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Hengbin Wang Date

SYNTHESIS OF CYCLOPROPANES AND DIHYDROFURANS BY METAL CARBENOID REACTIONS

By

Hengbin Wang
Doctor of Philosophy

Chemistry

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Accepted:

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Dean of the James T. Laney School of Graduate Studies

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Date

SYNTHESIS OF CYCLOPROPANES AND DIHYDROFURANS BY METAL CARBENOID REACTIONS

By

HENGBIN WANG

M.Sc., Shanghai Institute of Materia Medica, Chinese Academy of Sciences

Advisor: Huw M. L. Davies, Ph.D.

An abstract of

A dissertation submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

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Doctor of Philosophy

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2012

Abstract

SYNTHESIS OF CYCLOPROPANES AND DIHYDROFURANS BY METAL CARBENOID REACTIONS

By Hengbin Wang

Rhodium-catalyzed carbenoid reactions of donor/acceptor diazo compounds afford the product in high yield and with high stereoselectivity. The primary objective of this thesis is to explore the new reactivity of donor/acceptor carbenoids, especially in a multicatalytic process.

The first chapter of the thesis is devoted to studying the cyclopropanation of electron-deficient alkenes through donor/acceptor carbenoid intermediates. Under the optimized conditions, the cyclopropanation reaction of electron-deficient alkenes was achieved in high yields and with high diastereo- and enantioselectivity.

The second chapter focuses on the synthesis of dihydrofurans through sequential transition metal-catalyzed reactions. A triple cascaded reaction sequence was developed. The reaction process begins with a rhodium-catalyzed cyclopropanation, followed by a silver-catalyzed ring-opening reaction. The last step is a gold-catalyzed cyclization reaction. Starting with alkynyl-ketone diazo compounds, this reaction sequence afforded polycyclic benzo-fused dihydrofurans in high yield. A one-pot protocol for the cascaded reactions was then developed. The progress of applying this methodology to the synthesis of natural products is also described.

The third chapter presents the development on the synthesis of dihydrofurans by C-H functionalizations. Through the rhodium-catalyzed intramolecular C-H insertion reaction, the core structure of lithospermic acid was constructed in a highly diastereo- and enantioselective manner. An intermolecular process for the enantioselective synthesis of dihydrofurans is also described. The reaction sequence features the combination of two distinct types of C-H functionalizations. The process begins with a rhodium-catalyzed C-H insertion reaction of TBS benzyl ethers with donor/acceptor carbenoids, followed by the deprotection of the TBS group to afford adol-type alcohols. Lastly, the palladium-catalyzed C-H functionalization reaction of those alcohols produces dihydrofurans with high regio-, diastereo- and enantioselectivity.

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To my family

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Abbreviations

p-ABSA	*para*-acetamindobenzenesulfonyl azide
Ac	acetyl
APCI	atmospheric-pressure chemical ionization
Ar	aryl
atm	atmosphere
br.	broad
Bu	butyl
c	concentration for specific rotation measurements
calcd.	calculated
conc.	concentrated
Cy	cyclohexyl
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DCM	dichloromethane
de	diastereomeric excess
DMAP	4-dimethylaminopyridine
DMB	2,2-dimethylbutane
DMF	*N*,*N*-dimethylformamide
DMI	1,3-dimethyl-2-imidazolidinone
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
E	entgegen (opposite)
EDG	electron-donating group
ee	enantiomeric excess
eq	equation
equiv	equivalent
ESI	electrospray ionization

Et	ethyl
EWG	electron-withdrawing group
g	gram
h	hour
HMQC	heteronuclear multiple-quantum correlation
HPLC	high performance liquid chromatography
Hz	hertz
kcal	kilocalorie
IR	infrared
L	ligand
LG	leaving group
m	meta
M	metal
Me	methyl
min	minute
mol	mole
m.p.	melting point
MS	molecular sieves
NMR	nuclear magnetic resonance
N.O.	not observed
NOE	nuclear Overhauser effect
o	ortho
p	para
Ph	phenyl
PhMe	toluene
por	porphyrin
Pr	propyl
r.t.	room temperature
recrx	recrystallization
R_f	retention factor

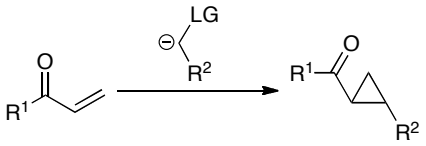
SiO_2	silica gel
TBAF	tetra-*n*-butylammonium fluoride
TBS	*tert*-butyldimethylsilyl
TEA	triethylamine
temp	temperature
Tf	triflyl (trifluoromethanesulfonyl)
TFA	trifluoroacetate
TFT	α,α,α-trifluorotoluene
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
t_R	retention time
TsOH	*p*-toluenesulfonic acid
Z	Zusammen (together)
$[\alpha]_D$	specific rotation at wavelength of sodium D line
Δ	heat at reflux
$\mu\omega$	microwave

Chapter I: Asymmetric Cyclopropanation of Electron-Deficient Alkenes *via* Carbenoid Reactions

1.1 Introduction

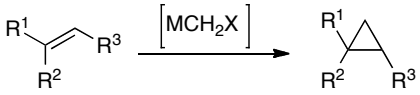
Cyclopropanes are important structural motifs in natural products and bioactive compounds.[1-4] The opening of cyclopropane ring leads to a number of synthetically valuable intermediates. Designing stereoselective methods to access cyclopropanes is an active field in organic chemistry.[5-7] Different types of reactions have been developed, including Michael-initiated addition[8-14] (eq **1.1**), Simmons-Smith type[15-17] (eq **1.2**) and metal carbenoid-mediated cyclopropanations[18-24] (eq **1.3**). Among these methods, metal carbenoid-mediated cyclopropanations are the most often utilized due to their high regio- and stereoselectivity.

Michael-initiated cyclopropanation



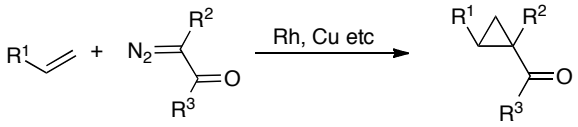
(**eq 1.1**)

Simmons-Smith type cyclopropanation



(**eq 1.2**)

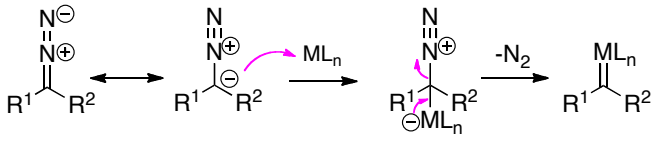
Metal carbenoid-mediaed cyclopropanation



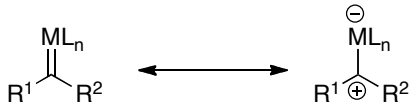
(**eq 1.3**)

Usually, reactive metal carbenoids are generated in situ from transition metal-catalyzed decomposition of diazo compounds[25,26] (Scheme **1.1**). The reaction starts with the coordination of the diazo compound to the metal catalyst, followed by an irreversible nitrogen extrusion to form the metal carbenoid. The metal-stabilized carbenoid behaves

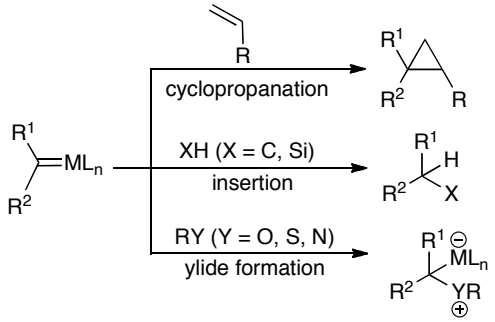
as a highly electrophilic species. Back bonding from the metal is considered to be relatively limited, and the carbenoid can be regarded as a metal bound carbocation as illustrated by the ylide-like resonance structure in Scheme **1.2**.[25] Various reactions have been developed by trapping the carbenoid intermediate with different nucleophiles[27-30] (Scheme **1.3**). A wide variety of transition metals is capable of catalyzing the decomposition of diazo compounds, but rhodium and copper are the most broadly used.[25,31]



Scheme 1.1 Mechanism for the formation of a metal carbenoid



Scheme 1.2 Resonance structures of a metal carbenoid



Scheme 1.3 Typical carbenoid reactions

Metal carbenoids can be divided into three classes, based on the substituent adjacent to the carbene center: acceptor, acceptor/acceptor and donor/acceptor carbenoids (Figure

1.1).[25] The acceptor and acceptor/acceptor carbenoids, containing one or two electron-withdrawing groups (EWG) respectively, are highly reactive species because the acceptor group is unable to stabilize the highly electrophilic carbene center. Different from these two conventional carbenoids, the donor/acceptor carbenoid has an electron-donating group (EDG) adjacent to the carbene center. This donor group can stabilize the electrophilic carbene and thus improve the selectivity of the reaction. The development of donor/acceptor carbenoid reactions is the central theme of the research in the Davies group.

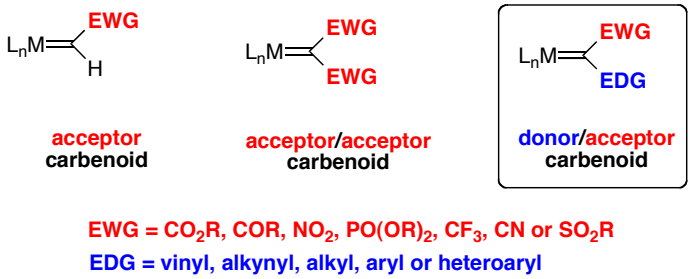
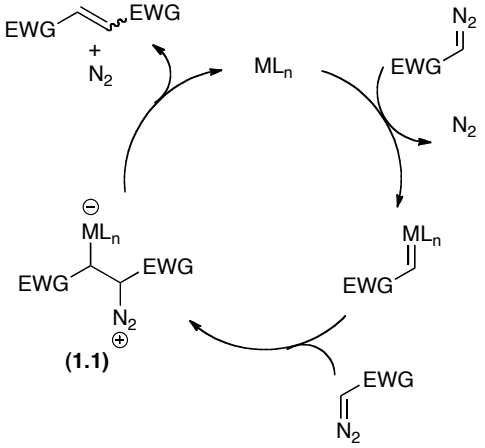


Figure 1.1 Three classes of metal carbenoids

The acceptor carbenoid was the first and the most widely used class of metal carbenoids.[31-34] This type of metal-carbenoid is highly electrophilic and has been used in a number of organic reactions. The acceptor/acceptor carbenoid is even more electrophilic. The formation of this type of metal carbenoid usually requires more reactive catalysts. The major challenges associated with these carbenoid intermediates are controlling regioselectivity, stereoselectivity and the formation of carbene dimers. These issues are especially problematic for intermolecular reactions.[32,35] A possible mechanism for the formation of carbene dimers is shown in Scheme **1.4**. A metal carbenoid is generated through the previous illustrated pathway. The negatively polarized carbon of another diazo compound attacks the carbon of the metal carbenoid to afford intermediate

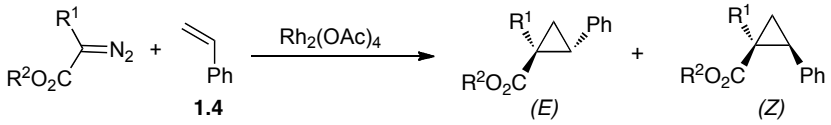
1.1. Subsequent extrusion of nitrogen and catalyst regeneration produces the carbene dimer.



Scheme **1.4** Mechanism for the formation of carbene dimer

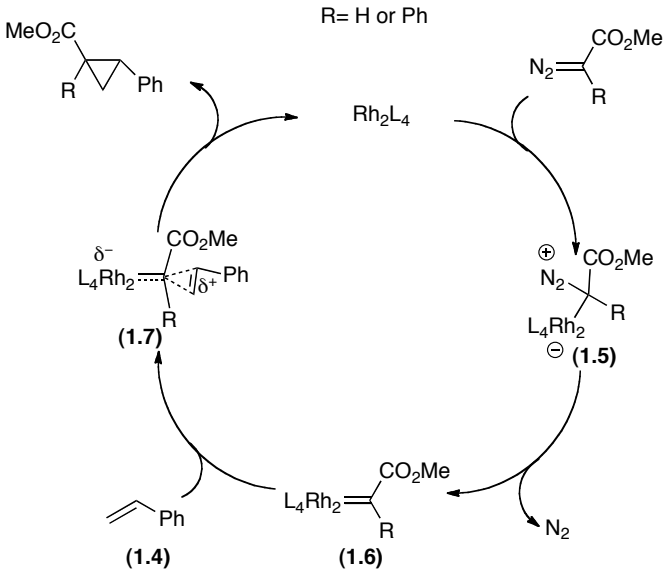
Donor/acceptor carbenoids, developed by the Davies group, have an electron-withdrawing group on one side and an electron-donating group on the other side of the carbenoid center. The donor substituent can stabilize the positive charge of the carbenoid carbon and thus improve the chemoselectivity of the reaction. This behavior is supported by both computational studies[36,37] and experimental results.[38] Table **1.1** illustrates the difference between the dirhodium(II) acetate catalyzed cyclopropanation of styrene with acceptor and donor/acceptor carbenoids. The reaction with ethyl diazoacetate **1.2** produced the cyclopropane in a less than 2:1 ratio of *E/Z* mixture favoring product in *E*-configuration. A great improvement of the diastereoselectivity was observed with the reaction of donor/acceptor carbenoids. The reaction of methyl phenyldiazoacetate **1.3** afforded the cyclopropane products in a >30:1 *E/Z* ratio.

Table 1.1 Diastereoselectivity of cyclopropanation reactions with acceptor and donor/acceptor carbenoids



entry	R^1	R^2	diazo	*E/Z* ratio
1	H	Et	**1.2**	1.8:1
2	Ph	Me	**1.3**	>30:1

The generally accepted mechanism of rhodium-catalyzed cyclopropanation is shown in Scheme **1.5**. The computational study on the cyclopropanation of styrene was carried out with dirhodium formate as the model for rhodium carboxylates. The calculation shows that the step of cyclopropanation (from **1.4** + **1.6** to **1.7**) for methyl diazoacetate is enthalpically barrierless, while a higher potential energy barrier (4.5 kcal/mol) was calculated for the reaction of methyl phenyldiazoacetate on this step. The calculation studies showed that the donor/acceptor carbenoid is much more stabilized than an acceptor carbenoid and consequently, the activation energy for the subsequent cyclopropanation step is higher. The computational results are consistent with the improved chemoselectivity observed in the reactions of donor/acceptor carbenoids compared to the acceptor carbenoids.



Scheme 1.5 Reaction pathway of the rhodium-catalyzed cyclopropanation

1.1.1 Asymmetric cyclopropanation of donor/acceptor carbenoids

With the development of chiral dirhodium(II) catalysts, highly diastereo- and enantioselective cyclopropanations of a variety of donor/acceptor carbenoids have been developed. Figure **1.2** shows several representative chiral dirhodium complexes developed by the Davies group.

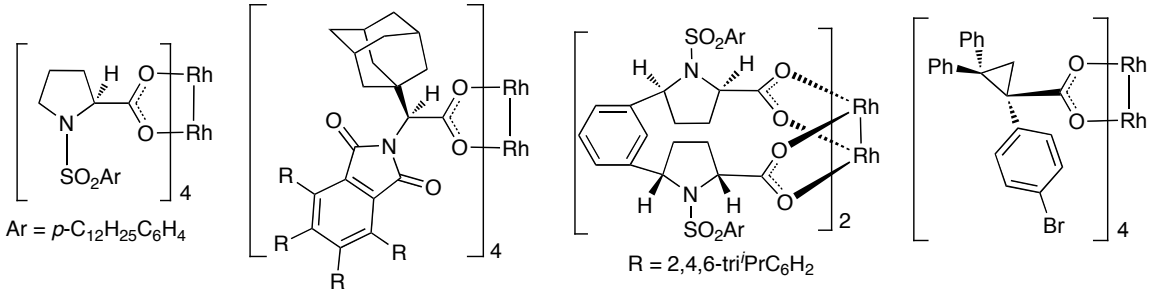
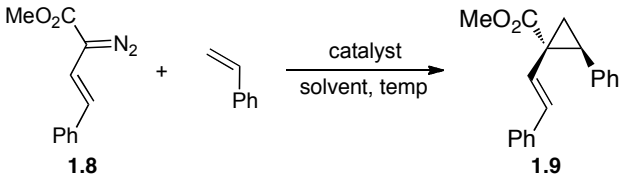


Figure 1.2 Representative chiral dirhodium(II) catalysts

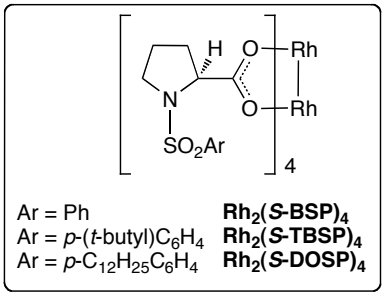
$Rh_2(DOSP)_4$ is the first generation of the Davies catalysts and still one of the most broadly used chiral dirhodium catalysts. It was derived from prolinate-based $Rh_2(BSP)_4$ developed by McKervey and coworkers.[39] $Rh_2(DOSP)_4$ was designed according to the

fact that hydrocarbons are the optimal solvents for high enantioselectivity of $Rh_2(BSP)_4$ catalyzed carbenoid reactions (Table **1.2**).[40] With dichloromethane as solvent, the $Rh_2(BSP)_4$ catalyzed cyclopropanation of styrene with phenylvinyldiazo compound **1.8** afforded product **1.9** in 74% ee (entry 1). By switching the solvent to benzene, the cyclopropanation catalyzed by $Rh_2(BSP)_4$ afforded **1.9** in 87% ee (entry 1.2). Similar results were also obtained from the reaction catalyzed by $Rh_2(TBSP)_4$, which has a *tert*-butyl group substituted on the *N*-arylsulfonyl groups of the ligands (entry 3). The alkyl substituents on the aryl ring improve the solubility of the catalyst, and the reaction can be performed in pentane resulting in higher enantioselectivity (entry 4). $Rh_2(DOSP)_4$, which has dodecanyls groups replacing the *tert*-butyl groups of $Rh_2(TBSP)_4$, has even more solubility in hydrocarbon solvents. With this improved solubility in pentane, the $Rh_2(DOSP)_4$ catalyzed cyclopropanation can be conducted in pentane at -78 ^oC, which produced **1.9** in 98% ee (entry 6).[40-42]

Table 1.2 Solvent effects on the rhodium-catalyzed cyclopropanation



entry	catalyst	solvent	temp (°C)	ee (%)
1	Rh_2(*S*-BSP)$_4$	DCM	23	74
2	Rh_2(*S*-BSP)$_4$	benzene	23	87
3	Rh_2(*S*-TBSP)$_4$	benzene	23	86
4	Rh_2(*S*-TBSP)$_4$	pentane	23	90
5	Rh_2(*S*-DOSP)$_4$	pentane	23	92
6	Rh_2(*S*-DOSP)$_4$	pentane	-78	98



To understand and predict the stereoselectivity of the Rh_2(*S*-DOSP)$_4$ catalyzed cyclopropanation reaction, a predicative model was proposed by isotope experiments and computational studies.[36,37,42] Rh_2(*S*-DOSP)$_4$ is considered to adopt a D_2 symmetric arrangement with the arylsulfonyl groups of the alternating ligands oriented toward opposite faces of the complex. The blocking arylsulfonyl groups adopt a highly angled propeller arrangement and tend to sterically block adjacent quadrants. As shown in Figure **1.3**, there is only one open site for the alkene to approach. The alkene is proposed to approach the metal carbenoid complex in an "end-on" fashion through a concerted non-synchronous transition state. This model was consistent with the observed products of the cyclopropanation reaction of donor/acceptor carbenoids.

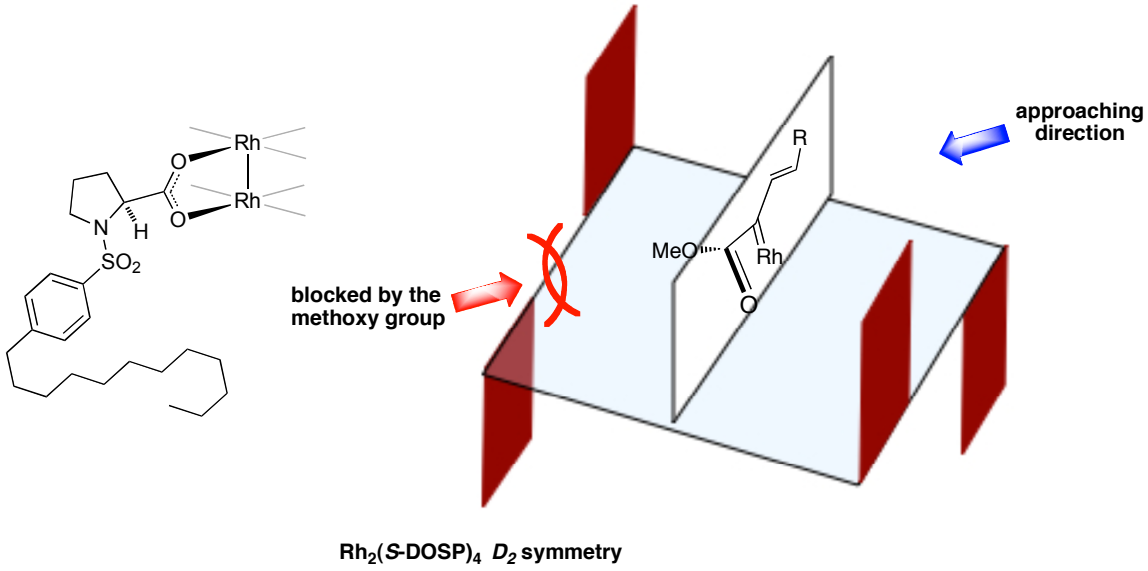


Figure 1.3 Predicative model of Rh_2(*S*-DOSP)$_4$

Rh_2(PTAD)$_4$ is the second generation of the Davies catalysts and an analogue of the Hashimoto catalyst Rh_2(PTTL)$_4$. With bulky adamantyl groups replacing the *tert*-butyl groups,[43,44] Rh_2(PTAD)$_4$ demonstrates better stereocontrol in some reactions.[45] This catalyst is considered to adopt a C_4 symmetric arrangement with all ligands aligned up.[46]

The intermolecular cyclopropanation of styrene derivatives and electron rich alkenes with donor/acceptor carbenoids has been well studied. Protocols have been set up for the reaction involving diazo compounds flanked with various donor and acceptor groups. $Rh_2(DOSP)_4$ and $Rh_2(PTAD)_4$ demonstrate complementary catalytic ability towards this reaction (Figure **1.4**). Generally, the $Rh_2(DOSP)_4$ catalyzed cyclopropanation reaction generates products with high enantioselectivity when the donor group of diazo compounds is aryl,[41,47] heteroaryl[48], styryl[40,42] or alkynyl group.[49] For the diazo compounds having siloxyvinyl as the donor group, high enantioselectivity can be obtained from the reaction catalyzed by $Rh_2(PTAD)_4$.[46] In terms of the acceptor group, $Rh_2(DOSP)_4$ is the optimum catalyst when the acceptor group of the diazo compounds is methyl ester, whereas $Rh_2(PTAD)_4$ showed good catalytic ability for the reaction of diazo compounds with phosphate,[45] trifluoromethyl,[18] nitrile[19] or ketone[20] as the acceptor group.

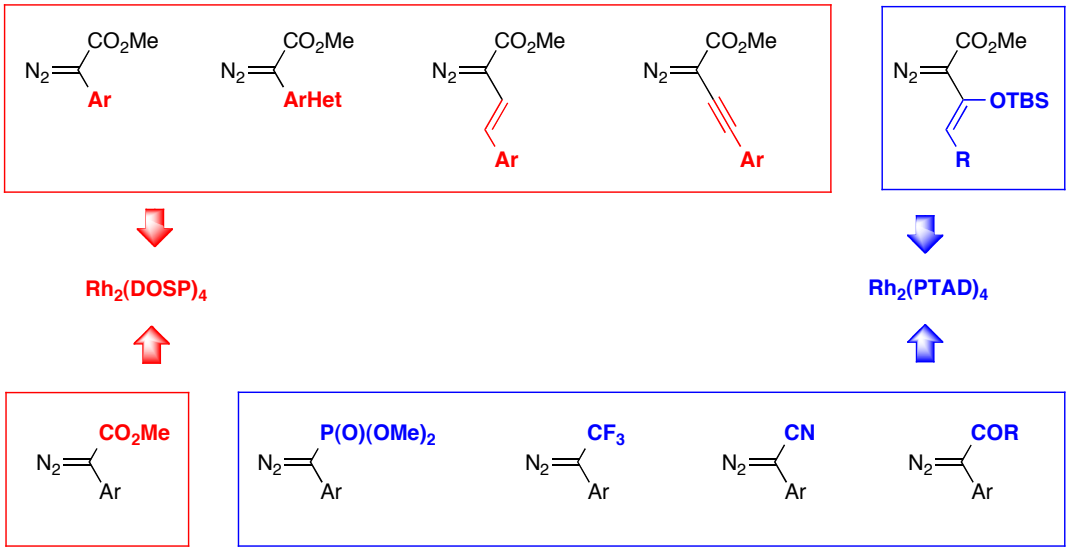
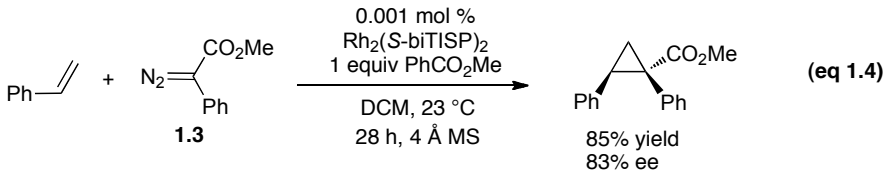


Figure 1.4 Complementary reactivity of $Rh_2(DOSP)_4$ and $Rh_2(PTAD)_4$ towards the cyclopropanation reaction with donor/acceptor carbenoids

Rh_2(biTISP)$_2$ is the third generation of the Davies catalysts. This bridged catalyst is bulky and conformationally constrained. The bridging nature of the ligands is considered to confine the catalyst into a D_2 symmetry orientation, in which the arylsulfonyl groups adopts an 'up-down-up-down' arrangement.[38] Different from Rh_2(DOSP)$_4$ and Rh_2(PTAD)$_4$, this catalyst behaves better in dichloromethane than in hexane or pentane.[50,51] This means a broadened substrate scope can be expected for the Rh_2(biTISP)$_2$-catalyzed reaction because they can include substrates that are hard to dissolve in nonpolar solvents. The Rh_2(biTISP)$_2$ catalyzed cyclopropanation can be conducted at extremely low catalyst loadings (eq **1.4**).[52] With only 0.001 mol % Rh_2(biTISP)$_2$ and methyl benzoate as additive, the cyclopropanation of styrene with diazo compound **1.3** furnished the product in good yield (85%) and with high enantioselectivity (83%). Although Rh_2(biTISP)$_2$ has been demonstrated as a robust catalyst, the complicated synthesis of this catalyst limits its use.



Rh_2(BTPCP)$_4$ is another bulky catalyst recently developed by the Davies group.[21] Like Rh_2(biTISP)$_2$, this catalyst also performs better in dichloromethane. The synthesis of this catalyst is relatively easy and its chiral ligand can be synthesized in a highly stereoselective manner through rhodium-catalyzed cyclopropanation of alkenes with aryldiazoacetates (eq **1.5**). Computational studies with this catalyst suggest it adopts a D_2 symmetric arrangement. A predictive model of this catalyst was also put forth (Figure **1.5**).

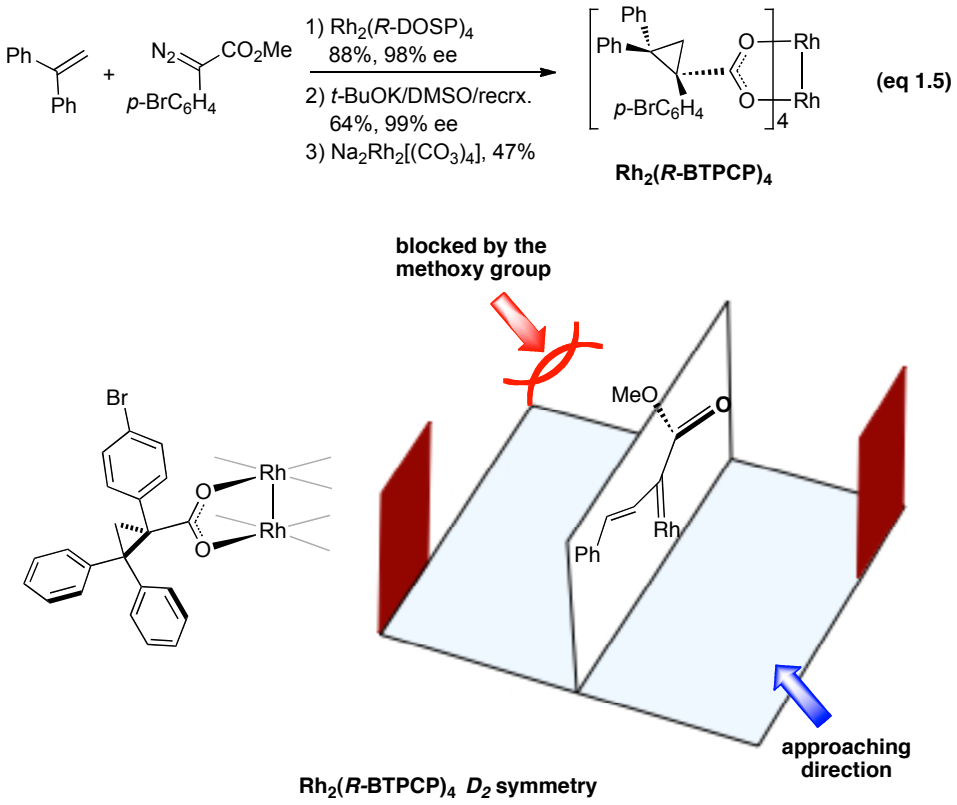
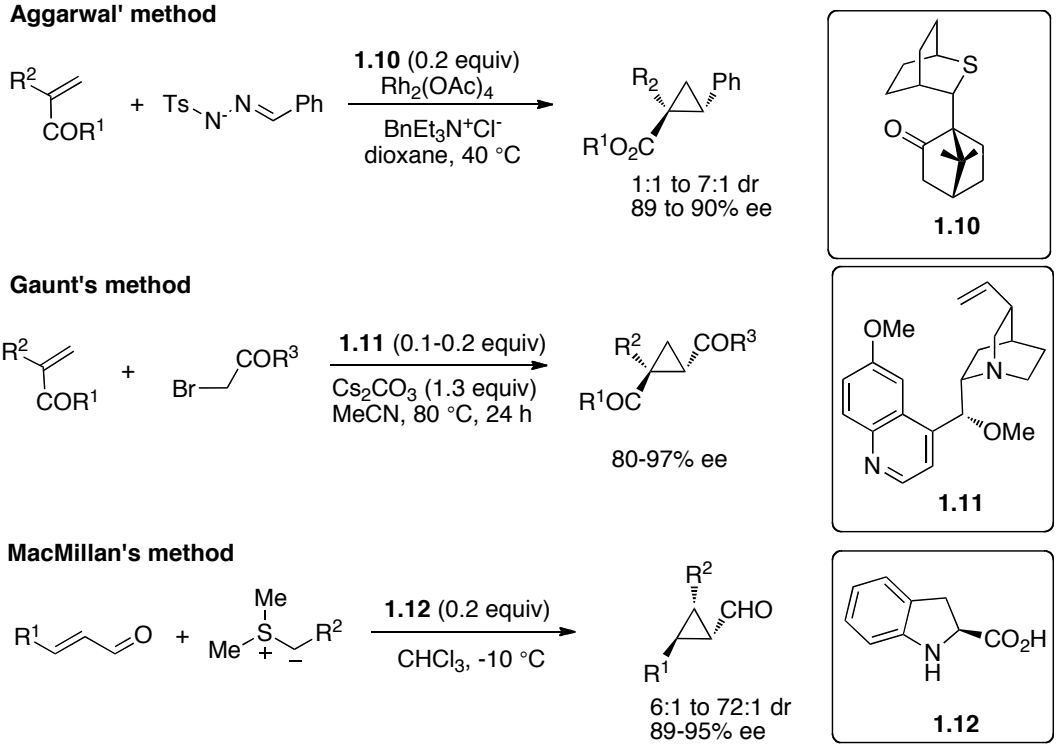


Figure 1.5 Predictive model of Rh_2(*R*-BTPCP)$_4$

1.1.2 Cyclopropanation of electron-deficient alkenes

Alkenes with a pendant electron-withdrawing group are good electrophiles. The cyclopropanation of these types of alkenes are mainly achieved through Michael-initiated cycloaddition of α,β-unsaturated carbonyl compounds with ylides. The asymmetric cyclopropanation of ylides was previous accomplished using stoichiometric amount of chiral reactants[53,54] before catalytic methods were discovered. Catalytic enantioselective cyclopropanation reactions with ylides were developed by the Aggarwal,[8,55] Gaunt[10-12] and MacMillan[9] groups. Although all of their reactions use organocatalysts, different strategies were employed (Scheme **1.6**). Both of the methods developed by Aggarwal and Gaunt used organocatalysts to generate ylides in situ, but with different catalysts and precursors. The approach taken by the Aggarwal group generated reactive ylides through

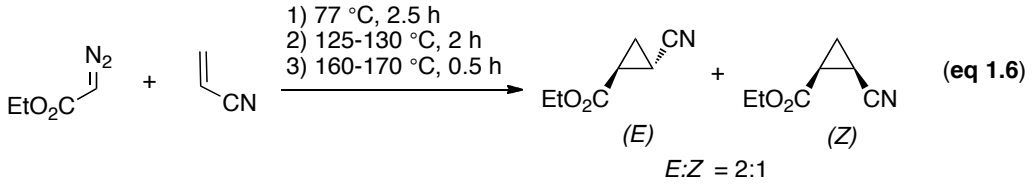
reactions of rhodium carbenoids with sulfide catalysts. Cyclopropanes were synthesized with high enantioselectivity but moderate diastereoselectivity, and the yields were also moderate. The Gaunt group used α-halo carbonyl compounds and tertiary amine catalysts to form ylides. The reaction of these ylides with α,β-unsaturated carbonyl compounds produced the cyclopropanes in high yields and with high enantioselectivity. Different from those two methods, the protocol developed by the MacMillan group proceeds by activating the olefin substrates with a secondary amine catalyst. The reactions afforded cyclopropane products with high diastereo- and enantioselectivity, but the substrates are confined to α,β-unsaturated aldehydes.



Scheme 1.6 Cyclopropanations of electron-deficient alkenes with ylides

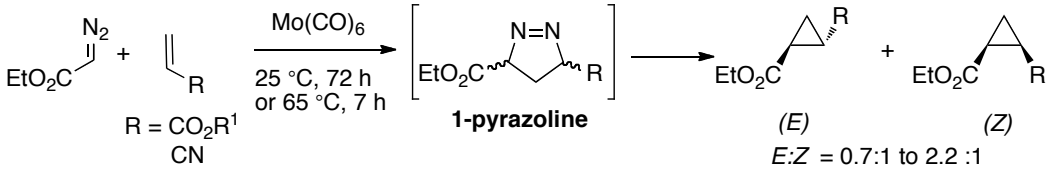
It is known that cyclopropanes can be synthesized by the reaction of acrylonitrile and ethyl diazoacetate under thermal conditions (eq **1.6**).[56,57] The evolution of nitrogen gas was not observed until the reaction temperature reached 125 °C. The diastereoselectivity

of this reaction was low (2:1 ratio of *E*/*Z* isomers). A 1,3-dipolar-cycloaddition/pyrazoline-decomposition pathway was suggested.



(**eq 1.6**)

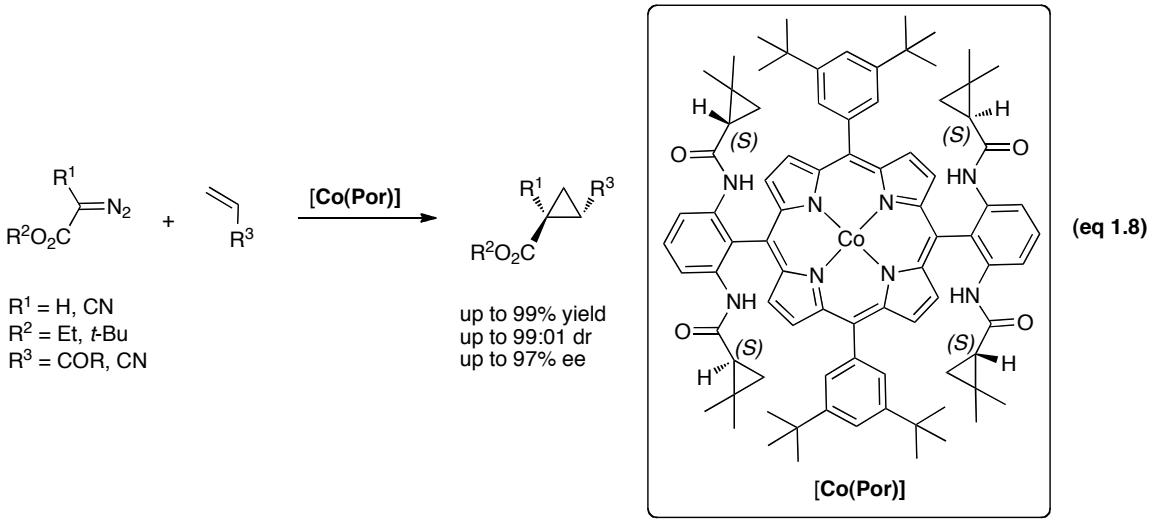
Employing molybdenum hexacarbonyl or molybdenum(II) acetate, a relative milder condition for the cyclopropanation of electron-deficient alkenes through 1,3-dipolar-cycloaddition/pyrazoline-decomposition was developed by the Doyle group (eq **1.7**).[58,59] The effect of molybdenum is to inhibit the tautomerization of 1-pyrazoline to the more stable 2-pyrazoline, which cannot undergo the decomposition to form cyclopropanes. The cyclopropanes synthesized under this condition are mixtures of diastereomers.



(**eq 1.7**)

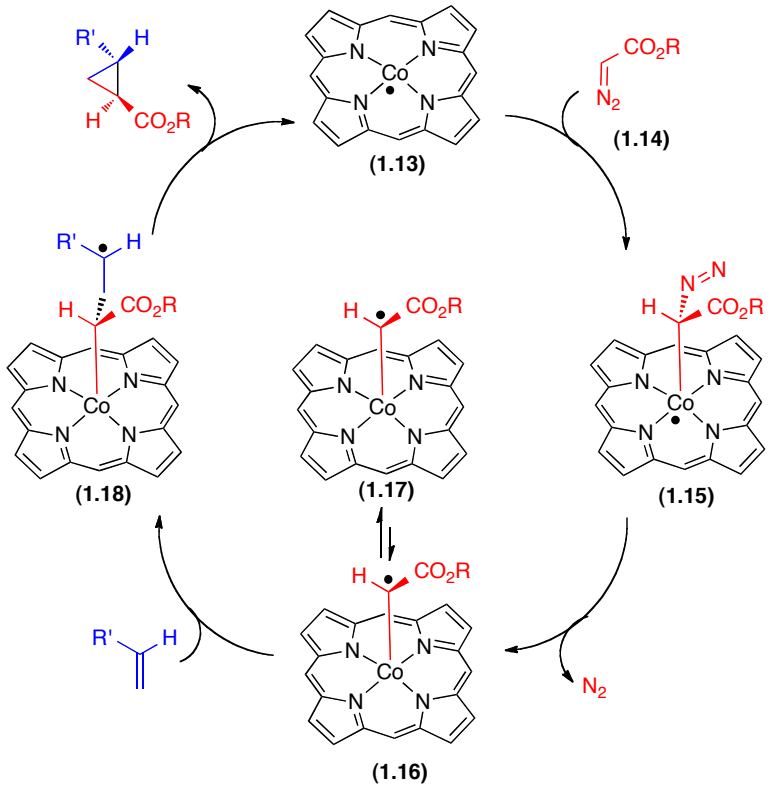
Transition metal-catalyzed carbenoid reactions have been broadly used for cyclopropanation of styrene derivatives or electron rich alkenes, but its applications to electron-deficient alkenes are problematic due to the electrophilic nature of metal carbenoids. The cyclopropanations of electron-deficient alkenes with metal carbenoids usually go through other pathways instead of a carbenoid process, such as [2+2] addition/reductive elimination for the palladium- and ruthenium-catalyzed reaction;[60-63] or radical addition-substitution for the cobalt-catalyzed reaction. Among those efforts,[64-66] the most effective catalyst for the cyclopropanation of electron deficient alkenes is the chiral porphyrin/cobalt(II) complex developed by Zhang and coworkers.[67-69] In the presence of this D_2 symmetric catalyst, reactions of electron-deficient alkenes with

acceptor or acceptor/acceptor diazo compounds produced cyclopropanes in high yields and with high stereoselectivity (eq **1.8**). Beside electron-deficient alkenes, the porphyrin/cobalt(II) can also catalyze the cyclopropanation of aryl, alkyl substituted alkenes.[70]



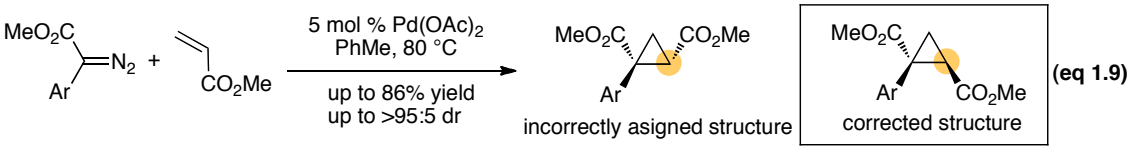
(eq 1.8)

Computational studies showed that the porphyrin/cobalt catalyzed cyclopropanation goes through a diradical addition-substitution pathway (Scheme **1.7**).[71] The reaction initiated with porphyrin/cobalt catalyst **1.13** reacting with diazo compound **1.14** to form intermediate **1.15**. The nitrogen extrusion of **1.15** generated the 'terminal carbene' intermediate **1.16**, which exists in an equilibrium with the more stable 'bridging carbene' **1.17**. The structure of **1.16** is a carbon-centered radical and can be described as a one-electron-reduced Fischer-type carbene.[72] The 'bridging carbene' **1.17** is a stable structure and not capable of reacting with olefin substrates. The cyclopropanation reaction proceeds by the addition of 'carbene radical' **1.16** to the double bond of an olefin *via* radical addition to form radical intermediate **1.18**. The subsequent collapse of this intermediate provides the cyclopropane product.



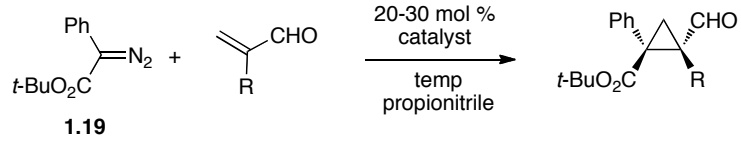
Scheme 1.7 Mechanism of the porphyrin/cobalt catalyzed cyclopropanation of olefins

Compared to acceptor and acceptor/acceptor diazo compounds, donor/acceptor diazo compounds as starting materials for the cyclopropanation of electron deficient alkenes is less studied. Among the several efforts, stereoselective results were only obtained from a palladium-catalyzed reaction and Lewis-acid catalyzed transformations. The palladium-catalyzed cyclopropanation of olefins bearing electron-withdrawing groups was developed by the Wang group (eq **1.9**).[73] Both [2+2] addition/reductive-elimination and 1,3-dipolar-cycloaddtion/pyrazoline-decomposition pathways were suggested. The structure of the major isomer of the palladium-catalyzed reaction was incorrectly assigned, which will be discussed in detail in Section **1.2**.

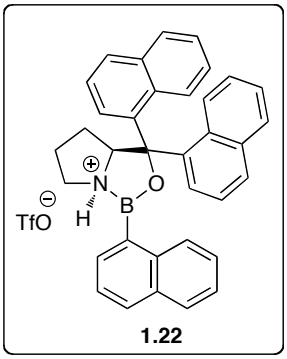


The Lewis acid-promoted cyclopropanation of electron-deficient alkenes with donor/acceptor diazo compound was not published until 2007. Through electrophilic activation of aldehyde, the titanium BINOLate-catalyzed enantioselective cyclopropanation was first studied by Maruoka and coworkers (Table **1.3**).[74] With this catalyst, the reaction of diazo compound **1.19** and alkene **1.20** yielded the cyclopropane in 57% ee (entry 1). The enantioselectivity of this Lewis acid catalyzed reaction was lately improved by the Hwang and Ryu groups. In the presence of oxazaborolidinium catalyst **1.22**, the reaction of **1.19** and **1.21** produced the cyclopropane in 91% ee (entry 2).[75]

Table 1.3 Lewis acids catalyzed cyclopropanation of electron-deficient alkenes



entry	R	alkene	catalyst	temp (°C)	yield of *trans* (%)	dr	ee (%)
1	OBz	**1.20**	Ti(O*i*-Pr)$_4$ /(*S*)-BINOL	0	44	12:1	57
2	Me	**1.21**	**1.22**	-45	63	10:1	91

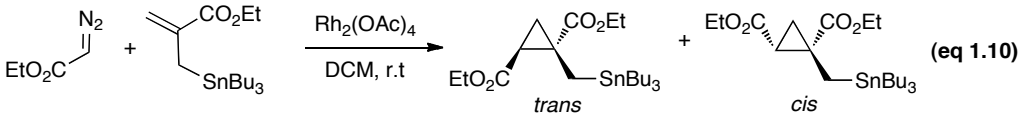


1.22

1.2 Results and discussion

The cyclopropanation of alkenes bearing electron-withdrawing group provides the product with multi-functional groups. These cyclopropanes can be potentially converted to valuable synthetic intermediates through functional group manipulations.[76,77] Enantioselective cyclopropanation reaction of electron-deficient alkenes has been developed *via* organocatalysis, Lewis acid and cobalt catalysis, but the reaction of this type of alkenes proceeding through carbenoid intermediates were unknown. Although the

rhodium-catalyzed carbenoid reaction is one of the most widely used methods to synthesize cyclopropanes, it has barely been studied for the cyclopropanation of electron-deficient alkenes. The only reported rhodium-catalyzed cyclopropanation of electron-deficient alkenes is the $Rh_2(OAc)_4$ catalyzed cyclopropanation of alkene **1.23** with ethyl diazoacetate **1.2** (eq **1.10**),[66] which produced cyclopropanes with almost no diastereocontrol (*trans:cis* = 1.7:1). The mechanism of this reaction has not been determined.

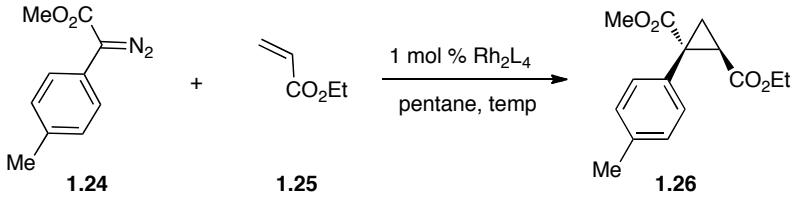


To examine the possibly enantioselective cyclopropanation with electron-deficient alkenes through a rhodium-catalyzed reaction of donor/acceptor carbenoids, the reaction between diazo compound **1.24** and alkene **1.25** in refluxing pentane was examined (Table **1.4**). Remarkably, the reaction catalyzed by Rh_2(*S*-DOSP)$_4$ generated cyclopropane **1.26** in 59% yield and with 77% ee (entry 1). Encouraged by this result, other commonly used rhodium catalysts were tested. Although the reaction with these catalysts produced the cyclopropane in good yields, the level of asymmetric induction in these reactions was low (entries 2-6). The breakthrough was made when dirhodium(II) tetrachlorophthalimido-carboxylates were applied to this cyclopropanation reaction. In the presence of Rh_2(*S*-PTTL)$_4$, the cyclopropane product was generated with only 27% ee, but the enantioselectivity increased to 74% ee after changing the catalyst to Rh_2(*S*-TCPTTL)$_4$ (entries 6 and 7). The size of the alkyl group on the ligand also influences the enantioselectivity of the products. The reaction catalyzed by Rh_2(*S*-TCPTV)$_4$, which has relatively smaller *iso*-propyl groups instead of *tert*-butyl groups found in Rh_2(*S*-

TCPTTL)$_4$, afforded **1.26** with lower enantioselectivity compared to the reaction catalyzed by Rh$_2$(*S*-TCPTTL)$_4$ (entry 8). The reaction catalyzed by Rh$_2$(*S*-TCPTAD)$_4$, which has bulky adamantyl groups replacing the *tert*-butyl groups produced the cyclopropane with higher enantioselectivity than the reaction catalyzed by Rh$_2$(*S*-TCPTTL)$_4$ (entry 9). When the reaction was performed at room temperature, cyclopropane **1.26** was formed with similar enantioselectivity but in much lower yield compared to the refluxing conditions (entry 10). In all cases, the cyclopropanation catalyzed by those dirhodium catalysts proceeded with high diastereoselectivity.

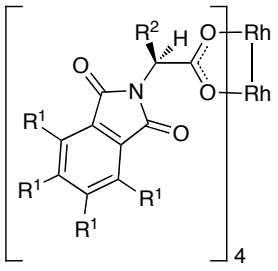
Compared to the reactions performed in pentane, the cyclopropanation conducted in dichloromethane afforded the product in higher yield but lower ee (entry 1, Table **1.5**). In term of stereoselectivity, tetrabromophthalimido-based catalyst Rh$_2$(*S*-TBPTTL)$_4$, which has poor solubility even in refluxing pentane, behaved better in dichloromethane than Rh$_2$(*S*-TCPTAD)$_4$ (entry 2). At room temperature, no cyclopropane product was observed from the reaction catalyzed by either Rh$_2$(*S*-TCPTAD)$_4$ or Rh$_2$(*S*-TBPTTL)$_4$ (entries 3 and 4).

Table 1.4 Optimization of the cyclopropanation of ethyl acrylate

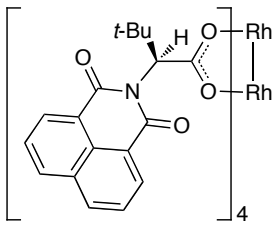


entry	catalyst	temperature (°C)	dr[a]	yield[b] (%)	ee (%)
1	Rh_2(*S*-DOSP)$_4$	36	>97:3	59	77
2	Rh_2(*S*-PTAD)$_4$	36	>97:3	70	35
3	Rh_2(*S*-BTPCP)$_4$	36	92:8	70	5
4	Rh_2(*S*-NTTL)$_4$	36	>97:3	69	24
5	Rh_2(*S*-BPTV)$_4$	36	>97:3	65	5
6	Rh_2(*S*-PTTL)$_4$	36	>97:3	68	27
7	Rh_2(*S*-TCPTTL)$_4$	36	>97:3	71	74
8	Rh_2(*S*-TCPTV)$_4$	36	>97:3	62	65
9	**Rh_2(*S*-TCPTAD)$_4$**	**36**	**>97:3**	**61**	**84**
10	Rh_2(*S*-TCPTAD)$_4$	23	>97:3	22	82

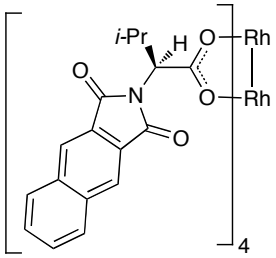
[a] Determined by crude NMR. [b] Isolated yield.



R^1 = H, R^2 = *t*-Bu **Rh_2(*S*-PTTL)$_4$**
R^1 = H, R^2 = adamantyl **Rh_2(*S*-PTAD)$_4$**
R^1 = Cl, R^2 = *t*-Bu **Rh_2(*S*-TCPTTL)$_4$**
R^1 = Cl, R^2 = *i*-Pr **Rh_2(*S*-TCPTV)$_4$**
R^1 = Cl, R^2 = adamantyl **Rh_2(*S*-TCPTAD)$_4$**

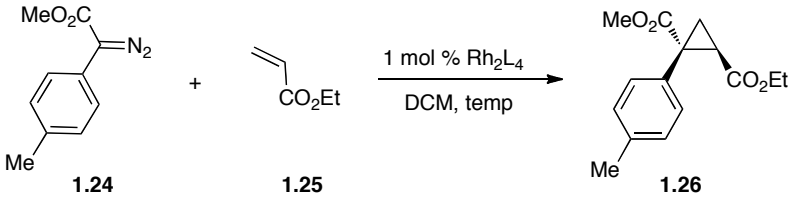


Rh_2(*S*-NTTL)$_4$

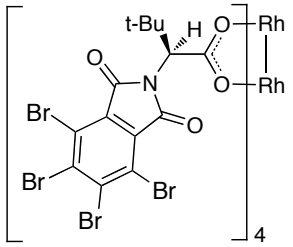


Rh_2(*S*-BPTV)$_4$

Table 1.5 Cyclopropanation reactions performed in dichloromethane



entry	catalyst	temp (°C)	dr[a]	yield[b] (%)	ee (%)
1	Rh_2(*S*-TCPTAD)$_4$	40	92:8	81	71
2	Rh_2(*S*-TBPTTL)$_4$	40	>97:3	62	79
3[c]	Rh_2(*S*-TCPTAD)$_4$	23	-	N.O.	-
4	Rh_2(*S*-TBPTTL)$_4$	23	-	N.O.	-



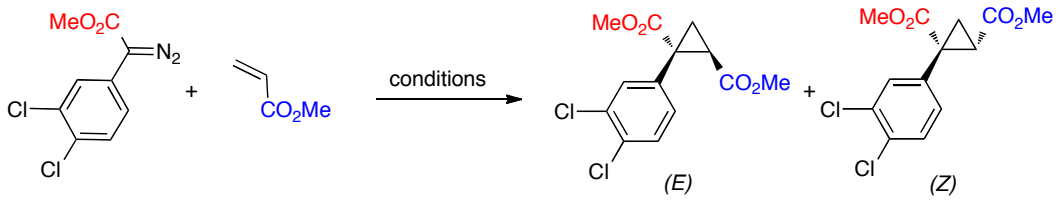
Rh$_2$(*S*-TBPTTL)$_4$

[a] Determined by crude NMR. [b] Isolated yield. [c] N.O. = not observed.

The Wang group has previously published a palladium-catalyzed cyclopropanation reaction of methyl acrylate with aryldiazo compounds.[73] The spectral and physical property of the major diastereomer is the same as the cyclopropane generated by Rh_2(TCPTAD)$_4$ catalyzed reaction. The Wang group rendered the major diastereomer of their palladium-catalyzed reaction in a *Z*-configuration as shown in compound **1.29**, but the major diastereomer generated from the rhodium-catalyzed reaction usually adopts a *E*-configuration as in compound **1.28**. To clarify the stereochemistry of this reaction, both rhodium- and palladium-catalyzed reactions of diazo compound **1.27** with methyl acrylate were performed (Table **1.6**). The reaction catalyzed by $Pd(OAc)_2$ provided cyclopropanes as a mixture of 85:15 ratio of diastereomers (entry 1), while the Rh_2(TCPTAD)$_4$ catalyzed the reaction produced the cyclopropane as a single regioisomer with 92% ee. The major diastereomers of those two reactions are the same based on NMR analysis (entry 2). ^{1}H-NMR showed that the signals of the methoxy groups of the major diastereomer from the palladium-catalyzed reaction are presented at relative high

field (3.67 and 3.53 ppm), while those of the minor isomer are presented at 4.00 and 3.75 ppm. This result indicates that both methoxy groups of the major isomer are shielded, which would be the expected behaviors of the *E*-isomer because the aryl group would shield the methyl ester protons. This would suggest that Wang had incorrectly assigned the structure of the major isomer in their palladium-catalyzed studies.

Table 1.6 Palladium- and rhodium-catalyzed cyclopropanations



1.27 **1.28** **1.29**

entry	coditions	dr[a] (*E*/*Z*)	yield[b] (%)	ee of *E* (%)
1	5 mol % $Pd(OAc)_2$, PhMe, 80 °C	85:15	43	-
2	1 mol % Rh_2(*S*-TCPTAD$_4$), pentane, 36 °C	>97:3	70	92

[a] Based on crude NMR. [b] Isolated yield.

The stereochemical configuration of **1.28** was further confirmed by NOE experiment (Figure **1.6**). HMQC experiment indicated that the H_a is on the carbon substituted with a methyl ester group, and protons (H_b and H_c) are on the same carbon of the cyclopropane ring. Only H_a was enhanced when H_c at 7.08 ppm was irradiated. This indicates that the cyclopropane **1.28** is in the *E* isomer because NOE enhancement of two protons (H_a and H_b) would be expected if the product was the *Z* isomer. The X-ray crystallographic structures of the analogues (**1.50** and **1.51**) of **1.28**, derived from the reaction of *tert*-butyl *p*-bromophenyldiazoacetate with phenyl acrylate and methyl 2-fluoroacrylate, were obtained. Both of the two crystal structures demonstrated the Rh_2(TCPTAD)$_4$ catalyzed reaction produced cyclopropanes in *E*-configuration.

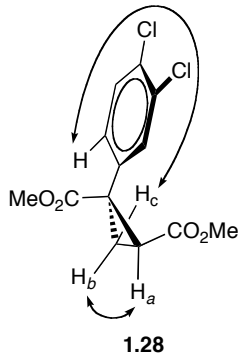
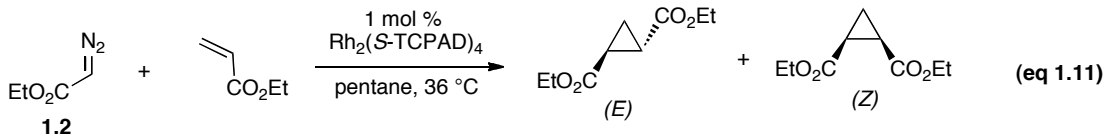
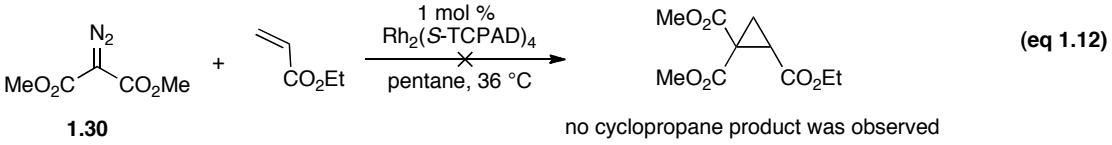


Figure 1.6 NOE experiment of cyclopropane **1.28**

The cyclopropanation of ethyl acrylate with acceptor and acceptor/acceptor diazo compounds were also evaluated. Under the optimized conditions, the reaction of ethyl diazoacetate **1.2** produced cyclopropanes as a mixture of two diastereomers (*E*:*Z* = 5.3:1, eq **1.11**). Compared to the reaction of donor/acceptor diazo compounds, the absence of donor group resulted in a decrease of diastereoselectivity. This is in accord with other experimental observations on the stereoselectivity of the reaction with acceptor and donor/acceptor carbenoids. No cyclopropane product was observed from the reaction of acceptor/acceptor diazo compound **1.30** with ethyl acrylate (eq **1.12)**.

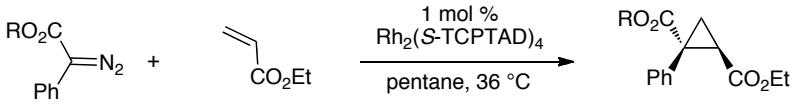




The influence of the ester group on the enantioselectivity of this rhodium-catalyzed cyclopropanation was then studied (Table **1.7**). The reaction of methyl phenyldiazoacetate produced the cyclopropane **1.31** in 83% yield and with 86% ee (entry

1). Similar results were obtained from the reaction of ethyl phenyldiazoacetate (entry 2). However, an increase of enantioselectivity was achieved when the diazo compound with bulky *t*-butyl ester was used (entry 4).

Table 1.7 Effect of the ester group on the enantioselectivity of the cyclopropanation reaction



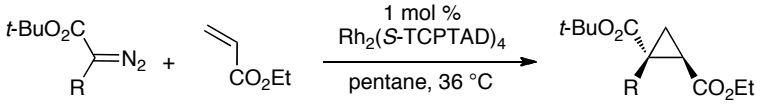
entry	R	product	dr[a]	yield[b] (%)	ee (%)
1	Me	**1.31**	97:3	83	86
2	Et	**132**	>97:3	78	85
3	*n*-Bu	**1.33**	>97:3	84	81
4	*t*-Bu	**1.34**	>97:3	78	91

[a] Determined by crude NMR. [b] Isolated yield.

A series of *tert*-butyl aryldiazoacetates were synthesized and subjected to the cyclopropanation reaction (Table **1.8**). The reaction of *t*-butyl *p*-methylphenyldiazoacetate produced the cyclopropane **1.35** in 61% yield and with 89% ee (entry 1). By increasing the electron density of the aryl group with a methoxy group replacing the methyl group, product **1.36** was provided in higher yield but the same level of asymmetric induction (entry 2). Improved enantioselectivity was observed for the cyclopropanation reaction with aryldiazoacetates having substituents at *meta*-position, products **1.37**-**1.39** were all obtained in high yield and over 90% ee (entries 3-5). The diastereoselectivity of the reaction decreased when less electron-rich aryl groups were used. The cyclopropanation reaction with *t*-butyl *p*-trifluoromethylphenyldiazoacetate provided product **1.41** in 64% yield and with 91% ee, but the diastereoselectivity decreased to 90:10 (entry 7). The carbenoid with a highly electron-deficient aryl group

resulted in significantly lower reaction yield. Cyclopropane **1.42** was isolated in only 22% yield from the reaction of *p*-nitrophenyldiazoacetate (entry 8).

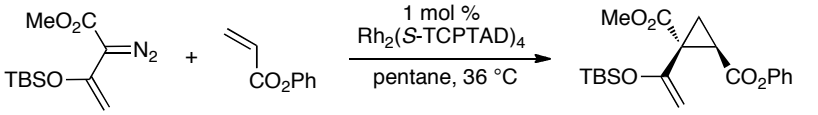
Table 1.8 Cyclopropanation reaction of ethyl acrylate with aryldiazo compounds



entry	R	prodcut	dr[a]	yield[b] (%)	ee (%)
1	*p*-MeC_6H_4	**1.35**	95:5	61	89
2	*p*-$MeOC_6H_4$	**1.36**	>97:3	83	88
3	*m*-$MeOC_6H_4$	**1.37**	96:4	75	94
4	3,4-*di*$MeOC_6H_3$	**1.38**	>97:3	91	93
5	2-naphthyl	**1.39**	95:5	86	94
6	*p*-BrC_6H_4	**1.40**	96:4	89	93
7	*p*-$CF_3C_6H_4$	**1.41**	90:10	64	91
8[c]	*p*-$NO_2C_6H_4$	**1.42**	92:8	22	91

[a] Determined by crude NMR. [b] Isolated yield. [c] The diazo compound was dissolved in pentane/DCM (v/v) = 10:1.

A cyclopropanation study with vinyldiazo compounds and acrylates was also conducted (eq **1.13**). Under the optimized conditions, the cyclopropanation of phenyl acrylate **1.44** with methyl siloxyvinyldiazoacetate **1.43** generated cyclopropane **1.45** in 41% yield and with 95% ee. This result shows the potential of applying this reaction to other vinyl carbenoids. Decomposition of product **1.45** to the subsequent ketone was observed after storage at room temperature for more than 72 h.



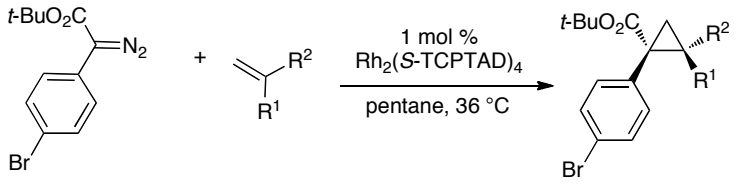
1.43 **1.44** **1.45**

41% yield, >97:3 dr, 95% ee

(eq 1.13)

The substrate scope of alkenes was next studied (Table **1.9**). The cyclopropanation of methyl acrylate provided cyclopropane **1.46** in excellent yield and with enantioselectivity (entry 1) Increasing the size of the ester group did not reduce the reaction yield. Cyclopropanes **1.47** and **1.48** were synthesized in high yield and with high enantioselectivity (entries 2 and 3). Besides alkenes with aliphatic ester groups, phenyl acrylate also behaved well for this cyclopropanation reaction (entry 5). Compared to the reaction of acrylates, the cyclopropanation of alkenes bearing amide groups afforded products **1.51** and **1.52** in good yields (51-59%) and with excellent diastereo- and enantioselectivities (entries 6 and 7). Reactions of 2-substituted methyl acrylate were also studied. When R^2 = F, the enantioselectivity of cyclopropane **1.53** decreased to 87% ee, but no loss of yield or diastereoselectivity was observed (entry 8). By further increasing the size of R^2 to a methyl group, both the reaction yield and stereoselectivity decreased. The reaction of such arylate produced cyclopropane **1.54** in 55% yield and with 84:16 dr and 77% ee (entry 9). Products **1.50** and **1.53** were crystalline, and their absolute and relative configurations were determined by X-ray crystallography (Figures **1.7** and **1.8**).

Table 1.9 Alkene substrate scope



entry	R^1	R^2	product	dr[a]	yield[b] (%)	ee (%)
1	CO_2Me	H	**1.46**	96:4	91	96
2	CO_2n-Bu	H	**1.47**	92:8	81	93
3	CO_2t-Bu	H	**1.48**	>97:3	86	93
4	CO_2Bn	H	**1.49**	96:4	47	90
5	CO_2Ph	H	**1.50**	97:3	74	92
6	$CONMe_2$	H	**1.51**	>97:3	51	94
7	CON(OMe)Me	H	**1.52**	>97:3	59	92
8	CO_2Me	F	**1.53**	>97:3	84	87
9	CO_2Me	Me	**1.54**	84:16	55	77

[b] Determined by crude NMR. [a] Isolated yield.

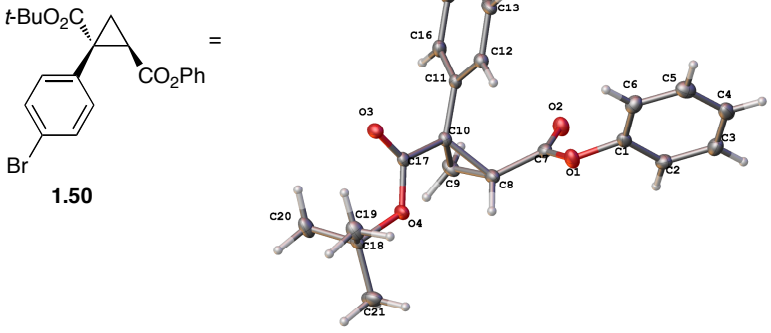


Figure 1.7 X-ray crystallographic structure of cyclopropane **1.50**

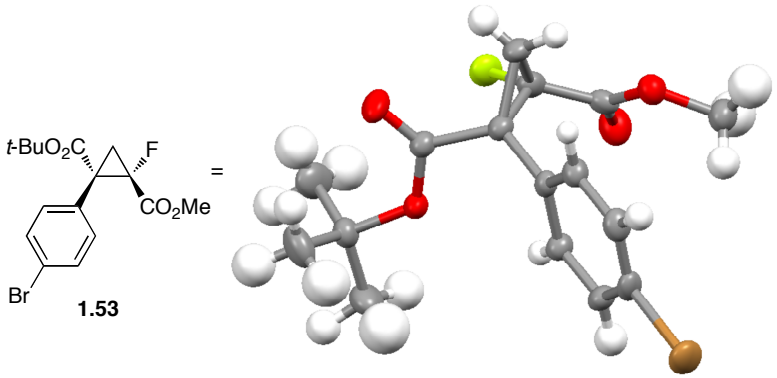
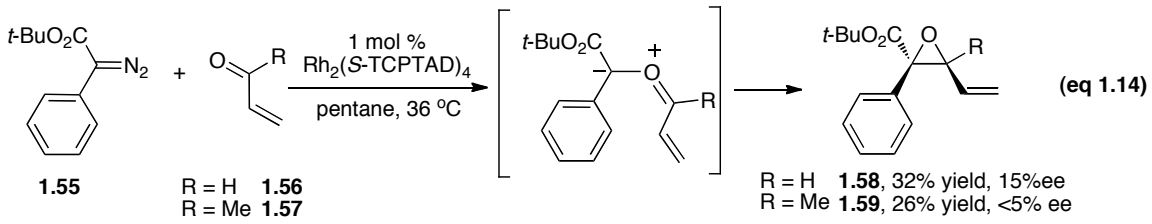


Figure 1.8 X-ray crystallographic structure of cyclopropane **1.53**

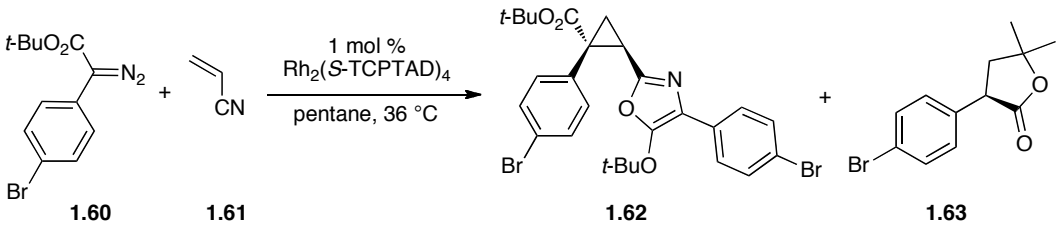
Under the optimized conditions, the reactions of acrolein **1.56** or α,β-unsaturated ketone **1.57** with diazo compound **1.55** produced epoxides **1.58** and **1.59** separately. No formation of cyclopropanes was observed (eq **1.14**). The formation of epoxides from rhodium-catalyzed reaction of donor/acceptor carbenoids has been reported and ylide intermediate was proposed.[79,80] Similar to the previous studies, there was almost no asymmetric induction for the Rh_2(TCPTAD)$_4$ catalyzed epoxidations. The epoxide **1.58** was synthesized in 15% ee and **1.59** was obtained as a racemic mixture.



The reaction of acrylonitrile **1.61** produced an interesting oxazole-substituted cyclopropane (Table **1.10**). With one equiv of diazo compound **1.60** and an excess amount of acrylonitrile as starting materials, cyclopropane **1.62** was isolated in 52% yield and with 97% ee, while the reaction of one equiv of **1.61** and an excess amount of **1.60** produced not only cyclopropane **1.62** in the same ee but also γ-lactone **1.63** in 65% ee.

Lactone **1.63** was formed *via* an intramolecular C–H insertion at one methyl group of the *tert*-butyl ester. The absolute configuration of cyclopropane **1.62** was assigned by X-ray crystallography (Figure **1.9**). The stereochemistry of *γ*-lactone **1.63** was tentatively assigned as *R*-configuration.

Table 1.10 Cyclopropanation of acrylonitrile with donor/acceptor carbenoids



1.60 **1.61** **1.62** **1.63**

entry	ratio (**1.60**:**1.61**)	yield of **1.62** (%)	ee of **1.62** (%)	yield of **1.63** (%)	ee of **1.63** (%)
1	1:5	52	97	-	-
2	2:1	48	97	24	65

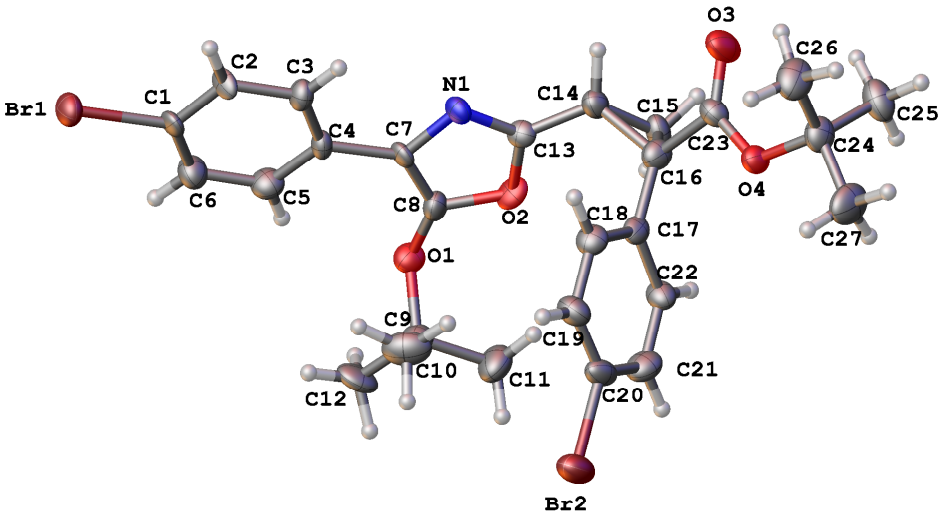
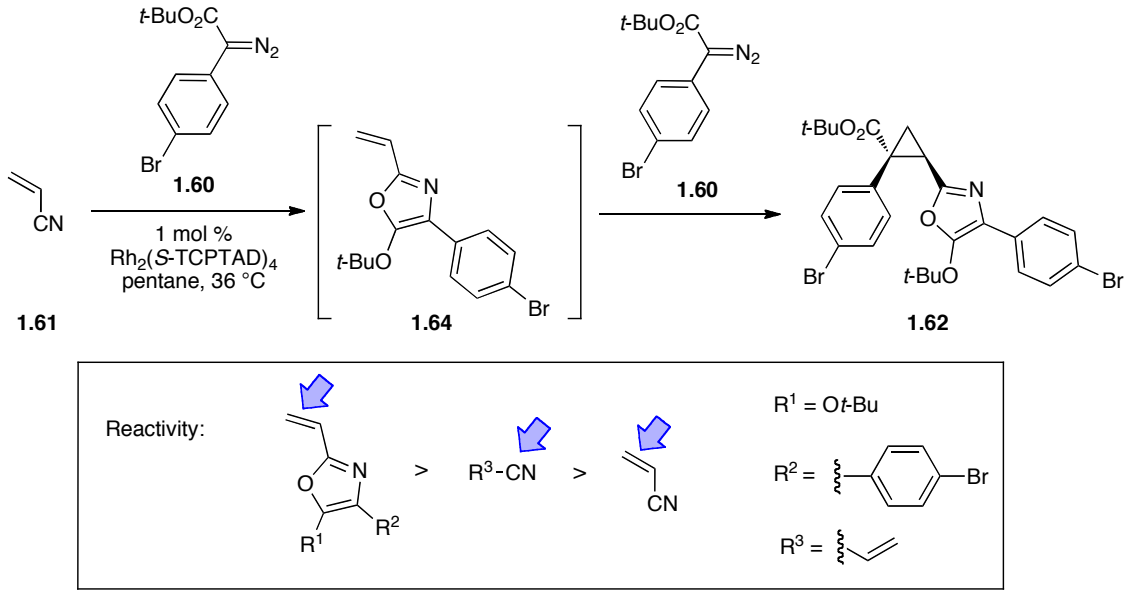


Figure 1.9 X-ray crystallographic structure of product **1.62**

The relative reactivity of alkenes and the nitrile group could be deducted from the fact that only one cyclopropane product **1.62** was synthesized even when the reaction started

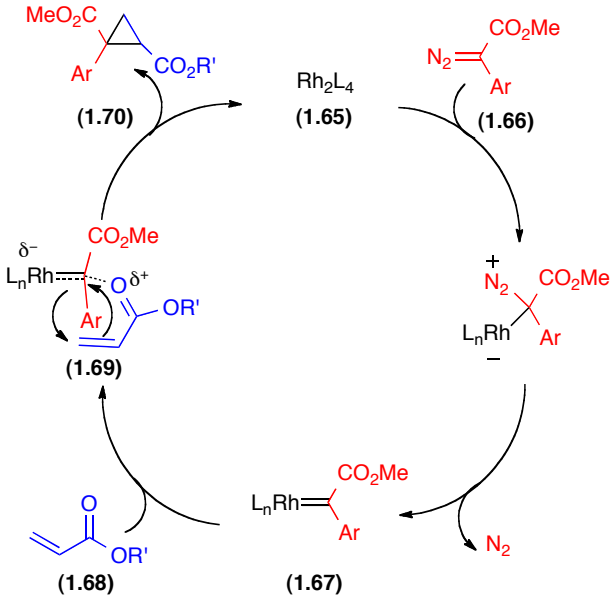
with an excess amount of acrylonitrile **1.61** (Scheme **1.8**). The reaction begins with a cycloaddition between diazo compound **1.60** and the nitrile group of **1.61** to produce an oxazole-substituted alkene **1.64**. As no **1.64** was observed from the crude mixture even when the reaction started with **1.60** as limiting reagent, this electron-rich alkene **1.64** must react fast with another molecular of the diazo compound to form cyclopropane **1.62**. The general reactivity can be summarized as oxazole-substituted alkene **1.64** > nitrile group > terminal alkene adjacent to nitrile.



Scheme 1.8 Relative reactivity of alkenes and the nitrile group

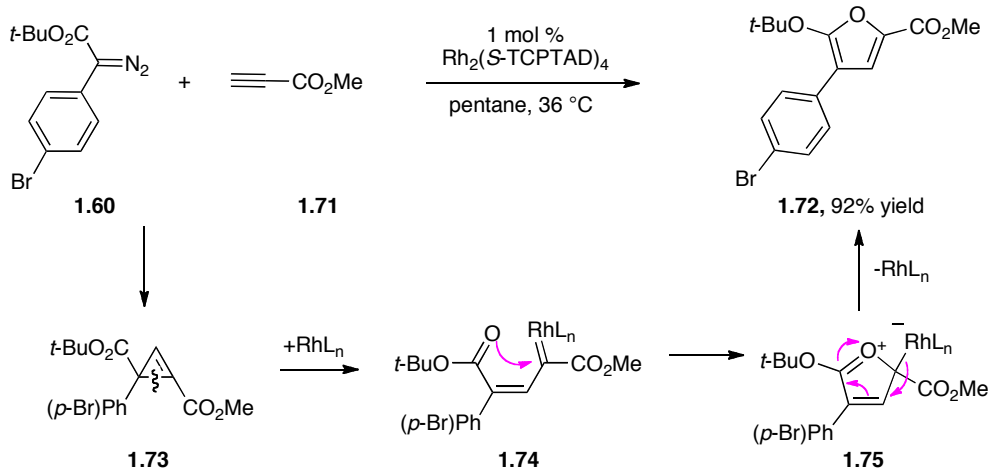
Since the rhodium carbenoid is electrophilic, it was surprising to see the rhodium-catalyzed cyclopropanations of electron deficient alkenes proceeded so well. Unlike palladium- and ruthenium-catalyzed cyclopropanations, dirhodium(II) tetracarboxylates are not capable of undergoing [2+2] addition as suggested for those reactions. The Davies group has previously reported that methyl benzoate is an effective additive in rhodium-catalyzed reactions. The interaction between the carbonyl group of the additive and the rhodium carbenoid might be the explanation for the effect of the additive. Similar

interaction between the α,β-unsaturated carbonyl substrates and rhodium carbenoid could be the rational for this cyclopropanation reaction. The generation of epoxides from the reaction of aldehydes and ketone also indicates that carbonyl groups are involved in the reaction process. Based on these experimental results, a possible mechanism was put forth (Scheme **1.9**). The reaction of rhodium catalyst **1.65** and diazo compound **1.66** produced rhodium carbenoid **1.67** after the extrusion of nitrogen. The carbonyl group of acrylate **1.68** attacks **1.67** to form intermediate **1.69**, which draws the alkene close the reactive carbene and the following [2+1] cycloaddition affords cyclopropane **1.70**. Current study can not rule out the direct reaction between the alkene group of the substrate and donor/acceptor carbenoids, which was postulated as one of the possible mechanisms for the cyclopropanation of methyl *trans*-cinnamate with diazomethane.[81] Further studies are needed to clarify the intriguing mechanism.



Scheme 1.9 Proposed mechanism for the rhodium-catalyzed cyclopropanation of electron-deficient alkenes

Aiming to expand this method to the cyclopropenation of electron deficient alkynes, the reaction of diazo compound **1.60** and methyl propiolate **1.71** was carried out. Interestingly, trisubstituted furan **1.72** was produced instead of the expected cyclopropene product. The furan product was obtained as a single isomer in 92% yield. A similar 2,4,5-trisubstituted furan was previously obtained during the study of the cyclopropenation of phenylacetylene. The mechanism for the formation of this product is considered to proceed through a cyclopropene intermediate.[82] Based on that, a plausible mechanism for the formation of **1.72** is proposed (Scheme **1.10**). The rhodium-catalyzed reaction of **1.60** and **1.71** generates cyclopropene **1.73**, which is converted immediately to rhodium carbenoid **1.74** *via* a ring opening of the cyclopropene. Zwitterionic intermediate **1.75** was then formed by intramolecular reaction of the rhodium carbenoid with the carbonyl of *t*-butyl ester group. The following transformation leads to the furan product **1.72**. The structure of **1.72** was unambiguously assigned by X-ray crystallography (Figure **1.10**).



Scheme 1.10 Reaction of methyl propiolate with diazo compound **1.60**

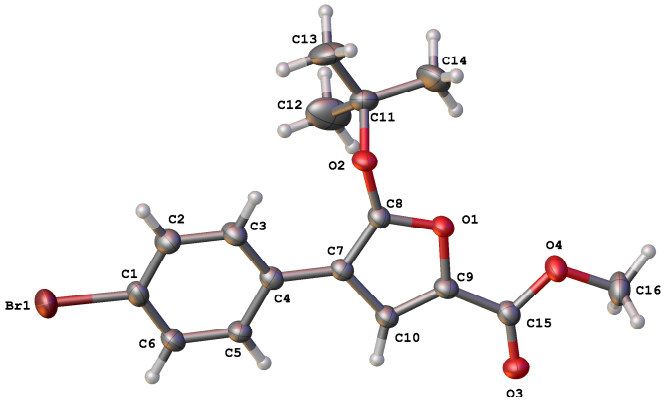


Figure 1.10 X-ray crystallographic structure of product **1.72**

1.3 Conclusion

Through rhodium-catalyzed carbenoid reactions, cyclopropanation reactions of α,β-unsaturated esters or amides with aryldiazoacetates were achieved. The products were obtained in high yield and with high diastereo- and enantioselectivity. The absolute configurations of products **1.50** and **1.53** were unambiguously assigned by X-ray crystallography and absolute configuration of the remainder of the cyclopropanation products were tentatively assigned by analogy. A mechanism for this unexpected transformation is proposed.

Chapter II: Synthesis of Fused Dihydrofurans *via* Transition Metal-Catalyzed Sequential Reactions

2.1 Introduction

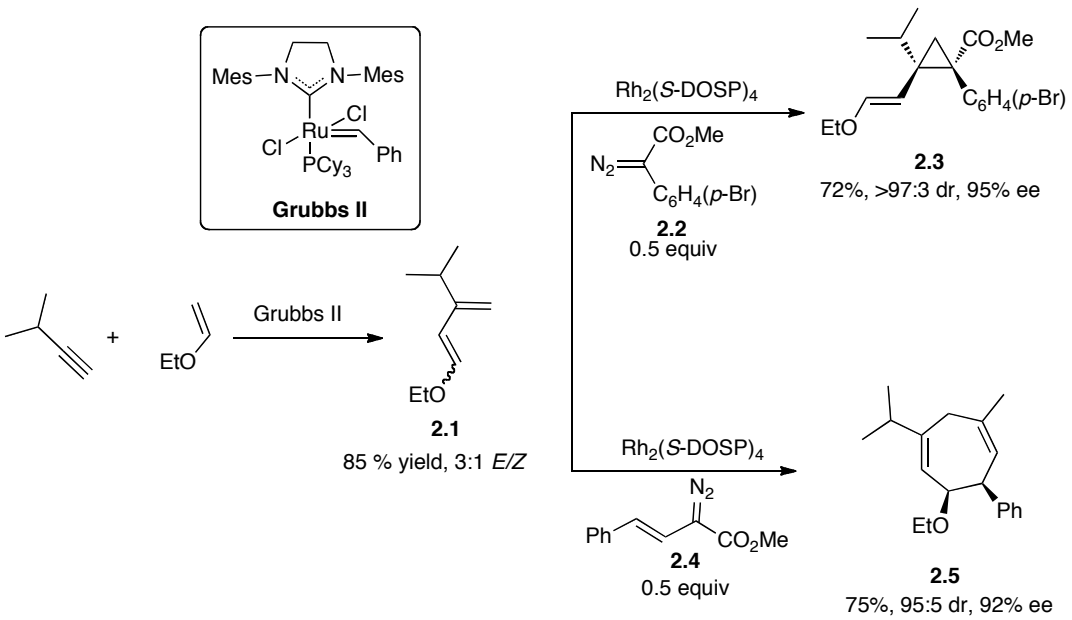
A feature of metal-catalyzed reactions of diazo compounds is the formation of high-energy metal carbenoid intermediates under very mild reaction conditions. The resulting carbenoid reactions often generate strained or reactive products, capable of undergoing further transformations.[25,29] The Davies group has developed a variety of cascade reactions using carbenoid intermediates, including ylide formation/[3+2] cycloaddition,[83] ylide formation/[2,3] sigmatropic rearrangement,[84,85] and cyclopropanation/Cope rearrangement.[86-88] Alternatively, a cascade sequence can be achieved through multicatalytic processes consisting of the carbenoid reaction and another transition metal-catalyzed reaction.[89-91] The Davies group has been interested in developing synthetic sequences that combine the rhodium-catalyzed reactions with other complementary metal-catalyzed reactions to provide orthogonal reactivity.[92-94]

2.1.1 Ruthenium- and rhodium-catalyzed sequential reactions

Rhodium-catalyzed carbenoid reactions proceed under mild reaction conditions. The reaction is highly selective and compatible with a number of different functional groups. These characterizes make the reaction suitable to be combined with other catalytic reactions.[93]

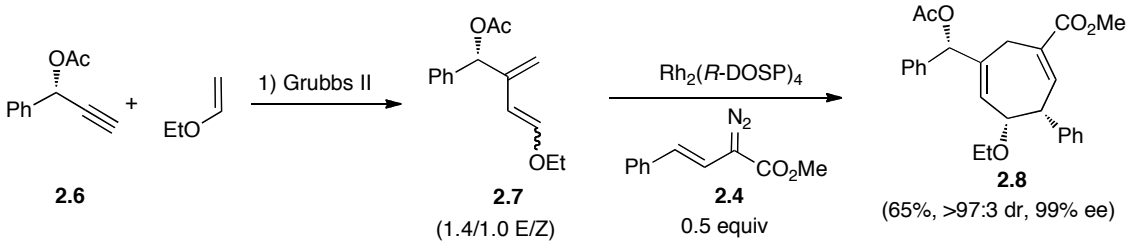
The rhodium-catalyzed asymmetric cyclopropanation/Cope rearrangement is a powerful method to construct seven-membered rings.[87,88,95-98] Through the reaction of vinyldiazo compounds and dienes, highly functionalized cycloheptadienes can be synthesized with high levels of diastereo- and enantioselectivity. This method has been

applied to the total synthesis of natural products.[99-102] As a highly selective process, rhodium-catalyzed carbenoid reactions can potentially differentiate the mixture of dienes, such as the mixture of *E/Z* dienes generated by the ruthenium-catalyzed enyne metathesis.[103,104] Employing the enyne metathesis developed by the Diver group, election rich dienes **2.1** were afforded as a mixture of 3:1 *E/Z*-isomers. The reaction used the second-generation of the Grubbs catalysts and tolerated a variety of functionalities on the alkyne. The cyclopropanation reaction was firstly conducted to evaluate the differentiation study (Scheme **2.1**). The $Rh_2(DOSP)_4$ catalyzed cyclopropanation of dienes **2.1** selectively reacted with the terminal double bond of (*E*)-**2.1** and afforded product **2.3** with high diastereo- (>97:3 dr) and enantioselectivity (95% ee). Changing the reactant from aryldiazoacetate **2.2** to phenylvinyldiazoacetate **2.4**, cycloheptadiene **2.5** was selectively synthesized with high diastereo- and enantioselectivity from the reaction of the 3:1 ratio of mixture of (*E/Z*)-**2.1**.



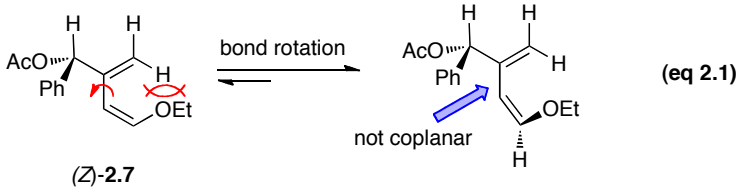
Scheme 2.1 Ruthenium- and rhodium-catalyzed reaction sequence

Besides the differentiation between the alkene geometries, stereodifferentiation was also achieved when chiral dienes **2.7** was used as substrates (Scheme **2.2**). Through ruthenium-catalyzed enyne metathesis of chiral phenyl propargyl acetate **2.6**, chiral diene **2.7** was generated as a mixture of 1.4:1.0 ratio of *E/Z*-isomers. Rh_2(*R*-DOSP)$_4$ was the matched catalyst and the reaction of **2.7** with diazo compound **2.4** produced cycloheptadiene **2.8** as a single diastereomer in 65% yield.



Scheme 2.2 Double diastereodifferentiation

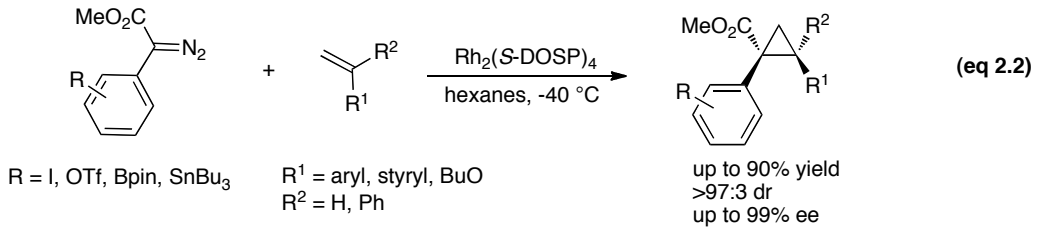
The observed selective reaction of *E*-**2.7** over its *Z*-isomer is because the ethoxy group in *Z*-**2.7** is twisted out from planarity due to the steric repulsion. Hence, the donation of electrons to the terminal double bond is limited (eq **2.1**), which results in the low reactivity of the *Z*-**2.7**



2.1.2 Rhodium- and palladium-catalyzed sequential reactions

Metal-catalyzed cross-coupling reaction is one of the most effective ways to construct complicated organic compounds through a carbon-carbon bond formation step.[105,106] Since dirhodium(II) catalysts do not react with the common functionalities used in cross-coupling reactions, the rhodium-catalyzed carbenoid reaction can be combined with

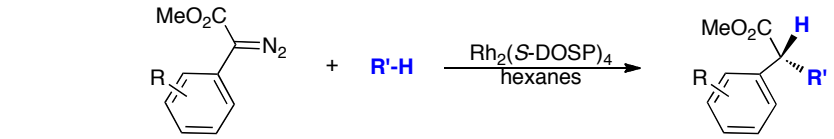
cross-coupling reactions as a new strategy for diversified synthesis. An example is the rhodium- and palladium-catalyzed reaction sequence developed by the Davies group.[94] The process began with the synthesis of coupling partners *via* the rhodium-catalyzed cyclopropanation and C–H functionalization with diazo compounds bearing common functionalities used in cross-coupling reactions, such as iodides, triflates, organoborons, and organotins. The $Rh_2(DOSP)_4$ catalyzed cyclopropanation reaction with these diazo compounds afforded the products as single diastereomers in high yields and with high enantioselectivity (eq **2.2**). These results indicate that the iodide, organoboron, organostannane, and triflate group do not interfere with the cyclopropanation reaction.

