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EXPLORATION OF HIGH SYMMETRY DIRHODIUM CATALYSTS
AND THE REACTION OF DONOR/ACCEPTOR CARBENOIDS WITH
ALCOHOLS

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in Chemistry

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Abstract

EXPLORATION OF HIGH SYMMETRY DIRHODIUM CATALYSTS AND THE REACTION OF DONOR/ACCEPTOR CARBENOIDS WITH ALCOHOLS

By Zhanjie Li

Chiral dirhodium complex catalyzed decomposition of diazo compounds results in a wide range of useful and highly stereoselective transformations. The symmetry of the catalyst has been considered as an important factor in its ability to induce stereoselectivity. In the first chapter of this dissertation, a series of highly symmetric dirhodium complexes containing *mono*, *di*, and *tetra*-binaphthylphosphate ligands were synthesized. The influences of substituents at the 3,3'- and 4,4',6,6'- positions of the binaphthyl scaffold on the complex's catalytic reactivity were systematically studied. The synthesis of chiral dirhodium carboxylate complexes containing adamantyl groups was also briefly explored. Two of this type of complexes were effectively synthesized in very short sequence from aryldiazoacetates and adamantane.

The second chapter of this dissertation focused on the reaction of donor/acceptor carbenoids with alcohols. A novel tandem ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols or propargylic alcohols was discovered and systematically studied. α -Hydroxycarboxylate derivatives containing one tertiary alcohol stereocenter were synthesized with excellent stereoselectivity (up to >97:3 dr and >99% ee), when dirhodium tetraproline, $\text{Rh}_2(\text{S-DOSP})_4$, was used as catalyst. It was found that chirality of the catalyst had dominant effect on the configuration of the tertiary alcohol stereocenter in the product, and the chirality of the alcohols had dominant effect on the second stereocenter generated in the rearrangement. Donor/acceptor carbenoids had distinct advantage than the conventional acceptor and acceptor/acceptor carbenoid in favor of the [2,3]-sigmatropic rearrangement. A highly enantioselective [1,2]-Stevens rearrangement between donor/acceptor carbenoids and tertiary benzyl alcohol was also briefly studied. α -Hydroxycarboxylates containing two adjacent quaternary centers were formed in 78-94% ee.

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To my wife, Yuxia and my daughters, Tia and Sarah

Table of Contents

Chapter 1 Design and Synthesis of Highly Symmetric Chiral Dirhodium(II) Complexes for Carbenoid Chemistry	1
1.1 Introduction.....	1
1.1.1 Dirhodium carboxylates.....	4
1.1.1.1 Proline derived dirhodium complexes.....	4
1.1.1.2 Phthalimide derived dirhodium complexes.....	8
1.1.2 Dirhodium carboxamidates.....	12
1.1.3 Dirhodium binaphthylphosphate complexes.....	16
1.2 Results and discussion.....	18
1.2.1 Synthesis of dirhodium binaphthylphosphate complexes.....	18
1.2.1.1 Dirhodium tetrabinaphthylphosphate complexes (Rh_2L_4).....	20
1.2.1.2 Dirhodium complexes containing mixed ligands ($\text{Rh}_2\text{L}_n(\text{OAc})_{(4-n)}$).....	25
1.2.2 Synthesis of dirhodium phosphinate complex.....	36
1.2.3 Synthesis of chiral dirhodium carboxylate complexes.....	40
1.3 Conclusion.....	45
1.4 Experimental.....	46
1.4.1 General information.....	46
1.4.2 Synthetic procedures and characterization.....	47
References.....	103

Chapter 2 Highly Enantioselective C–C Bond Formation by Rhodium-Catalyzed Tandem Ylide Formation/[2,3]-Sigmatropic Rearrangement between Donor/Acceptor Carbenoids and Allylic Alcohols/Propargylic Alcohols.....	110
2.1 Introduction.....	110
2.1.1 Intermolecular cyclopropanation.....	111
2.1.2 Intermolecular C–H insertion.....	117
2.1.3 Ylide formation.....	122
2.2 Results and discussion.....	128
2.2.1 New discovery.....	128
2.2.2 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols – generation of one stereogenic center.....	131
2.2.2.1 Optimal reaction conditions.....	133
2.2.2.2 Effect of allylic alcohols.....	136
2.2.2.3 Effect of carbenoid structure.....	138
2.2.2.4 Effect of chiral alcohol	140
2.2.2.5 Reactions of styryldiazoacetate 7 with racemic allylic alcohols.....	141
2.2.2.6 Other features.....	147
2.2.3 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols – generation of two stereogenic centers.....	151

2.2.3.1 Reactions with enantiomerically pure allylic alcohols.....	151
2.2.3.2 Rationale of the stereoselectivity.....	163
2.2.3.3 Further transformation	167
2.2.4 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols containing silyl group.....	171
2.2.5 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and propargylic alcohols.....	174
2.2.5.1 Reactions with achiral propargylic alcohols.....	175
2.2.5.2 Reactions with chiral tertiary propargylic alcohols.....	182
2.2.5.3 Reactions with chiral secondary propargylic alcohols.....	186
2.2.5.4 Stereoselective cyclization of α -allenic alcohols.....	188
2.2.5.5 Rationale of the stereoselectivity.....	189
2.2.6 Highly enantioselective intermolecular [1,2]-Stevens rearrangement between donor/acceptor carbenoids and tertiary alcohols.....	192
2.3 Conclusion.....	197
2.4 Experimental.....	199
2.4.1 General information.....	199
2.4.2 Synthetic procedures and characterization for chapter 2.2.1 and 2.2.2.....	200
2.4.3 Synthetic procedures and characterization for chapter 2.2.3.....	246
2.4.4 Synthetic procedures and characterization for chapter 2.2.4.....	282
2.4.5 Synthetic procedures and characterization for chapter 2.2.5.....	289
2.4.6 Synthetic procedures and characterization for chapter 2.2.6.....	343

References.....	350
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Appendix Crystal Structure Determination.....	361
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List of Schemes

Scheme 1.1: Rh ₂ (OAc) ₄ catalyzed O–H insertion reaction.....	2
Scheme 1.2: Rh ₂ (<i>S</i> -BNP) ₄ catalyzed intramolecular C–H insertion reaction.....	4
Scheme 1.3: Synthesis of (+)-erogorgiaene via an enantiodivergent process.....	7
Scheme 1.4: Synthesis of (-)-colombiasin A (17) and (-)-elisapterosin B (18).....	7
Scheme 1.5: Cyclopropanation catalyzed by Rh ₂ (<i>S</i> -biTISP) ₂	8
Scheme 1.6: Enantioselective intermolecular 1,3-dipolar cycloaddition catalyzed by Rh ₂ (<i>S</i> -BPTV) ₄	10
Scheme 1.7: Rh ₂ (<i>R</i> -PTAD) ₄ -catalyzed [4 + 3] cycloaddition reaction.....	10
Scheme 1.8: Dipolar cycloaddition catalyzed by Rh ₂ (<i>S</i> -BNP) ₄	16
Scheme 1.9: [1, 3]-dipolar cycloaddition catalyzed by Rh ₂ (<i>R</i> -DDBNP) ₄	17
Scheme 1.10: Sulfur ylide/[2,3]-sigmatropic rearrangement catalyzed by Rh ₂ (<i>S</i> -BNP) ₄	17
Scheme 1.11: Intramolecular aziridination catalyzed by Rh ₂ (<i>R</i> -BNP) ₄	17
Scheme 1.12: Intramolecular C–H insertion catalyzed by Rh ₂ (<i>S</i> -BNP) ₂ (HCO ₃) ₂	18
Scheme 1.13: Synthesis of complexes 91 and 115	21
Scheme 1.14: Cyclopropanation catalyzed by complex 91 and 115	21
Scheme 1.15: Synthesis of complexes 92 and 123	24
Scheme 1.16: Cyclopropanation catalyzed by complex 92 and 123	24
Scheme 1.17: Synthesis of <i>cis</i> -Rh ₂ ((<i>R</i> , <i>R</i>)-DTPI) ₂ (OAc) ₂	25

Scheme 1.18: Synthesis of <i>trans-syn</i> -Rh ₂ ((<i>R, R</i>)-DTPI) ₂ (OAc) ₂	26
Scheme 1.19: Synthesis of <i>trans</i> -Rh ₂ (OAc) ₂ (TFA) ₂ (129).....	27
Scheme 1.20: Synthesis of <i>trans</i> - Rh ₂ (<i>R</i> -BNP) ₂ (OAc) ₂ (131).....	27
Scheme 1.21: Synthesis of <i>cis</i> -Rh ₂ L ₂ (OAc) ₂ complexe 132 and 133	27
Scheme 1.22: Synthesis of <i>trans</i> -Rh ₂ L ₂ (OAc) ₂	30
Scheme 1.23: Cyclopropanation catalyzed by complexes <i>cis</i> - and <i>trans</i> -Rh ₂ L ₂ (OAc) ₂	32
Scheme 1.24: Synthesis of ligand 148	34
Scheme 1.25: Synthesis of complex 150-151	34
Scheme 1.26: Cyclopropanation catalyzed by complexes Rh ₂ L(OAc) ₃	35
Scheme 1.27: Proposed chiral dirhodium phosphinate 160	37
Scheme 1.28: Proposed synthesis of chiral dirhodium phosphinate 162	38
Scheme 1.29: Synthesis of <i>racemic</i> - 161	39
Scheme 1.30: Resolution of <i>racemic</i> - 161	40
Scheme 1.31: Synthesis of Rh ₂ (<i>S</i> -PTAD) ₄	42
Scheme 1.32: Proposed synthesis of the variants of Rh ₂ (<i>S</i> -PTAD) ₄	42
Scheme 1.33: Synthesis of Dirhodium complex 182 and 183	43
Scheme 1.34: Rh ₂ (<i>S</i> -DOSP) ₄ catalyzed C–H insertion of aryldiazoacetate 189 and adamantane.....	44
Scheme 2.1: Cyclopropanation of phenyldiazoacetate 6 with 1,1-disubstituted alkene	113
Scheme 2.2: Cyclopropanation of styryldiazoacetate 7 with <i>trans</i> -alkene	114

Scheme 2.3: Cyclopropanation of <i>p</i> -bromophenyldiazoacetate 30 with trisubstituted alkene	114
Scheme 2.4: Cyclopropanation of other donor/acceptor carbenoid precursors with styrene.....	115
Scheme 2.5: Tandem cyclopropanation/Cope rearrangement between vinyldiazoacetate and diene.....	116
Scheme 2.6: [4+3] cycloaddition between siloxyvinyldiazoacetate 41 and pyrroles.....	116
Scheme 2.7: [4+3] cycloaddition in the synthesis of (-)-5- <i>epi</i> -vibsanin.....	116
Scheme 2.8: C–H insertion of phenyldiazoacetate with 2-methylbutane.....	119
Scheme 2.9: C–H insertion of aryldiazoacetates adjacent to oxygen.....	120
Scheme 2.10: Asymmetric synthesis of Venlafaxine.....	120
Scheme 2.11: Asymmetric synthesis of Ritalin.....	121
Scheme 2.12: Synthesis of (+)-sertraline.....	121
Scheme 2.13: Enantiodivergent reaction between vinyldiazoacetate 64 with racemic dihydronaphthalene 65	122
Scheme 2.14: Asymmetric O–H insertion of phenyldiazoacetate 6 with water.....	124
Scheme 2.15: Intramolecular N–H insertion of diazoketoester 91	125
Scheme 2.16: Rh(II) and Cu catalyzed O–H insertion.....	125
Scheme 2.17: Three component reactions of aryldiazoacetates.....	126
Scheme 2.18: The epoxide formation with phenyldiazoacetate 6	127

Scheme 2.19: Sulfur ylide formation/[2,3]-sigmatropic rearrangement with aryldiazoacetate 12	127
Scheme 2.20: Reaction of phenyldiazoacetate 6 with (<i>E</i>)-4-methylpent-2-ene 97	129
Scheme 2.21: Reaction of phenyldiazoacetate 6 with allylic alcohols.....	129
Scheme 2.22: Tandem ylide formation/[2,3]-sigmatropic rearrangement between allylic alcohol and phenyldiazoacetate.....	130
Scheme 2.23: Rationale of the reaction of allylic alcohol with donor/acceptor carbenoids.....	132
Scheme 2.24: Reaction of allyl methyl ether 105 with phenyldiazoacetate 6	133
Scheme 2.25: Reactions of alcohol 101 with conventional carbenoids.....	139
Scheme 2.26: Reaction of styryldiazoacetate 7 with primary allylic alcohol 109	145
Scheme 2.27: Reactions of styryldiazoacetate 7 with <i>cis</i> -(1 <i>R</i> ,5 <i>R</i>)-(-)-pulegol 152	146
Scheme 2.28: Reactions of styryldiazoacetate 7 with thiol 159	150
Scheme 2.29: Reaction of alcohol 185 with styryldiazoacetate 7	166
Scheme 2.30: Reaction of alcohol 100 with aryldiazoacetate 121	166
Scheme 2.31: Synthesis of compound 189	168
Scheme 2.32: Oxy-Cope rearrangement of (2<i>S</i>, 3<i>S</i>)- 177	169
Scheme 2.33: Oxy-Cope rearrangement of (2<i>R</i>, 3<i>S</i>)- 177	169
Scheme 2.34: Oxy-Cope rearrangement of (<i>R</i>)- 125	170
Scheme 2.35: Synthesis of α -hydroxycarboxylates through halodesilylation-coupling strategy.....	171
Scheme 2.36: Synthesis of α -allenic alcohols with donor/acceptor carbenoids and propargylic alcohols.....	175

Scheme 2.37: Reactions of propargyl alcohol 199	176
Scheme 2.38: Reactions of tertiary propargyl alcohols.....	177
Scheme 2.39: Effect of carbenoid structure on the reaction selectivity.....	178
Scheme 2.40: Reaction of racemic alcohol 259 with styryldiazoacetate 7	183
Scheme 2.41: Reaction of racemic alcohol 261 with <i>p</i> -bromophenylvinyl diazoacetate 218	184
Scheme 2.42: Reactions of chiral secondary alcohol 269 with styryldiazoacetate 7	188
Scheme 2.43: Formation of 2,5-dihydrofurans.....	189
Scheme 2.44: Asymmetric [1,2]-Stevens rearrangement catalyzed by Rh ₂ (<i>S</i> -PTTL) ₄	192
Scheme 2.45: Formation of compound 273	193
Scheme 2.46: Formation of compound 277 and 278	193
Scheme 2.47: Reaction of alcohol 280 with phenyldiazoacetate 6	196
Scheme 2.48: Possible mechanism of the [1,2]-Stevens rearrangement	196

List of Tables

Table 1.1: Intramolecular C–H insertion of diazoacetate 84	15
Table 1.2: Cyclopropanation of phenyldiazoacetate with styrene.....	19
Table 1.3: Rh ₂ (O ₂ PMe ₂) ₄ and Rh ₂ (OAc) ₄ mediated cyclopropanations.....	36
Table 1.4: cyclopropanation catalyzed by complex 182 and 183	44
Table 2.1: Effect of rhodium carbenoid structure on the cyclopropanation diastereoselectivity.....	112
Table 2.2: Cyclopropanation of styryldiazoacetate 7 with alkenes.....	113

Table 2.3: Intermolecular C–H insertion of ethyl diazoacetate with 2-methylbutane.....	119
Table 2.4: C–H insertion of aryldiazoacetates with cycloalkanes.....	120
Table 2.5: Asymmetric N–H insertion of aryldiazoacetates with carbamate.....	123
Table 2.6: Asymmetric O–H insertion of phenyldiazoacetate 6 with alcohols.....	124
Table 2.7: Effects of dirhodium catalyst and solvent on the ratio of 99/103	135
Table 2.8: Effect of temperature and the amount of allylic alcohol on the ratio of 99/103	135
Table 2.9: Effect of allyl alcohols on the formation of [2,3]-sigmatropic rearrangement products.....	137
Table 2.10: Reactions of alcohol 101 with different donor/acceptor carbenoids.....	138
Table 2.11: Effect of the alcohol chirality on the product formation.....	140
Table 2.12: Reactions of styryldiazoacetate 7 with secondary allylic alcohols.....	143
Table 2.13: Reactions of styryldiazoacetate 7 with tertiary allylic alcohols.....	144
Table 2.14: Effect of catalyst loading.....	148
Table 2.15: Reaction of styryldiazoacetate with alcohol mixture.....	149
Table 2.16: Reaction of phenyldiazoacetate with allylic amines.....	150
Table 2.17: Reaction of (<i>S, E</i>)- 108 with different diazoacetates.....	152
Table 2.18: Reaction of pent-3-en-2-ol (108) with styryldiazoacetate 7	155
Table 2.19: Reaction of (<i>S</i>)-allylic alcohol with styryldiazoacetate 7	157
Table 2.20: Reaction of (<i>R</i>) and (<i>S</i>)- 183 with styryldiazoacetate 7	160
Table 2.21: Reaction of (<i>R, E</i>)- 170 with styryldiazoacetate 7	162
Table 2.22: Reaction of racemic alcohol 193 with donor/acceptor carbenoids.....	172

Table 2.23: Reaction of alcohol 196 with styryldiazoacetate 7	173
Table 2.24: Reaction of arylvinyldiazoacetates with alcohol 205	179
Table 2.25: Reaction of alcohol 223–237 with styryldiazoacetate 7	181
Table 2.26: Reaction of alcohol 253–255 with styryldiazoacetate 7	182
Table 2.27: Reaction of enantiomerically pure alcohol 259 with styryldiazoacetate.....	185
Table 2.28: Reactions of racemic alcohol 263 and 264 with styryldiazoacetate 7	186
Table 2.29: Reactions of chiral secondary alcohol 267 with styryldiazoacetate 7	187
Table 2.30: Reaction of alcohol 279 and 280 with arylvinyldiazoacetates.....	195

List of Figures

Figure 1.1: The structure of $\text{Rh}_2(\text{OAc})_4$	1
Figure 1.2: Dirhodium prolinates complexes.....	2
Figure 1.3: Schematic representation of the D_2 -symmetric ligand arrangement of $\text{Rh}_2(S\text{-DOSP})_4$	5
Figure 1.4: Model of the enantioselective cyclopropanation catalyzed by $\text{Rh}_2(S\text{-DOSP})_4$	6
Figure 1.5: Second-generation dirhodium prolinates complexes.....	8
Figure 1.6: Phthalimide derived dirhodium complexes.....	9
Figure 1.7: The model for the enantiodivergent reaction between racemic 39 and 40 with $\text{Rh}_2(S\text{-PTAD})_4$ as catalyst.....	12
Figure 1.8: Chiral dirhodium carboxamidates.....	14
Figure 1.9: Possible isomers of the chiral dirhodium carboxamidates.....	14

Figure 1.10: Matched and mismatched catalyst design.....	15
Figure 1.11: Dirhodium binaphthylphosphonate complexes.....	17
Figure 1.12: Molecular model of Rh ₂ (<i>S</i> -BNP) ₄ , and the substituent influence at 3,3'-position of the BNP.....	20
Figure 1.13: The aromatic region of the ¹ H and ¹³ C-NMR spectra of complex 131 and 132	29
Figure 1.14: Molecular models of <i>trans</i> -Rh ₂ (<i>S</i> -BNP) ₂ (OAc) ₂ and <i>cis</i> -Rh ₂ (<i>S</i> -BNP) ₂ (OAc) ₂	29
Figure 1.15: Structure of complex 143 and 144	32
Figure 1.16: Molecular model of the (<i>S</i>)-enantiomer of complex 141 (top view).....	33
Figure 1.17: Structure of Rh ₂ (<i>S</i> -PTAD) ₄ (30) and Rh ₂ (<i>S</i> -TCPTAD) ₄ (37).....	41
Figure 2.1: Classification of carbenoid intermediates.....	110
Figure 2.2: Chiral dirhodium carboxylate catalysts developed by the Davies group.....	111
Figure 2.3: Carbenoid induced C–H insertion.....	118
Figure 2.4: Natural products synthesized by the combined C–H activation/Cope rearrangement strategy.....	122
Figure 2.5: X-ray structure of compound 142	144
Figure 2.6: X-ray structure of compound 153	146
Figure 2.7: X-ray structure of compound 166	153
Figure 2.8: X-ray structure of compound 177	158
Figure 2.9: X-ray structure of compound 181	158
Figure 2.10: X-ray structure of compound (2<i>R</i> , 3<i>R</i>)- 184	160

Figure 2.11: X-ray structure of compound (2<i>R</i>, 3<i>S</i>)-184.....	161
Figure 2.12: Transition state analysis of (<i>R</i>) and (<i>S</i>) allylic alcohol with donor/acceptor carbenoid.....	165
Figure 2.13: X-ray structure of compound (2<i>R</i>, 3<i>R</i>)-187.....	166
Figure 2.14: X-ray structure of compound (2<i>R</i>, 3<i>S</i>)-187.....	167
Figure 2.15: X-ray structure of compound 243	180
Figure 2.16: X-ray structure of compound (2<i>R</i>, 4<i>S</i>)-260.....	185
Figure 2.17: X-ray structure of compound (2<i>S</i>, 4<i>R</i>)-268.....	188
Figure 2.18: Transition state analysis for the formation of α -allylic alcohol.....	190
Figure 2.19: X-ray structure of compound 283	195

List of Abbreviations

Ac	Acetyl
<i>p</i> -ABSA	4-Acetamidobenzenesulfonyl azide
Ar	Aryl
BNP	Binaphthylphosphate
BINOL	1,1'-bi-2-naphthol
Boc	<i>tert</i> -Butyloxycarbonyl
Br	Bromine
<i>t</i> -Bu	<i>tert</i> -Butyl
DBU	1,8-Diazabicyclo[5,4,0]undec-7-ene
DCM (CH ₂ Cl ₂)	Dichloromethane
2,2-DMB	2,2-Dimethylbutane
DMAD	Dimethyl acetylenedicarboxylate
DOSP	<i>N</i> -(4-dodecylbenzenesulfonyl)prolinate
dr	Diastereomeric ratio
ee	Enantiomeric excess
EDG	Electron-donating group
ESI	Electrospray ionization
Et	Ethyl
EWG	Electron-withdrawing group
Equiv.	Equivalent
FAB-MS	Fast atom bombardment mass spectroscopy

HCl	Hydrochloric acid
<i>c</i> -Hex	Cyclohexyl
Hz	Hertz
HPLC	High-performance liquid chromatography
IR	Infrared spectroscopy
K ₂ Cr ₂ O ₇	Potassium dichromate
L	Ligand
M	Metal
Me	Methyl
MeO	Methoxy
MEPY	Methyl 2-oxopyrrolidine-5-carboxylate
MOM	Methoxymethyl
Mes	Mesityl
NaHMDS	Sodium bis(trimethylsilyl)amide
nOe	Nuclear Overhauser effect
NOESY	Nuclear Overhauser effect spectroscopy
OAc	Acetate
OEt	Ethoxy
OOct	Octanoate
Ph	Phenyl
Piv	Pivalate
POCl ₃	Phosphorous oxychloride
<i>i</i> Pr	Isopropyl

Rh	Rhodium
rt	Room temperature
TBS	<i>tert</i> -Butyldimethylsilyl
TBSP	(4- <i>tert</i> -butylphenyl)sulfonyl-prolinate
TFA	Trifluoroacetic acid (trifluoroacetyl)
THF	Tetrahydrofuran
TISP	2,4,6-tri-iso-propyl-benzenesulfonyl
TMEDA	<i>N,N,N',N'</i> -Tetramethylethylenediamine
TMS	Trimethylsilyl
TPA	Triphenylacetate

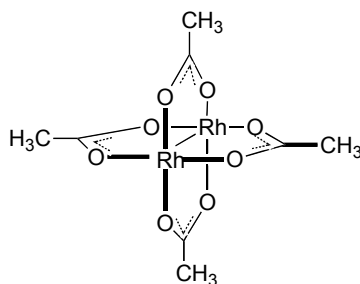
CHAPTER ONE

Design and Synthesis of High Symmetry Chiral Dirhodium(II) Complexes

1.1 Introduction

Dirhodium(II) complexes are well known as effective catalysts for the decomposition of diazocarbonyl compounds. The generated metal carbenoid intermediates can participate in a wide variety of synthetically useful transformations such as cyclopropanation, C–H insertion, and ylide formation with excellent efficiency and chemoselectivity.¹

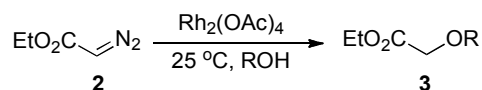
Figure 1.1 The structure of $\text{Rh}_2(\text{OAc})_4$



The first dirhodium(II) complex used as catalyst for the decomposition of diazocarbonyl compounds was dirhodium tetraacetate ($\text{Rh}_2(\text{OAc})_4$, **1**). In 1973, Teysse and co-workers found that dirhodium tetraacetate had much superior catalytic activity over copper catalysts to decompose ethyl diazoacetate (**2**) in the presence of alcohols, producing the O–H insertion products in nearly quantitative yield (Scheme 1.1).² Since then, it has become one of the most widely used catalysts for metal carbene

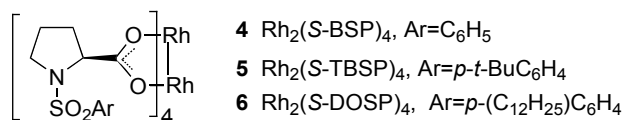
transformations. Dirhodium tetraacetate contains four bridging acetate ligands symmetrically positioned around the dirhodium core, which provides the whole molecule a dimeric “paddlewheel” complex with D_{4h} symmetry (Figure 1.1).³ The dirhodium core consists of a strong Rh–Rh single bond (originally considered as a triple bond because of the short bond distance 2.386 Å, compared with the expected Rh–Rh single bond 2.7–2.8 Å), and it provides the complex excellent ability to form adducts at its two axial coordination sites. These are considered to be the site of its catalytic activity during the carbenoid transformations. Dirhodium tetraacetate also serves as a parent compound to synthesize other dirhodium(II) complexes. Ligand exchange procedures, mainly done by refluxing dirhodium tetraacetate with excess of the incoming ligands (carboxylate, carboxamidate, phosphate, among others), give access to a wide variety of other dirhodium complexes containing similar paddlewheel dirhodium framework. In the 1990s, the introduction of chiral ligands opened enormous opportunities for the design and synthesis of chiral dirhodium complexes, and the study of their catalytic activity promoted the metal carbenoid chemistry to unprecedented levels of stereocontrol. There are three general classes of chiral dirhodium complexes widely used as catalysts in the asymmetric carbenoid transformations with high stereoselectivity: dirhodium carboxylates derived from *N*-sulfonyl proline or *N*-phthalimido amino acids, dirhodium carboxamidates, and dirhodium binaphthylphosphates.¹

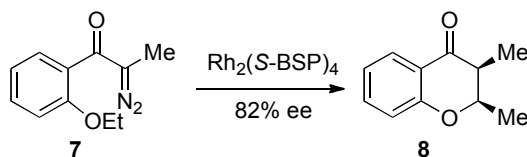
Scheme 1.1 $\text{Rh}_2(\text{OAc})_4$ catalyzed O–H insertion reaction



To rationalize the high asymmetric induction obtained in the carbenoid transformations, different models have been developed and successfully applied to predict the stereochemistry of the reaction. Symmetry of these dirhodium complexes has been considered as a critical factor.⁴ Traditionally, symmetry has been an important structural feature in the development of efficient chiral ligands, such as the C_2 -symmetric chiral biphosphines,⁵ bis(oxazolines) (Box's),⁶ and N,N -bis(salicylidine)ethylenediamines (Salen),⁷ C_3 -symmetric chiral tris(pyrazolyl)borates,⁸ and D_2 or D_4 -symmetric chiral porphyrins.⁹ Because of the ligand's symmetry property, their metal complexes are able to selectively activate the reagent and favor the attack on one specific face, and subsequently form the product with good stereoselectivity. The paddlewheel framework of the dirhodium complexes, however, provides an unusual ability to arrange identical chiral ligands of low symmetry around the dirhodium core and form a complex with higher symmetry. This high symmetric property allows these complexes to form the carbenoid intermediate in a highly selective manner, but also effectively define the approach of the substrate to the carbenoid intermediate and subsequently form product with high stereoselectivity.

Figure 1.2 Dirhodium prolinates complexes



Scheme 1.2 Rh₂(*S*-BSP)₄ catalyzed intramolecular C–H insertion reaction

1.1.1 Dirhodium carboxylates

1.1.1.1 Proline derived dirhodium complexes

Dirhodium complexes containing chiral carboxylate ligands were first synthesized by Brunner. Their initial evaluation in the cyclopropanation of ethyl diazoacetate with styrene gave very low enantioselectivity (<12% ee).¹⁰ Considering that the carboxylate ligand's chiral center is placed far away from the axial coordination sites of rhodium led to the preliminary conclusion that dirhodium carboxylate complexes would not be effective as chiral catalysts.¹¹ However, soon after Brunner, McKervy and co-workers discovered that dirhodium proline, Rh₂(*S*-BSP)₄ (**4**) (Figure 1.2) can selectively catalyze the intramolecular C–H insertion reaction of **7** with good enantioselectivity (82% ee) (Scheme 1.2).¹² This discovery quickly led to Davies' synthesis of Rh₂(*S*-TBSP)₄ (**5**) and Rh₂(*S*-DOSP)₄ (**6**). These catalysts have good solubility in hydrocarbon solvents and have been broadly used for asymmetric transformations of donor/acceptor substituted carbenoids.

Since their initial application as catalysts in the asymmetric cyclopropanation of styryldiazoacetate with alkenes in 1993,¹³ dirhodium prolinates, particularly Rh₂(*S*-DOSP)₄ (**6**) have been widely used as excellent catalysts in a vast array of asymmetric

transformations of donor/acceptor carbenoids, such as intermolecular cyclopropanation,¹⁴ [4+3] cycloaddition,¹⁵ cyclopropanation,¹⁶ C–H activation,^{1b,17} tandem C–H activation/Cope Rearrangement,¹⁸ and tandem ylide formation/[2,3]-sigmatropic rearrangement reaction.¹⁹ $\text{Rh}_2(\text{S-DOSP})_4$ (**6**) was considered to adopt a D_2 -symmetric conformation with the four *N*-arylsulfonyl groups having an up-down-up-down arrangement around the dirhodium core in solution (Figure 1.3).^{4,14a,20} Although the proline groups in the complex have considerable conformational mobility, the four *N*-arylsulfonyl groups must adopt either an “up” or “down” orientation in order to avoid getting into the periphery of the dirhodium carboxylate core and causing steric conflicts with the adjacent ligand. In spite of other possible arrangements, the overall up-down-up-down arrangement is the most reasonable to explain the high asymmetric induction of $\text{Rh}_2(\text{S-DOSP})_4$ in the carbenoid transformations. A model based on the combination of ¹³C kinetic isotope study and density functional theory calculation of the cyclopropanation of phenyldiazoacetate and alkene is shown in Figure 1.4.²¹ On each face of the complex (only top face is shown), the two arylsulfonyl groups adopt a propeller-like arrangement and this tends to sterically block adjacent quadrants. As shown in Figure 1.4, quadrant I and III are blocked and the alkene approaches the carbenoid through the less hindered quadrant IV.

Figure 1.3 Schematic representation of the D_2 -symmetric ligand arrangement of $\text{Rh}_2(\text{S-DOSP})_4$

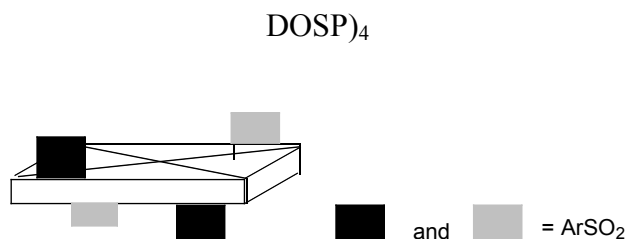
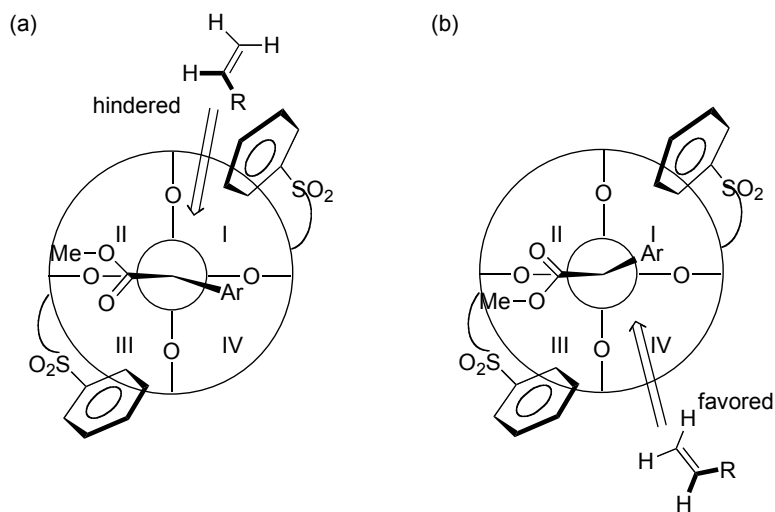


Figure 1.4 Model of the enantioselective cyclopropanation catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$



This model has been successfully applied to explain not only the highly diastereoselective and enantioselective cyclopropanation between aryldiazoacetate and alkenes catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$, but also the $\text{Rh}_2(\text{DOSP})_4$ catalyzed C–H activation and C–H activation/Cope rearrangement.^{15b,18,22} One of the most impressive examples is the successful prediction of the stereochemical outcome between the reaction of racemic dihydronaphthalene **9** and carbenoid derived from diazo **10** during the total synthesis of (+)-erogorgiaene (Scheme 1.3).^{18b,d} With the catalyst's D_2 -symmetric conformation ($\text{Rh}_2(\text{R-DOSP})_4$ as catalyst), in order to avoid the steric conflict between methyl and the arylsulfonyl blocking group, only (*S*)-**9** can react with the carbenoid through the C–H activation/Cope rearrangement to give **11**, on the other hand, (*R*)-**9** will react with the carbenoid to give cyclopropanation product **12**. This strategy has also been applied to the synthesis of (–)-colombiasin A (**17**) and (–)-elisapterosin B (**18**) (Scheme 1.4).^{18d}

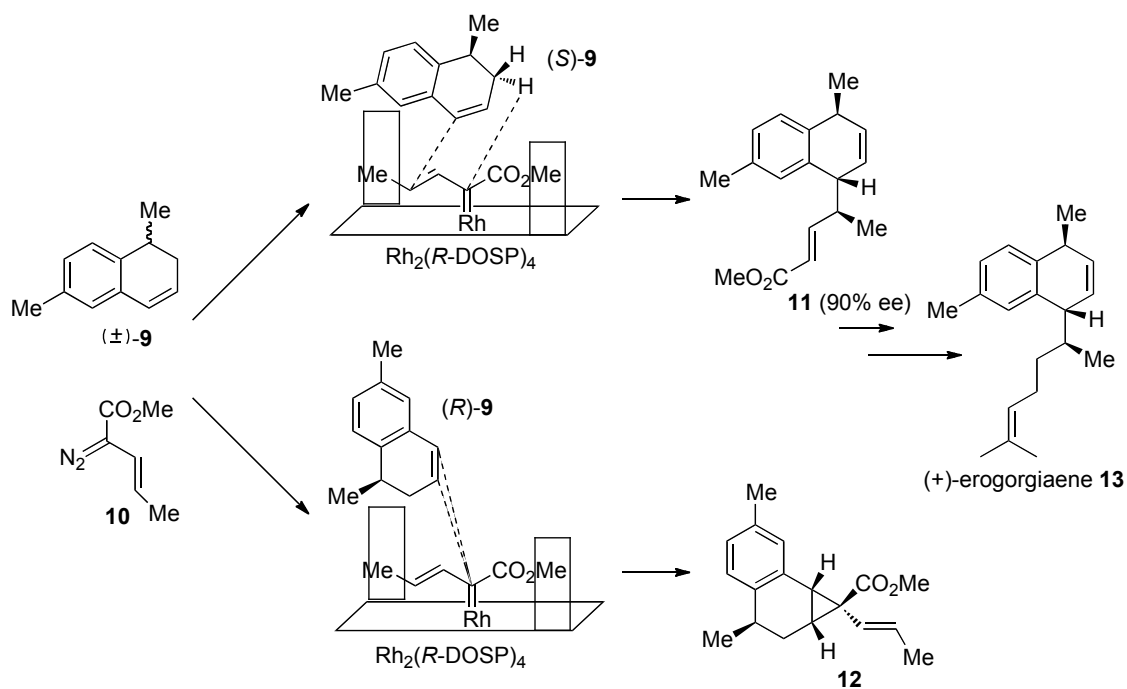
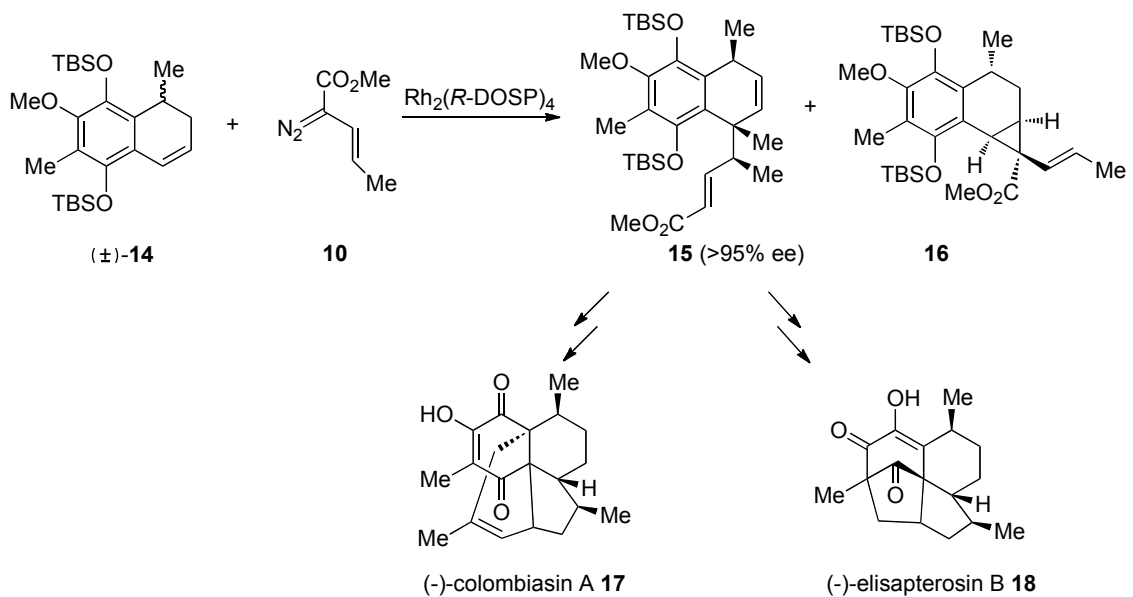
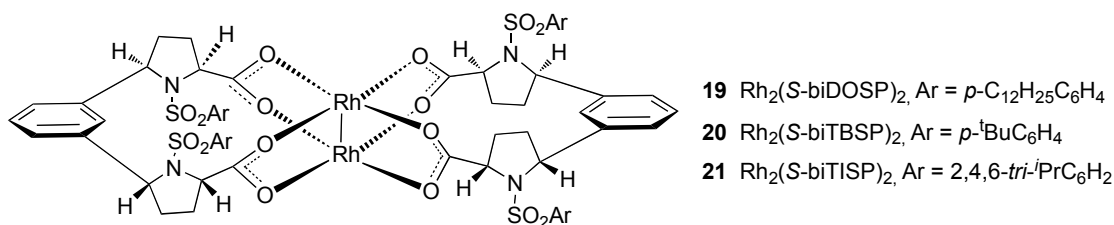
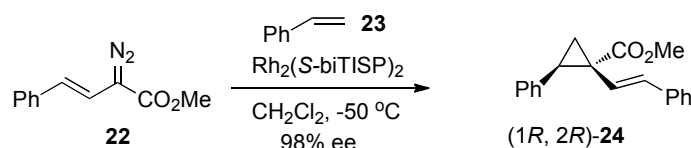
Scheme 1.3 Synthesis of (+)-erogorgiaene via an enantiodivergent process**Scheme 1.4** Synthesis of (-)-colombiasin A (17) and (-)-elisapterosin B (18)

Figure 1.5 Second-generation dirhodium prolineate complexes**Scheme 1.5** Cyclopropanation catalyzed by $\text{Rh}_2(\text{S-biTISP})_2$ 

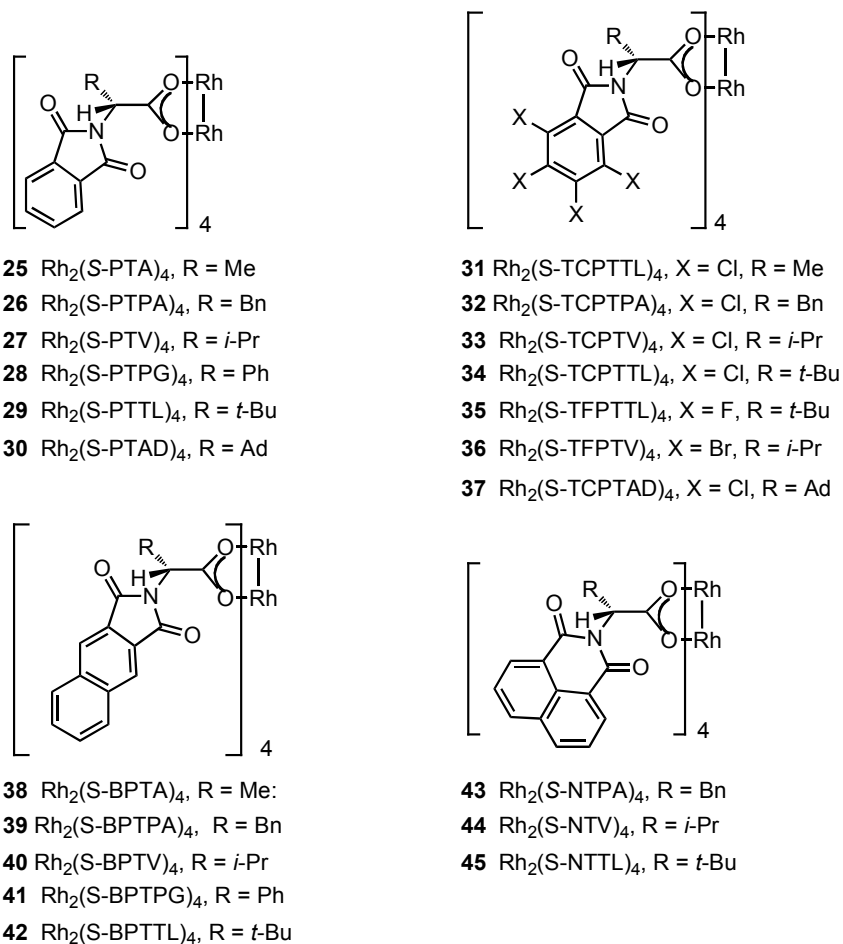
The second generation D_2 -symmetric dirhodium prolineate complexes **19–21** were synthesized with the design strategy of locking the four *N*-arylsulfonyl groups into the up-down-up-down arrangement with a *meta*-substituted benzene tether (Figure 1.5).²³ These catalysts offer a distinct advantage over $\text{Rh}_2(\text{S-DOSP})_4$ as high asymmetric induction can be achieved even when dichloromethane used as solvent (Scheme 1.5). In the cyclopropanation of styrene with methyl styryldiazoacetate (**22**) catalyzed by $\text{Rh}_2(\text{S-biTISP})_2$, cyclopropane **24** was formed with 98% ee.

1.1.1.2 Phthalimide derived dirhodium complexes

Ikegami, Hashimoto and co-workers synthesized a series of dirhodium carboxylate complexes with *N*-phthalimide protected amino acid as ligands (Figure 1.6).^{1a,1b} The R groups may vary, but in most cases the catalyst with R as *t*-butyl gave superior enantioselectivity over others. Replacing the hydrogen atoms on the phenyl with halogen atoms produced more active complexes **31–37**.²⁴ Complexes **38–42** were also synthesized

by extending the length of the phthalimide moiety.²⁵ As an application of the highly enantioselective C–H insertion into adamantane methodology, Davies synthesized $\text{Rh}_2(\text{S-PTAD})_4$ (**30**) and $\text{Rh}_2(\text{S-TCPTAD})_4$ (**37**) containing bulky adamantyl groups.²⁶ Müller also synthesized complexes **43–45** with a similar scaffold using 1,8-naphthoyl as the protecting group.²⁷

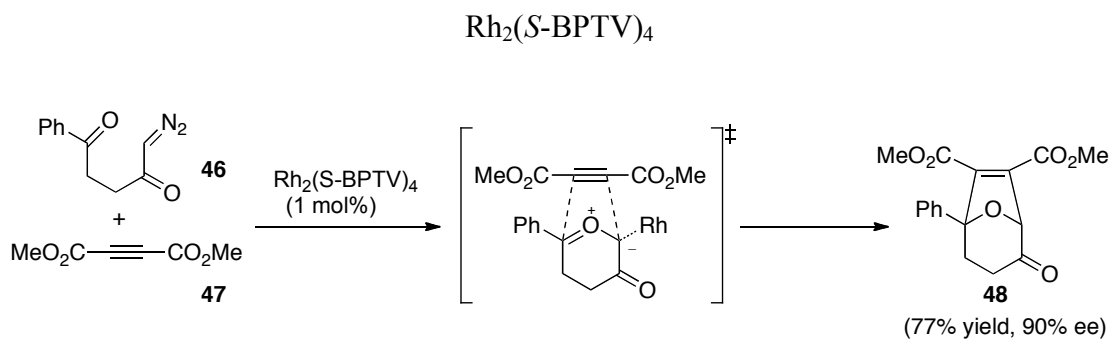
Figure 1.6 Phthalimide derived dirhodium complexes



Phthalimide derived dirhodium complexes have been widely used in cyclopropanation,^{27b,28} C–H activation,^{1a,1b} C–H amination,^{24,26b,27a,c} and ylide formation/cycloaddition reactions with very high enantioselectivity.²⁵ Scheme 1.6 shows

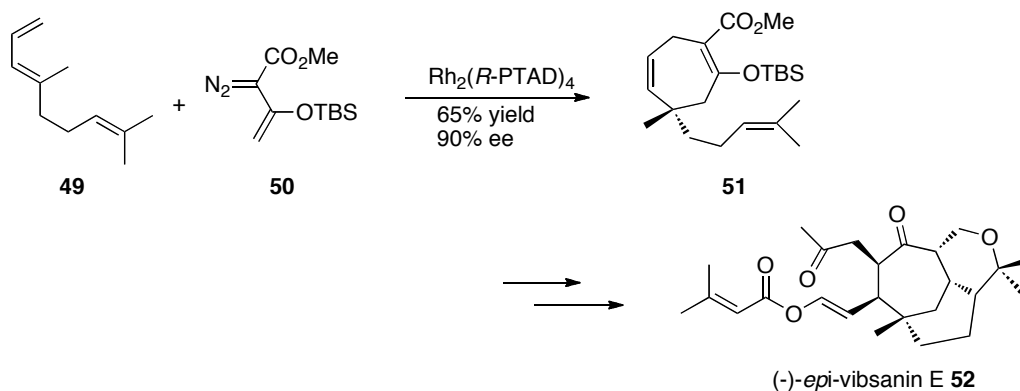
the $\text{Rh}_2(\text{S-BPTV})_4$ catalyzed tandem intermolecular 1,3-dipolar cycloaddition of diazoketone **45** and dimethyl acetylenedicarboxylate (DMAD) **46**. The reaction involves a chiral rhodium(II)-associated carbonyl ylide intermediate and produced **48** in 77% yield and 90% ee.²⁵

Scheme 1.6 Enantioselective intermolecular 1,3-dipolar cycloaddition catalyzed by



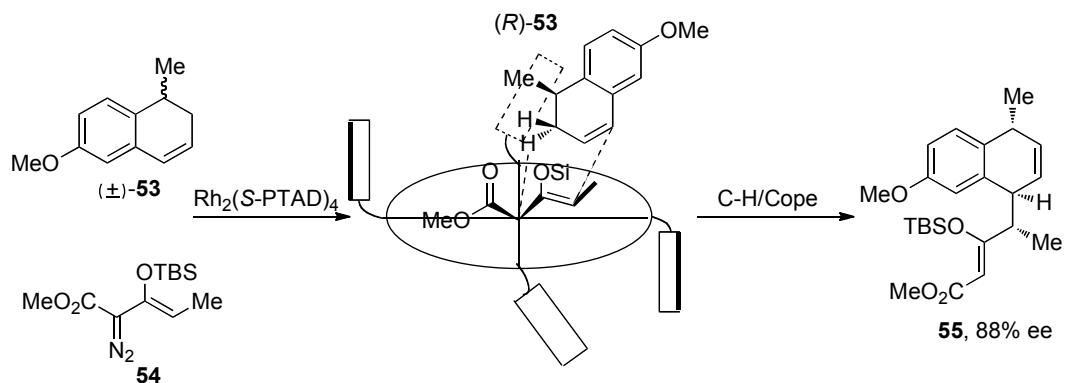
Davies and co-workers also used the $\text{Rh}_2(\text{R-PTAD})_4$ -catalyzed [4 + 3] cycloaddition between vinylsiloxydiazooacetate **49** and diene **50** to rapidly generate the cycloheptane core (**51**) of (-)-*epi*-vibsanin E in 65% yield and 90% ee (Scheme 1.7). Conversion of **51** to (-)-*epi*-vibsanin E was achieved in a very efficient manner.²⁹

Scheme 1.7 $\text{Rh}_2(\text{R-PTAD})_4$ -catalyzed [4 + 3] cycloaddition reaction



Hashimoto proposed that phthalimide derived dirhodium complexes had C_2 -symmetric conformation based on the X-ray crystal structure of $\text{Rh}_2(\text{S-PTPA})_4$.³⁰ The two adjacent phthalimido groups are positioned on the top face of the complex and the other two are positioned on the bottom face. Davies adopted this C_2 -symmetric model to $\text{Rh}_2(\text{S-PTAD})_4$ and successfully predicted the stereochemical outcome of the reaction between racemic dihydronaphthalene **53** and siloxyvinyl diazoacetate **54** catalyzed by $\text{Rh}_2(\text{S-PTAD})_4$.^{18c} As shown in Figure 1.7, the carbenoid has the favorable conformation with the bulky siloxyvinyl group away from the phthalimide plate. Meanwhile, the two phthalimide plates on the top face block the back face of the carbenoid, only (*R*)-**53** with the methyl group pointing out could attack the carbenoid from the front open side and go through the C–H activation/Cope rearrangement to form product **55** containing three stereogenic centers in 88% ee.

Recently, Fox and Charette independently reported that the $\text{Rh}_2(\text{S-PTTL})_4$ had C_4 symmetry by its X-ray crystal structure, with the four phthalimido groups on one face of the complex and the four *t*-butyl groups on the other face.^{28b, c} The X-ray crystal structure of $\text{Rh}_2(\text{S-PTAD})_4$ also had similar symmetric character.³¹ However, the 700 MHz ^1H - ^{13}C heteronuclear NOESY experiments by Charette suggests that $\text{Rh}_2(\text{S-PTTL})_4$ has mobile conformation in the solution. Thus there remains some uncertainties about the arrangement of the ligands in this class of catalysts.

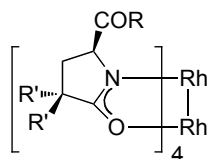
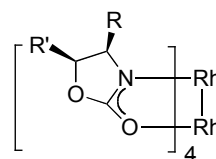
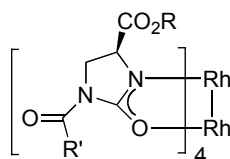
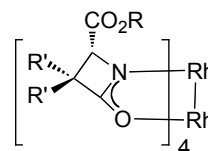
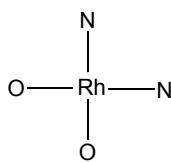
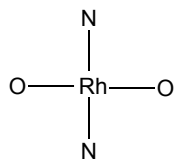
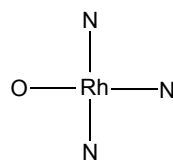
Figure 1.7 The model for the enantiodivergent reaction between racemic **53** and **54**with $\text{Rh}_2(\text{S-PTAD})_4$ as catalyst

1.1.2 Dirhodium carboxamidates

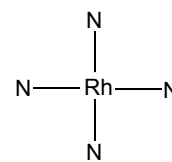
The chiral dirhodium carboxamidates with ligands based on enantiomerically pure 2-oxopyrrolidine, 2-oxazolidinone, *N*-acylimidazolidin-2-one and 2-azetidinone derivatives were developed by Doyle and co-workers (Figure 1.8).¹ Because of the electron-rich character, they are catalytically less active than dirhodium carboxylates. However they are very effective catalysts in the decomposition of diazoacetates and diazoacetamide derivatives and widely used for intramolecular cyclopropanation,³² intermolecular cyclopropanation,³³ and intramolecular C–H insertion reactions,¹¹ often resulting in reactions proceeding in >90% ee. Because of the unsymmetrical bridging ligands, there are four different geometries (based on the positions of nitrogens and oxygens on each rhodium): (2,2)-*cis*, (2,2)-*trans*, (3,1), and (4,0) (Figure 1.9). However, monitoring the ligand exchange process with LC-MS, they found that the complex with (2,2)-*cis* geometry was the dominant isomer, and all of the other isomers also isomerized into this major isomer upon heating.³⁴ This (2,2)-*cis* geometry was also consistently found in the X-ray structures of different dirhodium carboxamidate complexes, such as $\text{Rh}_2(5R-$

MEPY)₄ and Rh₂(4*S*-MEOX)₄.³⁵ In these two complexes, the two ester groups in the ligands oriented in counterclockwise fashion and effectively block one side of the carbenoid intermediate. The intramolecular approach of the substrate can only take place from the open side, producing the product with high stereoselectivity.

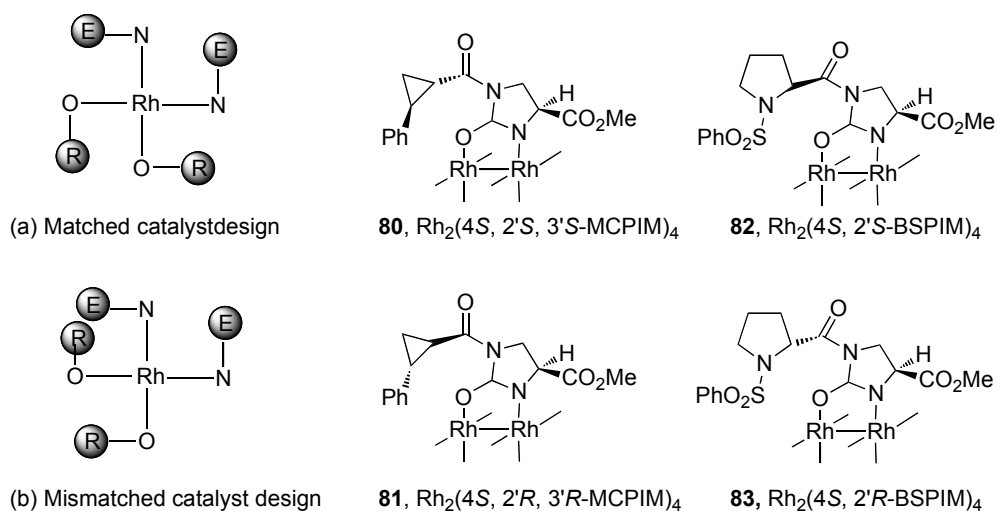
The further development of this (2,2)-*cis* geometry strategy is the synthesis of imidazolidinone carboxylate catalysts with chiral *N*-acyl attachments (Figure 1.10).³⁶ In the matched catalyst Rh₂(4*S*, 2'*S*, 3'*S*-MCPIM)₄ (**80**) and Rh₂(4*S*, 2'*S*-BSPIM)₄ (**82**), the orientation of the ester and *N*-acyl side chains are in the same direction, forming a counterclockwise spiral (determined by their X-ray structures). This orientation is particularly well suited to intramolecular reactions in which the active site for reaction is tethered to the dirhodium(II) axial coordination site. On the other hand, in the mismatched catalyst Rh₂(4*S*, 2'*R*, 3'*R*-MCPIM)₄ (**81**) and Rh₂(4*S*, 2'*R*-BSPIM)₄ (**83**), the orientation of the ester and *N*-acyl side chains are in the opposite direction (also determined by their X-ray structures). This orientation provides a barrier to stereoselectivity enhancement in intramolecular transformations.

Figure 1.8 Chiral dirhodium carboxamidates**56** Rh₂(5S-MEPY)₄, R = OMe, R' = H**57** Rh₂(5S-NEPY)₄, R = OCH₂CMe₃, R' = H**58** Rh₂(5S-ODPY)₄, R = O(CH₂)₁₇CH₃, R' = H**59** Rh₂(5S-DMAP)₄, R = NMe₂, R' = H**60** Rh₂(5S-dFMEPY)₄, R = OMe, R' = F**61** Rh₂(4S-MEOX)₄, R = CO₂Me, R' = H**62** Rh₂(4S-THREOX)₄, R = CO₂Me, R' = Me**63** Rh₂(4R-BNOX)₄, R = PhCH₂, R' = H**64** Rh₂(4R-IPOX)₄, R = *i*-Pr, R' = H**65** Rh₂(4R-PHOX)₄, R = Ph, R' = H**66** Rh₂(4S-MPOX)₄, R = Me, R' = Ph**67** Rh₂(4S-MACIM)₄, R = R' = Me**68** Rh₂(4S-MBOIM)₄, R = Me, R' = Ph**69** Rh₂(4S-MCHIM)₄, R = Me, R' = ^cC₆H₁₁CH₂**70** Rh₂(4S-EPPIM)₄, R = Et, R' = PhCH₂CH₂**71** Rh₂(4S-MPPIM)₄, R = Me, R' = PhCH₂CH₂**72** Rh₂(4S-BPPIM)₄, R = ⁱ-Bu, R' = PhCH₂CH₂**73** Rh₂(4S-BNAZ)₄, R = PhCH₂, R' = H**74** Rh₂(4S-IBAZ)₄, R = ^t-Bu, R' = H**75** Rh₂(4S-MEAZ)₄, R = Me, R' = H**76** Rh₂(4S-CHAZ)₄, R = ^cC₆H₁₁, R' = H**77** Rh₂(4R-dFIBAZ)₄, R = *i*-Pr, R' = F**78** Rh₂(4R-dFCHAZ)₄, R = ^cC₆H₁₁, R' = F**79** Rh₂(S, S/R-MENTHAZ)₄, R = S/R-menthyl, R' = H**Figure 1.9** Possible isomers of the chiral dirhodium carboxamidates(2,2)-*cis*(2,2)-*trans*

(3,1)



(4,0)

Figure 1.10 Matched and mismatched catalyst design**Table 1.1** Intramolecular C–H insertion of diazoacetate **84**

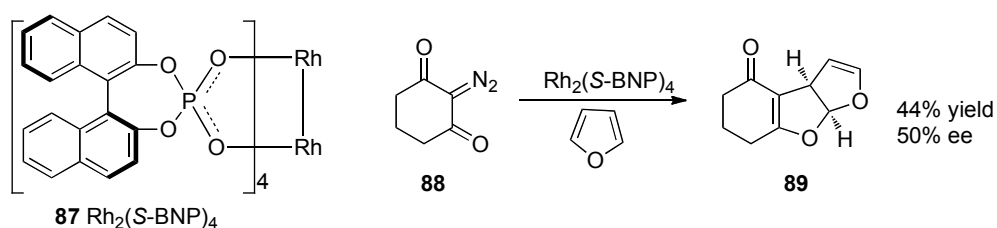
entry	Rh(II)	yield, %	85 : 86	ee of 85 , %	ee of 86 , %
1	80	78	99 : 1	97	nd
2	81	63	80 : 20	72	13
3	82	88	97 : 3	99	>99
4	83	89	98 : 2	74	33

The data for the intramolecular C–H insertion of diazoacetate **84** catalyzed by complexes **80–83** are summarized in Table 1.1. With catalyst **80** and **82**, extremely high diastereoselectivity (up to 99:1) and enantioselectivity (up to 99% ee) were obtained (Table 1.1, entries 1, 3). However, much lower selectivity in terms of the enantioselectivity was observed with **81** and **83** as catalyst (Table 1.1, entries 2, 4).³⁶

1.1.3 Dirhodium binaphthylphosphate complexes

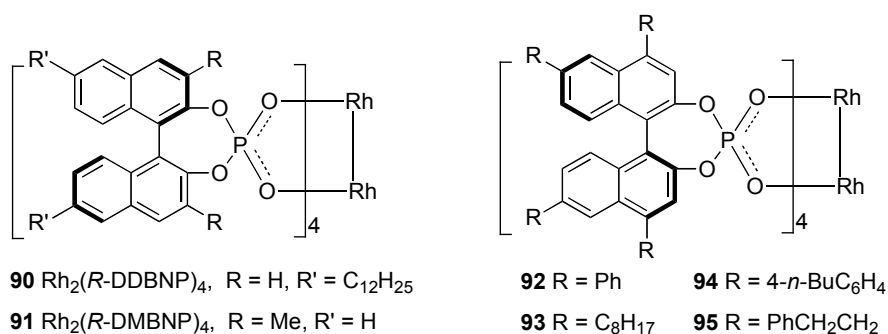
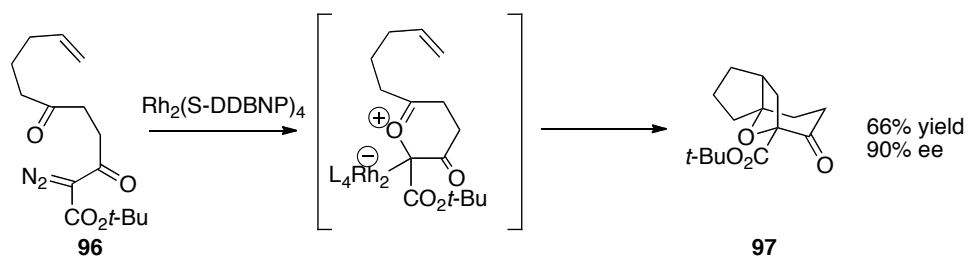
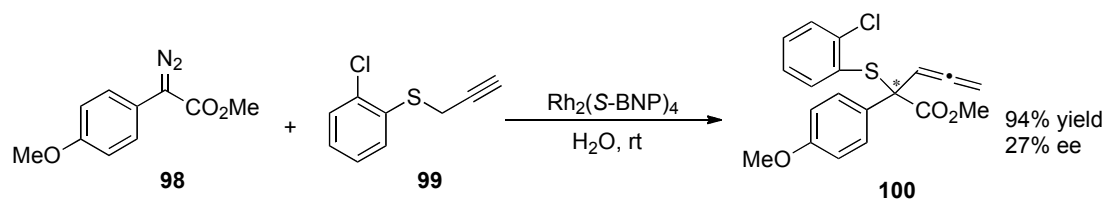
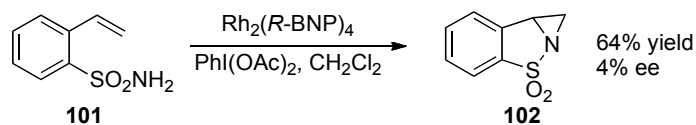
$\text{Rh}_2(\text{S-BNP})_4$ (**87**) with the C_2 -symmetric binaphthylphosphate as ligands has D_4 symmetry. It was first synthesized by Pirrung in 1992 and used for the asymmetric dipolar cycloaddition reaction with moderate enantioselectivity (Scheme 1.8).³⁷

Scheme 1.8 Dipolar cycloaddition catalyzed by $\text{Rh}_2(\text{S-BNP})_4$



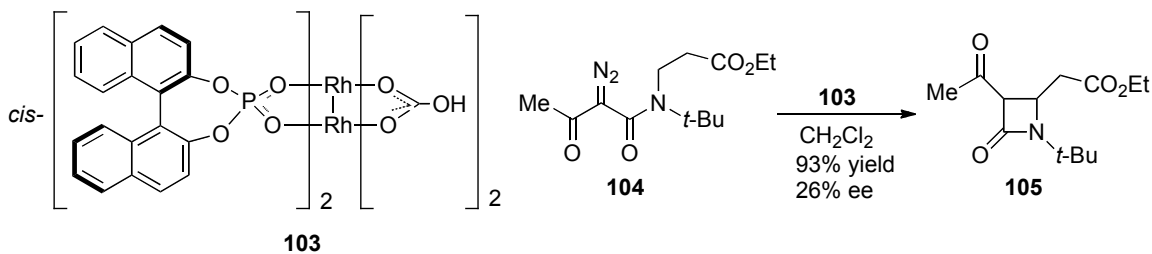
A variety of binaphthylphosphate catalysts have been explored by Hodgson and co-workers.³⁸ The general strategy was to add substituents at the different positions of the binaphthyl scaffold (Figure 1.11). Among those, $\text{Rh}_2(\text{R-DDBNP})_4$ with *n*-dodecyl chain at 6,6'-positions gave the best result. The tricyclic product **97** derived from the [1,3]-dipolar cycloaddition of the diazoacetoacetate **96** was isolated in 66% yield and 90% ee (Scheme 1.9).^{38c}

However, in many other reactions, these complexes had very limited success. $\text{Rh}_2(\text{S-BNP})_4$ -catalyzed reaction of *p*-methoxyphenyldiazoacetate **98** and sulfide **99** gave the sulfur ylide/[2,3]-sigmatropic rearrangement product **100** in 94% yield, but only 27% ee (Scheme 1.10).^{39a} The intramolecular aziridination of sulfonamide **101** with $\text{Rh}_2(\text{R-BNP})_4$ as catalyst produced **102** in 64% yield and 4% ee (Scheme 1.11).^{39b}

Figure 1.11 Dirhodium binaphthylphosphate complexes**Scheme 1.9** [1, 3]-dipolar cycloaddition catalyzed by $\text{Rh}_2(\text{R-DDBNP})_4$ **Scheme 1.10** Sulfur ylide/[2,3]-sigmatropic rearrangement catalyzed by $\text{Rh}_2(\text{S-BNP})_4$ **Scheme 1.11** Intramolecular aziridination catalyzed by $\text{Rh}_2(\text{R-BNP})_4$ 

The only dirhodium complex with mixed binaphthylphosphate ligands is $\text{Rh}_2(\text{S-BNP})_2(\text{HCO}_3)_2$ **103**.⁴⁰ The intramolecular C–H insertion of diazo **104** with complex **103** as catalyst produced compound **105** in 93% yield and 26% ee (Scheme 1.12).

Scheme 1.12 Intramolecular C–H insertion catalyzed by $\text{Rh}_2(\text{S-BNP})_2(\text{O}_3\text{CH})_2$



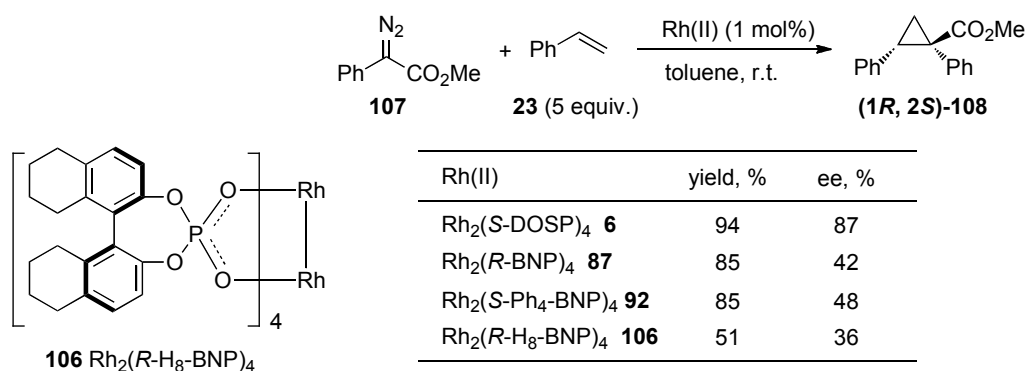
1.2 Results and discussion

1.2.1 Synthesis of dirhodium(II) binaphthylphosphate complexes

Compared with the dirhodium carboxylate and carboxamidate complexes, dirhodium binaphthylphosphates have limited success as catalysts in asymmetric carbenoid transformations. However, from the symmetry point of view, they have the possibility of functioning as very effective catalysts. There are two further advantages: 1. The synthesis of a wide range of binaphthylphosphoric acids is established, since they have been widely used as chiral Brønsted acid catalysts in various enantioselective reactions such as transfer hydrogenation, Friedel-Crafts reaction, Mannich reaction, Aza Diels-Alder reaction, Aza-ene-type reaction, and Pictet-Spengler reaction;⁴¹ 2. Dirhodium binaphthylphosphate complexes have comparatively rigid structures, and therefore, ligand modification may have great influence on their catalytic activity. For many years, the Davies group has been interested in the synthesis and application of this type of

complexes in the rhodium-catalyzed donor/acceptor carbenoid transformations.⁴² Dr Monica Grazini-Rocha and Dr Janelle L. Thompson synthesized complex **92** with 4,4',6,6'-tetraphenylbinaphthylphosphate as ligand, and complex **106** with partially hydrogenated binaphthylphosphate as ligand. Their initial evaluation in the cyclopropanation of phenyldiazoacetate **107** and styrene **23** is summarized in Table 1.2.^{42c} Complex **87**, **92**, and **106** had much lower enantioselectivity than $\text{Rh}_2(\text{S-DOSP})_4$, and cyclopropane **108** was formed in 51-85% yield with <50% ee. Meanwhile, compared with $\text{Rh}_2(\text{R-BNP})_4$ **87**, ligand modification in complex **92** and **106** did not substantially improve their asymmetric induction in the reaction.

Table 1.2 Cyclopropanation of phenyldiazoacetate with styrene



In order to further explore this chemistry, dirhodium tetrabinaphthylphosphate complexes (Rh_2L_4) containing different substituents at the (3,3')- or (4,4',6,6')- positions of the binaphthyl scaffold and other complexes ($\text{Rh}_2\text{L}_n(\text{OAc})_{(4-n)}$) containing mixed binaphthylphosphate and acetate ligands were synthesized and evaluated in various carbenoid transformations.

1.2.1.1 Dirhodium *tetrakis*-binaphthylphosphate complexes (Rh_2L_4)

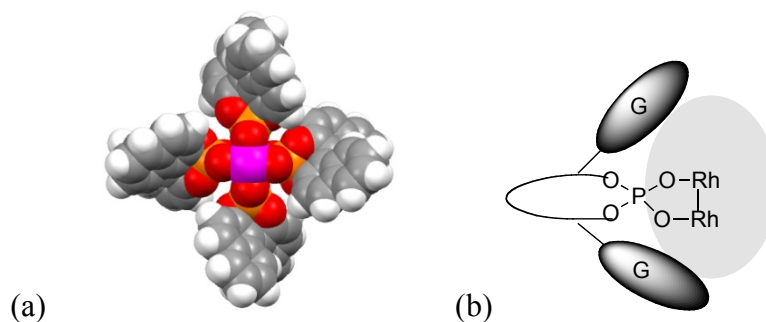
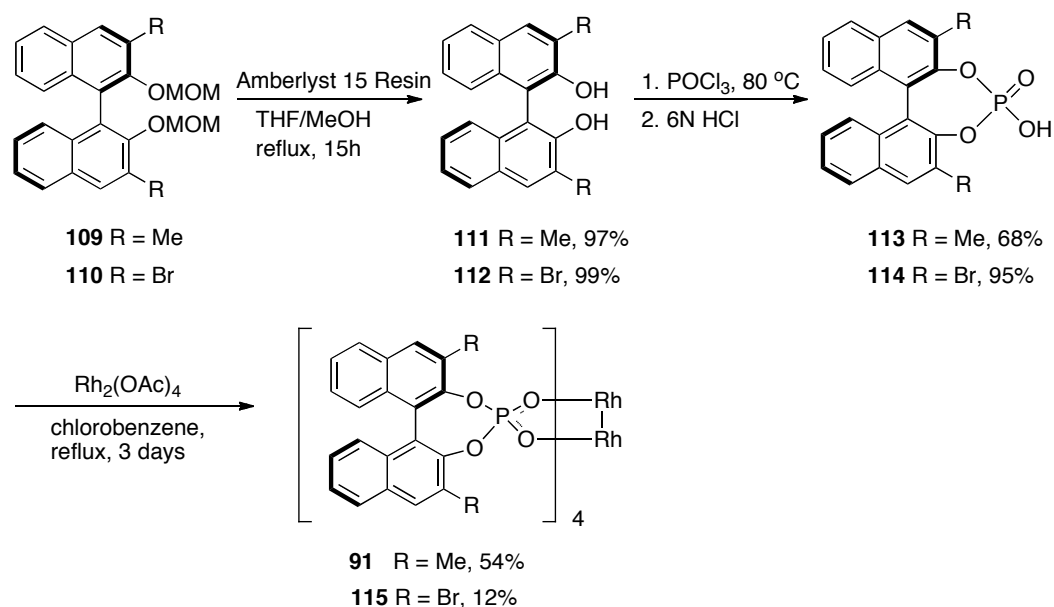
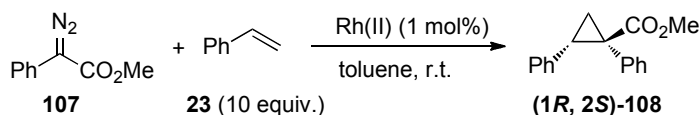


Figure 1.12 (a) Molecular model of $\text{Rh}_2(\text{S-BNP})_4$ (top view),
 (b) The substituent influence at 3,3'-position of the BNP

The molecular model of $\text{Rh}_2(\text{S-BNP})_4$ is shown in Figure 1.12(a). Besides its high symmetric character, the model also highlights the short distance between the (3,3')-positions of the binaphthyl scaffold and the axial site of the dirhodium core (Figure 1.12(b)). With the vision that substituents at these two positions might effectively influence its catalytic activity and asymmetric induction during the reaction, complex **91** ($\text{R} = \text{Me}$) and **115** ($\text{R} = \text{Br}$) were synthesized (Scheme 1.13). Deprotection of the MOM protected BINOL derivative **109** and **110** with Amberlyst 15 resin produced diols **111** and **112** in 97% and 99% yield. The diols were then treated with POCl_3 in pyridine, followed by hydrolysis with HCl to give the binaphthyl phosphoric acid **113** in 68% yield and **114** in 95% yield. The ligand exchange of **113** and **114** with $\text{Rh}_2(\text{OAc})_4$ in refluxing chlorobenzene produced complexes **91** in 54% yield and **115** in 15% yield. Both complexes were characterized by ^1H , ^{13}C , ^{31}P -NMR, and MS analysis.

Scheme 1.13 Synthesis of complexes **91** and **115**Scheme 1.14 Cyclopropanation catalyzed by complex **91** and **115**

Rh(II)	dr ^a	yield, % ^b	ee, % ^c
91	>97:3	50	26
115	94:6	58	55

^a Determined by ¹H-NMR of the crude reaction mixture.

^b Isolated yield of the major diastereomer.

^c Determined by chiral HPLC.

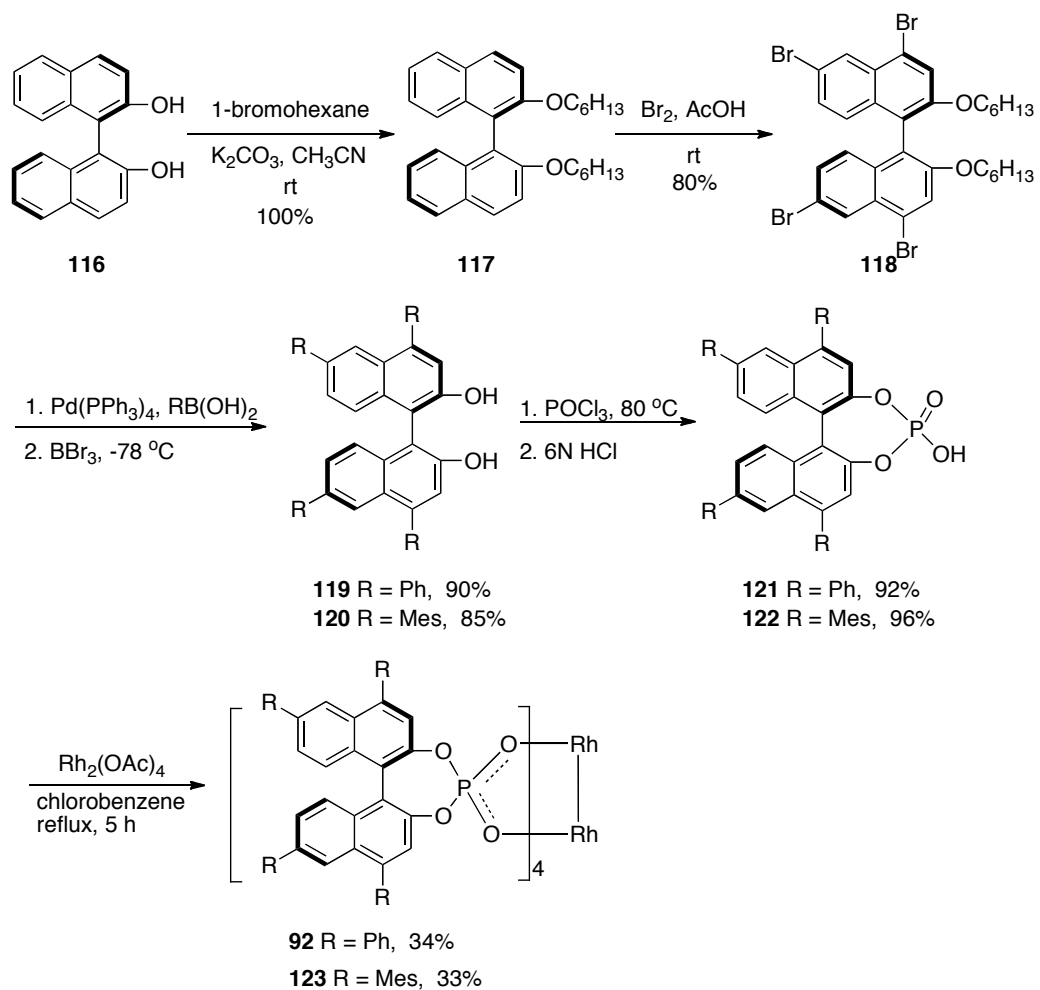
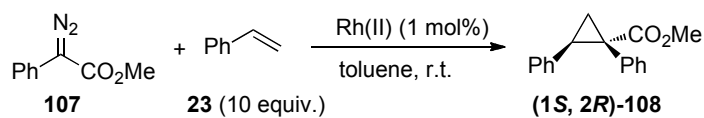
Donor/acceptor carbenoids derived from rhodium catalyzed decomposition of aryldiazoacetates and vinyldiazoacetates have shown superior selectivity compared to the traditional acceptor carbenoids and acceptor/acceptor carbenoids.^{1b,1c} In particular, the rhodium catalyzed cyclopropanation between phenyldiazoacetate **107** and styrene **23** has been well studied through both experimental and theoretical study.^{14a,21,22} This reaction

was chosen as a standard reaction to test the catalytic activity of complex **91** and **115** (Scheme 1.14). With complex **91** as catalyst, cyclopropane **108** was formed in 50% yield with >97:3 diastereomeric ratio favoring the *E*-diastereomer. The high diastereoselectivity was similar to that observed with $\text{Rh}_2(\text{S-DOSP})_4$. The enantioselectivity, however, was very poor (26% ee). The absolute configuration of the major enantiomer, (**1R, 2S**)-**108**, was assigned by comparing its HPLC trace with the known (**1S, 2R**)-**108**.^{14d} Hodgson has reported that even sterically small substituents at the 3,3'-positions of the binaphthyl scaffold would result in a considerable loss of enantiocontrol due to the possible steric congestion at the axial binding sites on the dirhodium core.^{38a} For example, the enantioselectivity of [1,3]-dipolar cycloaddition product **97** dropped dramatically from 64% ee to 7% ee by switching the catalyst from $\text{Rh}_2(\text{R-BNP})_4$ (**87**) to complex **91** (Scheme 1.9). This steric congestion can also be used to explain the low enantioselectivity of cyclopropane **108** catalyzed by complex **91**. Although the bromide groups in complex **115** had a similar steric effect as the methyl groups in complex **91**, the higher enantioselectivity of cyclopropane **108** obtained with complex **115** (55% ee) indicated that the electronic withdrawing effect of the bromide groups might have profound effect on its catalytic reactivity. Overall, compared with $\text{Rh}_2(\text{R-BNP})_4$, complex **115** did not demonstrate significant improvement (42% ee versus 55% ee).

The influence of bulky substituents at the (4,4',6,6')- positions of the binaphthyl scaffold was also studied. Since the previous studies showed that a phenyl group at these positions did not improve the catalyst's asymmetric induction in the cyclopropanation of donor/acceptor carbenoid with styrene,^{42b} the bulkier mesityl group was chosen. The

synthesis of binaphthyl phosphoric acid **122** and its rhodium complex **123** is outlined in Scheme 1.15. First, (*R*)-BINOL (**116**) was quantitatively converted into its hexyl ether (**117**), which was then treated with bromine in acetic acid to give the (4,4',6,6')-tetrabromo derivative **118** in 80% yield.^{38c} Suzuki coupling between mesitylboronic acid and **118** with Pd(PPh₃)₄ as catalyst, followed by deprotection of the hexyl group with BBr₃ and the standard phosphonation with POCl₃/HCl gave **121** in good yield (~81% yield over 2 steps). Ligand exchange of Rh₂(OAc)₄ with **121** was done in refluxing chlorobenzene to produce complex **123** in 33% yield. To compare the catalyst activities, complex **92** was also synthesized by following the same sequence.

High diastereoselectivity favoring the *E*-diastereomer was also observed in the cyclopropanation reaction of phenyldiazoacetate **107** and styrene with complexes **92** and **123** as catalyst (Scheme 1.16). The enantioselectivities, however, were still much lower than that of Rh₂(*S*-DOSP)₄ (43% ee with **92**, 33% ee with **123**). Surprisingly, (**1S, 2R**)-**108** was obtained as the major enantiomer in both reactions. The opposite asymmetric induction of complex **92** and **123** to that of Rh₂(*R*-BNP)₄ indicated that the substituents at the (4,4',6,6')-position of the binaphthyl scaffold had considerable influence on the carbenoid conformation. Further studies are needed in order to achieve a better understanding of this switch in stereoselectivity.

Scheme 1.15 Synthesis of complexes **92** and **123**Scheme 1.16 Cyclopropanation catalyzed by complex **92** and **123**

Rh(II)	dr ^a	yield, % ^b	ee, % ^c
92	>97:3	85	43
123	>97:3	60	33

^a Determined by ¹H-NMR of the crude reaction mixture.

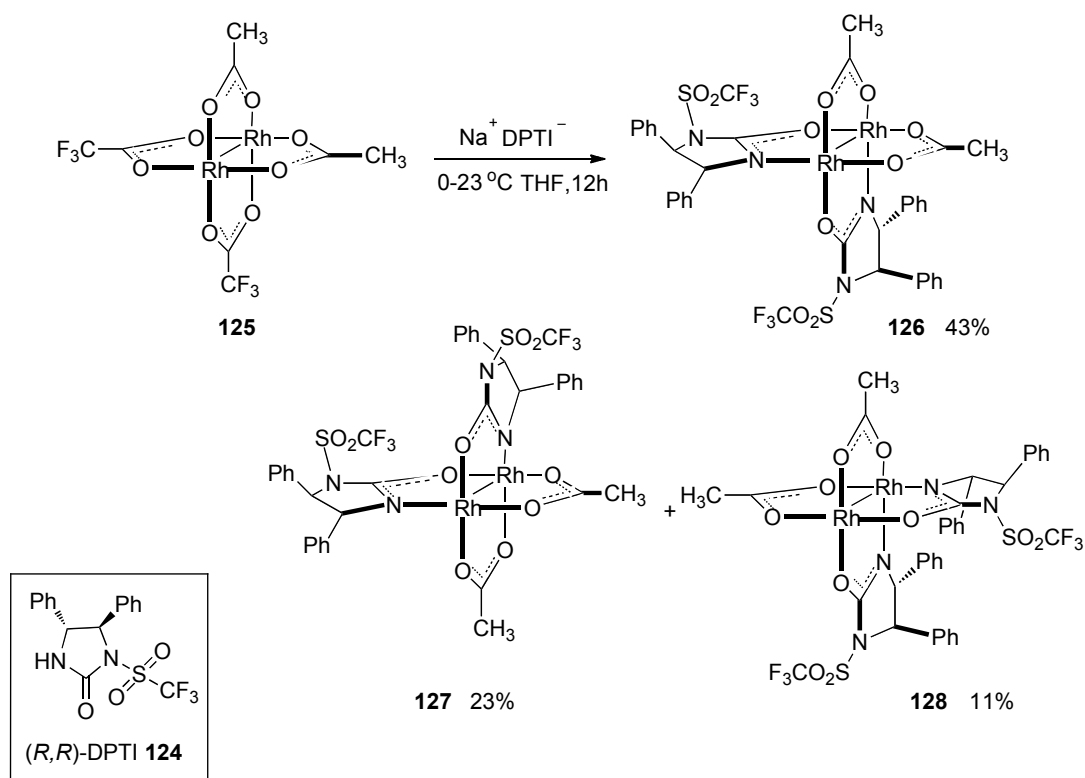
^b Isolated yield of the major diastereomer.

^c Determined by chiral HPLC.

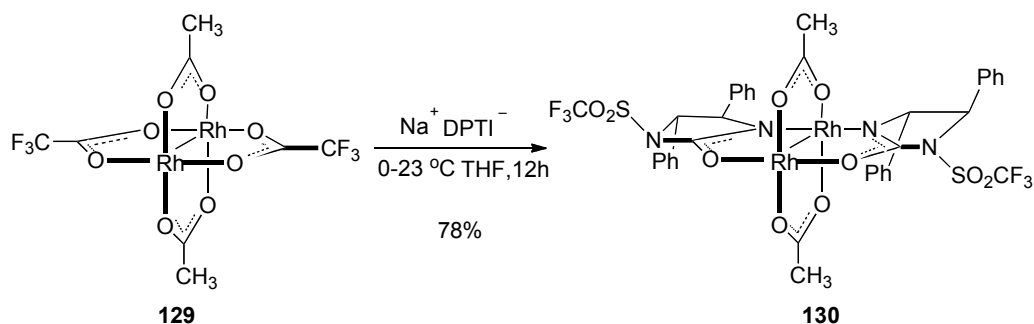
1.2.1.2 Dirhodium complexes containing mixed ligands ($\text{Rh}_2\text{L}_n(\text{OAc})_{(4-n)}$)

The selective synthesis of dirhodium complexes containing mixed ligands was achieved by Corey and co-workers in 2005.⁴³ Chiral carboxamidate (*R, R*)-DTPI (**124**) was treated with NaHMDS at $-78\text{ }^\circ\text{C}$, followed by the addition of *cis*- $\text{Rh}_2(\text{OAc})_2(\text{TFA})_2$ (**125**), producing a mixture of *cis*- $\text{Rh}_2((R, R)\text{-DTPI})_2(\text{OAc})_2$ (**126-128**) in 77% combined yield (Scheme 1.17). Similarly, *trans-syn*- $\text{Rh}_2((R, R)\text{-DTPI})_2(\text{OAc})_2$ (**130**) was selectively formed in 78% yield by treating (*R, R*)-DTPI (**124**) with NaHMDS followed by the addition of *trans*- $\text{Rh}_2(\text{OAc})_2(\text{TFA})_2$ (**129**) (Scheme 1.18).

Scheme 1.17 Synthesis of *cis*- $\text{Rh}_2((R, R)\text{-DTPI})_2(\text{OAc})_2$



Scheme 1.18 Synthesis of *trans-syn*-Rh₂((*R,R*)-DTPI)₂(OAc)₂

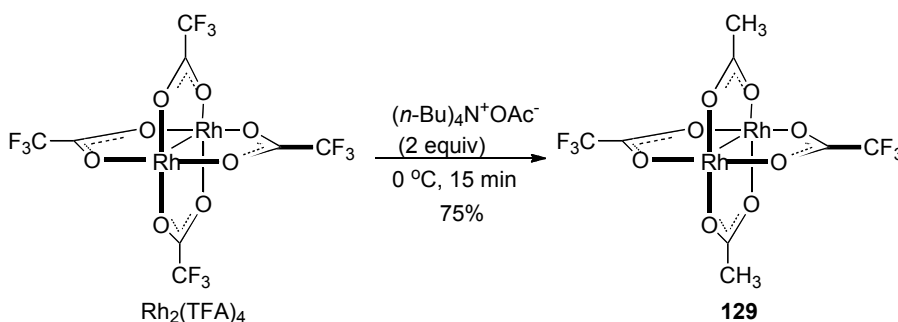


1.2.1.2.1 Dirhodium *bis*-binaphthylphosphate complexes (Rh₂L₂(OAc)₂)

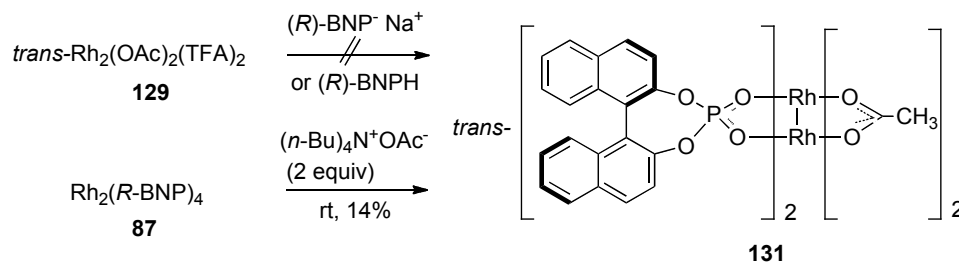
With the vision that dirhodium complexes containing both binaphthylphosphate and acetate ligands could also be synthesized by following Corey's procedure, this catalyst design project shifted to a new direction. First, the complexes containing two unsubstituted binaphthylphosphates and two acetates were chosen as targets. Following Corey's procedure, *trans*-Rh₂(OAc)₂(TFA)₂ (**129**) was prepared from the reaction of Rh₂(TFA)₄ with 2 equivalent *tetra*-butylammonium acetate in 75% yield (Scheme 1.19). Sodium binaphthylphosphate ((*R*)-BNP⁻Na⁺) was then mixed with *trans*-Rh₂(OAc)₂(TFA)₂ (**129**) under various conditions including different temperatures (rt or reflux) and solvents (acetonitrile, methanol, methanol/water, chloroform, and chloroform/water), but formation of the desired complex *trans*-Rh₂(*R*-BNP)₂(OAc)₂ (**131**) was not observed. The low basicity of the phosphate could be the reason for its poor reactivity towards the ligand exchange with *trans*-Rh₂(OAc)₂(TFA)₂. Ligand exchange of (*R*)-BNP-H and *trans*-Rh₂(OAc)₂(TFA)₂ at different temperatures also produced a complex mixture. Eventually, *trans*-Rh₂(*R*-BNP)₂(OAc)₂ (**131**) was produced in 14%

yield by treating $\text{Rh}_2(\text{R-BNP})_4$ (**87**) with 2 equivalent *tetra*-butylammonium acetate (Scheme 1.20).

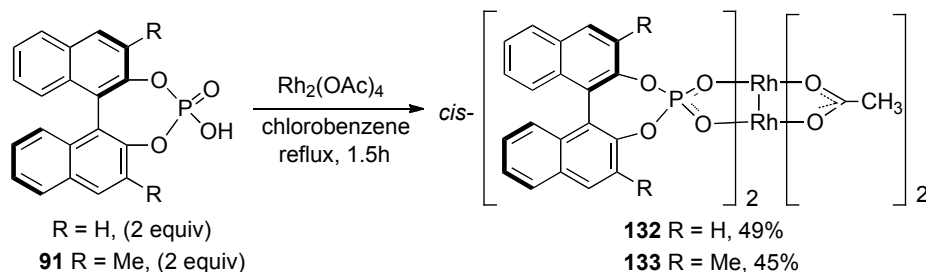
Scheme 1.19 Synthesis of *trans*- $\text{Rh}_2(\text{OAc})_2(\text{TFA})_2$ (**129**)



Scheme 1.20 Synthesis of *trans*- $\text{Rh}_2(\text{R-BNP})_2(\text{OAc})_2$ (**131**)



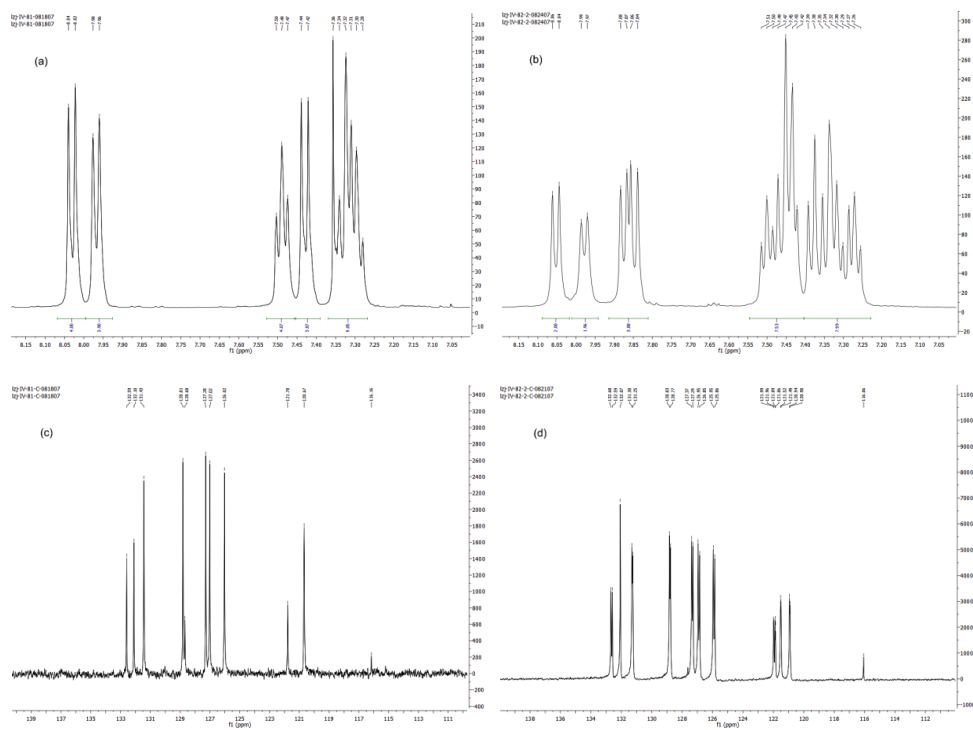
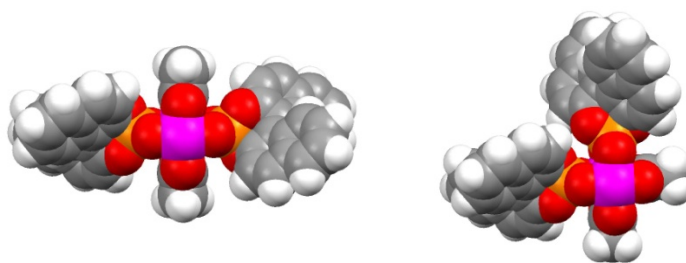
Scheme 1.21 Synthesis of *cis*- $\text{Rh}_2\text{L}_2(\text{OAc})_2$ complexes **132** and **133**

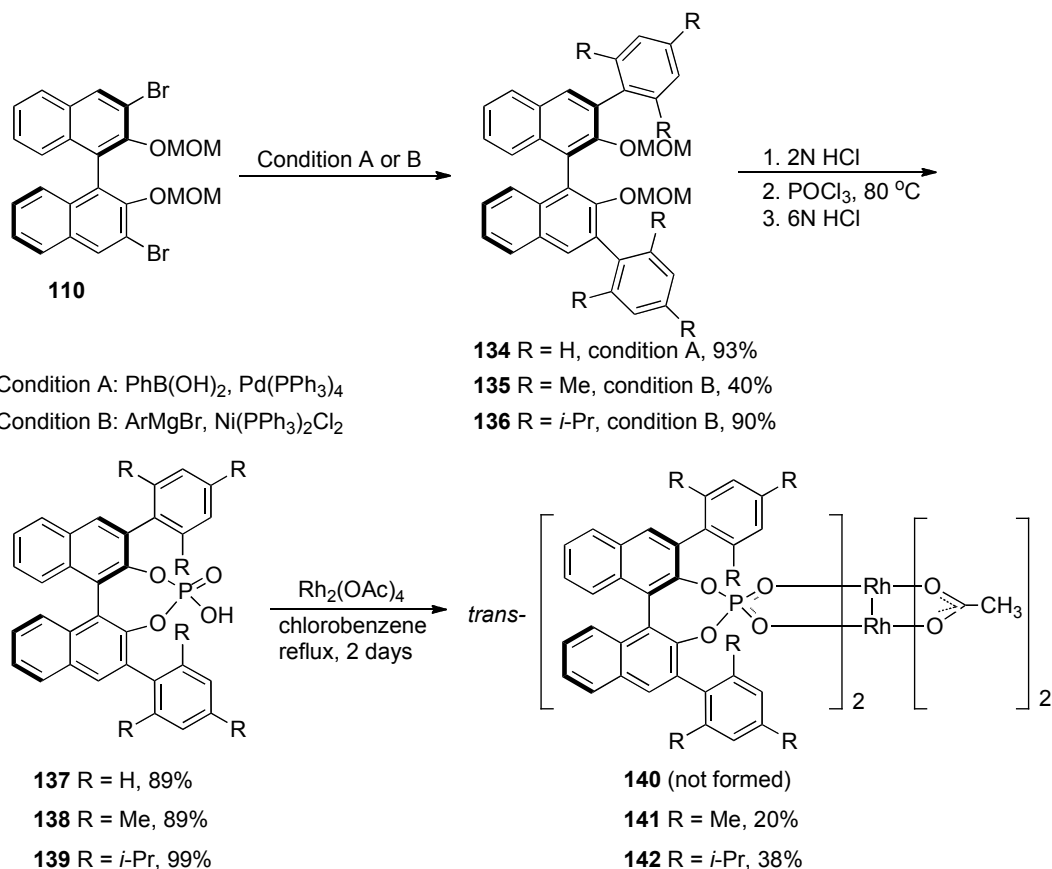


The ligand exchange of *(R)*-BNP-H and $\text{Rh}_2(\text{OAc})_4$ (ratio: 2:1) in refluxing chlorobenzene smoothly gave *cis*- $\text{Rh}_2(\text{R-BNP})_2(\text{OAc})_2$ (**132**) in 49% yield (Scheme 1.21).

Complex **133** with methyl at the (3,3')-position of the binaphthyl scaffold was also synthesized in the similar way in 45% yield.

The structure determination of complexes **131–133** was based on their NMR spectra (Figure 1.13). Although complexes **131** and **132** have similar FAB-MS spectrum, their NMR spectra (solvent: CD₂Cl₂) are quite different. For *trans*-Rh₂(*R*-BNP)₂(OAc)₂ (**131**), the aromatic region of its ¹H and ¹³C-NMR shows the signals of only one binaphthylphosphate ligand (Figure 1.13, a and c). While for *cis*-Rh₂(*R*-BNP)₂(OAc)₂ (**132**), the aromatic region of its ¹H and ¹³C-NMR shows the signals of two binaphthylphosphate ligands (Figure 1.13, b and d). This difference between **131** and **132** can be explained from a consideration of their conformation (Figure 1.14). *trans*-Rh₂(*R*-BNP)₂(OAc)₂ (**131**) is highly symmetric (*D*₂) and the two chiral ligands are magnetically equivalent. But *cis*-Rh₂(*R*-BNP)₂(OAc)₂ (**132**) is only *C*₂-symmetric, the different chemical environment between two chiral ligands results in the difference in the NMR spectra. Complex **133** also has similar character to complex **132** with the signals from two magnetically nonequivalent chiral ligands in the ¹H and ¹³C-NMR spectra. The preference of the two binaphthylphosphate ligands to adopt *cis*- arrangement in **132** and **133** is also consistent with the ligand arrangement during the synthesis of *cis*-Rh₂(TFA)₂(OAc)₂, in which the more electron-withdrawing trifluoroacetate (TFA) disfavors the displacement of acetate at the *trans* position.⁴³

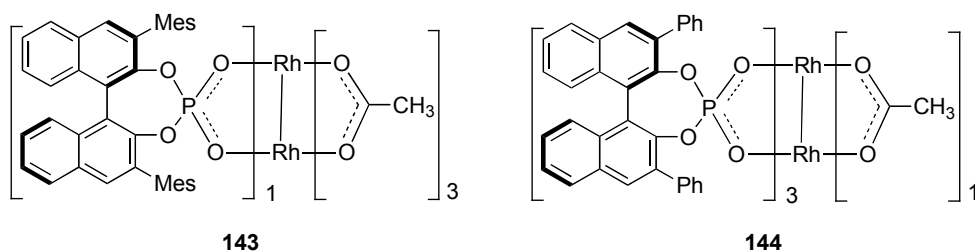
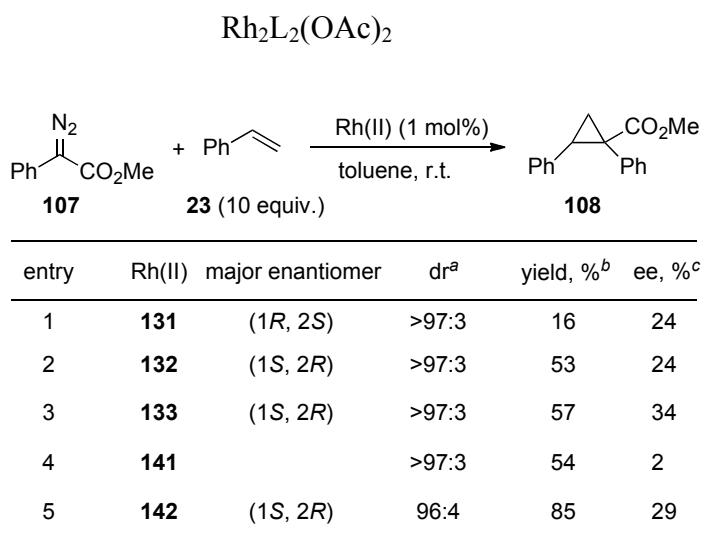
Figure 1.13 The aromatic region of the ^1H and ^{13}C -NMR spectra of complex **131** and**132****Figure 1.14** Molecular models of *trans*- $\text{Rh}_2(\text{S-BNP})_2(\text{OAc})_2$ and *cis*- $\text{Rh}_2(\text{S-BNP})_2(\text{OAc})_2$ 

Scheme 1.22 Synthesis of *trans*-Rh₂L₂(OAc)₂

With the perspective that a complex with higher symmetry could have better asymmetric induction, and the fact that the binaphthylphosphate ligand such as **113** prefers the *cis*-arrangement around the dirhodium core during the standard ligand exchange with Rh₂(OAc)₄, ligands with bulky substituents at the (3,3')-positions of the binaphthyl scaffold were chosen as targets. The hypothesis is that these bulky substituents such as mesityl and 2,4,6-triisopropylphenyl will prevent the second chiral ligand from getting onto the *cis* position of the first chiral ligand during the ligand exchange. Instead, the second chiral ligand will prefer to exchange with the acetate at the

trans position of the first chiral ligand and form highly symmetric complex *trans*-Rh₂L₂(OAc)₂.

To test this hypothesis, ligands **137–139** were successfully synthesized (Scheme 1.22). Pd(PPh₃)₄ catalyzed Suzuki coupling of phenylboronic acid and BINOL derivative **110** gave compound **134** in 93% yield. For the synthesis of compound **135** and **136** containing bulky substituents, Ni-catalyzed crossing couple of Grignard reagent and BINOL derivative **110** was used, and the reaction gave **135** and **136** in 40% and 90% yield, respectively. After hydrolysis with HCl and phosphonation with POCl₃/HCl, binaphthylphosphoric acids **137–139** were obtained in very high yield (89-99%). Ligand exchange of **138** (R = Me) and Rh₂(OAc)₄ (ratio of **138** : Rh₂(OAc)₄: 2:1) in refluxing chlorobenzene for 2 days produced complex **141** containing two chiral ligands at *trans* position in 20% yield, the major byproduct was complex **143** containing only one chiral ligand (40% yield). Ligand exchange of **139** (R = *i*-Pr) with Rh₂(OAc)₄ (ratio of **139** : Rh₂(OAc)₄ : 2.5:1) under similar condition produced complex **142** in 38% yield. The structure of complex **141** and **142** were assigned based on their ¹H and ¹³C-NMR spectra, which demonstrated their symmetric character with two magnetically equivalent chiral ligands. The ligand exchange of **137** (R = H) with Rh₂(OAc)₄ (ratio of **137** : Rh₂(OAc)₄: 1:1 to 2.5:1), however, produced a complex mixture with complex **144** containing three chiral ligands in 12% isolated yield.

Figure 1.15 Structure of complex **143** and **144**Scheme 1.23 Cyclopropanation catalyzed by complexes *cis*- and *trans*-

^a Determined by ¹H-NMR of the crude reaction mixture.

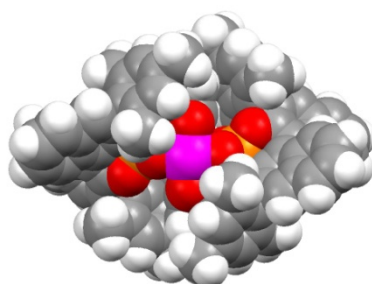
^b Isolated yield of the major diastereomer.

^c Determined by chiral HPLC.

Unfortunately, the standard cyclopropanation reaction with complexes **131–133**, **141**, and **142** as catalyst produced cyclopropane **108** with very low enantiomeric excess (24–30% ee) (Scheme 1.23). Opposite asymmetric induction was also observed with these complexes. Complex **131** catalyzed reaction produced (**1*R*, 2*S***)-**108** as the major enantiomer, while complex **132**, **133**, and **142** catalyzed reactions produced (**1*S*, 2*R***)-**108** as the major enantiomer. Catalyst decomposition was observed with complex **141**, and cyclopropane **108** was isolated in 54% yield in racemic form. Comparing the molecular

models of complexes **131–132** (Figure 1.14) and that of complex **141** (Figure 1.16), two reasonable possibilities could be drawn to explain the low asymmetric induction of these complexes. First, with unsubstituted binaphthylphosphate ligand, complexes **131**, **132** and **133** might be sterically too open to achieve good asymmetric induction. Second, the highly substituted aryl groups at the (3,3')- positions of the binaphthyl scaffold in the complex **142** might sterically cover the axial site of the dirhodium core and hence decrease the enantioselectivity of the reaction.

Figure 1.16 Molecular model of the (*S*)-enantiomer of complex **141** (top view)



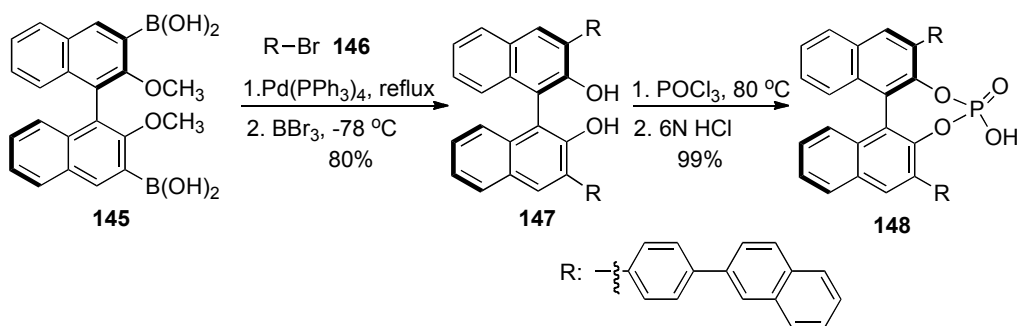
1.2.1.2.2 Dirhodium *mono*-binaphthylphosphate complexes ($\text{Rh}_2\text{L}(\text{OAc})_3$)

As a further extension of this project, the synthesis of dirhodium complexes containing only one binaphthylphosphate and three acetates was also explored. Apparently, very bulky substituents at the (3,3')- position of the binaphthyl scaffold are needed in order to achieve good enantioselectivity.

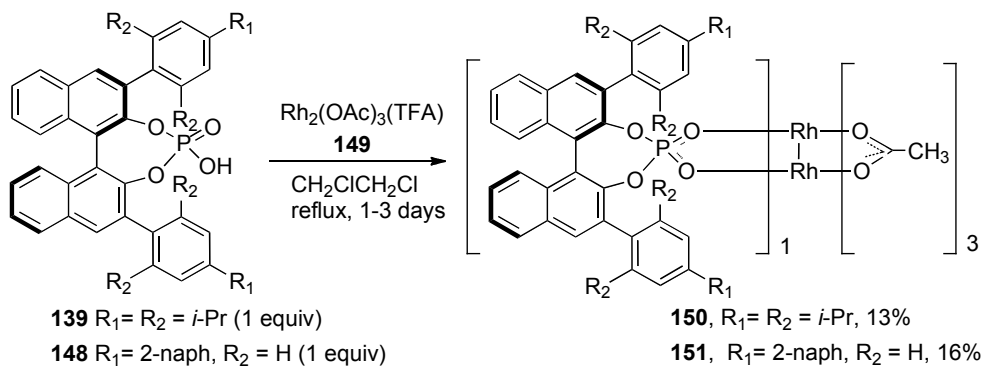
(*R*)-3,3'-bis(4-(2-naphthyl)-phenyl)binaphthylphosphoric acid **148** was synthesized following a similar procedure to the other ligands, starting with the Suzuki coupling of BINOL boronic acid **145** and aryl bromide **146**, as outlined in Scheme 1.24. Bear and

co-workers reported that the rate constants for the successive formation of *mono*, *di*, *tri*, and *tetra*-trifluoroacetate dirhodium complex during the ligand exchange of $\text{Rh}_2(\text{OAc})_4$ with trifluoroacetic acid had the ratio of 1:2:0.1:0.025.^{44,45} To synthesize the dirhodium complex containing only one binaphthylphosphate, $\text{Rh}_2(\text{OAc})_3(\text{TFA})$ (**149**) was used instead of $\text{Rh}_2(\text{OAc})_4$ in order to selectively exchange the more labile trifluoroacetate (TFA) with the chiral ligand. However, both ligand exchange reactions of **139** and **148** with $\text{Rh}_2(\text{OAc})_3(\text{TFA})$ gave the desired complexes **150** and **151** in very low yield (13–16%) (Scheme 1.25).

Scheme 1.24 Synthesis of ligand **148**

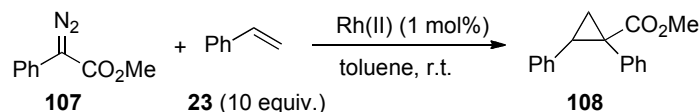


Scheme 1.25 Synthesis of complex **150-151**



A distinct difference among complexes **143**, **150** and **151** was observed from their evaluation with the standard cyclopropanation reaction (Scheme 1.26). Although all of these three complexes produced cyclopropane **108** in similar low yield (50–65%), the enantioselectivities were quite different. Complex **143** containing mesityl gave cyclopropane **108** with only 11% ee, while complexes **150** and **151** containing 2,4,6-triisopropylphenyl and 4-(2-naphthyl)-phenyl produced **108** with much higher enantioselectivity (48% ee and 54% ee, respectively). Considering that these two complexes only contain one chiral ligand, the results are very surprising. Further optimization of these catalysts might eventually lead to the discovery of new and efficient catalysts.

Scheme 1.26 Cyclopropanation catalyzed by complexes $\text{Rh}_2\text{L}(\text{OAc})_3$



entry	Rh(II)	major enantiomer	dr ^a	yield, % ^b	ee, % ^c
1	143	(1 <i>R</i> , 2 <i>S</i>)	>97:3	52	11
2	150	(1 <i>S</i> , 2 <i>R</i>)	>97:3	65	54
3	151	(1 <i>S</i> , 2 <i>R</i>)	>97:3	50	48

^a Determined by ¹H-NMR of the crude reaction mixture.

^b Isolated yield of the major diastereomer.

^c Determined by chiral HPLC.

In summary, chiral dirhodium complexes containing *mono*, *di*, and *tetra* binaphthylphosphate ligands were synthesized and fully characterized. Although the initial evaluation with the cyclopropanation of phenyldiazoacetate and styrene did not show improved asymmetric induction when compared with $\text{Rh}_2(\text{R-BNP})_4$, the novel and versatile method to synthesize these complexes could provide valuable information for

the further development of this project. This study also showed that dirhodium complexes containing only one binaphthylphosphate ligand with bulky substituents at the (3,3')-position of the binaphthyl scaffold gave similar asymmetric induction as dirhodium tetrabinaphthylphosphate $\text{Rh}_2(\text{R-BNP})_4$.

1.2.2 Synthesis of dirhodium phosphinate complex

Table 1.3 $\text{Rh}_2(\text{O}_2\text{PMe}_2)_4$ and $\text{Rh}_2(\text{OAc})_4$ mediated cyclopropanations

$\text{R-CH=CH}_2 + \text{EtO-C(=O)-CHN}_2 \xrightarrow[\text{DCM}]{\text{Rh(II) (1 mol\%)}}$

156
157
158

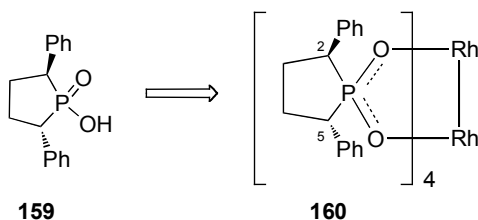
entry	alkene	$\text{Rh}_2(\text{O}_2\text{PMe}_2)_4$		$\text{Rh}_2(\text{OAc})_4$	
		yield	<i>trans/cis</i> ratio	yield	<i>rans/cis</i> ratio
1	23	88	1.8	93	1.6
2	153	83	3.0	90	3.8
3	154	80	5.6	91	6.5
4	155	83	4.0	78	1.0

152 $\text{Rh}_2(\text{O}_2\text{PMe}_2)_4$

The synthesis of the dirhodium phosphinate complex is not well documented. To date, there is only one report from Capretta and co-workers in 2006.⁴⁶ Dirhodium dimethylphosphinate ($\text{Rh}_2(\text{O}_2\text{PMe}_2)_4$) (**152**) was prepared in 62% yield from the ligand exchange of dimethylphosphinic acid and $\text{Rh}_2(\text{OAc})_4$ in refluxing chlorobenzene. Its X-ray structure showed that this complex possessed a unique propeller structure with a long Rh–Rh single bond (2.4379 Å). Initial evaluation of $\text{Rh}_2(\text{O}_2\text{PMe}_2)_4$ in the cyclopropanation of ethyl diazoacetate with various alkenes produced cyclopropanes with selectivity comparable to $\text{Rh}_2(\text{OAc})_4$ (Table 1.3, entries 1–3). When electron-rich alkene 2-methoxyprop-1-ene (**155**) was used as substrate, the reaction gave even better

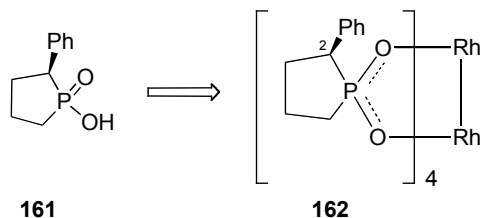
diastereoselectivity than $\text{Rh}_2(\text{OAc})_4$ (entry 4, *trans/cis* ratio: 4.0 with $\text{Rh}_2(\text{O}_2\text{PMe}_2)_4$, 1.0 with $\text{Rh}_2(\text{OAc})_4$).

Scheme 1.27 Proposed chiral dirhodium phosphinate **160**



Inspired by Capretta's work, a project aiming to synthesize chiral dirhodium phosphinate complexes was undertaken in the Davies group. It was envisioned that the C_2 -symmetric cyclic phosphinic acid **159** would be able to afford the D_4 -symmetric dirhodium complex **160** (Scheme 1.27). Meanwhile, the phenyl groups at the (2, 5)-positions of the phosphinate would be close to the axial site of the complex and have proper influence on the complex's asymmetric induction during the carbenoid reaction. The five member ring moiety of the phosphinate would also define the orientation of the phenyl groups and the symmetry of the complex. The following molecular modeling study showed that this complex was highly symmetric with four phenyl groups oriented around each axial site of the complex. However, it also showed that both axial sites were completely blocked by the four phenyl groups. To avoid this problem, attention turned to its analogue **162** containing only one phenyl group in the ligand, with the hope that its four ligands could have proper arrangement around the dirhodium core and generate **162** as a highly symmetric complex. Ideally, there will be only two phenyl groups around each axial site of **162** with either *cis* or *trans* arrangement.

Scheme 1.28 Proposed synthesis of chiral dirhodium phosphinate **162**

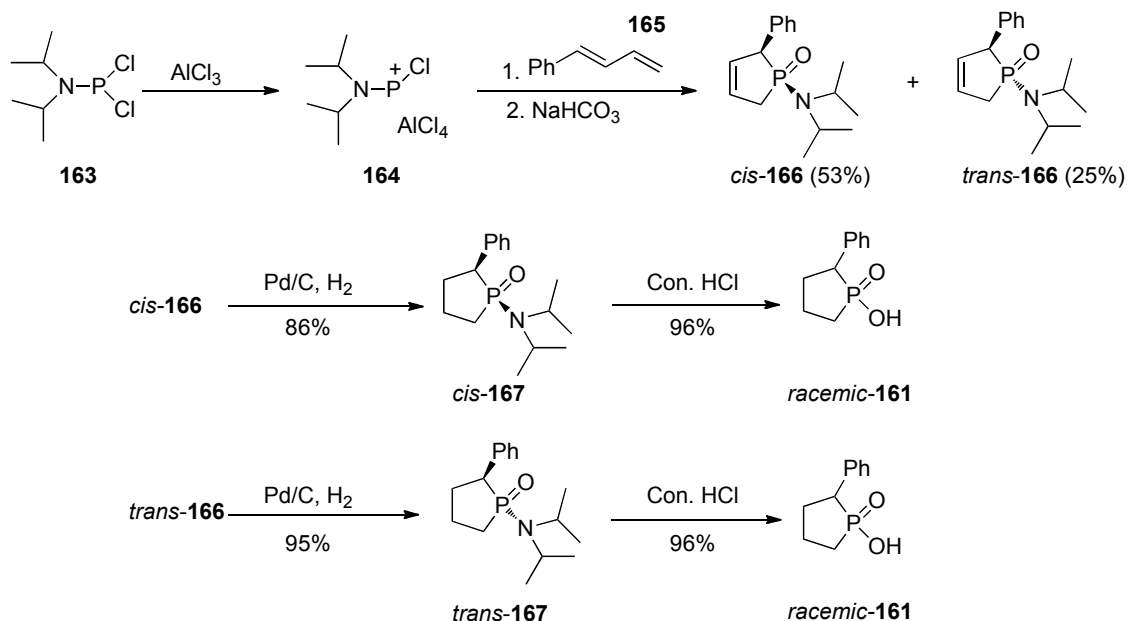


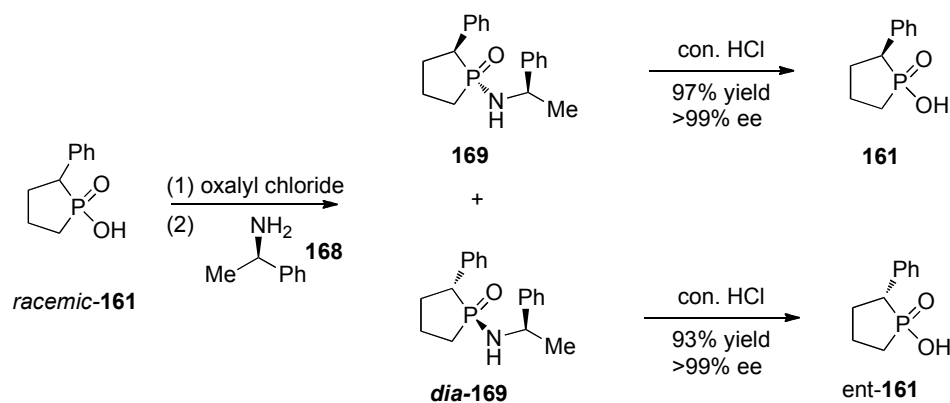
Logically, complex **162** could be synthesized from the ligand exchange of cyclic phosphinic acid **161** with $\text{Rh}_2(\text{OAc})_4$ by following a procedure similar to the synthesis of dirhodium binaphthylphosphate complexes (Scheme 1.28). The synthesis of *racemic-161* followed the procedure reported by Fiaud.⁴⁷ First, Diisopropylphosphoramidous dichloride (**163**) underwent chloride ion abstraction by aluminum trichloride to form phosphonium ion (**164**), which then underwent a cycloaddition reaction with (*E*)-1-phenyl-1,3-butadiene (**165**) at 0 °C,⁴⁸ followed by aqueous hydrolysis with NaHCO_3 to afford a 2:1 diastereomeric mixture of *cis*- and *trans-166* in 78% combined yield (Scheme 1.29). These two diastereomers were easily separated by flash chromatography. The relative configurations of *cis*- and *trans-166* were assigned by their $^1\text{H-NMR}$ spectra. For *cis-166*, the CH in the isopropyl group was shielded by the phenyl group and had chemical shift at 2.9 ppm. While for *trans-166*, the CH in the isopropyl group had chemical shift at 3.3 ppm. Both diastereomers of **166** were smoothly transformed into *racemic-161* through hydrogenation/hydrolysis sequence in good yields (Scheme 1.29).

Scheme 1.30 shows the resolution of *racemic-161*. *Racemic-161* was first converted into the acid chloride with oxalyl chloride, which was then reacted with (*R*)-methylbenzylamine (**168**) to produce a mixture containing two *trans* isomers **169** and *dia-169* as the major components (67% combined yield, separated by flash

chromatography). The relative stereochemistries of these two *trans* isomers were tentatively assigned by comparison with the corresponding *cis* isomers which were also isolated in 4.4% combined yield. For *trans* isomers **169** and *dia*-**169**, the chemical shifts of CH (~ 4.4 ppm) and CH₃ (~ 1.5 ppm) in the amine moiety are much higher than the chemical shift of similar CH (~ 4.1 ppm) and CH₃ (~ 1.1 ppm) in the *cis* isomers. Presumably, the shielding effect of phenyl group on the phospholane ring results in the lower chemical shift of CH and CH₃ in the *cis* isomers. Both **169** and *dia*-**169** were hydrolyzed in concentrated HCl to produce **161** and its enantiomer in almost quantitative yield with >99% ee. The enantiomeric purity was determined by chiral HPLC after converting the acid into the methyl ester with diazomethane.

Scheme 1.29 Synthesis of *racemic*-**161**

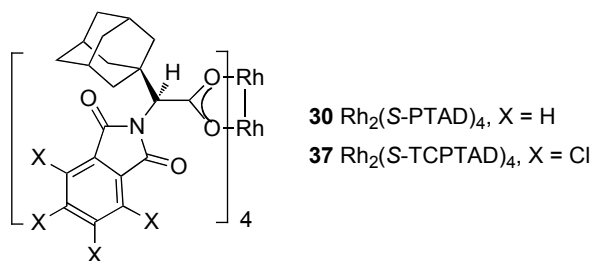


Scheme 1.30 Resolution of *racemic*-161

Unfortunately, the ligand exchange of enantiomerically pure phosphinic acid **161** with $\text{Rh}_2(\text{OAc})_4$ in chlorobenzene at 150–160 °C failed to generate the desired dirhodium complex. Formation of precipitates always occurred during heating and the color of the solution changed from green to brown in one hour. It is possible that the phosphinic acid decomposed upon heating at high temperature, and this led to the closure of this project.

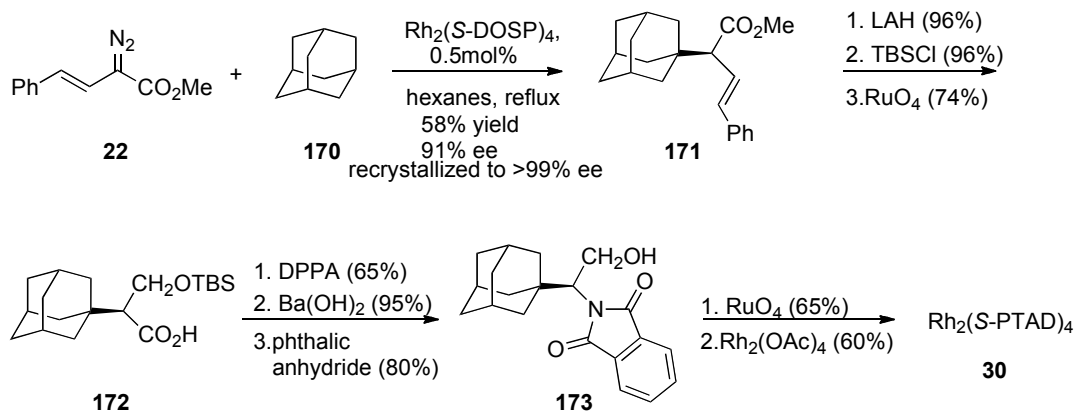
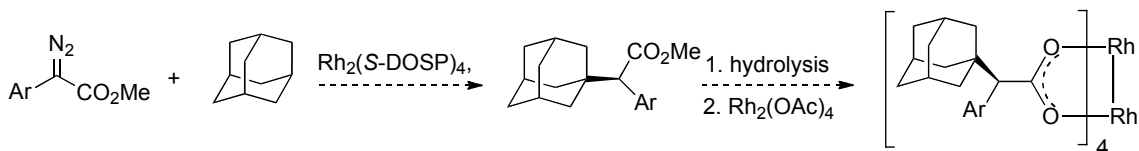
1.2.3 Synthesis of chiral dirhodium carboxylate complexes

Dirhodium tetracarboxylates derived from adamantylglycine, such as $\text{Rh}_2(S\text{-PTAD})_4$ (**30**) and $\text{Rh}_2(S\text{-TCPTAD})_4$ (**37**) developed by Davies and co-workers (Figure 1.17), have received increasing attention as excellent catalysts in a range of asymmetric transformations of donor/acceptor carbenoids, such as cyclopropanation,^{26a,49} C–H activation,^{14g} combined C–H activation/Cope rearrangement,^{18e} amination,^{26b} and [4+3]-cycloaddition.^{29,50} High diastereoselectivity and enantioselectivity were routinely obtained in these transformations. The bulky adamantyl group in these catalysts is considered to be an important contributor to their good performance.

