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Expanding The Scope of Reactions and Applications for Dirhodium(II) Tetracarboxylate
Catalyzed Carbene Reactions Toward C–H Insertion and Cyclopropanation.

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A dissertation submitted to the faculty of the
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Abstract

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By Yasir Naeem

The utilization of rhodium carbenes in catalyst-directed C–H functionalization, specifically in C–H insertion chemistry, has emerged as a potent synthetic method. A crucial advancement in this field entails harnessing the synergy between donor/acceptor carbenes and chiral dirhodium tetracarboxylate catalysts. The primary objective of the research detailed in this thesis is to employ our advanced next-generation chiral dirhodium catalysts for the attainment of highly site- and stereoselective C–H functionalization reactions mediated by donor/acceptor carbenes. This thesis is structured into four chapters. The first chapter provides an overview of general knowledge on dirhodium tetracarboxylate catalysts, focusing on selective carbene chemistry in C–H functionalization.

The second chapter focuses on catalyst-controlled C–H functionalization using donor/acceptor carbenes, highlighting its efficiency in achieving high levels of site and stereoselectivity. This research extends the scope of donor/acceptor carbene C–H functionalization to systems where the acceptor group is phosphonate. The sterically demanding phosphonate group resulted in significantly higher selectivity for primary sites over more crowded positions compared to the previously studied carboxylate ester group. The methodology's effectiveness was demonstrated by the late-stage primary C–H functionalization of estrone, adapalene, (*S*)-naproxen, clofibrate, and gemfibrozil derivatives.

The third chapter explores C–H functionalization chemistry for modifying triarylamine derivatives with carboxylic esters and norbornene, which are important for materials applications. Specifically, various triarylamines and 4,4'-bis(diarylamino)biphenyl were subjected to C(sp²)–H functionalization using a diazoacetate bearing a protected carboxylic acid functional group, in the presence of a dirhodium tetracarboxylate catalyst. This approach potentially provides straightforward access to a diverse array of Hole-Transport Materials (HTMs) with different functional groups.

The fourth and the final chapter of the thesis is focused on developing a novel approach for synthesizing aryl and heteroaryl diazo phosphonates using a palladium-catalyzed cross-coupling reaction. This method relies on readily available aryl iodides as starting materials, therefore avoiding the need for the hazardous diazo transfer reagent, 4-Acetamidobenzenesulfonyl azide, which is commonly used in traditional diazo transfer reactions to create different diazo phosphonate compounds. As a result, this approach enables the rapid and efficient creation of a diverse library of valuable diazo phosphonate compounds. The diazo phosphonate compounds synthesized in this thesis were subsequently subjected to cyclopropanation reactions using our next generation dirhodium tetracarboxylate catalyst.

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Acknowledgements

The past five years of my Ph.D. journey have been both challenging and transformative. Beginning this path was daunting enough, but with the onset of the pandemic soon after I started, it became even more difficult. The global crisis brought unprecedented challenges, and like many others, I faced an incredibly tough time, far away from the comfort of my family while striving to keep focused on my studies and research. Being separated from my loved ones was especially hard, given that both of my parents are elderly and have health concerns. The uncertainty of those times was overwhelming, but it also pushed me to grow, adapt, and persevere in ways I had never imagined.

These years have been more than just an academic pursuit; they have been a period of deep personal growth, resilience, and discovery. The struggles have been numerous, but each hurdle has been a steppingstone, shaping not only my research but also my character. As I look back on this journey, I realize how precious and meaningful these years have been. They have taught me the value of perseverance, the strength of community, and the importance of staying true to one's goals, no matter how difficult the path may become.

Reaching this point would not have been possible without the support, guidance, and encouragement of many wonderful individuals, to whom I am deeply indebted. I would like to express my heartfelt gratitude to my advisor, Professor Huw M. L. Davies, whose invaluable mentorship and unwavering support have been the cornerstone of my Ph.D. experience. His patience, profound knowledge, and insightful guidance have not only directed my research but also inspired me to think critically and creatively. I am sincerely grateful for the freedom he provided me to explore my ideas and for his constant encouragement, which fueled my confidence and drive throughout this journey.

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To my family

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List of abbreviations

Ac acetyl

APCI atmospheric pressure chemical ionization

Ar aryl

Bn benzyl

Bu butyl

brsm based on recovered starting material

c.a. approximately

Cbz carboxybenzyl

Cy cyclohexyl

dba bis(dibenzylideneacetone)

DBU 1,8-diazabicycloundec-7-ene

DCC *N,N*-dicyclohexylcarbodiimide

1,2-DCE 1,2-dichloroethane

DCM dichloromethane

DIAD diisopropyl azodicarboxylate

DMAP *N,N*-4-(dimethylamino)pyridine

DMA dimethylacetamide

DMB 2,2-dimethylbutane

DMF dimethylformamide

dppe 1,2-bis(diphenylphosphino)ethane

dppf 1,1'-bis(diphenylphosphino)ferrocene

dr diastereomeric ratio

EDG electron-donating group

ee enantiomeric excess

Et ethyl

equiv. equivalents

EWG electron-withdrawing group

HFIP Hexafluoro-2-propanol

HPLC high performance liquid chromatography

HRMS high-resolution mass spectrometry

Imid. Imidazole

IR infrared spectroscopy

L ligand

LDA lithium diisopropylamide

M metal

m.p. melting point

Me methyl

min minute

mmol millimoles

MS molecular sieves

NMR nuclear magnetic resonance

N.R. no reaction

N.O. not observed

***o*-NBSA** ortho-nitrobenzenesulfonyl azide

***p*-ABSA** para-acetamidobenzenesulfonyl azide

Ph phenyl

rt room temperature

r.r. regioisomeric ratio

SFC Supercritical fluid chromatography

SiO₂ silica gel

TBAF tetrabutylammonium fluoride

TBS tert-butyldimethylsilyl

TCE 2,2,2-trichloroethyl

TEA triethylamine

temp temperature

TFE 2,2,2-trifluoroethyl

THF tetrahydrofuran

TLC thin layer chromatography

TMS trimethylsilyl

Ts tosyl

TS transition state

Chapter 1: Introduction of Donor/acceptor Carbene and Dirhodium Tetracarboxylate Catalysts Chemistry

1.1 Introduction

The innovative strategy of C–H functionalization, recognized for synthesizing complex molecules, marks a departure from the conventional dependence on directing groups to govern molecular assembly. This approach introduces a distinct paradigm for organic synthesis. Simultaneously, the dynamic field of rhodium catalysis has attracted considerable attention owing to its unique reactivity and selectivity in asymmetric C–H functionalization reactions.¹⁻¹³ Recent years have witnessed noteworthy advancements in Rh-catalyzed asymmetric C–H functionalization reactions, spanning catalyst design, reaction development, and mechanistic exploration.¹⁴⁻²⁴

The importance of transition metal-catalyzed carbene reactions has experienced exponential growth in recent years, emerging as increasingly vital in organic synthetic chemistry.²⁵⁻²⁷ In this context, dirhodium tetracarboxylate catalysis have demonstrated exceptional proficiency in facilitating highly selective reactions involving donor/acceptor carbenes.²⁸⁻³¹ The proposed mechanism for the dirhodium-catalyzed carbene reaction is depicted in **(Figure 1.1)**.^{32,33} The catalytic cycle begins with the union of dirhodium complex **1.1** and diazo compound **1.2**, leading to dissociation of nitrogen from the rhodium-diazo compound complex **1.3**, which results in the formation of the rhodium carbene intermediate **1.4**. This highly electrophilic rhodium carbene **1.4** then approaches the substrate (**1.5a or 1.5b**) in the subsequent step. The process unfolds in a concerted manner, creating a three-membered-ring transition state (**1.6a or 1.6b**). Finally, the carbene reaction product (**1.7a or**

1.7b) is generated, and dirhodium catalysis **1.1** is released to initiate the succeeding catalytic cycle.³³⁻

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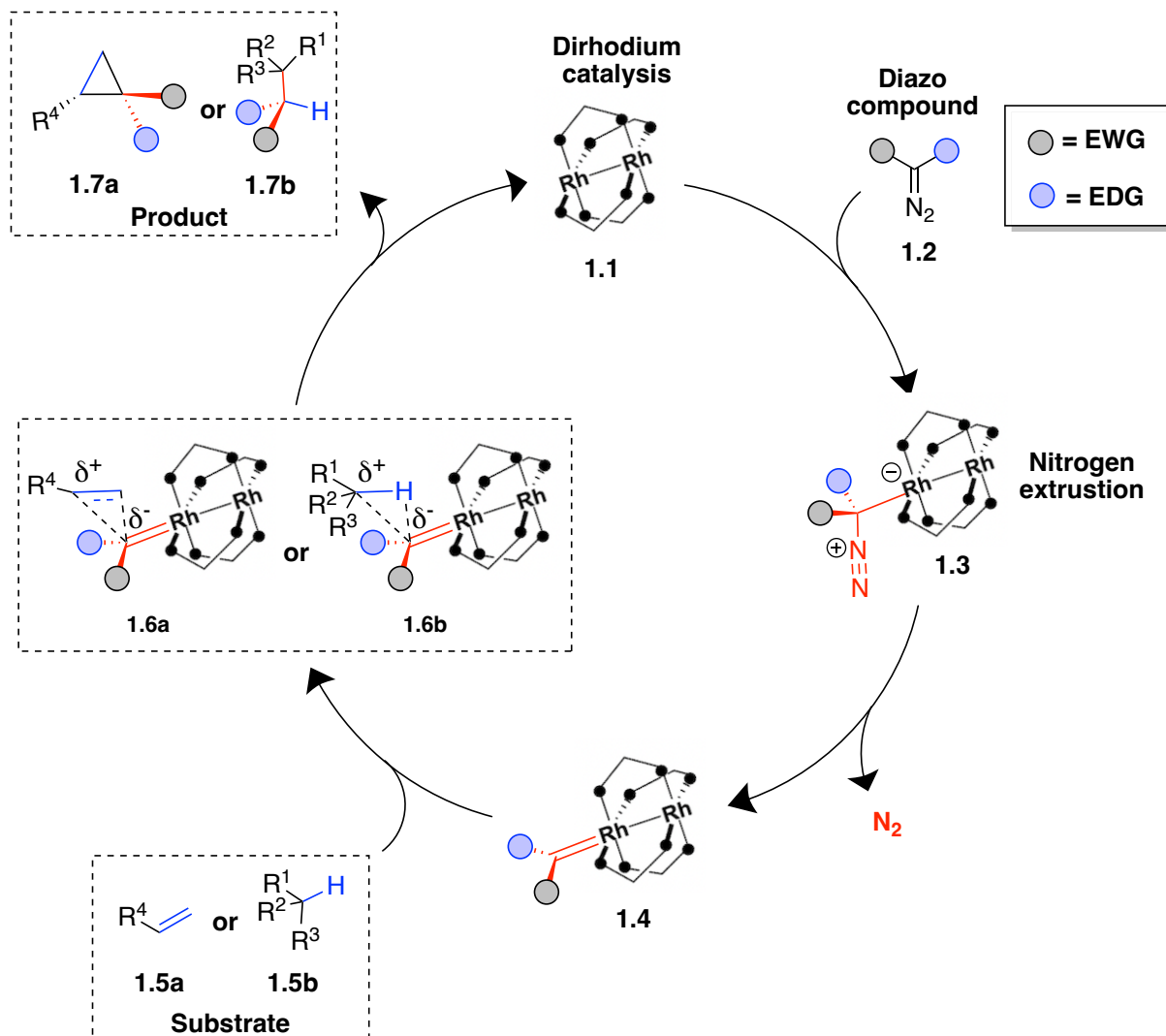


Figure 1.1 Generally accepted mechanism for dirhodium catalyzed carbene reaction.

Early investigations in this field focused on the dirhodium-catalyzed reaction involving carbenoids substituted with acceptor-only and acceptor–acceptor groups. The acceptor-only variant features an electron-withdrawing group, rendering the carbene intermediate exceptionally

electrophilic and intensely active. However, both acceptor-only carbene **1.7** and acceptor/acceptor carbene **1.8** often exhibit excessive reactivity, leading to widespread use in intramolecular C–H insertion reactions. Nonetheless, the reactive nature of these systems frequently results in low selectivity and complex product distributions when applied in intermolecular reactions.^{18,38}

A groundbreaking solution to address these challenges came with the development of donor/acceptor carbenes **1.9** pioneered by the Davies group. In contrast to the highly electrophilic acceptor-only carbene **1.7** and the acceptor/acceptor carbene **1.8**, donor/acceptor carbene **1.9** incorporates an electron-donating group that moderates the electronic nature of the carbenoid. This moderation stabilizes the metal complex, providing exceptional levels of selectivity across a wide range of intermolecular transformations (**Figure 1.2**).^{19,39}

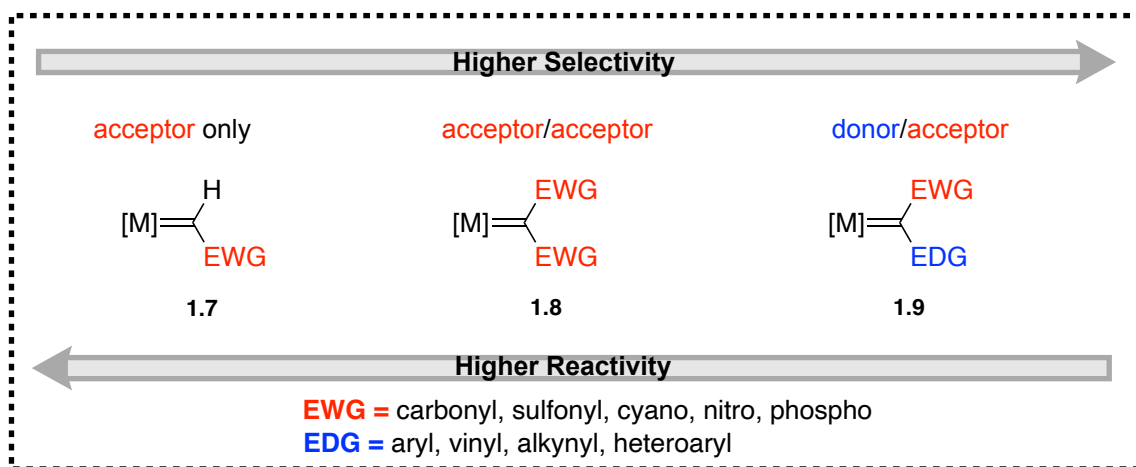


Figure 1.2 Major classes of metal-stabilized carbenes.

While various metals such as copper,^{40,41} palladium,^{42,43} silver,^{44,45} and gold^{46,47} have been utilized in metallocarbene chemistry to decompose carbene precursors and generate metallocarbenes, the development of rhodium catalysts for diazo compound decomposition has significantly expanded the scope of metallocarbene transformations.⁴⁸ Rhodium(II) catalysts are typically categorized into four major types based on the structure of their ligands: rhodium carboxylates, rhodium phosphates,

rhodium carboxamides, and ortho-metalated aryl phosphine rhodium complexes (**Figure 1.3**). In metallocarbene chemistry, rhodium catalysts are usually dirhodium complexes, where only one of the two rhodium atoms binds to the carbene center while the other serves as an electron bowl.^{49,50}

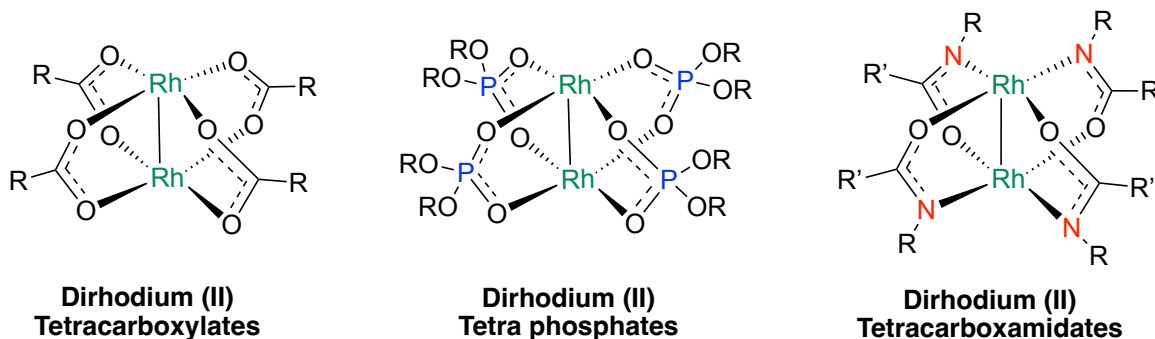


Figure 1.3 General structures of dirhodium(II) catalysts.

Rhodium (II) carboxylates are exceptionally effective catalysts for decomposing diazo compounds. An early example, dirhodium tetraacetate $\text{Rh}_2(\text{OAc})_4$, features four symmetrically arranged bridging acetate ligands around two rhodium atoms, forming a dimeric "paddlewheel" complex with D_{4h} -symmetry. Additionally, substituting the simple acetate ligands in dirhodium tetraacetate with chiral, non-racemic ligands can introduce asymmetry in reactions involving rhodium carbene species.⁴⁸

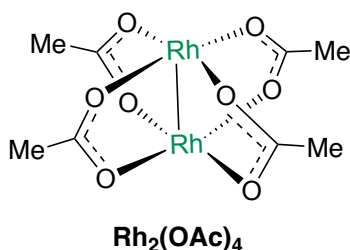


Figure 1.4 Structure of a dirhodium "paddlewheel" complex, rhodium tetraacetate.

The first class of rhodium catalysts for donor/acceptor carbenes is the arylsulfonylprolinates, initially developed by McKervy.^{28,51,52} A representative catalyst in this class is $\text{Rh}_2(\text{S-BSP})_4$. The scope of these catalysts was later expanded by Davies and coworkers that include $\text{Rh}_2(\text{S-TBSP})_4$ and $\text{Rh}_2(\text{S-DOSP})_4$, which have proven to be exceptional catalysts in carbene C–H functionalization and cyclopropanation.⁵³ The enhanced stereo control in hydrocarbon solvents is believed to result from solvent-induced ligand orientation, leading to an overall D_2 symmetry. The second-generation catalyst, $\text{Rh}_2(\text{S-bi-TISP})_4$, features a rigid bridging structure and can achieve high asymmetric induction even in non-hydrocarbon solvents.⁵⁴

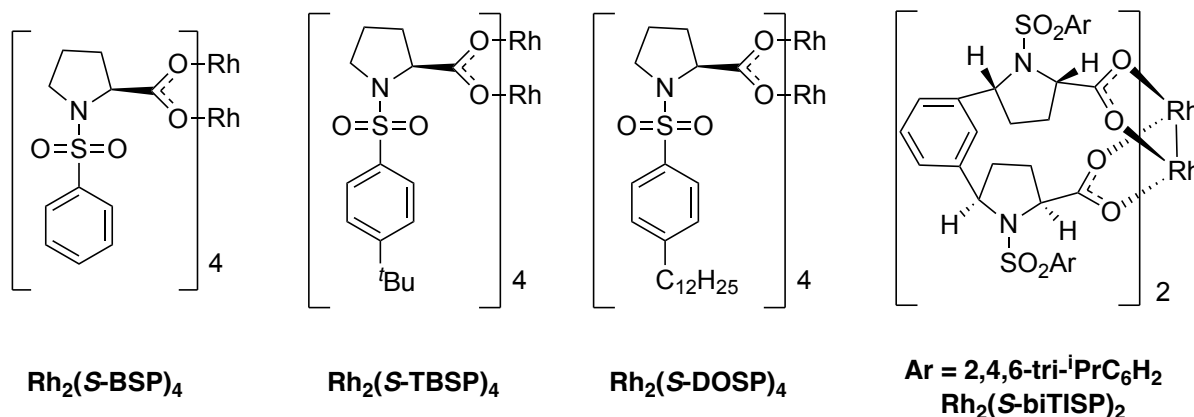
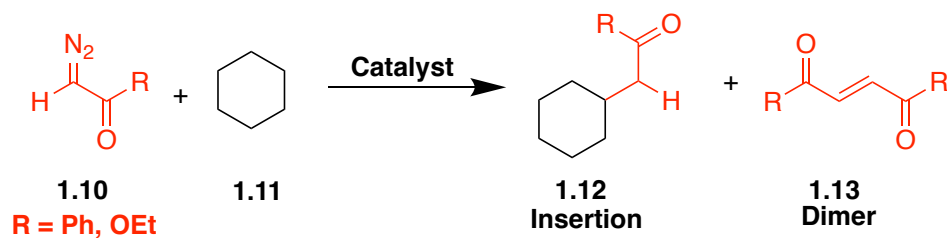


Figure 1.5 First generation dirhodium catalysts containing chiral proline ligands.

One of the early instances of carbene-induced C–H functionalization was accomplished by Scott and colleagues. In their work, they demonstrated that the decomposition of acceptor-only carbenes using copper (II) sulfate and copper (I) chloride as a catalyst proved to be an effective method for functionalizing cyclohexane when employed as a solvent. However, a significant portion of diazo self-dimerization occurred as a side product. In contrast, catalysis with cupric sulfate or cuprous chloride resulted in the absence of surviving diazo compounds, yielding the C–H functionalization product in 9–24% yield along with large amounts of dimer product (**Table 1.1**).^{1,44} Since that time,

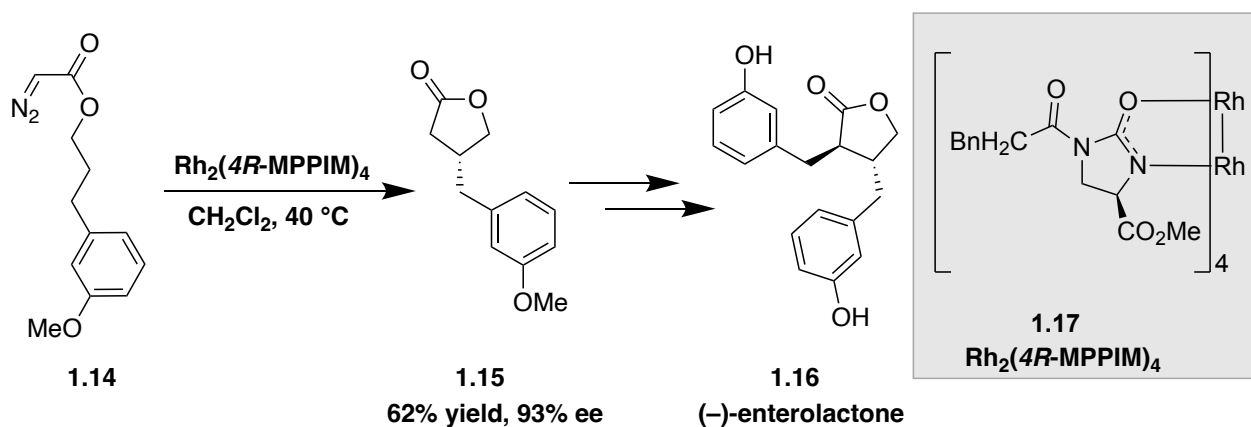
several research groups have endeavored to develop novel catalysts for conducting C–H insertion reactions, employing various metals such as rhodium, iridium, ruthenium, or palladium.¹⁹



Diazo	Catalyst	Insertion	Dimer
	CuSO ₄	24%	40%
	CuCl	15%	61%
	CuSO ₄	17%	9%
	CuCl	9%	29%

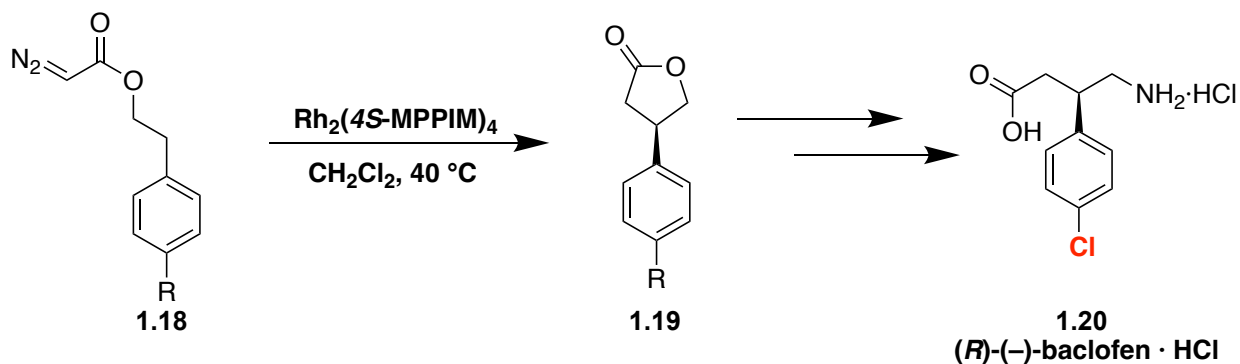
Table 1.1 C–H functionalization product of cyclohexane using copper catalyst.

In the context of C–H functionalization reactions, the emphasis is often placed on intramolecular processes where a specific C–H bond is situated in proximity to the diazo functionality. This becomes especially critical when dealing with acceptor-only carbenes, as they tend to be more challenging to control (**Scheme 1.1**).⁵⁵ This strategy is illustrated in the synthesis of (–)-enterolactone (**1.16**) through a Rh₂(4*R*-MPPIM)₄ (**1.17**)-catalyzed intramolecular C–H functionalization. In this instance, the diazo compound (**1.14**) features an acceptor-only group, making it highly electrophilic. The selective functionalization of a C–H bond occurs resulting in the production of the product (**1.15**) with an outstanding level of regio- and stereocontrol providing 62% yield and 93% ee. However, the benzylic position remained unfunctionalized due to the preferential formation of the 5-membered ring.⁴⁹

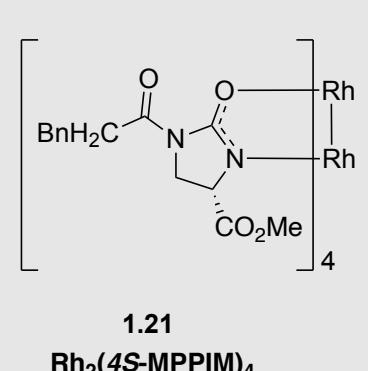


Scheme 1.1 C–H functionalization of (–)-enterolactone using acceptor-only carbene.

Another exemplification is apparent in the synthesis of (*R*)-(–)-baclofen (**1.20**), where a comparable intramolecular cyclization, utilizing (**1.18**) as the substrate, was orchestrated by the same catalyst (**1.21**) with exceptional precision in both regio- and stereocontrol. In this specific instance, the benzylic position underwent functionalization through site-selective activation driven by electronic factors. The resulting product (**1.19**) was attained with a notable asymmetric induction, yielding between 52% and 98%, and an impressive 91-95% enantiomeric excess (ee) (**Table 1.2**).⁵⁶ The crucial step in the enantioselective synthesis of the GABA_B receptor agonist (*R*)-(–)-baclofen involves the intramolecular C–H insertion of an acceptor-substituted carbenoid, catalyzed by the chiral rhodium carboxamidate catalyst Rh₂(4*S*-MPPIM)₄.⁴⁹



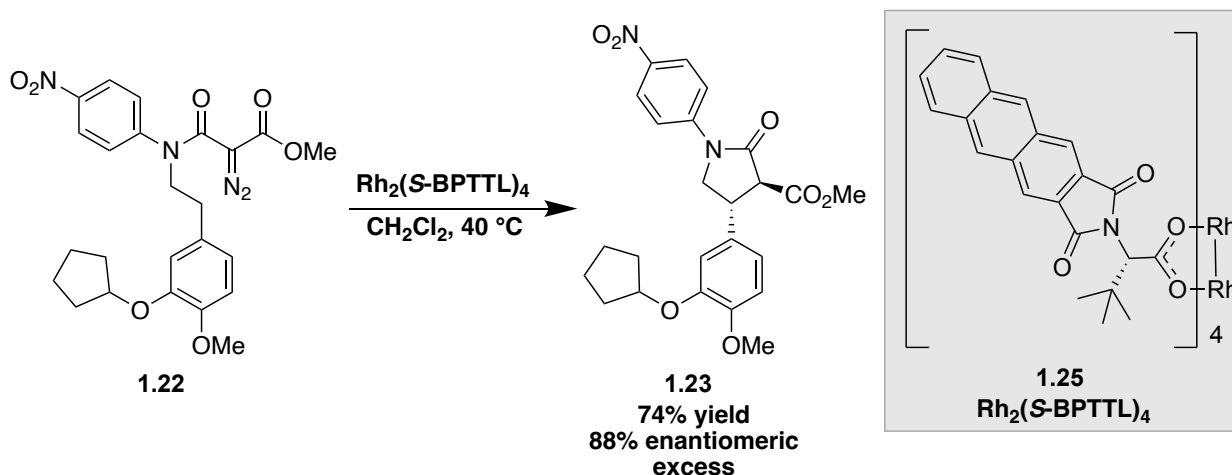
R	yield, %	ee, %
CH ₂ C ₆ H ₅	56	91
C ₂ H ₅	52	96
CH ₂ CH(CH ₃) ₂	60	95
OCH ₃	> 98	93
<i>p</i> -ClC ₆ H ₄	81	95

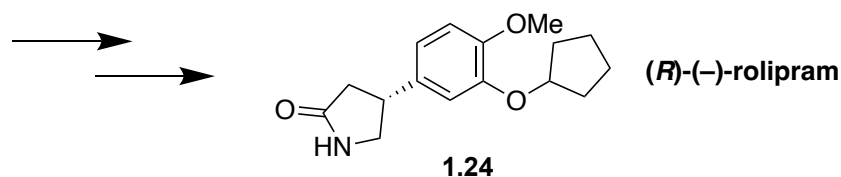


1.21
Rh₂(4S-MPPIM)₄

Table 1.2 Intramolecular C–H insertion of an acceptor-substituted carbenoid to form (*R*)-(–)-baclofen.

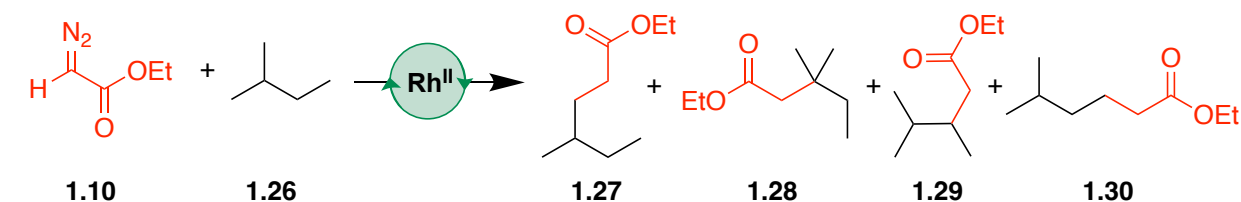
Hashimoto demonstrated the synthetic utility of the *N*-*p*-nitrophenyl substituent as a site-controlling element in the synthesis of several pharmaceutically relevant targets (**Scheme 1.2**).⁵⁷ The GABA_B receptor agonist, (*R*)-(–)-baclofen (**1.20**), and the phosphodiesterase type IV inhibitor (*R*)-(–)-rolipram (**1.23**) were efficiently prepared, with intramolecular C–H activation serving as a key step. This intramolecular C–H insertion involved an acceptor/acceptor-substituted carbenoid and was catalyzed by the chiral rhodium carboxylate catalyst Rh₂(*S*-BPTTL)₄. The resulting product (**1.23**) was attained with a notable asymmetric induction, yielding 94%, and an impressive 88% enantiomeric excess (ee).⁴⁹





Scheme 1.2 C–H functionalization of (*R*)-(-)-rolipram using acceptor/acceptor carbene.

The challenges associated with achieving regioselectivity in carbene-induced C–H functionalization initially led to significant advancements primarily in systems favorable to intramolecular reactions. However, the scope of intramolecular reactions may be limited, as they require multiple synthetic steps to prepare the substrate, which also acts as the diazo compound in this context. In contrast, intermolecular reactions offer a more versatile and practical approach to C–H functionalization, eliminating the need for a "tether" to control regioselectivity. This strategy has been successfully employed in the synthesis of several pharmaceutical agents, including (–)-enterolactone, (*R*)-(2)-baclofen, and (*R*)-(2)-rolipram as previously mentioned.



tetrakis(9-triptycenecarboxylate) (9-trp)	Rh^{II} Cat.	1.27 C₁	1.28 C₂	1.29 C₃	1.30 C₄
	Rh ₂ (OAc) ₄	1	8	90	1
	Rh ₂ (TFA) ₄	2	25	66	4
	Rh ₂ (9-trp) ₄	18	19	27	36

Table 1.3 C–H functionalization of 2-methylbutane with ethyl diazoacetate.

Traditional acceptor-only and acceptor-acceptor metallocarbenes exhibit high reactivity, often leading to poor selectivity.¹⁹ For instance, in the functionalization of 2-methylbutane using the acceptor-only diazo compound ethyl diazoacetate (**1.10**) (Table 1.3), when Rh₂(OAc)₄ was the catalyst, a mixture of products was obtained, with product (**1.29**) (resulting from insertion into the secondary C₃ position) being the major product. When electron-deficient catalyst Rh₂(TFA)₄ resulted in the more electron-rich tertiary (**1.28**) and secondary (**1.29**) products becoming the major products. Finally, using a bulky Rh₂(9-trp)₄ catalyst increased the ratio of primary C–H insertion products (**1.27** and **1.30**). Although there was a general preference for methylene C–H insertion, the regioselectivity remained poor, despite the influence of catalysts on site-selectivity in these reactions.⁵⁸

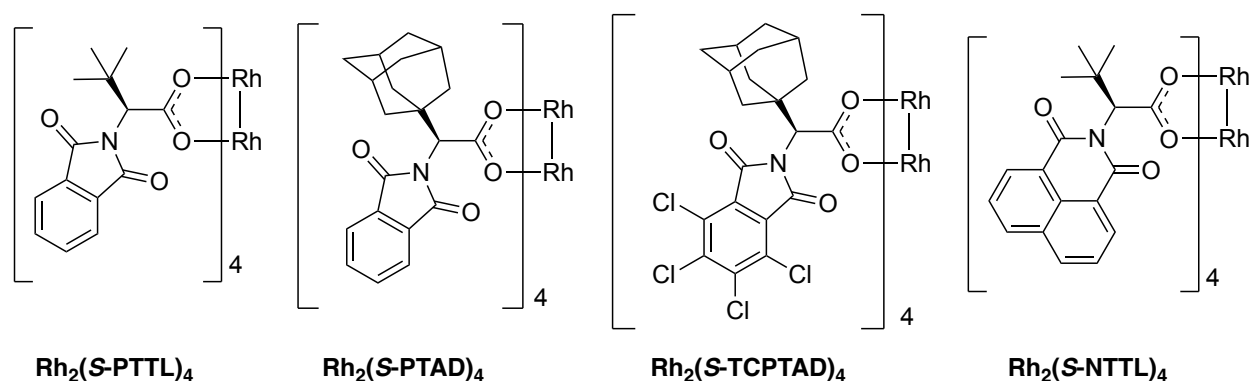


Figure 1.6 Second generation catalysts: phthalimide/naphthalimide-protected chiral ligands.

A second generation of dirhodium catalysts, ligated with N-phthalimidyl amino acids, was initially developed by Hashimoto.⁵⁹⁻⁶¹ The most notable catalyst in this class is Rh₂(S-PTTL)₄. Another catalyst in this family, Rh₂(S-PTAD)₄, reported by the Davies group, features an adamantyl group in place of a tert-butyl group (Figure 1.6).⁶² These catalysts are highly versatile, as a wide variety of chiral amino acids can be readily obtained from commercial sources. They typically adopt a C₄-symmetrical structure, and their reactivities and structural characteristics will be discussed in subsequent chapters.

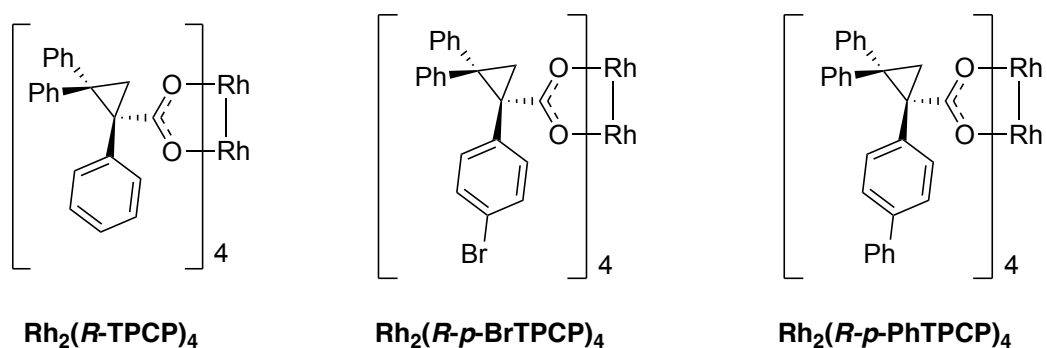


Figure 1.7 Third generation catalysts chiral TriPhenylCycloPropane (TPCP) ligands.

The third-generation catalysts are based on a chiral cyclopropane carboxylate ligands, synthesized through rhodium-catalyzed cyclopropanation reactions (**Figure 1.7**).⁶³ The initial example in this family is $\text{Rh}_2(\text{R-}p\text{-Br-TPCP})_4$, and the catalyst library has since been expanded to include the functionalized variant $\text{Rh}_2(\text{R-}p\text{-Ph-TPCP})_4$ via palladium cross coupling reaction.^{20,64} These catalysts can adopt a wide range of conformations, providing unique selectivity. Many are sterically demanding, allowing them to regioselectively functionalize the most accessible primary and secondary C–H bonds. However, synthesizing these cyclopropane ligands requires screening for a suitable catalyst for the asymmetric cyclopropanation step.^{65,66}

Catalytic carbene-transfer reactions represent a highly valuable class of transformations in organic synthesis. In the past decade, rhodium-bound donor/acceptor carbenes have greatly advanced in organometallic chemistry, enabling a wide range of valuable transformations, particularly in intermolecular carbene chemistry. These transformations include cyclopropanation,⁶⁷⁻⁷⁰ cyclopropanation,^{71,72} C–H functionalization,⁴⁹ cycloaddition,^{73,74} ylide formation,^{75,76} and vinylogous^{77,78} reactivity (**Figure 1.8**), all of which produce valuable components for further derivatization, total synthesis of natural products, and the creation of medically relevant compounds.⁷⁹⁻⁸²

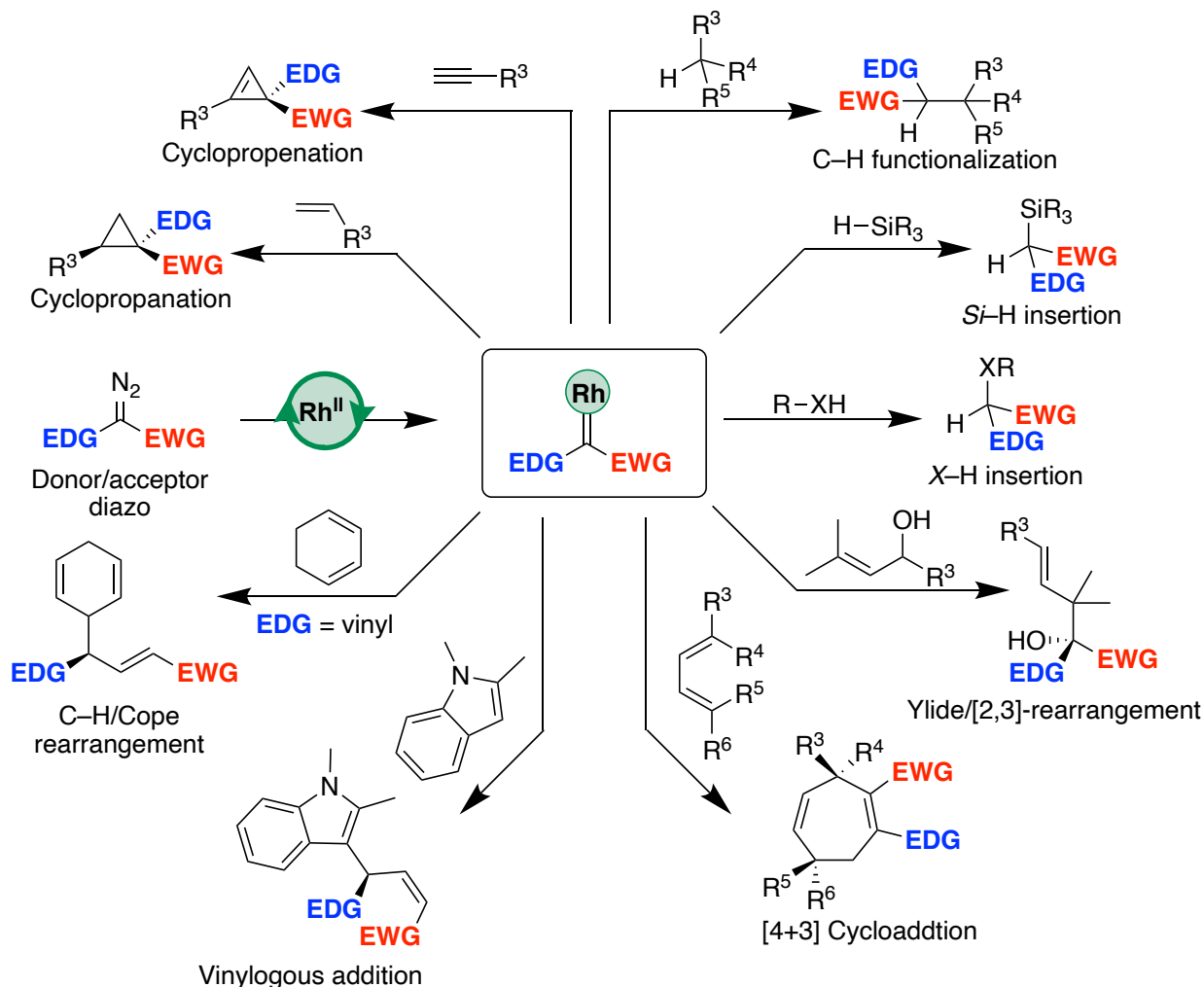
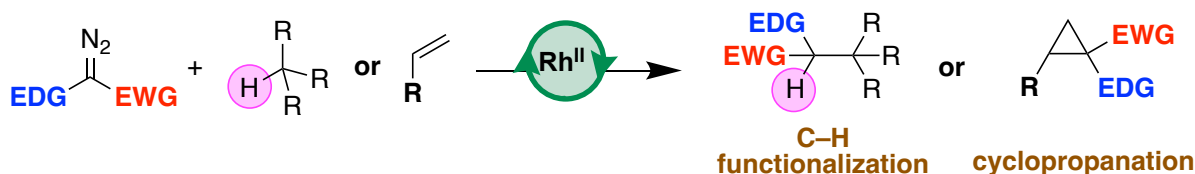


Figure 1.8 Selected reaction of donor/acceptor metallocarbenes.

Donor/acceptor rhodium carbenes exhibit enhanced sensitivity to both steric and electronic factors, enabling selective functionalization at primary, secondary, and tertiary sites. Competition experiments between different substrates reveal the general reactivity trends of various C–H bonds toward functionalization (**Figure 1.9**). Sites that stabilize positive charge build-up are particularly susceptible to C–H functionalization. For instance, 1,4-cyclohexadiene undergoes C–H functionalization 26,000 times faster than cyclohexane, surpassing even the reaction rate of styrene cyclopropanation. C–H sites adjacent to a heteroatom, such as those in tetrahydrofuran and *N*-Boc-

pyrrolidine, react over 1,000 times faster than cyclohexane. However, the rate of C–H functionalization is not solely dictated by electronic factors. For example, the insertion into tertiary C–H bonds of 2-methylbutane and 2,3-dimethylbutane, which should be electronically more favorable than secondary C–H bonds, occurs over 10 times slower than in cyclohexane.



26,000	24,000	2700	1700	1.0	0.66	0.078	0.011

Figure 1.9 Rates of reactivity for rhodium carbene C–H insertion of various substrates.

The electronic nature of the C–H bond is crucial in concerted asynchronous hydride transfers during C–H insertion events. The most reactive C–H bond is the one that best stabilizes a carbocation in the transition state (**Figure 1.10**). Therefore, considering electronic effects, the reactivity order is tertiary > secondary > primary C–H bonds. However, donor/acceptor rhodium carbenes are sterically demanding, making the steric nature of the C–H bond also a factor in selectivity and reactivity. From a steric perspective, reactivity decreases from primary to secondary to tertiary C–H bonds. Balancing these factors, C–H insertion reactions typically occur preferentially at secondary sites.⁸³

An important aspect of the Davies group's C–H functionalization program is the strategic use of donor/acceptor carbenes with the appropriate rhodium catalyst. This approach has been

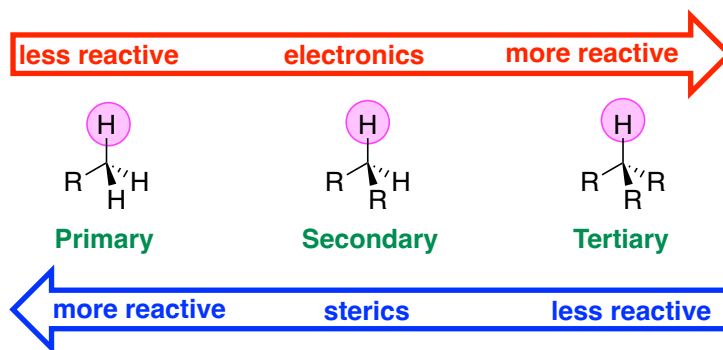
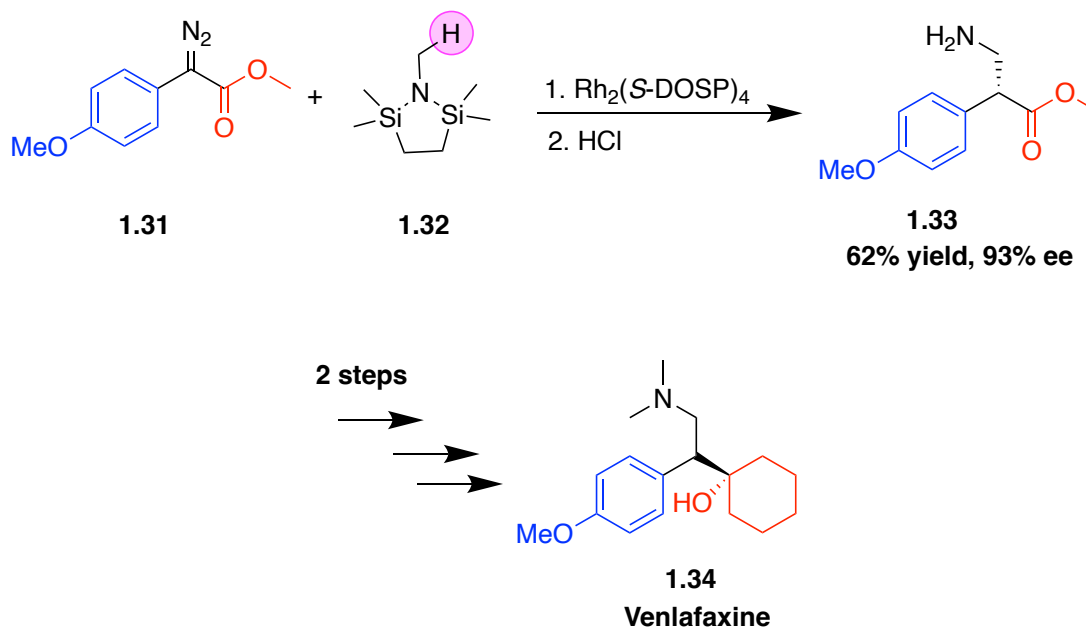


Figure 1.10 Electronic and steric effects of C–H insertion with donor/acceptor carbenes.

applied to functionalizing primary C–H bonds in important synthetic targets (**Scheme 1.3**). For instance, protected methylamine (**1.32**), used with donor/acceptor carbene (**1.31**) in the presence of $\text{Rh}_2(\text{S-DOSP})_4$, produced the desired product (**1.33**) with a 62% isolated yield and 93% ee.⁸⁴ This product was further derivatized to form venlafaxine, a medication classified as a selective serotonin and norepinephrine reuptake inhibitor (SNRI).⁸⁵



Scheme 1.3 C–H functionalization of venlafaxine using protected methylamine.

In the Davies group, significant progress has been made in developing catalysts capable of functionalizing challenging C–H bonds, particularly when the bond is not electronically activated (**Figure 1.11**). Significant progress has been made in developing catalysts capable of functionalizing challenging C–H bonds in the Davies group, significantly when the bond of interest is neither electronically activated nor adjacent to a directing group. This approach is exemplified by the selective functionalization of pentane derivatives using donor/acceptor carbenes (**Figure 1.11**). Notably, the catalyst $\text{Rh}_2[\text{R-3,5-di}(p\text{-}^t\text{BuPh})\text{TPCP}]_4$ has demonstrated functionalizing the most accessible secondary C–H bond in these substrates.⁶⁶ Following this discovery, related efforts have enabled the site-selective functionalization of the most accessible primary C–H bonds using the bulkier catalyst $\text{Rh}_2[\text{R-3,5-tris}(p\text{-}^t\text{BuPh})\text{TPCP}]_4$ and tertiary C–H bonds using $\text{Rh}_2(\text{R-TCPTAD})_4$. Based on the steric elements of these catalysts, these changes have expanded the scope from simple hydrocarbons to more complex targets, such as for cholesteryl, phytol pivalate, and vitamin E derivatives.^{23,24,86}

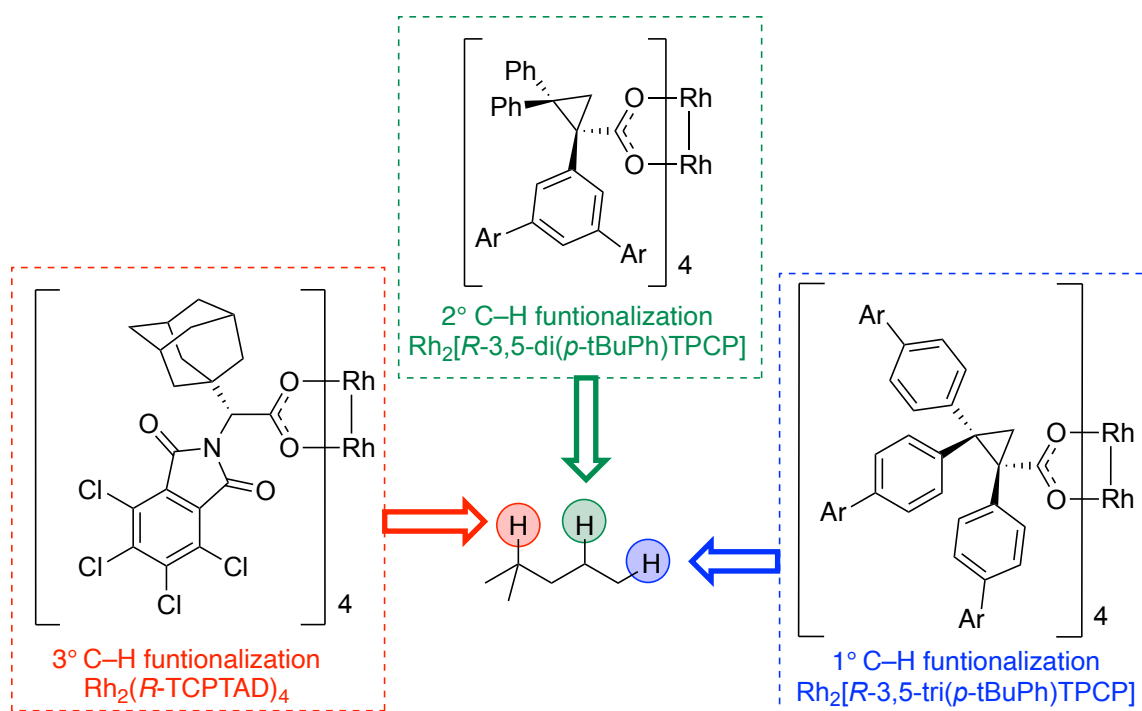
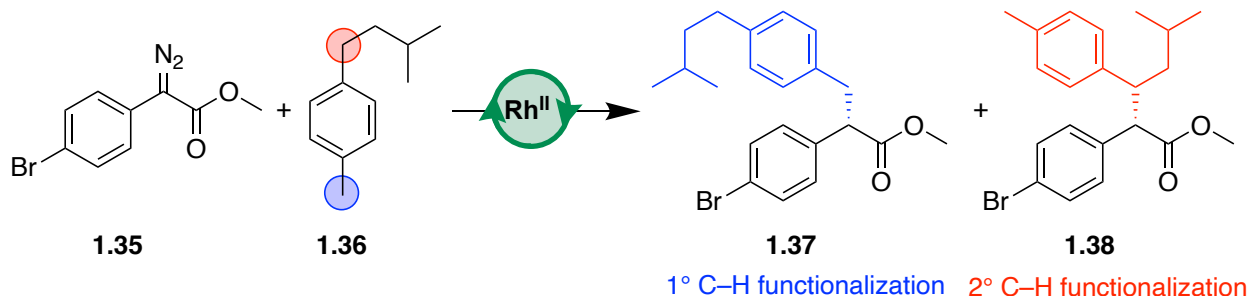


Figure 1.11 Selective C–H functionalization of not electronically activated pentane derivatives.

Recently, Davies and coworkers demonstrated that these catalysts can efficiently modify less reactive primary methyl groups that are more accessible due to steric factors (**Table 1.4**). In particular, when substrate (**1.36**), which featured competing secondary and primary C–H bonds, was subjected to functionalization using $\text{Rh}_2(R\text{-DOSP})_4$ as the catalyst, the secondary C–H insertion product (**1.38**) became the major product with a combined 70% yield with 77% ee for (**1.37**). In contrast, utilizing a bulkier $\text{Rh}_2(R\text{-}p\text{-PhTPCP})_4$ catalyst resulted in the exclusive production of product (**1.37**) with an excellent yield of 82% with 95% ee. Considering the steric properties of these catalysts, these modifications have broadened the range of applicable substrates beyond basic hydrocarbons to encompass more intricate compounds, including (–)- α -Cedrene and steroid derivatives.²⁰



entry	catalyst	yield%	1.37 : 1.38	ee for 1.37
1	$\text{Rh}_2(R\text{-DOSP})_4$	70% ^a	1 : 1.7	77%
2	$\text{Rh}_2(R\text{-}p\text{-PhTPCP})_4$	82% ^b	>20 : 1	95%

^aCombined yield for **1.37** and **1.38**. ^bYield for **1.9**.

Table 1.4 Selective C–H Functionalization Activated Primary C–H Bonds.

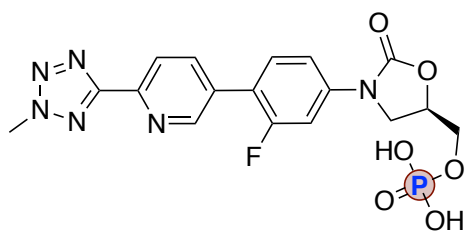
1.12 Conclusion

In summary, extensive research has been conducted on the chemistry involving rhodium-bound donor/acceptor carbenes, resulting in numerous valuable transformations. C–H insertion is particularly interesting, as it offers a novel approach for functionalizing activated and unactivated bonds. Despite the longstanding recognition of rhodium carbene chemistry, it has evolved into a potent approach for selectively modifying simple molecules and intricate targets. A key factor contributing to its effectiveness is the introduction of donor/acceptor carbenes. The once challenging task of managing their high reactivity has been successfully mitigated through ongoing refinement of their structures. The primary focus of this thesis revolves around broadening the range of reactions involving donor/acceptor carbenes using dirhodium tetracarboxylate catalyst through efficient, and selective transformations.

Chapter 2: Enantioselective Intermolecular C–H Functionalization of Primary Benzylic C–H Bonds Using ((Aryl)(diazo)methyl)phosphonates

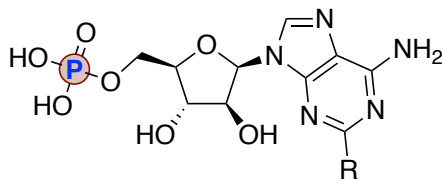
2.1 Introduction

The synthesis of phosphonate-containing compounds continues to be a topic of interest due to their relevance in various fields.^{87,88} Phosphorus-containing compounds hold biological significance and are extensively used in numerous industrial, medicinal, and synthetic applications. Tedizolid phosphate (Sivextro) is a key protein synthesis inhibitor that targets the 50S ribosomal subunit and belongs to the oxazolidinone class of antibiotics. Vidarabine monophosphate, a phosphorylated form of vidarabine, is effective in treating systemic herpes virus infections. Cardiovascular drugs such as fostedil and mifobate are currently in clinical trials (**Scheme 2.0**).⁸⁹⁻⁹¹ Compounds featuring a phosphorus functionality at the α -position relative to the diazo group, known as λ^3 and λ^5 -phosphorus-containing α -diazo compounds, constitute a large and highly versatile class of reagents in organic chemistry. These compounds are especially valuable in synthesizing phosphonate- and phosphine oxide-functionalized molecules. Due to their high reactivity, diazo groups can participate in various chemical transformations, including C–H functionalization and cyclopropenation.^{92,93} The importance of synthesizing a comprehensive library of different phosphonate classes containing compounds is of most interest. Traditional synthesis of phosphonate containing molecules employs the Michael-Arbuzov reaction developed in the past. Modern-day techniques have allowed mass production of elemental phosphorus in various forms, particularly phosphonates or phosphonic acids.⁹⁴⁻⁹⁶



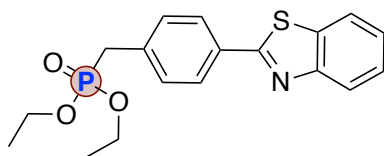
**Tedizolid Phosphate
(Sivextro)**

Treats acute bacterial skin
and skin structure infections



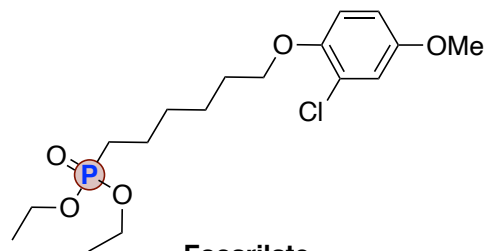
R = H, Vidarabine Monophosphate
R = F, Fludarabine Phosphate
R = NH₂, Triciribine Phosphate

Antiviral, active against herpes viruses, poxviruses,
rhabdoviruses, hepadnaviruses and some RNA tumour viruses



Fostedil

Cardiovascular drug



Fosarilate

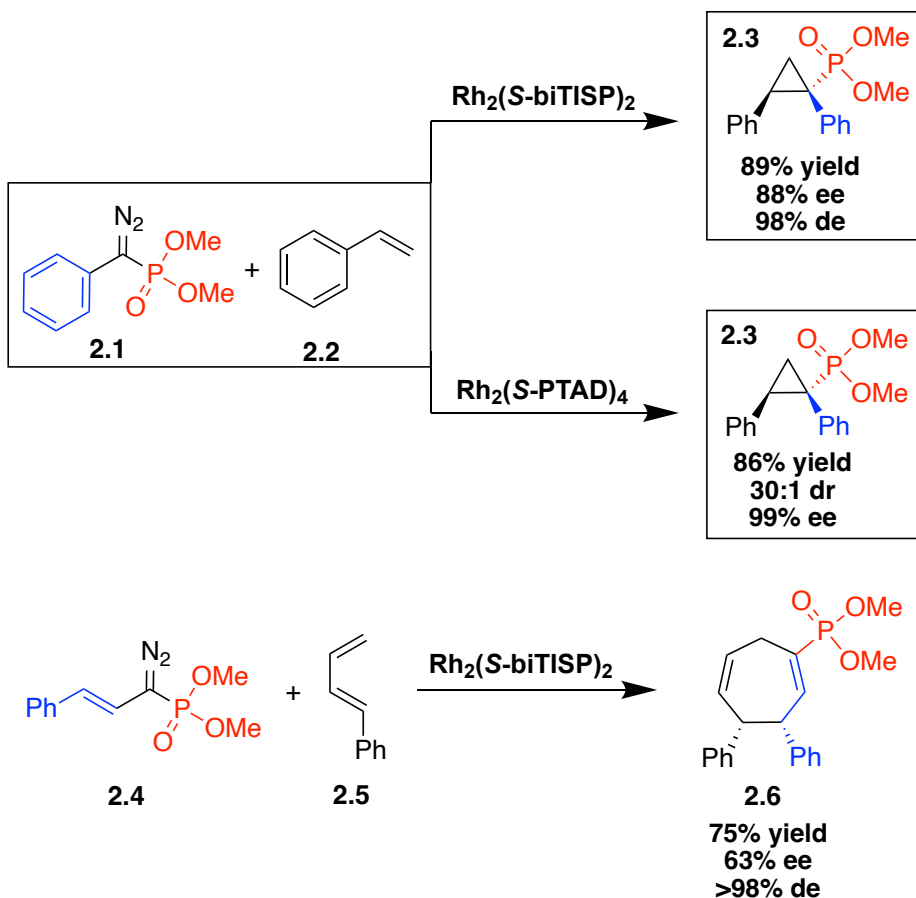
Antiviral drug

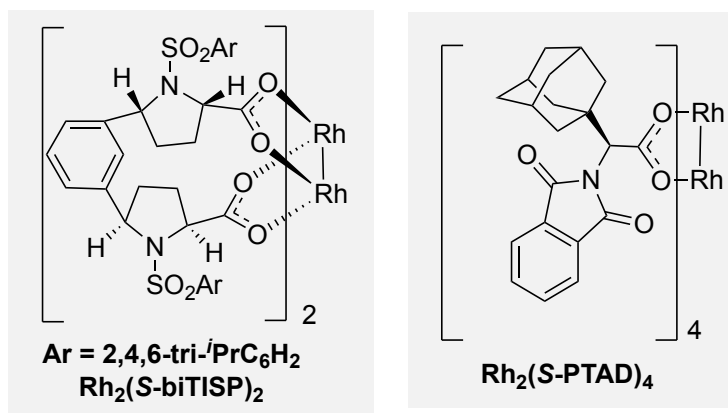
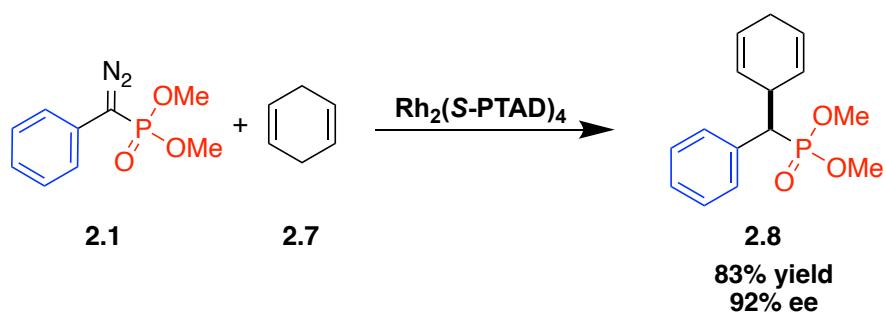
Scheme 2.0 Structures of phosphonate drugs and bioactive molecules.

Catalyst-controlled C–H functionalization using donor/acceptor carbenes is an efficient process capable of high site control and stereo control levels. This study demonstrated that the scope of the donor/acceptor carbene C–H functionalization could be extended to systems where the acceptor group is phosphonate. Recently, rhodium catalyzed intermolecular C–H functionalization with ((aryl)(diazo) methyl)phosphonates has surfaced as a promising alternative to the conventional α -diazoacetate compounds used as carbene precursors.⁹⁷⁻⁹⁹ Davies and coworker have made significant advances in the field of selective intermolecular carbene reactions by pioneering the concept of donor/acceptor carbenes and creating a variety of chiral catalysts with different steric and electronic characteristics for various uses.^{19,37,48,49}

In 2004, Davies and coworkers introduced a general method for the enantioselective synthesis of cyclopropylphosphonates with a quaternary stereocenter, using *D*₂-symmetric dirhodium complexes as catalysts, specifically Rh₂(*S*-biTISP)₂ (**Scheme 2.1**). The asymmetric

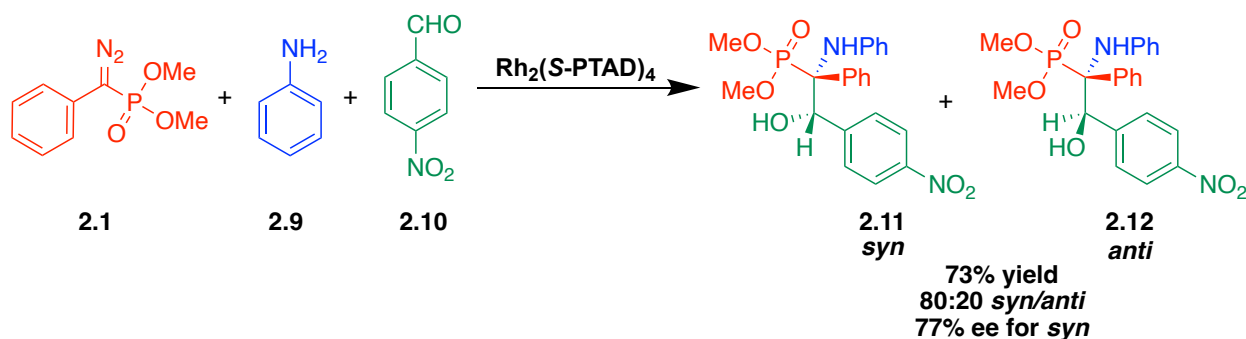
cyclopropanation of arylphosphonyldiazoalkanes catalyzed by $\text{Rh}_2(\text{S-biTISP})_2$ is highly stereoselective. Additionally, the first example of an asymmetric cyclopropanation/Cope rearrangement using a vinylphosphonyldiazoalkane has been successfully demonstrated.¹⁰⁰ In 2006, Davies and coworkers demonstrated that the phthalimido catalyst $\text{Rh}_2(\text{S-PTAD})_4$ is a promising alternative to $\text{Rh}_2(\text{S-biTISP})_2$. While $\text{Rh}_2(\text{S-biTISP})_2$ has proven to be highly effective, it has certain limitations, particularly due to the complex steps required to access this catalyst. Furthermore, the C–H activation of 1,4-cyclohexadiene by diazophosphonate using the phthalimido catalyst $\text{Rh}_2(\text{S-PTAD})_4$ was demonstrated, achieving a high yield of 83% and excellent enantioselectivity of 92% ee.⁶²





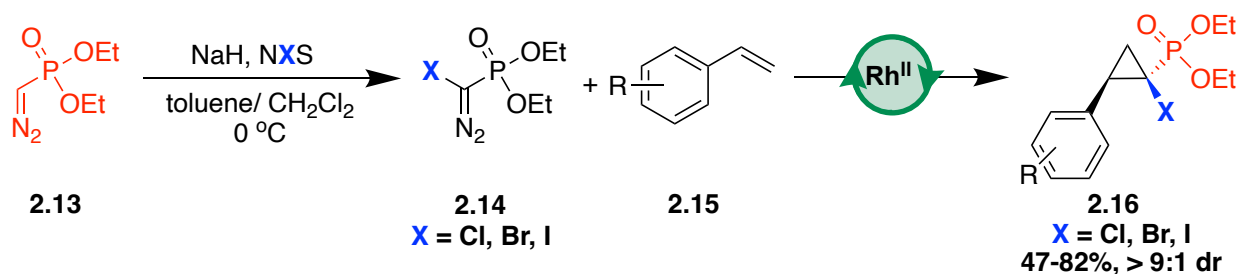
Scheme 2.1 Cyclopropanation and C–H functionalization using dirhodium catalyst.

In 2012, Che and coworkers developed a highly enantioselective metal-catalyzed three-component coupling reaction of diazophosphonates, anilines, and electron-deficient aldehydes. Using the chiral rhodium catalyst $\text{Rh}_2(\text{S-PTAD})_4$, a series of α -amino- β -hydroxyphosphonates were obtained in good to high yields and with good to high enantioselectivities (**Scheme 2.2**).⁹⁷ They examined C–H insertion reactions for the three-component coupling reactions (**2.1**, **2.9**, and **2.10**). With $\text{Rh}_2(\text{S-PTAD})_4$ as the catalyst, compounds (**2.11** and **2.12**) were obtained in a 73% yield, with a syn/anti ratio of 80:20 and an enantioselectivity of 77% ee for the syn product. Notably, the high degree of enantio-control provides evidence supporting the involvement of a metal-bound ammonium ylide intermediate during the nucleophilic addition step.



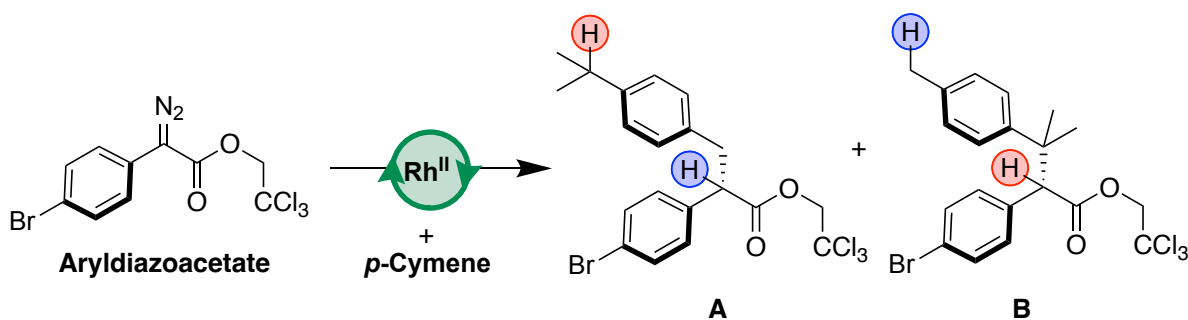
Scheme 2.2 Dirhodium catalyzed enantioselective reaction of diazophosphonates, anilines, and electron-deficient aldehydes.

In 2012, Hansen and coworkers developed a convenient, one-pot procedure for the generation of halodiazophosphonates and their subsequent diastereoselective intermolecular cyclopropanation with styrene derivatives with various dirhodium catalysts (**Scheme 2.3**).¹⁰¹ Moderate to high yields as well as high diastereomeric ratios were obtained, and low catalyst loadings of 0.1 mol % was achieved. Therefore, a solution of diethyl diazomethylphosphonate (**2.13**) in dry dichloromethane was added dropwise over a period of 2 h to a mixture containing $\text{Rh}_2(\text{esp})_2$, NXS, NaH, and styrene (**2.15**) at 0 °C in a one-pot reaction mixture. This reaction yielded cyclopropane (**2.16**) in an isolated yield from 47-82%, predominantly as a >9:1 trans/cis mixture, with minimal dimerization of the diazo compound.



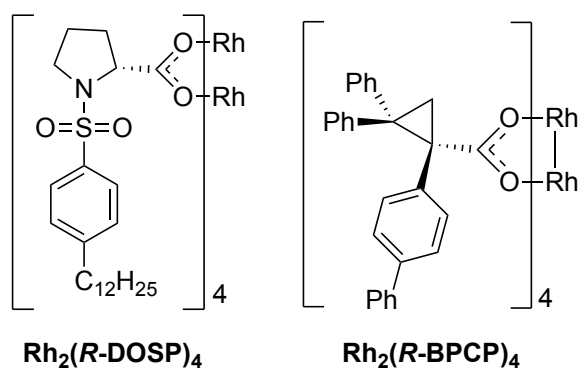
Scheme 2.3 One-pot procedure of Halodiazophosphonates for diastereoselective intermolecular Rh(II) catalyzed cyclopropanation.

In 2014, Davies and coworkers demonstrated that dirhodium tetraproline-catalyzed reactions of aryldiazoacetates tend to preferentially functionalize secondary and tertiary C–H bonds due to a balance of steric and electronic effects. Conversely, the bulkier dirhodium tetrakis(triarylcyclopropanecarboxylate) catalysts, such as dirhodium tetrakis[(*R*)-(1-(biphenyl)-2,2-diphenylcyclopropanecarboxylate)] [$\text{Rh}_2(\text{R-BPCP})_4$], is more effective in targeting activated primary C–H bonds. This approach offers a highly selective method for the C–H functional-ization of primary C–H bonds and has been successfully applied to complex molecules like (–)- α -cedrene and a steroid. This research demonstrates that highly site-selective C–H functional-ization can be achieved without using directing groups. The standard dirhodium catalyst, $\text{Rh}_2(\text{R-DOSP})_4$ was used it gave a mixture of primary and tertiary C–H functionalization products (**A**:**B** = 1:4). However, when $\text{Rh}_2(\text{R-BPCP})_4$ was used, the primary C–H functionalization product **A** was selectively formed (**A**:**B** >20:1) in 75% isolated yield and 97% ee (**Table 2.1**).²⁰



catalyst	ratio A:B	yield	ee (%) A
$\text{Rh}_2(\text{R-DOSP})_4$	1:4	72	73
$\text{Rh}_2(\text{R-BPCP})_4$	>20:1	75	97

Table 2.1 C–H functionalization of isopropyltoluene using $\text{Rh}_2(\text{R-BPCP})_4$.



The reaction involving aryldiazophosphonates is particularly significant to Davies's group due to the synthetic challenge of introducing stereocenters at the alpha positions of phosphonates. The tetrahedral nature of phosphonates presents more steric hindrance than trigonal esters, which could be beneficial for selective primary C–H functionalization. Previously, Davies's group demonstrated that cyclopropanation of styrenes using diazophosphonates resulted in high yields, diastereoselectivity, and enantioselectivity, as illustrated in (**Scheme 2.1**). Significant advancements have been made in developing synthetically useful processes using directing groups that coordinate with metal catalysts, thereby organizing the system to react with a specific C–H bond.¹⁰²⁻¹⁰⁵ Although this method has been highly effective, achieving site selectivity through catalyst control without the need for a directing group would be preferable. A practical strategy involves group transfer reactions that do not require prior coordination to directing groups.¹⁰⁶ The most common group transfer reactions involve transition-metal-catalyzed carbenes,^{19,24,107,108} nitrenes,^{109,110} and oxo species.¹¹¹⁻¹¹³ Recent advancements have further refined this approach by employing synthetic enzymes that offer site- and stereoselectivity.^{114,115}

The metal-catalyzed reactions of diazo compounds are highly versatile in organic synthesis. The high-energy metal carbenoid intermediates can facilitate various valuable transformations, such as cyclopropanation, ylide formation, and C–H insertion. Among these, metal carbenoids'

intermolecular C–H insertion is the most adaptable reaction for stereoselective C–H functionalization. The most selective system has been the donor/acceptor carbenes because they have several components that can be manipulated to influence the outcome of the C–H functionalization. The donor/acceptor carbenes have proven to be the most selective system due to their multiple components, which can be adjusted to influence the outcome of C–H functionalization (**Figure 2.1**).¹¹⁶ The acceptor group ensures that the carbene is sufficiently electrophilic to be capable of reacting with C–H bonds, whereas the donor group modulates the reactivity, making the system highly susceptible to catalyst control.



Figure 2.1 C–H functionalization with donor/acceptor carbenes.

Various chiral dirhodium catalysts have been developed to control the regio- and stereochemical outcomes of C–H functionalization reactions.^{24,117} Most research has focused on using aryldiazoacetates as carbene precursors, enabling selective reactions at primary, secondary, or tertiary C–H bonds based on the chosen catalyst.^{23,66,86} Fine-tuning can be achieved by altering the donor and acceptor groups. For instance, while methyl esters (**2.17**) are effective carbene precursors for functionalizing activated C–H bonds (benzylic, allylic, or α to oxygen or nitrogen),¹⁹ trichloroethyl esters (**2.18**) are superior for reactions at unactivated C–H bonds.^{23,66} To further broaden the scope of C–H functionalization with donor/acceptor carbenes, we explored using phosphonates as the acceptor group (**2.1**). This approach offers exciting possibilities because the resulting carbenes are more sterically demanding than their ester counterparts.

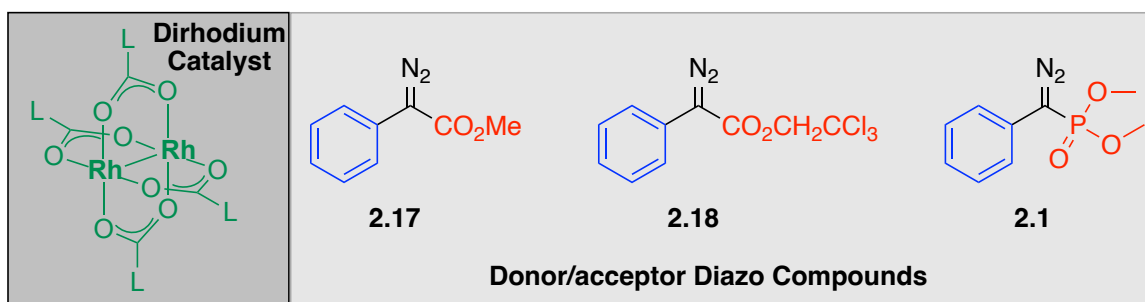
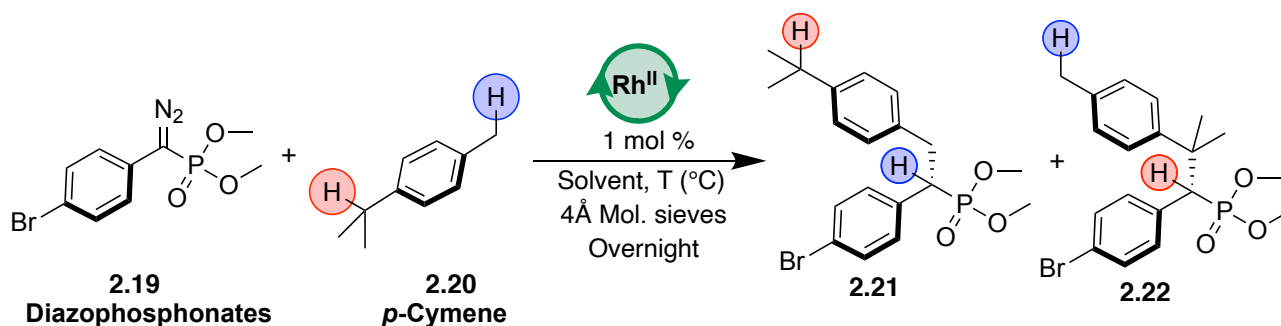


Figure 2.2 Chiral dirhodium catalysts and donor/acceptor diazo compounds.

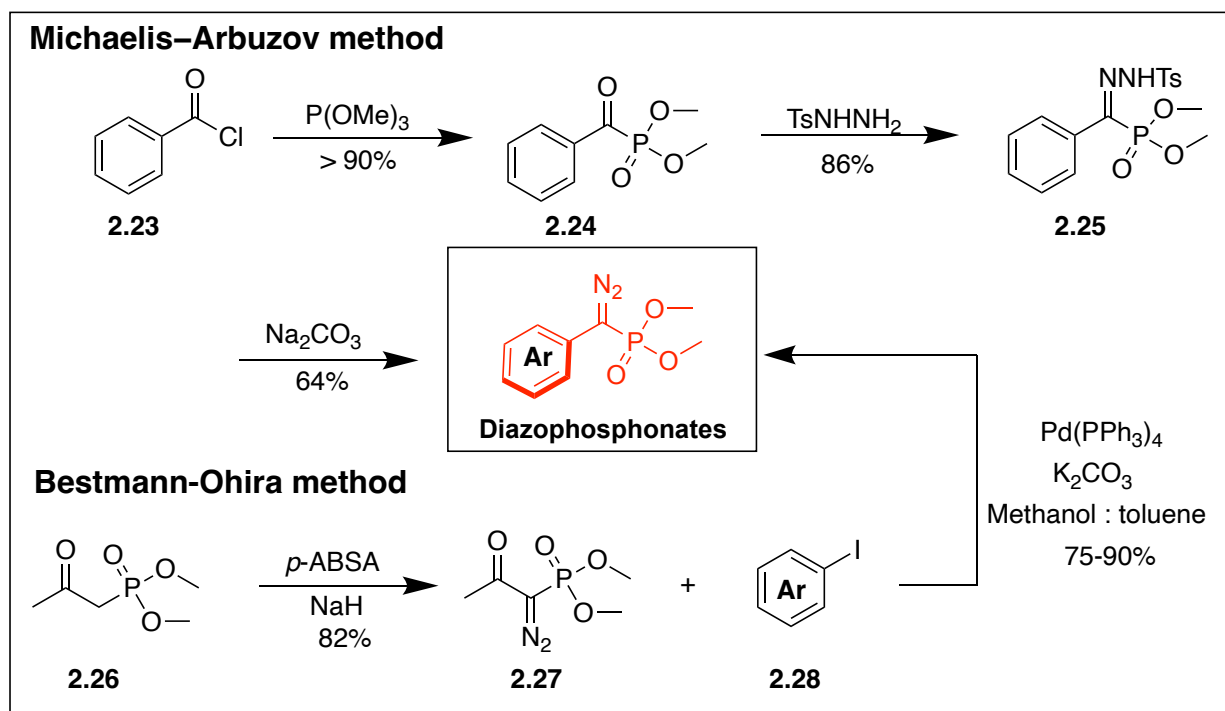
The initial catalyst studies were conducted by an exchange graduate student, Dr. Bianca Matsuo, from the Federal University of São Carlos in Brazil. She utilized four different types of rhodium catalysts, as shown in (Table 2.2) below. An excess amount of *p*-Cymene was used along with various solvent screenings. The reactions involved the slow addition of the diazo compound and were stirred overnight. The reaction did not reach completion, yielding very poor results of about 20-30% yield and the ratio of the products **2.21** and **2.22** were not provided. Her catalyst screening determined that $\text{Rh}_2(\text{R-PTAD})_4$ is the optimum catalyst and it produced an unexpected C–H insertion at the primary position of *p*-Cymene, although with poor yields.



entry	cat.	solvent	temp.	yield, %
1	$\text{Rh}_2(\text{R-PTAD})_4$	Pentane	50 °C	22%
2	$\text{Rh}_2(\text{R-PTAD})_4$	DCM	40 °C	30%
3	$\text{Rh}_2(\text{S-TPPTTL})_4$	DCE	84 °C	—
4	$\text{Rh}_2(\text{S-TCPTAD})_4$	DCE	84 °C	—
5	$\text{Rh}_2(\text{S-2-Cl-5-Br-TPCP})_4$	Pentane	50 °C	—

Table 2.2 Initial catalyst studies.

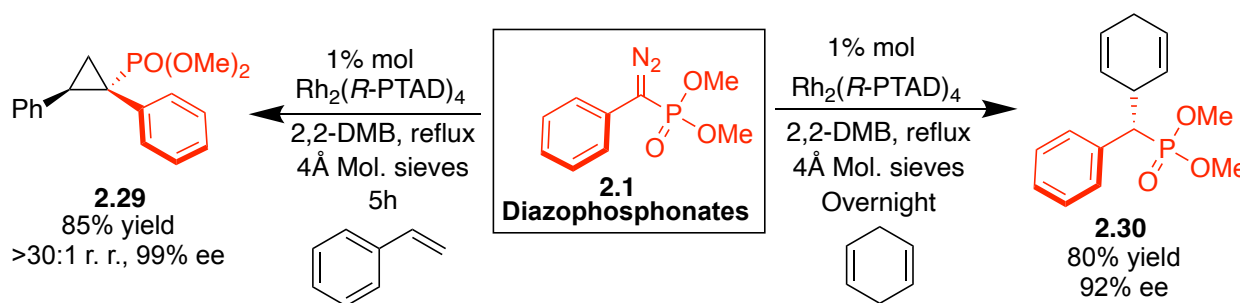
Like any other graduate student in Davies's lab, it is essential to synthesize the appropriate diazo species due to their extensive use in our research. Two methods are commonly employed to synthesize diazophosphonates: the Bestmann-Ohira method and the Michaelis-Arbuzov reaction (**Scheme 2.4**).¹¹⁸⁻¹²⁴ We successfully synthesized diazophosphonates using both techniques. However, the Michaelis-Arbuzov method involves three steps and takes three days to complete. In contrast, the Bestmann-Ohira method, which consists of only two steps, can be completed in less than two days with high yields, and is compatible with many different aromatic partners.^{124,125}



Scheme 2.4 Synthetic method for diazophosphonate using Bestmann-Ohira or Michaelis-Arbuzov methods.

Once a large batch of diazophosphonates was synthesized, we conducted several standard reactions previously reported in the literature (**Scheme 2.5**). These included enantioselective intermolecular cyclopropanation and C-H insertion of cyclohexa-1,4-diene, which achieved high yields (80-85%) (**2.29 and 2.30**) and excellent diastereoselectivity and enantioselectivity (92-99% ee), consistent with our previously reported data. The success of these reactions was attributed to

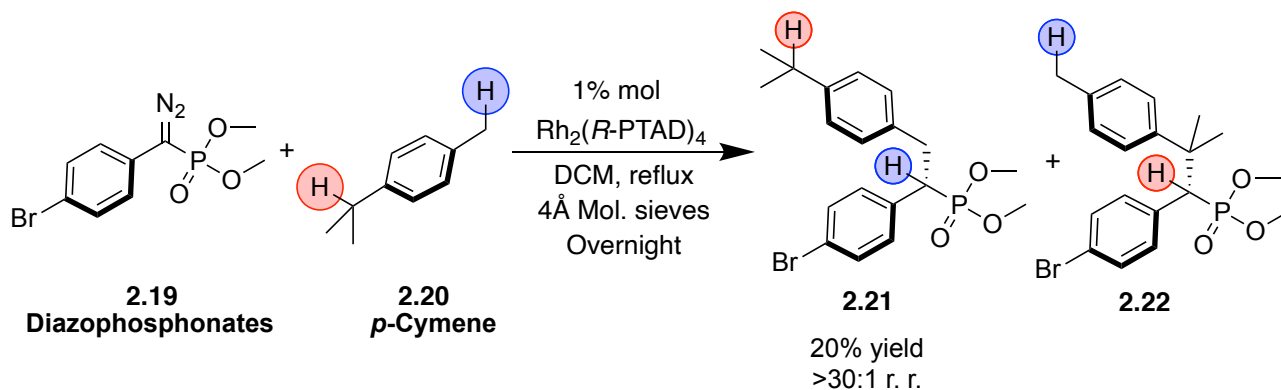
conducting them under drying conditions with 4Å molecular sieves, reflux condition and using 2,2-DMB as a solvent. 2,2-Dimethylbutane, a branched alkane (C₆H₁₄), was once widely used as a solvent in various chemical processes. However, due to evolving industrial standards, environmental regulations, and the availability of safer alternatives, its use has significantly declined. It has been discontinued in many countries, including the United States. One major factor behind this decline is its volatility and flammability, which present safety risks, particularly in large-scale reactions. Furthermore, as industries increasingly adopt greener and more sustainable practices, 2,2-dimethylbutane, a hydrocarbon-based solvent, falls short due to its lack of biodegradability and its contribution to volatile organic compound (VOC) emissions. Its reduced use reflects the broader shift toward environmentally friendly and safer solvent alternatives in both academic and industrial contexts.



Scheme 2.5 Enantioselective intermolecular cyclopropanation and C–H functionalization.

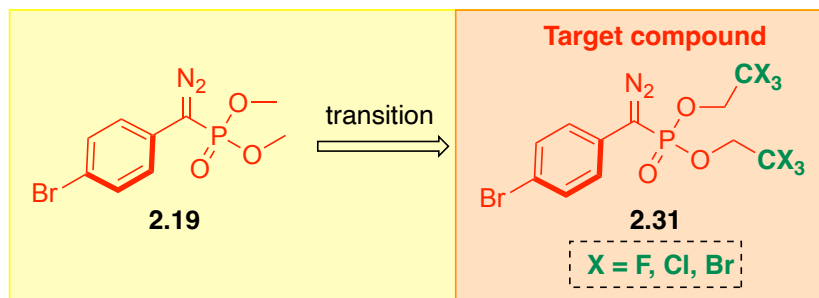
To assess the steric profile of diazophosphonates, we examined the reaction with *p*-Cymene (**Scheme 2.6**). Conducting the experiment under the same conditions as previously described yielded results similar to Dr. Bianca's; the reaction did not reach completion, and diazophosphonate was recovered without any side products. This study confirmed that $\text{Rh}_2(\text{R-PTAD})_4$ produced the C–H functionalization product (**2.21**) with a low yield of 20% but showed a strong preference towards

primary C–H functionalization site (>30:1 r.r.). This result demonstrated a significant difference because, typically, $\text{Rh}_2(\text{R-PTAD})_4$, being a non-bulky catalyst, reacts at tertiary or secondary sites rather than primary sites when aryldiazoacetates are used.

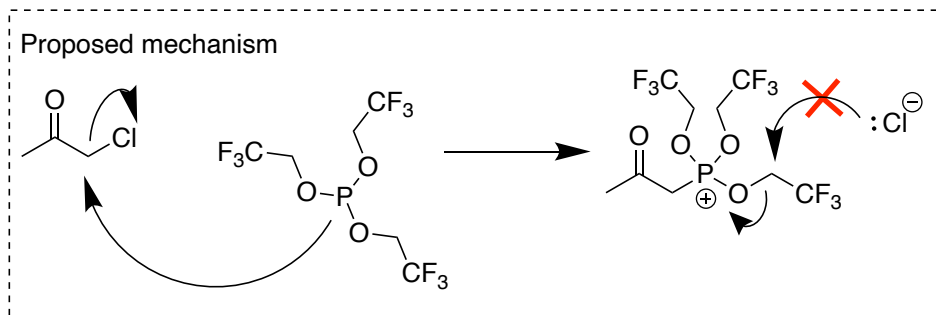
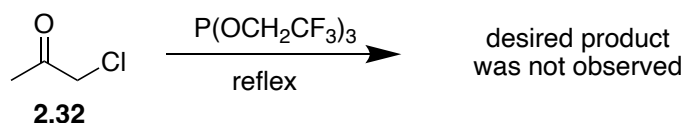


Scheme 2.6 C–H functionalization on *p*-cymene using diazophosphonate.

Building on our previous work on diazoacetates, we discovered that replacing the methyl ester group with trihaloethyl esters significantly improved the C–H functionalization of both activated and unactivated C–H bonds with high yields and enantioselectivity. However, synthesizing phosphonates containing trihaloethyl esters proved challenging as they had not been previously reported. Neither the Bestmann–Ohira method nor the Michaelis–Arbuzov reaction succeeded in synthesizing diazophosphonates with trihaloethyl esters (**Figure 2.3**). As shown in the schemes, esterification and the $\text{S}_{\text{N}}2$ steps did not occur due to the electronic and inductive effects of the halogens.



Bestmann-Ohira method



Michaelis-Arbuzov method

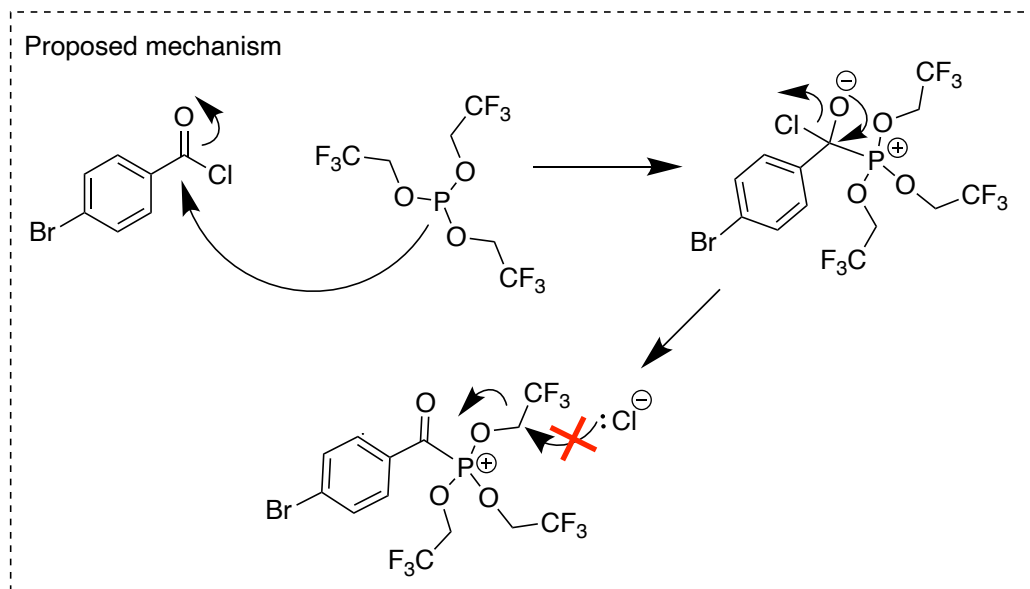
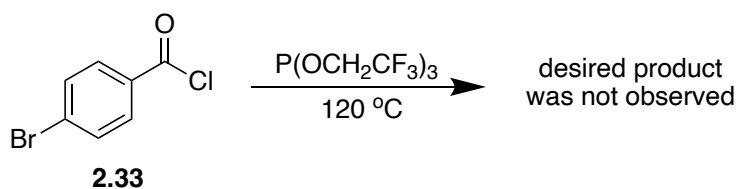
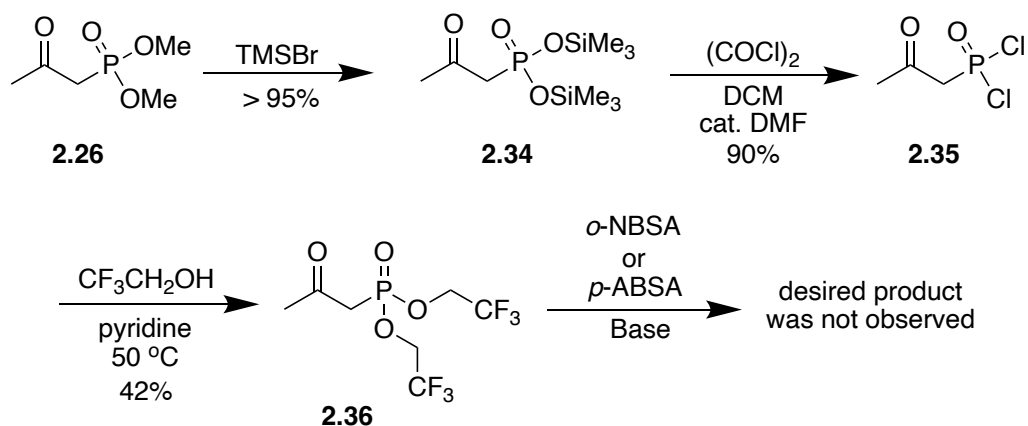


Figure 2.3 Bestmann-Ohira and Michaelis-Arbuzov methods proposed mechanism.

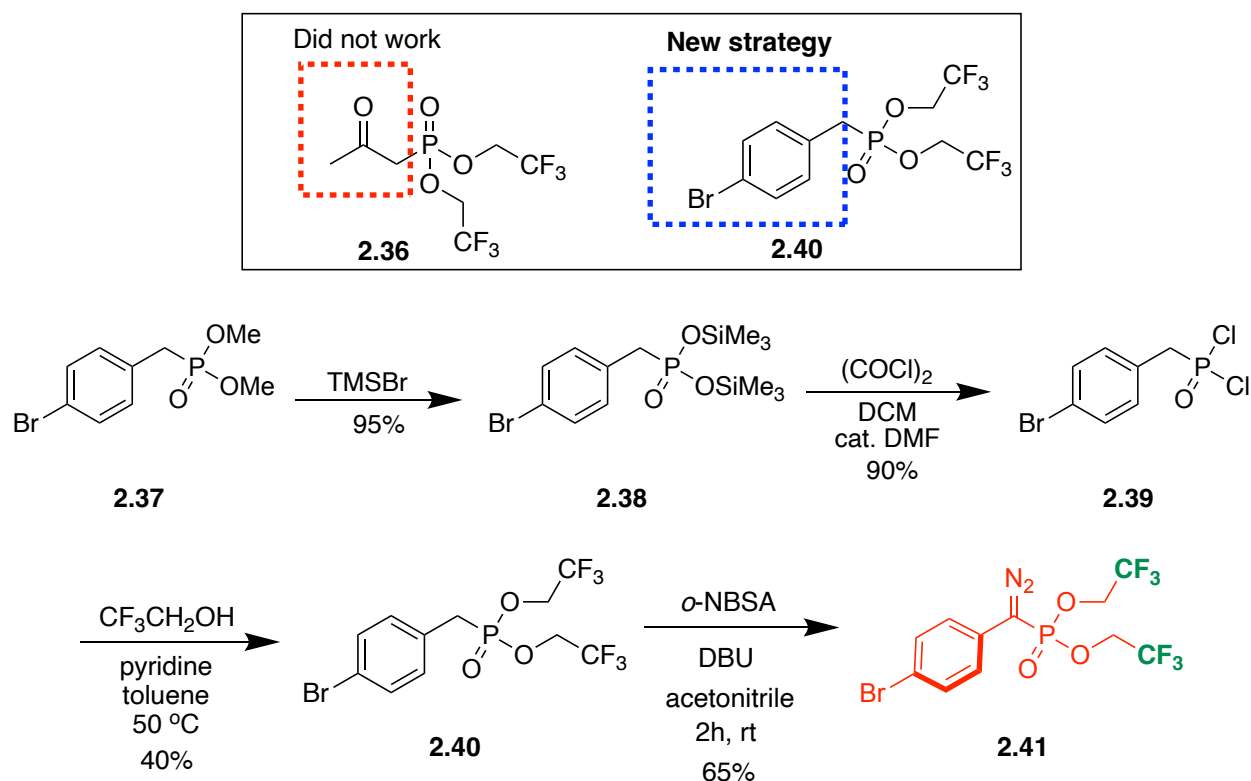
The Still-Gennari method, later refined by Molnar and coworkers, provided an esterification technique to attach a trifluoroethyl ester functional group (**Scheme 2.7**).¹²⁶⁻¹²⁸ This process involved

using trimethylsilyl bromide (TMSBr) to remove the methyl ester forming (**2.34**) in excellent yield 95%, followed by chlorination with oxalyl chloride (COCl)₂ forming (**2.35**) with 90% yield. The resulting product was then reacted with 2,2,2-trifluoroethanol in the presence of a base to complete the esterification product (**2.36**) in 42% yield. However, when this intermediate was used in the diazo transfer reaction, it resulted in multiple unverified products without forming the desired diazophosphonate.



Scheme 2.7 Preparation of trihaloethyl esters diazophosphonates.

We revised our strategy and applied the Still-Gennari method with a new species dimethyl (4-bromobenzyl)phosphonate (**2.37**) (**Scheme 2.8**). Using trimethylsilyl bromide (TMSBr), we removed the methyl ester, forming (**2.38**) in an excellent yield of 95%, followed by chlorination with oxalyl chloride (COCl)₂, forming (**2.39**) with a 90% yield. The resulting product was then reacted with 2,2,2-trifluoroethanol in the presence of a base to complete the esterification, producing (**2.40**) in moderate yield of 40%. This intermediate was used in the diazo transfer reaction with *o*-Nitrobenzenesulfonyl Azide (*o*-NBSA) in the presence of DBU, producing the desired product (**2.41**) with a 65% yield.

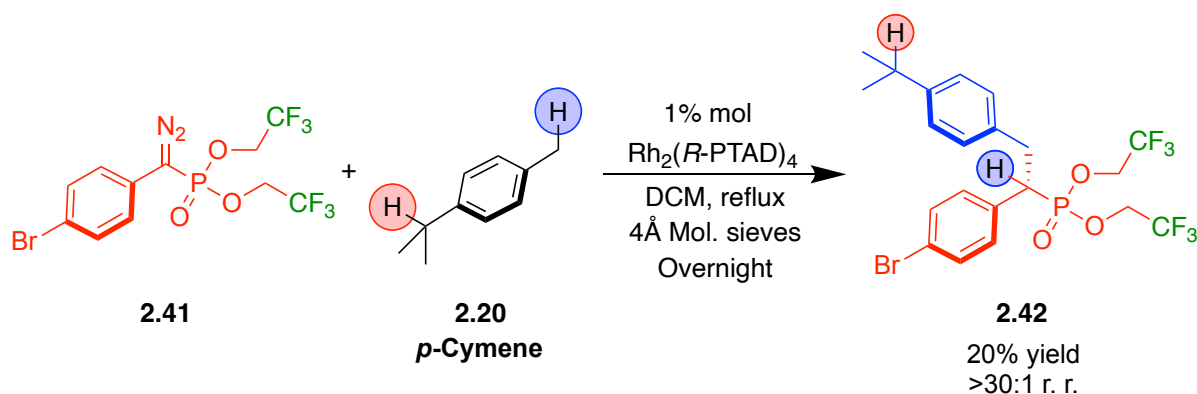


Scheme 2.8 Still-Gennari method to produce bis(trifluoroethyl) diazophosphonate.

In investigations into C–H functionalization using aryldiazoacetate, it was frequently observed that substituting the methyl ester with a trihaloethyl ester led to improved performance.^{23,66,86,129} Building on this observation, we explored the potential of trifluoroethyl diazophosphonate (**2.41**) to enhance C–H functionalization in a similar manner (**Scheme 2.9**). To gauge the selectivity of the phosphonate, we employed *p*-Cymene (**2.20**) as the model substrate, which contains both tertiary and primary benzylic C–H bonds. Initial trials under standard conditions yielded slow reactions and low conversions, with only 20% yield (**2.42**). Even with a catalyst loading increased to 5% mol, the yield remained at 20%.

The Davies lab's plans for the phosphonate products could provide valuable context for understanding their significance in the broader scope of our research. Phosphonates are versatile

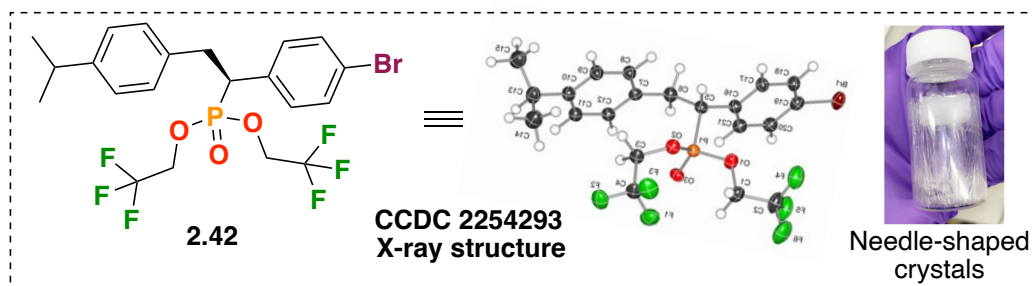
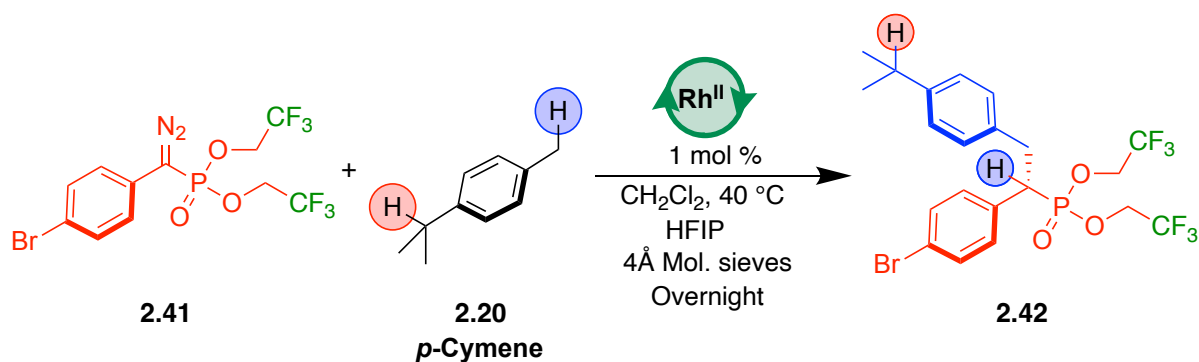
intermediates with applications in areas such as catalysis, medicinal chemistry, and material science like mentioned above.⁸⁹⁻⁹¹ In terms of deprotection, trihalocarboxylate esters represent an interesting class of compounds. The use of Zn dust for deprotection is a known strategy, typically employed for reducing functional groups or cleaving protective groups under mild conditions. However, whether Zn dust can effectively react with trifluoromethyl esters is less certain. Therefore, experimental validation would be needed to confirm its reactivity under these conditions.



Scheme 2.9 C–H functionalization of trifluoroethyl diazophosphate.

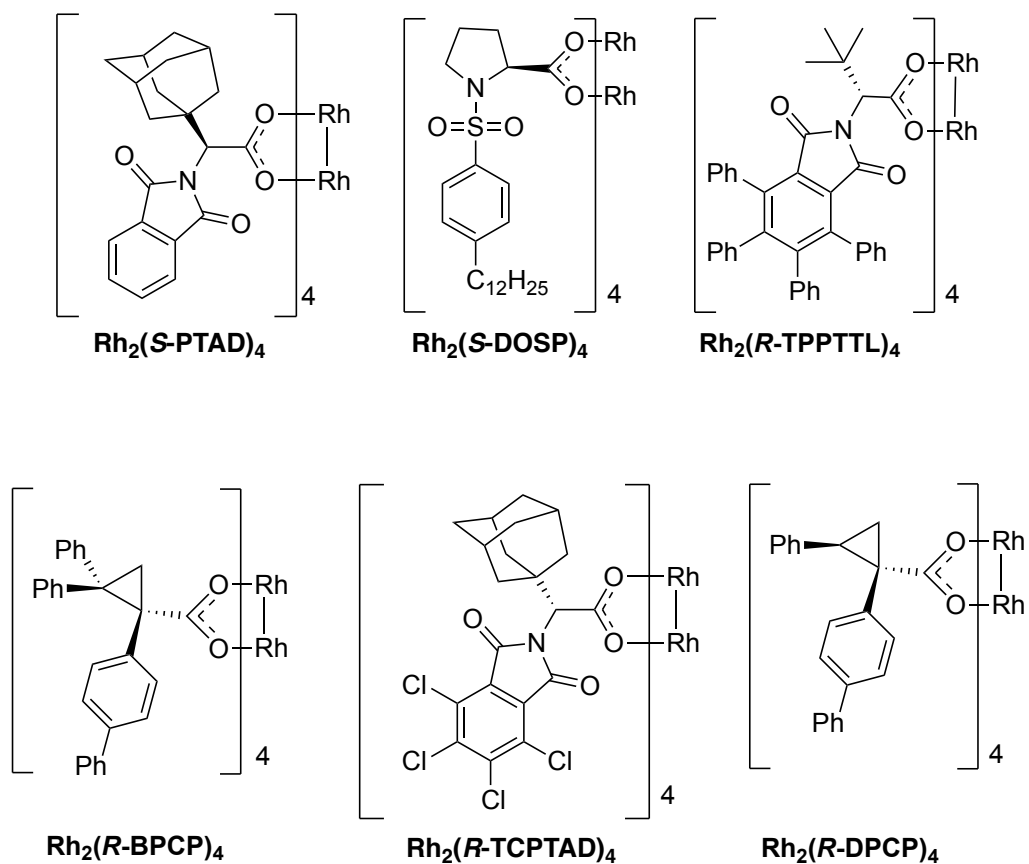
Further examination revealed that the reaction was moisture-sensitive, necessitating the use of activated molecular sieves and 20 equivalents of Hexafluoro-2-propanol (HFIP) for effective transformation. The beneficial effect of HFIP aligns with recent studies, which demonstrate that HFIP in donor/acceptor carbene reactions prevents interference from water and various other nucleophilic contaminants.¹³⁰ The initial phase of the study aimed to identify the optimal chiral catalyst for C–H functionalization and the use of HFIP as an additive. We tested this by examining the C–H functionalization of *p*-Cymene (**2.20**) (Table 2.3). The reaction proceeded cleanly, yielding (**2.42**) in 59%, with a (>30:1 d.r.) and (65% ee) when $\text{Rh}_2(\text{S-PTAD})_4$ was used (entry 1). Using the standard dirhodium catalyst, $\text{Rh}_2(\text{S-DOSP})_4$, resulted in a good product yield (75%) but low enantioselectivity (67% ee) for the C–H functionalization product (**2.32**), with a strong preference

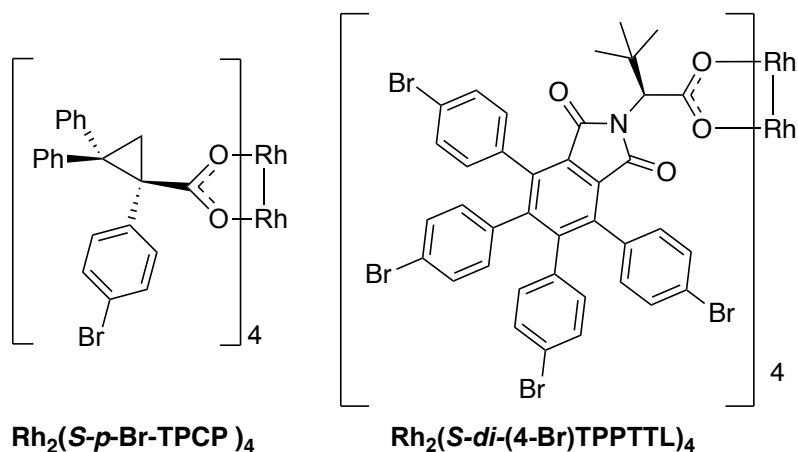
for the primary C–H bond (>30:1 r.r.) (**entry 2**). In contrast, Rh₂(R-TPPTTL)₄ yielded (**2.42**) in 82%, with a (>30:1 d.r.) and (83% ee) (**entry 3**). Other catalysts such as Rh₂(R-BPCP)₄, Rh₂(R-TCPTAD)₄, Rh₂(R-DPCP)₄, and Rh₂(*S-p*-Br-TPCP)₄, produced very low yields and poor enantioselectivity. The most effective catalyst was Rh₂(*S-di*-(4-Br)TPPTTL)₄, which provided an 84% yield for (**2.42**), with a >30:1 d.r. and very high asymmetric induction (98% ee). The absolute configuration of (**2.42**), confirmed by X-ray crystallography, was consistent with that observed for the methyl phosphonate derivatives.



entry	catalyst	yield, %	r.r.	ee, %
1	$\text{Rh}_2(\text{S-PTAD})_4$	59%	>30:1	65%
2	$\text{Rh}_2(\text{S-DOSP})_4$	75%	>30:1	67%
3	$\text{Rh}_2(\text{R-TPPTTL})_4$	82%	>30:1	–83%
4	$\text{Rh}_2(\text{R-BPCP})_4$	24%	>30:1	–20%
5	$\text{Rh}_2(\text{R-TCPTAD})_4$	33%	>30:1	–60%
6	$\text{Rh}_2(\text{R-DPCP})_4$	trace	–	–
7	$\text{Rh}_2(\text{S-}i\text{-}p\text{-Br-TPCP})_4$	trace	–	–
8	$\text{Rh}_2(\text{S-}di\text{-(4-Br)TPPTTL})_4$	84%	>30:1	98%

Table 2.3 Catalysts screening for trifluoroethylphosphonate with *p*-Cymene.

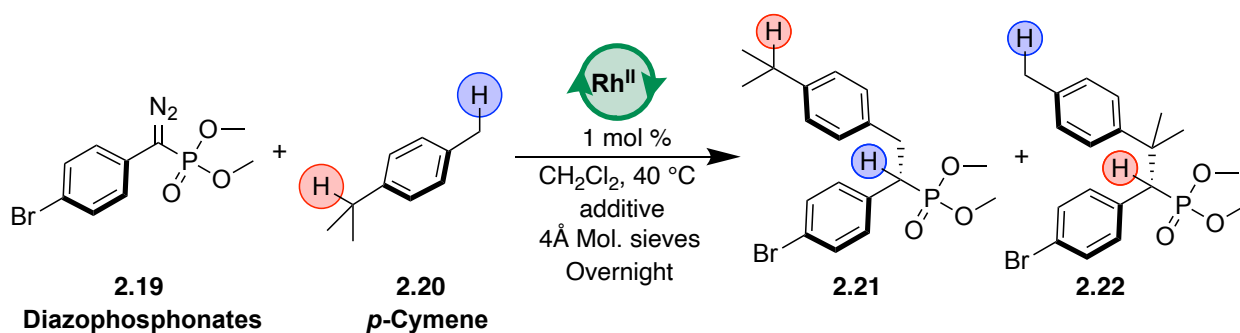




Hexafluoroisopropanol (HFIP) has become an important additive in C–H functionalization reactions, especially those involving metal carbenoid intermediates. Its effectiveness is due to several key properties. HFIP is a highly polar solvent with low nucleophilicity, making it ideal for stabilizing reactive intermediates without participating in the reaction. This stabilization is crucial for maintaining the integrity of metal carbenoids and ensuring the smooth progression of the functionalization process.¹³¹⁻¹³³ HFIPs strong hydrogen-bond-donating ability allows it to interact with and deactivate nucleophilic species, such as water or other contaminants, which could otherwise quench reactive intermediates or disrupt the catalytic cycle. This interaction helps preserve the reactivity of the carbenoid intermediates.¹³⁴⁻¹³⁶ HFIP often enhances the reactivity and selectivity in C–H functionalization reactions. For example, in the functionalization of benzylic C–H bonds, HFIP can increase the reaction rate and the yield of the desired product. Additionally, it has been observed to improve regio- and stereoselectivity, leading to higher enantioselectivity and regioselectivity.^{137,138} Furthermore, HFIP can stabilize the catalytic species involved in C–H functionalization. By preventing the deactivation of catalysts through coordination or precipitation, HFIP ensures that the catalysts remain active throughout the reaction, enhancing overall efficiency. Overall, HFIP unique properties as a solvent and additive make it an invaluable component in C–H

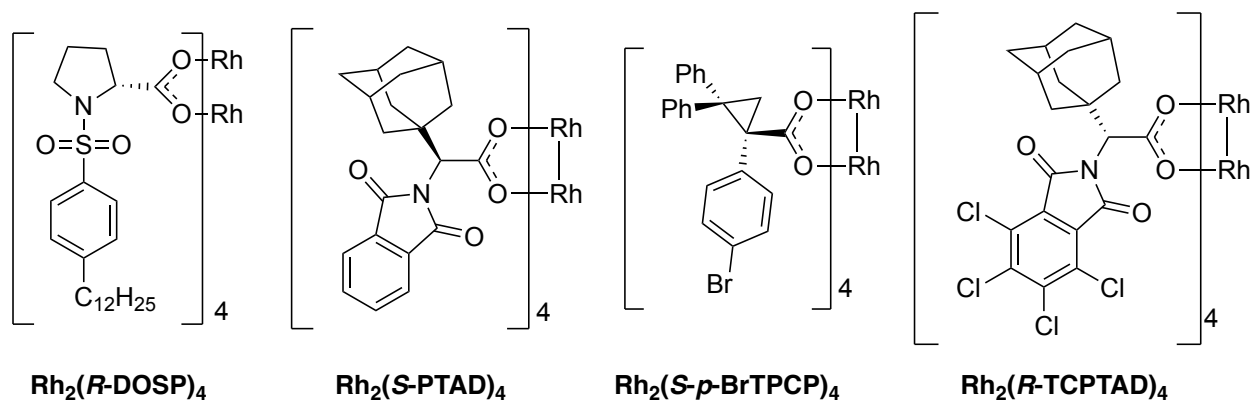
functionalization reactions, improving both the efficiency and selectivity of these transformations.^{130,139-141}

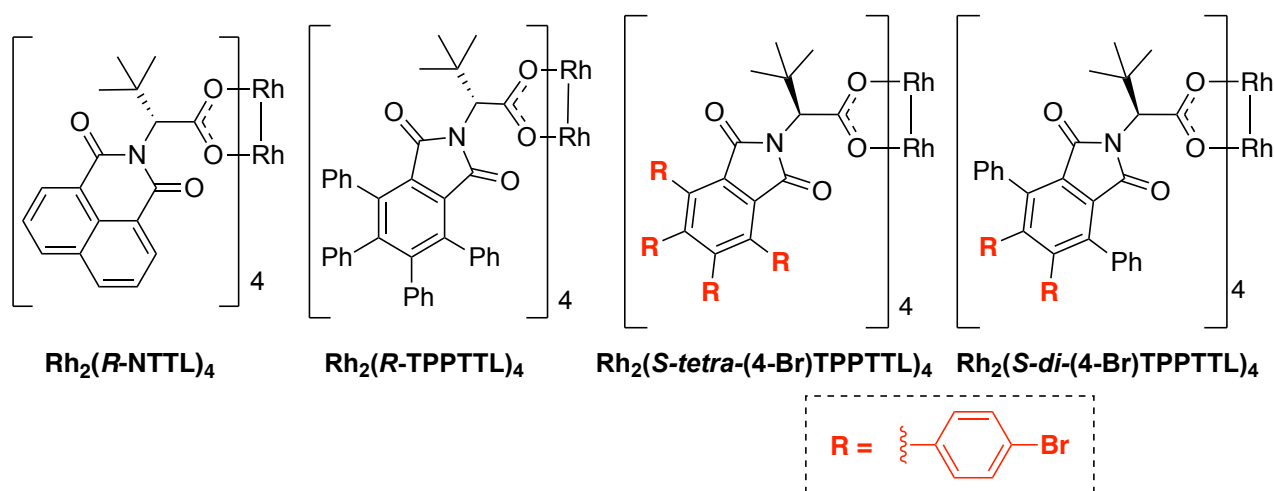
After establishing the viability of C–H functionalization at benzylic sites using trifluoroethyl diazophosphonate (**2.41**), we extended the same conditions to diazophosphonate (**2.19**). This diazophosphonate (**2.19**) was synthesized more readily through an Arbuzov reaction from 4-bromobenzyl bromide, followed by a well-established diazo transfer reaction.⁶² The standard dirhodium catalyst, Rh₂(S-DOSP)₄, yielded a good product yield 80% but low enantioselectivity (48% ee) for the C–H functionalization product (**2.21**), showing a strong preference for the primary C–H bond (>30:1 r.r.) (**entry 3**). Having demonstrated the viability of C–H functionalization at benzylic sites using diazophosphonate (**2.19**), we conducted an optimization study with a series of well-established chiral catalysts (**Table 2.4**). The bulky triarylcyclopropane carboxylate catalyst, Rh₂(*S-p*-Br-TPCP)₄,²⁰ which is highly effective for C–H functionalization with aryldiazoacetates, only produced a trace amount of the desired product (**2.21**) (**entry 4**). In contrast, the phthalimido-derived catalyst Rh₂(*S*-PTAD)₄, known for its efficiency in cyclopropanation reactions, afforded the product (**2.21**) in a 75% isolated yield with 83% ee (**entry 2**).⁶² The naphthalimido-derived catalyst Rh₂(*R*-NTTL)₄,¹⁴² along with the related phthalimido catalysts Rh₂(*R*-TCPTAD)₄,⁸⁶ and Rh₂(*R*-TPPTTL)₄,¹⁴³ all performed well, achieving 92–93% ee and good yields (**entries 5-7**). We recently prepared an extended series of Rh₂(*R*-TPPTTL)₄ derivatives and evaluated these as well.¹¹⁷ The tetrabromo derivative, Rh₂(*S*-tetra-(4-Br)TPPTTL)₄, showed improved enantioselectivity (97% ee) but had a low yield (35%) (**entry 8**). Conversely, the dibromo derivative, Rh₂(*S-di*-(4-Br)TPPTTL)₄, was exceptionally effective, producing (**2.21**) in 82% yield and 99% ee (**entry 9**).



entry	catalyst	additive	yield, %	r.r.	ee, %
1	Rh ₂ (S-PTAD) ₄	—	20%	—	—
2	Rh ₂ (S-PTAD) ₄	HFIP	75%	>30:1	83%
3	Rh ₂ (<i>R</i> -DOSP) ₄	HFIP	80%	>30:1	–48%
4	Rh ₂ (<i>S-p</i> -Br-TPCP) ₄	HFIP	trace	—	—
5	Rh ₂ (<i>R</i> -TCPTAD) ₄	HFIP	65%	>30:1	–93%
6	Rh ₂ (<i>R</i> -NTTL) ₄	HFIP	77%	>30:1	–92%
7	Rh ₂ (<i>R</i> -TPPTL) ₄	HFIP	81%	>30:1	–92%
8	Rh ₂ (<i>S-tetra</i> -(4-Br)TPPTL) ₄	HFIP	35%	>30:1	97%
9	Rh ₂ (<i>S-di</i> -(4-Br)TPPTL) ₄	HFIP	82%	>30:1	99%

Table 2.4 Catalyst optimization C–H functionalization of *p*-Cymene using diazophosphonate.





The site-selectivity profile of diazophosphonate differs significantly from that of aryldiazoacetates in similar reactions (**Figure 2.4**). Previous studies demonstrated that the $\text{Rh}_2(\text{S-tetra-(4-Br)TPPTTL})_4$ catalyzed reaction of aryldiazoacetate (**2.43**) with (**2.20**) predominantly produced the tertiary C–H functionalization product (**2.44**) over the primary C–H functionalization product (**2.45**) (>20:1 r.r.), the opposite of what was observed with diazophosphonate (**2.19**) (**Scheme 2.10**).¹¹⁷ This suggests that the size of the electron-withdrawing group can influence the site-selectivity of C–H functionalization in donor/acceptor carbene reactions. The high asymmetric induction by these catalysts has been previously discussed.¹⁴³ The ligand self-assembles into C_4 -symmetric bowl-shaped structures with 16 aryl rings on the periphery, which are tilted to create induced helical chirality. This ligand motif has shown high asymmetric induction in various carbene C–H functionalization reactions. Notably, the carbene face selectivity in reactions with aryldiazophosphonates is opposite to that seen with aryldiazoacetates, further highlighting the influence of the electron-withdrawing group size on selectivity.¹¹⁷

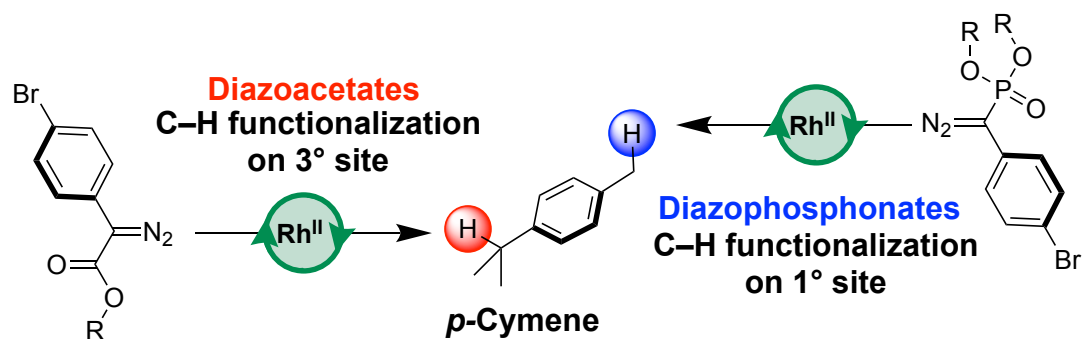
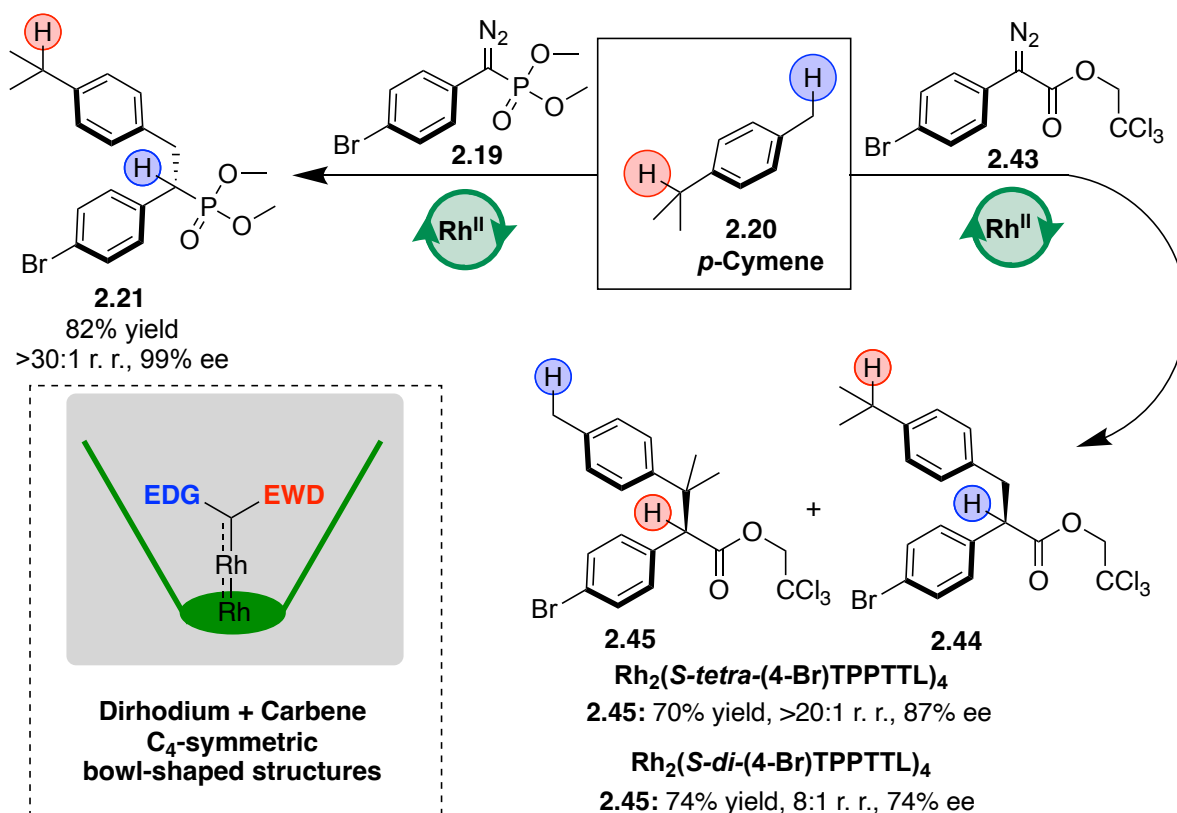
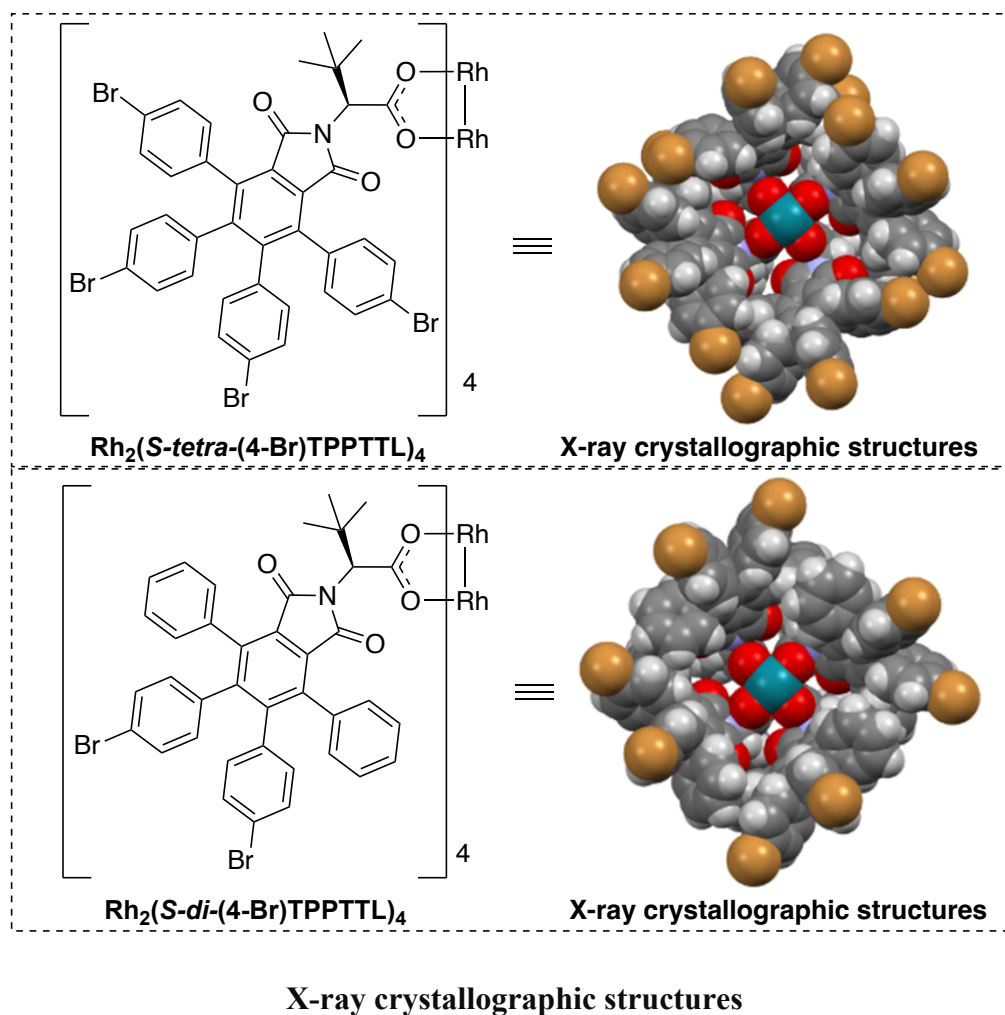


Figure 2.4 Aryldiazoacetates and arylphosphonates C-H functionalization comparison.



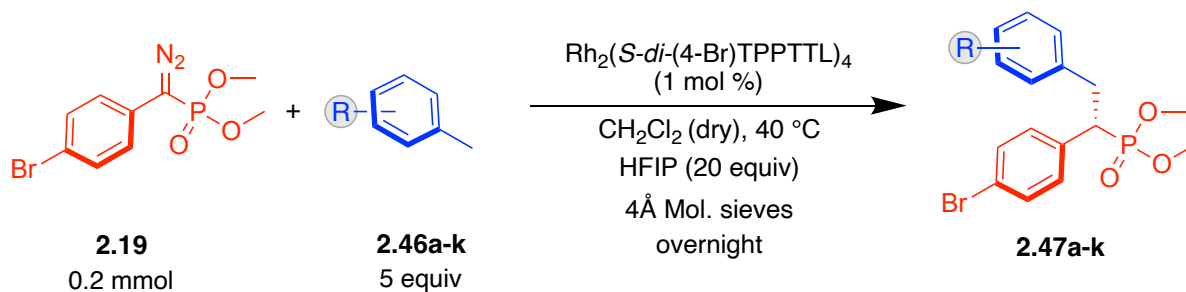
Scheme 2.10 C-H functionalization of *p*-cymene with aryldiazoacetate and arylphosphonate.



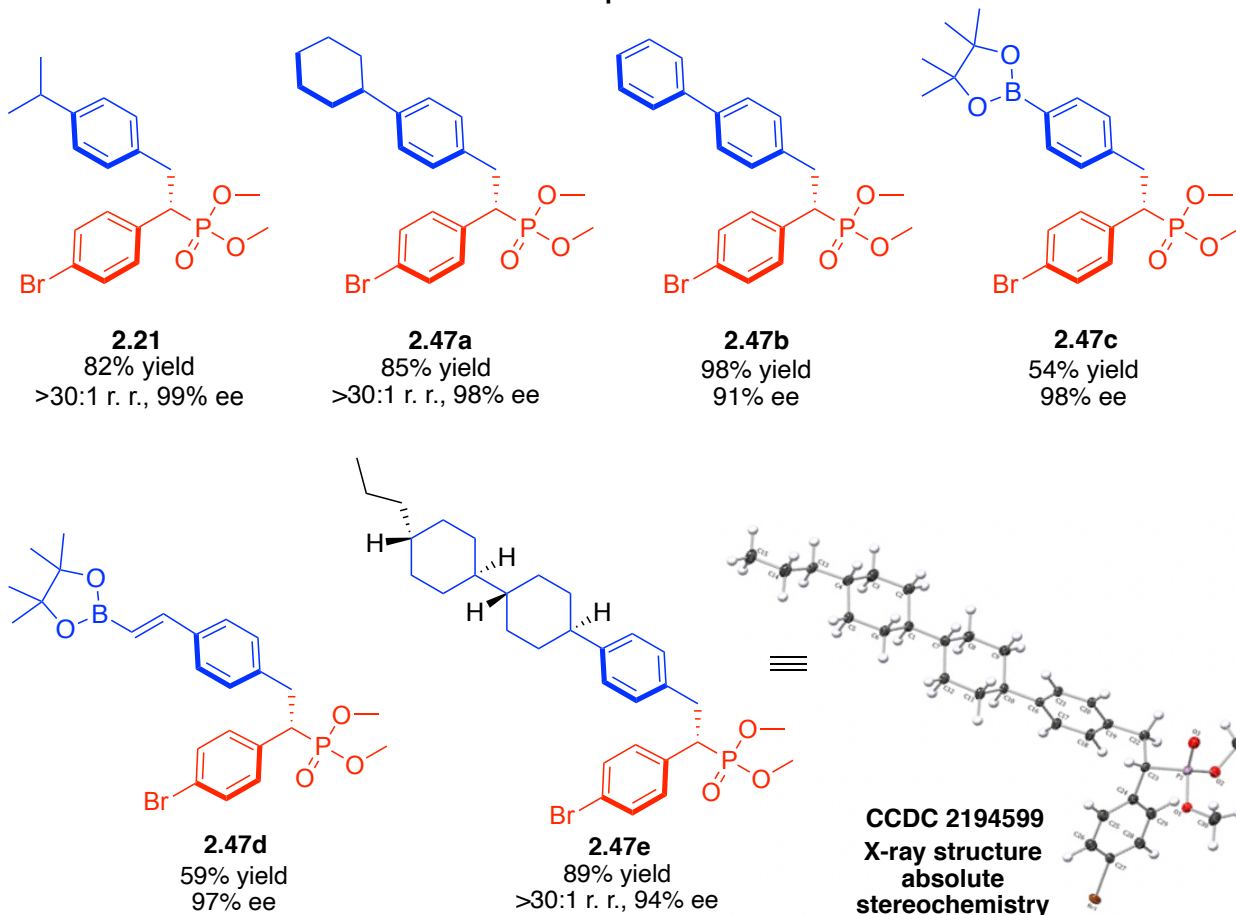
After establishing Rh₂(S-*di*-(4-Br)TPPTTL)₄ as the optimal catalyst, we explored the reaction scope with a series of representative substrates, as shown in (Table 2.3). The reactions with substrates (2.46a–k) to form (2.47a–k) demonstrate that various functional groups are compatible with this chemistry (Scheme 2.11). Notable examples include boronates (2.47c and 2.47d), alkynes (2.47f, 2.47j, and 2.47k) no cyclopropanation was formed, alkene (2.47d) no cyclopropanation was formed, and methoxy (2.47g, 2.47h, and 2.47i). Despite the presence of potentially competing C–H bonds in many substrates, all reactions occur cleanly at the primary benzylic site. A striking example is (2.46e), which contains an extended bicyclohexyl side chain that does not interfere with the

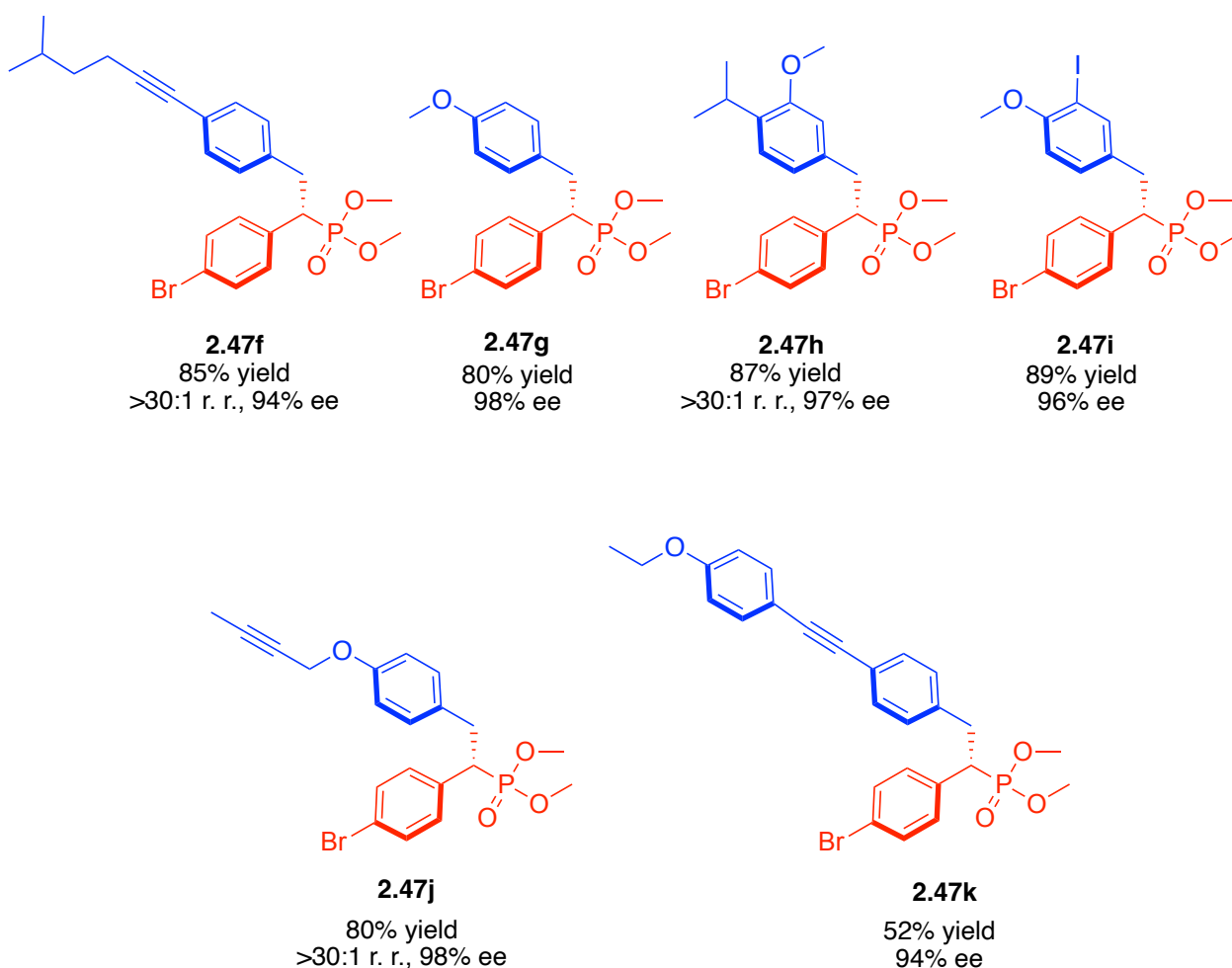
reaction. Moreover, all reactions exhibit high enantioselectivity, ranging from 91% to 98% ee.

Crystal structure of (**2.47e**) was achieved and used to determine the absolute configurations by X-ray crystallography. The absolute configurations of the other C–H functionalization products were tentatively assigned by analogy.



C–H Functionalization of representative substrates



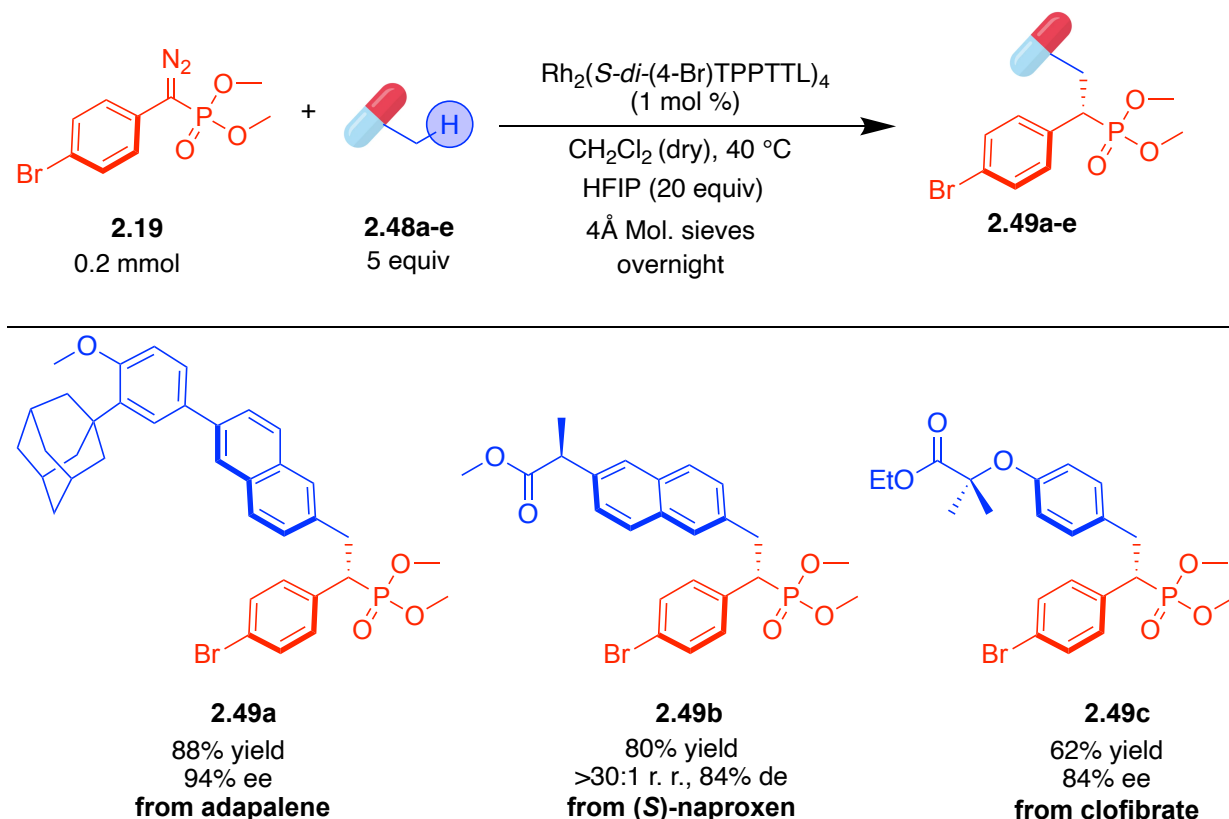


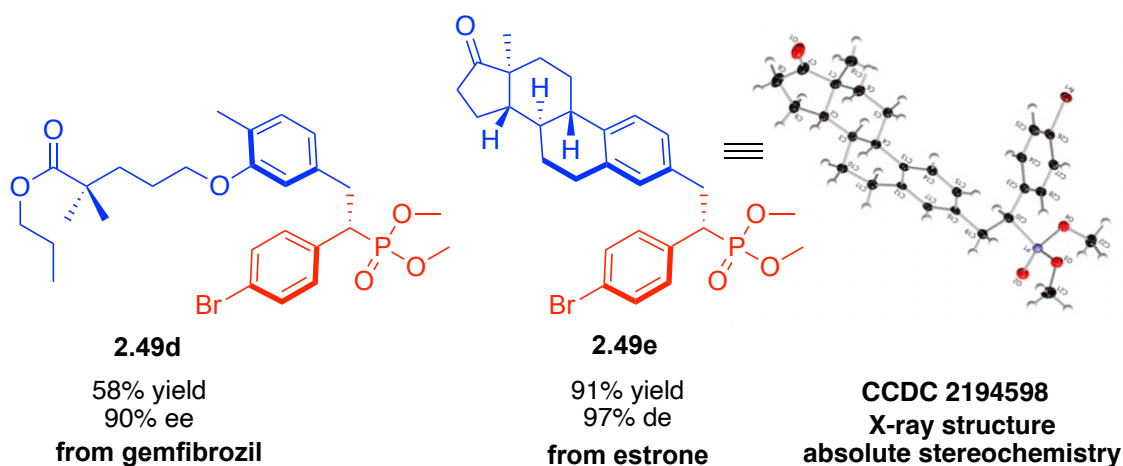
Scheme 2.11 Scope of primary benzylic C–H functionalization.

Rhodium catalysts typically do not form cyclopropanation products with internal alkynes due to both electronic and steric factors associated with the alkyne's structure. Internal alkynes have substituents on both carbons of the triple bond, which creates steric hindrance around the alkyne. This makes it more challenging for the Rh-catalyst to approach and react with the alkyne in the specific geometry required for cyclopropanation. Internal alkynes are generally less reactive than terminal alkynes in cyclopropanation reactions. The presence of substituents on both carbons of the alkyne can alter the electron density around the triple bond, making it less suitable for the

cyclopropenation process, which requires efficient orbital overlap between the alkyne and the catalyst. Rhodium catalysts tend to coordinate to alkynes in a way that favors terminal alkynes due to easier access and less steric bulk. This coordination often leads to more favorable transition states with terminal alkynes for forming three-membered rings, while internal alkynes are less accommodating in this regard.³³⁰

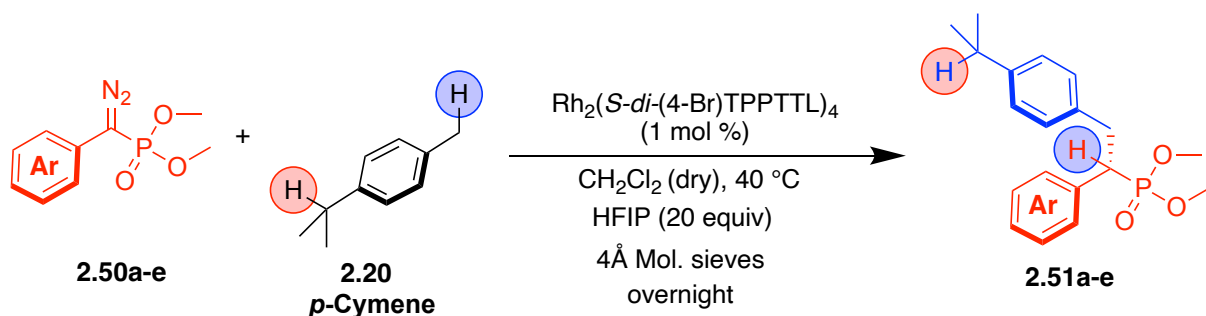
The phosphonate group is much more sterically demanding than the earlier studied carboxylate ester group, leading to much higher selectivity for a primary site versus more sterically crowded positions. The effectiveness of this methodology has been demonstrated by the late-stage primary C–H functionalization of estrone, adapalene, (*S*)-naproxen, clofibrate, and gemfibrozil derivatives (**Scheme 2.12**). The C–H functionalization of primary benzylic sites in substrates derived from pharmaceutical agents (**2.48a–e**), producing (**2.49a–e**) with 84–97% ee (or d.e. for chiral substrates). Crystals of (**2.49e**) were obtained and used to determine the absolute configurations by X-ray crystallography.

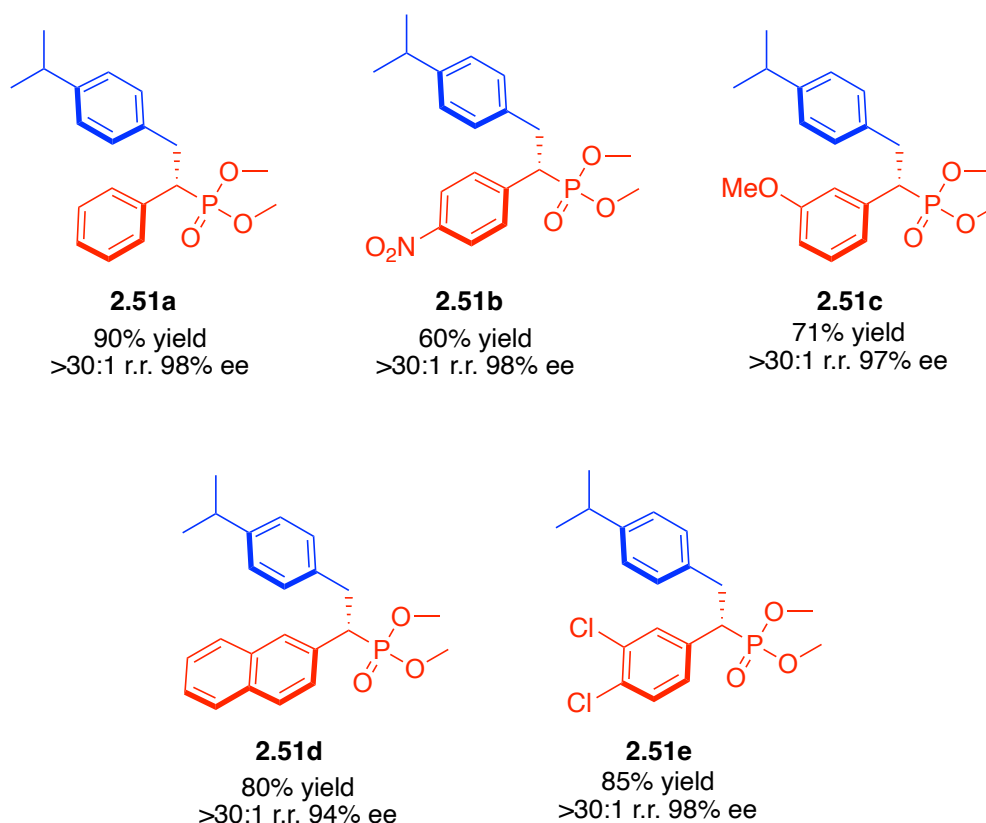




Scheme 2.12 Late-stage C–H functionalization of drug-like derivatives.

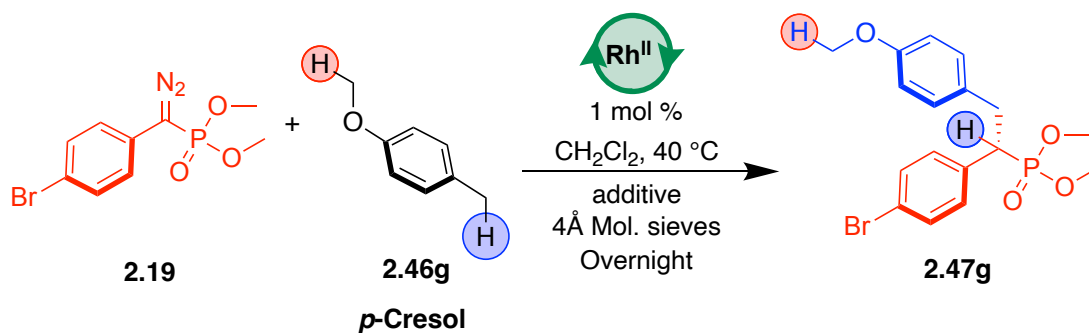
The reaction can be applied to a range of diazophosphonates (**2.50a–e**) as can be seen in the representative reaction with *p*-Cymene (**2.20**) (scheme 2.13). In all cases, the reaction occurs cleanly at the primary benzylic site to form (**2.51a–e**) (>30:1 r.r.). Furthermore, the enantioselectivity is high in all the cases. Compounds (**2.51a**, **2.51b**, and **2.51e**) were each formed in 98% ee, while slightly lower levels of enantioselectivity were observed for the meta-methoxyphenyl analogue (**2.51c**) (97% ee) and the 2-naphthyl analogue (**2.51d**) (94% ee). All the diazophosphonates derivatives provided moderate to excellent yields from 60%–90% with (>20:1 r.r.) in all cases.





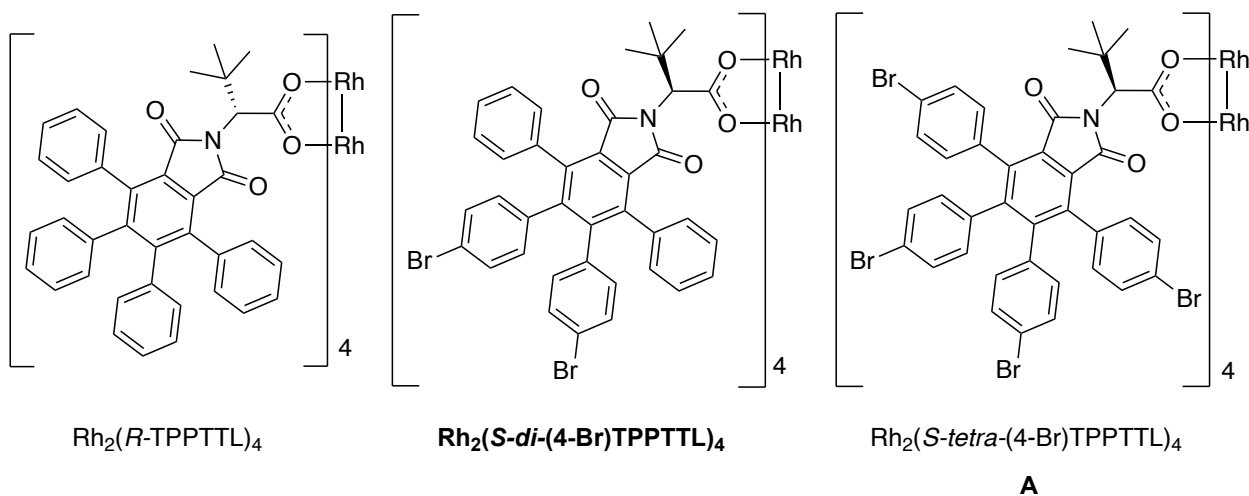
Scheme 2.13 C–H functionalization with modified aryldiazophosphonate derivatives.

All the extended $\text{Rh}_2(R\text{-TPPTTL})_4$ derivatives performed well in benzylic C–H functionalization, but $\text{Rh}_2(S\text{-di-(4-Br)-TPPTTL})_4$ was the best (**Table 2.5**) the enantioselective C–H functionalization with the complete series of $\text{Rh}_2(R\text{-TPPTTL})_4$ derivatives. Having demonstrated the viability of C–H functionalization at benzylic sites using diazophosphonate (**2.1**), we conducted an optimization study with a series of newly established chiral catalysts with *p*-Cresol. The reaction proceeded cleanly, yielding (**2.47g**) in 83%, with a (>30:1 d.r.) and (90% ee) when $\text{Rh}_2(S\text{-TPPTTL})_4$ was used (**entry 1**). Other catalysts such as A, B, C, and D provided moderate to good yields (34–80%), with a (>30:1 d.r.) and (73–97% ee) (**entry 2–5**). The most effective catalyst was $\text{Rh}_2(S\text{-di-(4-Br)TPPTTL})_4$, which provided an 80% yield for (**2.47g**), with a >30:1 d.r. and very high asymmetric induction (97% ee).



entry	catalyst	yield, %	r.r.	ee, %
1	$\text{Rh}_2(\text{R-TPPTTL})_4$	83%	>30:1	-90
2	A	34%	>30:1	97
3	B	43%	>30:1	73
4	C	50%	>30:1	94
5	D	80%	>30:1	94
6	$\text{Rh}_2(\text{S-di-(4-Br)TPPTTL})_4$	80%	>30:1	97

Table 2.5 Catalysts screening for *p*-cresol with extended $\text{Rh}_2(\text{R-TPPTTL})_4$ derivatives.



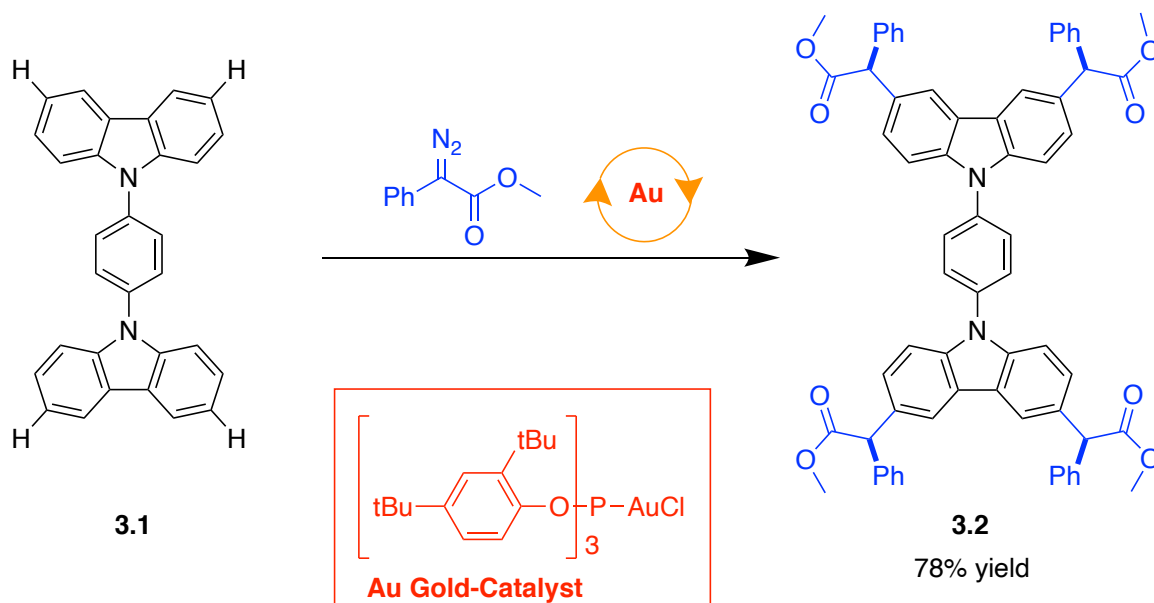
trifluoroethyl derivatives can also be utilized when needed. A particularly notable finding of this study is that the tetrahedral phosphonate group is significantly more sterically demanding than the trigonal ester group, enhancing the preference for primary C–H functionalization over more sterically congested sites. This demonstrates that the nature of the acceptor group can dramatically influence site selectivity, offering intriguing new opportunities for further refinement of carbene-induced C–H functionalization chemistry.

Chapter 3: Dirhodium C–H Functionalization of Hole-Transport Materials**3.1 Introduction**

C–H functionalization reactions provide a straightforward approach to introducing new functional groups onto organic scaffolds without pre-functionalizing the substrate molecule.¹⁴⁴⁻¹⁵¹ In this context, metal-catalyzed carbene transfer reactions for C–H functionalization have become a crucial strategy for forming new carbon-carbon bonds.^{18,37,152} The choice of catalyst can typically control the reactivity and site-selectivity of these reactions. Previous studies using precious metal catalysts such as rhodium,^{19,151,153} gold,¹⁵⁴⁻¹⁵⁷ palladium,¹⁵⁸⁻¹⁶² and others¹⁶³⁻¹⁶⁵ have shown the potential of this method for the selective functionalization of specific C–H bonds. In this study, we demonstrate that dirhodium tetracarboxylate catalysts and donor/acceptor carbenoid chemistry can be utilized to insert carboxylic esters group into sp^2 C–H bonds of a simple to complex triarylamine and a 4,4'-bis(diarylamino)biphenyl, respectively. We demonstrate that dirhodium catalysts uniquely enable multiple C–H functionalization reactions, facilitating the introduction of up to four carbene fragments onto molecules containing multiple triarylamine units.

This technique potentially provides an efficient way to access a variety of hole-transport materials (HTMs) with diverse functional groups. HTMs based on triarylamine derivatives are crucial in organic electronics, including organic light-emitting diodes and perovskite solar cells. In certain applications, triarylamine derivatives with suitable binding groups have been employed to functionalize surfaces, while in others, they have been incorporated as side chains into polymers to enhance the processibility of HTMs for device applications. Nevertheless, there are limited strategies for incorporating a single surface-binding group or polymerizable group into triarylamine materials.

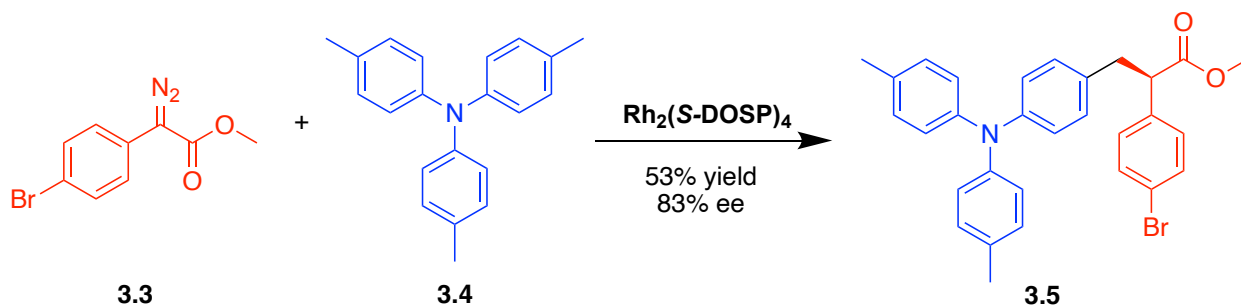
In 2020, Rene and coworkers reported on the multi C–H functionalization reaction of aryldiazoacetates with carbazole heterocycles (**Scheme 3.1**). They demonstrated that gold catalysts play a distinct role in enabling multiple C–H functionalization reactions, allowing the introduction of up to six carbene fragments onto molecules containing multiple carbazole units or linking multiple carbazole units into a single molecule. The best results were achieved by using a gold-catalyst (Au^{I} complex) with phosphite-derived ligand tris(2,4-di-*tert*-butylphenyl)phosphite in diluted reaction mixture and a reaction time of 3 hours, which provided 78% yield of (**3.2**). This method enables the linkage of two carbazole fragments and opens new pathways for the synthesis of polycarbazoles through C–H functionalization of simple and readily accessible building blocks.¹⁶⁶



Scheme 3.1 Multi C–H functionalization reactions via carbene transfer reaction.

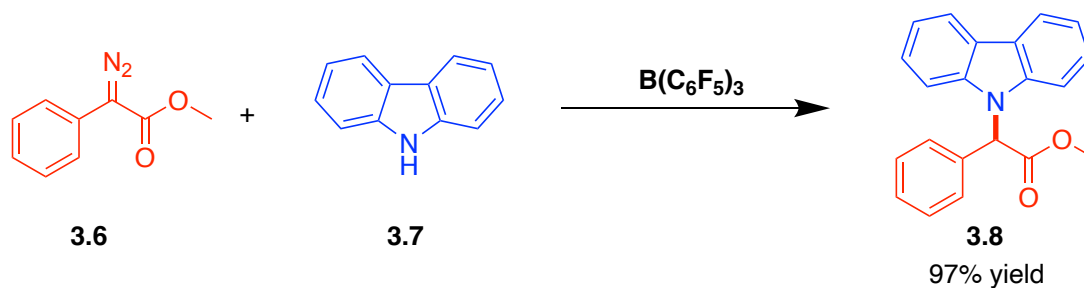
In 2003, Davies and coworkers demonstrated that effective C–H activation of benzylic methyl groups can be achieved as long as the aromatic ring is at least *p*-trisubstituted (**Scheme 3.2**).¹⁶⁷ The aromatic functionalization sterically protects the ring from electrophilic attack by the rhodium carbenoid intermediates. When the reactions are catalyzed by $\text{Rh}_2(\text{S-DOSP})_4$, high levels of

asymmetric induction is obtained. A very interesting example of this chemistry is the reaction of donor/acceptor carbene (**3.3**) with tritolyllamine (**3.4**) in the presence of $\text{Rh}_2(\text{S-DOSP})_4$. When the reaction was conducted with an excess amount of tritolyllamine, the C–H activation product was obtained in 53% yield and 81% ee.



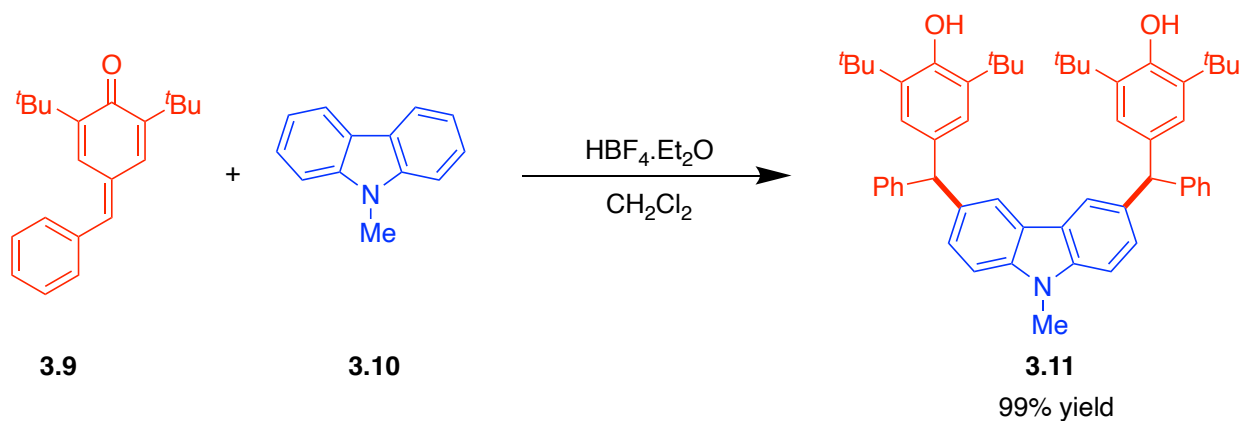
Scheme 3.2 C–H functionalization reaction of tritolyllamine.

In 2021, Koenigs and coworkers reported the tris(pentafluorophenyl)borane-catalyzed reaction of carbazole heterocycles with aryldiazoacetates (**Scheme 3.3**).¹⁶⁸ They detailed the Lewis acid-catalyzed N–H and C–H functionalization of both unprotected and protected carbazole heterocycles using aryldiazoacetates. Employing tris(pentafluorophenyl)borane as the catalyst, this transformation exhibits high selectivity, which is explained by the principles of hard and soft Lewis acids and bases. This approach overcomes the limitations of N–H functionalization reactions with borane catalysts and allows for such reactions with weakly basic aniline derivatives. The reaction of carbazole (**3.7**) with methyl phenyldiazoacetate (**3.6**) as a model reaction using tris(pentafluorophenyl)borane as catalyst with 1,2-DCE solvent gave a high yield of the N–H functionalization product (**3.8**) without the formation of byproducts.



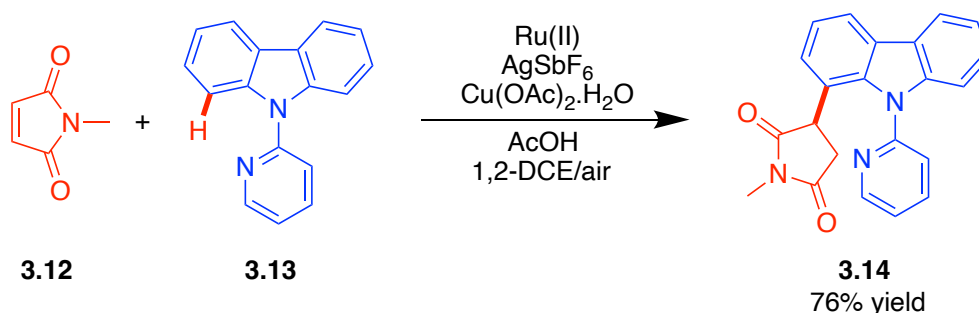
Scheme 3.3 C–N functionalization reaction of carbazole with aryldiazoacetates.

In 2022, Anand and coworkers introduced a metal- and additive-free method for directly synthesizing 3,6-bis-diarylmethylcarbazole and mono-diarylmethylcarbazole derivatives (**Scheme 3.4**).¹⁶⁹ This straightforward protocol allows for the preparation of substituted carbazole derivatives in moderate to excellent yields while demonstrating good tolerance to various functional groups. Notably, some of the 3,6-disubstituted carbazoles exhibited interesting photophysical properties, suggesting their potential applications as host materials in OLEDs.



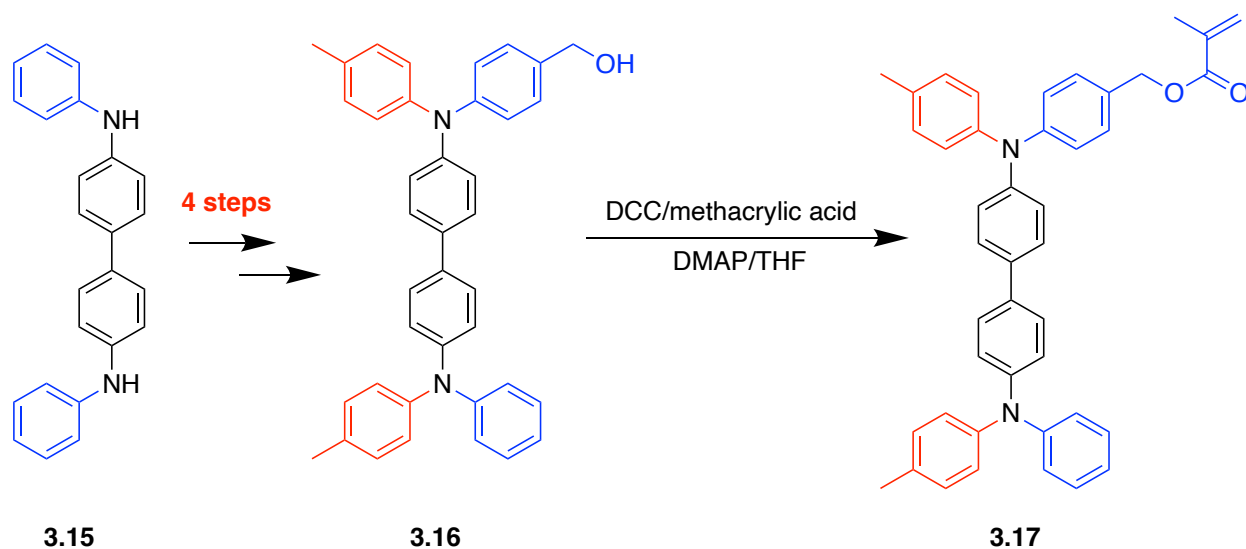
Scheme 3.4 Metal and additive free method for functionalizing carbazoles.

Lee and coworkers devised a transition metal-catalyzed C–H functionalization method to attach variously functionalized succinimide moieties to carbazole rings. This approach, which utilizes a directing group, offers a quickly install succinimides at the C-2 position of indole molecules through direct oxidation and C–H activation processes starting from indolines (**Scheme 3.5**).¹⁷⁰ The reaction carried out using (**3.12**) with (**2.13**) along with [Ru(*p*-cymene)Cl₂]₂ (5 mol%)/AgSbF₆ (20 mol%) in the presence of Cu(OAc)₂·H₂O (1 equiv.) gave (**3.14**) in yields of 76%.



Scheme 3.5 Directing group method for directing group carbazole.

In 2002, Marder and coworkers have synthesised and characterised hole-transport polymers with cinnamate and chalcone groups as photo-crosslinking moieties. The synthesis and molecular structures of methacrylate monomers with hole-transport moieties and crosslinking moieties are shown in (**Schemes 3.6**). The monomer (**3.17**) was synthesized from hydroxy-functionalised compounds by reaction with methacrylic acid, using 1,3-dicyclohexylcarbo-diimide (DCC) as a dehydrating agent and 4-dimethylaminopyridine (DMAP) as a catalyst. This multistep synthesis for species (**3.17**) provided an overall yield of 80%. Pure monomer (**3.17**) was obtained by recrystallisation of the crude product from a tetrahydrofuran and methanol solution.



Scheme 3.6 Synthesis of bis(diarylamino)biphenyl-functionalized methacrylate monomer.

Hole-transport materials (HTMs) based on triarylamines, particularly bis(diarylamino)biphenyls, have found extensive use in various organic electronic devices, primarily organic light-emitting diodes,¹⁷¹ and more recently in perovskite solar cells (PSCs).^{172,173} These materials include small molecules like spiro-OMeTAD and main-chain polymers such as PTAA (**Figure 3.1**).

Another innovative approach involves pendant triaryamine-based moieties connected by side chains to a non-redox-active main chain. This method offers the advantage of varying the HT moiety and polymer main chain to optimize redox and morphological properties. Furthermore, comonomers with cross-linking groups can be introduced to enable thermal or photochemical cross-linking after deposition, which is valuable for fabricating multilayer devices from solution.^{174,175} Additionally, monolayers consisting of HTM moieties bound to an ITO surface have been effective in PSCs, employing carboxylic acid as binding groups.^{176,177}

Attaching a single polymerizable or surface-anchoring functional group to a simple triaryamine or bis(diarylamino)biphenyl often requires a multistep synthesis. For example, polymerizable bis(diarylamino)biphenyl derivatives have been created by first incorporating a

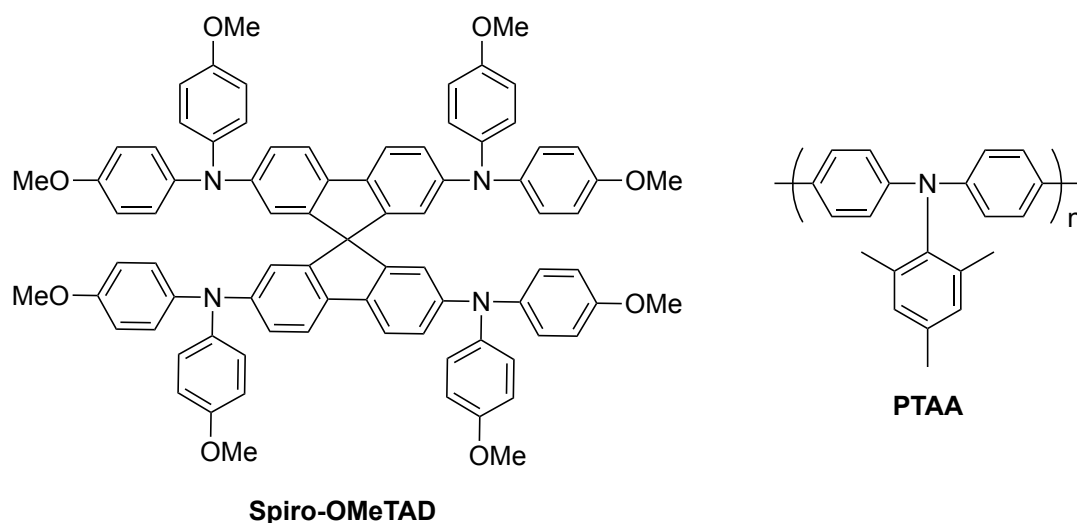


Figure 3.1 Examples of hole-transporting triarylamine derivatives.

protected alcohol on one of the bromoarenes, then performing multiple Buchwald–Hartwig Pd-catalyzed C–N bond-forming reactions, followed by deprotection and esterification with methacrylic acid as shown is (**scheme 3.6**).¹⁷⁸ Alternatively, a more symmetrical bis(diarylamino)-biphenyl moiety can undergo a Vilsmeier reaction to form a formyl derivative, which is then reduced to an alcohol and subsequently esterified.¹⁷⁴

Recently, rhodium carbenes' C–H functionalization chemistry has emerged as a potent synthetic technique, introducing new methods for constructing complex molecules.^{37,49,179} Diazo compounds are among the most frequently used precursors in transition-metal-catalyzed carbene reactions. These compounds, when reacted with specific transition-metal complexes—particularly dirhodium tetracarboxylate catalysts—transform into highly electrophilic metal carbenes.¹⁸ These carbenes can then undergo various functional transformations, including C–H insertion products.¹⁷⁹ Significant progress has been achieved in both C(sp³)-H and C(sp²)-H insertion reactions. For example, the asymmetric arylation of diazo compounds with primary benzylic C–H bonds and aniline has been catalyzed by an achiral dirhodium complex.^{180,181} These reactions are governed by a

balance of electronic and steric effects, with C–H insertion favored at sites that stabilize positive charge buildup on the carbon (**Figure 3.2**).³⁷

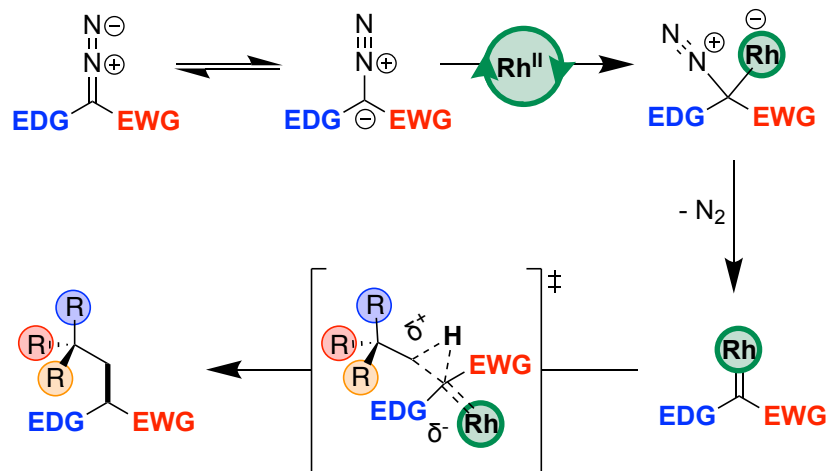


Figure 3.2 Formation of carbene and rhodium catalyzed C–H functionalization, and electronic and steric effects on-site selectivity.

This work presents the utilization of dirhodium carbene chemistry to insert carboxylic esters functional groups into the C(sp²)–H bonds of a basic triarylamine and complex bis(diarylamino)biphenyl moiety. This straightforward approach offers a simple means of synthesizing HTMs and may prove especially beneficial for attaching identical functional groups to various triarylamine derivatives. This approach holds promise, especially when aiming to attach identical functional groups to various triarylamine derivatives. Additionally, we investigate the susceptibility of electron-rich aromatic rings to electrophilic substitution reactions with donor/acceptor carbenes using dirhodium catalysts, provided the aromatic ring lacks steric hindrance. Hence, we employ this chemistry to assess the feasibility of inserting trichloroethyl ester into the C–H bonds of triarylamine products.¹⁸²

2,2,2-Trichloroethyl aryldiazoacetates were selected as the preferred diazo substrates due to the ease with which the trichloroethyl ester functional group can be deprotected to yield a carboxylic

acid. This deprotection occurs in a single step via reductive cleavage using zinc dust. This property can potentially be utilized for surface-binding chemistry in material applications (**Figure 3.3**). Furthermore, the triarylamine framework is commonly used in materials and pharmaceutical chemistry, necessitating efficient methods to introduce multiple functional groups.^{183,184} This is particularly valuable for the development of photoluminescent materials.¹⁸⁴

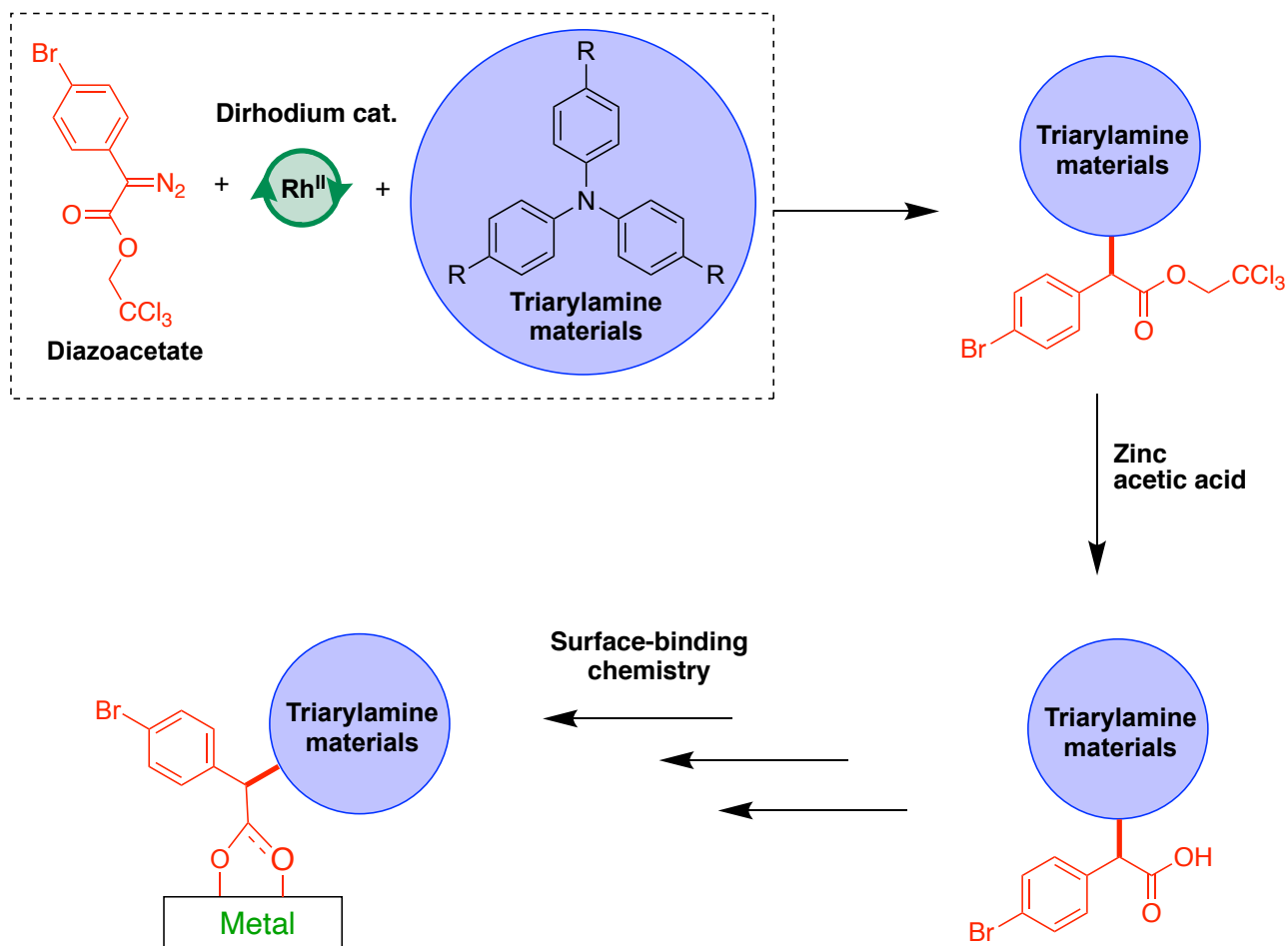
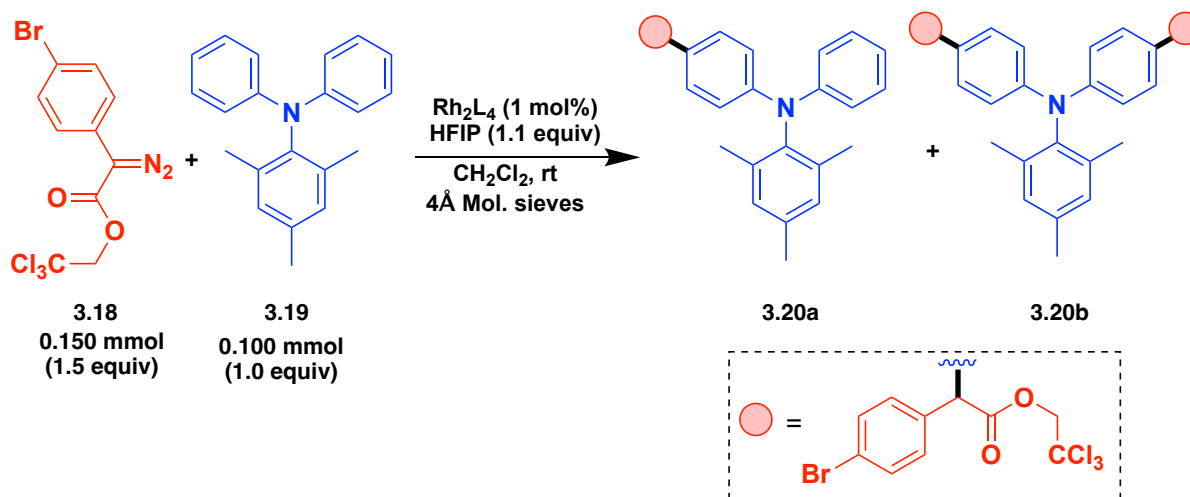


Figure 3.3 Deprotection and surface-binding chemistry

The efficiency and rapid catalyst turnover of dirhodium catalyst were crucial for achieving both site selectivity and reactivity in these reactions. Consequently, such a catalytic system can potentially overcome the synthetic challenge of multi-C–H functionalization reactions. When a simple triarylamine, **(3.19)**, was reacted with diazoacetate **(3.18)** in the presence of the achiral catalyst Rh₂(Oct)₄ (rhodium(II)octanoate), and HFIP (1,1,1,3,3,3-hexafluoro-2-propanol) as an additive, the result was C–H insertion product into the para-C(sp²)-H bond of **(3.19)**, yielding a mixture of single-insertion product **(3.20A)** in 42% yield along with double-insertion product **(3.20B)** in 20% yield (**Table 3.1, entry 1**).

The role of HFIP is to prevent interference from trace water contaminants, as discussed in chapter 2, and the diazo compound was added slowly to avoid carbene dimerization. We tested a range of chiral dirhodium catalysts for enantioselectivity in these reactions; however, no enantioselectivity was observed in any of the reactions. As summarized in (**Table 3.1, entries 2**), Rh₂(*S*-DOSP)₄ resulted in no enantioselectivity but yielded relatively high amounts of products **(3.20A)** in 65% yield and **(3.20B)** in 31% yield. The bulky triarylcyclopropane carboxylate catalyst, Rh₂(*S-p*-Br-TPCP)₄, which is highly effective for C–H functionalization with aryldiazoacetates, produced the desired products **(3.20A)** in 48% yield with 20% ee for **(3.20A)** and **(3.20B)** in 19% yield (**entry 3**). Rh₂(*S-p*-Br-TPCP)₄ was the only catalyst that exhibited poor enantioselectivity, while the other catalysts remained achiral and did not provide any enantioselectivity. When Rh₂(*S*-2-Cl-5-Br-TPCP)₄ catalyst was used it provided products **(3.20A)** in 44% yield and **(3.20B)** in 33% yield (**entry 4**). The naphthalimido-derived catalyst Rh₂(*R*-NTTL)₄ was used it also provided excellent yields for the desired products **(3.20A)** in 68% yield and **(3.20B)** in 30% yield (**entry 5**) like Rh₂(*S*-DOSP)₄. Other catalysts such as Rh₂(*R*-PTAD)₄, Rh₂(*R*-TCPTAD)₄, Rh₂(*S*-TPPTTL)₄,

and $\text{Rh}_2[\text{S-di-(4-Br)-di-(4-}^t\text{BuPh)TPPTTL}]_4$ produced only monosubstituted product (**3.20A**) with moderate to good yields (51-75%) (**entries 6-9**). Although $\text{Rh}_2(\text{S-DOSP})_4$ and $\text{Rh}_2(\text{R-NTTL})_4$ they both afforded relatively high yields of (**3.20A** and **3.20B**), and therefore $\text{Rh}_2(\text{S-DOSP})_4$ was used for the reactions described in the following sections.



entry	cat.	% yield (3.20a)	% yield (3.20b)
1	$\text{Rh}_2(\text{Oct})_4$	40	20
2	$\text{Rh}_2(\text{S-DOSP})_4$	65	31
3	$\text{Rh}_2(\text{S-p-Br-TPCP})_4$	48	19
4	$\text{Rh}_2(\text{S-2-Cl-5-Br-TPCP})_4$	44	33
5	$\text{Rh}_2(\text{R-NTTL})_4$	68	30
6	$\text{Rh}_2(\text{R-PTAD})_4$	75	—
7	$\text{Rh}_2(\text{R-TCPTAD})_4$	51	—
8	$\text{Rh}_2(\text{S-TPPTTL})_4$	62	—
9	$\text{Rh}_2[\text{S-di-(4-Br)-di-(4-}^t\text{BuPh)TPPTTL}]_4$	64	—

Table 3.1 Catalyst Screening with diazoacetate and triarylamine.

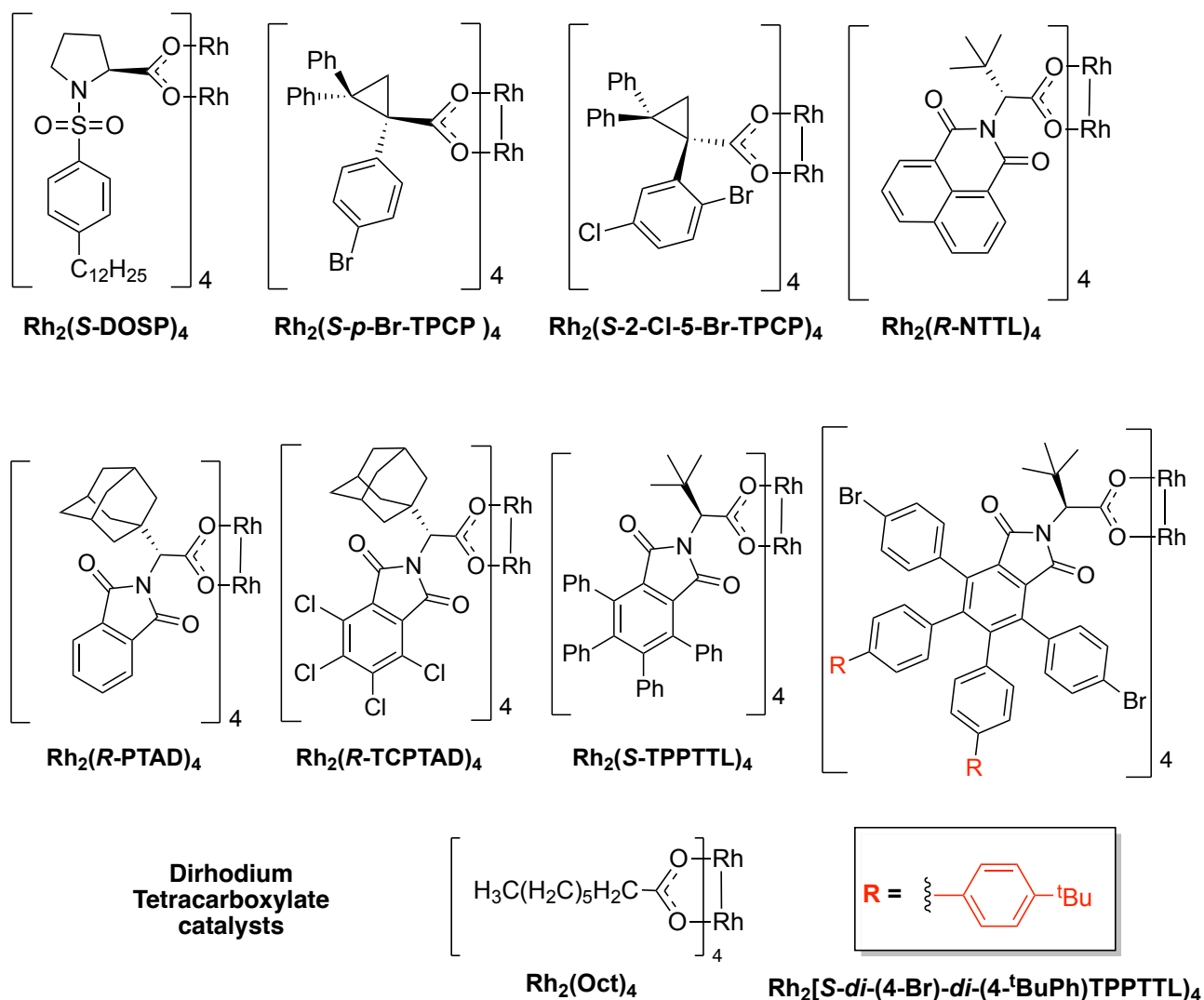
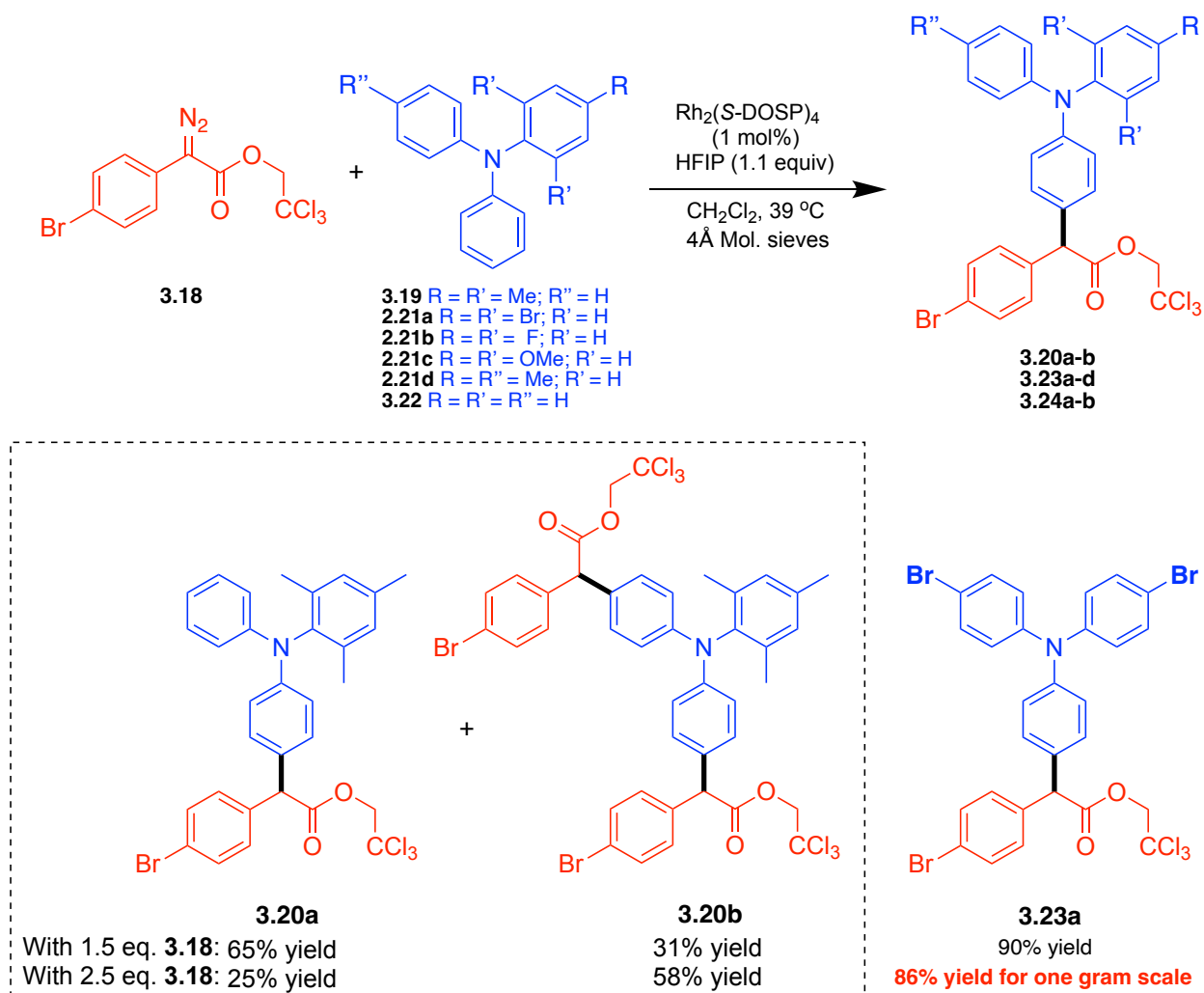
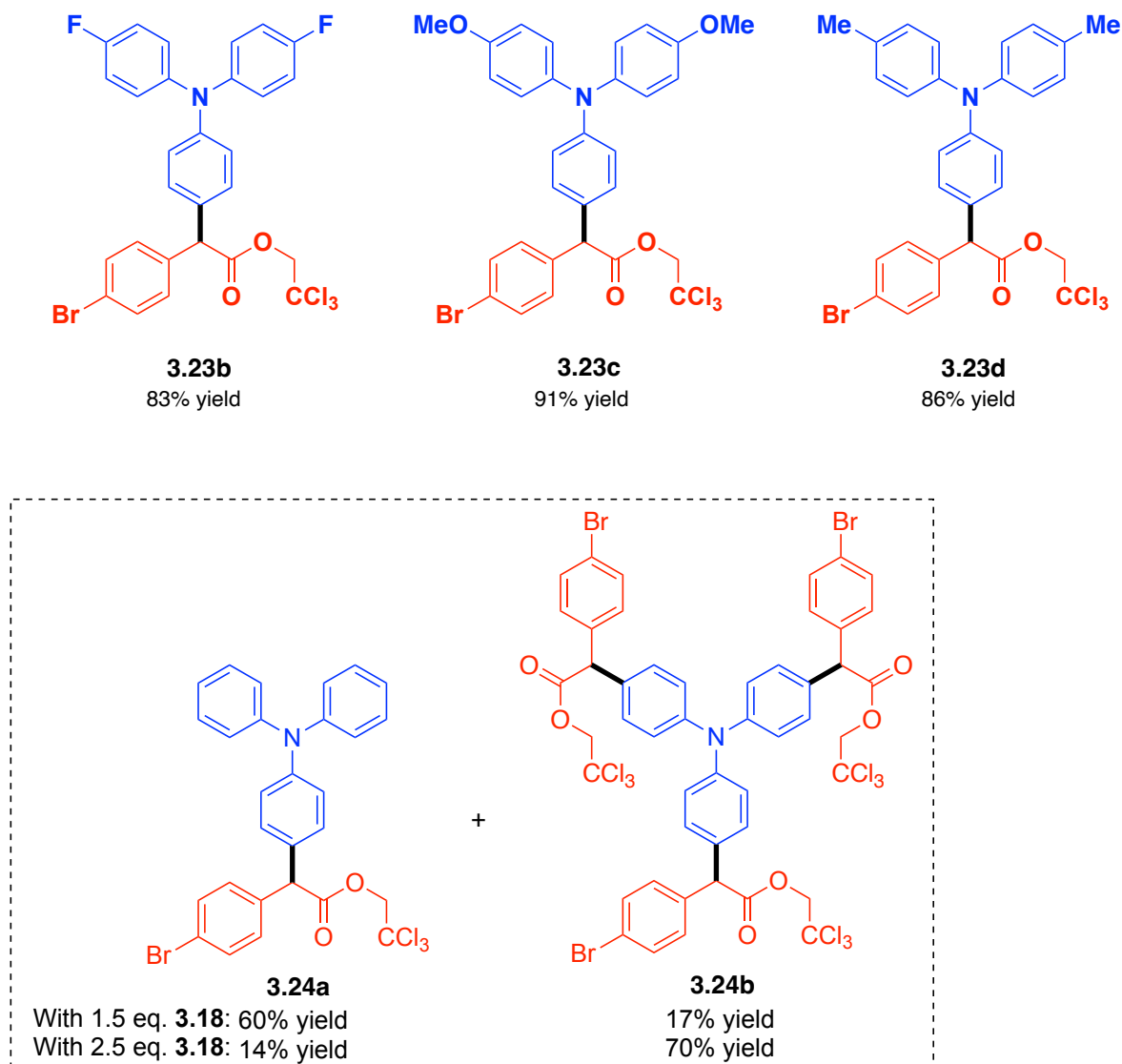


Figure 3.4 Dirhodium tetracarboxylate catalysts structures.