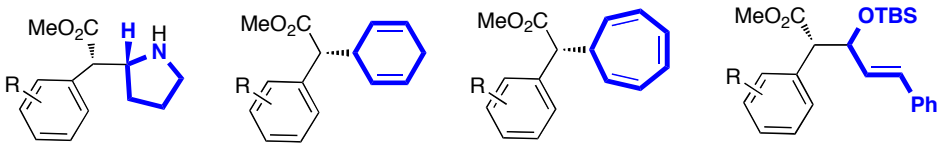


(eq 2.2)

Compared to the cyclopropanation reaction, the intermolecular C–H insertion reaction of these functionalized diazo compounds is more demanding and suitable substrates are required. In the presence of an iodide, organoboron and triflate group, the C–H insertion reaction of representative substrates furnished the products with good enantioselectivity (Table **2.1**). Compared to the reaction of simpler aryldiazoacetates, lower yields and stereoselectivity were observed for some substrates.

Table 2.1 Synthesis of coupling partners *via* C–H insertion





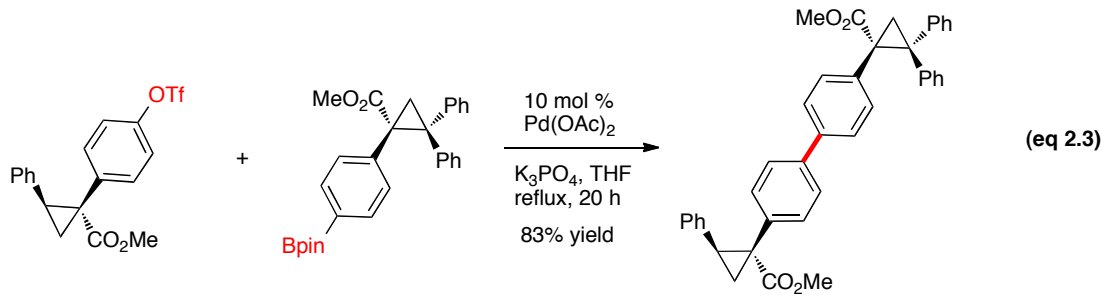
up to 48% yield
up to 85% ee
>94% de

up to 74% yield
up to 95% ee

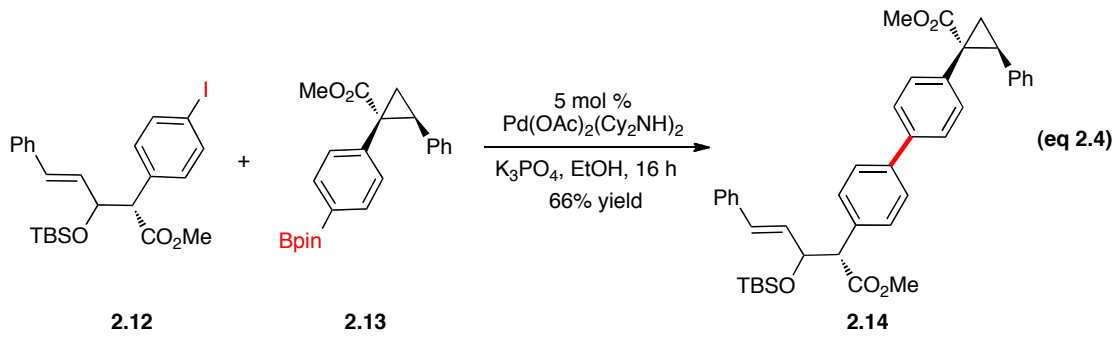
up to 58% yield
up to 95% ee

up to 95% yield
up to 89% ee
>94% de

With these functionalized cyclopropanes and C–H insertion products in hand, the subsequent palladium-catalyzed coupling reactions were conducted (eq **2.3**). In the presence of $Pd(OAc)_2$, the reaction of aryltriflate **2.9** and arylboronate **2.10** afforded the coupling product **2.11** in 83% yield. Beside aryltriflates, aryliodides can also react with organoborons to form the coupling product. For example, the DAPCy (*trans*-$(Cy_2NH)_2Pd(OAc)_2$) catalyzed coupling reaction of the C–H insertion product **2.12** with cyclopropane **2.13** afforded **2.14** in 66% yield (eq **2.4**).



2.9 **2.10** **2.11** **(eq 2.3)**



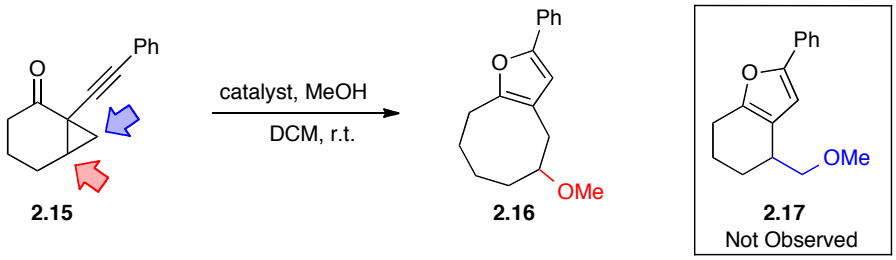
2.12 **2.13** **2.14**

2.1.3 Synthesis of heterocycles *via* cycloisomerization reaction

Cyclopropanes are readily accessible and highly strained organic compounds. The strain energy of the cyclopropane ring is about 27.5 kcal/mol.[107,108] Elaborating these three-membered ring cycloalkanes comprises a major research area in organic chemistry. In recent years, homogeneous gold-catalyzed reactions have been widely developed.[109-114] One class of gold-catalyzed reactions is the rearrangement of alkynyl cyclopropanyl ketones.[115-121] A number of heterocycles could be rapidly synthesized in high yield and with high selectivity *via* these transformations.

The gold-catalyzed cycloisomerization of alkynyl cyclopropanyl ketones was first developed by Schmalz and coworker. In the presence of a Lewis acid, fused furans were produced in high yield and with high selectivity (Table **2.2**).[115] A number of Lewis acids were able to catalyze this transformation, including $Cu(OTf)_2$, $Yb(OTf)_3$, AgOTf, AuCl, $AuCl_3$, etc, but the best result was obtained with $Ph_3PAuOTf$. In the presence of such catalyst, full conversion of **2.15** was achieved in less than 10 min and product **2.16** was isolated in 91% yield. Interestingly, the reaction generated product **2.16** exclusively and no formation of **2.17** was observed with any of these catalysts.

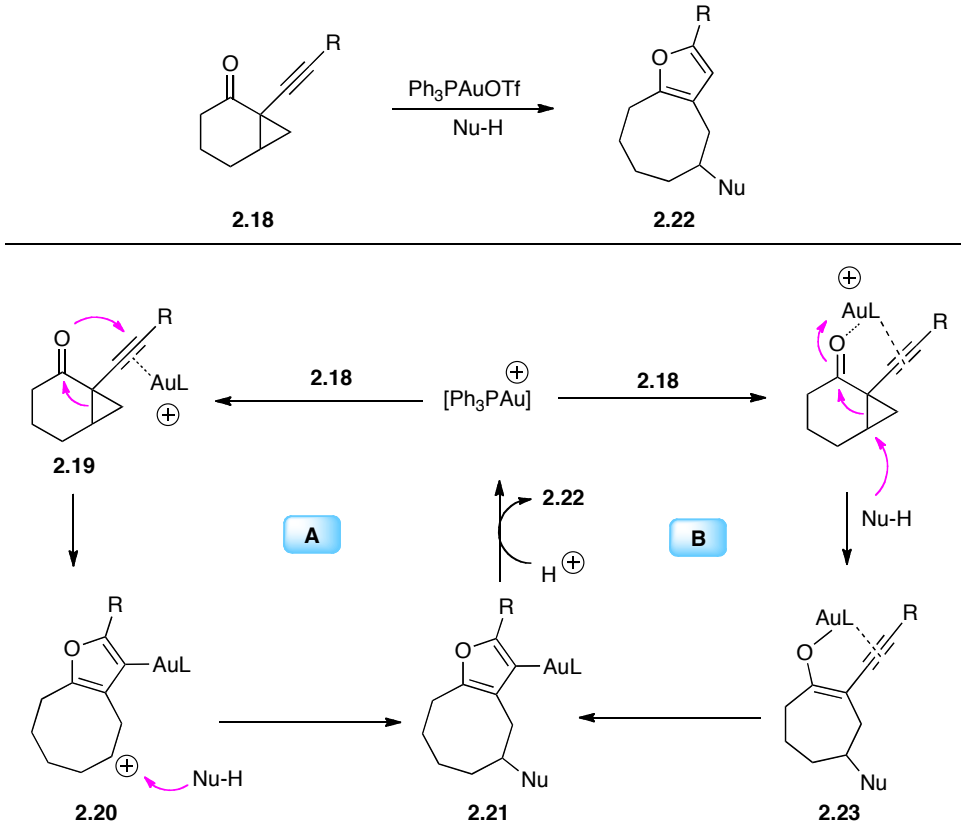
Table 2.2 Effective Lewis acid catalysts for the reaction of **2.15**



2.15 **2.16** **2.17** Not Observed

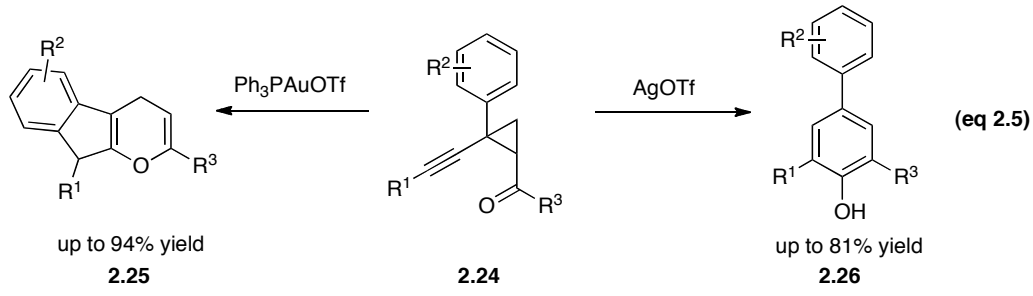
entry	catalyst	amount (mol %)	time	yield (%)
1	none	-	24 h	0
2	$Cu(OTf)_2$	5	16 h	74
3	$Yb(OTf)_3$	5	24 h	70
4	AuCl	5	1 h	66
5	$AuCl_3$	5	1 h	68
6	AgOTf	5	1 h	85
7	$Ph_3PAuOTf$	5	< 5 min	90
8	$Ph_3PAuOTf$	1	< 10 min	91

Two plausible mechanisms (**A** and **B**) were proposed for this transformation (Scheme **2.3**). In catalytic cycle **A**, the reaction begins with the coordination of a cationic gold catalyst to the alkyne group of reactant **2.18** to generate intermediate **2.19**. The subsequent opening of the cyclopropane ring followed by nucleophilic attack of the carbonyl on the gold-activated triple bond generates carbocation **2.20**, which is then trapped by a nucleophile to form intermediate **2.21**. The next protonation and demetalation afford product **2.22**. Alternatively, the opening of the cyclopropane ring can be assisted by the nucleophile, which results in the formation of intermediate **2.23** (cycle **B**). The subsequent ring closing reaction forms intermediate **2.21**, which would then undergo the same transformation as described above to furnish product **2.22**.

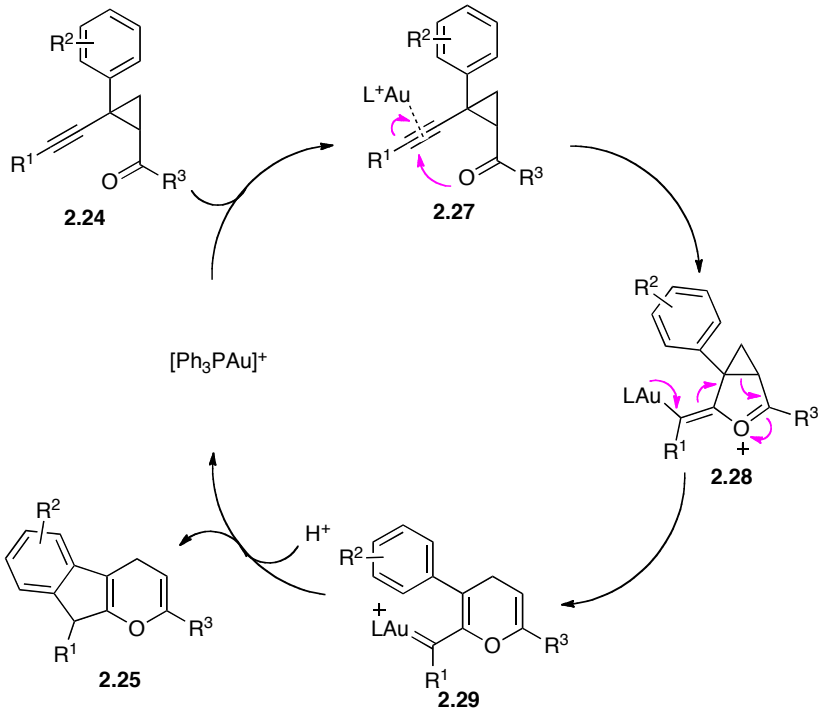


Scheme 2.3 Proposed mechanism for the gold-catalyzed reaction of **2.18**

By changing the substituents on the cyclopropane ring, the gold-catalyzed cycloisomerization reaction can lead to completely different classes of products. Starting with cyclopropane derivative **2.24**, Zhang and coworkers developed a new method to selective synthesize pyran-fused indenes and phenols (eq **2.5**). In contrast to the reaction discussed above, the silver- and gold-catalyzed reaction of **2.24** developed by the Zhang group provided phenol **2.26** and indene **2.25** separately.[116]

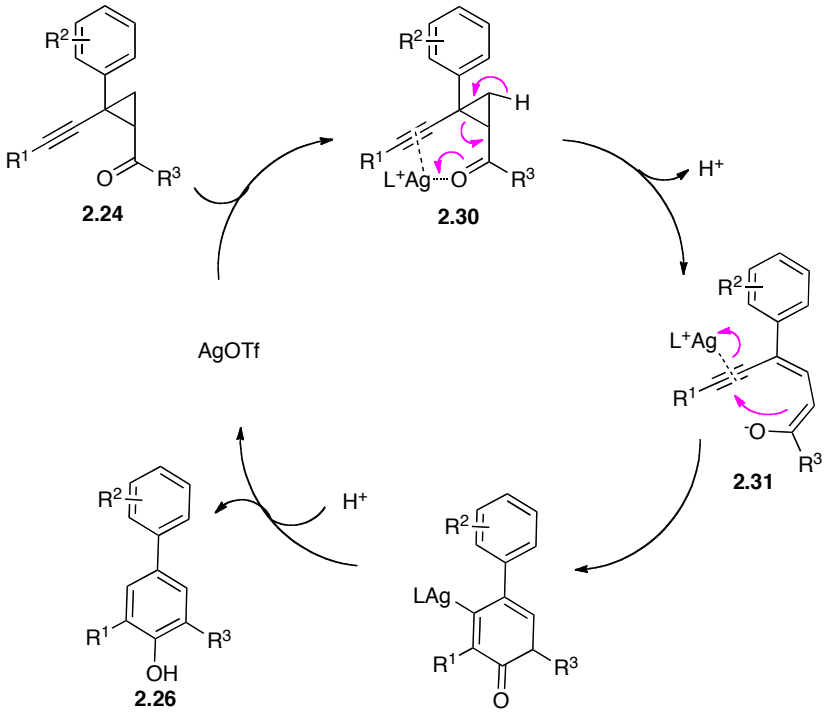


Mechanisms for the formation of both **2.25** and **2.26** were proposed. Scheme **2.4** shows the mechanism for the gold-catalyzed reaction. A cationic Au(I) catalyst first coordinates to the triple bond in **2.24** to form intermediate **2.27**. The subsequent nucleophilic attack of the carbonyl group to the gold-activated alkyne group generates intermediate **2.28**, which undergoes the opening of the cyclopropane ring to provide intermediate **2.29**. The next intramolecular Friedel-Crafts reaction and protodemetallation afford product **2.25**.



Scheme 2.4 Mechanism for the gold-catalyzed reaction of **2.24**

The proposed mechanism for the silver-catalyzed reaction is shown in Scheme **2.5**. The process is initiated with the coordination of AgOTf with both the triple bond and the ketone group to form intermediate **2.30**. This would induce the opening of the cyclopropane ring to generate intermediate **2.31**. The subsequent cyclization, protodemetalation, and aromatization furnish product **2.26**.

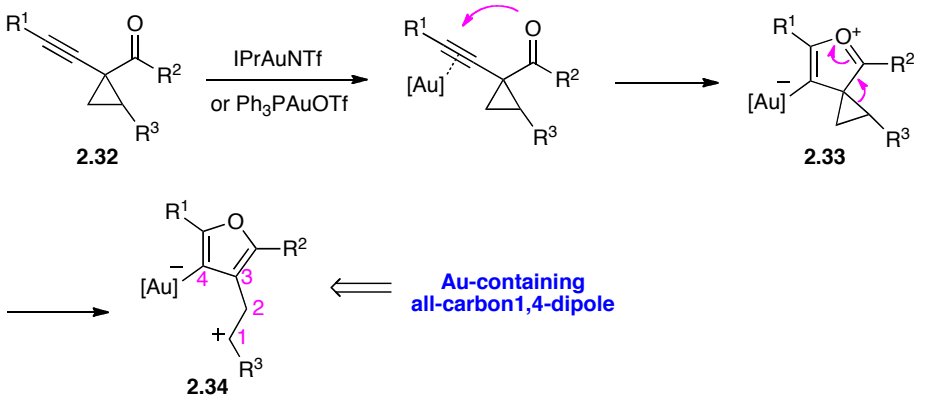


Scheme 2.5 Mechanism for the silver-catalyzed reaction of **2.24**

2.1.4 Generation of all carbon dipoles *via* cycloisomerization of alkynyl cyclopropanyl ketones

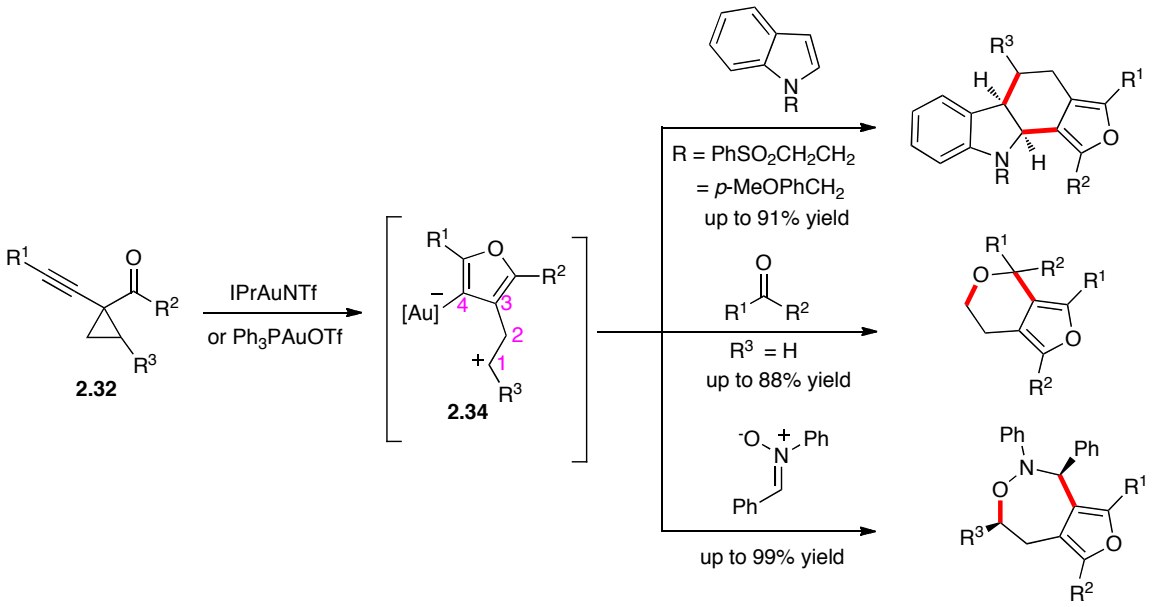
In the presence of a Lewis acid, alkynyl cyclopropanyl ketones can be isomerized to all carbon 1,3- or 1,4-dipoles. By trapping these dipole intermediates, a number of synthetically useful reactions have been developed.[117-121]

Inspired by the work of the Schmalz group, Zhang and coworkers developed a new class of gold-containing all carbon 1,4-dipoles though the cycloisomerization of cyclopropane **2.32** (Scheme **2.6**). The process begins with the coordination of a cationic gold catalyst to the alkyne group, which induces the intramolecular nucleophilic attack of the carbonyl onto the triple bond to furnish intermediate **2.33**. The subsequent opening of the cyclopropane ring forms 1,4-dipole **2.34**.



Scheme 2.6 Formation of Au-containing all-carbon 1,4-dipole

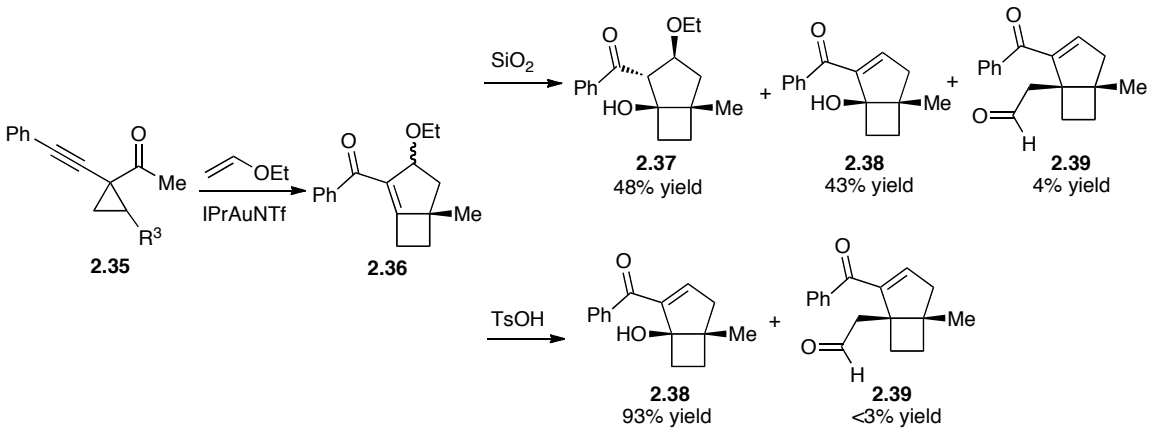
Through this dipole intermediate **2.34**, the gold-catalyzed [4+2] reaction has been applied to alkenes, ketones, aldehydes, etc.[117] A formal [4+3] reaction with nitrones was also achieved. Those reactions provide a simple method to synthesize furan derivatives in high yield (Scheme **2.7**).[121]



Scheme 2.7 Gold-catalyzed 1,4-dipolar cycloaddition

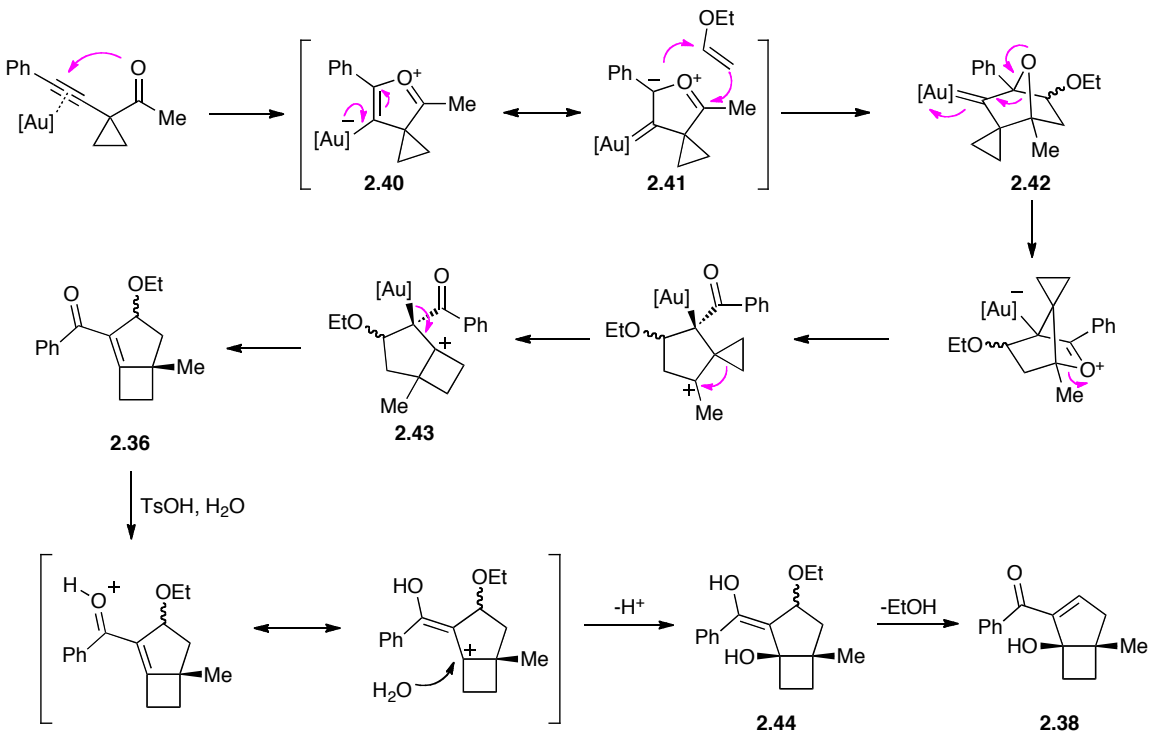
In contrast to the above reactions, the reaction of ethyl vinyl ether with alkynyl cyclopropanyl ketone **2.35** did not provide the anticipated tetrasubstituted furan product but an unstable compound, which decomposed on silica gel to three compounds **2.37**-

2.39 (Scheme **2.8**).[118] By analysis of these compounds, the unstable product generated from the reaction was deducted to be diastereomers of enone **2.36**. Selective formation of product **2.38** was achieved by treating the reaction mixture with Brønsted acid TsOH.



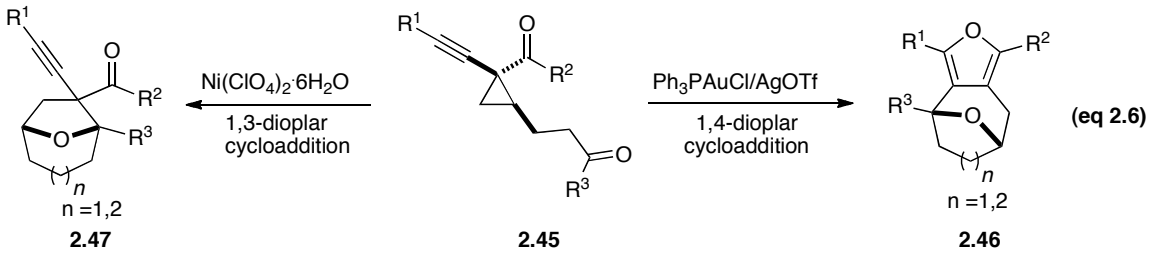
Scheme 2.8 Gold-catalyzed reaction of **2.35** with ethyl vinyl ether

A mechanism for the formation of **2.38** has been proposed (Scheme **2.9**). Instead of the 1,4-dipole, this reaction is considered to proceed *via* a 1,3-dipole intermediate. The reaction begins with the cyclization of the carbonyl group onto the gold-activated alkyne group to form intermediate **2.40**. A resonance structure of **2.40** is dipole **2.41**, which can undergo a 1,3-dipolar cycloaddition with ethyl vinyl ether to generate bicyclic intermediate **2.42**. The subsequent opening of the bicyclo ring and then the cyclopropane ring afford intermediate **2.43**. The elimination of the gold catalyst in **2.43** affords enone **2.36**. Intermediate **2.44** is obtained by treating **2.36** with TsOH. The tautomerization of **2.44** and elimination of EtOH provide the observed product **2.38**.[118]



Scheme 2.9 Proposed mechanism for gold-catalyzed reaction of vinyl ether

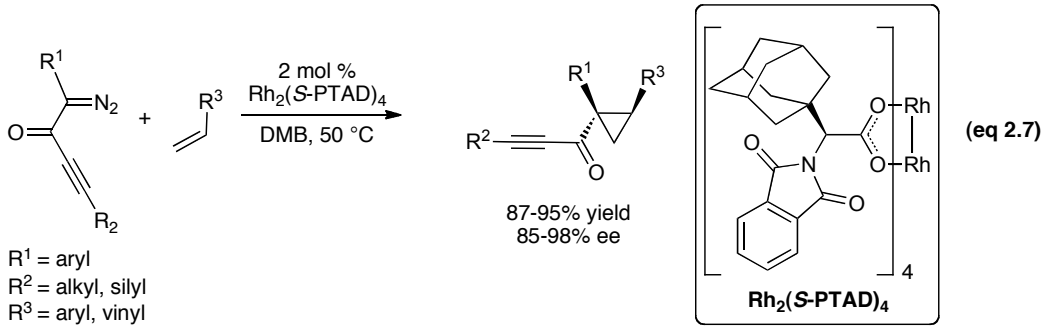
The above discussion shows that substrates can influence the reaction pathway. Another way to achieve selective 1,3- or 1,4-dipolar cycloaddition is changing the catalyst. During the exploration of the intramolecular reaction of alkynyl cyclopropanyl ketone **2.45**, Wang and coworkers found that the reaction produced tricyclic furan **2.46** exclusively *via* a 1,4-dipolar cycloaddition when $Ph_3PAuOTf$ was used as catalyst. In contrast, the reaction of **2.45** afforded the bicyclic compound **2.47** as the only product *via* a 1,3-dipolar cycloaddition when $Ni(ClO_4)_2{\cdot}6H_2O$ was used as catalyst (eq **2.6**).[119]



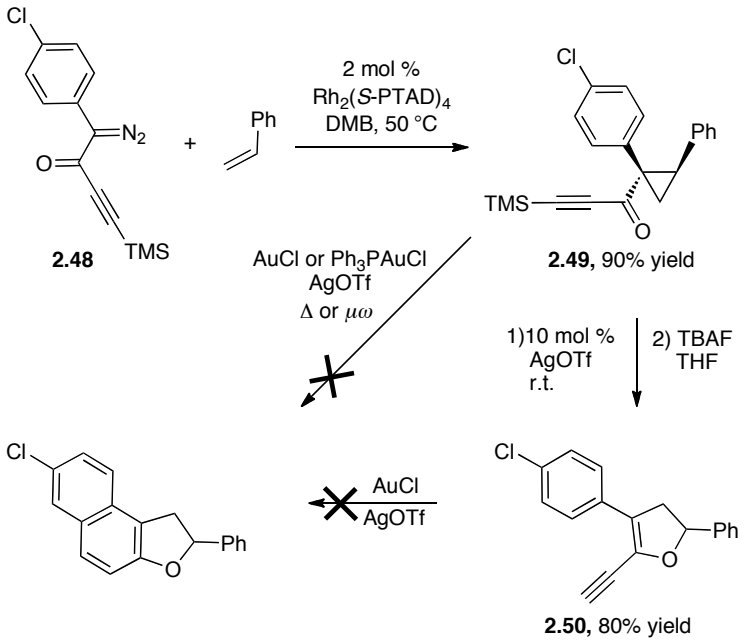
2.2 Results and discussion

2.2.1 Sequential reactions for the synthesis of fused dihydrofurans

During the study of the rhodium-catalyzed cyclopropanation of alkenes with α-aryldiazoketones, a new class of alkynyl-substituted cyclopropanes was developed (eq **2.7**).[20] As the resulting cyclopropane products have multiple reactive sites, such as the cyclopropyl ketone and the alkyne functionalities, they would be ideal substrates for multiple metal-catalyzed cascade reactions. A triple cascade process was designed for the rapid synthesis of polycyclic benzo-fused dihydrofurans. The first step is a rhodium-catalyzed cyclopropanation of alkenes with α-aryldiazoketones, which is followed by a silver-catalyzed ring expansion to dihydrofurans. Lastly, a gold-catalyzed cyclization to afford benzo-fused dihydrofurans.



The study began with the reaction of the *p*-chlorophenyldiazoketone **2.48** by previous graduate student, Justin Denton (Scheme **2.10**). A rhodium-catalyzed cyclopropanation of styrene with diazo compound **2.48** generated the cyclopropyl ketone **2.49** in 90% yield. Treatment of **2.49** with silver triflate (AgOTf) and TBAF resulted in desilylation and ring expansion to form **2.50**. However, the subsequent gold-catalyzed cyclization between the alkyne group and the phenyl ring in **2.50** was problematic. Under a variety of reaction conditions, no more than trace amounts of the polycyclic product were ever observed starting from **2.49** or **2.50**.

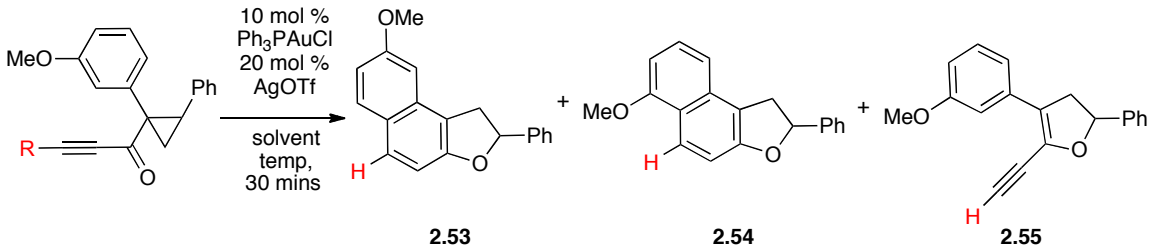


Scheme 2.10 Initial study of the gold-catalyzed cyclization reaction

A possible explanation for the failure of Justin Denton's gold-catalyzed cyclization studies is that the gold-activated complex is electrophilic and would require an electron-rich aromatic ring for effective ring closure.[122,123] Therefore the reaction sequence was repeated with the *m*-methoxy derivative **2.51** (Table **2.3**). The reaction was conducted under both thermal condition and microwave irradiation. With microwave irradiation, the reaction of **2.51** produced the fused dihydrofuran as two regioisomers (**2.53** and **2.54)** together with uncyclized dihydrobenzofuran **2.55** (entry 1). Under these conditions, proto-desilylation is observed. It was then reasoned that utilizing the desilylated alkynyl-ketone cyclopropane **2.52**, which has a proton replacing the TMS group, would result in higher yield of **2.53** and **2.54**. Employing the same reaction conditions as for **2.51**, the silver- and gold-catalyzed reaction of **2.52** resulted in complete conversion to the desired tricyclic dihydrofurans **2.53** and **2.54** with none of the uncyclized **2.55** remaining (entry

2). Further improvement of the reaction yield was achieved by conducting the reaction in less polar solvent under thermal conditions (entry 3).

Table 2.3 Ag/Au catalyzed cyclization of the cyclopropanes bearing an electron-rich phenyl group



2.53 **2.54** **2.55**

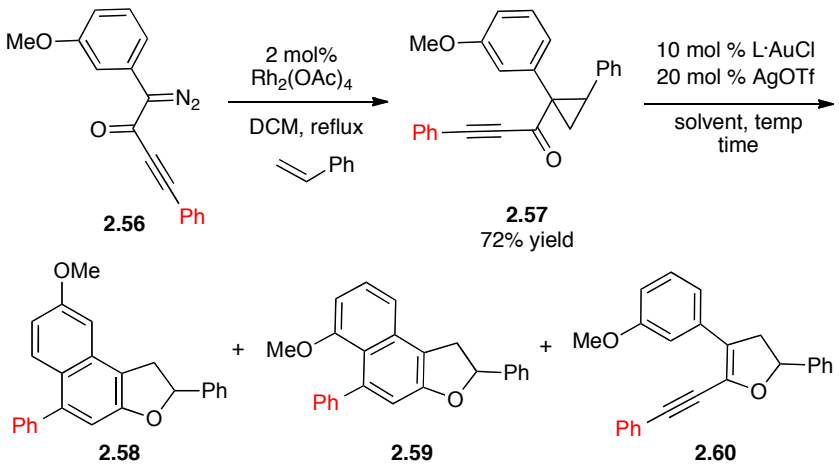
entry	R	cyclopropane	conditon	solvent	temp (°C)	combied yields[a] (%)	ratio[b] **(2.53+2.54)**: **2.55**
1	TMS	**2.51**	microwave	DCM	100	29	1.9:1
2	H	**2.52**	microwave	DCM	100	60	1:0
3[c]	H	**2.52**	thermal	PhMe	100	76	1:0

[a] Isolated yields. [b] Determined by crude NMR. [c] The reaction was stirred for 3 h at the reaction temperature.

Since the reaction conducted under thermal conditions provided the tricyclic dihydrofurans in higher yield than the reaction under microwave irradiations, further optimization studies were employing thermal conditions. The reaction of cyclopropane **2.57** was chosen to perform the subsequent optimization study because the low yield accompanying the synthesis of the diazo compound having a terminal alkyne group, which is required for the synthesis of cyclopropane **2.52** (Table **2.4**). The triphenylphosphine ligand was found to be important for this cyclization reaction. Without this ligand, the Au(I) catalyzed reaction of **2.57** did not go to completion after 24 h refluxing in dichloromethane (entry 1). In contrast, complete conversion of cyclopropane **2.57** to the cyclized dihydrofurans **2.58** and **2.59** was achieved in only 0.5 h when the reaction was catalyzed by Ph_3P/Au(I) (entry 2). Further studies showed that

toluene was the ideal solvent for this gold-catalyzed cyclization reaction and polycyclic dihydrofuran products were isolated in nearly quantitative yield (entry 4). A similar yield was also obtained from the reaction conducted in a cosolvent system consisting of a 1:2 volume ratio of dichloromethane and toluene (entry 6). As will be discussed later, this mixed-solvent system became the foundation of a one-pot procedure for this transformation. Without the extra amount of the AgOTf, complete conversion of cyclopropane **2.57** to dihydrofurans **2.58** and **2.59** were also observed, but the yield decreased.

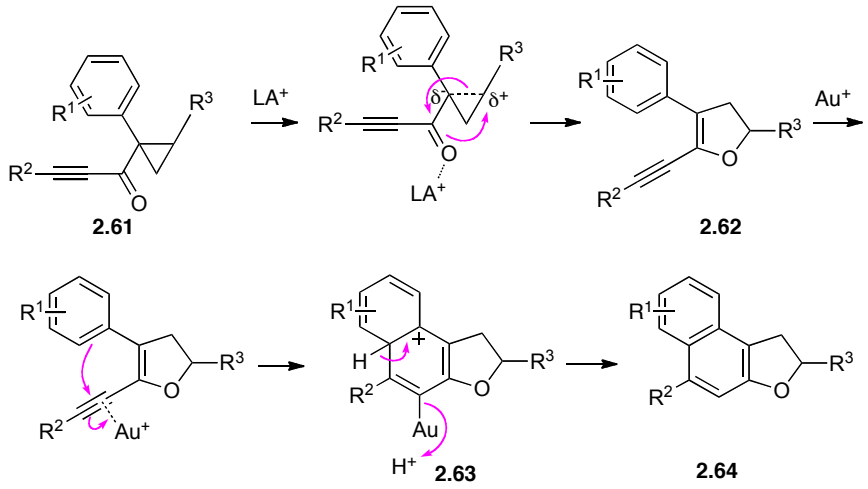
Table 2.4 Optimization of the cyclization reaction



entry	L·AuCl	solvent (v/v)	temp (°C)	time (h)	ratio[a] (**2.58**:**2.59**:**2.60**)	yield[b] %
1	AuCl	DCM	reflux	24	2.4: 1:1	59[c]
2	Ph_3PAuCl	DCM	reflux	0.5	2.8:1:0	78
3	Ph_3PAuCl	DCE	reflux	0.5	2.0:1:0	83
4	**Ph_3PAuCl**	**PhMe**	**85**	**0.5**	**2.5:1:0**	**99**
5	Ph_3PAuCl	DCM/PhMe (1/1)	reflux	0.5	1.6:1:0	91
6	Ph_3PAuCl	DCM/PhMe (1/2)	reflux	0.5	1.8:1:0	99
7[d]	Ph_3PAuCl	DCM/PhMe (1/2)	reflux	0.5	1.6:1:0	84

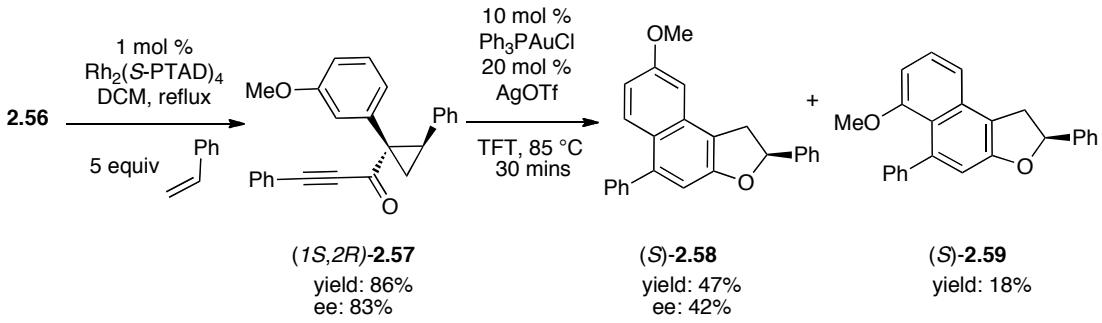
[a] Determinded by crude NMR. [b] Combined yield of compounds **2.58** and **2.59** from **2.57**.
[c] Combined yield of compounds **2.58**, **2.59** and **2.60**. [d] 10 mol % AgOTf was used.

A mechanism for the Ag/Au catalyzed cyclization reaction is proposed (Scheme **2.11)**. AgOTf is expected to act as a Lewis acid and induce rearrangement of the cyclopropyl ketone **2.61** to form the dihydrofuran **2.62**. The following gold-catalyzed benzannulation would form intermediate **2.63**, which upon deprotonation and protodemetalation would afford the tricyclic product **2.64**.



Scheme 2.11 Proposed mechanism of the cyclization reaction

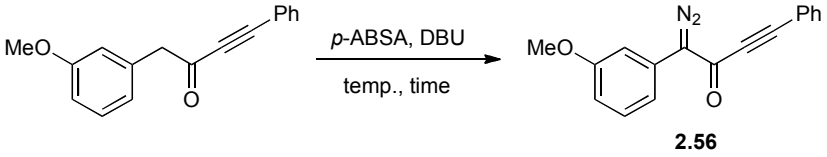
Since this type of cyclopropane can be synthesized with high levels of enantioselectivity, the dihydrofuran products obtained *via* this reaction sequence could be enantio-enriched if there is only minimal loss of enantioselectivity during the opening of the cyclopropane ring. To test the possibility, the cyclization reaction of chiral **2.57** (83% ee), which was synthesized by the Rh_2(*S*-PTAD)$_4$ catalyzed cyclopropanation of styrene with **2.56**, was conducted (Scheme **2.12**). Unfortunately, the silver- and gold-catalyzed reaction afforded the major product (*S*)-**2.58** in only 42% ee. Due to this observation, the following study of this cascaded process focused on the development of a racemic reaction.



Scheme 2.12 Cyclization reaction of chiral cyclopropane (*1S,2R*)-**2.57**

In order to study the scope of this reaction, a reliable synthetic route towards the alkynyl cyclopropanyl ketone has to be developed. The synthesis of this class of alkynyl-ketone diazo compounds was first optimized (Table **2.5**). It was found that warming up the reaction to room temperature caused a decrease in the reaction yield (entries 1 and 2). Further studies showed that the yield of **2.56** increased with a shorter reaction time. When the diazo transfer reaction was conducted in only 5 min, diazo compound **2.56** was produced in 91% yield (entries 3-6).

Table 2.5 Optimization study of the diazo transfer reaction



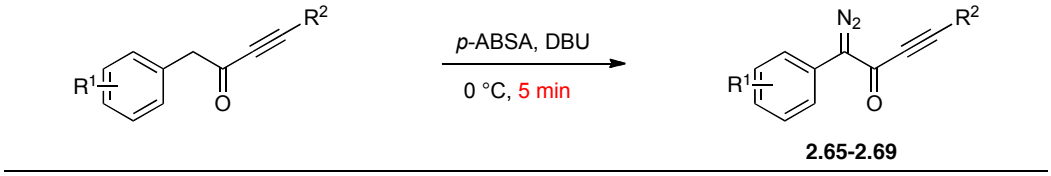
2.56

entry	temperature (°C)	time (min)	isolated yield (%)
1[a]	0 then 23	60 then 60	47
2	0	150	63
3	0	60	84
4	0	30	86
5	0	15	87
6	**0**	**5**	**91**
7	23	5	72

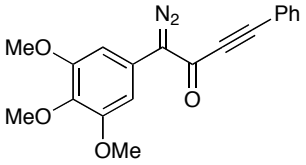
[a] The reaction was stirred at 0 °C for 60 min and 23 °C for 60 min

These optimized conditions were found to be quite general for the synthesis of alkynyl-ketone diazo compounds. Employing this protocol, diazo compounds **2.65-2.69** were synthesized in high yields (Table **2.6**). The only exception is the synthesis of diazo compound **2.70**, which can only be produced when triethylamine was used as base instead of DBU (eq **2.8**).

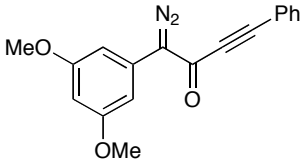
Table 2.6 Synthesis of the alkynyl-ketone diazo compounds



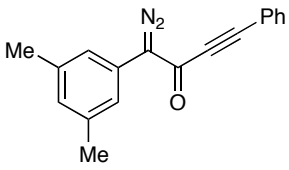
2.65-2.69



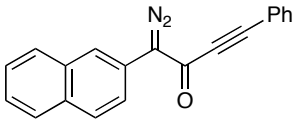
2.65, 87% yield



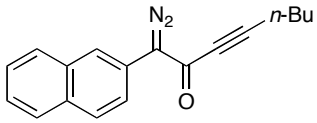
2.66, 86% yield



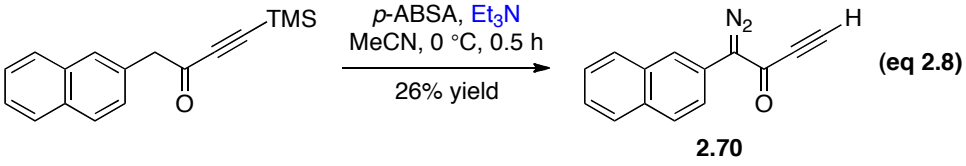
2.67, 88% yield



2.68, 88% yield



2.69, 83% yield

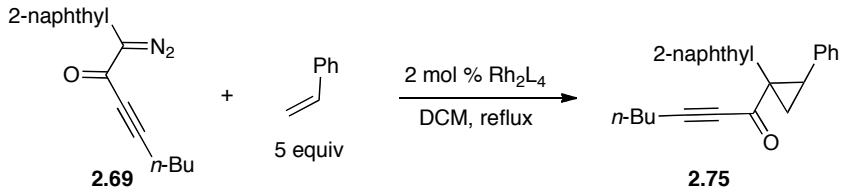


2.70 **(eq 2.8)**

Although the $Rh_2(OAc)_4$ catalyzed cyclopropanation of styrene with diazo compound **2.56** provided the product in good yield, this reaction is not general and low to moderate yields were observed for the reaction of some alkynyl-ketone diazo compounds. For example, the $Rh_2(OAc)_4$ catalyzed cyclopropanation of styrene with **2.73** provided the desired product in 57% yield (entry 1, Table **2.7**). Optimization of the rhodium-catalyzed

cyclopropanation with **2.73** was conducted in dichloromethane because cyclopropanation with this class of diazo compounds attempted in PhMe and TFT produced none of the desired cyclopropane product. The study of the rhodium catalysts showed that the electron-deficient $Rh_2(TFA)_4$ exhibited the best catalytic ability. In the presence of such catalyst, the reaction of **2.73** produced cyclopropane **2.74** in 78% yield.

Table 2.7 Optimization of the rhodium-catalyzed cyclopropanation reaction



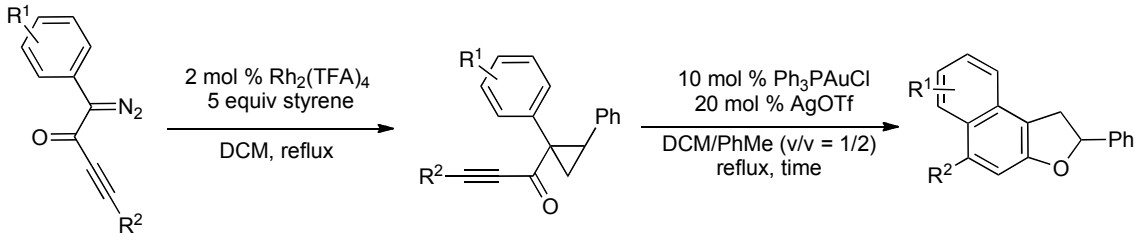
entry	catalysts	yield[a] (%)
1	$Rh_2(OAc)_4$	57
2	$Rh_2(Oct)_4$	56
3	$Rh_2(OPiv)_4$	55
4	$Rh_2(esp)_4$	51
5	$Rh_2(S\text{-PTAD})_4$	62
6	**$Rh_2(TFA)_4$**	**78**

[a] Isolated yield.

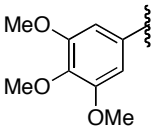
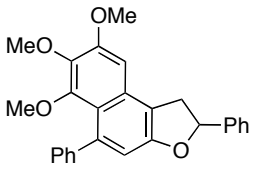
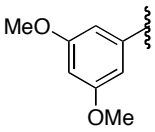
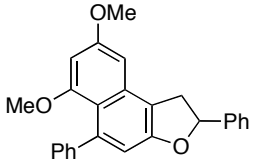
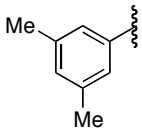
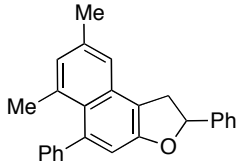
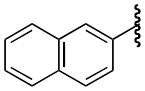
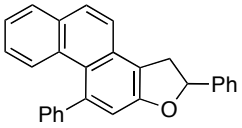
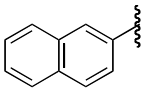
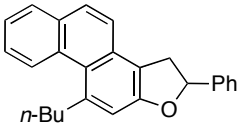
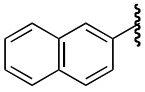
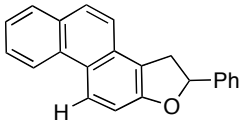
This optimized reaction condition worked well for the cyclopropanations of alkynyl-ketone diazo compounds (Table **2.8**). Under these conditions, cyclopropanes **2.71**-**2.75** were synthesized as single diastereomers in high yields. The reason for the moderate yield observed with **2.76** might be the instability of diazo compound **2.70**. All of the cyclopropanes synthesized were subjected to the following silver/gold catalyzed reactions. Although cyclopropanes **2.71** and **2.72**, with methoxy group on each side of the phenyl ring, are more sterically hindered than **2.57**, polycyclic products **2.77** and **2.78** were obtained in high yields after a period of 2 h (entries 1 and 2). The cyclization reaction of 2-naphthyl cyclopropane **2.74** generated product **2.80** as a single regioisomer in high yield (entry 4). The structure of **2.80** was confirmed by X-ray crystallographic

analysis (Figure **2.1**). The same selectivity was also observed for the reaction of other 2-naphthyl derivatives **2.81** and **2.82** (entries 5 and 6).

Table 2.8 Sequential reactions of diazo ketones with styrene



2.65-2.70 **2.71-2.76** **2.77-2.82**

entry	R^1	R^2	diazo	cyclopropane	yield[b] (%)	time[a] (h)	product	structure	yield[b] (%)
1		Ph	**2.65**	**2.71**	80	2	**2.77**		99
2		Ph	**2.66**	**2.72**	89	2	**2.78**		79
3		Ph	**2.67**	**2.73**	94	2	**2.79**		99
4		Ph	**2.68**	**2.74**	72	2	**2.80**		96
5		*n*-Bu	**2.69**	**2.75**	78	6	**2.81**		90
6		H	**2.70**	**2.76**	39	0.5	**2.82**		92

[a] The reactions were monitored by TLC and heating was stopped when all the starting materials were consumed. [b] Isolated yields.

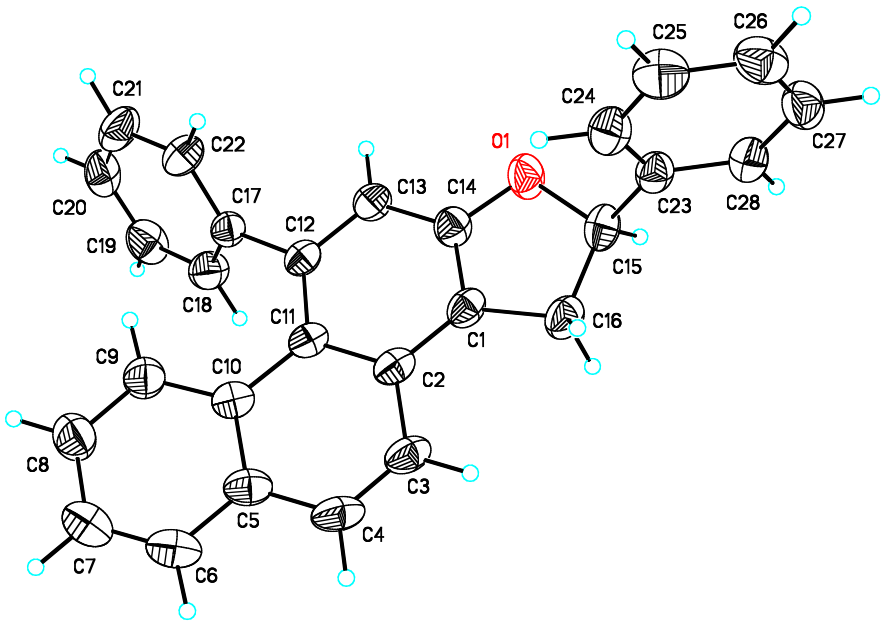
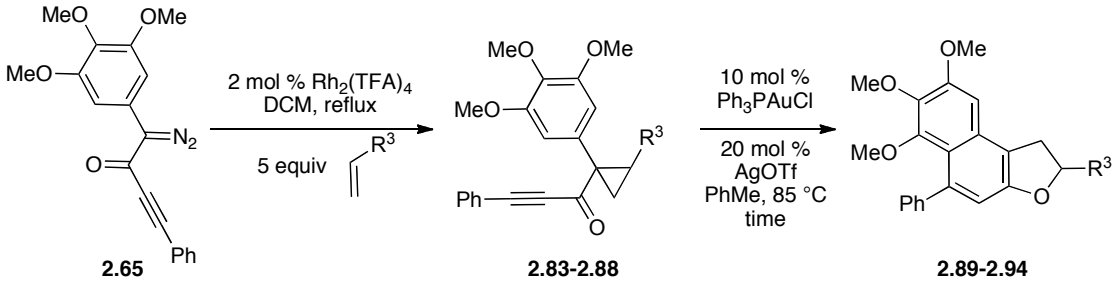


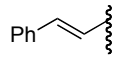
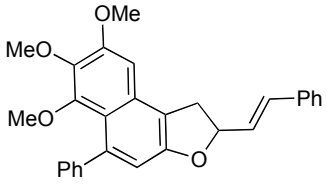
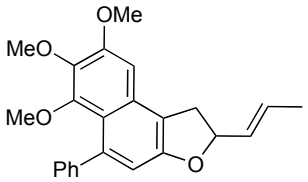
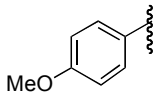
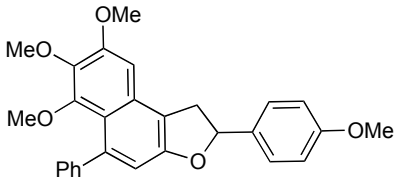
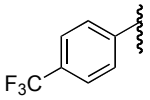
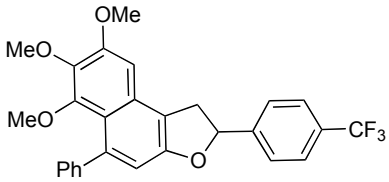
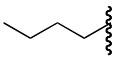
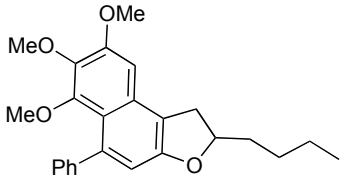
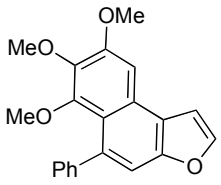
Figure 2.1 X-ray crystallographic structure of compound **2.80**

The reaction of trimethoxy-substituted diazo compound **2.65** was applied to a range of alkenes (Table **2.9**). In general, reactions using toluene as solvent provided better yields than the mixed-solvent conditions. In addition to alkenes, dienes also behaved well in this reaction sequence (entries 1 and 2). Different reactivities were observed for the Ag/Au catalyzed reactions of cyclopropane derivatives originating from electron rich styrenes and electron poor styrenes. The reaction with 4-methoxystyrene provided the polycyclic product **2.91** in low yield (entry 3). In contrast, the reaction with 4-(trifluoromethyl)styrene produced **2.92** in excellent yield (entry 4). Instead of a dihydrofuran product, the Ag/Au catalyzed reaction of cyclopropanyl acetate **2.88** generated benzofuran **2.94** in 48% yield (entry 6).

Table 2.9 Sequential reactions of **2.65** with alkenes

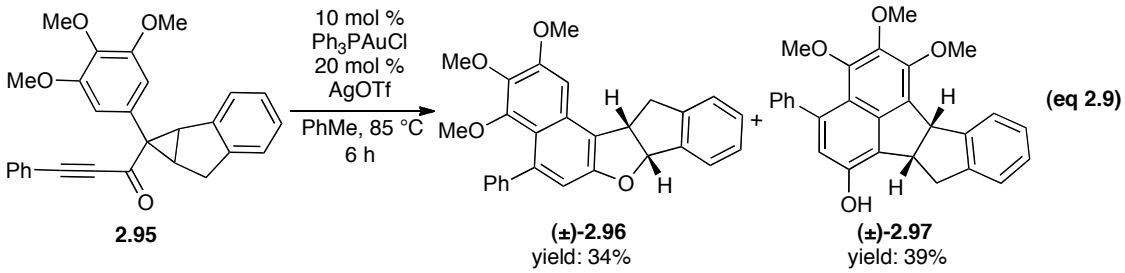


2.65 **2.83-2.88** **2.89-2.94**

entry	R^3	cyclopropane	yield[b] (%)	time[a] (h)	prodcut	structure	yield[b] (%)
1		**2.83**	80	6	**2.89**		80
2		**2.84**	70	6	**2.90**		62
3		**2.85**	82	6	**2.91**		21
4		**2.86**	66	6	**2.92**		93
5		**2.87**	34	2	**2.93**		89
6		**2.88**	46	6	**2.94**		48

[a] The reactions were monitored by TLC and heating was stopped when all the starting materials were consumed. [b] Isolated yields.

The attempted annulation of cyclopropane **2.95**, which was derived from diazo compound **2.65** and indene, gave an unexpected result as it produced not only the expected product **2.96** but also phenol **2.97** (eq **2.9**). The structure of **2.97** was confirmed by the X-ray crystallography (Figure **2.2**).



2.95

(±)-2.96
yield: 34%

(±)-2.97
yield: 39%

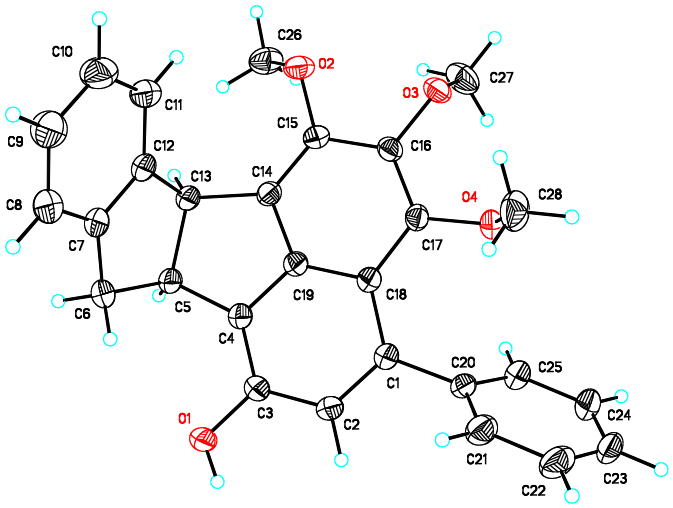
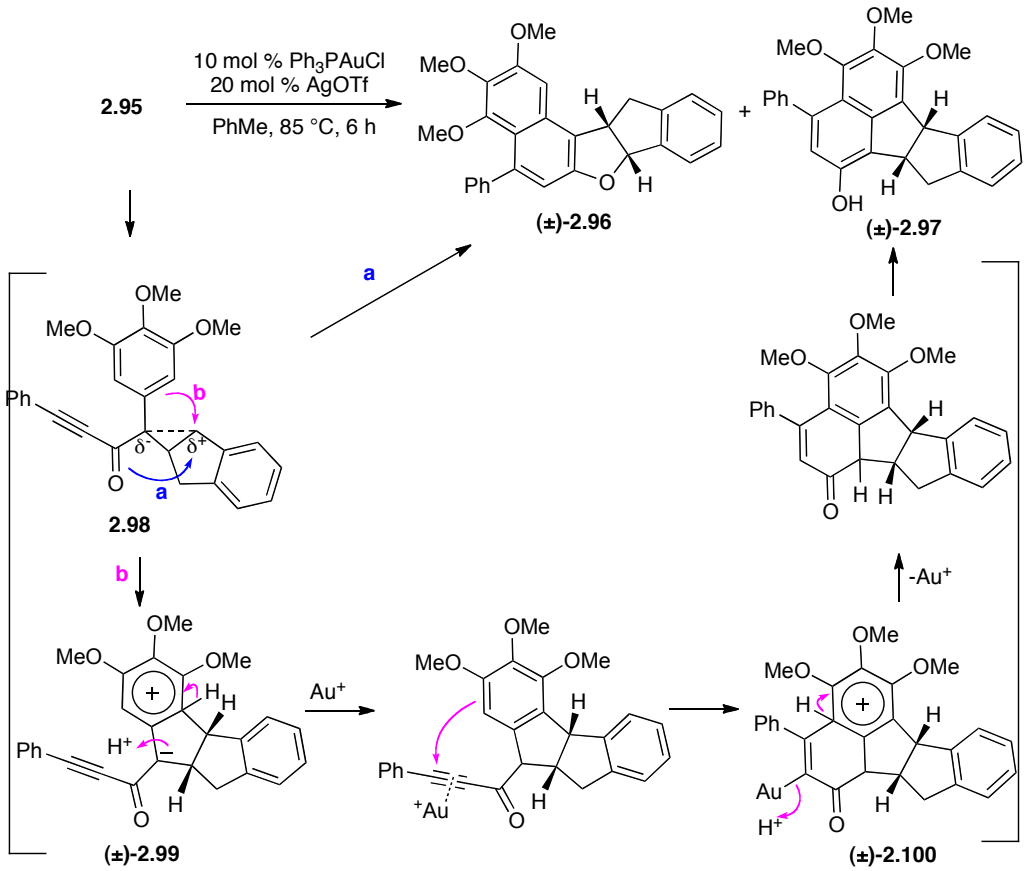


Figure 2.2 X-ray crystallographic structure of compound **2.97**

All efforts of converting **2.96** to **2.97**, with silver-, gold-catalysts or trifluoromethanesulfonic acid, were unsuccessful. This suggested that **2.96** and **2.97** were generated by different reaction pathway (Scheme **2.13**). The unexpected formation of phenol **2.97** might be caused by the ring stain of the tricyclic cyclopropane **2.95** and the nucleophilicity of the trimethoxyphenyl group. Different from the generation of product **2.96** constructed *via* route **a** as shown in **2.98**, the formation of **2.97** could be initiated with the opening of the cyclopropane ring assisted by the trimethoxyphenyl ring (route

b), which leads to intermediate **2.99**. This intermediate could then undergo aromatization, protonation and gold-catalyzed benzannulation to provide **2.100**. The following proto-demetalation and tautomerization would supply **2.97**.

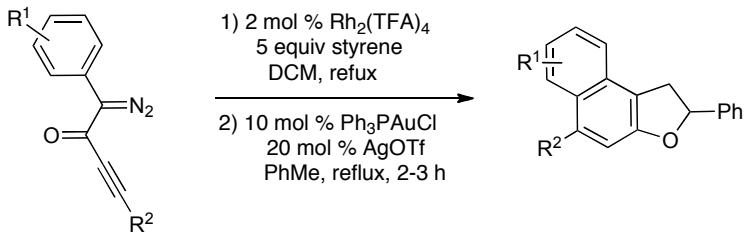


Scheme 2.13 Reaction of cyclopropane **2.95** to generate **2.96** and **2.97**

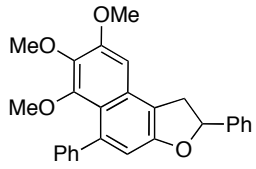
A one-pot procedure was also developed for the sequential reactions (Table **2.10**). This was based on the successful cyclization employing the cosolvent system of dichloromethane and toluene. The first step was the rhodium-catalyzed cyclopropanation reaction with dichloromethane as solvent. After finishing this step, the reaction was cooled down to room temperature, followed by adding silver-, gold-catalysts and toluene. The resulting mixture was heated to reflux again and the reaction was monitored by TLC.

Heating was stopped after all of the cyclopropane was consumed. This one-pot procedure resulted in the formation of **2.77**-**2.80** in similar yields to the two-step sequence.

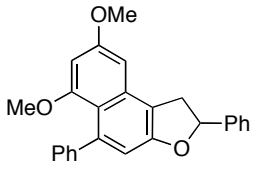
Table 2.10 Examples of the one-pot procedure



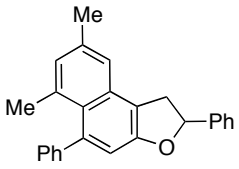
2.65-2.68 **2.77-2.80**



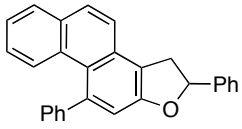
2.77, 74% yield



2.78, 74% yield



2.79, 82% yield

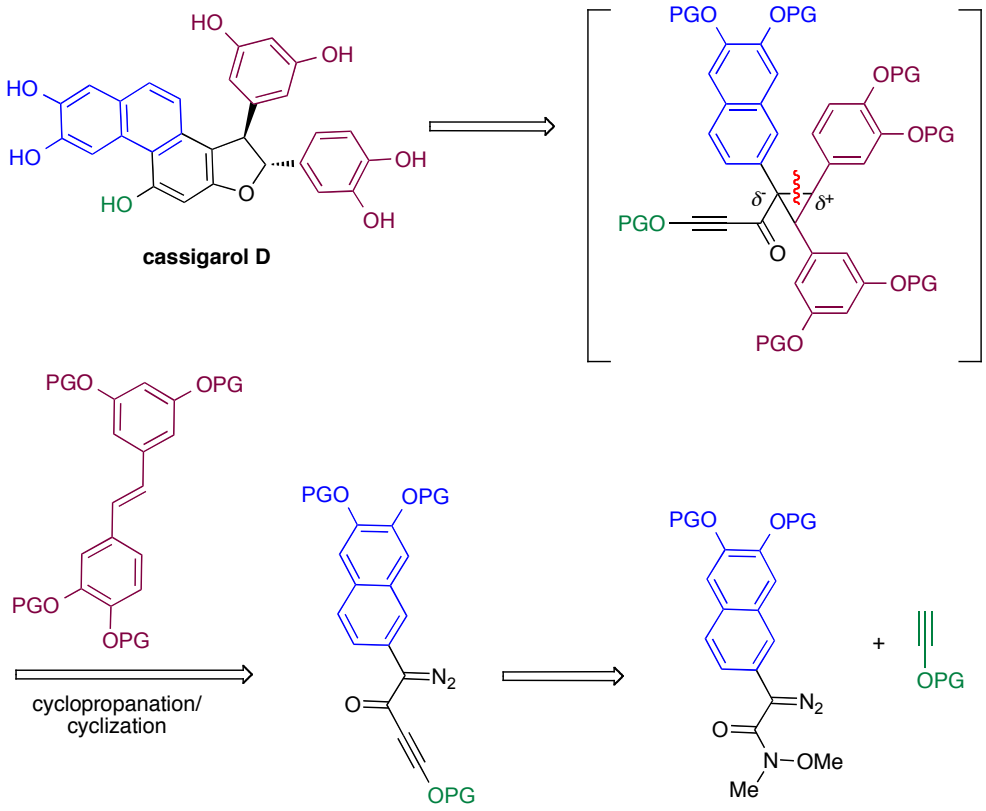


2.80, 72% yield

2.2.2 Application of the sequential reactions to the synthesis of cassigarol D

By transition metal-catalyzed sequential reactions, polycyclic dihydrofurans can be rapidly synthesized from simple alkenes and alkynyl-ketone diazo compounds as shown in section **2.2.1**. One way to showcase this methodology would be its applications to the synthesis of natural products. With its dihydrofuran core structure, cassigarol D was considered as an ideal target for this reaction sequence. Cassigarol D was first isolated in 1992 by Kozawa and coworkers from *Cassia garrettiana Craib* (Thai name: Samae Saan) - a medicinal plant in Thailand.[124] This natural product is an oligomer of piceatannol, which belongs to the resveratrol family of natural prodcuts.[125] Because of the potent bioactivity of resveratrol, the study of synthesizing the oligomers of resveratrol has drawn great attention from the chemical field.

The synthesis of oligomers of resveratrol was mainly achieved by the Snyder group *via* halogen-mediated Friedel-Crafts cyclization reactions developed by the group.[126-128] To date, there has been no reported synthesis of cassigarol D. It is envisioned that this natural product could be rapidly synthesized through the cyclopropanation/cyclization process (Scheme **2.14**). The regioselectivity of the cycloaddition step might be governed by the electronic effect. The 3,4-disubstitued-phenyl group would be more capable of stabilizing the partial positive charge built up during the opening of the cyclopropane ring, which would lead to the formation of the 2,3-disubstituted dihydrofuran core structure of the natural product.

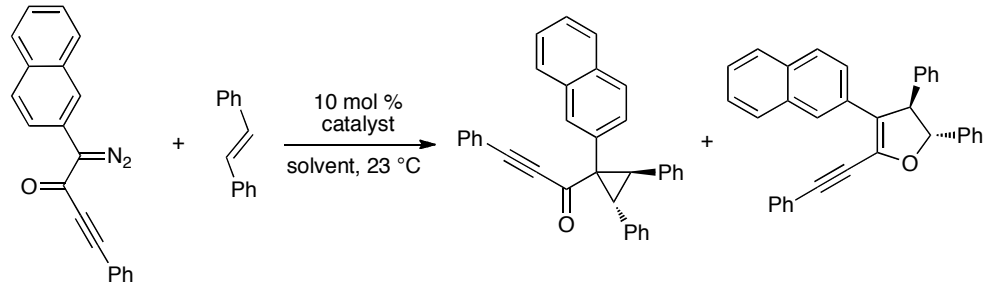


Scheme 2.14 Retro-synthesis of cassigarol D

The proposed synthesis of cassigarol D would start with the cyclopropanation of a *trans*-stilbene derivative. However, *trans*-disubstituted alkenes have been known to be

inert substrates to the rhodium-catalyzed cyclopropanation. A possible solution is to conduct the cyclopropanation with silver catalyst, which is able to catalyze the cyclopropanation of *trans*-disubstituted alkenes with aryldiazoacetates.[129] However, the reactivity of the alkynyl-ketone diazo towards silver catalysis was unknown. To evaluate the cyclopropanation reaction with this class of diazo compounds, the reaction of **2.68** with *trans*-stilbene was conducted and different silver catalysts were tested (Table **2.11**). Although silver hexafluoroantimonate showed good catalytic ability in the cyclopropanation of disubstituted alkenes with aryldiazo compounds, applying it to the reaction of alkynyl-ketone diazo compound **2.68** generated neither cyclopropane **2.101** nor the ring-opening product **2.102** (entry 1). Cyclopropane **2.101** was obtained from the reaction catalyzed by silver tetrafluoroborate or silver triflate, but the reaction yields were low (21-22%). In addition to the cyclopropane, the ring-opening product **2.102** was also observed (entries 3 and 4). The formation of **2.102** was reduced when the cyclopropanation was conducted in toluene or TFT (entries 5 and 6). The use of gold catalyst did not afford any of the desired products (entry 7).

Table 2.11 Optimization of the cyclopropanation of *trans*-stilbene



2.68 **2.101** **2.102**

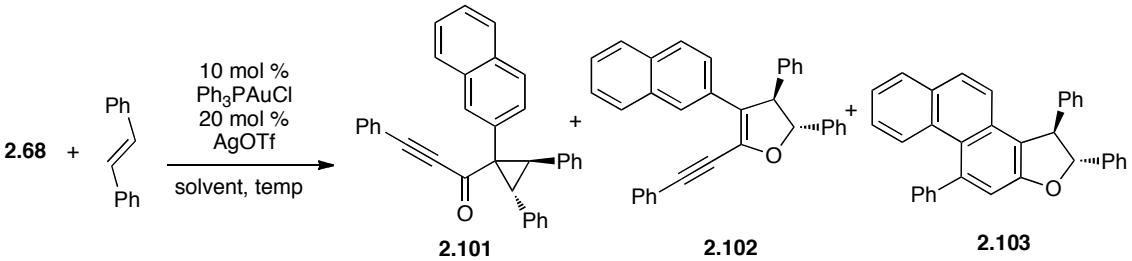
entry	catalyst	solvent	ratio[a] of **2.101:2.102**	yield[b,c] of **2.101** (%)
1	$AgSbF_6$	DCM	-	N.O.
2	$AgNTf_2$	DCM	-	N.O.
3	$AgBF_4$	DCM	4:1	21
4	AgOTf	DCM	5:1	22
5	AgOTf	PhMe	20:1	29
6	AgOTf	TFT	20:1	32
7	$Ph_3PAuOTf$	DCM	-	N.O.

[a] Determined by crude NMR. [b] Isolated yield. [c] N.O. = not observed.

Although the reaction yield is not ideal, this study demonstrates that the cyclopropanation step for proposed synthesis is feasible. As silver catalysts can catalyze not only the cyclopropanation but also the ring-opening reaction, it would be possible to develop a protocol to synthesize the polycyclic dihydrofuran directly from the diazo compound. To this end, the reaction of diazo compound **2.68** with *trans*-stilbene was conducted in the presence of both silver and gold catalysts (Table **2.12**). With dichloromethane as solvent, the reaction produced the desired polycyclic dihydrofuran **2.103** in 47% yield and no uncyclized dihydrobenzofuran **2.102** was left (entry 1). The sequential reaction performed in chloroform produced **2.103** together with uncyclized dihydrofuran **2.102** (entry 2). By changing the solvent to a less polar PhMe, the Ag/Au

catalyzed reaction afforded a mixture of three compounds, including cyclized product **2.103**, uncyclized dihydrofuran **2.102**, and also cyclopropane **2.101** (entry 3).

Table 2.12 Ag/Au catalyzed sequential reactions through a one-pot procedure



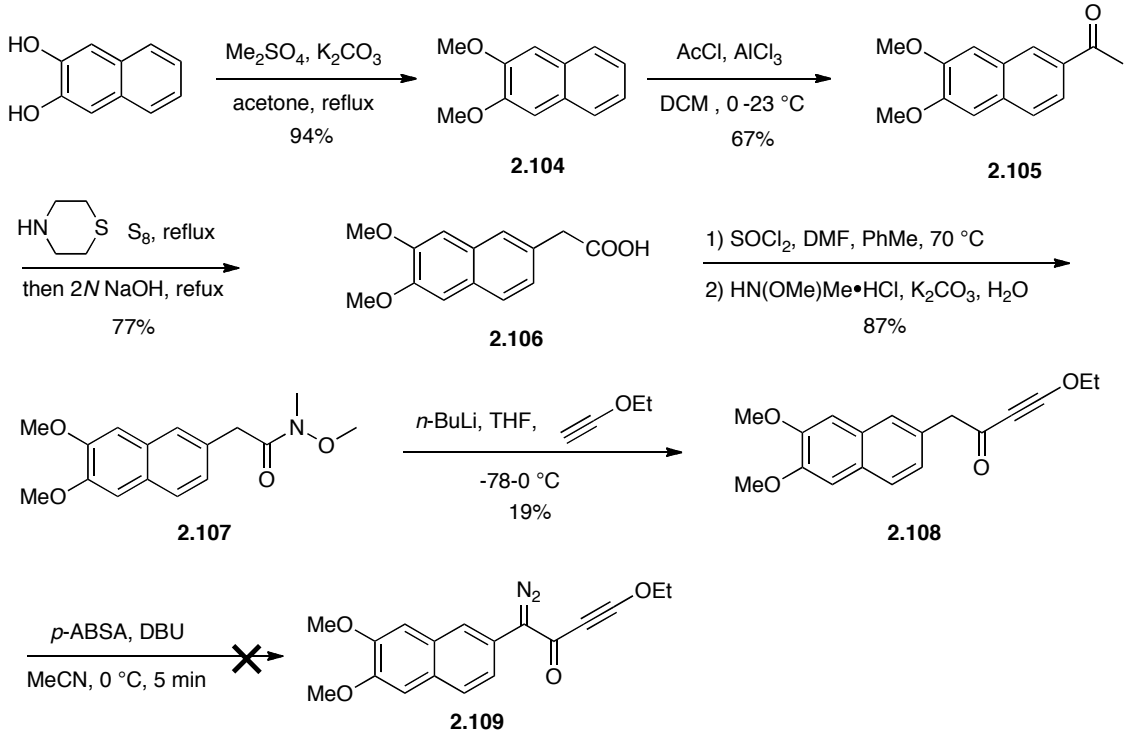
2.101 **2.102** **2.103**

entry	solvent	temp (°C)	ratio[a] of **2.101:2.102:2.103**	yield[b] of **2.103** (%)
1	**DCM**	**40**	**0:0:1**	**47**
2	$CHCl_3$	61	0:1:3	49
3	PhMe	85	2:1:1	15

[a] Determined by crude NMR. [b] Isolated yield.

The following study focused on the synthesis of the diazo compound **2.109**. Although the diazo compound with methoxyalkynyl group would be ideal for the final deprotection step to reveal the phenol group, the ethoxyacetylene is commercially available and selected to test the reactivity of the diazo compound. A six-step synthetic sequence was developed (Scheme **2.15**). The synthesis started with the methylation of hydroxyl groups of commercially available 2,3-dihydroxynaphthalene, which afforded **2.104** in high yield. A subsequent Friedel-Crafts acetylation produced two regioisomers favoring the formation of **2.105** (67% yield).[130] A Willgerodt-Kindler homologation and basic hydrolysis converted compound **2.105** to dimethoxynathphylacetic acid **2.106** in 73% yield.[131] Amide formation and incorporation of the alkynyl group provided diazo precursor **2.108**, which was only characterized by ^{1}H-NMR and subjected to the

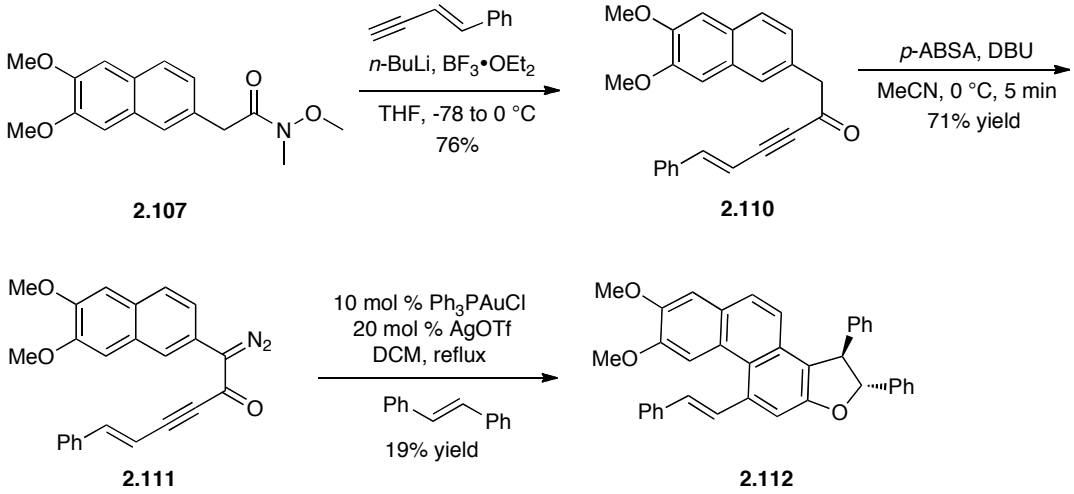
subsequent diazo transfer reaction directly. Unfortunately, no formation of **2.109** was observed.



Scheme 2.15 Attempts on the synthesis of diazo compound **2.109**

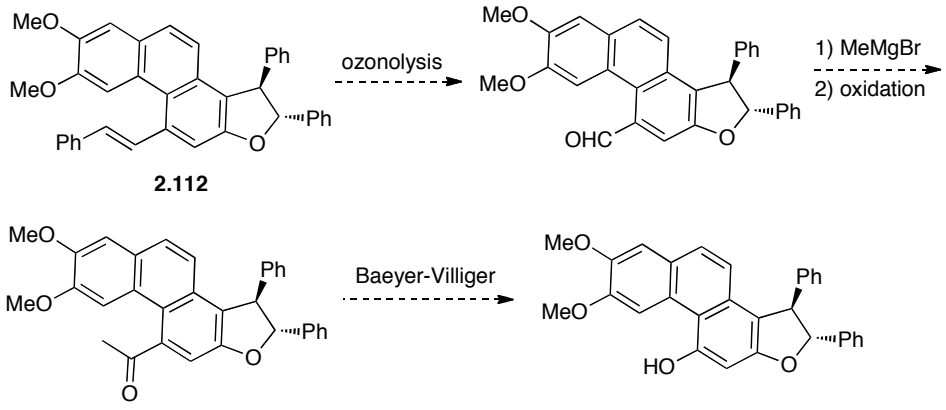
The unsuccessful synthesis of diazo compound **2.109** might be caused by the ethoxy-alkynyl group. Therefore, a diazo compound with a latent hydroxyl precursor, which can be converted to a hydroxyl group, has to be synthesized. After several attempts, styryl group was found as a potential hydroxyl precursor. The union of weinreb amide **2.107** and styryl acetylene produced diazo precursor **2.110** in 76% yield. The subsequent diazo transfer afforded **2.111** in 71% yield. This diazo compound was unstable and decomposed overnight even when it was stored at -20 °C. As a result, the diazo compound **2.111** has to be immediately used in the following reaction after purification. Under the previous developed protocol for the Ag/Au catalyzed sequential reactions, the reaction of diazo compound **2.111** and *trans*-stilbene produced the tetracyclic

dihydrofuran compound **2.112** in 19% yield (Scheme **2.16**). One possible reason for the low yield is the instability of the diazo compound.



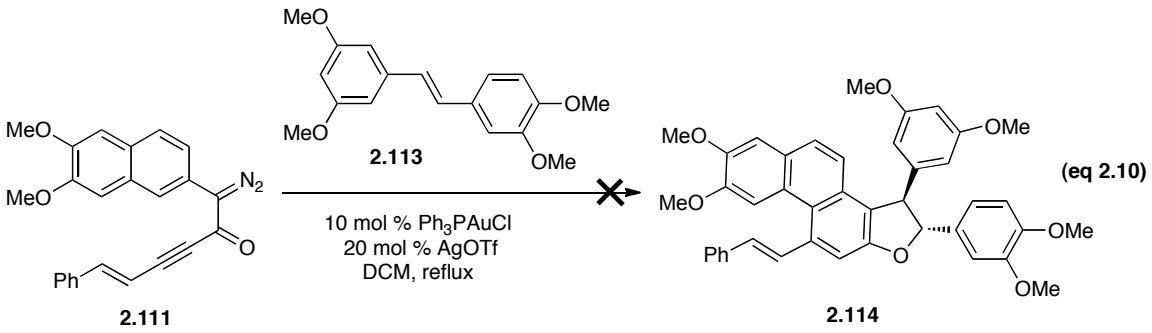
Scheme 2.16 Synthesis and cascade reactions of diazo compound **2.111**

To achieve the synthesis of cassigarol D, the styryl group of in the polycyclic dihydrofuran has to be converted to a hydroxyl group, which can be achieved by the follwing reactions (Scheme **2.17**): Transforming the double bond of the styryl to an aldehyde group by ozonolysis. The aldehyde could then be converted to an acetyl group by the nucleophilic addition with MeMgBr and subsequent oxidation. Lastly, a Baeyer-Villiger reaction would transform the acetyl group to the hydroxyl group.[132]

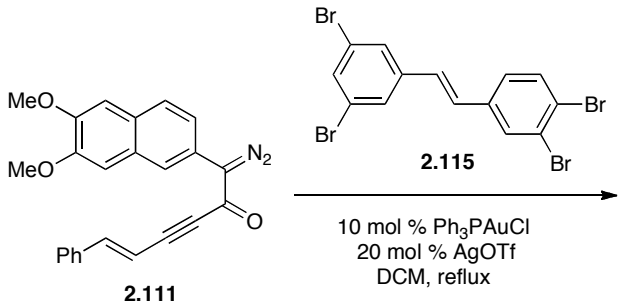


Scheme 2.17 Potential transformations of the styryl group to a hydroxyl group

Stilbene **2.113** was readily synthesized *via* a Horner-Wadsworth-Emmons reaction of commercially available 3,5-dimethoxybenzyl bromide and 3,4-dimethoxybenzyl aldehyde.[133] The reaction of diazo compound **2.111** and stilbene **2.113** was then conducted (eq **2.10**). Unfortunately, this reaction did not produce the desired dihydrofuran **2.114** but rather a mixture of inseparable compound. A possible reason for the ineffective reaction might be the *para*-methoxy group, which stabilized the partial charge on the benzylic carbon formed during the ring expansion process and thus disfavored the formation of the dihydrofuran. This can be related to what was observed during the exploration of the Rh/Ag/Au catalyzed sequential reaction. The reactions of cyclopropane **2.85**, derived from *para*-methoxystyrene, produced the polycyclic dihydrofuran **2.91** in only 21% yield (Section **2.2.1**).



The less electron-rich stilbene **2.115** was then synthesized and applied to the Ag/Au catalyzed sequential reactions (eq **2.11**). Only dimers of the diazo compound and unreacted stilbene were isolated, no adduct was formed by the reaction of the diazo compound **2.111** and stilbene **2.115**.



(eq 2.11)

Although the synthesis cassigarol D has not been successful, the study showed that 2,3-disubstituted polycyclic dihydrofurans could be rapidly constructed through Ag/Au catalyzed sequential reactions. To achieve the proposed synthesis, it is necessary to further optimize the reaction condition and change the functional groups on the stilbene to balance its reactivity and selectivity.

2.3 Conclusion

A class of polycyclic dihydrofuran derivatives was synthesized in high yields by means of three sequential transition-metal-catalyzed reactions. A one-pot procedure for this transformation was also established. This sequence illustrates the potential of carbenoid chemistry to initiate a cascade sequence of reactions. The progress on application of this method to the synthesis of cassigarol D is also discussed. Current results demonstrate that it is possible to synthesize the natural product through this cyclopropane/cyclization sequence, but further optimization of the reaction conditions and the functionalities of the stilbene substrate are necessary.

Chapter III: Synthesis of Dihydrobenzofurans *via* Sequential C–H Functionalizations

3.1 Introduction

C–H functionalization methodologies offer new strategies for the disconnection of natural products and a number of elegant synthetic applications have been described recently.[134-141] Two distinct types of metal-catalyzed C–H functionalization processes are becoming broadly effective (Figure **3.1**).[142,143] One of them is the C–H insertion by a metal bound carbene, nitrene or oxo intermediate and the other is the C–H activation initiated by inserting a metal complex into a C–H bond. The C–H functionalization developed by the Davies group belongs to the first type: insertions of a C–H bond with reactive metal carbenoids, which were generated by metal-catalyzed decomposition of donor/acceptor diazo compounds.

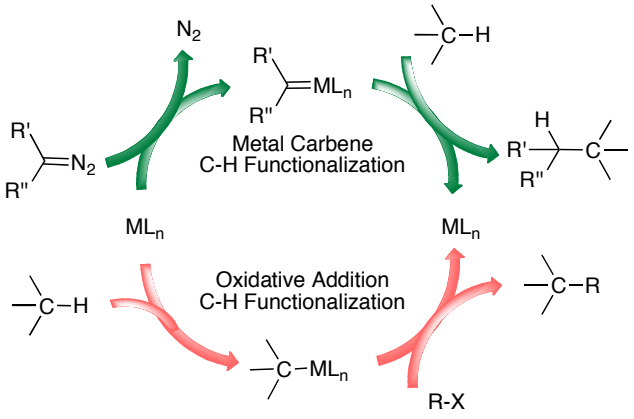


Figure 3.1 Two distinct types of C–H functionalizations

The major challenge of C–H functionalization is the control of regio-, diastereo- and enantioselectivity. Early advances in C–H functionalization with carbenoids were mainly achieved intramolecularly. The reacting C–H bond was brought close to the metal-carbenoid center by a tether group, which makes regioselective C–H functionalization

possible. The major breakthrough in intermolecular C–H functionalization was made by the Davies group with the more selective donor/acceptor carbenoids as the reactive intermediates. The donor group stabilizes the electron-deficient metal carbenoid and thus highly stereoselective intermolecular C–H functionalizations can be achieved. The general order of the reactivity of different type of C–H bonds was studied through competition studies (Figure **3.2**).[143]

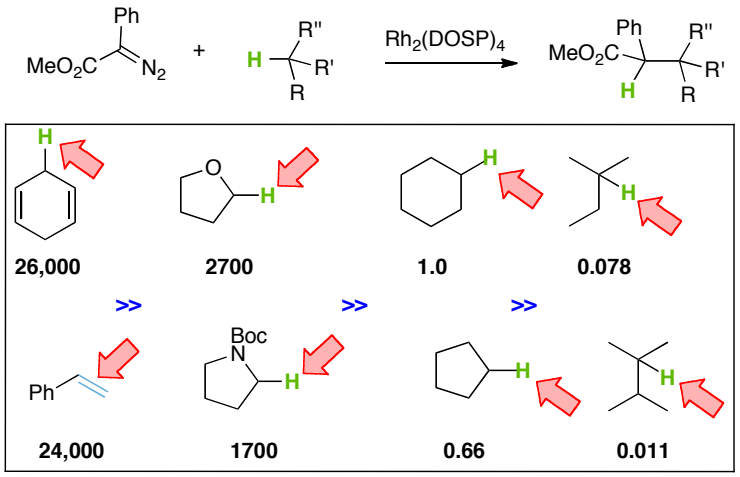


Figure 3.2 Relative reactivity of different C–H bonds

The reactivity of C–H bonds can be enhanced by functional groups that stabilize positive charges built-up at the carbon site of the C–H bond, such as aryl, alkene, oxygen or nitrogen groups (Figure **3.3**).[144-150] Although the reacting sites α to oxygen are highly active to the C–H functionalization, the C–H bonds β to oxygen do not undergo insertion due to the inductive effect of oxygen.[151] The rhodium-catalyzed C–H functionalization is compatible with a variety of functional groups, including halides, triflates and boronates, ethers, esters, ketones and carbamates. Alkenes and aromatic rings can also be tolerated in the reaction as long as they are sterically or electronically protected from potential cyclopropanations.