Figure 1.17 Structure of $\text{Rh}_2(\text{S-PTAD})_4$ (**30**) and $\text{Rh}_2(\text{S-TCPTAD})_4$ (**37**)

The key step in the Davies' synthesis of $\text{Rh}_2(\text{S-PTAD})_4$ and $\text{Rh}_2(\text{S-TCPTAD})_4$ is $\text{Rh}_2(\text{S-DOSP})_4$ -catalyzed highly enantioselective C–H insertion into adamantane (**170**) with methyl styryldiazoacetate (**22**) (91% ee for compound **171**) (Scheme 1.31). After recrystallization, adamantyl derivative **171** could be enriched to >99% ee. Although this C–H insertion strategy allowed the quick establishment of the necessary stereocenter in the ligand, the other transformations were very lengthy, including a three-step sequence to convert **171** to **172**: LiAlH_4 -mediated reduction, protection of the alcohol, and oxidative cleavage of the alkene; another three-step sequence: Curtius rearrangement, hydrolysis, and protection of the amine to convert **172** to the protected amino alcohol **173**; then the oxidation of **173** to the carboxylic acid and ligand exchange with $\text{Rh}_2(\text{OAc})_4$ to generate $\text{Rh}_2(\text{S-PTAD})_4$.^{26a}

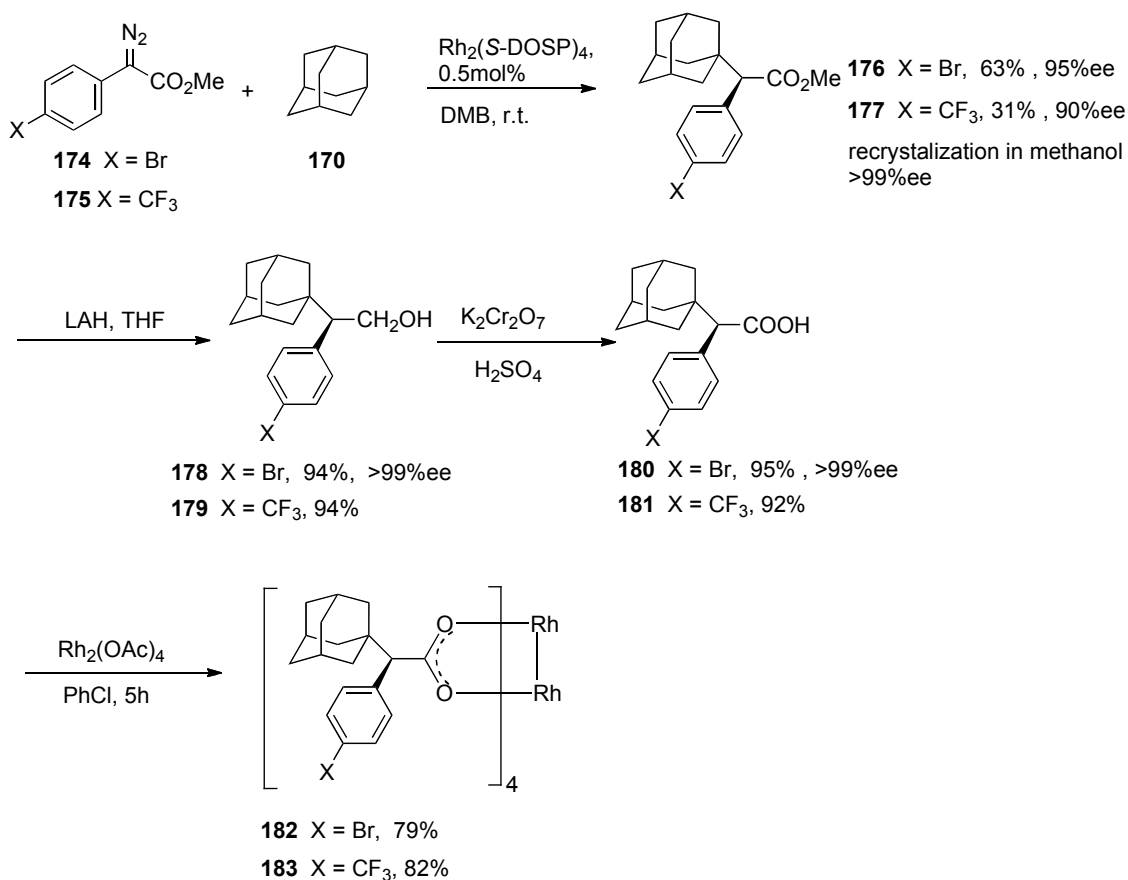
It was envisioned that the variants of $\text{Rh}_2(\text{S-PTAD})_4$ containing aryl instead of phthalimido group could be synthesized in a very concise sequence: C–H insertion, hydrolysis of the ester and ligand exchange with $\text{Rh}_2(\text{OAc})_4$ (Scheme 1.32). Besides the demonstration of Davies' highly enantioselective C–H insertion methodology and the possible benefits derived from the bulky adamantyl groups in the final dirhodium complex, the high efficiency of this sequence was very attractive.

Scheme 1.31 Synthesis of $\text{Rh}_2(\text{S-PTAD})_4$ Scheme 1.32 Proposed synthesis of the variants of $\text{Rh}_2(\text{S-PTAD})_4$ 

Dirhodium carboxylate complexes **182** and **183** containing *p*-bromophenyl and *p*-trifluoromethylphenyl as the aryl groups were chosen as the targets, and their syntheses are outlined in Scheme 1.33. $\text{Rh}_2(\text{S-DOSP})_4$ -catalyzed C–H insertion of *p*-bromophenyldiazoacetate **174** into adamantane produced **176** in 63% yield and 95% ee, its enantiomeric purity was further enriched to >99% ee by recrystallization from methanol. The (*R*) configuration of **174** was tentatively assigned according to **171**, assuming that a similar asymmetric induction occurred in the reaction. The hydrolysis of **176** with LiOH did not work well, so a two-step sequence including a LiAlH_4 -mediated reduction to convert **176** to alcohol **178** and the oxidation of alcohol **178** to carboxylic acid **180** with $\text{K}_2\text{Cr}_2\text{O}_7$ was taken. Carboxylic acid **180** was synthesized in >90% yield and >99% ee. Ligand exchange of **180** with $\text{Rh}_2(\text{OAc})_4$ produced complex **182** in 79%

yield. Complex **183** containing CF₃- on the phenyl group was also synthesized following a similar sequence.

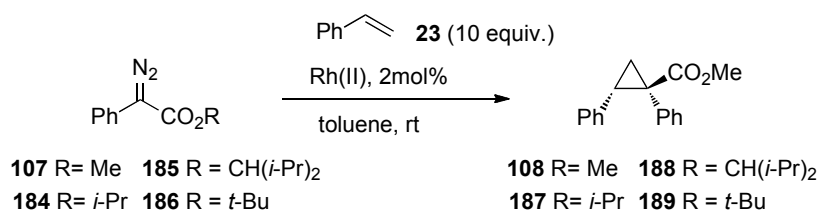
Scheme 1.33 Synthesis of Dirhodium complex **182** and **183**



The standard cyclopropanation of phenyldiazoacetate **107** and styrene with complex **182** as catalyst produced cyclopropane **108** in 69% yield with >97:3 d.r., but only 16% ee (Table 1.4, entry 1). Increasing the ester size of the phenyldiazoacetate from methyl to isopropyl and diisopropylmethyl resulted in better enantioselectivities (entry 2, 3). Further increasing the ester size to *t*-butyl caused a drastic loss of enantioselectivity, and cyclopropane **189** was formed in only 4% ee (entry 4). Complex **183** had better

asymmetric induction than complex **182**, and cyclopropane **187** could be formed in 67% ee when the reaction was conducted at -78 °C (entry 7).

Table 1.4 Cyclopropanation catalyzed by complex **182** and **183**



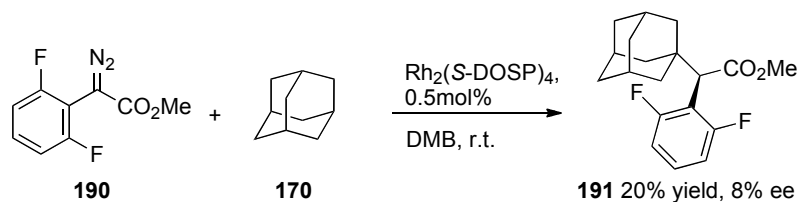
entry	R	Rh(II)	yield, %	dr ^a	ee, %
1	Me	182	69	>97:3	16
2	<i>i</i> -Pr	182	81	>97:3	34
3	CH(<i>i</i> -Pr) ₂	182	37	>97:3	47
4	<i>t</i> -Bu	182	42	>97:3	4
5	<i>i</i> -Pr	183	65	>97:3	54
6 ^b	<i>i</i> -Pr	183	65	>97:3	55
7 ^{b,c}	<i>i</i> -Pr	183	31	>97:3	67
8 ^b	CH(<i>i</i> -Pr) ₂	183	54	>97:3	53

^a Determined by the ¹H-NMR of the crude reaction mixture.

^b Hexanes used as solvent.

^c The reaction was conducted at -78 °C

Scheme 1.34 Rh₂(*S*-DOSP)₄ catalyzed C–H insertion of aryldiazoacetate **190** and adamantane



The small size of the aryl group in complexes **182** and **183** was considered to be the reason for their moderate asymmetric induction in the cyclopropanation reaction. Hence

aryldiazoacetate **190** with 2,6-difluorophenyl as the aryl group was synthesized, but the C–H insertion into adamantane produced compound **191** in only 20% yield and 8% ee (Scheme 1.34).

Recently, a comprehensive study of $\text{Rh}_2(\text{S-PTAD})_4$ catalyzed cyclopropanation reaction with a wide variety of aryldiazoacetates was carried out in the Davies group. This study showed that the interaction between the phthalimido group of the catalyst and the aryl group of the diazoacetate had dramatic effect on the enantioselectivity of the reaction. These results provide valuable insights for the re-evaluation of complexes **182** and **183**, and the further study is being carried out by other group members of the Davies group.

1.3 Conclusion

The synthesis of highly symmetric and efficient dirhodium complexes for the asymmetric transformation of donor/acceptor carbenoid was studied. Chiral dirhodium complexes containing *mono*, *di*, and *tetra* binaphthylphosphate ligands were synthesized and fully characterized. Their catalytic reactivities were evaluated by the cyclopropanation of phenyldiazoacetate and styrene, and moderate enantioselectivities were obtained. The synthesis of chiral dirhodium phosphinate complex was also attempted, but the ligand exchange with $\text{Rh}_2(\text{OAc})_4$ failed to generate the corresponding complex. The synthesis of chiral dirhodium carboxylate complex containing admantyl groups was also briefly explored, and two complexes were successfully synthesized. The evaluation of these two complexes by the cyclopropanation of phenyldiazoacetate and styrene generated cyclopropanes with up to 67% enantiomeric excess.

1.4 Experimental

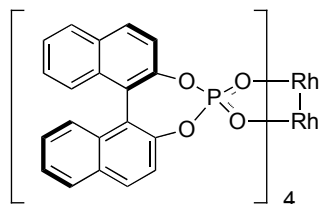
1.4.1 General Information

^1H NMR spectra were recorded on 500 MHz Varian spectrometer, and ^{13}C NMR spectra were recorded on 300 MHz Gemini spectrometer at 75 MHz with the sample solvent being CDCl_3 and reference against TMS unless otherwise noted. ^{31}P NMR spectra were recorded on 400 MHz Varian spectrometer at 162 MHz with 85% H_3PO_4 as external standard. Coupling constants were taken from the spectra directly and are uncorrected. Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were collected on a Nicolet iS10 FT-IR spectrometer as neat films. Mass spectral determinations were carried out by GC-MS (EI), LC-MS (ESI) in the Instrument Center, Department of Chemistry, SUNY University at Buffalo. Elemental analysis were performed by Atlantic Microlabs Inc., Norcross GA. Analytical TLC was performed on Whatman 0.25 mm aluminum backed silica gel (60F-254) plates using UV light and/or phosphomolybdic acid (PMA) stain for visualization. Glassware was dried in an oven (90 °C) overnight or flame dried under vacuum prior to use. Reactions were conducted under argon atmosphere unless otherwise stated. All heating was done with a silicone oil bath. Column chromatography was carried out on Merck silica gel 60 (230-400 mesh). All reaction solvents (CH_3CN , CH_2Cl_2 , hexanes, diethyl ether, THF and toluene) were dried by passing through activated A2 alumina columns (Grubbs type solvent purifier) and degassed (by bubbling argon gas through for 5-10 min) prior to use. Commercially available reagents were used without additional purification unless noted. Optical rotations were measured using a Jasco DIP-370 digital

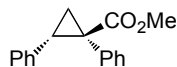
polarimeter. The 3-D modeling was carried out with Spartan software, based on the fixed dirhodium core from the X-ray structure of $\text{Rh}_2(\text{S-BNP})_4$.

1.4.2 Synthetic procedures and characterization

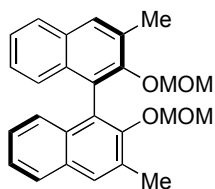
***Tetrakis*[(*R*)-1,1'-binaphthylphosphate] dirhodium ($\text{Rh}_2(\text{R-BNP})_4$ (**87**))**



Prepared by following the literature procedure.³⁷ To a 25 ml round bottom flask equipped with a Soxhlet extractor containing a 1:1 molecular sieves and Na_2CO_3 mixture, was added (*R*)-1,1'-binaphthylhydrogen phosphate (1.5 g, 4.3 mmol, 14 equiv.), $\text{Rh}_2(\text{OAc})_4$ (132 mg, 0.3 mmol) and 15 ml of chlorobenzene. The mixture was heated to reflux at 160 °C for 3 days, then solvent was distilled out. The residue was extracted with dichloromethane. After filtration, the dichloromethane solution was concentrated under vacuum to give the crude product, which was purified by flash chromatography on silica gel eluting with benzene/acetonitrile (50:1). The complex **87** was isolated as a green-yellow solid (343 mg, 72% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.87 (d, $J = 8.5$ Hz, 8H), 7.83 (d, $J = 9.0$ Hz, 8H), 7.62 (d, $J = 9.0$ Hz, 8H), 7.47-7.43 (m, 16H), 7.30 (t, $J = 8.0$ Hz, 8H); IR (neat): 1590, 1507, 1464, 1325, 1231, 1204, 1057, 964, 948, 883, 816, 750, 730 cm^{-1} ; HRMS (FAB) m/z : calcd for $\text{C}_{80}\text{H}_{48}\text{O}_{16}\text{P}_4\text{Rh}_2 \text{M}^+$, 1593.9997; found: 1594.0057. Data are consistent with the literature.

(1*R*,2*S*)-Methyl 1,2-diphenylcyclopropanecarboxylate (108)

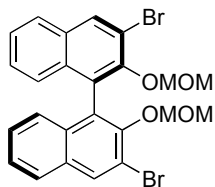
Methyl phenyldiazoacetate (**107**) (60 mg, 0.34 mmol, 1 equiv.) in 2 mL of degassed toluene was added to the solution of Rh(II) catalyst (**91**) (5.8 mg, 0.0034 mmol, 1 mol%) and styrene (0.39 mL, 3.4 mmol, 10 equiv.) in 2 mL of toluene at room temperature over 2 h. After addition, the solution was stirred for 2 h, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with hexanes/acetate (95:5) to afford cyclopropane **108** as a white solid (43 mg, 50% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.11–7.09 (m, 3H), 7.03–7.00 (m, 5H), 6.76–6.74 (m, 2H), 3.63 (s, 3H), 3.11 (dd, *J* = 9.5, 7.0 Hz, 1H), 2.13 (dd, *J* = 9.5, 5.0 Hz, 1H), 1.86 (dd, *J* = 7.0, 5.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 174.4, 136.4, 134.8, 132.0, 128.1, 127.8, 127.1, 126.4, 52.7, 37.5, 33.2, 20.6; IR (neat): 1714, 1498, 1433, 1254, 1191, 695 cm⁻¹; HRMS (APCI) *m/z*: calcd for C₁₇H₁₆O₂ [M+H]⁺: 253.12231, found: 253.12238. HPLC analysis: 26% ee, (*R*, *R*)-Whelk O1, 2.0% isopropanol/hexanes, 0.8 mL/min, UV: 254 nm, *t_R*: 10.3 min (major), 11.9 min (minor). Data are consistent with the reference.^{14d}

(*R*)-3,3'-Dimethyl-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (109)

Prepared by following the literature procedure.⁵¹ To a solution of (*R*)-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (1.0 g, 2.7 mmol) in 45 mL of diethyl ether, was

slowly added *n*-BuLi solution (1.6M in hexanes, 5.0 mL, 8.0 mmol). The mixture was stirred at room temperature for 3 h under argon. Then 30 mL of THF was added. After 1 h, the deep brown suspension was cooled to 0 °C, iodomethane (0.5 ml, 8.0 mmol) was added quickly. The reaction mixture was warmed to room temperature and stirred for 45 min. Then it was quenched with aqueous saturated NH₄Cl. The organic phase was separated, washed with brine, dried over MgSO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with hexanes/ethyl acetate (10:1) to afford **109** as a white solid (0.94 g, 87% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.81–7.79 (m, 4H), 7.38–7.35 (m, 2H), 7.22–7.19 (m, 4H), 4.60 (d, *J* = 6.0 Hz, 2H), 4.49 (d, *J* = 5.5 Hz, 2H), 2.84 (s, 6H), 2.58 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 153.2, 133.0, 131.6, 131.0, 129.8, 127.1, 126.2, 125.6, 125.4, 124.9, 98.7, 56.5, 17.9. Data are consistent with the literature.

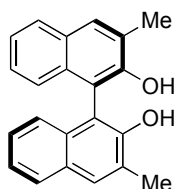
(*R*)-3,3'-Dibromo-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (110)



Prepared by following the literature procedure.⁵¹ In a 500 mL of round bottom flask, was added (*R*)-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (9.2 g, 24.5 mmol) and 420 mL of diethyl ether. *n*-BuLi (2.5 M in hexanes, 29.4 mL, 73.5 mmol) was slowly added. The solution was stirred at room temperature for 3 h. Then 270 mL of THF was added, and the mixture was stirred at room temperature for another 1 h. After cooled 0 °C, 2-dibromotetrachloroethane (23.9 g, 73.5 mmol) was added to the flask in one portion. The

solution was allowed warm to room temperature and stirred for 4 h, then quenched with aqueous saturated NH_4Cl . The solvent was removed under vacuum, the residue was extracted with diethyl ether. The combined ether solution was dried over MgSO_4 , filtered, and concentrated to give the crude, which was purified by flash chromatography on silica gel eluting with hexanes/ethyl acetate (20:1) to afford **110** as a white solid (10.4 g, 80% yield). ^1H NMR (500 MHz, CDCl_3): δ 8.27 (s, 2H), 7.80 (d, $J = 8.5$ Hz, 2H), 7.44 (t, $J = 8.0$ Hz, 2H), 7.30 (t, $J = 8.0$ Hz, 2H), 7.18 (d, $J = 8.5$ Hz, 2H), 4.82 (m, 4H), 2.56 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 150.1, 133.1, 133.0, 131.5, 127.4, 126.9, 126.5, 126.0, 117.4, 99.1, 56.3; HRMS (EI): calcd for $\text{C}_{24}\text{H}_{20}\text{O}_4\text{Br}_2 \text{M}^+$: 529.9723, found: 529.9734.

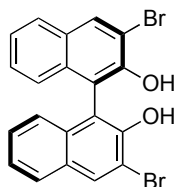
(R)-3,3'-Dimethyl-2,2'-dihydroxy-1,1'-binaphthyl (111)



Prepared by following the literature procedure.⁵¹ To a solution of (*R*)-3,3'-dimethyl-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (**109**) (0.78 g, 1.9 mmol) in THF/MeOH (1:1, 40 mL) were added Amberlyst 15 resin (1.5 g). The mixture was heated to reflux for 15 h under argon, then cooled to room temperature and filtered. The filtrate was concentrated under vacuum. The residue was purified by flash chromatography eluting with hexanes/ethyl acetate (10:1) to afford **111** as a white solid (0.59 g, 97% yield). ^1H NMR (500 MHz, CDCl_3): δ 7.81–7.80 (m, 4H), 7.32 (t, $J = 7.5$ Hz, 2H), 7.22 (t, $J = 7.0$ Hz, 2H), 7.07 (d, $J = 8.5$ Hz, 2H), 5.10 (s, 2H), 2.50 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ

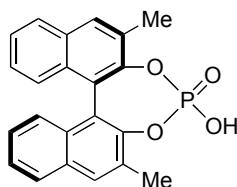
152.1, 132.1, 130.7, 129.4, 127.5, 127.0, 126.4, 124.0, 123.9, 110.5, 17.0. Data are consistent with the literature.

(*R*)-3,3'-Dibromo-2,2'-dihydroxy-1,1'-binaphthyl (112)



Prepared by following the procedure for compound **111**, using (*R*)-3,3'-dibromo-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (**110**) (1.5 g, 2.82 mmol) in THF/MeOH (1:1, 100 mL) and Amberlyst 15 resin (2.0 g). The crude material was purified by flash chromatography on silica gel eluting with hexanes/ethyl acetate (10:1) and afforded **112** as a white solid (1.24 g, 99% yield). ¹H NMR (500 MHz, CDCl₃): δ 8.25 (s, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 5.54 (s, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 148.1, 132.8, 129.8, 127.6, 127.4, 124.9, 124.6, 114.7, 112.3. Data are consistent with the literature.⁵¹

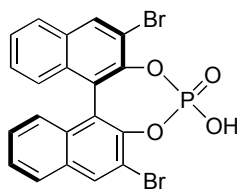
(*R*)-3,3'-Dimethyl-1,1'-binaphthylhydrogen phosphate (113)



Prepared by following the literature procedure.^{38c} To a solution of (*R*)-3,3'-dimethyl-2,2'-dihydroxy-1,1'-binaphthyl (**111**) (635 mg, 2.0 mmol) in 10 mL of pyridine, was slowly added POCl₃ (0.3 mL, 3.2 mmol). The reaction mixture was heated to 80 °C for 2.5 h,

then cooled to room temperature and 0.1 mL of water was added. The reaction mixture was reheated to 80 °C for 90 min, then cooled to room temperature and concentrated under vacuum. To this residue, was added 15 mL of 6N aqueous HCl and the mixture was heated to 80 °C for 90 min. The white precipitate was filtered, washed with water thoroughly, and dried under vacuum. Further purification on silica gel eluting with dichloromethane/methanol (4:1) afforded **113** as a white solid (518 mg, 68% yield). $[\alpha]_D^{20} -434.2^\circ$ (c 1.0, CHCl_3). $^1\text{H NMR}$ (500 MHz, $\text{MeOH-}d_4$): δ 7.89–7.86 (m, 4H), 7.39 (s, 2H), 7.14 (s, 4H), 2.62 (s, 6H); $^{13}\text{C NMR}$ (75 MHz, $\text{MeOH-}d_4$): δ 149.5 (d , $J = 9.7$ Hz), 132.6, 131.8, 130.8, 128.6, 127.7, 126.2, 125.9, 123.3, 17.9; $^{31}\text{P NMR}$ (162 MHz, $\text{MeOH-}d_4$): 3.4; IR (neat): 1504, 1414, 1260, 1238, 1208, 1181, 1148, 1089, 1016, 965, 907, 749, 732 cm^{-1} ; HRMS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{17}\text{O}_4\text{P}$ $[\text{M-H}]^-$: 375.07917, found: 375.07916.

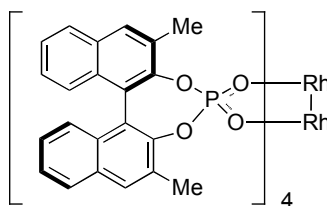
(R)-3,3'-Dibromo-1,1'-binaphthylhydrogen phosphate (114)



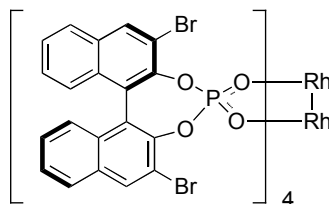
Prepared by following the procedure for compound **113**, using (*R*)-3,3'-dibromo-2,2'-dihydroxy-1,1'-binaphthyl (**112**) (1.23 g, 2.7 mmol) in 15 mL of pyridine and POCl_3 (0.42 mL, 4.5 mmol). The white precipitate was filtered, washed with water, dried under vacuum. To completely remove the small amount of pyridine impurity, this white solid was dissolved with dichloromethane, washed with 1N aqueous HCl, dried over MgSO_4 , and filtered. The solution was concentrated under vacuum to afford **114** as a white solid.

Weight: 1.33 g, 95% yield. ^1H NMR (500 MHz, $\text{CDCl}_3+\text{DMSO}-d_6$): δ 8.31 (s, 2H), 7.87 (d, $J = 8.0$ Hz, 2H), 7.48 (t, $J = 7.5$ Hz, 2H), 7.29 (t, $J = 7.5$ Hz, 2H), 7.22 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (75 MHz, $\text{CDCl}_3+\text{DMSO}-d_6$): δ 149.9 (d, $J = 9.7$ Hz, C), 133.2 (CH), 131.4 (C), 131.0 (C), 127.1 (CH), 126.6 (CH), 126.4 (CH), 126.1 (CH), 122.8 (C), 114.5 (d, $J = 3.4$ Hz, C); ^{31}P NMR (162 MHz, $\text{CDCl}_3+\text{DMSO}-d_6$): δ 2.2; MS (ESI) m/z : 503, 505, 507 ($[\text{M}-\text{H}]^-$, intensity: 1:2:1).

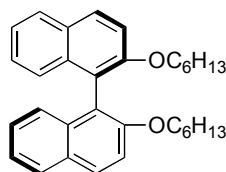
***Tetrakis*[(*R*)-3,3'-dimethyl-1,1'-binaphthylphosphate] dirhodium (**91**)**



Prepared by following the procedure for compound **87**, using $\text{Rh}_2(\text{OAc})_4$ (31 mg, 0.07 mmol), (*R*)-3,3'-dimethyl-1,1'-binaphthylhydrogen phosphate (**113**) (376 mg, 1 mmol), and 7 mL of chlorobenzene. The mixture was heated at 150–160 °C for 3 days, then the solvent was distilled out. The residue was dissolved with diethyl ether and passed through a short silica gel column. The green band was collected and concentrated. The residue was further purified on silica gel eluting with dichloromethane/diethyl ether (10:1) to afford **91** as a green solid (65 mg, 54% yield). ^1H NMR (500 MHz, CDCl_3): δ 7.76 (d, $J = 8.5$ Hz, 8H), 7.61 (s, 8H), 7.36 (t, $J = 7.5$ Hz, 8H), 7.18 (d, $J = 8.5$ Hz, 8H), 7.72 (t, $J = 8.0$ Hz, 8H), 2.24 (s, 24H); ^{13}C NMR (75 MHz, CDCl_3): δ 147.2 (m), 131.4, 131.1, 130.9, 130.0, 127.4, 127.1, 125.1, 125.0, 121.4, 17.7; ^{31}P NMR (162 MHz, CDCl_3): δ 20.8; MS (FAB): 1706 (M^+ , 100%), 1331 ($[\text{M}-\text{L}]^+$, 42%), 956 ($[\text{M}-2\text{L}]^+$, 45%).

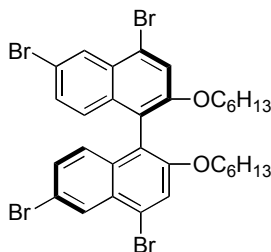
Tetrakis[(*R*)-3,3'-dibromo-1,1'-binaphthylphosphate] dirhodium (115)

Prepared by following the procedure for compound **87**, using $\text{Rh}_2(\text{OAc})_4$ (105 mg, 0.23 mmol), (*R*)-3,3'-dibromo-1,1'-dinaphthylhydrogen phosphate (**114**) (0.96 g, 1.9 mmol), and 20 mL of chlorobenzene. The mixture was heated to 150-160 °C for 3 days. Then it was passed through a short dry silica gel column, and washed with hexanes, dichloromethane, and diethyl ether. The diethyl ether solution was collected and concentrated. The residue was separated by flash chromatography on silica gel eluting with benzene/acetonitrile (30:1). The first green band was collected, and concentrated under vacuum to afford **115** as a yellow-green solid (61 mg, 12% yield). $[\alpha]_{\text{D}}^{25} -190.9^\circ$ (c 0.18, CHCl_3). ^1H NMR (500 MHz, CDCl_3): δ 8.09 (s, 8H), 7.74 (d, $J = 8.5$ Hz, 8H), 7.40 (t, $J = 7.5$ Hz, 8H), 7.18 (t, $J = 7.0$ Hz, 8H), 7.11 (d, $J = 8.5$ Hz, 8H); ^{13}C NMR (75 MHz, CDCl_3): δ 144.6 (d, $J = 4.5$ Hz), 133.5, 131.6, 131.1, 127.2, 127.0, 126.4, 126.1, 122.7, 115.2; ^{31}P NMR (162 MHz, CDCl_3): δ 21.5; IR (neat): 1396, 1239, 1214, 1065(s), 976, 749 cm^{-1} ; MS (FAB) m/z : 2225 (M^+).

(*R*)-2,2'-Dihexyloxy-1,1'-binaphthyl (117)

Prepared by following the literature procedure.⁵² To a solution of (*R*)-BINOL (6.04 g, 21 mmol) and 1-bromohexane (12 mL, 105 mmol) in acetonitrile (100 mL) was added K₂CO₃ (15 g, 105 mmol) at room temperature. The mixture was heated to reflux for 16 h. After cooled to room temperature, water was added and the mixture was extracted with hexanes. Combined hexane solution was washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with hexanes/ethyl acetate (50:1 to 20:1) to afford **117** as slight yellow oil (9.58 g, quantitative). ¹H NMR (500 MHz, CDCl₃): δ 7.90 (d, *J* = 9.0 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 9.0 Hz, 2H), 7.30–7.26 (m, 2H), 7.20–7.14 (m, 4H), 3.95–3.87 (m, 4H), 1.41–1.34 (m, 4H), 1.06–0.88 (m, 12H), 0.73 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 154.5, 134.2, 129.3, 129.0, 127.7, 126.0, 125.5, 123.3, 120.8, 115.9, 69.8, 31.3, 29.3, 25.3, 22.4, 13.9. Data are consistent with the literature.

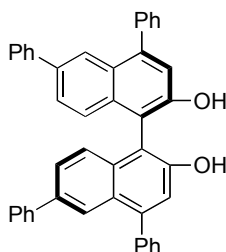
(*R*)-4,4'-6,6'-Tetrabromo-2,2'-hexyloxy-1,1'-binaphthyl (118)



Prepared by following the literature procedure.⁵² To a solution of (*R*)-2,2'-dihexyloxy-1,1'-binaphthyl (**117**) (9.5 g, 21 mmol) in 200 mL of acetic acid in a 500 mL round bottom flask was added bromine (11 mL, 214 mmol) over 30 min at room temperature. The resulting solution was stirred at room temperature for 6 h, then cooled to 0 °C. Aqueous 25% NaHSO₃ solution (100 mL) was added to quench the excess bromine. The

mixture was extracted with ethyl acetate. Combined acetate solution was washed with brine, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with hexanes/ ethyl acetate (100:1) and afforded **118** as slight yellow oil (13.7 g, 85% yield). ^1H NMR (500 MHz, CDCl_3): δ 8.39 (d, $J = 2.0$ Hz, 2H), 7.70 (s, 2H), 7.31 (dd, $J = 9.0, 2.0$ Hz, 2H), 6.96 (d, $J = 8.5$ Hz, 2H), 3.97–3.87 (m, 4H), 1.43–1.38 (m, 4H), 1.09–0.90 (m, 12H), 0.74 (t, $J = 7.0$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 154.4, 133.1, 130.5, 129.3, 128.8, 127.3, 122.4, 120.3, 119.2, 119.2, 69.8, 31.2, 29.0, 25.3, 22.4, 13.8. Data are consistent with the literature.

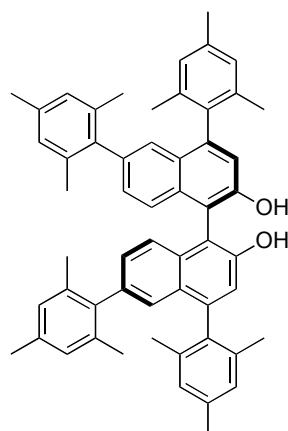
(*R*)-4,4'-6,6'-Tetraphenyl-2,2'-dihydroxy-1,1'-binaphthyl (119)



Prepared by following the literature procedure.⁵² To a solution of (*R*)-4,4',6,6'-tetrabromo-2,2'-hexyloxy-1,1'-binaphthyl (**118**) (1.58 g, 2.05 mmol) and phenylboronic acid (1.25 g, 10.25 mmol) in 40 mL of THF, was added $\text{Pd}(\text{PPh}_3)_4$ (284 mg, 12 mol%) and aqueous K_2CO_3 (2M, 24 mL). The mixture was degassed with argon for 10 min, then heated to reflux for 48 h. After cooling down to room temperature, it was poured into a mixture of ethyl acetate and water. The aqueous layer was extracted with ethyl acetate. Combined acetate solution was washed with brine, dried over Na_2SO_4 , and concentrated under vacuum. The residue was dissolved in 40 mL of dichloromethane and cooled to -78 °C, BBR_3 (1M in DCM, 6 mL) was slowly added. The reaction mixture was then warmed

to room temperature and stirred for 24 h. Water was added to quench the reaction. The aqueous layer was extracted with dichloromethane. Combined dichloromethane solution was washed with brine, dried over Na_2SO_4 and concentrated to give the crude product, which was purified by flash chromatography on silica gel eluting with hexane/ethyl acetate (5:1) to afford **119** as pale foamy solid (1.09 g, 90% yield). ^1H NMR (500 MHz, CDCl_3): δ 8.18 (s, 2H), 7.67–7.30 (m, 26H), 5.23 (br., 2H); ^{13}C NMR (75 MHz, CDCl_3): δ 152.3, 144.2, 141.0, 139.8, 137.0, 133.2, 129.9, 128.8, 128.5, 128.2, 127.8, 127.3, 127.2, 127.1, 125.3, 124.8, 119.2, 110.4. Data are consistent with the literature.

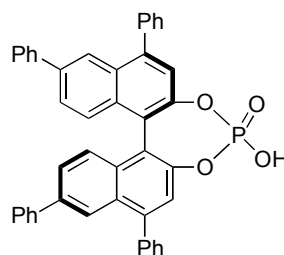
(R)-4,4'-6,6'-Tetra(2,4,6-trimethylphenyl)-2,2'-dihydroxy-1,1'-binaphthyl (120)



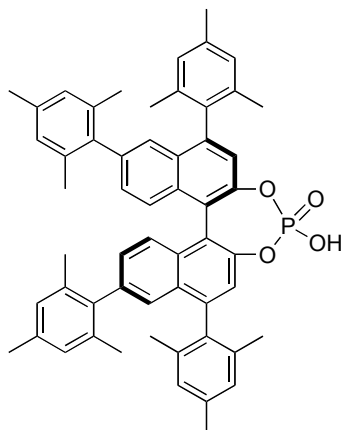
Prepared by following the procedure for compound **119**, using (*R*)-4,4',6,6'-tetrabromo-2,2'-hexyloxy-1,1'-binaphthyl (**118**) (1.56 g, 2.02 mmol), 2,4,6-trimethylphenylboronic acid (2.00 g, 12.12 mmol), $\text{Pd}(\text{PPh}_3)_4$ (284 mg, 12 mol%), and aqueous K_2CO_3 (2M, 24 mL). The mixture was heated to reflux for 3 days. The crude product after the deprotection with BBr_3 was purified by flash chromatography on silica gel eluting with hexane/ethyl acetate (10:1) to afford **120** as a white solid (1.30 g, 85% yield). $[\alpha]_D^{20}$ -23.2° (*c* 0.1, CHCl_3). ^1H NMR (500 MHz, CDCl_3): δ 7.44(s, 1H), 7.42 (s, 1H), 7.26 (s,

2H), 7.22 (d, $J = 1.5$ Hz, 2H), 7.20 (d, $J = 1.5$ Hz, 1H), 7.19 (d, $J = 1.5$ Hz, 1H), 6.98 (s, 4H), 6.90 (d, $J = 4.0$ Hz, 4H), 5.23 (s, 2H), 2.35 (s, 6H), 2.29 (s, 6H), 2.03 (s, 12H), 1.97 (s, 6H), 1.96 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 152.4, 142.9, 138.8, 137.1, 136.7, 136.6, 136.5, 136.4, 136.2, 136.2, 135.9, 132.4, 129.5, 128.5, 128.3, 128.1, 126.5, 124.5, 118.6, 110.0, 21.1, 20.9, 20.9, 20.4, 20.3; IR (neat): 3536, 2918, 1612, 1592, 1480, 1376, 1194, 1175, 1138, 850 cm^{-1} ; HRMS (EI) m/z : calcd. for $\text{C}_{56}\text{H}_{54}\text{O}_2$ M^+ : 758.4118, found: 758.4106.

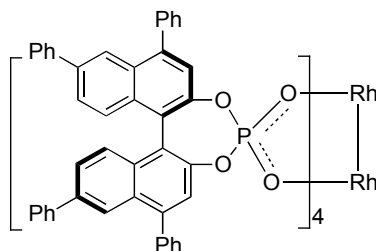
(*R*)-4,4'-6,6'-Tetraphenyl-1,1'-binaphthylhydrogen phosphate (121)



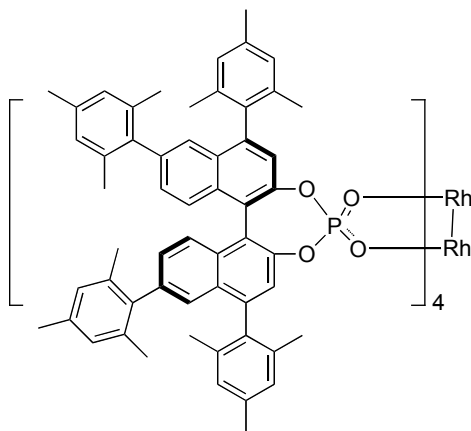
Prepared by following the procedure for compound **113**, using (*R*)-4,4',6,6'-tetraphenyl-2,2'-dihydroxy-1,1'-binaphthyl (**119**) (0.83 g, 1.4 mmol) in 7 mL of pyridine, and POCl_3 (0.21 mL, 2.2 mmol). The white precipitate was filtered, washed with water, and dried under vacuum. Yield: 0.84 g, 92% yield. ^1H NMR (500 MHz, $\text{DMSO}-d_6$): δ 8.14 (s, 2H), 7.79 (dd, $J = 9.0, 1.5$ Hz, 2H), 7.70 (m, 4H), 7.64–7.53 (m, 12H), 7.47–7.43 (m, 6H), 7.35 (t, $J = 7.0$ Hz, 2H); ^{31}P NMR (162 MHz, $\text{DMSO}-d_6$): δ 3.0; MS (ESI) m/z : 651 ($[\text{M}-\text{H}]^-$, 100%). Data are consistent with the literature.^{38c}

(R)-4,4'-6,6'-(2,4,6-Trimethylphenyl)-1,1'-binaphthylhydrogen phosphate (122)

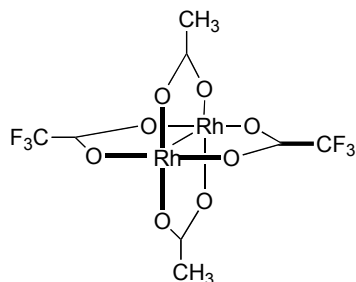
Prepared by following the procedure for compound **113**, using (*R*)-4,4',6,6'-(2,4,6-trimethylphenyl)-2,2'-dihydroxy-1,1'-binaphthyl (**120**) (1.0 g, 1.4 mmol) in 7 mL of pyridine, and POCl₃ (0.19 mL, 2.1 mmol). The white precipitate was filtered, washed with water, and dried under vacuum. Yield: 1.07 g, 96%. $[\alpha]_{\text{D}}^{20}$ -23.2° (*c* 1.1, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.41 (s, 2H), 7.28 (s, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.93 (s, 2H), 6.91 (s, 4H), 6.89 (s, 2H), 2.31 (s, 6H), 2.29 (s, 6H), 2.00 (s, 6H), 1.99 (s, 6H), 1.92 (s, 6H), 1.88 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 147.7 (d, *J* = 9.1 Hz), 142.9, 139.1, 138.6, 137.6, 137.3, 137.3, 136.2, 136.6, 136.5, 135.9, 132.0, 131.1, 128.9, 128.7, 128.6, 128.2, 126.7, 122.5, 121.0, 21.6, 21.5, 21.3, 21.3, 20.9, 20.8; ³¹P NMR (162 MHz, CDCl₃): δ 4.4; IR (neat): 2918, 1612, 1574, 1480, 1442, 1020, 968, 851 cm⁻¹; HRMS (ESI) *m/z*: calcd for C₅₆H₅₃O₄P M⁺: 820.36870, found: 820.36884.

Tetrakis-[(*R*)-4,4'-6,6'-tetraphenyl-1,1'-binaphthylphosphate] dirhodium (92**)**

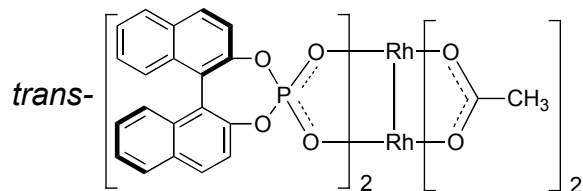
Prepared by following the procedure for compound **87**, using $\text{Rh}_2(\text{OAc})_4$ (25 mg, 0.05 mmol) and (*R*)-4,4',6,6'-tetraphenyl-1,1'-binaphthylhydrogen phosphate (**121**) (262 mg, 0.40 mmol), and 7 mL of chlorobenzene. The mixture was heated to 150-160 °C for 5 h, then all of the solvent was distilled out. The residue was purified with 50-70% of dichloromethane in petroleum ether on a silica gel column. The blue band was collected and concentrated. Further purification using the same condition to afford **92** as a blue-green solid (37 mg, 34%). $[\alpha]_D^{20} -38.9^\circ$ (*c* 0.19, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3): 8.21 (d, $J = 8.2$ Hz, 8H), 7.72 (d, $J = 8.0$ Hz, 8H), 7.52–7.70 (m, 32H), 7.50 (d, $J = 8.0$ Hz, 8H), 7.39–7.47 (m, 24H), 7.29–7.39 (m, 24H), 7.10 (d, $J = 7.0$ Hz, 8H); $^{31}\text{P NMR}$ (162 MHz, CDCl_3): 17.3; IR (neat): 1587, 1570, 1363, 1342, 1212, 1152, 1059, 974, 897, 758, 698 cm^{-1} ; MS (FAB) m/z : 2812 (M^+). Data are consistent with the literature.^{38c}

Tetrakis-[(*R*)-4,4'-6,6'-(2,4,6-trimethylphenyl)-1,1'-binaphthylphosphate]**dirhodium (123)**

Prepared by following the procedure for compound **87**, using $\text{Rh}_2(\text{OAc})_4$ (25 mg, 0.05 mmol), (*R*)-4,4',6,6'-(2,4,6-trimethylphenyl)-1,1'-binaphthylhydrogen phosphate (**122**) (328 mg, 0.4 mmol), and 10 mL of chlorobenzene. The mixture was heated to 150-160 °C for 2 days. The solvent was distilled out, and the resulting residue was dissolved with dichloromethane, passed a short silica column, the first blue band was collected and concentrated under vacuum. The residue was further purified on silica gel with 20-40% dichloromethane in hexanes to afford **123** as a blue-green solid (57 mg, 33% yield). $[\alpha]_D^{20} +119.2^\circ$ (c 0.21, CHCl_3). ^1H NMR (500 MHz, CDCl_3): δ 7.51 (m, 8H), 7.34 (s, 8H), 7.12 (s, 4H), 7.08 (s, 4H), 7.00 (m, 8H), 6.87 (s, 20H), 6.79 (s, 4H), 6.74 (s, 4H), 6.72 (s, 4H), 2.27 (s, 24H), 2.19 (s, 12H), 2.17 (s, 12H), 1.95–1.90 (m, 60H), 1.79–1.75 (m, 36H); ^{31}P NMR (162 MHz, CDCl_3): 18.4; IR (neat): 1611, 1573, 1478, 1450, 1210, 1185, 1057, 969, 906, 849, 729 cm^{-1} ; MA (FAB) m/z : 3485 (M^+).

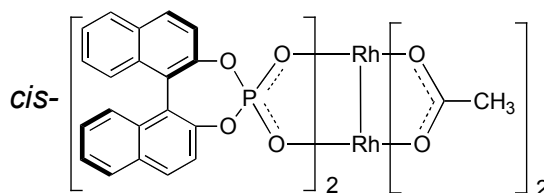
***Trans*-Rh₂(OAc)₂(TFA)₂ (**129**)**

Prepared by following the literature procedure.⁴³ Rh₂(TFA)₄ (270 mg, 0.41 mmol) was dissolved with 6 mL of acetonitrile in a 25 mL round bottom flask under argon. The solution was cooled to 0 °C and *n*-tetrabutylammonium acetate (250 mg, 0.82 mmol) was added in one portion. The solution was stirred for 15 min and the solvent was removed under vacuum. The residue was separated by flash chromatography on silica gel eluting with dichloromethane/acetonitrile (98:2). The first purple band was collected and concentrated to afford **129** as purple solid (106 mg, 47% yield). *R_f* 0.51 (10% acetonitrile/benzene). ¹H NMR (500 MHz, CDCl₃): δ 2.45 (s, the coordinated acetonitrile), 1.99 (s, 6H); ¹⁹F NMR (376 MHz, CDCl₃): δ -74.1; MS (ECI, reaction gas: isobutane) *m/z*: 550.7 ([M+H]⁺, 100%), 591.7 ([M+CH₃CN]⁺, 26%), 606.7 ([M+C₄H₁₀+H]⁺, 46%). Data are consistent with the literature.

***Trans*-Rh₂(OAc)₂(*R*-BNP)₂ (**131**)**

$\text{Rh}_2(\text{R-BNP})_4$ (**87**) (70 mg, 0.044 mmol) and *n*-tetrabutylammonium acetate (26 mg, 0.088 mmol) were dissolved with 3 mL of dichloromethane at room temperature under argon. The solution was stirred for 7 h, then concentrated under vacuum. The residue was separated by flash chromatography on silica gel eluting with benzene/acetonitrile (50:1 to 10:1). The first green band was the unreacted $\text{Rh}_2(\text{R-BNP})_4$, the second green band was collected and concentrated to afford **131** as a green solid (6 mg, 14% yield). R_f 0.11 (benzene/ CH_3CN 10:1). $[\alpha]_D^{20} +18.5^\circ$ (c 0.1, CHCl_3). ^1H NMR (500 MHz, CD_2Cl_2): δ 8.03 (d, $J = 8.5$ Hz, 4H), 7.96 (d, $J = 8.0$ Hz, 4H), 7.48 (t, $J = 7.5$ Hz, 4H), 7.42 (d, $J = 9.0$ Hz, 4H), 7.35-7.28 (m, 8H), 2.22 (s, 6H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 194.6 (C), 147.7 (m, C), 132.6 (C), 132.1 (C), 131.4 (CH), 128.8 (CH), 127.3 (CH), 127.0 (CH), 126.0 (CH), 121.8 (C), 120.7 (CH), 24.7 (CH_3); ^{31}P NMR (162 MHz, CD_2Cl_2): 18.1; IR (neat): 1557, 1508, 1464, 1412, 1231, 1193, 1060, 946, 948, 884 cm^{-1} ; MS (FAB) m/z : 1018.3 (M^+ , 100%), 959.1 ($[\text{M-OAc}]^+$, 41%), 670.9 ($[\text{M-BNP}]^+$, 31%); HRMS (FAB) m/z : calcd for $\text{C}_{44}\text{H}_{30}\text{O}_{12}\text{P}_2\text{Rh}_2$ M^+ : 1017.9317, found: 1017.9302.

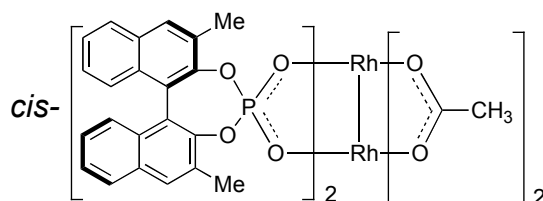
***Cis*- $\text{Rh}_2(\text{OAc})_2(\text{R-BNP})_2$ (**132**)**



In a 25 ml round bottom flask equipped with a short-path distillation apparatus, was added (*R*)-BNP (0.1 g, 0.28 mmol, 2.0 equiv.), $\text{Rh}_2(\text{OAc})_4$ (63 mg, 0.14 mmol) and 10 mL of chlorobenzene. The solution was heated to 160 °C to distill out chlorobenzene. At the same time, new chlorobenzene was added into the flask to maintain the same amount

of chlorobenzene in the flask. This process was kept going for 1.5 h, then all the chlorobenzene was distilled out. The residue was dissolved with dichloromethane, and passed through a short silica gel column to remove the unreacted ligand. The filtrate was concentrated under vacuum and the residue was separated by flash chromatography on silica gel eluting with benzene/acetonitrile (50:3). The third green band was collected and concentrated to afford **132** as a green solid (72 mg, 49% yield). $[\alpha]_D^{20}$ -107.2° (c 0.1, CHCl_3). ^1H NMR (500 MHz, CD_2Cl_2): δ 8.05 (d, $J = 8.5$ Hz, 2H), 7.98 (d, $J = 8.5$ Hz, 2H), 7.88–7.84 (m, 4H), 7.51–7.25 (m, 16H), 2.16 (s, 6H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 193.9 (C), 148.1 (C, d, $J = 9.7$ Hz), 147.92 (d, $J = 9.7$ Hz, C), 132.7 (C), 132.6 (C), 132.1 (C), 132.1 (C), 131.3 (CH), 131.2 (CH), 128.8 (CH), 128.8 (CH), 127.3 (CH), 127.3 (CH), 126.9 (CH), 126.8 (CH), 126.0 (CH), 125.9 (CH), 122.0 (C, d, $J = 2.2$ Hz), 121.9 (C, d, $J = 1.7$ Hz), 121.5 (CH, d, $J = 2.8$ Hz), 120.9 (CH, d, $J = 2.2$ Hz), 23.2 (CH_3); ^{31}P NMR (162 MHz, CD_2Cl_2): 17.1; IR (neat): 1557, 1508, 1421, 1232, 1086, 1061, 964, 947, 881 cm^{-1} ; MS (FAB) m/z : 1018.4 (M^+ , 100%), 959.2 ($[\text{M}-\text{OAc}]^+$, 17%), 670.8 ($[\text{M}-\text{BNP}]^+$, 45%); HRMS (FAB) m/z : calcd. for $\text{C}_{44}\text{H}_{30}\text{O}_{12}\text{P}_2\text{Rh}_2$ M^+ : 1017.9317, found: 1017.9351.

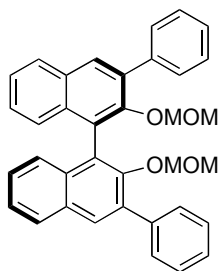
***Cis*-bis(*R*)-3,3'-dimethyl-1,1'-binaphthylphosphate]diacetate dirhodium (**133**)**



Prepared by following the procedure for compound **132**, using $\text{Rh}_2(\text{OAc})_4$ (66 mg, 0.15 mmol) and (*R*)-3,3'-dimethyl-1,1'-binaphthylhydrogen phosphate (**113**) (113 mg, 0.30

mmol, 2 equiv.). The crude material was separated by flash chromatography on silica gel eluting with benzene/acetonitrile (10:1 to 7:1). The third blue band was collected and concentrated to afford **133** as a green solid (72 mg, 45% yield). $[\alpha]_D^{20}$ -35.6° (*c* 0.11, CHCl₃). ¹H NMR (600 MHz, CDCl₃): δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.79 (s, 2H), 7.69 (s, 2H), 2.48 (s, 12H), 2.09 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 193.4, 147.2 (d, *J* = 9.4 Hz), 147.1 (d, *J* = 9.1 Hz), 131.8, 131.7, 131.4, 131.3, 130.6 (d, *J* = 2.6 Hz), 130.4, 130.0 (d, *J* = 2.6 Hz), 127.7, 127.6, 127.3, 127.1, 125.5, 121.9 (d, *J* = 2.3 Hz), 121.8 (d, *J* = 2.2 Hz), 23.3, 18.1, 17.3; ³¹P NMR (162 MHz, CDCl₃): δ 19.3; IR (neat): 1557, 1416, 1240, 1085, 1064, 1045, 926, 875, 749, 731 cm⁻¹; HRMS (APCI) *m/z*: calcd for C₄₈H₃₈O₁₂P₂Rh₂ [M+H]⁺: 1075.00214, found: 1075.01840.

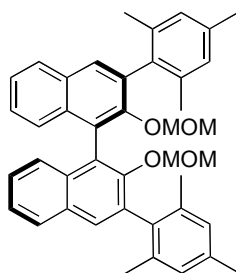
(*R*)-(+)- 3,3'-Diphenyl-2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (134)



Prepared by following the literature procedure.⁵¹ To a solution of (*R*)-3,3'-dibromo-2,2'-bis(methoxymethoxy)-1,1'-dinaphthyl (**8**) (1.0 g, 1.88 mmol) in 13 mL of degassed dimethoxyethane, were added phenylboronic acid (0.8 g, 6.58 mmol), aqueous Na₂CO₃ (2M, 5 mL, 9.78 mmol), and Pd(PPh₃)₄ (0.22 g, 0.19 mmol). The reaction mixture was heated to reflux for 24 h under argon. Then it was cooled to room temperature, and concentrated under vacuum. The residue was extracted with dichloromethane, and the combined dichloromethane solution was washed with brine, dried over MgSO₄, and

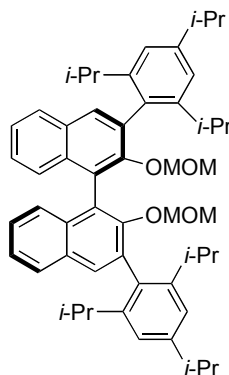
concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with hexanes/ethyl acetate (95:5) to afford **134** as a white solid (0.92 g, 93% yield). ^1H NMR (500 MHz, CDCl_3): δ 7.95 (s, 2H), 7.89 (d, $J = 7.5$ Hz, 2H), 7.76 (m, 4H), 7.47 (t, $J = 8.0$ Hz, 4H), 7.37–7.47 (m, 4H), 7.28–7.29 (m, 4H), 4.40 (d, $J = 6.0$ Hz, 2H), 4.37 (d, $J = 6.0$ Hz, 2H), 2.34 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 151.3, 139.0, 135.5, 133.6, 130.8, 130.5, 129.6, 128.3, 127.8, 127.3, 126.5, 126.4, 126.3, 125.1, 98.5, 55.8; HRMS (EI) m/z : calcd for $\text{C}_{36}\text{H}_{30}\text{O}_4$ M^+ : 526.2139, found: 526.2139. Data are consistent with the literature.

(R) -3,3'-Bis(2,4,6-trimethylphenyl)-2,2'-bis(methoxymethoxy)-1,1-dinaphthyl (135)

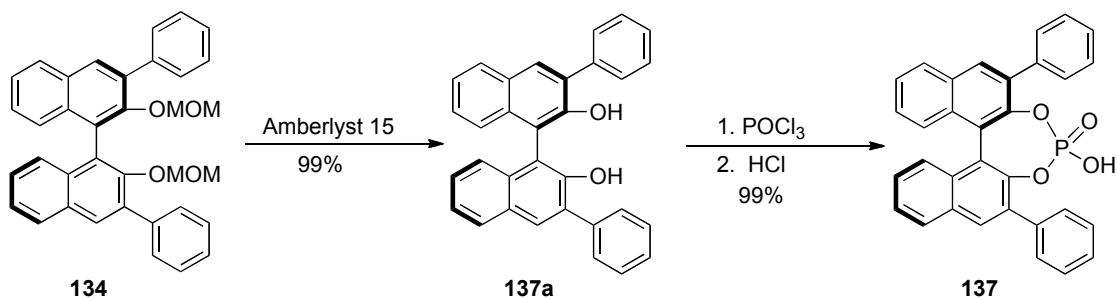


Preparation of the Grignard reagent: In a flame-dry 25 mL round bottom flask equipped with a condenser, was added magnesium (0.33 g, 13.6 mmol). 2-bromomesitylene (1.5 g, 7.5 mmol) was dissolved with 8 mL of diethyl ether and 2 mL of this solution was added to the flask. After 5 min, 0.05 mL of 1,2-dibromoethane was added to the flask, the reaction was initiated and began to reflux. The remaining 2-bromomesitylene ether solution was slowly added. The mixture was heated to reflux for 24 h, and cooled to room temperature.

The coupling reaction: In a 100 mL of round bottom flask was added $\text{Ni}(\text{PPh}_3)_2\text{Cl}_2$ (170 mg, 0.24 mmol), (*R*)-3,3'-dibromo-2,2'-bis(methoxymethoxy)-1,1-dinaphthyl (**110**) (1.0 g, 1.8 mmol), and 25 mL of diethyl ether. The mesitylmagnesium bromide solution was slowly added to the flask. The reaction mixture was stirred at room temperature for 10 min, then heated to reflux for 24 h. After cooled to room temperature, it was quenched with saturated NH_4Cl and extracted with diethyl ether. The ether solution was dried over MgSO_4 , filtered, and concentrated under vacuum. The residue was purified by flash chromatography eluting with hexanes/diethyl ether (30:1) to afford **135** as a white solid (0.46 g, 40% yield). $[\alpha]_D^{20} -6.5^\circ$ (*c* 1.1, CHCl_3). ^1H NMR (500 MHz, CDCl_3): δ 7.83 (d, $J = 8.0$ Hz, 2H), 7.72 (s, 2H), 7.39 (t, $J = 7.5$ Hz, 2H), 7.36–7.27 (m, 4H), 6.97 (s, 2H), 6.96 (s, 2H), 4.31 (d, $J = 6.0$ Hz, 2H), 4.28 (d, $J = 6.0$ Hz, 2H), 2.32 (s, 6H), 2.30 (s, 6H), 2.22 (s, 6H), 2.15 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 151.9 (C), 137.1 (C), 136.8 (C), 136.6 (C), 135.5 (C), 134.6 (C), 133.6 (C), 130.8 (C), 130.7 (CH), 128.0 (CH), 127.7 (CH), 126.3 (C), 126.2 (CH), 126.1 (CH), 124.9 (CH), 97.9 (CH_2), 55.5 (CH_3), 21.1 (CH_3), 20.9 (CH_3), 20.6 (CH_3); IR (neat): 1156, 998, 973, 733 cm^{-1} ; HRMS (EI) m/z : calcd for $\text{C}_{42}\text{H}_{42}\text{O}_4$: 610.3078, found: 610.3093.

(R)-3,3'-Bis(2,4,6-triisopropylphenyl)-2,2'-bis(methoxymethoxy)-1,1-dinaphthyl**(136)**

Prepared by following the procedure for compound **135**. Magnesium (0.78 g, 32 mmol) and 2,4,6-triisopropylphenyl bromide (5.0 g, 17 mmol) were used to prepare the corresponding Grignard reagent. Ni(PPh₃)₂Cl₂ (340 mg, 0.51 mmol) and (*R*)-3,3'-dibromo-2,2'-bis(methoxymethoxy)-1,1-dinaphthyl (**110**) (2.0 g, 3.7 mmol) were used during the coupling reaction with the Grignard reagent. The crude was purified by flash chromatography on silica gel eluting with hexane/ether (50:1) to afford **136** as a foamy white solid (2.63 g, 90% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.83 (d, *J* = 7.5 Hz, 2H), 7.78 (s, 2H), 7.38–7.43 (m, 4H), 7.29–7.32 (m, 2H), 7.09 (s, 2H), 7.06 (s, 2H), 4.22 (s, 4H), 2.80–2.95 (m, 6H), 2.25 (s, 6H), 1.18–1.29 (m, 30H), 1.00 (d, *J* = 6.5 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 152.3, 148.3, 147.4, 146.9, 134.2, 133.6, 133.2, 131.0, 130.4, 127.8, 126.2, 126.0, 125.9, 124.8, 120.7, 120.5, 97.6, 55.1, 34.3, 31.0, 30.8, 25.8, 25.3, 24.1, 23.2, 23.1; HRMS (ESI) *m/z*: calcd for C₅₄H₆₆O₄ [M+Na]⁺: 801.4853, found: 801.4842.

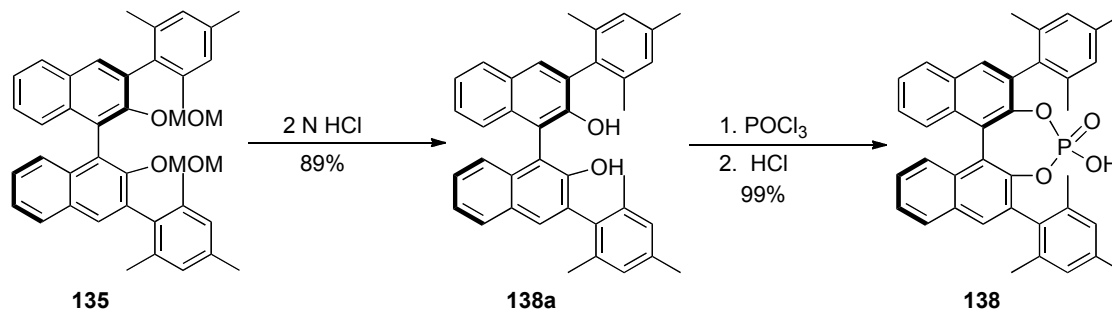
(R)- 3,3'-Diphenyl -1,1'-dinaphthylhydrogen phosphate (137)

Diol **137a** was prepared by following the literature procedure.⁵⁰ To a solution of (*R*)-(+)-3,3'-diphenyl -2,2'-bis(methoxymethoxy)-1,1'-binaphthyl (**134**) (0.91 g, 1.73 mmol) in 28 mL of THF/MeOH (1:1) were added Amberlyst 15 resin (1.0 g). The mixture was heated to reflux for 15 h under argon, then cooled to room temperature and filtered. The filtrate was concentrated under vacuum. The residue was purified by flash chromatography eluting with hexanes/ethyl acetate (10:1) to afford diol **137a** as a white solid (0.76 g, 99%). ¹H NMR (500 MHz, CDCl₃): δ 8.00 (s, 2H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 7.5 Hz, 4H), 7.47 (t, *J* = 7.5 Hz, 4H), 7.36–7.41 (m, 4H), 7.29–7.32 (m, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 5.34 (s, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 150.1, 137.5, 133.0, 131.3, 130.7, 129.6, 129.4, 128.4, 127.7, 127.3, 124.3, 124.2, 112.4.

Phosphoric acid **137** was prepared by following the procedure for compound **113**, using diol **137a** (887 mg, 2.0 mmol) in 10 mL of pyridine and POCl₃ (0.3 mL, 3.2 mmol). The white precipitate was filtered and washed with water. Then it was dissolved with dichloromethane, washed with 1N aqueous HCl to completely remove pyridine, dried over Na₂SO₄, filtered, and concentrated under vacuum to afford **137** as a pale solid (1.0 g, 99% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.98 (s, 2H), 7.94 (d, *J* = 8.0 Hz, 2H), 7.58

(d, $J = 7.0$ Hz, 4H), 7.49 (t, $J = 7.0$ Hz, 2H), 7.37 (d, $J = 8.5$ Hz, 2H), 7.30 (t, $J = 7.5$ Hz, 2H), 7.24 (t, $J = 7.5$ Hz, 4H), 7.16 (t, $J = 7.5$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3): δ 144.9 (d, $J = 9.0$ Hz), 137.1, 134.1 (d, $J = 2.8$ Hz), 132.1, 131.4, 131.2, 129.8, 128.3, 128.1, 127.3, 127.0, 126.3, 125.7, 122.7; ^{31}P NMR (162 MHz, CDCl_3): δ 2.5; IR (neat): 1498, 1410, 1269, 1245, 1181, 1151, 1020, 961, 894, 765, 750, 699 cm^{-1} ; HRMS (ESI) m/z : calcd for $\text{C}_{32}\text{H}_{21}\text{O}_4\text{P}^+$: 500.11830, found: 500.11832.

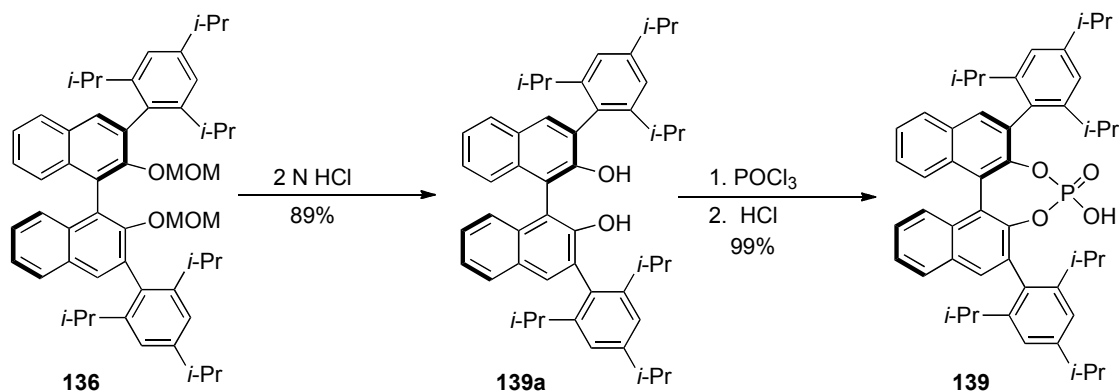
(*R*)- 3,3'- Bis(2,4,6-trimethylphenyl)-1,1'-dinaphthylhydrogen phosphate (138)



In a 100 ml RB flask, was added (*R*)-3,3'-bis(2,4,6-trimethylphenyl)-2,2'-bis(methoxymethoxy)-1,1'-dinaphthyl (**135**) (0.44 g, 0.73 mmol), 7 mL of 2N HCl ether solution, and 7 mL of methanol. The solution was heated to reflux for 12 h. After cooled to room temperature, saturated aqueous NaHCO_3 was carefully added to neutralize the solution. The solvent was removed under vacuum. The residue was extracted with diethyl ether, and the ether solution was washed with brine, dried over Na_2SO_4 , and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with hexanes/diethyl ether (20:1) to afford diol **138a** as a foamy solid (0.34 g, 89% yield). $[\alpha]_D^{20} +34.8^\circ$ (c 1.3, CHCl_3). ^1H NMR (500 MHz, CDCl_3): δ 7.87 (d, $J = 8.0$ Hz, 2H), 7.74 (s, 2H), 7.38 (t, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 2H), 7.24 (m, 2H),

7.00 (s, 4H), 4.99 (s, 2H), 2.34 (s, 6H), 2.14 (s, 6H), 2.07 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 150.0 (C), 137.7 (C), 137.1 (C), 137.1 (C), 133.4 (C), 132.9 (C), 130.6 (CH), 129.4 (C), 128.5 (CH), 128.4 (CH), 128.2 (CH), 126.8 (CH), 124.5 (CH), 123.8 (CH), 112.9 (C), 21.1 (CH_3), 20.5 (CH_3), 20.4 (CH_3); IR (neat): 3525, 1437, 1259, 1234, 908, 733 cm^{-1} ; HRMS (EI) m/z : calcd for $\text{C}_{38}\text{H}_{34}\text{O}_2 \text{M}^+$: 522.2553, found: 522.2558.

Phosphoric acid **138** was prepared by following the procedure for compound **113**, using diol **138a** (325 mg, 0.62 mmol) in 5 mL of pyridine and POCl_3 (0.09 mL, 0.93 mmol). The white precipitate was filtered and washed with water. Then it was dissolved with diethyl ether, washed with 1N aqueous HCl to completely remove pyridine, and dried over Na_2SO_4 . After filtration, the solution was concentrated under vacuum to afford **138** as a white solid (360 mg, 99% yield). ^1H NMR (500 MHz, CDCl_3): δ 7.92 (d, $J = 8.5$ Hz, 2H), 7.79 (s, 2H), 7.50 (t, $J = 7.5$ Hz, 2H), 7.39–7.30 (m, 4H), 6.79 (s, 2H), 6.76 (s, 2H), 2.10 (s, 6H), 2.06 (s, 6H), 1.96 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 145.3 (C, $J = 9.2$ Hz), 137.1 (C), 136.9 (C), 136.8 (C), 132.9 (C), 132.9 (C, $J = 2.8$ Hz), 131.9 (C), 131.7 (CH), 131.5 (C), 128.3 (CH), 128.2 (CH), 127.7 (CH), 127.1 (CH), 126.3 (CH), 125.7 (CH), 122.2 (C, $J = 2.2$ Hz), 20.9 (CH_3), 20.9 (CH_3), 20.3 (CH_3); ^{31}P NMR (162 MHz, CDCl_3): δ 2.8; IR (neat): 1279, 1194, 1024, 908, 752, 733 cm^{-1} ; MS (ESI) m/z : 585 ($[\text{M}+\text{H}]^+$, 100%).

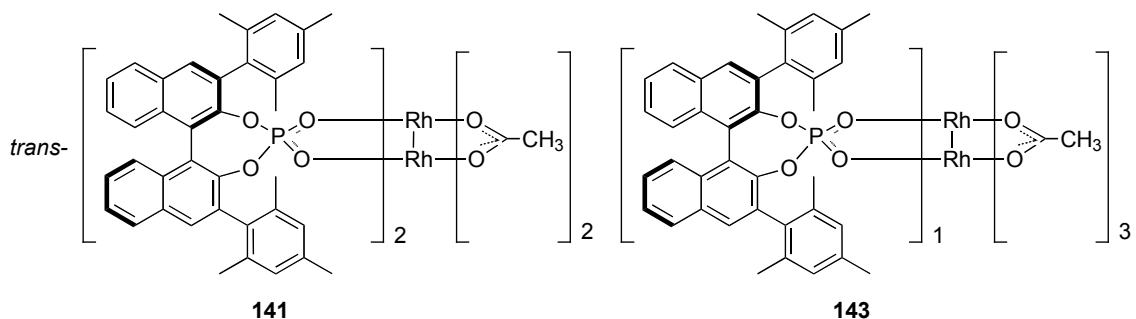
(R)-3,3'-Bis(2,4,6-triisopropylphenyl)-1,1'-dinaphthylhydrogen phosphate (139)

Diol **139a** was prepared by following the procedure for diol **138a**, using (*R*)-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-bis(methoxymethoxy)-1,1-dinaphthyl (**136**) (2.62 g, 3.37 mmol), 30 mL of 2N HCl ether solution, and 30 mL of methanol. The crude product was purified by flash chromatography on silica gel eluting with hexanes/diethyl ether (40:1) to afford diol **139a** as a foamy solid (2.30 g, 99% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.76 (s, 2H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.31–7.28 (m, 4H), 7.14 (s, 2H), 7.12 (s, 2H), 4.92 (s, 2H), 2.97–2.94 (m, 2H), 2.86–2.83 (m, 2H), 2.70–2.67 (m, 2H), 1.31 (d, *J* = 7.0 Hz, 12H), 1.18 (d, *J* = 7.0 Hz, 6H), 1.10–1.08 (m, 12H), 1.02 (d, *J* = 6.5 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 150.6, 149.1, 147.8, 147.7, 133.4, 130.6, 130.4, 129.1, 129.0, 128.2, 126.6, 124.5, 123.8, 121.2, 121.2, 113.1, 34.3, 30.9, 30.8, 24.3, 24.3, 24.0, 23.9, 23.9, 23.7. Data are consistent with the literature.⁵³

Phosphoric acid **139** was prepared by following the procedure for compound **113**, using diol **139a** (1.38 g, 2.0 mmol) in 10 mL of pyridine, and POCl₃ (0.3 mL, 3.2 mmol). The white precipitate was filtered, washed with water, and dried under vacuum to afford **139** (1.48 g, 99% yield). [α]_D²⁰ –33.1° (*c* 0.38, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.88

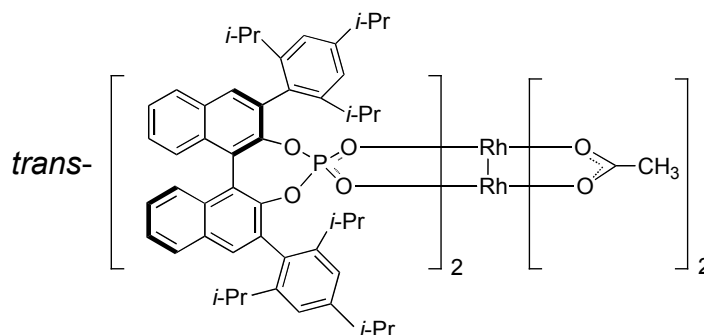
(d, $J = 7.5$ Hz, 2H), 7.79 (s, 2H), 7.49–7.46 (m, 2H), 7.31–7.28 (m, 4H), 6.92 (s, 4H), , 2.82–2.79 (m, 2H), 2.62–2.58 (m, 4H), 1.20 (d, $J = 7.0$ Hz, 12H), 1.02–0.98 (m, 12H), 0.90 (d, $J = 7.0$ Hz, 6H), 0.80 (d, $J = 5.5$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 147.9, 147.3, 146.4 (d, $J = 9.6$ Hz), 141.3, 132.5, 132.4, 131.8, 130.8, 128.0, 127.3, 126.4, 126.0, 125.3, 122.2, 121.0, 120.1, 34.1, 30.8, 30.7, 26.1, 24.9, 24.0, 23.9, 23.3, 23.2; ^{31}P NMR (162 MHz, CDCl_3): δ 2.4; IR (neat): 2960, 1606, 1460, 1411, 1362, 1241, 1197, 1020, 997, 970, 904, 750, 732 cm^{-1} ; MS (ESI) m/z : 751 ($[\text{M}-\text{H}]^-$, 100%); HRMS (ESI) m/z : calcd for $\text{C}_{50}\text{H}_{57}\text{O}_4\text{P}$ M^+ : 752.40000, found: 752.39901.

***Trans*[(*R*)- 3,3'-bis(2,4,6-trimethylphenyl)-1,1'-binaphthyl phosphate] diacetate dirhodium (141) and *Mono*[(*R*)- 3,3'-bis(2,4,6-trimethylphenyl)-1,1'-binaphthyl phosphate] triacetate dirhodium (143)**



Prepared by following the procedure for compound **87**, using $\text{Rh}_2(\text{OAc})_4$ (69 mg, 0.15 mmol), (*R*)-3,3'-bis(2,4,6-trimethyl-phenyl)-1,1'-binaphthylhydrogen phosphate (**138**) (182 mg, 0.30 mmol), and 6 mL of chlorobenzene. The mixture was heated to 150-160 °C for 2 days. Then chlorobenzene was distilled out. The residue was further purified on silica gel eluting with hexanes/diethyl ether (3:1 to 1:2). The first green band was collected and concentrated under vacuum to afford **141** as a green solid (51 mg, 22%

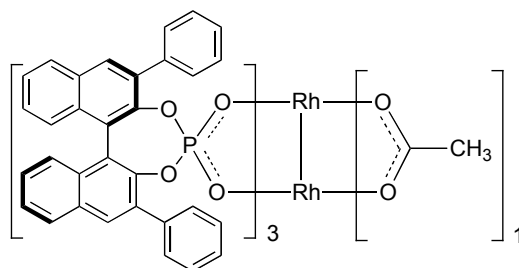
yield). The second green band was collected and concentrated under vacuum to afford **143** as a green solid (60 mg, 40% yield). Compound **141**: $[\alpha]_D^{20} +220.1^\circ$ (*c* 0.11, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.80 (d, *J* = 8.5 Hz, 4H), 7.59 (s, 4H), 7.39 (t, *J* = 7.5 Hz, 4H), 7.19 (t, *J* = 7.5 Hz, 4H), 7.09 (d, *J* = 9.0 Hz, 4H), 6.99 (s, 4H), 6.72 (s, 4H), 2.37 (s, 12H), 2.23 (s, 12H), 1.79 (s, 12H), 0.97 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 193.1 (C), 145.7 (C), 137.1 (C), 136.7 (C), 136.6 (C), 133.8 (C), 132.6 (C), 132.1 (C), 131.5 (CH), 131.2 (C), 128.5 (CH), 127.8 (CH), 127.6 (CH), 126.7 (CH), 126.2 (CH), 125.4 (CH), 122.2 (C), 22.0 (CH₃), 21.7 (CH₃), 21.1 (CH₃), 20.2 (CH₃); ³¹P NMR: (162 MHz, CDCl₃): δ 17.9; IR (neat): 1557, 1434, 1411, 1068, 974, 909, 731 cm⁻¹; HRMS (APCI) *m/z*: calcd for C₈₀H₇₀O₁₂P₂Rh₂ [M+H]⁺: 1491.25254, found: 1491.27799. Compound **143**: $[\alpha]_D^{20} +160.8^\circ$ (*c* 0.08, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.63 (s, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.15 (d, *J* = 7.5 Hz, 2H), 7.07 (s, 2H), 6.77 (s, 2H), 2.37 (s, 6H), 2.28 (s, 6H), 1.88 (s, 3H), 1.86 (s, 6H), 1.43 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 192.2 (C), 191.4 (C), 145.6 (d, *J*_{C-P} = 9.7 Hz, C), 137.3 (C), 136.7 (C), 134.1 (C), 132.6 (C), 132.1 (C), 131.7 (CH), 131.3 (C), 128.6 (CH), 127.9 (CH), 127.6 (CH), 126.8 (CH), 126.3 (CH), 125.5 (CH), 122.4 (C), 22.9 (CH₃), 22.4 (CH₃), 21.7 (CH₃), 21.1 (CH₃), 20.3 (CH₃); ³¹P NMR: (162 MHz, CDCl₃): δ 16.9; IR (neat): 1573, 1415, 1083, 910, 731 cm⁻¹; MS (FAB) *m/z*: 966 (M⁺, 17%), 907 ([M-OAc]⁺, 100%).

Trans*-bis[(*R*)-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthylphosphate]*diacetate dirhodium (142)**

Prepared by following the procedure for compound **87**, using $\text{Rh}_2(\text{OAc})_4$ (88 mg, 0.2 mmol), (*R*)-3,3'-bis(2,4,6-triisopropyl-phenyl)-1,1'-binaphthylhydrogen phosphate (**139**) (376 mg, 0.5 mmol), and 10 mL of chlorobenzene. The mixture was heated to 150-160 °C for 2 days. Then chlorobenzene was distilled out. The residue was dissolved with dichloromethane, passed through a short silica column, the green band was collected and concentrated under vacuum. The residue was further purified on silica gel eluting with hexanes/ ether (5:1) to afford **142** as a brown solid (141 mg, 38% yield). $[\alpha]_D^{25} +220.3^\circ$ (*c* 0.2, CHCl_3). ^1H NMR (500 MHz, CDCl_3): δ 7.80 (d, $J = 8.5\text{Hz}$, 4H), 7.71 (s, 4H), 7.40 (t, $J = 8.0\text{ Hz}$, 4H), 7.20 (t, $J = 7.0\text{ Hz}$, 4H), 7.15 (s, 4H), 7.09 (d, $J = 8.5\text{ Hz}$, 4H), 6.88 (s, 4H), 2.87–2.84 (m, 4H), 2.75–2.73 (m, 4H), 2.52–2.49 (m, 4H), 1.70 (d, $J = 6.5\text{ Hz}$, 12H), 1.24 (d, $J = 7.0\text{ Hz}$, 36H), 0.97 (d, $J = 6.5\text{ Hz}$, 12H), 0.92 (s, 6H), 0.84 (d, $J = 7.0\text{ Hz}$, 12H); ^{13}C NMR (75 MHz, CDCl_3): δ 192.2, 147.8, 147.8, 146.2, 133.1, 132.5, 132.0, 131.7, 130.6, 127.8, 127.0, 126.0, 125.4, 122.1, 121.7, 120.2, 34.2, 30.8, 30.6, 26.4, 24.9, 24.6, 24.1, 23.7, 23.5, 23.0; ^{31}P NMR (162MHz, CDCl_3): δ 17.8; IR (neat): 1557, 1415, 1215, 1192, 1064(s), 974, 889, 753 cm^{-1} ; MS (FAB) m/z : 1827 (M^+ , 16%), 767 ([M-

OAc]⁺, 26%), 1707 ([M-2OAc]⁺, 100%); HRMS (+ESI) m/z: calcd for C₁₀₄H₁₁₈O₁₂P₂Rh₂ [M+K]⁺: 1865.58402, found 1865.59037.

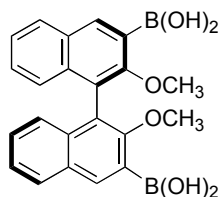
Tris-[(*R*)-3,3'-diphenyl-binaphthylphosphate] monoacetate dirhodium (144)



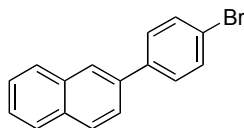
Prepared by following the procedure for compound **87**, using Rh₂(OAc)₄ (88 mg, 0.2 mmol), (*R*)-3,3'-diphenyl -1,1'-dinaphthylhydrogen phosphate (**137**) (275 mg, 0.5 mmol, 2.5 equiv.), and 10 mL of chlorobenzene. The mixture was heated to 150-160 °C for 1.5 days. After cooled to room temperature, it was passed through a short dry silica gel column, washed with hexanes, 60% dichloromethane/hexanes and dichloromethane (100%). The blue band washed down by pure dichloromethane was collected and concentrated. The residue was further purified by flash chromatography on silica gel column eluting with benzene/acetonitrile (50:1) to afford **144** as a blue-green solid (40 mg, 12% yield). $[\alpha]_D^{20} -160.4^\circ$ (*c* 0.18, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 8.05–7.99 (m, 8H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.76 (s, 2H), 7.52–7.16 (m, 36H), 6.51 (t, *J* = 7.5 Hz, 4H), 6.44 (t, *J* = 7.5 Hz, 4H), 6.14 (t, *J* = 7.0 Hz, 2H), 6.07 (t, *J* = 7.5 Hz, 2H), 1.12 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 151.9, 145.4 (d, *J* = 9.7 Hz), 144.9 (d, *J* = 9.7 Hz), 144.7 (d, *J* = 9.7 Hz), 137.3, 137.2, 136.9, 135.0, 135.0, 134.0, 132.1, 132.0, 131.8, 131.5, 131.4, 131.4, 131.3, 129.5, 129.4, 128.4, 128.1, 128.1, 128.0, 127.8, 127.6, 127.2, 126.9, 126.9, 126.7, 126.6, 126.2, 125.9, 125.9, 125.6, 123.6, 123.5, 123.0, 22.2; ³¹P

NMR (162 MHz, CDCl₃) δ 21.2, 19.3; IR (neat): 3056, 3013, 1498, 1413, 1060, 972, 750 cm⁻¹; MS (FAB) m/z : 1763 (M⁺, 100%), 1703 ([M-OAc]⁺, 35%), 1263 ([M-L]⁺, 57%), 1203 ([M-OAc-L]⁺, 88%); HRMS (+ESI) m/z : calcd for C₉₈H₆₃O₁₄P₃Rh₂ [M+K]⁺: 1801.11724, found 1801.13411.

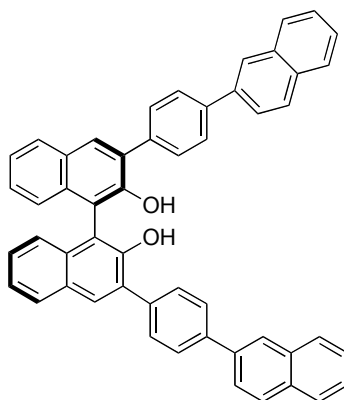
(R)-3,3'-Bis(dihydroxyborane)-2,2'-dimethoxy-1,1'-binaphthyl (145)



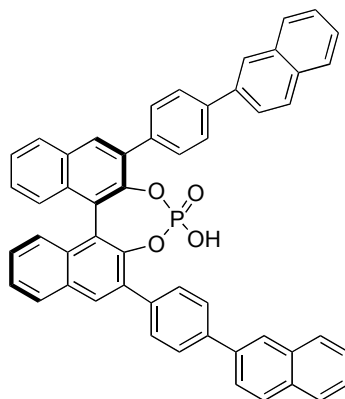
Prepared by following the literature procedure.⁵⁴ To a solution of TMEDA (4.42 mL, 29 mmol) in 150 mL of diethyl ether was added *n*-BuLi (2.5M in hexanes, 11.7 mL, 29 mmol) at room temperature. The solution was stirred for 30 min, solid (*R*)-2,2'-dimethoxy-1,1'-dinaphthyl (3.05 g, 9.7 mmol) was added in one portion, and the reaction mixture was stirred for 3 h. The resulting light brown suspension was cooled to -78 °C, and triethyl borate (11.6 mL, 68 mmol) was slowly added over 10 min. The solution was allowed to warm to room temperature and stirred overnight. Then it was cooled to 0 °C, aqueous 1M HCl (75 mL) was added and the mixture was stirred for 4 h at room temperature. The ether layer was separated, washed (aqueous 1N HCl, brine), dried over Na₂SO₄, and concentrated under vacuum to give the crude product as a pale yellow solid, which was further recrystallized in toluene to afford **145** as a white solid (1.40 g, 36% yield). ¹H NMR (500 MHz, CDCl₃): δ 8.62 (s, 2H), 7.99 (d, J = 8.0 Hz, 2H), 7.44(d, J = 7.5 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.5 Hz, 2H), 6.19 (s, 4H), 3.31 (s, 6H). Data are consistent with the lieterature.

2-(4'-Bromophenyl)naphthalene (146)

Prepared by following the literature procedure.⁵⁴ In a 100 mL round bottom flask, was added 2-naphthylboronic acid (1.55 g, 9.0 mmol), Ba(OH)₂·8H₂O (8.95 g, 28.3 mmol), Pd(PPh₃)₄ (219 mg, 0.19 mmol), 1-bromo-4-iodobenzene (3.21 g, 11.3 mmol), and 40 mL of degassed dioxane/H₂O (3:1) solution. The mixture was heated to reflux for 24 h under argon. Then it was cooled to room temperature and concentrated under vacuum. The residue was extracted with dichloromethane. The dichloromethane solution was washed with 1M aqueous HCl, brine, dried over Na₂SO₄, then concentrated under vacuum to give the crude product which was purified by flash chromatography on silica gel eluting with hexanes to afford **146** (1.49 g, 58% Yield). ¹H NMR (500 MHz, CDCl₃): δ 7.99 (s, 1H), 7.91–7.85 (m, 3H), 7.68 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.61–7.56 (m, 4H), 7.52–7.47 (m, 2H). Data are consistent with the lieterature.

(*R*)-3,3'-Bis(4-naphthalen-2-yl-phenyl)-1,1'-binaphthyl-2,2'-diol (147)

Prepared by following the literature procedure.⁵⁴ To a solution of (*R*)-3,3'-Bis(dihydroxyborane)-2,2'-dimethoxy-1,1-dinaphthyl (**145**) (437 mg, 1.09 mmol) in 8 mL of degassed dioxane/H₂O (3:1) solution was added 2-(4'-bromophenyl)naphthalene (**146**) (925 mg, 3.27 mmol), Ba(OH)₂·8H₂O (1.03 g, 3.27 mmol), and Pd(PPh₃)₄ (138 mg, 0.12 mmol). The reaction mixture was heated to reflux for 40 h under argon, then cooled to room temperature. The solvent was removed under vacuum, and the residue was extracted with dichloromethane. The dichloromethane solution was washed with 1M aqueous HCl, brine, dried over Na₂SO₄, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate to give the coupling product. To a solution of the coupling product in dichloromethane (20 mL) was added BBr₃ (1M in CH₂Cl₂, 2.45 ml, 2.45 mmol) at 0 °C, then it was warmed to room temperature and stirred for 24 h. The mixture was poured into a mixture of dichloromethane/water. The organic layer was separated, washed with brine, dried over anhydrous Na₂CO₃, and concentrated under vacuum. The crude product was further purified by flash chromatography on silica gel eluting with hexanes/ dichloromethane (3:1 to 3:2) to afford **147** as a white solid (602 mg, 80% yield). [α]_D²⁰ -158.6° (*c* 1.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 8.12 (s, 4H), 7.97–7.81 (m, 18H), 7.53–7.48 (m, 4H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 5.44 (s, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 150.3, 140.5, 138.0, 136.5, 133.7, 132.9, 132.7, 131.4, 130.3, 130.1, 129.5, 128.5, 128.2, 127.6, 127.4, 126.3, 126.0, 125.8, 125.5, 124.4, 124.3, 112.4. Data are consistent with the literature.

(R)-3,3'-Bis(4-naphthalen-2-yl-phenyl)-1,1'-binaphthylhydrogen phosphate (148)

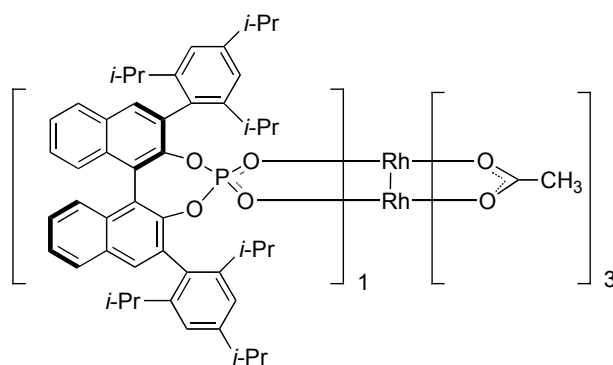
Prepared by following the procedure for compound **113**, using (*R*)-3,3'-Bis(4-naphthalen-2-yl-phenyl)-1,1'-binaphthyl-2,2'-diol (**147**) (345 mg, 0.5 mmol) in 2.5 mL of pyridine, and POCl₃ (0.07 mL, 0.8 mmol). The white precipitate was filtered, and washed with water. Then it was dissolved with dichloromethane, washed with aqueous 1N HCl, dried over Na₂SO₄, filtered, and concentrated under vacuum to afford **148** (371mg, 99% yield). ¹H NMR (500 MHz, DMSO-*d*₆): δ 8.34 (s, 2H), 8.27 (s, 2H), 8.15 (d, *J* = 8.5 Hz, 2H), 8.05–8.01 (m, 8H), 7.97–7.94 (m, 8H), 7.56–7.51 (m, 6H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 145.5 (d, *J* = 9.6 Hz), 138.9, 136.9, 136.4, 133.4, 133.2, 133.2, 132.3, 131.5, 130.9, 130.7, 130.5, 128.7, 128.5, 128.2, 127.4, 126.7, 126.6, 126.4, 126.1, 126.0, 125.6, 125.2, 124.9, 122.4; ³¹P NMR (162 MHz, DMSO-*d*₆): δ 1.5.

Rh₂(OAc)₃(TFA) (149)

n-Tetrabutylammonium acetate (1.14 g, 3.78 mmol, 2.2 equiv.) was added to Rh₂(TFA)₄ (1.12 g, 1.7 mmol) solution in 22 mL of acetonitrile at 0 °C. After 15 min, the solution was concentrated under vacuum. The residue was separated by flash chromatography on

silica gel eluting with dichloromethane/acetonitrile (98:2 to 90:10). Concentration of the third purple band afforded **149** as a purple solid (0.42 g, 49% yield). ^1H NMR: (500 MHz, CDCl_3): δ 1.98 (s, 6H), 1.97 (s, 3H); ^{13}C NMR (75 MHz, acetone- d_6): δ 191.4, 22.9, 22.8; ^{19}F NMR (376 MHz, CDCl_3): δ -74.1; IR (neat): 1638, 1560, 1433, 1197, 1160, 864, 712, 697, 617 cm^{-1} ; HRMS (FAB) m/z : calcd for $\text{C}_8\text{H}_9\text{O}_8\text{F}_3\text{Rh}_2$ M^+ : 495.8354, found: 495.8331.

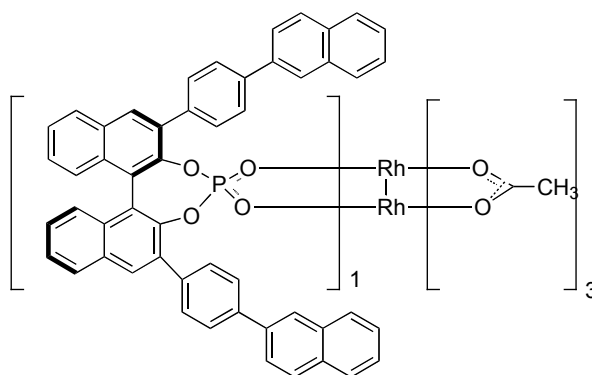
***Mono*[(*R*)-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'-binaphthylphosphate] triacetate dirhodium (**150**)**



In a 25 mL round bottom flask equipped with Soxhlet extractor filled with 1:1 Na_2CO_3 and molecular sieves, was added $\text{Rh}_2(\text{OAc})_3(\text{TFA})$ (**149**) (58 mg, 0.1 mmol), (*R*)-3,3'-Bis(2,4,6-triisopropylphenyl)-1,1'-binaphthylhydrogen phosphate (**139**) (75 mg, 0.1 mmol), and 5 mL of 1,2-dichloroethane. The mixture was heated to 110-120 $^\circ\text{C}$ for 1.5 days. Then the solvent was distilled out. The residue was dissolved with dichloromethane, passed through a short silica column, washed with dichloromethane and diethyl ether. The ether solution was collected and concentrated under vacuum. The residue was further purified on silica gel eluting with dichloromethane/diethyl ether (10:1) to afford **150** as a green solid (15 mg, 13% yield). ^1H NMR (500 MHz, CDCl_3): δ

7.81 (d, $J = 8.5$ Hz, 2H), 7.65 (s, 2H), 7.41(t, $J = 7.5$ Hz, 2H), 7.20–7.17 (m, 4H), 6.94–6.91 (m, 4H), 2.97–2.94 (m, 2H), 2.89–2.85 (m, 2H), 2.68–2.64 (m, 2H), 1.86 (s, 3H), 1.44 (d, $J = 6.0$ Hz, 6H), 1.33 (d, $J = 7.0$ Hz, 6H), 1.25–1.23 (m, 12H), 1.19–1.09 (m, 12H), 0.84 (d, $J = 7.0$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 192.4, 148.2, 147.9, 147.3, 146.3 (d, $J = 9.1$ Hz), 133.9, 132.8, 132.7, 131.7, 131.6, 130.5, 127.8, 127.0, 126.2, 125.4, 122.0, 120.6, 34.0, 31.3, 30.6, 25.9, 24.8, 24.1, 23.9, 23.8, 23.1, 22.6; ^{31}P NMR (162 MHz, CDCl_3): δ 15.2; IR (neat): 1567, 1415, 1073, 750 cm^{-1} ; MS (FAB) m/z : 1075 ($[\text{M-OAc}]^+$, 82%).

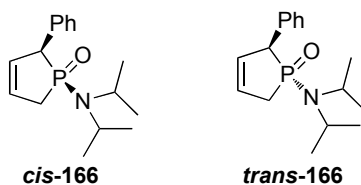
***Mono*[(*R*)-3,3'-Bis(4-naphthalen-2-yl-phenyl)-1,1'-binaphthylphosphate] triacetate dirhodium (151)**



Prepared by following the procedure for compound **151**, using $\text{Rh}_2(\text{OAc})_3(\text{TFA})$ (**149**) (58 mg, 0.1 mmol), (*R*)-3,3'-bis(4-naphthalen-2-yl-phenyl)-1,1'-binaphthylhydrogen phosphate (**148**) (75 mg, 0.1 mmol), and 6 mL of 1,2-dichloroethane. The mixture was heated to 120 °C for 3 days. Then it was concentrated under vacuum. The residue was separated by flash chromatography on silica gel eluting with dichloromethane/diethyl ether (20:1). The first green band was collected, concentrated, and further purified on

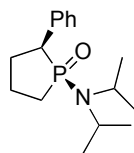
silica gel eluting with benzene/acetonitrile (10:1) to afford **151** as a green solid (18 mg, 16% yield). $[\alpha]_D^{20} -82.6^\circ$ (c 0.10, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 8.08 (s, 2H), 7.93 (s, 2H), 7.90–7.84 (m, 12H), 7.80–7.76 (m, 6H), 7.51–7.44 (m, 6H), 7.22 (s, 4H), 1.86 (s, 3H), 1.37 (s, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 192.4, 191.9, 145.0 (d, $J = 9.6$ Hz), 139.7, 138.0, 136.8, 133.7, 132.7, 132.1, 132.0, 131.1, 130.4, 128.5, 128.3, 128.2, 128.0, 127.6, 127.4, 127.1, 126.4, 126.3, 125.9, 125.8, 125.6, 125.4, 122.8, 23.3, 22.6; $^{31}\text{P NMR}$ (162 MHz, CDCl_3): δ 16.1; IR (neat): 1570, 1419, 1075, 747 cm^{-1} ; HRMS (FAB) m/z : calcd for $\text{C}_{58}\text{H}_{41}\text{O}_{10}\text{PRh}_2 \text{M}^+$: 1134.0542, found: 1134.0575.

1-[(*N,N*)-Diisopropylamino]-1-oxo-2-phenylphosphol-3-ene (**166**)

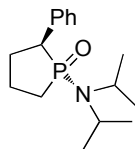


Prepared by following the literature procedure.⁴⁶ *N*-diisopropylphosphamidous dichloride (2.02 g, 10 mmol) was added to a stirred suspension of AlCl_3 (1.27 g, 9.5 mmol) in 15 mL of dichloromethane at room temperature under argon. After 45 min, the clear yellow solution was cooled to 0 °C, and (*E*)-1-phenyl-butadiene solution (1.17 g in 40 mL of dichloromethane) was slowly added. The reaction mixture was stirred at 0 °C for 24 h, then poured into a mixture of 40 mL of aqueous EDTA (0.2 M) and 20 mL of aqueous saturated NaHCO_3 solution. The biphasic mixture was stirred vigorously for 4 h at 0 °C, then filtered with a celite pad. The dichloromethane layer was separated, washed with saturated NaHCO_3 , 1M HCl, and brine, then dried over Na_2SO_4 , concentrated under vacuum to give the crude product as light yellow oil. Purification by flash

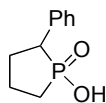
chromotography on silica gel (ethyl acetate/ethanol: 50:1 to 50:3) afforded **cis-166** (1.46 g, 53% yield) and **trans-166** (0.69 g, 25% yield). **cis-166**: light yellow solid. ^1H NMR (500 MHz, CDCl_3): δ 7.32–7.20 (m, 5H), 6.18 (d, $J = 30.0$ Hz, 2H), 4.10 (d, $J = 21.0$ Hz, 1H), 3.04–2.96 (m, 2H), 2.72–2.54 (m, 2H), 1.05 (d, $J = 7.0$ Hz, 6H), 0.78 (d, $J = 7.0$ Hz, 6H); ^{13}C NMR: (75 MHz, CDCl_3): δ 136.3 (d, $J = 5.7$ Hz, C), 131.5 (d, $J = 18.0$ Hz, CH), 128.1 (d, $J = 2.8$ Hz, CH), 127.7 (d, $J = 4.0$ Hz, CH), 127.3 (d, $J = 12.5$ Hz, CH), 126.2 (d, $J = 2.8$ Hz, CH), 51.5 (d, $J = 79.0$ Hz, CH), 46.0 (d, $J = 3.4$ Hz, CH), 31.8 (d, $J = 77.0$ Hz, CH_2), 23.0 (d, $J = 2.0$ Hz, CH_3), 22.7 (d, $J = 2.0$ Hz, CH_3); ^{31}P NMR: (162 MHz, CDCl_3): δ 64.3; IR (neat): 1493, 1451, 1403, 1366, 1229, 1206, 1154, 992, 882, 765, 691, 639 cm^{-1} ; HRMS (APCI) m/z : calcd for $\text{C}_{16}\text{H}_{24}\text{NOP}$ $[\text{M}+\text{H}]^+$: 278.16683, found: 278.16688. **trans-166**: light yellow solid. M.p.: 66–67 $^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3): δ 7.33–7.17 (m, 5H), 6.17–5.95 (m, 2H), 3.68 (d, $J = 10.0$ Hz, 1H), 3.39–3.31 (m, 2H), 2.62–2.45 (m, 2H), 1.27 (d, $J = 7.0$ Hz, 6H), 1.24 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 135.8 (d, $J = 6.8$ Hz, C), 133.1 (d, $J = 17.7$ Hz, CH), 128.5 (d, $J = 4.6$ Hz, CH), 128.0 (d, $J = 2.2$ Hz, CH), 127.3 (d, $J = 12.0$ Hz, CH), 126.3 (d, $J = 2.8$ Hz, CH), 48.7 (d, $J = 74.4$ Hz, CH), 45.5 (d, $J = 4.6$ Hz, CH), 31.6 (d, $J = 80.1$ Hz, CH_2), 22.8 (d, $J = 1.0$ Hz, CH_3), 22.6 (d, $J = 1.0$ Hz, CH_3); ^{31}P NMR (162 MHz, CDCl_3): δ 60.2; IR (neat): 2965, 1491, 1453, 1400, 1367, 1225, 1207, 1182, 1156, 1108, 993, 880, 764, 729, 697, 688 cm^{-1} ; HRMS (APCI) m/z : calcd for $\text{C}_{16}\text{H}_{24}\text{NOP}$ $[\text{M}+\text{H}]^+$: 278.16683, found: 278.16682; Anal. Calcd. for $\text{C}_{16}\text{H}_{24}\text{NOP}$: C, 69.29; H, 8.72; N, 5.05. Found: C, 69.07; H, 8.68; N, 5.04.

Cis-1-[(N,N)-diisopropylamino]-1-oxo-2-phenylphospholane (cis-167)

In the bottle of the hydrogenation reactor, was added solution of *cis-1-[(N,N)-diisopropylamino]-1-oxo-2-phenylphosphol-3-ene (cis-166)* (1.0 g in 5 mL of methanol) and 5% Pd-C (0.8 g, 10 mol%). The system was purged with hydrogen for three times, then filled with hydrogen (50 bar) and reacted for 24 h at room temperature. The mixture was passed through a celite pad, and the filtrate was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (ethyl acetate/ethanol 50:3) to afford ***cis-167*** as a white solid (0.87 g, 86% yield). M.p.: 141–142 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.34–7.19(m, 5H), 3.45–3.37 (m, 1H), 2.95–2.86 (m, 2H), 2.44–2.35 (m, 1H), 2.22–2.13 (m, 1H), 2.04–1.94 (m, 1H), 1.76–1.70 (m, 1H), 1.11 (d, *J* = 6.5 Hz, 6H), 0.73 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 136.9 (d, *J* = 4.0 Hz, C), 128.1 (d, *J* = 1.7 Hz, CH), 127.9 (d, *J* = 4.6 Hz, CH), 126.1 (d, *J* = 2.2 Hz, CH), 47.8 (d, *J* = 79.0 Hz, CH), 45.5 (d, *J* = 4.0 Hz, CH), 29.5 (d, *J* = 12.6 Hz, CH₂), 28.3 (d, *J* = 76.1 Hz, CH₂), 22.4 (s, CH₃), 22.3 (s, CH₃), 21.0 (d, *J* = 7.4 Hz, CH₂); ³¹P NMR (162 MHz, CDCl₃): δ 66.3; IR (neat): 2964, 1497, 1450, 1401, 1366, 1250, 1205, 1191, 1154, 1134, 989, 758, 690 cm⁻¹; HRMS (APCI) *m/z*: calcd for C₁₆H₂₆NOP [M+H]⁺: 280.18248, found: 280.18254; Anal. Calcd. for C₁₆H₂₆NOP: C, 68.79; H, 9.38; N, 5.01. Found: C, 68.97; H, 9.42; N, 5.02.

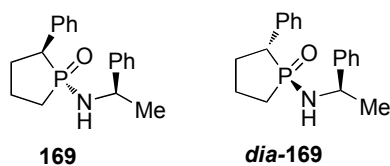
***Trans*-1-[(*N,N*)-diisopropylamino]-1-oxo-2-phenylphospholane (*trans*-167)**

Prepared by following the procedure for *cis*-167, using *trans*-1-[(*N,N*)-diisopropylamino]-1-oxo-2-phenylphosphol-3-ene (*trans*-166) (0.5 g in 5 mL of methanol) and 5% Pd-C(0.4 g, 10 mol%). The crude product was purified by flash chromatography on silica gel eluting with ethyl acetate to afford *trans*-167 as white solid (0.47 g, 95% yield). M.p.: 121–123 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.36–7.18 (m, 5H), 3.29–3.20 (m, 2H), 2.75–2.69 (m, 1H), 2.26–2.12 (m, 3H), 1.97–1.90 (m, 2H), 1.68–1.64 (m, 1H), 1.25 (d, $J = 7.0$ Hz, 6H), 1.05 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 137.0 (d, $J = 4.6$ Hz, C), 129.1 (d, $J = 5.2$ Hz, CH), 127.9 (s, CH), 126.1 (d, $J = 1.7$ Hz, CH), 46.0 (d, $J = 76.1$ Hz, CH), 45.3 (d, $J = 5.2$ Hz, CH), 32.1 (d, $J = 15.4$ Hz, CH_2), 27.0 (d, $J = 81.3$ Hz, CH_2), 23.2 (s, CH_3), 22.6 (d, $J = 1.1$ Hz, CH_3), 21.7 (d, $J = 5.6$ Hz, CH_2); ^{31}P NMR: (162 MHz, CDCl_3): δ 61.6; IR (neat): 2966, 1493, 1453, 1367, 1208, 1189, 1156, 1367cm^{-1} ; HRMS (APCI) m/z : calcd for $\text{C}_{16}\text{H}_{26}\text{NOP}$ $[\text{M}+\text{H}]^+$: 280.18248, found: 280.18251; Anal. Calcd. for $\text{C}_{16}\text{H}_{26}\text{NOP}$: C, 68.79; H, 9.38; N, 5.01. Found: C, 68.85; H, 9.46; N, 5.01.

1-Hydroxy-1-oxo-2-phenylphospholane (racemic 161)

A mixture of *cis*-1-[(*N,N*)-diisopropylamino]-1-oxo-2-phenylphospholane (***cis*-167**) in 35 mL of concentrated HCl was heated to 117-120 °C for 3.5 days. Then it was cooled to room temperature, diluted with water, and basified with 10% aqueous NaOH. After extracted with dichloromethane for 3 times, the aqueous solution was acidified with HCl, and extracted with dichloromethane. The dichloromethane solution was dried over Na₂SO₄, concentrated under vacuum to afford **racemic 161** as a white solid (0.54 g, 96% yield). M.p.: 95–96 °C. ¹H NMR (500 MHz, CDCl₃): δ 9.54 (br., 1H), 7.29–7.20 (m, 5H), 3.02–2.94 (m, 1H), 2.28–2.17 (m, 1H), 2.08–1.97 (m, 2H), 1.80–1.61 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 135.6 (d, *J* = 5.7 Hz, C), 128.3 (d, *J* = 5.7 Hz, CH), 128.2 (d, *J* = 1.7 Hz, CH), 126.5 (d, *J* = 2.2 Hz, CH), 45.3 (d, *J* = 89.3 Hz, CH), 30.3 (d, *J* = 16.6 Hz, CH₂), 25.0 (d, *J* = 90.4 Hz, CH₂), 20.4 (d, *J* = 8.6 Hz, CH₂); ³¹P NMR (162 MHz, CDCl₃): δ 73.9; IR (neat): 1601, 1495, 1451, 1256, 1164, 1089, 968, 759, 698 cm⁻¹; MS (ESI) *m/z*: 195 ([*M*-H]⁻, 100%); HRMS (APCI) *m/z*: calcd for C₁₀H₁₃O₂P [*M*+H]⁺: 197.07259, found: 197.07265; Anal. Calcd. for C₁₀H₁₃O₂P: C, 61.22; H, 6.73. Found: C, 61.25; H, 6.73.

1-[*N*-(*R*)-(1-Methyl)benzylamino]-1-oxo-2-phenylphospholane (**169**)



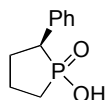
To the solution of 1-hydroxy-1-oxo-2-phenylphospholane (**racemic 161**) (0.7 g, 3.6 mmol) in 20 mL of THF was slowly added oxalyl chloride (1.39 mL, 16.5 mmol, 4.5 equiv.) at 0 °C. The solution was stirred at room temperature for 2 h and concentrated

under vacuum. The residue was dissolved with 10 mL of anhydrous benzene, cooled to 10 °C, and (*R*)-(+)-methylbenzylamine (1.40 mL, 11.0 mmol, 3 equiv.) in 5 mL of anhydrous benzene was slowly added. The reaction mixture was stirred at room temperature for one day, and heated to reflux for one day. Then it was concentrated under vacuum. The residue was dissolved with dichloromethane, washed with 0.5 N aqueous HCl, dried over Na₂SO₄, and concentrated under vacuum. The crude product was separated by flash chromatography on silica gel eluting with ethyl acetate/ethanol (10:1) to afford compound **169** and its diastereomer *dia*-**169**. Compound **169**: white solid, 0.30 g, 27% yield. M.p.: 163–164 °C. $[\alpha]_D^{20}$ -76.4° (*c* 1.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.38–7.13 (m, 10H), 4.40–4.37 (m, 1H), 2.72–2.65 (m, 2H), 2.27–2.17 (m, 1H), 2.12–2.02 (m, 2H), 1.88–1.78 (m, 2H), 1.59–1.51 (m, 1H), 1.48 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 145.1 (C), 136.4 (C), 128.8 (d, *J* = 5.1 Hz, CH), 128.6 (CH), 128.3 (CH), 127.3 (CH), 126.5 (CH), 126.1 (CH), 50.8 (CH), 45.5 (d, *J* = 80.0 Hz, CH), 32.5 (d, *J* = 14.8 Hz, CH₂), 26.4 (d, *J* = 71.0 Hz, CH₂), 25.9 (d, *J* = 17.8 Hz, CH₃), 21.3 (d, *J* = 6.8 Hz, CH₂); ³¹P NMR (162 MHz, CDCl₃): δ 59.1; IR (neat): 3197, 1601, 1493, 1449, 1253, 1174, 1126, 1093, 759, 699 cm⁻¹; HRMS (APCI) *m/z*: calcd for C₁₈H₂₂NOP [M+H]⁺: 300.15118, found: 300.15114. *dia*-**169**: white solid, 0.43 g, 40% yield. M.p.: 128–130 °C. $[\alpha]_D^{20}$ +157.8° (*c* 1.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.37–7.16 (m, 10H), 4.41–4.36 (m, 1H), 2.89–2.83 (m, 2H), 2.28–2.20 (m, 1H), 2.14–2.03 (m, 2H), 1.91–1.85 (m, 2H), 1.62–1.57 (m, 1H), 1.50 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 145.1, 136.8 (d, *J* = 5.1 Hz), 128.7 (d, *J* = 5.2 Hz), 128.6, 128.3, 127.2, 126.4, 125.9, 50.6, 44.9 (d, *J* = 80.7 Hz), 32.6 (d, *J* = 14.8 Hz), 27.3 (d, *J* = 83.0 Hz), 26.1 (d, *J* = 5.1 Hz), 21.1 (d, *J* = 6.8 Hz); ³¹P NMR (162 MHz, CDCl₃): δ 58.5;

IR(neat): 3179, 1601, 1493, 1450, 1252, 1173, 1124, 1089, 757, 697 cm^{-1} ; HRMS

(APCI) m/z : calcd for $\text{C}_{18}\text{H}_{22}\text{NOP}$ $[\text{M}+\text{H}]^+$: 300.15118, found: 300.15120.

1-Hydroxy-1-oxo-2-phenylphospholane (enantiopure **161**)

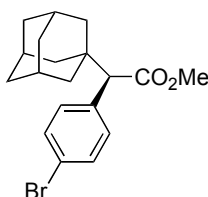


The solution of 1-[*N*-(*R*)-(1-methyl)benzylamino]-1-oxo-2-phenylphospholane (**169**) (0.30 g) in 17 mL of concentrated HCl was heated to reflux for 1 day under argon. Then it was cooled to room temperature, diluted with water, then basified with 10% aqueous NaOH. The solution was extracted with dichloromethane. The aqueous part was acidified with HCl, and extracted with dichloromethane. The dichloromethane solution was dried over Na_2SO_4 , filtered, and concentrated under vacuum to afford enantiopure **169** as a white solid (0.19 g, 97% yield). $[\alpha]_D^{25} +1.8^\circ$ (c 1.0, CHCl_3). The spectra data are identical as racemic **161**.

To determine the enantiomeric excess, enantiopure **161** was converted into the methyl ester following the following procedure: compound **161** (6 mg) was dissolved with 1 mL of diethyl ether in the outside tube of the diazomethane-generator. MNNG (1-methyl-3-nitro-1-nitrosoguanidine, 68 mg) was added to the inside tube with 0.3 mL of water. The diazomethane-generator was assembled and held together by tightening the 32 mm screw cap. Its lower part was immersed in an ice bath and 0.3 mL of 5 N aqueous NaOH was slowly added through the septum via a syringe with a narrow gauge needle (No. 22). After 2 h, the cap was removed, and the solution was concentrated with air stream. The

residue was used for HPLC analysis without purification. HPLC analysis: >99% ee, CHIRALCEL OD-H, 5% isopropanol/hexanes, 0.8 mL/min, UV 254nm, t_R : 19.0 min (major), 34.5 min (major), 20.1 min (minor), 24.6 min (minor).

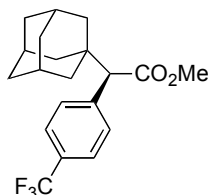
Methyl (*R*)-2-adamantyl-2-(4-bromophenyl)acetate (**176**)



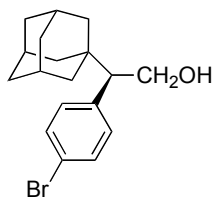
Prepared by following the literature procedure.^{26a} The solution of methyl 4-bromophenyldiazoacetate (**174**) (2.00 g in 60 mL of degassed 2,2-dimethylbutane) was added to a solution of $\text{Rh}_2(\text{S-DOSP})_4$ (75 mg, 0.04 mmol, 0.5 mol%) and adamantane (2.14 g, 15.68 mmol, 2 equiv.) in 40 mL of degassed 2,2'-dimethylbutane with a syringe pump over 2 h at room temperature. The resulting solution was stirred for 2 h, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with 4% diethyl ether in petroleum ether to afford **176** as a white solid (1.78 g, 63% yield, 95% ee). $[\alpha]_D^{20} -15.3^\circ$ (c 1.6, CHCl_3). M.p.: 127–129 °C; ^1H NMR (500 MHz, CDCl_3): δ 7.41 (d, $J = 8.5$ Hz, 2H), 7.25 (d, $J = 8.5$ Hz, 2H), 3.64 (s, 3H), 3.23 (s, 1H), 1.95 (s, 3H), 1.68–1.46 (m, 12H); ^{13}C NMR (75 MHz, CDCl_3): δ 172.7 (C), 133.8 (C), 131.8 (CH), 130.7 (CH), 121.2 (C), 62.3 (CH), 51.3 (CH_3), 39.7 (CH_2), 36.6 (CH_2), 36.2 (C), 28.5 (CH); IR (neat): 2906, 2848, 1734, 1488, 1447, 1434, 1341, 1263, 1198, 1152, 1075, 1011, 834 cm^{-1} ; HRMS (EI) m/z : calcd. for $\text{C}_{19}\text{H}_{23}\text{BrO}_2$ M^+ : 362.0876, found: 362.0886. Data are consistent with the literature. To determine the ee, small amount of compound **176** was reduced to alcohol with LiAlH_4 . HPLC analysis:

95% ee, (*S, S*)-Whelk O1, 20% isopropanol/hexanes, 0.6 mL/min, UV: 230 nm, t_R : 15.1 min (minor), 26.7 min (major).

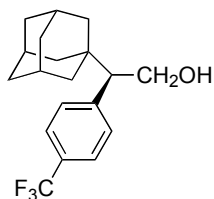
Methyl (*R*)-2-adamantyl-2-(4-trifluoromethylphenyl)acetate (177**)**



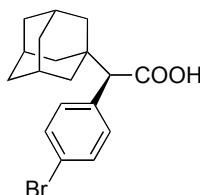
Prepared by following the procedure for **176**, using methyl 4-trifluoromethylphenyldiazoacetate (**175**) (2.0 g), $\text{Rh}_2(\text{S-DOSP})_4$ (77 mg, 0.04 mmol, 0.5 mol%), and adamantane (2.2 g, 16.4 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with 1.5% diethyl ether in petroleum ether to afford compound **177** as white solid (0.87 g, 31% yield). M.p.: 124–126 °C; $[\alpha]_D^{20}$ -12.1° (c 1.0, CHCl_3); R_f , 0.28 (1.5% diethyl ether/petroleum ether); ^1H NMR (500 MHz, CDCl_3): δ 7.55 (d, J = 8.5 Hz, 2H), 7.51 (2H, d, J = 8.5 Hz, 2H), 3.65 (s, 3H), 3.34 (s, 1H), 1.96 (s, 3H), 1.70–1.49 (m, 12H); ^{13}C NMR (75 MHz, CDCl_3): δ 172.5 (C), 138.9 (C), 130.4 (CH), 124.5 (q, $^3J_{\text{CF}}$ = 3.4 Hz, CH), 129.3 (q, $^2J_{\text{CF}}$ = 32 Hz, C), 124.2 (q, $^1J_{\text{CF}}$ = 272 Hz, C), 62.7 (CH), 51.4 (CH_3), 39.8 (CH_2), 36.6 (CH_2), 36.5 (C), 28.5 (CH); IR (neat): 2907, 2850, 1735, 1325, 1154, 1126, 1113, 1069 cm^{-1} ; HRMS (EI) m/z : calcd. for $\text{C}_{20}\text{H}_{23}\text{F}_3\text{O}_2$ M^+ : 352.1645, found: 352.1643; Anal. Calcd. for $\text{C}_{20}\text{H}_{23}\text{F}_3\text{O}_2$: C, 68.17; H, 6.58. Found: C, 67.94; H, 6.54. HPLC analysis: 90% ee, (*S, S*)-Whelk O1, 0.3 % isopropanol/hexanes, 0.5 mL/min, UV: 230 nm, t_R : 13.3 min (minor), 14.7 min (major).

(R)-2-Adamantyl-2-(4-bromophenyl)ethanol (178)

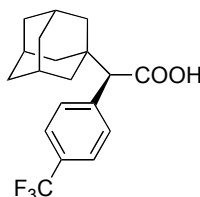
LiAlH₄ solution (2.4 M in THF, 0.8 mL, 0.7 equiv.) was added dropwise to methyl (*R*)-2-adamantanyl-2-(4-bromophenyl)acetate (**176**, >99% ee) (1.0 g, 2.75 mmol) in 15 mL of THF at 0 °C. After addition, the solution was stirred for 1 h at 0 °C, then warmed to room temperature and stirred for another 3 h. Then it was carefully quenched with water at 0 °C. The mixture was concentrated under vacuum and the residue was extracted with diethyl ether (3 x 50 mL). The combined ether solution was dried over Na₂SO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with diethyl ether/petroleum ether (10 to 30%) to afford compound **178** as white solid (0.87 g, 94% yield). $[\alpha]_D^{20} +1.0^\circ$ (*c* 1.3, CHCl₃). M.p.: 159–161 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.45 (d, *J* = 7.5 Hz, 2H), 7.06 (d, *J* = 7.5 Hz, 2H), 4.07 (dd, *J* = 11.0, 4.5 Hz, 1H), 3.98 (t, *J* = 11.0 Hz, 1H), 2.50 (dd, *J* = 11.0, 4.5 Hz, 1H), 1.92 (s, 3H), 1.66–1.39 (m, 12H); ¹³C NMR (75 MHz, CDCl₃): δ 138.8 (C), 131.6 (CH), 131.1 (CH), 120.5 (C), 61.4 (CH₂), 59.6 (CH), 40.6 (CH₂), 36.9 (CH₂), 34.9 (C), 28.5 (CH); IR (neat): 3258, 2903, 2847, 1489, 1045, 1009 cm⁻¹; HRMS (EI) *m/z*: calcd for C₁₈H₂₃BrO M⁺: 334.0927, found: 334.0922; Anal. Calcd. for C₁₈H₂₃BrO: C, 64.48; H, 6.91. Found: C, 64.32; H, 6.86. HPLC analysis: >99% ee, (*S, S*)-Whelk O1, 20% isopropanol/hexanes, 0.6 mL/min, UV: 230 nm, *t*_R: 15.1 min (minor), 26.7 min (major).

(R)-2-Adamantyl-2-(4-trifluoromethylphenyl)ethanol (179)

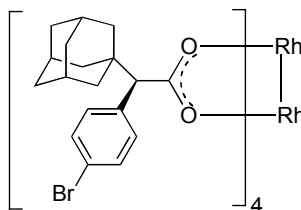
Prepared by following the procedure for **178**, using LiAlH_4 solution (2.4 M in THF, 0.8 mL, 0.7 equiv.), Methyl (*R*)-2-adamantanyl-2-(4-trifluoromethylphenyl)acetate (**177**) (0.3 g, 0.85 mmol). The crude product was purified by flash column chromatography on silica gel eluting with 10% ethyl acetate/hexanes to afford compound **179** as a white solid (0.26 g, 94% yield). M.p.: 129–131 °C. $[\alpha]_D^{20} +4.4^\circ$ (c 1.1, CHCl_3). R_f , 0.30 (10% ethyl acetate/hexanes); $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.58 (d, $J = 8.0$ Hz, 2H), 7.30 (d, $J = 7.5$ Hz, 2H), 4.11 (dd, $J = 11.0, 4.5$ Hz, 1H), 4.03 (t, $J = 11.0$ Hz, 1H), 2.61 (dd, $J = 11.0, 4.5$ Hz, 1H), 1.93 (s, 3H), 1.66–1.39 (m, 12H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 144.0 (C), 130.1 (CH), 124.8 (q, $^3J_{\text{CF}} = 4.0$ Hz, CH), 128.8 (q, $^2J_{\text{CF}} = 32$ Hz, C), 124.3 (q, $^1J_{\text{CF}} = 272$ Hz, C), 61.3 (CH), 59.9 (CH), 40.6 (CH_2), 36.8 (CH_2), 35.0 (C), 28.5 (CH); IR (neat): 3300 (broad), 2906, 2850, 1326, 1164, 1123, 1070 cm^{-1} ; HRMS (EI) m/z : calcd for $\text{C}_{19}\text{H}_{23}\text{F}_3\text{O M}^+$: 324.1696, found: 324.1705; Anal. Calcd. for $\text{C}_{19}\text{H}_{23}\text{F}_3\text{O}$: C, 70.35; H, 7.15. Found: C, 70.58; H, 7.21. HPLC analysis: 99% ee, (*R, R*)-Whelk O1, 15% isopropanol/hexanes, 0.8 mL/min, UV: 230 nm, t_R : 7.0 min (major), 9.4 min (minor).

(R)- 2-Adamantyl-2-(4-bromophenyl)acetic acid (180)

(*R*)-2-adamantanyl-2-(4-bromophenyl)ethanol (**178**) (0.2 g, 0.6 mmol) in 10 mL of acetone was added to the solution of $K_2Cr_2O_7$ (0.26 g, 0.9 mmol, 1.5 equiv.) in 6 mL of 1.5M aqueous H_2SO_4 at 0 °C. After addition, the mixture was warmed to room temperature and stirred for 2 h, then 10 mL of diethyl ether was added. The ether layer was separated and concentrated under vacuum. The residue was extracted with diethyl ether (3 x 15 mL). The combined ether solution was washed with brine, dried over Na_2SO_4 , and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel eluting hexanes/ethyl acetate (10:1 to 8:1) to afford compound **180** as a white solid (198 mg, 95% yield). M.p.: 210–212 °C. $[\alpha]_D^{20}$ -14.5° (*c* 1.5, $CHCl_3$). 1H NMR (500 MHz, $CDCl_3$): δ 12.0–10.0 (br., 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 3.24 (s, 1H), 1.96 (s, 3H), 1.69–1.53 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.4 (C), 133.3 (C), 131.9 (CH), 130.9 (CH), 121.5 (C), 62.6 (CH), 39.7 (CH_2), 36.6 (CH_2), 36.1 (C), 28.5 (CH); IR (neat): 2903, 2848, 1692, 1448, 1267, 1213 cm^{-1} ; MS (ESI, -c): 347 ($[M-H]^-$, 100%); HRMS (EI) m/z : calcd for $C_{18}H_{21}BrO_2$ M^+ : 348.0719, found: 348.0724; Anal. Calcd. for $C_{18}H_{21}BrO_2$: C, 61.90; H, 6.06. Found: C, 62.00; H, 6.12. HPLC analysis: >99% ee, (*S,S*)-whelk O1, 1.0% isopropanol/hexanes, 0.6 mL/min, UV: 230 nm, t_R : 20.7 min (major), 30.5 min (minor).

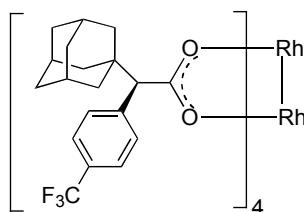
(R)- 2-Adamantyl-2-(4-trifluoromethylphenyl)acetic acid (181)

Prepared by following the procedure for **180**, using (*R*)-2-adamantanyl-2-(4-trifluoromethylphenyl)ethanol (**179**) (0.23 g, 0.72 mmol), $K_2Cr_2O_7$ (0.32 g, 1.1 mmol, 1.5 equiv.), and 6 mL of 1.8M aqueous H_2SO_4 . The crude product was purified by flash chromatography on silica gel eluting with hexanes/acetate (8:1 to 5:1) to afford compound **181** as a white solid (225 mg, 92% yield). M.p.: 142-145 °C. $[\alpha]_D^{20} -16.3^\circ$ (*c* 1.2, $CHCl_3$). R_f , 0.28 (hexanes/ethyl acetate 5:1); 1H NMR (500 MHz, $CDCl_3$): δ 12.0–10.0 (broad, 1H), 7.55 (d, $J = 8.5$ Hz, 2H), 7.50 (d, $J = 8.0$ Hz, 2H), 3.35 (s, 1H), 1.97 (s, 3H), 1.70-1.56 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5 (C), 138.4 (C), 130.5 (CH), 124.6 (q, $^3J_{CF} = 3.4$ Hz, CH), 129.5 (q, $^2J_{CF} = 32$ Hz, C), 124.2 (q, $^1J_{CF} = 272$ Hz, C), 63.1 (CH), 39.8 (CH_2), 36.5 (CH_2), 36.4 (C), 28.5 (CH); IR (neat): 2906, 2850, 1697, 1618, 1446, 1431, 1410, 1326, 1224, 1163, 1129, 1070, 1021, 908, 845, 735 cm^{-1} ; HRMS (EI) *m/z*: calcd. for $C_{19}H_{21}F_3O_2$ M^+ : 338.1488, found: 338.1492.

(R)- 2-Adamantyl-2-(4-bromophenyl)acetate dirhodium (II,II) complex (182)

In a 10 ml of round bottom flask equipped with a short distill path, was added (*R*)-2-adamantyl-2-(4-bromophenyl)acetic acid (**180**) (160 mg, 0.46 mmol, 6 equiv.), Rh₂(OAc)₄ (33 mg, 0.08 mmol, 1 equiv.) and 4 mL of dry chlorobenzene. The solution was stirred for 10 min at room temperature, then heated to 160-170 °C to distill out chlorobenzene. Proper amount of chlorobenzene was added at the same time to maintain the same amount of solvent in the flask. This process was continued for 5 h. Then the solution was concentrated under vacuum. The residue was purified by flash chromatography on silica gel eluting with hexanes/acetate (20:1) to afford compound **182** as a green solid (96 mg, 79% yield). $[\alpha]_D^{20} + 20.1^\circ$ (*c* 0.1, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.27 (d, *J* = 8.5 Hz, 8H), 6.85 (d, *J* = 8.5 Hz, 8H), 2.91 (s, 4H), 1.73 (s, 12H), 1.51 (m, 12H), 1.30–1.19 (m, 36H); ¹³C NMR (75 MHz, CDCl₃): δ 192.2 (C), 135.0 (C), 131.7 (CH), 130.3 (CH), 120.7 (C), 65.6 (CH), 40.0 (CH₂), 36.5 (CH₂), 36.2 (C), 28.5 (CH); IR (neat): 2905, 2848, 1582, 1487, 1390 cm⁻¹; HRMS (-ESI) *m/z*: calcd for C₇₄H₈₀Br₄O₈Rh₂ [M+CF₃CO₂]⁻: 1707.05526, found 1707.05389.