Having established the optimal conditions to selectively introduce donor/acceptor carbene fragments derived from **(3.18)** onto triarylamine **(3.19)**, we explored the scope of the $\text{Rh}_2(\text{S-DOSP})_4$ catalyzed reaction with different triarylamine derivatives (**(3.19)**, **(3.21a-d)**, and **(3.22)**, **Scheme 3.7**), which produced the corresponding C–H functionalization products (**(3.20a-b)**, **(3.23a-d)**, and **(3.24a-b)**) in excellent yield (**Scheme 3.7**). As noted above and in **Table 1**, the 2,4,6-substituted triarylamine **(3.19)** provided **(3.20a)** with an isolated yield of 65% as a major product and **(3.20b)** with an isolated yield of 31% as a minor product. An excess amount of diazo compound **(3.19)** provided

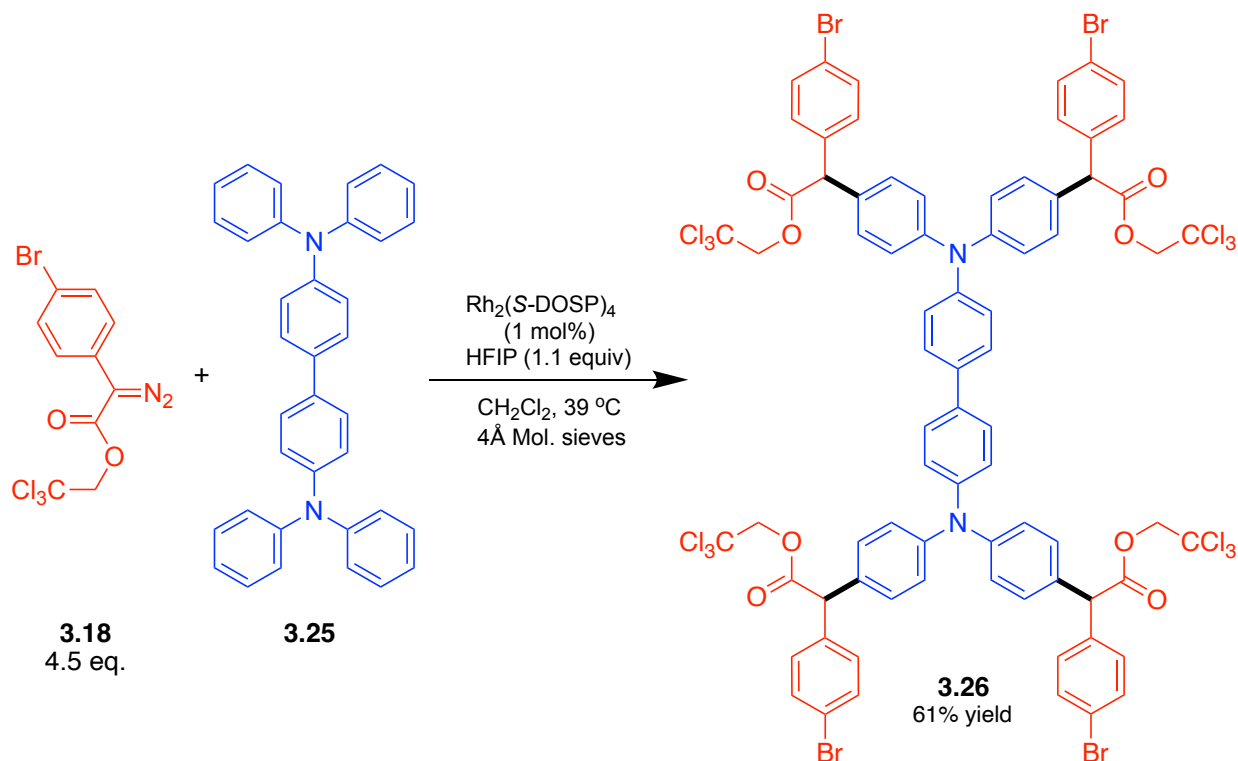
(**3.20a**) in an isolated yield of 25% as a minor product and (**3.20b**) with an isolated yield of 58% as a major product. 4,4'-Disubstituted triarylamines (**3.21a-d**), which had no functional group at para position, afforded singly functionalized products, all in isolated yields of (83-91%) regardless of the electron-donating or -withdrawing characteristics of the 4,4'-substituents. Triarylamines (**3.22**), containing no functional group at para positions, reacted with 1.5 equivalent of (**3.18**) to give (**3.24a**) in an isolated yield of 60% as a major product and triply substituted (**3.24b**) in an isolated yield of 17% as a minor product. Excess amount of diazo compound (**3.18**) provides (**3.24a**) in an isolated yield of 14% as a minor product and triply substituted (**3.24b**) in an isolated yield of 70% as a major product.





Scheme 3.7 C(sp²)-H functionalization of triarylamines derivatives.

We also extended the reaction to a more complex system involving triarylamines, specifically 4,4'-bis(diarylamino)biphenyl with diazoacetate (**Scheme 3.8**). The 4,4'-bis(diarylamino)biphenyl substrate (**3.25**) has four potentially reactive para positions without any functional groups. Using an excess amount of diazo compound (**3.18**) and one equivalent of 4,4'-bis(diarylamino)biphenyl substrate (**3.25**) with Rh₂(*S*-DOSP)₄, we obtained the tetra-functionalized product (**3.26**) in an isolated yield of 61%, albeit without any enantioselectivity.



Scheme 3.8 C–H functionalization 4,4'-bis(diarylamino)biphenyl substrate.

Proposed mechanism for understanding no enantioselectivity.

The proposed mechanism for the dirhodium-catalyzed carbene reaction is depicted in (Figure 3.5). The catalytic cycle begins with the combination of the dirhodium complex **3.27** and diazo compound **3.28**, leading to the dissociation of nitrogen from the diazo compound to form **3.29**, resulting in the formation of the rhodium carbene intermediate **3.30**. This highly electrophilic rhodium carbene **3.30** then approaches the substrate **3.31** in the subsequent step. The process unfolds in a concerted manner, creating a three-membered-ring transition state **3.32**, which would typically result in a cyclopropanation product. However, due to the strong electron-donating nature of the nitrogen functional group at the para position, electrons are donated into the aromatic ring, causing the three-membered ring to break open, ultimately forming the final product C(sp²)–H functionalization product **3.33** without any enantioselectivity. While this lack of enantioselectivity is observed in the case of triaryl amines, it is not a universal feature of all aromatic C–H

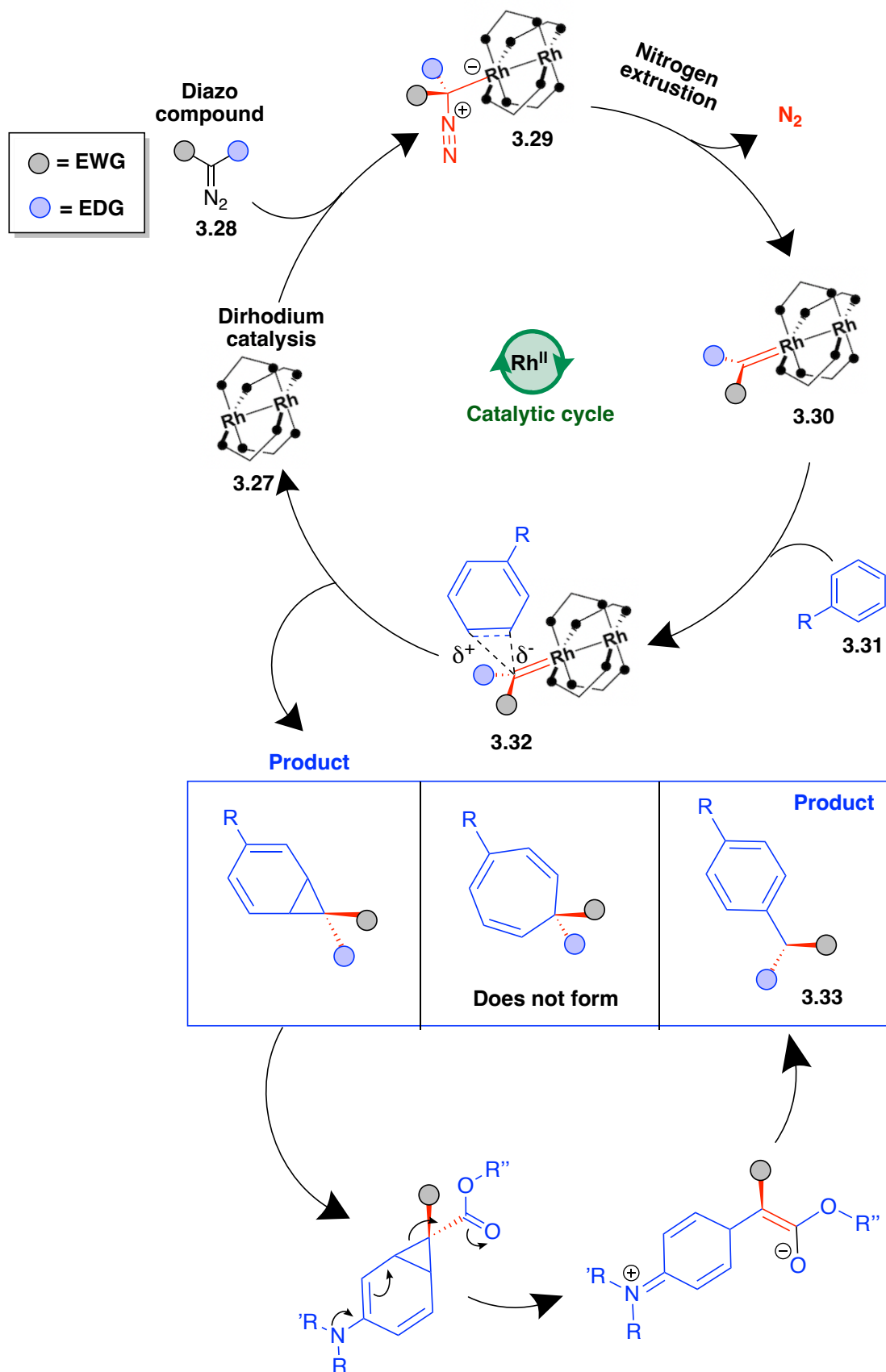
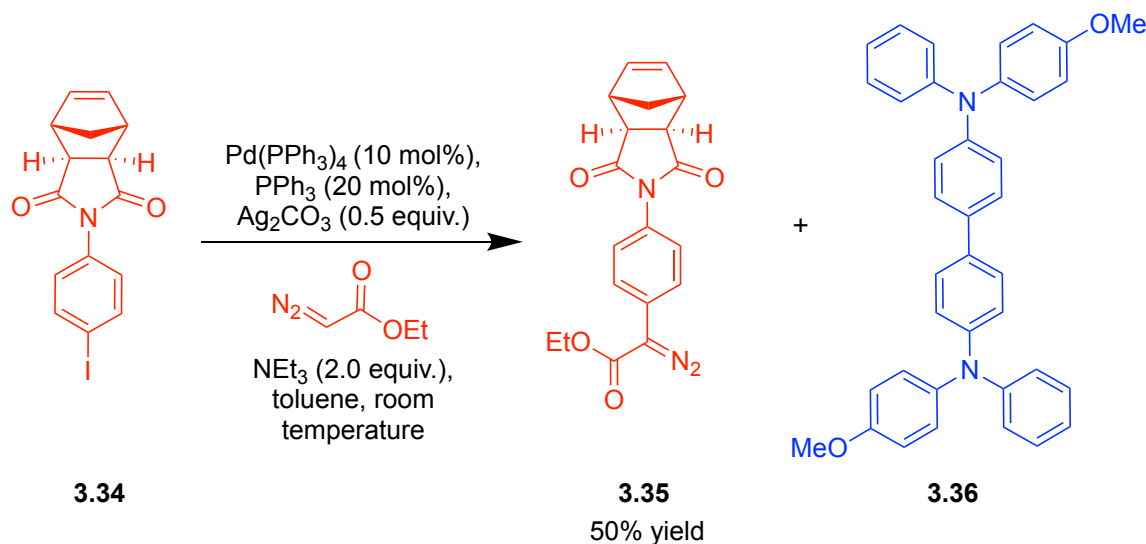
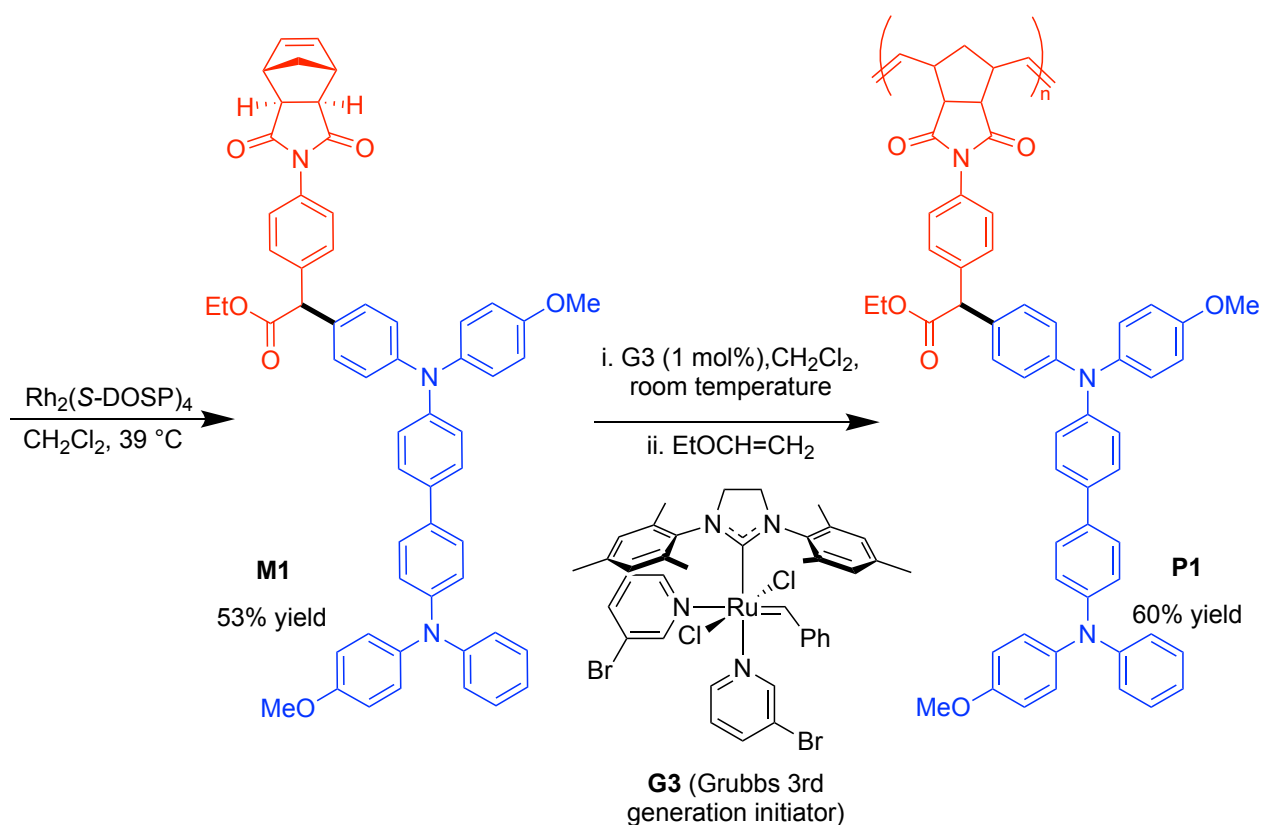


Figure 3.5 Proposed mechanism for dirhodium-catalyzed carbene reaction.

functionalizations catalyzed by dirhodium complexes with donor-acceptor diazos. The strong electron-donating properties of the para-substituted nitrogen group are unique to triarylamines, suggesting that this behavior is context-specific rather than a general characteristic of these catalysts and substrates.

In collaboration with the Seth Marder group at the University of Colorado Boulder, we explored the feasibility of using the dirhodium chemistry established by Davies and coworkers to insert a polymerizable diazo containing a norbornene group into the C–H bond of a bis(diarylamino)biphenyl derivative using $\text{Rh}_2(\text{S-DOSP})_4$ (**Scheme 3.9**). An aryldiazoacetate containing a norbornene functional group was obtained via palladium-catalyzed cross-coupling reactions.¹²⁹ Intermediate (**3.34**) was reacted with ethyl diazoacetate in the presence of silver carbonate to produce (**3.35**) with a 50% yield. Slow addition of (**3.35**) to a solution of **MeO-TPD** (**3.36**) led to the formation of the product (**M1**) with a 50% isolated yield. **P1** was successfully synthesized using the Grubbs third-generation catalyst initiator G3,^{185,186} achieving a 60% isolated yield. This material was then passed to our collaborators for electrochemical property studies, which are discussed in our paper published in the Journal of Organic Chemistry (JOC).¹⁸⁷





Scheme 3.9 C(sp²)-H functionalization of a Bis(Diarylamino)biphenyl with a Norbornene.

3.2 Conclusion

In conclusion, we have demonstrated the practicality and effectiveness of C-H functionalization chemistry for modifying triarylamine derivatives with groups essential for materials applications, such as carboxylic esters and norbornene. All triarylamines were shown to undergo C(sp²)-H activation with a diazoacetate bearing a protected carboxylic acid functional group in the presence of dirhodium tetracarboxylate catalyst Rh₂(S-DOSP)₄. The reaction of a bis(diarylamino)biphenyl with a new diazoacetate containing a norbornene functional group provided a straightforward route to the monomer (**M1**) for synthesizing the hole-transport polymer

(P1) using Grubbs third-generation catalyst. The C–H functionalization chemistry employed in this study could also be useful for introducing other significant functional groups into Hole-Transport Materials (HTMs) derivatives, such as phosphonic esters for surface modifications or benzocyclobutane for thermal crosslinking of HTMs.

Chapter 4: Synthesis of Aryl- and Hetro Diazophosphonates by Palladium-Catalyzed Cross-Coupling Reactions.

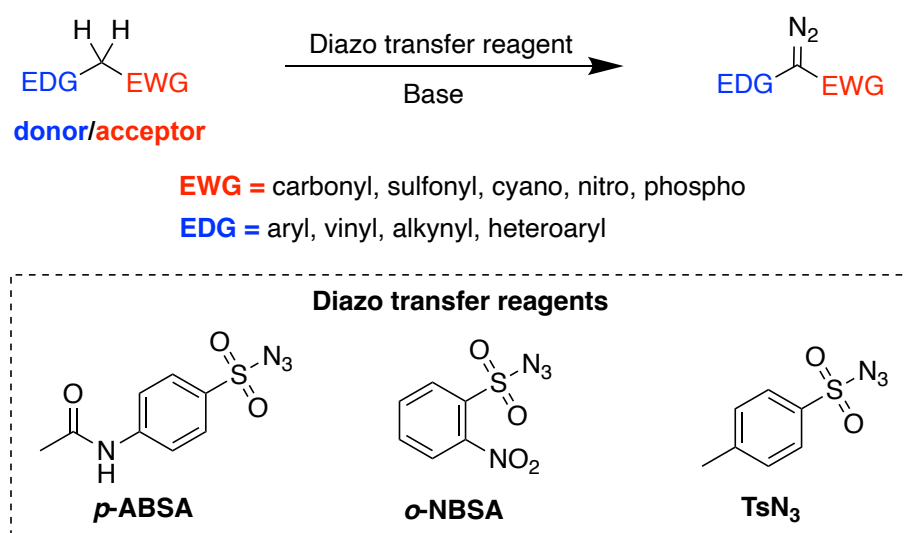
4.1 Introduction

Application of diazo compounds has become a standard method in organic synthesis, serving as both fundamental building blocks and adaptable reagents.¹⁸⁸⁻¹⁹² Notably, their role in carbene chemistry stands out as particularly noteworthy.^{37,191,193,194} When subjected to either photochemical or thermal conditions, diazo compounds undergo dinitrogen extrusion, facilitating the generation of free carbenes.¹⁹⁵⁻¹⁹⁸ Yet, the inherent reactivity of these carbenes often leads to issues of selectivity in reactions.^{192,199-201}

To address this challenge, transition metal-catalyzed diazo decomposition emerges as a solution. Through this process, highly reactive but stabilized transient metallocarbene complexes are formed.^{44,202,203} These complexes demonstrate an exceptional ability to undergo diverse transformations, characterized by remarkable levels of stereo-, and regioselectivity. Consequently, this advancement marks a significant stride forward in the domain of metallocarbene chemistry.^{204,205}

Aryldiazoacetates have been extensively investigated as precursors for producing donor/acceptor-substituted metallocarbenes, known for their remarkable reactivity and selectivity across a range of transformations.^{107,206} While historically receiving less attention in organic synthesis compared to diazocarboxylates, α -diazophosphonates have garnered increased interest in recent years, particularly for synthesizing diverse phosphonic acid derivatives.^{107,207} Notably, α -aryl- α -diazophosphonates play a crucial role in generating phosphonate-containing cyclopropanes, allenes, α,β -unsaturated phosphonates, imines, and diarylphosphonates.^{208,209}

The Regitz diazo transfer reaction, as depicted in (Scheme 4.1), is widely regarded as the most commonly used approach for obtaining donor/acceptor diazo compounds. This method involves using substrates that contain suitable acidic protons and employing sulfonyl azides as the diazo transfer reagents.^{210,211} Initially, tosyl azide was the preferred choice for diazo transfer reactions. However, the Davies group later introduced *p*-acetamidobenzenesulfonyl azide as a safer alternative, which has since become the standard diazo transfer reagent.²¹² However, these conventional conditions are found to be less effective for synthesizing diazophosphonate derivatives.

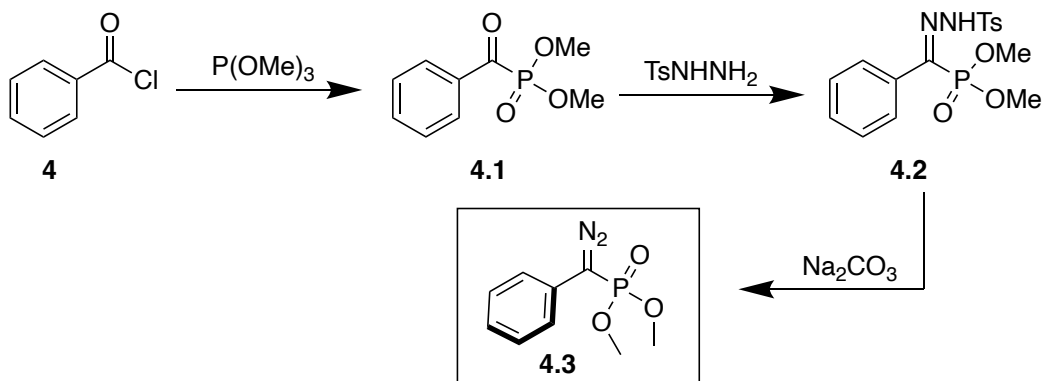


Scheme 4.1. Diazo transfer reaction for diazo synthesis

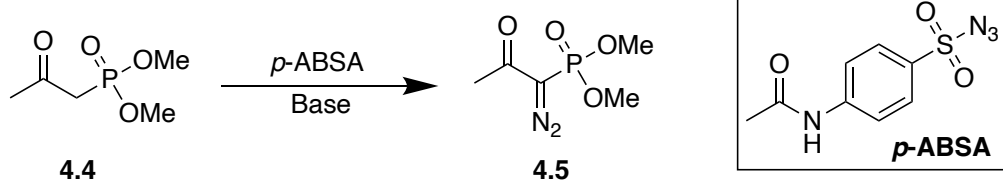
The sulfonyl azide-mediated diazo transfer reaction, pioneered by Regitz and coworker, has proven effective for synthesizing various compounds such as aryldiazoacetates, diazoketones, 2-diazo-1,3-dicarbonyl compounds, α -arylsulfonylcarboxylates, α -phosphonoacetates, and α -phosphonoketones.²¹⁰ However, this straightforward approach has not been widely employed for the preparation of α -aryldiazophosphonates. Few examples with relatively low yields are documented in the literature. Nonetheless, two methods currently utilized for synthesizing diazophosphonates are the Michaelis–Arbuzov method^{125,213–217} and the Bestmann–Ohira method^{121,218–222} (Scheme 4.2).

However, the scope of diazophosphonates remains limited, as these two methods can only synthesize a restricted range of substrates.

Michaelis–Arbuzov method

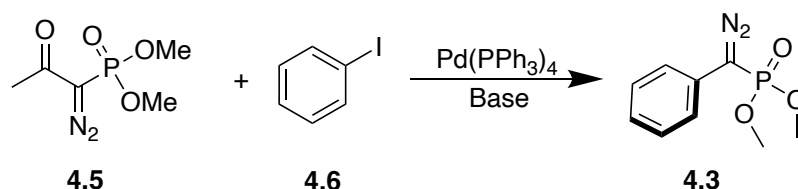


Bestmann–Ohira method



Scheme 4.2 Michaelis–Arbuzov and Bestmann–Ohira methods.

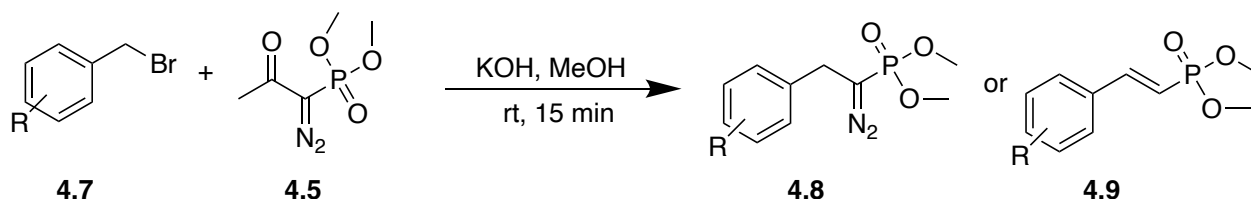
In 2014, Wang and coworkers developed a room temperature, Palladium(0)-catalyzed deacylative cross-coupling method for aryl iodides and acyldiazocarbonyl compounds. This reaction was conducted under mild conditions and allowed for the synthesis of aryldiazophosphonates. However, the range of applicable compounds in this reaction was relatively restricted (**Scheme 4.3**). Despite this limitation, the coupling reaction employed readily accessible starting materials, proceeded at room temperature, and exhibited compatibility with a few functional groups.¹²⁴ Nevertheless, it is constrained by its inability to accommodate various functional groups and its exclusion of heterocycles within its range.



Scheme 4.3 Palladium(0)-Catalyzed Deacylative Cross-Coupling.

In 2014, Rastogi and colleagues reported a study on the nucleophilic displacement of alkyl bromides using the Bestmann-Ohira reagent. The reaction yielded either dimethyl diazoalkylphosphonates **4.8** or (*E*)-vinylphosphonates **4.9**, depending on the substituent present. The dimethyl diazoalkylphosphonates could be easily transformed into (*E*)-vinylphosphonates by the addition of Cu, resulting in quantitative yields upon nitrogen elimination. Interestingly, benzyl bromides with electron-withdrawing substituents at the ortho- or para- positions underwent nitrogen elimination, leading to the corresponding styrylphosphonates **4.9**. This observation was attributed to the acidity of the benzylic proton, which facilitated 1,2-migration in these substrates (**Scheme 4.4**).

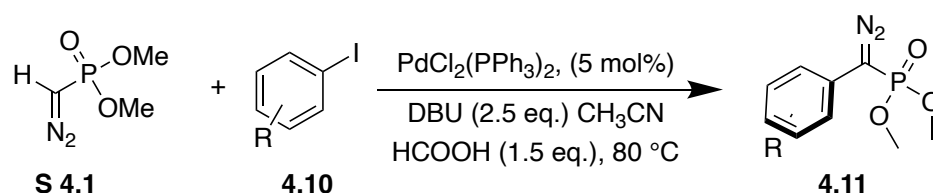
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Scheme 4.4 Selective synthesis of α-diazoalkylphosphonates or vinylphosphonates via nucleophilic substitution of alkyl bromides.

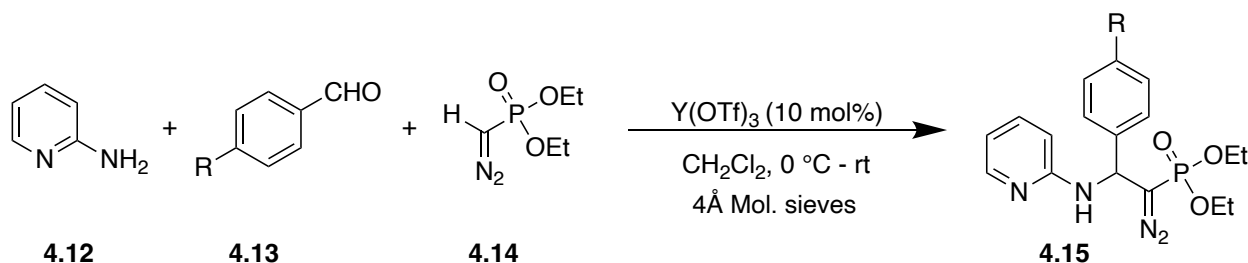
In 2014, Beletskaya and coworkers conducted a study on the Pd-catalyzed arylation of diethyl diazomethylphosphonate **S 4.1** (**Scheme 4.5**). Following the screening of several reaction

conditions, $\text{PdCl}_2(\text{PPh}_3)_4$, acetonitrile, and DBU were identified as the preferred catalyst, solvent, and base, respectively. Notably, the presence of formic acid as a reducing agent for $\text{Pd}(0)$ species generation was found to be a crucial parameter. The study observed a significant influence of the electronic effect of the substituent present in the aromatic ring on the yield. The best yields were obtained when using aryl iodides with electron-withdrawing substituents as starting materials, which shows the limitation of this method.²²⁴



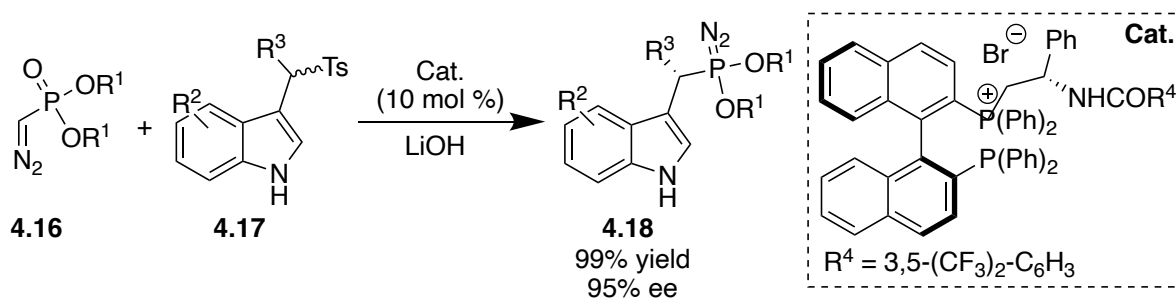
Scheme 4.5 Synthesis of Dimethyl α -Aryl- α -diazomethylphosponates.

In 2013, Gevorgyan and coworkers presented the development of a three-component coupling (3-CC) reaction involving 2-aminoazines, aromatic aldehydes, and diazo-compounds. The reaction resulted in the production of polyfunctional β -amino- α -diazo-compounds with the assistance of a heterocycle. This process involved an unprecedented addition of a diazo compound to an imine. Subsequently, the obtained diazoesters were successfully converted into important heterocycles and β -amino acid derivatives (**Scheme 4.6**).²²⁵



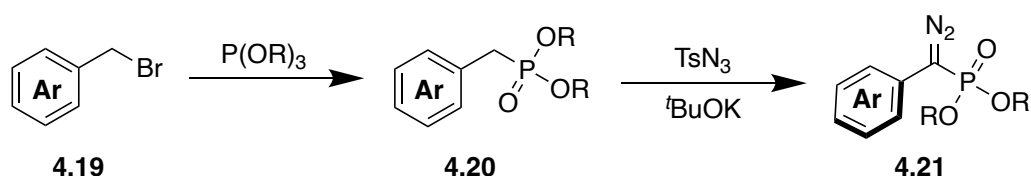
Scheme 4.6 $\text{Y}(\text{OTf})_3$ Catalyzed Three-Component Reaction.

In 2022, Peng and coworkers developed an enantioselective addition of α -diazomethylphosphonate to vinylogous imines derived from 2-unsubstituted sulfonylindoles, catalyzed by P-based phase-transfer catalysts. They introduced a set of trifunctional monophosphonium phase-transfer BINAP catalysts, incorporating axial and central chirality simultaneously for the first time, serving as nucleophile, phase-transfer agent, and hydrogen bond donor. The most effective catalyst was successfully applied in the asymmetric addition of α -diazomethylphosphonates to vinylogous imines formed in situ from 2-unsubstituted sulfonyl indoles, yielding the desired product **4.18** with up to 99% yield and 95% enantioselectivity (**Scheme 4.7**).²²⁶



Scheme 4.7 Diazomethylphosphonate Catalyzed by a Trifunctional BINAP-Based Monophosphonium Salt.

In 2023, Titanyuk and coworkers introduced an efficient diazo group transfer reaction as a versatile strategy for synthesizing α -aryl- α -diazophosphonates. This approach utilizes readily available starting materials (benzylphosphonates and TsN₃), along with a straightforward basic reagent, potassium tert-butoxide, and demonstrates compatibility with a limited number of functional groups (**Scheme 4.8**).²²⁷ It is worth noting that this method exhibits high reactivity and is time-sensitive, requiring monitoring through TLC to prevent decomposition. However, it has limitations, notably in its intolerance for several functional groups and the absence of heterocycles in its scope.



Scheme 4.8 Synthesis of Aryldiazophosphonates via a Diazo Transfer Reagent.

Drawing inspiration from the research conducted by Wang and our previous studies on diazoacetates,^{124,129} we proposed that a comparable approach could be utilized for the production of aryl- and hetero-diazophosphonates. Considering the versatile nature of diazophosphonates as reagents and the limitations of current methodologies, there is a critical demand for an alternative, universally adaptable synthetic pathway for these substances. In this study, we introduce a palladium(0)-catalyzed cross-coupling process involving aryl or hetero iodide and acceptor-only diazophosphonate compounds, operating under mild reaction conditions at room temperature. This coupling reaction presents a highly effective and widely applicable method for generating aryl- and hetero-diazophosphonate compounds, which are increasingly utilized as precursors for the production of donor/acceptor-substituted metallocarbenes.

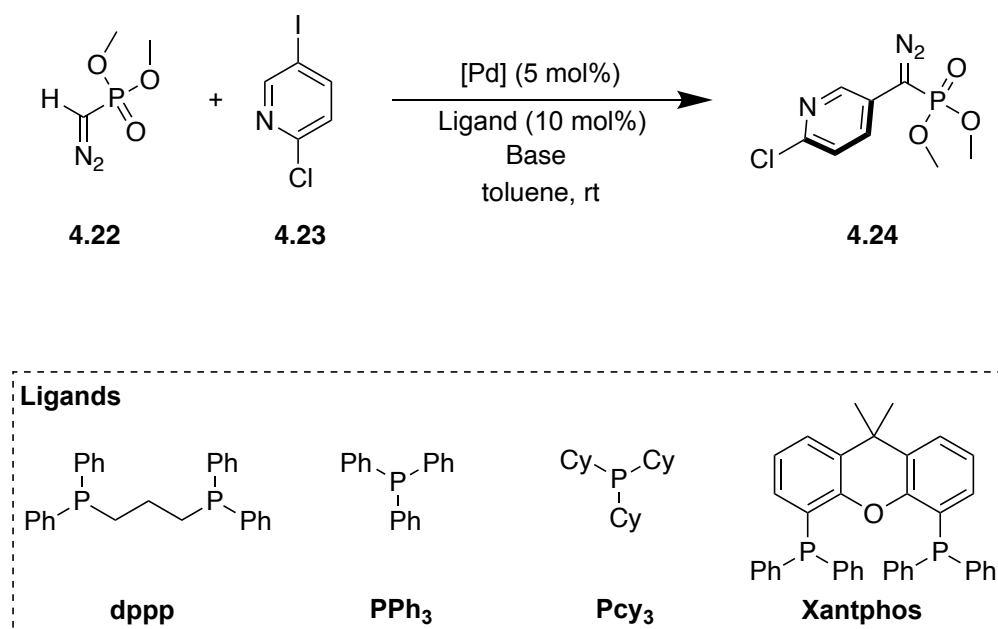
At the outset of this investigation, hetero iodide **4.23** and acceptor-only diazophosphonate **4.22** were chosen as the model substrates for investigating the coupling reaction (**Table 4.1**). The optimization process for reaction conditions entailed the addition of 5 mol% [Pd(PPh₃)₄], 10 mol% of a ligand, 1.0 equivalent of base, and 15 mL of toluene. Initial experiments using various palladium catalysts without employing any ligand and with 1.0 equivalent of K₂CO₃ yielded notably poor results. However, utilizing palladium tetrakis(triphenylphosphine) (5 mol%) produced product **4.24** with a 15% yield.

Further exploration involved testing different ligands. When 1,3-Bis(diphenylphosphino)propane (dppp) was employed at 10 mol%, product **4.24** was obtained in an 18% yield with 1.0 equivalent of K₂CO₃ (**Entry 5**). Xantphos at 10 mol% provided a 25% yield (**Entry**

6). Tricyclohexylphosphine (Pcy₃) at 10 mol% resulted in a 17% yield (**Entry 7**). Interestingly, using Triphenylphosphine (PPh₃) at 10 mol% doubled the yield to 33% (**Entry 8**), indicating promising results.

Subsequently, the impact of the base was examined. A mixture of K₂CO₃ and NEt₃ enhanced the yield from 33% to 40%. Moreover, the utilization of a combination of Cs₂CO₃ and NEt₃ resulted in a 52% yield, whereas the combination of Ag₂CO₃ and NEt₃ produced the most favorable outcome, delivering a yield of 58% for product **4.24**. With the refined reaction conditions (**Table 4.1, Entry 11**), we then proceeded to explore the substrate diversity using a range of aryl and hetero iodides, as depicted in (**Table 4.2**)

Table 4.1. Optimization of the reaction conditions.^[a]

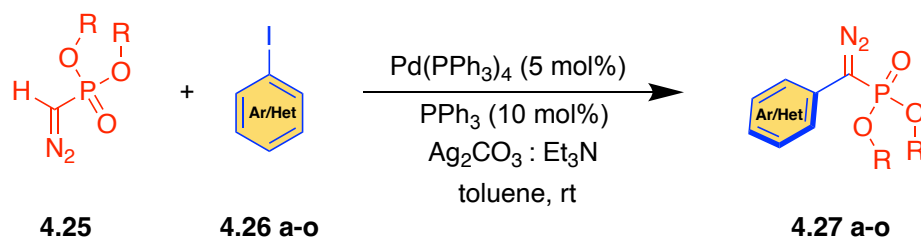


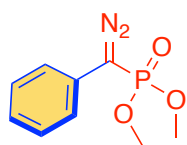
entry	[Pd]	ligand	base	yield
1	Pd(PPh ₃) ₄	—	K ₂ CO ₃	15%
2	Pd ₂ (dba) ₃	—	K ₂ CO ₃	—
3	Pd(dppf)Cl ₂	—	K ₂ CO ₃	—
4	Pd(PPh ₃)Cl ₂	—	K ₂ CO ₃	12%
5	Pd(PPh ₃) ₄	dppp	K ₂ CO ₃	18%
6	Pd(PPh ₃) ₄	Xantphos	K ₂ CO ₃	25%
7	Pd(PPh ₃) ₄	Pcy ₃	K ₂ CO ₃	17%
8	Pd(PPh ₃) ₄	PPh ₃	K ₂ CO ₃	33%
9	Pd(PPh ₃) ₄	PPh ₃	K ₂ CO ₃ : Et ₃ N	40%
10	Pd(PPh ₃) ₄	PPh ₃	Cs ₂ CO ₃ : Et ₃ N	52%
11	Pd(PPh₃)₄	PPh₃	Ag₂CO₃ : Et₃N	58%

[a] **Standard reaction conditions:** Acceptor diazophosphonate **4.22** (dimethyl (diazomethyl) phosphonate, 3.19 mmol, 1.3 equiv), hetro halide **4.23** (2.45 mmol, 1.0 equiv), NEt₃ (2.45 mmol, 1.0 equiv), Ag₂CO₃ (1.84 mmol, 0.75 equiv), Pd(PPh₃)₄ (5 mol%), and ligand (10 mol%) in 15 mL of toluene at room temperature for 6 hours (monitor by TLC).

Once the optimal conditions were established, the reaction's scope was explored using a range of representative substrates, as outlined in (Table 4.2). The reactions with substrates **4.26 a–o**, resulting in the formation of products **4.27a–o**, demonstrated compatibility with various functional groups (Table 4.2). Impressively versatile, the reaction accommodated different p-substituted aryl- and hetero derivatives, including both electron-withdrawing and electron-donating groups. Substrates **4.26a–d**, either lacking functional groups or containing halogens, yielded products **4.27a–d** with excellent yields ranging from 83% to 91%. Notably, substrate **4.26a** underwent a multigram scale reaction, providing a remarkable 86% yield **4.27a** for a five-gram scale reaction. Substrate **4.26e**, containing a dioxol functional group, resulted in product **4.27e** with a good yield of 80%. Of particular interest is the compatibility of the boron pinacolate group, which afforded

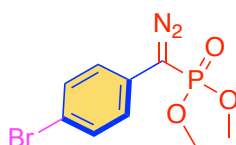
product **4.18f** with an impressive 85% yield, offering a valuable synthetic handle for further modifications. The reactions could also be applied to substrates derived from pharmaceutical agents **4.26g–j**, yielding products **4.27g–j** with moderate to good yields ranging from 53% to 75%. To demonstrate the broader applicability of this methodology, several diazophosphonates containing heteroaryl fragments commonly found in pharmaceuticals were synthesized, resulting in products **4.27k–o** with decent yields ranging from 40% to 67%. Nevertheless, substrates containing pyridine without any halogen yielded approximately 10%, and substrates with a functional group on the ortho position resulted in only a trace amount of the product. The key differences in the reaction conditions are the presence of an additional PPh₃ ligand beyond what is provided by Pd(PPh₃)₄, and the use of a combination of Ag₂CO₃ and Et₃N as bases. A plausible hypothesis for the role of the additional PPh₃ ligand is that it could influence the coordination environment around palladium, stabilizing certain intermediates or affecting the catalytic cycle's overall efficiency. This could enhance the catalyst's activity or selectivity. Regarding the combination of Ag₂CO₃ and Et₃N, Ag₂CO₃ likely serves as a mild oxidizing agent, facilitating the turnover of the palladium catalyst by assisting in the reoxidation of Pd(0) to Pd(II). Et₃N, on the other hand, acts as a base to neutralize any acidic byproducts formed during the reaction, ensuring that the reaction proceeds under favorable conditions.¹²⁹ However, these effects were determined purely through empirical observations rather than a mechanistic study, it would be accurate to state that these conditions were optimized experimentally, without a definitive mechanistic explanation for their roles.



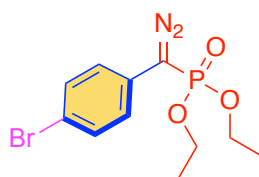


4.27a
88% yield

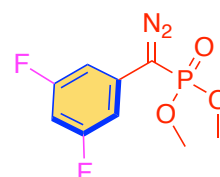
86 % yield
for five gram-scale



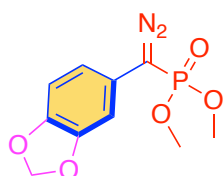
4.27b
90% yield



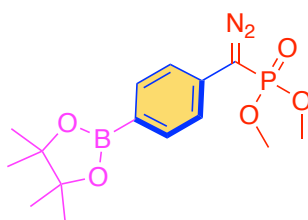
4.27c
83% yield



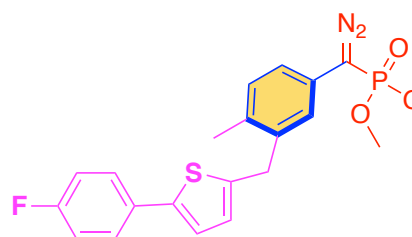
4.27d
91% yield



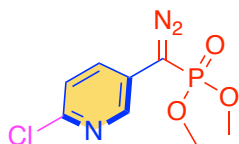
4.27e
80% yield
Dioxol



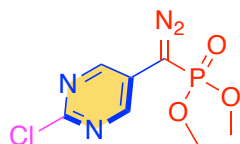
4.27f
85% yield
Boron



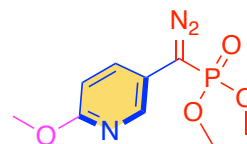
4.27g
75% yield
Canagliflozin



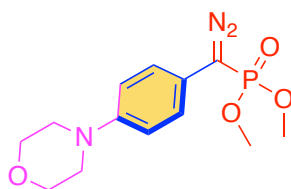
4.27k
58% yield
Pyridine



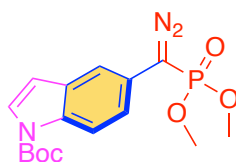
4.27l
40% yield
Pyrimidine



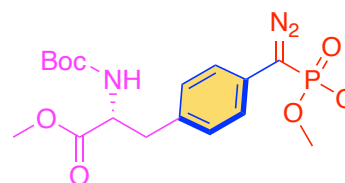
4.27m
60% yield
Pyridine



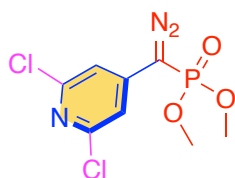
4.27h
55% yield
Morpholine



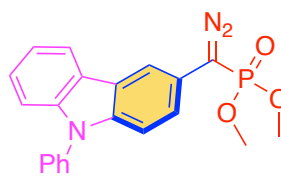
4.27i
60% yield
Indole



4.27j
53% yield
Amino Acid



4.27n
54% yield
Pyridine



4.27o
67% yield
Carbazole

Unsuccessful substrates (~10% yield to trace amount of product)

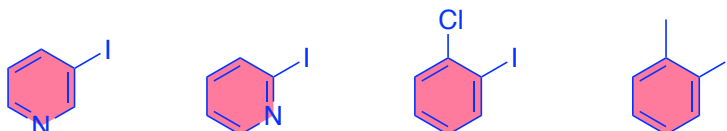
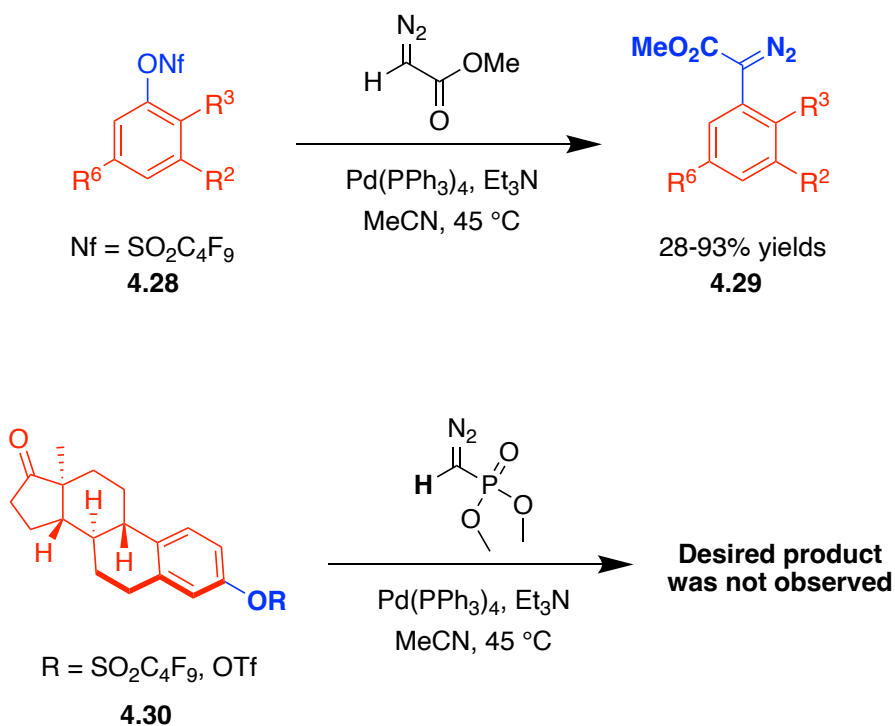


Table 4.2 Scope of palladium-catalyzed cross-coupling reactions.

Additionally, Reissig and coworkers developed an efficient method for preparing pyrid-4-yl-substituted methyl diazoacetates (**4.29**) through palladium-catalyzed couplings of pyrid-4-yl nonaflates (**4.28**) with methyl diazoacetate. After optimizing the reaction conditions, the transformation was found to have a broad scope, allowing for the synthesis of a series of pyrid-4-yl-substituted methyl diazoacetates in moderate to high yields.²²⁸ We also attempted to apply this method to compounds containing a phenol functional group by converting them into nonaflates or triflates to avoid the multi-step process of introducing an iodo functional group. However, this approach proved ineffective with acceptor-only diazophosphonate, as no desired product was generated. Additionally, we tried using compound **4.30** with the optimized reaction conditions we developed, but it still did not yield any desired product.



Scheme 4.9 Nonaflates or triflates coupling reaction.

A plausible reaction mechanism is proposed in **Figure 4.1**. The process begins with the oxidative addition of an aryl or heteroaryl iodide to the palladium(0) catalyst, resulting in the formation of intermediate **4.33**. This intermediate then coordinates with the diazo substrate to form intermediate **4.34**. Next, due to the presence of a base, deprotonation occurs, converting **4.34** into intermediate **4.35**. Finally, reductive elimination from **4.35** produces the coupling product **4.36** and regenerates the palladium(0) catalyst.¹²⁴

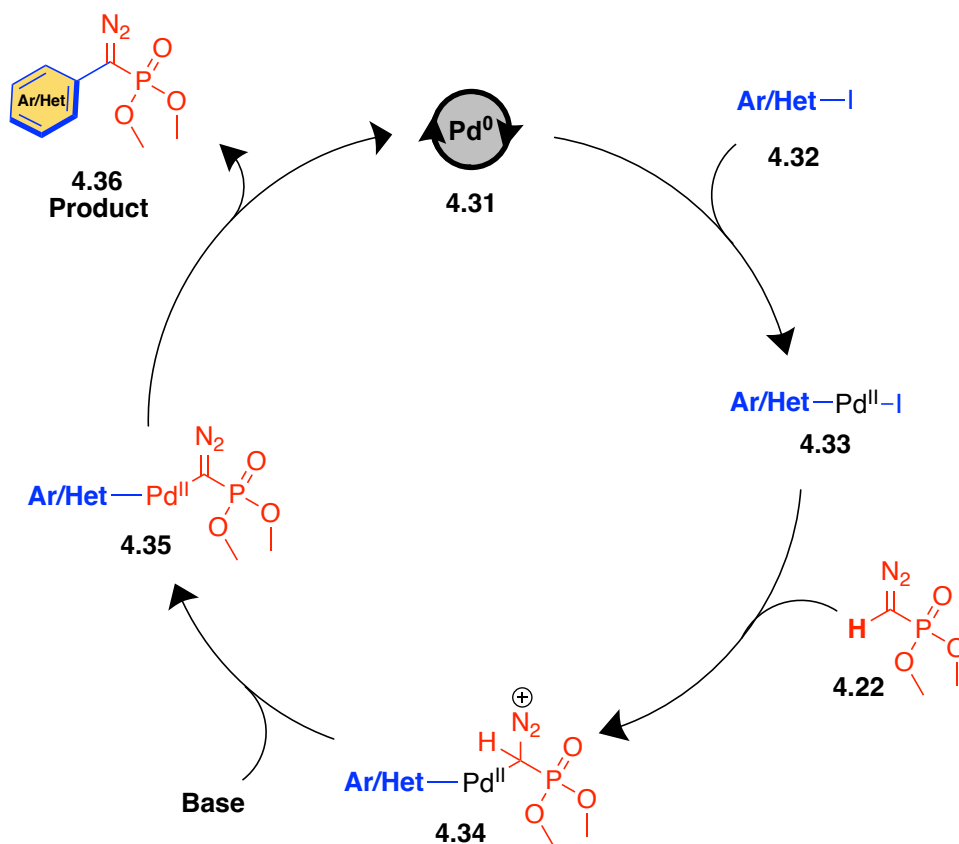


Figure 4.1 Proposed mechanism.

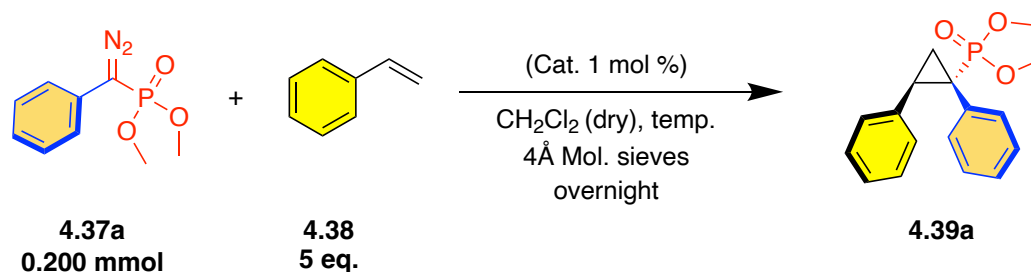
The cross-coupling reaction produced several novel aryl- and heteroaryl- diazophosphonates, many of which had not been previously used in enantioselective rhodium-catalyzed reactions. To explore their potential, we evaluated one of the compounds in the cyclopropanation of styrene using various rhodium catalysts and conditions, including dry dichloromethane at both reflux and room temperature. The initial phase of the research involved identifying the most effective chiral catalyst for the cyclopropanation reaction (**Table 4.3**). The preliminary experiments utilizing standard reaction conditions with the dirhodium catalyst, $\text{Rh}_2(\text{S-DOSP})_4$, resulted in a moderate yield of 65%. However, the enantioselectivity level of the cyclopropanation product **4.39a** was unsatisfactory at 20% ee, with a diastereomeric ratio of (>20:1) (**Table 4.3, entry 1**).

The phthalimido-derived catalyst $\text{Rh}_2(\text{S-PTAD})_4$, which had been shown to be effective in cyclopropanation reactions with **4.37a** gave the desired product **4.39a** in 85% isolated yield with 94% ee and (>30:1 d.r.) (**entry 2**). The phthalimido-derived catalyst $\text{Rh}_2(\text{S-TPPTTL})_4$ performed well, generating **4.39a** in 41% ee and in good yield of 88% with (30:1 d.r.) (**entry 3**). The use of the bulky triarylcyclopropanecarboxylate catalyst, $\text{Rh}_2(\text{S-}i\text{-Ph-TPCP})_4$, resulted in a satisfactory yield of 72% for the desired product **4.39a** (**entry 4**) with 60% ee and (20:1 d.r.). In contrast, the naphthalimido-derived catalyst $\text{Rh}_2(\text{S-NTTL})_4$ exhibited excellent performance, providing **4.39a** in 80% ee with a high yield of 90% and (30:1 d.r.) (**entry 5**). Subsequently, we synthesized an extended range of $\text{Rh}_2(\text{S-NTTL})_4$ derivatives, which were also subjected to evaluation. The tetraphenyl derivative, $\text{Rh}_2(\text{S-TPNTTL})_4$, gave improved enantioselectivity (90% ee), and excellent yield (92%) with (30:1 d.r.) (**entry 6**), whereas $\text{Rh}_2(\text{S-di}(4\text{'Bu})\text{PhNTTL})_4$ was found to be similar to $\text{Rh}_2(\text{S-TPNTTL})_4$, generating **4.39a** in 90% yield and 92% ee (**entry 7**).

All extended $\text{Rh}_2(\text{S-NTTL})_4$ derivatives demonstrated strong performance in cyclopropanation reactions, with PTAD and NTTL derivatives being the most effective. We also investigated the effect of temperature since all reactions were initially conducted under reflux conditions to determine if similar or superior results could be achieved. At room temperature, the catalyst $\text{Rh}_2(\text{S-PTAD})_4$ yielded 86% with 95% ee (**entry 8**). The catalyst $\text{Rh}_2(\text{S-mono}(4\text{'Bu})\text{PhNTTL})_4$ provided an excellent yield of 90% with a diastereomeric ratio (d.r.) of 30:1 and 88% ee (**entry 9**) at room temperature. The $\text{Rh}_2(\text{S-TPNTTL})_4$ catalyst at room temperature showed high efficiency with a 91% yield and 92% ee (**entry 10**), although it was not as effective as $\text{Rh}_2(\text{S-PTAD})_4$. The catalyst $\text{Rh}_2(\text{S-di}(4\text{'Br})\text{TPPTTL})_4$ achieved a good yield of 85% with a diastereomeric ratio (d.r.) of 30:1 but exhibited poor enantioselectivity at 26% ee (**entry 11**) at room temperature. However, when 20 equivalents of HFIP (Hexafluoro-2-propanol) additive were introduced, the catalyst maintained a comparable yield of 83% while significantly improving enantioselectivity from 26% ee to 56% ee (**entry 12**), retaining a

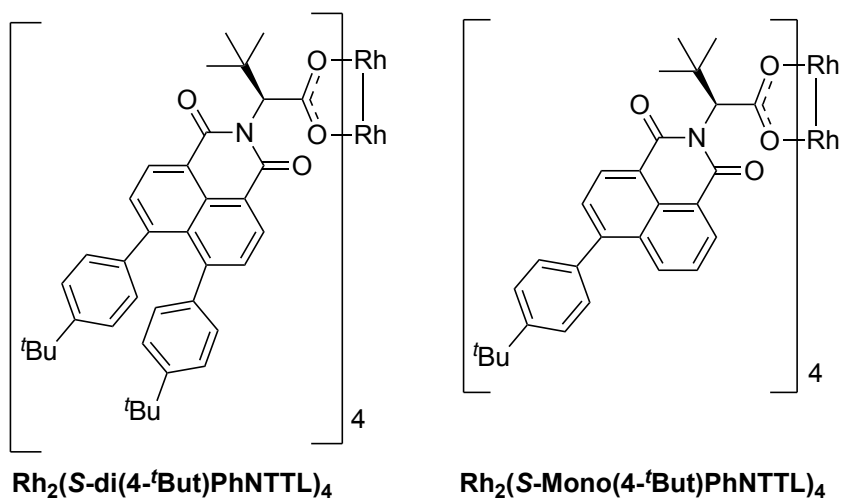
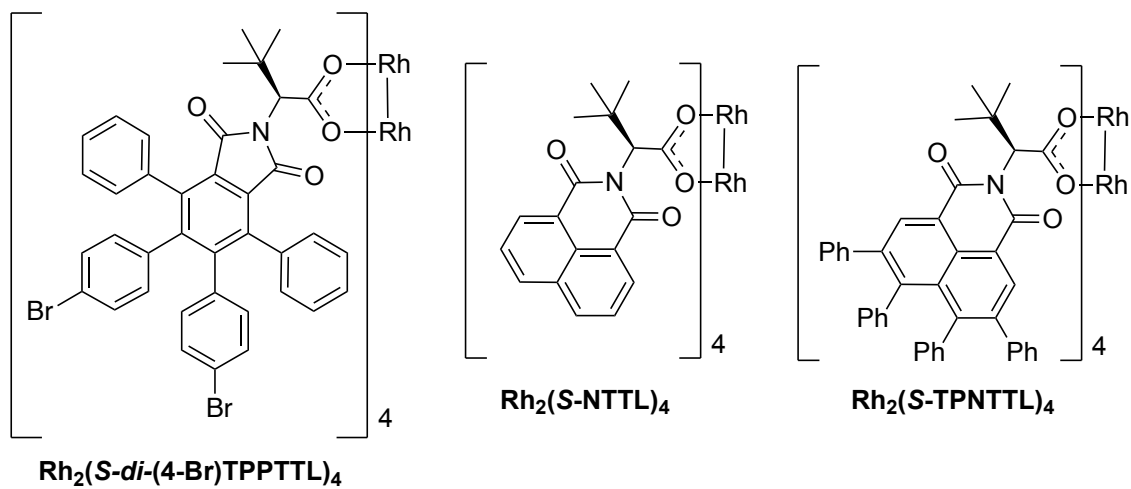
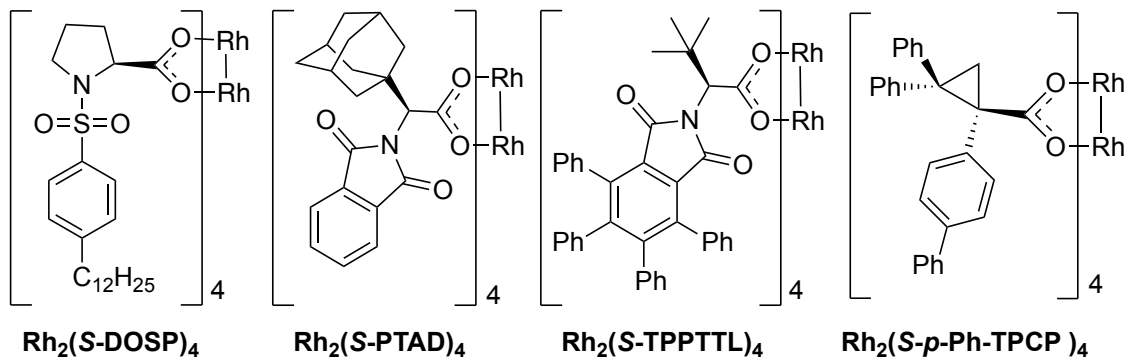
diastereomeric ratio (d.r.) of 30:1 at room temperature. Additionally, the experiment with the bulkier catalyst $\text{Rh}_2(\text{S-di}(3,5\text{'Bu})\text{PhNTTL})_4$ showed significantly higher effectiveness than $\text{Rh}_2(\text{S-PTAD})_4$, achieving a 92% yield with 96% ee and a d.r. of greater than 30:1 (**entry 11**).

Table 4.3. Catalyst optimization studies cyclopropanation reactions.^a



Entry	Catalyst	Temp. (°C)	yield, %	d.r.	ee, %
1	$\text{Rh}_2(\text{S-DOSP})_4$	40 °C	65%	> 20:1	20%
2	$\text{Rh}_2(\text{S-PTAD})_4$	40 °C	85%	> 30:1	94%
3	$\text{Rh}_2(\text{S-TPPTTL})_4$	40 °C	88%	> 30:1	41%
4	$\text{Rh}_2(\text{S-}p\text{-Ph-TPCP})_4$	40 °C	72%	20:1	60%
5	$\text{Rh}_2(\text{S-NTTL})_4$	40 °C	90%	> 30:1	80%
6	$\text{Rh}_2(\text{S-TPNTTL})_4$	40 °C	92%	> 30:1	90%
7	$\text{Rh}_2(\text{S-di}(4\text{'Bu})\text{PhNTTL})_4$	40 °C	90%	> 30:1	92%
8	$\text{Rh}_2(\text{S-PTAD})_4$	23 °C	86%	> 30:1	95%
9	$\text{Rh}_2(\text{S-Mono}(4\text{'Bu})\text{PhNTTL})_4$	23 °C	90%	> 30:1	88%
10	$\text{Rh}_2(\text{S-TPNTTL})_4$	23 °C	91%	> 30:1	92%
11	$\text{Rh}_2(\text{S-di}(4\text{'Br})\text{TPPTTL})_4$	23 °C	85%	> 30:1	26%
12 ^b	$\text{Rh}_2(\text{S-di}(4\text{'Br})\text{TPPTTL})_4$	23 °C	83%	> 30:1	56%
13	$\text{Rh}_2(\text{S-di}(3,5\text{'Bu})\text{PhNTTL})_4$	23 °C	92%	> 30:1	96%

^a Reaction conditions: To a mixture of **4.28** (1.0 mmol) and [Rh] catalyst (1 mol %) in dry CH_2Cl_2 solvent (5.0 mL) was added a solution of **4.27a** (0.2mmol) in dry CH_2Cl_2 solvent (10.0 mL) via an automatic syringe pump over 5 hours. The mixture was stirred overnight, and all reactions were performed with freshly distilled dry CH_2Cl_2 stored over activated 4 Å molecular sieves. ^b 20 equiv. of HFIP (Hexafluoro-2-propanol) was added as an additive.



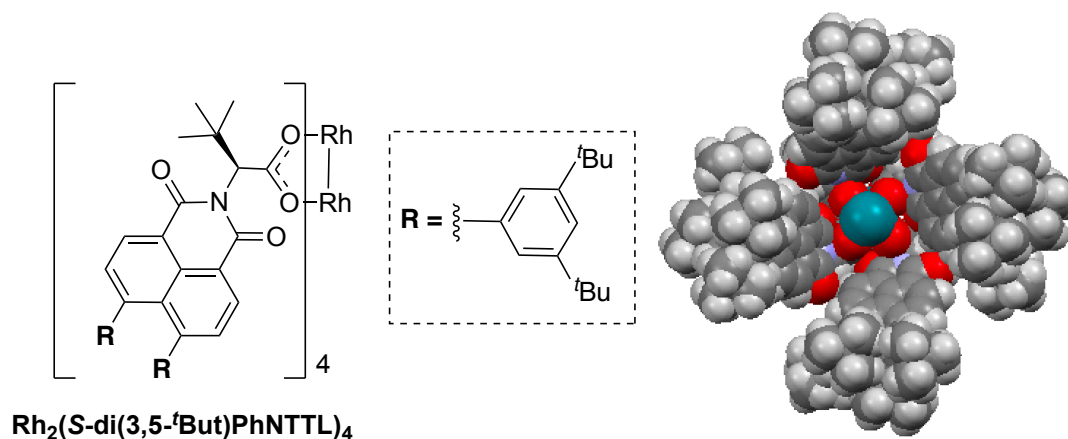
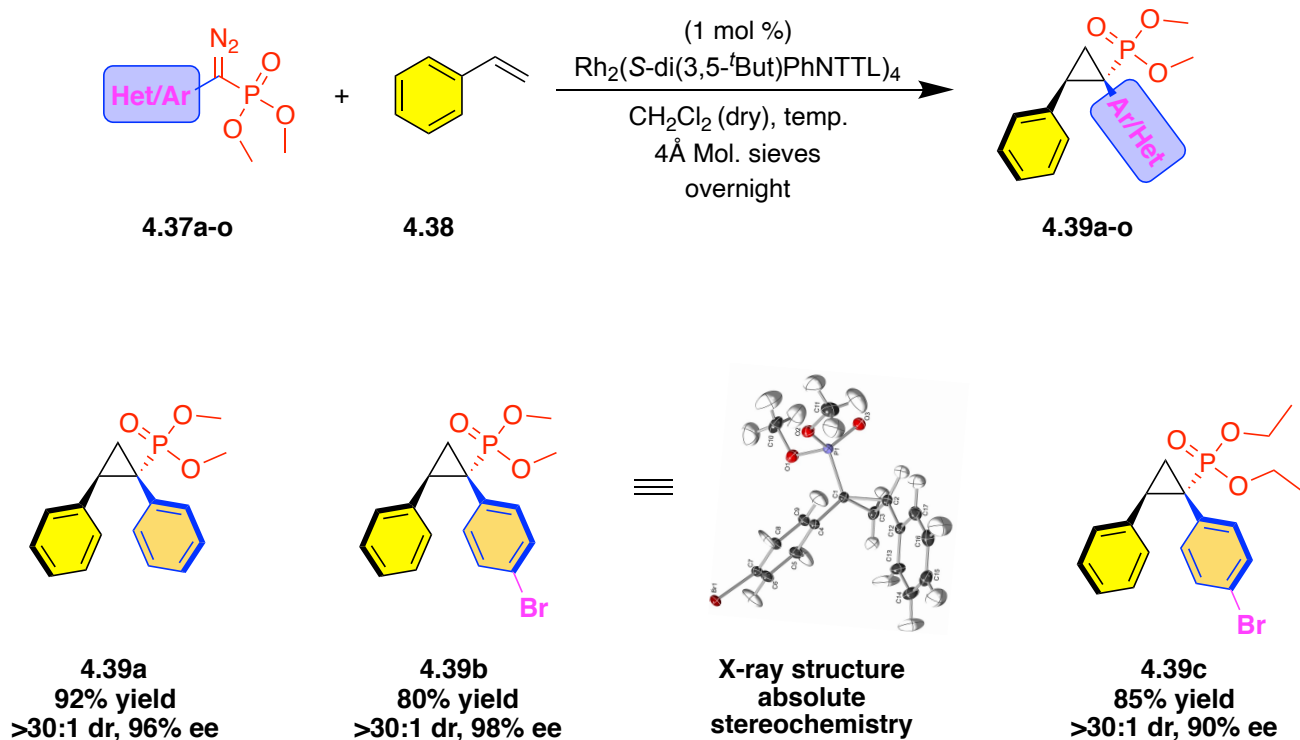


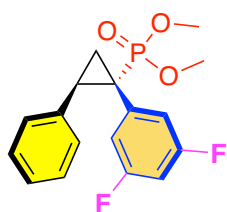
Figure 4.2 Chiral dirhodium catalyst.

Once Rh₂(S-di(3,5-*t*Bu)PhNTTL)₄ was identified as the optimal catalyst, the reaction scope was evaluated using a series of representative diazo substrates, as shown in **Table 4.4**. The reactions with substrates **4.37a-o**, leading to products **4.39a-o**, highlight the functional groups compatible with this chemistry (**Table 4.4**). Catalyst Rh₂(S-di(3,5-*t*Bu)PhNTTL)₄, which proved effective in cyclopropanation reactions with **4.37a**, delivered the desired product **4.39a** in 92% isolated yield with 96% ee and (>30:1 d.r.). The similar diazo compound **4.37b**, bearing a bromide at the para position, showed high efficacy with this catalyst, providing **4.39b** in 80% isolated yield with 98% ee and (>30:1 d.r.). Diazo compound **4.37c**, carrying an ethyl ester functional group, yielded **4.39c** in 85% isolated yield with 90% ee and (>30:1 d.r.). Compound **4.37d**, bearing a dibromide at the meta positions, providing **4.39d** in 78% isolated yield with 90% ee and (>30:1 d.r.). Compound **4.37e**, containing a dioxol functional group, providing **4.39e** in 84% isolated yield with 97% ee and (>30:1 d.r.). Compound **4.37f**, containing a boronate functional group, which is highly useful in cross-coupling reactions, produced **4.39f** in 75% isolated yield with 86% ee and (>30:1 d.r.). Diazo **4.37g**, containing a thiophene and fluorophenyl at the meta position, produced **4.39g** in 68% isolated yield with 90% ee and (>30:1 d.r.). Similarly, Diazo **4.37h**, containing morpholine group, which is used for inhibitor purposes, provided **4.39h** in 55% isolated yield with 88% ee and

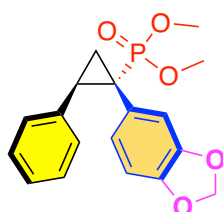
(>30:1 d.r.). Diazo compound **4.37i**, which includes an indol, provided **4.39i** 72% isolated yield with 66% ee and (>30:1 d.r.) Diazo compound **4.37j**, which contains an amino acid produced **4.39j** in 63% yield with 96% de.

The heterocycle-containing compound **4.37k** yielded **4.39k** in 70% isolated yield with an impressive 99% ee and (>30:1 d.r.). Diazo compound **4.37l**, containing chloropyrimidine produced **4.39l** in 53% yield with 97% ee and (>30:1 d.r.). A heterocycle-containing diazo compound **4.37m**, bearing a methoxy at the para position, showed high efficacy with this catalyst providing **4.39m** in 75% isolated yield with 99% ee and (>30:1 d.r.). Diazo compound **4.37n**, containing 2,6-dichloropyridine produced **4.39n** in 60% yield, however with a low enantioselectivity of 41% ee. Finally, diazo compound **4.37o**, bearing a carbazole, providing **4.39 o** in 81% isolated yield with 96% ee and (>30:1 d.r.).

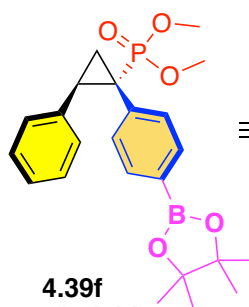




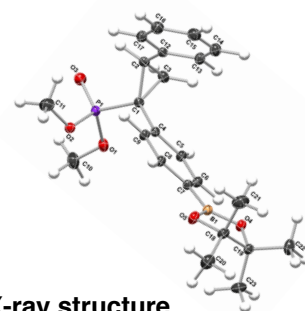
4.39d
78% yield
>30:1 dr, 90% ee



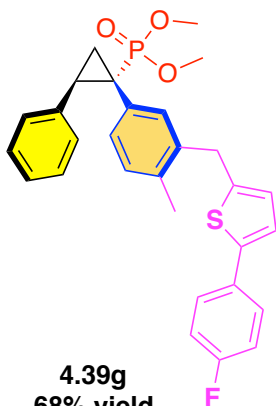
4.39e
84% yield
>30:1 dr, 97% ee



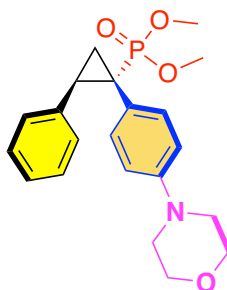
4.39f
75% yield
>30:1 dr, 86% ee



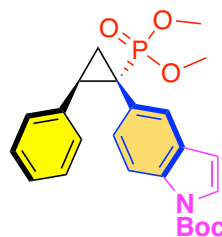
**X-ray structure
absolute
stereochemistry**



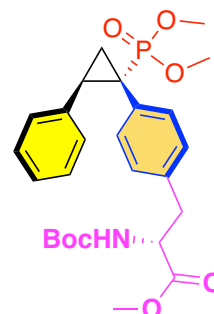
4.39g
68% yield
>30:1 dr, 90% ee



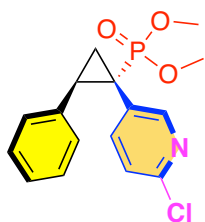
4.39h
55% yield
>30:1 dr, 88% ee



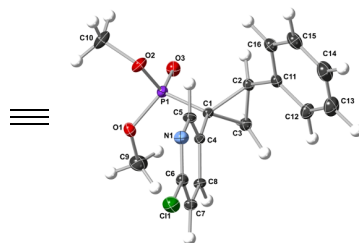
4.39i
72% yield
>30:1 dr, 66% ee



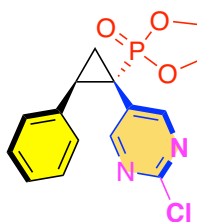
4.39j
63% yield
96% de



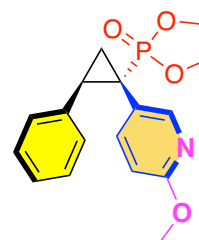
4.39k
70% yield
>30:1 dr, 99% ee



**X-ray structure
absolute
stereochemistry**



4.39l
53% yield
>30:1 dr, 97% ee



4.39m
75% yield
>30:1 dr, 99% ee

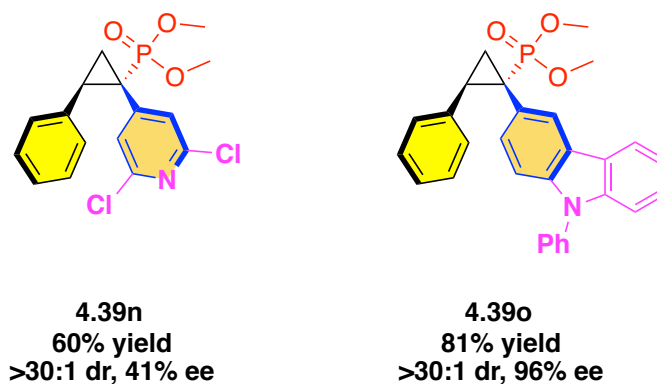


Table 4.4 Test of diazo compounds in cyclopropanation reactions.

In 2010, Katsuki and coworkers demonstrated that Ir(salen) complexes can efficiently catalyze enantioselective cyclopropanation. They showed that cyclopropanation can be achieved using donor/acceptor-substituted diazo compounds like R-phenyl-R-diazophosphonate as carbenoid precursors. These reactions provided highly enantioenriched cyclopropanes, yielding 96% isolated product with 86% enantiomeric excess (ee).²²⁹ To further explore this reaction, we applied our newly developed catalyst and successfully obtained highly enantioenriched cyclopropanes **4.41** with 95% isolated yield and 95% ee, surpassing previously reported enantioselectivity.

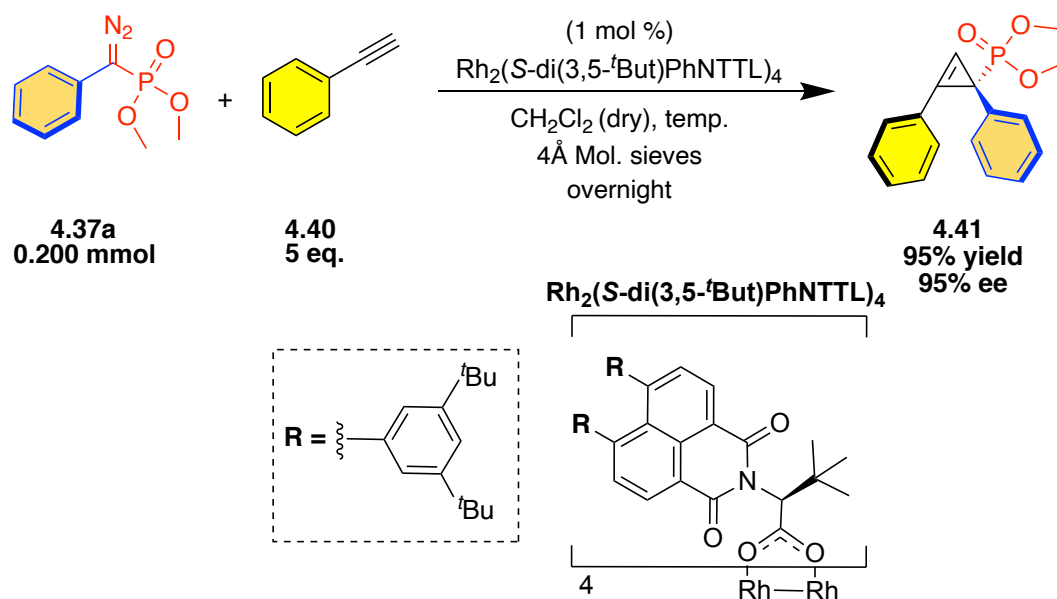


Table 4.5 Enantioselective Cyclopropanation.

4.2 Conclusion

We have developed a highly efficient palladium(0)-catalyzed cross-coupling reaction that introduces a new approach for synthesizing aryl- and heteroaryl-diazophosphonates. This method employs readily available starting materials, proceeds at room temperature, and is tolerant of a wide variety of functional groups, making it a versatile tool for diazo compound synthesis. To optimize this process, the addition of an extra phosphine ligand was required to prevent the decomposition of the diazo products. These easily accessible diazo compounds are expected to broaden the range and flexibility of donor-acceptor metallocarbene chemistry.

Rhodium-catalyzed cyclopropanation and C–H functionalization offer versatile and efficient approaches to constructing complex molecular structures. The distinct reactivity of rhodium catalysts enables highly regio- and stereoselective transformations, often under mild conditions. Rhodium carbenoids are particularly powerful in facilitating cyclopropanation, allowing the formation of three-membered rings with broad functional group compatibility. Additionally, rhodium-catalyzed C–H activation expands the possibilities for direct functionalization of otherwise inert C–H bonds, streamlining the modification of organic molecules without pre-functionalization. These advancements hold great potential for synthetic chemistry, especially in the development of pharmaceuticals, agrochemicals, and natural product synthesis.

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Experimental Section

General Information

All chemicals were used as purchased or purified according to Purification of Common Laboratory Chemicals if necessary. All chemical reagents were purchased from commercial sources and used as received unless otherwise noted. ^1H , ^{13}C , ^{19}F , and ^{31}P NMR spectra were recorded at either 400, 500 or 600 MHz on Bruker spectrometer or Varian spectrometer, (^{13}C at 101, or 151 MHz), 400 or 600 MHz on Bruker spectrometer, (^{19}F at 376 or 565) on Bruker-400 or Bruker-600 spectrometers, and (^{31}P at 162 or 243 MHz) on Bruker-400 or Bruker-600 spectrometers and all were reported in parts per million (ppm). All NMR samples solvent were performed using deuterated chloroform (CDCl_3) solvent unless otherwise noted. Coupling constant (J) values are recorded in Hertz (Hz). Abbreviations for ^1H NMR signals coupling are as follows: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of a doublet, ddd = doublet of a doublet of a doublet, dtd doublet of a triplet of a doublet. Mass spectral determinations were carried out by FTMS+p-NSI or APCI as ionization source unless otherwise noted. Reactions were carried out under argon in flame-dried or oven-dried glassware before use unless otherwise specified. Dichloromethane used for C–H functionalization reactions were dried using calcium hydride (CaH_2) and stored under argon overnight before use in 4 Å molecular sieves and degassed for one hour with argon. Thin-layer chromatography (TLC) analysis was performed with aluminum-sheet silica gel plates, visualizing with UV light, and staining with potassium permanganate (aqueous KMnO_4), ceric ammonium molybdate (CAM), or phosphomolybdic acid (PMA). Flash column chromatography was carried out on Merck silica gel 60 Å (230–400 mesh). Solvents THF, Et_2O , CH_3CN , CH_2Cl_2 , trifluorotoluene, and toluene were dried by solvent purifier. The dirhodium catalysts were prepared using the published procedures: $\text{Rh}_2(\text{R-DOSP})_4$,¹ $\text{Rh}_2(\text{S-PTAD})_4$,^{2,3} $\text{Rh}_2(\text{R-TPPTTL})_4$,⁴ $\text{Rh}_2(\text{R-TCPTAD})_4$,⁵ $\text{Rh}_2(\text{R-NTTL})_4$,⁶ $\text{Rh}_2(\text{S-DPCP})_4$, $\text{Rh}_2(\text{S-}i\text{-}p\text{-Br-TPCP})_4$,⁷ $\text{Rh}_2(\text{S-tetra-(4-Br)TPPTTL})_4$, $\text{Rh}_2(\text{S-di-(4-Br)TPPTTL})_4$.

Br)-di(4-*t*BuPh)TPPTTL)₄, Rh₂(*S-di*-(3,5-diCF₃Ph)TPPTTL)₄, Rh₂(*S-di*-(3,5-diBr)TPPTTL)₄, and Rh₂(*S-di*-(4-Br)TPPTTL)₄.⁸

Infrared (IR) spectra were collected on a Nicolet Impact Series 10 FT-IR spectrometer.

Mass spectrometric determinations were carried out on a Thermo Finnigan Exactive Plus Mass spectrometer with electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) Quadrupole-Orbitrap Mass spectrometer with ESI and APCI.

Melting points (m.p.) were measured in open capillary tubes with a Mel-Temp Electrothermal melting points apparatus and are uncorrected.

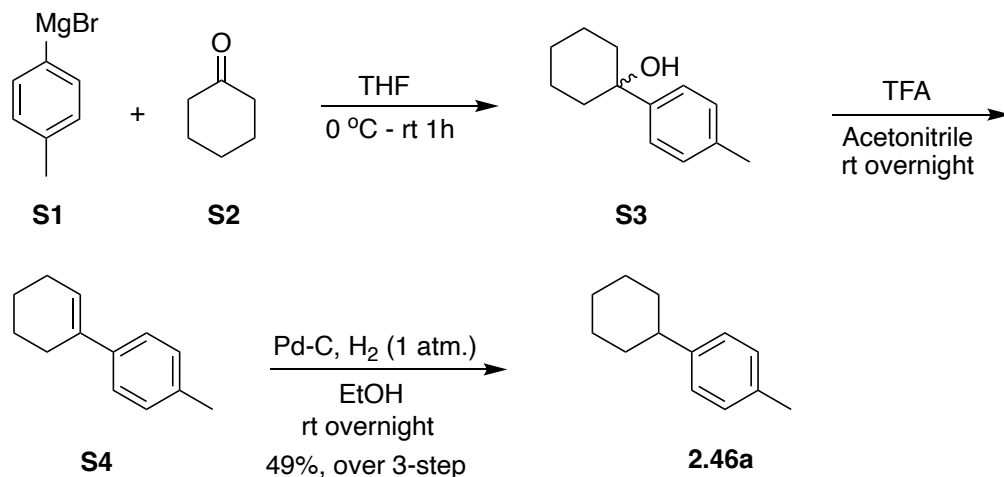
Enantiomeric excess (ee) data were obtained on Agilent 1100, or Agilent 1290 Infinity II instruments, eluting the purified products using a mixed solution of HPLC-grade 2-propanol (*i*PrOH) and *n*-hexane. Supercritical Fluid Chromatography (SFC) was performed on a Waters Acquity UPC2 system using methanol/isopropanol with 0.2% formic acid in supercritical carbon dioxide as eluent.

Coupling constants are uncorrected:

When it is stated that “coupling constants are uncorrected,” it typically means that the reported values of coupling constants (*J* values) are directly taken from the spectral data without applying any corrections or refinements. The values are raw and have not undergone advanced processing or theoretical adjustments to refine their accuracy.

Experimental section for chapter 2: Enantioselective Intermolecular C–H Functionalization of Primary Benzylic C–H Bonds Using ((Aryl)(diazo)methyl)phosphonates.

Preparation and Characterization of Substrates.



1-cyclohexyl-4-methylbenzene (2.46a)

To a stirred solution of *p*-tolylmagnesium bromide **S1** (3.5 g, 1 equiv.) in THF (42 mL) at 0 °C under argon, cyclohexanone **S2** (1.8 g, 0.9 equiv.) in THF (8 mL) was added dropwise. The reaction mixture was stirred for 1 hour at the room temperature, quenched with sat. NH₄Cl, and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄, and the residue was evaporated under reduced pressure to remove the volatile materials. The crude product was purified by flash column chromatography silica gel (hexanes/ethyl acetate 20:1) to afford 1-(*p*-tolyl)cyclohexan-1-ol **S3** (2.0 g, 60%) as colorless oil.

To a stirred solution of 1-(*p*-tolyl)cyclohexan-1-ol **S3** (1.0 g, 5.0 mmol) was dissolved in acetonitrile (10 mL), then TFA (0.4 mL, 1.0 equiv.) was added at room temperature. The reaction mixture was stirred for overnight, diluted with ethyl acetate, washed with sat. NaHCO₃, dried over Na₂SO₄, and evaporated to afford 1-(4-Methylphenyl)cyclohexene **S4** (0.85 g) as colorless oil.

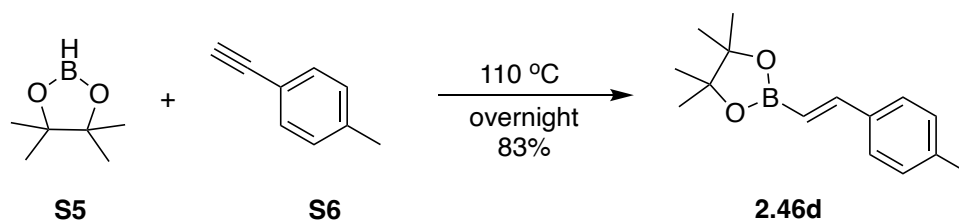
To a stirred solution 1-(4-Methylphenyl)cyclohexene **S4** (0.85 g, 4.9 mmol) in ethanol (25 mL), was added palladium on activated carbon (Pd/C 5%, 0.26 g). The reaction solution was purged

with hydrogen balloon for 15 minutes and then went overnight under hydrogen balloon. Then, the reaction was filtered over a short path of Celite, concentrated in vacuum, and the crude mixture was purified by flash column chromatography (SiO₂; hexanes/EtOAc, 25:1 gradient; R_f = 0.87 in 9:1 hexanes/EtOAc) to afford the final product **2.46a** as colorless oil (0.77 g, 49%, 3-step).

Spectroscopic data are in agreement with those reported in the literature.⁹⁻¹¹

¹H NMR (600 MHz, CDCl₃) δ 7.12 (s, 4H), 2.48 (ddt, J = 11.5, 8.8, 3.5 Hz, 1H), 2.33 (s, 3H), 1.90 – 1.82 (m, 4H), 1.76 (ddq, J = 1.6, 3.3, 12.8 Hz, 1H), 1.47 – 1.35 (m, 4H), 1.26 (tdd, J = 13.5, 8.1, 4.0 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃): δ 145.2, 135.2, 129.0, 126.8, 44.3, 34.9, 27.1, 26.3, 21.0.



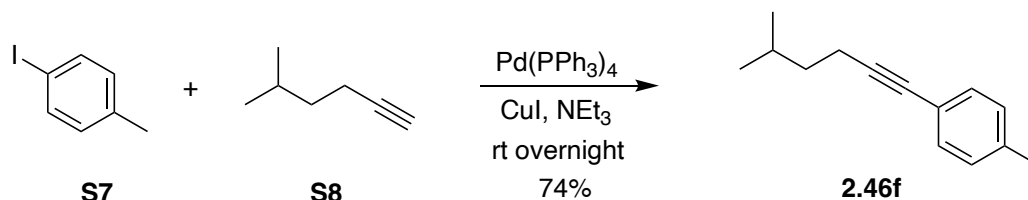
(*E*)-4,4,5,5-tetramethyl-2-(4-methylstyryl)-1,3,2-dioxaborolane (2.46d)

To a stirred solution of phenylacetylene **S6** (17.2 mmol, 1 equiv.), and **S5** pinacolborane (34.4 mmol, 2 equiv.) under an argon atmosphere at room temperature, and the reaction mixture was heated to 110 °C and stirred for overnight. Then, the reaction was cooled to room temperature and was quenched with water. The crude mixture was extracted with ethyl acetate (3×25 mL) and the organic layer was dried over anhydrous Na₂SO₄ and was concentrated under vacuum. The crude mixture was purified by flash column chromatography (SiO₂; hexanes/DCM, 7:3 gradient; R_f = 0.79 in 9:1 hexanes/DCM) to afford the product **2.46d** as light-yellow oil (3.5 g, 83% yield).

Spectroscopic data are in agreement with those reported in the literature.¹³

¹H NMR (600 MHz, CDCl₃) δ 7.39 (d, *J* = 7.8 Hz, 3H), 7.36 (s, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.11 (d, *J* = 18.4 Hz, 1H), 2.34 (s, 3H), 1.31 (s, 12H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 149.5, 139.0, 134.8, 129.3, 127.0, 83.3, 24.8, 21.3.

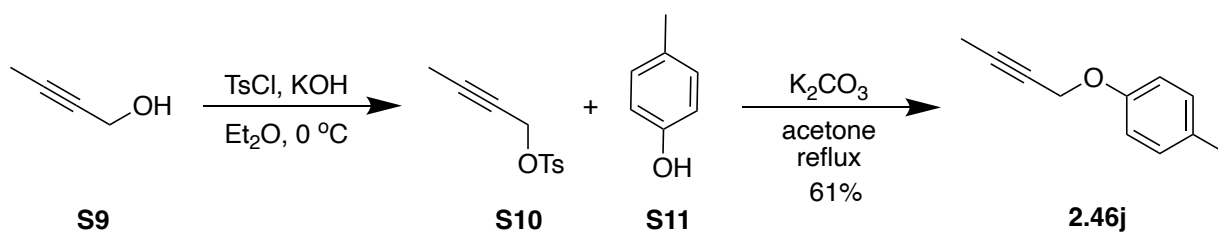


1-methyl-4-(5-methylhex-1-yn-1-yl)benzene (2.46f)

To a stirred solution of 4-iodotoluene **S7** (14 mmol, 3.0 g), 5-methyl-1-hexyne **S8** (21 mmol, 2.0 g, 1.5 equiv.), Pd(PPh₃)₄ (2.5 mol%, 400 mg), CuI (5 mol%, 130 mg) under argon atmosphere, triethylamine (40 mL) was added, and the reaction mixture was stirring at room temperature overnight. Then, the reaction was quenched with saturated aqueous ammonium chloride and the crude mixture was extracted with ether, washed by brine, dried over anhydrous MgSO₄, concentrated in vacuum. The crude mixture was purified by flash column chromatography (SiO₂; hexanes/EtOAc, 50:1 gradient; *R_f* = 0.85 in 9:1 hexanes/EtOAc) to afford the product **2.46f** as colorless oil (1.90 g, 74% yield). Spectroscopic data are in agreement with those reported in the literature.¹²

¹H NMR (600 MHz, CDCl₃) δ 7.27 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 2.40 (t, *J* = 7.4 Hz, 2H), 2.33 (s, 3H), 1.76 (dp, *J* = 13.4, 6.7 Hz, 1H), 1.50 (q, *J* = 7.4 Hz, 2H), 0.94 (dd, *J* = 6.6, 0.8 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 137.4, 131.4, 128.9, 121.0, 89.7, 80.4, 37.8, 27.3, 22.2, 21.4, 17.4.



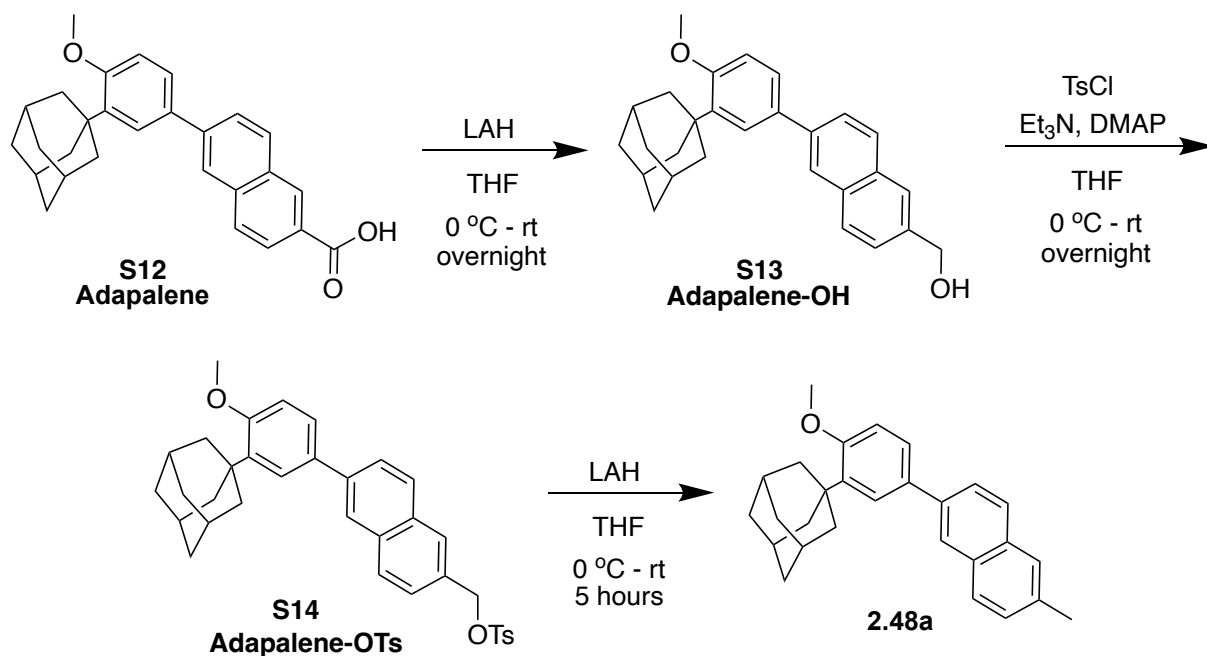
1-(but-2-yn-1-yloxy)-4-methylbenzene (2.46j)

To a solution of 2-butyne-1-ol **S9** (3.0 g, 42.8 mmol) in diethyl ether (100 mL) at 0 °C was added *p*-toluenesulfonyl chloride (8.98 g, 47.1 mmol) and crushed KOH (12 g) sequentially. The resulting mixture was stirred at 0 °C for 1 h before it was poured into an ice-water mixture. Ethyl ether (50 mL) was added, and the organic phase was separated, dried over MgSO₄, and concentrated to give **S10** as light-yellow oil.

To a solution of *p*-cresol **S11** (3.00 g, 27.7 mmol) and **S10** (2.66 g, 41.6 mmol) in acetone (40 mL) was added K₂CO₃ (4.60 g, 33.3 mmol). The mixture was stirred at reflux for 18 h and then cooled to rt. The solvent was removed under vacuum and hexane was added to the residue. The organic phase was washed with water and brine, dried over anhydrous Na₂SO₄, concentrated, and purified by flash chromatography (SiO₂; hexanes/EtOAc, 20:1 gradient; *R_f* = 0.90 in 9:1 hexanes/EtOAc) to afford the final product **2.46j** as colorless oil (2.70 g, 61% yield). Spectroscopic data are in agreement with those reported in the literature.¹⁴

¹H NMR (600 MHz, CDCl₃) δ 7.10 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.63 (q, *J* = 2.1 Hz, 2H), 2.31 (s, 3H), 1.87 (t, *J* = 2.4 Hz, 3H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 156.0, 130.7, 130.1, 114.9, 83.8, 74.5, 56.7, 20.8, 3.9.



1-(2-methoxy-5-(6-methylnaphthalen-2-yl)phenyl)adamantane (2.48a).

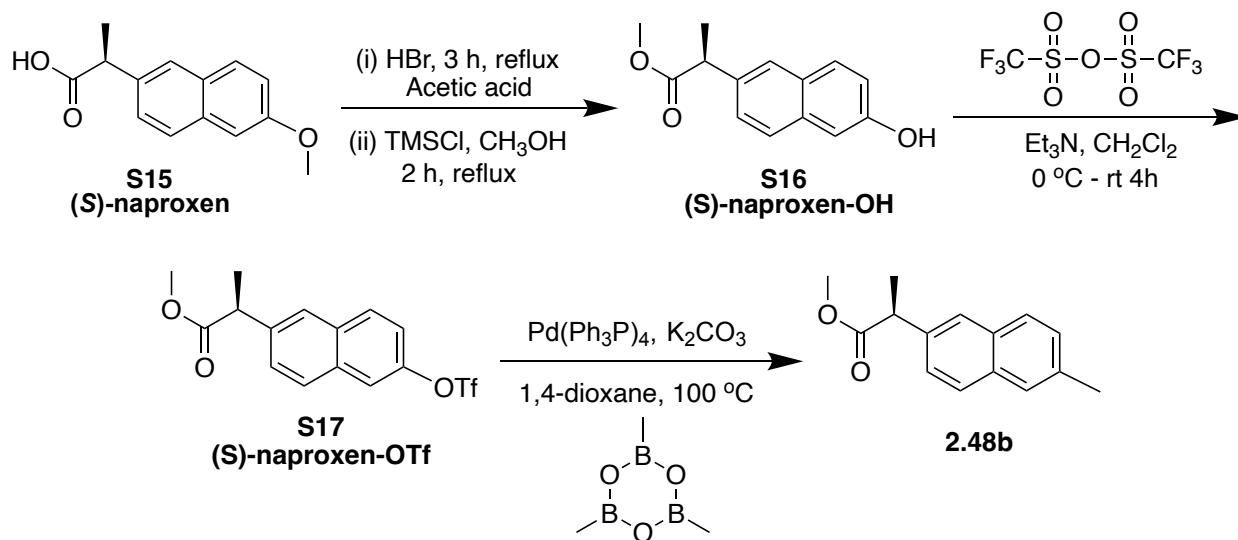
To a stirred solution of adapalene **S12** (1.1 g, 2.67 mmol) and THF (25 mL) were added under argon atmosphere. LiAlH₄ (202 mg, 5.33 mmol) was added slowly at 0 °C, and then the mixture was stirred at room temperature overnight. The reaction was quenched by water (4 mL) and then extracted with dichloromethane, dried over Na₂SO₄, and evaporated to give the naphthyl alcohol product **S13**. The naphthyl alcohol **S13** compound was used directly for the next reaction.

Adapalene alcohol **S13** was dissolved in dry THF (25 mL) and Et₃N (0.23 mL, 1.68 mmol) was added at 0 °C under argon atmosphere. Then TsCl (213 mg, 1.12 mmol) followed by DMAP (6 mg, 0.05 mmol) were added to the resulting reaction mixture and stirring was continued overnight at room temperature. The reaction mixture was quenched with aqueous saturated NH₄Cl solution. Afterwards it was extracted with EtOAc, washed with water, brine and dried over anhydrous MgSO₄. The organic extracts were filtered and concentrated under reduced pressure to give **S14**. The tosylated adapalene compound **S14** was used directly for the next reaction.

Compound **S14** was dissolved in anhydrous THF (20 mL) and LiAlH₄ (85 mg, 2.24 mmol) was added at 0°C under argon atmosphere. The reaction mixture was warmed to room temperature and stirring was continued for next 5 h. The reaction was quenched with aqueous saturated NH₄Cl solution at 0 °C and the white precipitate was filtered. The filtrate was taken up in EtOAc, washed with water, brine and dried over anhydrous MgSO₄. The crude mixture was filtered, and the solvent was removed under reduced pressure to remove the volatile materials. The crude product was purified by flash column chromatography silica gel (SiO₂; hexanes/EtOAc, 20:1 gradient; R_f = 0.90 in 9:1 hexanes/EtOAc) to afford the product **2.48a** as white solid (0.82 g, 51% yield). Spectroscopic data are in agreement with those reported in the literature.^{9, 15}

¹H NMR (600 MHz, CDCl₃) δ 7.95 (d, *J* = 1.9 Hz, 1H), 7.64 (dd, *J* = 8.6, 16.8 Hz, 2H), 7.58 (s, 1H), 7.50 (dd, *J* = 2.0, 8.7 Hz, 1H), 7.34 (dd, *J* = 1.7, 8.5 Hz, 1H), 7.29 (d, *J* = 2.6 Hz, 1H), 7.26 (dd, *J* = 2.4, 8.6 Hz, 1H), 6.73 (d, *J* = 8.6 Hz, 1H), 3.81 (s, 3H), 2.50 (s, 3H), 2.06 (s, 9H), 1.76 (d, *J* = 2.5 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 158.8, 139.2, 138.4, 135.5, 133.7, 132.8, 132.4, 128.8, 128.2, 127.9, 126.2, 126.1, 125.8, 125.1, 112.4, 55.5, 41.0, 38.1, 37.5, 29.5, 22.1.



Methyl (*S*)-2-(6-methylnaphthalen-2-yl)propanoate (2.48.b).

To (*S*)-naproxen **S15** (3 g, 13 mmol) in acetic acid (20 mL) was added 48% HBr (11.0 g, 7.37 mL, 65.1 mmol) at 0 °C. The mixture was stirred at reflux for 3 h and then cooled to room temperature, water (50 mL) was added to precipitate out the product, which was isolated by filtration. To the crude product was added methanol (35 mL) and TMSCl (1.7 g, 2.0 mL, 15.6 mmol), and the mixture was stirred at room temperature for 2 h. The solvent was removed in vacuo, resulting in a tan solid compound **S16**, which was dissolved in CH₂Cl₂ (25 mL). Following the addition of triethylamine (2.6 g, 3.6 mL, 26.1 mmol) at 0 °C, trifluoromethanesulfonic anhydride (4.9 g, 2.9 mL, 15.7 mmol) was added dropwise and the mixture was warmed to room temperature and allowed to stir for 4 h. The mixture was then diluted with diethyl ether, quenched with 1 M HCl, and washed with saturated sodium bicarbonate and brine. The organic layer was dried over MgSO₄ and then concentrated, resulting in the (*S*)-naproxen-OTf product **S17** (4.5 g, 72%).¹⁶

A clean oven-dried and flame-dried 50 mL round bottom flask equipped with activated 4 Å molecular sieves, and a magnetic stir-bar was evacuated and purged with argon (2-3 times). After cooling down to room temperature and charged with (*S*)-naproxen-OTf compound **S17** (2.1 g, 5.8 mmol), Pd(PPh₃)₄ (5.0 mol%, 335 mg, 290 μmol) and K₂CO₃ (2.4 g, 17.4 mmol, 3.0 equiv.). Freshly distilled and degassed 1,4-dioxane (25 ml) was added, and the resulting solution was stirred for 5 min. Then trimethylboroxine (1.0 g, 17.4 mmol, 3.0 equiv.) was introduced, and the mixture was stirred at 100 °C for overnight and then cooled to room temperature. Then, the reaction was filtered over a pad of Celite, concentrated in vacuum, and the crude mixture was purified by flash column chromatography. (SiO₂; hexanes:EtOAc, 10:1 to 1:1 gradient; R_f = 0.75 in 9:2 hexanes:EtOAc), which afforded **2.48.b** as a white solid (1.03 g, 65% yield).

m.p. 44-46 °C.

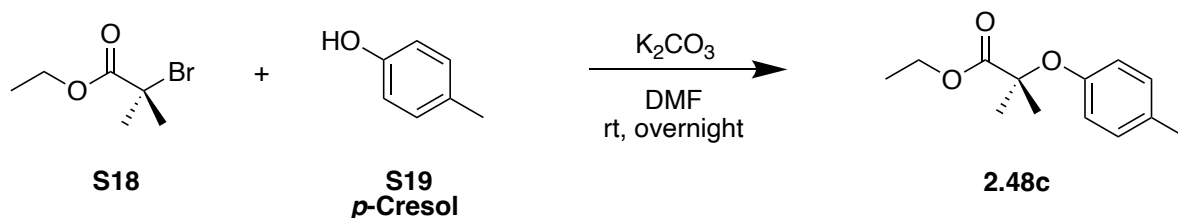
¹H NMR (600 MHz, CDCl₃) δ 7.75–7.69 (m, 3H), 7.59 (s, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 3.89 (q, *J* = 7.1 Hz, 1H), 3.68 (s, 3H), 2.51 (s, 3H), 1.60 (d, *J* = 7.2 Hz, 3H).

(Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 175.4, 137.4, 135.8, 133.1, 132.0, 128.8, 128.0, 127.9, 126.9, 126.2, 126.0, 52.4, 45.8, 22.0, 18.9.

IR (neat) 2978, 1735, 1607, 1504, 1434, 1376, 1329, 1251, 1195, 1167, 1093, 1066, 912, 882, 817, 657, 477, 462, 435, 424, 416, 404 cm⁻¹.

HRMS (APCI) calcd. for C₁₅H₁₆O₂ [M - H]⁻ 227.1078, found 227.1080.

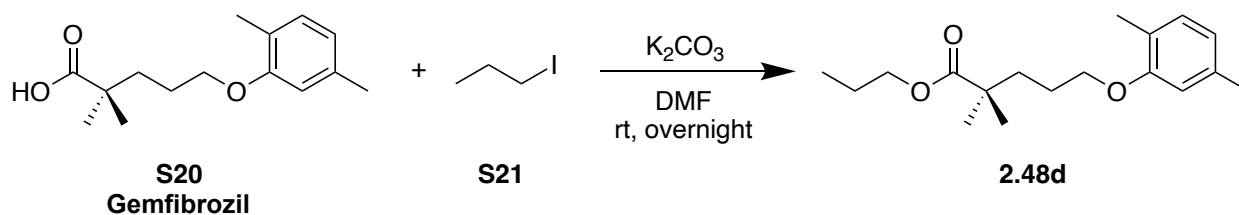


Ethyl 2-methyl-2-(*p*-tolylxy)propanoate (**2.48c**).

To a solution of *p*-Cresol **S19** (2.0 g, 18.5 mmol) and K₂CO₃ (5.11 g, 37.0 mmol) in 20 mL DMF was added ethyl 2-bromoisobutyrate **S18** (2.41 g, 12.3 mmol) at room temperature and the reaction was stirred overnight. Then the reaction was diluted with 25 mL EtOAc and washed with sat. brine (3×25 mL). The organic layer was dried over anhydrous Na₂SO₄ and was concentrated under vacuum. The crude mixture was purified by flash column chromatography (SiO₂; hexanes/EtOAc, 50:1 gradient; R_f = 0.78 in 9:1 hexanes/EtOAc) to afford the product **2.48c** as colorless oil (2.2 g, 35% yield). Spectroscopic data are in agreement with those reported in the literature.¹⁸

¹H NMR (600 MHz, CDCl₃) δ 7.03 (d, *J* = 8.8 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 4.24 (d, *J* = 7.2 Hz, 2H), 2.27 (s, 3H), 1.26 (d, *J* = 7.2 Hz, 3H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 174.8, 153.4, 132.0, 129.9, 119.8, 79.4, 61.7, 25.7, 20.9, 14.4.

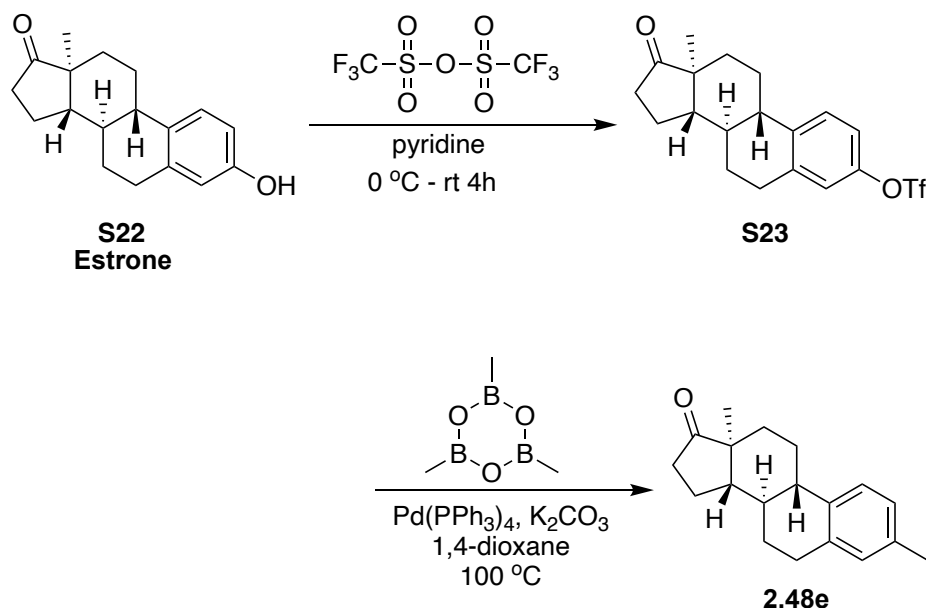


Propyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (2.48d).

To a solution of gemfibrozil **S20** (2.0 g, 7.99 mmol) and K_2CO_3 (1.3 g, 16.00 mmol) in 25 mL DMF was added 1-iodopropane **S21** (2.72 g, 10.4 mmol) at room temperature and the reaction was stirred overnight. Then the reaction was diluted with 25 mL EtOAc and washed with sat. brine (3×25 mL). The organic layer was dried over anhydrous Na_2SO_4 and was concentrated under vacuum. The crude mixture was purified by flash column chromatography (SiO_2 ; hexanes/EtOAc, 20:1 gradient; $R_f = 0.77$ in 9:1 hexanes/EtOAc) to afford the product **2.48d** as colorless oil (1.90 g, 81% yield). Spectroscopic data are in agreement with those reported in the literature.¹⁷

^1H NMR (400 MHz, CDCl_3) δ 7.00 (d, $J = 7.4$ Hz, 1H), 6.66 (dd, $J = 1.6, 7.5$ Hz, 1H), 6.61 (d, $J = 1.6$ Hz, 1H), 4.03 (t, $J = 6.6$ Hz, 2H), 3.92 (t, $J = 5.6$ Hz, 2H), 2.31 (s, 3H), 2.18 (s, 3H), 1.84 – 1.61 (m, 6H), 1.22 (s, 6H), 0.95 (t, $J = 7.4$ Hz, 3H). (Coupling constants are uncorrected)

^{13}C NMR (101 MHz, CDCl_3) δ 178.2, 157.3, 136.8, 130.6, 123.9, 121.0, 112.3, 68.3, 66.3, 42.4, 37.5, 25.5, 22.4, 21.7, 16.1, 10.8.



(8*R*,9*S*,13*S*)-3,13-dimethyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (2.48e**).**

To a stirred solution of Estrone **S22** (2.5 g, 9.3 mmol) in pyridine (25 mL) at 0 °C under argon, trifluoromethanesulfonic anhydride (1.55 mL, 9.3 mmol) was dropwise added causing the solution to turn orange. The reaction mixture was stirred at room temperature for 4 hours. Then, the reaction was diluted with DCM (20 mL) and washed with water and brine, dried over anhydrous Na_2SO_4 . The residue was evaporated under reduced pressure to remove the volatile materials. The crude product was purified by flash column chromatography providing estrone trifluoromethanesulfonic ester **S23** (2.4 g yield).¹⁹

To a stirred solution of estrone trifluoromethanesulfonic ester **S23** (2.4 g, 5.9 mmol, 1.0 equiv.), $\text{Pd}(\text{PPh}_3)_4$ (207 mg, 3.0 mol%) and K_2CO_3 (2.5 g, 17.9 mmol, 3.0 equiv.). Freshly distilled and degassed 1,4-dioxane (50 mL) was added, and the resulting solution was stirred for 5 min. Then trimethylboroxine (TMB) (17.9 mmol, 3.0 equiv.) was introduced, and the vial was then sealed by a screw cap and stirred at 100 °C overnight. The crude mixture was filtered over a pad of Celite, and the solvent was removed under reduced pressure to remove the volatile materials. The crude product

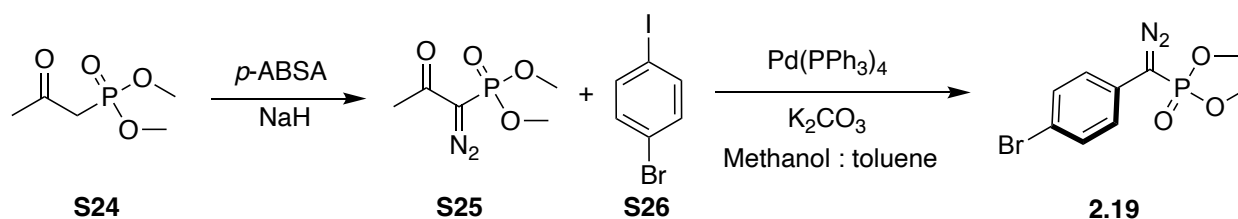
was purified by flash column chromatography silica gel (SiO₂; hexanes:EtOAc, 10:1 to 1:1 gradient; R_f = 0.81 in 9:2 hexanes:EtOAc) to afford the product **2.48e** as white solid (0.82 g, 51% yield). Spectroscopic data are in agreement with those reported in the literature.^{15, 20}

¹H NMR (600 MHz, CDCl₃) δ 7.19 (d, J = 7.9 Hz, 1H), 6.98 (dd, J = 1.9, 7.9 Hz, 1H), 6.93 (s, 1H), 2.91 – 2.86 (m, 2H), 2.50 (dd, J = 8.8, 18.9 Hz, 1H), 2.45 – 2.39 (m, 1H), 2.29 (s, 3H), 2.18 – 2.10 (m, 1H), 2.09 – 1.92 (m, 3H), 1.68 – 1.39 (m, 7H), 0.90 (s, 3H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 137.0, 136.6, 135.7, 130.1, 126.9, 125.6, 50.8, 48.4, 44.6, 38.6, 36.2, 31.9, 29.7, 26.9, 26.1, 21.9, 21.2, 14.2.

Procedure for the synthesis of phosphonate diazo compounds:

Bestmann-Ohira method.²¹⁻²³



To a 250 mL flask was added a solution of dimethyl 2-oxopropylphosphonate **S24** (6.26 g, 37.7 mmol) in toluene (160 mL) and THF (30 mL) was stirred at 0 °C for 30 min. Sodium hydride (60% dispersion in mineral oil, 1.66 g, 41.5 mmol) was slowly added into the flask and the solution was stirred at 0 °C for 1 hour under nitrogen, *p*-ABSA (9.96 g, 41.5 mmol) was added in one portion and the reaction was warmed to room temperature and stirring was continued overnight. The reaction mixture was filtered through celite, and the residue was evaporated under reduced pressure to remove the volatile materials. The crude diazo product was purified by flash column chromatography on silica gel (petroleum ether : EtOAc, 1:1) giving product **S25** (6.1 g , 84%) as a yellow liquid. Spectroscopic data are in agreement with those reported in the literature.²⁴

^1H NMR (400 MHz, CDCl_3) δ 3.79 (d, $J_{\text{HP}} = 11.9$ Hz, 6H), 2.21 (s, 3H). (Coupling constants are uncorrected)

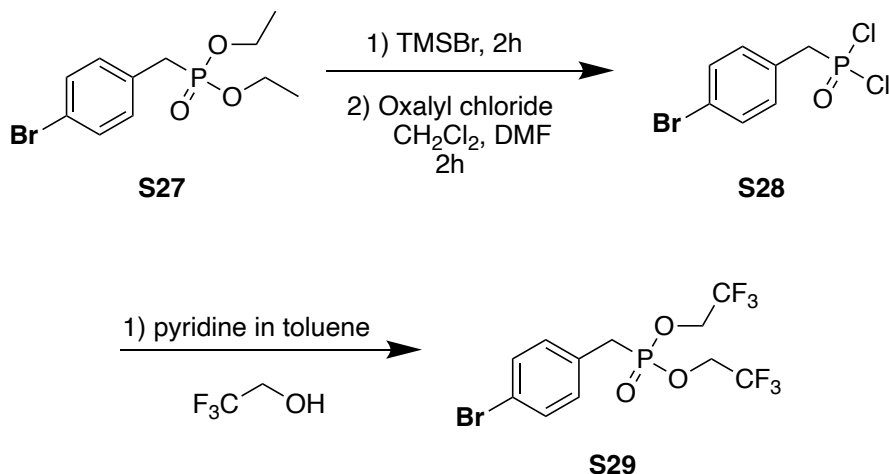
^{13}C NMR (101 MHz, CDCl_3) δ 190.07 (d, $J_{\text{CP}} = 13.1$ Hz), 63.73 (d, $J_{\text{CP}} = 220.5$ Hz), 53.80 (d, $J_{\text{CP}} = 5.6$ Hz), 27.34 (d, $J_{\text{CP}} = 1.3$ Hz).

^{31}P NMR (162 MHz, CDCl_3) δ 14.21.

To a 50 mL flask was added $\text{Pd}(\text{PPh}_3)_4$ (232 mg, 5 mol%), K_2CO_3 (1.0 g, 8.0 mmol, 2.0 equiv.) and 1-bromo-4-iodobenzene **S26** (1.0 g, 4.0 mmol, 1.0 equiv.) were suspended in a mixture of methanol and toluene (20 mL, 1:1) under nitrogen. Dimethyl (1-diazo-2-oxopropyl)phosphonate **2.19** (1.0 g, 5 mmol, 1.3 equiv.) was then added drop wise, and the resulting solution was stirred at room temperature for 5 h. The reaction mixture was filtered through a silica gel plug, eluted with ethyl acetate, and the filtrate solvent was evaporated in vacuo to remove the volatile materials. The crude diazo product was purified by flash column chromatography on silica gel (petroleum ether : EtOAc, 1:1) giving product **4** (90% yield) as a yellow liquid. Spectroscopic data are in agreement with those reported in the literature. (This procedure is used to synthesize all the (Aryl(diazo)methyl)phosphonates derivatives)²⁵

^1H NMR (600 MHz, CDCl_3) δ 3.83 (d, $J = 11.8$ Hz, 6H), 2.26 (s, 3H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 190.3 (d, $J = 13.1$ Hz), 63.9 (d, $J = 221.1$ Hz), 53.9 (d, $J = 5.5$ Hz), 27.5.



Bis(2,2,2-trifluoroethyl) (4-bromobenzyl)phosphonate (2.41).

Bromotrimethylsilane (TMSBr) (6.45 mL, 48.8 mmol) was added dropwise over 30 min to diethyl (4-bromobenzyl)phosphonate **S27** (5.0 g, 16.3 mmol) under N₂ at room temperature. The mixture was stirred for 2 h, then evaporated under reduced pressure to give crude product (6.4 g, 99%) as a light-yellow liquid. To this crude material in CH₂Cl₂ (35 mL) and DMF (40 μ L) oxalyl chloride (4.2 mL, 49.0 mmol) was added dropwise accompanied by intense gas evolution. The mixture was stirred for 2 hours at room temperature, then evaporated under reduced pressure to give the crude product **S28** (4.6 g, 98%) as a brownish liquid.^{28, 29}

To a solution of 2,2,2-trifluoroethanol (500 μ L, 7.0 mmol) in pyridine (10 mL) (4-bromobenzyl)phosphonic dichloride **S28** (1.0 g, 3.5 mmol) in toluene (5 mL) was added at 50 °C under N₂. The mixture was stirred for overnight, then quenched with 1 M NaHSO₄ (100 mL) and the aqueous phase was extracted with toluene (2 $\times$ 20 mL). The combined organic phases were washed with H₂O (20 mL), 1 M NaHCO₃ (20 mL), and brine (2 $\times$ 15 mL), then dried over anhydrous Na₂SO₄ and was concentrated under vacuum to give crude product **S29** (0.62 g, 43%) as a white solid.

¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, *J* = 8.5 Hz, 2H), 7.17 (dd, *J* = 2.7, 8.5 Hz, 2H), 4.39–4.16 (m, 4H), 3.28 (d, *J*_{HP} = 22.3 Hz, 2H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 132.5 (d, *J*_{CP} = 3.4 Hz), 131.8 (d, *J*_{CP} = 7.1 Hz), 128.5 (d, *J*_{CP} = 9.7 Hz), 122.8 (dq, *J*_{CP} = 7.5, *J*_{CF} = 278.1 Hz), 122.3 (d, *J*_{CP} = 5.2 Hz), 62.7 (dq, *J*_{CP} = 6.5, *J*_{CF} = 38.1 Hz), 33.3 (d, *J*_{CP} = 140.8 Hz).

¹⁹F NMR (376 MHz, CDCl₃) δ -75.30 (t, *J* = 8.0 Hz).

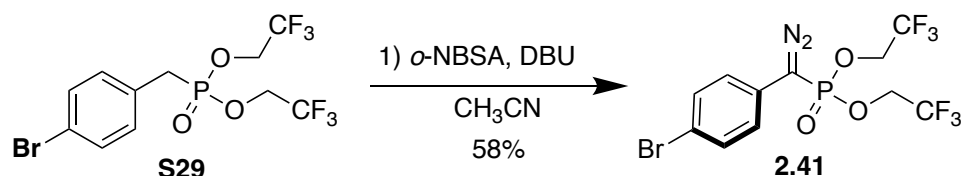
³¹P NMR (162 MHz, CDCl₃) δ 28.78.

IR (neat): 3020, 2921, 2850, 1489, 1464, 1419, 1401, 1291, 1263, 1221, 1168, 1105, 1085, 1073, 1012, 966, 894, 856, 828, 814, 749, 709, 655, 647, 627, 550, 526, 503, 477, 445, 434, 426 cm⁻¹.

m.p. 167-172 °C.

HRMS (+p APCI) calcd. for C₁₁H₁₀BrF₆O₃P [M + H]⁺ 414.9527, found 414.9517.

Bis(2,2,2-trifluoroethyl) ((4-bromophenyl)(diazo)methyl)phosphonate (2.41).



To a mixture of bis(2,2,2-trifluoroethyl) (4-bromobenzyl) phosphonate **S29** (0.62 g, 1.5 mmol) and ortho-nitrobenzenesulfonyl azide (*o*-NBSA) (0.41 g, 1.8 mmol) were dissolved in 25 mL anhydrous CH₃CN. The solution was kept stirring at room temperature and DBU (0.34 mL, 2.2 mmol) was added dropwise to the solution. The color of the solution gradually turned orange and it was quenched after 2 hours by diluting it with 50 mL Et₂O followed by adding 50 mL NH₄Cl (sat.)

solution. Extract the aqueous layer with Et₂O (3×25 mL), and the organic layer was dried over anhydrous Na₂SO₄ and was concentrated under vacuum. The crude mixture was purified by flash column chromatography. (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.68 in 1:1

hexanes/EtOAc) which afforded major product **2.41** as a yellow-orange oil (410 mg, 58% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.51 (d, *J* = 8.3 Hz, 2H), 7.03 (d, *J* = 8.5 Hz, 2H), 4.53–4.37 (m, 4H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 133.0, 124.8 (d, *J* = 4.7 Hz), 124.2 (d, *J* = 10.3 Hz), 122.5 (qd, *J* = 9.7, 277.6 Hz), 120.1, 63.3 (qd, *J* = 4.4, 38.3 Hz).

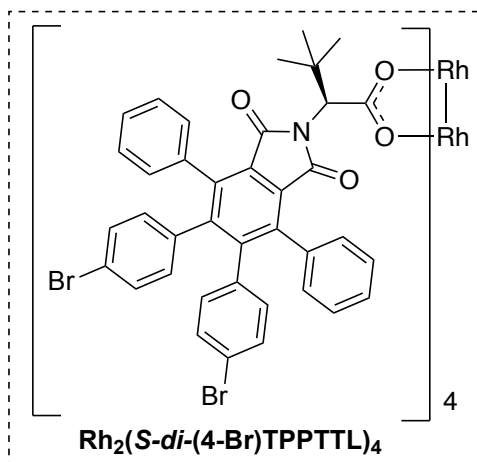
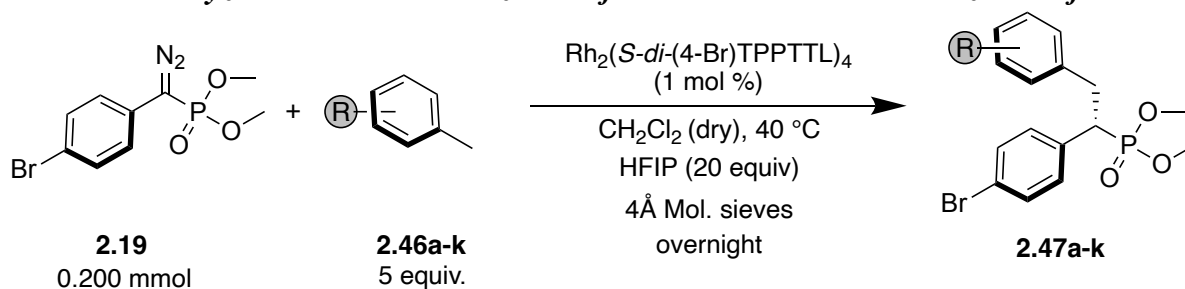
¹⁹F NMR (565 MHz, CDCl₃) δ -74.94 (t, *J* = 8.1 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 20.22.

IR (neat): 2971, 2085, 1585, 1562, 1490, 1455, 1490, 1455, 1519, 1286, 1258, 1163, 1094, 1055, 1008, 960, 876, 812, 715, 657, 585, 550, 515, 482, 468, 433, 419, 413, 404 cm⁻¹.

HRMS (+p APCI) calcd. for C₁₁H₈BrF₆N₂O₃P [M + H]⁺ 440.9432, found 440.9423.

Rhodium Catalyzed C–H Functionalization of Substrates and Characterization of Products.

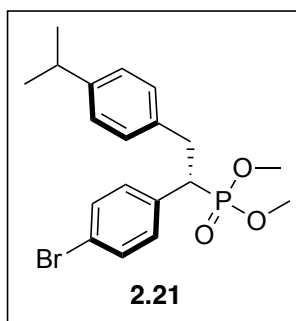


General Procedure for C-H Functionalization with Diazophosphonates.

A clean oven-dried and flame-dried 25.0 mL round bottom flask (flask-A) equipped with activated 4 Å molecular sieves, and a magnetic stir-bar was evacuated and purged with argon (2-3 times). After cooling down to room temperature, **2.46a-k** (5 equiv., 1.00 mmol) followed by $\text{Rh}_2(\text{S-di-(4-Br)TPPTTL})_4$ (6.2 mg, 0.01 equiv.), and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (20 equiv.) were then added. The flask was once again evacuated and purged with argon (3-5 times) and anhydrous CH_2Cl_2 (5.0 mL) was added. The flask and its contents were then set to stir at reflux (40 °C) using a hotplate under an argon atmosphere. To a second oven-dried round bottom flask (flask-B), that was evacuated and purged with argon was added dimethyl ((4-bromophenyl)(diazo) methyl)phosphonate, **2.19** (61 mg, 0.20 mmol). flask-B and its contents were evacuated and purged with argon (2-3 times) and anhydrous CH_2Cl_2 (10.0 mL) was then added to obtain a solution of the diazo-compound. The solution was transferred into a 12.0 mL plastic syringe. Using a well-calibrated syringe-pump, a slow

addition of the diazo solution into the stirring solution of flask-A under an inert atmosphere was initiated. After the complete addition of the solution (5 h), the residual diazo compound in the 12.0 mL plastic syringe was rinsed with anhydrous CH_2Cl_2 (1.0 mL) and transferred dropwise into the stirring reaction mixture of flask-A. The resulting solution was refluxed for 7 to 9 hours (overnight) before concentrating the solution under reduced pressure. Purification by flash column chromatography on silica gel (hexanes : EtOAc) was used to afford the final products.

Dimethyl (*S*)-(1-(4-bromophenyl)-2-(4-isopropylphenyl) ethyl)phosphonate (2.21**).**



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.35 in 1:1 hexanes/EtOAc), which afforded major product **2.21** as a colorless oil (67 mg, 82% yield).

^1H NMR (600 MHz, CDCl_3) δ 7.39 (d, J = 8.6 Hz, 2H), 7.15 (dd, J = 2.3, 8.5 Hz, 2H), 7.02 (d, J = 7.7 Hz, 2H), 6.89 (d, J = 7.9 Hz, 2H), 3.70 (d, J_{HP} = 10.7 Hz, 3H), 3.52 (d, J_{HP} = 10.5 Hz, 3H), 3.40 (ddd, J = 3.9, 9.4, 13.8 Hz, 1H), 3.28 (ddd, J = 3.9, 11.2, 22.3 Hz, 1H), 3.10 (ddd, J = 9.3, 11.2, 14.2 Hz, 1H), 2.81 (hept, J = 7.0 Hz, 1H), 1.18 (dd, J = 1.4, 6.9 Hz, 6H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 147.0, 135.7 (d, J_{CP} = 16.1 Hz), 134.7 (d, J_{CP} = 6.6 Hz), 131.6 (d, J_{CP} = 2.4 Hz), 131.1 (d, J_{CP} = 6.8 Hz), 128.6, 126.4, 121.2 (d, J_{CP} = 3.9 Hz), 53.1 (dd, J_{CP} = 7.2, 108.0 Hz), 45.7 (d, J_{CP} = 136.5 Hz), 35.6 (d, J_{CP} = 2.8 Hz), 33.6, 24.0, 23.9.

^{31}P NMR (243 MHz, CDCl_3) δ 29.83.

IR (neat): 2954, 1738, 1513, 1487, 1446, 1365, 1231, 1215, 1054, 1031, 1011, 868, 826, 759, 634, 553 cm^{-1} .

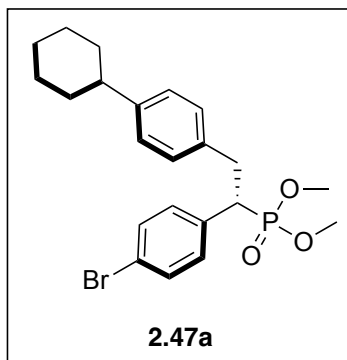
$[\alpha]^{20}_{\text{D}}$: + 41.9° (c 0.40, CHCl_3)

HRMS (+p APCI) calcd. for $\text{C}_{19}\text{H}_{24}\text{BrO}_3\text{P}$ $[\text{M} + \text{H}]^+$ 411.0719, found 411.0718.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 3.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm)

indicated 99% ee: t_R (major enantiomer) = 25.5 min, t_R (minor enantiomer) = 23.3 min.

Dimethyl (*S*)-(1-(4-bromophenyl)-2-(4-cyclohexylphenyl) ethyl) phosphonate (2.47a**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.40 in 1:1 hexanes/EtOAc), which afforded major product **2.47a** as a colorless oil (77 mg, 85% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.39 (d, J = 8.2 Hz, 2H), 7.15 (dd, J = 2.3, 8.6 Hz, 2H), 7.00 (d, J = 7.9 Hz, 2H), 6.89 (d, J = 7.9 Hz, 2H),

3.69 (d, J_{HP} = 10.8 Hz, 3H), 3.51 (d, J_{HP} = 10.5 Hz, 3H), 3.39 (ddd, J = 3.9, 9.4, 13.6, Hz, 1H), 3.28 (ddd, J = 3.95, 10.95, 22.09 Hz, 1H), 3.09 (ddd, J = 9.3, 11.0, 14.3 Hz, 1H), 2.44–2.35 (m, 1H), 1.82 – 1.77 (m, 4H), 1.71 (d, J = 13.1 Hz, 1H), 1.38–1.28 (m, 4H), 1.25 – 1.18 (m, 1H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 146.6, 136.1 (d, J_{CP} = 16.1 Hz), 135.0 (d, J_{CP} = 6.6 Hz), 131.9 (d, J_{CP} = 2.3 Hz), 131.4 (d, J_{CP} = 6.9 Hz), 129.0, 127.07, 121.6 (d, J_{CP} = 4.0 Hz), 53.5 (dd, J_{CP} = 7.2, 107.8 Hz), 46.0 (d, J_{CP} = 136.4 Hz), 44.4, 36.0 (d, J_{CP} = 2.9 Hz), 34.8 (d, J_{CP} = 5.6 Hz), 27.2, 26.5.

³¹P NMR (243 MHz, CDCl₃) δ 29.85.

IR (neat): 2955, 1513, 1488, 1460, 1405, 1363, 1244, 1182, 1053, 1029, 1010, 908, 868, 825, 760, 729, 644, 634, 621, 575, 553, 479, 436, 406 cm⁻¹.

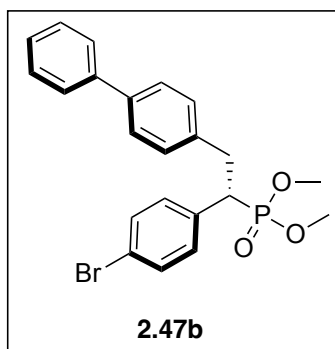
$[\alpha]^{20}_D$: +109.2° (c 3.50, CHCl₃)

HRMS (+p APCI) calcd. for C₂₂H₂₈BrO₃P [M + H]⁺ 451.1032, found 451.1038.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 2.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm)

indicated 98% ee: t_R (major enantiomer) = 33.2 min, t_R (minor enantiomer) = 29.8 min.

Dimethyl (S)-(2-([1,1'-biphenyl]-4-yl)-1-(4-bromophenyl) ethyl) phosphonate (2.47b).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.39 in 1:1 hexanes/EtOAc), which afforded major product **2.47b** as a white solid (79 mg, 89% yield). **m.p.** 139-142°C.

¹H NMR (400 MHz, CDCl₃) δ 7.57–7.49 (m, 2H), 7.43–7.36 (m, 6H),

7.34–7.28 (m, 1H), 7.17 (dd, *J* = 2.2, 8.6 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 2H), 3.73 (d, *J*_{HP} = 10.8 Hz, 3H), 3.54 (d, *J*_{HP} = 10.5 Hz, 3H), 3.48 (ddd, *J* = 3.7, 9.0, 13.3 Hz, 1H), 3.33 (ddd, *J* = 3.7, 11.3, 21.8 Hz, 1H), 3.17 (ddd, *J* = 8.8, 11.2, 13.9 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 141.0, 139.6, 138.0, 137.8, 134.8 (d, *J*_{CP} = 6.4 Hz), 132.0 (d, *J*_{CP} = 2.4 Hz), 131.4 (d, *J*_{CP} = 6.9 Hz), 129.5, 129.1, 127.5, 127.3 (d, *J*_{CP} = 7.9 Hz), 121.7 (d, *J*_{CP} = 3.9 Hz), 53.5 (dd, *J*_{CP} = 7.1, 76.7 Hz), 46.0 (d, *J*_{CP} = 136.9 Hz), 36.1 (d, *J*_{CP} = 2.6 Hz).

³¹P NMR (162 MHz, CDCl₃) δ 29.63.

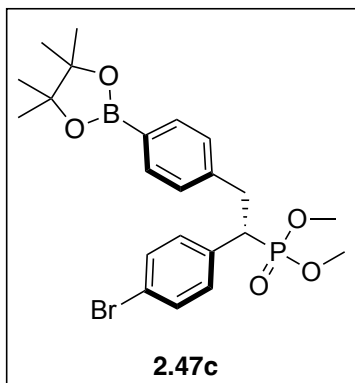
IR (neat): 2922, 1487, 1247, 1181, 1057, 1033, 1011, 833, 758, 699, 596, 553, 529, 512, 500, 292 cm⁻¹.

[α]²⁰_D: + 68.7° (c 0.70, CHCl₃)

HRMS (+p APCI) calcd. for C₂₂H₂₂BrO₃P [M + H]⁺ 445.0563, found 445.0571.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 4.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 91% ee: *t_R* (major enantiomer) = 28.7 min, *t_R* (minor enantiomer) = 26.5 min.

Dimethyl (S)-(1-(4-bromophenyl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl)phosphonate (2.47c).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.38 in 1:1 hexanes/EtOAc), which afforded major product **2.47c** as a colorless oil (53 mg, 54% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.60 (d, J = 7.7 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 7.12 (dd, J = 2.3, 8.5 Hz, 2H), 6.97 (d, J = 7.9 Hz, 2H),

3.72 (d, J_{HP} = 10.7 Hz, 3H), 3.52 (d, J_{HP} = 10.5 Hz, 3H), 3.44 (ddd, J = 3.8, 8.9, 13.3 Hz, 1H), 3.29 (ddd, J = 3.9, 11.4, 22.1 Hz, 1H), 3.12 (ddd, J = 8.8, 11.4, 14.0 Hz, 1H), 1.31 (bs, 12H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 142.0 (d, J_{CP} = 16.4 Hz), 135.1, 134.6 (d, J_{CP} = 6.3 Hz), 132.0 (d, J_{CP} = 2.5 Hz), 132.4 (d, J_{CP} = 7.1 Hz), 128.6, 125.9, 121.7 (d, J_{CP} = 3.7 Hz), 84.9, 53.5 (dd, J_{CP} = 7.2, 112.1 Hz), 45.9 (d, J_{CP} = 137.1 Hz), 36.6 (d, J_{CP} = 2.7 Hz), 30.7, 25.2 (d, J_{CP} = 3.8 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 29.60.

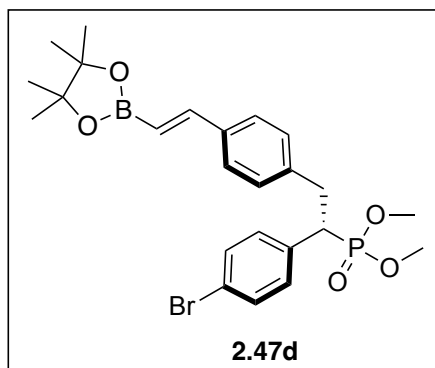
IR (neat): 2978, 2953, 1611, 1487, 1447, 1398, 1340, 1320, 1248, 1213, 1183, 1166, 1144, 1089, 1056, 1032, 1012, 962, 859, 827, 771, 753, 734, 658, 613, 557, 519, 498 cm⁻¹.

$[\alpha]^{20}_D$: + 17.9° (c 0.30, CHCl₃)

HRMS (+p APCI) calcd. for C₂₂H₂₉BBrO₅P [M + H]⁺ 494.1138, found 494.1151.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 5.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 98% ee: t_R (major enantiomer) = 12.6 min, t_R (minor enantiomer) = 15.2 min.

Dimethyl (*S,E*)-(1-(4-bromophenyl)-2-(4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethyl)phosphonate (2.47d**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.45 in 9:1 hexanes/EtOAc), which afforded major product **2.47d** as a colorless oil (61 mg, 59%).

¹H NMR (600 MHz, CDCl₃) δ 7.37 (d, *J* = 8.3 Hz, 2H), 7.33–7.26 (m, 3H), 7.12 (dd, *J* = 2.2, 8.5 Hz, 2H), 6.94 (d, *J* = 8.2

Hz, 2H), 6.07 (d, *J* = 18.5 Hz, 1H), 3.71 (d, *J_{HP}* = 10.7 Hz, 3H), 3.52 (d, *J_{HP}* = 10.5 Hz, 3H), (ddd, *J* = 3.8, 8.7, 13.5 Hz, 1H), 3.27 (ddd, *J* = 4.1, 11.2, 22.2 Hz, 1H), 3.11 (ddd, *J* = 9.4, 11.2, 14.2 Hz, 1H), 1.29 (s, 12H). (Coupling constants are uncorrected) **¹³C NMR (151 MHz, CDCl₃)** δ 149.4, 139.8, 136.1, 134.6, 132.0 (d, *J_{CP}* = 2.2 Hz), 131.4 (d, *J_{CP}* = 6.9 Hz), 129.4, 127.4, 121.7, 83.7, 53.5 (dd, *J_{CP}* = 7.2, 116.0 Hz), 45.9 (d, *J_{CP}* = 137.1 Hz), 36.4, 30.1, 25.1 (d, *J_{CP}* = 3.3 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 29.54.

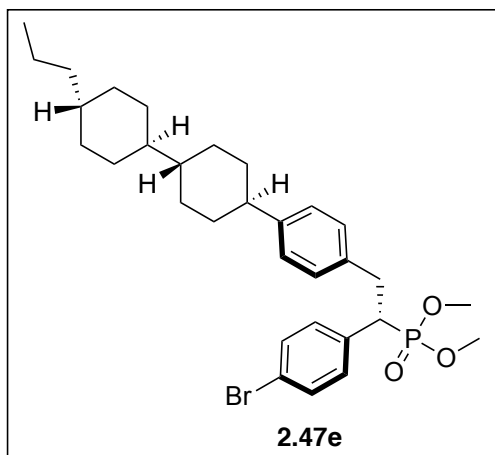
IR (neat): 2977, 1625, 1570, 1511, 1455, 1412, 1380, 1370, 1346, 1319, 1271, 1218, 1206, 1141, 1107, 995, 969, 900, 852, 845, 798, 760, 679, 644, 575, 495 cm⁻¹.

[α]²⁰_D: + 43.6° (c 0.50, CHCl₃)

HRMS (+p APCI) calcd. for C₂₃H₂₈BrO₃P [M + H]⁺ 520.1294, found 520.1303.

SFC analysis: (Chiralpak AS-3, 3 μm particle size, 150 mm x 3 mm, 7.0% MeOH/IPA, with 0.2% Formic Acid, 2.5 mL/min, 280 nm) indicated 97% ee: *t_R* (minor enantiomer) = 1.4 min, *t_R* (major enantiomer) = 2.2 min.

Dimethyl ((1*S*)-1-(4-bromophenyl)-2-(4-((1'*s*,4'*R*)-4'-ethyl-[1,1'-bi(cyclohexan)]-4-yl)phenyl)ethyl)phosphonate (2.47e**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 9:1 gradient; *R_f* = 0.62 in 9:1 hexanes/EtOAc), which afforded major product **2.47e** as a white solid (102 mg, 89%).

m.p. 135-138 °C.

¹H NMR (600 MHz, CDCl₃) δ 7.38 (d, *J* = 7.8 Hz, 2H), 7.15 (dd, *J* = 2.3, 8.6 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H),

6.88 (d, *J* = 8.1 Hz, 2H), 3.69 (d, *J*_{HP} = 10.8 Hz, 3H), 3.51 (d, *J*_{HP} = 10.6 Hz, 3H), 3.38 (ddd, *J* = 3.9, 9.3, 13.8 Hz, 1H), 3.31 – 3.24 (m, 1H), 3.09 (ddd, *J* = 9.3, 11.1, 14.3 Hz, 1H), 2.34 (tt, *J* = 3.3, 12.2 Hz, 1H), 1.85 – 1.77 (m, 4H), 1.77 – 1.70 (m, 4H), 1.37 – 1.26 (m, 4H), 1.16 – 1.07 (m, 6H), 1.05 – 0.94 (m, 3H), 0.87 (t, *J* = 7.3 Hz, 3H). (Coupling constants are uncorrected).

¹³C NMR (151 MHz, CDCl₃) δ 146.4, 136.1 (d, *J*_{CP} = 16.1 Hz), 135.0 (d, *J*_{CP} = 6.6 Hz), 131.9 (d, *J*_{CP} = 2.4 Hz), 131.4 (d, *J*_{CP} = 7.0 Hz), 128.9, 127.1, 121.6 (d, *J*_{CP} = 3.8 Hz), 53.5 (dd, *J*_{CP} = 7.2, 107.6 Hz), 46.0 (d, *J*_{CP} = 136.5 Hz), 44.5, 43.7, 43.3, 40.2, 38.0, 36.0 (d, *J*_{CP} = 2.8 Hz), 34.9 (d, *J*_{CP} = 3.9 Hz), 34.0, 30.7, 30.5, 20.4, 14.8.

³¹P NMR (162 MHz, CDCl₃) δ 29.87.

IR (neat): 2950, 2913, 2848, 1513, 1486, 1449, 1405, 1247, 1197, 1098, 1052, 1022, 977, 879, 823, 773, 737, 707, 643, 623, 600 cm⁻¹.

[α]²⁰_D: + 75.6° (c 0.95, CHCl₃)

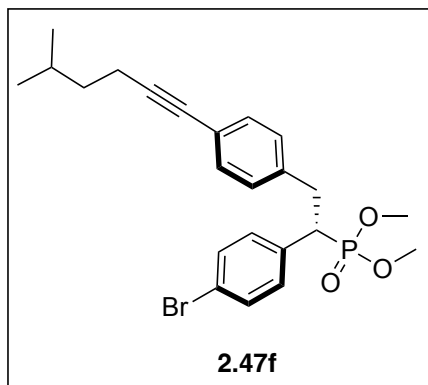
HRMS (+p APCI) calcd. for C₃₁H₄₄BrO₃P [M + H]⁺ 575.2284, found 575.2295.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 1.5% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm)

indicated 94% ee: *t_R* (minor enantiomer) = 24.6 min, *t_R* (major enantiomer) = 30.2 min.

The crystal structure information for compound (**2.47e**) is located in the crystallography section.

Dimethyl (S)-(1-(4-bromophenyl)-2-(4-(5-methylhex-1-yn-1-yl)phenyl)ethyl)phosphonate
(2.47f).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.40 in 1:1 hexanes/EtOAc), which afforded major product **2.47f** as a colorless oil (79 mg, 85%).

¹H NMR (600 MHz, CDCl₃) δ 7.37 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 7.9 Hz, 2H),

3.71 (dd, J_{HP} = 1.3, 10.7 Hz, 3H), 3.52 (dd, J_{HP} = 1.3, 10.5 Hz, 3H), 3.40 (ddd, J = 3.9, 8.8, 13.3 Hz, 1H), 3.24 (ddd, J = 3.7, 11.1, 22.1 Hz, 1H), 3.08 (ddd, J = 9.0, 11.1, 14.3 Hz, 1H), 2.37 (t, J = 7.5 Hz, 2H), 1.72 (hept, J = 6.7 Hz, 1H), 1.47 (q, J = 7.4 Hz, 2H), 0.90 (d, J = 6.6 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 138.2 (d, J_{CP} = 16.1 Hz), 134.6 (d, J_{CP} = 6.2 Hz), 132.0 (d, J_{CP} = 2.3 Hz), 131.8, 131.4 (d, J_{CP} = 6.9 Hz), 129.0, 122.5, 121.7 (d, J_{CP} = 3.5 Hz), 90.8, 80.5, 53.5 (dd, J_{CP} = 7.1, 117.4 Hz), 46.0 (d, J_{CP} = 137.1 Hz), 38.0, 36.4 (d, J_{CP} = 2.5 Hz), 27.6, 22.5, 17.7.

³¹P NMR (243 MHz, CDCl₃) δ 29.48.

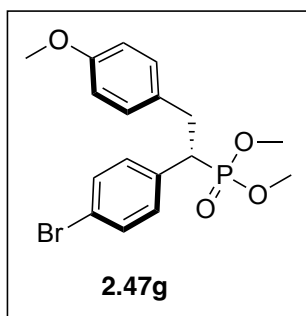
IR (neat): 3028, 2954, 2869, 2238, 1733, 1510, 1488, 1466, 1244, 1182, 1058, 1034, 1012, 908, 830, 731, 568 cm⁻¹.

$[\alpha]^{20}_D$: + 115.5° (c 0.50, CHCl₃)

HRMS (+p APCI) calcd. for C₂₃H₂₈BrO₃P [M + H]⁺ 463.1032, found 463.1039.

HPLC analysis: (Chiralcel ASH, 25 cm x 4.6 mm, 5.0% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: t_R (minor enantiomer) = 9.4 min, t_R (major enantiomer) = 16.7 min.

Dimethyl (S)-(1-(4-bromophenyl)-2-(4-methoxyphenyl)ethyl)phosphonate (2.47g).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.40 in 1:1 hexanes/EtOAc), which afforded **2.47g** as a colorless oil (64 mg, 80% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.38 (d, J = 8.6 Hz, 2H), 7.12 (dd, J = 2.2, 8.5 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.69 (d, J = 8.7 Hz, 2H), 3.73 (s,

3H), 3.72 (d, J_{HP} = 10.5 Hz, 3H), 3.52 (d, J_{HP} = 10.5 Hz, 3H), 3.38 (ddd, J = 3.9, 8.7, 14.1 Hz, 1H), 3.24 (ddd, J = 3.8, 11.4, 22.1 Hz, 1H), 3.06 (ddd, J = 8.9, 11.4, 14.1 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 158.4, 134.8 (d, J_{CP} = 6.3 Hz), 132.0 (d, J_{CP} = 2.3 Hz), 131.4 (d, J_{CP} = 7.0 Hz), 130.7 (d, J_{CP} = 16.9 Hz), 130.1, 121.6 (d, J_{CP} = 3.9 Hz), 114.0, 55.5, 53.5 (dd, J_{CP} = 7.2, 112.2 Hz), 46.3 (d, J_{CP} = 136.2 Hz), 35.6 (d, J_{CP} = 2.8 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 29.83.

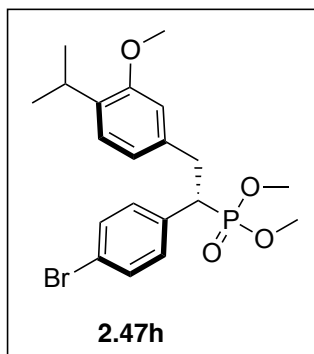
IR (neat): 2954, 2922, 2852, 1716, 1513, 1487, 1462, 1246, 1180, 1034, 1011, 904, 828, 730, 628, 534, 483 cm⁻¹.

$[\alpha]^{20}_D$: + 55.3° (c 0.40, CHCl₃)

HRMS (+p APCI) calcd. for C₁₇H₂₀BrO₄P [M + H]⁺ 399.0355, found 399.0360.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 1.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 98% ee: t_R (minor enantiomer) = 24.7 min, t (major enantiomer) = 28.0 min.

Dimethyl (*S*)-(1-(4-bromophenyl)-2-(4-isopropyl-3-methoxyphenyl)ethyl)phosphonate (2.47h**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; *R_f* = 0.34 in 1:1 hexanes/EtOAc), which afforded **2.47h** as a colorless oil (77 mg, 87% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.17 (dd, *J* = 2.2, 8.5 Hz, 2H), 6.99 (d, *J* = 7.7 Hz, 1H), 6.54 (dd, *J* = 1.7, 7.7 Hz, 1H),

6.35 (d, *J* = 1.8 Hz, 1H), 3.71 (d, *J*_{HP} = 10.7 Hz, 3H), 3.64 (s, 3H), 3.54 (d, *J*_{HP} = 10.5 Hz, 3H), 3.39 (ddd, *J* = 3.7, 9.2, 13.4 Hz, 1H), 3.27 (ddd, *J* = 3.8, 11.4, 22.1 Hz, 1H), 3.18 (hept, *J* = 7.0 Hz, 1H), 3.10 (ddd, *J* = 8.7, 11.3, 14.1 Hz, 1H), 1.13 (dd, *J* = 4.8, 6.9 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 156.8, 137.2 (d, *J*_{CP} = 16.6 Hz), 135.5, 135.2 (d, *J*_{CP} = 6.5 Hz), 131.9 (d, *J*_{CP} = 2.5 Hz), 131.5 (d, *J*_{CP} = 7.1 Hz), 126.2, 121.6 (d, *J*_{CP} = 3.9 Hz), 121.1, 111.4, 55.6, 53.5 (dd, *J*_{CP} = 7.1, 108.5 Hz), 46.1 (d, *J*_{CP} = 136.5 Hz), 36.4 (d, *J*_{CP} = 2.8 Hz), 26.8, 23.0 (d, *J*_{CP} = 8.5 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 29.78.

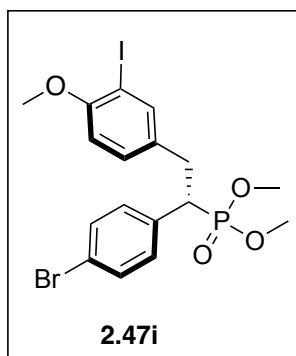
IR (neat): 2955, 2855, 1610, 1577, 1506, 1488, 1463, 1417, 1349, 1251, 1184, 1162, 1093, 1057, 1035, 1011, 957, 867, 826, 768, 731, 636, 548, 501, 479 cm⁻¹.

[α]²⁰_D: + 72.8° (c 0.50, CHCl₃)

HRMS (+p APCI) calcd. for C₂₀H₂₆BrO₄P [M + H]⁺ 441.0825, found 441.0824.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 3.0% *i*-PrOH/hexanes, 0.5 mL/min, 230 nm) indicated 97% ee: *t_R* (major enantiomer) = 37.5 min, *t* (minor enantiomer) = 39.9 min.

Dimethyl (S)-(1-(4-bromophenyl)-2-(3-iodo-4-methoxyphenyl) ethyl)phosphonate (2.47i).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.34 in 1:1 hexanes/EtOAc), which afforded **2.47i** as a colorless oil (93 mg, 89% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, J = 2.2 Hz, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.13 (dd, J = 2.2, 8.6 Hz, 2H), 6.82 (dd, J = 2.2, 8.4 Hz, 1H),

6.58 (d, J = 8.4 Hz, 1H), 3.79 (s, 3H), 3.72 (d, J_{HP} = 10.8 Hz, 3H), 3.52 (d, J_{HP} = 10.6 Hz, 3H), 3.34 (ddd, J = 3.9, 8.8, 13.3 Hz, 1H), 3.21 (ddd, J = 4.1, 11.0, 21.9 Hz, 1H), 3.01 (ddd, J = 9.2, 11.1, 13.9 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 157.1, 139.9, 134.6 (d, J_{CP} = 6.4 Hz), 132.9 (d, J_{CP} = 16.5 Hz), 132.1 (d, J_{CP} = 2.4 Hz), 131.4 (d, J_{CP} = 6.9 Hz), 130.2, 121.8 (d, J_{CP} = 3.8 Hz), 110.9, 86.1, 56.6, 53.5 (dd, J_{CP} = 7.2, 81.4 Hz), 46.2 (d, J_{CP} = 136.9 Hz), 35.2 (d, J_{CP} = 2.6 Hz).

³¹P NMR (162 MHz, CDCl₃) δ 29.38.

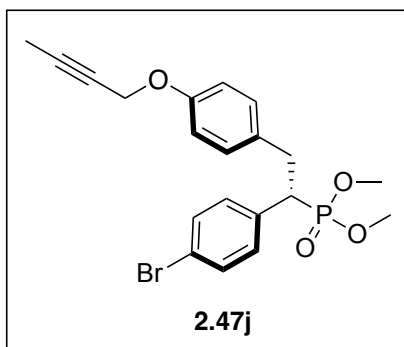
IR (neat): 3001, 2960, 2833, 1582, 1566, 1472, 1439, 1414, 1326, 1283, 1241, 1227, 1181, 1168, 1159, 1090, 1060, 1028, 988, 859, 840, 821, 762, 679, 651, 563 cm⁻¹.

$[\alpha]^{20}_D$: +116.2° (c 0.90, CHCl₃)

HRMS (+p APCI) calcd. for C₁₇H₁₉BrO₄IP [M + H]⁺ 524.9337, found 524.9322.

HPLC analysis: (Chiralcel ODH, 25 cm x 4.6 mm, 3.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 96% ee: t_R (major enantiomer) = 23.8 min, t (minor enantiomer) = 34.6 min.

Dimethyl (*S*)-(1-(4-bromophenyl)-2-(4-(but-2-yn-1-yloxy)phenyl)ethyl)phosphonate (2.47j**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.38 in 1:1

hexanes/EtOAc), which afforded **2.47j** as a colorless oil (70 mg, 85% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.38 (d, J = 8.4 Hz, 2H), 7.13 (dd,

J = 2.2, 8.5 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.76 (d, J = 8.7 Hz, 2H), 4.56 (q, J = 2.3 Hz, 2H),

3.71 (d, J_{HP} = 10.7 Hz, 3H), 3.52 (d, J_{HP} = 10.5 Hz, 3H), 3.38 (ddd, J = 4.0, 8.9, 13.5 Hz, 1H), 3.24

(ddd, J = 4.0, 11.1, 22.1 Hz, 1H), 3.06 (ddd, J = 9.2, 11.2, 14.2 Hz, 1H), 1.84 (t, J = 2.3 Hz, 3H).

(Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 156.8, 134.9 (d, J_{CP} = 6.2 Hz), 132.0 (d, J_{CP} = 2.2 Hz), 131.4 (d, J_{CP}

= 6.9 Hz), 130.0, 125.9, 121.6 (d, J_{CP} = 3.7 Hz), 115.0, 84.0, 74.4, 56.8, 53.5 (dd, J_{CP} = 7.2, 111.5

Hz), 46.3 (d, J_{CP} = 136.5 Hz), 35.7 (d, J_{CP} = 2.7 Hz), 4.0.

³¹P NMR (243 MHz, CDCl₃) δ 29.74.

IR (neat): 3032, 2981, 2920, 2227, 1612, 1585, 1509, 1488, 1455, 1370, 1293, 1217, 1177, 1141,

1110, 1052, 1012, 964, 854, 816, 770, 715, 702, 626, 576, 550, 508, 497, 489 cm⁻¹.

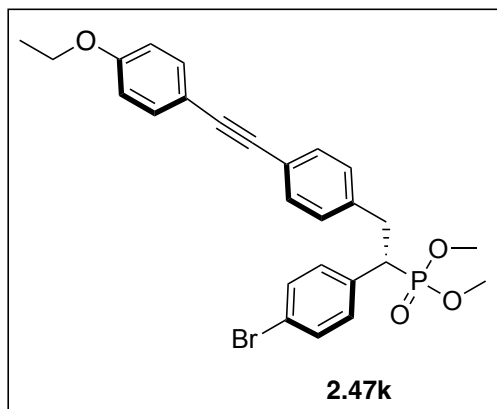
$[\alpha]^{20}_D$: + 70.5° (c 1.00, CHCl₃)

HRMS (+p APCI) calcd. for C₂₀H₂₂BrO₄P [M + H]⁺ 437.0512, found 437.0511.

HPLC analysis: (Chiralcel ODH, 25 cm x 4.6 mm, 5.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm)

indicated 98% ee: t_R (major enantiomer) = 22.3 min, t (minor enantiomer) = 31.6 min.

Dimethyl (*S*)-(1-(4-bromophenyl)-2-(4-((4-ethoxyphenyl)ethynyl)phenyl)ethyl) phosphonate (2.47k).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; *R_f* = 0.39 in 1:1 hexanes/EtOAc), which afforded **2.47k** as a colorless oil (53 mg, 52% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.41 (d, *J* = 8.7 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.12

(dd, *J* = 2.2, 8.5 Hz, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.04 (q, *J* = 7.0 Hz, 2H), 3.73 (d, *J*_{HP} = 10.8 Hz, 3H), 3.53 (d, *J*_{HP} = 10.6 Hz, 3H), 3.43 (ddd, *J* = 3.9, 8.7, 14.1 Hz, 1H), 3.26 (ddd, *J* = 3.9, 11.6, 22.1 Hz, 1H), 3.11 (ddd, *J* = 9.2, 11.4, 14.0 Hz, 1H), 1.42 (t, *J* = 7.0 Hz, 4H).

(Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 159.3, 138.7 (d, *J*_{CP} = 16.4 Hz), 134.5 (d, *J*_{CP} = 6.5 Hz), 133.3, 132.1 (d, *J*_{CP} = 2.3 Hz), 131.7, 131.4 (d, *J*_{CP} = 6.8 Hz), 129.1, 122.1, 121.8 (d, *J*_{CP} = 3.8 Hz), 115.5, 114.8, 89.8, 88.0, 63.9, 53.6 (dd, *J*_{CP} = 7.2, 119.5 Hz), 46.0 (d, *J*_{CP} = 137.2 Hz), 36.5 (d, *J*_{CP} = 2.6 Hz), 15.1.

³¹P NMR (243 MHz, CDCl₃) δ 29.44.

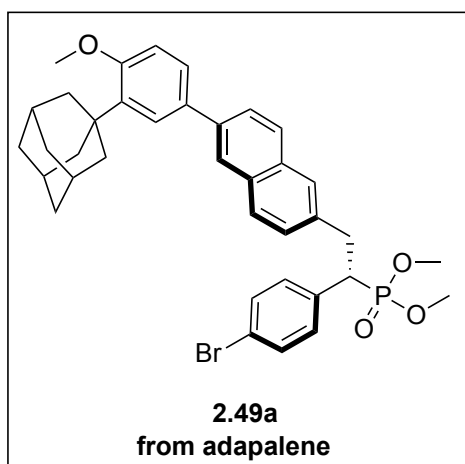
IR (neat): 2979, 2952, 2926, 2849, 1602, 1569, 1516, 1488, 1476, 1392, 1284, 1246, 1174, 1115, 1034, 1011, 921, 872, 830, 769, 706, 635, 617, 595, 570, 549 cm⁻¹.

[α]_D²⁰: + 41.9° (c 0.70, CHCl₃)

HRMS (+p APCI) calcd. for C₂₀H₂₂BrO₄P [M + H]⁺ 437.0512, found 437.0511.

SFC analysis: (ChiralCel OJ-3, 3 μm particle size, 150 mm x 3 mm, 10.0% MeOH/IPA with 0.2% Formic Acid, 2.5 mL/min, 280 nm) indicated 94% ee: *t_R* (major enantiomer) = 4.9 min, *t_R* (minor enantiomer) = 5.6 min.

Dimethyl ((1*S*)-2-(6-(3-(adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)-1-(4-bromophenyl)ethyl)phosphonate (2.49a**).**



The material was purified by flash chromatography (SiO₂;

hexanes/EtOAc, 10:0 to 1:1 gradient; *R_f* = 0.39 in 1:1

hexanes/EtOAc), which afforded **2.49a** as a white solid (116 mg, 88% yield).

m.p. 144-148 °C.

¹H NMR (600 MHz, CDCl₃): δ 7.87 (d, *J* = 1.8 Hz, 1H),

7.74 – 7.64 (m, 3H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.48 (dd, *J* =

2.3, 8.4 Hz, 1H), 7.43 (d, *J* = 1.5 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.17 (dd, *J* = 2.1, 6.4 Hz, 2H),

7.11 (dd, *J* = 1.8, 8.4 Hz, 1H), 7.00 – 6.95 (m, 1H), 3.89 (s, 3H), 3.74 (d, *J*_{HP} = 10.7 Hz, 3H), 3.61

(ddd, *J* = 3.8, 8.9, 13.6 Hz, 1H), 3.55 (d, *J*_{HP} = 10.7 Hz, 3H), 3.46 – 3.37 (m, 1H), 3.29 (ddd, *J* = 8.9,

11.3, 14.1 Hz, 1H), 2.16 (d, *J* = 2.9 Hz, 6H), 2.09 (d, *J* = 4.6 Hz, 3H), 1.82 – 1.75 (m, 6H).

(Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 158.9, 139.2, 139.1, 136.0, 135.9, 134.7 (d, *J* = 6.2 Hz), 133.5,

132.8, 132.5, 132.0 (d, *J* = 2.5 Hz), 131.4 (d, *J* = 6.8 Hz), 128.5, 128.2, 127.6 (d, *J* = 19.0 Hz), 126.2

(d, *J* = 2.1 Hz), 125.9, 125.1, 121.68 (d, *J* = 3.8 Hz), 112.4, 55.5, 53.6 (dd, *J* = 7.2, 114.4 Hz), 46.1

(d, *J* = 136.7 Hz), 41.0, 37.5 (d, *J* = 3.9 Hz), 36.7 (d, *J* = 2.7 Hz), 29.5.

³¹P NMR (243 MHz, CDCl₃) δ 29.64.

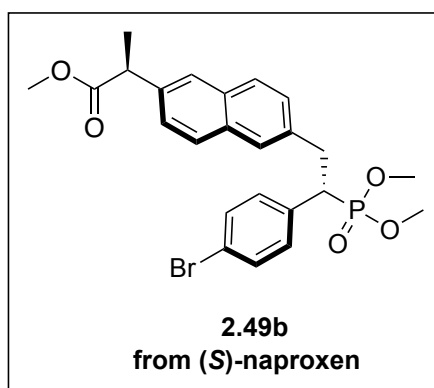
IR (neat): 2902, 2849, 1488, 1237, 1182, 1058, 1031, 880, 817, 757, 561, 492, 287, 479, 429, 217, 412, 406 cm⁻¹.

[α]²⁰_D: + 80.2° (c 2.50, CHCl₃)

HRMS (+p APCI) calcd. for C₃₇H₄₀BrO₄P [M + H]⁺ 659.1920, found 659.1927.

SFC analysis: (Chiralpak AS-3, 3 μ m particle size, 150 mm x 3 mm, 10.0% MeOH/IPA, with 0.2% Formic Acid, 2.5 mL/min, 280 nm) indicated 94% ee: t_R (minor enantiomer) = 1.8 min, t_R (major enantiomer) = 2.2 min.

Methyl (*S*)-2-(6-((*S*)-2-(4-bromophenyl)-2-(dimethoxyphosphoryl)ethyl)naphthalen-2-yl)propanoate (2.49b**).**



The material was purified by flash chromatography (SiO₂;

hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.35 in 1:1

hexanes/EtOAc), which afforded **2.49b** as a colorless oil (81 mg, 80% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, J = 8.4 Hz, 3H), 7.42 – 7.32 (m, 4H), 7.15 (dd, J = 2.3, 8.6 Hz, 2H), 7.10 (dd, J = 1.8,

8.4 Hz, 1H), 3.85 (q, J = 7.1 Hz, 1H), 3.73 (d, J_{HP} = 10.7 Hz, 3H), 3.65 (s, 3H), 3.64 – 3.50 (m, 4H), 3.39 (ddd, J = 3.8, 11.2, 21.7 Hz, 1H), 3.27 (ddd, J = 8.4, 11.4, 14.0 Hz, 1H), 1.56 (d, J = 7.3 Hz, 3H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 175.3, 138.1, 136.3 (d, J_{CP} = 16.6 Hz), 134.7 (d, J_{CP} = 6.5 Hz), 132.7 (d, J_{CP} = 33.5 Hz), 132.0 (d, J_{CP} = 2.4 Hz), 131.4 (d, J_{CP} = 6.9 Hz), 128.3 (d, J_{CP} = 6.4 Hz), 127.6 (d, J_{CP} = 14.1 Hz), 126.2 (d, J_{CP} = 9.8 Hz), 121.7, 53.6 (dd, J_{CP} = 7.2, 75.3 Hz), 52.4, 46.1 (d, J_{CP} = 137.0 Hz), 45.8, 36.6, 18.9.

³¹P NMR (162 MHz, CDCl₃) δ 29.58.

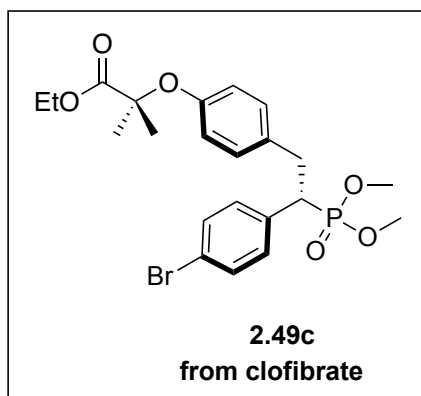
IR (neat): 2952, 1851, 1732, 1606, 1488, 1455, 1377, 1329, 1246, 1197, 1056, 1031, 1011, 888, 820, 767, 732, 556, 499, 479 cm⁻¹.

$[\alpha]^{20}_D$: + 85.5° (c 1.00, CHCl₃)

HRMS (+p APCI) calcd. for C₂₄H₂₆BrO₅P [M + H]⁺ 505.0774, found 505.0777.

SFC analysis: (Chiralpak AS-3, 3 μ m particle size, 150 mm x 3 mm, 5.0% MeOH/IPA, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 84% ee: t_R (minor enantiomer) = 1.4 min, t_R (major enantiomer) = 1.8 min.

Ethyl (*S*)-2-(4-(2-(4-bromophenyl)-2-(dimethoxyphosphoryl)ethyl)phenoxy)-2-methylpropanoate (2.49c**).**



The material was purified by flash chromatography (SiO₂;

hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.32 in 1:1

hexanes/EtOAc), which afforded **2.49c** as a colorless oil (62 mg, 62% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.36 (d, J = 8.6 Hz, 2H), 7.10

(dd, J = 2.3, 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 6.64 (d, J =

8.7 Hz, 2H), 4.18 (qd, J = 1.5, 7.1 Hz, 2H), 3.70 (d, J_{HP} = 10.8 Hz, 3H), 3.51 (d, J_{HP} = 10.5 Hz, 3H), 3.36 (ddd, J = 4.0, 8.7, 13.2 Hz, 1H), 3.21 (ddd, J = 4.1, 11.2, 22.1 Hz, 1H), 3.03 (ddd, J = 9.5, 11.2, 14.1 Hz, 1H), 1.53 (s, 6H), 1.18 (t, J = 7.1 Hz, 3H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 174.6, 154.3, 134.8 (d, J_{CP} = 6.2 Hz), 132.4 (d, J_{CP} = 16.1 Hz),

131.9 (d, J_{CP} = 2.2 Hz), 131.4 (d, J_{CP} = 7.1 Hz), 129.8, 121.6 (d, J_{CP} = 3.8 Hz), 119.3, 79.4, 61.7,

53.5 (dd, J_{CP} = 7.1, 114.5 Hz), 46.2 (d, J_{CP} = 136.7 Hz), 35.8 (d, J_{CP} = 2.7 Hz), 25.7 (d, J_{CP} = 32.9 Hz), 14.4.

³¹P NMR (243 MHz, CDCl₃) δ 29.71.

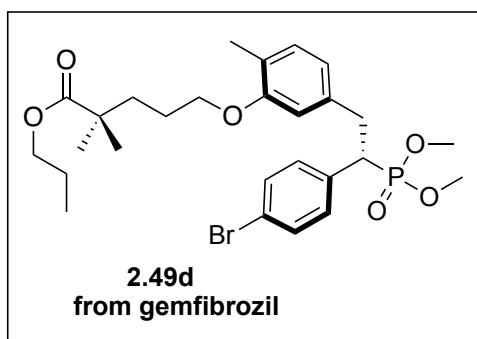
IR (neat): 2988, 2553, 2850, 1731, 1508, 1488, 1466, 1382, 1283, 1239, 1178, 1140, 1056, 1031, 1011, 971, 912, 830, 766, 731, 645, 559, 520, 508, 476 cm⁻¹.

$[\alpha]^{20}_D$: + 28.7° (c 0.40, CHCl₃)

HRMS (+p APCI) calcd. for C₂₂H₂₈BrO₆P [M + H]⁺ 499.0880, found 499.0885.

SFC analysis: (Chiralpak AS-3, 3 μ m particle size, 150 mm x 3 mm, 5.0% MeOH/IPA, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 84% ee: t_R (minor enantiomer) = 1.4 min, t_R (major enantiomer) = 2.0 min.

Propyl (*S*)-5-(5-(2-(4-bromophenyl)-2-(dimethoxyphosphoryl)ethyl)-2-methylphenoxy)-2,2-dimethylpentanoate (2.48d**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.40 in 1:1 hexanes/EtOAc)), which afforded **2.48d** as a colorless oil (66 mg, 58% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.39 (d, J = 8.4 Hz, 2H), 7.14 (dd, J = 2.2, 8.6 Hz, 2H), 6.90 (dd, J = 0.9, 7.5 Hz, 1H), 6.45 (dd, J = 1.6, 7.5 Hz, 1H), 6.28 (d, J = 1.7 Hz, 1H), 4.02 (t, J = 6.6 Hz, 2H), 3.79 – 3.69 (m, 4H), 3.68 – 3.60 (m, 1H), 3.54 (d, J_{HP} = 10.5 Hz, 3H), 3.37 (ddd, J = 3.7, 8.8, 14.2 Hz, 1H), 3.25 (ddd, J = 3.6, 11.5, 22.1 Hz, 1H), 3.06 (ddd, J = 8.3, 11.5, 14.0 Hz, 1H), 2.10 (s, 3H), 1.67 – 1.58 (m, 6H), 1.21 (s, 7H), 0.94 (t, J = 7.4 Hz, 3H).

(Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 178.2, 157.1, 137.3 (d, J_{CP} = 16.7 Hz), 135.0 (d, J_{CP} = 6.3 Hz), 131.9 (d, J_{CP} = 2.3 Hz), 131.5 (d, J_{CP} = 6.8 Hz), 130.7, 125.2, 121.6 (d, J_{CP} = 3.8 Hz), 120.8, 111.9, 68.3, 66.3, 53.5 (dd, J_{CP} = 7.0, 107.6 Hz), 46.2 (d, J_{CP} = 136.5 Hz), 42.4, 37.4, 36.4 (d, J_{CP} = 2.6 Hz), 25.5 (d, J_{CP} = 15.5 Hz), 22.4, 16.1, 10.8.

³¹P NMR (243 MHz, CDCl₃) δ 29.76.

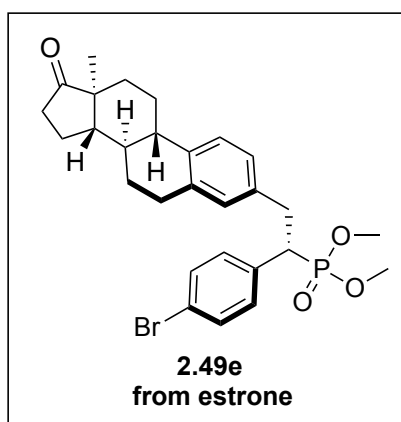
IR (neat): 2954, 2921, 2850, 1724, 1509, 1488, 1473, 1253, 1192, 1144, 1057, 1034, 1012, 871, 828, 770, 560, 552, 540, 534, 498, 490, 485, 477 cm⁻¹.

[α]²⁰ D: + 55.3° (c 0.80, CHCl₃)

HRMS (+p APCI) calcd. for $C_{27}H_{38}BrO_6P$ $[M + H]^+$ 569.1662, found 569.1671.

SFC analysis: (Chiralpak AS-3, 3 μ m particle size, 150 mm x 3 mm, 5.0% MeOH/IPA, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 90% ee: t_R (minor enantiomer) = 2.3 min, t_R (major enantiomer) = 2.7 min.

Dimethyl ((1*S*)-1-(4-bromophenyl)-2-((8*R*,9*S*,13*S*)-13-methyl-17-oxo-7,8,9,11,12,13, 14,15,16, 17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)ethyl)phosphonate (2.48e).



The material was purified by flash chromatography (SiO₂;

hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.38 in 1:1

hexanes/EtOAc), which afforded **2.48e** as a white solid (99 mg,

91% yield). **m.p.** 123-126 °C.

¹H NMR (600 MHz, CDCl₃) δ 7.40 (d, J = 8.3 Hz, 2H), 7.16 (d, J = 8.3 Hz, 2H), 7.08 (d, J = 7.9 Hz, 1H), 6.76 (d, J = 7.9 Hz, 1H),

6.68 (s, 1H), 3.72 (d, J_{HP} = 10.6 Hz, 2H), 3.53 (d, J_{HP} = 10.6 Hz, 3H), 3.37 (t, J = 11.9 Hz, 1H), 3.33 – 3.25 (m, 1H), 3.08 (q, J = 11.1 Hz, 1H), 2.84 – 2.70 (m, 2H), 2.49 (dd, J = 18.9, 8.8 Hz, 1H), 2.36 – 2.32 (m, 1H), 2.21 (d, J = 10.8 Hz, 1H), 2.19 – 2.08 (m, 1H), 2.07 – 1.99 (m, 1H), 1.99 – 1.91 (m, 2H), 1.65 – 1.32 (m, 6H), 0.89 (s, 3H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 138.2, 136.7, 136.2 (d, J_{CP} = 16.0 Hz), 135.0 (d, J_{CP} = 7.0 Hz), 131.9, 131.5 (d, J_{CP} = 6.7 Hz), 129.8, 126.3, 125.6, 121.6, 53.4 (dd, J_{CP} = 7.5, 107.9 Hz), 50.9, 48.3, 45.8 (d, J_{CP} = 136.9 Hz), 44.6, 38.4, 36.2, 35.7, 31.9, 30.1, 29.6, 26.8, 26.0, 21.9, 14.2.

³¹P NMR (243 MHz, CDCl₃) δ 29.83.

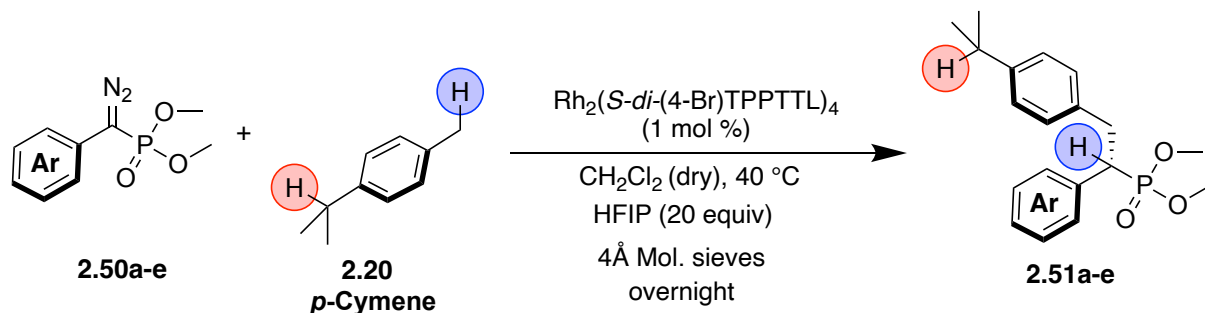
IR (neat): 2926, 1737, 1487, 1248, 1055, 1032, 1011, 824, 767, 552, 515, 504, 493, 485, 471, 466 cm^{-1} .

$[\alpha]^{20}_D$: + 78.4° (c 1.00, CHCl₃)

HRMS (+p APCI) calcd. for C₂₈H₃₄BrO₄P [M + H]⁺ 545.1451, found 545.1463.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 7.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 98% ee: *t*_R (major enantiomer) = 36.8 min, *t* (minor enantiomer) = 46.9 min.

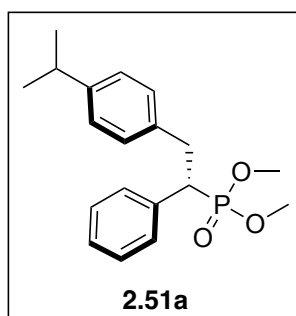
The crystal structure information for compound (**2.48e**) is located in the crystallography section.



A clean oven-dried and flame-dried 25.0 mL round bottom flask (flask-A) equipped with activated 4 Å molecular sieves, and a magnetic stir-bar was evacuated and purged with argon (2-3 times). After cooling down to room temperature, **2.20** (5 equiv., 1.00 mmol) followed by $\text{Rh}_2(\text{S-di-(4-Br)TPPTTL})_4$ (6.2 mg, 0.01 equiv.), and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (20 equiv.) were then added. The flask was once again evacuated and purged with argon (3-5 times) and anhydrous CH_2Cl_2 (5.0 mL) was added. The flask and its contents were then set to stir at reflux (40 °C) using a hotplate under an argon atmosphere. To a second oven-dried round bottom flask (flask-B), that was evacuated and purged with argon was added aryldiazophosphonates **2.50a-e** (0.20 mmol). flask-B and its contents were evacuated and purged with argon (2-3 times) and anhydrous CH_2Cl_2 (10.0 mL) was then added to obtain a solution of the diazo-compound. The solution was transferred into a 12.0 mL plastic syringe. Using a well-calibrated syringe-pump, a slow addition of the diazo solution into the stirring solution of flask-A under an inert atmosphere was initiated. After the complete addition of the solution (5 h), the residual diazo compound in the

12.0 mL plastic syringe was rinsed with anhydrous CH_2Cl_2 (1.0 mL) and transferred dropwise into the stirring reaction mixture of flask-A. The resulting solution was refluxed for 7 to 9 hours (overnight) before concentrating the solution under reduced pressure. Purification by flash column chromatography on silica gel (hexanes : EtOAc) was used to afford the final products.

Dimethyl (*S*)-(2-(4-isopropylphenyl)-1-phenylethyl)phosphonate (2.51a**)**



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 10:0 to 1:1 gradient; $R_f = 0.38$ in 1:1 hexanes/EtOAc), which afforded **2.51a** as a colorless oil (63 mg, 90% yield).

^1H NMR (600 MHz, CDCl_3) δ 7.27 – 7.20 (m, 5H), 7.18 (td, $J = 1.9, 6.6$ Hz, 1H), 6.97 (d, $J = 7.9$ Hz, 2H), 6.88 (d, $J = 7.9$ Hz, 2H), 3.64 (d, $J_{\text{HP}} =$

10.7 Hz, 3H), 3.42 (d, $J_{\text{HP}} = 10.7$ Hz, 3H), 3.37 (td, $J = 5.0, 9.9$ Hz, 1H), 3.30 (ddd, $J = 4.0, 10.6, 22.1$ Hz, 1H), 3.14 (dt, $J = 10.4, 14.0$ Hz, 1H), 2.76 (hept, $J = 6.9$ Hz, 1H), 1.13 (dd, $J = 2.0, 7.0$ Hz, 6H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 147.1, 136.6 (d, $J_{\text{CP}} = 15.8$ Hz), 135.9 (d, $J_{\text{CP}} = 6.6$ Hz), 129.8 (d, $J_{\text{CP}} = 6.7$ Hz), 129.0, 128.8 (d, $J_{\text{CP}} = 2.5$ Hz), 127.6 (d, $J_{\text{CP}} = 3.1$ Hz), 126.6, 53.4 (dd, $J_{\text{CP}} = 7.1, 125.5$ Hz), 46.6 (d, $J_{\text{CP}} = 135.9$ Hz), 36.2 (d, $J_{\text{CP}} = 2.7$ Hz), 33.9, 24.3 (d, $J_{\text{CP}} = 3.3$ Hz).

^{31}P NMR (243 MHz, CDCl_3) δ 30.67.

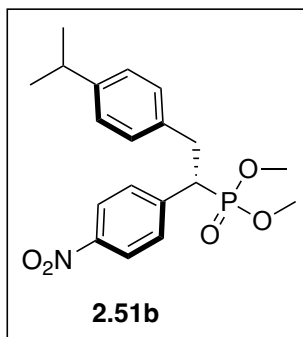
IR (neat): 2956, 1513, 1495, 1454, 1248, 1248, 1183, 1056, 1029, 826, 775, 762, 747, 699, 592, 574, 563, 563, 549, 535, 525, 510, 506, 497, 489, 483 cm^{-1} .

$[\alpha]^{20}_{\text{D}}$: +93.5° (c 4.50, CHCl_3)

HRMS (+p APCI) calcd. for $\text{C}_{19}\text{H}_{25}\text{O}_3\text{P}$ $[\text{M} + \text{H}]^+$ 333.1614, found 333.1619.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 2.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 98% ee: t_R (minor enantiomer) = 21.1 min, t (major enantiomer) = 28.6 min.

Dimethyl (2-(4-isopropylphenyl)-1-(4-nitrophenyl)ethyl)phosphonate (**2.51b**)



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; *R_f* = 0.32 in 1:1 hexanes/EtOAc), which afforded **2.51b** as a colorless oil (48 mg, 60%).

¹H NMR (600 MHz, CDCl₃) δ 8.12 (d, *J* = 8.7 Hz, 2H), 7.44 (dd, *J* = 2.2, 8.7 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 3.74 (d,

*J*_{HP} = 10.7 Hz, 3H), 3.58 (d, *J*_{HP} = 10.7 Hz, 3H), 3.51 – 3.42 (m, 2H), 3.15 (dt, *J* = 10.0, 13.4 Hz, 1H), 2.80 (p, *J* = 6.9 Hz, 1H), 1.16 (dd, *J* = 2.2, 6.9 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 147.7, 147.5, 143.9 (d, *J*_{CP} = 6.4 Hz), 135.4 (d, *J*_{CP} = 16.0 Hz), 130.6 (d, *J*_{CP} = 6.8 Hz), 128.9, 126.9, 124.0 (d, *J*_{CP} = 2.3 Hz), 53.6 (dd, *J*_{CP} = 7.0, 66.7 Hz), 46.7 (d, *J*_{CP} = 136.2 Hz), 36.0 (d, *J*_{CP} = 3.3 Hz), 33.9, 24.2 (d, *J*_{CP} = 4.2 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 28.73.

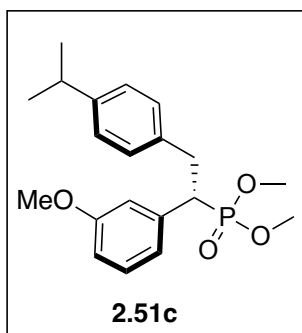
IR (neat): 2955, 1513, 1488, 1460, 1405, 1363, 1244, 1182, 1053, 1029, 1010, 908, 868, 825, 760, 729, 644, 634, 621, 575, 553, 479 cm⁻¹.

[α]²⁰_D: + 82.2° (c 2.00, CHCl₃)

HRMS (+p APCI) calcd. for C₁₉H₂₄NO₅P [M + H]⁺ 378.1465, found 378.1473

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 2.0% *i*-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 98% ee: *t_R* (minor enantiomer) = 25.1 min, *t* (major enantiomer) = 26.6 min.

Dimethyl (2-(4-isopropylphenyl)-1-(3-methoxyphenyl)ethyl)phosphonate (2.51c)



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.38 in 1:1 hexanes/EtOAc), which afforded **2.51c** as a colorless oil (51 mg, 71%).

¹H NMR (600 MHz, CDCl₃) δ 7.18 (t, J = 7.9 Hz, 1H), 7.02 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 7.6 Hz, 1H), 6.82 (d, J =

2.2 Hz, 1H), 6.76 (dd, J = 2.2, 8.3 Hz, 1H), 3.76 (s, 3H), 3.68 (d, J_{HP} = 10.7 Hz, 3H), 3.49 (d, J_{HP} = 10.5 Hz, 3H), 3.39 (ddd, J = 4.1, 10.0, 14.1 Hz, 1H), 3.29 (ddd, J = 4.1, 10.7, 22.0 Hz, 1H), 3.15 (dt, J = 10.4, 14.0 Hz, 1H), 2.80 (hept, J = 6.9 Hz, 1H), 1.18 (dd, J = 1.4, 7.0 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 159.9 (d, J_{CP} = 2.3 Hz), 147.1, 137.4 (d, J_{CP} = 6.5 Hz), 136.6 (d, J_{CP} = 15.9 Hz), 129.7 (d, J_{CP} = 2.4 Hz), 129.0, 126.6, 122.2 (d, J_{CP} = 6.7 Hz), 115.5 (d, J_{CP} = 7.1 Hz), 113.1 (d, J_{CP} = 3.1 Hz), 55.6, 53.4 (dd, J_{CP} = 7.0, 126.4 Hz), 46.6 (d, J_{CP} = 135.9 Hz), 36.2 (d, J_{CP} = 2.8 Hz), 34.0, 24.3 (d, J_{CP} = 4.2 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 30.55.

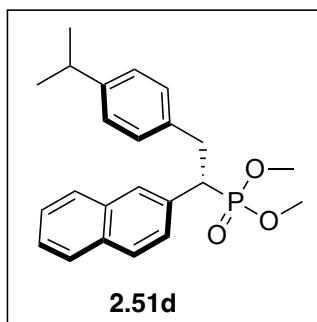
IR (neat): 2960, 2833, 1582, 1566, 1472, 1439, 1414, 1326, 1283, 1241, 1227, 1181, 1168, 1159, 1090, 1060, 1028, 988, 859, 840, 821, 763, 679, 651, 563, 478 cm⁻¹.

$[\alpha]^{20}_D$: + 77.5° (c 4.40, CHCl₃)

HRMS (+p APCI) calcd. for C₂₀H₂₇O₄P [M + H]⁺ 363.1718, found 363.1725.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 2.0% *i*-PrOH/hexanes, 1.0 mL/min, 280 nm) indicated 97% ee: t_R (minor enantiomer) = 11.9 min, t (major enantiomer) = 26.1 min.

Dimethyl (2-(4-isopropylphenyl)-1-(naphthalen-2-yl)ethyl)phosphonate (2.51d)



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.40 in 1:1 hexanes/EtOAc), which afforded **2.51d** as a colorless oil (61 mg, 80%).

¹H NMR (600 MHz, CDCl₃) δ 7.78 (dt, J = 5.4, 14.8 Hz, 3H), 7.71 (s, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.46 – 7.42 (m, 2H), 6.98 (d, J = 8.0 Hz,

2H), 6.94 (d, J = 8.0 Hz, 2H), 3.69 (d, J_{HP} = 10.6 Hz, 3H), 3.55 – 3.46 (m, 2H), 3.44 (d, J_{HP} = 10.6 Hz, 3H), 3.30 (dt, J = 11.1, 14.4 Hz, 1H), 2.77 (hept, J = 6.9 Hz, 1H), 1.14 (dd, J = 3.3, 6.9 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 147.13, 136.49 (d, J_{CP} = 15.7 Hz), 133.69 (d, J_{CP} = 2.5 Hz), 133.40 (d, J_{CP} = 6.8 Hz), 132.95 (d, J_{CP} = 2.2 Hz), 129.02, 128.86 (d, J_{CP} = 8.8 Hz), 128.48 (d, J_{CP} = 2.1 Hz), 128.20, 127.96, 127.58 (d, J_{CP} = 5.3 Hz), 126.62, 126.36, 126.16, 53.43 (dd, J_{CP} = 7.0, 120.9 Hz), 46.68 (d, J_{CP} = 135.8 Hz), 36.07 (d, J_{CP} = 2.7 Hz), 33.92, 24.25.

³¹P NMR (243 MHz, CDCl₃) δ 30.50.

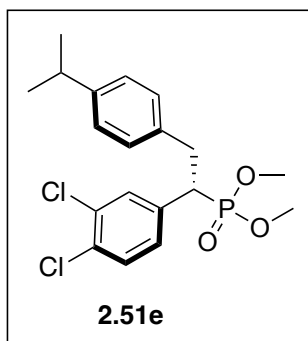
IR (neat): 2955, 1600, 1508, 1461, 1363, 1245, 1184, 1053, 1030, 861, 759, 650, 575, 545, 503, 476, 456 cm⁻¹.