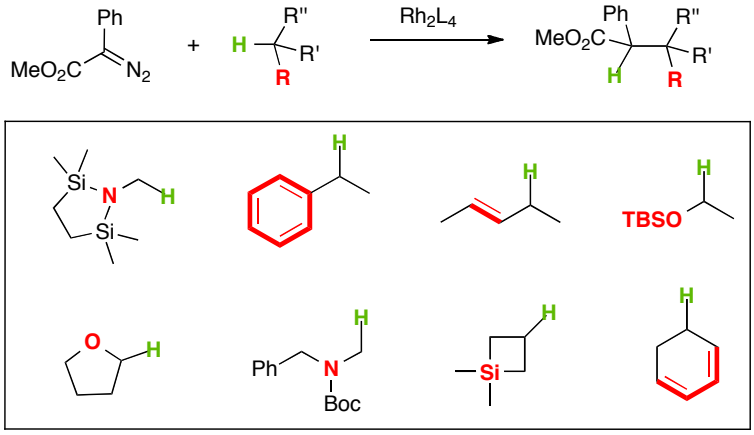


Figure 3.3 Common functional groups used to activate the C–H bonds

In order to understand the mechanism and stereoselectivity of rhodium-catalyzed C–H functionalizations, computational studies were conducted, which examined the reaction of methyl phenyldiazoacetate with 1,4-cyclohexadiene and cyclopentane.[36] It was found that the C–H insertion occurs *via* a concerted nonsynchronous process involving considerable hydride transfer character. The calculations demonstrated that the C–H–C angle was 165° in the reaction of 1,4-cyclohexadiene and 127° in the reaction of cyclopentane, which means that the C–H bond is nearly orthogonal in its approach to the carbenoid plane (Figure **3.4**).

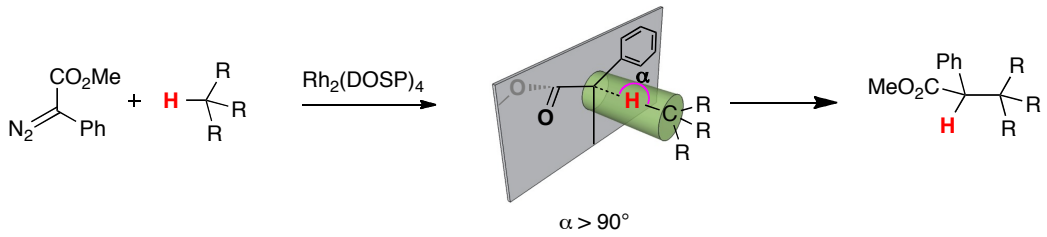


Figure 3.4 Approach angle between the C–H bond vector and the carbenoid plane

Based on the computational studies, a predictive model of the C–H functionalization reaction of donor/acceptor carbenoids was proposed (Figure **3.5**).[36,37] In this model, the O–C–O plane of the ester group is almost perpendicular to the carbenoid plane, so the

ester acts like a sterically demanding group. The three groups (**S**, **M**, **L**) connected to the site of C–H functionalization approach in a staggered relationship to the metal carbenoid. The largest group of the substrate orients away from the rhodium complex, while the smallest group is in gauche positions to both the ester group and rhodium catalyst. The resulting C–H insertion product is shown in the Newman projection below. The model provides not only a rational for the stereoselectivity of the C–H functionalization reaction but also is a useful predictive tool for the stereoselectivity of the C–H functionalization.

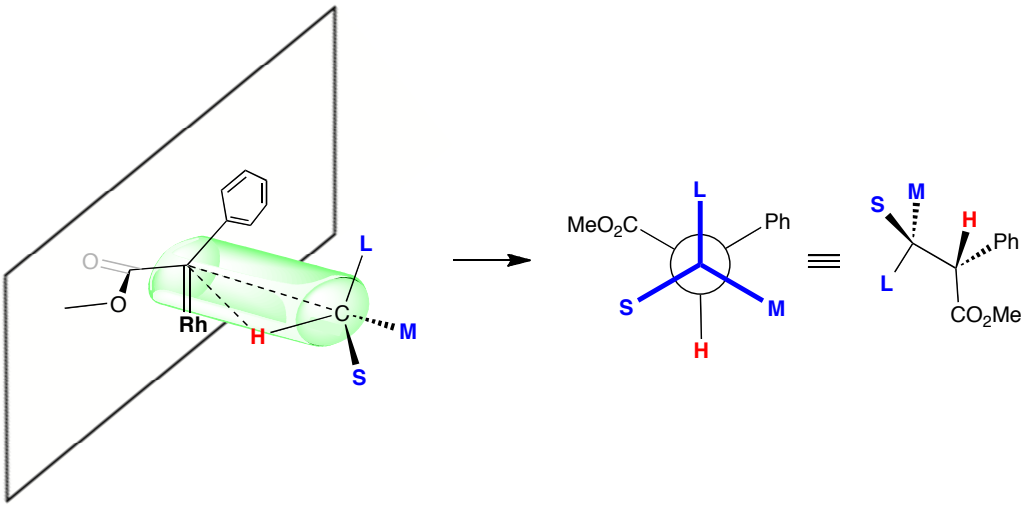


Figure 3.5 Predictive model of C–H insertions of donor/acceptor carbenoids

3.1.1 Synthesis of lactones *via* intramolecular C–H insertions

Intramolecular C–H functionalization represents an effective method for the synthesis of lactams and lactones.[152] The synthesis of *β*, *γ* and *δ*–lactones from acceptor and acceptor/acceptor carbenoids has ample precendences.[153,154] The intramolecular C–H insertion reactions occur in moderate to high yields and prefer the formation of *γ*–lactones. Although four-membered rings are more strained, the selective synthesis of *β*-lactone can also be achieved by means of C–H insertions, especially when donor/acceptor carbenoids are used.[155,156]

Though exceptions are known, the general reactivity of C–H bonds toward intramolecular C–H insertion can be summarized as tertiary > secondary > primary. The C–H insertion favors the reaction with an equatorial C–H bond over an axial C–H bond. Ligands of the rhodium catalysts also play an important role in the rhodium-catalyzed C–H functionalizations (Figure **3.6**). For the formation of lactams and lactones through C–H insertion reactions, the decrease of the electrophilic character of the ligands (pfb > OAc > acam, cap) causes decreased reactivity but increased selectivity.

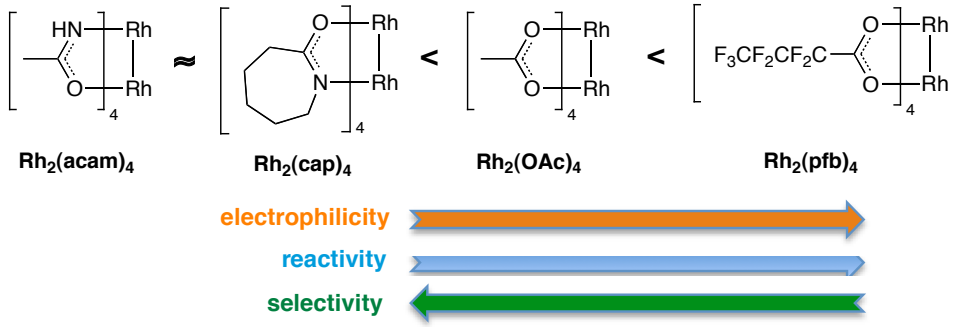
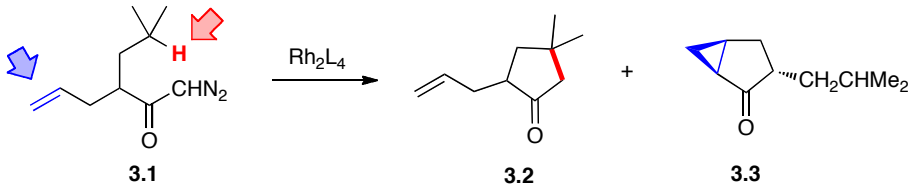


Figure 3.6 Ligand effect on the intramolecular C–H functionalizations

Compared to $Rh_2(cap)_4$ and $Rh_2(OAc)_4$, $Rh_2(pfb)_4$ is more reactive for intramolecular C–H functionalizations. Hence, the selective formation of a γ–lactone over a cyclopropanation reaction is possible with this electrophilic catalyst (Table **3.1**).[157] In the presence of $Rh_2(cap)_4$, the reaction of diazo compound **3.1** produced cyclopropane **3.3** as the only product (entry 1). Changing the catalyst to $Rh_2(OAc)_4$, a mixture of cyclopropane **3.3** and lactone **3.2** was formed (entry 2). With further increased electrophilic character, the $Rh_2(pfb)_4$ catalyzed reaction of **3.1** generated γ–lactone **3.2** as the only product *via* an intramolecular C–H insertion reaction (entry 3).

Table 3.1 Selective cyclopropanations and C–H functionalizations

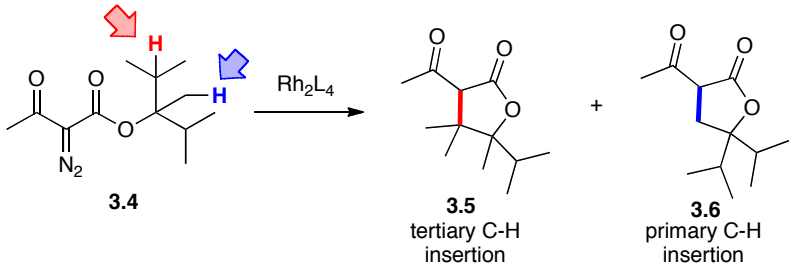


3.1 **3.2** **3.3**

entry	catalyst	ratio of **3.2**:**3.3**
1	$Rh_2(cap)_4$	0:100
2	$Rh_2(OAc)_4$	56:44
3	$Rh_2(pfb)_4$	100:0

When more than one C–H site exists in the substrate, the reaction catalyzed by $Rh_2(pfb)_4$ usually affords the product as a mixture. The chemoselectivity can be improved by employing less electrophilic catalysts. For instance, diazo compound **3.4** can undergo insertion either into a tertiary C–H or a primary C–H bond (Table **3.2**). With the reactive $Rh_2(pfb)_4$, the reaction produced a 1:2 ratio of mixture of lactones **3.5** and **3.6** (entry 1). Changing the catalyst to the less electrophilic $Rh_2(OAc)_4$, the insertion into the more electron-rich tertiary C–H bond dominated and products **3.5** and **3.6** were generated as a 9:1 ratio of mixture favoring the formation of lactone **3.5** *via* the tertiary C–H insertion reaction (entry 2). Exclusive formation of **3.5** was possible by further reducing the electron withdrawing ability of the ligands (entry 3). In the presence of $Rh_2(acam)_4$, no primary C–H insertion product **3.6** was observed from the reaction of diazo compound **3.4**.

Table 3.2 Ligand effect on the selectivity of intramolecular C–H functionalizations



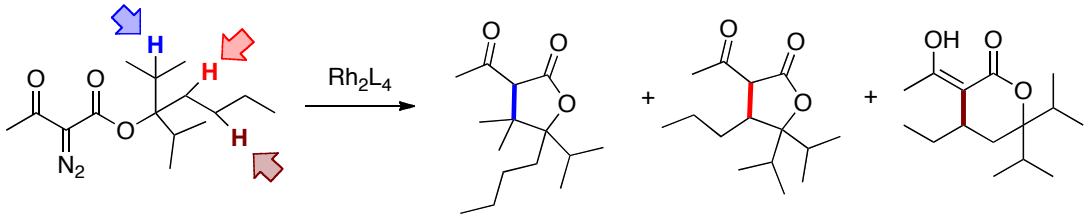
3.4 | **3.5** tertiary C-H insertion | **3.6** primary C-H insertion

entry	catalyst	combined yield (%)	ratio of **3.5**:**3.6**
1	$Rh_2(pfb)_4$	61	29:61
2	$Rh_2(OAc)_4$	97	90:10
3	$Rh_2(acam)_4$	89	>99:1

Although the insertion into a tertiary C–H bond is electronically favored, it is also considered sterically disfavored. As a result, the order of the reactivity of C–H bonds (tertiary > secondary > primary) can be disturbed. By replacing the methyl group of diazo compound **3.4** with an *n*-butyl alkyl chain and thus creating a bulkier environment around the tertiary C–H bond of **3.7**, Doyle and coworkers discovered that the reaction of **3.7** preferred the insertion into a secondary C–H bond instead of the tertiary C–H bond. Interestingly, catalysts had little influence on the selectivity of this transformation (Table **3.3**). Under thermal conditions, the reaction of diazo compound **3.7** generated two secondary C–H insertion products: *γ*–lactone **3.9** and *δ*–lactone **3.10** in a 1:1 ratio. No tertiary C–H insertion product **3.8** was observed (entry 1). In the presence of a rhodium catalyst, selective formation of lactone **3.9** *via* a secondary C–H insertion was achieved. The reaction catalyzed by $Rh_2(pfb)_4$ produced lactones **3.9** and **3.10** as a mixture in about 4:1 ratio favoring *γ*–lactone **3.9**. A trace amount of the tertiary C–H insertion product **3.8** was also observed (entry 2). The preference for the formation of lactone **3.9** was more

prominent for the reactions catalyzed by $Rh_2(OAc)_4$ and $Rh_2(cap)_4$, which afforded γ–lactone **3.9** as essentially the only product (entries 3 and 4).

Table 3.3 Competitive insertions of tertiary and secondary C–H bonds



3.7

3.8 tertiary C-H insertion

3.9 secondary C-H insertion

3.10 secondary C-H insertion

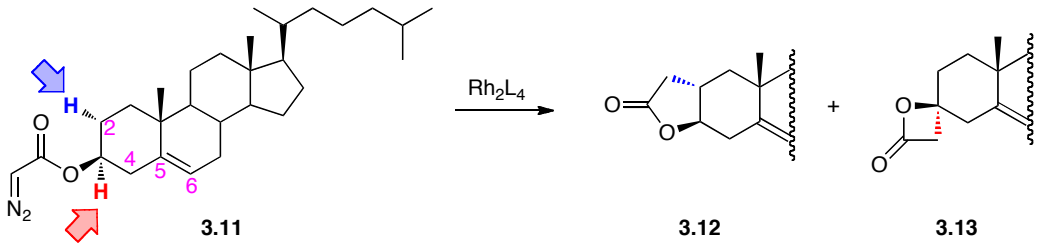
entry	catalyst	combined yield (%)	ratio of **3.8:3.9:3.10**
1[a]	-	-	0:1:1
2	$Rh_2(pfb)_4$	74	6:76:18
3	$Rh_2(OAc)_4$	88	3:97:0
4	$Rh_2(cap)_4$	79	4:96:0

[a] thermal, 200 °C

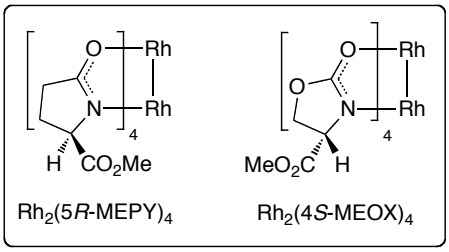
Besides the formation of γ–lactones, four-membered ring lactones can also be prepared through intramolecular C–H functionalization. Selective synthesis of five or four-membered ring products employing a steroidal system was achieved by the Doyle group (Table **3.4**).[156] With the *R*-enantiomer of selected catalysts, γ–lactone **3.12** was formed as the major product from the reaction of diazo compound **3.11**. The highest selectivity was obtained when the reaction was catalyzed by $Rh_2(5R\text{-MEPY})_4$ (entry 1). By switching to the *S*-enantiomer of the catalysts, selective synthesis of β–lactone **3.13** was realized. The best selectivity for this product was obtained when the reaction was catalyzed by $Rh_2(4S\text{-MEOX})_4$ (entry 4). Interestingly, no product was generated from C–H insertion at the secondary site at C-4-position. Although the rationale behind the inhibition of the C–H

insertion at C-4-position is not clear, it was proposed that the double bond at C5 and C6 was responsible for this selectivity.

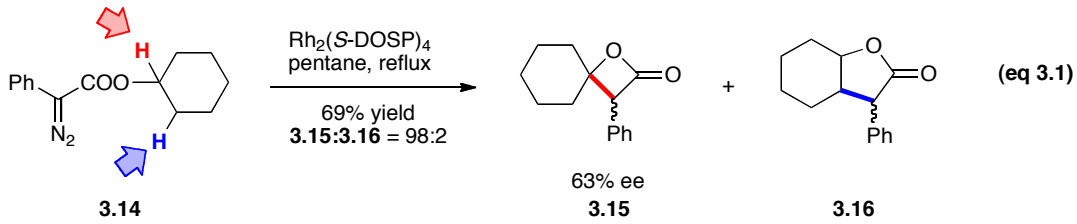
Table 3.4 Selective synthesis of γ– and β–lactones



entry	catalyst	yield (%)	ratio of **3.12:3.13**
1	**Rh_2(5*R*-MEPY)$_4$**	**81**	**94:6**
2	Rh_2(4*R*-MEOX)$_4$	81	89:11
3	Rh_2(5*S*-MEPY)$_4$	74	33:67
4	**Rh_2(4*S*-MEOX)$_4$**	**80**	**10:90**

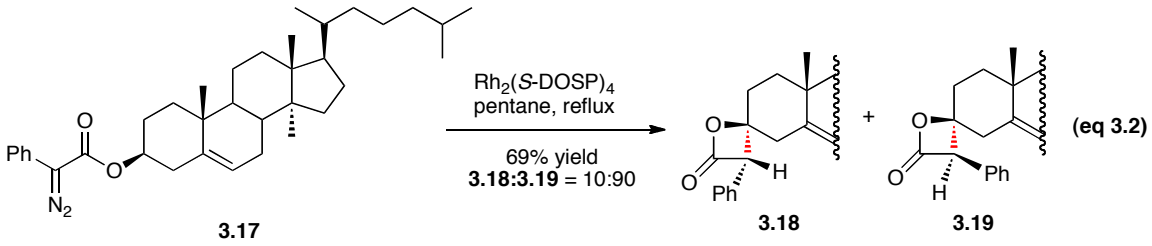


With the increased selectivity generated by the introduction of a donor group, the C–H insertion reaction of donor/acceptor diazo compound **3.14** preferred to react with a more electron-rich tertiary C–H bond over a secondary C–H bond. This resulted in the selective formation of β–lactone **3.15**.[155] Optimization studies showed that the best catalyst for this transformation was Rh_2(DOSP)$_4$. In the presence of such catalyst, the reaction of diazo compound **3.14** produced four-membered ring product **3.15** in moderate enantioselectivity (63% ee). Remarkably, only a trace amount of five-membered ring product **3.16** was observed (eq **3.1**).



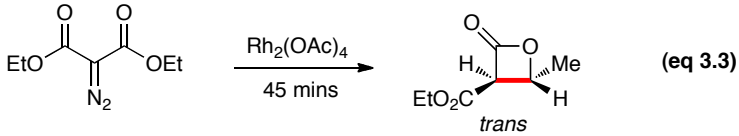
3.14 **3.15** **3.16**

The preference for the formation of *β*–lactones was also observed in the reaction of sophisticated steroidal systems.[156] In the presence of Rh_2(*S*-DOSP)$_4$, diazo compound **3.17** favored the exclusive formation of a diastereomeric mixture of *β*–lactones **3.18** and **3.19** (eq **3.2**). The products were obtained in good yield (69%) and with good diastereoselectivity (**3.18**:**3.19** = 10:90).

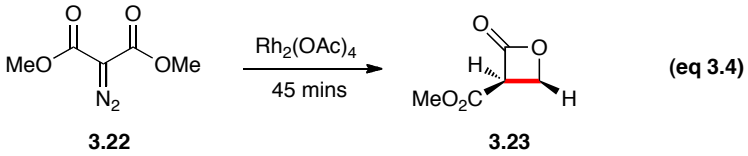


3.17 **3.18** **3.19**

Reactions of secondary and primary C–H bonds have also been used to prepare *β*–lactones. Most of these studies involve the reaction of acceptor/acceptor carbenoids, in which a low reactivity of the primary C–H bond has been observed.[153,158] In the presence of $Rh_2(OAc)_4$, full conversion of diazo compound **3.20** was achieved in 45 min and *β*–lactone **3.21** was produced quantitatively through secondary C–H insertion into the ethyl ester group (eq **3.3**). However, the insertion into a primary C–H bond is slow. In the presence $Rh_2(OAc)_4$, only 25% of diazo compound **3.22** was consumed after 24 h and product **3.23** was isolated in 24% yield (eq **3.4**).[159]



3.20 **3.21**



3.22 **3.23**

3.1.2 Synthesis of benzofurans *via* C–H insertion reactions

Benzofurans represent common subunits in a wide range of natural products and pharmaceuticals.[160,161] Therefore, the development of new methodologies for the construction of such structural motif is of particular importance in the synthetic community.[162-164] The intramolecular C–H insertion catalyzed by a chiral dirhodium complex is one of the most popular ways to stereoselectively synthesize benzofurans. Complementary results can be obtained from prolinate-based $Rh_2(DOSP)_4$ and phthalimidocarboxylate-based $Rh_2(PTTL)_4$ or $Rh_2(PTAD)_4$. Generally, $Rh_2(DOSP)_4$ shows good catalytic ability for primary and tertiary C–H insertions, while $Rh_2(PTTL)_4$ and $Rh_2(PTAD)_4$ behave better for secondary C–H insertions (Figure **3.7**).[45,165,166]

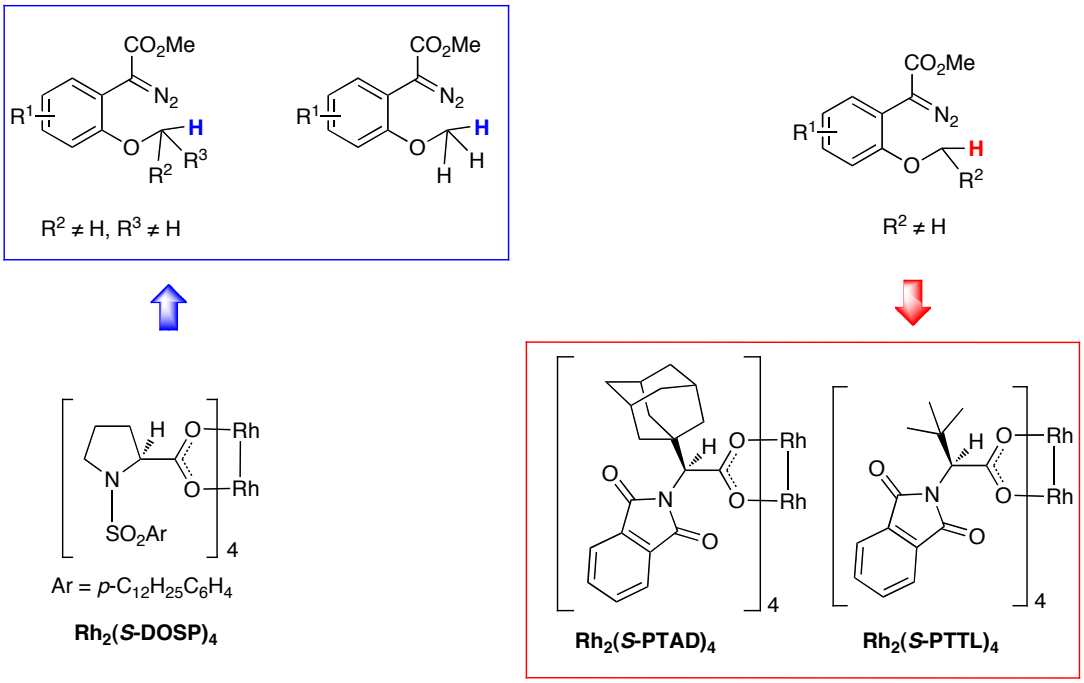
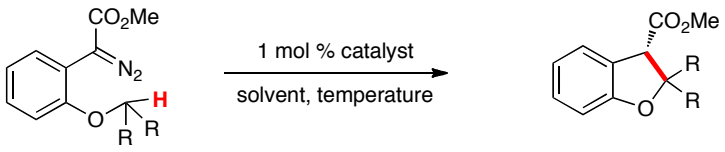


Figure 3.7 Complementary reactivity of $Rh_2(DOSP)_4$ and $Rh_2(PTAD)_4$

As shown in Table **3.5**, both $Rh_2(DOSP)_4$ and $Rh_2(PTTL)_4$ were effective catalysts for primary C–H insertion reactions to synthesize benzofurans, but higher asymmetric induction was obtained with $Rh_2(DOSP)_4$ (entries 1 and 2). The difference between the catalytic ability of these two catalysts is especially prominent with the reaction of tertiary C–H bonds. In the presence of $Rh_2(DOSP)_4$, the tertiary C–H insertion reaction afforded the benzofuran product in nearly quantitatively yield and with 94% ee (entry 3), whereas the $Rh_2(PTTL)_4$ catalyzed reaction at -78 °C produced this product in 88% yield but with only 22% ee (entry 4).[165]

Table 3.5 Insertions into primary and tertiary C–H bonds

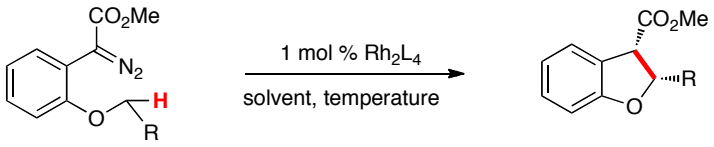


entry	R	catalyst	solvent	temperature (°C)	yield (%)	ee (%)
1	H	Rh_2(*S*-DOSP)$_4$	DCM	-50	70	68
2	H	Rh_2(*S*-PTTL)$_4$	PhMe	-23	69	44
3	Me	Rh_2(*S*-DOSP)$_4$	hexanes	-50	98	94
4	Me	Rh_2(*S*-PTTL)$_4$	PhMe	-78	88	22

Unlike the C–H insertion reactions of primary and tertiary C–H bonds, the optimum catalysts for secondary C–H insertion reactions are phthalimidocarboxylate-based $Rh_2(PTTL)_4$ and $Rh_2(PTAD)_4$ (Table **3.6**).[45,166] The $Rh_2(DOSP)_4$ catalyzed secondary C–H insertion produced the dihydrobenzofuran with moderate stereoselectivity (entry 1). A great improvement of the diastereo- and enantioselectivity was achieved by changing the catalyst to $Rh_2(PTTL)_4$ (entry 2). In the presence of this catalyst, the secondary C–H insertion product was synthesized as a single diastereomer in 90% ee (entry 3). Further

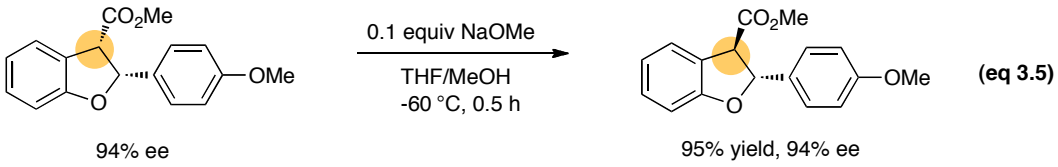
improvement of the enantioselectivity was observed by employing the bulkier $Rh_2(PTAD)_4$ catalyst (entry 4).

Table 3.6 Insertions into secondary C–H bonds



entry	R	catalyst	solvent	temperature (°C)	yield (%)	dr (*cis*:*trans*)	ee (%)
1	Me	Rh_2(*S*-DOSP)$_4$	hexanes	-50	85	80:20	60
2	Me	Rh_2(*S*-PTTL)$_4$	PhMe	-78	63	94:4	96
3	Ph	Rh_2(*S*-PTTL)$_4$	PhMe	-60	87	>97:3	90
4	Ph	Rh_2(*S*-PTAD)$_4$	PhMe	-60	79	>97:3	95

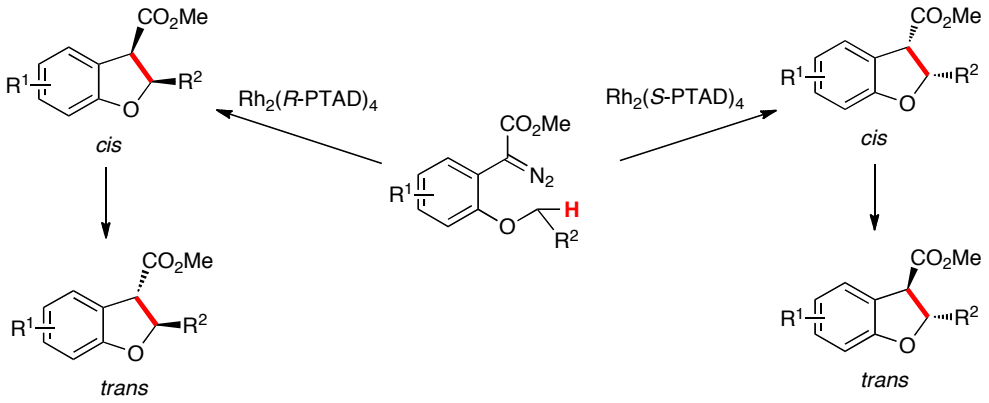
The rhodium-catalyzed secondary C–H insertion reaction produced the major product in a *cis* configuration with respect to the protons. Both Hashimoto and Davies groups demonstrated that those *cis*-dihydrobenzofurans could be quantitatively equilibrated to the corresponding *trans* dihydrobenzofurans under basic condition (eq **3.5**). No loss of the enantioselectivity was observed for this transformation.



94% ee

95% yield, 94% ee

By this intramolecular secondary C–H insertion reaction, all four isomers of the dihydrobenzofuran compounds are readily accessible. The two *cis*-dihydrobenzofurans can be synthesized through the insertion reaction catalyzed by the *R*- or *S*-dirhodium complex. The following equilibration under basic conditions leads to the two *trans*-dihydrobenzofurans (Scheme **3.1**).



Scheme 3.1 Stereoselective synthesis of the four isomers of the dihydrobenzofuran through the intramolecular C–H functionalization reaction

Since the first publication of the rhodium-catalyzed intramolecular C–H insertion to synthesize benzofurans, such methods have been applied by different groups in the synthesis of natural products (Figure **3.8**).[139,167-170] However, the application of this method to synthesis suffers from the necessity to synthesize poly-substituted aromatic substrates for the intramolecular reaction. In order to achieve acceptable levels of asymmetric induction, both a chiral catalyst and an auxiliary are often required. In this context, the enantioselective intermolecular synthesis of the dihydrobenzofuran motif would be significantly more appealing. In this chapter, recent developments in the synthesis of dihydrobenzofurans through intermolecular C–H functionalizations are discussed. The approach features the combination of two different types of C–H functionalizations, including a rhodium-catalyzed intermolecular C–H insertion and a palladium-catalyzed C–H functionalization/C–O cyclization.

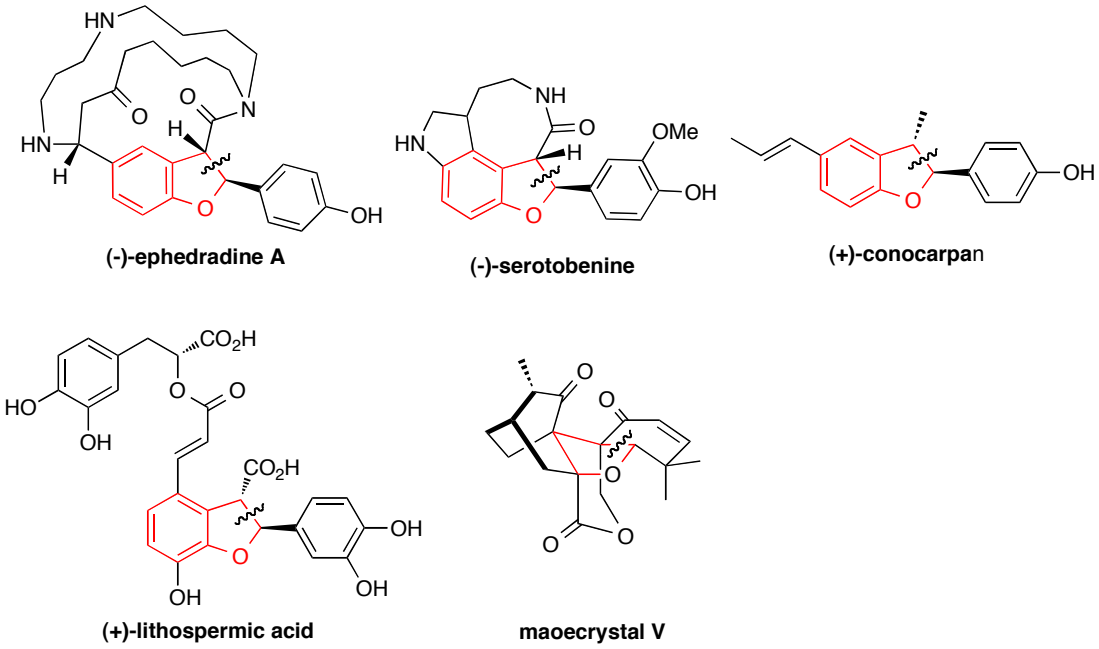


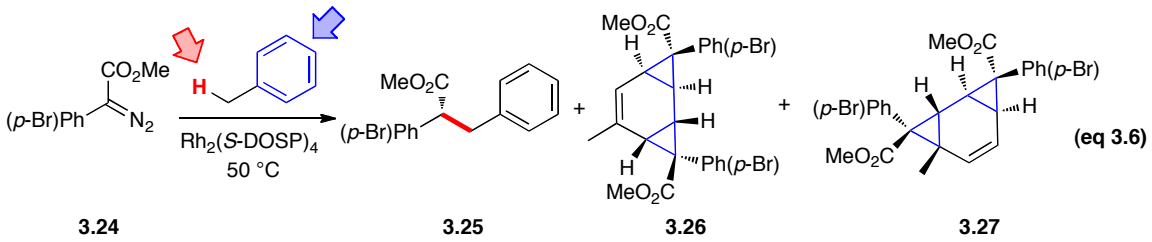
Figure 3.8 Applications of the intramolecular C–H insertion reaction to the synthesis of natural products

3.1.3 Intermolecular insertions into benzylic C–H bonds

The intermolecular C–H functionalization has been mainly achieved by the Davies group with the development of donor/acceptor carbenoids. With chiral dirhodium catalysts, protocols for stereoselective intermolecular C–H insertions of a variety of systems have been developed. In particular, the C–H functionalization of cyclohexane, 2-methylbutane, and adamantane, as well as alkanes with activated sites, such as allylic, benzylic and α to nitrogen or oxygen, have been investigated.

The activation of C–H bonds with a phenyl group has two different effects. Firstly, the reactivity of the C–H bond can be improved by the phenyl group; on the other hand, the alkyl substituent on the phenyl ring can also increase the electron density of the benzene ring and thus potentially favor a cyclopropanation reaction. As a result, the C–H functionalization of a benzylic C–H bond might compete with the cyclopropanation of

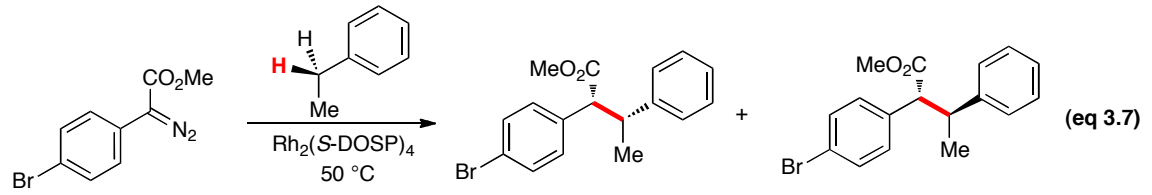
the phenyl ring, especially when the C–H insertion involves the reaction of less reactive primary C–H bonds, such as the reaction of toluene. In the presence of $Rh_2(DOSP)_4$, the reaction of diazo compound **3.24** with toluene afforded a mixture of C–H insertion and cyclopropanation products favoring the biscyclopropanation product **3.26** (eq **3.6**).[147]



3.24 **3.25** **3.26** **3.27**

50% combined yield; ratio of **3.25**:**3.26**:**3.27** = 28:58:16

In contrast to the insertion into primary C–H bonds, the reaction of more electron-rich secondary C–H bonds favors the formation of C–H insertion products over cyclopropanes (eq **3.7**). The $Rh_2(DOSP)_4$ catalyzed reaction of **3.24** with ethylbenzene produced two diastereomers **3.28** and **3.29** in a 5:1 ratio favoring the isomer **3.28**, which was formed in 86% ee.[147]

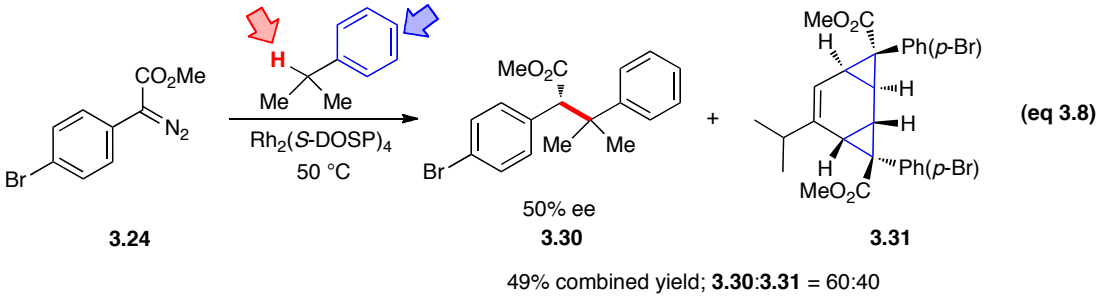


3.24 **3.28** **3.29**

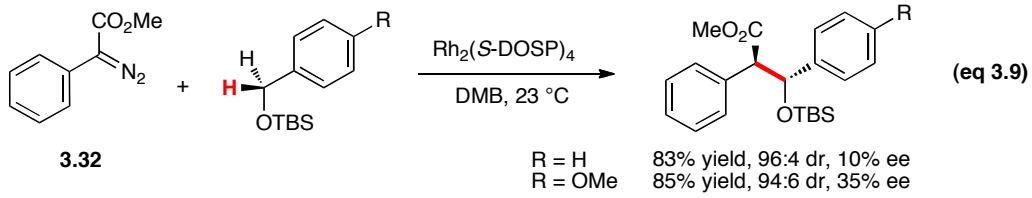
49% combined yield; ratio of **3.28**:**3.29** = 84:16

The C–H insertion into a tertiary C–H bond is electronically favored, but sterically disfavored. The strong steric hindrance slows down the intermolecular C–H insertion and the cyclopropanation of the phenyl ring again starts to compete. In the presence of $Rh_2(DOSP)_4$, the reaction of **3.24** with isopropylbenzene generated a mixture of C–H insertion product **3.30** and biscyclopropanation product **3.31** (eq **3.8**). The steric

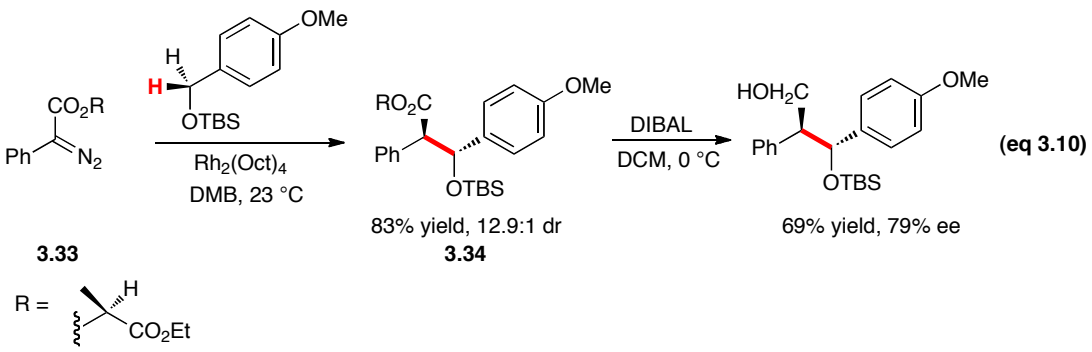
hindrance also influenced the asymmetric induction of the C–H insertion and product **3.30** was obtained in only 50% ee.



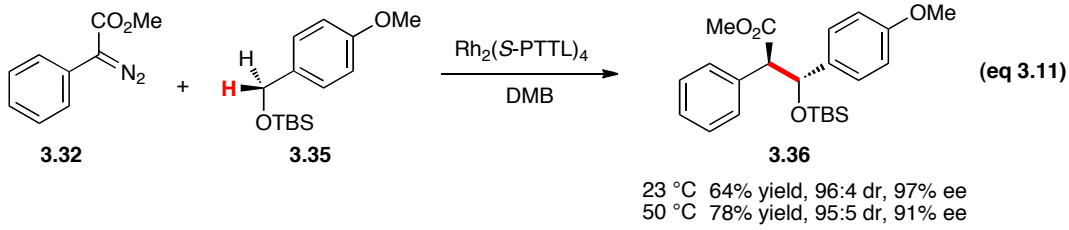
Further activation of benzylic C–H bonds can be achieved by the incorporation of another activating group, such as an OTBS group. The reaction of diazo compound **3.32** with TBS benzyl ether can be conducted at room temperature, from which the major diastereomer produced is in a syn configuration (eq **3.9**). This is opposite from the reaction of ethylbenzene. Unfortunately, the asymmetric induction for this $Rh_2(DOSP)_4$ catalyzed reaction was low.[144]



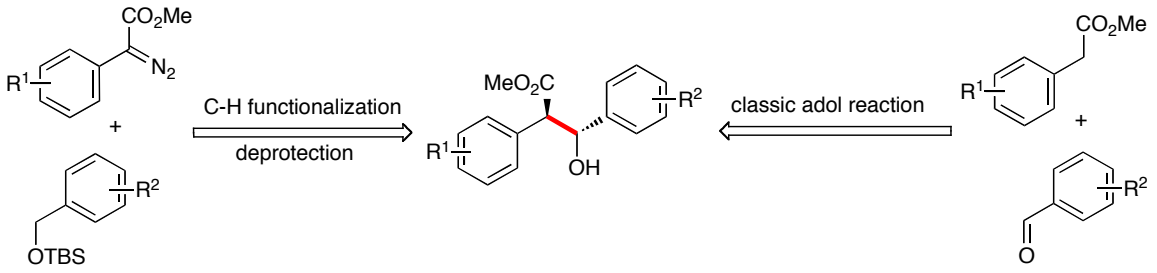
In order to improve the enantioselectivity of this transformation, two different methods were employed: one by using chiral auxiliary and achiral catalyst; the other by optimization of the chiral catalysts. The reaction of diazo compound **3.33** bearing a chiral auxiliary was first evaluated. The incorporation of the bulky chiral auxiliary increased the stereoselectivity of the reaction with no decrease in yield. After subsequent reduction to the corresponding alcohol, the enantioselectivity of the C–H insertion product was determined to be 79% ee (eq **3.10**).[144]



Subsequent optimization studies of the chiral rhodium catalysts showed that $Rh_2(PTTL)_4$ was the optimum catalyst for this benzylic C–H insertion reaction. In the presence of such catalyst, the reaction of **3.32** and TBS benzyl ether **3.35** conducted at room temperature produced the C–H insertion product **3.36** in good yield, and with excellent diastereo- and enantioselectivity. By performing the reaction in refluxing 2,2-dimethylbutane, the reaction yield was improved to 78% with little decrease of the diastereo- and enantioselectivity (eq **3.11**).[144]



The C–H insertion of TBS benzyl ether with aryldiazoacetates generated a class of compounds with high diastereo- and enantioselectivity. Furthermore, additional functional group manipulations of those products can lead to valuable intermediates. After deprotection of the TBS group, this intermolecular C–H insertion reaction can be considered as a surrogate for the adol reaction (Scheme **3.2**). A protocol to remove the silyl group of these C–H insertion products was developed to furnish the alcohols in high yields without any loss of the stereoselectivity (Section **2.2**).

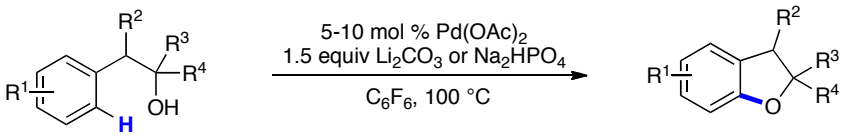


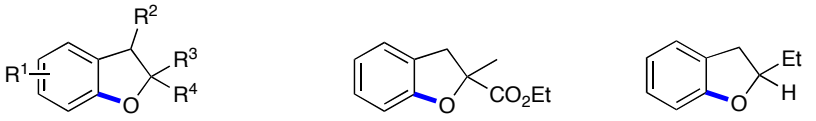
Scheme 3.2 Intermolecular C–H insertion as a surrogate of the adol reaction

3.1.4 Palladium-catalyzed C–H functionalization/C–O cyclization for the synthesis of benzofurans

In 2010, the Yu group developed a protocol to synthesize benzofurans through a palladium-catalyzed intramolecular C–H functionalization/C–O cyclization.[171] This reaction worked well with tertiary alcohols, and benzofurans were synthesized in high yields (Table **3.7**). For secondary alcohols or alcohols bearing an electron-deficient substituent at the α-position, the palladium-catalyzed C–H functionalization reaction produced benzofurans in moderate yield. Competitive oxidation of secondary alcohols to the ketone was observed as the major by-product.

Table 3.7 Palladium-catalyzed C–H functionalization/C–O cyclization



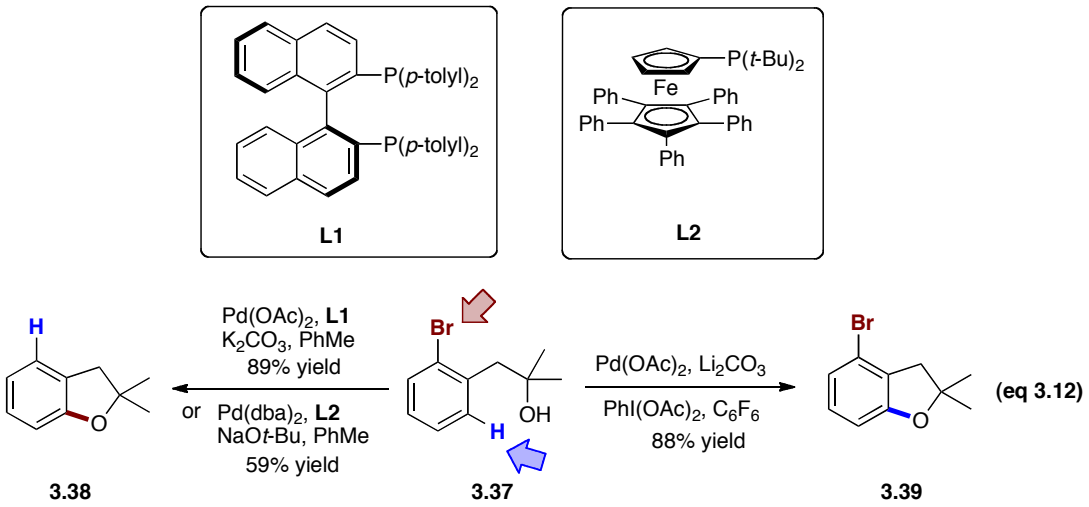


70-91% | 50% | 42%

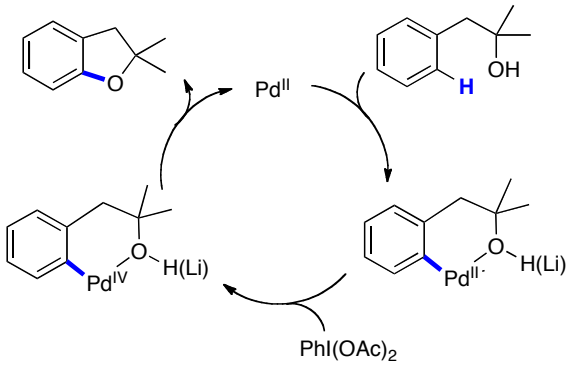
R^1 = EDG, EWG
R^2 = H, Me, Ph
R^3, $R^4 \neq$ H

For a substrate possessing both an *ortho*-hydrogen and *ortho*-bromo substituent, for example compound **3.37**, benzofurans can be synthesized through selective activation of

the C–H or C–Br bond (eq **3.12**). Under the condition developed by the Buchwald and Hartwig groups, the reaction of **3.37** generated benzofuran **3.38** through the C–Br activation/C–O cyclization,[172,173] while employing the protocol developed by the Yu group, benzofuran **3.39** was synthesized through C–H functionalization. Under this C–H functionalization, the bromo group is left untouched and can be used for further transformations.

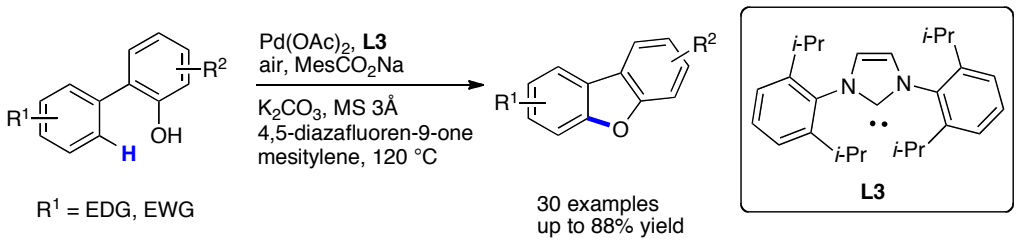


As strong oxidant $PhI(OAc)_2$ was used for this reaction, a Pd(II)/Pd(IV) mechanism was proposed (Scheme **3.3**). Since the benzofuran product can also be generated under base-free conditions, the formation of the [Pd(II)-OR] species as the C–H activation precursor is unlikely because its formation under neutral conditions is disfavored. Thus, the hydroxyl group was suggested to coordinate with Pd(II) as a neutral σ donor.



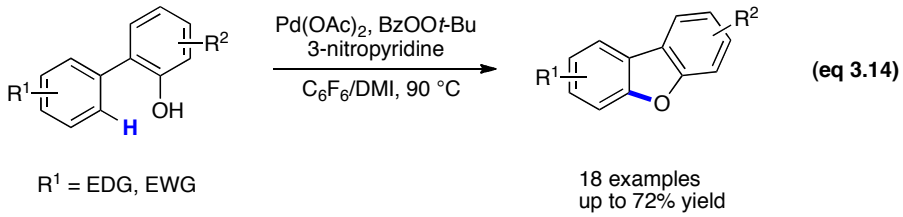
Scheme 3.3 Proposed mechanism for the palladium-catalyzed C–H functionalization/C–O cyclization

One limitation of the above methodology is the use of phenolic substrates. $PhI(OAc)_2$ is a strong oxidant and will tend to oxidize phenols and even methoxybenzene derivatives. During the study of synthesizing dibenzofurans through C–H functionalization of phenols, Liu and coworkers discovered that air was an effective oxidant for this transformation. In the presence of a palladium catalyst and NHC ligand, dibenzofurans were synthesized in good yield (eq **3.13**). A Pd(0)/Pd(II) catalytic cycle was proposed for this reaction, and the C–O reductive elimination was identified as the rate-limiting step. Since the key step for this reaction is the C–O reductive elimination, the reaction yield could be potentially improved by promoting this step with bulky additives. Among all the reagents tested, sodium 2,4,6-trimethylbenzoate ($MesCO_2Na$) exhibited the best effect.[174]



(eq 3.13)

With a peroxybenzoate as the oxidant, the Yoshikai group reported another C–H functionalization reaction to synthesize dibenzofurans (eq **3.14**). Different from the method developed by the Liu group, this reaction went through a Pd(II)/Pd(IV) catalytic cycle, and the C–H cleavage was identified as the rate-liming step for this transformation.[175]

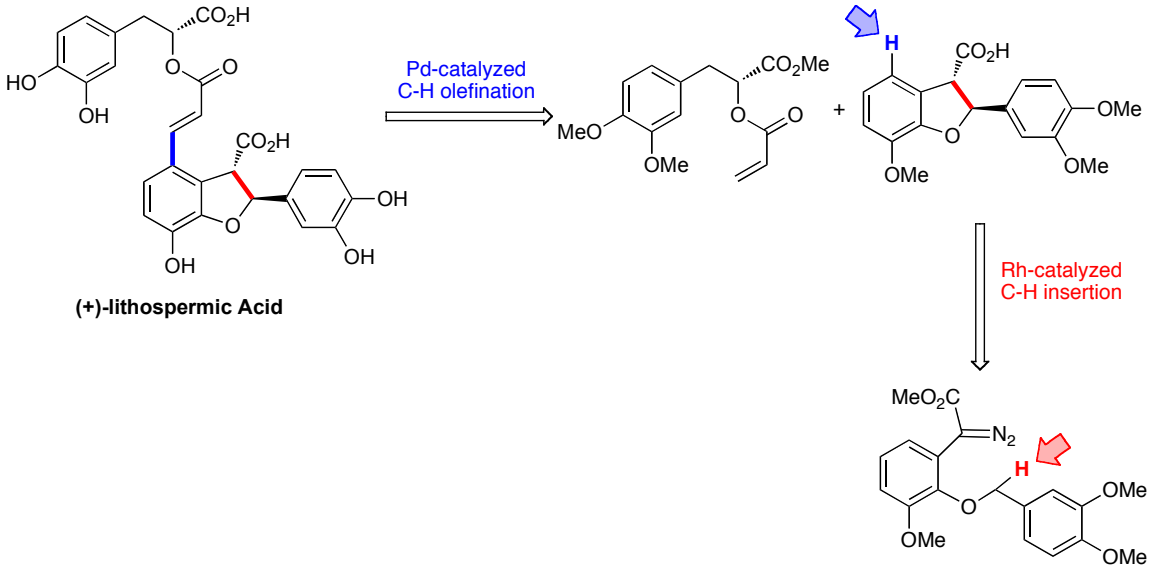


(eq 3.14)

3.2 Results and discussion

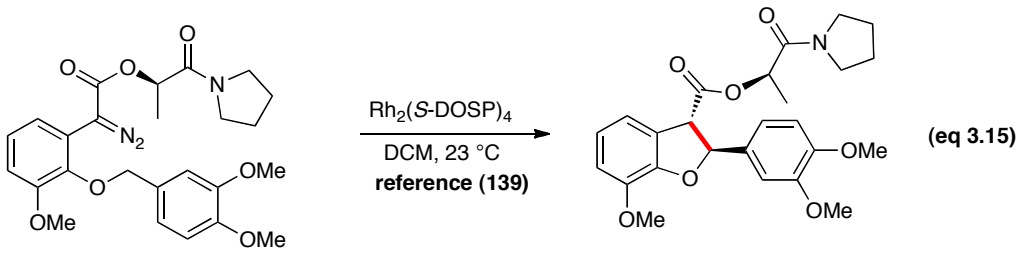
3.2.1 Application of the intramolecular C–H insertion to the synthesis of the core structure of lithospermic acid

Lithospermic acid is an bioactive component of *Salvia miltiorrhiza* (also known as Danshen), a traditional Chinese medicine used to treat cardiovascular and cerebrovascular diseases.[139] Because of its potent bioactivity, the synthesis of lithospermic acid has attracted considerable synthetic interest. The first total synthesis of this natural product was achieved by the Ellman and Bergman groups and in 5.9% overall yield over 10 linear steps.[141] Lately, the Yu group accomplished the synthesis of this compound in 11% overall yield over 12 linear steps. The reaction featured a late-stage palladium-catalyzed C–H olefination and a rhodium-catalyzed intramolecular C–H insertion reaction (Scheme **3.4**).

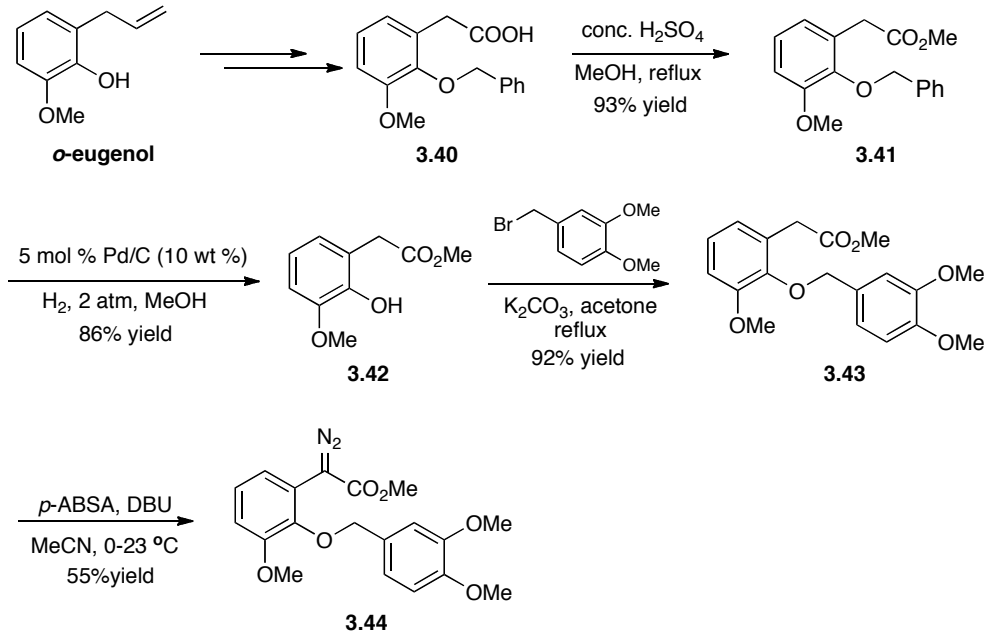


Scheme 3.4 Retro-synthesis of lithospermic acid by the Yu group

Although the methodology to synthesize dihydrobenzofurans *via* rhodium-catalyzed intramolecular C–H insertions was previously reported, the application in the synthesis of lithospermic acid was problematic. In order to develop a catalytic, asymmetric method to synthesize the dihydrobenzofuran core structure of this natural product, a collaboration between the Davies group and the Yu group was established. Although the Yu group lately achieved the synthesis of the dihydrobenzofuran intermediate by an intramolecular C–H functionalization, both a chiral rhodium catalyst and a chiral auxiliary were required and the product was obtained in only 8:1 dr (eq **3.15**). Our study demonstrated that the synthesis of this dihydrofuran core structure could be optimized and avoid the use of a chiral auxiliary. This was then followed by an alternative intermolecular enantioselective route to synthesize dihydrobenzofurans using two distinct types of C–H functionalization reactions.



The required diazo compound **3.44** for the intramolecular reaction can be synthesized from commercially available *o*-eugenol over six steps (Scheme **3.5**). Employing the published procedure,[139] phenylacetic acid **3.40** was prepared in two steps from *o*-eugenol. The subsequent esterification and deprotection afforded phenol **3.42** in high yield over two steps. A nucleophilic addition of 3,4-dimethoxybenzyl group followed by a diazo transfer reaction supplied diazo compound **3.44**.

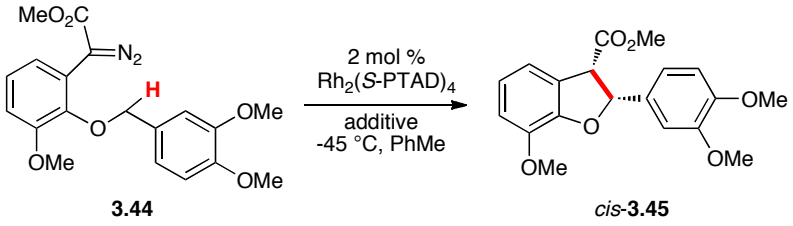


Scheme 3.5 Synthesis of diazo compound **3.44**

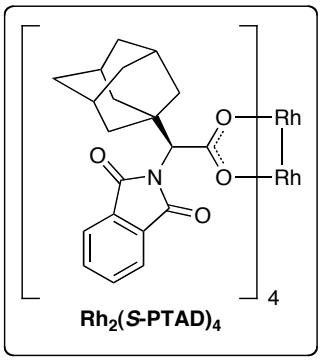
With diazo compound **3.44** in hand, the rhodium-catalyzed C–H insertion reaction was studied. Previous results from the Davies group have shown that $Rh_2(PTAD)_4$ is the optimum catalyst for intramolecular insertions into secondary benzylic C–H bonds.[45] As

a result, the study of the reaction of diazo compound **3.44** was started with $Rh_2(PTAD)_4$ (Table **3.8**). Although the reaction at -45 °C produced *cis*-dihydrobenzofuran **3.45** as a single diastereomer with 84% ee, the isolated yield was only 20% (entry 1). The major byproduct of the reaction was an alcohol generated by the reaction of the carbenoid with moisture. To suppress the formation of this by-product, drying reagents were examined. Calcium chloride was then identified as an effective additive for this transformation (entries 4 and 5). In the presence of five equiv of $CaCl_2$, the reaction yield was improved to 63% without any change of the enantioselectivity. As far as we are aware, this is the first time that $CaCl_2$ has been used as an additive for rhodium-catalyzed carbenoid chemistry.

Table 3.8 Optimization of the drying reagents



3.44 *cis*-**3.45**



Rh_2(*S*-PTAD)$_4$

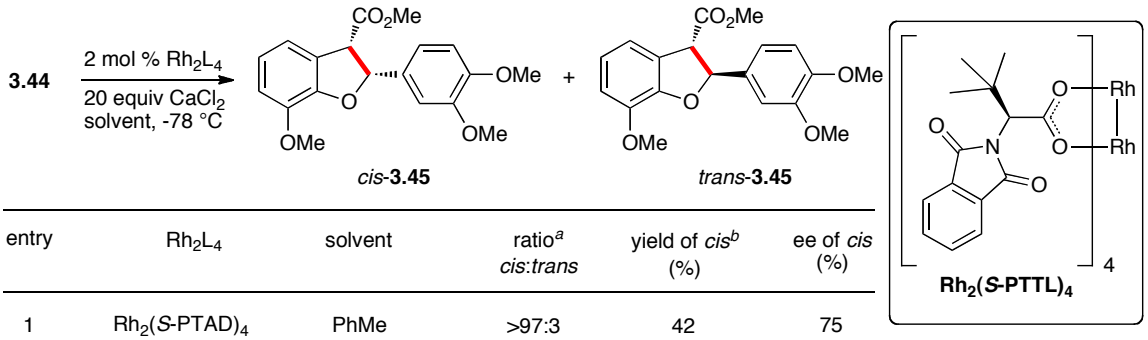
entry	additive (equiv)	ratio[a] *cis: trans*	yield of *cis*-**3.45**[b] (%)	ee of *cis*-**3.45** (%)
1	-	>97:3	20	84
2	MS 4Å	>97:3	4	-
3	$MgSO_4$ (20)	97:3	13	-
4	$CaCl_2$ (20)	>97:3	55	84
5	**$CaCl_2$ (5)**	**>97:3**	**63**	**87**

[a] Determined by crude NMR.[b] Islated yield.

In order to improve the asymmetric induction, the reaction was attempted at a lower temperature (Table **3.9**). However, the reaction performed at -78 °C proceeded slowly and the dihydrobenzofuran product was obtained in decreased yield and

enantioselectivity (entry 1). Compared to the reaction catalyzed by $Rh_2(PTAD)_4$, the $Rh_2(PTTL)_4$ catalyzed reaction produced the dihydrobenzofuran in similar level of asymmetric induction but lower yield (entry 2). The solvent is an important component for this reaction to achieve high diastereoselectivity. The reaction performed in toluene afforded *cis*-dihydrobenzofuran **3.45** as a single diastereomer, while the reaction conducted in dichloromethane furnished the products as mixture of diastereomers with a 6:1 ratio favoring the *cis*-isomer (entry 3).

Table 3.9 Intramolecular C–H insertions performed at -78 °C

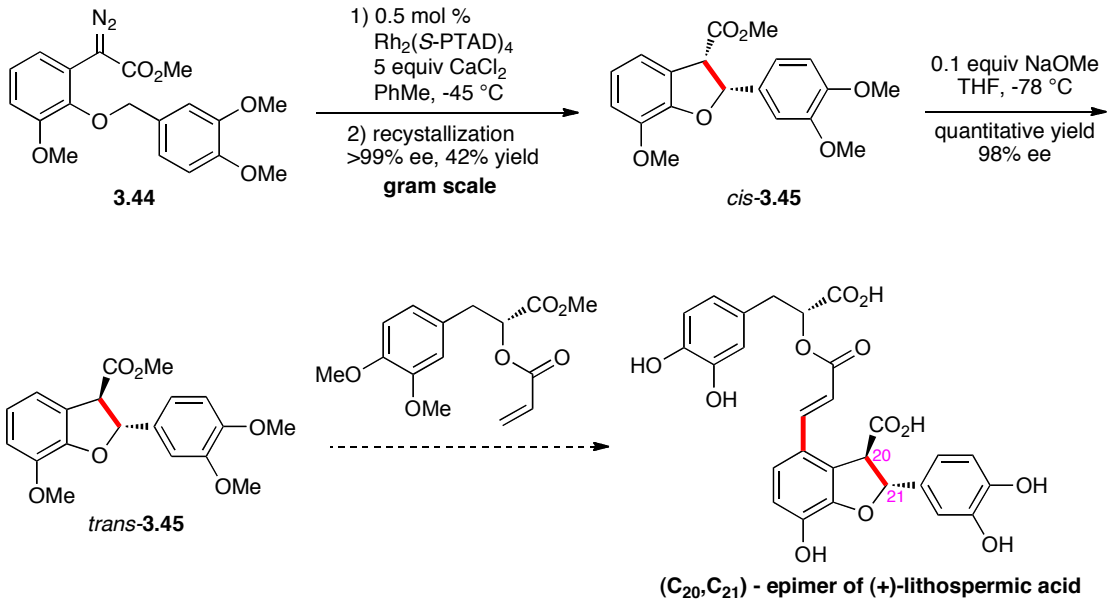


entry	Rh_2L_4	solvent	ratio[a] *cis*:*trans*	yield of *cis*[b] (%)	ee of *cis* (%)
1	Rh_2(*S*-PTAD)$_4$	PhMe	>97:3	42	75
2	Rh_2(*S*-PTTL)$_4$	PhMe	>97:3	28	74
3	Rh_2(*S*-PTAD)$_4$	DCM	86:14	38	79

[a] Determined by crude NMR. [b] Islated yield.

The optimized protocol was successfully applied to a gram scale reaction (Scheme **3.6**). The catalyst loading could be decreased to 0.5 mol % and the product was purified by recrystallization, which provided *cis*-dihydrobenzofuran **3.45** as a single enantiomer in 42% yield from the diazo compound. Under basic conditions, *cis*-**3.45** was equilibrated to the desired *trans*-**3.45** quantitatively, which is the opposite enantiomer of the lithospermic dihydrobenzofuran core structure. Under the protocols developed by the Yu group in their synthesis of lithospermic acid, the following C–H olefination and deprotection reactions would afford the epimer of the natural product.[139] Simply by

switching the catalyst to Rh_2(*R*-PTAD)$_4$, the enantiomer of the dihydrobenzofuran core structure in the natural product could be synthesized with high stereoselectivity through this reaction sequence.

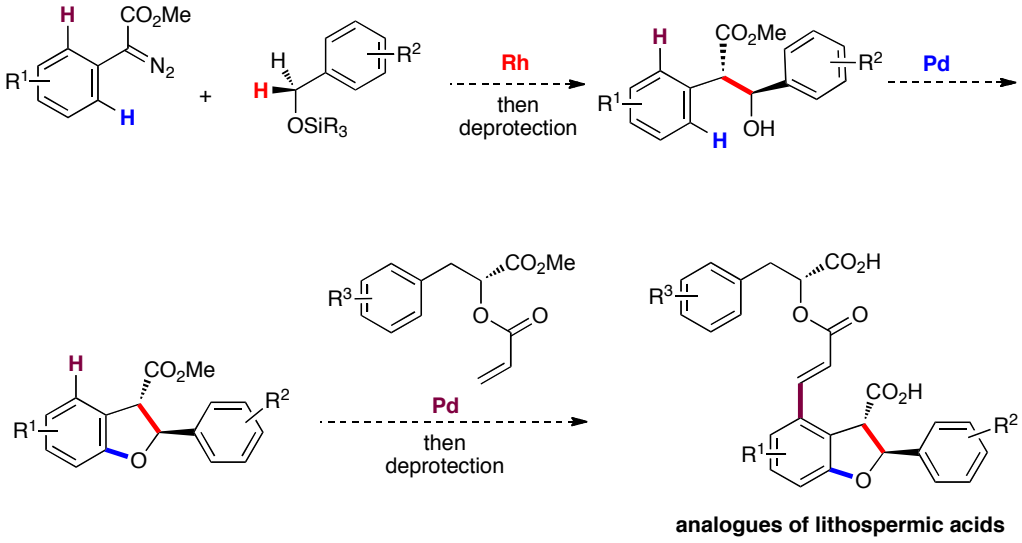


Scheme 3.6 Synthesis of *trans*-dihydrobenzofuran **3.45**

3.2.2 Synthesis of dihydrobenzofurans *via* sequential C–H functionalizations

Although the intramolecular C–H insertion works well for the synthesis of the dihydrobenzofuran moiety of lithospermic acid, the application of this method to the synthesis of analogues of this natural product is limited by the tedious synthesis of the diazo compounds required for the intramolecular reactions. This problem could be potentially solved by synthesizing dihydrobenzofuran moieties through enantioselective intramolecular C–H functionalizations. To this end, a reaction sequence to access dihydrobenzofurans through complementary C–H functionalization reactions was developed (Scheme **3.7**). The sequence combined the rhodium- and palladium-catalyzed

C–H functionalizations that were studied individually by the Davies group and the Yu group. In principle, a library of analogues of lithospermic acid could be rapidly synthesized *via* this reaction sequence. This methodology has the potential to facilitate the study of the bioactivities of this natural product and its derivatives. The reaction sequence started with a rhodium-catalyzed intermolecular C–H insertion, followed by the deprotection of the TBS groups to afford adol-type alcohols. The palladium-catalyzed C–H functionalization/C–O cyclization of those alcohols would furnish the desired dihydrobenzofurans. After hydrolysis to carboxylic acids, analogues of lithospermic acid could possibly be synthesized *via* a palladium-catalyzed Heck-type C–H olefination and the subsequent deprotection reaction.

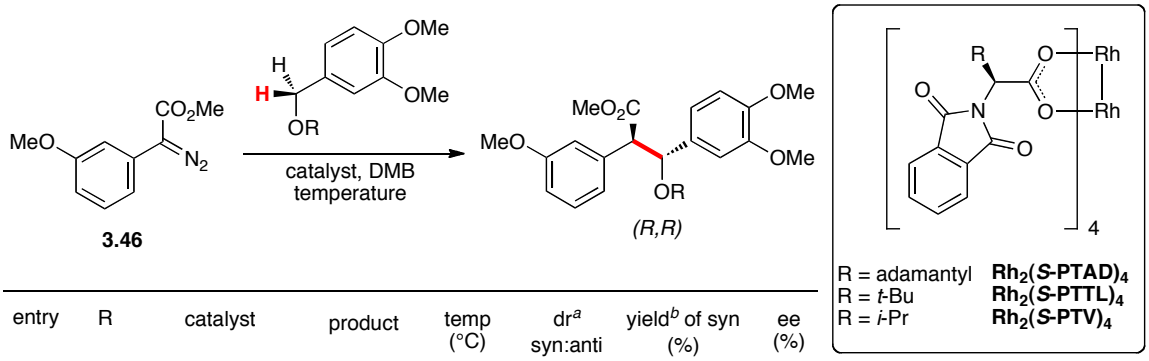


Scheme 3.7 Designing diversified synthesis of lithospermic acid analogues utilizing sequential C–H functionalizations

The Yu group shown that the palladium-catalyzed C–H functionalization/C–O cyclization reaction did not work well for a secondary alcohol or any alcohol bearing an electron-withdrawing substituent,[139] while the rhodium-catalyzed C–H insertion products are secondary alcohols with ester groups at the *β*-position. As a result, the feasibility of

the proposed palladium-catalyzed C–H functionalization of those alcohols was uncertain. In addition, a mild and efficient method to remove the TBS protecting group without epimerization would be required. To this end, the reaction of aryldiazoacetate **3.46** with TMS and TBS benzyl ethers was evaluated (Table **3.10**). As previously reported,[144] the best chiral dirhodium complex for the enantioselective benzylic C–H insertion reaction was Rh_2(PTTL)$_4$ (entries 2-4). In the presence of such catalyst, C–H insertion product **3.27** was obtained in 59% yield and with 92% ee (entry 2). By replacing the TMS group with the more electron-rich TBS group, both the yield and the enantioselectivity of this C–H insertion reaction were improved (entry 5).

Table 3.10 C–H insertion reaction of silyl benzyl ethers with diazo compound **3.46**



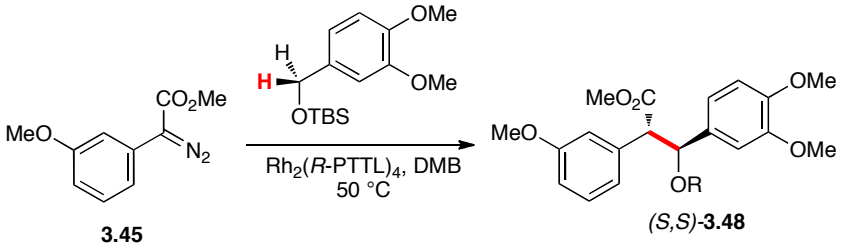
entry	R	catalyst	product	temp (°C)	dr[a] syn:anti	yield[b] of syn (%)	ee (%)
1	TMS	Rh_2(Oct)$_4$	**3.47**	23	93:7	62	-
2	TMS	Rh_2(*S*-PTTL)$_4$	**3.47**	50	91:9	59	92
3	TMS	Rh_2(*S*-PTAD)$_4$	**3.47**	50	89:11	44	66
4	TMS	Rh_2(*S*-PTV)$_4$	**3.47**	50	85:15	52	30
5	TBS	Rh_2(*S*-PTTL)$_4$	**3.48**	50	97:3	65	96

[a] Determined on crude NMR. [b] Isolated yield.

Aiming to apply this reaction sequence to the diversified synthesis of natural products, the further study of this reaction sequence focused on the synthesis of (*S*,*S*)-dihydrobenzofurans using Rh_2(*R*-PTTL)$_4$. In order to facilitate the potential large-scale

application, the catalyst loading of the C–H insertion reaction was studied (Table **3.11**). The reaction employing 0.5 mol % Rh_2(*R*-PTTL)$_4$ afforded the C–H insertion products in identical yield and stereoselectivity compared to the reaction with 1 mol % catalyst (entries 1 and 2). The further decrease of the catalyst loading to 0.1 mol % also had no influence on the diastereo- and enantioselectivity of **3.48** but the reaction yield was lowered to 40% (entry 3). Lastly, the concentration of the reaction had little influence on either the yield or the enantioselectivity (entry 4).

Table 3.11 Study of the catalyst loading



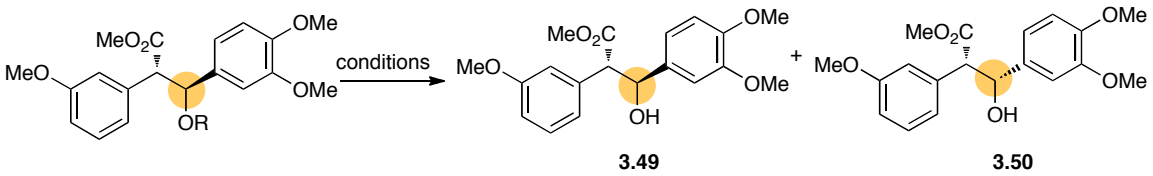
entry	catalyst loading (mol %)	concentration (mol/L)	dr[a] syn:anti	yield[b] of syn (%)	ee (%)
1	1	0.05	>93:7	70	95
2	0.5	0.05	>93:7	64	94
3	0.1	0.05	>93:7	40	93
4	0.5	0.1	>93:7	67	95

[a] Determined by crude NMR. [b] Isolated yield.

Conditions to remove the silyl-protecting group were then investigated (Table **3.12**). Treatment of the C–H insertion product **3.48** with TBAF caused the decomposition, 3,4-dimethoxybenzaldehyde was generated presumably through a retro-adol process (entry 1). It was then found that the silyl group could be smoothly removed by treating the C–H insertion product with HCl, which provided the corresponding alcohol in good yield (entries 2 and 3). No epimerization was observed under these conditions. Attempts to

deprotect compound **3.48** using HF resulted in a mixture of syn and anti alcohols (entry 4).

Table 3.12 Optimization of deprotection conditions

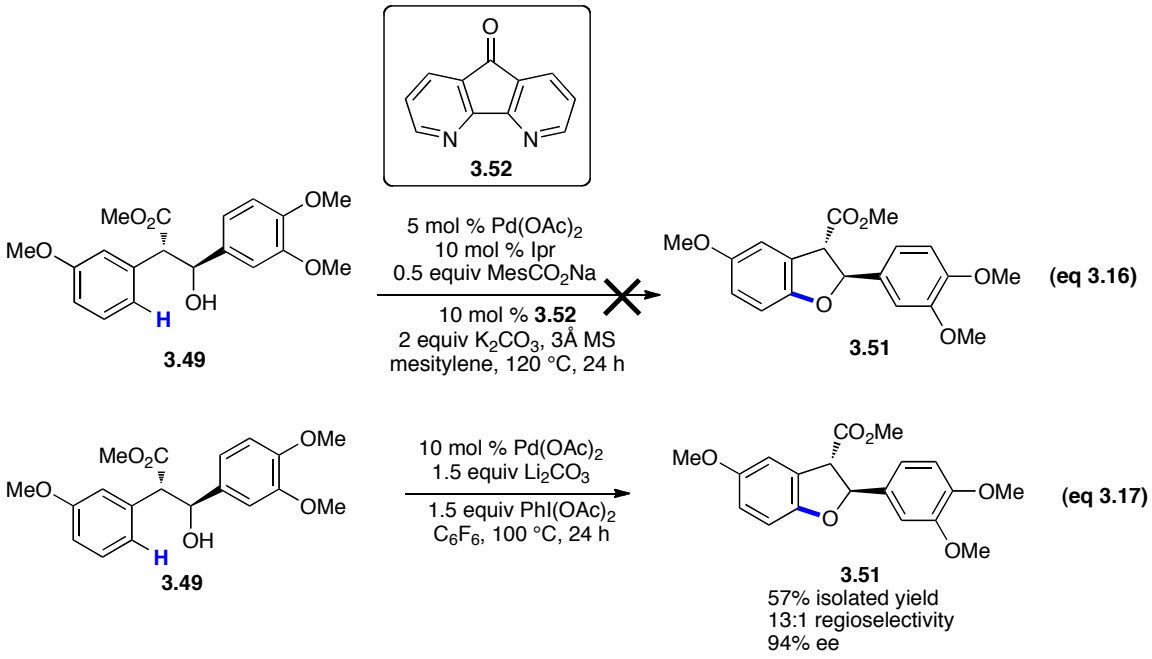


3.49 **3.50**

entry	R	reactant	conditions	yield[a] of **3.49** (%)	yield[a] of **3.50** (%)
1[b]	TMS	**3.47**	TBAF (1 *M*), THF, 0 °C	N.O.	N.O.
2	TMS	**3.47**	2*N* HCl, EtOH, 23 °C	94	-
3	TBS	**3.48**	conc. HCl, EtOH, 23 °C	80	-
4	TBS	**3.48**	48 wt % HF, MeCN, 23 °C	40	55

[a] Isolated yield. [b] N.O. = not observed.

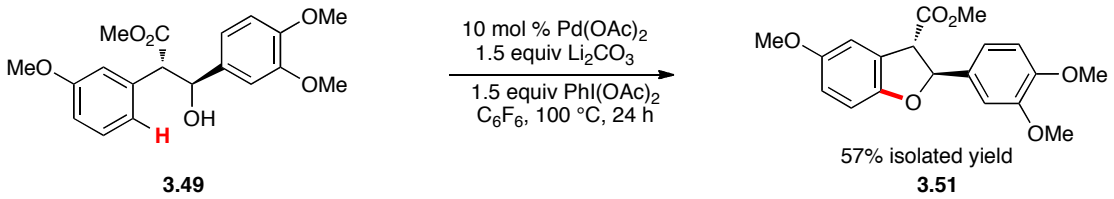
With alcohol **3.49** in hand, the synthesis of dihydrobenzofurans through palladium-catalyzed C–H functionalizations was evaluated. Alcohol **3.49** was subjected to protocols developed for the synthesis of dibenzofurans and benzofurans. Under the reaction condition developed by the Liu group, no dihydrobenzofuran product was observed using alcohol **3.49** as precursor (eq **3.16**). Again, the major product of the reaction was determined to be 3,4-dimethoxybenzaldehyde. Switching to the protocol developed by the Yu group, dihydrobenzofuran product **3.51** was formed in 57% yield with no loss of enantioselectivity. In addition, the product was obtained with good control of regioselectivity, favoring ring closure at the position *para* to the methoxy group (eq **3.17**). It should be noted that 3,4-dimethoxybenzaldehyde was also observed (~10%) as a by-product under these conditions.



Variation of these reaction conditions did not improve the yield or regioselectivity (Table **3.13**). At decreased reaction temperature, the reaction of alcohol **3.49** produced dihydrobenzofuran **3.51** in low yield (entry 2). The oxidant played a key role in this transformation. The yield of the product decreased after reducing the amount of the oxidant to one equiv (entry 3). Inorganic bases were intensely screened, among which only Na_2HPO_4 showed the comparable performance to Li_2CO_3 (entry 4). Dihydrobenzofuran **3.51** was also formed from the reaction under base-free conditions, but the yield was lower than the reaction with Li_2CO_3 as base (entry 5). The yield of the base-free reaction could be improved by increasing the amount of oxidant and reaction temperature but remained lower than the results obtained under standard reaction conditions (entries 6). With one equiv of oxidant, the reaction performed in dichloroethane provided the dihydrobenzofuran **3.51** in comparable yield to the reaction under standard conditions, however the conversion and regioselectivity were lower (entry 7). Efforts to improve the conversion by increasing the amount of oxidant only resulted in

a decrease of the reaction yield (Entry 8). Although NMI and peroxides played an important role for the synthesis of dibenzofuran developed by Yoshikai group,[175] the use of such reagents in this reaction resulted in no formation of dihydrobenzofurans (entries 9 and 10).

Table 3.13 Optimization of the palladium-catalyzed C–H functionalization



3.49 **3.51**

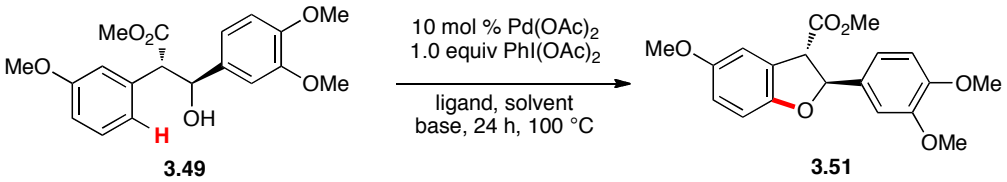
entry	variation from the standard conditon	r.r.[a]	NMR yield[b] (%)	conversion[b] (%)
1	none	13:1	60	>95
2	80 °C instead of 100 °C	14:1	32	90
3	1.0 equiv $PhI(OAc)_2$	17:1	39	83
4	Na_2HPO_4 instead of Li_2CO_3	>20:1	58	>95
5	no Li_2CO_3	10:1	28	>95
6	2.0 equiv $PhI(OAc)_2$, no Li_2CO_3, 140 °C, 6 h	>20:1	50	>95
7	DCE instead of C_6F_6, 1.0 equiv $PhI(OAc)_2$	8:1	58	77
8	DCE instead of C_6F_6	6:1	26	>95
9[c]	C_6F_6/DMI (3:2)	-	N.O.[d]	-
10	TBHP or BzOO*t*-Bu instead of $PhI(OAc)_2$	-	N.O.[d]	-

[a] Ratio of regioisomers. [b] Calculated with dibromomethane as internel standard. [c] DMI = 1,3-Dimethyl-2-imidazolidinone. [d] N.O. = not observed.

Inspired by the effective C–H oxygenation of arenes with palladium/pyridine type catalysts developed by the Sanford group,[176,177] the effect of pyridine and bipyridine ligands on this palladium-catalyzed C–H functionalization was studied (Table **3.14**). Although pyridine appeared to inhibit this C–H functionalization reaction, 2,2'-bipyridine showed some potential (entries 1 and 2). Next, the ratio of the ligands and palladium

catalyst was examined. When the ratio of 2,2'-bipyridine to $Pd(OAc)_2$ was 0.1-0.75, the reaction produced dihydrobenzofuran **3.51** in moderated yields (entries 2-4). The C–H functionalization was totally inhibited when a 1:1 ratio of ligand/palladium was used (entry 5). In the presence of bipyridine, the reaction conversion was typically inferior (50-70%). Various conditions were attempted to improve the conversion and reaction yield. The addition of base (Li_2CO_3) or prolonging the reaction time (48 h) slightly improved conversions of the starting material but result in similar or lower yield (entries 6 and 7). Full conversion of the starting material was achieved by increasing the amount of the oxidant to 1.5 equiv. However, the reaction yield remained lower than the standard reaction (entry 8). The choice of solvents plays an important role for the regioselectivity of the reaction, which was improved to 25:1 by changing the solvent from dichloroethane to hexafluorobenzene (entry 9). Although full conversion of the starting material was observed by increasing the amount of oxidant, the reaction yield was not better than the results obtained from the standard reaction (entry 8). Further enhancement of the regioselectivity (>30:1) was observed after changing the ligand from bipyridine to phenantroline, but the dihydrobenzofuran product was only produced in only 45% yield (entry 11).

Table 3.14 Optimization of the ligands



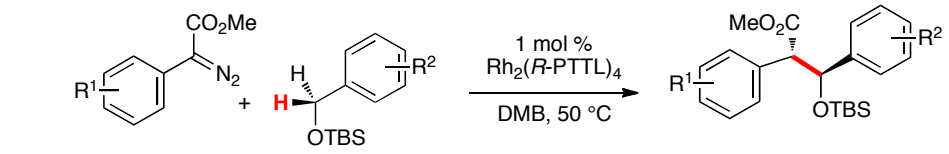
3.49 **3.51**

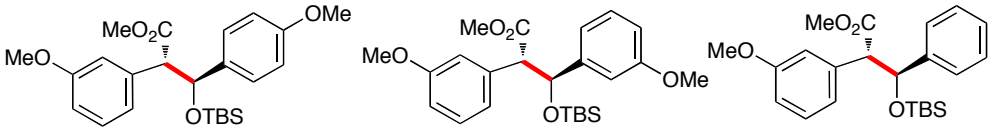
entry	ligand	ratio ligand/$Pd(OAc)_2$	base (1.5 equiv)	solvent	r.r.[a]	yield[b] (%)	conversion[b] (%)
1	pyridine	0.75	-	DCE	>30:1	15	59
2	2,2'-bipyridine	0.1	-	DCE	9:1	49	70
3[c]	2,2'-bipyridine	0.5	-	DCE	11:1	45	65
4	2,2'-bipyridine	0.75	-	DCE	10:1	46	68
5	2,2'-bipyridine	1	-	DCE	-	<1	38
6	2,2'-bipyridine	0.5	Li_2CO_3	DCE	14:1	46	79
7[d]	2,2'-bipyridine	0.5	-	DCE	10:1	35	77
8[e]	2,2'-bipyridine	0.5	-	DCE	10:1	53	>95
9[e]	**2,2'-bipyridine**	**0.5**	**-**	**C_6F_6**	**25:1**	**56**	**93**
10[e]	2,2'-bipyridine	0.5	Li_2CO_3	C_6F_6	17:1	37	87
11[e]	phenanthroline	0.5	Li_2CO_3	C_6F_6	>30:1	45	>95

[a] ratio of regioisomers. [b] CH_2Br_2 was used as internel standard. [c] 35% isolated yield. [d] 48 h reaction time.
[e] 1.5 equiv of $PhI(OAc)_2$ was used.

In order to better understand this reaction sequence, the substrate scope was then studied. A variety of aryldiazoacetates and TBS protected benzyl alcohols were subjected to the Rh_2(*R*-PTTL)$_4$ catalyzed C–H insertion reaction. As shown in Table **3.15**, most of the C–H insertion products were obtained in high yield (74-92% yield). The lowest yield was found for compound **3.54**, which was isolated in 58% yield. All of these products were synthesized with high diastereoselectivity (94:6 to >97:3) and high enantioselectivity (93-99% ee). For the synthesis of dihydrobenzofurans **3.57**-**3.59**, TFT was used as a co-solvent in order to improve the solubility of the starting material. Using other co-solvents (dichloromethane and toluene) or TFT as the only solvent resulted in low yield or no formation of the desired product.

Table 3.15 Scope of the rhodium-catalyzed C–H functionalization

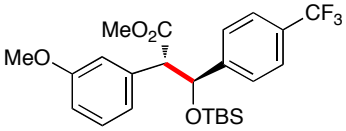




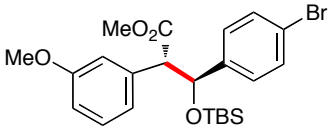
3.52, 76% yield
>97:3 dr, 93% ee

3.53, 58% yield
>97:3 dr, 95%ee

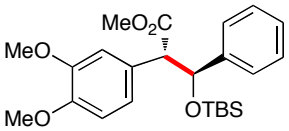
3.54, 86% yield
>97:3 dr, 96%ee



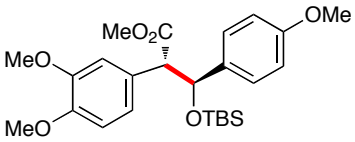
3.55, 86% yield
> 97:3 dr, 98% ee



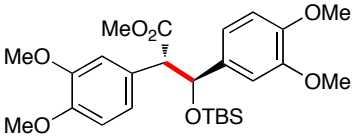
3.56, 92% yield
>97:3 dr, 98% ee



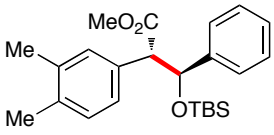
3.57, 86% yield[a]
>97:3 dr, 97%ee



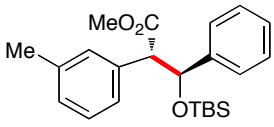
3.58, 74% yield[a]
>97:3 dr, 97%ee



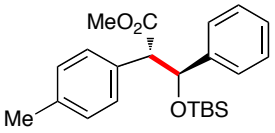
3.59, 77% yield[a]
>97:3 dr, 97%ee



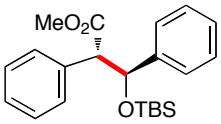
3.60, 92% yield
94:6 dr, 99%ee



3.61, 77% yield
>97:3 dr, 98% ee



3.62, 78% yield
>97:3 dr, 99% ee

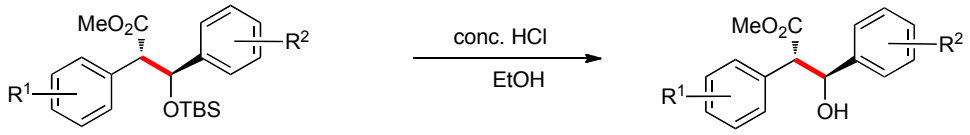


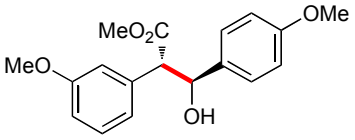
3.63, 76% yield
>97:3 dr, 95%ee

a: the reaction was performed by adding a solution of the diazo compond in DMB/TFT (v/v = 3/1) to a reluxing solution of TBS benzyl ether in DMB.