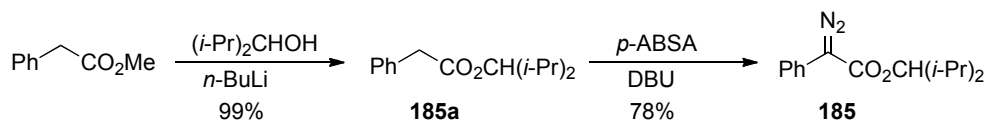
(*R*)-2-Adamantyl-2-(4-trifluoromethylphenyl)acetate dirhodium (II,II) complex (183)



Prepared by following the procedure for **182**, using (*R*)-2-adamantyl-2-(4-trifluoromethylphenyl)acetic acid (**181**) (200 mg, 0.59 mmol, 6 equiv.), Rh₂(OAc)₄ (44

mg, 0.01 mmol, 1 equiv.) and 5 mL of dry chlorobenzene. The ligand exchange was continued for 7 h. Then the solution was concentrated under vacuum. The residue was purified by flash chromatography on silica gel eluting with hexane/acetate (10:1) to afford compound **183** as a green solid (127 mg, 82% yield). $[\alpha]_D^{20} +63.9^\circ$ (*c* 0.1, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.41 (d, *J* = 8.5 Hz, 8H), 7.10 (d, *J* = 8.0 Hz, 8H), 3.03 (s, 4H), 1.71 (s, 12H), 1.50–1.17 (m, 48H); ¹³C NMR (75 MHz, CDCl₃): δ 191.7 (C), 140.2 (C), 130.3 (CH), 128.7 (q, ²*J*_{CF} = 32 Hz, C), 124.3 (q, ¹*J*_{CF} = 272 Hz, C), 124.0 (q, ³*J*_{CF} = 3.4 Hz, CH), 65.9 (CH), 40.0 (CH₂), 36.4 (CH₂), 36.4 (C), 28.5 (CH); IR (neat): 2907, 2850, 1582, 1393, 1326, 1165, 1127, 1070, 1020, 908, 735 cm⁻¹; HRMS (-ESI) *m/z*: calcd for C₇₆H₈₀F₁₂O₈Rh₂ [M+CF₃CO₂]⁻: 1667.36275, found 1667.35995.

2,4-Dimethyl-3-pentyl phenyldiazoacetate(**185**)

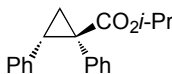


n-BuLi (10.6 mL, 2.5M in hexanes, 26.6 mmol) was added to 2,4-dimethyl-3-pentanol (3.73 mL, 26.6 mmol) in 60 mL of THF at -10 °C. The solution was stirred for 10 min, and methyl phenylacetate (2.0 g, 13.3 mmol) in 20 mL of THF was added slowly. The reaction mixture was warmed to room temperature and stirred overnight. It was concentrated under vacuum, the residue was extracted with dichloromethane (3 x 50 mL). The combined dichloromethane solution was washed with water, dried over Na₂SO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with 2% diethyl ether /pentane to afford compound **185a** as colorless oil (3.1 g, 99% yield). *R*_f, 0.47 (2% diethyl ether/pentane); ¹H NMR (500 MHz, CDCl₃):

7.33–7.23 (m, 5H), 4.57 (t, $J = 6.5$ Hz, 1H), 3.63 (s, 2H), 1.85 (m, 2H), 0.80 (d, $J = 7.0$ Hz, 6H), 0.79 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): 171.5 (C), 134.4 (C), 129.3 (CH), 128.4 (CH), 126.9 (CH), 82.9 (CH), 41.7 (CH_2), 29.3 (CH), 19.4 (CH_3), 17.0 (CH_3); IR (neat): 2966, 2936, 1731, 1258, 1130, 974 cm^{-1} ; HRMS (EI): calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2 \text{M}^+$: 234.1614, found: 234.1611.

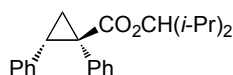
DBU was added to the solution of 2,4-dimethyl-3-pentyl phenylacetate (**185a**) (2.95 g, 12.6 mmol, 1 equiv.) and *p*-ABSA (3.63 g, 15.1 mmol, 1.2 equiv.) in 30 mL of acetonitrile in one portion at 0 °C. The reaction mixture was stirred overnight with temperature rising to room temperature. Then it was quenched with aqueous saturated NH_4Cl . The mixture was extracted with diethyl ether (3 x 50 mL), and the combined ether solution was washed with water (2x100 mL), dried over MgSO_4 , and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with 1% diethyl ether/pentane to afford compound **185** as orange oil (2.56 g, 78% yield). ^1H NMR (500 MHz, CDCl_3): 7.50 (d, $J = 8.5$ Hz, 2H), 7.38 (t, $J = 8.5$ Hz, 2H), 7.17 (t, $J = 7.5$ Hz, 1H), 4.76 (t, $J = 6.5$ Hz, 1H), 1.96 (m, 2H), 0.93 (d, $J = 6.5$ Hz, 6H), 0.91 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): 165.3 (C), 128.8 (CH), 128.5 (C), 125.6 (CH), 123.8 (CH), 83.4 (CH), 29.5 (CH), 19.6 (CH_3), 17.2 (CH_3); IR (neat): 2967, 2083, 1704, 1499, 1465, 1389, 1371, 1357, 1333, 1243, 1165, 1132, 1097, 1012, 996, 755, 691 cm^{-1} .

(1*R*, 2*S*)-Isopropyl 1,2-diphenylcyclopropanecarboxylate (187)



Isopropyl phenyldiazoacetate (**184**) (58 mg, 0.28 mmol, 1 equiv.) in 2 mL of degassed toluene was added to the solution of Rh(II) catalyst (**182**) (9.0 mg, 0.0056 mmol, 2 mol%) and styrene (0.33 mL, 2.8 mmol, 10 equiv.) in 2 mL of toluene at room temperature over 2 h. After addition, the solution was stirred for 1 h, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with hexanes/acetate (95:5) to afford cyclopropane **187** as a white solid (65 mg, 81% yield). M.p.: 63–66 °C. $[\alpha]_D^{20}$ -6.2° (*c* 2.1, CHCl₃). ¹H NMR (500 MHz, CDCl₃): δ 7.10–7.00 (m, 8H), 6.77–6.75 (m, 2H), 4.99 (m, 1H), 3.06 (dd, *J* = 9.5, 7.0 Hz, 1H), 2.10 (dd, *J* = 9.5, 5.0 Hz, 1H), 1.85 (dd, *J* = 7.0, 5.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): 173.3, 136.8, 135.1, 132.1, 128.3, 127.8, 127.7, 126.9, 126.4, 68.7, 38.0, 32.9, 21.9, 20.0; IR (neat): 1708, 1253, 1168, 1107, 1092, 782, 762, 695 cm⁻¹; HRMS (APCI) *m/z*: calcd for C₁₉H₂₀O₂ [M+H]⁺: 281.15361, found: 281.15373. HPLC analysis: 34% ee, (*R*, *R*)-Whelk O1, 2% isopropanol/hexanes, 1.0 mL/min, UV 254 nm, *t*_R: 6.6 min (major), 7.9 min (minor).

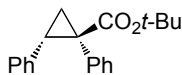
(1*R*, 2*S*)-2,4-Dimethylpentan-3-yl 1,2-diphenylcyclopropanecarboxylate (188)



Prepared by following the procedure for compound **186**, using 2,4-dimethyl-3-pentyl phenyldiazoacetate (**185**) (74 mg, 0.28 mmol, 1 equiv.), Rh(II) (**182**) (9.0 mg, 0.0056 mmol, 2 mol%), and styrene (0.33 mL, 2.8 mmol, 10 equiv.). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (100:1) to afford cyclopropane **188** as clear oil (35 mg, 37% yield). *R*_f 0.22 (pentane/diethyl

ether 50:1). $[\alpha]_D^{20}$ -5.2° (*c* 1.8, CHCl₃). ¹H NMR (500 MHz, CDCl₃): 7.10–7.01 (m, 8H), 6.79–7.77 (m, 2H), 4.56 (t, *J* = 6.0 Hz, 1H), 3.08 (dd, *J* = 9.0, 7.5 Hz, 1H), 2.12 (dd, *J* = 9.5, 5.0 Hz, 1H), 1.84 (dd, *J* = 7.5, 5.0 Hz, 1H), 1.82–1.71 (m, 2H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.80 (d, *J* = 6.5 Hz, 3H), 0.73 (d, *J* = 6.5 Hz, 3H), 0.65 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): 173.6 (C), 136.7 (C), 135.2 (C), 131.9 (CH), 128.0 (CH), 127.7 (CH), 127.4 (CH), 126.7 (CH), 126.2 (CH), 83.4 (CH), 37.7 (C), 32.5 (CH), 29.4 (CH), 29.4 (CH), 19.9 (CH₂), 19.5 (CH₃), 19.5 (CH₃), 17.0 (CH₃), 16.9 (CH₃); IR (neat): 2965, 2932, 1712, 1256, 1170, 697 cm⁻¹; HRMS (EI) *m/z*: calcd for C₂₃H₂₈O₂ M⁺: 336.2084, found: 336.2085. HPLC analysis: 47% ee, OJ, 0.2% isopropanol/hexanes, 0.8 mL/min, UV 254 nm, *t*_R: 7.2 min (major), 12.0 min (minor).

(1*R*, 2*S*)-tert-Butyl 1,2-diphenylcyclopropanecarboxylate (189)

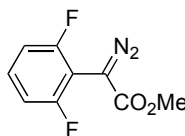


Prepared by following the procedure for compound **187**, using *t*-butyl phenyldiazoacetate (**186**) (40 mg, 0.18 mmol, 1 equiv.), Rh(II) (**182**) (5.8 mg, 0.0056 mmol, 2 mol%), and styrene (0.20 mL, 1.8 mmol, 10 equiv.). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (50:1) to afford cyclopropane **189** as a white solid (22 mg, 42% yield). M.p.: 82–83 °C. ¹H NMR (500 MHz, CDCl₃): 7.11–7.00 (m, 8H), 6.77–7.75 (m, 2H), 4.56 (t, *J* = 6.0 Hz, 1H), 3.00 (dd, *J* = 9.0, 7.5 Hz, 1H), 2.06 (dd, *J* = 9.5, 5.0 Hz, 1H), 1.80 (dd, *J* = 7.5, 5.0 Hz, 1H), 1.39 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): 172.9, 137.0, 135.5, 132.0, 128.2, 127.8, 127.6, 126.8, 126.3, 81.0, 38.8, 32.5, 28.2, 19.8; IR (neat): 1709, 1367, 1272, 1254, 1154, 696

cm⁻¹; HRMS (APCI) *m/z*: calcd for C₂₀H₂₂O₂ [M+H]⁺: 295.16926, found: 295.16972.

HPLC analysis: 4% ee, (*S, S*)-whelk O1, 2.0% isopropanol/hexanes, 0.8 mL/min, UV 254 nm, *t_R*: 7.6 min (major), 6.9 min (minor).

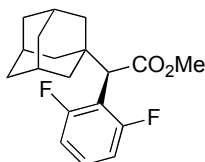
Methyl 2,6-difluorophenyldiazoacetate (**190**)



2,6-difluorophenylacetic acid (3.4 g, 20 mmol) was dissolved with 50 mL of methanol. A few drops of concentrated H₂SO₄ was added, and the solution was heated to reflux overnight. Then it was cooled to room temperature, 100 mL of diethyl ether and 100 mL of water were added. The ether layer was separated, dried over MgSO₄, concentrated under vacuum to give the corresponding methyl ester as colorless oil. The solution of this oil and *p*-ABSA (4.8 g, 20 mmol, 1 equiv.) in 50 mL of acetonitrile was cooled to 0 °C, DBU (3.2 mL, 21.6 mmol, 1.08 equiv.) was added in one portion. The reaction mixture was stirred overnight with temperature rising to room temperature. Then it was quenched with aqueous saturated NH₄Cl. The mixture was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with water (2 x 100 mL), dried over MgSO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with 6% diethyl ether/petroleum ether to afford compound **190** as a yellow solid (2.0 g, 48% yield). ¹H NMR (500 MHz, CDCl₃): 7.37–7.31(m, 1H), 7.00–6.95 (m, 2H), 3.84 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): 164.8 (C), 160.4 (dd, *J* = 5.7, 252.0 Hz, C), 130.9 (t, *J* = 10.0 Hz, CH), 111.9–111.5 (m, CH), 103.4 (C), 52.3 (CH₃); IR (neat): 2105, 1713, 1493, 1469, 1437, 1272, 1237, 1195, 1161, 1035,

1001, 786, 745 cm^{-1} ; HRMS (EI) m/z : calcd. for $\text{C}_9\text{H}_6\text{F}_2\text{N}_2\text{O}_2$ M^+ : 212.0392, found: 212.0400.

Methyl 2-adamantyl-2-(2,6-difluorophenyl)acetate (191)



The solution of Methyl 2,6-difluorophenyldiazoacetate (**190**) (100 mg, 0.47 mmol) in 3 mL of degassed 2,2'-dimethylbutane was added to a solution of $\text{Rh}_2(\text{S-DOSP})_4$ (4.5 mg, 0.5 mol%) and adamantane (130 mg, 0.94 mmol, 2 equiv.) in 2 mL of degassed 2,2-dimethylbutane with a syringe pump over 2 h at room temperature. After addition, the solution was stirred overnight, then concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with 5% ether in petroleum ether to afford compound **191** as a white solid (30 mg, 20% yield). M.p.: 69–72 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.25–7.19 (m, 1H), 6.88 (t, $J = 9.0$ Hz, 2H), 3.66 (s, 1H), 3.60 (s, 3H), 1.95 (s, 3H), 1.87–1.59 (m, 12H); ^{13}C NMR (75 MHz, CDCl_3): 170.9 (C), 161.4 (dd, $J = 247.9, 8.0$ Hz, C), 128.6 (t, $J = 10.5$ Hz, CH), 113.9 (t, $J = 19.1$ Hz, C), 111.3 (d, $J = 24.1$ Hz, CH), 51.4 (CH_3), 50.0 (CH), 39.3 (CH_2), 36.9 (CH_2), 28.6 (CH); IR (neat): 2903, 2849, 1747, 1622, 1590, 1467, 1264, 1229, 1198, 1156, 1020, 997, 973, 790, 756 cm^{-1} ; HRMS (EI) m/z : calcd for $\text{C}_{19}\text{H}_{22}\text{F}_2\text{O}_2$ M^+ : 320.1582, found: 320.1581. HPLC analysis: 8% ee, CHIRALCEL OD-H, 0.3% isopropanol/hexanes, 0.5 mL/min, UV 230 nm, t_R : 13.3 min (major), 14.7 min (minor).

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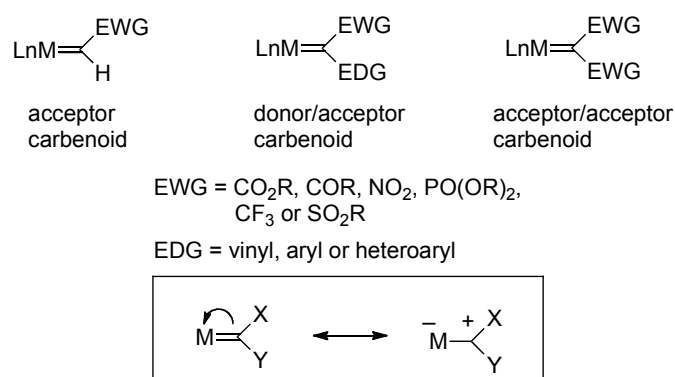
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Chapter 2 Highly Enantioselective C–C Bond Formation by Rhodium-Catalyzed Tandem Ylide Formation/[2,3]-Sigmatropic Rearrangement between Donor/Acceptor Carbenoids and Allylic Alcohols/Propargylic Alcohols

2.1 Introduction

Transition metal catalyzed decomposition of diazo compounds results in a wide variety of useful transformations, such as cyclopropanation, C–H and X–H insertion, and ylide formation.¹ It is generally accepted that these transformations involve highly electrophilic carbenoid intermediates.² Due to their high reactivity, it has been very challenging to achieve high levels of chemo and stereoselectivity. A large number of transition metal catalyst systems have been developed in the past two decades in order to address these challenges.^{1,3-7}

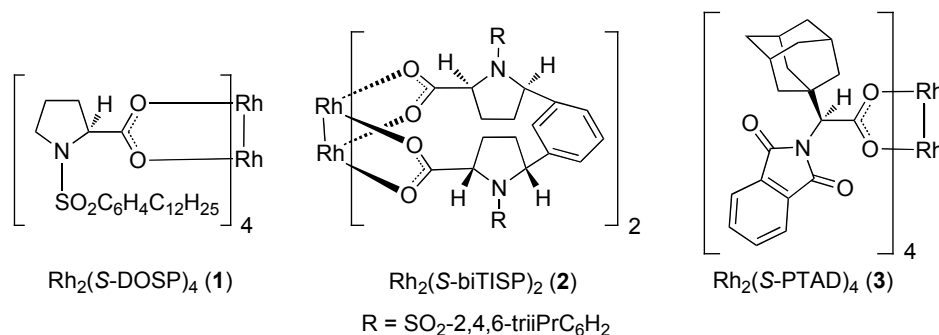
Figure 2.1 Classification of carbenoid intermediates



A different strategy developed by the Davies group is to attenuate the carbenoid reactivity with both an electron-withdrawing group and an electron-donating group (Figure 2.1).^{1b,8} Compared with the traditional carbenoids containing only one electron

withdrawing group (acceptor carbenoids) or two electron withdrawing groups (acceptor/acceptor carbenoids), donor/acceptor substituted carbenoids are more stable and are capable of a range of intermolecular transformations with high chemoselectivity. Most importantly, excellent enantioselectivity in these carbenoid transformations was also realized with the utilization of chiral dirhodium catalysts, such as $\text{Rh}_2(\text{S-DOSP})_4$ (**1**), $\text{Rh}_2(\text{S-biTISP})_2$ (**2**) and $\text{Rh}_2(\text{S-PTAD})_4$ (**3**) (Figure 2.2).

Figure 2.2 Chiral dirhodium carboxylate catalysts developed by the Davies group

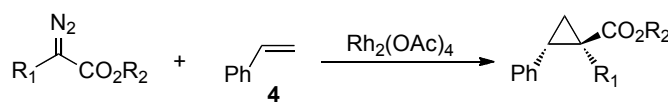


2.1.1 Intermolecular cyclopropanation

The transition metal catalyzed decomposition of alkyldiazoacetate in the presence of alkenes has been an excellent method for the synthesis of cyclopropanes.^{1a} Although many catalysts,^{3,4,6-7} particularly copper catalysts in the early days, had been successfully applied to the intermolecular version of this transformation, dirhodium catalysts have achieved very limited success. The major limitation is that, in general, the reactions are not particularly stereoselective, as can be seen in the $\text{Rh}_2(\text{OAc})_4$ -catalyzed cyclopropanation of ethyl diazoacetate (**5**) with styrene. The diastereomeric ratio of cyclopropane **8** was only 1.8:1 slightly favoring the *trans* isomer (Table 2.1, entry 1). The

introduction of donor/acceptor substituted carbenoids, however, completely changed this poor selectivity. The reactions of methyl phenyldiazoacetate (**6**) and methyl styryldiazoacetate (**7**) (the two most widely used donor/acceptor carbenoid precursors) with styrene produced cyclopropanes **9** and **10** with >30:1 and >50:1 diastereomeric ratio, respectively (entries 2 and 3).⁹

Table 2.1 Effect of rhodium carbenoid structure on the cyclopropanation diastereoselectivity



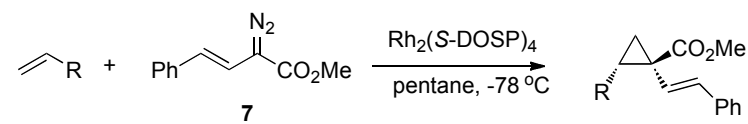
entry	R ₁	R ₂	diazo	product	<i>E/Z</i> ratio
1	H	Et	5	8	1.8:1
2	Ph	Me	6	9	>30:1
3	<i>trans</i> -PhCH=CH	Me	7	10	>50:1

When dirhodium tetraproline, Rh₂(*S*-DOSP)₄, was used as catalyst, the cyclopropanation of styryldiazoacetate **7** with a wide range of monosubstituted alkenes generated cyclopropanes **10** and **18–24** with very high diastereoselectivity (dr 15:1 to >40:1), as well as high enantioselectivity (90–98% ee) (Table 2.2).¹⁰ Aryl groups containing either electron withdrawing (such as Cl) or electron donating groups (such as OMe) were all tolerated in the reaction (entries 1–3). The reaction with simple alkenes also worked very well (entries 4–8). Because of the catalyst's high reactivity and excellent solubility in the hydrocarbon solvent, the reactions were able to be conducted at -78 °C.

Rh₂(*S*-DOSP)₄-catalyzed cyclopropanation of 1,1'-disubstituted alkene **25** with phenyldiazoacetate **6** produced tetrasubstituted cyclopropane **26** with an *E/Z* ratio of

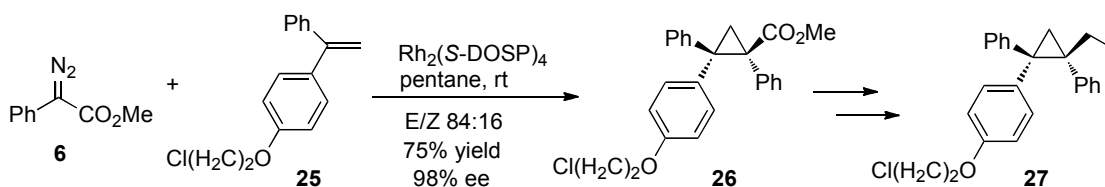
84:16, the major diastereomer was isolated in 75% yield and 98% ee (Scheme 2.1).¹¹ Considering that the diastereocontrol was caused by the distant para substituents on the aryl groups, the high diastereoselectivity of this reaction is remarkable. Cyclopropane **26** was transformed into the Tamoxifen analogue **27** in a few standard steps.¹²

Table 2.2 Cyclopropanation of styryldiazoacetate **7** with alkenes



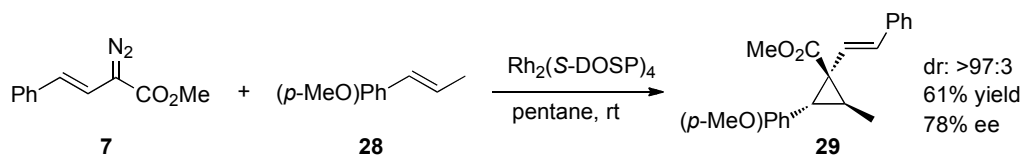
entry	R		temp, °C	product	ee, %	yield, %
1	C ₆ H ₅	4	-78	10	98	68
2	<i>p</i> -ClC ₆ H ₄	11	-78	18	>97	70
3	<i>p</i> -MeOC ₆ H ₄	12	-78	19	90	41
4	AcO	13	-78	20	95	26
5	EtO	14	-78	21	93	65
6	<i>n</i> -Bu	15	25	22	>90	63
7	Et	16	25	23	>95	65
8	<i>i</i> -Pr	17	25	24	95	58

Scheme 2.1 Cyclopropanation of phenyldiazoacetate **6** with 1,1-disubstituted alkene



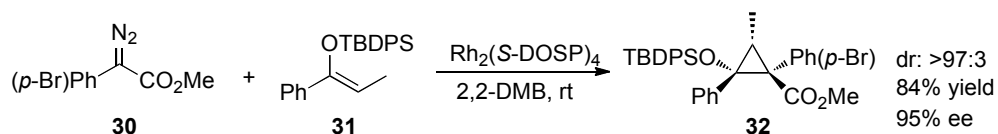
Although a *trans* double bond is generally considered to be too sterically crowded for cyclopropanation,¹⁰ due to the electronic activation by the *p*-methoxy group, *trans*-anethole (**28**) reacted with styryldiazoacetate **7** to smoothly generate tetrasubstituted cyclopropane **29** in 61% yield, >97:3 dr and 78% ee (Scheme 2.2).¹⁴

Scheme 2.2 Cyclopropanation of styryldiazoacetate **7** with *trans*-alkene

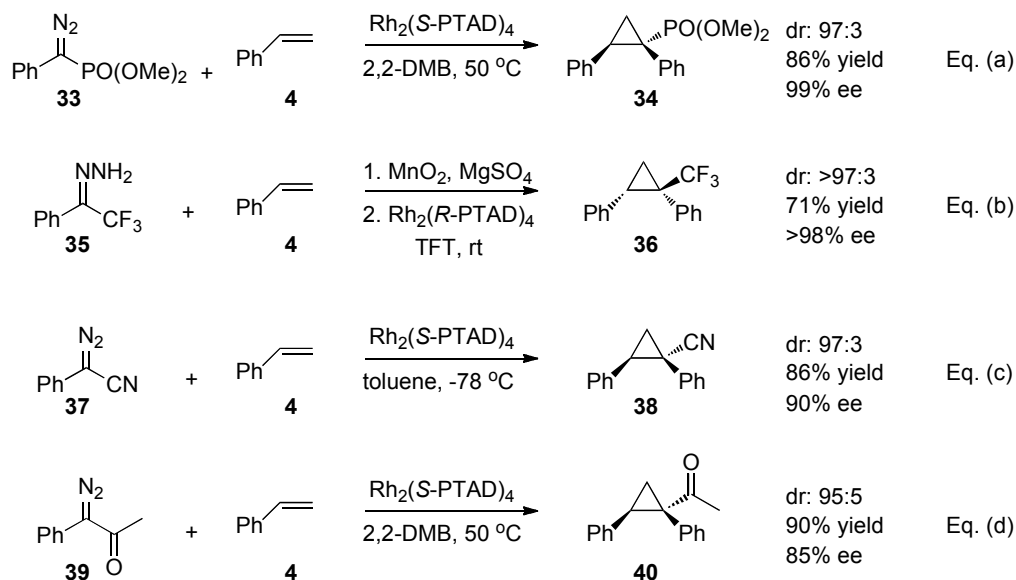


Cyclopropanation by aryldiazoacetates and electron rich trisubstituted alkenes were also extensively studied.¹⁵ Rh₂(S-DOSP)₄-catalyzed reaction of *p*-bromophenyldiazoacetate (**30**) with silyl enol ether **31** generated pentasubstituted cyclopropane **32** as a single diastereomer in 84% isolated yield and 95% ee (Scheme 2.3). This stereoselective synthesis of highly functionalized cyclopropanes effectively broadened the scope of the cyclopropanation chemistry.

Scheme 2.3 Cyclopropanation of *p*-bromophenyldiazoacetate **30** with trisubstituted alkene



In recent years, donor/acceptor carbenoids were also expanded to include diazo substrates containing phosphate, trifluoromethyl, cyano, and ketones as the electron withdrawing groups. Rh₂(PTAD)₄-catalyzed cyclopropanation reactions of these carbenoid precursors with styrene are summarized in Scheme 2.4. High diastereo- and enantioselectivity were routinely observed in these reactions.¹⁶⁻¹⁹

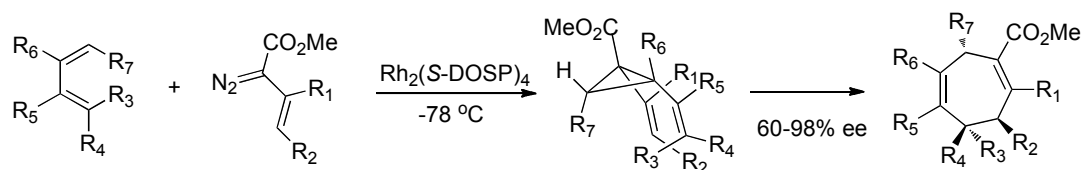
Scheme 2.4 Cyclopropanation of other donor/acceptor carbenoid precursors with styrene


Asymmetric synthesis of highly functionalized cycloheptadienes was achieved through a tandem cyclopropanation/Cope rearrangement of vinyl diazoacetates and dienes (Scheme 2.5).²⁰ The initial cyclopropanation step produces *cis*-divinylcyclopropane in a highly selective manner, which then undergoes a Cope rearrangement through a boat transition state to form a cycloheptadiene with full control of stereochemistry at three stereogenic centers. A variety of dienes, including cyclopentadiene and furan can be used for this transformation.

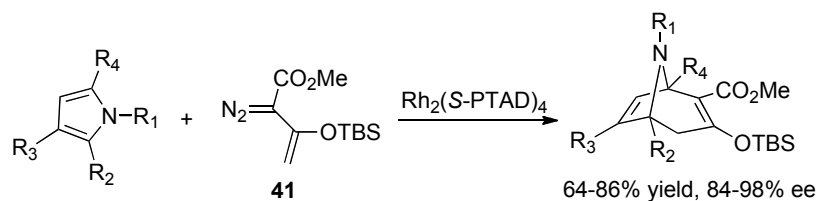
A recent development of the tandem cyclopropanation/Cope rearrangement is the asymmetric synthesis of tropanes by $\text{Rh}_2(\text{S-PTAD})_4$ -catalyzed [4+3] cycloaddition between siloxyvinyl diazoacetate (**41**) and pyrroles.²¹ A variety of highly substituted tropanes were synthesized in 64–86% yield and 84–98% ee (Scheme 2.6). The [4+3] cycloaddition between diazo **41** and diene **42** also leads to the rapid generation of the

cycloheptane core (**43**) of (-)-5-*epi*-vibsanin (**44**) in 65% yield and 90% ee (Scheme 2.7).²²

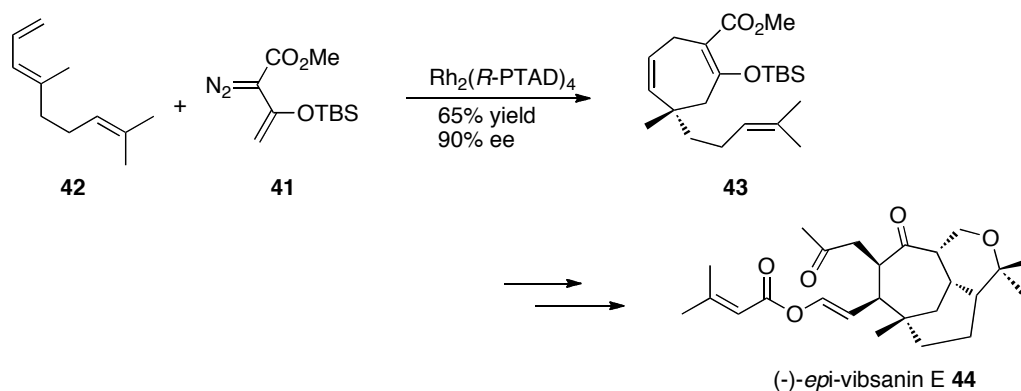
Scheme 2.5 Tandem cyclopropanation/Cope rearrangement between vinyldiazoacetate and diene



Scheme 2.6 [4+3] cycloaddition between siloxyvinyldiazoacetate **41** and pyroles



Scheme 2.7 [4+3] cycloaddition in the synthesis of (-)-5-*epi*-vibsanin E



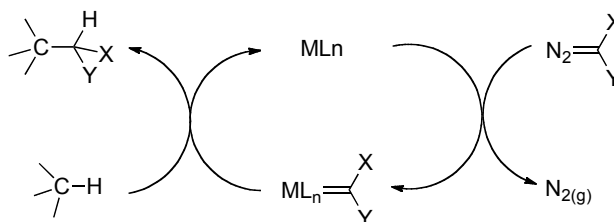
2.1.2 Intermolecular C–H insertion

Carbon–hydrogen bond (C–H) functionalization has been extensively studied in the past two decades, and considerable progress has been achieved.^{1,23} Distinct from the traditional approach of conducting transformations on the pre-existing functional groups, C–H functionalization relies on the selective modification of ubiquitous C–H bonds in organic molecules. This approach has the potential to dramatically shorten the complex molecule synthesis sequence and improve the synthetic efficiency and atom economy. However, in order to be synthetically practical, C–H functionalization has to overcome two fundamental challenges: 1. The inert nature of most C–H bonds; 2. The selective functionalization of a single C–H bond within a complex molecule. One strategy to overcome these two challenges is to use transition metals to react with the C–H bonds and produce far more reactive C–M bonds which can then be converted to new functional groups under mild conditions.²³ In order to achieve selectivity, directing groups are needed to bind to the metal center and selectively deliver the catalyst to the proximal C–H bond. Another strategy that has been shown to be very successful is to use highly electrophilic carbenoid intermediate generated from the metal (particularly rhodium) catalyzed decomposition of diazo compounds to directly insert into the C–H bonds (Figure 2.3).¹

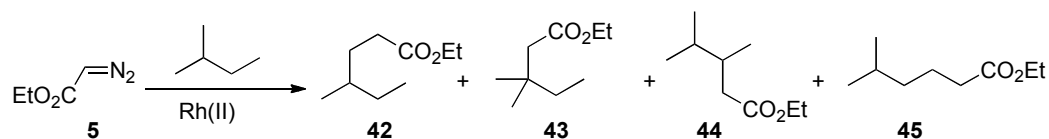
The traditional acceptor carbenoids and acceptor/acceptor carbenoids have been successfully applied to the intramolecular C–H insertion transformations.^{1d} Particularly, chiral dirhodium carboxamidates catalyzed decomposition of alkyl diazoacetates has been extensively studied by Doyle and co-workers. The generated carbenoids undergo

intramolecular C–H insertion to form five-member ring with high diastereoselectivity and enantioselectivity. However, these conventional carbenoids are too reactive for highly chemoselective intermolecular C–H insertion. Also, carbene dimerization is a favorable competing side reaction. One example is the rhodium catalyzed C–H insertion of ethyl diazoacetate (**5**) into 2-methylbutane (Table 2.3).²⁴ All of the four possible C–H insertion products were formed, although the catalysts had a profound influence on the product distribution.

Figure 2.3 Carbenoid induced C–H insertion

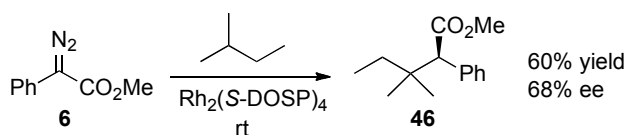


The donor/acceptor carbenoids, however, are much more chemoselective and less prone to carbene dimerization than the conventional acceptor carbenoids and acceptor/acceptor carbenoids.²⁵ Combined with chiral dirhodium catalysts, particularly $Rh_2(S-DOSP)_4$, a wide range of highly diastereoselective and enantioselective intermolecular C–H insertion reactions have been successfully developed.^{1b,8c} An illustrative example of the distinguished chemoselectivity in these systems is the $Rh_2(S-DOSP)_4$ -catalyzed C–H insertion of phenyldiazoacetate (**6**) with 2-methylbutane (Scheme 2.8).²⁶ Selective insertion into the tertiary C–H bond produced compound **46** in 60% yield and 68% ee.

Table 2.3 Intermolecular C–H insertion of ethyl diazoacetate with 2-methylbutane

entry	Rh(II)	ratio of 42:43:44:45
1	Rh ₂ (OAc) ₄	5:8:90:1
2	Rh ₂ (9-trp) ₄	18:18:27:37
3	Rh ₂ (TFA) ₄	5:25:66:4

Rh₂(9-trp)₄: Dirhodium(II) tetrakis(9-triptycenecarboxylate)

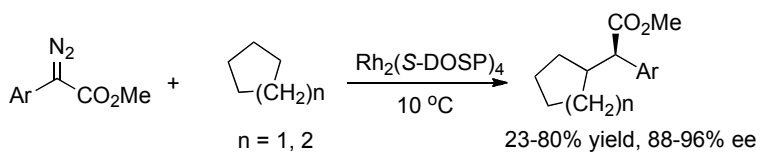
Scheme 2.8 C–H insertion of phenyldiazoacetate with 2-methylbutane

High enantioselectivity was routinely observed in the Rh₂(S-DOSP)₄-catalyzed C–H insertion of aryldiazoacetates with cycloalkanes (Table 2.4).²⁶ Either *para*-, *meta*-, or *ortho*-substituted aryldiazoacetates all reacted efficiently with the cycloalkanes and produced compounds **49–54** in 47–80% yield and 90–96% ee.

Rhodium catalyzed intermolecular C–H insertion of donor/acceptor carbenoids also provides valuable new strategies for organic synthesis. For example, C–H insertion adjacent to oxygen produces compounds that would be commonly derived from an Aldol reaction (Scheme 2.9).^{27–29} C–H insertion adjacent to nitrogen produces compounds that would be commonly derived from the Mannich reaction.^{30–33} Some excellent

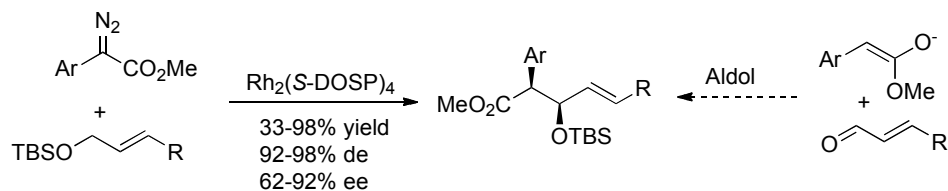
demonstrations of this novel strategy include the concise and highly stereoselective synthesis of drug motifs Venlafaxine (**57**) (Scheme 2.10) and Ritalin (**59**) (Scheme 2.11).

Table 2.4 C–H insertion of aryldiazoacetates with cycloalkanes

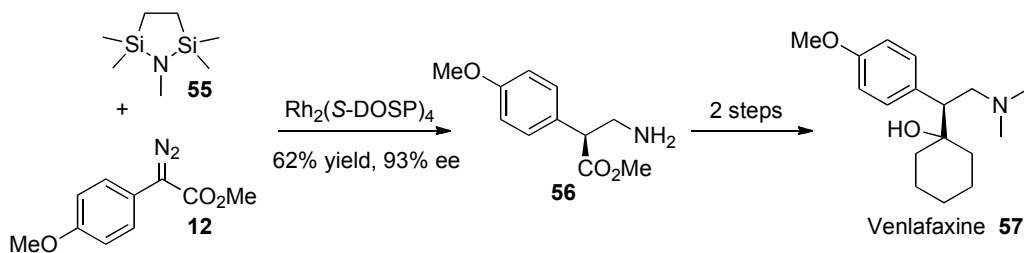


entry	Ar	n	product	yield, %	ee, %
1	C ₆ H ₅	1	49	72	96
2	<i>p</i> -ClC ₆ H ₄	1	50	70	95
3	C ₆ H ₅	2	51	80	95
4	<i>p</i> -ClC ₆ H ₄	2	52	76	94
5	<i>o</i> -ClC ₆ H ₄	2	53	81	90
6	<i>m</i> -ClC ₆ H ₄	2	54	47	94

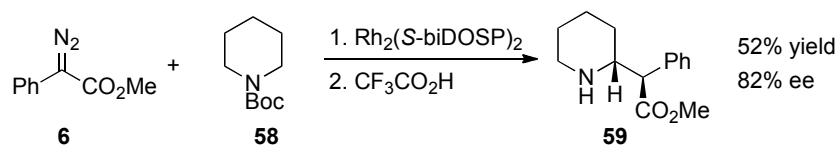
Scheme 2.9 C–H insertion of aryldiazoacetates adjacent to oxygen



Scheme 2.10 Asymmetric synthesis of Venlafaxine

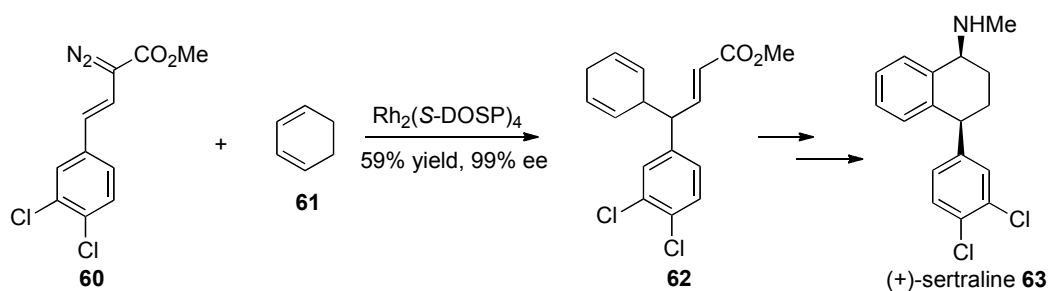


Scheme 2.11 Asymmetric synthesis of Ritalin



When vinyl diazoacetates were used as the donor/acceptor carbenoid precursor, combined C–H activation/Cope rearrangement occurred.³⁴⁻³⁹ Extremely high enantioselectivity is characteristic of this type of transformation. $\text{Rh}_2(\text{S-DOSP})_4$ -catalyzed reaction of methyl 3,4-dichlorophenylvinyl diazoacetate (**60**) with 1,3-cyclohexadiene (**61**) produced the combined C–H activation/Cope rearrangement product **62** in 59% yield and 99% ee, which could be converted into (+)-sertraline using standard operations (Scheme 2.12).³⁴

Scheme 2.12 Synthesis of (+)-sertraline



The $\text{Rh}_2(\text{R-DOSP})_4$ -catalyzed reaction of vinyl diazoacetate **64** with racemic dihydronaphthalene **65** involved an enantiodivergent process (Scheme 2.13).⁴⁰ Only (*R*)-**65** reacted with the carbenoid through combined C–H activation/Cope rearrangement to form compound **66** in 90% ee with the concomitant establishment of all three stereogenic centers. On the other hand, (*S*)-**65** reacted with the carbenoid to form cyclopropane **67**.

This remarkable reactivity has been applied to the highly efficient synthesis of a number of natural products derived from the West Indian gorgonian coral *Pseudopterogorgia elisabethae*, such as (+)-erogorgiaene (**68**), (-)-colombiasin A (**69**) and (-)-elisapterosin B (**70**) (Figure 2.4).⁴⁰⁻⁴²

Scheme 2.13 Enantiodivergent reaction between vinyl diazoacetate **64** with racemic dihydronaphthalene **65**

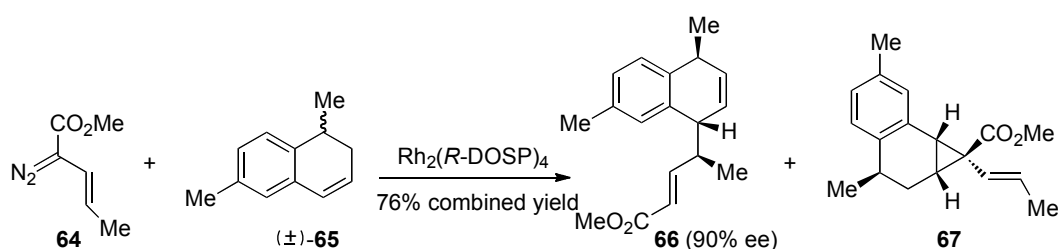
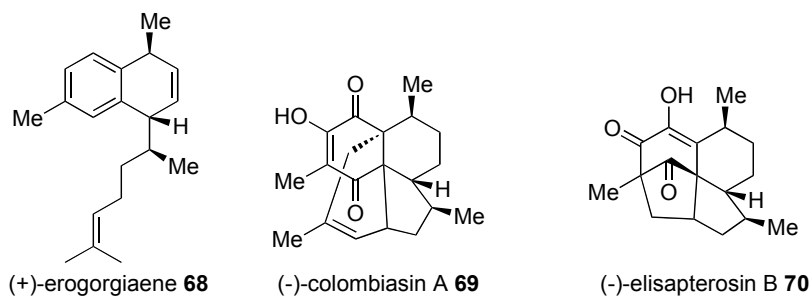


Figure 2.4 Natural products synthesized by the combined C–H activation/Cope rearrangement strategy



2.1.3 Ylide formation

The highly electrophilic carbenoid intermediate derived from the transition metal catalyzed decomposition of diazo compounds can readily react with heteroatoms including oxygen, sulfur, and nitrogen to form ylides. The generated ylides are usually very reactive and can further undergo a wide variety of transformations, such as X–H

insertion (X can be oxygen, nitrogen and sulfur), [2,3]-sigmatropic rearrangement, Stevens rearrangement, and 1,3-dipolar cycloaddition.^{1,43}

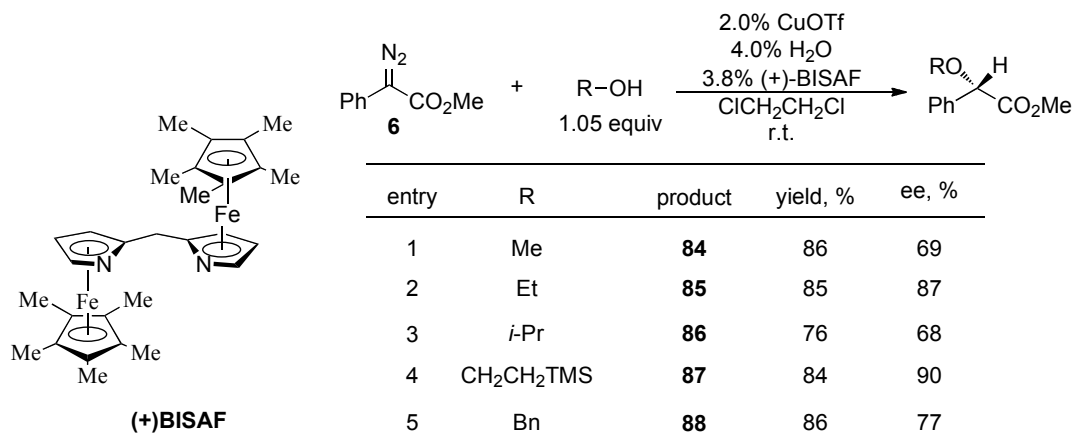
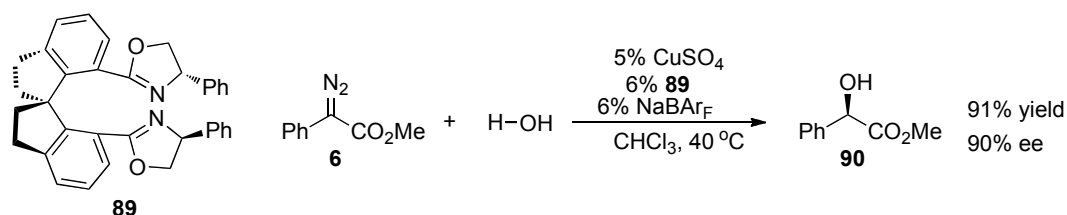
Donor/acceptor carbenoids have been successfully used for the highly enantioselective O–H and N–H insertions. The copper/planar-chiral ligand (-)-bpy* catalyst system developed by Fu and co-workers accomplished the N–H insertion of a wide range of aryldiazoacetates with carbamate **71** in good yield and enantioselectivity (Table 2.5).⁴⁴ AgSbF₆ works as co-catalyst to generate the halide-free copper complex. This method provides an efficient entry for the asymmetric synthesis of α -amino acids.

Table 2.5 Asymmetric N–H insertion of aryldiazoacetates with carbamate

entry	Ar	diazo	product	yield, %	ee, %
1	C ₆ H ₅	72	79	75	94
2	<i>p</i> -MeOC ₆ H ₄	73	80	61	95
3	<i>p</i> -(NHBoc)C ₆ H ₄	74	81	77	91
4	2-MeC ₆ H ₄	75	82	71	81
5	3-MeC ₆ H ₄	76	83	75	88
6	2-naphthyl	77	84	73	91
7	3-thienyl	78	85	48	80

(-)-BPY*

The copper/planar-chiral ligand (+)-BISAF catalyst system was effective in the asymmetric O–H insertion of phenyldiazoacetate **6** with a variety of alcohols, such as methanol, ethanol, and benzylalcohol.⁴⁵ The highest enantioselectivity was obtained with 2-trimethylsilylethanol as substrate, and the O–H insertion product **87** was formed in 84% yield and 90% ee (Table 2.6).

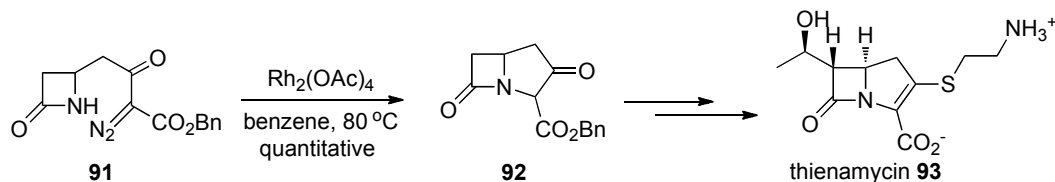
Table 2.6 Asymmetric O–H insertion of phenyldiazoacetate **6** with alcohols**Scheme 2.14** Asymmetric O–H insertion of phenyldiazoacetate **6** with water

Highly enantioselective O–H insertion of phenyldiazoacetate **6** with water was also achieved with the copper/chiral spirobox (**89**) catalyst system by Zhou and co-workers.⁴⁶ α -hydroxyphenylacetate (**90**) was formed in 91% yield and 90% ee (Scheme 2.14).

Dirhodium carboxylates have been introduced as highly efficient catalysts in the carbenoid O–H and N–H insertion reactions since 1970s.⁴⁷⁻⁴⁸ The most notable application is the Rh₂(OAc)₄-catalyzed intramolecular insertion into a β -lactam N–H bond, a key step in the Merck synthesis of thienamycin (Scheme 2.15).⁴⁹ Bicyclic ketoester **92** was formed in quantitative yield. However, compared with the success of the asymmetric cyclopropanation and C–H insertion reactions, chiral dirhodium catalysts have not proved to be effective in the asymmetric O–H and N–H insertion reactions.⁵⁰ The reaction of phenyldiazoacetate **6** with alcohols catalyzed by various chiral dirhodium

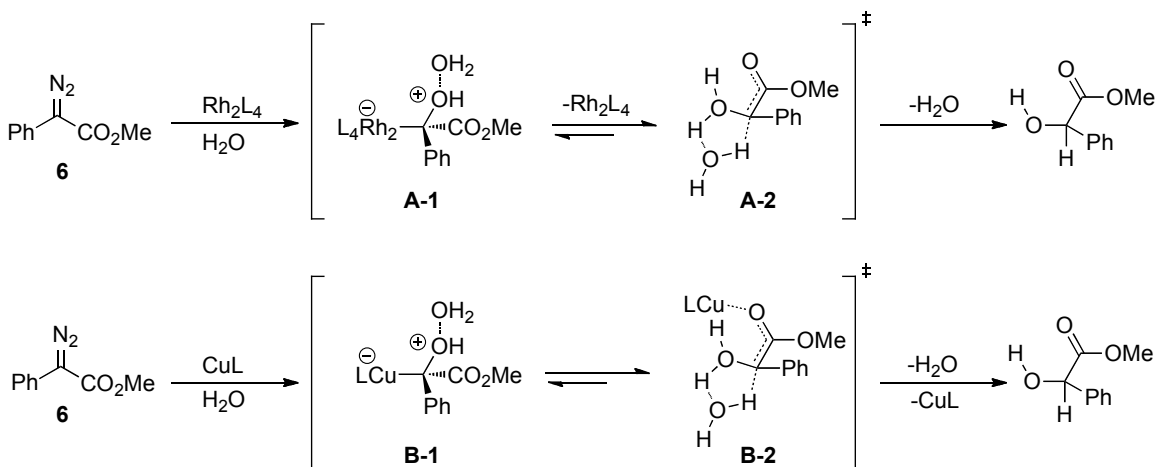
carboxylates produced the O–H insertion products in excellent yield, while all in racemic form.⁵¹

Scheme 2.15 Intramolecular N–H insertion of diazoketoester **91**



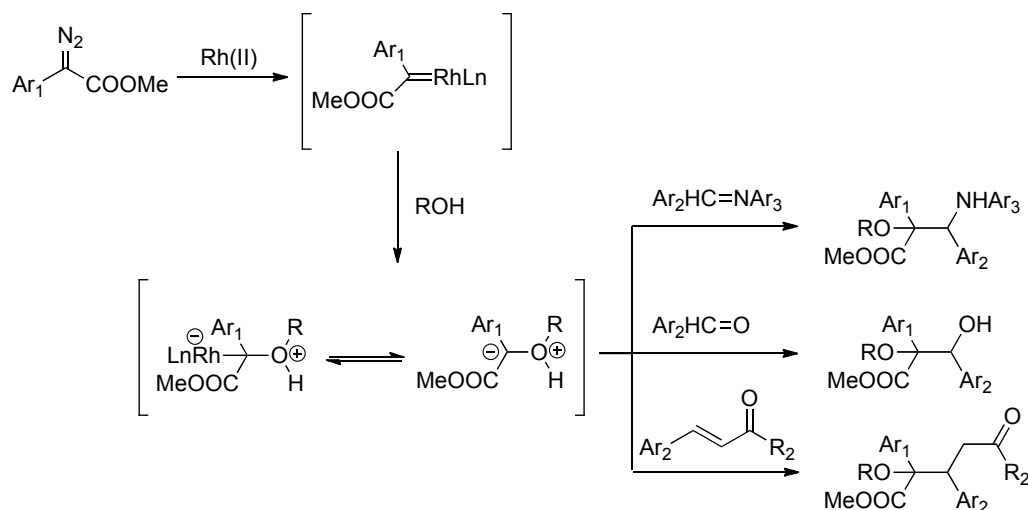
The dramatic difference between chiral copper and dirhodium catalysts on the asymmetric O–H insertion of phenyldiazoacetate **6** was studied by Yu using density functional theory (DFT) calculations with the B3LYP functional.⁵² The computational results showed that a water-catalyzed [1,2]-proton shift process was much more favorable than the widely accepted direct [1,2]-proton shift with both catalysts (Scheme 2.16). The free ylide **A-2** is the reactive precursor for the [1,2]-proton shift in the Rh(II)-catalyzed O–H insertion, while the copper-associated ylide **B-2** is the reactive precursor for the [1,2]-proton shift in the Cu-catalyzed O–H insertion. The neutral character of dirhodium catalyst might be responsible for its easy dissociation from the ylide intermediate.

Scheme 2.16 Rh(II) and Cu catalyzed O–H insertion



Besides the O–H and N–H insertion, donor/acceptor carbenoids also found broad application in the three-component reactions with alcohols and aldehydes (or imines).⁵³⁻⁵⁷ The oxonium ylide derived from the aryldiazoacetate and alcohol has proper stability to “delay” the [1,2]-proton shift and works as nucleophile to attack imine,^{54,56} aldehyde,⁵⁵ or α,β -unsaturated carbonyl compounds (Scheme 2.17).⁵⁷ A variety of compounds containing one quaternary center were formed with very high diastereoselectivity. In the case of using a chiral co-catalyst to activate the imine or carbonyl, high enantioselectivity was also achieved. In most of these reactions, $\text{Rh}_2(\text{OAc})_4$ was used as catalyst to decompose the aryldiazoacetates. Although it was proposed that the equilibrium of the metal-associated ylide and the free ylide exist during the reaction, racemic product was formed when chiral dirhodium catalyst such as $\text{Rh}_2(S\text{-DOSP})_4$ was used.⁵³

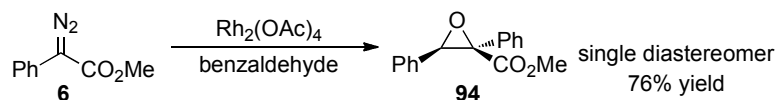
Scheme 2.17 Three component reactions of aryldiazoacetates



The reaction of donor/acceptor carbenoids with aldehydes is a highly diastereoselective method for the synthesis of epoxides.⁵⁸ Trisubstituted epoxide **94** was formed as a single diastereomer in 76% yield from the reaction of phenyldiazoacetate **6** with benzaldehyde

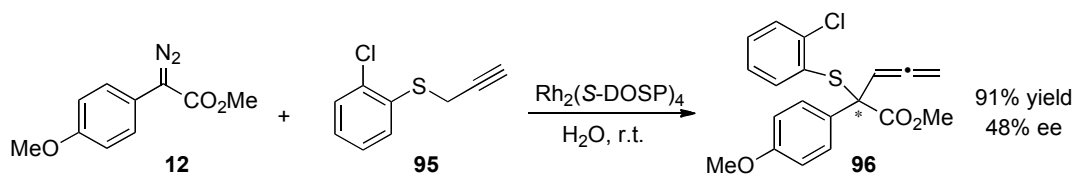
(Scheme 2.18). In a similar fashion to the O–H insertion and three-component reaction involving oxonium ylides derived from donor/acceptor carbenoids, chiral dirhodium catalysts did not have any asymmetric influence on the epoxide formation. With $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst, compound **94** was formed in racemic form.

Scheme 2.18 The epoxide formation with phenyldiazoacetate **6**



Donor/acceptor carbenoids have also been used for the sulfur ylide associated transformations, in which chiral dirhodium catalysts usually give moderate enantioselectivity on the product formation.⁵⁹⁻⁶⁰ $\text{Rh}_2(\text{S-DOSP})_4$ -catalyzed sulfur ylide formation/[2,3]-sigmatropic rearrangement between *p*-methoxyphenyldiazoacetate **12** and aryl allyl sulfide **95** produced allene **96** bearing one quaternary center in 91% yield and 48% ee (Scheme 2.19).⁵⁹

Scheme 2.19 Sulfur ylide formation/[2,3]-sigmatropic rearrangement with aryl diazoacetate **12**



Compared with its outstanding performance in the intermolecular cyclopropanation and C–H insertion reactions, it is surprising that $\text{Rh}_2(\text{S-DOSP})_4$ has poor asymmetric influence in the donor/acceptor carbenoid ylide transformations. Although the dissociation of metal to form the free ylide intermediate is the most reasonable

explanation, how to prevent this dissociation process and achieve high stereoselectivity remains a challenge.

2.2 Results and discussion

2.2.1 New discovery

Extensive experimental and calculation studies show that the C–H functionalizations by donor/acceptor substituted rhodium carbenoids proceed through a concerted nonsynchronous manner, with positive charge buildup on the carbon to be functionalized.²⁵ A site that can stabilize this positive charge will be reactive toward C–H functionalization. Meanwhile, steric influence is also critical. If the site is too crowded, C–H functionalization will be blocked, even when the site is electronically activated.

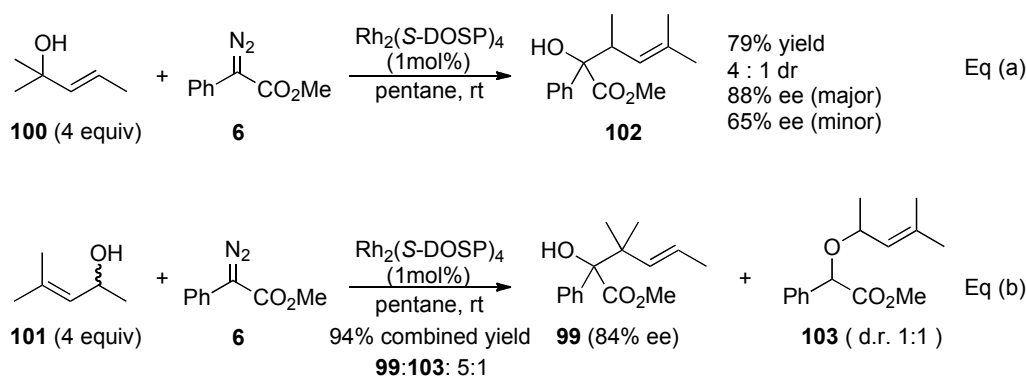
During the study of selective C–H functionalization of the tertiary C–H bonds with donor/acceptor carbenoids, (*E*)-4-methylpent-2-ene (**97**) was chosen as substrate. It contains two allylic C–H bonds that could be functionalized, and it was anticipated that the allylic tertiary C–H bond at 4-position would be more reactive than the allylic primary C–H bond at 1-position. The reaction of **97** with phenyldiazoacetate **6** catalyzed by Rh₂(*S*-DOSP)₄ worked smoothly to give one product in 34% yield, which was initially assigned as compound **98** largely based on its ¹H NMR spectrum (Scheme 2.20). This assignment was also consistent with the original hypothesis that the allylic tertiary C–H bond would be more reactive. However, upon very careful analysis of its ¹³C NMR spectrum, two questions arose: 1. The chemical shift of the benzylic tertiary carbon was ~80 ppm which is further down field than that of similar compounds (~60 ppm),⁶¹ 2. This carbon signal had similar intensity as the carbonyl carbon which suggested it could be a

quaternary carbon. Indeed, a follow-up DEPT spectrum confirmed it was a quaternary carbon. Combined with HRMS spectrum and D₂O exchange experiment, this product was determined to be compound **99**, containing a tertiary hydroxy group at the benzylic position (eventually, compound **98** was isolated in 10% yield from the reaction of **6** with another batch of alkene **97**. Its ¹³C NMR spectrum showed that the chemical shift of the benzylic carbon was 61.6 ppm).

Scheme 2.20 Reaction of phenyldiazoacetate **6** with (*E*)-4-methylpent-2-ene **97**



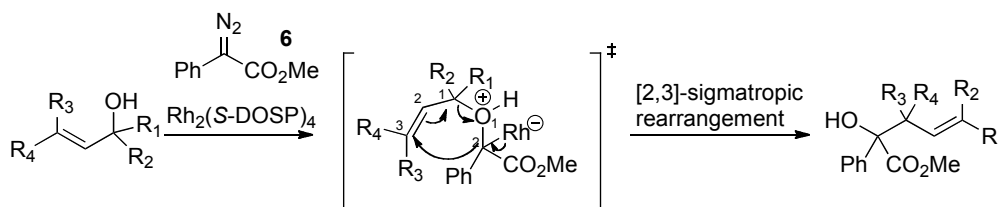
Scheme 2.21 Reaction of phenyldiazoacetate **6** with allylic alcohols



Considering the possibility that this unexpected product **99** might result from an alcohol impurity in the sample of alkene **97**, allylic alcohol **100** and **101** were tested in reactions with phenyldiazoacetate **6** (Scheme 2.21). Interestingly, the reaction of alcohol

100 with **6** produced another α -hydroxycarboxylate **102** as a 4:1 diastereomeric mixture in 79% combined yield and 88% ee for the major diastereomer and 65% ee for the minor diastereomer (Eq (a)). Meanwhile, no O–H insertion product was detected in this reaction. The reaction of alcohol **101** with **6**, however, produced a 5:1 mixture of compound **99** and the O–H insertion product **103** in 94% combined yield (Eq (b)). The major product, compound **99** was formed in 84% ee. Based on these results, it was concluded that allylic alcohol **101** was the impurity in the sample of alkene **97**. A reasonable mechanism for this reaction is shown in Scheme 2.22. The reaction of **6** with alcohol **100** and **101** went through a tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement process and produced α -hydroxycarboxylate **102** and **99**, respectively.

Scheme 2.22 Tandem ylide formation/[2,3]-sigmatropic rearrangement between allylic alcohol and phenyldiazoacetate



Since the O–H insertion between carbenoid and alcohol has been a well-established reaction, it is very surprisingly that the reaction of phenyldiazoacetate **6** with allylic alcohol **100** or **101** gave the [2,3]-sigmatropic rearrangement product as the major product. Moreover, considering the fact that chiral dirhodium catalysts always have very low asymmetric induction in the O–H insertion reactions, it is more interesting that the [2,3]-sigmatropic rearrangement product **99** and **102** were formed with good

enantioselectivity (65–88% ee). In order to understand this newly discovered transformation, a series of detailed studies were undertaken.

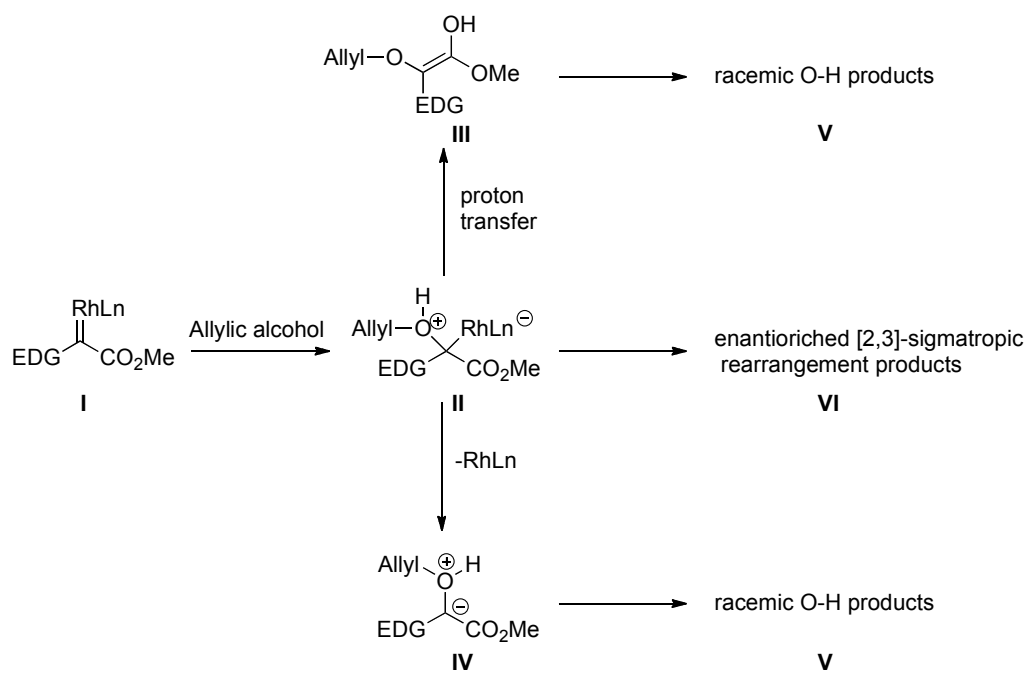
2.2.2 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols –generation of one stereogenic center

It is generally accepted that the formation of achiral enol intermediate **III** through proton transfer process and the formation of free ylide **IV** through the dissociation of rhodium catalyst from metal associated ylide **II** are the major causes of the racemic O–H insertion product formation in rhodium catalyzed carbenoid O–H insertions (Scheme 2.23).⁵² It would be reasonable to propose that the newly discovered tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between the allylic alcohol and phenyldiazoacetate **6** involves a relatively stable metal associated ylide **II** as the major intermediate. Two factors would favor its formation: 1. a highly substituted allyl moiety would effectively stabilize the positive charge in ylide **II** and subsequently suppress the achiral enol **III** formation. 2. nonpolar solvents, such as 2,2-dimethylbutane and pentane, could suppress the dissociation of rhodium catalyst from ylide **II** and subsequently suppress the free ylide **IV** formation.

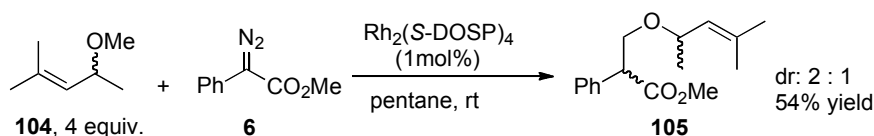
Considering these factors, the reaction of 4-methoxy-2-methylpent-2-ene (**104**) and phenyldiazoacetate **6** in pentane would have better selectivity favoring the [2,3]-sigmatropic rearrangement than the reaction of alcohol **101** and **6**. Compound **104** contains similar highly substituted allyl moiety as **101**, but does not have the free OH group for the competing O–H insertion reaction, these structural features would make the formation of the metal associated ylide intermediate more favorable. Unfortunately,

instead of forming the [2,3]-sigmatropic rearrangement product, the reaction of **104** and **6** in pentane with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst produced the C–H insertion product **105** as a 2:1 diastereomeric mixture in 54% yield (Scheme 2.24). Even though it is a failure in terms of the desired rearrangement transformation, it is still a most compelling example of the complementary influence of steric and electronic effects on the regioselectivity of C–H functionalization. The allylic C–H bond of **104** is electronically highly activated, but, due to its overwhelming steric influence with donor/acceptor carbenoids, C–H functionalization at the methyl group preferentially occurs.

Scheme 2.23 Rationale of the reaction of allylic alcohol with donor/acceptor carbenoids



Scheme 2.24 Reaction of allyl ether **105** with phenyldiazoacetate **6**



After finding out that the hydroxyl group was necessary for the tandem ylide formation/[2,3]-sigmatropic rearrangement reaction, our focus turned to the use of allylic alcohols as starting material. The optimal reaction conditions favoring the formation of [2,3]-sigmatropic rearrangement product, as well as the systematic study including the effects of dirhodium catalyst, solvent, substrates, and carbenoids on the reaction selectivity were all extensively explored.

2.2.2.1 Optimal reaction conditions

In order to establish the optimal reaction conditions for the formation of [2,3]-sigmatropic rearrangement products, the reaction of alcohol **101** and phenyldiazoacetate **6** was chosen as a standard reaction. The reaction outcomes under different conditions are summarized in Table 2.7. The solvent had a significant effect on the ratio of [2,3]-sigmatropic rearrangement product **99** and O-H insertion product **103** (entries 1-3). Using pentane as solvent, the ratio of **99/103** was 5:1. However, it decreased to 3:1 when toluene was used as solvent, and further decreased to 1:1 when more polar solvents such as dichloromethane were used. The enantioselectivity of **99** also decreased from 84% ee to 74% ee when the solvent was changed from pentane to dichloromethane, which was consistent with previous observation that $\text{Rh}_2(\text{S-DOSP})_4$ had better asymmetric induction in a nonpolar hydrocarbon solvent.¹⁰ The other two excellent chiral dirhodium catalysts

for the reactions of aryldiazoacetates are $\text{Rh}_2(\text{S-PTAD})_4$ and $\text{Rh}_2(\text{S-biTISP})_2$. But neither of these were as effective as $\text{Rh}_2(\text{S-DOSP})_4$ at favoring the formation of **99** over **103** (entries 4-5). Compound **99** was formed in only 37% ee with the opposite major enantiomer in $\text{Rh}_2(\text{S-biTISP})_2$ -catalyzed reaction. Interestingly, the common achiral dirhodium catalysts, such as $\text{Rh}_2(\text{OAc})_4$, $\text{Rh}_2(\text{OOct})_4$ and the very electrophilic $\text{Rh}_2(\text{TFA})_4$ all strongly favored the O–H insertion product formation (entries 6-9). The only exception was $\text{Rh}_2(\text{esp})_2$, developed by Du Bois,⁶² which slightly favored the [2,3]-sigmatropic rearrangement product formation with the ratio of **99/103** as 2:1 (entry 11). In all of these reactions, O–H insertion product **103** was formed as a 1:1 diastereomeric mixture, and both diastereomers had <10% ee in the chiral catalyst catalyzed reactions.

After finding out that $\text{Rh}_2(\text{S-DOSP})_4$ and pentane gave the best selectivity favoring the [2,3]-sigmatropic rearrangement product formation, the influence of temperature and stoichiometries were also studied (Table 2.8). The reaction of phenyldiazoacetate **6** and 4 equiv. of racemic **101** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst and pentane as solvent at room temperature gave a slightly higher ratio of **99/103** (6:1), compared with the reaction with only 2 equiv. of racemic **101** (entry 2). Further increasing the amount of **101** to 10 equiv. decreased this ratio to 4:1 (entry 3). The temperature also had slight influence on the reaction selectivity (entry 4-5). The reaction at either 40 °C or 0 °C produced a 4:1 mixture of **99** and **103**. Notably, under all of these conditions, compound **99** was isolated in very good enantiomeric excess (81-91% ee).

Table 2.7 Effects of dirhodium catalyst and solvent on the ratio of **99/103**

Reaction scheme showing the reaction of allylic alcohol **101** (2 equiv.) and diazo ester **6** with Rh(II) (1 mol%) in pentane at room temperature for 1 hour, yielding products **99** and **103**.

entry	Rh(II)	solvent	99/103 ^a	yield of (99 + 103), % ^b	ee of 99 , % ^c
1	Rh ₂ (S-DOSP) ₄	pentane	5:1	94	84
2	Rh ₂ (S-DOSP) ₄	toluene	3:1	75	83
3	Rh ₂ (S-DOSP) ₄	CH ₂ Cl ₂	1:1	65	74
4	Rh ₂ (S-PTAD) ₄	pentane	2:1	86	78
5	Rh ₂ (S-biTISP) ₂	pentane	1:1	69	-37
6	Rh ₂ (OAc) ₄	pentane	1:6	82	
7	Rh ₂ (OOct) ₄	pentane	1:5	94	
8	Rh ₂ (TFA) ₄	pentane	1:4	92	
9	Rh ₂ (TPA) ₄	CH ₂ Cl ₂	1:8	79	
10	Rh ₂ (OPiv) ₄	pentane	1:1	67	
11	Rh ₂ (esp) ₂	pentane	2:1	49	

^a Determined by crude ¹H-NMR. ^b Isolated yield. ^c Determined by chiral HPLC.

Table 2.8 Effect of temperature and the amount of allylic alcohol on the ratio of **99/103**

Reaction scheme showing the reaction of allylic alcohol **101** and diazo ester **6** with Rh₂(S-DOSP)₄ (1 mol%) in pentane, yielding products **99** and **103**.

entry	101	temp.	99/103 ^a	yield of (99 + 103), % ^b	ee of 99 , % ^c
1	2 equiv.	rt	5:1	94	84
2	4 equiv.	rt	6:1	86	86
3	10 equiv.	rt	4:1	77	88
4	4 equiv.	0 °C	4:1	81	91
5	4 equiv.	40 °C	4:1	99	81

^a Determined by crude ¹H-NMR. ^b Isolated yield. ^c Determined by chiral HPLC.

Based on these results in Table 2.7 and 2.8, it was concluded that the optimal reaction conditions for the selective formation of [2,3]-sigmatropic rearrangement product were to use 4 equiv. of alcohol and pentane as solvent. The reaction should be carried out at room temperature with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst.

2.2.2.2 Effect of allylic alcohols

The optimal reaction conditions were then applied to the reactions of phenyldiazoacetate **6** with a variety of allylic alcohols. The results are summarized in Table 2.9. Tertiary allylic alcohol and primary allylic alcohol had completely different influences on the reaction outcome. The reaction of **6** with tertiary alcohol **106** gave clean [2,3]-sigmatropic rearrangement product **113** in 70% yield and 79% ee, and no trace of the competing O–H insertion product was observed (entry 1). However, the reaction of **6** with primary allylic alcohol **112** gave clean O–H insertion product **119** in 63% yield and no trace of the competing [2,3]-sigmatropic rearrangement product was observed (entry 8). As typical with rhodium catalyzed O–H insertion reactions, **119** was afforded in racemic form. The reaction of **6** with secondary allylic alcohol **108** produced a 4:1 mixture of [2,3]-sigmatropic rearrangement product **115** and the competing O–H insertion product, and **115** was isolated as a 1:1 diastereomeric mixture in 66% yield, 90% ee and 85% ee for each diastereomer (entry 4). The substituent on the terminal double bond was also important for the reaction selectivity. Tertiary allylic alcohol **107** containing an unsubstituted terminal double bond only had a 5:1 ratio favoring the [2,3]-sigmatropic rearrangement product formation (entry 3). While secondary allylic alcohol **110** containing an unsubstituted terminal double bond had 1:14 ratio strongly favoring the O–H insertion product formation (entry 6).

Table 2.9 Effect of allyl alcohols on the formation of [2,3]-sigmatropic rearrangement

products

entry	alcohol	[2,3]-sigma/ O-H insertion ^a	major product	yield, % ^b	ee, % ^c
1	106	>20:1	113	70	79
2 ^{d,f}	100	>20:1	102	79	88, 65
3	107	5:1	114	40	79
4 ^e	108	4:1	115	66	90, 85
5	109	1:16	116	84	0
6	110	1:14	117	61	5, 6
7	111	1: >20	118	72	5
8	112	1: >20	119	63	0

^a Determined by crude ¹H-NMR. ^b Isolated yield of the major product. ^c ee of the major product, determined by chiral HPLC. ^d 4 : 1 diastereomers. ^e 1 : 1 diastereomers. ^f the reaction was conducted at 40 °C.

2.2.2.3 Effect of carbenoid structure

Table 2.10 Reactions of alcohol **101** with different donor/acceptor carbenoids

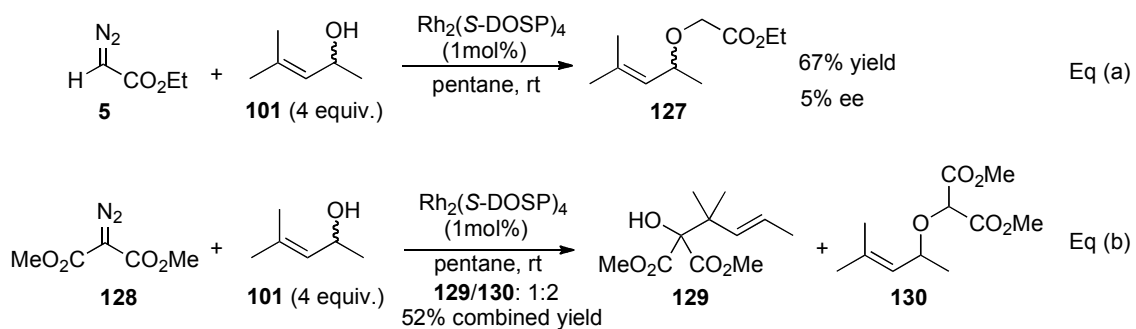
entry	R	[2,3]-sigma/ O-H insertion ^a	[2,3]-sigmatropic rearrangement product	yield, % ^b	ee, % ^c
1	<i>p</i> -(MeO)Ph 12	1:2		17	92
2	<i>p</i> -BrPh 30	7:1		70	88
3	Et 120	4:1		46	92 ^d
4	Ph 7	10:1		70	95
5	<i>p</i> -BrPh 121	10:1		56	98

^a Determined by crude ¹H-NMR. ^b Isolated yield. ^c Determined by chiral HPLC. ^d Determined by ¹H NMR with addition of Eu(tfc)₃.

Having established that highly substituted allylic alcohols prefer the [2,3]-sigmatropic rearrangement product formation, the effect of carbenoid structure on the reaction selectivity was carried out. Different donor/acceptor carbenoid precursors were reacted with racemic alcohol **101**, and the results are summarized in Table 2.10. *p*-bromophenyldiazoacetate (**30**) gave slightly higher selectivity than phenyldiazoacetate (**6**), and [2,3]-sigmatropic rearrangement product **123** was isolated in 70% yield and 88% ee (entry 2). However, *p*-methoxyphenyldiazoacetate (**12**) gave much lower selectivity, and its reaction with **101** produced a 1:2 mixture slightly favoring the O–H insertion, the [2,3]-sigmatropic rearrangement product **122** was isolated in only 17% yield and 92% ee

(entry 1). Vinyldiazoacetates are another type of widely used donor/acceptor carbenoid precursors. The reaction of styryldiazoacetate **7** with **101** produced a 10:1 mixture strongly favoring the [2,3]-sigmatropic rearrangement product formation, and compound **125** was isolated in 70% yield and 95% ee (entry 4).

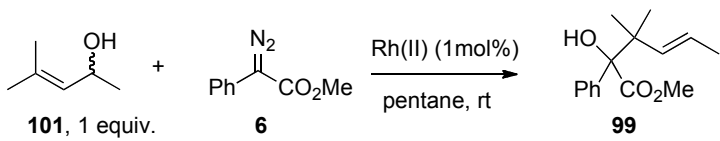
Scheme 2.25 Reactions of alcohol **101** with conventional carbenoids



The reaction of **101** with the conventional carbenoids was also studied (Scheme 2.25). No [2,3]-sigmatropic rearrangement product was observed in the reaction of **101** with ethyl diazoacetate (**5**) and O–H insertion product **127** was formed in 67% yield and 5% ee. The reaction with diazomalonate **128** produced a 1:2 mixture favoring the O–H insertion product formation in 52% combined yield.

This study demonstrated that the carbenoid structure had significant influence on the reaction selectivity between [2,3]-sigmatropic rearrangement and O–H insertion. Donor/acceptor carbenoids displayed better selectivity than the conventional acceptor carbenoids and acceptor/acceptor carbenoids in favor of the [2,3]-sigmatropic rearrangement.

2.2.2.4 Effect of chiral alcohol

Table 2.11 Effect of the alcohol chirality on the product formation


Entry	configuration of 101	Rh(II)	configuration of 99	yield, % ^a	ee, % ^b
1	(<i>R/S</i>)	Rh ₂ (<i>S</i> -DOSP) ₄	<i>S</i>	69	88
2	(<i>S</i>) 84 %ee	Rh ₂ (<i>S</i> -DOSP) ₄	<i>S</i>	61	85
3	(<i>R</i>) 83 %ee	Rh ₂ (<i>S</i> -DOSP) ₄	<i>S</i>	59	94
4	(<i>R/S</i>)	Rh ₂ (<i>R</i> -DOSP) ₄	<i>R</i>	74	87

^a Isolated yield . ^b Determined by chiral HPLC.

One of the most unexpected features of this newly discovered tandem ylide formation/[2,3]-sigmatropic rearrangement transformation was the high asymmetric induction obtained, despite the fact in many cases racemic allylic alcohols were used as starting material. To explore the effect of alcohol chirality on the reaction selectivity, the reactions of phenyldiazoacetate **6** with enantioenriched alcohol **101** were carried out, and the results are summarized in Table 2.11. In all of these reactions, a stoichiometric amount of alcohol **101** was used. The reaction of **6** with racemic (*R/S*)-**101** gave the [2,3]-sigmatropic rearrangement product (*S*)-**99** in 69% isolated yield and 88% ee (entry 1). The formation of (*S*)-**99** in higher than 50% yield indicated that both enantiomers of **101** were capable of generating (*S*)-**99**. This was confirmed by conducting the reaction with enantioenriched alcohol **101**. The reaction of **6** with (*S*)-**101** (84% ee) produced (*S*)-**99** in 61% isolated yield and 85% ee, while the reaction of **6** with (*R*)-**101** (83% ee) also produced (*S*)-**99** in 59% isolated yield and 94% ee. All the reactions went with high

efficiency, and the moderate yields were due to the difficult separation on the chromatography from the O–H insertion byproducts, which were formed in 10-15% yield. The control reaction of racemic (*R/S*)-**101** with **6** using $\text{Rh}_2(\text{R-DOSP})_4$ as catalyst produced (*R*)-**99** in 74% isolated yield and 87% ee. These results clearly demonstrated that the chiral catalyst had the dominant effect on the configuration of the tertiary alcohol stereogenic center in the [2,3]-sigmatropic rearrangement product.

2.2.2.5 Reactions of styryldiazoacetate **7** with racemic allylic alcohols

Since styryldiazoacetate **7** had improved selectivity and favored the [2,3]-sigmatropic rearrangement product formation, further study focused on the reactions of different allylic alcohols with **7**. Lowering the reaction temperature from room temperature to 0 °C, and using only 1 equivalent of racemic alcohol **101**, [2,3]-sigmatropic rearrangement product **125** still formed in 66% isolated yield and 98% ee from the reaction of **7** with **101**. This excellent chemo- and stereoselectivity could also relay to the reactions of **7** with a wide range of allylic alcohols containing different R groups on the carbinol carbon (Table 2.12). Different alkyl groups including very bulky *t*-butyl are all tolerated very well and the [2,3]-sigmatropic rearrangement products formed in 66-73% yield and 94-98% ee (entries 1-5). Functional groups such as protected ketones and alcohol were also compatible, and extremely high enantioselectivity was routinely obtained (entries 6-11, 95-98% ee). The reaction of **7** with 1 equivalent alcohol **135** containing an unsubstituted terminal double bond gave [2,3]-sigmatropic rearrangement product **144** in only 32% yield, presumably because of other possible competing reactions with the active double bond. The yield of **144** could be increased to 69% by using 4 equivalent alcohol **135**.

Similar differences were also observed in the reaction of **7** with alcohol **137**. Using 4 equivalent **137**, [2,3]-sigmatropic rearrangement product **146** was formed in higher yield than in the reaction using only 1 equivalent **137** (50% yield versus 23% yield, entries 9-10). In all of these reactions, the ratio of [2,3]-sigmatropic rearrangement over O-H insertion was higher than 10:1. The only exception that gave lower ratio was the reaction of **7** with alcohol **139** which contained an electron withdrawing ester group at the β -position of the carbinol carbon. A mixture of [2,3]-sigmatropic rearrangement and O-H insertion product was formed in 80% combined yield. Even though the chemoselectivity was low, [2,3]-sigmatropic rearrangement product **148** was still formed in 94% ee (entry 12).

Excellent enantioselectivity was also observed in the reactions of styryldiazoacetate **7** with tertiary allylic alcohols (Table 2.13). Compared with phenyldiazoacetate **6**, the reactions of **7** with tertiary alcohols **106** and **107** produced the [2,3]-sigmatropic rearrangement products with much higher enantioselectivity (entries 1-2). Particularly, for the reaction of **7** with alcohol **107**, no competing O-H insertion product was observed.

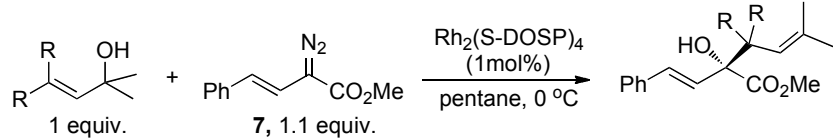
Table 2.12 Reactions of styryldiazoacetate **7** with secondary allylic alcohols

Reaction scheme: A secondary allylic alcohol (1 equiv.) reacts with styryldiazoacetate **7** (1.1 equiv.) in the presence of $\text{Rh}_2(\text{S-DOSP})_4$ (1 mol%) in pentane at 0 °C to form a product with a hydroxyl group and a CO_2Me group.

entry	R		ylide-[2,3]-sig / O-H insertion ^a	product	yield, % ^b	ee, % ^c
1	Me	101	15:1	125	66	98
2	<i>i</i> -Pr	131	> 20 :1	140	68	97
3	<i>i</i> -Bu	132	> 20 :1	141	66	96
4	<i>t</i> -Bu	133	> 20 :1	142	71	94
5	n-Hex	134	10:1	143	73	96
6		135	10:1	144	32	97
7 ^d		135	10:1	144	69	95
8		136	20: 1	145	69	95
9		137	10:1	146	23	98
10 ^d		137	10:1	146	50	98
11		138	10:1	147	70	97
12		139	5: 1	148	80 ^e	94

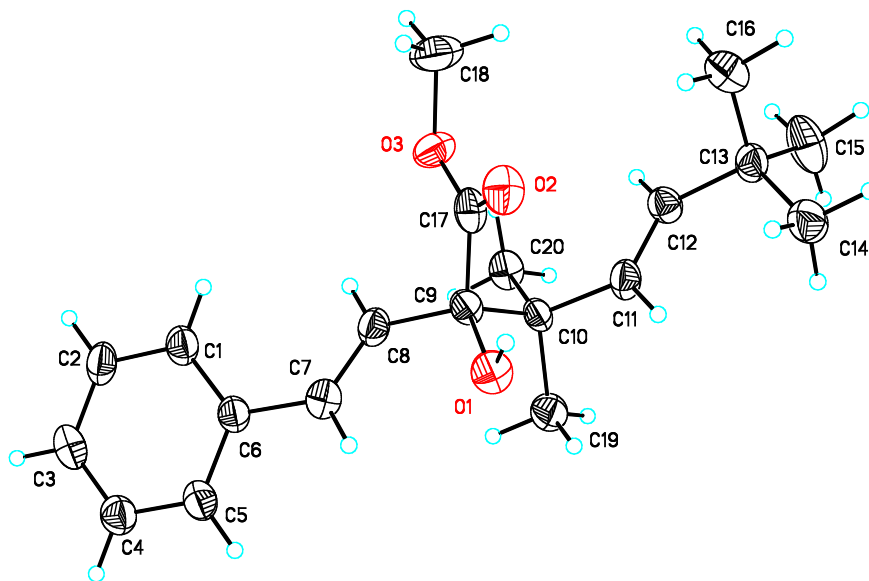
^a Determined by crude ¹H-NMR. ^b Isolated yield of major product. ^c Determined by chiral HPLC.

^d 4 equiv alcohol was used. ^e combined yield of **148** and the O-H insertion by product.

Table 2.13 Reactions of styryldiazoacetate **7** with tertiary allylic alcohols


entry	R	ylide-[2,3]-sig / O-H insertion ^a	product	yield, % ^b	ee, % ^c
1	Me 106	> 20:1	149	62	93
2	H 107	> 20:1	150	45	96

^a Determined by crude ¹H-NMR. ^b Isolated yield of major product. ^c Determined by chiral HPLC.

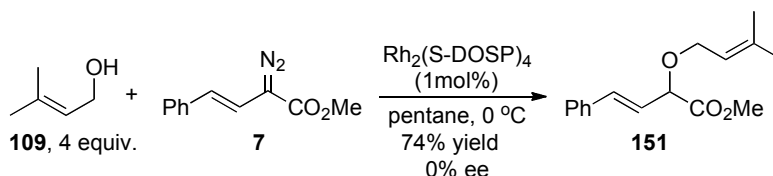
Figure 2.5 X-ray structure of compound **142**

Compound **142** was recrystallized from cold hexanes, and its absolute configuration was determined to be (*R*) by the X-ray crystallography (Figure 2.5). The drawn absolute configurations of other [2,3]-sigmatropic rearrangement products were tentatively

assigned according to **142**, assuming that a similar mode of asymmetric induction occurred for all of the substrates.

Similar to the reaction of phenyldiazoacetate **6** with primary allylic alcohols (Table 2.9), the reaction of styryldiazoacetate **7** with 3-methylbut-2-en-1-ol (**109**) gave racemic O–H insertion product **151** in 74% yield (Scheme 2.26). No [2,3]-sigmatropic rearrangement product was observed in the reaction.

Scheme 2.26 Reaction of styryldiazoacetate **7** with primary allylic alcohol **109**



The synthetic potential of the tandem ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols can be demonstrated from the reaction of styryldiazoacetate **7** with *cis*-(1*R*,5*R*)-(-)-pulegol (**152**) (Scheme 2.27). When $\text{Rh}_2(\text{S-DOSP})_4$ was used as catalyst, the reaction of **7** and **152** produced a 6:1 diastereomeric mixture in 64% combined yield. The major diastereomer **153** was selectively recrystallized from hexanes, and both its relative and absolute configurations were determined by the X-ray crystallography (Figure 2.6). The observed (*R*) configuration at the tertiary alcohol stereocenter was consistent with the (*R*) configuration in compound **142**, supporting the assumption that a similar mode of asymmetric induction occurred for all of the substrates. When $\text{Rh}_2(\text{R-DOSP})_4$ was used as catalyst, the reaction of **7** and **152** produced a 10:1 diastereomeric mixture of the [2,3]-sigmatropic

rearrangement products in 74% combined yield. The major diastereomer **154** was the same as the minor diastereomer in the reaction of **7** and **152** catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$, and the configuration at the tertiary alcohol stereocenter was assigned as (*S*). This assignment was also consistent with the previous results that the chiral catalyst had dominant effect on the configuration at the tertiary alcohol stereocenter in the [2,3]-sigmatropic rearrangement products (Table 2.11).

Scheme 2.27 Reactions of styryldiazoacetate **7** with *cis*-(1*R*,5*R*)-(-)-pulegol **152**

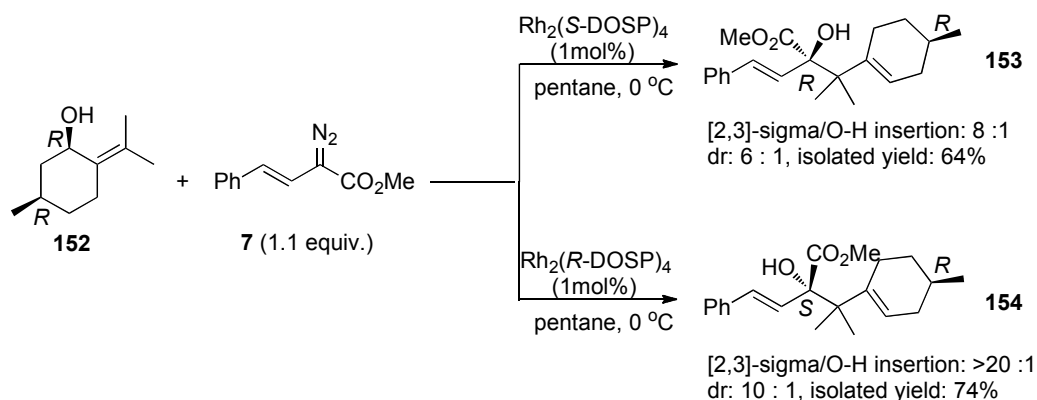
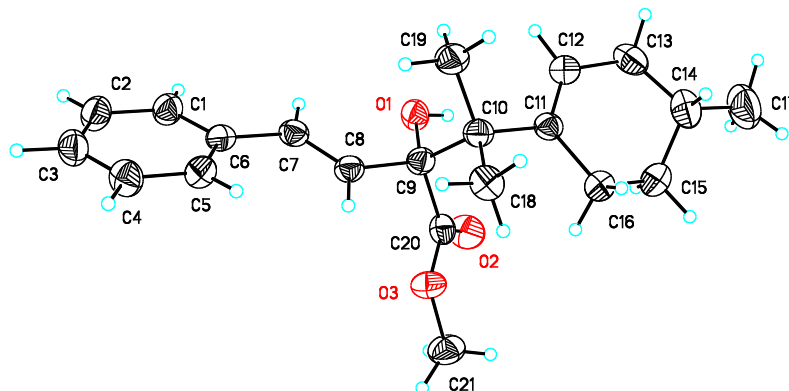
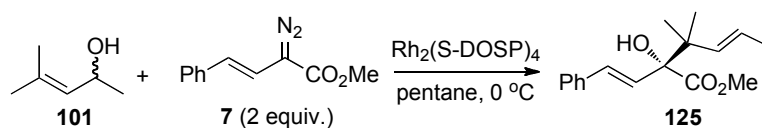


Figure 2.6 X-ray structure of compound **153**



2.2.2.6 Other features

Dirhodium prolinates have been used as efficient catalysts with extremely low loading in a variety of donor/acceptor carbenoid transformations.⁶³ To explore if this was applicable to the tandem ylide formation/[2,3]-sigmatropic rearrangement reactions between donor/acceptor carbenoids and allylic alcohols, the reaction of styryldiazoacetate **7** with racemic alcohol **101** was chosen as a standard reaction. To ensure the efficient conversion of alcohol **101** under low catalyst conditions, 2 equivalent of **7** was used. With 1 mol% of $\text{Rh}_2(\text{S-DOSP})_4$, the reaction of **7** and **101** produced the [2,3]-sigmatropic rearrangement product **125** in 67% yield and 98% ee (Table 2.14, entry 1), the same as the previous reaction using only 1.1 equivalent of **7** (Table 2.12, entry 1). Lowering the catalyst loading to 0.1 mol%, compound **125** was isolated in 63% yield and 91% ee (entry 4). With CaCl_2 as additive, the reaction with 0.01 mol% catalyst loading produced **125** in 51% yield and 96% ee (entry 6). It is proposed that CaCl_2 traps the moisture in the solution and prevent the catalyst decomposition.⁶³ High enantioselectivity is a distinctive character of this reaction under low catalyst loadings. With 0.001 mol% catalyst loading, even though most of **7** could not get decomposed and **125** was isolated in only 9% yield, the ee of **125** was still as high as 96%.

Table 2.14 Effect of catalyst loading

entry	Rh ₂ (S-DOSP) ₄	yield, % ^a	ee, % ^b
1	1 mol%	67	98
2	0.5 mol%	65	96
3	0.2 mol%	66	96
4	0.1 mol%	63	91
5	0.01mol%	11	90
6 ^c	0.01mol%	51	96
7 ^c	0.001mol%	9	96

^a Isolated yield. ^b Determined by chiral HPLC.

^c CaCl₂ used as additive.

The reactions of styryldiazoacetate **7** with a mixture of allylic alcohol **101** and alkyl alcohol revealed another interesting feature of the tandem ylide formation/[2,3]-sigmatropic rearrangement reaction (Table 2.15). O–H insertion product **158** was the major product in the reaction of **7** with a mixture containing equal amount of **101** and 1-propanol (**155**) (45% isolated yield), and [2,3]-sigmatropic rearrangement product **125** was formed in only 3% yield (entry 1). In contrast, no O–H insertion with alkyl alcohols was detected in the reactions of **7** with a mixture of **101** and secondary alcohol **156** or tertiary alcohol **157** (entries 2-3), and the only product that could be isolated in both reactions was [2,3]-sigmatropic rearrangement product **125**. Diazo dimerization accounts for the low yield of **123** in both reactions, and further optimization with slower addition of diazo solution are required in order to improve the yield. These results indicated that the oxonium ylide formation between the steric demanding donor/acceptor carbenoid and alcohol was a reversible process. The [2,3]-sigmatropic rearrangement was far less

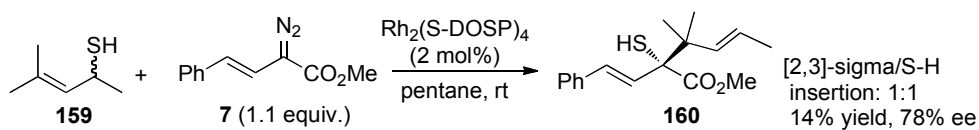
favorable than the [1,2]-proton shift from a primary carbinol, but far more favorable than the [1,2]-proton shift from a secondary and tertiary carbinol. This reactivity difference could lead to an efficient method for selective functionalization of different types of hydroxyl groups in more complex scaffolds.

Table 2.15 Reaction of styryldiazoacetate with alcohol mixture

entry	saturated alcohol	product	yield, % ^a	ee, % ^b
1 ^c	155	158	45	ND
2	156	125	23	98
3	157	125	14	98

^a Isolated yield. ^b Determined by chiral HPLC. ^c compound **125** was also formed in 3% yield and 99% ee

Substrates similar to allylic alcohol **101**, containing other heteroatoms such as sulfur and nitrogen, were also briefly investigated. The reaction of styryldiazoacetate **7** with 4-methylpent-3-ene-2-thiol (**159**) produced a 1:1 mixture of [2,3]-sigmatropic rearrangement product **160** and the S–H insertion product (Scheme 2.28). The low selectivity could be explained by the favorable [1,2]-proton shift due to the weaker S–H bond. Moreover, the pink solution of this reaction also indicated that thiol **159** poisoned the catalyst. Compound **160** was only isolated in 14% yield and 78% ee, and its absolute configuration was assigned as (*R*) assuming that a similar asymmetric induction occurred as its alcohol analogue.

Scheme 2.28 Reactions of styryldiazoacetate **7** with thiol **159**


The reactions of phenyldiazoacetate **6** with allylic amines were summarized in Table 2.16. Neither N–H insertion nor [2,3]-sigmatropic rearrangement product was observed in the reaction with Boc-protected secondary amine **161**. With primary amine **162**, clean N–H insertion product **163** was formed in 36% isolated yield.

Table 2.16 Reaction of phenyldiazoacetate with allylic amines

entry	allylic amine	product	yield, % ^a
1	 161	ND	
2	 162	 163	36

^a Isolated yield.

2.2.3 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols – generation of two stereogenic centers.

2.2.3.1 Reactions with enantiomerically pure allylic alcohols

The tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and racemic allylic alcohols such as **101**, **131-139** provided an efficient method to synthesize α -hydroxycarboxylate compounds containing two adjacent quaternary centers including one tertiary alcohol stereocenter with high enantioselectivity. The effect that the chiral dirhodium catalyst dominates the configuration of the tertiary alcohol stereocenter was particularly noteworthy.

In order to further expand the scope of this chemistry and particularly to improve the understanding of how the chirality of alcohol effects the product formation, (*E*)-pent-3-en-2-ol (**108**) was chosen as substrate. Previous studies showed that the reaction of racemic alcohol **108** with phenyldiazoacetate **6** produced a 1:1 diastereomeric mixture of [2,3]-sigmatropic rearrangement product **115** containing two adjacent stereocenters with good enantioselectivity (85-90% ee) (Table 2.9, entry 4). It was envisioned that the diastereomeric ratio of **115** could be influenced by the chirality of alcohol **108**. Indeed, the reaction of enantiomerically pure (*S, E*)-**108** (>99% ee) and phenyldiazoacetate **6** with Rh₂(*S*-DOSP)₄ as catalyst produced (*2S, 3R*)-**115** as the major diastereomer (dr: 94:6) in 56% isolated yield and >99% ee (Table 2.17, entry 1). This high diastereoselectivity and extremely high enantioselectivity were also apparent in the reaction of (*S, E*)-**108** with

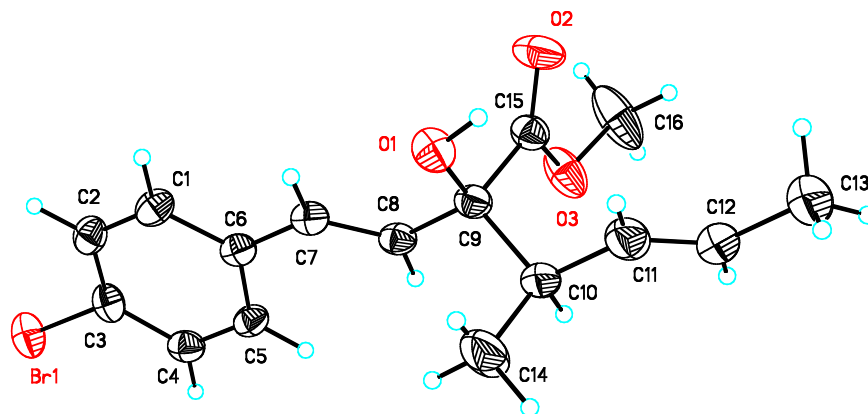
other donor/acceptor carbenoid precursors (Table 2.17, entries 2-4). Compound **166** was readily recrystallized from hexanes and its relative and absolute configuration was determined by the X-ray crystallography as (2*R*, 3*R*) (Figure 2.7). The observed (*R*) configuration at the tertiary alcohol stereocenter in **166** is consistent with the compounds from the reaction of donor/acceptor carbenoids with racemic allylic alcohols such as **101**, **131-139** (section 2.2.2). The absolute configurations of compound (2*S*, 3*R*)-**115**, (2*S*, 3*R*)-**165**, and (2*R*, 3*R*)-**167** were assigned according to **166**, assuming that a similar mode of asymmetric induction occurred in all the reactions.

Table 2.17 Reaction of (*S*, *E*)-**108** with different diazoacetates

entry	R	product	dr ^a	yield, % ^b	ee, % ^c
1	Ph 6		94:6	56	>99
2	<i>p</i> -BrPh 30		90:10	66	>99
3	(<i>E</i>)- <i>p</i> -BrPhCH=CH 121		94:6	69	>99
4	CH ₂ =CH 164		79:21	43	99

^a Determined by crude ¹H-NMR. ^b Isolated yield of the major diastereomer. ^c ee of the major diastereomer, determined by chiral HPLC.

Figure 2.7 X-ray structure of compound **166**



The high diastereoselectivity and extremely high enantioselectivity in Table 2.17 indicated that the chirality of the allylic alcohol could be effectively transferred to the second stereocenter produced during the rearrangement step. To further confirm it, both **(S, E)-108** (99% ee) and **(R, E)-108** (97% ee) were used as substrates, and the results of their reactions with styryldiazoacetates **7** were summarized in Table 2.18. The reaction of **(S, E)-108** (99% ee) and **7** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst produced **(2R, 3R)-168** in 70% isolated yield and >99% ee (entry 1), its absolute stereochemistry was assigned according to that of compound **166**. Interestingly, the reaction of **(R, E)-108** (97% ee) and **7** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst produced another diastereomer of **(2R, 3R)-168** in 64% isolated yield and >99% ee (entry 2) and its absolute stereochemistry was assigned as **(2R, 3S)**, assuming that the chiral catalyst dominates the configuration of the tertiary alcohol stereocenter. More interestingly, the reaction of **(S, E)-108** and **7** with $\text{Rh}_2(\text{R-DOSP})_4$ as catalyst produced the opposite enantiomer of **(2R, 3S)-168** (determined by

chiral HPLC), and it was assigned as **(2*S*, 3*R*)-168** (entry 3). Similarly, the reaction of **(*R*, *E*)-108** and **7** with $\text{Rh}_2(\text{R-DOSP})_4$ as catalyst produced the opposite enantiomer of **(2*R*, 3*R*)-168** (determined by chiral HPLC), and it was assigned as **(2*S*, 3*S*)-168** (entry 4). Overall, through the combination of the enantiomerically pure allylic alcohol **108** and chiral dirhodium catalyst, all of the four stereoisomers of **168** were produced with high diastereo- and enantioselectivity (dr: >90:10, >99% ee). These results also confirmed that the chiral catalyst dominates the configuration of the tertiary alcohol stereocenter, while the chirality of the allylic alcohol dominates the second stereocenter produced during the rearrangement step. As a control experiment, the reaction of racemic **108** and **7** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst produced a 1:1 diastereomeric mixture of **168** in 72% combined yield, both diastereomers had very high enantiomeric excess (97, 98% ee, entry 6).

The geometry of the alkene was also critical for the product stereochemistry. The reaction of **(*S*, *Z*)-108** (98% ee) with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst produced **(2*R*, 3*S*)-168** as the major diastereomer, which has the opposite configuration at the 3-position comparing with **(2*R*, 3*R*)-168** produced from the reaction of **(*S*, *E*)-108** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst (entry 5 versus entry 1). In this case, however, the reaction gave lower diastereoselectivity (dr: 75:25), and **(2*R*, 3*S*)-168** was isolated in 35% yield and >99% ee.

Table 2.18 Reaction of pent-3-en-2-ol (**108**) with styryldiazoacetate **7**

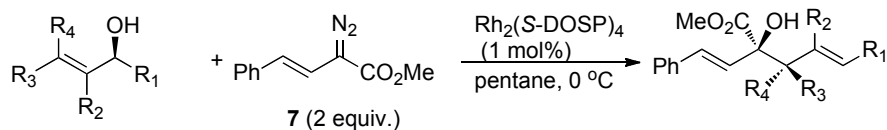
Reaction scheme: **108** + **7** (2 equiv.) $\xrightarrow[\text{pentane, 0 } ^\circ\text{C}]{\text{Rh(II) (1 mol\%)}}$ **168**

entry	allylic alcohol	Rh(II)	product	dr ^a	yield, % ^b	ee, % ^c
1	(<i>S, E</i>)- 108 99% ee	Rh ₂ (<i>S</i> -DOSP) ₄	 (<i>2R, 3R</i>)- 168	92:8	70	>99
2	(<i>R, E</i>)- 108 97% ee	Rh ₂ (<i>S</i> -DOSP) ₄	 (<i>2R, 3S</i>)- 168	91:9	64	>99
3	(<i>S, E</i>)- 108 99% ee	Rh ₂ (<i>R</i> -DOSP) ₄	 (<i>2S, 3R</i>)- 168	92:8	54	>99
4	(<i>R, E</i>)- 108 97% ee	Rh ₂ (<i>R</i> -DOSP) ₄	 (<i>2S, 3S</i>)- 168	95:5	78	>99
5	(<i>S, Z</i>)- 108 98% ee	Rh ₂ (<i>S</i> -DOSP) ₄	 (<i>2R, 3S</i>)- 168	75:25	35	>99
6	(<i>rac, E</i>)- 108	Rh ₂ (<i>S</i> -DOSP) ₄	 (<i>2R, 3R</i>)- 168 (<i>2R, 3S</i>)- 168	50:50	72	97, 98

^a Determined by crude ¹H-NMR. ^b Isolated yield of the major diastereomer. ^c ee of the major diastereomer, determined by chiral HPLC.

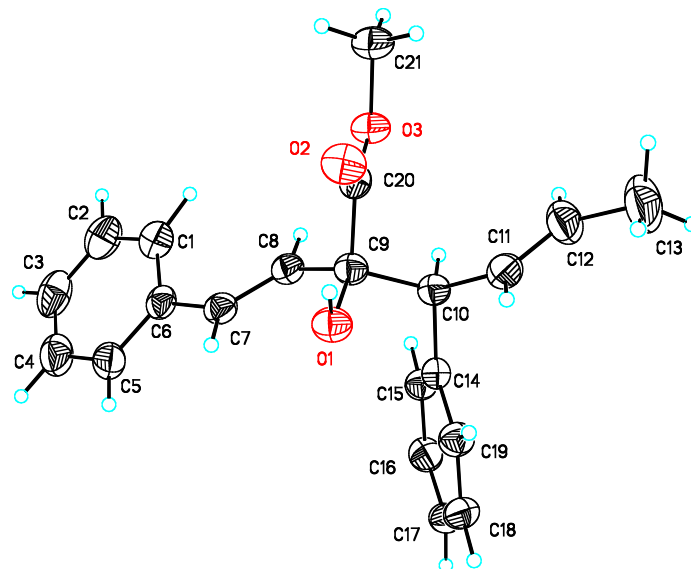
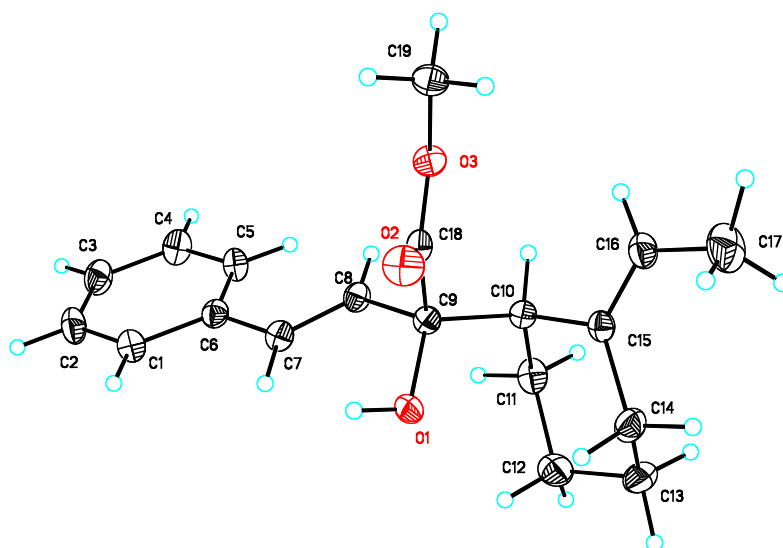
A variety of other enantiomerically pure (*S*)-allylic alcohols were obtained from the kinetic resolution of the racemic material by either enzymatic resolution or by Sharpless enantioselective epoxidation (See experimental). Their reactions with styryldiazoacetate **7** with Rh₂(*S*-DOSP)₄ as catalyst were summarized in Table 2.19. Products **176-182** with two adjacent stereocenters including one tertiary alcohol stereocenter were formed with extremely high diastereo- and enantioselectivity (Table 2.19, entry 1-6, dr: >95:5, >99% ee). In all of these reactions, the competing O—H insertion product could not be detected from the ¹H NMR spectra of the crude reaction mixture. Substituent R₁ group such as methyl and isopropyl, R₂ group such as methyl, R₃ group such as *n*-pentyl, phenyl, and trimethylsilyl, were all tolerated in the reaction (entries 1-4). The reaction of (*S*)-1-cyclohexenylethanol **174** also gave compound **181** in 77% isolated yield with >97:3 dr and >99% ee. Most impressively, the reaction of (*S*, *E*)-4, 8-dimethylnona-3,7-dien-2-ol (**175**) and **7** produced compound **182** containing two adjacent quaternary centers as a 95:5 inseparable diastereomeric mixture in 63% isolated yield and >99% ee for the major diastereomer.

Both compounds **177** and **181** were recrystallized from hexanes and their relative and absolute configurations were determined by the X-ray crystallography, which are consistent with that of **166** (Figure 2.8, 2.9). These two X-ray structures also confirmed that a similar mode of asymmetric induction occurred for all the substrates in this tandem ylide formation/[2,3]-sigmatropic rearrangement transformation between donor/acceptor carbenoids and enantiomerically pure allylic alcohols.

Table 2.19 Reaction of (*S*)-allylic alcohol with styryldiazoacetate **7**

entry	allylic alcohol	product	dr ^a	yield, % ^b	ee, % ^c
1	 169 , 99% ee	 176	>97:3	83	>99
2	 170 , 99% ee	 177	>97:3	71	>99
3	 171 , 99% ee	 178	>97:3	42	99
4	 172 , 99% ee	 179	>97:3	75	>99
5	 173 , 97% ee	 180	96:4	61	>99
6	 174 , 99% ee	 181	>97:3	77	>99
7	 175 , 99% ee	 182	95:5	63	>99

^a Determined by crude ¹H-NMR. ^b Isolated yield of the major diastereomer. ^c ee of the major diastereomer, determined by chiral HPLC.

Figure 2.8 X-ray structure of compound **177****Figure 2.9** X-ray structure of compound **181**

The highly diastereo- and enantioselective synthesis of **176-182** gave rise to the question: can all of the four stereoisomers of **176-182** be synthesized through the combination of chiral alcohol and chiral dirhodium catalyst, in the same manner as the synthesis of all four stereoisomers of **168** in Table 2.18?

To answer this question, the compatibility of R_1 and R_3 with the chiral dirhodium catalyst was studied, with the possibility that a large R_1 or R_3 group might result in a mismatch situation with the chiral catalyst and subsequently prevent the reaction from taking place. First, (*E*)-1-cyclohexylbut-2-en-1-ol **183** containing R_1 as cyclohexyl group was chosen. With $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst, the reaction of (*S*, *E*)-**183** and styryldiazoacetate **7** produced (**2R**, **3R**)-**184** in 86% isolated yield with high diastereo- and enantioselectivity (dr: >97:3, >99% ee, Table 2.20, entry 1). Its relative and absolute configuration was determined by the X-ray crystallography (Figure 2.10), which is also consistent with previous products derived from the reaction of (*S*)-alcohol and **7** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst (Table 2.19). Interestingly, the reaction of (*R*, *E*)-**183** with **7** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst produced (**2R**, **3S**)-**184** in 74% isolated yield with high diastereo- and enantioselectivity (dr: >97:3, >99% ee, Table 20, entry 2). The relative and absolute configuration of (**2R**, **3S**)-**184** was also determined by its X-ray crystallography (Figure 2.11). These two reactions not only demonstrated that both (*R*) and (*S*) allylic alcohol with a bulky group at the carbinol position were compatible with the $\text{Rh}_2(\text{S-DOSP})_4$ catalyst, but also confirmed that the chirality of the catalyst dominated the configuration of the tertiary alcohol stereocenter, and the chirality of the alcohol could be

effectively transferred to the second stereocenter generated during the rearrangement step.

Table 2.20 Reaction of (*R*) and (*S*)-**183** with styryldiazoacetate **7**

entry	allylic alcohol	Rh(II)	product	dr ^a	yield, % ^b	ee, % ^c
1	(<i>S</i> , <i>E</i>)- 183 >98% ee	Rh ₂ (<i>S</i> -DOSP) ₄	 (<i>2R</i> , <i>3R</i>)- 184	>97:3	86	>99
2	(<i>R</i> , <i>E</i>)- 183 >98% ee	Rh ₂ (<i>S</i> -DOSP) ₄	 (<i>2R</i> , <i>3S</i>)- 184	>97:3	74	>99

^a Determined by crude ¹H-NMR. ^b Isolated yield of the major diastereomer. ^c ee of the major diastereomer, determined by chiral HPLC.

Figure 2.10 X-ray structure of compound (*2R*, *3R*)-**184**

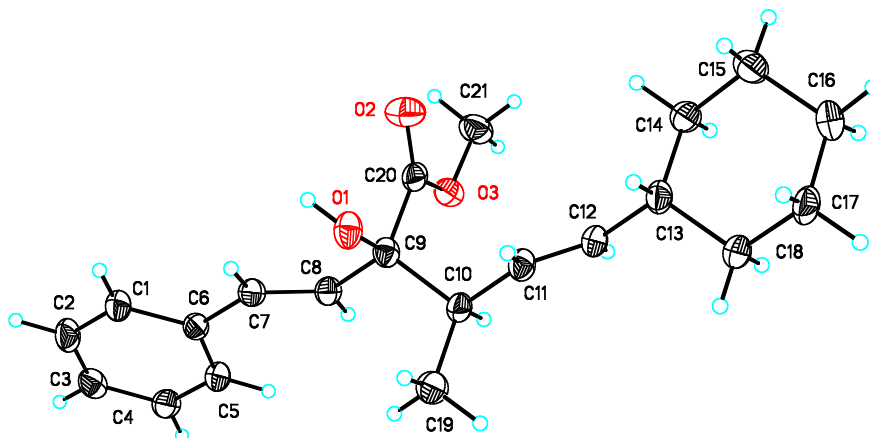
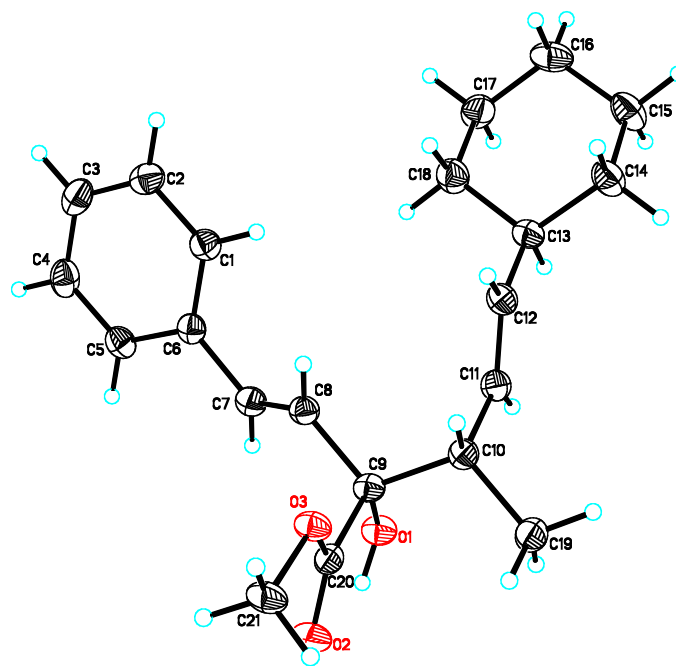


Figure 2.11 X-ray structure of compound **(2*R*, 3*S*)-184**



Focus then turned to how the size of R_3 group effected the reaction outcome. With R_3 group as phenyl, as described in Table 2.19, the reaction of **(*S*, *E*)-170** and styryldiazoacetate **7** with $\text{Rh}_2(\text{*S*-DOSP})_4$ as catalyst had a match situation, and produced **(2*R*, 3*S*)-177** with excellent result (dr: >97:3, 71% isolated yield, >99% ee, Table 2.21, entry 1 (same as Table 2.19, entry 2)). However, when $\text{Rh}_2(\text{*R*-DOSP})_4$ was used as catalyst, a mismatch situation occurred. The diastereoselectivity of the reaction dropped to 86:14 (entry 2). The isolated yield of **(2*S*, 3*S*)-177** also dramatically dropped to 30%. Even though an inferior result was obtained in this mismatched reaction, the high enantiomeric excess of **(2*S*, 3*S*)-177** (>99%) was still an excellent example of the highly

stereoselective nature of the tandem oxonium ylide formation/[2, 3]-sigmatropic rearrangement of donor/acceptor carbenoids with enantiomerically pure allylic alcohols.

Table 2.21 Reaction of (*R, E*)-**170** with styryldiazoacetate **7**

entry	allylic alcohol	Rh(II)	product	dr ^a	yield, % ^b	ee, % ^c
1	(<i>S, E</i>)- 170 >99% ee	Rh ₂ (<i>S</i> -DOSP) ₄	 (<i>2R, 3S</i>)- 177	>97:3	71	>99
2	(<i>S, E</i>)- 170 >99% ee	Rh ₂ (<i>R</i> -DOSP) ₄	 (<i>2S, 3S</i>)- 177	86:14	30	>99

^a Determined by crude ¹H-NMR. ^b Isolated yield of the major diastereomer. ^c ee of the major diastereomer, determined by chiral HPLC.

With these results in hand, it would be reasonable to predict that either (*R*) or (*S*) allylic alcohol **169**, **172**, **173**, **174** containing small R₃ groups will be compatible with both Rh₂(*S*-DOSP)₄ and Rh₂(*R*-DOSP)₄, and all of the four stereoisomers of their [2,3]-sigmatropic rearrangement products with styryldiazoacetate **7** could be synthesized with very high stereoselectivity. But for allylic alcohols containing large R₃ group, such as **171** (R₃ as trimethylsilyl), only two stereoisomers could be synthesized with very high stereoselectivity, and only in the cases where the chirality of the alcohol matches the chirality of the catalyst.

2.2.3.2 Rationale of the stereoselectivity

With the established model for the D_2 symmetric $\text{Rh}_2(\text{S-DOSP})_4$ catalyst,¹⁰ it is proposed that the alcohol approaches the carbenoid from the front open face to form the oxonium ylide, which subsequently goes through the [2,3]-sigmatropic rearrangement via an envelope transition state and produces the final product. Two other important assumptions include: 1. the oxonium ylide intermediate should be a rhodium-associated ylide instead of a free ylide due to the high asymmetric induction of the chiral dirhodium catalyst on the product formation; 2. this rhodium-associated ylide involves inversion of configuration at the rhodium-bound carbon to release the metal during the rearrangement step. Both assumptions had also been used by Doyle et al to explain the stereochemical outcome of the chiral dirhodium carboxamides catalyzed oxonium formation/[2,3]-sigmatropic rearrangement between ethyl diazoacetate (EDA) and cinnamyl methyl ether.⁶⁴ Calculation studies on the lithium associated anionic [2,3]-sigmatropic rearrangement system by Houk also support the configuration inversion at the metal associated carbon center.⁶⁵ The detailed role of the hydroxy group in the transformation is not clear. It is possible that the hydrogen bonding between the hydroxy group and the carbonyl of the ester group in the oxonium intermediate is also critical for this highly stereoselective transformation.

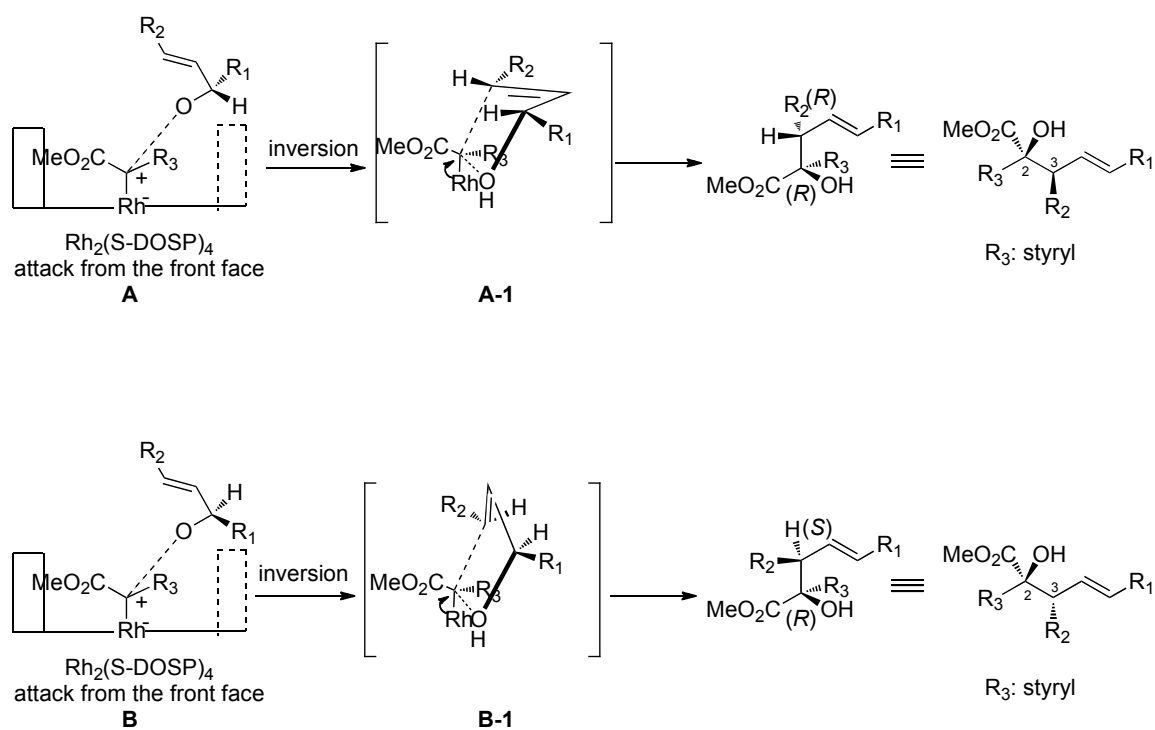
In order to explain the influence of the alcohol chirality on the product formation, two different transition states were proposed (Figure 2.12). In the reaction of (*S*)-alcohol and carbenoid derived from styryldiazoacetate **7** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst, the reaction goes through an envelope transition state **A-1** to form the product with (*2R*, *3R*)

configuration. However, in the reaction of (*R*)-alcohol with the same carbenoid, the reaction goes through a different envelope transition state **B-1** to form the product with (*2R, 3S*) configuration in order to avoid the steric conflict between R₁ group and the left blocking group (arylsulfonyl) of the catalyst. In addition to the ability to explain the stereochemistry of all the products from (*R*) and (*S*) allylic alcohol with donor/acceptor carbenoids, these two transition states also explain the good compatibility of the large R₁ group in either (*R*) or (*S*) allylic alcohols with the chiral dirhodium catalysts (see Table 2.20). This compatibility can be further confirmed with R₁ as *t*-butyl group. The low diastereomeric ratio of **186** (dr: 59:41) in the reaction of racemic alcohol **185** and 0.6 equivalent **7** with Rh₂(*S*-DOSP)₄ as catalyst indicated that both enantiomer of **185** had similar reactivity during the reaction (Scheme 2.29).

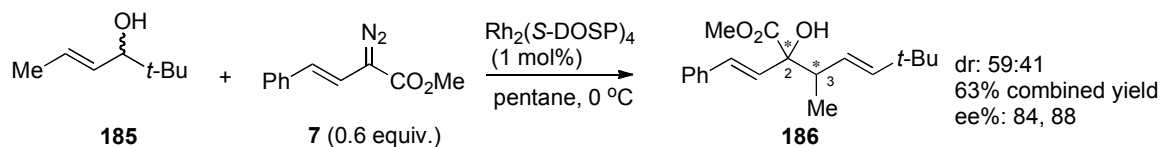
It is reasonable to propose that the orientation of R₂ group in the transition state **A-1** is more favorable than that in **B-1** taking account of the steric interaction between R₂ and the left blocking group (arylsulfonyl) from the catalyst. The reactivity difference derived from this orientation difference was demonstrated in the reaction of (*S*)-**170** with styryldiazoacetate **7** (Table 2.21), in which (*S*)-**170** matches with Rh₂(*S*-DOSP)₄, and mismatches with Rh₂(*R*-DOSP)₄. Another example is the reaction of (*E*)-2-methylpent-3-en-2-ol (**100**) and *p*-bromostyryldiazoacetate **121** with Rh₂(*S*-DOSP)₄ as catalyst (Scheme 2.30), in which (*2R, 3R*)-**187** and (*2R, 3S*)-**187** were produced as a 3:1 diastereomeric mixture. With alcohol **100**, the orientation of methyl group on the double bond in the transition state determined the reaction diastereoselectivity. Clearly, Transition state **A-1** (affording the major diastereomer (*2R, 3R*)-**187**) is about three times more favorable than

transition state **B-1** (affording the minor diastereomer **(2*R*, 3*S*)-187**). The relative and absolute configuration of **(2*R*, 3*R*)-187** and **(2*R*, 3*S*)-187** were determined by their X-ray crystallographies (Figure 2.13, 2.14).