$[\alpha]^{20}_D$: + 97.7° (c 1.00, CHCl₃)

HRMS (+p APCI) calcd. for C₂₃H₂₇O₃P [M + H]⁺ 383.1771, found 383.1777.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 3.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 94% ee: t_R (minor enantiomer) = 25.4 min, t (major enantiomer) = 39.5 min.

Dimethyl (1-(3,4-dichlorophenyl)-2-(4-isopropylphenyl)ethyl)phosphonate (**2.51e**)



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.35 in 1:1 hexanes/EtOAc), which afforded **2.51e** as a colorless oil (68 mg, 85%).

¹H NMR (600 MHz, CDCl₃) δ 7.33 (d, J = 8.5 Hz, 2H), 7.16 – 7.11 (m, 1H), 7.04 (d, J = 7.8 Hz, 2H), 6.90 (d, J = 7.8 Hz, 2H), 3.72 (d, J_{HP} = 10.6

Hz, 3H), 3.58 (d, J_{HP} = 10.6 Hz, 3H), 3.40 (ddd, J = 4.0, 9.3, 13.7 Hz, 1H), 3.27 (ddd, J = 4.0, 11.1, 22.5 Hz, 1H), 3.12 – 3.02 (m, 1H), 2.82 (hept, J = 6.9 Hz, 1H), 1.18 (d, J = 6.9 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 136.37 (d, J_{CP} = 6.2 Hz), 135.70 (d, J_{CP} = 15.7 Hz), 132.80 (d, J_{CP} = 2.7 Hz), 131.68 (d, J_{CP} = 3.8 Hz), 131.60 (d, J_{CP} = 7.2 Hz), 130.71 (d, J_{CP} = 2.5 Hz), 129.04 (d, J_{CP} = 6.8 Hz), 128.94, 126.81, 53.54 (dd, J_{CP} = 7.0, 84.3 Hz), 45.81 (d, J_{CP} = 137.1 Hz), 35.93 (d, J_{CP} = 2.8 Hz), 33.98, 24.27 (d, J_{CP} = 2.4 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 29.26.

IR (neat): 2956, 1514, 1468, 1398, 1239, 1239, 1184, 1133, 1029, 894, 823, 761, 731, 704, 678, 596, 565, 506, 494, 478, 470, 459, 441, 422, 411, 406 cm⁻¹.

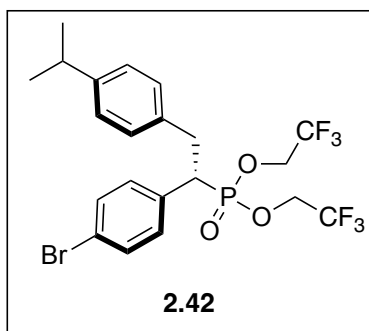
$[\alpha]^{20}_D$: + 145.1° (c 1.00, CHCl₃)

HRMS (+p APCI) calcd. for C₁₉H₂₃Cl₂O₃P [M + H]⁺ 401.0835, found 401.0842.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 4.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 98% ee: t_R (minor enantiomer) = 13.5 min, t (major enantiomer) = 16.4 min.

Bis(2,2,2-trifluoroethyl) (S)-(1-(4-bromophenyl)-2-(4-isopropylphenyl)ethyl)phosphonate

(2.42)



The material was purified by flash chromatography (SiO₂;

hexanes/EtOAc, 10:0 to 1:1 gradient; R_f = 0.55 in 1:1

hexanes/EtOAc), which afforded **2.42** as a colorless oil (92 mg,

84%). **m.p.** 75-77 °C.

¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.42 (m, 2H), 7.20 – 7.14 (m,

2H), 7.09 – 7.04 (m, 2H), 6.97 – 6.92 (m, 2H), 4.34 – 4.15 (m, 2H), 4.08 (ddq, J = 8.1, 9.3, 12.2 Hz, 1H), 3.89 – 3.76 (m, 1H), 3.52 – 3.34 (m, 2H), 3.23 – 3.09 (m, 1H), 2.82 (hept, J = 7.0 Hz, 1H), 1.19 (d, J = 7.0 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 147.9, 135.0 (d, J_{CP} = 15.3 Hz), 133.2 (d, J_{CP} = 6.7 Hz), 132.3 (d, J_{CP} = 2.7 Hz), 131.3 (d, J_{CP} = 7.3 Hz), 129.0, 123.7 (qd, J_{CP} = 4.2, J_{CF} = 278.24 Hz), 123.6 (qd, J_{CP} = 4.2, J_{CF} = 278.24 Hz), 126.9, 63.0 (qd, J_{CP} = 6.5, J_{CF} = 37.8 Hz), 62.3 (qd, J_{CP} = 6.5, J_{CF} = 37.8 Hz), 46.3 (d, J_{CP} = 136.7 Hz), 35.6 (d, J_{CP} = 2.6 Hz), 34.0, 24.3 (d, J_{CP} = 3.1 Hz).

¹⁹F NMR (376 MHz, CDCl₃) δ -75.23 (t, J = 8.1 Hz), -75.51 (t, J = 8.0 Hz). (Coupling constants are uncorrected)

³¹P NMR (162 MHz, CDCl₃) δ 30.43.

IR (neat): 2963, 1489, 1456, 1418, 1290, 1251, 1167, 1102, 1070, 1012, 962, 870, 835, 710, 652, 540, 481 cm⁻¹.

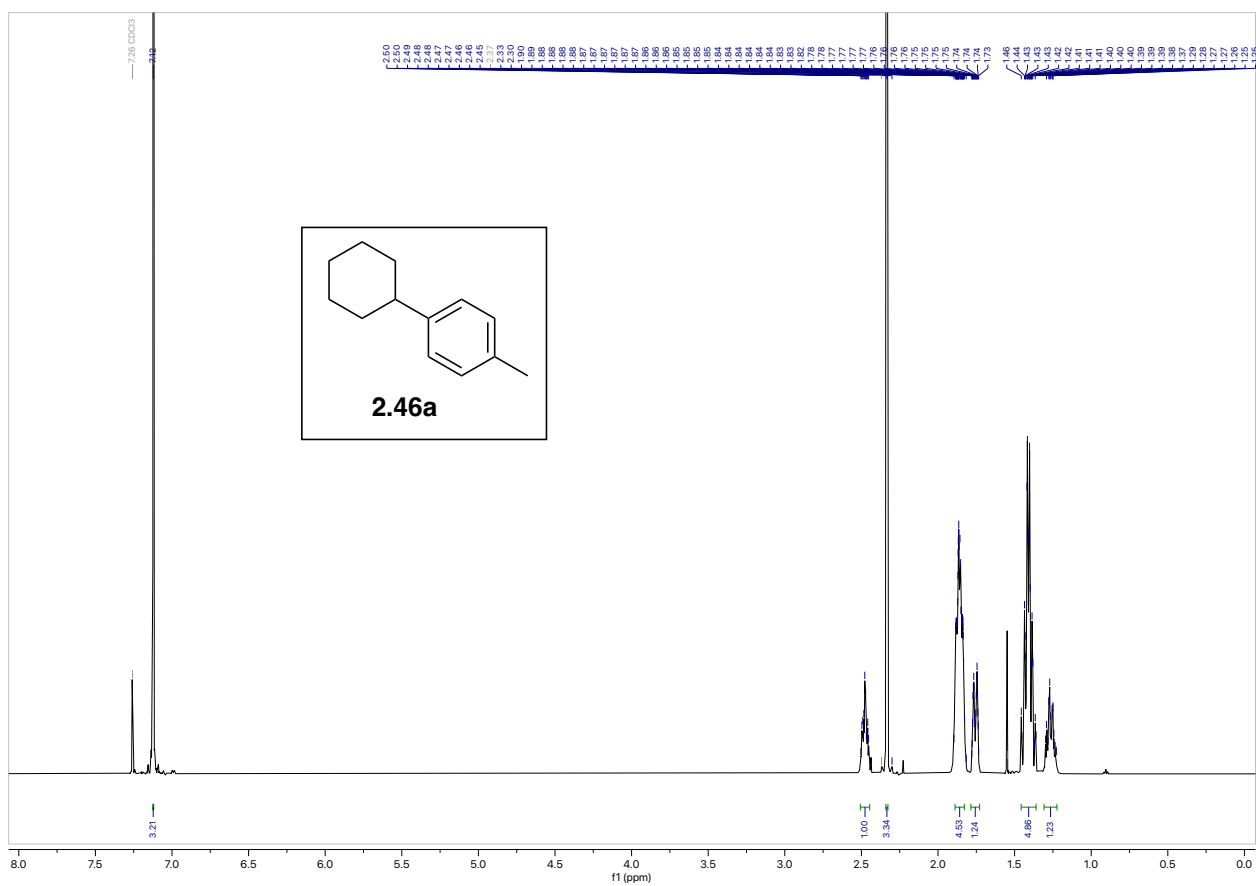
$[\alpha]^{20}_D$: + 82.6° (c 0.50, CHCl₃)

HRMS (+p APCI) calcd. for C₁₉H₂₃Cl₂O₃P 401.0835, found 401.0842.

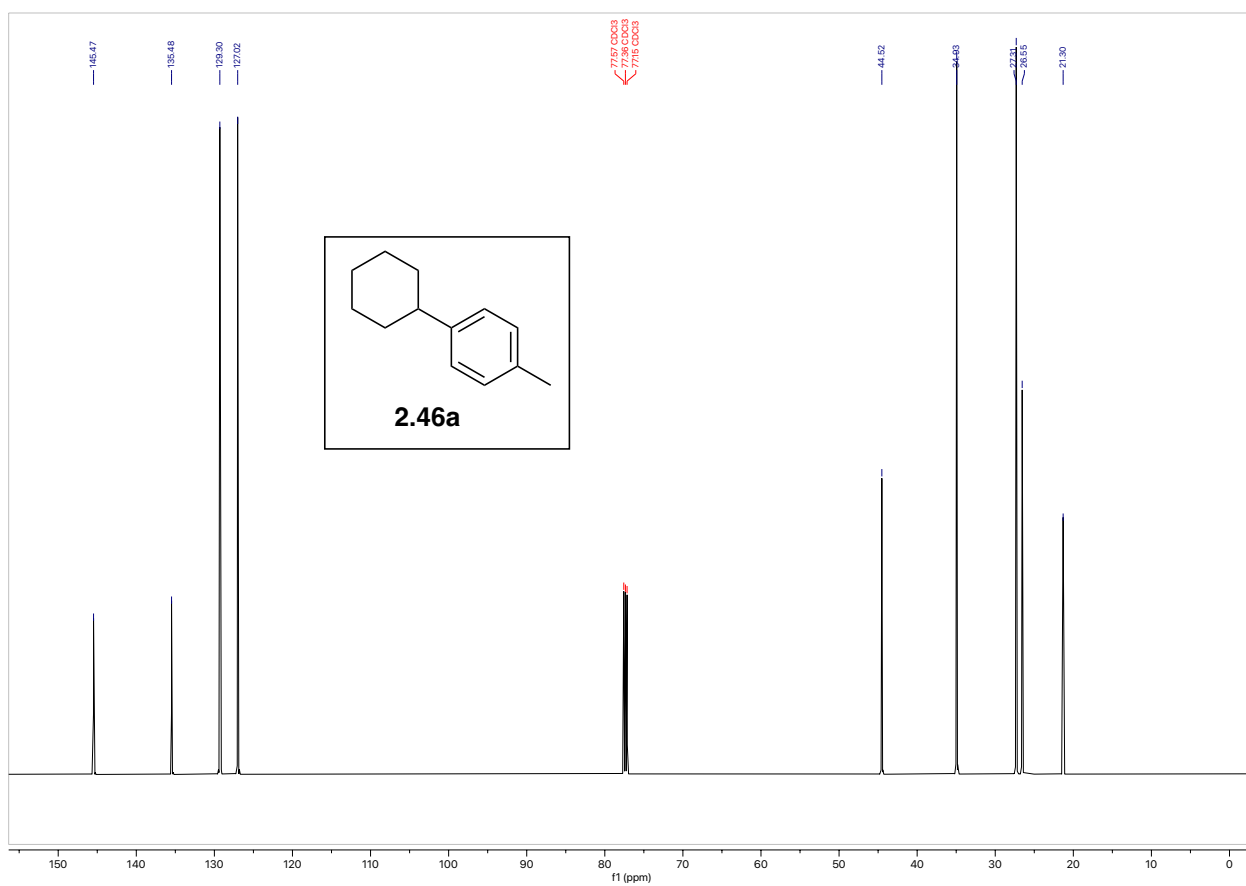
HPLC analysis: (Chiralcel ODH, 25 cm x 4.6 mm, 1.0% *i*-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 99% ee: t_R (minor enantiomer) = 11.2 min, t (major enantiomer) = 15.8 min.

The crystal structure information for compound (**2.42**) is located in the crystallography section

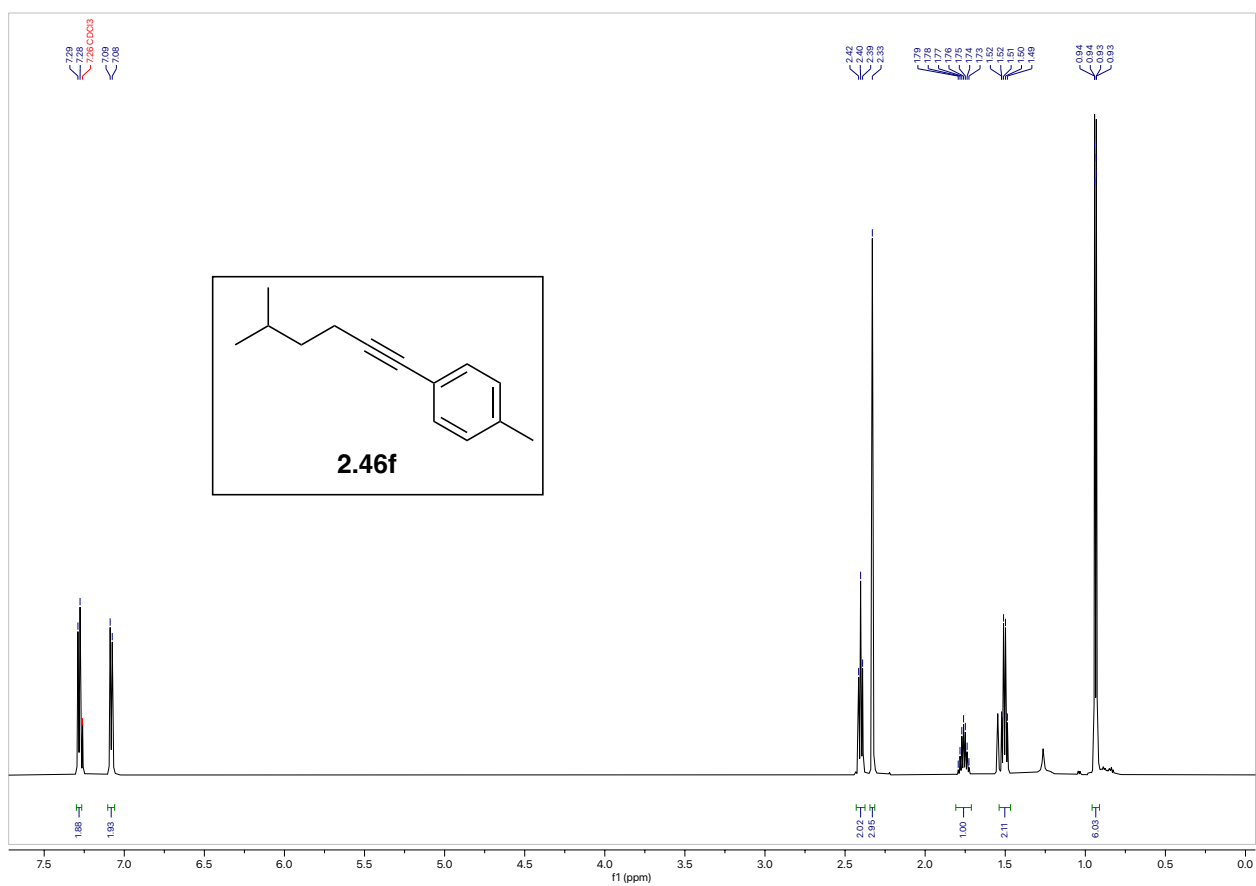
^1H NMR, ^{13}C NMR, ^{19}F NMR, and ^{31}P NMR Spectroscopic Data.



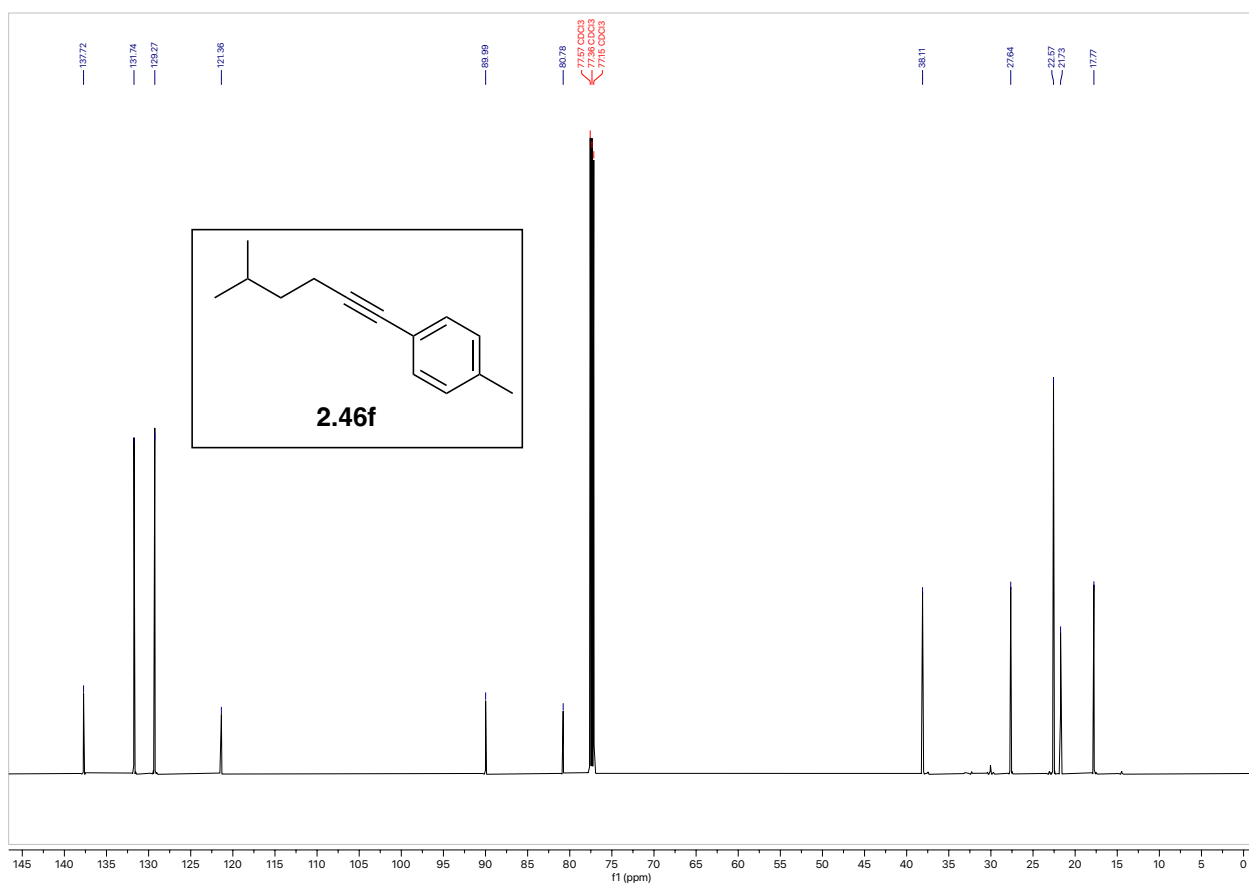
^1H NMR spectrum (600 MHz, Chloroform- d) (s, 7.26 ppm) of **2.46a**.

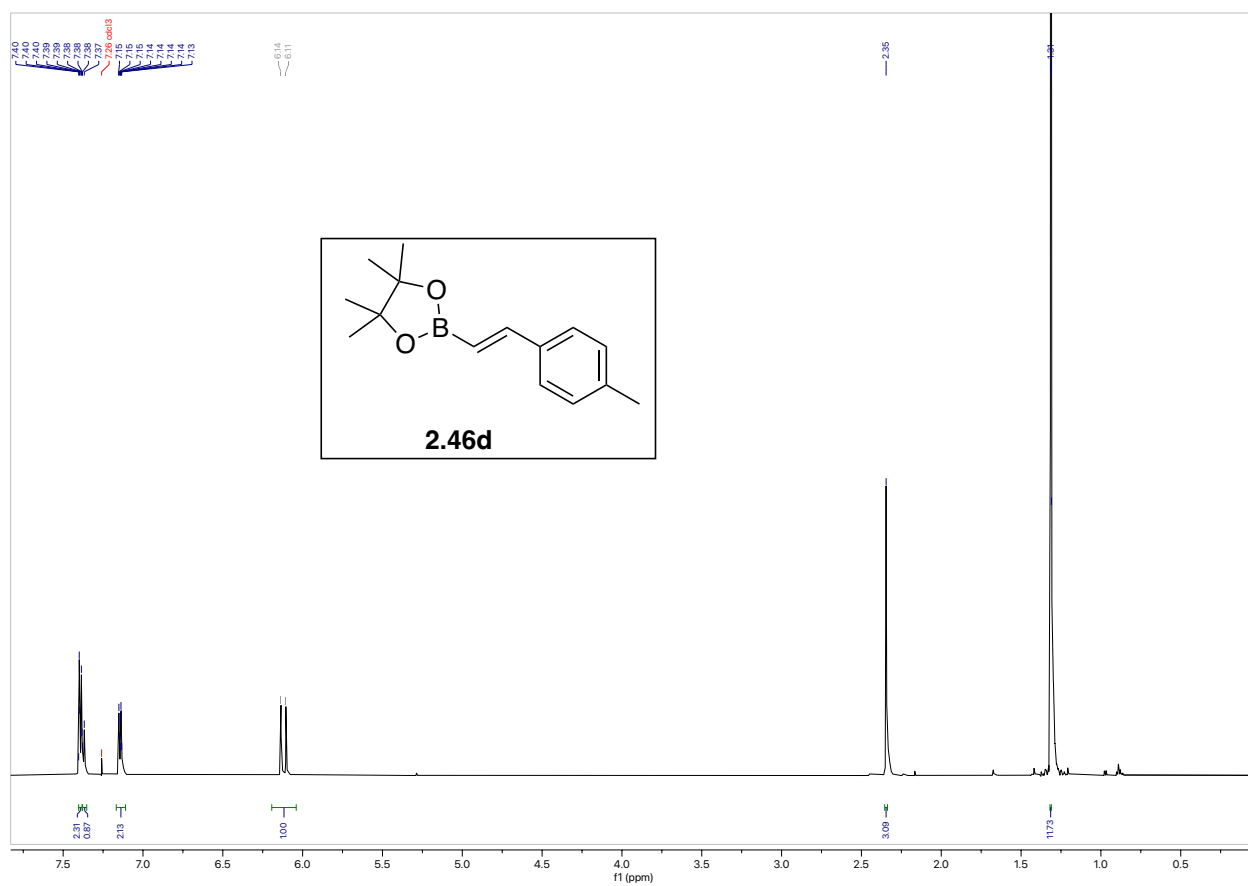


^{13}C NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.46a**.

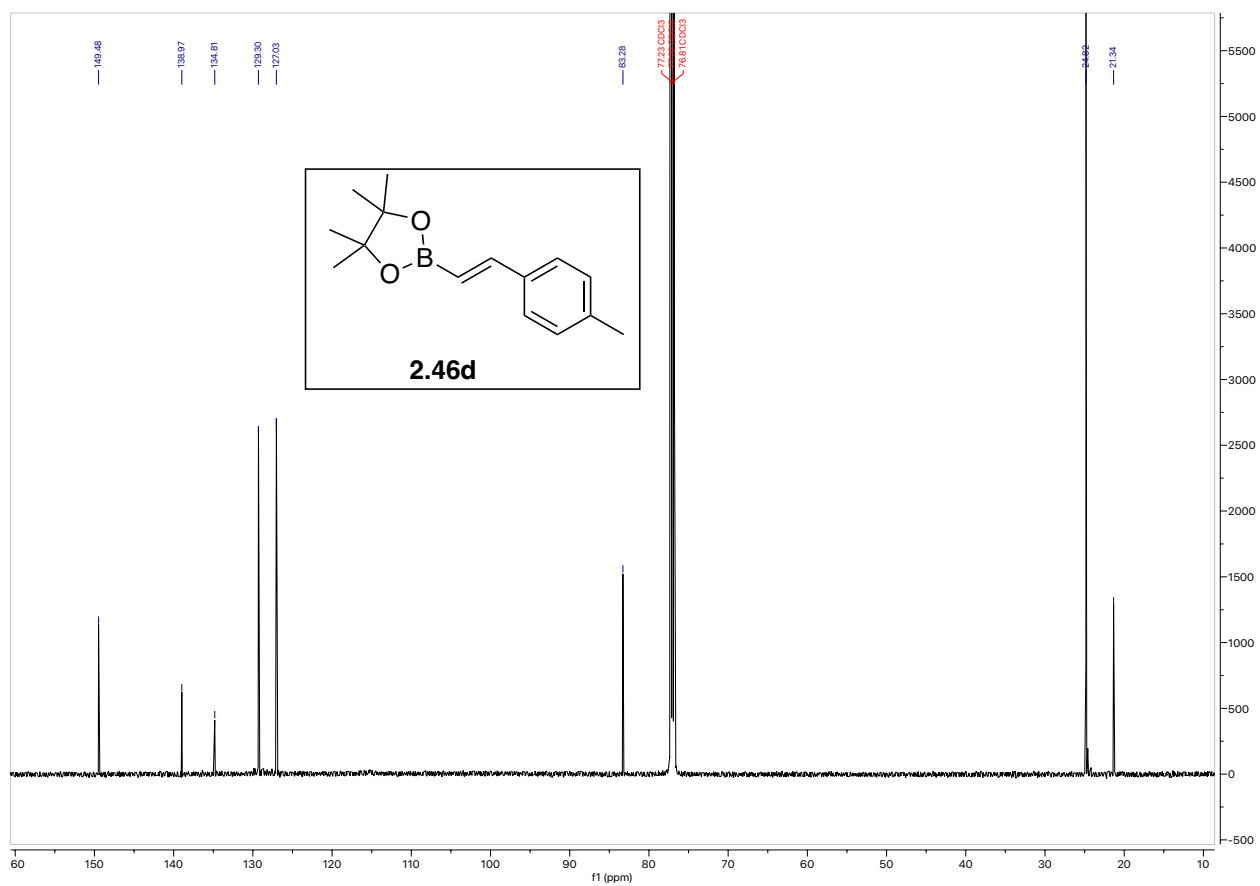


^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.46f**.

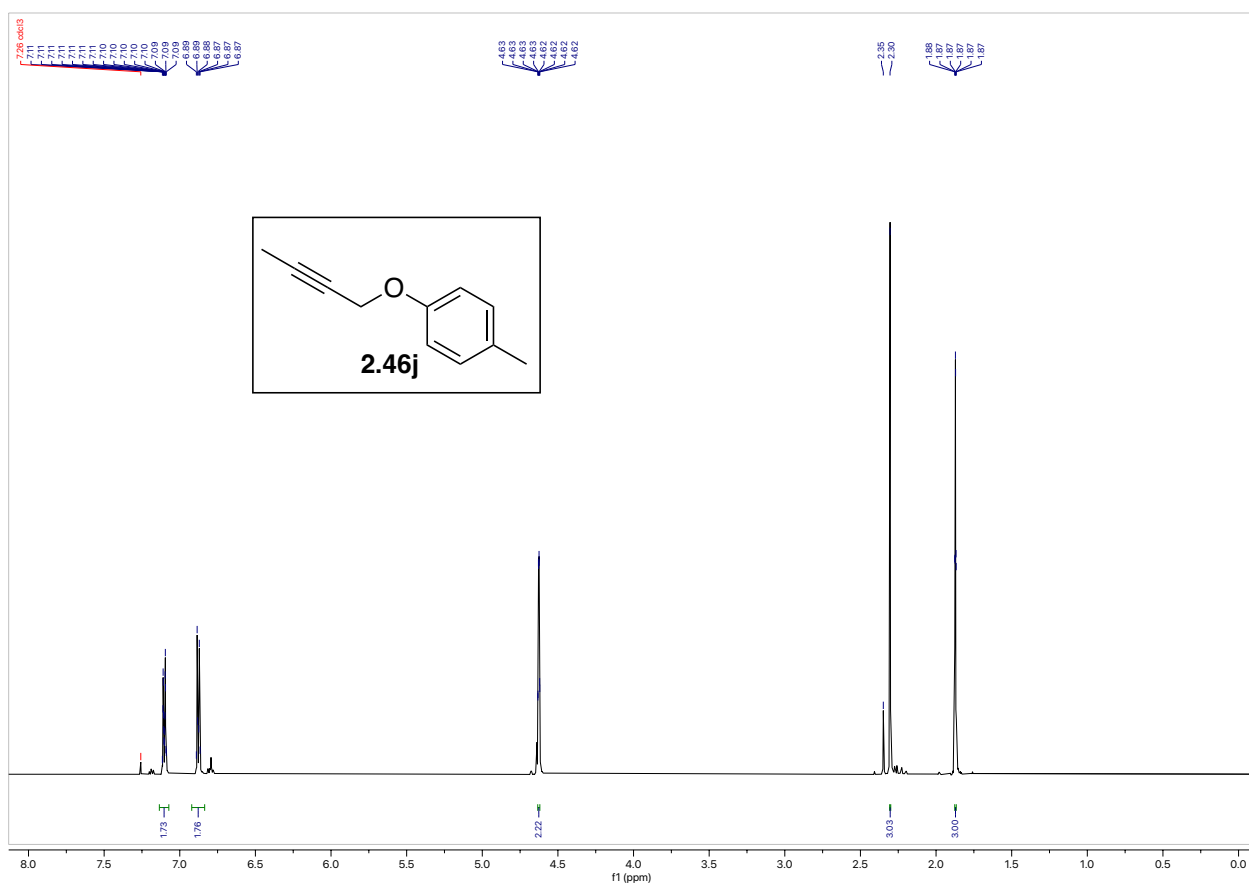




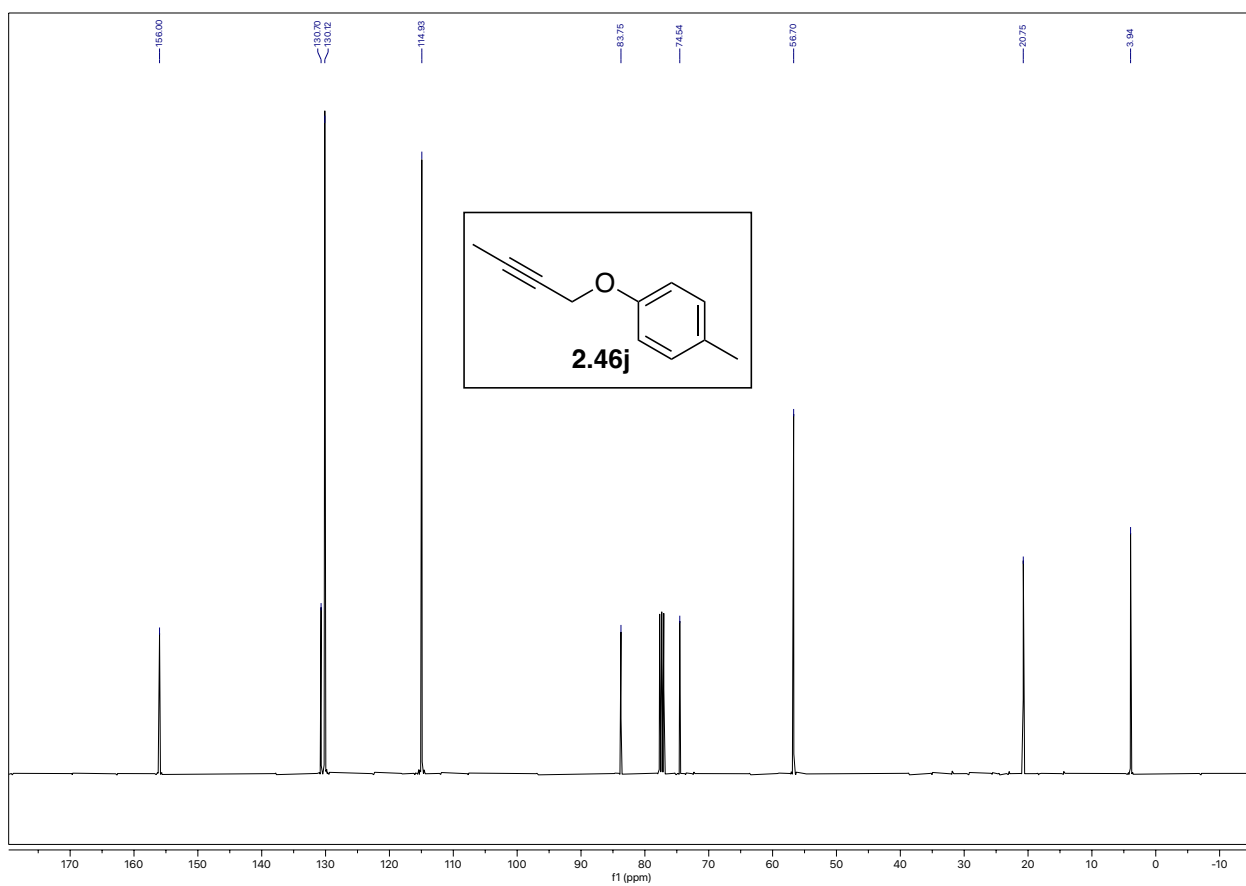
^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.46d**.



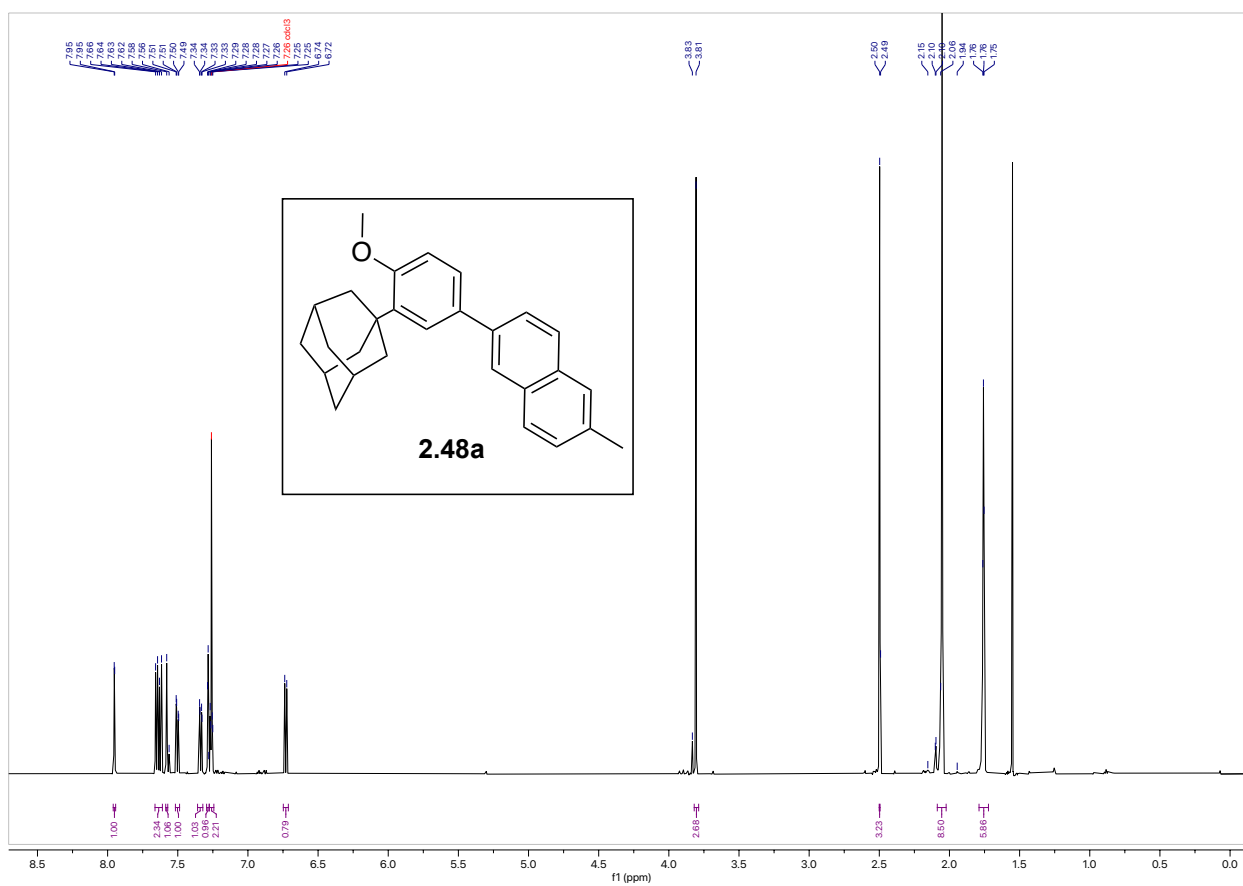
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.46d**.

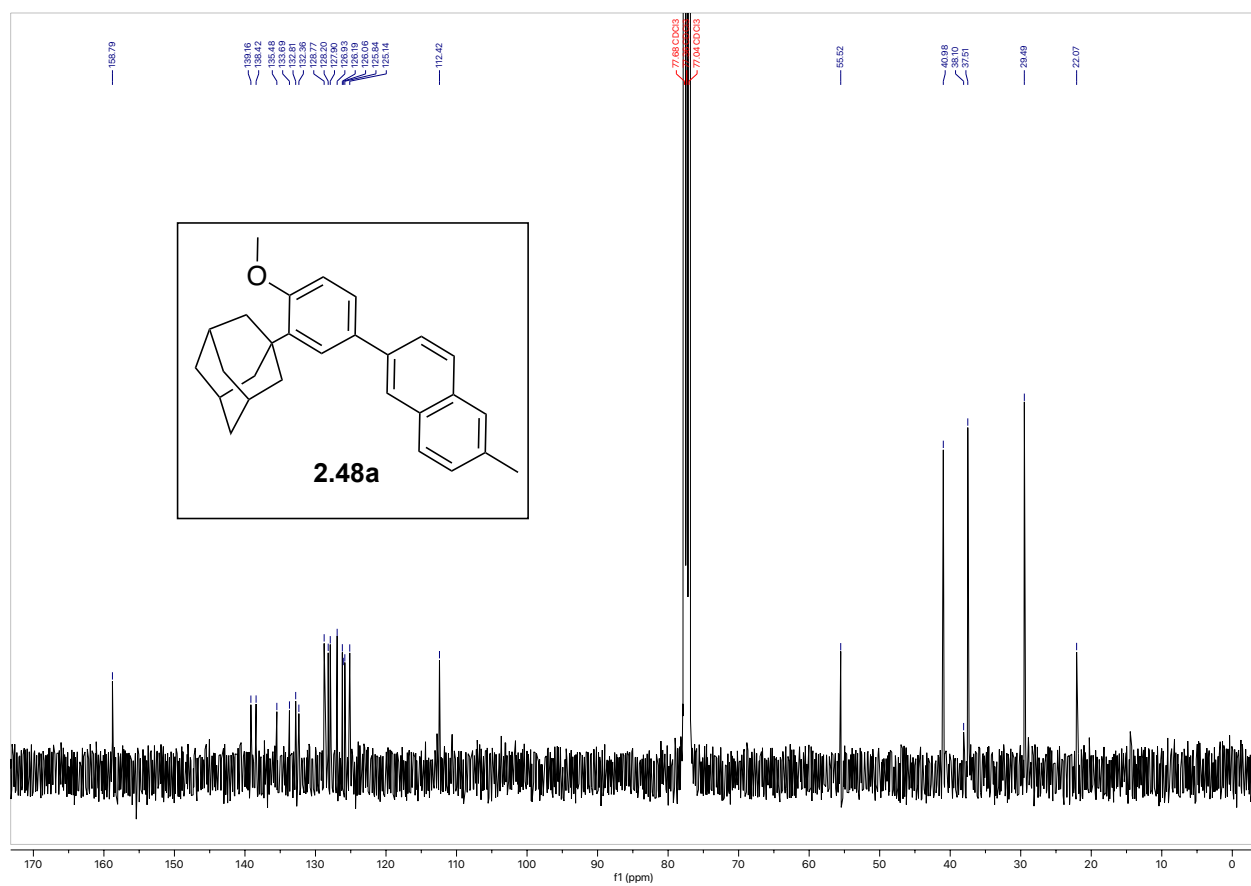


¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.46j**.

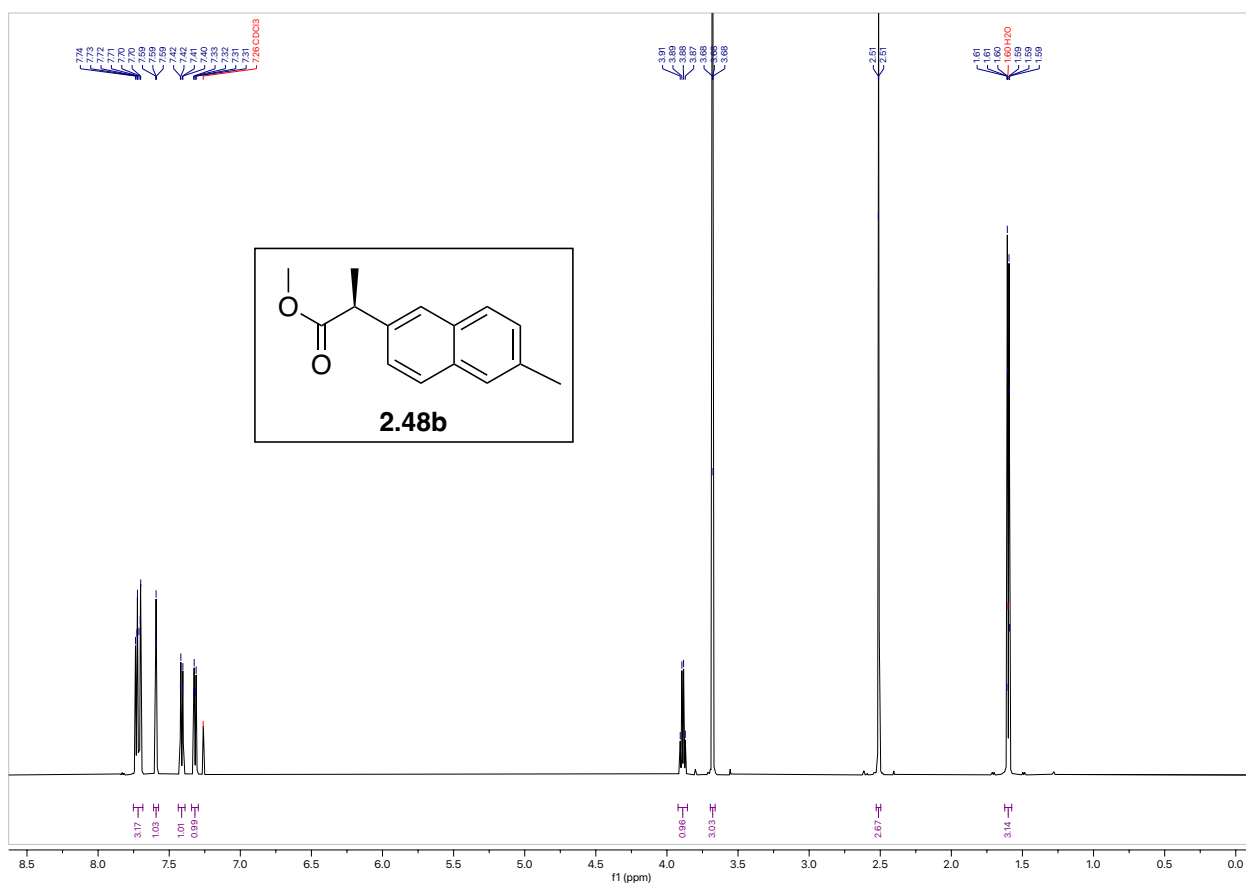


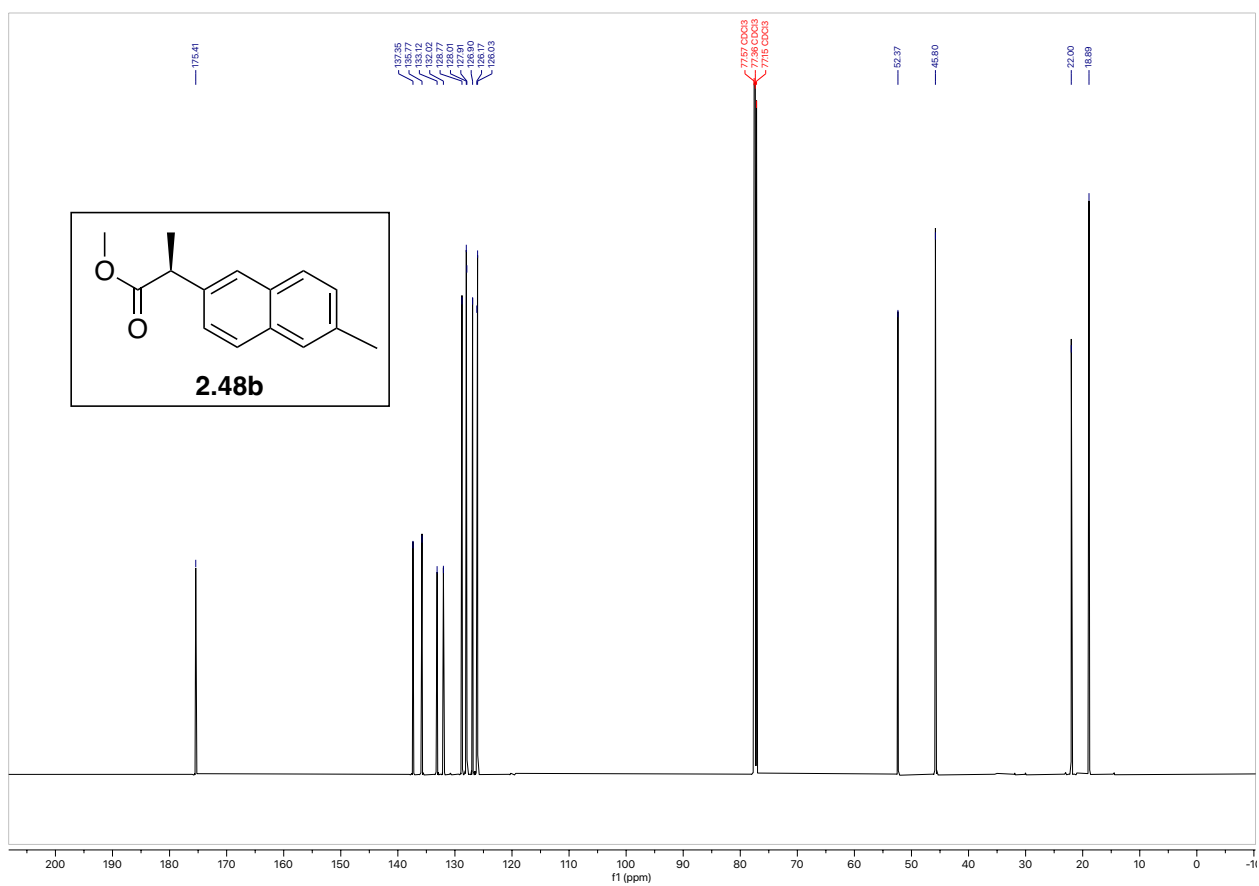
^{13}C NMR spectrum (101 MHz, CDCl_3) of **2.46j**.

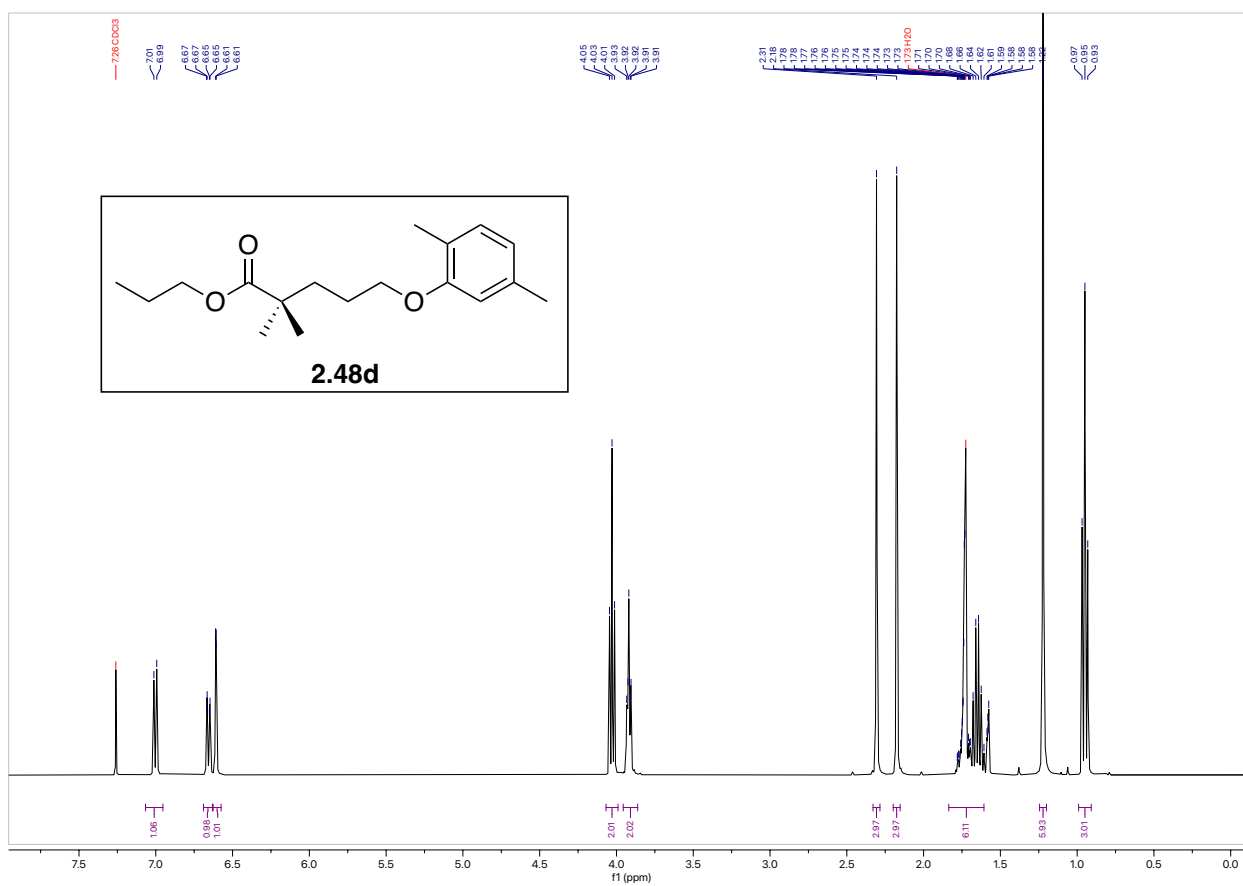




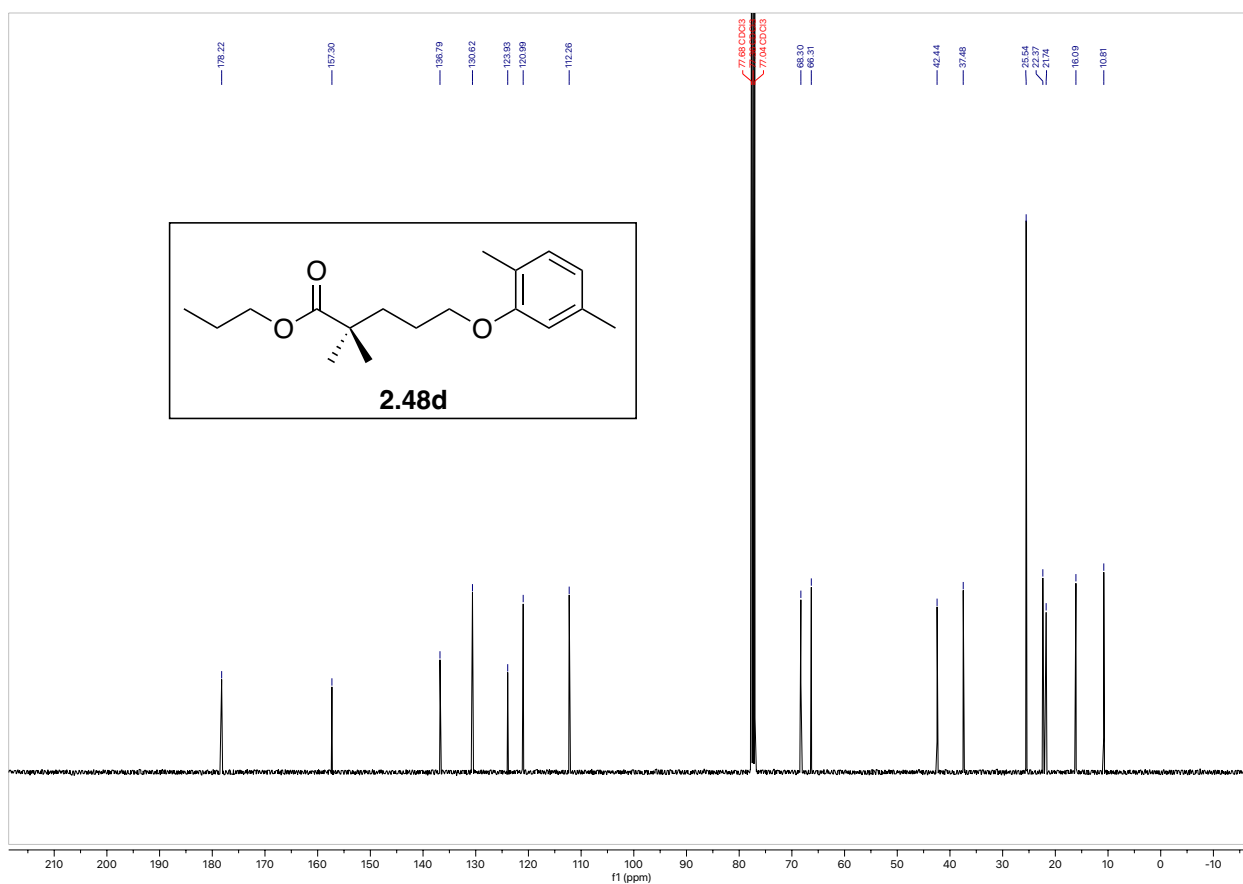
¹³C NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.48a.**

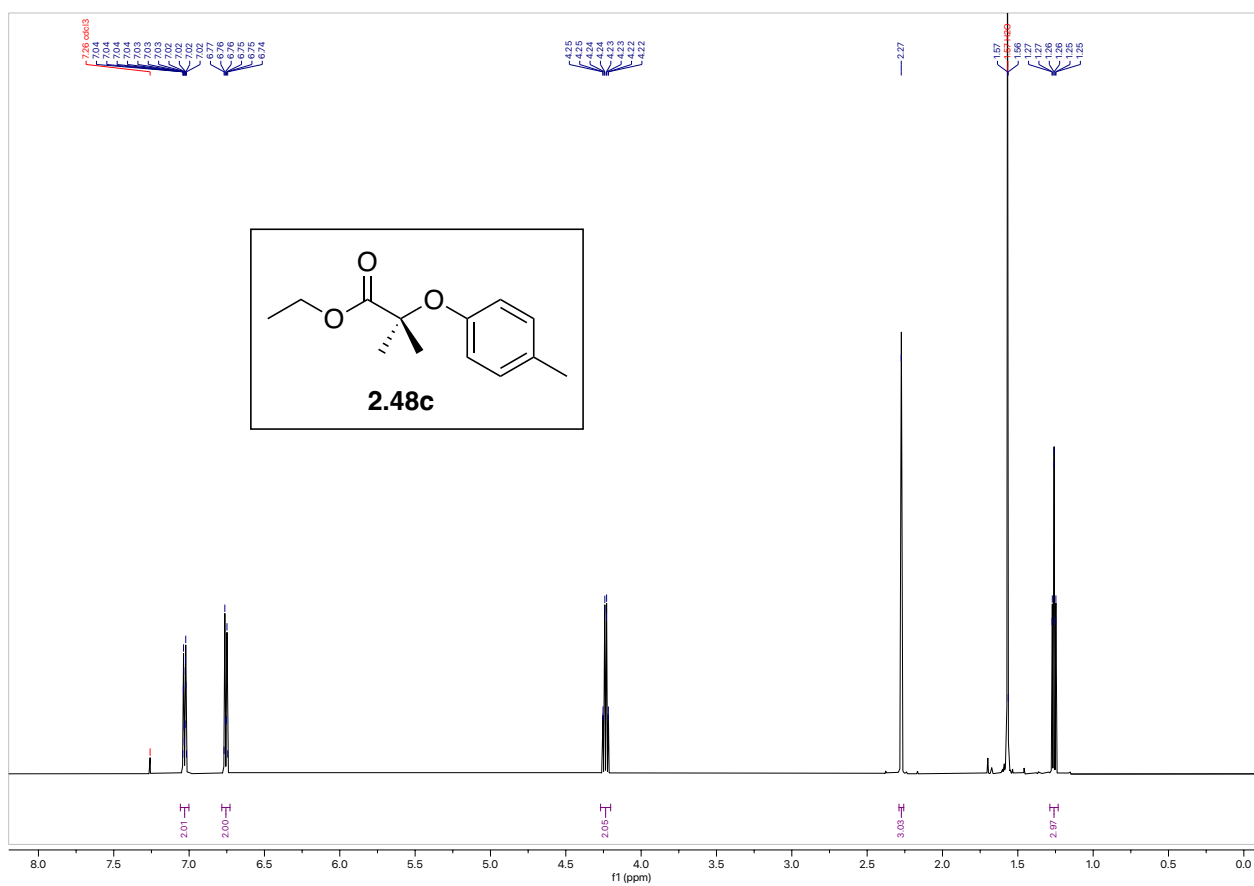




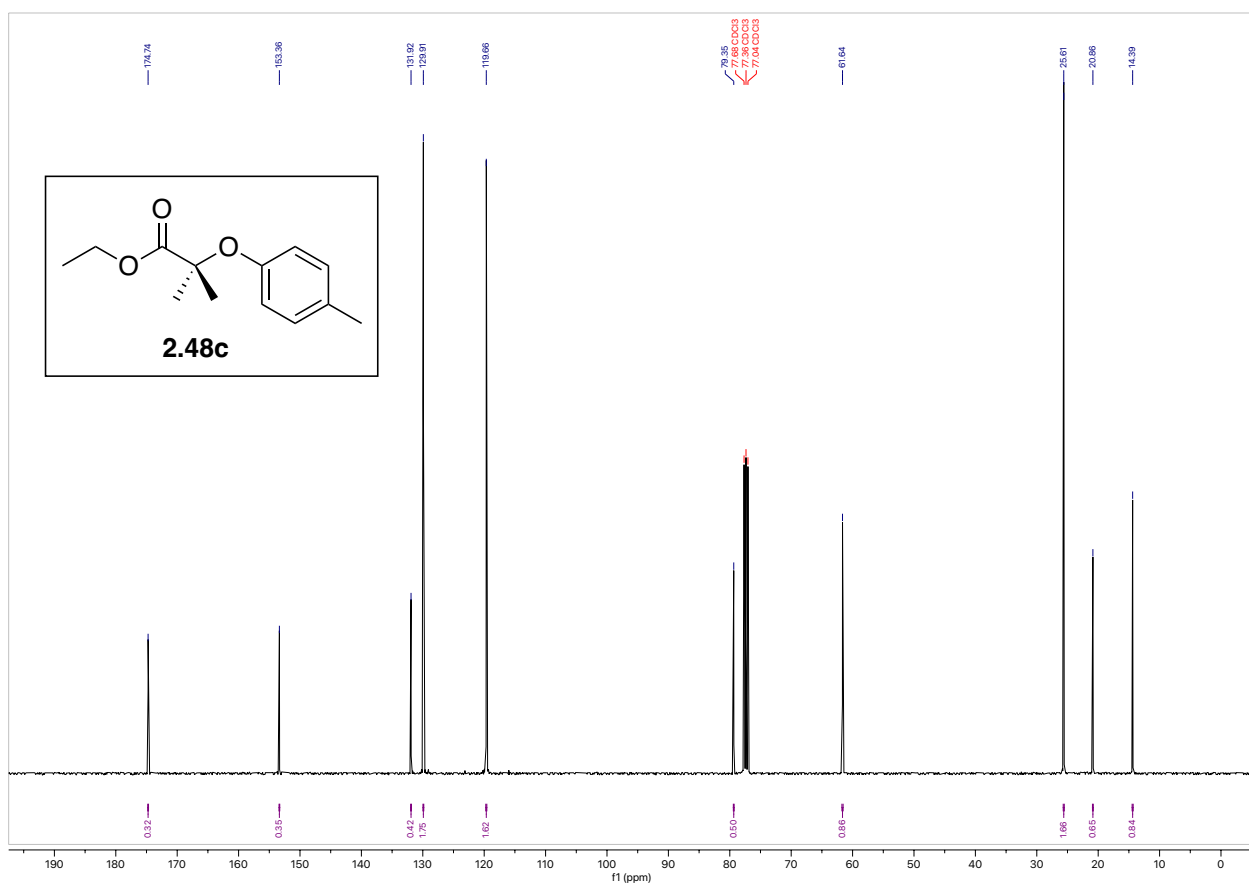


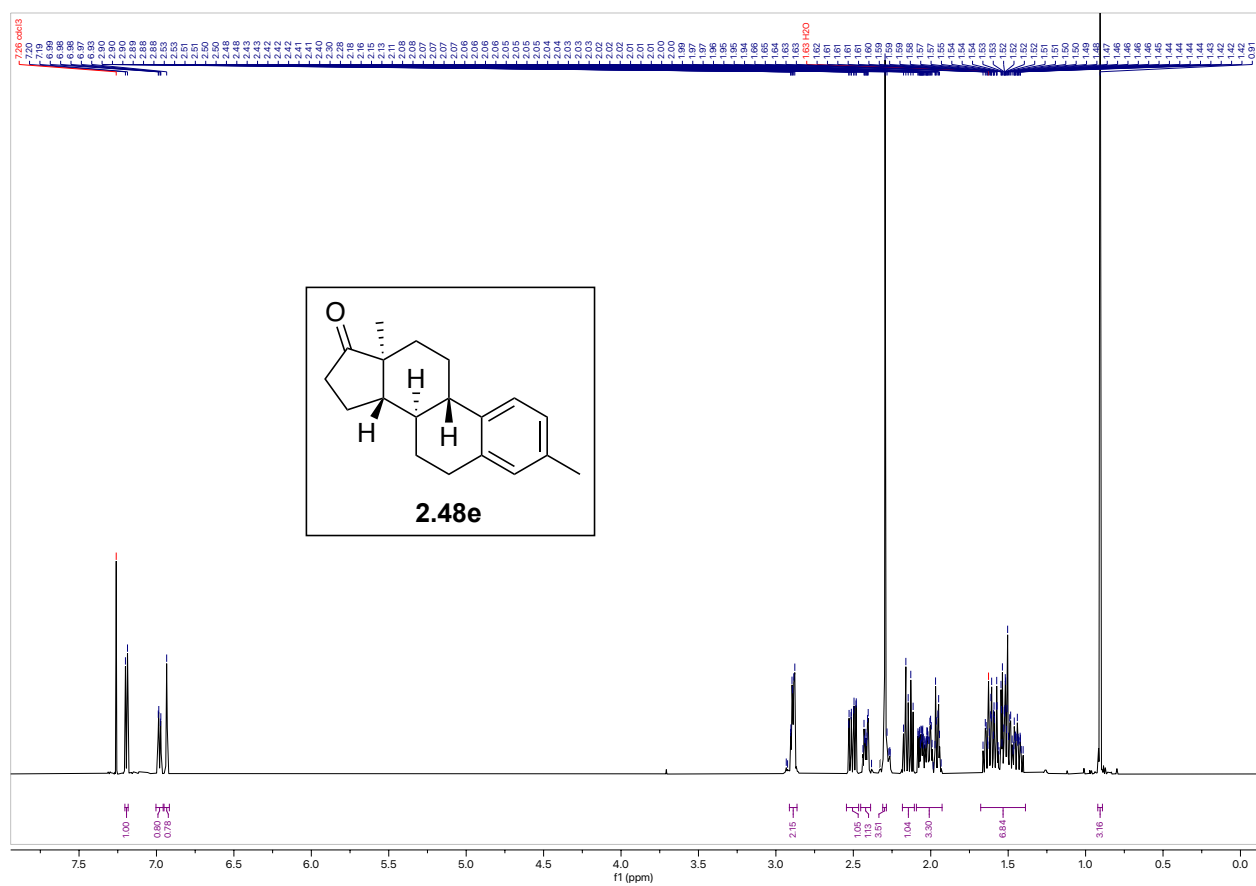
^1H NMR spectrum (600 MHz, Chloroform- d) (s, 7.26 ppm) of **2.48d**.



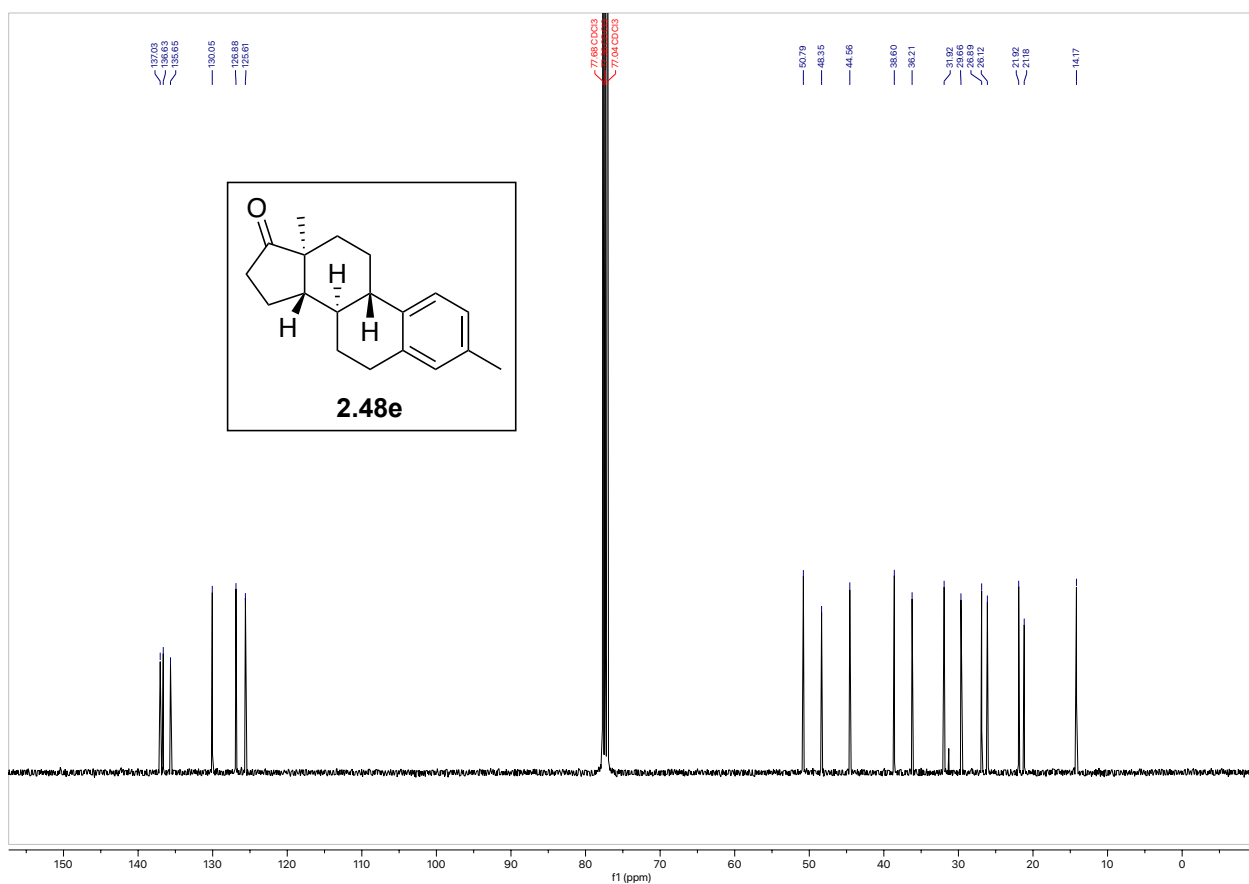


¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.48c**.

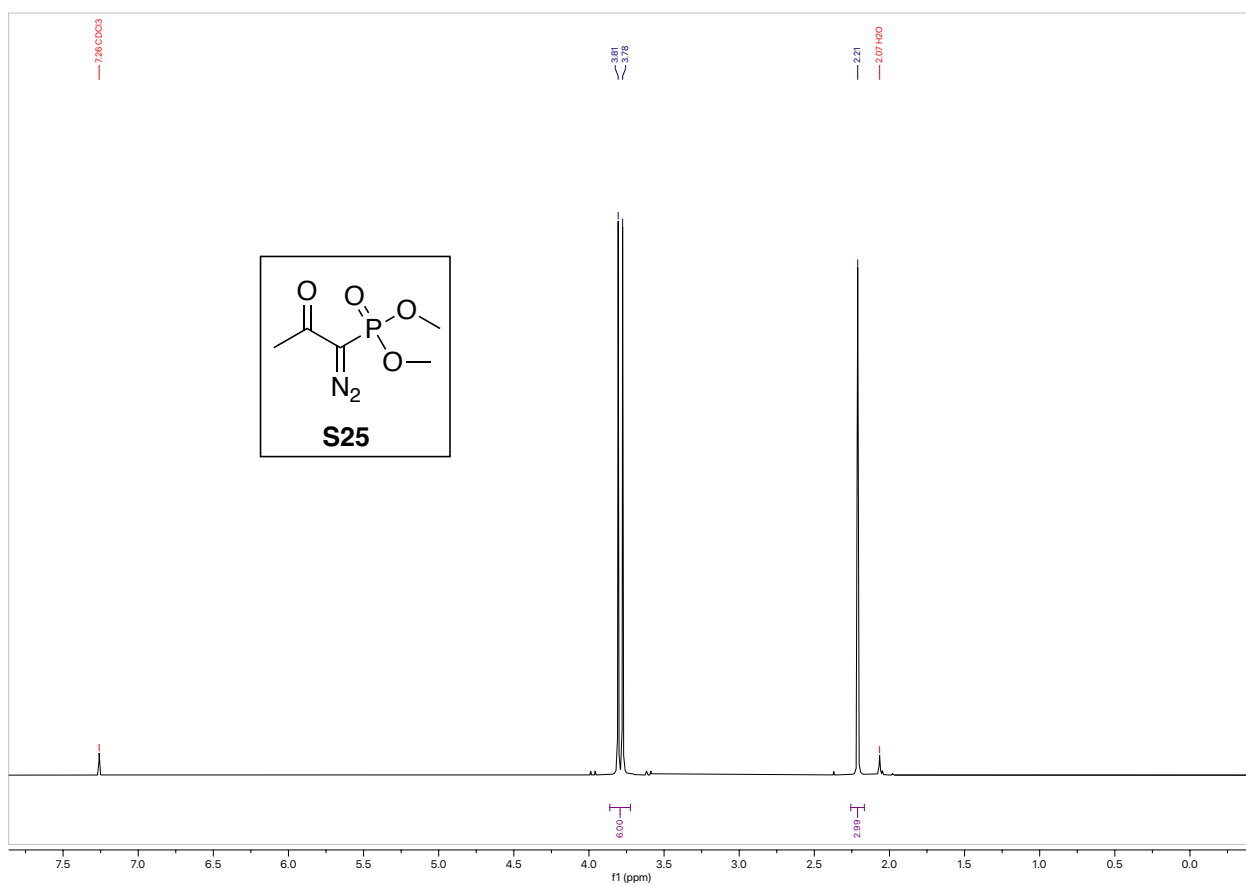




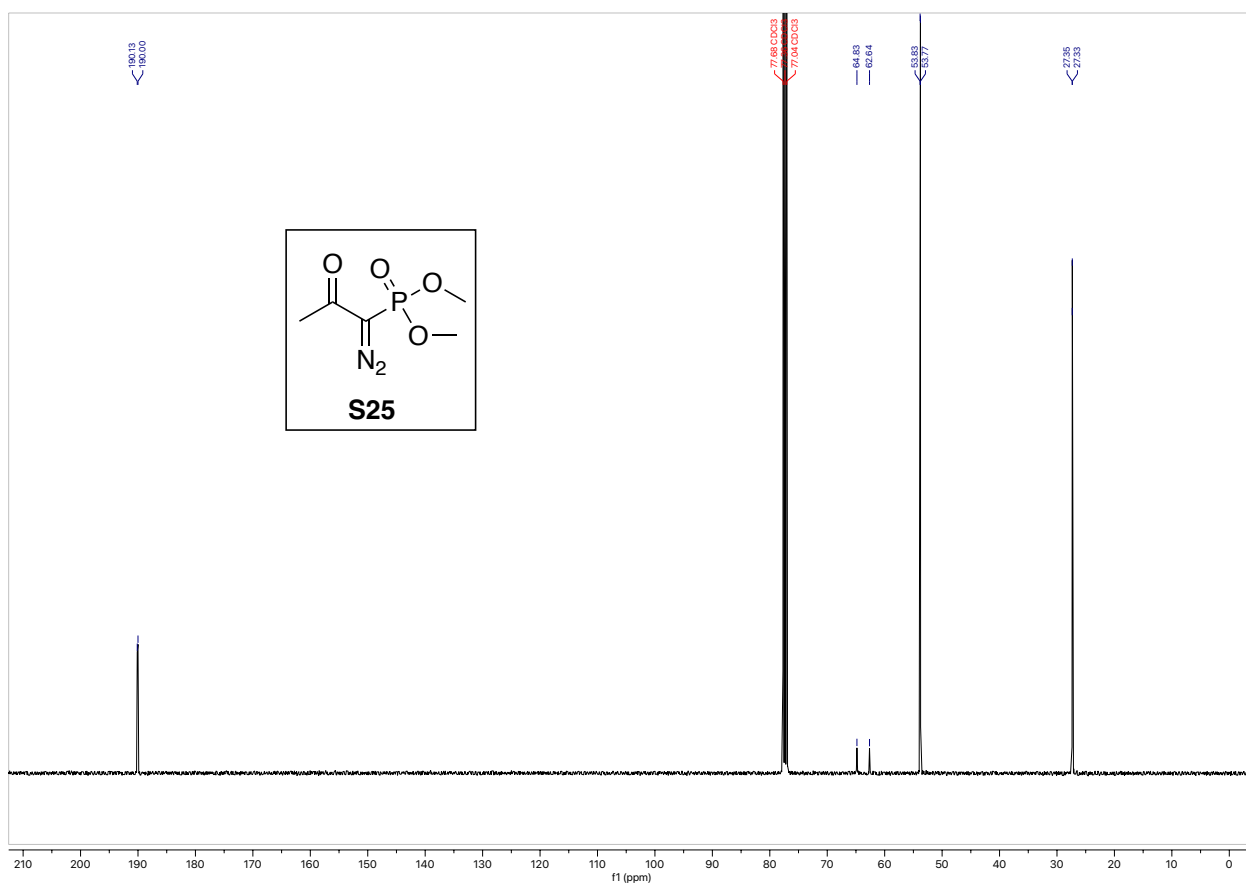
^1H NMR spectrum (600 MHz, CDCl_3) (s, 7.26 ppm) of **2.48e**.



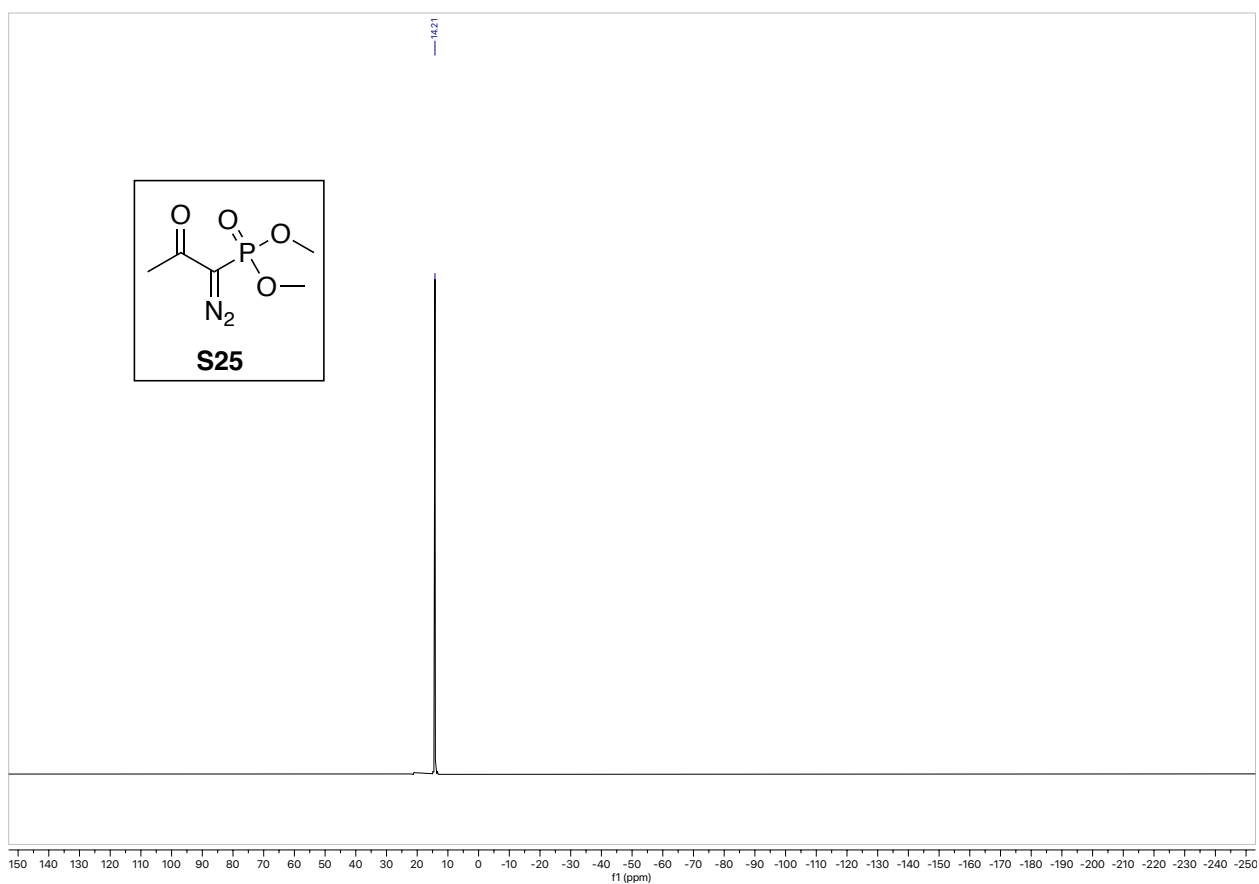
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.48e**.



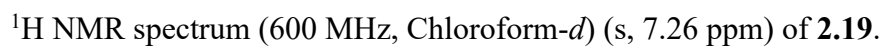
^1H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **S25**.

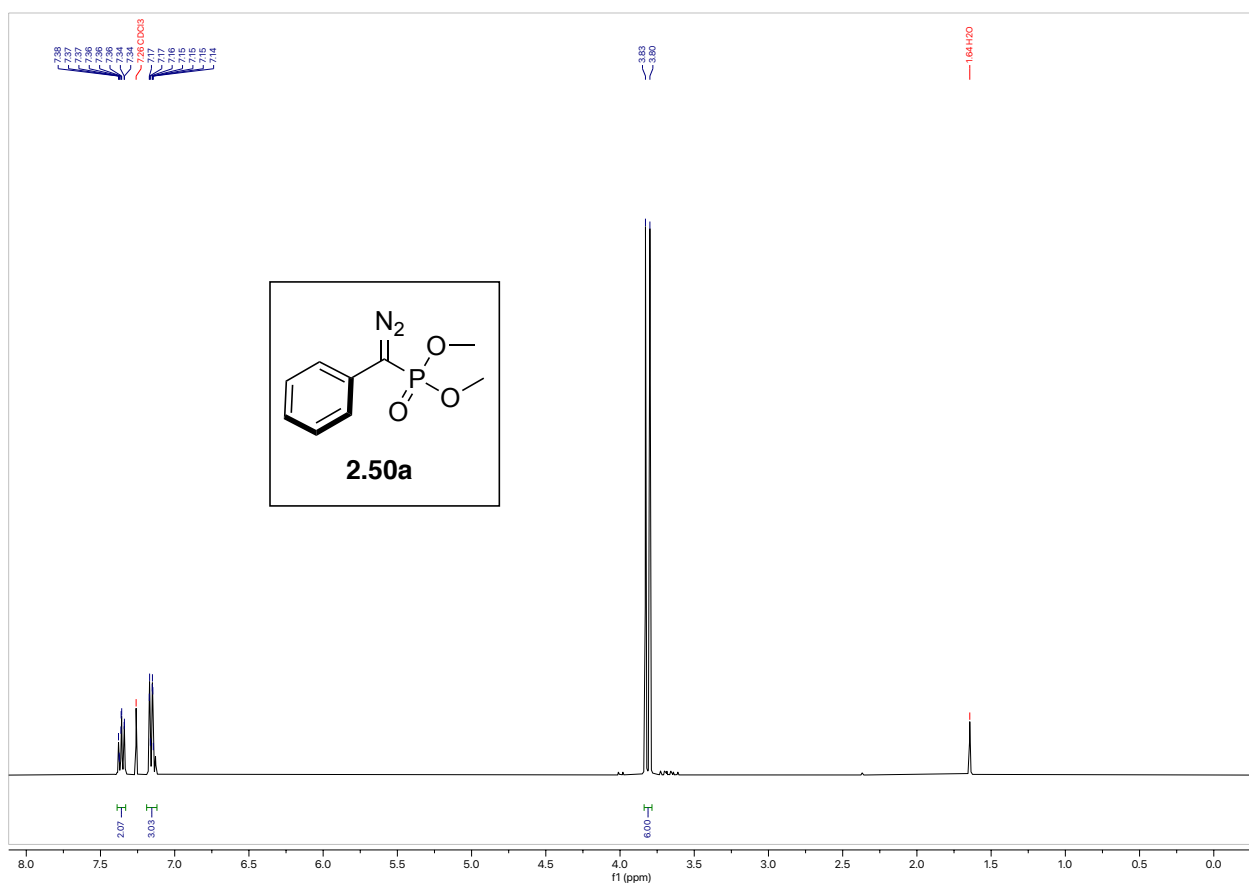


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **S25**.

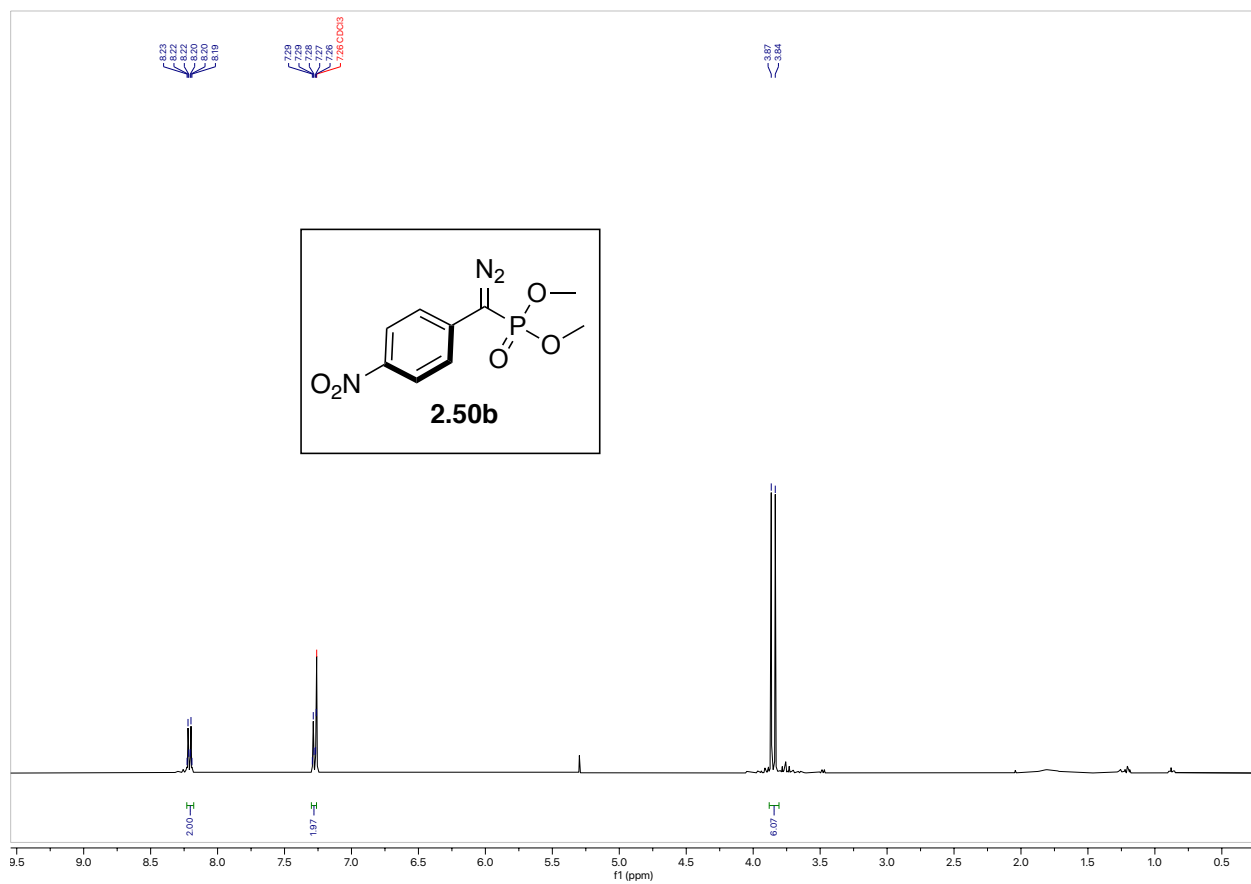


^{31}P NMR spectrum (162 MHz, Chloroform- d) of **S25**.

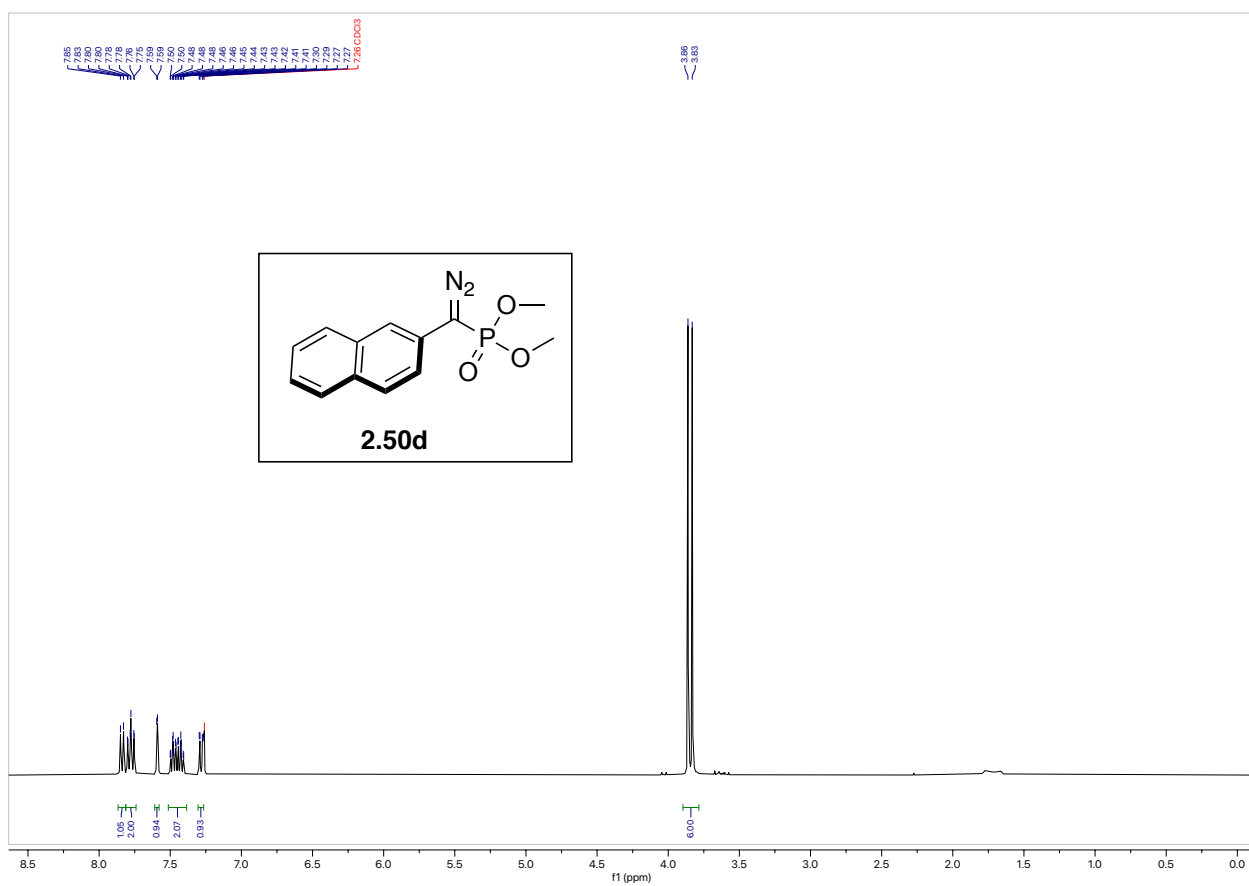




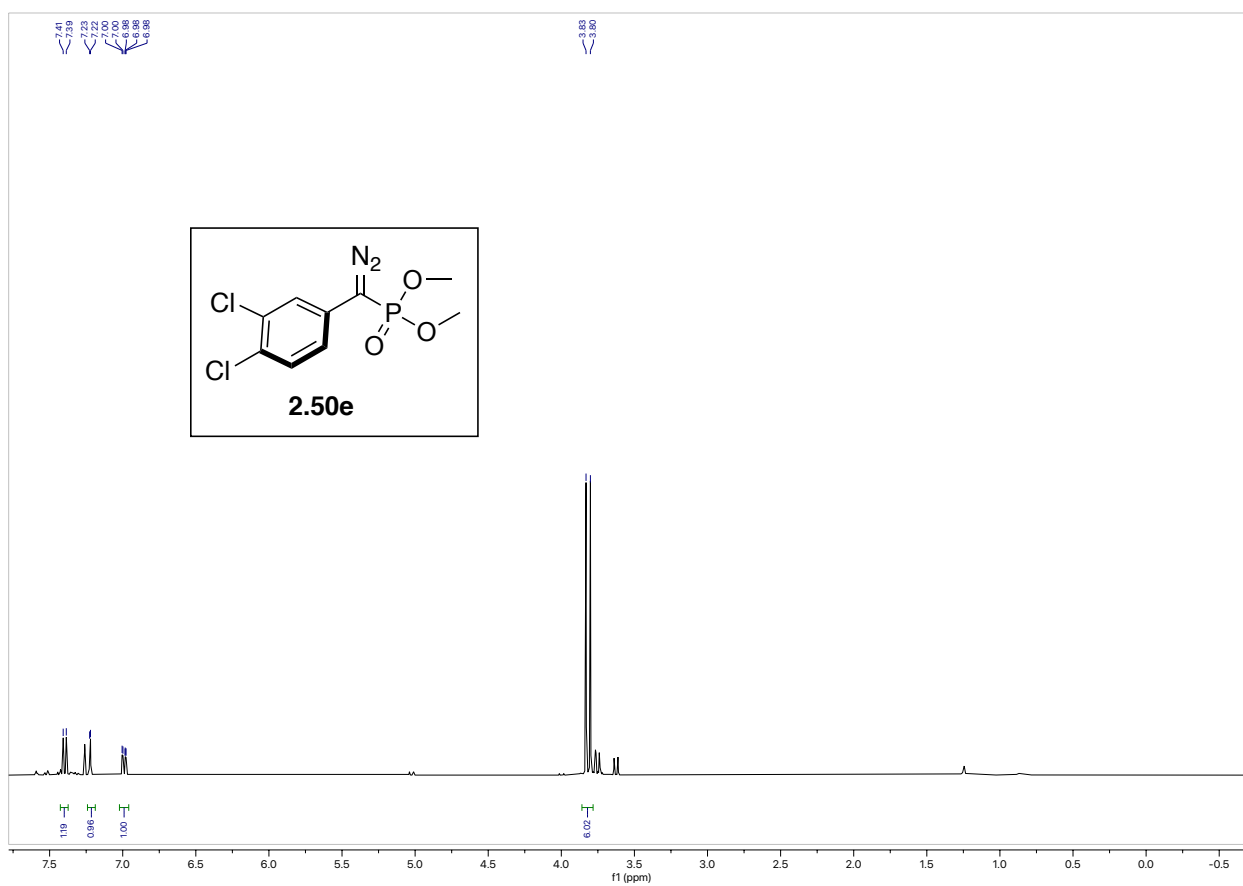
^1H NMR spectrum (400 MHz, CDCl_3) (s, 7.26 ppm) of **2.50a**.



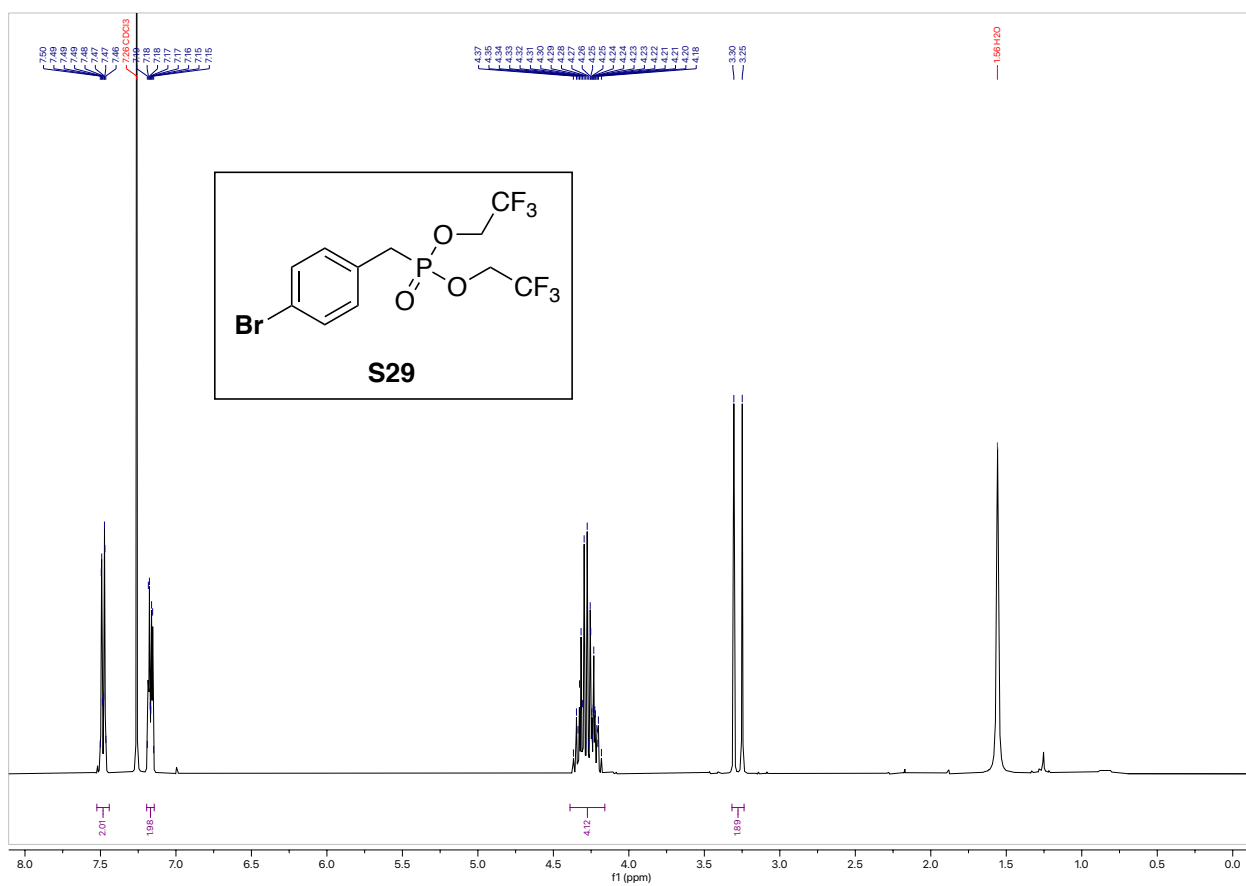




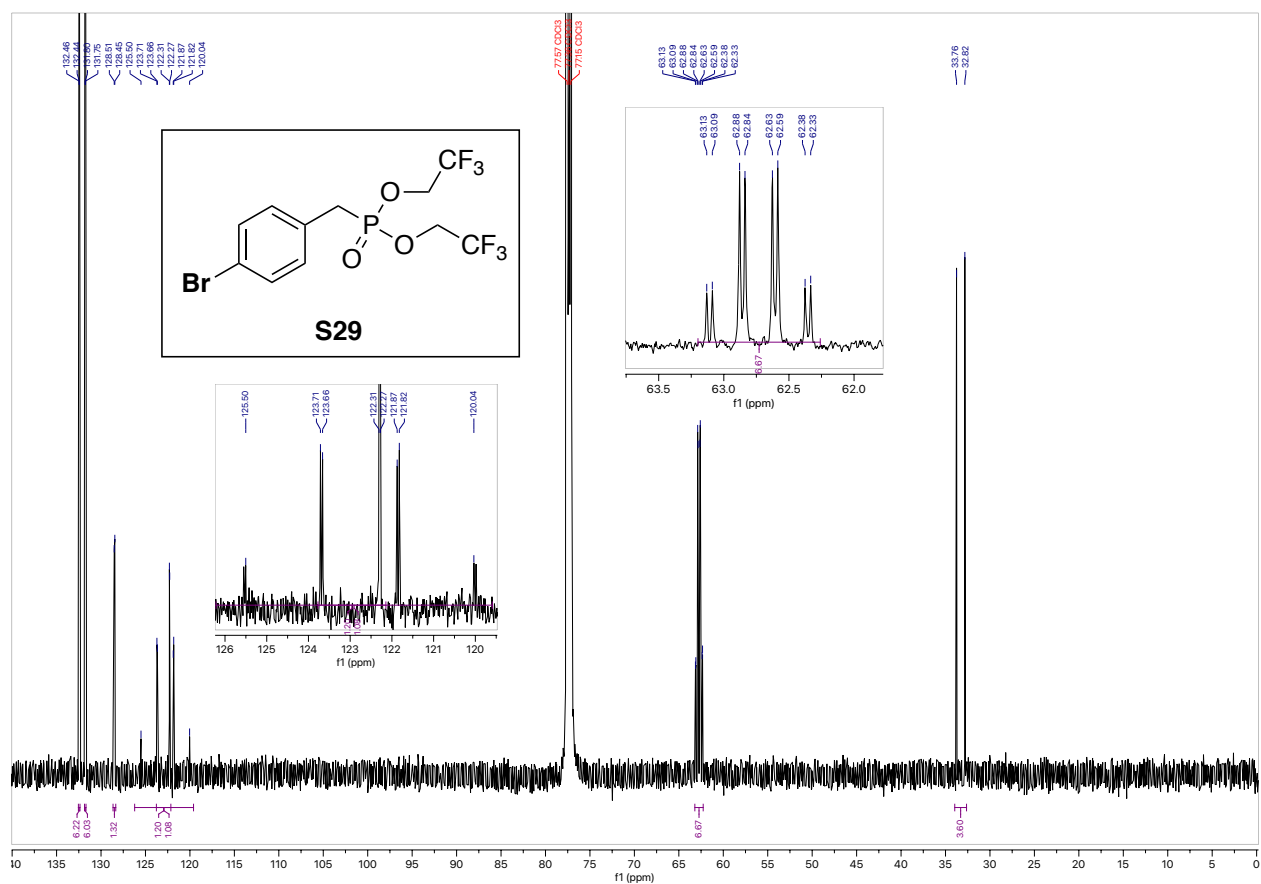
^1H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.50d**.



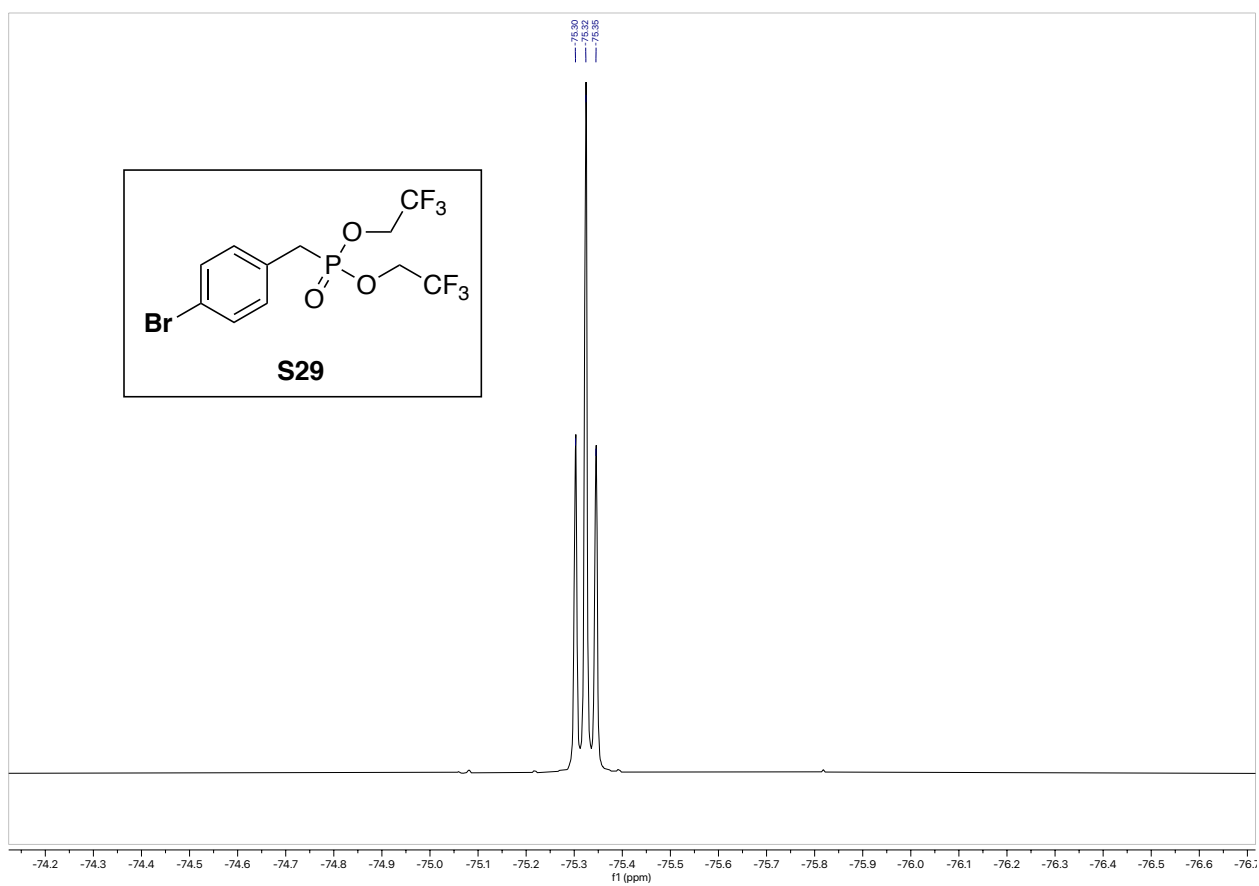
^1H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.50e**.



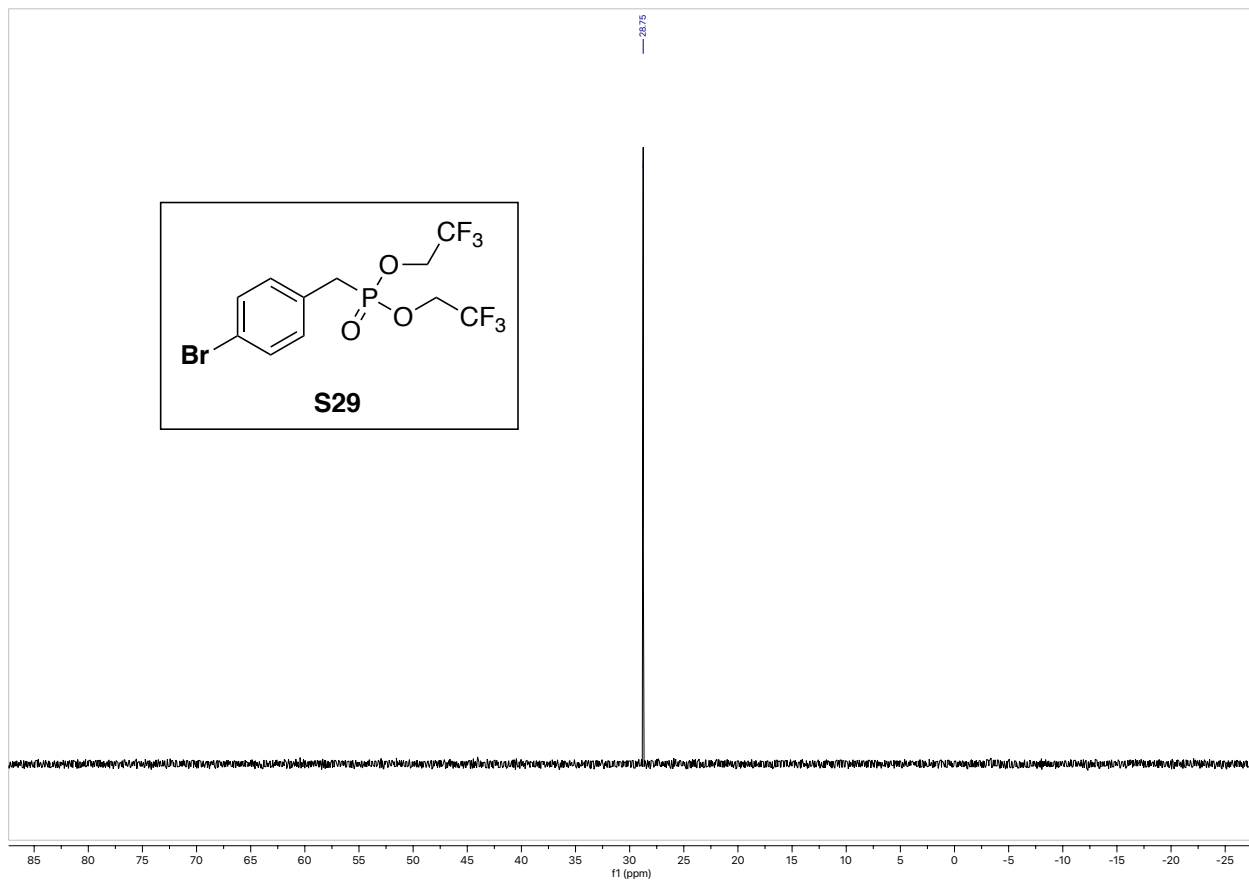
¹H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **S29**.



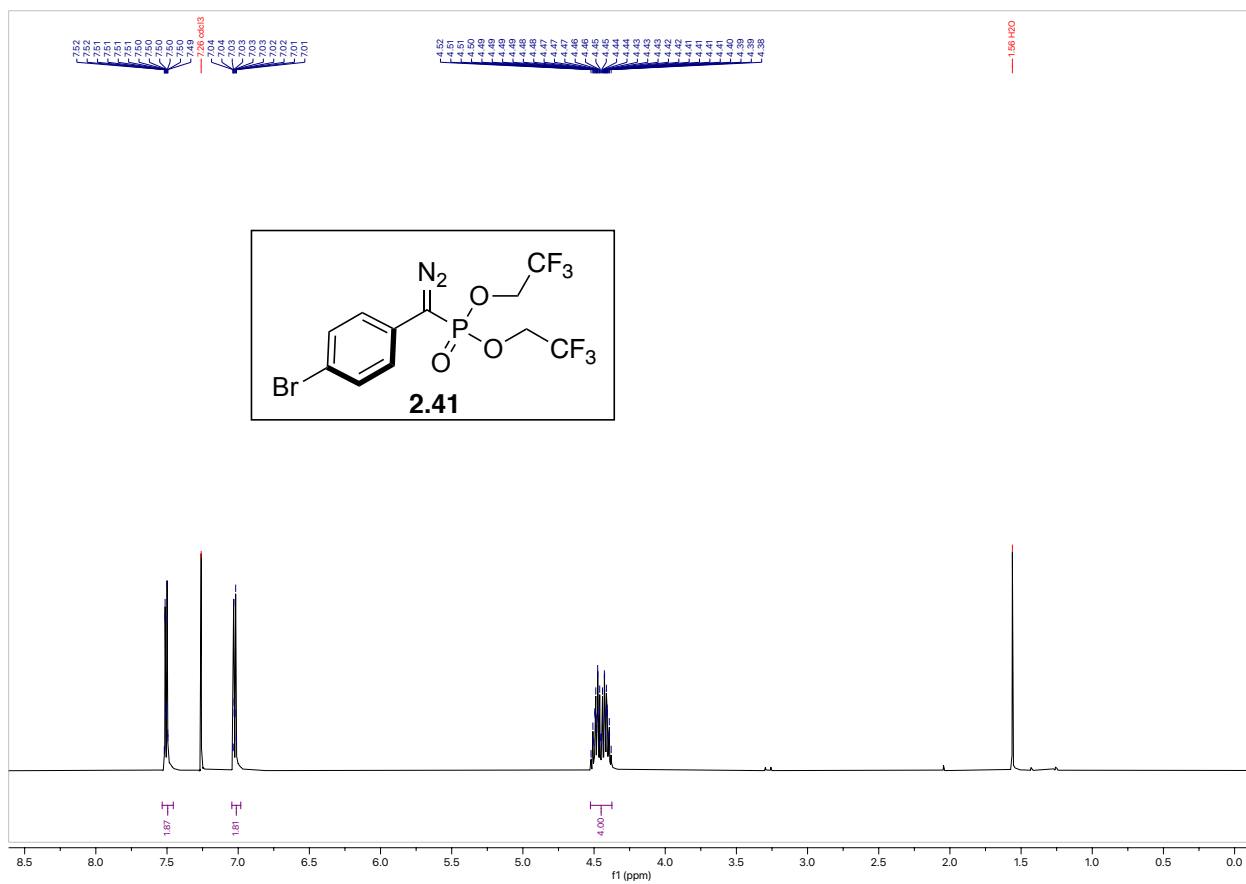
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **S29**.



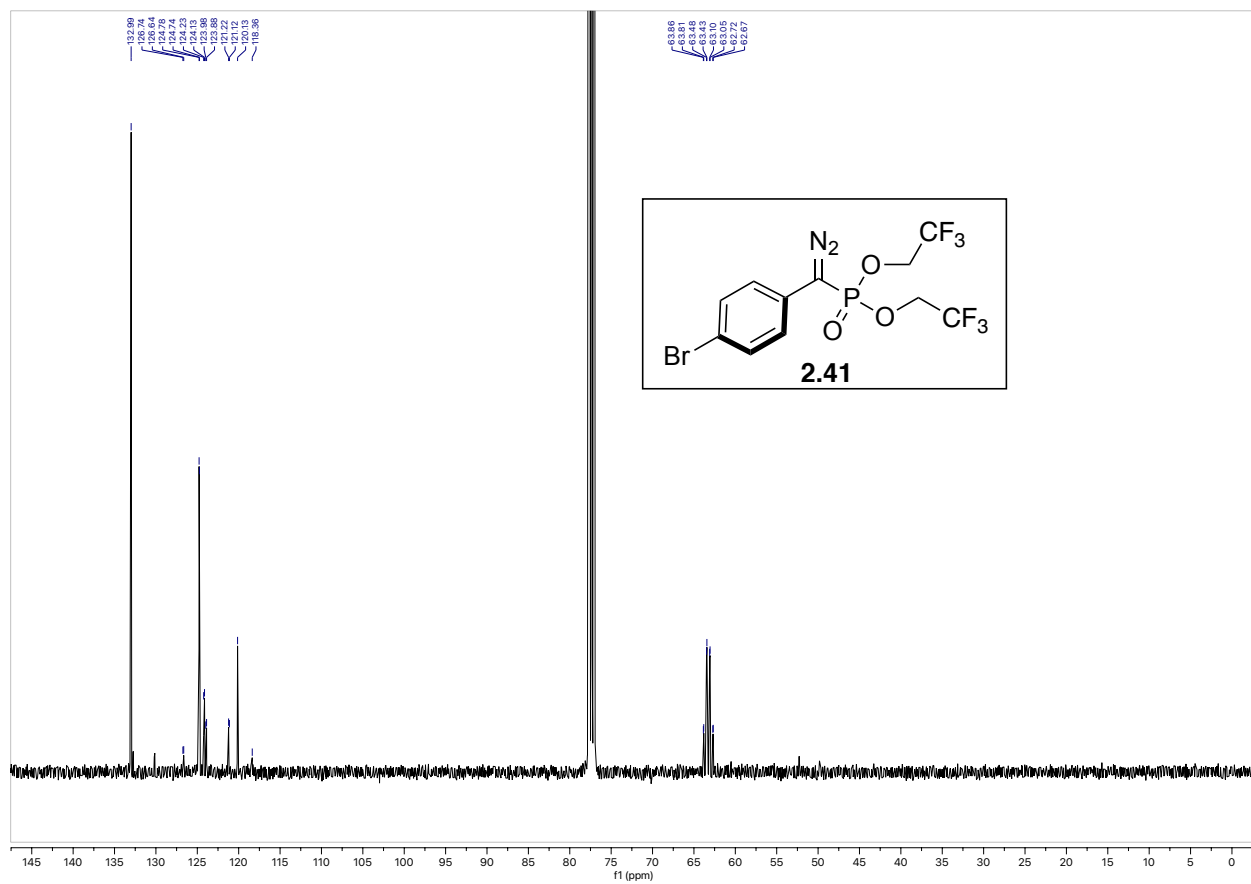
^{19}F NMR spectrum (376 MHz, Chloroform- d) of **S29**.



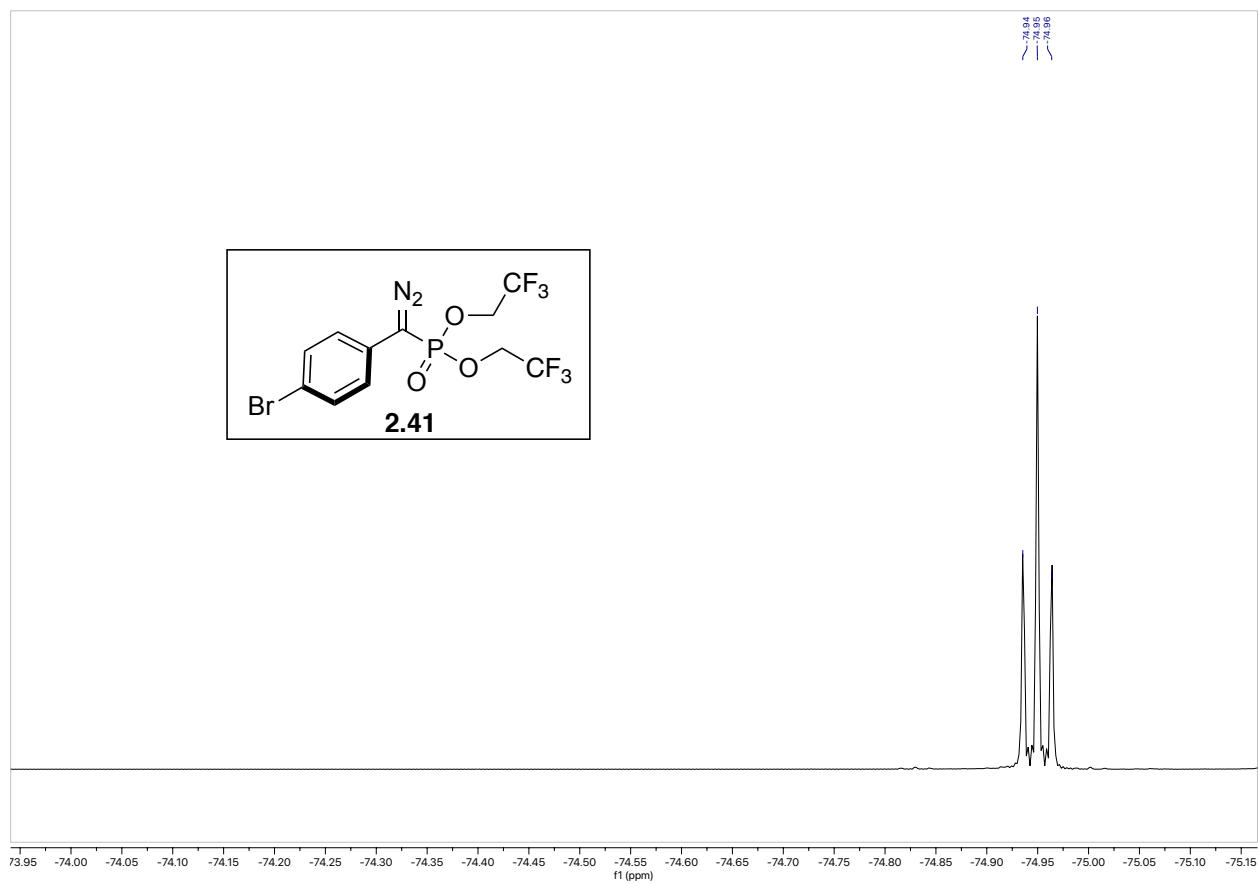
^{31}P NMR spectrum (162 MHz, Chloroform-d) of **S29**.



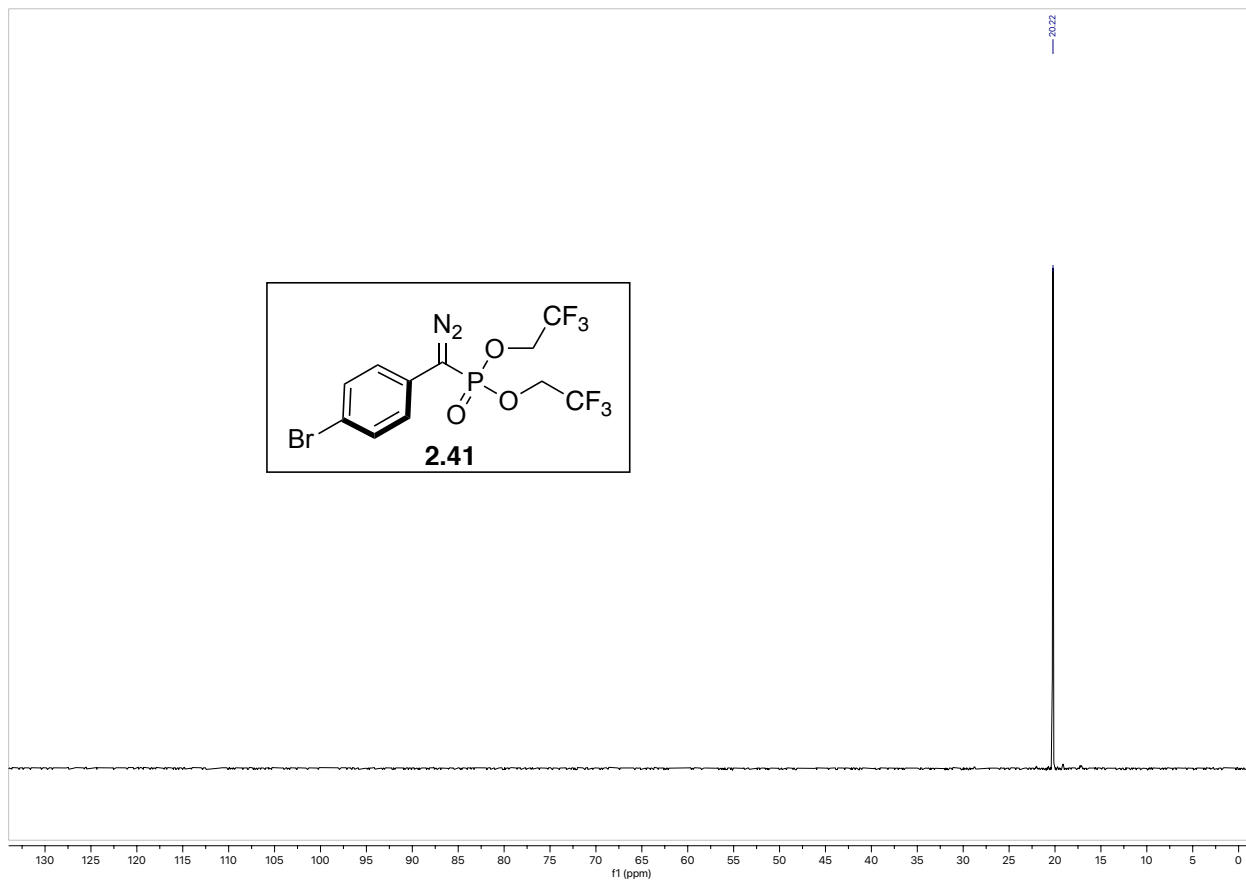
^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.41**.



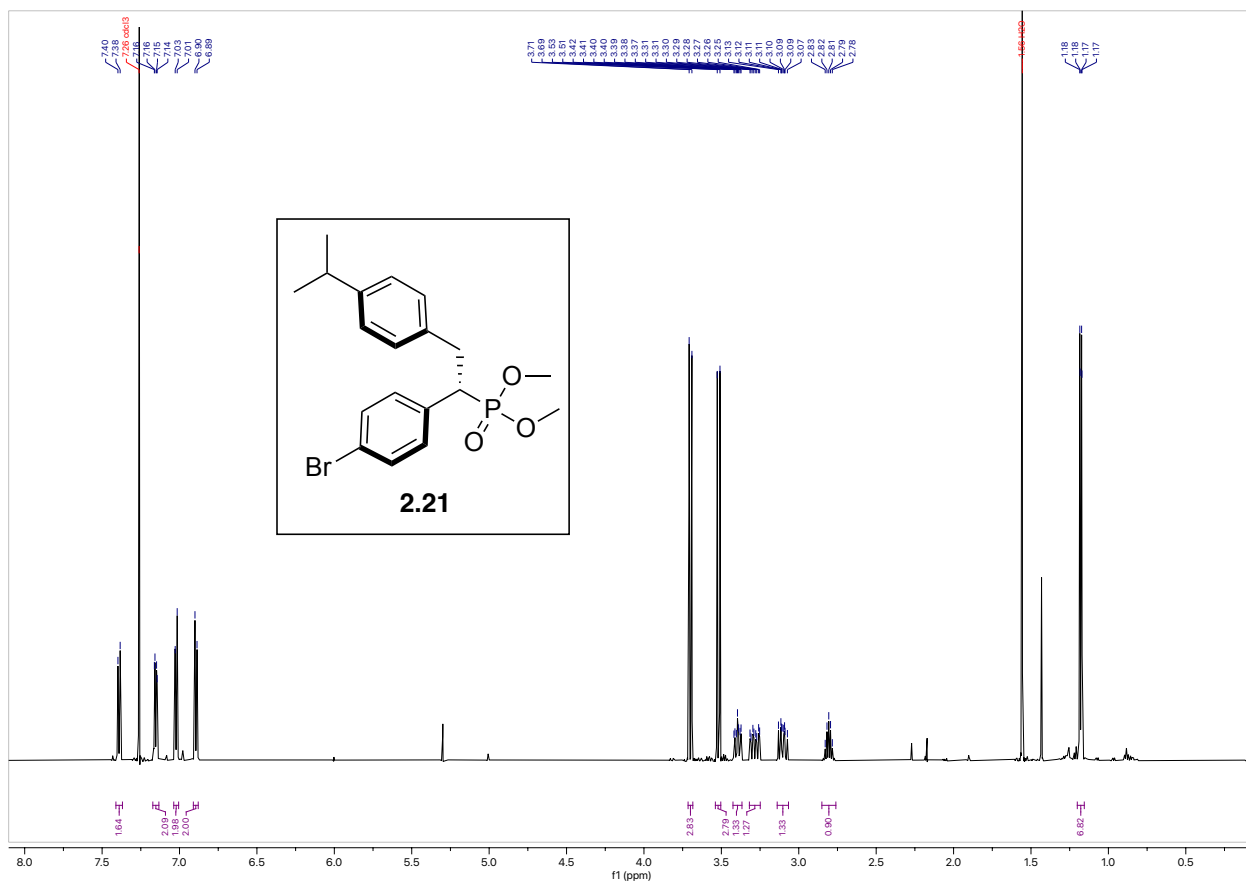
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.41**.



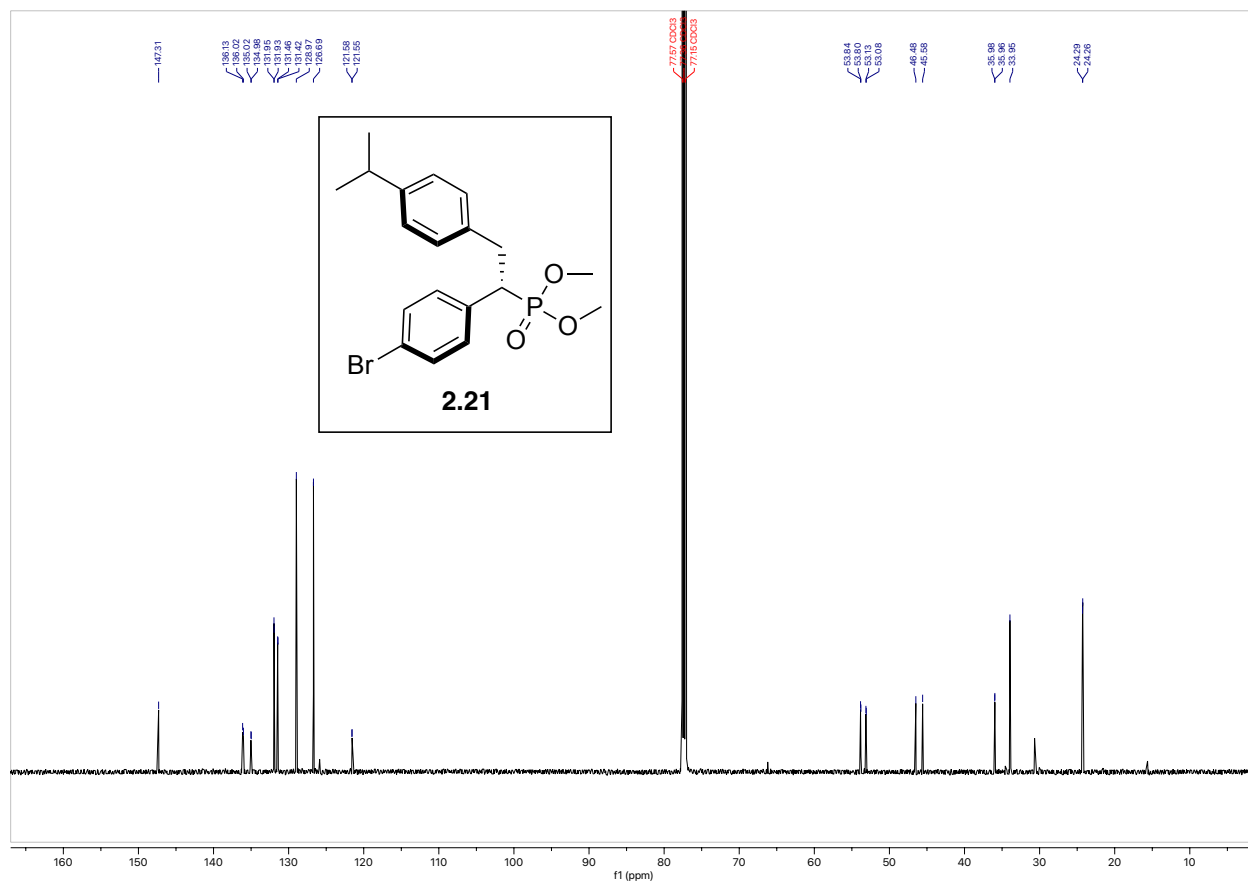
^{19}F NMR spectrum (565 MHz, Chloroform- d) of **2.41**.



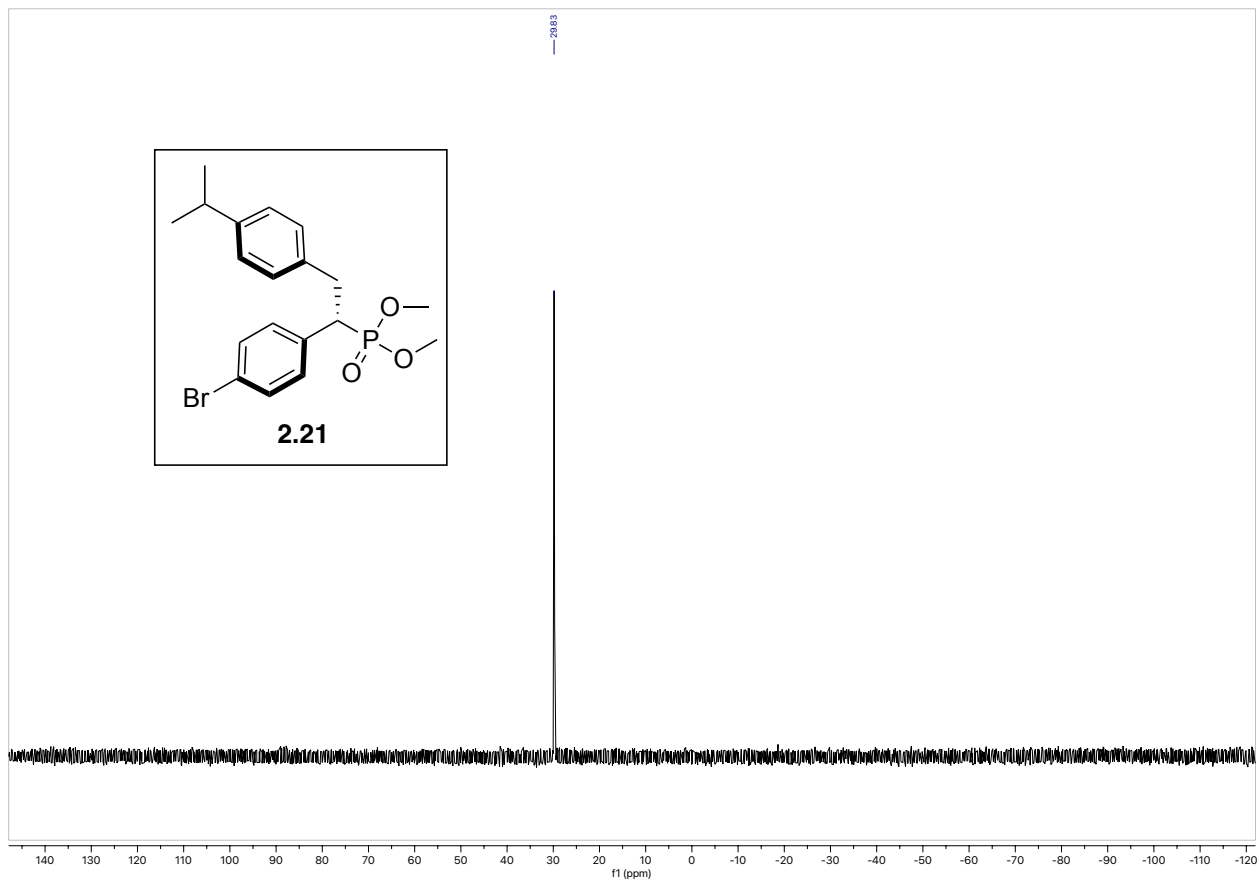
^{31}P NMR spectrum (243 MHz, Chloroform- d) of **2.41**.



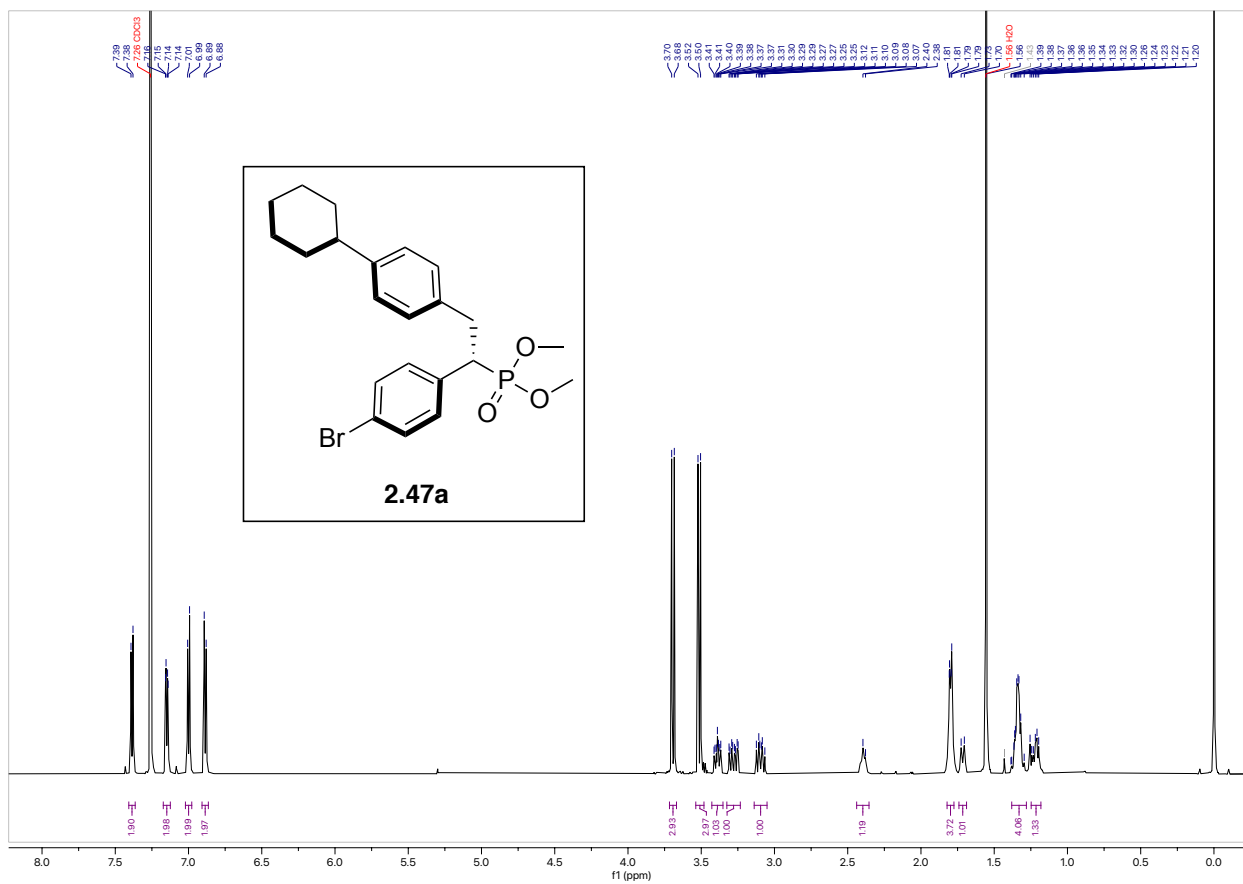
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.21**.



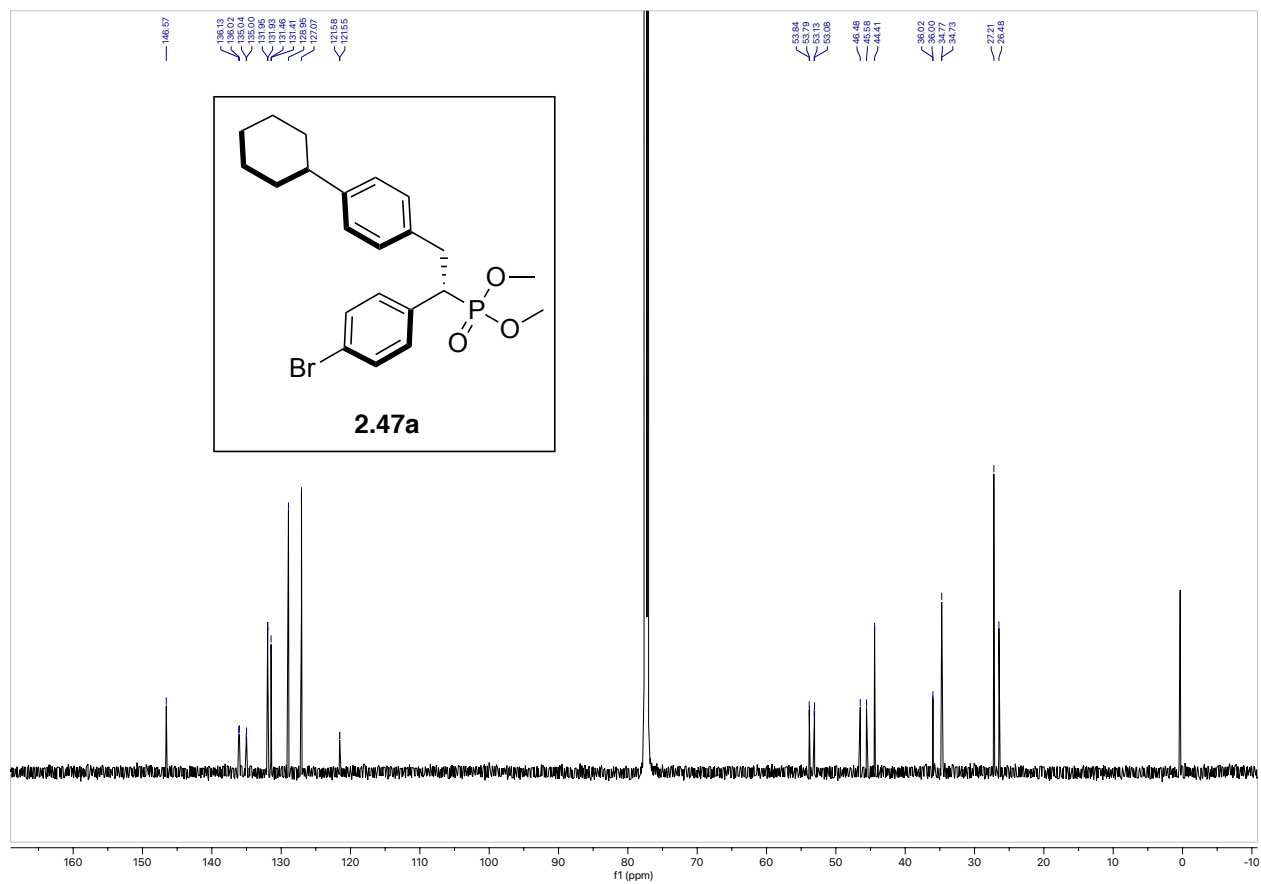
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.21**.

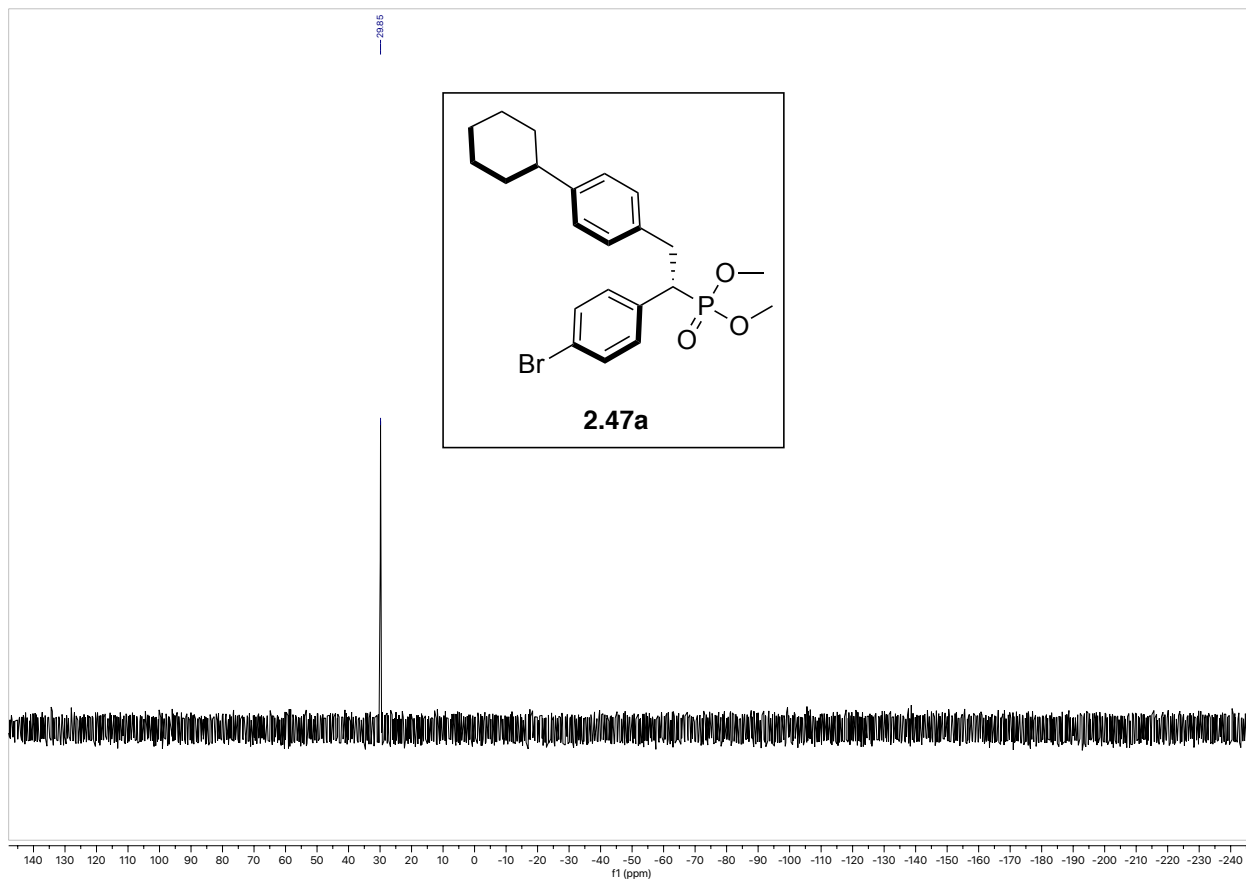


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.21**.

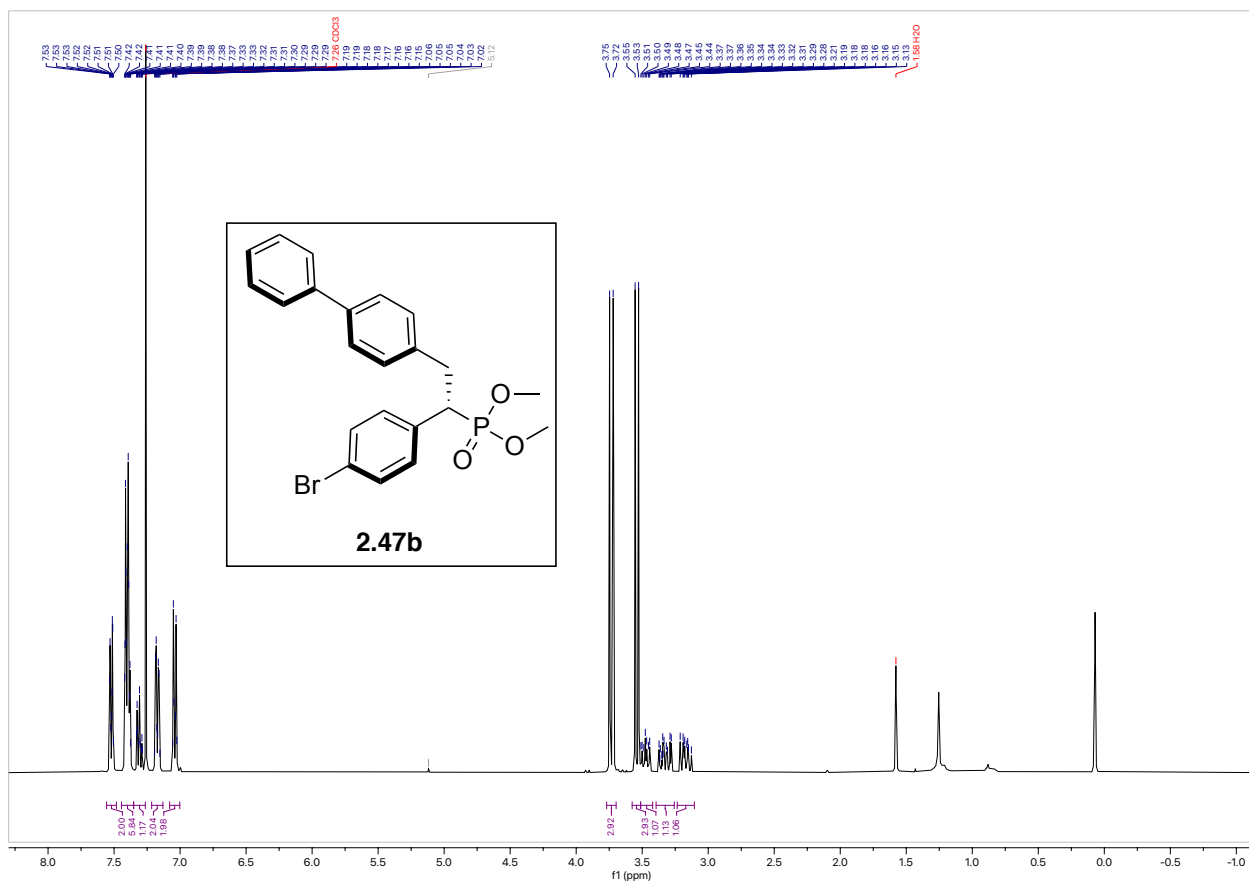


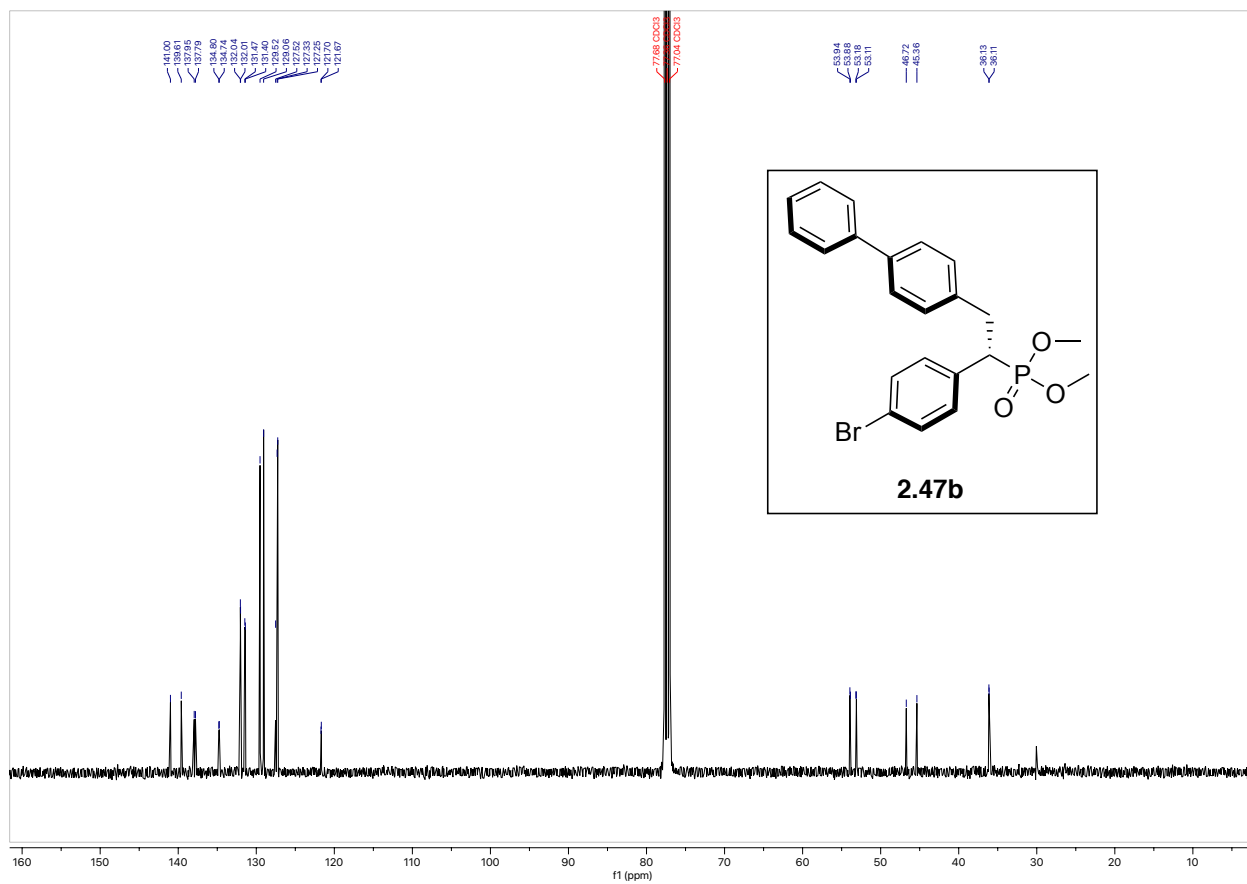
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.47a**.



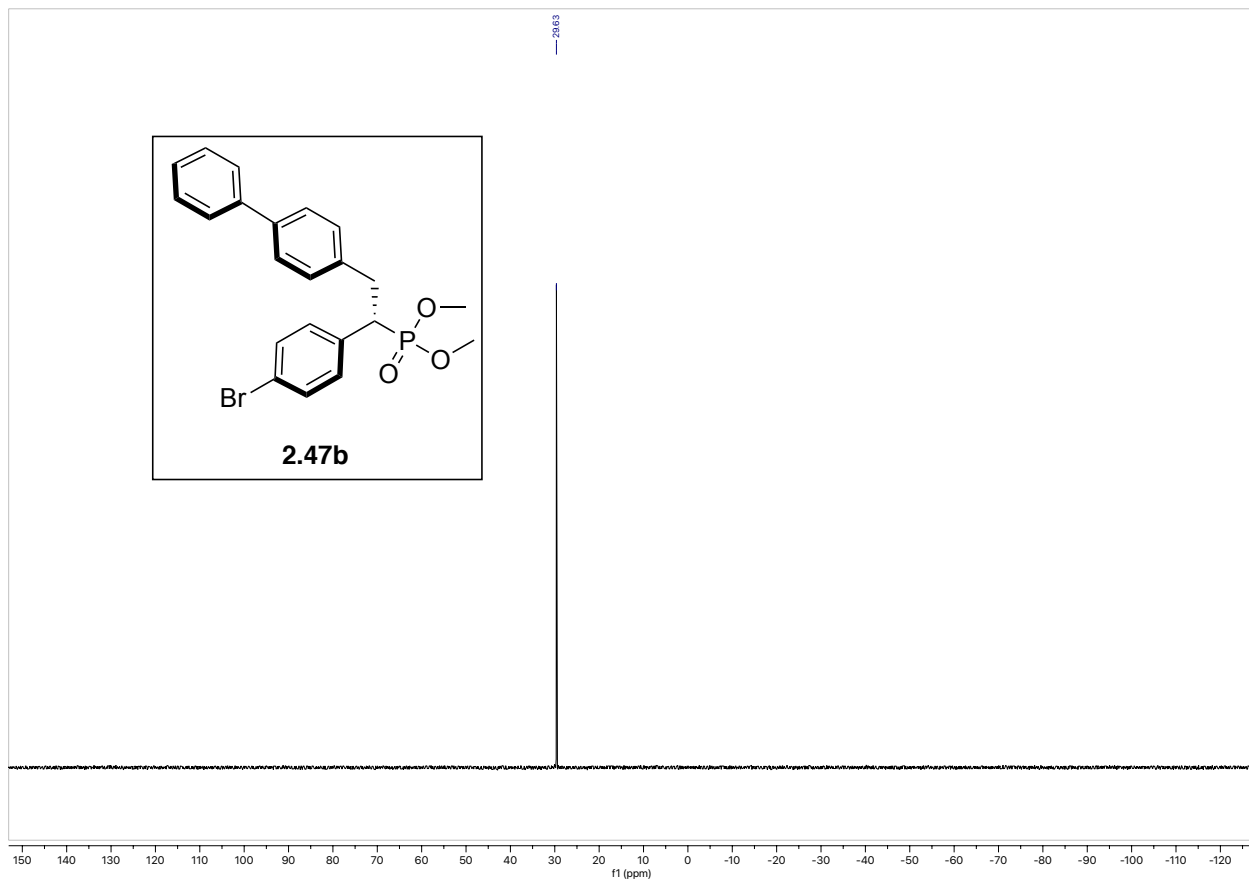


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47a**.

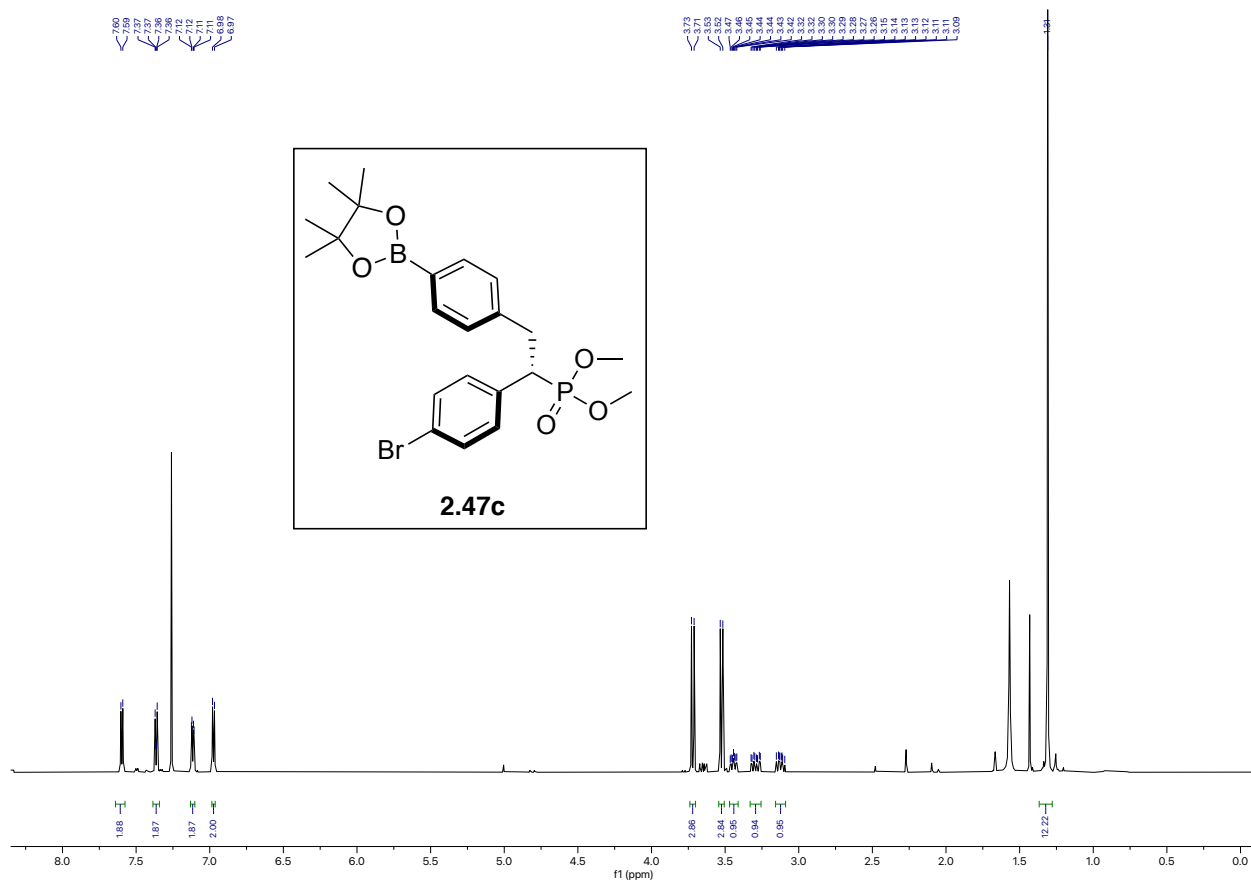


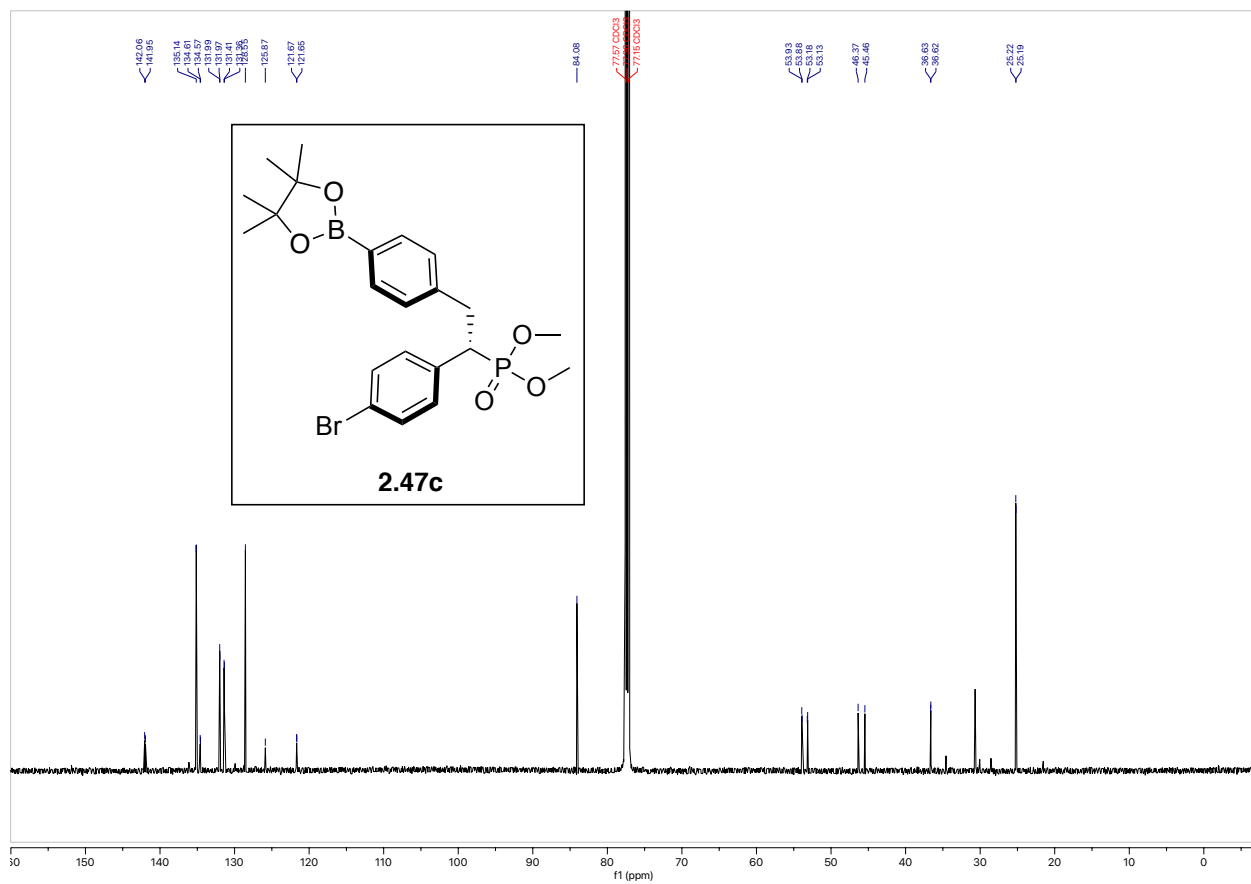


¹³C{¹H} NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47b**.

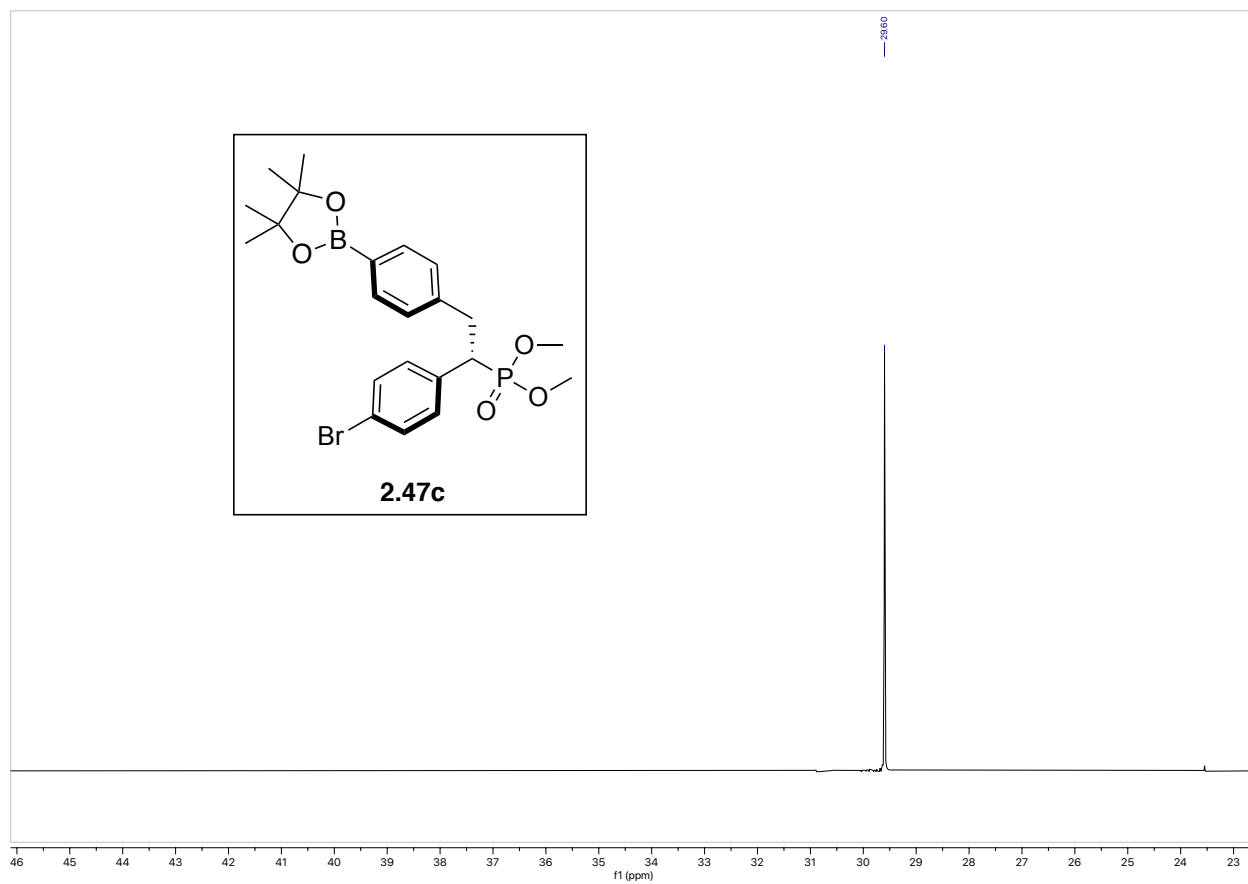


^{31}P NMR spectrum (162 MHz, Chloroform-*d*) of **2.47b**.



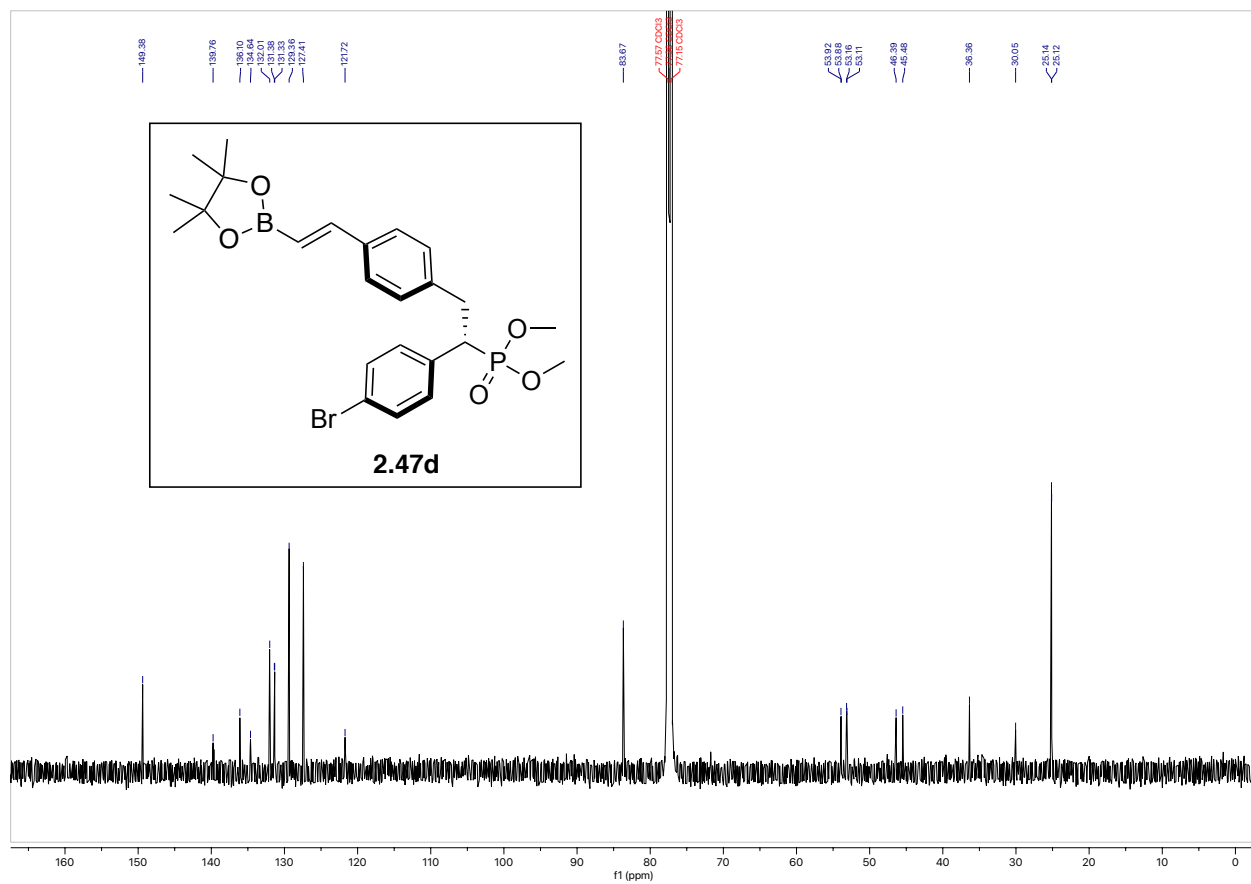


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47c**.

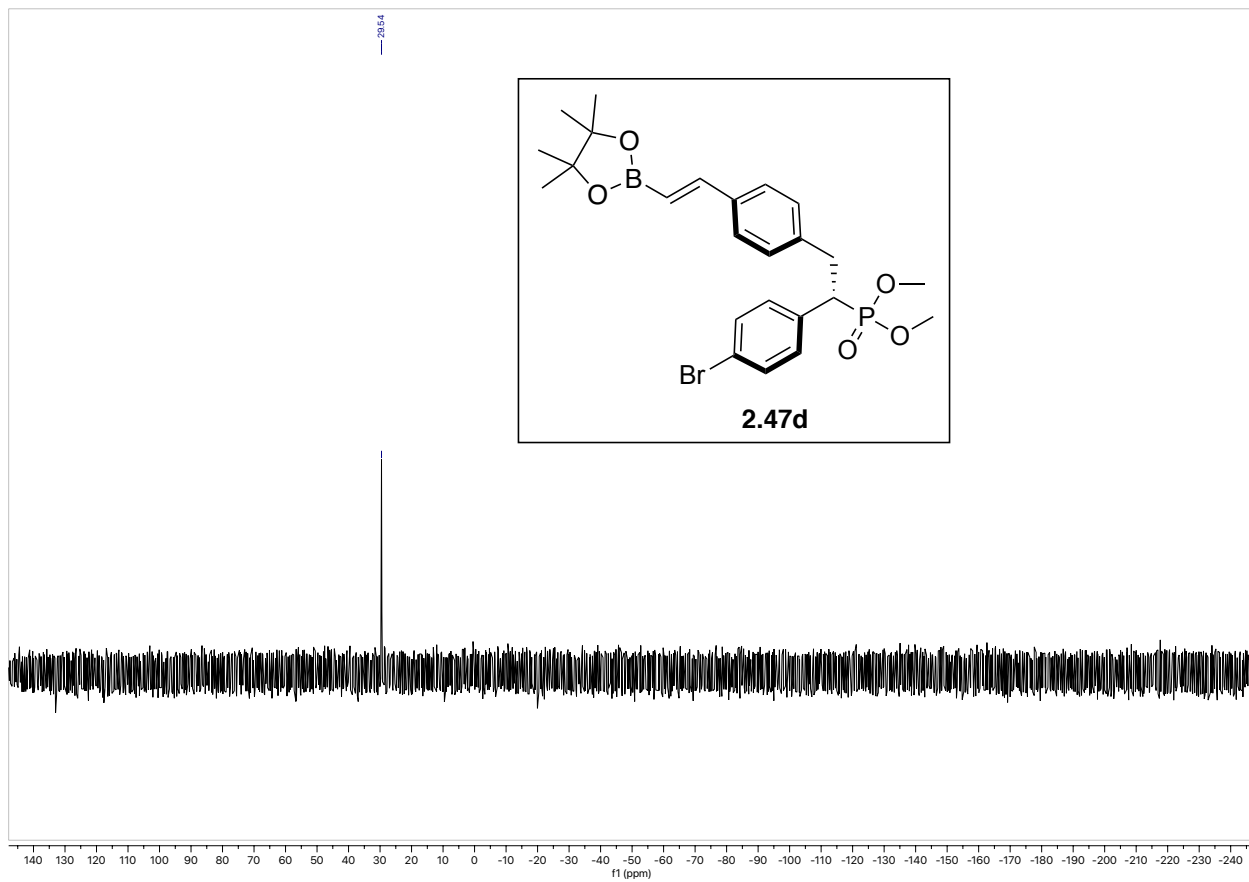


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47c**.

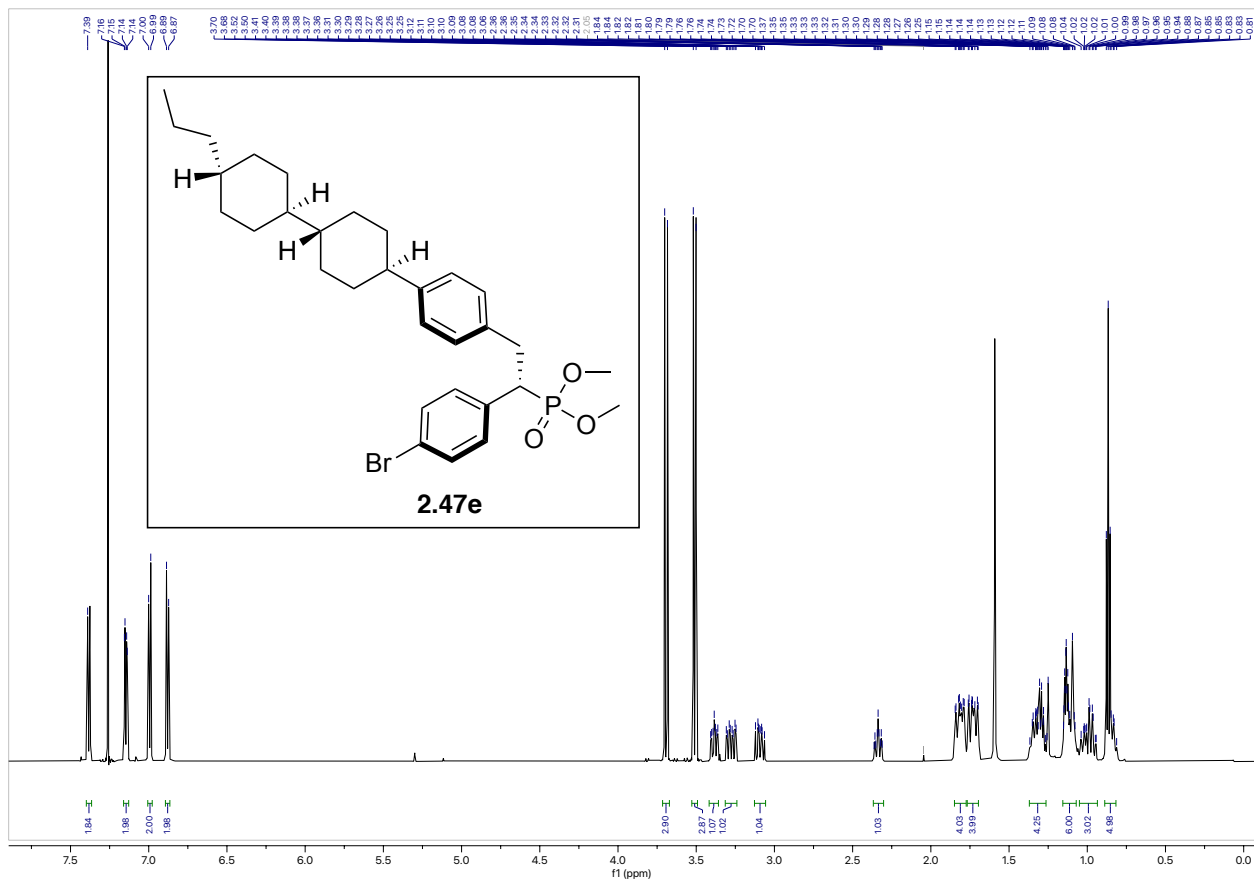


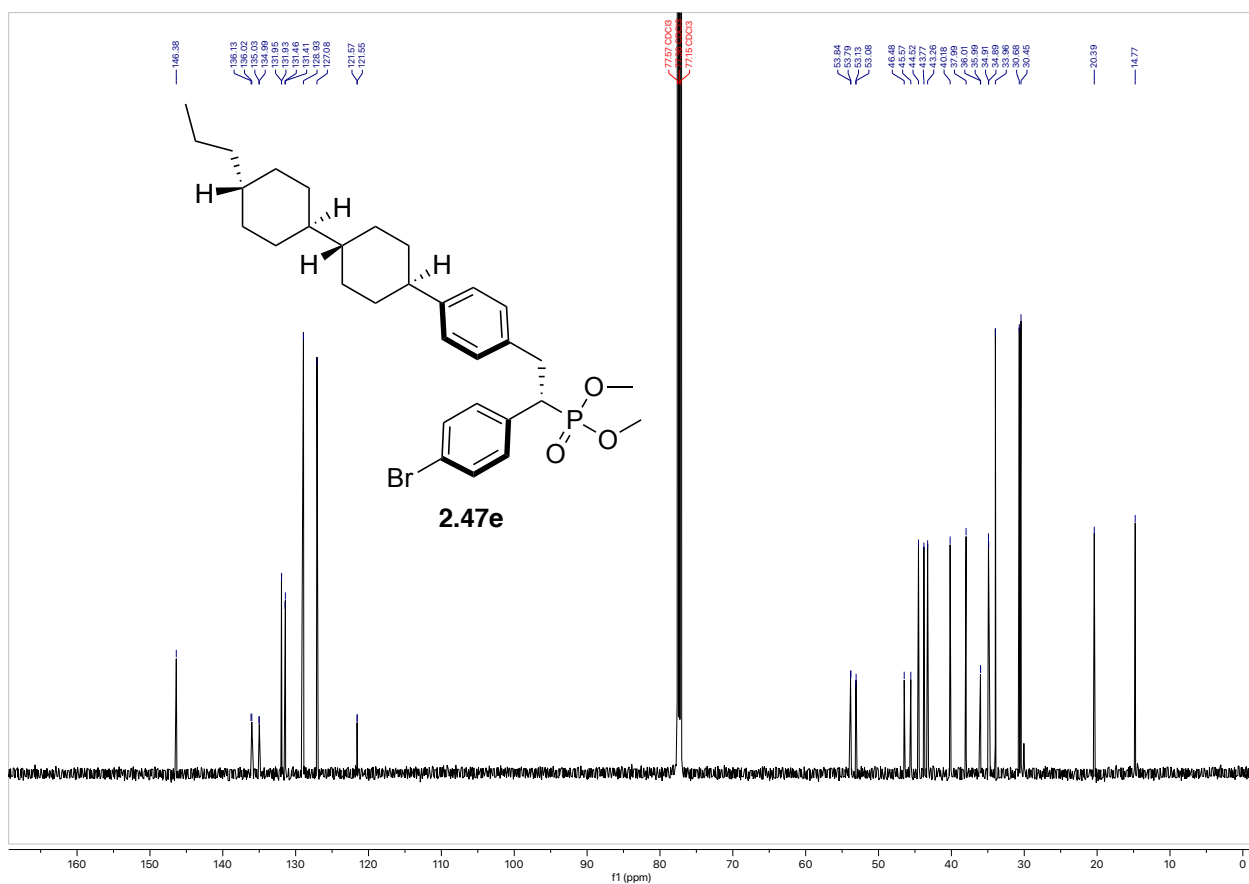


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47.d**.

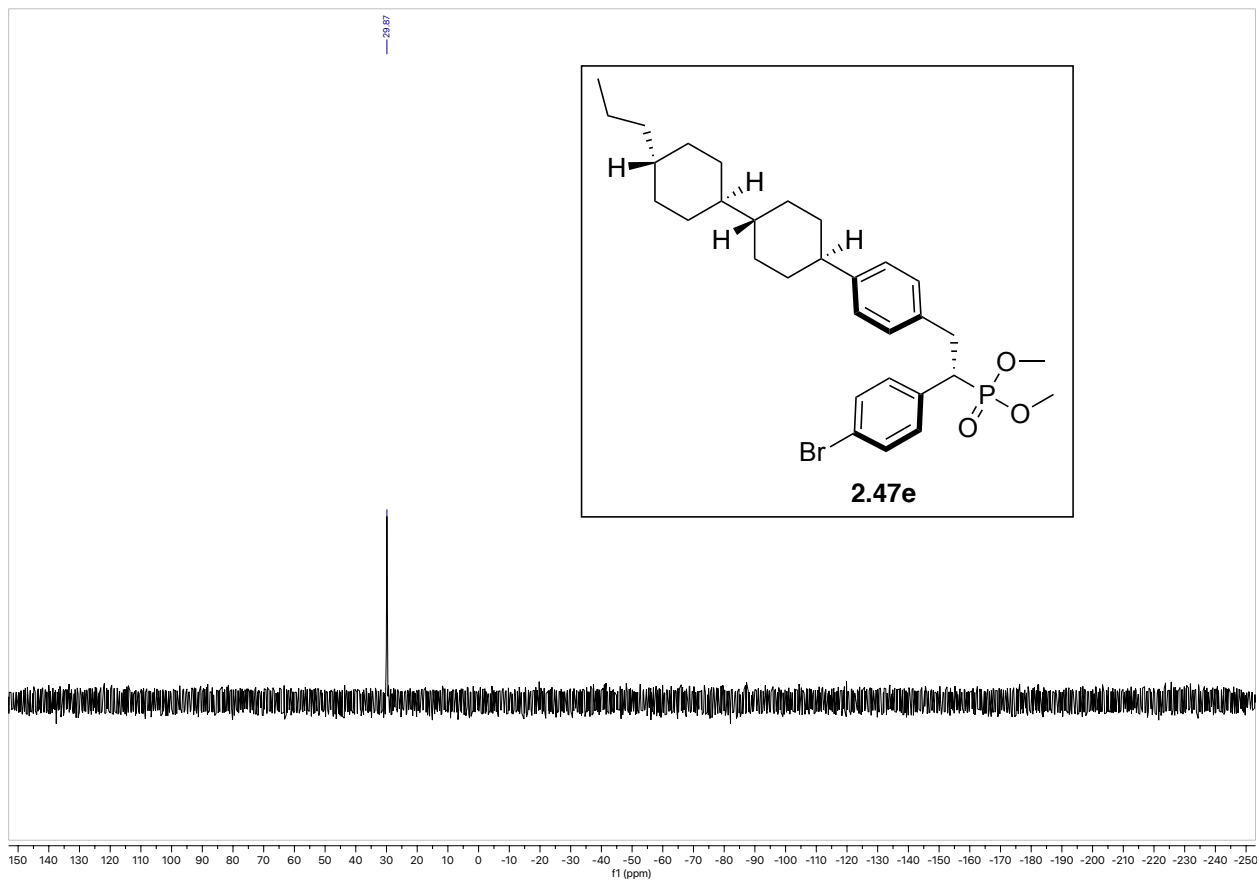


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47d**.

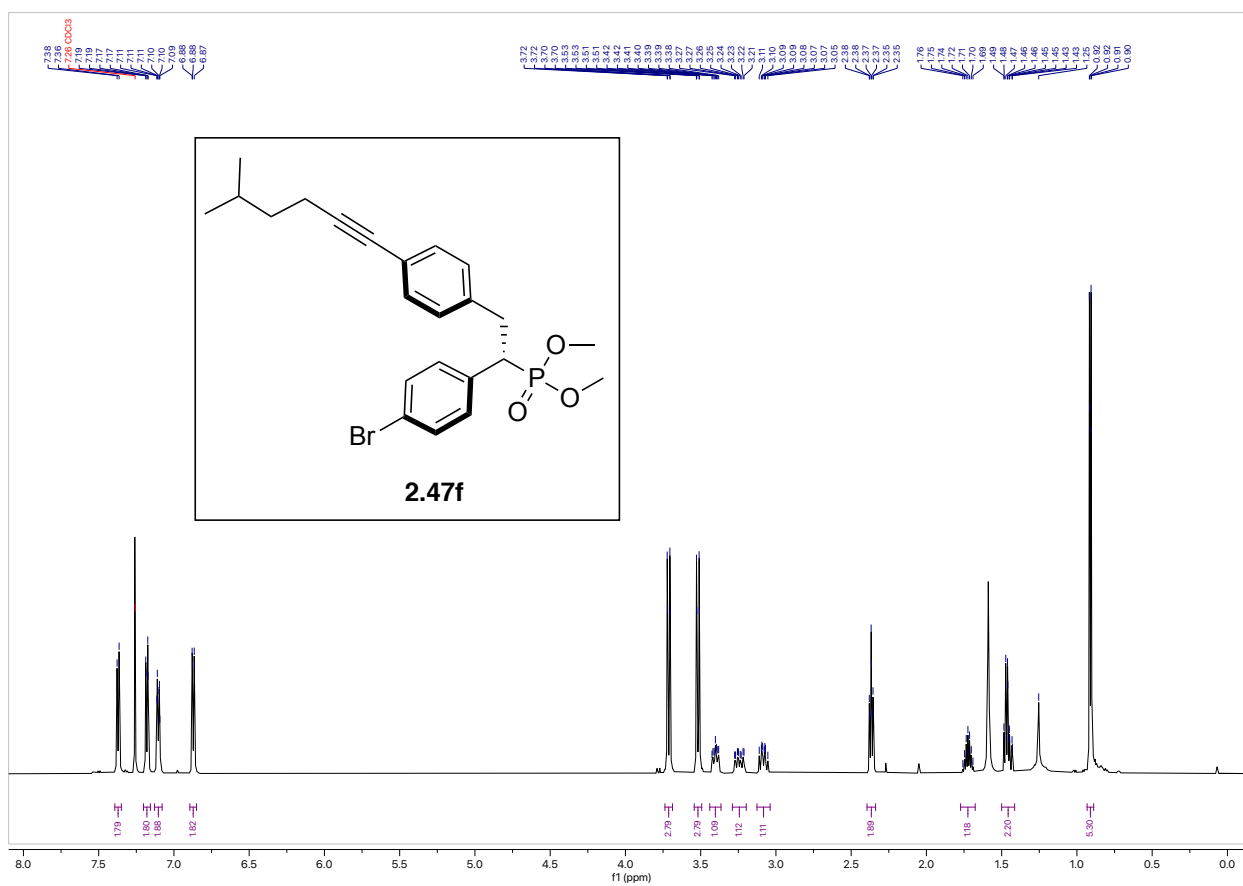




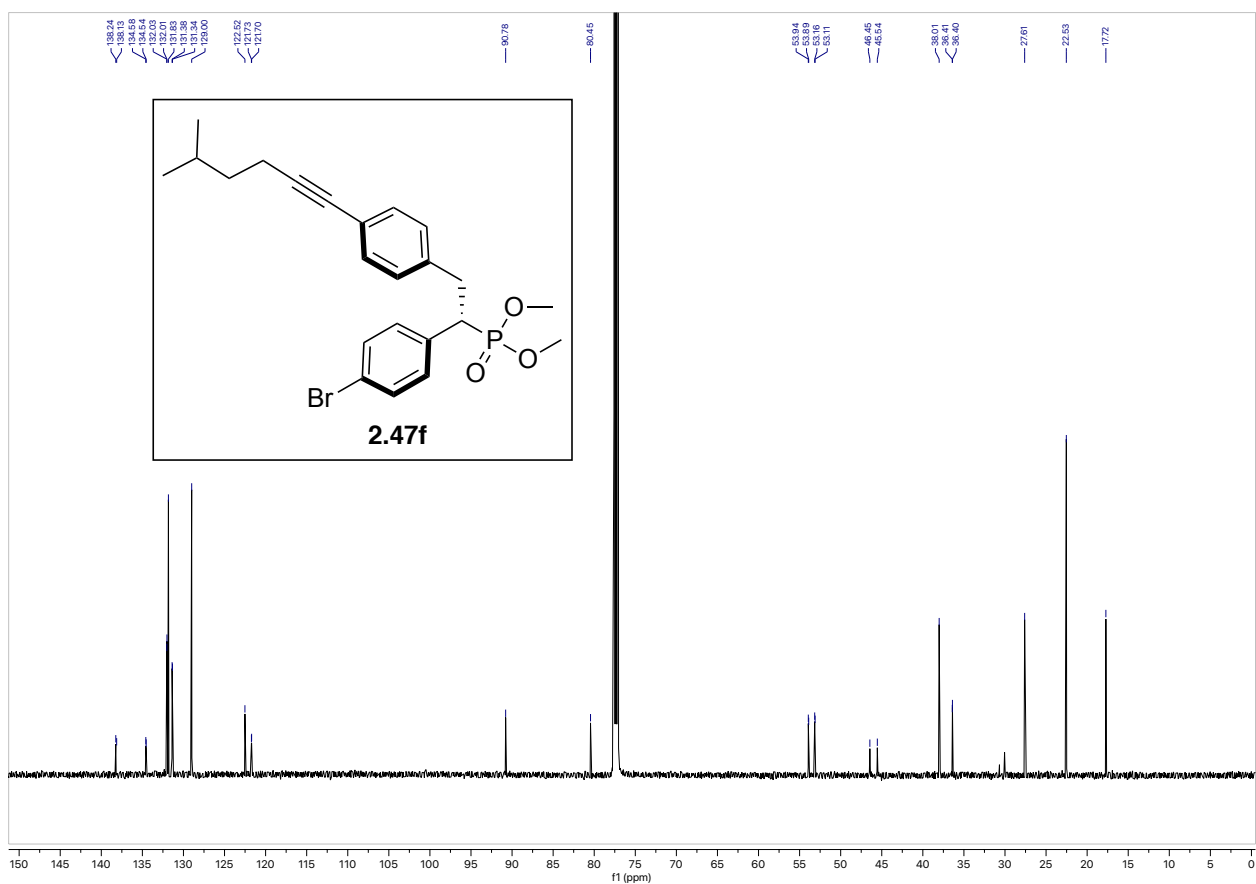
¹³C{¹H} NMR spectrum (151 MHz, Chloroform-d) (t, 77.36 ppm) of **2.47e**.



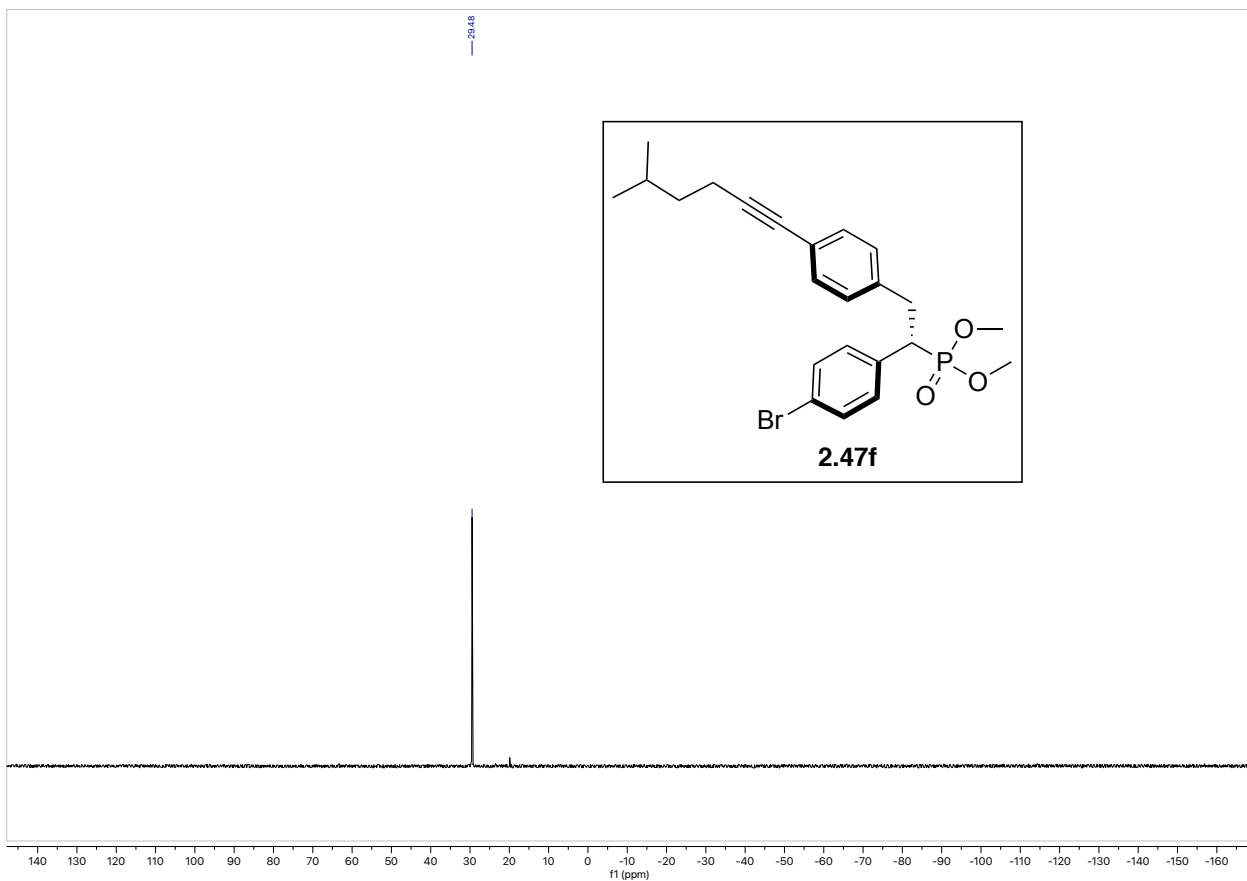
^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47e**



¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.47f**.