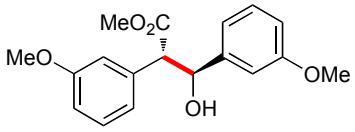
Under the optimum deprotection conditions, those C–H insertion products were converted to the corresponding alcohols in high yield (72-94%). Furthermore, no epimerizations was observed for the deprotection reaction (Table **3.16**).

Table 3.16 Deprotection of the TBS group

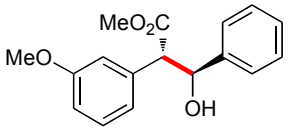




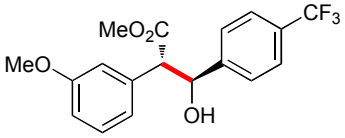
3.64, 83% yield



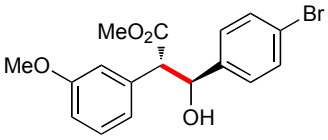
3.65, 87% yield



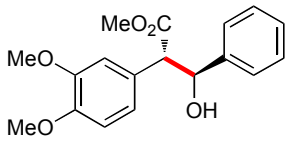
3.66, 94% yield



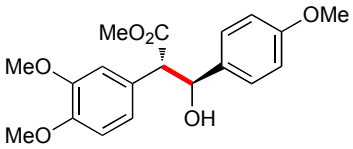
3.67, 78% yield



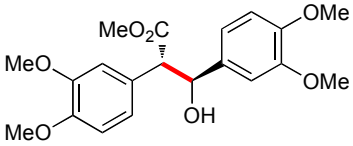
3.68, 88% yield



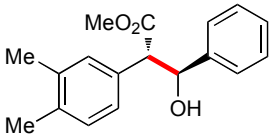
3.69, 82% yield



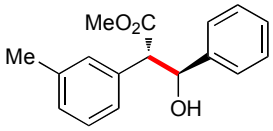
3.70, 85% yield



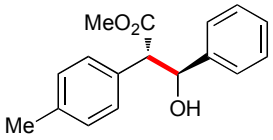
3.71, 78% yield



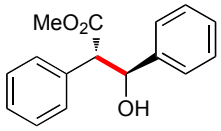
3.72, 83% yield



3.73, 81% yield



3.74, 85% yield

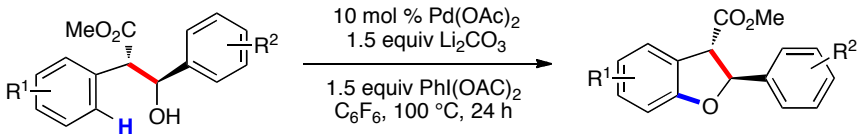


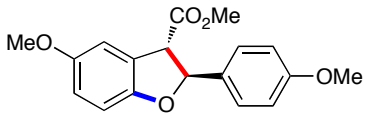
3.75, 79% yield

All these alcohols were then cyclized to the corresponding dihydrobenzofurans employing the standard palladium-catalyzed C–H functionalization conditions (Table **3.17**). No loss of the enantioselectivies for this palladium-catalyzed reaction has been observed. Some of the dihydrobenzofurans (**3.51**, **3.76**, **3.82** and **3.83**) have been synthesized in half-gram to gram scale. In cases where a mixture of regioisomers could have been formed, the reaction favored the less sterically hinder C–H bond, such as the position *para* to a methoxy group (**3.76-3.85**). All of the dihydrofurans were synthesized in high regioselectivity (13:1 to >30:1). The palladium-catalyzed C–H functionalization

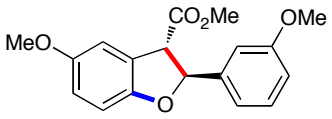
favors the cyclization onto an electron rich aromatic ring and dihydrobenzofurans **3.76-3.83** were produced in 24 h. However, in the case of **3.81-3.83**, containing two methoxy groups in the reacting phenyl ring, increased amount of aromatized benzofurans by-products were observed by crude ^{1}H-NMR analysis. Without methoxy substituents on the phenyl ring, more vigorous reaction conditions have to be used. For the synthesis of dihydrobenzofurans **3.84-3.87**, the reaction with Na_2HPO_4 as base provided better results than those with Li_2CO_3. Full conversion of the alcohols to dihydrobenzofuran **3.84** and **3.85** was achieved by increasing the catalyst loading (20 mol %) and prolonging the reaction time (48-72 h). Without the electron-donating substituents at the *para*-position, the syntheses of products **3.86** and **3.87** have to be conducted at a higher temperature (120 °C).

Table 3.17 Scope of the palladium-catalyzed C–H functionalizations

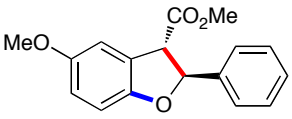




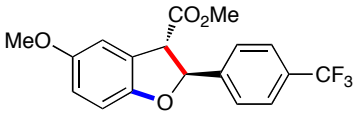
3.76
56% yield, 13:1 rr, 93% ee



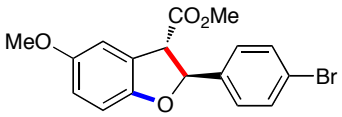
3.77
41% yield, 14:1 rr, 93% ee



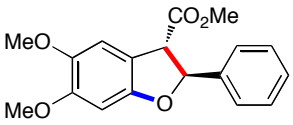
3.78
63% yield, 14:1 rr, 96% ee



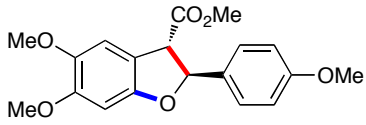
3.79
61% yield, 15:1 rr, 93% ee



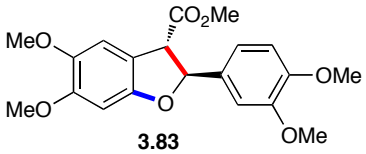
3.80
61% yield, 15:1 rr, 93% ee



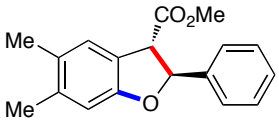
3.81[b]
47% yield, >30:1 rr, 93% ee



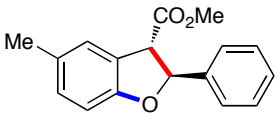
3.82
43% yield, >30:1 rr, 97% ee



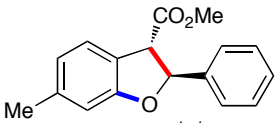
3.83
40% yield, > 30:1 rr, 99% ee



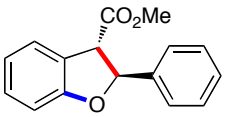
3.84[a,b,c]
45% yield, >30:1 rr, 99% ee



3.85[a,b,d]
44% yield, >30:1 rr, 98% ee



3.86[a,b,d,e]
46% yield, 99% ee

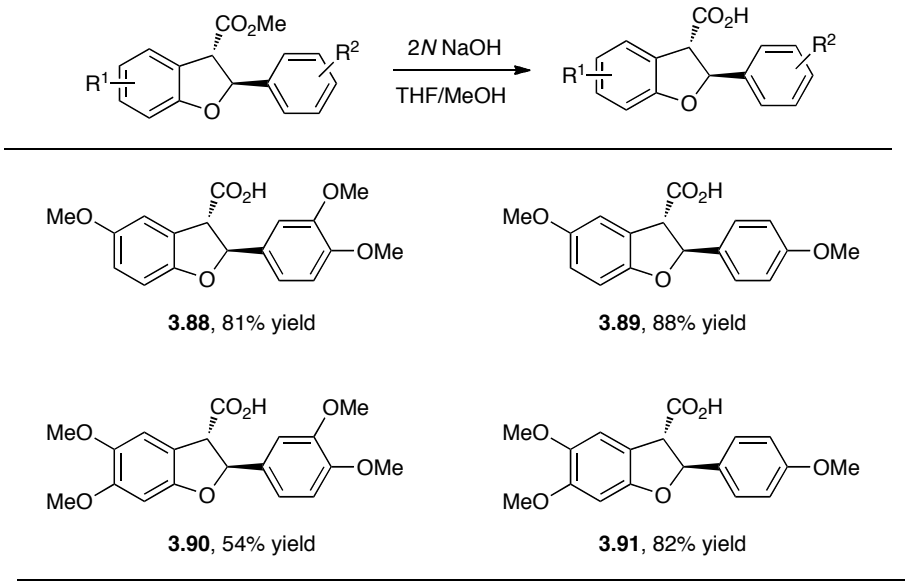


3.87[a,b,d,e]
39% yield, 97% ee

[a] 20 mol % of $Pd(OAc)_2$ was used. [b] Na_2HPO_4 was used as base. [c] Reaction time was 48 h.
[d] Reaction time was 72 h, [e] Reaction temperature was 120 °C.

The dihydrobenzofurans synthesized through the sequential C–H functionalizations have the potential to be further functionalized by a third C–H functionalization, such as a palladium-catalyzed Heck-type reaction. The carboxylic acids for the C–H olefination were obtained by hydrolysis of the methyl esters under saponification conditions (Table **3.18**). The absolute configuration of carboxylic acid **3.91** derived from **3.82** was unambiguously assigned by X-ray crystallography and extended by analogy to other dihydrobenzofurans (Figure **3.9**).

Table 3.18 Hydrolysis of the methyl ester



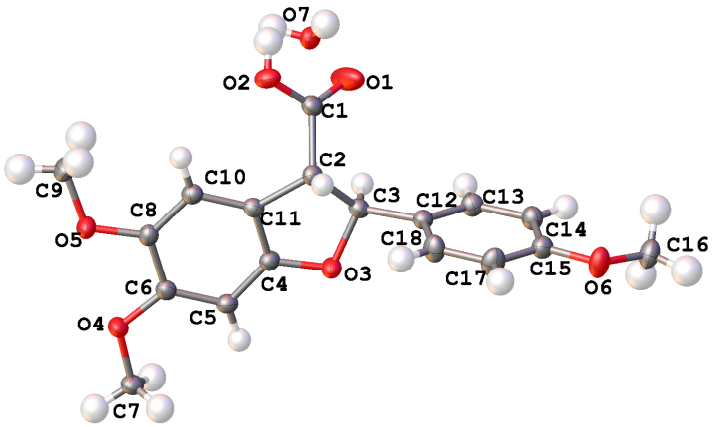
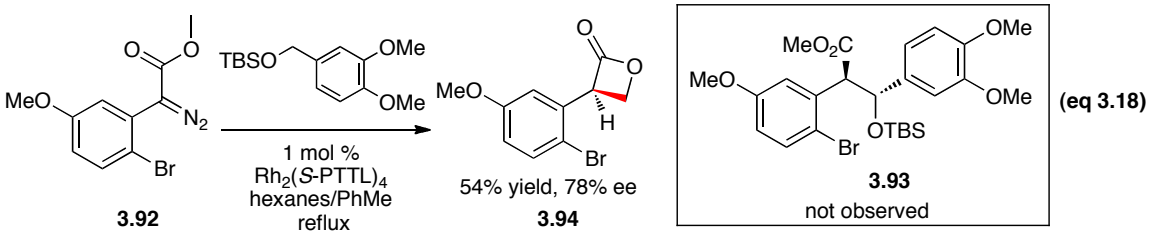


Figure 3.9 X-ray crystallographic structure of product **3.91**

3.2.3 Synthesis of *β*-lactones *via* reactions of donor/acceptor carbenoid

During the exploration of synthesizing dihydrobenzofurans through sequential C–H functionalizations, an unexpected transformation was discovered. In attempts to synthesize C–H insertion product **3.93**, the reaction of diazo compound **3.92** and TBS

3,4-dimthoxybenzyl ether afforded *β*-lactone **3.94** as the only reaction product, which derived from an intramolecular primary C–H insertion reaction (eq **3.18**). The absolute configuration of **3.94** was assigned by X-ray crystallography (Figure **3.10**). Although the synthesis of *β*-lactones *via* intramolecular C–H insertion reactions has been previous studied, the insertion into primary C–H bonds is typically observed in low yield when more reactive acceptor/acceptor diazo compounds are used. The formation of **3.94** is the first example of an intramolecular primary C–H insertion into the methyl ester group of donor/acceptor diazo compounds.



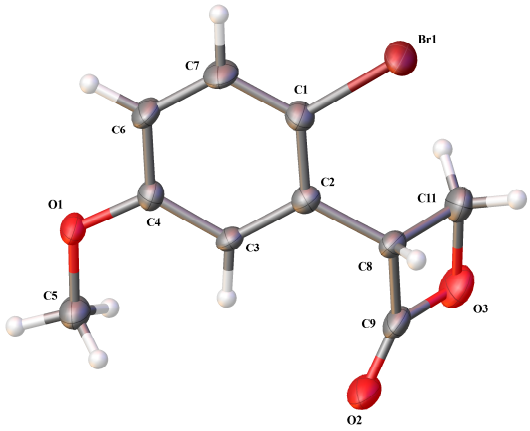
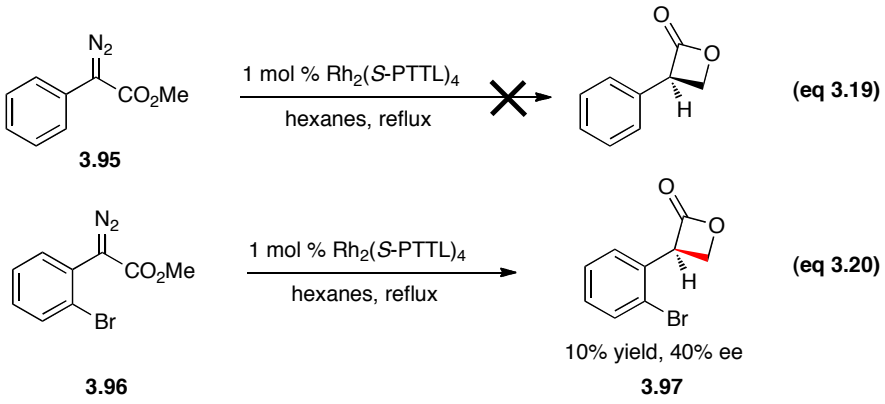


Figure 3.10 X-ray crystallographic structure of product **3.94**

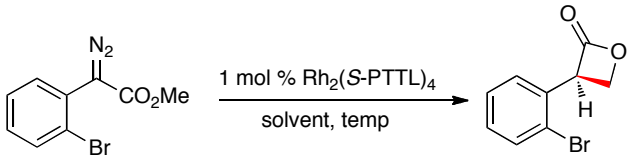
The *ortho*-bromo substituent might play an important role in this unusual intramolecular primary C–H insertion reaction. In order to test this hypothesis, control experiment of diazo compounds **3.95** and **3.96** was conducted. In the presence of $Rh_2(PTTL)_4$, no *β*-lactone product was formed from the reaction of methyl

phenyldiazoacetate **3.95** (eq **3.19**). The reaction between this diazo compound and the hydrocarbon solvent was observed, which generated an inseparable mixture of C–H insertion products. Under the same reaction condition, the reaction of *ortho*-bromo-substituted diazo compound **3.96** produced *β*-lactone **3.97** in 10% yield and 40% ee (eq **3.20**). Again, the major by-product of this reaction was also the C–H insertion products formed by the reaction of **3.96** with the solvent.



In order to improve the yield and enantioselectivity, optimization of the reaction of diazo compound **3.96** was next performed (Table **3.19**). Halogenated solvents were used to overcome the reaction between this diazo compound and hydrocarbon solvents. By switching the solvent from hexanes to dichloromethane, the yield of *β*-lactone **3.97** increased to 40%; however, the enantioselectivity decreased to 30% ee (entries 3 and 4).

Table 3.19 Optimization of the reaction of diazo compound **3.96**



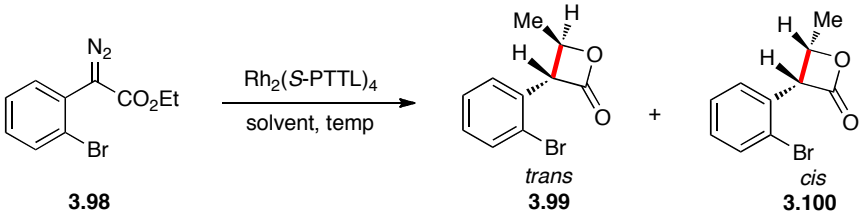
3.96 **3.97**

entry	solvent	temp (°C)	yield[a] (%)	ee (%)
1	DMB	50	2	42
2	PhMe	60	<1	-
3	**DCM**	**40**	**45**	**30**
4	DCE	84	43	32
5	TFT	60	<1	-

[a] Isolated yield.

In contrast to the above reaction, the C–H insertion into the methylene of ethyl ester of **3.98** generated *β*-lactones as two diastereomers **3.99** and **3.100** in high yield. The reason behind this is that secondary C–H bonds are more electron-rich and thus prone to undergo the C–H insertion reaction compared to primary C–H bonds. NOE experiment revealed that the major isomer is in a *trans*-configuration with respect to the protons. With increased reactivity, the reaction of **3.98** can also be performed in hydrocarbons. With DMB as solvent, the intramolecular C–H insertion reaction produced a 6.7:1 ratio of diastereomeric mixture of **3.99** and **3.100** in 82% combined yields (Table **3.20**).

Table 3.20 Intramolecular secondary C–H insertion of diazo compound **3.98**



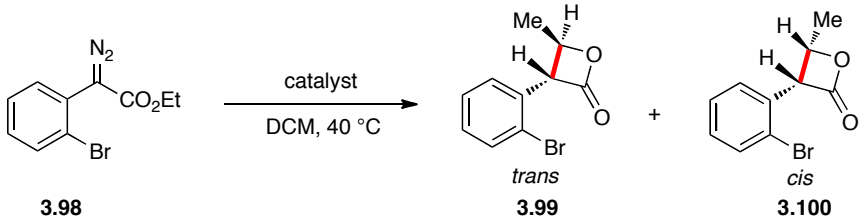
3.98 *trans* **3.99** *cis* **3.100**

entry	solvent	temp (°C)	combined yield (%)	dr[a] (*trans*:*cis*)	ee of *trans* (%)
1	DCM	40	80	88:12	60
2	DCM	23	38	89:11	64
3	DMB	50	82	87:13	63

[a] Determined by crude NMR.

Further optimization of the reaction conditions focused on the chiral dirhodium(II) complexes (Table **3.21**). In the presence of those examined catalysts, diastereomer **3.99** was isolated as the major product, with the only exception of $Rh_2(BTPCP)_4$. The reaction catalyzed by $Rh_2(BTPCP)_4$ produced a mixture of diastereomers in a 4:1 ratio favoring **3.100** (entry 1). Compared to the rhodium phthalimidocarboxylate, the prolinate $Rh_2(DOSP)_4$ catalyzed reaction afforded **3.99** with only 26% ee (entry 2). The best result was obtained from the reaction catalyzed by $Rh_2(TCPTTL)_4$. In the presence of this catalyst, the reaction conducted in dichloromethane furnished *β*-lactones **3.99** and **3.100** as a 9:1 ratio of diastereomeric mixture and the major diastereomer was formed with 60% ee (entry 5). By changing the solvent to pentane, both the yield and enantioselectivity were improved (89% combined yield, 71% ee of product **3.99**), however, the diastereoselectivity decreased to 5:1 (entry 6). Although *β*-lactones were obtained in high yields from the reaction performed at reflux, only trace amount of the products was observed when the reaction was conducted at room temperature (entry 7). The use of $Rh_2(PTAD)_4$ and $Rh_2(TCPTAD)_4$ did not lead to a better selectivity (entries 8 and 9).

Table 3.21 Optimization of the catalysts

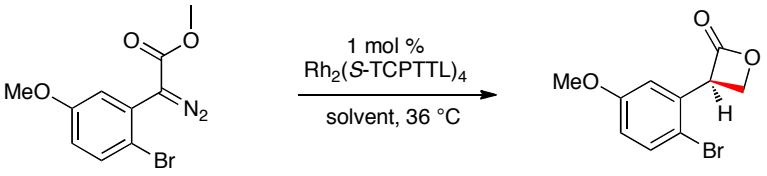


3.98 **3.99** **3.100**

entry	catalyst	combined yield[a] (%)	dr[b] (*trans*:*cis*)	ee of *trans* (%)	ee of *cis* (%)
1	Rh_2(*R*-BTPCP)$_4$	59	21:79	-	52
2	Rh_2(*S*-DOSP)$_4$	58	81:19	26	48
3	Rh_2(*S*-NTTL)$_4$	57	86:14	61	-29
4	Rh_2(*R*-TCPTV)$_4$	60	79:21	-69	-47
5	**Rh_2(*S*-TCPTTL)$_4$**	**70**	**90: 10**	**60**	**62**
6[c]	**Rh_2(*S*-TCPTTL)$_4$**	**89**	**83: 17**	**71**	**76**
7[d]	Rh_2(*S*-TCPTTL)$_4$	trace	-	-	-
8	Rh_2(*S*-PTAD)$_4$	71	83:17	59	-
9	Rh_2(*S*-TCPTAD)$_4$	64	83: 17	59	65

[a] Isolated yield. [b] Determined by crude NMR. [c] Reaction performed in pentane at 36 °C. [d] Reaction performed in pentane at 23 °C.

Since Rh_2(TCPTTL)$_4$ was found to be the optimum catalyst for the synthesis of *β*-lactone *via* the intramolecular C–H insertion reaction, the primary C–H insertion reaction of diazo compound **3.92** was re-examined. In the presence of this catalyst, the reaction performed in dichloromethane afforded *β*-lactone **3.94** in 60% yield and with 84% ee, while the reaction conducted in pentane generated the product with slightly higher level of asymmetric induction but in only 22% yield (eq **3.21**).

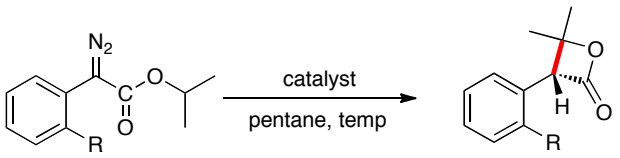


3.92 **3.94** **(eq 3.21)**

DCM: 60% yield, 84% ee
Pentane: 22% yield, 87% ee

Although the synthesis of *β*-lactone through tertiary C–H insertions has been previously studied, only moderate level of enantioselectivity was observed.[155] Since *ortho*-bromo group was found to improve the reactivity of the intramolecular C–H reaction, it was thought that the asymmetric induction of the tertiary C–H insertion reaction might be improved by such substituent. In order to test this hypothesis, diazo compound **3.101** was synthesized and subjected to the intramolecular C–H insertion reaction (Table **3.22**). In the presence of $Rh_2(TCPTTL)_4$, the reaction of diazo compound **3.101** produced *β*-lactone **3.103** in 90% yield but with only 45% ee (entry 1). Changing the catalyst to $Rh_2(DOSP)_4$ resulted in lower enantioselectivity (entry 3). Compared to the reaction of diazo compound **3.102** (entry 4),[155] the *ortho*-bromo lowered the enantioselectivity instead of improving it. This observation indicated that steric effect is the key factor for the enantioselective synthesis *β*-lactone *via* the intramolecular insertion into a tertiary C–H bond. The bromo substituent at the *ortho*-position increased the steric environment around the tertiary C–H bond in **3.101**, which led to a loose transition state and resulted in the low level of asymmetric induction. The insertion into the tertiary C–H bond was so reactive that *β*-lactone **3.101** could also be synthesized from the reaction conducted at 0 °C, but the enantioselectivity remains moderate (entry 2).

Table 3.22 Intramolecular insertion at the tertiary C–H bond



entry	catalyst	R	diazo compound	temp (°C)	product	yield[a] (%)	ee (%)
1	Rh_2(*S*-TCPTTL)$_4$	Br	**3.101**	36	**3.103**	90	45
2	Rh_2(*S*-TCPTTL)$_4$	Br	**3.101**	0	**3.103**	50	48
3	Rh_2(*S*-DOSP)$_4$	Br	**3.101**	36	**3.103**	89	13
4[b]	Rh_2(*S*-DOSP)$_4$	H	**3.102**	36	**3.104**	69	63

[a] Isolated yield. [b] Reference (155).

3.3 Conclusion

Through the catalytic enantioselective intramolecular C–H insertion, a protocol for the construction of the dihydrobenzofuran core structure of lithospermic acid was established. Through rhodium-catalyzed intermolecular C–H insertion and the following palladium-catalyzed C–H functionalization, a new reaction sequence for rapidly construction of dihydrobenzofurans was set up. Products were isolated in a highly regio-, diastereo- and enantioselective fashion. A new method to access β-lactones was also discovered during these studies.

Experimental Section

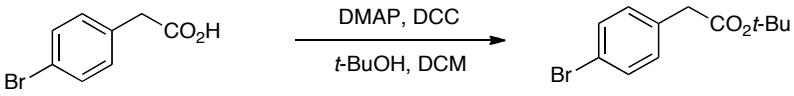
General methods

^{1}H Nuclear Magnetic Resonance (^{1}H-NMR) and ^{13}C Nuclear Magnetic Resonance (^{13}C-NMR) spectra were recorded on Varian Mercury 300, INOVA 400, VNMR 400, INOVA 600 and UNITY 600 MHz. NMR spectra were recorded in deuterated chloroform ($CDCl_3$) or acetone (CD_3COCD_3) at room temperature unless otherwise stated. The NMR data were presented as follows: chemical shift in ppm with tetramethylsilane (TMS, δ = 0.00 ppm) for ^{1}H-NMR and the residual of chloroform (δ = 77.0 ppm with chapters I and III; 77.23 ppm with chapter II) for ^{13}C-NMR as internal standards, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet, br. = broad), coupling constant (*J*/Hz), integration. IR spectra were collected on a Nicolet iS10 from Thermo Scientific and reported in unit of cm^{-1}. Mass spectra were recorded on a Finnigan LTQ FTMS mass spectrometer. Optical rotations were measured on a Jasco *p*-2000 polarimeter (concentration in g/100ml). Melting points were measured on a MEL-TEMP of Electrothermal (uncorrected).

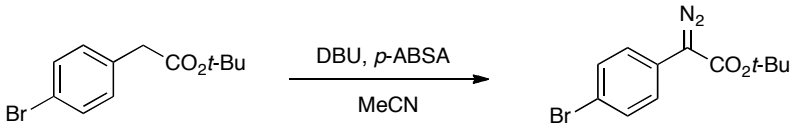
All reactions were performed under an argon atmosphere in oven or flamed dried glassware. Acetonitrile, tetrahydrofuran, dichloromethane and toluene were dried by a solvent purification system (passed through activated alumina columns). Analytical TLC was performed on silica gel plates using UV light or phosphomolybdic acid stain. Flash column chromatography was performed on silica gel 60Å (230-400 mesh) from Sorbent Technologies. Unless otherwise noted, all other chemical reagents were obtained from commercial sources and used as received.

Experimental for Chapter I: Asymmetric Cyclopropanation of Electron-Deficient Alkenes *via* Carbenoid Reactions

Exemplified procedure for the synthesis of *tert*-butyl aryldiazoacetate:



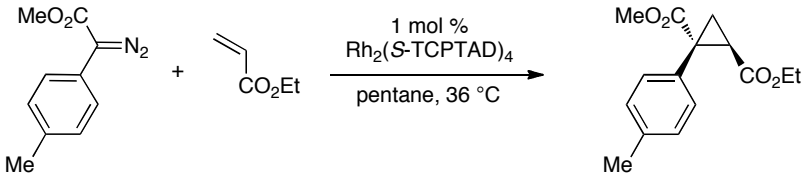
methyl *p*-bromophenylacetate (S1): To a solution of *p*-bromophenylacetic acid (6.2 g, 0.029 mol, 1 equiv), *tert*-butanol (6.8 g, 0.092 mol, 3 equiv) and DMAP (2.9 g, 0.024 mol, 0.8 equiv) in dichloromethane (30 ml) at 0 °C was added DCC (6.7 g, 0.032 mol, 1.1 equiv) slowly. The resulting mixture was warmed up slowly in the ice-water bath to room temperature and stirred overnight. The solid was filtered off and washed with hexanes. The filtrate was concentrated in vacuo and purified by flash chromatography (silica gel, hexanes:diethyl ether = 20:1) to afford the product as a pale yellow oil (5.0 g, 64% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.2 Hz, 2H), 3.48 (s, 2H), 1.43 (s, 9H).



methyl *p*-bromophenyldiazoacetate (S2): To a solution of **S1** (9.2 g, 0.034 mol, 1 equiv) and *p*-ABSA (12.2 g, 0.51 mol, 1.5 equiv) in acetonitrile at 0 °C was added DBU (10.0 ml, 0.067 mol, 2 equiv) in one portion. The resulting mixture was warmed up slowly in the ice-water bath to room temperature and stirred for 72 hours. The reaction was quenched with saturated ammonium chloride solution and then extracted with diethyl

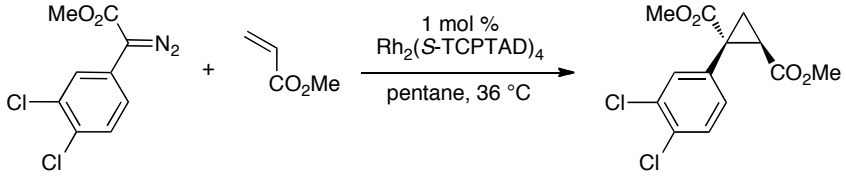
ether. The combined the organic layers were dried over magnesium sulfate. The solid was filtered off and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:diethyl ether = 20:1) to afford the product as a yellow solid (8.0 g, 79% yield). The spectroscopic data were consistent with the published values.[178] ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.6 Hz, 2H), 7.35 (d, J = 8.6 Hz, 2H), 1.54 (s, 9H).

General procedure (A) - the Rh_2(*S*-TCPTAD)$_4$ catalyzed cyclopropanations of electron deficient alkenes: Under argon atmosphere, to a solution of alkene (5 equiv) and Rh_2(*S*-TCPTAD)$_4$ (0.01 equiv) in pentane (5 ml) at reflux was added a solution of diazo compound (0.3-0.5 mmol, 1 equiv) in pentane (5 ml) over 2 hours. The resulting mixture was stirred at reflux for an additional hour before cooling down to room temperature. The solvent was removed under vacuum and the crude mixture was purified by flash chromatography.

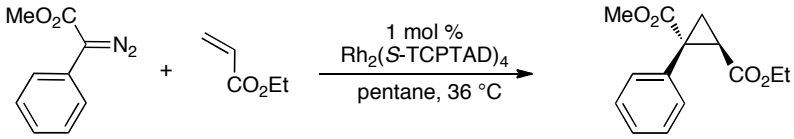


(1*R*,2*R*)-2-ethyl 1-methyl 1-(*p*-tolyl)cyclopropane-1,2-dicarboxylate (1.26): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.14 ml, 1.28 mmol, 5 equiv), methyl *p*-methylphenyldiazoacetate (48.1 mg, 0.25 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (5.5 mg, 0.0026 mmol, 0.01 equiv) afforded the product as a colorless oil (40.7 mg, 61% yield) after purification by flash chromatography. R_f = 0.27 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -81.2 (c 0.99, $CHCl_3$); FTIR (neat): 2954, 1720, 1519, 1436, 1398, 1381,

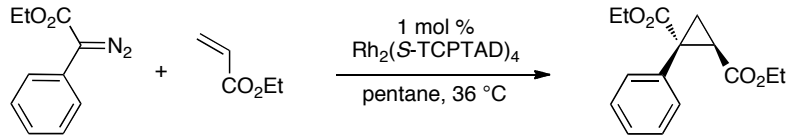
1257, 1181, 1159, 1097, 1037 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.14 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 3.98-3.80 (m, 2H), 3.64 (s, 3H), 2.72 (dd, J = 8.3, 6.7 Hz, 1H), 1.99 (dd, J = 6.5, 4.4 Hz, 1H), 1.86 (dd, J = 8.5, 4.4 Hz, 1H), 1.01 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.0, 169.0, 137.3, 131.5, 130.3, 128.8, 60.8, 52.9, 36.2, 29.7, 21.2, 19.5, 13.9; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{15}H_{18}O_4{}^{23}Na_1$, 285.1097; found, 285.1098; HPLC analysis: 84% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 9.05 min, minor; t_R = 10.25 min, major).



(1*R*,2*R*)-dimethyl 1-(3,4-dichlorophenyl)cyclopropane-1,2-dicarboxylate (1.28): Following the general procedure **(A)**, the reaction of methyl acrylate (0.14 ml, 1.55 mmol, 5 equiv), methyl 3,4-dichlorophenyldiazoacetate (71.5 mg, 0.29 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.0 mg, 0.0029 mmol, 0.01 equiv) afforded the product as a colorless oil (62.2 mg, 70% yield) after purification by flash chromatography. R_f = 0.33 (hexanes:ethyl acetate = 10:1); $[\alpha]_D{}^{20}$ -61.3 (c 0.87, $CHCl_3$); FTIR (neat): 2953, 1726, 1475, 1436, 1260, 1207, 1207, 1165, 1135, 1095, 1032 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.3 Hz, 1H), 7.35 (d, J = 2.1 Hz, 1H), 7.08 (dd, J = 8.3, 2.1 Hz, 1H), 3.66 (s, 3H), 3.53 (s, 3H), 2.76 (dd, J = 8.5, 6.6 Hz, 1H), 1.96 (dd, J = 6.6, 4.6 Hz, 1H), 1.92 (dd, J = 8.5, 4.6 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.7, 169.1, 134.9, 132.5, 132.1, 132.0, 130.1, 129.8, 53.1, 52.2, 35.7, 29.5, 19.7; HRMS (ESI) *m/z*: $[M-H]^-$ calcd. for $C_{13}H_{11}O_4{}^{35}Cl_2$, 301.0040; found, 301.0040; HPLC analysis: 92% ee (AD-H, hexane, 1.0 mL/min, λ = 210 nm, t_R = 18.49 min, minor; , t_R = 20.69 min, major).

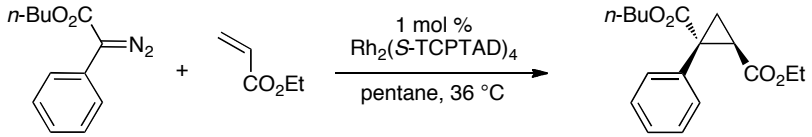


(1*R*,2*R*)-2-ethyl 1-methyl 1-phenylcyclopropane-1,2-dicarboxylate (1.31): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.16 ml, 1.47 mmol, 5 equiv), methyl phenyldiazoacetate (58.3 mg, 0.33 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.0 mg, 0.0029 mmol, 0.01 equiv) afforded the product as a colorless oil (68.2 mg, 83% yield) after purification by flash chromatography. R_f = 0.27 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -78.7 (c 1.06, $CHCl_3$); FTIR (neat): 2954, 1719, 1436, 1382, 1254, 1185, 1100, 1036 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33-7.22 (m, 5H), 3.94-3.78 (m, 2H), 3.65 (s, 3H), 2.74 (dd, *J* = 8.5, 6.6 Hz, 1H), 2.02 (dd, *J* = 6.6, 4.5 Hz, 1H), 1.88 (dd, *J* = 8.5, 4.4 Hz, 1H), 0.97 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.8, 168.9, 134.6, 130.5, 128.0, 127.7, 60.8, 52.9, 36.5, 29.7, 19.4, 13.8; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{16}O_4{}^{23}Na_1$, 271.0941; found, 271.0940; HPLC analysis: 86% ee (*SS*-Whelk, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 16.92 min, minor; t_R = 22.97 min, major).



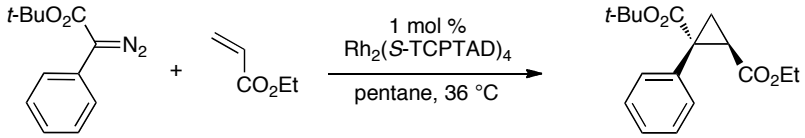
(1*R*,2*R*)-diethyl 1-phenylcyclopropane-1,2-dicarboxylate (1.32): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.27 ml, 2.48 mmol, 5 equiv), ethyl phenyldiazoacetate (89.3 mg, 0.47 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.2 mg, 0.0049 mmol, 0.01 equiv) afforded the product as a colorless oil (95.7 mg, 78% yield)

after purification by flash chromatography. R_f = 0.27 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -67.2 (c 1.06, $CHCl_3$); FTIR (neat): 2981, 1717, 1447, 1382, 1367, 1252, 1193, 1158, 1096, 1037 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32-7.22 (m, 5H), 4.18-4.02 (m, 2H), 3.93-3.77 (m, 2H), 2.73 (dd, *J* = 8.5, 6.6 Hz, 1H), 2.02 (dd, *J* = 6.5, 4.5 Hz, 1H), 1.87 (dd, *J* = 8.5, 4.4 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.1, 168.9, 134.6, 130.6, 127.8, 127.5, 61.6, 60.6, 36.7, 29.5, 19.03, 13.9, 13.7; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{15}H_{19}O_4$, 263.1291; found, 263.1278; HPLC analysis: 85% ee (*SS*-Whelk, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 16.11 min, minor; , t_R = 22.03 min, major).

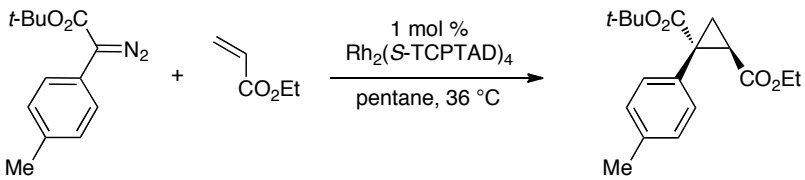


(1*R*,2*R*)-1-butyl 2-ethyl 1-phenylcyclopropane-1,2-dicarboxylate (1.33): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.27 ml, 2.48 mmol, 5 equiv), *n*-butyl phenyldiazoacetate (110.0 mg, 0.50 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.5 mg, 0.0050 mmol, 0.01 equiv) afforded the product as a colorless oil (123.3 mg, 84% yield) after purification by flash chromatography. R_f = 0.30 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -64.1 (c 1.08, $CHCl_3$); FTIR (neat): 2961, 2874, 1720, 1498, 1448, 1380, 1255, 1193, 1164, 1100, 1037 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32-7.22 (m, 5H), 4.13-3.96 (m, 2H), 3.94-3.78 (m, 2H), 2.73 (dd, *J* = 8.4, 6.6 Hz, 1H), 2.02 (dd, *J* = 6.5, 4.5 Hz, 1H), 1.91-1.83 (m, 1H), 1.51 (tt, *J* = 7.2, 6.8 Hz, 2H), 1.24 (qt, *J* = 7.6, 7.2 Hz, 2H), 0.97 (t, *J* = 7.1 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.1, 168.9, 134.7, 130.4, 127.8, 127.5, 65.4, 60.6, 36.7, 30.3, 29.4, 19.0, 18.8, 13.7,

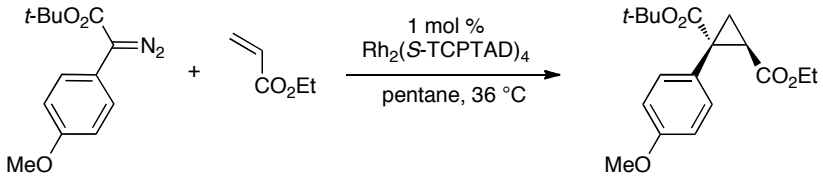
13.5; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{22}O_4{}^{23}Na_1$, 313.1410; found, 313.1310; HPLC analysis: 81% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 9.64 min, minor; , t_R = 0.74 min, major).



(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-phenylcyclopropane-1,2-dicarboxylate (1.34): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.27 ml, 2.48 mmol, 5 equiv), *t*-butyl phenyldiazoacetate (114.8 mg, 0.53 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (9.8 mg, 0.0047 mmol, 0.01 equiv) afforded the product as a colorless oil (118.9 mg, 78% yield) after purification by flash chromatography. R_f = 0.30 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -61.9 (c 1.00, $CHCl_3$); FTIR (neat): 2979, 1713, 1448, 1393, 1382, 1368, 1254, 1196, 1151, 1098 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32-7.19 (m, 5H), 3.92-3.78 (m, 2H), 2.66 (dd, *J* = 8.4, 6.5 Hz, 1H), 1.97 (dd, *J* = 6.4, 4.4 Hz, 1H), 1.81 (dd, *J* = 8.4, 4.4 Hz, 1H), 1.37 (s, 9H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 171.0, 169.3, 135.19, 130.5, 127.8, 127.3, 81.6, 60.6, 37.7, 29.0, 27.8, 18.7, 13.8; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{23}O_4$, 291.1591; found, 291.1592; HPLC analysis: 91% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 6.16 min, major; , t_R = 6.96 min, minor).

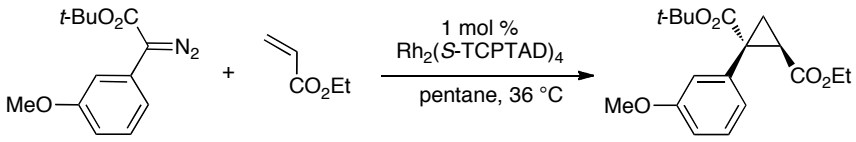


(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(*p*-tolyl)cyclopropane-1,2-dicarboxylate (1.35): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.16 ml, 1.47 mmol, 5 equiv), *t*-butyl *p*-methylphenyldiazoacetate (72.2 mg, 0.31 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.6 mg, 0.0031 mmol, 0.01 equiv) afforded the product as a colorless oil (57.7 mg, 61% yield) after purification by flash chromatography. R_f = 0.39 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -58.1 (c 1.02, $CHCl_3$); FTIR (neat): 2979, 1714, 1518, 1457, 1393, 1381, 1368, 1271, 1254, 1196, 1153, 1098, 1035 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.12 (d, J = 8.2 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 3.95-3.81 (m, 2H), 2.63 (dd, J = 8.4, 6.4 Hz, 1H), 2.31 (s, 3H), 1.94 (dd, J = 6.4, 4.4 Hz, 1H), 1.79 (dd, J = 8.4, 4.4 Hz, 1H), 1.37 (s, 9H), 0.99 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.1, 169.3, 136.8, 132.0, 130.2, 128.5, 81.4, 60.6, 37.4, 28.9, 27.8, 21.1, 18.6, 13.8; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{25}O_4$, 305.1747; found, 305.1751; HPLC analysis: 89% ee (AD-H, hexane, 1.0 mL/min, λ = 230 nm, t_R = 5.39 min, minor; , t_R = 6.31 min, major).



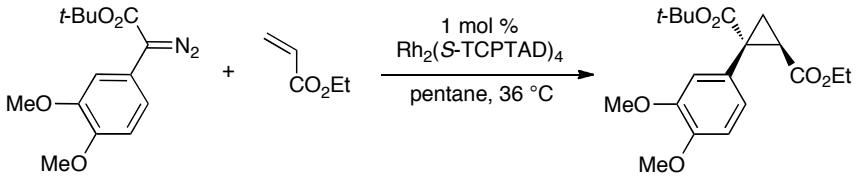
(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(4-methoxyphenyl)cyclopropane-1,2-dicarboxylate (1.36): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.27 ml, 2.48 mmol, 5 equiv), *t*-butyl *p*-methoxyphenyldiazoacetate (124.1 mg, 0.50 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.4 mg, 0.0049 mmol, 0.01 equiv) afforded the product as a colorless oil (143.0 mg, 89% yield) after purification by flash chromatography. R_f = 0.16 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -46.5 (c 0.97, $CHCl_3$); FTIR (neat): 2979, 1715,

1614, 1516, 1458, 1393, 1382, 1368, 1273, 1246, 1197, 1152, 1098 cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.16 (d, J = 8.7 Hz, 2H), 6.80 (d, J = 8.7 Hz, 2H), 3.94-3.83 (m, 2H), 3.78 (s, 3H), 2.62 (dd, J = 8.3, 6.4 Hz, 1H), 1.93 (dd, J = 6.4, 4.4 Hz, 1H), 1.79 (dd, J = 8.4, 4.3 Hz, 1H), 1.37 (s, 9H), 1.00 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.1, 169.1, 158.5, 131.3, 127.0, 113.0, 81.2, 60.4, 54.9, 36.8, 28.9, 27.6, 18.6, 13.8; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{25}O_5$, 321.1697; found, 321.1696; HPLC analysis: 88% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 230 nm, t_R = 9.88 min, minor; t_R = 11.87 min, major).

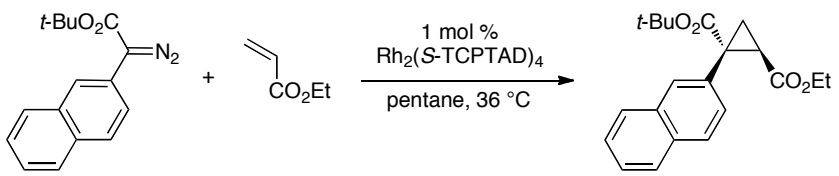


(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(3-methoxyphenyl)cyclopropane-1,2-dicarboxylate (1.37): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.16 ml, 1.47 mmol, 5 equiv), *t*-butyl *p*-methylphenyldiazoacetate (76.6 mg, 0.31 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.6 mg, 0.0031 mmol, 0.01 equiv) afforded the product as a colorless oil (74.4 mg, 75% yield) after purification by flash chromatography. R_f = 0.17 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -58.4 (c 1.02, $CHCl_3$); FTIR (neat): 2979, 1716, 1603, 1585, 1455, 1382, 1273, 1256, 1238, 1195, 1154, 1102 cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.18 (td, J = 7.7, 0.7 Hz, 1H), 6.84 (dt, J = 7.8, 1.2, 1H), 6.80-6.77 (m, 2H), 3.92-3.84 (m, *2*H), 3.78 (s, 3H), 2.64 (dd, J = 8.4, 6.5 Hz, 1H), 1.95 (dd, J = 6.4, 4.4 Hz, 1H), 1.79 (dd, J = 8.4, 4.4 Hz, 1H), 1.37 (s, 9H), 0.98 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.8, 169.2, 159.0, 136.6, 128.6, 122.9, 116.1, 112.8, 81.5, 60.6, 55.0, 37.6, 28.9, 27.7, 18.7, 13.8; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{24}O_5{}^{23}Na_1$,

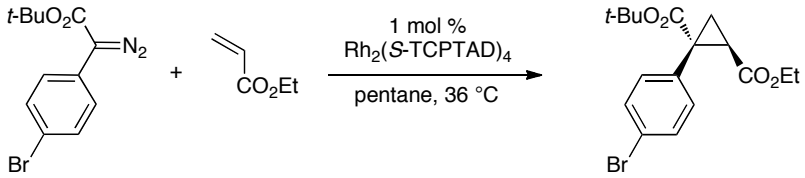
343.1516; found, 343.1517; HPLC analysis: 94% ee (AD-H, hexane, 1.0 mL/min, λ = 230 nm, t_R = 9.34 min, minor; t_R = 10.17 min, major).



(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(3,4-dimethoxyphenyl)cyclopropane-1,2-dicarboxylate (1.38): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.27 ml, 2.47 mmol, 5 equiv), *t*-butyl 3,4-dimethoxyphenyldiazoacetate (140.5 mg, 0.50 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.8 mg, 0.0051 mmol, 0.01 equiv) afforded the product as a colorless oil (161.8 mg, 91% yield) after purification by flash chromatography. R_f = 0.23 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -52.0 (c 1.00, $CHCl_3$); FTIR (neat): 2978, 1713, 1590, 1518, 1464, 1413, 1393, 1381, 1368, 1251, 1227, 1194, 1140, 1097, 1028 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.81 (dd, J = 8.2, 1.9 Hz, 1H), 6.78-6.76 (m, 2H), 3.94-3.86 (m, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 2.63 (dd, J = 8.4, 6.4 Hz, 1H), 1.95 (dd, J = 6.4, 4.4 Hz, 1H), 1.79 (dd, J = 8.4, 4.4 Hz, 1H), 1.38 (s, 9H), 1.01 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.9, 169.1, 148.0, 148.0, 127.4, 122.5, 113.4, 110.1, 81.3, 60.5, 55.53, 55.46, 37.2, 28.9, 27.6, 18.6, 13.8; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{19}H_{26}O_6{}^{23}Na_1$, 373.1622; found, 373.1621; HPLC analysis: 93% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 19.79 min, major; t_R = 26.90 min, minor).

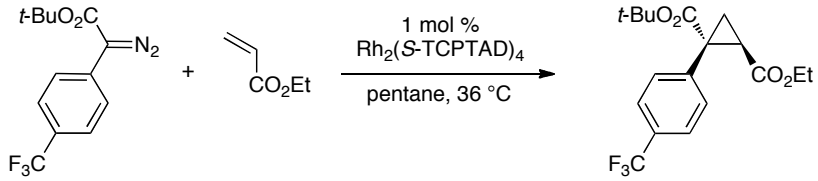


(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(naphthalen-2-yl)cyclopropane-1,2-dicarboxylate (1.39): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.27 ml, 2.47 mmol, 5 equiv), *t*-butyl 2-naphtyldiazoacetate (127.8 mg, 0.48 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.6 mg, 0.0050 mmol, 0.01 equiv) afforded the product as a colorless oil (140.2 mg, 86% yield) after purification by flash chromatography. R_f = 0.23 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -16.2 (c 0.95, $CHCl_3$); FTIR (neat): 2979, 2360, 1716, 1457, 1394, 1382, 1369, 1276, 1256, 1190, 1153, 1130 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 9.2, 4.5 Hz, 2H), 7.75-7.72 (m, 2H), 7.47-7.41 (m, 2H), 7.36 (dd, *J* = 8.4, 1.8 Hz, 1H), 3.89-3.71 (m, 2H), 2.73 (dd, *J* = 8.4, 6.4 Hz, 1H), 2.10 (dd, *J* = 6.4, 4.4 Hz, 1H), 1.90 (dd, *J* = 8.4, 4.4 Hz, 1H), 1.36 (s, 9H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.9, 169.1, 133.0, 132.64, 132.60, 129.2, 128.5, 127.7, 127.5, 127.2, 125.7 (2xC), 81.7, 60.6, 37.8, 29.1, 27.7, 18.8, 13.7; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{21}H_{24}O_4{}^{23}Na_1$, 363.1567; found, 363.1567; HPLC analysis: 94% ee (AD-H, hexane, 1.0 mL/min, λ = 230 nm, t_R = 8.10 min, major; t_R = 9.17 min, minor).



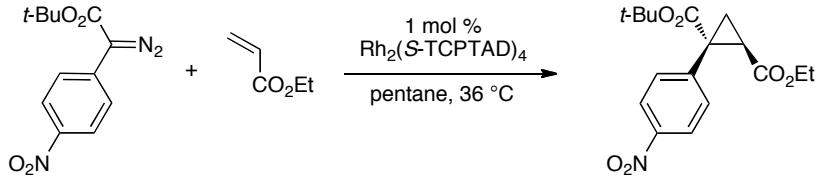
(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(4-bromophenyl)cyclopropane-1,2-dicarboxylate (1.40): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.27 ml, 2.47 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (151.3 mg, 0.51 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.6 mg, 0.0050 mmol, 0.01 equiv) afforded the product as a colorless oil (166.7 mg, 89% yield) after purification by flash chromatography. R_f = 0.39 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -38.4 (c 0.92, $CHCl_3$); FTIR (neat): 2979, 1715,

1490, 1394, 1381, 1368, 1276, 1254, 1197, 1150, 1094, 1033, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 3.96-3.82 (m, 2H), 2.65 (dd, J = 8.4, 6.5 Hz, 1H), 1.92 (dd, J = 6.4, 4.5 Hz, 1H), 1.82 (dd, J = 8.5, 4.5 Hz, 1H), 1.37 (s, 9H), 1.01 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.7, 168.9, 147.2, 143.0, 131.5, 123.1, 82.6, 61.1, 37.4, 29.2, 27.8, 19.1, 14.0; HRMS (ESI) *m/z*: $[M+NH_4]^+$ calcd. for $C_{17}H_{25}O_4N_1{}^{79}Br_1$, 386.0962; found, 386.0962; HPLC analysis: 93% ee (AD-H, hexane, 0.25 mL/min, λ = 230 nm, t_R = 22.13 min, minor; t_R = 24.31 min, major).

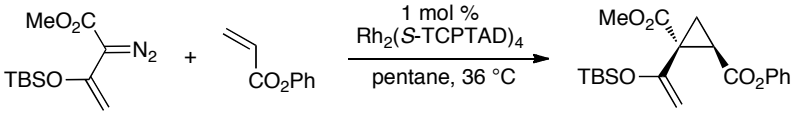


(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(4-(trifluoromethyl)phenyl)cyclopropane-1,2-dicarboxylate (1.41): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.16 ml, 1.47 mmol, 5 equiv), *t*-butyl *p*-trifluoromethyphenyldiazoacetate (87.5 mg, 0.31 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.1 mg, 0.0029 mmol, 0.01 equiv) afforded the product as a colorless oil (70.1 mg, 64% yield) after purification by flash chromatography. R_f = 0.33 (hexanes:ethyl acetate = 10:1); $[\alpha]_D{}^{20}$ -43.7 (c 0.92, $CHCl_3$); FTIR (neat): 2982, 1720, 1620, 1458, 1395, 1370, 1325, 1275, 1201, 1158, 1126, 1067, 1035, 1019 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 3.88 (qd, J = 7.1, 2.6 Hz, 2H), 2.69 (dd, J = 8.4, 6.5 Hz, 1H), 1.98 (dd, J = 6.4, 4.5 Hz, 1H), 1.87 (dd, J = 8.5, 4.5 Hz, 1H), 1.37 (s, 9H), 0.97 (t, J = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.2, 169.0, 139.4, 130.9, 129.50 (q, J = 32 Hz), 122.9 (q, J = 269 Hz), 124.8 (q, J = 4 Hz), 82.2, 60.9, 37.4, 291, 27.8, 18.8, 13.8; HRMS (ESI) *m/z*:

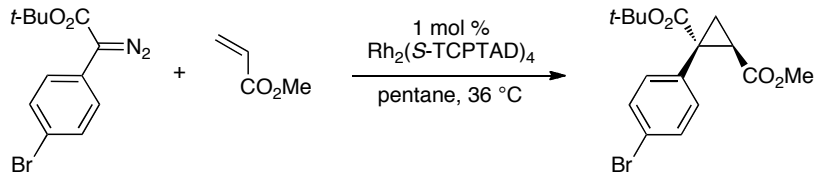
$[M+NH_4]^+$ calcd. for $C_{18}H_{25}O_4N_1F_3$, 376.1730; found, 376.1733; HPLC analysis: 91% ee (*SS*-Whelk, 1% *i*-PrOH hexane, 1 mL/min, λ = 210 nm, t_R = 6.21 min, minor; t_R = 7.61 min, major).



(1*R*,2*R*)-1-*tert*-butyl 2-ethyl 1-(4-nitrophenyl)cyclopropane-1,2-dicarboxylate (1.42): Following the general procedure **(A)**, the reaction of ethyl acrylate (0.17 ml, 1.56 mmol, 5 equiv), *t*-butyl *p*-nitrophenyldiazoacetate (75.3 mg, 0.29 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.6 mg, 0.0031 mmol, 0.01 equiv) afforded the product as a yellow oil (21.5 mg, 22% yield) after purification by flash chromatography. R_f = 0.29 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -9.5 (c 1.02, $CHCl_3$); FTIR (neat): 2980, 2358, 1719, 1603, 1522, 1457, 1394, 1382, 1369, 1348, 1294, 1257, 1200, 1154, 1096 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 2H), 3.98-3.85 (m, 2H), 2.73 (dd, *J* = 8.5, 6.5 Hz, 1H), 1.98 (dd, *J* = 6.4, 4.6 Hz, 1H), 1.92 (dd, *J* = 8.5, 4.6 Hz, 1H), 1.37 (s, 9H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.7, 168.9, 147.2, 143.0, 131.5, 123.1, 82.6, 61.1, 37.4, 29.2, 27.8, 19.1, 14.0; HRMS (ESI) *m/z*: $[M-H]^-$ calcd. for $C_{17}H_{20}O_6N_1$, 334.1296; found, 334.1297; HPLC analysis: 91% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 13.22 min, minor; t_R = 17.75 min, major).

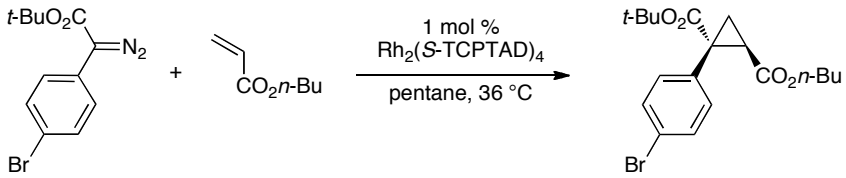


(1*R*,2*R*)-1-methyl 2-phenyl 1-(1-((*tert*-butyldimethylsilyl)oxy)vinyl)cyclopropane-1,2-dicarboxylate (1.45): Following the general procedure **(A)**, the reaction of phenyl acrylate (0.17 ml, 1.05 mmol, 5 equiv), methyl *tert*-butyldimethylsiloxyvinyldiazoacetate (**1.43**, 75.3 mg, 0.29 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (4.4 mg, 0.0021 mmol, 0.01 equiv) afforded the product as a colorless oil (38.3 mg, 41% yield) after purification by flash chromatography. R_f = 0.40 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -74.2 (c 0.95, $CHCl_3$); FTIR (neat): 2955, 2857, 1720, 1640, 1592, 1494, 1436, 1387, 1268, 1162, 1140, 1070, 1005 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34 (t, J = 7.9 Hz, 2H), 7.19 (t, J = 7.4 Hz, 2H), 7.10 (d, J = 7.6 Hz, 2H), 4.41 (d, J = 1.7 Hz, 1H), 4.37 (d, J = 1.7 Hz, 1H), 3.74 (s, 3H), 2.75 (dd, J = 8.3, 6.7 Hz, 1H), 1.93 (dd, J = 6.6, 4.5 Hz, 1H), 1.71 (dd, J = 8.4, 4.4 Hz, 1H), 0.88 (s, 9H), 0.22 (s, 3H), 0.18 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.8, 167.5, 152.0, 150.7, 129.1, 125.6, 121.3, 95.0, 52.6, 38.4, 27.8, 25.5, 20.7, 18.0, -4.3, -5.8; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{20}H_{29}O_5{}^{28}Si_1$, 377.1779; found, 377.1780; HPLC analysis: 94% ee (AD-H, 0.5% *i*-PrOH in hexane 1.0 mL/min, λ = 210 nm, t_R = 8.07 min, major; t_R = 10.00 min, minor).



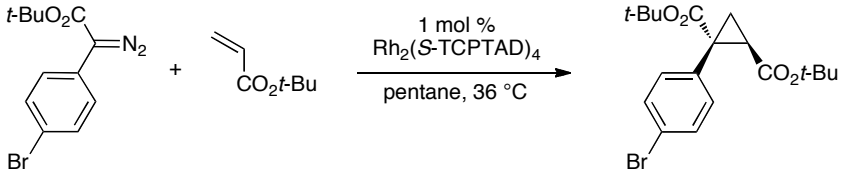
(1*R*,2*R*)-1-*tert*-butyl 2-methyl 1-(4-bromophenyl)cyclopropane-1,2-dicarboxylate (1.46): Following the general procedure **(A)**, the reaction of methyl acrylate (0.14 ml, 1.55 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (91.3 mg, 0.31 mmol, 1 equiv)

and Rh_2(*S*-TCPTAD)$_4$ (6.2 mg, 0.0029 mmol, 0.01 equiv) afforded the product as a colorless oil (102.2 mg, 89% yield) after purification by flash chromatography. R_f = 0.31 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -44.5 (c 1.06, $CHCl_3$); FTIR (neat): 2978, 1716, 1439, 1383, 1278, 1256, 1205, 1154, 1090, 1012 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 3.46 (s, 3H), 2.67 (dd, J = 8.4, 6.5 Hz, 1H), 1.92 (dd, J = 6.4, 4.5 Hz, 1H), 1.83 (dd, J = 8.5, 4.5 Hz, 1H), 1.36 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.4, 169.5, 134.3, 132.1, 131.0, 121.5, 82.0, 52.0, 37.2, 28.8, 27.8, 18.8; HRMS (APCI) *m/z*: $[M-H]^-$ calcd. for $C_{16}H_{18}O_4{}^{79}Br_1$, 353.0394; found, 353.0396; HPLC analysis: 96% ee (AD-H, hexane, 0.25 mL/min, λ = 230 nm, t_R = 26.00 min, major; t_R = 32.15 min, minor).

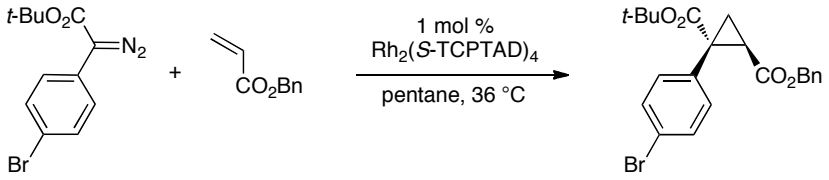


(1*R*,2*R*)-1-*tert*-butyl 2-butyl 1-(4-bromophenyl)cyclopropane-1,2-dicarboxylate (1.47): Following the general procedure **(A)**, the reaction of *n*-butyl acrylate (0.22 ml, 1.53 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (94.6 mg, 0.32 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.5 mg, 0.0031 mmol, 0.01 equiv) afforded the product as a colorless oil (102.3 mg, 81% yield) after purification by flash chromatography. R_f = 0.30 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -32.3 (c 1.06, $CHCl_3$); FTIR (neat): 2961, 1718, 1490, 1457, 1395, 1369, 1277, 1256, 1200, 1155, 1094, 1070, 1012 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 3.88-3.77 (m, 2H), 2.65 (dd, J = 8.4, 6.5 Hz, 1H), 1.91 (dd, J = 6.4, 4.5 Hz, 1H), 1.82 (dd, J = 8.5, 4.4 Hz, 1H), 1.37 (s, 9H), 1.35-1.29 (m, 2H), 1.24-1.12 (m, 2H), 0.85 (t, J = 7.3 Hz, 3H); ^{13}C-

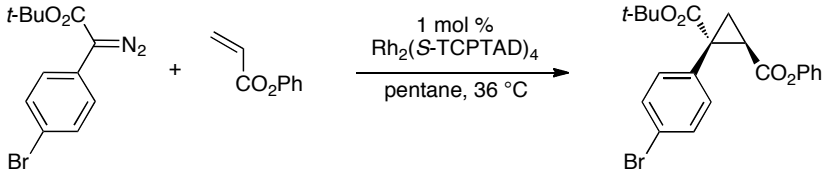
NMR (100 MHz, $CDCl_3$) δ 170.4, 169.1, 134.5, 132.4, 131.0, 121.4, 81.9, 64.7, 37.1, 30.4, 29.0, 27.8, 18.9, 18.7, 13.5; HRMS (APCI) *m/z*: $[M-H]^-$ calcd. for $C_{19}H_{24}O_4{}^{79}Br_1$, 395.0863; found, 395.0865; HPLC analysis: 93% ee (AD-H, hexane, 1.0 mL/min, λ = 230 nm, t_R = 5.95 min, minor; t_R = 6.84 min, major).



(1*R*,2*R*)-di-*tert*-butyl 1-(4-bromophenyl)cyclopropane-1,2-dicarboxylate (1.48): Following the general procedure **(A)**, the reaction of *t*-butyl acrylate (0.37 ml, 2.53 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (137.3 mg, 0.46 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.4 mg, 0.0049 mmol, 0.01 equiv) afforded the product as a white solid (157.1 mg, 86% yield) after purification by flash chromatography. m.p. 51-53 $^{\circ}$C; R_f = 0.30 (hexanes:ethyl acetate = 10:1); $[\alpha]_D{}^{20}$ -32.6 (c 0.98, $CHCl_3$); FTIR (neat): 2978, 2932, 1716, 1490, 1457, 1392, 1368, 1279, 1255, 1217, 1145, 1140, 1095, 1012 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 2.55 (dd, *J* = 8.4, 6.5 Hz, 1H), 1.85 (dd, *J* = 6.5, 4.4 Hz, 1H), 1.76 (dd, *J* = 8.5, 4.4 Hz, 1H), 1.37 (s, 9H), 1.19 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.6, 168.0, 134.5, 132.4, 130.8, 121.3, 81.8, 81.0, 37.0, 30.0, 27.8, 27.7, 18.7; HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{19}H_{25}O_4{}^{79}Br_1{}^{39}K_1$, 435.0568; found, 435.0569; HPLC analysis: 93% ee (AD-H, hexane, 0.25 mL/min, λ = 230 nm, t_R = 17.65 min, minor; t_R = 19.09 min, major).

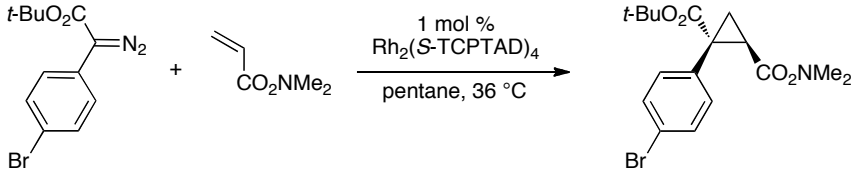


(1*R*,2*R*)-2-benzyl 1-*tert*-butyl 1-(4-bromophenyl)cyclopropane-1,2-dicarboxylate (1.49): Following the general procedure **(A)**, the reaction of benzyl acrylate (0.23 ml, 1.50 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (87.8 mg, 0.30 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.3 mg, 0.0030 mmol, 0.01 equiv) afforded the product as a colorless oil (59.3 mg, 47% yield) after purification by flash chromatography. R_f = 0.30 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -11.5 (c 0.91, $CHCl_3$); FTIR (neat): 2977, 1716, 1490, 1456, 1393, 1368, 1256, 1191, 1152, 1089, 1012 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33-7.29 (m, 5H), 7.13-7.08 (m, 2H), 7.03 (d, J = 8.4 Hz, 2H), 4.91 (d, J = 12.1 Hz, 1H), 4.82 (d, J = 12.1 Hz, 1H), 2.70 (dd, J = 8.4, 6.5 Hz, 1H), 1.92 (dd, J = 6.4, 4.5 Hz, 1H), 1.82 (dd, J = 8.4, 4.5 Hz, 1H), 1.35 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.3, 169.0, 135.3, 134.2, 132.1, 131.1, 128.6, 128.5, 128.3, 121.5, 82.0, 66.9, 37.4, 29.0, 27.8, 18.9; HRMS (APCI) *m/z*: $[M-H]^-$ calcd. for $C_{22}H_{22}O_4{}^{79}Br_1$, 429.0707; found, 429.0707; HPLC analysis: 90% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 7.69 min, minor; t_R = 13.60 min, major).



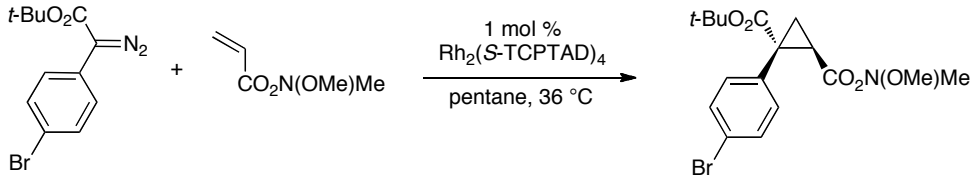
(1*R*,2*R*)-1-*tert*-butyl 2-phenyl 1-(4-bromophenyl)cyclopropane-1,2-dicarboxylate (1.50): Following the general procedure **(A)**, the reaction of phenyl acrylate (219.7 mg, 1.48 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (91.6 mg, 0.31 mmol, 1 equiv)

and Rh_2(*S*-TCPTAD)$_4$ (6.8 mg, 0.0032 mmol, 0.01 equiv) afforded the product as a white solid (94.6 mg, 74% yield) after purification by flash chromatography. m.p. 135-137 °C; R_f = 0.40 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -54.8 (c 1.01, $CHCl_3$); FTIR (neat): 2978, 1757, 1717, 1593, 1491, 1457, 1382, 1369, 1279, 1254, 1198, 1155, 1140, 1107, 1093, 1071, 1012 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2H), 7.31-7.21 (m, 5H), 7.15 (t, J = 7.4 Hz, 1H), 6.66 (d, J = 7.7 Hz, 2H), 2.90 (dd, J = 8.4, 6.4 Hz, 1H), 2.10 (dd, J = 6.4, 4.7 Hz, 1H), 1.95 (dd, J = 8.4, 4.7 Hz, 1H), 1.40 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.2, 167.6, 150.3, 134.1, 132.4, 131.2, 129.3, 125.8, 121.8, 121.1, 82.3, 37.8, 29.0, 27.9, 19.0; HRMS (APCI) *m/z*: $[M-H]^-$ calcd. for $C_{21}H_{20}O_4{}^{79}Br_1$, 415.0550; found, 415.0551; HPLC analysis: 93% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 7.99 min, minor; t_R = 13.14 min, major).

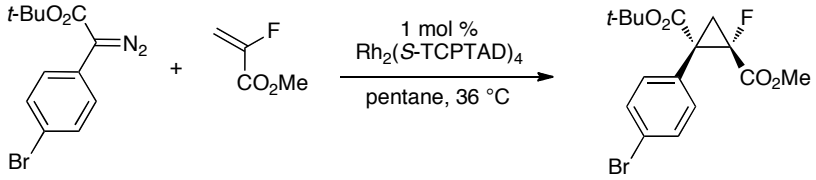


(1*R*,2*R*)-*tert*-butyl 1-(4-bromophenyl)-2-(dimethylcarbamoyl)cyclopropanecarboxylate (1.51): Following the general procedure **(A)**, the reaction of *N,N*-dimethylacrylamide (0.15 ml, 1.46 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (93.9 mg, 0.32 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.7 mg, 0.0032 mmol, 0.01 equiv) afforded the product as a white solid (62.2 mg, 52% yield) after purification by flash chromatography. m.p. 137-139 °C; R_f = 0.40 (hexanes:acetone = 2:1); $[\alpha]_D^{20}$ +41.6 (c 1.23, $CHCl_3$); FTIR (neat): 2977, 1714, 1652, 1490, 1457, 1399, 1368, 1341, 1279, 1256, 1156, 1084, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.5 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 3.21 (s, 3H), 2.79 (s, 3H), 2.78-2.74 (m, 1H), 2.13 (dd, J = 6.3, 4.3 Hz, 1H), 1.69 (dd, J =

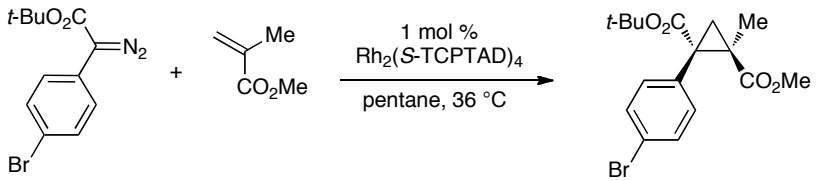
8.5, 4.3 Hz, 1H), 1.38 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.1, 167.1, 134.2, 131.8, 131.0, 121.330, 81.7, 37.1, 36.6, 35.5, 28.6, 27.8, 18.0; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{23}O_3N_1{}^{79}Br_1$, 368.0856; found, 368.0857; HPLC analysis: 94% ee (AD-H, 3% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 17.88 min, minor; t_R = 21.63 min, major).



(1*R*,2*R*)-*tert*-butyl 1-(4-bromophenyl)-2-(methoxy(methyl)carbamoyl)cyclopropane-carboxylate (1.52): Following the general procedure **(A)**, the reaction of *N,O*-dimethylacrylamide (286.5 mg, 2.49 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (156.8 mg, 0.53 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.6 mg, 0.0050 mmol, 0.01 equiv) afforded the product as a white solid (119.1 mg, 59% yield) after purification by flash chromatography. m.p. 100-102 $^{\circ}$C; R_f = 0.20 (hexanes:ethyl acetate = 4:1); $[\alpha]_D{}^{20}$ +65.7 (c 1.05, $CHCl_3$); FTIR (neat): 2976, 2935, 1716, 1670, 1490, 1459, 1415, 1392, 1368, 1323, 1275, 1256, 1155, 1116, 1082, 1012 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 3.82 (s, 3H), 3.09-2.95 (m, 4H), 2.02 (dd, *J* =6.4, 4.3 Hz, 1H), 1.79 (dd, *J* = 8.4, 4.3 Hz, 1H), 1.38 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.0, 169.5, 134.3, 132.3, 130.9, 121.3, 81.6, 61.6, 36.9, 32.8, 27.8, 27.4, 17.4; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{23}O_4N_1{}^{79}Br_1$, 384.0805; found, 384.0806; HPLC analysis: 92% ee (AD-H, 5% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 7.20 min, minor; t_R = 10.51 min, major).

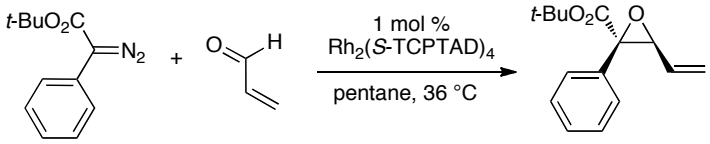


(1*R*,2*S*)-1-*tert*-butyl 2-methyl 1-(4-bromophenyl)-2-fluorocyclopropane-1,2-dicarboxylate (1.53): Following the general procedure **(A)**, the reaction of methyl 2-fuoroacrylate (0.14 ml, 1.50 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (91.2 mg, 0.31 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.3 mg, 0.0030 mmol, 0.01 equiv) afforded the product as a white solid (95.9 mg, 84% yield). m.p. 77-79 $^{\circ}$C; R_f = 0.30 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ +27.2 (c 0.84, $CHCl_3$); FTIR (neat): 2978, 1749, 1729, 1490, 1440, 1395, 1369, 1355, 1325, 1276, 1256, 1237, 1198, 1155, 1107, 1077, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 3.55 (s, 3H), 2.58 (dd, J = 17.9, 7.1 Hz, 1H), 2.13 (dd, J = 9.2, 7.2 Hz, 1H), 1.41 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.3 (d, J = 25.4 Hz), 164.83 (d, J = 3.9 Hz), 131.4 (d, J = 1.4 Hz), 131.39 (d = 1.9 Hz), 131.27, 122.1, 83.0, 79.8 (d, J =241.1 Hz), 81.1, 78.7, 52.6, 43.0 (d, J = 1.9 Hz), 27.74, 21.34 (d, J = 10.1 Hz); HRMS (ESI) *m/z*: $[M+NH_4]^+$ calcd. for $C_{16}H_{22}O_4N_1{}^{79}Br_1F_1$, 390.0711; found, 390.0712; HPLC analysis: 87% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 230 nm, t_R = 6.60 min, major; t_R = 7.50 min, minor).



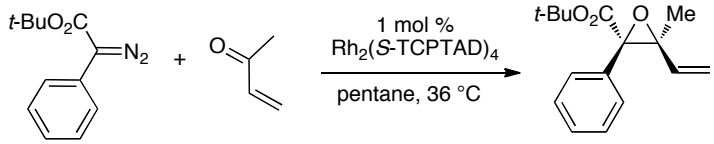
(1*S*,2*R*)-1-*tert*-butyl 2-methyl 1-(4-bromophenyl)-2-methylcyclopropane-1,2-dicarboxylate (1.54): Following the general procedure **(A)**, the reaction of metyl

methacrylate (0.27 ml, 2.52 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (145.3 mg, 0.49 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.2 mg, 0.0049 mmol, 0.01 equiv) afforded the product as a white solid (98.6 mg, 55% yield) after purification by flash chromatography. m.p. 82-84 °C; R_f = 0.37 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ +31.0 (c 1.08, $CHCl_3$); FTIR (neat): 2976, 1717, 1489, 1457, 1436, 1394, 1368, 1320, 1275, 1254, 1195, 1158, 1116, 1101, 1073, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 8.6 Hz, 2H), 3.32 (s, 3H), 2.03 (d, J = 5.2 Hz, 1H), 1.75 (d, J = 5.2 Hz, 1H), 1.50 (s, 3H), 1.38 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.4, 168.2, 135.9, 132.0, 130.7, 121.3, 82.0, 51.8, 42.2, 32.1, 27.8, 21.9, 15.7; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{21}O_4{}^{79}Br_1{}^{23}Na_1$, 391.0515; found, 391.0518; HPLC analysis: 77% ee (AD-H, hexane, 1.0 mL/min, λ = 230 nm, t_R = 5.20 min, major; t_R = 5.74 min, minor).

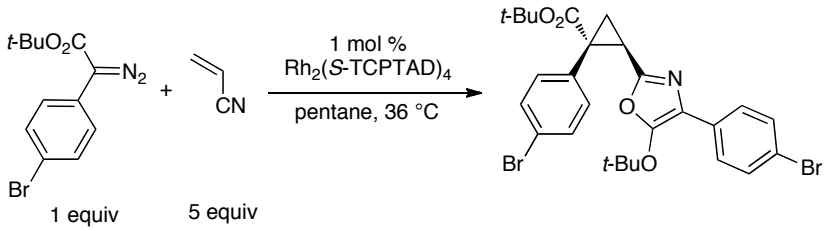


***tert*-butyl 2-phenyl-3-vinyloxirane-2-carboxylate (1.58):** Following the general procedure **(A)**, the reaction of methyl methacrylate (0.07 ml, 1.03 mmol, 5 equiv), *t*-butyl phenyldiazoacetate (46.0 mg, 0.21 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (4.4 mg, 0.0021 mmol, 0.01 equiv) afforded the product as a colorless oil (16.4 mg, 32% yield) after purification by flash chromatography. R_f = 0.39 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -3.3 (c 0.69, $CHCl_3$); FTIR (neat): 2980, 2108, 1742, 1727, 1450, 1394, 1369, 1333, 1258, 1206, 1190, 1156, 1106 cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.56 (dd, J = 8.0, 1.3 Hz, 2H), 7.39-7.31 (m, 3H), 5.78 (ddd, J = 17.3, 10.5, 7.4 Hz, 1H), 5.60 (d, J = 17.1 Hz, 1H), 5.44 (d, J = 10.6 Hz, 1H), 3.50 (d, J = 7.4 Hz, 1H), 1.49 (s, 9H); ^{13}C-NMR (100 MHz,

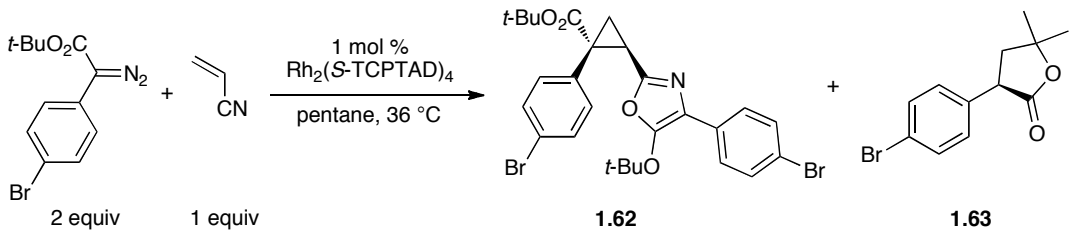
$CDCl_3$) δ 166.4, 135.2, 131.4, 128.4, 128.3, 126.3, 121.9, 83.0, 65.3, 28.0, 27.7; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{15}H_{18}O_3{}^{23}Na_1$, 269.1148; found, 269.1147; HPLC analysis: 15% ee (OD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 230 nm, t_R = 4.42 min, minor; t_R = 4.90 min, major).



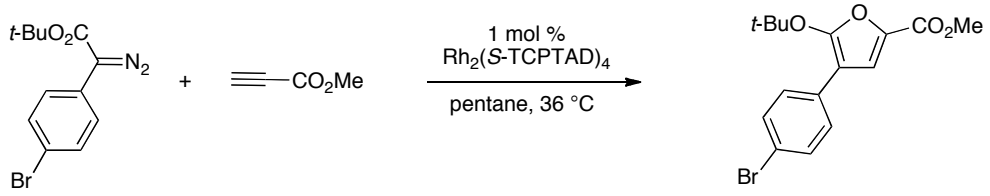
***tert*-butyl 3-methyl-2-phenyl-3-vinyloxirane-2-carboxylate (1.59):** Following the general procedure **(A)**, the reaction of 3-buten-2-one (0.20 ml, 2.44 mmol, 5 equiv), *t*-butyl phenyldiazoacetate (108.9 mg, 0.50 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (10.5 mg, 0.0050 mmol, 0.01 equiv) afforded the product as a colorless oil (34.3 mg, 26% yield) after purification by flash chromatography. R_f = 0.39 (hexanes:ethyl acetate = 10:1); R_f = 0.38 (hexanes:ethyl acetate = 10:1); FTIR (neat): 2927, 2854, 2358, 1725, 1455, 1393, 1369, 1250, 1158, 1084, 1069, 1031, 1010 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.38-7.29 (m, 3H), 5.31 (dd, *J* = 17.2, 1.8 Hz, 1H), 5.22 (dd, *J* = 17.2, 10.4 Hz, 1H), 5.13 (dd, *J* = 10.4, 1.8 Hz, 1H), 1.60 (s, 3H), 1.57 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 167.6, 135.8, 133.9, 128.0, 127.9, 127.7, 119.1, 82.7, 69.9, 65.0, 28.0, 17.1; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{16}H_{20}O_3{}^{23}Na_1$, 283.1305; found, 283.1305. HPLC analysis: <5% ee (AD-H, hexane, 0.25 mL/min, λ = 210 nm, t_R = 20.96 min, minor; t_R = 22.02 min, major).



(1*R*,2*R*)-*tert*-butyl 1-(4-bromophenyl)-2-(4-(4-bromophenyl)-5-(*tert*-butoxy)oxazol-2-yl)cyclopropanecarboxylate (1.62): Following the general procedure **(A)**, the reaction of acrylonitrile (0.10 ml, 1.52 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (93.8 mg, 0.32 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (5.9 mg, 0.0028 mmol, 0.01 equiv) afforded the product as a white solid (97.5 mg, 52% yield) after purification by flash chromatography. m.p. 133-135 $^{\circ}$C; R_f = 0.39 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -87.0 (c 1.02, $CHCl_3$); FTIR (neat): 2977, 2932, 1715, 1636, 1584, 1489, 1394, 1369, 1303, 1254, 1152, 1097, 1071, 1012 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 3.13 (dd, J = 9.2, 6.8 Hz, 1H), 2.09 (dd, J = 9.2, 4.8 Hz, 1H), 2.01 (dd, J = 6.8, 4.9 Hz, 1H), 1.39 (s, 9H), 1.05 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.2, 151.6, 151.1, 134.6, 132.5, 131.3, 131.1, 130.2, 126.5, 121.5, 120.0, 119.3, 86.0, 81.8, 36.7, 27.9, 27.8, 25.2, 18.5; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{24}O_4{}^{23}Na_1$, 590.0536; found, 590.0541; HPLC analysis: 97% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 5.43 min, minor; t_R = 6.27 min, major).



3-(4-bromophenyl)-5,5-dimethyldihydrofuran-2(3*H*)-one (1.63): White solid (24% yield); m.p. 70-72 °C; R_f = 0.29 (hexanes:ethyl acetate = 4:1); $[\alpha]_D^{20}$ 0.37 (c 0.80, $CHCl_3$); FTIR (neat): 2976, 2933, 1765, 1489, 1389, 1375, 1299, 1272, 1258, 1185, 1140, 1114, 1074, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H), 4.00 (dd, J = 11.9, 9.1 Hz, 1H), 2.57 (dd, J = 12.8, 9.1 Hz, 1H), 2.19 (t, J = 12.4 Hz, 1H), 1.54 (s, 3H), 1.49 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.9, 135.8, 131.9, 129.7, 121.5, 82.2, 46.3, 43.8, 28.8, 26.8; HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{12}H_{13}O_2{}^{79}Br_1{}^{39}K_1$, 306.9731; found, 306.9732; HPLC analysis: 65% ee (AD-H, 5% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 15.56 min, major; t_R = 16.79 min, minor).

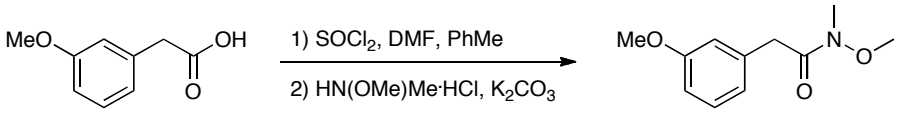


methyl 4-(4-bromophenyl)-5-(*tert*-butoxy)furan-2-carboxylate (1.72): Following the general procedure **(A)**, the reaction of methyl propiolate (0.13 ml, 1.46 mmol, 5 equiv), *t*-butyl *p*-bromophenyldiazoacetate (90.4 mg, 0.30 mmol, 1 equiv) and Rh_2(*S*-TCPTAD)$_4$ (6.5 mg, 0.0031 mmol, 0.01 equiv) afforded the product as a white solid (99.1 mg, 92% yield) after purification by flash chromatography. m.p. 130-132 °C R_f = 0.27 (hexanes:ethyl acetate = 10:1); FTIR (neat): 2976, 2933, 1765, 1489, 1456, 1389,1375, 1299, 1272, 1258, 1185, 1140, 1114, 1074, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.8 Hz, 2H), 7.40 (s, 1H), 3.88 (s, 3H), 1.49 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.7, 156.4, 135.1, 131.6, 130.4, 127.4, 120.0, 118.4,

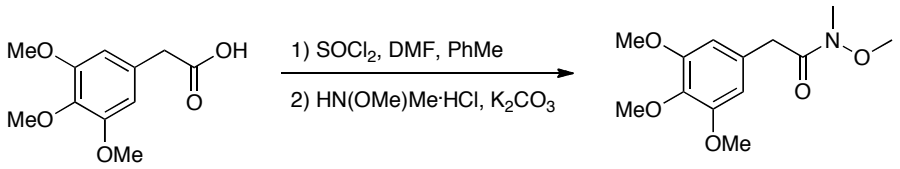
106.4, 87.0, 51.7, 28.9; Anal. Calcd. for $C_{16}H_{17}BrO_4$: C, 54.41; H, 4.85. Found: C, 54.23; H, 4.74.

Experimental for Chapter II: Synthesis of Fused Dihydrobenzofurans *via* Sequential Reactions

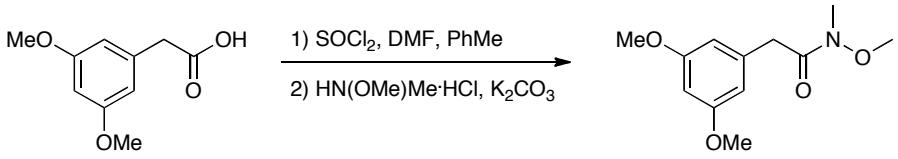
General procedure (B) – synthesis of weinreb amides: Under argon atmosphere, an oven dried two-neck round-bottom flask was charged with phenylacetic acid (10 mmol, 1 equiv) in toluene (20 ml). The flask was connected to a thermometer and water condenser. To this solution at 70 ºC was added dimethylformamide (0.50 mmol, 0.05 equiv) in one portion and then thionyl chloride (12 mmol, 1.2 equiv) over 30 minutes. After stirring at this temperature for an additional 2.5 hours, the reaction was cooled down to 0 ºC and *N,O*-dimethylhydroxylamine hydrochloride (15 mmol, 1.5 equiv) was added. To this solution at 0 ºC, a solution of potassium carbonate (40 mmol, 4 equiv) in water (10 ml) was added over 30 minutes. The ice was allowed to melt and the resulting mixture was stirred overnight. 2*N* hydrochloride acid solution was then added slowly (caution: gas evolution). Diethyl ether was added and layers were separated. The aqueous layer was extracted with diethyl ether two more times. The combined organic layers were washed with saturated sodium bicarbonate solution, water and brine subsequently. After drying over magnesium sulfate, the organics were filtered through a plug of silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography to afford the product.



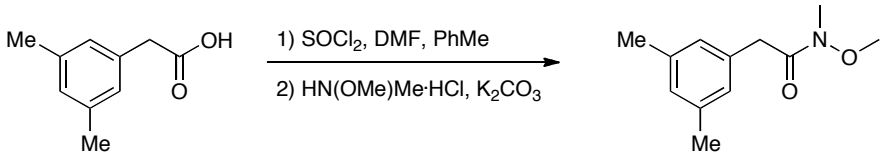
***N*-methoxy-2-(3-methoxyphenyl)-*N*-methylacetamide (B1):** Following the general procedure **(B)**, the reaction of 3-methoxyphenylacetic acid (3.63 g, 0.022 mmol) afforded the product as a yellow oil (4.16 g, 91% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1). FTIR (neat): 2938, 2836, 1657, 1597, 1584, 1490, 1455, 1435, 1379, 1256, 1148, 1045, 1004 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, J = 8.4, 7.6 Hz, 1H), 6.89-6.86 (m, 2H), 6.79 (dd, J = 8.4, 2.3 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 2H), 3.61 (s, 3H), 3.20 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.1, 158.9, 135.8, 128.5, 120.8, 114.2, 111.3, 60.3, 54.1, 38.4, 31.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{11}H_{16}N_1O_3$, 210.1125; found, 120.1124.



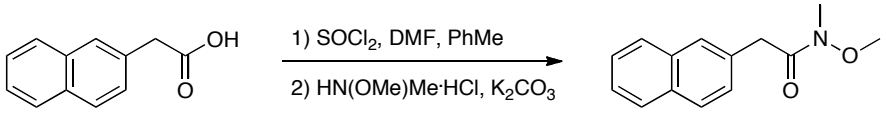
***N*-methoxy-*N*-methyl-2-(3,4,5-trimethoxyphenyl)acetamide (B2):** Following the general procedure **(B)**, the reaction of 3,4,5-trimethoxyphenylacetic acid (4.8215 g, 0.022 mmol) afforded the product as an orange solid (5.6264 g, 98% yield) after purification by flash chromatography (silica gel, ethyl acetate). m.p. 46-49 ºC; FTIR (neat): 2934, 2834, 1662, 1591, 1427, 1334, 1120, 1002 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.52 (s, 2H), 3.85 (s, 6H), 3.83 (s, 3H), 3.71 (s, 2H), 3.65 (s, 3H), 3.21 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.5, 152.5, 136.1, 130.0, 105.8, 60.7, 60.0, 55.3, 38.6, 31.5; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{13}H_{20}N_1O_5$, 270.1336; found, 270.1332.