Figure 2.12 Transition state analysis of (*R*) and (*S*) allylic alcohol with donor/acceptor carbenoid



Scheme 2.29 Reaction of alcohol **185** with styryldiazoacetate **7**



Scheme 2.30 Reaction of alcohol **100** with aryldiazoacetate **121**

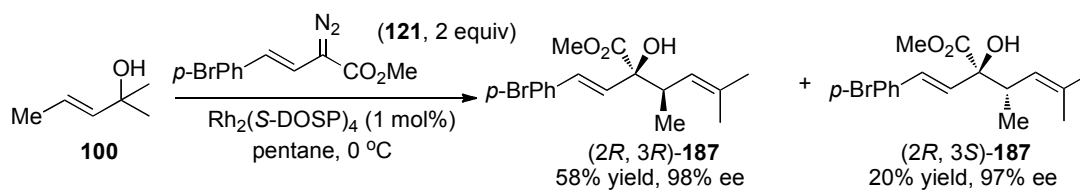


Figure 2.13 X-ray structure of compound **(2R,3R)-187**

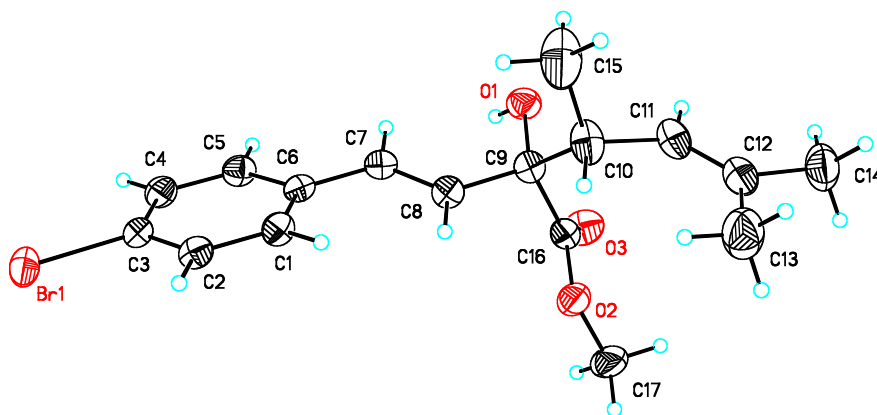
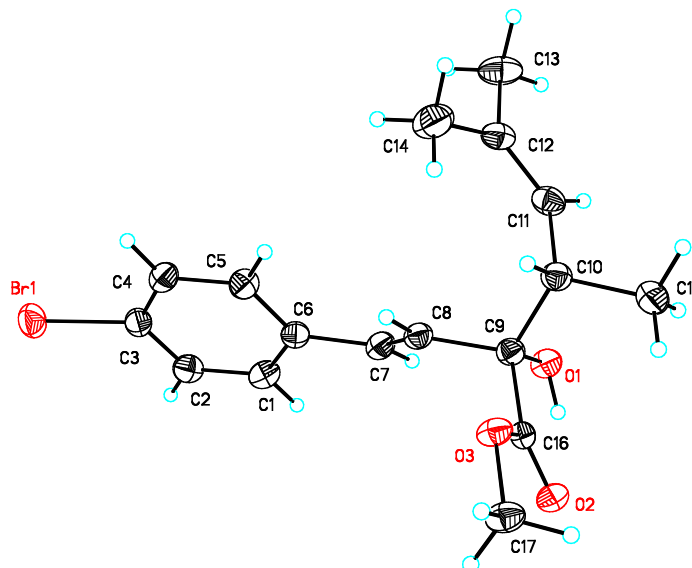


Figure 2.14 X-ray structure of compound (**2*R*, 3*S***)-**187**



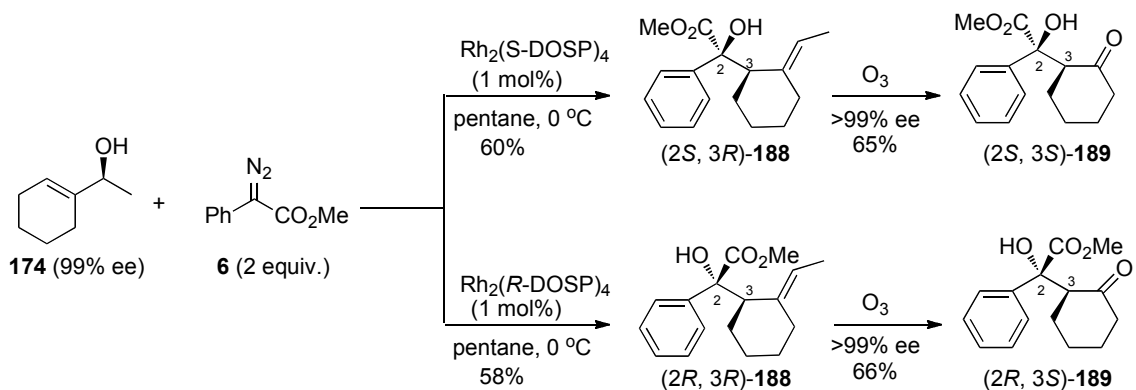
2.2.3.3 Further transformation

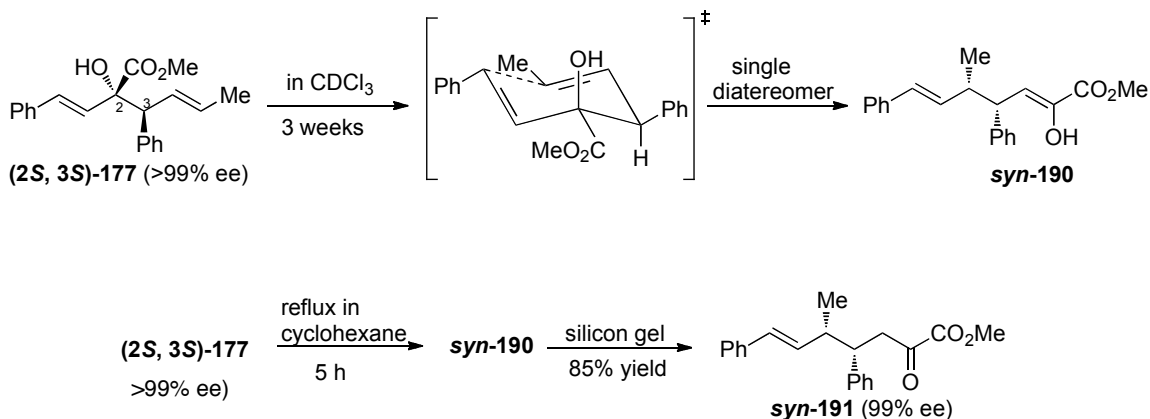
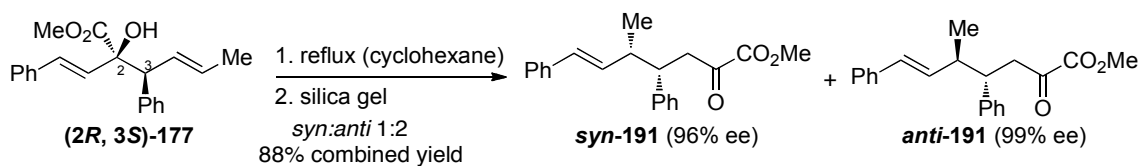
The synthesis of α -hydroxycarboxylate compounds containing a β -carbonyl moiety has been extensively studied.⁶⁶ Among those, the asymmetric aldol reaction between α -keto ester and ketone catalyzed by organocatalysts such as proline has been most successful in terms of high diastereo- and enantioselectivity.^{66a-c}

The tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and enantiomerically pure allylic alcohols provides a highly stereoselective method to synthesize the α -hydroxycarboxylate compounds. Particularly, the excellent diastereoselective and enantioselective control on the product formation by the chiral dirhodium catalyst and the chiral allylic alcohol give a unique opportunity to selectively synthesize each of the four possible stereoisomers. As a further demonstration

of this powerful method, the two diastereomers of **189** were chosen to be prepared (Scheme 2.31). The reaction of alcohol (*S*)-**174** and phenyldiazoacetate **6** catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$ produced (**2S, 3R**)-**188** in 60% yield, the subsequent ozonolysis provided (**2S, 3S**)-**189** in 65% yield and >99% ee. Similarly, the reaction of (*S*)-**174** and **6** catalyzed by $\text{Rh}_2(\text{R-DOSP})_4$, followed with ozonolysis to give (**2R, 3S**)-**189** in 66% yield and >99% ee. Both (**2S, 3S**)-**189** and (**2R, 3S**)-**189** are known compounds, and their spectral data are consistent with the literature.^{66a,c} Although this is a two-step sequence to synthesize α -hydroxycarboxylate compounds containing β -carbonyl moiety, the excellent and predictable stereocontrol on the product formation offers an attractive advantage over the conventional methods to synthesize this type of compounds.

Scheme 2.31 Synthesis of compound **189**



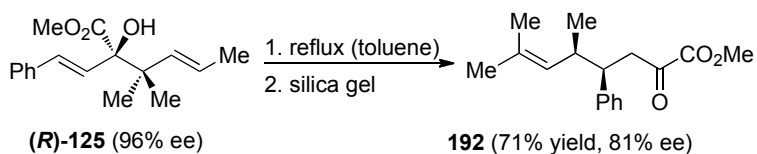
Scheme 2.32 Oxy-Cope rearrangement of (2*S*, 3*S*)-177Scheme 2.33 Oxy-Cope rearrangement of (2*R*, 3*S*)-177

Another important transformation of compounds derived from tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols is the oxy-Cope rearrangement. Originally, it was found that (2*S*, 3*S*)-177 (>99% ee) in CDCl₃ at room temperature slowly rearranged into enol **190** as a single diastereomer (Scheme 2.32). Presumably, this oxy-Cope rearrangement goes through a very favorable chair transition state with the ester, phenyl, and methyl groups at the equatorial positions, and the hydroxyl group at the axial position. This rearrangement could be much faster at higher temperature. Upon refluxing in cyclohexane for only 5 hours (80 °C), (2*S*, 3*S*)-177 quantitatively rearranged to enol *syn*-190 as a single diastereomer, which tautomerized upon addition of silica gel into α -keto ester *syn*-191 in

85% yield and 99% ee (Scheme 2.32). In contrast, reflux of **(2*R*, 3*S*)-177** (>99% ee) for 5 hours, followed with the tautomerization on silica gel produced a 2:1 diastereomeric mixture with ***syn*-191** as the minor diastereomer (Scheme 2.33). The major diastereomer, ***anti*-191**, was formed in 99% ee. It is apparent that the preferred equatorial orientation of phenyl group at the 3-position eroded the diastereoselectivity, both chair and boat transition states might get involved in the rearrangement process.

This low diastereoselectivity limitation could be avoided by using compounds containing two methyl groups at the 3-position (Scheme 2.34). **(*R*)-125** (96% ee) was refluxed in toluene for 5 hours, followed with the tautomerization on silica gel to produce α -keto ester **192** as a single diastereomer in 71% yield and 81% ee.

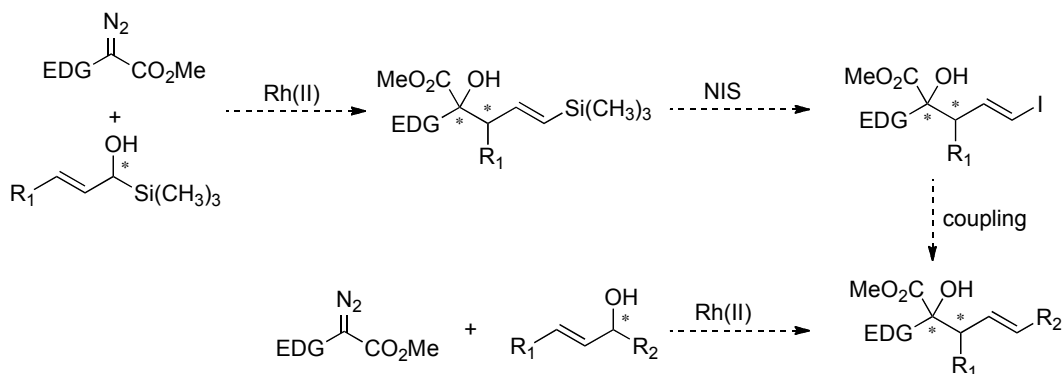
Scheme 2.34 Oxy-Cope rearrangement of (*R*)-**125**



It should be noted that both the relative and absolute configuration of **191** and **192** have not been unambiguously determined. More detailed studies of this oxy-Cope rearrangement chemistry are being carried out by other group members of the Davies group.

2.2.4 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols containing silyl group

Scheme 2.35 Synthesis of α -hydroxycarboxylates through halodesilylation-coupling strategy



Vinylsilane can be easily converted into vinyl iodide upon treatment of *N*-iodosuccinimide (NIS) with retention of olefin geometry.^{67,68} Vinyl iodide can undergo a wide variety of transition metal catalyzed cross coupling reaction, such as NHK coupling,⁶⁹ Sonogashira coupling,⁷⁰ Heck coupling,⁷¹ and Suzuki coupling.⁷² It was envisioned that vinylsilanes derived from the tandem ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoid and allylic alcohols containing silyl groups on the carbinol position would be also easily converted to the corresponding vinyl iodides. Combined with the well-established coupling methods, these vinyl iodides could be further converted into much more complex molecules (Scheme 2.35). Although it is a two-step sequence, it could avoid the tedious synthesis of complex chiral allylic alcohol, particularly those containing other functional groups.

Table 2.22 Reaction of racemic alcohol **193** with donor/acceptor carbenoids

entry	R	product	[2,3]-sigma/O-H insertion ^a	yield, % ^b	ee, % ^c
1	Ph 6	194	>20:1	72	88
2	(<i>E</i>)-PhCH=CH 7	195	>20:1	69	92

^a Determined by crude ¹H-NMR. ^b Isolated yield. ^c Determined by chiral HPLC.

This study started with racemic allylic alcohol **193**. Its reaction with both phenyldiazoacetate **6** and styryldiazoacetate **7** worked very well and produced the [2,3]-sigmatropic rearrangement product **194** in 72% yield with 88% ee, and **195** in 69% yield with 92% ee, respectively (Table 2.22). In both reactions, the competing O–H insertion product couldn't be detected from the ¹H-NMR of the crude reaction mixture. The (*R*) configuration of **194** and **195** was assigned according other analogues in section 2.2.2.

The excellent selectivity of [2,3]-sigmatropic rearrangement over O–H insertion was also observed in the reactions of secondary allylic alcohol **196** with styryldiazoacetate **7**. However, the poor diastereoselectivity of these reactions was in sharp contrast with that of other reactions involving secondary allylic alcohols without trimethylsilyl group (section 2.2.3). In order to have a full understanding, a detailed study was carried out and the results are summarized in Table 2.23. First, the reaction of racemic **196** with **7** produced a 1:1 diastereomeric mixture of **197** in 35% combined yield with moderate enantioselectivity (71 and 69% ee, entry 1). With either (*R*) or (*S*) enantioenriched **196**, the diastereoselectivity of the reaction kept constantly around 3:1, with the major

diastereomer 97-98% ee and the minor diastereomer <26% ee (entries 2-5). The relative and absolute configuration of **(2R, 3R)-197** (entry 2) and **(2S, 3R)-197** (entry 3) were assigned based on the configuration of other similar compounds from the reaction of enantiomerically pure allylic alcohols and styryldiazoacetate **7** with chiral dirhodium catalyst (section 2.3), while the other products were assigned based on the HPLC traces comparing with these two.

Table 2.23 Reaction of alcohol **196** with styryldiazoacetate **7**

entry	196	Rh(II)	dr ^a	major product ^b	minor product ^b	
1	<i>(rac, E)</i> - 196	Rh ₂ (S-DOSP) ₄	50:50	<i>(2R, 3R)</i> - 197 20% yield, 71% ee	<i>(2R, 3S)</i> - 197 15% yield, 69% ee	
2	<i>(S, E)</i> - 196 82% ee	Rh ₂ (S-DOSP) ₄	71:29	<i>(2R, 3R)</i> - 197 33% yield, 97% ee	<i>(2S, 3R)</i> - 197 13% yield, 25% ee	
3	<i>(S, E)</i> - 196 82% ee	Rh ₂ (R-DOSP) ₄	72:28	<i>(2S, 3R)</i> - 197 36% yield, 98% ee	<i>(2R, 3R)</i> - 197 11% yield, 23% ee	
4	<i>(R, E)</i> - 196 85% ee	Rh ₂ (S-DOSP) ₄		<i>(2R, 3S)</i> - 197 rt 28% yield, 97% ee	<i>(2S, 3S)</i> - 197 10% yield, 26% ee	
			75:25	0 °C	35% yield, 97% ee	6% yield, 11% ee
			75:25	40 °C	34% yield, 96% ee	7% yield, 21% ee
5	<i>(R, E)</i> - 196 85% ee	Rh ₂ (R-DOSP) ₄	76:24	<i>(2S, 3S)</i> - 197 31% yield, 98% ee	<i>(2R, 3S)</i> - 197 8% yield, 26% ee	
6	<i>(rac, Z)</i> - 196	Rh ₂ (S-DOSP) ₄	55:45	<i>(2R, 3R)</i> - 197 14% yield, 84% ee	<i>(2R, 3S)</i> - 197 11% yield, 88% ee	

^a Determined by crude ¹H-NMR. ^b Yield was isolated yield, and the ee was determined by chiral HPLC.

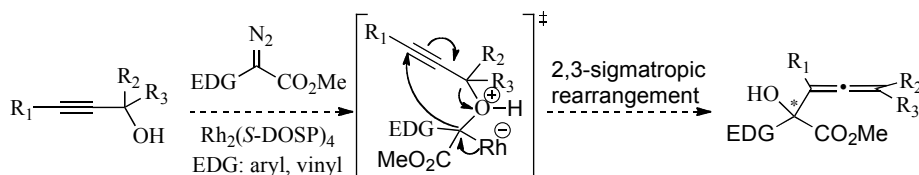
Through careful comparison of the absolute configuration of the two diastereomers of **197** (entries 2-5), it is found that the minor diastereomer in each reaction always had the opposite configuration at the tertiary alcohol stereocenter, compared with that of the major diastereomer. Previous study showed that the chiral catalyst dominated the

configuration of this tertiary alcohol stereocenter during the rearrangement step (section 2.2.2 and 2.2.3, particularly Scheme 2.29). The low diastereomeric ratio of **197** in all the reactions, however, showed that this effect from the chiral catalyst was very limited for alcohol **196**. More studies are needed to understand whether the large size of trimethylsilyl group or other effects are responsible for this decline.

2.2.5 Tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and propargylic alcohols.

α -Allenic alcohols are versatile and useful intermediates in organic synthesis due to their unique reactivities and the ease of further conversion into compounds with other functional groups.⁷³ They are generally prepared by allenylation of carbonyl compounds (aldehydes in most cases), and a variety of enantioselective synthesis have also been developed.^{74,75} The enantioselective synthesis of α -allenic alcohols containing a tertiary alcohol stereocenter, however, remains a formidable challenge. The success with the studies of the tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and allylic alcohols prompted us to explore the reactions of donor/acceptor carbenoids with propargylic alcohols. It would be reasonable to propose that these reactions would also go through a similar oxonium ylide formation/[2,3]-sigmatropic rearrangement process to form α -allenic alcohols containing a tertiary alcohol stereocenter (Scheme 2.36).

Scheme 2.36 Synthesis of α -allenic alcohols with donor/acceptor carbenoids and propargylic alcohols

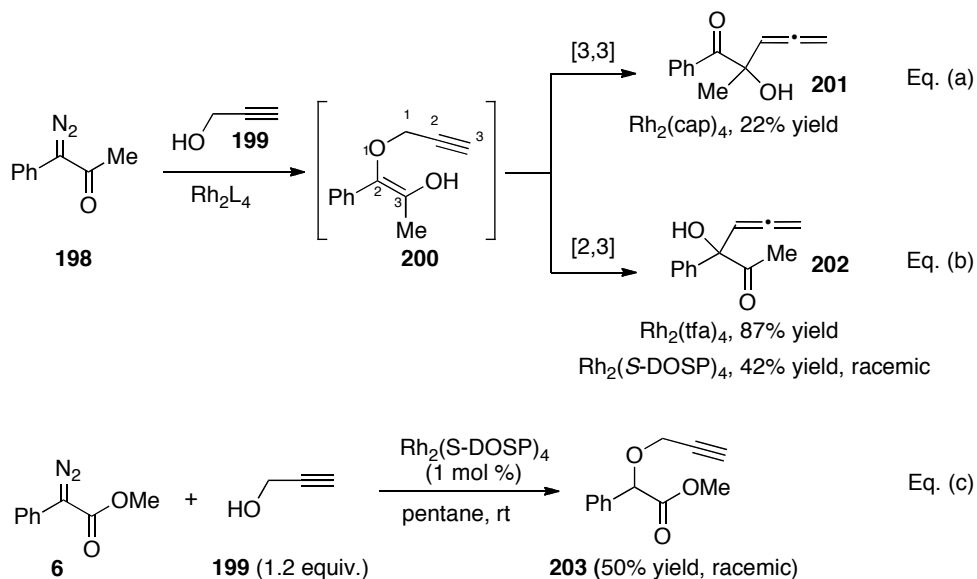


2.2.5.1 Reactions with achiral propargylic alcohols

Although rhodium catalyzed sulfonium ylide formation/[2,3]-sigmatropic rearrangement between propargyl sulfide and carbenoid has been extensively studied, there was no report using propargyl alcohols for a similar transformation due to the competing O–H insertion.^{1a,c} The only exception was the rhodium catalyzed reaction of diazoketone **198** with propargyl alcohol **199**.⁷⁶ It was reported that the O–H insertion between the carbenoid and alcohol **199** formed alkoxy enol intermediate **200**, which can either go through a [3,3]-sigmatropic rearrangement to give tertiary α -allenic alcohol **201** when electron rich $\text{Rh}_2(\text{cap})_4$ was used as catalyst (Scheme 2.37, Eq (a)), or go through a [2,3]-sigmatropic rearrangement to give α -allenic alcohol **202** when electrodeficient $\text{Rh}_2(\text{tfa})_4$ was used as catalyst (Eq (b)). Interestingly, when $\text{Rh}_2(\text{S-DOSP})_4$ was used as catalyst, α -allenic alcohol **202** was selectively formed in 42% isolated yield in racemic form, presumably due to the achiral enol intermediate formation. In order to achieve enantioselectivity for the [2,3]-sigmatropic rearrangement process, it was envisioned that the enol intermediate formation could be suppressed by using diazo ester instead of diazo ketone as the carbenoid precursor since the carbonyl in the ester would be much less nucleophilic than that in the ketone, and subsequently less prone to trap the proton and form the enol intermediate. To our surprise, the reaction of phenyldiazoacetate **6** with

propargyl alcohol **199** catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$ did not give any allene product. Instead, the racemic O–H insertion product **203** was isolated in 50% yield (Eq. (c)).

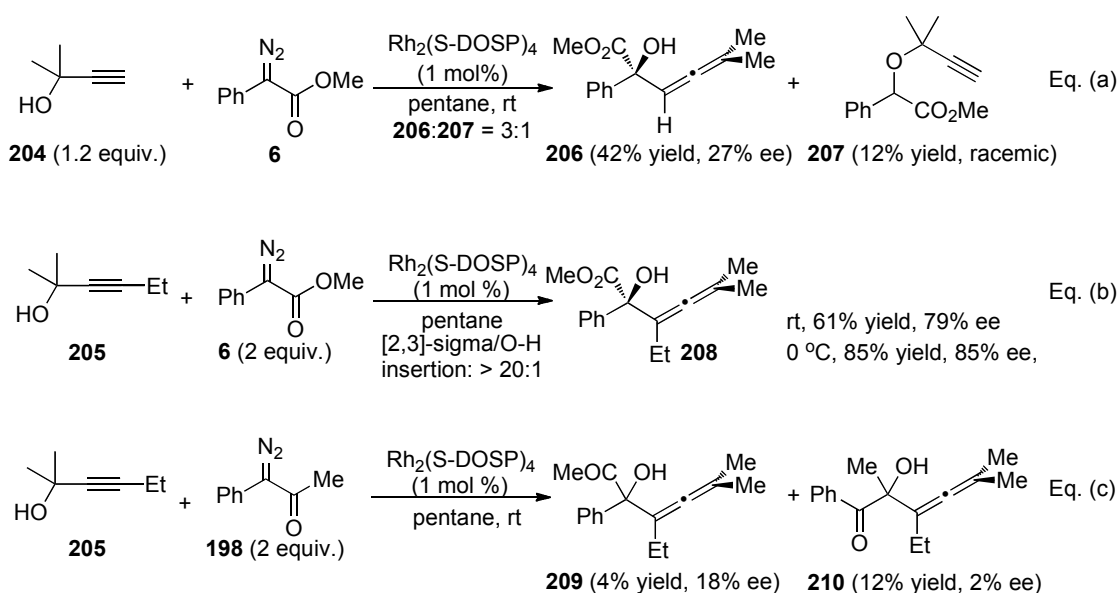
Scheme 2.37 Reactions of propargyl alcohol **199**



Previous studies showed that tertiary allylic alcohol had superior selectivity than secondary and primary allylic alcohols in favor of the [2,3]-sigmatropic rearrangement during its reaction with donor/acceptor carbenoids (Table 2.9). In order to promote the rearrangement, tertiary propargylic alcohol, 2-methyl-3-butyn-2-ol (**204**) was used instead of propargyl alcohol **199** (Scheme 2.38, Eq (a)). The reaction of **204** with phenyldiazoacetate **6** gave a 3:1 mixture of [2,3]-sigmatropic rearrangement product **206** and O–H insertion product **207**. Compound **206** was formed in 42% yield and 27% ee. As a typical rhodium catalyzed O–H insertion reaction, compound **207** was formed as racemate in 12% isolated yield. A dramatic change was observed when 2-methyl-3-hexyne-2-ol (**205**) was used (Eq (b)). [2,3]-sigmatropic rearrangement product **208** was cleanly formed in 61% isolated yield with 79% ee when the reaction was carried out at

room temperature. Further, on lowering the reaction temperature to 0 °C, **208** was cleanly formed in 85% isolated yield with 85% ee without any detection of the O–H insertion product from the crude ¹H NMR spectrum. However, this excellent chemo- and stereoselectivity did not work with diazo ketone **198** (Eq (c)). The reaction of **205** with **198** produced a mixture of [2,3]-sigmatropic rearrangement product **209** and [3,3]-sigmatropic rearrangement product **210**. Compound **209** was only isolated in 4% yield and 18% ee.

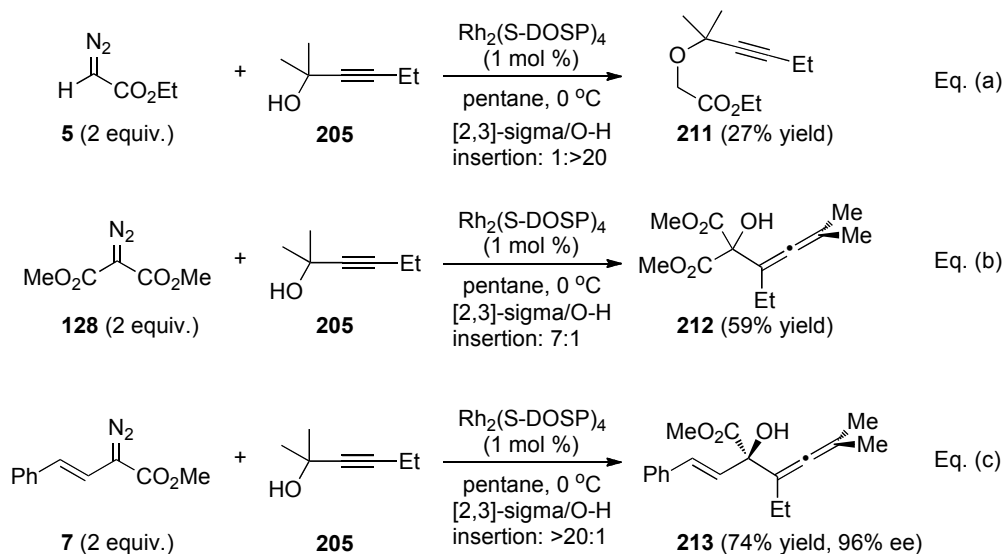
Scheme 2.38 Reactions of tertiary propargyl alcohols



After finding that the reaction of tertiary propargylic alcohol **205** and diazo ester **6** gave the best chemo- and stereoselectivity in favor of the [2,3]-sigmatropic rearrangement product formation, attention turned to test other diazo esters. Not surprisingly, the O–H insertion product **211** was the only isolable product from the reaction of ethyl diazoacetate **5** with **205** (Scheme 2.39, Eq (a)). The reaction of methyl diazomalonate **128** with **205** gave a mixture of [2,3]-sigmatropic rearrangement product

212 and the O–H insertion product with a ratio of 7:1, and **212** was isolated in 59% yield (Scheme 2.39, Eq (b)). In contrast with the conventional diazo ester **5** and **128**, the reaction of styryldiazoacetate **7** with **205** gave clean [2,3]-sigmatropic rearrangement product **213** in 74% isolated yield and 96% ee (Scheme 2.39, Eq (c)). As phenyldiazoacetate **6** and styryldiazoacetate **7** are widely used donor/acceptor carbenoid precursors, these results clearly demonstrated that donor/acceptor carbenoids had much better selectivity in favor of the [2,3]-sigmatropic rearrangement than the conventional carbenoids containing only one or two electron withdrawing groups.

Scheme 2.39 Effect of carbenoid structure on the reaction selectivity



The excellent chemo- and stereoselectivity were also apparent in the reactions of other arylvinyldiazoacetates with alcohol **205** (Table 2.24). The electron-withdrawing groups such as Br-, CF₃, Cl- on the aryl group were tolerated in the reactions and [2,3]-sigmatropic rearrangement product **218–212** were formed with good yield and very high enantioselectivity (Table 2.24, entries 1-4, 77–85% yield, 85–97% ee). Even though low yield of [2,3]-sigmatropic rearrangement product **222** was obtained in the reaction of

diazoacetate **217** and **205** (34% yield), its high enantioselectivity was still impressive (92% ee, entry 4). In all of these cases, no competing O–H insertion products were observed from the $^1\text{H-NMR}$ spectra of the crude reaction mixture.

Table 2.24 Reaction of arylvinyl diazoacetates with alcohol **205**

entry	R	product	yield, % ^a	ee, % ^b
1	211	218	81	97
2	214	219	85	96
3	215	220	81	85
4	216	221	77	96
5	217	222	34	92

^a Isolated yield. ^b Determined by chiral HPLC.

Further exploration with other propargylic alcohols showed that the reactions had very broad substrate scope, and high enantioselectivities were routinely obtained in all of the cases (Table 2.25). Alkyl groups (linear or cyclic, entries 1–6), TBS protected alcohols (entries 8–9) and substituents containing phenyl groups (entries 10–13) were all compatible in the reaction, even though other active C–H activation or cyclopropanation sites were present in these substrates. Alcohols with very bulky R groups such as *t*-butyl and trimethylsilyl, however, gave lower yield (entry 14–15), due to the competing [1,2]-

shift product formation (section 2.2.6). Compound **243** was recrystallized from hexanes and its absolute configuration was determined to be (*R*) by X-ray crystallography (Figure 2.15). The drawn absolute configuration of the other products is the tentatively assigned stereochemistry, assuming that a similar mode of asymmetric induction occurs for all the substrates.

Figure 2.15 X-ray structure of compound **243**

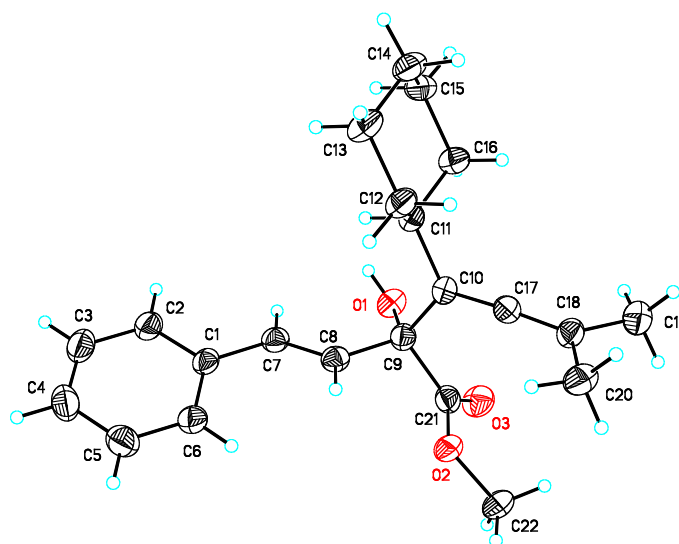
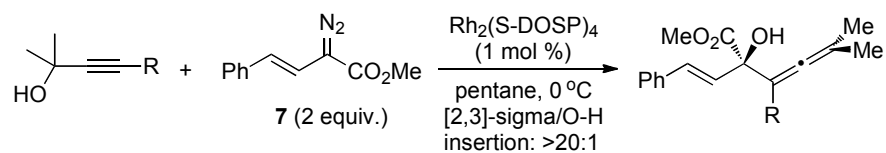


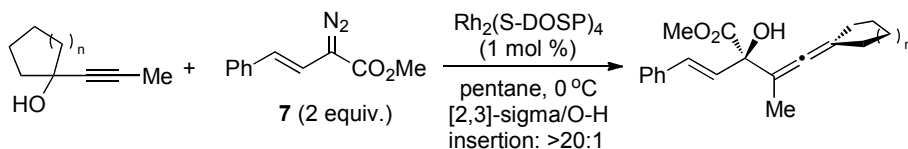
Table 2.25 Reaction of alcohol **223-237** with styryldiazoacetate **7**

entry	R	alcohol	product	yield, % ^a	ee, % ^b
1	CH ₃	223	238	77	96
2	<i>n</i> -C ₄ H ₉	224	239	86	95
3	<i>n</i> -C ₁₀ H ₂₁	225	240	88	96
4	OEt	226	241	44	95
5		227	242	60	92
6		228	243	78	98
7		229	244	51	97
8		230	245	66	90
9		231	246	84	96
10		232	247	72	97
11		233	248	59	94
12		234	249	44	92
13		235	250	79	95
14		236	251	44	96
15		237	252	37	94

^a Isolated yield. ^b Determined by chiral HPLC.

Instead of dimethyl groups, alcohol **253–255** containing cyclic subunits were also good substrates for the α -allenic alcohol formation (Table 2.26). Compound **256–258** containing five, six, and seven member rings were cleanly formed in 69–85% yield with 88–94% ee.

Table 2.26 Reaction of alcohol **253–255** with styryldiazoacetate **7**



entry	n	alcohol	product	yield, % ^a	ee, % ^b
1	1	253	256	69	88
2	2	254	257	85	94
3	3	255	258	82	95

^a Isolated yield. ^b Determined by chiral HPLC.

2.2.5.2 Reactions with chiral tertiary propargylic alcohols

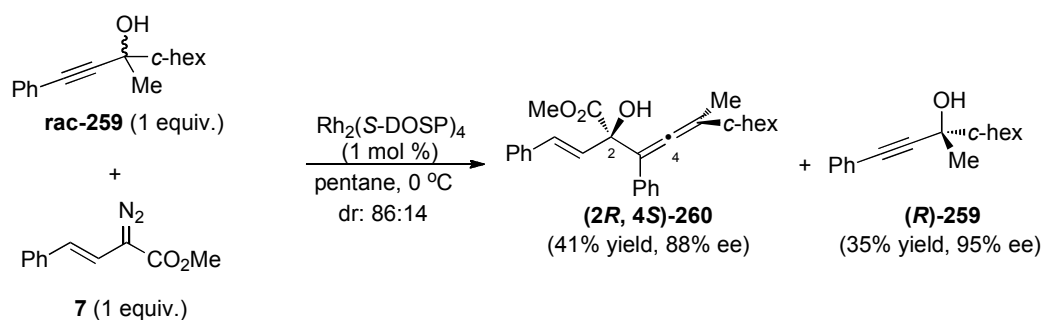
Previous studies of the tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and chiral allylic alcohols showed that the chiral catalyst dominated the tertiary alcohol stereocenter, and the chirality of the alcohol could be effectively transferred to the second stereocenter during the rearrangement (section 2.2.3). With the perspective that this stereocontrol could also be applied to the reactions of donor/acceptor carbenoids and chiral propargylic alcohols, the following studies were carried out.

A more effective way to do these studies would be to use racemic propargylic alcohols as starting material and avoid the tedious synthesis of enantiomerically pure alcohols. For this purpose, alcohol **259**, containing methyl and cyclohexyl groups on the carbinol position, was chosen with the hope that the size difference between these two

groups could cause the two enantiomers of **259** to have different reactivity during their reaction with donor/acceptor carbenoids. The ideal situation would be that one enantiomer of **259** could react with the carbenoids, while another enantiomer could not react and subsequently get enriched during the reaction.

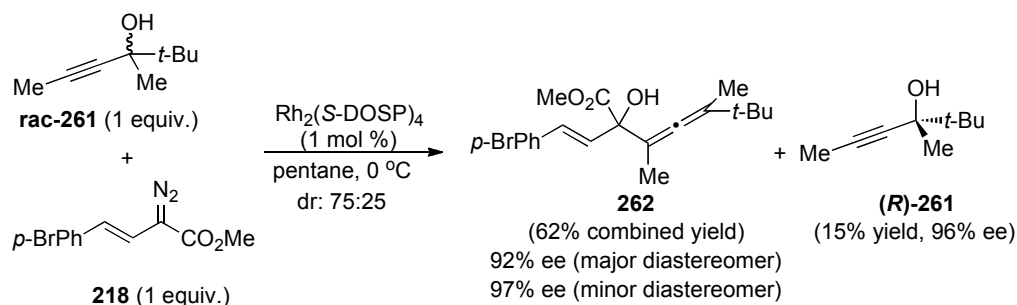
Gratefully, the reaction of racemic alcohol **259** with styryldiazoacetate **7** worked smoothly to produce α -allenic alcohol **260** with good diastereoselectivity (Scheme 2.40, dr: 86:14). The major diastereomer (**2R, 4S**)-**260** was isolated in 41% yield and 88% ee. More interestingly, (**R**)-**259** was also isolated in 35% yield and 95% ee. The absolute configuration of (**R**)-**259** was assigned according to its analogue (**R**)-**261** (96% ee, $[\alpha]_D^{20}$: +1.94° (*c* 6.03, Et₂O), lit. +1.44° (*c* 6.03, Et₂O)) from the reaction of racemic **261** and *p*-bromophenylvinyl diazoacetate **218** (Scheme 2.41).

Scheme 2.40 Reaction of racemic alcohol **259** with styryldiazoacetate **7**



Scheme 2.41 Reaction of racemic alcohol **261** with *p*-bromophenylvinyl diazoacetate

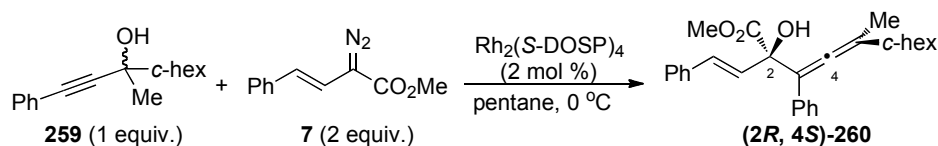
218



The reaction of racemic alcohol **259** and styryldiazoacetate **7** was carried out on a one gram scale to provide **(R)-259** (0.35 g, 31% yield, 96% ee) with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst and **(S)-259** (0.38 g, 34% yield, 95% ee) with $\text{Rh}_2(\text{R-DOSP})_4$ as catalyst, respectively. With the enantiomerically pure alcohol **259** in hand, their reactions with styryldiazoacetate **7** were carried out and the results revealed an interesting match/mismatch issue between the chiral alcohol and the chiral catalyst (Table 2.27). The reaction of **7** and **(S)-259** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst and the reaction of **7** and **(R)-259** with $\text{Rh}_2(\text{R-DOSP})_4$ as catalyst resulted in matched reactions, and the [2,3]-sigmatropic rearrangement products were formed as single diastereomer with extremely high enantioselectivity (>97:3 dr, >99% ee, Table 2.27, entry 1 and 3). However, The reaction of **7** and **(S)-259** with $\text{Rh}_2(\text{R-DOSP})_4$ as catalyst and the reaction of **7** and **(R)-259** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst resulted in mismatched reactions, and the [2,3]-sigmatropic rearrangement products were formed as 2:1 diastereomeric mixtures (entries 2 and 3). The α -allenic alcohol **260** from the reaction of **(S)-259** and **7** with $\text{Rh}_2(\text{S-DOSP})_4$ as catalyst was recrystallized from cold hexanes (entry 1, >99% ee), and its X-ray crystallography determined that the absolute configuration of the tertiary

alcohol stereocenter was (*R*) and the configuration of the chiral allene moiety was (*S*) (Figure 2.16). The (*R*) configuration at the tertiary alcohol stereocenter was also consistent with that of compound **243** (Figure 2.15).

Table 2.27 Reaction of enantiomerically pure alcohol **259** with styryldiazoacetate **7**



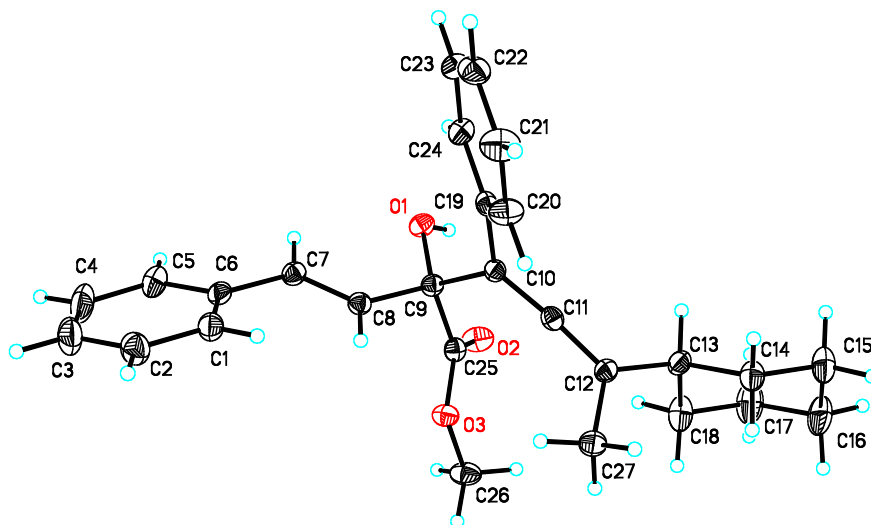
entry	259	Rh(II)	dr ^a	yield, %	ee of (2R, 4S)- 260 , % ^d
1	<i>S</i> , 95% ee	Rh ₂ (<i>S</i> -DOSP) ₄	>97 : 3	70 ^b	99
2	<i>S</i> , 95% ee	Rh ₂ (<i>R</i> -DOSP) ₄	37 : 63	42 ^c	51
3	<i>R</i> , 96% ee	Rh ₂ (<i>R</i> -DOSP) ₄	>97 : 3	79 ^b	-99 ^e
4	<i>R</i> , 96% ee	Rh ₂ (<i>S</i> -DOSP) ₄	32 : 68	39 ^c	-59 ^e

^a Determined by crude ¹H-NMR. ^b Isolated yield of the major diastereomer.

^c ee Combined isolated yield of both diastereomers. ^d Determined by chiral HPLC.

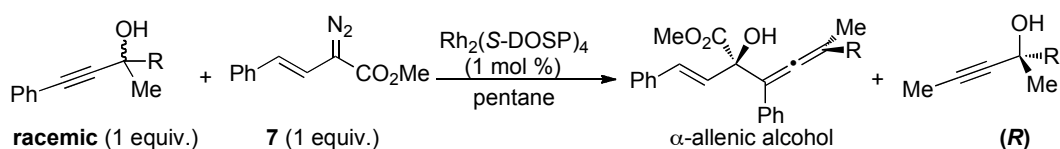
^e "-" signifies the opposite enantiomeric series.

Figure 2.16 X-ray structure of compound (**2R, 4S**)-**260**



Besides alcohol **259**, other racemic alcohols such as **263** and **264** containing large *iso*-propyl and *t*-butyl groups can also be used in the reaction with styryldiazoacetate **7** (Table 2.28). The (*R*)-**263** and (*R*)-**264** were enriched to 81% ee and 77% ee, respectively (entries 1 and 2). Meanwhile, the major diastereomer of α -allenenic alcohol **265** and **266** were also formed in high enantioselectivity (93% ee), and their absolute configuration was assigned according to compound (**2R, 4S**)-**260**. Further lowering the reaction temperature to $-45\text{ }^{\circ}\text{C}$ did not significantly enhance the stereoselectivity (entry 3).

Table 2.28 Reactions of racemic alcohol **263** and **264** with styryldiazoacetate **7**



entry	R	alcohol	temp., $^{\circ}\text{C}$	dr ^a	α -allenenic alcohol		<i>(R)</i> -alcohol		
					yield, % ^b	ee, % ^c	yield, % ^d	ee, % ^e	
1	<i>i</i> -Pr	263	0	77 : 23	265	47	93	36	81
2	<i>t</i> -Bu	264	0	87 : 13	266	50	93	42	77
3	<i>t</i> -Bu	264	-45	87 : 13	266	44	97	50	65

^a Determined by crude $^1\text{H-NMR}$. ^b Combined yield of two diastereomers. ^c ee of the major diastereomer, determined by chiral HPLC. ^d Isolated yield. ^e Determined by chiral HPLC

2.2.5.3 Reactions with chiral secondary propargylic alcohols

The reaction of styryldiazoacetate **7** with secondary chiral propargylic alcohol was also briefly investigated. Both enantiomerically pure (*R*)- and (*S*)- alcohol **267** were synthesized following the literature procedure.⁷⁷ Their reactions with styryldiazoacetate **7** are summarized in Table 2.29. Similar to the reactions of **7** with tertiary alcohol **259** (Table 2.27), the combination of (*R*)-**267** and $\text{Rh}_2(\text{S-DOSP})_4$ resulted in a mismatch situation and only small amount of α -allenenic alcohol **268** could be observed from the ^1H

NMR of the crude reaction mixture (entry 1). The combination of (*R*)-**267** and Rh₂(*R*-DOSP)₄ or (*S*)-**267** and Rh₂(*S*-DOSP)₄ produced much better results. Both (**2S, 4R**)-**268** and (**2R, 4S**)-**268** were isolated in ~30% yield and >99% ee. Their absolute configurations were assigned according to the X-ray crystallography of (**2S, 4R**)-**268** (Figure 2.17). The low selectivity between [2,3]-sigmatropic rearrangement and O–H insertion was the major cause of the low isolated yields of **268** (ratio of [2,3]-sigma/O–H insertion: 1:1).

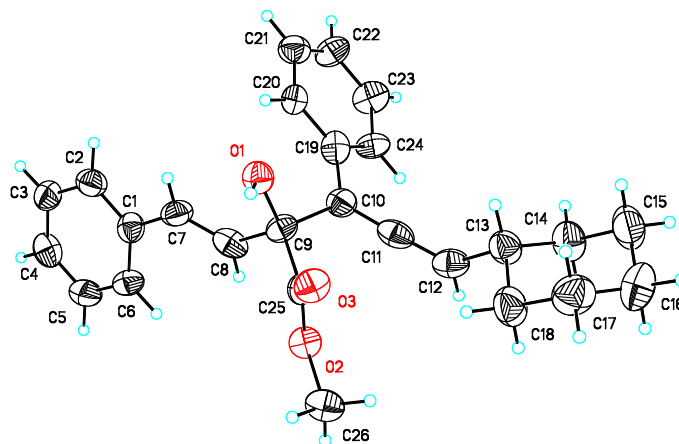
Table 2.29 Reactions of chiral secondary alcohol **267** with styryldiazoacetate **7**

entry	configuration of 267	Rh(II)	α -allenic alcohol		
				yield, % ^a	ee, % ^b
1	(<i>R</i>), 97% ee	Rh ₂ (<i>S</i> -DOSP) ₄	ND	<5	
2	(<i>R</i>), 97% ee	Rh ₂ (<i>R</i> -DOSP) ₄	(2S, 4R)-268	33	>99
3	(<i>S</i>), 97% ee	Rh ₂ (<i>S</i> -DOSP) ₄	(2R, 4S)-268	31	>99

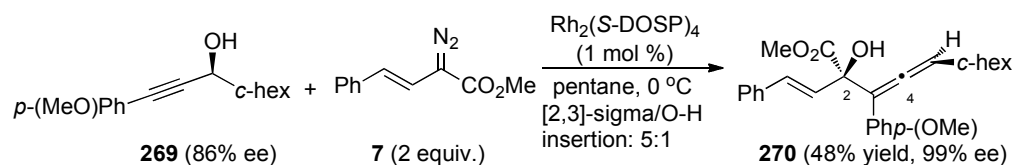
^a Isolated yield. ^b ee determined by chiral HPLC.

Since the ability to stabilize the positive charge in the oxonium ylide intermediate is critical for the selectivity between [2,3]-sigmatropic rearrangement and O–H insertion (section 2.2.2), it is expected that adding the electron donating methoxy group on the para position of phenyl in alcohol **268** would effectively stabilize the positive charge in the ylide intermediate and hence favor the [2,3]-sigmatropic rearrangement. Indeed, using alcohol **269** (86% ee) as substrate, the ratio of [2,3]-sigmatropic rearrangement over O–H insertion improved from 1:1 to 5:1 compared with alcohol **267**, and α -allenic alcohol **270** was isolated in 48% yield and 99% ee (Scheme 2.42).

Figure 2.17 X-ray structure of compound (**2*S***, **4*R***)-**268**



Scheme 2.42 Reactions of chiral secondary alcohol **269** with styryldiazoacetate **7**

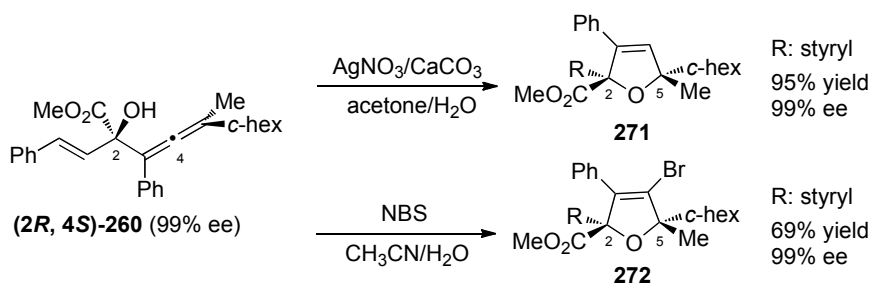


2.2.5.4 Stereoselective cyclization of α -allenic alcohols

One of the most favorable transformations of α -allenic alcohols is their stereoselective conversion into 2,5-dihydrofurans.⁷³ This transformation has also been successfully applied to the total synthesis of a variety of natural products containing the 2,5-dihydrofuran subunit such as Amphidinolide X and Y,⁷⁸ and Boivinnianin B.⁷⁹ The highly substituted α -allenic alcohols synthesized from the reactions of arylvinylidiazooacetates and tertiary propargylic alcohols can also be easily transformed into various 2,5-dihydrofuran derivatives with the >99% chirality transfer (Scheme 2.43). Treatment of (**2*R***, **4*S***)-**260** (99% ee) with AgNO₃ and CaCO₃ or NBS, 2,5-dihydrofurans **271** and **272** containing two quaternary stereocenters were smoothly formed as single

diastereomers in 69-95% yield and 99% ee. The chirality on the allene moiety was effectively transferred to the stereocenter at the 5-position of the dihydrofuran ring. NOE study of **271** and **272** showed that the ester group at 2-position and the methyl group at 5-position were on the same side of the furan ring in both compounds. Their absolute configurations were assigned assuming that the stereocenter at 2-position did not change during the cyclization step.

Scheme 2.43 Formation of 2,5-dihydrofurans

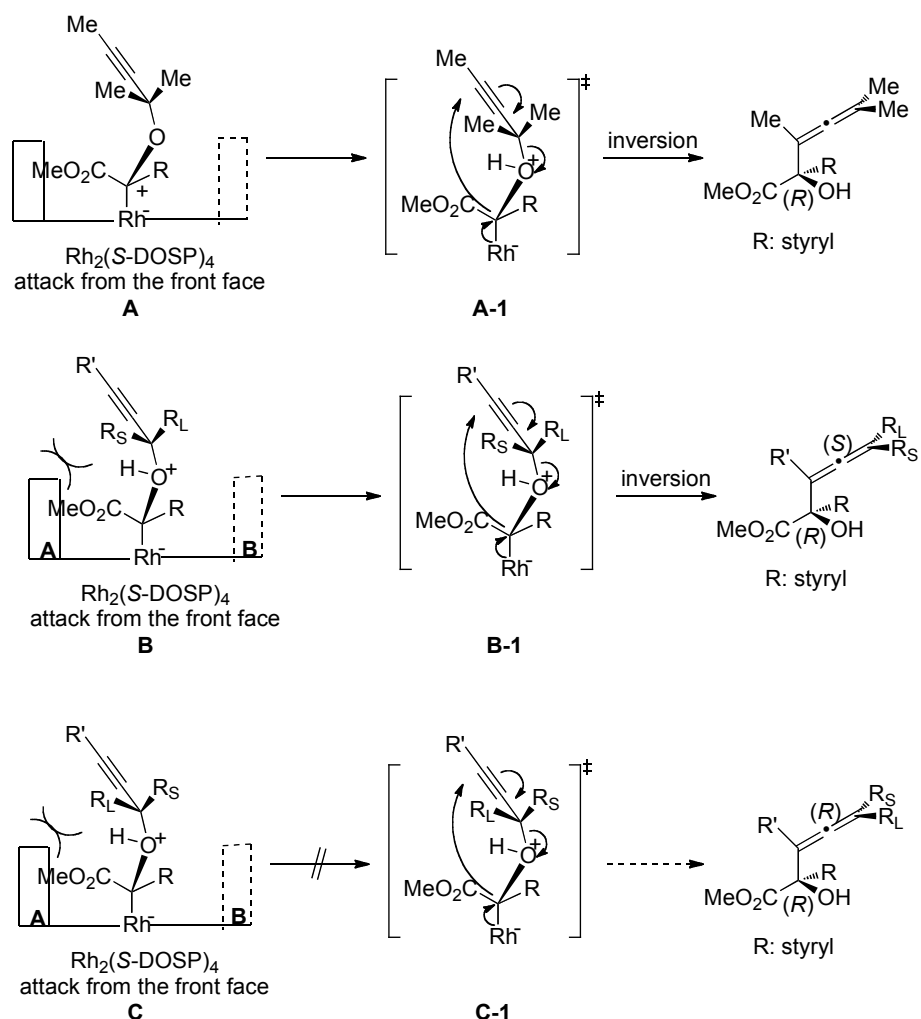


2.2.5.5 Rationalization of the stereoselectivity

All of the α -allenic alcohols derived from the reaction of styryldiazoacetate **7** and various propargylic alcohols catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$ had the same (*R*) configuration at the tertiary alcohol stereocenter. This is also consistent with all of the products derived from the reaction of **7** and various allylic alcohols catalyzed by the same catalyst (section 2.2.1-2.2.4). This extraordinary consistency signifies that similar ylide intermediates are involved in all of the reactions. Therefore, some important assumptions used for the transition state analysis of the [2,3]-sigmatropic rearrangement between donor/acceptor carbenoid and allylic alcohols (section 2.2.3) were also applied here. They included the catalyst $\text{Rh}_2(\text{S-DOSP})_4$ D_2 -symmetric conformation and the chirality inversion of the rhodium associated carbon stereocenter during the rearrangement. A simple transition

state analysis using alcohol **223** as substrate was shown in Figure 2.18. Alcohol **223** approaches the carbenoid from the front open side to form ylide **A-1**, which subsequently goes through the [2,3]-sigmatropic rearrangement via a rigid five-center transition state along with the inversion of the rhodium associated carbon stereocenter and gives rise to the product with (*R*) configuration at the tertiary alcohol stereocenter.

Figure 2.18 Transition state analysis for the formation of α -allenic alcohol



When the chiral propargylic alcohol containing two different groups as R_L and R_S on the carbinol position is used as substrate, this alcohol would also approach the carbenoid

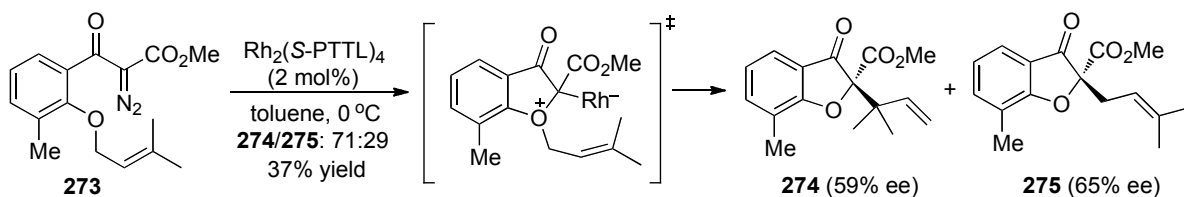
in a similar way as alcohol **223**. Experimental data shows that the carbenoid prefers to react with the (*S*)-alcohol and produces the [2,3]-sigmatropic rearrangement product with (*R*)-configuration at the tertiary alcohol stereocenter and (*S*)-configuration at the chiral allene moiety. These results support the transition state analysis (ylide formation, followed with the [2,3]-sigmatropic rearrangement) shown in Figure 2.18.B with R_S group of the (*S*)-alcohol on the left and R_L group on the right. This arrangement would have the minimum steric interaction between the R groups of the alcohol and the blocking groups of the carbenoid.

High level of kinetic resolution in the reactions of styryldiazoacetate **7** with various racemic propargylic alcohols (Scheme 2.40, Table 2.28) might also originate from this type of steric interaction. In a mismatched reaction with (*R*)-alcohol, a similar analysis will have R_L group of the (*R*)-alcohol on the left side and its strong steric interaction with blocking group A will prevent the following [2,3]-sigmatropic rearrangement process (Figure 2.18, C). One possible factor that could enhance this match/mismatch effect is the hydrogen bonding between the carbonyl of the ester and the hydroxyl group of the alcohol in the oxonium ylide. This hydrogen bonding can further draw the R groups of the alcohol closer to blocking group A. Of course, more detailed studies, particularly the theoretical calculation studies will eventually lead to an improved and more accurate understanding of this chemistry.

2.2.6 Highly enantioselective intermolecular [1,2]-Stevens rearrangement between donor/acceptor carbenoids and tertiary alcohols

[1,2]-Stevens rearrangement of ylides derived from metal carbenoid and heteroatoms such as nitrogen, sulfur and oxygen is a very useful synthetic method, particularly for the construction of medium-size heterocycles through ring expansion.^{1a,80} Dirhodium tetraacetate ($\text{Rh}_2(\text{OAc})_4$) is one of the most widely used catalysts in this chemistry. The asymmetric [1,2]-Stevens rearrangement has also been observed as the competing reaction with the [2,3]-sigmatropic rearrangement in the chiral dirhodium complex catalyzed ylide transformations.⁸¹ One such examples is the $\text{Rh}_2(\text{S-PTTL})_4$ catalyzed decomposition of diazo **273** (Scheme 2.44).^{81b} The major product in this reaction is compound **274**, derived from the [2,3]-sigmatropic rearrangement of the oxonium ylide intermediate. The minor product, compound **275** was formed from the [1,2]-Stevens rearrangement of the same ylide intermediate in 65% ee.

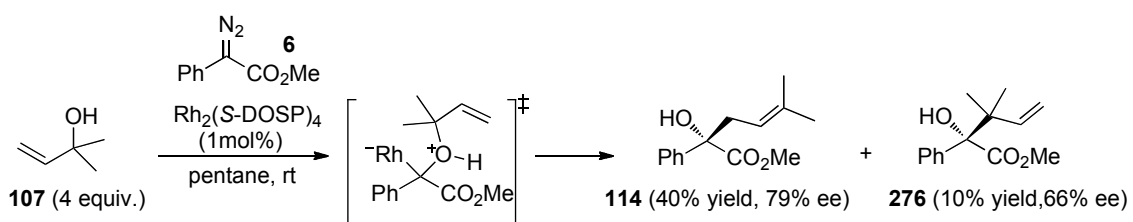
Scheme 2.44 Asymmetric [1,2]-Stevens rearrangement catalyzed by $\text{Rh}_2(\text{S-PTTL})_4$



During the study of tandem ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoid and allylic alcohols (chapter 2.2.2), tertiary allylic alcohol **107** was used as substrate to react with phenyldiazoacetate **6**. Surprisingly, besides the expected [2,3]-sigmatropic rearrangement product **114**, compound **276** was also isolated

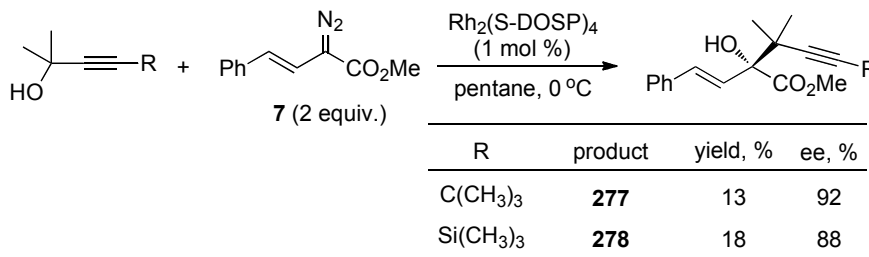
in 10% yield and 66% ee (Scheme 2.45). Presumably, both compound **114** and **276** were formed from the same oxonium ylide intermediate, and stabilization of the positive charge by the tertiary carbon moiety in the ylide intermediate contributed the [1,2]-Stevens rearrangement product formation.

Scheme 2.45 Formation of compound **273**

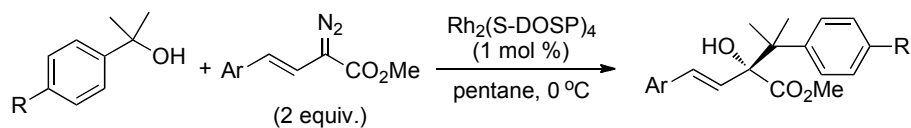


[1,2]-Stevens rearrangement products were also observed as byproducts in the reaction of styryldiazoacetate **7** with tertiary propargylic alcohols. In most cases, they were formed in <2% yield. Much higher yield was obtained when alcohol containing large group on the triple bond was used as substrate. For example, with R as trimethylsilyl and *t*-butyl, [1,2]-Stevens rearrangement products **277** and **278** could be isolated in 13–18% yield and 88–92% ee (Scheme 2.46).

Scheme 2.46 Formation of compound **277** and **278**

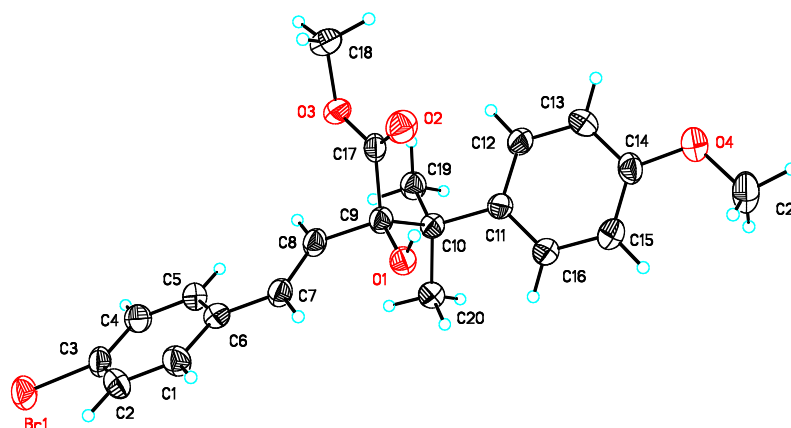


Impressed with the highly enantioselective formation of compound **277** and **278**, a further study to develop this methodology was undertaken. Initially, alcohol **279** was chosen as substrate with the expectation that the tertiary benzylic carbon would effectively stabilize the positive charge in the ylide intermediate and subsequently suppress the competing O–H insertion reaction. Indeed, no O–H insertion product was observed in the reaction of **279** with styryldiazoacetate **7** catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$. However, [1,2]-Stevens rearrangement product **281** was formed in only 21% isolated yield due to a lot of other unknown product formation (Table 2.30, entry 1). A much cleaner reaction was observed when alcohol **280** containing methoxy group on the para position of phenyl was used as substrate (entry 2). The low yield of **282** was due to its difficult separation with the diazo dimerization byproducts (48% yield). The reaction of **280** with *p*-bromophenylvinyl diazoacetate **218** produced [1,2]-Stevens rearrangement product **283** in 40% yield and 87% ee (entry 3), which could be further enriched to 94% ee through recrystallization from hexanes. Its X-ray crystallography determined the absolute configuration of the tertiary alcohol stereocenter as (*R*) (Figure 2.19). The configurations of all of the other [1,2]-Stevens rearrangement products were tentatively assigned as (*R*), assuming that a similar mode of asymmetric induction occurred in all the reactions.

Table 2.30 Reaction of alcohol **279** and **280** with arylvinyl diazoacetates

entry	R	Ar	alcohol	product	yield, % ^a	ee, % ^b
1	H	Ph	279	281	21	88
2	OMe	Ph	280	282	48	94
3	OMe	<i>p</i> -BrPh	280	283	40	87

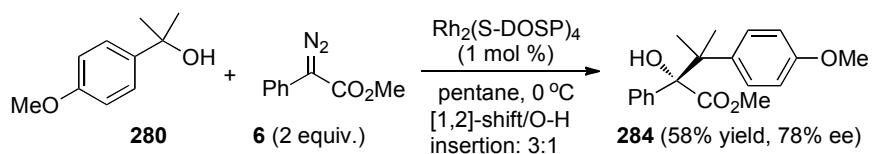
^a Isolated yield. ^b ee determined by chiral HPLC.

Figure 2.19 X-ray structure of compound **283**

Low selectivity between [1,2]-Stevens rearrangement and O–H insertion reaction was observed when phenyldiazoacetate **6** was used as the donor/acceptor carbenoid precursor (Scheme 2.47). The reaction of **6** with alcohol **280** produced a 3:1 mixture of [1,2]-Stevens rearrangement product **284** and the O–H insertion product. Compound **284** was isolated in 58% yield and 78% ee. (Note: the reaction in Table 2.30, entry 3 and the

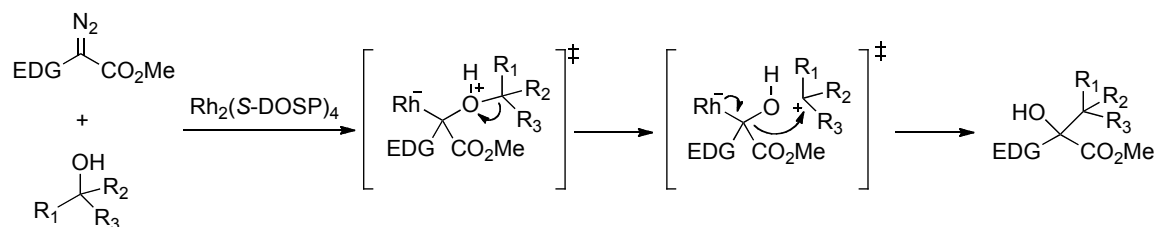
reaction in Scheme 2.47 were conducted by undergraduate student Robbin Hoggins under my supervision).

Scheme 2.47 Reaction of alcohol **280** with phenyldiazoacetate **6**



The mechanism of the [1,2]-Stevens rearrangement has been extensively studied via various calculations.⁸² Generally it is considered as a diradical mechanism, through the homolytic dissociation of the migrating group to form a radical couple, followed with the radical coupling. It has been documented that the [1,2]-Stevens rearrangement of oxonium ylide also goes through this rapid radical dissociation-recombination mechanism.^{81b,83} The [1,2]-Stevens rearrangement of donor/acceptor carbenoids with tertiary alcohols, however, suggest that the reaction might involve a carbocation intermediate, since the ability of the tertiary alcohols to stabilize the carbocation intermediate is critical for the rearrangement to occur (Scheme 2.48).

Scheme 2.48 Possible mechanism of the [1,2]-Stevens rearrangement



The (*R*) configuration of the tertiary alcohol stereocenter in the [1,2]-Stevens rearrangement product is consistent with the products derived from the reaction of

donor/acceptor carbenoids with allylic alcohols and propargylic alcohols catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$, which suggests that the oxonium ylide intermediates with similar configuration are involved in all of these transformations. Presumably, the tertiary alcohol approaches the carbenoid in a similar trajectory to the allylic alcohols and propargylic alcohols to form the oxonium ylide, then this ylide will undergo the carbocation intermediate formation and the rapid C–C bond formation with inversion of configuration at the rhodium-bound carbon. Further studies to elucidate a more detailed understanding of the mechanism are underway in the Davies group.

2.3 Conclusion

A novel tandem oxonium ylide formation/[2,3]-sigmatropic rearrangement of donor/acceptor carbenoids and allylic alcohols/propargylic alcohols was discovered and the scope and limitations were explored. α -Hydroxycarboxylate derivatives were synthesized with very high stereoselectivity (up to >97:3 dr and >99% ee). Dirhodium tetraperchlorate, $\text{Rh}_2(\text{S-DOSP})_4$, was the best catalyst for this type of transformation, and its chirality dominated the configuration of the tertiary alcohol stereocenter in the product. When chiral allylic alcohols were used as substrates, the chirality of the alcohol was effectively transformed to the second stereocenter in the product. When chiral propargylic alcohols were used as substrates, the chirality of the alcohol was effectively transformed to the allene moiety in the product. These studies not only provide a novel and efficient method to synthesize α -hydroxycarboxylate derivatives with high stereoselectivity, but also demonstrate that the donor/acceptor carbenoids have superior

reactivity over the conventional acceptor carbenoid and acceptor/acceptor carbenoids to suppress the competing O–H insertion reaction.

A highly enantioselective [1,2]-Stevens rearrangement between donor/acceptor carbenoids and tertiary alcohols was also briefly studied. α -Hydroxycarboxylate derivatives containing two adjacent quaternary centers were synthesized in 20–60% yield and 78–94% ee.

2.4 Experimental

2.4.1 General Information

All experiments were performed under anhydrous conditions in an argon atmosphere with oven-dried glassware. Pentane was dried by a solvent-purification system (passed through activated alumina columns) and degassed with argon before use. ^1H -NMR spectra were recorded at either 400 MHz on an INOVA-400 spectrometer, or at 600 MHz on an INOVA-600 spectrometer. ^{13}C -NMR and DEPT spectra were recorded at 100 MHz, or 150 MHz on the same instruments. NMR spectra were recorded in deuterated chloroform (CDCl_3) solutions, with residual chloroform (δ 7.27 ppm for ^1H NMR and δ 77.23 ppm for ^{13}C -NMR) taken as the internal standard, and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants were taken from the spectra directly and are uncorrected. IR spectra were collected on a Nicolet iS10 FT-IR spectrometer as neat films. Mass spectra determinations were carried out on a Thermo Finnigan LTQ-FTMS spectrometer with ESI or APCI ionization. Optical rotations were measured on JASCO P-2000 polarimeter. Elemental analysis was performed by Atlantic Microlab Inc, P. O. Box 2288, Norcross, Georgia. GC-MS analysis was performed on Shimadzu GC-17A, column condition: 80 °C, keep 1 min, then 10 °C/min to 250 °C, keep 5 min. GC analysis was performed on Agilent 7890A, column condition: 30 °C for 1 min, then increase to 180 °C at a rate of 5 °C /min, then keep 5 min. Analytical TLC was performed on silica gel plates using UV light or stained with 5% phosphomolybdic acid-ethanol

solution. Flash column chromatography was performed with silica gel 60 A (230-400 mesh).

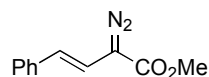
2.4.2 Synthetic procedures and characterization for Chapter 2.2.1 and 2.2.2

2.4.2.1 General procedure of the $\text{Rh}_2(\text{S-DOSP})_4$ -catalyzed tandem ylide formation/[2,3]-sigmatropic rearrangement of carbenoid with allylic alcohol:

A solution of $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol %) and allylic alcohol (0.5 - 2.0 mmol, 1- 4 equiv.) in 1 mL of degassed pentane was cooled to 0 °C with ice bath under argon. Diazo solution (0.5 - 0.55 mmol, 1 - 1.1 equiv.) in 5 mL of degassed pentane was added by syringe pump over 1 h. The syringe was rinsed with another 1 mL of degassed pentane and added to the reaction mixture. After addition, the solution was stirred for 30 min at 0 °C, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel.

2.4.2.2 Characterization of compounds in Chapter 2.2.1 and 2.2.2

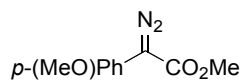
Methyl styryldiazoacetate (7)



Prepared by following the literature procedure.³⁷ A solution of benzaldehyde (6.1 mL, 60 mmol, 1 equiv.) and carboxyethyltriphenylphosphonium chloride (26.7 g, 72 mmol, 1.2 equiv.) in 130 mL of THF was cooled to 0 °C under argon. Potassium *t*-butoxide (16.8 g, 150 mmol, 2.5 equiv.) in 80 mL of THF was slowly added over 30 min with cannula.

After addition, the solution was stirred at 0 °C for 30 min, then warmed to room temperature and stirred for 20 min. Dimethyl sulfate (11.4 mL, 120 mmol, 2.0 equiv.) was added in one portion, and the solution was stirred at room temperature for 2.5 h. Then it was cooled to 0 °C, *p*-ABSA (18.7 g, 78 mmol, 1.3 equiv.) was added in one portion, followed with the rapid addition of DBU (11.7 mL, 78 mmol, 1.3 equiv.). The reaction mixture was stirred at 0 °C for 4 h, then warmed to room temperature and concentrated under vacuum. The residue was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (12:1) to afford compound **7** as red oil (9.9 g, 82% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.36–7.31 (m, 4H), 7.20 (t, *J* = 7.0 Hz, 1H), 6.47 (d, *J* = 16.5 Hz, 1H), 6.19 (d, *J* = 16.5 Hz, 1H), 3.85 (s, 3H). Data are consistent with the literature.⁸⁴

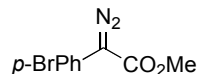
Methyl *p*-methoxyphenyldiazoacetate (**12**)



Prepared by following the literature procedure.²⁶ In a 500 mL round bottom flask, was added methyl *p*-methoxyphenylacetate (11.4 g, 63 mmol), *p*-ABSA (18.2 g, 76 mmol, 1.2 equiv.), and 120 mL of acetonitrile. DBU (13.6 mL, 91 mmol, 1.4 equiv.) was slowly added. The solution was stirred at room temperature for 12 h. Then 100 mL of saturated NH₄Cl was added. The mixture was extracted with diethyl ether (3 x 100 mL), the combined ether solution was washed with brine, dried over MgSO₄, and concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1) to afford compound **12** as orange solid (5.6 g,

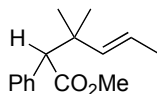
43% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.39 (d, $J = 9.2$ Hz, 2H), 6.94 (d, $J = 9.2$ Hz, 2H), 3.85 (s, 3H), 3.81 (s, 3H). Data are consistent with the literature.²⁶

Methyl *p*-bromophenyldiazoacetate (**30**)

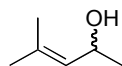


Prepared by following the literature procedure.²⁶ In a 250 mL round bottom flask, was added *p*-bromophenylacetic acid (10.6 g, 49 mmol) and 150 mL of methanol. Acetyl chloride (1.5 mL) was slowly added, and the solution was stirred at room temperature overnight. Then it was concentrated under vacuum. 30 mL of water was added to the residue, the mixture was extracted with diethyl ether (3 x 100 mL). The combined ether solution was dried over MgSO_4 , and concentrated under vacuum to give the corresponding ester which was used without further purification.

Methyl *p*-bromophenylacetate from last step was dissolved with 100 mL of acetonitrile and cooled to 0 °C. Then *p*-ABSA (14.2 g, 59 mmol, 1.2 equiv.) was added in one portion, followed with DBU (8.8 mL, 59 mmol, 1.2 equiv.). The mixture was stirred at room temperature overnight, then concentrated under vacuum. To the residue, was added 100 mL of saturated NH_4Cl . The mixture was extracted with diethyl ether (3 x 100 mL), the combined ether solution was washed with brine, dried over MgSO_4 , and concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (9:1) to afford compound **30** as orange solid (11.1 g, 88% yield). ^1H NMR (500 MHz, CDCl_3): δ 7.49 (d, $J = 9.0$ Hz, 2H), 7.36 (d, $J = 9.0$ Hz, 2H), 3.87 (s, 3H). Data are consistent with the literature.²⁶

(E)-Methyl 3,3-dimethyl-2-phenylhex-4-enoate (98)

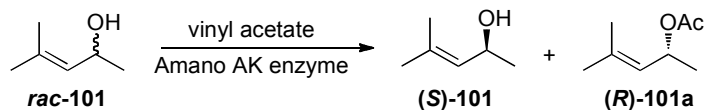
A solution of $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol %) and 4-methyl-pent-2-ene (**97**) (0.65 mL, 5 mmol, 10 equiv.) in 1 mL of degassed 2,2-dimethylbutane was heated to reflux (50 °C) under argon. Methyl phenyldiazoacetate (**6**) (88mg, 0.5 mmol) in 5 mL of degassed 2,2-dimethylbutane was added by syringe pump over 5 h. After addition, the solution was stirred for 30 min at 50 °C, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **98** as clear oil (12mg, 10% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.37–7.35 (m, 2H), 7.31–7.26 (m, 3H), 5.61 (dq, $J = 15.6, 1.6$ Hz, 1H), 5.28 (dq, $J = 15.6, 6.4$ Hz, 1H), 3.63 (s, 3H), 3.49 (s, 1H), 1.69 (dd, $J = 6.4, 1.6$ Hz, 3H), 1.06 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.4 (C), 138.2 (CH), 136.0 (C), 130.3 (CH), 127.8 (CH), 127.3 (CH), 123.0 (CH), 61.6 (CH), 51.6 (CH_3), 39.6 (C), 26.7 (CH_3), 24.6 (CH_3), 18.3 (CH_3); IR (neat): 1736, 1454, 1433, 1362, 1199, 1165, 1140, 1022, 974, 738, 702 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{15}\text{H}_{21}\text{O}_2$ $[\text{M}+\text{H}]^+$: 233.15361, found: 233.15334.

4-Methylpent-3-en-2-ol (rac-101)

Prepared by following the literature procedure.⁸⁶ The suspension of LiAlH_4 (4.9 g, 0.13 mol) in 100 mL of diethyl ether was cooled to 0 °C with ice-bath. A solution of 4-methyl-

3-penten-2-one (25.0 g, 0.25 mol) in 100 mL of diethyl ether was slowly added. After addition, the mixture was stirred at room temperature for 1h, then cooled to 0 °C, and carefully quenched with cold water. 15 mL of 15% aqueous NaOH solution and 50 mL of water were added to the mixture. The organic layer was separated, washed with brine, and dried over MgSO₄. After filtration, the solution was concentrated under vacuum, and the crude material was distilled with kugelrohr under vacuum to afford compound **101** as clear liquid (20.5 g, 80% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.12 (d, *J* = 8.4 Hz, 1H), 4.48-4.44 (m, 1H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.69 (d, *J* = 1.2 Hz, 3H), 1.40 (br., 1H), 1.22 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 133.3 (C), 129.3 (CH), 64.4 (CH), 25.4 (CH₃), 23.4 (CH₃), 17.8 (CH₃). Data are consistent with the literature.⁸⁶

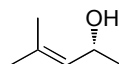
(S)-4-Methylpent-3-en-2-ol ((S)-101)



Prepared by following the literature procedure.⁸⁷ To the solution of racemic alcohol **101** (5.0 g, 0.05 mol) and vinyl acetate (12.5 mL, 0.14 mol, 2.8 equiv) in 250 mL of hexanes, was added Amano AK enzyme (2.5 g) and 4 Å molecular sieves (3.0 g). The mixture was stirred vigorously at room temperature for 15 h. After filtration, the solution was concentrated and the crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1 to 1:1) to afford **(S)-101** (2.2 g, 44% yield) and **(R)-101a** (2.7 g, 38% yield). **(S)-101**: Chiral capillary GC analysis: 69% ee, CHIRALDEX B-PM column, *t_R*: 5.31 min (minor), 6.74 min (major). This material was

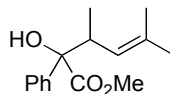
further enriched to 84% ee following the same procedure. **(R)-101a**: $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 5.56–5.55 (m, 1H), 5.18–5.14 (m, 1H), 2.02 (s, 3H), 1.72 (d, $J = 1.2$ Hz, 3H), 1.71 (d, $J = 1.2$ Hz, 3H), 1.26 (d, $J = 6.4$ Hz, 3H).

(R)-4-Methylpent-3-en-2-ol ((R)-101)



(R)-101a (2.6 g) was dissolved with KOH solution (6.0 g, 0.11 mol) in 15 mL of ethanol/ H_2O (7:3). The solution was heated to reflux for 2.5 h. After cooled to 0 °C, 100 mL of cold water was added, and the solution was neutralized with aqueous HCl. The solution was extracted with diethyl ether. The combined diethyl ether solution was dried over MgSO_4 , and concentrated to give the crude product, which was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 2:1) to afford **(R)-101** (1.0 g, 56% yield). Chiral capillary GC analysis: 83% ee, CHIRALDEX B-PM column, t_R : 5.31 min (major), 6.74 min (minor).

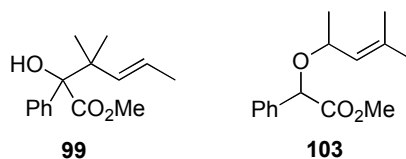
Methyl 2-hydroxy-3,5-dimethyl-2-phenylhex-4-enoate (102)



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (93 mg, 0.5 mmol) and (*E*)-2-methylpent-3-en-2-ol (**100**) (202 mg, 2.0 mmol, 4 equiv.) at 40 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **102**: pure major diastereomer (80 mg), a mixture of two

diastereomers (7 mg), and pure minor diastereomer (18 mg). Combined yield: 105 mg, 79% yield. **Major diastereomer:** clear oil, $[\alpha]_D^{20} +75.2^\circ$ (c 1.0, CHCl_3). R_f 0.32 (pentane/diethyl ether 10:1). ^1H NMR (600 MHz, CDCl_3): δ 7.71 (d, $J = 8.4$ Hz, 2H), 7.37 (t, $J = 8.4$ Hz, 2H), 7.29 (t, $J = 7.2$ Hz, 1H), 5.25 (d, $J = 10.2$ Hz, 1H), 3.76 (s, 1H), 3.70 (s, 3H), 3.36–3.33 (m, 1H), 1.72 (d, $J = 1.2$ Hz, 3H), 1.71 (d, $J = 1.2$ Hz, 3H), 0.77 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 176.1 (C), 140.7 (C), 133.1 (C), 128.3 (CH), 127.7 (CH), 126.4 (CH), 124.9 (CH), 80.9 (C), 53.2 (CH_3), 40.8 (CH), 26.3 (CH_3), 18.2 (CH_3), 14.5 (CH_3); IR (neat): 3511, 1723, 1447, 1436, 1250, 1151, 1122, 1013, 727, 699 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 231.13796, found: 231.13802. Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$: C, 72.55; H, 8.12. Found: C, 72.70, H, 8.18. HPLC analysis: 88% ee, (*S,S*)- Whelk- O1, 0.3% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm, t_R : 8.5 min (major), 10.3 min (minor). **Minor diastereomer:** white solid. $[\alpha]_D^{20} +6.1^\circ$ (c 1.0, CHCl_3). M.p.: 94–95 $^\circ\text{C}$. R_f 0.26 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.57 (dd, $J = 8.8, 1.6$ Hz, 2H), 7.32–7.22 (m, 3H), 4.99 (d, $J = 10.0$ Hz, 1H), 3.81 (s, 3H), 3.72 (s, 1H), 3.36–3.32 (m, 1H), 1.49 (s, 3H), 1.42 (s, 3H), 1.01 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 176.1 (C), 141.4 (C), 132.7 (C), 127.9 (CH), 127.5 (CH), 126.2 (CH), 124.2 (CH), 81.3 (C), 53.5 (CH_3), 40.6 (CH), 25.9 (CH_3), 18.1 (CH_3), 16.4 (CH_3); IR (neat): 3515, 1723, 1447, 1436, 1246, 1123, 730, 698 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$ $[\text{M}+\text{H}]^+$: 249.14852, found: 249.14854. Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$: C, 72.55; H, 8.12. Found: C, 72.29, H, 8.23. HPLC analysis: 65% ee, CHIRAL PAK AS-H, 0.3% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm, t_R : 9.6 min (major), 12.5 min (minor).

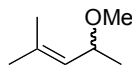
(*S, E*)-Methyl 2-hydroxy-3,3-dimethyl-2-phenylhex-4-enoate (99) and **methyl 2-((4-methylpent-3-en-2-yl)oxy)-2-phenylacetate (103)**



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (91 mg, 0.5 mmol) and 4-methylpent-3-en-2-ol (**101**) (racemic, 203 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded pure compound **99** (clear oil, 77 mg), mixture of compound **99** and compound **103** (1st diastereomer) (clear oil, 26 mg), and pure compound **103** (2nd diastereomer) (clear oil, 8 mg). Combined yield: 111 mg, 86% yield. **Compound 99**: $[\alpha]_D^{20}$ -30.4° (*c* 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.71–7.68 (m, 2H), 7.34–7.28 (m, 3H), 5.65 (m, 1H), 5.39–5.34 (m, 1H), 3.84 (s, 3H), 3.66 (s, 1H), 1.68 (dd, *J* = 6.4, 1.6 Hz, 3H), 1.09 (s, 3H), 1.04 (s, 3H); With the addition of D₂O, peak at 3.66 ppm disappeared; ¹³C NMR (100 MHz, CDCl₃): δ 174.7 (C), 138.8 (C), 136.8 (CH), 127.7 (CH), 127.6 (CH), 127.3 (CH), 124.3 (CH), 83.1 (C), 52.9 (CH₃), 44.3 (C), 23.5 (CH₃), 23.3 (CH₃), 18.5 (CH₃); IR (neat): 3502, 1717, 1447, 1434, 1227, 1161, 1061, 978, 745, 701 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₅H₂₀O₃ [M+H]⁺: 249.14852, found: 249.14862. Anal. Calcd for C₁₅H₂₀O₃: C, 72.55; H, 8.12. Found: C, 72.34, H, 8.29. HPLC analysis: 86% ee, (*S, S*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, *t*_R: 10.2 min (major), 12.6 min (minor). **Compound 103**: 1st diastereomer: ¹H NMR (400 MHz, CDCl₃): δ 7.46–7.43 (m, 2H), 7.37–7.30 (m, 3H), 5.10–5.07 (m, 1H), 4.98 (s,

1H), 4.39–4.35 (m, 1H), 3.72 (s, 3H), 1.74 (d, $J = 1.2$ Hz, 3H), 1.63 (d, $J = 1.2$ Hz, 3H), 1.32 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.6 (C), 137.4 (C), 136.5 (C), 128.7 (CH), 128.5 (CH), 127.3 (CH), 126.6 (CH), 77.5 (CH), 71.4 (CH), 52.3 (CH_3), 26.0 (CH_3), 21.8 (CH_3), 18.2 (CH_3); IR (neat): 1750, 1451, 1435, 1207, 1170, 1117, 1070, 728, 696 cm^{-1} ; GC-MS analysis: t_{R} : 9.05 min, m/z 55 (68%), 67 (78%), 77 (61%), 79 (75%), 83 (100%), 107 (82%), 166 (3%). HPLC analysis: 10% ee, (*S,S*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, t_{R} : 14.7 min (major), 17.5 min (minor). **2nd diastereomer**: ^1H NMR (400 MHz, CDCl_3): δ 7.46–7.44 (m, 2H), 7.37–7.32 (m, 3H), 5.15–5.12 (m, 1H), 4.92 (s, 1H), 4.14–4.10 (m, 1H), 3.67 (s, 3H), 1.75 (d, $J = 1.2$ Hz, 3H), 1.51 (d, $J = 1.2$ Hz, 3H), 1.26 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.9 (C), 137.4 (C), 136.3 (C), 128.7 (CH), 128.6 (CH), 127.6 (CH), 126.6 (CH), 77.9 (CH), 70.5 (CH), 52.4 (CH_3), 26.1 (CH_3), 21.8 (CH_3), 18.3 (CH_3); IR (neat): 1757, 1435, 1204, 1168, 1114, 1067, 729, 697 cm^{-1} ; GC-MS analysis: t_{R} : 9.25 min, m/z 55 (67%), 67 (96%), 77 (72%), 79 (89%), 83 (95%), 107 (100%), 166 (3%). HPLC analysis: 7% ee, (*S,S*)-Whelk-O1, 1.0 % isopropanol/hexanes, 0.7 mL/min, UV 230 nm, t_{R} : 14.9 min (major), 23.1 min (minor).

4-Methoxy-2-methylpent-2-ene (104)

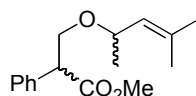


Prepared by following the literature procedure.⁸⁵ A solution of 4-methyl-3-penten-2-ol (**101**) (5.5 g, 54 mmol) in 6 mL of diethyl ether was slowly added to the suspension of NaH (1.8 g, 71 mmol, 1.3 equiv.) in 25 mL of diethyl ether under argon. The mixture was

heated to reflux for 1 h. After cooled to room temperature, MeI (5.4 mL, 87 mmol, 1.6 equiv.) was slowly added, and the solution was relaxed for another 8 h. Then it was carefully quenched with water at 0 °C, the mixture was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over K₂CO₃, and concentrated under vacuum. The crude material was distilled with kugelrhor under vacuum to afford compound **104** as clear oil (3.8 g, 61% yield). ¹H NMR (600 MHz, CDCl₃): δ 5.07–5.03 (m, 1H), 4.06–3.99 (m, 1H), 3.24 (s, 3H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.68 (d, *J* = 1.2 Hz, 3H), 1.18 (d, *J* = 6.4 Hz, 3H). Data are consistent with the literature.

85

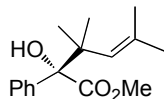
Methyl 3-((4-methylpent-3-en-2-yl)oxy)-2-phenylpropanoate (**105**)



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (91 mg, 0.5 mmol) and 4-methoxy-2-methylpent-2-ene (**104**) (racemic, 230 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1 to 10:1), and afforded compound **105** as an inseparable diastereomeric mixture (clear oil, dr: 2:1, 75 mg, 54% yield). **Major diastereomer:** ¹H NMR (400 MHz, CDCl₃): δ 7.33–7.26 (m, 5H), 5.10–5.07 (m, 1H), 4.22–4.13 (m, 1H), 4.02 (t, *J* = 9.2 Hz, 1H), 3.88 (dd, *J* = 9.2, 5.2 Hz, 1H) 3.69 (s, 3H), 3.50 (dd, *J* = 9.2, 5.2 Hz, 1H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.64 (d, *J* = 1.6 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H); IR (neat): 1738, 1454, 1435, 1202, 1164, 1104, 1077, 699 cm⁻¹; GC-MS analysis: Major diastereomer: *t*_R: 10.27 min, *m/z* 55 (70%), 67 (37%), 83 (100%), 99 (18%), 118 (10%),

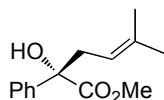
150 (18%); Minor diastereomer: t_R : 10.21 min, m/z 55 (64%), 67 (23%), 83 (100%), 99 (16%), 118 (11%), 150 (17%).

(S)-Methyl 2-hydroxy-3,3,5-trimethyl-2-phenylhex-4-enoate (113)



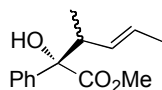
Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (91 mg, 0.5 mmol) and 2,4-dimethylpent-3-en-2-ol (**106**) (239 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **113** as clear oil (98 mg, 72% yield). $[\alpha]_D^{20}$ -32.0° (c 1.0, CHCl_3). R_f 0.33 (pentane/diethyl ether 5:1). $^1\text{H NMR}$ (600 MHz, CDCl_3): δ 7.73–7.72 (m, 2H), 7.33–7.27 (m, 3H), 5.22 (s, 1H), 3.85 (s, 3H), 3.69 (s, 1H), 1.71 (s, 3H), 1.49 (s, 3H), 1.22 (s, 3H), 1.17 (s, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3): δ 174.9 (C), 138.9 (C), 133.2 (C), 129.8 (CH), 127.8 (CH), 127.7 (CH), 127.3 (CH), 83.9 (C), 53.0 (CH_3), 45.0 (C), 29.2 (CH_3), 25.3 (CH_3), 25.2 (CH_3), 19.0 (CH_3); IR (neat): 3500, 1717, 1446, 1434, 1249, 1178, 1063, 1023, 746, 701 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}]^+$: 263.16417, found: 263.16412. Anal. Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3$: C, 73.25; H, 8.45. Found: C, 73.42, H, 8.32. HPLC analysis: 79% ee, (*S,S*) Whelk-O1, 0.3 % isopropanol/hexanes, 1.0 mL/min, UV: 230 nm, t_R : 7.2 min (major), 8.5 min (minor).

(S)-Methyl 2-hydroxy-5-methyl-2-phenylhex-4-enoate (114)



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (90 mg, 0.5 mmol) and 2-methylbut-3-en-2-ol (**107**) (178 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **114** as clear oil (49 mg, 40% yield). $[\alpha]_D^{20} +13.7^\circ$ (c 1.0, CHCl_3); R_f 0.17 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.63–7.61 (m, 2H), 7.39–7.29 (m, 3H), 5.16–5.13 (m, 1H), 3.77 (s, 3H), 3.64 (s, 1H), 2.98 (dd, $J = 14.8, 7.2$ Hz, 1H), 2.69 (dd, $J = 14.8, 7.2$ Hz, 1H), 1.72 (d, $J = 0.8$ Hz, 3H), 1.65 (d, $J = 0.8$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3): δ 175.6 (C), 141.8 (C), 136.6 (C), 128.4 (CH), 127.9 (CH), 125.6 (CH), 117.7 (CH), 78.6 (C), 53.3 (CH_3), 38.8 (CH_2), 26.2 (CH_3), 18.3 (CH_3); IR (neat): 3511, 1727, 1447, 1436, 1231, 1101, 1072, 730, 697 cm^{-1} ; HRMS (+ESI) m/z : calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{NH}_4]^+$: 252.15942, found: 252.15957. HPLC analysis: 79% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, t_R : 22.9 min (major), 20.7 min (minor).

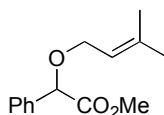
Methyl 2-hydroxy-3-methyl-2-phenylhex-4-enoate (**115**)



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (92 mg, 0.5 mmol) and (*E*)-pent-3-en-2-ol (**108**) (racemic, 172 mg, 2.0 mmol, 4 equiv.) at rt. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **115** (81 mg, 66% yield). **1st diastereomer**: clear oil, $[\alpha]_D^{20} +70.9^\circ$ (c 1.0, CHCl_3). R_f 0.32 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.69–7.67 (m, 2H), 7.38–7.29 (m, 3H), 5.61 (dq, $J = 15.2, 6.4$ Hz, 1H), 5.53–5.47 (m, 1H), 3.74 (s,

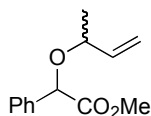
3H), 3.67 (s, 1H), 3.10 (m, 1H), 1.69 (dd, $J = 6.4, 1.6$ Hz, 3H), 0.81 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 175.9 (C), 140.4 (C), 131.6 (CH), 128.3 (CH), 127.7 (CH), 127.4 (CH), 126.3 (CH), 81.2 (C), 53.3 (CH_3), 45.2 (CH), 18.4 (CH_3), 14.2 (CH_3); IR (neat): 3507, 1724, 1447, 1435, 1244, 1140, 1005, 966, 759, 727, 698 cm^{-1} ; HRMS (+ESI) m/z : calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{NH}_4]^+$: 252.15942, found: 252.15958. Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$: C, 71.77; H, 7.74. Found: C, 71.75, H, 7.85. HPLC analysis: 90% ee, (*S,S*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, t_{R} : 9.3 min (major), 10.5 min (minor). **2nd diastereomer**: $[\alpha]_{\text{D}}^{20}$ -12.6° (c 1.0, CHCl_3). R_f , 0.23 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.62–7.59 (m, 2H), 7.35–7.25 (m, 3H), 5.31 (dq, $J = 15.2, 6.4$ Hz, 1H), 5.23–5.17 (m, 1H), 3.80 (s, 3H), 3.67 (s, 1H), 3.15 (m, 1H), 1.48 (d, $J = 6.4$ Hz, 3H), 1.08 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 175.8 (C), 141.1 (C), 130.3 (CH), 128.2 (CH), 127.6 (CH), 127.3 (CH), 126.3 (CH), 81.1 (C), 53.5 (CH_3), 44.4 (CH), 18.2 (CH_3), 15.7 (CH_3); IR (neat): 3511, 1724, 1447, 1435, 1238, 1192, 1138, 1072, 1022, 1007, 966, 729, 698 cm^{-1} ; HRMS (+ESI) m/z : calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{NH}_4]^+$: 252.15942, found: 252.15952. Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$: C, 71.77; H, 7.74. Found: C, 71.98, H, 7.87. HPLC analysis: 85% ee, CHIRAL PAK AS-H, 0.3% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, t_{R} : 11.2 min (major), 13.3 min (minor).

Methyl 2-((3-methylbut-2-en-1-yl)oxy)-2-phenylacetate (116)



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (93 mg, 0.5 mmol) and 3-methylbut-2-en-1-ol (**109**) (179 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **116** as clear oil (104 mg, 84% yield). ¹H-NMR (400 MHz, CDCl₃): δ 7.47–7.45 (m, 2H), 7.39–7.33 (m, 3H), 5.41–5.37 (m, 1H), 4.93 (s, 1H), 4.04 (d, *J* = 7.2 Hz, 2H), 3.72 (s, 1H), 1.76 (s, 3H), 1.62 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 171.5 (C), 138.3 (C), 136.7 (C), 128.7 (CH), 128.6 (CH), 127.4 (CH), 120.2 (CH), 79.6 (CH), 65.8 (CH₂), 52.3 (CH₃), 25.9 (CH₃), 18.1 (CH₃); IR (neat): 1750, 1453, 1435, 1206, 1169, 1093, 1070, 1010, 728, 696 cm⁻¹; HRMS (+ESI) *m/z*: calcd for C₁₄H₁₈O₃ [M+NH₄]⁺: 252.15942, found: 252.15902. HPLC analysis: 0% ee, (*S*, *S*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, *t*_R: 31.2 min, 49.4 min.

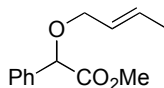
Methyl 2-(but-3-en-2-yloxy)-2-phenylacetate (**117**)



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (92 mg, 0.5 mmol) and but-3-en-2-ol (**110**) (racemic, 157 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **117** (71 mg, 61% yield). **1st diastereomer**: clear oil, *R*_f 0.27 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.41–7.45 (m, 2H), 7.38–7.30 (m, 3H), 5.78–5.70 (m, 1H), 5.23–5.18 (m, 2H), 5.01 (s, 1H), 4.02 (m, 1H), 3.73 (s, 3H), 1.38 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 172.2 (C), 139.4

(CH), 137.1 (C), 128.7 (CH), 128.6 (CH), 127.4 (CH), 117.3 (CH₂), 78.0 (CH), 76.8 (CH), 52.3 (CH₃), 21.5 (CH₃); IR (neat): 1749, 1208, 1170, 1095, 1072, 990, 926, 728, 696 cm⁻¹; HRMS (+ESI) *m/z*: calcd for C₁₃H₁₆O₃ [M+NH₄]⁺: 238.14377, found: 238.14396. HPLC analysis: 6% ee, (*S,S*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, *t*_R: 13.3 min (major), 17.9 min (minor). **2nd diastereomer**: clear oil, *R*_f 0.20 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.47–7.45 (m, 2H), 7.40–7.27 (m, 3H), 5.82–5.74 (m, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 5.15 (d, *J* = 16.8 Hz, 1H), 4.98 (s, 1H), 3.82 (m, 1H), 3.68 (s, 3H), 1.31 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 171.6 (C), 139.3 (CH), 137.0 (C), 128.8 (CH), 128.7 (CH), 127.5 (CH), 117.5 (CH₂), 78.2 (CH), 75.8 (CH), 52.4 (CH₃), 21.6 (CH₃); IR (neat): 1755, 1205, 1169, 1093, 1071, 994, 920, 729, 697 cm⁻¹; HRMS (+ESI) *m/z*: calcd for C₁₃H₁₆O₃ [M+NH₄]⁺: 238.14377, found: 238.14399. HPLC analysis: 5% ee, (*S,S*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, *t*_R: 33.5 min (major), 20.8 min (minor).

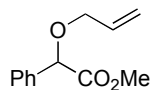
(*E*)-Methyl 2-(but-2-en-1-yloxy)-2-phenylacetate (118)



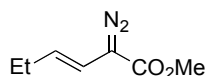
Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (0.089 g, 0.5 mmol) and (*E*)-but-2-en-1-ol (**111**) (150 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **118** as clear oil (81 mg, 72% yield). *R*_f 0.18 (pentane/diethyl ether 10:1). ¹H-NMR (400 MHz, CDCl₃): δ 7.46–7.39 (m, 2H), 7.39–7.33 (m, 3H), 5.77–5.70 (m, 1H), 5.65–5.58 (m, 1H), 4.95 (s, 1H), 4.00 (m, 2H), 3.72 (s,

1H), 1.72 (dd, $J = 6.0, 0.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.6 (C), 136.6 (C), 131.0 (CH), 128.8 (CH), 128.7 (CH), 127.5 (CH), 126.8 (CH), 79.6 (CH), 70.3 (CH_2), 52.4(CH_3), 17.9 (CH_3); IR (neat): 1750, 1453, 1435, 1206, 1170, 1099, 1062, 1014, 966, 728, 696 cm^{-1} ; HRMS (+ESI) m/z : calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{NH}_4]^+$: 238.14377, found: 238.14341. HPLC analysis: 5% ee, (*R, R*)-Whelk-O1, 0.7% isopropanol/hexanes, 0.8 mL/min, UV 230 nm, t_{R} : 20.0 min (major), 15.9 min (minor).

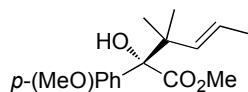
Methyl 2-(allyloxy)-2-phenylacetate (**119**)



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (87 mg, 0.5 mmol) and prop-2-en-1-ol (**112**) (117 mg, 2.0 mmol, 4 equiv.) at rt. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **119** as clear oil (65 mg, 63% yield). R_f 0.18 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.47–7.45 (m, 2H), 7.39–7.34 (m, 3H), 5.98–5.91 (m, 1H), 5.29 (dq, $J = 17.2, 1.6$ Hz, 1H), 5.24 (dq, $J = 10.4, 1.2$ Hz, 1H), 4.96 (s, 1H), 4.06 (dt, $J = 6.0, 1.2$ Hz, 2H), 3.72 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.4 (C), 136.5 (C), 133.9 (CH), 128.9 (CH), 128.8 (CH), 127.5 (CH), 118.4 (CH_2), 79.8 (CH), 70.5 (CH_2), 52.4(CH_3); IR (neat): 1750, 1454, 1434, 1258, 1207, 1171, 1097, 1071, 1015, 924, 729, 696 cm^{-1} ; HRMS (+ESI) m/z : calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$ $[\text{M}+\text{NH}_4]^+$: 224.12812, found: 224.12779. HPLC analysis: 1% ee, (*R, R*)-Whelk-O1, 1.0% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, t_{R} : 13.7 min, 16.9 min.

(E)-Methyl 2-diazohehex-3-enoate (120)

Prepared by following the literature procedure.⁸⁸ *Trans*-3-hexenoate (4.0 g, 31 mmol) and *p*-ABSA (11.2 g, 47 mmol, 1.5 equiv.) was dissolved with 100 mL of acetonitrile and cooled to 0 °C with ice bath. DBU (7.0 mL, 47 mmol, 1.5 equiv.) was slowly added. The reaction mixture was stirred at room temperature for 3 h, then quenched with saturated NH₄Cl (10 mL), and extracted with diethyl ether (3 x 100 mL). The combined ether solution was washed with brine, dried over MgSO₄, and concentrated under vacuum. The crude material was purified on silica gel eluting with pentane/diethyl ether (30:1) to afford compound **120** as orange oil (1.5 g, 31% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.72 (dt, *J* = 16.0, 1.6 Hz, 1H), 5.37 (dt, *J* = 16.0, 6.4 Hz, 1H), 3.80 (s, 3H), 2.23–2.15 (m, 2H), 1.03 (t, *J* = 7.6 Hz, 3H), ; HRMS (+APCI) *m/z*: calcd for C₇H₁₁O₂N₂ [M+H]⁺: 155.08150, found: 155.08152.

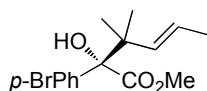
(S, E)-Methyl 2-hydroxy-2-(4-methoxyphenyl)-3,3-dimethylhex-4-enoate (122)

Prepared by following the general procedure with methyl *p*-methoxyphenyldiazoacetate (**12**) (108 mg, 0.5 mmol) and 4-methylpent-3-en-2-ol (**101**) (racemic, 209 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (5:1), and afforded compound **122** as clear oil (25 mg, 17% yield).

$[\alpha]_D^{20}$ -17.8° (*c* 0.8, CHCl₃). *R_f*, 0.27 (pentane/diethyl ether 5:1). ¹H NMR (600 MHz, CDCl₃): δ 7.61 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 5.64 (dd, *J* = 15.6, 1.8 Hz, 1H), 5.35 (dq, *J* = 15.6, 6.6 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.60 (s, 1H), 1.67 (dd, *J* = 6.6, 1.8 Hz, 3H), 1.06 (s, 3H), 1.01 (s, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 174.9 (C), 159.1 (C), 136.9 (CH), 130.9 (C), 129.0 (CH), 124.3 (CH), 112.6 (CH), 82.8 (C), 55.4 (CH₃), 52.9 (CH₃), 44.4 (C), 22.5 (CH₃), 22.3 (CH₃), 18.5 (CH₃); IR (neat): 3500, 1717, 1608, 1509, 1440, 1298, 1246, 1177, 1090, 1068, 1035, 978, 830. 802, 778 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₆H₂₂O₄ [M+NH₄]⁺: 296.18564, found: 296.18526. HPLC analysis: 92% ee, (*S,S*)-whelk O1, 1.0% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm, *t_R*: 15.7 min (major), 18.8 min (minor). O–H insertion products were also isolated from this reaction (combined yield of two diastereomers: 47 mg, 31% yield). **1st diastereomer of the O–H insertion product:** ¹H NMR (600 MHz, CDCl₃): δ 7.35 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 5.06 (d, *J* = 9.6 Hz, 1H), 4.91 (s, 1H), 4.35–4.31 (m, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 1.74 (s, 3H), 1.61 (s, 3H), 1.28 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 172.8 (C), 159.9 (C), 136.4 (C), 130.9 (C), 129.6 (C), 128.7 (CH), 126.7 (CH), 114.1 (CH), 77.0 (CH), 71.2 (CH), 55.4 (CH₃), 52.2 (CH₃), 26.0 (CH₃), 21.7 (CH₃), 18.2 (CH₃); IR (neat): 1749, 1611, 1512, 1246, 1208, 1170, 1117, 1104, 1066, 1033, 827, 794 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₆H₂₂O₄ [M+NH₄]⁺: 296.18564, found: 296.18521. HPLC analysis: 7% ee, (*S,S*)-whelk O1, 1.0% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm, *t_R*: 22.2 min (major), 30.4 min (minor). **2nd diastereomer of the O–H insertion product:** ¹H NMR (600 MHz, CDCl₃): δ 7.35 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 5.11 (d, *J* = 9.6 Hz, 1H), 4.86 (s, 1H), 4.13–4.08 (m, 1H), 3.81

(s, 3H), 3.67 (s, 3H), 1.74 (s, 3H), 1.51 (s, 3H), 1.24 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 172.1 (C), 159.9 (C), 136.1 (C), 129.4 (C), 128.9 (CH), 126.7 (CH), 114.1 (CH), 77.4 (CH), 70.1 (CH), 55.4 (CH_3), 52.3 (CH_3), 26.0 (CH_3), 21.8 (CH_3), 18.3 (CH_3); IR (neat): 1755, 1733, 1610, 1511, 1440, 1246, 1206, 1169, 1115, 1102, 1067, 1032, 829, 794 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{16}\text{H}_{22}\text{O}_4$ $[\text{M}+\text{NH}_4]^+$: 296.18564, found: 296.18520. HPLC analysis: 2% ee, (*S,S*)-whelk O1, 1.0% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm, t_R : 36.2 min (minor), 64.9 min (major).

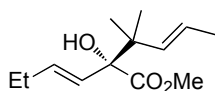
(*S,E*)-Methyl 2-(4-bromophenyl)-2-hydroxy-3,3-dimethylhex-4-enoate (123**)**



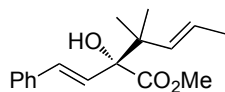
Prepared by following the general procedure with methyl *p*-bromophenyldiazoacetate (**30**) (129 mg, 0.5 mmol) and 4-methylpent-3-en-2-ol (**101**) (racemic, 204 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **123** as clear oil (116 mg, 70% yield). $[\alpha]_D^{20}$ -8.3° (c 1.0, CHCl_3). R_f 0.32 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.57 (d, $J = 8.8$ Hz, 2H), 7.42 (d, $J = 8.8$ Hz, 2H), 5.61 (d, $J = 15.6$ Hz, 1H), 5.33 (dq, $J = 15.6, 6.4$ Hz, 1H), 3.84 (s, 3H), 3.70 (s, 1H), 1.68 (dd, $J = 6.4, 1.6$ Hz, 3H), 1.05 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.3 (C), 137.8 (C), 136.3 (CH), 130.3 (CH), 129.6 (CH), 124.8 (CH), 122.0 (C), 82.7 (C), 53.2 (CH_3), 44.4 (C), 23.4 (CH_3), 23.1 (CH_3), 18.5 (CH_3); IR (neat): 3510, 1719, 1486, 1229, 1160, 1076, 1009, 978, 821, 783, 731 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{15}\text{H}_{19}\text{O}_3\text{Br}$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 309.04847, found: 309.04841. Anal. Calcd for $\text{C}_{15}\text{H}_{19}\text{O}_3\text{Br}$: C, 55.06; H, 5.85. Found: C,

55.28, H, 5.87. HPLC analysis: 88% ee, (*S,S*) Whelk-O1, 0.3% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm, t_R : 10.8 min (major), 12.5 min (minor).

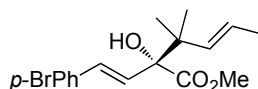
(*R,E*)-Methyl 2-hydroxy-2-((*E*)-2-methylpent-3-en-2-yl)hex-3-enoate (124**)**



Prepared by following the general procedure with (*E*)-methyl 2-diazohept-3-enoate (**120**) (154 mg, 1.0 mmol, 2 equiv.) and 4-methylpent-3-en-2-ol (**101**) (racemic, 51 mg, 0.5 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1 to 10:1), and afforded compound **124** as clear oil (53 mg, 46% yield). $[\alpha]_D^{20}$ -42.1° (*c* 1.2, CHCl₃). R_f 0.33 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 5.92 (dt, *J* = 15.2, 6.4 Hz, 1H), 5.71 (d, *J* = 15.2 Hz, 1H), 5.54 (d, *J* = 15.6 Hz, 1H), 5.43 (dq, *J* = 15.6, 6.0 Hz, 1H), 3.77 (s, 3H), 3.23 (s, 1H), 2.13–2.05 (m, 2H), 1.69 (dd, *J* = 6.0, 1.2 Hz, 3H), 1.06 (s, 3H), 1.01 (s, 3H), 1.00 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.7 (C), 136.6 (CH), 134.1 (CH), 126.2 (CH), 124.0 (CH), 81.3 (C), 52.7 (CH₃), 43.8 (C), 25.6 (CH₂), 23.0 (CH₃), 22.9 (CH₃), 18.5 (CH₃), 13.8 (CH₃); IR (neat): 3517, 2963, 1723, 1436, 1383, 1260, 1237, 1165, 1147, 1118, 976 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₃H₂₂O₃ [M+H-H₂O]⁺: 209.15361, found: 209.15353. Enantiomeric excess was determined as 92% ee by ¹H NMR of compound **124** with addition of Eu(tfc)₃, 3.90 ppm (OCH₃, major enantiomer), 3.87 (OCH₃, minor enantiomer).

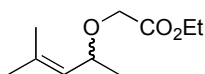
(*R, E*)-Methyl 2-hydroxy-3,3-dimethyl-2-((*E*)-styryl)hex-4-enoate (125**)**

Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (113 mg, 0.55 mmol, 1.1 equiv.) and 4-methylpent-3-en-2-ol (**101**) (racemic, 50 mg, 0.5 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **125** as clear oil (91 mg, 66% yield). $[\alpha]_D^{20}$ -26.1° (*c* 1.0, CHCl₃). *R_f*, 0.35 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.41 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.25 (m, 1H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.61 (dd, *J* = 16.0, 1.6 Hz, 1H), 5.53–5.46 (m, 1H), 3.80 (s, 3H), 3.44 (s, 1H), 1.72 (dd, *J* = 6.0, 0.8 Hz, 3H), 1.14 (s, 3H), 1.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.2 (C), 137.0 (C), 136.4 (CH), 130.9 (CH), 128.7 (CH), 127.8 (CH), 127.4 (CH), 126.9 (CH), 124.4 (CH), 81.8 (C), 52.9 (CH₃), 44.4 (C), 23.1 (CH₃), 23.0 (CH₃), 18.5 (CH₃); IR (neat): 3507, 1722, 1447, 1435, 1235, 1132, 972, 753, 740, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₇H₂₂O₃ [M+H]⁺: 275.16417, found: 275.16420. Anal. Calcd for C₁₇H₂₂O₃: C, 74.42; H, 8.08. Found: C, 74.27, H, 8.25. HPLC analysis: 98% ee, (*S, S*) Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm, *t_R*: 12.8 min (major), 15.2 min (minor).

(*R, E*)-Methyl 2-(4-bromostyryl)-2-hydroxy-3,3-dimethylhex-4-enoate (126**)**

Prepared by following the general procedure with methyl *p*-bromophenylvinyl diazoacetate (**121**) (315 mg, 1.1 mmol, 1.1 equiv.) and 4-methylpent-3-en-2-ol (**101**) (racemic, 102 mg, 1.0 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1 to 10:1), and afforded compound **126** as a white solid (204 mg, 56% yield). M.p.: 54-57 °C. $[\alpha]_D^{20}$ -12.0° (*c* 1.0, CHCl₃). *R_f*, 0.46 (pentane/diethyl ether 7:1). ¹H NMR (600 MHz, CDCl₃): δ 7.43 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 6.76 (d, *J* = 16.2 Hz, 1H), 6.47 (d, *J* = 16.2 Hz, 1H), 5.57 (d, *J* = 16.2 Hz, 1H), 5.48 (dq, *J* = 16.2, 7.2 Hz, 1H), 3.80 (s, 3H), 3.43 (s, 1H), 1.70 (dd, *J* = 6.6, 1.8 Hz, 3H), 1.12 (s, 3H), 1.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 174.8 (C), 136.1 (CH), 135.7 (C), 131.6 (CH), 129.7 (CH), 128.2 (CH), 128.0 (CH), 124.3 (CH), 121.3 (C), 81.6 (C), 52.8 (CH₃), 44.2 (C), 22.9 (CH₃), 22.8 (CH₃), 18.3 (CH₃); IR (neat): 3511, 1722, 1487, 1435, 1236, 1134, 1072, 1036, 1008, 974, 815, 790, 750, 707 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₇H₂₁O₃Br [M+H]⁺: 353.07468, found: 353.07462. HPLC analysis: 98% ee, (*R, R*) Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm, *t_R*: 11.2 min (minor), 12.2 min (major).

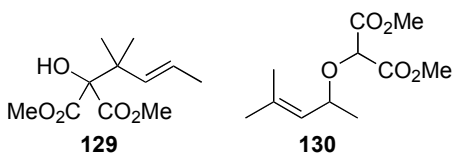
Ethyl 2-((4-methylpent-3-en-2-yl)oxy)acetate (**127**)



Prepared by following the general procedure with ethyl diazoacetate (**5**) (62 mg, 0.5 mmol) and 4-methylpent-3-en-2-ol (**101**) (racemic, 204 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (5:1), and afforded compound **127** as clear oil (68 mg, 67% yield). *R_f*, 0.33 (pentane/diethyl

ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 5.06–5.03 (m, 1H), 4.33–4.26 (m, 1H), 4.21 (q, $J = 7.2$ Hz, 2H), 4.02 (d, $J = 16.4$ Hz, 1H), 3.95 (d, $J = 16.4$ Hz, 1H), 1.73 (d, $J = 1.2$ Hz, 3H), 1.65 (d, $J = 1.2$ Hz, 3H), 1.29–1.24 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.2 (C), 136.5 (C), 126.4 (CH), 72.4 (CH), 65.2 (CH_2), 60.8 (CH_2), 25.9 (CH_3), 21.5 (CH_3), 18.2 (CH_3), 14.4 (CH_3); IR (neat): 1754, 1197, 1125 cm^{-1} ; Chiral-GC: 5% ee, CHIRALDEX B-DM (60 $^\circ\text{C}$, 2 $^\circ\text{C}/\text{min}$ to 150 $^\circ\text{C}$, keep 5 min), t_{R} : 17.9 min (major), 17.7 min (minor). GC-MS analysis: t_{R} : 4.28 min, m/z 55 (47%), 67 (100%), 83 (36%), 99 (35%), 171 (2%).

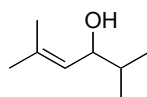
(*E*)-Dimethyl 2-hydroxy-2-(2-methylpent-3-en-2-yl)malonate (129) and dimethyl 2-((4-methylpent-3-en-2-yl)oxy)malonate (130)



Prepared by following the general procedure with methyl diazomalonnate (**128**) (81 mg, 0.5 mmol) and 4-methylpent-3-en-2-ol (**101**) (racemic, 203 mg, 2.0 mmol, 4 equiv.) at room temperature. The crude was purified on silica gel eluting with pentane/diethyl ether (3:1), and afforded compound **129** and **130** as an inseparable mixture, clear oil (65 mg, 52% yield). R_f 0.28 (pentane/diethyl ether 3:1). **Compound 129**: ^1H NMR (600 MHz, CDCl_3): δ 5.64 (dq, $J = 15.6, 1.2$ Hz, 1H), 5.47 (dq, $J = 15.6, 6.6$ Hz, 1H), 3.78 (s, 6H), 1.67 (dd, $J = 6.0, 1.2$ Hz, 3H), 1.20 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.3 (C), 168.1 (C), 167.5 (C), 138.0 (C), 135.5 (CH), 125.4 (CH), 124.7 (CH), 83.4 (C), 76.1 (CH), 72.9 (CH), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 43.1 (C), 25.9 (CH_3), 23.2 (CH_3),

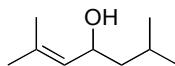
21.5 (CH₃), 18.4 (CH₃), 18.2 (CH₃); HRMS (+APCI) *m/z*: calcd for C₁₁H₁₈O₅ [M+H]⁺: 231.1227, found: 231.1228. **Compound 130**: ¹H NMR (600 MHz, CDCl₃): δ 5.04 (d, *J* = 9.6 Hz, 1H), 4.55 (s, 1H), 4.37-4.33 (m, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 1.73 (s, 3H), 1.65 (s, 3H), 1.30 (d, *J* = 6.6 Hz, 3H).

2,5-Dimethylhex-4-en-3-ol (131)



3-methyl-2-butanal (4.0 g, 47 mmol) in 20 mL of diethyl ether was slowly added to the isopropyl magnesium bromide solution (28 mL, 2.0 M in diethyl ether) at 0 °C. After addition, the reaction mixture was stirred for 1 h at room temperature. Then it was cooled to 0 °C and carefully quenched with cold saturated NH₄Cl. The mixture was extracted with diethyl ether (3 x 50 mL). The combined ether solution was dried over MgSO₄ and concentrated under vacuum. The crude material was distilled with kugelrohr under vacuum to afford compound **131** as clear liquid (4.8 g, 78% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.19 (d, *J* = 9.0 Hz, 1H), 4.07–4.04 (m, 1H), 1.75 (s, 3H), 1.69 (s, 3H), 1.68–1.66 (m, 1H), 1.30 (d, *J* = 3.6 Hz, 1H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H).

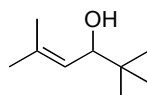
2,6-Dimethylhept-2-en-4-ol (132)



Prepared by following the procedure for compound **131**, using 3-methyl-2-butanal (4.0 g, 47 mmol) and isobutyl magnesium bromide solution (29 mL, 2.0 M in THF). The crude

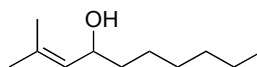
product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) to afford compound **132** as clear liquid (5.1 g, 75% yield). ^1H NMR (400 MHz, CDCl_3): δ 5.15 (d, $J = 8.8$ Hz, 1H), 4.43 (q, $J = 7.6$ Hz, 1H), 1.73 (s, 3H), 1.70 (s, 3H), 1.68–1.60 (m, 1H), 1.53–1.46 (m, 1H), 1.30–1.24 (m, 1H), 0.93 (d, $J = 6.4$ Hz, 3H), 0.91 (d, $J = 6.4$ Hz, 3H).

2,2,5-Trimethylhex-4-en-3-ol (133)



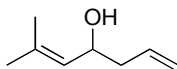
t-Butyl lithium solution (1.7 M in pentane, 33 mL) was slowly added to the 3-methyl-2-butanal solution (4.0 g, 47 mmol) in 20 mL of diethyl ether at 0 °C. After addition, the reaction mixture was stirred for 4 h at 0 °C. Then it was carefully quenched with cold saturated NH_4Cl . The mixture was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over MgSO_4 and concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **133** as clear liquid (2.3 g, 34% yield). ^1H NMR (400 MHz, CDCl_3): δ 5.24 (d, $J = 9.2$ Hz, 1H), 4.00 (d, $J = 9.2$ Hz, 1H), 1.75 (s, 3H), 1.69 (s, 3H), 0.90 (s, 9H).

2-Methyldec-2-en-4-ol (134)



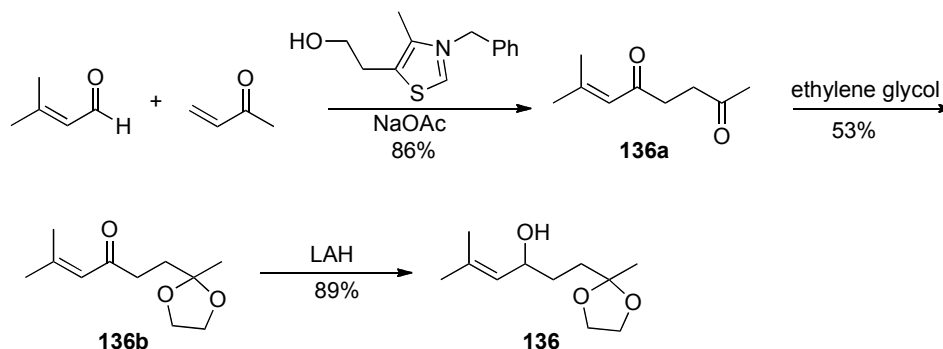
Prepared by following the procedure for compound **131**, using 3-methyl-2-butanal (4.0 g, 47 mmol) and hexyl magnesium bromide solution (29 mL, 2.0 M in THF). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) to afford Compound **134** as clear liquid (7.3 g, 90% yield). ^1H NMR (400 MHz, CDCl_3): δ 5.15 (d, $J = 9.2$ Hz, 1H), 4.34 (q, $J = 6.8$ Hz, 1H), 1.73 (s, 3H), 1.69 (s, 3H), 1.59–1.29 (m, 10H), 0.88 (t, $J = 6.8$ Hz, 3H).

6-Methylhepta-1,5-dien-4-ol (**135**)



Prepared by following the procedure for compound **131**, using 3-methyl-2-butanal (4.0 g, 47 mmol) and allyl magnesium bromide solution (57 mL, 1.0 M in diethyl ether). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) to afford compound **135** as clear liquid (4.2 g, 70% yield). ^1H NMR (600 MHz, CDCl_3): δ 5.81–5.78 (m, 1H), 5.21–5.11 (m, 3H), 4.43–4.39 (m, 1H), 2.28 (t, $J = 6.0$ Hz, 2H), 1.73 (s, 3H), 1.70 (s, 3H), 1.54 (d, $J = 3.6$ Hz, 1H).

5-Methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-4-en-3-ol (**136**)



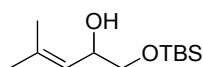
Prepared by following the literature procedure.⁸⁹ To the solution of 3-methyl-2-butanal (10.0 g, 119 mmol) and 3-buten-2-one (8.3 g, 119 mmol) in 100 mL of ethanol, was added 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium (3.2 g, 12 mmol, 10 mol%) and sodium acetate (3.9 g, 47 mmol). The reaction mixture was heated to reflux for 20 h. After cooled to room temperature, it was concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (2:1 to 1:1) to afford compound **136a** as yellow oil (15.8 g, 86% yield). ¹H NMR (600 MHz, CDCl₃): δ 6.10 (s, 1H), 2.72 (s, 4H), 2.21 (s, 3H), 2.13 (s, 3H), 1.89 (s, 3H).

To the solution of compound **136a** (4.0 g, 26 mmol) in 250 mL of toluene, was added ethylene glycol (2.8 g, 44 mmol, 1.7 equiv.), and pyridium tosylate (1.0 g, 3.9 mmol, 15 mol%). The reaction mixture was heated to reflux with continuous removal of water with a Dean-Stark apparatus for 16 h. Then it was cooled to room temperature, and concentrated under vacuum. The residue was diluted with diethyl ether (100 mL), washed with saturated NaHCO₃, dried over MgSO₄, and concentrated under vacuum. The crude was purified flash chromatography on silica gel eluting with pentane/diethyl ether (2:1) to afford compound **136b** as yellow oil (2.7 g, 53% yield). ¹H NMR (600 MHz, CDCl₃): δ 6.08 (s, 1H), 2.51 (t, *J* = 7.2 Hz, 2H), 2.14 (s, 3H), 1.98 (t, *J* = 7.2 Hz, 2H), 1.88 (s, 3H), 1.32 (s, 3H).

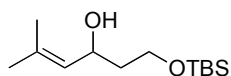
The solution of compound **136b** (2.7 g, 14 mmol) in 20 mL of diethyl ether was slowly added to the suspension of LiAlH₄ (0.3 g, 7mmol, 0.5 equiv.) in 20 mL of diethyl ether at 0 °C. After addition, the reaction mixture was stirred at room temperature for 1 h. Then it was carefully quenched with 10% aqueous NaOH at 0 °C. The ether solution was

separated, washed with brine, dried over MgSO₄, and concentrated under vacuum. The crude product was purified flash chromatography on silica gel eluting with hexanes/acetate (1:1) to afford compound **136** as clear oil (2.4 g, 89% yield). ¹H NMR (600 MHz, CDCl₃): δ 5.18 (d, *J* = 9.0 Hz, 1H), 4.35 (q, *J* = 7.2 Hz, 1H), 3.98–3.93 (m, 4H), 1.80 (br., 1H), 1.76–1.66 (m, 3H), 1.72 (s, 3H), 1.68 (s, 3H), 1.60–1.54 (m, 1H), 1.33 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 135.1 (C), 128.2 (CH), 110.1 (C), 68.7 (CH), 64.8 (CH₂), 35.2 (CH₂), 32.2 (CH₂), 25.9 (CH₃), 24.0 (CH₃), 18.4 (CH₃). Data are consistent with the literature.

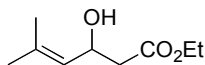
1-((*tert*-Butyldimethylsilyloxy)-4-methylpent-3-en-2-ol (**137**)



Prepared by following the procedure for compound **131**, using *t*-butyldimethylsilyloxyacetaldehyde (2.0 g, 12 mmol) and 2-methyl-1-propenyl magnesium bromide solution (0.5M in THF, 30 mL). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **137** as clear oil (1.9 g, 73% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.09 (d, *J* = 7.2 Hz, 1H), 4.42–4.36 (m, 1H), 3.55 (dd, *J* = 10.0, 3.6 Hz, 1H), 3.39 (dd, *J* = 10.0, 8.4 Hz, 1H), 2.53 (d, *J* = 2.4 Hz, 1H), 1.73 (d, *J* = 0.4 Hz, 3H), 1.70 (d, *J* = 0.4 Hz, 3H), 0.91 (s, 9H), 0.08 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 137.5 (C), 123.3 (CH), 69.4 (CH), 67.1 (CH₂), 26.1 (CH₃), 26.0 (C), 18.6 (CH₃), 18.5 (CH₃), -5.1 (CH₃), -5.2 (CH₃); IR (neat): 3416 (broad), 1253, 1113, 1059, 835, 776 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₂H₂₆O₂Si [M+H-H₂O]⁺: 213.1669, found: 213.1668.