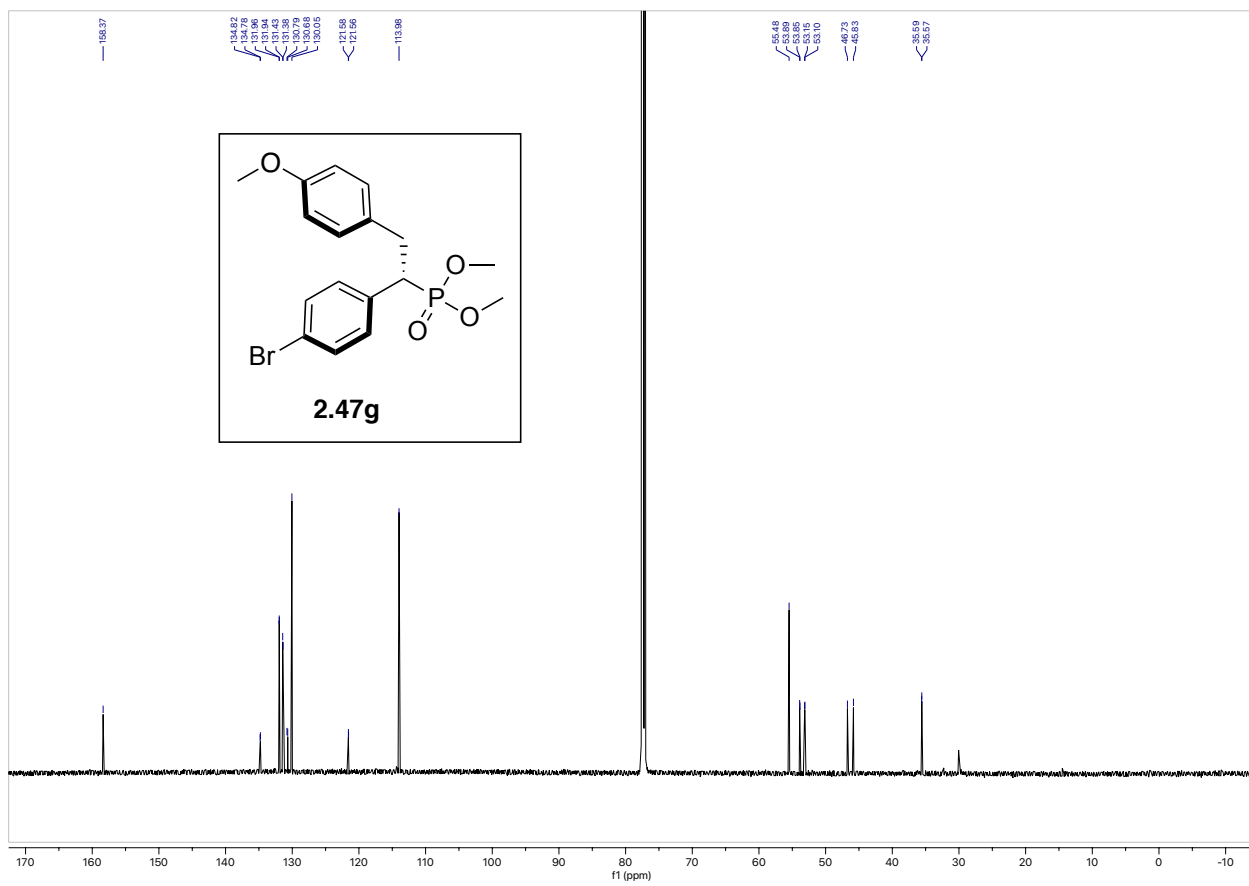


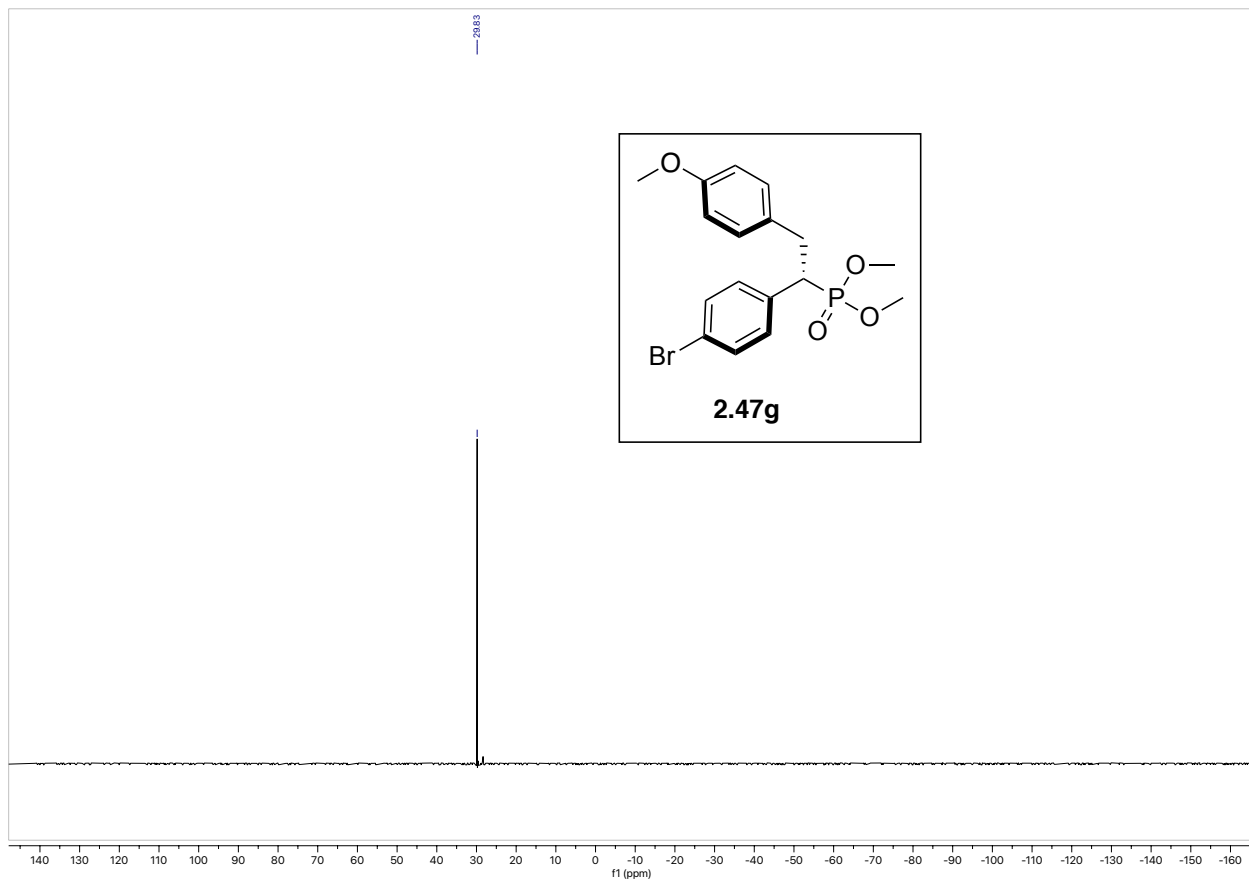
¹³C{¹H} NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47f**.



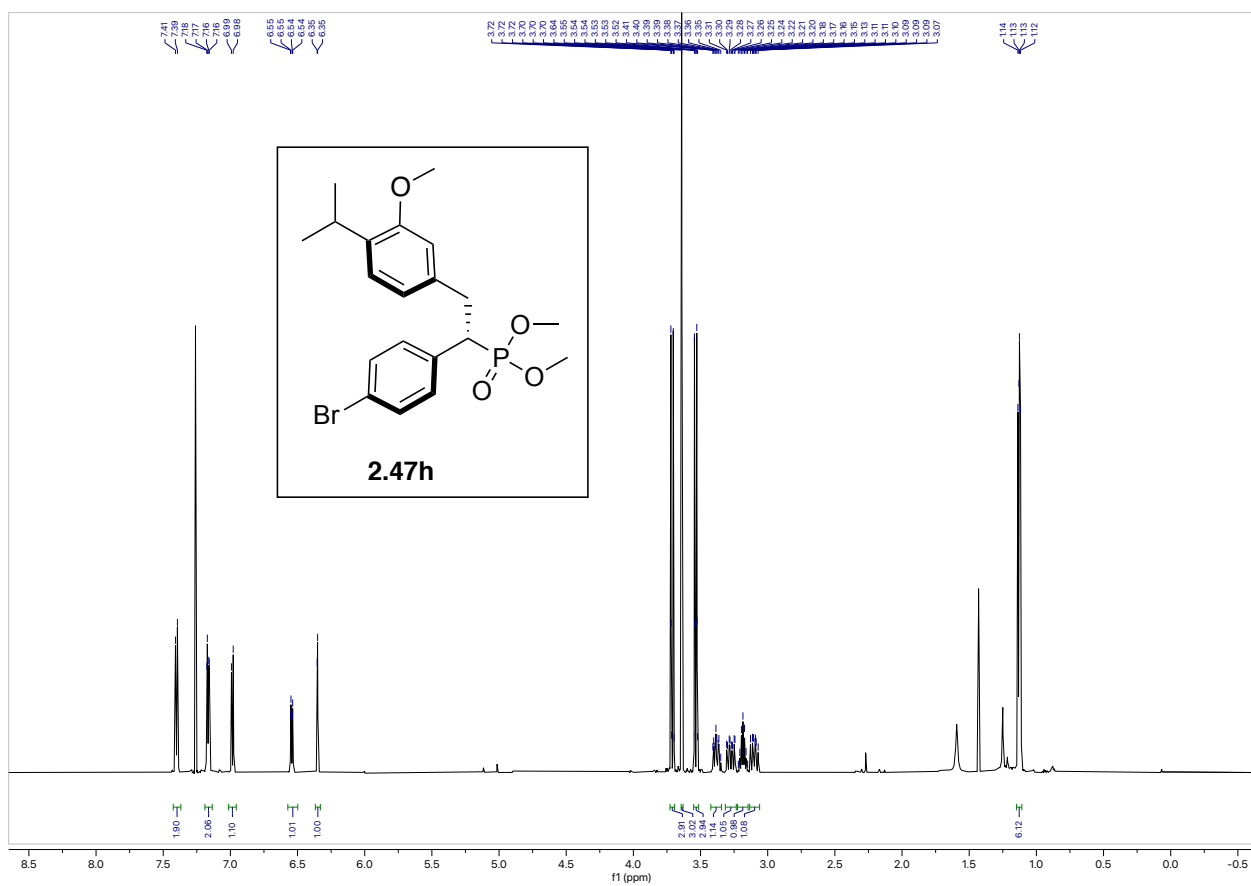
^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47f**.

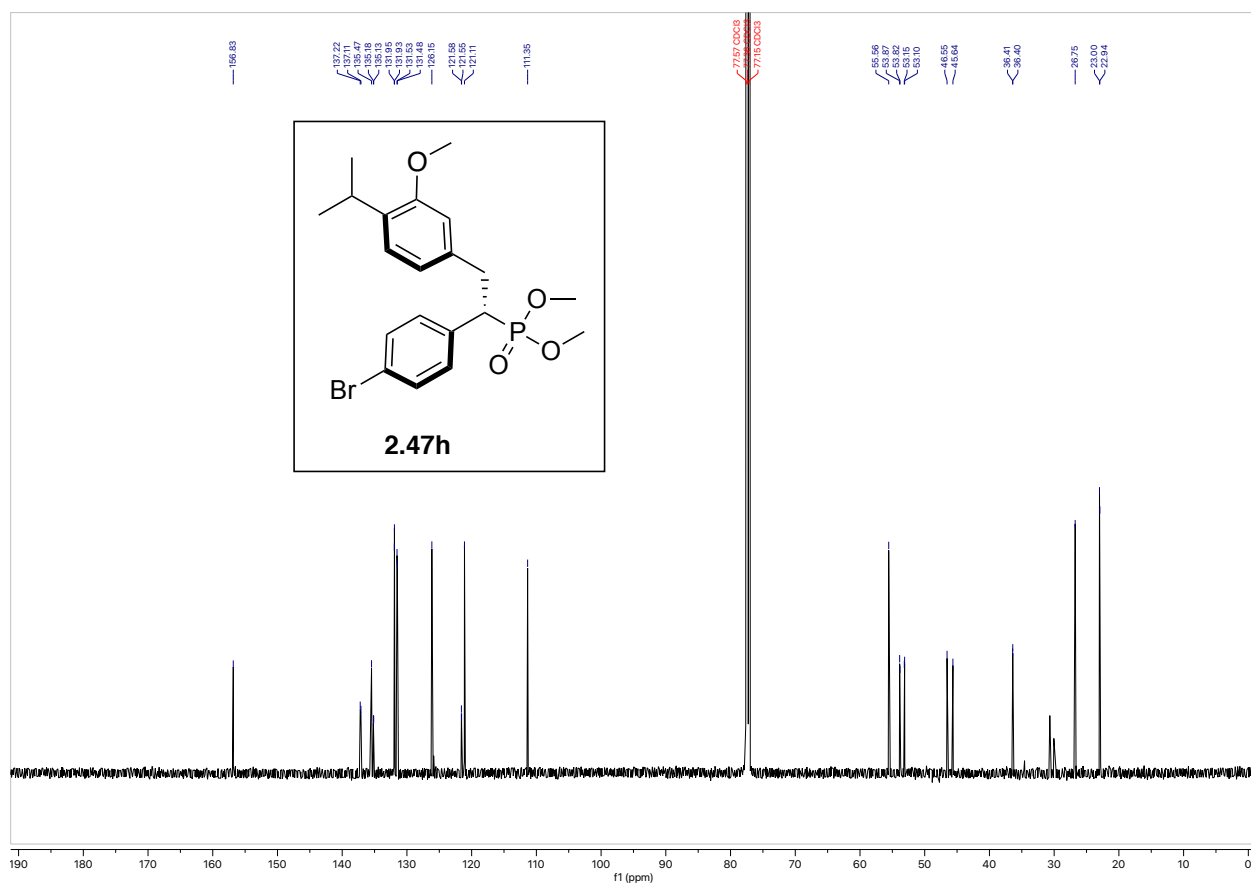




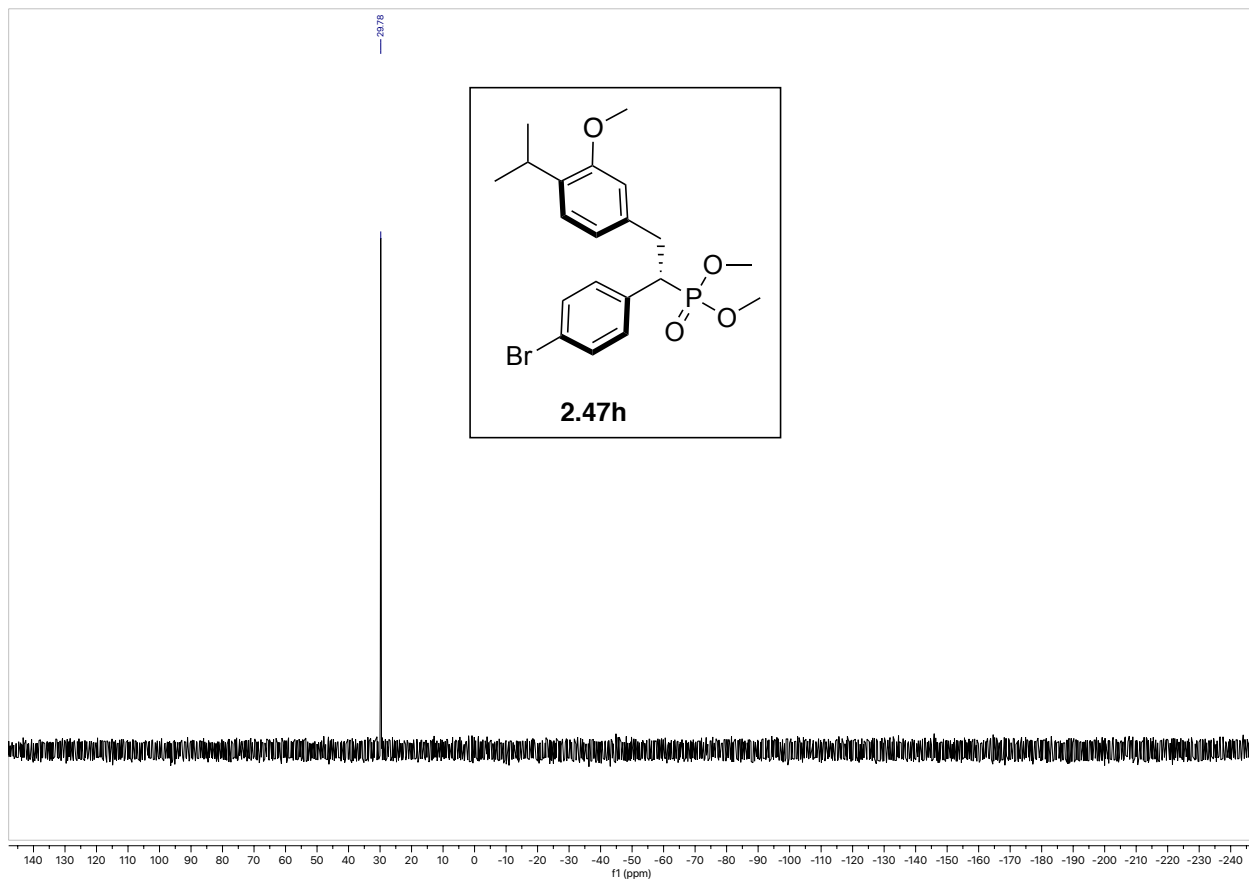


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47g**.

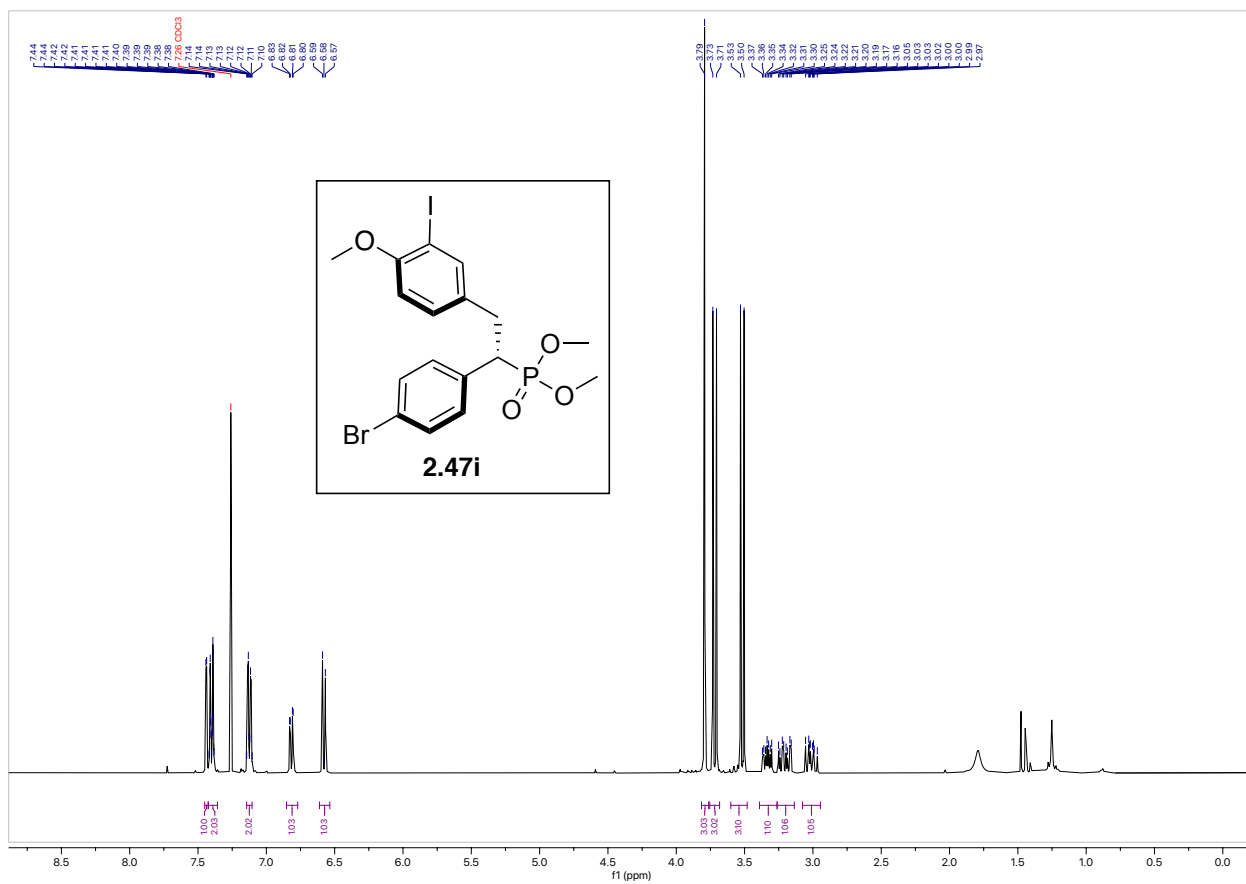




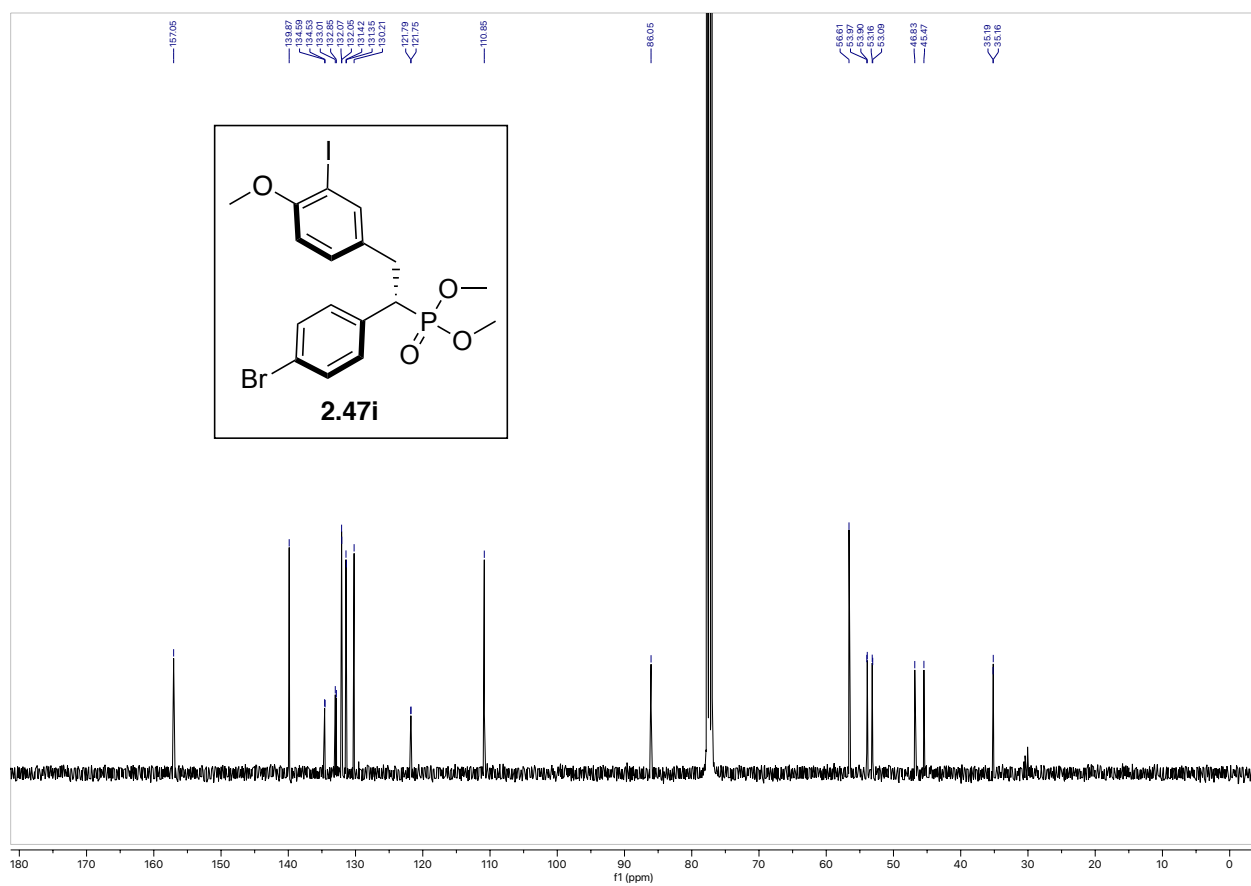
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47h**.



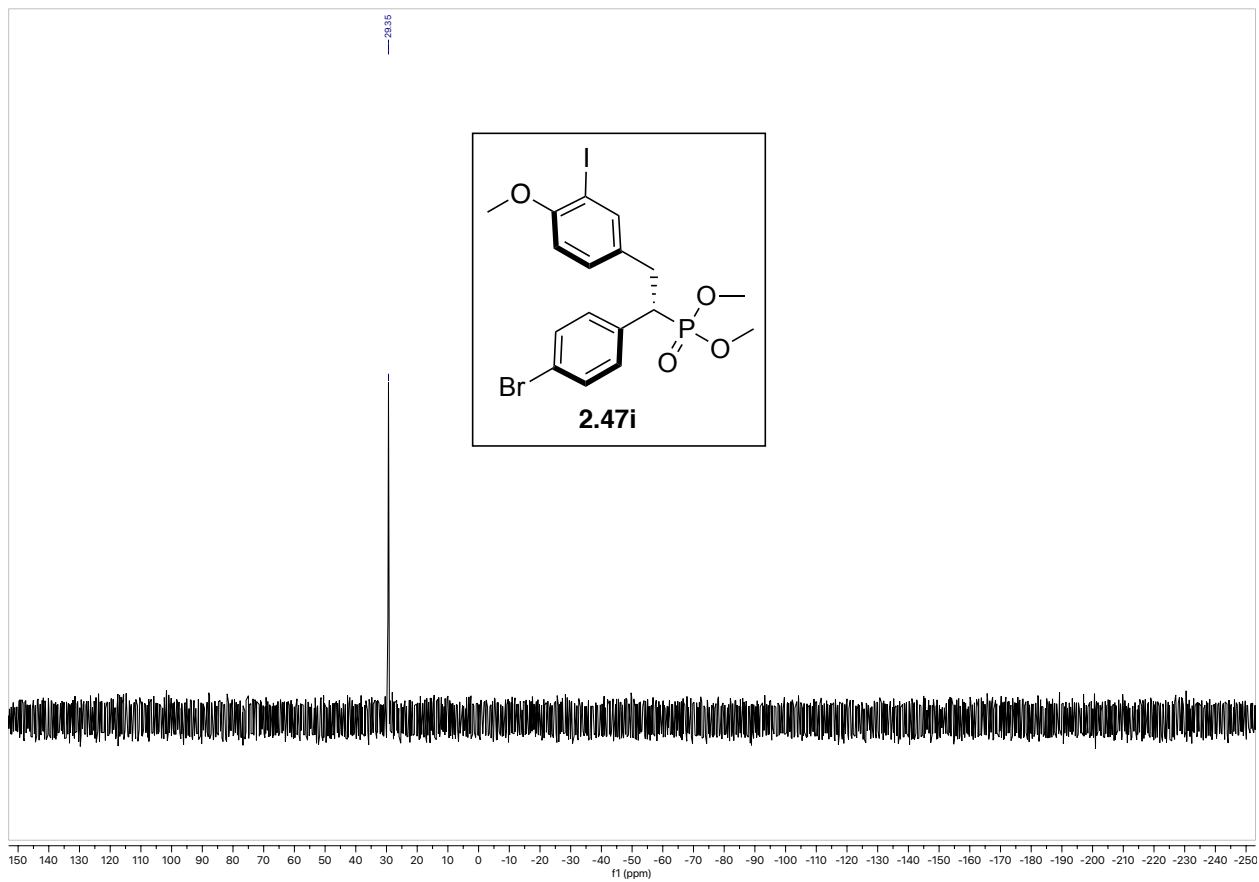
^{31}P NMR spectrum (243 MHz, Chloroform- d) of **2.47h**.



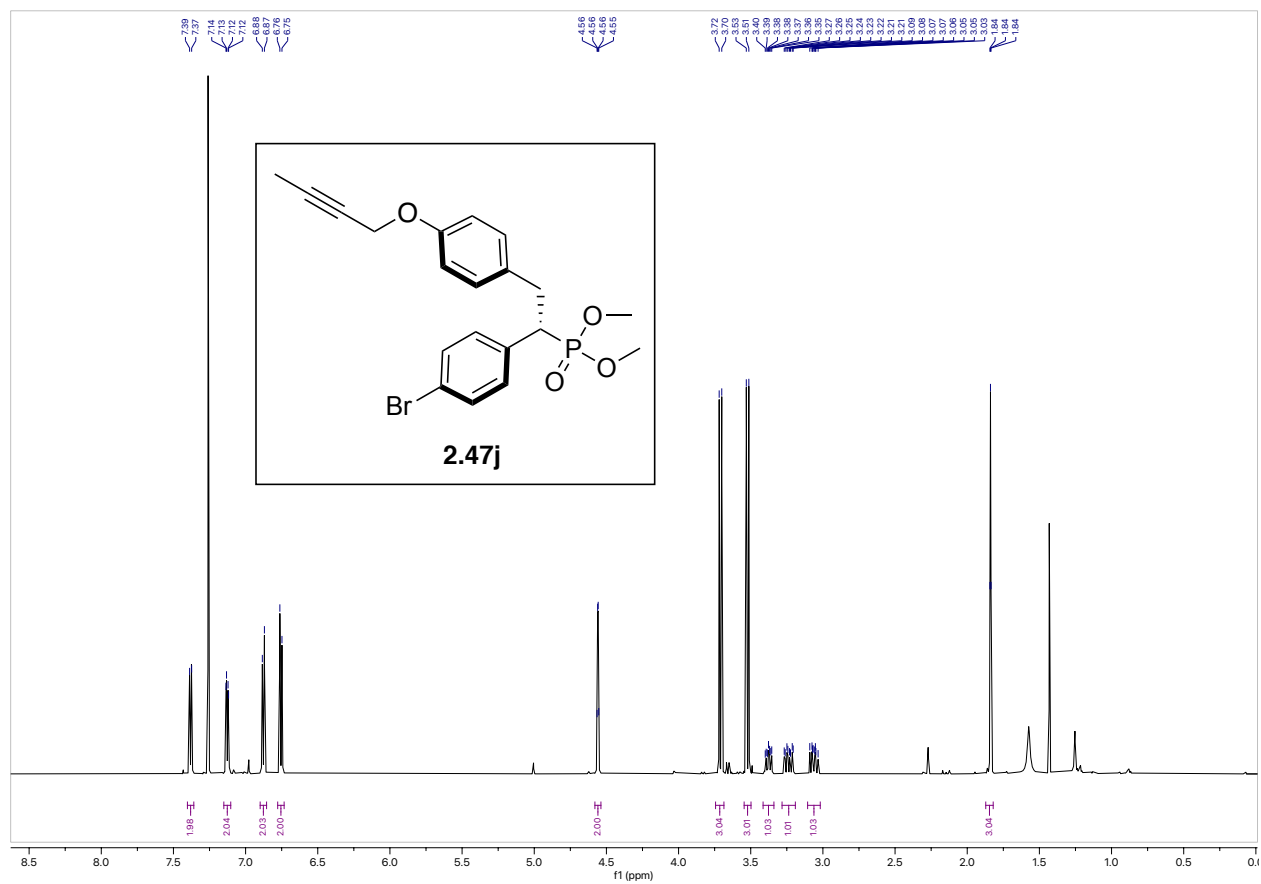
¹H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.47i**.



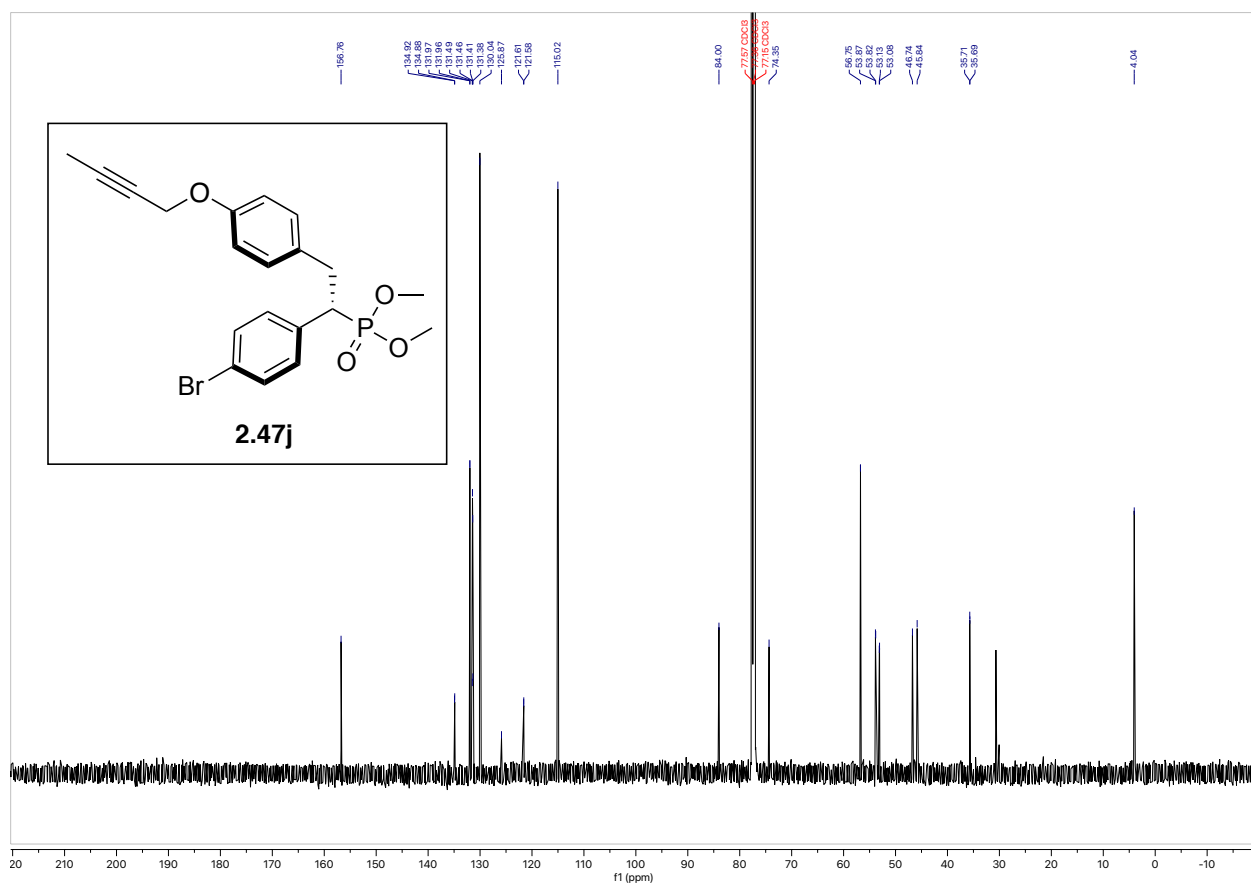
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47i**.



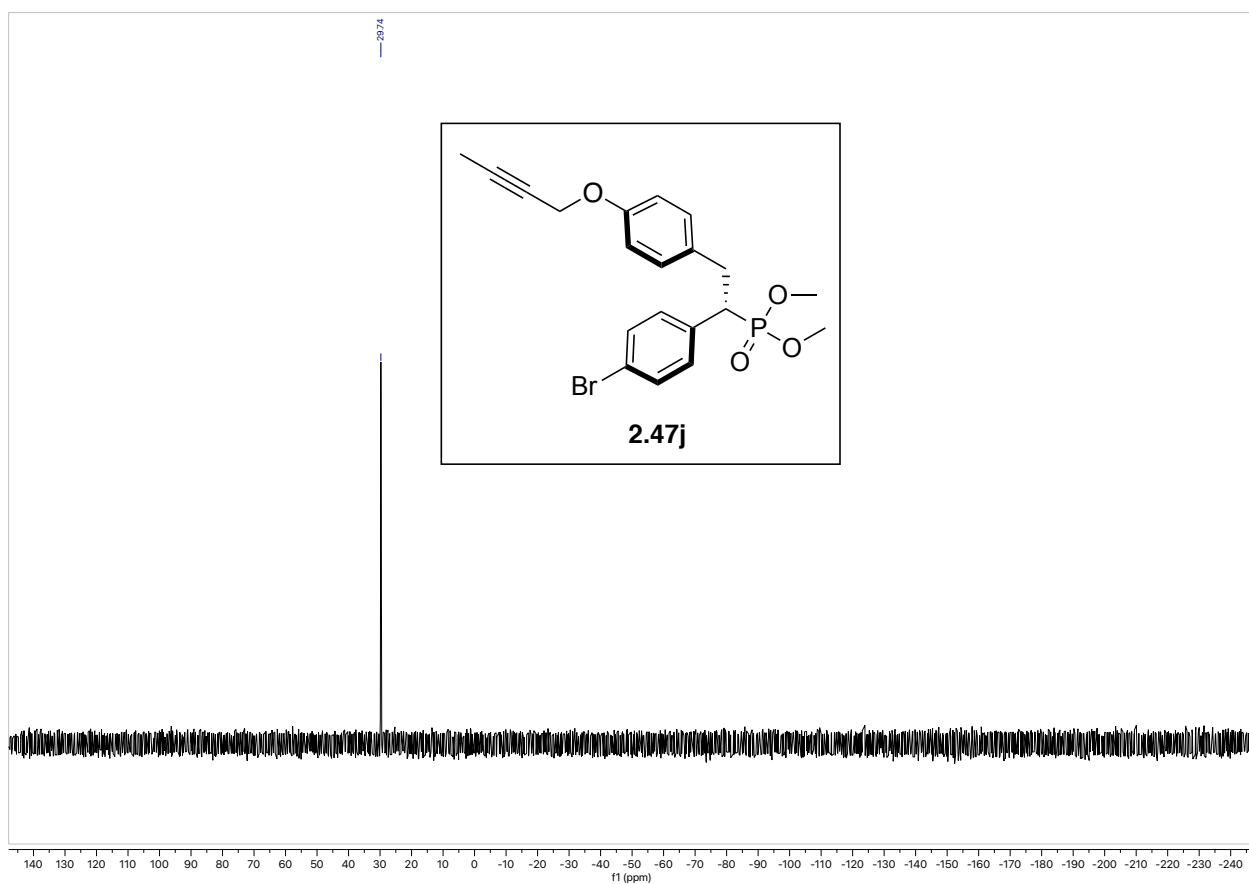
^{31}P NMR spectrum (162 MHz, Chloroform-*d*) of **2.47i**.



¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.47j**.

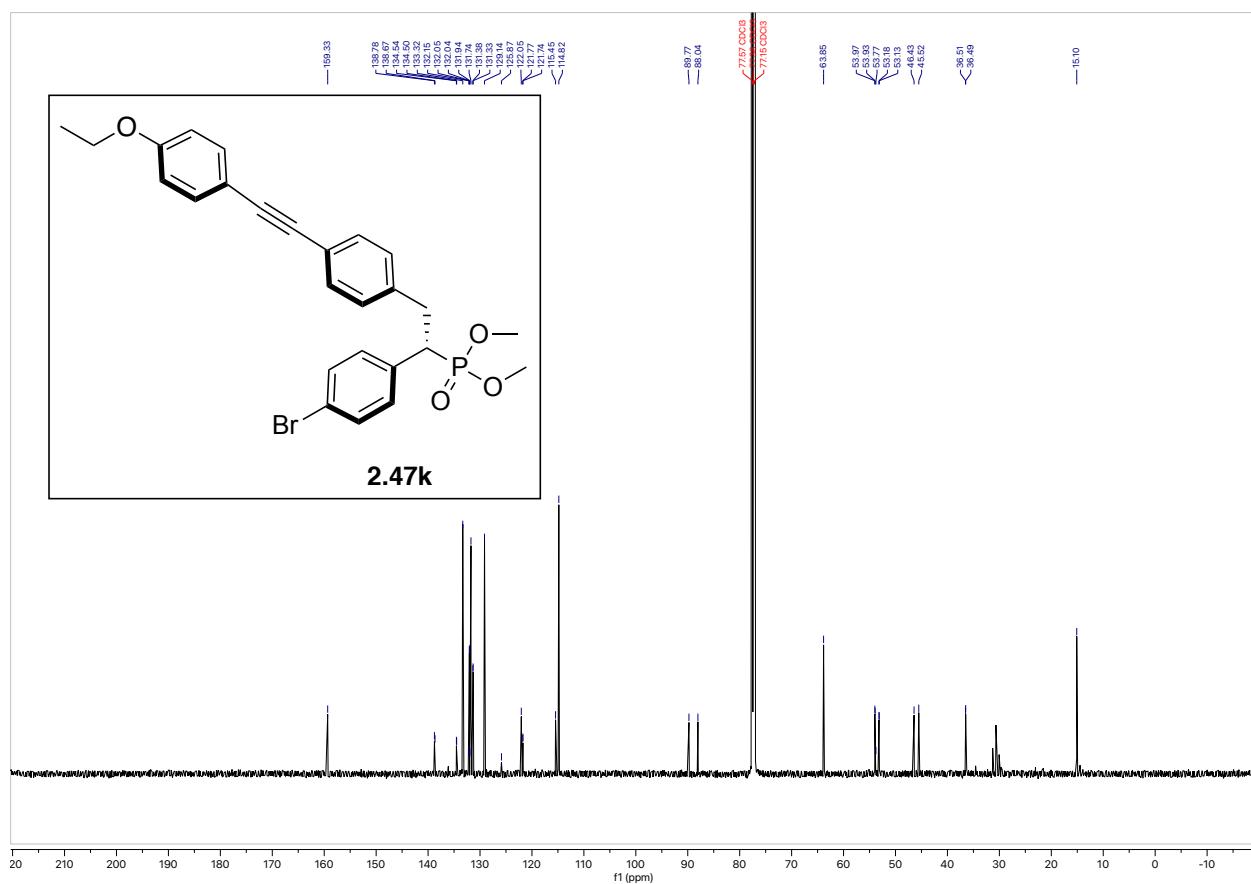


¹³C{¹H} NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47j**.

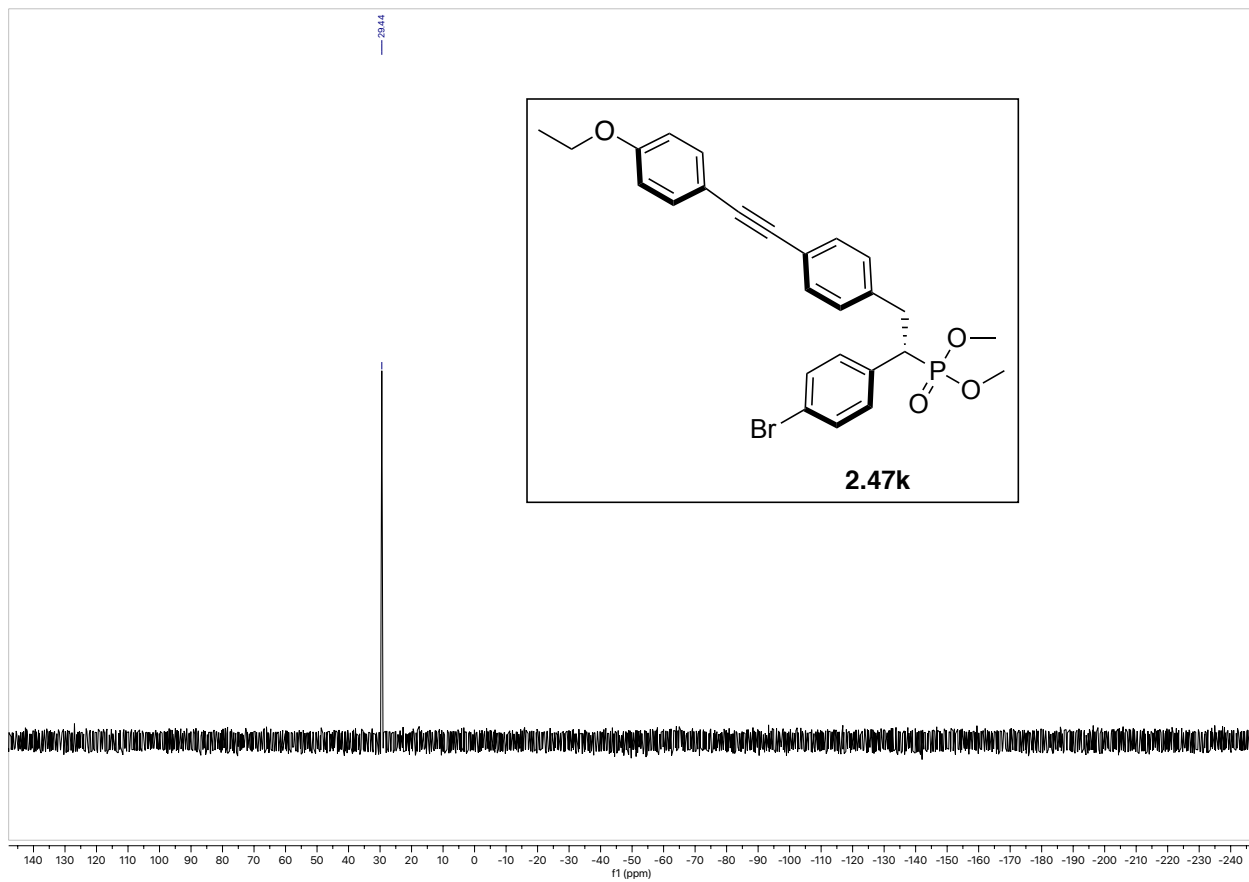


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47j**.

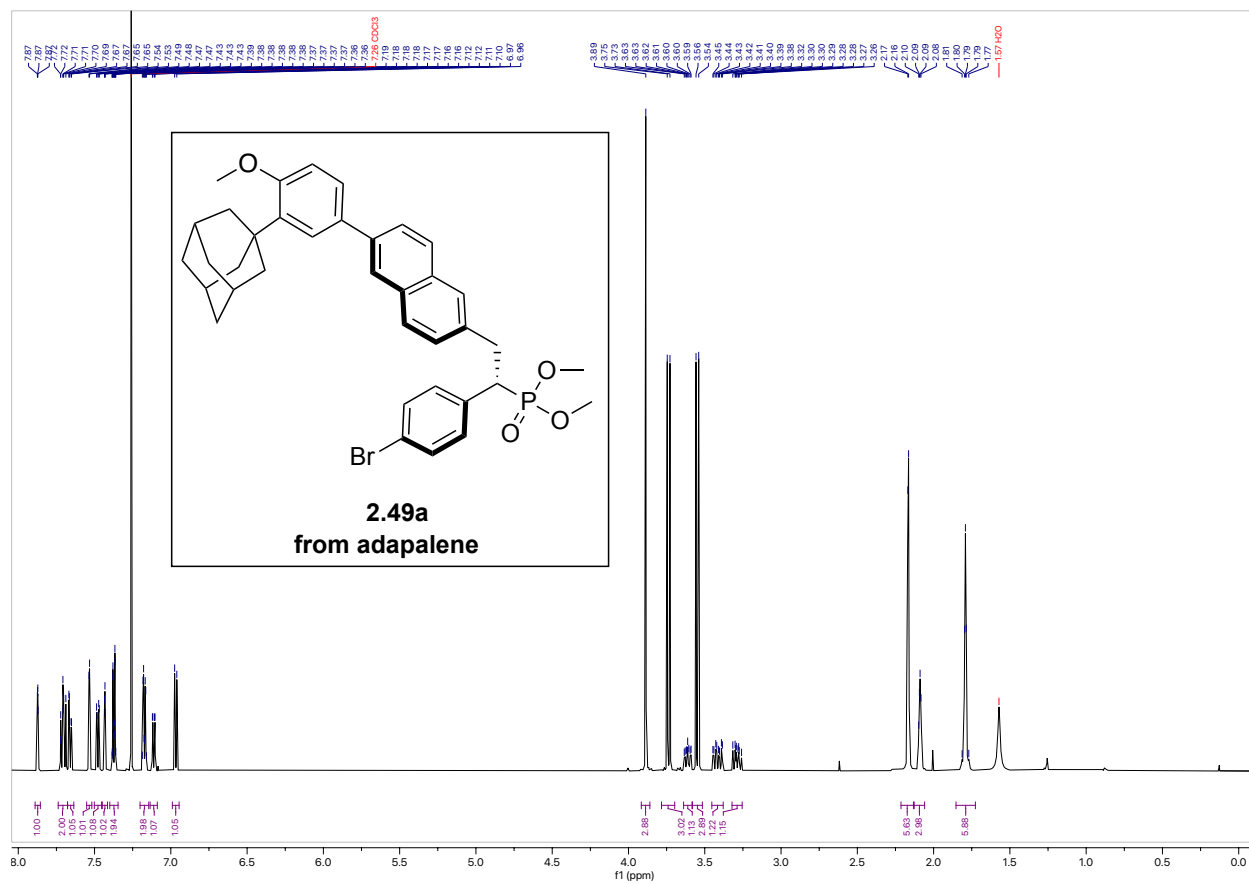


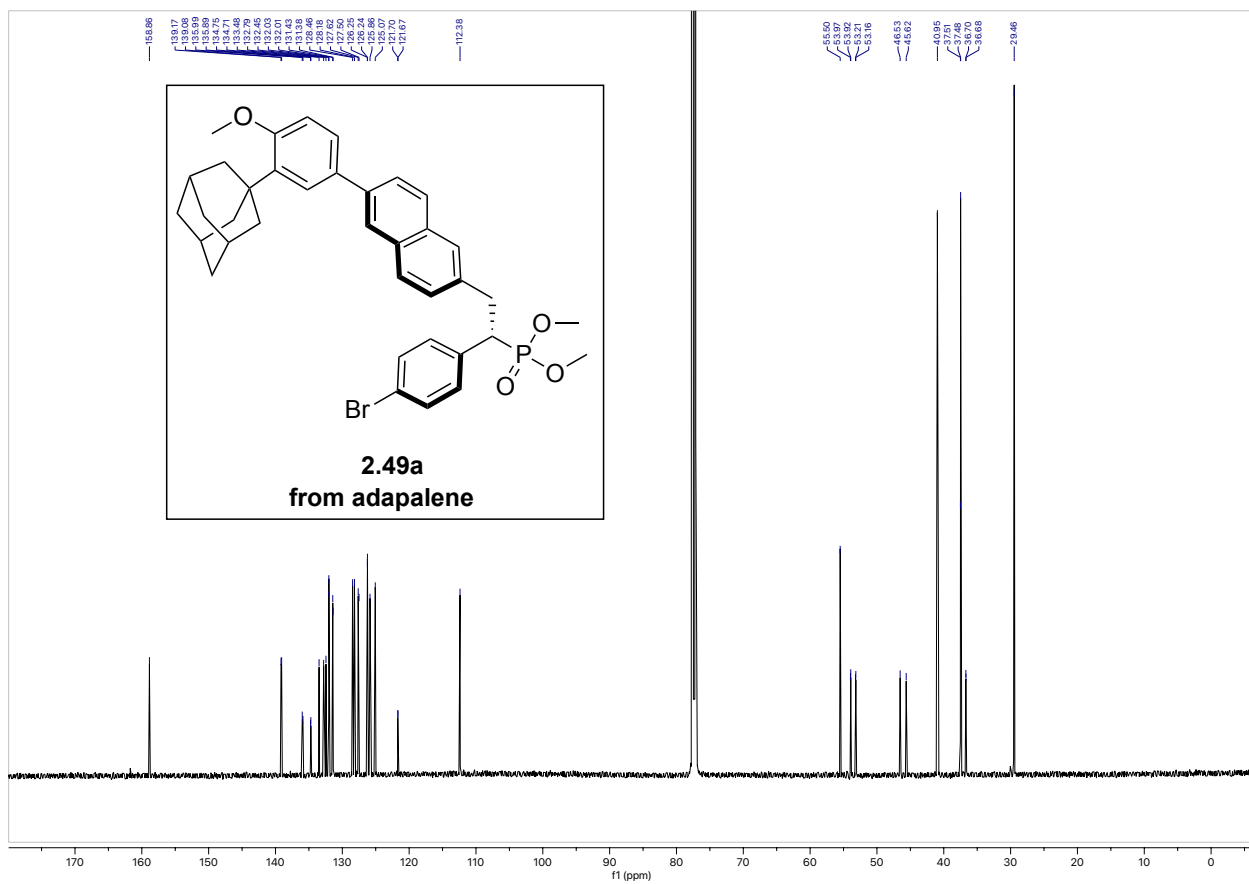


¹³C{¹H} NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.47k**.

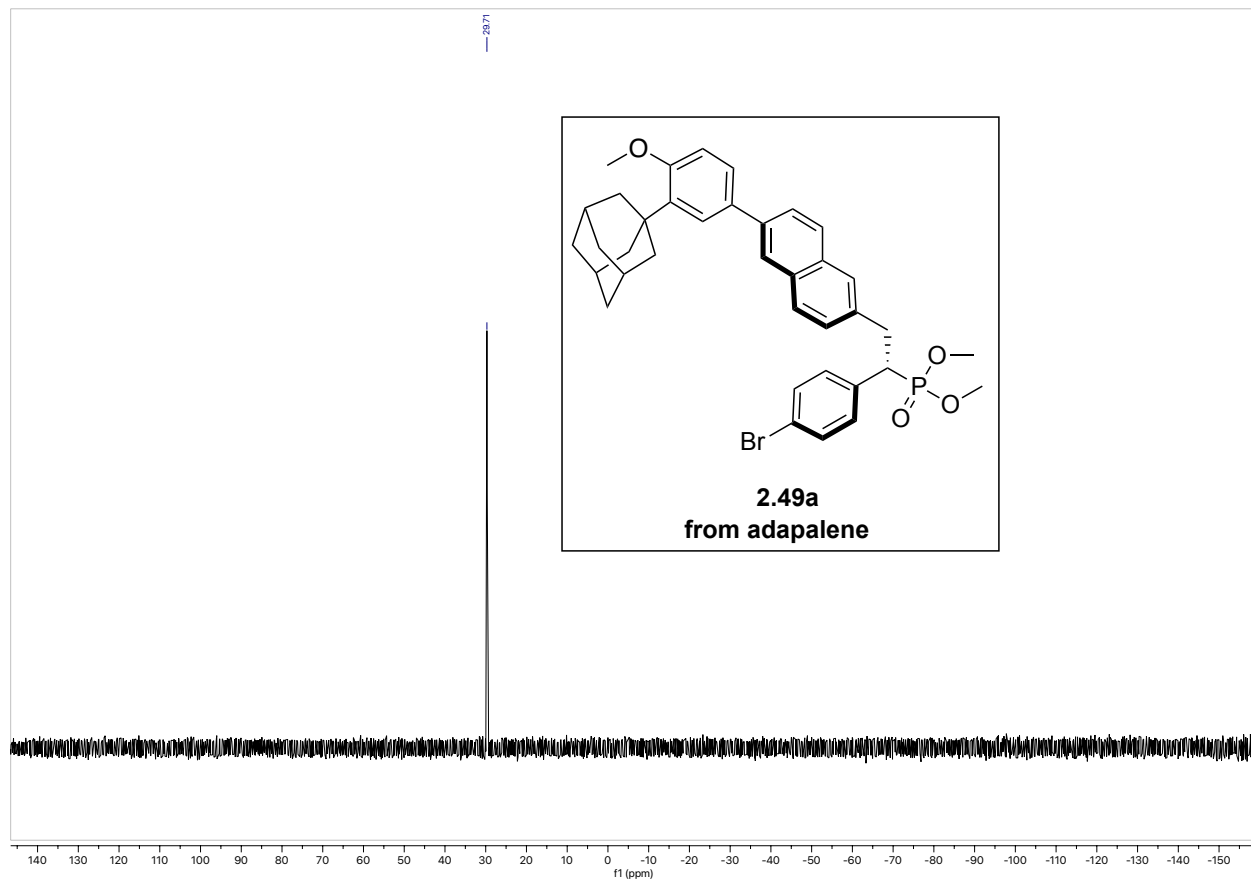


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.47k**.

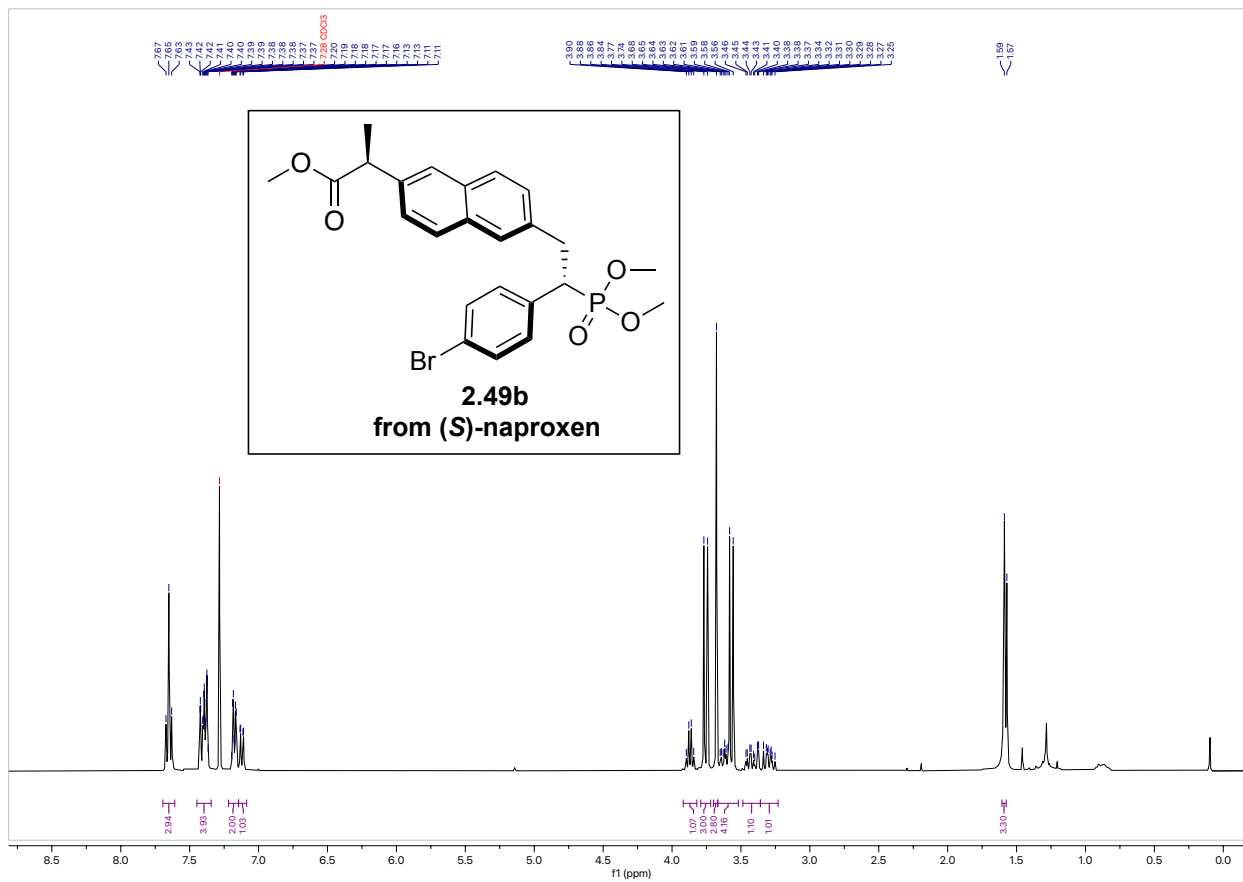




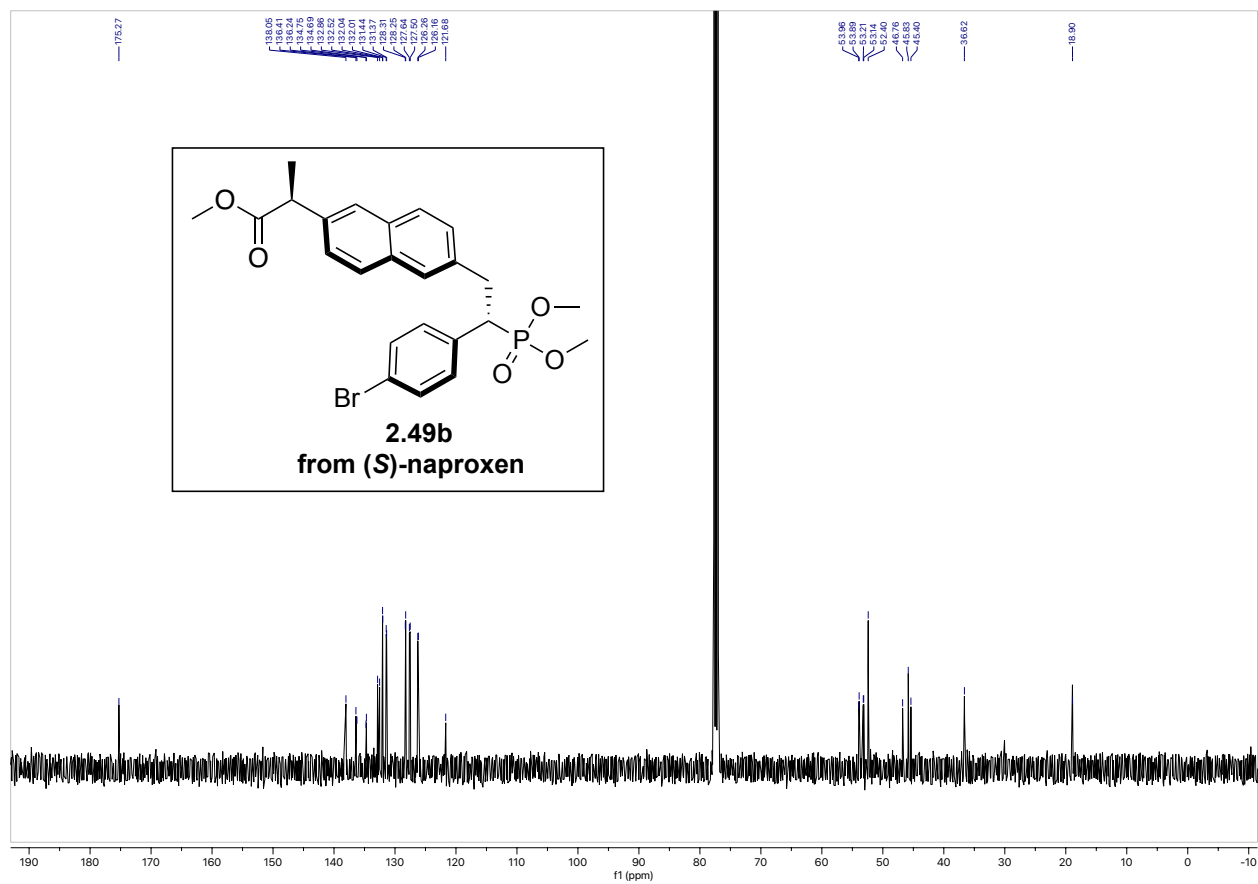
¹³C{¹H} NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.49a**.



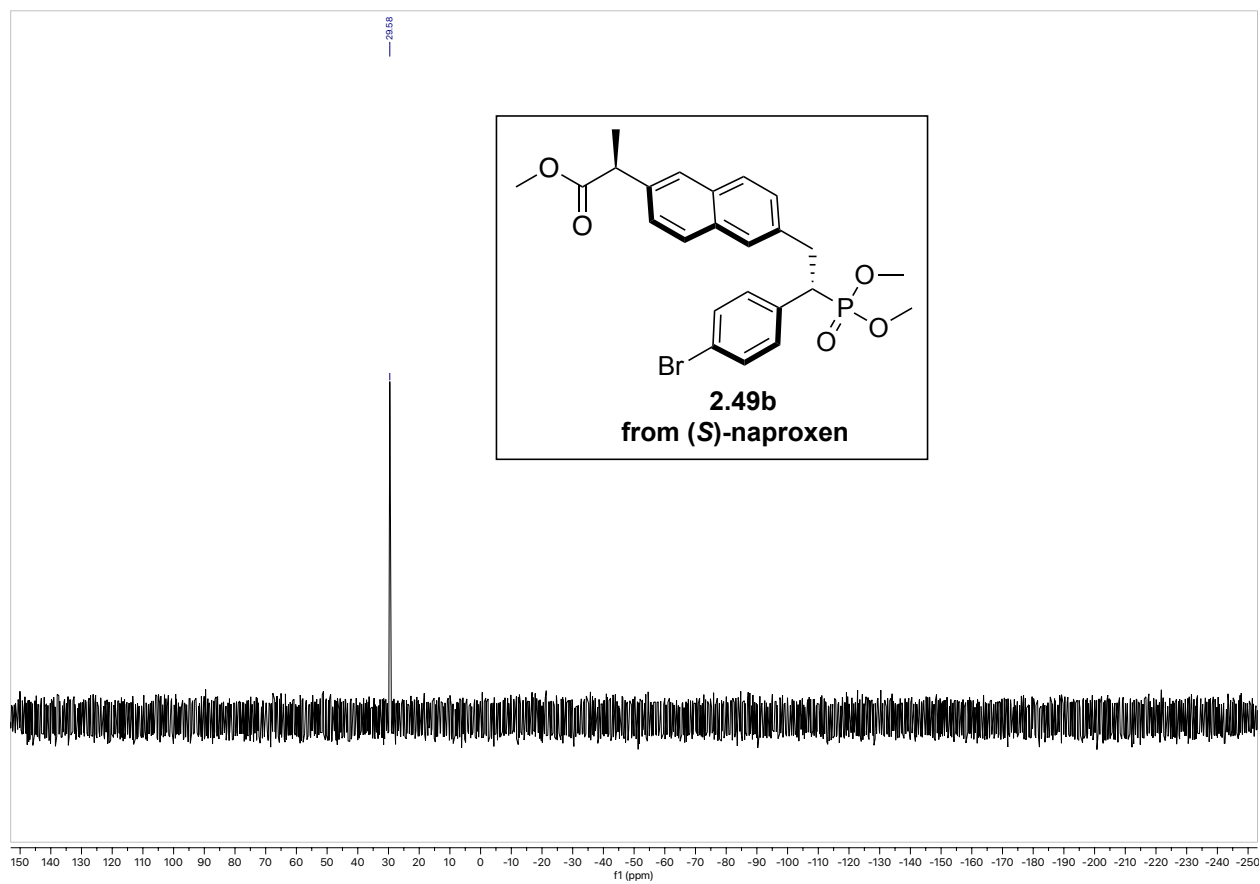
^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.49a**.



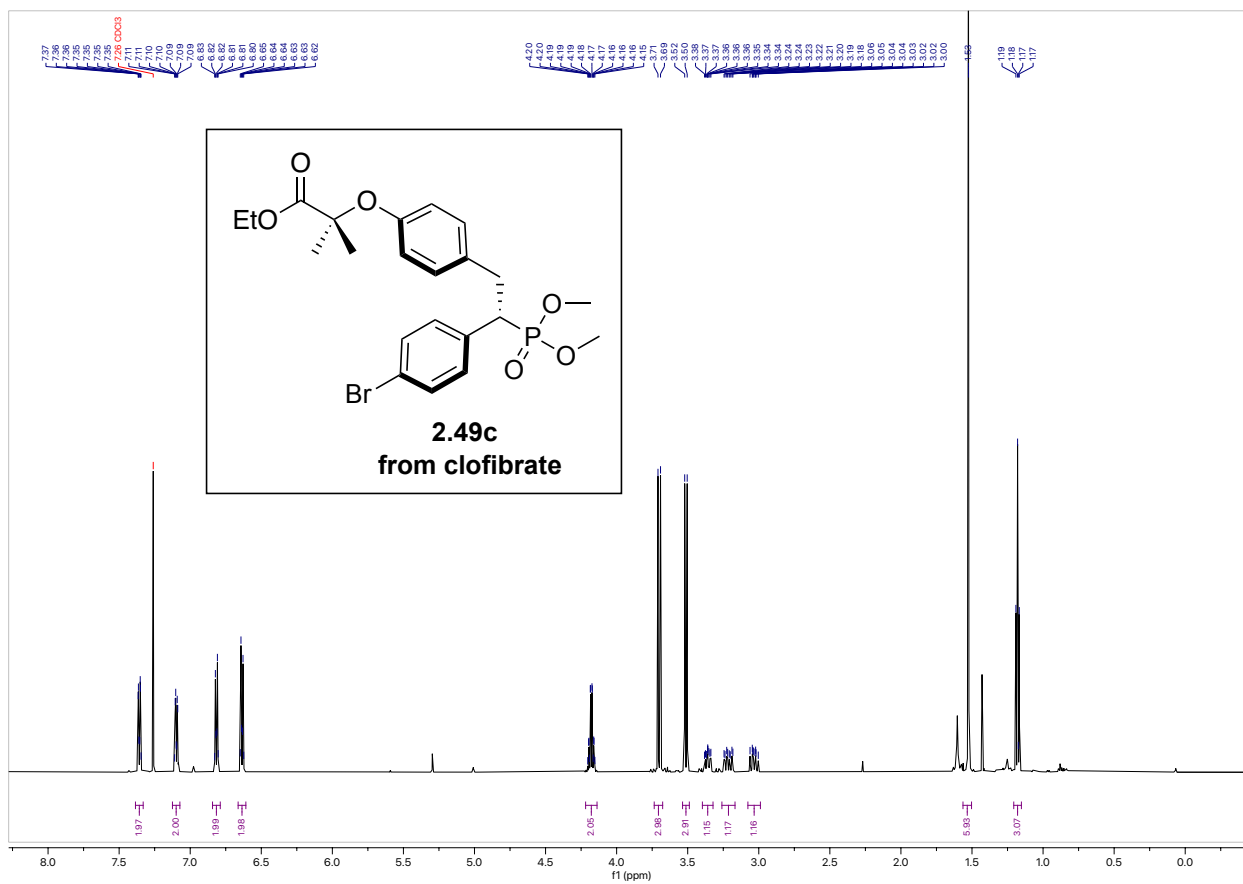
^1H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.49b**.



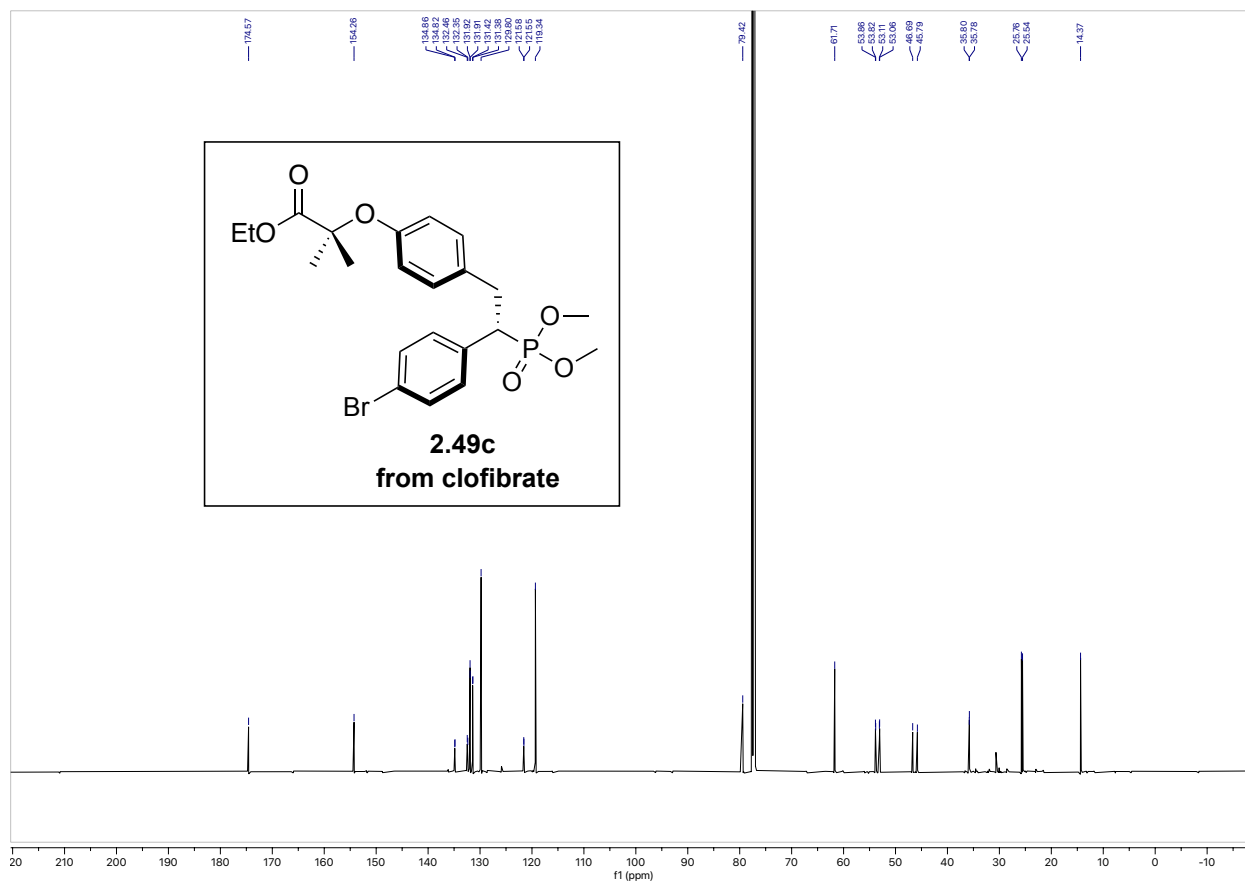
¹³C{¹H} NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.49b**.



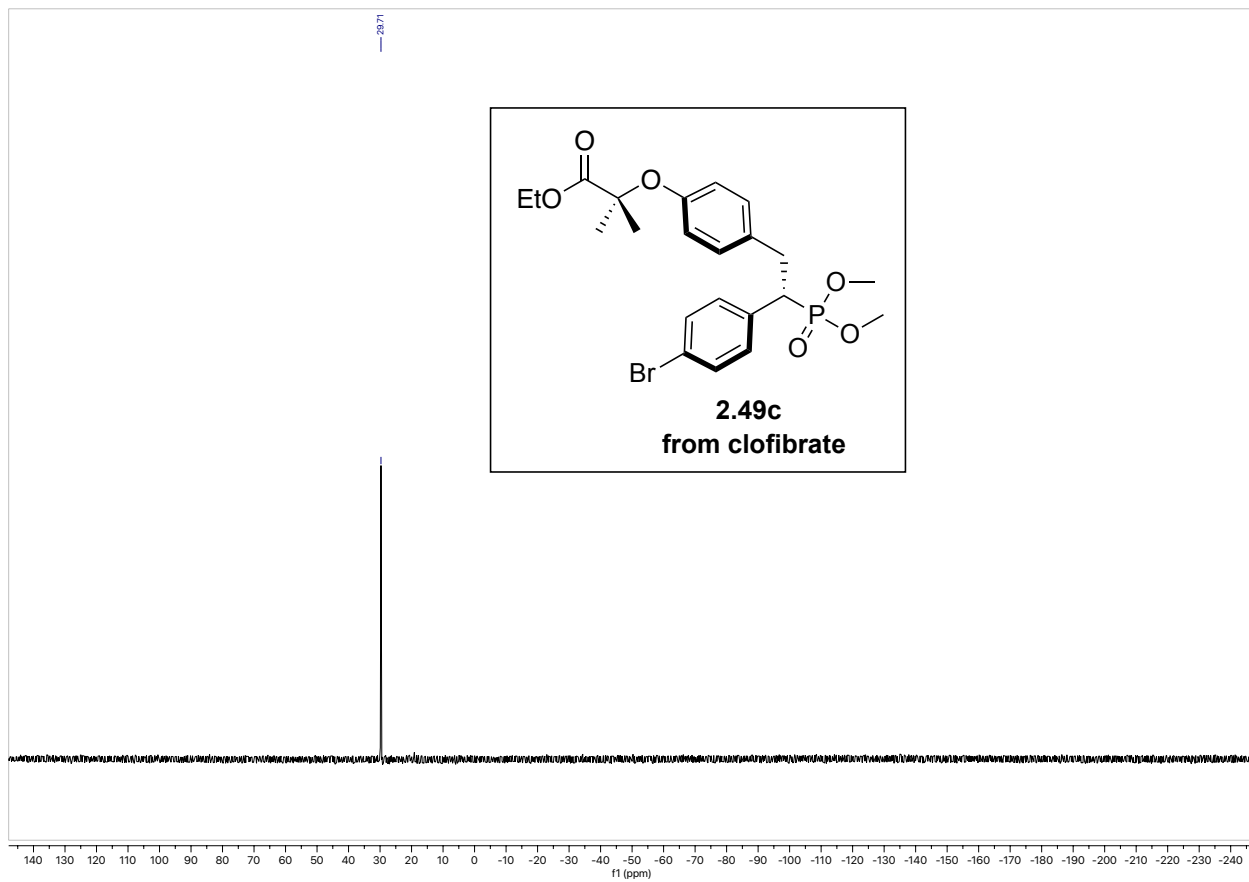
^{31}P NMR spectrum (162 MHz, Chloroform- d) of **2.49b**.



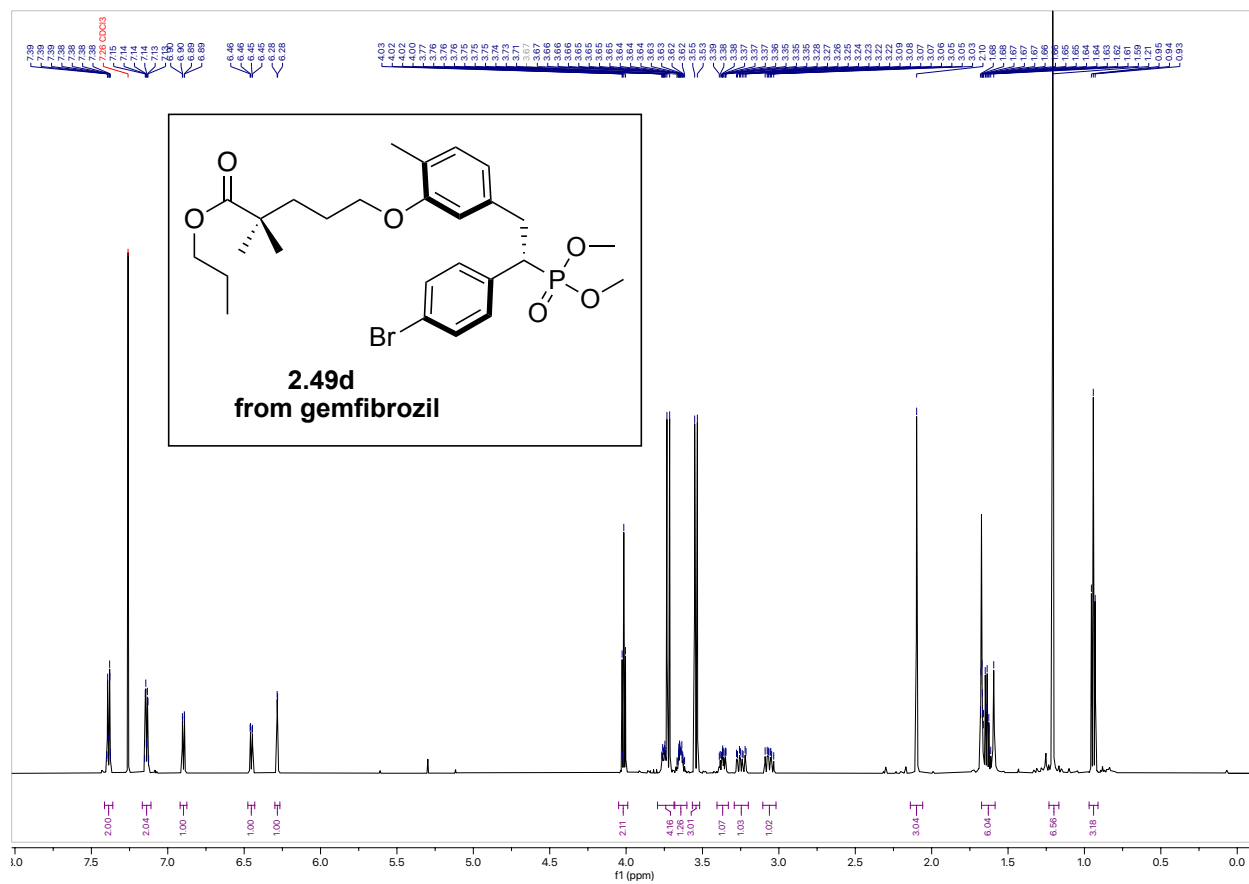
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.49c**.

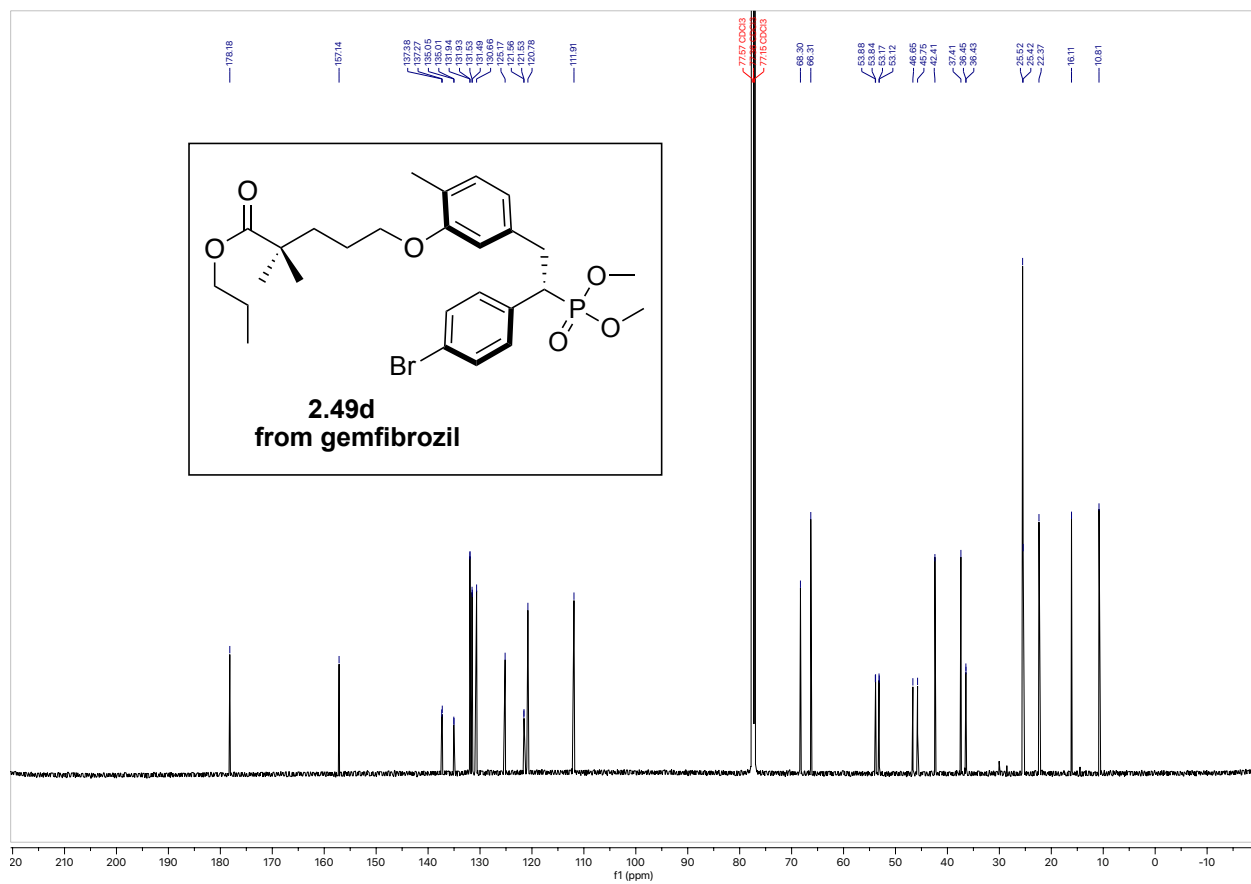


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.49c**.

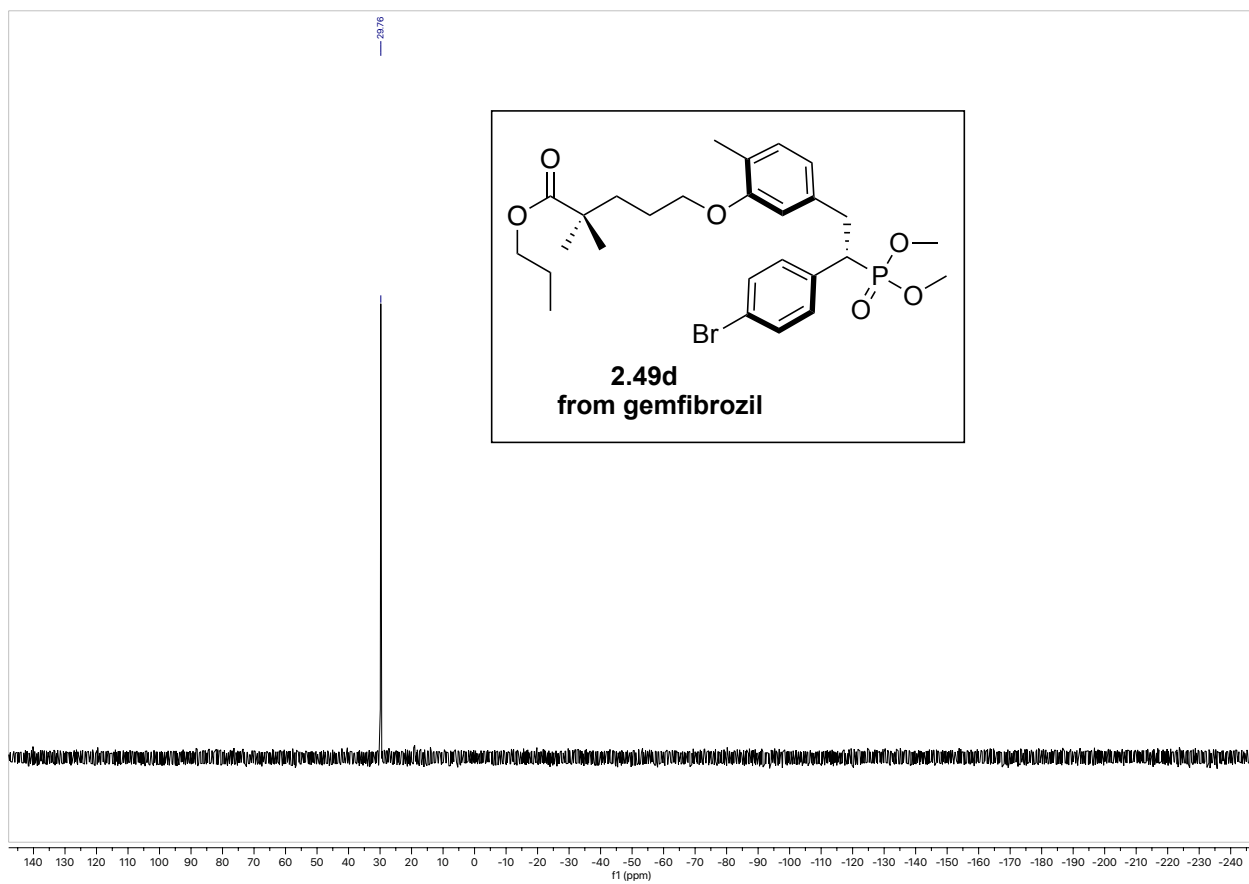


^{31}P NMR spectrum (243 MHz, Chloroform- d) of **2.49c**.

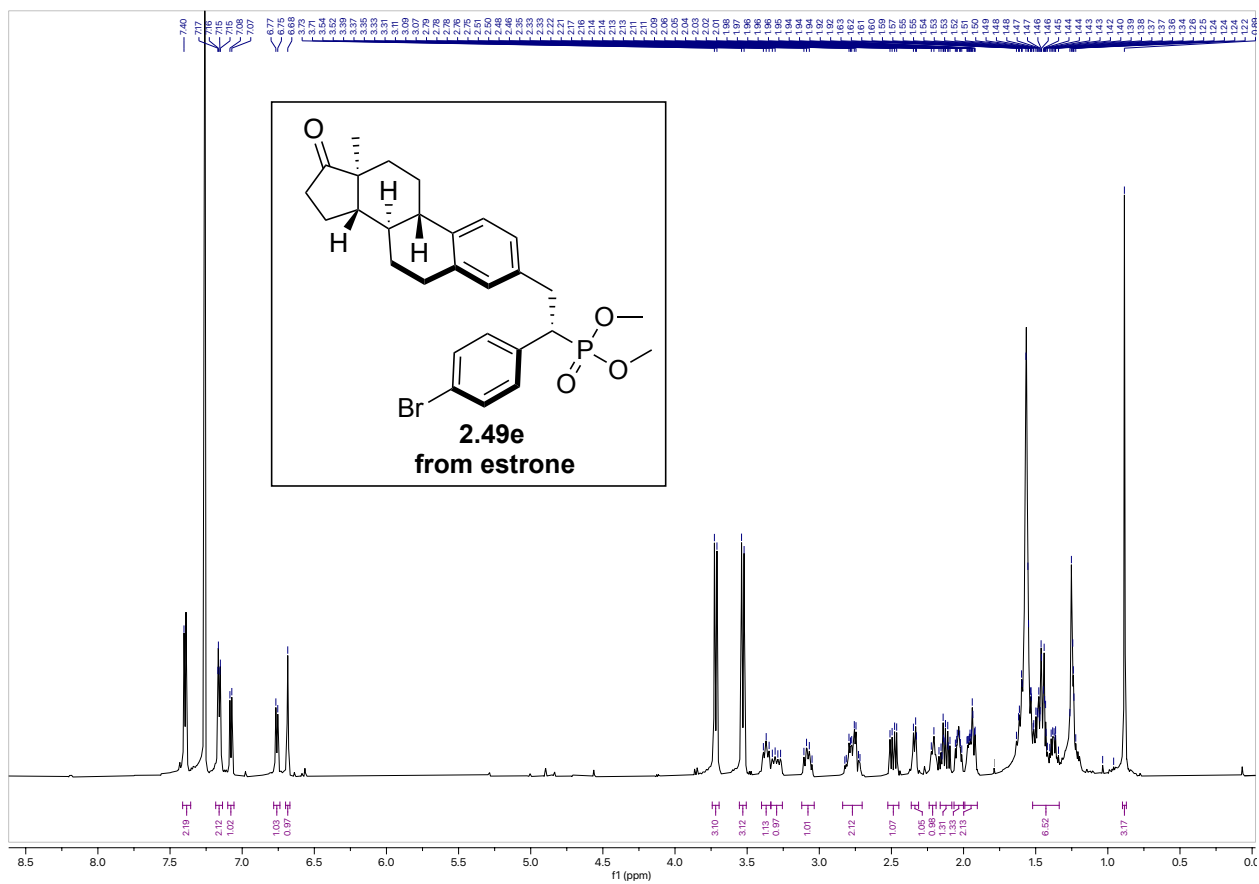




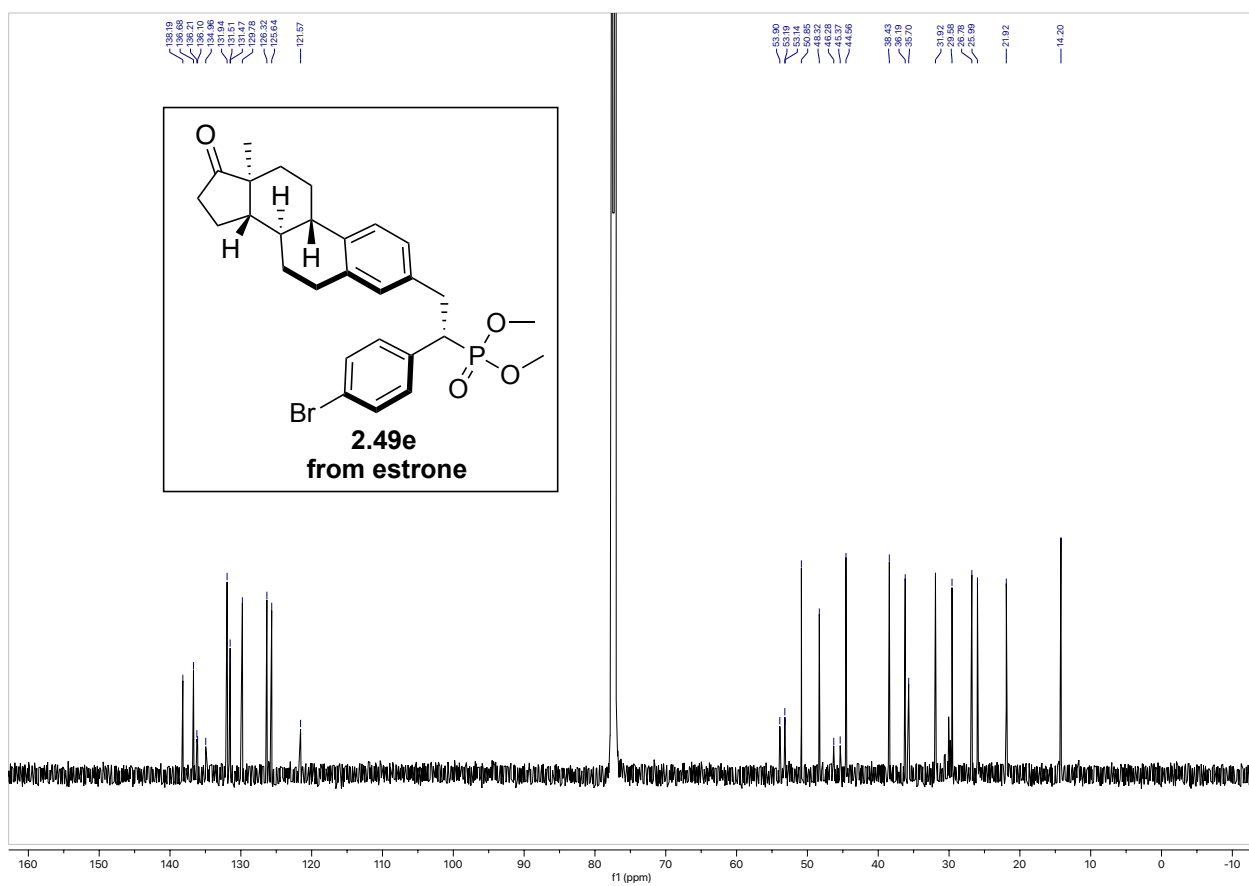
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.49d**.



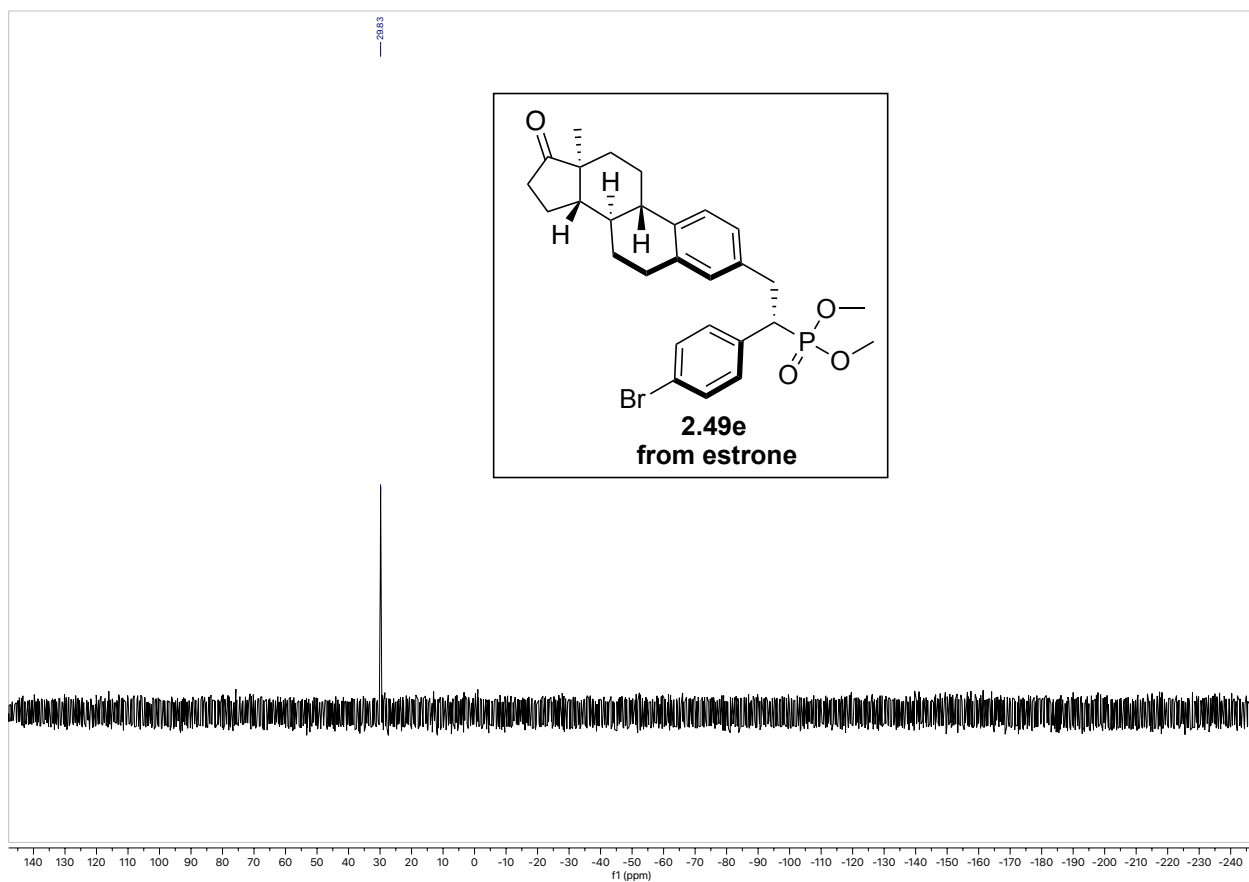
^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.49d**.



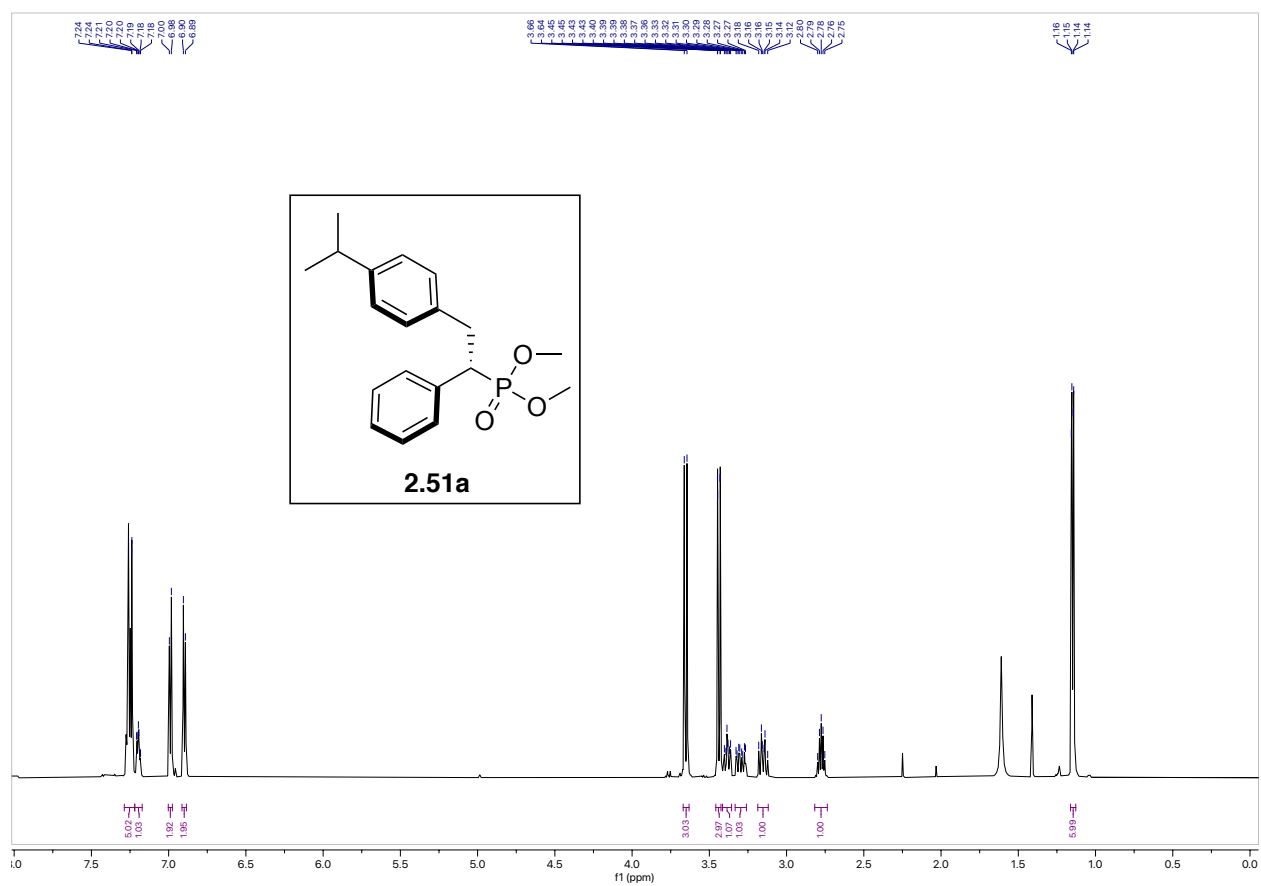
^1H NMR spectrum (600 MHz, CDCl_3) of **2.49e**.



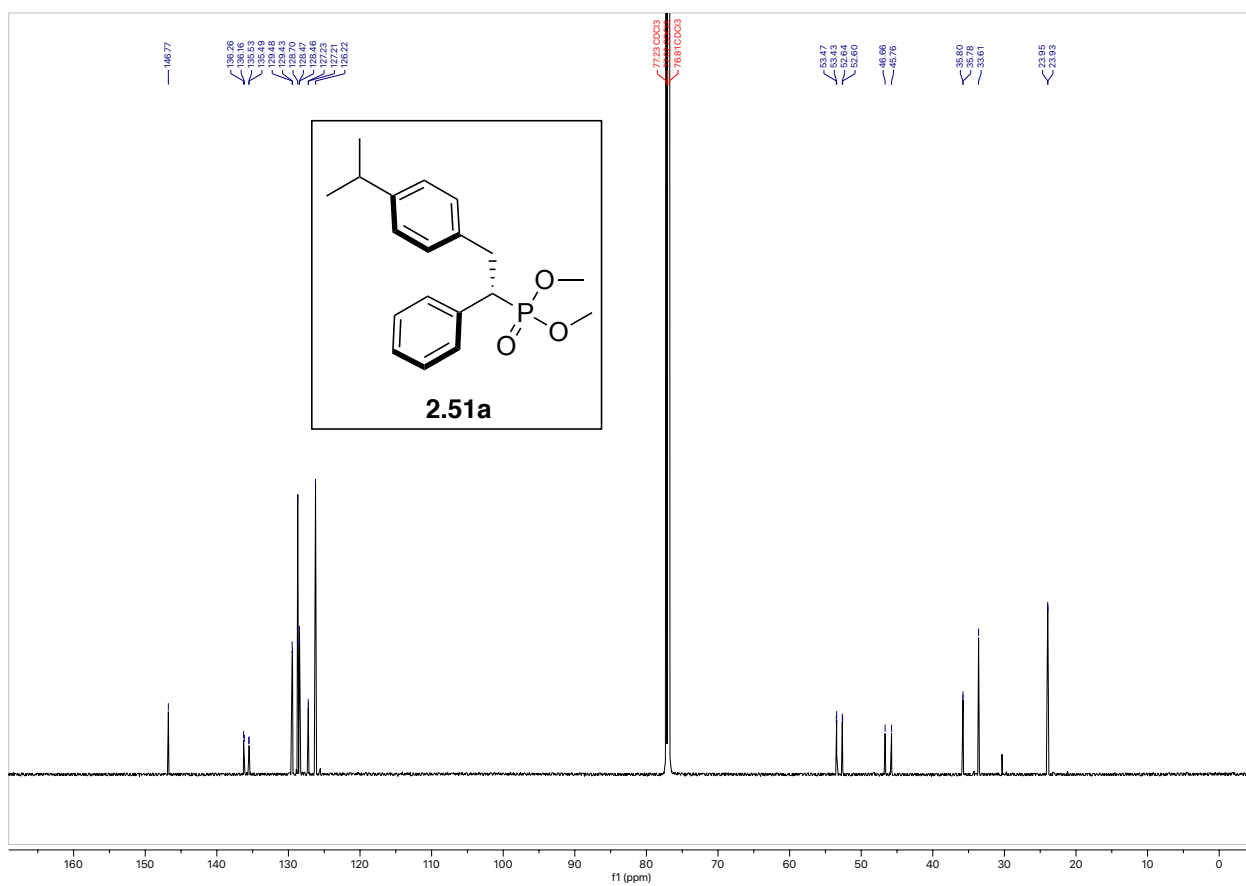
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.49e**.

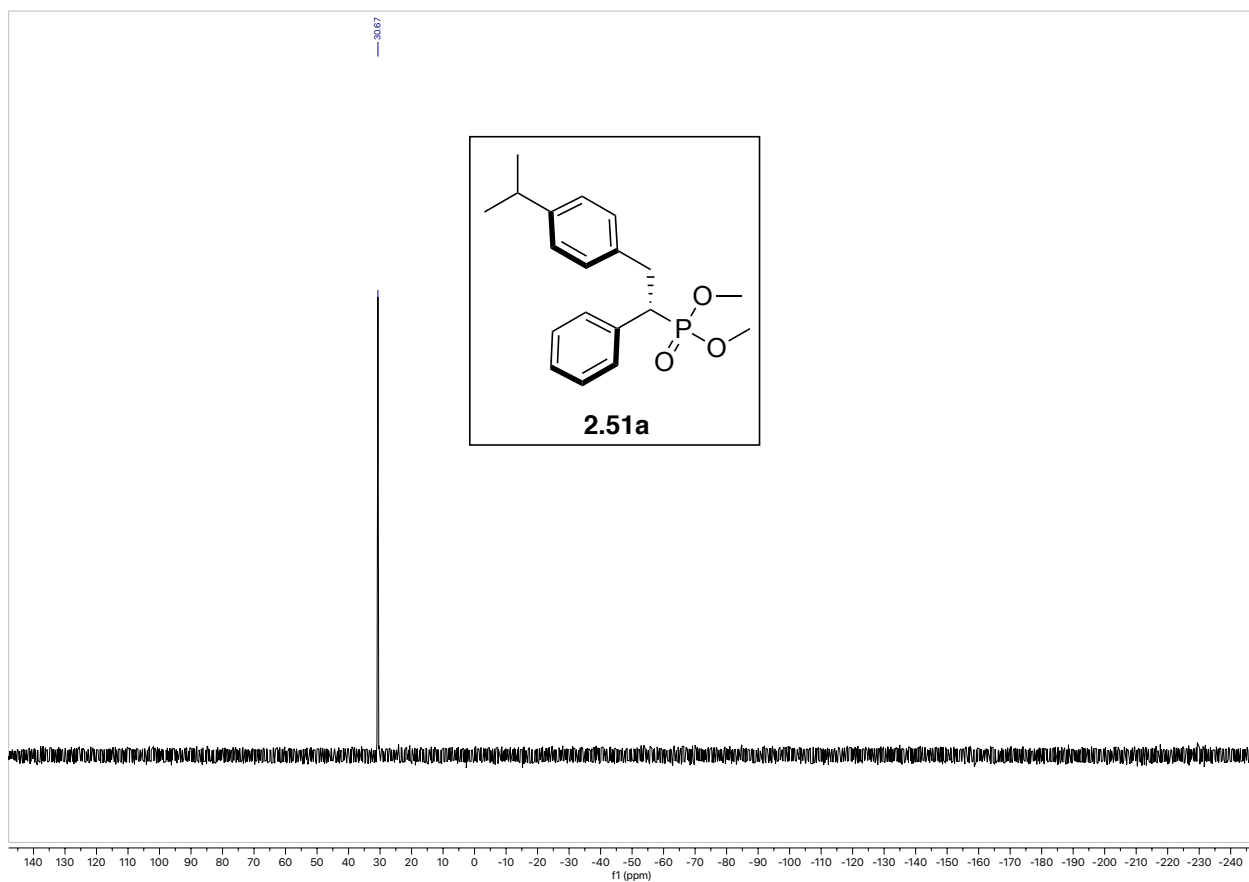


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.49e**.

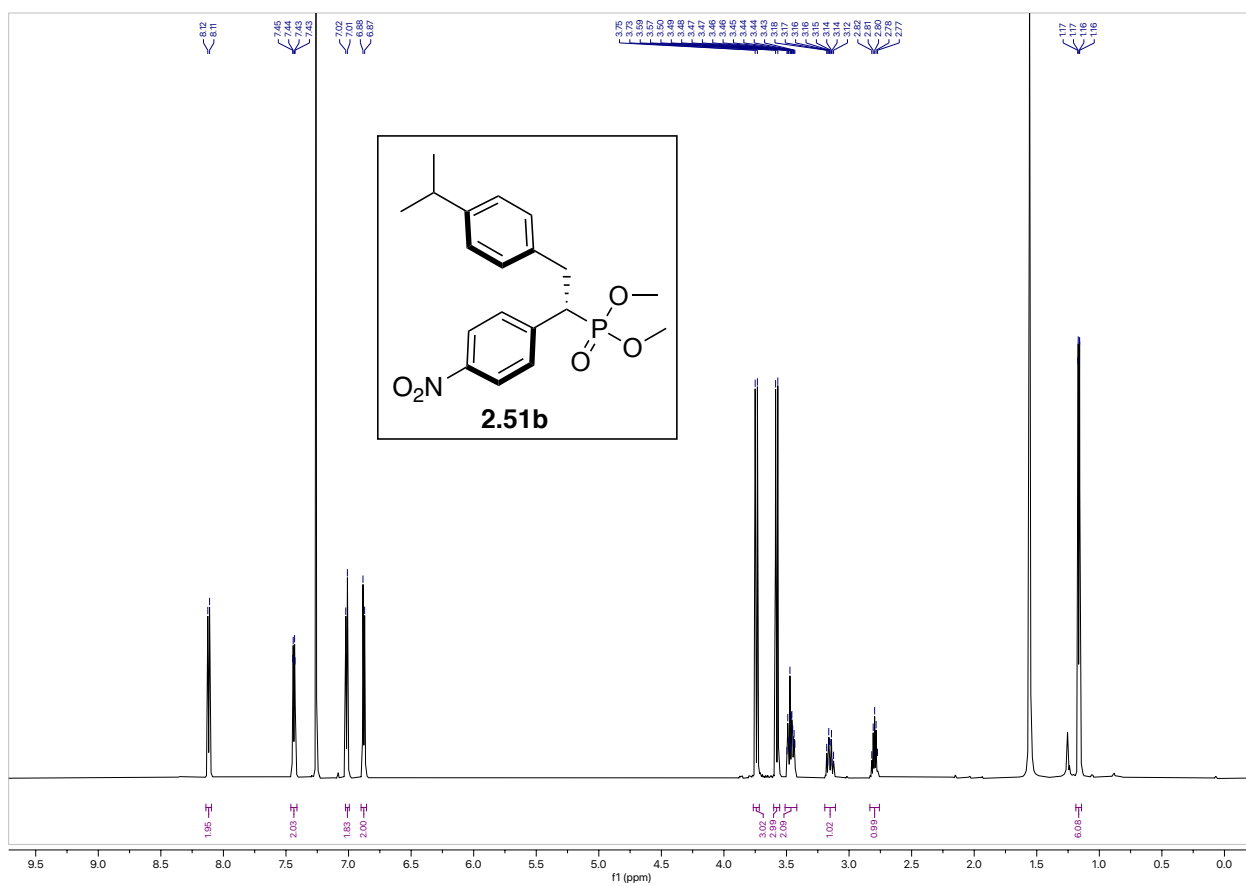


¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.51a**.

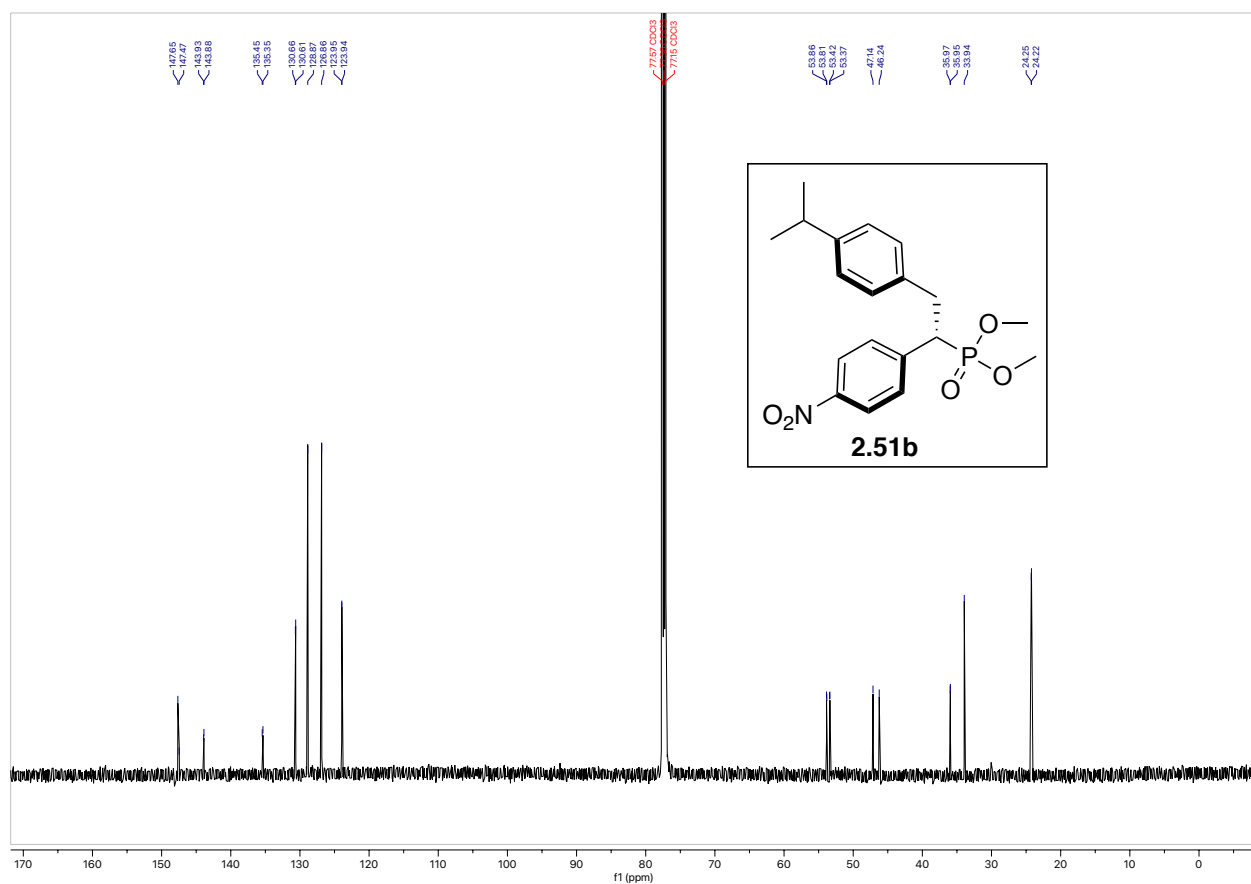




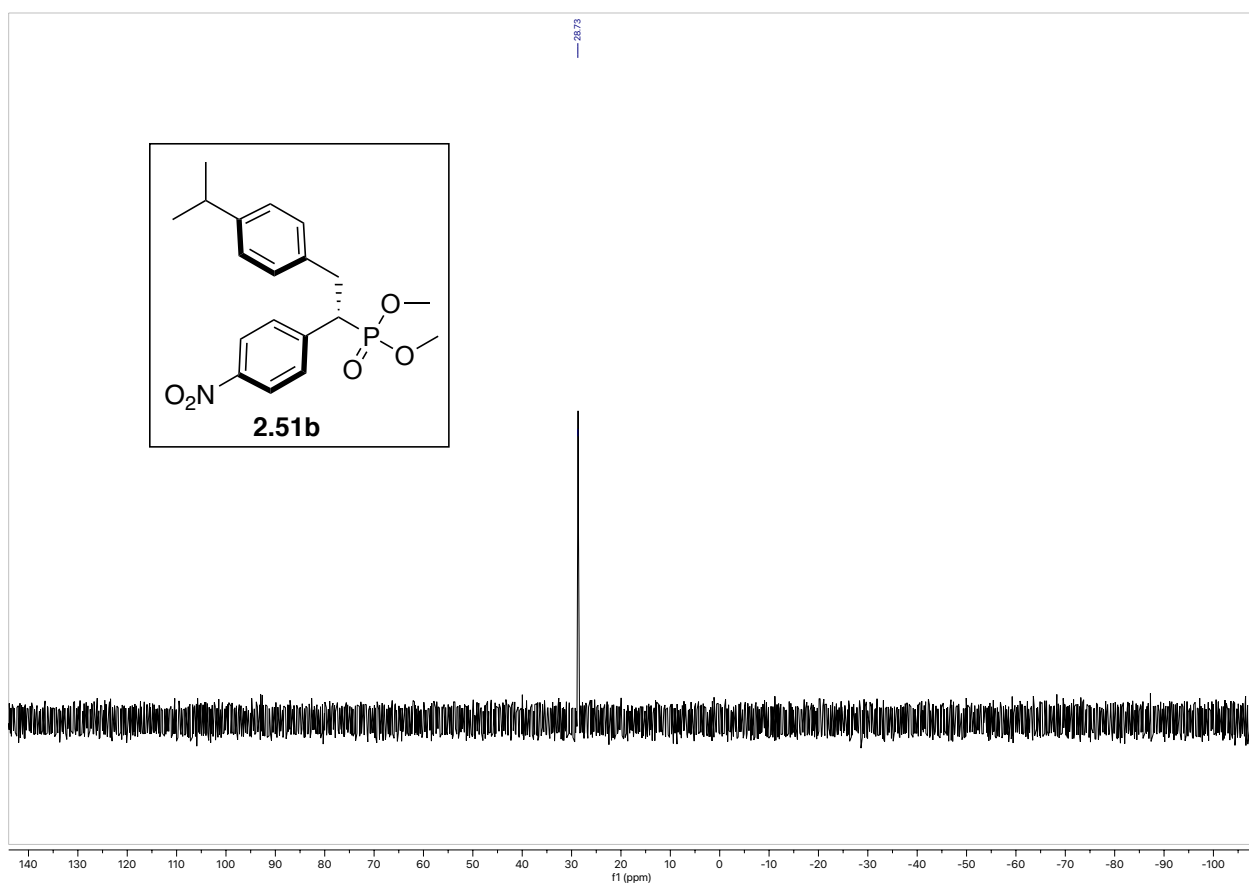
^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.51a**.



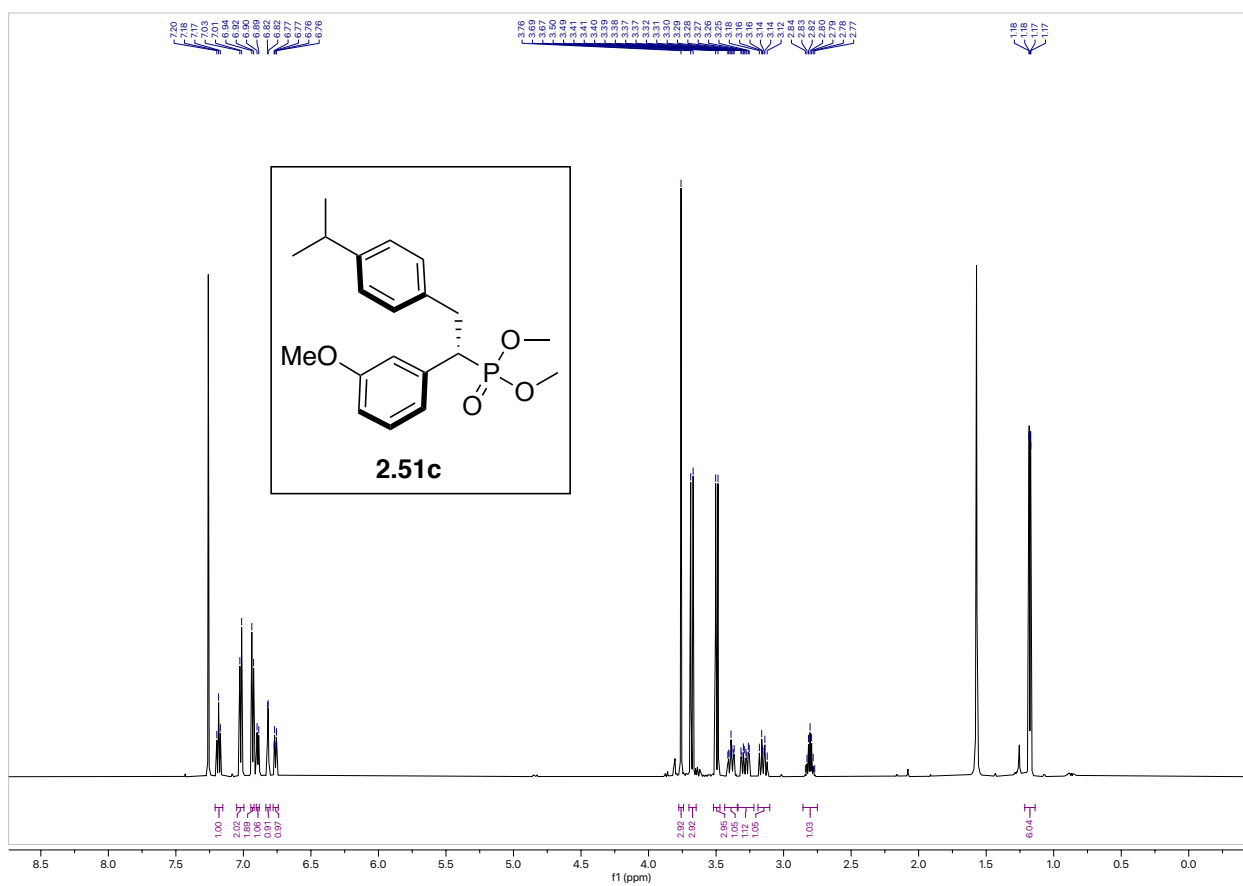
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.51b**.

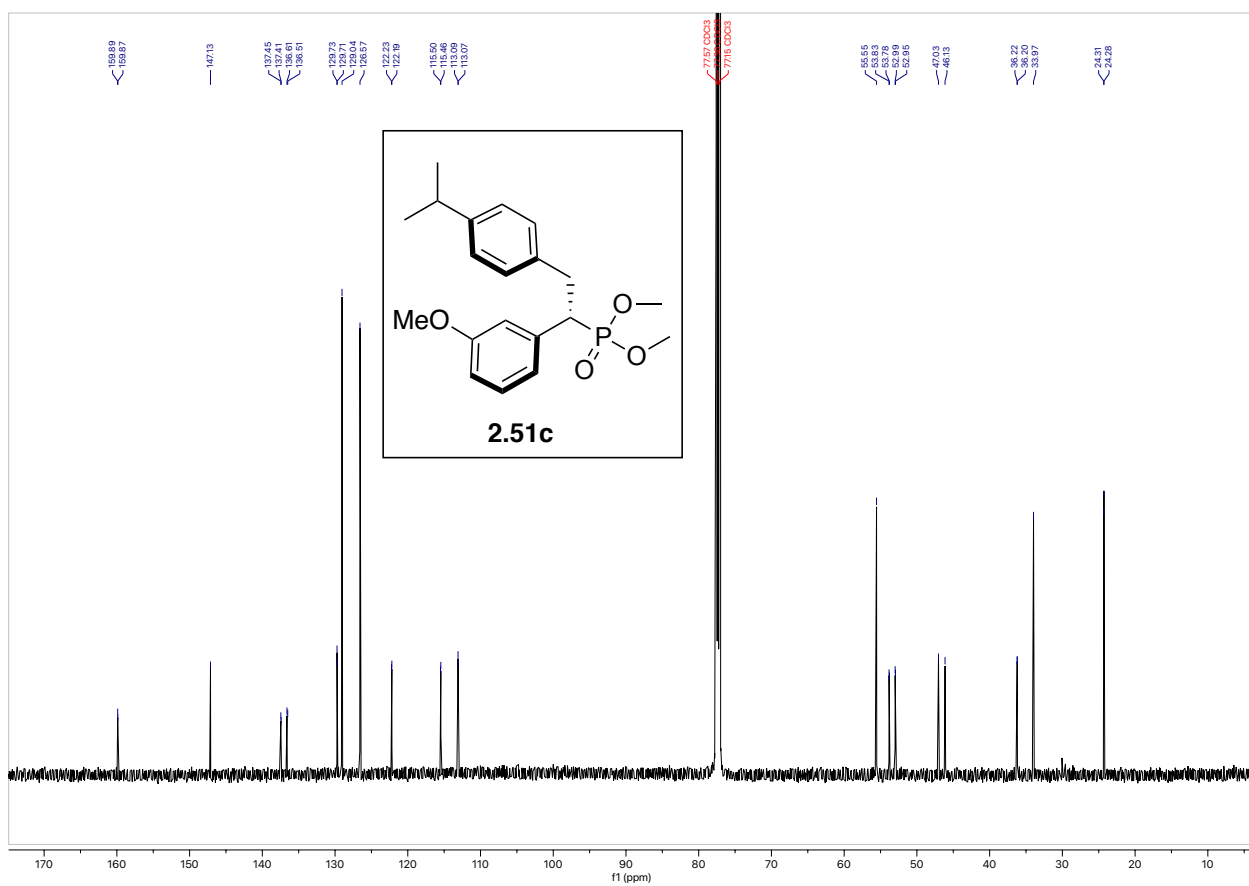


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.51b**.

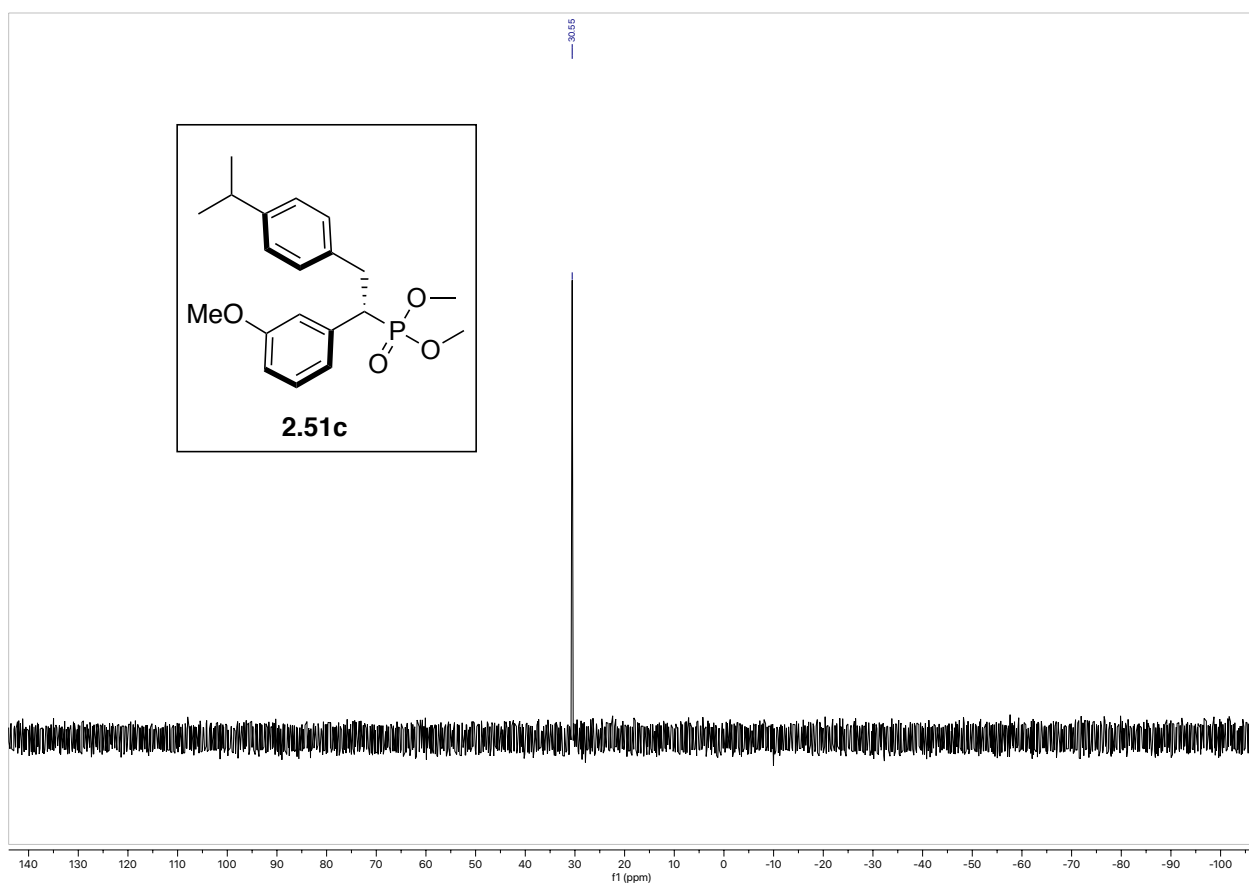


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.51b**.

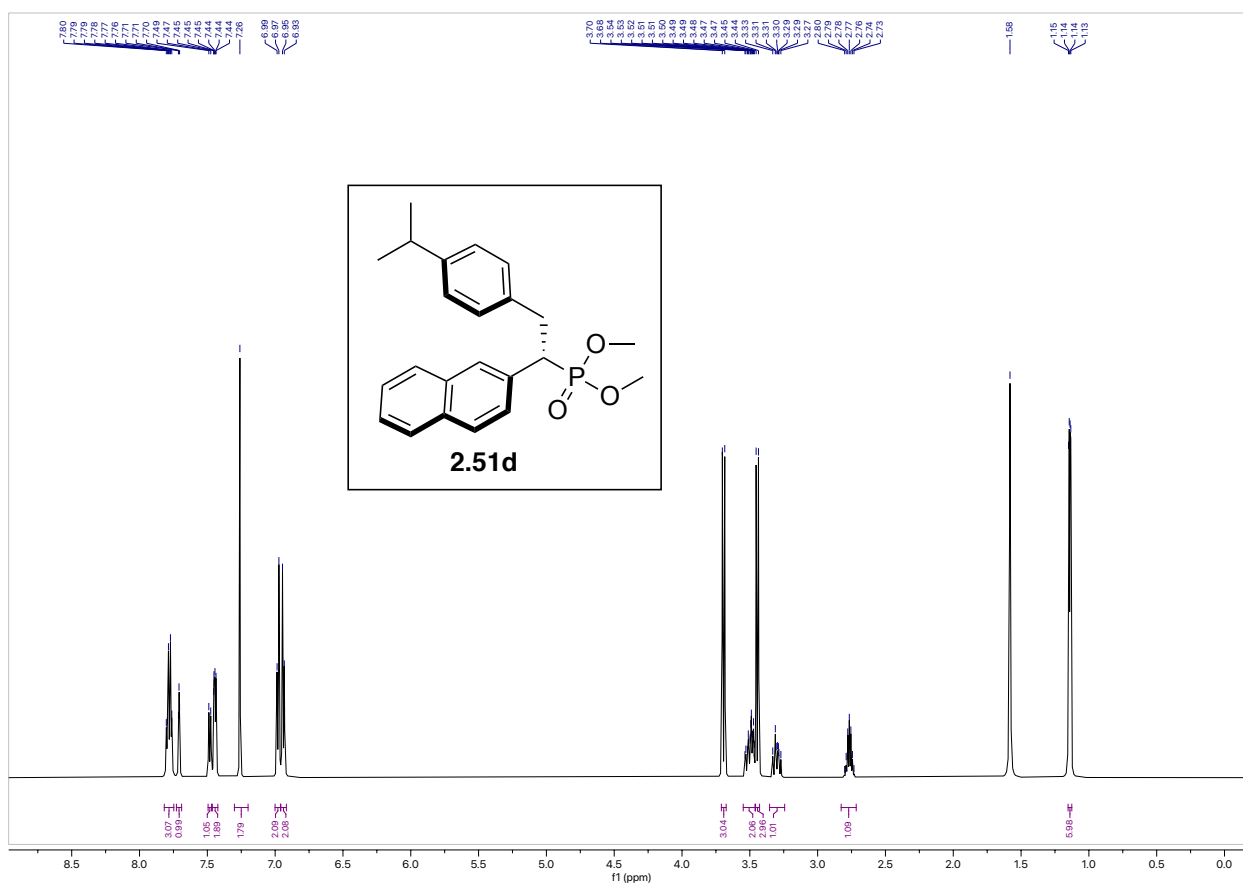




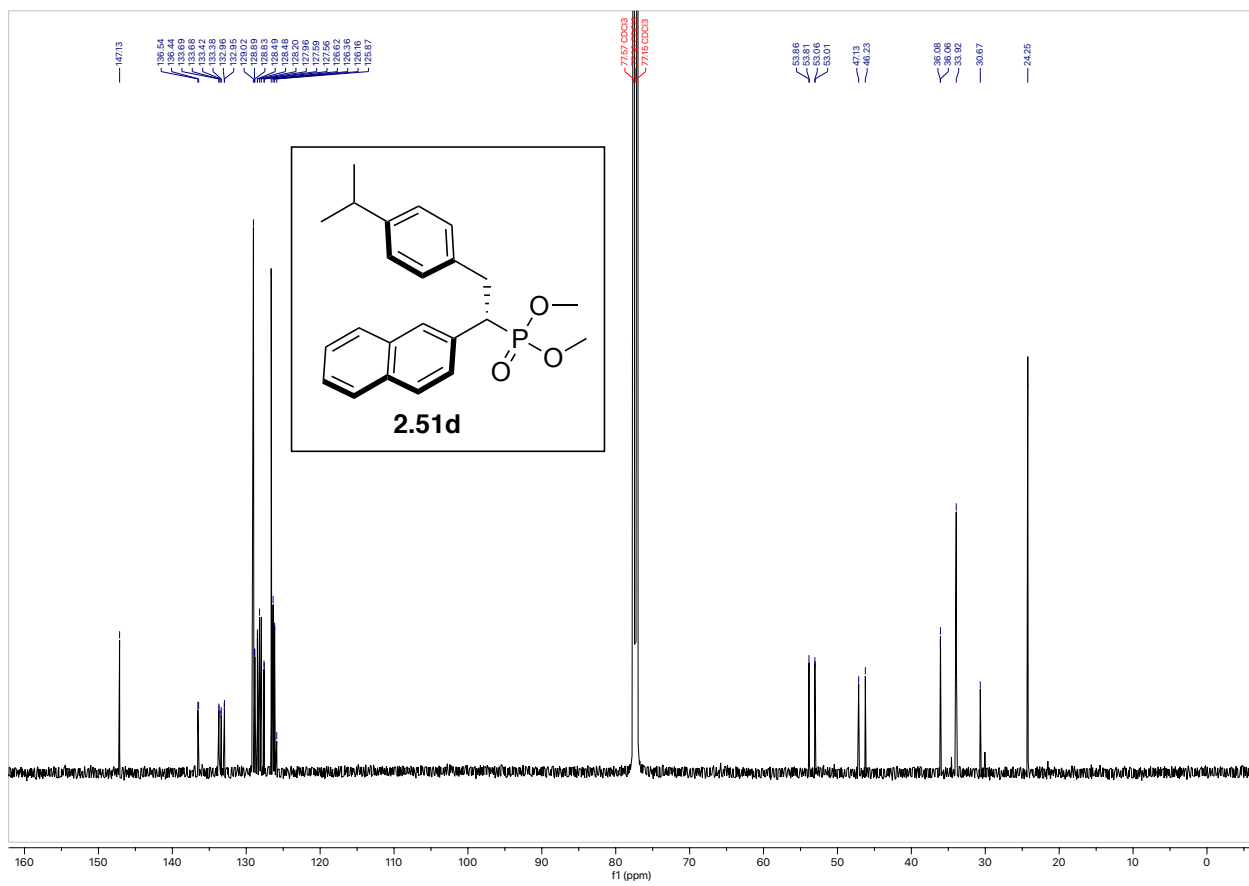
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.51c**.



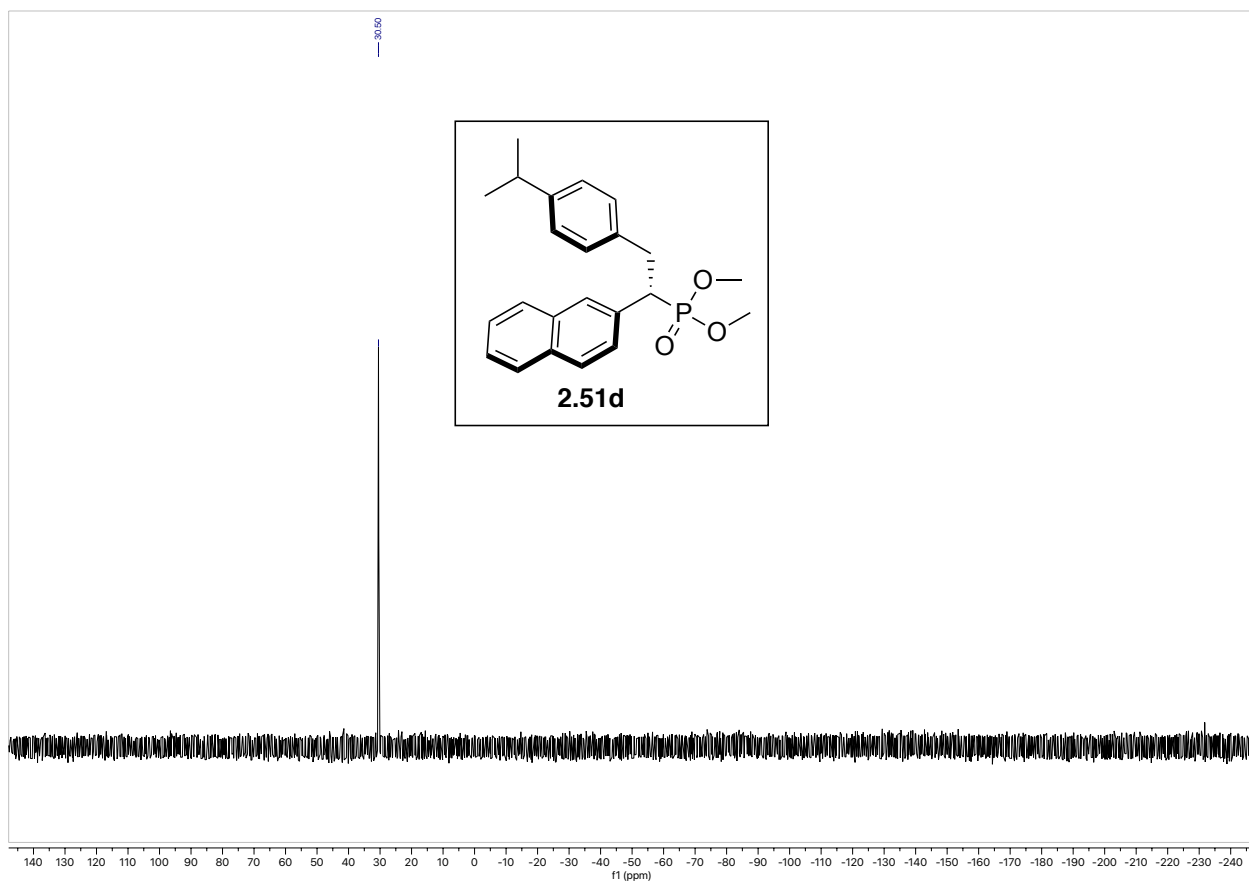
^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.51c**.



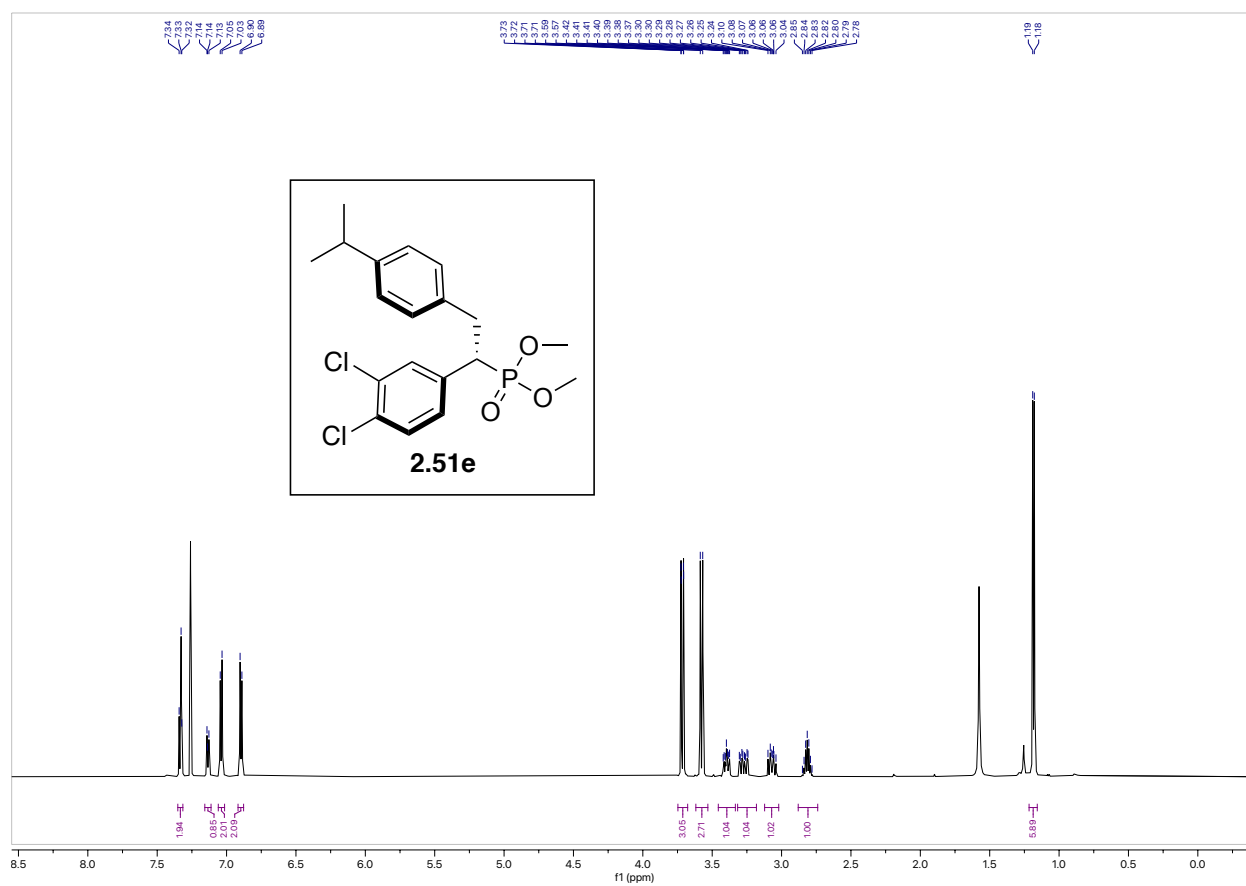
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **2.51d**.



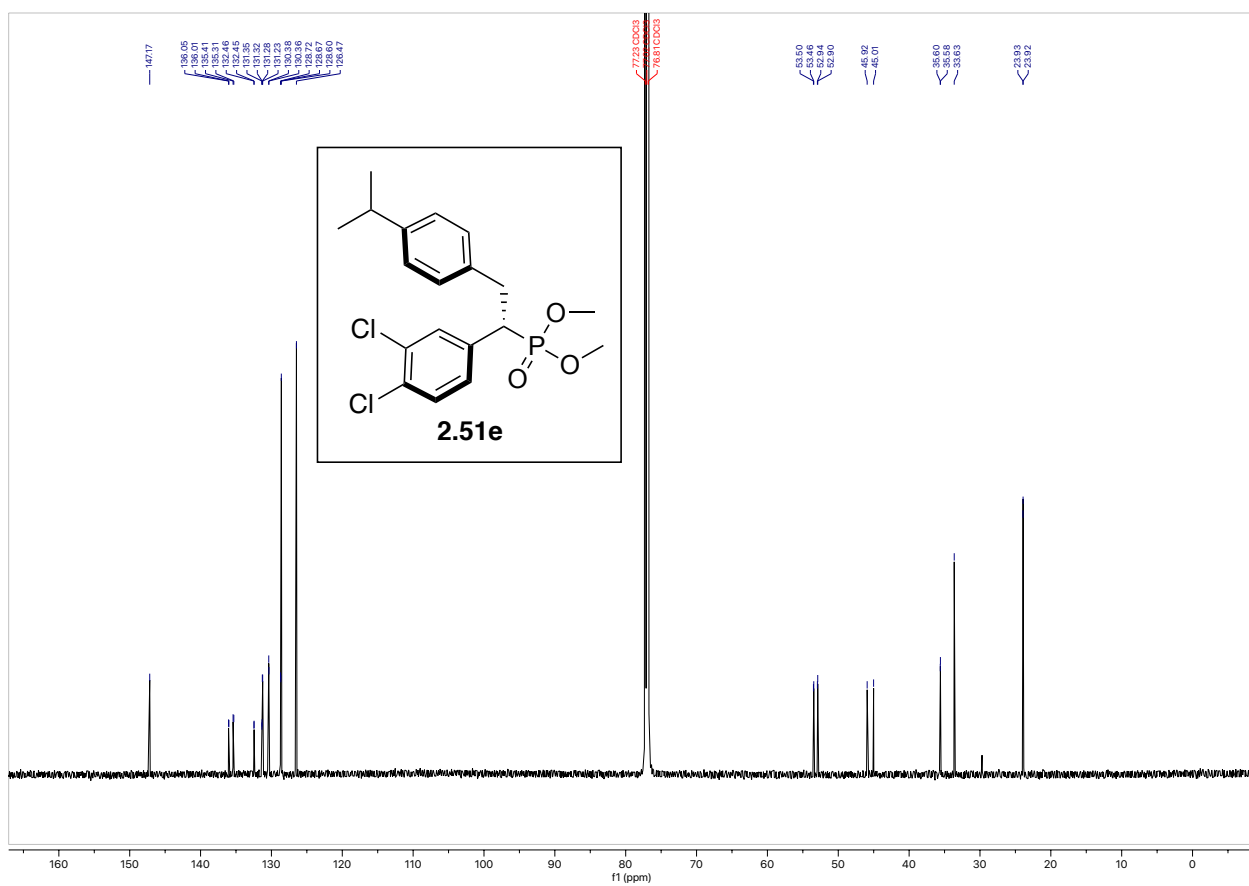
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **2.51d**.

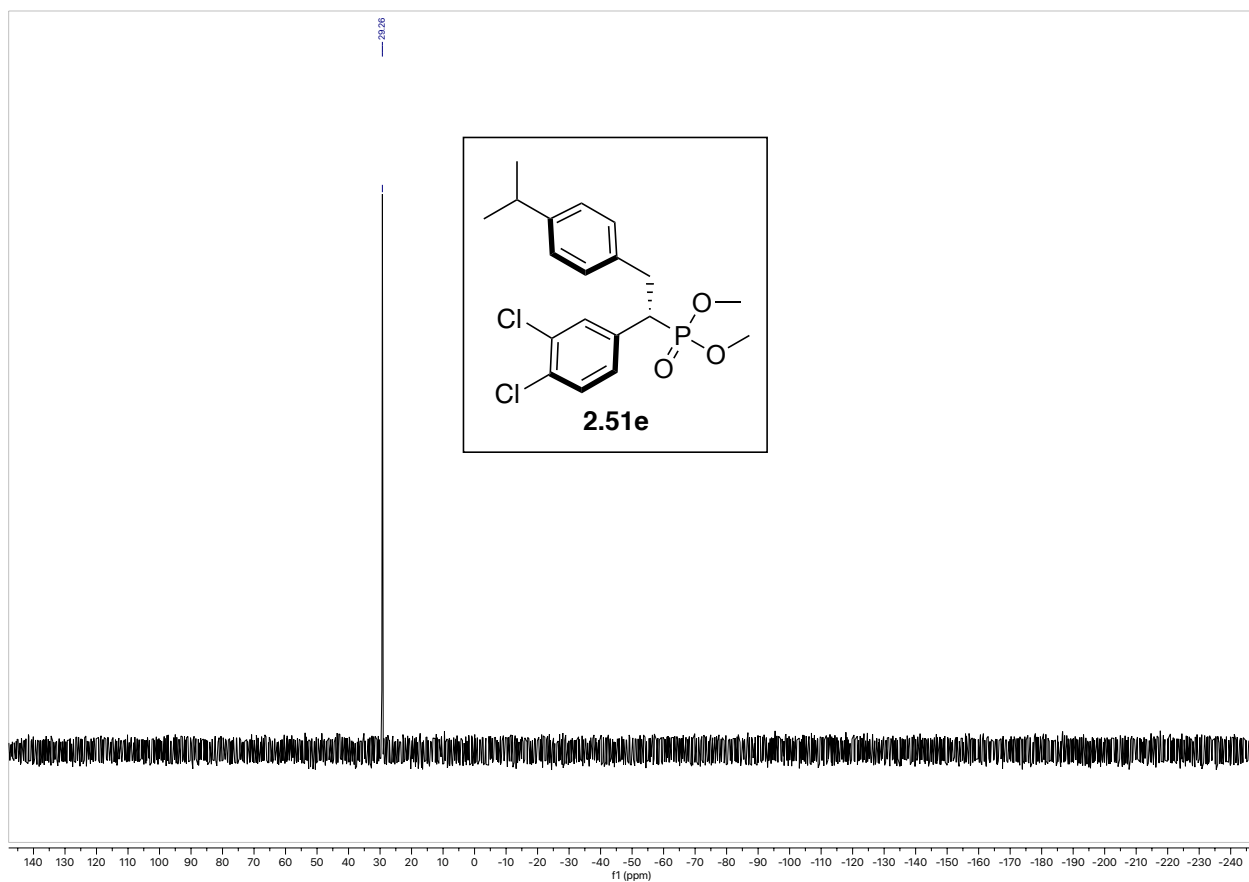


^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.51d**.

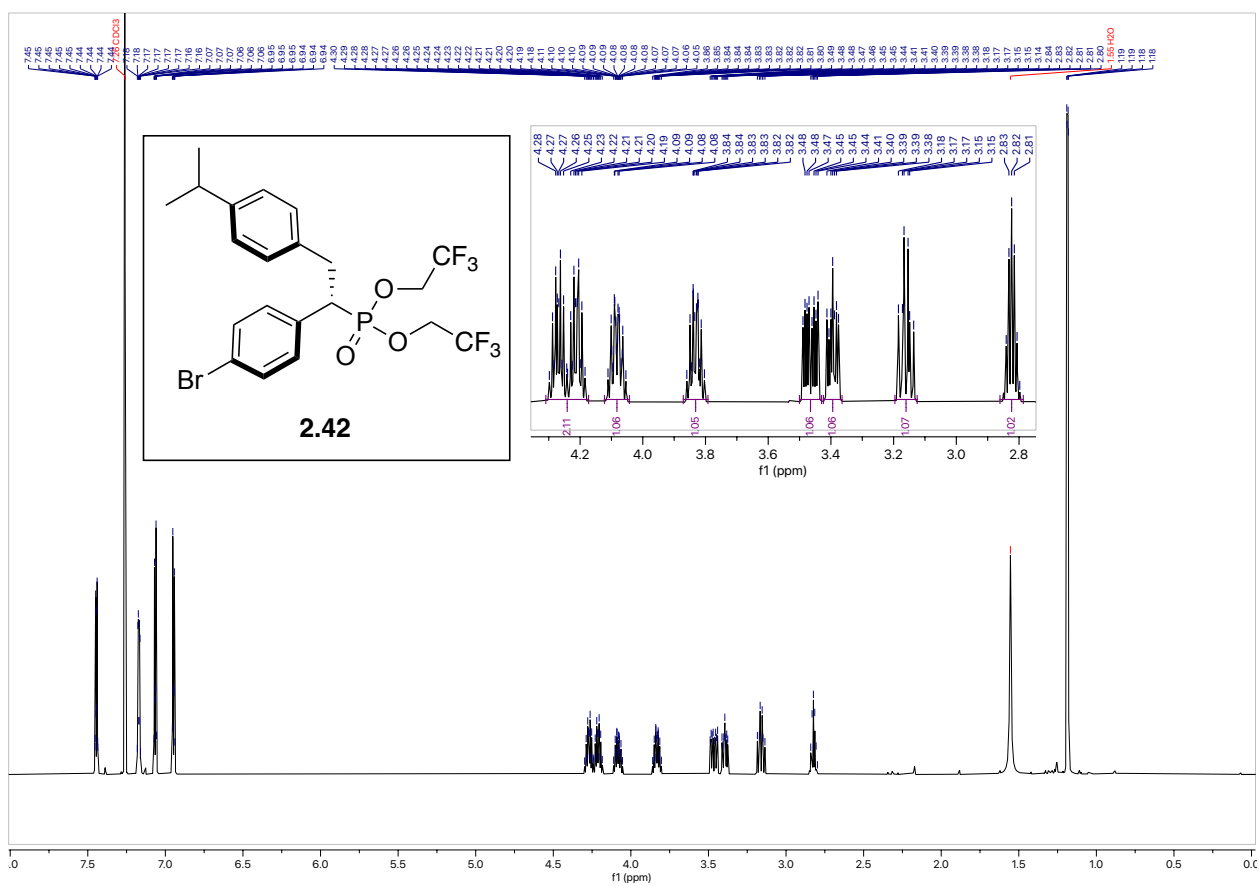


^1H NMR spectrum (600 MHz, CDCl_3) (s, 7.26 ppm) of **2.51e**.

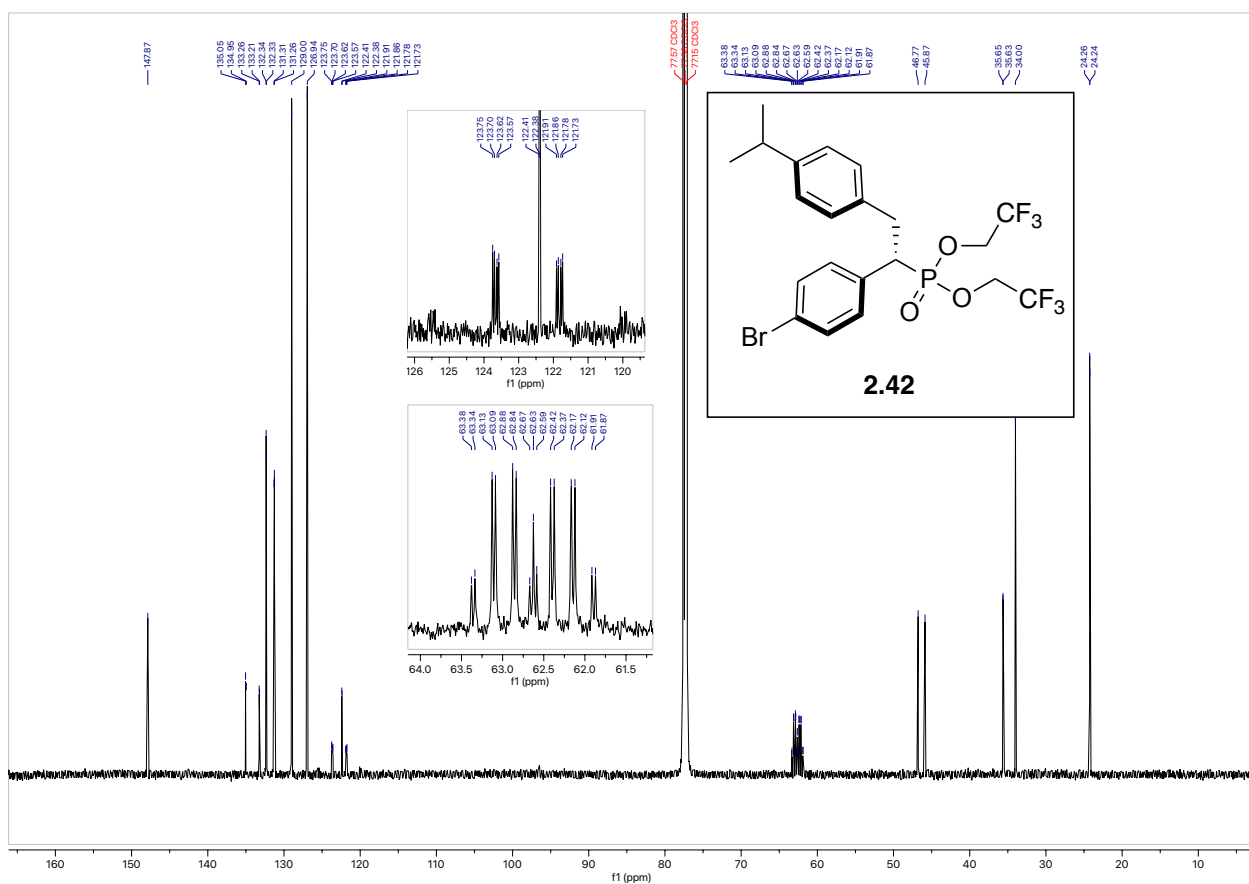




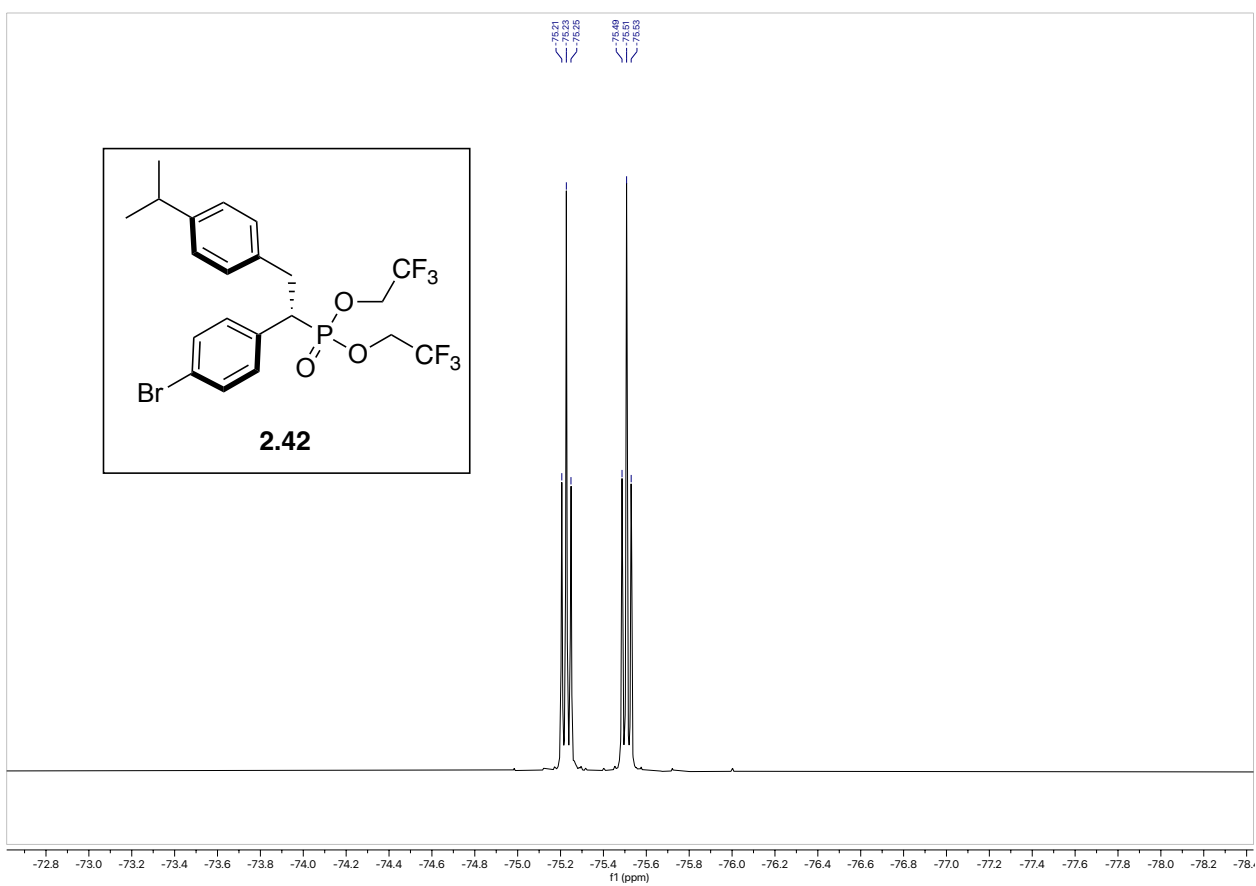
^{31}P NMR spectrum (243 MHz, Chloroform-*d*) of **2.51e**.



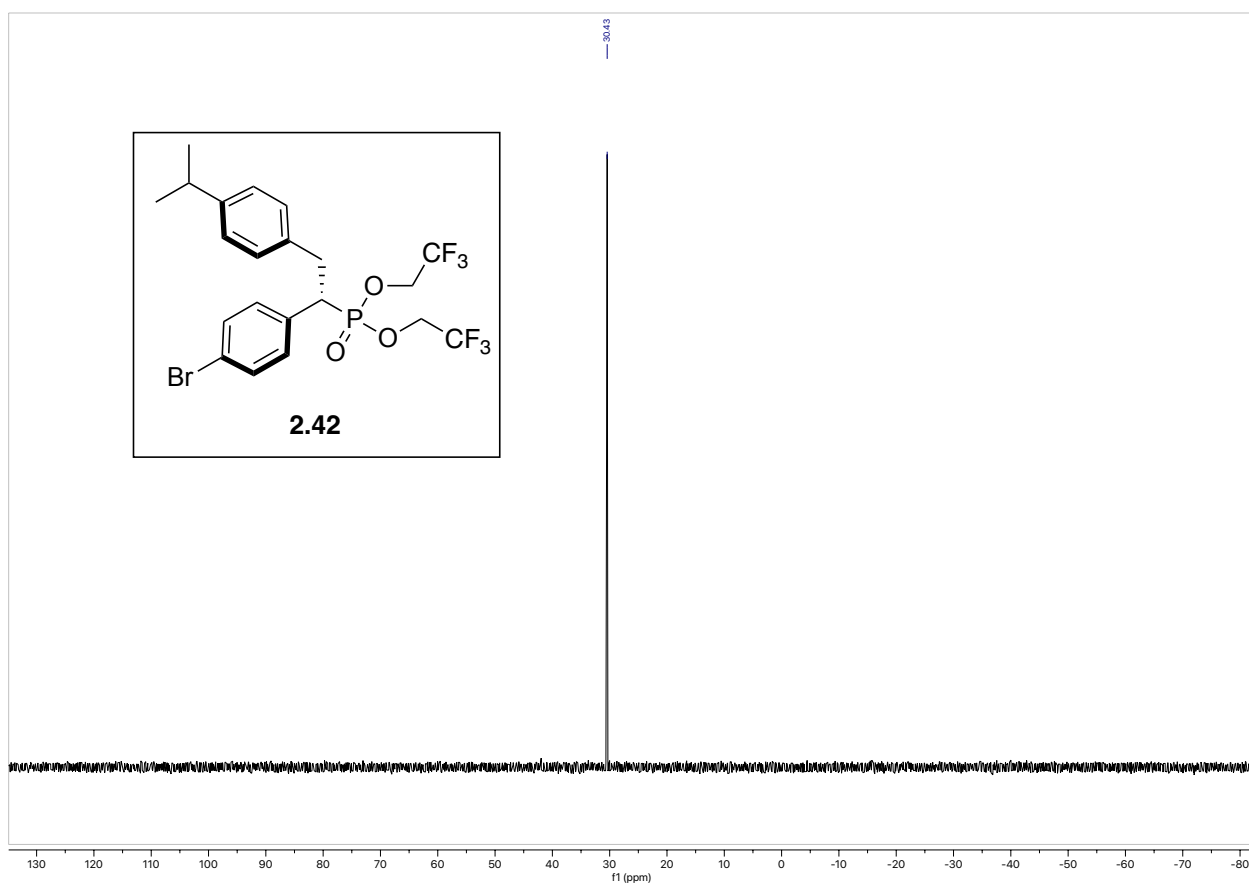
¹H NMR spectrum (600 MHz, Chloroform-d) of (s, 7.26 ppm) of **2.42**.



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-d) of (t, 77.36 ppm) of **2.42**.

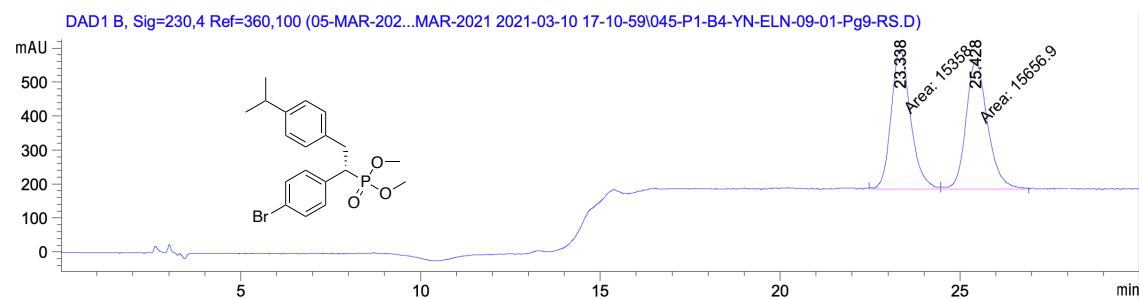


^{19}F NMR spectrum (376 MHz, Chloroform-d) of **2.42**.



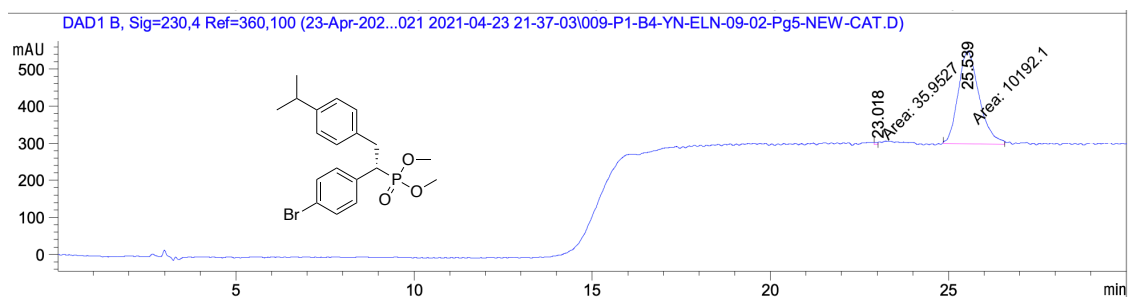
^{31}P NMR spectrum (162 MHz, Chloroform-d) of **2.42**.

Enantioselectivity Determination by HPLC or SFC



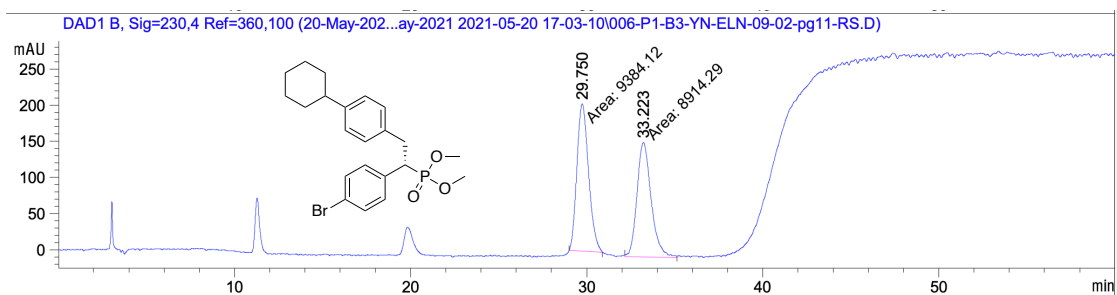
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.338	MF	0.6247	1.53580e4	409.71216	49.5182
2	25.428	FM	0.6982	1.56569e4	373.71921	50.4818

Totals : 3.10149e4 783.43137



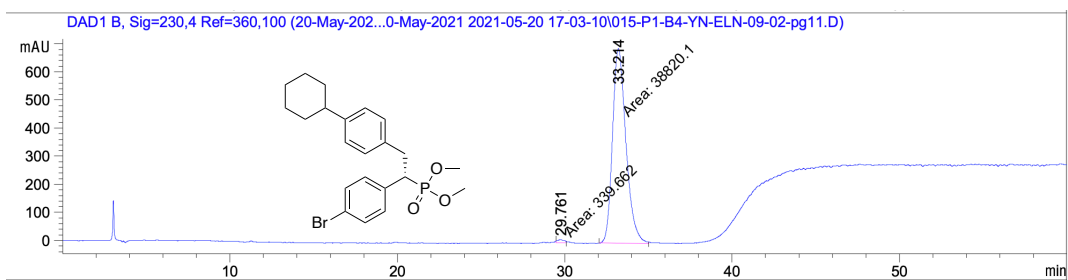
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.018	MM	0.1011	35.95274	5.92440	0.3515
2	25.539	MM	0.6825	1.01921e4	248.88594	99.6485

Totals : 1.02280e4 254.81034



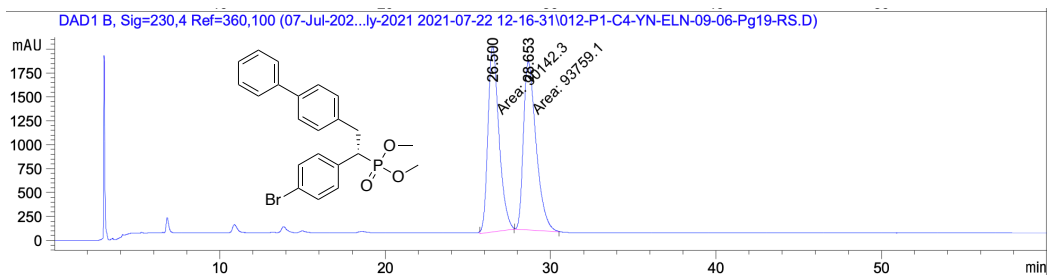
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.750	MM	0.7670	9384.11621	203.90833	51.2838
2	33.223	MM	0.9359	8914.29004	158.74568	48.7162

Totals : 1.82984e4 362.65401



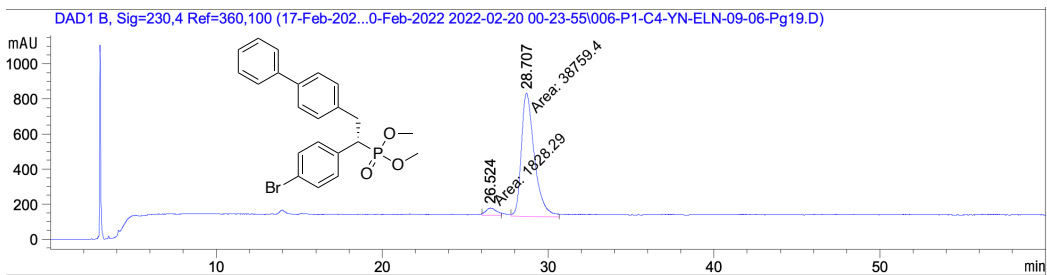
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.761	MM	0.4746	339.66165	11.92875	0.8674
2	33.214	MM	0.9334	3.88201e4	693.16809	99.1326

Totals : 3.91597e4 705.09684



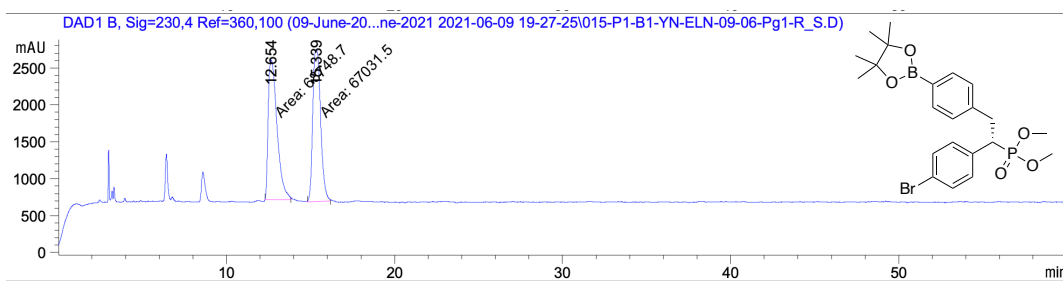
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.500	MM	0.7761	9.01423e4	1935.90735	49.0166
2	28.653	MM	0.8871	9.37591e4	1761.58472	50.9834

Totals : 1.83901e5 3697.49207



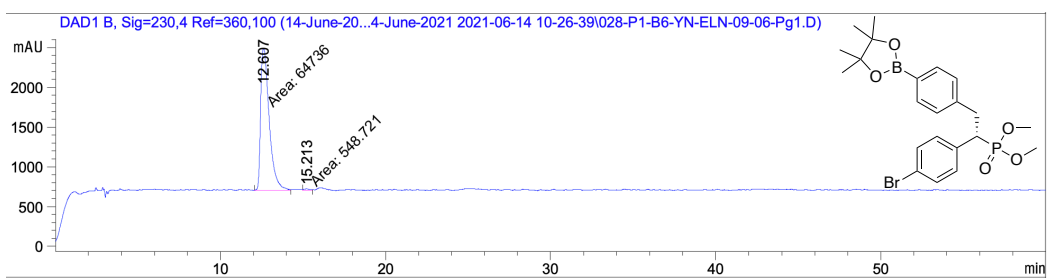
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.524	MM	0.7563	1828.28589	40.29083	4.5045
2	28.707	MM	0.9187	3.87594e4	703.18109	95.4955

Totals : 4.05877e4 743.47192



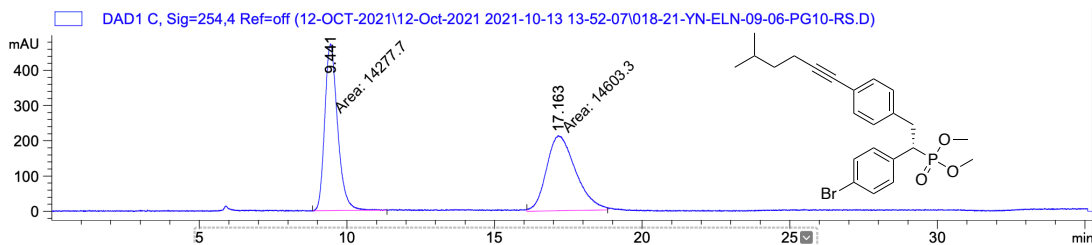
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.654	MM	0.6063	6.87487e4	1889.84363	50.6324
2	15.339	MM	0.5407	6.70315e4	2066.25659	49.3676

Totals : 1.35780e5 3956.10022

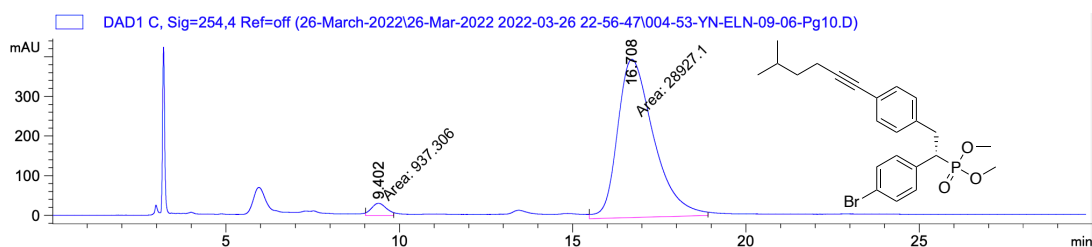


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.607	MM	0.6034	6.47360e4	1788.11292	99.1595
2	15.213	MM	0.4084	548.72058	22.39397	0.8405

Totals : 6.52847e4 1810.50688



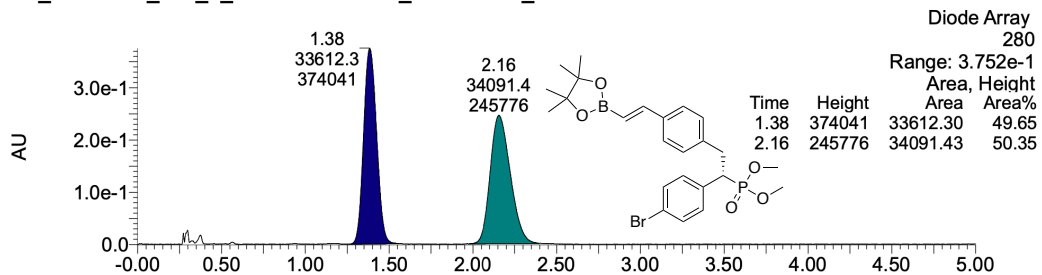
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.441	MM	0.5020	1.42777e4	474.00946	49.4364
2	17.163	MM	1.1377	1.46033e4	213.92677	50.5636
Totals :				2.88810e4	687.93623	



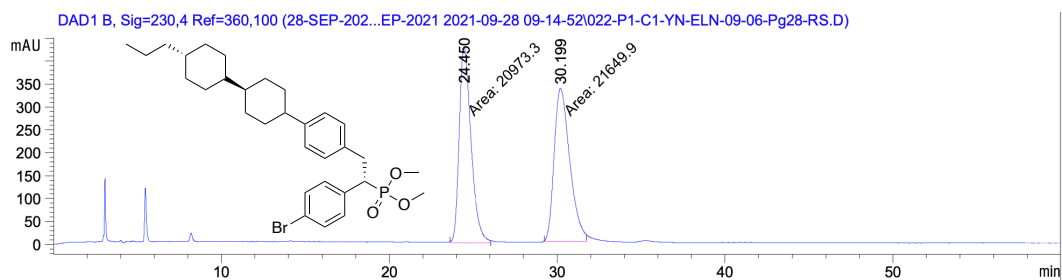
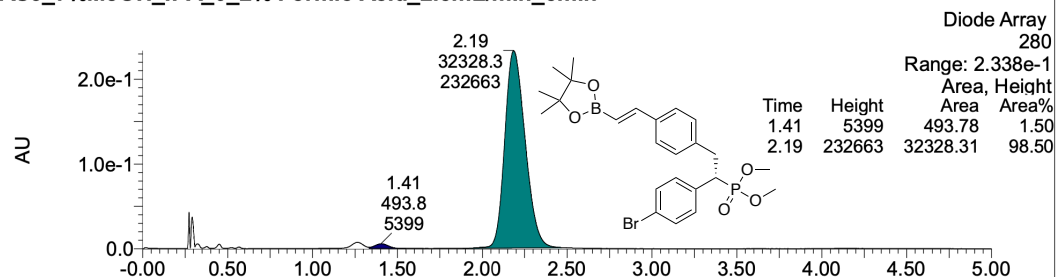
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.402	MM	0.5095	937.30646	30.66275	3.1385
2	16.708	MM	1.2074	2.89271e4	399.29587	96.8615
Totals :				2.98644e4	429.95862	

SFC

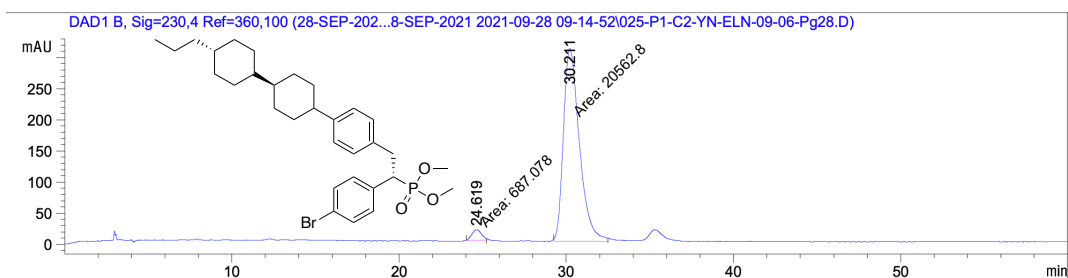
AS3_7%MeOH_IPA_0_2% Formic Acid_2.5mL/min_5min



AS3_7%MeOH_IPA_0_2% Formic Acid_2.5mL/min_5min

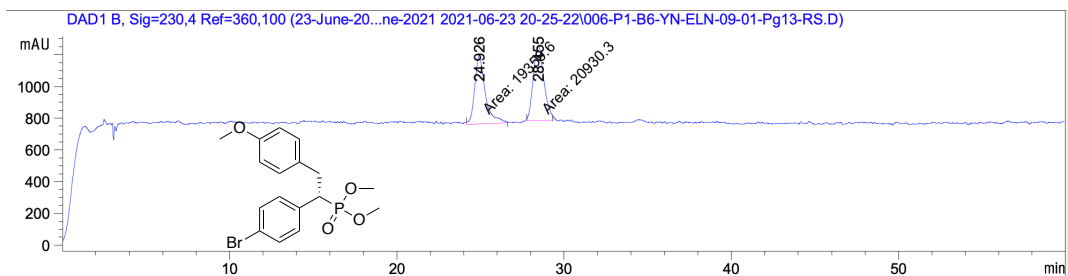


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.450	MM	0.8188	2.09733e4	426.92914	49.2063
2	30.199	MM	1.0779	2.16499e4	334.76395	50.7937



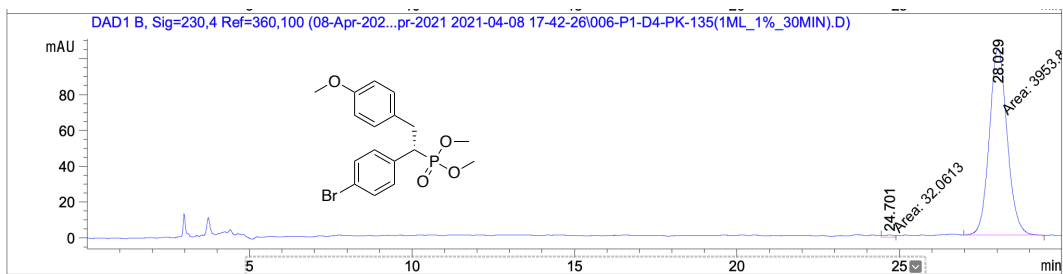
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.619	MM	0.6734	687.07770	17.00618	3.2333
2	30.211	MM	1.1054	2.05628e4	310.04095	96.7667

Totals : 2.12498e4 327.04713



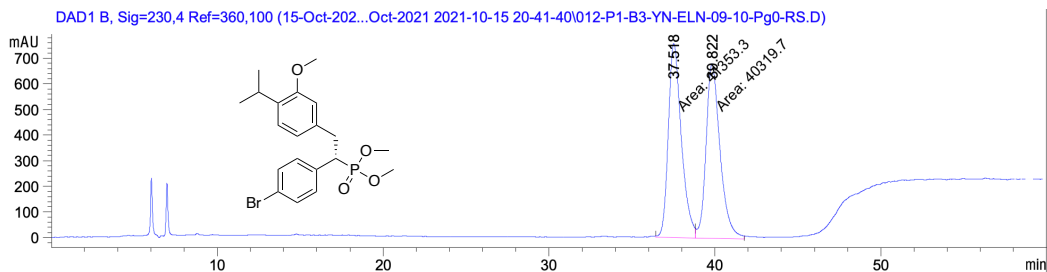
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.926	MM	0.7497	1.93596e4	430.39493	48.0508
2	28.455	MM	0.7438	2.09303e4	468.96695	51.9492

Totals : 4.02899e4 899.36188



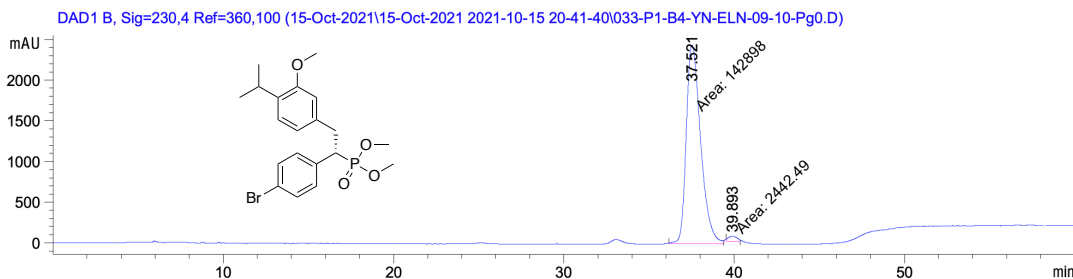
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.701	MM	0.4098	32.06128	1.30389	0.8044
2	28.029	MM	0.6325	3953.86230	104.19036	99.1956

Totals : 3985.92358 105.49425



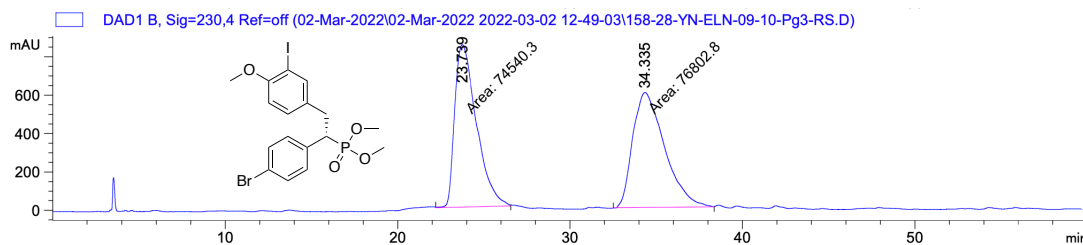
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.518	MF	0.9105	4.13533e4	756.97668	50.6328
2	39.822	FM	0.9853	4.03197e4	681.99347	49.3672

Totals : 8.16730e4 1438.97015



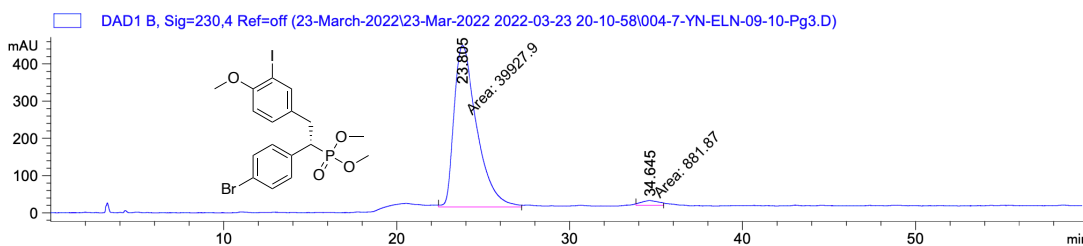
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.521	MM	0.9765	1.42898e5	2439.02441	98.3195
2	39.893	MM	0.6191	2442.48633	65.75668	1.6805

Totals : 1.45340e5 2504.78109



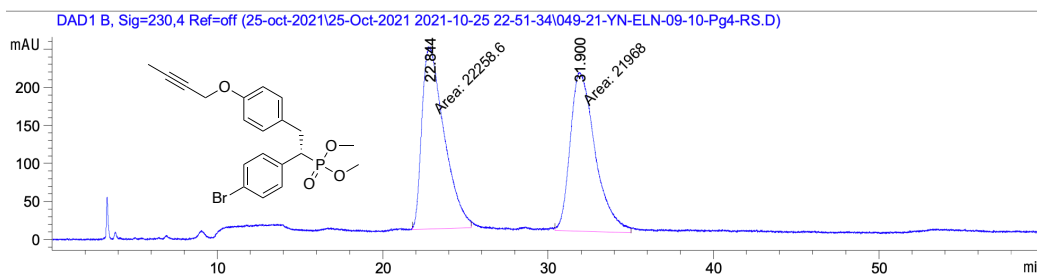
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.739	MM	1.4669	7.45403e4	846.90216	49.2525
2	34.335	MM	2.1364	7.68028e4	599.16113	50.7475

Totals : 1.51343e5 1446.06329



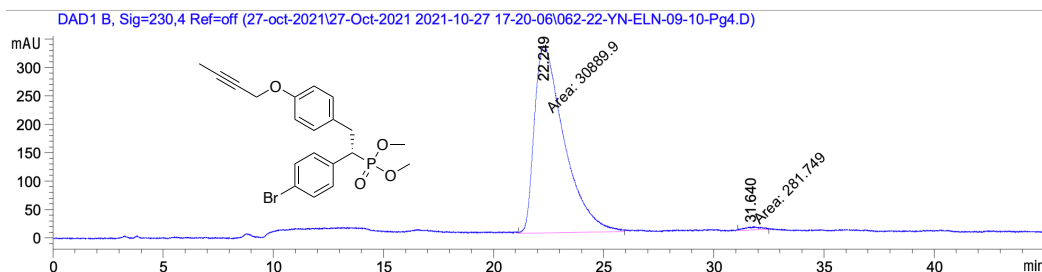
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.805	MM	1.5338	3.99279e4	433.86063	97.8391
2	34.645	MM	1.1665	881.87042	12.59987	2.1609

Totals : 4.08098e4 446.46049



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.844	MM	1.5467	2.22586e4	239.84695	50.3286
2	31.900	MM	1.7526	2.19680e4	208.91402	49.6714

Totals : 4.42266e4 448.76097

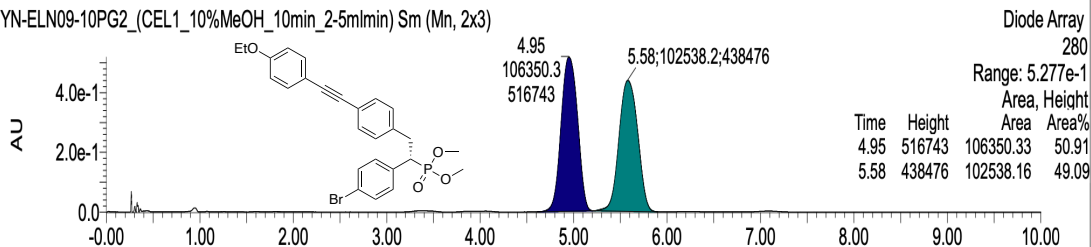


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.249	MM	1.5584	3.08899e4	330.35114	99.0961
2	31.640	MM	0.7416	281.74908	6.33182	0.9039

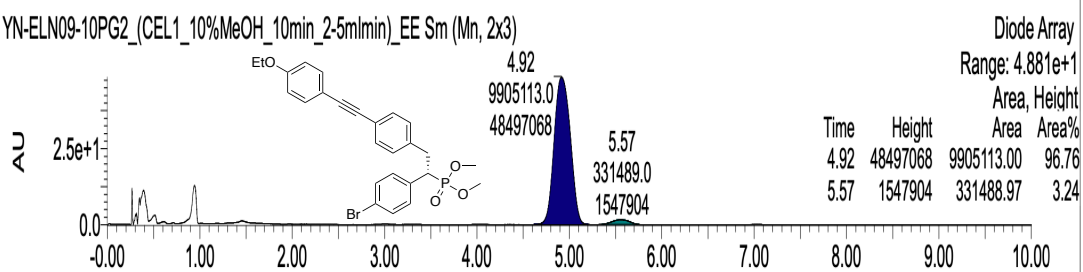
Totals : 3.11717e4 336.68296

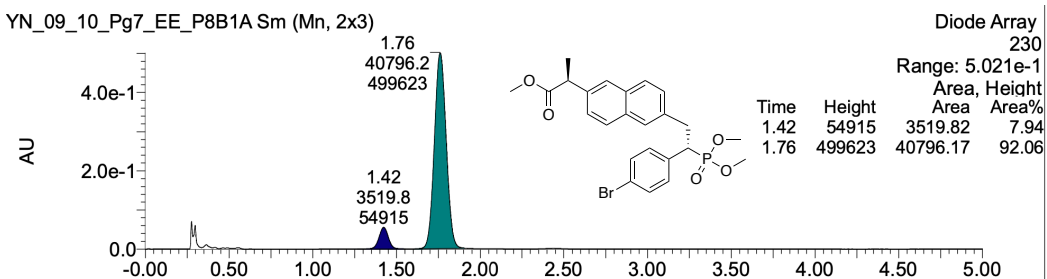
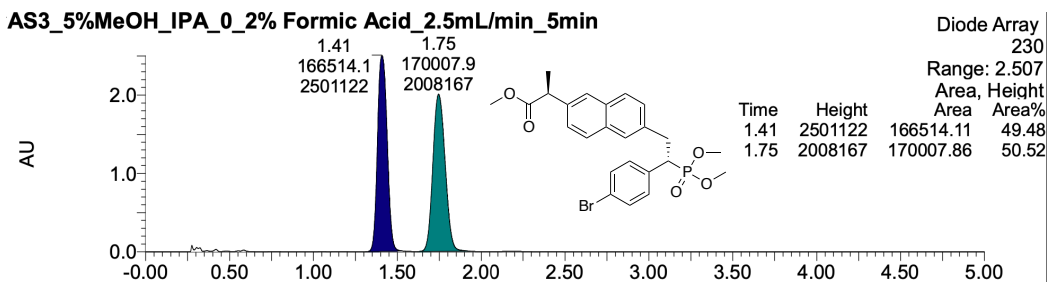
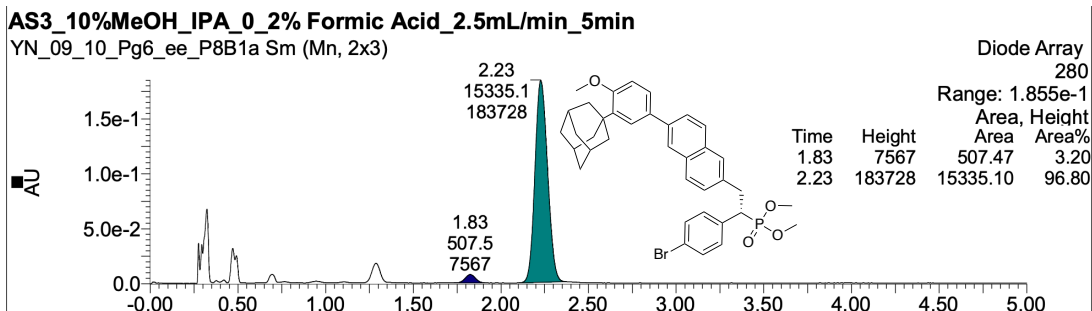
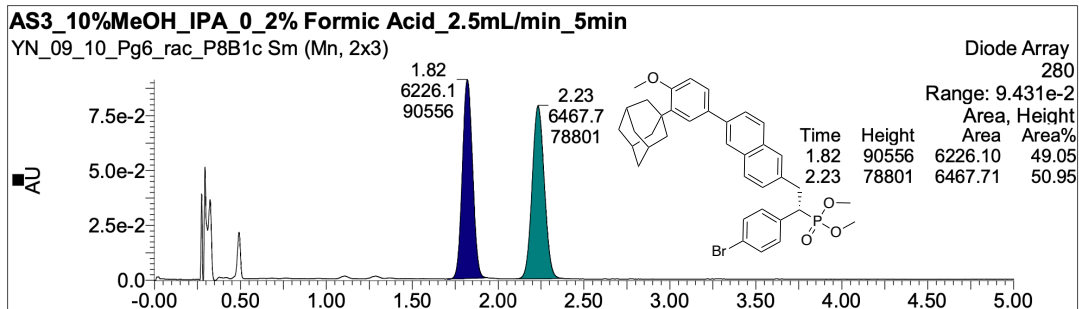
SFC

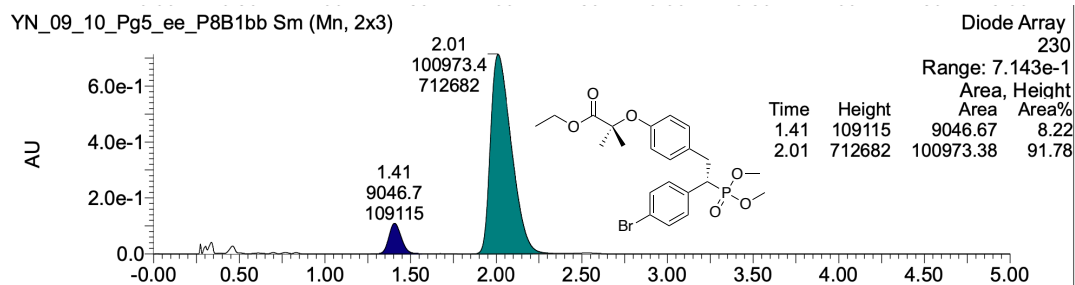
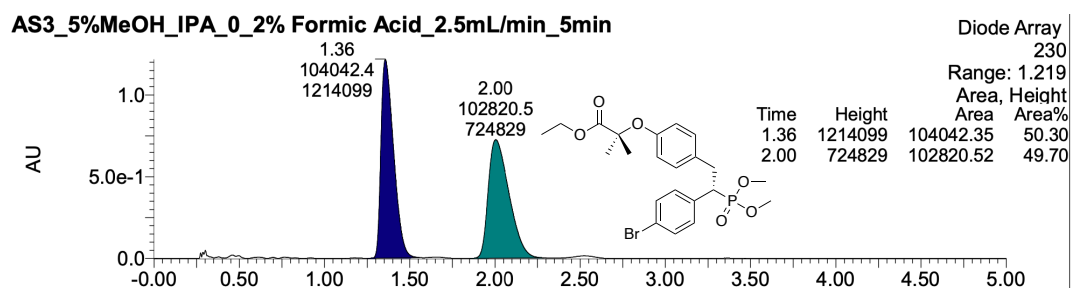
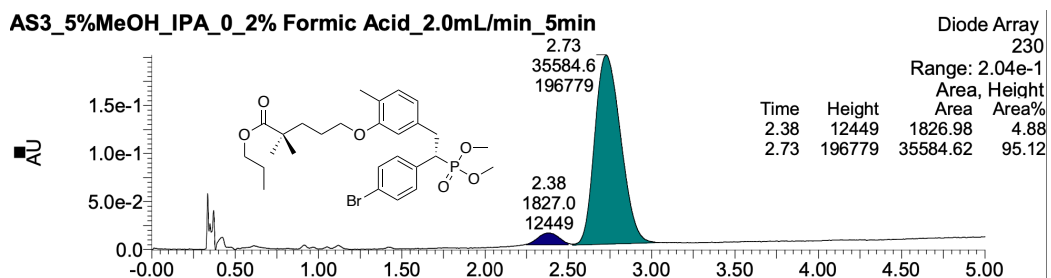
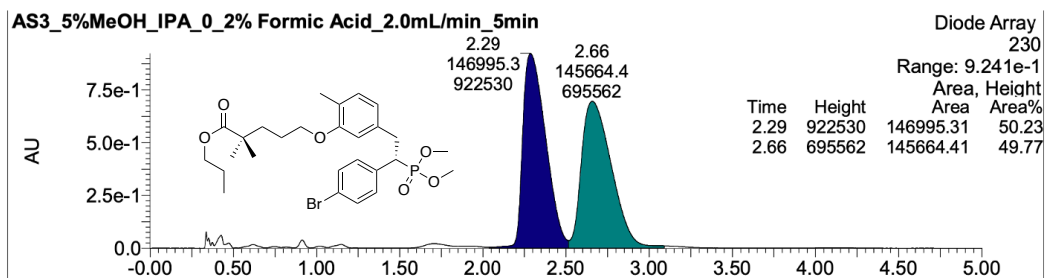
YN-ELN09-10PG2_(CEL1_10%MeOH_10min_2-5mlmin)_Sm (Mn, 2x3)

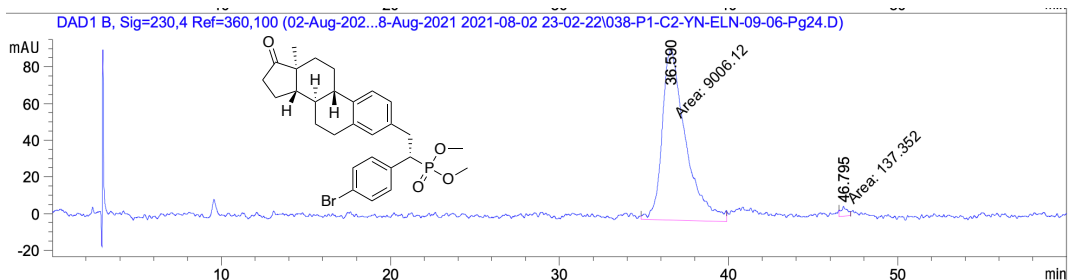
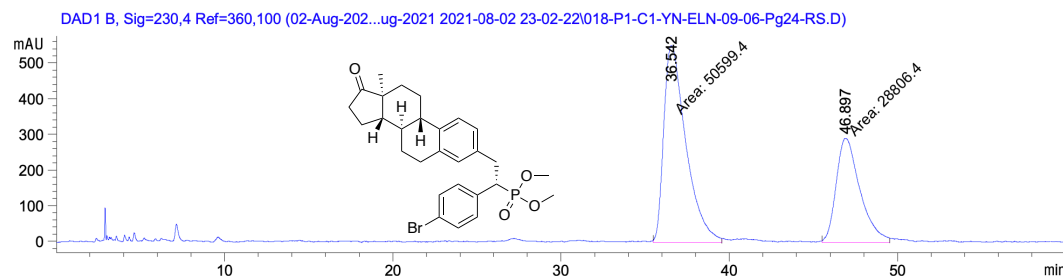


YN-ELN09-10PG2_(CEL1_10%MeOH_10min_2-5mlmin)_EE Sm (Mn, 2x3)



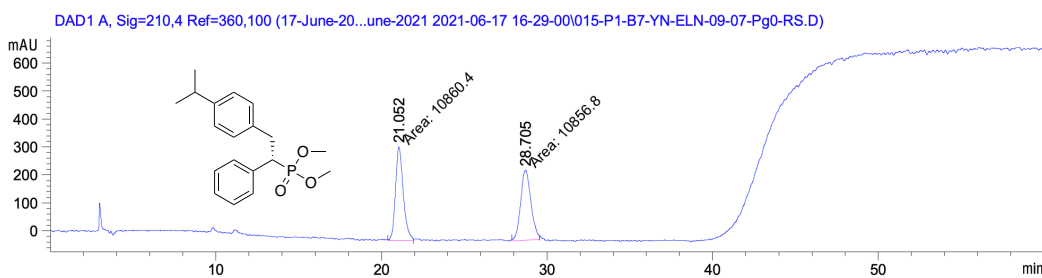






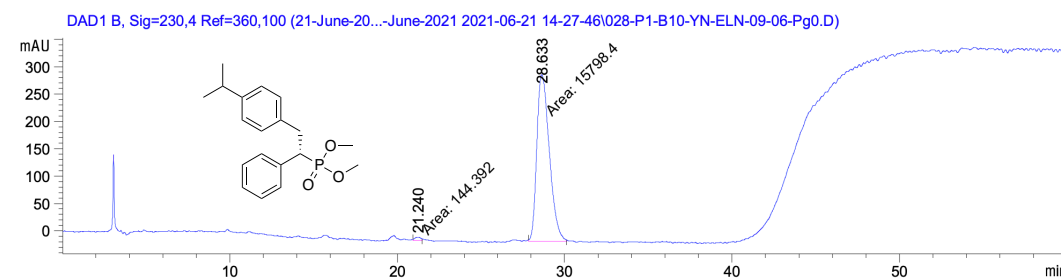
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.590	MM	1.6095	9006.12012	93.26187	98.4978
2	46.795	MM	0.4318	137.35229	5.30115	1.5022

Totals : 9143.47241 98.56303



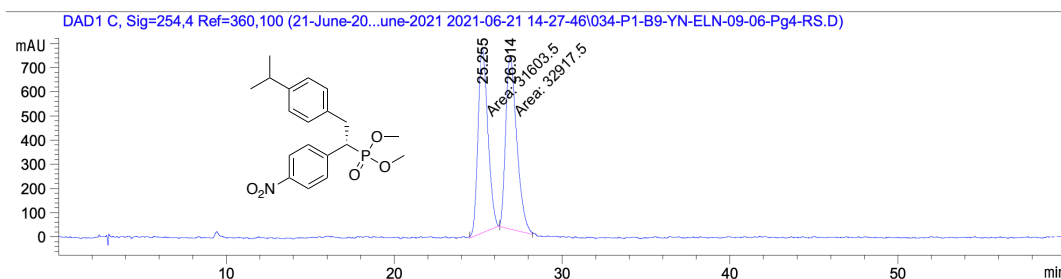
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.052	MM	0.5436	1.08604e4	332.99515	50.0083
2	28.705	MM	0.7235	1.08568e4	250.09103	49.9917

Totals : 2.17171e4 583.08618



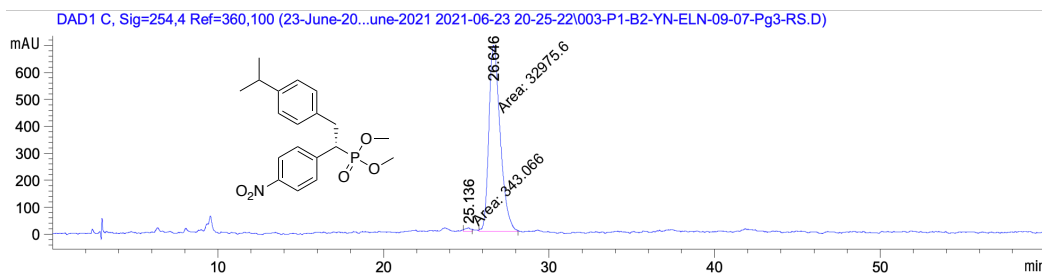
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.240	MM	0.4317	144.39218	5.57509	0.9057
2	28.633	MM	0.8646	1.57984e4	304.54202	99.0943

Totals : 1.59428e4 310.11711



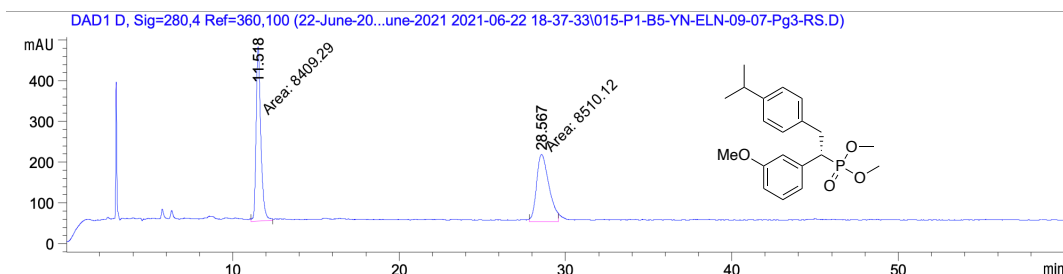
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.255	MM	0.6873	3.16035e4	766.32025	48.9817
2	26.914	MM	0.7733	3.29175e4	709.44983	51.0183

Totals : 6.45210e4 1475.77008



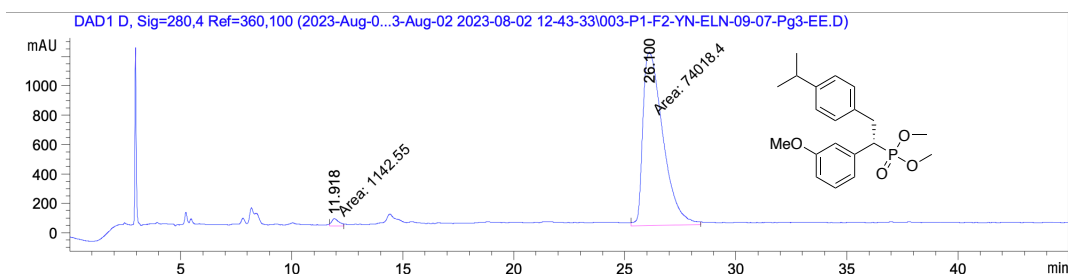
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.136	MM	0.4261	343.06598	13.41953	1.0297
2	26.646	MM	0.7956	3.29756e4	690.74866	98.9703

Totals : 3.33187e4 704.16819



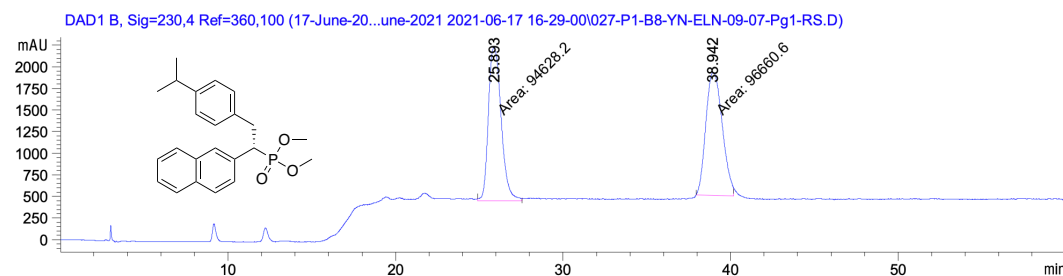
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.518	MM	0.3274	8409.29492	428.14645	49.7020
2	28.567	MM	0.8622	8510.12402	164.49858	50.2980

Totals : 1.69194e4 592.64503



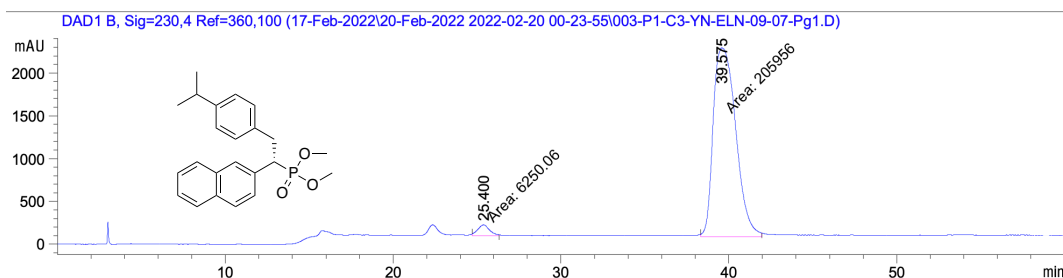
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.918	MM	0.3863	1142.54785	49.29086	1.5201
2	26.100	MM	1.0459	7.40184e4	1179.53149	98.4799

Totals : 7.51609e4 1228.82236



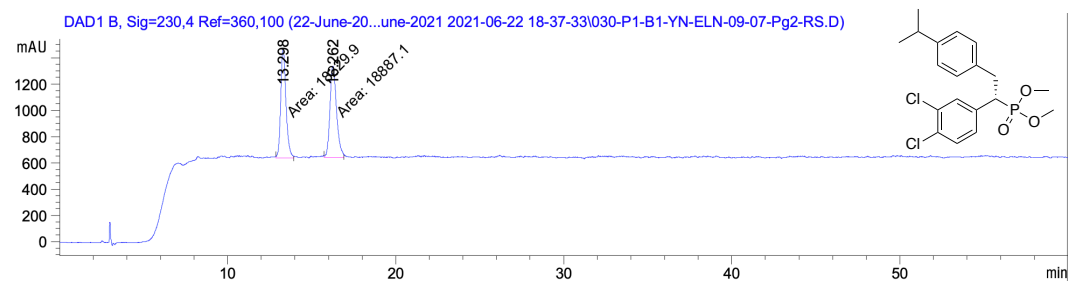
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.893	MM	0.8840	9.46282e4	1784.02478	49.4687
2	38.942	MM	1.1325	9.66606e4	1422.53210	50.5313

Totals : 1.91289e5 3206.55688



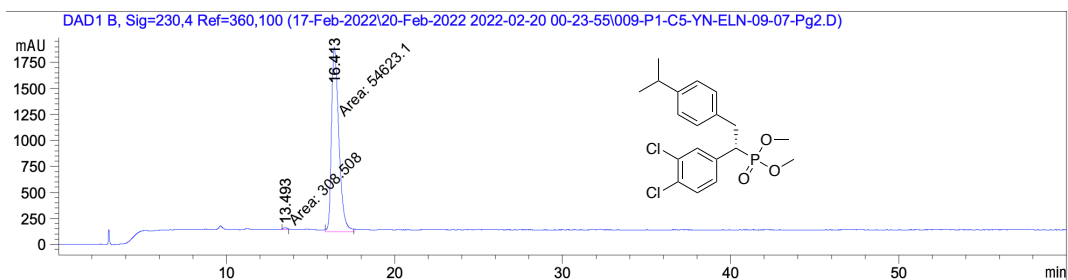
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.400	MM	0.8248	6250.06104	126.29051	2.9453
2	39.575	MM	1.5548	2.05956e5	2207.67676	97.0547

Totals : 2.12206e5 2333.96727



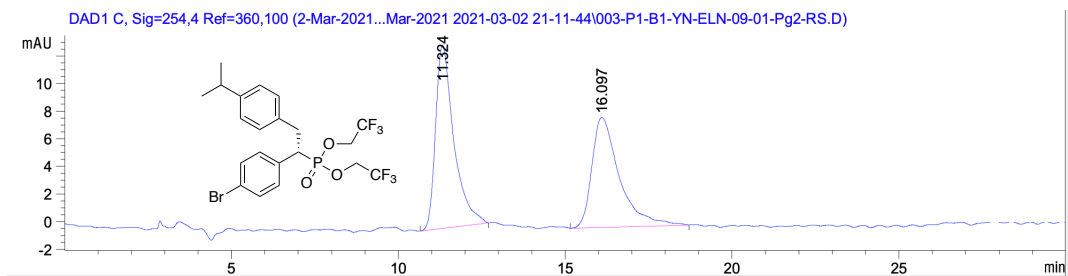
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.298	MM	0.3642	1.82299e4	834.27338	49.1147
2	16.262	MM	0.4532	1.88871e4	694.51489	50.8853

Totals : 3.71171e4 1528.78827



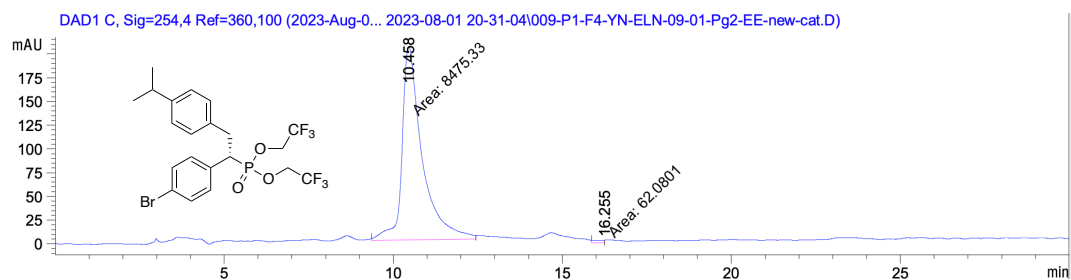
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.493	MM	0.2854	308.50833	18.01846	0.5616
2	16.413	MM	0.5135	5.46231e4	1772.96472	99.4384

Totals : 5.49316e4 1790.98318



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.324	BB	0.5649	506.80612	13.28964	52.6348
2	16.097	BB	0.8439	456.06689	7.96670	47.3652

Totals : 962.87302 21.25634



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.458	MM	0.6945	8475.32617	203.40036	99.2728
2	16.255	MM	0.3564	62.08010	2.90310	0.7272

Totals : 8537.40628 206.30346

References for Chapter 2

1. Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J., Asymmetric Cyclopropanations by Rhodium(II) N-(Arylsulfonyl)prolinate Catalyzed Decomposition of Vinyldiazomethanes in the Presence of Alkenes. Practical Enantioselective Synthesis of the Four Stereoisomers of 2-Phenylcyclopropan-1-amino Acid. *J. Am. Chem. Soc.* **1996**, *118* (29), 6897-6907.
2. Callot, H. J.; Metz, F., Rhodium(II)2,4,6-triarylbenzoates : improved catalysts for the syn cyclopropanation of z-olefins. *Tetrahedron* **1985**, *41* (20), 4495-4501.
3. Reddy, R. P.; Lee, G. H.; Davies, H. M. L., Dirhodium Tetracarboxylate Derived from Adamantylglycine as a Chiral Catalyst for Carbenoid Reactions. *Org. Lett.* **2006**, *8* (16), 3437-3440.
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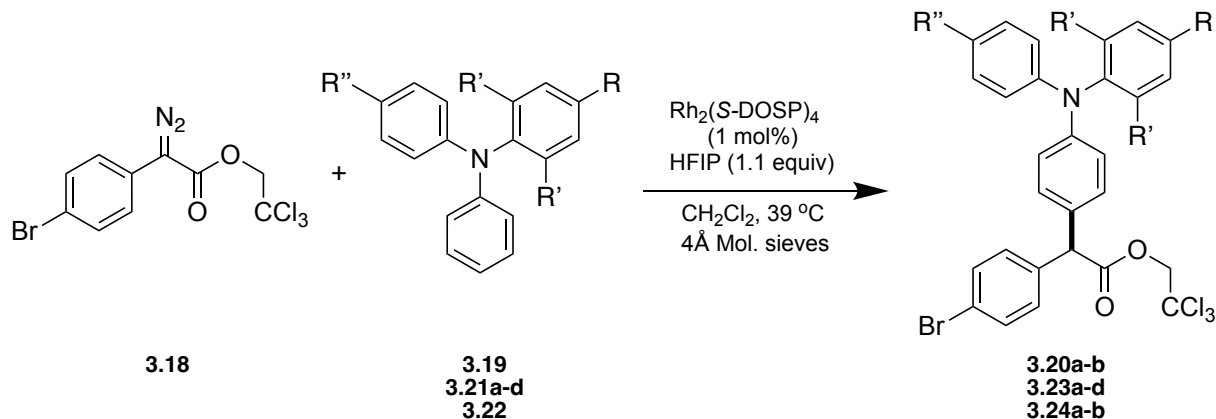
Experimental section for chapter 3: Dirhodium C–H Functionalization of Hole-Transport Materials

General Information Chapter 3

Chemicals were obtained from commercial sources and used as received unless stated otherwise. $\text{Rh}_2(\text{R-DOSP})_4$,¹ $\text{Rh}_2(\text{S-PTAD})_4$,^{2,3} $\text{Rh}_2(\text{R-TPPTTL})_4$,⁴ $\text{Rh}_2(\text{R-TCPTAD})_4$,⁵ $\text{Rh}_2(\text{R-NTTL})_4$,⁶ $\text{Rh}_2(\text{S-DPCP})_4$, $\text{Rh}_2(\text{S-}p\text{-Br-TPCP})_4$,⁷ $\text{Rh}_2(\text{S-tetra-(4-Br)TPPTTL})_4$, $\text{Rh}_2(\text{S-}di\text{-(4-Br)-di(4-}^t\text{BuPh)TPPTTL})_4$, $\text{Rh}_2(\text{S-}di\text{-(3,5-diCF}_3\text{Ph)TPPTTL})_4$, $\text{Rh}_2(\text{S-}di\text{-(3,5-diBr)TPPTTL})_4$, and $\text{Rh}_2(\text{S-}di\text{-(4-Br)TPPTTL})_4$.⁸ Synthesized based on the literature reports. All operations involved in synthesis were performed under an atmosphere of nitrogen or argon using standard Schlenk techniques. ^1H NMR and ^{13}C NMR spectra were recorded in CDCl_3 on Varian 500, 600, or 700 MHz spectrometers. The chemical shifts (δ) are reported in parts per million (ppm).