2-(3,5-dimethoxyphenyl)-*N*-methoxy-*N*-methylacetamide (B3): Following the general procedure **(B)**, the reaction of 3,5-dimethoxyphenylacetic acid (0.4923 g, 2.51 mmol) afforded the product as an orange oil (0.5271 g, 88%) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1). The spectroscopic data were consistent with the published values.[179] ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.47 (d, J = 2.2 Hz, 2H), 6.36 (t, J = 2.2 Hz, 1H), 3.78 (s, 6H), 3.71 (s, 2H), 3.62 (s, 3H), 3.20 (s, 3H).

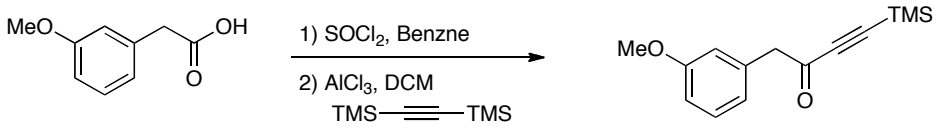


2-(3,5-dimethylphenyl)-*N*-methoxy-*N*-methylacetamide (B4): Following the general procedure **(B)**, the reaction of 3,5-dimethylphenylacetic acid (5.1139 g, 0.031 mmol) afforded the product as a yellow oil (6.2362 g, 97% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 2:1). FTIR (neat): 2918, 1660, 1605, 1463, 1412, 1376, 1005, 851 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.91 (s, 2H), 6.88 (s, 1H), 3.70 (s, 2H), 3.62 (s, 3H), 3.20 (s, 3H), 2.29 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4, 137.7, 134.6, 128.3, 126.9, 61.1, 39.0, 32.0, 21.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{12}H_{18}N_1O_2$, 208.1332; found 208.1332.



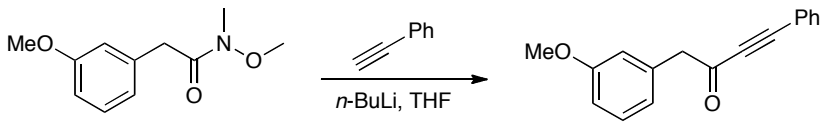
***N*-methoxy-*N*-methyl-2-(naphthalen-2-yl)acetamide (B5):** Following the general procedure **(B)**, the reaction of 2-naphthylacetic acid (2.5002 g, 0.013 mmol) afforded the product as a yellow oil (2.6984 g, 88%) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1). m.p. 55-57 ºC; FTIR (neat): 3052, 2936, 1652, 1413, 1379, 1169, 1002 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.84-7.76 (m, 3H), 7.74 (s, 1H), 7.49-7.4 (m, 3H), 3.94 (s, 2H), 3.61 (s, 3H), 3.21 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.5, 133.6, 132.6, 132.5, 128.2, 127.9, 127.7 (br., 3xC), 126.1, 125.7, 61.4, 39.7, 32.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{14}H_{16}N_1O_2$, 230.1176; found, 230.1176.

General procedure (C) – synthesis of diazo precursors: Under argon atmosphere, an oven dried round-bottom flask was charged with acetylene derivatives (1.3-4.0 equiv) in tetrahydrofuran (5 ml). To this solution at -78 ºC was added *n*-butyllithium (2.5 M in hexanes, 1.3-4.0 equiv) dropwise. The resulting mixture was stirred at -78 ºC for 5 more minutes and then room temperature 30 minutes. After cooling back to -78 ºC again, a solution of weinreb amide (5 mmol, 1 equiv) in tetrahydrofuran (5 ml) was added over 30 minutes. After another 5 minutes' stirring at -78 ºC, the dry ice/acetone bath was replaced by an ice/water bath and the reaction was stirred for 30 more minutes in the bath before being poured into a saturated solution of ammonium chloride. Diethyl ether was added and layers were separated. The aqueous layer was extracted with diethyl ether two more times and the combined organic layers were washed with brine. After drying over magnesium sulfate, the organics were filtered through a plug of silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography to afford the product.

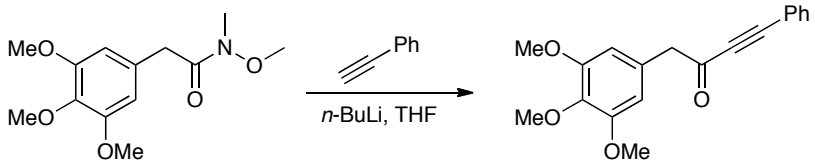


1-(3-methoxyphenyl)-4-(trimethylsilyl)but-3-yn-2-one (C1): Under argon atmosphere, to a solution of 3-methoxypenylacetic acid (2.4823 g, 0.015 mol, 1.0 equiv) in benzene (25 ml) at reflux was added a solution of thionyl chloride (4.4 ml, 0.060 mol, 4 equiv) over 30 minutes. The reaction was stirred at reflux for an additional 1.5 hours and then overnight at room temperature. The resulting mixture was concentrated under vacuum and then dried over a vacuum line for two hours. The residue was dissolved in dichloromethane (10 ml) and mixed with a solution of bis(trimethylsilyl)acetylene (2.7852, 0.016 mmol, 1 equiv). The whole mixture was added over 30 minutes to a suspension of aluminum chloride (0.7610 g, 5.71 mmol, 1 equiv) in dichloromethane (70 ml) at 0 ºC. The resulting mixture was stirred at 0 ºC for 30 minutes and room temperature for 1 hour. After cool the reaction to 0 ºC again, 2*N* HCl (150 ml) was added carefully. Layers were separated and the aqueous one was extracted with dichloromethane two more times. The combined organic layers were washed with saturated sodium bicarbonate solution, water and brine subsequently. The organics were then dried over magnesium sulfate, filtered through a plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 10:1) to afford the product (2.0042 g, 54%) as a pale yellow oil. FTIR (neat): 2960, 2153, 1673, 1599, 1585, 1491, 1466, 1455, 1436, 1252, 1217, 1149, 1097, 1047 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.26 (t, J = 7.6 Hz, 1H), 6.86-6.80 (m, 3H), 3.81 (s, 3H), 0.2 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 184.0, 159.5, 134.0, 129.3, 121.9, 115.2,

112.6, 101.5, 99.3, 54.7, 51.6, -1.2. HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{14}H_{19}O_2{}^{28}Si_1$, 247.1149; found, 247.1153.

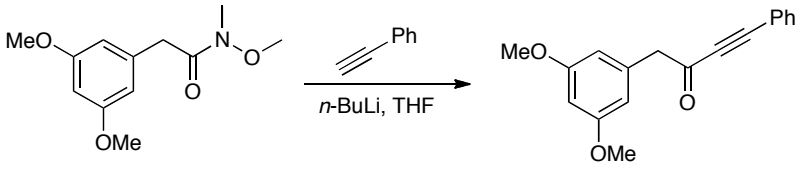


1-(3-methoxyphenyl)-4-phenylbut-3-yn-2-one (C2): Following the general procedure **(C)**, the reaction of phenylacetylene (0.50 ml, 4.58 mmol, 1.3 equiv), *n*-butyllithium (2.5 M in hexanes, 1.90 ml, 4.75 mmol, 1.3 equiv) and **B1** (0.7654 g, 3.66 mmol) afforded the product as a pale yellow oil (0.6038 g, 66% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 2937, 2835, 2200, 1662, 1597, 1584, 1489, 1254, 1073 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.0 Hz, 2H), 7.43 (d, J = 7.3 Hz, 1H), 7.41-7.33 (m, 2H), 7.32-7.26 (m, 1 H), 6.91 (d, J = 7.3 Hz, 1H), 6.89-6.83 (m, 2H), 3.91 (s, 2H), 3.81 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 184.8, 159.8, 134.6, 133.0, 130.8, 129.6, 128.6, 122.2, 119.7, 115.4, 112.9, 92.7, 87.7, 55.1, 52.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{15}O_2$, 251.1067; found, 251.1067.

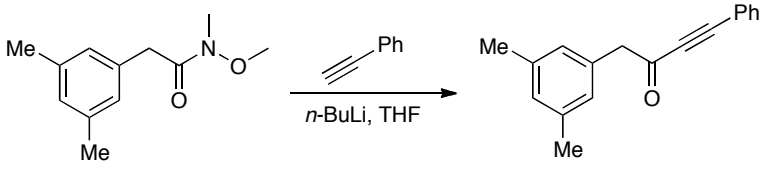


4-phenyl-1-(3,4,5-trimethoxyphenyl)but-3-yn-2-one (C3): Following the general procedure **(C)**, the reaction of phenylacetylene (0.51 ml, 4.64 mmol, 4 equiv), *n*-butyllithium (2.5 M in hexanes, 1.80 ml, 4.50 mmol, 4 equiv) and **B2** (0.3455 g, 1.17 mmol, 1 equiv) afforded the product as a yellow solid (0.2728 g, 75% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1, then 1:1).

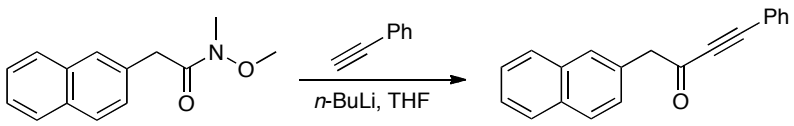
m.p. 51-54 ºC; FTIR (neat): 2934, 2202, 1661, 1590, 1421, 1238, 1128, 1042 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.51-7.43 (m, 3H), 7.41-7.34 (m, 2H), 6.53 (s, 2H), 3.87 (s, 2H), 3.86 (s, 6H), 3.85 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 185.0, 153.3, 137.2, 133.0, 130.1, 128.74, 128.66, 119.7, 106.8, 92.9, 87.7, 60.8, 56.1, 52.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{19}O_4$, 311.1278; found, 311.1279.



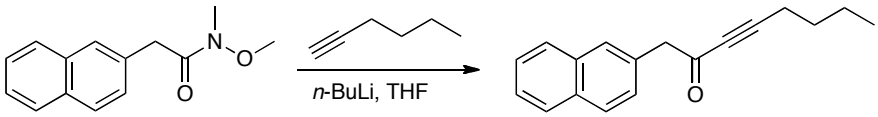
1-(3,5-dimethoxyphenyl)-4-phenylbut-3-yn-2-one (C4): Following the general procedure **(C)**, the reaction of phenylacetylene (0.11 ml, 1.00 mmol, 4 equiv), *n*-butyllithium (2.5 M in hexanes, 0.40 ml, 1.00 mmol, 4 equiv) and **B3** (0.0608 g, 0.25 mmol, 1 equiv) afforded the product as a pale yellow oil (0.0576 g, 81% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 5:1). FTIR (neat): 2935, 2200, 1661, 1593, 1456, 1429, 1293, 1204, 1147, 1062 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 7.6 Hz, 2H), 7.44 (d, J = 7.3 Hz, 1H), 7.36 (dd, J = 7.6, 7.3 Hz, 2H), 6.47 (d, J = 2.1 Hz, 2H), 6.42 (t, J = 2.1 Hz, 1H), 3.86 (s, 2H), 3.79 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 184.9, 161.0, 135.2, 133.1, 130.9, 128.7, 119.8, 107.9, 99.5, 92.8, 87.7, 55.3, 52.4; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{17}O_3$, 281.1172; found, 281.1173.



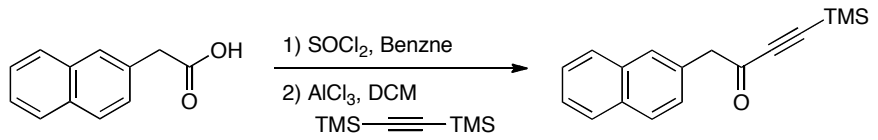
1-(3,5-dimethylphenyl)-4-phenylbut-3-yn-2-one (C5): Following the general procedure **(C)**, the reaction of phenylacetylene (2.80 ml, 0.025 mol, 3.4 equiv), *n*-butyllithium (2.5 M in hexanes, 10.0 ml, 0.025 mol, 3.4 equiv) and **B4** (1.5168 g, 7.32 mmol, 1 equiv) afforded the product as a pale yellow oil (1.2711 g, 70% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 2918, 2201, 1663, 1605, 1489, 1293, 1273, 1072 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.3 Hz, 1H), 7.36 (dd, J = 8.0, 7.3 Hz, 2H), 6.94 (br.s, 3H), 3.86 (s, 2H), 2.32 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 185.2, 138.1, 133.0, 132.9, 130.8, 129.0, 128.6, 127.7, 119.9, 92.5, 87.9, 52.1, 21.2; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{17}O_1$, 249.1274; found, 249.1274.



1-(naphthalen-2-yl)-4-phenylbut-3-yn-2-one (C6): Following the general procedure **(C)**, the reaction of phenylacetylene (0.90 ml, 8.25 mmol, 1.3 equiv), *n*-butyllithium (2.5 M in hexanes, 1.90 ml, 8.25 mmol, 1.3 equiv) and **B5** (1.4361 g, 6.26 mmol, 1 equiv) afforded the product as a yellow solid (0.7584 g, 45% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 5:1). m.p. 57-62 ºC; FTIR (neat): 3051, 2893, 2199, 1670, 1488, 1325, 1071 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.89-7.80 (m, 3H), 7.78 (s, 1H), 7.53-7.38 (m, 6H), 7.36-7.28 (m, 2H), 4.10 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 185.3, 133.7, 133.2, 132.8, 131.0, 130.8, 128.9, 128.7, 128.5, 127.91, 127.87 (2xC), 126.4, 126.1, 119.9, 93.2, 88.0, 52.5; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{20}H_{15}O_1$, 271.1117; found, 271.1118.



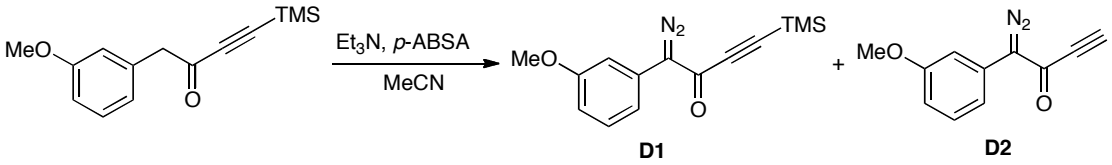
1-(naphthalen-2-yl)oct-3-yn-2-one (C7): Following the general procedure **(C)**, the reaction of 1-hexyne (0.56 ml, 4.72 mmol, 4 equiv), *n*-butyllithium (2.5 M in hexanes, 1.90 ml, 4.75 mmol, 4 equiv) and **B5** (0.2718 g, 1.19 mmol, 1 equiv) afforded the product as an orange oil (0.2029 g, 68% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 2957, 2208, 1667, 1238, 1159, 794 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.87-7.77 (m, 3H), 7.71 (s, 1H), 7.52-7.43 (m, 2H), 7.36 (dd, J = 8.4, 1.4 Hz, 1H), 3.97 (s, 2H), 2.29 (t, J = 7.0 Hz, 2H), 1.49-1.37 (m, 2H), 1.27 (dq, J = 14.9, 7.3 Hz, 2H), 0.81 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 185.4, 133.6, 132.7, 130.9, 128.7, 128.4, 127.80, 127.78 (2xC), 126.3, 126.0, 96.9, 81.0, 52.5, 29.6, 21.9, 18.8, 13.5; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{19}O_1$, 251.1430; found, 251.1434.



1-(naphthalen-2-yl)-4-(trimethylsilyl)but-3-yn-2-one (C8): Under argon atmosphere, to a solution of 2-naphthylacetic acid (1.0062 g, 5.40 mmol, 1.0 equiv) in benzene (10 ml) at reflux was added a solution of thionyl chloride (0.47 ml, 6.46 mmol, 1.2 equiv) in benzene (5 ml) over 30 minutes. The reaction was stirred at reflux for an additional 2.5 hours. It was then cooled down to room temperature and concentrated in vacuo. The residue was dried over a vacuum line for two hours and then dissolved in

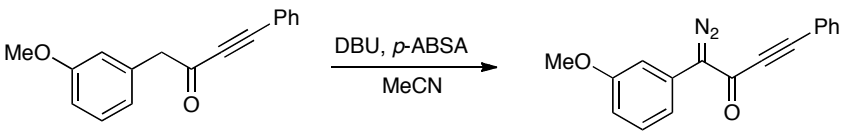
dichloromethane (10 ml). After adding bis(trimethylsilyl)acetylene (1.3 ml, 5.75 mmol, 1.1 equiv) to this solution, the whole mixture was added over one hour into a suspension of aluminum chloride (0.7610 g, 5.71 mmol, 1.1 equiv) in dichloromethane (20 ml) cooled at 0 ºC by an ice/water bath. The ice was allowed to melt and the reaction was stirred overnight. 2*N* HCl and diethyl ether was added. After the separation of layers, the aqueous one was extracted with diethyl ether two more times. The combined organic layers were washed with saturated sodium bicarbonate solution, water and brine subsequently. The organics were then dried over magnesium sulfate, filtered through a plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 10:1) to afford the product (1.0776 g, 75%) as a yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.84-7.79 (m, 3H), 7.72 (s, 1H), 7.49-7.46 (m, 2H), 7.36 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.00 (s, 2H), 0.16 (s, 9H).

General procedure (D) - synthesis of alkynyl-ketone diazo compounds: Under argon atmosphere, an oven dried round-bottom flask was charged with diazo precursor (0.5 mmol, 1 equiv) and *p*-acetamidobenzenesulfonyl azide (*p*-ABSA, 0.6 mmol, 1.2 equiv) in acetonitrile (5 ml). To this solution at 0 ºC was added 1,8-dizaobicyclo[5.4.0]undec-7-ene (DBU, 0.75 mmol, 1.5 equiv) in one portion. After stirring at 0 ºC for 5 more minutes, the reaction was quenched with saturated sodium bicarbonate solution. Diethyl ether was added and layers were separated. The aqueous layer was extracted with diethyl ether two more times. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through a plug of silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography.

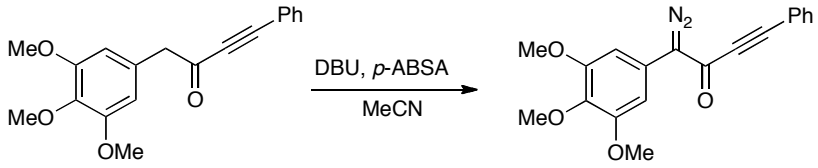


1-diazo-1-(3-methoxyphenyl)-4-(trimethylsilyl)but-3-yn-2-one (D1): Under argon atmosphere, to a solution of **C1** (1.6317 g, 6.63 mmol, 1 equiv) and *p*-ABSA (1.9228 g, 8.00 mmol, 1.2 equiv) in acetonitrile (50 ml) at 0 °C was added triethylamine (1.80 ml, 13.0 mmol, 2 equiv) in one portion. The resulting mixture was stirred at 0 °C for 1 hour and then concentrated to a small volume, which was purified by silica gel to afford **D1** (0.6217 g, 34% yield) as an orange oil and **D2** (0.1301 g, 10% yield) as a yellow solid. FTIR (neat): 2082, 1599, 1492, 1465, 1452, 1348, 1292, 1246, 1214, 1178, 1123, 1041 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32 (t, J = 8.1 Hz, 1H), 7.27-7.20 (m, 1H), 7.05 (d, J = 7.1 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 3.82 (s, 3H), 0.26 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.6, 160.1, 130.0, 125.8, 116.6, 112.8, 110.6, 99.2, 97.8, 78.8, 55.3, -0.6; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{14}H_{17}O_2{}^{28}Si_1$, 245.0992; found, 245.0992.

1-diazo-1-(3-methoxyphenyl)but-3-yn-2-one (D2): Yellow solid, FTIR (neat): 3234, 2090, 1596, 1496, 1465, 1451, 1431, 1363, 1334, 1317, 1245, 1208, 1176, 1119, 1031 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 8.1 Hz, 1H), 7.28-7.22 (m, 1H), 7.05 (ddd, J = 7.8, 1.7, 0.8 Hz, 1H), 6.85-6.79 (m, 1H), 3.83 (s, 3H), 3.26 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.8, 160.1, 130.1, 125.5, 116.7, 113.1, 110.7, 79.1, 78.6, 55.4; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{11}H_9O_2$, 173.0597; found, 173.0599.

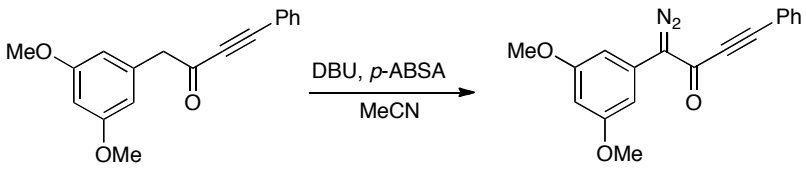


1-diazo-1-(3-methoxyphenyl)-4-phenylbut-3-yn-2-one (2.56): Following the general procedure **(D)**, the reaction of **C2** (0.0954 g, 0.38 mmol) afforded the product as a yellow solid (0.0960 g, 91% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 3001, 2942, 2203, 2084, 1601, 1576, 1489, 1366, 1230, 1204, 1050 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.0 Hz, 2H), 7.49-7.45 (m, 1H), 7.42-7.37 (m, 2H), 7.33 (d, J = 8.0 Hz, 1H), 7.29 (br.s, 1H), 7.11 (d, J = 7.8 Hz, 1H), 6.82 (d, J = 7.8 Hz, 1H), 3.84 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.6, 160.0, 132.7, 130.8, 129.9, 128.7, 125.8, 119.6, 116.4, 112.7, 110.3, 90.1, 84.9, 78.6, 55.2; HRMS (APCI) *m/z*: $[M-N_2+H]^+$ calcd. for $C_{17}H_{13}O_2$, 249.0910; found, 249.0909.

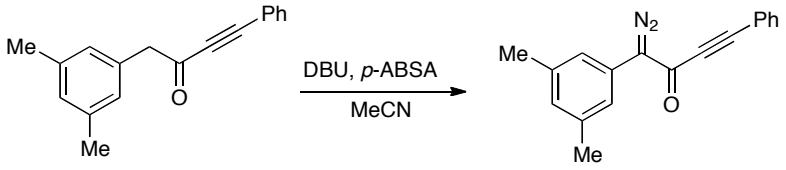


1-diazo-4-phenyl-1-(3,4,5-trimethoxyphenyl)but-3-yn-2-one (2.65): Following the general procedure **(D)**, the reaction of **C3** (0.1236 g, 0.40 mmol) afforded the product as an orange solid (0.1164 g, 87% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 1:2). FTIR (neat): 2938, 2204, 2088, 1592, 1572, 1505, 1443, 1415, 1298, 1241, 1208, 1125, 1114 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.56 (br.s, 2H), 7.48 (t, J = 7.3 Hz, 1H), 7.38-7.42 (m, 2H), 6.84 (s, 2H), 3.89 (s, 6H), 3.87 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.1, 153.8, 137.2, 133.7, 132.8, 130.9, 128.8, 119.7, 102.3,

90.4, 85.1, 78.6, 61.0, 56.3; HRMS (APCI) *m/z*: $[M\text{-}N_2+H]^+$ calcd. for $C_{19}H_{17}O_4$, 309.1121; found, 309.1122.

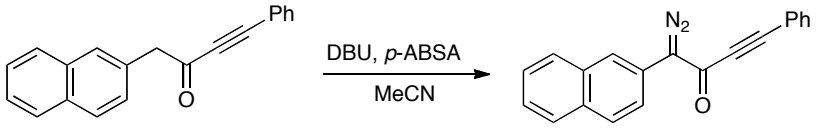


1-diazo-1-(3,5-dimethoxyphenyl)-4-phenylbut-3-yn-2-one (2.66): Following the general procedure **(D)**, the reaction of **C4** (0.2352 g, 0.84 mmol) afforded the product as a yellow solid (0.2223 g, 86% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2968, 2203, 2079, 1593, 1479, 1285, 1184, 1150, 974 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.3 Hz, 2H), 7.47 (t, J = 7.7 Hz, 1H), 7.40 (dd, J = 7.7, 7.3 Hz, 2H), 6.80 (d, J = 1.6 Hz, 2H), 6.38 (br.s, 1H), 3.82 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.9, 161.2, 132.8, 130.8, 128.8, 126.6, 119.7, 102.8, 99.3, 90.5, 85.0, 78.9, 55.5; HRMS (APCI) *m/z*: $[M\text{-}N_2+H]^+$ calcd. for $C_{18}H_{15}O_3$, 279.1016; found, 279.1017.

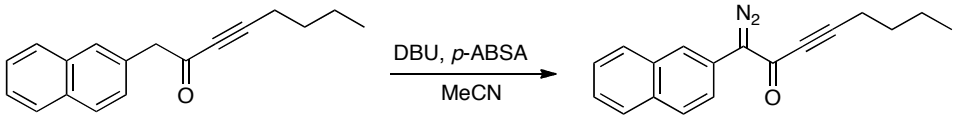


1-diazo-1-(3,5-dimethylphenyl)-4-phenylbut-3-yn-2-one (2.67): Following the general procedure **(D)**, the reaction of **C5** (0.1095 g, 0.44 mmol) afforded the product as a yellow solid (0.1069 g, 88%) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 2916, 2207, 2077, 1589, 1354, 1285, 1274, 1242, 843 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 6.6 Hz, 2H), 7.46 (t, J = 7.4

Hz, 1H), 7.39 (dd, *J* =7.4, 6.6 Hz, 2H), 7.22 (s, 2H), 6.92 (s, 1H), 2.35 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.1, 138.8, 132.9, 130.8, 129.2, 128.8, 124.2, 122.8, 119.9, 90.5, 86.3, 78.6, 21.6; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{15}N_2O_1$, 275.1179; found, 275. 1179.

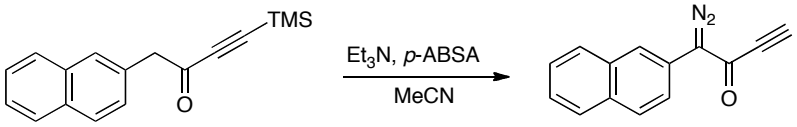


1-diazo-1-(naphthalen-2-yl)-4-phenylbut-3-yn-2-one (2.68): Following the general procedure **(D)**, except using dichloromethane to conduct the partition, the reaction of **C6** (0.4458 g, 1.65 mmol) afforded the product as an orange solid (0.4282 g, 88% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 3058, 2206, 2187, 2084, 1585, 1329, 1191, 1098 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.91 (d, *J* = 9.0 Hz, 1H), 7.88-7.79 (m, 2H), 7.67-7.35 (m, 8H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 133.7, 133.0, 132.4, 131.0, 129.0, 128.9, 128.1, 127.9, 127.0, 126.6, 124.3, 122.3, 121.8, 120.0, 85.2, 79.1, due to solubility issue, two signals attributed to C=N_2 and C=O were not observed; HRMS (APCI) *m/z*: $[M-N_2+H]^+$ calcd. for $C_{20}H_{13}O_1$, 269.0961; found, 269.0955.



1-diazo-1-(naphthalen-2-yl)oct-3-yn-2-one (2.69): Following the general procedure **(D)**, the reaction of **C7** (0.2714 g, 1.08 mmol, 1 equiv) afforded the product as a yellow solid (0.2472 g, 83% yield) after purification by flash chromatography (silica gel,

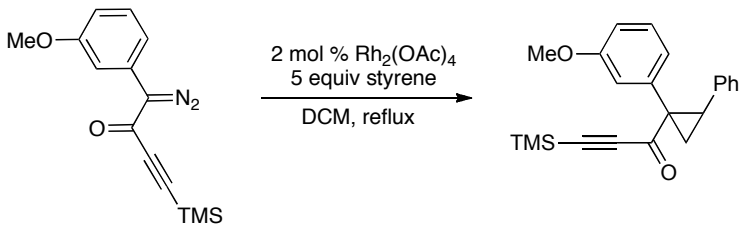
pentane:diethyl ether = 10:1). FTIR (neat): 3048, 2955, 2931, 2226, 2091, 1586, 1357, 1247, 1178, 819 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (br.s, 1H), 7.87 (d, J = 8.6 Hz, 1H), 7.85-77 (m, 2H), 7.56 (dd, J = 8.6, 1.6 Hz, 1H), 7.53-7.43 (m, 2H), 2.43 (t, J = 6.8 Hz, 2H), 1.69-1.54 (m, 2H), 1.53-1.34 (m, 2H), 0.94 (t, J = 6.7 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.9, 133.6, 132.2, 128.8, 128.0, 127.8, 126.8, 126.4, 123.8, 122.2, 121.9, 94.1, 78.5, 78.1, 29.8, 22.1, 18.8, 13.6; HRMS (APCI) *m/z*: $[2M-2N_2+H]^+$ calcd. for $C_{36}H_{33}O_2$, 497.2475; found, 497.2483.



1-diazo-1-(naphthalen-2-yl)but-3-yn-2-one (2.70): Under argon atmosphere, to a solution of **C8** (0.3331 g, 1.25 mmol, 1 equiv) and *p*-ABSA (0.3703 g, 1.54 mmol, 1.2 equiv) in acetonitrile (5 ml) at 0 ºC was added triethylamine (0.35 ml, 2.53 mmol, 2.0 equiv) in one portion. The reaction mixture was then stirred at 0 ºC for 30 minutes before the addition of saturated sodium bicarbonate solution. Diethyl ether was added and layers were separated. The aqueous layer was extracted with diethyl ether two more times. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through a plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 5:1) to afford the product (0.0704 g, 26% yield) as a yellow solid. FTIR (neat): 3293, 3232, 3055, 2410, 2311, 2088, 1590, 1329, 813 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (br.s, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.83 (dd, J = 8.2, 1.9 Hz, 2H), 7.55 (dd, J = 8.2, 1.9 Hz, 1H), 7.53-7.44 (m, 2H), 3.29 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.1, 133.6, 132.3, 129.0, 128.1, 127.9, 127.0,

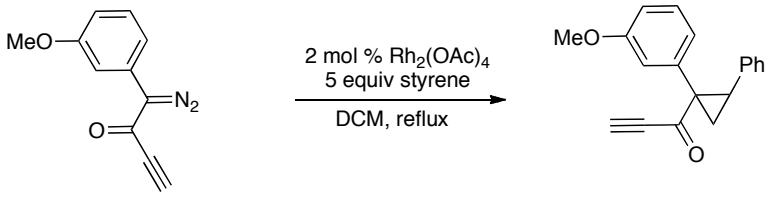
126.6, 124.2, 122.1, 121.2, 79.4, 78.9 (2xC); HRMS (APCI) *m/z*: $[2M-2N_2+H]^+$ calcd. for $C_{28}H_{17}O_2$, 385.1223; found, 385.1218.

General procedure (E) - the $Rh_2(TFA)_4$ catalyzed cyclopropanation reaction: Under argon atmosphere, a flame dried round-bottom flask was charged with alkene derivative (2.50 mmol, 5 equiv) and $Rh_2(TFA)_4$ (0.010 mmol, 0.02 equiv) in dichloromethane (2 ml). To this solution at reflux was added a solution of diazo compound (0.50 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. After stirring at reflux for an additional hour, the reaction mixture was cooled down to room temperature and concentrated in vacuo. The residue was purified by flash chromatography.



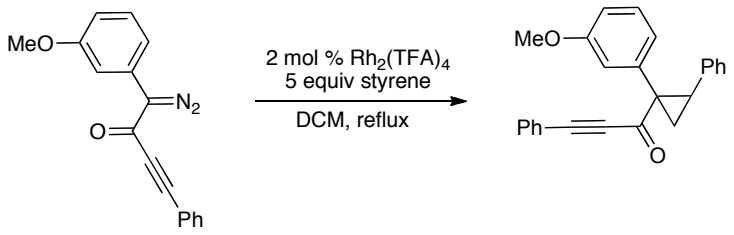
1-(1-(3-methoxyphenyl)-2-phenylcyclopropyl)-3-(trimethylsilyl)prop-2-yn-1-one (2.51): Under argon atmosphere, a flame dried round-bottom flask was charged with styrene (0.20 ml, 1.74 mmol, 5 equiv) and $Rh_2(OAc)_4$ (2.3 mg, 0.0052 mmol, 0.02 equiv) in dichloromethane (2 ml). To this solution at reflux was added a solution of **D1** (0.1029g, 0.38 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. After stirring at reflux for an additional hour, the reaction mixture was cooled down to room temperature and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 20:1) to afford the product as a pale yellow oil (0.1555 g, 88% yield). FTIR (neat): 1647, 1601, 1582, 1225, 1204, 1130, 1080, 1041 cm^{-1}; ^{1}H-NMR (400

MHz, $CDCl_3$) δ 7.10-7.02 (m, 4H), 6.82 (dd, J = 6.5, 3.0 Hz, 2H), 6.73-6.68 (m, 1H), 6.66 (d, J = 7.6 Hz, 1H), 6.56-6.51 (m, 1H), 3.56 (s, 3H), 3.23 (dd, J = 9.2, 7.7 Hz, 1H), 2.30 (dd, J = 9.3, 4.7 Hz, 1H), 2.00 (dd, J = 7.5, 4.8 Hz, 1H), 0.05 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 186.8, 159.0, 136.2, 128.7, 128.1, 127.9, 126.7, 125.0, 118.0, 113.5, 102.1, 100.8, 55.0, 47.8, 36.5, 23.2, -1.0; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{22}H_{25}O_2{}^{28}Si_1$, 349.1618; found, 349.1623.

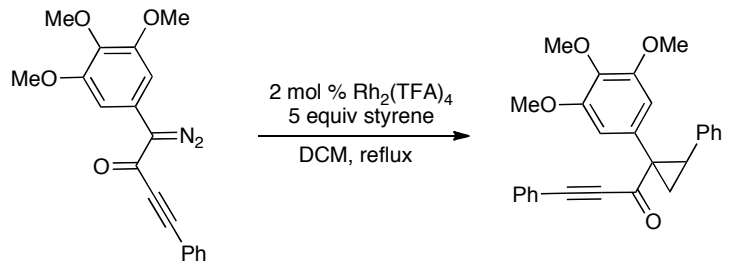


1-(1-(3-methoxyphenyl)-2-phenylcyclopropyl)prop-2-yn-1-one (2.52): Under argon atmosphere, a flame dried round-bottom flask was charged with styrene (0.35 ml, 3.0 mmol, 5 equiv) and $Rh_2(OAc)_4$ (2.6 mg, 0.0059 mmol, 0.02 equiv) in dichloromethane (2 ml). To this solution at reflux was added a solution of **D2** (0.1201g, 0.60 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. After stirring at reflux for an additional hour, the reaction mixture was cooled down to room temperature and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 50:1 then 15:1) to afford the product as a pale yellow oil (0.1160 g, 70% yield). FTIR (neat): 3219, 2087, 1643, 1610, 1582, 1489, 1453, 1434, 1287, 1229, 1199, 1130, 1047, 1020, 1041 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.15-7.01 (m, 4H), 6.81 (dd, J = 6.5, 2.9 Hz, 2H), 6.70 (dd, J = 8.2, 2.4 Hz, 1H), 6.64 (d, J = 7.6 Hz, 1H), 6.56-6.48 (m, 1H), 3.57 (s, 3H), 3.26 (dd, J = 9.2, 7.8 Hz, 1H), 3.11 (s, 1H), 2.33 (dd, J = 9.4, 5.0 Hz, 1H), 2.05 (dd, J = 7.6, 5.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 186.4, 159.1, 135.8, 135.4, 128.9,

128.2, 128.0, 126.9, 124.9, 117.9, 113.7, 81.7, 80.1, 55.2, 47.7, 36.3, 22.9; HRMS (APCI) *m/z*: $[M]^+$ calcd. for $C_{19}H_{16}O_2$, 276.1145; found, 276.1149.



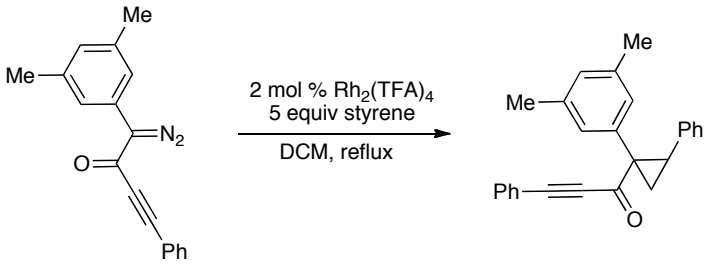
1-(1-(3-methoxyphenyl)-2-phenylcyclopropyl)-3-phenylprop-2-yn-1-one (2.57): Following the general procedure **(E)**, the reaction of styrene (0.72 ml, 6.26 mmol, 5 equiv) and **2.56** (0.3462 g, 1.25 mmol, 1 equiv) afforded the product as a pale yellow foam (0.3833 g, 87% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 2935, 2200, 1639, 1600, 1582, 1489, 1275, 1039 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37 (t, J = 7.4 Hz, 1H), 7.29-7.25 (m, 2H), 7.20-7.19 (m, 2H), 7.14-7.09 (m, 4H), 6.87-6.85 (m, 2H), 6.79-6.74 (m, 2H), 6.62 (s, 1H), 3.59 (s, 3H), 3.29 (dd, J = 9.3, 7.5 Hz, 1H), 2.38 (dd, J = 9.3, 4.7 Hz, 1H), 2.05 (dd, J = 7.5, 4.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.1, 159.1, 136.7, 136.3, 133.2, 130.8, 128.8, 128.5, 128.2, 127.9, 126.7, 125.2, 120.0, 118.0, 113.6, 94.9, 87.4, 55.1, 48.0, 36.6, 23.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{21}O_2$, 353.1536; found, 353.1535.



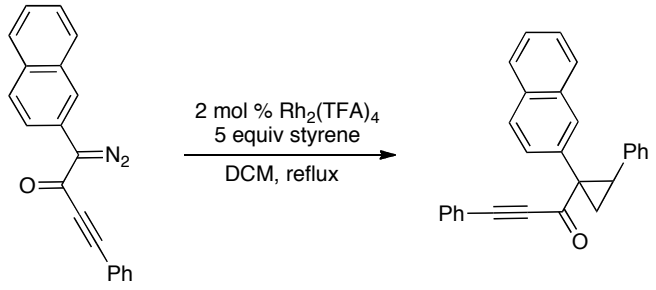
3-phenyl-1-(2-phenyl-1-(3,4,5-trimethoxyphenyl)cyclopropyl)prop-2-yn-1-one (2.71): Following the general procedure **(E)**, the reaction of styrene (0.05 ml, 0.43 mmol, 5 equiv) and **2.56** (0.0278 g, 0.083 mmol, 1 equiv) afforded the product as a pale yellow foam (0.0274 g, 80% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 1:1). FTIR (neat): 2998, 2192, 1643, 1584, 1508, 1452, 1412, 1288, 1238, 1120, 995 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39 (t, J = 7.3 Hz, 1H), 7.29 (d, J = 7.6 Hz, 2H), 7.23 (d, J = 7.3 Hz, 2H), 7.17-7.10 (m, 3H), 6.89-6.87 (m, 2H), 6.29 (s, 2H), 3.82 (s, 3H), 3.60 (s, 6H), 3.26 (dd, J = 9.2, 7.7 Hz, 1H), 2.40 (dd, J = 9.2, 4.8 Hz, 1H), 2.03 (dd, J = 7.7, 4.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.3, 152.7, 137.5, 136.5 (2xC), 133.4, 131.0, 128.7, 128.3, 128.1, 126.9, 120.1, 110.1, 95.0, 87.4, 61.0, 56.2, 48.2, 37.0, 23.6; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{25}O_4$, 413.1747; found 413.1750.

1-(1-(3,5-dimethoxyphenyl)-2-phenylcyclopropyl)-3-phenylprop-2-yn-1-one (2.72): Following the general procedure **(E)**, the reaction of styrene (0.06 ml, 0.52 mmol, 5 equiv) and **2.66** (0.0312 g, 0.10 mmol, 1 equiv) afforded the product as a pale yellow oil (0.0346 g, 89% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 5:1). FTIR (neat): 2935, 2202, 1640, 1593, 1455, 1424, 1277, 1203, 1152, 1122, 1066 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 7.0 Hz, 1H),

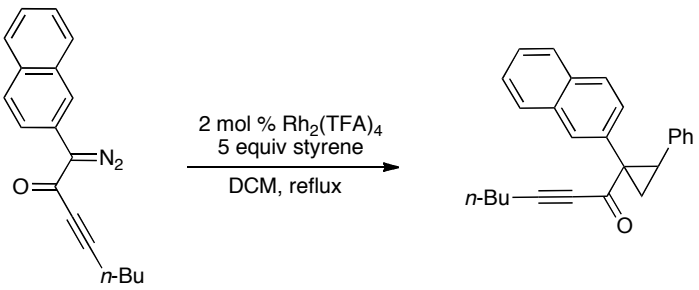
7.31-7.23 (m, 4H), 7.13-7.11 (m, 3H), 6.89 (dd, J = 7.0, 2.2 Hz, 2H), 6.33 (t, J = 2.2 Hz, 1H), 6.27 (d, J = 2.2 Hz, 2H), 3.59 (s, 6H), 3.27 (dd, J = 9.3, 7.7 Hz, 1H), 2.36 (dd, J = 9.3, 4.8 Hz, 1H), 2.04 (dd, J = 7.7, 4.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.0, 160.3, 137.5, 136.5, 133.4, 130.9, 128.7, 128.3, 128.0, 126.8, 120.2, 110.9, 100.4, 94.8, 87.4, 55.4, 48.3, 36.7, 23.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{23}O_3$, 383.1642; found, 383.1641.



1-(1-(3,5-dimethylphenyl)-2-phenylcyclopropyl)-3-phenylprop-2-yn-1-one (2.73): Following the general procedure **(E)**, the reaction of styrene (0.06 ml, 0.52 mmol, 5 equiv) and **2.67** (0.0277 g, 0.10 mmol, 1 equiv) afforded the product as a pale yellow oil (0.0334 g, 94% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1). FTIR (neat): 3029, 2916, 2201, 1636, 1603, 1489, 1276, 1197, 1070 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.35 (m, 1H), 7.32-7.28 (m, 2H), 7.23-7.18 (m, 2H), 7.13-7.06 (m, 3H), 6.88-6.81 (m, 3H), 6.71 (s, 2H), 3.25 (dd, J = 9.2, 7.6 Hz, 1H), 2.37 (dd, J = 9.2, 4.7 Hz, 1H), 2.17 (s, 6H), 2.02 (dd, J = 7.6, 4.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.7, 137.2, 136.6, 134.8, 133.4, 130.8, 130.6, 129.2, 128.6, 128.3, 127.9, 126.7, 120.3, 94.8, 87.5, 48.0, 36.7, 23.3, 21.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{23}O_1$, 351.1743; found, 351.1742.

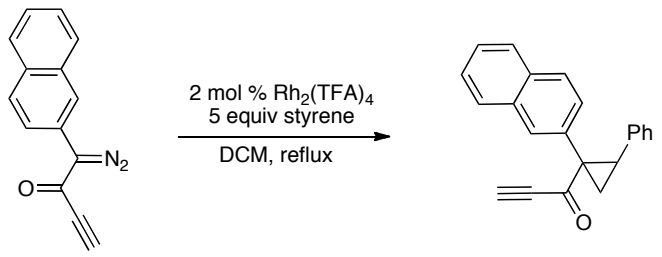


1-(1-(naphthalen-2-yl)-2-phenylcyclopropyl)-3-phenylprop-2-yn-1-one (2.74): Following the general procedure **(E)**, the reaction of styrene (0.30 ml, 2.61 mmol, 5 equiv) and **2.68** (0.1569 g, 0.53 mmol, 1 equiv) afforded the product as a yellow solid (0.1427 g, 72% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 5:1). m.p. 111-113 ºC; FTIR (neat): 3056, 2924, 2198, 1640, 1275, 1197, 1119 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.81-7.69 (m, 3H), 7.62 (d, J = 8.3 Hz, 1H), 7.50-7.38 (m, 2H), 7.28 (t, J = 7.6 Hz, 1H), 7.19-7.09 (m, 3H), 7.07-7.00 (m, 3H), 6.96 (d, J = 7.3 Hz, 2H), 6.87 (dd, J = 5.7, 3.5 Hz, 2H), 3.37 (dd, J = 9.2, 7.7 Hz, 1H), 2.48 (dd, J = 9.2, 4.8 Hz, 1H), 2.20 (dd, J = 7.7, 4.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.3, 136.2, 133.31, 133.26, 133.1, 132.9, 131.9, 130.8, 130.6, 128.5, 128.3, 128.1, 128.0, 127.7, 127.4, 126.8, 126.2, 126.0, 119.9, 95.3, 87.7, 48.3, 36.9, 23.5; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{21}O_1$, 373.1587; found, 373.1585.



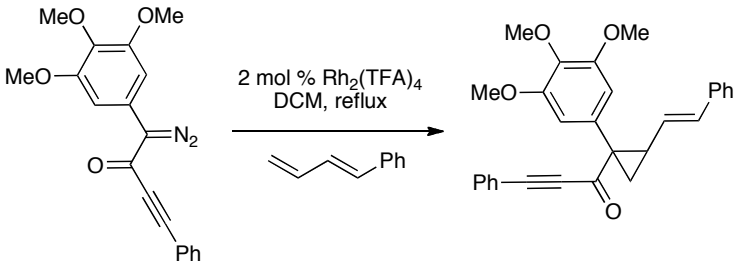
1-(1-(naphthalen-2-yl)-2-phenylcyclopropyl)hept-2-yn-1-one (2.75): Following the general procedure **(E)**, the reaction of styrene (0.06 ml, 0.52 mmol, 5 equiv) and **2.69**

(0.0277 g, 0.10 mmol, 1 equiv) afforded the product as a colorless oil (0.0276 g, 78% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 10:1 then 5:1). FTIR (neat): 3055, 2956, 2930, 2210, 1645, 1241, 1207, 1154, 946 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.71 (br.s, 2H), 7.62 (s, 1H), 7.55 (d, J = 8.2 Hz, 1H), 7.41 (dd, J = 5.3, 2.9 Hz, 2H), 7.06 (d, J = 8.2 Hz, 1H), 7.01 (br.s, 3H), 6.82 (d, J = 2.0 Hz, 2H), 3.30 (t, J = 8.3 Hz, 1H), 2.38 (dd, J = 8.3, 3.9 Hz, 1H), 2.19-2.02 (m, 3H), 1.18-1.03 (m, 2H), 1.0-0.9 (dt, J = 9.5, 7.0 Hz, 2H), 0.58 (t, J = 7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.5, 136.3, 133.2, 133.0, 132.8, 131,5, 130.4, 128.2, 128.0, 127.9, 127.7, 127.3, 126.7, 126.0, 125.9, 98.7, 80.2, 47.9, 36.3, 29.5, 23.2, 21.7, 18.8, 13.4; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_1$ 353.1900; found, 353.1903.

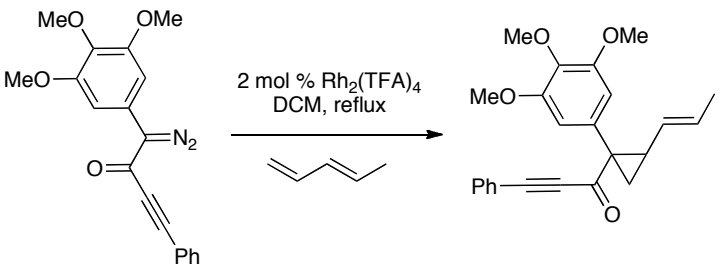


1-(1-(naphthalen-2-yl)-2-phenylcyclopropyl)prop-2-yn-1-one (2.76): Following the general procedure **(E)**, the reaction of styrene (0.19 ml, 1.65 mmol, 5 equiv) and **2.70** (0.0717 g, 0.33 mmol, 1 equiv) afforded the product as a yellow oil (0.0374 g, 39% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 5:1). FTIR (neat): 3275, 3057, 2093, 1652, 1232, 747 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.77-7.67 (m, 2H), 7.62 (s, 1H), 7.57 (d, J = 8.5 Hz, 1H), 7.47-7.39 (m, 2H), 7.06 (d, J = 1.5 Hz, 1H), 7.05-6.96 (m, 3H), 6.87-6.77 (m, 2H), 3.36 (dd, J = 9.3, 7.7 Hz, 1H), 3.07 (s, 1H), 2.45 (dd, J = 9.3, 4.9 Hz, 1H), 2.20 (dd, J = 7.6, 4.9 Hz, 1H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 186.6, 135.7, 133.2, 132.9, 131.9, 131.7, 130.2, 128.3, 128.1, 128.0, 127.8,

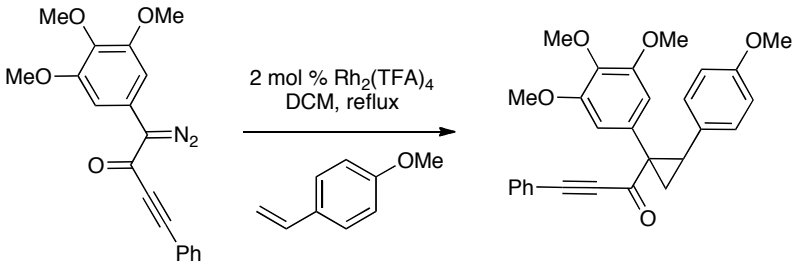
127.5, 126.9, 126.3, 126.0, 82.0, 80.2, 47.9, 36.6, 23.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{22}H_{17}O_1$ 297.1274; found, 297.1271.



(*E*)-3-phenyl-1-(2-styryl-1-(3,4,5-trimethoxyphenyl)cyclopropyl)prop-2-yn-1-one (2.83): Following the general procedure **(E)**, the reaction of 4-phenyl-1,3-butadiene (0.6513 g, 5.01 mmol, 5 equiv) and **2.65** (0.3303 g, 0.98 mmol, 1 equiv) afforded the product as a pale yellow oil (0.3426 g, 80% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1, then 1:1). FTIR (neat): 2936, 2198, 1640, 1585, 1413, 1235, 1123, 1095, 755 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (t, J = 7.2 Hz, 1H), 7.34-7.22 (m, 7H), 7.22-7.15 (m, 2H), 6.69-6.63 (m, 3H), 5.41 (dd, J = 15.9, 9.5 Hz, 1H), 3.91 (s, 3H), 3.77 (s, 6H), 2.85 (ddd, J = 9.5, 9.2, 6.9 Hz, 1H), 2.32 (dd, J = 9.2, 4.4 Hz, 1H), 1.65 (dd, J = 6.9, 4.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.2, 153.1, 137.8, 137.1, 133.3, 131.9, 131.0, 129.1, 128.8 (2xC), 127.5, 126.1, 120.1, 109.6, 95.1, 87.2, 61.1, 56.3 (2xC), 46.5, 35.9, 25.9; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}O_4$ 439.1904; found, 439.1901.

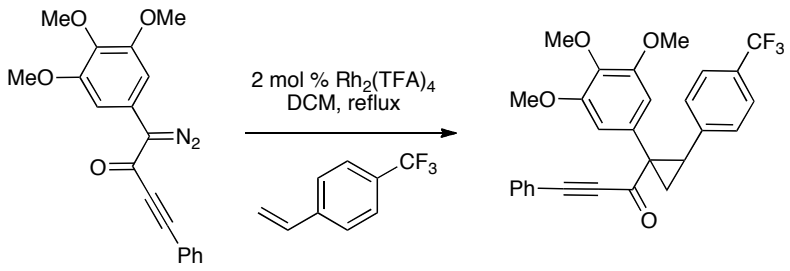


(*E*)-3-phenyl-1-(2-(prop-1-en-1-yl)-1-(3,4,5-trimethoxyphenyl)cyclopropyl)prop-2-yn-1-one (2.84): Following the general procedure **(E)**, the reaction of *trans*-piperylene (0.20 ml, 1.98 mmol, 5 equiv) and **2.65** (0.1364 g, 0.41 mmol, 1 equiv) afforded the product as a pale yellow oil (0.1067 g, 70% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2936, 2200, 1639, 1585, 1412, 1234, 1122, 1098 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (t, J = 7.4 Hz, 1H), 7.34-7.22 (m, 4H), 6.60 (s, 2H), 5.76-5.64 (m, 1H), 4.71 (ddd, J = 15.3, 9.4, 1.3 Hz, 1H), 3.91 (s, 3H), 3.84 (s, 6H), 2.66 (dd, J = 16.4, 9.2 Hz, 1H), 2.17 (dd, J = 9.2, 4.1 Hz, 1H), 1.63 (dd, J = 6.8, 1.3 Hz, 3H), 1.49 (dd, J = 6.8, 4.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.5, 152.9, 137.6, 133.2, 132.0, 130.8, 129.7, 128.6, 127.9, 120.1, 109.6, 94.5, 87.2, 61.0, 56.3, 45.8, 35.4, 25.3, 18.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{24}H_{25}O_4$ 377.1747; found, 377.1742.



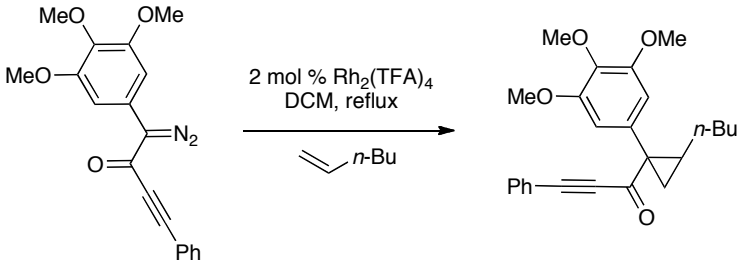
1-(2-(4-methoxyphenyl)-1-phenylcyclopropyl)-3-phenylprop-2-yn-1-one (2.85): Following the general procedure **(E)**, the reaction of 4-methoxystyrene (0.33 ml, 2.48

mmol, 5 equiv) and **2.65** (0.1659 g, 0.49 mmol, 1 equiv) afforded the product as a pale yellow foam (0.1782 g, 82% yield) after purification by flash chromatography (silica gel, dichloromethane:methanol = 200:1). FTIR (neat): 2936, 2837, 2201, 1637, 1586, 1514, 1413, 1247, 1124, 908 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 7.4 Hz, 1H), 7.33-7.20 (m, 4H), 6.80 (d, J = 8.5 Hz, 2H), 6.68 (d, J = 8.5 Hz, 2H), 6.30 (s, 2H), 3.82 (s, 3H), 3.72 (s, 3H), 3.63 (s, 6H), 3.22 (dd, J = 9.1, 8.0 Hz, 1H), 2.39 (dd, J = 9.1, 4.6 Hz, 1H), 1.96 (dd, J = 8.0, 4.6 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.2, 158.7, 152.7, 137.5, 133.3, 131.0, 130.9, 129.3, 128.7, 128.4, 120.1, 113.5, 110.1, 94.8, 87.5, 61.0, 56.1, 55.4, 48.1, 36.8, 23.6; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{27}O_5$ 443.1853; found, 443.1846.

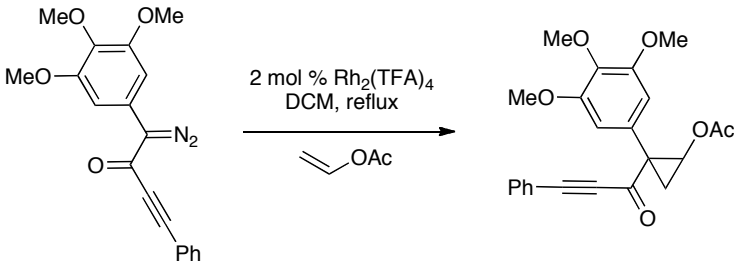


3-phenyl-1-(2-(4-(trifluoromethyl)phenyl)-1-(3,4,5-trimethoxyphenyl)cyclopropyl) prop-2-yn-1-one (2.86): Following the general procedure **(E)**, the reaction of 4-(trifluoromethyl)styrene (0.37ml, 2.50 mmol, 5 equiv) and **2.65** (0.1681 g, 0.50 mmol, 1 equiv) afforded the product as a pale yellow oil (0.1595 g, 66% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2938, 2201, 1643, 1586, 1413, 1324, 1118, 1067 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44-7.36 (m, 3H), 7.29 (dd, J = 8.0, 7.4 Hz, 2H), 7.22 (d, J = 7.4 Hz, 2H), 6.99 (d, J = 8.2 Hz, 2H), 6.27 (s, 2H), 3.83 (s, 3H), 3.61 (s, 6H), 3.30 (dd, J = 9.0, 7.6 Hz, 1H), 2.42 (dd, J = 9.0,

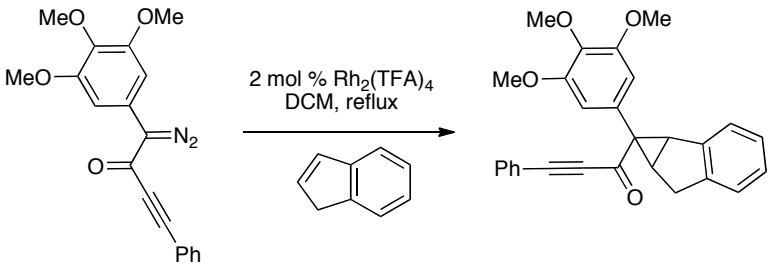
4.8 Hz, 1H), 2.04 (dd, J = 7.6, 4.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 186.7, 152.9, 141.1, 137.9, 133.3, 131.1, 130.3, 128.8 (q, J = 32.4 Hz), 128.7, 128.5, 124.4 (q, J = 270.4 Hz), 124.9 (q, J = 3.6 Hz), 119.9, 110.0, 95.7, 87.3, 61.0, 56.2, 48.4, 35.9, 23.9; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{24}F_3O_4$ 481.1621; found, 481.1617.



1-(2-butyl-1-(3,4,5-trimethoxyphenyl)cyclopropyl)-3-phenylprop-2-yn-1-one (2.86): Following the general procedure **(E)**, the reaction of 1-hexene (0.28 ml, 2.26 mmol, 5 equiv) and **2.65** (0.1529 g, 0.45 mmol, 1 equiv) afforded the product as a pale yellow oil (0.0605 g, 34% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 3:1). FTIR (neat): 2931, 2201, 1644, 1586, 1236, 1126 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (t, J = 7.0 Hz, 1H), 7.34-7.24 (m, 4H), 6.59 (s, 2H), 3.90 (s, 3H), 3.86 (s, 6H), 2.12-2.05 (m, 1H), 1.94 (dd, J = 9.2, 3.7 Hz, 1H), 1.58-1.46 (m, 1H), 1.45-1.36 (m, 2H), 1.32-1.19 (m, 3H), 0.86 (t, J = 7.2 Hz, 3H), 0.81-0.70 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 188.7, 153.0, 137.7, 133.2, 132.3 130.8, 128.7, 120.3, 109.2, 94.0, 87.4, 61.1, 56.3, 45.1, 32.5, 31.7, 30.6, 25.6, 22.7, 14.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{29}O_4$ 393.2060; found, 393.2062.



1-(2-acetyl-1-(3,4,5-trimethoxyphenyl)cyclopropyl)-3-phenylprop-2-yn-1-one (2.88): Following the general procedure **(E)**, the reaction of vinyl acetate (0.28 ml, 2.71 mmol, 5 equiv) and **2.65** (0.1809 g, 0.54 mmol, 1 equiv) afforded the product as a yellow solid (0.0980 g, 46% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 1:1). m.p. 102-105 ºC; FTIR (neat): 2939, 2205, 1750, 1632, 1587, 1241, 1148, 1024, 1002 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41 (t, J = 7.2 Hz, 1H), 7.30 (dd, J = 7.6, 7.2 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 6.63 (s, 2H), 4.84 (dd, J = 7.0, 4.8 Hz, 1H), 3.91 (s, 3H), 3.84 (s, 6H), 2.20 (dd, J = 7.0, 5.8 Hz, 1H), 1.91 (s, 3H), 1.85 (dd, J = 5.8, 4.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 185.7, 171.2, 153.1, 137.9, 133.2, 131.1, 129.9, 128.7, 119.8, 108.8, 95.7, 87.2, 61.0, 60.6, 56.3, 44.5, 22.1, 20.9; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{23}H_{23}O_6$ 395.1489; found, 395.1484.



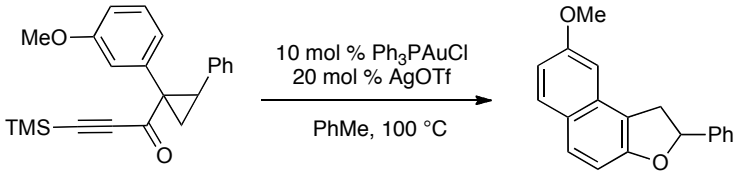
3-phenyl-1-(1-(3,4,5-trimethoxyphenyl)-1,1a,6,6a-tetrahydrocyclopropa[*a*]inden-1-yl)prop-2-yn-1-one (2.95): Following the general procedure **(E)**, the reaction of indene (0.59 ml, 5.07 mmol, 5 equiv) and **2.65** (0.3392 g, 1.01 mmol, 1 equiv) afforded the

product as a pale yellow solid (0.3018 g, 70% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 1:1). m.p. 153-155 ºC; FTIR (neat): 2926, 2197, 1635, 1587, 1452, 1414, 1146, 1120, 1024 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.3 Hz, 1H), 7.37 (dd, J = 7.6, 7.2 Hz, 1H), 7.30-7.23 (m, 2H), 7.21-7.16 (m, 2H), 7.13 (t, J = 7.3 Hz, 1H), 6.99 (t, J = 7.3 Hz, 1H), 6.84 (d, J = 7.6 Hz. 1H), 6.25 (br.s, 2H), 3.78 (s, 3H), 3.64 (br.s, 6H), 3.60 (d, J = 6.7 Hz, 1H), 3.29 (dd, J = 18.1, 6.5 Hz, 1H), 3.10 (dd, J = 6.7, 6.5 Hz, 1H), 2.83 (d, J = 18.1 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.1, 152.7, 143.7, 141.7, 137.2, 133.3, 130.9, 128.6, 128.5, 126.9, 126.4, 124.93, 124.86, 120.1, 110.4, 95.0, 87.8, 60.9, 56.2, 49.6, 44.9, 35.5, 34.0; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{25}O_4$ 425.1747; found, 425.1742.

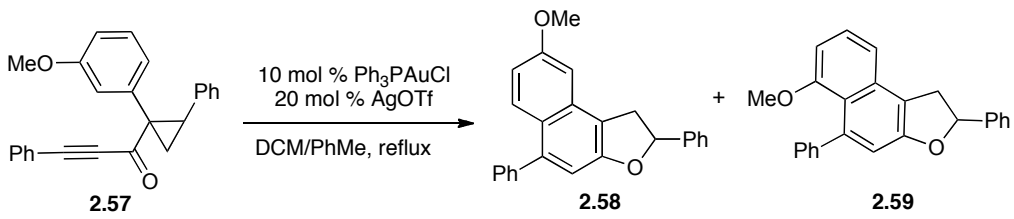
General procedure (F) - the Ag/Au catalyzed cycloaddition reaction: Under argon atmosphere, a flame dried round-bottom flask was wrapped with aluminum foil and charged with cyclopropane derivative (0.1 mmol, 1 equiv), chlorotriphenylphosphine gold (I) (0.01 mol, 0.1 equiv) and silver trifluoromethanesulfonate (0.02 mmol, 0.2 equiv) in dichloromethane/toluene (2 ml / 4 ml). The reaction mixture was heated to reflux and monitored by TLC. After all the starting material was consumed, the reaction mixture was cooled down to room temperature and filtered through a plug of silica gel. The filtrate was concentrated in vacuo and purified by flash chromatography.

General procedure (G) - the Ag/Au catalyzed cycloaddition reaction in toluene: Under argon atmosphere, a flame dried two neck round-bottom flask was wrapped with aluminum foil and charged with cyclopropane derivative (0.1 mmol, 1 equiv),

chlorotriphenylphosphine gold (I) (0.01 mol, 0.1 equiv) and silver trifluoromethanesulfonate (0.02 mmol, 0.2 equiv) in toluene (4 ml). A water condenser and thermometer were connected. The reaction was heated to 85 °C and monitored by TLC. After all the starting material was consumed, the reaction mixture was cooled down to room temperature and filtered through a plug of silica gel. The filtrate was concentrated in vacuo and purified by flash chromatography.



8-methoxy-2-phenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.53): Following the general procedure **(G)** but at 100 °C, the reaction of **2.52** (0.0346 g, 0.13 mmol, 1 equiv) afforded the product as a white solid (0.0163 g, 47% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 30:1). FTIR (neat): 2924, 1621, 1603, 1583, 1515, 1495, 1472, 1453, 1434, 1372, 1306, 1262, 1203, 1182, 11154, 1062 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 9.0 Hz, 1H), 7.65 (d, J = 8.6 Hz, 1H), 7.50-7.29 (m, 5H), 7.05 (d, J = 8.7 Hz, 1H), 6.98 (dd, J = 8.9, 2.5 Hz, 1H), 6.80 (d, J = 2.3 Hz, 1H), 5.96 (dd, J = 9.7, 8.0 Hz, 1H), 3.90-3.85 (m, 4H), 3.44 (dd, J = 15.3, 7.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.7, 157.9, 142.5, 132.1, 130.5, 129.1, 128.9, 128.2, 126.0, 124.9, 117.3, 115.7, 109.5, 101.3, 84.8, 55.4, 37.6; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{17}O_2$, 227.1223; found 277.1222

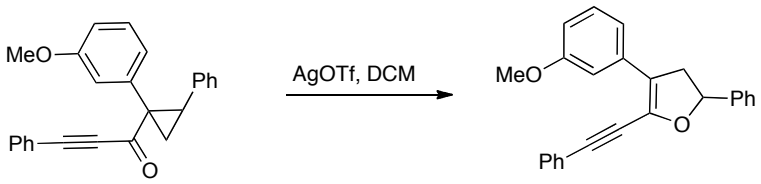


2.57 **2.58** **2.59**

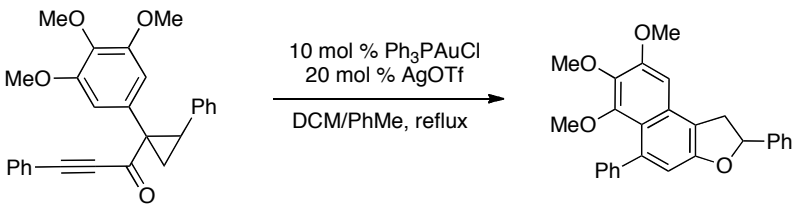
8-methoxy-2,5-diphenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.58): Following the general procedure **(F)**, the reaction of **2.57** (0.0298 g, 0.088 mmol) afforded the product as a white solid (0.0196 g, 66% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 30:1, then 10:1). m.p. 98-101 ºC; FTIR (neat): 2931, 1620, 1588, 1471, 1342, 1220, 1141, 1030, 851 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 9.2 Hz, 1H), 7.49-7.47 (m, 6H), 7.42-7.38 (m, 3H), 7.35-7.31 (m, 1H), 7.02 (s, 1H), 6.92 (dd, J = 9.2, 2.5 Hz, 1H), 6.85 (d, J = 2.5 Hz, 1H), 5.99 (dd, J = 9.5, 7.9 Hz, 1H), 3.95 (dd, J = 15.2, 9.5 Hz, 1H), 3.91 (s, 3H), 3.49 (dd, J = 15.2, 7.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.5, 157.4, 142.5, 142.1, 141.0, 132.6, 130.2, 129.1, 128.9, 128.4, 128.3, 127.5, 126.0, 123.1, 116.7, 115.6, 110.7, 101.6 84.8, 55.4, 37.8; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{21}O_2$, 353.1536; found 353.1539.

6-methoxy-2,5-diphenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.59): Purified by flash chromatography (silica gel, pentane:diethyl ether = 30:1, then 10:1) to afford the product (0.0100 g, 33% yield) as a white solid. m.p. 134-137 ºC; FTIR (neat): 2929, 1618, 1577, 1340, 1255, 1164, 975 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.2 Hz, 2H), 7.41 -7.31 (m, 9H), 7.20 (d, J = 8.3 Hz, 1H), 6.99 (s, 1H), 6.63 (d, J = 7.6 Hz, 1H), 5.97 (dd, J = 9.7, 7.8 Hz, 1H), 3.96 (dd, J = 15.6, 9.7 Hz, 1H), 3.53-3.47 (dd, J = 15.6, 7.8 Hz, 1H), 3.45 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.8, 156.7, 145.6, 142.4, 141.2, 133.1, 128.9, 128.8, 128.7, 128.3 127.4, 126.9,126.04, 125.98, 119.4, 117.8, 116.2, 114.6, 103.9,

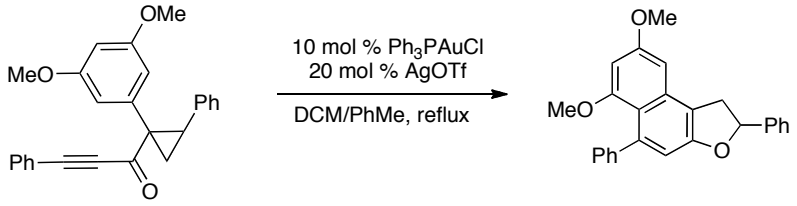
85.0, 55.3, 38.1, one more signal attributed to the slow equilibrium of the conformations of the compound at room temperature; carbons between δ 128.8 and 128.7 are not chemically equivalent; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{21}O_2$, 353.1536; found 353.1540.



4-(3-methoxyphenyl)-2-phenyl-5-(phenylethynyl)-2,3-dihydrofuran (2.60): Under argon atmosphere, an aluminum foil wrapped round-bottom flask was charged with **2.57** (0.1749 g, 0.50 mmol, 1 equiv) and silver trifluoromethansulfonate (0.0244 g, 0.095 mmol, 0.2 equiv) in dichloromethane (5 ml). The reaction was then stirred at reflux for 24 hours. After cooling down to room temperature, the solvent was removed under vacuo and the crude residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 10:1) to afford product (0.078 g, 46% yield) as a yellow oil. FTIR (neat): 3031, 2931, 2204, 1596, 1490, 1270, 1217, 1146 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 6.7, 3.1 Hz, 2H), 7.47 (d, J = 7.0 Hz, 2H), 7.43-7.26 (m, 9H), 6.80 (dt, J =6.4, 2.5 Hz, 1H), 5.69 (dd, J = 9.9, 8.9 Hz, 1H), 3.80 (s, 3H), 3.59 (dd, J = 15.7, 9.9 Hz, 1H), 3.21 (dd, J = 15.7, 8.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.8, 142.1, 134.9, 134.4, 131.9, 129.5, 129.3, 128.9, 128.7, 128.3, 126.1, 122.2, 119.5, 118.5, 112.9, 111.1, 96.7, 81.70, 81.68, 55.4, 41.4; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{21}O_2$ 353.1536; found, 353.1535.

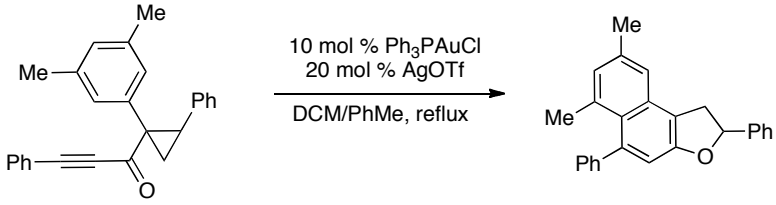


6,8-dimethoxy-2,5-diphenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.77): Following the general procedure **(F)**, the reaction of **2.61** (0.0305 g, 0.073 mmol) afforded the product as a pale yellow oil (0.0303 g, 99% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2935, 1615, 1470, 1418, 1331, 1260, 1119, 1038 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.2 Hz, 2H), 7.43-7.29 (m, 8H), 6.87 (s, 1H), 6.65 (s, 1H), 5.96 (dd, J = 10.0, 7.8 Hz, 1H), 3.96 (s, 3H), 3.92 (dd, J = 15.2, 10.0 Hz, 1H), 3.85 (s, 3H), 3.46 (dd, J = 15.2, 7.8 Hz, 1H), 3.25 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.4, 154.0, 151.1, 144.6, 142.5, 140.4, 140.3, 129.3, 129.0, 128.9, 128.3, 127.0, 126.2, 126.0, 118.2, 117.1, 113.2, 98.3, 84.7, 61.3, 60.8, 56.0, 38.2; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{25}O_4$, 413.1747; found, 413.1746.



6,8-dimethoxy-2,5-diphenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.78): Following the general procedure **(F)**, the reaction of **2.72** (0.0218 g, 0.057 mmol) afforded the product as a pale yellow oil (0.0173 g, 79% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2928, 2853, 1618, 1585, 1344, 1236, 1158, 1136, 1025 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.2 Hz, 2H), 7.39 (dd, J = 8.0, 7.2 Hz, 2H), 7.34-7.29 (m, 6H), 6.83 (s, 1H), 6.45 (d, J = 2.2 Hz, 1H),

6.29 (d, J = 2.2 Hz, 1H), 5.97 (dd, J = 9.8, 7.9 Hz, 1H), 3.96-3.87 (m, 4H), 3.49-3.40 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.2, 159.0, 157.3, 145.5, 142.5, 141.3, 133.8, 128.9, 128.8, 128.7, 128.2, 126.8, 125.99, 125.97, 117.0, 115.2, 112.2, 96.7, 94.5, 84.8, 55.5, 55.2, 38.2, one more signal attributed to the slow equilibrium of the conformations of the compound at room temperature; carbons between δ 128.8 and 128.7 are not chemically equivalent; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{23}O_3$, 383.1642; found, 383.1644.

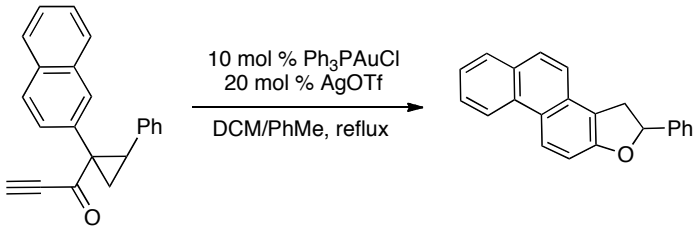


6,8-dimethyl-2,5-diphenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.79): Following the general procedure **(F)**, the reaction of **2.73** (0.0318 g, 0.091 mmol) afforded the product as a yellow solid (0.0315 g, 99% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 50:1). m.p. 80-83 ºC; FTIR (neat): 3029, 2842, 1610, 1583, 1443, 1342, 1210, 1072, 976 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.2 Hz, 2H), 7.40-7.32 (m, 9H), 6.96 (s, 1H), 6.92 (s, 1H), 5.97 (dd, J = 9.8, 8.0 Hz, 1H), 3.97 (dd, J = 15.5, 9.8 Hz, 1H), 3.51 (dd, J = 15.5, 8.0 Hz, 1H), 2.43 (s, 3H), 1.94 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.8, 145.3, 142.6, 142.2, 136.5, 136.2, 132.6, 129.74, 129.66, 129.62, 128.9, 128.2, 127.75, 127.71, 127.0, 126.0, 125.4, 121.2, 117.9, 114.4, 84.9, 38.2, 25.4, 21.6, two more signals attributed to the slow equilibrium of the conformations of the compound at room temperature; carbons between δ 129.66 and

129.62, δ 127.75 and 127.71 are not chemically equivalent; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{23}O_1$, 351.1743; found, 351.1744.

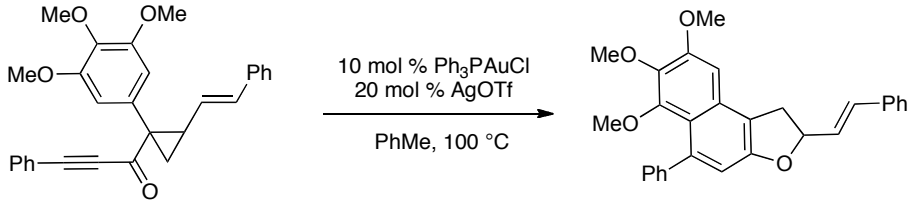
2,10-diphenyl-2,3-dihydrophenanthro[2,1-*b*]furan (2.80): Following the general procedure **(F)**, the reaction **2.74** (0.0238 g, 0.064 mmol) afforded the product as a white solid (0.0228 g, 96% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 20:1). m.p. 141-143 ºC; FTIR (neat): 3026, 2917, 1595, 1575, 1442, 1435, 1211, 1161, 977 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.9 Hz, 1H), 7.56 (dd, *J* = 11.4, 8.9 Hz, 2H), 7.51-7.30 (m, 11H), 7.11 (s, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.01 (dd, *J* = 9.5, 8.0 Hz, 1H), 4.04 (dd, *J* = 15.6, 9.5 Hz, 1H), 3.58 (dd, *J* = 15.6, 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.3, 145.6, 142.30, 142.27, 132.3, 131.4, 130.8, 129.2 (2xC), 129.0, 128.9, 128.8, 128.4, 128.0, 127.3, 126.1, 125.3, 125.1, 123.3, 122.9, 120.4, 114.6, 85.2, 38.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{21}O$, 373.1592; found, 373.1590.

10-butyl-2-phenyl-2,3-dihydrophenanthro[2,1-*b*]furan (2.81): Following the general procedure **(F)**, the reaction of **2.75** (0.0343 g, 0.097 mmol) afforded the product as a pale yellow oil (0.0307 g, 90% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 20:1). FTIR (neat): 3033, 2954, 2928, 1612, 1598, 1581, 1455, 1271, 1081 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 8.6 Hz, 1H), 7.86 (dd, J = 8.0, 1.6 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.59 (td, J = 7.0, 1.6 Hz, 1H), 7.55-7.44 (m, 4H), 7.39 (t, J = 7.3 Hz, 2H), 7.35-7.30 (m, 1H), 7.18 (s, 1H), 5.96 (dd, J = 9.5, 8.1 Hz, 1H), 3.98 (dd, J = 15.2, 9.5 Hz, 1H), 3.53 (dd, J = 15.2, 8.1 Hz, 1H), 3.47-3.34 (m, 2H), 1.96-1.89 (m, 2H), 1.65-1.55 (m, 2H), 1.04 (t, J = 7.3 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.5, 142.42, 142.38, 132.3, 131.9, 131.0, 129.2, 128.9, 128.32, 128.29, 126.8, 126.09, 126.06, 125.0, 124.2, 123.5, 119.2, 113.7, 85.0, 38.5, 38.1, 33.2, 23.2, 14.2; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_1$, 353.1900; found, 353.1900.



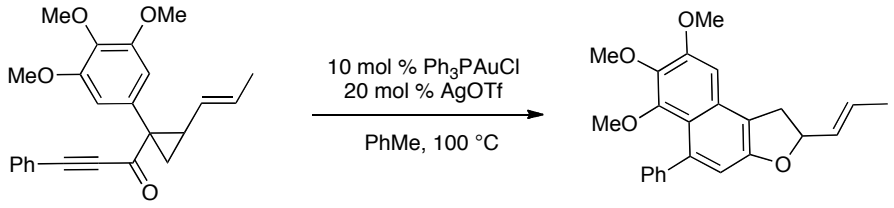
2-phenyl-2,3-dihydrophenanthro[2,1-*b*]furan (2.82): Following the general procedure **(F)**, the reaction of **2.76** (0.0374 g, 0.13 mmol) afforded the product as a pale yellow oil (0.0343 g, 92% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 20:1). FTIR (neat): 3063, 2930, 1619, 1462, 1267, 814 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.58 (t, J = 8.4 Hz, 2H), 7.85 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.63 (td, J = 7.2, 1.2 Hz, 1H), 7.56-7.43 (m, 4H), 7.39 (dd, J = 7.6, 7.2 Hz, 2H), 7.36-7.26 (m, 2H), 5.99 (dd, J = 9.7, 8.0 Hz, 1H), 4.00 (dd, J = 15.5, 9.7 Hz, 1H),

3.55 (dd, J = 15.5, 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.3, 142.3, 131.3, 130.8, 129.5, 129.0, 128.9, 128.33, 128.26, 127.1, 126.0, 125.6, 125.1, 123.9, 122.6, 122.5, 120.7, 110.7, 85.1, 37.7; HRMS (APCI) *m/z*: $[M\text{-}C_6H_5]^+$ calcd. for $C_{16}H_{11}O_1$, 219.0804; found, 219.0804.

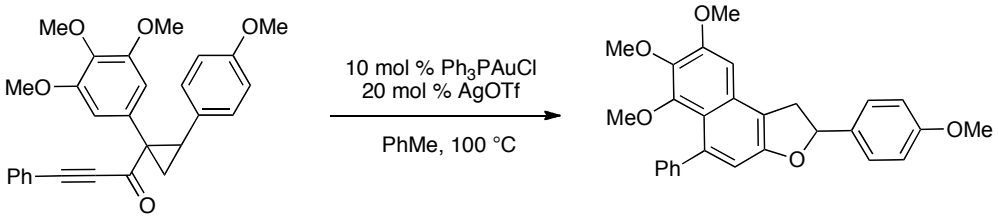


(*E*)-6,7,8-trimethoxy-5-phenyl-2-styryl-1,2-dihydronaphtho[2,1-*b*]furan (2.89): Following the general procedure **(G)**, the reaction of **2.83** (0.0305 g, 0.070 mmol) afforded the product as a pale yellow oil (0.0243 g, 80% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 3:1). FTIR (neat): 2928, 1615, 1581, 1466, 1420, 1335, 1257, 1120, 1043 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.3 Hz, 2H), 7.39-7.29 (m, 7H), 7.25 (d, J = 4.6 Hz, 1H), 6.82 (s, 1H), 6.77 (d, J = 15.8 Hz, 1H), 6.67 (s, 1H), 6.46 (dd, J = 15.8, 7.5 Hz, 1H), 5.65-5.52 (m, 1H), 3.98 (s, 3H), 3.85 (s, 3H), 3.72 (dd, J = 15.2, 9.6 Hz, 1H), 3.34 (dd, J = 15.2, 7.3 Hz, 1H). 3.24 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.1, 154.0, 151.0, 144.6, 140.3, 140.2, 136.4, 132.5, 129.3, 129.0, 128.9, 128.8, 128.7, 128.2, 127.0, 126.9, 126.2, 118.1, 117.3, 113.3, 98.2, 84.2, 61.3, 60.8, 56.0, 36.0, one more signal attributed to the slow equilibrium of the conformations of the compound at room temperature; carbons between δ 129.0 and 128.9 are not chemically equivalent; ^{13}C-NMR (150 MHz, $CDCl_3$, 55 ºC) δ 156.3, 154.2, 151.2, 144.8, 140.5, 140.4, 136.7, 132.4, 129.5, 129.1, 129.0, 128.8, 128.2, 127.00, 126.96,

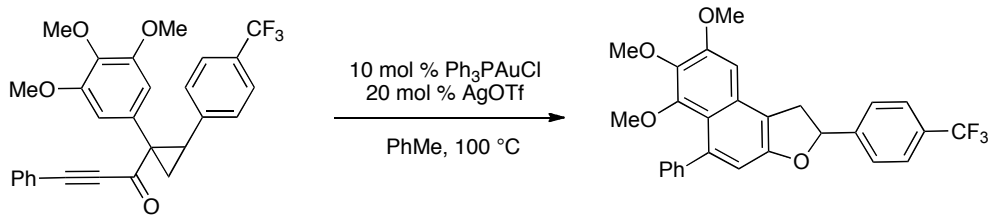
126.2, 118.3, 117.3, 113.4, 98.5, 84.2, 61.2, 60.7, 56.0, 36.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{27}O_4$, 439.1904; found, 439.1900.



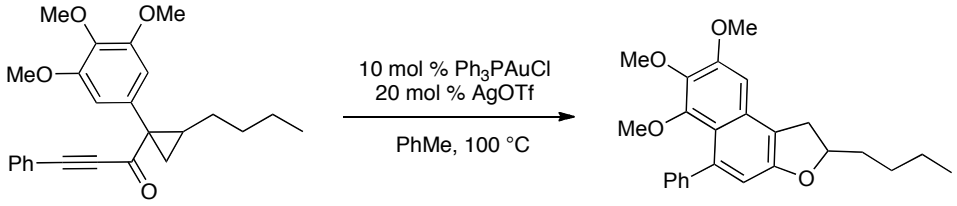
(*E*)-6,7,8-trimethoxy-5-phenyl-2-(prop-1-en-1-yl)-1,2-dihydronaphtho[2,1-*b*]furan (2.90): Following the general procedure **(G)**, the reaction of **2.84** (0.0512 g, 0.14 mmol) afforded the product as a pale yellow oil (0.0319 g, 62% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 3:1). FTIR (neat): 2934, 2249, 1614, 1581, 1466, 1420, 1374, 1335, 1256, 1120, 1042 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5H), 6.77, (s, 1H), 6.64 (s, 1H), 5.98-5.85 (m, 1H), 5.82-5.71 (m, 1H), 5.35 (dd, J = 8.8, 8.0 Hz, 1H), 3.97 (s, 3H), 3.85 (s, 3H), 3.60 (dd, J = 15.3, 9.5 Hz, 1H), 3.28-3.15 (m, 4H), 1.77 (dd, J = 6.4, 1.6 Hz, 3H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 156.1, 153.9, 151.0, 144.7, 140.14, 140.09, 130.8, 129.8, 129.3, 129.0, 128.9, 127.0, 126.1, 118.0, 117.5, 113.3, 98.2, 84.5, 61.3, 60.7, 55.9, 35.7, 17.9, one more signal attributed to the slow equilibrium of the conformations of the compound at room temperature; carbons between δ 129.0 and 128.9 are not chemically equivalent; ^{13}C-NMR (150 MHz, $CDCl_3$, 55 ºC) δ 156.3, 154.1, 151.1, 144.9, 140.34, 140.27, 131.1, 129.43, 129.40, 129.0, 127.0, 126.1, 118.2, 117.5, 113.4, 98.4, 84.4, 61.2, 60.7, 56.0, 35.8, 17.8; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{24}H_{25}O_4$, 377.1747; found, 377.1741.



6,7,8-trimethoxy-2-(4-methoxyphenyl)-5-phenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.91): Following the general procedure **(G)**, the reaction of **2.85** (0.1553 g, 0.35 mmol) afforded the product as a pale yellow oil (0.0324 g, 21% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2933, 1614, 1581, 1513, 1466, 1335, 1247, 1121, 1040, 829 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43-7.28 (m, 7H), 6.91 (d, J = 8.5 Hz, 2H), 6.84 (s, 1H), 6.66 (s, 1H), 5.91 (dd, J = 9.5, 7.9 Hz, 1H), 3.96 (s, 3H), 3.88-3.83 (m, 4H), 3.81 (s, 3H), 3.46 (dd, J = 15.3, 7.9 Hz, 1H), 3.24 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.7, 156.4, 154.0, 151.0, 144.7, 140.3, 140.2, 134.4, 129.2, 129.0, 128.9, 127.5, 127.0, 126.2, 118.1, 117.2, 114.3, 113.3, 98.3, 84.7, 61.3, 60.8, 56.0, 55.5, 38.0, one more signal attributed to the slow equilibrium of the conformations of the compound at room temperature; carbons between δ 129.0 and 128.9 are not chemically equivalent; ^{13}C-NMR (150 MHz, $CDCl_3$, 55 ºC) δ 159.9, 156.5, 154.2, 151.2, 144.9, 140.5, 140.4, 134.6, 129.4, 129.1, 127.5, 127.0, 126.2, 118.4, 117.2, 114.4, 113.4, 98.5, 84.8, 61.2, 60.7, 56.0, 55.6, 38.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{27}O_5$, 443.1853; found, 443.1846.

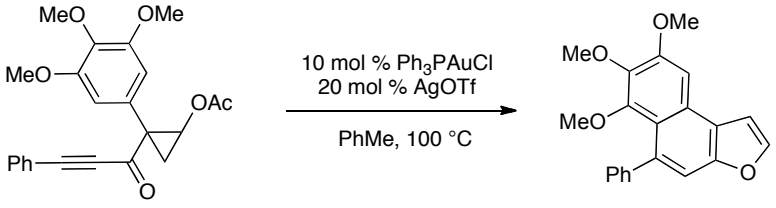


6,7,8-trimethoxy-5-phenyl-2-(4-(trifluoromethyl)phenyl)-1,2-dihydronaphtho[2,1-*b*]furan (2.92): Following the general procedure **(G)**, the reaction of **2.86** (0.0329 g, 0.068 mmol) afforded the product as a pale yellow oil (0.0305 g, 93% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2933, 1615, 1581, 1467, 1421, 1323, 1162, 1118, 1066, 1042 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 7.42-7.30 (m, 5H), 6.89 (s, 1H), 6.63 (s, 1H), 6.02 (dd, J = 9.8, 7.4 Hz, 1H), 4.03-3.93 (m, 4H), 3.85 (s, 3H), 3.41 (dd, J = 15.3, 7.4 Hz, 1H), 3.25 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.2, 154.1, 151.1, 146.6, 144.5, 140.7, 140.4, 130.4 (q, J = 32.2 Hz), 129.2, 128.9, 124.3 (q, J = 270.5 Hz), 127.0, 126.3, 126.1, 125.9 (q, J = 3.7 Hz), 118.4, 116.5, 113.1, 98.2, 83.7, 61.3, 60.8, 56.0, 38.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{24}F_3O_4$, 481.1621; found, 481.1617.

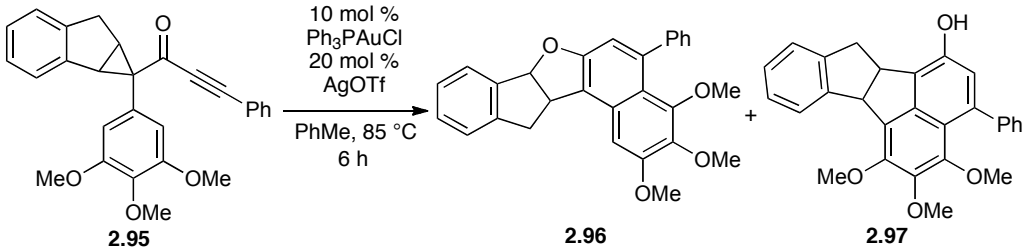


2-butyl-6,7,8-trimethoxy-5-phenyl-1,2-dihydronaphtho[2,1-*b*]furan (2.93): Following the general procedure **(G)**, the reaction of **2.87** (0.0513 g, 0.13 mmol) afforded the product as a pale yellow oil (0.0456 g, 89% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 3:1). FTIR (neat): 2931, 1616, 1582, 1466, 1338, 1258, 1121, 1044 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 5H), 6.76 (s, 1H), 6.65 (s, 1H), 5.02-4.94 (m, 1H), 3.99 (s, 3H), 3.85 (s, 3H), 3.53 (dd, J = 15.2, 9.3 Hz, 1H), 3.23 (s, 3H), 3.10 (dd, J = 15.2, 7.6 Hz, 1H), 1.99-1.86 (m, 1H), 1.86-

1.70 (m, 1H), 1.65-1.35 (m, 4H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 156.4, 153.9, 151.0, 144.7, 140.1, 140.0, 129.4, 129.0, 127.0, 126.1, 117.8, 117.5, 113.4, 98.2, 84.2, 61.3, 60.8, 56.0, 36.4, 35.1, 27.8, 22.9, 14.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{29}O_4$, 393.2060; found, 393.2061.