1-((*tert*-Butyldimethylsilyloxy)-5-methylhex-4-en-3-ol (138)

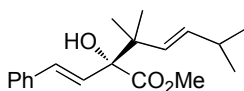
Prepared by following the procedure for compound **131**, using *t*-butyldimethylsilyloxy-1-propanal⁹⁰ (2.2 g, 12 mmol) and 2-methyl-1-propenyl magnesium bromide solution (0.5 M in THF, 30 mL). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **138** as clear oil (1.9 g, 68% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.21 (m, 1H), 4.61–4.55 (m, 1H), 3.88–3.75 (m, 2H), 2.95 (d, *J* = 2.8 Hz, 1H), 1.82–1.73 (m, 1H), 1.72 (d, *J* = 0.8 Hz, 3H), 1.68 (d, *J* = 0.8 Hz, 3H), 1.66–1.59 (m, 1H), 0.90 (9H, s), 0.07 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 134.5 (C), 127.9 (CH), 68.4 (CH), 62.0 (CH₂), 39.4 (CH₂), 26.0 (CH₃), 25.9 (C), 18.3 (CH₃), -5.3 (CH₃); IR (neat): 3384 (broad), 1254, 1098, 835, 775 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₃H₂₈O₂Si [M+H-H₂O]⁺: 227.1825, found: 227.1826.

Ethyl 3-hydroxy-5-methylhex-4-enoate (139)

Prepared by following the literature procedure.⁹¹ Ethyl acetate (5.7 mL, 75 mmol) was added to the LDA solution (49 mL, 98 mmol, 1.3 equiv.) in 150 mL of THF at -78 °C. The reaction mixture was stirred for 30 min, and 3-methyl-2-butenal (5.5 mL, 75 mmol) was slowly added. The reaction mixture was stirred for another 1 h and quenched with glacial acetic acid (12 g in 100 mL of THF). Then it was warmed to room temperature, and added 100 mL of saturated NaHCO₃. The organic layer was separated. The aqueous

layer was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over MgSO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (1:1) to afford compound **139** as red oil (9.4 g, 73% yield). ¹H NMR (600 MHz, CDCl₃): δ 5.21 (d, *J* = 9.0 Hz, 1H), 4.80–4.76 (m, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.72 (d, *J* = 4.2 Hz, 1H), 2.55–2.45 (m, 2H), 1.73 (s, 3H), 1.71 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H). Data are consistent with literature.

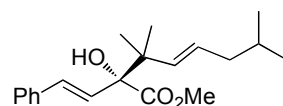
(*R, E*)-Methyl 2-hydroxy-3,3,6-trimethyl-2-((*E*)-styryl)hept-4-enoate (140)



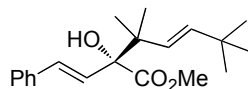
Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (113 mg, 0.55 mmol, 1.1 equiv.) and 2,5-dimethylhex-4-en-3-ol (**131**) (racemic, 64 mg, 0.5 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **140** as clear oil (103 mg, 68% yield). [α]_D²⁰ -26.3° (*c* 1.0, CHCl₃). *R_f*, 0.33 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.41 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.27–7.23 (m, 1H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.55 (dd, *J* = 16.0, 1.2 Hz, 1H), 5.40 (dd, *J* = 16.0, 9.2 Hz, 1H), 3.80 (s, 3H), 3.45 (s, 1H), 2.33–2.28 (m, 1H), 1.15 (s, 3H), 1.07 (s, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.2 (C), 137.0 (C), 136.9 (CH), 132.5 (CH), 130.9 (CH), 128.7 (CH), 127.8 (CH), 127.4 (CH), 126.8 (CH), 81.9 (C), 52.9 (CH₃), 44.1 (C), 31.6 (CH), 23.0 (CH₃), 22.9 (CH₃); IR (neat): 3511, 1722, 1237, 1135, 974, 755, 740, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₉H₂₆O₃ [M+H-

$\text{H}_2\text{O}]^+$: 285.18491, found: 285.18503. Anal. Calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$: C, 75.46; H, 8.67. Found: C, 75.25, H, 8.73. HPLC analysis: 97% ee, CHIRALCEL OD-H, 0.3% isopropanol/hexanes, 1.0 mL/min, UV: 254 nm, t_{R} : 14.7 min (major), 16.1 min (minor).

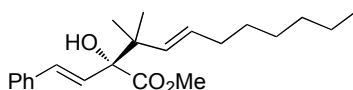
(*R, E*)-Methyl 2-hydroxy-3,3,7-trimethyl-2-((*E*)-styryl)oct-4-enoate (141**)**



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (117 mg, 0.55 mmol, 1.1 equiv.) and 2,6-dimethylhept-2-en-4-ol (**132**) (racemic, 71 mg, 0.5 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **141** as clear oil (104 mg, 66% yield). $[\alpha]_{\text{D}}^{20}$ -25.2° (*c* 1.0, CHCl_3). R_f , 0.37 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.41 (d, $J = 7.2$ Hz, 2H), 7.35 (t, $J = 7.2$ Hz, 2H), 7.25 (m, 1H), 6.85 (d, $J = 16.0$ Hz, 1H), 6.52 (d, $J = 16.0$ Hz, 1H), 5.58 (d, $J = 15.2$ Hz, 1H), 5.46 (dt, $J = 15.2, 7.2$ Hz, 1H), 3.81 (s, 3H), 3.47 (s, 1H), 1.94 (t, $J = 6.4$ Hz, 2H), 1.66–1.61 (m, 1H), 1.16 (s, 3H), 1.10 (s, 3H), 0.91 (d, $J = 5.6$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.3 (C), 137.0 (C), 136.5 (CH), 130.9 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 127.4 (CH), 126.9 (CH), 81.7 (C), 53.0 (CH_3), 44.4 (C), 42.4 (CH_2), 28.7 (CH), 23.2 (CH_3), 23.0 (CH_3), 22.5 (CH_3); IR (neat): 3512, 1723, 1238, 1071, 974, 754, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 299.20056, found: 299.20068. Anal. Calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3$: C, 75.91; H, 8.92. Found: C, 75.70, H, 9.06. HPLC analysis: 96% ee, (*S, S*) Whelk-O1, 0.2% isopropanol/hexanes, 1.0 mL/min, UV: 254 nm, t_{R} : 8.4 min (major), 9.9 min (minor).

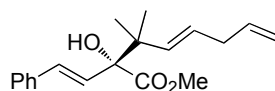
(*R, E*)-Methyl 2-hydroxy-3,3,6,6-tetramethyl-2-((*E*)-styryl)hept-4-enoate (142)

Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (113 mg, 0.55 mmol, 1.1 equiv.) and 2,2,5-trimethylhex-4-en-3-ol (**133**) (racemic, 71 mg, 0.5 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **142** as a white crystal (112 mg, 71% yield). $[\alpha]_D^{20}$ -23.8° (*c* 1.0, CHCl₃). *R_f* 0.32 (pentane/diethyl ether 10:1). M.p. 75-77 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.41 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.31 (m, 1H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.51 (d, *J* = 16.0 Hz, 1H), 5.46 (d, *J* = 16.0 Hz, 1H), 3.79 (s, 3H), 3.45 (s, 1H), 1.16 (s, 3H), 1.07 (s, 3H), 1.03 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 175.2 (C), 140.6 (CH), 137.1 (C), 130.9 (CH), 130.1 (CH), 128.7 (CH), 127.7 (CH), 127.4 (CH), 126.8 (CH), 81.9 (C), 52.8 (CH₃), 43.9 (C), 33.1 (C), 29.9 (CH₃), 23.1 (CH₃), 22.9 (CH₃); IR (neat): 3511, 1724, 1240, 1158, 1129, 975, 755, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₀H₂₈O₃ [M+H-H₂O]⁺: 299.20056, found: 299.20071. Anal. Calcd for C₂₀H₂₈O₃: C, 75.91; H, 8.92. Found: C, 75.75, H, 8.93. HPLC analysis: 94% ee, CHIRALPAK AD-H, 0.2% isopropanol/hexanes, 1.0 mL/min, UV: 254 nm, *t_R*: 17.5 min (major), 14.2 min (minor).

(*R, E*)-Methyl 2-hydroxy-3,3-dimethyl-2-((*E*)-styryl)undec-4-enoate (143)

Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (114 mg, 0.55 mmol, 1.1 equiv.) and 2-methyldec-2-en-4-ol (**134**) (racemic, 85 mg, 0.5 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (30:1), and afforded compound **143** as clear oil (125 mg, 73% yield). $[\alpha]_D^{20}$ -18.9° (*c* 1.0, CHCl₃). *R_f*, 0.34 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.26 (m, 1H), 6.83 (d, *J* = 16.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.58 (d, *J* = 15.6 Hz, 1H), 5.46 (dt, *J* = 15.6, 6.8 Hz, 1H), 3.80 (s, 3H), 3.44 (s, 1H), 2.04 (q, *J* = 6.4 Hz, 2H), 1.38–1.29 (m, 8H), 1.14 (s, 3H), 1.08 (s, 3H), 0.89 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.2 (C), 137.0 (C), 135.4 (CH), 130.9 (CH), 130.1 (CH), 128.7 (CH), 127.8 (CH), 127.4 (CH), 126.9 (CH), 81.8 (C), 52.9 (CH₃), 44.3 (C), 33.1 (CH₂), 31.9 (CH₂), 29.8 (CH₂), 29.0 (CH₂), 23.1 (CH₂), 23.0 (CH₃), 22.8 (CH₃), 14.3 (CH₃); IR (neat): 3511, 1723, 1447, 1435, 1237, 1135, 974, 754, 740, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₂H₃₂O₃ [M+H-H₂O]⁺: 327.23186, found: 327.23206. Anal. Calcd for C₂₂H₃₂O₃: C, 76.70; H, 9.36. Found: C, 76.57, H, 9.48. HPLC analysis: 96% ee, (s, s) Whelk-O1, 0.2% isopropanol/hexanes, 1.0 mL/min, UV: 254 nm, *t_R*: 8.4 min (major), 9.9 min (minor).

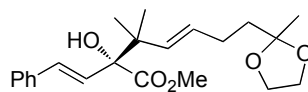
(*R, E*)-Methyl 2-hydroxy-3,3-dimethyl-2-((*E*)-styryl)octa-4,7-dienoate (144**)**



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (111 mg, 0.5 mmol) and 6-methylhepta-1,5-dien-4-ol (**135**) (racemic, 256 mg, 2.0 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1 to 10:1), and

afforded compound **144** as clear oil (114 mg, 69% yield). $[\alpha]_D^{20}$ -22.1° (c 1.0, CHCl_3). R_f , 0.27 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.32 (t, $J = 7.2$ Hz, 2H), 7.25 (m, 1H), 6.85 (d, $J = 16.0$ Hz, 1H), 6.50 (d, $J = 16.0$ Hz, 1H), 5.87–5.80 (m, 1H), 5.66 (dt, $J = 16.0, 1.2$ Hz, 1H), 5.48 (dt, $J = 16.0, 6.4$ Hz, 1H), 5.08–4.99 (m, 2H), 3.80 (s, 3H), 3.48 (s, 1H), 2.83–2.79 (m, 2H), 1.17 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.2 (C), 137.3 (CH), 136.9 (C), 136.8 (CH), 131.1 (CH), 128.7 (CH), 127.8 (CH), 127.3 (CH), 127.1 (CH), 126.9 (CH), 115.2 (CH_2), 81.8 (C), 53.0 (CH_3), 44.5 (C), 37.1 (CH_2), 23.1 (CH_3), 22.9 (CH_3); IR (neat): 3508, 1722, 1447, 1434, 1204, 1132, 973, 911, 754, 740, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{19}\text{H}_{24}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 283.16926, found: 283.16940. Anal. Calcd for $\text{C}_{19}\text{H}_{24}\text{O}_3$: C, 75.97; H, 8.05. Found: C, 75.69, H, 8.05. HPLC analysis: 95% ee, (*S,S*) Whelk-O1, 0.2% isopropanol/hexanes, 1.0 mL/min, UV: 254 nm, t_R : 9.6 min (major), 11.1 min (minor).

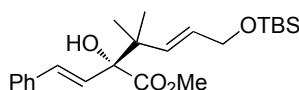
(*R, E*)-Methyl 2-hydroxy-3,3-dimethyl-7-(2-methyl-1,3-dioxolan-2-yl)-2-((*E*)-styryl)hept-4-enoate (145**)**



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (115 mg, 0.55 mmol, 1.1 equiv.) and 5-methyl-1-(2-methyl-1,3-dioxolan-2-yl)hex-4-en-3-ol (**136**) (racemic, 103 mg, 0.5 mmol) at 0°C . The crude was purified on silica gel eluting with pentane/diethyl ether (3:1 to 2:1), and afforded compound **145** as clear oil (133 mg, 69% yield). $[\alpha]_D^{20}$ -26.3° (c 1.0, CHCl_3). R_f , 0.23 (pentane/diethyl ether 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.41 (d, $J = 8.0$ Hz, 2H), 7.34 (t, $J = 7.6$ Hz, 2H), 7.24 (m, 1H), 6.82 (d,

$J = 16.0$ Hz, 1H), 6.50 (d, $J = 16.0$ Hz, 1H), 5.58 (d, $J = 15.6$ Hz, 1H), 5.48 (dt, $J = 15.6$, 6.0 Hz, 1H), 3.98–3.93 (m, 4H), 3.79 (s, 3H), 3.55 (s, 1H), 2.19–2.13 (m, 2H), 1.74–1.70 (m, 2H), 1.61 (s, 3H), 1.14 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.9 (C), 136.9 (C), 135.3 (CH), 130.9 (CH), 129.7 (CH), 128.7 (CH), 127.7 (CH), 127.3 (CH), 126.8 (CH), 110.0 (C), 81.7 (C), 64.8 (CH_2), 52.8 (CH_3), 44.3 (C), 39.1 (CH_3), 27.8 (CH_2), 23.9 (CH_3), 23.1 (CH_3), 22.9 (CH_3); IR (neat): 3508, 1723, 1447, 1435, 1134, 1058, 1040, 974, 754, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{22}\text{H}_{30}\text{O}_5$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 357.20604, found: 357.20607. Anal. Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_5$: C, 70.56; H, 8.07. Found: C, 70.41, H, 8.17. HPLC analysis: 95% ee, CHIRALCEL OD-H, 3.0% isopropanol/hexanes, 0.8 mL/min, UV: 254 nm, t_{R} : 10.3 min (major), 12.0 min (minor).

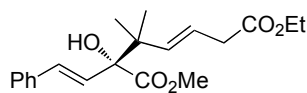
(*R*, *E*)-Methyl 6-((*tert*-butyldimethylsilyl)oxy)-2-hydroxy-3,3-dimethyl-2-(*E*)-styryl)hex-4-enoate (146**)**



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (106 mg, 0.5 mmol) and 1-((*tert*-butyldimethylsilyl)oxy)-4-methylpent-3-en-2-ol (**137**) (racemic, 466 mg, 2.0 mmol, 4 equiv.) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **146** as clear oil (107 mg, 50% yield). $[\alpha]_{\text{D}}^{20}$ -13.6° (c 1.0, CHCl_3). R_f 0.51 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.41 (d, $J = 6.8$ Hz, 2H), 7.32 (t, $J = 6.8$ Hz, 2H), 7.25 (m, 1H), 6.85 (d, $J = 16.0$ Hz, 1H), 6.48 (d, $J = 16.0$ Hz, 1H), 5.85 (dt, $J = 16.0$, 1.6 Hz, 1H), 5.57 (dt, $J = 16.0$, 5.2 Hz, 1H), 4.20 (dd, $J = 5.2$, 1.6 Hz, 2H), 3.81 (s, 3H), 3.49 (s, 1H), 1.16 (s, 3H),

(CH), 126.2 (CH), 81.7 (C), 63.5 (CH₂), 52.9 (CH₃), 44.5 (C), 36.7 (CH₂), 26.1 (CH₃), 23.0 (CH₃), 22.9 (CH₃), 18.5 (C), -5.0 (CH₃); IR (neat): 3512, 1724, 1251, 1134, 1098, 974, 834, 774 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₄H₃₈O₄Si [M+H-H₂O]⁺: 401.25065, found: 401.25075. Anal. Calcd for C₂₄H₃₈O₄Si: C, 68.86; H, 9.15. Found: C, 69.09, H, 9.16. HPLC analysis: 97% ee, (*S, S*) Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm, *t*_R: 10.7 min (major), 12.3 min (minor).

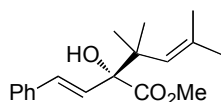
(*R, E*)-1-Ethyl 7-methyl 6-hydroxy-5,5-dimethyl-6-((*E*)-styryl)hept-3-enedioate (148**)**



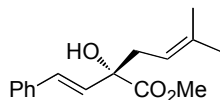
Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (116 mg, 0.55 mmol, 1.1 equiv.) and (**139**) (racemic, 88 mg, 0.5 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (4:1), and afforded a mixture of compound **148** the O–H insertion products as clear oil (141 mg, 80% yield). Pure **148** was obtained by preparative HPLC. [α]_D²⁰ -17.7° (*c* 1.0, CHCl₃). *R*_f, 0.33 (pentane/diethyl ether 2:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.27–7.23 (m, 1H), 6.84 (d, *J* = 15.6 Hz, 1H), 6.48 (d, *J* = 15.6 Hz, 1H), 5.76 (d, *J* = 15.6 Hz, 1H), 5.59 (dq, *J* = 15.6, 6.8 Hz, 1H), 4.14 (q, *J* = 6.8 Hz, 2H), 3.81 (s, 3H), 3.54 (s, 1H), 3.08 (dd, *J* = 7.2, 1.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.17 (s, 3H), 1.11 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.1 (C), 172.1 (C), 139.7 (CH), 136.9 (C), 131.3 (CH), 128.8 (CH), 127.9 (CH), 127.1 (CH), 126.9 (CH), 121.5 (CH), 81.7 (C), 60.8 (CH₂), 53.1 (CH₃), 44.6 (C), 38.5 (CH₂), 22.9 (CH₃), 22.7 (CH₃), 14.4 (CH₃); IR (neat): 3507, 1729, 1241, 1161, 1029, 975, 756, 693 cm⁻¹; HRMS (+ESI) *m/z*: calcd for C₂₀H₂₆O₅ [M+Na]⁺:

369.16725, found: 369.16717. Anal. Calcd for C₂₀H₂₆O₅: C, 69.34; H, 7.56. Found: C, 69.44, H, 7.66. HPLC analysis: 94% ee, CHIRALCEL OD-H, 1.5% isopropanol/hexanes, 0.8 mL/min, UV: 254 nm, *t*_R: 14.1 min (minor), 25.6 min (major).

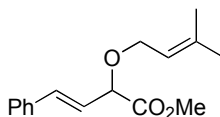
(*R, E*)-Methyl 2-hydroxy-3,3,5-trimethyl-2-styrylhex-4-enoate (149)



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (113 mg, 0.56 mmol, 1.1 equiv.) and 2,4-dimethylpent-3-en-2-ol (**106**) (58 mg, 0.51 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound **149** as clear oil (92 mg, 62% yield). $[\alpha]_D^{20}$ -46.1° (*c* 1.0, CHCl₃). *R*_f 0.25 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.43 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.26 (m, 1H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.54 (d, *J* = 16.0 Hz, 1H), 5.22 (m, 1H), 3.82 (s, 3H), 3.51 (s, 1H), 1.76 (d, *J* = 1.6 Hz, 3H), 1.75 (d, *J* = 1.6 Hz, 3H), 1.28 (s, 3H), 1.22 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.4 (C), 137.0 (C), 133.3 (C), 131.0 (CH), 129.3 (CH), 128.7 (CH), 127.8 (CH), 127.5 (CH), 126.9 (CH), 82.7 (C), 53.1 (CH₃), 44.9 (C), 29.2 (CH₃), 25.0 (CH₃), 24.8 (CH₃), 19.4 (CH₃); IR (neat): 3511, 1720, 1447, 1435, 1251, 1143, 974, 754, 741, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₈H₂₄O₃ [M+H-H₂O]⁺: 271.16926, found: 271.16937. Anal. Calcd for C₁₈H₂₄O₃: C, 74.97; H, 8.39. Found: C, 74.75, H, 8.55. HPLC analysis: 93% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.8 mL/min, UV: 254 nm, *t*_R: 10.5 min (major), 12.1 min (minor).

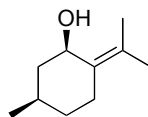
(S, E)-Methyl 2-hydroxy-5-methyl-2-styrylhex-4-enoate (150)

Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (113 mg, 0.56 mmol, 1.1 equiv.) and 2-methylbut-3-en-2-ol (**107**) (44 mg, 0.51 mmol) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1 to 5:1), and afforded compound **150** as clear oil (60 mg, 45% yield). $[\alpha]_D^{20}$ -14.1° (*c* 1.0, CHCl₃). R_f 0.15 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.43 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.27 (m, 1H), 6.87 (d, *J* = 16.0 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.17 (t, *J* = 7.2 Hz, 1H), 3.82 (s, 3H), 3.41 (s, 1H), 2.71 (dd, *J* = 14.8, 7.2 Hz, 1H), 2.50 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.75 (s, 3H), 1.68 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.4 (C), 136.6 (C), 136.5 (C), 130.1 (CH), 129.9 (CH), 128.7 (CH), 127.9 (CH), 126.9 (CH), 117.3 (CH), 77.8 (C), 53.2 (CH₃), 38.6 (CH₂), 26.2 (CH₃), 18.2 (CH₃); IR (neat): 3515, 1730, 1447, 1436, 1228, 1128, 971, 745, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₆H₂₀O₃ [M+H-H₂O]⁺: 243.13796, found: 243.13806. Anal. Calcd for C₁₆H₂₀O₃: C, 73.82; H, 7.74. Found: C, 73.67, H, 7.85. HPLC analysis: 96% ee, CHIRALCEL OD-H, 0.1% isopropanol/hexanes, 0.8 mL/min, UV: 254 nm, *t*_R: 15.6 min (major), 14.6 min (minor).

(E)-Methyl 2-((3-methylbut-2-en-1-yl)oxy)-4-phenylbut-3-enoate (151)

Prepared by following the general procedure with methyl stryldiazoacetate (**7**) (103 mg, 0.5 mmol) and 3-methylbut-2-en-1-ol (**109**) (193 mg, 2.0 mmol, 4 equiv.) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1 to 5:1), and afforded compound **151** as clear oil (98 mg, 74% yield). R_f , 0.28 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.40 (m, 2H), 7.33 (m, 2H), 7.25 (m, 1H), 6.76 (d, $J = 16.0$ Hz, 1H), 6.23 (dd, $J = 16.0, 6.8$ Hz, 1H), 5.40 (m, 1H), 4.57 (dd, $J = 6.8, 1.6$ Hz, 1H), 4.10 (m, 2H), 3.77 (s, 3H), 1.76 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.5 (C), 138.5 (C), 136.1 (C), 134.3 (CH), 128.7 (CH), 128.3 (CH), 126.8 (CH), 124.2 (CH), 120.3 (CH), 78.7 (CH), 66.0 (CH_2), 52.4 (CH_3), 25.9 (CH_3), 18.2 (CH_3); IR (neat): 1749, 1448, 1435, 1257, 1171, 1133, 1071, 1013, 966, 735, 690 cm^{-1} ; HPLC analysis: 0% ee, CHIRALCEL OD-H, 1.0% isopropanol/hexanes, 0.8 mL/min, UV: 254 nm, t_R : 13.1 min, 15.4 min.

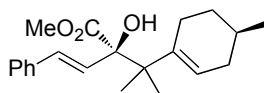
***cis*-(1*R*,5*R*)-(-)-Pulegol (**152**)**



Prepared by following the literature procedure.⁹² The suspension of NaBH_4 (0.8 g, 21mmol, 1.1 equiv.) in 42 mL of ethanol was slowly added to the (*R*)-(+)-pulegone solution (3.0 g, 20 mmol) in 36 mL of ethanol at 0 °C. After addition, the reaction mixture was stirred at room temperature for 2 h. Then 50 mL of brine was added, and the solution was extracted with hexanes (3 x 50 mL). The combined hexanes solution was dried over MgSO_4 and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with hexanes/acetate (5:1) to afford compound

152 as a white solid (1.6 g, 53% yield). ^1H NMR (600 MHz, CDCl_3): δ 4.72 (t, $J = 4.8$ Hz, 1H), 2.40–2.20 (m, 2H), 1.79 (s, 3H), 1.69 (s, 3H), 1.83–1.68 (m, 2H), 1.61–1.55 (m, 2H), 1.48–1.42 (m, 1H), 1.23 (s, 1H), 1.12 (d, $J = 6.8$ Hz, 3H). Data are consistent with literature.

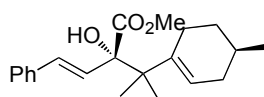
(*R*, *E*)-Methyl 2-hydroxy-2-(2-((*R*)-4-methylcyclohex-1-en-1-yl)propan-2-yl)-4-phenylbut-3-enoate (153**)**



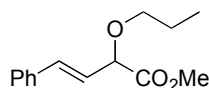
Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (116 mg, 0.57 mmol, 1.1 equiv.) and *cis*-(1*R*, 5*R*)-(-)-pulegol (**152**) (83 mg, 0.54 mmol) with $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol%) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **153** as a diastereomeric mixture (white solid, dr: 10:1, 113 mg, 64% yield). R_f , 0.44 (pentane/diethyl ether 10:1). Further recrystallization in cold hexanes afforded pure compound **150** as a white crystal suitable for X-ray spectroscopy analysis. M.p.: 81–83 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.41 (d, $J = 7.6$ Hz, 2H), 7.33 (t, $J = 8.0$ Hz, 2H), 7.24 (t, $J = 7.2$ Hz, 1H), 6.82 (d, $J = 16.0$ Hz, 1H), 6.52 (d, $J = 16.0$ Hz, 1H), 5.64 (m, 1H), 3.76 (s, 3H), 3.36 (s, 1H), 2.18–1.94 (m, 3H), 1.73–1.55 (m, 3H), 1.26 (s, 3H), 1.14 (s, 3H), 1.16–1.08 (m, 1H), 0.94 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.0 (C), 140.6 (C), 137.2 (C), 130.5 (CH), 128.7 (CH), 127.7 (CH), 127.5 (CH), 126.8 (CH), 124.5 (CH), 81.4 (C), 52.8 (CH₃), 47.3 (C), 34.7 (CH₂), 31.8 (CH₂), 28.1 (CH), 27.2 (CH₂), 23.4 (CH₃), 23.3 (CH₃), 22.0 (CH₃); IR (neat): 3515, 1725, 1448, 1434, 1248,

1127, 1072, 1040, 975, 754, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{28}\text{O}_3$ [$\text{M}+\text{H}-\text{H}_2\text{O}$] $^+$: 311.20056, found: 311.20089. Anal. Calcd for $\text{C}_{21}\text{H}_{28}\text{O}_3$: C, 76.79; H, 8.59. Found: C, 76.58, H, 8.61.

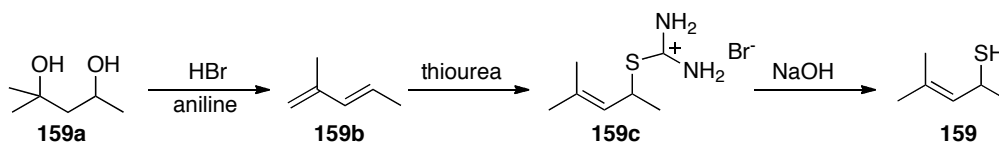
(S, E)-Methyl 2-hydroxy-2-(2-((R)-4-methylcyclohex-1-en-1-yl)propan-2-yl)-4-phenylbut-3-enoate (154)



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (113 mg, 0.56 mmol, 1.1 equiv.) and *cis*-(1*R*, 5*R*)-(-)-pulegol (**152**) (77 mg, 0.50 mmol) with $\text{Rh}_2(\text{R-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol%) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **154** as a diastereomeric mixture (dr: 10:1, clear oil, 122 mg, 74% yield). R_f , 0.44 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42 (d, $J = 7.6$ Hz, 2H), 7.34 (t, $J = 7.6$ Hz, 2H), 7.25 (m, 1H), 6.83 (d, $J = 16.0$ Hz, 1H), 6.56 (d, $J = 16.0$ Hz, 1H), 5.62 (m, 1H), 3.78 (s, 3H), 3.41 (s, 1H), 2.30–2.16 (m, 2H), 2.00–1.92 (m, 1H), 1.74–1.55 (m, 3H), 1.28 (s, 3H), 1.17 (s, 3H), 1.18–1.12 (m, 1H), 0.95 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.2 (C), 141.1 (C), 137.1 (C), 130.4 (CH), 128.7 (CH), 128.0 (CH), 127.7 (CH), 126.8 (CH), 124.0 (CH), 82.2 (C), 52.8 (CH_3), 47.1 (C), 34.7 (CH_2), 31.7 (CH_2), 28.0 (CH), 27.0 (CH_2), 24.7 (CH_3), 22.2 (CH_3), 21.9 (CH_3); IR (neat): 3509, 1723, 1448, 1435, 1249, 1154, 1127, 975, 906, 753, 733, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{28}\text{O}_3$ [$\text{M}+\text{H}-\text{H}_2\text{O}$] $^+$: 311.20056, found: 311.20097.

(E)-Methyl 4-phenyl-2-propoxybut-3-enoate (158)

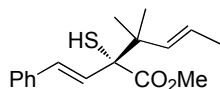
A solution of $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol %), 4-methylpent-3-en-2-ol (**101**) (racemic, 50 mg, 0.5 mmol), and 1-propanol (0.04 mL, 0.5 mmol) in 2 mL of degassed pentane was cooled to 0 °C with ice bath under argon. Methyl styryldiazoacetate (**7**) (105 mg, 0.5 mmol) in 5 mL of degassed pentane was added by syringe pump over 1 h. After addition, the solution was stirred for 2 h with temperature rising to room temperature, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **158** as clear oil (54 mg, 45% yield). R_f , 0.34 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.38 (d, $J = 7.2$ Hz, 2H), 7.30 (t, $J = 7.6$ Hz, 2H), 7.26-7.22 (m, 1H), 6.75 (d, $J = 16.0$ Hz, 1H), 6.22 (dd, $J = 16.0, 6.8$ Hz, 1H), 4.51 (dd, $J = 6.8, 1.6$ Hz, 1H), 3.76 (s, 3H), 3.54–3.42 (m, 2H), 1.74–1.62 (m, 2H), 0.94 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.6 (C), 136.2 (C), 134.0 (CH), 128.8 (CH), 128.3 (CH), 126.9 (CH), 124.3 (CH), 80.1 (CH), 71.9 (CH_2), 52.4 (CH_3), 23.0 (CH_2), 10.7 (CH_3). Compound **125** was also isolated in 4 mg (3% yield, 99% ee) from the reaction mixture.

4-Methylpent-3-ene-2-thiol (159)

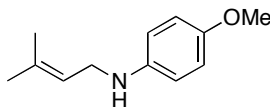
Prepared by following the literature procedure.⁹³ The mixture of 2-methylpentane-2,4-diol (**159a**) (100 mL), aqueous HBr (48%, 2 mL), and aniline (1.6 mL) was heated to reflux and distilled with vigreux column at 130 °C to get a two phase mixture. The top phase was separated, washed with water, dried over MgSO₄, and further distilled with the vigreux column. The fraction at 74 °C was collected to give diene **159b** as clear liquid (19 g). ¹H NMR (400 MHz, CDCl₃): δ 6.15 (18.0 Hz, 1H), 5.66 (dq, *J* = 18.0, 6.0 Hz, 1H), 4.83 (s, 2H), 1.82 (s, 3H), 1.77 (d, *J* = 6.0 Hz, 3H).

Diene **159b** (19 g) was added to a solution of thiourea (19.4 g of thiourea dissolved in 35 mL of 48% aqueous HBr solution) at 10 °C. The reaction mixture was shaken vigorously with cooling. After 5-6 min, the mixture solidified, and the cake, after another 30min, was shaken into a slurry with 25 mL of 20% aqueous HBr solution. The solid was filtered, resuspended in acetone (50 mL), filtered, and dried under vacuum to afford compound **159c** as a white solid (36 g, 65% yield).

Compound **159c** (20 g) was added in portions to a cold solution of NaOH (5 g) and NaCN (63 mg) in 25 mL of water. After 2 h, the reaction mixture was extracted with pentane (3 x 50 mL). The combined pentane solution was dried over MgSO₄, concentrated under vacuum to give the crude product, which was further distilled to afford the pure thiol **159** as clear oil with characteristic odour of thiol (4.5 g, 46% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.16 (d, *J* = 10.0 Hz, 1H), 3.93–3.85 (m, 1H), 1.69 (s, 3H), 1.67 (s, 3H), 1.35 (d, *J* = 6.8 Hz, 3H).

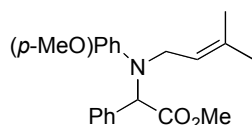
(*R, E*)-Methyl 2-mercapto-3,3-dimethyl-2-styrylhex-4-enoate (160)

A solution of $\text{Rh}_2(\text{S-DOSP})_4$ (21 mg, 0.011 mmol, 2 mol %) and 4-methylpent-3-ene-2-thiol (**159**) (75 mg, 0.65 mmol) in 2 mL of degassed pentane was stirred at room temperature (pink solution) under argon. Methyl styryldiazoacetate (**7**) (145 mg, 0.71 mmol, 1.1 equiv.) in 6 mL of degassed pentane was added by syringe pump over 1 h. After addition, the solution was stirred for 30 min, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (50:1 to 30:1), and afforded compound **160** as clear oil (27 mg, 14% yield). R_f , 0.63 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.34 (t, $J = 7.6$ Hz, 2H), 7.28–7.22 (m, 1H), 6.75 (d, $J = 16.0$ Hz, 1H), 6.65 (d, $J = 16.0$ Hz, 1H), 5.66 (dq, $J = 15.6, 1.6$ Hz, 1H), 5.51 (dq, $J = 15.6, 6.4$ Hz, 1H), 3.76 (s, 3H), 2.47 (s, 1H), 1.73 (dd, $J = 6.4, 1.2$ Hz, 3H), 1.25 (s, 3H), 1.20 (s, 3H); HRMS (+APCI) m/z : calcd for $\text{C}_{17}\text{H}_{23}\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$: 291.14133, found: 291.14151. HPLC analysis: 78% ee, CHIRALCEL OD-H, 0.2% isopropanol/hexanes, 1.0 mL/min, UV: 254 nm, t_R : 8.6 min (minor), 10.2 min (major).

4-Methoxy-*N*-(3-methylbut-2-en-1-yl)aniline (162)

Prepared by following the literature procedure.⁹⁴ The solution of 3-methyl-2-butenal (1.2 g, 14 mmol) and *p*-anisidine (2.0 g, 16 mmol) in 100 mL of dichloromethane/acetic acid (99:1) was stirred for 45 min at 0 °C. NaB(OAc)₃H was then added in portions. After addition, it was warmed to room temperature and stirred for 6 h. The reaction mixture was carefully quenched with 50 mL of cold water. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 x 125 mL). The combined dichloromethane solution was washed with brine, dried over MgSO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1 to 5:1), and afforded compound **162** as clear oil (1.87 g, 69% yield). ¹H NMR (400 MHz, CDCl₃): δ 6.79 (d, *J* = 8.8 Hz, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 5.34 (t, *J* = 6.8 Hz, 1H), 3.76 (s, 3H), 3.66 (d, *J* = 6.8 Hz, 2H), 3.33 (s, 1H), 1.75 (s, 3H), 1.71 (s, 3H).

Methyl 2-((4-methoxyphenyl)(3-methylbut-2-enyl)amino)-2-phenylacetate (163)



A solution of Rh₂(*S*-DOSP)₄ (10 mg, 0.005 mmol, 1 mol %) and 4-methoxy-N-(3-methylbut-2-enyl)aniline (**162**) (88 mg, 0.5 mmol) in 2 mL of degassed pentane was heated to reflux (pink solution) under argon. Methyl phenyldiazoacetate (**6**) (176 mg, 1.0 mmol, 2 equiv.) in 9 mL of degassed pentane was added by syringe pump over 1 h. After addition, the solution was stirred for 30 min, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl

ether (10:1), and afforded compound **163** as clear oil (57 mg, 36% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.39–7.31 (m, 5H), 6.89–6.86 (m, 2H), 6.83–6.80 (m, 2H), 5.37 (s, 1H), 5.05 (t, $J = 6.4$ Hz, 1H), 3.85–3.79 (m, 1H), 3.77 (s, 3H), 3.70 (s, 3H), 3.68–3.64 (m, 1H), 1.61 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.8 (C), 153.7 (C), 143.4 (C), 136.5 (C), 133.7 (C), 129.0 (CH), 128.7 (CH), 128.2 (CH), 122.2 (CH), 119.3 (CH), 114.5 (CH), 68.0 (CH), 55.7 (CH_3), 52.1 (CH_3), 48.1 (CH_2), 25.9 (CH_3), 17.9 (CH_3); IR (neat): 1743, 1508, 1452, 1241, 1194, 1154, 1040, 815, 724, 697 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{25}\text{O}_3\text{N}$ $[\text{M}+\text{H}]^+$: 340.19072, found: 340.19108.

2.4.3 Synthetic procedures and characterization for Chapter 2.2.3

2.4.3.1 General procedure I: the enzymatic resolution of allylic alcohols⁸⁷

To a vigorously stirred solution of racemic allylic alcohol (2 g, 1 equiv) and vinyl acetate (2.7 equiv) in 100 mL of hexanes was added Amano AK enzyme (0.6 g, 30% weight) and molecular sieves (1 g). The mixture was allowed to proceed at room temperature with periodic aliquotting and analysis by chiral GC or HPLC. After the enantiomeric excess of the alcohol exceeded 98%, the mixture was filtered and concentrated under vacuum. Flash chromatography of the crude material on silica gel afforded the enantiomerically pure (*S*)-alcohol.

2.4.3.2 General procedure II: the kinetic resolution of allylic alcohols by Sharpless enantioselective epoxidation⁹⁵

The solution of racemic allylic alcohol (10 mmol, 1 equiv) and D-(-)-DIPT (2.55 mL, 12 mmol, 1.2 equiv) in 100 mL of dichloromethane was cooled to -20 °C. Then $\text{Ti}(i\text{-OPr})_4$

(3.00 mL, 10 mmol, 1.0 equiv) was slowly added. The solution was stirred for 30 min and followed with the slow addition of TBHP (5.5 M in decane, 1.1 mL, 6 mmol, 0.6 equiv). After stirring at -20 °C for 15 h, the reaction was quenched with cold citric acid/FeSO₄ solution (33 g of FeSO₄ and 11 g of citric acid were dissolved in 100 mL of water). The mixture was stirred vigorously at room temperature until two layers were formed. The organic layer was separated and the aqueous layer was extracted with dichloromethane. The combined organic solution was concentrated under vacuum, and the residue was dissolved with 100 mL of diethyl ether. To this ether solution was added 10 mL of NaOH solution (30 g of NaOH and 5 g of NaCl were dissolved in 90 mL of water) at 0 °C. The mixture was stirred for 1 h at 0 °C, then 100 mL of water was added to dissolve the solid formed during the reaction. The ether solution was separated, dried over MgSO₄, filtered, and concentrated under vacuum. Flash chromatography of the crude material on silica gel afforded the enantiomerically pure (*S*)-alcohol.

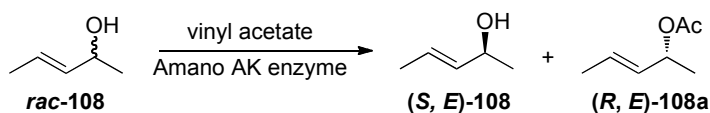
2.4.3.3 General procedure III: the Rh₂(*S*-DOSP)₄-catalyzed tandem ylide formation/[2,3]-sigmatropic rearrangement of donor/acceptor carbenoid with enantiomerically pure allylic alcohol

A solution of enantiomerically pure allylic alcohol (0.5 mmol, 1 equiv) and Rh₂(*S*-DOSP)₄ (0.005 mmol, 1 mol%) in 1 mL of degassed pentane was cooled to 0 °C with ice bath under argon. Diazo solution (1 mmol, 2 equiv) in 9 mL of degassed pentane (1 mmol, 2 equiv) was added by syringe pump over 90 min. After addition, the reaction mixture was stirred for 2 h with temperature rising to room temperature. Then it was

concentrated under vacuum, the crude material was purified by flash chromatography on silica gel to afford the desired product.

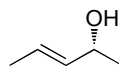
2.4.3.4. Synthetic procedures and characterization in Chapter 2.2.3

(*S, E*)-Pen-3-en-2-ol ((*S, E*)-108)



Prepared by following the general procedure **I** with racemic (*E*)-pen-3-en-2-ol (**108**) (3.0 g, 34.8 mmol, 1 equiv), vinyl acetate (8.7 mL, 94.0 mmol, 2.7 equiv), and Amano AK enzyme (1.0 g, 30% weight). The reaction mixture was stirred for 8 h at room temperature and filtered. After concentration, the residue was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 2:1) to afford (*S, E*)-**108** as clear oil (0.95 g, 63% yield). Chiral capillary GC analysis: 99% ee, CHIRALDEX B-PM column, t_R : 5.10 min (minor), 5.27 min (major). $[\alpha]_D^{20}$ -14.5° (*c* 3.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 5.66 (dq, *J* = 15.2, 6.4 Hz, 1H), 5.53 (dd, *J* = 15.2, 6.4 Hz, 1H), 4.26 (m, 1H), 1.69 (d, *J* = 6.8 Hz, 3H), 1.29 (d, *J* = 6.4 Hz, 3H).

(*R, E*)-Pen-3-en-2-ol ((*R, E*)-108)

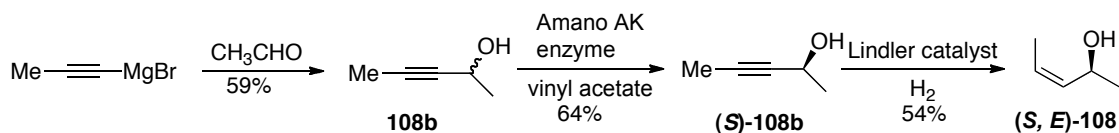


Prepared by following the general procedure **I** with racemic (*E*)-pen-3-en-2-ol (**108**) (3.0 g, 34.8 mmol, 1 equiv), vinyl acetate (8.7 mL, 94.0 mmol, 2.7 equiv), and Amano AK enzyme (1.0 g, 30% weight). The reaction mixture was stirred for 4 h at room

temperature and filtered. After concentration, the residue was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 2:1) to afford (*R*, *E*)-pent-3-en-2-yl acetate ((*R*, *E*)-**108a**) as clear oil (1.5 g). Chiral capillary GC analysis: 85% ee, CHIRALDEX B-PM column t_R : 6.34 min (minor), 6.90 min (major). ^1H NMR (400 MHz, CDCl_3): δ 5.72 (dq, $J = 15.2, 6.4$ Hz, 1H), 5.51–5.45 (m, 1H), 5.33–5.27 (m, 1H), 2.03 (s, 3H), 1.70 (dd, $J = 6.4, 0.8$ Hz, 3H), 1.28 (d, $J = 6.4$ Hz, 3H).

(*R*, *E*)-pent-3-en-2-yl acetate (85% ee, 1.5 g, 11.7 mmol, 1 equiv) was dissolved with KOH solution (3.9 g of KOH dissolved in 7 mL of ethanol and 3 mL of water, 70.2 mmol, 6 equiv) and heated to reflux for 3.5 h. After cooled to room temperature, the solution was carefully neutralized with aqueous HCl, and extracted with diethyl ether. The combined ether solution was dried over MgSO_4 , filtered, and concentrated to give (*R*, *E*)-**108** as clear oil. This material was subject to the second enzyme resolution for 4 h, and purification on silica gel gave (*R*, *E*)-pent-3-en-2-yl acetate (0.43 g, 99% ee). Finally a second hydrolysis of this acetate afforded (*R*, *E*)-**108** as clear oil (0.19 g, 13% overall yield). Chiral capillary GC analysis: 97% ee, CHIRALDEX B-PM column t_R : 5.10 min (major), 5.27 min (minor). The ^1H -NMR spectra was identical as (*S*, *E*)-**108**.

(*S*, *Z*)-3-Penten-2-ol ((*S*, *Z*)-**108**)

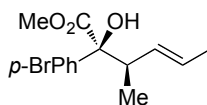


To a solution of 1-propynylmagnesium bromide (0.5 M in THF, 100 mL, 50 mmol, 1 equiv) was slowly added acetaldehyde (5.6 mL, 100 mmol, 2 equiv) in 50 mL of diethyl

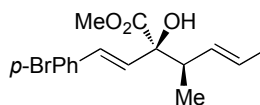
ether at 0 °C. After addition, the reaction mixture was stirred 5 h with temperature rising to room temperature. Then it was quenched with aqueous saturated NH₄Cl, the organic phase was separated and washed with brine, dried over MgSO₄, concentrated under vacuum. The crude was distilled under reduced pressure (20 mmHg) at 70-80 °C to afford racemic 3-pentyn-2-ol (**108b**) as clear oil (2.50 g, 59% yield). ¹H NMR (400 MHz, CDCl₃): δ 4.50–4.48 (m, 1H), 1.84 (d, *J* = 2.0 Hz, 3H), 1.42 (d, *J* = 6.4 Hz, 3H).

To the solution of racemic 3-pentyn-2-ol (**108b**) (1.35 g, 11.9 mmol) in 50 mL of vinyl acetate was added Amano AK enzyme (0.4 g, 30% weight). The mixture was stirred at 30 °C for 20 h. After the filtration, the solution was concentrated under vacuum. Purification by flash chromatography on silica gel (pentane/Et₂O, 10:1 to 3:1) afforded (*S*)-(+)-3-pentyn-2-ol ((**S**)-**108b**) as a clear oil (0.43 g, 64% recovery). $[\alpha]_D^{20}$ -36.9° (*c* 6.9, CHCl₃). Chiral capillary GC analysis: 98% ee, CHIRALDEX B-PM column, *t*_R: 7.21 min (minor), 7.38 min (major).

To the solution of (*S*)-(+)-3-pentyn-2-ol ((**S**)-**108b**) (215 mg, 2.56 mmol) in 2 mL of pentane were added Pd on CaCO₃ poisoned with Pb (Lindlar catalyst, 12.4 mg) and one drop of quinoline. The flask was purged with H₂ and stirred for 20 h at room temperature. The suspension was filtered and the solution was concentrated under vacuum. Purification by flash chromatography on silica gel (pentane/Et₂O, 5:1 to 3:1) afforded (**S**, **Z**)-**108** as a clear oil (120 mg, 54% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.55–5.54 (m, 2H), 4.71–4.66 (m, 1H), 1.68 (dd, *J* = 6.4, 1.2 Hz, 3H), 1.36 (s, 1H), 1.25 (d, *J* = 6.4 Hz, 3H). Data are consistent with the literature.⁹⁶

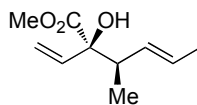
(2*S*, 3*R*, *E*)-Methyl 2-(4-bromophenyl)-2-hydroxy-3-methylhex-4-enoate (165)

Prepared by following the general procedure **III** with (***S*, *E***)-**108** (99% ee, 45 mg, 0.5 mmol, 1 equiv), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and *p*-bromophenyldiazoacetate **30** (259 mg, 1 mmol, 2 equiv). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1) to afford **165** as clear oil (109 mg, 66% yield). $[\alpha]_D^{20} +80.3^\circ$ (*c* 1.0, CHCl₃). *R_f*: 0.54 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.55 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 5.59 (dq, *J* = 15.2, 6.4 Hz, 1H), 5.46 (ddq, *J* = 15.2, 8.4, 1.6 Hz, 1H), 3.74 (s, 3H), 3.66 (s, 1H), 3.02 (m, 1H), 1.68 (dd, *J* = 6.4, 1.2 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.4 (C), 139.5 (C), 131.4 (CH), 131.3 (CH), 128.3 (CH), 127.7 (CH), 121.9 (C), 81.0 (C), 53.5 (CH₃), 45.3 (CH), 18.4 (CH₃), 14.1 (CH₃); IR (neat): 3503, 1728, 1486, 1436, 1395, 1246, 1141, 1090, 1075, 1010, 966, 824, 780, 745, 719 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₄H₁₇O₃Br [M+H-H₂O]⁺: 295.03282, found: 295.03308. HPLC analysis: >99% ee, CHIRALPAK AD-H, 1.0% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm. *t_R*: 13.8 (minor), 17.5 min (major).

(2*R*, 3*R*, *E*)-Methyl 2-(4-bromostyryl)-2-hydroxy-3-methylhex-4-enoate (166)

Prepared by following the general procedure **III** with (*S, E*)-**108** (99% ee, 44 mg, 0.5 mmol, 1 equiv), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and *p*-bromophenylvinyl diazoacetate **121** (281 mg, 1 mmol, 2 equiv, in 9 mL of pentane and 0.5 mL of toluene). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford **166** as a white solid (119 mg, 69% yield). M.p.: 76–78 °C. [α]_D²⁰ +35.2° (*c* 1.0, CHCl₃). *R*_f 0.36 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 15.6 Hz, 1H), 6.24 (d, *J* = 15.6 Hz, 1H), 5.51 (dq, *J* = 15.2, 6.0 Hz, 1H), 5.38 (ddq, *J* = 15.2, 8.8, 1.6 Hz, 1H), 3.77 (s, 3H), 3.32 (s, 1H), 2.68–2.60 (m, 1H), 1.65 (dd, *J* = 6.4, 1.6 Hz, 1H), 0.99 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.4 (C), 135.6 (C), 131.8 (CH), 131.2 (CH), 130.0 (CH), 129.7 (CH), 128.4 (CH), 127.5 (CH), 121.7 (C), 80.5 (C), 53.2 (CH₃), 44.9 (CH), 18.3 (CH₃), 14.2 (CH₃); IR (neat): 3512, 1731, 1487, 1435, 1243, 1145, 1072, 1009, 972, 817, 754, 725 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₆H₁₉O₃Br [M+H-H₂O]⁺: 321.04847, found: 321.04923. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm. *t*_R: 13.8 (minor), 14.9 min (major).

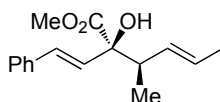
(2*R*, 3*R*, *E*)-Methyl 2-hydroxy-3-methyl-2-vinylhex-4-enoate (167)



Prepared by following the general procedure **III** with (*S, E*)-**108** (99% ee, 45 mg, 0.5 mmol, 1 equiv), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and vinyl diazoacetate **164** (160 mg, 1.25 mmol, 2.5 equiv). The diazo solution in 5 mL of pentane was added by syringe pump over 60 min. After addition, the reaction mixture was stirred for 20 min at 0 °C.

Then it was concentrated under vacuum, the crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1) to afford **167** as clear oil (41 mg, 43% yield). $[\alpha]_D^{20}$ -52.8° (c 1.0, CHCl_3). R_f 0.39 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 3.75 (s, 3H), 3.14 (s, 1H), 2.58–2.54 (m, 1H), 1.64 (dd, $J = 6.4, 1.2$ Hz, 1H), 0.96 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.6 (C), 137.7 (CH), 131.4 (CH), 127.2 (CH), 116.2 (CH_2), 80.6 (C), 53.0 (CH_3), 44.3 (CH), 18.3 (CH_3), 14.0 (CH_3); IR (neat): 3519, 2975, 2935, 1732, 1437, 1264, 1244, 1159, 993, 969, 930 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{10}\text{H}_{17}\text{O}_2$ $[\text{M}+\text{H}]^+$: 185.11722, found: 185.11726. Chiral capillary GC analysis: 99% ee, CHIRALDEX B-PM column, t_R : 14.7 min (major), 15.2 min (minor).

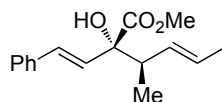
(2*R*, 3*R*, *E*)-Methyl 2-hydroxy-3-methyl-2-styrylhex-4-enoate ((2*R*, 3*R*)-168)



Prepared by following the general procedure **III** with (*S*, *E*)-**108** (99% ee, 44 mg, 0.5 mmol, 1 equiv), $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 1 mol%) and styryldiazoacetate **7** (205 mg, 1 mmol, 2 equiv). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford (**2*R*, 3*R*)-168** as clear oil (93 mg, 70% yield). $[\alpha]_D^{20}$ $+19.7^\circ$ (c 1.0, CHCl_3). R_f 0.25 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42–7.41 (m, 2H), 7.35–7.31 (m, 2H), 7.25–7.23 (m, 1H), 6.85 (d, $J = 15.6$ Hz, 1H), 6.26 (d, $J = 15.6$ Hz, 1H), 5.52 (dq, $J = 15.2, 6.0$ Hz, 1H), 5.40 (ddq, $J = 15.2, 8.4, 1.6$ Hz, 1H), 3.78 (s, 3H), 3.33 (s, 1H), 2.70–2.63 (m, 1H), 1.67 (dd, $J = 6.0, 1.6$ Hz, 3H), 1.02 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.6 (C), 137.7

(C), 131.4 (CH), 130.8 (CH), 129.2 (CH), 128.7 (CH), 127.9 (CH), 127.3 (CH), 126.8 (CH), 80.5 (C), 53.1 (CH₃), 44.9 (CH), 18.3 (CH₃), 14.2 (CH₃); IR (neat): 3514, 1731, 1448, 1436, 1243, 1144, 971, 749, 716, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₆H₂₀O₃ [M+H-H₂O]⁺: 243.13796, found: 243.13791. Anal. Calcd. for C₁₆H₂₀O₃: C: 73.82; H 7.74. Found: C, 74.11, H, 7.87. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. *t*_R: 17.6 min (major), 21.9 min (minor).

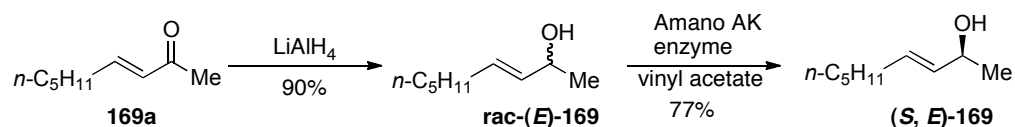
(2*S*, 3*R*, *E*)-Methyl 2-hydroxy-3-methyl-2-styrylhex-4-enoate ((2*S*, 3*R*)-168)



Prepared by following the general procedure **III** with (*S*, *E*)-**108** (99% ee, 45 mg, 0.5 mmol, 1 equiv.), Rh₂(*R*-DOSP)₄ (10 mg, 1 mol%) and styryldiazoacetate **7** (202 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (15:1) to afford (**2*S*, 3*R*)-168 as clear oil (73 mg, 54% yield). [α]_D²⁰ +53.1° (*c* 1.0, CHCl₃). *R*_f: 0.21 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.41–7.39 (m, 2H), 7.34–7.31 (m, 2H), 7.27–7.23 (m, 1H), 6.78 (d, *J* = 15.6 Hz, 1H), 6.28 (d, *J* = 15.6 Hz, 1H), 5.52 (dq, *J* = 15.6, 6.4 Hz, 1H), 5.40 (ddq, *J* = 15.2, 7.6, 1.6 Hz, 1H), 3.82 (s, 3H), 3.38 (s, 1H), 2.74–2.67 (m, 1H), 1.65 (dd, *J* = 6.0, 1.6 Hz, 3H), 1.01 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.6 (C), 136.8 (C), 130.5 (CH), 130.4 (CH), 129.9 (CH), 128.7 (CH), 127.8 (CH), 127.4 (CH), 126.8 (CH), 79.9 (C), 53.3 (CH₃), 44.9 (CH), 18.3 (CH₃), 15.3 (CH₃); IR (neat): 3515, 1727, 1448, 1436, 1236, 1152, 966, 746, 716, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for**

$C_{16}H_{20}O_3$ $[M+H-H_2O]^+$: 243.13796, found: 243.13803. Anal. Calcd. for $C_{16}H_{20}O_3$: C: 73.82; H, 7.74. Found: C, 73.62; H, 7.85. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_R : 18.5 (minor), 19.9 min (major).

(*S, E*)-Non-3-en-2-ol ((*S, E*)-169)

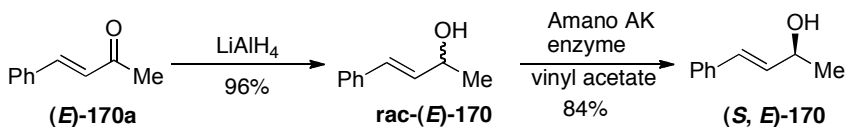


To a solution of (*E*)-3-nonen-2-one (3.0 g, 21.4 mmol, 1 equiv.) in 30 mL of methanol was slowly added $NaBH_4$ (0.9 g, 22.9 mmol, 1.07 equiv) solution in 30 mL of methanol at 0 °C. After addition, the reaction mixture was warmed to room temperature and stirred for 3 h. Then it was quenched with saturated aqueous NH_4Cl . The mixture was concentrated under vacuum, and the residue was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over $MgSO_4$, and concentrated under vacuum to give the crude product, which was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) to afford racemic (*E*)-169 as clear oil (2.7 g, 90% yield). 1H NMR (400 MHz, $CDCl_3$): δ 5.64 (1H, dt, $J = 15.6, 6.8$ Hz, 1H), 5.51 (dd, $J = 15.6, 6.8$ Hz, 1H), 4.29–4.25 (m, 1H), 2.01 (q, $J = 6.8$ Hz, 2H), 1.42–1.29 (m, 6H), 1.26 (d, $J = 6.0$ Hz, 3H), 0.89 (t, $J = 7.2$ Hz, 3H).

The synthesis of (*S, E*)-12 followed the general procedure I with racemic (*E*)-169 (2.0 g, 14.7 mmol, 1 equiv.), vinyl acetate (3.7 mL, 39.6 mmol, 2.7 equiv.), and Amano AK enzyme (0.6 g, 30% weight). The reaction mixture was stirred for 3 h at room temperature and filtered. After concentration, the residue was purified by flash

chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) to afford (**S**, **E**)-**169** as clear oil (0.77 g, 77% yield). $[\alpha]_D^{20} -10.2^\circ$ (c 1.3, CHCl_3) (lit. for (**R**, **E**)-**169**: $[\alpha]_D^{20} +10.68^\circ$ (c 1.03, CHCl_3), 97% ee).^{97a} The ^1H NMR data are identical as racemic (**E**)-**169**. Chiral capillary GC analysis: 99% ee, CHIRALDEX B-PM column, t_R : 15.10 min (minor), 14.17 min (major).

(S, E)-4-Phenylbut-3-en-2-ol ((S, E)-170)

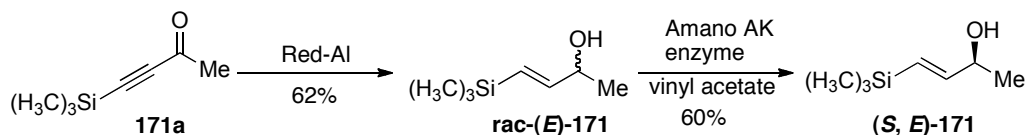


To a solution of (**E**)-4-phenylbut-3-en-2-one (5.0 g, 34.2 mmol, 1 equiv.) in 50 mL of methanol was slowly added NaBH_4 (1.4 g, 36.6 mmol, 1.07 equiv.) in 50 mL of methanol at 0 °C. After addition, the reaction mixture was warmed to room temperature and stirred for 2 h. Then it was quenched with saturated aqueous NH_4Cl . The mixture was concentrated under vacuum, and the residue was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over MgSO_4 , and concentrated under vacuum to give the crude product, which was purified by flash chromatography on silica gel eluting with hexanes/ethyl acetate (3:1) to afford racemic (**E**)-**170** as a white solid (4.9 g, 96% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.40 (d, $J = 7.6$ Hz, 2H), 7.33 (t, $J = 7.6$ Hz, 2H), 7.27–7.23 (m, 1H), 6.58 (d, $J = 16.0$ Hz, 1H), 6.28 (dd, $J = 16.0, 6.4$ Hz, 1H), 4.54–4.47 (m, 1H), 1.63 (d, $J = 4.0$ Hz, 1H), 1.38 (d, $J = 6.4$ Hz, 3H).

The synthesis of (**S**, **E**)-**170** followed the general procedure **I** with racemic (**E**)-**170** (1.0 g, 6.7 mmol, 1 equiv.), vinyl acetate (1.7 mL, 18.2 mmol, 2.7 equiv.), and Amano AK

enzyme (0.5 g, 20% weight). The reaction mixture was stirred for 24 h at room temperature and filtered. After concentration, the residue was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) to afford (*S, E*)-**170** as a white solid (0.43 g, 84% yield). $[\alpha]_D^{20} -33.9^\circ$ (*c* 5.2, CHCl₃) (lit. $[\alpha]_D^{20} -24.2^\circ$ (*c* 5.2, CHCl₃), 98% ee).^{97b} The ¹H NMR data are the same as racemic (*E*)-**170**. Chiral HPLC analysis: 99% ee, CHIRALCEL OD-H, 5% isopropanol/hexanes, 0.6 mL/min, UV: 254nm. *t*_R: 21.9 min (minor), 35.6 min (major).

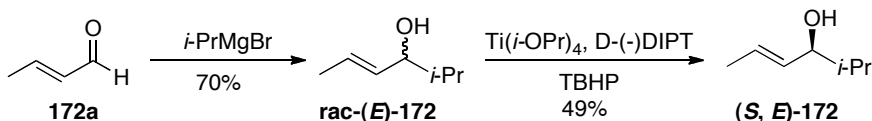
(*S, E*)-4-(Trimethylsilyl)but-3-en-2-ol ((*S, E*)-171)



4-(trimethylsilyl)but-3-yn-2-ol (2.6 g, 18.2 mmol, 1 equiv) in 40 mL of diethyl ether was cooled to 0 °C, Red-Al (11.0 mL, 36.4 mmol, 2 equiv.) was slowly added. The reaction mixture was allowed to warm up to room temperature over 2 h, and quenched with 1 mL of water and 2 mL of 3.6 M H₂SO₄ at 0 °C. 100 mL of water and 100 mL of diethyl ether were added to the solution. The ether solution was separated, and the aqueous part was washed with diethyl ether. The combined ether solution was washed with brine, dried over MgSO₄, filtered, and concentrated to give the crude product. Purification on silica gel by flash chromatography eluting with pentane/diethyl ether (10:1 to 5:1) afforded racemic (*E*)-**171** as clear oil (1.62 g, 62% yield).⁹⁸ ¹H NMR (400 MHz, CDCl₃): δ 6.09 (dd, *J* = 18.8, 5.2 Hz, 1H), 5.84 (d, *J* = 18.8 Hz, 1H), 4.31–4.27 (m, 1H), 1.53 (d, *J* = 4.8 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 3H), 0.08 (s, 9H). Data are consistent with the literature.⁹⁹

racemic (*E*)-**171** (1.0 g, 6.9 mmol, 1 equiv.) in 30 mL of pentane was added vinyl acetate (3.2 mL, 34.6 mmol, 5 equiv.) and Amano AK enzyme (0.5 g, 50% weight). The mixture was heated to reflux for 15 h. After filtration, the solution was concentrated. The residue was purified by flash chromatography eluting with pentane/diethyl ether (10:1 to 5:1) to afford (*S, E*)-**171** as clear oil (0.30 g, 60% yield).¹⁰⁰ $[\alpha]_{\text{D}}^{20} +5.2^{\circ}$ (*c* 1.3, CHCl₃). The ¹H NMR data are identical as racemic (*E*)-**171**. Chiral capillary GC analysis: 99% ee, CHIRALDEX B-PM column, *t*_R: 11.58 min (major), 11.89 min (minor).

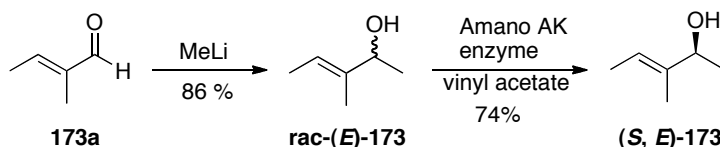
(*S, E*)-2-Methylhex-4-en-3-ol ((*S, E*)-172**)**



Isopropylmagnesium bromide solution (2.0 M in diethyl ether, 43 mL, 85.6 mmol, 1.2 equiv.) was cooled to 0 °C with ice bath. Crotonaldehyde (**172a**) (5.0 g, 71.3 mmol) in 10 mL of diethyl ether was slowly added. After addition, the ice bath was removed and the reaction was stirred at room temperature for 1 h. Then it was quenched with saturated aqueous NH₄Cl. The organic layer was separated and the aqueous layer was washed with diethyl ether. The combined ether solution was dried over MgSO₄, filtered, and concentrated under vacuum. The crude was distilled under vacuum at 65 °C to afford racemic (*E*)-**172** as clear oil (5.7 g, 70% yield). ¹H NMR (400 MHz, CDCl₃): δ 6.65 (dq, *J* = 15.2, 6.4 Hz, 1H), 5.50 (dd, *J* = 15.2, 7.2 Hz, 1H), 3.77 (t, *J* = 6.8 Hz, 1H), 1.71 (dd, *J* = 6.4, 1.2 Hz, 1H), 1.69–1.67 (m, 1H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.88 (d, *J* = 7.2 Hz, 3H).

The synthesis of (*S, E*)-**172** followed the general procedure **II** with racemic (*E*)-**172** (1.14 g, 10 mmol). Flash chromatography of the crude product on silica gel eluting with pentane/diethyl ether (10:1 to 5:1) afforded (*S, E*)-**172** as clear oil (0.28 g, 49% yield). $[\alpha]_D^{20} +10.4^\circ$ (*c* 3.7, CHCl₃). The ¹H NMR data identical as racemic (*E*)-**172**. Chiral capillary GC analysis: 99% ee, CHIRALDEX B-PM column, *t*_R: 9.83 min (minor), 9.85 min (major).

(*S, E*)-3-Methylpent-3-en-2-ol ((*S, E*)-173**)**

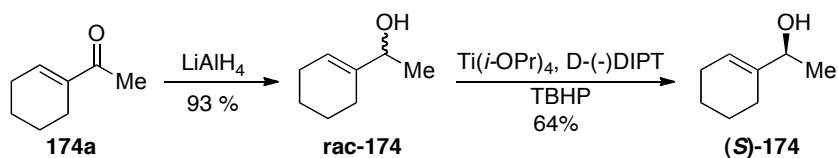


To the solution of (*E*)-2-methyl-2-butanal (**173a**) (4.4 g, 52.4 mmol) in 100 mL of THF was slowly added MeLi solution (1.6 M in diethyl ether, 39 mL, 62.5 mmol, 1.2 equiv.) at 0 °C. After addition, the reaction was stirred at 0 °C for 4 h, and quenched with saturated aqueous NH₄Cl. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined ether solution was washed with brine, dried over MgSO₄, filtered, and concentrated under vacuum. Flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) afforded racemic (*E*)-**173** as clear oil (4.5 g, 86% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.49 (q, *J* = 6.4 Hz, 1H), 4.25–4.19 (m, 1H), 1.63 (s, 3H), 1.61 (d, *J* = 7.2 Hz, 3H), 1.39 (br., 1H), 1.25 (d, *J* = 6.0 Hz, 3H). Data are consistent with the literature.¹⁰¹

The synthesis of (*S, E*)-**173** followed the general procedure **I** with racemic (*E*)-**173** (3.5 g, 34.8 mmol, 1 equiv.), vinyl acetate (8.7 mL, 94.0 mmol, 2.7 equiv.), and Amano AK

enzyme (1.0 g, 29% weight). The reaction mixture was stirred for 12 h at room temperature and filtered. After concentration, the residue was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) to afford (*S, E*)-**173** as clear oil (1.29 g, 74% yield). $[\alpha]_D^{20}$ -11.7° (*c* 2.3, CHCl₃). The ¹H NMR data are identical as racemic (*E*)-**173**. Chiral capillary GC analysis: 97% ee, CHIRALDEX B-PM column, *t*_R: 8.76 min (minor), 8.98 min (major).

(*S*)-1-Cyclohexenylethanol ((*S*)-**174**)

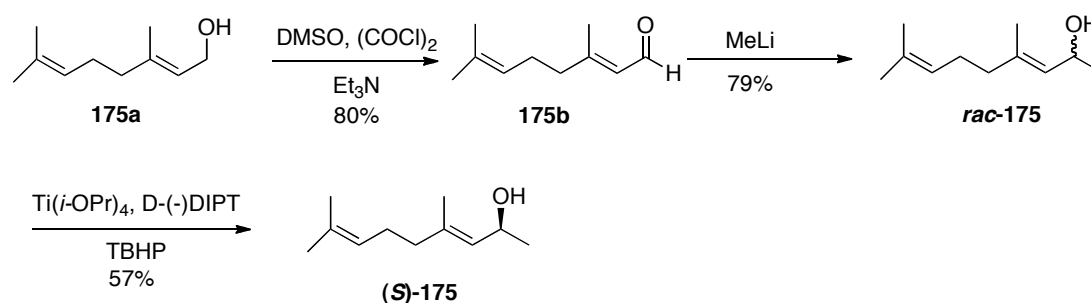


To the solution of lithium aluminum hydride (0.6 g, 16.7 mmol, 0.5 equiv.) in 15 mL of diethyl ether at 0 °C, was slowly added 1-acetylcyclohexene (**174a**) (4.0 g, 32.2 mmol, 1 equiv.) in 15 mL of diethyl ether. After addition, the reaction mixture was warmed to room temperature and stirred 1 h. Then it was cooled to 0 °C and quenched with cold water, followed with 5 mL of 10% sulfuric acid. The ether solution was separated, washed with saturated NaHCO₃, dried over MgSO₄, filtered, and concentrated under vacuum. The crude product was distilled at 100 °C under vacuum to afford racemic **174** as clear oil (3.8 g, 93% yield). ¹H NMR (600 MHz, CDCl₃): δ 5.67 (d, *J* = 0.6 Hz, 1H), 4.17 (q, *J* = 6.0 Hz, 1H), 2.06-1.98 (m, 4H), 1.67–1.54 (m, 4H), 1.42 (br., 1H), 1.26 (d, *J* = 6.0 Hz, 3H).

The synthesis of (*S*)-**174** followed the general procedure **II** racemic **174** (1.20 g, 10 mmol). Flash chromatography of the crude product on silica gel eluting with

pentane/diethyl ether (5:1) afforded (**S**)-**174** as clear oil (0.39 g, 64% yield). $[\alpha]_D^{20} -3.0^\circ$ (*c* 2.4, EtOH) (lit. for (**R**)-**174**: $[\alpha]_D^{20} +3.29^\circ$ (*c* 2.49, EtOH), >98% ee).^{95b} The ¹H NMR data are identical as racemic (**E**)-**174**. Chiral capillary GC analysis: 99% ee, CHIRALDEX B-PM column, *t*_R: 16.50 min (minor), 16.60 min (major).

(S, E)-4,8-Dimethylnona-3,7-dien-2-ol (175)

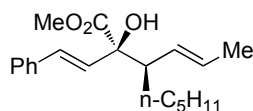


Dimethyl sulfoxide (6.5 mL, 90.7 mmol, 2.8 equiv.) was slowly added to the oxalyl chloride (4.1 mL, 48.6 mmol, 1.5 equiv.) in 40 mL of dichloromethane at -78 °C. The solution was stirred for 1.5 h, then geraniol (**175a**) (5.0 g, 32.4 mmol, 1 equiv.) in 60 mL of dichloromethane was slowly added. After stirring for 2 h at -78 °C, triethylamine (24.0 mL, 171.7 mmol, 5.3 equiv.) was slowly added. The solution was allowed to warm to room temperature and stirred overnight. Then it was poured into 100 mL of water. The organic layer was separated, and the aqueous layer was washed with saturated aqueous NH₄Cl, dried over MgSO₄, filtered, and concentrated to give the crude product, which was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford the geranial (**175b**) as clear oil (3.9 g, 80% yield). ¹H NMR (400 MHz, CDCl₃): δ 9.99 (d, *J* = 8.0 Hz, 1H), 5.88 (d, *J* = 8.0 Hz, 1H), 5.07 (m, 1H), 2.24–2.19 (m, 4H), 2.17 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H).

Methyl lithium solution (1.6 M in diethyl ether, 21 mL, 33.3 mmol, 1.3 equiv) was slowly added to the geranial solution (3.9 g, 25.6 mmol, 1 equiv) in 150 mL of diethyl ether at -78 °C. After stirring for 1.5 h, it was quenched with 1 mL of aqueous HCl. The organic layer was separated, washed with water, brine, dried over MgSO₄, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (6:1 to 3:1) to afford racemic **175** as clear oil (3.4 g, 79% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.21(d, *J* = 8.4 Hz, 1H), 5.09 (t, *J* = 6.8 Hz, 1H), 4.61–4.55 (m, 1H), 2.12–2.07 (m, 2H), 2.01–1.97 (m, 2H), 1.68 (s, 6H), 1.60 (s, 3H), 1.33 (br., 1H), 1.23 (d, *J* = 6.8 Hz, 3H). Data are consistent with the literature.¹⁰²

The synthesis of (**S**)-**175** followed the general procedure **II** with racemic **175** (1.68 g, 10 mmol). Flash chromatography of the crude product on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) afforded (**S**)-**175** as a clear oil (0.49 g, 57% yield). $[\alpha]_D^{20}$ -25.8° (*c* 3.3, CHCl₃). The ¹H NMR data are identical as racemic (**E**)-**175**. Chiral capillary GC analysis: 99% ee, CHIRALDEX B-PM column, *t*_R: 18.92 min (minor), 19.32 min (major).

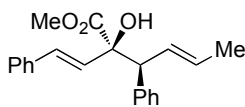
(2*R*, 3*R*)-Methyl 2-hydroxy-3-((*E*)-prop-1-enyl)-2-styryloctanoate (176)



Prepared by following the general procedure **III** with (*S*, *E*)-**169** (99% ee, 71 mg, 0.5 mmol, 1 equiv.), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and styryldiazoacetate **7** (206 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel

eluting with pentane/diethyl ether (30:1 to 20:1) to afford **176** as clear oil (131 mg, 83% yield). $[\alpha]_D^{20}$ -4.5° (c 1.0, CHCl_3). R_f 0.38 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42–7.39 (m, 2H), 7.34–7.30 (m, 2H), 7.26–7.22 (m, 1H), 6.84 (d, J = 16.0 Hz, 1H), 6.24 (d, J = 16.0 Hz, 1H), 5.48 (dq, J = 15.2, 6.4 Hz, 1H), 5.31 (ddq, J = 15.2, 9.2, 1.6 Hz, 1H), 3.75 (s, 3H), 3.40 (s, 1H), 2.39 (t, J = 11.2 Hz, 1H), 1.67 (dd, J = 6.4, 1.6 Hz, 3H), 1.53–1.50 (m, 1H), 1.31–1.08 (m, 7H), 0.84 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.6 (C), 136.7 (C), 130.8 (C), 130.2 (CH), 129.4 (CH), 128.7 (CH), 128.7 (CH), 127.8 (CH), 126.8 (CH), 80.9 (C), 53.1 (CH_3), 50.9 (CH), 31.9 (CH_2), 27.7 (CH_2), 27.4 (CH_2), 22.8 (CH_2), 18.3 (CH_3), 14.2 (CH_3); IR (neat): 3515, 1731, 1447, 1436, 1242, 1228, 1136, 972, 753, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 299.20056, found: 299.20031. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm. t_R : 13.7 (major), 16.8 min (minor).

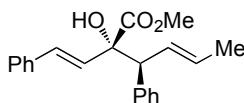
(2*R*, 3*S*, *E*)-Methyl 2-hydroxy-3-phenyl-2-styrylhex-4-enoate ((2*R*, 3*S*)-177)



Prepared by following the general procedure **III** with (*S*, *E*)-**170** (99% ee, 77 mg, 0.5 mmol, 1 equiv.), $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 1 mol%) and styryldiazoacetate **7** (203 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 10:1) to afford **(2*R*, 3*S*)-177** as a white solid (119 mg, 71% yield). M.p.: 112–114 $^\circ\text{C}$. $[\alpha]_D^{20}$ -148.5° (c 1.1, CHCl_3). R_f 0.27 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.34–7.32 (m, 2H), 7.27–

7.14 (m, 8H), 6.55 (d, $J = 16.0$ Hz, 1H), 6.26 (d, $J = 16.0$ Hz, 1H), 5.94 (ddq, $J = 15.2$, 9.2, 1.6 Hz, 1H), 5.31 (dq, $J = 15.2$, 6.8 Hz, 1H), 3.82 (s, 3H), 3.81 (d, $J = 9.2$ Hz, 1H), 3.59 (s, 1H), 1.69 (dd, $J = 6.4$, 1.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.1 (C), 139.4 (C), 136.7 (C), 130.8 (CH), 129.5 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.6 (CH), 128.2 (CH), 127.7 (CH), 127.0 (CH), 126.7 (CH), 80.9 (C), 57.2 (CH_3), 53.3 (CH_3), 18.4 (CH_3); IR (neat): 3506, 1728, 1448, 1436, 1239, 1140, 1118, 969, 745, 696 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 305.15361, found: 305.15353. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm. t_{R} : 25.3 (major), 32.0 min (minor).

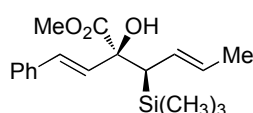
(2*S*, 3*S*, *E*)-Methyl 2-hydroxy-3-phenyl-2-styrylhex-4-enoate ((2*S*, 3*S*)-177)



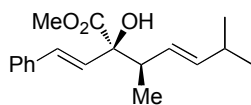
Prepared by following the general procedure **III** with (*S*, *E*)-**170** (99% ee, 74 mg, 0.5 mmol, 1 equiv.), $\text{Rh}_2(\text{R-DOSP})_4$ (10 mg, 1 mol%) and styryldiazoacetate **7** (213 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 10:1) to afford (**2*S*, 3*S*)-177 as a white solid (49 mg, 30% yield). M.p.: 96–97 °C. $[\alpha]_{\text{D}}^{20} +53.0^\circ$ (c 0.6, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ 7.45–7.43 (m, 2H), 7.37–7.22 (m, 8H), 6.88 (d, $J = 16.0$ Hz, 1H), 6.35 (d, $J = 16.0$ Hz, 1H), 5.87 (ddq, $J = 15.2$, 8.8, 1.6 Hz, 1H), 5.53 (ddq, $J = 15.2$, 6.4, 0.8 Hz, 1H), 3.82 (d, $J = 8.4$ Hz, 1H), 3.64 (s, 3H), 3.52 (s, 1H), 1.65 (dd, $J = 6.4$, 1.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.7 (C), 140.1 (C), 136.8 (C), 131.1 (CH), 129.5 (CH), 129.4 (CH), 129.1 (CH), 128.8 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.3 (CH),**

126.9 (CH), 80.5 (C), 56.7 (CH₃), 53.1 (CH₃), 18.4 (CH₃); IR (neat): 3508, 1732, 1448, 1436, 1244, 1135, 966, 747, 701 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₁H₂₂O₃ [M+H-H₂O]⁺: 305.15361, found: 305.15353. HPLC analysis: >99% ee, CHIRALPAK AD-H, 0.8% isopropanol/hexanes, 0.8 mL/min, UV: 254 nm. *t_R*: 25.8 (major), 38.9 min (minor).

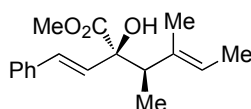
(2*S*, 3*R*, *E*)-Methyl 2-hydroxy-2-styryl-3-(trimethylsilyl)hex-4-enoate (178**)**



Prepared by following the general procedure **III** with (*S*, *E*)-**171** (99% ee, 73 mg, 0.5 mmol, 1 equiv.) and Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and styryldiazoacetate **7** (208 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 20:1) to afford **178** as a white solid (68 mg, 42% yield). M.p.: 58–60 °C. [α]_D²⁰ -63.7° (*c* 1.0, CHCl₃). *R_f* 0.50 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.40–7.38 (m, 2H), 7.35–7.31 (m, 2H), 7.26–7.23 (m, 1H), 6.82 (d, *J* = 15.6 Hz, 1H), 6.26 (d, *J* = 15.6 Hz, 1H), 5.50–5.34 (m, 2H), 3.72 (s, 3H), 3.61 (s, 1H), 2.12 (d, *J* = 7.0 Hz, 1H), 1.67 (d, *J* = 4.8 Hz, 3H), 0.02 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 176.1 (C), 136.8 (C), 131.1 (CH), 129.8 (CH), 128.8 (CH), 127.8 (CH), 127.5 (CH), 126.8 (CH), 80.5 (C), 53.1 (CH₃), 43.9 (CH), 18.4 (CH₃), -0.3 (CH₃); IR (neat): 3512, 2953, 1728, 1448, 1436, 1245, 1233, 1099, 973, 872, 839, 748, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₈H₂₆O₃Si [M+H-H₂O]⁺: 301.16184, found: 301.16197. HPLC analysis: 99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. *t_R*: 13.1 min (major), 16.5 min (minor).

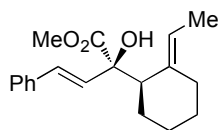
(2*R*, 3*R*, *E*)-Methyl 2-hydroxy-3,6-dimethyl-2-styrylhept-4-enoate (179)

Prepared by following the general procedure **III** with (*S*, *E*)-**172** (99% ee, 59 mg, 0.5 mmol, 1 equiv.), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and styryldiazoacetate **7** (201 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 20:1) to afford **179** as clear oil (112 mg, 75% yield). $[\alpha]_D^{20} +28.8^\circ$ (*c* 1.0, CHCl₃). *R_f*: 0.43 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.43–7.41 (m, 2H), 7.35–7.31 (m, 2H), 7.27–7.23 (m, 1H), 6.86 (d, *J* = 16.0 Hz, 1H), 6.26 (d, *J* = 16.0 Hz, 1H), 5.46 (dd, *J* = 16.0, 6.8 Hz, 1H), 5.34 (dd, *J* = 16.0, 8.8 Hz, 1H), 3.77 (s, 3H), 3.36 (s, 1H), 2.66–2.59 (m, 1H), 2.29–2.21 (m, 1H), 1.02 (d, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.6 (C), 140.2 (CH), 136.7 (C), 130.8 (CH), 129.3 (CH), 128.7 (CH), 127.9 (CH), 127.3 (CH), 126.9 (CH), 80.7 (C), 53.0 (CH₃), 45.0 (CH), 31.3 (CH), 22.9 (CH₃), 22.8 (CH₃), 14.2 (CH₃); IR (neat): 3515, 1731, 1448, 1436, 1236, 1142, 972, 747, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₈H₂₄O₃ [M+H-H₂O]⁺: 271.16926, found: 271.16939. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. *t_R*: 15.9 (major), 19.6 min (minor).

(2*R*, 3*R*, *E*)-Methyl 2-hydroxy-3,4-dimethyl-2-styrylhex-4-enoate (180)

Prepared by following the general procedure **III** with (*S, E*)-**173** (97% ee, 45 mg, 0.5 mmol, 1 equiv.), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and styryldiazoacetate **7** (214 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1) to afford **180** as clear oil (86 mg, 61% yield). $[\alpha]_D^{20} +29.4^\circ$ (*c* 1.0, CHCl₃). *R_f*, 0.30 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.43–7.41 (m, 2H), 7.35–7.31 (m, 2H), 7.27–7.23 (m, 1H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 5.38 (dq, *J* = 6.8, 1.2 Hz, 1H), 3.76 (s, 3H), 3.32 (s, 1H), 2.70 (q, *J* = 7.2 Hz, 1H), 1.65 (t, *J* = 1.2 Hz, 3H), 1.58 (dd, *J* = 6.8, 0.8 Hz, 3H), 1.08 (d, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.8 (C), 136.8 (C), 136.7 (C), 130.5 (CH), 129.8 (CH), 128.7 (CH), 127.8 (CH), 126.8 (CH), 122.3 (CH), 81.3 (C), 52.9 (CH₃), 49.7 (CH), 14.0 (CH₃), 13.6 (CH₃), 12.8 (CH₃); IR (neat): 3513, 1729, 1448, 1436, 1248, 1145, 973, 742, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₇H₂₂O₃ [M+H-H₂O]⁺: 257.15361, found: 257.15360. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. *t_R*: 17.3 (major), 33.4 min (minor).

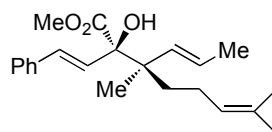
(*R, E*)-Methyl 2-((*R, E*)-2-ethylidenecyclohexyl)-2-hydroxy-4-phenylbut-3-enoate (181)



Prepared by following the general procedure **III** with (*S*)-**174** (99% ee, 64 mg, 0.5 mmol, 1 equiv.), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and styryldiazoacetate **7** (202 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting

with pentane/diethyl ether (30:1) to afford **181** as a white solid (117 mg, 77% yield). M.p.: 136–137 °C. $[\alpha]_D^{20}$ -58.6° (*c* 1.0, CHCl₃). *R_f*, 0.47 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42–7.39 (m, 2H), 7.33–7.29 (m, 2H), 7.25–7.21 (m, 1H), 6.86 (d, *J* = 16.0 Hz, 1H), 6.24 (d, *J* = 16.0 Hz, 1H), 5.24 (q, *J* = 6.8 Hz, 1H), 3.74 (s, 3H), 3.40 (s, 1H), 2.61 (t, *J* = 5.2 Hz, 1H), 2.30–2.25 (m, 2H), 1.89–1.82 (m, 2H), 1.68–1.53 (m, 2H), 1.57 (d, *J* = 6.8 Hz, 3H), 1.44–1.32 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 176.1 (C), 139.3 (C), 136.7 (C), 130.8 (CH), 130.6 (CH), 128.7 (CH), 127.9 (CH), 126.9 (CH), 118.5 (CH), 82.6 (C), 53.1 (CH₃), 48.9 (CH), 27.5 (CH₂), 27.4 (CH₂), 27.3 (CH₂), 24.0 (CH₂), 13.1 (CH₃); IR (neat): 3503, 1729, 1447, 1242, 1159, 1133, 973, 749, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₉H₂₄O₃ [M+H-H₂O]⁺: 283.16926, found: 283.16897. HPLC analysis: >99% ee, CHIRALPAK AD-H, 0.3% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm. *t_R*: 29.7 (minor), 33.1 min (major).

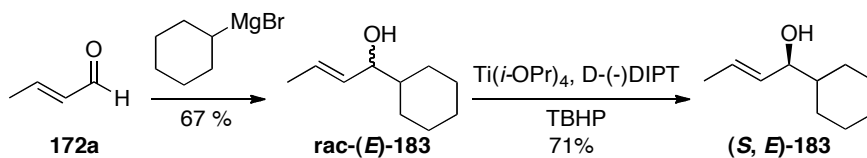
(2*R*, 3*R*)-Methyl 2-hydroxy-3,7-dimethyl-3-((*E*)-prop-1-enyl)-2-styryloct-6-enoate (182)



Prepared by following the general procedure **III** with (*S*, *E*)-**175** (99% ee, 85 mg, 0.5 mmol, 1 equiv.), Rh₂(*S*-DOSP)₄ (10 mg, 1 mol%) and styryldiazoacetate **7** (200 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 10:1) to afford **182** as a diastereomeric mixture (dr: 95:5, clear oil, 109 mg, 63% yield). $[\alpha]_D^{20}$ -29.4° (*c* 1.0, CHCl₃). *R_f*, 0.44

(pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.40 (d, $J = 7.2$ Hz, 2H), 7.31(d, $J = 7.2$ Hz, 2H), 7.24–7.21 (m, 1H), 6.81 (d, $J = 15.6$ Hz, 1H), 6.46 (d, $J = 15.6$ Hz, 1H), 5.55 (d, $J = 15.6$ Hz, 1H), 5.43 (dq, $J = 15.6, 6.0$ Hz, 1H), 5.07 (t, $J = 7.6$ Hz, 1H), 3.79 (s, 3H), 3.50 (s, 1H), 1.84–1.77 (m, 2H), 1.74 (d, $J = 6.0$ Hz, 3H), 1.65 (s, 3H), 1.61–1.56 (m, 1H), 1.42–1.34 (m, 1H), 1.12 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.2 (C), 137.0 (C), 134.8 (CH), 131.3 (C), 130.9 (CH), 128.7 (CH), 127.8 (CH), 127.7 (CH), 126.9 (CH), 125.9 (CH), 125.1 (CH), 82.4 (C), 53.0 (CH_3), 47.6 (C), 35.2 (CH_2), 25.9 (CH_3), 23.0 (CH_2), 18.6 (CH_3), 17.8 (CH_3), 17.7 (CH_3); IR (neat): 3507, 1721, 1448, 1436, 1376, 1240, 1144, 975, 753, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{22}\text{H}_{30}\text{O}_3$ $[\text{M}+\text{H}]^+$: 343.22677, found: 343.22640. HPLC analysis: >99% ee (major diastereomer), CHIRALPAK AD-H, 0.3% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm. t_{R} : 29.7 (minor), 18.1 min (major).

(*S, E*)-1-Cyclohexylbut-2-en-1-ol (*S, E*)-183

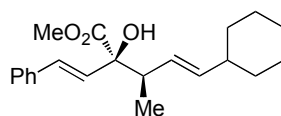


Cyclohexylmagnesium bromide solution (1.0 M in THF, 32 mL, 32.0 mmol, 1.5 equiv.) was cooled to 0 °C with ice bath. Crotonaldehyde (**172a**) (1.5 g, 21.4 mmol) in 10 mL of THF was slowly added over 10 min. After addition, the ice bath was removed and the reaction was stirred at room temperature for 1 h. Then it was quenched with saturated aqueous NH_4Cl . The organic layer was separated and the aqueous layer was washed with diethyl ether. The combined ether solution was dried over MgSO_4 , filtered, and

concentrated under vacuum. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford racemic (**E**)-**183** as clear oil (2.2 g, 67% yield). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 5.62 (dq, $J = 15.2, 6.4$ Hz, 1H), 5.48 (ddq, $J = 15.2, 7.6, 1.2$ Hz, 1H), 3.79–3.74 (m, 1H), 1.88–1.64 (m, 5H), 1.72 (dd, $J = 6.8, 1.6$ Hz, 3H), 1.40 (d, $J = 3.6$ Hz, 3H), 1.39–0.93 (m, 6H).

The synthesis of (**S, E**)-**183** followed the general procedure **II** with racemic (**E**)-**173** (1.54 g, 10 mmol). Flash chromatography of the crude product on silica gel eluting with pentane/diethyl ether (5:1) afforded (**S, E**)-**183** as clear oil (0.55 g, 71% yield). $[\alpha]_{\text{D}}^{20} +12.5^\circ$ (c 2.7, EtOH) (lit. for (**R, E**)-**183**: $[\alpha]_{\text{D}}^{20} -13.33^\circ$ (c 2.76, EtOH), >94% ee).^{95b} The $^1\text{H NMR}$ data are identical as racemic (**E**)-**183**. The enantiomeric excess was determined to be >98% from the $^1\text{H-NMR}$ of its MTPA ester.

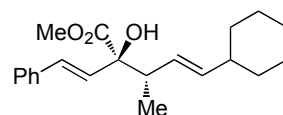
(2R, 3R, E)-Methyl 5-cyclohexyl-2-hydroxy-3-methyl-2-styrylpent-4-enoate ((2R, 3R)-184)



Prepared by following the general procedure **III** with (**S, E**)-**183** (>98% ee, 78 mg, 0.5 mmol, 1 equiv.), $\text{Rh}_2(\text{S-DOSP})_4$ (9 mg, 1 mol%) and styryldiazoacetate **7** (204 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1 to 10:1) to afford (**2R, 3R**)-**184** as a white solid (143 mg, 86% yield). M.p.: 130–131 °C. $[\alpha]_{\text{D}}^{20} +34.1^\circ$ (c 1.0, CHCl_3). R_f 0.43 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.43–7.41 (m, 2H), 7.34–

7.31 (m, 2H), 7.26–7.23 (m, 1H), 6.86 (d, $J = 16.0$ Hz, 1H), 6.26 (d, $J = 16.0$ Hz, 1H), 5.43 (dd, $J = 15.6, 6.4$ Hz, 1H), 5.34 (dd, $J = 15.6, 8.4$ Hz, 1H), 3.77 (s, 3H), 3.35 (s, 1H), 2.66–2.58 (m, 1H), 1.92–1.88 (m, 1H), 1.74–1.64 (m, 1H), 1.31–1.13 (m, 4H), 1.08–1.04 (m, 1H), 1.02 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.6 (C), 139.0 (CH), 136.7 (C), 130.8 (CH), 129.2 (CH), 128.8 (CH), 127.9 (CH), 127.8 (CH), 126.8 (CH), 80.8 (C), 53.1 (CH_3), 45.1 (CH), 40.9 (CH), 33.4 (CH_2), 33.3 (CH_2), 26.3 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 14.2 (CH_3); IR (neat): 3516, 2922, 2849, 1730, 1447, 1243, 1144, 971, 747, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{28}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 311.20056, found: 311.20048. HPLC analysis: >99% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_{R} : 16.4 min (major), 19.9 min (minor).

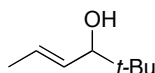
(2*R*, 3*R*, *E*)-Methyl 5-cyclohexyl-2-hydroxy-3-methyl-2-styrylpent-4-enoate ((2*R*, 3*S*)-184)



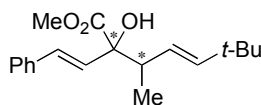
Prepared by following the general procedure **III** with **(*R*, *E*)-183** (>98% ee, 80 mg, 0.5 mmol, 1 equiv.), $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 1 mol%) and styryldiazoacetate **7** (205 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1 to 10:1) to afford **(2*R*, 3*S*)-184** as a white solid (126 mg, 74% yield). M.p.: 82–84 °C. $[\alpha]_{\text{D}}^{20}$ -83.6° (c 1.0, CHCl_3). R_f , 0.31 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.41–7.39 (m, 2H), 7.35–7.31 (m, 2H), 7.27–7.23 (m, 1H), 6.78 (d, $J = 16.0$ Hz, 1H), 6.29 (d, $J = 16.0$ Hz, 1H),

5.45 (dd, $J = 15.6, 6.4$ Hz, 1H), 5.33 (ddd, $J = 15.6, 8.4, 1.2$ Hz, 1H), 3.83 (s, 3H), 3.40 (s, 1H), 2.70–2.67 (m, 1H), 1.95–1.88 (m, 1H), 1.70–1.59 (m, 1H), 1.29–1.06 (m, 4H), 1.06–1.00 (m, 1H), 1.03 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.7 (C), 139.1 (CH), 136.9 (C), 130.2 (CH), 130.0 (CH), 128.6 (CH), 127.7 (CH), 127.0 (CH), 126.8 (CH), 79.9 (C), 53.2 (CH_3), 45.3 (CH), 40.8 (CH), 33.3 (CH_2), 33.2 (CH_2), 26.3 (CH_2), 26.1 (CH_2), 26.0 (CH_2), 15.5 (CH_3); IR (neat): 3517, 2922, 2849, 1728, 1447, 1239, 1160, 966, 746, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{28}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 311.20056, found: 311.20070. HPLC analysis: >99% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_R : 29.2 min (minor), 37.5 min (major).

2,2-Dimethylhex-4-en-3-ol (185)



t-Butyl lithium solution (1.7 M in pentane, 40 mL, 68 mmol, 1.2 equiv.) was added slowly to the crotonaldehyde (4.0 g, 57 mmol) in 100 mL of diethyl ether at 0 °C. After addition, the solution was stirred for 4 h, and then quenched with aqueous saturated NH_4Cl . The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over MgSO_4 , filtered, and concentrated. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **185** as clear oil (2.85 g, 44% yield). ^1H NMR (400 MHz, CDCl_3): δ 5.67 (dq, $J = 15.2, 6.0$ Hz, 1H), 5.55 (ddq, $J = 15.2, 7.2, 1.6$ Hz, 1H), 3.69 (dd, $J = 7.6, 2.8$ Hz, 1H), 1.72 (dd, $J = 6.0, 0.8$ Hz, 3H), 1.39 (s, 1H), 0.90 (s, 9H).

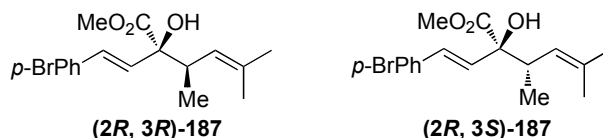
Methyl 2-hydroxy-3,6,6-trimethyl-2-styrylhept-4-enoate (186)

To a solution of (*E*)-2,2-dimethylhex-4-en-3-ol (**185**) (129 mg, 1.0 mmol, 1 equiv.) and $\text{Rh}_2(\text{S-DOSP})_4$ (19 mg, 1 mol%) in 2 mL of degassed pentane at 0 °C, was added the solution of styryldiazoacetate **7** in 5 mL of pentane and (128 mg, 0.6 mmol, 0.6 equiv.) by syringe pump over 1 h. After addition, the reaction mixture was stirred for 30min at 0 °C. Then it was concentrated under vacuum, the residue was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1) to afford 1st diastereomer of **186** (41 mg, 21% yield) and 2nd diastereomer of **186** (81 mg, 42% yield).

1st diastereomer: clear oil. $[\alpha]_{\text{D}}^{20} +32.4^\circ$ (*c* 1.0, CHCl_3). R_f , 0.37 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.43–7.41 (m, 2H), 7.35–7.31 (m, 2H), 7.27–7.23 (m, 1H), 6.86 (d, $J = 16.0$ Hz, 1H), 6.26 (d, $J = 16.0$ Hz, 1H), 5.51 (d, $J = 15.6$ Hz, 1H), 5.29 (dd, $J = 15.6, 8.8$ Hz, 1H), 3.76 (s, 3H), 3.37 (s, 1H), 2.66–2.58 (m, 1H), 1.02 (d, $J = 7.2$ Hz, 3H), 0.99 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 175.6 (C), 144.0 (CH), 136.7 (C), 130.8 (CH), 129.3 (CH), 128.8 (CH), 127.9 (CH), 126.9 (CH), 124.9 (CH), 80.8 (C), 53.0 (CH_3), 45.1 (CH), 33.1 (C), 29.8 (CH_3), 14.3 (CH_3); IR (neat): 3515, 2953, 1731, 1448, 1435, 1364, 1243, 1202, 1141, 974, 757, 745, 713, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 285.18491, found: 285.18464. HPLC analysis: 84% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_R : 14.8 min (major), 16.5 min (minor). **2nd diastereomer:** white solid. M.p.: 68–71 °C. $[\alpha]_{\text{D}}^{20} -69.8^\circ$ (*c* 1.0, CHCl_3). R_f , 0.25 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ

7.39–7.36 (m, 2H), 7.33–7.29 (m, 2H), 7.24–7.21 (m, 1H), 6.75 (d, $J = 16.0$ Hz, 1H), 6.25 (d, $J = 16.0$ Hz, 1H), 5.51 (dd, $J = 15.6, 0.4$ Hz, 1H), 5.24 (dd, $J = 15.6, 8.8$ Hz, 1H), 3.82 (s, 3H), 3.36 (s, 1H), 2.70–2.62 (m, 1H), 1.02 (d, $J = 6.8$ Hz, 3H), 0.94 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.8 (C), 144.3 (CH), 136.9 (C), 130.1 (CH), 128.7 (CH), 127.7 (CH), 126.7 (CH), 124.3 (CH), 80.0 (C), 53.2 (CH_3), 45.5 (CH), 33.1 (C), 29.9 (CH_3), 15.6 (CH_3); IR (neat): 3518, 2957, 1729, 1448, 1436, 1363, 1238, 1203, 1162, 1131, 969, 758, 745, 713, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$ [$\text{M}+\text{H}-\text{H}_2\text{O}$] $^+$: 285.18465, found: 285.18464. HPLC analysis: 89% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_{R} : 31.9 min (minor), 39.0 min (major).

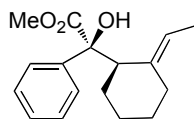
(2R, 3R)-Methyl 2-(4-bromostyryl)-2-hydroxy-3,5-dimethylhex-4-enoate ((2R, 3R)-187) and **(2R, 3S)-methyl 2-(4-bromostyryl)-2-hydroxy-3,5-dimethylhex-4-enoate ((2R, 3S)-187)**



Prepared by following the general procedure **III** with (*E*)-2-methylpent-3-en-2-ol (**100**) (53 mg, 0.5 mmol, 1 equiv.), $\text{Rh}_2(\text{S-DOSP})_4$ (9 mg, 1 mol%) and *p*-bromophenylvinyl diazoacetate **121** (280 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1 to 15:1) to afford **(2R, 3R)-187** (white solid, 108 mg, 58% yield) and **(2R, 3S)-187** (white solid, 37 mg, 20% yield). **(2R, 3R)-187**: M.p.: 105–106 °C. $[\alpha]_{\text{D}}^{20} +42.4^\circ$ (c 1.0, CHCl_3).

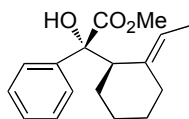
R_f , 0.26 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.44 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 8.4$ Hz, 2H), 6.80 (d, $J = 15.6$ Hz, 1H), 6.28 (d, $J = 15.6$ Hz, 1H), 5.12 (d, $J = 10.4$ Hz, 1H), 3.74 (s, 3H), 3.40 (s, 1H), 2.93–2.89 (m, 1H), 1.70 (d, $J = 1.2$ Hz, 3H), 1.63 (d, $J = 1.2$ Hz, 3H), 0.95 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.6 (C), 135.7 (C), 133.3 (C), 131.9 (CH), 130.3 (CH), 129.7 (CH), 128.4 (CH), 124.6 (CH), 121.6 (C), 80.3 (C), 53.1 (CH_3), 40.3 (CH), 26.2 (CH_3), 18.1 (CH_3), 14.6 (CH_3); IR (neat): 3513, 1730, 1487, 1436, 1246, 1206, 1136, 1073, 1009, 974, 851, 816, 797, 757, 729 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{17}\text{H}_{21}\text{O}_3\text{Br}$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 335.06412, found: 335.06427. HPLC analysis: 98% ee, CHIRALCEL OD-H, 0.2% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_R : 44.6 min (minor), 51.3 min (major). **(2R, 3S)-187**: M.p.: 84–87 °C. $[\alpha]_D^{20}$ -9.8° (c 1.0, CHCl_3). R_f , 0.21 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42 (d, $J = 8.4$ Hz, 2H), 7.22 (d, $J = 8.4$ Hz, 2H), 6.68 (d, $J = 16.0$ Hz, 1H), 6.22 (d, $J = 16.0$ Hz, 1H), 5.02 (d, $J = 10.4$ Hz, 1H), 3.84 (s, 3H), 3.40 (s, 1H), 2.97–2.89 (m, 1H), 1.66 (d, $J = 1.2$ Hz, 3H), 1.62 (d, $J = 1.2$ Hz, 3H), 0.95 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.7 (C), 135.9 (C), 133.5 (C), 131.8 (CH), 130.5 (CH), 129.0 (CH), 128.3 (CH), 124.1 (CH), 121.5 (C), 80.4 (C), 53.4 (CH_3), 40.7 (CH), 26.1 (CH_3), 18.5 (CH_3), 15.8 (CH_3); IR (neat): 3515, 1728, 1487, 1436, 1244, 1205, 1161, 1129, 1072, 1009, 972, 815, 796, 727 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{17}\text{H}_{21}\text{O}_3\text{Br}$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 335.06412, found: 335.06409. HPLC analysis: 97% ee, CHIRALPAK AS-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_R : 13.2 min (major), 16.4 min (minor).

(S)-Methyl 2-((R, E)-2-ethylidenecyclohexyl)-2-hydroxy-2-phenylacetate ((2S, 3R)-188)



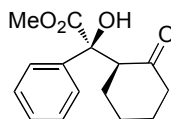
Prepared by following the general procedure **III** with **(S)-174** (99% ee, 63 mg, 0.5 mmol, 1 equiv), $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 1 mol%) and phenyldiazoacetate **6** (179 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 10:1) to afford **(2S, 3R)-188** as clear oil (83 mg, 60% yield). $[\alpha]_D^{20} +0.4^\circ$ (*c* 2.2, CHCl_3). R_f 0.52 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.69 (d, $J = 7.2$ Hz, 2H), 7.36 (t, $J = 7.6$ Hz, 2H), 7.31–7.27 (m, 1H), 5.38 (q, $J = 6.8$ Hz, 1H), 3.74 (s, 1H), 3.73 (s, 3H), 3.01 (t, $J = 5.2$ Hz, 1H), 2.49–2.42 (m, 1H), 2.23–2.17 (m, 1H), 1.86–1.77 (m, 1H), 1.62 (d, $J = 6.8$ Hz, 3H), 1.60–1.56 (m, 1H), 1.47–1.27 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.4 (C), 141.7 (C), 139.7 (C), 128.3 (CH), 127.6 (CH), 126.3 (CH), 118.0 (CH), 82.9 (C), 53.3 (CH_3), 50.8 (CH), 27.8 (CH_2), 27.7 (CH_2), 27.5 (CH_2), 24.4 (CH_2), 13.3 (CH_3); IR (neat): 3497, 2930, 1724, 1446, 1247, 1176, 1160, 1139, 728, 712, 698 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{17}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}]^+$: 275.16417, found: 275.16398.

(R)-Methyl 2-((R, E)-2-ethylidenecyclohexyl)-2-hydroxy-2-phenylacetate ((2R, 3R)-188)



Prepared by following the general procedure **III** with **(S)-174** (99% ee, 65 mg, 0.5 mmol, 1 equiv.), $\text{Rh}_2(\text{R-DOSP})_4$ (10 mg, 1 mol%) and phenyldiazoacetate **6** (180 mg, 1 mmol, 2 equiv.). The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 10:1) to afford **(2R, 3R)-188** as clear oil (82 mg, 58% yield). $[\alpha]_D^{20}$ -79.4° (c 1.0, CHCl_3). R_f 0.47 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.54 (d, $J = 7.2$ Hz, 2H), 7.28 (t, $J = 8.0$ Hz, 2H), 7.22–7.18 (m, 1H), 4.82 (q, $J = 6.8$ Hz, 1H), 3.94 (s, 1H), 3.74 (s, 3H), 3.08–3.06 (m, 1H), 2.49–2.43 (m, 1H), 1.95–1.84 (m, 2H), 1.69–1.45 (m, 5H), 1.30 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 176.6 (C), 141.7 (C), 136.2 (C), 128.0 (CH), 127.3 (CH), 126.1 (CH), 120.0 (CH), 82.5 (C), 53.6 (CH_3), 50.1 (CH), 30.3 (CH_2), 28.4 (CH_2), 27.7 (CH_2), 25.7 (CH_2), 13.0 (CH_3); IR (neat): 3502, 2927, 1722, 1447, 1243, 1139, 1124, 730, 697 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{17}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}]^+$: 275.16417, found: 275.16395.

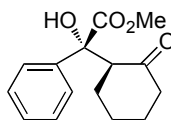
(S)-Methyl 2-hydroxy-2-((S)-2-oxocyclohexyl)-2-phenylacetate ((2S, 3S)-189)



The solution of **(2S, 3R)-188** (61 mg, 0.22 mmol) in 10 mL of dichloromethane was cooled to -78°C . O_3 gas was bubbled through the solution until a stable blue color appeared. The excess O_3 in the solution was removed by passing air for 10 min. Then dimethylsulfide (0.04 mL, 0.55 mmol, 2.5 equiv) was added. The solution was stirred for 24 h with temperature rising to room temperature. It was concentrated under vacuum and the crude material was purified by flash chromatography on silica gel eluting with

pentane/diethyl ether (3:1) to afford **(2*S*, 3*S*)-189** as clear oil (38 mg, 65% yield). $[\alpha]_{\text{D}}^{20}$ -175.5° (*c* 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.59 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.32–7.27 (m, 1H), 3.91 (s, 1H), 3.74 (s, 3H), 3.43 (dd, *J* = 12.0, 6.0 Hz, 1H), 2.47–2.38 (m, 2H), 2.11–2.06 (m, 1H), 1.83–1.80 (m, 1H), 1.68–1.54 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 213.4, 175.3, 138.9, 128.6, 128.0, 125.4, 77.9, 59.0, 53.2, 42.6, 27.8, 27.4, 25.1; IR (neat): 3520, 2947, 1731, 1703, 1448, 1434, 1245, 1211, 1132, 729, 698 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₅H₁₈O₄ [M+H]⁺: 263.12779, found: 263.12763. HPLC analysis: >99% ee, CHIRALPAK AD-H, 10% isopropanol/hexanes, 0.5 mL/min, UV 254 nm, *t*_R: 28.5 min (minor), 33.6 min (major). Data are consistent with the literature.^{66a}

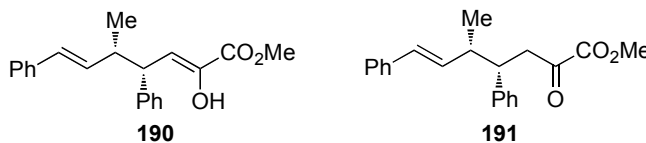
(*R*)-Methyl 2-hydroxy-2-((*S*)-2-oxocyclohexyl)-2-phenylacetate ((*2R*, 3*S*)-189)



Prepared by following the procedure for **(2*S*, 3*S*)-189**, using **(2*R*, 3*R*)-188** (75 mg, 0.27 mmol) as starting material. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (2:1) to afford **(2*R*, 3*S*)-189** as clear oil (48 mg, 66% yield). $[\alpha]_{\text{D}}^{20}$ -28.9° (*c* 1.3, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.50 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.31–7.29 (m, 1H), 4.21 (s, 1H), 3.79 (s, 3H), 3.22 (dd, *J* = 12.8, 5.28 Hz, 1H), 2.44–2.31 (m, 2H), 2.13–2.00 (m, 2H), 1.92–1.58 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 213.0 (C), 173.5 (C), 140.5 (C), 128.5 (CH), 128.1 (CH), 125.7 (CH), 79.6 (C), 59.7 (CH), 53.0 (CH₃), 43.2 (CH₂), 30.7 (CH₂), 28.0 (CH₂), 25.5

(CH₂); IR (neat): 3502, 1948, 1728, 1699, 1449, 1434, 1242, 1206, 1130, 729, 699 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₅H₁₈O₄ [M+H]⁺: 263.12779, found: 263.12771. HPLC analysis: >99% ee, CHIRALPAK AD-H, 10% isopropanol/hexanes, 0.5 mL/min, UV 254 nm, *t*_R: 33.1 min (major), 38.2 min (minor). Data are consistent with the literature.^{66c}

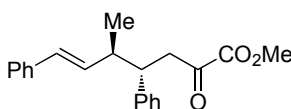
(2*Z*, 6*E*)-Methyl 2-hydroxy-5-methyl-4,7-diphenylhepta-2,6-dienoate (190) and (*E*)-methyl *Syn*-5-methyl-2-oxo-4,7-diphenylhept-6-enoate (*syn*-191)



The solution of (**2*S*, 3*S*)-177 (36 mg, 0.11 mmol, 0.016 M) in 7 mL of cyclohexane was heated to reflux for 5 h. 1 mL of solution was taken out and concentrated under vacuum. Its ¹H-NMR spectrum showed the quantitative formation of **190**. Then the solution was cooled to room temperature and 1 g of silica gel was added. The mixture was stirred vigorously at room temperature for 5 h, then filtered and concentrated under vacuum to give *syn*-**191** as clear oil (31 mg, 85% yield). Compound **190**: ¹H NMR (400 MHz, CDCl₃): δ 7.34–7.20 (m, 10H), 6.39 (d, *J* = 15.6 Hz, 1H), 6.15 (dd, *J* = 15.6, 8.0 Hz, 1H), 5.92 (dd, *J* = 10.4, 1.6 Hz, 1H), 5.63 (d, *J* = 1.6 Hz, 1H), 3.81 (d, *J* = 9.2 Hz, 1H), 3.77 (s, 3H), 2.75–2.70 (m, 1H), 1.00 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 166.1 (C), 142.8 (C), 139.4 (C), 138.0 (C), 134.1 (CH), 129.9 (CH), 128.7 (CH), 128.7 (CH), 128.3 (CH), 127.2 (CH), 126.7 (CH), 126.4 (CH), 116.2 (CH), 53.1 (CH₃), 48.1 (CH), 43.3 (CH), 19.3 (CH₃); IR (neat): 3448, 1703, 1494, 1441, 1245, 968, 749, 698 cm⁻¹. Compound *syn*-**191**: [α]_D²⁰ -109.3° (*c* 1.0, CHCl₃). *R*_f 0.45 (pentane/diethyl ether 5:1).**

^1H NMR (400 MHz, CDCl_3): δ 7.35–7.29 (m, 6H), 7.24–7.22 (m, 4H), 6.43 (d, $J = 16.0$ Hz, 1H), 5.95 (dd, $J = 16.0, 9.2$ Hz, 1H), 3.52 (s, 3H), 3.42 (dd, $J = 16.8, 7.6$ Hz, 1H), 3.18 (dt, $J = 9.2, 7.6$ Hz, 1H), 3.01 (dd, $J = 16.8, 7.6$ Hz, 1H), 2.56–2.46 (m, 1H), 0.88 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 193.2 (C), 161.2 (C), 142.9 (C), 137.1 (C), 134.9 (CH), 131.0 (CH), 128.8 (CH), 128.3 (CH), 127.6 (CH), 127.0 (CH), 126.4 (CH), 52.9 (CH_3), 47.6 (CH), 44.9 (CH), 44.6 (CH_2), 19.4 (CH_3); IR (neat): 1727, 1494, 1452, 1284, 1260, 1242, 1065, 971, 750, 695 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}]^+$: 323.16417, found: 323.16427. HPLC analysis: 99.6% ee, (*R*, *R*)-Whelk O1, 0.8% isopropanol/hexanes, 0.8 mL/min, UV 254 nm, t_{R} : 28.2 min (major), 64.0 min (minor).

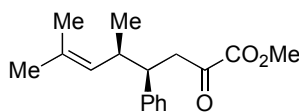
***Anti*-5-methyl-2-oxo-4,7-diphenylhept-6-enoate (*anti*-191)**



The solution of (**2*R*, 3*S***)-**177** (>99% ee) (53 mg, 0.17 mmol, 0.016 M) in 10 mL of cyclohexane was heated to reflux for 5 h. Then the solution was cooled to room temperature and 0.5 g of silica gel was added. The mixture was stirred vigorously at room temperature for 5 h, then filtered and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford pure **syn-191** (13 mg), the mixture of **syn-191** and **syn-191** (7 mg), pure **anti-191** (27 mg). Combined yield: 47 mg, 88% yield. **Anti-191**: clear oil. $[\alpha]_{\text{D}}^{20} -5.8^\circ$ (c 1.0, CHCl_3). R_f 0.36 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.30–7.15

(m, 10H), 6.30 (dd, $J = 16.0, 0.8$ Hz, 1H), 5.95 (dd, $J = 16.0, 8.0$ Hz, 1H), 3.76 (s, 3H), 3.40–3.32 (m, 1H), 3.28 (t, $J = 6.8$ Hz, 2H), 2.65–2.61 (m, 1H), 1.05 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 193.4 (C), 161.7 (C), 140.9 (C), 137.6 (C), 132.8 (CH), 130.6 (CH), 128.9 (CH), 128.7 (CH), 128.4 (CH), 127.4 (CH), 126.9 (CH), 126.3 (CH), 53.1 (CH_3), 46.0 (CH), 42.6 (CH_2), 42.0 (CH), 18.2 (CH_3); IR (neat): 1728, 1494, 1452, 1244, 1066, 972, 750, 695 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}]^+$: 323.16417, found: 323.16432. HPLC analysis: 99.7% ee, (*R, R*)-Whelk O1, 0.8% isopropanol/hexanes, 0.8 mL/min, UV 254 nm, t_R : 47.3 min (major), 67.6 min (minor).

Methyl 5,7-dimethyl-2-oxo-4-phenyloct-6-enoate (**192**)



The solution of (***R***)-**125** (100 mg, 0.36 mmol, 0.016 M) in 23 mL of toluene was heated to reflux for 4 h. TLC showed that all of (***R***)-**125** was consumed. The solution was cooled to room temperature and 2 g of silica gel was added. The mixture was stirred vigorously at room temperature for 5 h, then filtered and concentrated under vacuum. The crude material was further by flash chromatography on silica gel eluting with pentane/diethyl ether (15:1) to afford **192** as clear oil (70 mg, 71% yield). $[\alpha]_D^{20} +63.5^\circ$ (c 1.0, CHCl_3). R_f , 0.23 (pentane/diethyl ether 10:1). Compound **192**: ^1H NMR (400 MHz, CDCl_3): δ 7.30–7.26 (m, 2H), 7.21–7.17 (m, 3H), 4.88 (d, $J = 10.0$ Hz, 1H), 3.77 (s, 3H), 3.28–3.20 (m, 1H), 3.03–2.95 (m, 2H), 2.62–2.52 (m, 1H), 1.68 (d, $J = 1.2$ Hz, 3H), 1.65 (d, $J = 1.2$ Hz, 3H), 0.70 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 193.2 (C), 161.4 (C),

143.3 (C), 132.8 (C), 130.2 (CH), 128.6 (CH), 128.3 (CH), 126.7 (CH), 53.0 (CH₃), 48.3 (CH), 44.6 (CH₂), 39.0 (CH), 26.0 (CH₃), 19.5 (CH₃), 18.4 (CH₃); IR (neat): 1728, 1452, 1268, 1239, 1096, 1061, 762, 701 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₇H₂₂O₃ [M+H]⁺: 275.16417, found: 275.16393. HPLC analysis: 81% ee, (*R, R*)-whelk O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, *t*_R: 22.3 min (minor), 34.3 min (major).

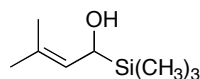
2.4.4 Synthetic procedures and characterization for Chapter 2.2.4

2.4.4.1 General procedure :

A solution of Rh₂(*S*-DOSP)₄ (10 mg, 0.005 mmol, 1 mol %) and allylic alcohol (0.5 mmol, 1 equiv.) in 1 mL of degassed pentane was cooled to 0 °C with ice bath under argon. diazo solution (0.55 mmol, 1.1 equiv.) in 5 mL of degassed pentane was added by syringe pump over 1 h. The syringe was rinsed with another 1 mL of degassed pentane and added to the reaction mixture. After addition, the solution was stirred for 30 min at 0 °C, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel.

2.4.4.2 Characterization in Chapter 2.2.4

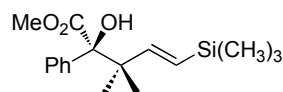
3-Methyl-1-(trimethylsilyl)but-2-en-1-ol (193)



Prepared by following the literature procedure.¹⁰³ *n*-butyl lithium solution (2.5 M in hexanes, 15 mL, 38 mmol, 1.1 equiv.) was slowly added to the 3-methyl-2-buten-1-ol

solution (3.0 g, 35 mmol) in 20 mL of THF at $-78\text{ }^{\circ}\text{C}$. After 1 h of stirring, TMSCl (4.5 mL, 35 mmol) was added, and the solution was stirred for another 2.5 h. *sec*-butyl lithium solution (1.4 M in cyclohexane, 30 mL, 42 mmol, 1.2 equiv.) was slowly added, and the solution was stirred for 2 h. Then it was warmed to room temperature, and quenched with aqueous saturated NH_4Cl . THF was removed under vacuum. The residue was extracted with diethyl ether (3 x 50 mL), and the combined ether solution was dried over MgSO_4 , filtered, and concentrated under vacuum. The crude product was purified on silica gel eluting with pentane/diethyl ether (5:1), and afforded compound **193** as clear oil (1.2 g, 22% yield). ^1H NMR (400 MHz, CDCl_3): δ 5.27 (d, $J = 10.4$ Hz, 1H), 4.17 (d, $J = 10.4$ Hz, 1H), 1.75 (s, 3H), 1.62 (s, 3H), 1.13 (s, 1H), 0.04 (s, 9H).

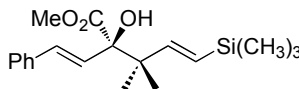
(*S*, *E*)-Methyl 2-hydroxy-3,3-dimethyl-2-phenyl-5-(trimethylsilyl)pent-4-enoate (194**)**



Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (91 mg, 0.52 mmol) and 3-methyl-1-(trimethylsilyl)but-2-en-1-ol (**193**) (racemic, 82 mg, 0.51 mmol) at $0\text{ }^{\circ}\text{C}$. The crude material was purified on silica gel eluting with pentane/diethyl ether (30:1), and afforded compound **194** as clear oil (115 mg, 72% yield). $[\alpha]_{\text{D}}^{20} -12.7^{\circ}$ (c 1.0, CHCl_3). R_f 0.36 (pentane/diethyl ether 10:1). ^1H NMR (600 MHz, CDCl_3): δ 7.70–7.67 (m, 2H), 7.31–7.27 (m, 3H), 6.23 (d, $J = 15.2$ Hz, 1H), 5.55 (d, $J = 15.2$ Hz, 1H), 3.83 (s, 3H), 3.73 (s, 1H), 1.07 (s, 6H), 0.07 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.7 (C), 151.7 (CH), 138.7 (C), 128.3 (CH), 127.8 (CH), 127.8 (CH), 127.3 (CH), 83.0 (C), 53.0 (CH_3), 46.2 (C), 22.8 (CH_3), 22.5 (CH_3), -1.0 (CH_3); IR (neat): 3502, 2953,

1720, 1246, 1065, 867, 835, 743, 701 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{17}\text{H}_{26}\text{O}_3\text{Si}$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 289.16184, found: 289.16180. HPLC analysis: 88% ee, (*S,S*)-whelk O1, 0.3% isopropanol/hexanes, 0.7 mL/min, UV: 230 nm, t_R : 7.5 min (major), 8.5 min (minor).

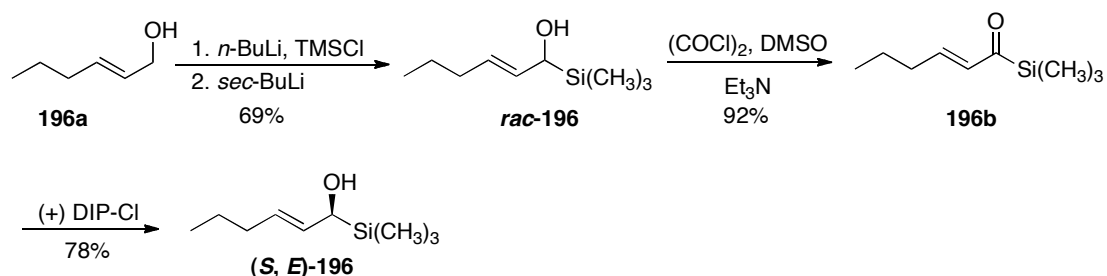
(*R,E*)-Methyl 2-hydroxy-3,3-dimethyl-2-((*E*)-styryl)-5-(trimethylsilyl)pent-4-enoate (195)



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (115 mg, 0.57 mmol, 1.1 equiv.) and 3-methyl-1-(trimethylsilyl)but-2-en-1-ol (**193**) (racemic, 81 mg, 0.51 mmol) at 0 °C. The crude material was purified on silica gel eluting with pentane/diethyl ether (20:1), and afforded compound **195** as clear oil (117 mg, 69% yield). $[\alpha]_D^{20}$ -15.7° (c 1.0, CHCl_3). R_f 0.26 (pentane/diethyl ether 10:1). ^1H NMR (600 MHz, CDCl_3): δ 7.38 (d, $J = 7.8$ Hz, 2H), 7.31 (t, $J = 7.2$ Hz, 2H), 7.23 (t, $J = 7.2$ Hz, 1H), 6.83 (d, $J = 15.6$ Hz, 1H), 6.46 (d, $J = 15.6$ Hz, 1H), 6.18 (d, $J = 19.2$ Hz, 1H), 5.69 (d, $J = 19.2$ Hz, 1H), 3.77 (s, 3H), 3.46 (s, 1H), 1.14 (s, 3H), 1.07 (s, 3H), 0.07 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 175.1 (C), 151.4 (CH), 137.0 (C), 131.0 (CH), 128.7 (CH), 128.4 (CH), 127.8 (CH), 127.2 (CH), 126.8 (CH), 81.6 (C), 52.9 (CH_3), 46.3 (C), 22.4 (CH_3), 22.2 (CH_3), -1.0 (CH_3); IR (neat): 3512, 1724, 1245, 1145, 1126, 974, 866, 834, 739, 690 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{19}\text{H}_{28}\text{O}_3\text{Si}$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 315.17749, found: 315.17745. Anal. Calcd for $\text{C}_{19}\text{H}_{28}\text{O}_3\text{Si}$: C, 68.63; H, 8.49. Found: C, 68.90, H,

8.65. HPLC analysis: 92% ee, CHIRALCEL OD-H, 0.3% isopropanol/hexanes, 0.7 mL/min, UV: 254 nm, t_R : 13.3 min (major), 11.6 min (minor).

(*S, E*)-1-(Trimethylsilyl)hex-2-en-1-ol ((*S, E*)-196)



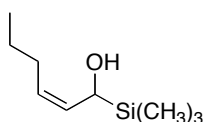
Racemic (*E*)-196 was prepared literature procedure.¹⁰³ *n*-butyl lithium solution (2.5 M in hexanes, 31 mL, 77 mmol, 1.1 equiv.) was slowly added to the *trans*-2-hexen-1-ol (**196a**) solution (7.0 g, 70 mmol) in 40 mL of THF at -78 °C. After 1 h of stirring, TMSCl (8.9 mL, 70 mmol) was added, and the solution was stirred for another 2.5 h. *sec*-butyl lithium solution (1.4 M in cyclohexane, 60 mL, 84 mmol, 1.2 equiv.) was slowly added, and the solution was stirred for 2 h. Then it was warmed to room temperature, and quenched with aqueous saturated NH₄Cl. THF was removed under vacuum. The residue was extracted with diethyl ether (3 x 50 mL), and the combined ether solution was dried over MgSO₄, filtered, and concentrated under vacuum. The crude product was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded racemic (*E*)-196 as clear oil (8.3 g, 69% yield). ¹H NMR (400 MHz, CDCl₃): δ 5.59 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.46 (dt, *J* = 15.6, 6.4 Hz, 1H), 3.91 (d, *J* = 6.4 Hz, 1H), 2.02 (q, *J* = 7.2 Hz, 2H), 1.44–1.35 (m, 2H), 0.90 (t, *J* = 7.6 Hz, 3H), 0.03 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 131.6, 127.7, 68.6, 34.8, 23.0, 13.8, -4.0. Data are consistent with the literature.

DMSO (3.7 mL, 52 mmol, 2.8 equiv.) was slowly added to the oxalyl chloride solution (2.4 mL, 28 mmol, 1.5 equiv.) in 20 mL of dichloromethane at -78 °C. After stirred for 1.5 h racemic (**E**)-**196** (3.2 g, 18 mmol, 1.0 equiv.) in 30 mL of dichloromethane was added, and the solution was stirred for 2 h at -78 °C. Triethylamine (13.4 mL, 96 mmol, 5.3 equiv.) was then added, and the solution was warmed to 0 °C and stirred for 2.5 h. The reaction mixture was poured into 50 mL of water, the organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 x 50 mL). The combined dichloromethane solution was washed with dilute aqueous HCl, dried over MgSO₄, filtered, and concentrated under vacuum. The crude product was purified on silica gel eluting with pentane/diethyl ether (15:1), and afforded compound **196b** as yellow oil (2.9 g, 92% yield). ¹H NMR (600 MHz, CDCl₃): δ 6.76 (dt, *J* = 16.2, 6.6 Hz, 1H), 6.22 (d, *J* = 16.2 Hz, 1H), 2.24 (q, *J* = 7.2 Hz, 2H), 1.52 (m, 2H), 0.96 (t, *J* = 7.8 Hz, 3H), 0.25 (s, 9H).

The solution of **196b** (1.2 g, 7.6 mmol) in 10 mL of THF was added to (+)-DIPCl (3.9 g, 12.1 mmol, 1.6 equiv.) in 10 mL of THF at -10 °C. The mixture was stirred for 20 h, then warmed to room temperature and concentrated under vacuum. The residue was mixed with diethanolamine (3.8 g, 36.0 mmol, 4.7 equiv.) in 50 mL diethyl ether. The mixture was vigorously stirred at room temperature for 24 h. After filtration, the solution was concentrated under vacuum. The crude product was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded compound (**S**, **E**)-**196** as yellow oil (1.0 g, 78% yield). $[\alpha]_{\text{D}}^{20} -37.0^{\circ}$ (*c* 1.0, CHCl₃).¹⁰³ The ¹H NMR data are identical as the racemic (**E**)-

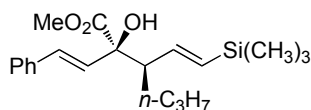
196. Chiral capillary GC analysis: 82% ee, CHIRALDEX B-PM column, t_R : 13.68 min (major), 13.87 min (minor).