Infrared (IR) spectra were collected on a Nicolet Impact Series 10 FT-IR. Mass spectrometric determinations were carried out on a Thermo Fisher Scientific Exactive Plus Orbitrap Mass spectrometer with electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI), or a Thermo Fisher Scientific Q-Exactive HF Quadrupole-Orbitrap Mass spectrometer with ESI.

Experimental section for chapter 3: Dirhodium C–H Functionalization of Hole-Transport Materials.



General Procedure for C–H Functionalization with 2,2,2-Trichloroethyl Esters

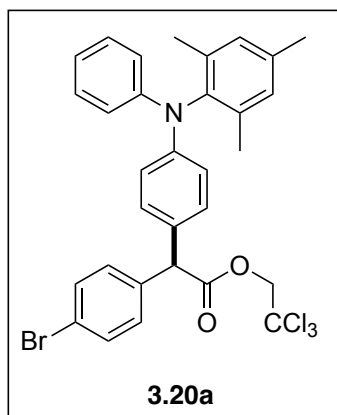
A clean oven-dried and flame-dried 8.0 mL scintillation vial (vial-A) equipped with a few activated 4 Å molecular sieves and a magnetic stir bar was evacuated and purged with argon (2–3 times). After cooling down to room temperature, the relevant triarylamine (**3.19**, **3.21a–d**, or **3.22**, 1.0 equiv, 0.200 mmol) followed by $\text{Rh}_2(\text{S-DOSP})_4$ (3.79 mg, 0.01 equiv), and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (1.1 equiv) were then added. The vial was once again evacuated and purged with argon (3–5 times) and anhydrous CH_2Cl_2 (0.5 mL) was added. The vial and its contents were then set to stir at reflux (39 °C) under an argon atmosphere using a hot plate. To a second oven-dried vial (vial-B) that was evacuated and purged with argon was added 2,2,2-trichloroethyl-2-(4-bromophenyl)-2-diazoacetate, **3.18** (1.0 to 4.5 equiv). Vial-B and its contents were evacuated and purged with argon (2–3 times), and anhydrous CH_2Cl_2 (2.0 mL) was then added to obtain a 0.1 M solution of the diazo compound. The 0.1 M solution was transferred into a 5.0 mL plastic syringe (12.46 mm diameter). Using a well-calibrated syringe pump, slow addition of the diazo solution into the stirring solution of vial-A under an inert atmosphere was initiated. After the complete addition of the solution (3 h), the residual diazo compound in the 5.0 mL plastic syringe was rinsed with anhydrous CH_2Cl_2 (0.5 mL) and transferred dropwise into the stirring reaction mixture of vial-A. An additional 30 min was allowed before concentrating the solution under reduced pressure. Purification by flash column chromatography on silica gel (hexane/EtOAc) was used to afford the final product.

Gram-Scale Procedure for C–H Functionalization with 2,2,2-Trichloroethyl Esters.

A clean oven-dried and flame-dried 100.0 mL round-bottom flask (flask-A) equipped with activated 4 Å molecular sieves and a magnetic stir bar was evacuated and purged with argon (2–3

times). After cooling down to room temperature, **3.21a** (1.04 g, 2.48 mmol) followed by $\text{Rh}_2(\text{S-DOSP})_4$ (47.0 mg, 0.01equiv), and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (1.1 equiv) were then added. The flask was once again evacuated and purged with argon (3–5 times) and anhydrous CH_2Cl_2 (10.0 mL) was added. The flask and its contents were then set to stir at reflux (39 °C) under an argon atmosphere using a hotplate. To a second oven-dried round-bottom flask (flask-B) that was evacuated and purged with argon was added 2,2,2-trichloroethyl-2-(4-bromophenyl)-2-diazoacetate, **3.18** (0.924 g, 1.0 equiv, 2.48 mmol). Flask-B and its contents were evacuated and purged with argon (2–3 times), and anhydrous CH_2Cl_2 (25.0 mL) was then added to obtain a solution of the diazo compound. The solution was transferred into a 30.0 mL plastic syringe. Using a well-calibrated syringe pump, slow addition of the diazo solution into the stirring solution of flask-A under an inert atmosphere was initiated. After the complete addition of the solution (3 h), the residual diazo compound in the 30.0 mL plastic syringe was rinsed with anhydrous CH_2Cl_2 (1.0 mL) and transferred drop wise into the stirring reaction mixture of flask-A. An additional 30 min was allowed before concentrating the solution under reduced pressure. Purification by flash column chromatography on silica gel (hexanes : EtOAc) was used to afford the final product.

2,2,2-Trichloroethyl-2-(4-bromophenyl)-2-(4-(mesityl(phenyl)-amino)phenyl)acetate (3.20a)



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 10:0 to 9:1 gradient; $R_f = 0.62$ in 9:1 hexanes/EtOAc), which afforded major product **3.20a** as a colorless gel (82 mg, 65%).

^1H NMR (600 MHz, CDCl_3) δ 7.47 (d, $J = 8.5$ Hz, 2H), 7.27–7.24 (m, 2H), 7.18 (t, $J = 8.0$ Hz, 2H), 7.13 (d, $J = 8.8$ Hz, 2H), 6.97 (d, $J = 8.9$ Hz, 2H), 6.94–6.90 (m, 4H), 6.88 (t, $J = 7.3$ Hz, 1H), 5.02 (s, 1H), 4.79 (s, 2H), 2.32 (s, 3H), 1.97 (s, 6H).

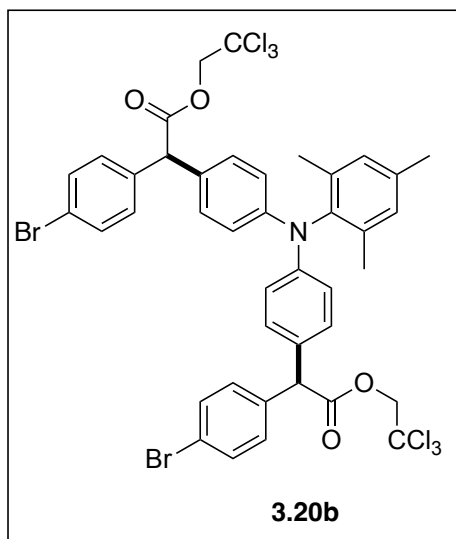
^{13}C { ^1H } NMR (101 MHz, CDCl_3) δ 171.1, 146.0, 140.2, 137.9, 137.4, 137.3, 132.1, 130.7, 130.3, 129.6, 129.4, 129.2, 121.9, 121.3, 120.1, 119.7, 95.0, 74.7, 55.9, 21.4, 18.9.

HRMS (ESI) calcd for $\text{C}_{31}\text{H}_{27}\text{BrCl}_3\text{NO}_2$ $[\text{M} + \text{H}]^+$ 630.0363, found, 630.0385.

IR (neat): 2950, 1752, 1593, 1506, 1490, 1406, 1374, 1374, 1307, 1260, 1178, 1128, 1074, 1028, 1011, 908, 853, 828, 755, 732, 695, 605, 671, 551, 497 cm^{-1} .

HPLC analysis: (R,R-Whelk column, 1% isopropanol in hexane, 1.0 mLmin $^{-1}$, 1 mg mL $^{-1}$, 15 min, UV 230 nm) retention times of 5.8 min(major) and 6.5 min (minor) 20% ee when using $\text{Rh}_2(\text{S-}p\text{-Br-TPCP})_4$ in place of $\text{Rh}_2(\text{S-DOSP})_4$.

bis(2,2,2-Trichloroethyl)-2,2'-((4-mesitylazanediy)bis(4,1-phenylene))bis(2-(4-bromophenyl)-acetate) (3.20b).



The minor product **3.20b** (R_f = 0.39 in 9:1 hexanes/EtOAc) was obtained from the same column as **3.20a** as a colorless gel (61 mg, 31%).

^1H NMR (600 MHz, CDCl_3) δ 7.46 (d, J = 8.5 Hz, 4H), 7.25 (d, J = 8.5 Hz, 5H), 7.12 (d, J = 8.6 Hz, 4H), 6.91 (d, J = 8.9 Hz, 6H), 5.02 (s, 2H), 4.78 (s, 4H), 2.31 (s, 3H), 1.94 (s, 6H).

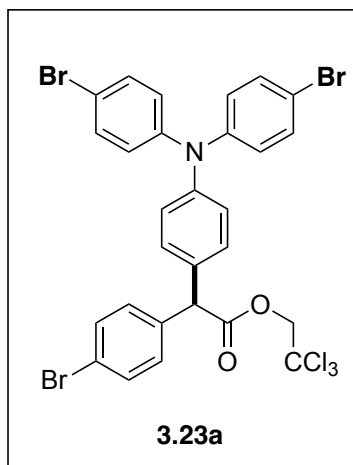
^{13}C { ^1H } NMR (151 MHz, CDCl_3) δ 171.0, 145.7, 139.9, 137.8, 137.4, 137.3, 132.1, 130.7, 130.3, 129.6, 129.6, 121.9,

119.9, 95.0, 74.7, 55.9, 21.4, 18.8. **HRMS (ESI)** calcd for $\text{C}_{41}\text{H}_{33}\text{Br}_2\text{Cl}_6\text{NO}_4$ $[\text{M} + \text{H}]^+$ 970.8907, found, 970.8888.

IR (neat): 2951, 1749, 1601, 1504, 1487, 1406, 1369, 1307, 1260, 1179, 1124, 1073, 1026, 1011, 907, 853, 829, 763, 730, 649, 571, 552, 529, 496, 449 cm^{-1} .

When an excess amount of **3.18** (2.5 equiv) was used the isolated yield of **3.20b** was (113 mg, 58%) that of **3.20a** is (31 mg, 25%).

2,2,2-Trichloroethyl-2-(4-(bis(4-bromophenyl)amino)phenyl)-2-(4-bromophenyl)acetate
(3.23a).



The material was purified by flashchromatography (SiO₂;

hexanes/EtOAc, 10:0 to 9:1 gradient; R_f = 0.58 in 9:1

hexanes/EtOAc), which afforded **3.23a** as a colorless gel (134mg, 90% yield) (1.55 g, 84% yield for one gram-scale).

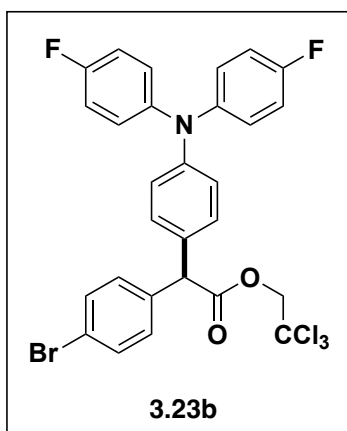
¹H NMR (600 MHz, CDCl₃) δ 7.51 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.8 Hz, 4H), 7.28 (d, J = 8.2 Hz, 4H), 7.22 (d, J = 8.2 Hz, 2H), 7.02 (d, J = 8.6 Hz, 2H), 6.94 (d, J = 8.8 Hz, 4H), 5.07 (s, 1H), 4.82 (s, 2H).

¹³C {¹H} NMR (151 MHz, CDCl₃) δ 170.8, 146.8, 146.5, 137.0, 132.8, 132.3, 132.2, 130.7, 130.0, 126.1, 124.3, 122.1, 116.3, 95.0, 74.7, 56.0.

HRMS (APCI) calcd for C₂₈H₁₉Br₃Cl₃NO₂ [M + H]⁺ 743.8104, found, 743.8107.

IR (neat): 3032, 2952, 1750, 1607, 1507, 1578, 1507, 1482, 1406, 1369, 1311, 1270, 1177, 1128, 1071, 1010, 906, 820, 765, 730, 669, 649, 571, 537, 510, 458 cm⁻¹.

2,2,2-Trichloroethyl-2-(4-(bis(4-fluorophenyl)amino)phenyl)-2-(4-bromophenyl)acetate
(3.23b).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 9:1 gradient; R_f = 0.62 in 9:1 hexanes/EtOAc), which afforded **3.23b** as a colorless foam (104 mg, 83% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 7.15 (d, J = 8.6 Hz, 2H), 7.04–6.99 (m, 4H), 6.98–6.89

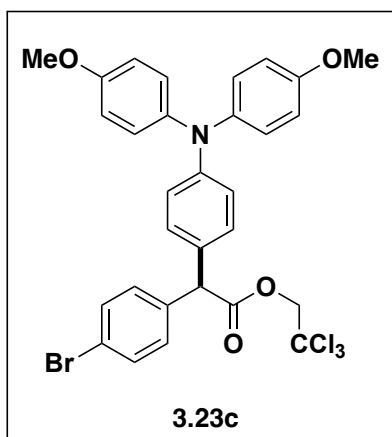
(m, 6H), 5.03 (s, 1H), 4.79 (s, 2H).

¹³C {¹H} NMR (101 MHz, CDCl₃) δ 170.9, 160.6, 158.2, 147.9, 143.8 (d, J = 2.8 Hz), 137.2, 132.1, 130.7 (d, J = 7.8 Hz), 129.8, 126.6 (d, J = 8.0 Hz), 122.4, 122.0, 116.6 (d, J = 22.6 Hz), 95.0, 74.7, 55.9.

HRMS (APCI) calcd for C₂₈H₁₉BrCl₃F₂NO₂ [$M + H$]⁺ 623.9705, found, 623.9708.

IR (neat): 2954, 1750, 1604, 1498, 1406, 1369, 1311, 1276, 1215, 1188, 1127, 1093, 1073, 1010, 906, 829, 797 763, 728, 671, 649, 632, 564, 516 cm⁻¹.

2,2,2-Trichloroethyl-2-(4-(bis(4-methoxyphenyl)amino)phenyl)-2-(4-bromophenyl) acetate (3.23c).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 7:3 gradient; R_f = 0.83 in 7:3 hexanes/EtOAc), which afforded **3.23c** as a colorless gel (118 mg, 91% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.47 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H), 7.03 (d, J = 7.8 Hz, 4H), 6.86

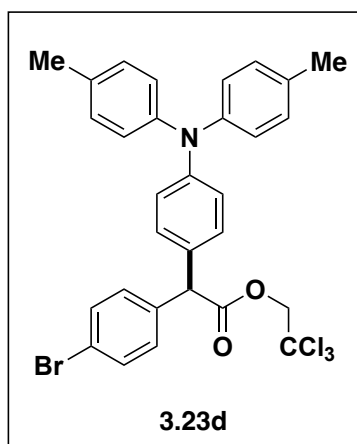
(d, $J = 8.8$ Hz, 2H), 6.81 (d, $J = 7.8$ Hz, 4H), 5.02 (s, 1H), 4.79 (q, $J = 11.9$ Hz, 2H), 3.79 (s, 6H).

^{13}C { ^1H } NMR (101 MHz, CDCl_3) δ 171.1, 156.3, 148.7, 141.0, 137.5, 132.1, 130.7, 129.4, 128.8, 127.1, 121.9, 120.5, 115.0, 95.0, 74.7, 55.8 (two peaks separated by 0.03 ppm).

HRMS (APCI) calcd for $\text{C}_{30}\text{H}_{25}\text{BrCl}_3\text{NO}_4$ $[\text{M} + \text{H}]^+$ 648.0124, found, 648.0099.

IR (neat): 2952, 2834, 1750, 1605, 1501, 1463, 1440, 1369, 1319, 1274, 1237, 1179, 1127, 1073, 1033, 1011, 905, 827, 780, 762, 726, 648, 571, 525, 502 cm^{-1} .

2,2,2-Trichloroethyl-2-(4-bromophenyl)-2-(4-(di-p-tolylamino)-phenyl)acetate (3.23d)



The material was purified by flash chromatography (SiO_2 ;

hexanes/EtOAc, 10:0 to 9:2 gradient; $R_f = 0.56$ in 9:1

hexanes/EtOAc), which afforded **3.23d** as a colorless foam (106 mg, 86% yield).

^1H NMR (400 MHz, CDCl_3) δ 7.47 (d, $J = 8.5$ Hz, 2H), 7.26 (d, $J = 8.5$ Hz, 2H), 7.13 (d, $J = 8.6$ Hz, 2H), 7.06 (d, $J = 8.3$ Hz, 4H), 6.98–6.94 (m, 6H), 5.03 (s, 1H), 4.80 (q, $J = 11.9$ Hz, 2H), 2.31

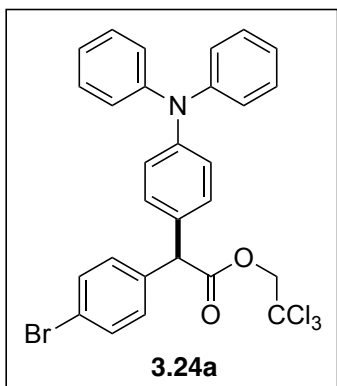
(s, 6H).

^{13}C { ^1H } NMR (101 MHz, CDCl_3) δ 171.1, 148.1, 145.4, 137.4, 133.1, 132.1, 130.7, 130.3, 130.0, 129.5, 125.1, 122.5, 121.9, 95.0, 74.7, 55.9, 21.2.

HRMS (APCI) calcd for $\text{C}_{30}\text{H}_{25}\text{BrCl}_3\text{NO}_2$ $[\text{M} + \text{H}]^+$ 616.0207, found, 616.0209.

IR (neat): 3026, 2919, 2245, 1750, 1604, 1504, 1488, 1406, 1369, 1319, 1292, 1271, 1211, 1179, 1125, 1073, 1011, 906, 814, 762, 728, 648, 568, 511, 457 cm^{-1} .

2,2,2-Trichloroethyl-2-(4-bromophenyl)-2-(4-(diphenylamino)-phenyl)acetate (3.24a)



3.24a as major product (60%) and **3.24b** as minor product (17%).

The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 9:1 gradient; *R_f* = 0.53 in 9:1 hexanes/EtOAc), which afforded major product **3.24a** as a colorless gel (70 mg, 60%).

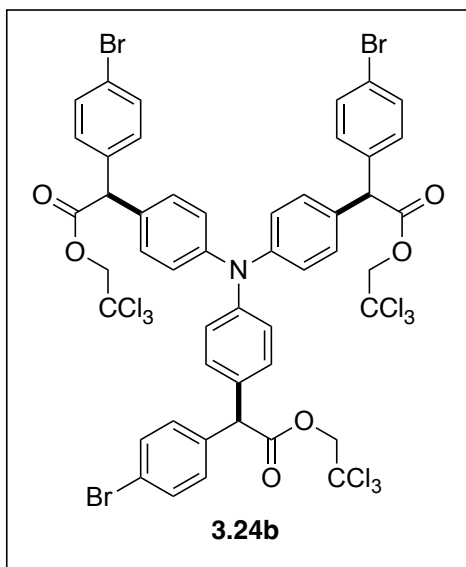
¹H NMR (400 MHz, CDCl₃) δ 7.49 (d, *J* = 8.4 Hz, 2H), 7.31–7.21 (m, 6H), 7.18 (d, *J* = 6.7 Hz, 2H), 7.08 (d, *J* = 7.5 Hz, 4H), 7.06–6.99 (m, 4H), 5.05 (s, 1H), 4.81 (t, *J* = 1.7 Hz, 2H).

¹³C {¹H} NMR (101 MHz, CDCl₃) δ 171.0, 148.2, 147.8, 147.8, 137.2, 132.1, 131.0, 130.7, 129.7, 129.6, 129., 124.9, 124.5, 123.7, 123.5, 123.0, 122.0, 95.0, 74.7, 56.0.

HRMS (ESI) calcd for C₂₈H₂₁BrCl₃NO₂ [M + H]⁺ 587.9894, found, 587.9901.

IR (neat): 3034, 2952, 1751, 1588, 1507, 1487, 1449, 1406, 1369, 1329, 1313, 1275, 1177, 1127, 1073, 1027, 1011, 908, 830, 753, 731, 695, 636, 621, 571, 531, 510, 449, 426 cm⁻¹.

Tris(2,2,2-trichloroethyl)-2,2',2''-(nitrilotris-(benzene-4,1-diyl))tris(2-(4-bromophenyl) acetate) (3.24b).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 10:0 to 9:1 gradient; *R_f* = 0.39 in 9:1 hexanes/EtOAc), which afforded minor product **3.24b** as a colorless foam (43 mg, 17%):

¹H NMR (600 MHz, CDCl₃) δ 7.47 (d, *J* = 8.6 Hz, 6H), 7.25 (d, *J* = 8.6 Hz, 6H), 7.17 (d, *J* = 8.6 Hz, 6H), 6.99 (d, *J* = 8.6 Hz, 6H), 5.04 (s, 3H), 4.79 (s, 6H).

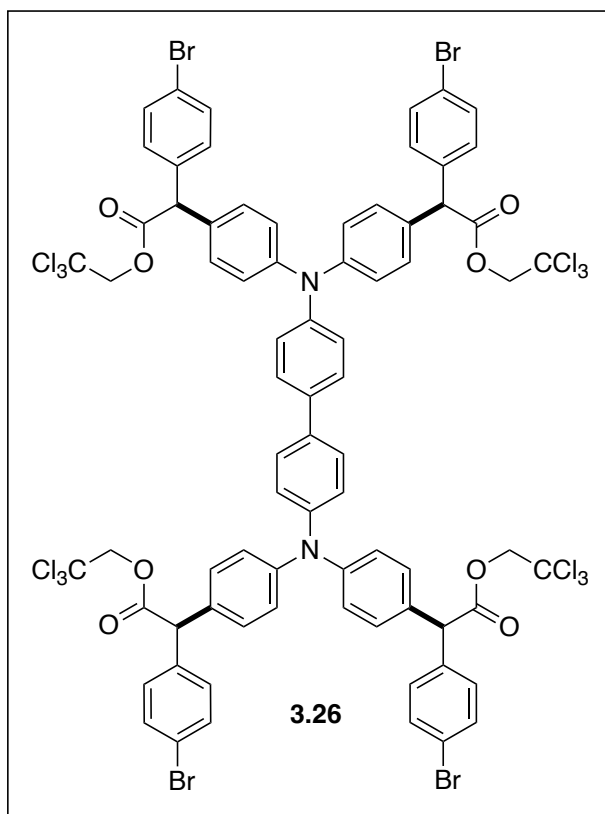
^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 170.9, 147.1, 137.1, 132.2, 132.1, 130.7, 129.9, 124.6, 122.1, 95.0, 74.7, 56.0.

HRMS (ESI) calcd for $\text{C}_{48}\text{H}_{33}\text{Br}_3\text{Cl}_9\text{NO}_6$ $[\text{M} + \text{H}]^+$ 1270.7022, found, 1270.7027.

IR (neat): 3031, 2953, 1749, 1602, 1505, 1487, 1445, 1406, 1369, 1323, 1275, 1180, 1127, 1073, 1011, 907, 831, 763, 717, 649, 571, 536, 501, 465 cm^{-1} .

When an excess amount of diazo derivative (3.5 equiv) was used, the major product of **3.22** is **3.24b** in an isolated yield of 70% and the minor product is **3.24a** in an isolated yield of 14%.

Tetrakis(2,2,2-trichloroethyl)-2,2',2'',2'''-([1,1'-biphenyl]-4,4'-diylbis(azanetriyl))tetrakis (benzene-4,1-diyl)tetrakis(2-(4-bromo-phenyl) acetate) (3.26).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 10:0 to 9:1 gradient; R_f = 0.55 in 9:1 hexanes/EtOAc), which afforded **3.26** as a colorless foam (226 mg, 61% yield using 4.5 equiv diazo derivative).

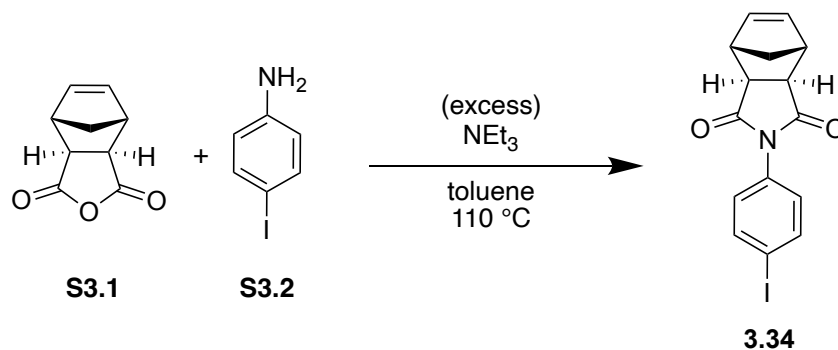
^1H NMR (600 MHz, CDCl_3) δ 7.48 (d, J = 8.5 Hz, 8H), 7.43 (d, J = 8.6 Hz, 4H), 7.27 (d, J = 8.5 Hz, 8H), 7.19 (d, J = 8.6 Hz, 8H), 7.09 (d, J = 8.6 Hz, 4H), 7.05 (d, J = 8.6 Hz, 8H), 5.05 (s, 4H), 4.80 (s, 8H).

^{13}C $\{^1\text{H}\}$ NMR (151 MHz, CDCl_3) δ 170.9, 147.3, 146.5, 137.1, 135.6, 132.2, 131.8, 130.7,

129.8, 127.8, 125.0, 124.4, 122.1, 95.0, 74.7, 56.0.

HRMS (ESI) calcd for $C_{76}H_{52}Br_4Cl_{12}N_2O_8$ $[M + H]^+$ 1855.67140, found, 1855.67295.

IR (neat): 3031, 2953, 2250, 1903, 1748, 1600, 1505, 1488, 1406, 1369, 1321, 1273, 1179, 1126, 1073, 1010, 905, 824, 762, 726, 649, 571, 529, 502, 464 cm^{-1} .



(3a*R*,4*R*,7*S*,7a*S*)-2-(4-iodophenyl)-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoisindole-1,3(2*H*)-dione (3.34).

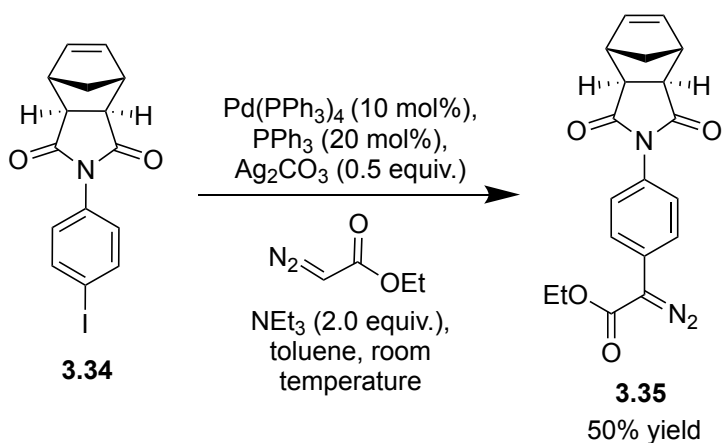
To a 40 mL toluene solution of ethyl **S3.1** (2.0 g, 12.2 mmol) were added 4-iodoaniline **S3.2** (4.0 g, 18 mmol) and NEt_3 (2.0 mL). The resulting mixture was allowed to stir at reflux (achieving using a heating block containing sand) for 15 h. The reaction mixture was cooled down to room temperature, and a white precipitate was formed. The solid was filtered, rinsed with toluene, and dried to get the desired product as white crystals (3.0 g, 8.0 mmol), 67% yield.

1H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, $J = 8.6$ Hz, 2H), 7.04 (d, $J = 8.6$ Hz, 2H), 6.35 (t, $J = 1.9$ Hz, 2H), 3.40 (t, $J = 1.8$ Hz, 2H), 2.85 (d, $J = 1.3$ Hz, 2H), 1.62 (dt, $J = 9.9, 1.6$ Hz, 1H), 1.43 (d, $J = 9.9$ Hz, 1H).

^{13}C { 1H } NMR (126 MHz, $CDCl_3$) δ 176.8, 138.5, 138.1, 131.6, 128.2, 94.2, 48.0, 46.0, 43.1.

HRMS (ESI) calcd for $C_{15}H_{13}INO_2$ $[M + H]^+$ 365.9985, found, 365.9991.

Calcd for $C_{15}H_{12}INO_2$: C, 49.34; H, 3.31; N, 3.84. Found: C, 49.13; H, 3.23; N, 3.88.



Ethyl 2-diazo-2-(4-((3*aR*,4*R*,7*S*,7*aS*)-1,3-dioxo-1,3,3*a*,4,7,7*a*-hexahydro-2*H*-4,7-methanoisoindol-2-yl)phenyl)acetate (3.35).

$\text{Pd(PPh}_3)_4$ (664 mg, 0.574 mmol, 10 mol %), PPh_3 (300 mg, 1.14 mmol, 20 mol %), compound **3.34** (2.1 g, 5.75 mmol, 1.0 equiv), and Ag_2CO_3 (792 mg, 2.87 mmol, 0.5 equiv) was suspended in toluene (25.0 mL) under nitrogen, followed by addition of NEt_3 (1.16 g, 11.5 mmol, 2.0 equiv) and ethyl diazoacetate (1.31 g, 11.5 mmol, 2.0 equiv). The resulting reaction was stirred at room temperature overnight and then filtered through a short path of silica gel, eluting with ethyl acetate. The volatile compounds were removed in vacuo, and the residue was purified by column chromatography (3:2 Hex/EtOAc) to give the product as a yellow solid **3.35** (1.0 g, 2.8 mmol), 50%.

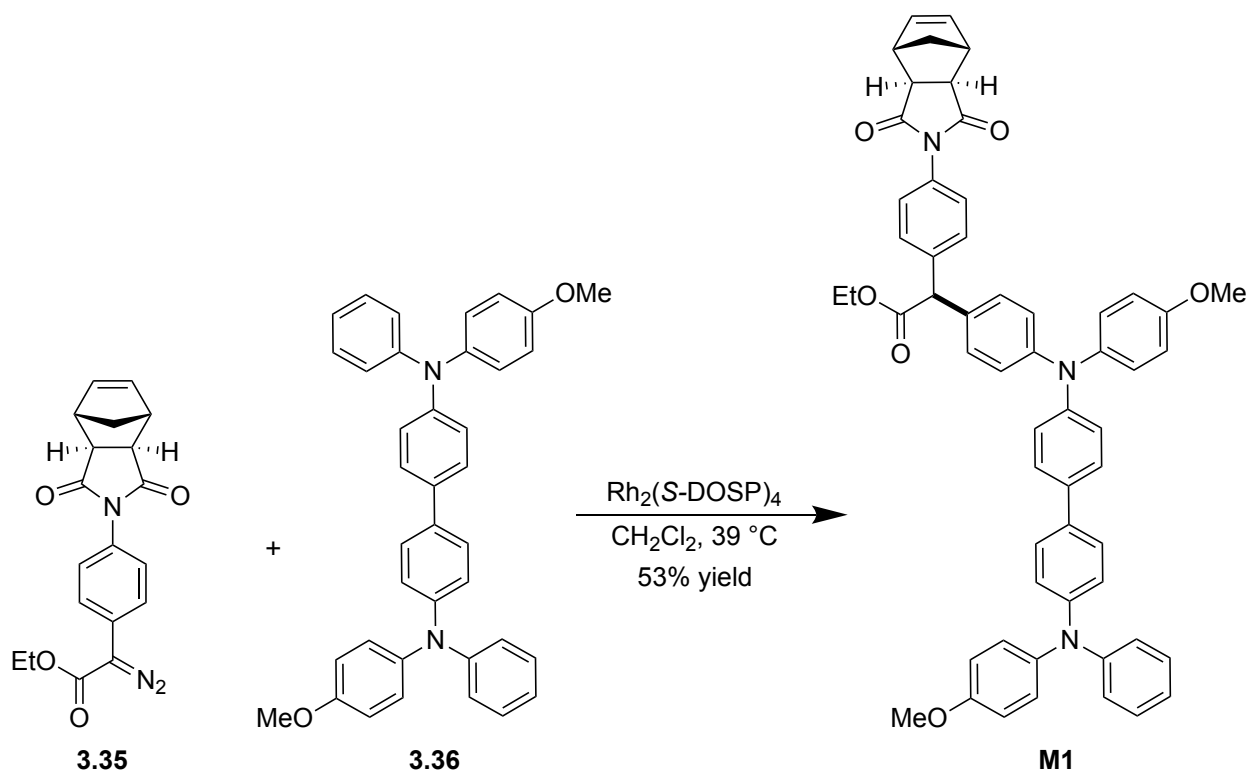
^1H NMR (500 MHz, CDCl_3) δ 7.60–7.53 (m, 2H), 7.33–7.27 (m, 2H), 6.35 (t, $J=1.9$ Hz, 2H), 4.34 (q, $J=7.2$ Hz, 2H), 3.41 (t, $J=1.8$ Hz, 2H), 2.86 (d, $J=1.3$ Hz, 2H), 1.62 (dt, $J=9.8, 1.6$ Hz, 1H), 1.48 (d, $J=9.9$ Hz, 1H), 1.34 (t, $J=7.1$ Hz, 3H).

^{13}C { ^1H } NMR (126 MHz, CDCl_3) δ 177.2, 164.9, 138.2, 129.3, 126.9, 126.6, 124.5, 63.7, 61.3, 48.0, 46.0, 43.2, 14.6.

HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{21}\text{N}_4\text{O}_4$ [$\text{M} + \text{NH}_4$] $^+$ 369.1557, found, 369.1560.

Calcd for $\text{C}_{19}\text{H}_{21}\text{N}_4\text{O}_4$: C, 64.95; H, 4.88; N, 11.96. Found: C, 64.48; H, 4.98; N, 10.88 (we were unable to obtain analysis within acceptable limits despite several attempts).

Synthesis of Norbornene-Bis(diarylamino)biphenyl Monomer, **M1**.



In a 20 mL vial with a stir bar, **3.36** (100 mg, 0.182 mmol) and $\text{Rh}_2(\text{S-DOSP})_4$ (4.2 mg, 0.0022 mmol, 1.2 mol %) were added, capped, evacuated, and refilled with nitrogen three times. Anhydrous CH_2Cl_2 (1.0 mL added) was used to dissolve all the solids. In another vial, **3.35** (92 mg, 0.26 mmol) was added, evacuated, and refilled three times. Dry CH_2Cl_2 (5.0 mL) was added to dissolve all solids, and then the yellow solution was taken into a syringe and added dropwise to the vial containing MeO-TPD over 2 h. The reaction mixture was stirred overnight at reflux (achieved using a heating block containing sand). The solvent was evaporated under reduced pressure to yield a crude product, in which mass spectrometry indicated the presence of both the desired compound and a minor product identified as a double-insertion product. The desired product, **M1**, was purified by column chromatography (3:2 hexane/EtOAc) and obtained as a pale yellow solid (85 mg, 0.075 mmol), 53%.

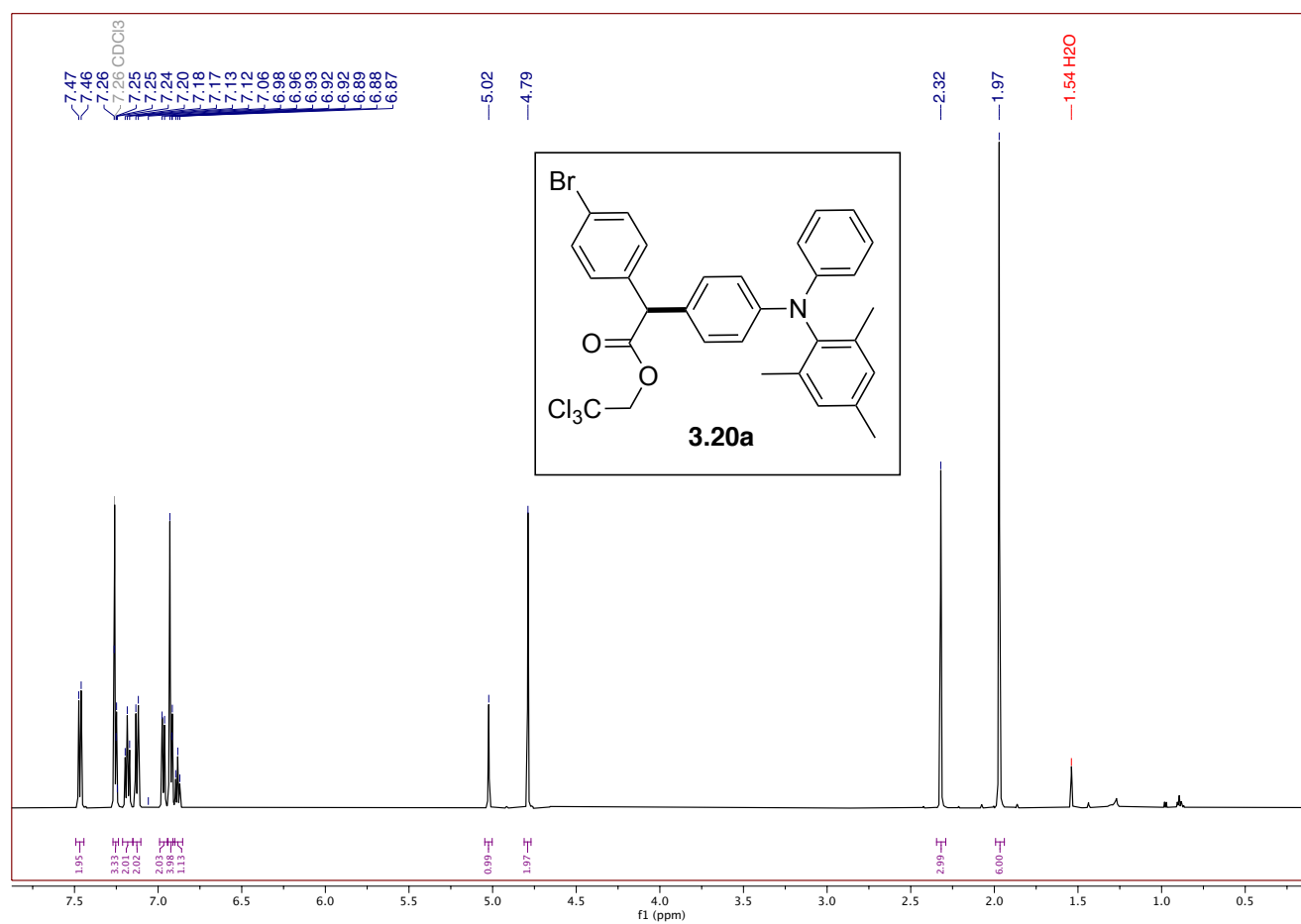
¹H NMR (700 MHz, CDCl₃) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.43–7.36 (d, *J* = 8.3, 4H), 7.25–7.20 (m, 4H), 7.16 (d, *J* = 8.3 Hz, 2H), 7.12–7.03 (m, 10H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.95 (m, 1H), 6.85 (dd, *J* = 9.0, 3.6 Hz, 4H), 6.35 (m, 2H), 4.93 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.40 (m, 2H), 2.85 (d, *J* = 1.4 Hz, 2H), 1.61 (d, *J* = 9.9, 1.6 Hz, 1H), 1.47 (d, *J* = 9.9, 1.6 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H).

¹³C {¹H} NMR (176 MHz, CDCl₃) δ 177.2, 172.3, 171.3, 156.5, 156.3, 148.2, 147.4, 147.1, 146.8, 140.8, 140.5, 139.7, 138.1, 134.4, 134.2, 131.5, 130.9, 129.5, 129.3, 129.2, 127.6, 127.5, 127.3, 123.3, 123.2, 123.0, 122.7, 122.1, 114.9 (two peaks separated by 0.03 ppm), 61.5, 60.5, 56.3, 55.6, 48.0, 46.0, 43.1, 21.2, 14.3, 14.3.

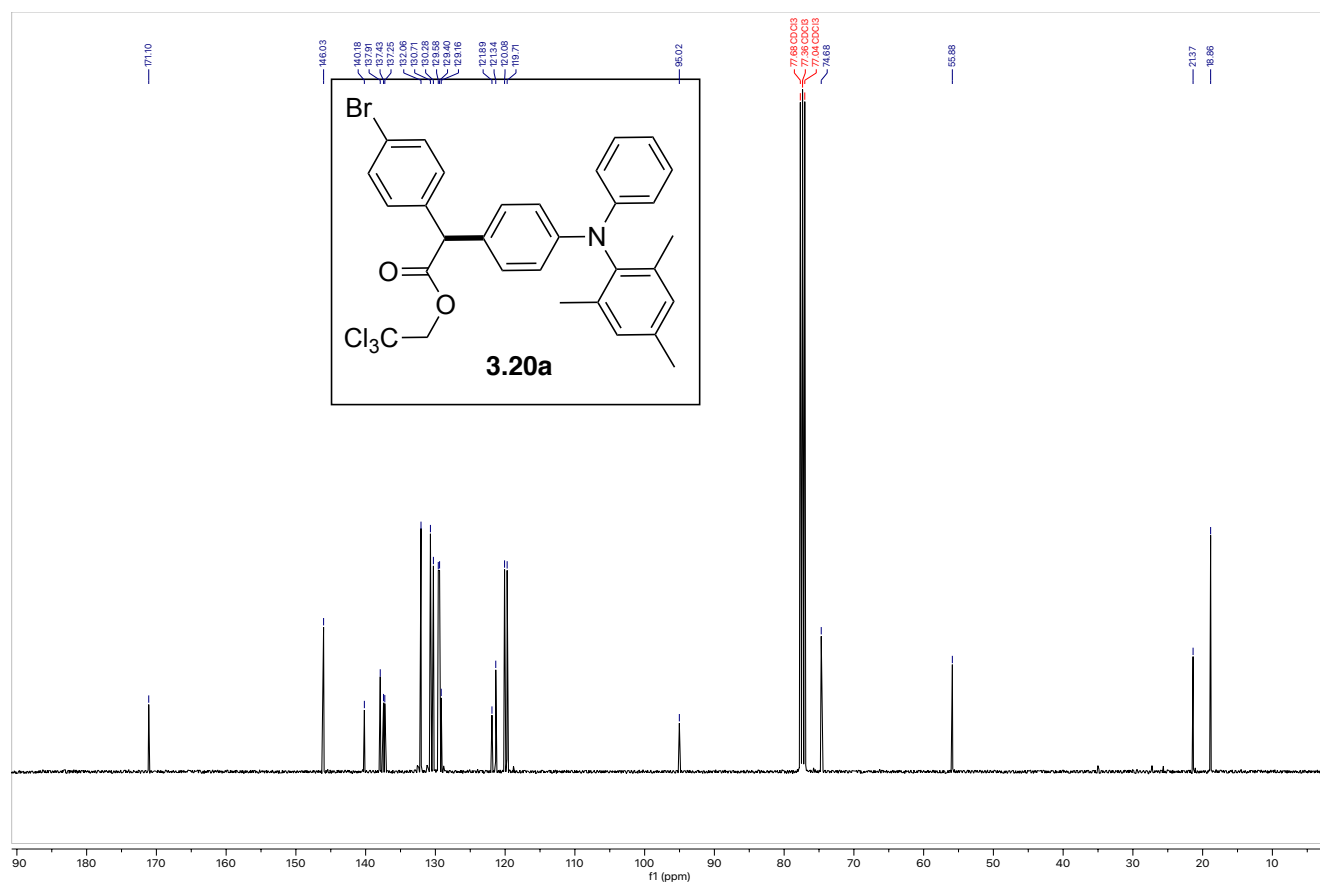
HRMS (ESI) calcd for C₅₇H₅₀N₃O₆ [M + H]⁺, 872.3694; found, 872.3678. [Minor double-insertion product (not isolated pure):

ERMS(EI) calcd C₇₆H₆₇N₄O₁₀ [M + H]⁺, 1195.4852; found, 1195.4832.

^1H NMR, ^{13}C NMR Spectroscopic Data and HPLC.



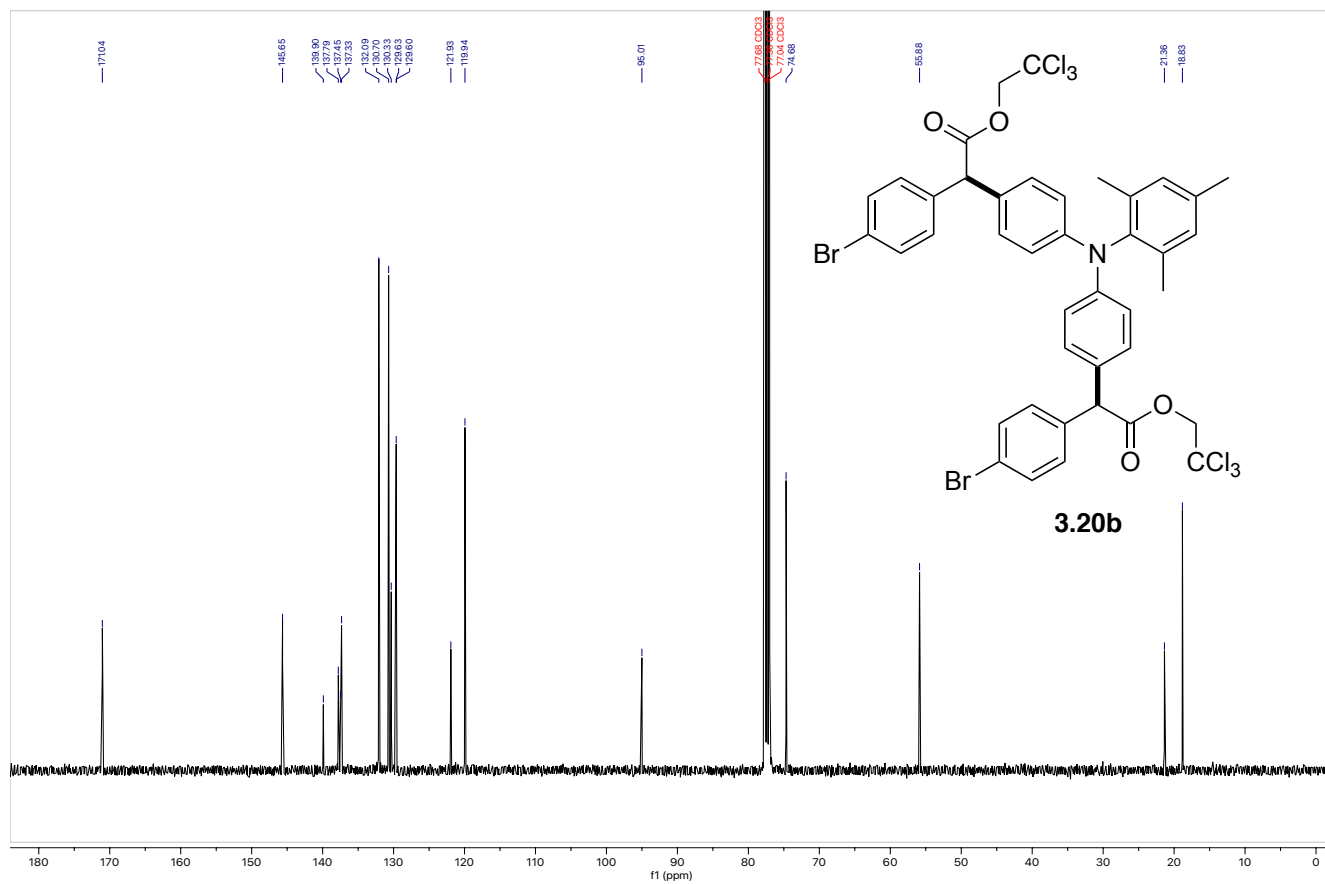
^1H NMR spectrum (600 MHz, Chloroform-d) of **3.20a**.



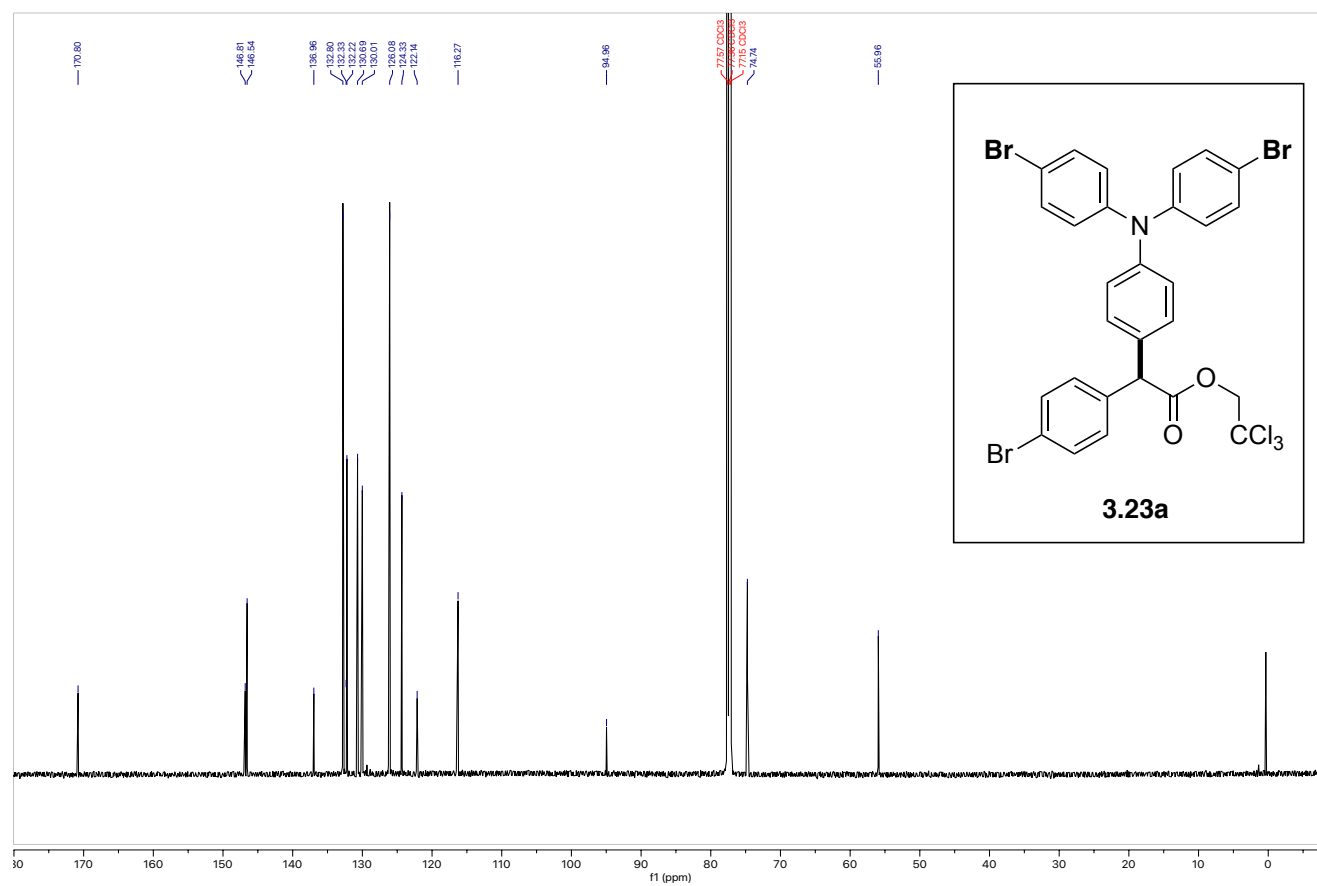
¹³C{¹H} NMR spectrum (101 MHz, Chloroform-d) of **3.20a**.

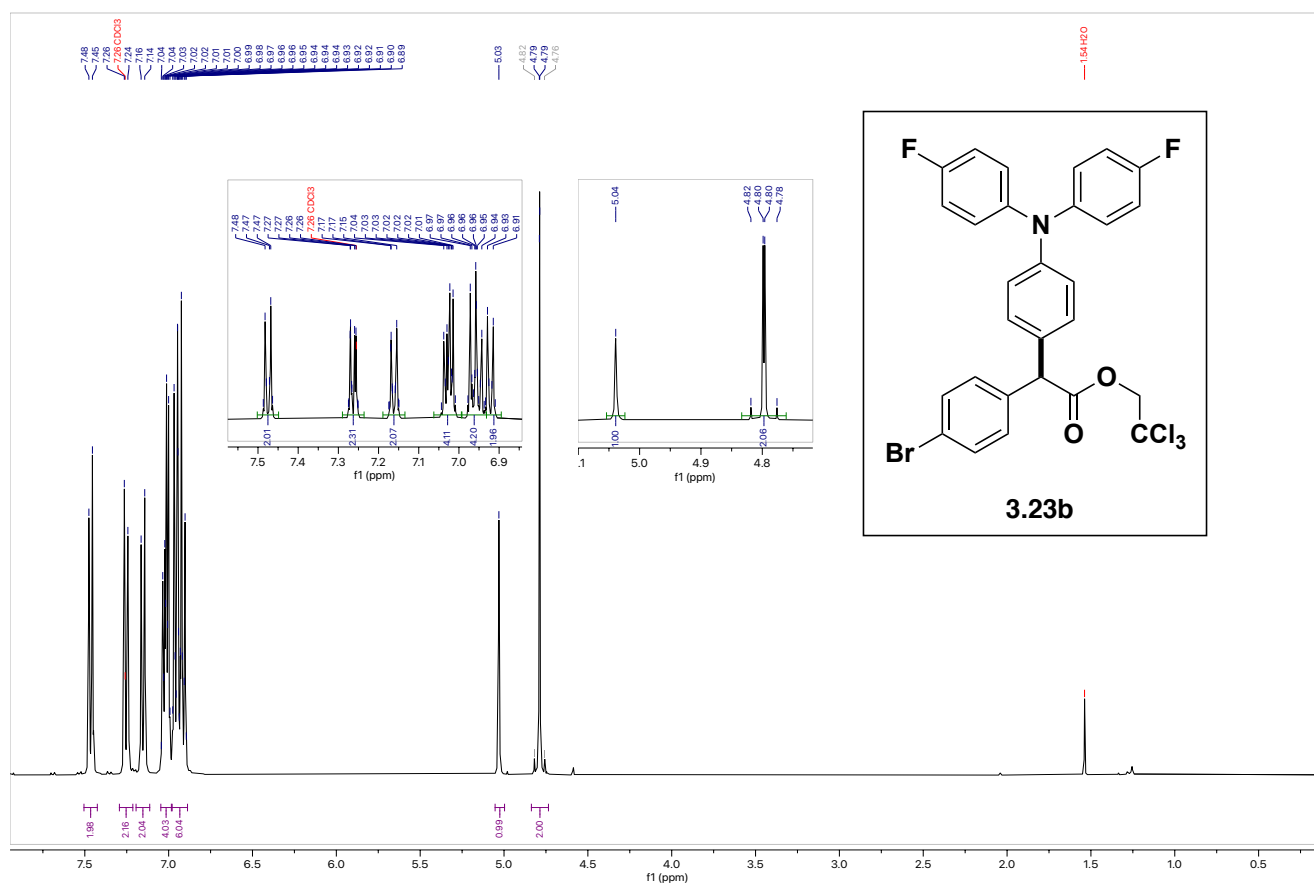


¹H NMR spectrum (600 MHz, Chloroform-d) of **3.20b**.

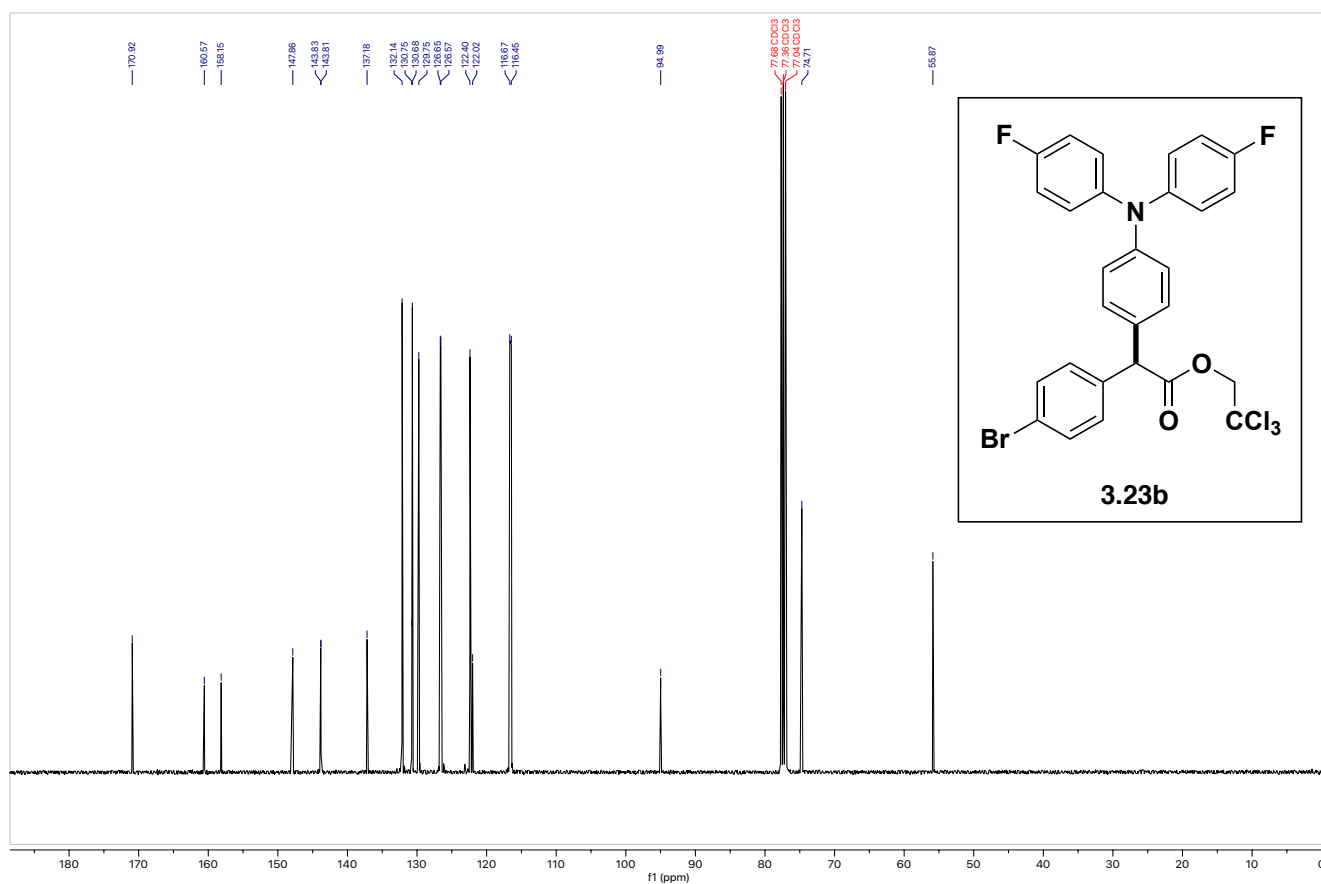


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-d) of **3.20b**.

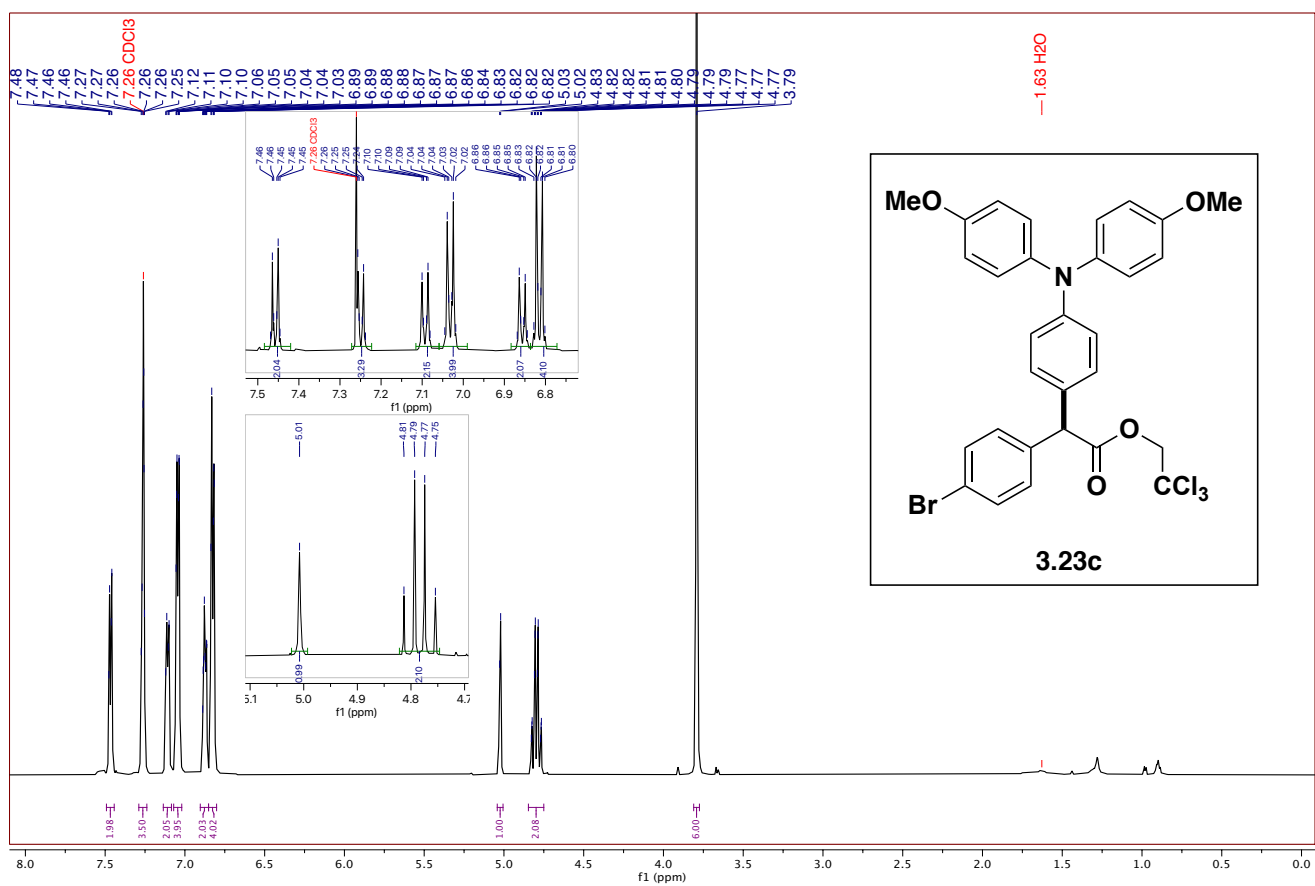




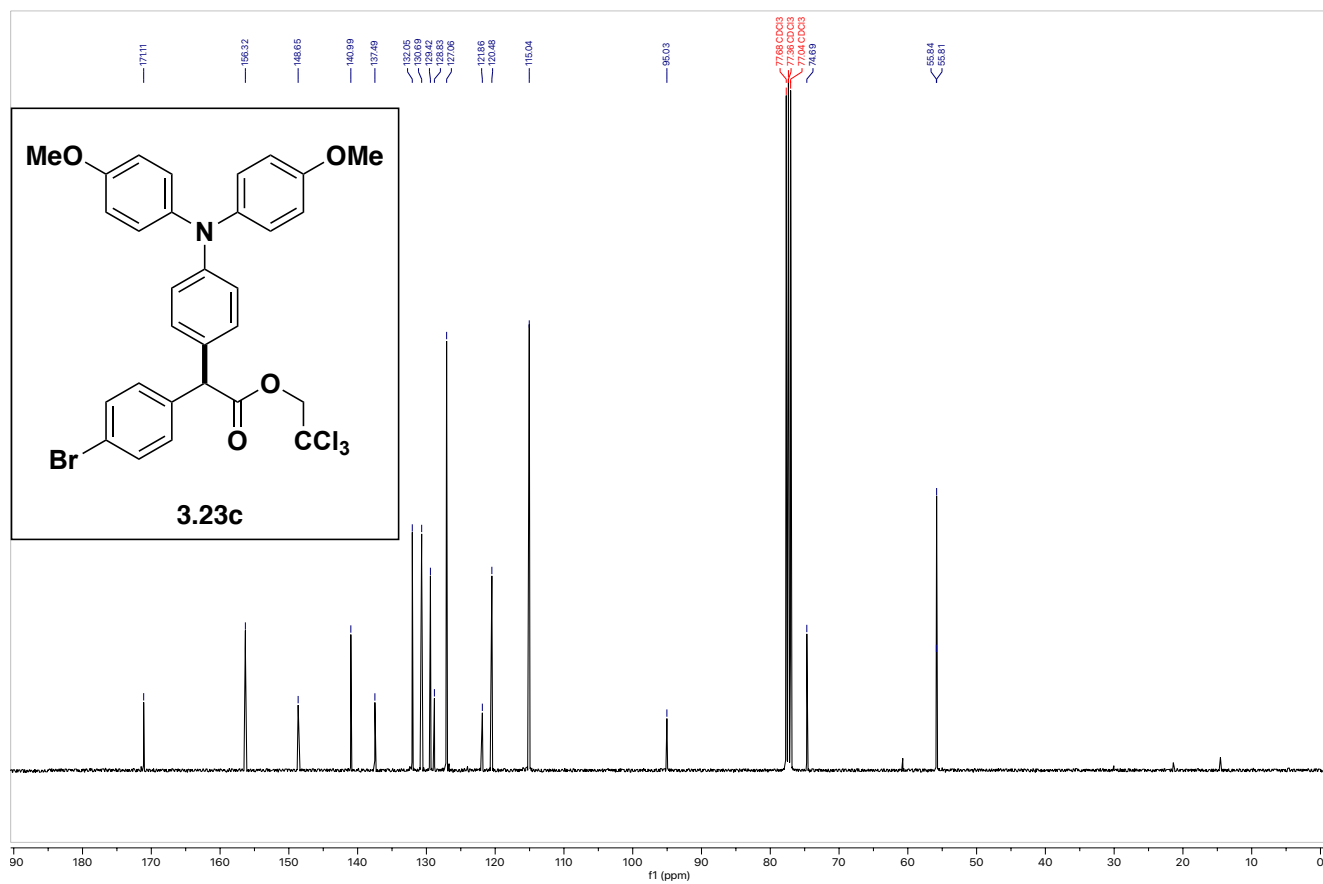
¹H NMR spectrum (400 MHz, Chloroform-d) of **3.23b**.



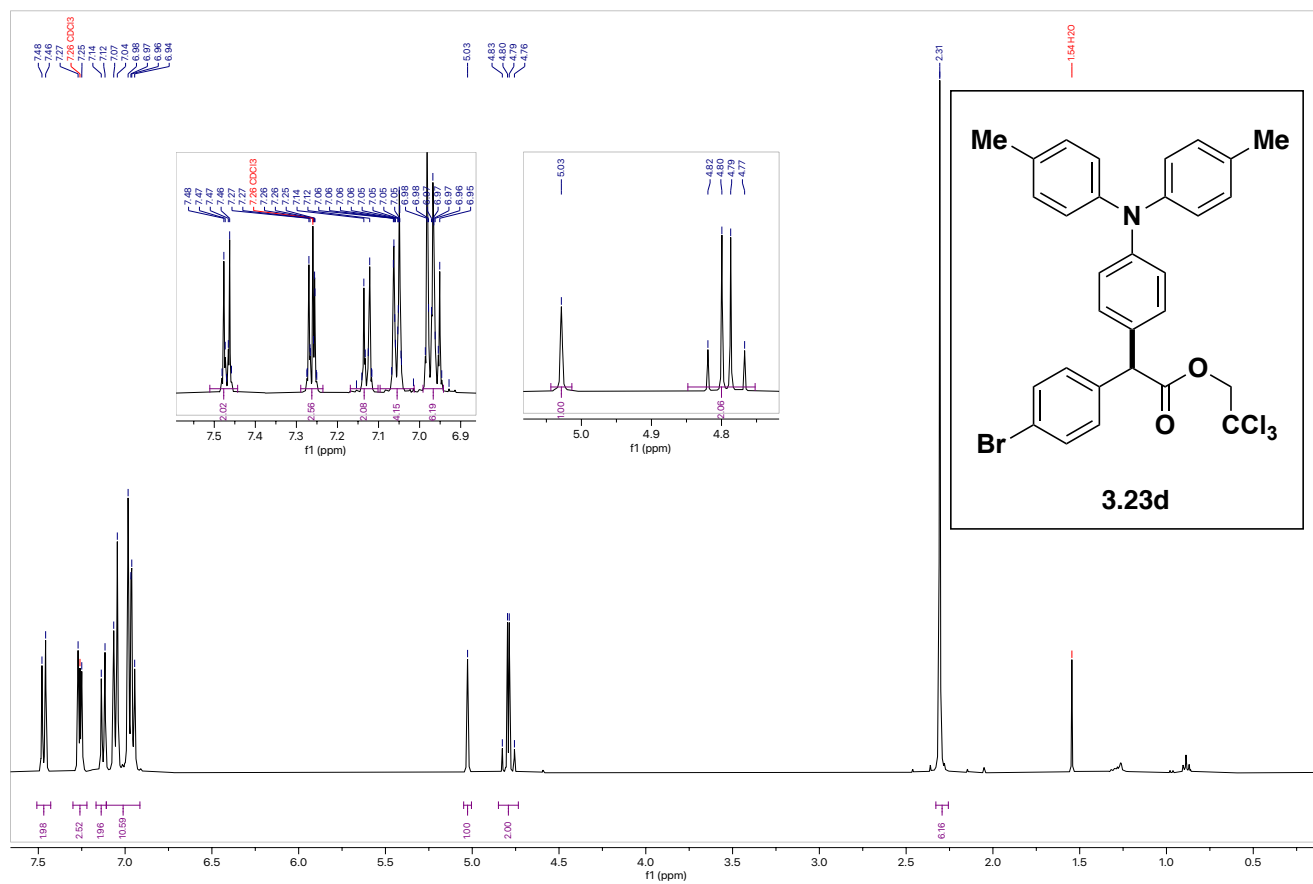
¹³C{¹H} NMR spectrum (101 MHz, Chloroform-d) of **3.23b**.



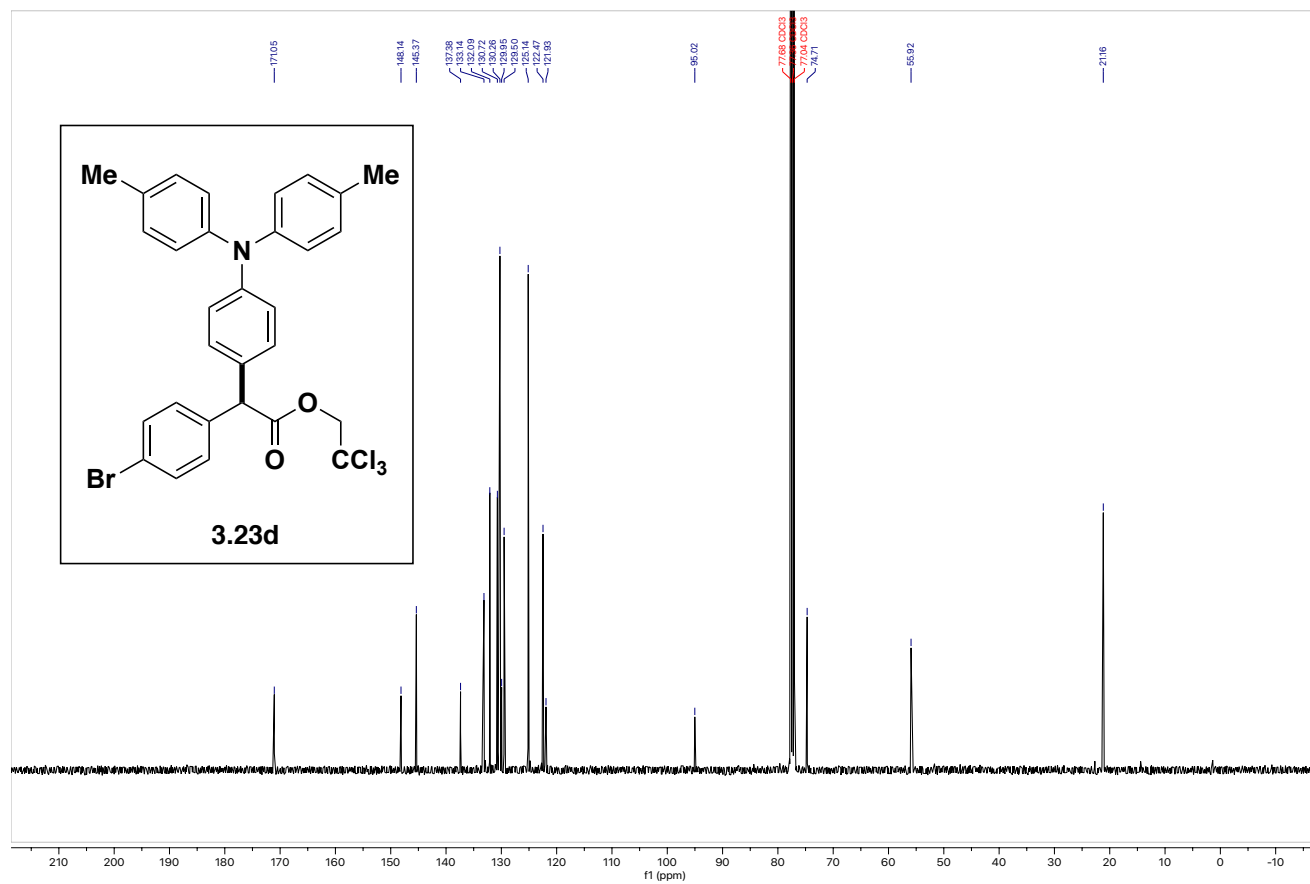
¹H NMR spectrum (600 MHz, Chloroform-d) of **3.23c**.



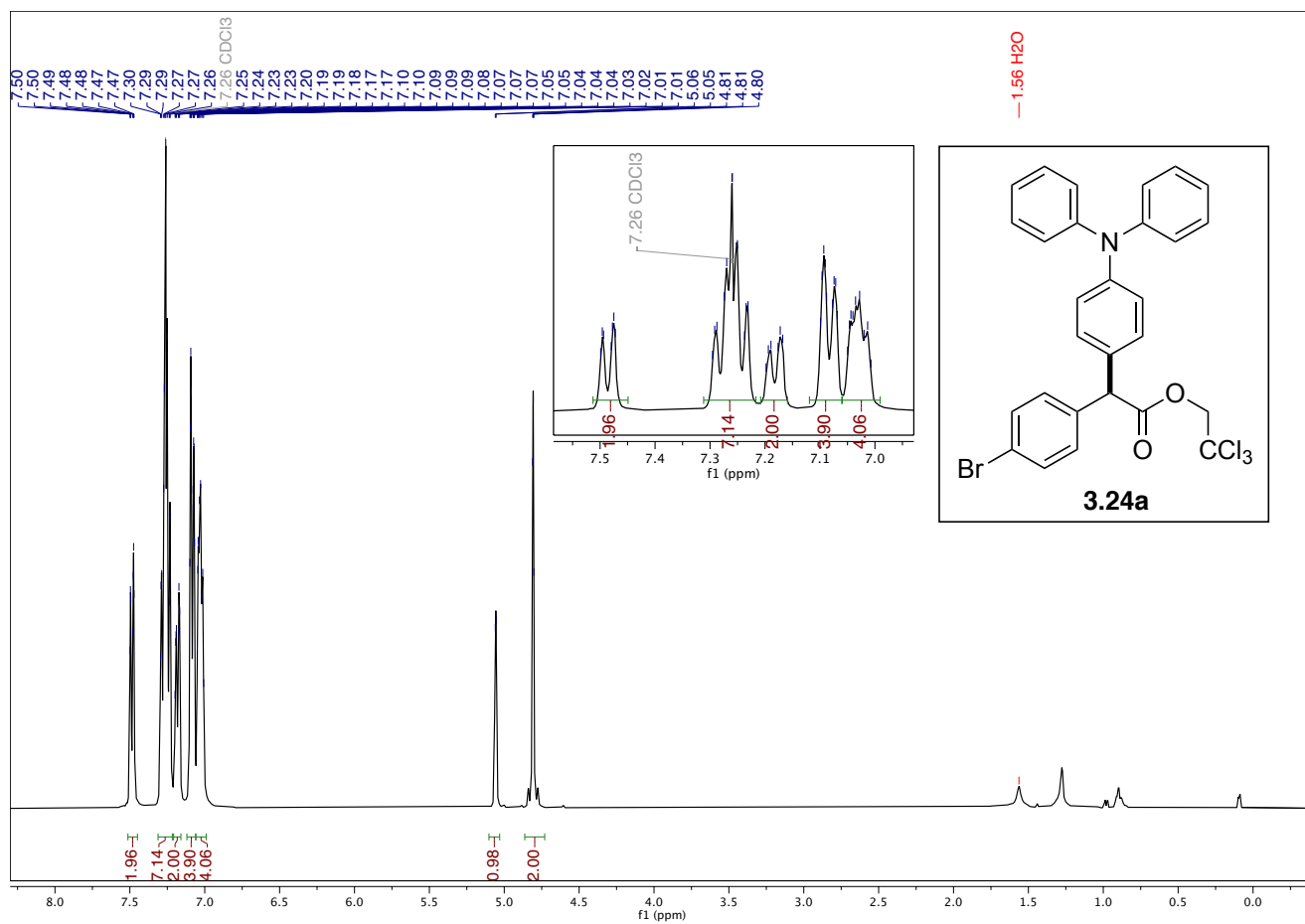
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-d) of **3.23c**.



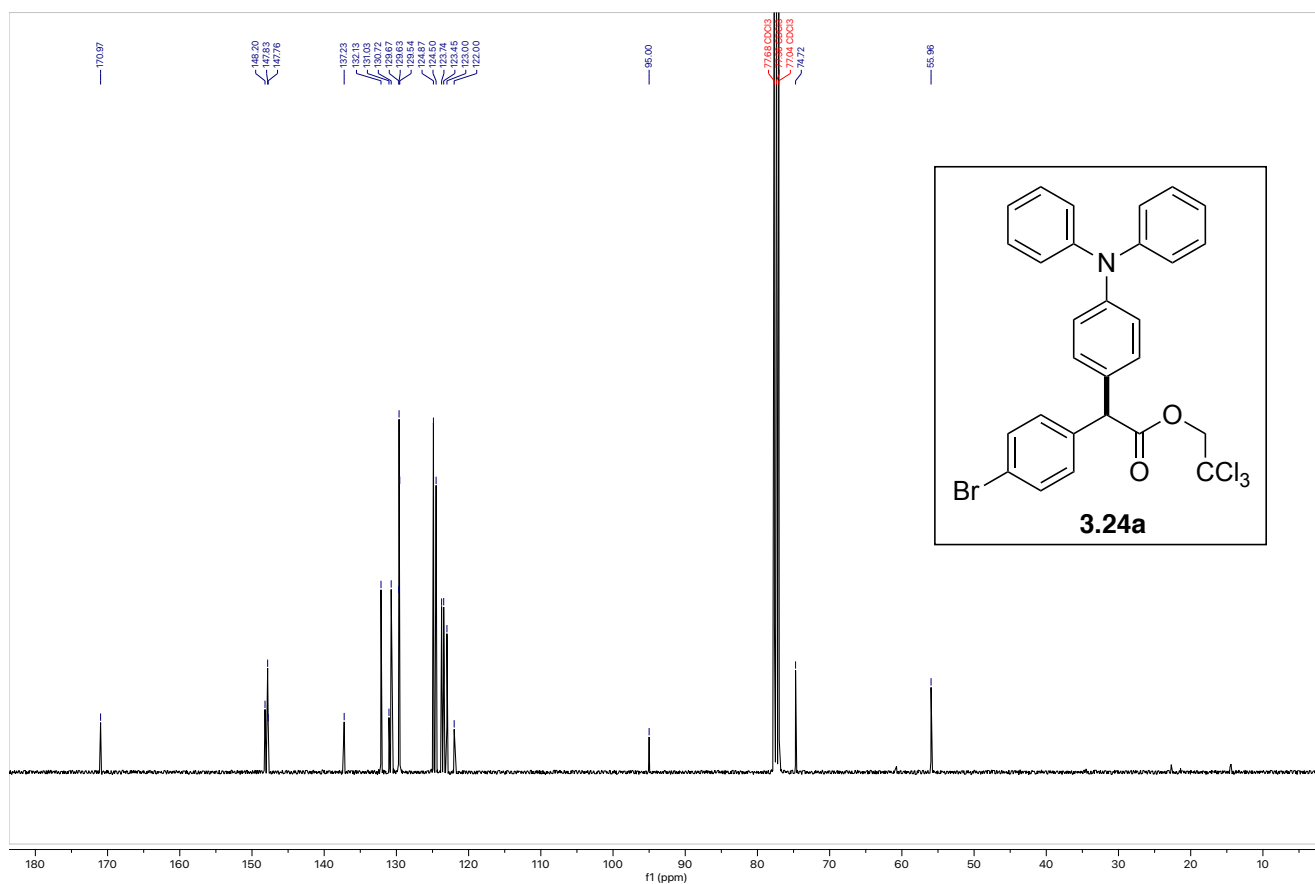
¹H NMR spectrum (400 MHz, Chloroform-d) of **3.23d**.



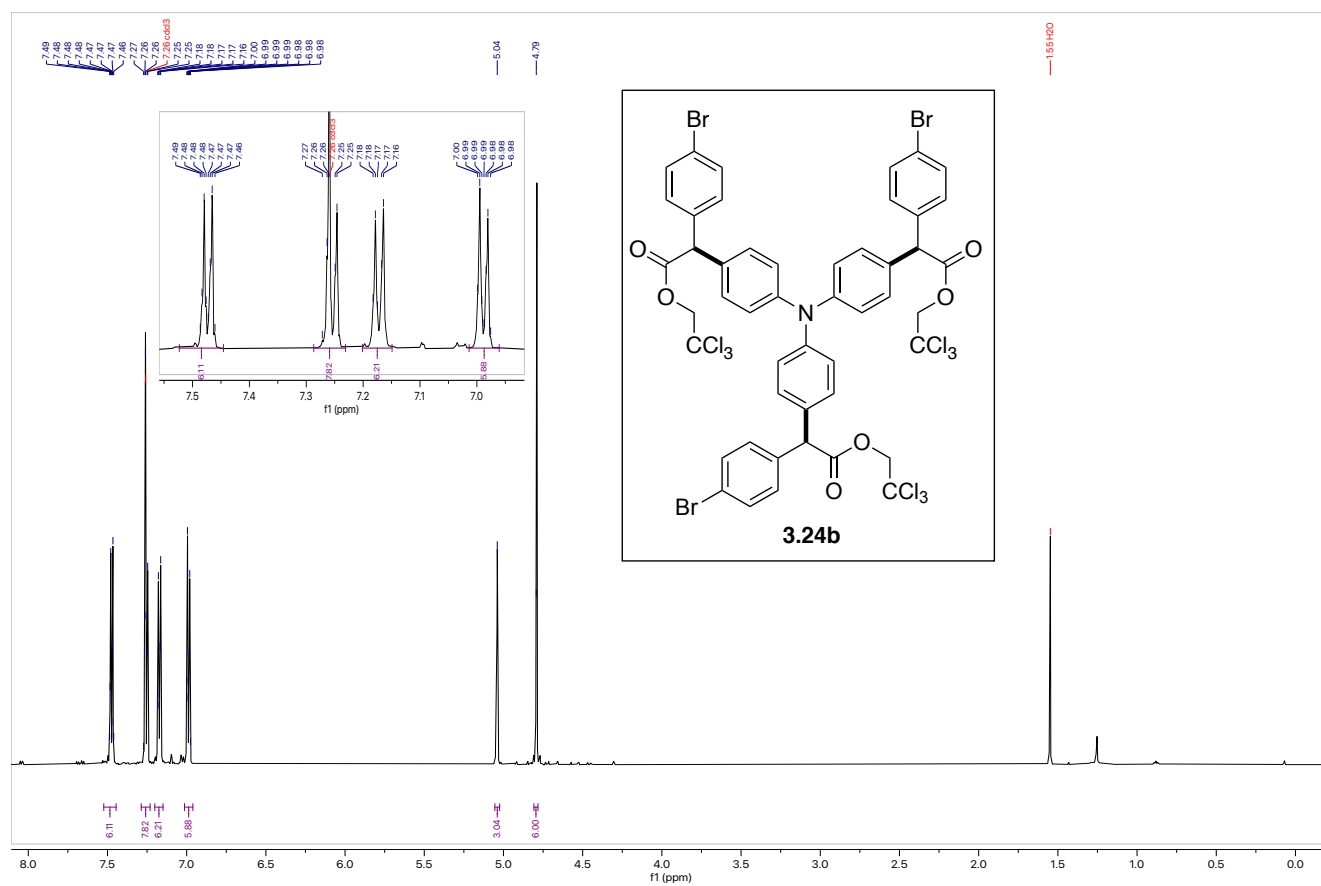
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-d) of **3.23d**.



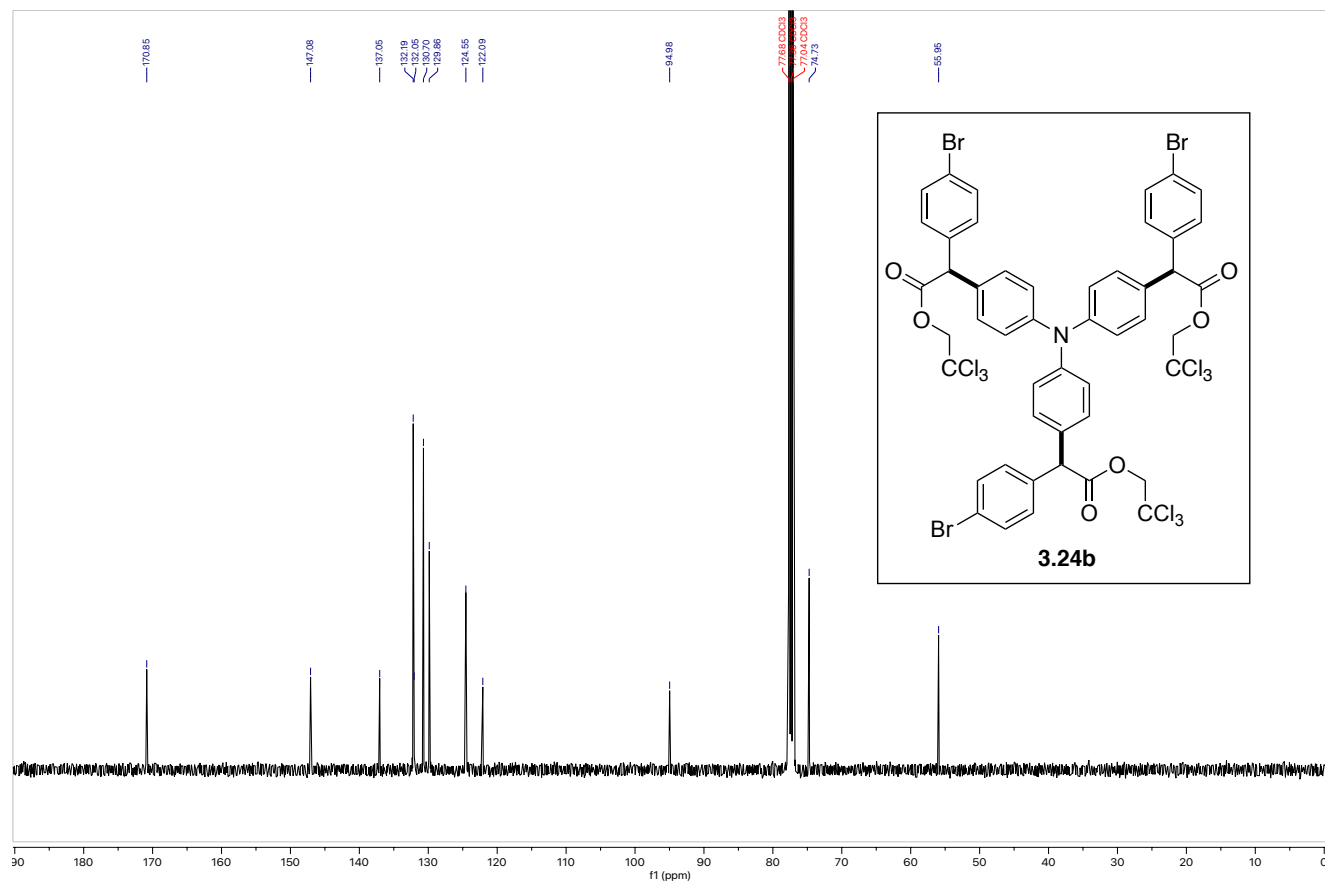
¹H NMR spectrum (400 MHz, Chloroform-d) of **3.24a**.



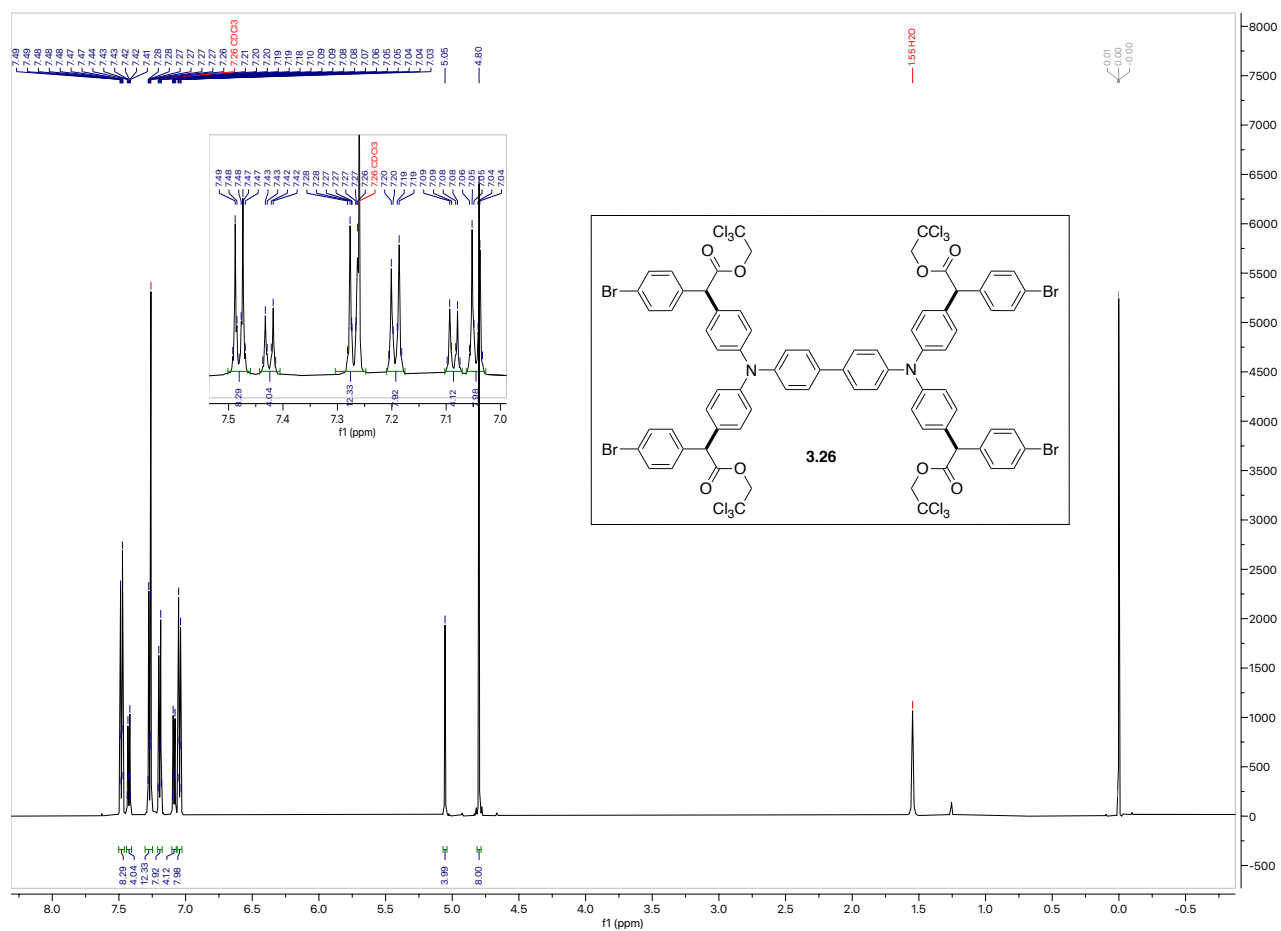
¹³C{¹H} NMR spectrum (101 MHz, Chloroform-d) of **3.24a**.

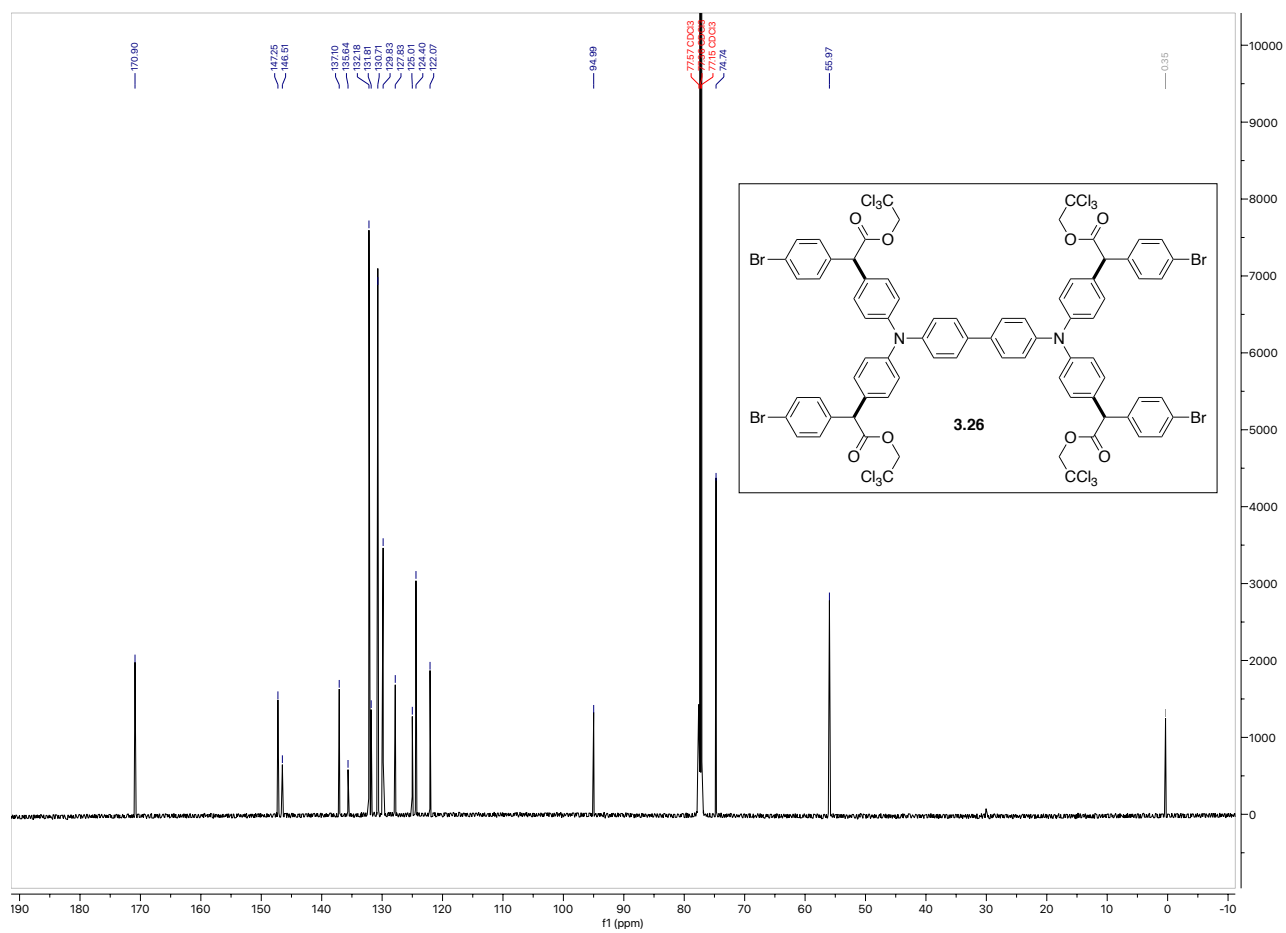


^1H NMR spectrum (600 MHz, Chloroform-d) of **3.24b**.

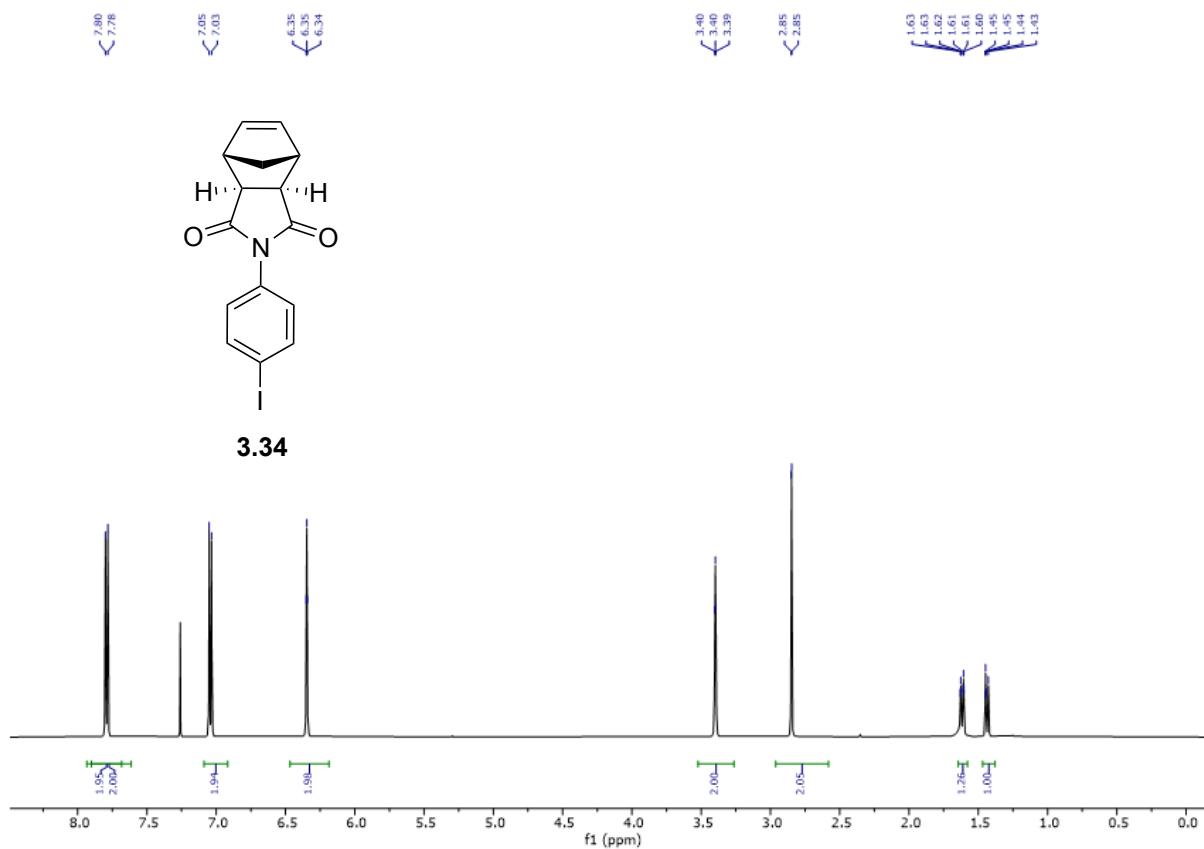


^{13}C NMR spectrum (101 MHz, CDCl_3) of **3.24b**.

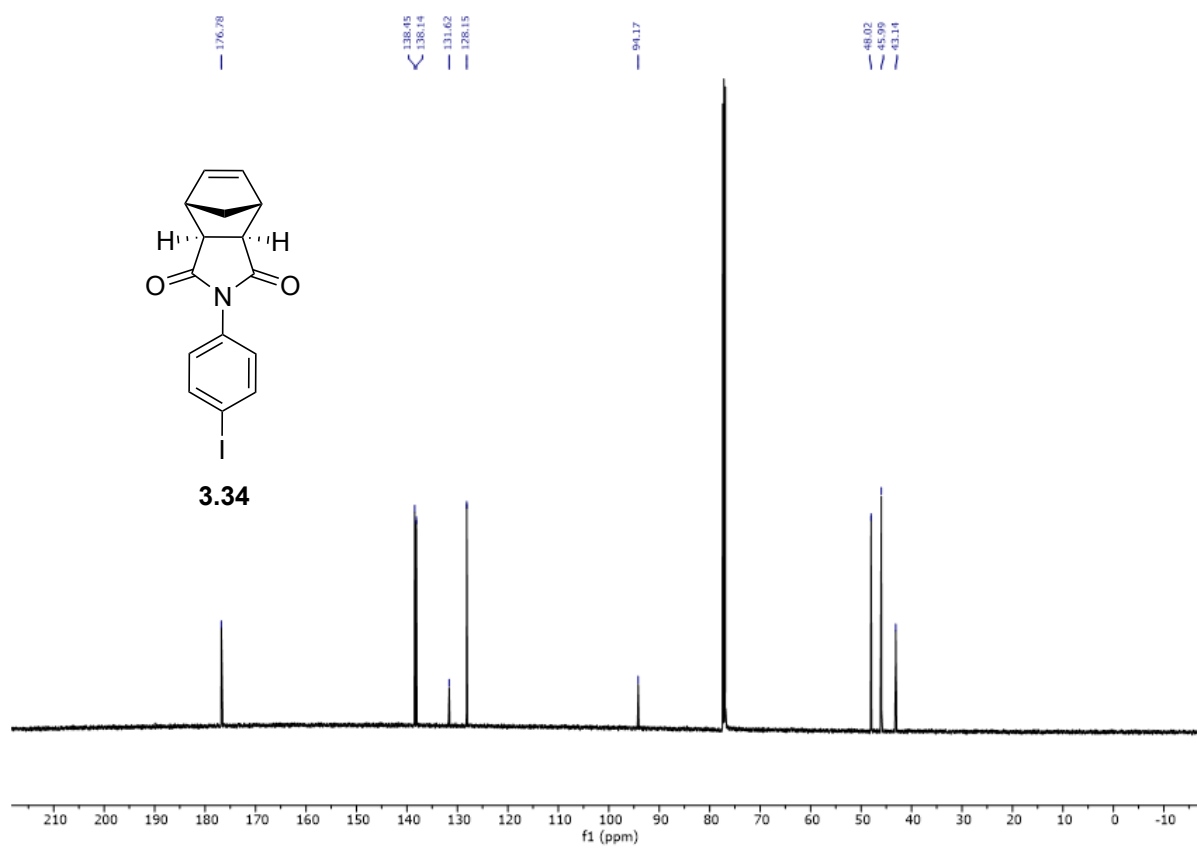




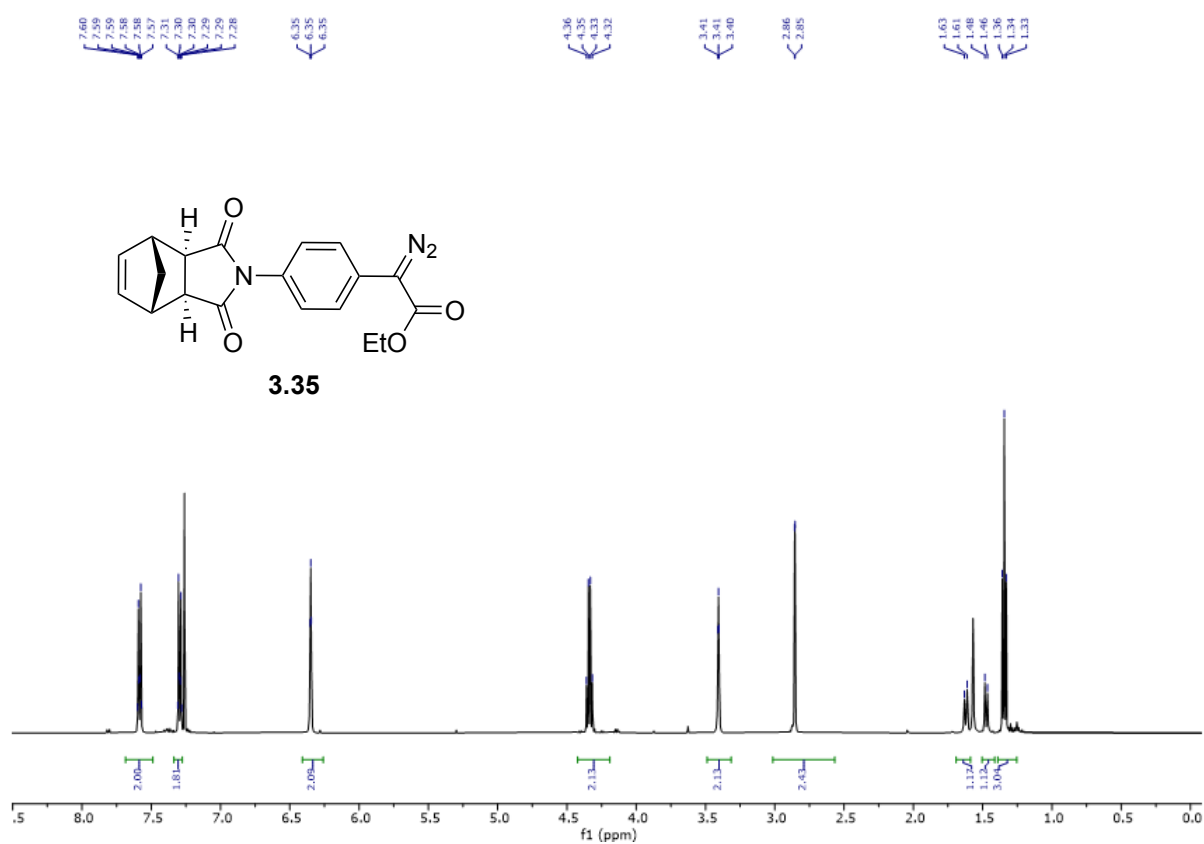
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-d) of **3.26**.



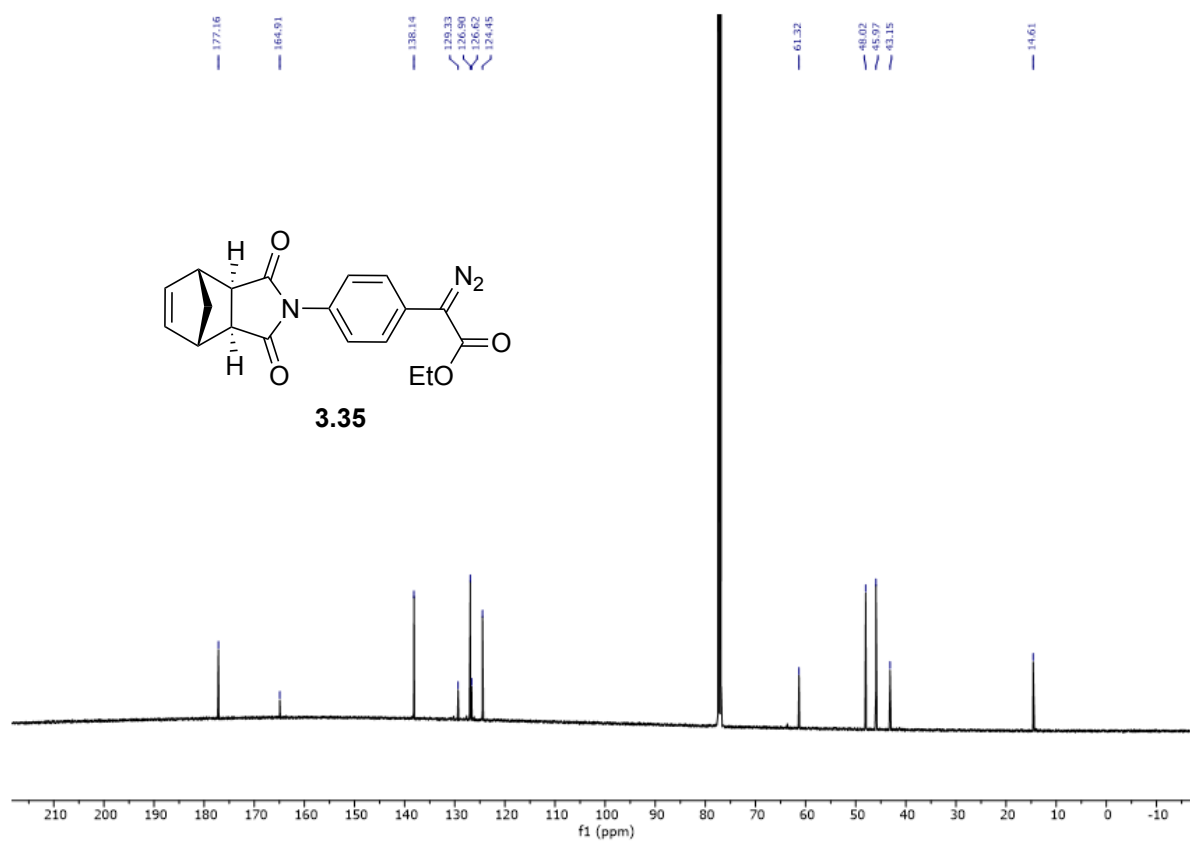
^1H NMR spectrum (500 MHz, Chloroform-d) of **3.34**.



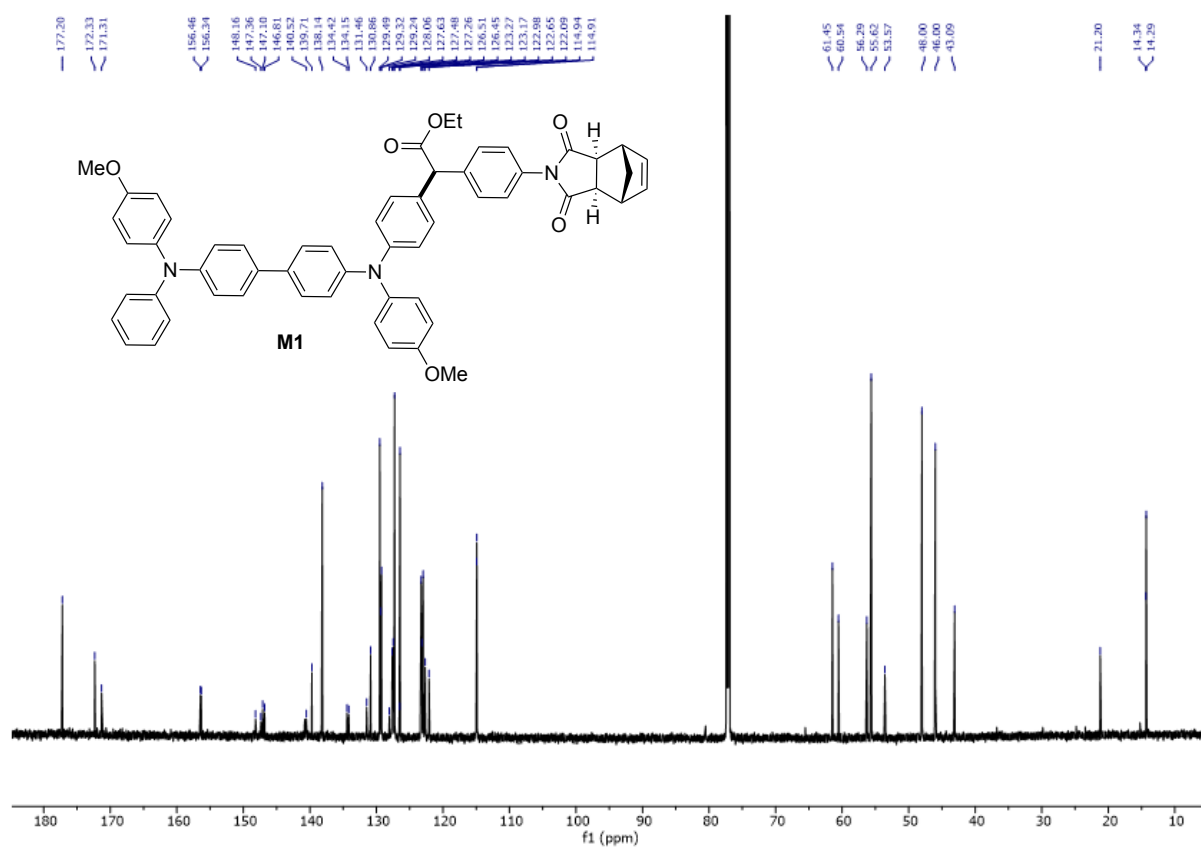
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (126 MHz, Chloroform-d) of **3.34**.



¹H NMR spectrum (500 MHz, Chloroform-d) of **3.35**.

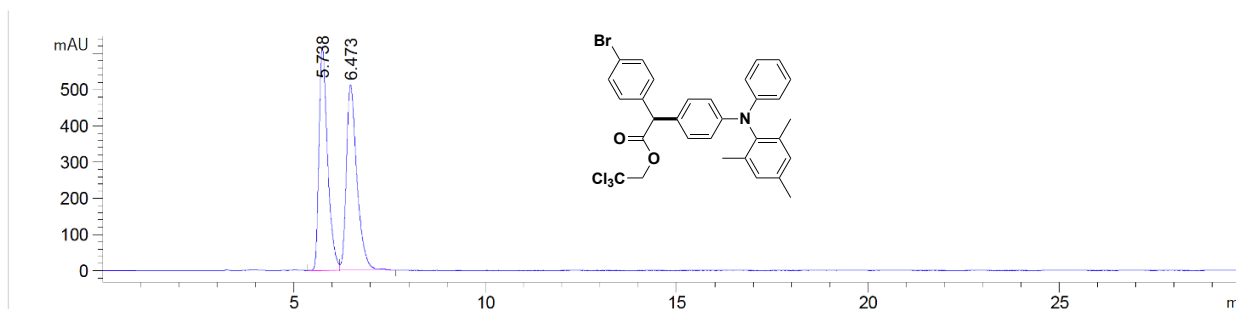


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (126 MHz, Chloroform-d) of **3.35**.



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (176 MHz, Chloroform-d) of **M1**.

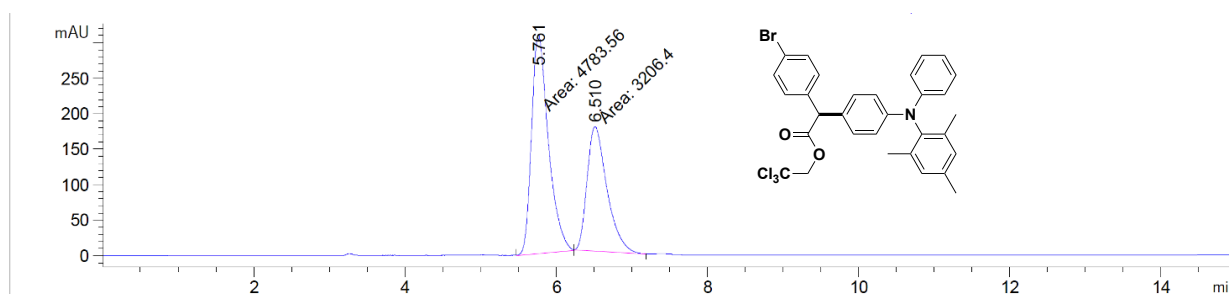
HPLC Traces



Signal 2: DAD1 B, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.738	VV R	0.2300	9639.89258	617.98462	49.4060
2	6.473	VV R	0.2640	9871.70898	511.92154	50.5940

Totals : 1.95116e4 1129.90616



Signal 2: DAD1 B, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.761	MM	0.2580	4783.55713	309.04507	59.8696
2	6.510	MM	0.3046	3206.39819	175.44948	40.1304

Totals : 7989.95532 484.49455

HPLC trace synthesized using $\text{Rh}_2(S\text{-}p\text{-Br-TPCP})_4$ catalyst

References for Chapter 3

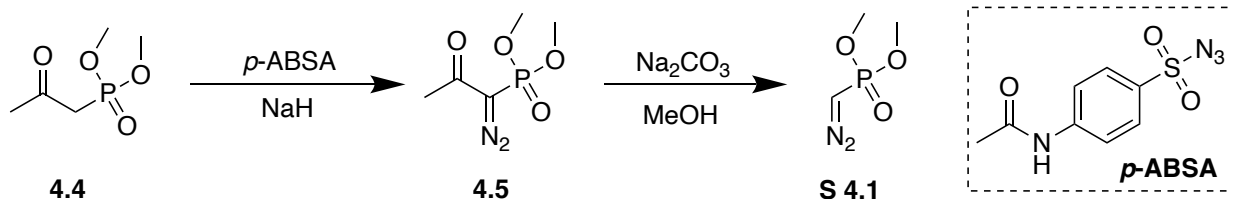
1. Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J., Asymmetric Cyclopropanations by Rhodium(II) N-(Arylsulfonyl)prolinate Catalyzed Decomposition of Vinyldiazomethanes in the Presence of Alkenes. Practical Enantioselective Synthesis of the Four Stereoisomers of 2-Phenylcyclopropan-1-amino Acid. *J. Am. Chem. Soc.* **1996**, *118* (29), 6897-6907.
2. Callot, H. J.; Metz, F., Rhodium(II)2,4,6-triarylbenzoates : improved catalysts for the syn cyclopropanation of z-olefins. *Tetrahedron* **1985**, *41* (20), 4495-4501.
3. Reddy, R. P.; Lee, G. H.; Davies, H. M. L., Dirhodium Tetracarboxylate Derived from Adamantylglycine as a Chiral Catalyst for Carbenoid Reactions. *Org. Lett.* **2006**, *8* (16), 3437-3440.
4. Fu, J.; Ren, Z.; Bacsá, J.; Musaev, D. G.; Davies, H. M. L., Desymmetrization of cyclohexanes by site- and stereoselective C–H functionalization. *Nature* **2018**, *564* (7736), 395-399.
5. Reddy, R. P.; Davies, H. M. L., Dirhodium Tetracarboxylates Derived from Adamantylglycine as Chiral Catalysts for Enantioselective C–H Aminations. *Org. Lett.* **2006**, *8* (22), 5013-5016.
6. Ghanem, A.; Gardiner, M. G.; Williamson, R. M.; Müller, P., First X-ray Structure of a N-Naphthaloyl-Tethered Chiral Dirhodium(II) Complex: Structural Basis for Tether Substitution Improving Asymmetric Control in Olefin Cyclopropanation. *Chem. Eur. J.* **2010**, *16* (11), 3291-3295.
7. Qin, C.; Boyarskikh, V.; Hansen, J. H.; Hardcastle, K. I.; Musaev, D. G.; Davies, H. M. L., D₂-Symmetric Dirhodium Catalyst Derived from a 1,2,2-Triarylcyclopropanecarboxylate Ligand: Design, Synthesis and Application. *J. Am. Chem. Soc.* **2011**, *133* (47), 19198-19204.

8. Garlets, Z. J.; Boni, Y. T.; Sharland, J. C.; Kirby, R. P.; Fu, J.; Bacsa, J.; Davies, H. M. L., Design, Synthesis, and Evaluation of Extended C₄-Symmetric Dirhodium Tetracarboxylate Catalysts. *ACS Catal.* **2022**, *12* (17), 10841-10848.

Experimental section for chapter 4: Synthesis of Aryl- and Hetroaryl Diazophosphonates by Palladium-catalyzed Cross-coupling Reactions and Cyclopropanation.

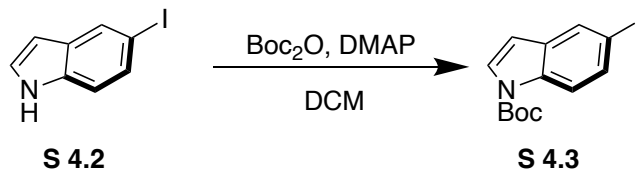
Procedure for the synthesis of phosphonate diazo compounds:

Bestmann-Ohira method

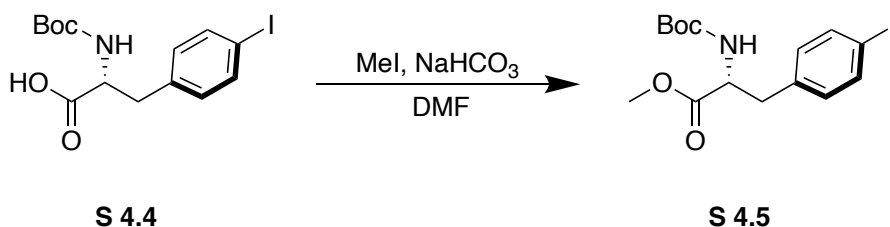


To a 250 mL flask was added a solution of dimethyl 2-oxopropylphosphonate **4.4** (6.26 g, 37.7 mmol) in toluene (160 mL) and THF (30 mL) was stirred at 0 °C for 30 min. Sodium hydride (60% dispersion in mineral oil, 1.66 g, 41.5 mmol) was slowly added into the flask and the solution was stirred at 0 °C for 1 hour under nitrogen, *p*-ABSA (9.96 g, 41.5 mmol) was added in one portion and the reaction was warmed to room temperature and stirring was continued overnight. The reaction mixture was filtered through celite, and the residue was evaporated under reduced pressure to remove the volatile materials. The crude diazo product was purified by flash column chromatography on silica gel (petroleum ether : EtOAc, 1:1) giving product **4.5** (6.1 g , 84%) as a yellow liquid. Spectroscopic data are in agreement with those reported in the literature.

A solution of **4.5** (1.9 g, 10 mmol) in 10 mL of MeOH was stirred with Sodium carbonate (5 mmol) at room temperature for 15 min (monitored by TLC). The reaction mixture was filtered off, and the residue was evaporated under reduced pressure to remove the volatile materials. The crude diazo product was purified by flash column chromatography on silica gel (petroleum ether: EtOAc, 1:1) giving product **S 4.1** (1.3 g, 85%) as a yellow liquid. Spectroscopic data are in agreement with those reported in the literature.¹⁻³

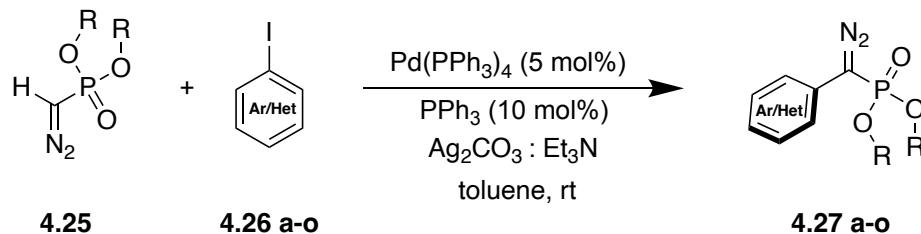


A solution of 5-iodoindole (2.00 g, 8.229 mmol) in dry methylene chloride (40 mL) was treated with di-tert-butyl dicarbonate (2.155 g, 9.875 mmol) and 4-dimethylaminopyridine (201 mg, 1.646 mmol) was added at room temperature and the solution was stirred at room temperature for 16 hours. The crude product was purified by flash column chromatography on silica gel (petroleum ether : EtOAc, 1:1) giving product **S 4.3** as a colorless oil (2.57 g, 91%). Spectroscopic data are in agreement with those reported in the literature.⁴



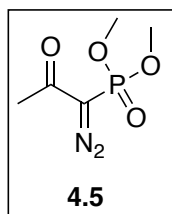
A solution of halogenated amino acid (5.00 g, 12.8 mmol) in DMF (35 mL) was treated with NaHCO_3 (1.61 g, 19.2 mmol) and iodomethane (2.72 g, 19.2 mmol) was added and the solution was stirred at room temperature for 4 hours (monitored by TLC). The organic layer was separated, and the aqueous layer was extracted with DCM. The combined organic layers were dried (Na_2SO_4), concentrated and the residue was purified by flash column chromatography on silica gel (hexane : EtOAc, 6:1) to give compound **S 4.5** as a white solid (4.7 g, 90% yield). Spectroscopic data are in agreement with those reported in the literature.⁵

General Procedure: Palladium-catalyzed cross-coupling reaction:



Pd(PPh₃)₄ (142 mg, 0.12 mmol, 5 mol%), PPh₃ (64.3 mg, 0.25 mmol, 10 mol%), aryl iodide (2.45 mmol, 1.0 equiv), and Ag₂CO₃ (507 mg, 1.84 mmol, 0.75 equiv) were suspended in toluene (15 mL) under an argon atmosphere. NEt₃ (0.34 mL, 2.45 mmol, 1.0 equiv) and dimethyl (diazomethyl)phosphonate (478 mg, 3.19 mmol, 1.3 equiv) were then added to the mixture. The reaction was stirred at room temperature for 4–6 hours (monitor by TLC), after which it was filtered through a short silica gel column using ethyl acetate as the eluent. The volatiles were removed under reduced pressure, and the residue was purified by column chromatography to yield the desired products.

Dimethyl (1-diazo-2-oxopropyl)phosphonate. ⁷



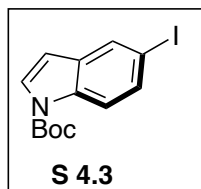
¹H NMR (600 MHz, CDCl₃) δ 3.83 (d, *J* = 11.8 Hz, 6H), 2.26 (s, 3H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 190.3 (d, *J* = 13.1 Hz), 63.9 (d, *J* = 221.1 Hz), 53.9

(d, *J* = 5.5 Hz), 27.5.

³¹P NMR (243 MHz, CDCl₃) δ 14.30.

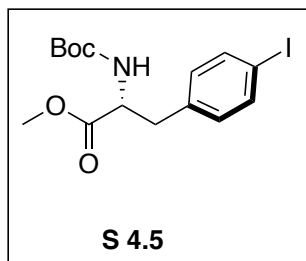
Tert-butyl 5-iodo-1*H*-indole-1-carboxylate (S 4.3). ⁴



¹H NMR (600 MHz, CDCl₃) 7.90 (s, 1H), 7.57 (d, *J* = 9.1 Hz, 1H), 7.55 (s, 1H), 6.49 (d, *J* = 3.7 Hz, 1H), 1.67 (d, *J* = 1.4 Hz, 1H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 149.8, 134.8, 133.2, 133.0, 130.1, 127.0, 117.4, 106.6, 87.0, 84.5, 28.5.

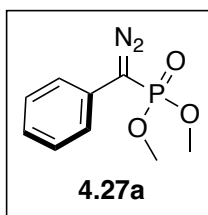
(*R*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-iodophenyl)propanoic acid (S 4.5).⁵



^1H NMR (600 MHz, CDCl_3) δ 7.64 (d, $J = 7.1$ Hz, 2H), 6.90 (d, $J = 7.8$ Hz, 2H), 5.00 (d, $J = 8.2$ Hz, 1H), 4.59 (d, $J = 7.0$ Hz, 1H), 3.80 – 3.71 (m, 3H), 3.10 (dd, $J = 5.7, 14.1$ Hz, 1H), 3.00 (dd, $J = 6.1, 14.0$ Hz, 1H), 1.44 (s, 9H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 172.4, 155.3, 137.9, 136.1, 131.7, 92.9, 80.4, 54.5, 52.7, 38.2, 28.6.

Dimethyl (diazo(phenyl)methyl)phosphonate (4.27a).⁶



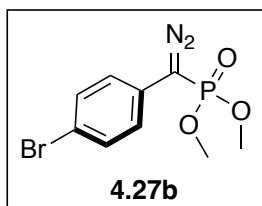
The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.35$ in 1:1 hexanes/EtOAc), which afforded major product **4.27a** as a yellow oil (486 mg, 88% yield). For a 5-gram scale (6.48 g, 86% yield)

^1H NMR (600 MHz, CDCl_3) δ 7.35 (t, $J = 7.7$ Hz, 2H), 7.15 (d, $J = 7.8$ Hz, 3H), 3.80 (d, $J_{\text{HP}} = 11.9$ Hz, 6H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 129.6, 126.6 (d, $J_{\text{CP}} = 9.4$ Hz), 125.6, 122.9 (d, $J_{\text{CP}} = 4.4$ Hz), 53.4 (d, $J_{\text{CP}} = 5.0$ Hz), 50.1 (d, $J_{\text{CP}} = 228.6$ Hz).

^{31}P NMR (243 MHz, CDCl_3) δ 20.89.

Dimethyl ((4-bromophenyl)(diazo)methyl)phosphonate (4.27b).⁶



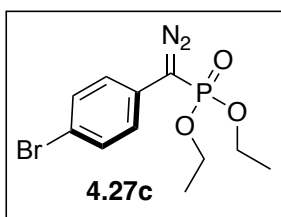
The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.35$ in 1:1 hexanes/EtOAc), which afforded major product **4.27b** as a yellow oil (485 mg, 90% yield).

^1H NMR (600 MHz, CDCl_3) δ 7.46 (d, $J = 8.6$ Hz, 2H), 7.02 (d, $J = 8.7$ Hz, 2H), 3.80 (d, $J_{\text{HP}} = 11.9$ Hz, 6H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 132.7, 126.0 (d, $J_{\text{CP}} = 9.9$ Hz), 124.4 (d, $J_{\text{CP}} = 4.6$ Hz), 119.0, 53.6 (d, $J_{\text{CP}} = 5.1$ Hz), 50.2 (d, $J_{\text{CP}} = 228.9$ Hz).

^{31}P NMR (243 MHz, CDCl_3) δ 20.00.

Diethyl (diazo(phenyl)methyl)phosphonate (4.27c). ⁷



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.35$ in 1:1 hexanes/EtOAc), which afforded major product **4.27c** as a yellow oil (487 mg, 83% yield).

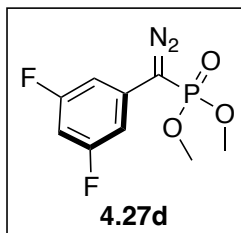
^1H NMR (400 MHz, CDCl_3) δ 7.41 (d, $J = 8.6$ Hz, 2H), 7.01 (d, $J = 8.7$

Hz, 2H), 4.31 – 3.96 (m, 4H), 1.29 (t, $J_{\text{HP}} = 7.1$ Hz, 6H). (Coupling constants are uncorrected)

^{13}C NMR (101 MHz, CDCl_3) δ 132.5, 126.2 (d, $J_{\text{CP}} = 9.8$ Hz), 124.4 (d, $J_{\text{CP}} = 4.5$ Hz), 118.7, 63.3 (d, $J_{\text{CP}} = 5.1$ Hz), 50.9 (d, $J_{\text{CP}} = 226.3$ Hz), 16.4 (d, $J_{\text{CP}} = 6.8$ Hz).

^{31}P NMR (162 MHz, CDCl_3) δ 16.40.

Dimethyl (diazo(3,5-difluorophenyl)methyl)phosphonate (4.27d).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.35$ in 1:1 hexanes/EtOAc), which afforded major product **4.27d** as a yellow oil (495 mg, 91% yield).

^1H NMR (400 MHz, CDCl_3) δ 6.70 – 6.63

(m, 2H), 6.55 (tt, $J_{\text{HF}} = 2.2, 8.8$ Hz, 1H), 3.81 (d, $J_{\text{HP}} = 12.0$ Hz, 6H). (Coupling constants are uncorrected)

^{13}C NMR (101 MHz, CDCl_3) δ 163.9 (dd, $J_{\text{CF}} = 13.8$, 248.4 Hz), 131.2 (q, $J_{\text{CF}} = 11.1$ Hz), 105.9 – 105.42 (m), 100.8 (t, $J_{\text{CF}} = 25.6$ Hz), 53.7 (d, $J_{\text{CP}} = 5.2$ Hz), 51.4 (d, $J_{\text{CP}} = 229.1$ Hz).

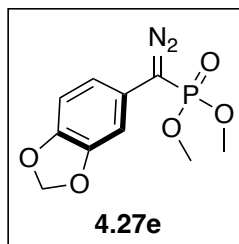
^{31}P NMR (162 MHz, CDCl_3) δ 18.65.

^{19}F NMR (376 MHz, CDCl_3) δ -108.19.

IR (neat): 2983, 2907, 2075, 1621, 1585, 1489, 1443, 1392, 1368, 1295, 1256, 1186, 1164, 1120, 1096, 1043, 1012, 969, 814, 795, 710, 670 cm^{-1} .

HRMS (+p ESI) calcd. for $\text{C}_9\text{H}_9\text{F}_2\text{N}_2\text{O}_3\text{P}$ $[\text{M} + \text{H}]^+$ 263.0392, found 263.0391.

Dimethyl (benzo[d][1,3]dioxol-5-yl(diazo)methyl)phosphonate (4.27e).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.30$ in 1:1 hexanes/EtOAc), which afforded major product **4.27e** as a yellow oil (437 mg, 80% yield).

^1H NMR (600 MHz, CDCl_3) δ 6.82 (d, $J_{\text{HP}} = 8.3$ Hz, 1H), 6.69 (s, 1H), 6.63 (d, $J_{\text{HP}} = 8.2$ Hz, 1H), 5.96 (s, 2H), 3.80 (d, $J_{\text{HP}} = 12.0$ Hz, 6H). (Coupling constants are uncorrected)

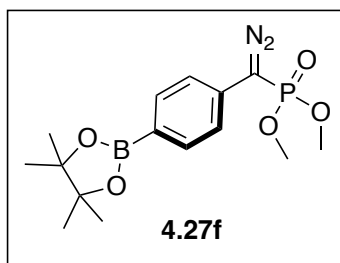
^{13}C NMR (151 MHz, CDCl_3) δ 149.1, 146.1, 119.6 (d, $J_{\text{CP}} = 9.8$ Hz), 116.8 (d, $J_{\text{CP}} = 4.7$ Hz), 109.6, 104.4 (d, $J_{\text{CP}} = 4.4$ Hz), 101.7, 53.5 (d, $J_{\text{CP}} = 5.0$ Hz), 49.7 (d, $J_{\text{CP}} = 230.0$ Hz).

^{31}P NMR (243 MHz, CDCl_3) δ 21.22.

IR (neat): 2953, 2077, 1608, 1504, 1491, 1446, 1343, 1255, 1231, 1187, 1138, 1111, 1020, 932, 875, 832, 798, 721, 668 cm^{-1} .

HRMS (+p ESI) calcd. for $\text{C}_{10}\text{H}_{11}\text{N}_2\text{O}_5\text{P}$ $[\text{M} + \text{H} - \text{N}_2]^+$, 243.0415, found 243.0412.

Dimethyl (diazo(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methyl)phosphonate (4.27f).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.35 in 1:1 hexanes/EtOAc), which afforded major product **4.27f** as an orange solid (465 mg, 85% yield).

m.p. 103-106 °C.

¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 3.80 (d, *J*_{HP} = 12.0 Hz, 6H), 1.33 (s, 12H). (Coupling constants are uncorrected)

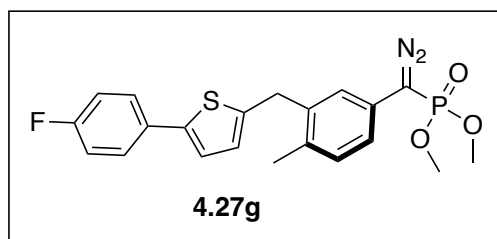
¹³C NMR (101 MHz, CDCl₃) δ 136.0, 130.0 (d, *J*_{CP} = 9.5 Hz), 129.7, 121.9 (d, *J*_{CP} = 4.5 Hz), 84.17, 53.5 (d, *J*_{CP} = 5.0 Hz), 51.0 (d, *J*_{CP} = 227.6 Hz), 25.2.

³¹P NMR (162 MHz, CDCl₃) δ 20.39.

IR (neat): 2977, 2852, 2080, 1605, 1548, 1462, 1398, 1360, 1326, 1294, 1263, 1213, 1185, 1167, 1143, 1110, 1092, 1018, 966, 927, 858, 831, 799, 783, 736, 696, 670, 654 cm⁻¹.

HRMS (+p ESI) calcd. for C₁₅H₂₂BN₂O₅P [*M* + *H*]⁺ 352.1469, found 352.1473.

Dimethyl (diazo(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)methyl)phosphonate (4.27g).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.30 in 1:1 hexanes/EtOAc), which afforded major product **4.27g** as a yellow oil (397 mg, 75% yield). (To conduct a more

thorough analysis of this compound, 2D NMR spectroscopy is required. The starting material for this synthesis was sourced from Ambeed and is identified by CAS No. 898566-17-1 and Catalog

No. A126498. However, there is a possibility that the compound purchased from the vendor may not be as pure as claimed. Impurities or inconsistencies in the quality of the starting material could impact the results of subsequent reactions or analyses. Therefore, it is crucial to verify the purity and identity of the compound using additional techniques, such as NMR, to ensure that the material meets the required specifications for the intended research which can be done by chemist who are also working on this project.)

^1H NMR (600 MHz, CDCl_3) δ 7.47 (d, $J = 7.0$ Hz, 2H), 7.17 (d, $J = 7.8$ Hz, 1H), 7.06 – 6.97 (m, 5H), 6.68 (d, $J = 3.7$ Hz, 1H), 4.11 (s, 2H), 3.79 (d, $J_{\text{HP}} = 11.8$ Hz, 6H), 2.30 (s, 3H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 162.4 (d, $J_{\text{CF}} = 246.9$ Hz), 143.1, 142.0, 139.7, 134.0, 131.8, 131.1 (d, $J_{\text{CP}} = 3.5$ Hz), 127.4 (d, $J_{\text{CP}} = 8.0$ Hz), 126.4, 124.1, 124.0 (d, $J_{\text{CP}} = 4.4$ Hz), 123.0, 121.6 (d, $J_{\text{CP}} = 4.4$ Hz), 116.1 (d, $J_{\text{CF}} = 21.7$ Hz), 53.4 (d, $J_{\text{CP}} = 5.0$ Hz), 49.7 (d, $J_{\text{CP}} = 229.1$ Hz), 34.5, 19.3.

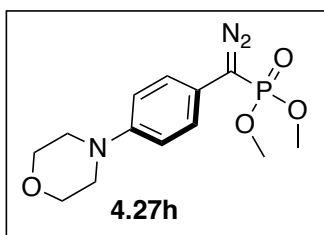
^{31}P NMR (243 MHz, CDCl_3) δ 21.16.

^{19}F NMR (565 MHz, CDCl_3) δ -114.99.

IR (neat): 2952, 2849, 2241, 2072, 1595, 1500, 1477, 1457, 1363, 1331, 1232, 1181, 985, 906, 830, 809, 760, 745, 725, 697 cm^{-1} .

HRMS (+p ESI) calcd. for $\text{C}_{21}\text{H}_{20}\text{FN}_2\text{O}_3\text{PS}$ $[\text{M} + \text{Na}]^+$ 453.0809, found 453.0804.

Dimethyl (diazo(4-morpholinophenyl)methyl)phosphonate (4.27h).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.35$ in 1:1 hexanes/EtOAc), which afforded major product **4.27h** as a yellow oil (297 mg, 55% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.09 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.86 (t, *J* = 4.9 Hz, 4H), 3.80 (d, *J*_{HP} = 11.9 Hz, 6H), 3.14 (t, *J* = 4.9 Hz, 4H). (Coupling constants are uncorrected)

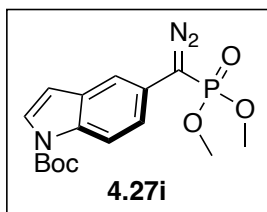
¹³C NMR (101 MHz, CDCl₃) δ 149.6, 124.5 (d, *J*_{CP} = 4.4 Hz), 117.1, 116.7 (d, *J*_{CP} = 9.6 Hz), 67.2, 53.4 (d, *J*_{CP} = 5.1 Hz), 49.6.

³¹P NMR (162 MHz, CDCl₃) δ 21.82.

IR (neat): 2955, 2852, 2080, 1608, 1515, 1489, 1449, 1438. 1380. 1296. 1234. 1182. 1118. 1018. 974, 926, 830, 788, 757, 721, 696 cm⁻¹.

HRMS (+p ESI) calcd. for C₁₃H₁₈N₃O₄P [M + H]⁺ 312.1108, found 312.1115.

***Tert*-butyl 5-(diazo(dimethoxyphosphoryl)methyl)-1*H*-indole-1-carboxylate (**4.27i**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.30 in 1:1 hexanes/EtOAc), which afforded major product **4.27i** as an orange solid (319 mg, 60% yield).

m.p. 101-104 °C.

¹H NMR (600 MHz, CDCl₃) δ 8.12 (s, 1H), 7.59 (s, 1H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.10 (dd, *J* = 2.0, 8.8 Hz, 1H), 6.52 (dd, *J* = 0.8, 3.7 Hz, 1H), 3.82 (d, *J*_{HP} = 11.9 Hz, 6H), 1.67 (s, 9H). (Coupling constants are uncorrected)

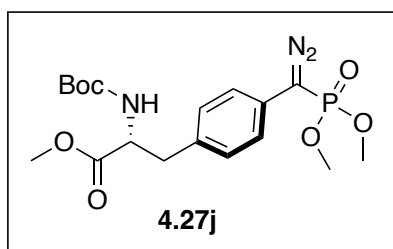
¹³C NMR (151 MHz, CDCl₃) δ 149.9, 133.6, 131.9, 127.2, 120.4 (d, *J* = 9.5 Hz), 119.7 (d, *J* = 4.8 Hz), 116.5, 115.7 (d, *J*_{CP} = 4.2 Hz), 107.3, 84.3, 53.5 (d, *J*_{CP} = 5.0 Hz), 49.6 (d, *J*_{CP} = 228.6 Hz), 28.5.

³¹P NMR (243 MHz, CDCl₃) δ 21.67.

IR (neat): 2978, 2074, 1732, 1575, 1469, 1369, 1346, 1290, 1247, 1165, 113, 1085, 1020, 895, 833, 801, 765, 725 cm⁻¹.

HRMS (+p APCI) calcd. for C₁₆H₂₀N₃O₅P [M + H]⁺ 366.1213, found 366.1212.

Methyl (*R*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(diazo(dimethoxyphosphoryl)methyl)phenyl)propanoate (4.27j).



The material was purified by flash chromatography (SiO₂;

hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.25 in 1:1

hexanes/EtOAc), which afforded major product **4.27j** as a yellow oil (279 mg, 53% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.13 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.8 Hz, 2H), 5.01 (d, J = 8.3 Hz, 1H), 4.59 (d, J = 7.1 Hz, 1H), 3.83 (d, J_{HP} = 11.9 Hz, 6H), 3.74 (s, 3H), 3.12 (dd, J = 5.6, 14.0 Hz, 1H), 3.03 (dd, J = 6.1, 14.0 Hz, 1H), 1.43 (s, 9H). (Coupling constants are uncorrected)

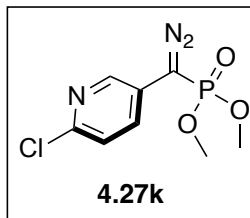
¹³C NMR (151 MHz, CDCl₃) δ 172.5, 155.4, 133.5, 130.6, 125.3 (d, J_{CP} = 9.6 Hz), 123.1 (d, J_{CP} = 4.4 Hz), 80.3, 54.7, 53.5 (d, J_{CP} = 5.0 Hz), 52.6, 50.0 (d, J_{CP} = 228.8 Hz), 38.1, 28.6.

³¹P NMR (243 MHz, CDCl₃) δ 20.81.

IR (neat): 3301, 2954, 2077, 1745, 1711, 1610, 1513, 1444, 1391, 1365, 1296, 1252, 1166, 1020, 972, 838, 800 cm⁻¹.

HRMS (+p APCI) calcd. for C₁₈H₂₆N₃O₇P [M + H]⁺ 428.1581, found 428.1583.

Dimethyl ((6-chloropyridin-3-yl)(diazo)methyl)phosphonate (4.27k).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.27k** as a yellow oil (318 mg, 58% yield).

¹H NMR (400 MHz, CDCl₃) δ 8.21 (d, J = 2.7 Hz, 1H), 7.45 (dd, J = 2.7, 8.5 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H), 3.83 (d, J_{HP} = 11.9 Hz, 6H). (Coupling constants are uncorrected)

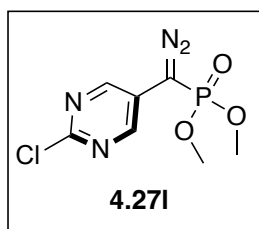
¹³C NMR (101 MHz, CDCl₃) δ 148.4, 143.8 (d, J_{CP} = 4.6 Hz), 132.8 (d, J_{CP} = 4.0 Hz), 124.9, 123.3 (d, J_{CP} = 10.0 Hz), 60.7, 53.8 (d, J_{CP} = 5.4 Hz).

^{31}P NMR (162 MHz, CDCl_3) δ 18.51.

IR (neat): 2955, 2083, 1549, 1515, 1467, 1380, 1307, 1260, 1184, 1111, 1019, 967, 928, 834, 803, 787, 749, 722, 695, 656 cm^{-1} .

HRMS (+p ESI) calcd. for $\text{C}_8\text{H}_9\text{ClN}_3\text{O}_3\text{P}$ $[\text{M} + \text{H}]^+$ 262.0142, found 262.0148.

Dimethyl ((2-chloropyrimidin-5-yl)(diazo)methyl)phosphonate (4.27l).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.27l** as a yellow oil (218 mg, 40% yield).

^1H NMR (400 MHz, CDCl_3) δ 8.45 (s, 2H), 3.86 (d, J_{HP} = 11.9 Hz, 6H).

(Coupling constants are uncorrected)

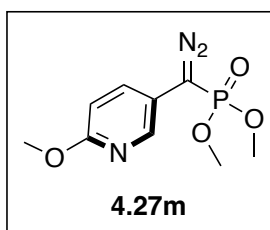
^{13}C NMR (101 MHz, CDCl_3) δ 158.1, 153.1 (d, J_{CP} = 3.9 Hz), 122.3 (d, J_{CP} = 10.2 Hz), 55.7 (dd, J_{CP} = 6.0, 186.4 Hz), 54.0 (d, J_{CP} = 5.5 Hz).

^{31}P NMR (162 MHz, CDCl_3) δ 16.98.

IR (neat): 2956, 1085, 1667, 1549, 1468, 1380, 1308, 1261, 1184, 1110, 1021, 967, 835, 803, 786, 749, 729 cm^{-1}

HRMS (+p APCI) calcd. for $\text{C}_7\text{H}_8\text{ClN}_4\text{O}_3\text{P}$ $[\text{M} + \text{H}]^+$ 263.0095, found 263.0102.

Dimethyl (diazo(6-methoxypyridin-3-yl)methyl)phosphonate (4.27m).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.15 in 1:1 hexanes/EtOAc), which afforded major product **4.27m** as a yellow oil (327 mg, 60% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.02 (s, 1H), 7.40 (dd, *J* = 2.6, 8.8 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 3.92 (d, *J* = 1.7 Hz, 3H), 3.81 (d, *J*_{HP} = 11.9 Hz, 6H). (Coupling constants are uncorrected)

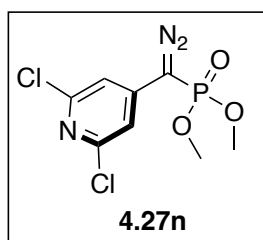
¹³C NMR (151 MHz, CDCl₃) δ 162.9, 142.0 (d, *J*_{CP} = 4.3 Hz), 134.3 (d, *J*_{CP} = 4.3 Hz), 115.6 (d, *J*_{CP} = 9.9 Hz), 112.0, 53.9, 53.6 (d, *J*_{CP} = 5.4 Hz), 46.8 (d, *J*_{CP} = 232.0 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 20.50.

IR (neat): 2952, 2849, 2241, 2072, 1595, 1500, 1477, 1457, 1363, 1331, 1232, 1181, 1018, 985, 906, 830, 809, 760, 745, 725, 697, 662 cm⁻¹.

HRMS (+p APCI) calcd. for C₉H₁₂N₃O₄P [M + H]⁺ 258.0638, found 258.0644.

Dimethyl (diazo(2,6-dichloropyridin-4-yl)methyl)phosphonate (4.27n).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R*_f = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.27n** as a yellow oil (292 mg, 54% yield).

¹H NMR (600 MHz, CDCl₃) δ 6.98 (s, 2H), 3.84 (d, *J*_{HP} = 11.9 Hz, 6H).

(Coupling constants are uncorrected)

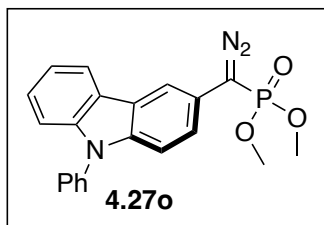
¹³C NMR (151 MHz, CDCl₃) δ 151.5, 143.3 (d, *J*_{CP} = 10.3 Hz), 115.2 (d, *J*_{CP} = 4.5 Hz), 54.0 (d, *J*_{CP} = 5.1 Hz), 52.4 (d, *J*_{CP} = 227.4 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 15.87.

IR (neat): 2955, 2097, 1573, 1521, 1426, 1385, 1306, 1265, 1174, 1114, 1020, 981, 843, 810, 750, 668 cm⁻¹.

HRMS (+p APCI) calcd. for C₈H₈Cl₂N₃O₃P [M + H]⁺ 295.9753, found 295.9753.

Dimethyl (diazo(9-phenyl-9H-carbazol-3-yl)methyl)phosphonate (4.27o).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.30 in 1:1 hexanes/EtOAc), which afforded major product **4.27o** as a yellow oil (354 mg, 67% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.17 (d, J = 7.8 Hz, 1H), 7.97 (s, 1H), 7.63 (t, J = 7.9 Hz, 2H), 7.57 (d, J = 8.3 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.47 – 7.41 (m, 3H), 7.32 (t, J = 7.2 Hz, 1H), 7.29 – 7.26 (m, 1H), 3.89 (d, J_{HP} = 11.9 Hz, 6H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 141.5, 139.5, 137.7, 130.3, 127.9, 127.3, 126.8, 124.7, 122.9, 121.9 (d, J_{CP} = 4.2 Hz), 120.8, 120.5, 117.0 (d, J_{CP} = 9.3 Hz), 115.4 (d, J_{CP} = 4.3 Hz), 111.2, 110.3, 53.5 (d, J_{CP} = 4.9 Hz), 49.5 (d, J_{CP} = 229.0 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 22.11.

IR (neat): 3061, 2951, 2849, 2072, 1595, 1501, 1477, 1458, 1363, 1331, 1301, 1233, 1186, 1022, 985, 906, 832, 809, 762, 746, 728, 699, 662 cm⁻¹.

HRMS (+p ESI) calcd. for C₂₁H₁₈N₃O₃P [M + H – N₂]⁺ 364.1097, found 364.1097.

The SFC system employed supercritical fluid CO₂ with various cosolvents, including HPLC-grade methanol, acetonitrile, ethanol, isopropanol, or mixtures such as 1:1 methanol (MeOH) with 0.2% formic acid, 1:1 ethanol (Ethanol) with 0.2% formic acid, 1:1 ethanol (Ethanol) with 0.2% formic acid, and 1:1:1 ethanol:isopropanol (Ethanol:IPA) with 20 mM ammonium formate. The SFC columns used in the system included: Trefoil AMY1 (2.5 μ m, 3.0 mm x 150 mm), Trefoil CEL1 (2.5 μ m, 3.0 mm x 150 mm), Trefoil CEL2 (2.5 μ m, 3.0 mm x 150 mm), Regis (S,S) Whelk-O 1 Kromasil (3.5 μ m, 3.0 mm x 150 mm), ChiralPak AD-3 (3.0 μ m, 3.0 mm x 150 mm SFC), ChiralCel OZ-3 (3.0 μ m, 3.0 mm x 150 mm), ChiralCel OD-3 (3.0 μ m, 3.0 mm x 150 mm SFC), ChiralCel OX-3 (3.0 μ m, 3.0 mm x 150 mm SFC), ChiralCel OJ-3 (3.0 μ m, 3.0 mm x 150 mm

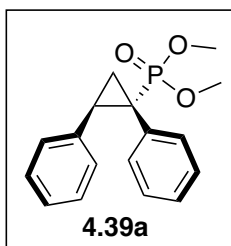
SFC), and ChiralPak AS-3 (3.0 μm , 3.0 mm x 150 mm SFC). In general, chiral HPLC or SFC conditions were determined by obtaining separation of the racemic products using $\text{Rh}_2(\text{esp})_4$ as a catalyst.

IR spectra were collected on a Nicolet iS10 FT-IR spectrometer. Mass spectra were taken on a Thermo Finnigan LTQ-FTMS spectrometer with APCI, ESI or NSI. Melting points (m.p.) were measured in open S3 capillary tubes with a Mel-Temp Electrothermal melting points apparatus and are uncorrected.

General Procedure for Cyclopropanation with Diazophosphonates.

A clean oven-dried and flame-dried 25.0 mL round bottom flask (flask-A) equipped with activated 4 Å molecular sieves, and a magnetic stir-bar was evacuated and purged with argon (2-3 times). After cooling down to room temperature, **styrene or phenylacetylene** (5 equiv., 1.00 mmol) followed by $\text{Rh}_2(\text{Cat.})$ (0.01 equiv.) was then added. The flask was once again evacuated and purged with argon (3-5 times) and anhydrous CH_2Cl_2 (3.0 mL) was added. The flask and its contents were then set to stir at room temperature using a hotplate under an argon atmosphere. To a second oven-dried round bottom flask (flask-B), that was evacuated and purged with argon was added diazophosphonates, (0.20 mmol). flask-B and its contents were evacuated and purged with argon (2-3 times) and anhydrous CH_2Cl_2 (10.0 mL) was then added to obtain a solution of the diazo-compound. The solution was transferred into a 12.0 mL plastic syringe. Using a well-calibrated syringe-pump, a slow addition of the diazo solution into the stirring solution of flask-A under an inert atmosphere was initiated. After the complete addition of the solution (5 h), the residual diazo compound in the 12.0 mL plastic syringe was rinsed with anhydrous CH_2Cl_2 (1.0 mL) and transferred dropwise into the stirring reaction mixture of flask-A. The resulting solution was stirred for 5 to 7 hours before concentrating the solution under reduced pressure. Purification by flash column chromatography on silica gel (hexanes : EtOAc) was used to afford the final products.

Dimethyl ((1*S*,2*R*)-1,2-diphenylcyclopropyl)phosphonate (4.39a).⁸



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.39a** as a colorless oil (55 mg, 92% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.12 (dd, *J* = 2.0, 5.2 Hz, 3H), 7.10 – 7.02 (m, 5H), 6.78 – 6.72 (m, 2H), 3.74 (d, *J*_{HP} = 10.6 Hz, 3H), 3.69 (d, *J*_{HP} = 10.6 Hz, 3H), 3.02 (ddd, *J*_{HP} = 6.6, 9.0, 16.6 Hz, 1H), 2.07 (ddd, *J*_{HP} = 5.2, 9.0, 17.4 Hz, 1H), 1.74 (ddd, *J*_{HP} = 5.2, 6.6, 12.5 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 136.3 (d, *J*_{CP} = 2.7 Hz), 133.9 (d, *J*_{CP} = 2.0 Hz), 132.5 (d, *J*_{CP} = 4.0 Hz), 128.3, 128.2 (d, *J*_{CP} = 2.5 Hz), 128.0, 127.5 (d, *J*_{CP} = 2.8 Hz), 126.6, 53.5, 29.7 (d, *J*_{CP} = 186.6 Hz), 27.3 (d, *J*_{CP} = 1.9 Hz), 16.9 (d, *J*_{CP} = 3.3 Hz).

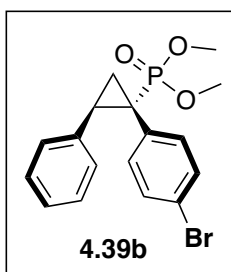
³¹P NMR (243 MHz, CDCl₃) δ 29.13.

The NMR data are consistent with the published data.⁸

SFC analysis: (OJ-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 254 nm) indicated 96% ee: *t_R* (minor enantiomer) = 0.79 min, *t_R* (major enantiomer) = 0.87 min.

[α]²⁰ D: –50.1° (c 0.60, CHCl₃)

Dimethyl ((1*S*,2*R*)-1-(4-bromophenyl)-2-phenylcyclopropyl)phosphonate (4.39b).⁸



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.24 in 1:1 hexanes/EtOAc), which afforded major product **4.39a** as a colorless oil (61 mg, 80% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.25 (d, *J* = 12.4 Hz, 2H), 7.09 (m, 2H), 6.92 (d, *J* = 8.3 Hz, 2H), 6.76 (d, *J* = 7.3 Hz, 2H), 3.75 (dd, *J*_{HP} = 1.7, 10.6 Hz, 3H), 3.70 (dd, *J*_{HP} = 1.7, 10.5 Hz, 3H), 3.03 (ddd, *J*_{HP} = 6.6, 9.0, 16.2 Hz, 1H), 2.06 (ddd, *J*_{HP} = 5.3, 8.9, 16.6 Hz, 1H), 1.70 (ddd, *J*_{HP} = 6.0, 8.8, 12.2 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 135.8 (d, *J*_{CP} = 2.6 Hz), 134.2 (d, *J*_{CP} = 3.8 Hz), 133.2, 131.4 (d, *J*_{CP} = 2.3 Hz), 128.3 (d, *J*_{CP} = 7.2 Hz), 126.9, 121.8 (d, *J*_{CP} = 3.4 Hz), 53.6 (dd, *J*_{CP} = 6.5, 10.1 Hz), 29.2 (d, *J*_{CP} = 187.8 Hz), 27.4, 16.7 (d, *J*_{CP} = 3.0 Hz).

³¹P NMR (243 MHz, CDCl₃) 28.46.

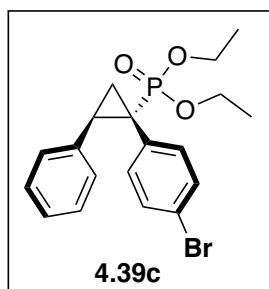
The NMR data are consistent with the published data.⁸

SFC analysis: (OJ-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 98% ee: *t*_R (minor enantiomer) = 1.07 min, *t*_R (major enantiomer) = 1.23 min.

The crystal structure information for compound (**4.39b**) is located in the crystallography section.

[α]²⁰ D: −65.7° (c 2.00, CHCl₃)

Diethyl ((1*S*,2*R*)-1-(4-bromophenyl)-2-phenylcyclopropyl)phosphonate (4.39c**).⁸**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R*_f = 0.24 in 1:1 hexanes/EtOAc), which afforded major product **4.39c** as a colorless oil (70 mg, 85% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.24 (d, *J* = 8.1 Hz, 2H), 7.12 – 7.06 (m, 3H), 6.93 (d, *J* = 6.9 Hz, 2H), 6.79 – 6.72 (m, 2H), 4.14 – 3.99 (m, 4H), 3.01 (ddd, *J*_{HP} = 6.6, 8.8, 16.1 Hz, 1H), 2.05 (ddd, *J*_{HP} = 5.2, 8.9, 17.2 Hz, 1H), 1.72 – 1.60 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 3H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 136.1 (d, $J_{\text{CP}} = 2.5$ Hz), 134.3 (d, $J_{\text{CP}} = 4.0$ Hz), 133.5, 131.3 (d, $J_{\text{CP}} = 2.2$ Hz), 128.3, 128.2, 126.8, 121.6 (d, $J_{\text{CP}} = 3.5$ Hz), 62.9 (t, $J_{\text{CP}} = 6.0$ Hz), 30.0 (d, $J_{\text{CP}} = 187.0$ Hz), 27.5, 16.9 (d, $J_{\text{CP}} = 3.3$ Hz), 16.8 (t, $J_{\text{CP}} = 6.1$ Hz).

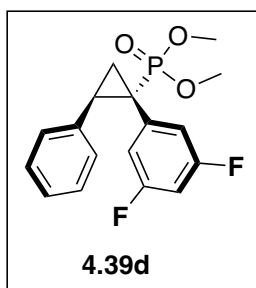
^{31}P NMR (243 MHz, CDCl_3) δ 25.60.

The NMR data are consistent with the published data. ⁸

SFC analysis: (OJ-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 90% ee: t_{R} (major enantiomer) = 1.93 min, t_{R} (minor enantiomer) = 3.96 min.

$\alpha]^{20}_{\text{D}}$: -48.8° (c 0.60, CHCl_3)

Dimethyl ((1*S*,2*R*)-1-(3,5-difluorophenyl)-2-phenylcyclopropyl)phosphonate (4.39d).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.20$ in 1:1 hexanes/EtOAc), which afforded major product **4.39d** as a colorless oil (53 mg, 78% yield)

^1H NMR (400 MHz, CDCl_3) δ 7.12 (dd, $J = 1.9, 5.0$ Hz, 3H), 6.79 (dd, $J = 4.3, 7.6$ Hz, 2H), 6.65 – 6.53 (m, 3H), 3.79 (d, $J_{\text{HP}} = 10.7$ Hz, 3H), 3.73 (d, $J_{\text{HP}} = 10.7$ Hz, 3H), 3.04 (ddd, $J_{\text{HP}} = 6.7, 9.0, 16.1$ Hz, 1H), 2.06 (ddd, $J_{\text{HP}} = 5.4, 9.0, 17.1$ Hz, 1H), 1.74 (ddd, $J_{\text{HP}} = 5.4, 6.7, 12.2$ Hz, 1H). (Coupling constants are uncorrected)

^{13}C NMR (101 MHz, CDCl_3) δ 162.6 (ddd, $J_{\text{CF}} = 2.6, 13.1, 248.2$ Hz), 138.3 – 138.0 (m), 135.2 (d, $J_{\text{CP}} = 2.6$ Hz), 128.4, 128.2, 127.2, 115.8 – 115.0 (m), 103.4 (td, $J_{\text{CF}} = 2.7, 25.2$ Hz), 53.7 (t, $J_{\text{CP}} = 6.4$ Hz), 29.4 (d, $J_{\text{CP}} = 188.2$ Hz), 27.8 (d, $J_{\text{CP}} = 2.0$ Hz), 16.5 (d, $J_{\text{CP}} = 3.2$ Hz).

^{19}F NMR (565 MHz, CDCl_3) δ -110.39.

^{31}P NMR (243 MHz, CDCl_3) δ 27.80.

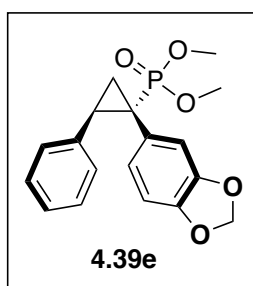
IR (neat): 3468, 2954, 2851, 2239, 2151, 1622, 1595, 1498, 1435, 1346, 1242, 1183, 1119, 1067, 1051, 1031, 1003, 993, 952, 906, 873, 829, 806, 772, 733, 696, 685 cm^{-1} .

HRMS (+p APCI) calcd. for $\text{C}_{17}\text{H}_{17}\text{F}_2\text{O}_3\text{P}$ $[\text{M} + \text{H}]^+$ 439.0956, found 439.0957.

HPLC analysis: (Chiralcel ASH, 25 cm x 4.6 mm, 3.0% i-PrOH/hexanes, 1.0 mL/min, 210 nm) indicated 90% ee: t_R (major enantiomer) = 21.37 min, t_R (minor enantiomer) = 53.41 min.

$[\alpha]^{20}_D$: -26.6° (c 0.72, CHCl_3)

Dimethyl ((1*S*,2*R*)-1-(benzo[*d*][1,3]dioxol-5-yl)-2-phenylcyclopropyl)phosphonate (4.39e).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.16 in 1:1 hexanes/EtOAc), which afforded major product **4.39e** as a colorless oil (58 mg, 84% yield)

^1H NMR (600 MHz, CDCl_3) δ 7.15 – 7.05 (m, 3H), 6.79 (dd, J = 2.6, 7.1 Hz, 2H), 6.64 – 6.46 (m, 3H), 5.87 (d, J = 5.2 Hz, 2H), 3.76 (d, J_{HP} = 10.6 Hz, 3H), 3.72 (d, J_{HP} = 10.6 Hz, 3H), 2.97 (ddd, J_{HP} = 6.6, 9.0, 16.1 Hz, 1H), 2.03 (ddd, J_{HP} = 5.2, 9.0, 17.3 Hz, 1H), 1.68 (ddd, J_{HP} = 5.9, 9.0, 12.1 Hz, 1H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 147.4 (d, J_{CP} = 2.4 Hz), 147.1 (d, J_{CP} = 3.0 Hz), 136.2, 128.4, 128.2, 126.8, 126.1 (d, J_{CP} = 4.9 Hz), 112.7 (d, J_{CP} = 3.8 Hz), 108.1 (d, J_{CP} = 2.7 Hz), 101.3, 53.7 (dd, J_{CP} = 6.5, 16.4 Hz), 31.3 (d, J_{CP} = 285.8 Hz), 30.1, 27.5, 23.1.

^{31}P NMR (243 MHz, CDCl_3) δ 29.27.

IR (neat): 3459, 2952, 2922, 2852, 1605, 1502, 1488, 1457, 1438, 1344, 1230, 1183, 1100, 1063, 1031, 969, 934, 902, 871, 836, 761, 726, 697 cm^{-1} .

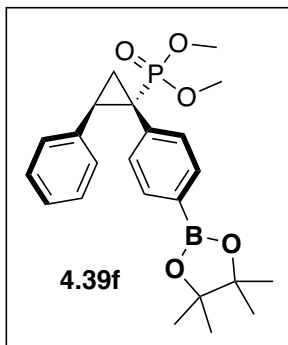
HRMS (+p APCI) calcd. for $\text{C}_{18}\text{H}_{19}\text{O}_5\text{P}$ $[\text{M} + \text{H}]^+$ 347.1043, found 347.1042.

SFC analysis: (AS-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 97% ee: t_R (major enantiomer) = 1.73 min, t_R (minor

enantiomer) = 2.93 min.

$[\alpha]^{20}_{\text{D}}$: -44.3° (c 0.60, CHCl_3)

Dimethyl ((1*S*,2*R*)-2-phenyl-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)cyclopropyl)phosphonate (2.39f).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.39f** as a colorless oil (64 mg, 75% yield).

^1H NMR (600 MHz, CDCl_3) δ 7.56 (d, J = 7.6 Hz, 2H), 7.06 (dt, J = 2.3, 6.2 Hz, 5H), 6.78 – 6.74 (m, 2H), 3.73 (d, J_{HP} = 10.5 Hz, 3H), 3.67 (d, J_{HP} = 10.4 Hz, 3H), 3.03 (ddd, J_{HP} = 6.6, 8.9, 16.2 Hz, 1H), 2.08 (ddd, J_{HP} = 5.1, 8.9, 17.4 Hz, 1H), 1.74 (ddd, J_{HP} = 5.8, 8.9, 12.3 Hz, 1H), 1.30 (s, 12H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 137.2, 136.1 (d, J_{CP} = 2.4 Hz), 134.6 (d, J_{CP} = 2.2 Hz), 131.9 (d, J_{CP} = 3.7 Hz), 128.3, 128.1, 126.7, 84.1, 53.7 (d, J_{CP} = 6.5 Hz), 53.6 (d, J_{CP} = 6.5 Hz), 29.9 (d, J_{CP} = 186.0 Hz), 27.4, 25.2 (d, J_{CP} = 20.3 Hz), 16.9 (d, J_{CP} = 3.3 Hz).

^{31}P NMR (243 MHz, CDCl_3) δ 28.91.

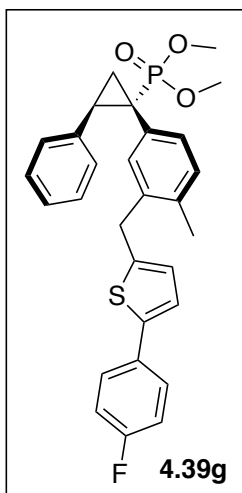
IR (neat): 2978, 1609, 1499, 1457, 1398, 1359, 1321, 1248, 1185, 1144, 1096, 1085, 1065, 1030, 963, 939, 870, 858, 828, 766, 732, 698, 675, 658 cm^{-1} .

HRMS (+p APCI) calcd. for $\text{C}_{23}\text{H}_{30}\text{BO}_5\text{P}$ $[\text{M} + \text{H}]^+$ 428.2033, found 428.2035.

SFC analysis: (OJ-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 86% ee: t_R (major enantiomer) = 1.37 min, t_R (minor enantiomer) = 2.21 min.

$[\alpha]^{20}_{\text{D}}$: -56.8° (c 1.00, CHCl_3)

Dimethyl ((1*S*,2*R*)-1-(3-((5-(4-fluorophenyl)thiophen-2-yl)methyl)-4-methylphenyl)-2-phenylcyclopropyl)phosphonate (4.39g**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.18 in 1:1 hexanes/EtOAc), which afforded major product **4.39g** as a colorless oil (69 mg, 68% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.47 (dd, *J* = 5.3, 8.8 Hz, 2H), 7.09 – 7.01 (m, 5H), 6.98 – 6.92 (m, 3H), 6.90 (s, 1H), 6.79 (d, *J* = 8.1 Hz, 2H), 6.29 (d, *J* = 3.5 Hz, 1H), 3.94 (s, 2H), 3.73 (d, *J* = 10.5 Hz, 3H), 3.69 (d, *J* = 10.3 Hz, 3H), 3.00 (ddd, *J* = 6.6, 8.9, 16.1 Hz, 1H), 2.19 (s, 3H), 2.05 (ddd, *J* = 5.2, 9.0, 17.3

Hz, 1H), 1.74 (ddd, *J* = 5.2, 6.6, 12.2 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 162.1 (d, *J_{CF}* = 246.6 Hz), 143.3, 141.3, 137.6 (d, *J_{CP}* = 2.6 Hz), 136.0 (d, *J_{CP}* = 2.4 Hz), 135.5 (d, *J_{CP}* = 3.0 Hz), 133.4 (d, *J_{CP}* = 3.9 Hz), 131.2 (d, *J_{CP}* = 2.1 Hz), 130.9 (d, *J_{CP}* = 3.4 Hz), 130.6 (d, *J_{CP}* = 4.2 Hz), 130.2 (d, *J_{CP}* = 2.4 Hz), 128.1, 127.8, 127.1 (d, *J_{CF}* = 7.9 Hz), 126.3, 125.9, 122.6, 115.8 (d, *J_{CF}* = 22.0 Hz), 53.2 (dd, *J_{CP}* = 6.6, 18.8 Hz), 33.9, 29.6, 28.4, 27.0, 19.1, 16.4 (d, *J_{CP}* = 3.2 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 29.41.

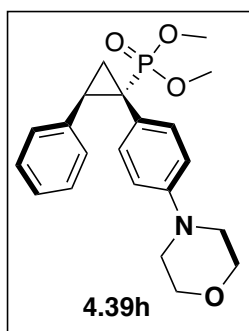
IR (neat): 2985, 1746, 1612, 1508, 1431, 1368, 1212, 1180, 1128, 1074, 1034, 983, 908, 850, 818, 796, 728, 685 cm⁻¹.

HRMS (+p APCI) calcd. for C₂₉H₂₈FO₃PS [*M* + *H*]⁺ 507.1554, found 507.1556.

SFC analysis: (SSWhelk, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 90% ee: *t_R* (minor enantiomer) = 7.92 min, *t_R* (major enantiomer) = 8.39 min.

(To conduct a more thorough analysis of compound **4.39g**, 2D NMR spectroscopy is required)

Dimethyl ((1*S*,2*R*)-1-(4-morpholinophenyl)-2-phenylcyclopropyl)phosphonate (4.39h).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.30 in 1:1 hexanes/EtOAc), which afforded major product **4.39h** as a colorless oil (43 mg, 55% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.12 – 7.03 (m, 3H), 6.94 (dd, *J* = 2.2, 8.8 Hz, 2H), 6.77 (dd, *J* = 2.2, 5.2 Hz, 2H), 6.66 (dd, *J* = 2.1, 8.8 Hz, 2H), 3.80 (t, *J* =

4.8 Hz, 4H), 3.73 (dd, *J_{HP}* = 2.0, 10.5 Hz, 3H), 3.69 (dd, *J_{HP}* = 2.0, 10.5 Hz, 3H), 3.07 (t, *J* = 4.8 Hz, 4H), 2.97 (ddd, *J_{HP}* = 6.7, 9.0, 16.2 Hz, 1H), 2.03 (ddd, *J_{HP}* = 5.6, 9.0, 17.3 Hz, 1H), 1.66 (ddd, *J_{HP}* = 5.8, 9.0, 12.1 Hz, 1H). (Coupling constants are uncorrected)

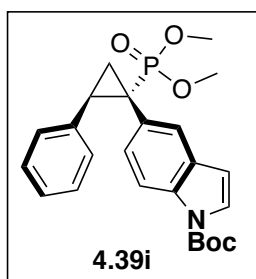
¹³C NMR (151 MHz, CDCl₃) δ 150.4, 136.5, 133.2 (d, *J_{CP}* = 3.9 Hz), 128.4, 128.0, 126.5, 124.6, 115.2, 67.2, 53.6 (dd, *J_{CP}* = 6.6, 13.5 Hz), 49.3, 28.9 (d, *J_{CP}* = 188.2 Hz), 27.3, 17.1 (d, *J_{CP}* = 3.1 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 29.71.

IR (neat): 3460, 2953, 2850, 1610, 1517, 1451, 1380, 1303, 1233, 1183, 1121, 1096, 1065, 1027, 963, 931, 862, 827, 773, 736, 698 cm⁻¹.

SFC analysis: (AS-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 88% ee: *t_R* (major enantiomer) = 3.78 min, *t_R* (minor enantiomer) = 5.31 min.