6,7,8-trimethoxy-5-phenylnaphtho[2,1-*b*]furan (2.94): Following the general procedure **(G)**, the reaction of **2.88** (0.0412 g, 0.10 mmol) afforded the product as a pale yellow oil (0.0166 g, 48% yield) after purification by flash chromatography (silica gel, pentane:diethyl ether = 2:1). FTIR (neat): 2934, 1617, 1474, 1392, 1357, 1259, 1120, 1035 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 2.1 Hz, 1H), 7.43-7.31 (m, 6H), 7.29 (s, 1H), 7.19 (d, J = 1.2 Hz, 1H), 4.06 (s 3H), 3.89 (s, 3H), 3.26 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 153.6, 151.9, 151.2, 144.8, 144.3, 141.3, 136.1, 129.1, 127.0, 126.2, 126.0, 121.8, 119.2, 113.8, 105.6, 99.6, 61.3, 60.9, 56.1; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{21}H_{19}O_4$, 335.1278; found, 335.1273.

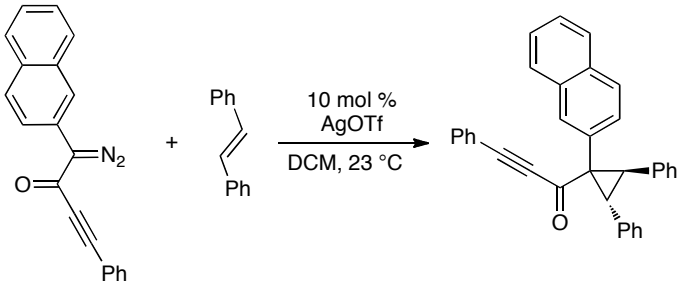


2,3,4-trimethoxy-5-phenyl-12,12a-dihydro-7a*H*-indeno[1,2-*b*]naphtho[1,2-*d*]furan (2.96): Following the general procedure **(G)**, the reaction of **2.95** (0.1962 g, 0.46 mmol) afforded the product as a white solid (0.0658 g, 34% yield) after purification by flash chromatography (pentane:dichloromethane = 1:2, then 1:4). m.p. 148-150 ºC; FTIR (neat): 2936, 1613, 1581, 1465, 1420, 1374, 1338, 1260, 1243, 1120, 1045 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 5.0, 3.5 Hz, 1H), 7.41-7.18 (m, 8H), 6.83 (s, 1H), 6.72 (s, 1H), 6.41 (d, J = 8.8 Hz, 1H), 4.66 (td, J = 8.8, 2.6 Hz, 1H), 4.05 (s, 3H), 3.86 (s, 3H), 3.71 (dd, J = 16.6, 8.8 Hz, 1H), 3.46 (dd, J = 16.5, 2.6 Hz, 1H), 3.21 (s, 3H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 155.5, 153.9, 151.3, 144.6, 142.8, 141.0, 140.6, 140.1, 129.7, 129.1, 128.9, 128.8, 127.5, 126.9, 126.3, 126.1, 125.4, 120.8, 118.4, 113.8, 98.0, 91.8, 61.3, 60.7, 56.0, 44.7, 38.5, one more signal attributed to the slow equilibrium of the conformations of the compound at room temperature; carbons between δ 128.9 and 128.8 are not chemically equivalent; ^{13}C-NMR (150 MHz, $CDCl_3$, 55 ºC) δ 155.8, 154.1, 151.4, 144.8, 142.9, 141.1, 140.8, 140.3, 129.7, 129.3, 128.9, 127.6, 126.9, 126.3, 126.1, 125.4, 120.9, 118.6, 113.9, 98.3, 91.9, 61.2, 60.7, 56.1, 44.9, 38.6; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{25}O_4$, 425.1747; found, 425.1743.

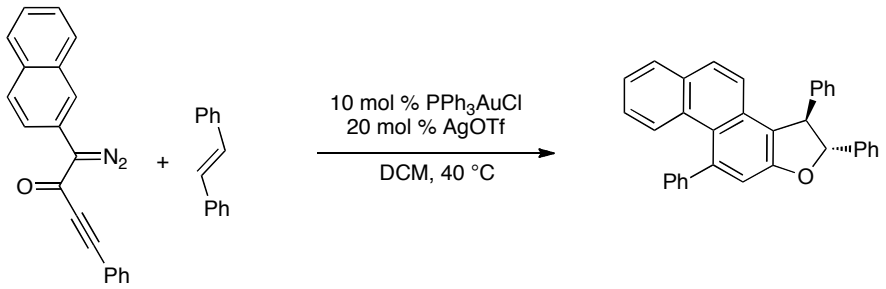
1,2,3-trimethoxy-4-phenyl-11,11a-dihydro-6b*H*-indeno[1,2-*a*]acenaphthylen-6-ol (2.97): Purified by flash chromatography (silica gel, pentane:dichloromethane = 1:2, then 1:4) to afford the product (0.0771 g, 39% yield) as a yellow solid. m.p. 117-119 ºC; FTIR (neat): 3331, 2918, 1589, 1457, 1445, 1384, 1337, 1310, 1285, 1247, 1214, 1113, 1052, 1033, 1021 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.0 Hz, 1H), 7.33 (br.s, 5H), 7.17 (br.s, 3H), 6.75 (s, 1H), 5.45 (d, J = 7.2 Hz, 1H), 5.01 (s, 1H), 4.58 (t, J = 7.2 Hz,

1H), 4.13 (s, 3H), 3.90 (s, 3H), 3.67 (dd, J = 16.5, 10.1 Hz, 1H), 3.46 (d, J = 16.5 Hz, 1H), 3.16 (s, 3H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 148.5, 147.3, 145.4, 144.7, 142.5, 142.3, 138.0, 137.7, 130.2, 129.6 (2xC), 127.4, 127.3, 127.12, 127.06, 126.6, 126.3, 125.2, 121.4, 117.4, 61.5, 61.0, 60.8, 54.7, 44.9, 37.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{28}H_{25}O_4$, 425.1747; found, 424.1743.

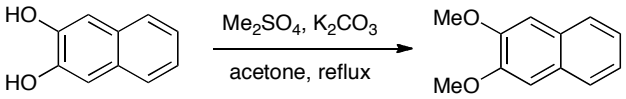
The one-pot procedure for the triple cascaded reactions: Under argon atmosphere, a two neck round-bottom flask was charged with alkene (1.0 mmol, 5 equiv) and $Rh_2(TFA)_4$ (0.004 mmol, 0.02 equiv) in dichloromethane (2 ml). A water condenser and thermometer were connected. To this solution at reflux was added a solution of diazo compound (0.2 mmol, 1 equiv) in dichloromethane (2 ml) over 3 h. The reaction was stirred at reflux for an additional hour before cooling down to room temperature. To this solution at room temperature was added chlorotriphenylphosphine gold (I) (0.02 mol, 0.1 equiv) and silver trifluoromethanesulfonate (0.04 mmol, 0.2 equiv) and toluene (8 ml). The round-bottom flask was wrapped with aluminum foil and the reaction mixture was heated to reflux. The reaction was monitored by TLC and heating was stopped when all the cyclopropane was converted to the final product. After cooling down to room temperature, the resulting mixture was filtered through a plug of silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography.



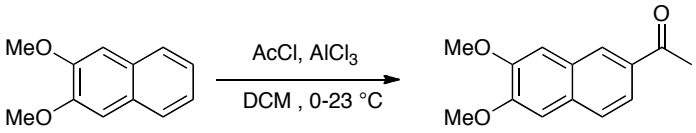
1-(1-(naphthalen-2-yl)-2,3-diphenylcyclopropyl)-3-phenylprop-2-yn-1-one (2.101): Under argon atmosphere, an aluminum foil wrapped round-bottom flask was charged with *trans*-stilbene (0.17 g, 0.94 mmol, 5 equiv), silver trifluoromethanesulfonate (0.0052 g, 0.020 mmol, 0.1 equiv) and dichloromethane (2 ml). To this solution at room temperature was added a solution of diazo compound **2.68** (0.055 g, 0.19 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. The reaction was stirred for another 30 minutes at this temperature before the removal of solvent. The crude residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 10:1) to afford the product as white foam (0.024 g, 29% yield). FTIR (neat): 3060, 2193, 1637, 1628, 1284, 1042, 828; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.82-7.79 (m, 2H), 7.71 (d, J = 8.8 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.50-7.47 (m, 2H), 7.40-7.37 (t, J = 7.6 Hz, 2H); 7.31-7.22 (m, 3H), 7.13-7.02 (m, 7H), 6.77 (d, J = 8.0 Hz, 2H), 4.18 (d, J = 8.4 Hz, 1H), 3.96 (d, J = 8.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 183.4 (C), 136.4 (C), 135.4 (C), 134.1 (C), 133.4 (C), 133.2 (CH), 133.0 (C), 131.7 (CH), 130.6 (CH), 130.1 (CH), 129.8 (CH), 128.6 (CH), 128.43 (CH), 128.41 (CH), 128.26 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 127.5 (CH), 126.8 (CH), 126.4 (CH), 126.3 (CH), 120.0 (C), 95.1 (C), 89.0 (C), 55.5 (C), 41.6 (CH), 36.9 (CH); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{34}H_{25}O_1$, 449.1911; found, 499.1907.



2,3,10-triphenyl-2,3-dihydrophenanthro[2,1-b]furan (2.103): Under argon atmosphere, an aluminum foil wrapped round-bottom flask was charged with trans-stilbene (0.15 g, 0.84 mmol, 5 equiv), silver trifluoromethanesulfonate (0.0084 g, 0.033 mmol, 0.2 equiv) and dichloromethane (5 ml). To this solution at reflux was added a solution of diazo compound **2.68** (0.050 g, 0.17 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. After stirring at this temperature for another 2 hours, the reaction was cooled down to room temperature and then filtered through a plug of silica gel. After the removal of solvent, the crude residue was purified by flash chromatography (silica gel, pentane:diethyl ether = 50:1) to afford the product as a white gum (0.035 g, 47% yield). FTIR (neat): 3028, 1596, 1575, 1493, 1452, 1380, 1286, 1214, 1053, 984; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.51-7.23 (m, 19H), 7.04 (td, J = 7.6, 1.2 Hz, 1H), 5.76 (d, J = 6.1 Hz, 1H), 5.0 (d, J = 5.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.0 (C), 145.5 (C), 143.3 (C), 143.2 (C), 141.8 (C), 132.1 (C), 131.4 (C), 131.1 (C), 129.3 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.4 (CH), 128.2 (CH), 128.0 (CH), 127.5 (CH), 127.4 (CH), 125.8 (CH), 125.2 (CH), 125.1 (CH), 124.0 (C), 122.8 (CH), 122.3 (C), 114.7 (CH), 93.9 (CH), 58.2 (CH); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. For $C_{34}H_{25}O_1$, 449.1900; found, 499.1896.

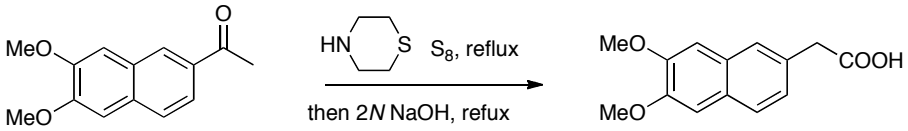


2,3-dimethoxynaphthalene (2.104): To a suspension of 2,3-dihydroxynaphthalene (20.0 g, 0.13 mol, 1 equiv) and potassium carbonate (38.0 g, 0.28 mol, 2 equiv) in acetone (300 ml) was added dimethyl sulfate (26.5 ml, 0.28 mol, 2 equiv) through a dropping funnel over 30 minutes. The reaction was then heated up to reflux and stirred overnight. After cooling down to room temperature, the reaction mixture was filtered through silica gel and concentrated in vacuo. The residue was dissolved in dichloromethane and washed with water three times. The combined organic layers were dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude product was obtained as a yellow solid, which was directly used for next step. The spectroscopic data were consistent with the published values.[130] ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.68-7.64 (m, 2H), 7.34-7.30 (m, 2H), 7.08 (s, 2H), 3.97 (s, 6H).



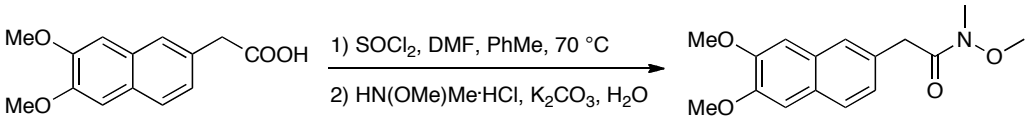
1-(6,7-dimethoxynaphthalen-2-yl)ethanone (2.105): To a suspension of aluminum chloride (6.15 g, 0.046 mol, 1.9 equiv) in dichloromethane (20 ml) at 0 $^{\circ}$C was added acetyl chloride (3.3 ml, 0.046 mol, 1.9 equiv) dropwise. The reaction was stirred at this temperature for 10 minutes before the addition of a solution of **2.104** (4.57 g, 0.024 mol, 1 equiv) in dichloromethane (10 ml). The reaction was warmed up slowly in the ice-water bath to room temperature and stirred overnight. Water was then added slowly (caution: gas evolution). After the separation of layers, the aqueous one was extracted with

dichloromethane three times and the combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 3:1) to afford the product as a yellow solid (3.73 g, 67% yield). The spectroscopic data were consistent with the published values.[130] ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.90 (dd, J = 8.5, 1.3 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.22 (s, 1H), 7.14 (s, 1H), 4.03 (s, 3H), 4.02 (s, 3H), 2.69 (s, 3H).



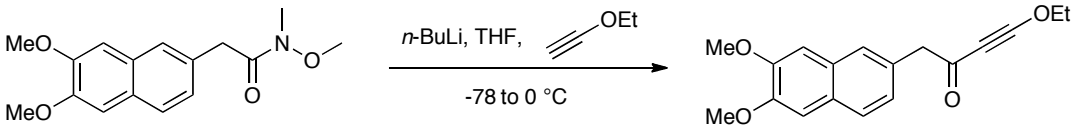
2-(6,7-dimethoxynaphthalen-2-yl)acetic acid (2.106) A mixture of **2.105** (1.59 g, 0.0069 mol, 1equiv), sulfur (0.45 g, 0.14 mol, 2 equiv) and morpholine (1.80 ml, 0.21 mol, 3 equiv) was stirred overnight at reflux. After cooling down to room temperature, a solution of sodium hydroxide (2.17 g, 0.054 mol, 8 equiv) in water (10 ml) and neat benzyl ammonium chloride (0.084 g, 0.0037 mol, 0.05 equiv) were added. The reaction was heated to reflux again and stirred overnight. It was then cooled down to room temperature and 2*N* HCl solution was added until the pH~7. The solid was collected by filtration and washed with 2*N* HCl till the filtrate's pH~1. The filtrated was then extracted with ethyl acetate three times and the combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel, washed with acetone and concentrated in vacuo to afford the crude product as a yellow solid (1.53g, 77% yield). m.p. 141-143 $^{\circ}$C; FTIR (neat): 2945 (br.), 1695, 1512, 1492 1424, 1251, 1208, 1163, 1130, 1006, 855 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OCD_3) δ 7.68 (d, J = 8.2 Hz, 1H), 7.64

(s, 1H), 7.28 (dd, J = 8.2, 1.5 Hz, 1H), 7.25 (s, 1H), 7.23 (s, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.72 (s, 2H); ^{13}C-NMR (100 MHz, CD_3OCD_3) δ 173.5 (C), 151.0 (C), 150.7 (C), 131.3 (C), 130.3 (C), 129.1 (C), 127.4 (CH), 127.2 (CH), 126.5 (CH), 107.1 (2xCH), 55.9 (CH_3), 41.5 (CH_2); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{14}H_{15}O_4$, 247.0965; found, 247.0966.



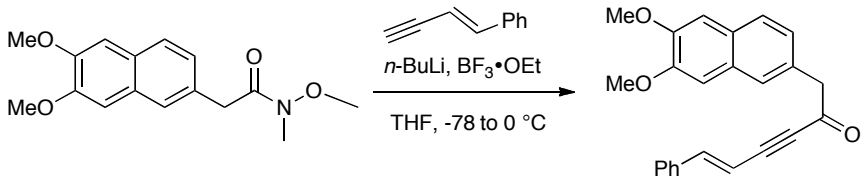
2-(6,7-dimethoxynaphthalen-2-yl)-N-methoxy-N-methylacetamide (2.107): To a solution of **2.106** (1.5980 g, 6.49 mmol, 1 equiv) in toluene (20 ml) at 70 °C was added *N,N*-diemthylformade (0.01 ml, 0.00014 mmol, 0.02 equiv) in one portion and thionyl chloride (0.60 ml, 8.25 mol, 1.3 equiv) over 30 minutes. After stirring at this temperature for two additional hours, the reaction was cooled down to 0 °C. To this solution at 0 °C was added *N,O*-dimethoxyamide hydrochloride (0.9609 g, 9.85 mol, 1.5 equiv) in one portion and a solution of potassium carbonate (3.5925 g, 0.026 mol, 4 equiv) in water (10 ml) over 30 minutes. The reaction was then warmed up slowly in the ice-water bath slowly to room temperature and stirred overnight. 2*N* HCl was added slowly into the reaction mixture. After the separation of layers, the aqueous one was extracted with ethyl acetate three times and the combined organic layers were washed with a saturated sodium bicarbonate solution, brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 1:2) to afford the product as a yellow oil (1.6350 g, 87% yield). FTIR (neat): 2937, 1659, 1609, 1512, 1491, 1463, 1437, 1420, 1382, 1255, 1206,

1163, 1131, 1008 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0 Hz, 1H), 7.61 (s, 1H), 7.29 (dd, J = 8.4, 1.6 Hz, 1H), 7.09 (s, 1H), 7.08 (s, 1H), 3.98 (6H, 2xCH_3), 3.89 (s, 2H), 3.60 (s, 3H), 3.21 (s, 3H). ^{13}C-NMR (100 MHz, CD_3OCD_3) δ 172.2 (C), 149.2 (C), 148.9 (C), 130.3 (C), 128.8 (C), 127.6 (C), 126.1 (CH), 125.9 (CH), 125.4 (CH), 105.74 (CH), 105.71 (CH), 60.8 (CH_3), 55.3 (2xCH_3), 38.9 (CH_2), 31.76 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{16}H_{20}O_4N_1$, 290.1387; found, 290.1387.



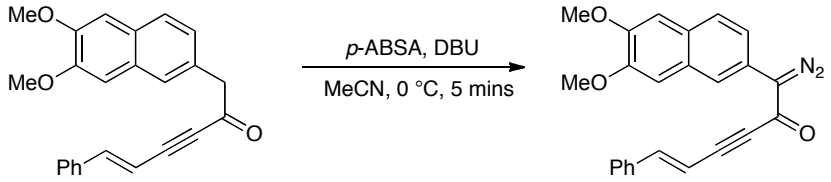
1-(6,7-dimethoxynaphthalen-2-yl)-4-ethoxybut-3-yn-2-one (2.108): Under argon atmosphere, to a solution of ethyl ethylnyl ether (~40 wt % in hexanes, 1.35 g, 7.70 mmol, 4 equiv) in THF at -78 °C was added *n*-butyllithium (2.5 M in hexanes, 2.70 ml, 6.75 mmol, 3.5 equiv) over 30 minutes. The reaction was then stirred at -78 °C for 5 minutes and room temperature for 30 minutes. After being chilled back to -78 °C, a solution of **2.107** (0.56 g, 1.94 mmol, 1 equiv) in THF (5 ml) was added over 30 minutes. The reaction was stirred at -78 °C for another 5 minutes and then 0 °C for 1 hour. The reaction was quenched with a saturated solution of ammonium chloride. The layers were separated and the aqueous one was extracted with diethyl ether three times. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 3:1) to afford the product as an orange oil (0.11 g, 19% yield). The compound was directly used for the next step. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 8.1 Hz, 1H), 7.56 (s, 1H), 7.24 (dd, J = 8.4, 1.5

Hz, 1H), 7.11 (s, 1H), 7.09 (s, 1H), 4.15 (q, J = 7.2 Hz, 2H), 4.00 (s, 6H), 3.88 (s, 2H), 1.29 (t, J = 7.2 Hz, 3H).

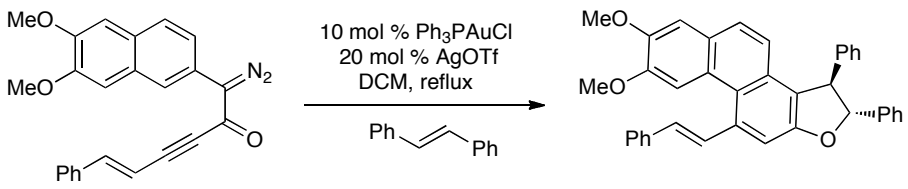


(*E*)-1-(6,7-dimethoxynaphthalen-2-yl)-6-phenylhex-5-en-3-yn-2-one (2.110): To a solution of styrylacetylene (179.3 mg, 1.40 mmol, 2.3 equiv) in THF (2 ml) at -78 °C, *n*-BuLi (2.5 M in hexanes, 0.48 ml, 1.20 mmol, 2 equiv) was added slowly. The reaction was stirred for 5 minutes before the addition of BF_3•OEt_2 (0.17 ml, 1.35 mmol, 2.2 equiv). The resulting mixture was stirred for 15 minutes at this temperature. A solution of **2.107** (175.1 mg, 0.605 mmol, 1 equiv) in THF (2 ml) was then added slowly. After stirring the mixture for 2 hour at -78 °C, acetic acid (0.20 ml) and BF_3•OEt_2 (0.20 ml) were added subsequently. The reaction was slowly warmed up to -20 °C over 1 hour and then quenched with saturated sodium bicarbonate solution. The aqueous solution was extracted with diethyl ether three times and the combined organic layers were dried over magnesium sulfate. The solid was filtered off and the filtrate was concentrated in vacuo. The crude residue was purified by chromatography (silica gel, hexanes:ethyl acetate = 5:1 then 3:1) to afford the product as a yellow solid (164.1 mg, 76% yield). R_f = 0.23 (hexanes: ethyl acetate = 4:1). FTIR (neat): 3003, 2937, 2829, 2253, 2171, 1656, 1606, 1574, 1511, 1489, 1463, 1449, 1436, 1419, 1407, 1277, 1253, 1204, 1162, 1129, 1032, 1005 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.3 Hz, 1H), 7.60 (s, 1H), 7.35 (br.s, 5H), 7.29-7.25 (m, 1H), 7.12 (d, J = 4.3 Hz, 2H), 7.05 (d, J = 16.3 Hz, 1H), 6.17 (d, J = 16.3 Hz, 1H), 4.00 (s, 5H), 4.00 (s, 3H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 185.1 (C),

149.6 (C), 149.4 (C), 148.0 (CH), 134.9 (C), 130.0 (CH), 129.2 (C), 128.9 (C), 128.8 (CH), 128.2 (C), 127.1 (CH), 126.8 (CH), 126.7 (CH), 126.0 (CH), 106.0 (2xCH), 105.0 (CH), 92.6 (C), 89.8 (C), 55.8 (2xCH_3), 52.(CH_2); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{24}H_{21}O_3$, 357.1482; found, 357.1492.

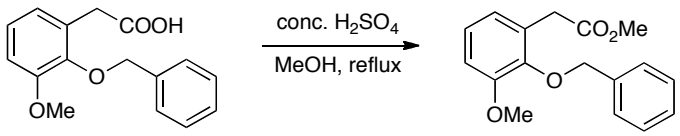


(*E*)-1-diazo-1-(6,7-dimethoxynaphthalen-2-yl)-6-phenylhex-5-en-3-yn-2-one (2.111): Under argon atmosphere, to a solution of **2.110** (104.1 mg, 0.29 mmol, 1 equiv) and *p*-ABSA (113.2 mg, 0.47 mmol, 1.6 equiv) in acetonitrile (5 ml) at 0 °C was added DBU (0.09 ml, 0.60 mmol, 2 equiv) in one portion. The resulting mixture was stirred at this temperature for 5 minutes and then quenched with saturated sodium bicarbonate solution. The aqueous solution was extracted with dichloromethane three times. The combined organic layers were dried over magnesium sulfate. The solid was filtered off and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 3:1) to afford the product as an orange solid (79.6 mg, 71% yield). This compound was immediately used for the next step. FTIR (neat): 3059, 3027, 2932, 2837, 1615, 1596, 1578, 1523,1509, 1479, 1453, 1437, 1393, 1356, 1262, 1226, 1164, 1154, 1093, 1074 1052, 1023 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.08 (br.s, 1H), 7.74 (d, J = 8.6 Hz, 1H), 7.54-7.32 (m, 6H), 7.15-7.11 (m, 3H), 6.29 (d, J = 16.3 Hz, 1H), 4.01 (s, 3H), 4.01 (s, 3H).

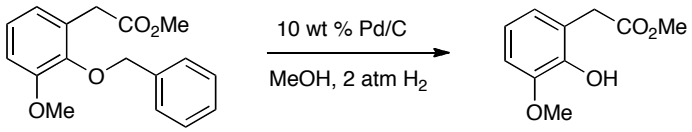


7,8-dimethoxy-2,3-diphenyl-10-((*E*)-styryl)-2,3-dihydrophenanthro[2,1-*b*]furan (2.112): Under argon atmosphere, to a solution of *trans*-stilbene (235.1 mg, 1.30 mmol, 5 equiv), AgOTf (13.9 mg, 0.054 mmol, 0.2 equiv) and Ph_3PAuCl (13.0 mg, 0.026 mmol, 0.1 equiv) in dichloromethane (5 ml) at reflux was added a solution of **2.111** (101.4 mg, 0.27 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. The resulting mixture was stirred overnight at this temperature (8 hours). After cooling down to room temperature, the solvent was removed under vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 9:1, 4:1 then 2:1) to afforded the product was a yellow gum (27.1 mg, 19% yield). R_f = 0.25 (hexanes: ethyl acetate = 5:1); FTIR (neat): 3003, 2937, 2829, 2253, 2171, 1656, 1606, 1574, 1511, 1489, 1463, 1449, 1436, 1419, 1407, 1277, 1253, 1204, 1162, 1129, 1032, 1005 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.96 (d, J = 16.1 Hz, 1H), 7.65 (d, J = 7.8 Hz, 2H), 7.55-7.09 (m, 18H), 5.70 (d, J = 5.8 Hz, 1H), 4.96 (d, J = 5.8 Hz, 1H), 3.99 (s, 3H), 3.71 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.6 (C), 148.1 (C), 147.8 (C), 143.2 (C), 141.7 (C), 138.5 (C), 137.4 (C), 133.3 (CH), 129.8 (C), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.2 (C), 127.84 (CH), 127.80 (CH), 127.4 (CH), 127.2 (CH), 126.8 (2xC), 126.3 (CH), 125.5 (CH), 124.4 (C), 122.2 (CH), 120.9 (CH), 111.3 (CH), 108.9 (CH), 108.3 (CH), 93.5 (CH), 57.9 (CH), 55.8 (CH_3), 55.6 (CH_3); HRMS (APCI) *m/z*: $[M]^+$ calcd. for $C_{38}H_{30}O_3$, 534.2190; found, 534.2203.

Experimental of Chapter III: Synthesis of Dihydrobenzofurans *via* Sequential C–H Functionalizations

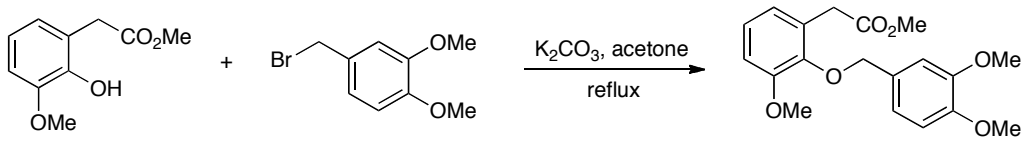


methyl 2-(2-(benzyloxy)-3-methoxyphenyl)acetate (3.41): A solution of 2-(2-(benzyloxy)-3-methoxyphenyl)acetic acid (1.72 g, 0.0063 mol) and concentrated sulfuric acid (3 drops) in methanol (50 ml) was stirred at reflux for 24 hours. After cooling down to room temperature, aqueous saturated sodium bicarbonate solution was added. The solution was extracted with diethyl ether three times. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo to afford the product as a yellow oil (1.68 g, 93% yield). The crude product was directly used for the next step. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44-7.46 (m, 2H), 7.39-7.30 (m, 3H), 7.04 (t, J = 8.0 Hz, 1H), 6.89 (dd, J = 8.0, 1.2 Hz, 1H), 6.82 (dd, J = 8.0, 1.2 Hz, 1H), 5.03 (s, 2H), 3.89 (s, 3H), 3.61 (s, 5H).

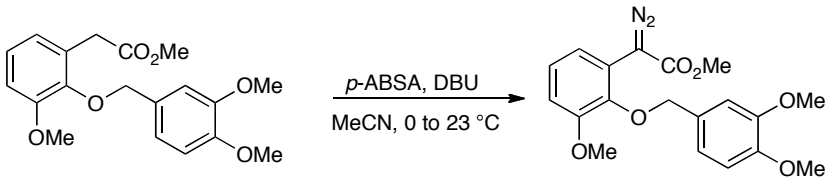


methyl 2-(2-hydroxy-3-methoxyphenyl)acetate (3.42): A suspension of palladium on activated carbon (10 wt%, 0.18 g, 0.17 mmol, 0.05 equiv) and **3.41** (0.93 g, 3.37 mmol, 1 equiv) in methanol (50 ml) was shaken overnight in a hydrogenator under hydrogen atmosphere (2 atm). The resulting reaction mixture was filtered through silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography (silica

gel, hexanes:diethyl ether = 2:1) to afford the product as a colorless oil (0.51 g, 86% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.84-6.78 (m, 3H), 5.88 (s, 1H), 3.89 (s, 3H), 3.71 (s, 3H), 3.68 (s, 2H).

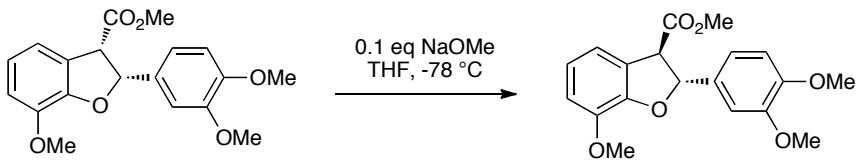


methyl 2-(2-((3,4-dimethoxybenzyl)oxy)-3-methoxyphenyl)acetate (3.43): Under argon atmosphere, a mixture of **3.42** (0.51 g, 2.59 mmol, 1 equiv), 4-(bromomethyl)-1,2-dimethoxybenzene (0.96 g, 4.16 mmol, 1.6 equiv), and potassium carbonate (0.72 g, 5.24 mmol, 2 equiv) and acetone (30 ml) was stirred overnight at reflux. After cooling down to room temperature, the reaction mixture was filtered through silica gel and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:acetone = 4:1) to afford the product as pale yellow oil (0.83 g, 92% yield). FTIR (neat): 2951, 2837, 1734, 1515, 1476, 1464, 1261, 1239, 1209, 1157, 1138, 1077, 1026; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.04 (t, J = 8.0 Hz, 2H), 6.95 (dd, J = 8.0, 1.6 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.85-6.81 (m, 2H), 4.98 (s, 2H), 3.97 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H), 3.63 (s, 3H), 3.59 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.0 (C), 152.7 (C), 148.8 (C), 148.7 (C), 146.0 (C), 130.3 (C), 128.6 (C), 123.9 (CH), 122.6 (CH), 120.8 (CH), 111.61 (CH), 111.59 (CH), 110.7 (CH), 74.4 (CH_2), 55.8 (CH_3), 55.69 (CH_3), 55.66 (CH_3), 51.7 (CH_3), 35.6 (CH_2); HRMS (APCI) *m/z*: $[M-H]^-$ calcd. for $C_{19}H_{21}O_6$, 345.1344; found, 345.1341;

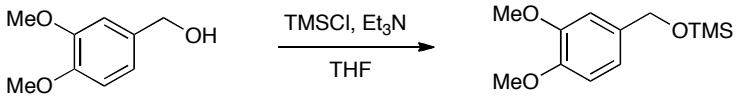


methyl 2-diazo-2-(2-((3,4-dimethoxybenzyl)oxy)-3-methoxyphenyl)acetate(3.44): Under argon atmosphere, to a solution of **3.43** (0.83 g, 2.39 mmol, 1 equiv) and *p*-ABSA (0.76 g, 3.16 mmol, 1.3 equiv) in acetonitrile (10 ml) at 0 °C was added DBU (0.55 ml, 3.68 mmol, 1.5 equiv) in one portion. The reaction was warmed up slowly in the ice-water bath to room temperature and stirred for 3 days. It was quenched with saturated aqueous ammonium chloride solution and then extracted with diethyl ether three times. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:acetone = 5:1) to afford the product as a yellow oil (0.49 g, 55% yield). FTIR (neat): 2953, 2838, 2097, 1701, 1517, 1471, 1264, 1159, 1030; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.15-7.08 (m, 2H), 6.95 (d, J = 1.6 Hz, 1H), 6.88 (dd, J = 7.6, 2.0 Hz, 1H), 6.83 (dd, J = 8.4, 1.6 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 4.94 (s, 2H), 3.91 (s, 3H), 3.88 (s, 6H), 3.75 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.0 (C), 152.7 (C), 149.0 (C), 148.8 (C), 143.8 (C), 129.2 (C), 124.4 (CH), 121.5 (CH), 121.4 (CH), 120.6 (C), 111.7 (CH), 111.3 (CH), 110.7 (CH), 75.4 (CH_2), 55.9 (CH_3), 55.8 (CH_3), 55.6 (CH_3), 51.8 (CH_3), one missing carbon attributed to C=N_2; HRMS (APCI) *m/z*: $[M-N_2+H]^+$ calcd. for $C_{19}H_{21}O_6$, 345.1333; found, 345.1331.

(2*R*,3*S*)-methyl 2-(3,4-dimethoxyphenyl)-7-methoxy-2,3-dihydrobenzofuran-3-carboxylate (*cis*-3.45): Under argon atmosphere, to a mixture of **3.44** (0.57 g, 1.53 mmol, 1 equiv), calcium chloride (0.85 g, 7.66 mmol, 5 equiv) and toluene (8 ml) at -45 °C was added Rh_2(*S*-PTAD)$_4$ (0.013 g, 0.0079 mmol, 0.005 equiv) in one portion. After stirring at this temperature for 30 minutes, the reaction mixture was filtered though a plug of silica gel and then concentrated in vacuo. ^{1}H-NMR was used to determine the diastereomeric ratio (dr >97:3) and the crude residue was purified by recrystallization. The crude mixture was dissolved in hot solvents of diethyl ether and hexanes. After sitting overnight at room temperature, white needles (0.22 g, 42%) were collected. $[\alpha]_D^{25}$ +106.4 (c 1.53, $CHCl_3$); FTIR (neat): 2940, 2837, 1731, 1593, 1524, 1492, 1468, 1452, 1338, 1302, 1202, 1185, 1162, 1087, 1024, 1011, 965; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.95-6.81 (m, 6H), 5.98 (d, J = 10.0 Hz, 1H), 4.55 (d, J = 9.6 Hz, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.86 (s, 3H), 3.29 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.6 (C), 149.01 (C), 148.99 (C), 148.8 (C), 144.8(C), 129.2 (C), 126.1 (C), 122.0 (CH), 119.2 (CH), 117.8 (CH), 112.6 (CH), 110.6 (CH), 109.6 (CH), 86.6 (CH), 56.1 (CH_3), 56.0 (CH_3), 55.9 (CH_3), 54.5 (CH), 51.9 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{21}O_6$, 345.1333; found, 345.1331; HPLC analysis: 99% ee (AD-H, 20% *i*-PrOH in hexane, 0.7 mL/min, λ = 254 nm, t_R = 22.2 min, minor; t_R = 25.4 min, major). The mother liquid was concentrated in vacuo and purified by flash chromatography (silica gel, pentane:acetone = 5:1) to afford the product as a white power (0.11 g, 20%).



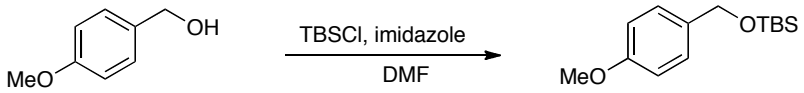
(2*R*,3*R*)-methyl 2-(3,4-dimethoxyphenyl)-7-methoxy-2,3-dihydrobenzofuran-3-carboxylate (*trans*-3.45): To a solution of *cis*-**3.45** (0.0531 g, 0.15 mmol, 1 equiv) in THF at -45 °C was added sodium methoxide (0.5 M in MeOH, 0.03 ml, 0.015 mmol, 0.1 equiv) in one portion. The reaction was stirred at this temperature for 1 hour before being poured into a PH = 7 buffer. After the separation of layers, the aqueous one was extracted with diethyl ether three times. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude mixture was purified by flash chromatography (silica gel, pentane:acetone = 5:1) to afford the product as a pale yellow oil (0.0500 g, 94% yield). $[\alpha]_D^{25}$ -51.5 (c 1.11, $CHCl_3$); FTIR (neat): 2952, 2837, 1735, 1593, 1262, 1236, 1199, 1160, 1139, 1088, 1025, cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.00-6.95 (m, 3H), 6.91 (t, J = 7.2 Hz, 1H), 6.85 (t, J = 7.6 Hz, 2H), 6.08 (d, J = 8.0 Hz, 1H), 4.36 (d, J = 8.4 Hz, 1H), 3.90 (s, 3H), 3.88, (s, 3H), 3.87 (s, 3H), 3.82 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.2 (C), 149.18 (C), 149.16 (C), 147.8 (C), 144.6 (C), 132.5 (C), 125.1 (C), 121.5 (CH), 118.8 (CH), 117.0 (CH), 112.5 (CH), 111.1 (CH), 109.2 (CH), 86.6 (CH), 55.1 (CH_3), 56.02 (CH_3), 55.96 (CH), 55.9 (CH_3), 52.6 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{21}O_6$, 345.1333; found, 345.1331; HPLC analysis: 98% ee (AD-H, 10% *i*-PrOH in hexane, 0.7 mL/min, λ = 254 nm, t_R = 20.7 min, minor; t_R = 26.1 min, major).



((3,4-dimethoxybenzyl)oxy)trimethylsilane (S3): To a solution of 3,4-dimethoxybenzyl alcohol (1.84 g, 0.011 mol, 1 equiv) and triethylamine (2.30 ml, 0.017 mol, 1.5 equiv) in THF (40 ml) at 0 °C was added chlorotrimethylsilane (1.70ml, 0.013mol, 1.2) over 30

minutes. The reaction was warmed up slowly in the ice-water bath to room temperature and stirred overnight. The reaction mixture was then filtered through silica gel, washed with diethyl ether, and concentrated in vacuo. The crude residue was purified by flash chromatography (hexanes:diethyl ether = 4:1) to afford the product as pale yellow oil (2.50 g, 95% yield). R_f = 0.26 (hexanes:diethyl ether = 5:1); FTIR (neat): 2954, 2835, 1514, 1464, 1250, 1234, 1156, 1137, 1070, 1029 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.89 (s, 1H), 6.87-6.81 (m, 2H), 4.63 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 0.15 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.7 (C), 147.9 (C), 133.3 (C), 118.6 (CH), 110.7 (CH), 110.0 (CH), 64.2 (CH_2), 55.5 (CH_3), 55.3 (CH_3), 0.7 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{20}O_3{}^{23}Na_1{}^{28}Si_1$, 263.1074; found, 263.1074.

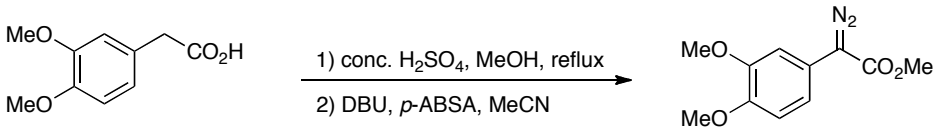
Exemplified procedure for the synthesis of TBS benzyl ether:



***tert*-butyl((4-methoxybenzyl)oxy)dimethylsilane (S4):** A mixture of *p*-methoxybenzyl alcohol (2.0102 g, 0.015 mol, 1 equiv), imidazole (1.4917 g, 0.022 mol, 1.5 equiv), and DMF (10 ml) was stirred at room temperature until a clear solution was obtained. The reaction was cooled to 0 $^{\circ}$C and a solution of TBSCl (2.1956 g, 0.015 mol, 1 equiv) in DMF (10 ml) was then added over 30 minutes. The reaction was warmed up slowly in the ice-water bath to room temperature and stirred overnight. The reaction was diluted with water and extracted with diethyl ether till TCL indicated there was no product left in the aqueous layer. The combined organic layers were washed with brine and dried over magnesium sulfate. The solid was filtered off and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:diethyl ether

= 5:1) to afford the product as a colorless oil (2.9992 g, 82% yield). The spectroscopic data were consistent with the published values.[180] ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 4.68 (s, 2H), 3.80 (s, 3H), 0.93 (s, 9H), 0.09 (s, 6H).

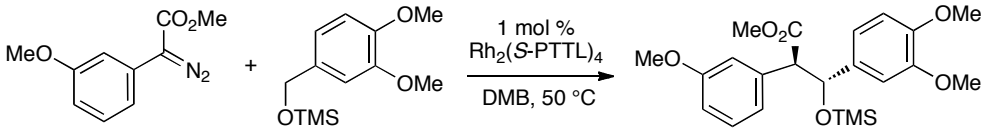
Exemplified procedure for the synthesis of methyl aryldiazoacetate:



methyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate (S5): A mixture of 3,4-dimethoxyphenylacetic acid (10.4 g, 0.053 mol), concentrated sulfuric acid (10 drops) and methanol (60 ml) was stirred overnight at reflux. After cooling down to room temperature, saturated sodium bicarbonate solution was added. The aqueous solution was extracted with diethyl ether three times. The combined organic layers were washed with saturated sodium bicarbonate solution, water, brine, and dried over magnesium sulfate. The solid was filtered off and the filtrate was concentrated in vacuo. After drying over a vacuum line, the crude product (10.0835 g, 0.480 mol, 1 equiv) was dissolved in acetonitrile (80 ml) and *p*-ABSA (17.2512 g, 0.072 mol, 1.5 equiv) was added. The reaction mixture was cooled to 0 $^{\circ}$C and then DBU (14.5 ml, 0.097 mol, 2 equiv) was added in one portion. The reaction was warmed up slowly in the ice-water bath to room temperature and stirred overnight. It was quenched with saturated ammonium chloride solution and extracted with diethyl ether till no product left in the aqueous layer. The combined organic layers were washed with water, brine, dried over magnesium sulfate and concentrated in vacuo. The crude residue was purified by flash chromatography

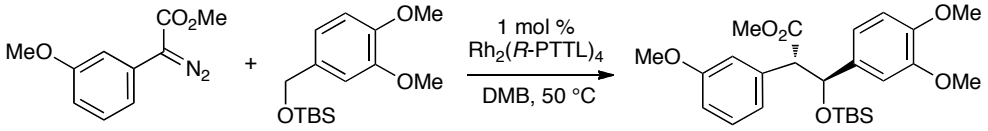
(silica gel, hexanes:ethyl acetate = 5:1) to afford the product as an orange solid (8.774 g, 70% yield over two steps). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.19 (d, J = 1.2 Hz, 1H), 6.93-6.87 (m, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.86 (s, 3H).

General procedure (H) - the rhodium-catalyzed inter-molecular C–H insertion: Under argon atmosphere, an oven dried round bottom flask was charged with TBS ether (1 mmol, 1 equiv) and Rh_2(*R*-PTTL)$_4$ (0.01 mmol, 0.01 equiv) in 2,2-dimethylbutane (5 ml). To this solution at reflux was added a solution of diazo compound (2 mmol, 2 equiv) in 2,2-dimethylbutane (5 ml) [or α,α,α-trifluorotoluene/2,2-dimethylbutane (v/v = 1/3)] over 3 hours. The reaction was then stirred at this temperature for another 1 hour. After cooling down to room temperature, the solvent was removed under vacuum and crude NMR was taken. The crude residue was then purified by flash chromatography.



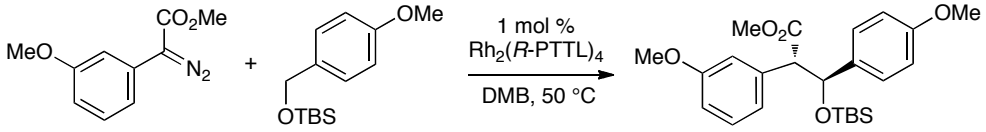
(2*R*,3*R*)-methyl 3-(3,4-dimethoxyphenyl)-2-(3-methoxyphenyl)-3-((trimethylsilyl)-oxy)propanoate (3.47): Following the general procedure **(H)**, the reaction of **S2** (0.12 g, 0.51 mmol, 1 equiv), methyl *m*-methoxypehnyldiazoacetate (0.21 g, 1.0 mmol, 2 equiv) and Rh_2(*S*-PTTL)$_4$ (0.0066 g, 0.0053 mmol, 0.01 equiv) afforded the product as a colorless oil (0.14 g, 64% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 3:1). R_f = 0.18 (hexanes:diethyl ether = 3:1); $[\alpha]_D^{20}$ +55.1 (c 1.42, $CHCl_3$); FTIR (neat): 2753, 2836, 1734, 1598, 1516, 1464, 1435, 1258, 1151, 1081, 876, 840, 752, 694 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.20 (t, J = 7.9 Hz, 1H), 6.99-6.96 (m, 2H), 6.88-6.85 (m, 2H), 6.80 (dd, J = 8.1, 2.0 Hz, 1H), 6.75 (d, J = 7.9 Hz, 1H), 5.08 (d, J

= 8.5 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H), 3.74 (d, *J* = 8.8 Hz, 1H), -0.24 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9 (C), 159.3 (C), 148.4 (C), 148.2 (C), 137.8 (C), 135.2 (C), 128.8 (CH), 121.6 (CH), 118.9 (CH), 114.5 (CH), 113.0 (CH), 110.2 (CH), 109.6 (CH), 76.3 (CH), 61.1 (CH), 55.7 (CH_3), 55.6 (CH_3), 55.1 (CH_3), 51.6 (CH_3), -0.4 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{22}H_{30}O_6{}^{23}Na_1{}^{28}Si_1$, 441.1704; found, 441.1704; HPLC analysis: 92% ee (OD-H, 1% *i*-PrOH in hexane, 0.7 mL/min, λ = 254 nm, t_R = 12.9 min, minor; t_R = 18.4 min, major).



(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-3-(3,4-dimethoxyphenyl)-2-(3-methoxyphenyl)propanoate (3.48): Following the general procedure **(H)**, the reaction of TBS benzyl ether (11.2 g, 0.040 mol, 1 equiv), methyl *m*-methoxypehnyldiazoacetate (16.9 g, 0.082 mol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (246.5 mg, 0.20 mmol, 0.005 equiv) afforded the product as a colorless oil (12.8 g, 70% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 5:1). R_f = 0.24 (hexanes:ethyl acetate = 4:1); $[\alpha]_D{}^{20}$ -62.5 (c 1.25, $CHCl_3$); FTIR (neat): 2951, 2855, 1734, 1599, 1515, 1464, 1435, 1257, 1237, 1151, 1028, 867 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.9 Hz, 1H), 7.06-6.96 (m, 2H), 6.92-6.80 (m, 3H), 6.77 (d, *J* = 8.2 Hz, 1H), 5.09 (d, *J* = 8.5 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.81 (s, 3H), 3.74 (d, *J* = 8.6 Hz, 1H), 3.47 (s, 3H), 0.65 (s, 9H), -0.33 (s, 3H), -0.34 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9 (C), 159.3 (C), 148.3 (C), 148.2 (C), 137.7 (C), 135.3 (C), 128.8 (CH), 121.9 (CH), 119.1 (CH), 114.8 (CH), 113.1 (CH), 110.1 (CH), 109.7 (CH), 76.7 (CH), 61.5 (CH), 55.6 (CH_3), 55.1

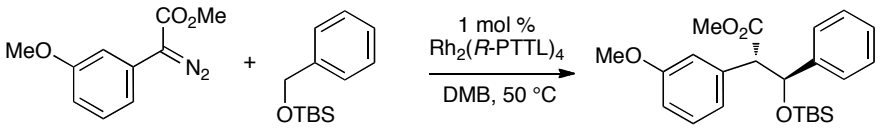
(2xCH_3), 51.6 (CH_3), 25.4 (CH_3), 17.8 (C), -5.0 (CH_3), -5.8 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{25}H_{36}O_7{}^{23}Na_1{}^{28}Si_1$, 483.2173; found, 483.2175; HPLC analysis: 95% ee (OD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 5.55 min, major; t_R = 8.10 min, minor).



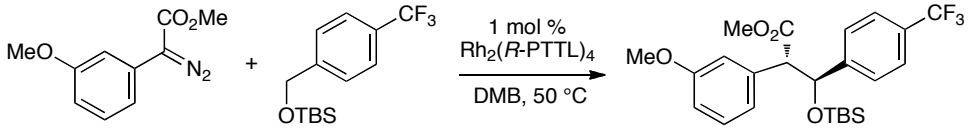
(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2-(3-methoxyphenyl)-3-(4-methoxyphenyl)propanoate (3.52): Following the general procedure **(H)**, the reaction of TBS benzyl ether (3.7846 g, 0.015 mol, 1 equiv), methyl *m*-methoxypehnyldiazoacetate (6.1755 g, 0.030 mol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (79.6 mg, 0.064 mmol, 0.004 equiv) afforded the product as a colorless oil (4.91 g, 76% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 10:1). R_f = 0.14 (hexanes:ethyl acetate = 10:1); $[\alpha]_D{}^{20}$ -63.9 (c 2.38, $CHCl_3$); FTIR (neat): 2952, 2855, 1734, 1610, 1600, 1512, 1464, 1246, 1171, 1079, 1036, 858 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.05-6.98 (m, 2H), 6.83-6.81 (m, 3H), 5.05 (d, *J* = 9.0 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.75 (d, *J* = 9.0 Hz, 1H), 3.44 (s, 3H), 0.62 (s, 9H), -0.35 (s, 3H), -0.38 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.8 (C), 159.3 (C), 158.9 (C), 137.9 (C), 134.8 (C), 128.8 (CH), 127.9 (CH), 121.6 (CH), 114.6 (CH), 113.1 (CH), 113.0 (CH), 76.6 (CH), 61.5 (CH), 55.0 (CH_3), 54.8 (CH_3), 51.4 (CH_3), 25.3 (CH_3), 17.7 (C), -5.1 (CH_3), -5.9 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{24}H_{34}O_5{}^{39}K_1{}^{28}Si_1$, 469.1807; found, 469.1814; HPLC analysis: 93%

ee (OD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 4.14 min, major; t_R = 5.37 min, minor).

(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2,3-bis(3-methoxyphenyl)propanoate (3.53): Following the general procedure **(H)**, the reaction of TBS benzyl ether (0.4961 g, 1.97 mmol, 1 equiv), methyl *m*-methoxypehnyldiazoacetate (0.8024 g, 3.89 mmol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (24.4 mg, 0.020 mmol, 0.01 equiv) afforded the product as a colorless oil (0.4942 g, 58% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 10:1). R_f = 0.29 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -57.1 (c 0.51, MeOH); FTIR (neat): 2952, 2856, 1735, 1600, 1586, 1489, 1465, 1434, 1258, 1151, 1095, 1047 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.04-6.96 (m, 2H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 2.0 Hz, 1H), 6.86-6.74 (m, 1H), 6.78 (dd, *J* = 8.1, 2.6 Hz, 1H), 5.11 (d, *J* = 8.7 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.75 (d, *J* = 8.7 Hz, 1H), 3.47 (s, 3H), 0.65 (s, 9H), -0.32 (s, 3H), -0.34 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.8 (C), 159.3 (C), 159.2 (C), 144.3 (C), 137.6 (C), 128.8 (CH), 128.7 (CH), 121.8 (CH), 119.2 (CH), 114.8 (CH), 113.4 (CH), 113.1 (CH), 111.9 (CH), 76.8 (CH), 61.4 (CH), 55.0 (CH_3), 54.9 (CH_3), 51.5 (CH_3), 25.4 (CH_3), 17.7 (C), -5.1 (CH_3), -5.8 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{24}H_{34}O_5{}^{23}Na_1{}^{28}Si_1$, 453.2068; found, 453.2077; HPLC analysis: 95% ee (OD-H, hexane, 1.0 mL/min, λ = 280 nm, t_R = 4.32 min, major; t_R = 5.83 min, minor).

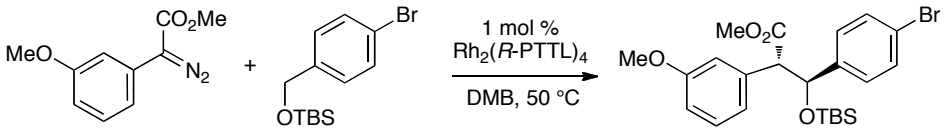


(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2-(3-methoxyphenyl)-3-phenylpropanoate (3.54): Following the general procedure **(H)**, the reaction of TBS benzyl ether (0.1207 g, 0.54 mmol, 1 equiv), methyl *m*-methoxypehnyldiazoacetate (0.2208 g, 1.07 mmol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (6.8 mg, 0.0055 mmol, 0.01 equiv) afforded the product as a colorless oil (0.1871 g, 86% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 20:1). R_f = 0.29 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -68.1 (c 0.98, MeOH); FTIR (neat): 2952, 2929, 2836, 1735, 1600, 1586, 1491, 1454, 1434, 1257, 1150, 1088, 1071 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 8.1, 1.4 Hz, 2H), 7.32-7.18 (m, 4H), 7.01 (dd, *J* = 6.9, 1.3 Hz, 2H), 6.85-6.79 (m, 1H), 5.11 (d, *J* = 8.9 Hz, 1H), 3.82 (s, 3H), 3.78 (d, *J* = 8.9 Hz, 1H), 3.43 (s, 3H), 0.63 (s, 9H), -0.34 (s, 3H), -0.38 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.8 (C), 159.4 (C), 142.7 (C), 137.8 (C), 128.9 (CH), 127.8 (CH), 127.6 (CH), 126.9 (CH), 121.8 (CH), 114.7 (CH), 113.2 (CH), 77.1 (CH) 61.5 (CH), 55.1 (CH_3), 51.5 (CH_3), 25.4 (CH_3), 17.7 (C), -5.07 (CH_3), -5.79 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{23}H_{33}O_4{}^{28}Si_1$, 401.2143; found, 401.2142; HPLC analysis: 96% ee (OD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 3.94 min, major; t_R = 5.02 min, minor).



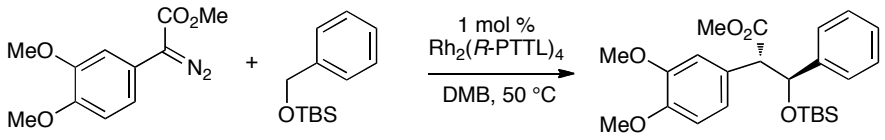
(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2-(3-methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)propanoate (3.55): Following the general procedure **(H)**, the

reaction of TBS benzyl ether (0.5810 g, 2.00 mmol, 1 equiv), methyl *m*-methoxypehnyldiazoacetate (0.8580 g, 4.16 mmol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (25.0 mg, 0.020 mmol, 0.01 equiv) afforded the product as a colorless oil (0.8082 g, 86% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 20:1); R_f = 0.39 (hexanes:ethyl acetate = 10:1). $[\alpha]_D^{20}$ -62.7 (c 1.00, MeOH); FTIR (neat): 2953, 2857, 1733, 1600, 1586, 1492, 1464, 1435, 1323, 1259, 1163, 1124, 1087, 1066, 1017 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.01-6.94 (m, 2H), 6.83 (dd, *J* = 8.2, 2.5 Hz, 1H), 5.17 (d, *J* = 8.7 Hz, 1H), 3.81 (s, 3H), 3.75 (d, *J* = 8.9 Hz, 1H), 3.46 (s, 3H), 0.65 (s, 9H), -0.34 (s, 3H), -0.37 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.6 (C), 159.5 (C), 146.9 (C), 137.2 (C), 129.8 (C, q, *J* = 31.9 Hz), 129.1 (C), 127.3 (CH), 124.1 (CH, q, *J* = 270.4 Hz), 124.8 (CH, q, *J* = 3.8 Hz), 121.7 (CH), 114.8 (CH), 113.3 (CH), 76.4 (CH), 61.2 (CH), 55.0 (CH_3), 52.0 (CH_3), 25.3 (CH_3), 17.7 (C), -5.1 (CH_3), -5.9 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{24}H_{31}O_4F_3{}^{23}Na_1{}^{28}Si_1$, 491.1836; found, 491.1855; HPLC analysis: 95% ee (OD-H, hexane, 1.0 mL/min, λ = 280 nm, t_R = 4.32 min, major; t_R = 5.83 min, minor).



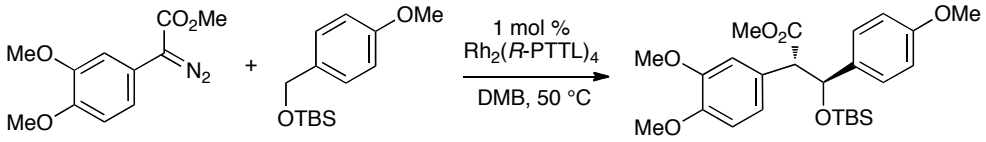
(2*S*,3*S*)-methyl 3-(4-bromophenyl)-3-((*tert*-butyldimethylsilyl)oxy)-2-(3-methoxyphenyl)propanoate (3.56): Following the general procedure **(H)**, the reaction of TBS benzyl ether (0.3050 g, 1.01 mmol, 1 equiv), methyl *m*-methoxypehnyldiazoacetate (0.4145 g, 2.01 mmol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (24.4 mg,

0.010 mmol, 0.01 equiv) afforded the product as a colorless oil (0.4465 g, 92% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 20:1). R_f = 0.35 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -76.0 (c 1.08, MeOH); FTIR (neat): 2952, 2929, 1735, 1600, 1486, 1464, 1435, 1258, 1163, 1105, 1086, 1011 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 7.21 (d, J = 8.2 Hz, 1H), 7.00-6.96 (m, 2H), 6.83 (dd, J = 2.4, 1.2 Hz, 1H), 5.07 (d, J = 8.9 Hz, 1H), 3.81 (s, 3H), 3.72 (d, J = 8.9 Hz, 1H), 3.46 (s, 3H), 0.64 (s, 9H), -0.35 (s, 3H), -0.37 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.4 (C), 159.3 (C), 141.8 (C), 137.3 (C), 130.9 (CH), 128.9 (CH), 128.5 (CH), 121.5 (CH), 121.3 (C), 114.7 (CH), 113.1 (CH), 76.3 (CH), 61.1 (CH), 54.8 (CH_3), 51.4 (CH_3), 25.3 (CH_3), 17.6 (C), -5.15 (CH_3), -5.92 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{23}H_{31}O_4{}^{79}Br^{39}K_1{}^{28}Si_1$, 517.0807; found, 517.0820; HPLC analysis: 98% ee (OD-H, hexane, 1.0 mL/min, λ = 280 nm, t_R = 3.90 min, major; t_R = 5.06 min, minor).



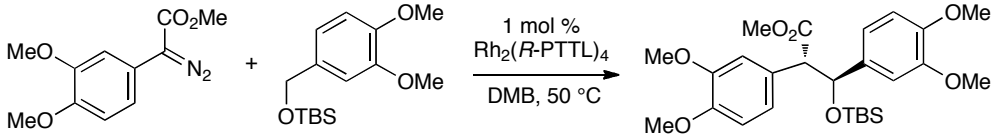
(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2-(3,4-dimethoxyphenyl)-3-phenylpropanoate (3.57): Following the general procedure **(H)**, the reaction of TBS benzyl ether (0.4291 g, 1.93 mmol, 1 equiv), methyl 3,4-dimethoxypehnyldiazoacetate (0.9160 g, 3.88 mmol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (24.3 mg, 0.019 mmol, 0.01 equiv) afforded the product as a colorless oil (0.7123 g, 86% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 10:1). R_f = 0.20 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -62.9 (c 0.99, MeOH); FTIR (neat): 2951, 2931, 2856, 1733, 1515,

1464, 1454, 1262, 1153, 1090, 1072, 1029 cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.34-7.29 (m, 2H), 7.29-7.25 (m, 2H), 7.25-7.21 (m, 1H), 7.01 (d, J = 2.0 Hz, 1H), 6.90 (dd, J = 8.3, 2.0 Hz, 1H), 6.79 (d, J = 8.1 Hz, 1H), 5.11 (d, J = 8.5 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.73 (d, J = 8.5 Hz, 1H), 3.45 (s, 3H), 0.67 (s, 9H), -0.29 (s, 3H), -0.36 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.2 (C), 148.4 (C), 148.3 (C), 142.6 (C), 128.7 (C), 127.8 (CH), 127.5 (CH), 126.8 (CH), 121.8 (CH), 112.6 (CH), 110.7 (CH), 77.1 (CH), 60.9 (CH), 55.9 (CH_3), 55.8 (CH_3), 51.6 (CH_3), 25.4 (CH_3), 17.8 (C), -5.0 (CH_3), -5.6 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{23}H_{34}O_5{}^{23}Na_1{}^{28}Si_1$, 453.2068; found, 453.2076; HPLC analysis: 99% ee (OD-H, hexane, 0.25 mL/min, λ = 280 nm, t_R = 23.54 min, major; t_R = 25.19 min, minor).



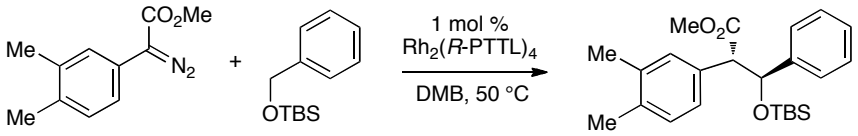
(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2-(3,4-dimethoxyphenyl)-3-(4-methoxyphenyl)propanoate (3.58): Following the general procedure **(H)**, the reaction of TBS benzyl ether (3.7831 g, 0.015 mol, 1 equiv), methyl 3,4-dimethoxypehnyldiazo-acetate (7.0709 g, 0.030 mol, 0.004 equiv) and Rh_2(*R*-PTTL)$_4$ (73.1 mg, 0.059 mmol, 0.01 equiv) afforded the product as a colorless oil (5.1334 g, 74 % yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 5:1). R_f = 0.25 (hexanes:ethyl acetate = 5:1); $[\alpha]_D{}^{20}$ -63.7 (c 1.83, $CHCl_3$); FTIR (neat): 2952, 2855, 2255, 1732, 1512, 1463, 1246, 1172, 1143, 1029, 911 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 1.9 Hz, 1H), 6.91 (dd, J = 8.2, 2.0 Hz, 1H), 6.83 - 6.77 (m, 3H), 5.06 (d, J = 8.4 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.80 (s, 3H), 3.71 (d, J

= 8.4 Hz, 1H), 3.46 (s, 3H), 0.65 (s, 9H), -0.31 (s, 3H), -0.36 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.2 (C), 158.8 (C), 148.4 (C), 148.3 (C), 134.8 (C), 128.9 (C), 127.9 (CH), 121.7 (CH), 113.1 (CH), 112.5 (CH), 110.7 (CH), 76.6 (CH), 61.0 (CH), 55.8 (CH_3), 55.7 (CH_3), 55.0 (CH_3), 51.5 (CH_3), 25.4 (CH_3), 17.7 (C), -5.0 (CH_3), -5.7 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{25}H_{36}O_7{}^{39}K_1{}^{28}Si_1$, 499.1913; found, 499.1920; HPLC analysis: 96% ee (AD-H, 5% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 11.65 min, minor; t_R = 12.61 min, major).

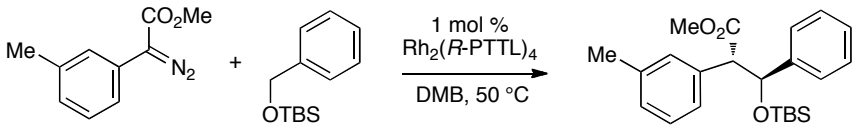


(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2,3-bis(3,4-dimethoxyphenyl)propanoate (3.59): Following the general procedure **(H)**, the reaction of TBS benzyl ether (3.6903 g, 0.013 mol, 1 equiv), methyl 3,4-dimethoxypehnyldiazoacetate (6.1853 g, 0.026 mol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (75.6 mg, 0.061 mmol, 0.005 equiv) afforded the product as a colorless oil (4.9495 g, 77% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 2:1). R_f = 0.14 (hexanes:ethyl acetate = 4:1); $[\alpha]_D{}^{20}$ -64.2 (c 1.08, $CHCl_3$); FTIR (neat): 2952, 2855, 2255, 1732, 1514, 1464, 1259, 1237, 1140, 1083, 1027, 910 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.05 (s, 1H), 6.91-6.73 (m, 5H), 5.08 (d, *J* = 8.2 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 6H), 3.82 (s, 3H), 3.69 (d, *J* = 8.2 Hz, 1H), 3.49 (s, 3H), 0.68 (s, 9H), -0.29 (s, 3H), -0.33 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.1 (C), 148.3 (C), 148.20 (C), 148.16 (C), 148.0 (C), 135.2 (C), 128.6 (C), 121.8 (CH), 118.9 (CH), 112.5 (CH), 110.5 (CH), 110.0 (CH), 109.6 (CH), 76.6 (CH), 60.8 (CH), 55.7 (CH_3), 55.6 (CH_3), 55.5 (2xCH_3), 51.4 (CH_3), 25.3 (CH_3), 17.7

(C), -5.1 (CH_3), -5.8 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{26}H_{38}O_7{}^{39}K_1{}^{28}Si_1$, 529.2018; found, 529.2026; HPLC analysis: 97% ee (AD-H, 5% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 15.21 min, minor; t_R = 15.95 min, major).



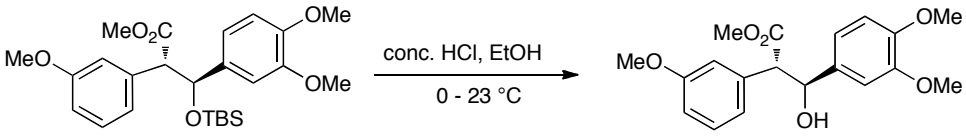
(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2-(3,4-dimethylphenyl)-3-phenylpropanoate (3.60): Following the general procedure **(H)**, the reaction of TBS benzyl ether (0.2190 g, 0.985 mmol, 1 equiv), methyl 3,4-dimethylpehnyldiazoacetate (0.4200 g, 2.06 mmol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (12.2 mg, 0.0098 mmol, 0.01 equiv) afforded the product as a white solid (0.3615 g, 92% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 9:1). R_f = 0.21 (hexanes:diethyl ether = 10:1). m.p. 68-70 $^{\circ}$C; $[\alpha]_D{}^{20}$ -84.8 (c 1.37, $CHCl_3$); FTIR (neat): 2951, 2928, 2856, 1736, 1455, 1435, 1251, 1154, 1091, 1072 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38-7.31 (m, 2H), 7.31-7.22 (m, 3H), 7.19 (d, *J* = 1.8 Hz, 1H), 7.14 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 5.08 (d, *J* = 8.9 Hz, 1H), 3.73 (d, *J* = 9.0 Hz, 1H), 3.41 (s, 3H), 2.25 (s, 3H), 2.24 (s, 3H), 0.62 (s, 9H), -0.38 (s, 3H), -0.39 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.3 (C), 143.0 (C), 136.0 (C), 135.5 (C), 133.8 (C), 130.7 (CH), 129.3 (CH), 127.9 (CH), 127.5 (CH), 127.0 (CH), 126.5 (CH), 77.0 (CH), 61.1 (CH), 51.5 (CH_3), 25.4 (CH_3), 19.6 (CH_3), 19.3 (CH_3), 17.8 (C), -5.0 (CH_3), -5.8 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{24}H_{34}O_3{}^{23}Na_1{}^{28}Si_1$, 421.2169; found, 421.2179; HPLC analysis: 99% ee (OD-H, hexane, 1.0 mL/min, λ = 254 nm, t_R = 3.53 min, major; t_R = 3.86 min, minor).



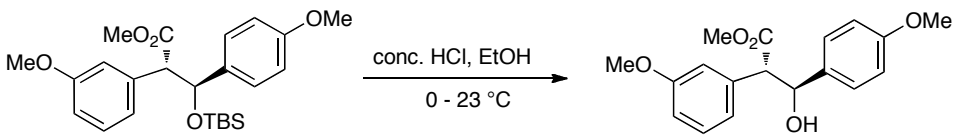
(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-3-phenyl-2-(m-tolyl)propanoate (3.61): Following the general procedure **(H)**, the reaction of TBS benzyl ether (0.4230 g, 1.90 mmol, 1 equiv), methyl 3,4-dimethoxypehnyldiazoacetate (0.7266 g, 3.82 mmol, 2 equiv) and Rh_2(*R*-PTTL)$_4$ (23.5 mg, 0.019 mmol, 0.01 equiv) afforded the product as a colorless oil (0.5650 g, 77% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 15:1). R_f = 0.47 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -74.3 (c 1.11, $CHCl_3$); FTIR (neat): 2951.9, 2928, 2856, 1736, 1608, 1471, 1455, 1435, 1251, 1164, 1090, 1072 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39-7.33 (m, 2H), 7.32-7.15 (m, 6H), 7.10-7.06 (m, 1H), 5.08 (d, *J* = 9.0 Hz, 1H), 3.76 (d, *J* = 9.0 Hz, 1H), 3.42 (s, 3H), 2.35 (s, 3H), 0.62 (s, 9H), -0.38 (s, 3H), -0.40 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9 (C), 142.8 (C), 137.4 (C), 136.3 (C), 130.1 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 127.5 (CH), 126.8 (CH), 126.1 (CH), 77.0 (CH), 61.4 (CH), 51.3 (CH_3), 25.3 (CH_3), 21.2 (CH_3), 17.7 (C), -5.1 (CH_3), -5.9 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{23}H_{32}O_3{}^{23}Na_1{}^{28}Si_1$, 407.2012; found, 407.2024; HPLC analysis: 98% ee (OD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 254 nm, t_R = 3.53 min, major; t_R = 4.20 min, minor).

General procedure (I) – deprotection of the TBS group: To a solution of TBS ether (0.5 mmol, 1 equiv) in ethanol (10 ml) at 0 $^{\circ}$C, was added concentrated hydrochloric acid (0.82 ml, 20 equiv) dropwise. The reaction was then warmed up slowly in the bath to room temperature and monitored by TLC (usually 24 hours). A saturated aqueous solution of sodium bicarbonate was added carefully and the resulting mixture was

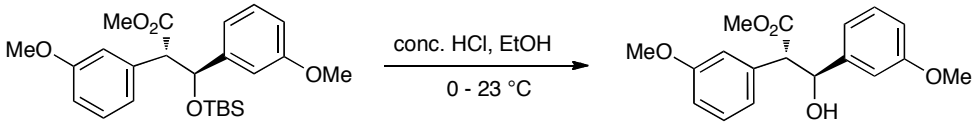
extracted with ethyl acetate three times. The combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate, water and brine. The organics were combined and dried over anhydrous magnesium sulfate. After filtration, the filtrate was concentrated under vacuum and the crude residue was purified by flash chromatography.



(2*S*,3*S*)-methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-(3-methoxyphenyl)propanoate (3.49): Following the general procedure **(I)**, the reaction of **3.48** (3.6903 g, 0.013 mol) afforded the product as a white solid (0.1552 g, 80% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 3:2). R_f = 0.24 (hexanes:ethyl acetate = 3:2). m.p. 101-104 $^{\circ}$C; $[\alpha]_D^{20}$ -89.7 (c 1.28, $CHCl_3$); FTIR (neat): 3411 (br.), 2923, 2836, 2360, 1732, 1598, 1522, 1464, 1259, 1236, 1154, 1143, 1041, 1022 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30-7.23 (m, 1H), 6.97-6.84 (m, 4H), 6.84-6.79 (m, 2H), 5.24 (dd, J = 7.6, 2.3 Hz, 1H), 3.87 (s, 3H), 3.83-3.81 (m, 4H), 3.80 (s, 3H), 3.55 (s, 3 H), 2.53 (d, J = 2.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6 (C), 159.6 (C), 148.6 (C), 148.5 (C), 136.2 (C), 133.4 (C), 129.5 (CH), 121.4(CH), 118.9 (CH), 114.6 (CH), 113.4 (CH), 110.6 (CH), 109.6 (CH), 74.8 (CH), 59.6 (CH), 55.8 (CH_3), 55.7 (CH_3), 55.1 (CH_3), 52.0 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{19}H_{22}O_6{}^{23}Na_1$, 369.1309; found, 369.1309.

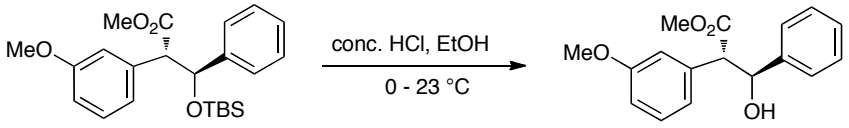


(2*S*,3*S*)-methyl 3-hydroxy-2-(3-methoxyphenyl)-3-(4-methoxyphenyl)propanoate (3.64): Following the general procedure **(I)**, the reaction of **3.52** (0.3213 g, 0.75 mmol) afforded the product as a white solid (0.1959 g, 83% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1). R_f = 0.21 (hexanes:ethyl acetate = 3:1). m.p. 70-72 °C; $[\alpha]_D^{20}$ -49.3 (c 1.87, $CHCl_3$); FTIR (neat): 3495 (br.), 2952, 2837, 1731, 1609, 1599, 1585, 1513, 1491, 1455, 1435, 1318, 1247, 1172, 1032 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39-7.23 (m, 3H), 7.01-6.93 (m, 2H), 6.92-6.83 (m, 3H), 5.23 (dd, J = 8.2, 2.4 Hz, 1H), 3.83 (d, J = 7.9 Hz, 1H), 3.80 (s, 6H), 3.53 (s, 3H), 2.37 (d, J = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4 (C), 159.7 (C), 159.2 (C), 136.4 (C), 133.0 (C), 129.6 (CH), 127.9 (CH), 121.3 (CH), 114.5 (CH), 113.6 (CH), 113.5 (CH), 74.7 (CH), 59.8 (CH), 55.2 (2xCH_3), 51.9 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{20}O_5{}^{23}Na_1$, 339.1203; found, 339.1205.

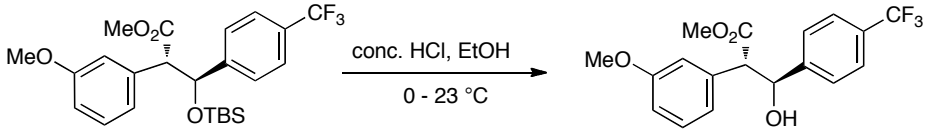


(2*S*,3*S*)-methyl 3-hydroxy-2,3-bis(3-methoxyphenyl)propanoate (3.65): Following the general procedure **(I)**, the reaction of **3.53** (0.0935 g, 0.22 mmol) afforded the product as a white solid (0.0599 g, 87% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 3:1). R_f = 0.26 (hexanes:ethyl acetate = 3:1); $[\alpha]_D^{20}$ -90.0 (c 0.93, $CHCl_3$); FTIR (neat): 3501 (br.), 2951, 2836, 1732, 1599, 1586, 1489, 1455, 1435, 1320, 1259, 1151, 1042 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.20 (m, 2H), 6.95-6.84 (m, 5H), 6.83-6.79 (m, 1H), 5.27 (dd, J = 7.5, 2.2 Hz, 1H), 3.84 (d, J = 7.5 Hz, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 3.56 (s, 3H), 2.57 (d, J = 2.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ

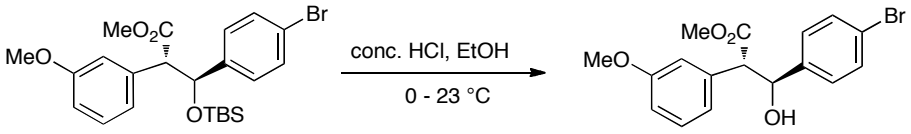
172.5 (C), 159.5 (C), 159.4 (C), 142.5 (C), 136.1 (C), 129.4 (CH), 129.1 (CH), 121.4 (CH), 118.8 (CH), 114.5 (CH), 113.7 (CH), 113.4 (CH), 111.7 (CH), 74.7 (CH), 59.4 (CH), 55.1 (CH_3), 55.0 (CH_3), 51.9 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{20}O_5{}^{23}Na_1$, 339.1203; found, 339.1202.



(2*S*,3*S*)-methyl 3-((*tert*-butyldimethylsilyl)oxy)-2,3-diphenylpropanoate (3.66): Following the general procedure **(I)**, the reaction of **3.54** (0.2290 g, 0.57 mmol) afforded the product as a white solid (0.1451 g, 89% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 5:1). R_f = 0.17 (hexanes:ethyl acetate = 5:1). m.p. 71-73 °C; $[\alpha]_D{}^{20}$ -107.7 (c 1.13, $CHCl_3$); FTIR (neat): 3494 (br.), 3031, 2950, 2836, 1731, 1599, 1584, 1490, 1454, 1434, 1319, 1259, 1192, 1049, 1082, 1041, 1024 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33-7.19 (m, 6H), 6.92 (d, *J* = 7.7 Hz, 1H), 6.90-6.87 (m, 1H), 6.83 (dd, *J* = 8.1, 2.3 Hz, 1H), 5.23 (dd, *J* = 8.0, 0.8 Hz 1H), 3.83 (d, *J* = 7.9 Hz, 1H), 3.74 (s, 3H), 3.48 (s, 3H), 2.65 (d, *J* = 1.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.5 (C), 159.6 (C), 140.8 (C), 136.2 (C), 129.8 (CH), 128.1 (CH), 127.9 (CH), 126.6 (CH), 121.3 (CH), 114.5 (CH), 113.4 (CH), 74.91 (CH), 59.59 (CH), 55.08 (CH_3), 51.88 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{18}O_4{}^{23}Na_1$, 309.1097; found, 309.1102.

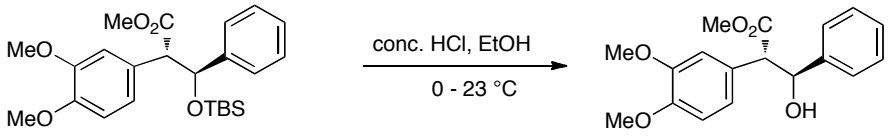


(2*S*,3*S*)-methyl 3-hydroxy-2-(3-methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)-propanoate (3.67): Following the general procedure **(I)**, the reaction of **3.55** (0.7509 g, 1.60 mmol) afforded the product as a white solid (0.4407 g, 78% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 3:1). R_f = 0.32 (hexanes:ethyl acetate = 3:1). m.p. 89-91 °C; $[\alpha]_D^{20}$ -109.2 (c 0.98, $CHCl_3$); FTIR (neat): 3486 (br.), 2954, 1733, 1600, 1492, 1436, 1325, 1262, 1164, 1123, 1068, 1017 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 7.28-7.22 (m, 1H), 6.87 (d, J = 2.0 Hz, 1H), 6.84 (dd, J = 11.2, 2.1 Hz, 2H), 5.36 (dd, J = 7.1, 2.3 Hz, 1H), 3.83 (s, 1H), 3.77 (s, 3H), 3.58 (s, 3H), 2.79 (d, J = 2.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6 (C), 159.7 (C), 144.8 (C), 135.4 (C), 130.0 (C, q, J = 32.2 Hz) 129.6 (CH), 127.0 (CH), 125.4 (C, q, J = 270.6 Hz), 125.1 (CH, q, J = 3.8 Hz), 121.4 (CH), 114.7 (CH), 113.6 (CH), 74.2 (CH), 59.2 (CH), 55.1 (CH_3), 52.2 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{17}O_4F_3{}^{23}Na_1$, 377.0971; found, 377.0969.

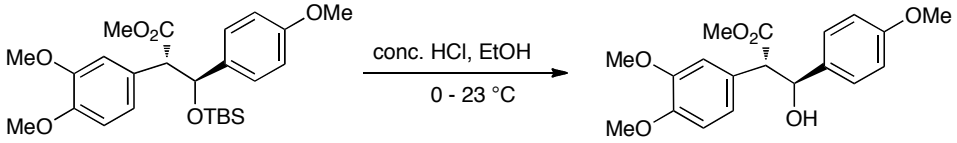


(2*S*,3*S*)-methyl 3-(4-bromophenyl)-3-hydroxy-2-(3-methoxyphenyl)propanoate (3.68): Following the general procedure **(I)**, the reaction of **3.56** (0.8784 g, 1.83 mmol) afforded the product as a white solid (0.5868 g, 88% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). R_f = 0.27 (hexanes:ethyl acetate = 4:1); $[\alpha]_D^{20}$ -109.0 (c 0.97, MeOH); FTIR (neat): 3485 (br.), 2951, 2836, 1732, 1599, 1585, 1490, 1454, 1435, 1320, 1261, 1193, 1164, 1070, 1050, 1010 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.3 Hz, 2H), 7.29-7.22 (m, 1H), 7.19 (d, J = 8.4 Hz, 2H),

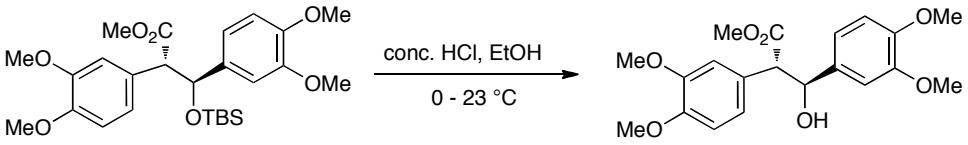
6.91-6.83 (m, 3H), 5.25 (dd, J = 7.4, 1.5 Hz, 1H), 3.77-3.79 (m, 4H), 3.56 (s, 3H), 2.65 (d, J = 2.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4 (C), 159.5 (C), 139.9 (C), 135.7 (C), 131.2 (CH), 129.5 (CH), 128.3 (CH), 121.7 (CH), 121.3 (C), 114.6 (CH), 113.4 (CH), 74.1 (CH), 59.3 (CH), 55.0 (CH_3), 52.0 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{17}H_{17}O_4{}^{79}Br^{39}K_1$, 402.9942; found, 402.9949.



(2*S*,3*S*)-methyl 2-(3,4-dimethoxyphenyl)-3-hydroxy-3-phenylpropanoate (3.69): Following the general procedure **(I)**, the reaction of **3.57** (0.3444 g, 0.80 mmol) afforded the product as a white solid (0.2083 g, 82% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 2:1). R_f = 0.31 (hexanes:ethyl acetate = 3:2). m.p. 118-120 °C; $[\alpha]_D{}^{20}$ -115.6 (c 0.95, MeOH); FTIR (neat): 3505 (br.), 2951, 2836, 1632, 1515, 1454, 1329, 1263, 1240, 1190, 1143, 1026 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 5H), 6.90 (dd, J = 8.3, 2.0 Hz, 1H), 6.86-6.80 (m, 2H), 5.26 (dd, J = 7.4, 2.0 Hz, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 3.81 (d, J = 7.4 Hz, 1H), 3.55 (s, 3H), 2.61 (d, J = 2.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6 (C), 148.5 (C), 148.4 (C), 140.8 (C), 127.9 (CH), 127.6 (CH), 126.9 (C), 126.3 (CH), 121.1 (CH), 111.8 (CH), 110.7 (CH), 74.7 (CH), 58.8 (CH), 55.5 (2xCH_3), 51.61 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{20}O_5{}^{23}Na_1$, 339.1203; found, 339.1202.

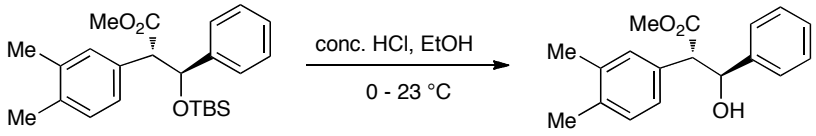


(2*S*,3*S*)-methyl 2-(3,4-dimethoxyphenyl)-3-hydroxy-3-(4-methoxyphenyl)propanoate (3.70): Following the general procedure **(I)**, the reaction of **3.58** (0.2647 g, 0.57 mmol) afforded the product as a white solid (0.1715 g, 85% yield) after purification by flash chromatography. R_f = 0.24 (hexanes:ethyl acetate = 3:2). m.p. 107-109 °C; $[\alpha]_D^{20}$ -94.9 (c 1.37, $CHCl_3$); FTIR (neat): 3501 (br.), 2952, 2837, 2253, 1731, 1611, 1513, 1464, 1244, 1142, 1025, 909 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29-7.22 (m, 2H), 6.92 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.86 (m, 4H), 5.20 (d, *J* = 7.8, 1.9 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.81-3.74 (m, 4H), 3.54 (s, 3H), 2.45 (d, *J* = 2.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.5 (C), 158.9 (C), 148.5 (C), 148.4 (C), 133.0 (C), 127.6 (CH), 127.2 (C), 121.1 (CH), 113.2 (CH), 111.7 (CH), 110.8 (CH), 74.4 (CH), 59.0 (CH), 55.5 (2xCH_3), 54.8 (CH_3), 51.6 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{19}H_{22}O_6{}^{23}Na_1$, 369.1309; found, 369.1314.

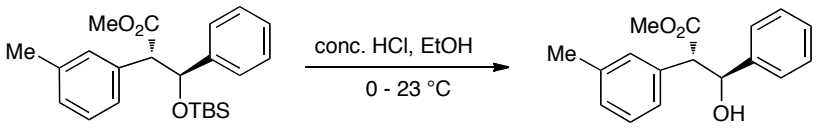


(2*S*,3*S*)-methyl 2,3-bis(3,4-dimethoxyphenyl)-3-hydroxypropanoate (3.71): Following the general procedure **(I)** the reaction of **3.59** (4.9495 g, 0.011 mol) afforded the product as a white solid (3.1492 g, 78% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1 then 1:2). R_f = 0.19 (hexanes:ethyl acetate = 1:1). m.p. 141-143 °C; $[\alpha]_D^{20}$ -86.3 (c 1.01, $CHCl_3$); FTIR (neat): 3469 (br.), 2957, 2837, 1726, 1712, 1593, 1516, 1463, 1421, 1257, 1235, 1023 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.93-6.87 (m, 3H), 6.86-6.78 (m, 3H), 5.21 (dd, *J* = 7.7, 2.2 Hz, 1H), 3.88 (s, 3H), 3.873 (s, 3H), 3.870 (s, 3H), 3.83 (s, 3H), 3.78 (d, *J* = 7.7 Hz, 1H), 3.56 (s, 3H), 2.52 (d, *J* = 2.2

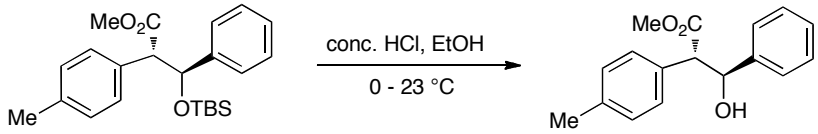
Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4 (C), 148.4 (C), 148.2 (C), 148.1(C), 148.0 (C), 133.4 (C), 127.0 (C), 121.0 (CH), 118.5 (CH), 111.6 (CH), 110.6 (CH), 110.2 (CH), 109.3 (CH), 74.3 (CH), 58.8 (CH), 55.31 (2xCH_3), 55.29 (CH_3), 55.2 (CH_3), 51.4 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{20}H_{24}O_7{}^{23}Na_1$, 399.1414; found, 399.1420.



(2*S*,3S)-methyl 2-(3,4-dimethylphenyl)-3-hydroxy-3-phenylpropanoate (3.72): Following the general procedure **(I)**, the reaction of **3.60** (0.3511 g, 0.90 mmol) afforded the product as a white solid (0.2112 g, 83% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 9:1). R_f = 0.50 (hexanes:ethyl acetate = 3:1). m.p. 86-88 $^{\circ}$C; $[\alpha]_D{}^{20}$ -48.3 (c 1.39, $CHCl_3$); FTIR (neat): 3522, 3031, 2949, 1732, 1503, 1454, 1435, 1331, 1281, 1219, 1153, 1043, 1024 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 7.15 (s, 1H), 7.11 (d, *J* = 1.2 Hz, 2H), 5.25 (dd, *J* = 8.3, 2.3 Hz, 1H), 3.82 (d, *J* = 8.2 Hz, 1H), 3.49 (s, 3H), 2.37 (d, *J* = 2.3 Hz, 1H), 2.26 (s, 3H), 2.25 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.54 (C), 141.08 (C), 136.73 (C), 136.17 (C), 132.19 (C), 130.00 (CH), 129.78 (CH), 128.04 (CH), 127.75 (CH), 126.58 (CH), 126.20 (CH), 74.92 (CH), 59.33 (CH), 51.66 (CH_3), 19.64 (CH_3), 19.26 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{20}O_3{}^{23}Na_1$, 307.1308; found, 307. 1304.



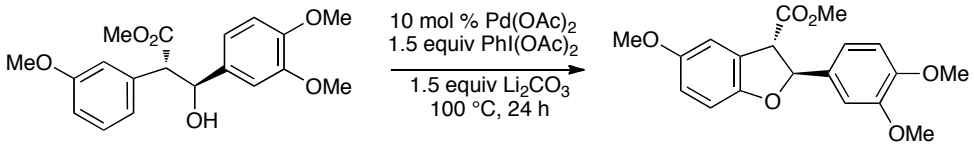
(2*S*,3*S*)-methyl 3-hydroxy-3-phenyl-2-(m-tolyl)propanoate (3.73): Following the general procedure **(I)**, the reaction of **3.61** (0.2685 g, 0.70 mmol) afforded the product as a white solid (0.1536 g, 81% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 9:1). R_f = 0.24 (hexanes:ethyl acetate = 4:1). m.p. 81-85 °C; $[\alpha]_D^{20}$ -44.4 (c 1.27, $CHCl_3$); FTIR (neat): 3500 (br.), 3031, 2951, 1732, 1606, 1493, 1454, 1435, 1332, 1281, 1192, 1164, 1043, 1024 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 5H), 7.22 (d, J = 7.4 Hz, 1H), 7.20-7.11 (m, 3H), 5.27 (dd, J = 8.0, 2.3 Hz, 1H), 3.84 (d, J = 8.1 Hz, 1H), 3.51 (s, 3H), 2.44 (d, J = 2.3 Hz, 1H), 2.35 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4 (C), 141.0 (C), 138.0 (C), 134.7 (C), 129.6 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.7 (CH), 126.5 (CH), 125.9 (CH), 74.8 (CH), 59.6 (CH), 51.6 (CH_3), 21.2 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{18}O_3{}^{23}Na_1$, 293.1148; found, 293.1148.