(Z)-1-(Trimethylsilyl)hex-2-en-1-ol ((Z)-196)



Compound **(Z)-196** was synthesized by the same procedure as racemic **(E)-196** with *cis*-2-hexen-1-ol (3.5 g, 35 mmol) as starting material. The crude product was purified on silica gel eluting with pentane/diethyl ether (10:1), and afforded racemic **(Z)-196** as yellow oil (3.8 g, 63% yield). ^1H NMR (400 MHz, CDCl_3): δ 5.47 (t, $J = 10.0$ Hz, 1H), 5.40–5.34 (m, 1H), 4.25 (d, $J = 9.6$ Hz, 1H), 2.10–1.80 (m, 2H), 1.44–1.30 (m, 3H), 0.91 (t, $J = 7.2$ Hz, 3H), 0.05 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 130.9 (CH), 129.5 (CH), 64.2 (CH), 30.2 (CH_2), 23.2 (CH_2), 14.1 (CH_3), -3.9 (CH_3).

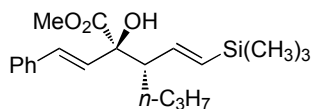
(2R, 3R)-Methyl 2-hydroxy-2-styryl-3-((E)-2-(trimethylsilyl)vinyl)hexanoate ((2R, 3R)-197)



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (115 mg, 0.57 mmol, 1.1 equiv) and (*S, E*)-1-(trimethylsilyl)hex-2-en-1-ol (**(S, E)-196**) (82% ee, 87 mg, 0.5 mmol) and $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 1 mol%) at room temperature. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl

ether (30:1) to afford **(2R, 3R)-197** as clear oil (57 mg, 33% yield). $[\alpha]_D^{20} +6.7^\circ$ (c 1.0, CHCl_3). R_f 0.38 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 2H), 7.27–7.24 (m, 1H), 6.87 (d, $J = 15.6$ Hz, 1H), 6.25 (d, $J = 15.6$ Hz, 1H), 5.87 (dd, $J = 18.4, 8.8$ Hz, 1H), 5.71 (d, $J = 18.4$ Hz, 1H), 3.74 (s, 3H), 3.45 (s, 1H), 2.51–2.45 (m, 1H), 1.53–1.47 (m, 1H), 1.42–1.27 (m, 2H), 1.14–1.09 (m, 1H), 0.86 (t, $J = 6.8$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 175.4 (C), 145.6 (CH), 136.7 (C), 134.8 (CH), 131.0 (CH), 129.2 (CH), 128.8 (CH), 127.9 (CH), 126.9 (CH), 80.8 (C), 54.8 (CH), 53.1 (CH_3), 29.4 (CH_2), 20.8 (CH_2), 14.2 (CH_3), -1.0 (CH_3); IR (neat): 3515, 2954, 1732, 1247, 1234, 1136, 997, 973, 867, 836, 752, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{20}\text{H}_{30}\text{O}_3\text{Si}$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 329.19318, found: 329.19318. HPLC analysis: 97% ee, (*S, S*)-DACH DNB, 0.2% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. t_R : 37.2 min (major), 50.6 min (minor). **(2S, 3R)-197** was also isolated as a white solid from this reaction (22 mg, 13% yield). Its spectra data are identical as that of compound **(2R, 3S)-197**.

(2R, 3S)-Methyl 2-hydroxy-2-styryl-3-((E)-2-(trimethylsilyl)vinyl)hexanoate ((2R, 3S)-197)



Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (113 mg, 0.56 mmol, 1.1 equiv.) and (*R, E*)-1-(trimethylsilyl)hex-2-en-1-ol (**(R, E)-196**) (85% ee, 88 mg, 0.5 mmol) and $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 1 mol%) at room temperature. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl

ether (30:1) to afford **(2R, 3S)-197** as a white solid (50 mg, 28% yield). M.p.: 79–81 °C. $[\alpha]_D^{20}$ -58.5° (*c* 0.9, CHCl₃). *R_f*, 0.25 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.27–7.24 (m, 1H), 6.87 (d, *J* = 15.6 Hz, 1H), 6.25 (d, *J* = 15.6 Hz, 1H), 5.87 (dd, *J* = 18.4, 8.8 Hz, 1H), 5.71 (d, *J* = 18.4 Hz, 1H), 3.74 (s, 3H), 3.45 (s, 1H), 2.51–2.45 (m, 1H), 1.53–1.47 (m, 1H), 1.42–1.27 (m, 2H), 1.14–1.09 (m, 1H), 0.86 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 175.8 (C), 144.6 (CH), 136.9 (C), 135.1 (CH), 130.1 (CH), 130.0 (CH), 128.6 (CH), 127.7 (CH), 126.8 (CH), 79.9 (C), 55.2 (CH), 53.3 (CH₃), 31.1 (CH₂), 20.7 (CH₂), 14.2 (CH₃), -1.0 (CH₃); IR (neat): 3526, 2954, 1725, 1247, 1231, 1143, 868, 836, 756, 742, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₀H₃₀O₃Si [M+H-H₂O]⁺: 329.19318, found: 329.19319. Anal. Calcd for C₁₆H₂₀O₃: C, 69.32; H, 8.73. Found: C, 769.52; H, 8.92. HPLC analysis: 97% ee, CHIRALCEL OD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV: 254nm. *t_R*: 13.1 min (minor), 14.6 min (major). **(2S, 3S)-197** was also isolated as clear oil from this reaction (17 mg, 10% yield). Its spectra data are identical as that of compound **(2R, 3R)-197**.

2.4.5 Synthetic procedures and characterization for Chapter 2.2.5

2.4.5.1 General procedure I: synthesis of tertiary propargylic alcohols:

n-Butyl lithium solution (2.5 M in hexanes, 5.3 mL, 13.2 mmol, 1.1 equiv.) was slowly added to the alkyne solution (11.9 mmol, 1 equiv.) in 50 mL of THF at -78 °C. After 30 min, acetone (1.0 mL, 13.2 mmol, 1.1 equiv.) was slowly added. The reaction was stirred for 1 h with temperature rising to room temperature, then quenched with aqueous

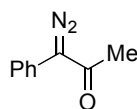
saturated NH_4Cl . The mixture was extracted with diethyl ether (3 x 50 mL), and the combined ether solution was washed with brine, dried over MgSO_4 , filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel.

2.4.5.2 General procedure II: the $\text{Rh}_2(\text{S-DOSP})_4$ -catalyzed tandem ylide formation/[2,3]-sigmatropic rearrangement of donor/acceptor carbenoid with propargylic alcohol:

A solution of $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol %) and propargylic alcohol (0.5 mmol) in 1 mL of degassed pentane was cooled to 0 °C with ice bath under argon. Diazo (1.0 mmol, 2 equiv.) in 9 mL of degassed pentane was added by syringe pump over 1.5 h. After addition, the solution was stirred for 2 h with temperature rising to room temperature, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel.

2.4.5.3 characterization for Chapter 2.2.5

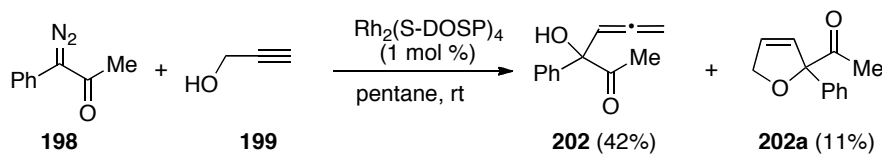
1-Diazo-1-phenylpropan-2-one (198)



Prepared by following the literature procedure.¹⁹ The solution of phenylacetone (2.5 g, 18.6 mmol) and *p*-ABSA (5.4 g, 22.3 mmol, 1.2 equiv.) in 125 mL of acetonitrile was cooled to 0 °C with ice bath under argon. DBU (3.3 mL, 22.1 mmol, 1.2 equiv.) was

slowly added. The solution was stirred for 1 h at 0 °C and 1 h at room temperature. Saturated aqueous NaHCO₃ solution (100 mL) and diethyl ether (100 mL) were added. The organic layer was separated, and the aqueous layer was extracted with diethyl ether. The combined organic solution was dried over MgSO₄, filtered, and concentrated under vacuum. The crude material was purified on silica gel eluting with pentane/diethyl ether (10:1 to 5:1) to afford compound **198** as orange crystal (2.6 g, 86% yield). ¹H NMR (600 MHz, CDCl₃): δ 7.49 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 8.4 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 2.37 (s, 3H). Data are consistent with the literature.

3-Hydroxy-3-phenylhexa-4,5-dien-2-one (**202**)

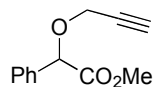


To a solution of Rh₂(*S*-DOSP)₄ (19 mg, 0.01 mmol, 1 mol %) and propargyl alcohol (**199**) (67 mg, 1.2 mmol, 1.2 equiv.) in 1 mL of degassed pentane and 0.5 mL of toluene, was added diazo ketone (**198**) (161 mg, 1.0 mmol) in 9 mL of degassed pentane by syringe pump over 1.5 h at room temperature. After addition, the solution was stirred for 30 min, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1 to 10:1) to afford compound **202** as clear oil (80 mg, 42% yield). ¹H NMR (400 MHz, CDCl₃): δ 7.53 (d, *J* = 6.8 Hz, 2H), 7.42-7.27 (m, 3H), 5.81 (t, *J* = 6.4 Hz, 1H), 5.02 (dd, *J* = 6.8, 1.2 Hz, 2H), 4.61 (s, 1H), 2.12 (s, 3H). Data are consistent with the literature.⁷⁶ HPLC analysis: 0% ee (Note). Compound **202a** was also isolated as byproduct from this reaction (clear oil, 21

mg, 11% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.48-7.45 (m, 2H), 7.37 (t, $J = 7.6$ Hz, 2H), 7.32-7.28 (m, 1H), 6.24 (dt, $J = 6.4, 2.4$ Hz, 1H), 6.04 (dt, $J = 6.0, 1.6$ Hz, 1H), 4.92-4.83 (m, 2H), 2.22 (s, 3H). Data are consistent with the literature.⁷⁶ HPLC analysis: 0% ee, (*R, R*)-whelk O1, 0.5% isopropanol/hexanes, 0.8 mL/min, UV: 230 nm. t_{R} : 12.7 min, 16.4 min.

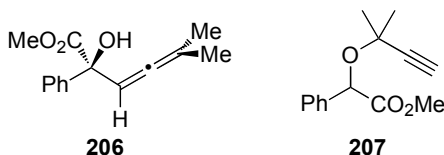
Note: Compound **202** was converted to compound **202a** by treating with AgBF_4 in order to determine the enantiomeric excess.

Methyl 2-phenyl-2-(prop-2-ynoxy)acetate (**203**)



Prepared by following the general procedure **II** with methyl phenyldiazoacetate (**6**) (177 mg, 1.0 mmol), propargyl alcohol (**199**) (70 mg, 1.2 mmol, 1.2 equiv.), and $\text{Rh}_2(\text{S-DOSP})_4$ (20 mg, 0.01 mmol, 1 mol%) at room temperature. The crude material was purified on silica gel eluting with pentane/diethyl ether (10:1 to 7:1) to afford compound **203** as clear oil (103 mg, 50% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.47-7.44 (m, 2H), 7.41-7.34 (m, 3H), 5.23 (s, 1H), 4.32 (dd, $J = 15.6, 2.4$ Hz, 1H), 4.16 (dd, $J = 15.6, 2.4$ Hz, 1H), 3.73 (s, 3H), 2.49 (t, $J = 2.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.8 (C), 135.5 (C), 129.2 (CH), 128.9 (CH), 127.7 (CH), 78.8 (CH), 75.9 (C), 56.4 (CH_2), 52.6 (CH_3); IR (neat): 3284, 1746, 1455, 1436, 1263, 1210, 1174, 1097, 1074, 1024, 731, 696 cm^{-1} ; HPLC analysis: 0% ee, (*R, R*)-Whelk-O1, 1.0% isopropanol/hexanes, 0.7 mL/min. UV 230 nm. t_{R} : 20.0 min, 27.6 min.

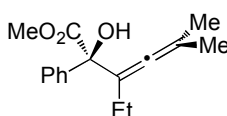
(S)-Methyl 2-hydroxy-5-methyl-2-phenylhexa-3,4-dienoate (206) and Methyl 2-(2-methylbut-3-yn-2-yloxy)-2-phenylacetate (207)



Prepared by following the general procedure **II** with methyl phenyldiazoacetate (**6**) (176 mg, 1.0 mmol), 2-methyl-3-butyn-2-ol (**204**) (84 mg, 1.2 mmol, 1.2 equiv.), and $\text{Rh}_2(\text{S-DOSP})_4$ (20 mg, 0.01 mmol, 1 mol%) at room temperature. The crude material was purified on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **206** (clear oil, 97 mg, 42% yield) and compound **207** (clear oil, 28 mg, 12% yield). Compound **206**: $[\alpha]_D^{20} +20.9^\circ$ (c 1.0, CHCl_3). R_f 0.26 (pentane/diethyl ether 5:1). ^1H NMR (600 MHz, CDCl_3): δ 7.60 (d, $J = 7.8$ Hz, 2H), 7.37 (t, $J = 7.8$ Hz, 2H), 7.33–7.30 (m, 1H), 5.56–5.54 (m, 1H), 3.76 (s, 3H), 3.74 (s, 1H), 1.75 (d, $J = 3.0$ Hz, 3H), 1.73 (d, $J = 2.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 200.5 (C), 174.6 (C), 141.0 (C), 128.2 (CH), 128.1 (CH), 126.6 (CH), 101.1 (C), 94.3 (CH), 78.0 (C), 53.3 (CH_3), 20.4 (CH_3), 20.3 (CH_3); IR (neat): 3498, 1728, 1448, 1435, 1252, 1186, 1173, 734, 697 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{14}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 215.10666, found: 215.10657. HPLC analysis: 27% ee, CHIRALPAK AD-H, 1.0% isopropanol/hexanes, 0.7 mL/min. UV 230 nm. t_R : 31.4 min (major), 34.4 min (minor). Compound **207**: R_f 0.37 (pentane/diethyl ether 5:1). ^1H NMR (600 MHz, CDCl_3): δ 7.47 (d, $J = 7.2$ Hz, 2H), 7.36 (t, $J = 7.8$ Hz, 2H), 7.33–7.30 (m, 1H), 5.39 (s, 1H), 3.73 (s, 3H), 2.48 (s, 1H), 1.58 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.7 (C), 137.9 (C), 128.7 (CH), 128.5 (CH),

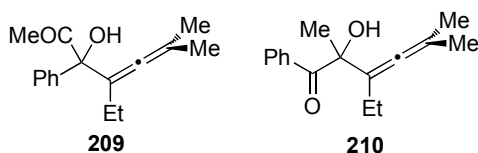
127.1 (CH), 85.5 (CH), 76.2 (CH), 73.4 (C), 72.4 (C), 52.4 (CH₃), 29.6 (CH₃), 29.4 (CH₃); IR (neat): 3282, 1754, 1454, 1535, 1382, 1366, 1274, 1229, 1206, 1152, 1090, 1069, 1015, 723, 696 cm⁻¹; HPLC analysis: 0% ee, (*R*, *R*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min. UV 230 nm. *t*_R: 16.3 min, 21.6 min.

(*R*)-Methyl 3-ethyl-2-hydroxy-5-methyl-2-phenylhexa-3,4-dienoate (208)



Prepared by following the general procedure **II** with methyl phenyldiazoacetate (**6**) (180 mg, 1 mmol) and 2-methylhex-3-yn-2-ol (**205**) (59 mg, 0.5 mmol) at room temperature. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) and afforded Compound **208** as clear oil (115 mg, 85% yield). $[\alpha]_D^{20} +144.5^\circ$ (*c* 1.0, CHCl₃). *R*_f 0.21 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.63–7.60 (m, 2H), 7.38–7.27 (m, 3H), 3.87 (s, 1H), 3.71 (s, 3H), 2.05–1.96 (m, 1H), 1.86–1.76(m, 1H), 1.73 (s, 3H), 1.71 (s, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 199.2 (C), 175.0 (C), 139.6 (C), 127.9 (CH), 127.8 (CH), 127.4 (CH), 107.9 (C), 100.4 (C), 81.9 (C), 53.2 (CH₃), 20.7 (CH₃), 20.6 (CH₂), 20.4 (CH₃), 12.5 (CH₃); IR (neat): 3501, 1724, 1448, 1435, 1251, 1187, 1172, 1059, 740, 698 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₆H₂₀O₃ [M+H-H₂O]⁺: 243.1379, found: 243.1380. Anal. Calcd for C₁₆H₂₀O₃: C, 73.82; H, 7.74. Found: C, 73.56; H, 7.86. HPLC analysis: 85% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.7 mL/min. UV 230 nm. *t*_R: 22.4 min (major), 29.4 min (minor).

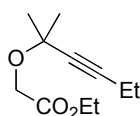
4-Ethyl-3-hydroxy-6-methyl-3-phenylhepta-4,5-dien-2-one (209) and 3-ethyl-2-hydroxy-2,5-dimethyl-1-phenylhexa-3,4-dien-1-one (210)



Prepared by following the general procedure **II** with 1-diazo-1-phenylpropan-2-one (**198**) (160 mg, 1.0 mmol, 2 equiv.), 2-methylhex-3-yn-2-ol (**205**) (59 mg, 0.5 mmol) at room temperature. The crude material was purified on silica gel eluting with pentane/diethyl ether (30:1) to afford Compound **209** (clear oil, 5 mg, 4% yield) and Compound **210** (clear oil, 15 mg, 12% yield). Compound **209**: R_f 0.50 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.54–7.51 (m, 2H), 7.40–7.36 (m, 2H), 7.34–7.29 (m, 1H), 4.66 (s, 1H), 2.12–2.04 (m, 1H), 2.02 (s, 3H), 1.98–1.90 (m, 1H), 1.80 (s, 3H), 1.69 (s, 3H), 0.98 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 208.6, 199.4, 139.8, 128.6, 128.1, 127.7, 106.2, 100.3, 85.6, 25.7, 21.1, 21.0, 20.4, 12.4; IR (neat): 3451, 1708, 1448, 1355, 1212, 1183, 1172, 1131, 1060, 750, 702 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{16}\text{H}_{20}\text{O}_2$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 227.14304, found: 227.14286. Anal. HPLC analysis: 18% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.7 mL/min. UV 230 nm. t_R : 12.8 min (minor), 21.4 min (major). Compound **210**: ^1H NMR (400 MHz, CDCl_3): δ 8.16 (d, $J = 8.0$ Hz, 2H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.44 (t, $J = 7.2$ Hz, 2H), 4.71 (s, 1H), 2.17–2.08 (m, 1H), 1.83 (s, 3H), 1.77 (s, 3H), 1.68–1.62 (m, 1H), 1.60 (s, 3H), 0.91 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 203.5, 199.2, 133.7, 133.6, 129.9, 128.4, 109.5, 101.5, 79.5, 26.5, 21.0, 20.7, 19.8, 12.5; IR (neat): 3452, 2965, 2931, 1669, 1598, 1449, 1363,

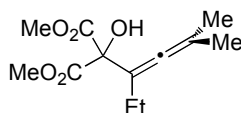
1246, 1176, 1134, 1067, 958, 905, 712, 689 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{16}\text{H}_{20}\text{O}_2$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 227.14304, found: 227.14288. HPLC analysis: 2% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.7 mL/min. UV 230 nm. t_R : 18.3 min (minor), 20.6 min (major).

Ethyl 2-(2-methylhex-3-yn-2-yloxy)acetate (211)



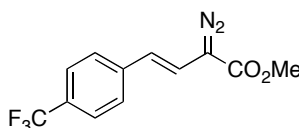
Prepared by following the general procedure **II** with ethyl diazoacetate (**5**) (122 mg, 1 mmol, 2 equiv.) and 2-methylhex-3-yn-2-ol (**205**) (60 mg, 0.5 mmol) at 0 °C. The crude material was purified on silica gel eluting with pentane/diethyl ether (10:1 to 5:1) to afford compound **211** as clear oil (29 mg, 27% yield). R_f 0.44 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 4.21 (q, $J = 7.2$ Hz, 2H), 4.20 (s, 2H), 2.19 (q, $J = 7.6$ Hz, 2H), 1.46 (s, 6H), 1.28 (t, $J = 7.2$ Hz, 3H), 1.12 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.2 (C), 87.2 (C), 80.7 (C), 71.9 (C), 62.9 (CH_2), 60.9 (CH_2), 29.2 (CH_3), 14.4 (CH_3), 14.1 (CH_3), 12.5 (CH_2); IR (neat): 2981, 1761, 1732, 1378, 1251, 1186, 1152, 1115, 1034 cm^{-1} .

Dimethyl 2-hydroxy-2-(5-methylhexa-3,4-dien-3-yl)malonate (212)



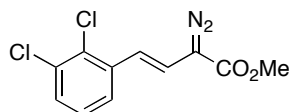
Prepared by following the general procedure **II** with methyl diazomalonate (**128**) (170 mg, 1 mmol, 2 equiv., dissolved with 1 mL of toluene and 8 mL of pentane) and 2-methylhex-3-yn-2-ol (**205**) (61 mg, 0.5 mmol) at 0 °C. The crude material was purified on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) to afford compound **212** as clear oil (79 mg, 59% yield). R_f 0.14 (pentane/diethyl ether 3:1). ^1H NMR (400 MHz, CDCl_3): δ 3.81 (s, 6H), 3.76 (s, 1H), 2.03 (q, $J = 7.2$ Hz, 2H), 1.71 (s, 6H), 0.98 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 199.7 (C), 170.5 (C), 104.0 (C), 101.8 (C), 81.9 (C), 53.4 (CH_3), 20.7 (CH_2), 20.3 (CH_3), 12.4 (CH_3); IR (neat): 3481, 1736, 1436, 1249, 1222, 1116, 1086, 1022 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{12}\text{H}_{18}\text{O}_5$ $[\text{M}+\text{H}]^+$: 243.12270, found: 243.12264.

(E)-Methyl 2-diazo-4-(4-(trifluoromethyl)phenyl)but-3-enoate (214)

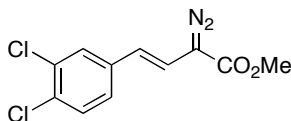


Prepared by following the procedure of Davies.³⁷ This compound was made available by Dr James R. Manning.¹⁰⁴

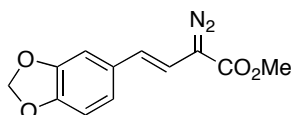
(E)-Methyl 2-diazo-4-(2,3-dichlorophenyl)but-3-enoate (215)



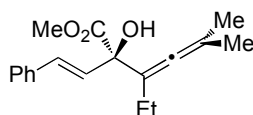
Prepared by following the procedure of Davies.³⁷ This compound was made available by Dr James R. Manning.¹⁰⁴

(E)-Methyl 2-diazo-4-(3,4-dichlorophenyl)but-3-enoate (216)

Prepared by following the procedure of Davies.³⁷ This compound was made available by Dr James R. Manning.¹⁰⁴

(E)-Methyl 4-(benzo[d][1,3]dioxol-5-yl)-2-diazobut-3-enoate (217)

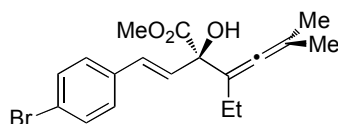
Prepared by following the procedure of Davies.³⁷ This compound was made available by Dr James R. Manning.¹⁰⁴

(R, E)-Methyl 3-ethyl-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (213)

Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (209 mg, 1 mmol, 2 equiv.) and 2-methylhex-3-yn-2-ol (**205**) (56 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **213** as clear oil (106 mg, 74% yield). $[\alpha]_D^{20} +59.9^\circ$ (c 1.0, CHCl_3). R_f , 0.28 (pentane/diethyl ether 5:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.41 (d, $J = 7.6$ Hz, 2H), 7.33 (t, $J = 7.6$ Hz, 2H), 7.25 (t, $J = 7.6$ Hz, 1H), 6.86 (d, $J = 15.6$ Hz, 1H),

6.45 (d, $J = 15.6$ Hz, 1H), 3.79 (s, 3H), 3.56 (s, 1H), 2.13–2.03 (m, 1H), 2.01–1.91 (m, 1H), 1.76 (s, 3H), 1.72 (s, 3H), 0.97 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 199.1 (C), 175.1 (C), 137.0 (C), 129.9 (CH), 128.8 (CH), 128.7 (CH), 127.8 (CH), 126.9 (CH), 107.4 (C), 101.0 (C), 79.3 (C), 53.3 (CH_3), 20.7 (CH_3), 20.6 (CH_2), 20.5 (CH_3), 12.6 (CH_3); IR (neat): 3507, 1731, 1448, 1435, 1247, 1128, 971, 751, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{18}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 269.1536, found: 269.1531. HPLC analysis: 96% ee, CHIRALPAK AD-H, 1.0% isopropanol/hexanes, 0.6 mL/min. UV 254 nm. t_{R} : 20.4 min (major), 23.9 min (minor).

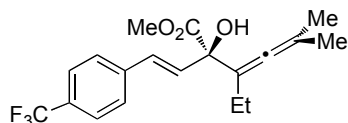
(*R, E*)-Methyl 2-(4-bromostyryl)-3-ethyl-2-hydroxy-5-methylhexa-3,4-dienoate (218**)**



Prepared by following the general procedure **II** with methyl *p*-bromophenylvinyl diazoacetate (**121**) (281 mg, 1 mmol, 2 equiv.) and 2-methylhex-3-yn-2-ol (**205**) (58 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **218** as clear oil (153 mg, 81% yield). $[\alpha]_{\text{D}}^{20} +63.8^\circ$ (c 1.0, CHCl_3). R_f 0.25 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.40 (d, $J = 8.8$ Hz, 2H), 7.23 (d, $J = 8.8$ Hz, 2H), 6.76 (d, $J = 16.0$ Hz, 1H), 6.40 (d, $J = 16.0$ Hz, 1H), 3.75 (s, 3H), 3.53 (s, 1H), 2.06–1.97 (m, 1H), 1.95–1.86 (m, 1H), 1.71 (s, 3H), 1.67 (s, 3H), 0.92 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 199.0 (C), 174.8 (C), 135.9 (C), 131.8 (CH), 129.5 (CH), 128.7 (CH), 128.4 (CH), 121.5 (C), 107.3 (C), 101.1 (C), 79.2 (C), 53.3 (CH_3), 20.6 (CH_3), 20.5

(CH₂), 12.5 (CH₃); IR (neat): 3504, 1730, 1487, 1435, 1243, 1128, 1072, 1008, 972, 810, 742 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₈H₂₁O₃Br [M+H-H₂O]⁺: 347.0641, found: 347.0640. HPLC analysis: 97% ee, (*S,S*)-Whelk O1, 0.5% isopropanol/hexanes, 0.7 mL/min. UV 254nm. *t*_R: 15.0 min (major), 17.7 min (minor).

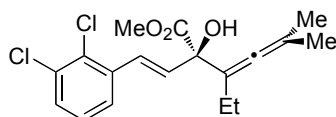
(*R,E*)-Methyl 3-ethyl-2-hydroxy-5-methyl-2-(4-(trifluoromethyl)styryl)hexa-3,4-dienoate (219)



Prepared by following the general procedure **II** with vinyl diazoacetate **214** (356 mg, 1 mmol, 2 equiv.) and 2-methylhex-3-yn-2-ol (**205**) (58 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **219** as clear oil (155 mg, 85% yield). [α]_D²⁰ +46.6° (*c* 1.0, CHCl₃). *R*_f 0.25 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 16.0 Hz, 1H), 6.55 (d, *J* = 16.0 Hz, 1H), 3.80 (s, 3H), 3.61 (s, 1H), 2.11–2.01 (m, 1H), 2.00 (m, 1H), 1.96 (m, 1H), 1.76 (s, 3H), 1.71 (s, 3H), 0.97 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 199.1 (C), 174.8 (C), 140.5 (C), 131.4 (CH), 129.6 (C, q, ²*J*_{CF} = 31.9 Hz), 128.6 (CH), 127.0 (CH), 125.7 (CH, q, ³*J*_{CF} = 3.8 Hz), 107.2 (C), 101.3 (C), 79.2 (C), 53.4 (CH₃), 20.6 (CH₃), 20.5 (CH₂), 12.5 (CH₃); IR (neat): 3504, 1732, 1615, 1437, 1322, 1247, 1162, 1121, 1105, 1067, 822 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₉H₂₁O₃F₃ [M+H-H₂O]⁺: 337.14099, found: 337.14099. Anal. Calcd for C₁₉H₂₁F₃O₃: C, 64.40; H, 5.97. Found: C, 64.30, H,

5.85. HPLC analysis: 96% ee, CHIRALCEL OD-H, 0.5% isoprpanol/hexanes, 0.8mL/min. UV 254 nm. t_R : 8.5 min (major), 9.5 min (minor).

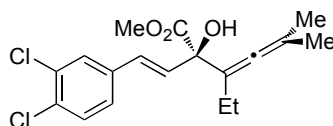
(*R, E*)-Methyl 2-(2,3-dichlorostyryl)-3-ethyl-2-hydroxy-5-methylhexa-3,4-dienoate (220)



Prepared by following the general procedure **II** with vinyl diazoacetate **215** (273 mg, 1 mmol, 2 equiv., dissolved with 2 mL of toluene and 8 mL of pentane) and 2-methylhex-3-yn-2-ol (**205**) (60 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **220** as white solid (155 mg, 81% yield). M.p.: 95–96 °C. $[\alpha]_D^{20} +31.8^\circ$ (c 1.0, CHCl₃). R_f 0.43 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.40 (dd, J = 7.6, 1.6 Hz, 1H), 7.34 (dd, J = 7.6, 1.6 Hz, 1H), 7.23 (d, J = 16.0 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H), 6.43 (d, J = 16.0 Hz, 1H), 3.79 (s, 3H), 3.62 (s, 1H), 2.11–2.02 (m, 1H), 2.00–1.91 (m, 1H), 1.75 (s, 3H), 1.71 (s, 3H), 0.97 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 199.1 (C), 174.6 (C), 137.7 (C), 133.5 (C), 132.9 (CH), 131.7 (C), 129.4 (CH), 127.2 (CH), 126.6 (CH), 125.5 (CH), 107.2 (C), 101.1 (C), 79.3 (C), 53.3 (CH₃), 20.6 (CH₃), 20.6 (CH₃), 20.4 (CH₂), 12.5 (CH₃); IR (neat): 3484, 1730, 1449, 1266, 1253, 1238, 1181, 1157, 1128, 1042, 974, 963, 775 cm⁻¹; HRMS (+APCI) m/z : calcd for C₁₈H₂₀O₃Cl₂ [M+H-H₂O]⁺: 337.07566, found: 337.07569. HPLC analysis: 85 %ee, (*S*,

S)-Whelk O1, 0.5% isoprpanol/hexanes, 0.7 mL/min. UV 254nm. t_R : 17.1 min (major), 19.5 min (minor).

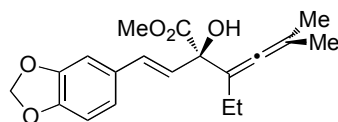
(*R*, *E*)-Methyl 2-(3,4-dichlorostyryl)-3-ethyl-2-hydroxy-5-methylhexa-3,4-dienoate (221)



Prepared by following the general procedure with **II** vinyl diazoacetate **216** (272 mg, 1 mmol, 2 equiv., dissolved with 3 mL of toluene and 7 mL of pentane) and 2-methylhex-3-yn-2-ol (**205**) (59 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **221** as slight yellow solid (143 mg, 77% yield). M.p.: 64–67 °C. $[\alpha]_D^{20} +68.8^\circ$ (c 1.0, CHCl₃). R_f 0.29 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.47 (d, J = 2.0 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.21 (dd, J = 8.4, 2.0 Hz, 1H), 6.77 (d, J = 16.0 Hz, 1H), 6.44 (d, J = 16.0 Hz, 1H), 3.80 (s, 3H), 3.55 (s, 1H), 2.08–1.98 (m, 1H), 1.98–1.88 (m, 1H), 1.75 (s, 3H), 1.71 (s, 3H), 0.96 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 199.0 (C), 174.7 (C), 137.1 (C), 132.8 (C), 131.4 (C), 130.8 (CH), 130.6 (CH), 128.4 (CH), 127.7 (CH), 126.2 (CH), 107.2 (C), 101.3 (C), 79.2 (C), 53.4 (CH₃), 20.6 (CH₃), 20.4 (CH₂), 12.5 (CH₃); IR (neat): 3501, 1731, 1472, 1391, 1242, 1131, 1028, 971, 813 cm⁻¹; HRMS (+APCI) m/z : calcd for C₁₈H₂₀O₃Cl₂ [M+H-H₂O]⁺: 337.07566, found: 337.07548. Anal. Calcd for C₁₈H₂₀O₃ Cl₂: C, 60.86; H, 5.67. Found: C, 61.15, H,

5.54. HPLC analysis: 96% ee, (*R, R*)-Whelk O1, 0.5% isopropanol/hexanes, 0.7 mL/min. UV 254nm. t_R : 13.5 min (minor), 14.6 min (major).

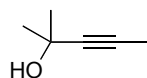
(*R, E*)-Methyl 2-(2-(benzo[d][1,3]dioxol-5-yl)vinyl)-3-ethyl-2-hydroxy-5-methylhexa-3,4-dienoate (222)



Prepared by following the general procedure **II** with vinyl diazoacetate **217** (247 mg, 1 mmol, 2 equiv., dissolved with 7 mL of toluene and 4 mL of pentane) and 2-methylhex-3-yn-2-ol (**205**) (58 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **222** as clear oil (59 mg, 34% yield). $[\alpha]_D^{20} +69.3^\circ$ (c 1.0, CHCl_3). R_f 0.20 (pentane/diethyl ether 5:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.94 (d, $J = 1.6$ Hz, 1H), 6.84 (dd, $J = 8.0, 1.6$ Hz, 1H), 6.77–6.74 (m, 2H), 6.27 (d, $J = 15.6$ Hz, 1H), 5.96 (s, 2H), 3.78 (s, 3H), 3.53 (s, 1H), 2.08–2.01 (m, 1H), 1.98–1.89 (m, 1H), 1.74 (s, 3H), 1.71 (s, 3H), 0.96 (t, $J = 7.6$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 198.9 (C), 175.1 (C), 148.2 (C), 147.4 (C), 131.4 (C), 129.4 (CH), 126.9 (CH), 121.6 (CH), 108.5 (CH), 107.5 (C), 106.1 (CH), 101.2 (CH_2), 101.0 (C), 79.2 (C), 53.3 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 20.5 (CH_2), 12.6 (CH_3); IR (neat): 3501, 1731, 1504, 1490, 1445, 1249, 1232, 1037, 970, 930, 804 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{19}\text{H}_{22}\text{O}_5$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 313.14344, found: 313.14325. Anal. Calcd for $\text{C}_{19}\text{H}_{22}\text{O}_5$: C, 69.07; H, 6.71. Found: C, 68.88, H, 6.71.

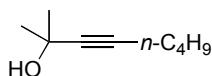
HPLC analysis: 92% ee, (*R, R*)-Whelk O1, 1.0% isopropanol/hexanes, 0.8 mL/min. UV 254nm. t_R : 15.9 min (minor), 17.2 min (major).

2-Methylpent-3-yn-2-ol (**223**)



Acetone (1.0 mL, 13.2 mmol) in 10 mL of THF was slowly added to the 1-propynylmagnesium bromide solution (0.5 M in THF, 52 mL, 25.9 mmol, 1.9 equiv.) at 0 °C. After addition, the solution was stirred 30 min at 0 °C, and 1 h at room temperature. Then it was cooled to 0 °C, and quenched with aqueous saturated NH_4Cl . The mixture was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over MgSO_4 , filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (2:1 to 1:1) to afford compound **223** as slightly yellow oil (1.1 g, 83% yield). ^1H NMR (400 MHz, CDCl_3): δ 1.93 (s, 1H), 1.82 (s, 3H), 1.49 (s, 6H).

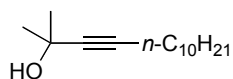
2-Methyloct-3-yn-2-ol (**224**)



Prepared by following the general procedure **I** with 1-hexyne (1.0 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **224** as clear oil (1.3 g, 75% yield). ^1H NMR (600 MHz, CDCl_3): δ 2.19 (t, $J = 7.2$ Hz, 2H), 1.87 (d, $J = 4.8$ Hz, 1H), 1.50 (s,

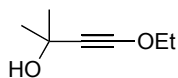
6H), 1.47–1.46 (m, 2H), 1.44–1.38 (m, 2H), 0.92 (t, $J = 7.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 85.4 (C), 82.4 (C), 65.2 (C), 31.8 (CH_3), 30.9 (CH_2), 22.0 (CH_2), 18.4 (CH_2), 13.7 (CH_3); IR (neat): 3354, 2979, 2959, 1458, 1362, 1239, 1164, 945 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_9\text{H}_{16}\text{O}$ $[\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}]^+$: 183.17434, found: 183.17445.

2-Methyltetradec-3-yn-2-ol (225)



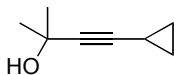
Prepared by following the general procedure **I** with 1-dodecyne (2.0 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **225** as clear oil (2.0 g, 74% yield). ^1H NMR (600 MHz, CDCl_3): δ 2.18 (t, $J = 7.2$ Hz, 2H), 1.86 (s, 1H), 1.50 (s, 6H), 1.38–1.27 (m, 16H), 0.89 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 85.3 (C), 82.7 (C), 65.4 (C), 32.1 (CH_2), 31.9 (CH_3), 31.9 (CH_3), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 22.8 (CH_2), 18.7 (CH_2), 14.2 (CH_3); IR (neat): 3350, 2923, 2854, 1459, 1362, 1239, 1164, 947 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{15}\text{H}_{28}\text{O}$ $[\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}]^+$: 267.26824, found: 267.26841.

4-Ethoxy-2-methylbut-3-yn-2-ol (226)



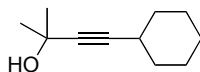
Prepared by following the general procedure **I** with ethyl ethynyl ether (1.7 g, 50% wt in hexanes). The crude product was used for the carbenoid reaction without further purification. ^1H NMR (400 MHz, CDCl_3): δ 4.07 (q, $J = 7.2$ Hz, 2H), 1.50 (s, 6H), 1.36 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 91.4, 74.4, 65.1, 43.5, 32.4, 14.3; IR (neat): 3385, 2979, 2259, 1376, 1167, 1113, 995, 951, 870 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_7\text{H}_{12}\text{O}_2$ $[\text{M}+\text{H}]^+$: 129.09101, found: 129.09107.

4-Cyclopropyl-2-methylbut-3-yn-2-ol (**227**)



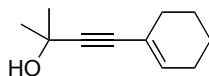
Prepared by following the general procedure **I** with cyclopropylacetylene (1.6 g, 23.8 mmol, 1.0 equiv.), *n*-butyl lithium (2.5 M in hexanes, 10.6 mL, 26.4 mmol, 1.1 equiv.), and acetone (2.0 mL, 26.4 mmol, 1.1 equiv.). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) to afford compound **227** as clear oil (2.8 g, 92% yield). ^1H NMR (400 MHz, CDCl_3): δ 1.87 (s, 1H), 1.48 (s, 6H), 1.27–1.20 (m, 1H), 0.78–0.74 (m, 2H), 0.68–0.64 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 85.5 (C), 80.6 (C), 65.2 (C), 31.8 (CH_2), 8.2 (CH_2), -0.6 (C); IR (neat): 3351, 1361, 1246, 1162, 1029, 998, 946, 877, 813 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_8\text{H}_{12}\text{O}$ $[\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}]^+$: 167.14304, found: 167.14316.

4-Cyclohexyl-2-methylbut-3-yn-2-ol (**228**)

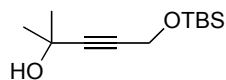


Prepared by following the general procedure **I** with cyclohexylacetylene (1.3 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (6:1) to afford compound **228** as clear oil (1.6 g, 80% yield). ^1H NMR (400 MHz, CDCl_3): δ 2.40–2.32 (m, 1H), 1.87 (s, 1H), 1.78–1.64 (m, 4H), 1.56–1.50 (m, 1H), 1.50 (s, 6H), 1.45–1.26 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 86.5 (C), 85.3 (C), 65.2 (C), 32.8 (CH_2), 31.9 (CH_3), 31.9 (CH_3), 28.9 (CH), 26.0 (CH_2), 24.9 (CH_2); IR (neat): 3347, 2928, 2853, 1448, 1361, 1238, 1164, 1142, 946, 867 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{11}\text{H}_{18}\text{O}$ [$\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}$] $^+$: 209.18999, found: 209.19012.

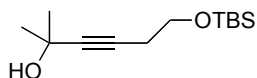
4-(Cyclohex-1-en-1-yl)-2-methylbut-3-yn-2-ol (**229**)



Prepared by following the general procedure **I** with 1-ethynylcyclohexene (1.3 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (4:1) to afford compound **229** as clear oil (1.4 g, 69% yield). ^1H NMR (400 MHz, CDCl_3): δ 6.10–6.08 (m, 1H), 2.14–2.06 (m, 4H), 1.93 (s, 1H), 1.66–1.57 (m, 4H), 1.54 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 135.0 (CH), 120.3 (C), 91.4 (C), 83.9 (C), 65.6 (C), 31.7 (CH_3), 29.4 (CH_2), 25.7 (CH_2), 22.4 (CH_2), 21.6 (CH_2); IR (neat): 3344, 2979, 2929, 1437, 1360, 1272, 1247, 1164, 1151, 1135, 951, 919, 893, 841 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{11}\text{H}_{16}\text{O}$ [$\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}$] $^+$: 207.17434, found: 207.17448.

5-((*tert*-Butyldimethylsilyl)oxy)-2-methylpent-3-yn-2-ol (230)

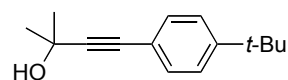
Prepared by following the general procedure **I** with *tert*-butyldimethyl(prop-2-yn-1-yloxy)silane (2.0 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1 to 3:1) to afford compound **230** as clear oil (2.2 g, 80% yield). ^1H NMR (400 MHz, CDCl_3): δ 4.34 (s, 2H), 1.89 (s, 1H), 1.52 (s, 6H), 0.92 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 89.7 (C), 80.9 (C), 65.2 (C), 51.9 (CH_2), 31.5 (CH_3), 26.0 (CH_3), 18.4 (C), -4.9 (CH_3); IR (neat): 3363, 2931, 2859, 1363, 1254, 1097, 836, 778 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{12}\text{H}_{24}\text{O}_2\text{Si}$ $[\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}]^+$: 271.20879, found: 271.20895.

6-((*tert*-Butyldimethylsilyl)oxy)-2-methylhex-3-yn-2-ol (231)

Prepared by following the general procedure **I** with (but-3-yn-1-yloxy)(*tert*-butyl)dimethylsilane (2.2 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **231** as clear oil (2.3 g, 81% yield). ^1H NMR (600 MHz, CDCl_3): δ 3.70 (t, $J = 6.6$ Hz, 2H), 2.41 (t, $J = 6.6$ Hz, 2H), 1.86 (s, 1H), 1.50 (s, 6H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 86.4 (C), 79.4 (C), 65.2 (C), 62.0 (CH_2), 31.8 (CH_3), 31.8 (CH_3), 26.0 (CH_3), 23.1 (CH_2), 18.4 (C), -5.1 (CH_3); IR (neat): 3365, 2955, 2930, 1254,

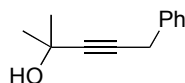
1107, 837, 776 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{13}\text{H}_{26}\text{O}_2\text{Si}$ $[\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}]^+$: 285.22444, found: 285.22461.

4-(4-(*tert*-Butyl)phenyl)-2-methylbut-3-yn-2-ol (**233**)

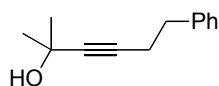


Prepared by following the general procedure **I** with 4-*t*-butylphenylacetylene (1.9 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **233** as white solid (2.0 g, 79% yield). ^1H NMR (600 MHz, CDCl_3): δ 7.36 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.4$ Hz, 2H), 2.09 (s, 1H), 1.62 (s, 6H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 151.6 (C), 131.5 (CH), 125.4 (CH), 119.9 (C), 93.3 (C), 82.4 (C), 65.8 (C), 34.9 (C), 37.7 (CH_3), 31.3 (CH_3); IR (neat): 3334, 2959, 1508, 1465, 1363, 1265, 1159, 1146, 959, 904, 836 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{15}\text{H}_{20}\text{O}$ $[\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}]^+$: 259.20564, found: 259.20580.

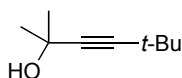
2-Methyl-5-phenylpent-3-yn-2-ol (**234**)



Prepared by following the general procedure **I** with 3-phenyl-1-propyne (1.4 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) to afford compound **234** as yellow oil (1.5 g, 72% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.34–7.32 (m, 5H), 3.63 (s, 2H), 1.56 (s, 6H).

2-Methyl-6-phenylhex-3-yn-2-ol (235)

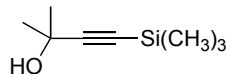
Prepared by following the general procedure **I** with 4-phenyl-1-butyne (1.5 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (4:1 to 3:1) to afford compound **235** as clear oil (1.4 g, 65% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.31 (t, $J = 7.6$ Hz, 2H), 7.24–7.22 (m, 3H), 2.82 (t, $J = 7.6$ Hz, 2H), 2.48 (t, $J = 7.6$ Hz, 2H), 1.83 (s, 1H), 1.48 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 140.7 (C), 128.6 (CH), 128.4 (CH), 126.3 (CH), 86.2 (C), 81.7 (C), 65.2 (C), 35.2 (CH_2), 31.7 (CH_3), 31.7 (CH_3), 20.9 (CH_2); IR (neat): 3362, 1454, 1362, 1238, 1163, 949, 748, 698 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{13}\text{H}_{16}\text{O}$ [$\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}$] $^+$: 231.17434, found: 231.17451.

2,5,5-Trimethylhex-3-yn-2-ol (236)

Prepared by following the general procedure **I** with 3,3-dimethylbutyne (1.0 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **236** as clear oil (1.2 g, 69% yield). ^1H NMR (400 MHz, CDCl_3): δ 1.85 (br., 1H), 1.49 (s, 6H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 90.9 (C), 83.7 (C), 65.3 (C), 32.0 (CH_3), 31.2 (CH_3), 27.3 (C); IR (neat):

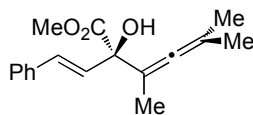
3286, 2970, 1361, 1276, 1164, 1146, 942, 858 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_9\text{H}_{16}\text{O}$ $[\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}]^+$: 183.17434, found: 183.17445.

2-Methyl-4-(trimethylsilyl)but-3-yn-2-ol (237)



Prepared by following the general procedure **I** with trimethylsilylacetylene (1.2 g, 11.9 mmol). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (6:1) to afford compound **237** as white solid (1.6 g, 86% yield). ^1H NMR (400 MHz, CDCl_3): δ 1.95 (s, 1H), 1.52 (s, 6H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 110.8, 86.1, 65.5, 31.6, 0.1; IR (neat): 3269, 2988, 2869, 1251, 1221, 1143, 970, 917, 838, 758 cm^{-1} .

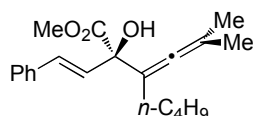
(R, E)-Methyl 2-hydroxy-3,5-dimethyl-2-styrylhexa-3,4-dienoate (238)



Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (212 mg, 1 mmol, 2 equiv.) and 2-methylpent-3-yn-2-ol (**223**) (49 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **238** as clear oil (105 mg, 77% yield). $[\alpha]_D^{20} +59.4^\circ$ (c 1.0, CHCl_3). R_f 0.41 (pentane/diethyl ether 3:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 2H), 7.27–7.23 (m, 1H), 6.87 (d, $J = 16.0$ Hz, 1H), 6.44 (d, $J = 16.0$ Hz, 1H), 3.80 (s, 3H), 3.54 (s, 1H), 1.73 (s, 3H), 1.69 (s, 6H); ^{13}C NMR (100

MHz, CDCl₃): δ 199.5 (C), 175.0 (C), 137.0 (C), 130.0 (CH), 128.7 (CH), 128.4 (CH), 127.8 (CH), 126.8 (CH), 100.1 (C), 98.5 (C), 79.3 (C), 53.3 (CH₃), 20.6 (CH₃), 20.5 (CH₃), 14.4 (CH₃); IR (neat): 3507, 1730, 1436, 1245, 1129, 1070, 971, 752, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₇H₂₀O₃⁺: 255.13796, found: 255.13797. HPLC analysis: 96% ee, CHIRALPAK AD-H, 1.0% isoprpanol/hexanes, 0.6 mL/min. UV 254nm. *t*_R: 27.3 min (major), 37.7 min (minor).

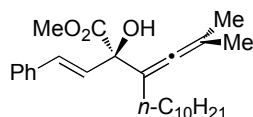
(*R, E*)-Methyl 2-hydroxy-3-(2-methylprop-1-enylidene)-2-styrylheptanoate (239)



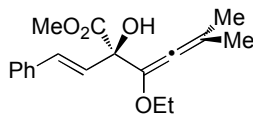
Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (208 mg, 1 mmol, 2 equiv.) and 2-methyloct-3-yn-2-ol (**224**) (71 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **239** as clear oil (136 mg, 86% yield). [α]_D²⁰ +41.3° (*c* 1.0, CHCl₃). *R*_f 0.20 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.27–7.23 (m, 1H), 6.87 (d, *J* = 16.0 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 3.79 (s, 3H), 3.58 (s, 1H), 2.09–1.91 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.42–1.28 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 199.2 (C), 175.1 (C), 137.0 (C), 129.8 (CH), 128.7 (CH), 128.7 (CH), 127.8 (CH), 126.8 (CH), 105.6 (C), 100.4 (C), 79.4 (C), 53.2 (CH₃), 30.2 (CH₂), 26.9 (CH₂), 22.5 (CH₂), 20.6 (CH₃), 20.5 (CH₃), 14.2 (CH₃); IR (neat): 3507, 2853, 2929, 1731, 1448, 1435, 1246, 1129, 1100, 1071, 971, 754, 692 cm⁻¹; HRMS (+ESI) *m/z*: calcd for C₂₀H₂₆O₃

$[M+Na]^+$: 337.17742, found: 377.17754. HPLC analysis: 95% ee, CHIRALPAK AD-H, 0.5% isoprpanol/hexanes, 0.7 mL/min. UV 254nm. t_R : 26.8 min (major), 36.9 min (minor).

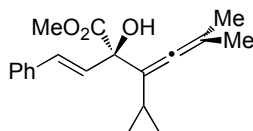
(*R, E*)-Methyl 2-hydroxy-3-(2-methylprop-1-enylidene)-2-styryltridecanoate (240)



Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (207 mg, 1 mmol, 2 equiv.) and 2-methyltetradec-3-yn-2-ol (**225**) (115 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **240** as clear oil (181 mg, 88% yield). $[\alpha]_D^{20} +30.8^\circ$ (c 1.0, $CHCl_3$). R_f , 0.20 (pentane/diethyl ether 10:1). 1H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, $J = 7.2$ Hz, 2H), 7.30 (t, $J = 6.8$ Hz, 2H), 7.25–7.21 (m, 1H), 6.85 (d, $J = 15.6$ Hz, 1H), 6.43 (d, $J = 15.6$ Hz, 1H), 3.76 (s, 3H), 3.54 (s, 1H), 2.06–1.88 (m, 2H), 1.73 (s, 3H), 1.69 (s, 3H), 1.36–1.24 (m, 16H), 0.87 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.2 (C), 175.1 (C), 137.0 (C), 129.8 (CH), 128.7 (CH), 128.7 (CH), 127.8 (CH), 126.9 (CH), 105.6 (C), 100.4 (C), 79.4 (C), 53.2 (CH₃), 32.1 (CH₂), 30.0 (CH₂), 29.8 (CH₂), 29.5 (CH₂), 29.4 (CH₂), 28.1 (CH₂), 27.2 (CH₂), 22.9 (CH₂), 20.6 (CH₃), 20.5 (CH₃), 14.3 (CH₃); IR (neat): 3512, 2923, 2853, 1732, 1448, 1435, 1247, 1130, 1071, 971, 752, 691 cm^{-1} ; HRMS (+ESI) m/z : calcd for $C_{26}H_{38}O_3$ $[M+Na]^+$: 421.27132, found: 421.27150. HPLC analysis: 96% ee, CHIRALPAK AD-H, 0.5% isoprpanol/hexanes, 0.7 mL/min. UV 254nm. t_R : 20.0 min (major), 26.2 min (minor).

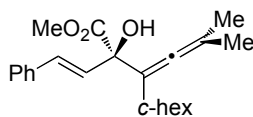
(*R, E*)-Methyl 3-ethoxy-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (241)

Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (205 mg, 1 mmol, 2 equiv.) and 4-ethoxy-2-methylbut-3-yn-2-ol (**226**) (61 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether/triethylamine (5:1:1% to 3:1:1%) to afford compound **241** as clear oil (63 mg, 44% yield). $[\alpha]_D^{20}$ -125.5° (*c* 1.0, CHCl₃). *R_f*, 0.29 (pentane/diethyl ether/triethylamine 3:1:1%). ¹H NMR (400 MHz, CDCl₃): δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.27–7.23 (m, 1H), 6.91 (d, *J* = 16.0 Hz, 1H), 6.35 (d, *J* = 16.0 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 1H), 3.68–3.62 (m, 2H), 1.89 (s, 3H), 1.79 (s, 3H), 1.23 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 186.4 (C), 173.9 (C), 136.9 (C), 130.3 (CH), 130.1 (C), 128.7 (CH), 127.8 (CH), 126.9 (CH), 126.6 (CH), 114.4 (C), 78.1 (C), 64.6 (CH₂), 53.5 (CH₃), 22.9 (CH₃), 22.8 (CH₃), 14.5 (CH₃); IR (neat): 3504, 1736, 1436, 1243, 1173, 1143, 1072, 1056, 970, 760, 737, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₈H₂₂O₄ [M+H-H₂O]⁺: 285.14852, found: 285.14859. HPLC analysis: 95% ee, CHIRALPAK AD-H, 1.2% isopropanol/hexanes, 0.8 mL/min. UV 254nm. *t_R*: 26.4 min (minor), 44.1 min (major).

(*R, E*)-Methyl 3-cyclopropyl-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (242)

Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (207 mg, 1 mmol, 2 equiv.) and 4-cyclopropyl-2-methylbut-3-yn-2-ol (**227**) (63 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **242** as clear oil (91 mg, 60% yield). $[\alpha]_D^{20}$ -15.0° (*c* 1.0, CHCl₃). *R_f* 0.15 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42 (d, *J* = 6.8 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.26–7.23 (m, 1H), 6.90 (d, *J* = 16.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 3.80 (s, 3H), 3.68 (s, 1H), 1.72 (s, 3H), 1.68 (s, 3H), 1.33–1.27 (m, 1H), 0.69–0.66 (m, 2H), 0.40–0.35 (m, 1H), 0.30–0.26 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 197.3 (C), 175.1 (C), 137.0 (C), 129.7 (CH), 128.8 (CH), 128.7 (CH), 127.8 (CH), 126.9 (CH), 109.6 (C), 101.9 (C), 79.2 (C), 53.2 (CH₃), 20.7 (CH₃), 8.7 (CH), 7.9 (CH₂), 7.0 (CH₂); IR (neat): 3507, 1731, 1448, 1435, 1244, 1204, 1120, 1071, 1014, 968, 751, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₉H₂₂O₃ [M+H-H₂O]⁺: 281.15361, found: 281.15330. HPLC analysis: 92% ee, CHIRALCEL OD-H, 0.5% isoprpanol/hexanes, 0.7 mL/min. UV 254nm. *t_R*: 21.0 min (major), 25.9 min (minor).

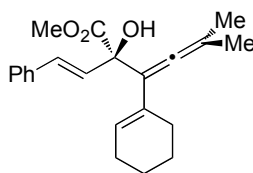
(*R, E*)-Methyl 3-cyclohexyl-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (243)



Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (210 mg, 1 mmol, 2 equiv.) and 4-cyclohexyl-2-methylbut-3-yn-2-ol (**228**) (85 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (15:1 to 10:1) to afford compound **243** as white solid (136 mg, 78%

yield). M.p.: 135–137 °C. $[\alpha]_D^{20} +17.2^\circ$ (*c* 1.0, CHCl₃). *R_f*, 0.19 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.41 (d, *J* = 6.8 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.26–7.23 (m, 1H), 6.86 (d, *J* = 16.0 Hz, 1H), 6.44 (d, *J* = 16.0 Hz, 1H), 3.77 (s, 3H), 3.53 (s, 1H), 1.95–1.89 (m, 1H), 1.80–1.77 (m, 2H), 1.75 (s, 3H), 1.71 (s, 3H), 1.70–1.60 (m, 3H), 1.29–1.05 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ 199.6 (C), 175.2 (C), 137.1 (C), 129.7 (CH), 128.8 (CH), 128.7 (CH), 127.8 (CH), 126.9 (CH), 111.4 (C), 101.0 (C), 79.5 (C), 53.2 (CH₃), 37.2 (CH), 34.6 (CH₂), 24.6 (CH₂), 26.8 (CH₂), 26.8 (CH₂), 26.2 (CH₂), 20.7 (CH₃), 20.6 (CH₃); IR (neat): 3524, 2925, 2849, 1728, 1447, 1249, 1128, 1107, 973, 756, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₂H₂₈O₃ [M+H-H₂O]⁺: 323.20056, found: 323.20068. Anal. Calcd for C₂₂H₂₈O₃: C, 77.61; H, 8.29. Found: C, 77.45, H, 8.23. HPLC analysis: 98% ee, CHIRALCEL OD-H, 0.5% isoprpanol/hexanes, 0.7 mL/min. UV 254nm. *t_R*: 13.6 min (major), 19.0 min (minor).

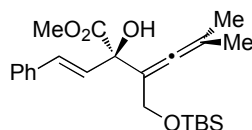
(*R, E*)-Methyl 3-cyclohexenyl-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (244)



Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (212 mg, 1 mmol, 2 equiv.) and 4-cyclohexenyl-2-methylbut-3-yn-2-ol (**229**) (83 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **244** as clear oil (87 mg, 51% yield). $[\alpha]_D^{20} -103.9^\circ$ (*c* 1.0, CHCl₃). *R_f*, 0.43 (pentane/diethyl ether 3:1). ¹H NMR (400 MHz, CDCl₃): δ 7.39 (d, *J* = 6.8 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.27–7.23 (m, 1H), 6.85 (d, *J* = 15.6

Hz, 1H), 6.41 (d, $J = 15.6$ Hz, 1H), 5.94 (m, 1H), 3.78 (s, 3H), 3.66 (s, 1H), 2.10–2.02 (m, 4H), 1.79 (s, 3H), 1.70 (s, 3H), 1.68–1.52 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ 202.7 (C), 175.6 (C), 137.1 (C), 131.0 (C), 130.5 (CH), 129.5 (CH), 128.7 (CH), 127.7 (CH), 126.8 (CH), 125.0 (CH), 124.9 (CH), 108.5 (C), 100.4 (C), 79.0 (C), 53.4 (CH_3), 28.2 (CH_2), 26.0 (CH_2), 23.1 (CH_2), 22.3 (CH_2), 20.5 (CH_3), 20.4 (CH_3); IR (neat): 3501, 2927, 1730, 1447, 1435, 1244, 1131, 1070, 970, 754, 737, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{22}\text{H}_{26}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 321.18491, found: 321.18497. HPLC analysis: 97% ee, CHIRALCEL OD-H, 0.8% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 11.8 min (major), 15.6 min (minor).

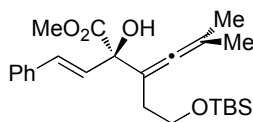
(*R*, *E*)-Methyl 3-((*tert*-butyldimethylsilyloxy)methyl)-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (245**)**



Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (210 mg, 1 mmol, 2 equiv.) and 5-(*tert*-butyldimethylsilyloxy)-2-methylpent-3-yn-2-ol (**230**) (117 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **245** as clear oil (137 mg, 66% yield). $[\alpha]_{\text{D}}^{20} -23.8^\circ$ (c 1.0, CHCl_3). R_f 0.33 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.39 (d, $J = 7.2$ Hz, 2H), 7.32 (t, $J = 6.8$ Hz, 2H), 7.26–7.22 (m, 1H), 6.88 (d, $J = 16.0$ Hz, 1H), 6.44 (d, $J = 16.0$ Hz, 1H), 4.37 (d, $J = 12.4$ Hz, 1H), 4.32 (s, 1H), 4.22 (d, $J = 11.6$ Hz, 1H), 3.78 (s, 3H), 1.79 (s, 3H), 1.71 (s, 3H), 0.91 (s,

9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 199.9 (C), 174.3 (C), 137.0 (C), 129.6 (CH), 129.1 (CH), 128.7 (CH), 127.8 (CH), 126.9 (CH), 104.1 (C), 100.3 (C), 78.4 (C), 62.6 (CH_2), 53.1 (CH_3), 26.0 (CH_3), 20.4 (CH_3), 20.3 (CH_3), 18.5 (C), -5.3 (CH_3), -5.3 (CH_3); IR (neat): 3502, 1733, 1249, 1135, 1071, 1050, 971, 835, 777, 753, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{23}\text{H}_{34}\text{O}_4\text{Si}$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 385.21935, found: 385.21890. HPLC analysis: 90% ee, CHIRALCEL OD-H, 0.5% isoprpanol/hexanes, 0.8 mL/min. UV 254nm. t_{R} : 7.1 min (major), 8.6 min (minor).

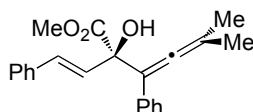
(*R*, *E*)-Methyl 3-(2-(*tert*-butyldimethylsilyloxy)ethyl)-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (246)



Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (208 mg, 1 mmol, 2 equiv.) and 5-(*tert*-butyldimethylsilyloxy)-2-methylpent-3-yn-2-ol (**231**) (124 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **246** as clear oil (179 mg, 84% yield). $[\alpha]_{\text{D}}^{20} +51.0^\circ$ (c 1.0, CHCl_3). R_f , 0.35 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.41 (d, $J = 7.6$ Hz, 2H), 7.32 (t, $J = 7.2$ Hz, 2H), 7.26–7.22 (m, 1H), 6.87 (d, $J = 16.0$ Hz, 1H), 6.45 (d, $J = 16.0$ Hz, 1H), 4.42 (s, 1H), 3.76 (s, 3H), 3.68 (t, $J = 6.8$ Hz, 2H), 2.25 (td, $J = 6.8, 1.4$ Hz, 2H), 1.74 (s, 3H), 1.70 (s, 3H), 0.92 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 200.0 (C), 174.4 (C), 137.0 (C), 129.8 (CH), 129.2 (CH), 128.7 (CH), 127.7 (CH), 126.9 (CH), 102.4 (C), 100.0 (C),

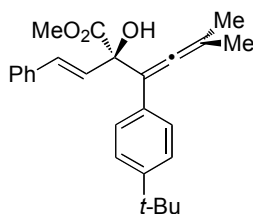
79.1 (C), 66.6 (CH₂), 52.9 (CH₃), 31.2 (CH₂), 26.1 (CH₃), 20.6 (CH₃), 20.5 (CH₃), 18.5 (C), -5.2 (CH₃); IR (neat): 3510, 1732, 1250, 1129, 1092, 971, 834, 775, 752, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₃H₃₄O₄Si [M+H-H₂O]⁺: 399.23555, found: 399.23502. HPLC analysis: 96% ee, CHIRALPAK AD-H, 0.8% isoprpanol/hexanes, 0.8 mL/min. UV 254nm. *t*_R: 12.5 min (major), 14.3 min (minor).

(*R, E*)-Methyl 2-hydroxy-5-methyl-3-phenyl-2-styrylhexa-3,4-dienoate (247)

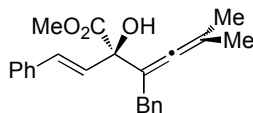


Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (207 mg, 1 mmol, 2 equiv.) and 2-methyl-4-phenylbut-3-yn-2-ol (**232**) (81 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1 to 7:1) to afford compound **247** as white solid (121 mg, 72% yield). M.p.: 126–128 °C. [α]_D²⁰ -55.8° (*c* 1.0, CHCl₃). *R*_f 0.22 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.47–7.44 (m, 2H), 7.41–7.39 (m, 2H), 7.35–7.19 (m, 6H), 3.81 (s, 1H), 3.75 (s, 3H), 1.87 (s, 3H), 1.81 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 203.0 (C), 175.2 (C), 136.8 (C), 135.5 (C), 130.4 (CH), 129.5 (CH), 128.7 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.0 (CH), 126.9 (CH), 106.9 (C), 100.8 (C), 79.4 (C), 53.5 (CH₃), 20.3 (CH₃); IR (neat): 3495, 1729, 1598, 1494, 1447, 1247, 1131, 1071, 971, 751, 693 cm⁻¹; HRMS (+ESI) *m/z*: calcd for C₂₂H₂₂O₃ [M+Na]⁺: 357.14612, found: 357.14629. HPLC analysis: 97% ee, CHIRALCEL OD-H, 1.0% isoprpanol/hexanes, 0.8 mL/min. UV 254nm. *t*_R: 13.9 min (major), 19.6 min (minor).

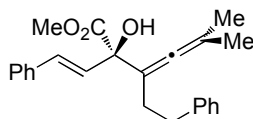
(*R, E*)-Methyl 3-(4-*tert*-butylphenyl)-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (248)



Prepared by following the general procedure **II** with methyl styryldiazoacetate (205 mg, 1 mmol, 2 equiv.) and 4-(4-*tert*-butylphenyl)-2-methylbut-3-yn-2-ol (**233**) (111 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1) to afford compound **248** as white solid (118 mg, 59% yield). M.p.: 108–111 °C. $[\alpha]_D^{20}$ -50.1° (*c* 1.0, CHCl₃). *R_f* 0.33 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.41–7.24 (m, 9H), 6.94 (d, *J* = 15.6 Hz, 1H), 6.51 (d, *J* = 15.6 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 1H), 1.86 (s, 3H), 1.80 (s, 3H), 1.30 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 202.8 (C), 175.2 (C), 149.8 (C), 136.9 (C), 132.2 (C), 130.3 (CH), 129.6 (CH), 128.7 (CH), 127.9 (CH), 127.8 (CH), 126.9 (CH), 125.3 (CH), 106.7 (C), 100.7 (C), 79.4 (C), 53.5 (CH₃), 34.6 (C), 31.5 (CH₃), 20.3 (CH₃); IR (neat): 3501, 2954, 1731, 1447, 1362, 1247, 1131, 1071, 970, 837, 755, 734, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₆H₃₀O₃ [M+H-H₂O]⁺: 373.21621, found: 373.21623. HPLC analysis: 94% ee, CHIRALPAK AD-H, 0.8% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t_R*: 30.0 min (major), 54.6 min (minor).

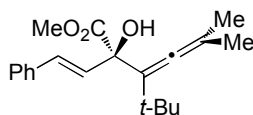
(*R, E*)-Methyl 3-benzyl-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (249)

Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (205 mg, 1 mmol, 2 equiv.) and 2-methyl-5-phenylpent-3-yn-2-ol (**234**) (90 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (10:1 to 5:1) to afford compound **249** as clear oil (79 mg, 44% yield). $[\alpha]_D^{20} +46.9^\circ$ (*c* 1.0, CHCl₃). *R_f*, 0.26 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.39–7.31 (m, 4H), 7.28–7.25 (m, 3H), 7.20–7.18 (m, 3H), 6.90 (d, *J* = 15.6 Hz, 1H), 6.43 (d, *J* = 15.6 Hz, 1H), 3.66 (s, 1H), 3.65 (s, 3H), 3.38 (d, *J* = 2.0 Hz, 2H), 1.66 (s, 3H), 1.61 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 201.1 (C), 174.8 (C), 140.1 (C), 136.9 (C), 130.0 (CH), 129.3 (CH), 128.7 (CH), 128.7 (CH), 128.1 (CH), 127.8 (CH), 126.9 (CH), 126.0 (CH), 105.2 (C), 100.4 (C), 79.0 (C), 53.2 (CH₃), 34.7 (CH₂), 20.2 (CH₃); IR (neat): 3499, 1729, 1494, 1448, 1435, 1247, 1128, 970, 757, 732, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₃H₂₄O₃ [M+H-H₂O]⁺: 331.16926, found: 331.16918. HPLC analysis: 92% ee, CHIRALCEL OD-H, 0.8% isoprpanol/hexanes, 0.8 mL/min. UV 254nm. *t_R*: 15.5 min (major), 19.4 min (minor).

(*R, E*)-Methyl 2-hydroxy-5-methyl-3-phenethyl-2-styrylhexa-3,4-dienoate (250)

Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (204 mg, 1 mmol, 2 equiv.) and 2-methyl-6-phenylhex-3-yn-2-ol (**235**) (99 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **250** as white solid (149 mg, 79% yield). M.p.: 86–89 °C. $[\alpha]_D^{20} +31.0^\circ$ (*c* 1.0, CHCl₃). *R_f*, 0.45 (pentane/diethyl ether 3:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.30–7.25 (m, 3H), 7.21–7.16 (m, 3H), 6.89 (d, *J* = 16.0 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 3.78 (s, 3H), 3.60 (s, 1H), 2.74 (t, *J* = 8.0 Hz, 2H), 2.47–2.29 (m, 2H), 1.72 (s, 3H), 1.69 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 199.4 (C), 174.9 (C), 142.2 (C), 136.9 (C), 130.0 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 127.8 (CH), 126.9 (CH), 125.8 (CH), 105.0 (C), 101.1 (C), 79.4 (C), 53.3 (CH₃), 34.2 (CH₂), 28.7 (CH₂), 20.6 (CH₃), 20.5 (CH₃); IR (neat): 3503, 1729, 1496, 1448, 1435, 1247, 1127, 1071, 1030, 971, 749, 731, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₄H₂₆O₃ [M+H-H₂O]⁺: 345.18491, found: 345.18496. HPLC analysis: 95% ee, CHIRALPAK AD-H, 0.8% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t_R*: 35.4 min (minor), 39.9 min (major).

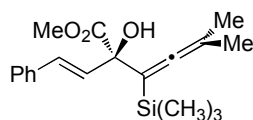
(*R, E*)-Methyl 3-*tert*-butyl-2-hydroxy-5-methyl-2-styrylhexa-3,4-dienoate (251**)**



Prepared by following the general procedure **II** with methyl styryldiazoacetate (211 mg, 1 mmol, 2 equiv.) and 2,5,5-trimethylhex-3-yn-2-ol (**236**) (70 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl

ether (20:1) to afford compound **251** as clear oil (68 mg, 44% yield). $[\alpha]_D^{20}$: -43.8° (c 1.0, CHCl_3). R_f 0.26 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.38 (d, $J = 7.2$ Hz, 2H), 7.32 (t, $J = 7.2$ Hz, 2H), 7.24 (t, $J = 7.2$ Hz, 1H), 6.78 (d, $J = 15.6$ Hz, 1H), 6.45 (d, $J = 15.6$ Hz, 1H), 3.78 (s, 3H), 3.60 (s, 1H), 1.75 (s, 3H), 1.67 (s, 3H), 1.14 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 201.9 (C), 176.2 (C), 137.2 (C), 131.3 (CH), 128.8 (CH), 128.6 (CH), 127.7 (CH), 126.8 (CH), 113.0 (C), 98.7 (C), 79.7 (C), 53.4 (CH_3), 35.5 (C), 31.3 (CH_3), 20.4 (CH_3); IR (neat): 3504, 1728, 1447, 1436, 1362, 1243, 1130, 970, 749, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{20}\text{H}_{26}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 297.18491, found: 297.18490. HPLC analysis: 96% ee, CHIRALCEL OD-H, 0.5% isoprpanol/hexanes, 0.7 mL/min. UV 254nm. t_R : 13.2 min (major), 20.8 min (minor).

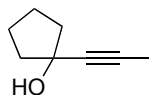
(*S, E*)-Methyl 2-hydroxy-5-methyl-2-styryl-3-(trimethylsilyl)hexa-3,4-dienoate (252)



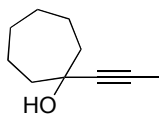
Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (203 mg, 1 mmol, 2 equiv.) and 2-methyl-4-(trimethylsilyl)but-3-yn-2-ol (**237**) (62 mg, 0.5 mmol) at 0°C . The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1) to afford compound **252** as clear oil (48 mg, 37% yield). $[\alpha]_D^{20}$ $+58.9^\circ$ (c 1.0, CHCl_3). R_f 0.23 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.40 (d, $J = 7.6$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 2H), 7.26–7.23 (m, 1H), 6.80 (d, $J = 16.0$ Hz, 1H), 6.44 (d, $J = 16.0$ Hz, 1H), 3.78 (s, 3H), 3.63 (s, 1H), 1.71 (s, 6H), 0.12 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 205.9 (C), 175.3 (C), 137.0 (C), 130.3 (CH), 129.0

(CH), 128.8 (CH), 127.8 (CH), 126.9 (CH), 101.0 (C), 93.2 (C), 79.1 (C), 53.3 (CH₃), 19.8 (CH₃), 19.7 (CH₃), 0.4 (CH₃); IR (neat): 3507, 1727, 1436, 1354, 1245, 1136, 1070, 971, 885, 838, 748, 691 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₉H₂₆O₃Si [M+H-H₂O]⁺: 313.16184, found: 313.16144. HPLC analysis: 94% ee, CHIRALCEL OD-H, 0.3% isoprpanol/hexanes, 0.7 mL/min. UV 254nm. *t*_R: 11.2 min (major), 15.9 min (minor).

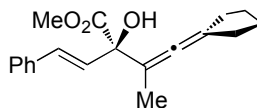
1-(Prop-1-yn-1-yl)cyclopentanol (**253**)



cyclopentanone (1.2 mL, 13.5 mmol, 1 equiv.) in 20 mL of THF was slowly added to the 1-propynylmagnesium bromide solution (0.5 M in THF, 50 mL, 25.0 mmol, 1.9 equiv.) at 0 °C. After addition, the solution was stirred overnight with temperature rising to room temperature. Then it was quenched with aqueous saturated NH₄Cl. The mixture was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over MgSO₄, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) to afford compound **253** as clear oil (1.4 g, 82% yield). ¹H NMR (400 MHz, CDCl₃): δ 1.94–1.90 (m, 4H), 1.83 (s, 3H), 1.82–1.80 (m, 2H), 1.76–1.70 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 83.4 (C), 78.9 (C), 74.6 (C), 42.4 (CH₂), 23.4 (CH₂), 3.5 (CH₃); IR (neat): 3363, 2962, 1222, 992 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₈H₁₂O [M+H-H₂O+iPrOH]⁺: 167.14304, found: 167.14315.

1-(Prop-1-yn-1-yl)cycloheptanol (255)

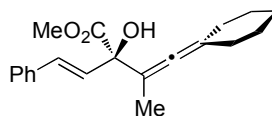
Prepared by following the procedure for compound **253**, using cycloheptanone (1.5 g, 13.0 mmol) as starting material. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) to afford compound **255** as clear oil (1.8 g, 91% yield). ^1H NMR (600 MHz, CDCl_3): δ 2.00–1.96 (m, 2H), 1.85 (s, 3H), 1.82–1.78 (m, 3H), 1.65–1.52 (m, 7H); ^{13}C NMR (100 MHz, CDCl_3): δ 84.4 (C), 79.1 (C), 71.9 (C), 43.4 (CH_2), 28.2 (CH_2), 22.3 (CH_2), 3.6 (CH_3); IR (neat): 3363, 2920, 2856, 1459, 1445, 1022, 997, 952 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{10}\text{H}_{16}\text{O}$ [$\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}$] $^+$: 195.17434. Found: 195.17445.

(*R, E*)-Methyl 4-cyclopentylidene-2-hydroxy-3-methyl-2-styrylbut-3-enoate (256)

Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (209 mg, 1 mmol, 2 equiv.) and 1-(prop-1-ynyl)cyclopentanol (**253**) (67 mg, 0.5 mmol) at 0 $^{\circ}\text{C}$. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1) to afford compound **256** as clear oil (111 mg, 69% yield). $[\alpha]_{\text{D}}^{20} +49.4^{\circ}$ (c 1.0, CHCl_3). R_f 0.29 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 2H), 7.27–7.23 (m, 1H), 6.88 (d, $J = 15.6$ Hz, 1H), 6.46 (d, $J = 15.6$ Hz, 1H), 3.80 (s, 3H), 3.58 (s, 1H), 2.43–2.26 (m, 4H),

1.72 (s, 3H), 1.71–1.63 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ 195.2 (C), 175.0 (C), 136.9 (C), 129.9 (CH), 127.7 (CH), 128.4 (CH), 127.8 (CH), 126.8 (CH), 107.1(C), 102.6 (C), 79.5 (C), 53.3 (CH_3), 31.4 (CH_2), 31.3 (CH_2), 27.3 (CH_2), 27.2 (CH_2), 14.5 (CH_3); IR (neat): 3502, 2951, 1728, 1435, 1245, 1128, 970, 750, 732, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{19}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 281.15361, found: 281.15359. HPLC analysis: 88% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 18.9 min (major), 29.4 min (minor).

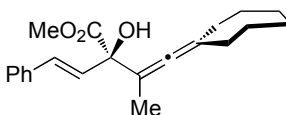
(*R, E*)-Methyl 4-cyclohexylidene-2-hydroxy-3-methyl-2-styrylbut-3-enoate (257)



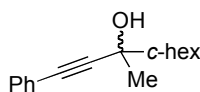
Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (206 mg, 1 mmol, 2 equiv.) and 1-(prop-1-ynyl)cyclohexanol (**254**) (72 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **257** as clear oil (139 mg, 85% yield). $[\alpha]_D^{20} +13.7^\circ$ (c 1.0, CHCl_3). R_f 0.31 (pentane/diethyl ether 7:1). ^1H NMR (400 MHz, CDCl_3): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 2H), 7.27–7.23 (m, 1H), 6.86 (d, $J = 16.0$ Hz, 1H), 6.48 (d, $J = 16.0$ Hz, 1H), 3.82 (s, 3H), 3.56 (s, 1H), 2.20–2.07 (m, 4H), 1.71 (s, 3H), 1.69–1.41 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 196.4 (C), 175.0 (C), 136.8 (C), 129.8 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 126.8 (CH), 105.7(C), 99.8 (C), 79.2 (C), 53.4 (CH_3), 31.5 (CH_2), 27.7 (CH_2), 27.5 (CH_2), 26.2 (CH_2), 14.8 (CH_3); IR (neat): 3508, 2926, 1728, 1435, 1243, 1132, 997, 971, 750, 731, 691 cm^{-1} ; HRMS

(+APCI) m/z : calcd for $C_{20}H_{24}O_3$ $[M+H-H_2O]^+$: 295.16926, found: 295.16892. HPLC analysis: 94% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 17.8 min (major), 22.6 min (minor).

(*R, E*)-Methyl 4-cycloheptylidene-2-hydroxy-3-methyl-2-styrylbut-3-enoate (258)

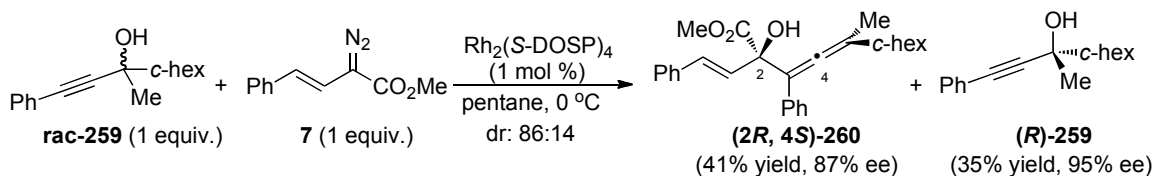


Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (210 mg, 1 mmol, 2 equiv.) and 1-(prop-1-ynyl)cyclohexanol (**254**) (76 mg, 0.5 mmol) at 0 °C. The crude was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (7:1) to afford compound **258** as clear oil (133 mg, 82% yield). $[\alpha]_D^{20}$ -0.2° (c 1.0, $CHCl_3$). R_f 0.33 (pentane/diethyl ether 5:1). 1H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 2H), 7.26–7.22 (m, 1H), 6.87 (d, $J = 16.0$ Hz, 1H), 6.48 (d, $J = 16.0$ Hz, 1H), 3.82 (s, 3H), 3.57 (s, 1H), 2.28 (t, $J = 6.8$ Hz, 2H), 2.20 (t, $J = 6.4$ Hz, 2H), 1.70 (s, 3H), 1.65–1.47 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.0 (C), 175.1 (C), 136.8 (C), 129.8 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 126.8 (CH), 107.7 (C), 99.7 (C), 79.1 (C), 53.4 (CH₃), 32.4 (CH₂), 32.3 (CH₂), 29.6 (CH₂), 29.4 (CH₂), 28.5 (CH₂), 28.4 (CH₂), 14.7 (CH₃); IR (neat): 3508, 2923, 1728, 1435, 1246, 1128, 971, 757, 732, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $C_{21}H_{26}O_3$ $[M+H-H_2O]^+$: 309.18491, found: 309.18488. HPLC analysis: 95% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 18.2 min (major), 22.0 min (minor).

2-Cyclohexyl-4-phenylbut-3-yn-2-ol (259)

Prepared by following the general procedure **I** with phenylacetylene (1.5 g, 15 mmol, 1.0 equiv.), cyclohexyl methyl ketone (2.1 g, 16.5 mmol, 1.1 equiv.), and *n*-butyl lithium (2.5 M in hexanes, 6.6 mL, 16.5 mmol, 1.1 equiv.). The crude product was purified by flash chromatography on silica gel (the column was washed with pentane/diethyl ether 5:1 with 1% triethylamine before loading the sample) eluting with pentane/diethyl ether (5:1) to afford compound **259** as clear oil (2.9 g, 85% yield). ^1H NMR (400 MHz, CDCl_3): δ 7.45–7.42 (m, 2H), 7.33–7.30 (m, 3H), 2.06–1.68 (m, 5H), 2.02 (s, 1H), 1.55 (s, 3H), 1.32–1.15 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 131.8 (CH), 128.4 (CH), 128.3 (CH), 123.1 (C), 92.7 (C), 84.1 (C), 71.7 (C), 49.1 (CH), 28.1 (CH_2), 27.6 (CH_2), 27.5 (CH_3), 27.5 (CH_3) 26.5 (CH_2), 26.4 (CH_2), 26.4 (CH_2); IR (neat): 3381, 2926, 2852, 1489, 1443, 1108, 1067, 928, 754, 690 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{16}\text{H}_{20}\text{O}$ $[\text{M}+\text{H}]^+$: 229.15869, found: 229.15855.

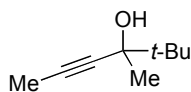
(2R, 4S)-Methyl 5-cyclohexyl-2-hydroxy-3-phenyl-2-styrylhexa-3,4-dienoate (260)
and (R)-2-cyclohexyl-4-phenylbut-3-yn-2-ol ((R)-259)



A solution of $\text{Rh}_2(\text{S-DOSP})_4$ (0.101 g, 0.05 mmol, 1 mol %) and racemic 2-cyclohexyl-4-phenylbut-3-yn-2-ol (**259**) (1.13 g, 5 mmol, 1 equiv.) in 10 mL of degassed pentane was stirred for 10 min at room temperature, then cooled to 0 °C with ice bath under argon. Styryldiazoacetate (**7**) (1.01 g, 5 mmol, 1 equiv.) in 40 mL of degassed pentane was added by syringe pump over 2 h. After addition, the solution was stirred for 2 h with temperature rising to room temperature, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel (the column was washed with pentane/diethyl ether/ triethylamine (20:1:1%) before loading the sample) eluting with pentane/diethyl ether (20:1, 10:1, 5:1, 3:1) to afford pure compound **260** (the absolute stereochemistry was assigned as **(2R, 4S)-260**) (white solid, 0.780 g), the mixture of compound **260** and its minor diastereomer (clear oil, 0.199 g). Combined yield: 0.979 g, 49% yield. **(R)-259** was also isolated in 0.354 g, 31% yield. Compound **260**: M.p.: 78–80 °C. $[\alpha]_D^{20}$ -70.8° (*c* 1.0, CHCl_3). R_f 0.31 (pentane/diethyl ether 5:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.50–7.48 (m, 2H), 7.38 (d, $J = 6.8$ Hz, 2H), 7.34–7.17 (m, 6H), 6.94 (d, $J = 16.0$ Hz, 1H), 6.51 (d, $J = 16.0$ Hz, 1H), 3.82 (s, 1H), 3.76 (s, 3H), 1.94–1.86 (m, 3H), 1.80 (s, 3H), 1.78–1.62 (m, 3H), 1.33–1.15 (m, 5H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 201.9 (C), 175.2 (C), 136.8 (C), 135.5 (C), 130.4 (CH), 129.6 (CH), 128.7 (CH), 128.3 (CH), 128.0 (CH), 127.9 (CH), 126.9 (CH), 126.8 (CH), 110.5 (C), 108.7 (C), 79.5 (C), 53.4 (CH_3), 42.5 (CH), 32.0 (CH_2), 26.7 (CH_2), 26.6 (CH_2), 26.4 (CH_2), 17.2 (CH_3); IR (neat): 3501, 2924, 2850, 1730, 1494, 1447, 1247, 1127, 1068, 969, 908, 750, 731, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{27}\text{H}_{30}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 385.21621, found: 385.21563. HPLC analysis: 87% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 27.4 min (major), 34.5 min (minor). **The minor**

diastereomer: $[\alpha]_D^{20}$: -50.8° (*c* 1.0, CHCl₃).); ¹H NMR (400 MHz, CDCl₃): δ 7.44–7.42 (m, 2H), 7.38–7.33 (m, 2H), 7.33–7.16 (m, 6H), 6.91 (d, *J* = 16.0 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 1H), 1.84 (s, 3H), 1.83–1.57 (m, 5H), 1.22–1.04 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 202.4 (C), 175.3 (C), 136.8 (C), 135.7 (C), 130.2 (CH), 129.9 (CH), 128.7 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 126.9 (CH), 126.8 (CH), 110.5 (C), 108.7 (C), 79.1 (C), 53.5 (CH₃), 42.2 (CH), 31.9 (CH₂), 31.7 (CH₂), 26.6 (CH₂), 26.5 (CH₂), 26.4 (CH₂), 17.1 (CH₃); IR (neat): 3503, 2924, 2851, 1730, 1494, 1447, 1246, 1136, 1069, 970, 753, 693 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₇H₃₀O₃ [M+H-H₂O]⁺: 385.21621, found: 385.21579. HPLC analysis: 88% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t*_R: 41.4 min (minor), 62.9 min (major). **(R)-259:** $[\alpha]_D^{20}$ -6.8° (*c* 1.0, CHCl₃). The ¹H NMR data are identical as racemic **259**. HPLC analysis: 96% ee, CHIRALCEL OD-H, 1.0% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t*_R: 17.8 min (major), 36.9 min (minor).

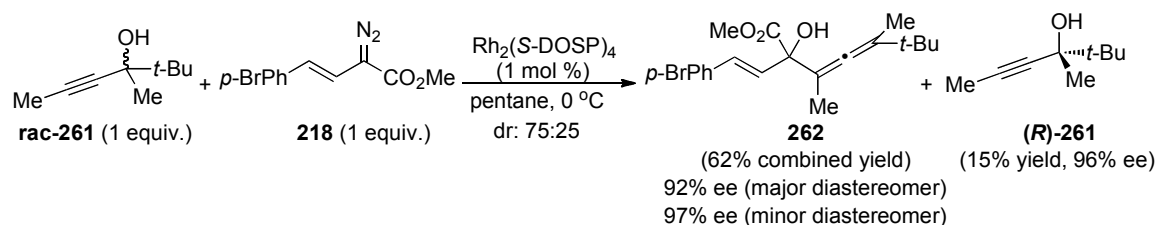
2,2,3-Trimethylhex-4-yn-3-ol (261)



pinacolone (2.6 g, 26.3 mmol, 1 equiv.) in 20 mL of THF was slowly added to the 1-propynylmagnesium bromide solution (0.5 M in THF, 100 mL, 50.0 mmol, 1.9 equiv.) at 0 °C. After addition, the solution was stirred overnight with temperature rising to room temperature. Then it was quenched with aqueous saturated NH₄Cl. The mixture was extracted with diethyl ether (3 x 50 mL). The combined ether solution was washed with brine, dried over MgSO₄, filtered, and concentrated under vacuum. The crude product

was purified by flash chromatography on silica gel (the column was washed with pentane/diethyl ether 20:1 with 1% triethylamine before loading the sample) eluting with pentane/diethyl ether (20:1 to 10:1) to afford compound **261** as clear oil (2.5 g, 68% yield). ^1H NMR (400 MHz, CDCl_3): δ 1.84 (s, 3H), 1.79 (s, 1H), 1.41 (s, 3H), 1.03 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 83.1 (C), 79.6 (C), 74.1 (C), 38.3 (C), 25.3 (CH_3), 25.1 (CH_3), 3.5 (CH_3); IR (neat): 3462, 2959, 1368, 1181, 1084, 997, 908 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_9\text{H}_{16}\text{O}$ [$\text{M}+\text{H}-\text{H}_2\text{O}+i\text{PrOH}$] $^+$: 183.17434, found: 183.17447.

(2*R*, 4*S*)-Methyl 2-hydroxy-3,5,6,6-tetramethyl-2-styrylhepta-3,4-dienoate (262) and (*R*)-2,2,3-trimethylhex-4-yn-3-ol ((*R*)-261)



Prepared by following the procedure for compound **260**, using $\text{Rh}_2(\text{S-DOSP})_4$ (0.103 g, 0.05 mmol, 1 mol %), racemic 2,2,3-trimethylhex-4-yn-3-ol (**261**) (0.702 g, 5 mmol, 1 equiv.), and *p*-bromophenylvinyl diazoacetate (**218**, 1.40 g, 5 mmol, 1 equiv., dissolved in 36 mL of degassed pentane and 4 mL of toluene). The crude material was purified by flash chromatography on silica gel (the column was washed with pentane/diethyl ether/triethylamine (20:1:1%) before loading the sample) eluting with pentane/diethyl ether (10:1) to give pure compound **262** (major diastereomer, clear oil, 0.873 g), mixture of two diastereomers of compound **262** and (*R*)-**261** which was further separated by distillation with Kugelrohr under vacuum to afford diastereomers of compound **262**

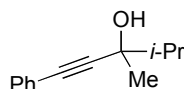
(0.173 g) and pure (**R**)-**261** (0.104 g), pure minor diastereomer of compound **262** (0.184 g, white solid). Combined yield of two diastereomers of **262**: 1.229 g, 62% yield.

Compound **262** (**major diastereomer**): $[\alpha]_D^{20} +52.8^\circ$ (*c* 1.0, CHCl₃). *R_f*, 0.43 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.41 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 16.0 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 3.77 (s, 3H), 3.53 (s, 1H), 1.66 (s, 3H), 1.63 (s, 3H), 1.03 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 198.4 (C), 174.8 (C), 135.8 (C), 131.8 (CH), 129.3 (CH), 128.9 (CH), 128.4 (CH), 121.6 (C), 111.7 (C), 101.2 (C), 79.3 (C), 53.3 (CH₃), 34.3 (C), 29.1 (CH₃), 14.9 (CH₃), 14.6 (CH₃); IR (neat): 3508, 2961, 1732, 1488, 1435, 1360, 1248, 1130, 1073, 1008, 973, 813, 790, 753, 716, 694 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₀H₂₅O₃Br [M+H-H₂O]⁺: 375.09542, found: 375.09577. HPLC analysis: 92% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t_R*: 13.4 min (major), 17.7 min (minor).

Compound **262** (**minor diastereomer**): $[\alpha]_D^{20} -4.0^\circ$ (*c* 1.2, CHCl₃). *R_f*, 0.36 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 16.0 Hz, 1H), 6.41 (d, *J* = 16.0 Hz, 1H), 3.77 (s, 3H), 3.57 (s, 1H), 1.69 (s, 3H), 1.67 (s, 3H), 0.96 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 198.5 (C), 174.7 (C), 135.7 (C), 131.8 (CH), 129.5 (CH), 128.5 (CH), 128.3 (CH), 121.5 (C), 111.7 (C), 101.2 (C), 78.9 (C), 53.4 (CH₃), 34.0 (C), 29.0 (CH₃), 14.8 (CH₃), 14.7 (CH₃); IR (neat): 3508, 2961, 1731, 1488, 1435, 1360, 1244, 1135, 1073, 1008, 972, 813, 790, 753, 717, 665 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₀H₂₅O₃Br [M+H-H₂O]⁺: 375.09542, found: 375.09580. HPLC analysis: 97% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t_R*: 14.6 min (major), 16.7 min (minor).

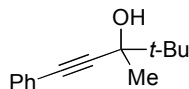
(R)-261: 0.104 g, 15% yield. $[\alpha]_D^{20} +1.9^\circ$ (*c* 6.0, CHCl₃). The ¹H NMR data are identical as racemic **261**. Chiral capillary GC analysis: 96% ee, CHIRALDEX B-PM column, *t*_R: 12.57 min (minor), 12.70 min (major).

3,4-Dimethyl-1-phenylpent-1-yn-3-ol (**263**)



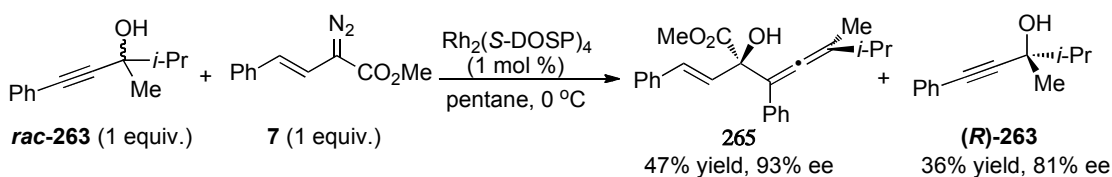
Prepared by following the general procedure **I** with phenylacetylene (1.5 g, 15 mmol, 1.0 equiv.), 3-methyl-2-butanone (1.4 g, 16.5 mmol, 1.1 equiv.), and *n*-butyl lithium (2.5 M in hexanes, 6.6 mL, 16.5 mmol, 1.1 equiv.). The crude product was purified by flash chromatography on silica gel (the column was washed with pentane/diethyl ether 5:1 with 1% triethylamine before loading the sample) eluting with pentane/diethyl ether (5:1) to afford compound **263** as clear oil (2.2 g, 79% yield). ¹H NMR (400 MHz, CDCl₃): δ 7.45–7.42 (m, 2H), 7.32–7.30 (m, 3H), 2.02 (s, 1H), 1.95–1.86 (m, 1H), 1.55 (s, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 131.8 (CH), 128.4 (CH), 128.3 (CH), 123.1 (C), 92.3 (C), 84.1 (C), 72.2 (C), 39.3 (CH), 27.4 (CH₃), 27.4 (CH₃), 18.1 (CH₃), 17.7 (CH₃); IR (neat): 3386, 2965, 1489, 1370, 1142, 1095, 1038, 1027, 921, 870, 754, 690 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₃H₁₆O [M+H-H₂O+i-PrOH]⁺: 231.17434, found: 231.17450.

3,4,4-Trimethyl-1-phenylpent-1-yn-3-ol (**264**)



Prepared by following the general procedure **I** with phenylacetylene (1.5 g, 15 mmol, 1.0 equiv.), pinacolone (1.6 g, 16.5 mmol, 1.1 equiv.), and *n*-butyl lithium (2.5 M in hexanes, 6.6 mL, 16.5 mmol, 1.1 equiv.). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether/triethylamine (10:1:1% to 5:1:1%) to afford compound **264** as clear oil (2.4 g, 80% yield). ¹H NMR (400 MHz, CDCl₃): δ 7.45–7.42 (m, 2H), 7.33–7.30 (m, 3H), 1.98 (s, 1H), 1.55 (s, 3H), 1.13 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 131.7 (CH), 128.4 (CH), 128.2 (CH), 123.2 (C), 93.1 (C), 84.0 (C), 74.5 (C), 38.6 (C), 25.4 (CH₃), 24.9 (CH₃); IR (neat): 3454, 2968, 1449, 1369, 1134, 1070, 1005, 927, 901, 754, 690 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₄H₁₈O [M+H]⁺: 203.14304, found: 203.14323.

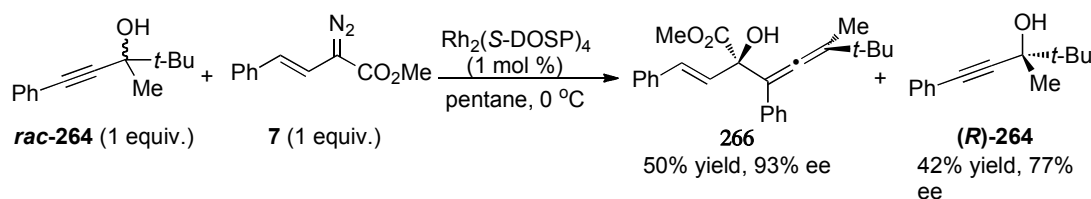
(2*R*, 4*S*)-Methyl 2-hydroxy-5,6-dimethyl-3-phenyl-2-styrylhepta-3,4-dienoate (265)



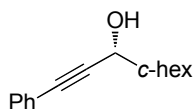
A solution of Rh₂(S-DOSP)₄ (20 mg, 0.01 mmol, 1 mol %) and racemic 3,4-dimethyl-1-phenylpent-1-yn-3-ol (**263**) (186 mg, 1 mmol, 1 equiv.) in 2 mL of degassed pentane was stirred for 10 min at room temperature, then cooled to 0 °C with ice bath under argon. Styryldiazoacetate (**7**) (206 mg, 1 mmol, 1 equiv.) in 9 mL of degassed pentane was added by syringe pump over 1.5 h. After addition, the solution was stirred for 2 h with temperature rising to room temperature, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel (the column was washed with pentane/diethyl ether/ triethylamine (20:1:1%) before loading the sample) eluting with

pentane/diethyl ether (10:1, 7:1, 5:1, 3:1) to afford pure compound **265** (clear oil, 47 mg), mixture of compound **260** and its minor diastereomer (clear oil, 121 mg). Combined yield: 168 mg, 47% yield. (**R**)-**263** was also isolated in 68 mg, 36% yield. Compound **265**: $[\alpha]_D^{20}$ -92.2° (*c* 1.0, CHCl₃). *R_f*, 0.25 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.48–7.45 (m, 2H), 7.39 (d, *J* = 6.8 Hz, 2H), 7.32–7.16 (m, 6H), 6.92 (d, *J* = 15.6 Hz, 1H), 6.49 (d, *J* = 15.6 Hz, 1H), 3.78 (s, 1H), 3.73 (s, 3H), 2.31–2.24 (m, 1H), 1.78 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 201.6 (C), 175.2 (C), 136.8 (C), 135.5 (C), 130.3 (CH), 129.6 (CH), 128.7 (CH), 128.3 (CH), 128.0 (CH), 127.9 (CH), 126.9 (CH), 126.9 (CH), 111.3 (C), 108.9 (C), 79.4 (C), 53.4 (CH₃), 32.9 (CH), 21.5 (CH₃), 17.1 (CH₃); IR (neat): 3500, 2960, 1730, 1494, 1447, 1435, 1246, 1129, 970, 746, 692 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₄H₂₆O₃ [M+H-H₂O]⁺: 345.18407, found: 345.18434. HPLC analysis: 93% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t_R*: 30.0 min (major), 36.9 min (minor). (**R**)-**263**: $[\alpha]_D^{20}$ -17.7° (*c* 2.0, CHCl₃). The ¹H NMR data are identical as racemic **263**. HPLC analysis: 81% ee, CHIRALCEL OD-H, 1.0% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. *t_R*: 19.1 min (major), 33.6 min (minor).

(2R, 4S)-Methyl 2-hydroxy-5,6,6-trimethyl-3-phenyl-2-styrylhepta-3,4-dienoate (266)

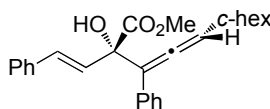


Prepared by following the procedure for compound **265**, using $\text{Rh}_2(\text{S-DOSP})_4$ (19 mg, 0.01 mmol, 1 mol %), racemic 3,4,4-trimethyl-1-phenylpent-1-yn-3-ol (**264**) (206 mg, 1 mmol, 1 equiv.), and styryldiazoacetate (**7**, 209 mg, 1 mmol, 1 equiv.). The crude material was purified by flash chromatography on silica gel (the column was washed with pentane/diethyl ether/ triethylamine (20:1:1%) before loading the sample) eluting with pentane/diethyl ether (7:1 to 5:1) to afford mixture of the two diastereomers of compound **266** and (**R**)-**264** (ratio of **266** and (**R**)-**264**: 1.2:1) (clear oil, 277 mg. calculated yield of **266**: 50% yield, calculated yield of (**R**)-**264**: 42% yield). Further purification was carried out by preparative HPLC. Compound **266**: $[\alpha]_{\text{D}}^{20}$ -98.9° (*c* 1.0, CHCl_3). R_f 0.34 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.49 (d, $J = 6.8$ Hz, 2H), 7.41 (d, $J = 6.8$ Hz, 2H), 7.35–7.20 (m, 6H), 6.94 (d, $J = 15.6$ Hz, 1H), 6.53 (d, $J = 15.6$ Hz, 1H), 3.81 (s, 1H), 3.76 (s, 3H), 1.80 (s, 3H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 201.5 (C), 175.3 (C), 136.8 (C), 136.5 (C), 130.4 (CH), 129.6 (CH), 128.7 (CH), 128.3 (CH), 127.9 (CH), 126.9 (CH), 126.8 (CH), 114.1 (C), 108.0 (C), 79.5 (C), 53.4 (CH_3), 34.8 (C), 29.1 (CH_3), 14.8 (CH_3); IR (neat): 3504, 2962, 1731, 1493, 1447, 1435, 1361, 1247, 1203, 1129, 1069, 967, 767, 739, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{25}\text{H}_{28}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 359.20056, found: 359.20061. HPLC analysis: 93% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_{R} : 25.9 min (major), 30.5 min (minor). (**R**)-**264**: $[\alpha]_{\text{D}}^{20}$ -3.9° (*c* 1.0, CHCl_3). The ^1H NMR data are identical as racemic compound **264**. HPLC analysis: 77% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_{R} : 17.6 min (major), 20.9 min (minor).

(R)-1-Cyclohexyl-3-phenylprop-2-yn-1-ol ((R)-267)

Prepared by following the literature procedure.⁷⁷ To a 50 mL of round bottom flask, was added zinc triflate (1.0 g, 2.7 mmol, 1.1 equiv.) and (+)-N-methylephedrine (0.54 g, 3.0 mmol, 1.2 equiv.). The flask was purged with argon for 15 min, then 7.5 mL of toluene and triethylamine (0.42 mL, 3.0 mmol, 1.2 equiv.) were added. The reaction mixture was stirred for 2 h at room temperature, followed with the addition of phenylacetylene (0.33 mL, 3.0 mmol, 1.2 equiv.). After stirred for 15 min, cyclohexanecarboxaldehyde (0.30 mL, 2.5 mmol, 1.0 equiv.) was added. The reaction mixture was stirred for 2 h, and quenched with aqueous saturated NH₄Cl. It was extracted with diethyl ether (3 x 15 mL). The combined ether solution was washed with brine, dried over MgSO₄, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **(R)-267** as clear oil (0.51 g, 96% yield). ¹H NMR (400 MHz, CDCl₃): δ 7.46–7.44 (m, 2H), 7.34–7.30 (m, 3H), 4.39 (t, *J* = 6.0 Hz, 1H), 1.95–1.63 (m, 6H), 1.32–1.13 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ 131.8 (CH), 128.4 (CH), 122.9 (C), 89.5 (C), 85.8 (C), 67.8 (CH), 44.5 (CH), 28.8 (CH₂), 28.4 (CH₂), 26.6 (CH₂), 26.1 (CH₂); IR (neat): 3339, 2923, 2851, 1489, 1449, 1021, 755, 690 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₅H₁₈O [M+H-H₂O+iPrOH]⁺: 257.18999, found: 257.19016. HPLC analysis: 97% ee, CHIRALCEL OD, 10% isopropanol/hexanes, 0.6 mL/min. UV 254 nm. *t*_R: 10.4 min (major), 22.1 min (minor). Data are consistent with the literature.

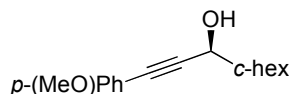
(2*S*, 4*R*)-Methyl 5-cyclohexyl-2-hydroxy-3-phenyl-2-styrylpenta-3,4-dienoate ((2*S*, 4*R*)-268)



Prepared by following the general procedure with **II** methyl styryldiazoacetate (**7**) (209 mg, 1.0 mmol, 2 equiv), (*R*)-1-cyclohexyl-3-phenylprop-2-yn-1-ol (**(R)-267**) (108 mg, 0.5 mmol), and $\text{Rh}_2(\text{R-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol%) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (20:1 to 10:1) to afford compound **(2*S*, 4*R*)-268** as white solid (65 mg, 33% yield). M.p.: 90–92 °C. $[\alpha]_D^{20} +89.1^\circ$ (*c* 1.0, CHCl_3). R_f 0.28 (pentane/diethyl ether 5:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.50–7.48 (m, 2H), 7.41–7.39 (m, 2H), 7.35–7.19 (m, 6H), 6.94 (d, $J = 16.0$ Hz, 1H), 6.52 (d, $J = 16.0$ Hz, 1H), 6.59 (d, $J = 6.0$ Hz, 1H), 3.81 (s, 1H), 3.75 (s, 3H), 2.20–2.10 (m, 1H), 1.88–1.67 (m, 5H), 1.37–1.15 (m, 5H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 203.9 (C), 174.9 (C), 136.7 (C), 134.9 (C), 130.5 (CH), 129.2 (CH), 128.7 (CH), 128.4 (CH), 128.0 (CH), 127.2 (CH), 127.0 (CH), 109.8 (C), 102.3 (CH), 79.1 (C), 53.6 (CH₃), 38.0 (CH), 33.3 (CH₂), 33.1 (CH₂), 26.3 (CH₂), 26.2 (CH₂); IR (neat): 3498, 2923, 2850, 1731, 1494, 1447, 1247, 1129, 1066, 970, 909, 890, 752, 735, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{26}\text{H}_{28}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 371.20056, found: 371.20103. HPLC analysis: >99% ee, CHIRALPAK AD-H, 1.2% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 57.3 min (major), 65.0 min (minor). The O–H insertion products were also isolated and characterized. **1st diastereomer of O–H insertion product**: 15 mg, 8% yield. $[\alpha]_D^{20} -64.6^\circ$ (*c* 0.58, CHCl_3). R_f 0.46 (pentane/diethyl ether 5:1). $^1\text{H NMR}$ (400 MHz, CDCl_3):

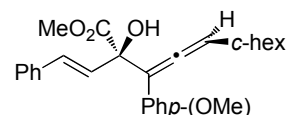
δ 7.46–7.40 (m, 4H), 7.34–7.20 (m, 6H), 6.83 (dd, $J = 1.2, 16.0$ Hz, 1H), 6.32 (dd, $J = 6.4, 16.0$ Hz, 1H), 5.08 (dd, $J = 1.2, 6.4$ Hz, 1H), 4.31 (d, $J = 6.0$ Hz, 1H), 3.80 (s, 3H), 2.02–1.69 (m, 6H), 1.32–1.20 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.7 (C), 136.4 (C), 133.4 (CH), 132.0 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 126.9 (CH), 124.4 (CH), 122.8 (C), 87.6 (C), 86.7 (C), 77.5 (CH), 74.4 (CH), 52.4 (CH_3), 43.1 (CH), 29.3 (CH_2), 28.6 (CH_2), 26.6 (CH_2), 26.2 (CH_2), 26.1 (CH_2); IR (neat): 2925, 2852, 1749, 1489, 1448, 1252, 1198, 1133, 1101, 1071, 1027, 965, 755, 735, 690 cm^{-1} ; HPLC analysis: 97% ee, CHIRALPAK AD-H, 0.7% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_{R} : 10.2 min (major), 13.5 min (minor). **2nd diastereomer of O–H insertion product**: 9 mg, 5% yield. $[\alpha]_{\text{D}}^{20} +254.7^\circ$ (c 0.85, CHCl_3). R_f , 0.40 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.48–7.43 (m, 4H), 7.37–7.29 (m, 6H), 6.82 (d, $J = 16.0$ Hz, 1H), 6.20 (dd, $J = 16.0, 7.6$ Hz, 1H), 4.92 (d, $J = 7.6$ Hz, 1H), 4.22 (d, $J = 6.4$ Hz, 1H), 3.75 (s, 3H), 2.01–1.67 (m, 6H), 1.32–1.14 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.3 (C), 136.0 (C), 125.6 (CH), 132.0 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.5 (CH), 127.0 (CH), 123.8 (CH), 122.9 (C), 87.6 (C), 86.7 (C), 78.2 (CH), 73.5 (CH), 52.5 (CH_3), 42.9 (CH), 29.5 (CH_2), 28.8 (CH_2), 26.6 (CH_2), 26.1 (CH_2); IR (neat): 2925, 2852, 1756, 1489, 1449, 1328, 1263, 1196, 1170, 1071, 1028, 968, 756, 691 cm^{-1} ; HPLC analysis: 97% ee, CHIRALPAK AD-H, 1.2% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_{R} : 20.0 min (major), 43.1 min (minor).

(S)-1-Cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-ol (269)



Prepared by following the procedure for compound **(R)-267**, using (-)-N-methylephedrine (0.54 g, 3.0 mmol, 1.1 equiv.) and 4-ethynylanisole (0.40 mL, 3.0 mmol, 1.2 equiv.). The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (3:1) to afford compound **269** as clear oil (0.61 g, 100% yield). $[\alpha]_D^{20} +9.7^\circ$ (*c* 1.5, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.38 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.37 (t, *J* = 6.0 Hz, 1H), 3.82 (s, 3H), 1.94–1.63 (m, 7H), 1.31–1.12 (m, 5H); ¹³C NMR (100 MHz, CDCl₃): δ 159.6 (C), 133.2 (CH), 115.0 (C), 113.9 (CH), 88.0 (C), 85.5 (C), 67.7 (CH), 55.3 (CH₃), 44.4 (CH), 28.8 (CH₂), 28.3 (CH₂), 26.5 (CH₂), 26.0 (CH₂); IR (neat): 3385, 2924, 2851, 1606, 1508, 1450, 1289, 1245, 1172, 1031, 830 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₆H₂₀O₂ [M+H-H₂O+iPrOH]⁺: 287.20056. Found: 287.20072. HPLC analysis: 86% ee, CHIRALCEL OD-H, 10% isopropanol/hexanes, 0.6 mL/min. UV 254 nm. *t*_R: 12.1 min (minor), 33.5 min (maor).

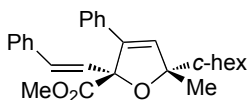
(2R, 4S)-Methyl 5-cyclohexyl-2-hydroxy-3-(4-methoxyphenyl)-2-styrylpenta-3,4-dienoate (270)



Prepared by following the general procedure **II** with methyl styryldiazoacetate (**7**) (206 mg, 1.0 mmol, 2 equiv.), (*S*)-1-cyclohexyl-3-(4-methoxyphenyl)prop-2-yn-1-ol (**269**) (127 mg, 0.5 mmol), and Rh₂(*S*-DOSP)₄ (10 mg, 0.005 mmol, 1 mol%) at 0 °C. The crude was purified on silica gel eluting with pentane/diethyl ether (10:1 to 5:1) to afford compound **270** as clear oil (105 mg, 48% yield). $[\alpha]_D^{20} -82.2^\circ$ (*c* 1.0, CHCl₃). *R*_f 0.33

(pentane/diethyl ether 3:1). ^1H NMR (400 MHz, CDCl_3): δ 7.43–7.39 (m, 4H), 7.33 (t, J = 8.0 Hz, 2H), 7.27–7.23 (m, 1H), 6.92 (d, J = 16.0 Hz, 1H), 6.82 (d, J = 8.8 Hz, 2H), 6.51 (d, J = 16.0 Hz, 1H), 5.55 (d, J = 6.0 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 1H), 3.75 (s, 3H), 2.20–2.18 (m, 1H), 1.90–1.64 (m, 5H), 1.36–1.10 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 203.4 (C), 175.0 (C), 158.8 (C), 136.7 (C), 130.5 (CH), 129.3 (CH), 129.2 (CH), 128.8 (CH), 128.0 (CH), 127.1 (C), 127.0 (CH), 113.8 (CH), 109.3 (C), 102.1 (CH), 79.3 (C), 55.4 (CH_3), 53.5 (CH_3), 38.0 (CH), 33.3 (CH_2), 33.1 (CH_2), 26.3 (CH_2), 26.3 (CH_2); IR (neat): 3491, 2923, 2849, 1731, 1605, 1509, 1448, 1245, 1178, 1131, 1031, 971, 933, 736, 693 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{27}\text{H}_{30}\text{O}_4$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 401.21112, found: 401.21104. HPLC analysis: 99% ee, CHIRALPAK AD-H, 3.0% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_{R} : 53.8 min (minor), 72.0 min (major).

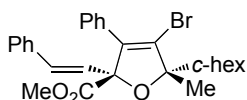
(2*R*, 5*S*)-Methyl 5-cyclohexyl-5-methyl-3-phenyl-2-styryl-2,5-dihydrofuran-2-carboxylate (271)



To the solution of **(2*R*, 4*S*)-260** (99% ee) (54 mg, 0.13 mmol) in 2.5 mL of acetone/ H_2O (4:1), was added AgNO_3 (25 mg, 0.14 mmol, 1.1 equiv.) and CaCO_3 (26 mg, 0.26 mmol, 2.0 equiv.) at room temperature. The reaction mixture was stirred in the dark for 24 h, then concentrated under vacuum. The residue was extracted with dichloromethane (3 x 15 mL). The combined dichloromethane solution was passed through a short celite pad, dried over MgSO_4 , filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1 to

10:1) to afford compound **271** as clear oil (52 mg, 95% yield). $[\alpha]_D^{20}$ -17.1° (c 1.0, CHCl_3). R_f 0.28 (pentane/diethyl ether 10:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.45–7.42 (m, 2H), 7.39–7.29 (m, 7H), 7.26–7.23 (m, 1H), 6.77 (d, $J = 15.6$ Hz, 1H), 6.69 (d, $J = 15.6$ Hz, 1H), 6.30 (s, 1H), 3.76 (s, 3H), 2.02–1.60 (m, 6H), 1.49 (s, 3H), 1.29–1.09 (s, 5H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 172.9 (C), 139.3 (C), 137.0 (C), 133.0 (C), 132.9 (CH), 132.8 (CH), 131.6 (CH), 128.7 (CH), 128.6 (CH), 128.1 (CH), 128.0 (CH), 127.6 (CH), 127.0 (CH), 93.9 (C), 92.0 (C), 52.8 (CH_3), 48.4 (CH), 28.9 (CH_2), 28.3 (CH_2), 26.8 (CH_2), 26.7 (CH_2), 22.8 (CH_3); IR (neat): 2926, 2851, 1733, 1447, 1243, 1159, 1070, 1036, 967, 912, 745, 691 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{27}\text{H}_{30}\text{O}_3$ $[\text{M}+\text{H}]^+$: 403.22677, found: 403.22727. HPLC analysis: 99% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 14.8 min (minor), 16.9 min (major).

(2R, 5S)-Methyl 4-bromo-5-cyclohexyl-5-methyl-3-phenyl-2-styryl-2,5-dihydrofuran-2-carboxylate (272)



(2R, 4S)-260 (99% ee) (51 mg, 0.13 mmol) and NBS (24 mg, 0.13 mmol) was dissolved with 2.0 mL of acetonitrile and 0.14 mL of H_2O . The solution was stirred for 3 h at room temperature, then quenched with 0.5 mL of aqueous NaHCO_3 , and concentrated under vacuum. The residue was extracted with dichloromethane (3 x 15 mL). The combined dichloromethane solution was washed with brine, dried over MgSO_4 , filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (30:1 to 20:1) to afford compound **272** as

clear oil (42 mg, 69% yield). $[\alpha]_D^{20} +0.7^\circ$ (c 1.0, CHCl_3). R_f 0.38 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.45–7.25 (m, 10H), 6.92 (d, $J = 16.0$ Hz, 1H), 6.38 (d, $J = 16.0$ Hz, 1H), 3.73 (s, 3H), 2.08 (d, $J = 12.8$ Hz, 1H), 1.93 (d, $J = 12.8$ Hz, 1H), 1.79–1.60 (m, 4H), 1.67 (s, 3H), 1.56–1.46 (m, 1H), 1.37–1.16 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.6 (C), 137.3 (C), 136.6 (C), 132.8 (C), 131.1 (CH), 129.4 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.1 (CH), 127.0 (CH), 126.7 (C), 126.0 (CH), 94.4 (C), 92.3 (C), 52.7 (CH_3), 45.0 (CH), 27.7 (CH_2), 27.0 (CH_2), 26.8 (CH_2), 26.7 (CH_2), 26.5 (CH_2), 23.4 (CH_3); IR (neat): 2930, 2851, 1735, 1492, 1448, 1237, 1160, 1069, 1022, 987, 972, 907, 747, 731, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{27}\text{H}_{29}\text{O}_3\text{Br}$ $[\text{M}+\text{H}]^+$: 481.13728, found: 481.13811. HPLC analysis: 99% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.8 mL/min. UV 254 nm. t_R : 9.3 min (minor), 10.5 min (major).

2.4.6 Synthetic procedures and characterization for Chapter 2.2.6

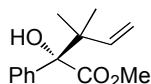
2.4.6.1 General procedure of the $\text{Rh}_2(\text{S-DOSP})_4$ -catalyzed tandem ylide formation/[1,2]-Stevens rearrangement of donor/acceptor carbenoid with tertiary alcohol:

A solution of $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol %) and tertiary alcohol (0.5 mmol) in 1 mL of degassed pentane was cooled to 0 °C with ice bath under argon. Diazo (1.0 mmol, 2 equiv.) in 9 mL of degassed pentane was added by syringe pump over 1.5 h. After addition, the solution was stirred for 2 h with temperature rising to room

temperature, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel.

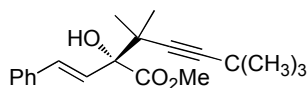
2.4.6.2 Characterization of Chapter 2.2.6

(*S*)-Methyl 2-hydroxy-3,3-dimethyl-2-phenylpent-4-enoate (**276**)



Isolated as byproduct from the synthesis of compound **114**. Compound **276**: clear oil, 13 mg, 10% yield. R_f 0.36 (pentane/diethyl ether 10:1). ^1H NMR (400 MHz, CDCl_3): δ 7.70 (dd, $J = 7.2, 1.2$ Hz, 2H), 7.34–7.27 (m, 3H), 6.07 (dd, $J = 17.6, 10.8$ Hz, 1H), 5.04 (d, $J = 10.8$ Hz, 1H), 4.97 (d, $J = 17.6$ Hz, 1H), 3.85 (s, 3H), 3.71 (s, 1H), 1.11 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.6 (C), 144.2 (CH), 138.7 (C), 127.8 (CH), 127.7 (CH), 127.4 (CH), 113.6 (CH_2), 82.9 (C), 53.1 (CH_3), 45.1 (C), 23.0 (CH_3), 22.7 (CH_3); IR (neat): 3502, 1719, 1447, 1435, 1250, 1162, 1101, 1067, 916, 743, 702 cm^{-1} ; HRMS (+ESI) m/z : calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{NH}_4]^+$: 252.15942, found: 252.15966. HPLC analysis: 66% ee, (*S, S*)-Whelk-O1, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, t_R : 10.7 min (major), 12.9 min (minor).

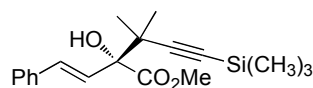
(*R, E*)-Methyl 2-hydroxy-3,3,6,6-tetramethyl-2-styrylhept-4-ynoate (**277**)



Isolated as byproduct from the synthesis of compound **251**. Compound **277**: clear oil, 21 mg, 13% yield. $[\alpha]_D^{20} +12.5^\circ$ (c 1.0, CHCl_3). R_f 0.33 (pentane/diethyl ether 10:1). ^1H

NMR (400 MHz, CDCl₃): δ 7.44 (d, $J = 7.2$ Hz, 2H), 7.34 (t, $J = 8.0$ Hz, 2H), 7.27–7.24 (m, 1H), 6.87 (d, $J = 16.0$ Hz, 1H), 6.68 (d, $J = 16.0$ Hz, 1H), 3.84 (s, 3H), 3.63 (s, 1H), 1.27 (s, 3H), 1.23 (s, 9H), 1.19 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 174.8 (C), 136.9 (C), 131.2 (CH), 128.8 (CH), 127.9 (CH), 126.9 (CH), 91.3 (C), 82.9 (C), 81.2 (C), 53.0 (CH₃), 39.5 (C), 31.4 (CH₃), 27.5 (C), 25.3 (CH₃), 24.8 (CH₃); IR (neat): 3509, 2969, 1724, 1448, 1436, 1361, 1285, 1256, 1220, 1205, 1161, 1141, 975, 756, 741, 692 cm⁻¹; HRMS (+APCI) m/z : calcd for C₂₀H₂₆O₃ [M+H-H₂O]⁺: 297.18491, found: 297.18491. HPLC analysis: 92% ee, CHIRALPAK AD-H, 0.5% isopropanol/hexanes, 0.7 mL/min, UV 254 nm, t_R : 15.2 min (minor), 22.4 min (major).

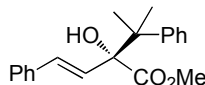
(*R, E*)-Methyl 2-hydroxy-3,3-dimethyl-2-styryl-5-(trimethylsilyl)pent-4-ynoate (278)



Isolated as byproduct from the synthesis of compound **252**. Compound **278**: clear oil, 24 mg, 18% yield. $[\alpha]_D^{20} +15.9^\circ$ (c 1.0, CHCl₃). R_f 0.29 (pentane/diethyl ether 10:1). ¹H NMR (400 MHz, CDCl₃): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.34 (t, $J = 7.6$ Hz, 2H), 7.32–7.26 (m, 1H), 6.88 (d, $J = 16.0$ Hz, 1H), 6.67 (d, $J = 16.0$ Hz, 1H), 3.85 (s, 3H), 3.68 (s, 1H), 1.30 (s, 3H), 1.23 (s, 3H), 0.19 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 174.6 (C), 136.8 (C), 131.5 (CH), 128.8 (CH), 127.9 (CH), 126.9 (CH), 126.6 (CH), 111.3 (C), 86.6 (C), 80.9 (C), 53.1 (CH₃), 40.4 (C), 25.0 (CH₃), 24.4 (CH₃), 0.34 (CH₃); IR (neat): 3508, 2160, 1725, 1249, 1161, 1142, 974, 871, 840, 758, 693 cm⁻¹; HRMS (+APCI) m/z : calcd for C₁₉H₂₆O₃Si [M+H-H₂O]⁺: 313.16184, found: 313.16189. HPLC analysis: 88% ee,

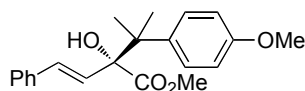
CHIRALPAK AD-H, 0.3% isopropanol/hexanes, 0.7 mL/min, UV 254 nm, t_R : 14.4 min (minor), 18.5 min (major).

(*R, E*)-Methyl 2-hydroxy-4-phenyl-2-(2-phenylpropan-2-yl)but-3-enoate (281**)**



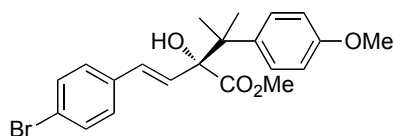
Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (177 mg, 1.0 mmol), 2-phenylpropan-2-ol (**279**) (69 mg, 1.2 mmol, 1.2 equiv.), and $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol%) at $^\circ\text{C}$. The crude material was purified on silica gel eluting with pentane/diethyl ether (10:1 to 5:1) to afford Compound **281** as white solid (33 mg, 21% yield). M.p.: 95–98 $^\circ\text{C}$. $[\alpha]_D^{20}$ -34.3 $^\circ$ (c 1.0, CHCl_3). R_f 0.52 (pentane/diethyl ether 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.45–7.42 (m, 4H), 7.38–7.24 (m, 6H), 6.87 (d, J = 16.0 Hz, 1H), 6.57 (d, J = 16.0 Hz, 1H), 3.65 (s, 3H), 3.37 (s, 1H), 1.62 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.7 (C), 144.7 (C), 137.0 (C), 131.4 (CH), 128.8 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.1 (CH), 126.9 (CH), 126.8 (CH), 82.3 (C), 52.9 (CH_3), 46.4 (C), 24.8 (CH_3), 23.8 (CH_3); IR (neat): 3509, 1723, 1447, 1435, 1241, 1163, 1134, 1103, 1072, 1032, 975, 776, 755, 734, 692 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{20}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 293.15361, found: 293.15363. HPLC analysis: 88% ee, CHIRALPAK AD-H, 1.0% isopropanol/hexanes, 0.8 mL/min, UV 254 nm, t_R : 19.0 min (minor), 21.4 min (major).

(*R, E*)-Methyl 2-hydroxy-2-(2-(4-methoxyphenyl)propan-2-yl)-4-phenylbut-3-enoate
(282)

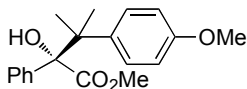


Prepared by following the general procedure with methyl styryldiazoacetate (**7**) (210 mg, 1.0 mmol), 2-(4-methoxyphenyl)propan-2-ol (**280**) (83 mg, 0.5 mmol), and $\text{Rh}_2(\text{S-DOSP})_4$ (10 mg, 0.005 mmol, 1 mol%) at 0 °C. The crude material was purified on silica gel eluting with pentane/diethyl ether (4:1) to afford compound **282** as slight yellow solid (82 mg, 48% yield). M.p.: 78–81 °C. $[\alpha]_D^{20}$ -33.1° (c 1.0, CHCl_3). R_f , 0.36 (pentane/diethyl ether 3:1). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.45–7.37 (m, 2H), 7.37–7.33 (m, 4H), 7.29–7.25 (m, 1H), 6.87–6.83 (m, 3H), 6.56 (d, $J = 15.6$ Hz, 1H), 3.82 (s, 3H), 3.68 (s, 3H), 3.36 (s, 1H), 1.59 (s, 3H), 1.45 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 174.8 (C), 158.3 (C), 137.0 (C), 136.8 (C), 131.3 (CH), 128.8 (CH), 128.7 (CH), 127.9 (CH), 127.3 (CH), 126.9 (CH), 113.0 (CH), 82.4 (C), 55.3 (CH_3), 52.9 (CH_3), 45.9 (C), 25.0 (CH_3), 24.1 (CH_3); IR (neat): 3507, 1725, 1513, 1248, 1187, 1165, 1137, 1035, 977, 832, 749, 693 cm^{-1} ; HRMS (+APCI) m/z : calcd for $\text{C}_{21}\text{H}_{24}\text{O}_4$ $[\text{M}+\text{H}-\text{H}_2\text{O}]^+$: 323.16417, found: 323.16424. HPLC analysis: 94% ee, CHIRALPAK AD-H, 1.0% isopropanol/hexanes, 0.6 mL/min, UV 254 nm, t_R : 54.3 min (minor), 69.8 min (major).