***Tert*-butyl 5-((1*S*,2*R*)-1-(dimethoxyphosphoryl)-2-phenylcyclopropyl)-1*H*-indole-1-carboxylate (4.39i).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.35 in 1:1 hexanes/EtOAc), which afforded major product **4.39i** as a yellow oil (64 mg, 72% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.87 (s, 1H), 7.51 (d, *J* = 3.5 Hz, 1H), 7.28 (t, *J* = 2.1 Hz, 1H), 7.06 – 7.01 (m, 3H), 7.00 (d, *J* = 8.6 Hz, 1H), 6.76 (dd, *J* = 2.9, 6.7 Hz, 2H), 6.41 (d, *J* = 3.7 Hz, 1H), 3.73 (d, *J*_{HP} = 10.6 Hz, 3H), 3.67 (d, *J*_{HP} = 10.5 Hz, 3H), 3.04 (ddd, *J*_{HP} = 6.6, 9.0, 16.1 Hz, 1H), 2.11 (ddd, *J*_{HP} = 5.1, 9.0, 17.5 Hz, 1H), 1.78 (ddd, *J*_{HP} = 5.1, 6.6, 12.1 Hz, 1H), 1.63 (s, 9H).

(Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 150.0, 136.5 (d, *J*_{CP} = 2.3 Hz), 130.7, 128.7 (d, *J*_{CP} = 3.5 Hz), 128.4, 128.1, 128.0, 126.6, 126.4, 125.1 (d, *J*_{CP} = 4.4 Hz), 114.9 (d, *J*_{CP} = 2.2 Hz), 107.5, 84.0, 53.6 (dd, *J*_{CP} = 6.7, 11.8 Hz), 29.7 (d, *J*_{CP} = 187.2 Hz), 28.5, 27.5, 17.4 (d, *J*_{CP} = 3.1 Hz).

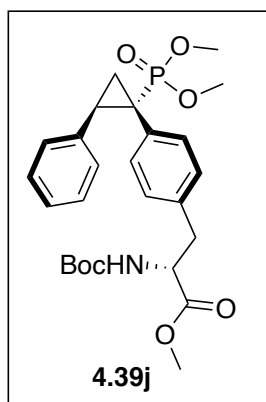
³¹P NMR (243 MHz, CDCl₃) δ 29.51.

IR (neat): 2979, 2951, 1732, 1499, 1470, 1437, 1369, 1343, 1331, 1303, 1281, 1244, 1211, 1160, 1137, 1091, 1065, 1025, 972, 912, 850, 828, 787, 768, 729, 698, 656 cm⁻¹.

HRMS (+p APCI) calcd. for C₂₄H₂₈NO₅P [M + H]⁺ 442.1778, found 442.1769.

SFC analysis: (AS-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 66% ee: *t*_R (major enantiomer) = 2.07 min, *t*_R (minor enantiomer) = 3.11 min.

Methyl (*R*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-((1*S*,2*R*)-1-(dimethoxyphosphoryl)-2-phenylcyclopropyl)phenyl)propanoate (4.39j).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R*_f = 0.18 in 1:1 hexanes/EtOAc), which afforded major product **4.39j** as a yellow oil (63 mg, 63% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.06 (dd, *J* = 1.9, 5.1 Hz, 3H), 6.98 (dd, *J* = 2.1, 8.2 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.70 (dd, *J* = 1.7, 4.9 Hz, 2H), 4.92 (d, *J* = 8.1 Hz, 1H), 4.50 (q, *J* = 6.5 Hz, 1H), 3.73 (d, *J*_{HP} = 10.6 Hz,

3H), 3.68 (d, $J_{\text{HP}} = 10.6$ Hz, 3H), 3.58 (s, 3H), 3.06 – 2.88 (m, 3H), 2.06 (ddd, $J_{\text{HP}} = 5.2, 9.0, 17.4$ Hz, 1H), 1.69 (ddd, $J_{\text{HP}} = 5.2, 6.6, 12.1$ Hz, 1H), 1.43 (s, 9H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 172.6, 172.4, 155.4 (d, $J_{\text{CP}} = 7.3$ Hz), 136.2, 135.3 (d, $J_{\text{CP}} = 17.1$ Hz), 132.7 (d, $J_{\text{CP}} = 4.0$ Hz), 129.1 (d, $J_{\text{CP}} = 2.4$ Hz), 128.3 (d, $J_{\text{CP}} = 4.0$ Hz), 128.0 (d, $J_{\text{CP}} = 7.1$ Hz), 126.7 (d, $J_{\text{CP}} = 11.6$ Hz), 80.3 (d, $J_{\text{CP}} = 13.0$ Hz), 54.6 (d, $J_{\text{CP}} = 9.7$ Hz), 53.7 – 53.5 (m), 52.4 (d, $J_{\text{CP}} = 5.5$ Hz), 38.3 (d, $J_{\text{CP}} = 14.4$ Hz), 29.4 (d, $J_{\text{CP}} = 187.4$ Hz), 28.7, 27.3, 17.0 (d, $J_{\text{CP}} = 10.6$ Hz).

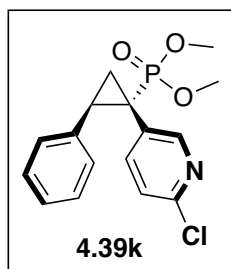
^{31}P NMR (243 MHz, CDCl_3) δ 28.92.

IR (neat): 3270, 2953, 2850, 1746, 1711, 1513, 1500, 1456, 1391, 1366, 1245, 1168, 1095, 1029, 964, 939, 868, 829, 774, 697, 681, 654 cm^{-1} .

HRMS (+p APCI) calcd. for $\text{C}_{26}\text{H}_{34}\text{NO}_7\text{P}$ $[\text{M} + \text{H}]^+$ 503.2067, found 503.2072.

$[\alpha]^{20}_{\text{D}}$: -22.9° (c 0.60, CHCl_3)

Dimethyl ((1*S*,2*R*)-1-(6-chloropyridin-3-yl)-2-phenylcyclopropyl)phosphonate (4.39k).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; $R_f = 0.20$ in 1:1 hexanes/EtOAc), which afforded major product **4.39k** as a colorless oil (47 mg, 70% yield).

^1H NMR (600 MHz, CDCl_3) δ 8.09 (t, $J = 2.4$ Hz, 1H), 7.23 (dt, $J = 2.2, 8.2$ Hz, 1H), 7.12 (dd, $J = 1.9, 5.0$ Hz, 3H), 7.04 (d, $J = 8.2$ Hz, 1H), 6.79 (dd, $J = 3.2, 6.4$ Hz, 2H), 3.75 (dd, $J_{\text{HP}} = 10.7, 13.2$ Hz, 6H), 3.09 (ddd, $J_{\text{HP}} = 6.6, 9.0, 16.0$ Hz, 1H), 2.11 (ddd, $J_{\text{HP}} = 5.5, 9.0, 17.1$ Hz, 1H), 1.76 (ddd, $J_{\text{HP}} = 5.5, 6.7, 12.1$ Hz, 1H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 153.1 (d, $J_{\text{CP}} = 4.5$ Hz), 150.5 (d, $J_{\text{CP}} = 3.2$ Hz), 142.7 (d, $J_{\text{CP}} = 3.5$ Hz), 134.9 (d, $J_{\text{CP}} = 2.5$ Hz), 129.7 (d, $J_{\text{CP}} = 2.1$ Hz), 128.6, 128.4, 127.4, 123.8 (d, $J_{\text{CP}} = 2.2$ Hz), 53.8 (d, $J_{\text{CP}} = 6.5$ Hz), 53.7 (d, $J_{\text{CP}} = 6.7$ Hz), 27.1 (d, $J_{\text{CP}} = 1.8$ Hz), 26.5 (d, $J_{\text{CP}} = 189.9$ Hz), 16.0 (d, $J_{\text{CP}} = 3.1$ Hz).

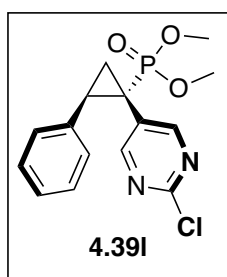
^{31}P NMR (243 MHz, CDCl_3) δ 27.54.

IR (neat): 2960, 1744, 1508, 1433, 1367, 1211, 1178, 1126, 1036, 981, 909, 848, 818, 728, 687 cm^{-1} .

HRMS (+p APCI) calcd. for $\text{C}_{16}\text{H}_{17}\text{ClNO}_3\text{P}$ $[\text{M} + \text{H}]^+$ 338.0707, found 338.0708.

SFC analysis: (AS-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 99% ee: t_R (major enantiomer) = 1.39 min, t_R (minor enantiomer) = 1.65 min.

Dimethyl ((1*S*,2*R*)-1-(2-chloropyrimidin-5-yl)-2-phenylcyclopropyl)phosphonate (4.39I).



The material was purified by flash chromatography (SiO_2 ; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.39I** as a colorless oil (36 mg, 53% yield).

^1H NMR (600 MHz, CDCl_3) δ 8.21 (d, J = 1.9 Hz, 2H), 7.19 – 7.14 (m, 3H), 6.83 (dd, J = 2.1, 7.0 Hz, 2H), 3.80 (d, J_{HP} = 10.8 Hz, 3H), 3.76 (d, J_{HP} = 10.8 Hz, 3H), 3.17 (ddd, J_{HP} = 6.7, 9.0, 15.9 Hz, 1H), 2.15 (ddd, J_{HP} = 5.7, 9.0, 16.9 Hz, 1H), 1.77 (ddd, J_{HP} = 5.7, 6.7, 12.1 Hz, 1H). (Coupling constants are uncorrected)

^{13}C NMR (151 MHz, CDCl_3) δ 162.7 (d, J_{CP} = 3.8 Hz), 160.2 (d, J_{CP} = 3.1 Hz), 134.1 (d, J_{CP} = 2.4 Hz), 129.0, 128.3, 128.0 (d, J_{CP} = 2.4 Hz), 127.9, 53.9 (dd, J_{CP} = 6.7, 15.5 Hz), 26.9, 24.2 (d, J_{CP} = 191.7 Hz), 15.4 (d, J_{CP} = 3.2 Hz).

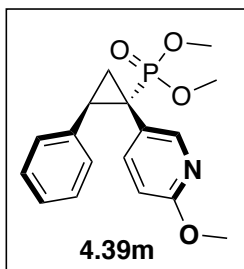
^{31}P NMR (243 MHz, CDCl_3) δ 26.57.

IR (neat): 2954, 1652, 1577, 1538, 1500, 1457, 1402, 1251, 1217, 1172, 1099, 1066, 1050, 1029, 965, 861, 832, 808, 794, 774, 762, 740, 728, 700 cm^{-1} .

HRMS (+p APCI) calcd. for $\text{C}_{15}\text{H}_{16}\text{ClN}_2\text{O}_3\text{P}$ $[\text{M} + \text{H}]^+$ 339.0660, found 339.0657.

SFC analysis: (OZ-3, 3 μ m particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 254 nm) indicated 97% ee: t_R (minor enantiomer) = 5.50 min, t_R (major enantiomer) = 7.65 min.

Dimethyl ((1*S*,2*R*)-1-(6-methoxypyridin-3-yl)-2-phenylcyclopropyl)phosphonate (4.39m**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; R_f = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.39m** as a colorless oil (50 mg, 75% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.89 (t, J = 2.5 Hz, 1H), 7.19 – 7.07 (m, 4H), 6.83 – 6.77 (m, 2H), 6.46 (d, J = 8.6 Hz, 1H), 3.85 (s, 3H), 3.76 (d, J_{HP} = 10.6 Hz, 3H), 3.72 (d, J_{HP} = 10.6 Hz, 3H), 3.03 (ddd, J_{HP} = 6.6, 9.0, 15.9 Hz, 1H), 2.07 (ddd, J_{HP} = 5.3, 9.0, 17.2 Hz, 1H), 1.72 (ddd, J_{HP} = 5.3, 6.6, 12.0 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (101 MHz, CDCl₃) δ 163.5 (d, J_{CP} = 2.2 Hz), 150.3 (d, J_{CP} = 4.9 Hz), 142.6 (d, J_{CP} = 3.1 Hz), 135.6 (d, J_{CP} = 2.5 Hz), 128.5, 128.4, 127.0, 122.8, 110.4 (d, J_{CP} = 2.1 Hz), 53.7, 53.6 (d, J_{CP} = 6.6 Hz), 26.9 (d, J_{CP} = 1.5 Hz), 16.3 (d, J_{CP} = 3.0 Hz).

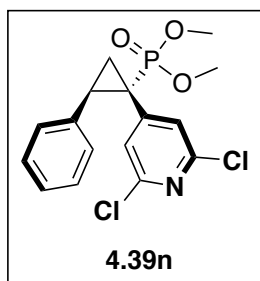
³¹P NMR (162 MHz, CDCl₃) δ 28.85.

IR (neat): 3461, 2952, 2849, 1605, 1567, 1493, 1458, 1374, 1284, 1247, 1182, 1098, 1065, 1024, 962, 941, 961, 861, 828, 762, 697 cm⁻¹.

HRMS (+p APCI) calcd. for C₁₇H₂₀NO₄P [M + H]⁺ 334.1203, found 334.1201.

SFC analysis: (AS-3, 3 μ m particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 99% ee: t_R (major enantiomer) = 1.47 min, t_R (minor enantiomer) = 2.49 min.

Dimethyl ((1*S*,2*R*)-1-(2,6-dichloropyridin-4-yl)-2-phenylcyclopropyl)phosphonate (4.39n**).**



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.39n** as a colorless oil (45 mg, 60% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.20 – 7.12 (m, 3H), 6.92 (s, 2H), 6.82 (d, *J* = 7.7 Hz, 2H), 3.82 (d, *J*_{HP} = 10.8 Hz, 3H), 3.76 (d, *J*_{HP} = 10.8 Hz, 3H), 3.11 (ddd, *J*_{HP} = 6.8, 8.9, 16.2 Hz, 1H), 2.09 (ddd, *J*_{HP} = 5.7, 9.0, 16.7 Hz, 1H), 1.77 (ddd, *J*_{HP} = 5.7, 6.2, 12.3 Hz, 1H). (Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 150.3 (d, *J*_{CP} = 2.2 Hz), 150.0 (d, *J*_{CP} = 3.1 Hz), 134.2 (d, *J*_{CP} = 3.3 Hz), 128.8, 128.1, 127.8, 126.3 (d, *J*_{CP} = 3.8 Hz), 53.9 (dd, *J*_{CP} = 2.4, 6.7 Hz), 28.6 (d, *J*_{CP} = 187.9 Hz), 28.0 (d, *J*_{CP} = 2.4 Hz), 15.7 (d, *J*_{CP} = 3.2 Hz).

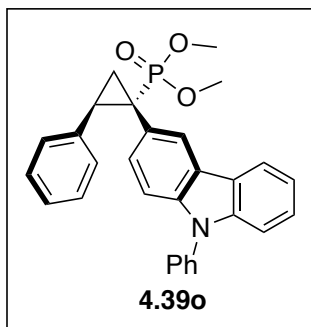
³¹P NMR (243 MHz, CDCl₃) δ 26.13.

IR (neat): 2953, 1578, 1532, 1500, 1457, 1362, 1248, 1164, 1139, 1097, 1066, 1026, 978, 949, 898, 831, 807, 790, 772, 724, 696 cm⁻¹.

HRMS (+p APCI) calcd. for C₁₆H₁₆Cl₂NO₃P [M + H]⁺ 372.0329, found 372.0320.

SFC analysis: (AS-3, 3 μm particle size, 150 mm x 3 mm, 20.0% IPA/Heptane, with 0.2% Formic Acid, 2.5 mL/min, 230 nm) indicated 41% ee: *t_R* (major enantiomer) = 2.81 min, *t_R* (minor enantiomer) = 4.59 min.

Dimethyl ((1*S*,2*R*)-2-phenyl-1-(9-phenyl-9*H*-carbazol-3-yl)cyclopropyl)phosphonate (4.39o).



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.20 in 1:1 hexanes/EtOAc), which afforded major product **4.39o** as a yellow oil (63 mg, 81% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.04 (dt, *J* = 1.0, 7.8 Hz, 1H), 7.91 (t, *J* = 1.8 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.52 – 7.49 (m, 2H), 7.44 – 7.41 (m,

1H), 7.39 – 7.37 (m, 2H), 7.30 – 7.22 (m, 1H), 7.13 (dt, *J* = 0.7, 8.5 Hz, 1H), 7.06 – 6.98 (m, 4H), 6.83 – 6.78 (m, 2H), 3.75 (d, *J_{HP}* = 10.5 Hz, 3H), 3.71 (d, *J_{HP}* = 10.5 Hz, 3H), 3.09 (ddd, *J_{HP}* = 6.6, 9.0, 16.0 Hz, 1H), 2.18 (ddd, *J_{HP}* = 5.1, 8.9, 17.5 Hz, 1H), 1.87 (ddd, *J_{HP}* = 5.1, 6.6, 12.5 Hz, 1H).

(Coupling constants are uncorrected)

¹³C NMR (151 MHz, CDCl₃) δ 141.3, 140.3 (d, *J_{CP}* = 2.1 Hz), 137.9, 136.5 (d, *J_{CP}* = 2.4 Hz), 130.6 (d, *J_{CP}* = 3.3 Hz), 130.1, 128.4, 128.1, 127.7, 127.3, 126.6, 126.3, 125.2, 124.3 (d, *J_{CP}* = 4.8 Hz), 123.5, 123.4 (d, *J_{CP}* = 1.5 Hz), 120.6, 120.3, 110.2, 109.5 (d, *J_{CP}* = 2.2 Hz), 53.7 (dd, *J_{CP}* = 6.7, 13.3 Hz), 29.9 (d, *J_{CP}* = 188.3 Hz), 27.6, 17.7 (d, *J_{CP}* = 3.2 Hz).

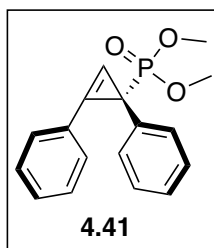
³¹P NMR (243 MHz, CDCl₃) δ 29.67.

IR (neat): 3470, 2957, 2853, 2104, 1589, 1536, 1460, 1296, 1239, 1184, 1014, 822, 773 cm⁻¹.

HRMS (+p APCI) calcd. for C₂₉H₂₆NO₃P [M + H]⁺ 468.1723.1203, found 468.1718.

HPLC analysis: (Chiralcel ADH, 25 cm x 4.6 mm, 3.0% i-PrOH/hexanes, 1.0 mL/min, 254 nm) indicated 96% ee: *t_R* (minor enantiomer) = 19.84 min, *t_R* (major enantiomer) = 23.78 min.

Dimethyl (*R*)-(1,2-diphenylcycloprop-2-en-1-yl)phosphonate (4.41).⁹



The material was purified by flash chromatography (SiO₂; hexanes/EtOAc, 9:1 to 1:1 gradient; *R_f* = 0.33 in 1:1 hexanes/EtOAc), which afforded major product

4.41 as a yellow oil (57 mg, 95% yield).

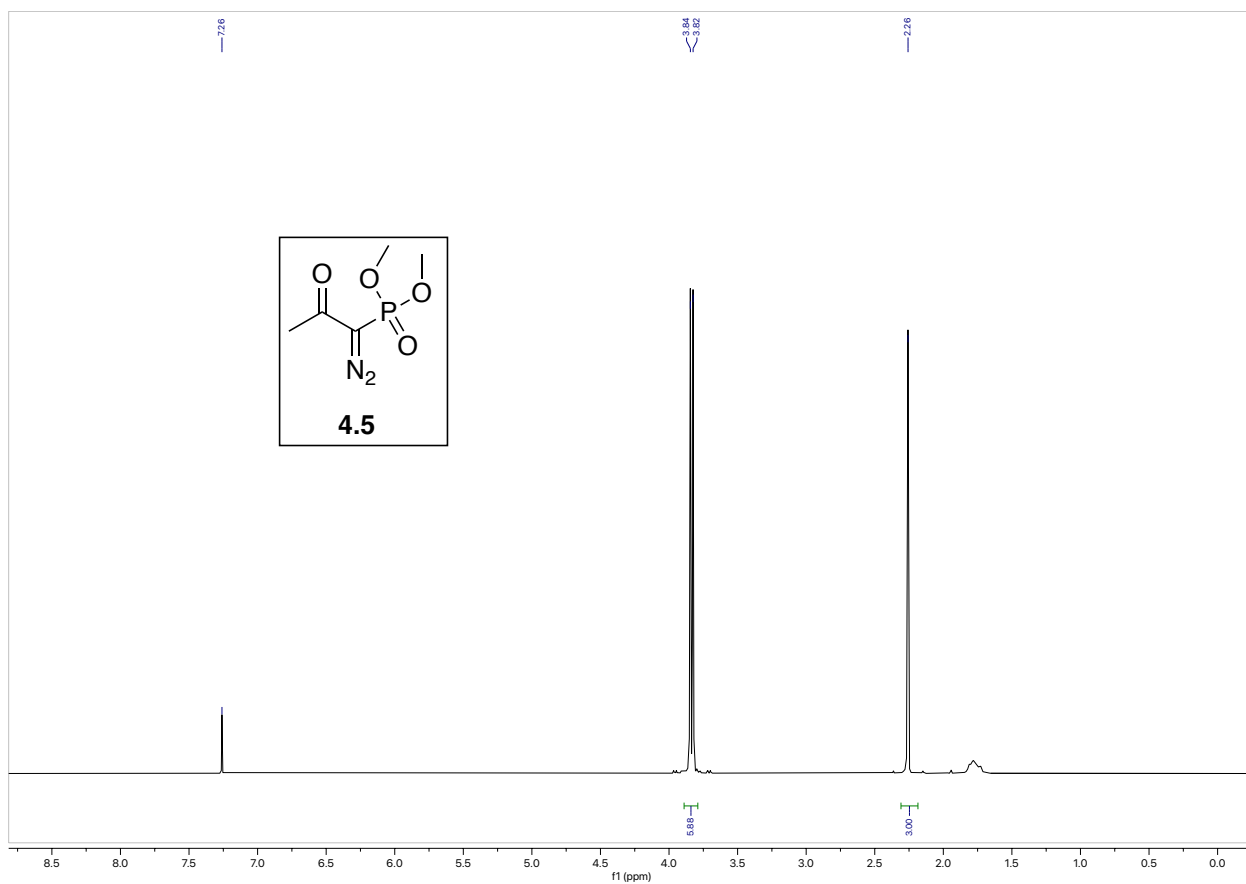
¹H NMR (600 MHz, CDCl₃) δ 7.70 (dd, *J* = 1.6, 8.0 Hz, 2H), 7.51 (dd, *J* = 1.0, 7.3 Hz, 2H), 7.48 – 7.36 (m, 3H), 7.31 – 7.25 (m, 3H), 7.21 (t, *J* = 7.4 Hz, 1H), 3.72 (d, *J* = 10.6 Hz, 3H), 3.68 (d, *J* = 10.5 Hz, 3H). (Coupling constants are uncorrected).

The NMR data are consistent with the published data.⁹

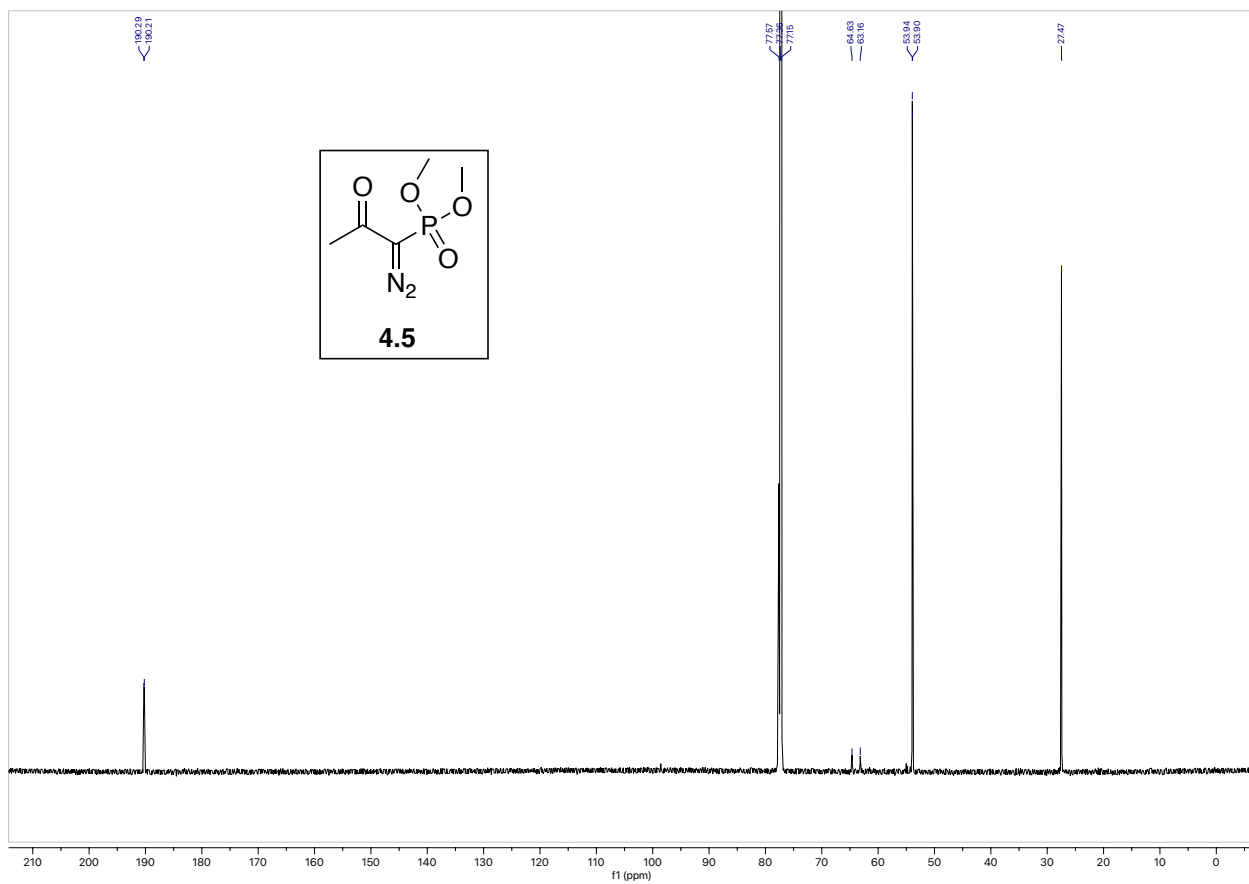
HPLC analysis: (Chiralcel ODH, 25 cm x 4.6 mm, 5.0% i-PrOH/hexanes, 1.0 mL/min, 230 nm) indicated 95% ee: *t_R* (major enantiomer) = 13.02 min, *t_R* (minor enantiomer) = 16.29 min. (The enantiomeric excess was determined by HPLC using the published procedure).

[α]²⁰ D: –38.5° (c 0.29, CHCl₃)

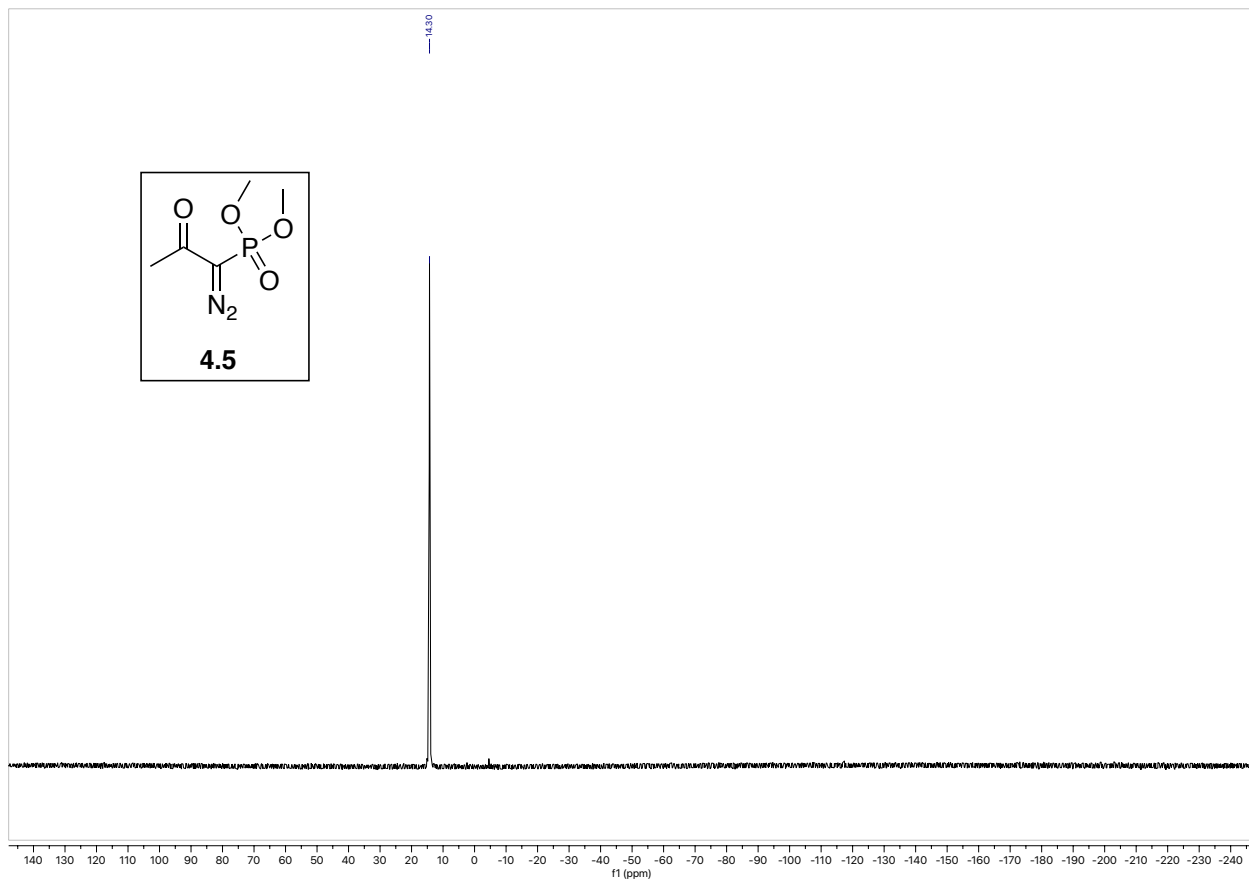
^1H NMR, ^{13}C NMR, ^{19}F NMR, and ^{31}P NMR Spectroscopic Data.



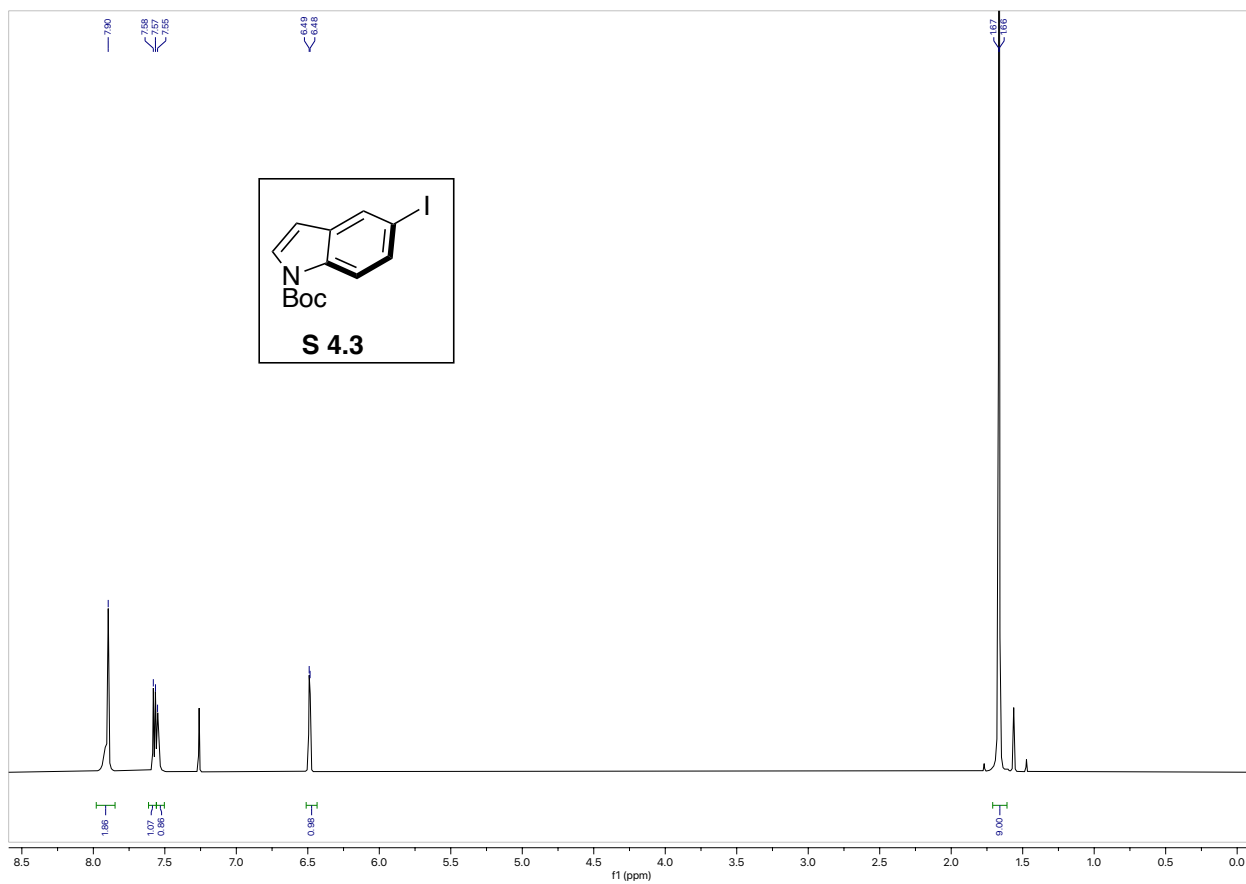
^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.5**.



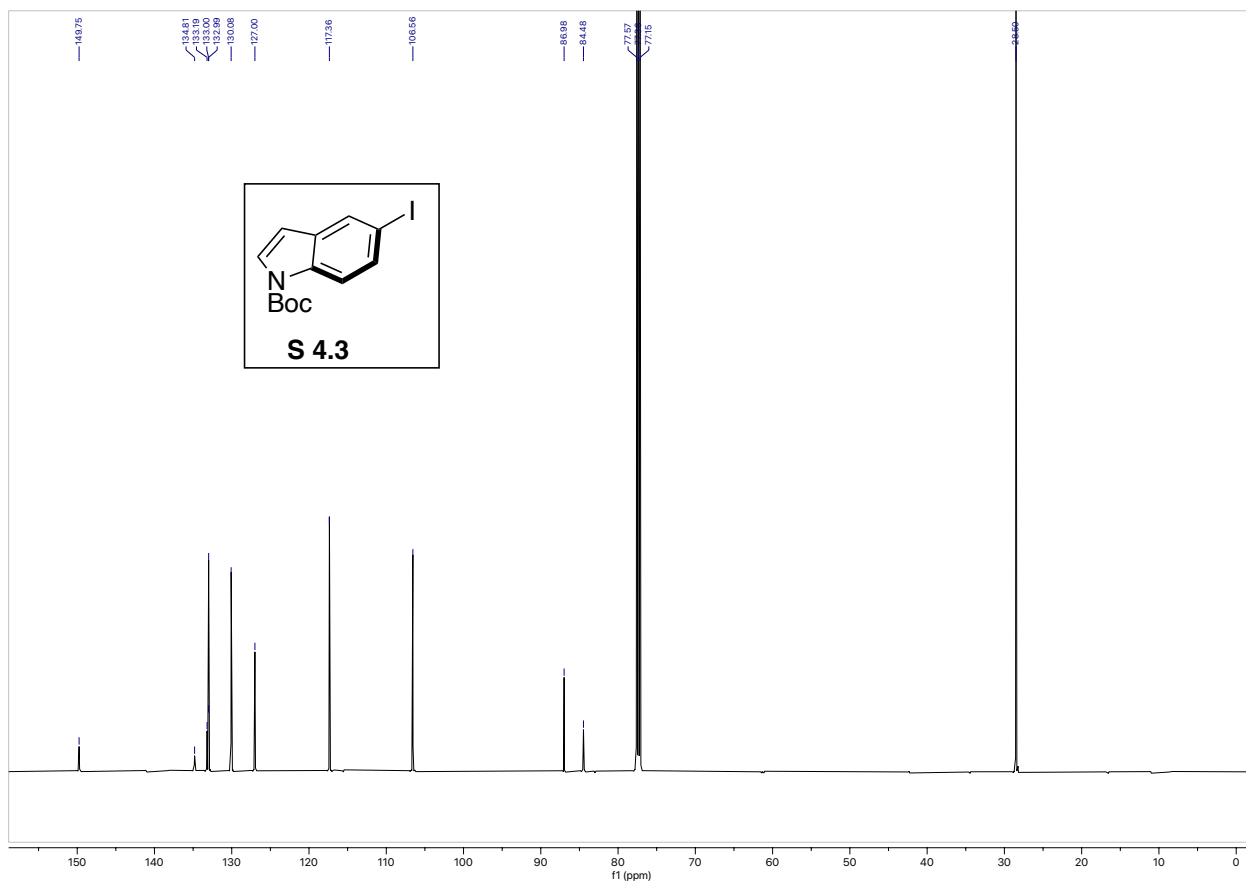
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform- d) (t, 77.36 ppm) of **4.5**.



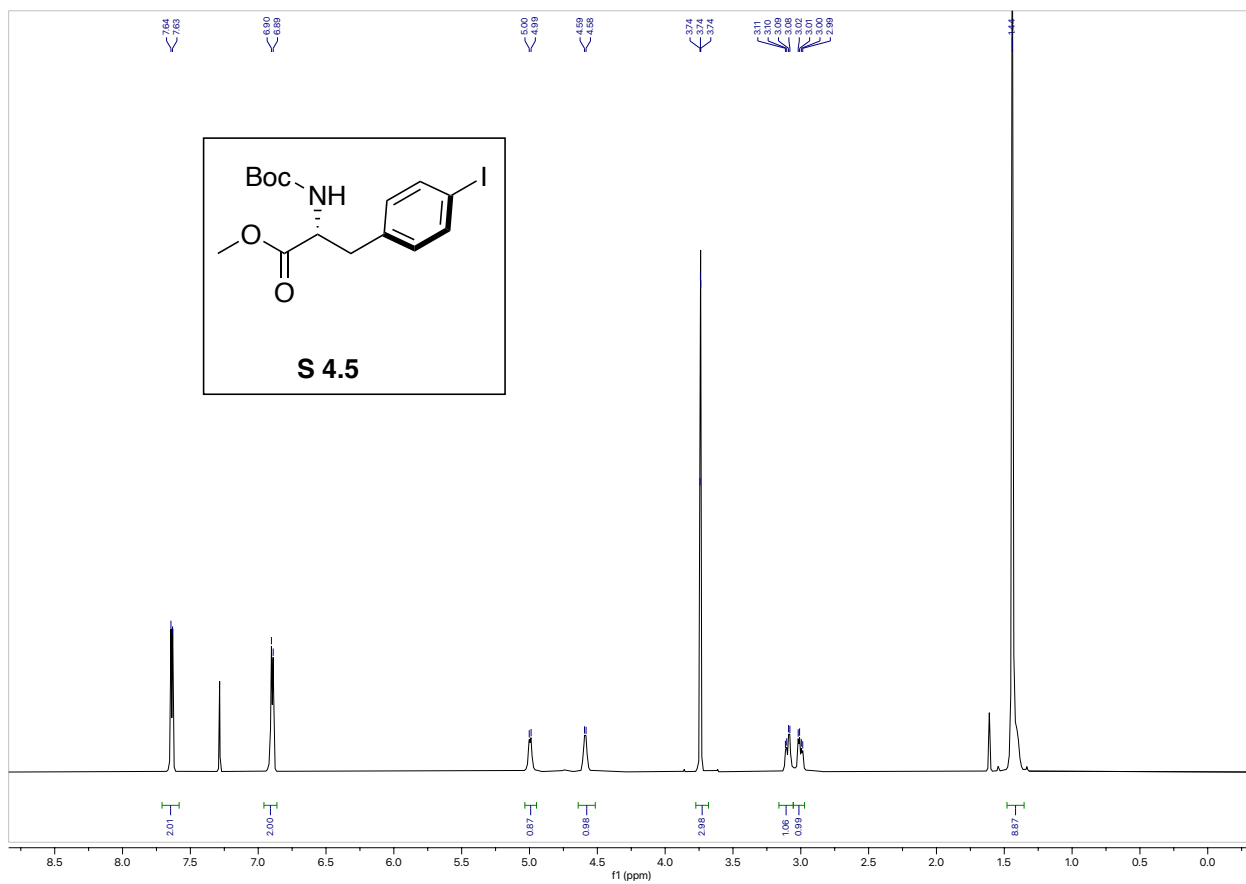
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.5**.



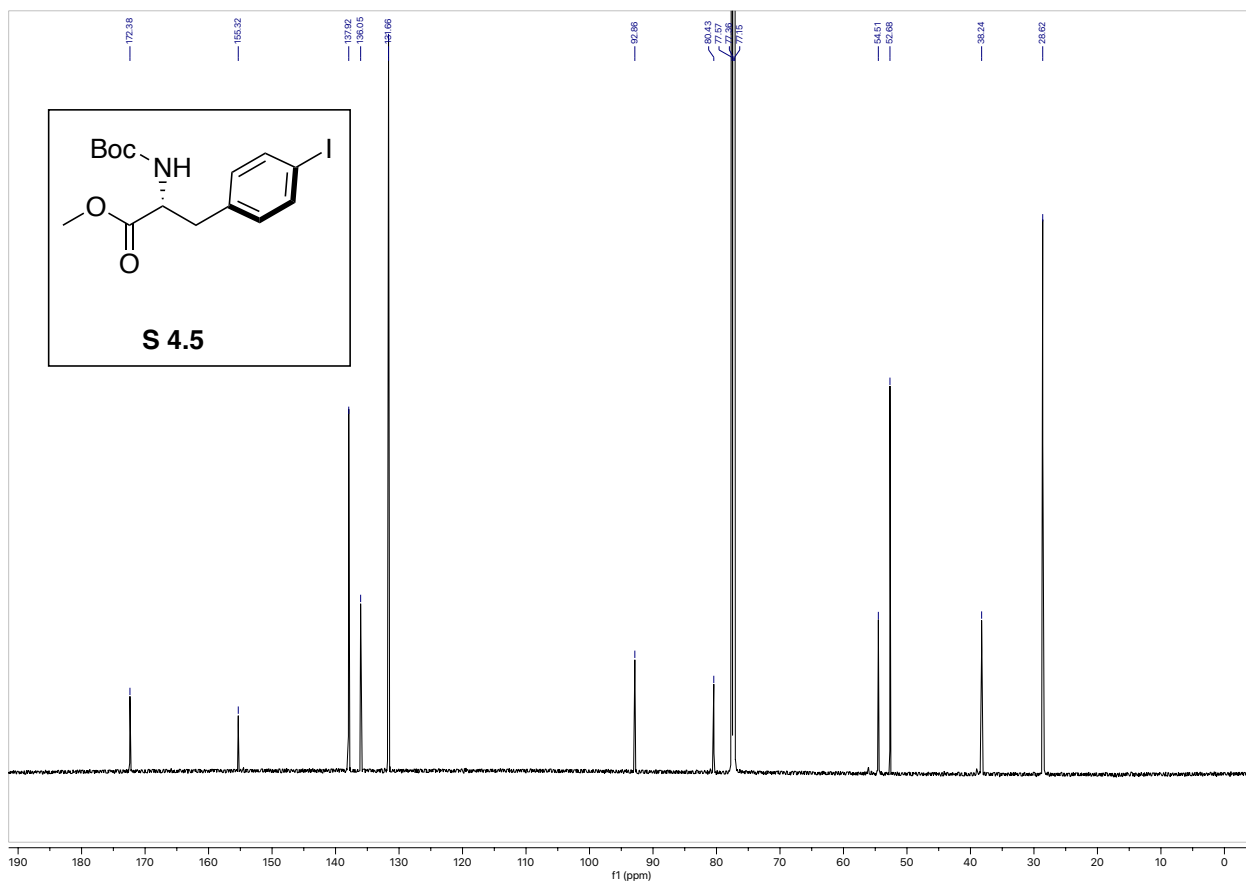
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **S4.3**.



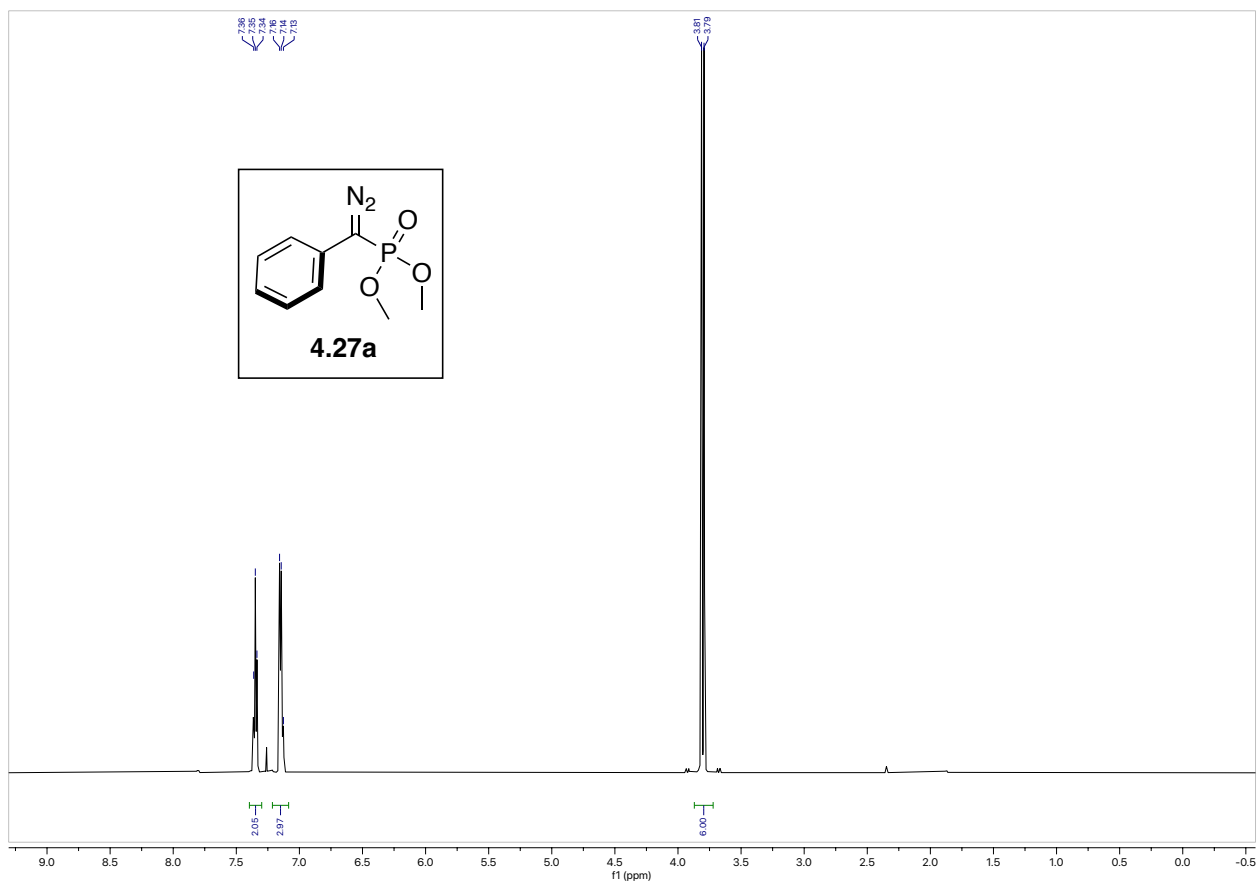
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **S 4.3**.



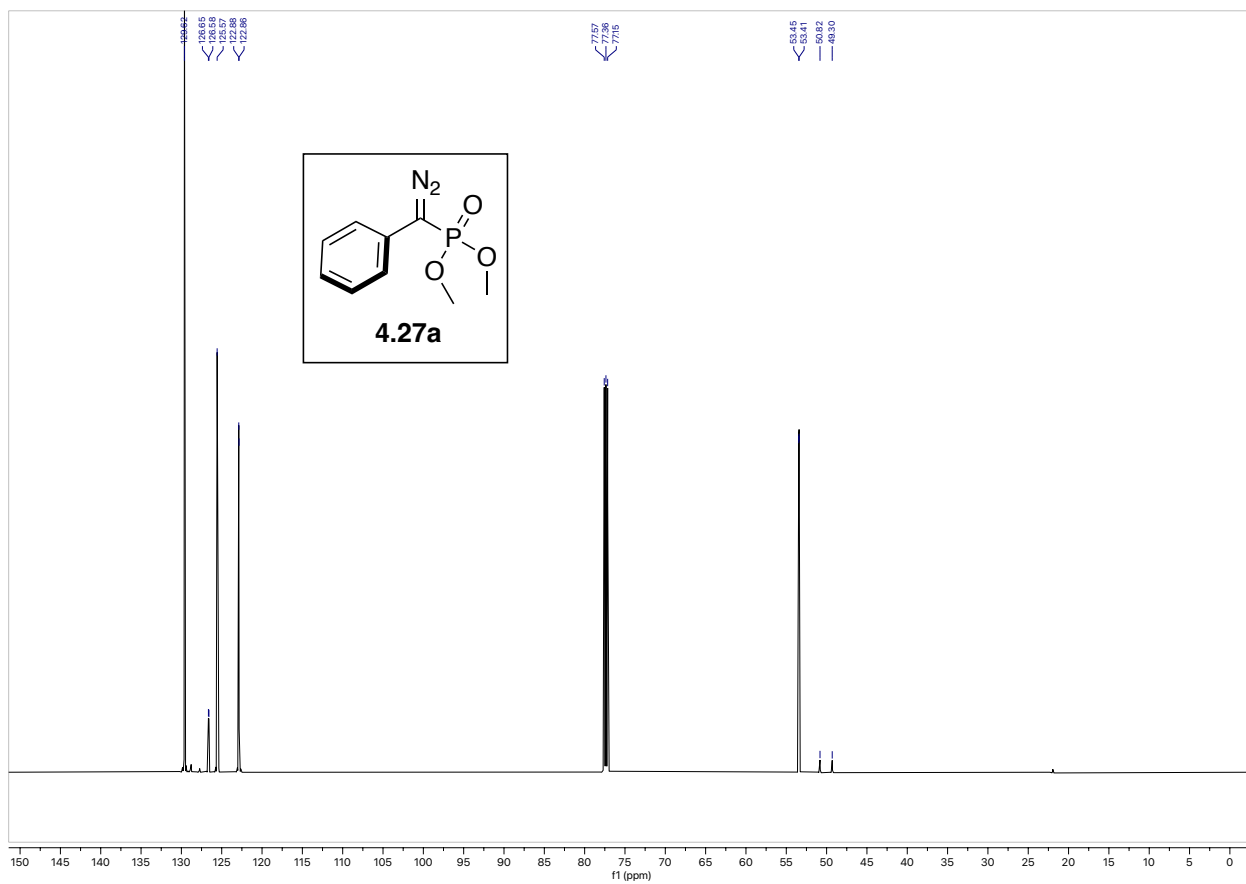
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **S 4.5**.



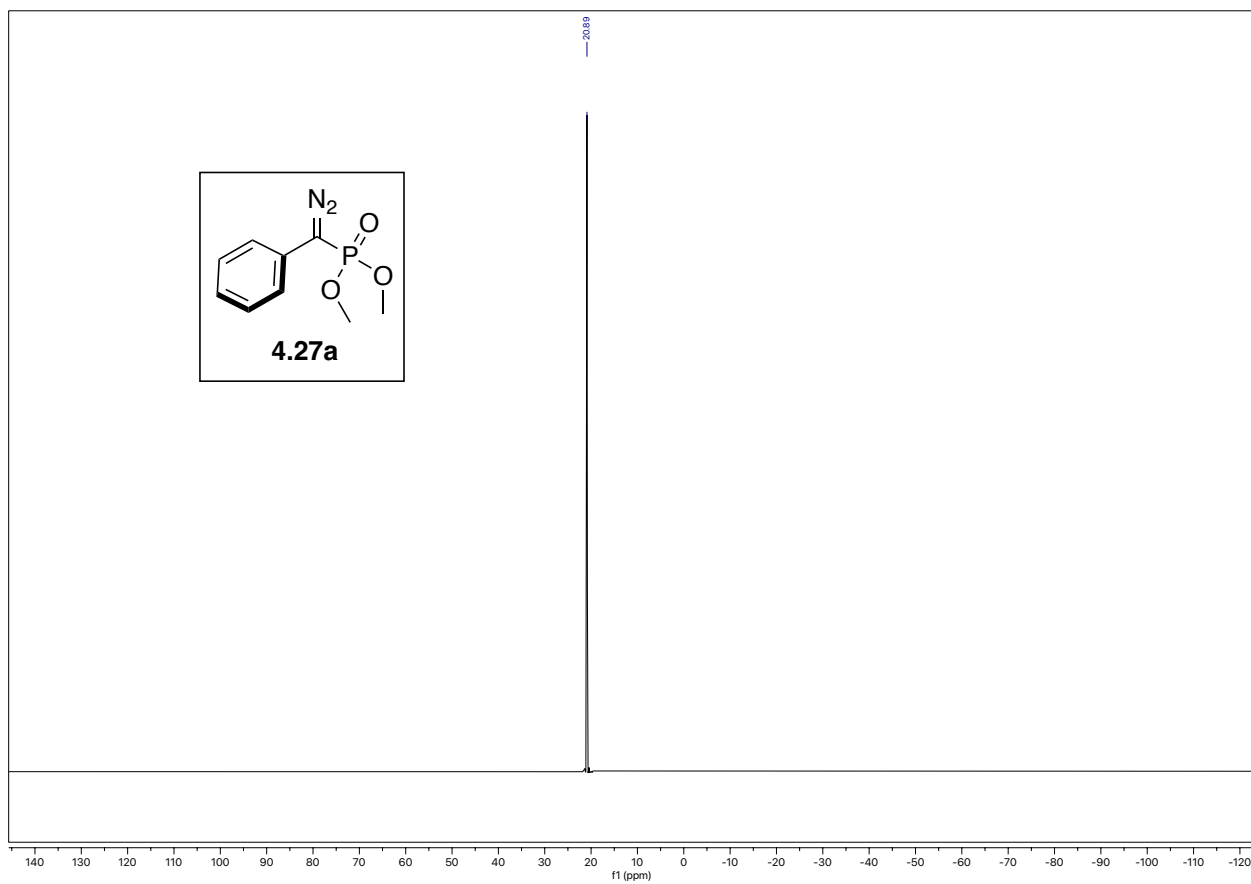
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **S 4.5**.



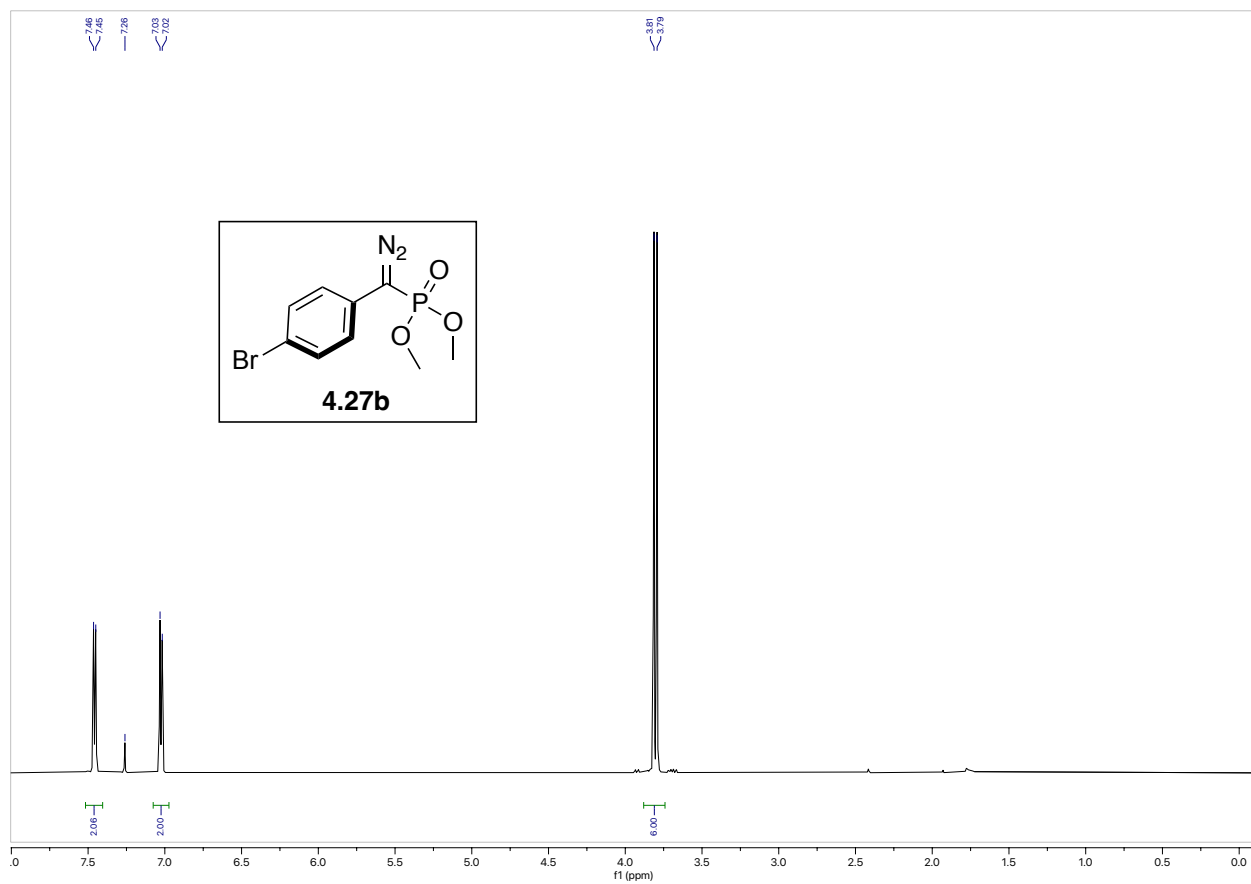
^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27a**.



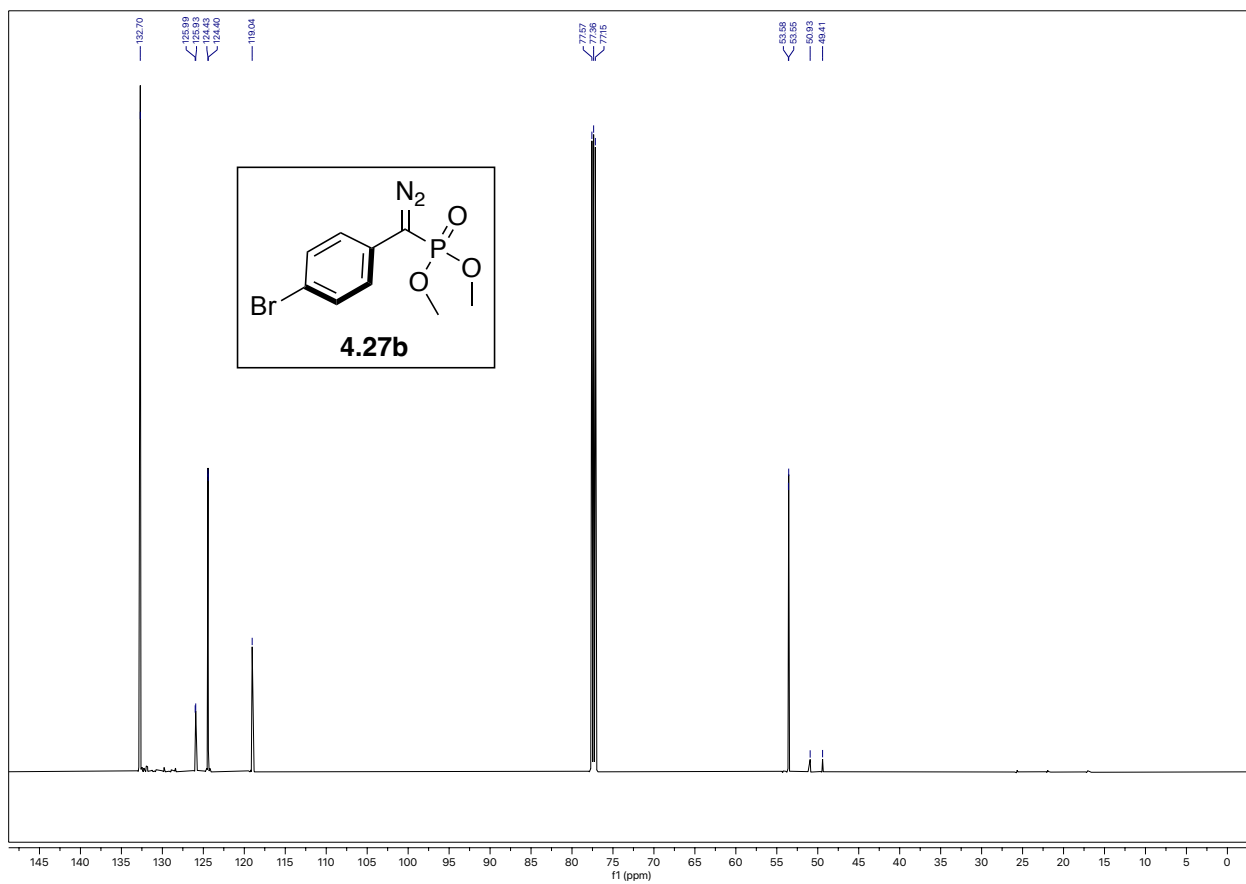
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27a**.



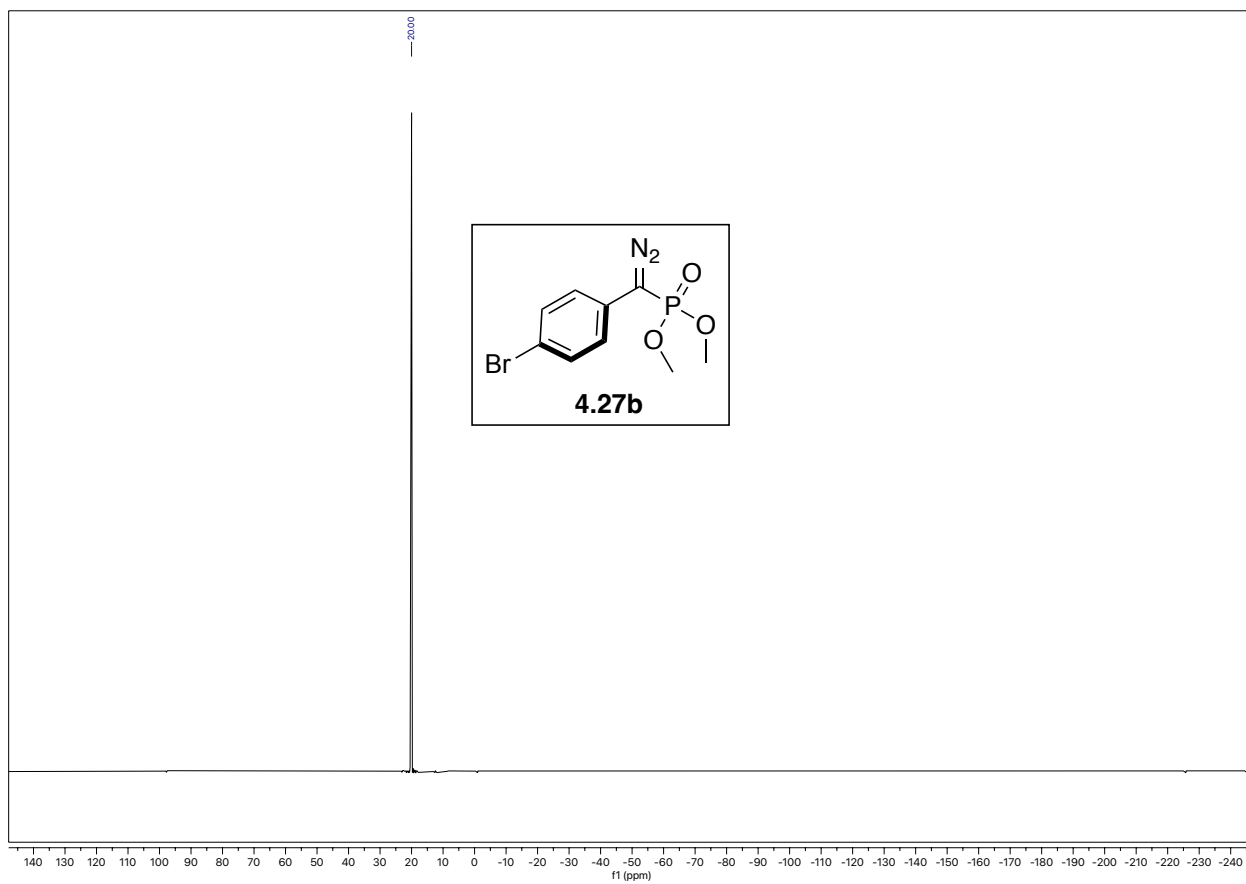
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27a**.



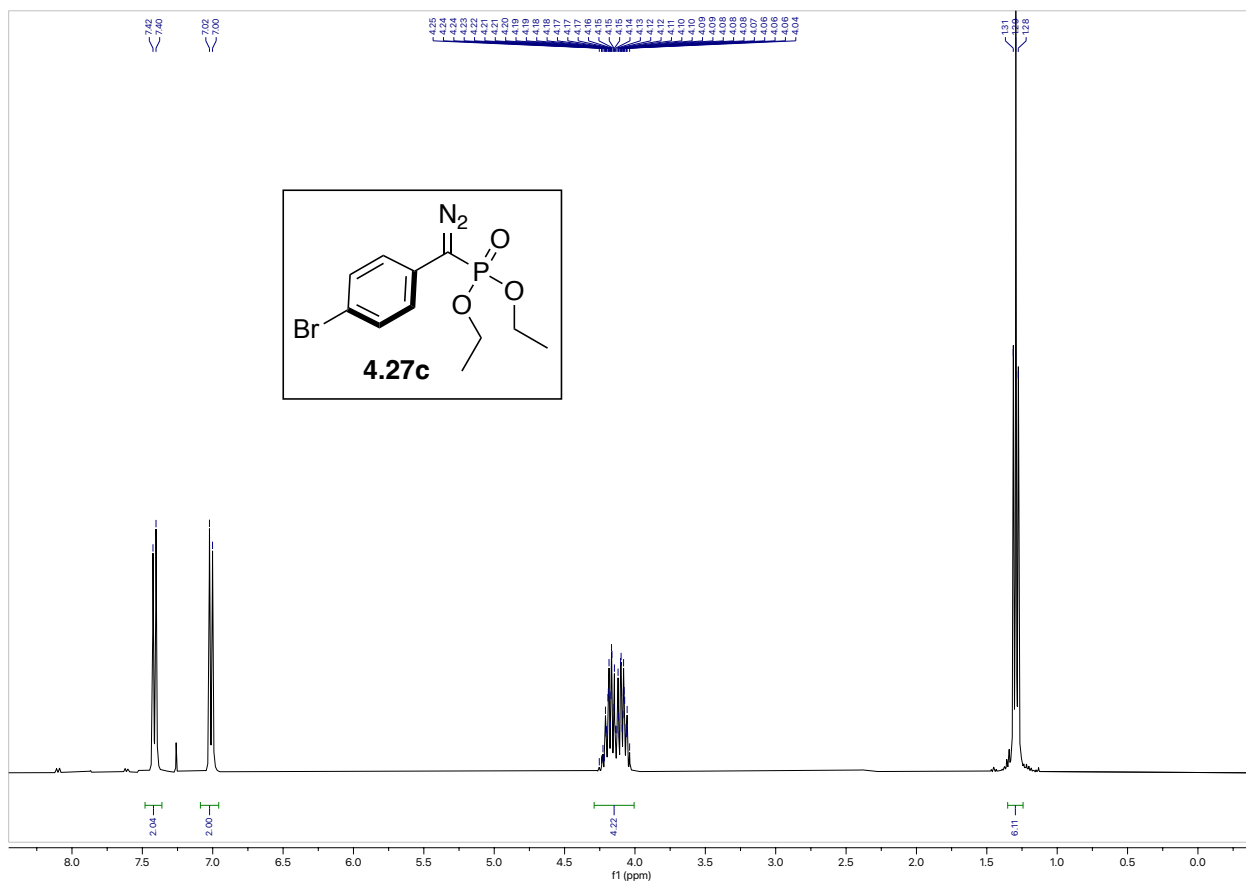
^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27b**.



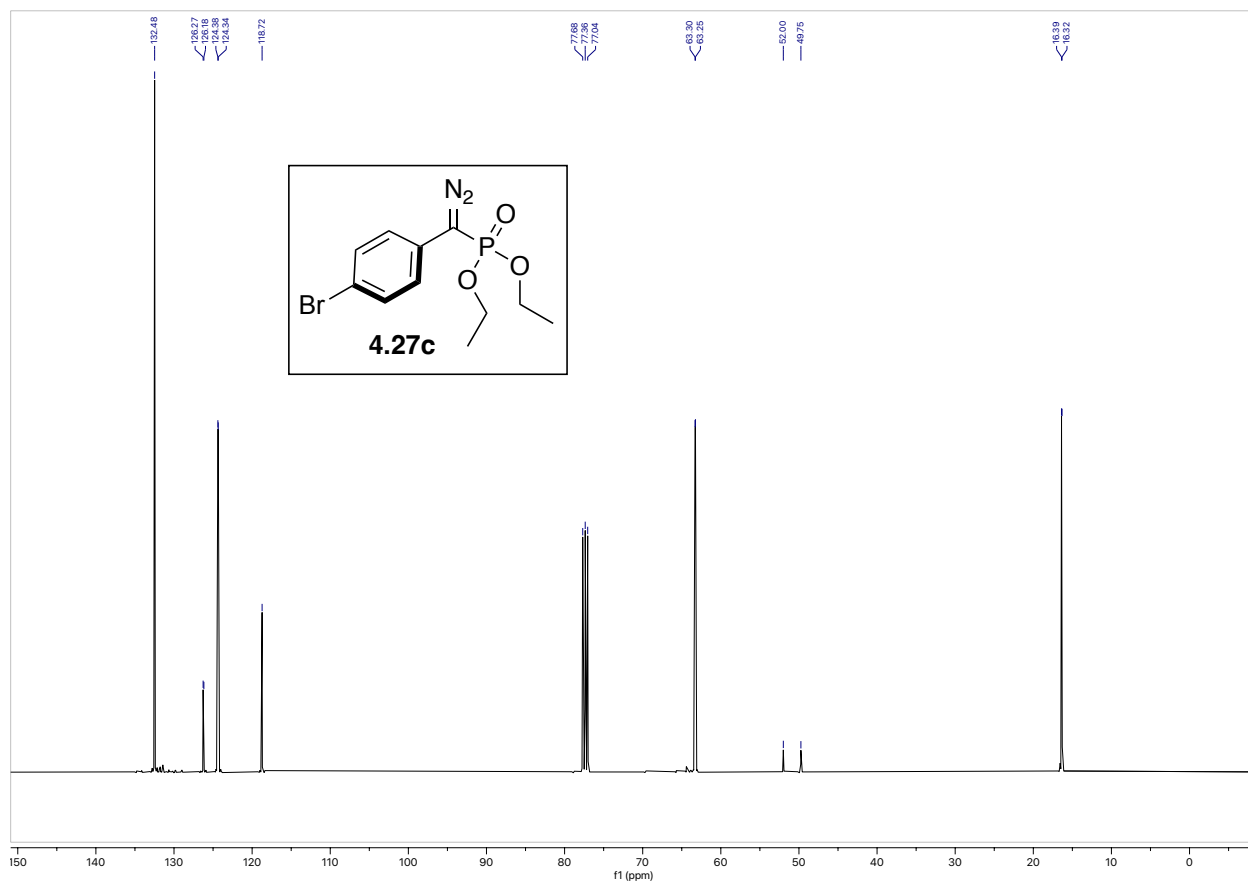
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27b**.



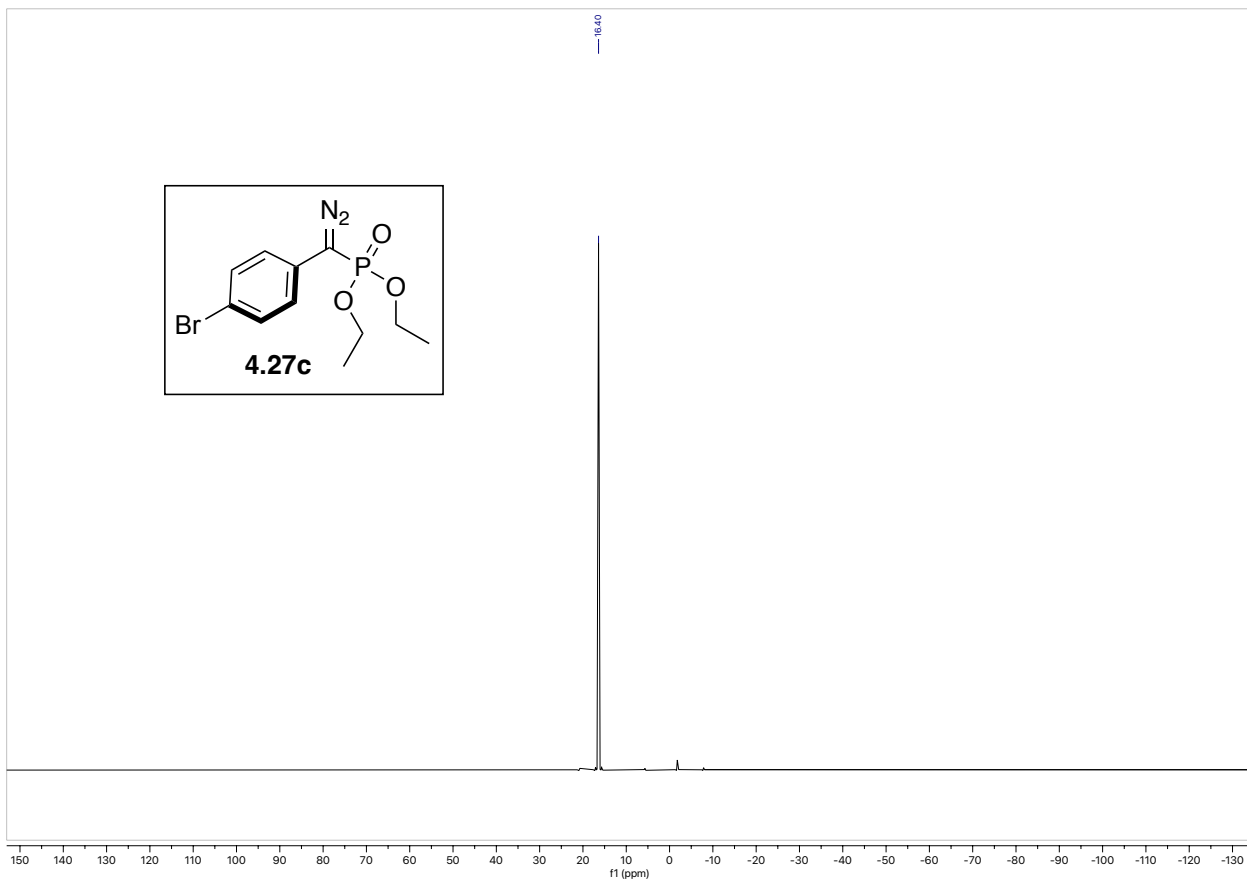
^{31}P NMR spectrum (243 MHz, Chloroform- d) of **4.27b**.



^1H NMR spectrum (400 MHz, CDCl_3) (s, 7.26 ppm) of **4.27c**.



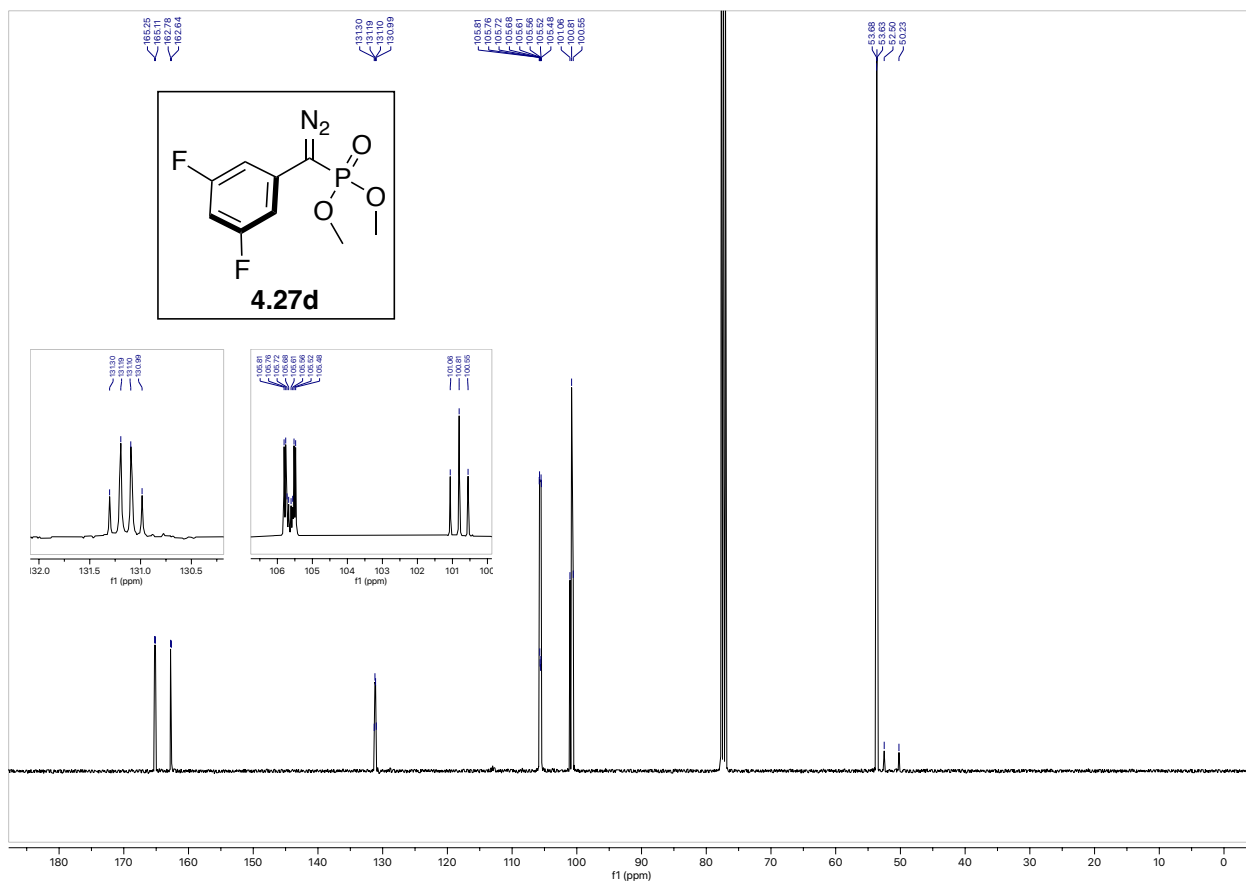
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27c**.



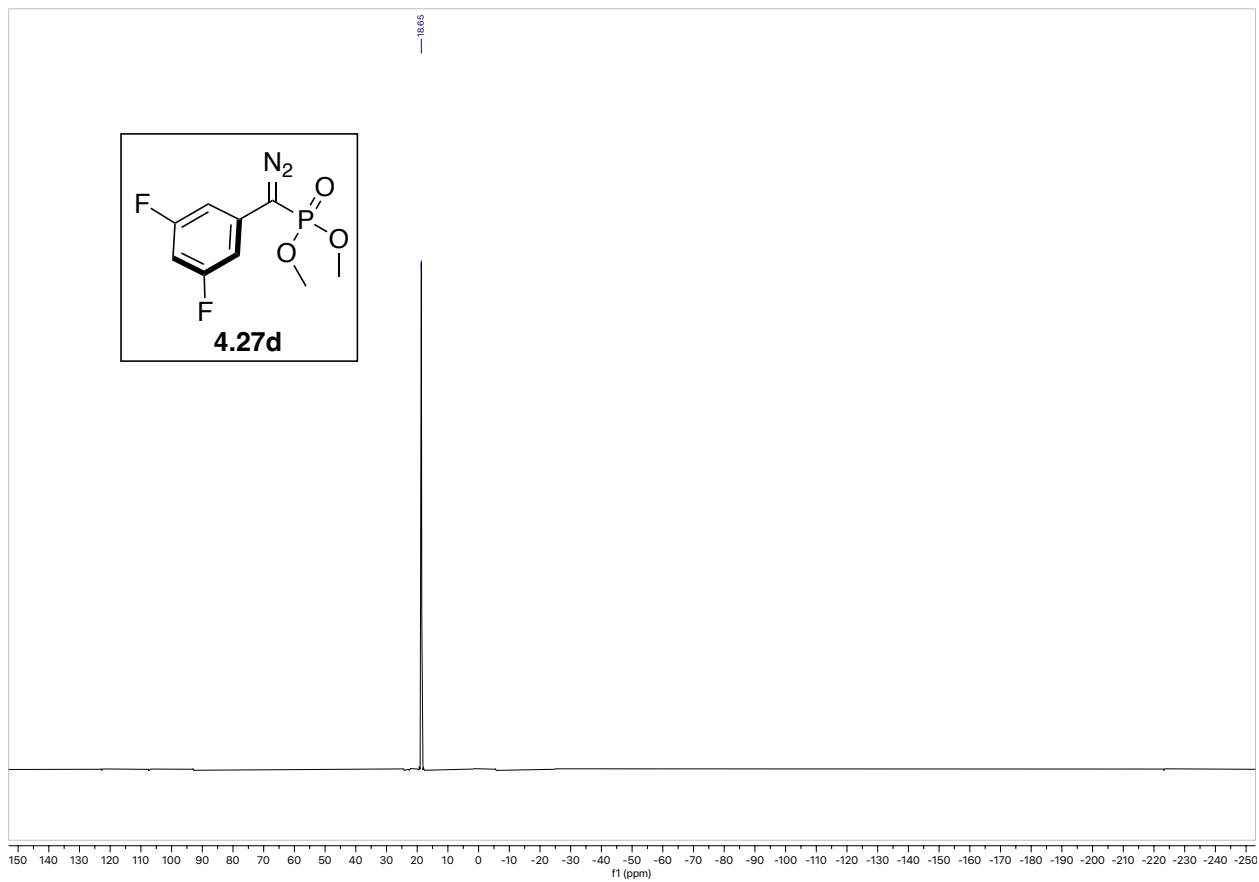
^{31}P NMR spectrum (162 MHz, Chloroform-d) of **4.27c**.



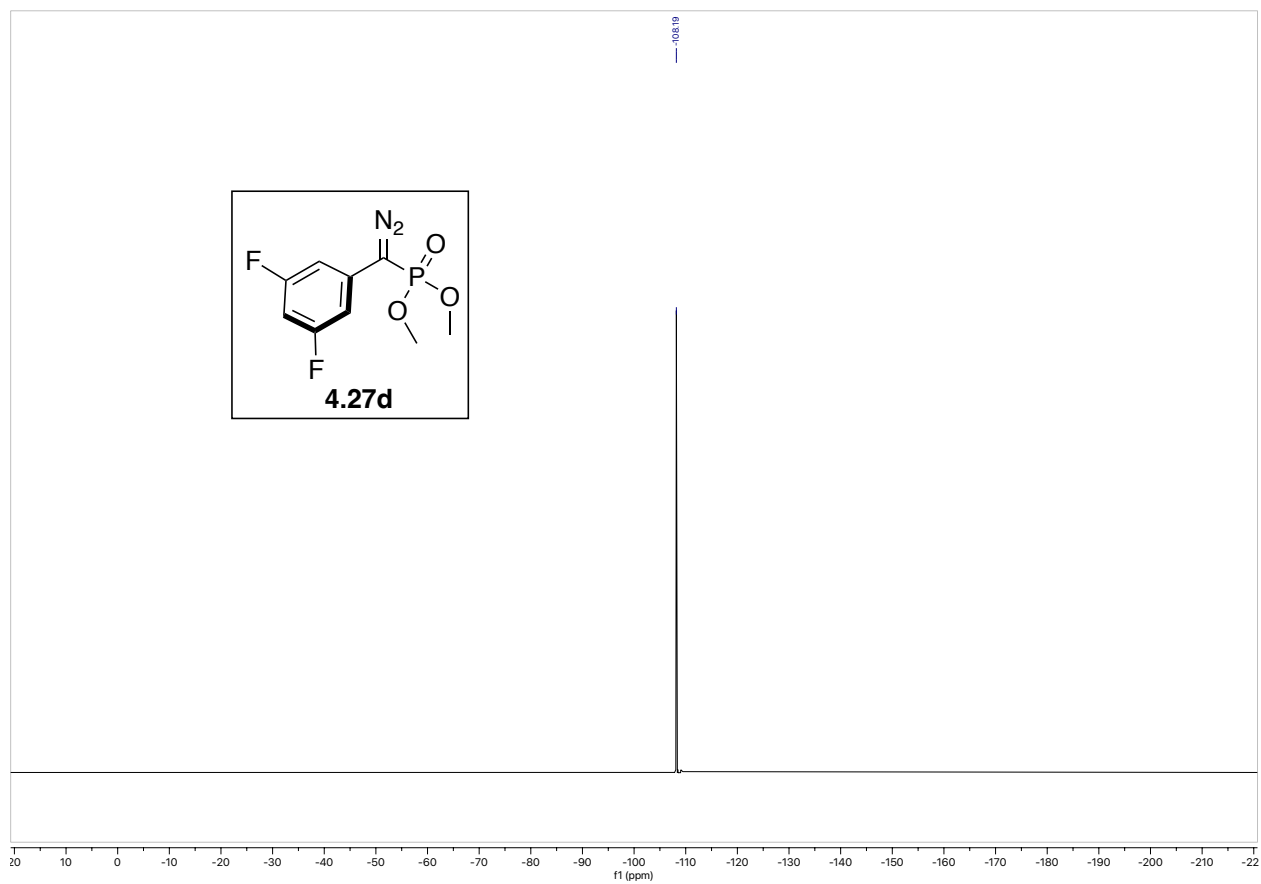
^1H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27d**.



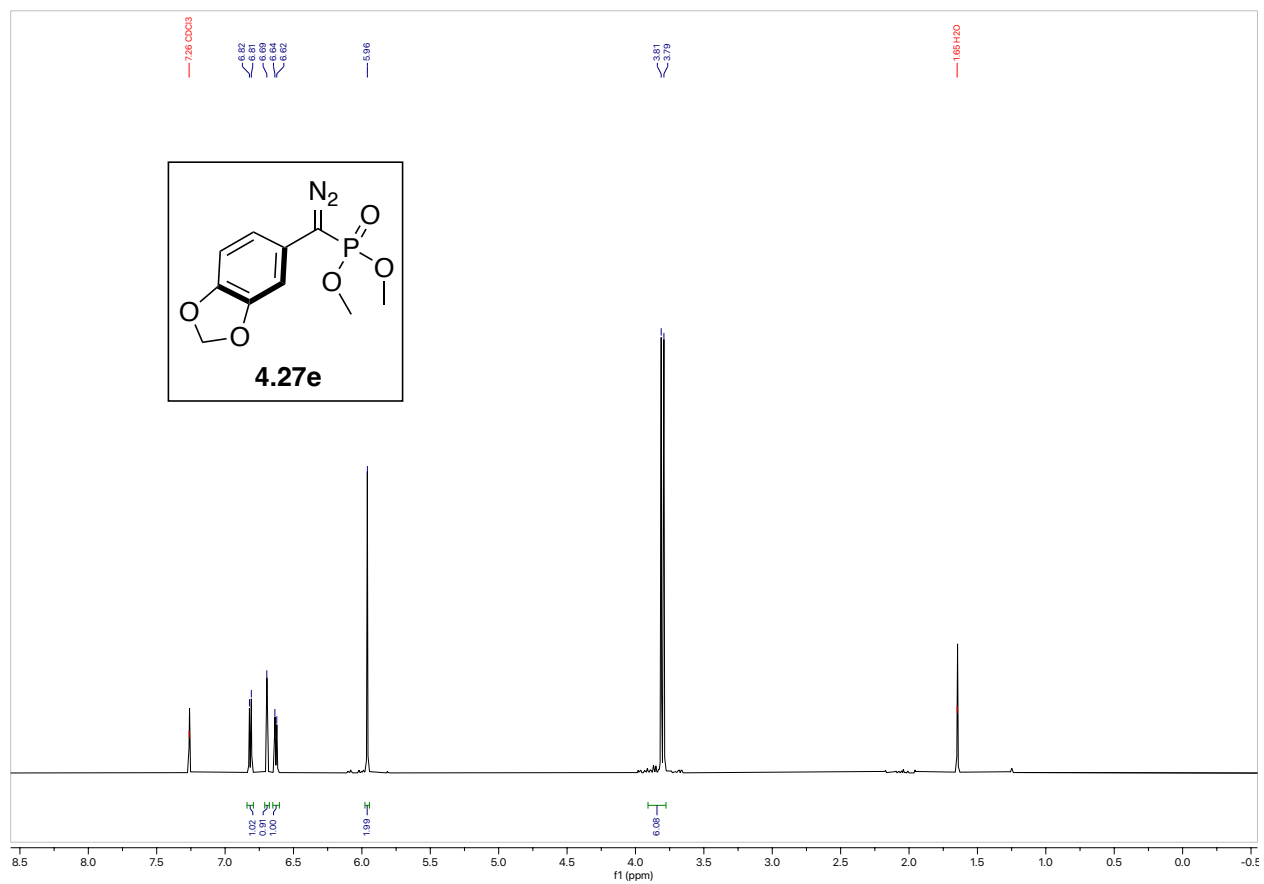
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27d**.



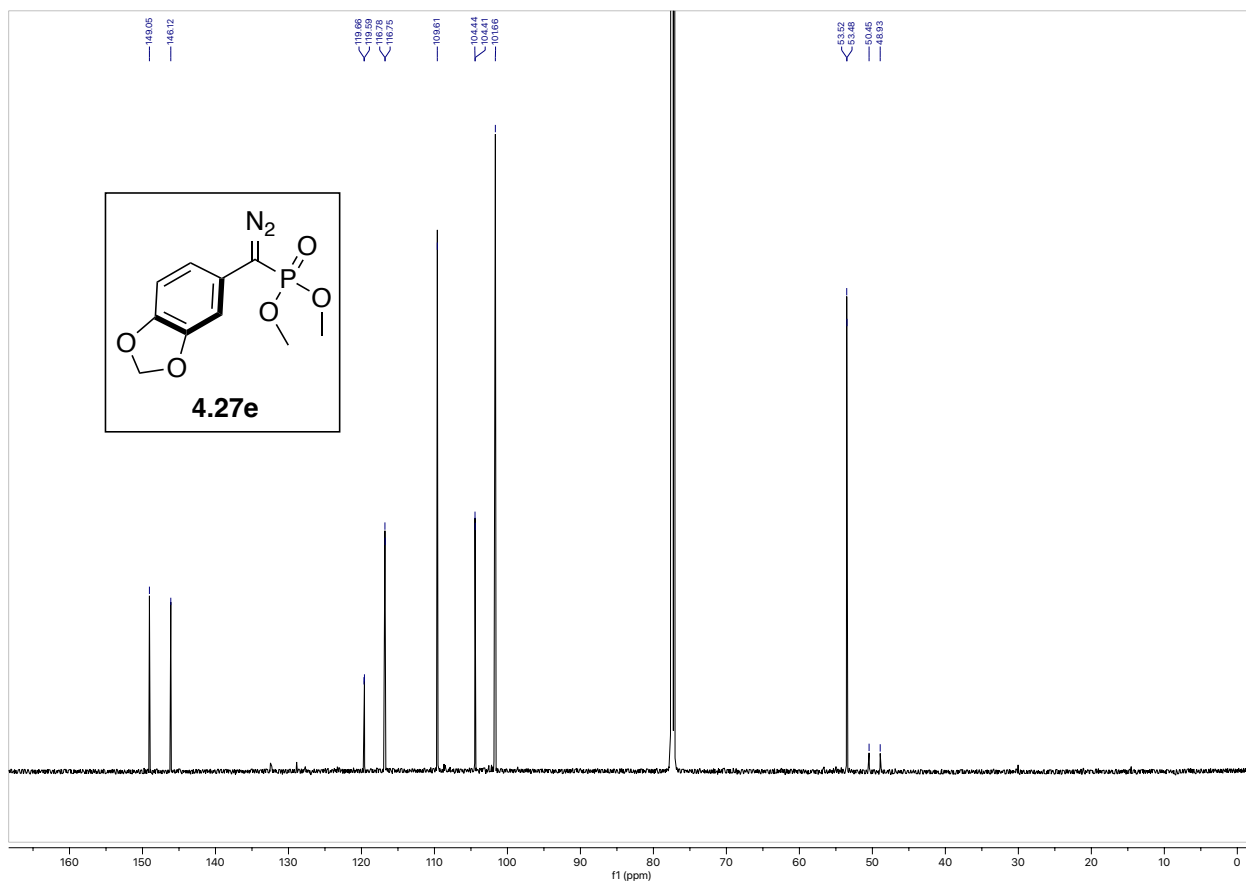
^{31}P NMR spectrum (162 MHz, Chloroform-d) of **4.27d**.



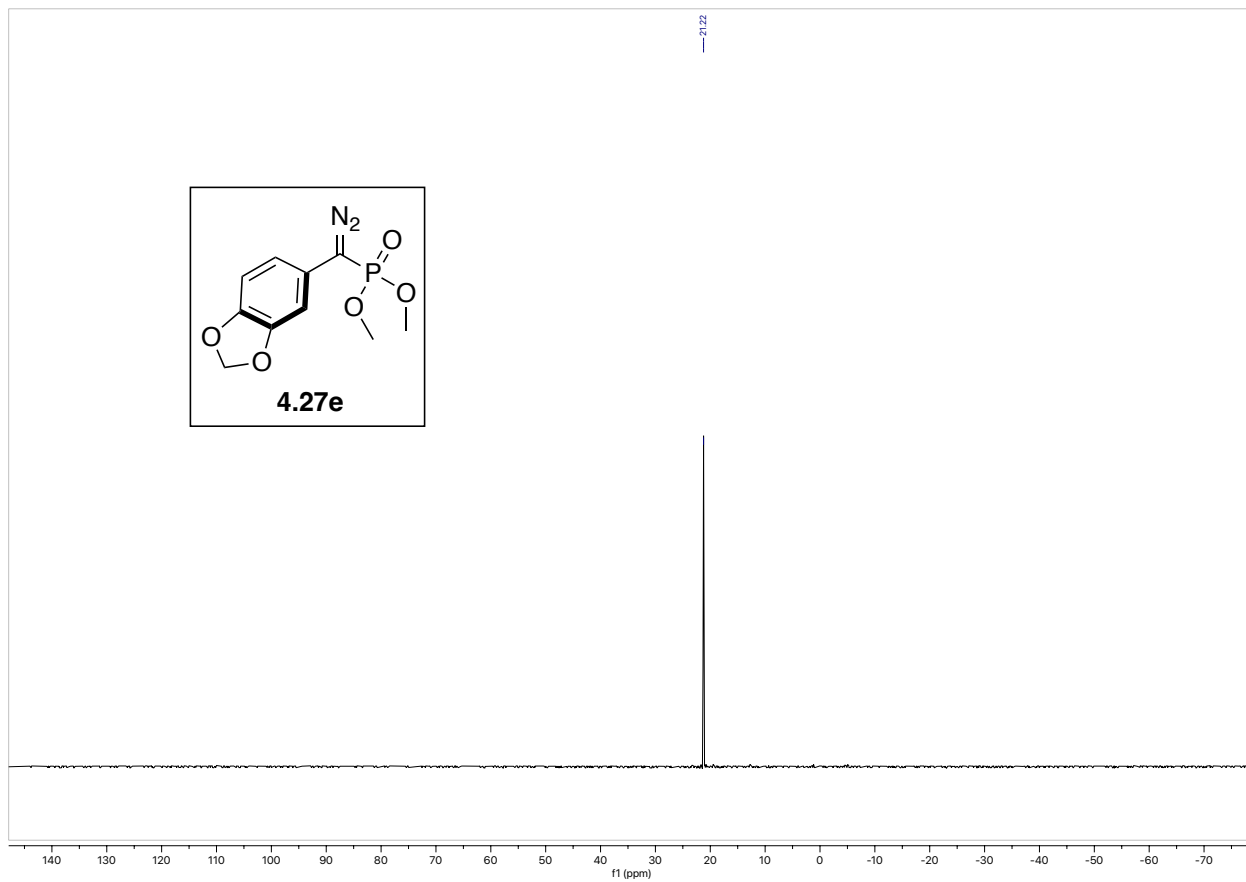
^{19}F NMR spectrum (376 MHz, Chloroform-d) of **4.27d**.



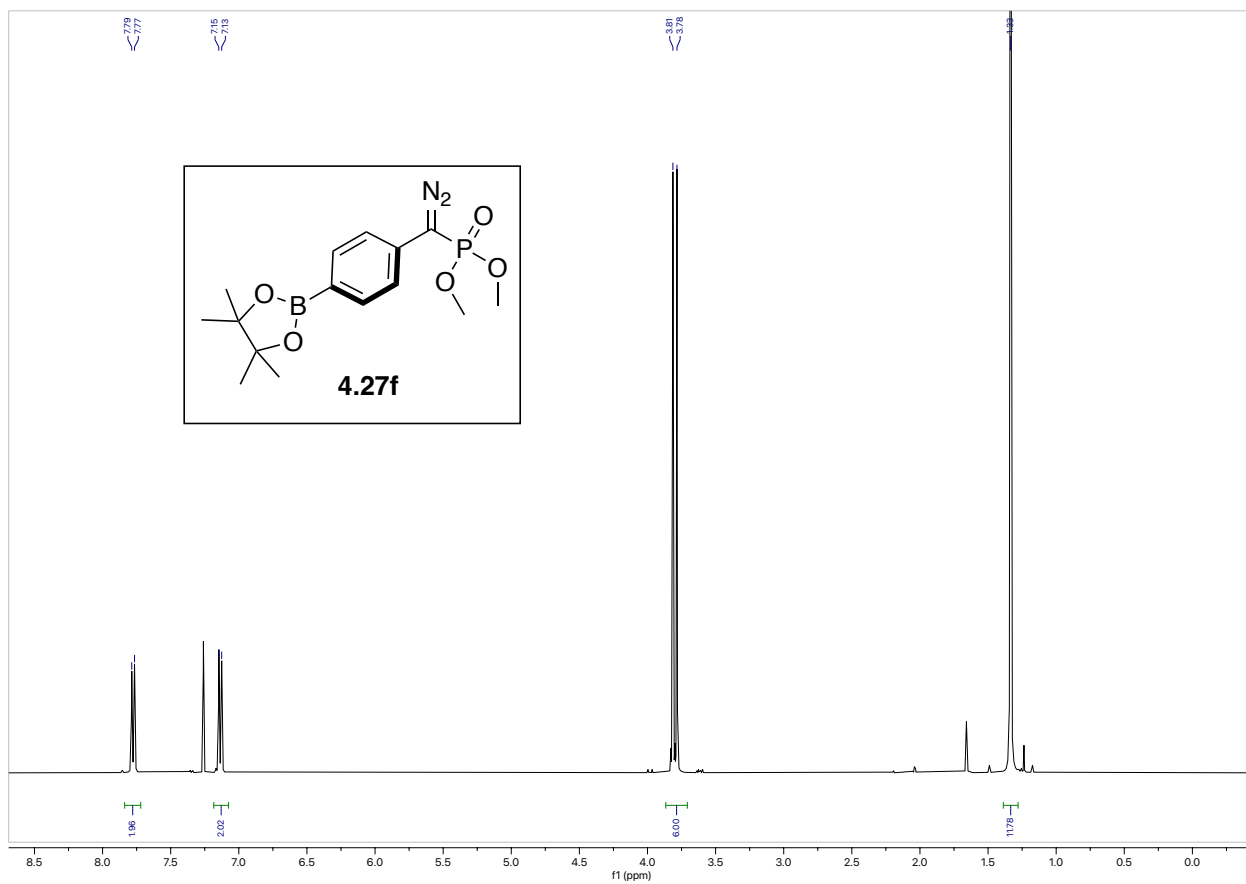
^1H NMR spectrum (600 MHz, CDCl_3) (s, 7.26 ppm) of **4.27e**.



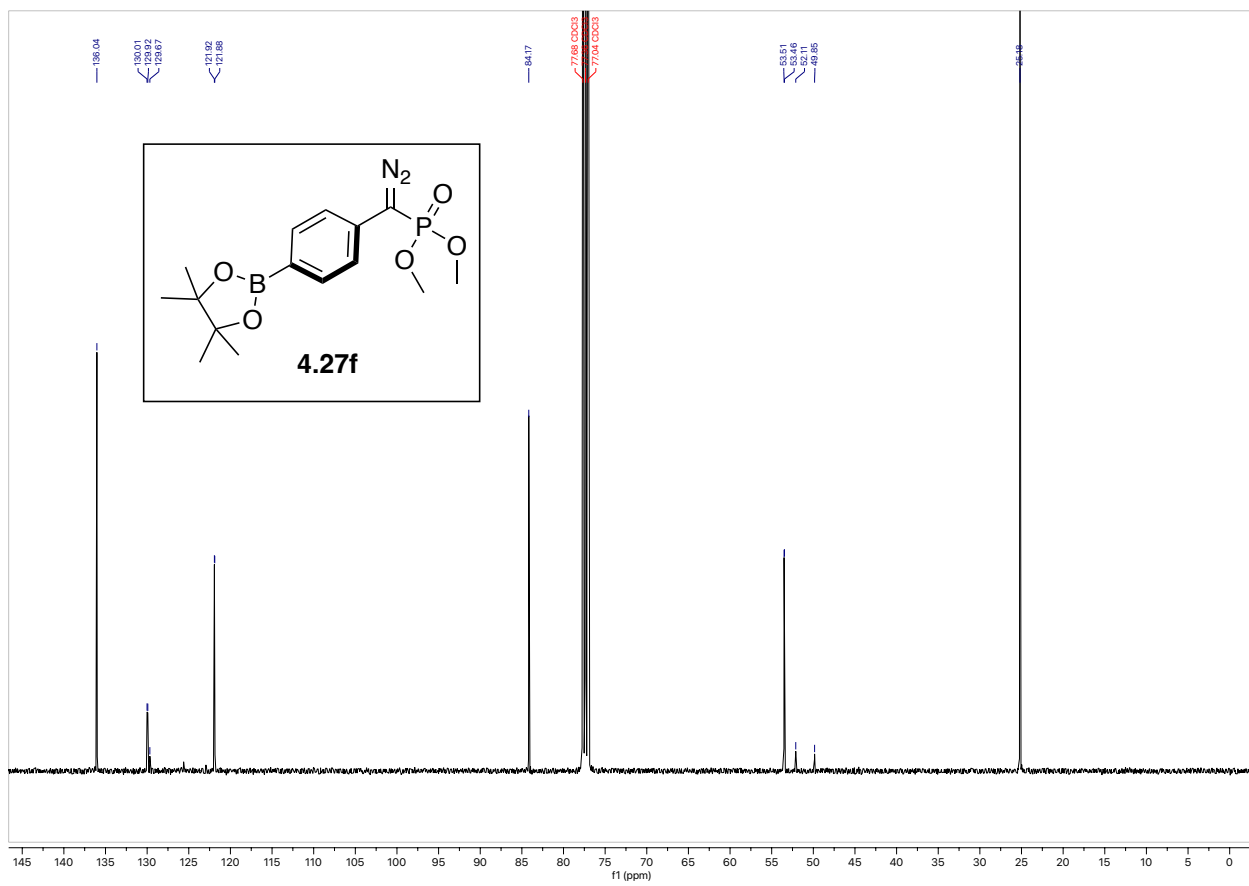
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27e**.



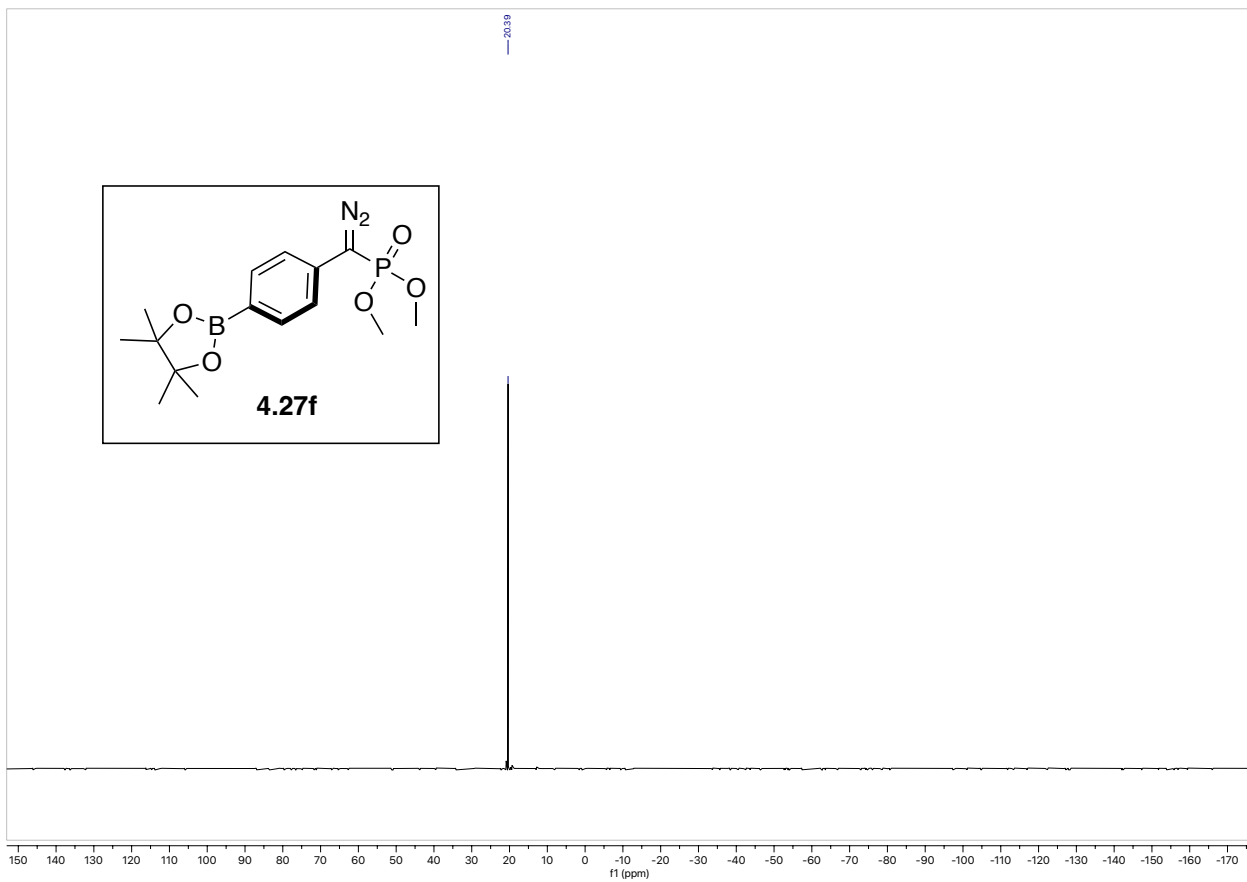
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27e**.



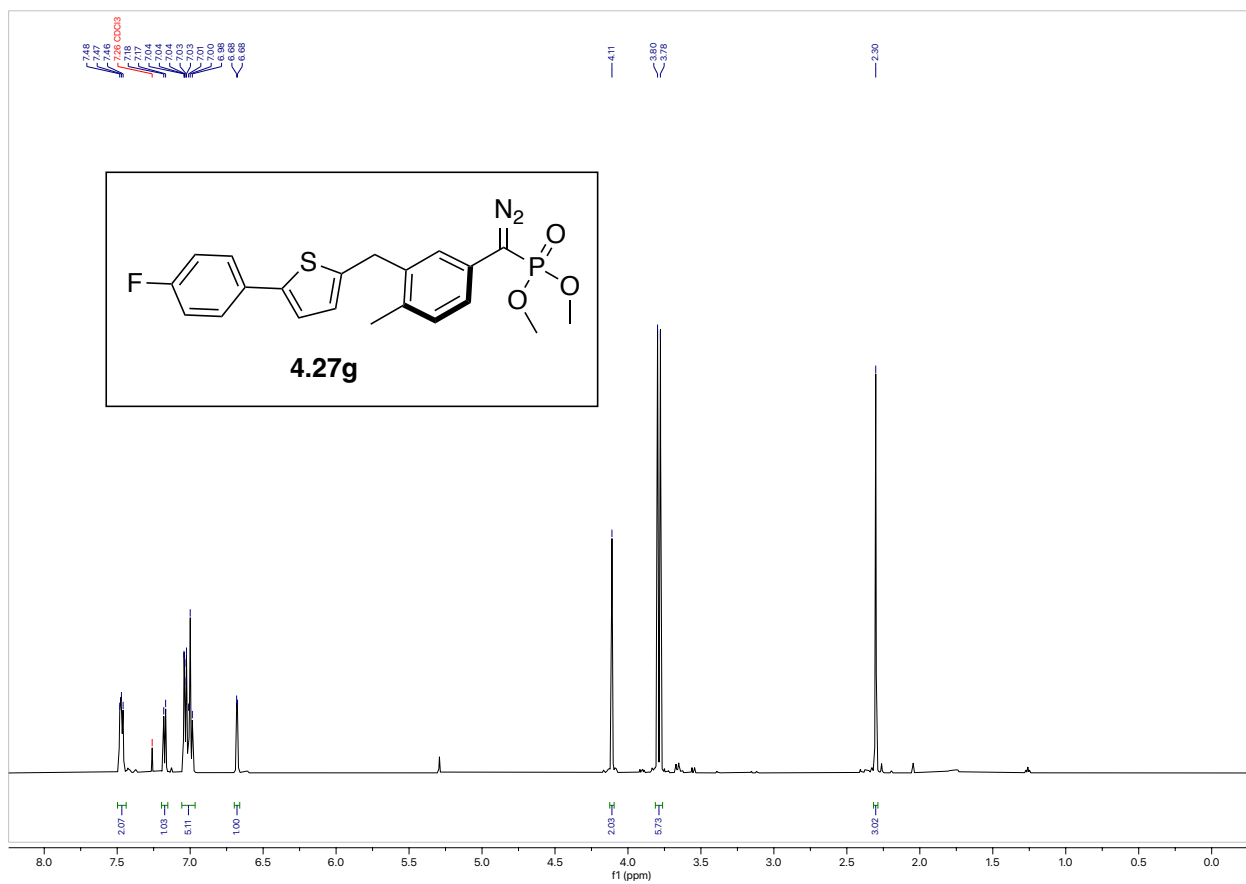
¹H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27f**.



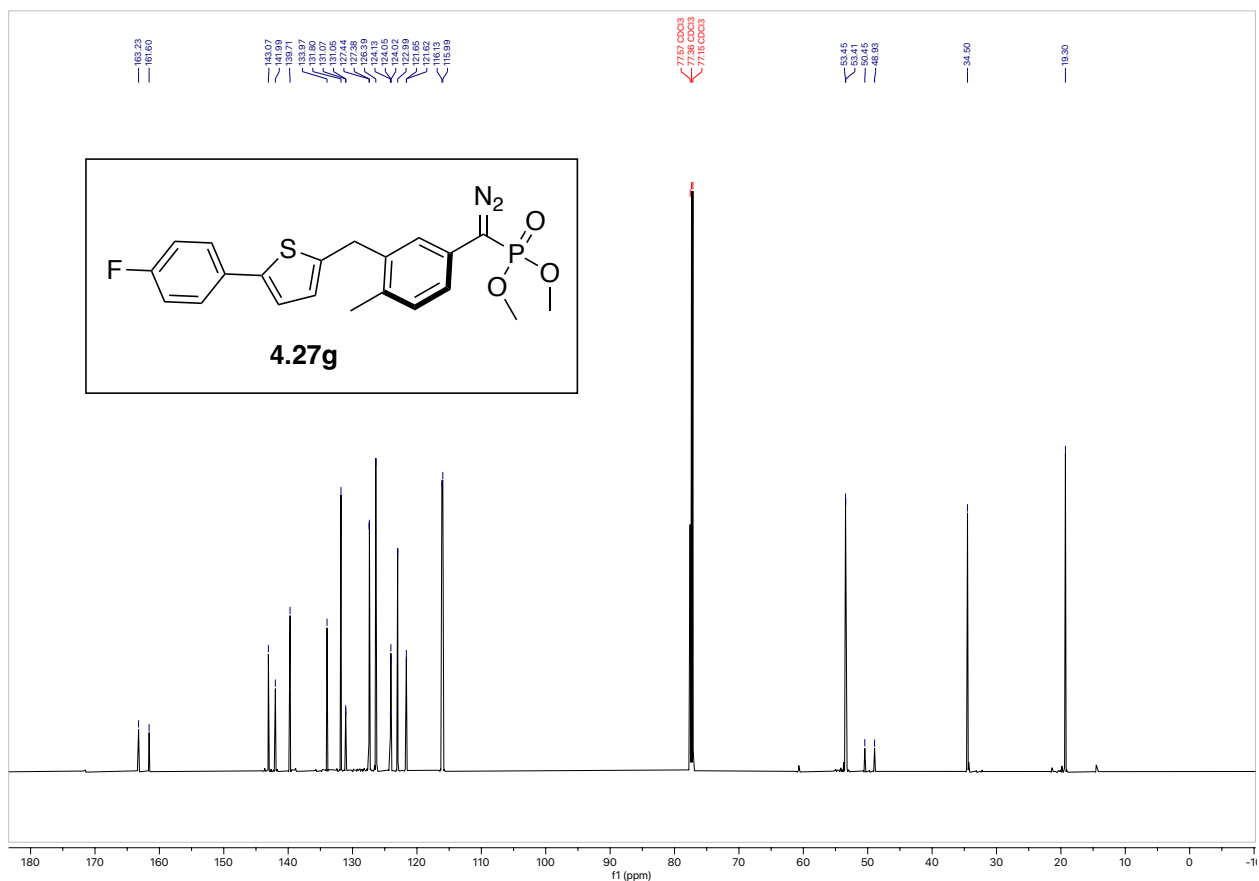
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform- d) (t, 77.36 ppm) of **4.27f**.

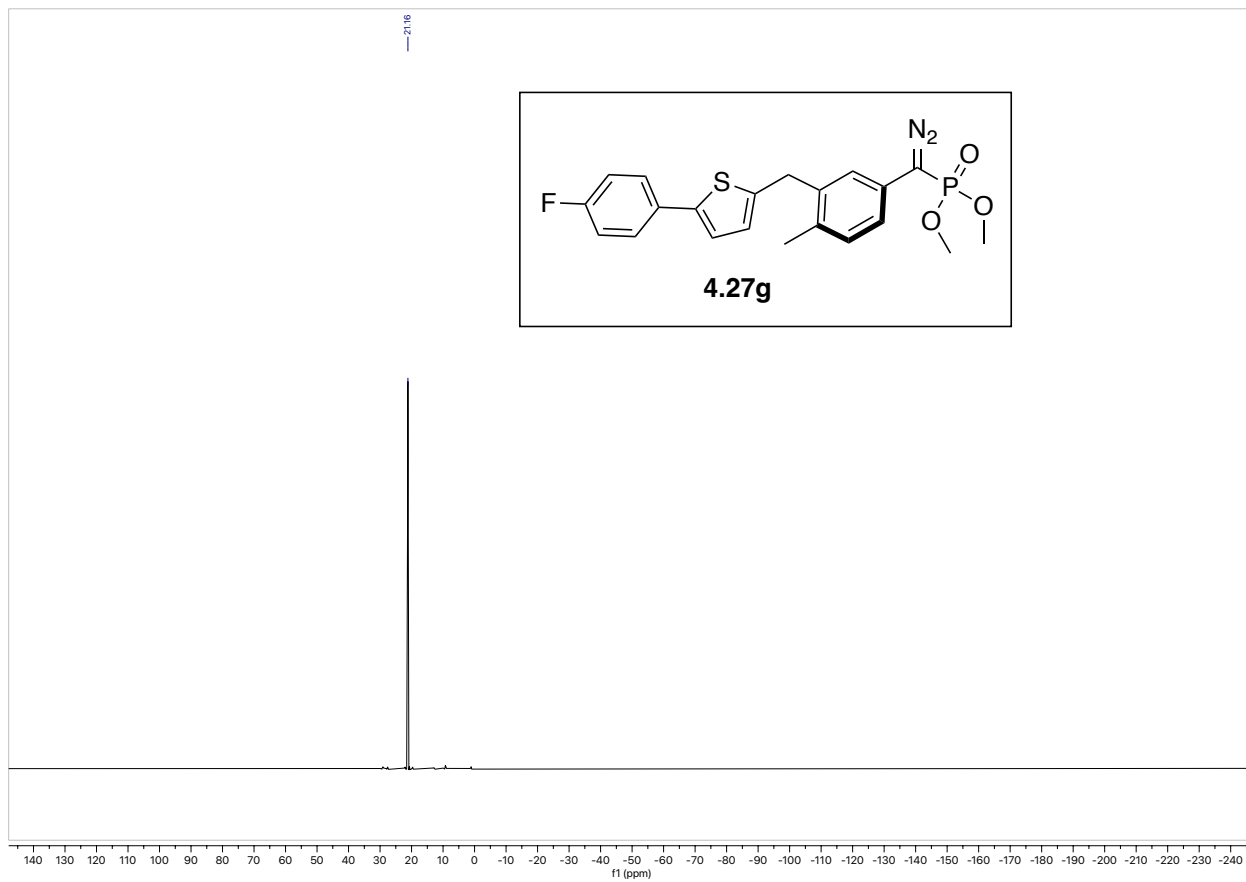


^{31}P NMR spectrum (162 MHz, Chloroform- d) of **4.27f**.

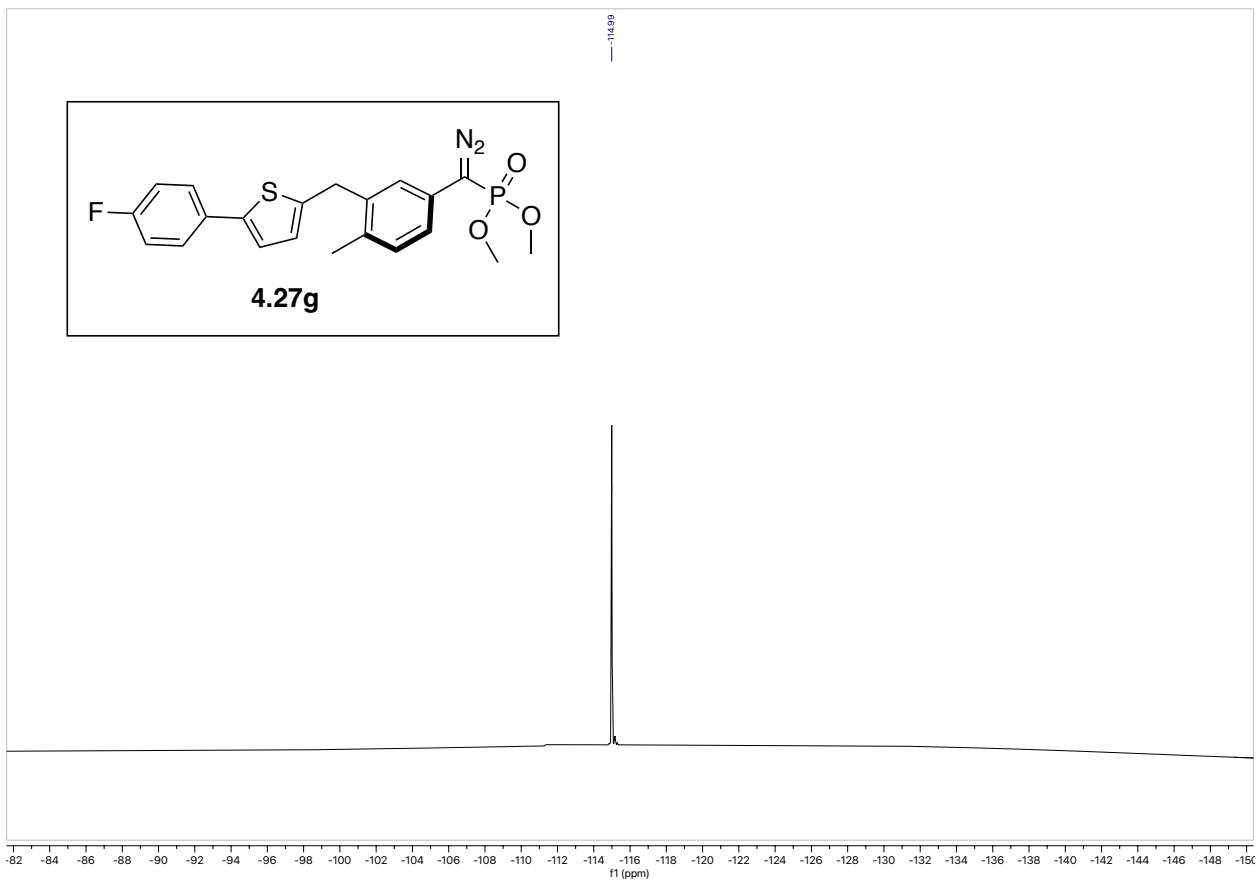


¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27g**.

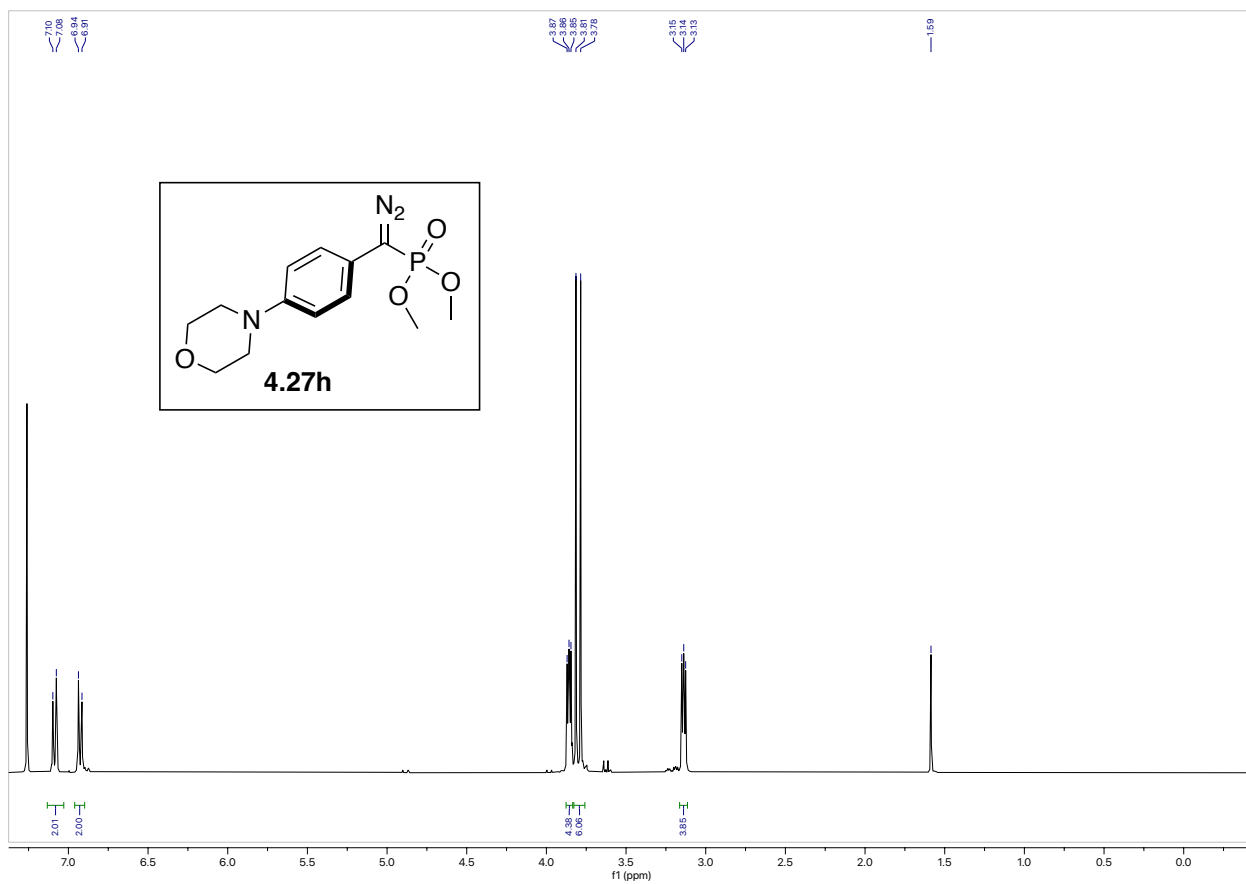




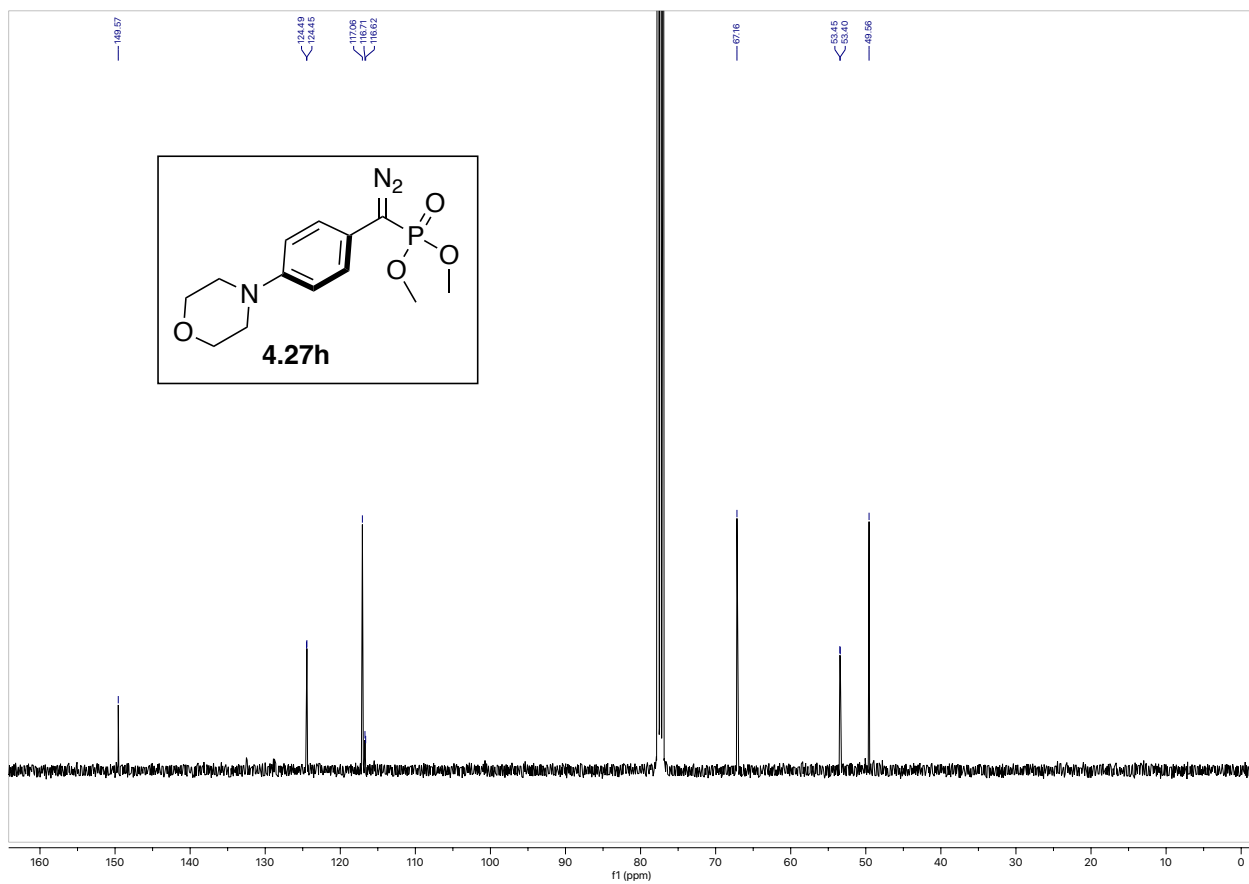
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27g**.



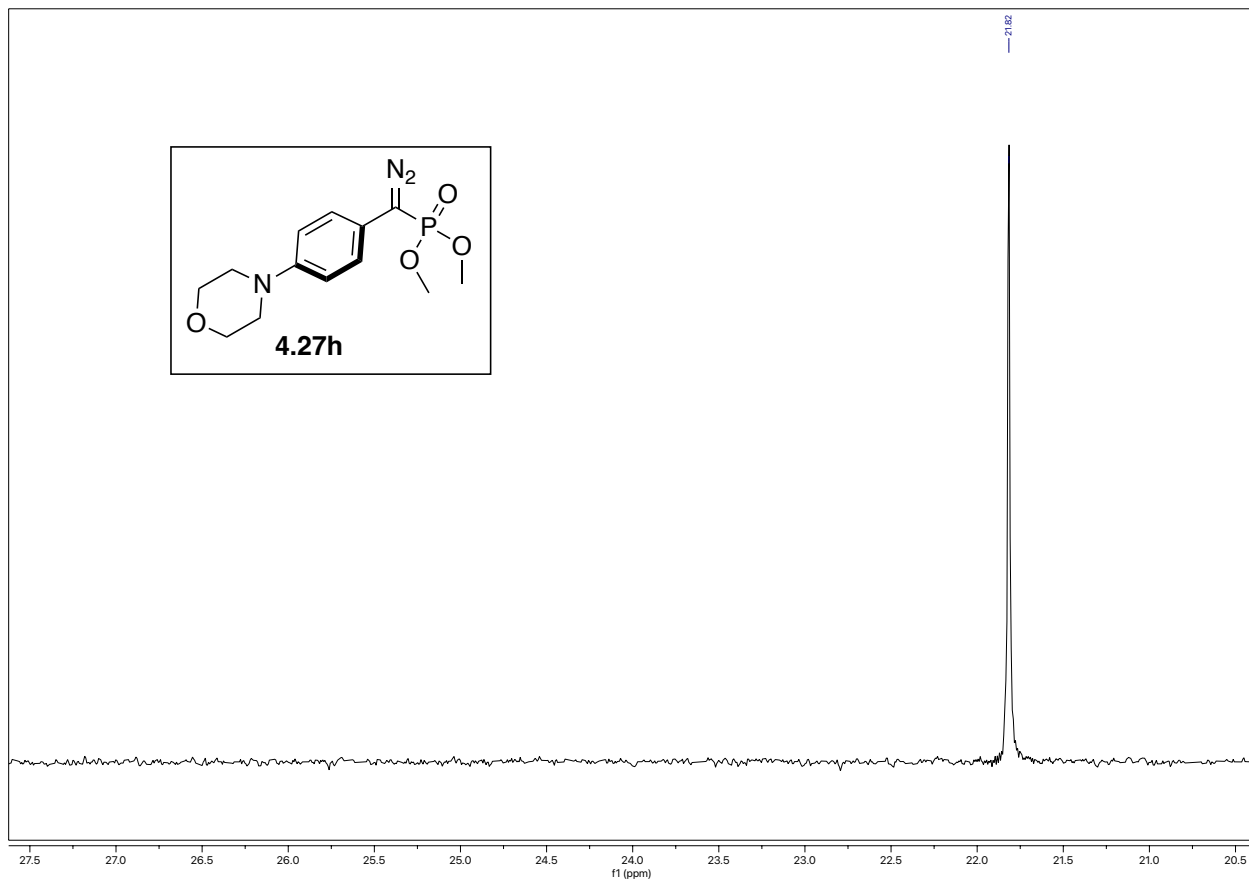
^{19}F NMR spectrum (565 MHz, Chloroform- d) of **4.27g**.



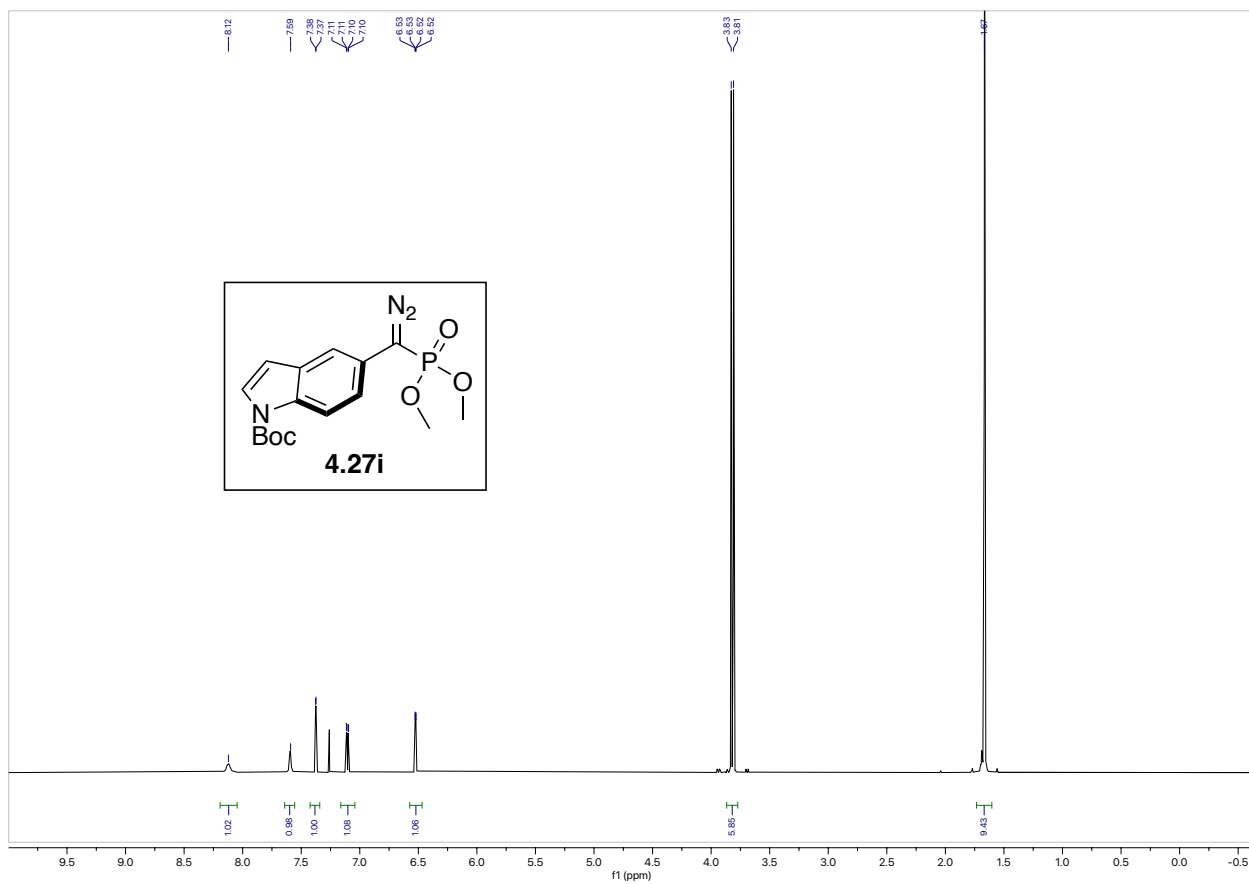
¹H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27h**.



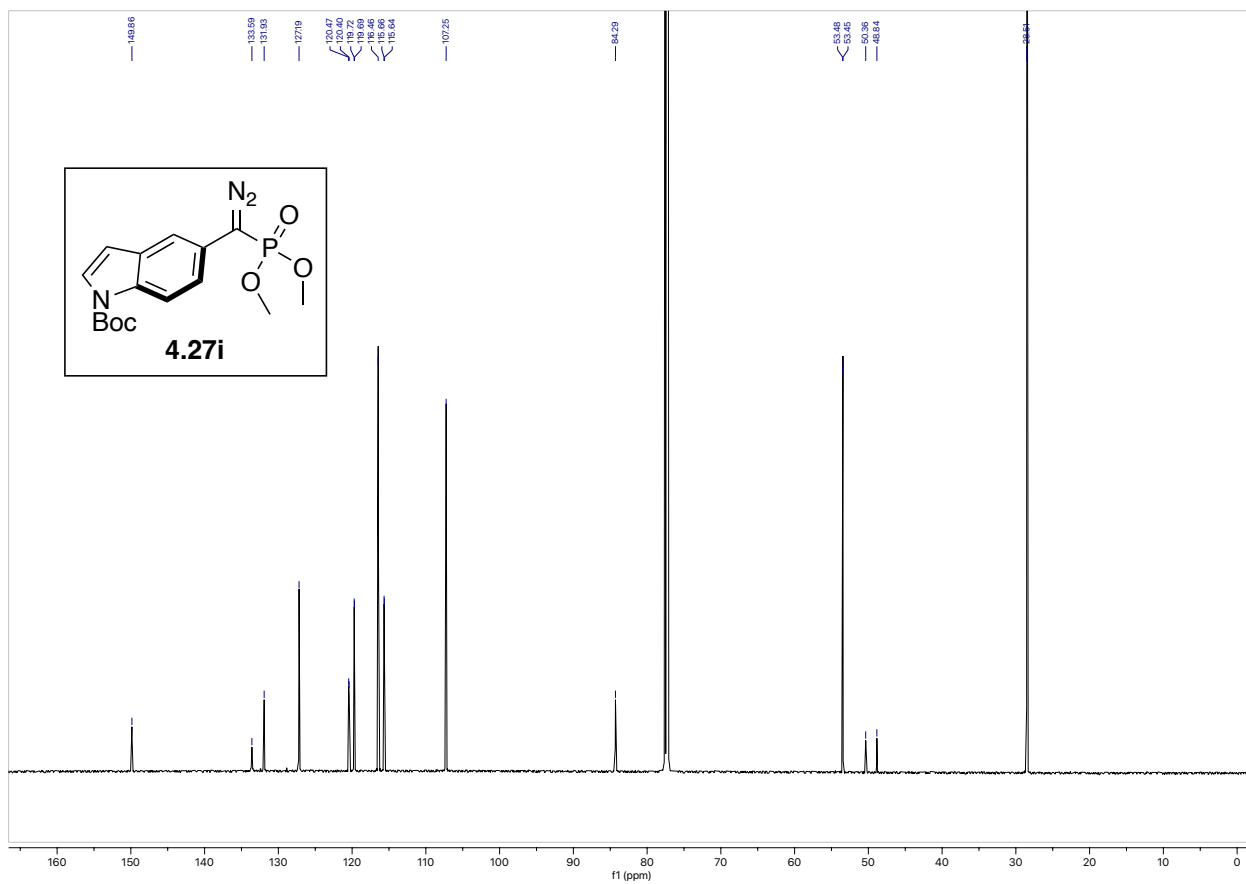
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27h**.



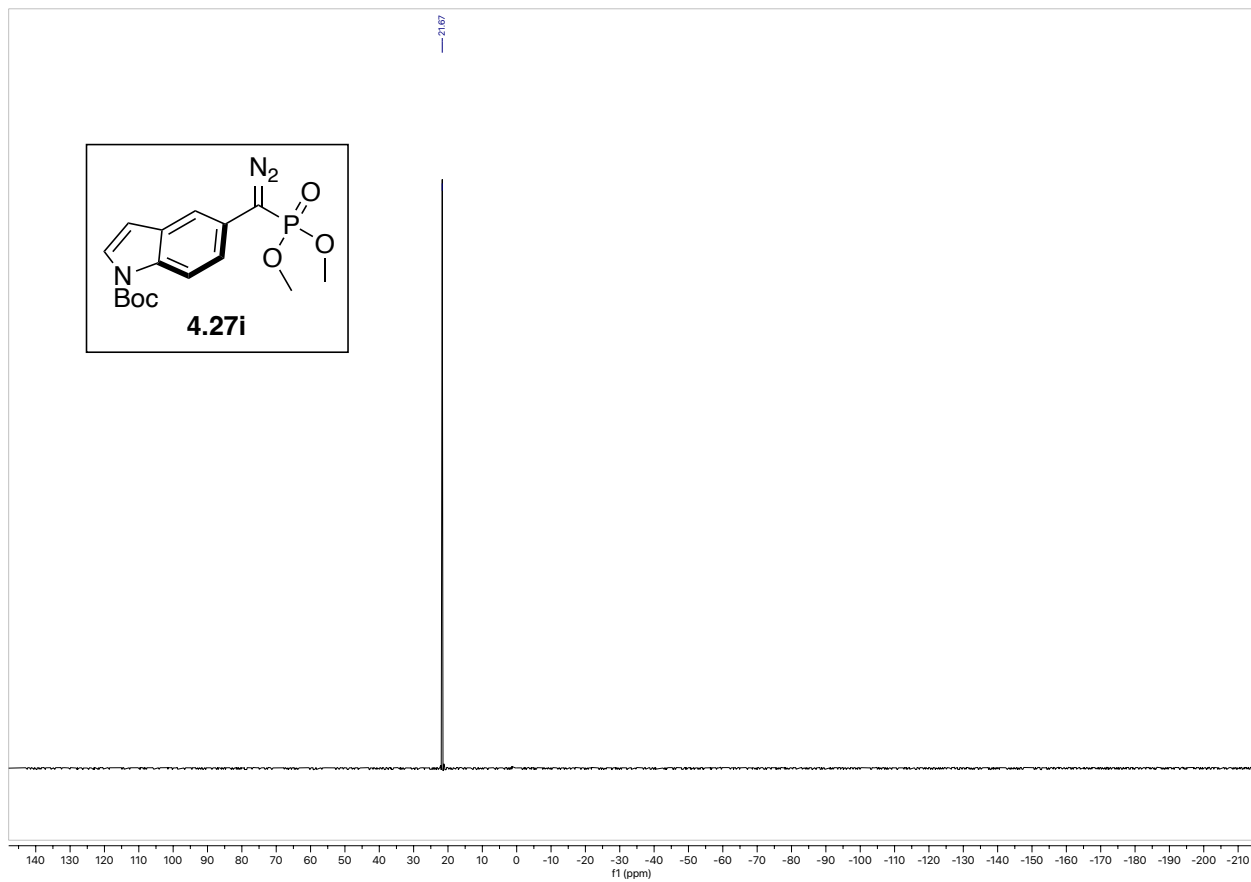
^{31}P NMR spectrum (162 MHz, Chloroform-d) of **4.27h**.



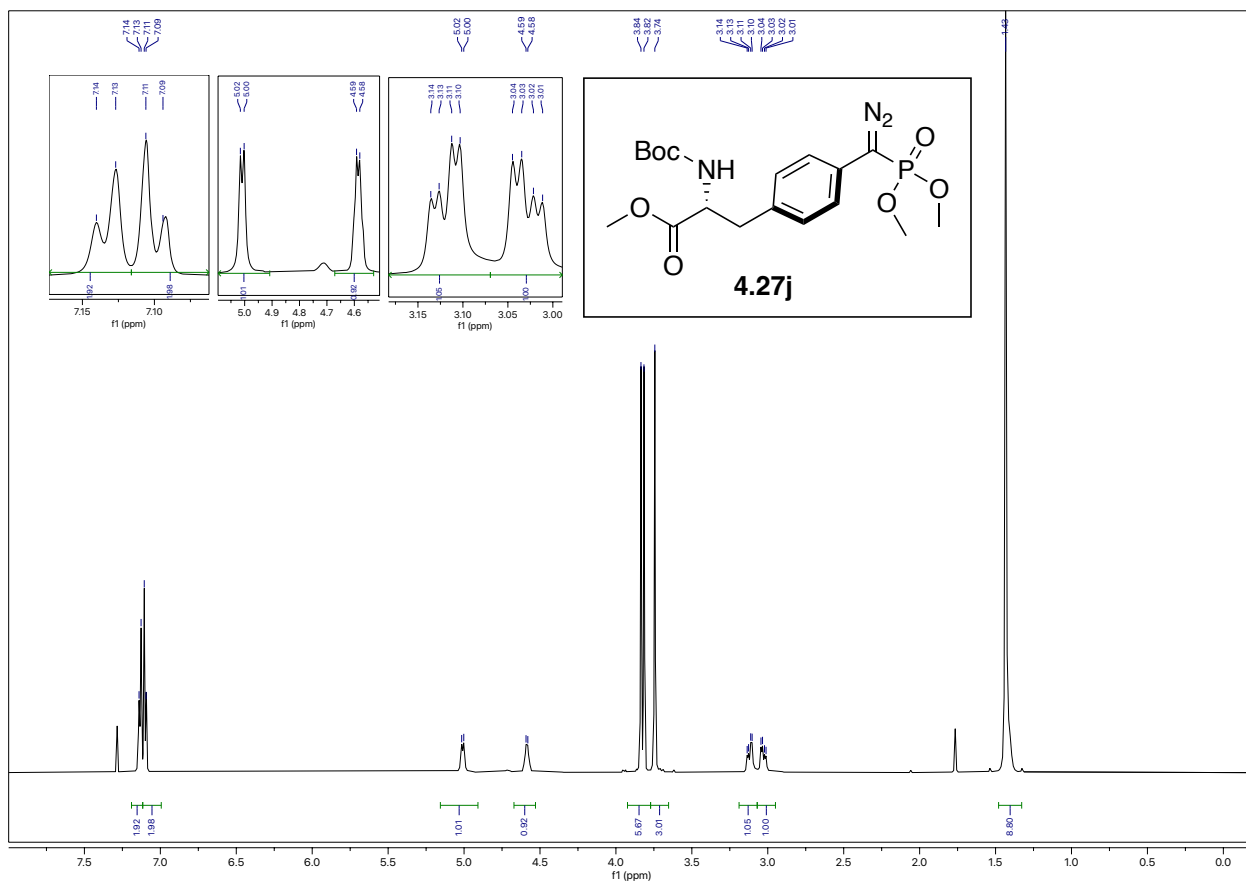
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27i**.

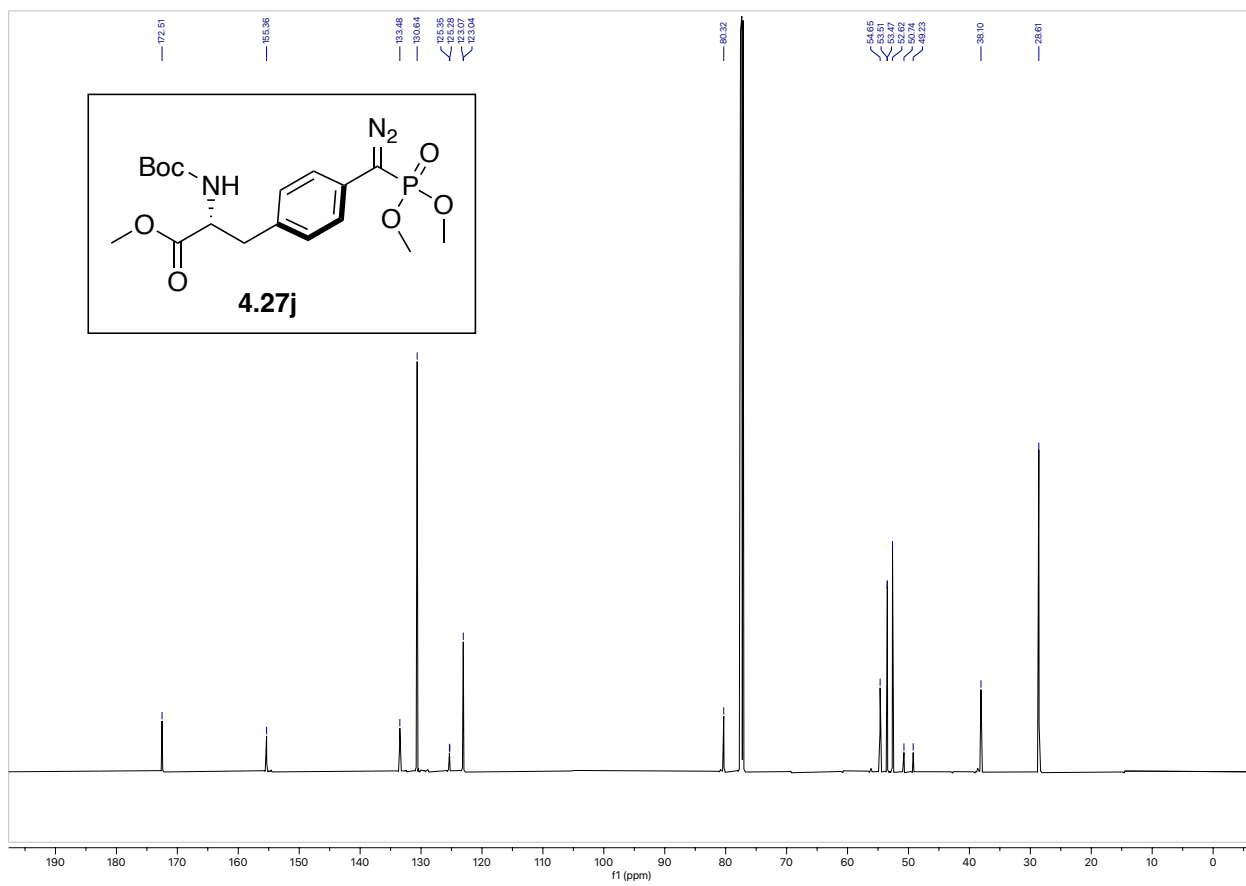


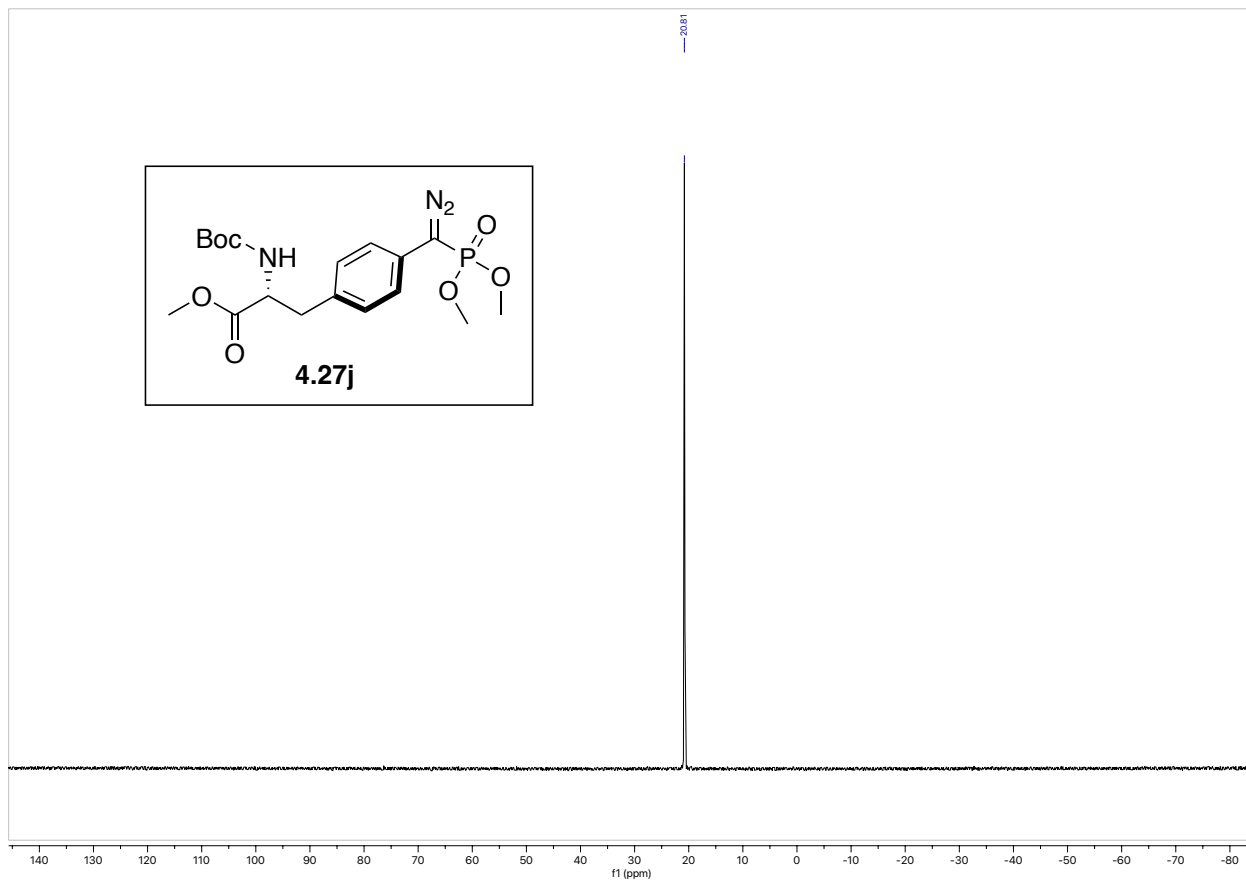
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27i**.



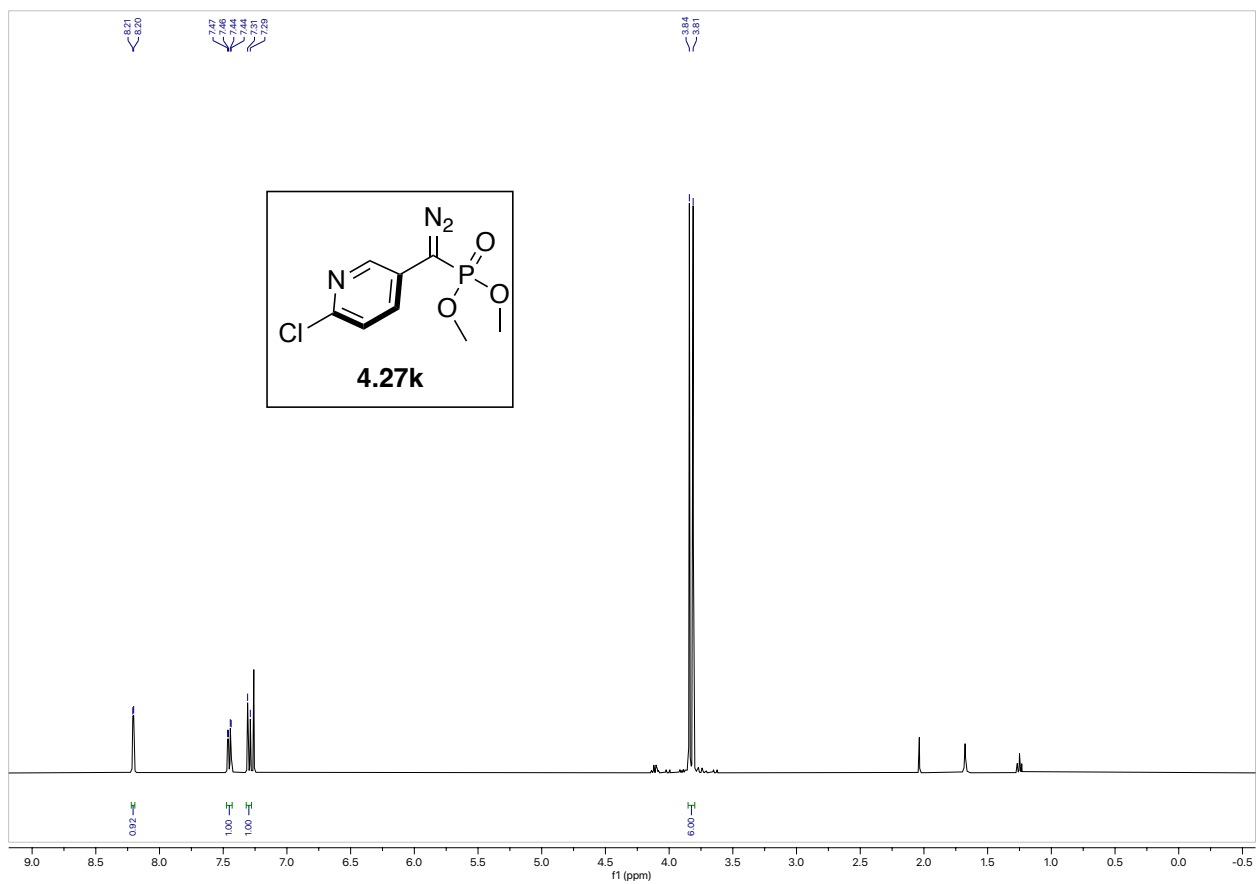
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27i**.



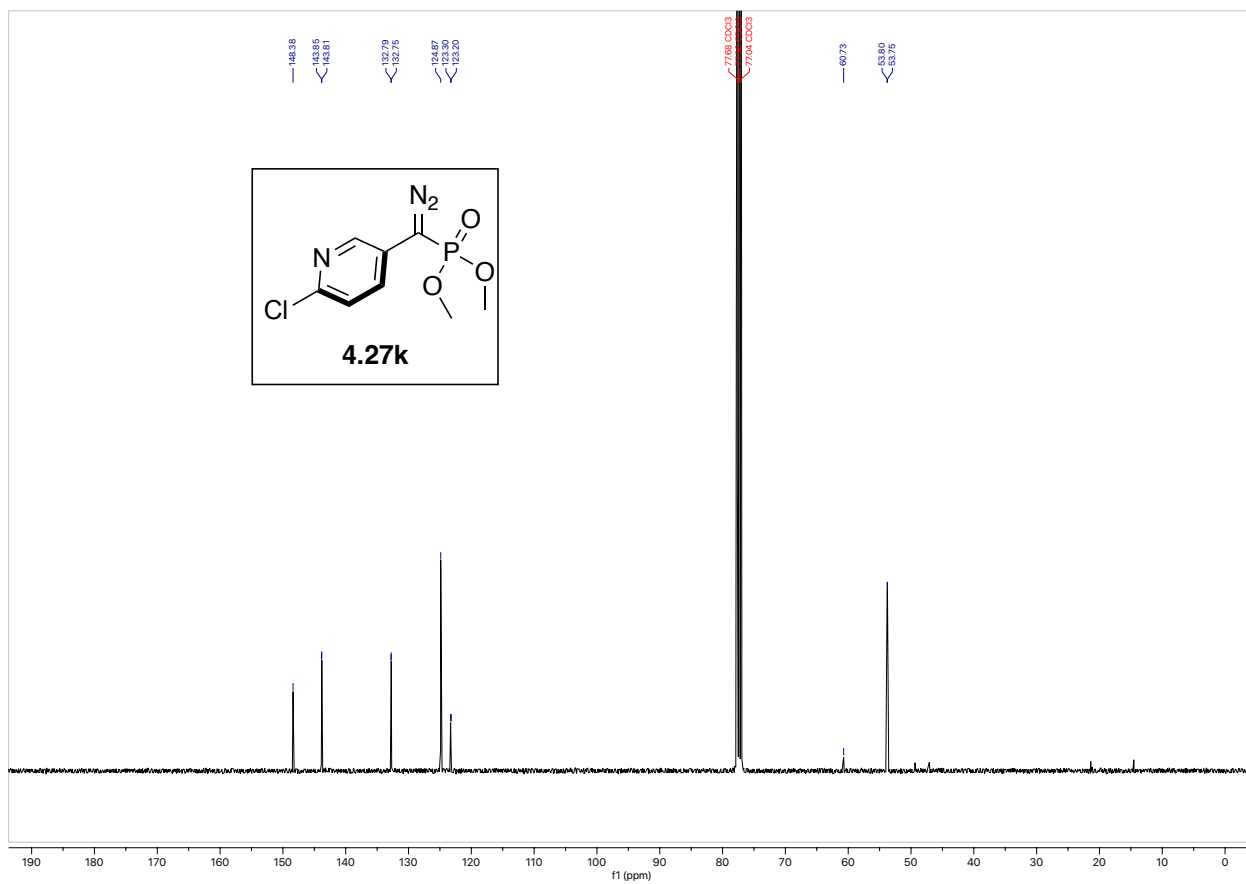




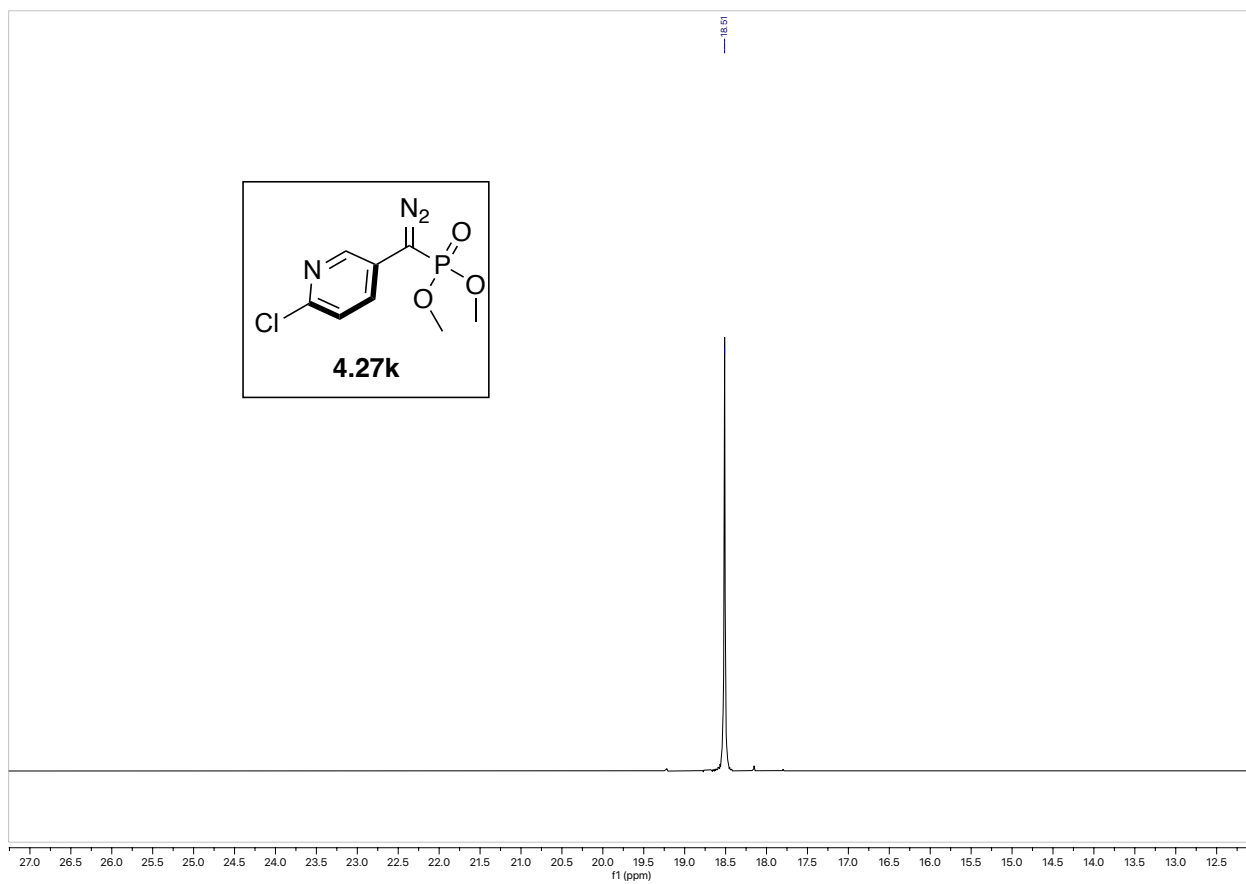
^{31}P NMR spectrum (162 MHz, Chloroform-d) of **4.27j**



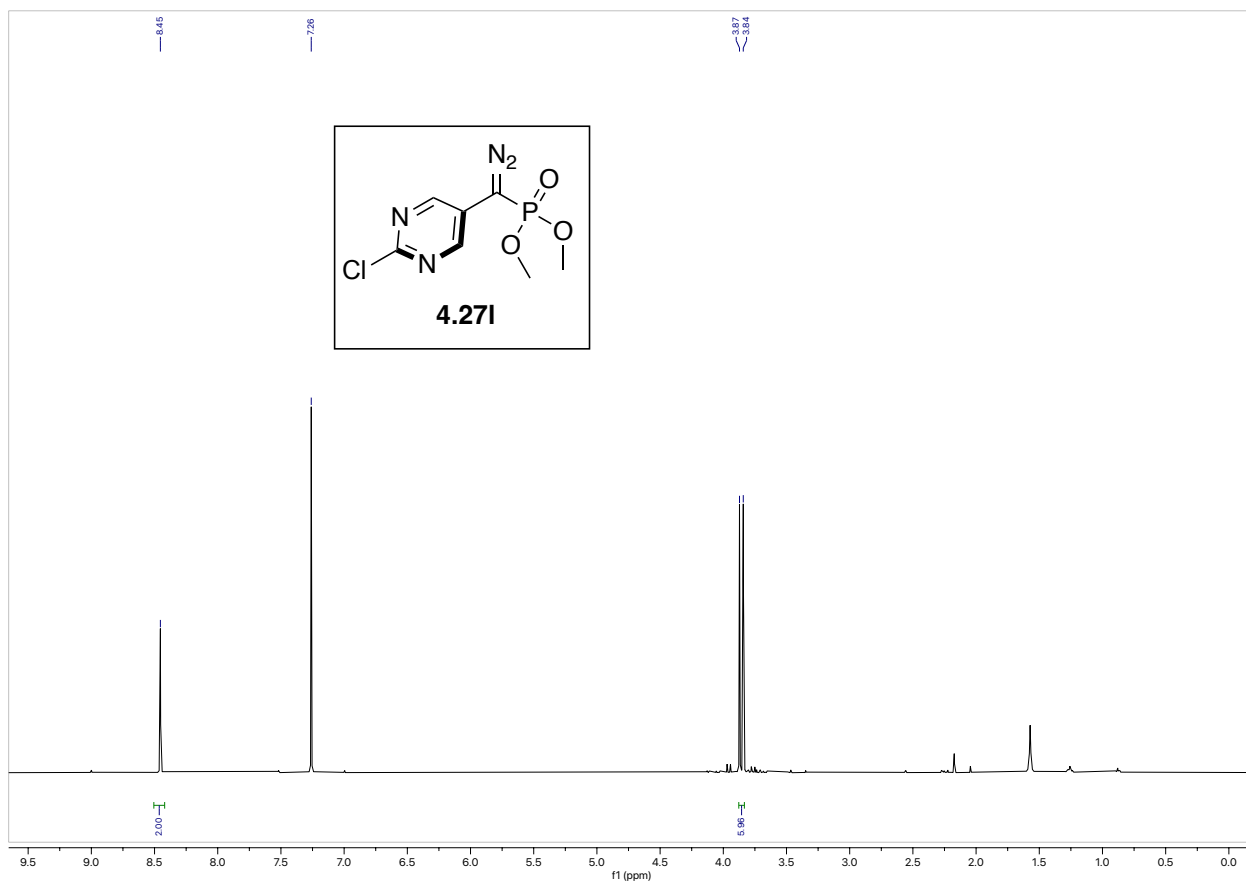
¹H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27k**.



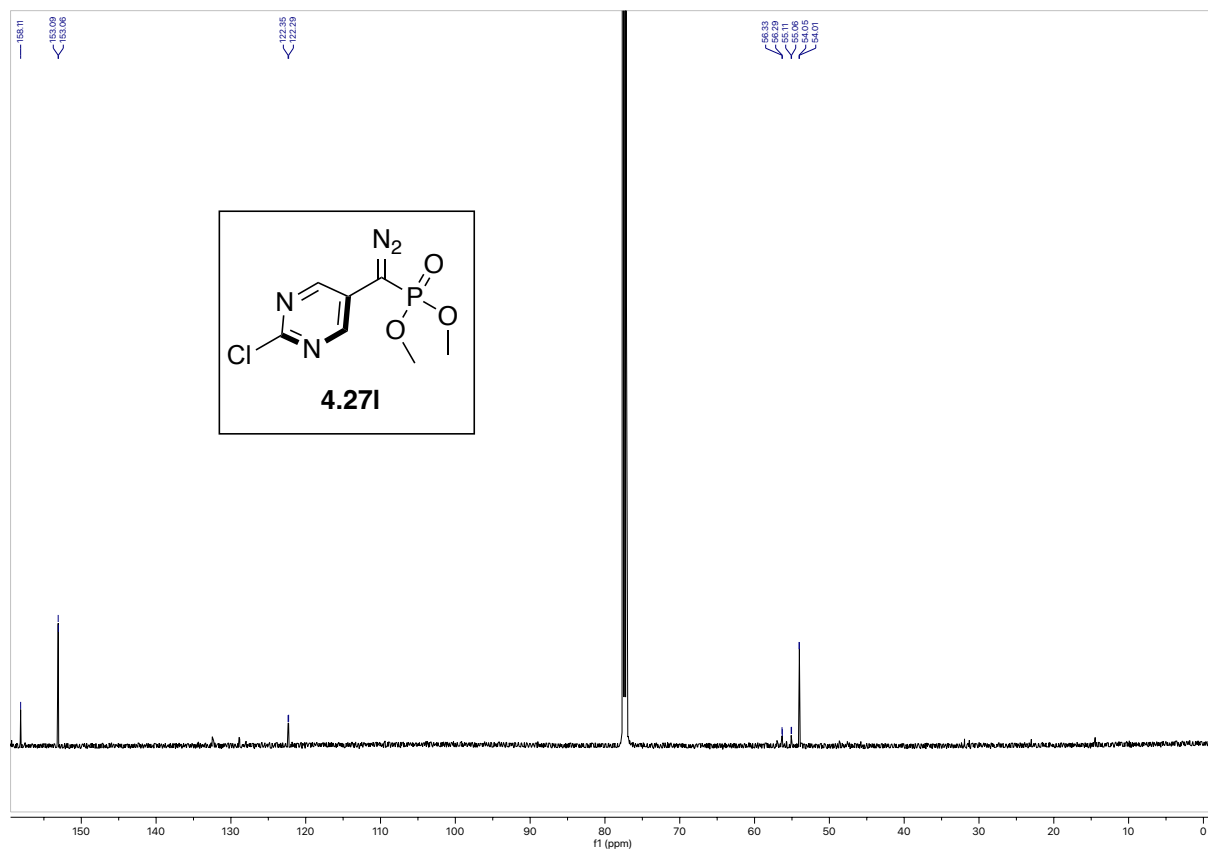
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform- d) (t, 77.36 ppm) of **4.27k**.



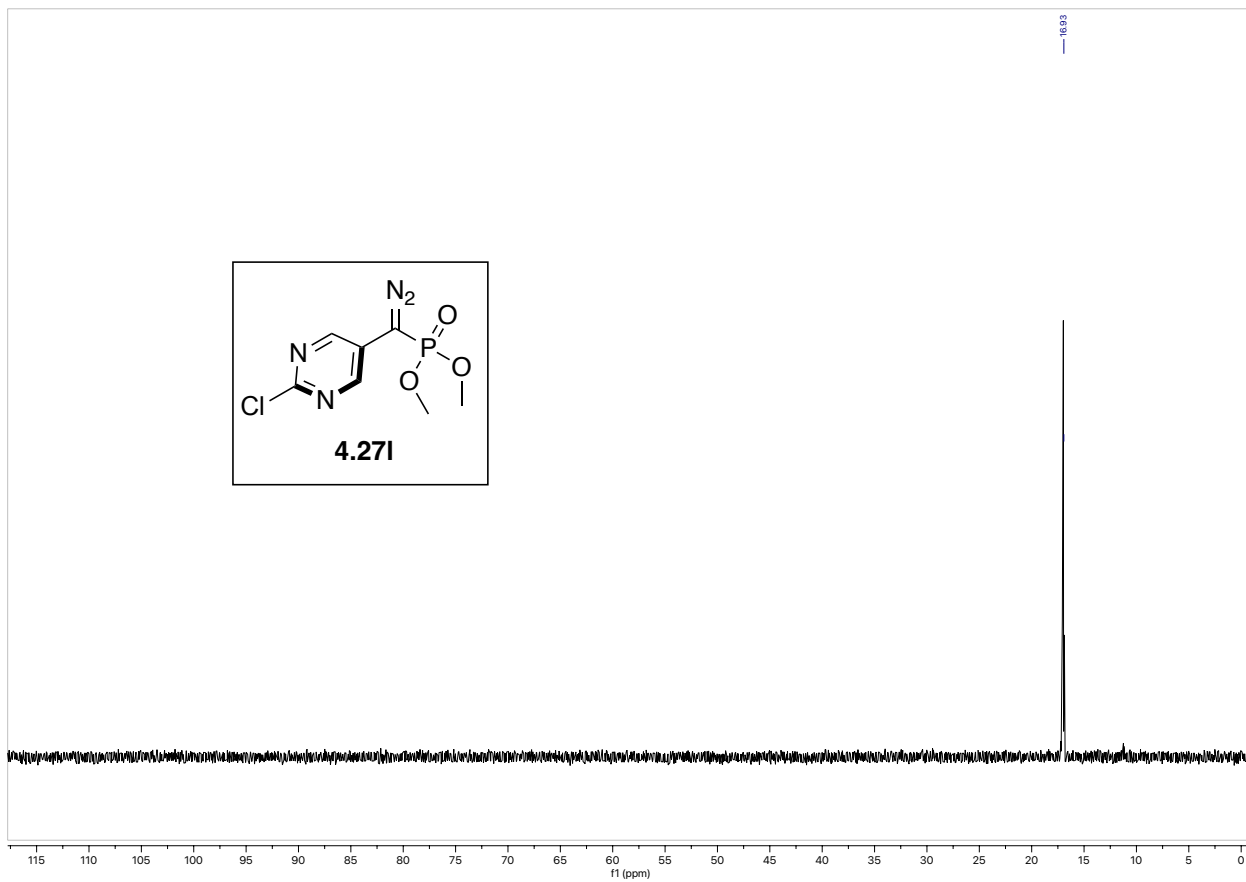
^{31}P NMR spectrum (162 MHz, Chloroform-d) of **4.27k**.



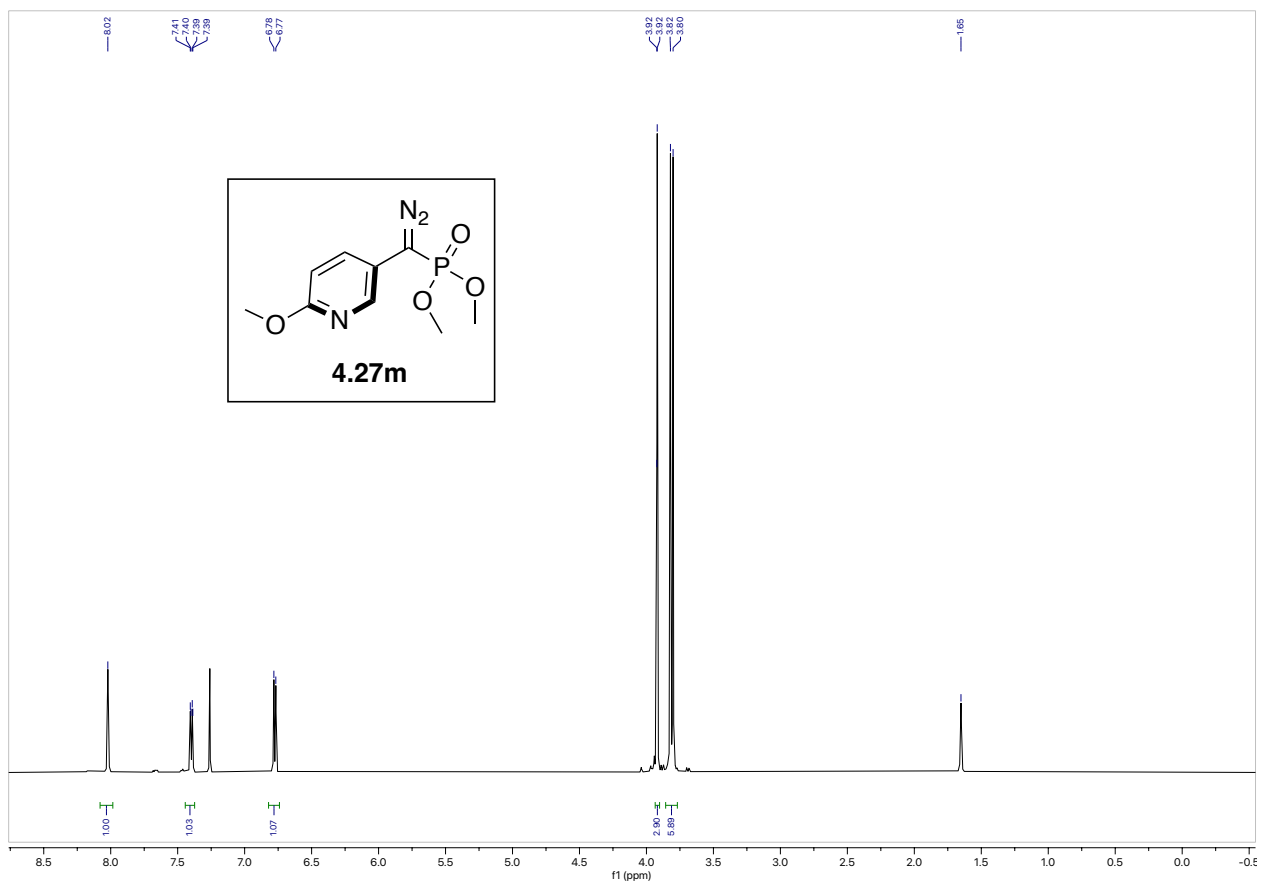
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27I**.



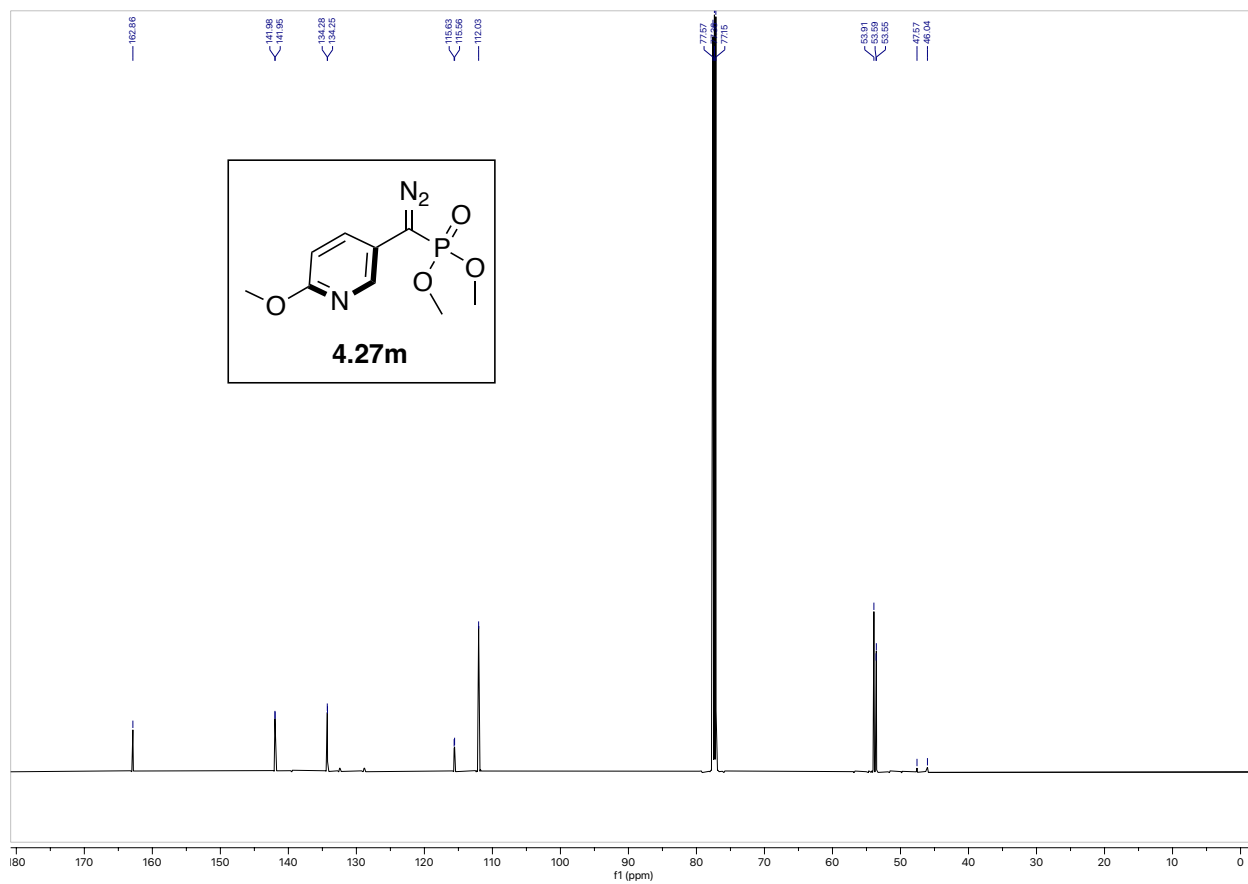
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27l**.



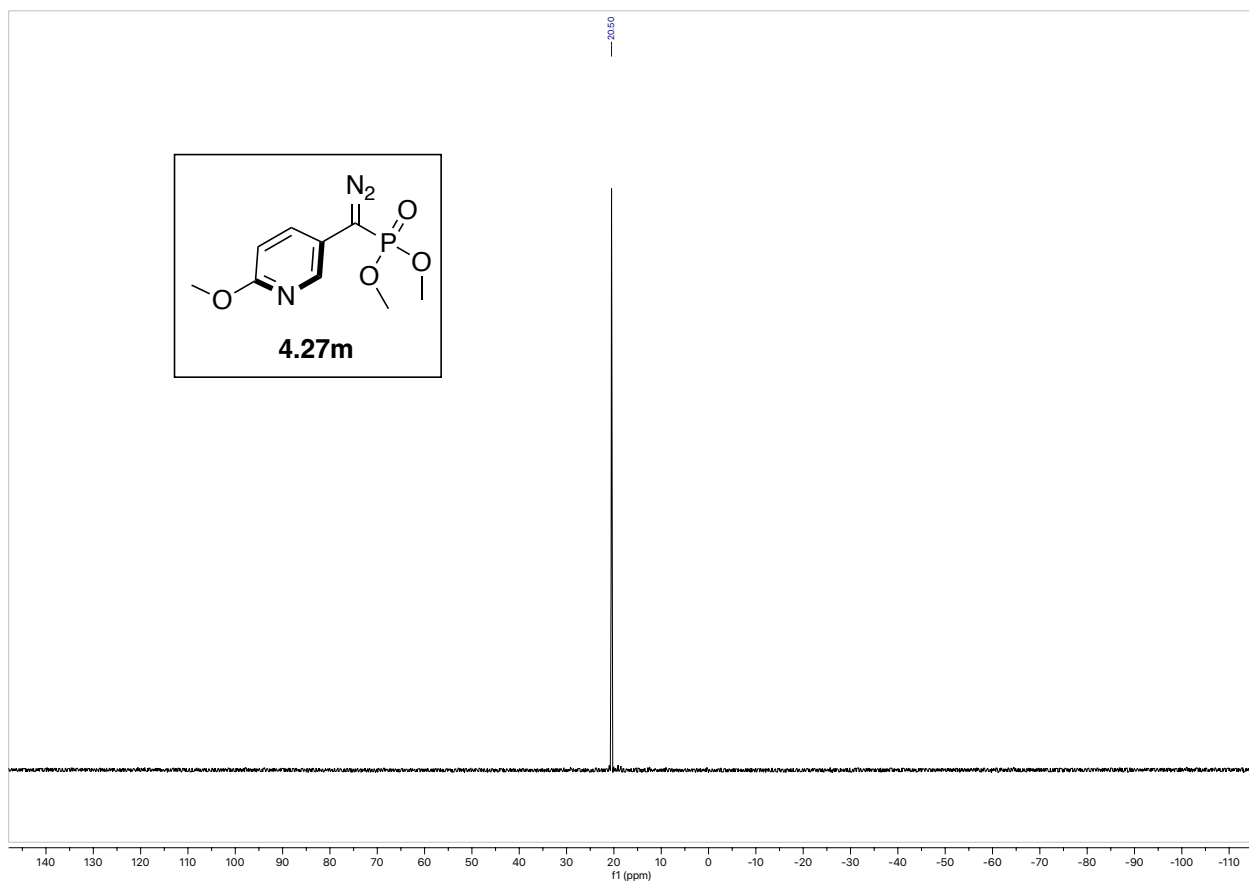
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27l**.



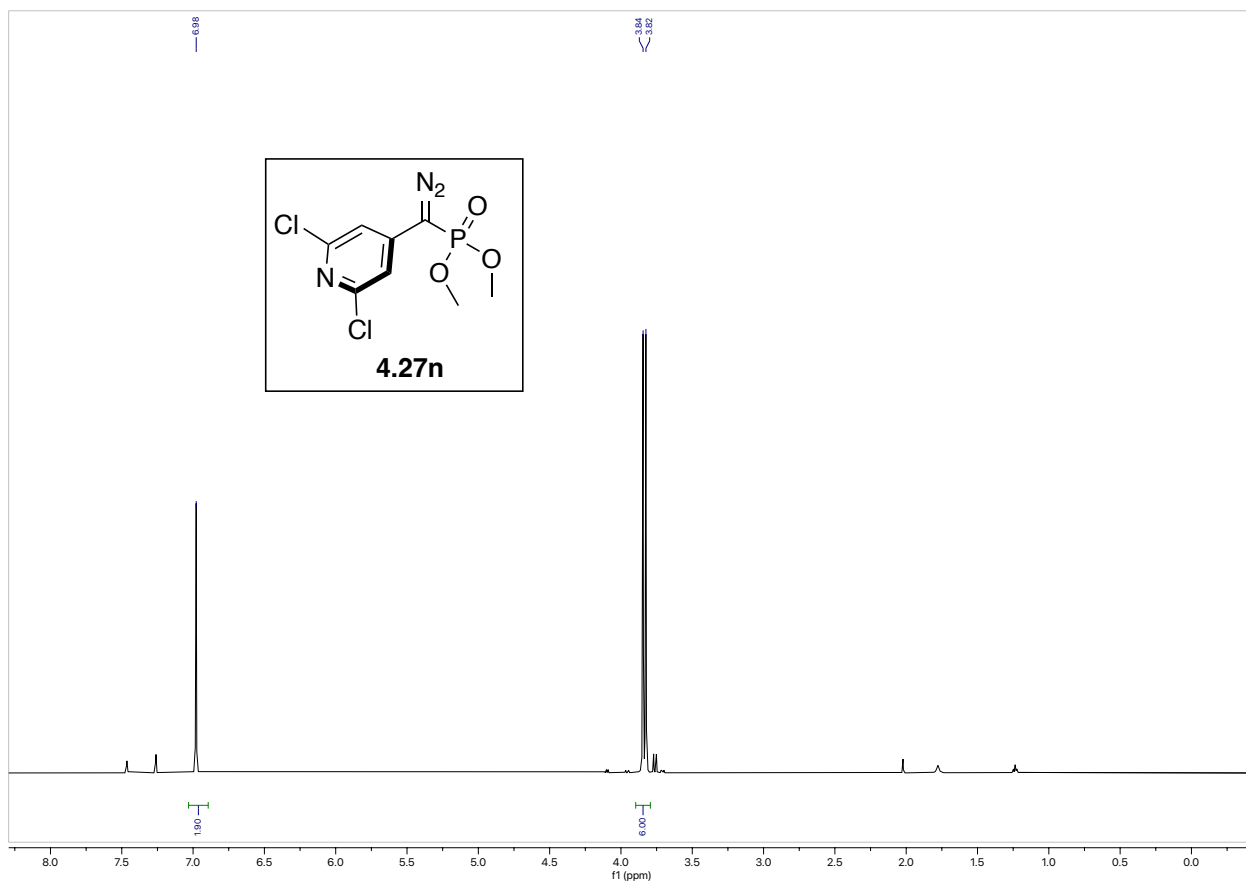
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27m**.



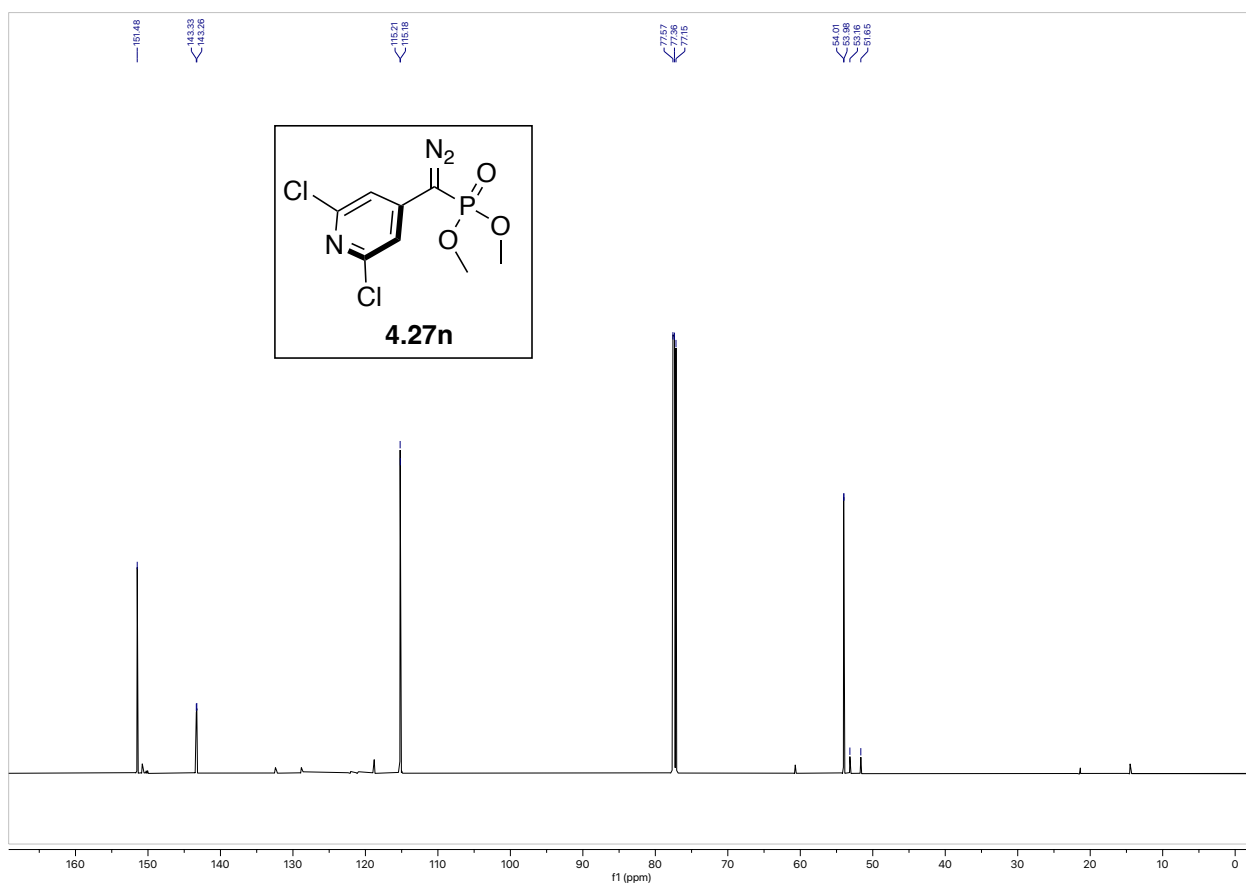
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27m**.



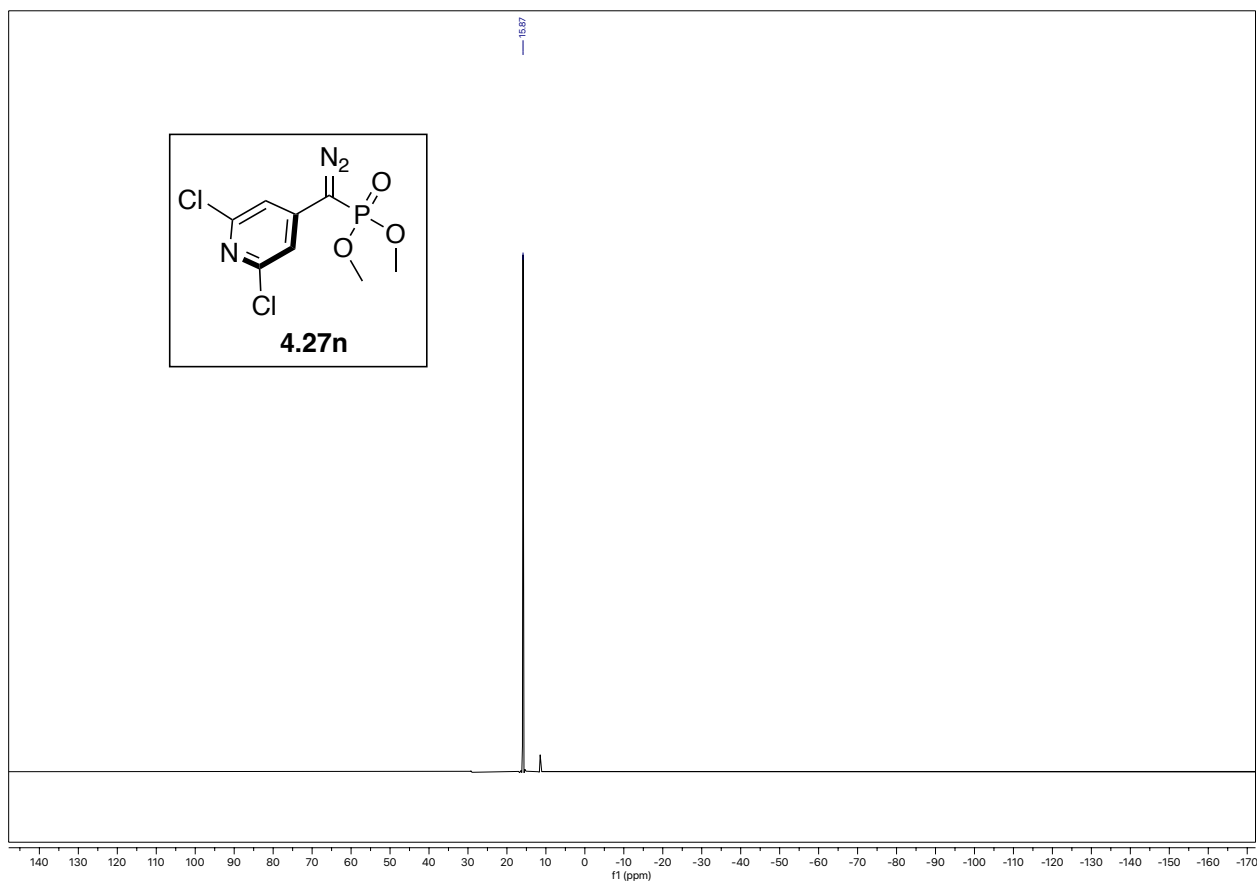
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27m**.