(2*S*,3*S*)-methyl 3-hydroxy-3-phenyl-2-(*p*-tolyl)propanoate (3.74): Following the general procedure **(I)**, the reaction of **3.62** (0.2854 g, 0.74 mmol) afforded the product as a white solid (0.1712 g, 85% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 9:1). R_f = 0.42 (hexanes:ethyl acetate = 4:1). m.p. 102-103 °C; $[\alpha]_D^{20}$ -50.6 (c 0.92, $CHCl_3$); FTIR (neat): 3051, 3031, 2950, 1733, 1513, 1454, 1435, 1332, 1279, 1496, 1156, 1041, 1024 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 7.25-7.22 (m, 2H), 7.15 (d, J = 7.9 Hz, 2H), 5.27 (dd, J = 7.7, 2.5 Hz, 1H), 3.85 (d, J = 7.7 Hz, 1H), 3.52 (s, 3H), 2.50 (d, J = 2.5 Hz, 1H), 2.34 (s, 3H); ^{13}C-NMR (100 MHz,

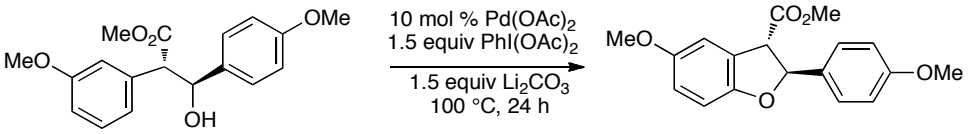
$CDCl_3$) δ 172.7 (C), 141.0 (C), 137.5 (C), 131.7 (C), 129.2 (CH), 128.8 (CH), 128.1 (CH), 127.7 (CH), 126.5 (CH), 74.8 (CH), 59.2 (CH), 51.7 (CH_3), 21.0 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{18}O_3{}^{23}Na_1$, 293.1148; found, 293.1148.

General procedure (J) - the palladium-catalyzed intramolecular C–H oxidation: A pressure tube (35 ml) was charged with alcohol (2 mmol, 1 equiv), lithium carbonate or Na_2HPO_4 (3 mmol, 1.5 equiv) and (diacetoxyiodo)benzene (3 mmol, 1.5 equiv) in hexaflurobenzene (2 ml). The tube was capped with Teflon cap and then placed in a 100°C oil bath. After stirring at this temperature for 24-72 hours, the reaction was cooling down to room temperature and filtered through a plug of silica gel. After the removal of solvent, crude NMR was taken. The crude residue was purified by flash chromatography.

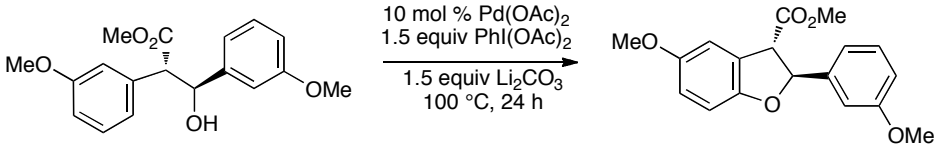


(2*S*,3*S*)-methyl 2-(3,4-dimethoxyphenyl)-5-methoxy-2,3-dihydrobenzofuran-3-carboxylate (3.51): Following the general procedure **(J)**, the reaction of **3.49** (18.7 mg, 0.054 mmol) afforded the product as a pale yellow oil (10.6 mg, 57% yield) after purification by flash chromatography (silica gel, hexanes:acetone = 9:1) to afford the product as a yellow oil (57% yield). R_f = 0.22 (hexanes:ethyl acetate = 3:1). $[\alpha]_D{}^{20}$ +54.6 (c 0.95, $CHCl_3$); FTIR (neat): 2952, 2835, 1736, 1594, 1516, 1487, 1464, 1435, 1263, 1236, 1206, 1160, 1138, 1026 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.97 (d, *J* = 8.2 Hz, 1 H), 6.93 (s, 2 H), 6.85 (d, *J* = 8.2 Hz, 1 H), 6.81 (br.s., 2 H), 6.02 (d, *J* = 8.2 Hz, 1 H), 4.28 (d, *J* = 7.9 Hz, 1 H), 3.88 (s, 3 H), 3.87 (s, 3 H), 3.83 (s, 3 H), 3.78 (s, 3 H); ^{13}C-

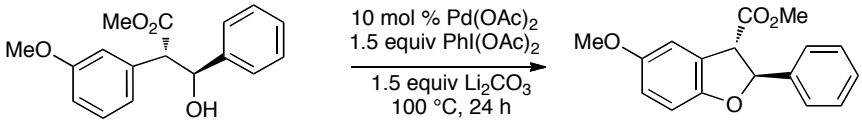
NMR (100 MHz, $CDCl_3$) δ 171.1 (C), 154.3(C), 153.3 (C), 149.1 (C), 149.0 (C), 132.8 (C), 124.7 (C), 118.3 (CH), 114.7 (CH), 111.03 (CH), 111.01 (CH), 109.8 (CH), 108.8 (CH), 85.8 (CH), 56.0 (CH_3), 55.9 (CH), 55.8 (2xCH_3), 52.6 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{21}O_6$, 345.1333; found, 345.1332. HPLC analysis: 94% ee (AD-H, 10% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 33.90 min, major; t_R = 35.92 min, minor).



(2*S*,3*S*)-methyl 5-methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran-3-carboxylate (3.76): Following the general procedure **(J)**, the reaction of **3.64** (64.0 mg, 0.20 mmol) afforded the product as a pale yellow oil (35.5 mg, 56% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). R_f = 0.33 (hexanes:acetone = 3:1); $[\alpha]_D^{20}$ +54.0 (c 0.70, $CHCl_3$); FTIR (neat): 2953, 2836, 1738, 1614, 1515, 1488, 1465, 1435, 1248, 1208, 1174, 1032, 832 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (m, 2H), 6.95-6.92 (m, 1 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 6.81-6.78 (m, 2 H), 6.02 (d, *J* = 7.7 Hz, 1 H), 4.25 (dd, *J* = 7.9, 0.9 Hz, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.78 (s, 3 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.0 (C), 159.5 (C), 154.2 (C), 153.2 (C), 132.5 (C), 127.1 (CH), 124.7 (C), 114.6 (CH), 113.9 (CH), 111.0 (CH), 109.7 (CH), 85.6 (CH), 55.84 (CH_3), 55.81 (CH), 55.1 (CH_3), 52.5 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{18}O_5{}^{23}Na_1$, 337.1047; found, 337.1050; HPLC analysis: 93% ee (AD-H, 10% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 21.90 min, minor; t_R = 23.96 min, major).

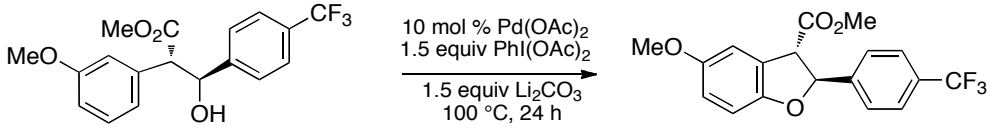


(2*S*,3*S*)-methyl 5-methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran-3-carboxylate (3.77): Following the general procedure **(J)**, the reaction of **3.65** (59.9 mg, 0.19 mmol) afforded the product as a pale yellow oil (24.7 mg, 41% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 9:1). R_f = 0.28 (hexanes:acetone =85:15); $[\alpha]_D^{20}$ +52.1 (c 0.80, MeOH); FTIR (neat): 2952, 2835, 1736, 1602, 1586, 1486, 1464, 1434, 1347, 1268, 1205, 1169, 1031 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31-7.26 (m, 1H), 6.98 (d, J = 8.3 Hz, 1H), 6.96-6.94 (m, 1H), 6.92 (d, J = 2.0 Hz, 1H), 6.88-6.81 (m, 2H), 6.81-6.76 (m, 1H), 6.07 (d, J = 7.5 Hz, 1H), 4.25 (d, J = 7.5 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.1 (C), 159.8 (C), 154.4 (C), 153.4 (C), 142.3 (C), 129.8 (CH), 124.5 (C), 117.9 (CH), 114.8 (CH), 113.7 (CH), 111.2 (CH), 111.1 (CH), 110.9 (CH), 85.5 (CH), 56.08 (CH), 56.05 (CH_3), 55.3 (CH_3), 52.7 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{18}O_5{}^{39}K_1$, 353.0786; found, 353.0788; HPLC analysis: 93% ee (AD-H, 10% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 14.62 min, minor; t_R = 15.51 min, major).



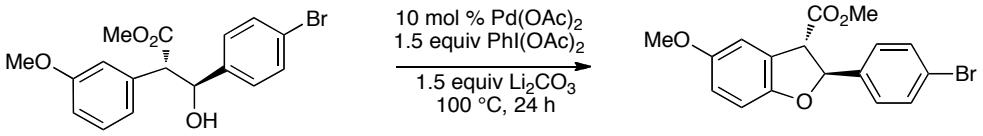
(2*S*,3*S*)-methyl 5-methoxy-2-phenyl-2,3-dihydrobenzofuran-3-carboxylate (3.78): Following the general procedure **(J)**, the reaction of **3.66** (58.2 mg, 0.19 mmol) afforded the product as a pale yellow oil (36.6 mg, 63% yield) after purification by flash

chromatography (silica gel, hexanes:ethyl acetate = 15:1). R_f = 0.23 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ +52.8 (c 0.76, $CHCl_3$); FTIR (neat): 2953, 1739, 1488, 1270, 1209, 1180, 1031 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.45-7.28 (m, 5H), 6.93 (d, J = 2.0 Hz, 1H), 6.82 (d, J = 8.8 Hz, 1H), 6.79 (dd, J = 8.9, 2.6 Hz, 1H), 6.09 (d, J = 7.6 Hz, 1H), 4.26 (d, J = 7.5 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.2 (C), 154.4 (C), 153.5 (C), 140.7 (C), 128.7 (CH), 128.3 (C), 125.7 (C), 124.5 (C), 114.9 (CH), 111.1 (CH), 109.9 (CH), 85.7 (CH), 56.11 (CH), 56.08 (CH_3), 52.7 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{16}O_6{}^{23}Na_1$, 307.0941; found, 307.0941. HPLC analysis: 96% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 21.17 min, major; t_R = 28.96 min, minor).

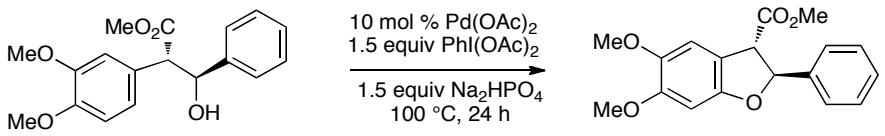


(2*S*,3*S*)-methyl 5-methoxy-2-(4-(trifluoromethyl)phenyl)-2,3-dihydrobenzofuran-3-carboxylate (3.79): Following the general procedure **(J)**, the reaction of **3.67** (58.2 mg, 0.19 mmol) afforded the product as a pale yellow oil (40.5 mg, 61% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 10:1). R_f = 0.34 (hexanes:ethyl acetate = 85:15); $[\alpha]_D^{20}$ +24.9 (c 0.76, MeOH); FTIR (neat): 2955, 1738, 1488, 1323, 1206, 1164, 1122, 1067, 1031, 1018, 991 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.2 Hz, 2H), 6.93 (dd, J = 2.0, 1.0 Hz, 1H), 6.86 (d, J = 8.6 Hz, 1H), 6.81 (dd, J = 8.9, 2.5 Hz, 1H), 6.15 (d, J = 7.5 Hz, 1H), 4.20 (d, J = 7.5 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.8 (C), 154.6 (C), 153.2 (C), 144.8 (C), 130.4 (C, q, J = 32.2 Hz), 126.0 (C, J = 270.8 Hz), 125.94

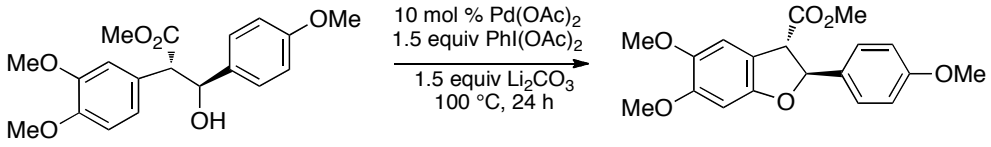
(CH), 125.7 (CH, *J* = 3.7 Hz), 124.0 (C), 115.0 (CH), 111.2 (CH), 110.0 (CH), 84.7 (CH), 56.1 (CH), 56.0 (CH_3), 52.8 (CH_3); HRMS (ESI) *m/z*: $[M-H]^-$ calcd. for $C_{18}H_{14}O_4F_3$, 351.0850; found, 351.0852. HPLC analysis: 98% ee (*SS*-Whelk, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 10.22 min, minor; t_R = 12.12 min, major).



(2*S*,3*S*)-methyl 2-(4-bromophenyl)-5-methoxy-2,3-dihydrobenzofuran-3-carboxylate (3.80): Following the general procedure **(J)**, the reaction of **3.68** (70.3 mg, 0.19 mmol) afforded the product as a pale yellow oil (42.8 mg, 61% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 10:1). R_f = 0.46 (hexanes:ethyl acetate = 4:1); $[\alpha]_D^{20}$ + 42.6 (c 1.16, MeOH); FTIR (neat): 2952, 1738, 1488, 1269, 1210, 1179, 1010 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50-7.30 (m, 5H), 6.88 (s, 1H), 6.55 (s, 1H), 6.09 (d, *J* = 7.0 Hz, 1H), 4.22 (d, *J* = 7.0 Hz, 1H), 3.87 (s, 3H), 3.83 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.9 (C), 154.5 (C), 153.2 (C), 139.7 (C), 131.8 (CH), 127.4 (CH), 124.2 (C), 122.2 (C), 114.9 (CH), 111.2 (CH), 109.9 (CH), 85.0 (CH), 56.0 (CH and CH_3), 52.8 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{15}O_4{}^{79}Br_1{}^{23}Na_1$, 385.0046; found, 385.0049. HPLC analysis: 98% ee (*SS*-Whelk, 2% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 13.70 min, minor; t_R = 15.68 min, major).

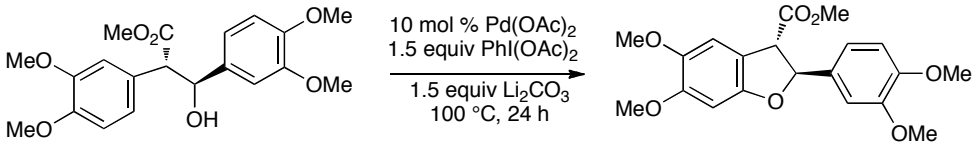


(2*S*,3*S*)-methyl 5,6-dimethoxy-2-phenyl-2,3-dihydrobenzofuran-3-carboxylate (3.81): Following the general procedure **(J)**, the reaction of **3.69** (63.4 mg, 0.20 mmol) afforded the product as a pale yellow oil (29.6 mg, 47% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 5:1). R_f = 0.34 (hexanes:ethyl acetate = 3:1); $[\alpha]_D^{20}$ + 23.3 (c 0.92, MeOH); FTIR (neat): 2952, 1737, 1503, 1454, 1267, 1215, 1190, 1166, 1106, 1025, 994 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48-7.29 (m, 5H), 6.88 (s, 1H), 6.55 (s, 1H), 6.09 (d, J = 6.9 Hz, 1H), 4.22 (d, J = 6.9 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.6 (C), 153.7 (C), 150.8 (C), 143.8 (C), 140.8 (C), 128.7 (CH), 128.3 (CH), 125.6 (CH), 113.2 (C), 108.8 (CH), 94.8 (CH), 86.0 (CH), 56.9 (CH_3), 56.1 (CH_3), 56.0 (CH), 52.7 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{18}H_{18}O_5{}^{39}K_1$, 353.0788; found, 353.0788. HPLC analysis: 97% ee (AD-H, 5% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 15.72 min, major; t_R = 20.60 min, minor).



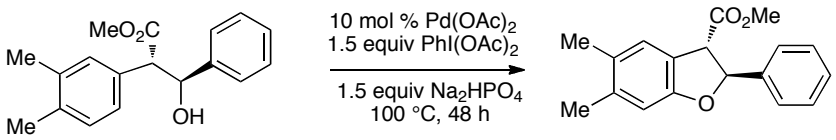
(2*S*,3*S*)-methyl 5,6-dimethoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran-3-carboxylate (3.82): Following the general procedure **(J)**, the reaction of **3.70** (1.3991 g, 4.04 mmol) afforded the product as a pale yellow oil (0.6048 g, 43% yield) after purification by flash chromatography (silica gel, dichloromethane:diethyl ether = 100:1, 50:1, then 10:1). R_f = 0.27 (hexanes:ethyl acetate = 3:1); $[\alpha]_D^{20}$ +49.7 (c 1.66, $CHCl_3$); FTIR (neat): 2953, 2836, 1736, 1613, 1504, 1455, 1249, 1216, 1190, 1168, 1167, 1031, 993 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 8.7 Hz, 2H), 6.93-6.85 (m, 3H),

6.52 (s, 1H), 6.02 (d, J = 7.2 Hz, 1H), 4.21 (dd, J = 7.3, 0.9Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.82 (s 3H), 3.81 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.3 (C), 159.4 (C), 153.4 (C), 150.5 (C), 143.5 (C), 132.5 (C), 126.9 (CH), 113.8 (CH), 113.3 (C), 108.7 (CH), 94.6 (CH), 85.8 (CH), 56.7 (CH_3), 55.8 (CH_3), 55.6 (CH), 54.9 (CH_3), 52.3 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. For $C_{19}H_{20}O_6{}^{23}Na_1$, 367.1152; found, 367.1156; HPLC analysis: 97% ee (AD-H, 20% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 25.58 min, major; t_R = 26.91 min, minor).

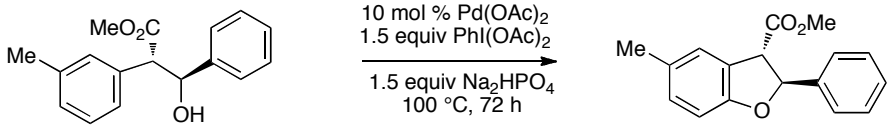


(2*S*,3*S*)-methyl 2-(3,4-dimethoxyphenyl)-5,6-dimethoxy-2,3-dihydrobenzofuran-3-carboxylate (3.83): Following the general procedure **(J)**, the reaction of **3.71** (1.8901 g, 5.02 mmol) afforded the product as a pale yellow oil (0.76 g, 40% yield) after purification by flash chromatography (silica gel, dichloromethane:diethyl ether = 100:1, 75:1, 50:1, 20:1, then 10:1). R_f = 0.43 (hexanes:ethyl acetate = 1:1); $[\alpha]_D{}^{20}$ +32.2 (c 1.09, $CHCl_3$); FTIR (neat): 2936, 2835, 2253, 1735, 1608, 1504, 1454, 1260, 1189, 1160, 1139, 1106, 1025, 994 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.96 (dd, J = 8.1, 2.0 Hz, 1H), 6.91 (d, J = 1.9 Hz, 1H), 6.89 (d, J = 0.9 Hz, 1H), 6.85 (d, J = 8.2 Hz, 1H), 6.54 (s, 1H), 6.02 (d, J = 7.8 Hz, 1H), 4.24 (dd, J = 7.8, 1.0 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 6H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.3 (C), 153.4 (C), 150.5 (C), 148.9 (C), 148.8 (C), 143.5 (C), 132.8 (C), 118.1 (CH), 113.2 (C), 110.9 (CH), 108.63 (CH), 108.59 (CH), 94.6 (CH), 85.9 (CH), 56.6 (CH_3), 55.8 (2xCH_3), 55.6 (CH_3), 55.5 (CH), 52.3 (CH_3); HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{20}H_{22}O_7{}^{23}Na_1$, 397.1258;

found, 397.1263; HPLC analysis: 99% ee (AD-H, 10% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 45.68 min, major; t_R = 47.12 min, minor).

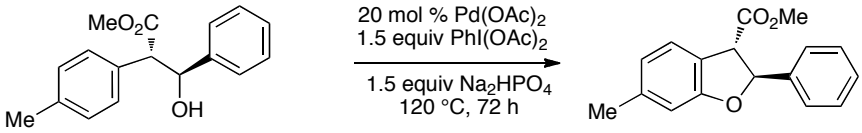


(2*S*,3*S*)-methyl 5,6-dimethyl-2-phenyl-2,3-dihydrobenzofuran-3-carboxylate (3.84): Following the general procedure **(J)**, the reaction of **3.72** (48.5 mg, 0.17 mmol) afforded the product as a pale yellow oil (21.5 mg, 45% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 25:1). R_f = 0.25 (hexanes:ethyl acetate = 95:5); $[\alpha]_D^{20}$ +36.0 (c 0.89, MeOH); FTIR (neat): 3031, 2951, 1738, 1493, 1455, 1261, 1193, 1173, 1008 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43-7.27 (m, 5H), 7.09 (s, 1H), 6.73 (s, 1H), 6.07 (d, *J* = 7.2 Hz, 1H), 4.21 (d, *J* = 7.1 Hz, 1H), 3.81 (s, 3H), 2.24 (s, 3H), 2.21 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.6 (C), 157.7 (C), 140.9 (C), 138.2 (C), 128.9 (C), 128.7 (CH), 128.2 (CH), 125.8 (CH), 125.7 (CH), 120.8 (C), 110.9 (CH), 85.6 (CH), 55.8(CH), 52.6 (CH_3), 20.2 (CH_3), 19.3 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{18}H_{18}O_3{}^{39}K_1$, 321.0887; found, 321.0889; HPLC analysis: 99% ee (AD-H, 0.5% *i*-PrOH in hexane, 1.0 mL/min, λ = 280 nm, t_R = 14.29 min, major; t_R = 19.31 min, minor).



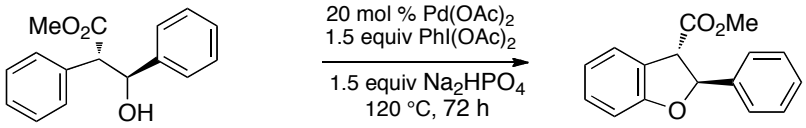
(2S,3S)-methyl 5-methyl-2-phenyl-2,3-dihydrobenzofuran-3-carboxylate (3.85): Following the general procedure **(J)**, the reaction of **3.73** (51.8 mg, 0.19 mmol) afforded

the product as a pale yellow oil (22.5 mg, 44% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 25:1). R_f = 0.25 (hexanes:ethyl acetate = 95:5); $[\alpha]_D^{20}$ +48.6 (c 0.79, MeOH); FTIR (neat): 3033, 2952, 1738, 1490, 1456, 1435, 1247, 1208, 1172 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43-7.28 (m, 5H), 7.15 (s, 1H), 7.04 (d, J = 8.2 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H), 6.09 (d, J = 7.5 Hz, 1H), 4.25 (d, J = 7.5 Hz, 1H), 3.83 (s, 3H), 2.31 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.4 (C), 157.2 (C), 140.8 (C), 130.3 (C), 130.1 (CH), 128.7 (CH), 128.3 (CH), 125.7 (CH), 125.5 (CH), 123.7 (C), 109.4 (CH), 85.6 (CH), 55.8 (CH), 52.7 (CH_3), 20.8 (CH_3); HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $C_{17}H_{16}O_3{}^{39}K_1$, 307.0731; found, 307.0732; HPLC analysis: 99% ee (*SS*-Whelk, 0% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 9.50 min, minor; t_R = 11.76 min, major).



(2*S*,3*S*)-methyl 6-methyl-2-phenyl-2,3-dihydrobenzofuran-3-carboxylate (3.86): Following the general procedure **(J)**, the reaction of **3.74** (52.2 mg, 0.19 mmol) afforded the product as a colorless oil (23.6 mg, 46% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 25:1). The spectroscopic data were consistent with the published values.[166] R_f = 0.25 (hexanes:ethyl acetate = 95:5); $[\alpha]_D^{20}$ +17.5 (c 0.27, MeOH); ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.39 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.1 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 6.75 (d, J = 6.9 Hz, 2H), 6.10 (d, J = 7.2 Hz, 1H), 4.23 (d, J = 7.2 Hz, 1H), 3.81 (s, 3H), 2.35 (s, 3H); HPLC

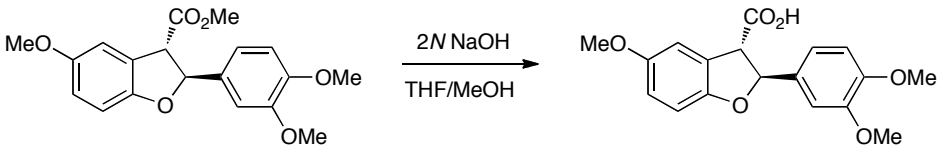
analysis: 99% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 10.64 min, major; t_R = 11.66 min, minor).



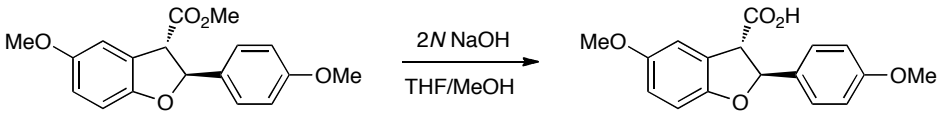
(2*S*,3*S*)-methyl 2-phenyl-2,3-dihydrobenzofuran-3-carboxylate (3.87): Following the general procedure **(J)**, the reaction of **3.75** (52.0 mg, 0.20 mmol) afforded the product as a colorless oil (19.9 mg, 39% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 25:1). The spectroscopic data were consistent with the published values.[166] R_f = 0.25 (hexanes:ethyl acetate = 95:5); $[\alpha]_D^{20}$ +49.3 (c 0.32, MeOH); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.32 (m, 6H), 7.29-7.21 (m, 1H), 6.97-6.89 (m, 2H), 6.12 (d, *J* = 7.5 Hz, 1H), 4.29 (d, *J* = 7.4 Hz, 1H), 3.83 (s, 3H); HPLC analysis: 97% ee (AD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 9.69 min, major; t_R = 10.72 min, minor).

General procedure (K) - hydrolysis of carboxylic esters: To a solution of dihydrobenzofuran ester (1.7 mmol) in THF (6.6 ml) and MeOH (10 ml) at 0 °C was added 2*N* sodium hydroxide solution (3.4 ml, 4 equiv) dropwise. The reaction was then stirred at this temperature for 1 hour and then room temperature. The reaction was stopped when TLC analysis indicated there was no starting material left (about 2 hour at room temperature). Hexane was added and the organic layer was discarded. The aqueous one was cooled down to 0 °C again and acidified with 2*N* HCl until pH ~1. The resulting aqueous solution was extracted with ethyl acetate three times. The combined organic

layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and then concentrated in vacuo. The crude residue was purified by flash chromatography.

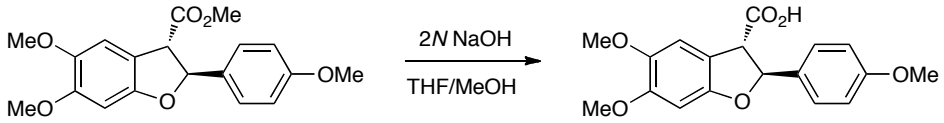


(2*S*,3*S*)-2-(3,4-dimethoxyphenyl)-5-methoxy-2,3-dihydrobenzofuran-3-carboxylic acid (3.88): Following the general procedure **(K)**, the reaction of **3.51** (0.5413 g, 1.57 mmol) afforded the product as a pale yellow oil (0.4202 g, 81% yield) after purification by flash chromatography (silica gel, dichloromethane:methanol = 50:1, 10:1 then 5:1). $[\alpha]_D^{20}$ +57.4 (c 1.26, $CHCl_3$); FTIR (neat): 3485-2591 (br.), 1736, 1712, 1595, 1517, 1488, 1465, 1424, 1263, 1236, 1183, 1139, 1026, 809 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.01-6.89 (m, 3H), 6.88-6.77 (m, 3H), 5.99 (d, J = 7.9 Hz, 1H), 4.31 (d, J = 7.8 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.77 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.0 (C), 154.2 (C), 153.2 (C), 149.0 (C), 148.9 (C), 132.6 (C), 124.1 (C), 118.3 (CH), 115.1 (CH), 111.0 (CH), 110.8 (CH), 109.8 (CH), 108.7 (CH), 85.6 (CH), 55.9 (CH_3), 55.72 (CH, 2xCH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{19}O_6$, 331.1176; found, 331.1175.

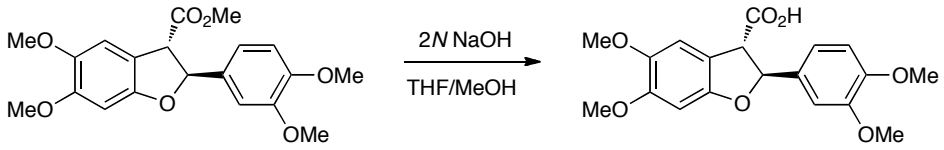


(2*S*,3*S*)-5-methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran-3-carboxylic acid (3.89): Following the general procedure **(K)**, the reaction of **3.76** (0.3438 g, 1.09 mmol) afforded the product as a pale yellow oil (0.2818 g, 88% yield) after purification by flash chromatography (silica gel, dichloromethane:acetone = 10:1, dotted with AcOH 0.05

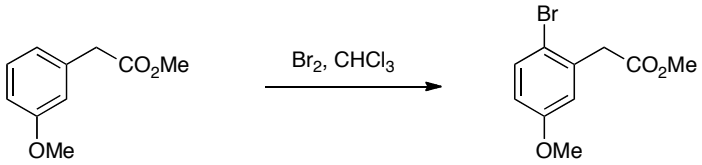
ml/100 ml). R_f = 0.31 (dichloromethane:methanol = 10:1). $[\alpha]_D^{20}$ +86.8 (c 0.95, $CHCl_3$); FTIR (neat): 3500-2594 (br.), 1708, 1612, 1514, 1486, 1465, 1435, 1246, 1204, 1173, 1030, 908 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 8.2 Hz, 2H), 6.98 (s, 1H), 6.89 (d, J = 8.6 Hz, 2H), 6.81 (s, 2 H), 6.00 (d, J = 7.8 Hz, 1H), 4.30 (d, J = 7.8 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.3 (C), 159.5 (C), 154.2 (C), 153.2 (C), 132.2 (C), 127.1 (CH), 124.0 (C), 115.2 (CH), 114.0 (CH), 110.8 (CH), 109.8 (CH), 85.3 (CH), 55.9 (CH_3), 55.7 (CH), 55.1 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{17}O_5$, 301.1071; found, 301.1071.



(2*S*,3*S*)-5,6-dimethoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran-3-carboxylic acid (3.90): Following the general procedure **(K)**, the reaction of **3.82** (0.5976 g, 1.74 mmol) afforded the product as a pale yellow oil (0.4715 g, 82% yield) after purification by flash chromatography (silica gel, dichloromethane:acetone = 10:1, dotted with AcOH 0.05 ml/100 ml). $[\alpha]_D^{20}$ +65.6 (c 1.07, $CHCl_3$); FTIR (neat): 3484-2604 (br.), 1735, 1710, 1613, 1514, 1504, 1464, 1455, 1249, 1216, 1191, 1167, 1105, 1031, 996 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 0.8 Hz, 1H), 6.90 (d, J = 8.8 Hz, 2H), 6.53 (s, 1H), 6.01 (d, J = 7.0 Hz, 1H), 4.26 (dd, J = 7.2, 0.9 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.81 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.6 (C), 159.5 (C), 153.5 (C), 150.7 (C), 143.7 (C), 132.4 (C), 127.0 (CH), 114.0 (CH), 112.7 (C), 108.7 (CH), 94.7 (CH), 85.6 (CH), 56.7 (CH_3), 55.9 (CH_3), 55.6 (CH), 55.1 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{19}O_6$, 331.1176; found, 331.1175.

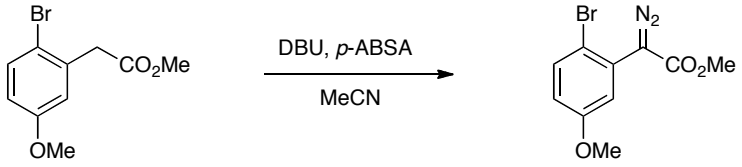


(2*S*,3*S*)-2-(3,4-dimethoxyphenyl)-5,6-dimethoxy-2,3-dihydrobenzofuran-3-carboxylic acid (2.91): Following the general procedure **(K)**, the reaction of **3.83** (0.5916 g, 1.74 mmol) afforded the product as a pale yellow oil (0.3105 g, 54% yield) after purification by flash chromatography (silica gel, dichloromethane:methanol = 50:1, 10:1 then 5:1). R_f = 0.29 (dichloromethane:methanol = 10:1); $[\alpha]_D^{20}$ +45.5 (c 0.99, $CHCl_3$); FTIR (neat): 3489-2592 (br.), 1735, 1609, 1517, 1503, 1464, 1454, 1262, 1216, 1190, 1163, 1140, 1025, 998 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.99-6.93 (m, 2H), 6.91 (s, 1H), 6.85 (d, J = 8.2 Hz, 1H), 6.55 (s, 1H), 6.01 (d, J = 7.3 Hz, 1H), 4.29 (d, J = 7.3 Hz, 1H), 3.88 (s., 3H), 3.87 (s, 6H), 3.85 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.3 (C), 153.5 (C), 150.8 (C), 149.1 (C), 149.0 (C), 143.8 (C), 132.8 (C), 118.3 (2xCH), 112.9 (C), 111.1 (CH), 108.73 (CH), 108.67 (CH), 94.8 (CH), 85.9 (CH), 56.7 (CH_3), 56.0 (CH_3), 55.8 (CH_3), 55.6 (CH); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{21}O_7$, 361.1282; found, 361.1281.



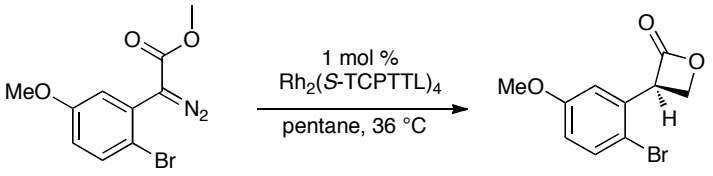
methyl 2-(2-bromo-5-methoxyphenyl)acetate (S6): A solution of 3-methoxyphenylacetic acid methyl ester (5.67 g, 0.031 mol, 1 equiv) in chloroform (25 ml) was placed in a water bath and bromine (1.70 ml, 0.033 mol, 1.05 equiv) was added

dropwise to this solution. The reaction was stirred overnight at room temperature. It was then quenched with saturated sodium thiosulfate solution. The resulting mixture was stirred for an additional hour at room temperature before the separation of layers. The aqueous layer was extracted with dichloromethane three times and the combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:diethyl ether = 3:1) to afford the product as colorless oil (5.93 g, 73% yield). The spectroscopic data were consistent with the published values.[181] R_f = 0.26 (hexanes:diethyl ether = 3:1); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.5 Hz, 1H), 6.85 (d, J = 3.1 Hz, 1H), 6.72 (dd, J = 8.7, 2.9 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 2H), 3.71 (s, 3H).



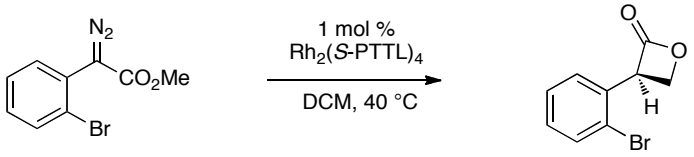
methyl 2-(2-bromo-4-methoxyphenyl)-2-diazoacetate (3.93): To a solution of **S6** (3.48 g, 0.013 mol, 1 equiv) and *p*-ABSA (4.20 g, 0.017 mol, 1.3 equiv) in acetonitrile (15 ml) at 0 $^{\circ}$C was added DBU (3.0 ml, 0.020 mol, 1.5 equiv) in one portion. The reaction was warmed up slowly in the ice-water bath to room temperature and stirred overnight. The reaction was quenched with saturated sodium bicarbonate solution. The aqueous solution was extracted with diethyl ether three times. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered through silica gel and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, petroleum ether:diethyl ether = 10:1 then 3:1) to afford the product as yellow solid (3.14 g, 82%

yield). FTIR (neat): 2953, 2838, 2095, 1699, 1589, 1567, 1470, 1435, 1339, 1279, 1233, 1191, 1153, 1073, 1034, 1014, 741 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 9.0 Hz, 1H), 7.06 (d, J = 3.1 Hz, 1H), 6.79 (dd, J = 8.8, 2.9 Hz, 1H), 3.85 (s, 3H), 3.80 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7 (C), 159.0 (C), 133.8 (CH), 126.3 (C), 117.7 (CH), 116.5 (CH), 114.5 (C), 55.5 (CH_3), 52.2 (CH_3); HRMS (APCI) *m/z*: $[M\text{-}N_2\text{+}H]^+$ calcd. for $C_{10}H_{10}O_3{}^{79}Br_1$, 256.9808; found, 256.9808.

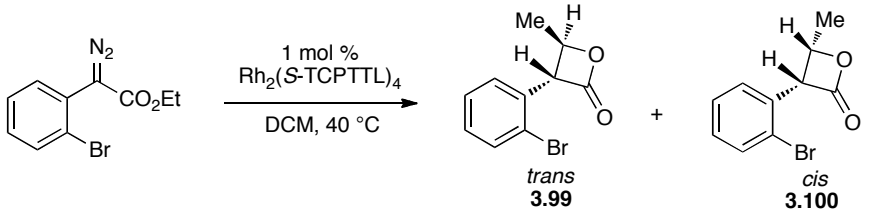


(*R*)-3-(2-bromo-5-methoxyphenyl)oxetan-2-one (3.94): Under argon atmosphere, to a solution of Rh_2(*S*-PTTL)$_4$ (86.4 mg, 0.069 mmol, 0.01 equiv) in pentane (80 ml) at reflux as added a solution of **3.93** (1.9556 g, 6.86 mmol, 1 equiv) in pentane (40 ml) over 3 hours. After stirring an additional hour at reflux, the reaction was cooled to room temperature and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:diethyl ether = 10:1) and then recrystallization, which was performed by dissolving the product in hot hexanes and then sitting it overnight at room temperature. The product was collected through filtration as a white solid (0.5240 g, 30% yield). R_f = 0.26 (hexanes:ethyl acetate = 5:1); $[\alpha]_D{}^{20}$ -150.2 (c 1.27, $CHCl_3$, 99% ee); FTIR (neat): 2939, 2838, 1819, 1594, 1572, 1471, 1417, 1332, 1295, 1241, 1168, 1108, 1063, 1017 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.8 Hz, 1H), 7.12 (d, J = 3.0 Hz, 1H), 6.78 (dd, J = 8.8, 3.0 Hz, 1H), 5.14 (dd, J = 6.6, 5.1 Hz, 1H), 4.78 (dd, J = 6.8, 5.2 Hz, 1H), 4.24 (dd, J = 5.2, 5.1 Hz, 1H), 3.81 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.6 (C), 159.3 (C), 133.7 (C), 133.5 (CH), 115.7 (CH), 113.7

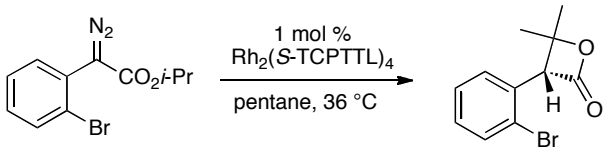
(CH), 113.4 (C), 66.6 (CH), 56.60 (CH), 55.57 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{10}H_{10}O_3{}^{79}Br_1$, 256.9808; found, 256.9807; HPLC analysis: 87% ee (AD-H, hexane, 1.0 mL/min, λ = 230 nm, t_R = 17.88 min, minor; t_R = 21.03 min, major). The enantioselectivity was enriched to 99% by recrystallization.



(*R*)-3-(2-bromophenyl)oxetan-2-one (3.97): Under argon atmosphere, to a solution of Rh_2(*S*-PTTL)$_4$ (12.6 mg, 0.001 mmol, 0.01 equiv) in dichloromethane (5 ml) at reflux as added a solution of methyl 2-bromophenylacetate (287.0 mg, 1.13 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. After stirring an additional hour at reflux, the reaction was cooled to room temperature and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:diethyl ether = 20:1 then 10:1) to afford the product as a colorless oil (0.1019 mg, 43% yield). R_f = 0.53 (hexanes:diethyl ether = 5:1); $[\alpha]_D{}^{20}$ -62.4 (c 1.20, $CHCl_3$); FTIR (neat): 2981, 1816, 1474, 1438, 1331, 1296, 1180, 1124, 1104, 1051, 1024 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.57 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.37 (td, *J* = 7.7, 1.1 Hz, 1H), 7.24 (td, *J* = 7.7, 1.6 Hz, 1H), 5.19 (dd, *J* = 6.7, 5.1 Hz, 1H), 4.79 (dd, *J* = 6.7, 5.4 Hz, 1H), 4.24 (dd, *J* = 5.4, 5.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.6 (C), 132.94 (C), 132.89 (CH), 129.8, (CH) 128.2 (CH), 128.0 (CH), 123.4 (C), 66.6 (CH_2), 56.7 (CH); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_9H_8O_1{}^{79}Br_1$, 226.9702; found, 226.9700; HPLC analysis: 32% ee (OD-H, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 230 nm, t_R = 10.23 min, t_R = major; t_R = 11.32 min, minor).



(3*R*,4*R*)-3-(2-bromophenyl)-4-methyloxetan-2-one (3.99): Under argon atmosphere, to a solution of Rh_2(*S*-TCPTTL)$_4$ (8.4 mg, 0.0047 mmol, 0.01 equiv) in dichloromethane (5 ml) at reflux as added a solution of *iso*-propyl 2-bromophenylacetate (128.4 mg, 0.48 mmol, 1 equiv) in dichloromethane (5 ml) over 3 hours. After stirring an additional hour at reflux, the reaction was cooled to room temperature and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 30:1) to afford the product as a white solid (80.5 mg, 70% yield). R_f = 0.32 (hexanes:ethyl acetate = 10:1); $[\alpha]_D^{20}$ -63.2 (c 2.06, $CHCl_3$, 60% ee); FTIR (neat): 2981, 1814, 1473, 1440, 1384, 1354, 1314, 1278, 1256, 1181, 1130, 1087, 1022 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, J = 8.0, 1.2 Hz, 1H), 7.47 (dd, J = 7.7, 1.6 Hz, 1H), 7.36 (td, J = 7.6, 1.2 Hz, 1H), 7.22 (td, J = 7.7, 1.7 Hz, 1H), 4.75 (d, J = 4.2 Hz, 1H), 4.56 (qd, J = 6.1, 4.2 Hz, 1H), 1.83 (d, J = 6.1 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.4 (C), 133.1 (CH), 132.9 (C), 129.9 (CH), 128.6 (CH), 128.2 (CH), 123.7 (C), 76.8 (CH), 62.3 (CH_2), 20.7 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{10}H_{10}O_2{}^{79}Br_1$, 240.9859; found, 240.9857; HPLC analysis: 76% ee (AD-H, 0.5% *i*Pr-OH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 20.60 min, major; t_R = 48.59 min, minor).



(3*R*,4*R*)-3-(2-bromophenyl)-4-methyloxetan-2-one (3.103): Under argon atmosphere, to a solution of Rh_2(*S*-TCPTTL)$_4$ (5.9 mg, 0.0033 mmol, 0.01 equiv) in pentane (5 ml) at reflux as added a solution of *iso*-propyl 2-bromophenylacetate (92.2 mg, 0.33 mmol, 1 equiv) in pentane (5 ml) over 3 hours. After stirring an additional hour at reflux, the reaction was cooled to room temperature and concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 20:1 then 10:1) to afford the product as a white solid (74.7 mg, 90% yield). R_f = 0.43 (hexanes:ethyl acetate = 10:1); FTIR (neat): 2978, 2932, 1809, 1472, 1439, 1387, 1378, 1262, 1241, 1213, 1118, 1133, 1071, 1024 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 8.0, 1.2 Hz, 1H), 7.47 (dd, J = 7.7, 1.6 Hz, 1H), 7.37 (td, J = 7.6, 1.2 Hz, 1H), 7.23 (td, J = 7.7, 1.7 Hz, 1H), 4.87 (s, 1H), 1.92 (s, 3H), 1.22 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.5 (C), 132.8 (C), 132.0 (CH), 129.7 (CH), 127.8 (CH), 123.8 (CH), 81.9 (C), 63.7 (CH), 27.5 (CH_3), 22.5 (CH_3); HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{11}H_{12}O_2{}^{79}Br_1$, 255.0015; found, 255.0020; HPLC analysis: 45% ee (*SS*-Whelk, 1% *i*-PrOH in hexane, 1.0 mL/min, λ = 210 nm, t_R = 11.32 min, major; t_R = 15.21 min, minor).

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Appendix

1. X-ray crystallographic structure of product 1.50

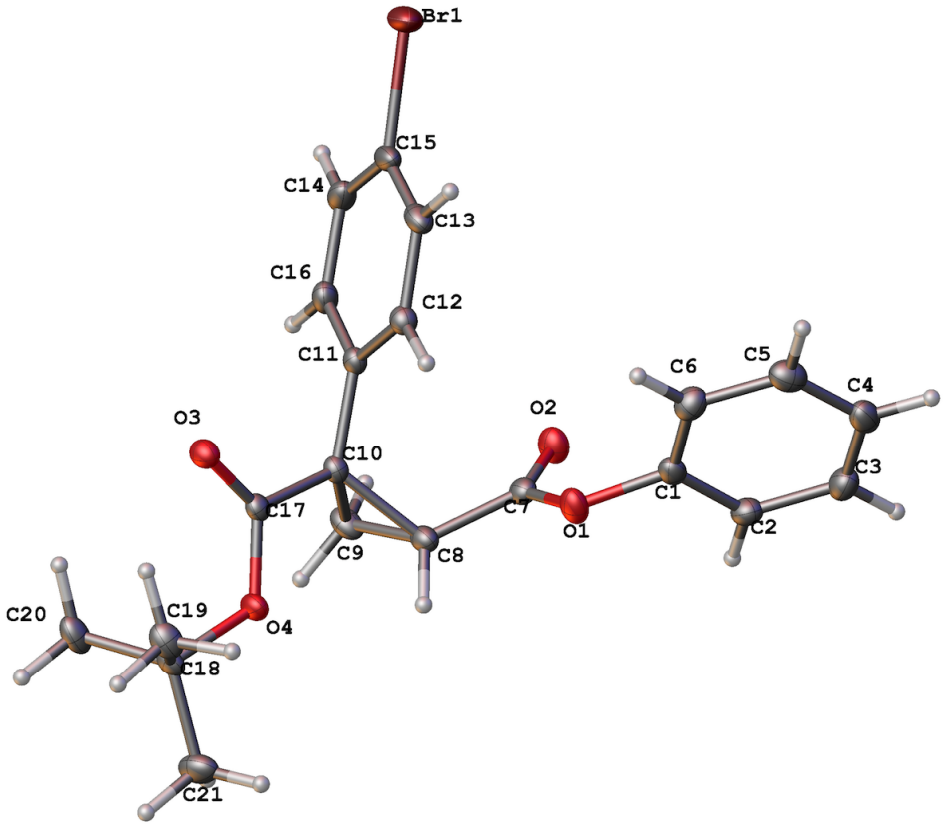

Table 1. Crystal data and structure refinement for product **1.50**

Identification code	HW-XVIII-046	
Empirical formula	C21 H21 Br O4	
Formula weight	417.29	
Temperature	173.2 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.0402(2) Å	α= 90°.
	b = 15.4144(4) Å	β= 90°.
	c = 20.7290(8) Å	γ = 90°.
Volume	1930.00(11) $Å^3$	
Z	4	
Density (calculated)	1.436 Mg/m^3	
Absorption coefficient	2.152 mm^{-1}	
F(000)	856	
Crystal size	0.472 x 0.451 x 0.346 mm^3	
Theta range for data collection	1.65 to 30.99°.	
Index ranges	-8<=h<=8, -21<=k<=21, -15<=l<=29	
Reflections collected	21661	
Independent reflections	6098 [R(int) = 0.0482]	
Completeness to theta = 30.99°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7464 and 0.5354	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6098 / 0 / 238	
Goodness-of-fit on F^2	1.020	
Final R indices [I>2sigma(I)]	R_1 = 0.0382, wR_2 = 0.0836	
R indices (all data)	R_1 = 0.0604, wR_2 = 0.0916	
Absolute structure parameter	0.006(7)	
Largest diff. peak and hole	0.349 and -0.357 e.$Å^{-3}$	

Table 2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$) for product **1.50**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Br(1)	-1109(1)	2618(1)	3356(1)	70(1)
C(1)	1296(3)	6901(1)	4382(1)	30(1)
C(2)	2868(3)	7495(1)	4195(1)	34(1)
C(3)	2435(4)	8010(2)	3664(1)	40(1)
C(4)	472(4)	7923(1)	3328(1)	40(1)
C(5)	-1062(4)	7314(2)	3522(1)	41(1)
C(6)	-670(3)	6797(2)	4055(1)	37(1)
C(7)	3213(3)	5848(1)	5026(1)	28(1)
C(8)	3116(3)	5493(1)	5690(1)	29(1)
C(9)	4540(3)	4747(2)	5872(1)	34(1)
C(10)	2112(3)	4579(1)	5764(1)	24(1)
C(11)	1386(3)	4113(1)	5169(1)	24(1)
C(12)	-535(3)	4373(1)	4852(1)	28(1)
C(13)	-1282(4)	3930(2)	4311(1)	36(1)
C(14)	-49(4)	3241(2)	4079(1)	39(1)
C(15)	1884(4)	2982(2)	4372(1)	41(1)
C(16)	2591(4)	3420(1)	4921(1)	33(1)
C(17)	718(3)	4419(1)	6353(1)	24(1)
C(18)	492(3)	4800(1)	7512(1)	28(1)
C(19)	-2022(3)	4875(2)	7540(1)	38(1)
C(20)	1273(4)	3924(2)	7740(1)	40(1)
C(21)	1588(4)	5528(2)	7879(1)	45(1)
O(1)	1555(2)	6435(1)	4961(1)	36(1)
O(2)	4465(2)	5656(1)	4605(1)	38(1)
O(3)	-716(2)	3876(1)	6375(1)	32(1)
O(4)	1295(2)	4945(1)	6840(1)	30(1)

Table 3. Bond lengths [Å] and angles [°] for product **1.50**

Br(1)-C(14)	1.891(2)
O(1)-C(1)	1.406(2)
O(1)-C(7)	1.357(2)
O(2)-C(7)	1.193(2)
O(3)-C(17)	1.205(2)
O(4)-C(17)	1.341(2)
O(4)-C(18)	1.492(2)
C(1)-C(2)	1.375(3)
C(1)-C(6)	1.377(3)
C(2)-C(3)	1.382(3)
C(3)-C(4)	1.382(3)
C(4)-C(5)	1.380(3)
C(5)-C(6)	1.383(3)
C(7)-C(8)	1.482(3)
C(8)-C(9)	1.484(3)
C(8)-C(10)	1.542(3)
C(9)-C(10)	1.506(3)
C(10)-C(11)	1.493(3)
C(10)-C(17)	1.503(3)
C(11)-C(12)	1.393(3)
C(11)-C(16)	1.392(3)
C(12)-C(13)	1.387(3)
C(13)-C(14)	1.384(3)
C(14)-C(15)	1.375(3)
C(15)-C(16)	1.391(3)
C(18)-C(19)	1.524(3)
C(18)-C(20)	1.507(3)
C(18)-C(21)	1.509(3)
C(2)-H(2)	0.9500
C(3)-H(3)	0.9500
C(4)-H(4)	0.9500
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(8)-H(8)	1.0000

C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(12)-H(12)	0.9500
C(13)-H(13)	0.9500
C(15)-H(15)	0.9500
C(16)-H(16)	0.9500
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800

C(1)-O(1)-C(7)	120.49(14)
C(17)-O(4)-C(18)	121.84(14)
O(1)-C(1)-C(2)	120.24(16)
O(1)-C(1)-C(6)	117.17(17)
C(2)-C(1)-C(6)	122.28(18)
C(1)-C(2)-C(3)	118.48(18)
C(2)-C(3)-C(4)	120.6(2)
C(3)-C(4)-C(5)	119.6(2)
C(4)-C(5)-C(6)	120.7(2)
C(1)-C(6)-C(5)	118.3(2)
O(1)-C(7)-O(2)	124.08(17)
O(1)-C(7)-C(8)	108.05(15)
O(2)-C(7)-C(8)	127.84(18)
C(7)-C(8)-C(9)	119.97(17)
C(7)-C(8)-C(10)	116.49(16)
C(9)-C(8)-C(10)	59.67(13)
C(8)-C(9)-C(10)	62.06(13)
C(8)-C(10)-C(9)	58.27(13)
C(8)-C(10)-C(11)	118.17(16)
C(8)-C(10)-C(17)	116.82(16)

C(9)-C(10)-C(11)	119.46(16)
C(9)-C(10)-C(17)	116.94(16)
C(11)-C(10)-C(17)	115.33(16)
C(10)-C(11)-C(12)	119.84(16)
C(10)-C(11)-C(16)	121.38(17)
C(12)-C(11)-C(16)	118.78(17)
C(11)-C(12)-C(13)	120.79(19)
C(12)-C(13)-C(14)	118.9(2)
Br(1)-C(14)-C(13)	118.86(17)
Br(1)-C(14)-C(15)	119.31(17)
C(13)-C(14)-C(15)	121.8(2)
C(14)-C(15)-C(16)	118.7(2)
C(11)-C(16)-C(15)	121.0(2)
O(3)-C(17)-O(4)	125.32(16)
O(3)-C(17)-C(10)	123.17(16)
O(4)-C(17)-C(10)	111.51(15)
O(4)-C(18)-C(19)	110.37(15)
O(4)-C(18)-C(20)	109.01(15)
O(4)-C(18)-C(21)	102.51(16)
C(19)-C(18)-C(20)	111.58(18)
C(19)-C(18)-C(21)	111.20(18)
C(20)-C(18)-C(21)	111.79(17)
C(1)-C(2)-H(2)	121.00
C(3)-C(2)-H(2)	121.00
C(2)-C(3)-H(3)	120.00
C(4)-C(3)-H(3)	120.00
C(3)-C(4)-H(4)	120.00
C(5)-C(4)-H(4)	120.00
C(4)-C(5)-H(5)	120.00
C(6)-C(5)-H(5)	120.00
C(1)-C(6)-H(6)	121.00
C(5)-C(6)-H(6)	121.00
C(7)-C(8)-H(8)	116.00
C(9)-C(8)-H(8)	116.00
C(10)-C(8)-H(8)	116.00
C(8)-C(9)-H(9A)	118.00

C(8)-C(9)-H(9B)	118.00
C(10)-C(9)-H(9A)	118.00
C(10)-C(9)-H(9B)	118.00
H(9A)-C(9)-H(9B)	115.00
C(11)-C(12)-H(12)	120.00
C(13)-C(12)-H(12)	120.00
C(12)-C(13)-H(13)	121.00
C(14)-C(13)-H(13)	121.00
C(14)-C(15)-H(15)	121.00
C(16)-C(15)-H(15)	121.00
C(11)-C(16)-H(16)	120.00
C(15)-C(16)-H(16)	119.00
C(18)-C(19)-H(19A)	110.00
C(18)-C(19)-H(19B)	110.00
C(18)-C(19)-H(19C)	109.00
H(19A)-C(19)-H(19B)	109.00
H(19A)-C(19)-H(19C)	109.00
H(19B)-C(19)-H(19C)	109.00
C(18)-C(20)-H(20A)	109.00
C(18)-C(20)-H(20B)	110.00
C(18)-C(20)-H(20C)	109.00
H(20A)-C(20)-H(20B)	109.00
H(20A)-C(20)-H(20C)	109.00
H(20B)-C(20)-H(20C)	109.00
C(18)-C(21)-H(21A)	110.00
C(18)-C(21)-H(21B)	109.00
C(18)-C(21)-H(21C)	109.00
H(21A)-C(21)-H(21B)	109.00
H(21A)-C(21)-H(21C)	109.00
H(21B)-C(21)-H(21C)	110.00

Table 4. Anisotropic displacement parameters ($Å^2x10^3$) for product **1.50**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	132(1)	49(1)	30(1)	-4(1)	-15(1)	-37(1)
C(1)	40(1)	26(1)	22(1)	-3(1)	4(1)	3(1)
C(2)	39(1)	32(1)	32(1)	-4(1)	0(1)	-6(1)
C(3)	51(1)	31(1)	38(1)	2(1)	6(1)	-6(1)
C(4)	56(1)	32(1)	31(1)	0(1)	0(1)	8(1)
C(5)	40(1)	44(1)	39(1)	-6(1)	-6(1)	6(1)
C(6)	36(1)	34(1)	42(1)	0(1)	6(1)	-4(1)
C(7)	31(1)	26(1)	27(1)	0(1)	2(1)	-8(1)
C(8)	32(1)	32(1)	22(1)	0(1)	1(1)	-7(1)
C(9)	25(1)	51(1)	26(1)	2(1)	-3(1)	-3(1)
C(10)	24(1)	26(1)	21(1)	2(1)	1(1)	2(1)
C(11)	28(1)	24(1)	20(1)	2(1)	3(1)	-1(1)
C(12)	28(1)	30(1)	26(1)	2(1)	0(1)	-2(1)
C(13)	40(1)	43(1)	26(1)	6(1)	-7(1)	-12(1)
C(14)	63(1)	34(1)	20(1)	1(1)	0(1)	-20(1)
C(15)	68(2)	26(1)	28(1)	-2(1)	11(1)	-2(1)
C(16)	44(1)	28(1)	28(1)	5(1)	2(1)	3(1)
C(17)	26(1)	26(1)	21(1)	3(1)	-2(1)	2(1)
C(18)	31(1)	36(1)	17(1)	0(1)	1(1)	0(1)
C(19)	33(1)	47(2)	33(1)	2(1)	3(1)	9(1)
C(20)	44(1)	48(1)	27(1)	8(1)	0(1)	15(1)
C(21)	51(1)	52(2)	32(1)	-13(1)	8(1)	-11(1)
O(1)	45(1)	38(1)	26(1)	5(1)	10(1)	6(1)
O(2)	40(1)	41(1)	32(1)	4(1)	11(1)	3(1)
O(3)	34(1)	37(1)	26(1)	0(1)	2(1)	-7(1)
O(4)	39(1)	33(1)	20(1)	-1(1)	4(1)	-8(1)

Table 5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2x10^3$) for product **1.50**

	x	y	z	U(eq)
H(2)	4221	7549	4425	41
H(3)	3496	8427	3529	48
H(4)	180	8281	2965	47
H(5)	-2402	7249	3287	49
H(6)	-1731	6380	4192	44
H(8)	2770	5917	6041	35
H(9A)	5094	4724	6322	41
H(9B)	5591	4526	5545	41
H(12)	-1343	4858	5007	34
H(13)	-2617	4098	4103	44
H(15)	2721	2512	4202	49
H(16)	3917	3243	5130	40
H(19A)	-2486	5420	7339	57
H(19B)	-2508	4866	7991	57
H(19C)	-2690	4386	7309	57
H(20A)	512	3468	7496	60
H(20B)	942	3858	8201	60
H(20C)	2874	3874	7672	60
H(21A)	3195	5496	7820	68
H(21B)	1235	5475	8339	68
H(21C)	1044	6086	7717	68

Table 6. Torsion angles [°] for product **1.50**

C(7)-O(1)-C(1)-C(2)	-66.8(2)
C(7)-O(1)-C(1)-C(6)	119.4(2)
C(1)-O(1)-C(7)-O(2)	-3.7(3)
C(1)-O(1)-C(7)-C(8)	177.80(16)
C(17)-O(4)-C(18)-C(19)	-62.5(2)
C(18)-O(4)-C(17)-O(3)	11.9(3)
C(18)-O(4)-C(17)-C(10)	-167.44(15)
C(17)-O(4)-C(18)-C(20)	60.4(2)
C(17)-O(4)-C(18)-C(21)	179.01(16)
O(1)-C(1)-C(6)-C(5)	173.34(19)
C(2)-C(1)-C(6)-C(5)	-0.3(3)
C(6)-C(1)-C(2)-C(3)	0.8(3)
O(1)-C(1)-C(2)-C(3)	-172.64(18)
C(1)-C(2)-C(3)-C(4)	-0.5(3)
C(2)-C(3)-C(4)-C(5)	-0.3(3)
C(3)-C(4)-C(5)-C(6)	0.9(4)
C(4)-C(5)-C(6)-C(1)	-0.6(3)
O(1)-C(7)-C(8)-C(10)	102.99(19)
O(2)-C(7)-C(8)-C(9)	-6.8(3)
O(1)-C(7)-C(8)-C(9)	171.65(17)
O(2)-C(7)-C(8)-C(10)	-75.4(3)
C(9)-C(8)-C(10)-C(11)	-108.95(19)
C(7)-C(8)-C(9)-C(10)	-105.0(2)
C(7)-C(8)-C(10)-C(9)	110.80(19)
C(9)-C(8)-C(10)-C(17)	106.52(18)
C(7)-C(8)-C(10)-C(17)	-142.68(17)
C(7)-C(8)-C(10)-C(11)	1.9(2)
C(8)-C(9)-C(10)-C(17)	-106.31(19)
C(8)-C(9)-C(10)-C(11)	106.75(19)
C(17)-C(10)-C(11)-C(16)	-108.5(2)
C(8)-C(10)-C(17)-O(3)	154.48(18)
C(8)-C(10)-C(11)-C(12)	-73.5(2)
C(8)-C(10)-C(11)-C(16)	106.5(2)
C(9)-C(10)-C(11)-C(12)	-141.04(19)

C(9)-C(10)-C(11)-C(16)	39.0(3)
C(17)-C(10)-C(11)-C(12)	71.5(2)
C(11)-C(10)-C(17)-O(4)	-171.70(15)
C(9)-C(10)-C(17)-O(3)	-139.4(2)
C(9)-C(10)-C(17)-O(4)	40.0(2)
C(8)-C(10)-C(17)-O(4)	-26.2(2)
C(11)-C(10)-C(17)-O(3)	9.0(3)
C(16)-C(11)-C(12)-C(13)	2.3(3)
C(10)-C(11)-C(16)-C(15)	179.01(19)
C(10)-C(11)-C(12)-C(13)	-177.72(18)
C(12)-C(11)-C(16)-C(15)	-1.0(3)
C(11)-C(12)-C(13)-C(14)	-1.9(3)
C(12)-C(13)-C(14)-Br(1)	178.29(16)
C(12)-C(13)-C(14)-C(15)	0.3(3)
C(13)-C(14)-C(15)-C(16)	1.0(3)
Br(1)-C(14)-C(15)-C(16)	-177.02(16)
C(14)-C(15)-C(16)-C(11)	-0.6(3)

Table 7. Hydrogen bonds for product **1.50** [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(2)-H(2)...O(1)#1	0.9500	2.4600	3.277(2)	144.00
C(8)-H(8)...O(4)	1.0000	2.4000	2.758(2)	100.00
C(19)-H(19C)...O(3)	0.9800	2.4100	2.971(3)	116.00
C(20)-H(20A)...O(3)	0.9800	2.5200	3.075(2)	116.00

Symmetry transformations used to generate equivalent atoms:
#1 1/2+x, 3/2-y, 1-z

2. X-ray crystallographic structure of 1.53

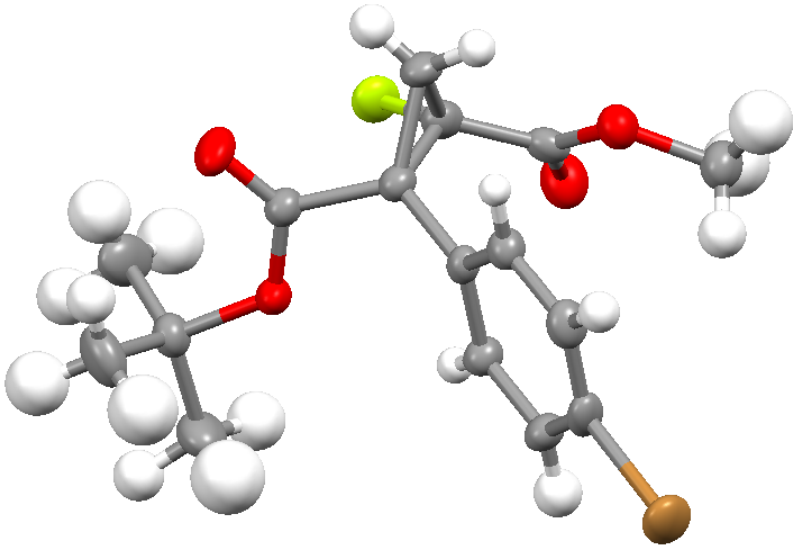

Table 1. Crystal data and structure refinement for product **1.53**

Identification code	
Empirical formula	$C_{16}HBrFO_4$
Formula weight	355.06
Temperature/K	173
Crystal system	orthorhombic
Space group	$P2_12_12$
a/Å	10.996(3)
b/Å	23.742(5)
c/Å	6.3573(15)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1659.7(7)
Z	4
ρ_{calc}mg/mm^3	1.421
m/mm^{-1}	2.498
F(000)	688.0
Crystal size/mm^3	0.516 × 0.255 × 0.232
2Θ range for data collection	3.43 to 59.11°
Index ranges	$-15 \leq h \leq 15$, $-32 \leq k \leq 30$, $-8 \leq l \leq 8$
Reflections collected	12942
Independent reflections	4650[R(int) = 0.0313]
Data/restraints/parameters	4650/0/271
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0387, wR_2 = 0.0889
Final R indexes [all data]	R_1 = 0.0480, wR_2 = 0.0928
Largest diff. peak/hole / e Å^{-3}	1.06/-0.32
Flack parameter	0.003(3)

Table 2. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for product **1.53.** U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{ij} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
Br1	667.6(3)	4162.85(18)	3671.7(7)	46.54(14)
F1	6587.3(18)	2714.8(9)	9305(4)	39.5(5)
O1	3774(2)	2271.3(11)	7391(4)	33.7(5)
O2	5571(3)	2320.0(12)	5694(4)	43.4(6)
O4	6013(3)	3817.3(13)	11992(4)	42.3(6)
O3	6161(2)	4025.6(9)	8552(4)	30.6(5)
C4	3775(3)	3524.4(13)	8064(5)	23.9(6)
C1	1922(3)	3896.4(15)	5465(5)	31.4(7)
C10	5719(3)	3750.2(13)	10200(5)	26.5(6)
C3	2580(3)	3528.3(13)	8771(5)	28.5(6)
C15	4032(3)	3702.3(14)	6025(5)	27.1(6)
C11	7168(3)	4436.5(14)	8756(6)	32.1(6)
C5	4783(3)	3320.3(14)	9479(5)	25.7(6)
C2	1649(3)	3718.3(16)	7457(6)	33.5(7)
C9	4595(3)	2834.4(16)	10978(5)	32.1(7)
C16	3109(3)	3889.2(15)	4706(5)	30.1(7)
C8	3188(4)	2037(2)	5537(6)	41.3(9)
C7	4935(3)	2417.6(14)	7189(5)	29.4(6)
C6	5349(3)	2745.3(15)	9063(5)	30.0(7)
C12	7380(5)	4603(2)	6477(7)	52.9(11)
C13	6778(5)	4932(2)	10069(9)	53.8(12)
C14	8274(4)	4139(2)	9625(9)	53.1(11)

Table 3. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for product **1.53**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+...+2hka \times b \times U_{12}]$

Atom	$\mathbf{U_{11}}$	$\mathbf{U_{22}}$	$\mathbf{U_{33}}$	$\mathbf{U_{23}}$	$\mathbf{U_{13}}$	$\mathbf{U_{12}}$
Br1	30.38(17)	51.9(2)	57.3(2)	8.82(19)	-17.59(16)	3.42(17)
F1	22.9(9)	44.4(12)	51.1(12)	6.5(9)	-7.8(8)	4.8(9)
O1	28.5(11)	35.8(13)	36.7(12)	0.1(10)	1.6(9)	-3.6(10)
O2	34.0(13)	50.0(16)	46.2(14)	-8.0(12)	10.4(11)	-3.7(12)
O4	41.4(14)	60.3(17)	25.2(11)	-0.4(11)	-2.1(10)	-16.3(13)
O3	31.5(11)	34.6(12)	25.6(10)	4.3(9)	-4.9(9)	-9.6(9)
C4	20.0(13)	25.5(14)	26.2(14)	-3.4(10)	-2.1(10)	0.6(11)
C1	22.4(14)	31.7(16)	40.1(17)	-1.5(13)	-11.9(13)	1.8(13)
C10	22.5(13)	32.7(15)	24.4(13)	0.7(11)	-0.1(11)	-0.5(13)
C3	25.2(13)	32.8(16)	27.5(14)	-2.1(14)	2.0(12)	-2.2(11)
C15	22.0(13)	34.0(15)	25.3(14)	1.1(12)	0.8(11)	0.2(11)
C11	27.3(14)	33.6(16)	35.4(16)	-0.8(15)	-0.4(14)	-5.4(13)
C5	22.6(13)	31.9(16)	22.7(13)	2.0(11)	-0.6(11)	-1.2(12)
C2	20.1(15)	39.0(19)	41.5(19)	-4.3(15)	2.0(13)	-0.4(14)
C9	32.7(17)	39.8(18)	23.9(15)	8.5(13)	-2.1(12)	-4.4(14)
C16	29.5(16)	36.2(17)	24.4(15)	3.3(13)	-3.9(12)	-0.4(14)
C8	36.7(19)	48(2)	39.1(19)	-0.1(17)	-3.8(15)	-8.6(18)
C7	29.8(15)	24.3(15)	34.0(15)	6.1(12)	4.1(13)	1.8(13)
C6	22.4(14)	33.4(17)	34.3(16)	6.4(13)	-2.7(11)	1.3(12)
C12	63(3)	55(3)	41(2)	10(2)	3(2)	-23(2)
C13	54(3)	39(2)	68(3)	-14(2)	9(2)	-12(2)
C14	22.9(16)	65(3)	71(3)	16(3)	-7.7(16)	-4(2)

Table 4. Bond Lengths for product **1.53**

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
Br1	C1	1.898(3)	C1	C16	1.392(5)
F1	C6	1.373(4)	C10	C5	1.520(5)
O1	C8	1.454(5)	C3	C2	1.396(5)
O1	C7	1.329(4)	C15	C16	1.390(5)
O2	C7	1.203(4)	C11	C12	1.520(6)
O4	C10	1.195(4)	C11	C13	1.506(6)
O3	C10	1.327(4)	C11	C14	1.511(5)
O3	C11	1.481(4)	C5	C9	1.511(4)
C4	C3	1.388(4)	C5	C6	1.523(5)
C4	C15	1.393(4)	C9	C6	1.488(5)
C4	C5	1.508(4)	C7	C6	1.494(5)
C1	C2	1.368(5)			

Table 5. Bond Angles for product **1.53**

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
C7	O1	C8	116.6(3)	C4	C5	C10	117.5(3)
C10	O3	C11	122.0(2)	C4	C5	C9	121.4(3)
C3	C4	C15	119.5(3)	C4	C5	C6	119.0(3)
C3	C4	C5	120.3(3)	C10	C5	C6	112.2(3)
C15	C4	C5	120.2(3)	C9	C5	C10	114.5(3)
C2	C1	Br1	120.0(3)	C9	C5	C6	58.7(2)
C2	C1	C16	121.5(3)	C1	C2	C3	119.5(3)
C16	C1	Br1	118.5(3)	C6	C9	C5	61.1(2)
O4	C10	O3	126.0(3)	C15	C16	C1	118.7(3)
O4	C10	C5	124.1(3)	O1	C7	C6	110.6(3)
O3	C10	C5	109.9(2)	O2	C7	O1	125.7(3)
C4	C3	C2	120.1(3)	O2	C7	C6	123.6(3)
C16	C15	C4	120.7(3)	F1	C6	C5	115.7(3)
O3	C11	C12	101.7(3)	F1	C6	C9	117.9(3)
O3	C11	C13	110.5(3)	F1	C6	C7	111.4(3)
O3	C11	C14	109.0(3)	C9	C6	C5	60.2(2)
C13	C11	C12	111.7(4)	C9	C6	C7	123.8(3)
C13	C11	C14	113.1(4)	C7	C6	C5	118.7(3)
C14	C11	C12	110.3(4)				

Table 6. Torsion Angles for product **1.53**

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Br1	C1	C2	C3	-179.4(3)	C10	C5	C6	F1	-2.8(4)
Br1	C1	C16	C15	179.1(2)	C10	C5	C6	C9	106.1(3)
O1	C7	C6	F1	156.6(3)	C10	C5	C6	C7	-139.2(3)
O1	C7	C6	C5	-65.2(4)	C3	C4	C15	C16	0.7(5)
O1	C7	C6	C9	6.4(4)	C3	C4	C5	C10	-113.5(3)
O2	C7	C6	F1	-25.5(5)	C3	C4	C5	C9	36.6(4)
O2	C7	C6	C5	112.6(4)	C3	C4	C5	C6	105.7(3)
O2	C7	C6	C9	-175.7(3)	C15	C4	C3	C2	-1.1(5)
O4	C10	C5	C4	129.4(4)	C15	C4	C5	C10	67.5(4)
O4	C10	C5	C9	-22.7(5)	C15	C4	C5	C9	-142.4(3)
O4	C10	C5	C6	-87.2(4)	C15	C4	C5	C6	-73.4(4)
O3	C10	C5	C4	-51.7(4)	C11	O3	C10	O4	4.3(5)
O3	C10	C5	C9	156.2(3)	C11	O3	C10	C5	-174.6(3)
O3	C10	C5	C6	91.7(3)	C5	C4	C3	C2	179.9(3)
C4	C3	C2	C1	0.5(5)	C5	C4	C15	C16	179.8(3)
C4	C15	C16	C1	0.2(5)	C5	C9	C6	F1	105.1(3)
C4	C5	C9	C6	107.1(3)	C5	C9	C6	C7	-106.4(3)
C4	C5	C6	F1	140.0(3)	C2	C1	C16	C15	-0.8(5)
C4	C5	C6	C9	-111.1(3)	C9	C5	C6	F1	-108.9(3)
C4	C5	C6	C7	3.6(4)	C9	C5	C6	C7	114.7(3)
C10	O3	C11	C12	176.9(3)	C16	C1	C2	C3	0.5(5)
C10	O3	C11	C13	-64.4(4)	C8	O1	C7	O2	-8.2(5)
C10	O3	C11	C14	60.4(4)	C8	O1	C7	C6	169.6(3)
C10	C5	C9	C6	-102.0(3)					

Table 7. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for product **1.53**

Atom	***x***	***y***	***z***	**U(eq)**
H3	2350(30)	3422(14)	10110(60)	19(8)
H16	3310(40)	3997(19)	3330(70)	43(12)
H2	870(40)	3695(16)	7860(60)	31(10)
H9A	3820(40)	2664(15)	11100(60)	26(9)
H9B	4950(40)	2839(18)	12170(70)	36(11)
H15	4860(40)	3686(15)	5550(60)	24(9)
H8A	2840(50)	2362(19)	4830(70)	42(11)
H8B	3800(60)	1820(30)	4690(90)	83(19)
H8C	2570(60)	1830(20)	6120(90)	75(17)
H13A	6520(40)	4846(19)	11440(70)	44(12)
H13B	7460(60)	5200(20)	10150(90)	74(18)
H13C	6050(70)	5100(30)	9280(100)	90(20)
H12A	8030(40)	4909(19)	6320(70)	47(11)
H12B	7540(50)	4250(20)	5540(80)	63(15)
H12C	6710(70)	4780(30)	6040(120)	100(30)
H14A	8170(50)	4110(20)	10940(100)	72(18)
H14B	8540(60)	3790(30)	8830(100)	83(19)
H14C	8970(60)	4400(20)	9420(80)	62(15)

Crystal Data for $C_{16}HBrFO_4$ (*M* =355.06): orthorhombic, space group $P2_12_12$ (no. 18), *a* = 10.996(3) Å, *b* = 23.742(5) Å, *c* = 6.3573(15) Å, *V* = 1659.7(7) Å^3, *Z* = 4, *T* = 173 K, μ(MoKα) = 2.498 mm^{-1}, *Dcalc* = 1.421 g/mm^3, 12942 reflections measured ($3.43 \leq 2\Theta \leq 59.11$), 4650 unique ($R_{int}$ = 0.0313) which were used in all calculations. The final R_1 was 0.0387 ($I > 2\sigma(I)$) and wR_2 was 0.0928 (all data).

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3. X-ray crystallographic structure of 1.62

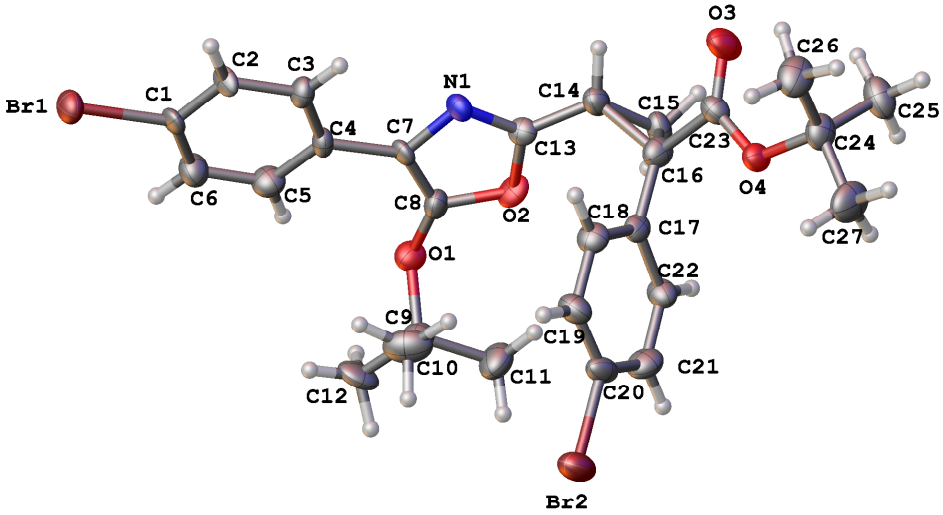

Table 1. Crystal data and structure refinement for product **1.62**

Identification code	hwxviii026	
Empirical formula	C27 H29 Br2 N O4	
Formula weight	591.33	
Temperature	173.2 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.4731(3) Å	α= 90º.
	b = 9.8670(4) Å	β= 90º.
	c = 41.1040(18) Å	γ= 90º.
Volume	2625.3(2) Å ^{3}	
Z	4	
Density (calculated)	1.496 Mg/m^3	
Absorption coefficient	3.120 mm^{-1}	
F(000)	1200	
Crystal size	0.366 x 0.335 x 0.098 mm^3	
Theta range for data collection	1.98 to 27.54º.	
Index ranges	-6<=h<=8, -12<=k<=12, -53<=l<=53	
Reflections collected	22383	
Independent reflections	6020 [R(int) = 0.0625]	
Completeness to theta = 27.54º	99.4 %	
Absorption correction	Numerical	
Max. and min. transmission	0.8326 and 0.4559	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6020 / 0 / 313	
Goodness-of-fit on F^2	1.140	
Final R indices [I>2sigma(I)]	R_1 = 0.0687, wR_2 = 0.1594	
R indices (all data)	R_1 = 0.0782, wR_2 = 0.1629	
Absolute structure parameter	0.102(19)	
Largest diff. peak and hole	1.210 and -1.426 e.Å^{-3}	

Table 2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$) for product **1.62**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Br(1)	-1110(1)	5372(1)	7783(1)	37(1)
Br(2)	5422(2)	6904(1)	5278(1)	50(1)
C(1)	1333(10)	5373(8)	7522(2)	28(1)
C(2)	2082(10)	4156(7)	7412(2)	26(2)
C(3)	3865(11)	4150(7)	7214(2)	29(1)
C(4)	4826(9)	5348(7)	7141(1)	24(1)
C(5)	4070(13)	6572(7)	7265(2)	36(2)
C(6)	2329(13)	6570(8)	7458(2)	38(2)
C(7)	6733(9)	5332(7)	6941(2)	23(1)
C(8)	7801(12)	6389(8)	6813(2)	30(2)
C(9)	6894(13)	8525(8)	6555(2)	36(2)
C(10)	5237(16)	7756(10)	6377(2)	55(3)
C(11)	8771(16)	8802(9)	6338(2)	51(2)
C(12)	6110(16)	9840(7)	6704(2)	47(2)
C(13)	9345(10)	4496(7)	6681(2)	25(1)
C(14)	10887(12)	3612(7)	6541(2)	31(2)
C(15)	11247(13)	3632(7)	6168(2)	32(2)
C(16)	12771(11)	4242(8)	6400(2)	33(2)
C(17)	9858(11)	4449(6)	5960(2)	28(1)
C(18)	7821(12)	4050(7)	5913(2)	32(2)
C(19)	6520(12)	4789(8)	5714(2)	36(2)
C(20)	7237(14)	5903(8)	5554(2)	35(2)
C(21)	9228(14)	6347(8)	5595(2)	40(2)
C(22)	10522(12)	5627(7)	5799(2)	31(2)
C(23)	11998(11)	2288(7)	6033(2)	29(2)
C(24)	12648(14)	1144(8)	5514(2)	37(2)
C(25)	14979(13)	1012(9)	5563(2)	45(2)
C(26)	11565(16)	-150(9)	5604(2)	51(2)
C(27)	12194(18)	1565(10)	5175(2)	56(3)

N(1)	7718(9)	4128(6)	6850(1)	26(1)
O(1)	7649(8)	7723(5)	6840(1)	32(1)
O(2)	9503(8)	5873(5)	6646(1)	30(1)
O(3)	12720(11)	1406(6)	6198(1)	48(2)
O(4)	11879(8)	2296(5)	5712(1)	31(1)

Table 3. Bond lengths [Å] and angles [º] for product **1.62**

Br(1)-C(1)	1.911(7)
Br(2)-C(20)	1.909(8)
O(1)-C(8)	1.325(9)
O(1)-C(9)	1.495(9)
O(2)-C(8)	1.394(9)
O(2)-C(13)	1.370(8)
O(3)-C(23)	1.199(9)
O(4)-C(23)	1.320(9)
O(4)-C(24)	1.486(9)
N(1)-C(7)	1.399(9)
N(1)-C(13)	1.312(9)
C(1)-C(2)	1.372(10)
C(1)-C(6)	1.371(11)
C(2)-C(3)	1.412(10)
C(3)-C(4)	1.369(10)
C(4)-C(5)	1.399(10)
C(4)-C(7)	1.484(8)
C(5)-C(6)	1.379(12)
C(7)-C(8)	1.357(10)
C(9)-C(10)	1.504(13)
C(9)-C(11)	1.533(13)
C(9)-C(12)	1.521(11)
C(13)-C(14)	1.446(10)
C(14)-C(15)	1.551(10)
C(14)-C(16)	1.486(10)
C(15)-C(16)	1.499(10)
C(15)-C(17)	1.478(10)
C(15)-C(23)	1.517(10)
C(17)-C(18)	1.390(10)
C(17)-C(22)	1.406(9)
C(18)-C(19)	1.382(11)
C(19)-C(20)	1.362(11)
C(20)-C(21)	1.371(13)
C(21)-C(22)	1.381(11)

C(24)-C(25)	1.528(12)
C(24)-C(26)	1.503(12)
C(24)-C(27)	1.482(12)
C(2)-H(2)	0.9500
C(3)-H(3)	0.9500
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(14)-H(14)	1.0000
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(18)-H(18)	0.9500
C(19)-H(19)	0.9500
C(21)-H(21)	0.9500
C(22)-H(22)	0.9500
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(8)-O(1)-C(9)	119.0(6)
C(8)-O(2)-C(13)	104.6(5)
C(23)-O(4)-C(24)	121.7(6)
C(7)-N(1)-C(13)	105.8(6)

Br(1)-C(1)-C(2)	118.5(5)
Br(1)-C(1)-C(6)	119.8(6)
C(2)-C(1)-C(6)	121.6(7)
C(1)-C(2)-C(3)	118.9(6)
C(2)-C(3)-C(4)	119.6(6)
C(3)-C(4)-C(5)	120.5(6)
C(3)-C(4)-C(7)	119.4(6)
C(5)-C(4)-C(7)	120.1(6)
C(4)-C(5)-C(6)	119.6(7)
C(1)-C(6)-C(5)	119.8(7)
N(1)-C(7)-C(4)	122.4(6)
N(1)-C(7)-C(8)	108.5(6)
C(4)-C(7)-C(8)	129.1(6)
O(1)-C(8)-O(2)	117.6(6)
O(1)-C(8)-C(7)	133.9(7)
O(2)-C(8)-C(7)	108.2(6)
O(1)-C(9)-C(10)	110.3(6)
O(1)-C(9)-C(11)	107.0(6)
O(1)-C(9)-C(12)	104.2(6)
C(10)-C(9)-C(11)	111.8(7)
C(10)-C(9)-C(12)	112.8(8)
C(11)-C(9)-C(12)	110.3(7)
O(2)-C(13)-N(1)	112.9(6)
O(2)-C(13)-C(14)	120.3(6)
N(1)-C(13)-C(14)	126.8(6)
C(13)-C(14)-C(15)	119.4(6)
C(13)-C(14)-C(16)	118.0(6)
C(15)-C(14)-C(16)	59.1(5)
C(14)-C(15)-C(16)	58.3(5)
C(14)-C(15)-C(17)	119.1(6)
C(14)-C(15)-C(23)	113.4(6)
C(16)-C(15)-C(17)	123.3(6)
C(16)-C(15)-C(23)	111.9(6)
C(17)-C(15)-C(23)	117.5(6)
C(14)-C(16)-C(15)	62.6(5)
C(15)-C(17)-C(18)	120.2(6)

C(15)-C(17)-C(22)	122.5(7)
C(18)-C(17)-C(22)	117.3(6)
C(17)-C(18)-C(19)	120.8(7)
C(18)-C(19)-C(20)	120.2(7)
Br(2)-C(20)-C(19)	119.6(6)
Br(2)-C(20)-C(21)	119.0(6)
C(19)-C(20)-C(21)	121.3(7)
C(20)-C(21)-C(22)	118.6(7)
C(17)-C(22)-C(21)	121.8(7)
O(3)-C(23)-O(4)	126.4(7)
O(3)-C(23)-C(15)	123.5(7)
O(4)-C(23)-C(15)	109.9(6)
O(4)-C(24)-C(25)	108.8(6)
O(4)-C(24)-C(26)	110.9(7)
O(4)-C(24)-C(27)	103.7(7)
C(25)-C(24)-C(26)	110.8(7)
C(25)-C(24)-C(27)	110.2(8)
C(26)-C(24)-C(27)	112.2(7)
C(1)-C(2)-H(2)	121.00
C(3)-C(2)-H(2)	121.00
C(2)-C(3)-H(3)	120.00
C(4)-C(3)-H(3)	120.00
C(4)-C(5)-H(5)	120.00
C(6)-C(5)-H(5)	120.00
C(1)-C(6)-H(6)	120.00
C(5)-C(6)-H(6)	120.00
C(9)-C(10)-H(10A)	109.00
C(9)-C(10)-H(10B)	109.00
C(9)-C(10)-H(10C)	110.00
H(10A)-C(10)-H(10B)	109.00
H(10A)-C(10)-H(10C)	109.00
H(10B)-C(10)-H(10C)	109.00
C(9)-C(11)-H(11A)	110.00
C(9)-C(11)-H(11B)	109.00
C(9)-C(11)-H(11C)	110.00
H(11A)-C(11)-H(11B)	109.00

H(11A)-C(11)-H(11C)	110.00
H(11B)-C(11)-H(11C)	109.00
C(9)-C(12)-H(12A)	109.00
C(9)-C(12)-H(12B)	109.00
C(9)-C(12)-H(12C)	110.00
H(12A)-C(12)-H(12B)	109.00
H(12A)-C(12)-H(12C)	109.00
H(12B)-C(12)-H(12C)	109.00
C(13)-C(14)-H(14)	116.00
C(15)-C(14)-H(14)	116.00
C(16)-C(14)-H(14)	116.00
C(14)-C(16)-H(16A)	118.00
C(14)-C(16)-H(16B)	118.00
C(15)-C(16)-H(16A)	117.00
C(15)-C(16)-H(16B)	117.00
H(16A)-C(16)-H(16B)	115.00
C(17)-C(18)-H(18)	120.00
C(19)-C(18)-H(18)	120.00
C(18)-C(19)-H(19)	120.00
C(20)-C(19)-H(19)	120.00
C(20)-C(21)-H(21)	121.00
C(22)-C(21)-H(21)	121.00
C(17)-C(22)-H(22)	119.00
C(21)-C(22)-H(22)	119.00
C(24)-C(25)-H(25A)	110.00
C(24)-C(25)-H(25B)	110.00
C(24)-C(25)-H(25C)	109.00
H(25A)-C(25)-H(25B)	110.00
H(25A)-C(25)-H(25C)	109.00
H(25B)-C(25)-H(25C)	109.00
C(24)-C(26)-H(26A)	109.00
C(24)-C(26)-H(26B)	109.00
C(24)-C(26)-H(26C)	110.00
H(26A)-C(26)-H(26B)	109.00
H(26A)-C(26)-H(26C)	109.00
H(26B)-C(26)-H(26C)	110.00

C(24)-C(27)-H(27A)	110.00
C(24)-C(27)-H(27B)	109.00
C(24)-C(27)-H(27C)	110.00
H(27A)-C(27)-H(27B)	109.00
H(27A)-C(27)-H(27C)	109.00
H(27B)-C(27)-H(27C)	109.00

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2x10^3$) for product **1.62**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	26(1)	39(1)	47(1)	2(1)	10(1)	0(1)
Br(2)	63(1)	46(1)	42(1)	7(1)	-2(1)	21(1)
C(1)	16(3)	35(4)	35(3)	5(3)	2(3)	12(3)
C(2)	11(3)	22(3)	46(4)	-1(3)	3(3)	-5(2)
C(3)	22(3)	37(4)	30(3)	-2(3)	4(3)	-2(3)
C(4)	18(3)	32(3)	23(3)	-4(3)	3(2)	2(3)
C(5)	38(4)	29(4)	42(4)	3(3)	1(4)	-5(3)
C(6)	37(4)	31(4)	44(4)	-3(3)	7(4)	2(3)
C(7)	13(3)	26(3)	31(3)	0(3)	-1(2)	6(3)
C(8)	29(4)	36(4)	24(3)	0(3)	6(3)	3(3)
C(9)	43(4)	26(4)	38(4)	4(3)	5(3)	0(3)
C(10)	57(6)	50(6)	58(5)	12(4)	-24(5)	-12(5)
C(11)	59(6)	42(5)	51(5)	7(4)	20(5)	-5(5)
C(12)	58(5)	24(4)	59(5)	0(3)	-8(5)	16(4)
C(13)	20(3)	23(3)	31(3)	0(3)	-3(2)	-6(3)
C(14)	33(4)	32(4)	28(3)	-3(3)	1(3)	7(3)
C(15)	41(4)	28(4)	29(3)	-5(3)	2(3)	-1(3)
C(16)	24(4)	41(4)	35(4)	-9(3)	1(3)	6(3)
C(17)	38(4)	18(3)	27(3)	-5(3)	7(3)	1(3)
C(18)	33(4)	25(4)	37(4)	1(3)	1(3)	-8(3)
C(19)	31(4)	30(4)	46(4)	2(3)	-4(3)	3(3)
C(20)	49(5)	31(4)	24(3)	-1(3)	-4(3)	14(4)
C(21)	52(6)	29(4)	40(4)	5(3)	4(4)	-7(4)
C(22)	29(3)	22(3)	42(4)	3(3)	4(3)	-2(3)
C(23)	26(3)	24(4)	37(4)	-2(3)	-1(3)	2(3)
C(24)	42(5)	34(4)	36(4)	-10(3)	5(4)	-1(4)
C(25)	33(5)	39(4)	64(6)	-16(4)	4(4)	-1(4)
C(26)	63(6)	34(5)	55(5)	-11(4)	12(4)	-7(4)