(*R*, *E*)-Methyl 4-(4-bromophenyl)-2-hydroxy-2-(2-(4-methoxyphenyl)propan-2-yl)but-3-enoate (283**)**



Prepared by following the general procedure with methyl *p*-bromophenylvinylidiazooacetate (**218**) (282 mg, 1.0 mmol), 2-(4-methoxyphenyl)propan-2-ol (**280**) (81 mg, 0.5 mmol), and Rh₂(*S*-DOSP)₄ (10 mg, 0.005 mmol, 1 mol%) at 0 °C. The crude material was purified on silica gel eluting with pentane/diethyl ether (5:1) to afford compound **283** as white solid (83 mg, 40% yield). M. p.: 127–128 °C. $[\alpha]_D^{20}$ -23.4° (*c* 1.0, CHCl₃). *R*_f 0.49 (pentane/diethyl ether 3:1). ¹H NMR (400 MHz, CDCl₃): δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.33–7.27 (m, 4H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 16.0 Hz, 1H), 6.54 (d, *J* = 16.0 Hz, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 3.36 (s, 1H), 1.57 (s, 3H), 1.43 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 174.5 (C), 158.3 (C), 136.6 (C), 135.9 (C), 131.9 (CH), 130.2 (CH), 128.7 (CH), 128.4 (CH), 128.1 (CH), 121.6 (C), 113.1 (CH), 82.3 (C), 55.3 (CH₃), 52.9 (CH₃), 45.9 (C), 25.0 (CH₃), 24.0 (CH₃); IR (neat): 3505, 1727, 1513, 1487, 1249, 1187, 1137, 1098, 1072, 1036, 1009, 978, 832 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₂₁H₂₃O₄Br [M+H-H₂O]⁺: 401.07468, found: 401.07467. HPLC analysis: 87% ee, CHIRALPAK AD-H, 1.5% isopropanol/hexanes, 0.8 mL/min, UV 254 nm, *t*_R: 27.5 min (major), 32.0 min (minor).

(R)-Methyl 2-hydroxy-3-(4-methoxyphenyl)-3-methyl-2-phenylbutanoate (284)

Prepared by following the general procedure with methyl phenyldiazoacetate (**6**) (182 mg, 1.0 mmol), 2-(4-methoxyphenyl)propan-2-ol (**280**) (86 mg, 0.5 mmol), and Rh₂(S-DOSP)₄ (10 mg, 0.005 mmol, 1 mol%) at 0 °C. The crude material was purified on silica gel eluting with pentane/diethyl ether (10:1) to afford pure compound **284** as clear oil (94 mg) and a mixture of **284** and the O-H insertion product (51 mg). Combined yield: 145 mg, 89% yield. Compound **284**: $[\alpha]_D^{20}$ -14.5° (*c* 1.0, CHCl₃). *R_f* 0.32 (pentane/diethyl ether 5:1). ¹H NMR (400 MHz, CDCl₃): δ 7.69–7.66 (m, 2H), 7.31–7.24 (m, 5H), 6.78 (d, *J* = 8.8 Hz), 3.79 (s, 3H), 3.66 (s, 3H), 3.58 (s, 1H), 1.48 (s, 3H), 1.33 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 174.2 (C), 158.2 (C), 138.8 (C), 137.0 (C), 129.4 (CH), 127.9 (CH), 127.8 (CH), 127.3 (CH), 112.7 (CH), 83.3 (C), 55.3 (CH₃), 52.9 (CH₃), 45.7 (C), 25.4 (CH₃), 24.6 (CH₃); IR (neat): 3498, 1717, 1512, 1246, 1187, 1065, 1035, 831, 735, 703 cm⁻¹; HRMS (+APCI) *m/z*: calcd for C₁₉H₂₂O₄ [M+Na]⁺: 337.14103, found: 337.14084. HPLC analysis: 87% ee, CHIRALPAK AD-H, 1.0% isopropanol/hexanes, 0.7 mL/min, UV 230 nm, *t_R*: 30.5 min (minor), 41.8 min (major).

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APPENDIX

1. Crystal structure of compound 142

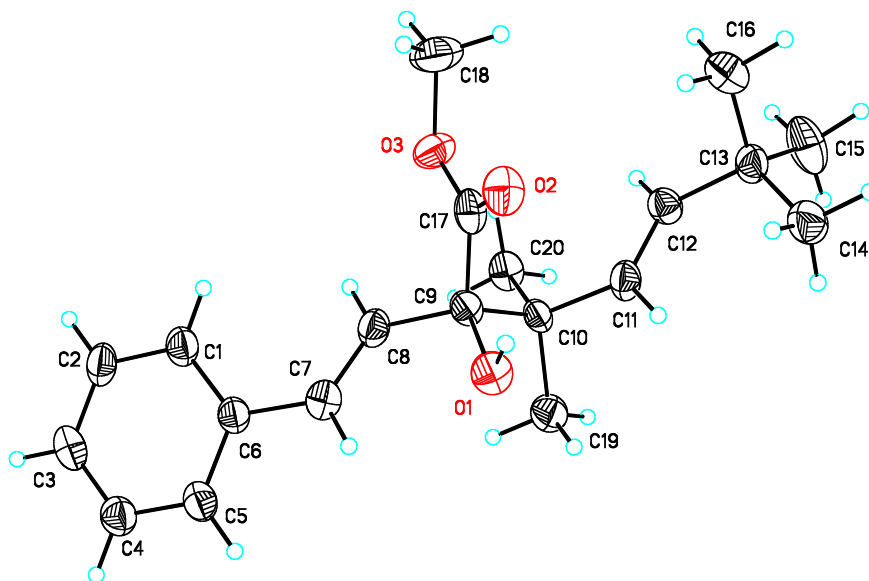
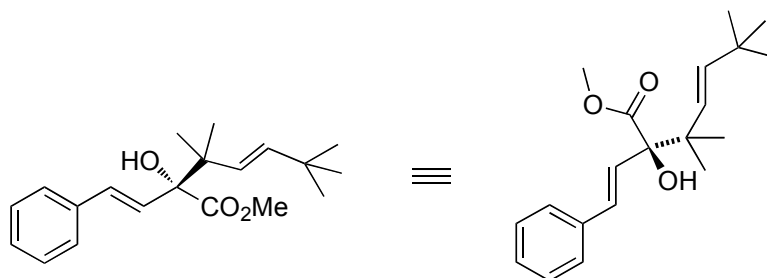


Table 1. Crystal data and structure refinement for compound **142**.

Compound	142	
Empirical formula	$C_{20} H_{28} O_3$	
Formula weight	316.42	
Temperature	172(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	$a = 5.9909(10)$ Å	$\alpha = 90^\circ$.
	$b = 9.1703(13)$ Å	$\beta = 90^\circ$.
	$c = 34.141(5)$ Å	$\gamma = 90^\circ$.
Volume	$1875.7(5)$ Å ³	
Z	4	
Density (calculated)	1.121 Mg/m ³	
Absorption coefficient	0.582 mm ⁻¹	
F(000)	688	
Crystal size	0.23 x 0.05 x 0.05 mm ³	
Theta range for data collection	2.59 to 65.52°.	
Index ranges	-6<=h<=5, -10<=k<=9, -34<=l<=40	
Reflections collected	7161	
Independent reflections	2888 [R(int) = 0.0718]	
Completeness to theta = 65.52°	93.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9715 and 0.8778	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2888 / 0 / 216	
Goodness-of-fit on F ²	1.010	
Final R indices [I>2sigma(I)]	R1 = 0.0545, wR2 = 0.1070	
R indices (all data)	R1 = 0.1525, wR2 = 0.1593	
Absolute structure parameter	0.0(6)	
Extinction coefficient	0.0024(3)	
Largest diff. peak and hole	0.371 and -0.365 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **142**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	5747(8)	-1434(5)	1768(2)	43(1)
C(2)	7071(9)	-2490(5)	1947(2)	47(2)
C(3)	6310(9)	-3238(6)	2271(2)	47(2)
C(4)	4214(9)	-2936(6)	2413(2)	45(1)
C(5)	2879(9)	-1886(5)	2240(1)	42(1)
C(6)	3614(8)	-1121(5)	1914(2)	36(1)
C(7)	2153(9)	-17(6)	1735(2)	40(1)
C(8)	2849(8)	1075(5)	1507(2)	39(1)
C(9)	1373(7)	2169(6)	1309(1)	35(1)
C(10)	1615(7)	3755(5)	1481(1)	32(1)
C(11)	359(8)	4785(5)	1221(2)	40(1)
C(12)	1232(9)	5813(5)	983(1)	38(1)
C(13)	-9(8)	6743(5)	694(2)	40(1)
C(14)	-2546(8)	6604(6)	727(2)	56(2)
C(15)	681(11)	8323(6)	746(2)	71(2)
C(16)	697(10)	6225(7)	288(2)	61(2)
C(17)	1833(9)	2193(6)	867(2)	43(1)
C(18)	4592(9)	2391(7)	371(1)	65(2)
C(19)	514(9)	3770(6)	1893(1)	47(2)
C(20)	4094(7)	4177(5)	1534(2)	41(1)
O(1)	-939(5)	1739(4)	1351(1)	44(1)
O(2)	406(6)	2086(4)	619(1)	50(1)
O(3)	4016(5)	2327(4)	787(1)	46(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound **142**.

C(1)-C(2)	1.394(7)	C(15)-H(15B)	0.9800
C(1)-C(6)	1.401(7)	C(15)-H(15C)	0.9800
C(1)-H(1)	0.9500	C(16)-H(16A)	0.9800
C(2)-C(3)	1.377(7)	C(16)-H(16B)	0.9800
C(2)-H(2)	0.9500	C(16)-H(16C)	0.9800
C(3)-C(4)	1.374(7)	C(17)-O(2)	1.207(6)
C(3)-H(3)	0.9500	C(17)-O(3)	1.341(6)
C(4)-C(5)	1.384(7)	C(18)-O(3)	1.463(5)
C(4)-H(4)	0.9500	C(18)-H(18A)	0.9800
C(5)-C(6)	1.388(6)	C(18)-H(18B)	0.9800
C(5)-H(5)	0.9500	C(18)-H(18C)	0.9800
C(6)-C(7)	1.471(7)	C(19)-H(19A)	0.9800
C(7)-C(8)	1.334(7)	C(19)-H(19B)	0.9800
C(7)-H(7)	0.9500	C(19)-H(19C)	0.9800
C(8)-C(9)	1.500(6)	C(20)-H(20A)	0.9800
C(8)-H(8)	0.9500	C(20)-H(20B)	0.9800
C(9)-O(1)	1.447(5)	C(20)-H(20C)	0.9800
C(9)-C(17)	1.533(7)	O(1)-H(1A)	0.8400
C(9)-C(10)	1.576(7)		
C(10)-C(11)	1.500(6)	C(2)-C(1)-C(6)	120.3(5)
C(10)-C(20)	1.545(6)	C(2)-C(1)-H(1)	119.9
C(10)-C(19)	1.551(6)	C(6)-C(1)-H(1)	119.9
C(11)-C(12)	1.350(6)	C(3)-C(2)-C(1)	120.7(5)
C(11)-H(11)	0.9500	C(3)-C(2)-H(2)	119.7
C(12)-C(13)	1.500(7)	C(1)-C(2)-H(2)	119.7
C(12)-H(12)	0.9500	C(4)-C(3)-C(2)	119.0(5)
C(13)-C(15)	1.517(7)	C(4)-C(3)-H(3)	120.5
C(13)-C(16)	1.527(7)	C(2)-C(3)-H(3)	120.5
C(13)-C(14)	1.529(7)	C(3)-C(4)-C(5)	121.2(5)
C(14)-H(14A)	0.9800	C(3)-C(4)-H(4)	119.4
C(14)-H(14B)	0.9800	C(5)-C(4)-H(4)	119.4
C(14)-H(14C)	0.9800	C(4)-C(5)-C(6)	120.7(5)
C(15)-H(15A)	0.9800	C(4)-C(5)-H(5)	119.7

C(6)-C(5)-H(5)	119.7	C(13)-C(14)-H(14B)	109.5
C(5)-C(6)-C(1)	118.1(5)	H(14A)-C(14)-H(14B)	109.5
C(5)-C(6)-C(7)	119.5(5)	C(13)-C(14)-H(14C)	109.5
C(1)-C(6)-C(7)	122.4(5)	H(14A)-C(14)-H(14C)	109.5
C(8)-C(7)-C(6)	124.9(5)	H(14B)-C(14)-H(14C)	109.5
C(8)-C(7)-H(7)	117.5	C(13)-C(15)-H(15A)	109.5
C(6)-C(7)-H(7)	117.5	C(13)-C(15)-H(15B)	109.5
C(7)-C(8)-C(9)	125.5(5)	H(15A)-C(15)-H(15B)	109.5
C(7)-C(8)-H(8)	117.2	C(13)-C(15)-H(15C)	109.5
C(9)-C(8)-H(8)	117.2	H(15A)-C(15)-H(15C)	109.5
O(1)-C(9)-C(8)	109.7(4)	H(15B)-C(15)-H(15C)	109.5
O(1)-C(9)-C(17)	105.8(4)	C(13)-C(16)-H(16A)	109.5
C(8)-C(9)-C(17)	110.4(4)	C(13)-C(16)-H(16B)	109.5
O(1)-C(9)-C(10)	107.6(4)	H(16A)-C(16)-H(16B)	109.5
C(8)-C(9)-C(10)	113.2(4)	C(13)-C(16)-H(16C)	109.5
C(17)-C(9)-C(10)	109.7(4)	H(16A)-C(16)-H(16C)	109.5
C(11)-C(10)-C(20)	113.2(4)	H(16B)-C(16)-H(16C)	109.5
C(11)-C(10)-C(19)	108.6(4)	O(2)-C(17)-O(3)	123.8(5)
C(20)-C(10)-C(19)	107.6(4)	O(2)-C(17)-C(9)	124.1(5)
C(11)-C(10)-C(9)	108.2(4)	O(3)-C(17)-C(9)	112.1(4)
C(20)-C(10)-C(9)	111.3(4)	O(3)-C(18)-H(18A)	109.5
C(19)-C(10)-C(9)	107.9(4)	O(3)-C(18)-H(18B)	109.5
C(12)-C(11)-C(10)	127.0(4)	H(18A)-C(18)-H(18B)	109.5
C(12)-C(11)-H(11)	116.5	O(3)-C(18)-H(18C)	109.5
C(10)-C(11)-H(11)	116.5	H(18A)-C(18)-H(18C)	109.5
C(11)-C(12)-C(13)	126.9(5)	H(18B)-C(18)-H(18C)	109.5
C(11)-C(12)-H(12)	116.5	C(10)-C(19)-H(19A)	109.5
C(13)-C(12)-H(12)	116.5	C(10)-C(19)-H(19B)	109.5
C(12)-C(13)-C(15)	109.3(5)	H(19A)-C(19)-H(19B)	109.5
C(12)-C(13)-C(16)	106.5(4)	C(10)-C(19)-H(19C)	109.5
C(15)-C(13)-C(16)	109.2(5)	H(19A)-C(19)-H(19C)	109.5
C(12)-C(13)-C(14)	113.4(5)	H(19B)-C(19)-H(19C)	109.5
C(15)-C(13)-C(14)	109.9(5)	C(10)-C(20)-H(20A)	109.5
C(16)-C(13)-C(14)	108.4(5)	C(10)-C(20)-H(20B)	109.5
C(13)-C(14)-H(14A)	109.5	H(20A)-C(20)-H(20B)	109.5

C(10)-C(20)-H(20C)	109.5	C(9)-O(1)-H(1A)	109.5
H(20A)-C(20)-H(20C)	109.5	C(17)-O(3)-C(18)	115.5(4)
H(20B)-C(20)-H(20C)	109.5		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **142**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	42(3)	31(3)	55(3)	2(3)	1(3)	1(3)
C(2)	42(3)	35(3)	64(4)	0(3)	0(3)	11(3)
C(3)	57(4)	32(3)	52(4)	5(3)	-12(3)	1(3)
C(4)	54(4)	38(3)	43(3)	-1(3)	0(3)	1(3)
C(5)	50(3)	35(3)	41(3)	3(3)	-4(3)	4(3)
C(6)	36(3)	31(3)	42(3)	2(3)	0(3)	2(3)
C(7)	38(3)	38(3)	44(3)	-3(3)	-3(3)	2(3)
C(8)	31(3)	36(3)	49(3)	1(3)	1(3)	6(3)
C(9)	23(3)	36(3)	46(3)	12(3)	-1(2)	-1(2)
C(10)	31(3)	28(3)	39(3)	9(3)	-2(2)	0(2)
C(11)	31(3)	36(3)	54(4)	5(3)	-3(3)	5(3)
C(12)	36(3)	36(3)	43(3)	5(3)	-2(3)	-3(3)
C(13)	40(3)	29(3)	52(3)	5(3)	4(3)	2(3)
C(14)	42(3)	65(4)	60(4)	19(4)	-1(3)	5(3)
C(15)	81(5)	37(3)	95(5)	16(4)	-24(4)	-8(4)
C(16)	72(4)	64(4)	45(3)	12(4)	1(3)	9(4)
C(17)	48(4)	25(3)	55(4)	1(3)	-4(3)	3(3)
C(18)	63(4)	92(5)	40(3)	-1(4)	15(3)	5(4)
C(19)	53(4)	49(4)	38(3)	2(3)	-1(3)	7(3)
C(20)	31(3)	38(3)	55(3)	2(3)	-8(3)	-6(3)
O(1)	28(2)	47(2)	58(2)	4(2)	-6(2)	-7(2)
O(2)	51(2)	46(2)	53(2)	-4(2)	-11(2)	3(2)
O(3)	37(2)	60(3)	40(2)	-3(2)	7(2)	5(2)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **142**.

	x	y	z	U(eq)
H(1)	6294	-923	1545	51
H(2)	8513	-2696	1846	57
H(3)	7221	-3951	2394	57
H(4)	3673	-3458	2634	54
H(5)	1445	-1685	2346	50
H(7)	598	-85	1786	48
H(8)	4413	1166	1467	46
H(11)	-1222	4705	1223	48
H(12)	2797	5964	1000	46
H(14A)	-2994	5605	662	84
H(14B)	-3257	7285	544	84
H(14C)	-3011	6835	995	84
H(15A)	169	8674	1002	106
H(15B)	7	8916	539	106
H(15C)	2310	8399	732	106
H(16A)	2313	6346	258	91
H(16B)	-76	6804	88	91
H(16C)	307	5194	256	91
H(18A)	4025	1518	239	97
H(18B)	6218	2436	343	97
H(18C)	3919	3261	254	97
H(19A)	720	4731	2013	70
H(19B)	1211	3024	2058	70
H(19C)	-1084	3564	1867	70
H(20A)	4855	4128	1280	62
H(20B)	4806	3499	1717	62
H(20C)	4194	5172	1637	62
H(1A)	-1511	1630	1128	66

Table 6. Torsion angles [°] for compound **142**.

C(6)-C(1)-C(2)-C(3)	-0.2(8)
C(1)-C(2)-C(3)-C(4)	0.5(8)
C(2)-C(3)-C(4)-C(5)	-0.8(8)
C(3)-C(4)-C(5)-C(6)	1.0(8)
C(4)-C(5)-C(6)-C(1)	-0.7(7)
C(4)-C(5)-C(6)-C(7)	179.7(5)
C(2)-C(1)-C(6)-C(5)	0.3(7)
C(2)-C(1)-C(6)-C(7)	179.9(5)
C(5)-C(6)-C(7)-C(8)	158.5(5)
C(1)-C(6)-C(7)-C(8)	-21.1(8)
C(6)-C(7)-C(8)-C(9)	177.1(5)
C(7)-C(8)-C(9)-O(1)	-8.8(7)
C(7)-C(8)-C(9)-C(17)	-125.1(5)
C(7)-C(8)-C(9)-C(10)	111.5(5)
O(1)-C(9)-C(10)-C(11)	-67.6(5)
C(8)-C(9)-C(10)-C(11)	170.9(4)
C(17)-C(9)-C(10)-C(11)	47.1(5)
O(1)-C(9)-C(10)-C(20)	167.5(4)
C(8)-C(9)-C(10)-C(20)	46.0(5)
C(17)-C(9)-C(10)-C(20)	-77.8(5)
O(1)-C(9)-C(10)-C(19)	49.7(5)
C(8)-C(9)-C(10)-C(19)	-71.8(5)
C(17)-C(9)-C(10)-C(19)	164.4(4)
C(20)-C(10)-C(11)-C(12)	13.2(7)
C(19)-C(10)-C(11)-C(12)	132.5(5)
C(9)-C(10)-C(11)-C(12)	-110.6(5)
C(10)-C(11)-C(12)-C(13)	173.6(5)
C(11)-C(12)-C(13)-C(15)	131.8(6)
C(11)-C(12)-C(13)-C(16)	-110.4(6)
C(11)-C(12)-C(13)-C(14)	8.7(8)
O(1)-C(9)-C(17)-O(2)	10.0(7)
C(8)-C(9)-C(17)-O(2)	128.7(5)
C(10)-C(9)-C(17)-O(2)	-105.9(6)

O(1)-C(9)-C(17)-O(3)	-169.1(4)
C(8)-C(9)-C(17)-O(3)	-50.4(6)
C(10)-C(9)-C(17)-O(3)	75.0(5)
O(2)-C(17)-O(3)-C(18)	2.2(8)
C(9)-C(17)-O(3)-C(18)	-178.7(5)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound **142** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	\angle (DHA)
O(1)-H(1A)...O(2)	0.84	2.12	2.643(5)	119.8

Symmetry transformations used to generate equivalent atoms:

2. Crystal structure of compound 153

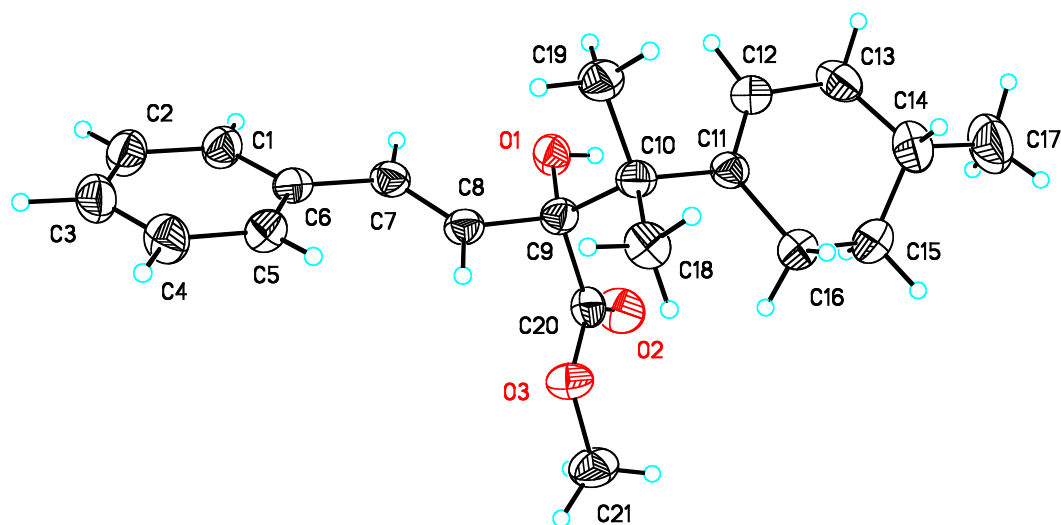
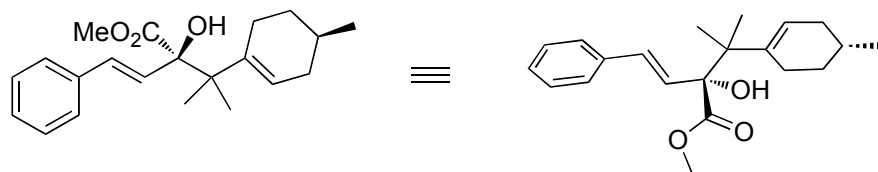


Table 1. Crystal data and structure refinement for compound **153**.

Compound	153	
Empirical formula	C ₂₁ H ₂₈ O ₃	
Formula weight	328.43	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 6.2766(3) Å	α = 90°.
	b = 19.1025(9) Å	β = 98.705(3)°.
	c = 7.8637(4) Å	γ = 90°.
Volume	931.99(8) Å ³	
Z	2	
Density (calculated)	1.170 Mg/m ³	
Absorption coefficient	0.605 mm ⁻¹	
F(000)	356	
Crystal size	0.37 x 0.16 x 0.12 mm ³	
Theta range for data collection	4.63 to 65.42°.	
Index ranges	-6 ≤ h ≤ 6, -21 ≤ k ≤ 20, -8 ≤ l ≤ 9	
Reflections collected	5742	
Independent reflections	2540 [R(int) = 0.0238]	
Completeness to theta = 65.42°	88.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9310 and 0.8072	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2540 / 1 / 329	
Goodness-of-fit on F ²	1.076	
Final R indices [I > 2σ(I)]	R1 = 0.0303, wR2 = 0.0801	
R indices (all data)	R1 = 0.0316, wR2 = 0.0811	
Absolute structure parameter	0.1(2)	
Largest diff. peak and hole	0.169 and -0.148 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **153**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	-6566(4)	-2022(1)	-1379(3)	38(1)
C(2)	-7076(4)	-1315(1)	-1469(3)	43(1)
C(3)	-5660(4)	-845(1)	-2034(2)	43(1)
C(4)	-3750(4)	-1085(1)	-2524(2)	42(1)
C(5)	-3263(4)	-1788(1)	-2443(2)	36(1)
C(6)	-4647(3)	-2272(1)	-1845(2)	31(1)
C(7)	-4158(3)	-3024(1)	-1687(2)	32(1)
C(8)	-2267(3)	-3325(1)	-1734(2)	31(1)
C(9)	-1852(3)	-4102(1)	-1593(2)	31(1)
C(10)	-1136(3)	-4409(1)	-3311(2)	33(1)
C(11)	-729(3)	-5200(1)	-3104(2)	31(1)
C(12)	-2315(4)	-5673(1)	-3472(2)	38(1)
C(13)	-1984(4)	-6451(1)	-3443(3)	45(1)
C(14)	334(4)	-6662(1)	-3334(3)	51(1)
C(15)	1720(4)	-6209(1)	-2039(3)	50(1)
C(16)	1544(4)	-5444(1)	-2534(3)	40(1)
C(17)	698(7)	-7439(2)	-2930(5)	72(1)
C(18)	871(4)	-4041(1)	-3758(3)	38(1)
C(19)	-2991(4)	-4253(1)	-4783(2)	41(1)
C(20)	-137(3)	-4252(1)	-7(2)	32(1)
C(21)	3166(4)	-3890(1)	1626(3)	47(1)
O(1)	-3772(2)	-4436(1)	-1282(2)	37(1)
O(2)	-285(3)	-4719(1)	984(2)	49(1)
O(3)	1494(2)	-3793(1)	152(2)	38(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound **153**.

C(1)-C(2)	1.388(3)	C(15)-H(22)	1.02(3)
C(1)-C(6)	1.395(3)	C(15)-H(23)	1.01(3)
C(1)-H(1)	0.96(3)	C(16)-H(24)	0.97(2)
C(2)-C(3)	1.383(3)	C(16)-H(25)	0.96(3)
C(2)-H(2)	0.95(3)	C(17)-H(18)	0.96(4)
C(3)-C(4)	1.391(3)	C(17)-H(19)	0.90(4)
C(3)-H(3)	1.02(3)	C(17)-H(20)	0.99(5)
C(4)-C(5)	1.376(3)	C(18)-H(12)	0.95(3)
C(4)-H(4)	0.98(3)	C(18)-H(13)	0.93(2)
C(5)-C(6)	1.398(3)	C(18)-H(14)	0.96(3)
C(5)-H(5)	0.90(3)	C(19)-H(9)	0.95(3)
C(6)-C(7)	1.470(3)	C(19)-H(10)	1.00(2)
C(7)-C(8)	1.324(3)	C(19)-H(11)	0.96(2)
C(7)-H(7)	0.92(2)	C(20)-O(2)	1.197(2)
C(8)-C(9)	1.508(2)	C(20)-O(3)	1.338(2)
C(8)-H(8)	0.99(2)	C(21)-O(3)	1.453(2)
C(9)-O(1)	1.417(2)	C(21)-H(26)	0.86(4)
C(9)-C(20)	1.546(3)	C(21)-H(27)	0.95(3)
C(9)-C(10)	1.598(2)	C(21)-H(28)	1.04(3)
C(10)-C(18)	1.529(3)	O(1)-H(10)	0.76(3)
C(10)-C(11)	1.537(3)		
C(10)-C(19)	1.541(3)	C(2)-C(1)-C(6)	121.4(2)
C(11)-C(12)	1.343(3)	C(2)-C(1)-H(1)	116.5(15)
C(11)-C(16)	1.504(3)	C(6)-C(1)-H(1)	121.9(15)
C(12)-C(13)	1.500(3)	C(3)-C(2)-C(1)	119.6(2)
C(12)-H(15)	0.96(2)	C(3)-C(2)-H(2)	121.8(14)
C(13)-C(14)	1.500(4)	C(1)-C(2)-H(2)	118.6(14)
C(13)-H(16)	0.93(3)	C(2)-C(3)-C(4)	119.9(2)
C(13)-H(17)	1.01(3)	C(2)-C(3)-H(3)	115.6(16)
C(14)-C(15)	1.509(3)	C(4)-C(3)-H(3)	124.5(16)
C(14)-C(17)	1.527(4)	C(5)-C(4)-C(3)	120.2(2)
C(14)-H(21)	1.06(2)	C(5)-C(4)-H(4)	121.7(16)
C(15)-C(16)	1.511(3)	C(3)-C(4)-H(4)	118.0(16)

C(4)-C(5)-C(6)	121.1(2)	H(16)-C(13)-H(17)	104(2)
C(4)-C(5)-H(5)	119.5(15)	C(13)-C(14)-C(15)	109.84(19)
C(6)-C(5)-H(5)	119.4(15)	C(13)-C(14)-C(17)	112.7(2)
C(1)-C(6)-C(5)	117.82(18)	C(15)-C(14)-C(17)	111.4(2)
C(1)-C(6)-C(7)	119.31(17)	C(13)-C(14)-H(21)	105.8(13)
C(5)-C(6)-C(7)	122.87(18)	C(15)-C(14)-H(21)	108.1(13)
C(8)-C(7)-C(6)	126.72(18)	C(17)-C(14)-H(21)	108.8(13)
C(8)-C(7)-H(7)	119.2(14)	C(14)-C(15)-C(16)	111.61(18)
C(6)-C(7)-H(7)	114.0(14)	C(14)-C(15)-H(22)	105.4(15)
C(7)-C(8)-C(9)	124.77(17)	C(16)-C(15)-H(22)	111.2(15)
C(7)-C(8)-H(8)	123.6(13)	C(14)-C(15)-H(23)	114.2(16)
C(9)-C(8)-H(8)	111.6(14)	C(16)-C(15)-H(23)	103.2(17)
O(1)-C(9)-C(8)	108.32(16)	H(22)-C(15)-H(23)	111(2)
O(1)-C(9)-C(20)	106.47(14)	C(11)-C(16)-C(15)	113.98(18)
C(8)-C(9)-C(20)	109.45(14)	C(11)-C(16)-H(24)	110.2(13)
O(1)-C(9)-C(10)	109.63(14)	C(15)-C(16)-H(24)	108.3(13)
C(8)-C(9)-C(10)	111.49(14)	C(11)-C(16)-H(25)	107.7(15)
C(20)-C(9)-C(10)	111.31(15)	C(15)-C(16)-H(25)	108.8(16)
C(18)-C(10)-C(11)	110.30(16)	H(24)-C(16)-H(25)	107.6(19)
C(18)-C(10)-C(19)	107.09(16)	C(14)-C(17)-H(18)	103(2)
C(11)-C(10)-C(19)	111.29(15)	C(14)-C(17)-H(19)	110(3)
C(18)-C(10)-C(9)	111.89(15)	H(18)-C(17)-H(19)	120(3)
C(11)-C(10)-C(9)	109.54(13)	C(14)-C(17)-H(20)	105(2)
C(19)-C(10)-C(9)	106.67(16)	H(18)-C(17)-H(20)	109(3)
C(12)-C(11)-C(16)	119.58(18)	H(19)-C(17)-H(20)	108(4)
C(12)-C(11)-C(10)	122.23(18)	C(10)-C(18)-H(12)	110.5(15)
C(16)-C(11)-C(10)	118.15(16)	C(10)-C(18)-H(13)	108.4(14)
C(11)-C(12)-C(13)	124.5(2)	H(12)-C(18)-H(13)	101.2(19)
C(11)-C(12)-H(15)	119.8(14)	C(10)-C(18)-H(14)	112.9(14)
C(13)-C(12)-H(15)	115.0(14)	H(12)-C(18)-H(14)	112.4(19)
C(14)-C(13)-C(12)	113.48(19)	H(13)-C(18)-H(14)	111(2)
C(14)-C(13)-H(16)	111.8(16)	C(10)-C(19)-H(9)	109.2(14)
C(12)-C(13)-H(16)	108.2(17)	C(10)-C(19)-H(10)	109.7(11)
C(14)-C(13)-H(17)	106.1(15)	H(9)-C(19)-H(10)	109.3(19)
C(12)-C(13)-H(17)	112.5(15)	C(10)-C(19)-H(11)	108.6(13)

H(9)-C(19)-H(11)	111(2)	H(26)-C(21)-H(27)	113(3)
H(10)-C(19)-H(11)	109.0(17)	O(3)-C(21)-H(28)	104.7(17)
O(2)-C(20)-O(3)	124.04(18)	H(26)-C(21)-H(28)	111(3)
O(2)-C(20)-C(9)	123.40(18)	H(27)-C(21)-H(28)	109(2)
O(3)-C(20)-C(9)	112.54(15)	C(9)-O(1)-H(10)	109(2)
O(3)-C(21)-H(26)	108(2)	C(20)-O(3)-C(21)	116.20(16)
O(3)-C(21)-H(27)	110(2)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **153**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
C(1)	32(1)	36(1)	47(1)	1(1)	7(1)	1(1)
C(2)	40(1)	42(1)	46(1)	-1(1)	6(1)	10(1)
C(3)	55(2)	33(1)	39(1)	0(1)	2(1)	7(1)
C(4)	52(2)	32(1)	41(1)	8(1)	5(1)	-2(1)
C(5)	34(1)	36(1)	37(1)	4(1)	5(1)	2(1)
C(6)	28(1)	33(1)	31(1)	-1(1)	0(1)	-1(1)
C(7)	31(1)	30(1)	35(1)	0(1)	2(1)	-5(1)
C(8)	27(1)	32(1)	34(1)	0(1)	2(1)	-3(1)
C(9)	27(1)	30(1)	36(1)	1(1)	5(1)	-2(1)
C(10)	32(1)	34(1)	32(1)	-1(1)	1(1)	-1(1)
C(11)	31(1)	34(1)	26(1)	-2(1)	4(1)	0(1)
C(12)	35(1)	40(1)	39(1)	-3(1)	2(1)	1(1)
C(13)	58(2)	36(1)	38(1)	-3(1)	-1(1)	-7(1)
C(14)	62(2)	41(1)	51(1)	-6(1)	13(1)	6(1)
C(15)	41(2)	47(1)	58(1)	-2(1)	-2(1)	11(1)
C(16)	34(1)	39(1)	45(1)	-4(1)	3(1)	2(1)
C(17)	93(3)	43(2)	79(2)	-10(1)	10(2)	11(2)
C(18)	42(1)	37(1)	36(1)	2(1)	11(1)	-5(1)
C(19)	43(2)	40(1)	36(1)	2(1)	-3(1)	2(1)
C(20)	37(1)	30(1)	30(1)	-1(1)	8(1)	3(1)
C(21)	42(2)	60(2)	35(1)	0(1)	-5(1)	2(1)
O(1)	33(1)	27(1)	50(1)	-1(1)	9(1)	-4(1)
O(2)	60(1)	41(1)	43(1)	11(1)	1(1)	-6(1)
O(3)	34(1)	44(1)	33(1)	4(1)	-2(1)	-5(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **153**.

	x	y	z	U(eq)
H(1)	-7540(40)	-2322(13)	-900(30)	50(6)
H(2)	-8360(40)	-1165(12)	-1080(30)	38(6)
H(3)	-6110(40)	-334(16)	-2040(30)	63(7)
H(4)	-2800(40)	-741(15)	-2950(30)	61(8)
H(5)	-2040(40)	-1939(13)	-2790(30)	40(6)
H(7)	-5300(40)	-3295(12)	-1490(30)	35(5)
H(8)	-950(40)	-3063(12)	-1880(30)	39(6)
H(9)	-4290(40)	-4445(14)	-4500(30)	47(6)
H(10)	-3160(30)	-3735(13)	-4940(20)	34(5)
H(11)	-2640(30)	-4455(12)	-5820(30)	40(6)
H(12)	580(40)	-3562(14)	-4000(30)	47(6)
H(13)	1130(40)	-4202(11)	-4820(30)	40(6)
H(14)	2120(40)	-4108(12)	-2900(30)	43(6)
H(15)	-3740(40)	-5522(12)	-3940(30)	41(6)
H(16)	-2830(40)	-6641(14)	-4410(30)	56(7)
H(17)	-2520(40)	-6682(14)	-2440(30)	50(6)
H(18)	-290(60)	-7665(19)	-3820(50)	93(11)
H(19)	620(70)	-7520(20)	-1820(60)	107(13)
H(20)	2190(80)	-7540(20)	-3130(50)	112(14)
H(21)	760(40)	-6558(12)	-4570(30)	44(6)
H(22)	1170(40)	-6296(14)	-890(40)	59(7)
H(23)	3310(50)	-6305(16)	-1940(30)	63(8)
H(24)	2210(30)	-5170(12)	-1560(30)	39(5)
H(25)	2340(40)	-5366(14)	-3460(30)	51(7)
H(26)	3930(60)	-4250(20)	1440(50)	91(12)
H(27)	2550(50)	-3932(16)	2650(40)	75(9)
H(28)	4070(50)	-3433(18)	1690(40)	76(9)
H(10)	-3530(50)	-4821(17)	-1080(40)	66(9)

Table 6. Torsion angles [°] for compound **153**.

C(6)-C(1)-C(2)-C(3)	0.1(3)
C(1)-C(2)-C(3)-C(4)	0.6(3)
C(2)-C(3)-C(4)-C(5)	-0.2(3)
C(3)-C(4)-C(5)-C(6)	-1.0(3)
C(2)-C(1)-C(6)-C(5)	-1.3(3)
C(2)-C(1)-C(6)-C(7)	178.53(17)
C(4)-C(5)-C(6)-C(1)	1.8(2)
C(4)-C(5)-C(6)-C(7)	-178.09(16)
C(1)-C(6)-C(7)-C(8)	-165.34(18)
C(5)-C(6)-C(7)-C(8)	14.5(3)
C(6)-C(7)-C(8)-C(9)	-179.02(15)
C(7)-C(8)-C(9)-O(1)	-4.1(2)
C(7)-C(8)-C(9)-C(20)	-119.84(19)
C(7)-C(8)-C(9)-C(10)	116.56(19)
O(1)-C(9)-C(10)-C(18)	177.22(15)
C(8)-C(9)-C(10)-C(18)	57.3(2)
C(20)-C(9)-C(10)-C(18)	-65.25(19)
O(1)-C(9)-C(10)-C(11)	-60.14(18)
C(8)-C(9)-C(10)-C(11)	179.92(15)
C(20)-C(9)-C(10)-C(11)	57.39(19)
O(1)-C(9)-C(10)-C(19)	60.42(19)
C(8)-C(9)-C(10)-C(19)	-59.5(2)
C(20)-C(9)-C(10)-C(19)	177.94(16)
C(18)-C(10)-C(11)-C(12)	-149.56(17)
C(19)-C(10)-C(11)-C(12)	-30.8(2)
C(9)-C(10)-C(11)-C(12)	86.9(2)
C(18)-C(10)-C(11)-C(16)	28.1(2)
C(19)-C(10)-C(11)-C(16)	146.77(18)
C(9)-C(10)-C(11)-C(16)	-95.52(19)
C(16)-C(11)-C(12)-C(13)	-3.2(3)
C(10)-C(11)-C(12)-C(13)	174.39(17)
C(11)-C(12)-C(13)-C(14)	-12.4(3)
C(12)-C(13)-C(14)-C(15)	43.2(2)

C(12)-C(13)-C(14)-C(17)	168.0(2)
C(13)-C(14)-C(15)-C(16)	-60.4(3)
C(17)-C(14)-C(15)-C(16)	174.0(3)
C(12)-C(11)-C(16)-C(15)	-13.6(3)
C(10)-C(11)-C(16)-C(15)	168.76(16)
C(14)-C(15)-C(16)-C(11)	45.4(3)
O(1)-C(9)-C(20)-O(2)	19.3(2)
C(8)-C(9)-C(20)-O(2)	136.19(19)
C(10)-C(9)-C(20)-O(2)	-100.1(2)
O(1)-C(9)-C(20)-O(3)	-159.22(14)
C(8)-C(9)-C(20)-O(3)	-42.4(2)
C(10)-C(9)-C(20)-O(3)	81.35(18)
O(2)-C(20)-O(3)-C(21)	0.6(3)
C(9)-C(20)-O(3)-C(21)	179.18(17)

Symmetry transformations used to generate equivalent atoms:

3. Crystal structure of compound 166

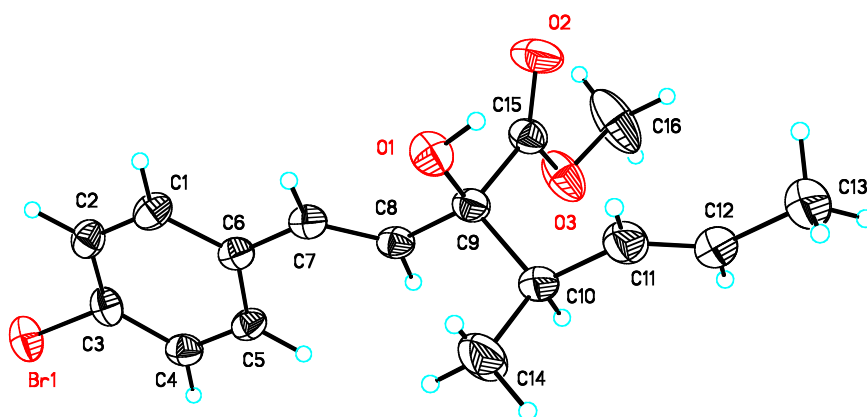
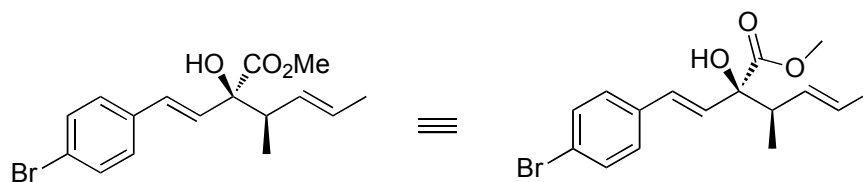


Table 1. Crystal data and structure refinement for compound **166**.

Compound	166	
Empirical formula	C ₁₆ H ₁₉ Br O ₃	
Formula weight	339.22	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2	
Unit cell dimensions	a = 7.9626(3) Å	α = 90°.
	b = 36.6534(11) Å	β = 90°.
	c = 5.6635(2) Å	γ = 90°.
Volume	1652.93(10) Å ³	
Z	4	
Density (calculated)	1.363 Mg/m ³	
Absorption coefficient	3.427 mm ⁻¹	
F(000)	696	
Crystal size	0.48 x 0.12 x 0.03 mm ³	
Theta range for data collection	2.41 to 67.55°.	
Index ranges	-8 ≤ h ≤ 8, -43 ≤ k ≤ 43, -6 ≤ l ≤ 6	
Reflections collected	10887	
Independent reflections	2788 [R(int) = 0.0324]	
Completeness to theta = 67.55°	94.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9042 and 0.2900	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2788 / 0 / 181	
Goodness-of-fit on F ²	1.089	
Final R indices [I > 2σ(I)]	R1 = 0.0368, wR2 = 0.0913	
R indices (all data)	R1 = 0.0401, wR2 = 0.0926	
Absolute structure parameter	0.02(3)	
Largest diff. peak and hole	0.452 and -0.340 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **166**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	3150(1)	1730(1)	4087(1)	52(1)
C(1)	1866(6)	2456(1)	9409(6)	40(1)
C(2)	2084(6)	2139(1)	8096(6)	40(1)
C(3)	2888(5)	2159(1)	5959(7)	37(1)
C(4)	3519(5)	2485(1)	5108(7)	38(1)
C(5)	3278(5)	2800(1)	6423(6)	35(1)
C(6)	2434(5)	2791(1)	8582(6)	32(1)
C(7)	2186(5)	3119(1)	10048(6)	34(1)
C(8)	2353(5)	3461(1)	9390(6)	33(1)
C(9)	2057(5)	3783(1)	10984(7)	35(1)
C(10)	3501(5)	4062(1)	10910(10)	48(1)
C(11)	3081(6)	4395(1)	12314(9)	52(1)
C(12)	2888(6)	4727(1)	11509(10)	63(1)
C(13)	2480(8)	5057(1)	12972(12)	80(2)
C(14)	5113(6)	3886(1)	11784(14)	90(2)
C(15)	420(5)	3973(1)	10211(6)	37(1)
C(16)	-950(8)	4287(2)	7148(9)	84(2)
O(1)	1834(4)	3667(1)	13352(4)	43(1)
O(2)	-765(4)	4008(1)	11467(6)	58(1)
O(3)	513(5)	4094(1)	8025(5)	59(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound **166**.

Br(1)-C(3)	1.906(3)	C(15)-O(3)	1.318(4)
C(1)-C(2)	1.389(5)	C(16)-O(3)	1.450(6)
C(1)-C(6)	1.392(5)	C(16)-H(16A)	0.9800
C(1)-H(1A)	0.9500	C(16)-H(16B)	0.9800
C(2)-C(3)	1.371(6)	C(16)-H(16C)	0.9800
C(2)-H(2A)	0.9500	O(1)-H(1B)	0.8400
C(3)-C(4)	1.383(5)		
C(4)-C(5)	1.388(5)	C(2)-C(1)-C(6)	121.2(3)
C(4)-H(4A)	0.9500	C(2)-C(1)-H(1A)	119.4
C(5)-C(6)	1.395(5)	C(6)-C(1)-H(1A)	119.4
C(5)-H(5A)	0.9500	C(3)-C(2)-C(1)	119.1(3)
C(6)-C(7)	1.475(5)	C(3)-C(2)-H(2A)	120.4
C(7)-C(8)	1.315(5)	C(1)-C(2)-H(2A)	120.4
C(7)-H(7A)	0.9500	C(2)-C(3)-C(4)	121.5(3)
C(8)-C(9)	1.504(5)	C(2)-C(3)-Br(1)	119.9(3)
C(8)-H(8A)	0.9500	C(4)-C(3)-Br(1)	118.6(3)
C(9)-O(1)	1.419(4)	C(3)-C(4)-C(5)	118.8(3)
C(9)-C(10)	1.540(5)	C(3)-C(4)-H(4A)	120.6
C(9)-C(15)	1.541(5)	C(5)-C(4)-H(4A)	120.6
C(10)-C(11)	1.494(6)	C(4)-C(5)-C(6)	121.1(3)
C(10)-C(14)	1.521(6)	C(4)-C(5)-H(5A)	119.4
C(10)-H(10A)	1.0000	C(6)-C(5)-H(5A)	119.4
C(11)-C(12)	1.308(6)	C(1)-C(6)-C(5)	118.2(3)
C(11)-H(11A)	0.9500	C(1)-C(6)-C(7)	119.2(3)
C(12)-C(13)	1.501(7)	C(5)-C(6)-C(7)	122.6(3)
C(12)-H(12A)	0.9500	C(8)-C(7)-C(6)	127.2(3)
C(13)-H(13A)	0.9800	C(8)-C(7)-H(7A)	116.4
C(13)-H(13B)	0.9800	C(6)-C(7)-H(7A)	116.4
C(13)-H(13C)	0.9800	C(7)-C(8)-C(9)	124.2(3)
C(14)-H(14A)	0.9800	C(7)-C(8)-H(8A)	117.9
C(14)-H(14B)	0.9800	C(9)-C(8)-H(8A)	117.9
C(14)-H(14C)	0.9800	O(1)-C(9)-C(8)	110.6(3)
C(15)-O(2)	1.189(5)	O(1)-C(9)-C(10)	108.6(3)

C(8)-C(9)-C(10)	112.8(3)	H(13A)-C(13)-H(13C)	109.5
O(1)-C(9)-C(15)	107.4(3)	H(13B)-C(13)-H(13C)	109.5
C(8)-C(9)-C(15)	108.5(3)	C(10)-C(14)-H(14A)	109.5
C(10)-C(9)-C(15)	108.9(3)	C(10)-C(14)-H(14B)	109.5
C(11)-C(10)-C(14)	111.3(4)	H(14A)-C(14)-H(14B)	109.5
C(11)-C(10)-C(9)	111.2(3)	C(10)-C(14)-H(14C)	109.5
C(14)-C(10)-C(9)	109.8(3)	H(14A)-C(14)-H(14C)	109.5
C(11)-C(10)-H(10A)	108.1	H(14B)-C(14)-H(14C)	109.5
C(14)-C(10)-H(10A)	108.1	O(2)-C(15)-O(3)	124.8(4)
C(9)-C(10)-H(10A)	108.1	O(2)-C(15)-C(9)	123.4(3)
C(12)-C(11)-C(10)	126.9(5)	O(3)-C(15)-C(9)	111.8(4)
C(12)-C(11)-H(11A)	116.5	O(3)-C(16)-H(16A)	109.5
C(10)-C(11)-H(11A)	116.5	O(3)-C(16)-H(16B)	109.5
C(11)-C(12)-C(13)	125.6(5)	H(16A)-C(16)-H(16B)	109.5
C(11)-C(12)-H(12A)	117.2	O(3)-C(16)-H(16C)	109.5
C(13)-C(12)-H(12A)	117.2	H(16A)-C(16)-H(16C)	109.5
C(12)-C(13)-H(13A)	109.5	H(16B)-C(16)-H(16C)	109.5
C(12)-C(13)-H(13B)	109.5	C(9)-O(1)-H(1B)	109.5
H(13A)-C(13)-H(13B)	109.5	C(15)-O(3)-C(16)	116.2(4)
C(12)-C(13)-H(13C)	109.5		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **166**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^*2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
Br(1)	69(1)	41(1)	46(1)	-2(1)	-4(1)	13(1)
C(1)	45(2)	46(2)	28(2)	6(2)	2(2)	-5(2)
C(2)	45(3)	39(2)	34(2)	9(2)	-3(2)	0(2)
C(3)	42(2)	35(2)	33(2)	-2(2)	-11(2)	6(2)
C(4)	32(2)	48(2)	33(2)	4(2)	0(2)	2(2)
C(5)	33(2)	40(2)	31(2)	6(1)	1(2)	-4(2)
C(6)	27(2)	42(2)	28(2)	6(1)	-6(1)	0(1)
C(7)	31(2)	43(2)	28(2)	3(1)	-2(2)	0(2)
C(8)	30(2)	43(2)	27(2)	4(2)	2(1)	3(1)
C(9)	30(2)	40(2)	35(2)	4(2)	2(2)	4(1)
C(10)	30(3)	41(2)	72(3)	-4(2)	7(2)	-2(2)
C(11)	40(3)	49(2)	68(3)	-12(2)	0(3)	-1(2)
C(12)	53(3)	46(2)	90(4)	-4(2)	24(3)	-6(2)
C(13)	65(4)	52(3)	123(5)	-21(3)	20(3)	-2(2)
C(14)	34(3)	55(3)	183(8)	-25(4)	-6(4)	5(2)
C(15)	37(3)	42(2)	33(2)	0(2)	3(2)	5(2)
C(16)	114(5)	85(4)	53(3)	-10(3)	-28(3)	61(4)
O(1)	54(2)	48(1)	28(1)	-1(1)	1(1)	8(1)
O(2)	33(2)	79(2)	60(2)	7(2)	10(2)	12(2)
O(3)	82(3)	60(2)	36(2)	3(1)	0(2)	34(2)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **166**.

	x	y	z	U(eq)
H(1A)	1320	2443	10898	48
H(2A)	1681	1912	8671	48
H(4A)	4106	2493	3649	45
H(5A)	3695	3026	5843	42
H(7A)	1871	3079	11645	41
H(8A)	2682	3508	7806	40
H(10A)	3674	4138	9230	57
H(11A)	2939	4362	13965	63
H(12A)	3017	4762	9857	76
H(13A)	2410	5272	11949	120
H(13B)	3364	5094	14153	120
H(13C)	1402	5020	13770	120
H(14A)	6031	4064	11718	136
H(14B)	5387	3676	10781	136
H(14C)	4960	3803	13416	136
H(16A)	-749	4364	5516	126
H(16B)	-1162	4501	8135	126
H(16C)	-1928	4125	7199	126
H(1B)	1469	3841	14166	65

Table 6. Torsion angles [°] for compound **166**.

C(6)-C(1)-C(2)-C(3)	0.6(6)
C(1)-C(2)-C(3)-C(4)	1.5(6)
C(1)-C(2)-C(3)-Br(1)	-178.4(3)
C(2)-C(3)-C(4)-C(5)	-2.2(6)
Br(1)-C(3)-C(4)-C(5)	177.7(3)
C(3)-C(4)-C(5)-C(6)	0.8(6)
C(2)-C(1)-C(6)-C(5)	-1.9(6)
C(2)-C(1)-C(6)-C(7)	-179.5(4)
C(4)-C(5)-C(6)-C(1)	1.2(6)
C(4)-C(5)-C(6)-C(7)	178.7(3)
C(1)-C(6)-C(7)-C(8)	-166.5(4)
C(5)-C(6)-C(7)-C(8)	16.0(6)
C(6)-C(7)-C(8)-C(9)	179.2(3)
C(7)-C(8)-C(9)-O(1)	9.0(5)
C(7)-C(8)-C(9)-C(10)	130.9(4)
C(7)-C(8)-C(9)-C(15)	-108.4(4)
O(1)-C(9)-C(10)-C(11)	-63.0(4)
C(8)-C(9)-C(10)-C(11)	174.0(4)
C(15)-C(9)-C(10)-C(11)	53.5(5)
O(1)-C(9)-C(10)-C(14)	60.6(5)
C(8)-C(9)-C(10)-C(14)	-62.4(5)
C(15)-C(9)-C(10)-C(14)	177.2(4)
C(14)-C(10)-C(11)-C(12)	121.6(6)
C(9)-C(10)-C(11)-C(12)	-115.7(5)
C(10)-C(11)-C(12)-C(13)	-179.4(5)
O(1)-C(9)-C(15)-O(2)	0.2(5)
C(8)-C(9)-C(15)-O(2)	119.7(4)
C(10)-C(9)-C(15)-O(2)	-117.2(4)
O(1)-C(9)-C(15)-O(3)	179.5(3)
C(8)-C(9)-C(15)-O(3)	-61.1(4)
C(10)-C(9)-C(15)-O(3)	62.1(4)
O(2)-C(15)-O(3)-C(16)	0.8(7)
C(9)-C(15)-O(3)-C(16)	-178.4(4)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound **166** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	\angle (DHA)
O(1)-H(1B)...O(3)#1	0.84	2.49	3.250(4)	150.5

Symmetry transformations used to generate equivalent atoms:

#1 x,y,z+1

4. Crystal structure of compound 177

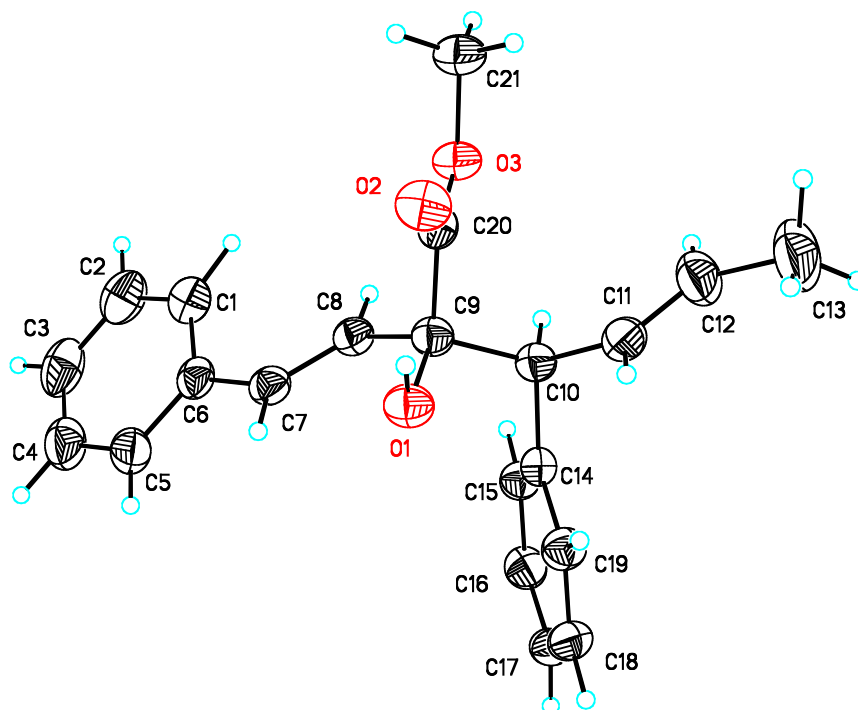
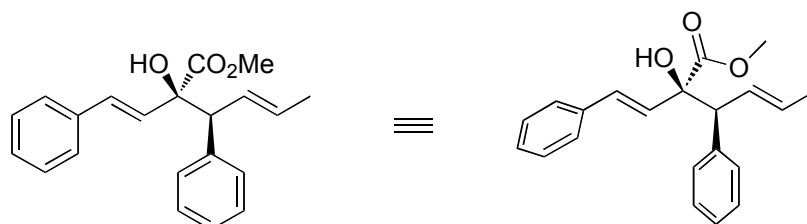


Table 1. Crystal data and structure refinement for compound **177**.

Compound	177	
Empirical formula	C ₂₁ H ₂₂ O ₃	
Formula weight	322.39	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 11.1117(5) Å	α = 90°.
	b = 5.5288(3) Å	β = 104.084(2)°.
	c = 14.6321(7) Å	γ = 90°.
Volume	871.89(7) Å ³	
Z	2	
Density (calculated)	1.228 Mg/m ³	
Absorption coefficient	0.646 mm ⁻¹	
F(000)	344	
Crystal size	0.42 x 0.17 x 0.16 mm ³	
Theta range for data collection	3.11 to 68.04°.	
Index ranges	-12 ≤ h ≤ 13, -6 ≤ k ≤ 5, -16 ≤ l ≤ 17	
Reflections collected	6114	
Independent reflections	2555 [R(int) = 0.0138]	
Completeness to theta = 68.04°	95.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9038 and 0.7732	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2555 / 1 / 305	
Goodness-of-fit on F ²	1.013	
Final R indices [I > 2σ(I)]	R1 = 0.0254, wR2 = 0.0692	
R indices (all data)	R1 = 0.0258, wR2 = 0.0697	
Absolute structure parameter	-0.20(16)	
Largest diff. peak and hole	0.143 and -0.133 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **177**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	7838(1)	8078(3)	2616(1)	44(1)
C(2)	9030(2)	9020(4)	2923(1)	54(1)
C(3)	9910(2)	7803(4)	3599(1)	56(1)
C(4)	9602(1)	5691(4)	3974(1)	54(1)
C(5)	8419(1)	4749(4)	3671(1)	43(1)
C(6)	7514(1)	5921(3)	2990(1)	33(1)
C(7)	6265(1)	4860(3)	2673(1)	33(1)
C(8)	5242(1)	6061(3)	2264(1)	31(1)
C(9)	3985(1)	4929(3)	1864(1)	31(1)
C(10)	2952(1)	6164(3)	2259(1)	31(1)
C(11)	1674(1)	5447(3)	1697(1)	39(1)
C(12)	817(2)	6987(4)	1279(1)	53(1)
C(13)	-479(2)	6317(7)	57(2)	79(1)
C(14)	3127(1)	5696(3)	3307(1)	30(1)
C(15)	3716(1)	7413(3)	3955(1)	34(1)
C(16)	3844(1)	7080(3)	4914(1)	39(1)
C(17)	3377(1)	5013(3)	5233(1)	39(1)
C(18)	2799(1)	3283(3)	4598(1)	40(1)
C(19)	2679(1)	3610(3)	3639(1)	36(1)
C(20)	3670(1)	5295(3)	790(1)	30(1)
C(21)	3394(2)	8006(3)	-470(1)	40(1)
O(1)	4001(1)	2406(2)	2035(1)	36(1)
O(2)	3484(1)	3623(2)	245(1)	41(1)
O(3)	3649(1)	7599(2)	539(1)	35(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound **177**.

C(1)-C(2)	1.392(2)	C(16)-C(17)	1.383(2)
C(1)-C(6)	1.395(2)	C(16)-H(16)	0.948(19)
C(1)-H(1)	1.031(19)	C(17)-C(18)	1.379(2)
C(2)-C(3)	1.384(3)	C(17)-H(17)	0.949(18)
C(2)-H(2)	0.97(3)	C(18)-C(19)	1.388(2)
C(3)-C(4)	1.368(3)	C(18)-H(18)	0.95(2)
C(3)-H(3)	0.93(2)	C(19)-H(19)	0.964(18)
C(4)-C(5)	1.383(2)	C(20)-O(2)	1.2049(17)
C(4)-H(4)	0.99(2)	C(20)-O(3)	1.3240(18)
C(5)-C(6)	1.392(2)	C(21)-O(3)	1.4510(16)
C(5)-H(5)	0.94(2)	C(21)-H(21A)	0.96(2)
C(6)-C(7)	1.4737(19)	C(21)-H(21B)	0.966(17)
C(7)-C(8)	1.327(2)	C(21)-H(21C)	0.94(2)
C(7)-H(7)	0.96(2)	O(1)-H(10)	0.882(19)
C(8)-C(9)	1.5122(18)		
C(8)-H(8)	0.989(19)	C(2)-C(1)-C(6)	57(16)
C(9)-O(1)	1.4166(18)	C(2)-C(1)-H(1)	118.5(11)
C(9)-C(20)	1.5388(17)	C(6)-C(1)-H(1)	120.8(11)
C(9)-C(10)	1.5624(19)	C(3)-C(2)-C(1)	120.01(19)
C(10)-C(11)	1.5100(18)	C(3)-C(2)-H(2)	122.3(12)
C(10)-C(14)	1.5198(17)	C(1)-C(2)-H(2)	117.6(12)
C(10)-H(10)	0.979(18)	C(4)-C(3)-C(2)	119.94(16)
C(11)-C(12)	1.313(2)	C(4)-C(3)-H(3)	117.6(13)
C(11)-H(11)	0.95(2)	C(2)-C(3)-H(3)	122.3(13)
C(12)-C(13)	1.503(3)	C(3)-C(4)-C(5)	120.25(17)
C(12)-H(12)	1.04(3)	C(3)-C(4)-H(4)	120.3(13)
C(13)-H(13A)	0.98(3)	C(5)-C(4)-H(4)	119.5(13)
C(13)-H(13B)	1.00(3)	C(4)-C(5)-C(6)	121.27(18)
C(13)-H(13C)	1.00(4)	C(4)-C(5)-H(5)	119.9(11)
C(14)-C(15)	1.388(2)	C(6)-C(5)-H(5)	118.7(11)
C(14)-C(19)	1.390(2)	C(5)-C(6)-C(1)	117.94(14)
C(15)-C(16)	1.387(2)	C(5)-C(6)-C(7)	120.07(14)
C(15)-H(15)	0.942(17)	C(1)-C(6)-C(7)	121.97(13)

C(8)-C(7)-C(6)	125.48(14)	C(15)-C(14)-C(19)	118.54(12)
C(8)-C(7)-H(7)	116.8(10)	C(15)-C(14)-C(10)	119.76(12)
C(6)-C(7)-H(7)	117.7(10)	C(19)-C(14)-C(10)	121.67(12)
C(7)-C(8)-C(9)	125.22(14)	C(16)-C(15)-C(14)	121.04(14)
C(7)-C(8)-H(8)	121.4(9)	C(16)-C(15)-H(15)	119.7(9)
C(9)-C(8)-H(8)	113.3(9)	C(14)-C(15)-H(15)	119.2(9)
O(1)-C(9)-C(8)	111.60(11)	C(17)-C(16)-C(15)	119.82(14)
O(1)-C(9)-C(20)	107.45(11)	C(17)-C(16)-H(16)	119.5(10)
C(8)-C(9)-C(20)	107.41(10)	C(15)-C(16)-H(16)	120.7(10)
O(1)-C(9)-C(10)	110.14(11)	C(18)-C(17)-C(16)	119.78(13)
C(8)-C(9)-C(10)	111.64(11)	C(18)-C(17)-H(17)	120.9(12)
C(20)-C(9)-C(10)	108.42(10)	C(16)-C(17)-H(17)	119.2(12)
C(11)-C(10)-C(14)	112.18(11)	C(17)-C(18)-C(19)	120.37(15)
C(11)-C(10)-C(9)	111.19(12)	C(17)-C(18)-H(18)	120.2(11)
C(14)-C(10)-C(9)	111.91(10)	C(19)-C(18)-H(18)	119.4(11)
C(11)-C(10)-H(10)	107.3(8)	C(18)-C(19)-C(14)	120.44(14)
C(14)-C(10)-H(10)	107.9(8)	C(18)-C(19)-H(19)	121.0(10)
C(9)-C(10)-H(10)	106.0(9)	C(14)-C(19)-H(19)	118.6(10)
C(12)-C(11)-C(10)	124.24(18)	O(2)-C(20)-O(3)	124.49(12)
C(12)-C(11)-H(11)	119.5(11)	O(2)-C(20)-C(9)	122.31(13)
C(10)-C(11)-H(11)	116.2(11)	O(3)-C(20)-C(9)	113.19(11)
C(11)-C(12)-C(13)	125.0(2)	O(3)-C(21)-H(21A)	104.5(11)
C(11)-C(12)-H(12)	117.8(13)	O(3)-C(21)-H(21B)	109.5(10)
C(13)-C(12)-H(12)	117.2(13)	H(21A)-C(21)-H(21B)	112.5(16)
C(12)-C(13)-H(13A)	107.7(17)	O(3)-C(21)-H(21C)	110.5(11)
C(12)-C(13)-H(13B)	109.3(14)	H(21A)-C(21)-H(21C)	109.6(18)
H(13A)-C(13)-H(13B)	109(2)	H(21B)-C(21)-H(21C)	110.1(15)
C(12)-C(13)-H(13C)	107.6(18)	C(9)-O(1)-H(10)	103.7(12)
H(13A)-C(13)-H(13C)	108(3)	C(20)-O(3)-C(21)	114.63(12)
H(13B)-C(13)-H(13C)	115(3)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **177**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
C(1)	41(1)	47(1)	47(1)	-1(1)	15(1)	0(1)
C(2)	48(1)	54(1)	65(1)	-10(1)	24(1)	-12(1)
C(3)	36(1)	79(1)	56(1)	-23(1)	14(1)	-11(1)
C(4)	35(1)	78(1)	46(1)	-4(1)	7(1)	7(1)
C(5)	38(1)	53(1)	40(1)	0(1)	11(1)	7(1)
C(6)	33(1)	40(1)	30(1)	-6(1)	11(1)	3(1)
C(7)	37(1)	34(1)	30(1)	0(1)	12(1)	1(1)
C(8)	34(1)	31(1)	29(1)	-1(1)	10(1)	0(1)
C(9)	33(1)	28(1)	31(1)	2(1)	8(1)	0(1)
C(10)	32(1)	31(1)	31(1)	3(1)	8(1)	0(1)
C(11)	35(1)	49(1)	35(1)	2(1)	10(1)	-4(1)
C(12)	38(1)	75(1)	41(1)	-3(1)	2(1)	11(1)
C(13)	37(1)	134(3)	58(1)	-13(2)	-1(1)	13(1)
C(14)	27(1)	33(1)	32(1)	3(1)	9(1)	3(1)
C(15)	35(1)	32(1)	35(1)	3(1)	10(1)	0(1)
C(16)	40(1)	42(1)	34(1)	-3(1)	8(1)	4(1)
C(17)	42(1)	46(1)	31(1)	8(1)	14(1)	10(1)
C(18)	43(1)	39(1)	43(1)	11(1)	19(1)	4(1)
C(19)	38(1)	34(1)	38(1)	2(1)	11(1)	-2(1)
C(20)	28(1)	31(1)	31(1)	-2(1)	8(1)	-1(1)
C(21)	52(1)	41(1)	28(1)	0(1)	10(1)	0(1)
O(1)	44(1)	28(1)	36(1)	1(1)	10(1)	-1(1)
O(2)	50(1)	36(1)	37(1)	-6(1)	7(1)	-3(1)
O(3)	45(1)	32(1)	27(1)	1(1)	9(1)	-1(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **177**.

	x	y	z	U(eq)
H(1)	7223(17)	8940(40)	2071(13)	54(5)
H(2)	9218(19)	10500(50)	2631(14)	64(6)
H(3)	10726(19)	8320(40)	3791(13)	62(5)
H(4)	10229(19)	4810(40)	4457(14)	65(6)
H(5)	8227(17)	3240(40)	3901(13)	53(5)
H(7)	6178(15)	3150(40)	2770(11)	40(4)
H(8)	5251(13)	7830(30)	2167(10)	35(4)
H(10)	3039(13)	7910(30)	2171(10)	28(4)
H(11)	1492(16)	3760(40)	1672(12)	46(5)
H(12)	1050(20)	8810(50)	1302(16)	77(7)
H(13A)	-620(30)	6980(60)	120(20)	111(10)
H(13B)	-1080(20)	7070(50)	1078(18)	99(9)
H(13C)	-520(30)	4510(70)	700(20)	103(10)
H(15)	3987(14)	8870(30)	3736(11)	31(4)
H(16)	4249(15)	8260(40)	5353(12)	43(4)
H(17)	3508(16)	4760(30)	5892(13)	48(5)
H(18)	2514(16)	1830(40)	4815(12)	45(5)
H(19)	2267(15)	2420(40)	3189(11)	39(4)
H(21A)	3422(17)	9740(40)	-534(13)	54(5)
H(21B)	2591(16)	7340(40)	-770(11)	43(4)
H(21C)	4009(16)	7290(40)	-719(12)	48(5)
H(10)	3795(16)	1770(30)	1466(13)	48(5)

Table 6. Torsion angles [°] for compound **177**.

C(6)-C(1)-C(2)-C(3)	0.7(2)
C(1)-C(2)-C(3)-C(4)	-0.9(3)
C(2)-C(3)-C(4)-C(5)	0.9(3)
C(3)-C(4)-C(5)-C(6)	-0.6(3)
C(4)-C(5)-C(6)-C(1)	0.4(2)
C(4)-C(5)-C(6)-C(7)	179.27(14)
C(2)-C(1)-C(6)-C(5)	-0.5(2)
C(2)-C(1)-C(6)-C(7)	-179.30(14)
C(5)-C(6)-C(7)-C(8)	158.53(14)
C(1)-C(6)-C(7)-C(8)	-22.7(2)
C(6)-C(7)-C(8)-C(9)	174.43(12)
C(7)-C(8)-C(9)-O(1)	4.06(19)
C(7)-C(8)-C(9)-C(20)	-113.46(14)
C(7)-C(8)-C(9)-C(10)	127.81(14)
O(1)-C(9)-C(10)-C(11)	-68.77(14)
C(8)-C(9)-C(10)-C(11)	166.66(12)
C(20)-C(9)-C(10)-C(11)	48.54(15)
O(1)-C(9)-C(10)-C(14)	57.56(14)
C(8)-C(9)-C(10)-C(14)	-67.01(14)
C(20)-C(9)-C(10)-C(14)	174.87(11)
C(14)-C(10)-C(11)-C(12)	110.54(17)
C(9)-C(10)-C(11)-C(12)	-123.28(16)
C(10)-C(11)-C(12)-C(13)	-176.81(16)
C(11)-C(10)-C(14)-C(15)	-137.08(14)
C(9)-C(10)-C(14)-C(15)	97.13(14)
C(11)-C(10)-C(14)-C(19)	40.96(18)
C(9)-C(10)-C(14)-C(19)	-84.83(15)
C(19)-C(14)-C(15)-C(16)	-0.78(19)
C(10)-C(14)-C(15)-C(16)	177.33(12)
C(14)-C(15)-C(16)-C(17)	-0.2(2)
C(15)-C(16)-C(17)-C(18)	0.7(2)
C(16)-C(17)-C(18)-C(19)	-0.3(2)
C(17)-C(18)-C(19)-C(14)	-0.7(2)

C(15)-C(14)-C(19)-C(18)	1.22(19)
C(10)-C(14)-C(19)-C(18)	-176.84(12)
O(1)-C(9)-C(20)-O(2)	0.15(16)
C(8)-C(9)-C(20)-O(2)	120.35(14)
C(10)-C(9)-C(20)-O(2)	-118.87(14)
O(1)-C(9)-C(20)-O(3)	-178.85(11)
C(8)-C(9)-C(20)-O(3)	-58.65(14)
C(10)-C(9)-C(20)-O(3)	62.13(13)
O(2)-C(20)-O(3)-C(21)	-0.83(18)
C(9)-C(20)-O(3)-C(21)	178.15(11)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound **177** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	\angle (DHA)
O(1)-H(10)...O(2)	0.882(19)	2.014(19)	2.6288(14)	125.7(16)

Symmetry transformations used to generate equivalent atoms:

5. Crystal structure of compound 181

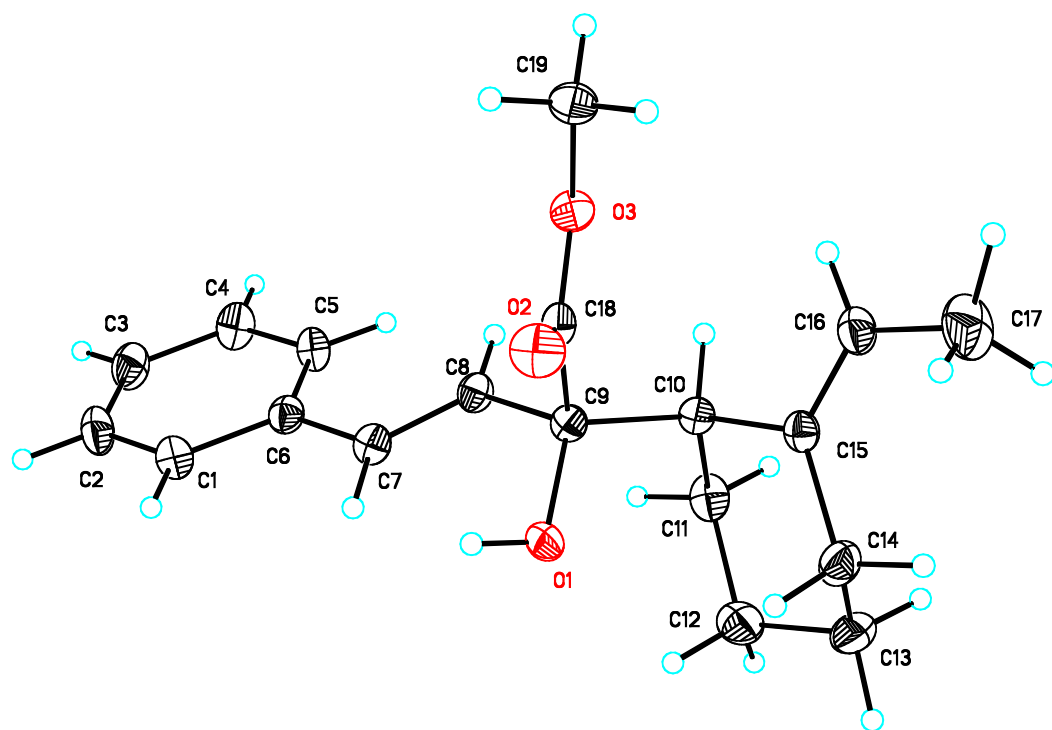
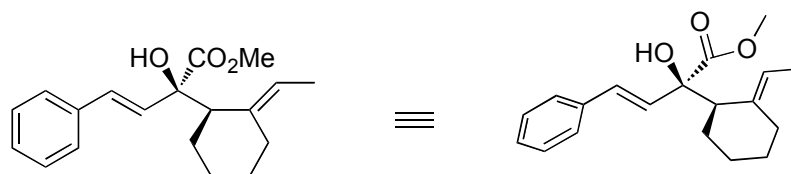


Table 1. Crystal data and structure refinement for compound **181**.

Compound	181	
Empirical formula	C ₁₉ H ₂₄ O ₃	
Formula weight	300.38	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 5.7546(12) Å	α = 104.48(2)°.
	b = 12.147(2) Å	β = 90.08(3)°.
	c = 12.151(2) Å	γ = 90.16(3)°.
Volume	822.4(3) Å ³	
Z	2	
Density (calculated)	1.213 Mg/m ³	
Absorption coefficient	0.641 mm ⁻¹	
F(000)	324	
Crystal size	0.34 x 0.10 x 0.09 mm ³	
Theta range for data collection	3.76 to 65.09°.	
Index ranges	-6 ≤ h ≤ 5, -14 ≤ k ≤ 14, -14 ≤ l ≤ 13	
Reflections collected	8095	
Independent reflections	3637 [R(int) = 0.0146]	
Completeness to theta = 65.09°	87.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9446 and 0.8115	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3637 / 3 / 398	
Goodness-of-fit on F ²	1.020	
Final R indices [I > 2σ(I)]	R1 = 0.0299, wR2 = 0.0860	
R indices (all data)	R1 = 0.0300, wR2 = 0.0861	
Absolute structure parameter	-0.02(16)	
Extinction coefficient	0.0100(9)	
Largest diff. peak and hole	0.194 and -0.138 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **181**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	-4649(4)	-10986(2)	-2261(2)	34(1)
C(2)	-6004(4)	-11964(2)	-2567(2)	38(1)
C(3)	-8104(4)	-11946(2)	-3097(2)	38(1)
C(4)	-8882(4)	-10946(2)	-3323(2)	37(1)
C(5)	-7531(4)	-9966(2)	-3029(2)	33(1)
C(6)	-5408(4)	-9967(2)	-2482(2)	27(1)
C(7)	-3926(4)	-8946(2)	-2136(2)	28(1)
C(8)	-4577(4)	-7892(2)	-2085(2)	26(1)
C(9)	-3022(3)	-6859(2)	-1670(2)	24(1)
C(10)	-3470(4)	-5963(2)	-2371(2)	25(1)
C(11)	-3018(4)	-6423(2)	-3647(2)	32(1)
C(12)	-493(4)	-6412(2)	-4000(2)	39(1)
C(13)	534(4)	-5221(2)	-3549(2)	41(1)
C(14)	317(4)	-4825(2)	-2261(2)	34(1)
C(15)	-2139(4)	-4862(2)	-1875(2)	25(1)
C(16)	-3171(4)	-4012(2)	-1138(2)	32(1)
C(17)	-2059(5)	-2903(2)	-520(3)	50(1)
C(18)	-3627(4)	-6326(2)	-421(2)	26(1)
C(19)	-6572(4)	-5466(2)	853(2)	35(1)
O(1)	-660(2)	-7197(1)	-1711(1)	29(1)
O(2)	-2234(3)	-6195(1)	336(2)	37(1)
O(3)	-5870(3)	-6047(1)	-287(1)	29(1)
C(1B)	-4419(4)	-4075(2)	-5532(2)	34(1)
C(2B)	-3119(5)	-3082(2)	-5360(2)	40(1)
C(3B)	-1047(5)	-3076(2)	-5918(2)	42(1)
C(4B)	-262(5)	-4052(2)	-6648(2)	40(1)
C(5B)	-1546(4)	-5054(2)	-6829(2)	35(1)
C(6B)	-3637(4)	-5079(2)	-6271(2)	28(1)
C(7B)	-5067(4)	-6121(2)	-6431(2)	27(1)

C(8B)	-4320(4)	-7171(2)	-6886(2)	26(1)
C(9B)	-5828(4)	-8222(2)	-7011(2)	26(1)
C(10B)	-5282(4)	-9103(2)	-8161(2)	25(1)
C(11B)	-5836(4)	-8652(2)	-9207(2)	33(1)
C(12B)	-8385(5)	-8737(2)	-9569(2)	41(1)
C(13B)	-9288(4)	-9943(2)	-9707(2)	42(1)
C(14B)	-8965(4)	-10334(2)	-8609(2)	36(1)
C(15B)	-6450(4)	-10245(2)	-8239(2)	27(1)
C(16B)	-5264(4)	-11087(2)	-7996(2)	32(1)
C(17B)	-6157(5)	-12257(2)	-8002(3)	52(1)
C(18B)	-5225(4)	-8773(2)	-6040(2)	27(1)
C(19B)	-2321(4)	-9659(2)	-5204(2)	37(1)
O(1B)	-8199(2)	-7920(1)	-6907(1)	29(1)
O(2B)	-6649(3)	-8945(1)	-5377(2)	38(1)
O(3B)	-2979(3)	-9029(1)	-6022(1)	30(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound **181**.

C(1)-C(2)	1.390(3)	C(14)-H(14B)	0.9900
C(1)-C(6)	1.401(3)	C(15)-C(16)	1.327(3)
C(1)-H(1A)	0.9500	C(16)-C(17)	1.509(3)
C(2)-C(3)	1.372(4)	C(16)-H(16A)	0.9500
C(2)-H(2A)	0.9500	C(17)-H(17A)	0.9800
C(3)-C(4)	1.386(3)	C(17)-H(17B)	0.9800
C(3)-H(3A)	0.9500	C(17)-H(17C)	0.9800
C(4)-C(5)	1.390(3)	C(18)-O(2)	1.199(3)
C(4)-H(4A)	0.9500	C(18)-O(3)	1.335(3)
C(5)-C(6)	1.390(3)	C(19)-O(3)	1.447(3)
C(5)-H(5A)	0.9500	C(19)-H(19A)	0.9800
C(6)-C(7)	1.474(3)	C(19)-H(19B)	0.9800
C(7)-C(8)	1.321(3)	C(19)-H(19C)	0.9800
C(7)-H(7A)	0.9500	O(1)-H(1B)	0.8400
C(8)-C(9)	1.518(3)	C(1B)-C(2B)	1.388(3)
C(8)-H(8A)	0.9500	C(1B)-C(6B)	1.398(3)
C(9)-O(1)	1.419(2)	C(1B)-H(1BA)	0.9500
C(9)-C(18)	1.535(3)	C(2B)-C(3B)	1.373(4)
C(9)-C(10)	1.562(3)	C(2B)-H(2BA)	0.9500
C(10)-C(15)	1.526(3)	C(3B)-C(4B)	1.370(4)
C(10)-C(11)	1.534(3)	C(3B)-H(3BA)	0.9500
C(10)-H(10A)	1.0000	C(4B)-C(5B)	1.391(3)
C(11)-C(12)	1.516(3)	C(4B)-H(4BA)	0.9500
C(11)-H(11A)	0.9900	C(5B)-C(6B)	1.386(3)
C(11)-H(11B)	0.9900	C(5B)-H(5BA)	0.9500
C(12)-C(13)	1.530(3)	C(6B)-C(7B)	1.479(3)
C(12)-H(12A)	0.9900	C(7B)-C(8B)	1.329(3)
C(12)-H(12B)	0.9900	C(7B)-H(7BA)	0.9500
C(13)-C(14)	1.524(4)	C(8B)-C(9B)	1.518(3)
C(13)-H(13A)	0.9900	C(8B)-H(8BA)	0.9500
C(13)-H(13B)	0.9900	C(9B)-O(1B)	1.411(3)
C(14)-C(15)	1.494(3)	C(9B)-C(18B)	1.535(3)
C(14)-H(14A)	0.9900	C(9B)-C(10B)	1.566(3)

C(10B)-C(15B)	1.521(3)	C(2)-C(3)-C(4)	119.8(2)
C(10B)-C(11B)	1.539(3)	C(2)-C(3)-H(3A)	120.1
C(10B)-H(10B)	1.0000	C(4)-C(3)-H(3A)	120.1
C(11B)-C(12B)	1.527(3)	C(3)-C(4)-C(5)	120.4(2)
C(11B)-H(11C)	0.9900	C(3)-C(4)-H(4A)	119.8
C(11B)-H(11D)	0.9900	C(5)-C(4)-H(4A)	119.8
C(12B)-C(13B)	1.522(4)	C(6)-C(5)-C(4)	120.53(19)
C(12B)-H(12C)	0.9900	C(6)-C(5)-H(5A)	119.7
C(12B)-H(12D)	0.9900	C(4)-C(5)-H(5A)	119.7
C(13B)-C(14B)	1.535(4)	C(5)-C(6)-C(1)	118.31(18)
C(13B)-H(13C)	0.9900	C(5)-C(6)-C(7)	122.69(18)
C(13B)-H(13D)	0.9900	C(1)-C(6)-C(7)	119.0(2)
C(14B)-C(15B)	1.511(3)	C(8)-C(7)-C(6)	125.8(2)
C(14B)-H(14C)	0.9900	C(8)-C(7)-H(7A)	117.1
C(14B)-H(14D)	0.9900	C(6)-C(7)-H(7A)	117.1
C(15B)-C(16B)	1.324(3)	C(7)-C(8)-C(9)	124.0(2)
C(16B)-C(17B)	1.509(3)	C(7)-C(8)-H(8A)	118.0
C(16B)-H(16B)	0.9500	C(9)-C(8)-H(8A)	118.0
C(17B)-H(17D)	0.9800	O(1)-C(9)-C(8)	110.04(16)
C(17B)-H(17E)	0.9800	O(1)-C(9)-C(18)	107.53(16)
C(17B)-H(17F)	0.9800	C(8)-C(9)-C(18)	107.64(16)
C(18B)-O(2B)	1.204(3)	O(1)-C(9)-C(10)	112.04(16)
C(18B)-O(3B)	1.332(3)	C(8)-C(9)-C(10)	110.64(16)
C(19B)-O(3B)	1.449(3)	C(18)-C(9)-C(10)	108.79(16)
C(19B)-H(19D)	0.9800	C(15)-C(10)-C(11)	112.04(17)
C(19B)-H(19E)	0.9800	C(15)-C(10)-C(9)	111.29(16)
C(19B)-H(19F)	0.9800	C(11)-C(10)-C(9)	113.30(17)
O(1B)-H(1BB)	0.8400	C(15)-C(10)-H(10A)	106.6
		C(11)-C(10)-H(10A)	106.6
C(2)-C(1)-C(6)	120.7(2)	C(9)-C(10)-H(10A)	106.6
C(2)-C(1)-H(1A)	119.6	C(12)-C(11)-C(10)	115.09(19)
C(6)-C(1)-H(1A)	119.6	C(12)-C(11)-H(11A)	108.5
C(3)-C(2)-C(1)	120.2(2)	C(10)-C(11)-H(11A)	108.5
C(3)-C(2)-H(2A)	119.9	C(12)-C(11)-H(11B)	108.5
C(1)-C(2)-H(2A)	119.9	C(10)-C(11)-H(11B)	108.5

H(11A)-C(11)-H(11B)	107.5	O(3)-C(19)-H(19B)	109.5
C(11)-C(12)-C(13)	109.88(19)	H(19A)-C(19)-H(19B)	109.5
C(11)-C(12)-H(12A)	109.7	O(3)-C(19)-H(19C)	109.5
C(13)-C(12)-H(12A)	109.7	H(19A)-C(19)-H(19C)	109.5
C(11)-C(12)-H(12B)	109.7	H(19B)-C(19)-H(19C)	109.5
C(13)-C(12)-H(12B)	109.7	C(9)-O(1)-H(1B)	109.5
H(12A)-C(12)-H(12B)	108.2	C(18)-O(3)-C(19)	115.93(18)
C(14)-C(13)-C(12)	111.32(18)	C(2B)-C(1B)-C(6B)	120.5(2)
C(14)-C(13)-H(13A)	109.4	C(2B)-C(1B)-H(1BA)	119.7
C(12)-C(13)-H(13A)	109.4	C(6B)-C(1B)-H(1BA)	119.7
C(14)-C(13)-H(13B)	109.4	C(3B)-C(2B)-C(1B)	120.3(2)
C(12)-C(13)-H(13B)	109.4	C(3B)-C(2B)-H(2BA)	119.9
H(13A)-C(13)-H(13B)	108.0	C(1B)-C(2B)-H(2BA)	119.9
C(15)-C(14)-C(13)	112.08(19)	C(4B)-C(3B)-C(2B)	119.9(2)
C(15)-C(14)-H(14A)	109.2	C(4B)-C(3B)-H(3BA)	120.1
C(13)-C(14)-H(14A)	109.2	C(2B)-C(3B)-H(3BA)	120.1
C(15)-C(14)-H(14B)	109.2	C(3B)-C(4B)-C(5B)	120.5(2)
C(13)-C(14)-H(14B)	109.2	C(3B)-C(4B)-H(4BA)	119.7
H(14A)-C(14)-H(14B)	107.9	C(5B)-C(4B)-H(4BA)	119.7
C(16)-C(15)-C(14)	123.95(19)	C(6B)-C(5B)-C(4B)	120.5(2)
C(16)-C(15)-C(10)	119.94(19)	C(6B)-C(5B)-H(5BA)	119.8
C(14)-C(15)-C(10)	116.10(18)	C(4B)-C(5B)-H(5BA)	119.8
C(15)-C(16)-C(17)	126.4(2)	C(5B)-C(6B)-C(1B)	118.33(19)
C(15)-C(16)-H(16A)	116.8	C(5B)-C(6B)-C(7B)	122.67(19)
C(17)-C(16)-H(16A)	116.8	C(1B)-C(6B)-C(7B)	119.0(2)
C(16)-C(17)-H(17A)	109.5	C(8B)-C(7B)-C(6B)	125.0(2)
C(16)-C(17)-H(17B)	109.5	C(8B)-C(7B)-H(7BA)	117.5
H(17A)-C(17)-H(17B)	109.5	C(6B)-C(7B)-H(7BA)	117.5
C(16)-C(17)-H(17C)	109.5	C(7B)-C(8B)-C(9B)	123.4(2)
H(17A)-C(17)-H(17C)	109.5	C(7B)-C(8B)-H(8BA)	118.3
H(17B)-C(17)-H(17C)	109.5	C(9B)-C(8B)-H(8BA)	118.3
O(2)-C(18)-O(3)	124.8(2)	O(1B)-C(9B)-C(8B)	110.44(16)
O(2)-C(18)-C(9)	123.2(2)	O(1B)-C(9B)-C(18B)	107.68(16)
O(3)-C(18)-C(9)	111.93(17)	C(8B)-C(9B)-C(18B)	108.20(16)
O(3)-C(19)-H(19A)	109.5	O(1B)-C(9B)-C(10B)	112.41(17)

C(8B)-C(9B)-C(10B)	110.07(17)	C(13B)-C(14B)-H(14C)	109.4
C(18B)-C(9B)-C(10B)	107.89(15)	C(15B)-C(14B)-H(14D)	109.4
C(15B)-C(10B)-C(11B)	111.44(17)	C(13B)-C(14B)-H(14D)	109.4
C(15B)-C(10B)-C(9B)	112.03(16)	H(14C)-C(14B)-H(14D)	108.0
C(11B)-C(10B)-C(9B)	112.95(16)	C(16B)-C(15B)-C(14B)	124.08(19)
C(15B)-C(10B)-H(10B)	106.6	C(16B)-C(15B)-C(10B)	120.13(19)
C(11B)-C(10B)-H(10B)	106.6	C(14B)-C(15B)-C(10B)	115.79(18)
C(9B)-C(10B)-H(10B)	106.6	C(15B)-C(16B)-C(17B)	127.1(2)
C(12B)-C(11B)-C(10B)	115.12(19)	C(15B)-C(16B)-H(16B)	116.4
C(12B)-C(11B)-H(11C)	108.5	C(17B)-C(16B)-H(16B)	116.4
C(10B)-C(11B)-H(11C)	108.5	C(16B)-C(17B)-H(17D)	109.5
C(12B)-C(11B)-H(11D)	108.5	C(16B)-C(17B)-H(17E)	109.5
C(10B)-C(11B)-H(11D)	108.5	H(17D)-C(17B)-H(17E)	109.5
H(11C)-C(11B)-H(11D)	107.5	C(16B)-C(17B)-H(17F)	109.5
C(13B)-C(12B)-C(11B)	110.50(18)	H(17D)-C(17B)-H(17F)	109.5
C(13B)-C(12B)-H(12C)	109.6	H(17E)-C(17B)-H(17F)	109.5
C(11B)-C(12B)-H(12C)	109.6	O(2B)-C(18B)-O(3B)	124.8(2)
C(13B)-C(12B)-H(12D)	109.6	O(2B)-C(18B)-C(9B)	122.9(2)
C(11B)-C(12B)-H(12D)	109.6	O(3B)-C(18B)-C(9B)	112.39(17)
H(12C)-C(12B)-H(12D)	108.1	O(3B)-C(19B)-H(19D)	109.5
C(12B)-C(13B)-C(14B)	111.24(19)	O(3B)-C(19B)-H(19E)	109.5
C(12B)-C(13B)-H(13C)	109.4	H(19D)-C(19B)-H(19E)	109.5
C(14B)-C(13B)-H(13C)	109.4	O(3B)-C(19B)-H(19F)	109.5
C(12B)-C(13B)-H(13D)	109.4	H(19D)-C(19B)-H(19F)	109.5
C(14B)-C(13B)-H(13D)	109.4	H(19E)-C(19B)-H(19F)	109.5
H(13C)-C(13B)-H(13D)	108.0	C(9B)-O(1B)-H(1BB)	109.5
C(15B)-C(14B)-C(13B)	111.1(2)	C(18B)-O(3B)-C(19B)	115.55(18)
C(15B)-C(14B)-H(14C)	109.4		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **181**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* 2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	36(1)	29(1)	35(1)	8(1)	0(1)	2(1)
C(2)	48(2)	25(1)	44(2)	13(1)	1(1)	0(1)
C(3)	47(1)	28(1)	38(1)	7(1)	-1(1)	-10(1)
C(4)	39(1)	36(1)	36(1)	11(1)	-7(1)	-10(1)
C(5)	38(1)	26(1)	35(1)	10(1)	-3(1)	-2(1)
C(6)	34(1)	25(1)	23(1)	5(1)	6(1)	-1(1)
C(7)	31(1)	29(1)	25(1)	8(1)	-2(1)	-1(1)
C(8)	28(1)	27(1)	24(1)	6(1)	0(1)	-2(1)
C(9)	22(1)	26(1)	24(1)	6(1)	0(1)	1(1)
C(10)	24(1)	25(1)	26(1)	5(1)	-2(1)	-1(1)
C(11)	42(1)	31(1)	23(1)	7(1)	-3(1)	-1(1)
C(12)	46(2)	43(1)	28(1)	10(1)	9(1)	11(1)
C(13)	34(1)	46(1)	46(2)	21(1)	13(1)	3(1)
C(14)	28(1)	33(1)	45(2)	16(1)	-2(1)	-4(1)
C(15)	26(1)	24(1)	27(1)	10(1)	-3(1)	-1(1)
C(16)	39(1)	24(1)	32(1)	7(1)	-1(1)	-1(1)
C(17)	67(2)	29(1)	48(2)	-2(1)	-2(2)	-6(1)
C(18)	29(1)	21(1)	29(1)	10(1)	-3(1)	-3(1)
C(19)	41(1)	32(1)	29(1)	3(1)	8(1)	3(1)
O(1)	23(1)	28(1)	36(1)	9(1)	-2(1)	2(1)
O(2)	37(1)	45(1)	29(1)	8(1)	-9(1)	0(1)
O(3)	31(1)	29(1)	25(1)	4(1)	2(1)	1(1)
C(1B)	39(1)	30(1)	34(1)	7(1)	4(1)	2(1)
C(2B)	52(2)	26(1)	37(1)	-1(1)	3(1)	-1(1)
C(3B)	53(2)	30(1)	41(2)	7(1)	-4(1)	-15(1)
C(4B)	41(1)	38(1)	39(1)	8(1)	2(1)	-11(1)
C(5B)	39(1)	29(1)	33(1)	3(1)	3(1)	-3(1)
C(6B)	33(1)	28(1)	24(1)	10(1)	-5(1)	-2(1)
C(7B)	32(1)	27(1)	23(1)	7(1)	-1(1)	-1(1)

C(8B)	26(1)	28(1)	24(1)	8(1)	-1(1)	0(1)
C(9B)	25(1)	25(1)	26(1)	5(1)	2(1)	1(1)
C(10B)	23(1)	24(1)	26(1)	6(1)	4(1)	0(1)
C(11B)	41(1)	32(1)	27(1)	9(1)	4(1)	3(1)
C(12B)	46(2)	47(1)	30(1)	11(1)	-3(1)	14(1)
C(13B)	33(1)	50(1)	36(1)	-2(1)	-9(1)	5(1)
C(14B)	28(1)	33(1)	41(1)	1(1)	-1(1)	-3(1)
C(15B)	26(1)	27(1)	25(1)	2(1)	4(1)	-3(1)
C(16B)	33(1)	26(1)	35(1)	6(1)	3(1)	1(1)
C(17B)	61(2)	33(1)	63(2)	17(1)	5(2)	-6(1)
C(18B)	30(1)	24(1)	25(1)	3(1)	1(1)	-4(1)
C(19B)	42(1)	38(1)	36(1)	18(1)	-4(1)	2(1)
O(1B)	25(1)	28(1)	31(1)	5(1)	3(1)	0(1)
O(2B)	37(1)	49(1)	32(1)	17(1)	7(1)	-2(1)
O(3B)	30(1)	31(1)	30(1)	12(1)	-1(1)	-1(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **181**.

	x	y	z	U(eq)
H(1A)	-3192	-11007	-1899	40
H(2A)	-5473	-12648	-2408	46
H(3A)	-9023	-12617	-3310	45
H(4A)	-10348	-10931	-3679	44
H(5A)	-8062	-9289	-3204	39
H(7A)	-2366	-9056	-1931	33
H(8A)	-6109	-7774	-2322	32
H(10A)	-5159	-5770	-2289	30
H(11A)	-3603	-7214	-3884	38
H(11B)	-3927	-5966	-4064	38
H(12A)	-380	-6638	-4840	46
H(12B)	397	-6966	-3694	46
H(13A)	2194	-5227	-3763	49
H(13B)	-286	-4681	-3902	49
H(14A)	1285	-5315	-1907	41
H(14B)	914	-4037	-2002	41
H(16A)	-4765	-4112	-986	38
H(17A)	-3211	-2429	-27	75
H(17B)	-1484	-2504	-1075	75
H(17C)	-759	-3055	-58	75
H(19A)	-8236	-5297	858	52
H(19B)	-5691	-4756	1103	52
H(19C)	-6263	-5954	1369	52
H(1B)	112	-6712	-1235	43
H(1BA)	-5853	-4072	-5144	41
H(2BA)	-3665	-2405	-4855	48
H(3BA)	-159	-2395	-5797	50
H(4BA)	1170	-4045	-7034	48
H(5BA)	-985	-5726	-7338	42

H(7BA)	-6640	-6034	-6189	33
H(8BA)	-2761	-7268	-7147	31
H(10B)	-3568	-9240	-8171	29
H(11C)	-5351	-7845	-9045	39
H(11D)	-4891	-9079	-9854	39
H(12C)	-9320	-8203	-8990	49
H(12D)	-8549	-8519	-10298	49
H(13C)	-8445	-10465	-10334	50
H(13D)	-10958	-9974	-9910	50
H(14C)	-9931	-9858	-7999	43
H(14D)	-9495	-11132	-8735	43
H(16B)	-3676	-10937	-7796	38
H(17D)	-4889	-12711	-7805	77
H(17E)	-6752	-12629	-8760	77
H(17F)	-7409	-12193	-7444	77
H(19D)	-647	-9810	-5258	55
H(19E)	-3174	-10382	-5364	55
H(19F)	-2696	-9213	-4435	55
H(1BB)	-8936	-8396	-6646	43

Table 6. Torsion angles [°] for compound **181**.

C(6)-C(1)-C(2)-C(3)	0.4(4)
C(1)-C(2)-C(3)-C(4)	-0.4(4)
C(2)-C(3)-C(4)-C(5)	1.0(4)
C(3)-C(4)-C(5)-C(6)	-1.5(4)
C(4)-C(5)-C(6)-C(1)	1.5(3)
C(4)-C(5)-C(6)-C(7)	-179.0(2)
C(2)-C(1)-C(6)-C(5)	-1.0(3)
C(2)-C(1)-C(6)-C(7)	179.5(2)
C(5)-C(6)-C(7)-C(8)	14.3(4)
C(1)-C(6)-C(7)-C(8)	-166.2(2)
C(6)-C(7)-C(8)-C(9)	177.0(2)
C(7)-C(8)-C(9)-O(1)	19.1(3)
C(7)-C(8)-C(9)-C(18)	-97.8(2)
C(7)-C(8)-C(9)-C(10)	143.5(2)
O(1)-C(9)-C(10)-C(15)	-63.7(2)
C(8)-C(9)-C(10)-C(15)	173.14(18)
C(18)-C(9)-C(10)-C(15)	55.1(2)
O(1)-C(9)-C(10)-C(11)	63.7(2)
C(8)-C(9)-C(10)-C(11)	-59.5(2)
C(18)-C(9)-C(10)-C(11)	-177.58(17)
C(15)-C(10)-C(11)-C(12)	45.0(2)
C(9)-C(10)-C(11)-C(12)	-82.0(2)
C(10)-C(11)-C(12)-C(13)	-52.9(3)
C(11)-C(12)-C(13)-C(14)	57.4(3)
C(12)-C(13)-C(14)-C(15)	-55.7(3)
C(13)-C(14)-C(15)-C(16)	-131.9(2)
C(13)-C(14)-C(15)-C(10)	48.6(2)
C(11)-C(10)-C(15)-C(16)	138.0(2)
C(9)-C(10)-C(15)-C(16)	-94.0(2)
C(11)-C(10)-C(15)-C(14)	-42.5(3)
C(9)-C(10)-C(15)-C(14)	85.5(2)
C(14)-C(15)-C(16)-C(17)	-3.4(4)
C(10)-C(15)-C(16)-C(17)	176.0(2)

O(1)-C(9)-C(18)-O(2)	3.3(2)
C(8)-C(9)-C(18)-O(2)	121.8(2)
C(10)-C(9)-C(18)-O(2)	-118.3(2)
O(1)-C(9)-C(18)-O(3)	-175.92(13)
C(8)-C(9)-C(18)-O(3)	-57.4(2)
C(10)-C(9)-C(18)-O(3)	62.53(19)
O(2)-C(18)-O(3)-C(19)	4.9(3)
C(9)-C(18)-O(3)-C(19)	-175.89(15)
C(6B)-C(1B)-C(2B)-C(3B)	0.1(4)
C(1B)-C(2B)-C(3B)-C(4B)	0.2(4)
C(2B)-C(3B)-C(4B)-C(5B)	-0.2(4)
C(3B)-C(4B)-C(5B)-C(6B)	-0.1(4)
C(4B)-C(5B)-C(6B)-C(1B)	0.4(3)
C(4B)-C(5B)-C(6B)-C(7B)	-179.9(2)
C(2B)-C(1B)-C(6B)-C(5B)	-0.4(3)
C(2B)-C(1B)-C(6B)-C(7B)	179.9(2)
C(5B)-C(6B)-C(7B)-C(8B)	16.5(3)
C(1B)-C(6B)-C(7B)-C(8B)	-163.8(2)
C(6B)-C(7B)-C(8B)-C(9B)	178.52(19)
C(7B)-C(8B)-C(9B)-O(1B)	17.5(3)
C(7B)-C(8B)-C(9B)-C(18B)	-100.1(2)
C(7B)-C(8B)-C(9B)-C(10B)	142.2(2)
O(1B)-C(9B)-C(10B)-C(15B)	-65.9(2)
C(8B)-C(9B)-C(10B)-C(15B)	170.57(17)
C(18B)-C(9B)-C(10B)-C(15B)	52.7(2)
O(1B)-C(9B)-C(10B)-C(11B)	61.0(2)
C(8B)-C(9B)-C(10B)-C(11B)	-62.6(2)
C(18B)-C(9B)-C(10B)-C(11B)	179.53(17)
C(15B)-C(10B)-C(11B)-C(12B)	45.6(3)
C(9B)-C(10B)-C(11B)-C(12B)	-81.5(2)
C(10B)-C(11B)-C(12B)-C(13B)	-52.2(3)
C(11B)-C(12B)-C(13B)-C(14B)	56.7(3)
C(12B)-C(13B)-C(14B)-C(15B)	-56.4(3)
C(13B)-C(14B)-C(15B)-C(16B)	-128.3(2)
C(13B)-C(14B)-C(15B)-C(10B)	51.3(2)

C(11B)-C(10B)-C(15B)-C(16B)	134.3(2)
C(9B)-C(10B)-C(15B)-C(16B)	-98.1(2)
C(11B)-C(10B)-C(15B)-C(14B)	-45.3(3)
C(9B)-C(10B)-C(15B)-C(14B)	82.4(2)
C(14B)-C(15B)-C(16B)-C(17B)	-2.0(4)
C(10B)-C(15B)-C(16B)-C(17B)	178.5(2)
O(1B)-C(9B)-C(18B)-O(2B)	3.6(2)
C(8B)-C(9B)-C(18B)-O(2B)	123.0(2)
C(10B)-C(9B)-C(18B)-O(2B)	-118.0(2)
O(1B)-C(9B)-C(18B)-O(3B)	-176.29(16)
C(8B)-C(9B)-C(18B)-O(3B)	-56.9(2)
C(10B)-C(9B)-C(18B)-O(3B)	62.15(19)
O(2B)-C(18B)-O(3B)-C(19B)	6.3(3)
C(9B)-C(18B)-O(3B)-C(19B)	-173.82(17)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound **181** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	\angle (DHA)
O(1)-H(1B)...O(3)#1	0.84	2.62	3.361(2)	148.5
O(1B)-H(1BB)...O(3B)#2	0.84	2.62	3.354(2)	146.7

Symmetry transformations used to generate equivalent atoms:

#1 $x+1, y, z$ #2 $x-1, y, z$

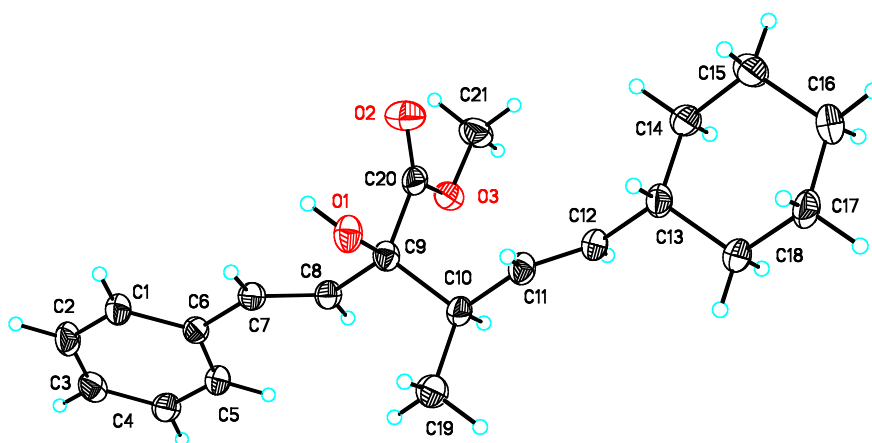
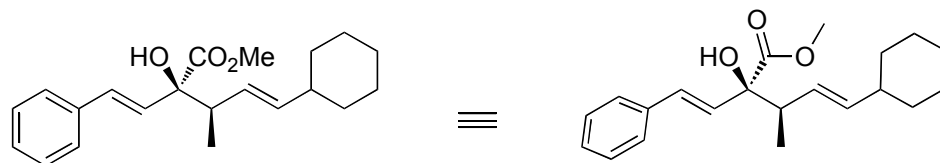
6. Crystal structure of compound (2*R*, 3*R*)-184

Table 1. Crystal data and structure refinement for compound **(2R, 3R)-184**.

Compound	(2R, 3R)-184	
Empirical formula	C ₂₁ H ₂₈ O ₃	
Formula weight	328.43	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 5.5849(4) Å	α = 116.623(5)°.
	b = 9.4558(6) Å	β = 94.611(6)°.
	c = 9.9361(7) Å	γ = 90.704(4)°.
Volume	466.88(6) Å ³	
Z	1	
Density (calculated)	1.168 Mg/m ³	
Absorption coefficient	0.604 mm ⁻¹	
F(000)	178	
Crystal size	0.25 x 0.18 x 0.09 mm ³	
Theta range for data collection	5.00 to 67.44°.	
Index ranges	-6<=h<=6, -11<=k<=11, -11<=l<=11	
Reflections collected	3568	
Independent reflections	1969 [R(int) = 0.0221]	
Completeness to theta = 67.44°	82.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9477 and 0.8637	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	1969 / 3 / 217	
Goodness-of-fit on F ²	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0448, wR2 = 0.1175	
R indices (all data)	R1 = 0.0484, wR2 = 0.1214	
Absolute structure parameter	0.0(3)	
Largest diff. peak and hole	0.200 and -0.203 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R, 3R**)-**184**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	-2307(5)	-9699(3)	-4730(4)	36(1)
C(2)	-640(6)	-10279(4)	-3999(4)	41(1)
C(3)	1493(5)	-9456(4)	-3307(4)	39(1)
C(4)	2021(5)	-8038(4)	-3343(4)	37(1)
C(5)	392(5)	-7454(3)	-4079(4)	33(1)
C(6)	-1791(5)	-8280(3)	-4788(3)	30(1)
C(7)	-3563(5)	-7712(3)	-5591(3)	30(1)
C(8)	-3141(4)	-6641(3)	-6066(3)	29(1)
C(9)	-5058(4)	-6134(3)	-6907(3)	29(1)
C(10)	-5068(4)	-4302(3)	-6244(3)	30(1)
C(11)	-6930(5)	-3852(3)	-7143(3)	32(1)
C(12)	-6537(5)	-3162(3)	-8004(3)	32(1)
C(13)	-8505(5)	-2727(3)	-8861(3)	33(1)
C(14)	-8172(6)	-3432(3)	-10550(3)	40(1)
C(15)	-10283(6)	-3052(4)	-11404(4)	47(1)
C(16)	-10576(6)	-1272(4)	-10739(4)	46(1)
C(17)	-10812(5)	-540(4)	-9054(4)	41(1)
C(18)	-8694(5)	-939(3)	-8215(4)	37(1)
C(19)	-5555(6)	-3570(4)	-4580(4)	41(1)
C(20)	-4571(5)	-6847(3)	-8577(4)	31(1)
C(21)	-1845(6)	-6927(4)	-10283(4)	44(1)
O(1)	-7369(3)	-6737(2)	-6853(3)	36(1)
O(2)	-5972(4)	-7755(3)	-9582(3)	49(1)
O(3)	-2447(3)	-6335(2)	-8750(2)	35(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound (**2R**, **3R**)-**184**.

C(1)-C(6)	1.396(4)	C(15)-H(15A)	0.9900
C(1)-C(2)	1.399(4)	C(15)-H(15B)	0.9900
C(1)-H(1A)	0.9500	C(16)-C(17)	1.516(5)
C(2)-C(3)	1.365(5)	C(16)-H(16A)	0.9900
C(2)-H(2A)	0.9500	C(16)-H(16B)	0.9900
C(3)-C(4)	1.387(4)	C(17)-C(18)	1.540(4)
C(3)-H(3A)	0.9500	C(17)-H(17A)	0.9900
C(4)-C(5)	1.390(4)	C(17)-H(17B)	0.9900
C(4)-H(4A)	0.9500	C(18)-H(18A)	0.9900
C(5)-C(6)	1.393(4)	C(18)-H(18B)	0.9900
C(5)-H(5A)	0.9500	C(19)-H(19A)	0.9800
C(6)-C(7)	1.475(4)	C(19)-H(19B)	0.9800
C(7)-C(8)	1.321(4)	C(19)-H(19C)	0.9800
C(7)-H(7A)	0.9500	C(20)-O(2)	1.198(4)
C(8)-C(9)	1.517(3)	C(20)-O(3)	1.329(3)
C(8)-H(8A)	0.9500	C(21)-O(3)	1.439(4)
C(9)-O(1)	1.419(3)	C(21)-H(21A)	0.9800
C(9)-C(20)	1.535(4)	C(21)-H(21B)	0.9800
C(9)-C(10)	1.553(3)	C(21)-H(21C)	0.9800
C(10)-C(11)	1.504(3)	O(1)-H(1B)	0.8400
C(10)-C(19)	1.529(4)		
C(10)-H(10A)	1.0000	C(6)-C(1)-C(2)	120.4(3)
C(11)-C(12)	1.317(4)	C(6)-C(1)-H(1A)	119.8
C(11)-H(11A)	0.9500	C(2)-C(1)-H(1A)	119.8
C(12)-C(13)	1.508(4)	C(3)-C(2)-C(1)	120.7(3)
C(12)-H(12A)	0.9500	C(3)-C(2)-H(2A)	119.6
C(13)-C(18)	1.524(4)	C(1)-C(2)-H(2A)	119.6
C(13)-C(14)	1.531(4)	C(2)-C(3)-C(4)	119.6(3)
C(13)-H(13A)	1.0000	C(2)-C(3)-H(3A)	120.2
C(14)-C(15)	1.537(4)	C(4)-C(3)-H(3A)	120.2
C(14)-H(14A)	0.9900	C(3)-C(4)-C(5)	120.3(3)
C(14)-H(14B)	0.9900	C(3)-C(4)-H(4A)	119.8
C(15)-C(16)	1.524(4)	C(5)-C(4)-H(4A)	119.8

C(4)-C(5)-C(6)	120.7(2)	C(14)-C(13)-H(13A)	107.7
C(4)-C(5)-H(5A)	119.7	C(13)-C(14)-C(15)	110.5(2)
C(6)-C(5)-H(5A)	119.7	C(13)-C(14)-H(14A)	109.5
C(5)-C(6)-C(1)	118.3(2)	C(15)-C(14)-H(14A)	109.5
C(5)-C(6)-C(7)	122.5(2)	C(13)-C(14)-H(14B)	109.5
C(1)-C(6)-C(7)	119.2(2)	C(15)-C(14)-H(14B)	109.5
C(8)-C(7)-C(6)	126.2(2)	H(14A)-C(14)-H(14B)	108.1
C(8)-C(7)-H(7A)	116.9	C(16)-C(15)-C(14)	111.2(3)
C(6)-C(7)-H(7A)	116.9	C(16)-C(15)-H(15A)	109.4
C(7)-C(8)-C(9)	123.1(2)	C(14)-C(15)-H(15A)	109.4
C(7)-C(8)-H(8A)	118.4	C(16)-C(15)-H(15B)	109.4
C(9)-C(8)-H(8A)	118.4	C(14)-C(15)-H(15B)	109.4
O(1)-C(9)-C(8)	110.6(2)	H(15A)-C(15)-H(15B)	108.0
O(1)-C(9)-C(20)	107.2(2)	C(17)-C(16)-C(15)	111.9(2)
C(8)-C(9)-C(20)	108.6(2)	C(17)-C(16)-H(16A)	109.2
O(1)-C(9)-C(10)	109.1(2)	C(15)-C(16)-H(16A)	109.2
C(8)-C(9)-C(10)	111.7(2)	C(17)-C(16)-H(16B)	109.2
C(20)-C(9)-C(10)	109.49(18)	C(15)-C(16)-H(16B)	109.2
C(11)-C(10)-C(19)	110.6(2)	H(16A)-C(16)-H(16B)	107.9
C(11)-C(10)-C(9)	110.0(2)	C(16)-C(17)-C(18)	111.1(3)
C(19)-C(10)-C(9)	110.3(2)	C(16)-C(17)-H(17A)	109.4
C(11)-C(10)-H(10A)	108.6	C(18)-C(17)-H(17A)	109.4
C(19)-C(10)-H(10A)	108.6	C(16)-C(17)-H(17B)	109.4
C(9)-C(10)-H(10A)	108.6	C(18)-C(17)-H(17B)	109.4
C(12)-C(11)-C(10)	126.9(2)	H(17A)-C(17)-H(17B)	108.0
C(12)-C(11)-H(11A)	116.5	C(13)-C(18)-C(17)	110.7(2)
C(10)-C(11)-H(11A)	116.5	C(13)-C(18)-H(18A)	109.5
C(11)-C(12)-C(13)	124.0(2)	C(17)-C(18)-H(18A)	109.5
C(11)-C(12)-H(12A)	118.0	C(13)-C(18)-H(18B)	109.5
C(13)-C(12)-H(12A)	118.0	C(17)-C(18)-H(18B)	109.5
C(12)-C(13)-C(18)	112.1(2)	H(18A)-C(18)-H(18B)	108.1
C(12)-C(13)-C(14)	111.8(2)	C(10)-C(19)-H(19A)	109.5
C(18)-C(13)-C(14)	109.8(2)	C(10)-C(19)-H(19B)	109.5
C(12)-C(13)-H(13A)	107.7	H(19A)-C(19)-H(19B)	109.5
C(18)-C(13)-H(13A)	107.7	C(10)-C(19)-H(19C)	109.5

H(19A)-C(19)-H(19C)	109.5	H(21A)-C(21)-H(21B)	109.5
H(19B)-C(19)-H(19C)	109.5	O(3)-C(21)-H(21C)	109.5
O(2)-C(20)-O(3)	125.3(3)	H(21A)-C(21)-H(21C)	109.5
O(2)-C(20)-C(9)	122.8(2)	H(21B)-C(21)-H(21C)	109.5
O(3)-C(20)-C(9)	111.9(2)	C(9)-O(1)-H(1B)	109.5
O(3)-C(21)-H(21A)	109.5	C(20)-O(3)-C(21)	115.9(2)
O(3)-C(21)-H(21B)	109.5		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R**, **3R**)-**184**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* 2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	44(1)	30(1)	38(2)	19(1)	5(1)	4(1)
C(2)	58(2)	32(2)	44(2)	24(1)	11(2)	14(1)
C(3)	48(2)	38(2)	35(2)	20(1)	7(1)	19(1)
C(4)	41(1)	33(1)	37(2)	15(1)	3(1)	8(1)
C(5)	38(1)	29(1)	37(2)	17(1)	3(1)	5(1)
C(6)	40(1)	25(1)	27(2)	12(1)	7(1)	9(1)
C(7)	31(1)	28(1)	30(2)	13(1)	2(1)	5(1)
C(8)	29(1)	27(1)	32(2)	14(1)	3(1)	6(1)
C(9)	25(1)	30(1)	34(2)	18(1)	-1(1)	3(1)
C(10)	34(1)	24(1)	34(2)	15(1)	1(1)	4(1)
C(11)	33(1)	28(1)	37(2)	17(1)	3(1)	8(1)
C(12)	37(1)	26(1)	36(2)	15(1)	3(1)	7(1)
C(13)	37(1)	28(1)	38(2)	19(1)	3(1)	6(1)
C(14)	52(2)	30(2)	33(2)	11(1)	2(1)	14(1)
C(15)	59(2)	45(2)	34(2)	16(2)	-4(2)	12(2)
C(16)	58(2)	41(2)	49(2)	30(2)	-2(2)	9(1)
C(17)	45(1)	27(1)	52(2)	21(1)	-1(1)	10(1)
C(18)	45(1)	27(1)	38(2)	15(1)	2(1)	9(1)
C(19)	51(2)	36(2)	37(2)	16(1)	5(1)	13(1)
C(20)	33(1)	25(1)	36(2)	15(1)	-3(1)	5(1)
C(21)	52(2)	49(2)	30(2)	16(1)	8(1)	7(1)
O(1)	29(1)	37(1)	49(1)	27(1)	2(1)	3(1)
O(2)	48(1)	51(1)	38(1)	12(1)	-5(1)	-6(1)
O(3)	36(1)	38(1)	31(1)	16(1)	2(1)	4(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R, 3R**)-**184**.

	x	y	z	U(eq)
H(1A)	-3799	-10273	-5188	43
H(2A)	-996	-11257	-3984	50
H(3A)	2609	-9853	-2804	46
H(4A)	3504	-7461	-2863	44
H(5A)	773	-6481	-4097	40
H(7A)	-5161	-8159	-5785	35
H(8A)	-1561	-6166	-5872	35
H(10A)	-3450	-3890	-6316	36
H(11A)	-8563	-4093	-7084	38
H(12A)	-4917	-2922	-8091	39
H(13A)	-10065	-3183	-8758	39
H(14A)	-8075	-4595	-10968	48
H(14B)	-6647	-2992	-10688	48
H(15A)	-9997	-3470	-12483	56
H(15B)	-11784	-3582	-11348	56
H(16A)	-9165	-762	-10922	56
H(16B)	-12025	-1071	-11256	56
H(17A)	-12341	-940	-8876	49
H(17B)	-10859	625	-8649	49
H(18A)	-7178	-455	-8314	44
H(18B)	-8928	-490	-7127	44
H(19A)	-5565	-2416	-4177	62
H(19B)	-4293	-3841	-4005	62
H(19C)	-7121	-3984	-4492	62
H(21A)	-257	-6478	-10288	66
H(21B)	-3050	-6621	-10863	66
H(21C)	-1818	-8084	-10743	66
H(1B)	-7372	-7727	-7209	54

Table 6. Torsion angles [°] for compound (**2R, 3R**)-184.

C(6)-C(1)-C(2)-C(3)	1.3(4)
C(1)-C(2)-C(3)-C(4)	-0.7(5)
C(2)-C(3)-C(4)-C(5)	0.0(5)
C(3)-C(4)-C(5)-C(6)	0.0(4)
C(4)-C(5)-C(6)-C(1)	0.6(4)
C(4)-C(5)-C(6)-C(7)	-179.5(3)
C(2)-C(1)-C(6)-C(5)	-1.2(4)
C(2)-C(1)-C(6)-C(7)	178.9(3)
C(5)-C(6)-C(7)-C(8)	17.8(4)
C(1)-C(6)-C(7)-C(8)	-162.3(3)
C(6)-C(7)-C(8)-C(9)	179.1(2)
C(7)-C(8)-C(9)-O(1)	10.7(4)
C(7)-C(8)-C(9)-C(20)	-106.7(3)
C(7)-C(8)-C(9)-C(10)	132.4(3)
O(1)-C(9)-C(10)-C(11)	-59.4(3)
C(8)-C(9)-C(10)-C(11)	178.0(2)
C(20)-C(9)-C(10)-C(11)	57.7(2)
O(1)-C(9)-C(10)-C(19)	62.8(3)
C(8)-C(9)-C(10)-C(19)	-59.8(3)
C(20)-C(9)-C(10)-C(19)	179.9(2)
C(19)-C(10)-C(11)-C(12)	124.9(3)
C(9)-C(10)-C(11)-C(12)	-113.0(3)
C(10)-C(11)-C(12)-C(13)	-179.2(3)
C(11)-C(12)-C(13)-C(18)	110.9(3)
C(11)-C(12)-C(13)-C(14)	-125.4(3)
C(12)-C(13)-C(14)-C(15)	176.6(2)
C(18)-C(13)-C(14)-C(15)	-58.3(3)
C(13)-C(14)-C(15)-C(16)	56.2(3)
C(14)-C(15)-C(16)-C(17)	-54.3(4)
C(15)-C(16)-C(17)-C(18)	54.3(4)
C(12)-C(13)-C(18)-C(17)	-176.6(2)
C(14)-C(13)-C(18)-C(17)	58.5(3)
C(16)-C(17)-C(18)-C(13)	-56.6(3)

O(1)-C(9)-C(20)-O(2)	-0.9(3)
C(8)-C(9)-C(20)-O(2)	118.7(3)
C(10)-C(9)-C(20)-O(2)	-119.1(3)
O(1)-C(9)-C(20)-O(3)	179.2(2)
C(8)-C(9)-C(20)-O(3)	-61.3(2)
C(10)-C(9)-C(20)-O(3)	60.9(2)
O(2)-C(20)-O(3)-C(21)	0.7(4)
C(9)-C(20)-O(3)-C(21)	-179.3(2)

Symmetry transformations used to generate equivalent atoms:

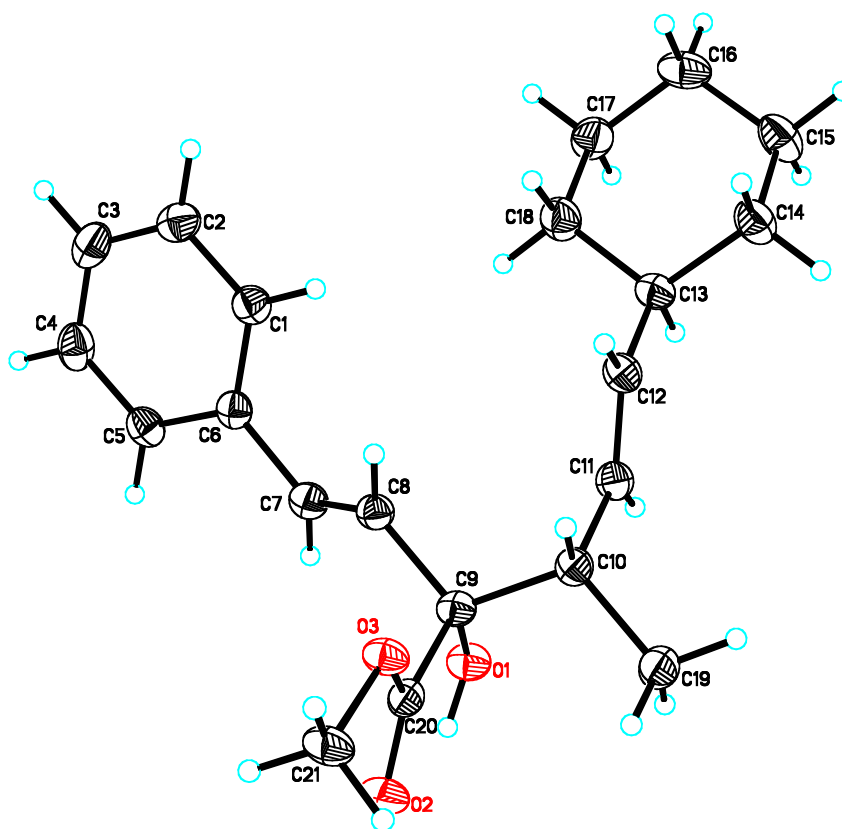
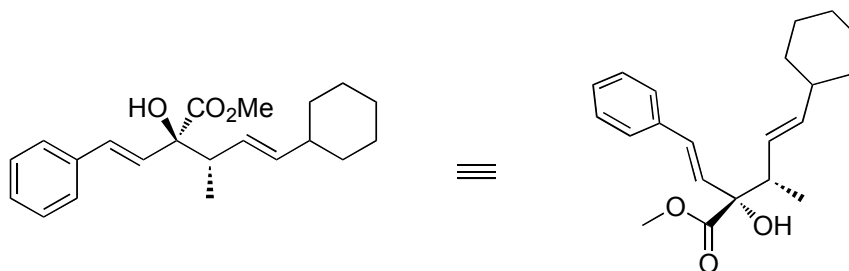
7. Crystal structure of compound (2*R*, 3*S*)-184

Table 1. Crystal data and structure refinement for compound **(2R, 3S)-184**.