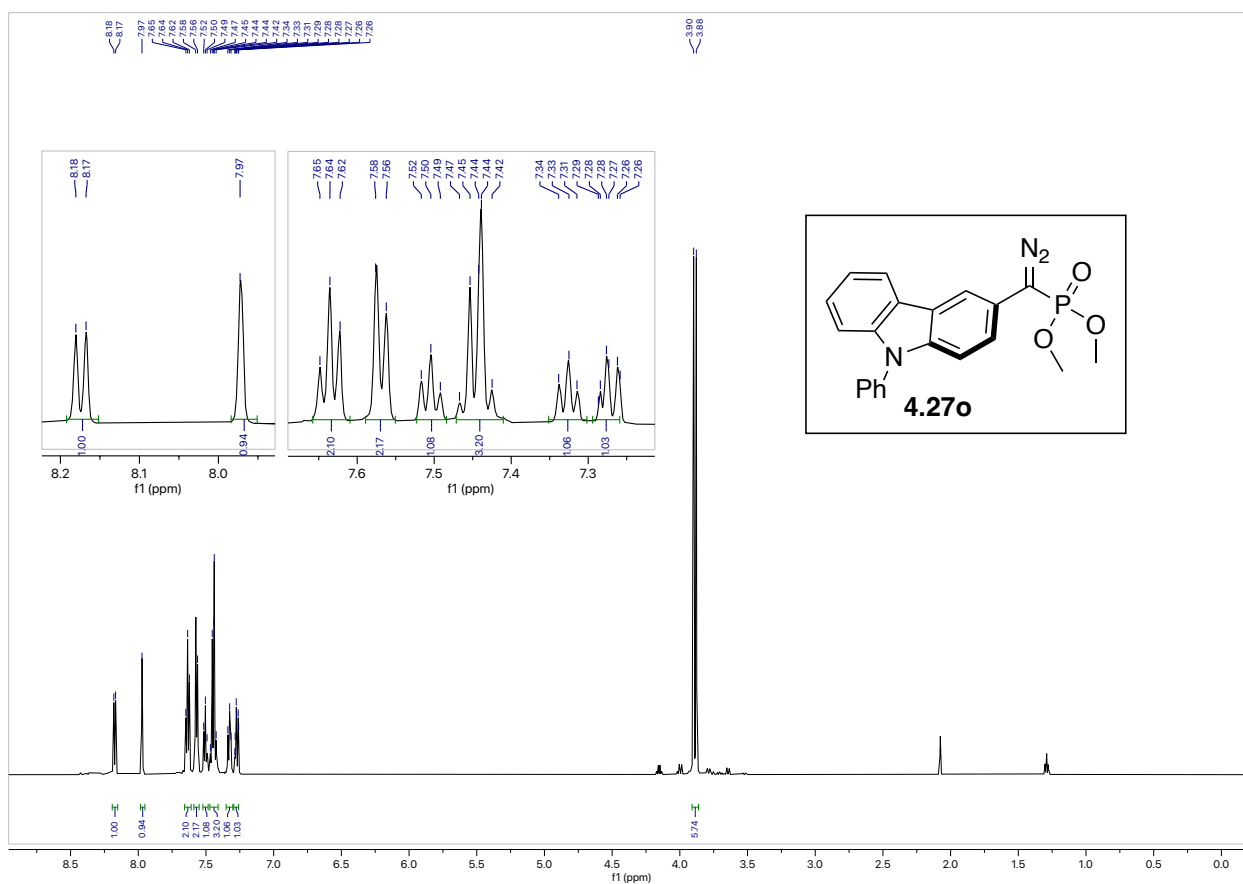
^1H NMR spectrum (600 MHz, CHCl_3) (s, 7.26 ppm) of **4.27n**.



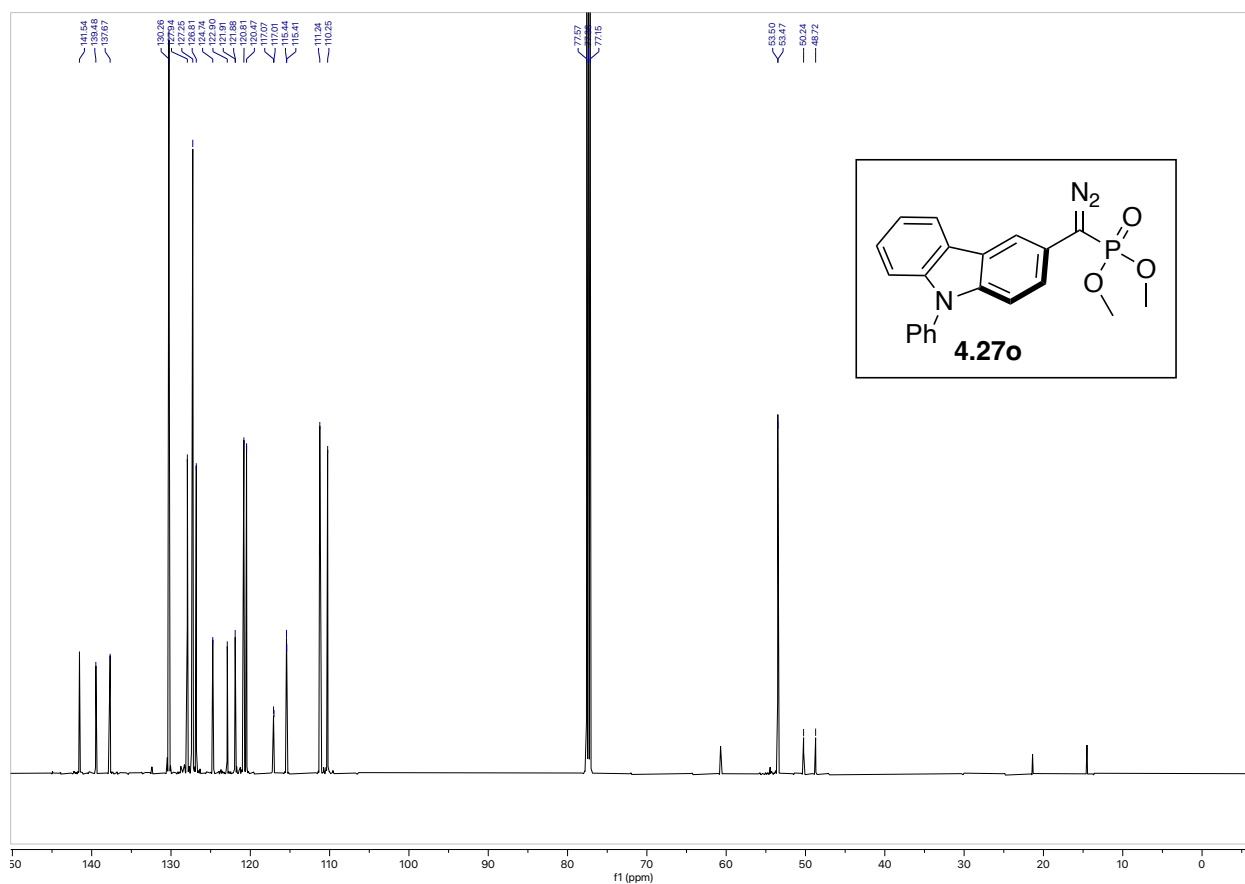
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27n**.



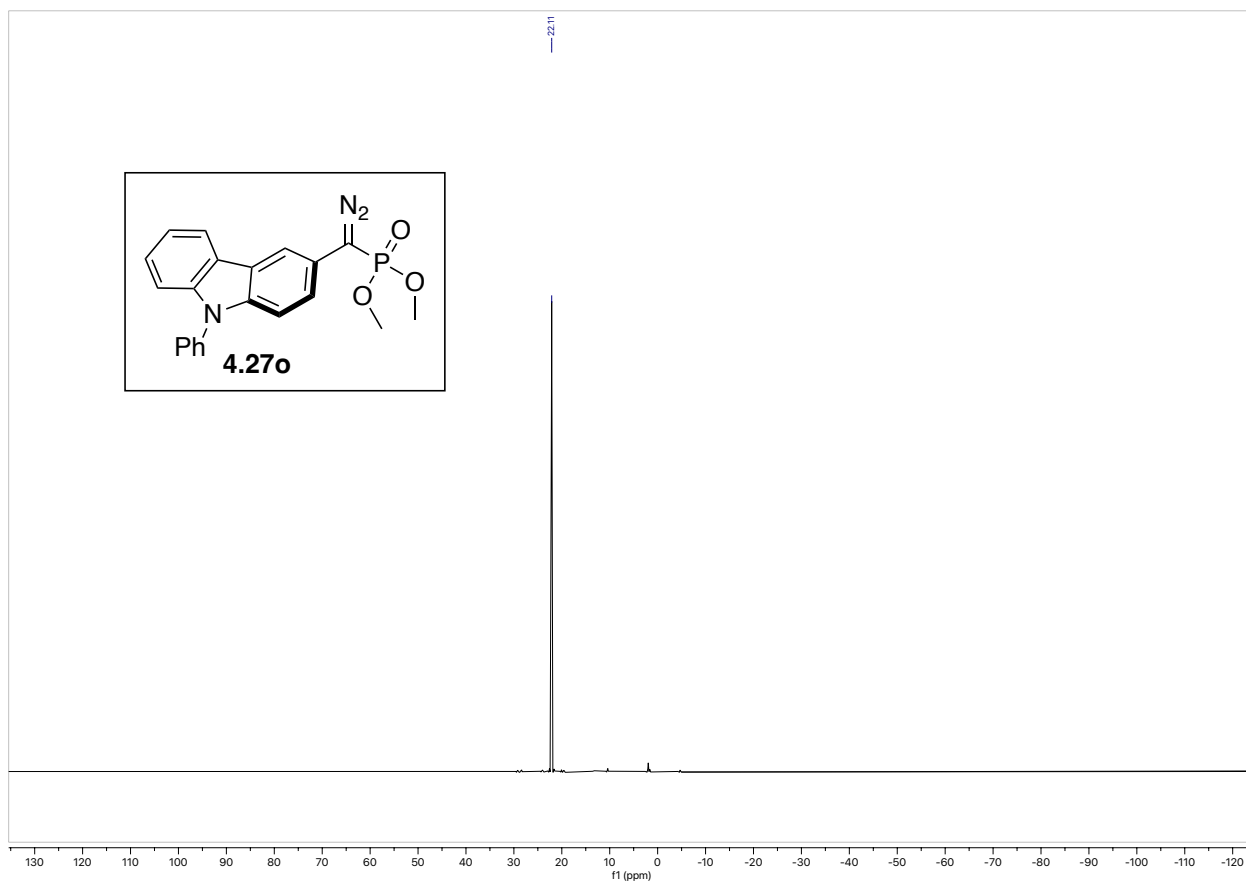
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27n**.



^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.27o**.

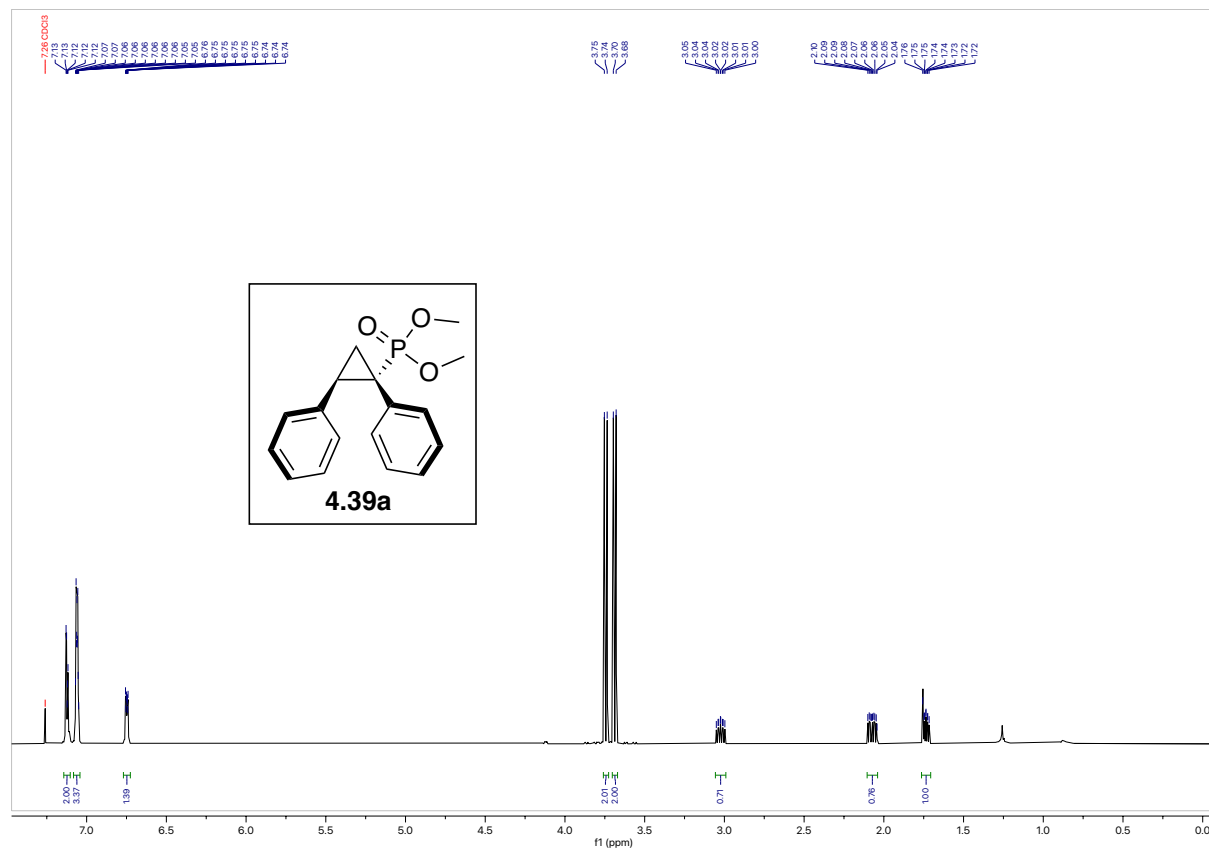


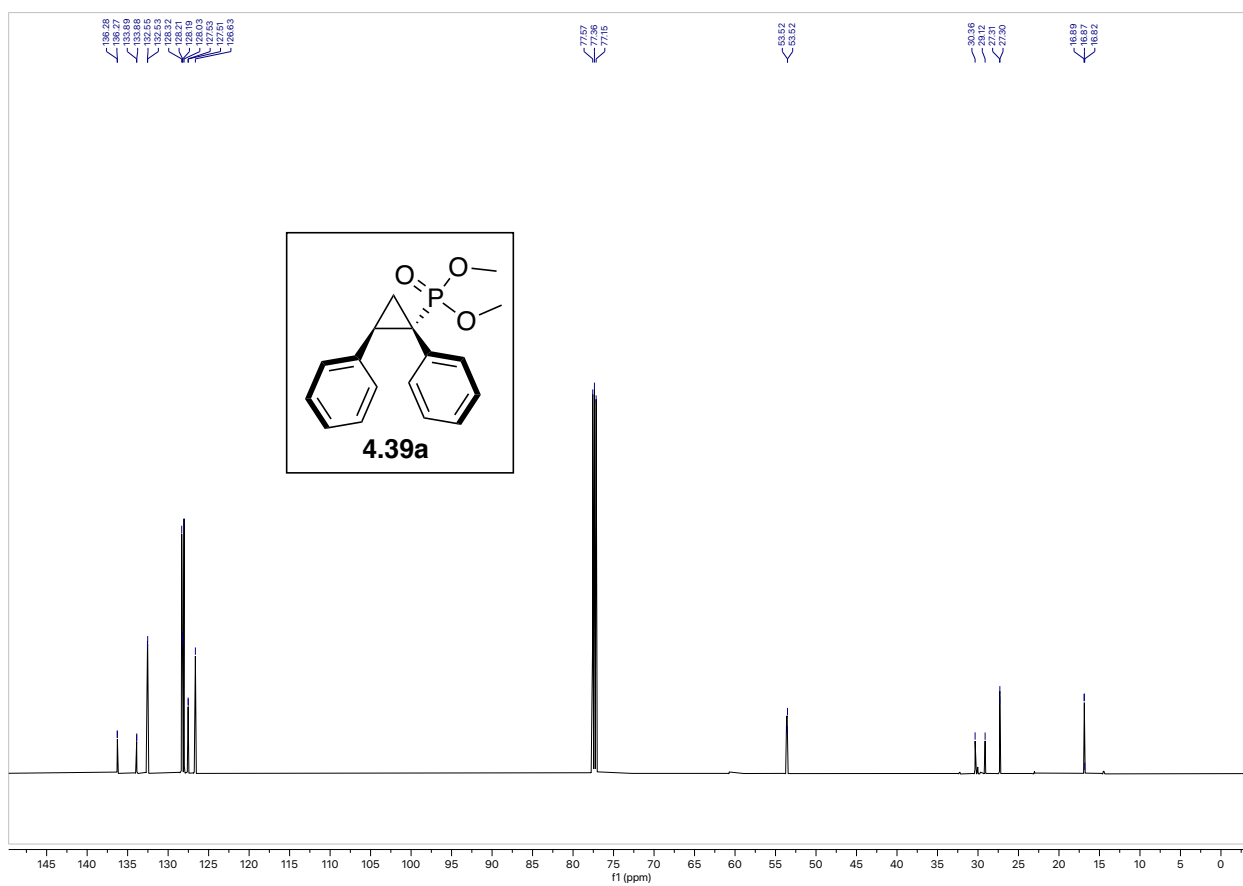
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.27o**.



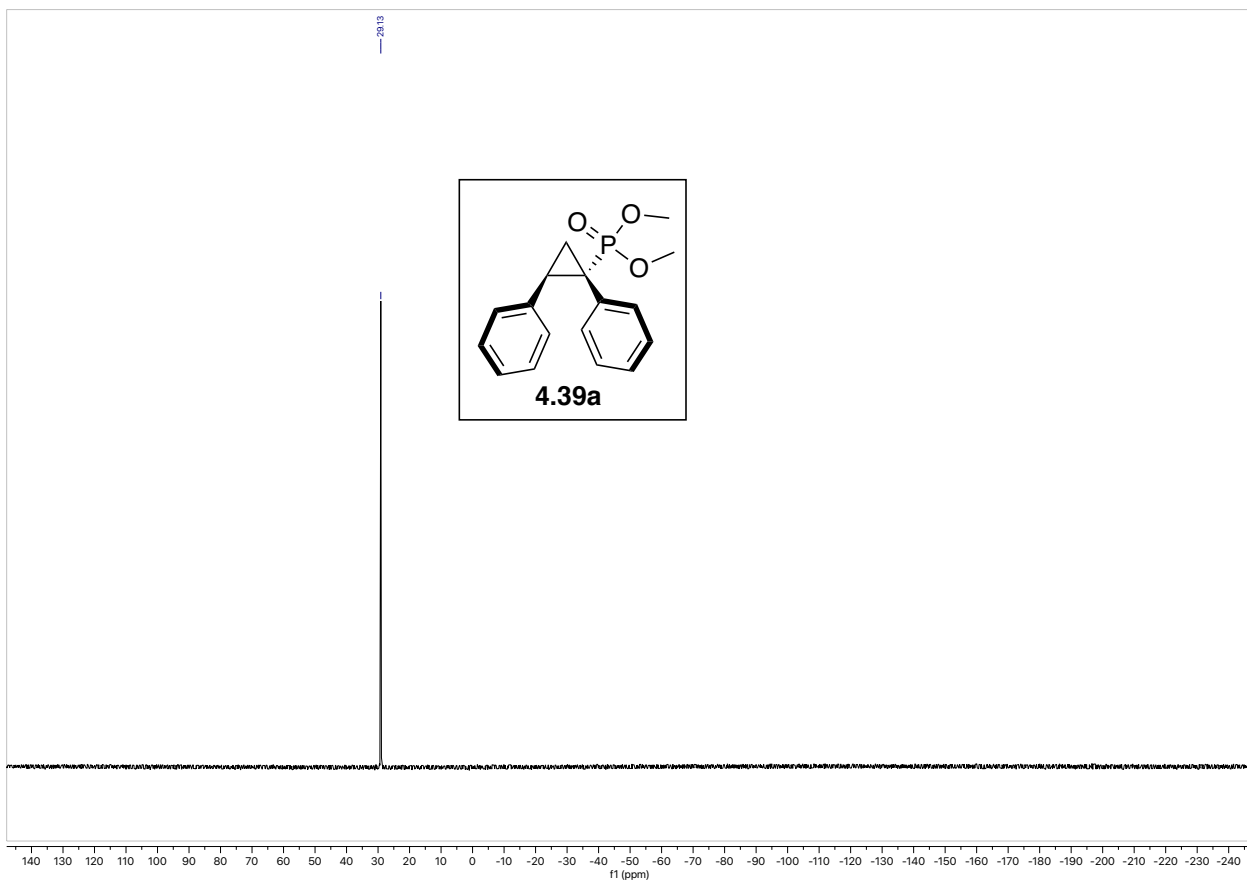
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.27o**.

Cyclopropanation ^1H NMR, ^{13}C NMR, ^{19}F NMR, and ^{31}P NMR Spectroscopic Data.

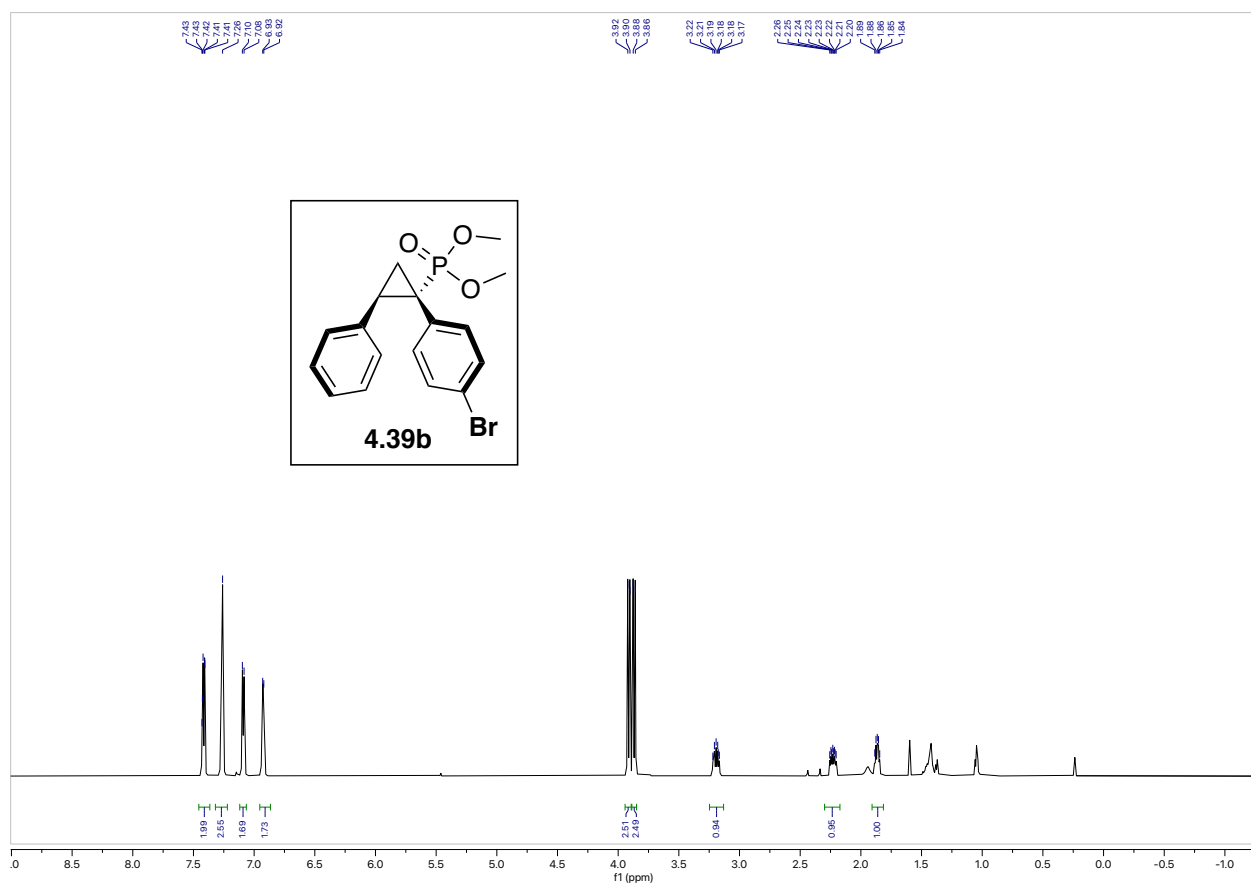




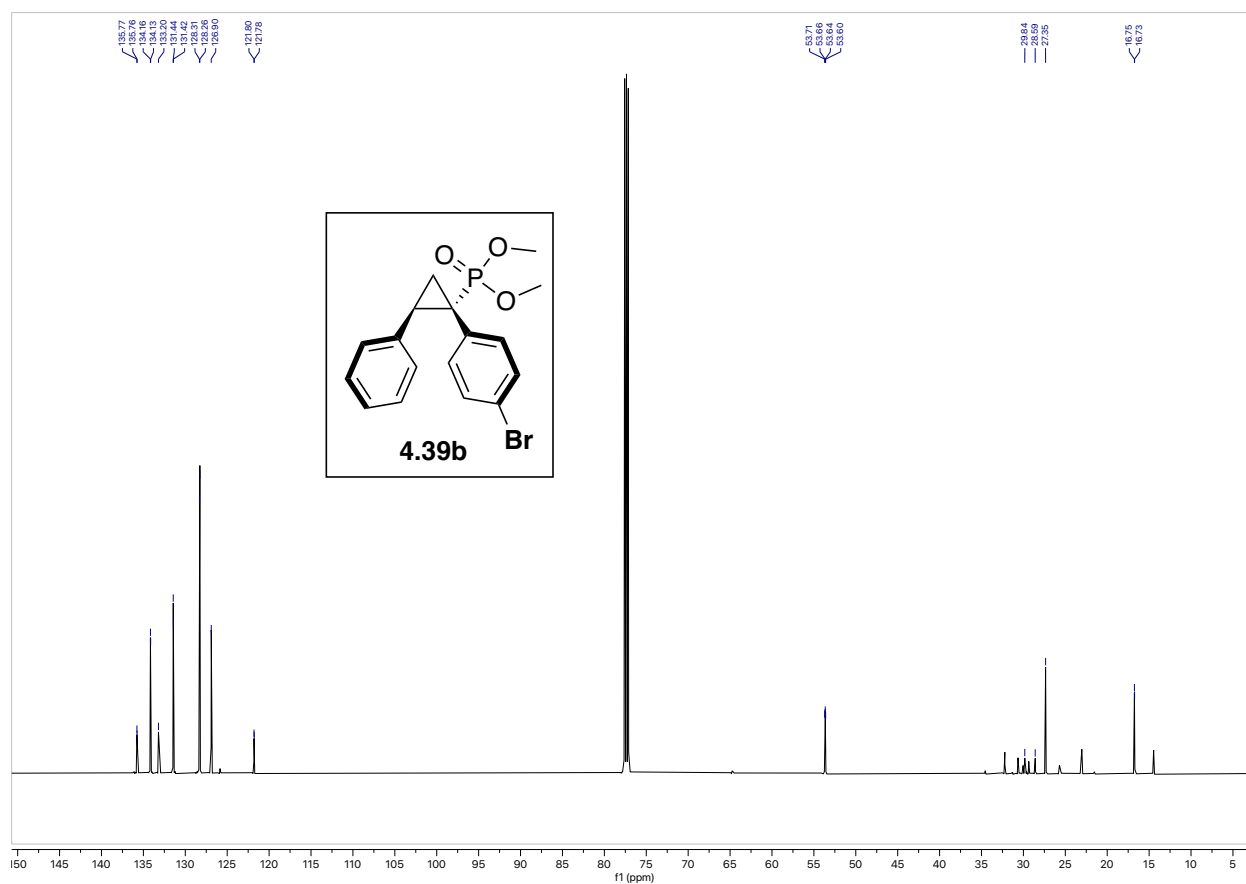
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39a**.



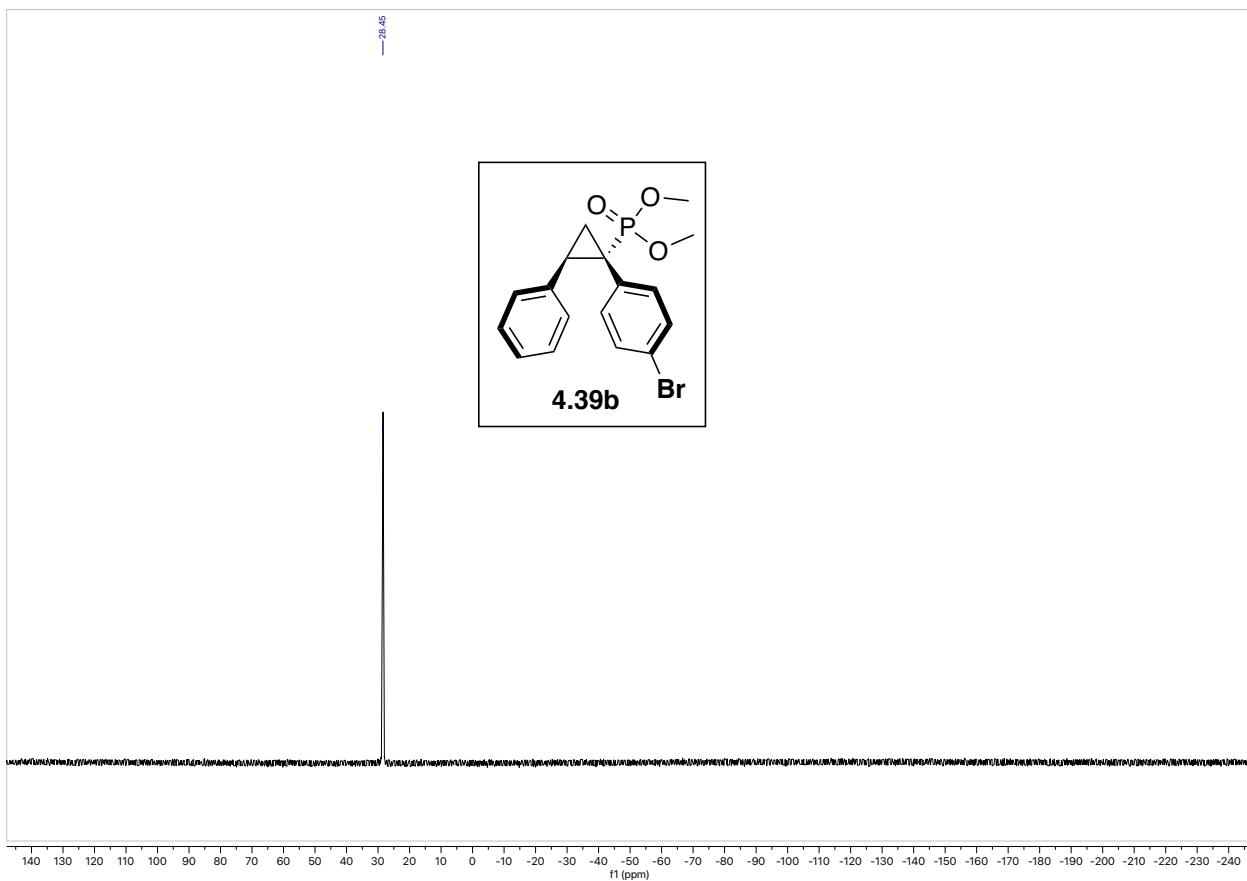
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39a**.



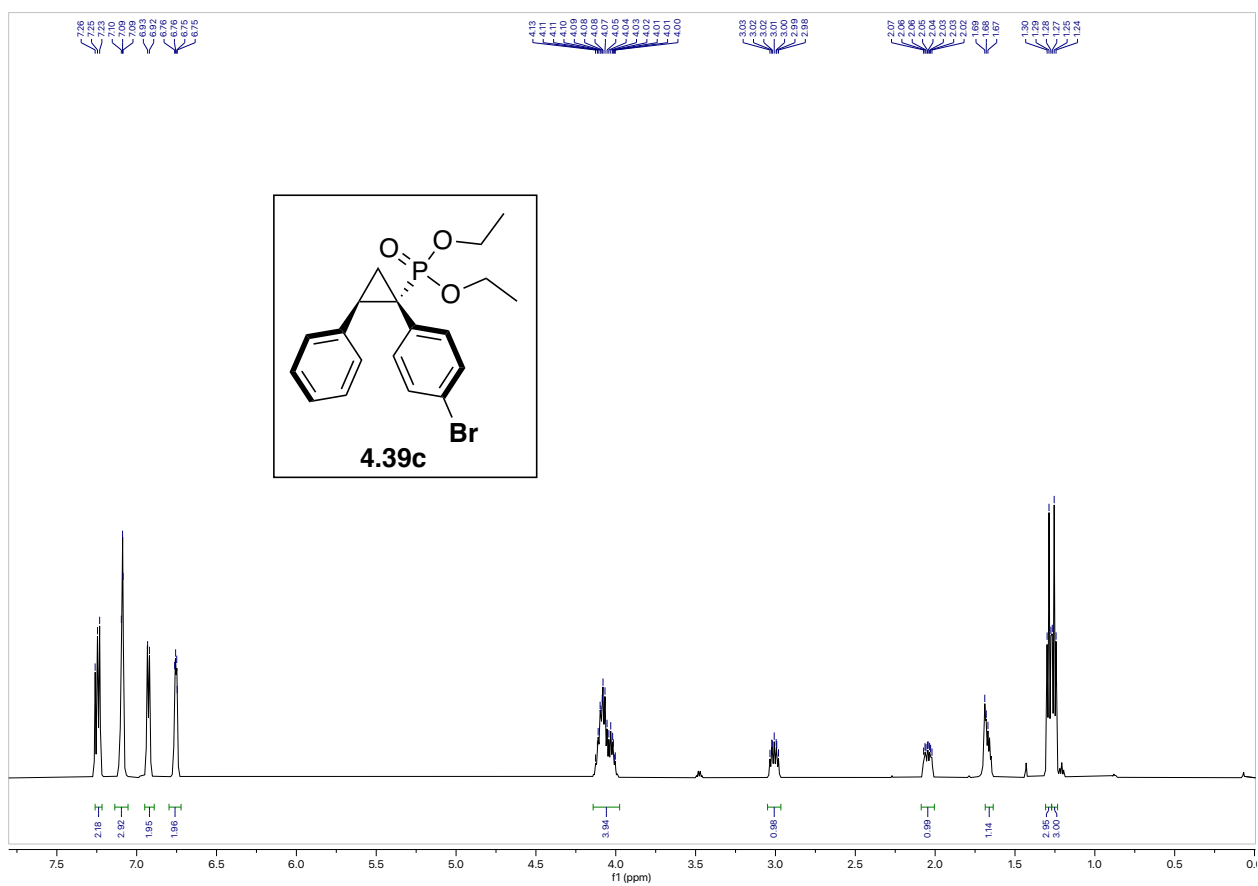
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39b**.

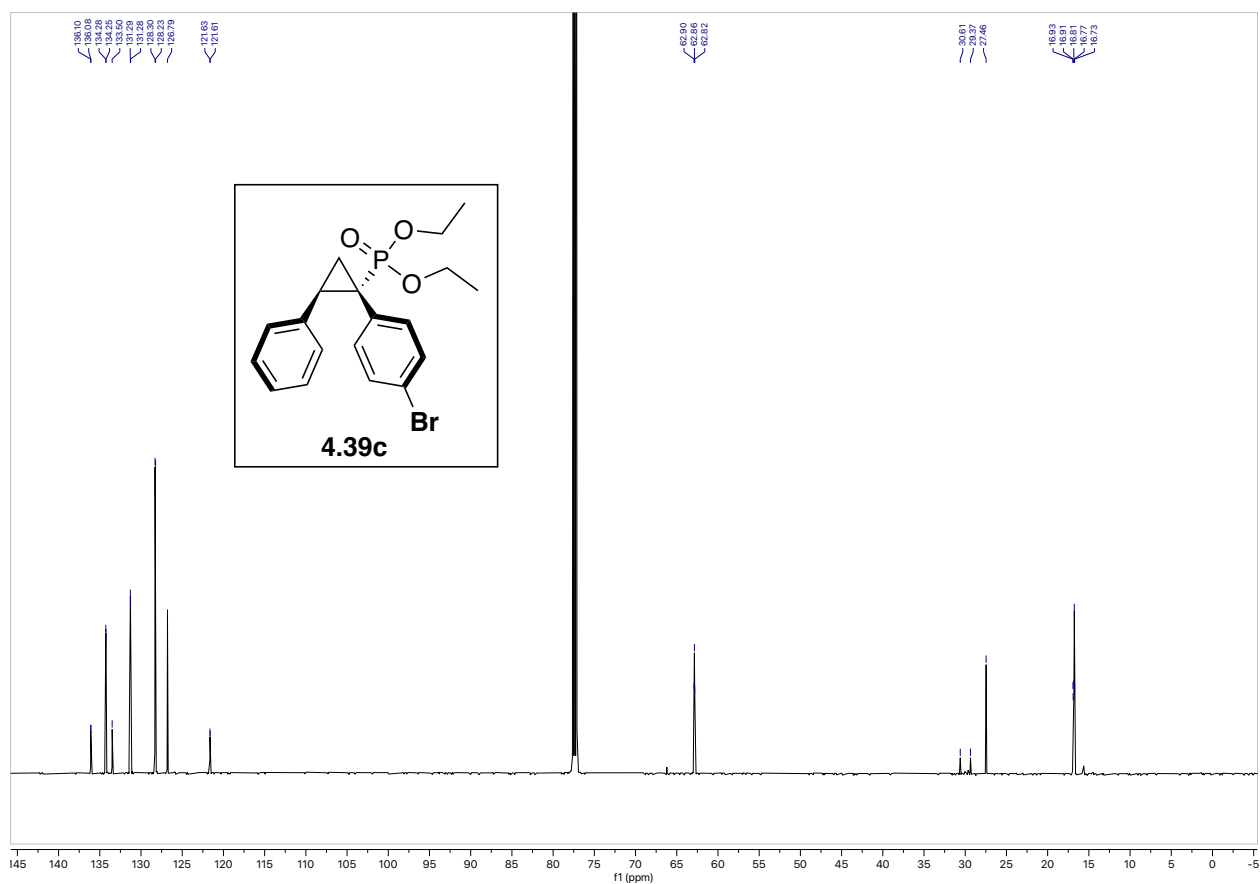


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39b**.

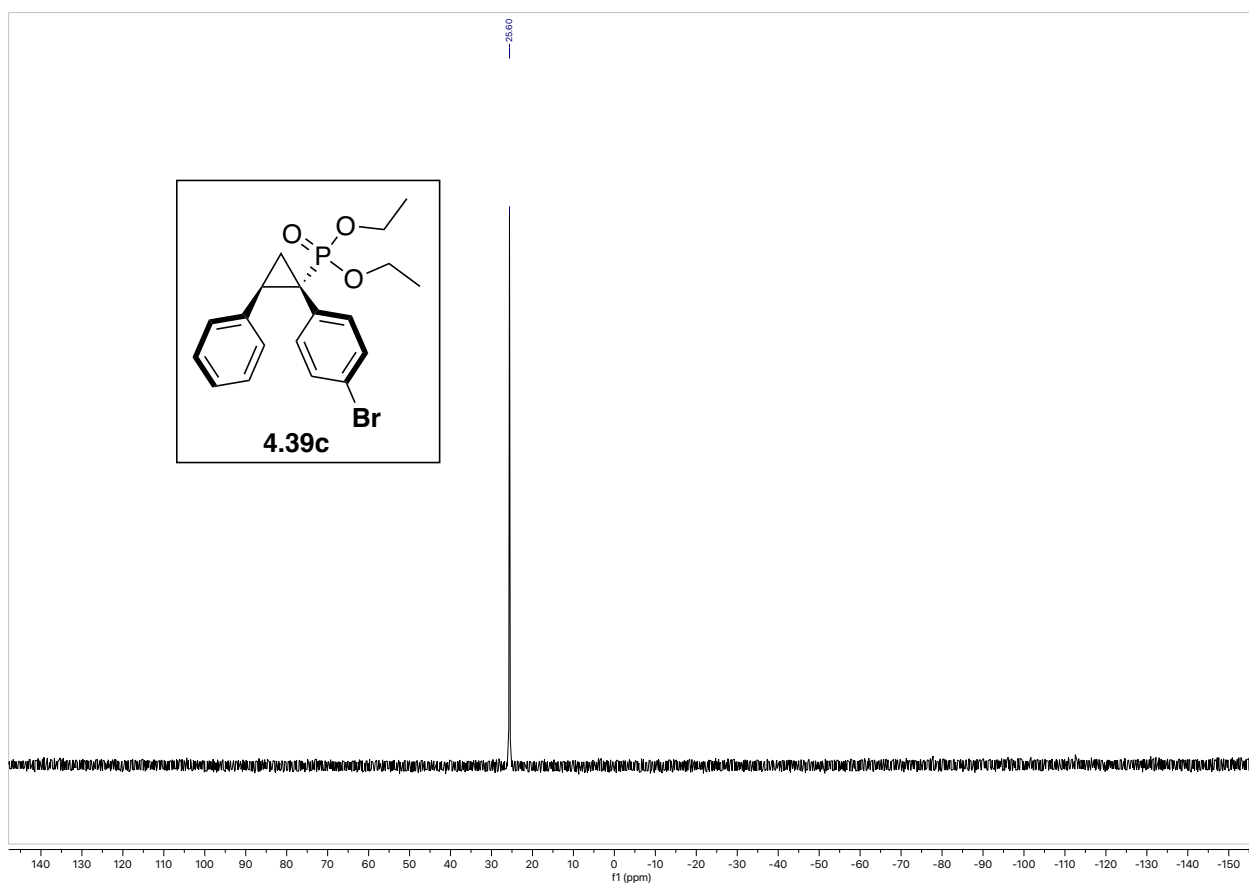


^{31}P NMR spectrum (243 MHz, Chloroform- d) of **4.39b**.

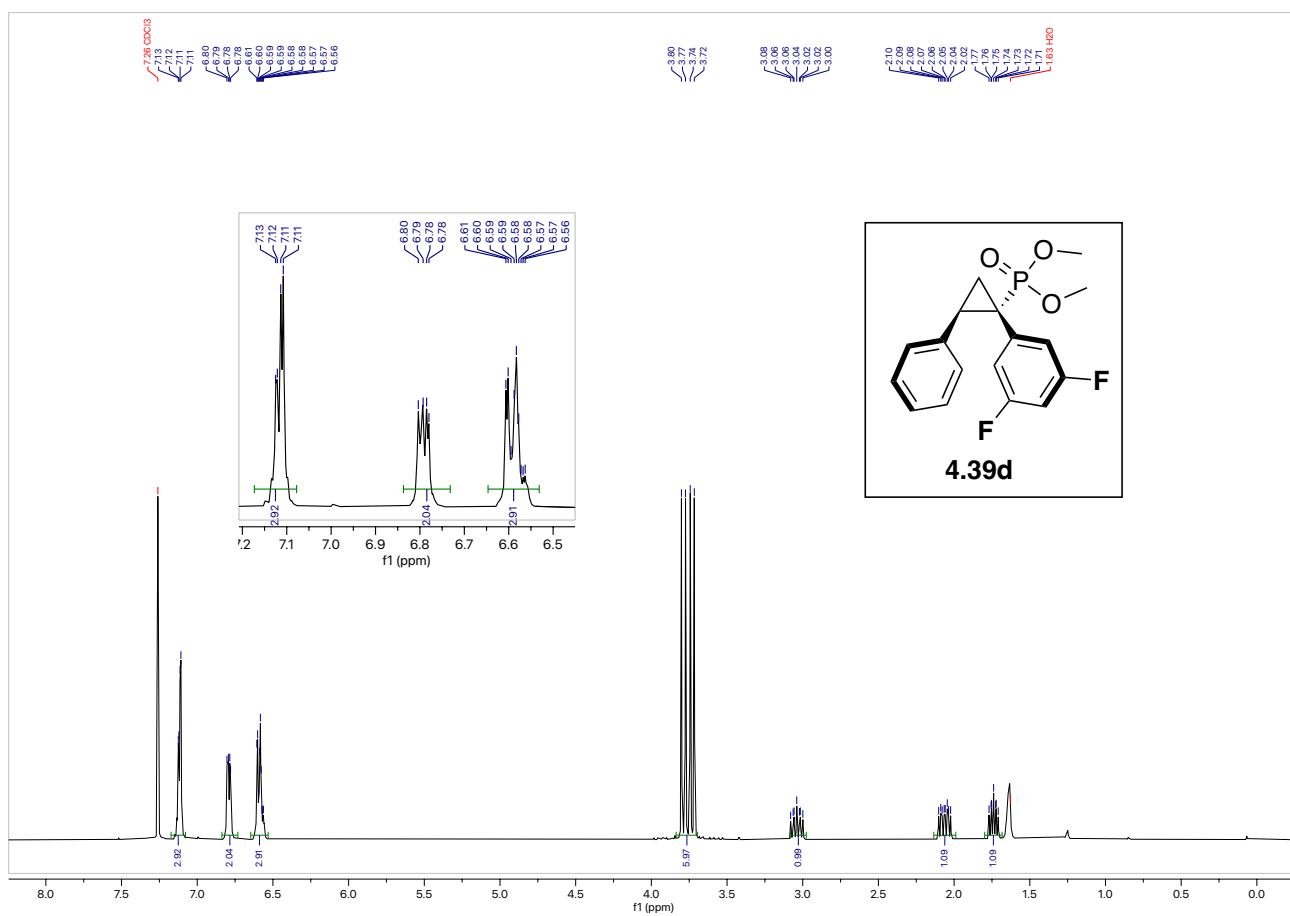




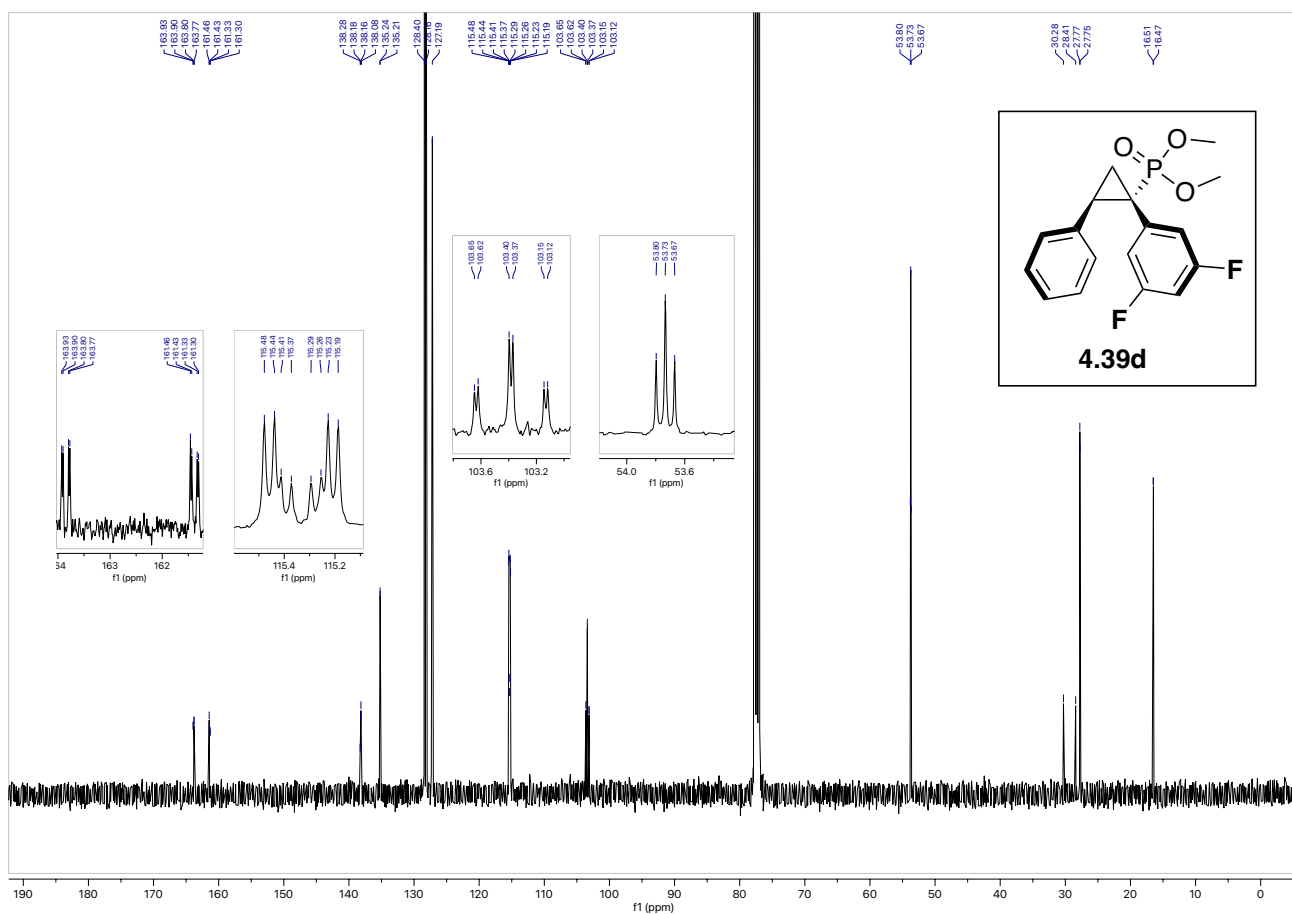
¹³C{¹H} NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39c**.



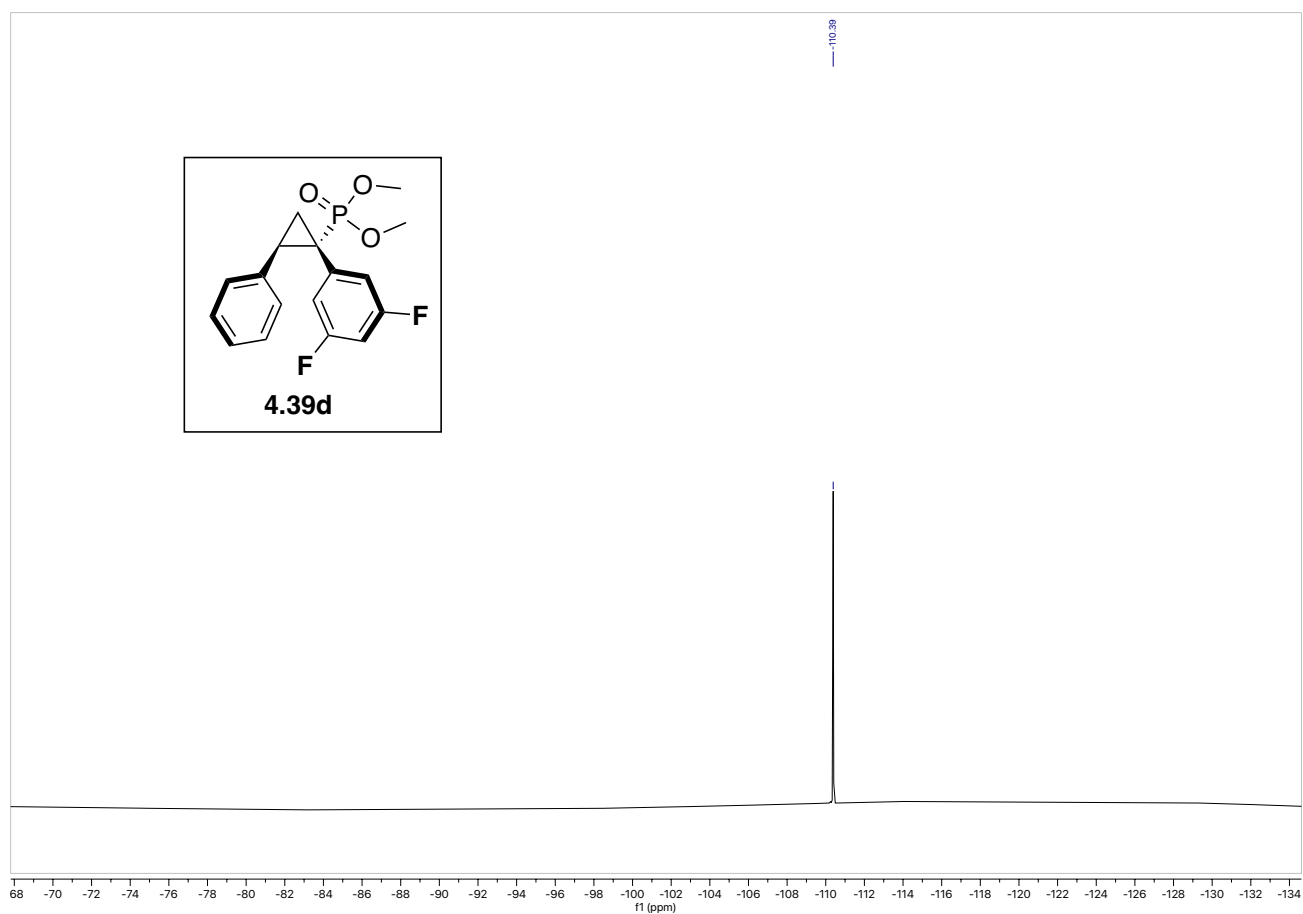
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39c**.



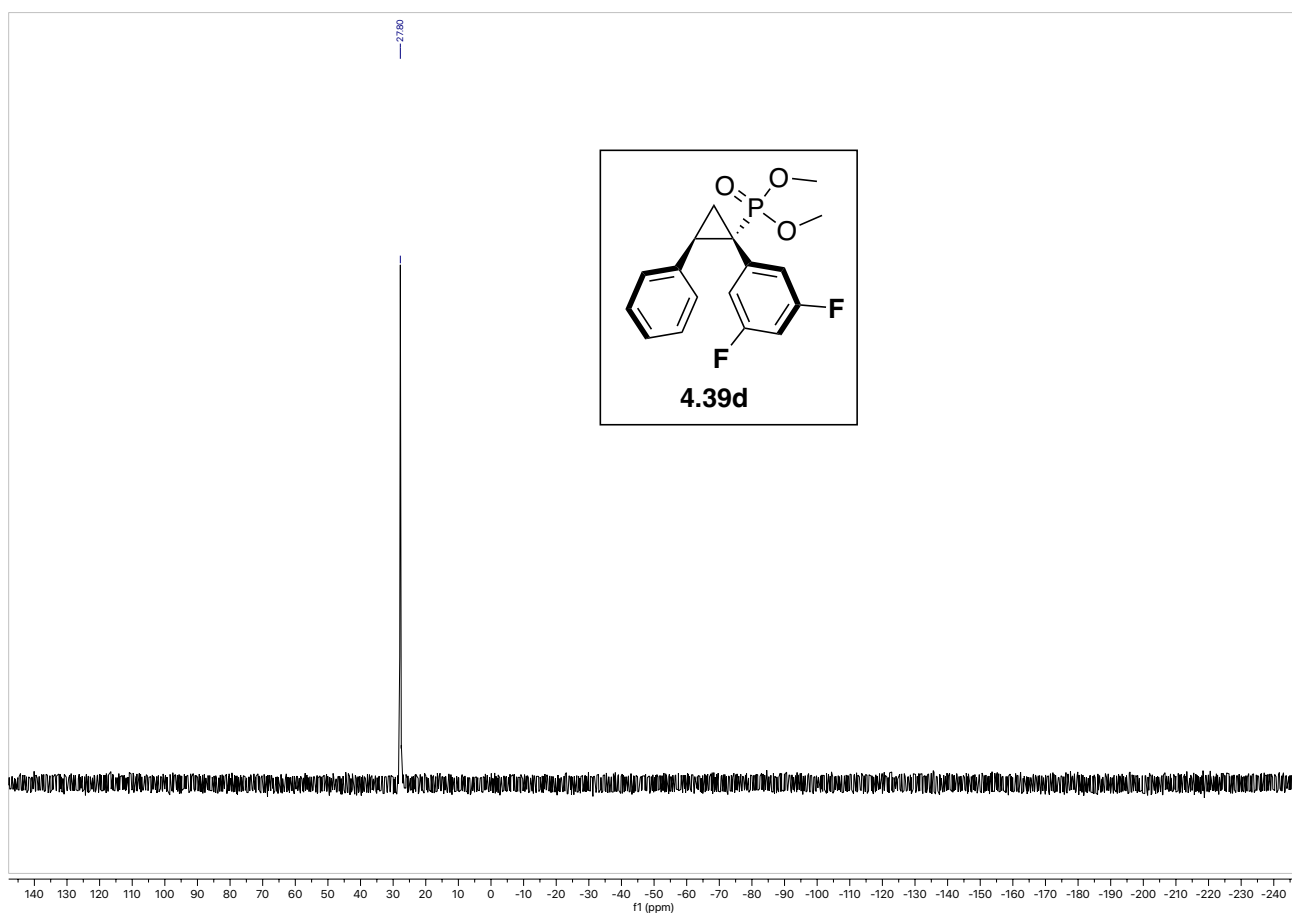
¹H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39d**.



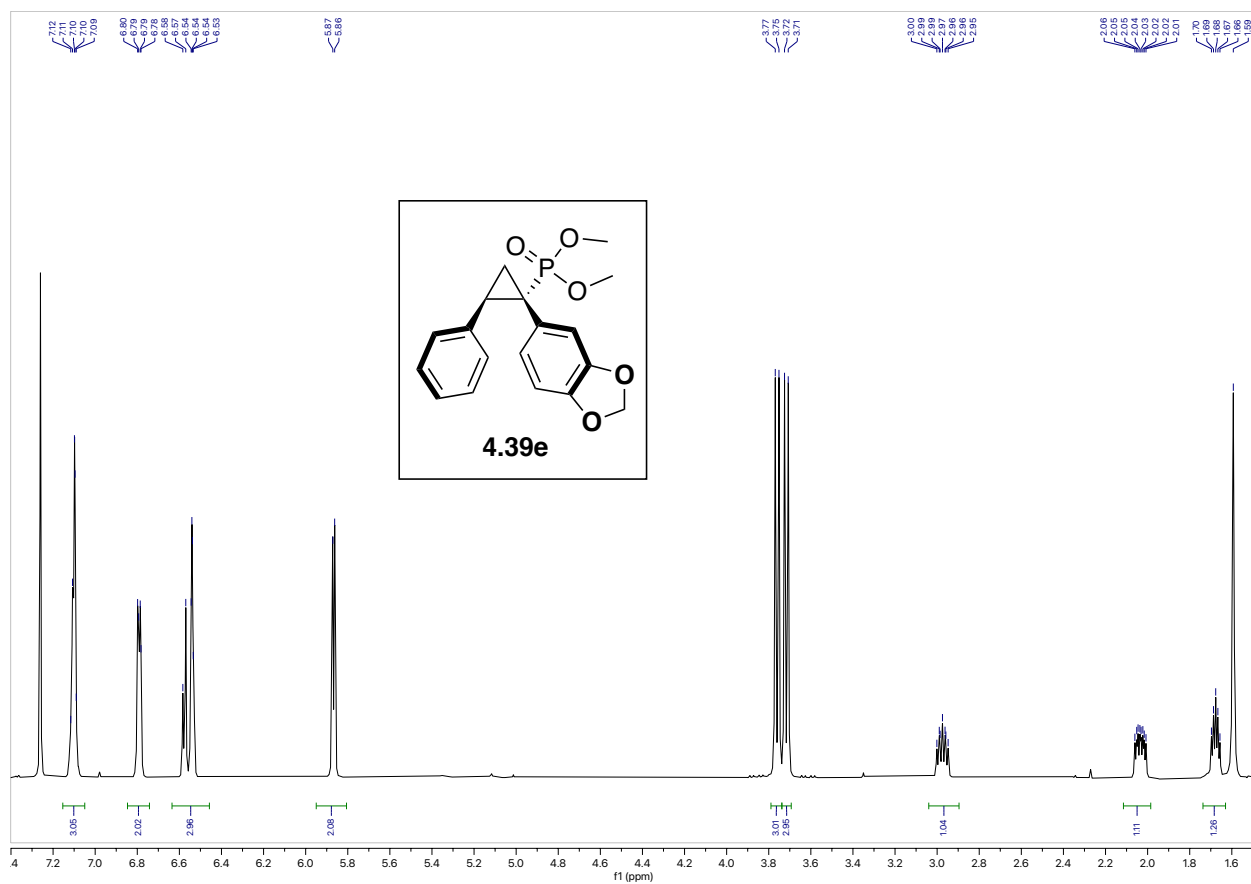
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39d**.



^{19}F NMR spectrum (565 MHz, Chloroform- d) of **4.39d**.

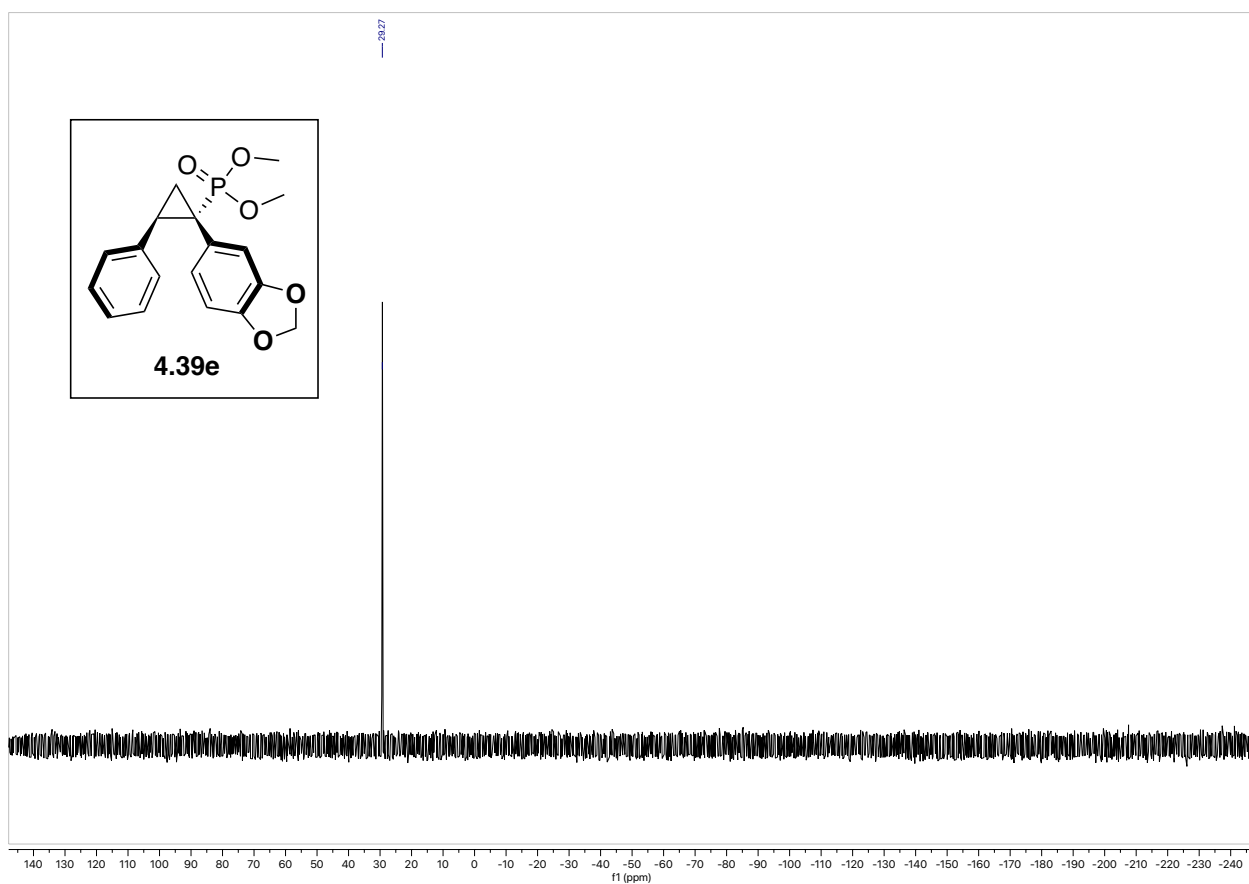


^{31}P NMR spectrum (243 MHz, Chloroform- d) of **4.39d**.

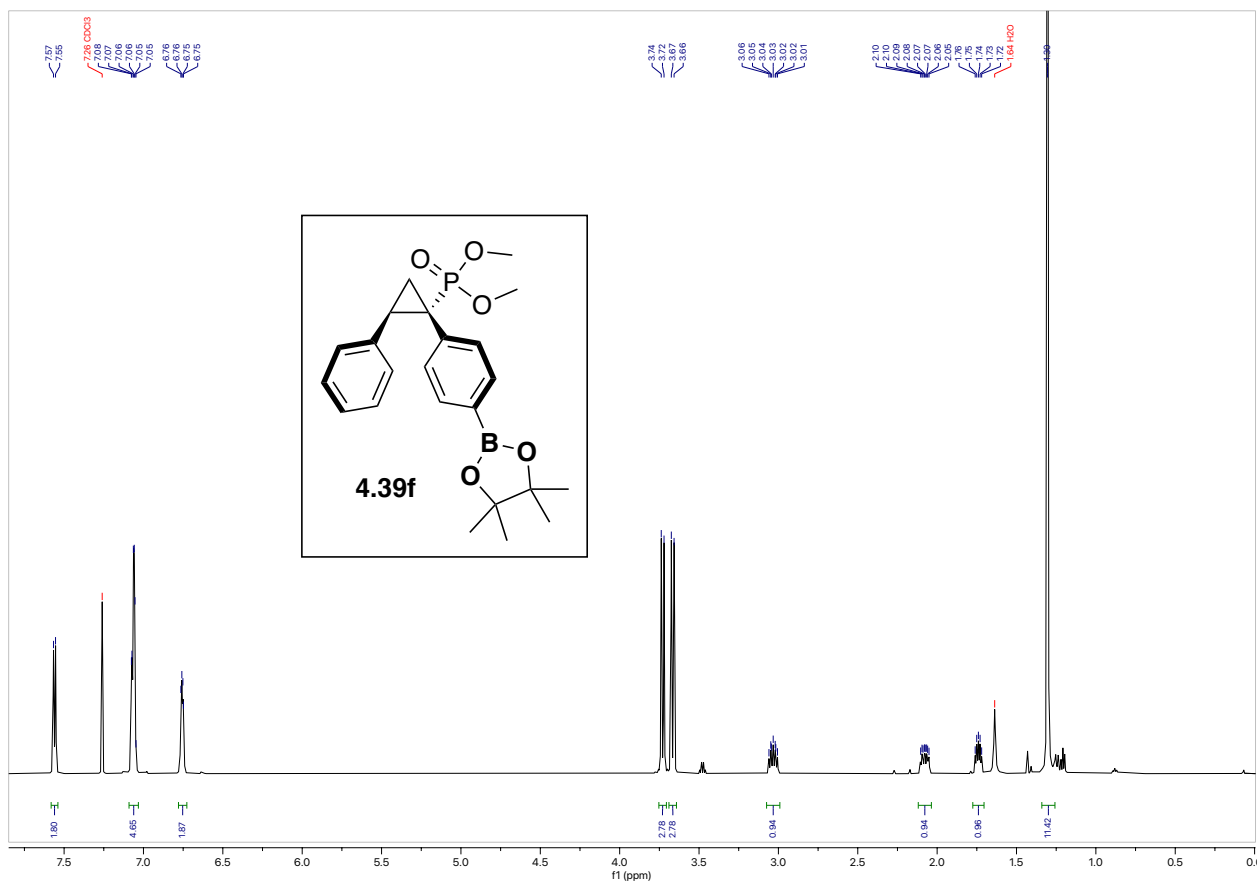


¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39e**.

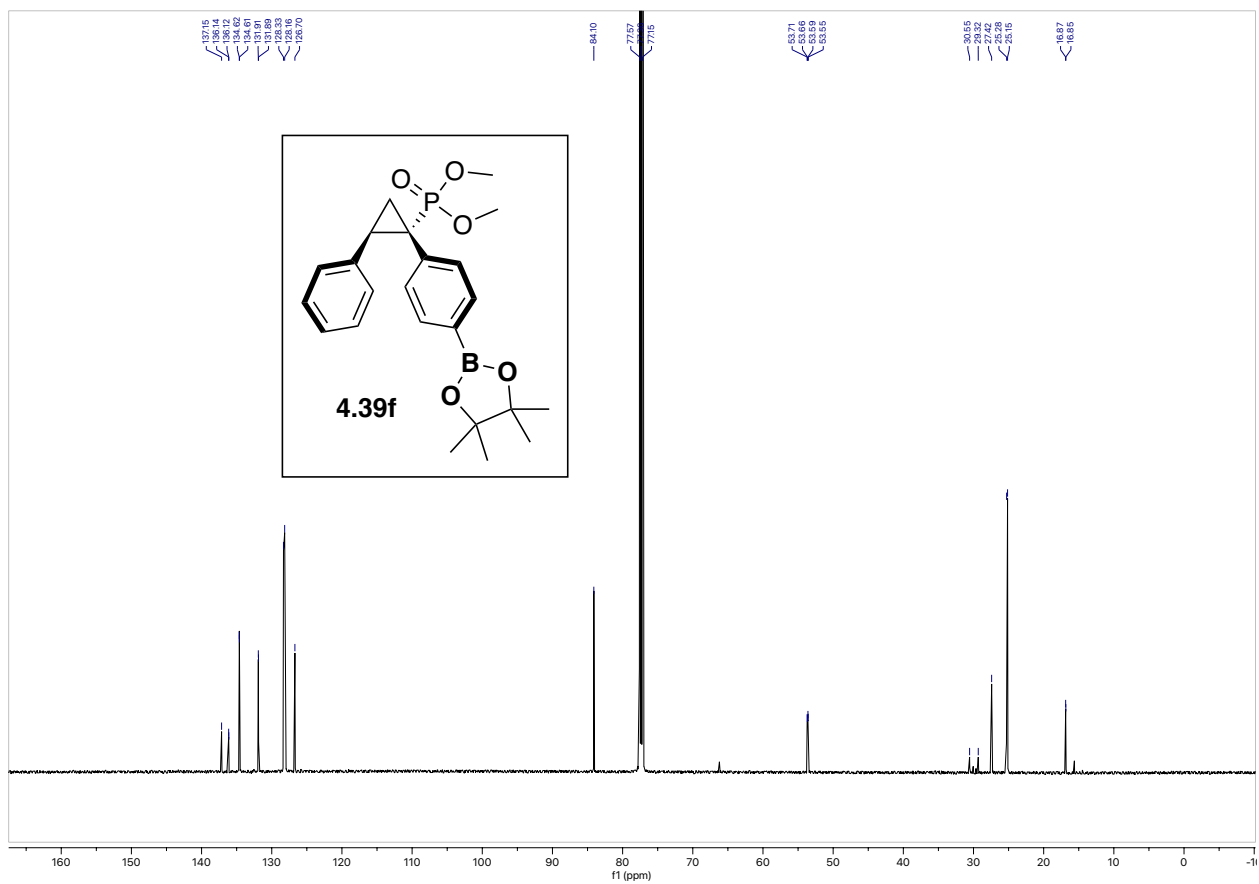




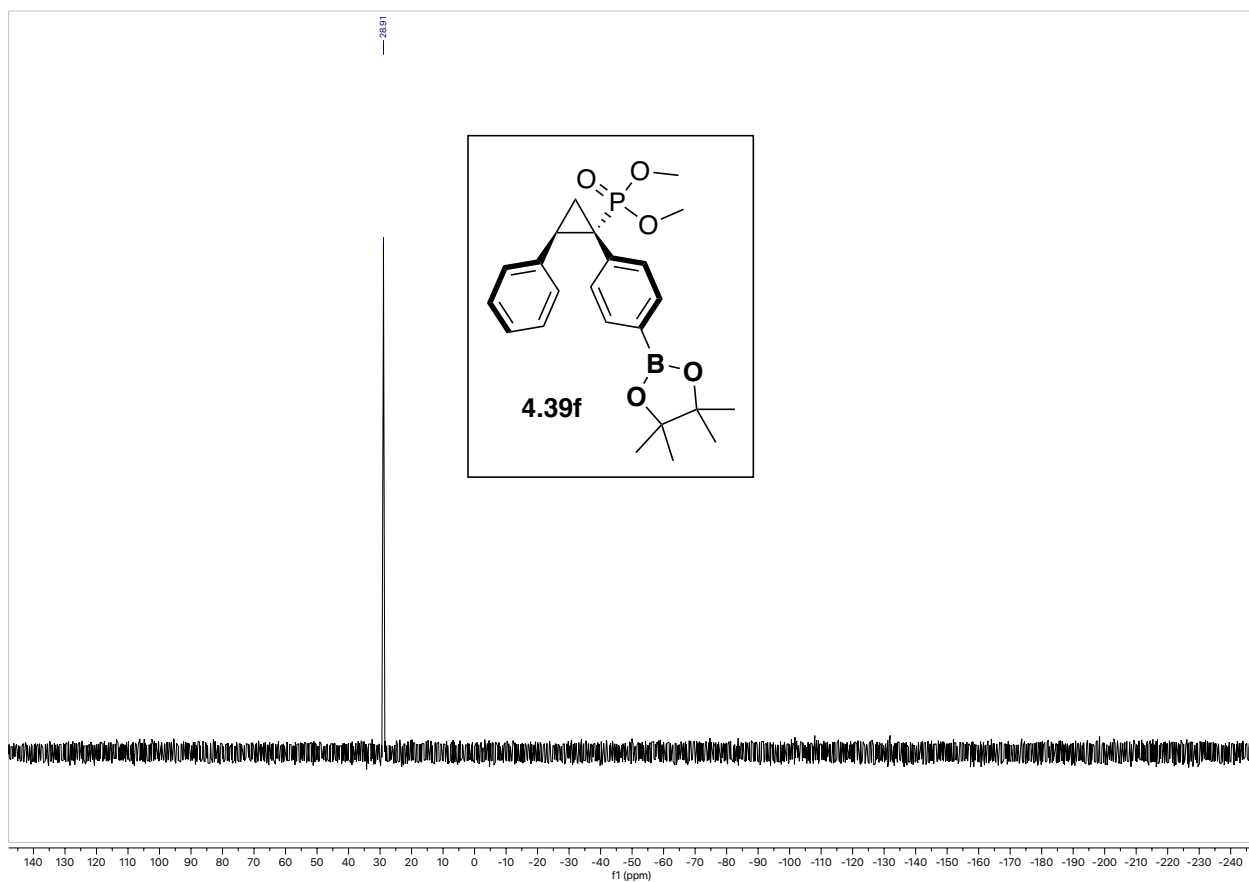
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39e**.



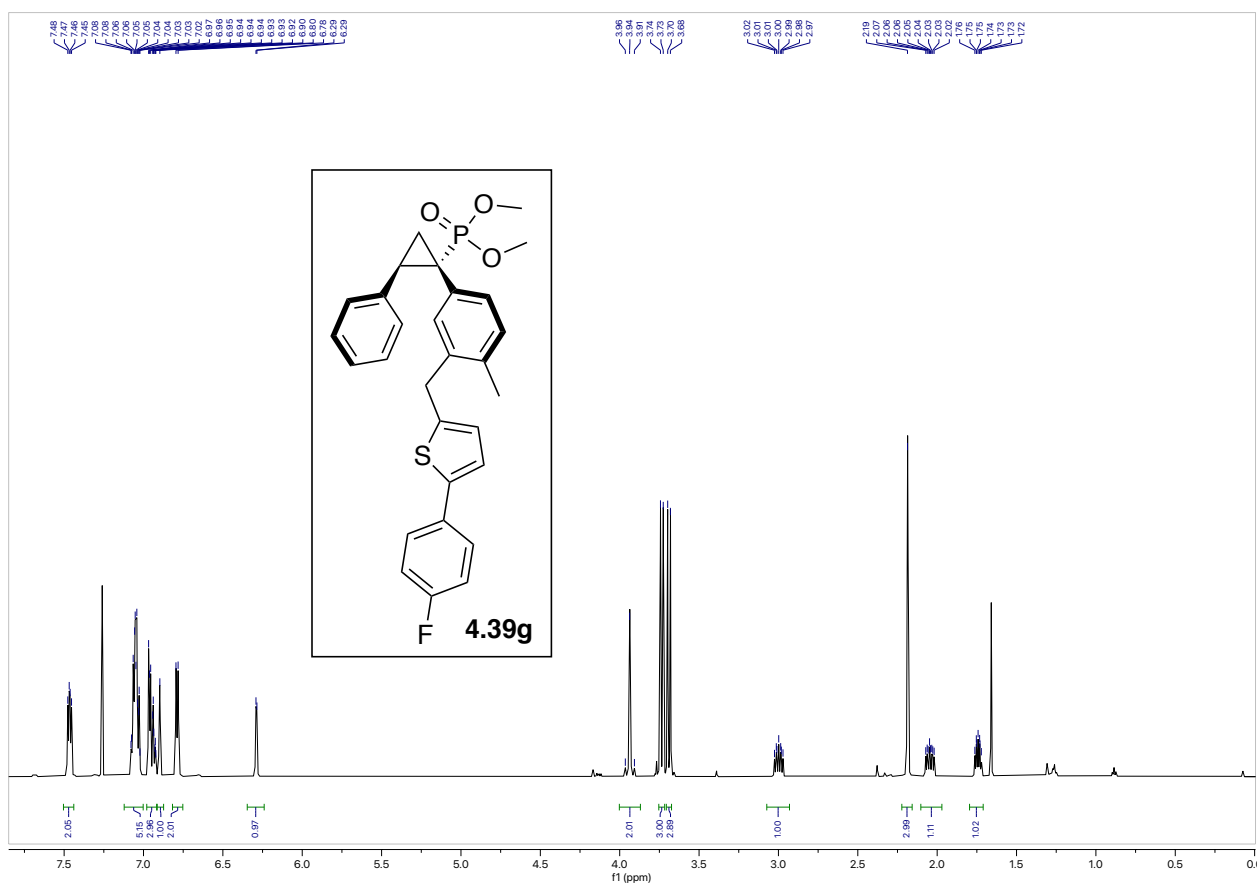
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39f**.



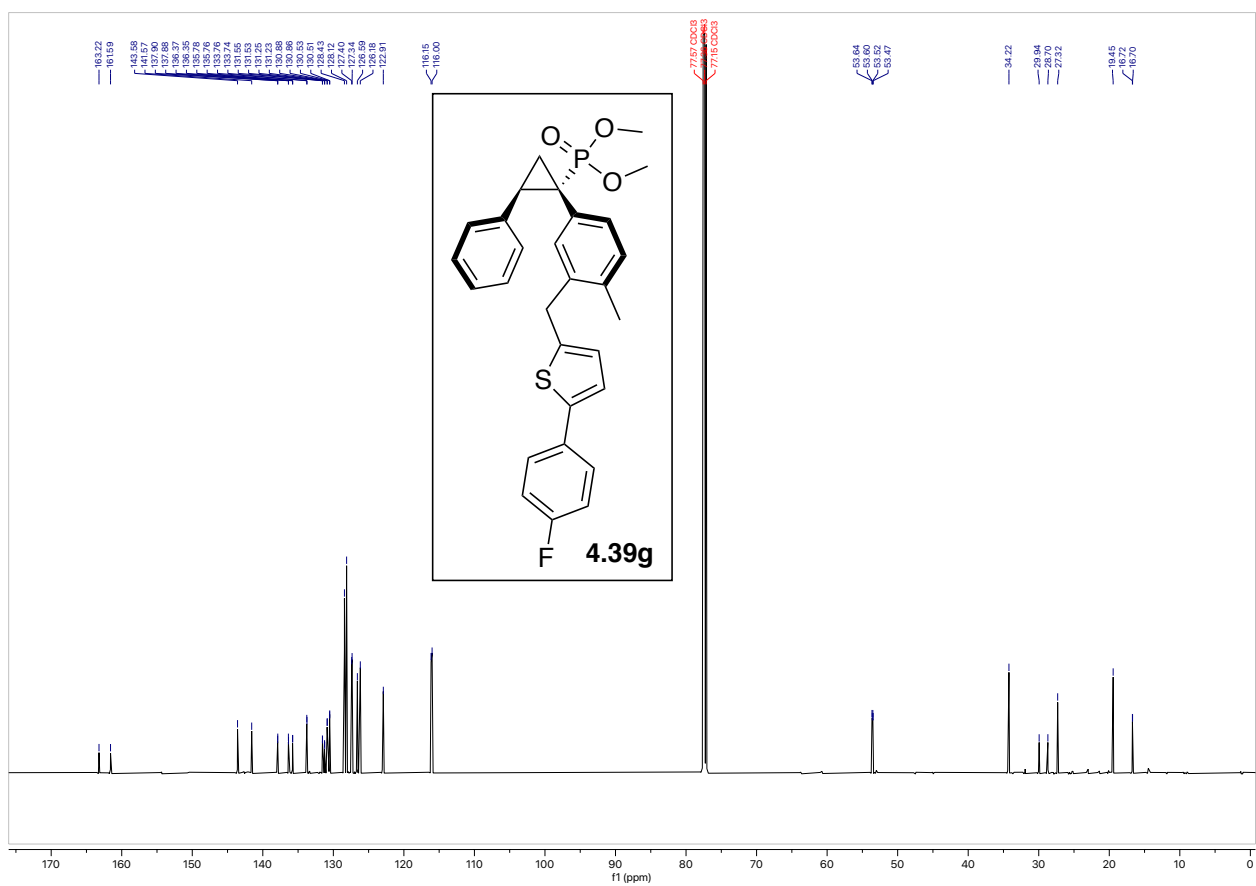
¹³C{¹H} NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39f**.



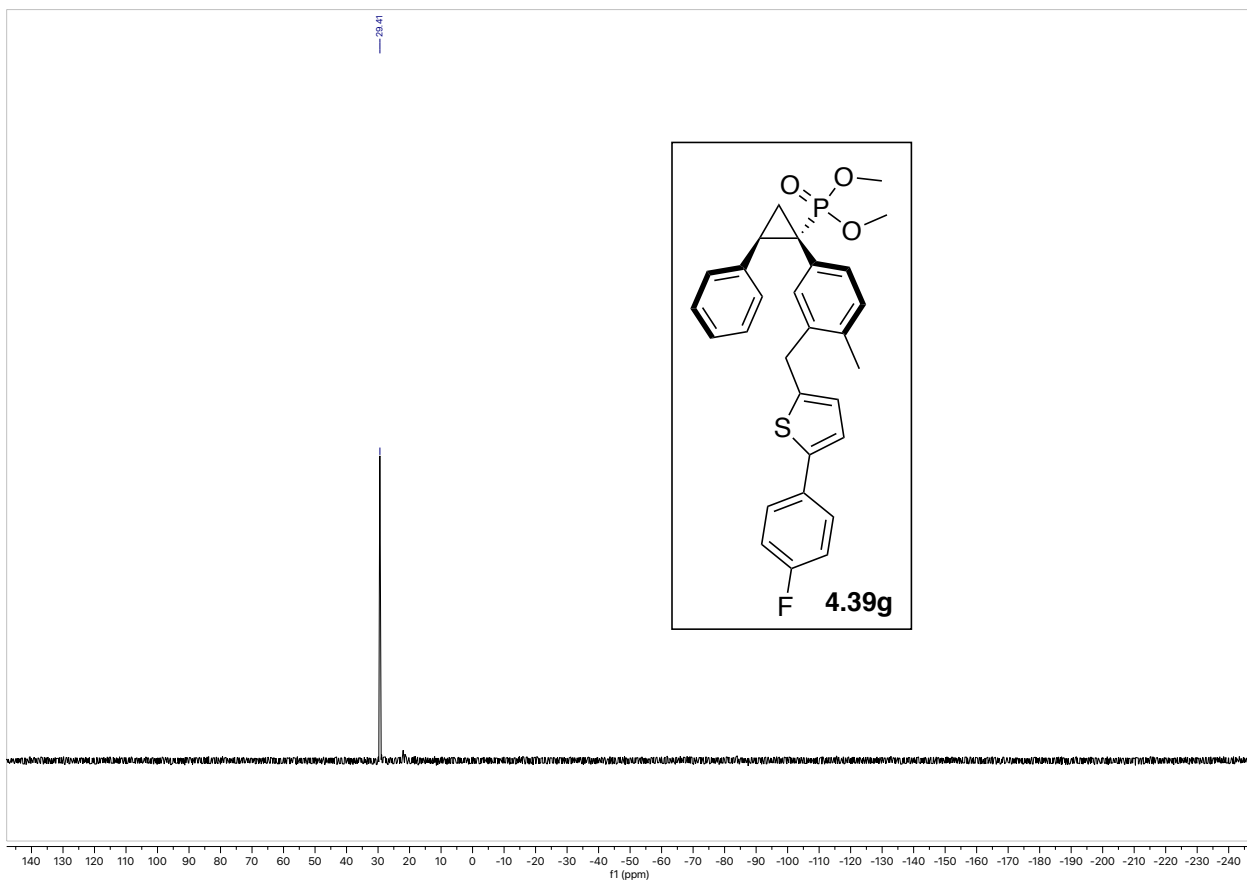
^{31}P NMR spectrum (243 MHz, Chloroform- d) of **4.39f**.



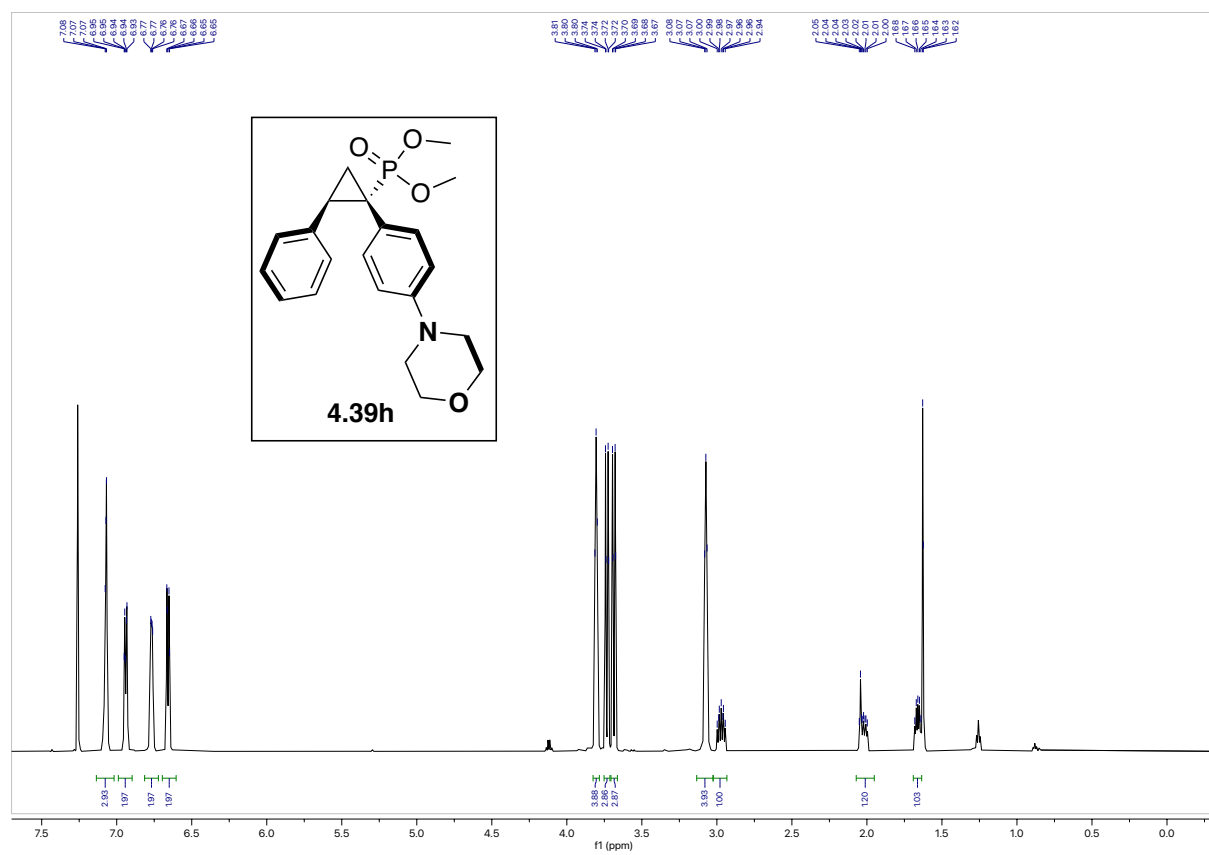
^1H NMR spectrum (600 MHz, Chloroform- d) (s, 7.26 ppm) of **4.39g**.



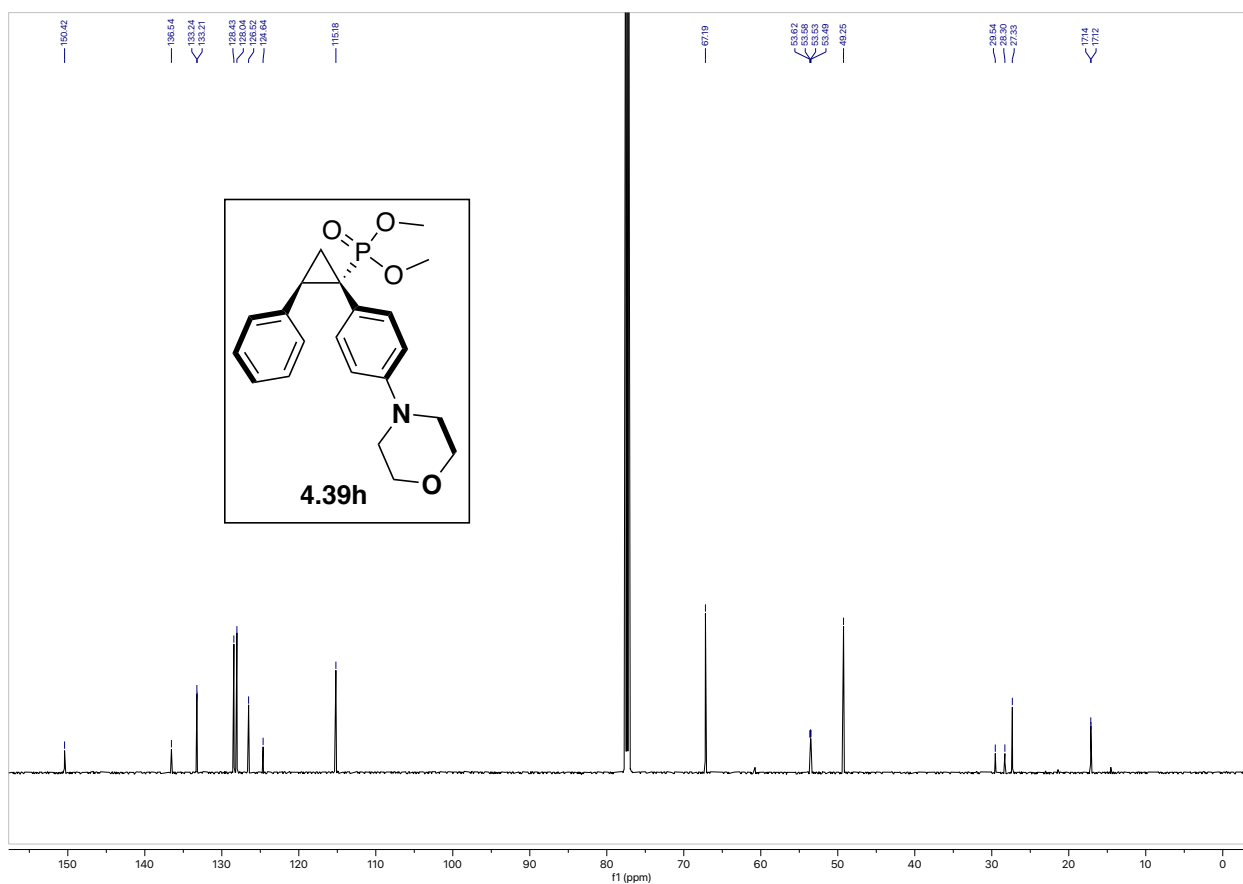
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39g**.

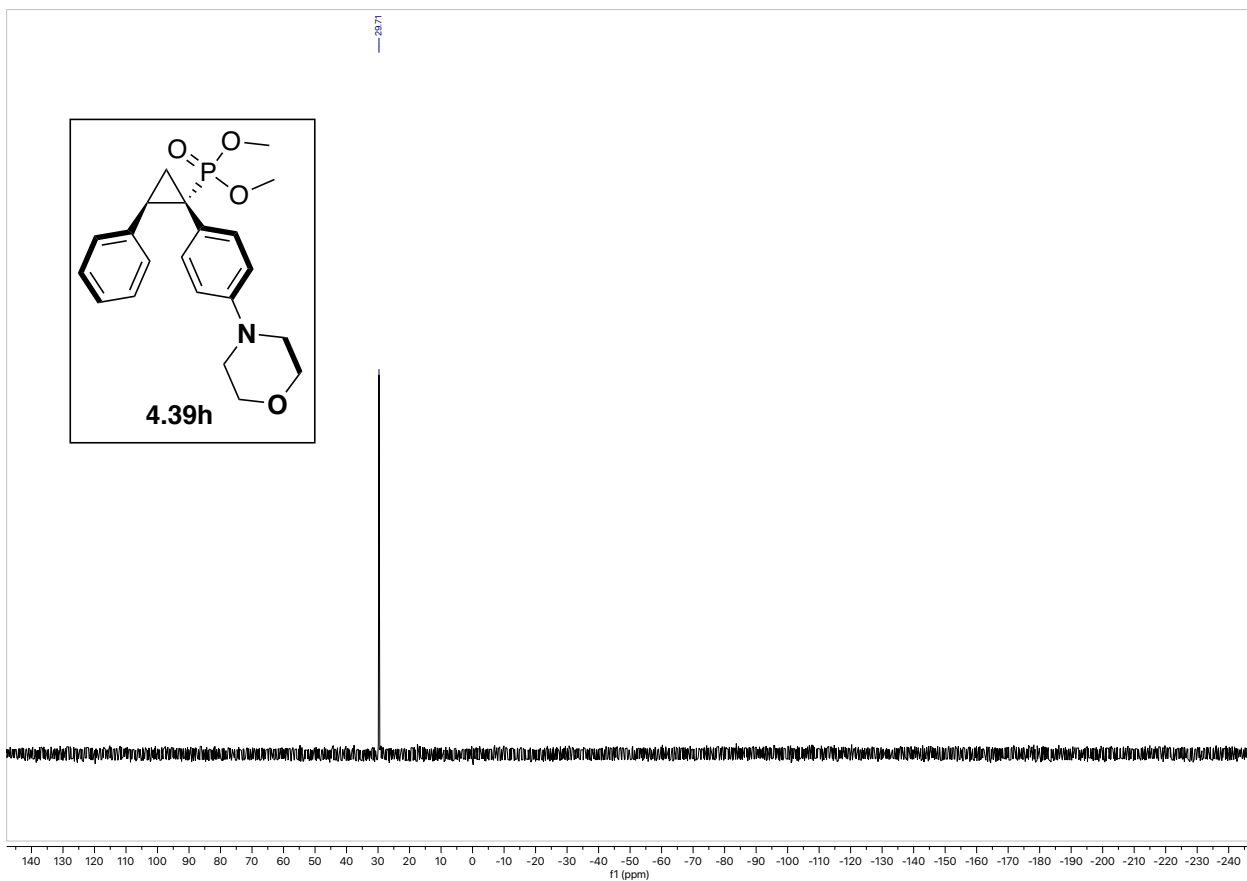


^{31}P NMR spectrum (243 MHz, Chloroform- d) of **4.39g**.

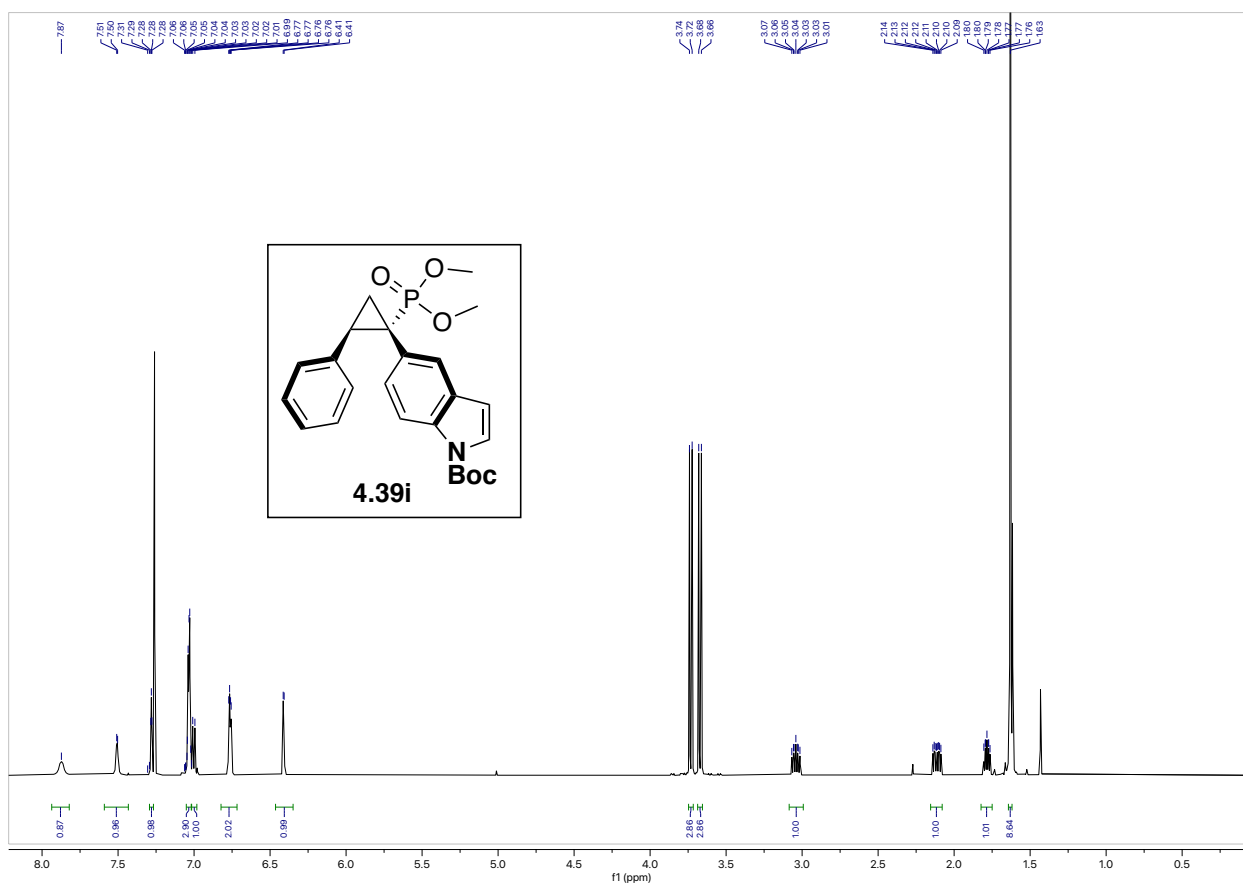


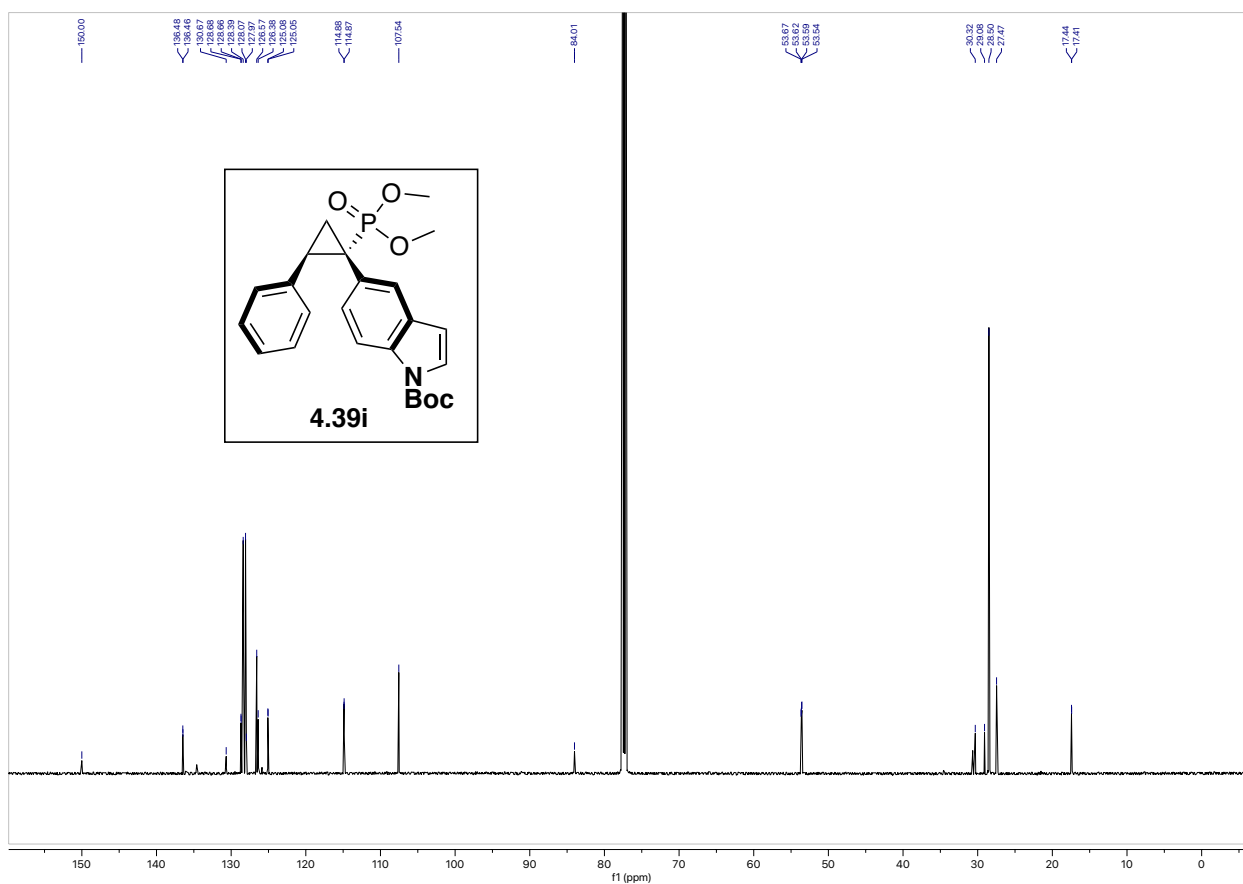
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39h**.

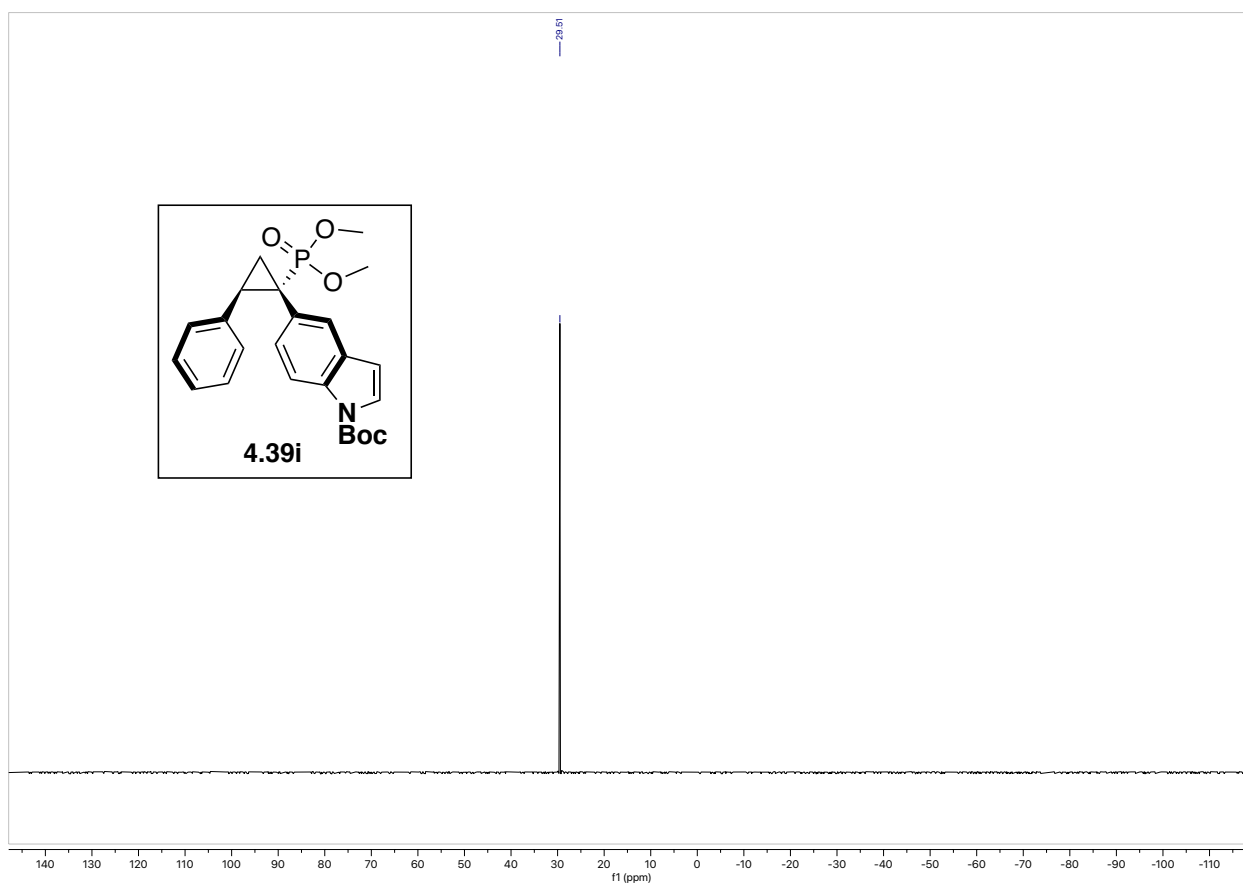




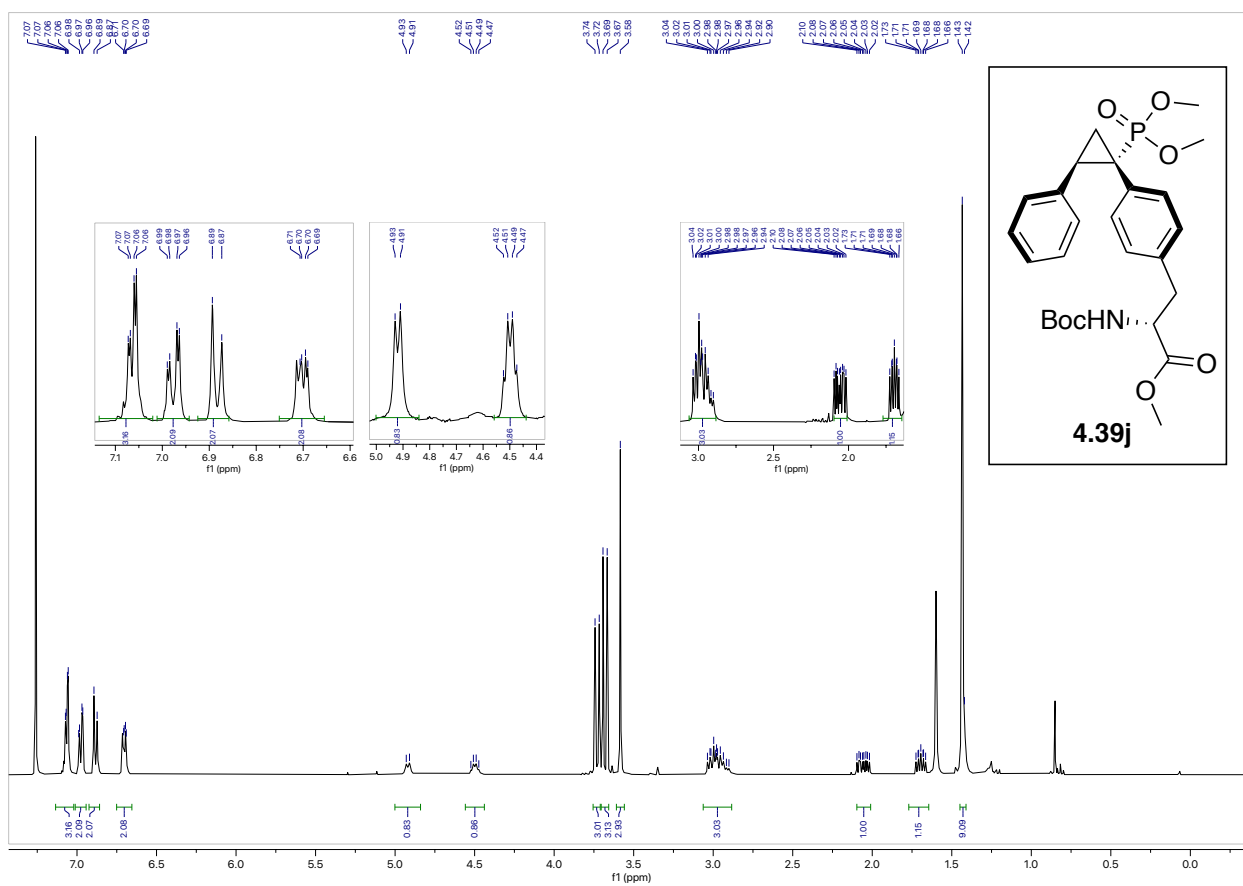
³¹P NMR spectrum (243 MHz, Chloroform-d) of **4.39h**.



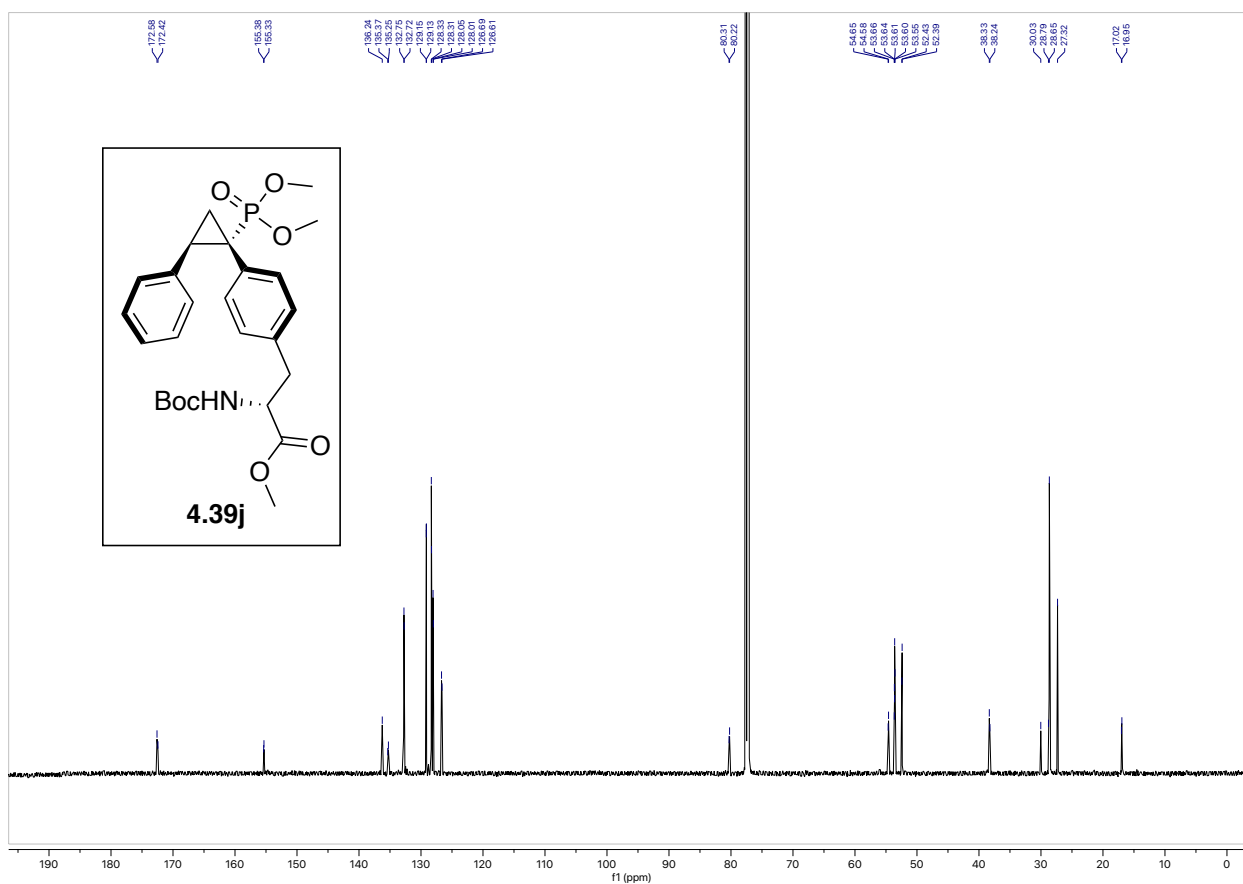




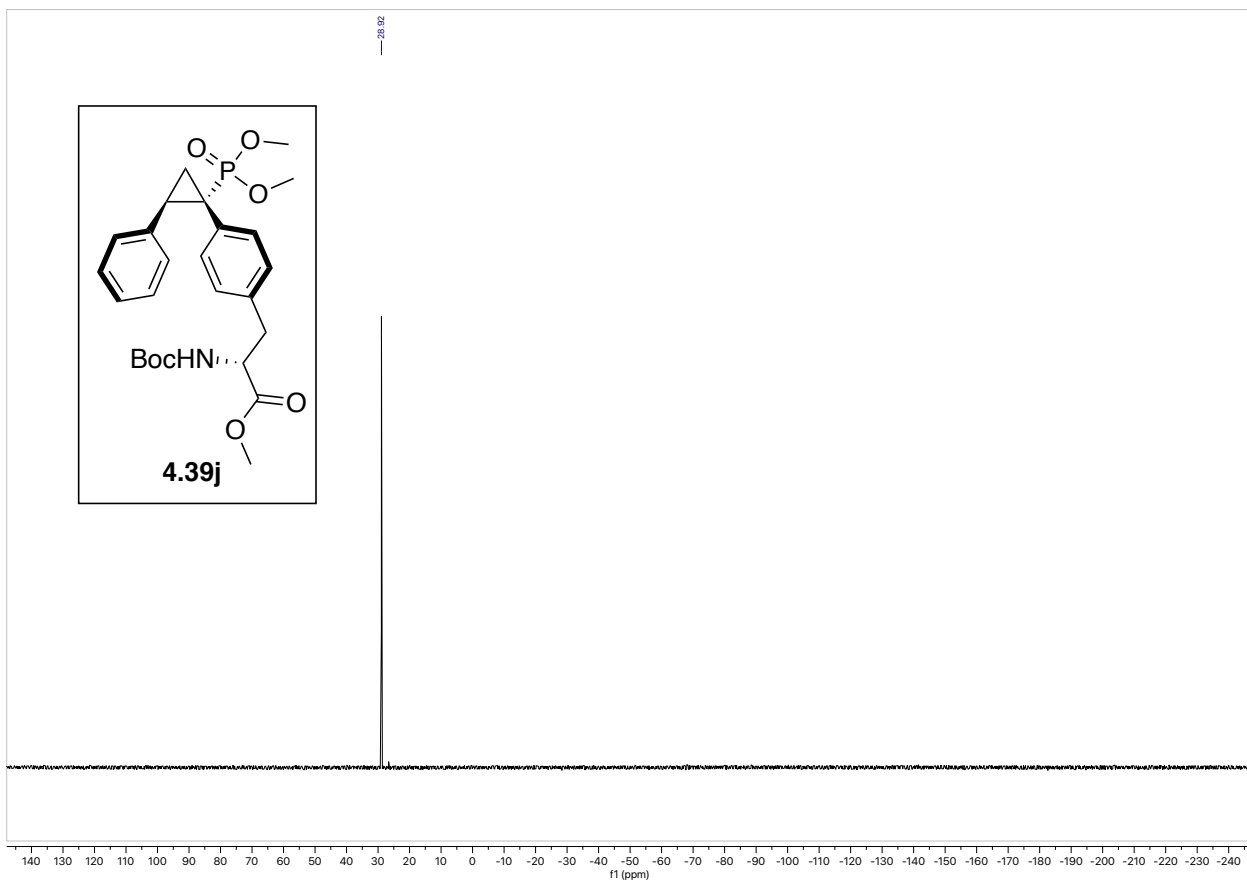
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39i**.



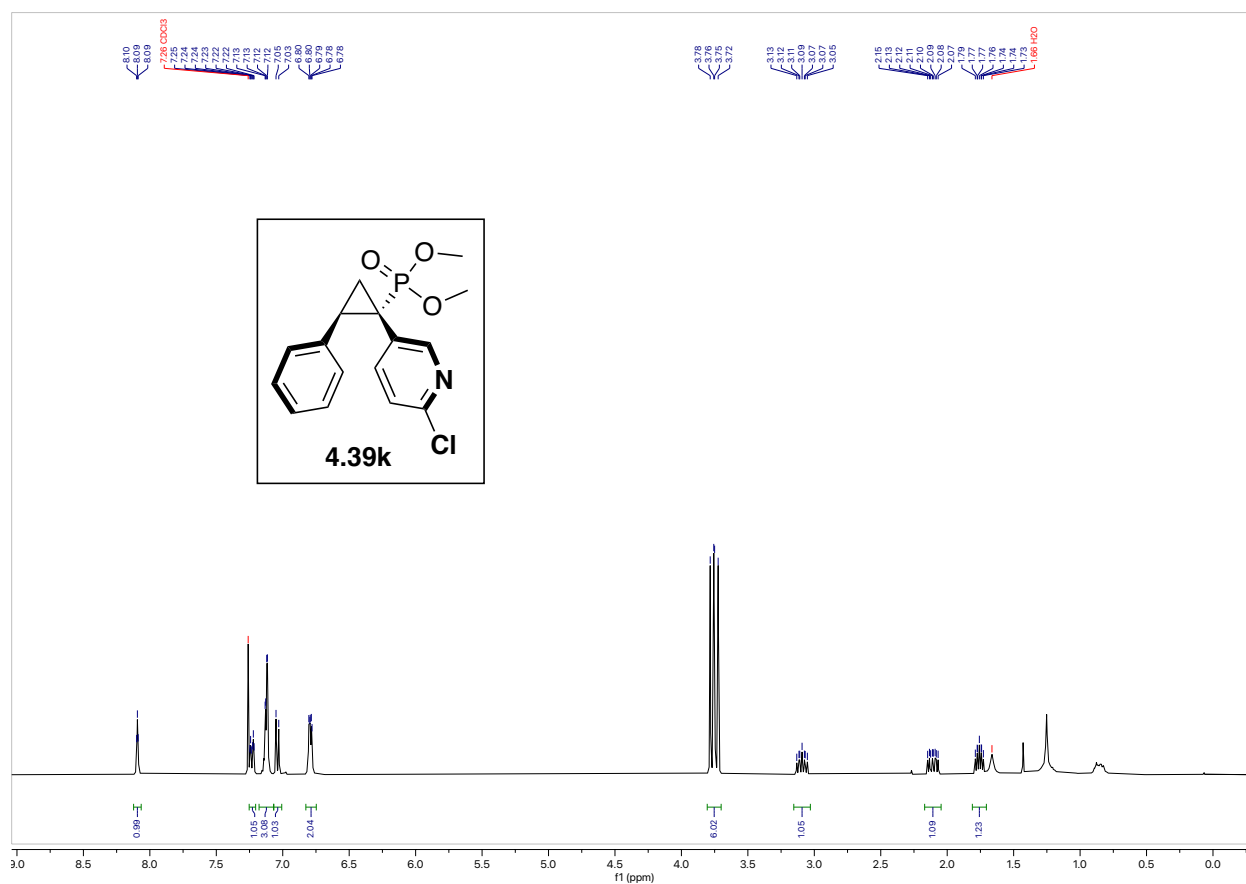
^1H NMR spectrum (400 MHz, CDCl_3) (s, 7.26 ppm) of **4.39j**.



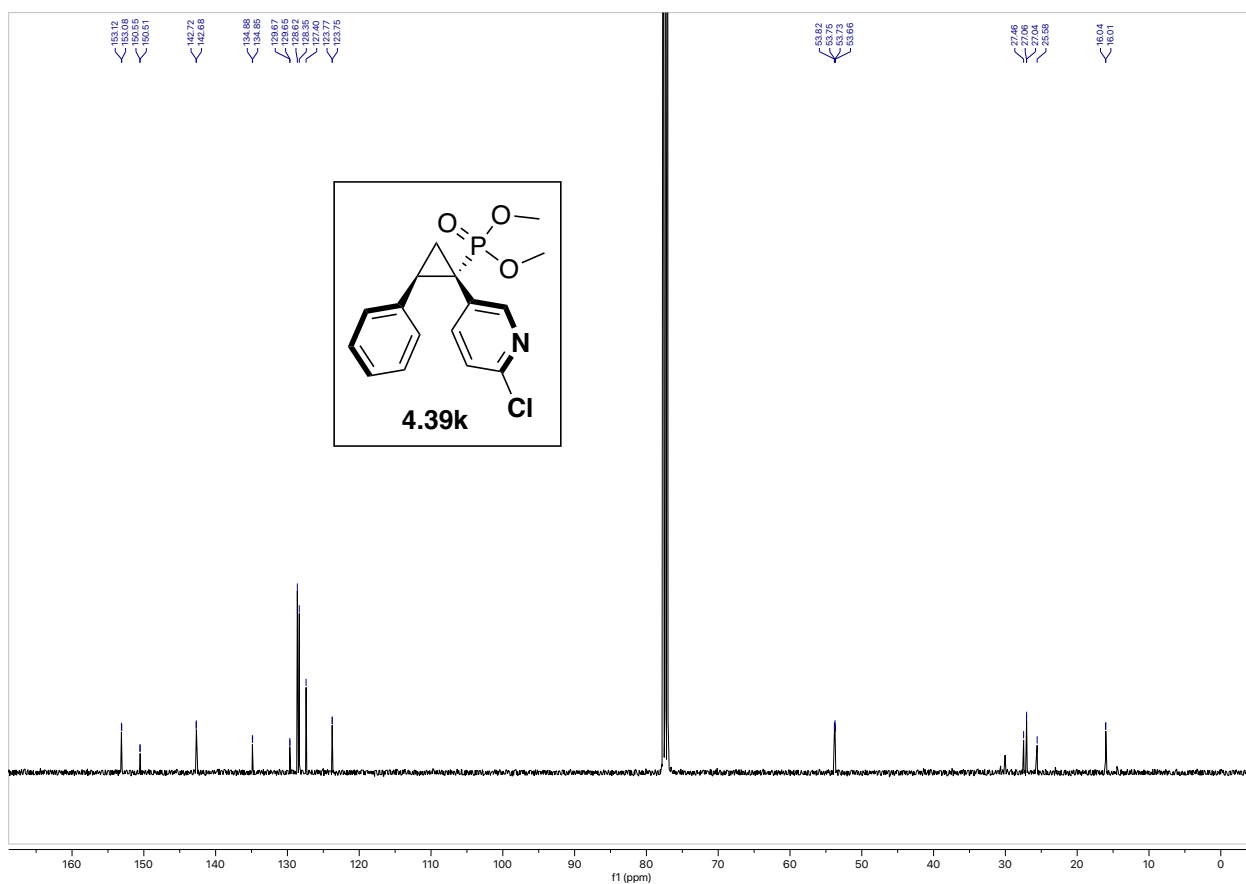
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39j**.



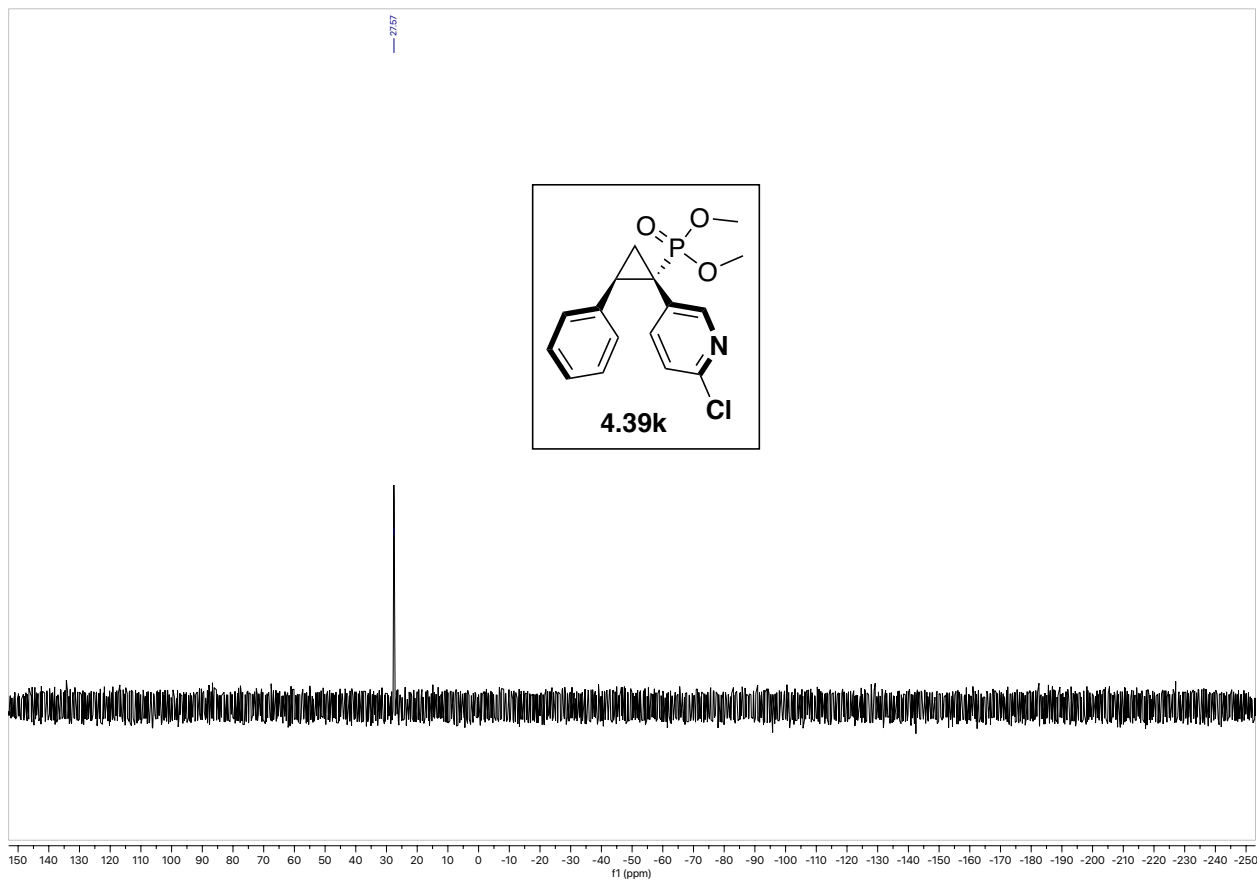
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39j**.



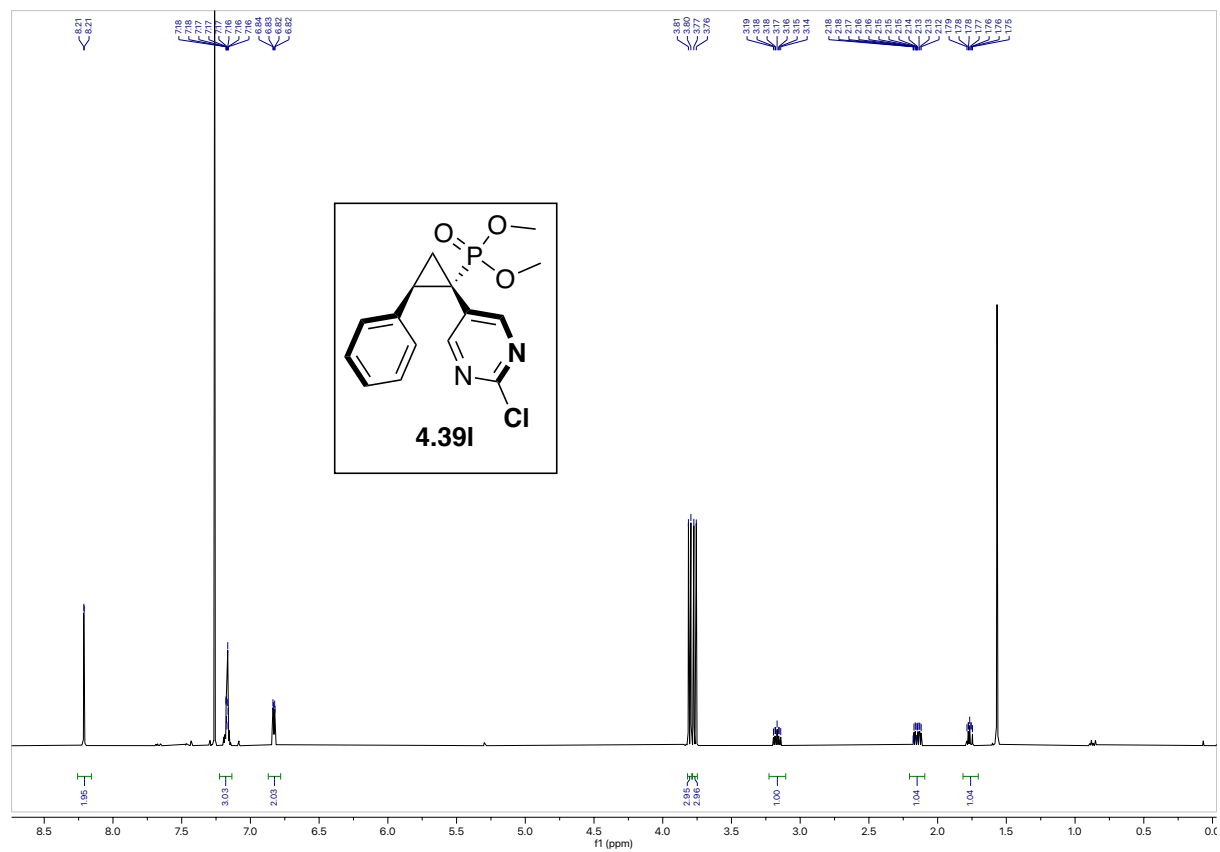
¹H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39k**.



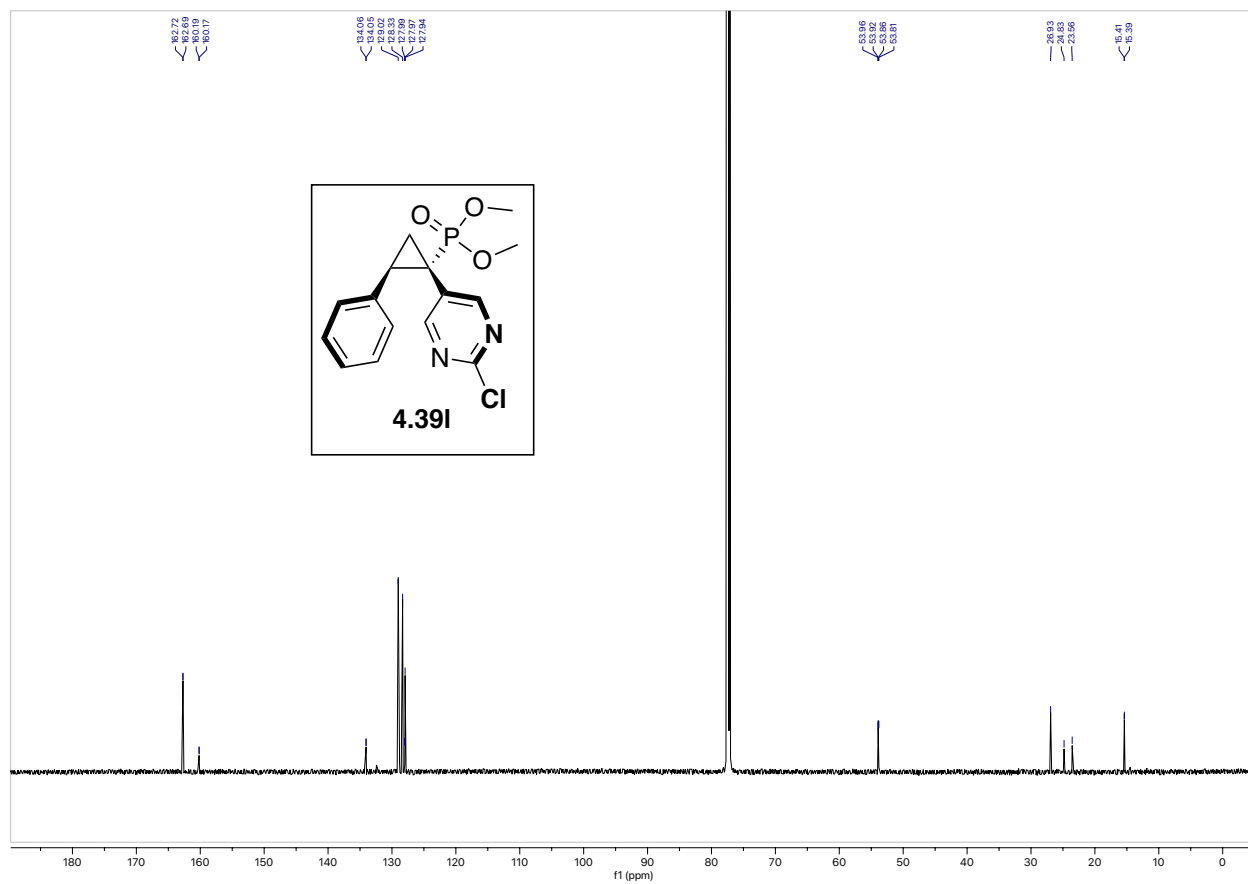
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, CDCl_3) (t, 77.36 ppm) of **4.39k**.

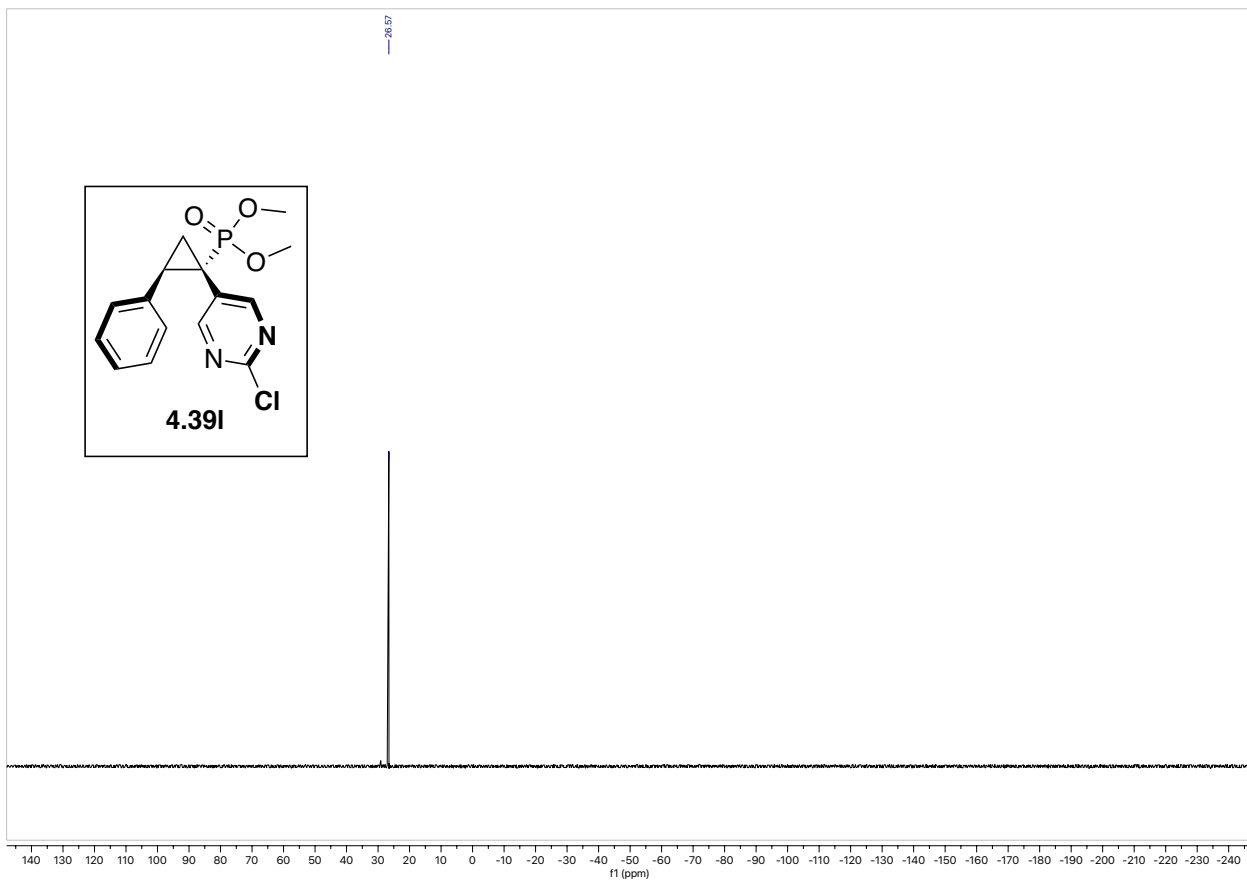


^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39k**.

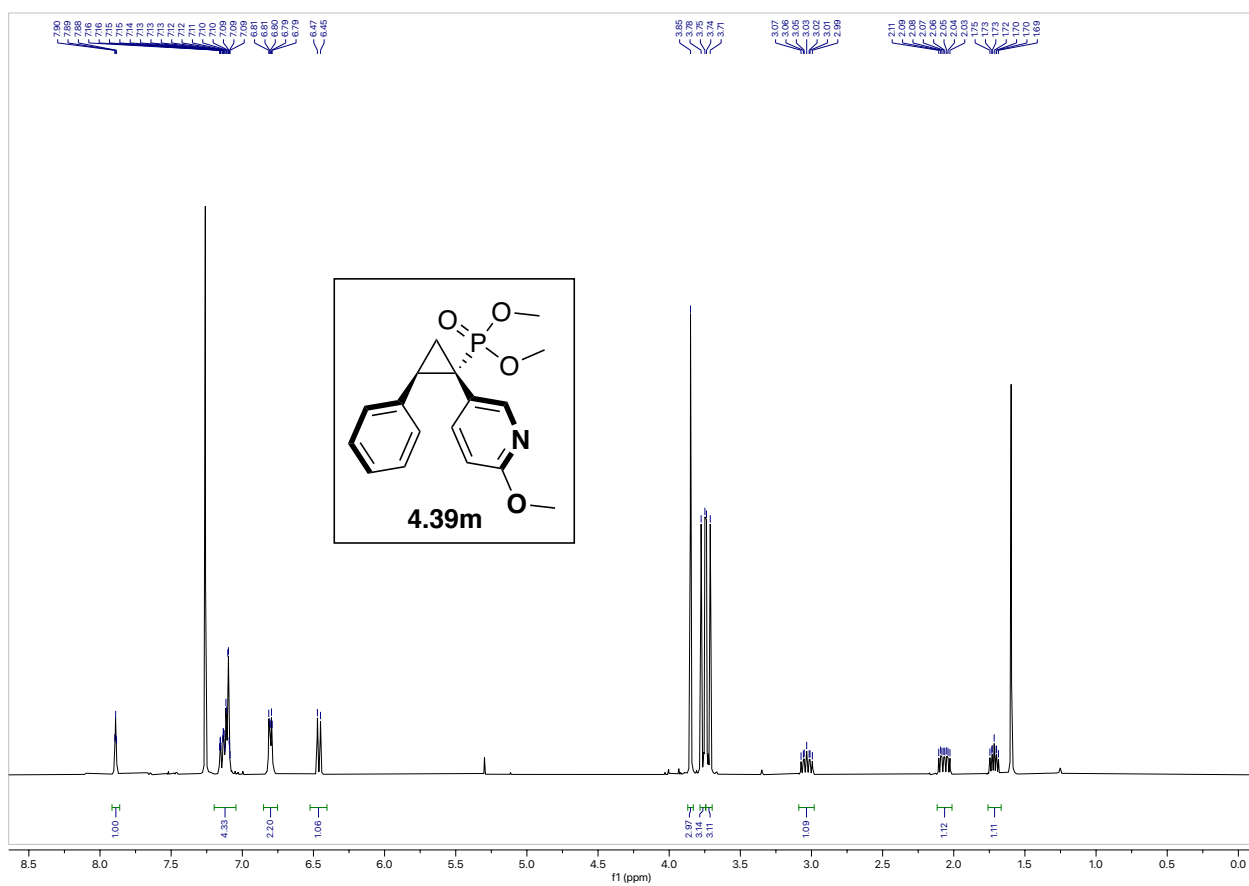


^1H NMR spectrum (600 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39I**.

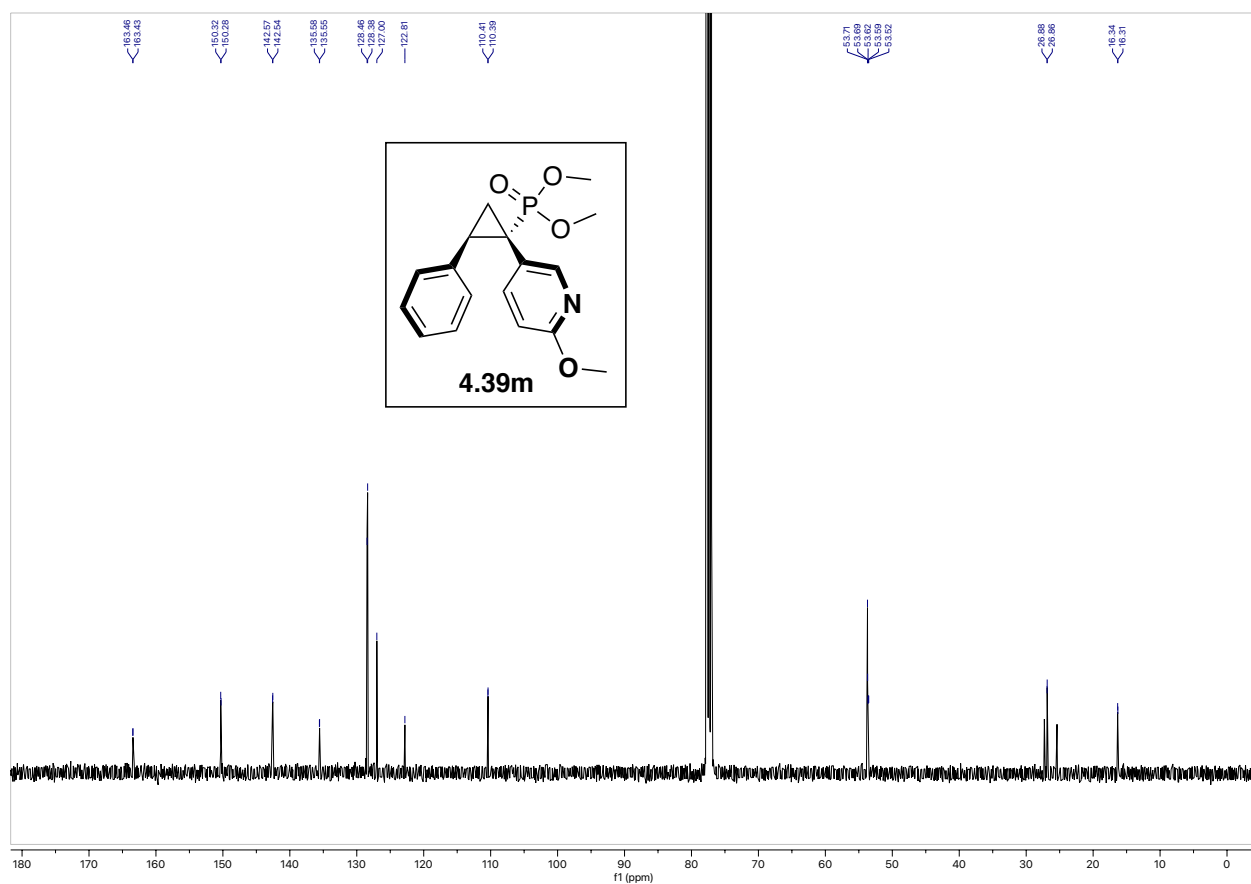




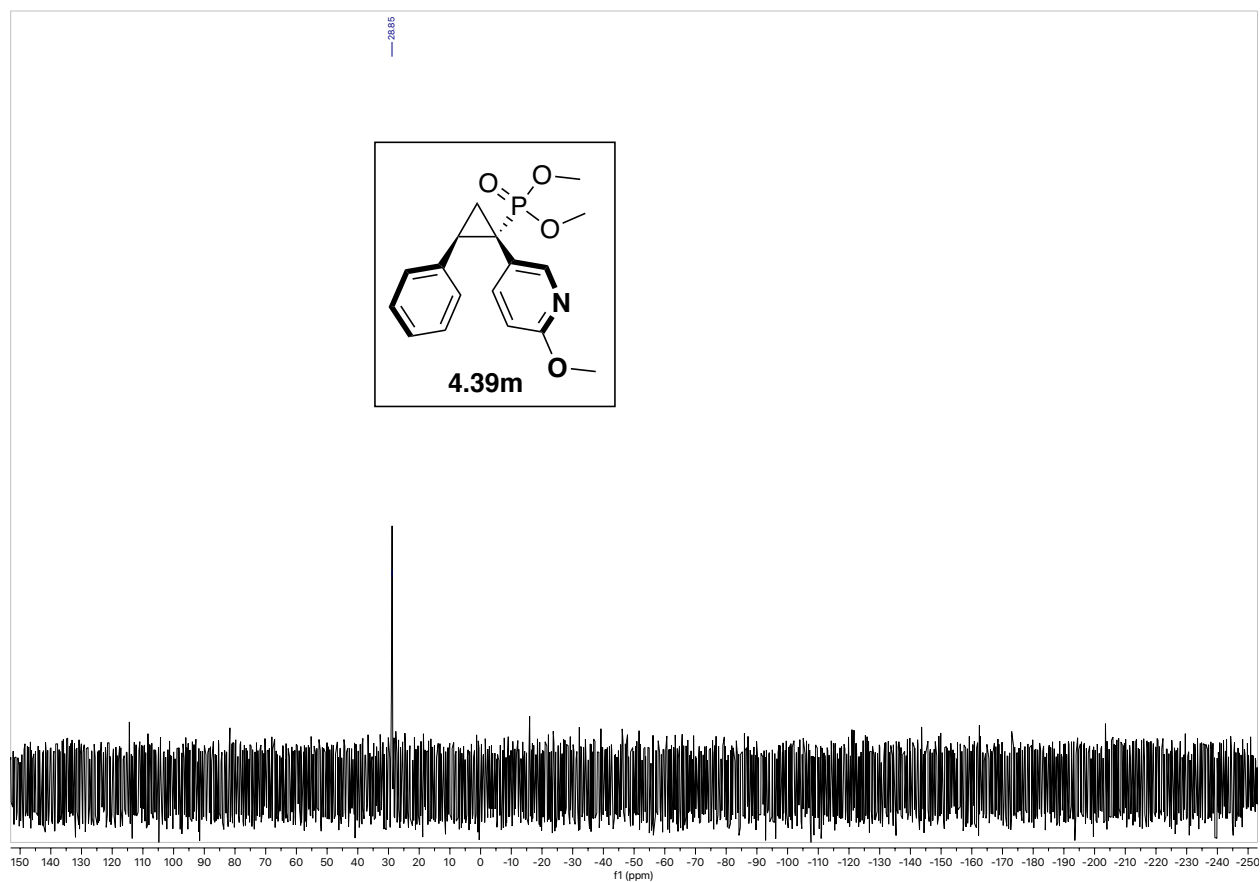
^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39I**.



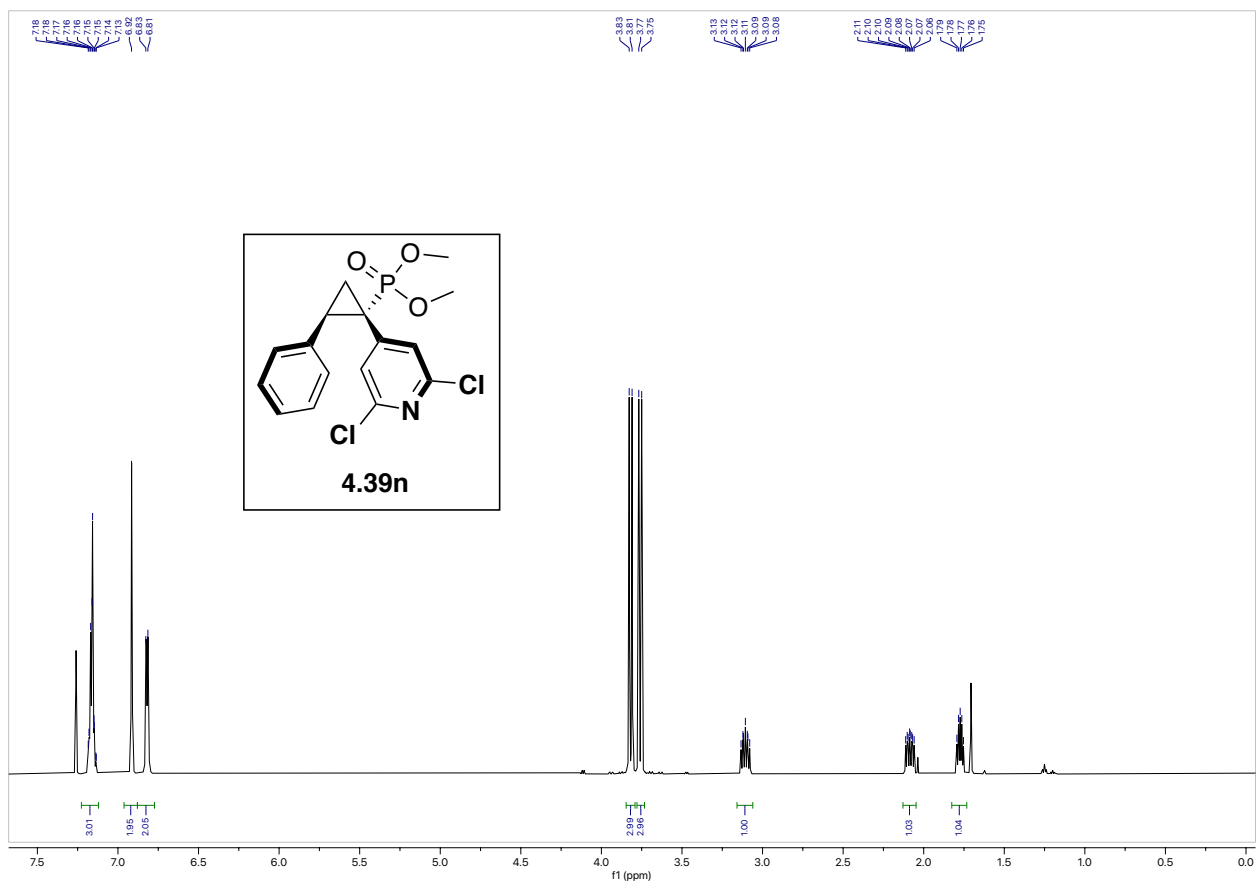
^1H NMR spectrum (400 MHz, Chloroform-*d*) (s, 7.26 ppm) of **4.39m**.

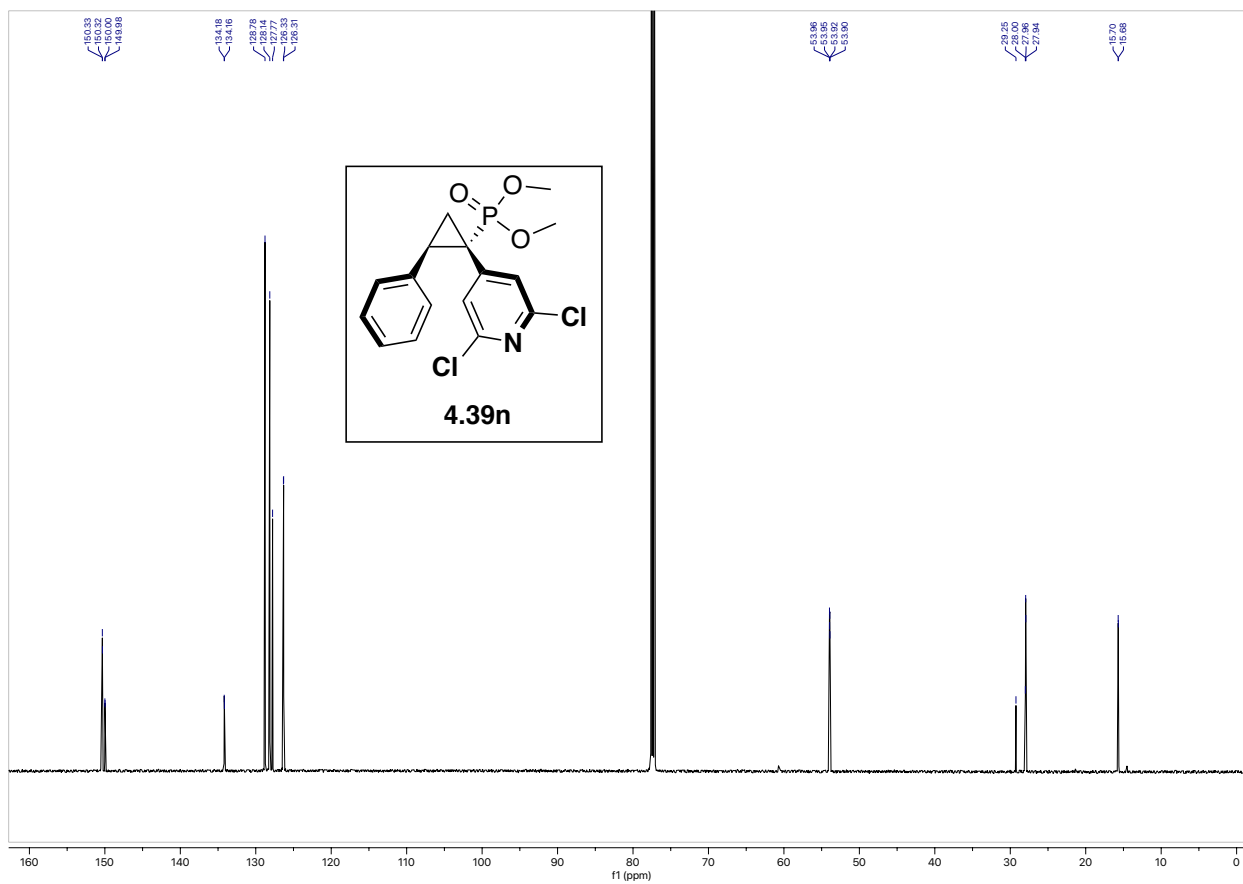


$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (101 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39m**.

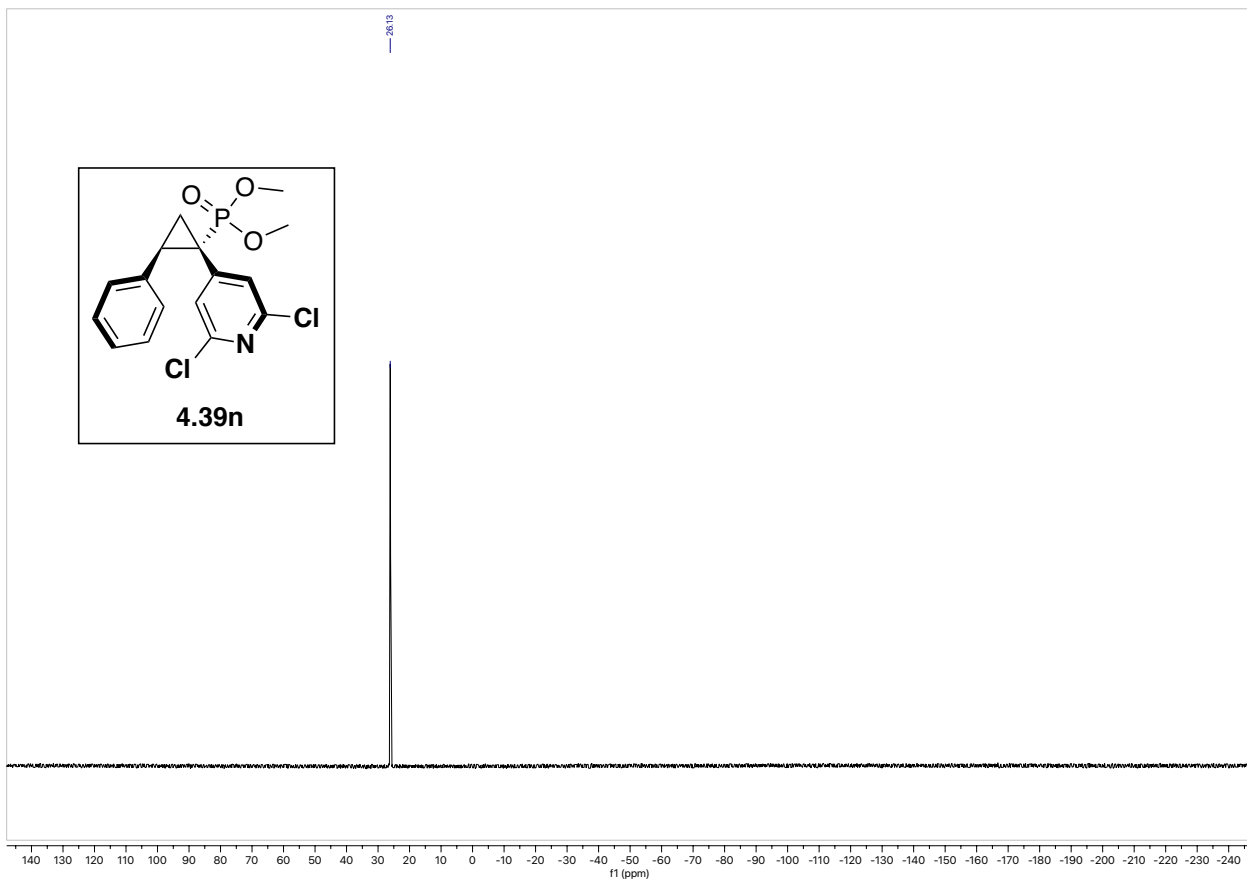


^{31}P NMR spectrum (162 MHz, Chloroform- d) of **4.39m**.

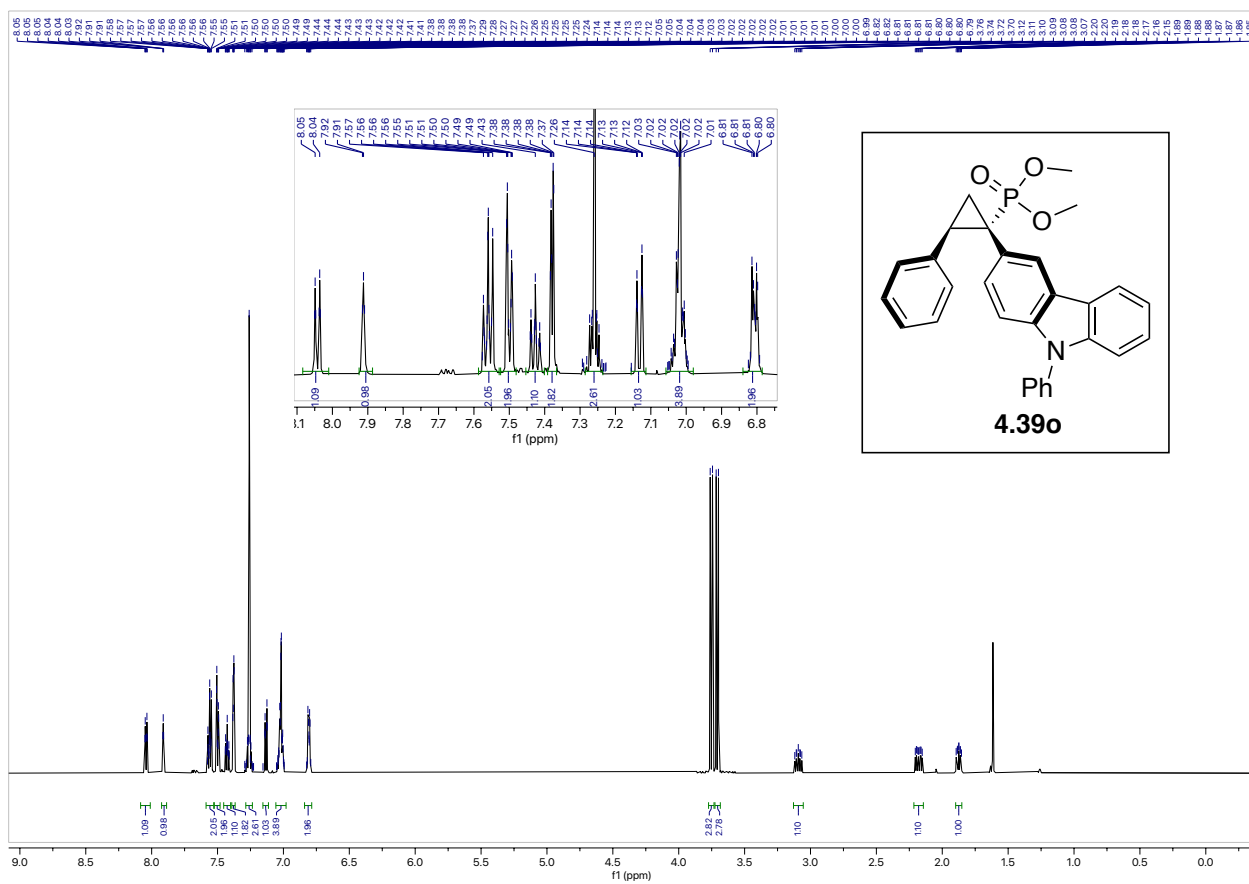




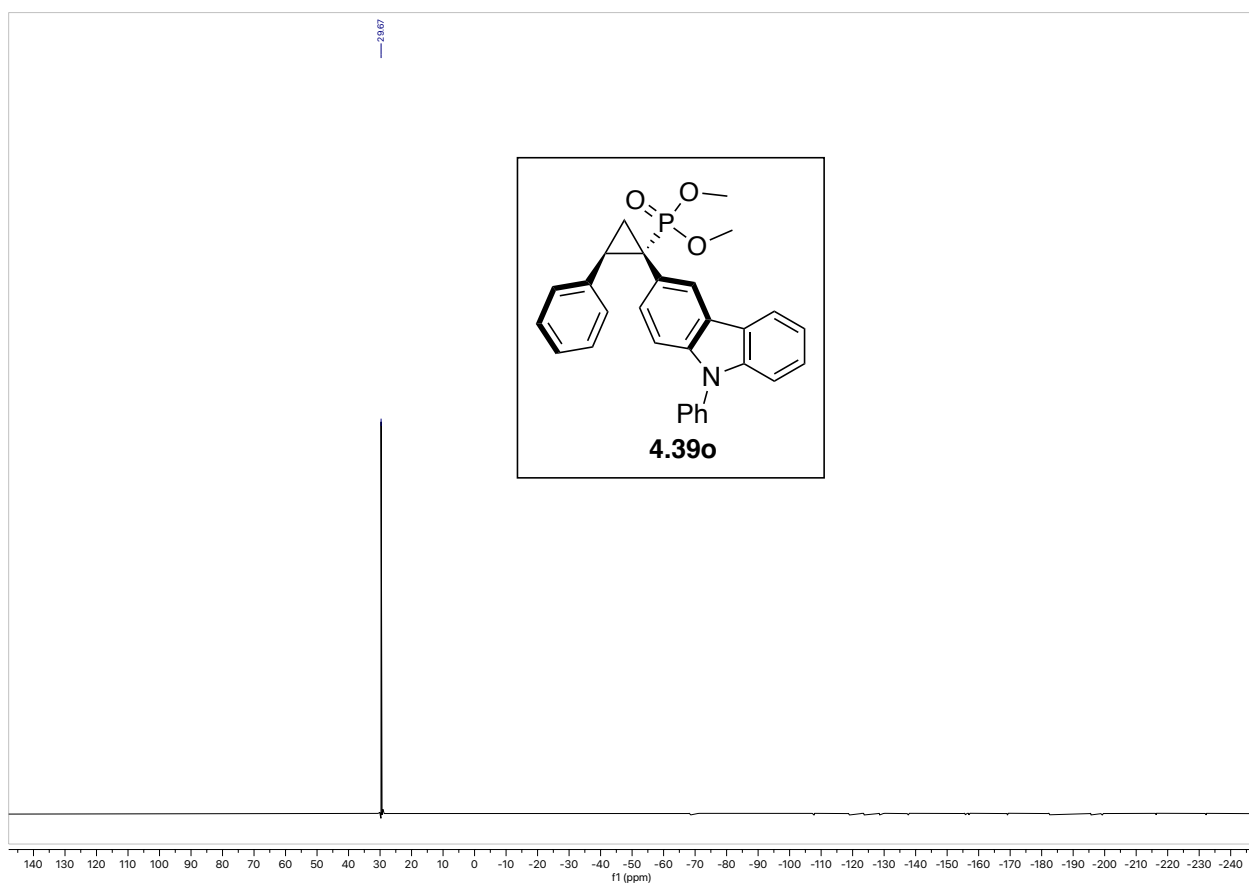
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (151 MHz, Chloroform-*d*) (t, 77.36 ppm) of **4.39n**.



^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39n**.

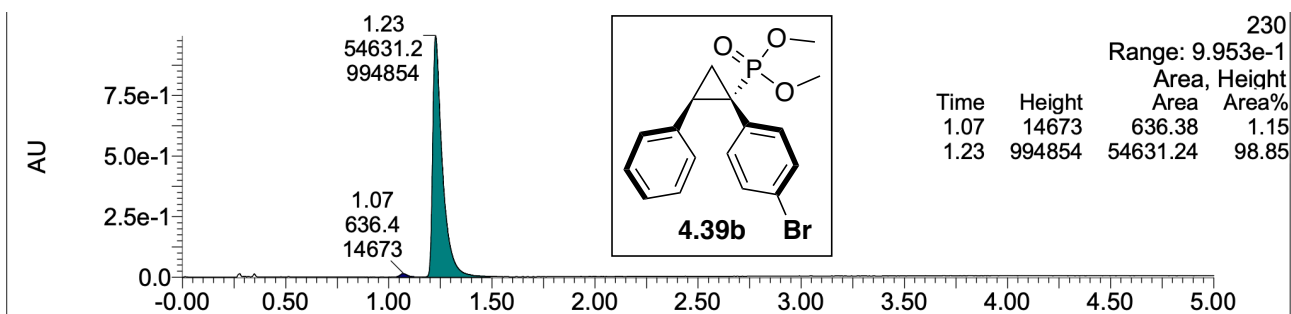
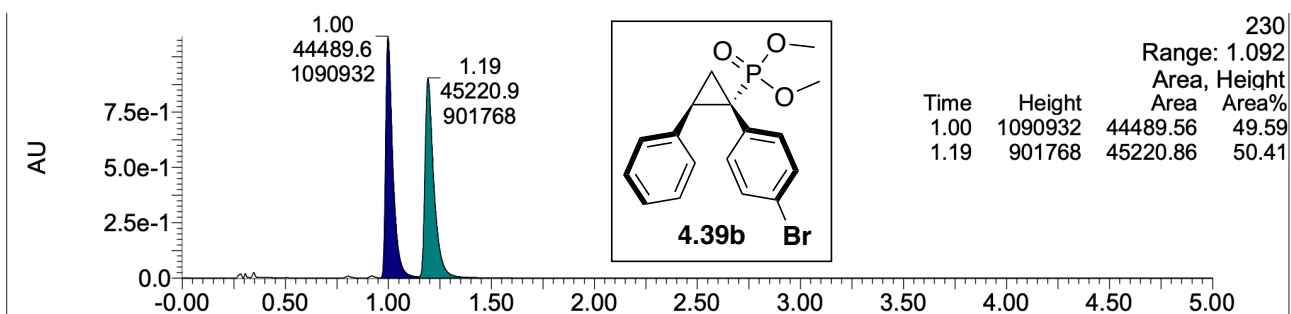
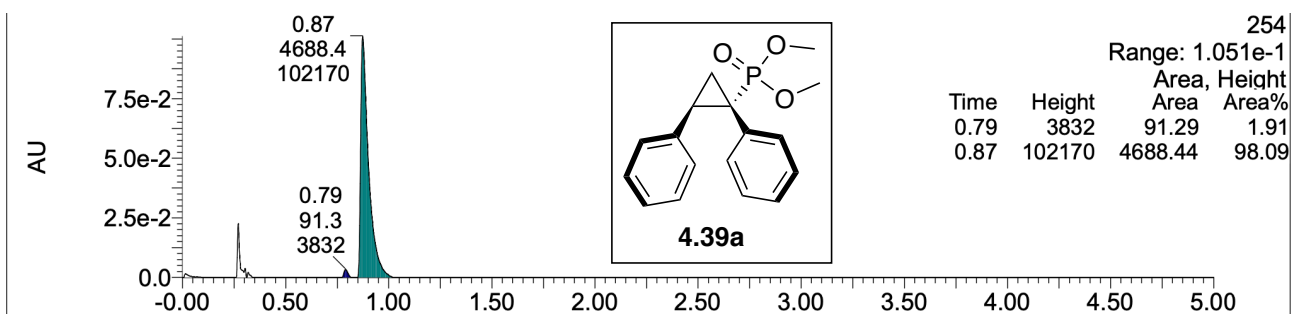
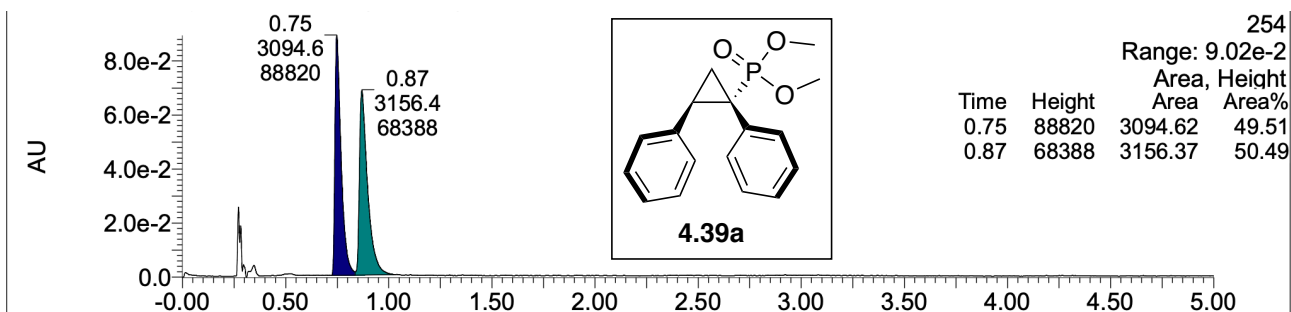


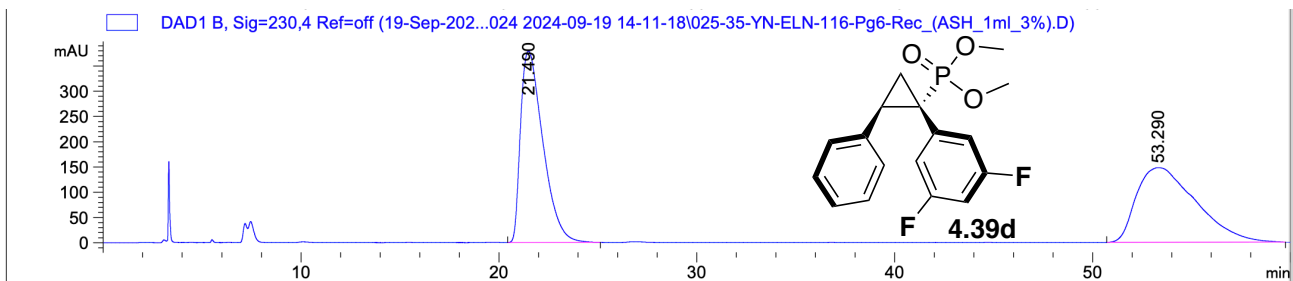
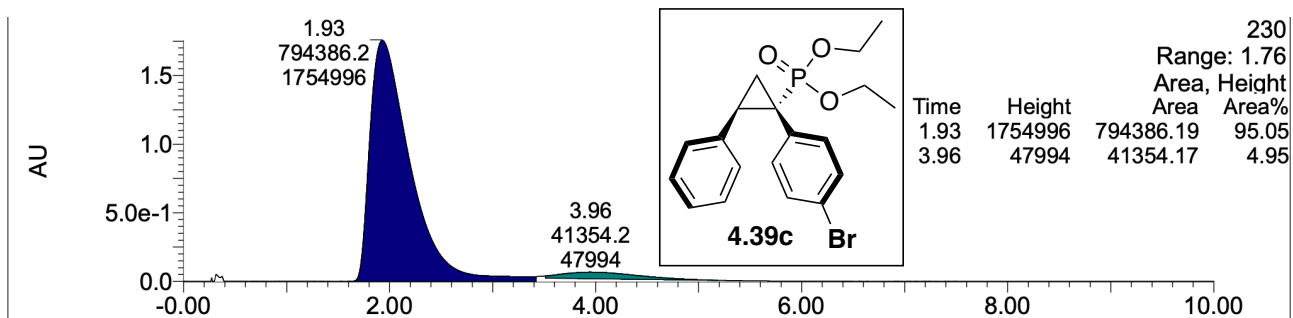
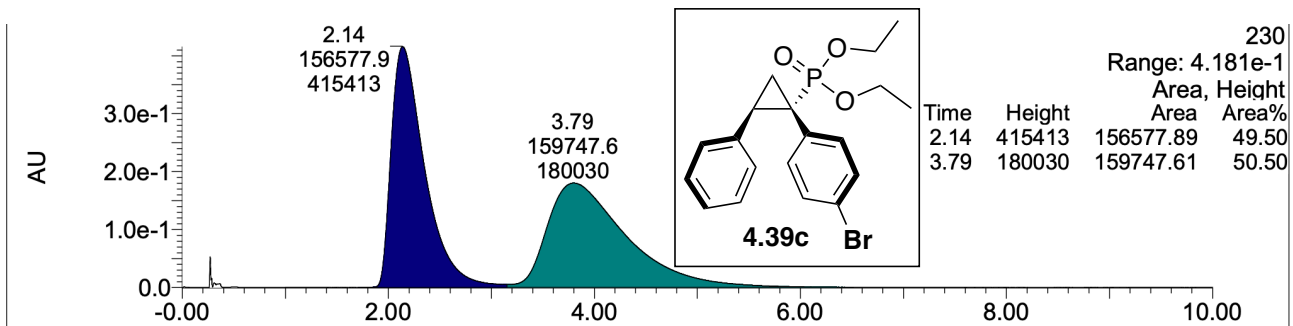
^1H NMR spectrum (600 MHz, CDCl_3) of **4.39o**.



^{31}P NMR spectrum (243 MHz, Chloroform-d) of **4.39o**.

Enantioselectivity Determination by HPLC or SFC

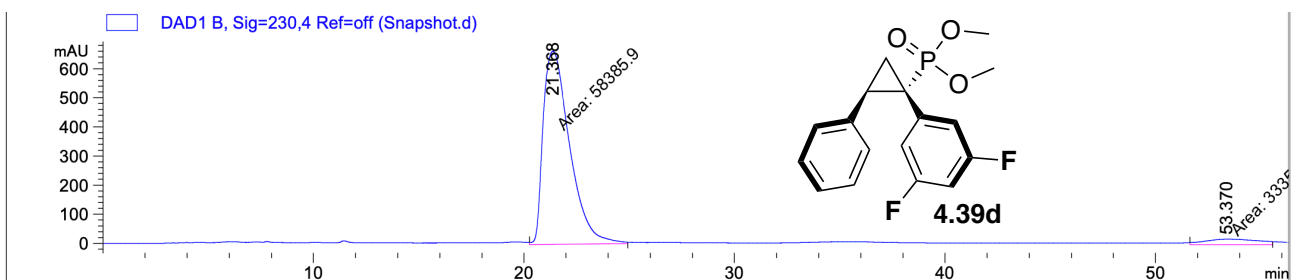




Signal 2: DAD1 B, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.490	BB	0.9190	2.96888e4	378.76147	49.0181
2	53.290	BB	2.4409	3.08782e4	147.73773	50.9819

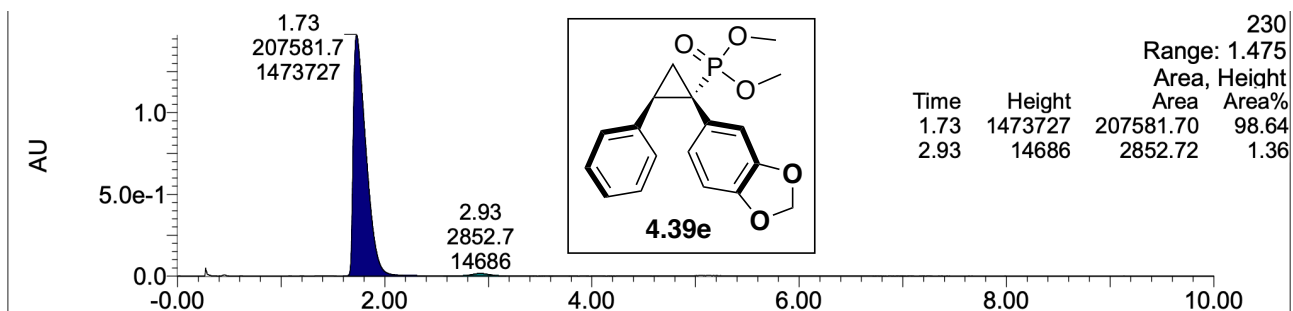
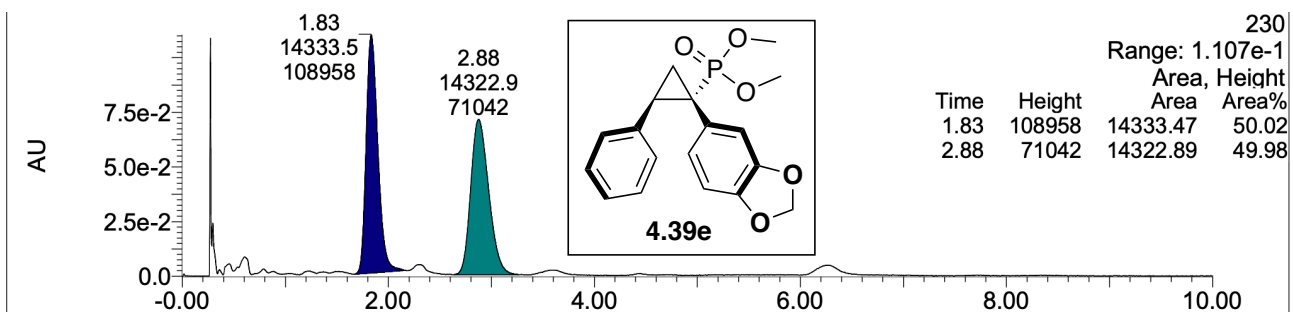
Totals : 6.05670e4 526.49921

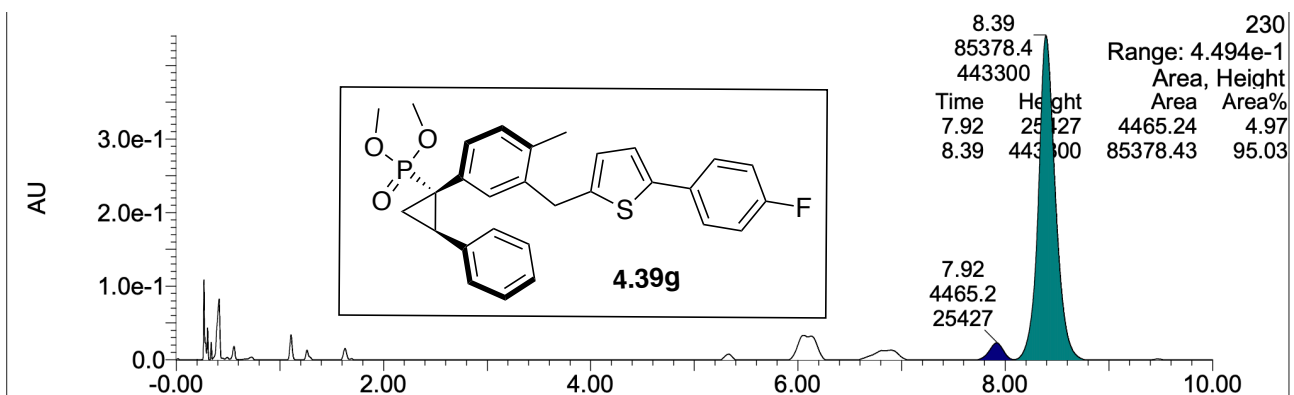
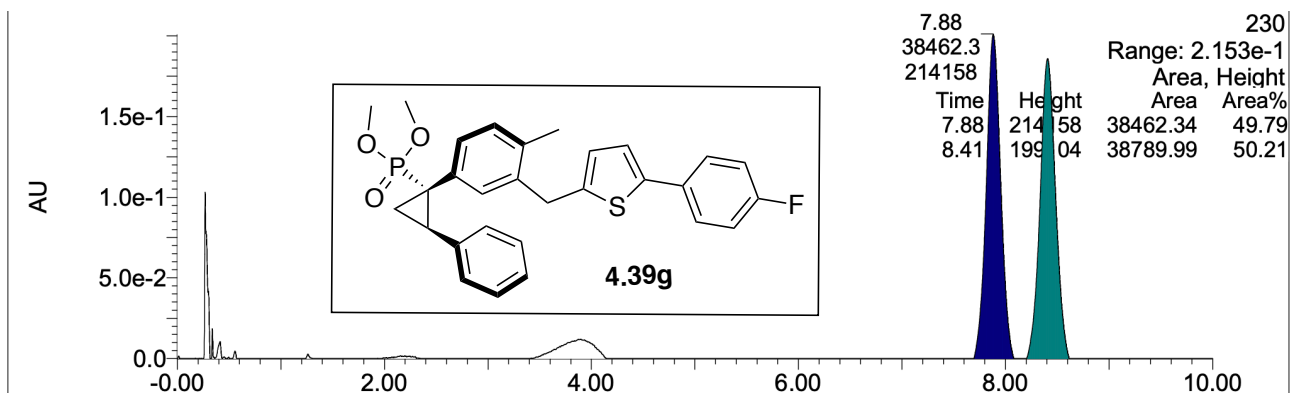
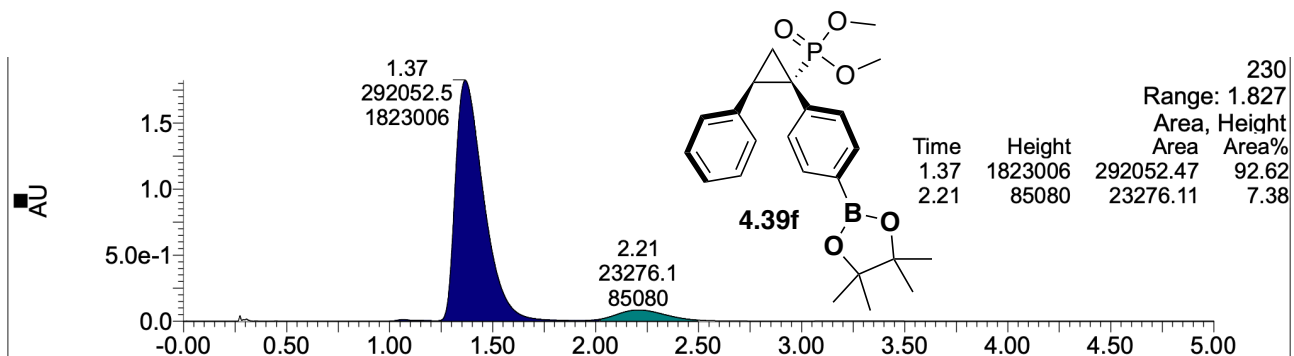
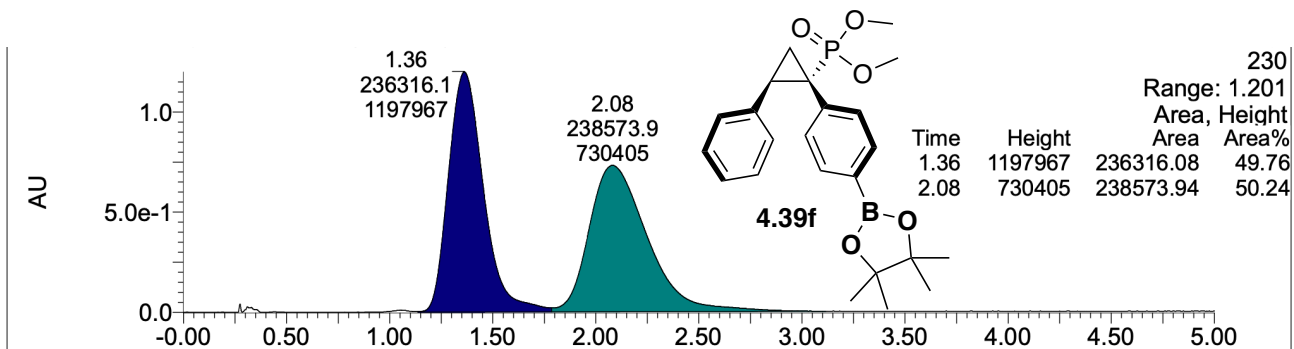


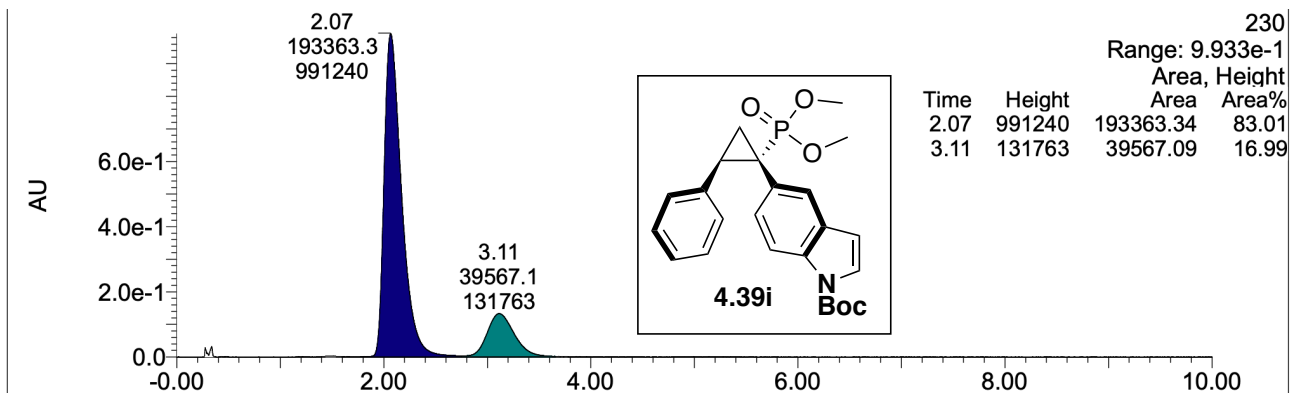
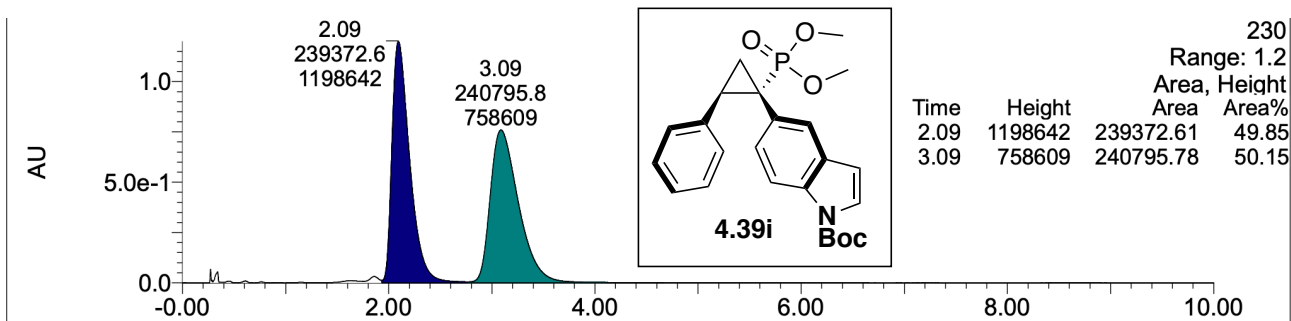
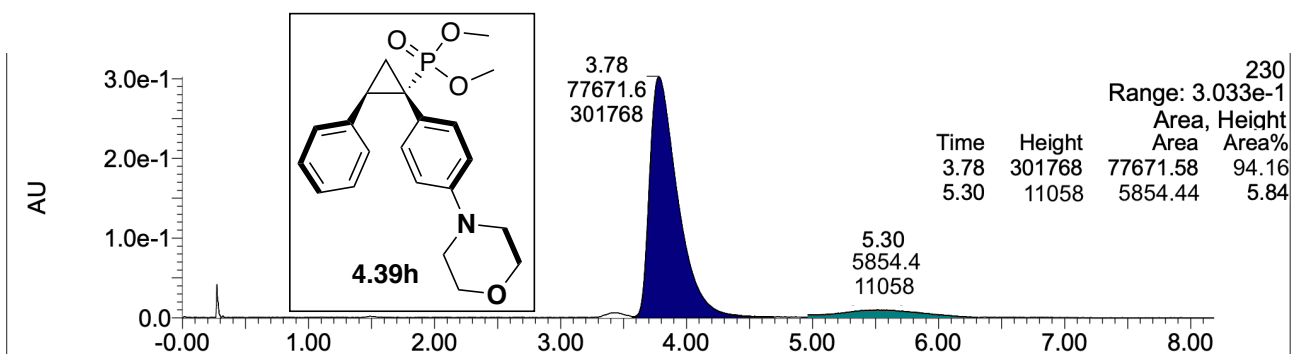
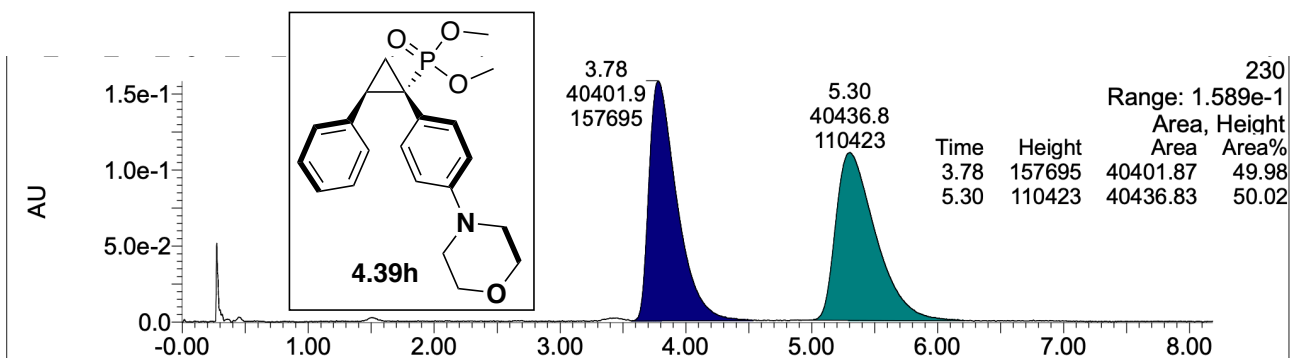
Signal 2: DAD1 B, Sig=230,4 Ref=off

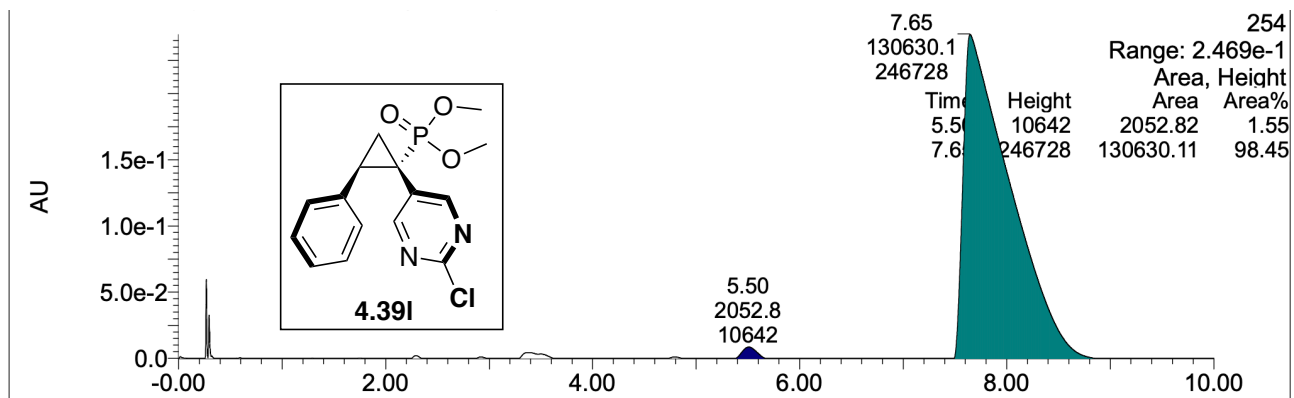
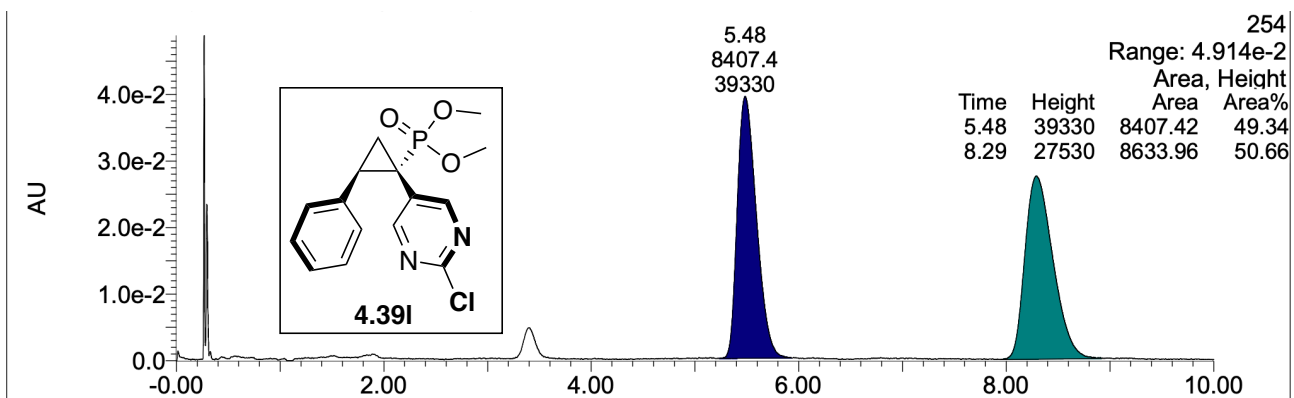
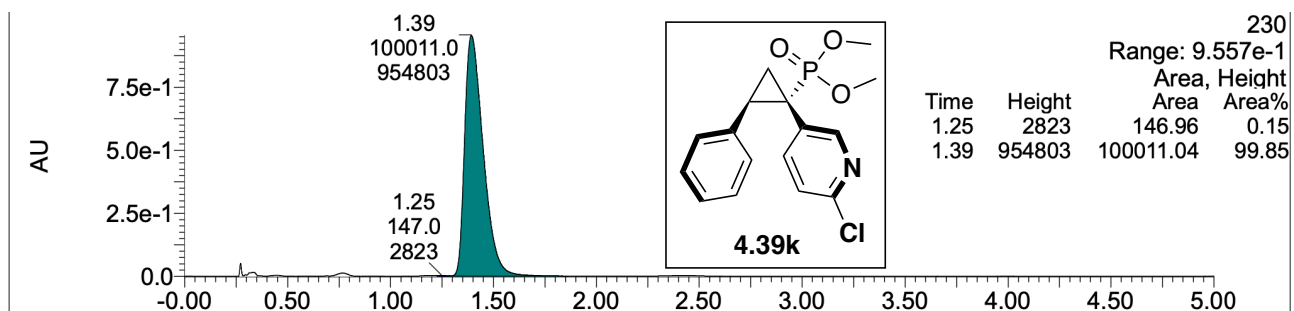
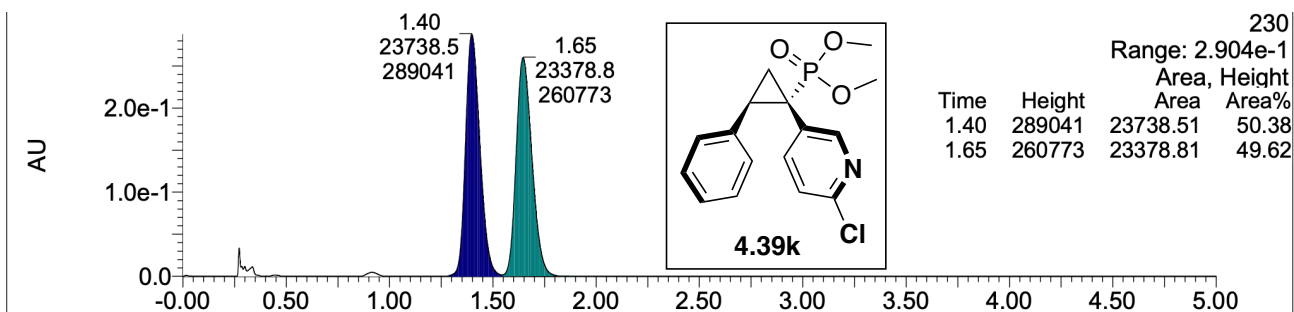
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.368	MM	1.4662	5.83859e4	663.68878	94.5962
2	53.370	MM	2.9732	3335.29956	18.69671	5.4038

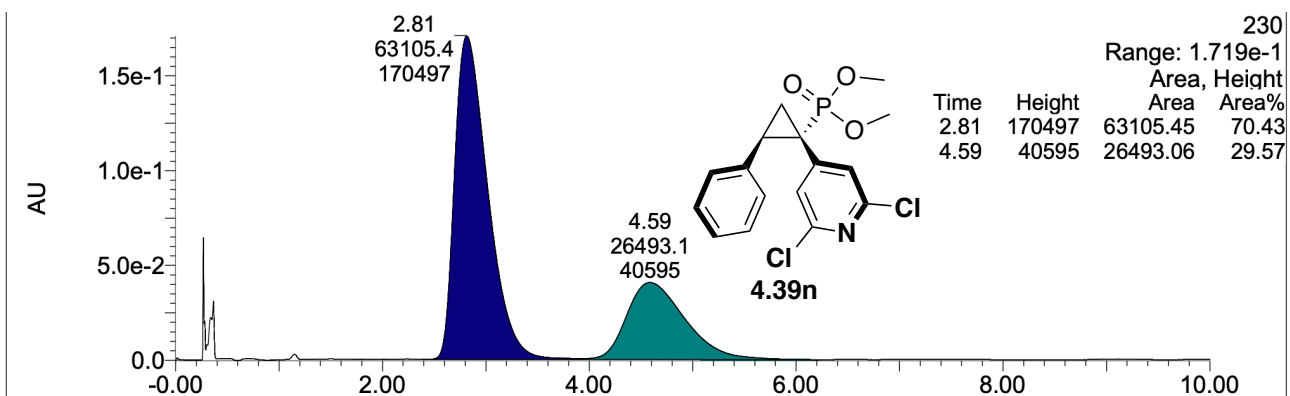
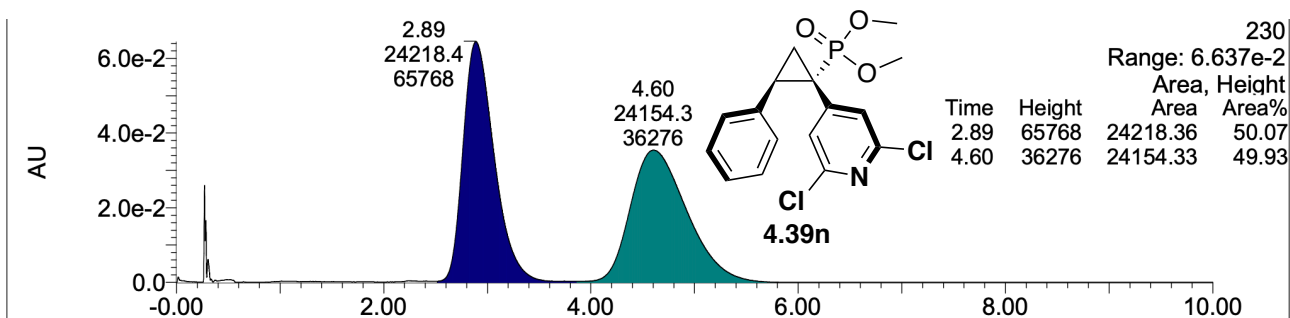
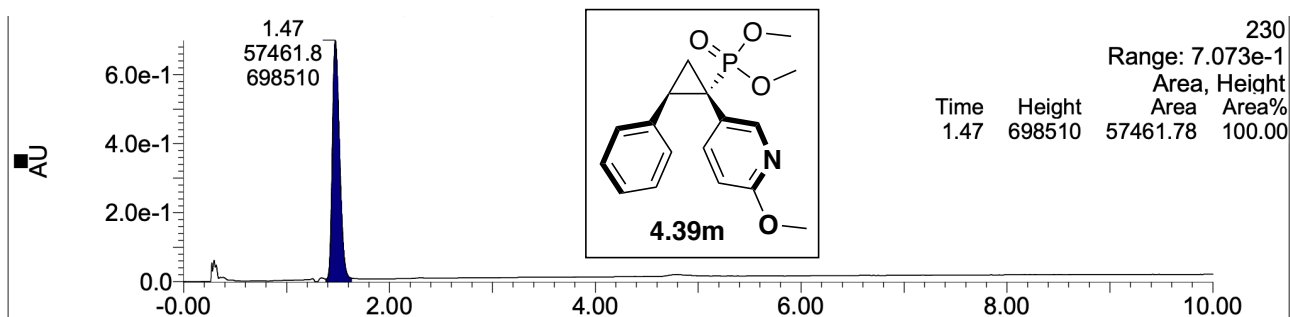
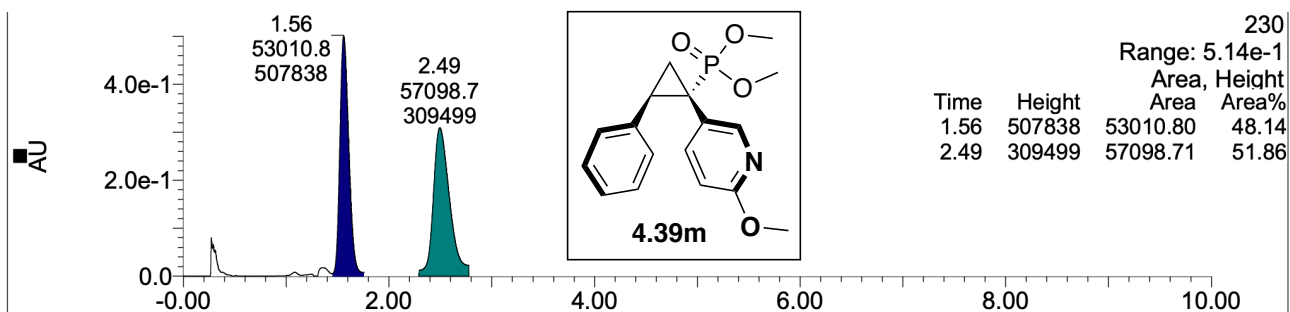
Totals : 6.17212e4 682.38549

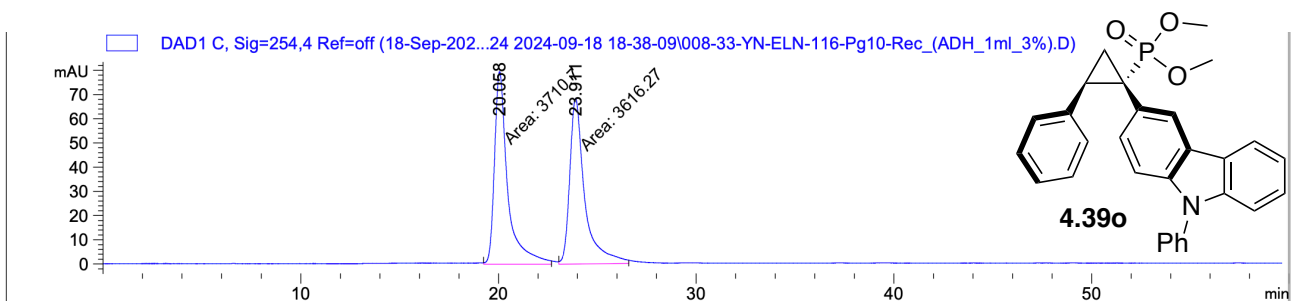








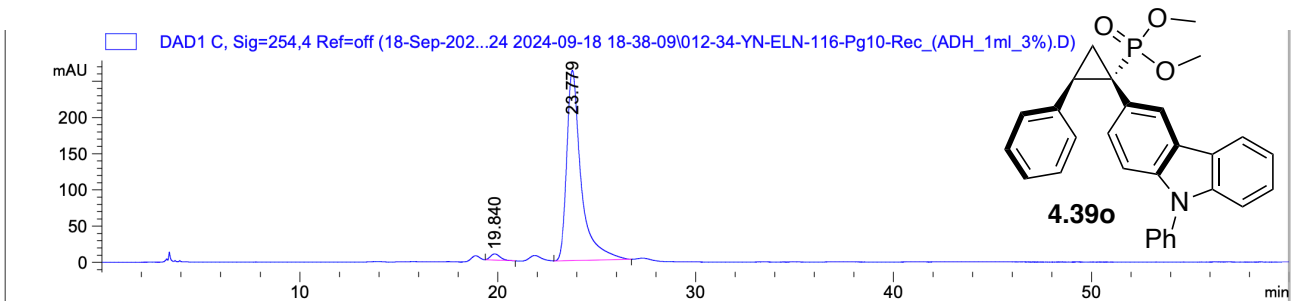




Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.058	MM	0.7771	3710.70142	79.58295	50.6444
2	23.911	MM	0.8804	3616.27075	68.45638	49.3556

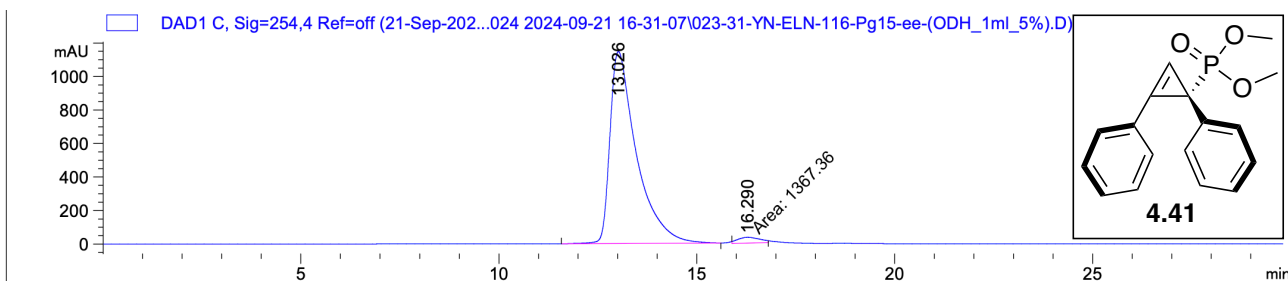
Totals : 7326.97217 148.03933



Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.840	BB	0.3942	286.00339	8.52900	2.1111
2	23.779	BB	0.6542	1.32616e4	262.60242	97.8889

Totals : 1.35476e4 271.13142



Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.026	BB	0.5564	5.31636e4	1145.58081	97.4925
2	16.290	MM	0.4673	1367.35583	34.50927	2.5075

Totals : 5.45309e4 1180.09008

References for Chapter 4

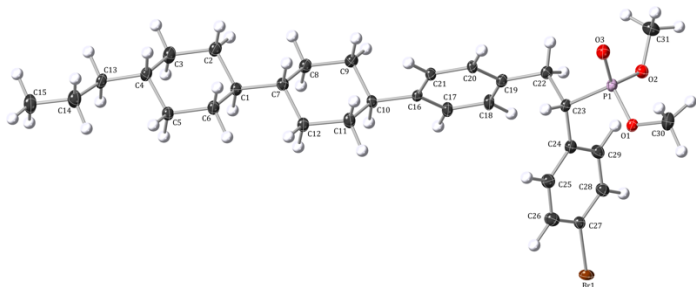
- (1) Liu, S.; Liang, Y.; Xu, L.; Dong, J. *Eur. J. Org. Chem.* **2024**, 27, e202301282.
- (2) Mayr, F.; Mohr, L.-M.; Rodriguez, E.; Bach, T. *Synthesis* **2017**, 49, 5238.
- (3) Ohira, S. *Synth. Commun.* **1989**, 19, 561.
- (4) Kong, W.-J.; Chen, X.; Wang, M.; Dai, H.-X.; Yu, J.-Q. *Org. Lett.* **2018**, 20, 284.
- (5) Shabani, S.; Hutton, C. A. *Org. Lett.* **2020**, 22, 11, 4557–4561.
- (6) Ye, F.; Wang, C.; Zhang, Y.; Wang, J. *Angew. Chem.* **2014**, 126, 11809–11812.
- (7) Beletskaya, I. P.; Titanyuk, I. D. *The Journal of Organic Chemistry* **2022**, 87.
- (8) Lee, G. H.; Davies, H. L. M. *Org. Lett.* **2004**, 6, 13, 2117–2120.
- (9) Uehara, M.; Suematsu, H.; Yasutomi, Y.; Katsuki, T. *J. Am. Chem. Soc.* **2011**, 133, 2, 170–171.