C(27)	85(7)	45(5)	37(5)	-14(4)	11(5)	1(5)
N(1)	17(3)	26(3)	35(3)	0(2)	-1(2)	2(2)
O(1)	38(3)	25(3)	33(3)	-2(2)	1(2)	-2(2)
O(2)	26(2)	32(3)	31(2)	1(2)	1(2)	-16(2)
O(3)	64(4)	43(3)	39(3)	-4(3)	1(3)	24(3)
O(4)	36(3)	27(3)	29(3)	-3(2)	2(2)	5(2)

Table 5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2x10^3$) for product **1.62**

	x	y	z	U(eq)
H(2)	1413	3331	7468	31
H(3)	4395	3320	7132	35
H(5)	4751	7399	7216	44
H(6)	1822	7395	7546	45
H(10A)	5831	6935	6281	83
H(10B)	4663	8329	6204	83
H(10C)	4137	7505	6529	83
H(11A)	9828	9285	6463	76
H(11B)	8347	9357	6152	76
H(11C)	9337	7941	6259	76
H(12A)	4723	9698	6793	71
H(12B)	6058	10544	6536	71
H(12C)	7045	10126	6879	71
H(14)	11086	2718	6651	37
H(16A)	14099	3762	6431	40
H(16B)	12873	5243	6406	40
H(18)	7318	3260	6018	38
H(19)	5120	4520	5689	43
H(21)	9707	7134	5485	49
H(22)	11897	5937	5831	37
H(25A)	15663	1845	5491	68
H(25B)	15498	242	5437	68
H(25C)	15272	864	5795	68
H(26A)	12023	-442	5820	76
H(26B)	11898	-854	5444	76
H(26C)	10069	2	5607	76
H(27A)	10728	1800	5155	83
H(27B)	12514	817	5026	83
H(27C)	13039	2355	5118	83

Table 6. Torsion angles [°] for product **1.62**

C(8)-O(1)-C(9)-C(11)	-85.1(8)
C(8)-O(1)-C(9)-C(12)	158.1(7)
C(8)-O(1)-C(9)-C(10)	36.7(9)
C(9)-O(1)-C(8)-C(7)	-109.2(9)
C(9)-O(1)-C(8)-O(2)	78.3(8)
C(13)-O(2)-C(8)-C(7)	0.6(7)
C(13)-O(2)-C(8)-O(1)	175.0(6)
C(8)-O(2)-C(13)-C(14)	-179.2(6)
C(8)-O(2)-C(13)-N(1)	0.4(7)
C(23)-O(4)-C(24)-C(25)	-63.4(8)
C(23)-O(4)-C(24)-C(27)	179.4(7)
C(23)-O(4)-C(24)-C(26)	58.7(9)
C(24)-O(4)-C(23)-O(3)	0.7(12)
C(24)-O(4)-C(23)-C(15)	175.8(6)
C(7)-N(1)-C(13)-C(14)	178.4(6)
C(7)-N(1)-C(13)-O(2)	-1.2(7)
C(13)-N(1)-C(7)-C(8)	1.6(7)
C(13)-N(1)-C(7)-C(4)	-179.0(6)
Br(1)-C(1)-C(2)-C(3)	178.9(5)
Br(1)-C(1)-C(6)-C(5)	-178.8(6)
C(6)-C(1)-C(2)-C(3)	-3.2(11)
C(2)-C(1)-C(6)-C(5)	3.3(12)
C(1)-C(2)-C(3)-C(4)	1.1(10)
C(2)-C(3)-C(4)-C(7)	178.3(6)
C(2)-C(3)-C(4)-C(5)	0.9(10)
C(3)-C(4)-C(7)-C(8)	172.6(7)
C(3)-C(4)-C(7)-N(1)	-6.7(9)
C(3)-C(4)-C(5)-C(6)	-0.8(11)
C(5)-C(4)-C(7)-N(1)	170.7(6)
C(5)-C(4)-C(7)-C(8)	-10.1(10)
C(7)-C(4)-C(5)-C(6)	-178.2(7)
C(4)-C(5)-C(6)-C(1)	-1.3(12)
C(4)-C(7)-C(8)-O(1)	6.2(13)
N(1)-C(7)-C(8)-O(2)	-1.4(8)

C(4)-C(7)-C(8)-O(2)	179.3(6)
N(1)-C(7)-C(8)-O(1)	-174.5(8)
O(2)-C(13)-C(14)-C(16)	8.4(9)
N(1)-C(13)-C(14)-C(15)	120.4(8)
O(2)-C(13)-C(14)-C(15)	-60.1(9)
N(1)-C(13)-C(14)-C(16)	-171.2(7)
C(16)-C(14)-C(15)-C(23)	102.1(7)
C(13)-C(14)-C(15)-C(16)	106.9(7)
C(13)-C(14)-C(15)-C(17)	-6.3(10)
C(13)-C(14)-C(16)-C(15)	-109.3(7)
C(16)-C(14)-C(15)-C(17)	-113.2(7)
C(13)-C(14)-C(15)-C(23)	-151.0(7)
C(23)-C(15)-C(16)-C(14)	-104.8(6)
C(17)-C(15)-C(16)-C(14)	106.1(8)
C(23)-C(15)-C(17)-C(22)	-105.9(8)
C(14)-C(15)-C(23)-O(3)	-17.1(11)
C(14)-C(15)-C(17)-C(18)	-70.5(9)
C(14)-C(15)-C(17)-C(22)	110.9(8)
C(16)-C(15)-C(17)-C(18)	-139.8(7)
C(16)-C(15)-C(17)-C(22)	41.6(10)
C(23)-C(15)-C(17)-C(18)	72.8(9)
C(17)-C(15)-C(23)-O(4)	22.4(9)
C(16)-C(15)-C(23)-O(3)	46.6(10)
C(16)-C(15)-C(23)-O(4)	-128.6(6)
C(14)-C(15)-C(23)-O(4)	167.7(6)
C(17)-C(15)-C(23)-O(3)	-162.4(7)
C(22)-C(17)-C(18)-C(19)	0.1(10)
C(15)-C(17)-C(22)-C(21)	177.2(7)
C(15)-C(17)-C(18)-C(19)	-178.6(7)
C(18)-C(17)-C(22)-C(21)	-1.4(10)
C(17)-C(18)-C(19)-C(20)	1.8(11)
C(18)-C(19)-C(20)-Br(2)	179.6(6)
C(18)-C(19)-C(20)-C(21)	-2.3(12)
C(19)-C(20)-C(21)-C(22)	1.0(12)
Br(2)-C(20)-C(21)-C(22)	179.1(6)
C(20)-C(21)-C(22)-C(17)	0.9(11)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for product **1.62**

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(3)-H(3)...N(1)	0.9500	2.5700	2.909(9)	101.00
C(5)-H(5)...O(1)	0.9500	2.4500	3.115(9)	127.00
C(11)-H(11C)...O(2)	0.9800	2.5900	3.191(10)	120.00
C(14)-H(14)...O(3)	1.0000	2.5000	2.850(9)	100.00
C(16)-H(16B)...O(2)	0.9900	2.4700	2.844(9)	102.00
C(25)-H(25C)...O(3)	0.9800	2.4000	3.018(10)	120.00
C(26)-H(26A)...O(3)	0.9800	2.4400	2.981(10)	114.00

Symmetry transformations used to generate equivalent atoms:

4. X-ray crystallographic structure of 1.72

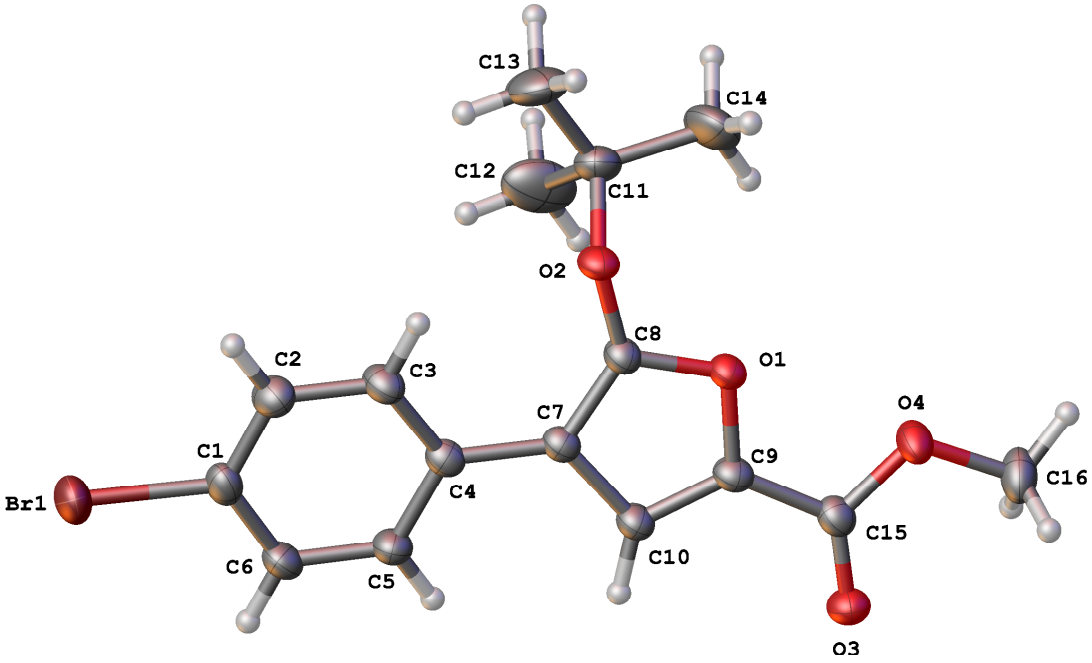

Table 1. Crystal data and structure refinement for product **1.72**

Identification code	hwxviii079	
Empirical formula	C16 H17 Br O4	
Formula weight	353.21	
Temperature	173.2 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 10.972(3) Å	α= 90º.
	b = 22.298(5) Å	β= 93.182(3)º.
	c = 6.4777(14) Å	γ = 90º.
Volume	1582.3(6) Å^3	
Z	4	
Density (calculated)	1.483 Mg/m^3	
Absorption coefficient	2.610 mm^{-1}	
F(000)	720	
Crystal size	0.689 x 0.514 x 0.104 mm^3	
Theta range for data collection	1.83 to 30.02º.	
Index ranges	-15<=h<=15, -31<=k<=31, -9<=l<=9	
Reflections collected	15749	
Independent reflections	4600 [R(int) = 0.0500]	
Completeness to theta = 30.02º	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7460 and 0.4420	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4600 / 0 / 194	
Goodness-of-fit on F^2	1.014	
Final R indices [I>2sigma(I)]	R_1 = 0.0481, wR_2 = 0.1099	
R indices (all data)	R_1 = 0.0814, wR_2 = 0.1247	
Largest diff. peak and hole	0.708 and -0.559 e.Å^{-3}	

Table 2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$) for product **1.72**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Br(1)	2711(1)	2982(1)	717(1)	46(1)
C(1)	2378(2)	3696(1)	2177(4)	31(1)
C(2)	2598(2)	4244(1)	1271(4)	33(1)
C(3)	2378(3)	4765(1)	2351(4)	31(1)
C(4)	1939(2)	4748(1)	4336(4)	25(1)
C(5)	1713(2)	4185(1)	5187(4)	30(1)
C(6)	1924(2)	3662(1)	4117(4)	32(1)
C(7)	1734(2)	5295(1)	5527(4)	24(1)
C(8)	2097(2)	5868(1)	5109(4)	25(1)
C(9)	1174(2)	5925(1)	8009(4)	26(1)
C(10)	1126(2)	5342(1)	7425(4)	25(1)
C(11)	3918(3)	6317(1)	3778(5)	38(1)
C(12)	4665(3)	5857(2)	4987(7)	68(1)
C(13)	4277(4)	6369(2)	1556(6)	64(1)
C(14)	3927(4)	6922(1)	4834(6)	62(1)
C(15)	712(2)	6218(1)	9819(4)	27(1)
C(16)	604(3)	7124(1)	11684(4)	41(1)
O(1)	1767(2)	6260(1)	6593(2)	27(1)
O(2)	2636(2)	6098(1)	3503(2)	28(1)
O(3)	152(2)	5958(1)	11095(3)	34(1)
O(4)	990(2)	6804(1)	9894(3)	34(1)

Table 3. Bond lengths [Å] and angles [º] for product **1.72**

Br(1)-C(1)	1.897(2)
O(1)-C(8)	1.364(3)
O(1)-C(9)	1.375(3)
O(2)-C(8)	1.328(3)
O(2)-C(11)	1.490(4)
O(3)-C(15)	1.205(3)
O(4)-C(15)	1.344(3)
O(4)-C(16)	1.445(3)
C(1)-C(2)	1.382(3)
C(1)-C(6)	1.379(4)
C(2)-C(3)	1.386(3)
C(3)-C(4)	1.398(4)
C(4)-C(5)	1.399(3)
C(4)-C(7)	1.467(3)
C(5)-C(6)	1.383(3)
C(7)-C(8)	1.370(3)
C(7)-C(10)	1.435(4)
C(9)-C(10)	1.353(3)
C(9)-C(15)	1.457(4)
C(11)-C(12)	1.505(5)
C(11)-C(13)	1.518(5)
C(11)-C(14)	1.513(4)
C(2)-H(2)	0.9500
C(3)-H(3)	0.9500
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(10)-H(10)	0.9500
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800

C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800

C(8)-O(1)-C(9)	105.98(17)
C(8)-O(2)-C(11)	119.41(19)
C(15)-O(4)-C(16)	115.7(2)
Br(1)-C(1)-C(2)	119.10(19)
Br(1)-C(1)-C(6)	119.80(17)
C(2)-C(1)-C(6)	121.1(2)
C(1)-C(2)-C(3)	119.2(2)
C(2)-C(3)-C(4)	121.3(2)
C(3)-C(4)-C(5)	117.7(2)
C(3)-C(4)-C(7)	122.1(2)
C(5)-C(4)-C(7)	120.2(2)
C(4)-C(5)-C(6)	121.4(2)
C(1)-C(6)-C(5)	119.3(2)
C(4)-C(7)-C(8)	128.1(2)
C(4)-C(7)-C(10)	127.16(19)
C(8)-C(7)-C(10)	104.76(19)
O(1)-C(8)-O(2)	116.80(17)
O(1)-C(8)-C(7)	111.6(2)
O(2)-C(8)-C(7)	131.5(2)
O(1)-C(9)-C(10)	110.4(2)
O(1)-C(9)-C(15)	119.44(19)
C(10)-C(9)-C(15)	130.2(2)
C(7)-C(10)-C(9)	107.3(2)
O(2)-C(11)-C(12)	108.8(2)
O(2)-C(11)-C(13)	101.8(3)
O(2)-C(11)-C(14)	109.2(3)
C(12)-C(11)-C(13)	112.5(3)
C(12)-C(11)-C(14)	112.5(3)
C(13)-C(11)-C(14)	111.4(3)
O(3)-C(15)-O(4)	124.5(2)

O(3)-C(15)-C(9)	123.4(2)
O(4)-C(15)-C(9)	112.2(2)
C(1)-C(2)-H(2)	120.00
C(3)-C(2)-H(2)	120.00
C(2)-C(3)-H(3)	119.00
C(4)-C(3)-H(3)	119.00
C(4)-C(5)-H(5)	119.00
C(6)-C(5)-H(5)	119.00
C(1)-C(6)-H(6)	120.00
C(5)-C(6)-H(6)	120.00
C(7)-C(10)-H(10)	126.00
C(9)-C(10)-H(10)	126.00
C(11)-C(12)-H(12A)	109.00
C(11)-C(12)-H(12B)	110.00
C(11)-C(12)-H(12C)	109.00
H(12A)-C(12)-H(12B)	109.00
H(12A)-C(12)-H(12C)	109.00
H(12B)-C(12)-H(12C)	109.00
C(11)-C(13)-H(13A)	109.00
C(11)-C(13)-H(13B)	109.00
C(11)-C(13)-H(13C)	109.00
H(13A)-C(13)-H(13B)	110.00
H(13A)-C(13)-H(13C)	109.00
H(13B)-C(13)-H(13C)	109.00
C(11)-C(14)-H(14A)	110.00
C(11)-C(14)-H(14B)	109.00
C(11)-C(14)-H(14C)	109.00
H(14A)-C(14)-H(14B)	109.00
H(14A)-C(14)-H(14C)	109.00
H(14B)-C(14)-H(14C)	109.00
O(4)-C(16)-H(16A)	109.00
O(4)-C(16)-H(16B)	109.00
O(4)-C(16)-H(16C)	110.00
H(16A)-C(16)-H(16B)	109.00
H(16A)-C(16)-H(16C)	109.00
H(16B)-C(16)-H(16C)	109.00

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2x10^3$) for product **1.72**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ...+ 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	55(1)	28(1)	57(1)	-14(1)	19(1)	-5(1)
C(1)	28(1)	25(1)	38(1)	-8(1)	2(1)	-2(1)
C(2)	39(2)	32(1)	28(1)	0(1)	6(1)	-3(1)
C(3)	40(2)	24(1)	28(1)	2(1)	3(1)	-5(1)
C(4)	26(1)	23(1)	26(1)	3(1)	-1(1)	-1(1)
C(5)	34(1)	24(1)	32(1)	2(1)	9(1)	-3(1)
C(6)	36(1)	21(1)	40(1)	2(1)	8(1)	-3(1)
C(7)	25(1)	21(1)	25(1)	2(1)	0(1)	-1(1)
C(8)	28(1)	21(1)	25(1)	2(1)	2(1)	0(1)
C(9)	29(1)	23(1)	27(1)	5(1)	2(1)	-2(1)
C(10)	29(1)	20(1)	27(1)	2(1)	4(1)	-2(1)
C(11)	33(2)	34(1)	46(2)	1(1)	12(1)	-8(1)
C(12)	34(2)	69(2)	100(3)	22(2)	-8(2)	-3(2)
C(13)	62(2)	69(2)	63(2)	0(2)	35(2)	-22(2)
C(14)	66(2)	46(2)	76(3)	-18(2)	20(2)	-31(2)
C(15)	31(1)	22(1)	29(1)	2(1)	1(1)	0(1)
C(16)	60(2)	30(1)	35(2)	-5(1)	9(1)	10(1)
O(1)	33(1)	20(1)	28(1)	2(1)	7(1)	-2(1)
O(2)	35(1)	24(1)	27(1)	5(1)	7(1)	-4(1)
O(3)	38(1)	30(1)	34(1)	2(1)	12(1)	-5(1)
O(4)	51(1)	21(1)	29(1)	0(1)	11(1)	0(1)

Table 5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for product **1.72**

	x	y	z	U(eq)
H(2)	2898	4262	-76	39
H(3)	2528	5142	1731	37
H(5)	1409	4161	6529	36
H(6)	1758	3283	4711	38
H(10)	758	5024	8138	30
H(12A)	4591	5468	4287	102
H(12B)	4368	5822	6381	102
H(12C)	5523	5981	5080	102
H(13A)	5109	6527	1533	95
H(13B)	3711	6640	795	95
H(13C)	4243	5972	905	95
H(14A)	3691	6874	6262	93
H(14B)	3348	7190	4089	93
H(14C)	4749	7094	4836	93
H(16A)	-289	7155	11613	62
H(16B)	960	7528	11711	62
H(16C)	878	6908	12941	62

Table 6. Torsion angles [°] for product **1.72**

C(8)-O(1)-C(9)-C(15)	179.4(2)
C(8)-O(1)-C(9)-C(10)	-0.4(2)
C(9)-O(1)-C(8)-C(7)	0.1(2)
C(9)-O(1)-C(8)-O(2)	176.64(19)
C(8)-O(2)-C(11)-C(12)	45.6(3)
C(8)-O(2)-C(11)-C(14)	-77.5(3)
C(11)-O(2)-C(8)-O(1)	72.8(3)
C(11)-O(2)-C(8)-C(7)	-111.5(3)
C(8)-O(2)-C(11)-C(13)	164.6(2)
C(16)-O(4)-C(15)-O(3)	1.9(4)
C(16)-O(4)-C(15)-C(9)	-177.8(2)
Br(1)-C(1)-C(6)-C(5)	178.42(17)
C(2)-C(1)-C(6)-C(5)	-1.5(3)
Br(1)-C(1)-C(2)-C(3)	-178.7(2)
C(6)-C(1)-C(2)-C(3)	1.2(4)
C(1)-C(2)-C(3)-C(4)	0.0(4)
C(2)-C(3)-C(4)-C(5)	-0.8(4)
C(2)-C(3)-C(4)-C(7)	178.2(2)
C(7)-C(4)-C(5)-C(6)	-178.6(2)
C(5)-C(4)-C(7)-C(10)	-10.9(4)
C(5)-C(4)-C(7)-C(8)	167.7(2)
C(3)-C(4)-C(5)-C(6)	0.5(4)
C(3)-C(4)-C(7)-C(8)	-11.4(4)
C(3)-C(4)-C(7)-C(10)	170.1(3)
C(4)-C(5)-C(6)-C(1)	0.6(3)
C(10)-C(7)-C(8)-O(1)	0.2(3)
C(4)-C(7)-C(10)-C(9)	178.3(2)
C(8)-C(7)-C(10)-C(9)	-0.5(3)
C(4)-C(7)-C(8)-O(1)	-178.6(2)
C(4)-C(7)-C(8)-O(2)	5.6(4)
C(10)-C(7)-C(8)-O(2)	-175.6(2)
C(10)-C(9)-C(15)-O(3)	-2.4(4)
C(10)-C(9)-C(15)-O(4)	177.2(2)
O(1)-C(9)-C(10)-C(7)	0.6(3)

C(15)-C(9)-C(10)-C(7)	-179.3(2)
O(1)-C(9)-C(15)-O(3)	177.7(2)
O(1)-C(9)-C(15)-O(4)	-2.6(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for product **1.72** [Å and º]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(3)-H(3)...O(2)	0.9500	2.4200	3.073(3)	126.00
C(5)-H(5)...O(3)#1	0.9500	2.3800	3.261(3)	154.00
C(10)-H(10)...O(3)#1	0.9500	2.4700	3.382(3)	162.00
C(14)-H(14A)...O(1)	0.9800	2.5400	3.065(4)	114.00
C(16)-H(16B)...O(4)#2	0.9800	2.5400	3.180(3)	123.00

Symmetry transformations used to generate equivalent atoms:
#1 2 #2 -x,1/2+y+1,1/2-z

5. The X-ray crystallographic structure of compound 2.80

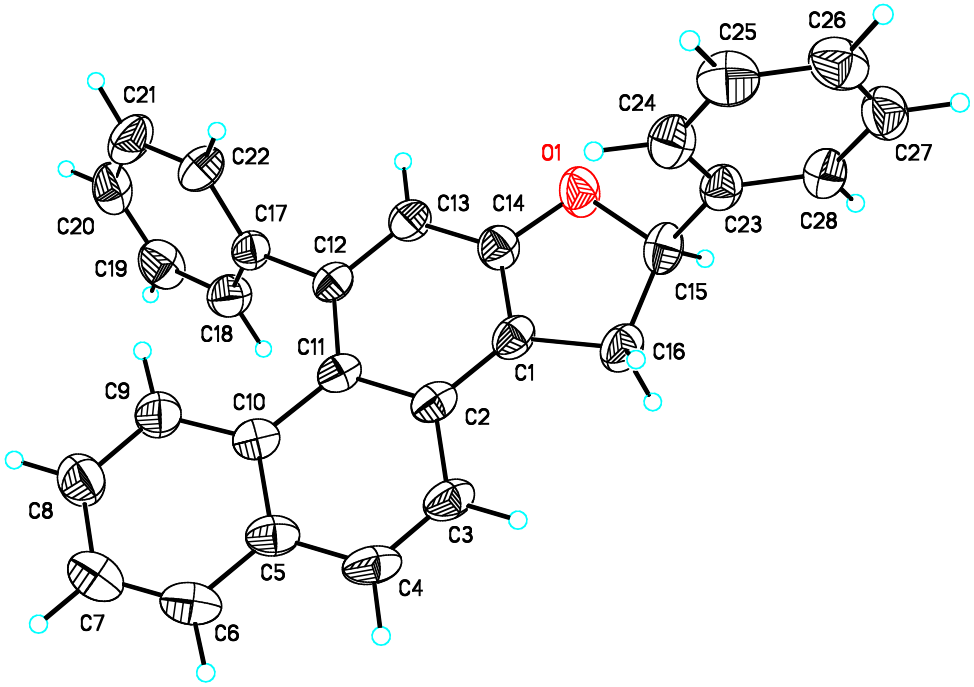

Table 1. Crystal data and structure refinement for product **2.80**

Identification code	hwxviii079	
Empirical formula	C16 H17 Br O4	
Formula weight	353.21	
Temperature	173.2 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 10.972(3) Å	α= 90º.
	b = 22.298(5) Å	β= 93.182(3)º.
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Volume	1582.3(6) Å^3	
Z	4	
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Absorption coefficient	2.610 mm^{-1}	
F(000)	720	
Crystal size	0.689 x 0.514 x 0.104 mm^3	
Theta range for data collection	1.83 to 30.02º.	
Index ranges	-15<=h<=15, -31<=k<=31, -9<=l<=9	
Reflections collected	15749	
Independent reflections	4600 [R(int) = 0.0500]	
Completeness to theta = 30.02º	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7460 and 0.4420	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4600 / 0 / 194	
Goodness-of-fit on F^2	1.014	
Final R indices [I>2sigma(I)]	R_1 = 0.0481, wR_2 = 0.1099	
R indices (all data)	R_1 = 0.0814, wR_2 = 0.1247	
Largest diff. peak and hole	0.708 and -0.559 e.Å^{-3}	

Table 2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$) for product **2.80**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Br(1)	2711(1)	2982(1)	717(1)	46(1)
C(1)	2378(2)	3696(1)	2177(4)	31(1)
C(2)	2598(2)	4244(1)	1271(4)	33(1)
C(3)	2378(3)	4765(1)	2351(4)	31(1)
C(4)	1939(2)	4748(1)	4336(4)	25(1)
C(5)	1713(2)	4185(1)	5187(4)	30(1)
C(6)	1924(2)	3662(1)	4117(4)	32(1)
C(7)	1734(2)	5295(1)	5527(4)	24(1)
C(8)	2097(2)	5868(1)	5109(4)	25(1)
C(9)	1174(2)	5925(1)	8009(4)	26(1)
C(10)	1126(2)	5342(1)	7425(4)	25(1)
C(11)	3918(3)	6317(1)	3778(5)	38(1)
C(12)	4665(3)	5857(2)	4987(7)	68(1)
C(13)	4277(4)	6369(2)	1556(6)	64(1)
C(14)	3927(4)	6922(1)	4834(6)	62(1)
C(15)	712(2)	6218(1)	9819(4)	27(1)
C(16)	604(3)	7124(1)	11684(4)	41(1)
O(1)	1767(2)	6260(1)	6593(2)	27(1)
O(2)	2636(2)	6098(1)	3503(2)	28(1)
O(3)	152(2)	5958(1)	11095(3)	34(1)
O(4)	990(2)	6804(1)	9894(3)	34(1)

Table 3. Bond lengths [Å] and angles [º] for product **2.80**

Br(1)-C(1)	1.897(2)
O(1)-C(8)	1.364(3)
O(1)-C(9)	1.375(3)
O(2)-C(8)	1.328(3)
O(2)-C(11)	1.490(4)
O(3)-C(15)	1.205(3)
O(4)-C(15)	1.344(3)
O(4)-C(16)	1.445(3)
C(1)-C(2)	1.382(3)
C(1)-C(6)	1.379(4)
C(2)-C(3)	1.386(3)
C(3)-C(4)	1.398(4)
C(4)-C(5)	1.399(3)
C(4)-C(7)	1.467(3)
C(5)-C(6)	1.383(3)
C(7)-C(8)	1.370(3)
C(7)-C(10)	1.435(4)
C(9)-C(10)	1.353(3)
C(9)-C(15)	1.457(4)
C(11)-C(12)	1.505(5)
C(11)-C(13)	1.518(5)
C(11)-C(14)	1.513(4)
C(2)-H(2)	0.9500
C(3)-H(3)	0.9500
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(10)-H(10)	0.9500
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800

C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800
C(8)-O(1)-C(9)	105.98(17)
C(8)-O(2)-C(11)	119.41(19)
C(15)-O(4)-C(16)	115.7(2)
Br(1)-C(1)-C(2)	119.10(19)
Br(1)-C(1)-C(6)	119.80(17)
C(2)-C(1)-C(6)	121.1(2)
C(1)-C(2)-C(3)	119.2(2)
C(2)-C(3)-C(4)	121.3(2)
C(3)-C(4)-C(5)	117.7(2)
C(3)-C(4)-C(7)	122.1(2)
C(5)-C(4)-C(7)	120.2(2)
C(4)-C(5)-C(6)	121.4(2)
C(1)-C(6)-C(5)	119.3(2)
C(4)-C(7)-C(8)	128.1(2)
C(4)-C(7)-C(10)	127.16(19)
C(8)-C(7)-C(10)	104.76(19)
O(1)-C(8)-O(2)	116.80(17)
O(1)-C(8)-C(7)	111.6(2)
O(2)-C(8)-C(7)	131.5(2)
O(1)-C(9)-C(10)	110.4(2)
O(1)-C(9)-C(15)	119.44(19)
C(10)-C(9)-C(15)	130.2(2)
C(7)-C(10)-C(9)	107.3(2)
O(2)-C(11)-C(12)	108.8(2)
O(2)-C(11)-C(13)	101.8(3)
O(2)-C(11)-C(14)	109.2(3)
C(12)-C(11)-C(13)	112.5(3)
C(12)-C(11)-C(14)	112.5(3)
C(13)-C(11)-C(14)	111.4(3)
O(3)-C(15)-O(4)	124.5(2)

O(3)-C(15)-C(9)	123.4(2)
O(4)-C(15)-C(9)	112.2(2)
C(1)-C(2)-H(2)	120.00
C(3)-C(2)-H(2)	120.00
C(2)-C(3)-H(3)	119.00
C(4)-C(3)-H(3)	119.00
C(4)-C(5)-H(5)	119.00
C(6)-C(5)-H(5)	119.00
C(1)-C(6)-H(6)	120.00
C(5)-C(6)-H(6)	120.00
C(7)-C(10)-H(10)	126.00
C(9)-C(10)-H(10)	126.00
C(11)-C(12)-H(12A)	109.00
C(11)-C(12)-H(12B)	110.00
C(11)-C(12)-H(12C)	109.00
H(12A)-C(12)-H(12B)	109.00
H(12A)-C(12)-H(12C)	109.00
H(12B)-C(12)-H(12C)	109.00
C(11)-C(13)-H(13A)	109.00
C(11)-C(13)-H(13B)	109.00
C(11)-C(13)-H(13C)	109.00
H(13A)-C(13)-H(13B)	110.00
H(13A)-C(13)-H(13C)	109.00
H(13B)-C(13)-H(13C)	109.00
C(11)-C(14)-H(14A)	110.00
C(11)-C(14)-H(14B)	109.00
C(11)-C(14)-H(14C)	109.00
H(14A)-C(14)-H(14B)	109.00
H(14A)-C(14)-H(14C)	109.00
H(14B)-C(14)-H(14C)	109.00
O(4)-C(16)-H(16A)	109.00
O(4)-C(16)-H(16B)	109.00
O(4)-C(16)-H(16C)	110.00
H(16A)-C(16)-H(16B)	109.00
H(16A)-C(16)-H(16C)	109.00
H(16B)-C(16)-H(16C)	109.00

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2x10^3$) for product **2.80**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	55(1)	28(1)	57(1)	-14(1)	19(1)	-5(1)
C(1)	28(1)	25(1)	38(1)	-8(1)	2(1)	-2(1)
C(2)	39(2)	32(1)	28(1)	0(1)	6(1)	-3(1)
C(3)	40(2)	24(1)	28(1)	2(1)	3(1)	-5(1)
C(4)	26(1)	23(1)	26(1)	3(1)	-1(1)	-1(1)
C(5)	34(1)	24(1)	32(1)	2(1)	9(1)	-3(1)
C(6)	36(1)	21(1)	40(1)	2(1)	8(1)	-3(1)
C(7)	25(1)	21(1)	25(1)	2(1)	0(1)	-1(1)
C(8)	28(1)	21(1)	25(1)	2(1)	2(1)	0(1)
C(9)	29(1)	23(1)	27(1)	5(1)	2(1)	-2(1)
C(10)	29(1)	20(1)	27(1)	2(1)	4(1)	-2(1)
C(11)	33(2)	34(1)	46(2)	1(1)	12(1)	-8(1)
C(12)	34(2)	69(2)	100(3)	22(2)	-8(2)	-3(2)
C(13)	62(2)	69(2)	63(2)	0(2)	35(2)	-22(2)
C(14)	66(2)	46(2)	76(3)	-18(2)	20(2)	-31(2)
C(15)	31(1)	22(1)	29(1)	2(1)	1(1)	0(1)
C(16)	60(2)	30(1)	35(2)	-5(1)	9(1)	10(1)
O(1)	33(1)	20(1)	28(1)	2(1)	7(1)	-2(1)
O(2)	35(1)	24(1)	27(1)	5(1)	7(1)	-4(1)
O(3)	38(1)	30(1)	34(1)	2(1)	12(1)	-5(1)
O(4)	51(1)	21(1)	29(1)	0(1)	11(1)	0(1)

Table 5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters (Å $^2x10^3$) for product **2.80**

	x	y	z	U(eq)
H(2)	2898	4262	-76	39
H(3)	2528	5142	1731	37
H(5)	1409	4161	6529	36
H(6)	1758	3283	4711	38
H(10)	758	5024	8138	30
H(12A)	4591	5468	4287	102
H(12B)	4368	5822	6381	102
H(12C)	5523	5981	5080	102
H(13A)	5109	6527	1533	95
H(13B)	3711	6640	795	95
H(13C)	4243	5972	905	95
H(14A)	3691	6874	6262	93
H(14B)	3348	7190	4089	93
H(14C)	4749	7094	4836	93
H(16A)	-289	7155	11613	62
H(16B)	960	7528	11711	62
H(16C)	878	6908	12941	62

Table 6. Torsion angles [°] for product **2.80**

C(8)-O(1)-C(9)-C(15)	179.4(2)
C(8)-O(1)-C(9)-C(10)	-0.4(2)
C(9)-O(1)-C(8)-C(7)	0.1(2)
C(9)-O(1)-C(8)-O(2)	176.64(19)
C(8)-O(2)-C(11)-C(12)	45.6(3)
C(8)-O(2)-C(11)-C(14)	-77.5(3)
C(11)-O(2)-C(8)-O(1)	72.8(3)
C(11)-O(2)-C(8)-C(7)	-111.5(3)
C(8)-O(2)-C(11)-C(13)	164.6(2)
C(16)-O(4)-C(15)-O(3)	1.9(4)
C(16)-O(4)-C(15)-C(9)	-177.8(2)
Br(1)-C(1)-C(6)-C(5)	178.42(17)
C(2)-C(1)-C(6)-C(5)	-1.5(3)
Br(1)-C(1)-C(2)-C(3)	-178.7(2)
C(6)-C(1)-C(2)-C(3)	1.2(4)
C(1)-C(2)-C(3)-C(4)	0.0(4)
C(2)-C(3)-C(4)-C(5)	-0.8(4)
C(2)-C(3)-C(4)-C(7)	178.2(2)
C(7)-C(4)-C(5)-C(6)	-178.6(2)
C(5)-C(4)-C(7)-C(10)	-10.9(4)
C(5)-C(4)-C(7)-C(8)	167.7(2)
C(3)-C(4)-C(5)-C(6)	0.5(4)
C(3)-C(4)-C(7)-C(8)	-11.4(4)
C(3)-C(4)-C(7)-C(10)	170.1(3)
C(4)-C(5)-C(6)-C(1)	0.6(3)
C(10)-C(7)-C(8)-O(1)	0.2(3)
C(4)-C(7)-C(10)-C(9)	178.3(2)
C(8)-C(7)-C(10)-C(9)	-0.5(3)
C(4)-C(7)-C(8)-O(1)	-178.6(2)
C(4)-C(7)-C(8)-O(2)	5.6(4)
C(10)-C(7)-C(8)-O(2)	-175.6(2)
C(10)-C(9)-C(15)-O(3)	-2.4(4)
C(10)-C(9)-C(15)-O(4)	177.2(2)
O(1)-C(9)-C(10)-C(7)	0.6(3)

C(15)-C(9)-C(10)-C(7)	-179.3(2)
O(1)-C(9)-C(15)-O(3)	177.7(2)
O(1)-C(9)-C(15)-O(4)	-2.6(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for product **2.80** [Å and º]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(3)-H(3)...O(2)	0.9500	2.4200	3.073(3)	126.00
C(5)-H(5)...O(3)#1	0.9500	2.3800	3.261(3)	154.00
C(10)-H(10)...O(3)#1	0.9500	2.4700	3.382(3)	162.00
C(14)-H(14A)...O(1)	0.9800	2.5400	3.065(4)	114.00
C(16)-H(16B)...O(4)#2	0.9800	2.5400	3.180(3)	123.00

Symmetry transformations used to generate equivalent atoms:
#1 2 #2 -x,1/2+y+1,1/2-z

6. The X-ray crystallographic structure of compound 2.97

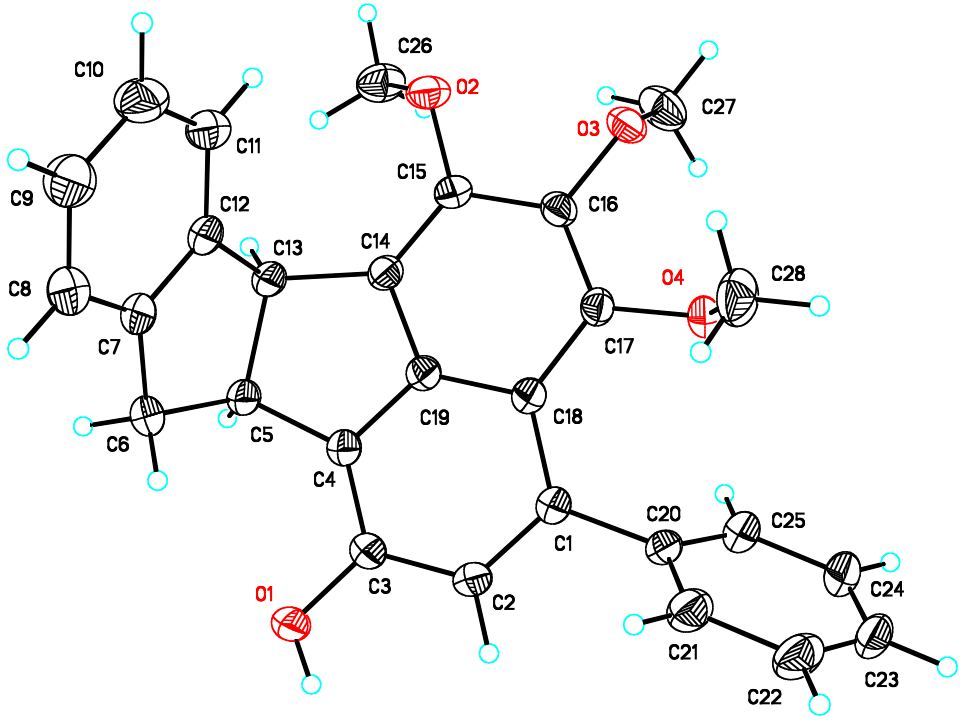

Table 1. Crystal data and structure refinement for product **2.97**

Identification code	hw_v_022b	
Empirical formula	C28 H24 O4	
Formula weight	424.47	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 11.1319(2) Å	α= 90°.
	b = 17.6950(2) Å	β= 113.7040(10)°.
	c = 13.8306(2) Å	γ= 90°.
Volume	2494.50(6) $Å^3$	
Z	4	
Density (calculated)	1.130 Mg/m^3	
Absorption coefficient	0.601 mm^{-1}	
F(000)	896	
Crystal size	0.27 x 0.24 x 0.13 mm^3	
Theta range for data collection	4.29 to 69.42°.	
Index ranges	-12<=h<=13, -21<=k<=18, -16<=l<=14	
Reflections collected	14475	
Independent reflections	4370 [R(int) = 0.0156]	
Completeness to theta = 69.42°	93.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9259 and 0.8545	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4370 / 0 / 289	
Goodness-of-fit on F^2	1.049	
Final R indices [I>2sigma(I)]	R_1 = 0.0412, wR_2 = 0.1280	
R indices (all data)	R_1 = 0.0444, wR_2 = 0.1313	
Largest diff. peak and hole	0.310 and -0.268 $e.Å^{-3}$	

Table 2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$) for product **2.97**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	-1016(1)	8508(1)	7125(1)	30(1)
C(2)	-95(1)	7940(1)	7301(1)	35(1)
C(3)	1249(1)	8033(1)	7954(1)	33(1)
C(4)	1683(1)	8715(1)	8433(1)	30(1
C(5)	3044(1)	8977(1)	9151(1)	31(1)
C(6)	4066(1)	8919(1)	8658(1)	36(1)
C(7)	4141(1)	9706(1)	8274(1)	34(1)
C(8)	4751(2)	9940(1)	7625(1)	43(1)
C(9)	4729(2)	10699(1)	7377(2)	53(1)
C(10)	4112(2)	11218(1)	7775(2)	52(1)
C(11)	3503(2)	10989(1)	8422(1)	40(1)
C(12)	3513(1)	10224(1)	8664(1)	32(1)
C(13)	2852(1)	9842(1)	9303(1)	30(1)
C(14)	1373(1)	9963(1)	8814(1)	28(1)
C(15)	604(1)	10581(1)	8740(1)	28(1)
C(16)	-758(1)	10541(1)	8081(1)	29(1)
C(17)	-1345(1)	9898(1)	7518(1)	29(1)
C(18)	-590(1)	9231(1)	7614(1)	28(1)
C(19)	762(1)	9297(1)	8264(1)	28(1)
C(20)	-2409(1)	8323(1)	6435(1)	32(1)
C(21)	-2732(2)	8090(1)	5401(1)	41(1)
C(22)	-4023(2)	7889(1)	4763(1)	50(1)
C(23)	-4986(2)	7920(1)	5142(1)	50(1)
C(24)	-4672(1)	8148(1)	6171(1)	48(1)
C(25)	-3394(1)	8346(1)	6811(1)	39(1)
C(26)	1772(2)	11257(1)	10322(1)	45(1)
C(27)	-1976(2)	11259(1)	8800(1)	49(1)
C(28)	-2982(2)	10188(1)	5862(1)	51(1)
O(1)	2139(1)	7463(1)	8134(1)	44(1)
O(2)	1047(1)	11269(1)	9214(1)	37(1)

O(3)	-1518(1)	11178(1)	7978(1)	33(1)
O(4)	-2665(1)	9916(1)	6906(1)	35(1)

Table 3. Bond lengths [Å] and angles [°] for product **2.97**

C(1)-C(2)	1.3864(18)
C(1)-C(18)	1.4354(17)
C(1)-C(20)	1.4940(16)
C(2)-C(3)	1.413(18)
C(2)-H(2A)	0.9500
C(3)-O(1)	1.3647(16)
C(3)-C(4)	1.3686(18)
C(4)-C(19)	1.4038(17)
C(4)-C(5)	1.5118(16)
C(5)-C(6)	1.5472(19)
C(5)-C(13)	1.5713(17)
C(5)-H(5A)	1.0000
C(6)-C(7)	1.5044(19)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(12)	1.388(2)
C(7)-C(8)	1.389(2)
C(8)-C(9)	1.384(2)
C(8)-H(8A)	0.9500
C(9)-C(10)	1.386(2)
C(9)-H(9A)	0.9500
C(10)-C(11)	1.384(2)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.3929(19)
C(11)-H(11A)	0.9500
C(12)-C(13)	1.5173(19)
C(13)-C(14)	1.5228(17)
C(13)-H(13A)	1.0000
C(14)-C(15)	1.3667(18)
C(14)-C(19)	1.4195(17)
C(15)-O(2)	1.3760(14)
C(15)-C(16)	1.4227(17)
C(16)-O(3)	1.3831(15)
C(16)-C(17)	1.3845(18)

C(17)-O(4)	1.3698(15)
C(17)-C(18)	1.4246(17)
C(18)-C(19)	1.4135(16)
C(20)-C(21)	1.389(2)
C(20)-C(25)	1.391(2)
C(21)-C(22)	1.396(2)
C(21)-H(21A)	0.9500
C(22)-C(23)	1.371(3)
C(22)-H(22A)	0.9500
C(23)-C(24)	1.382(3)
C(23)-H(23A)	0.9500
C(24)-C(25)	1.3849(19)
C(24)-H(24A)	0.9500
C(25)-H(25A)	0.9500
C(26)-O(2)	1.4161(17)
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(27)-O(3)	1.4282(18)
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-O(4)	1.4260(19)
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
O(1)-H(1A)	0.8400

C(2)-C(1)-C(18)	118.83(11)
C(2)-C(1)-C(20)	117.22(11)
C(18)-C(1)-C(20)	123.94(11)
C(1)-C(2)-C(3)	123.13(12)
C(1)-C(2)-H(2A)	118.4
C(3)-C(2)-H(2A)	118.4
O(1)-C(3)-C(4)	118.38(12)
O(1)-C(3)-C(2)	122.34(11)

C(4)-C(3)-C(2)	119.29(12)
C(3)-C(4)-C(19)	118.31(12)
C(3)-C(4)-C(5)	130.80(12)
C(19)-C(4)-C(5)	110.89(11)
C(4)-C(5)-C(6)	114.24(11)
C(4)-C(5)-C(13)	103.40(9)
C(6)-C(5)-C(13)	106.69(10)
C(4)-C(5)-H(5A)	110.7
C(6)-C(5)-H(5A)	110.7
C(13)-C(5)-H(5A)	110.7
C(7)-C(6)-C(5)	104.43(10)
C(7)-C(6)-H(6A)	110.9
C(5)-C(6)-H(6A)	110.9
C(7)-C(6)-H(6B)	110.9
C(5)-C(6)-H(6B)	110.9
H(6A)-C(6)-H(6B)	108.9
C(12)-C(7)-C(8)	120.48(13)
C(12)-C(7)-C(6)	111.50(12)
C(8)-C(7)-C(6)	128.01(13)
C(9)-C(8)-C(7)	119.07(14)
C(9)-C(8)-H(8A)	120.5
C(7)-C(8)-H(8A)	120.5
C(8)-C(9)-C(10)	120.43(15)
C(8)-C(9)-H(9A)	119.8
C(10)-C(9)-H(9A)	119.8
C(11)-C(10)-C(9)	120.89(15)
C(11)-C(10)-H(10A)	119.6
C(9)-C(10)-H(10A)	119.6
C(10)-C(11)-C(12)	118.74(14)
C(10)-C(11)-H(11A)	120.6
C(12)-C(11)-H(11A)	120.6
C(7)-C(12)-C(11)	120.40(13)
C(7)-C(12)-C(13)	111.70(12)
C(11)-C(12)-C(13)	127.86(12)
C(12)-C(13)-C(14)	111.71(10)
C(12)-C(13)-C(5)	103.45(10)

C(14)-C(13)-C(5)	104.99(9)
C(12)-C(13)-H(13A)	112.1
C(14)-C(13)-H(13A)	112.1
C(5)-C(13)-H(13A)	112.1
C(15)-C(14)-C(19)	118.32(11)
C(15)-C(14)-C(13)	132.71(11)
C(19)-C(14)-C(13)	108.67(10)
C(14)-C(15)-O(2)	125.37(11)
C(14)-C(15)-C(16)	118.76(11)
O(2)-C(15)-C(16)	115.79(11)
O(3)-C(16)-C(17)	118.73(11)
O(3)-C(16)-C(15)	118.37(11)
C(17)-C(16)-C(15)	122.87(11)
O(4)-C(17)-C(16)	118.36(11)
O(4)-C(17)-C(18)	121.59(11)
C(16)-C(17)-C(18)	120.01(12)
C(19)-C(18)-C(17)	115.40(11)
C(19)-C(18)-C(1)	116.04(11)
C(17)-C(18)-C(1)	128.55(11)
C(4)-C(19)-C(18)	124.39(11)
C(4)-C(19)-C(14)	111.06(11)
C(18)-C(19)-C(14)	124.54(11)
C(21)-C(20)-C(25)	118.47(12)
C(21)-C(20)-C(1)	119.75(13)
C(25)-C(20)-C(1)	121.72(12)
C(20)-C(21)-C(22)	120.13(15)
C(20)-C(21)-H(21A)	119.9
C(22)-C(21)-H(21A)	119.9
C(23)-C(22)-C(21)	120.80(15)
C(23)-C(22)-H(22A)	119.6
C(21)-C(22)-H(22A)	119.6
C(22)-C(23)-C(24)	119.45(13)
C(22)-C(23)-H(23A)	120.3
C(24)-C(23)-H(23A)	120.3
C(23)-C(24)-C(25)	120.18(16)
C(23)-C(24)-H(24A)	119.9

C(25)-C(24)-H(24A)	119.9
C(24)-C(25)-C(20)	120.97(14)
C(24)-C(25)-H(25A)	119.5
C(20)-C(25)-H(25A)	119.5
O(2)-C(26)-H(26A)	109.5
O(2)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
O(2)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
O(3)-C(27)-H(27A)	109.5
O(3)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
O(3)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
O(4)-C(28)-H(28A)	109.5
O(4)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
O(4)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
C(3)-O(1)-H(1A)	109.5
C(15)-O(2)-C(26)	116.17(10)
C(16)-O(3)-C(27)	113.51(10)
C(17)-O(4)-C(28)	113.60(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2x10^3$) for product **2.97**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	26(1)	30(1)	32(1)	-2(1)	8(1)	-1(1)
C(2)	32(1)	26(1)	40(1)	-6(1)	8(1)	-2(1)
C(3)	29(1)	28(1)	39(1)	-2(1)	9(1)	3(1)
C(4)	25(1)	28(1)	32(1)	0(1)	8(1)	0(1)
C(5)	24(1)	28(1)	34(1)	0(1)	6(1)	0(1)
C(6)	25(1)	34(1)	48(1)	-1(1)	12(1)	4(1)
C(7)	23(1)	35(1)	38(1)	-4(1)	7(1)	-2(1)
C(8)	37(1)	44(1)	53(1)	-3(1)	23(1)	0(1)
C(9)	57(1)	48(1)	66(1)	4(1)	40(1)	-2(1)
C(10)	61(1)	36(1)	71(1)	4(1)	38(1)	-3(1)
C(11)	42(1)	32(1)	50(1)	-5(1)	21(1)	-3(1)
C(12)	24(1)	33(1)	33(1)	-4(1)	5(1)	-4(1)
C(13)	25(1)	28(1)	30(1)	-3(1)	6(1)	-2(1)
C(14)	27(1)	27(1)	29(1)	0(1)	9(1)	-3(1)
C(15)	31(1)	24(1)	30(1)	0(1)	12(1)	-3(1)
C(16)	29(1)	25(1)	34(1)	4(1)	14(1)	3(1)
C(17)	23(1)	30(1)	32(1)	3(1)	11(1)	-1(1)
C(18)	25(1)	27(1)	31(1)	0(1)	10(1)	-1(1)
C(19)	26(1)	26(1)	29(1)	1(1)	10(1)	-1(1)
C(20)	28(1)	24(1)	37(1)	-1(1)	5(1)	-2(1)
C(21)	40(1)	37(1)	39(1)	-3(1)	7(1)	-4(1)
C(22)	51(1)	41(1)	38(1)	-4(1)	-3(1)	-7(1)
C(23)	31(1)	37(1)	59(1)	0(1)	-7(1)	-6(1)
C(24)	28(1)	42(1)	64(1)	-2(1)	8(1)	-5(1)
C(25)	29(1)	38(1)	43(1)	-4(1)	8(1)	-5(1)
C(26)	55(1)	37(1)	37(1)	-8(1)	13(1)	-5(1)
C(27)	55(1)	44(1)	60(1)	6(1)	36(1)	14(1)
C(28)	35(1)	62(1)	44(1)	11(1)	2(1)	2(1)
O(1)	31(1)	29(1)	58(1)	-10(1)	3(1)	5(1)
O(2)	43(1)	25(1)	37(1)	-3(1)	11(1)	-3(1)

O(3)	35(1)	26(1)	43(1)	4(1)	20(1)	6(1)
O(4)	22(1)	35(1)	44(1)	2(1)	9(1)	2(1)

Table 5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2x10^3$) for product **2.97**

	x	y	z	U(eq)
H(2A)	-381	7465	6967	41
H(5A)	3358	8706	9843	37
H(6A)	4929	8757	9192	44
H(6B)	3777	8554	8065	44
H(8A)	5178	9585	7356	52
H(9A)	5139	10865	6930	63
H(10A)	4107	11737	7600	63
H(11A)	3086	11347	8697	48
H(13A)	3253	9994	10063	35
H(21A)	-2075	8068	5128	50
H(22A)	-4235	7728	4057	60
H(23A)	-5863	7785	4700	60
H(24A)	-5334	8169	6439	57
H(25A)	-3187	8500	7519	47
H(26A)	2039	11772	10577	67
H(26B)	2554	10941	10492	67
H(26C)	1226	11048	10664	67
H(27A)	-2506	11719	8682	73
H(27B)	-1224	11293	9483	73
H(27C)	-2513	10819	8800	73
H(28A)	-3936	10188	5468	77
H(28B)	-2580	9859	5505	77
H(28C)	-2646	10703	5894	77
H(1A)	1789	7103	7720	65

Table 6. Torsion angles [°] for product **2.97**

C(18)-C(1)-C(2)-C(3)	0.9(2)
C(20)-C(1)-C(2)-C(3)	-178.69(13)
C(1)-C(2)-C(3)-O(1)	178.74(13)
C(1)-C(2)-C(3)-C(4)	-0.7(2)
O(1)-C(3)-C(4)-C(19)	-178.72(12)
C(2)-C(3)-C(4)-C(19)	0.8(2)
O(1)-C(3)-C(4)-C(5)	1.3(2)
C(2)-C(3)-C(4)-C(5)	-179.25(13)
C(3)-C(4)-C(5)-C(6)	58.41(19)
C(19)-C(4)-C(5)-C(6)	-121.59(12)
C(3)-C(4)-C(5)-C(13)	173.95(14)
C(19)-C(4)-C(5)-C(13)	-6.05(14)
C(4)-C(5)-C(6)-C(7)	98.60(12)
C(13)-C(5)-C(6)-C(7)	-15.00(13)
C(5)-C(6)-C(7)-C(12)	12.01(14)
C(5)-C(6)-C(7)-C(8)	-168.88(14)
C(12)-C(7)-C(8)-C(9)	0.2(2)
C(6)-C(7)-C(8)-C(9)	-178.80(15)
C(7)-C(8)-C(9)-C(10)	0.4(3)
C(8)-C(9)-C(10)-C(11)	-0.3(3)
C(9)-C(10)-C(11)-C(12)	-0.4(3)
C(8)-C(7)-C(12)-C(11)	-0.9(2)
C(6)-C(7)-C(12)-C(11)	178.26(12)
C(8)-C(7)-C(12)-C(13)	176.86(12)
C(6)-C(7)-C(12)-C(13)	-3.96(15)
C(10)-C(11)-C(12)-C(7)	1.0(2)
C(10)-C(11)-C(12)-C(13)	-176.40(14)
C(7)-C(12)-C(13)-C(14)	-118.17(12)
C(11)-C(12)-C(13)-C(14)	59.41(17)
C(7)-C(12)-C(13)-C(5)	-5.74(13)
C(11)-C(12)-C(13)-C(5)	171.84(13)
C(4)-C(5)-C(13)-C(12)	-108.03(11)
C(6)-C(5)-C(13)-C(12)	12.78(12)
C(4)-C(5)-C(13)-C(14)	9.22(13)

C(6)-C(5)-C(13)-C(14)	130.03(11)
C(12)-C(13)-C(14)-C(15)	-71.58(18)
C(5)-C(13)-C(14)-C(15)	176.96(13)
C(12)-C(13)-C(14)-C(19)	101.79(12)
C(5)-C(13)-C(14)-C(19)	-9.67(13)
C(19)-C(14)-C(15)-O(2)	-179.27(11)
C(13)-C(14)-C(15)-O(2)	-6.4(2)
C(19)-C(14)-C(15)-C(16)	-2.77(18)
C(13)-C(14)-C(15)-C(16)	170.10(13)
C(14)-C(15)-C(16)-O(3)	-177.49(11)
O(2)-C(15)-C(16)-O(3)	-0.66(16)
C(14)-C(15)-C(16)-C(17)	0.78(19)
O(2)-C(15)-C(16)-C(17)	177.61(11)
O(3)-C(16)-C(17)-O(4)	-1.84(18)
C(15)-C(16)-C(17)-O(4)	179.89(11)
O(3)-C(16)-C(17)-C(18)	-179.50(11)
C(15)-C(16)-C(17)-C(18)	2.24(19)
O(4)-C(17)-C(18)-C(19)	179.47(11)
C(16)-C(17)-C(18)-C(19)	-2.95(17)
O(4)-C(17)-C(18)-C(1)	0.6(2)
C(16)-C(17)-C(18)-C(1)	178.22(12)
C(2)-C(1)-C(18)-C(19)	-1.18(18)
C(20)-C(1)-C(18)-C(19)	178.42(12)
C(2)-C(1)-C(18)-C(17)	177.65(13)
C(20)-C(1)-C(18)-C(17)	-2.8(2)
C(3)-C(4)-C(19)-C(18)	-1.1(2)
C(5)-C(4)-C(19)-C(18)	178.86(11)
C(3)-C(4)-C(19)-C(14)	-179.89(12)
C(5)-C(4)-C(19)-C(14)	0.11(15)
C(17)-C(18)-C(19)-C(4)	-177.65(12)
C(1)-C(18)-C(19)-C(4)	1.33(18)
C(17)-C(18)-C(19)-C(14)	0.94(18)
C(1)-C(18)-C(19)-C(14)	179.92(12)
C(15)-C(14)-C(19)-C(4)	-179.29(11)
C(13)-C(14)-C(19)-C(4)	6.24(15)
C(15)-C(14)-C(19)-C(18)	1.96(19)

C(13)-C(14)-C(19)-C(18)	-172.51(11)
C(2)-C(1)-C(20)-C(21)	-59.30(18)
C(18)-C(1)-C(20)-C(21)	121.10(14)
C(2)-C(1)-C(20)-C(25)	117.90(15)
C(18)-C(1)-C(20)-C(25)	-61.71(18)
C(25)-C(20)-C(21)-C(22)	0.3(2)
C(1)-C(20)-C(21)-C(22)	177.58(12)
C(20)-C(21)-C(22)-C(23)	0.2(2)
C(21)-C(22)-C(23)-C(24)	-0.5(2)
C(22)-C(23)-C(24)-C(25)	0.2(2)
C(23)-C(24)-C(25)-C(20)	0.3(2)
C(21)-C(20)-C(25)-C(24)	-0.5(2)
C(1)-C(20)-C(25)-C(24)	-177.77(13)
C(14)-C(15)-O(2)-C(26)	-55.34(18)
C(16)-C(15)-O(2)-C(26)	128.07(13)
C(17)-C(16)-O(3)-C(27)	97.02(15)
C(15)-C(16)-O(3)-C(27)	-84.63(15)
C(16)-C(17)-O(4)-C(28)	87.96(15)
C(18)-C(17)-O(4)-C(28)	-94.43(15)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for product **2.97** [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1A)...O(3)#1	0.84	1.86	2.6745(13)	162.6

Symmetry transformations used to generate equivalent atoms:
#1 -x,y-1/2,-z+3/2

7. The X-ray crystallographic structure of product 3.91

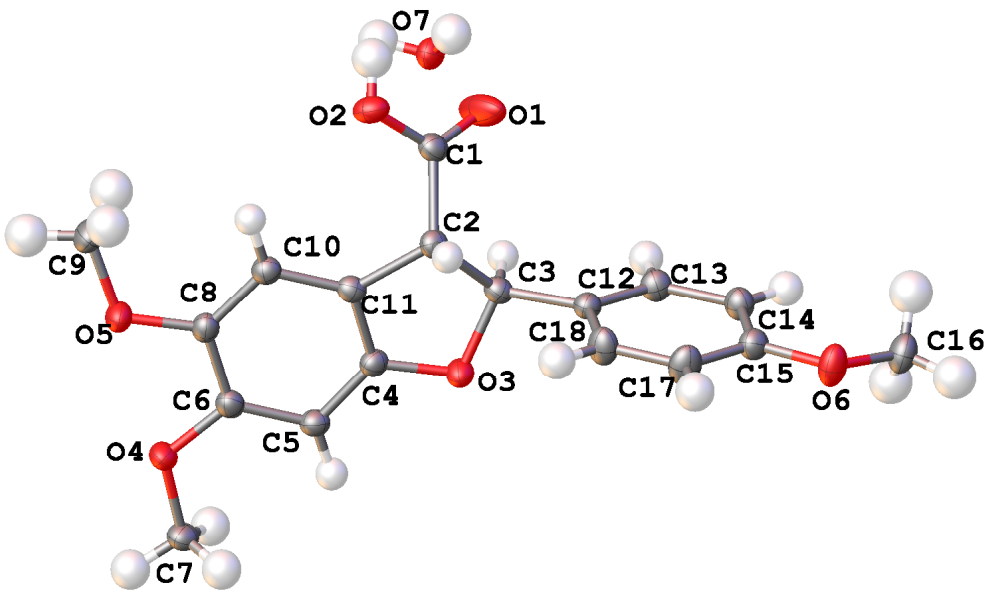

Table 1. Crystal data and structure refinement for product **3.91**

Identification code	hwxii014	
Empirical formula	C18 H20 O7	
Formula weight	348.34	
Temperature	173 K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.2635(3) Å	α= 90º.
	b = 5.08800(10) Å	β= 97.1880(10)º.
	c = 15.9439(4) Å	γ= 90º.
Volume	826.06(4) $Å^3$	
Z	2	
Density (calculated)	1.400 Mg/m^3	
Absorption coefficient	0.910 mm^{-1}	
F(000)	368	
Crystal size	0.467 x 0.43 x 0.311 mm^3	
Theta range for data collection	2.79 to 68.24º.	
Index ranges	-12<=h<=12, -6<=k<=6, -18<=l<=19	
Reflections collected	6079	
Independent reflections	2267 [R(int) = 0.0135]	
Completeness to theta = 68.24º	98.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7531 and 0.7143	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2267 / 5 / 302	
Goodness-of-fit on F^2	1.159	
Final R indices [I>2sigma(I)]	R_1 = 0.0352, wR_2 = 0.0842	
R indices (all data)	R_1 = 0.0353, wR_2 = 0.0844	
Absolute structure parameter	0.01(14)	
Largest diff. peak and hole	0.208 and -0.311 $e.Å^{-3}$	

Table 2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$) for product **3.91**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O(1)	9790(1)	4360(3)	3131(1)	26(1)
O(17)	7580(1)	-2027(3)	1407(1)	30(1)
O(18)	13433(1)	3609(3)	1479(1)	29(1)
O(20)	12272(1)	-122(3)	638(1)	31(1)
O(22)	6604(1)	3404(3)	6188(1)	35(1)
O(24)	6408(1)	1278(5)	1827(1)	62(1)
C(2)	8464(1)	3236(4)	2988(1)	22(1)
C(3)	8605(2)	628(3)	2512(1)	22(1)
C(4)	9845(1)	1175(4)	2108(1)	21(1)
C(5)	10463(2)	3283(4)	2524(1)	22(1)
C(6)	11676(2)	4234(4)	2356(1)	23(1)
C(7)	12242(1)	2959(4)	1726(1)	23(1)
C(8)	11607(2)	862(4)	1270(1)	23(1)
C(9)	10413(2)	-83(4)	1468(1)	22(1)
C(10)	7922(1)	3174(4)	3823(1)	22(1)
C(11)	8432(2)	1519(4)	4484(1)	31(1)
C(12)	7975(2)	1630(4)	5260(1)	33(1)
C(13)	6995(2)	3427(4)	5395(1)	26(1)
C(14)	6469(2)	5069(4)	4750(1)	27(1)
C(15)	6945(2)	4928(4)	3968(1)	26(1)
C(16)	7405(2)	34(4)	1885(1)	25(1)
C(19)	14160(2)	5684(4)	1927(1)	27(1)
C(21)	11607(2)	-1965(5)	68(1)	33(1)
C(23)	5705(2)	5426(4)	6366(1)	33(1)
O(1W)	5668(1)	-2600(3)	113(1)	28(1)

Table 3. Bond lengths [Å] and angles [º] for product **3.91**

O(1)-C(2)	1.467(2)
O(1)-C(5)	1.372(2)
O(17)-C(16)	1.322(2)
O(18)-C(7)	1.3712(18)
O(18)-C(19)	1.431(2)
O(20)-C(8)	1.380(2)
O(20)-C(21)	1.419(3)
O(22)-C(13)	1.373(2)
O(22)-C(23)	1.434(2)
O(24)-C(16)	1.197(2)
O(17)-H(17)	0.87(2)
O(1W)-H(1WA)	0.960(19)
O(1W)-H(1WB)	0.99(2)
C(2)-C(10)	1.507(2)
C(2)-C(3)	1.544(2)
C(3)-C(16)	1.517(2)
C(3)-C(4)	1.522(2)
C(4)-C(5)	1.374(3)
C(4)-C(9)	1.393(2)
C(5)-C(6)	1.392(2)
C(6)-C(7)	1.383(2)
C(7)-C(8)	1.405(3)
C(8)-C(9)	1.389(2)
C(10)-C(15)	1.383(3)
C(10)-C(11)	1.398(2)
C(11)-C(12)	1.378(2)
C(12)-C(13)	1.396(3)
C(13)-C(14)	1.382(2)
C(14)-C(15)	1.397(2)
C(2)-H(2)	0.95(2)
C(3)-H(3)	0.96(3)
C(6)-H(6)	0.96(2)
C(9)-H(9)	0.93(3)
C(11)-H(11)	0.93(3)

C(12)-H(12)	0.95(3)
C(14)-H(14)	0.96(3)
C(15)-H(15)	0.97(3)
C(19)-H(19B)	0.96(3)
C(19)-H(19A)	0.96(2)
C(19)-H(19C)	0.94(2)
C(21)-H(21B)	1.02(2)
C(21)-H(21C)	0.97(2)
C(21)-H(21A)	1.02(3)
C(23)-H(23C)	1.02(2)
C(23)-H(23A)	1.04(3)
C(23)-H(23B)	1.00(2)
C(2)-O(1)-C(5)	105.87(13)
C(7)-O(18)-C(19)	117.56(13)
C(8)-O(20)-C(21)	117.69(13)
C(13)-O(22)-C(23)	116.50(14)
C(16)-O(17)-H(17)	107.8(19)
H(1WA)-O(1W)-H(1WB)	107(2)
O(1)-C(2)-C(10)	107.96(12)
C(3)-C(2)-C(10)	118.92(16)
O(1)-C(2)-C(3)	105.63(12)
C(4)-C(3)-C(16)	114.22(12)
C(2)-C(3)-C(16)	112.12(13)
C(2)-C(3)-C(4)	100.68(13)
C(3)-C(4)-C(5)	107.38(13)
C(3)-C(4)-C(9)	132.45(16)
C(5)-C(4)-C(9)	120.11(15)
O(1)-C(5)-C(6)	122.60(16)
C(4)-C(5)-C(6)	123.25(15)
O(1)-C(5)-C(4)	114.14(14)
C(5)-C(6)-C(7)	116.36(16)
O(18)-C(7)-C(6)	124.48(16)
O(18)-C(7)-C(8)	114.03(14)
C(6)-C(7)-C(8)	121.48(14)
O(20)-C(8)-C(7)	114.43(14)
C(7)-C(8)-C(9)	120.68(15)

O(20)-C(8)-C(9)	124.89(16)
C(4)-C(9)-C(8)	118.04(17)
C(11)-C(10)-C(15)	118.29(14)
C(2)-C(10)-C(11)	122.24(15)
C(2)-C(10)-C(15)	119.33(15)
C(10)-C(11)-C(12)	120.94(17)
C(11)-C(12)-C(13)	119.90(17)
C(12)-C(13)-C(14)	120.20(15)
O(22)-C(13)-C(12)	115.85(16)
O(22)-C(13)-C(14)	123.95(16)
C(13)-C(14)-C(15)	119.07(17)
C(10)-C(15)-C(14)	121.61(16)
O(17)-C(16)-C(3)	112.38(14)
O(17)-C(16)-O(24)	123.44(17)
O(24)-C(16)-C(3)	124.19(18)
O(1)-C(2)-H(2)	105.9(13)
C(3)-C(2)-H(2)	109.1(13)
C(10)-C(2)-H(2)	108.6(12)
C(2)-C(3)-H(3)	115.6(15)
C(4)-C(3)-H(3)	106.8(13)
C(16)-C(3)-H(3)	107.5(14)
C(7)-C(6)-H(6)	120.7(12)
C(5)-C(6)-H(6)	122.9(12)
C(8)-C(9)-H(9)	122.3(12)
C(4)-C(9)-H(9)	119.6(12)
C(10)-C(11)-H(11)	119.5(14)
C(12)-C(11)-H(11)	119.5(14)
C(11)-C(12)-H(12)	115.3(14)
C(13)-C(12)-H(12)	124.8(14)
C(15)-C(14)-H(14)	119.9(14)
C(13)-C(14)-H(14)	121.0(14)
C(10)-C(15)-H(15)	117.5(14)
C(14)-C(15)-H(15)	120.9(14)
O(18)-C(19)-H(19B)	111.9(18)
O(18)-C(19)-H(19C)	108.8(17)
O(18)-C(19)-H(19A)	108.9(15)

H(19A)-C(19)-H(19C)	110.4(18)
H(19B)-C(19)-H(19C)	106(3)
H(19A)-C(19)-H(19B)	111(2)
O(20)-C(21)-H(21A)	111.0(13)
O(20)-C(21)-H(21B)	110.0(16)
H(21A)-C(21)-H(21B)	110.6(19)
H(21A)-C(21)-H(21C)	107(2)
O(20)-C(21)-H(21C)	105.9(14)
H(21B)-C(21)-H(21C)	111.8(18)
O(22)-C(23)-H(23B)	106.2(15)
O(22)-C(23)-H(23C)	109.4(16)
O(22)-C(23)-H(23A)	107.0(13)
H(23A)-C(23)-H(23C)	113(2)
H(23B)-C(23)-H(23C)	114.2(17)
H(23A)-C(23)-H(23B)	107(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2x10^3$) for product **3.91**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	25(1)	27(1)	27(1)	-7(1)	8(1)	-5(1)
O(17)	28(1)	29(1)	29(1)	-5(1)	-4(1)	-2(1)
O(18)	22(1)	38(1)	28(1)	-8(1)	8(1)	-8(1)
O(20)	26(1)	38(1)	29(1)	-12(1)	9(1)	-6(1)
O(22)	44(1)	40(1)	23(1)	4(1)	11(1)	12(1)
O(24)	28(1)	71(1)	80(1)	-41(1)	-15(1)	16(1)
C(2)	20(1)	23(1)	23(1)	1(1)	3(1)	-1(1)
C(3)	23(1)	22(1)	20(1)	3(1)	4(1)	-2(1)
C(4)	19(1)	21(1)	22(1)	3(1)	1(1)	-1(1)
C(5)	23(1)	24(1)	19(1)	0(1)	3(1)	-1(1)
C(6)	22(1)	25(1)	23(1)	-1(1)	1(1)	-3(1)
C(7)	20(1)	28(1)	21(1)	1(1)	2(1)	0(1)
C(8)	23(1)	26(1)	20(1)	-1(1)	3(1)	3(1)
C(9)	22(1)	22(1)	23(1)	0(1)	1(1)	0(1)
C(10)	21(1)	24(1)	22(1)	-1(1)	3(1)	-1(1)
C(11)	31(1)	34(1)	30(1)	4(1)	6(1)	11(1)
C(12)	39(1)	36(1)	24(1)	7(1)	4(1)	11(1)
C(13)	27(1)	30(1)	23(1)	0(1)	5(1)	-2(1)
C(14)	26(1)	28(1)	27(1)	1(1)	5(1)	5(1)
C(15)	26(1)	27(1)	25(1)	3(1)	3(1)	1(1)
C(16)	22(1)	27(1)	26(1)	1(1)	5(1)	-3(1)
C(19)	25(1)	31(1)	27(1)	-2(1)	4(1)	-8(1)
C(21)	35(1)	34(1)	30(1)	-11(1)	7(1)	-3(1)
C(23)	41(1)	32(1)	27(1)	-3(1)	12(1)	6(1)
O(1W)	25(1)	37(1)	23(1)	-1(1)	5(1)	0(1)

Table 5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2x10^3$) for product **3.91**

	x	y	z	U(eq)
H(2)	7956(19)	4430(50)	2623(12)	21(5)
H(3)	8780(20)	-890(60)	2861(14)	33(6)
H(6)	12103(19)	5710(50)	2647(12)	25(5)
H(9)	9961(19)	-1440(60)	1165(12)	24(5)
H(11)	9080(20)	300(60)	4395(13)	32(3)
H(12)	8380(20)	450(60)	5672(14)	32(3)
H(14)	5780(20)	6270(60)	4829(14)	32(3)
H(15)	6600(20)	6060(60)	3506(14)	32(3)
H(17)	6890(20)	-2180(60)	1038(15)	40(6)
H(19A)	14300(20)	5250(50)	2518(14)	28(5)
H(19B)	13720(30)	7350(70)	1841(16)	48(7)
H(19C)	14970(20)	5870(60)	1713(14)	38(6)
H(21A)	11450(20)	-3680(60)	367(14)	33(5)
H(21B)	10740(20)	-1190(60)	-206(15)	42(6)
H(21C)	12200(20)	-2340(50)	-346(13)	30(5)
H(23A)	6140(20)	7210(60)	6253(15)	38(6)
H(23B)	5650(20)	5330(60)	6989(15)	37(6)
H(23C)	4830(20)	5160(60)	5997(13)	32(6)
H(1WA)	6120(20)	-2780(60)	-376(11)	52(5)
H(1WB)	5160(30)	-940(40)	46(16)	52(5)

Table 6. Torsion angles [°] for product **3.91**

C(5)-O(1)-C(2)-C(3)	23.45(16)
C(5)-O(1)-C(2)-C(10)	151.67(15)
C(2)-O(1)-C(5)-C(4)	-13.08(19)
C(2)-O(1)-C(5)-C(6)	167.70(16)
C(19)-O(18)-C(7)-C(6)	2.5(2)
C(19)-O(18)-C(7)-C(8)	-178.45(15)
C(21)-O(20)-C(8)-C(7)	-170.69(16)
C(21)-O(20)-C(8)-C(9)	9.8(3)
C(23)-O(22)-C(13)-C(12)	173.32(16)
C(23)-O(22)-C(13)-C(14)	-7.4(3)
O(1)-C(2)-C(3)-C(4)	-24.21(14)
O(1)-C(2)-C(3)-C(16)	-146.03(13)
C(10)-C(2)-C(3)-C(4)	-145.57(13)
C(10)-C(2)-C(3)-C(16)	92.61(16)
O(1)-C(2)-C(10)-C(11)	-68.1(2)
O(1)-C(2)-C(10)-C(15)	107.46(18)
C(3)-C(2)-C(10)-C(11)	52.1(2)
C(3)-C(2)-C(10)-C(15)	-132.36(17)
C(2)-C(3)-C(4)-C(5)	16.94(16)
C(2)-C(3)-C(4)-C(9)	-165.85(18)
C(16)-C(3)-C(4)-C(5)	137.27(15)
C(16)-C(3)-C(4)-C(9)	-45.5(3)
C(2)-C(3)-C(16)-O(17)	172.58(13)
C(2)-C(3)-C(16)-O(24)	-7.6(3)
C(4)-C(3)-C(16)-O(17)	58.9(2)
C(4)-C(3)-C(16)-O(24)	-121.3(2)
C(3)-C(4)-C(5)-O(1)	-3.2(2)
C(3)-C(4)-C(5)-C(6)	175.97(15)
C(9)-C(4)-C(5)-O(1)	179.14(15)
C(9)-C(4)-C(5)-C(6)	-1.7(3)
C(3)-C(4)-C(9)-C(8)	-177.01(17)
C(5)-C(4)-C(9)-C(8)	-0.1(3)
O(1)-C(5)-C(6)-C(7)	-179.94(16)
C(4)-C(5)-C(6)-C(7)	0.9(3)

C(5)-C(6)-C(7)-O(18)	-179.49(16)
C(5)-C(6)-C(7)-C(8)	1.5(3)
O(18)-C(7)-C(8)-O(20)	-1.9(2)
O(18)-C(7)-C(8)-C(9)	177.66(16)
C(6)-C(7)-C(8)-O(20)	177.23(15)
C(6)-C(7)-C(8)-C(9)	-3.3(3)
O(20)-C(8)-C(9)-C(4)	-178.09(16)
C(7)-C(8)-C(9)-C(4)	2.5(3)
C(2)-C(10)-C(11)-C(12)	175.61(17)
C(15)-C(10)-C(11)-C(12)	0.0(3)
C(2)-C(10)-C(15)-C(14)	-175.76(16)
C(11)-C(10)-C(15)-C(14)	0.0(3)
C(10)-C(11)-C(12)-C(13)	-0.4(3)
C(11)-C(12)-C(13)-O(22)	-179.79(17)
C(11)-C(12)-C(13)-C(14)	0.9(3)
O(22)-C(13)-C(14)-C(15)	179.85(17)
C(12)-C(13)-C(14)-C(15)	-0.9(3)
C(13)-C(14)-C(15)-C(10)	0.5(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for product **3.91** [Å and º]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1W)-H(1WA)...O(18)#1	0.960(19)	2.00(2)	2.8731(16)	150(2)
O(1W)-H(1WA)...O(20)#1	0.960(19)	2.12(2)	2.8603(17)	133(2)
O(1W)-H(1WB)...O(1W)#2	0.99(2)	1.90(2)	2.892(2)	175(3)
O(17)-H(17)...O(1W)	0.87(2)	1.83(2)	2.6790(16)	169(2)
C(6)-H(6)...O(22)#3	0.96(2)	2.55(2)	3.463(2)	160.0(18)
C(9)-H(9)...O(17)	0.93(3)	2.54(2)	3.061(2)	115.7(16)
C(12)-H(12)...O(1)#4	0.95(3)	2.57(2)	3.421(2)	151(2)

Symmetry transformations used to generate equivalent atoms:
#1 _____+2_ #2
_____+1_
#3 _____+2_ #4
_____+2_

8. The X-ray crystallographic structure of product 3.94

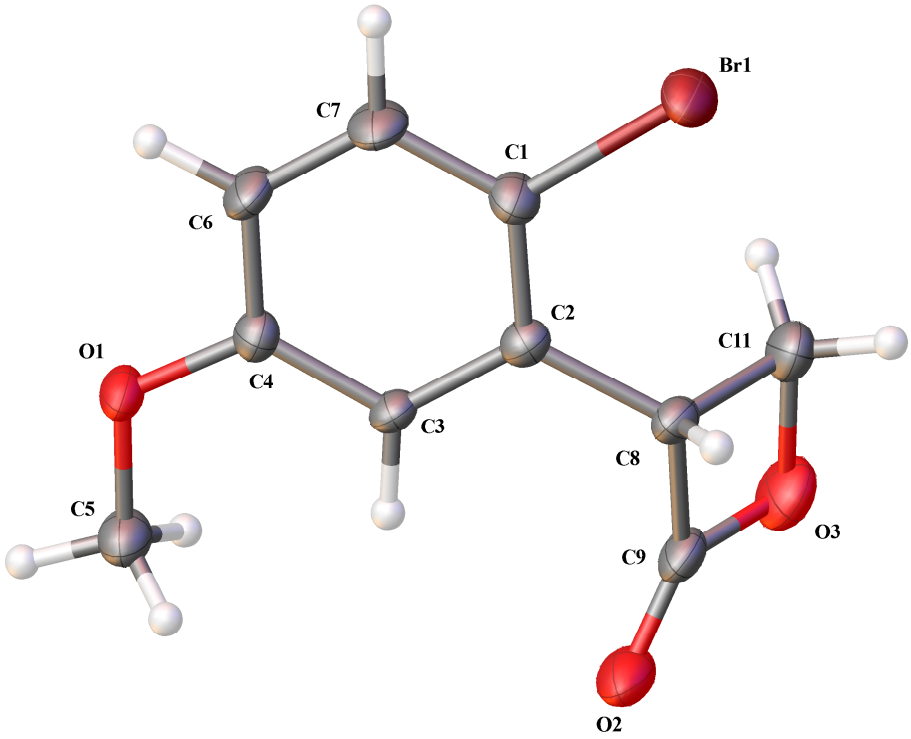

Table 1. Crystal data and structure refinement for product **3.94**

Identification code	hwxii114s	
Empirical formula	C10 H9 Br O3	
Formula weight	257.08	
Temperature	173.15 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21	
Unit cell dimensions	a = 6.2085(15) Å	α= 90°.
	b = 5.3383(12) Å	β= 95.715(4)°.
	c = 15.239(4) Å	γ= 90°.
Volume	502.5(2) $Å^3$	
Z	2	
Density (calculated)	1.699 Mg/m^3	
Absorption coefficient	4.067 mm^{-1}	
F(000)	256	
Crystal size	0.198 x 0.173 x 0.13 mm^3	
Theta range for data collection	2.69 to 30.78°.	
Index ranges	-8<=h<=8, -7<=k<=5, -21<=l<=21	
Reflections collected	3795	
Independent reflections	2647 [R(int) = 0.0213]	
Completeness to theta = 29.57°	98.3 %	
Absorption correction	Numerical	
Max. and min. transmission	0.3895 and 0.3174	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2353 / 19 / 161	
Goodness-of-fit on F^2	1.038	
Final R indices [I>2sigma(I)]	R_1 = 0.0341, wR_2 = 0.0793	
R indices (all data)	R_1 = 0.0378, wR_2 = 0.0813	
Absolute structure parameter	-0.012(12)	
Largest diff. peak and hole	0.694 and -0.270 $e.Å^{-3}$	

Table 2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$) for product **3.94**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Br(1)	5930(1)	-1446(1)	1962(1)	38(1)
O(1)	1859(4)	5811(5)	4319(2)	31(1)
C(9)	292(5)	3847(10)	985(2)	31(1)
C(3)	1785(4)	3850(9)	2871(2)	22(1)
C(8)	1858(5)	1852(7)	1371(2)	25(1)
C(4)	2662(5)	4196(6)	3737(2)	24(1)
O(2)	-1424(5)	4640(6)	1116(2)	47(1)
C(5)	64(6)	7335(8)	3995(2)	36(1)
O(3)	1538(5)	4589(6)	353(2)	44(1)
C(11)	3255(6)	2759(8)	662(2)	35(1)
C(2)	2730(5)	2179(6)	2321(2)	23(1)
C(1)	4552(5)	858(7)	2671(2)	29(1)
C(7)	5391(6)	1187(8)	3535(2)	36(1)
C(6)	4458(6)	2847(7)	4071(2)	33(1)

Table 3. Bond lengths [Å] and angles [°] for product **3.94**

Br(1)-C(1)	1.897(3)
O(1)-C(4)	1.367(4)
O(1)-C(5)	1.428(4)
C(9)-O(2)	1.182(5)
C(9)-O(3)	1.353(4)
C(9)-C(8)	1.520(5)
C(3)-C(4)	1.388(4)
C(3)-C(2)	1.394(5)
C(3)-H(3)	0.974(19)
C(8)-C(2)	1.504(4)
C(8)-C(11)	1.530(5)
C(8)-H(8)	0.982(8)
C(4)-C(6)	1.381(4)
C(5)-H(5A)	0.964(18)
C(5)-H(5B)	0.962(18)
C(5)-H(5C)	0.979(17)
O(3)-C(11)	1.487(5)
C(11)-H(11A)	0.982(8)
C(11)-H(11B)	0.982(8)
C(2)-C(1)	1.393(4)
C(1)-C(7)	1.378(5)
C(7)-C(6)	1.373(5)
C(7)-H(7)	0.978(19)
C(6)-H(6)	0.982(19)

C(4)-O(1)-C(5)	117.2(3)
O(2)-C(9)-O(3)	127.2(4)
O(2)-C(9)-C(8)	137.6(4)
O(3)-C(9)-C(8)	95.3(3)
C(4)-C(3)-C(2)	120.5(3)
C(4)-C(3)-H(3)	115(3)
C(2)-C(3)-H(3)	124(3)
C(2)-C(8)-C(9)	116.5(3)

C(2)-C(8)-C(11)	117.9(3)
C(9)-C(8)-C(11)	83.7(3)
C(2)-C(8)-H(8)	111(2)
C(9)-C(8)-H(8)	110(2)
C(11)-C(8)-H(8)	115(2)
O(1)-C(4)-C(6)	115.0(3)
O(1)-C(4)-C(3)	124.5(3)
C(6)-C(4)-C(3)	120.5(3)
O(1)-C(5)-H(5A)	107(2)
O(1)-C(5)-H(5B)	109(2)
H(5A)-C(5)-H(5B)	110(2)
O(1)-C(5)-H(5C)	114(2)
H(5A)-C(5)-H(5C)	108.5(18)
H(5B)-C(5)-H(5C)	108.7(17)
C(9)-O(3)-C(11)	91.4(3)
O(3)-C(11)-C(8)	89.6(3)
O(3)-C(11)-C(9)	41.65(19)
C(8)-C(11)-C(9)	47.9(2)
O(3)-C(11)-H(11A)	118(3)
C(8)-C(11)-H(11A)	117(2)
C(9)-C(11)-H(11A)	130(3)
O(3)-C(11)-H(11B)	108(2)
C(8)-C(11)-H(11B)	112(2)
C(9)-C(11)-H(11B)	119(2)
H(11A)-C(11)-H(11B)	110(3)
C(1)-C(2)-C(3)	117.9(3)
C(1)-C(2)-C(8)	120.7(3)
C(3)-C(2)-C(8)	121.4(3)
C(7)-C(1)-C(2)	121.1(3)
C(7)-C(1)-Br(1)	118.5(2)
C(2)-C(1)-Br(1)	120.3(2)
C(6)-C(7)-C(1)	120.6(3)
C(6)-C(7)-H(7)	120(3)
C(1)-C(7)-H(7)	119(3)
C(7)-C(6)-C(4)	119.3(3)
C(7)-C(6)-H(6)	123(3)

C(4)-C(6)-H(6)	118(3)

Table 4. Anisotropic displacement parameters ($Å^2x10^3$) for product **3.94**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	39(1)	42(1)	33(1)	-10(1)	-3(1)	22(1)
O(1)	34(1)	38(1)	18(1)	-6(1)	-4(1)	16(1)
C(9)	33(2)	39(2)	19(1)	-5(2)	-8(1)	11(2)
C(3)	20(1)	29(2)	18(1)	0(1)	-4(1)	6(1)
C(8)	23(1)	29(2)	21(2)	-5(1)	-4(1)	5(1)
C(4)	26(1)	29(2)	18(1)	-1(1)	1(1)	4(1)
O(2)	44(2)	64(2)	32(1)	-12(1)	-11(1)	27(1)
C(5)	37(2)	44(2)	26(2)	-5(2)	-4(2)	18(2)
O(3)	53(2)	53(2)	24(1)	6(1)	-4(1)	7(1)
C(11)	34(2)	52(2)	20(1)	-3(1)	1(1)	6(2)
C(2)	22(1)	26(2)	20(1)	1(1)	-1(1)	3(1)
C(1)	29(2)	32(2)	25(2)	-4(1)	0(1)	13(1)
C(7)	32(2)	46(2)	29(2)	-1(2)	-8(2)	21(2)
C(6)	32(2)	44(2)	19(1)	-3(1)	-8(1)	14(1)

Table 5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2x10^3$) for product **3.94**

	x	y	z	U(eq)
H(11A)	4700(30)	3400(90)	870(20)	35(9)
H(11B)	3350(60)	1510(60)	190(20)	35(11)
H(8)	1230(60)	180(30)	1270(30)	33(11)
H(6)	5060(70)	3180(110)	4681(16)	47(7)
H(3)	490(50)	4830(80)	2700(30)	47(7)
H(7)	6710(50)	290(80)	3760(30)	47(7)
H(5A)	-310(50)	8330(60)	4485(17)	35(9)
H(5B)	490(50)	8400(60)	3534(16)	36(9)
H(5C)	-1210(40)	6370(60)	3765(18)	22(9)

Table 6. Torsion angles [°] for product **3.94**

O(2)-C(9)-C(8)-C(2)	-61.4(7)
O(3)-C(9)-C(8)-C(2)	119.1(3)
O(2)-C(9)-C(8)-C(11)	-179.5(6)
O(3)-C(9)-C(8)-C(11)	1.0(3)
C(5)-O(1)-C(4)-C(6)	177.2(3)
C(5)-O(1)-C(4)-C(3)	-3.5(5)
C(2)-C(3)-C(4)-O(1)	179.3(3)
C(2)-C(3)-C(4)-C(6)	-1.5(5)
O(2)-C(9)-O(3)-C(11)	179.4(5)
C(8)-C(9)-O(3)-C(11)	-1.0(3)
C(9)-O(3)-C(11)-C(8)	1.0(3)
C(2)-C(8)-C(11)-O(3)	-117.6(3)
C(9)-C(8)-C(11)-O(3)	-0.9(3)
C(2)-C(8)-C(11)-C(9)	-116.7(4)
O(2)-C(9)-C(11)-O(3)	-5(4)
C(8)-C(9)-C(11)-O(3)	178.7(4)
O(2)-C(9)-C(11)-C(8)	177(4)
O(3)-C(9)-C(11)-C(8)	-178.7(4)
C(4)-C(3)-C(2)-C(1)	0.9(5)
C(4)-C(3)-C(2)-C(8)	-177.6(3)
C(9)-C(8)-C(2)-C(1)	-163.7(3)
C(11)-C(8)-C(2)-C(1)	-66.5(4)
C(9)-C(8)-C(2)-C(3)	14.7(5)
C(11)-C(8)-C(2)-C(3)	111.9(4)
C(3)-C(2)-C(1)-C(7)	0.1(5)
C(8)-C(2)-C(1)-C(7)	178.5(4)
C(3)-C(2)-C(1)-Br(1)	-179.9(3)
C(8)-C(2)-C(1)-Br(1)	-1.5(5)
C(2)-C(1)-C(7)-C(6)	-0.5(6)
Br(1)-C(1)-C(7)-C(6)	179.5(3)
C(1)-C(7)-C(6)-C(4)	-0.1(6)
O(1)-C(4)-C(6)-C(7)	-179.6(4)
C(3)-C(4)-C(6)-C(7)	1.1(6)