Compound	(2R, 3S)-184	
Empirical formula	C ₂₁ H ₂₈ O ₃	
Formula weight	328.43	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.4496(4) Å	a = 90°.
	b = 13.7116(8) Å	b = 90°.
	c = 25.4795(15) Å	g = 90°.
Volume	1903.9(2) Å ³	
Z	4	
Density (calculated)	1.146 Mg/m ³	
Absorption coefficient	0.592 mm ⁻¹	
F(000)	712	
Crystal size	0.41 x 0.09 x 0.07 mm ³	
Theta range for data collection	3.47 to 65.51°.	
Index ranges	-6<=h<=4, -16<=k<=16, -29<=l<=30	
Reflections collected	16001	
Independent reflections	3218 [R(int) = 0.0341]	
Completeness to theta = 65.51°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3218 / 0 / 218	
Goodness-of-fit on F ²	1.176	
Final R indices [I>2sigma(I)]	R1 = 0.0356, wR2 = 0.0832	
R indices (all data)	R1 = 0.0527, wR2 = 0.0970	
Absolute structure parameter	0.1(3)	
Extinction coefficient	0.0037(4)	
Largest diff. peak and hole	0.176 and -0.195 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2R, 3S)-184**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	8707(4)	4366(2)	9942(1)	39(1)
C(2)	9687(5)	4390(2)	10444(1)	45(1)
C(3)	8532(5)	3911(2)	10849(1)	50(1)
C(4)	6391(5)	3402(2)	10756(1)	48(1)
C(5)	5397(4)	3381(2)	10258(1)	40(1)
C(6)	6552(4)	3852(1)	9840(1)	34(1)
C(7)	5471(4)	3795(1)	9311(1)	37(1)
C(8)	6693(4)	3878(1)	8867(1)	34(1)
C(9)	5552(4)	3836(1)	8328(1)	32(1)
C(10)	6691(4)	4619(1)	7963(1)	35(1)
C(11)	6344(4)	5612(1)	8204(1)	37(1)
C(12)	8112(4)	6139(1)	8411(1)	37(1)
C(13)	7841(4)	7110(1)	8676(1)	38(1)
C(14)	9447(5)	7891(2)	8415(1)	50(1)
C(15)	9342(5)	8861(2)	8704(1)	56(1)
C(16)	10009(5)	8744(2)	9277(1)	55(1)
C(17)	8346(5)	8008(2)	9538(1)	52(1)
C(18)	8466(5)	7028(2)	9258(1)	49(1)
C(19)	5614(4)	4556(2)	7408(1)	45(1)
C(20)	5968(4)	2821(1)	8100(1)	33(1)
C(21)	8802(4)	1616(1)	7852(1)	42(1)
O(1)	2969(3)	3980(1)	8360(1)	40(1)
O(2)	4317(3)	2279(1)	7980(1)	45(1)
O(3)	8343(3)	2590(1)	8052(1)	36(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound (**2R, 3S**)-184.

C(1)-C(2)	1.387(3)	C(15)-H(15A)	0.9900
C(1)-C(6)	1.393(3)	C(15)-H(15B)	0.9900
C(1)-H(1A)	0.9500	C(16)-C(17)	1.511(3)
C(2)-C(3)	1.376(3)	C(16)-H(16A)	0.9900
C(2)-H(2A)	0.9500	C(16)-H(16B)	0.9900
C(3)-C(4)	1.380(3)	C(17)-C(18)	1.523(3)
C(3)-H(3A)	0.9500	C(17)-H(17A)	0.9900
C(4)-C(5)	1.379(3)	C(17)-H(17B)	0.9900
C(4)-H(4A)	0.9500	C(18)-H(18A)	0.9900
C(5)-C(6)	1.395(3)	C(18)-H(18B)	0.9900
C(5)-H(5A)	0.9500	C(19)-H(19A)	0.9800
C(6)-C(7)	1.473(2)	C(19)-H(19B)	0.9800
C(7)-C(8)	1.318(3)	C(19)-H(19C)	0.9800
C(7)-H(7A)	0.9500	C(20)-O(2)	1.207(2)
C(8)-C(9)	1.510(2)	C(20)-O(3)	1.338(2)
C(8)-H(8A)	0.9500	C(21)-O(3)	1.451(2)
C(9)-O(1)	1.424(2)	C(21)-H(21A)	0.9800
C(9)-C(20)	1.525(3)	C(21)-H(21B)	0.9800
C(9)-C(10)	1.549(3)	C(21)-H(21C)	0.9800
C(10)-C(11)	1.506(3)	O(1)-H(1B)	0.8400
C(10)-C(19)	1.533(3)		
C(10)-H(10A)	1.0000	C(2)-C(1)-C(6)	120.52(19)
C(11)-C(12)	1.315(3)	C(2)-C(1)-H(1A)	119.7
C(11)-H(11A)	0.9500	C(6)-C(1)-H(1A)	119.7
C(12)-C(13)	1.500(3)	C(3)-C(2)-C(1)	120.3(2)
C(12)-H(12A)	0.9500	C(3)-C(2)-H(2A)	119.9
C(13)-C(18)	1.527(3)	C(1)-C(2)-H(2A)	119.9
C(13)-C(14)	1.534(3)	C(2)-C(3)-C(4)	119.93(19)
C(13)-H(13A)	1.0000	C(2)-C(3)-H(3A)	120.0
C(14)-C(15)	1.522(3)	C(4)-C(3)-H(3A)	120.0
C(14)-H(14A)	0.9900	C(5)-C(4)-C(3)	120.1(2)
C(14)-H(14B)	0.9900	C(5)-C(4)-H(4A)	120.0
C(15)-C(16)	1.512(3)	C(3)-C(4)-H(4A)	120.0

C(4)-C(5)-C(6)	121.0(2)	C(14)-C(13)-H(13A)	108.2
C(4)-C(5)-H(5A)	119.5	C(15)-C(14)-C(13)	112.27(18)
C(6)-C(5)-H(5A)	119.5	C(15)-C(14)-H(14A)	109.2
C(1)-C(6)-C(5)	118.22(17)	C(13)-C(14)-H(14A)	109.2
C(1)-C(6)-C(7)	122.28(17)	C(15)-C(14)-H(14B)	109.2
C(5)-C(6)-C(7)	119.50(19)	C(13)-C(14)-H(14B)	109.2
C(8)-C(7)-C(6)	125.4(2)	H(14A)-C(14)-H(14B)	107.9
C(8)-C(7)-H(7A)	117.3	C(16)-C(15)-C(14)	111.4(2)
C(6)-C(7)-H(7A)	117.3	C(16)-C(15)-H(15A)	109.3
C(7)-C(8)-C(9)	124.8(2)	C(14)-C(15)-H(15A)	109.3
C(7)-C(8)-H(8A)	117.6	C(16)-C(15)-H(15B)	109.3
C(9)-C(8)-H(8A)	117.6	C(14)-C(15)-H(15B)	109.3
O(1)-C(9)-C(8)	110.42(16)	H(15A)-C(15)-H(15B)	108.0
O(1)-C(9)-C(20)	107.19(16)	C(17)-C(16)-C(15)	110.6(2)
C(8)-C(9)-C(20)	108.66(15)	C(17)-C(16)-H(16A)	109.5
O(1)-C(9)-C(10)	109.60(16)	C(15)-C(16)-H(16A)	109.5
C(8)-C(9)-C(10)	110.78(16)	C(17)-C(16)-H(16B)	109.5
C(20)-C(9)-C(10)	110.11(15)	C(15)-C(16)-H(16B)	109.5
C(11)-C(10)-C(19)	112.23(16)	H(16A)-C(16)-H(16B)	108.1
C(11)-C(10)-C(9)	109.36(15)	C(16)-C(17)-C(18)	110.97(19)
C(19)-C(10)-C(9)	111.16(17)	C(16)-C(17)-H(17A)	109.4
C(11)-C(10)-H(10A)	108.0	C(18)-C(17)-H(17A)	109.4
C(19)-C(10)-H(10A)	108.0	C(16)-C(17)-H(17B)	109.4
C(9)-C(10)-H(10A)	108.0	C(18)-C(17)-H(17B)	109.4
C(12)-C(11)-C(10)	124.7(2)	H(17A)-C(17)-H(17B)	108.0
C(12)-C(11)-H(11A)	117.7	C(17)-C(18)-C(13)	112.35(17)
C(10)-C(11)-H(11A)	117.7	C(17)-C(18)-H(18A)	109.1
C(11)-C(12)-C(13)	126.6(2)	C(13)-C(18)-H(18A)	109.1
C(11)-C(12)-H(12A)	116.7	C(17)-C(18)-H(18B)	109.1
C(13)-C(12)-H(12A)	116.7	C(13)-C(18)-H(18B)	109.1
C(12)-C(13)-C(18)	110.45(16)	H(18A)-C(18)-H(18B)	107.9
C(12)-C(13)-C(14)	111.61(17)	C(10)-C(19)-H(19A)	109.5
C(18)-C(13)-C(14)	110.21(19)	C(10)-C(19)-H(19B)	109.5
C(12)-C(13)-H(13A)	108.2	H(19A)-C(19)-H(19B)	109.5
C(18)-C(13)-H(13A)	108.2	C(10)-C(19)-H(19C)	109.5

H(19A)-C(19)-H(19C)	109.5	H(21A)-C(21)-H(21B)	109.5
H(19B)-C(19)-H(19C)	109.5	O(3)-C(21)-H(21C)	109.5
O(2)-C(20)-O(3)	123.51(18)	H(21A)-C(21)-H(21C)	109.5
O(2)-C(20)-C(9)	123.23(19)	H(21B)-C(21)-H(21C)	109.5
O(3)-C(20)-C(9)	113.26(17)	C(9)-O(1)-H(1B)	109.5
O(3)-C(21)-H(21A)	109.5	C(20)-O(3)-C(21)	114.62(16)
O(3)-C(21)-H(21B)	109.5		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R**, **3S**)-**184**. The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^* 2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	42(2)	37(1)	38(1)	-2(1)	2(1)	0(1)
C(2)	42(2)	44(1)	49(1)	-8(1)	-7(1)	6(1)
C(3)	64(2)	48(1)	37(1)	-3(1)	-8(1)	16(1)
C(4)	68(2)	42(1)	35(1)	3(1)	10(1)	8(1)
C(5)	45(2)	34(1)	41(1)	-2(1)	8(1)	-1(1)
C(6)	39(1)	29(1)	34(1)	-3(1)	3(1)	6(1)
C(7)	35(1)	34(1)	40(1)	-3(1)	1(1)	1(1)
C(8)	33(1)	31(1)	37(1)	-2(1)	-3(1)	1(1)
C(9)	24(1)	34(1)	38(1)	-3(1)	-2(1)	2(1)
C(10)	37(1)	32(1)	35(1)	-1(1)	-1(1)	3(1)
C(11)	38(1)	33(1)	39(1)	0(1)	-1(1)	3(1)
C(12)	38(1)	32(1)	41(1)	-1(1)	3(1)	2(1)
C(13)	38(1)	33(1)	44(1)	-3(1)	-1(1)	-2(1)
C(14)	61(2)	36(1)	52(1)	-1(1)	8(1)	-6(1)
C(15)	69(2)	35(1)	63(1)	-4(1)	16(1)	-7(1)
C(16)	48(2)	44(1)	73(2)	-21(1)	-5(1)	-1(1)
C(17)	67(2)	44(1)	44(1)	-7(1)	-5(1)	4(1)
C(18)	63(2)	39(1)	46(1)	-3(1)	2(1)	0(1)
C(19)	57(2)	40(1)	38(1)	0(1)	-4(1)	2(1)
C(20)	35(1)	36(1)	29(1)	2(1)	-2(1)	0(1)
C(21)	43(2)	31(1)	52(1)	-13(1)	-1(1)	1(1)
O(1)	30(1)	41(1)	49(1)	-6(1)	-2(1)	3(1)
O(2)	38(1)	40(1)	58(1)	-10(1)	-4(1)	-8(1)
O(3)	30(1)	31(1)	46(1)	-9(1)	-1(1)	1(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R, 3S**)-184.

	x	y	z	U(eq)
H(1A)	9510	4702	9665	47
H(2A)	11162	4739	10508	54
H(3A)	9208	3931	11192	60
H(4A)	5601	3066	11034	58
H(5A)	3903	3041	10199	48
H(7A)	3752	3688	9288	44
H(8A)	8417	3972	8888	40
H(10A)	8494	4490	7938	41
H(11A)	4734	5877	8206	44
H(12A)	9725	5878	8391	44
H(13A)	6088	7318	8645	46
H(14A)	11168	7660	8405	59
H(14B)	8894	7987	8049	59
H(15A)	10492	9326	8537	67
H(15B)	7666	9135	8676	67
H(16A)	11735	8526	9307	66
H(16B)	9856	9381	9457	66
H(17A)	6637	8252	9534	62
H(17B)	8846	7924	9909	62
H(18A)	7304	6570	9428	59
H(18B)	10138	6754	9296	59
H(19A)	6367	5056	7186	68
H(19B)	3837	4662	7423	68
H(19C)	5949	3910	7260	68
H(21A)	10575	1507	7827	63
H(21B)	8058	1548	7504	63
H(21C)	8081	1135	8092	63
H(1B)	2243	3481	8249	60

Table 6. Torsion angles [°] for compound (**2R, 3S**)-184.

C(6)-C(1)-C(2)-C(3)	-0.4(3)
C(1)-C(2)-C(3)-C(4)	0.1(3)
C(2)-C(3)-C(4)-C(5)	-0.6(3)
C(3)-C(4)-C(5)-C(6)	1.4(3)
C(2)-C(1)-C(6)-C(5)	1.1(3)
C(2)-C(1)-C(6)-C(7)	-179.01(18)
C(4)-C(5)-C(6)-C(1)	-1.6(3)
C(4)-C(5)-C(6)-C(7)	178.51(19)
C(1)-C(6)-C(7)-C(8)	26.0(3)
C(5)-C(6)-C(7)-C(8)	-154.1(2)
C(6)-C(7)-C(8)-C(9)	-178.80(18)
C(7)-C(8)-C(9)-O(1)	16.9(3)
C(7)-C(8)-C(9)-C(20)	-100.4(2)
C(7)-C(8)-C(9)-C(10)	138.6(2)
O(1)-C(9)-C(10)-C(11)	64.4(2)
C(8)-C(9)-C(10)-C(11)	-57.7(2)
C(20)-C(9)-C(10)-C(11)	-177.93(17)
O(1)-C(9)-C(10)-C(19)	-60.1(2)
C(8)-C(9)-C(10)-C(19)	177.83(16)
C(20)-C(9)-C(10)-C(19)	57.6(2)
C(19)-C(10)-C(11)-C(12)	-127.8(2)
C(9)-C(10)-C(11)-C(12)	108.4(2)
C(10)-C(11)-C(12)-C(13)	-177.13(17)
C(11)-C(12)-C(13)-C(18)	113.9(2)
C(11)-C(12)-C(13)-C(14)	-123.1(2)
C(12)-C(13)-C(14)-C(15)	-175.66(19)
C(18)-C(13)-C(14)-C(15)	-52.5(3)
C(13)-C(14)-C(15)-C(16)	55.1(3)
C(14)-C(15)-C(16)-C(17)	-56.8(3)
C(15)-C(16)-C(17)-C(18)	57.2(3)
C(16)-C(17)-C(18)-C(13)	-56.2(3)
C(12)-C(13)-C(18)-C(17)	177.0(2)
C(14)-C(13)-C(18)-C(17)	53.2(3)

O(1)-C(9)-C(20)-O(2)	-0.2(2)
C(8)-C(9)-C(20)-O(2)	119.2(2)
C(10)-C(9)-C(20)-O(2)	-119.3(2)
O(1)-C(9)-C(20)-O(3)	-179.55(15)
C(8)-C(9)-C(20)-O(3)	-60.2(2)
C(10)-C(9)-C(20)-O(3)	61.3(2)
O(2)-C(20)-O(3)-C(21)	-1.4(2)
C(9)-C(20)-O(3)-C(21)	178.03(14)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound (**2R, 3S**)-**184** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1B)...O(2)	0.84	2.11	2.6306(19)	119.5
O(1)-H(1B)...O(3)#1	0.84	2.50	3.2562(19)	150.0

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z

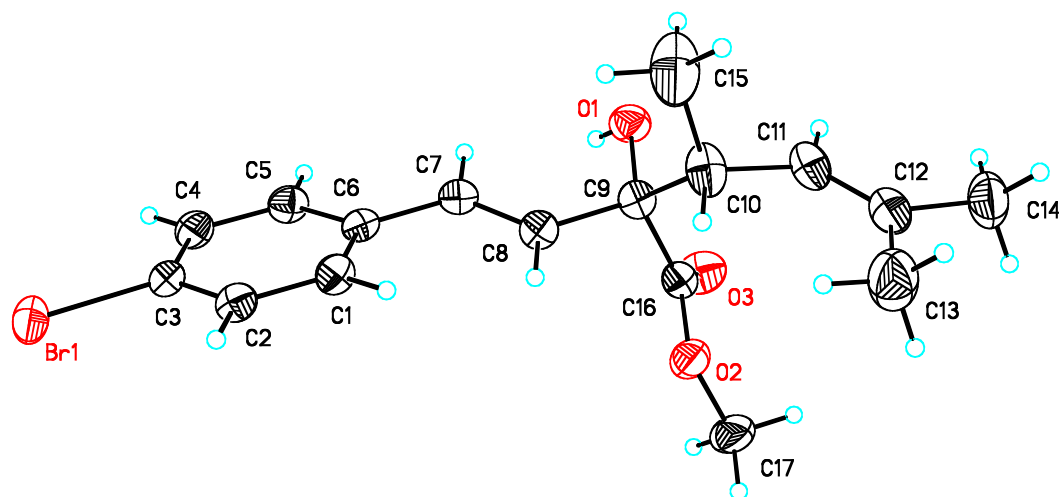
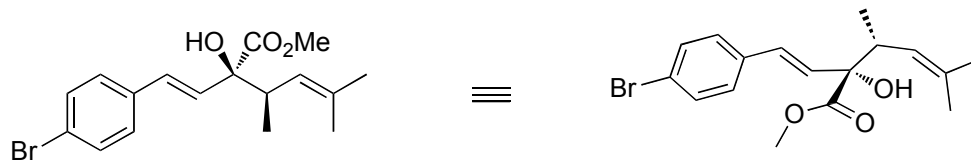
8. Crystal structure of compound (2*R*, 3*R*)-187

Table 1. Crystal data and structure refinement for compound **(2R, 3R)-187**.

Compound	(2R, 3R)-187	
Empirical formula	C ₁₇ H ₂₁ Br O ₃	
Formula weight	353.25	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 5.75640(10) Å	α = 90°.
	b = 7.8526(2) Å	β = 96.2410(10)°.
	c = 18.9358(4) Å	γ = 90°.
Volume	850.88(3) Å ³	
Z	2	
Density (calculated)	1.379 Mg/m ³	
Absorption coefficient	3.350 mm ⁻¹	
F(000)	364	
Crystal size	0.34 x 0.09 x 0.04 mm ³	
Theta range for data collection	2.35 to 69.29°.	
Index ranges	-6 ≤ h ≤ 6, -7 ≤ k ≤ 9, -22 ≤ l ≤ 21	
Reflections collected	5758	
Independent reflections	2337 [R(int) = 0.0180]	
Completeness to theta = 69.29°	97.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8693 and 0.3954	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2337 / 1 / 190	
Goodness-of-fit on F ²	1.050	
Final R indices [I > 2σ(I)]	R1 = 0.0236, wR2 = 0.0642	
R indices (all data)	R1 = 0.0240, wR2 = 0.0644	
Absolute structure parameter	0.015(17)	
Largest diff. peak and hole	0.291 and -0.219 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2R, 3R)-187**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	-4854(1)	-10060(1)	-11512(1)	54(1)
C(1)	-6265(3)	-10198(4)	-9419(1)	35(1)
C(2)	-5222(4)	-10414(3)	-10036(1)	37(1)
C(3)	-6337(3)	-9796(3)	-10670(1)	37(1)
C(4)	-8473(4)	-8986(4)	-10698(1)	41(1)
C(5)	-9495(4)	-8783(3)	-10075(1)	38(1)
C(6)	-8419(4)	-9359(3)	-9424(1)	32(1)
C(7)	-9576(4)	-9098(3)	-8779(1)	34(1)
C(8)	-8567(4)	-9218(3)	-8120(1)	36(1)
C(9)	-9806(4)	-8928(3)	-7462(1)	35(1)
C(10)	-9328(5)	-10419(3)	-6931(1)	49(1)
C(11)	-9992(4)	-9934(4)	-6206(1)	47(1)
C(12)	-8667(4)	-10035(5)	-5594(1)	49(1)
C(13)	-6186(6)	-10678(7)	-5514(2)	81(1)
C(14)	-9535(6)	-9519(5)	-4903(2)	67(1)
C(15)	-10641(12)	-12001(4)	-7210(2)	100(2)
C(16)	-8935(4)	-7275(3)	-7110(1)	36(1)
C(17)	-5703(5)	-5784(6)	-6568(2)	78(1)
O(1)	-12253(3)	-8780(2)	-7636(1)	44(1)
O(2)	-6633(3)	-7290(3)	-6929(1)	50(1)
O(3)	-10174(3)	-6117(3)	-7002(1)	54(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound (**2R, 3R**)-187.

Br(1)-C(3)	1.901(2)	C(15)-H(15B)	0.9800
C(1)-C(2)	1.380(3)	C(15)-H(15C)	0.9800
C(1)-C(6)	1.403(3)	C(16)-O(3)	1.187(3)
C(1)-H(1A)	0.9500	C(16)-O(2)	1.332(3)
C(2)-C(3)	1.386(3)	C(17)-O(2)	1.440(4)
C(2)-H(2A)	0.9500	C(17)-H(17A)	0.9800
C(3)-C(4)	1.380(3)	C(17)-H(17B)	0.9800
C(4)-C(5)	1.383(3)	C(17)-H(17C)	0.9800
C(4)-H(4A)	0.9500	O(1)-H(1B)	0.8400
C(5)-C(6)	1.393(3)		
C(5)-H(5A)	0.9500	C(2)-C(1)-C(6)	121.18(19)
C(6)-C(7)	1.467(3)	C(2)-C(1)-H(1A)	119.4
C(7)-C(8)	1.322(3)	C(6)-C(1)-H(1A)	119.4
C(7)-H(7A)	0.9500	C(1)-C(2)-C(3)	119.1(2)
C(8)-C(9)	1.517(3)	C(1)-C(2)-H(2A)	120.4
C(8)-H(8A)	0.9500	C(3)-C(2)-H(2A)	120.4
C(9)-O(1)	1.416(3)	C(4)-C(3)-C(2)	121.4(2)
C(9)-C(16)	1.520(3)	C(4)-C(3)-Br(1)	119.83(16)
C(9)-C(10)	1.548(3)	C(2)-C(3)-Br(1)	118.73(16)
C(10)-C(11)	1.515(3)	C(3)-C(4)-C(5)	118.7(2)
C(10)-C(15)	1.519(5)	C(3)-C(4)-H(4A)	120.7
C(10)-H(10A)	1.0000	C(5)-C(4)-H(4A)	120.7
C(11)-C(12)	1.318(3)	C(4)-C(5)-C(6)	121.8(2)
C(11)-H(11A)	0.9500	C(4)-C(5)-H(5A)	119.1
C(12)-C(14)	1.506(4)	C(6)-C(5)-H(5A)	119.1
C(12)-C(13)	1.507(4)	C(5)-C(6)-C(1)	117.7(2)
C(13)-H(13A)	0.9800	C(5)-C(6)-C(7)	119.50(19)
C(13)-H(13B)	0.9800	C(1)-C(6)-C(7)	122.75(19)
C(13)-H(13C)	0.9800	C(8)-C(7)-C(6)	125.7(2)
C(14)-H(14A)	0.9800	C(8)-C(7)-H(7A)	117.1
C(14)-H(14B)	0.9800	C(6)-C(7)-H(7A)	117.1
C(14)-H(14C)	0.9800	C(7)-C(8)-C(9)	124.5(2)
C(15)-H(15A)	0.9800	C(7)-C(8)-H(8A)	117.7

C(9)-C(8)-H(8A)	117.7	H(13B)-C(13)-H(13C)	109.5
O(1)-C(9)-C(8)	111.46(18)	C(12)-C(14)-H(14A)	109.5
O(1)-C(9)-C(16)	107.75(18)	C(12)-C(14)-H(14B)	109.5
C(8)-C(9)-C(16)	109.02(19)	H(14A)-C(14)-H(14B)	109.5
O(1)-C(9)-C(10)	108.4(2)	C(12)-C(14)-H(14C)	109.5
C(8)-C(9)-C(10)	110.65(19)	H(14A)-C(14)-H(14C)	109.5
C(16)-C(9)-C(10)	109.5(2)	H(14B)-C(14)-H(14C)	109.5
C(11)-C(10)-C(15)	110.8(3)	C(10)-C(15)-H(15A)	109.5
C(11)-C(10)-C(9)	110.7(2)	C(10)-C(15)-H(15B)	109.5
C(15)-C(10)-C(9)	110.3(3)	H(15A)-C(15)-H(15B)	109.5
C(11)-C(10)-H(10A)	108.3	C(10)-C(15)-H(15C)	109.5
C(15)-C(10)-H(10A)	108.3	H(15A)-C(15)-H(15C)	109.5
C(9)-C(10)-H(10A)	108.3	H(15B)-C(15)-H(15C)	109.5
C(12)-C(11)-C(10)	127.0(2)	O(3)-C(16)-O(2)	124.2(2)
C(12)-C(11)-H(11A)	116.5	O(3)-C(16)-C(9)	123.7(2)
C(10)-C(11)-H(11A)	116.5	O(2)-C(16)-C(9)	112.1(2)
C(11)-C(12)-C(14)	122.1(3)	O(2)-C(17)-H(17A)	109.5
C(11)-C(12)-C(13)	124.1(2)	O(2)-C(17)-H(17B)	109.5
C(14)-C(12)-C(13)	113.8(2)	H(17A)-C(17)-H(17B)	109.5
C(12)-C(13)-H(13A)	109.5	O(2)-C(17)-H(17C)	109.5
C(12)-C(13)-H(13B)	109.5	H(17A)-C(17)-H(17C)	109.5
H(13A)-C(13)-H(13B)	109.5	H(17B)-C(17)-H(17C)	109.5
C(12)-C(13)-H(13C)	109.5	C(9)-O(1)-H(1B)	109.5
H(13A)-C(13)-H(13C)	109.5	C(16)-O(2)-C(17)	115.0(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R**, **3R**)-**187**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* 2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	52(1)	76(1)	35(1)	-14(1)	7(1)	-3(1)
C(1)	36(1)	34(1)	34(1)	3(1)	-2(1)	5(1)
C(2)	34(1)	34(1)	41(1)	-4(1)	1(1)	2(1)
C(3)	37(1)	41(1)	31(1)	-6(1)	2(1)	-7(1)
C(4)	36(1)	53(2)	32(1)	3(1)	-6(1)	-3(1)
C(5)	32(1)	41(1)	40(1)	4(1)	-4(1)	3(1)
C(6)	31(1)	30(1)	35(1)	-1(1)	-2(1)	-3(1)
C(7)	31(1)	30(1)	40(1)	2(1)	1(1)	1(1)
C(8)	34(1)	35(1)	39(1)	-1(1)	3(1)	5(1)
C(9)	35(1)	33(1)	37(1)	2(1)	4(1)	5(1)
C(10)	72(2)	35(2)	42(1)	5(1)	14(1)	13(1)
C(11)	56(1)	41(1)	45(1)	8(1)	16(1)	6(2)
C(12)	55(1)	48(1)	46(1)	3(2)	15(1)	-2(2)
C(13)	59(2)	125(4)	57(2)	8(2)	4(1)	10(2)
C(14)	76(2)	84(3)	42(1)	2(2)	14(1)	2(2)
C(15)	212(6)	31(2)	60(2)	0(2)	28(3)	-18(2)
C(16)	36(1)	38(1)	36(1)	2(1)	6(1)	1(1)
C(17)	54(2)	123(3)	58(2)	-47(2)	18(1)	-35(2)
O(1)	35(1)	49(1)	49(1)	-5(1)	6(1)	-1(1)
O(2)	34(1)	75(1)	43(1)	-17(1)	6(1)	-4(1)
O(3)	53(1)	38(1)	72(1)	-11(1)	3(1)	6(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R, 3R**)-187.

	x	y	z	U(eq)
H(1A)	-5512	-10625	-8984	42
H(2A)	-3759	-10978	-10025	44
H(4A)	-9226	-8576	-11136	49
H(5A)	-10971	-8235	-10091	46
H(7A)	-11190	-8817	-8841	41
H(8A)	-6955	-9506	-8052	43
H(10A)	-7616	-10676	-6884	59
H(11A)	-11532	-9510	-6190	56
H(13A)	-5737	-10993	-5981	121
H(13B)	-6066	-11678	-5202	121
H(13C)	-5141	-9782	-5306	121
H(14A)	-11157	-9127	-4993	100
H(14B)	-8558	-8595	-4687	100
H(14C)	-9456	-10497	-4580	100
H(15A)	-10318	-12936	-6870	150
H(15B)	-10131	-12324	-7668	150
H(15C)	-12323	-11764	-7270	150
H(17A)	-4011	-5910	-6451	116
H(17B)	-6442	-5625	-6131	116
H(17C)	-6023	-4792	-6878	116
H(1B)	-12541	-7971	-7923	66

Table 6. Torsion angles [°] for compound (**2R, 3R**)-**187**.

C(6)-C(1)-C(2)-C(3)	-0.4(4)
C(1)-C(2)-C(3)-C(4)	-0.6(4)
C(1)-C(2)-C(3)-Br(1)	178.72(19)
C(2)-C(3)-C(4)-C(5)	0.5(4)
Br(1)-C(3)-C(4)-C(5)	-178.81(19)
C(3)-C(4)-C(5)-C(6)	0.6(4)
C(4)-C(5)-C(6)-C(1)	-1.4(4)
C(4)-C(5)-C(6)-C(7)	179.5(2)
C(2)-C(1)-C(6)-C(5)	1.3(4)
C(2)-C(1)-C(6)-C(7)	-179.7(2)
C(5)-C(6)-C(7)-C(8)	-163.8(2)
C(1)-C(6)-C(7)-C(8)	17.2(4)
C(6)-C(7)-C(8)-C(9)	179.5(2)
C(7)-C(8)-C(9)-O(1)	9.4(3)
C(7)-C(8)-C(9)-C(16)	-109.4(3)
C(7)-C(8)-C(9)-C(10)	130.1(3)
O(1)-C(9)-C(10)-C(11)	-72.7(3)
C(8)-C(9)-C(10)-C(11)	164.8(2)
C(16)-C(9)-C(10)-C(11)	44.6(3)
O(1)-C(9)-C(10)-C(15)	50.3(3)
C(8)-C(9)-C(10)-C(15)	-72.2(3)
C(16)-C(9)-C(10)-C(15)	167.6(3)
C(15)-C(10)-C(11)-C(12)	110.4(4)
C(9)-C(10)-C(11)-C(12)	-126.9(4)
C(10)-C(11)-C(12)-C(14)	-179.7(3)
C(10)-C(11)-C(12)-C(13)	-0.2(6)
O(1)-C(9)-C(16)-O(3)	1.3(3)
C(8)-C(9)-C(16)-O(3)	122.4(3)
C(10)-C(9)-C(16)-O(3)	-116.4(3)
O(1)-C(9)-C(16)-O(2)	-179.69(19)
C(8)-C(9)-C(16)-O(2)	-58.6(2)
C(10)-C(9)-C(16)-O(2)	62.6(3)
O(3)-C(16)-O(2)-C(17)	1.3(4)

C(9)-C(16)-O(2)-C(17) -177.8(2)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound (**2R, 3R**)-**187** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
O(1)-H(1B)...Br(1)#1	0.84	2.88	3.651(2)	154.1

Symmetry transformations used to generate equivalent atoms:

#1 $-x-2, y+1/2, -z-2$

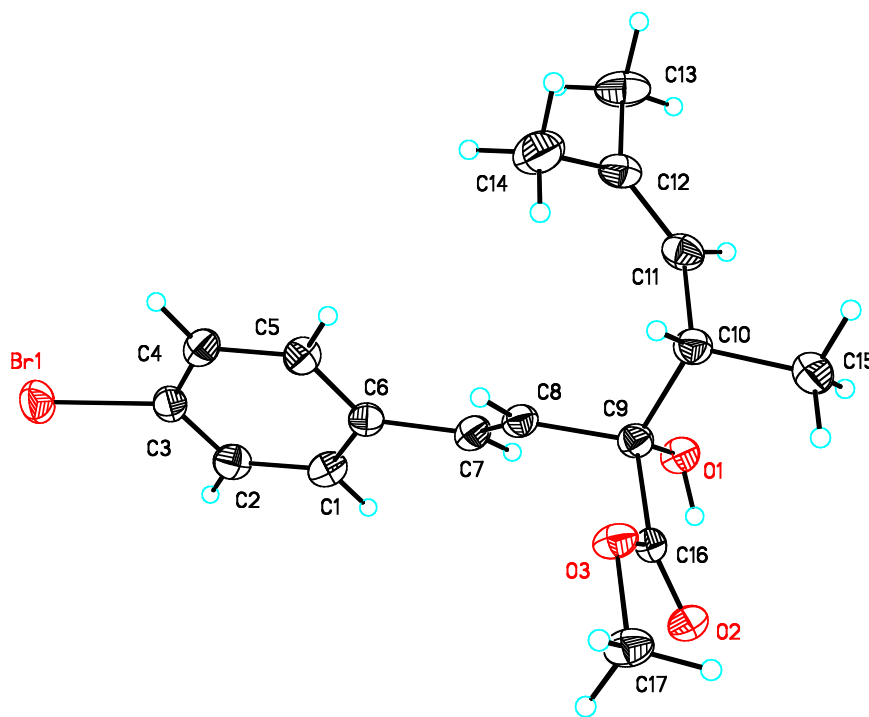
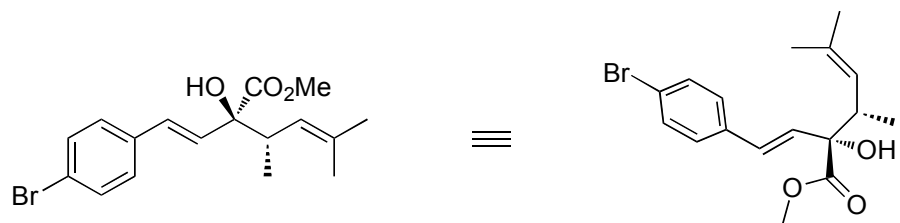
9. Crystal structure of compound (2*R*, 3*S*)-187

Table 1. Crystal data and structure refinement for compound **(2R, 3S)-187**.

Compound	(2R, 3S)-187	
Empirical formula	C ₁₇ H ₂₁ Br O ₃	
Formula weight	353.25	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.76370(10) Å	α = 90°.
	b = 13.8437(3) Å	β = 90°.
	c = 20.8594(5) Å	γ = 90°.
Volume	1664.39(6) Å ³	
Z	4	
Density (calculated)	1.410 Mg/m ³	
Absorption coefficient	3.426 mm ⁻¹	
F(000)	728	
Crystal size	0.34 x 0.17 x 0.05 mm ³	
Theta range for data collection	3.83 to 69.26°.	
Index ranges	-4 ≤ h ≤ 6, -16 ≤ k ≤ 15, -17 ≤ l ≤ 25	
Reflections collected	6741	
Independent reflections	2632 [R(int) = 0.0178]	
Completeness to theta = 69.26°	95.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8474 and 0.3888	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2632 / 0 / 190	
Goodness-of-fit on F ²	1.050	
Final R indices [I > 2σ(I)]	R1 = 0.0196, wR2 = 0.0524	
R indices (all data)	R1 = 0.0200, wR2 = 0.0527	
Absolute structure parameter	0.031(13)	
Largest diff. peak and hole	0.267 and -0.273 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2R, 3S)-187**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	1715(1)	10097(1)	204(1)	44(1)
C(1)	5431(3)	7638(2)	661(1)	33(1)
C(2)	4808(4)	8535(2)	421(1)	34(1)
C(3)	2675(3)	8916(1)	584(1)	32(1)
C(4)	1201(3)	8441(2)	997(1)	33(1)
C(5)	1838(4)	7537(1)	1230(1)	32(1)
C(6)	3950(3)	7116(1)	1059(1)	28(1)
C(7)	4665(3)	6149(2)	1281(1)	30(1)
C(8)	3295(4)	5436(1)	1455(1)	27(1)
C(9)	4129(3)	4445(1)	1655(1)	26(1)
C(10)	2961(3)	4112(1)	2288(1)	30(1)
C(11)	3655(3)	4766(2)	2830(1)	33(1)
C(12)	2419(4)	5462(2)	3098(1)	32(1)
C(13)	3391(4)	6053(2)	3646(1)	45(1)
C(14)	30(4)	5746(2)	2903(1)	50(1)
C(15)	3583(4)	3064(2)	2441(1)	41(1)
C(16)	3558(3)	3739(1)	1111(1)	24(1)
C(17)	662(3)	2967(2)	513(1)	34(1)
O(1)	6579(2)	4442(1)	1738(1)	31(1)
O(2)	5013(2)	3340(1)	795(1)	30(1)
O(3)	1281(2)	3628(1)	1022(1)	30(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound (**2R, 3S**)-187.

Br(1)-C(3)	1.8993(19)	C(15)-H(15B)	0.9800
C(1)-C(2)	1.387(3)	C(15)-H(15C)	0.9800
C(1)-C(6)	1.393(3)	C(16)-O(2)	1.200(2)
C(1)-H(1A)	0.9500	C(16)-O(3)	1.334(2)
C(2)-C(3)	1.380(3)	C(17)-O(3)	1.446(2)
C(2)-H(2A)	0.9500	C(17)-H(17A)	0.9800
C(3)-C(4)	1.378(3)	C(17)-H(17B)	0.9800
C(4)-C(5)	1.392(3)	C(17)-H(17C)	0.9800
C(4)-H(4A)	0.9500	O(1)-H(1B)	0.8400
C(5)-C(6)	1.396(3)		
C(5)-H(5A)	0.9500	C(2)-C(1)-C(6)	121.46(18)
C(6)-C(7)	1.476(3)	C(2)-C(1)-H(1A)	119.3
C(7)-C(8)	1.315(3)	C(6)-C(1)-H(1A)	119.3
C(7)-H(7A)	0.9500	C(3)-C(2)-C(1)	118.90(19)
C(8)-C(9)	1.513(3)	C(3)-C(2)-H(2A)	120.6
C(8)-H(8A)	0.9500	C(1)-C(2)-H(2A)	120.6
C(9)-O(1)	1.423(2)	C(4)-C(3)-C(2)	121.41(18)
C(9)-C(16)	1.535(2)	C(4)-C(3)-Br(1)	119.51(15)
C(9)-C(10)	1.552(2)	C(2)-C(3)-Br(1)	119.04(15)
C(10)-C(11)	1.502(3)	C(3)-C(4)-C(5)	119.02(19)
C(10)-C(15)	1.528(3)	C(3)-C(4)-H(4A)	120.5
C(10)-H(10A)	1.0000	C(5)-C(4)-H(4A)	120.5
C(11)-C(12)	1.322(3)	C(4)-C(5)-C(6)	121.09(19)
C(11)-H(11A)	0.9500	C(4)-C(5)-H(5A)	119.5
C(12)-C(14)	1.489(3)	C(6)-C(5)-H(5A)	119.5
C(12)-C(13)	1.513(3)	C(1)-C(6)-C(5)	118.04(18)
C(13)-H(13A)	0.9800	C(1)-C(6)-C(7)	119.10(18)
C(13)-H(13B)	0.9800	C(5)-C(6)-C(7)	122.86(18)
C(13)-H(13C)	0.9800	C(8)-C(7)-C(6)	126.85(19)
C(14)-H(14A)	0.9800	C(8)-C(7)-H(7A)	116.6
C(14)-H(14B)	0.9800	C(6)-C(7)-H(7A)	116.6
C(14)-H(14C)	0.9800	C(7)-C(8)-C(9)	124.48(18)
C(15)-H(15A)	0.9800	C(7)-C(8)-H(8A)	117.8

C(9)-C(8)-H(8A)	117.8	H(13B)-C(13)-H(13C)	109.5
O(1)-C(9)-C(8)	110.60(16)	C(12)-C(14)-H(14A)	109.5
O(1)-C(9)-C(16)	107.47(15)	C(12)-C(14)-H(14B)	109.5
C(8)-C(9)-C(16)	107.81(13)	H(14A)-C(14)-H(14B)	109.5
O(1)-C(9)-C(10)	109.04(15)	C(12)-C(14)-H(14C)	109.5
C(8)-C(9)-C(10)	111.51(16)	H(14A)-C(14)-H(14C)	109.5
C(16)-C(9)-C(10)	110.34(15)	H(14B)-C(14)-H(14C)	109.5
C(11)-C(10)-C(15)	110.65(16)	C(10)-C(15)-H(15A)	109.5
C(11)-C(10)-C(9)	110.22(16)	C(10)-C(15)-H(15B)	109.5
C(15)-C(10)-C(9)	110.98(16)	H(15A)-C(15)-H(15B)	109.5
C(11)-C(10)-H(10A)	108.3	C(10)-C(15)-H(15C)	109.5
C(15)-C(10)-H(10A)	108.3	H(15A)-C(15)-H(15C)	109.5
C(9)-C(10)-H(10A)	108.3	H(15B)-C(15)-H(15C)	109.5
C(12)-C(11)-C(10)	127.85(18)	O(2)-C(16)-O(3)	123.91(16)
C(12)-C(11)-H(11A)	116.1	O(2)-C(16)-C(9)	123.30(17)
C(10)-C(11)-H(11A)	116.1	O(3)-C(16)-C(9)	112.78(15)
C(11)-C(12)-C(14)	125.2(2)	O(3)-C(17)-H(17A)	109.5
C(11)-C(12)-C(13)	120.92(19)	O(3)-C(17)-H(17B)	109.5
C(14)-C(12)-C(13)	113.92(19)	H(17A)-C(17)-H(17B)	109.5
C(12)-C(13)-H(13A)	109.5	O(3)-C(17)-H(17C)	109.5
C(12)-C(13)-H(13B)	109.5	H(17A)-C(17)-H(17C)	109.5
H(13A)-C(13)-H(13B)	109.5	H(17B)-C(17)-H(17C)	109.5
C(12)-C(13)-H(13C)	109.5	C(9)-O(1)-H(1B)	109.5
H(13A)-C(13)-H(13C)	109.5	C(16)-O(3)-C(17)	114.69(14)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2R, 3S)-187**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* 2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	59(1)	31(1)	41(1)	5(1)	-8(1)	4(1)
C(1)	29(1)	32(1)	38(1)	-6(1)	3(1)	-3(1)
C(2)	39(1)	31(1)	33(1)	-1(1)	2(1)	-5(1)
C(3)	40(1)	25(1)	30(1)	-3(1)	-8(1)	0(1)
C(4)	32(1)	30(1)	37(1)	-4(1)	-2(1)	3(1)
C(5)	31(1)	30(1)	34(1)	1(1)	2(1)	-1(1)
C(6)	29(1)	26(1)	27(1)	-4(1)	-4(1)	-3(1)
C(7)	29(1)	29(1)	33(1)	-5(1)	-2(1)	2(1)
C(8)	28(1)	28(1)	26(1)	-5(1)	-2(1)	2(1)
C(9)	25(1)	29(1)	25(1)	-3(1)	-3(1)	1(1)
C(10)	31(1)	31(1)	26(1)	-3(1)	-1(1)	1(1)
C(11)	29(1)	43(1)	26(1)	-1(1)	-2(1)	-1(1)
C(12)	37(1)	34(1)	25(1)	-4(1)	3(1)	-6(1)
C(13)	46(1)	53(1)	38(1)	-18(1)	7(1)	-13(1)
C(14)	45(1)	58(2)	47(1)	-13(1)	-1(1)	12(1)
C(15)	56(1)	35(1)	32(1)	3(1)	2(1)	0(1)
C(16)	29(1)	22(1)	23(1)	3(1)	2(1)	2(1)
C(17)	29(1)	39(1)	33(1)	-11(1)	-2(1)	-1(1)
O(1)	25(1)	35(1)	34(1)	-6(1)	-3(1)	2(1)
O(2)	28(1)	30(1)	32(1)	-5(1)	4(1)	2(1)
O(3)	24(1)	35(1)	30(1)	-11(1)	-2(1)	2(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2R, 3S**)-**187**.

	x	y	z	U(eq)
H(1A)	6900	7374	553	39
H(2A)	5832	8882	148	41
H(4A)	-229	8726	1121	39
H(5A)	817	7200	1509	38
H(7A)	6287	6028	1299	36
H(8A)	1671	5552	1456	33
H(10A)	1241	4156	2233	35
H(11A)	5164	4666	3001	39
H(13A)	4957	5825	3749	68
H(13B)	2389	5982	4023	68
H(13C)	3457	6735	3521	68
H(14A)	-489	5334	2549	75
H(14B)	29	6423	2764	75
H(14C)	-1025	5670	3268	75
H(15A)	2818	2868	2840	61
H(15B)	5268	3005	2491	61
H(15C)	3061	2645	2090	61
H(17A)	-1031	2923	481	51
H(17B)	1304	2326	606	51
H(17C)	1295	3202	106	51
H(1B)	7201	4141	1433	47

Table 6. Torsion angles [°] for compound (**2R, 3S**)-**187**.

C(6)-C(1)-C(2)-C(3)	0.3(3)
C(1)-C(2)-C(3)-C(4)	2.4(3)
C(1)-C(2)-C(3)-Br(1)	-175.25(15)
C(2)-C(3)-C(4)-C(5)	-3.1(3)
Br(1)-C(3)-C(4)-C(5)	174.56(14)
C(3)-C(4)-C(5)-C(6)	1.1(3)
C(2)-C(1)-C(6)-C(5)	-2.2(3)
C(2)-C(1)-C(6)-C(7)	177.59(17)
C(4)-C(5)-C(6)-C(1)	1.5(3)
C(4)-C(5)-C(6)-C(7)	-178.29(18)
C(1)-C(6)-C(7)-C(8)	-154.44(19)
C(5)-C(6)-C(7)-C(8)	25.4(3)
C(6)-C(7)-C(8)-C(9)	177.64(16)
C(7)-C(8)-C(9)-O(1)	10.3(2)
C(7)-C(8)-C(9)-C(16)	-106.89(19)
C(7)-C(8)-C(9)-C(10)	131.84(18)
O(1)-C(9)-C(10)-C(11)	58.3(2)
C(8)-C(9)-C(10)-C(11)	-64.1(2)
C(16)-C(9)-C(10)-C(11)	176.11(16)
O(1)-C(9)-C(10)-C(15)	-64.6(2)
C(8)-C(9)-C(10)-C(15)	172.95(16)
C(16)-C(9)-C(10)-C(15)	53.2(2)
C(15)-C(10)-C(11)-C(12)	-134.1(2)
C(9)-C(10)-C(11)-C(12)	102.8(2)
C(10)-C(11)-C(12)-C(14)	-0.5(4)
C(10)-C(11)-C(12)-C(13)	179.75(19)
O(1)-C(9)-C(16)-O(2)	-5.5(2)
C(8)-C(9)-C(16)-O(2)	113.71(19)
C(10)-C(9)-C(16)-O(2)	-124.30(18)
O(1)-C(9)-C(16)-O(3)	175.31(15)
C(8)-C(9)-C(16)-O(3)	-65.5(2)
C(10)-C(9)-C(16)-O(3)	56.5(2)
O(2)-C(16)-O(3)-C(17)	0.9(3)

C(9)-C(16)-O(3)-C(17) -179.92(15)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound (**2R, 3S**)-**187** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1B)...O(2)	0.84	2.14	2.6467(18)	118.4
O(1)-H(1B)...O(3)#1	0.84	2.60	3.2936(18)	140.4

Symmetry transformations used to generate equivalent atoms:

#1 x+1,y,z

10. Crystal structure of compound 243

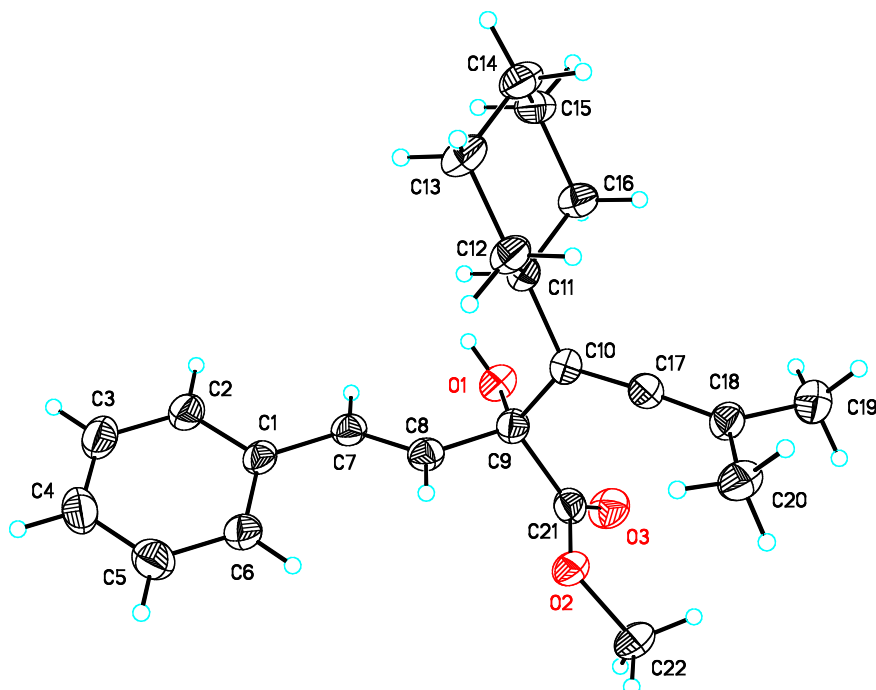
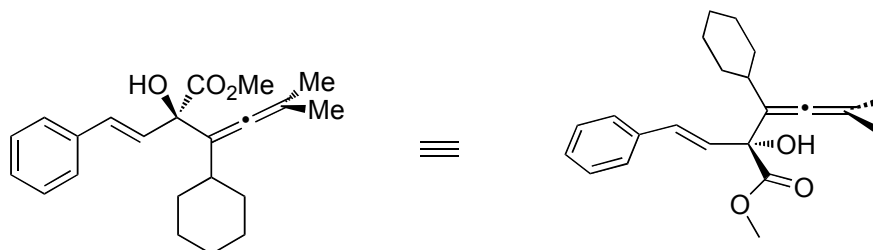


Table 1. Crystal data and structure refinement for compound **243**.

Compound	243	
Empirical formula	$C_{22} H_{28} O_3$	
Formula weight	340.44	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	$a = 5.9599(4)$ Å	$\alpha = 90^\circ$.
	$b = 14.1275(7)$ Å	$\beta = 92.370(5)^\circ$.
	$c = 11.3539(6)$ Å	$\gamma = 90^\circ$.
Volume	$955.16(9)$ Å ³	
Z	2	
Density (calculated)	1.184 Mg/m ³	
Absorption coefficient	0.609 mm ⁻¹	
F(000)	368	
Crystal size	0.33 x 0.27 x 0.11 mm ³	
Theta range for data collection	3.90 to 69.38°.	
Index ranges	-6 ≤ h ≤ 6, -16 ≤ k ≤ 16, -13 ≤ l ≤ 13	
Reflections collected	5844	
Independent reflections	2934 [R(int) = 0.0273]	
Completeness to theta = 69.38°	89.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9360 and 0.8243	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2934 / 1 / 226	
Goodness-of-fit on F ²	1.007	
Final R indices [I > 2σ(I)]	R1 = 0.0455, wR2 = 0.1037	
R indices (all data)	R1 = 0.0532, wR2 = 0.1116	
Absolute structure parameter	-0.1(3)	
Largest diff. peak and hole	0.246 and -0.292 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **243**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	2899(5)	3203(2)	2467(2)	33(1)
C(2)	1986(6)	3844(2)	3259(2)	40(1)
C(3)	3145(7)	4106(2)	4279(3)	49(1)
C(4)	5269(7)	3757(2)	4542(3)	49(1)
C(5)	6220(6)	3128(2)	3761(3)	45(1)
C(6)	5059(6)	2857(2)	2746(3)	38(1)
C(7)	1577(5)	2915(2)	1404(2)	32(1)
C(8)	2350(5)	2470(2)	480(2)	32(1)
C(9)	917(5)	2167(2)	-581(2)	33(1)
C(10)	1608(5)	2723(2)	-1677(2)	33(1)
C(11)	1140(5)	3789(2)	-1661(2)	33(1)
C(12)	3301(5)	4353(2)	-1846(3)	37(1)
C(13)	2840(6)	5422(2)	-1817(3)	43(1)
C(14)	1015(6)	5703(2)	-2703(3)	42(1)
C(15)	-1119(5)	5142(2)	-2539(3)	39(1)
C(16)	-663(5)	4067(2)	-2572(3)	37(1)
C(17)	2454(5)	2300(2)	-2580(2)	34(1)
C(18)	3366(5)	1844(2)	-3442(2)	35(1)
C(19)	1986(6)	1444(2)	-4460(3)	46(1)
C(20)	5843(6)	1687(2)	-3463(3)	42(1)
C(21)	1267(5)	1104(2)	-843(2)	35(1)
C(22)	3889(7)	-107(2)	-1134(3)	47(1)
O(1)	-1374(4)	2309(2)	-378(2)	39(1)
O(2)	3398(4)	845(1)	-732(2)	39(1)
O(3)	-271(4)	595(2)	-1144(2)	47(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound **243**.

C(1)-C(6)	1.401(4)	C(15)-C(16)	1.542(4)
C(1)-C(2)	1.403(4)	C(15)-H(15A)	0.9700
C(1)-C(7)	1.470(4)	C(15)-H(15B)	0.9700
C(2)-C(3)	1.374(4)	C(16)-H(16A)	0.9700
C(2)-H(2A)	0.9300	C(16)-H(16B)	0.9700
C(3)-C(4)	1.379(5)	C(17)-C(18)	1.308(4)
C(3)-H(3A)	0.9300	C(18)-C(20)	1.494(4)
C(4)-C(5)	1.392(5)	C(18)-C(19)	1.502(4)
C(4)-H(4A)	0.9300	C(19)-H(19A)	0.9600
C(5)-C(6)	1.374(4)	C(19)-H(19B)	0.9600
C(5)-H(5A)	0.9300	C(19)-H(19C)	0.9600
C(6)-H(6A)	0.9300	C(20)-H(20A)	0.9600
C(7)-C(8)	1.322(4)	C(20)-H(20B)	0.9600
C(7)-H(7A)	0.9300	C(20)-H(20C)	0.9600
C(8)-C(9)	1.509(4)	C(21)-O(3)	1.204(4)
C(8)-H(8A)	0.9300	C(21)-O(2)	1.323(4)
C(9)-O(1)	1.408(4)	C(22)-O(2)	1.455(4)
C(9)-C(21)	1.546(4)	C(22)-H(22A)	0.9600
C(9)-C(10)	1.543(4)	C(22)-H(22B)	0.9600
C(10)-C(17)	1.306(4)	C(22)-H(22C)	0.9600
C(10)-C(11)	1.532(4)	O(1)-H(1A)	0.8200
C(11)-C(16)	1.512(4)		
C(11)-C(12)	1.536(4)	C(6)-C(1)-C(2)	117.2(3)
C(11)-H(11A)	0.9800	C(6)-C(1)-C(7)	123.1(3)
C(12)-C(13)	1.537(4)	C(2)-C(1)-C(7)	119.7(3)
C(12)-H(12A)	0.9700	C(3)-C(2)-C(1)	121.3(3)
C(12)-H(12B)	0.9700	C(3)-C(2)-H(2A)	119.4
C(13)-C(14)	1.504(5)	C(1)-C(2)-H(2A)	119.4
C(13)-H(13A)	0.9700	C(4)-C(3)-C(2)	120.7(3)
C(13)-H(13B)	0.9700	C(4)-C(3)-H(3A)	119.6
C(14)-C(15)	1.516(4)	C(2)-C(3)-H(3A)	119.6
C(14)-H(14A)	0.9700	C(3)-C(4)-C(5)	119.0(3)
C(14)-H(14B)	0.9700	C(3)-C(4)-H(4A)	120.5

C(5)-C(4)-H(4A)	120.5	C(14)-C(13)-H(13A)	109.3
C(6)-C(5)-C(4)	120.5(3)	C(12)-C(13)-H(13A)	109.3
C(6)-C(5)-H(5A)	119.7	C(14)-C(13)-H(13B)	109.3
C(4)-C(5)-H(5A)	119.7	C(12)-C(13)-H(13B)	109.3
C(5)-C(6)-C(1)	121.2(3)	H(13A)-C(13)-H(13B)	107.9
C(5)-C(6)-H(6A)	119.4	C(13)-C(14)-C(15)	111.6(3)
C(1)-C(6)-H(6A)	119.4	C(13)-C(14)-H(14A)	109.3
C(8)-C(7)-C(1)	126.2(3)	C(15)-C(14)-H(14A)	109.3
C(8)-C(7)-H(7A)	116.9	C(13)-C(14)-H(14B)	109.3
C(1)-C(7)-H(7A)	116.9	C(15)-C(14)-H(14B)	109.3
C(7)-C(8)-C(9)	124.4(3)	H(14A)-C(14)-H(14B)	108.0
C(7)-C(8)-H(8A)	117.8	C(14)-C(15)-C(16)	111.2(3)
C(9)-C(8)-H(8A)	117.8	C(14)-C(15)-H(15A)	109.4
O(1)-C(9)-C(8)	110.4(2)	C(16)-C(15)-H(15A)	109.4
O(1)-C(9)-C(21)	108.0(2)	C(14)-C(15)-H(15B)	109.4
C(8)-C(9)-C(21)	110.7(2)	C(16)-C(15)-H(15B)	109.4
O(1)-C(9)-C(10)	110.6(2)	H(15A)-C(15)-H(15B)	108.0
C(8)-C(9)-C(10)	109.8(2)	C(11)-C(16)-C(15)	111.1(2)
C(21)-C(9)-C(10)	107.2(2)	C(11)-C(16)-H(16A)	109.4
C(17)-C(10)-C(11)	122.4(3)	C(15)-C(16)-H(16A)	109.4
C(17)-C(10)-C(9)	121.7(3)	C(11)-C(16)-H(16B)	109.4
C(11)-C(10)-C(9)	115.9(2)	C(15)-C(16)-H(16B)	109.4
C(16)-C(11)-C(10)	111.9(2)	H(16A)-C(16)-H(16B)	108.0
C(16)-C(11)-C(12)	110.4(2)	C(10)-C(17)-C(18)	176.7(3)
C(10)-C(11)-C(12)	110.7(2)	C(17)-C(18)-C(20)	121.8(3)
C(16)-C(11)-H(11A)	107.9	C(17)-C(18)-C(19)	122.0(3)
C(10)-C(11)-H(11A)	107.9	C(20)-C(18)-C(19)	116.2(3)
C(12)-C(11)-H(11A)	107.9	C(18)-C(19)-H(19A)	109.5
C(13)-C(12)-C(11)	110.8(3)	C(18)-C(19)-H(19B)	109.5
C(13)-C(12)-H(12A)	109.5	H(19A)-C(19)-H(19B)	109.5
C(11)-C(12)-H(12A)	109.5	C(18)-C(19)-H(19C)	109.5
C(13)-C(12)-H(12B)	109.5	H(19A)-C(19)-H(19C)	109.5
C(11)-C(12)-H(12B)	109.5	H(19B)-C(19)-H(19C)	109.5
H(12A)-C(12)-H(12B)	108.1	C(18)-C(20)-H(20A)	109.5
C(14)-C(13)-C(12)	111.7(3)	C(18)-C(20)-H(20B)	109.5

H(20A)-C(20)-H(20B)	109.5	O(2)-C(22)-H(22B)	109.5
C(18)-C(20)-H(20C)	109.5	H(22A)-C(22)-H(22B)	109.5
H(20A)-C(20)-H(20C)	109.5	O(2)-C(22)-H(22C)	109.5
H(20B)-C(20)-H(20C)	109.5	H(22A)-C(22)-H(22C)	109.5
O(3)-C(21)-O(2)	125.3(3)	H(22B)-C(22)-H(22C)	109.5
O(3)-C(21)-C(9)	121.9(3)	C(9)-O(1)-H(1A)	109.5
O(2)-C(21)-C(9)	112.8(2)	C(21)-O(2)-C(22)	115.5(2)
O(2)-C(22)-H(22A)	109.5		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **243**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	45(2)	23(1)	30(1)	1(1)	5(1)	-1(1)
C(2)	52(2)	35(2)	34(1)	-2(1)	6(1)	6(1)
C(3)	77(3)	36(2)	34(2)	-5(1)	6(2)	-1(2)
C(4)	68(3)	43(2)	35(2)	-1(1)	-9(2)	-12(2)
C(5)	50(2)	41(2)	44(2)	6(2)	-7(2)	-2(2)
C(6)	49(2)	29(2)	35(1)	2(1)	1(1)	2(1)
C(7)	37(2)	28(1)	32(1)	3(1)	5(1)	2(1)
C(8)	34(2)	28(2)	34(1)	3(1)	3(1)	0(1)
C(9)	38(2)	31(2)	29(1)	-1(1)	3(1)	-1(1)
C(10)	38(2)	31(2)	29(1)	-4(1)	1(1)	3(1)
C(11)	43(2)	28(2)	29(1)	-2(1)	4(1)	4(1)
C(12)	37(2)	28(2)	46(2)	-7(1)	-1(1)	2(1)
C(13)	39(2)	28(2)	60(2)	-10(1)	0(2)	0(1)
C(14)	51(2)	26(2)	49(2)	-1(1)	10(1)	3(1)
C(15)	43(2)	31(2)	44(2)	4(1)	-1(1)	6(1)
C(16)	37(2)	29(2)	44(2)	1(1)	0(1)	1(1)
C(17)	39(2)	31(2)	31(1)	1(1)	-2(1)	0(1)
C(18)	44(2)	29(2)	32(1)	-2(1)	4(1)	-1(1)
C(19)	53(2)	46(2)	40(2)	-8(1)	-1(2)	3(2)
C(20)	46(2)	32(2)	48(2)	-1(1)	5(2)	3(1)
C(21)	45(2)	32(2)	28(1)	1(1)	1(1)	-3(1)
C(22)	64(2)	25(2)	52(2)	-7(1)	-2(2)	6(1)
O(1)	41(1)	34(1)	44(1)	-3(1)	6(1)	0(1)
O(2)	47(1)	26(1)	42(1)	-5(1)	-4(1)	3(1)
O(3)	51(2)	34(1)	56(1)	-4(1)	-2(1)	-7(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **243**.

	x	y	z	U(eq)
H(2A)	568	4097	3091	48
H(3A)	2492	4524	4797	59
H(4A)	6052	3938	5230	59
H(5A)	7653	2890	3928	55
H(6A)	5720	2435	2235	45
H(7A)	54	3061	1380	39
H(8A)	3877	2335	484	39
H(11A)	605	3952	-882	40
H(12A)	4416	4191	-1233	45
H(12B)	3898	4184	-2600	45
H(13A)	2401	5601	-1034	51
H(13B)	4206	5762	-1981	51
H(14A)	1528	5597	-3492	50
H(14B)	699	6372	-2621	50
H(15A)	-2220	5305	-3159	47
H(15B)	-1736	5307	-1789	47
H(16A)	-2036	3727	-2422	44
H(16B)	-194	3891	-3350	44
H(19A)	430	1587	-4363	69
H(19B)	2185	770	-4487	69
H(19C)	2461	1719	-5182	69
H(20A)	6563	1971	-2779	63
H(20B)	6410	1970	-4160	63
H(20C)	6149	1020	-3465	63
H(22A)	5467	-230	-1020	71
H(22B)	3463	-164	-1956	71
H(22C)	3060	-557	-691	71
H(1A)	-1592	2870	-236	59

Table 6. Torsion angles [°] for compound **243**.

C(6)-C(1)-C(2)-C(3)	-1.3(4)
C(7)-C(1)-C(2)-C(3)	178.0(3)
C(1)-C(2)-C(3)-C(4)	1.2(5)
C(2)-C(3)-C(4)-C(5)	-0.4(5)
C(3)-C(4)-C(5)-C(6)	-0.3(5)
C(4)-C(5)-C(6)-C(1)	0.1(5)
C(2)-C(1)-C(6)-C(5)	0.7(4)
C(7)-C(1)-C(6)-C(5)	-178.6(3)
C(6)-C(1)-C(7)-C(8)	-14.5(4)
C(2)-C(1)-C(7)-C(8)	166.2(3)
C(1)-C(7)-C(8)-C(9)	178.4(3)
C(7)-C(8)-C(9)-O(1)	-7.8(4)
C(7)-C(8)-C(9)-C(21)	-127.4(3)
C(7)-C(8)-C(9)-C(10)	114.4(3)
O(1)-C(9)-C(10)-C(17)	-121.6(3)
C(8)-C(9)-C(10)-C(17)	116.3(3)
C(21)-C(9)-C(10)-C(17)	-4.0(4)
O(1)-C(9)-C(10)-C(11)	55.7(3)
C(8)-C(9)-C(10)-C(11)	-66.4(3)
C(21)-C(9)-C(10)-C(11)	173.3(2)
C(17)-C(10)-C(11)-C(16)	65.1(4)
C(9)-C(10)-C(11)-C(16)	-112.2(3)
C(17)-C(10)-C(11)-C(12)	-58.5(4)
C(9)-C(10)-C(11)-C(12)	124.2(3)
C(16)-C(11)-C(12)-C(13)	56.2(3)
C(10)-C(11)-C(12)-C(13)	-179.4(3)
C(11)-C(12)-C(13)-C(14)	-55.6(4)
C(12)-C(13)-C(14)-C(15)	55.0(4)
C(13)-C(14)-C(15)-C(16)	-54.9(3)
C(10)-C(11)-C(16)-C(15)	179.7(3)
C(12)-C(11)-C(16)-C(15)	-56.5(3)
C(14)-C(15)-C(16)-C(11)	56.0(3)
C(11)-C(10)-C(17)-C(18)	144(6)

C(9)-C(10)-C(17)-C(18)	-39(6)
C(10)-C(17)-C(18)-C(20)	-51(6)
C(10)-C(17)-C(18)-C(19)	129(6)
O(1)-C(9)-C(21)-O(3)	19.0(4)
C(8)-C(9)-C(21)-O(3)	140.0(3)
C(10)-C(9)-C(21)-O(3)	-100.3(3)
O(1)-C(9)-C(21)-O(2)	-162.8(2)
C(8)-C(9)-C(21)-O(2)	-41.8(3)
C(10)-C(9)-C(21)-O(2)	77.9(3)
O(3)-C(21)-O(2)-C(22)	6.9(4)
C(9)-C(21)-O(2)-C(22)	-171.2(2)

Symmetry transformations used to generate equivalent atoms:

Comparing experimental Parsons' Q-values with those from calculated dataset 1
Correlation coefficient 14.02, GooF 0.9354, Flack x -0.0765 (0.1232)

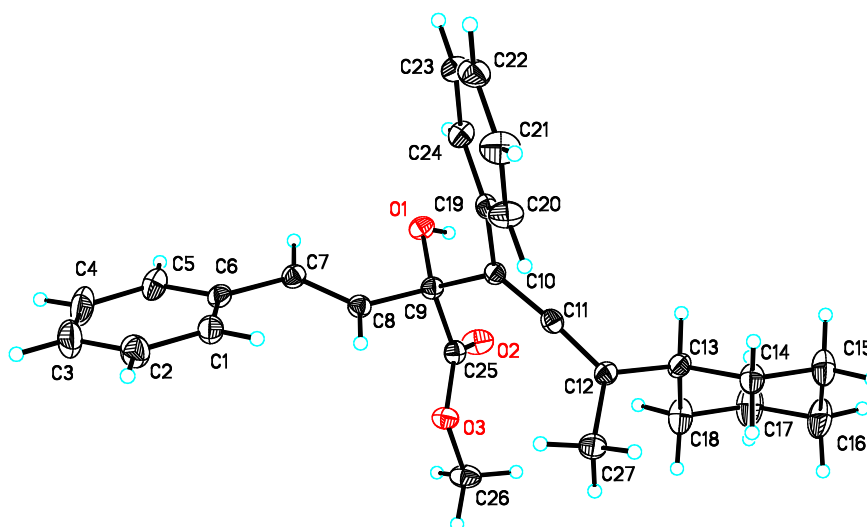
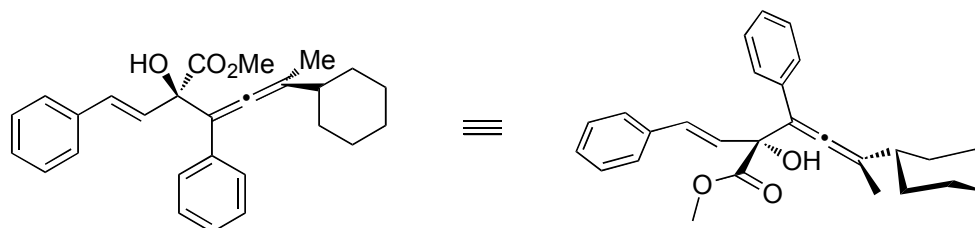
11. Crystal structure of compound (2*R*, 4*S*)-260

Table 1. Crystal data and structure refinement for compound **(2R, 4S)-260**.

Compound	(2R, 4S)-260	
Empirical formula	C ₂₇ H ₃₀ O ₃	
Formula weight	402.51	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.7202(2) Å	α = 90°.
	b = 14.8351(6) Å	β = 90°.
	c = 26.7155(11) Å	γ = 90°.
Volume	2267.07(15) Å ³	
Z	4	
Density (calculated)	1.179 Mg/m ³	
Absorption coefficient	0.593 mm ⁻¹	
F(000)	864	
Crystal size	0.54 x 0.25 x 0.15 mm ³	
Theta range for data collection	3.31 to 69.36°.	
Index ranges	-6 ≤ h ≤ 6, -16 ≤ k ≤ 18, -30 ≤ l ≤ 29	
Reflections collected	20515	
Independent reflections	4004 [R(int) = 0.0177]	
Completeness to theta = 69.36°	96.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9174 and 0.7399	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4004 / 0 / 271	
Goodness-of-fit on F ²	1.042	
Final R indices [I > 2σ(I)]	R1 = 0.0298, wR2 = 0.0754	
R indices (all data)	R1 = 0.0305, wR2 = 0.0761	
Absolute structure parameter	0.06(15)	
Largest diff. peak and hole	0.131 and -0.193 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2R, 4S)-260**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	12400(2)	7454(1)	6613(1)	38(1)
C(2)	13794(3)	7228(1)	6210(1)	48(1)
C(3)	13120(4)	7467(1)	5732(1)	60(1)
C(4)	11056(4)	7926(1)	5660(1)	63(1)
C(5)	9635(3)	8132(1)	6061(1)	45(1)
C(6)	10297(2)	7912(1)	6547(1)	32(1)
C(7)	8802(2)	8187(1)	6969(1)	31(1)
C(8)	9546(2)	8298(1)	7434(1)	28(1)
C(9)	8041(2)	8603(1)	7869(1)	27(1)
C(10)	8514(2)	7972(1)	8317(1)	26(1)
C(11)	9577(2)	8279(1)	8717(1)	28(1)
C(12)	10783(2)	8597(1)	9094(1)	30(1)
C(13)	9624(2)	8954(1)	9565(1)	33(1)
C(14)	10658(3)	8535(1)	10039(1)	41(1)
C(15)	9420(4)	8876(1)	10509(1)	53(1)
C(16)	9530(4)	9893(1)	10538(1)	61(1)
C(17)	8510(4)	10326(1)	10071(1)	65(1)
C(18)	9733(3)	9982(1)	9598(1)	50(1)
C(19)	7952(2)	6991(1)	8262(1)	28(1)
C(20)	9537(2)	6353(1)	8437(1)	41(1)
C(21)	9060(3)	5440(1)	8401(1)	51(1)
C(22)	7004(3)	5143(1)	8196(1)	43(1)
C(23)	5415(3)	5763(1)	8021(1)	40(1)
C(24)	5881(2)	6681(1)	8051(1)	35(1)
C(25)	8689(2)	9575(1)	8019(1)	29(1)
C(26)	11601(2)	10655(1)	8147(1)	42(1)
C(27)	13423(2)	8613(1)	9057(1)	39(1)
O(1)	5655(2)	8609(1)	7726(1)	32(1)
O(2)	7217(2)	10119(1)	8127(1)	43(1)

O(3) 10962(2) 9740(1) 8011(1) 32(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound (**2R**, **4S**)-**260**.

C(1)-C(2)	1.382(2)	C(15)-C(16)	1.512(2)
C(1)-C(6)	1.393(2)	C(15)-H(15A)	0.9900
C(1)-H(1A)	0.9500	C(15)-H(15B)	0.9900
C(2)-C(3)	1.379(2)	C(16)-C(17)	1.520(2)
C(2)-H(2A)	0.9500	C(16)-H(16A)	0.9900
C(3)-C(4)	1.376(3)	C(16)-H(16B)	0.9900
C(3)-H(3A)	0.9500	C(17)-C(18)	1.531(2)
C(4)-C(5)	1.380(2)	C(17)-H(17A)	0.9900
C(4)-H(4A)	0.9500	C(17)-H(17B)	0.9900
C(5)-C(6)	1.3917(19)	C(18)-H(18A)	0.9900
C(5)-H(5A)	0.9500	C(18)-H(18B)	0.9900
C(6)-C(7)	1.4734(18)	C(19)-C(24)	1.3902(18)
C(7)-C(8)	1.3222(18)	C(19)-C(20)	1.3912(18)
C(7)-H(7A)	0.9500	C(20)-C(21)	1.386(2)
C(8)-C(9)	1.5148(17)	C(20)-H(20A)	0.9500
C(8)-H(8A)	0.9500	C(21)-C(22)	1.370(2)
C(9)-O(1)	1.4173(15)	C(21)-H(21A)	0.9500
C(9)-C(25)	1.5421(17)	C(22)-C(23)	1.374(2)
C(9)-C(10)	1.5438(17)	C(22)-H(22A)	0.9500
C(10)-C(11)	1.3112(17)	C(23)-C(24)	1.3895(18)
C(10)-C(19)	1.4974(16)	C(23)-H(23A)	0.9500
C(11)-C(12)	1.3080(18)	C(24)-H(24A)	0.9500
C(12)-C(27)	1.5134(17)	C(25)-O(2)	1.2014(15)
C(12)-C(13)	1.5185(17)	C(25)-O(3)	1.3234(15)
C(13)-C(18)	1.5291(19)	C(26)-O(3)	1.4521(15)
C(13)-C(14)	1.5299(18)	C(26)-H(26A)	0.9800
C(13)-H(13A)	1.0000	C(26)-H(26B)	0.9800
C(14)-C(15)	1.527(2)	C(26)-H(26C)	0.9800
C(14)-H(14A)	0.9900	C(27)-H(27A)	0.9800
C(14)-H(14B)	0.9900	C(27)-H(27B)	0.9800

C(27)-H(27C)	0.9800	C(19)-C(10)-C(9)	118.41(10)
O(1)-H(1B)	0.8400	C(12)-C(11)-C(10)	175.44(13)
		C(11)-C(12)-C(27)	118.84(12)
C(2)-C(1)-C(6)	121.17(13)	C(11)-C(12)-C(13)	122.27(11)
C(2)-C(1)-H(1A)	119.4	C(27)-C(12)-C(13)	118.89(11)
C(6)-C(1)-H(1A)	119.4	C(12)-C(13)-C(18)	112.21(12)
C(3)-C(2)-C(1)	119.86(16)	C(12)-C(13)-C(14)	112.07(11)
C(3)-C(2)-H(2A)	120.1	C(18)-C(13)-C(14)	110.03(11)
C(1)-C(2)-H(2A)	120.1	C(12)-C(13)-H(13A)	107.4
C(4)-C(3)-C(2)	119.83(15)	C(18)-C(13)-H(13A)	107.4
C(4)-C(3)-H(3A)	120.1	C(14)-C(13)-H(13A)	107.4
C(2)-C(3)-H(3A)	120.1	C(15)-C(14)-C(13)	111.48(12)
C(3)-C(4)-C(5)	120.36(15)	C(15)-C(14)-H(14A)	109.3
C(3)-C(4)-H(4A)	119.8	C(13)-C(14)-H(14A)	109.3
C(5)-C(4)-H(4A)	119.8	C(15)-C(14)-H(14B)	109.3
C(4)-C(5)-C(6)	120.88(15)	C(13)-C(14)-H(14B)	109.3
C(4)-C(5)-H(5A)	119.6	H(14A)-C(14)-H(14B)	108.0
C(6)-C(5)-H(5A)	119.6	C(16)-C(15)-C(14)	110.71(13)
C(5)-C(6)-C(1)	117.87(13)	C(16)-C(15)-H(15A)	109.5
C(5)-C(6)-C(7)	119.47(13)	C(14)-C(15)-H(15A)	109.5
C(1)-C(6)-C(7)	122.64(11)	C(16)-C(15)-H(15B)	109.5
C(8)-C(7)-C(6)	124.52(12)	C(14)-C(15)-H(15B)	109.5
C(8)-C(7)-H(7A)	117.7	H(15A)-C(15)-H(15B)	108.1
C(6)-C(7)-H(7A)	117.7	C(15)-C(16)-C(17)	111.29(14)
C(7)-C(8)-C(9)	125.07(11)	C(15)-C(16)-H(16A)	109.4
C(7)-C(8)-H(8A)	117.5	C(17)-C(16)-H(16A)	109.4
C(9)-C(8)-H(8A)	117.5	C(15)-C(16)-H(16B)	109.4
O(1)-C(9)-C(8)	110.06(10)	C(17)-C(16)-H(16B)	109.4
O(1)-C(9)-C(25)	107.14(10)	H(16A)-C(16)-H(16B)	108.0
C(8)-C(9)-C(25)	109.96(10)	C(16)-C(17)-C(18)	111.20(15)
O(1)-C(9)-C(10)	112.42(10)	C(16)-C(17)-H(17A)	109.4
C(8)-C(9)-C(10)	108.35(9)	C(18)-C(17)-H(17A)	109.4
C(25)-C(9)-C(10)	108.90(9)	C(16)-C(17)-H(17B)	109.4
C(11)-C(10)-C(19)	121.09(11)	C(18)-C(17)-H(17B)	109.4
C(11)-C(10)-C(9)	120.21(11)	H(17A)-C(17)-H(17B)	108.0

C(13)-C(18)-C(17)	111.14(14)	C(23)-C(24)-C(19)	120.74(12)
C(13)-C(18)-H(18A)	109.4	C(23)-C(24)-H(24A)	119.6
C(17)-C(18)-H(18A)	109.4	C(19)-C(24)-H(24A)	119.6
C(13)-C(18)-H(18B)	109.4	O(2)-C(25)-O(3)	124.61(12)
C(17)-C(18)-H(18B)	109.4	O(2)-C(25)-C(9)	121.50(11)
H(18A)-C(18)-H(18B)	108.0	O(3)-C(25)-C(9)	113.89(10)
C(24)-C(19)-C(20)	117.80(12)	O(3)-C(26)-H(26A)	109.5
C(24)-C(19)-C(10)	122.98(11)	O(3)-C(26)-H(26B)	109.5
C(20)-C(19)-C(10)	119.21(11)	H(26A)-C(26)-H(26B)	109.5
C(21)-C(20)-C(19)	120.87(13)	O(3)-C(26)-H(26C)	109.5
C(21)-C(20)-H(20A)	119.6	H(26A)-C(26)-H(26C)	109.5
C(19)-C(20)-H(20A)	119.6	H(26B)-C(26)-H(26C)	109.5
C(22)-C(21)-C(20)	120.75(14)	C(12)-C(27)-H(27A)	109.5
C(22)-C(21)-H(21A)	119.6	C(12)-C(27)-H(27B)	109.5
C(20)-C(21)-H(21A)	119.6	H(27A)-C(27)-H(27B)	109.5
C(21)-C(22)-C(23)	119.22(13)	C(12)-C(27)-H(27C)	109.5
C(21)-C(22)-H(22A)	120.4	H(27A)-C(27)-H(27C)	109.5
C(23)-C(22)-H(22A)	120.4	H(27B)-C(27)-H(27C)	109.5
C(22)-C(23)-C(24)	120.61(13)	C(9)-O(1)-H(1B)	109.5
C(22)-C(23)-H(23A)	119.7	C(25)-O(3)-C(26)	114.60(10)
C(24)-C(23)-H(23A)	119.7		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2R, 4S)-260**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* 2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	44(1)	38(1)	32(1)	-1(1)	2(1)	-2(1)
C(2)	50(1)	47(1)	47(1)	-6(1)	10(1)	3(1)
C(3)	74(1)	66(1)	39(1)	-14(1)	17(1)	0(1)
C(4)	86(1)	78(1)	26(1)	-7(1)	-3(1)	0(1)
C(5)	57(1)	48(1)	32(1)	-4(1)	-7(1)	3(1)
C(6)	40(1)	26(1)	29(1)	-3(1)	-1(1)	-7(1)
C(7)	32(1)	30(1)	30(1)	1(1)	-4(1)	0(1)
C(8)	28(1)	28(1)	29(1)	1(1)	0(1)	-1(1)
C(9)	24(1)	30(1)	28(1)	0(1)	-2(1)	1(1)
C(10)	22(1)	30(1)	25(1)	-2(1)	1(1)	1(1)
C(11)	25(1)	30(1)	28(1)	2(1)	4(1)	4(1)
C(12)	27(1)	34(1)	28(1)	0(1)	-3(1)	0(1)
C(13)	29(1)	43(1)	28(1)	-5(1)	-3(1)	0(1)
C(14)	50(1)	41(1)	31(1)	2(1)	-1(1)	1(1)
C(15)	72(1)	57(1)	29(1)	-1(1)	4(1)	5(1)
C(16)	93(1)	59(1)	32(1)	-13(1)	0(1)	9(1)
C(17)	100(2)	54(1)	42(1)	-8(1)	4(1)	26(1)
C(18)	72(1)	43(1)	33(1)	0(1)	-1(1)	14(1)
C(19)	30(1)	30(1)	23(1)	-1(1)	4(1)	1(1)
C(20)	33(1)	34(1)	56(1)	3(1)	-7(1)	1(1)
C(21)	46(1)	34(1)	75(1)	5(1)	-5(1)	7(1)
C(22)	50(1)	28(1)	51(1)	-3(1)	9(1)	-4(1)
C(23)	42(1)	40(1)	39(1)	-8(1)	-1(1)	-9(1)
C(24)	38(1)	34(1)	33(1)	-2(1)	-5(1)	1(1)
C(25)	29(1)	31(1)	27(1)	2(1)	-1(1)	4(1)
C(26)	36(1)	29(1)	62(1)	-9(1)	6(1)	-3(1)
C(27)	26(1)	51(1)	39(1)	-2(1)	0(1)	0(1)
O(1)	25(1)	35(1)	36(1)	-1(1)	-6(1)	3(1)
O(2)	32(1)	34(1)	65(1)	-9(1)	-2(1)	6(1)

O(3) 27(1) 27(1) 42(1) -5(1) 4(1) -1(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2R, 4S)-260**.

	x	y	z	U(eq)
H(1A)	12885	7293	6941	46
H(2A)	15213	6908	6261	57
H(3A)	14077	7316	5454	72
H(4A)	10608	8101	5331	76
H(5A)	8186	8427	6004	55
H(7A)	7193	8292	6903	37
H(8A)	11148	8178	7500	34
H(13A)	7937	8780	9551	40
H(14A)	10511	7871	10021	49
H(14B)	12342	8685	10060	49
H(15A)	7766	8680	10503	63
H(15B)	10170	8613	10809	63
H(16A)	11177	10085	10577	74
H(16B)	8650	10102	10835	74
H(17A)	8687	10988	10092	78
H(17B)	6819	10187	10051	78
H(18A)	8973	10247	9299	59
H(18B)	11387	10178	9601	59
H(20A)	10966	6546	8583	49
H(21A)	10170	5015	8520	62
H(22A)	6681	4516	8174	52
H(23A)	3986	5562	7879	48
H(24A)	4771	7101	7927	42
H(26A)	13304	10721	8132	63
H(26B)	11056	10783	8487	63
H(26C)	10873	11079	7912	63

H(27A)	13908	8360	8735	58
H(27B)	14092	8253	9330	58
H(27C)	13977	9236	9084	58
H(1B)	4947	9015	7885	48

Table 6. Torsion angles [°] for compound (**2R, 4S**)-**260**.

C(6)-C(1)-C(2)-C(3)	0.8(2)
C(1)-C(2)-C(3)-C(4)	-0.3(3)
C(2)-C(3)-C(4)-C(5)	-1.3(3)
C(3)-C(4)-C(5)-C(6)	2.5(3)
C(4)-C(5)-C(6)-C(1)	-2.0(2)
C(4)-C(5)-C(6)-C(7)	176.56(14)
C(2)-C(1)-C(6)-C(5)	0.4(2)
C(2)-C(1)-C(6)-C(7)	-178.13(12)
C(5)-C(6)-C(7)-C(8)	-156.06(13)
C(1)-C(6)-C(7)-C(8)	22.41(19)
C(6)-C(7)-C(8)-C(9)	178.45(11)
C(7)-C(8)-C(9)-O(1)	9.52(16)
C(7)-C(8)-C(9)-C(25)	-108.28(13)
C(7)-C(8)-C(9)-C(10)	132.81(12)
O(1)-C(9)-C(10)-C(11)	-126.17(12)
C(8)-C(9)-C(10)-C(11)	111.98(12)
C(25)-C(9)-C(10)-C(11)	-7.60(15)
O(1)-C(9)-C(10)-C(19)	59.88(14)
C(8)-C(9)-C(10)-C(19)	-61.98(13)
C(25)-C(9)-C(10)-C(19)	178.44(10)
C(19)-C(10)-C(11)-C(12)	110.8(16)
C(9)-C(10)-C(11)-C(12)	-63.0(16)
C(10)-C(11)-C(12)-C(27)	-21.0(17)
C(10)-C(11)-C(12)-C(13)	158.7(16)
C(11)-C(12)-C(13)-C(18)	-106.59(15)
C(27)-C(12)-C(13)-C(18)	73.12(17)
C(11)-C(12)-C(13)-C(14)	129.02(13)
C(27)-C(12)-C(13)-C(14)	-51.27(17)

C(12)-C(13)-C(14)-C(15)	-178.04(12)
C(18)-C(13)-C(14)-C(15)	56.37(17)
C(13)-C(14)-C(15)-C(16)	-56.81(19)
C(14)-C(15)-C(16)-C(17)	56.2(2)
C(15)-C(16)-C(17)-C(18)	-55.9(2)
C(12)-C(13)-C(18)-C(17)	178.85(13)
C(14)-C(13)-C(18)-C(17)	-55.64(19)
C(16)-C(17)-C(18)-C(13)	55.8(2)
C(11)-C(10)-C(19)-C(24)	141.13(12)
C(9)-C(10)-C(19)-C(24)	-44.97(16)
C(11)-C(10)-C(19)-C(20)	-37.64(17)
C(9)-C(10)-C(19)-C(20)	136.26(12)
C(24)-C(19)-C(20)-C(21)	0.0(2)
C(10)-C(19)-C(20)-C(21)	178.86(14)
C(19)-C(20)-C(21)-C(22)	-0.5(3)
C(20)-C(21)-C(22)-C(23)	0.5(3)
C(21)-C(22)-C(23)-C(24)	0.1(2)
C(22)-C(23)-C(24)-C(19)	-0.6(2)
C(20)-C(19)-C(24)-C(23)	0.49(19)
C(10)-C(19)-C(24)-C(23)	-178.29(12)
O(1)-C(9)-C(25)-O(2)	19.44(16)
C(8)-C(9)-C(25)-O(2)	139.03(12)
C(10)-C(9)-C(25)-O(2)	-102.39(13)
O(1)-C(9)-C(25)-O(3)	-160.12(10)
C(8)-C(9)-C(25)-O(3)	-40.53(13)
C(10)-C(9)-C(25)-O(3)	78.06(13)
O(2)-C(25)-O(3)-C(26)	-0.05(18)
C(9)-C(25)-O(3)-C(26)	179.49(10)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound (**2R, 4S**)-**260** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	\angle (DHA)
O(1)-H(1B)...O(2)	0.84	2.19	2.6385(13)	113.5
O(1)-H(1B)...O(3)#1	0.84	2.54	3.2556(12)	143.3

Symmetry transformations used to generate equivalent atoms:

#1 $x-1, y, z$

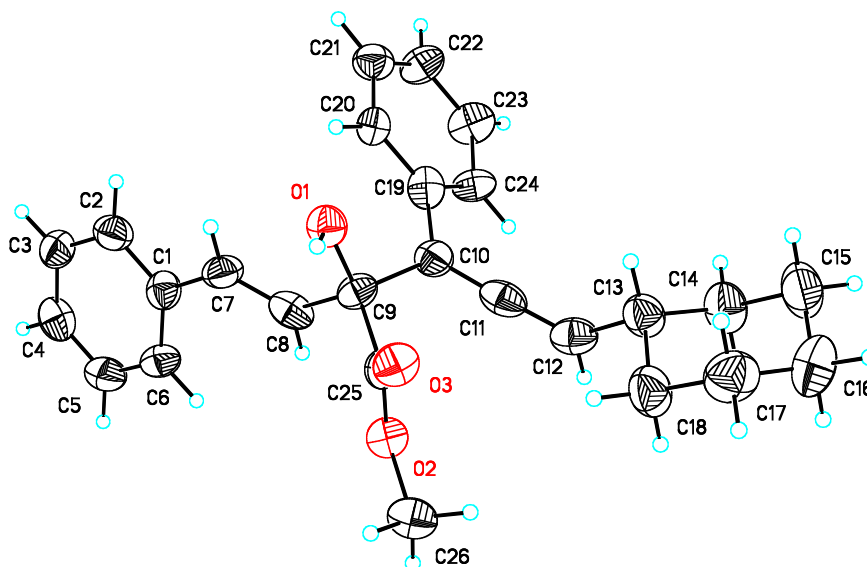
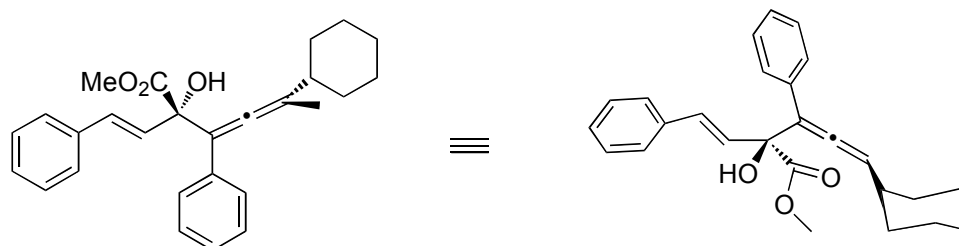
12. Crystal structure of compound (2*S*, 4*R*)-268

Table 1. Crystal data and structure refinement for compound **(2*S*, 4*R*)-268**.

Compound	(2<i>S</i>, 4<i>R</i>)-268	
Empirical formula	C ₂₆ H ₂₈ O ₃	
Formula weight	388.48	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.3970(11) Å	α = 90°.
	b = 15.026(4) Å	β = 90°.
	c = 26.570(5) Å	γ = 90°.
Volume	2154.6(8) Å ³	
Z	4	
Density (calculated)	1.198 Mg/m ³	
Absorption coefficient	0.607 mm ⁻¹	
F(000)	832	
Crystal size	0.30 x 0.08 x 0.03 mm ³	
Theta range for data collection	3.33 to 69.46°.	
Index ranges	-6<=h<=4, -18<=k<=16, -31<=l<=28	
Reflections collected	8134	
Independent reflections	3776 [R(int) = 0.1016]	
Completeness to theta = 69.46°	97.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9820 and 0.8390	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3776 / 0 / 263	
Goodness-of-fit on F ²	1.019	
Final R indices [I>2σ(I)]	R1 = 0.0688, wR2 = 0.0926	
R indices (all data)	R1 = 0.2561, wR2 = 0.1298	
Absolute structure parameter	-0.2(7)	
Extinction coefficient	0.0040(2)	
Largest diff. peak and hole	0.236 and -0.258 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2S, 4R)-268**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	-7215(17)	-2704(6)	-6498(3)	67(3)
C(2)	-5875(16)	-2115(6)	-6223(3)	77(3)
C(3)	-6661(17)	-1898(5)	-5726(3)	80(3)
C(4)	-8782(18)	-2274(6)	-5544(3)	82(3)
C(5)	-10071(17)	-2866(6)	-5827(4)	87(3)
C(6)	-9303(16)	-3077(5)	-6309(3)	69(2)
C(7)	-6239(14)	-2943(5)	-7005(3)	73(3)
C(8)	-7526(14)	-3288(5)	-7377(3)	70(3)
C(9)	-6510(14)	-3540(6)	-7898(3)	61(2)
C(10)	-7603(14)	-2925(6)	-8302(3)	67(3)
C(11)	-8895(16)	-3282(6)	-8669(4)	76(3)
C(12)	-10133(16)	-3620(5)	-9046(3)	79(3)
C(13)	-8900(16)	-3899(6)	-9547(3)	79(3)
C(14)	-10395(15)	-3545(5)	-9982(3)	92(3)
C(15)	-9268(18)	-3847(6)	-10482(3)	116(4)
C(16)	-9322(17)	-4847(7)	-10503(3)	120(4)
C(17)	-7795(17)	-5231(6)	-10082(3)	111(3)
C(18)	-8931(15)	-4905(5)	-9563(3)	99(3)
C(19)	-7340(18)	-1929(7)	-8252(3)	73(3)
C(20)	-5292(15)	-1545(6)	-8038(2)	73(3)
C(21)	-5043(16)	-602(6)	-8029(3)	79(3)
C(22)	-6867(16)	-96(6)	-8223(3)	83(3)
C(23)	-8915(16)	-474(6)	-8436(3)	87(3)
C(24)	-9134(16)	-1408(6)	-8447(3)	74(3)
C(25)	-7020(17)	-4524(6)	-8049(3)	67(3)
C(26)	-9954(12)	-5708(5)	-8051(2)	79(3)
O(1)	-3873(8)	-3421(3)	-7901(2)	69(2)
O(2)	-9319(9)	-4775(3)	-7917(2)	68(2)
O(3)	-5510(9)	-4961(3)	-8252(2)	75(2)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound (**2S**, **4R**)-**268**.

C(1)-C(6)	1.354(9)	C(16)-C(17)	1.504(9)
C(1)-C(2)	1.356(9)	C(16)-H(16A)	0.9900
C(1)-C(7)	1.491(9)	C(16)-H(16B)	0.9900
C(2)-C(3)	1.426(9)	C(17)-C(18)	1.586(8)
C(2)-H(2)	0.9500	C(17)-H(17A)	0.9900
C(3)-C(4)	1.365(8)	C(17)-H(17B)	0.9900
C(3)-H(3A)	0.9500	C(18)-H(18A)	0.9900
C(4)-C(5)	1.355(9)	C(18)-H(18B)	0.9900
C(4)-H(4A)	0.9500	C(19)-C(24)	1.348(9)
C(5)-C(6)	1.384(8)	C(19)-C(20)	1.370(9)
C(5)-H(5A)	0.9500	C(20)-C(21)	1.423(9)
C(6)-H(6A)	0.9500	C(20)-H(20A)	0.9500
C(7)-C(8)	1.314(8)	C(21)-C(22)	1.346(9)
C(7)-H(7A)	0.9500	C(21)-H(21A)	0.9500
C(8)-C(9)	1.537(9)	C(22)-C(23)	1.365(9)
C(8)-H(8A)	0.9500	C(22)-H(22A)	0.9500
C(9)-O(1)	1.434(7)	C(23)-C(24)	1.408(8)
C(9)-C(10)	1.535(9)	C(23)-H(23A)	0.9500
C(9)-C(25)	1.556(10)	C(24)-H(24A)	0.9500
C(10)-C(11)	1.314(10)	C(25)-O(3)	1.177(8)
C(10)-C(19)	1.509(10)	C(25)-O(2)	1.344(8)
C(11)-C(12)	1.306(9)	C(26)-O(2)	1.487(7)
C(12)-C(13)	1.547(9)	C(26)-H(26A)	0.9800
C(12)-H(12A)	0.9500	C(26)-H(26B)	0.9800
C(13)-C(14)	1.506(8)	C(26)-H(26C)	0.9800
C(13)-C(18)	1.513(8)	O(1)-H(1A)	0.8400
C(13)-H(13A)	1.0000		
C(14)-C(15)	1.528(9)	C(6)-C(1)-C(2)	121.0(9)
C(14)-H(14A)	0.9900	C(6)-C(1)-C(7)	121.9(9)
C(14)-H(14B)	0.9900	C(2)-C(1)-C(7)	117.0(9)
C(15)-C(16)	1.504(9)	C(1)-C(2)-C(3)	119.2(9)
C(15)-H(15A)	0.9900	C(1)-C(2)-H(2)	120.4
C(15)-H(15B)	0.9900	C(3)-C(2)-H(2)	120.4

C(4)-C(3)-C(2)	118.9(9)	C(18)-C(13)-H(13A)	110.5
C(4)-C(3)-H(3A)	120.6	C(12)-C(13)-H(13A)	110.5
C(2)-C(3)-H(3A)	120.6	C(13)-C(14)-C(15)	110.4(7)
C(5)-C(4)-C(3)	120.4(9)	C(13)-C(14)-H(14A)	109.6
C(5)-C(4)-H(4A)	119.8	C(15)-C(14)-H(14A)	109.6
C(3)-C(4)-H(4A)	119.8	C(13)-C(14)-H(14B)	109.6
C(4)-C(5)-C(6)	120.6(9)	C(15)-C(14)-H(14B)	109.6
C(4)-C(5)-H(5A)	119.7	H(14A)-C(14)-H(14B)	108.1
C(6)-C(5)-H(5A)	119.7	C(16)-C(15)-C(14)	108.8(8)
C(1)-C(6)-C(5)	119.8(9)	C(16)-C(15)-H(15A)	109.9
C(1)-C(6)-H(6A)	120.1	C(14)-C(15)-H(15A)	109.9
C(5)-C(6)-H(6A)	120.1	C(16)-C(15)-H(15B)	109.9
C(8)-C(7)-C(1)	126.0(8)	C(14)-C(15)-H(15B)	109.9
C(8)-C(7)-H(7A)	117.0	H(15A)-C(15)-H(15B)	108.3
C(1)-C(7)-H(7A)	117.0	C(15)-C(16)-C(17)	110.2(9)
C(7)-C(8)-C(9)	125.9(8)	C(15)-C(16)-H(16A)	109.6
C(7)-C(8)-H(8A)	117.1	C(17)-C(16)-H(16A)	109.6
C(9)-C(8)-H(8A)	117.1	C(15)-C(16)-H(16B)	109.6
O(1)-C(9)-C(10)	107.6(7)	C(17)-C(16)-H(16B)	109.6
O(1)-C(9)-C(8)	109.2(7)	H(16A)-C(16)-H(16B)	108.1
C(10)-C(9)-C(8)	110.2(7)	C(16)-C(17)-C(18)	108.4(8)
O(1)-C(9)-C(25)	107.0(7)	C(16)-C(17)-H(17A)	110.0
C(10)-C(9)-C(25)	108.8(7)	C(18)-C(17)-H(17A)	110.0
C(8)-C(9)-C(25)	113.8(7)	C(16)-C(17)-H(17B)	110.0
C(11)-C(10)-C(19)	121.3(9)	C(18)-C(17)-H(17B)	110.0
C(11)-C(10)-C(9)	118.6(9)	H(17A)-C(17)-H(17B)	108.4
C(19)-C(10)-C(9)	120.0(8)	C(13)-C(18)-C(17)	109.1(7)
C(12)-C(11)-C(10)	178.0(9)	C(13)-C(18)-H(18A)	109.9
C(11)-C(12)-C(13)	123.0(8)	C(17)-C(18)-H(18A)	109.9
C(11)-C(12)-H(12A)	118.5	C(13)-C(18)-H(18B)	109.9
C(13)-C(12)-H(12A)	118.5	C(17)-C(18)-H(18B)	109.9
C(14)-C(13)-C(18)	109.1(7)	H(18A)-C(18)-H(18B)	108.3
C(14)-C(13)-C(12)	109.6(7)	C(24)-C(19)-C(20)	119.6(10)
C(18)-C(13)-C(12)	106.8(7)	C(24)-C(19)-C(10)	118.3(9)
C(14)-C(13)-H(13A)	110.5	C(20)-C(19)-C(10)	122.0(9)

C(19)-C(20)-C(21)	120.1(9)	C(19)-C(24)-H(24A)	119.7
C(19)-C(20)-H(20A)	119.9	C(23)-C(24)-H(24A)	119.7
C(21)-C(20)-H(20A)	119.9	O(3)-C(25)-O(2)	127.0(9)
C(22)-C(21)-C(20)	119.1(9)	O(3)-C(25)-C(9)	121.8(9)
C(22)-C(21)-H(21A)	120.4	O(2)-C(25)-C(9)	111.2(8)
C(20)-C(21)-H(21A)	120.4	O(2)-C(26)-H(26A)	109.5
C(21)-C(22)-C(23)	121.0(9)	O(2)-C(26)-H(26B)	109.5
C(21)-C(22)-H(22A)	119.5	H(26A)-C(26)-H(26B)	109.5
C(23)-C(22)-H(22A)	119.5	O(2)-C(26)-H(26C)	109.5
C(22)-C(23)-C(24)	119.4(9)	H(26A)-C(26)-H(26C)	109.5
C(22)-C(23)-H(23A)	120.3	H(26B)-C(26)-H(26C)	109.5
C(24)-C(23)-H(23A)	120.3	C(9)-O(1)-H(1A)	109.5
C(19)-C(24)-C(23)	120.7(9)	C(25)-O(2)-C(26)	114.5(6)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **(2S, 4R)-268**.
 The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
C(1)	58(7)	78(7)	64(6)	1(5)	-2(6)	7(6)
C(2)	71(7)	78(7)	80(7)	13(5)	7(6)	-7(6)
C(3)	92(8)	75(7)	73(7)	-4(5)	-16(6)	-9(6)
C(4)	84(8)	94(9)	68(7)	7(6)	11(6)	22(7)
C(5)	87(8)	86(8)	89(7)	12(6)	12(7)	-19(7)
C(6)	64(7)	54(6)	90(7)	-4(5)	0(5)	-4(5)
C(7)	58(6)	71(6)	91(7)	8(5)	-6(5)	-15(5)
C(8)	56(6)	70(7)	85(7)	17(5)	25(5)	15(6)
C(9)	44(6)	62(6)	78(7)	-5(5)	-3(5)	0(5)
C(10)	48(6)	75(8)	77(7)	11(6)	-4(5)	0(6)
C(11)	58(7)	73(8)	97(8)	26(6)	18(6)	6(6)
C(12)	62(7)	68(7)	106(8)	8(6)	3(6)	-1(6)
C(13)	99(7)	66(7)	73(7)	3(5)	4(6)	5(6)
C(14)	113(8)	80(7)	84(6)	3(6)	-6(6)	27(7)
C(15)	156(9)	122(9)	70(7)	6(7)	-3(7)	2(9)
C(16)	134(9)	135(10)	91(8)	-34(8)	-16(7)	6(10)
C(17)	125(9)	85(8)	122(9)	-13(7)	4(7)	0(7)
C(18)	139(8)	91(8)	67(6)	-7(6)	10(6)	2(8)
C(19)	65(7)	87(8)	66(6)	-3(6)	2(5)	15(7)
C(20)	73(7)	83(7)	61(5)	6(5)	-12(5)	-10(6)
C(21)	86(7)	67(7)	83(6)	-1(5)	6(6)	-9(7)
C(22)	71(7)	68(7)	111(8)	-19(6)	-7(6)	1(6)
C(23)	70(7)	63(7)	129(8)	-2(6)	-7(6)	23(6)
C(24)	72(7)	51(6)	100(7)	-7(5)	4(5)	-10(6)
C(25)	62(7)	73(8)	66(6)	9(5)	-14(6)	-1(6)
C(26)	73(6)	61(5)	102(6)	5(5)	15(5)	11(6)
O(1)	71(4)	65(4)	71(4)	2(3)	-2(3)	7(3)
O(2)	63(4)	65(4)	75(3)	-4(3)	4(3)	8(4)
O(3)	73(4)	67(4)	83(4)	-12(3)	5(3)	4(4)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound (**2S**, **4R**)-**268**.

	x	y	z	U(eq)
H(2)	-4428	-1849	-6361	92
H(3A)	-5725	-1499	-5524	96
H(4A)	-9359	-2120	-5218	98
H(5A)	-11514	-3138	-5692	105
H(6A)	-10238	-3482	-6508	83
H(7A)	-4529	-2837	-7065	88
H(8A)	-9239	-3390	-7318	84
H(12A)	-11871	-3699	-9010	95
H(13A)	-7160	-3672	-9564	95
H(14A)	-10428	-2887	-9969	111
H(14B)	-12122	-3763	-9957	111
H(15A)	-10228	-3597	-10766	139
H(15B)	-7539	-3633	-10509	139
H(16A)	-8657	-5052	-10830	144
H(16B)	-11053	-5059	-10473	144
H(17A)	-6055	-5029	-10112	133
H(17B)	-7819	-5889	-10098	133
H(18A)	-10653	-5124	-9529	119
H(18B)	-7945	-5147	-9280	119
H(20A)	-4038	-1909	-7894	87
H(21A)	-3608	-334	-7889	94
H(22A)	-6726	534	-8212	100
H(23A)	-10182	-110	-8575	105
H(24A)	-10560	-1674	-8593	89
H(26A)	-11641	-5842	-7938	118
H(26B)	-8786	-6115	-7888	118
H(26C)	-9854	-5782	-8417	118
H(1A)	-3176	-3920	-7912	104

Table 6. Torsion angles [°] for compound (**2S**, **4R**)-**268**.

C(6)-C(1)-C(2)-C(3)	1.1(12)
C(7)-C(1)-C(2)-C(3)	-176.9(7)
C(1)-C(2)-C(3)-C(4)	-1.7(12)
C(2)-C(3)-C(4)-C(5)	2.2(13)
C(3)-C(4)-C(5)-C(6)	-2.1(14)
C(2)-C(1)-C(6)-C(5)	-1.0(12)
C(7)-C(1)-C(6)-C(5)	176.9(7)
C(4)-C(5)-C(6)-C(1)	1.5(13)
C(6)-C(1)-C(7)-C(8)	22.3(12)
C(2)-C(1)-C(7)-C(8)	-159.7(9)
C(1)-C(7)-C(8)-C(9)	-179.5(7)
C(7)-C(8)-C(9)-O(1)	5.5(11)
C(7)-C(8)-C(9)-C(10)	-112.4(9)
C(7)-C(8)-C(9)-C(25)	125.0(9)
O(1)-C(9)-C(10)-C(11)	120.8(8)
C(8)-C(9)-C(10)-C(11)	-120.2(9)
C(25)-C(9)-C(10)-C(11)	5.2(11)
O(1)-C(9)-C(10)-C(19)	-63.6(10)
C(8)-C(9)-C(10)-C(19)	55.3(10)
C(25)-C(9)-C(10)-C(19)	-179.2(7)
C(19)-C(10)-C(11)-C(12)	54(27)
C(9)-C(10)-C(11)-C(12)	-130(27)
C(10)-C(11)-C(12)-C(13)	39(27)
C(11)-C(12)-C(13)-C(14)	-133.3(9)
C(11)-C(12)-C(13)-C(18)	108.8(9)
C(18)-C(13)-C(14)-C(15)	-61.0(9)
C(12)-C(13)-C(14)-C(15)	-177.5(7)
C(13)-C(14)-C(15)-C(16)	61.3(10)
C(14)-C(15)-C(16)-C(17)	-61.5(11)
C(15)-C(16)-C(17)-C(18)	60.2(10)
C(14)-C(13)-C(18)-C(17)	59.2(9)
C(12)-C(13)-C(18)-C(17)	177.5(7)
C(16)-C(17)-C(18)-C(13)	-59.1(10)

C(11)-C(10)-C(19)-C(24)	26.0(13)
C(9)-C(10)-C(19)-C(24)	-149.5(7)
C(11)-C(10)-C(19)-C(20)	-150.9(8)
C(9)-C(10)-C(19)-C(20)	33.6(12)
C(24)-C(19)-C(20)-C(21)	-1.2(12)
C(10)-C(19)-C(20)-C(21)	175.7(7)
C(19)-C(20)-C(21)-C(22)	1.6(12)
C(20)-C(21)-C(22)-C(23)	-1.4(13)
C(21)-C(22)-C(23)-C(24)	0.7(13)
C(20)-C(19)-C(24)-C(23)	0.5(13)
C(10)-C(19)-C(24)-C(23)	-176.4(7)
C(22)-C(23)-C(24)-C(19)	-0.3(13)
O(1)-C(9)-C(25)-O(3)	-18.0(11)
C(10)-C(9)-C(25)-O(3)	98.0(9)
C(8)-C(9)-C(25)-O(3)	-138.7(9)
O(1)-C(9)-C(25)-O(2)	161.8(6)
C(10)-C(9)-C(25)-O(2)	-82.2(8)
C(8)-C(9)-C(25)-O(2)	41.1(9)
O(3)-C(25)-O(2)-C(26)	-0.6(12)
C(9)-C(25)-O(2)-C(26)	179.7(5)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound (**2S, 4R**)-**268** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1A)...O(3)	0.84	2.20	2.647(6)	113.2
O(1)-H(1A)...O(2)#1	0.84	2.45	3.191(6)	148.2

Symmetry transformations used to generate equivalent atoms:

#1 x+1,y,z

13. Crystal structure of compound 283

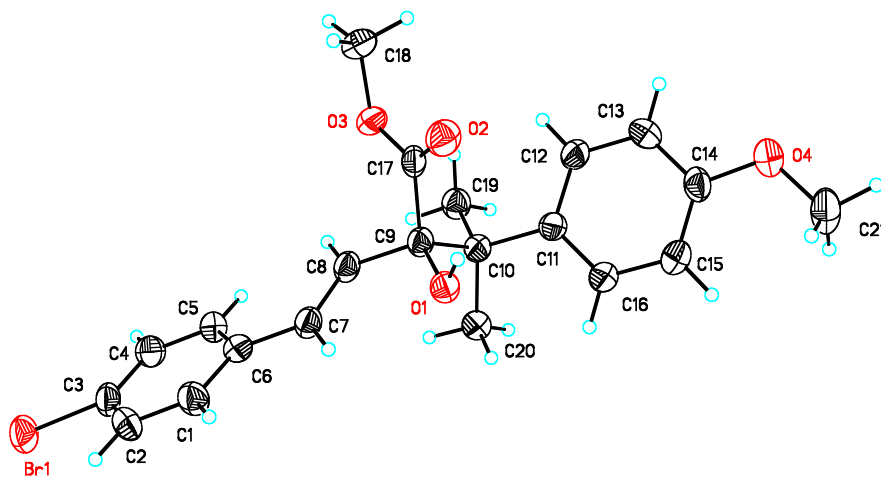
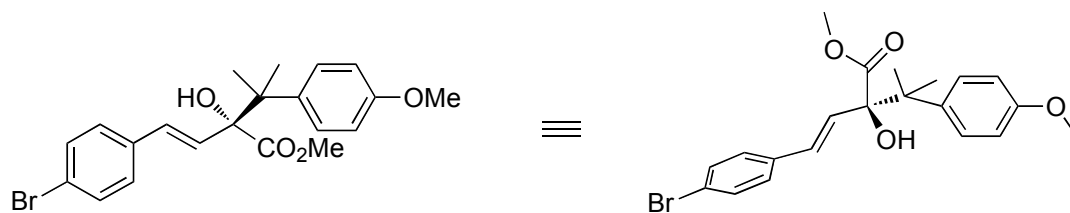


Table 1. Crystal data and structure refinement for compound **283**.

Compound	283	
Empirical formula	C ₂₁ H ₂₃ Br O ₄	
Formula weight	419.30	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 6.1466(9) Å	α = 90°.
	b = 11.3882(15) Å	β = 90°.
	c = 27.357(4) Å	γ = 90°.
Volume	1915.0(5) Å ³	
Z	4	
Density (calculated)	1.454 Mg/m ³	
Absorption coefficient	3.116 mm ⁻¹	
F(000)	864	
Crystal size	0.50 x 0.21 x 0.11 mm ³	
Theta range for data collection	3.23 to 66.59°.	
Index ranges	-7 ≤ h ≤ 7, -10 ≤ k ≤ 12, -32 ≤ l ≤ 32	
Reflections collected	16252	
Independent reflections	3227 [R(int) = 0.0428]	
Completeness to theta = 66.59°	96.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7256 and 0.3048	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3227 / 0 / 235	
Goodness-of-fit on F ²	1.010	
Final R indices [I > 2σ(I)]	R1 = 0.0334, wR2 = 0.0809	
R indices (all data)	R1 = 0.0378, wR2 = 0.0855	
Absolute structure parameter	0.04(2)	
Largest diff. peak and hole	0.638 and -0.408 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **283**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Br(1)	-4655(1)	-9774(1)	-2304(1)	50(1)
C(1)	-4348(6)	-6732(3)	-1474(1)	38(1)
C(2)	-3862(6)	-7801(3)	-1693(2)	41(1)
C(3)	-5341(7)	-8330(3)	-1989(1)	37(1)
C(4)	-7361(6)	-7826(3)	-2075(1)	36(1)
C(5)	-7846(6)	-6753(3)	-1858(1)	34(1)
C(6)	-6362(6)	-6188(3)	-1553(1)	31(1)
C(7)	-6801(5)	-5055(3)	-1312(1)	31(1)
C(8)	-8736(6)	-4542(3)	-1268(1)	30(1)
C(9)	-9107(5)	-3371(3)	-1023(1)	28(1)
C(10)	-10161(6)	-2459(3)	-1399(1)	30(1)
C(11)	-10408(6)	-1260(3)	-1147(1)	30(1)
C(12)	-12286(6)	-987(3)	-881(1)	36(1)
C(13)	-12516(6)	95(3)	-659(1)	40(1)
C(14)	-10920(6)	947(3)	-698(1)	35(1)
C(15)	-9058(6)	694(3)	-958(1)	35(1)
C(16)	-8812(6)	-403(3)	-1177(1)	33(1)
C(17)	-10559(6)	-3561(3)	-570(1)	29(1)
C(18)	-13537(6)	-4574(3)	-223(1)	39(1)
C(19)	-12373(6)	-2881(3)	-1594(1)	35(1)
C(20)	-8592(6)	-2376(3)	-1836(1)	36(1)
C(21)	-9652(8)	2863(3)	-493(2)	54(1)
O(1)	-7107(4)	-2911(2)	-854(1)	31(1)
O(2)	-10188(5)	-3102(2)	-183(1)	41(1)
O(3)	-12180(4)	-4309(2)	-647(1)	33(1)
O(4)	-11309(5)	1990(2)	-465(1)	49(1)

Table 3. Bond lengths [\AA] and angles [$^\circ$] for compound **283**.

Br(1)-C(3)	1.902(3)	C(17)-O(2)	1.203(4)
C(1)-C(2)	1.389(5)	C(17)-O(3)	1.327(4)
C(1)-C(6)	1.401(5)	C(18)-O(3)	1.460(4)
C(1)-H(1A)	0.9500	C(18)-H(18A)	0.9800
C(2)-C(3)	1.359(6)	C(18)-H(18B)	0.9800
C(2)-H(2A)	0.9500	C(18)-H(18C)	0.9800
C(3)-C(4)	1.388(6)	C(19)-H(19A)	0.9800
C(4)-C(5)	1.391(5)	C(19)-H(19B)	0.9800
C(4)-H(4A)	0.9500	C(19)-H(19C)	0.9800
C(5)-C(6)	1.394(5)	C(20)-H(20A)	0.9800
C(5)-H(5A)	0.9500	C(20)-H(20B)	0.9800
C(6)-C(7)	1.474(5)	C(20)-H(20C)	0.9800
C(7)-C(8)	1.331(5)	C(21)-O(4)	1.425(5)
C(7)-H(7A)	0.9500	C(21)-H(21A)	0.9800
C(8)-C(9)	1.509(4)	C(21)-H(21B)	0.9800
C(8)-H(8A)	0.9500	C(21)-H(21C)	0.9800
C(9)-O(1)	1.414(4)	O(1)-H(1B)	0.8400
C(9)-C(17)	1.543(5)		
C(9)-C(10)	1.598(4)	C(2)-C(1)-C(6)	120.8(3)
C(10)-C(11)	1.536(4)	C(2)-C(1)-H(1A)	119.6
C(10)-C(19)	1.537(5)	C(6)-C(1)-H(1A)	119.6
C(10)-C(20)	1.539(5)	C(3)-C(2)-C(1)	120.1(3)
C(11)-C(16)	1.386(5)	C(3)-C(2)-H(2A)	119.9
C(11)-C(12)	1.401(5)	C(1)-C(2)-H(2A)	119.9
C(12)-C(13)	1.380(5)	C(2)-C(3)-C(4)	121.0(3)
C(12)-H(12A)	0.9500	C(2)-C(3)-Br(1)	120.3(3)
C(13)-C(14)	1.384(5)	C(4)-C(3)-Br(1)	118.6(3)
C(13)-H(13A)	0.9500	C(3)-C(4)-C(5)	118.9(3)
C(14)-O(4)	1.369(4)	C(3)-C(4)-H(4A)	120.6
C(14)-C(15)	1.379(5)	C(5)-C(4)-H(4A)	120.6
C(15)-C(16)	1.392(5)	C(4)-C(5)-C(6)	121.4(3)
C(15)-H(15A)	0.9500	C(4)-C(5)-H(5A)	119.3
C(16)-H(16A)	0.9500	C(6)-C(5)-H(5A)	119.3

C(5)-C(6)-C(1)	117.8(3)	C(16)-C(15)-H(15A)	120.0
C(5)-C(6)-C(7)	123.5(3)	C(11)-C(16)-C(15)	122.0(3)
C(1)-C(6)-C(7)	118.7(3)	C(11)-C(16)-H(16A)	119.0
C(8)-C(7)-C(6)	126.1(3)	C(15)-C(16)-H(16A)	119.0
C(8)-C(7)-H(7A)	117.0	O(2)-C(17)-O(3)	124.0(3)
C(6)-C(7)-H(7A)	117.0	O(2)-C(17)-C(9)	122.5(3)
C(7)-C(8)-C(9)	124.3(3)	O(3)-C(17)-C(9)	113.4(3)
C(7)-C(8)-H(8A)	117.8	O(3)-C(18)-H(18A)	109.5
C(9)-C(8)-H(8A)	117.8	O(3)-C(18)-H(18B)	109.5
O(1)-C(9)-C(8)	109.9(3)	H(18A)-C(18)-H(18B)	109.5
O(1)-C(9)-C(17)	107.0(3)	O(3)-C(18)-H(18C)	109.5
C(8)-C(9)-C(17)	108.6(3)	H(18A)-C(18)-H(18C)	109.5
O(1)-C(9)-C(10)	108.8(3)	H(18B)-C(18)-H(18C)	109.5
C(8)-C(9)-C(10)	110.6(3)	C(10)-C(19)-H(19A)	109.5
C(17)-C(9)-C(10)	111.9(3)	C(10)-C(19)-H(19B)	109.5
C(11)-C(10)-C(19)	110.2(3)	H(19A)-C(19)-H(19B)	109.5
C(11)-C(10)-C(20)	110.9(3)	C(10)-C(19)-H(19C)	109.5
C(19)-C(10)-C(20)	107.7(3)	H(19A)-C(19)-H(19C)	109.5
C(11)-C(10)-C(9)	109.2(2)	H(19B)-C(19)-H(19C)	109.5
C(19)-C(10)-C(9)	112.2(3)	C(10)-C(20)-H(20A)	109.5
C(20)-C(10)-C(9)	106.6(3)	C(10)-C(20)-H(20B)	109.5
C(16)-C(11)-C(12)	117.2(3)	H(20A)-C(20)-H(20B)	109.5
C(16)-C(11)-C(10)	122.0(3)	C(10)-C(20)-H(20C)	109.5
C(12)-C(11)-C(10)	120.8(3)	H(20A)-C(20)-H(20C)	109.5
C(13)-C(12)-C(11)	120.8(3)	H(20B)-C(20)-H(20C)	109.5
C(13)-C(12)-H(12A)	119.6	O(4)-C(21)-H(21A)	109.5
C(11)-C(12)-H(12A)	119.6	O(4)-C(21)-H(21B)	109.5
C(12)-C(13)-C(14)	121.3(3)	H(21A)-C(21)-H(21B)	109.5
C(12)-C(13)-H(13A)	119.4	O(4)-C(21)-H(21C)	109.5
C(14)-C(13)-H(13A)	119.4	H(21A)-C(21)-H(21C)	109.5
O(4)-C(14)-C(15)	124.5(3)	H(21B)-C(21)-H(21C)	109.5
O(4)-C(14)-C(13)	116.7(3)	C(9)-O(1)-H(1B)	109.5
C(15)-C(14)-C(13)	118.8(3)	C(17)-O(3)-C(18)	115.9(3)
C(14)-C(15)-C(16)	119.9(3)	C(14)-O(4)-C(21)	117.1(3)
C(14)-C(15)-H(15A)	120.0		

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **283**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^* 2U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	68(1)	29(1)	53(1)	-5(1)	14(1)	7(1)
C(1)	30(2)	34(2)	50(2)	-3(2)	-4(2)	1(2)
C(2)	34(2)	33(2)	56(2)	2(2)	3(2)	9(2)
C(3)	51(2)	21(2)	38(2)	0(1)	8(2)	3(2)
C(4)	38(2)	34(2)	37(2)	-3(1)	1(2)	-1(2)
C(5)	35(2)	28(2)	39(2)	2(1)	2(2)	2(2)
C(6)	29(2)	29(2)	35(2)	0(1)	4(2)	-3(1)
C(7)	30(2)	25(2)	39(2)	2(1)	-3(1)	-3(1)
C(8)	29(2)	23(2)	39(2)	-1(1)	-3(2)	-4(1)
C(9)	26(2)	23(2)	35(2)	-2(1)	-1(1)	-2(1)
C(10)	27(2)	26(2)	36(2)	1(1)	2(2)	-1(1)
C(11)	30(2)	28(2)	31(2)	6(1)	3(2)	3(1)
C(12)	28(2)	28(2)	52(2)	2(2)	4(2)	-3(1)
C(13)	33(2)	38(2)	49(2)	-2(2)	9(2)	7(2)
C(14)	44(2)	24(2)	37(2)	2(1)	0(2)	6(2)
C(15)	38(2)	29(2)	39(2)	5(1)	-3(2)	-4(2)
C(16)	32(2)	29(2)	38(2)	2(1)	3(2)	0(2)
C(17)	29(2)	20(2)	40(2)	0(1)	-1(2)	2(1)
C(18)	37(2)	41(2)	39(2)	7(2)	6(2)	-6(2)
C(19)	33(2)	32(2)	40(2)	0(2)	-3(2)	0(2)
C(20)	36(2)	33(2)	40(2)	2(2)	6(2)	2(2)
C(21)	65(3)	29(2)	67(3)	-7(2)	-3(3)	0(2)
O(1)	24(1)	28(1)	42(1)	-4(1)	-3(1)	-2(1)
O(2)	47(2)	38(1)	37(1)	-5(1)	1(1)	-7(1)
O(3)	32(1)	31(1)	37(1)	0(1)	6(1)	-7(1)
O(4)	59(2)	31(2)	57(2)	-8(1)	11(2)	0(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound **283**.

	x	y	z	U(eq)
H(1A)	-3302	-6366	-1269	45
H(2A)	-2493	-8163	-1636	49
H(4A)	-8394	-8207	-2279	43
H(5A)	-9219	-6398	-1918	41
H(7A)	-5589	-4652	-1177	37
H(8A)	-9965	-4940	-1398	36
H(12A)	-13416	-1552	-852	44
H(13A)	-13794	258	-476	48
H(15A)	-7943	1267	-989	42
H(16A)	-7512	-568	-1351	40
H(18A)	-14676	-5132	-317	58
H(18B)	-14208	-3849	-102	58
H(18C)	-12637	-4920	36	58
H(19A)	-12958	-2297	-1822	53
H(19B)	-13385	-2981	-1320	53
H(19C)	-12187	-3632	-1763	53
H(20A)	-9181	-1828	-2079	54
H(20B)	-8425	-3154	-1985	54
H(20C)	-7172	-2095	-1724	54
H(21A)	-10116	3563	-313	81
H(21B)	-9395	3069	-836	81
H(21C)	-8306	2557	-349	81
H(1B)	-7216	-2742	-556	47

Table 6. Torsion angles [°] for compound **283**.

C(6)-C(1)-C(2)-C(3)	0.3(6)
C(1)-C(2)-C(3)-C(4)	-0.7(6)
C(1)-C(2)-C(3)-Br(1)	178.4(3)
C(2)-C(3)-C(4)-C(5)	0.9(6)
Br(1)-C(3)-C(4)-C(5)	-178.1(3)
C(3)-C(4)-C(5)-C(6)	-0.8(6)
C(4)-C(5)-C(6)-C(1)	0.5(5)
C(4)-C(5)-C(6)-C(7)	-179.7(3)
C(2)-C(1)-C(6)-C(5)	-0.2(5)
C(2)-C(1)-C(6)-C(7)	180.0(3)
C(5)-C(6)-C(7)-C(8)	14.5(6)
C(1)-C(6)-C(7)-C(8)	-165.7(4)
C(6)-C(7)-C(8)-C(9)	-179.2(3)
C(7)-C(8)-C(9)-O(1)	0.1(5)
C(7)-C(8)-C(9)-C(17)	-116.5(4)
C(7)-C(8)-C(9)-C(10)	120.3(4)
O(1)-C(9)-C(10)-C(11)	-56.3(3)
C(8)-C(9)-C(10)-C(11)	-177.1(3)
C(17)-C(9)-C(10)-C(11)	61.7(3)
O(1)-C(9)-C(10)-C(19)	-178.8(3)
C(8)-C(9)-C(10)-C(19)	60.4(4)
C(17)-C(9)-C(10)-C(19)	-60.9(3)
O(1)-C(9)-C(10)-C(20)	63.5(3)
C(8)-C(9)-C(10)-C(20)	-57.3(3)
C(17)-C(9)-C(10)-C(20)	-178.5(3)
C(19)-C(10)-C(11)-C(16)	-143.8(3)
C(20)-C(10)-C(11)-C(16)	-24.7(4)
C(9)-C(10)-C(11)-C(16)	92.5(4)
C(19)-C(10)-C(11)-C(12)	35.4(4)
C(20)-C(10)-C(11)-C(12)	154.6(3)
C(9)-C(10)-C(11)-C(12)	-88.3(4)
C(16)-C(11)-C(12)-C(13)	0.0(5)
C(10)-C(11)-C(12)-C(13)	-179.3(3)

C(11)-C(12)-C(13)-C(14)	0.9(6)
C(12)-C(13)-C(14)-O(4)	179.8(3)
C(12)-C(13)-C(14)-C(15)	-0.9(6)
O(4)-C(14)-C(15)-C(16)	179.2(3)
C(13)-C(14)-C(15)-C(16)	0.1(5)
C(12)-C(11)-C(16)-C(15)	-0.9(5)
C(10)-C(11)-C(16)-C(15)	178.4(3)
C(14)-C(15)-C(16)-C(11)	0.8(5)
O(1)-C(9)-C(17)-O(2)	17.3(4)
C(8)-C(9)-C(17)-O(2)	135.8(3)
C(10)-C(9)-C(17)-O(2)	-101.8(4)
O(1)-C(9)-C(17)-O(3)	-160.1(3)
C(8)-C(9)-C(17)-O(3)	-41.6(4)
C(10)-C(9)-C(17)-O(3)	80.8(3)
O(2)-C(17)-O(3)-C(18)	-0.7(5)
C(9)-C(17)-O(3)-C(18)	176.7(3)
C(15)-C(14)-O(4)-C(21)	-0.7(5)
C(13)-C(14)-O(4)-C(21)	178.5(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for compound **283** [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	\angle (DHA)
O(1)-H(1B)...O(2)	0.84	2.13	2.647(3)	119.2
O(1)-H(1B)...O(2)#1	0.84	2.56	3.282(3)	144.4

Symmetry transformations used to generate equivalent atoms:

#1 $x+1/2, -y-1/2, -z$