X-Ray Crystallographic Data for Compound 2.42, 2.47e, 2.49e, and 4.39b.

Crystal Data and Experimental for Compound 2.47e (CCDC 2194599).

Crystal data and structure refinement for compound 2.47e



Experimental. Single colorless needle-shaped crystals of compound **2.47e** were recrystallised from a mixture of DCM and pentane by slow evaporation. A suitable crystal with dimensions $0.23 \times 0.03 \times 0.02$ mm³ was selected and mounted on a loop with paratone on a XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was kept at a steady $T = 101(1)$ K during data collection. The structure was solved with the **ShelXT** 2018/2 (Sheldrick, 2018) solution and by using **Olex2** 1.5-alpha (Dolomanov et al., 2009) as the graphical interface. The model was refined with **olex2.refine** 1.5-alpha (Bourhis et al., 2015) using full matrix least squares minimisation on F^2 .

Crystal Data. C₃₁H₄₄BrO₃P, $M_r = 575.570$, triclinic, $P1$ (No. 1), $a = 5.48884(19)$ Å, $b = 11.0126(4)$ Å, $c = 24.3359(7)$ Å, $\alpha = 83.978(3)^\circ$, $\beta = 85.694(3)^\circ$, $\gamma = 83.124(3)^\circ$, $V = 1449.46(8)$ Å³, $T = 101(1)$ K, $Z = 2$, $Z' = 2$, $\mu(\text{Cu K}\alpha) = 2.678$, 15748 reflections measured, 7568 unique ($R_{\text{int}} = 0.0873$) which were used in all calculations. The final wR_2 was 0.1454 (all data) and R_1 was 0.0612 ($I \geq 2 \sigma(I)$).

Structure Quality Indicators

Reflections:	d min (Cu\lambda)	0.80	I/\sigma(I)	9.0	Rint	8.73%	Full 135.4°	99.1
	2\Theta=146.9°						94% to 146.9°	
Refinement:	Shift	-0.007	Max Peak	0.6	Min Peak	-0.4	GooF	1.038
							Hooft	-.05(3)

Compound	2.47e
Formula	C ₃₁ H ₄₄ BrO ₃ P
$D_{\text{calc.}} / \text{g cm}^{-3}$	1.319
μ / mm^{-1}	2.678
Formula Weight	575.570
Colour	colourless
Shape	needle-shaped
Size/mm ³	0.23×0.03×0.02
T/K	101(1)
Crystal System	triclinic
Flack Parameter	-0.05(3)
Hooft Parameter	-0.05(3)
Space Group	$P1$
$a/\text{\AA}$	5.48884(19)
$b/\text{\AA}$	11.0126(4)
$c/\text{\AA}$	24.3359(7)
$\alpha/^\circ$	83.978(3)
$\beta/^\circ$	85.694(3)
$\gamma/^\circ$	83.124(3)
$V/\text{\AA}^3$	1449.46(8)
Z	2
Z'	2
Wavelength/Å	1.54184
Radiation type	Cu K α
$\theta_{\text{min}}/^\circ$	3.66
$\theta_{\text{max}}/^\circ$	73.45
Measured Refl's.	15748
Indep't Refl's	7568
Refl's $I \geq 2 \sigma(I)$	6344
R_{int}	0.0873
Parameters	751
Restraints	851
Largest Peak	0.5986
Deepest Hole	-0.3505
GooF	1.0375
wR_2 (all data)	0.1454
wR_2	0.1367
R_1 (all data)	0.0748
R_1	0.0612

A colorless needle-shaped crystal with dimensions $0.23 \times 0.03 \times 0.02 \text{ mm}^3$ was mounted on a loop with paratone. Data were collected using a XtaLAB Synergy, Dualflex, HyPix diffractometer equipped with an Oxford Cryosystems low-temperature device operating at $T = 101(1) \text{ K}$.

Data were measured using ω scans with Cu $K\alpha$ radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlisPro 1.171.41.116a (Rigaku OD, 2021). The maximum resolution that was achieved was $\Theta = 73.45^\circ$ ($0.80 \text{ \AA}$).

The unit cell was refined using CrysAlisPro 1.171.41.116a (Rigaku OD, 2021) on 6826 reflections, 43% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using CrysAlisPro 1.171.41.116a (Rigaku OD, 2021). The final completeness is 99.09 % out to 73.45° in Θ . An analytical numeric absorption correction using a multifaceted crystal model based on expressions derived by R.C. Clark & J.S. Reid. (Clark, R. C. & Reid, J. S. (1995). Acta Cryst. A51, 887-897) was performed using CrysAlisPro 1.171.41.108a (Rigaku Oxford Diffraction, 2021). An empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm was also applied. The absorption coefficient μ of this material is 2.678 mm^{-1} at this wavelength ($\lambda = 1.54184 \text{ \AA}$) and the minimum and maximum transmissions are 0.654 and 0.947.

The structure was solved and the space group $P1$ (# 1 determined by the ShelXT 2018/2 (Sheldrick, 2018) structure solution program and refined by full matrix least squares minimisation on F^2 using version of **olex2.refine** 1.5-alpha (Bourhis et al., 2015). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. Hydrogen atom positions were calculated geometrically and refined refined using the Hirshfeld model.

Refinement was by using NoSpherA2, an implementation of non-spherical atom-form-factors (F. Kleemiss, H. Puschmann, O. Dolomanov, S.Grabowsky - <https://doi.org/10.1039/D0SC05526C> – 2020). NoSpherA2 implementation of HAR makes use of tailor-made aspherical atomic form factors calculated from a Hirshfeld-partitioned electron density (ED) not from spherical-atom form factors. The ED was calculated from a Gaussian basis set single determinant SCF wavefunction from DFT using selected functionals for a fragment of this crystal. The following options were used: SOFTWARE: ORCA PARTITIONING: NoSpherA2 INT ACCURACY: Normal METHOD: PBE BASIS SET: def2-SVP CHARGE: 0 MULTIPLICITY: 1 DATE: 2021-10-08_16-37-20

The value of Z' is 2. This means that there are two independent molecules in the asymmetric unit.

The Flack parameter was refined to $-0.05(3)$. Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2 results in $-0.05(3)$. Note: The Flack parameter is used to determine chirality of the crystal studied, the value should be near 0, a value of 1 means that the stereochemistry is wrong, and the model should be inverted. A value of 0.5 means that the crystal consists of a racemic mixture of the two enantiomers.

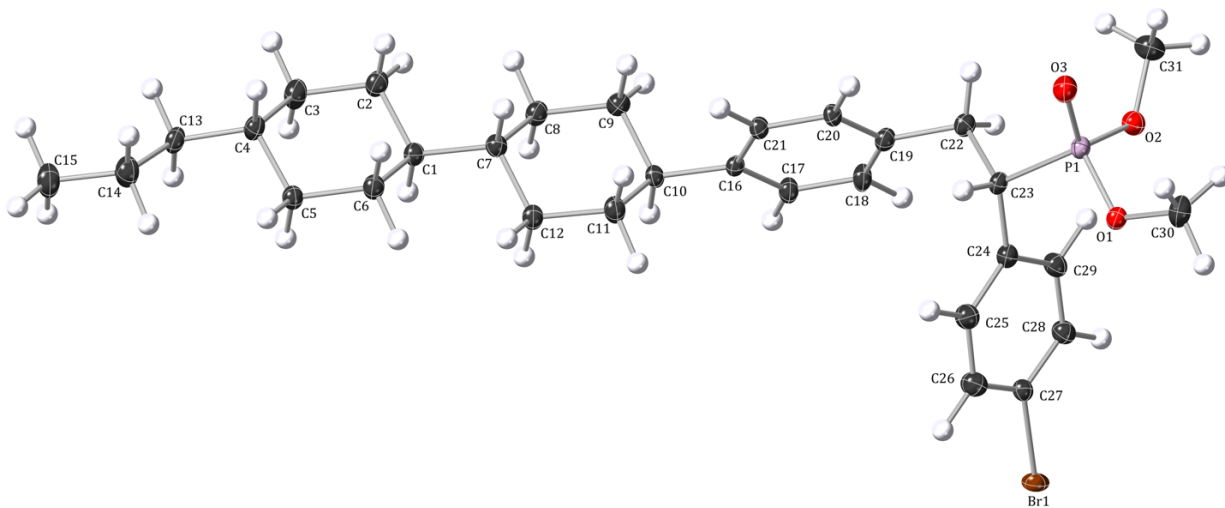


Figure S1: The molecular structure.

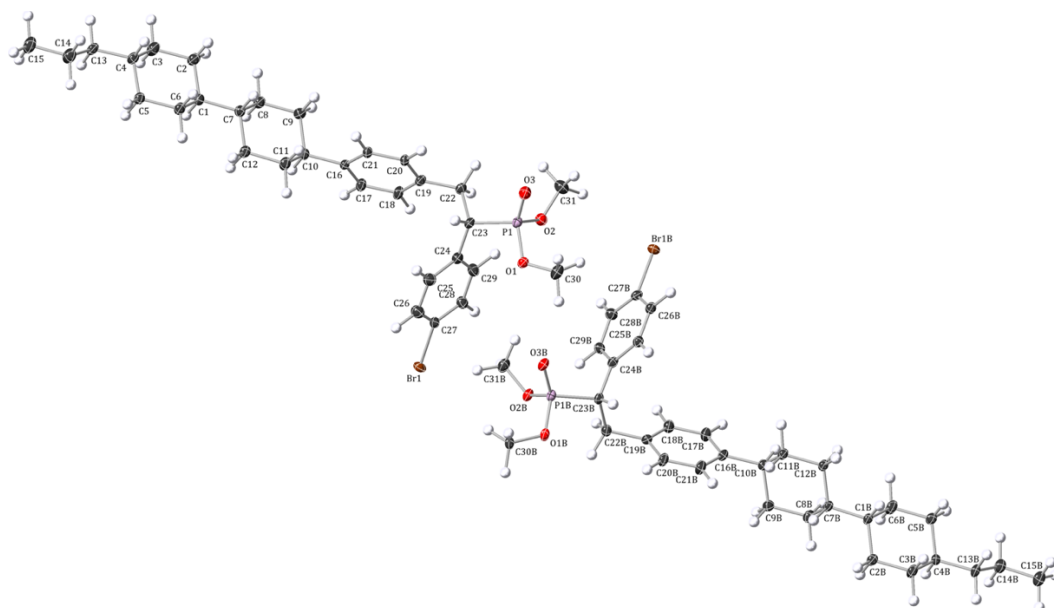


Figure S2: The asymmetric unit consists of two independent molecules.

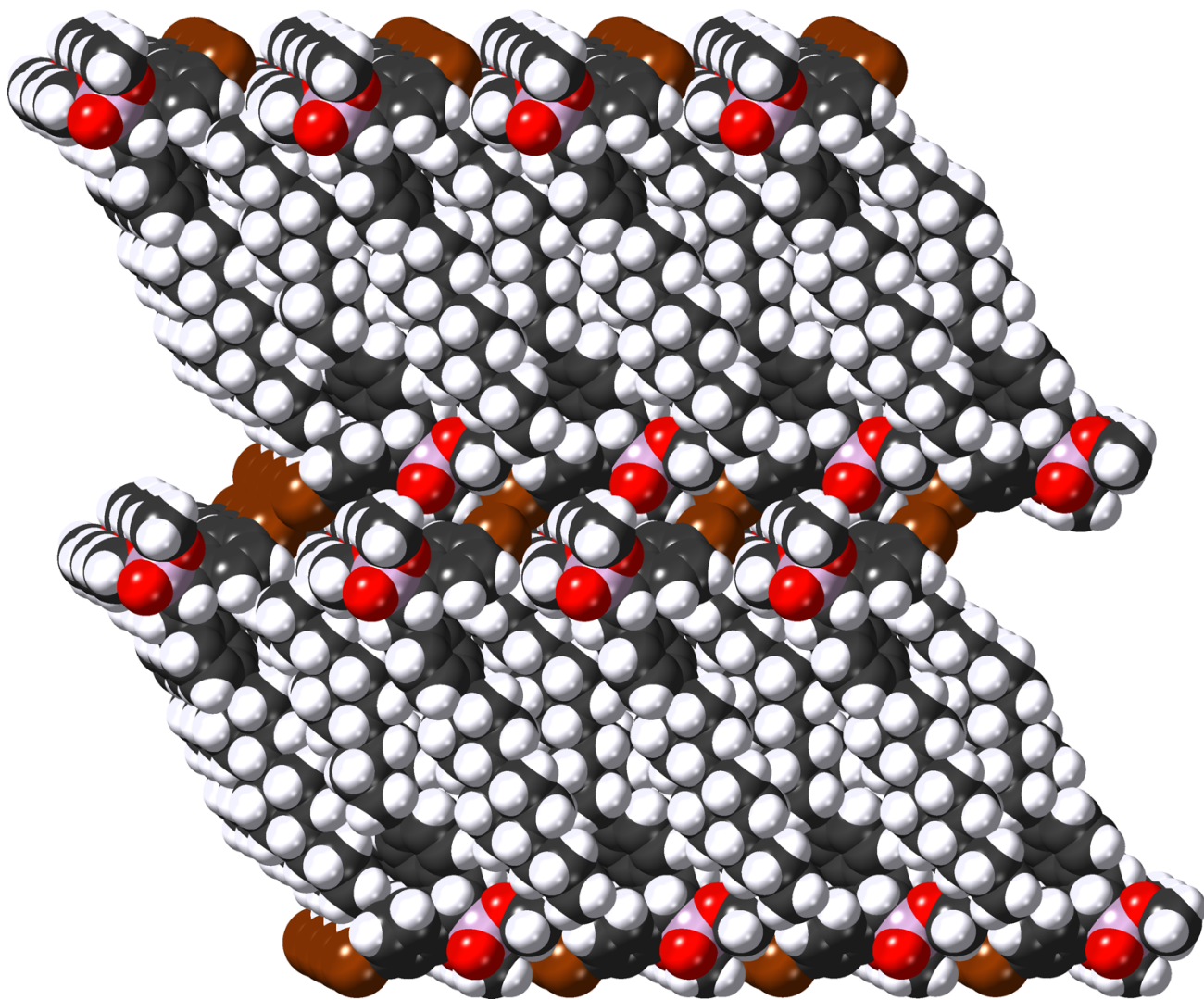


Figure S3: Molecular packing viewed along the a-crystallographic axis. The atoms are shown as spheres with van der Waals radii.

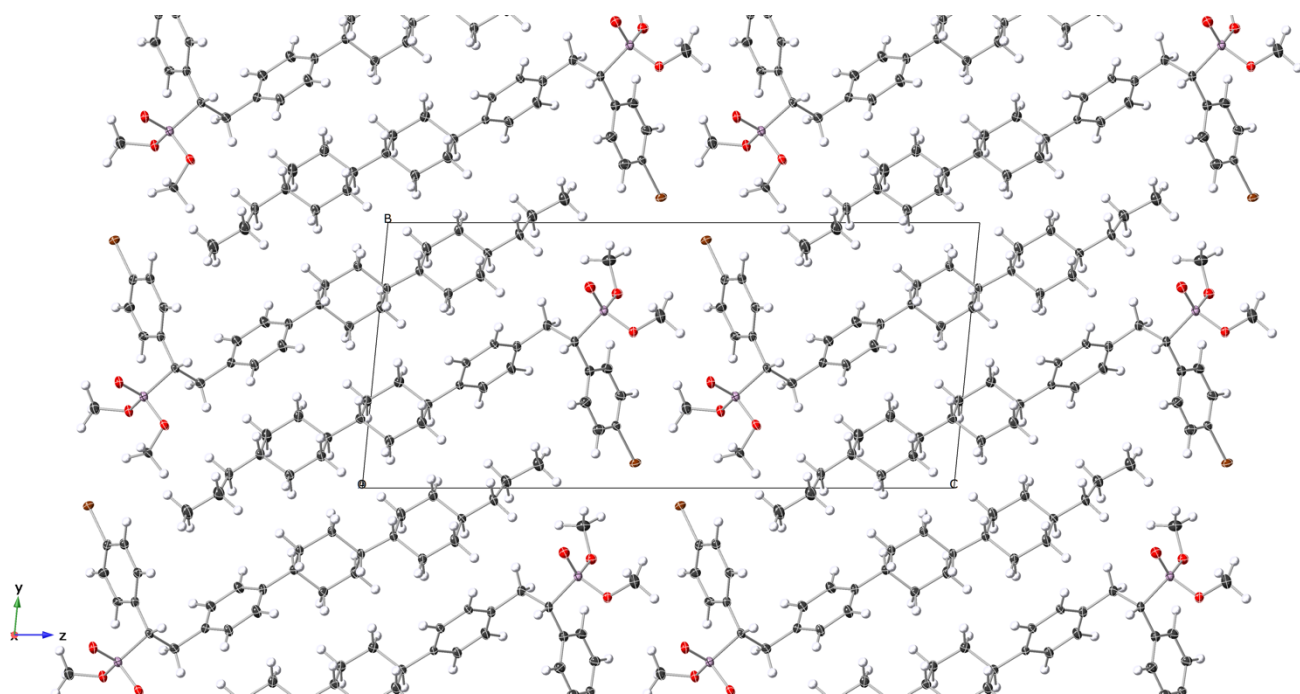


Figure S4: Molecular packing viewed along the a-crystallographic axis.

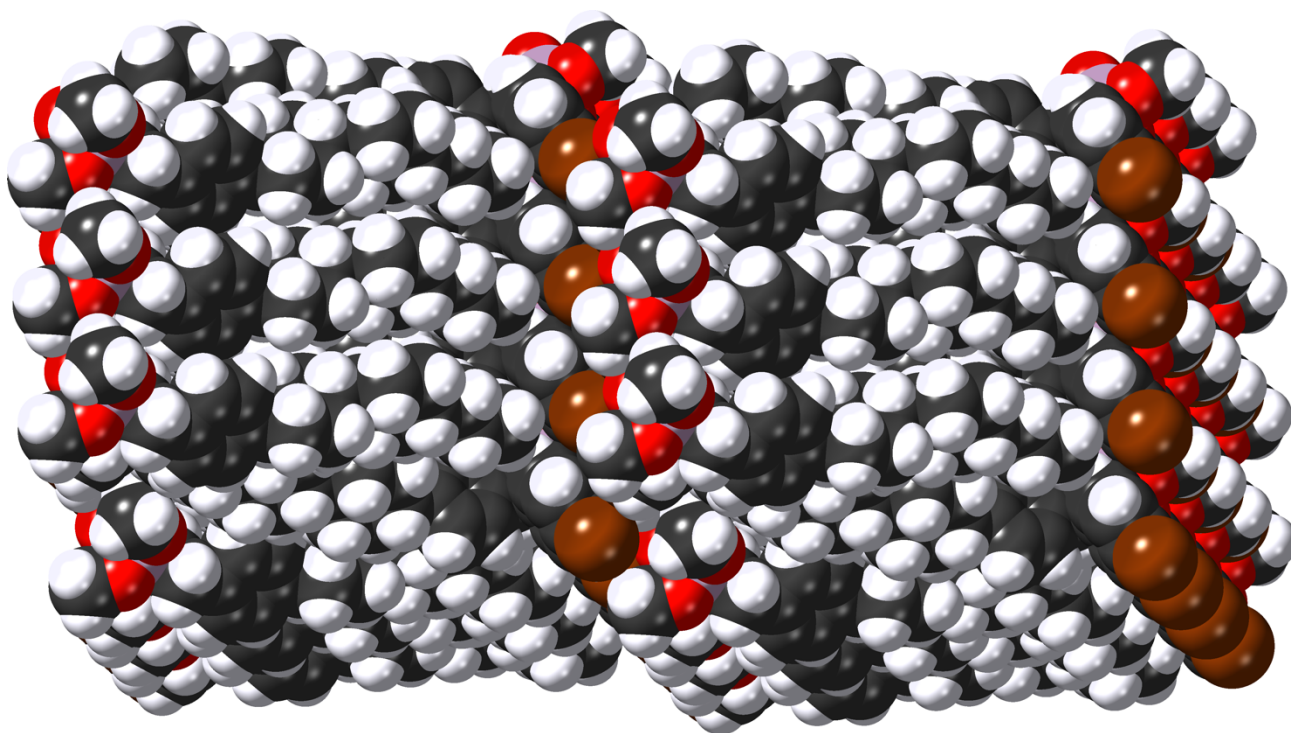


Figure S5: Molecular packing viewed along the b-crystallographic axis. The atoms are shown as spheres with van der Waals radii.

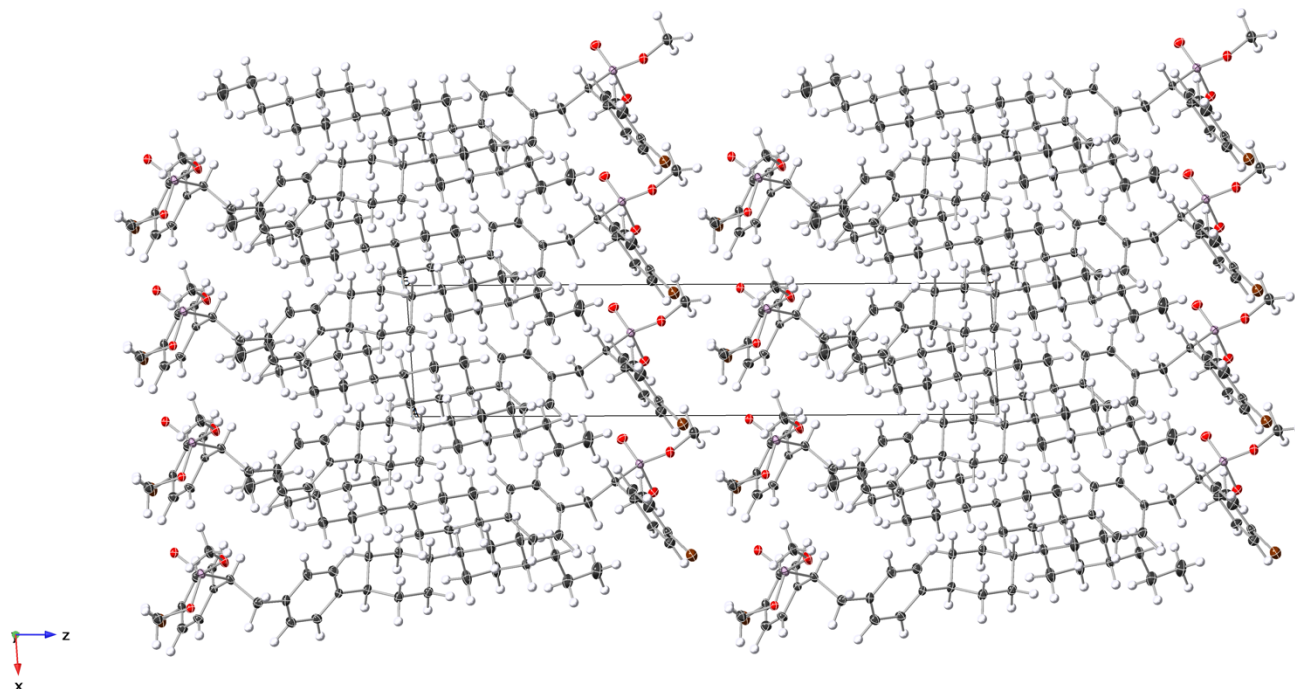


Figure S6: Molecular packing viewed along the b-crystallographic axis.

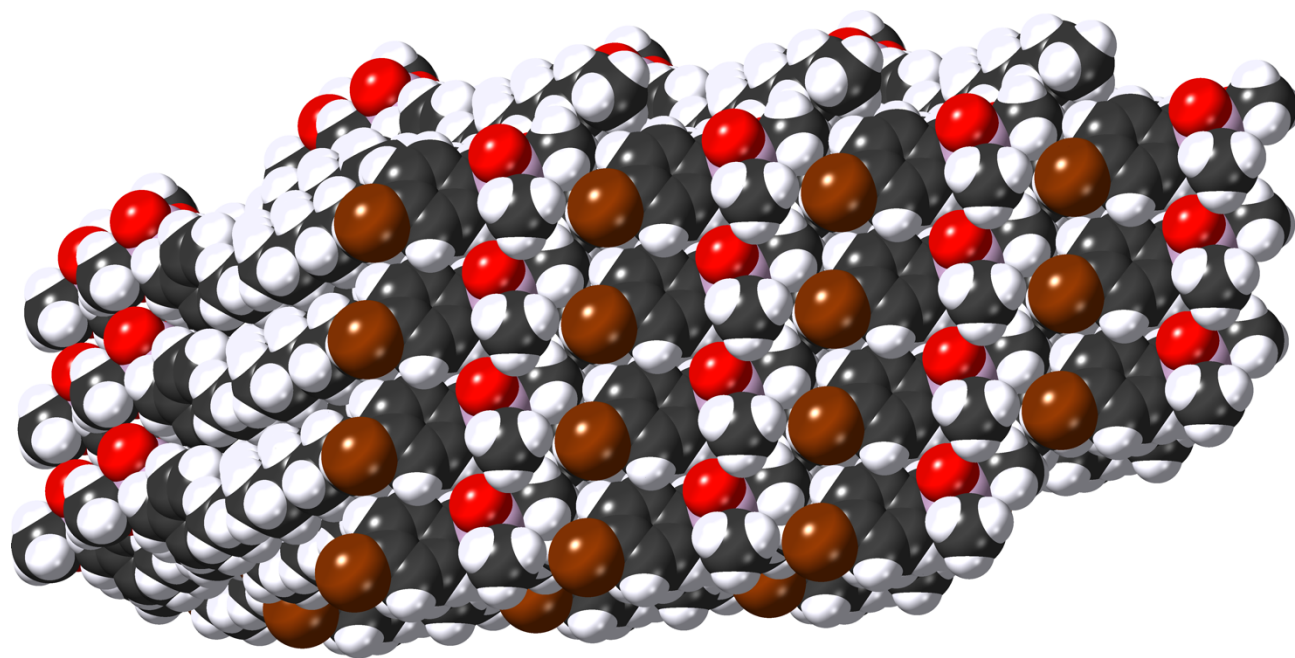
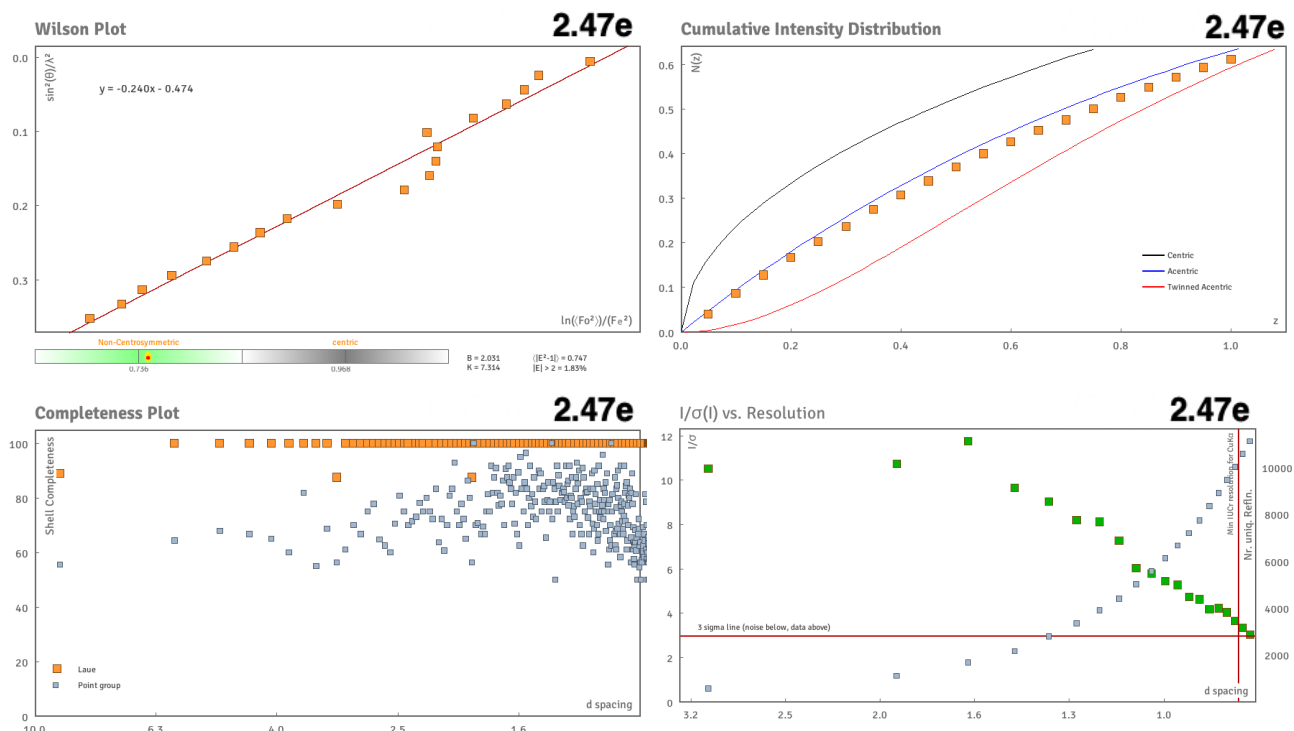
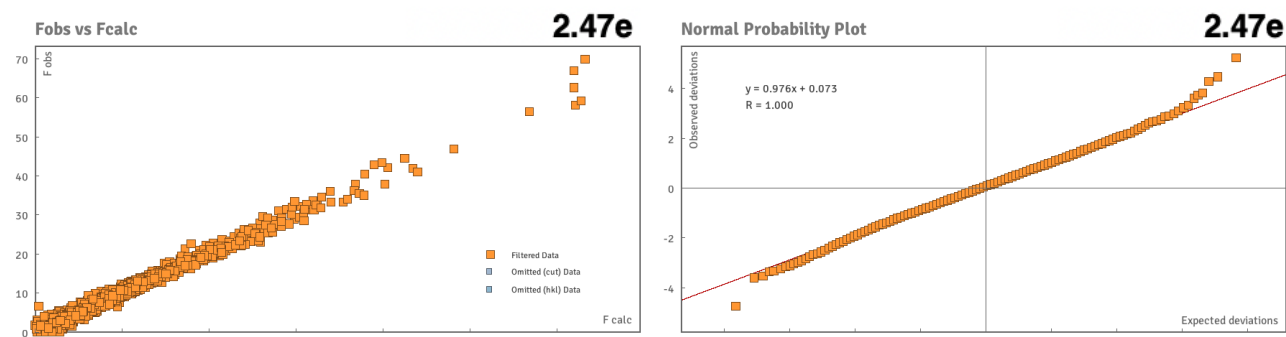


Figure S7: Molecular packing viewed along the c-crystallographic axis. The atoms are shown as spheres with van der Waals radii.

Data Plots: Diffraction Data



Data Plots: Refinement and Data



Reflection Statistics

Total reflections (after filtering)	15748	Unique reflections	7568
Completeness	0.648	Mean I/σ	6.98
$hkl_{\max}$ collected	(6, 13, 29)	$hkl_{\min}$ collected	(-6, -13, -25)
$hkl_{\max}$ used	(6, 13, 29)	$hkl_{\min}$ used	(-6, -13, -25)
Lim $d_{\max}$ collected	100.0	Lim $d_{\min}$ collected	0.77
$d_{\max}$ used	12.08	$d_{\min}$ used	0.8
Friedel pairs	2064	Friedel pairs merged	0
Inconsistent equivalents	2	R_{int}	0.0873
R_{sigma}	0.1106	Intensity transformed	0
Omitted reflections	0	Omitted by user (OMIT hkl)	1
Multiplicity	(3399, 2086, 1050, 526, 276, 128, 70, 24, 8, 1, 1)	Maximum multiplicity	11
Removed systematic absences	0	Filtered off (Shel/OMIT)	0

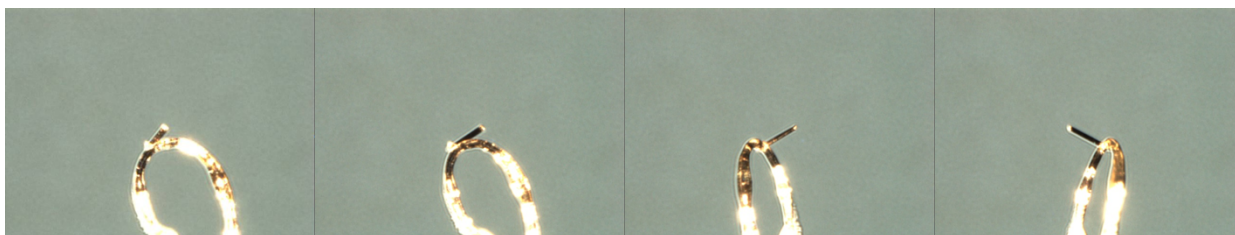


Table S4: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for compound **2.47e**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
Br1	10640.1(5)	949.0(5)	4573.9(4)	23.6(6)
C1	7114(8)	1910(4)	-664.2(14)	17.9(12)
O1	2802(6)	5881(3)	4324.2(12)	19.6(9)
P1	3669.8(19)	6685.0(13)	3793.2(7)	16.1(4)
C2	7679(10)	2716(4)	-1193.2(16)	25.4(14)
O2	5835(5)	7327(3)	3988.2(16)	20.7(9)
C3	8046(8)	1987(5)	-1699.8(18)	25.6(15)
O3	1763(5)	7557(3)	3521.7(16)	22.7(10)
C4	5916(8)	1282(4)	-1781.8(16)	19.5(13)
C5	5312(9)	495(4)	-1247.9(16)	19.4(13)
C6	4929(8)	1224(5)	-744.0(18)	21.8(14)
C7	6776(8)	2613(4)	-145.3(14)	17.7(12)
C8	8970(8)	3290(5)	-64.8(17)	20.8(13)
C9	8615(8)	4002(4)	448.2(15)	19.0(12)
C10	8065(7)	3164(4)	977.5(14)	18.1(12)
C11	5885(8)	2472(5)	901.8(18)	25.5(15)
C12	6247(10)	1785(4)	380.5(16)	24.0(14)
C13	6487(8)	527(5)	-2273.6(19)	23.0(15)
C14	4470(9)	-196(6)	-2413(3)	30.3(17)
C15	5209(11)	-898(7)	-2917(3)	40(2)
C16	7669(7)	3888(4)	1478.2(16)	15.5(12)
C17	9401(8)	3803(5)	1873.6(19)	21.5(14)
C18	9084(8)	4512(5)	2320(2)	21.6(13)
C19	6992(7)	5340(4)	2383.3(16)	18.9(12)
C20	5222(7)	5432(5)	1995.0(18)	18.1(13)
C21	5558(7)	4723(5)	1550.3(19)	18.3(13)
C22	6586(8)	6122(4)	2863.9(15)	20.7(13)
C23	5006(7)	5525(3)	3351.0(13)	16.1(11)
C24	6355(7)	4411(3)	3649(2)	17.0(12)
C25	5646(8)	3236(3)	3635(2)	23.3(14)
C26	6879(8)	2195(4)	3903(2)	27.2(15)
C27	8879(7)	2350(3)	4191(2)	18.4(12)
C28	9683(8)	3484(3)	4216(2)	21.8(14)
C29	8396(8)	4513(4)	3941(2)	20.7(13)
C30	1318(9)	6480(6)	4757(2)	27.2(15)
C31	6221(10)	8576(4)	3798(3)	27.2(16)
Br1B	5463.8(5)	9336.0(5)	5407.4(4)	24.1(6)
C1B	355(8)	8179(4)	10612.5(14)	18.9(12)
O1B	932(6)	2376(3)	6557.1(14)	22.5(10)
P1B	1900(2)	3448.6(13)	6158.1(6)	16.4(4)
C2B	-26(10)	7323(4)	11135.3(15)	25.7(14)
O2B	4527(5)	2897(3)	5930.8(13)	19.0(9)
C3B	-606(9)	8024(5)	11648.6(18)	26.8(15)
O3B	291(5)	3985(3)	5715.1(13)	19.9(9)

Atom	x	y	z	U_{eq}
C4B	1306(8)	8858(4)	11735.8(16)	17.7(12)
C5B	1687(10)	9710(4)	11209.8(17)	28.3(16)
C6B	2288(9)	9016(5)	10697.7(19)	30.2(16)
C7B	834(7)	7518(4)	10085.3(13)	16.8(12)
C8B	3392(7)	6817(5)	10022.5(17)	21.9(14)
C9B	3727(9)	6093(4)	9512.2(15)	20.4(13)
C10B	3165(7)	6925(4)	8979.5(14)	18.2(12)
C11B	632(7)	7655(5)	9042.8(18)	19.5(14)
C12B	349(9)	8362(4)	9559.2(15)	20.1(13)
C13B	612(8)	9553(5)	12242.8(19)	22.9(14)
C14B	2594(9)	10252(6)	12421(2)	28.7(16)
C15B	1785(11)	10901(7)	12937(3)	37(2)
C16B	3429(7)	6186(4)	8484.5(16)	16.9(12)
C17B	5357(8)	6261(5)	8082.0(18)	20.5(13)
C18B	5617(8)	5553(4)	7635(2)	20.9(13)
C19B	3966(7)	4721(4)	7579.0(16)	17.5(12)
C20B	2004(8)	4643(5)	7975.1(19)	22.1(14)
C21B	1748(8)	5357(5)	8418(2)	22.4(14)
C22B	4137(8)	3958(4)	7091.0(15)	20.1(13)
C23B	2354(7)	4524(3)	6644.6(13)	17.1(12)
C24B	3081(6)	5709(3)	6349(2)	16.7(12)
C25B	1504(7)	6803(3)	6347(2)	17.5(12)
C26B	2144(7)	7892(4)	6070(2)	19.6(12)
C27B	4427(7)	7857(3)	5786(2)	19.8(12)
C28B	6060(7)	6801(3)	5769(2)	20.7(14)
C29B	5363(7)	5719(4)	6056(2)	18.3(12)
C30B	222(10)	1329(4)	6321(3)	22.5(15)
C31B	5313(9)	3010(6)	5351.8(17)	25.2(14)

Table S5: Anisotropic Displacement Parameters ($\times 10^4$) for compound **2.47e**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \dots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	29.9(11)	13.7(10)	24.3(12)	3.4(7)	1.6(8)	2.3(8)
C1	19(3)	19(3)	16(2)	-1.4(16)	0.6(14)	-3.5(14)
O1	24(2)	20(2)	15.1(18)	-5.4(14)	-1.1(12)	-1.9(12)
P1	15.4(7)	18.2(8)	14.4(8)	-0.2(6)	-0.2(6)	-3.3(6)
C2	34(3)	28(3)	17(2)	-13(2)	-0.9(16)	-1.7(15)
O2	20(2)	21(2)	22(2)	-3.3(12)	-5.0(14)	-2.7(15)
C3	26(3)	36(3)	19(3)	-17(2)	0.8(18)	-5.2(19)
O3	19(2)	25(2)	23(2)	5.2(13)	-5.4(14)	-4.6(15)
C4	19(3)	25(3)	15(2)	-5.9(17)	-2.8(15)	-2.3(15)
C5	21(3)	21(3)	17(2)	-5.7(18)	-0.7(16)	-3.5(15)
C6	26(3)	23(3)	17(3)	-7.4(18)	0.5(17)	-3.7(18)
C7	16(2)	18(3)	18(2)	0.5(15)	0.0(14)	-3.7(14)
C8	22(3)	24(3)	17(3)	-5.0(17)	-0.5(16)	-2.3(17)
C9	16(3)	22(3)	19(2)	-4.6(18)	-0.5(15)	-0.8(15)
C10	23(3)	17(3)	15(2)	-2.9(16)	1.5(14)	-5.0(13)
C11	34(3)	26(3)	19(3)	-12.3(19)	1.3(17)	-6.0(19)
C12	33(3)	23(3)	17(2)	-9(2)	-0.8(16)	-3.9(15)
C13	29(3)	28(3)	13(3)	-8(2)	-0.7(18)	-3.2(18)
C14	35(3)	36(4)	24(3)	-15(2)	-4(2)	-7(2)
C15	58(5)	41(5)	25(4)	-16(3)	-3(3)	-12(3)
C16	19(2)	16(2)	12(2)	0.2(15)	-0.3(13)	-2.2(14)
C17	24(3)	22(3)	18(3)	3.5(18)	-6.2(15)	-6.5(17)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C18	23(3)	26(3)	17(3)	-0.4(17)	-4.3(16)	-8.0(17)
C19	21(2)	21(3)	14(2)	-1.7(16)	-0.1(14)	-2.3(15)
C20	22(3)	16(3)	15(2)	1.9(18)	-1.0(15)	-5.2(16)
C21	22(3)	17(3)	15(3)	2.4(16)	-1.4(15)	-4.1(16)
C22	26(3)	21(3)	15(2)	-5.1(17)	3.7(15)	-2.4(14)
C23	17(2)	20(2)	12(2)	-2.9(13)	0.1(13)	-2.4(12)
C24	14(2)	21(2)	17(3)	-3.1(12)	-0.6(15)	-2.7(14)
C25	25(3)	23(2)	24(3)	-6.9(14)	-6(2)	-2.3(15)
C26	32(3)	22(3)	28(3)	-4.5(15)	-6.3(18)	-0.9(17)
C27	22(2)	16(2)	16(3)	-0.2(13)	3.1(16)	-3.9(14)
C28	23(3)	19(2)	23(4)	-0.1(14)	-2.6(19)	-3.2(15)
C29	19(2)	19(3)	25(3)	-1.8(14)	-6.4(17)	-4.2(17)
C30	26(3)	37(4)	20(3)	-4(2)	-0.1(19)	-8(2)
C31	24(3)	22(3)	35(4)	-2.8(17)	-1(3)	-0.7(19)
Br1B	34.9(12)	15.0(10)	21.7(12)	-4.9(8)	1.4(8)	2.2(8)
C1B	26(3)	19(3)	13(2)	-6.0(17)	1.4(14)	-4.1(14)
O1B	32(2)	20.7(19)	16(2)	-5.2(13)	5.3(14)	-7.2(12)
P1B	17.2(7)	18.0(8)	14.2(9)	-0.9(6)	1.0(6)	-4.5(6)
C2B	42(4)	23(3)	15(2)	-14(2)	0.6(17)	-2.7(15)
O2B	16.6(18)	26(2)	14.1(19)	1.5(12)	-1.8(11)	-6.0(15)
C3B	38(3)	30(3)	15(3)	-18(2)	2.5(18)	-6.0(18)
O3B	19.1(19)	27(2)	14(2)	-1.9(15)	-1.9(12)	-5.0(14)
C4B	23(3)	15(3)	15(2)	-2.9(17)	0.3(15)	-4.0(15)
C5B	49(4)	22(3)	16(3)	-14(2)	-1.5(17)	-2.6(15)
C6B	45(3)	33(3)	17(3)	-22(2)	3.6(19)	-7.5(19)
C7B	19(3)	20(3)	12(2)	-0.5(16)	-3.8(13)	-3.4(13)
C8B	22(3)	26(3)	17(3)	4.5(18)	-5.1(16)	-4.0(18)
C9B	24(3)	20(3)	17(2)	2.3(18)	-4.3(15)	-1.6(15)
C10B	22(2)	18(3)	15(2)	-1.9(15)	-4.1(13)	-2.8(13)
C11B	24(3)	21(3)	13(3)	0.8(17)	-2.7(15)	-3.0(17)
C12B	25(3)	20(3)	14(2)	4.4(18)	-3.2(15)	-3.7(15)
C13B	30(3)	25(3)	15(3)	-3(2)	0.1(18)	-8.2(18)
C14B	39(3)	29(4)	21(3)	-8(2)	-5(2)	-7(2)
C15B	56(5)	34(4)	23(3)	-2(3)	-7(3)	-9(2)
C16B	16(2)	22(3)	13(2)	-2.4(15)	-2.6(14)	-3.7(14)
C17B	17(2)	25(3)	21(3)	-5.7(17)	1.2(15)	-8.0(16)
C18B	21(3)	22(3)	20(3)	-6.0(17)	2.2(17)	-5.7(17)
C19B	23(2)	17(3)	13(2)	-2.3(15)	-2.2(14)	-0.2(15)
C20B	27(3)	26(3)	16(3)	-11.0(18)	1.2(16)	-7.3(17)
C21B	22(3)	30(3)	19(3)	-8.8(18)	0.8(17)	-9.5(18)
C22B	23(3)	19(3)	18(2)	0.3(17)	-3.0(15)	-4.1(14)
C23B	19(3)	18(2)	14(2)	2.1(13)	2.6(13)	-4.7(12)
C24B	15(2)	21(2)	13(3)	1.3(12)	-0.2(15)	-2.4(13)
C25B	17(2)	19(2)	16(3)	1.7(13)	-1.9(17)	-3.4(15)
C26B	22(2)	21(3)	16(3)	-1.4(14)	-1.7(16)	-3.6(16)
C27B	25(2)	21(2)	13(3)	0.5(12)	-0.1(16)	0.2(14)
C28B	19(3)	20(2)	22(3)	-1.2(14)	-0.6(18)	-1.2(16)
C29B	16(2)	16(3)	20(3)	3.3(14)	4.2(16)	-2.3(17)
C30B	31(4)	18(3)	19(4)	-2.6(19)	3(3)	-7.6(19)
C31B	26(3)	31(4)	19(2)	1(3)	0.5(15)	-6.3(18)

Table S6: Bond Lengths in Å for compound **2.47e**.

Atom	Atom	Length/Å
Br1	C27	1.913(3)

Atom	Atom	Length/Å
C1	C2	1.519(3)
C1	C6	1.526(3)
C1	C7	1.538(3)
O1	P1	1.565(3)
O1	C30	1.448(3)
P1	O2	1.579(2)
P1	O3	1.478(2)
P1	C23	1.810(3)
C2	C3	1.529(3)
O2	C31	1.440(3)
C3	C4	1.515(3)
C4	C5	1.522(3)
C4	C13	1.520(3)
C5	C6	1.523(3)
C7	C8	1.525(3)
C7	C12	1.522(3)
C8	C9	1.531(3)
C9	C10	1.537(3)
C10	C11	1.526(3)
C10	C16	1.513(3)
C11	C12	1.533(3)
C13	C14	1.516(3)
C14	C15	1.521(3)
C16	C17	1.391(3)
C16	C21	1.403(3)
C17	C18	1.392(3)
C18	C19	1.388(3)
C19	C20	1.393(3)
C19	C22	1.512(3)
C20	C21	1.389(3)
C22	C23	1.552(3)
C23	C24	1.502(3)
C24	C25	1.400(3)
C24	C29	1.392(3)
C25	C26	1.385(3)
C26	C27	1.383(3)
C27	C28	1.382(3)
C28	C29	1.397(3)
Br1B	C27B	1.911(3)
C1B	C2B	1.519(3)
C1B	C6B	1.525(3)
C1B	C7B	1.532(3)
O1B	P1B	1.566(3)
O1B	C30B	1.446(3)
P1B	O2B	1.580(2)
P1B	O3B	1.475(3)
P1B	C23B	1.810(3)
C2B	C3B	1.530(3)
O2B	C31B	1.439(3)
C3B	C4B	1.516(3)
C4B	C5B	1.522(3)
C4B	C13B	1.520(3)
C5B	C6B	1.524(3)
C7B	C8B	1.524(3)
C7B	C12B	1.522(3)
C8B	C9B	1.533(3)
C9B	C10B	1.536(3)

Atom	Atom	Length/Å
C10B	C11B	1.526(3)
C10B	C16B	1.512(3)
C11B	C12B	1.535(3)
C13B	C14B	1.519(3)
C14B	C15B	1.520(3)
C16B	C17B	1.391(3)
C16B	C21B	1.402(3)
C17B	C18B	1.392(3)
C18B	C19B	1.387(3)
C19B	C20B	1.395(3)
C19B	C22B	1.516(3)
C20B	C21B	1.389(3)
C22B	C23B	1.549(3)
C23B	C24B	1.505(3)
C24B	C25B	1.396(3)
C24B	C29B	1.394(3)
C25B	C26B	1.383(3)
C26B	C27B	1.383(3)
C27B	C28B	1.383(3)
C28B	C29B	1.396(3)

Table S7: Bond Angles in ° for compound **2.47e**.

Atom	Atom	Atom	Angle/°
C6	C1	C2	109.0(3)
C7	C1	C2	113.3(3)
C7	C1	C6	113.3(3)
C30	O1	P1	118.7(3)
O2	P1	O1	103.9(2)
O3	P1	O1	116.60(19)
O3	P1	O2	113.4(2)
C23	P1	O1	101.75(17)
C23	P1	O2	107.84(18)
C23	P1	O3	112.2(2)
C3	C2	C1	112.1(3)
C31	O2	P1	122.4(3)
C4	C3	C2	114.2(3)
C5	C4	C3	109.2(3)
C13	C4	C3	110.9(3)
C13	C4	C5	112.4(3)
C6	C5	C4	113.0(3)
C5	C6	C1	113.1(3)
C8	C7	C1	113.2(3)
C12	C7	C1	112.5(3)
C12	C7	C8	108.7(3)
C9	C8	C7	113.0(3)
C10	C9	C8	111.8(3)
C11	C10	C9	109.7(3)
C16	C10	C9	111.1(3)
C16	C10	C11	112.5(3)
C12	C11	C10	112.4(3)
C11	C12	C7	113.2(3)
C14	C13	C4	116.3(3)
C15	C14	C13	112.1(4)
C17	C16	C10	122.3(3)

Atom	Atom	Atom	Angle/°
C21	C16	C10	120.8(3)
C21	C16	C17	116.8(3)
C18	C17	C16	122.2(3)
C19	C18	C17	120.2(3)
C20	C19	C18	118.6(3)
C22	C19	C18	121.6(3)
C22	C19	C20	119.8(3)
C21	C20	C19	120.7(3)
C20	C21	C16	121.4(3)
C23	C22	C19	111.8(3)
C22	C23	P1	109.7(2)
C24	C23	P1	114.6(3)
C24	C23	C22	113.0(3)
C25	C24	C23	121.6(3)
C29	C24	C23	120.7(3)
C29	C24	C25	117.7(3)
C26	C25	C24	122.4(3)
C27	C26	C25	117.5(3)
C26	C27	Br1	119.4(3)
C28	C27	Br1	117.8(2)
C28	C27	C26	122.7(3)
C29	C28	C27	118.2(3)
C28	C29	C24	121.4(3)
C6B	C1B	C2B	109.4(3)
C7B	C1B	C2B	113.7(3)
C7B	C1B	C6B	114.3(3)
C30B	O1B	P1B	118.7(3)
O2B	P1B	O1B	104.44(19)
O3B	P1B	O1B	116.10(19)
O3B	P1B	O2B	113.1(2)
C23B	P1B	O1B	101.14(17)
C23B	P1B	O2B	107.39(18)
C23B	P1B	O3B	113.49(19)
C3B	C2B	C1B	112.1(3)
C31B	O2B	P1B	122.7(3)
C4B	C3B	C2B	113.7(3)
C5B	C4B	C3B	109.0(3)
C13B	C4B	C3B	111.5(3)
C13B	C4B	C5B	112.6(3)
C6B	C5B	C4B	112.7(3)
C5B	C6B	C1B	112.9(3)
C8B	C7B	C1B	114.2(3)
C12B	C7B	C1B	113.3(3)
C12B	C7B	C8B	109.1(3)
C9B	C8B	C7B	112.5(3)
C10B	C9B	C8B	111.7(3)
C11B	C10B	C9B	110.5(3)
C16B	C10B	C9B	110.8(3)
C16B	C10B	C11B	112.4(3)
C12B	C11B	C10B	112.0(3)
C11B	C12B	C7B	112.1(3)
C14B	C13B	C4B	115.6(3)
C15B	C14B	C13B	112.6(4)
C17B	C16B	C10B	122.5(3)
C21B	C16B	C10B	120.9(3)
C21B	C16B	C17B	116.5(3)
C18B	C17B	C16B	122.1(3)

Atom	Atom	Atom	Angle/°
C19B	C18B	C17B	120.9(3)
C20B	C19B	C18B	117.9(3)
C22B	C19B	C18B	122.6(3)
C22B	C19B	C20B	119.4(3)
C21B	C20B	C19B	120.9(3)
C20B	C21B	C16B	121.7(3)
C23B	C22B	C19B	112.0(3)
C22B	C23B	P1B	112.6(2)
C24B	C23B	P1B	111.2(3)
C24B	C23B	C22B	112.9(3)
C25B	C24B	C23B	121.8(3)
C29B	C24B	C23B	119.6(3)
C29B	C24B	C25B	118.6(3)
C26B	C25B	C24B	122.2(3)
C27B	C26B	C25B	117.1(3)
C26B	C27B	Br1B	119.4(2)
C28B	C27B	Br1B	117.2(2)
C28B	C27B	C26B	123.4(3)
C29B	C28B	C27B	118.1(3)
C28B	C29B	C24B	120.7(3)

Table S8: Torsion Angles in ° for compound **2.47e**.

Atom	Atom	Atom	Atom	Angle/°
Br1	C27	C26	C25	179.5(5)
Br1	C27	C28	C29	-179.6(4)
C1	C2	C3	C4	55.2(5)
C1	C6	C5	C4	-55.6(5)
C1	C7	C8	C9	179.3(4)
C1	C7	C12	C11	-179.5(4)
O1	P1	O2	C31	-142.3(4)
P1	C23	C22	C19	-159.6(3)
P1	C23	C24	C25	120.0(4)
P1	C23	C24	C29	-61.4(4)
C2	C3	C4	C5	-52.4(5)
C2	C3	C4	C13	-176.8(4)
C3	C4	C5	C6	52.1(4)
C3	C4	C13	C14	-178.2(5)
C4	C13	C14	C15	178.9(6)
C7	C8	C9	C10	56.4(4)
C7	C12	C11	C10	-55.5(4)
C8	C9	C10	C11	-53.8(4)
C8	C9	C10	C16	-178.9(3)
C9	C10	C11	C12	53.4(4)
C9	C10	C16	C17	-106.9(5)
C9	C10	C16	C21	70.2(4)
C10	C16	C17	C18	177.0(5)
C10	C16	C21	C20	-177.1(5)
C16	C17	C18	C19	-0.1(7)
C16	C21	C20	C19	0.4(7)
C17	C18	C19	C20	0.7(7)
C17	C18	C19	C22	179.8(5)
C18	C19	C20	C21	-0.8(7)
C18	C19	C22	C23	-94.9(5)

Atom	Atom	Atom	Atom	Angle/°
C19	C22	C23	C24	71.2(4)
C22	C23	C24	C25	-113.4(4)
C22	C23	C24	C29	65.2(4)
C23	C24	C25	C26	179.4(5)
C23	C24	C29	C28	-179.4(5)
C24	C25	C26	C27	-0.1(7)
C24	C29	C28	C27	0.2(7)
C25	C26	C27	C28	-0.5(8)
C26	C27	C28	C29	0.5(7)
Br1B	C27B	C26B	C25B	-178.6(5)
Br1B	C27B	C28B	C29B	178.3(5)
C1B	C2B	C3B	C4B	-55.5(5)
C1B	C6B	C5B	C4B	55.8(5)
C1B	C7B	C8B	C9B	175.8(4)
C1B	C7B	C12B	C11B	-175.1(4)
O1B	P1B	O2B	C31B	132.2(4)
P1B	C23B	C22B	C19B	-164.2(3)
P1B	C23B	C24B	C25B	110.7(4)
P1B	C23B	C24B	C29B	-67.6(4)
C2B	C3B	C4B	C5B	53.7(5)
C2B	C3B	C4B	C13B	178.7(4)
C3B	C4B	C5B	C6B	-53.5(4)
C3B	C4B	C13B	C14B	170.4(5)
C4B	C13B	C14B	C15B	-178.8(5)
C7B	C8B	C9B	C10B	55.6(5)
C7B	C12B	C11B	C10B	-56.4(4)
C8B	C9B	C10B	C11B	-52.9(4)
C8B	C9B	C10B	C16B	-178.2(3)
C9B	C10B	C11B	C12B	53.4(4)
C9B	C10B	C16B	C17B	-108.6(4)
C9B	C10B	C16B	C21B	69.6(5)
C10B	C16B	C17B	C18B	178.3(5)
C10B	C16B	C21B	C20B	-178.0(5)
C16B	C17B	C18B	C19B	-1.1(7)
C16B	C21B	C20B	C19B	0.3(7)
C17B	C18B	C19B	C20B	1.8(7)
C17B	C18B	C19B	C22B	178.2(5)
C18B	C19B	C20B	C21B	-1.4(6)
C18B	C19B	C22B	C23B	-98.6(5)
C19B	C22B	C23B	C24B	68.9(4)
C22B	C23B	C24B	C25B	-121.6(4)
C22B	C23B	C24B	C29B	60.0(4)
C23B	C24B	C25B	C26B	-179.1(5)
C23B	C24B	C29B	C28B	178.7(5)
C24B	C25B	C26B	C27B	0.6(7)
C24B	C29B	C28B	C27B	0.1(7)
C25B	C26B	C27B	C28B	-0.1(7)
C26B	C27B	C28B	C29B	-0.3(7)

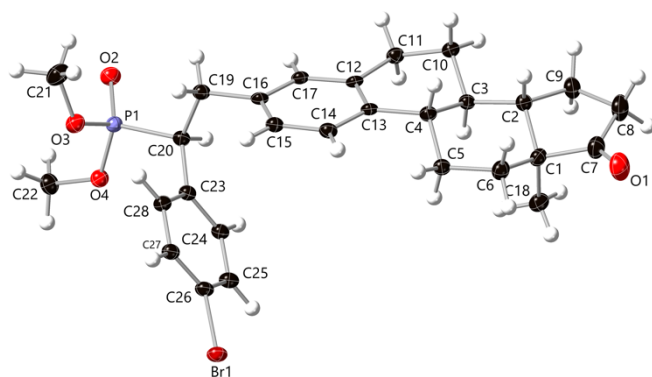
Table S9: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **compound 2.47e**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
H1	8686(9)	1225(4)	-608.4(14)	21.5(14)

Atom	x	y	z	U_{eq}
H2a	6181(10)	3442(4)	-1253.7(16)	30.5(17)
H2b	9328(10)	3141(4)	-1151.7(16)	30.5(17)
H3a	8337(8)	2617(5)	-2065(2)	30.8(18)
H3b	9693(9)	1345(5)	-1660.9(18)	30.8(18)
H4	4329(9)	1940(4)	-1867.7(16)	23.4(15)
H5a	3659(9)	75(4)	-1291.6(16)	23.2(16)
H5b	6795(9)	-236(4)	-1181.3(16)	23.2(16)
H6a	4607(8)	601(5)	-377.8(19)	26.1(17)
H6b	3305(8)	1880(5)	-787.8(18)	26.1(17)
H7	5197(9)	3296(4)	-196.4(14)	21.2(14)
H8a	9279(8)	3925(5)	-427.4(19)	24.9(16)
H8b	10594(8)	2631(5)	-28.9(18)	24.9(16)
H9a	10263(9)	4426(4)	491.0(15)	22.9(15)
H9b	7109(9)	4727(4)	394.8(15)	22.9(15)
H10	9655(8)	2492(4)	1038.6(14)	21.7(14)
H11a	5624(8)	1820(5)	1261(2)	30.6(19)
H11b	4238(9)	3118(5)	875.9(18)	30.6(19)
H12a	7760(10)	1062(4)	430.1(16)	28.8(17)
H12b	4606(10)	1355(4)	337.1(16)	28.8(17)
H13a	8111(9)	-112(5)	-2194.5(19)	27.6(17)
H13b	6939(8)	1142(5)	-2634(2)	27.6(17)
H14a	4039(9)	-838(6)	-2061(3)	36(2)
H14b	2829(9)	430(6)	-2492(3)	36(2)
H15a	5479(11)	-254(7)	-3278(3)	60(3)
H15b	6903(11)	-1490(7)	-2848(3)	60(3)
H15c	3770(11)	-1450(7)	-2983(3)	60(3)
H17	11041(8)	3168(5)	1832.9(19)	25.8(16)
H18	10469(8)	4418(5)	2618(2)	25.9(16)
H20	3574(8)	6061(5)	2040.2(18)	21.8(15)
H21	4167(8)	4815(5)	1254(2)	21.9(15)
H22a	8349(9)	6253(4)	3007.1(15)	24.9(16)
H22b	5674(8)	7017(4)	2725.3(15)	24.9(16)
H23	3603(7)	5231(3)	3183.0(13)	19.3(14)
H25	4085(9)	3136(3)	3407(2)	28.0(17)
H26	6301(8)	1300(4)	3887(2)	32.6(18)
H28	11257(9)	3572(3)	4441(2)	26.1(17)
H29	8997(8)	5405(4)	3954(2)	24.8(16)
H30a	-488(10)	6805(6)	4614(2)	41(2)
H30b	1141(9)	5832(6)	5120(2)	41(2)
H30c	2190(9)	7250(6)	4860(2)	41(2)
H31a	7133(10)	8608(4)	3387(3)	41(2)
H31b	4466(10)	9140(4)	3786(3)	41(2)
H31c	7357(10)	8920(4)	4079(3)	41(2)
H1B	-1357(9)	8770(4)	10566.1(14)	22.7(15)
H2Ba	-1525(10)	6793(4)	11088.4(15)	30.8(17)
H2Bb	1619(10)	6686(4)	11192.2(15)	30.8(17)
H3Ba	-760(9)	7367(5)	12009.9(19)	32.1(18)
H3Bb	-2372(9)	8572(5)	11612.1(18)	32.1(18)
H4B	3025(9)	8286(4)	11804.9(16)	21.2(15)
H5Ba	36(11)	10340(4)	11151.0(17)	33.9(19)
H5Bb	3174(11)	10247(4)	11257.6(17)	33.9(19)
H6Ba	2443(9)	9673(5)	10337(2)	36(2)
H6Bb	4052(10)	8467(5)	10735.4(19)	36(2)
H7B	-461(8)	6842(4)	10112.7(13)	20.1(14)
H8Ba	4752(8)	7461(5)	9990.4(17)	26.3(16)
H8Bb	3707(7)	6186(5)	10389.4(19)	26.3(16)
H9Ba	5602(9)	5658(4)	9474.7(15)	24.4(15)

Atom	x	y	z	U_{eq}
H9Bb	2517(9)	5376(4)	9565.5(15)	24.4(15)
H10B	4514(8)	7577(4)	8915.8(14)	21.8(14)
H11c	349(7)	8299(5)	8679.1(19)	23.4(17)
H11d	-765(8)	7032(5)	9070.5(18)	23.4(17)
H12c	-1498(10)	8831(4)	9595.8(15)	24.1(16)
H12d	1621(9)	9051(4)	9512.0(15)	24.1(16)
H13c	-998(9)	10199(5)	12160.0(19)	27.5(17)
H13d	102(8)	8903(5)	12585(2)	27.5(17)
H14c	4221(9)	9617(6)	12501(2)	34.4(19)
H14d	3078(9)	10926(6)	12086(3)	34.4(19)
H15d	191(11)	11558(7)	12855(3)	56(3)
H15e	1320(11)	10231(7)	13275(3)	56(3)
H15f	3268(11)	11376(7)	13047(3)	56(3)
H17B	6691(8)	6886(5)	8117.2(18)	24.6(16)
H18B	7121(8)	5653(4)	7329(2)	25.1(16)
H20B	669(8)	4020(5)	7937.1(19)	26.5(17)
H21B	218(8)	5272(5)	8718(2)	26.9(17)
H22c	6003(9)	3888(4)	6908.1(16)	24.1(15)
H22d	3712(8)	3039(4)	7235.8(16)	24.1(15)
H23B	720(7)	4729(3)	6844.0(13)	20.5(14)
H25B	-269(8)	6797(3)	6568(2)	21.0(15)
H26B	916(7)	8731(4)	6074(2)	23.6(15)
H28B	7819(8)	6813(3)	5542(2)	24.9(16)
H29B	6599(7)	4883(4)	6051(2)	22.0(15)
H30d	1452(10)	1128(4)	5964(3)	34(2)
H30e	325(10)	539(4)	6627(3)	34(2)
H30f	-1644(10)	1536(4)	6194(3)	34(2)
H31d	4734(9)	2263(6)	5155.7(17)	38(2)
H31e	4499(9)	3878(6)	5157.4(17)	38(2)
H31f	7298(10)	2973(6)	5306.6(17)	38(2)

Crystal Data and Experimental for Compound 2.49e (CCDC 2194598).



Experimental. Single colorless needle-shaped crystals of compound **2.49e** recrystallized from THF by slow evaporation. A suitable crystal with dimensions $0.28 \times 0.04 \times 0.02 \text{ mm}^3$ was selected and mounted on a loop with paratone on a XtaLAB Synergy-S diffractometer. The crystal was kept at a steady $T = 100.00(10) \text{ K}$ during data collection. The structure was solved with the **ShelXT** (Sheldrick, 2015) solution program using iterative methods and by using **Olex2** 1.3-alpha (Dolomanov et al., 2009) as the graphical interface. The model was refined with **ShelXL** 2018/3 (Sheldrick, 2015) using full matrix least squares minimisation on F^2 .

Crystal Data. $\text{C}_{28}\text{H}_{34}\text{BrO}_4\text{P}$, $M_r = 545.43$, monoclinic, $P2_1$ (No. 4), $a = 16.8546(7) \text{ \AA}$, $b = 6.1111(2) \text{ \AA}$, $c = 26.2684(10) \text{ \AA}$, $\beta = 105.468(4)^\circ$, $\alpha = \gamma = 90^\circ$, $V = 2607.66(18) \text{ \AA}^3$, $T = 100.01(10) \text{ K}$, $Z = 4$, $Z' = 2$, $\mu(\text{Cu K}\alpha) = 2.981$, 29380 reflections measured, 9667 unique ($R_{\text{int}} = 0.0715$) which were used in all calculations. The final wR_2 was 0.1083 (all data) and R_1 was 0.0446 ($I \geq 2\sigma(I)$).

Crystal data and structure refinement for compound **2.49e**.

Compound	2.49e
Formula	$\text{C}_{28}\text{H}_{34}\text{BrO}_4\text{P}$
$D_{\text{calc.}} / \text{g cm}^{-3}$	1.389
μ / mm^{-1}	2.981
Formula Weight	545.43
Color	colorless
Shape	needle-shaped
Size/ mm^3	$0.27 \times 0.05 \times 0.03$
T / K	100.01(10)
Crystal System	monoclinic
Flack Parameter	-0.021(16)
Hooft Parameter	-0.000(12)
Space Group	$P2_1$
$a / \text{\AA}$	16.8546(7)
$b / \text{\AA}$	6.1111(2)
$c / \text{\AA}$	26.2684(10)
$\alpha / ^\circ$	90
$\beta / ^\circ$	105.468(4)
$\gamma / ^\circ$	90
$V / \text{\AA}^3$	2607.66(18)
Z	4
Z'	2
Wavelength/ $\text{\AA}$	1.54184
Radiation type	Cu $\text{K}\alpha$
$\theta_{\text{min}} / ^\circ$	2.720
$\theta_{\text{max}} / ^\circ$	72.957
Measured Refl's.	29380
Indep't Refl's	9667
Refl's $I \geq 2\sigma(I)$	8623
R_{int}	0.0715
Parameters	692
Restraints	660
Largest Peak	0.448
Deepest Hole	-0.637
GooF	1.096
wR_2 (all data)	0.1083
wR_2	0.1044
R_1 (all data)	0.0524
R_1	0.0446

Structure Quality Indicators

Reflections:	d min (Cu α) $2\theta = 145.9^\circ$ 0.81	$I/\sigma(I)$ 12.9	R_{int} 7.15%	CAP 130.0° 95% to 145.9° 98.8
Refinement:	Shift -0.001	Max Peak 0.5	Min Peak -0.6	GooF 1.096
				Flack -0.021(16)

A colourless needle-shaped-shaped crystal with dimensions $0.27 \times 0.05 \times 0.03 \text{ mm}^3$ was mounted on a loop with paratone. Data were collected using a XtaLAB Synergy, Dualflex, HyPix diffractometer equipped with an

Oxford Cryosystems low-temperature device operating at $T = 100.01(10)$ K.

Data were measured using ω scans using Cu $K\alpha$ radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlisPro 1.171.41.108a (Rigaku OD, 2021). The maximum resolution that was achieved was $\Theta = 72.957^\circ$ ($0.81 \text{ \AA}$).

The unit cell was refined using CrysAlisPro 1.171.41.108a (Rigaku OD, 2021) on 5002 reflections, 17% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using CrysAlisPro 1.171.41.108a (Rigaku OD, 2021). The final completeness is 98.30 % out to 72.957° in Θ . A Gaussian absorption correction using a multifaceted crystal model based on expressions derived by R.C. Clark & J.S. Reid. (Clark, R. C. & Reid, J. S. (1995) was performed using CrysAlisPro 1.171.41.98a (Rigaku Oxford Diffraction, 2021). An empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm was also performed. The absorption coefficient μ of this material is 2.981 mm^{-1} at this wavelength ($\lambda = 1.54184 \text{ \AA}$) and the minimum and maximum transmissions are 0.700 and 0.961.

The structure was solved and the space group $P2_1$ (# 4) determined with the **ShelXT** (Sheldrick, 2015) solution program using iterative methods and refined by full matrix least squares minimisation on F^2 using version 2018/3 of **ShelXL** 2018/3 (Sheldrick, 2015). All non-hydrogen atoms were refined anisotropically. Most hydrogen atom positions were calculated geometrically and refined using the riding model, but some hydrogen atoms were refined freely.

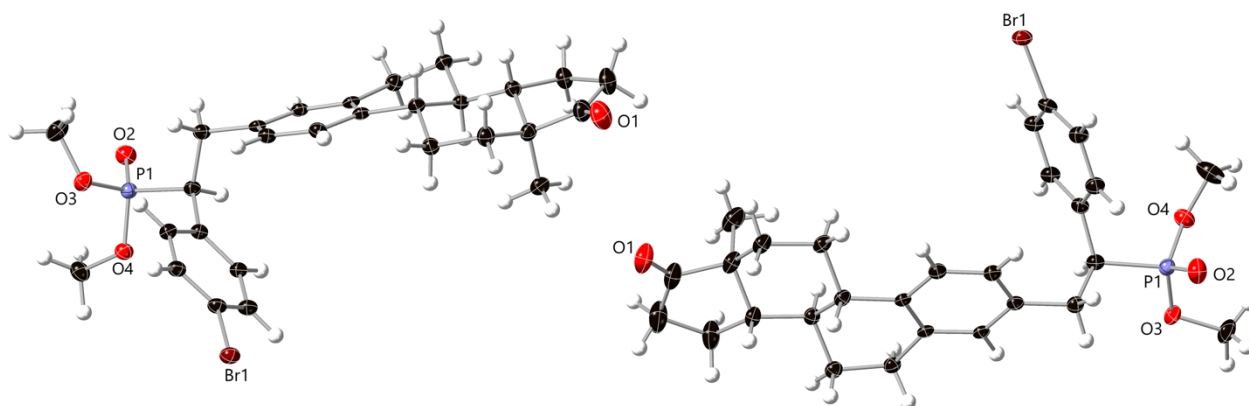


Figure S8: There are two molecules in the asymmetric unit that are rotamers of the $\text{PO}(\text{OCH}_3)_2$ group.

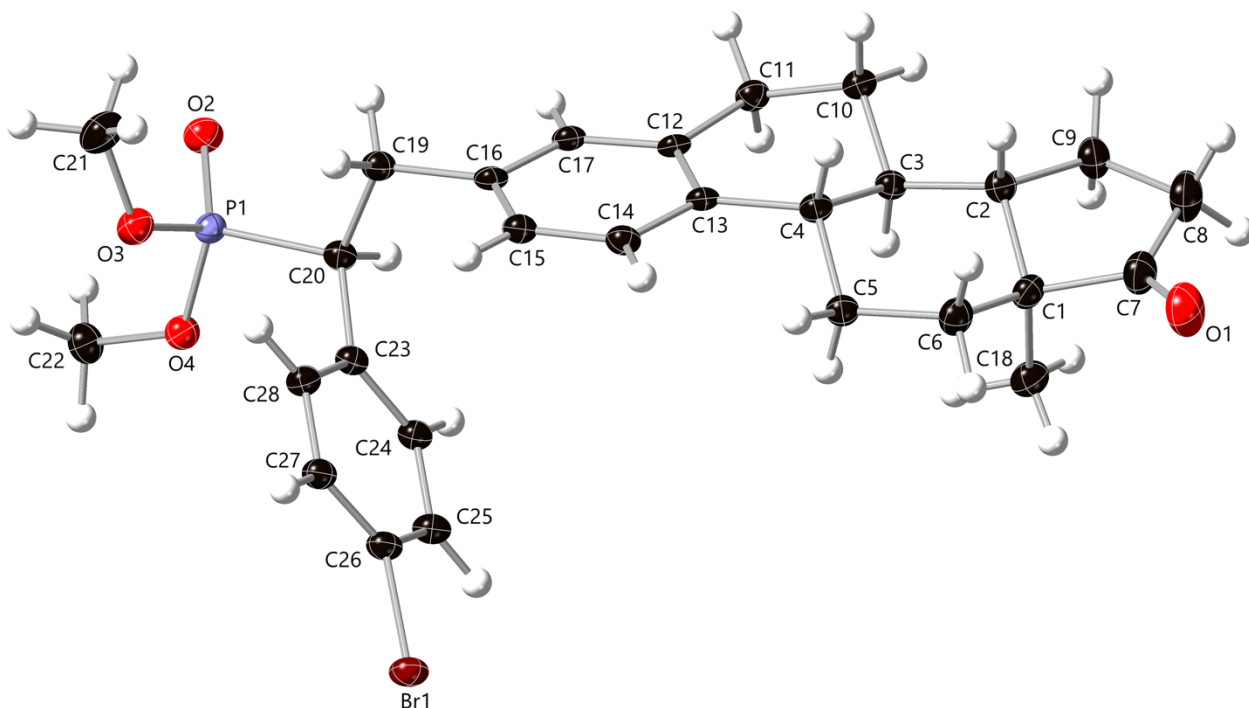
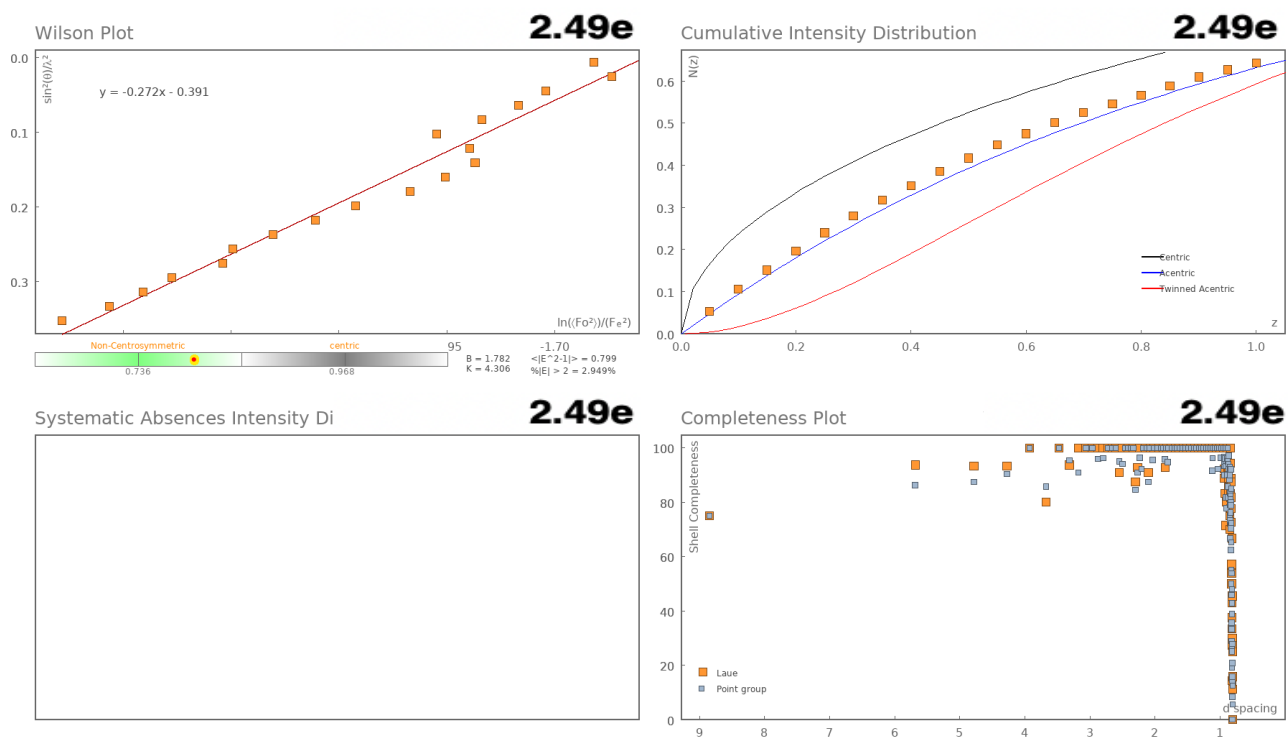
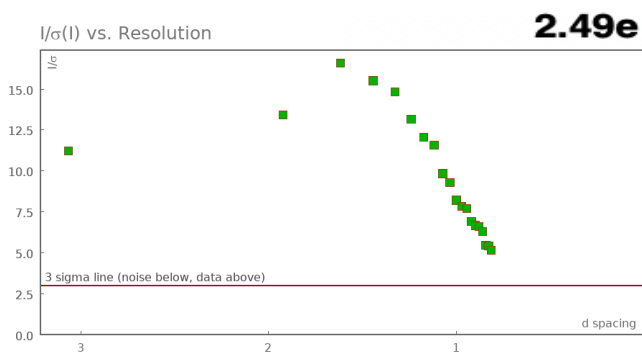


Figure S9: The molecular structure.

Data Plots: Diffraction Data





Data Plots: Refinement and Data

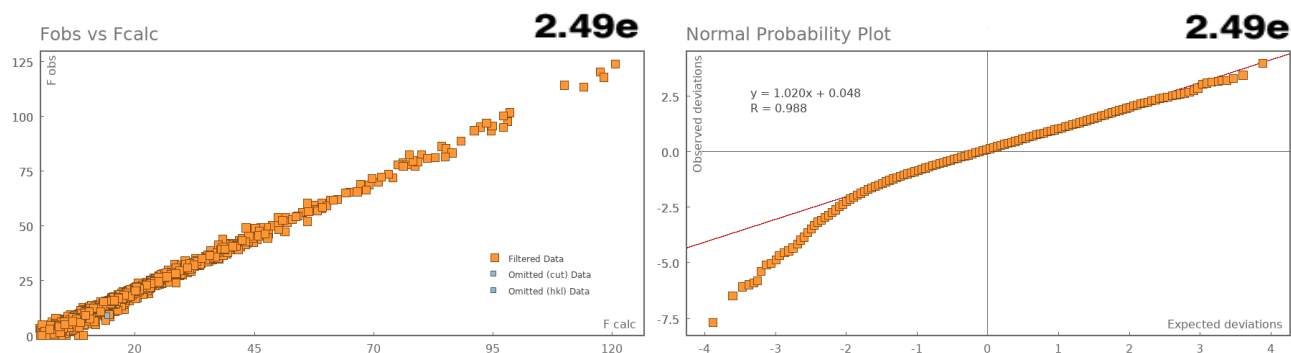


Table S11: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for compound **2.49e**. U_{eq} is defined as $1/3$ of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
Br1_1	9031.7(4)	3329.8(10)	8011.5(2)	23.54(18)
C1_1	3383(4)	3882(11)	6729(2)	26.7(10)
C2_1	3197(4)	5194(10)	6209(2)	24.8(11)
C3_1	3960(3)	6121(9)	6092(2)	18.6(10)
C4_1	4537(3)	4193(9)	6062(2)	18.4(9)
C5_1	4736(3)	2821(11)	6570(2)	23.0(11)
C6_1	3960(4)	1984(10)	6705(2)	25.5(12)
C7_1	2509(4)	3279(12)	6737(3)	33.2(12)
C8_1	1952(5)	5156(14)	6492(4)	47.9(18)
C9_1	2474(4)	6676(12)	6244(3)	38.7(15)
C10_1	3789(3)	7434(10)	5580(2)	20.6(11)
C11_1	4577(3)	8449(10)	5510(2)	19.6(10)
C12_1	5314(3)	6960(9)	5648.5(19)	15.6(9)
C13_1	5306(3)	4940(9)	5905(2)	16.4(9)
C14_1	6010(3)	3625(10)	6003(2)	19.6(10)
C15_1	6708(3)	4277(10)	5856(2)	19.8(10)
C16_1	6730(3)	6315(9)	5615(2)	17.1(9)
C17_1	6028(3)	7612(10)	5511.5(18)	16.5(9)
C18_1	3737(5)	5298(13)	7226(3)	37.3(16)
C19_1	7493(3)	7044(10)	5462(2)	19.6(10)
C20_1	8081(3)	8430(10)	5899.7(19)	18.6(10)
C21_1	9178(4)	12409(13)	5062(3)	34.7(15)

Atom	x	y	z	U_{eq}
C22_1	10308(5)	9377(15)	6480(3)	48(2)
C23_1	8360(3)	7244(9)	6426(2)	18.9(10)
C24_1	8211(3)	8126(10)	6875(2)	20.7(10)
C25_1	8428(3)	7025(10)	7358(2)	21.8(11)
C26_1	8789(3)	4977(10)	7369(2)	21.1(11)
C27_1	8969(3)	4053(10)	6932(2)	22.4(11)
C28_1	8750(4)	5195(10)	6455(2)	21.8(11)
O1_1	2298(3)	1574(9)	6897(2)	41.9(12)
O2_1	9356(2)	7546(8)	5451.7(17)	29.8(9)
O3_1	8617(3)	11297(7)	5319.1(15)	26.3(9)
O4_1	9574(2)	10441(7)	6176.1(16)	26.8(9)
P1_1	8967.6(9)	9295(3)	5685.4(5)	19.2(3)
Br1_2	-3864.4(4)	-2139.6(10)	6977.8(2)	23.27(17)
C1_2	1848(4)	-348(10)	8367(2)	21.6(10)
C2_2	1979(3)	794(10)	8904(2)	19.8(10)
C3_2	1172(3)	1638(9)	8984(2)	16.6(9)
C4_2	596(3)	-344(9)	8965(2)	17.4(9)
C5_2	468(3)	-1627(11)	8446(2)	19.9(10)
C6_2	1282(3)	-2303(11)	8336(2)	23.7(11)
C7_2	2730(4)	-870(12)	8381(3)	29.0(12)
C8_2	3282(4)	915(12)	8699(3)	35.2(14)
C9_2	2714(3)	2319(11)	8944(2)	26.2(12)
C10_2	1259(3)	2910(10)	9497(2)	19.1(10)
C11_2	427(3)	3855(10)	9509(2)	19.8(10)
C12_2	-276(3)	2263(9)	9348.4(19)	15.8(9)
C13_2	-208(3)	285(9)	9091(2)	15.9(9)
C14_2	-889(3)	-1139(9)	8972(2)	18.9(10)
C15_2	-1609(3)	-610(10)	9105(2)	19.0(10)
C16_2	-1688(3)	1364(9)	9349(2)	16.5(9)
C17_2	-1020(3)	2774(10)	9462.4(18)	17.3(9)
C18_2	1534(4)	1216(12)	7897(2)	28.7(13)
C19_2	-2470(3)	1939(10)	9493(2)	19.2(10)
C20_2	-3075(3)	3254(10)	9046.3(19)	17.5(10)
C21_2	-4342(4)	1223(12)	9901(2)	31.6(14)
C22_2	-5270(4)	6254(11)	8755(3)	28.8(14)
C23_2	-3317(3)	2003(9)	8529(2)	17.8(10)
C24_2	-3126(3)	2815(11)	8084.3(19)	19.3(10)
C25_2	-3297(4)	1621(10)	7616(2)	22.0(11)
C26_2	-3654(3)	-414(10)	7605(2)	20.1(10)
C27_2	-3865(3)	-1276(10)	8038(2)	20.6(10)
C28_2	-3691(3)	-65(9)	8501(2)	19.1(10)
O1_2	2965(3)	-2446(9)	8186.5(19)	41.6(12)
O2_2	-3711(2)	5707(7)	9722.1(15)	25.3(9)
O3_2	-4434(3)	2130(7)	9380.0(15)	23.7(9)
O4_2	-4513(2)	5145(7)	8751.0(15)	23.5(9)
P1_2	-3940.2(9)	4198(2)	9274.1(5)	17.6(3)

Table S12: Anisotropic Displacement Parameters ($\times 10^4$) for compound **2.49e**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \dots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1_1	25.6(3)	23.6(4)	18.9(3)	4.8(2)	1.5(2)	0.2(2)
C1_1	34(2)	25(2)	27(2)	-0.4(16)	17.0(16)	-4.1(16)
C2_1	25(2)	27(3)	26(2)	-0.2(19)	13.6(18)	-2.6(18)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C3_1	20.5(19)	19(2)	18(2)	-2.9(16)	6.8(16)	-1.7(15)
C4_1	22.6(19)	17(2)	16(2)	-1.6(16)	7.3(16)	-1.6(15)
C5_1	28(2)	22(3)	20(2)	3.3(19)	8.5(17)	-2(2)
C6_1	32(2)	25(2)	24(3)	1(2)	13(2)	-4.1(18)
C7_1	37(2)	32(2)	39(3)	-7(2)	25(2)	-6.7(18)
C8_1	40(3)	44(3)	70(5)	10(3)	34(3)	0(2)
C9_1	32(3)	34(3)	58(4)	4(3)	27(3)	3(2)
C10_1	22.9(19)	21(3)	18(2)	-1.8(18)	6.6(17)	-1.0(18)
C11_1	21.7(17)	19(2)	18(2)	2.6(19)	5.4(16)	1.7(16)
C12_1	20.1(17)	17.0(19)	9(2)	-0.7(15)	2.8(15)	0.0(14)
C13_1	19.8(17)	18.3(19)	11(2)	0.9(15)	2.9(16)	0.0(14)
C14_1	21.7(17)	18(2)	18(2)	3.1(19)	4.3(15)	1.4(15)
C15_1	21.4(19)	20(2)	17(2)	0.3(17)	3.7(18)	-0.4(16)
C16_1	19.7(17)	18.1(19)	12(2)	-2.7(15)	2.5(16)	-1.3(14)
C17_1	20.3(16)	18(2)	10(2)	-0.9(18)	3.2(14)	-0.9(14)
C18_1	53(4)	35(3)	29(3)	-6(2)	21(3)	-11(3)
C19_1	21.1(18)	21(3)	17(2)	-2.4(18)	5.7(16)	-0.6(17)
C20_1	21(2)	17(2)	17.5(16)	-0.7(15)	3.8(15)	1.2(18)
C21_1	38(3)	37(4)	35(3)	8(3)	20(3)	-9(3)
C22_1	30(3)	55(5)	48(4)	1(3)	-10(3)	4(3)
C23_1	19(2)	18.3(19)	17.8(16)	-0.5(14)	2.1(15)	-0.6(17)
C24_1	24(2)	19(2)	18.4(16)	-0.3(15)	3.2(15)	2(2)
C25_1	23(3)	22(2)	18.8(19)	1.4(16)	2.6(17)	2.4(18)
C26_1	19(2)	22(2)	19(2)	2.0(16)	-1.6(19)	2.0(18)
C27_1	25(3)	19(2)	21.4(18)	1.2(15)	2.8(16)	-2.1(19)
C28_1	25(3)	20(2)	20(2)	0.5(16)	4.8(18)	2.1(18)
O1_1	45(3)	36(2)	54(3)	-1(2)	31(2)	-8.8(19)
O2_1	30(2)	22(2)	41(2)	-8(2)	16.4(18)	-2.2(19)
O3_1	27(2)	29(2)	26(2)	9.1(17)	11.7(17)	-2.7(17)
O4_1	23.0(19)	29(2)	26(2)	-3.8(17)	0.6(16)	-4.1(17)
P1_1	19.7(7)	19.1(7)	19.4(7)	0.1(6)	6.2(6)	-1.7(6)
Br1_2	26.4(3)	25.2(4)	16.6(3)	-5.4(2)	2.9(2)	-0.5(3)
C1_2	22.4(19)	24(2)	20.2(19)	-0.7(15)	9.5(15)	1.1(15)
C2_2	17.9(18)	22(2)	20(2)	0.1(17)	5.2(15)	1.8(16)
C3_2	17.3(18)	16(2)	15.6(19)	0.6(16)	3.2(15)	0.9(15)
C4_2	20.0(18)	16(2)	15.8(19)	-0.8(16)	4.5(15)	-0.2(15)
C5_2	20(2)	22(3)	18.4(19)	-4.8(19)	4.9(15)	-1.4(19)
C6_2	23.6(19)	24(2)	26(3)	-3(2)	10.0(18)	0.9(17)
C7_2	24(2)	33(2)	33(3)	0(2)	12.7(18)	3.6(16)
C8_2	25(2)	37(3)	48(3)	-6(2)	18(2)	-1(2)
C9_2	20(2)	29(3)	32(3)	-1(2)	9(2)	-1.5(18)
C10_2	22.1(19)	19(3)	16.1(19)	-0.5(18)	5.4(16)	-0.5(19)
C11_2	22.2(17)	19(2)	18(2)	-3.6(19)	5.8(16)	-1.0(15)
C12_2	20.7(16)	16.8(18)	9(2)	-0.3(15)	2.9(15)	1.0(14)
C13_2	19.7(17)	16.8(18)	10(2)	-0.7(15)	2.0(15)	0.9(14)
C14_2	20.5(16)	18(2)	17(2)	-3.5(19)	2.7(15)	-0.2(14)
C15_2	20(2)	20(2)	16(2)	-0.6(17)	2.5(18)	0.5(16)
C16_2	19.3(17)	18.7(19)	10(2)	2.6(15)	1.1(15)	2.0(13)
C17_2	20.2(15)	20(2)	11(2)	-0.2(18)	2.8(14)	1.3(14)
C18_2	29(3)	36(3)	22(3)	5(2)	9(2)	2(2)
C19_2	20.1(19)	21(3)	16(2)	0.3(18)	3.3(15)	1.4(17)
C20_2	19(2)	17(2)	16.8(16)	-0.2(15)	3.4(14)	-0.5(18)
C21_2	42(4)	29(3)	28(2)	6(2)	16(2)	4(3)
C22_2	21(2)	34(3)	31(3)	2(3)	6(2)	9(2)
C23_2	18(2)	17.3(18)	16.6(16)	-0.3(14)	2.2(15)	0.8(16)
C24_2	20(2)	19(2)	16.9(16)	0.7(14)	2.5(15)	0(2)
C25_2	24(3)	23(2)	17.2(19)	-0.6(16)	1.9(18)	-0.2(18)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C26_2	21(2)	22(2)	16(2)	-2.9(16)	1.5(18)	0.9(18)
C27_2	20(2)	23(2)	17.6(17)	-1.9(14)	2.9(15)	2(2)
C28_2	22(3)	18.0(19)	16.7(19)	0.2(15)	5.0(18)	-0.7(17)
O1_2	29(2)	43(2)	56(3)	-13(2)	16(2)	6(2)
O2_2	28(2)	24(2)	24(2)	-7.9(17)	6.6(17)	2.3(18)
O3_2	27(2)	21(2)	23.8(17)	0.4(15)	9.4(15)	-5.1(17)
O4_2	21.3(18)	27(2)	21(2)	2.4(16)	5.3(15)	7.2(16)
P1_2	18.8(7)	17.1(7)	16.9(7)	-0.7(5)	5.1(5)	1.8(5)

Table S13: Bond Lengths in Å for compound **2.49e**.

Atom	Atom	Length/Å
Br1_1	C26_1	1.913(6)
C1_1	C2_1	1.542(9)
C1_1	C6_1	1.526(9)
C1_1	C7_1	1.524(8)
C1_1	C18_1	1.546(9)
C2_1	C3_1	1.510(8)
C2_1	C9_1	1.540(9)
C3_1	C4_1	1.543(8)
C3_1	C10_1	1.526(8)
C4_1	C5_1	1.537(8)
C4_1	C13_1	1.529(8)
C5_1	C6_1	1.531(8)
C7_1	C8_1	1.513(11)
C7_1	O1_1	1.212(9)
C8_1	C9_1	1.538(10)
C10_1	C11_1	1.521(8)
C11_1	C12_1	1.505(7)
C12_1	C13_1	1.409(8)
C12_1	C17_1	1.403(7)
C13_1	C14_1	1.400(8)
C14_1	C15_1	1.391(8)
C15_1	C16_1	1.402(8)
C16_1	C17_1	1.388(8)
C16_1	C19_1	1.514(8)
C19_1	C20_1	1.554(8)
C20_1	C23_1	1.519(7)
C20_1	P1_1	1.810(5)
C21_1	O3_1	1.467(7)
C22_1	O4_1	1.438(8)
C23_1	C24_1	1.382(8)
C23_1	C28_1	1.406(8)
C24_1	C25_1	1.394(8)
C25_1	C26_1	1.389(8)
C26_1	C27_1	1.384(8)
C27_1	C28_1	1.395(8)
O2_1	P1_1	1.470(4)
O3_1	P1_1	1.571(4)
O4_1	P1_1	1.579(4)
Br1_2	C26_2	1.909(5)

Atom	Atom	Length/Å
C1_2	C2_2	1.536(8)
C1_2	C6_2	1.517(8)
C1_2	C7_2	1.512(8)
C1_2	C18_2	1.540(9)
C2_2	C3_2	1.520(8)
C2_2	C9_2	1.532(8)
C3_2	C4_2	1.545(8)
C3_2	C10_2	1.529(7)
C4_2	C5_2	1.537(7)
C4_2	C13_2	1.527(8)
C5_2	C6_2	1.532(7)
C7_2	C8_2	1.530(10)
C7_2	O1_2	1.205(9)
C8_2	C9_2	1.547(9)
C10_2	C11_2	1.525(7)
C11_2	C12_2	1.505(8)
C12_2	C13_2	1.405(7)
C12_2	C17_2	1.398(7)
C13_2	C14_2	1.407(8)
C14_2	C15_2	1.388(8)
C15_2	C16_2	1.389(8)
C16_2	C17_2	1.386(8)
C16_2	C19_2	1.507(8)
C19_2	C20_2	1.558(7)
C20_2	C23_2	1.517(7)
C20_2	P1_2	1.812(5)
C21_2	O3_2	1.447(7)
C22_2	O4_2	1.447(7)
C23_2	C24_2	1.384(8)
C23_2	C28_2	1.406(8)
C24_2	C25_2	1.393(8)
C25_2	C26_2	1.379(8)
C26_2	C27_2	1.383(8)
C27_2	C28_2	1.386(8)
O2_2	P1_2	1.464(4)
O3_2	P1_2	1.579(4)
O4_2	P1_2	1.565(4)

Table S1: Bond Angles in ° for compound **2.49e**.

Atom	Atom	Atom	Angle/°
C2_1	C1_1	C18_1	113.4(6)
C6_1	C1_1	C2_1	109.8(5)
C6_1	C1_1	C18_1	110.7(6)
C7_1	C1_1	C2_1	99.7(5)
C7_1	C1_1	C6_1	116.5(5)
C7_1	C1_1	C18_1	106.3(5)
C3_1	C2_1	C1_1	113.1(5)
C3_1	C2_1	C9_1	121.5(5)
C9_1	C2_1	C1_1	103.3(5)
C2_1	C3_1	C4_1	107.9(5)
C2_1	C3_1	C10_1	113.9(5)
C10_1	C3_1	C4_1	109.2(4)
C5_1	C4_1	C3_1	111.4(4)
C13_1	C4_1	C3_1	112.2(5)
C13_1	C4_1	C5_1	113.1(4)

Atom	Atom	Atom	Angle/°
C6_1	C5_1	C4_1	112.4(5)
C1_1	C6_1	C5_1	110.4(5)
C8_1	C7_1	C1_1	107.7(6)
O1_1	C7_1	C1_1	125.9(6)
O1_1	C7_1	C8_1	126.4(6)
C7_1	C8_1	C9_1	106.1(6)
C8_1	C9_1	C2_1	102.8(6)
C11_1	C10_1	C3_1	110.8(4)
C12_1	C11_1	C10_1	114.6(5)
C13_1	C12_1	C11_1	122.2(5)
C17_1	C12_1	C11_1	118.5(5)
C17_1	C12_1	C13_1	119.4(5)
C12_1	C13_1	C4_1	120.5(5)
C14_1	C13_1	C4_1	121.2(5)
C14_1	C13_1	C12_1	118.3(5)
C15_1	C14_1	C13_1	121.6(5)
C14_1	C15_1	C16_1	120.4(5)
C15_1	C16_1	C19_1	120.5(5)
C17_1	C16_1	C15_1	118.2(5)
C17_1	C16_1	C19_1	121.3(5)
C16_1	C17_1	C12_1	122.1(5)
C16_1	C19_1	C20_1	112.6(4)
C19_1	C20_1	P1_1	110.2(4)
C23_1	C20_1	C19_1	113.2(5)
C23_1	C20_1	P1_1	109.9(4)
C24_1	C23_1	C20_1	120.6(5)
C24_1	C23_1	C28_1	119.3(5)
C28_1	C23_1	C20_1	120.2(5)
C23_1	C24_1	C25_1	121.7(6)
C26_1	C25_1	C24_1	117.5(5)
C25_1	C26_1	Br1_1	118.9(4)
C27_1	C26_1	Br1_1	118.3(4)
C27_1	C26_1	C25_1	122.8(5)
C26_1	C27_1	C28_1	118.5(6)
C27_1	C28_1	C23_1	120.2(5)
C21_1	O3_1	P1_1	117.3(4)
C22_1	O4_1	P1_1	121.8(5)
O2_1	P1_1	C20_1	114.4(3)
O2_1	P1_1	O3_1	116.5(3)
O2_1	P1_1	O4_1	113.6(2)
O3_1	P1_1	C20_1	102.2(3)
O3_1	P1_1	O4_1	102.1(2)
O4_1	P1_1	C20_1	106.5(2)
C2_2	C1_2	C18_2	112.9(5)
C6_2	C1_2	C2_2	110.0(5)
C6_2	C1_2	C18_2	111.7(5)
C7_2	C1_2	C2_2	100.1(5)
C7_2	C1_2	C6_2	115.8(5)
C7_2	C1_2	C18_2	105.9(5)
C3_2	C2_2	C1_2	111.4(4)
C3_2	C2_2	C9_2	121.5(5)
C9_2	C2_2	C1_2	104.7(5)
C2_2	C3_2	C4_2	107.9(4)
C2_2	C3_2	C10_2	114.5(4)
C10_2	C3_2	C4_2	109.8(4)
C5_2	C4_2	C3_2	111.4(4)
C13_2	C4_2	C3_2	112.5(4)

Atom	Atom	Atom	Angle/°
C13_2	C4_2	C5_2	113.4(4)
C6_2	C5_2	C4_2	112.6(4)
C1_2	C6_2	C5_2	111.0(5)
C1_2	C7_2	C8_2	108.3(5)
O1_2	C7_2	C1_2	126.2(6)
O1_2	C7_2	C8_2	125.5(6)
C7_2	C8_2	C9_2	105.6(5)
C2_2	C9_2	C8_2	102.3(5)
C11_2	C10_2	C3_2	109.7(4)
C12_2	C11_2	C10_2	114.2(5)
C13_2	C12_2	C11_2	122.1(5)
C17_2	C12_2	C11_2	118.7(5)
C17_2	C12_2	C13_2	119.2(5)
C12_2	C13_2	C4_2	120.8(5)
C12_2	C13_2	C14_2	118.2(5)
C14_2	C13_2	C4_2	121.0(5)
C15_2	C14_2	C13_2	121.1(5)
C14_2	C15_2	C16_2	121.1(5)
C15_2	C16_2	C19_2	121.1(5)
C17_2	C16_2	C15_2	117.8(5)
C17_2	C16_2	C19_2	121.1(5)
C16_2	C17_2	C12_2	122.6(5)
C16_2	C19_2	C20_2	111.8(4)
C19_2	C20_2	P1_2	109.8(3)
C23_2	C20_2	C19_2	112.4(5)
C23_2	C20_2	P1_2	114.1(3)
C24_2	C23_2	C20_2	120.6(5)
C24_2	C23_2	C28_2	118.6(5)
C28_2	C23_2	C20_2	120.7(5)
C23_2	C24_2	C25_2	121.2(6)
C26_2	C25_2	C24_2	118.5(5)
C25_2	C26_2	Br1_2	119.7(4)
C25_2	C26_2	C27_2	122.2(5)
C27_2	C26_2	Br1_2	118.1(4)
C26_2	C27_2	C28_2	118.5(6)
C27_2	C28_2	C23_2	120.9(5)
C21_2	O3_2	P1_2	123.0(4)
C22_2	O4_2	P1_2	120.4(4)
O2_2	P1_2	C20_2	113.7(3)
O2_2	P1_2	O3_2	113.7(2)
O2_2	P1_2	O4_2	116.2(2)
O3_2	P1_2	C20_2	108.2(3)
O4_2	P1_2	C20_2	101.0(2)
O4_2	P1_2	O3_2	102.7(2)

Table 215: Torsion Angles in ° for compound **2.49e**.

Atom	Atom	Atom	Atom	Angle/°
Br1_1	C26_1	C27_1	C28_1	176.3(4)
C1_1	C2_1	C3_1	C4_1	58.8(6)
C1_1	C2_1	C3_1	C10_1	-179.8(5)
C1_1	C2_1	C9_1	C8_1	-39.2(7)
C1_1	C7_1	C8_1	C9_1	10.5(8)
C2_1	C1_1	C6_1	C5_1	54.5(6)
C2_1	C1_1	C7_1	C8_1	-34.0(7)
C2_1	C1_1	C7_1	O1_1	144.1(7)

Atom	Atom	Atom	Atom	Angle/°
C2_1	C3_1	C4_1	C5_1	-56.1(6)
C2_1	C3_1	C4_1	C13_1	176.0(4)
C2_1	C3_1	C10_1	C11_1	175.9(5)
C3_1	C2_1	C9_1	C8_1	-167.3(6)
C3_1	C4_1	C5_1	C6_1	55.7(6)
C3_1	C4_1	C13_1	C12_1	-20.4(7)
C3_1	C4_1	C13_1	C14_1	161.0(5)
C3_1	C10_1	C11_1	C12_1	42.4(6)
C4_1	C3_1	C10_1	C11_1	-63.5(6)
C4_1	C5_1	C6_1	C1_1	-54.4(6)
C4_1	C13_1	C14_1	C15_1	179.1(5)
C5_1	C4_1	C13_1	C12_1	-147.4(5)
C5_1	C4_1	C13_1	C14_1	34.0(7)
C6_1	C1_1	C2_1	C3_1	-59.2(7)
C6_1	C1_1	C2_1	C9_1	167.7(5)
C6_1	C1_1	C7_1	C8_1	-152.0(6)
C6_1	C1_1	C7_1	O1_1	26.0(9)
C7_1	C1_1	C2_1	C3_1	178.0(5)
C7_1	C1_1	C2_1	C9_1	44.8(6)
C7_1	C1_1	C6_1	C5_1	166.8(5)
C7_1	C8_1	C9_1	C2_1	17.7(8)
C9_1	C2_1	C3_1	C4_1	-177.5(5)
C9_1	C2_1	C3_1	C10_1	-56.1(7)
C10_1	C3_1	C4_1	C5_1	179.6(5)
C10_1	C3_1	C4_1	C13_1	51.7(6)
C10_1	C11_1	C12_1	C13_1	-10.3(7)
C10_1	C11_1	C12_1	C17_1	169.2(4)
C11_1	C12_1	C13_1	C4_1	-0.8(7)
C11_1	C12_1	C13_1	C14_1	177.8(5)
C11_1	C12_1	C17_1	C16_1	-178.7(5)
C12_1	C13_1	C14_1	C15_1	0.5(8)
C13_1	C4_1	C5_1	C6_1	-176.9(5)
C13_1	C12_1	C17_1	C16_1	0.8(7)
C13_1	C14_1	C15_1	C16_1	1.5(8)
C14_1	C15_1	C16_1	C17_1	-2.3(8)
C14_1	C15_1	C16_1	C19_1	179.1(5)
C15_1	C16_1	C17_1	C12_1	1.2(8)
C15_1	C16_1	C19_1	C20_1	-93.2(6)
C16_1	C19_1	C20_1	C23_1	57.7(6)
C16_1	C19_1	C20_1	P1_1	-178.7(4)
C17_1	C12_1	C13_1	C4_1	179.7(5)
C17_1	C12_1	C13_1	C14_1	-1.6(7)
C17_1	C16_1	C19_1	C20_1	88.3(6)
C18_1	C1_1	C2_1	C3_1	65.3(7)
C18_1	C1_1	C2_1	C9_1	-67.8(7)
C18_1	C1_1	C6_1	C5_1	-71.5(6)
C18_1	C1_1	C7_1	C8_1	84.1(7)
C18_1	C1_1	C7_1	O1_1	-97.9(8)
C19_1	C16_1	C17_1	C12_1	179.8(5)
C19_1	C20_1	C23_1	C24_1	-122.0(6)
C19_1	C20_1	C23_1	C28_1	55.9(7)
C19_1	C20_1	P1_1	O2_1	-47.1(5)
C19_1	C20_1	P1_1	O3_1	79.8(4)
C19_1	C20_1	P1_1	O4_1	-173.5(4)
C20_1	C23_1	C24_1	C25_1	177.1(5)
C20_1	C23_1	C28_1	C27_1	-176.8(5)
C21_1	O3_1	P1_1	C20_1	-179.0(4)

Atom	Atom	Atom	Atom	Angle/°
C21_1	O3_1	P1_1	O2_1	-53.4(5)
C21_1	O3_1	P1_1	O4_1	71.0(5)
C22_1	O4_1	P1_1	C20_1	104.6(6)
C22_1	O4_1	P1_1	O2_1	-22.3(6)
C22_1	O4_1	P1_1	O3_1	-148.6(6)
C23_1	C20_1	P1_1	O2_1	78.3(4)
C23_1	C20_1	P1_1	O3_1	-154.8(4)
C23_1	C20_1	P1_1	O4_1	-48.0(5)
C23_1	C24_1	C25_1	C26_1	-1.1(8)
C24_1	C23_1	C28_1	C27_1	1.1(9)
C24_1	C25_1	C26_1	Br1_1	-176.0(4)
C24_1	C25_1	C26_1	C27_1	2.8(9)
C25_1	C26_1	C27_1	C28_1	-2.4(9)
C26_1	C27_1	C28_1	C23_1	0.5(9)
C28_1	C23_1	C24_1	C25_1	-0.8(8)
O1_1	C7_1	C8_1	C9_1	-167.5(7)
P1_1	C20_1	C23_1	C24_1	114.3(5)
P1_1	C20_1	C23_1	C28_1	-67.9(6)
Br1_2	C26_2	C27_2	C28_2	178.0(4)
C1_2	C2_2	C3_2	C4_2	60.8(6)
C1_2	C2_2	C3_2	C10_2	-176.7(5)
C1_2	C2_2	C9_2	C8_2	-39.0(6)
C1_2	C7_2	C8_2	C9_2	8.2(7)
C2_2	C1_2	C6_2	C5_2	55.1(6)
C2_2	C1_2	C7_2	C8_2	-31.4(6)
C2_2	C1_2	C7_2	O1_2	146.9(7)
C2_2	C3_2	C4_2	C5_2	-56.5(5)
C2_2	C3_2	C4_2	C13_2	174.8(4)
C2_2	C3_2	C10_2	C11_2	174.7(5)
C3_2	C2_2	C9_2	C8_2	-166.1(5)
C3_2	C4_2	C5_2	C6_2	53.6(7)
C3_2	C4_2	C13_2	C12_2	-18.2(7)
C3_2	C4_2	C13_2	C14_2	164.5(5)
C3_2	C10_2	C11_2	C12_2	45.9(6)
C4_2	C3_2	C10_2	C11_2	-63.8(6)
C4_2	C5_2	C6_2	C1_2	-52.5(6)
C4_2	C13_2	C14_2	C15_2	177.3(5)
C5_2	C4_2	C13_2	C12_2	-145.8(5)
C5_2	C4_2	C13_2	C14_2	36.9(7)
C6_2	C1_2	C2_2	C3_2	-61.1(6)
C6_2	C1_2	C2_2	C9_2	165.8(5)
C6_2	C1_2	C7_2	C8_2	-149.5(5)
C6_2	C1_2	C7_2	O1_2	28.8(9)
C7_2	C1_2	C2_2	C3_2	176.6(5)
C7_2	C1_2	C2_2	C9_2	43.5(6)
C7_2	C1_2	C6_2	C5_2	167.6(5)
C7_2	C8_2	C9_2	C2_2	18.6(7)
C9_2	C2_2	C3_2	C4_2	-175.1(5)
C9_2	C2_2	C3_2	C10_2	-52.6(7)
C10_2	C3_2	C4_2	C5_2	178.1(4)
C10_2	C3_2	C4_2	C13_2	49.4(6)
C10_2	C11_2	C12_2	C13_2	-14.6(7)
C10_2	C11_2	C12_2	C17_2	165.1(4)
C11_2	C12_2	C13_2	C4_2	0.5(7)
C11_2	C12_2	C13_2	C14_2	177.8(5)
C11_2	C12_2	C17_2	C16_2	-177.2(5)
C12_2	C13_2	C14_2	C15_2	0.0(8)

Atom	Atom	Atom	Atom	Angle/°
C13_2	C4_2	C5_2	C6_2	-178.2(5)
C13_2	C12_2	C17_2	C16_2	2.5(7)
C13_2	C14_2	C15_2	C16_2	1.5(8)
C14_2	C15_2	C16_2	C17_2	-0.9(8)
C14_2	C15_2	C16_2	C19_2	179.9(5)
C15_2	C16_2	C17_2	C12_2	-1.1(7)
C15_2	C16_2	C19_2	C20_2	-92.3(6)
C16_2	C19_2	C20_2	C23_2	59.1(6)
C16_2	C19_2	C20_2	P1_2	-172.7(4)
C17_2	C12_2	C13_2	C4_2	-179.3(5)
C17_2	C12_2	C13_2	C14_2	-1.9(7)
C17_2	C16_2	C19_2	C20_2	88.6(6)
C18_2	C1_2	C2_2	C3_2	64.4(6)
C18_2	C1_2	C2_2	C9_2	-68.7(6)
C18_2	C1_2	C6_2	C5_2	-71.1(6)
C18_2	C1_2	C7_2	C8_2	86.2(6)
C18_2	C1_2	C7_2	O1_2	-95.6(8)
C19_2	C16_2	C17_2	C12_2	178.1(5)
C19_2	C20_2	C23_2	C24_2	-118.2(6)
C19_2	C20_2	C23_2	C28_2	57.8(6)
C19_2	C20_2	P1_2	O2_2	62.6(5)
C19_2	C20_2	P1_2	O3_2	-64.8(4)
C19_2	C20_2	P1_2	O4_2	-172.2(4)
C20_2	C23_2	C24_2	C25_2	175.9(5)
C20_2	C23_2	C28_2	C27_2	-175.9(5)
C21_2	O3_2	P1_2	C20_2	99.2(5)
C21_2	O3_2	P1_2	O2_2	-28.1(5)
C21_2	O3_2	P1_2	O4_2	-154.5(5)
C22_2	O4_2	P1_2	C20_2	-175.2(5)
C22_2	O4_2	P1_2	O2_2	-51.7(5)
C22_2	O4_2	P1_2	O3_2	73.1(5)
C23_2	C20_2	P1_2	O2_2	-170.3(4)
C23_2	C20_2	P1_2	O3_2	62.4(4)
C23_2	C20_2	P1_2	O4_2	-45.0(5)
C23_2	C24_2	C25_2	C26_2	-0.8(8)
C24_2	C23_2	C28_2	C27_2	0.2(8)
C24_2	C25_2	C26_2	Br1_2	-177.9(4)
C24_2	C25_2	C26_2	C27_2	1.7(9)
C25_2	C26_2	C27_2	C28_2	-1.7(8)
C26_2	C27_2	C28_2	C23_2	0.7(8)
C28_2	C23_2	C24_2	C25_2	-0.2(8)
O1_2	C7_2	C8_2	C9_2	-170.0(7)
P1_2	C20_2	C23_2	C24_2	116.0(5)
P1_2	C20_2	C23_2	C28_2	-68.0(6)

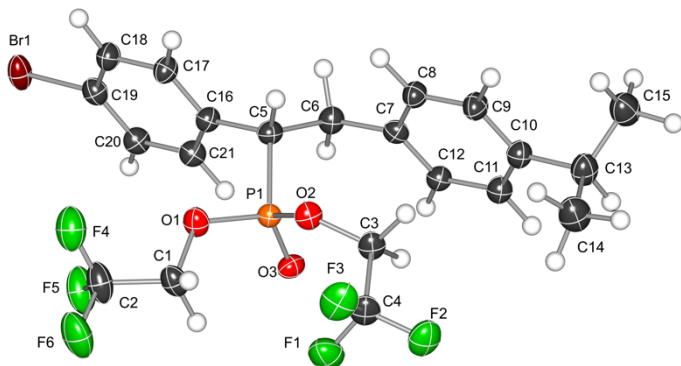
Table S3: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for compound **2.49e**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
H2_1	2964(4)	4115(16)	5920(4)	30
H3_1	4246(5)	7099(14)	6393(4)	22
H4_1	4223(5)	3212(14)	5770(4)	22
H5A_1	5086(5)	1539(17)	6528(2)	28
H5B_1	5063(5)	3736(15)	6871(4)	28

Atom	x	y	z	U_{eq}
H6A_1	3669(5)	907(16)	6429(4)	31
H6B_1	4118(4)	1211(13)	7055(4)	31
H8A_1	1753(5)	5956(16)	6768(5)	57
H8B_1	1461(7)	4601(15)	6214(5)	57
H9A_1	2673(5)	7983(19)	6475(4)	46
H9B_1	2154(5)	7189(14)	5885(5)	46
H10A_1	3543(4)	6446(14)	5273(4)	25
H10B_1	3379(6)	8621(16)	5587(2)	25
H11A_1	4479(3)	8922(11)	5132(4)	24
H11B_1	4705(3)	9795(17)	5737(3)	24
H14_1	6012(3)	2230(30)	6176(5)	24
H15_1	7181(12)	3320(20)	5920(3)	24
H17_1	6032(3)	9010(30)	5340(4)	20
H18A_1	4260(50)	5980(70)	7202(4)	56
H18B_1	3870(50)	4390(160)	7530(40)	56
H18C_1	3300(60)	6500(160)	7200(30)	56
H19A_1	7326(8)	7920(40)	5132(15)	24
H19B_1	7793(14)	5730(60)	5388(4)	24
H20_1	7820(20)	9580(100)	5948(4)	22
H21A_1	9326(5)	11360(20)	4790(6)	52
H21B_1	9690(50)	12880(150)	5300(30)	52
H21C_1	8890(50)	13940(160)	4830(30)	52
H22A_1	10480(20)	8300(120)	6260(20)	72
H22B_1	10190(60)	8680(190)	6820(40)	72
H22C_1	10660(40)	10790(80)	6570(40)	72
H24_1	7943(6)	9580(30)	6855(2)	25
H25_1	8328(4)	7679(16)	7679(7)	26
H27_1	9247(7)	2620(30)	6958(2)	27
H28_1	8869(4)	4561(16)	6137(7)	26
H2_2	2175(4)	-371(16)	9179(4)	24
H3_2	912(4)	2631(14)	8680(4)	20
H4_2	891(5)	-1360(14)	9255(4)	21
H5A_2	135(5)	-2974(18)	8463(2)	24
H5B_2	147(5)	-698(14)	8146(4)	24
H6A_2	1562(4)	-3433(16)	8602(4)	28
H6B_2	1168(3)	-2976(13)	7975(4)	28
H8A_2	3530(5)	1831(16)	8463(4)	42
H8B_2	3739(6)	249(14)	8983(4)	42
H9A_2	2991(4)	2701(12)	9322(5)	31
H9B_2	2543(4)	3702(18)	8737(3)	31
H10A_2	1467(4)	1910(14)	9807(4)	23
H10B_2	1669(5)	4128(16)	9522(2)	23
H11A_2	464(3)	4387(11)	9876(4)	24
H11B_2	305(4)	5155(17)	9266(3)	24
H14_2	-854(3)	-2510(30)	8795(5)	23
H15_2	-2063(11)	-1630(30)	9027(3)	23
H17_2	-1069(3)	4160(30)	9626(4)	21
H18A_2	940(50)	1720(40)	7882(3)	43
H18B_2	1510(50)	400(140)	7580(30)	43
H18C_2	1860(30)	2680(60)	7940(30)	43
H19A_2	-2331(4)	2833(14)	9826(4)	23
H19B_2	-2746(4)	559(17)	9564(2)	23
H20_2	-2771(4)	4596(17)	8982(2)	21
H21A_2	-4079(7)	-320(30)	9921(3)	47
H21B_2	-4890(20)	1160(150)	10010(20)	47
H21C_2	-4000(40)	2280(90)	10190(20)	47
H22A_2	-5563(7)	6786(16)	8375(8)	43

Atom	x	y	z	<i>U_{eq}</i>
H22B_2	-5130(40)	7570(70)	9010(20)	43
H22C_2	-5610(30)	5250(100)	8940(20)	43
H24_2	-2864(6)	4270(30)	8099(2)	23
H25_2	-3166(4)	2220(15)	7298(7)	26
H27_2	-4135(6)	-2720(30)	8018(2)	25
H28_2	-3832(4)	-664(15)	8815(7)	23

X-Ray Crystallographic Data for Compound 2.42 (CCDC 2254293).



Experimental. Single colourless needle-shaped crystals of compound **2.42**. The crystal was chosen from the sample as supplied. A suitable crystal with dimensions $0.49 \times 0.09 \times 0.06$ mm³ was selected and mounted on a loop with paratone on a XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was kept at a steady $T = 99.96(12)$ K during data collection. The structure was solved with the ShelXT 2018/2 (Sheldrick, 2018) solution program using dual methods and by using Olex2 1.5-alpha (Dolomanov et al., 2009) as the graphical interface. The model was refined with olex2.refine 1.5-alpha (Bourhis et al., 2015) using full matrix least squares minimisation on F^2 .

Crystal Data. C₂₁H₂₂BrF₆O₃P, $M_r = 547.275$, monoclinic, $P2_1$ (No. 4), $a = 14.0207(11)$ Å, $b = 5.7946(7)$ Å, $c = 14.8367(11)$ Å, $\beta = 103.512(8)^\circ$, $\alpha = \gamma = 90^\circ$, $V = 1172.03(19)$ Å³, $T = 99.96(12)$ K, $Z = 2$, $Z' = 1$, $\mu(\text{Cu } K\alpha) = 3.666$, 10893 reflections measured, 4188 unique ($R_{\text{int}} = 0.0736$) which were used in all calculations. The final wR_2 was 0.1735 (all data) and R_1 was 0.0625 ($I \geq 2 \sigma(I)$).

Crystal data and structure refinement for compound **2.42**.

Compound	2.42
Formula	C ₂₁ H ₂₂ BrF ₆ O ₃ P
$D_{\text{calc.}} / \text{g cm}^{-3}$	1.551
μ / mm^{-1}	3.666
Formula Weight	547.275
Colour	colourless
Shape	needle-shaped
Size/mm ³	0.49×0.09×0.06
T/K	99.96(12)
Crystal System	monoclinic
Flack Parameter	0.020(19)
Hooft Parameter	0.020(19)
Space Group	$P2_1$
$a/\text{\AA}$	14.0207(11)
$b/\text{\AA}$	5.7946(7)
$c/\text{\AA}$	14.8367(11)
$\alpha/^\circ$	90
$\beta/^\circ$	103.512(8)
$\gamma/^\circ$	90
$V/\text{\AA}^3$	1172.03(19)
Z	2
Z'	1
Wavelength/Å	1.54184
Radiation type	Cu $K\alpha$
$\theta_{\text{min}}/^\circ$	3.24
$\theta_{\text{max}}/^\circ$	73.30
Measured Refl's.	10893
Indep't Refl's	4188
Refl's $I \geq 2 \sigma(I)$	3472
R_{int}	0.0736
Parameters	418
Restraints	399
Largest Peak	0.8749
Deepest Hole	-0.8954
GooF	1.0331
wR_2 (all data)	0.1735
wR_2	0.1582
R_1 (all data)	0.0747
R_1	0.0625

Structure Quality Indicators

Reflections:	d min (Cu\α)	0.80	I/σ(I)	14.2	R _{int}	7.36%	Full 135.4°	97.4
	2Θ=146.6°				m=2.58		92% to 146.6°	
Refinement:	Shift	-0.005	Max Peak	0.9	Min Peak	-0.9	Goof	1.033
							Hooft	.020(19)

A colourless needle-shaped crystal with dimensions $0.49 \times 0.09 \times 0.06 \text{ mm}^3$ was mounted on a loop with paratone. Data were collected using a XtaLAB Synergy, Dualflex, HyPix diffractometer operating at $T = 99.96(12) \text{ K}$.

Data were measured using ω scans with Cu K_α radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlisPro 1.171.42.74a (Rigaku OD, 2022). The maximum resolution that was achieved was $\theta = 73.30^\circ$ ($0.80 \text{ \AA}$).

The unit cell was refined using CrysAlisPro 1.171.42.74a (Rigaku OD, 2022) on 2526 reflections, 23% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using CrysAlisPro 1.171.42.74a (Rigaku OD, 2022). The final completeness is 98.89 % out to 73.30° in θ . A gaussian absorption correction was performed using CrysAlisPro 1.171.42.74a (Rigaku Oxford Diffraction, 2022) Numerical absorption correction based on gaussian integration over a multifaceted crystal model Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.. The absorption coefficient μ of this material is 3.666 mm^{-1} at this wavelength ($\lambda = 1.54184 \text{ \AA}$) and the minimum and maximum transmissions are 0.429 and 0.942.

The structure was solved and the space group $P2_1$ (# 4) determined by the ShelXT 2018/2 (Sheldrick, 2018) structure solution program using dual methods and refined by full matrix least squares minimisation on F^2 using version of olex2.refine 1.5-alpha (Bourhis et al., 2015). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. Most hydrogen atom positions were calculated geometrically and refined using the riding model, but some hydrogen atoms were refined freely.

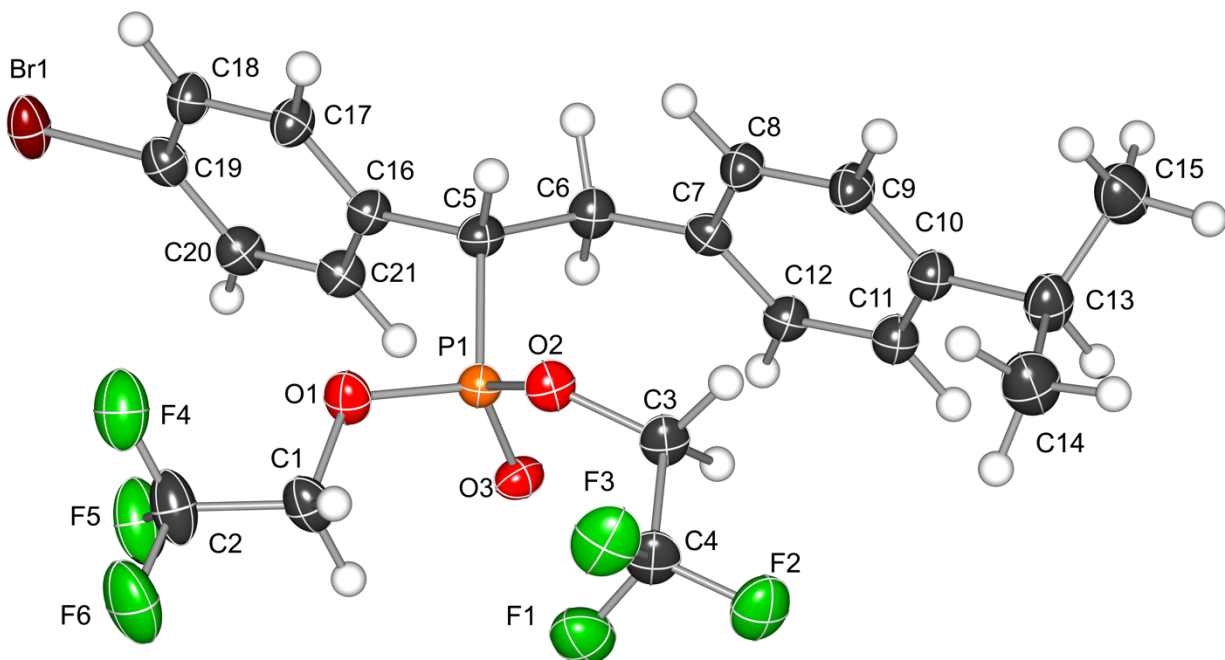


Figure S10:

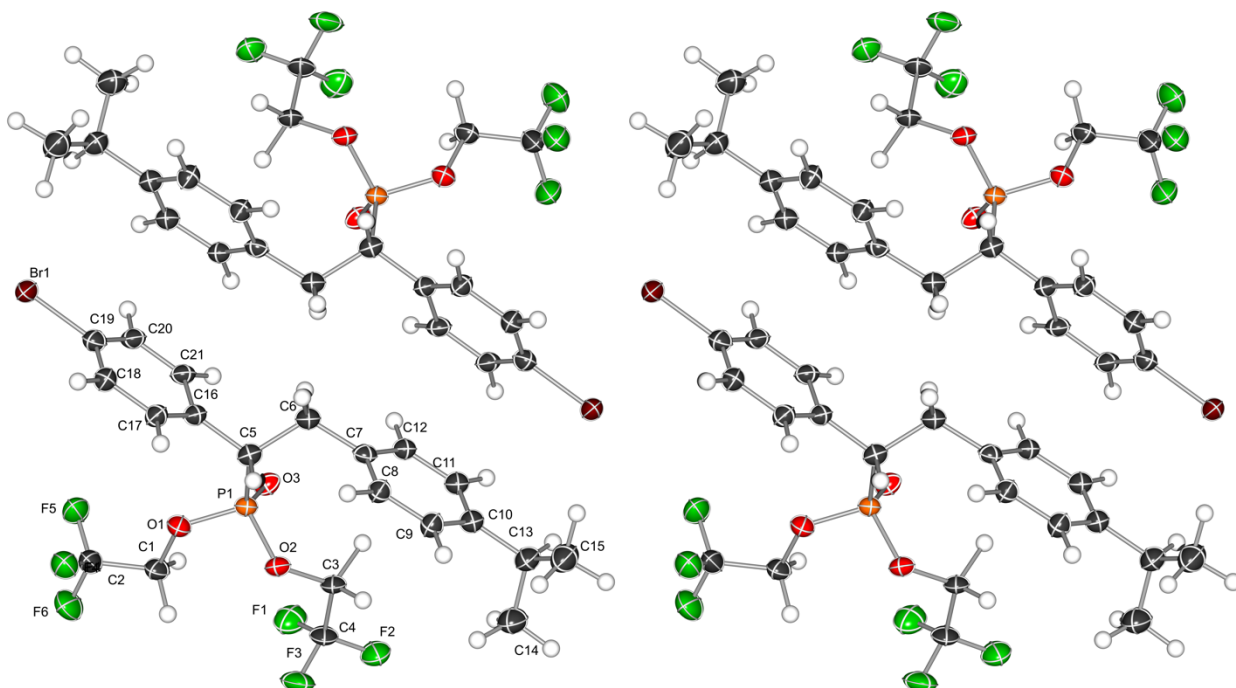
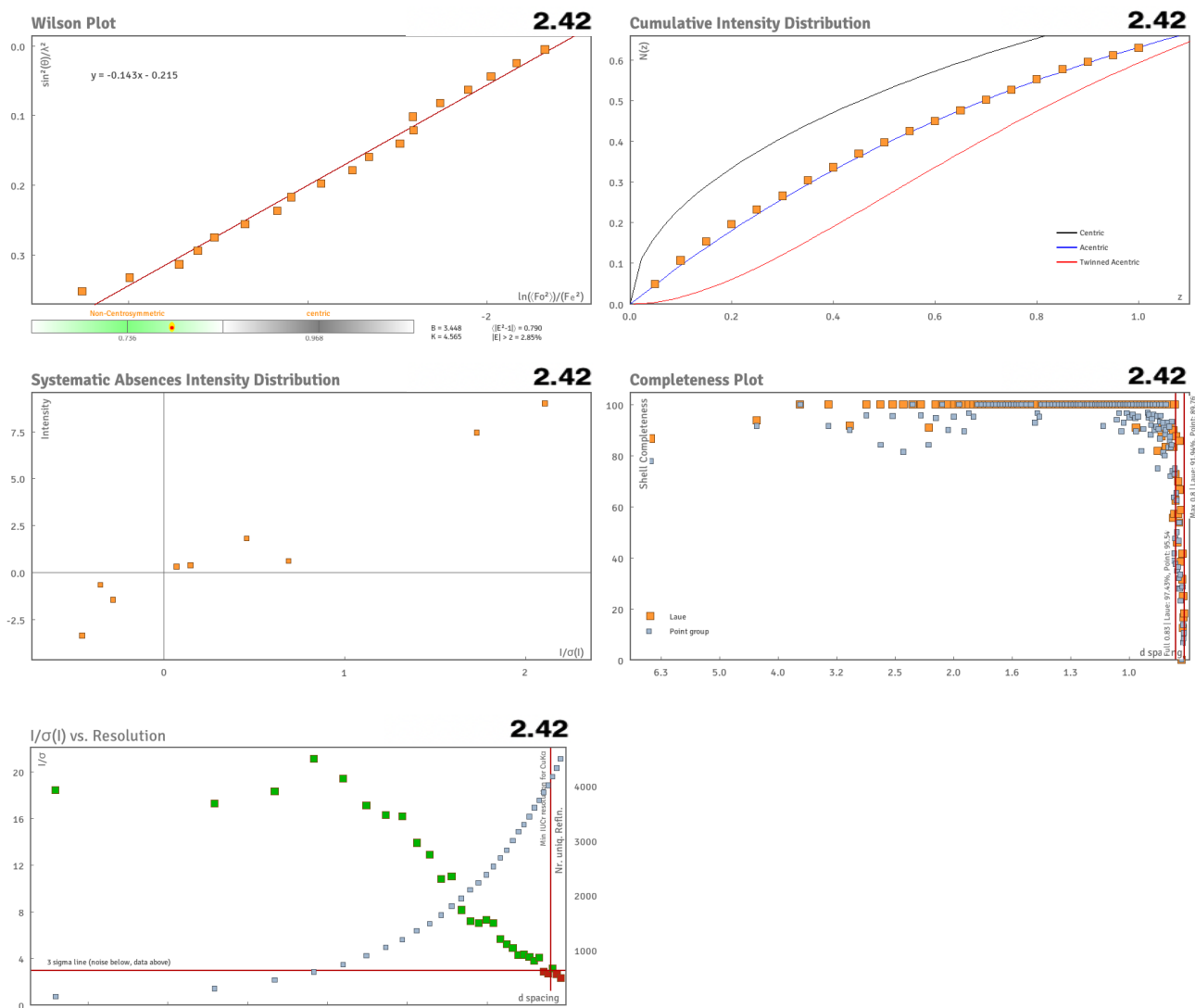


Figure S11:

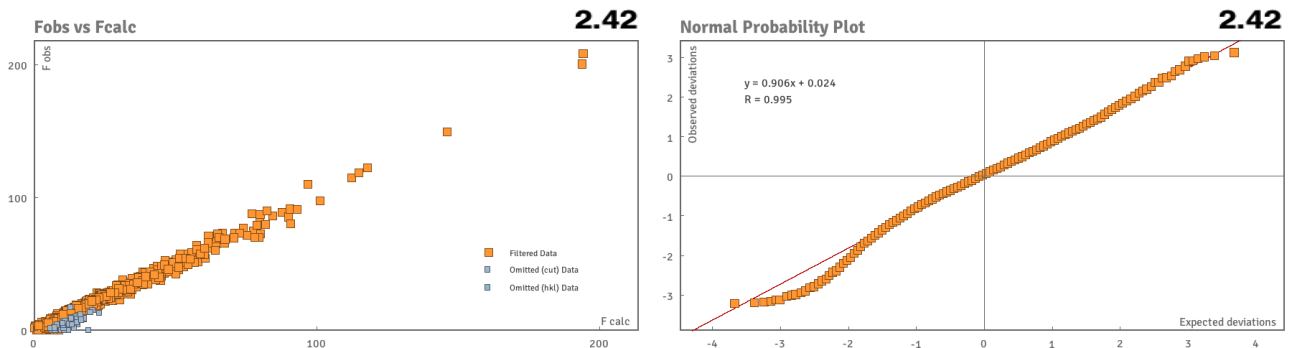
_olex2_refine_details: Refinement using NoSpherA2, an implementation of NON-SPHERical Atom-form-factors in Olex2. Please cite: F. Kleemiss et al. Chem. Sci. DOI 10.1039/D0SC05526C - 2021NoSpherA2 implementation of HAR makes use of tailor-made aspherical atomic form factors calculated on-the-fly from a Hirshfeld-partitioned electron density (ED) - not from spherical-atom form factors. The ED is calculated from a gaussian basis set single determinant SCF wave function - either Hartree-Fock or DFT using selected functionals - for a fragment of the crystal. This fragment can be embedded in an electrostatic crystal field by employing cluster charges or modelled using implicit solvation models, depending on the software used. The following options were used: SOFTWARE: ORCA PARTITIONING: NoSpherA2 INT ACCURACY: Normal METHOD: PBE BASIS SET: def2-SVP CHARGE: 0

exptl_absorpt_process_details: CrysAlisPro 1.171.42.74a (Rigaku Oxford Diffraction, 2022) Numerical absorption correction based on gaussian integration over a multifaceted crystal model Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

Data Plots: Diffraction Data



Data Plots: Refinement and Data



Reflection Statistics

Total reflections (after filtering)	10902	Unique reflections	4233
Completeness	0.898	Mean I/ σ	9.9
hkl _{max} collected	(14, 7, 18)	hkl _{min} collected	(-17, -6, -16)
hkl _{max} used	(16, 7, 18)	hkl _{min} used	(-17, -6, 0)
Lim d _{max} collected	100.0	Lim d _{min} collected	0.77
d _{max} used	13.63	d _{min} used	0.8
Friedel pairs	1313	Friedel pairs merged	0
Inconsistent equivalents	27	R _{int}	0.0735
R _{sigma}	0.0707	Intensity transformed	0
Omitted reflections	0	Omitted by user (OMIT hkl)	40
Multiplicity	(2426, 1637, 777, 407, 161, 52, 18)	Maximum multiplicity	8
Removed systematic absences	9	Filtered off (Shel/OMIT)	0

Table S18: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for compound **2.42**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
Br1	262.5(4)	7420.8(7)	4077.6(4)	49.1(2)
P1	4567.0(10)	4563(2)	7432.2(9)	29.9(3)
F2	7196(3)	1869(7)	9747(3)	62.1(12)
O3	4799(3)	2312(7)	7090(3)	37.0(8)
O1	3567(3)	4696(7)	7736(3)	41.2(10)
O2	5316(3)	5329(7)	8366(3)	37.3(9)
F1	5690(4)	956(7)	9222(3)	65.3(12)
F3	6065(4)	3760(7)	10174(3)	67.0(13)
F5	1823(3)	2140(8)	7508(3)	71.7(13)
F4	1890(3)	5184(8)	8345(3)	69.4(12)
F6	2069(4)	1830(8)	8992(3)	81.9(16)
C7	6285(4)	6759(9)	6608(4)	32.5(11)
C11	7859(4)	4834(11)	7069(4)	37.3(12)
C20	2118(5)	5288(11)	4814(4)	38.3(12)
C5	4449(4)	6940(9)	6621(4)	32.5(12)
C9	7639(5)	8541(11)	7706(5)	40.0(13)
C19	1534(4)	7228(12)	4848(4)	38.3(11)
C8	6671(4)	8609(11)	7185(4)	36.9(12)
C12	6887(4)	4897(10)	6537(4)	34.0(12)
C21	3056(4)	5192(10)	5378(4)	35.9(12)
C16	3418(4)	6997(10)	5997(4)	33.3(11)
C17	2826(4)	8912(10)	6011(4)	36.1(12)
C6	5236(4)	6828(11)	6055(4)	38.7(14)
C4	6300(5)	2717(13)	9461(4)	45.9(12)
C10	8253(5)	6639(10)	7653(4)	37.8(12)
C18	1879(4)	9035(11)	5451(4)	38.7(13)
C1	3368(5)	3162(11)	8422(4)	43.1(14)
C3	6271(4)	4368(11)	8657(4)	37.6(12)
C13	9287(5)	6495(13)	8245(5)	49.0(14)
C2	2270(5)	3104(14)	8305(5)	56.9(14)
C14	9286(6)	5722(14)	9208(5)	60.5(19)
C15	9877(6)	8639(13)	8217(6)	60.8(19)

Table S19: Anisotropic Displacement Parameters ($\times 10^4$) for compound **2.42**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \dots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	32.0(3)	81.3(5)	32.0(3)	-5.9(3)	3.3(2)	6.5(4)
P1	31.7(7)	34.5(7)	23.3(6)	0.1(6)	6.1(5)	0.1(6)
F2	56.2(19)	86(3)	41(2)	14.5(16)	5.3(13)	17.7(19)
O3	40.2(19)	32(2)	35.1(19)	4(2)	1.9(15)	1(2)
O1	38(2)	56(3)	30.3(19)	-0.7(17)	9.6(15)	5.8(17)
O2	40.2(19)	47(2)	22.4(18)	-1.5(15)	2.3(13)	-1.9(16)
F1	66(3)	69(3)	57(3)	-5.7(16)	7.0(18)	19.2(17)
F3	78(3)	98(3)	26.5(18)	14(2)	14.4(15)	7.7(16)
F5	46(2)	118(4)	49.5(19)	-17(2)	7.4(14)	-23.2(19)
F4	52(2)	107(3)	53(2)	-1.3(17)	17.2(18)	-13.3(18)
F6	62(3)	129(5)	61(2)	-22(2)	28.0(17)	6(2)
C7	38(2)	36(2)	25(2)	-1.0(12)	8.1(13)	4.9(14)
C11	37(2)	44(3)	30(2)	1.6(14)	6.3(15)	0.8(16)
H11	46(9)	54(8)	50(20)	11(4)	-2(6)	-11(6)
C20	41(2)	47(3)	25(2)	-3.4(14)	4.1(15)	-1.1(17)
H20	49(11)	54(12)	60(30)	10(5)	-10(8)	-22(9)
C5	36(2)	33(3)	28(2)	-0.2(14)	4.4(13)	0.7(16)
H5	42(11)	33(7)	27(13)	-3(3)	8(4)	1(5)
C9	35(2)	42(3)	41(3)	-0.9(14)	4.0(16)	-2.7(18)
H9	46(9)	54(8)	50(20)	11(4)	-2(6)	-11(6)
C19	39(2)	48(3)	29(2)	-5.0(13)	9.2(13)	1.8(16)
C8	33(2)	38(3)	38(3)	0.5(14)	5.0(16)	-0.7(16)
H8	46(9)	54(8)	50(20)	11(4)	-2(6)	-11(6)
C12	35(2)	38(3)	28(2)	0.4(13)	5.4(15)	0.3(17)
H12	46(9)	54(8)	50(20)	11(4)	-2(6)	-11(6)
C21	38(2)	40(3)	28(2)	-2.0(14)	3.8(15)	-3.2(16)
H21	49(11)	54(12)	60(30)	10(5)	-10(8)	-22(9)
C16	34(2)	37(3)	27(2)	0.4(13)	4.0(13)	-0.0(14)
C17	33(2)	39(3)	33(3)	1.6(14)	3.2(16)	-2.5(16)
H17	37(12)	41(11)	40(30)	4(5)	-1(8)	-6(8)
C6	38(2)	51(4)	26(2)	1.4(14)	6.8(13)	1.5(17)
H6a	43(11)	54(6)	33(8)	1(3)	7(4)	7(3)
H6b	37(10)	51(6)	27(8)	2(3)	6(4)	1(3)
C4	49(2)	63(3)	26(2)	3.3(13)	8.6(12)	16.0(14)
C10	36(2)	45(3)	31(2)	1.3(13)	6.3(15)	1.4(15)
C18	33(2)	47(3)	35(3)	2.0(14)	6.4(15)	-1.0(17)
H18	42(12)	62(16)	60(40)	14(7)	-13(10)	-23(12)
C1	41(2)	61(4)	28(2)	-8.0(16)	8.8(13)	4.3(18)
H1a	44(11)	61(5)	31(11)	-8(3)	14(4)	6(3)
H1b	42(10)	65(11)	29(4)	-9(4)	9(2)	3(3)
C3	38(2)	53(3)	20(2)	0.8(16)	3.8(14)	6.9(16)
H3a	43(11)	53(9)	22(6)	0(4)	7(3)	6(3)
H3b	41(7)	54(7)	16(11)	-1(3)	3(3)	8(3)
C13	40(3)	64(3)	39(3)	1.3(15)	1.8(16)	5.8(19)
H13	40(9)	65(6)	42(10)	2(3)	3(4)	7(3)
C2	40(2)	95(3)	38(2)	-13.2(15)	13.6(12)	-11.7(16)
C14	58(4)	76(5)	43(3)	-4(3)	2.7(19)	9(2)
H14a	60(9)	80(10)	44(11)	-2(4)	4(4)	9(4)
H14b	60(12)	77(6)	48(12)	-5(4)	3(5)	10(3)
H14c	58(5)	77(13)	47(9)	-4(4)	1(3)	9(4)
C15	47(4)	71(4)	58(4)	-5(2)	-1(3)	12(2)
H15a	47(12)	77(12)	58(5)	-5(5)	0(3)	13(3)
H15b	45(11)	72(7)	57(11)	-5(4)	-3(5)	11(4)
H15c	47(4)	77(13)	62(10)	-4(3)	-2(3)	12(5)

Table 4: Bond Lengths in Å for compound **2.42**.

Atom	Atom	Length/Å
Br1	C19	1.883(6)
P1	O3	1.464(4)
P1	O1	1.572(4)
P1	O2	1.594(4)
P1	C5	1.811(5)
F2	C4	1.324(8)
O1	C1	1.427(7)
O2	C3	1.421(7)
F1	C4	1.325(8)
F3	C4	1.324(8)
F5	C2	1.325(8)
F4	C2	1.324(9)
F6	C2	1.341(9)
C7	C8	1.400(8)
C7	C12	1.389(8)
C7	C6	1.508(8)
C11	H11	1.084(3)
C11	C12	1.406(8)
C11	C10	1.388(9)
C20	H20	1.040(3)
C20	C19	1.398(9)
C20	C21	1.385(9)
C5	H5	1.0831(16)
C5	C16	1.524(8)
C5	C6	1.537(8)
C9	H9	1.084(3)
C9	C8	1.396(9)
C9	C10	1.411(9)
C19	C18	1.388(9)
C8	H8	1.084(3)
C12	H12	1.084(3)
C21	H21	1.040(3)
C21	C16	1.407(8)
C16	C17	1.389(8)
C17	H17	1.040(3)
C17	C18	1.395(9)
C6	H6a	1.0830(11)
C6	H6b	1.0830(11)
C4	C3	1.523(8)
C10	C13	1.512(9)
C18	H18	1.040(3)
C1	H1a	1.0830(13)
C1	H1b	1.0830(13)
C1	C2	1.509(9)
C3	H3a	1.0831(19)
C3	H3b	1.0831(19)
C13	H13	1.0831(19)
C13	C14	1.498(10)
C13	C15	1.498(10)
C14	H14a	1.0830(19)
C14	H14b	1.0830(19)
C14	H14c	1.0830(19)
C15	H15a	1.0831(19)
C15	H15b	1.0831(19)
C15	H15c	1.0831(19)

Table S21: Bond Angles in ° for compound **2.42**.

Atom	Atom	Atom	Angle/°
O1	P1	O3	115.4(2)
O2	P1	O3	113.3(2)
O2	P1	O1	100.8(2)
C5	P1	O3	116.1(2)
C5	P1	O1	101.8(2)
C5	P1	O2	107.8(2)
C1	O1	P1	120.7(4)
C3	O2	P1	122.5(4)
C12	C7	C8	119.1(5)
C6	C7	C8	120.1(5)
C6	C7	C12	120.8(5)
C12	C11	H11	119.3(3)
C10	C11	H11	119.3(4)
C10	C11	C12	121.5(6)
C19	C20	H20	120.3(3)
C21	C20	H20	120.3(4)
C21	C20	C19	119.4(6)
H5	C5	P1	107(3)
C16	C5	P1	110.3(4)
C16	C5	H5	111(3)
C6	C5	P1	111.4(4)
C6	C5	H5	105(4)
C6	C5	C16	111.6(4)
C8	C9	H9	119.4(4)
C10	C9	H9	119.4(4)
C10	C9	C8	121.2(6)
C20	C19	Br1	120.3(5)
C18	C19	Br1	118.9(5)
C18	C19	C20	120.8(5)
C9	C8	C7	120.3(6)
H8	C8	C7	119.9(3)
H8	C8	C9	119.9(4)
C11	C12	C7	120.3(5)
H12	C12	C7	119(4)
H12	C12	C11	120(4)
H21	C21	C20	119.6(4)
C16	C21	C20	120.8(6)
C16	C21	H21	119.6(3)
C21	C16	C5	121.9(5)
C17	C16	C5	119.6(5)
C17	C16	C21	118.5(5)
H17	C17	C16	119.3(3)
C18	C17	C16	121.4(5)
C18	C17	H17	119.3(3)
C5	C6	C7	115.9(5)
H6a	C6	C7	108.3(3)
H6a	C6	C5	108.3(3)
H6b	C6	C7	108.3(3)
H6b	C6	C5	108.3(3)
H6b	C6	H6a	107.4
F1	C4	F2	107.8(6)
F3	C4	F2	107.9(5)
F3	C4	F1	107.5(5)

Atom	Atom	Atom	Angle/°
C3	C4	F2	109.5(5)
C3	C4	F1	112.1(5)
C3	C4	F3	111.9(6)
C9	C10	C11	117.7(6)
C13	C10	C11	120.6(6)
C13	C10	C9	121.7(6)
C17	C18	C19	119.0(6)
H18	C18	C19	120.5(4)
H18	C18	C17	120.5(3)
H1a	C1	O1	110.3(3)
H1b	C1	O1	110.3(3)
H1b	C1	H1a	108.5
C2	C1	O1	107.3(5)
C2	C1	H1a	110.3(4)
C2	C1	H1b	110.3(3)
C4	C3	O2	109.5(5)
H3a	C3	O2	109.8(3)
H3a	C3	C4	109.8(4)
H3b	C3	O2	109.8(3)
H3b	C3	C4	109.8(3)
H3b	C3	H3a	108.2
H13	C13	C10	105(3)
C14	C13	C10	110.8(6)
C14	C13	H13	101(4)
C15	C13	C10	113.5(6)
C15	C13	H13	112(3)
C15	C13	C14	113.5(7)
F4	C2	F5	108.2(6)
F6	C2	F5	107.9(6)
F6	C2	F4	108.0(5)
C1	C2	F5	111.6(5)
C1	C2	F4	112.6(6)
C1	C2	F6	108.3(6)
H14a	C14	C13	109.5
H14b	C14	C13	109.5
H14b	C14	H14a	109.5
H14c	C14	C13	109.5
H14c	C14	H14a	109.5
H14c	C14	H14b	109.5
H15a	C15	C13	109.5
H15b	C15	C13	109.5
H15b	C15	H15a	109.5
H15c	C15	C13	109.5
H15c	C15	H15a	109.5
H15c	C15	H15b	109.5

Table S22: Torsion Angles in ° for compound **2.42**.

Atom	Atom	Atom	Atom	Angle/°
Br1	C19	C20	C21	179.2(4)
Br1	C19	C18	C17	-179.0(4)
P1	O1	C1	C2	-159.5(5)
P1	O2	C3	C4	-105.9(5)
P1	C5	C16	C21	-63.8(5)
P1	C5	C16	C17	118.4(4)

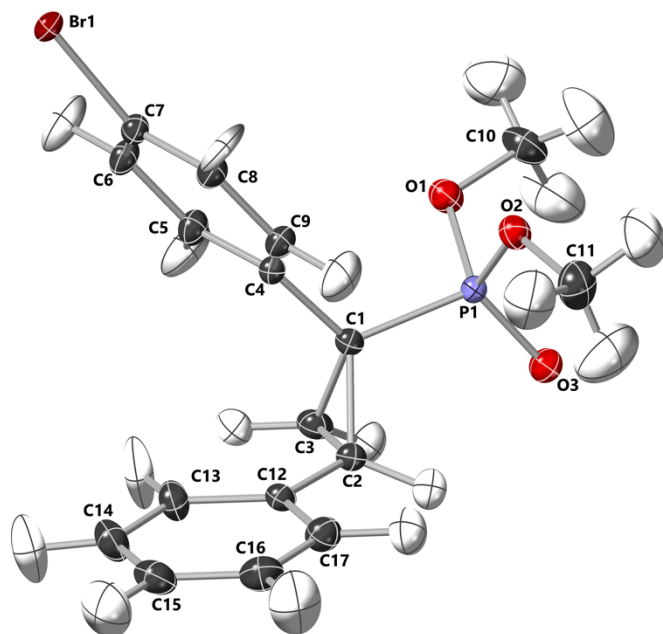
Atom	Atom	Atom	Atom	Angle/°
P1	C5	C6	C7	-56.1(4)
F2	C4	C3	O2	-178.3(5)
O1	C1	C2	F5	66.6(6)
O1	C1	C2	F4	-55.4(6)
O1	C1	C2	F6	-174.7(5)
O2	C3	C4	F1	62.1(5)
O2	C3	C4	F3	-58.8(5)
C7	C8	C9	C10	1.0(7)
C7	C12	C11	C10	-2.0(6)
C7	C6	C5	C16	-179.9(5)
C11	C10	C9	C8	-0.3(7)
C11	C10	C13	C14	-97.2(7)
C11	C10	C13	C15	133.7(7)
C20	C19	C18	C17	1.3(6)
C20	C21	C16	C5	-179.7(5)
C20	C21	C16	C17	-1.9(7)
C5	C16	C17	C18	180.0(5)
C9	C10	C13	C14	79.7(7)
C9	C10	C13	C15	-49.4(7)
C19	C18	C17	C16	-1.8(7)
C21	C16	C17	C18	2.1(6)

Table S23: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for compound **2.42**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
H11	8311(5)	3342(11)	7021(4)	53(10)
H20	1849(5)	3928(11)	4370(4)	58(16)
H5	4610(50)	8500(50)	7030(30)	34(7)
H9	7925(5)	9974(11)	8158(5)	53(10)
H8	6218(4)	10100(11)	7229(4)	53(10)
H12	6590(50)	3460(80)	6090(40)	53(10)
H21	3497(5)	3768(11)	5342(4)	58(16)
H17	3095(4)	10284(11)	6450(4)	41(16)
H6a	5148(4)	8316(11)	5601(4)	44(5)
H6b	5102(4)	5306(11)	5620(4)	39(5)
H18	1437(5)	10460(11)	5484(4)	60(20)
H1a	3641(5)	1451(11)	8330(4)	44(6)
H1b	3722(5)	3768(11)	9109(4)	45(6)
H3a	6458(4)	3451(11)	8085(4)	40(6)
H3b	6803(4)	5733(11)	8871(4)	38(5)
H13	9610(40)	5000(70)	7990(40)	50(6)
H14a	8808(6)	6832(14)	9492(5)	63(6)
H14b	9023(6)	3960(14)	9189(5)	63(6)
H14c	10024(6)	5813(14)	9638(6)	62(6)
H15a	9864(6)	9067(13)	7503(6)	63(6)
H15b	9567(6)	10050(14)	8533(6)	60(6)
H15c	10628(6)	8350(13)	8593(6)	64(6)

Submitted by: **Yasir Naeem**Solved by: **John Bacsá** **$R_1 = 1.58\%$**

Crystal Data and Experimental



Experimental. A single colorless crystal of **4.39b** with dimensions $0.25 \times 0.18 \times 0.05 \text{ mm}^3$ was selected and mounted on a loop with paratone on a XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was kept at a steady $T = 100(1) \text{ K}$ during data collection. The structure was solved with the ShelXT (Sheldrick, 2015) solution program using iterative methods and by using Olex2 1.5-alpha (Dolomanov et al., 2009) as the graphical interface. The model was refined with olex2.refine 1.5-alpha (Bourhis et al., 2015) using full matrix least squares minimisation on F^2 .

Crystal Data. $\text{C}_{17}\text{H}_{18}\text{BrO}_3\text{P}$, $M_r = 381.208$, orthorhombic, $P2_12_12_1$ (No. 19), $a = 6.5281(2) \text{ \AA}$, $b = 9.2356(3) \text{ \AA}$, $c = 27.8895(7) \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$, $V = 1681.48(9) \text{ \AA}^3$, $T = 158(80) \text{ K}$, $Z = 4$, $Z' = 1$, $\mu(\text{Cu } K\alpha) = 4.313$, 29021 reflections measured, 3452 unique ($R_{\text{int}} = 0.0535$) which were used in all calculations. The final wR_2 was 0.0347 (all data) and R_1

Compound	4.39b
Formula	$\text{C}_{17}\text{H}_{18}\text{BrO}_3\text{P}$
$D_{\text{calc.}} / \text{g cm}^{-3}$	1.506
μ / mm^{-1}	4.313
Formula Weight	381.208
Color	colorless
Shape	block-shaped
Size/ mm^3	$0.25 \times 0.18 \times 0.05$
T / K	158(80)
Crystal System	orthorhombic
Flack Parameter	-0.032(6)
Hooft Parameter	-0.032(6)
Space Group	$P2_12_12_1$
$a / \text{\AA}$	6.5281(2)
$b / \text{\AA}$	9.2356(3)
$c / \text{\AA}$	27.8895(7)
$\alpha / ^\circ$	90
$\beta / ^\circ$	90
$\gamma / ^\circ$	90
$V / \text{\AA}^3$	1681.48(9)
Z	4
Z'	1
Wavelength/ $\text{\AA}$	1.54184
Radiation type	Cu $K\alpha$
$\theta_{\text{min}} / ^\circ$	3.17
$\theta_{\text{max}} / ^\circ$	78.22
Measured Refl's.	29021
Indep't Refl's	3452
Refl's $I \geq 2 \sigma(I)$	3415
R_{int}	0.0535
Parameters	411
Restraints	309
Largest Peak	0.2098
Deepest Hole	-0.1553
GooF	1.1007
wR_2 (all data)	0.0347
wR_2	0.0345
R_1 (all data)	0.0161
R_1	0.0158

was 0.0158 ($I \geq 2 \sigma(I)$).

Structure Quality Indicators

Reflections:	d min (CuK α) 2 Θ =156.4°	0.79	I/ σ (I)	48.7	R _{int} m=8.39	5.35%	Full 135.4° 95% to 156.4°	98.7
Refinement:	Shift	-0.001	Max Peak	0.2	Min Peak	-0.2	GooF	1.101
							Hoof	-.032(6)

A colorless block-shaped crystal with dimensions $0.25 \times 0.18 \times 0.05$ mm³ was mounted on a loop with paratone. Data were collected using a XtaLAB Synergy, Dualflex, HyPix diffractometer operating at $T = 158(80)$ K.

Data were measured using ω scans with Cu K α radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlisPro system (CCD 43.128a 64-bit (release 20-06-2024)). The maximum resolution that was achieved was $\Theta = 78.22^\circ$ (0.79 Å).

The unit cell was refined using CrysAlisPro 1.171.43.121a (Rigaku OD, 2024) on 23439 reflections, 81% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using CrysAlisPro 1.171.43.121a (Rigaku OD, 2024). The final completeness is 99.78 % out to 78.22° in Θ . A numerical absorption correction based on gaussian integration over a multifaceted crystal model was performed using CrysAlisPro 1.171.42.74a (Rigaku Oxford Diffraction, 2022). An empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm was also used. The absorption coefficient μ of this material is 4.313 mm⁻¹ at this wavelength ($\lambda = 1.54184$ Å) and the minimum and maximum transmissions are 0.354 and 1.000.

The structure was solved and the space group $P2_12_12_1$ (# 19) determined by the ShelXT (Sheldrick, 2015) structure solution program using iterative methods and refined by full matrix least squares minimisation on F^2 using version of olex2.refine 1.5-alpha (Bourhis et al., 2015). All atoms were refined anisotropically. Hydrogen atom positions were located from the electron densities and freely refined using Hirshfeld scattering factors. Refinement was by using NoSpherA2, an implementation of non-spherical atom-form-factors (F. Kleemiss, H. Puschmann, O. Dolomanov, S. Grabowsky - <https://doi.org/10.1039/D0SC05526C> – 2020). NoSpherA2 implementation of HAR makes use of tailor-made aspherical atomic form factors calculated from a Hirshfeld-partitioned electron density (ED) not from spherical-atom form factors. The ED was calculated from a Gaussian basis set single determinant SCF wavefunction from DFT using selected functionals for a fragment of this crystal. This fragment was embedded in an electrostatic crystal field by employing cluster charges. The following options were used: SOFTWARE: ORCA PARTITIONING: NoSpherA2 INT ACCURACY: Normal METHOD: PBE BASIS SET: def2-TZVP CHARGE: 0 MULTIPLICITY: 1 SOLVATION: Ethanol DATE: 2024-09-15_11-56-33

There is a single formula unit in the asymmetric unit, which is represented by the reported sum formula. In other words: Z is 4 and Z' is 1. The moiety formula is C₁₇ H₁₈ Br O₃ P.

The Flack parameter was refined to -0.032(6). Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2 results in -0.032(6). The chiral atoms in this structure are: C1(S), C2(R). Note: The Flack parameter is used to determine chirality of the crystal studied, the value should be near 0, a value of 1 means that the stereochemistry is wrong and the model should be inverted. A value of 0.5 means that the crystal consists of a racemic mixture of the two enantiomers.

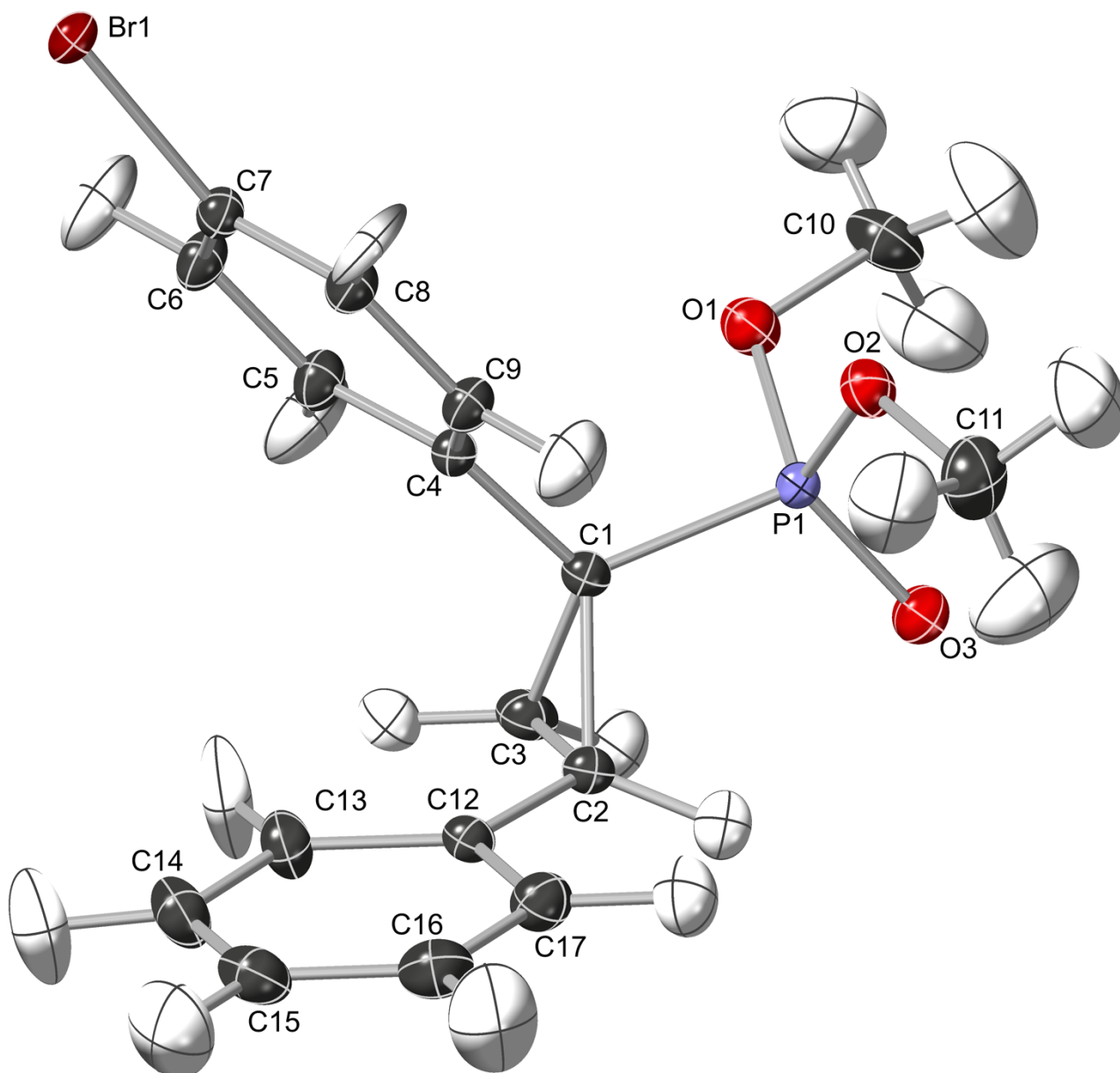


Figure 4 Thermal ellipsoidal representation (50% probability for all atoms, including hydrogens) of the molecular structure in the crystal. The chiral atoms in this structure are: C1(S), C2(R).

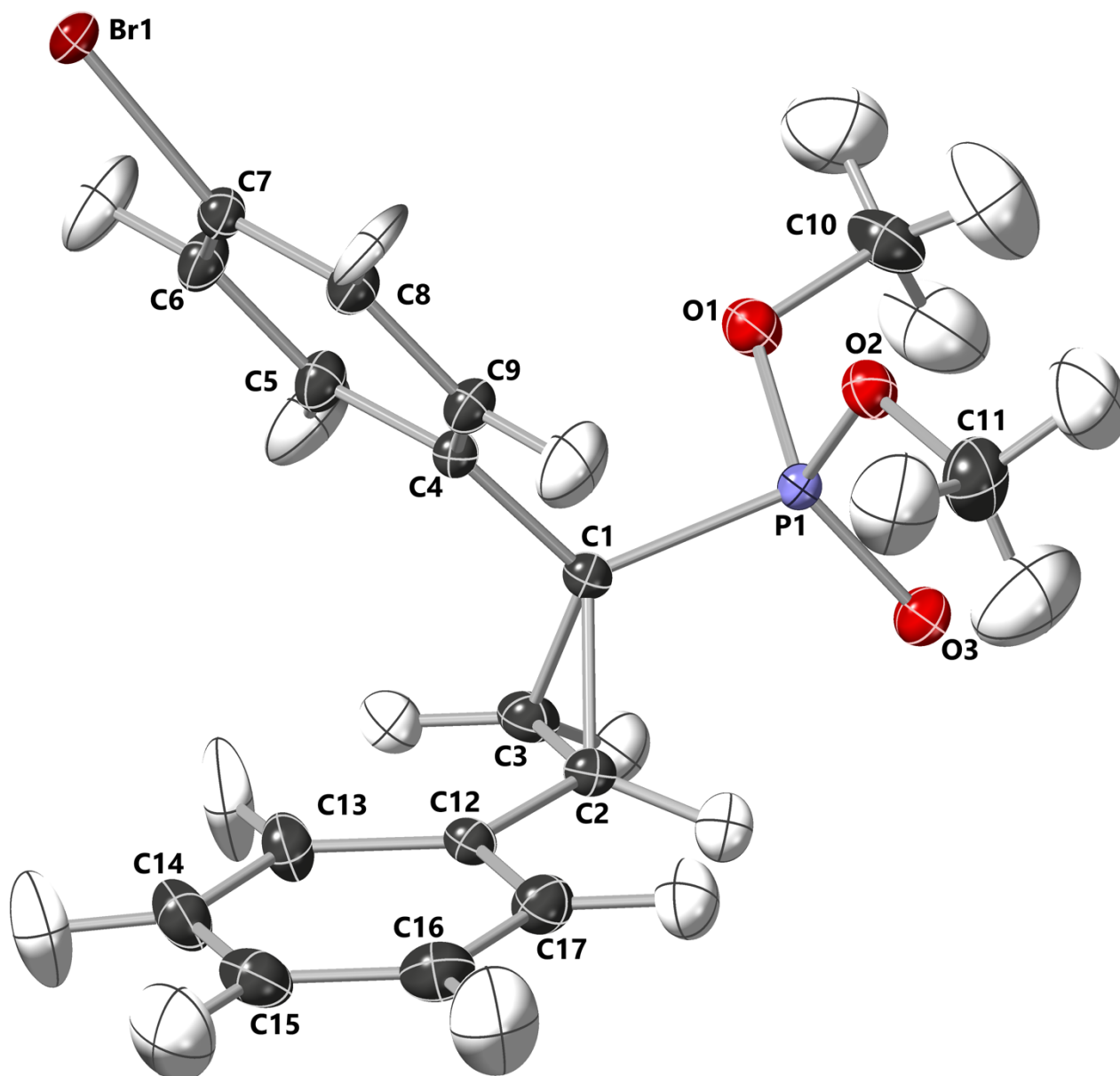


Figure 5 Thermal ellipsoidal representation (50% probability for all atoms, including hydrogens) of the molecular structure in the crystal. The chiral atoms in this structure are: C1(S), C2(R).

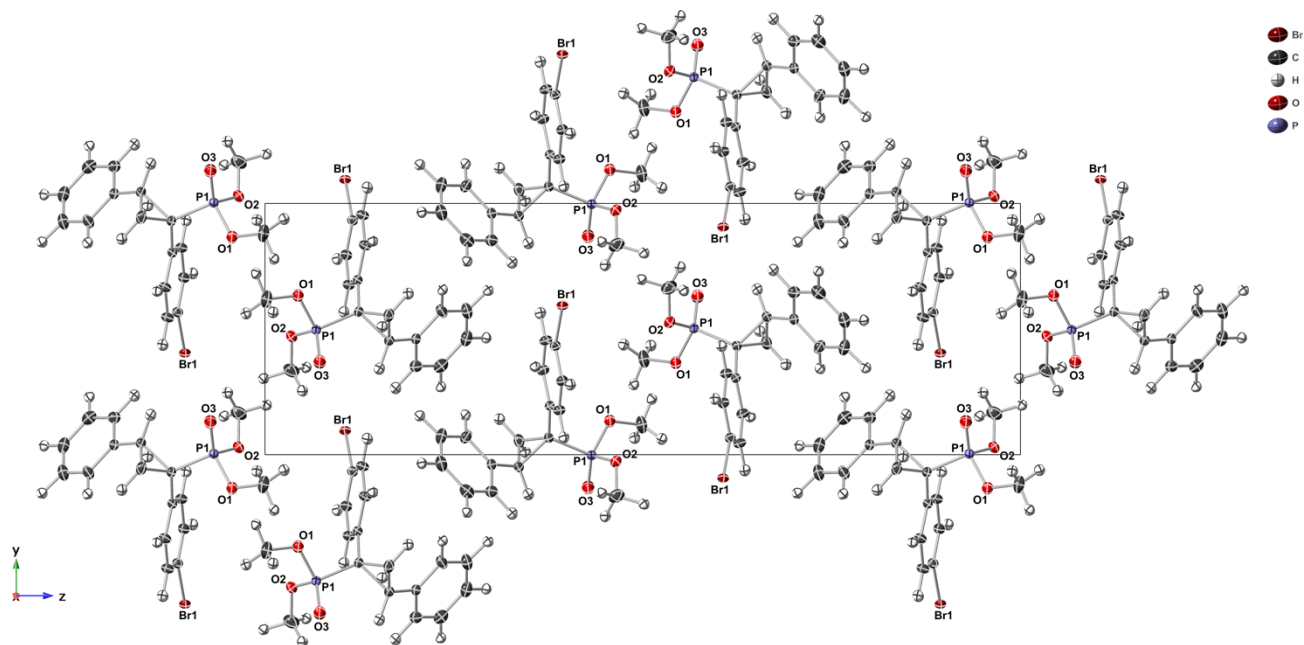
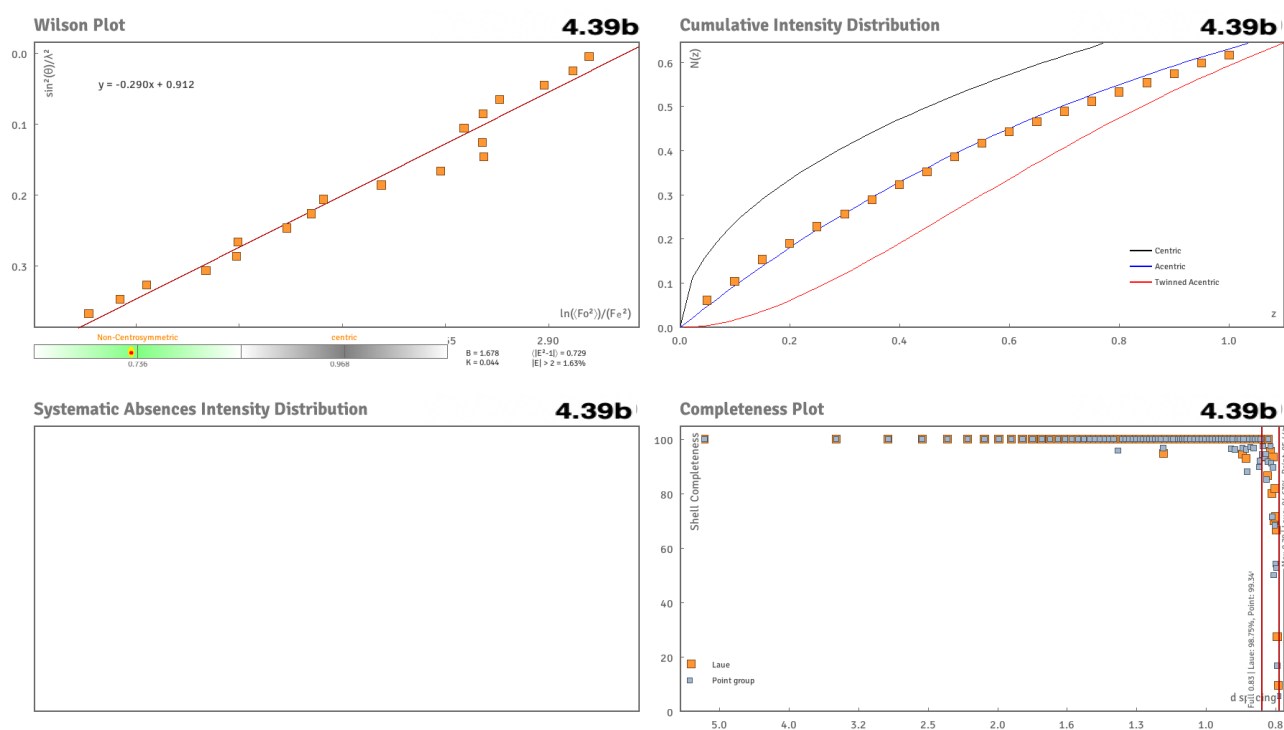
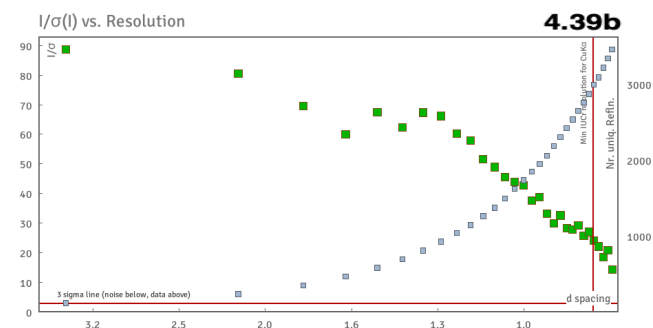


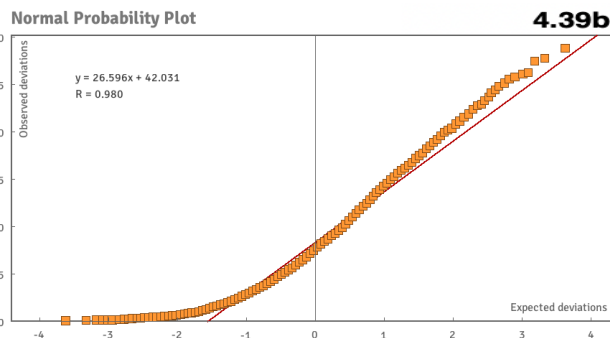
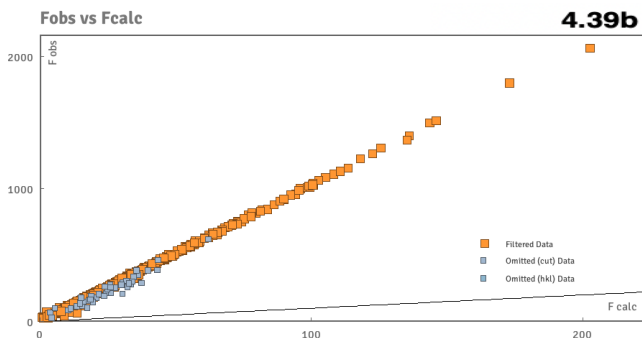
Figure 6 Molecular packing in the crystal structure

Data Plots: Diffraction Data





Data Plots: Refinement and Data



Reflection Statistics

Total reflections (after filtering)	28615	Unique reflections	3447
Completeness	0.953	Mean I/σ	45.24
$hkl_{\max}$ collected	(8, 11, 35)	$hkl_{\min}$ collected	(-8, -11, -27)
$hkl_{\max}$ used	(8, 11, 35)	$hkl_{\min}$ used	(-8, 0, 0)
Lim $d_{\max}$ collected	100.0	Lim $d_{\min}$ collected	0.77
$d_{\max}$ used	13.94	$d_{\min}$ used	0.79
Friedel pairs	2450	Friedel pairs merged	0
Inconsistent equivalents	19	R_{int}	0.0459
R_{sigma}	0.0181	Intensity transformed	0
Omitted reflections	185	Omitted by user (OMIT hkl)	0
Multiplicity	(2925, 1928, 1216, 983, 689, 426, 321, 254, 131, 82, 48, 54, 33, 21, 13, 2, 2)	Maximum multiplicity	26
Removed systematic absences	0	Filtered off (Shel/OMIT)	0



Table 5: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 4.39b. U_{eq} is defined as $1/3$ of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
Br1	564.7(5)	-945.6(3)	6062.12(11)	18.07(15)
C1	6362(2)	4317.1(14)	6241.9(4)	16.5(3)
C2	6153(2)	5472.0(15)	6642.4(5)	19.1(3)
C3	7948(2)	4448.7(16)	6638.3(5)	21.7(3)
C4	4933(2)	3046.3(14)	6229.7(4)	15.7(3)
C5	5647(2)	1651.0(15)	6323.3(4)	20.0(3)
C6	4345(2)	457.4(15)	6287.3(5)	20.6(3)
C7	2309(2)	670.4(14)	6158.0(4)	16.2(3)
C8	1558(2)	2053.5(15)	6071.4(5)	18.5(3)
C9	2875(2)	3235.2(14)	6107.4(5)	17.9(3)
C10	9452(3)	3811(2)	5017.6(5)	32.0(4)
C11	4176(3)	6649.6(18)	5347.2(6)	33.9(4)
C12	4468(2)	5391.8(14)	6999.8(4)	18.5(3)
C13	4308(3)	4286.7(16)	7339.2(5)	25.0(3)
C14	2706(3)	4277.0(19)	7669.6(5)	29.2(3)
C15	1235(2)	5363.1(19)	7666.4(5)	28.9(3)
C16	1377(3)	6463.1(18)	7327.9(5)	28.3(3)
C17	2983(2)	6472.5(16)	6999.7(5)	24.3(3)
O1	8175.9(16)	3660.7(11)	5436.5(3)	22.6(2)
O2	5231.7(16)	5283.4(11)	5353.5(3)	21.9(2)
O3	8523.5(17)	6303.7(12)	5723.9(3)	29.2(3)
P1	7182.9(14)	5031.2(10)	5678.0(3)	15.5(2)

Table 6: Anisotropic Displacement Parameters ($\times 10^4$) for **4.39b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \dots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	20.7(2)	12.8(2)	20.7(2)	-4.36(19)	-0.19(18)	0.38(16)
C1	19.8(6)	16.1(7)	13.7(5)	-1.9(5)	-1.9(5)	-0.1(5)
C2	24.1(8)	18.3(6)	15.0(6)	-3.9(5)	0.2(5)	-1.6(5)
H2	46(11)	24(5)	27(9)	-6(3)	4(6)	3(3)
C3	22.7(7)	25.6(8)	16.7(6)	-3.2(6)	-4.1(6)	-2.5(5)
H3a	25(5)	30(9)	41(9)	-4(3)	0(3)	1(6)
H3b	45(10)	30(6)	22(7)	-6(5)	-6(5)	2(3)
C4	19.6(7)	13.2(6)	14.3(5)	-0.9(5)	-1.5(4)	1.1(4)
C5	19.9(7)	16.4(6)	23.6(6)	-0.1(6)	-3.4(6)	4.1(5)
H5	24(4)	19(9)	76(14)	1(3)	-18(3)	4(7)
C6	21.8(7)	13.9(6)	26.1(6)	-1.3(6)	-4.3(6)	4.0(5)
H6	30(10)	16(5)	77(14)	0(3)	-12(7)	10(3)
C7	16.8(6)	15.0(7)	16.9(5)	-1.8(5)	-0.6(5)	1.5(4)
C8	17.8(6)	16.1(6)	21.5(6)	-0.8(5)	-2.1(6)	1.3(6)
H8	22(4)	8(8)	69(12)	-4(3)	-18(3)	3(6)
C9	17.9(6)	14.2(6)	21.7(6)	-0.2(5)	-1.4(5)	1.1(5)
H9	45(10)	21(5)	53(12)	9(3)	-5(7)	7(3)
C10	32.8(8)	44.6(10)	18.6(6)	0.8(9)	4.1(7)	-5.4(7)
H10a	51(6)	101(14)	46(11)	-25(4)	4(4)	-10(6)
H10b	70(12)	96(13)	46(8)	13(6)	-4(4)	18(5)
H10c	74(14)	58(5)	58(11)	5(3)	18(7)	-16(3)
C11	37.1(10)	27.3(8)	37.4(8)	12.8(8)	4.4(8)	7.7(7)
H11a	50(6)	46(12)	64(11)	11(4)	19(4)	3(6)
H11b	74(14)	48(11)	43(5)	24(7)	1(3)	13(3)
H11c	68(11)	39(8)	95(13)	6(4)	-15(5)	-5(4)
C12	24.3(7)	17.6(6)	13.7(5)	-0.6(6)	-3.1(6)	-0.7(4)
C13	29.2(8)	26.2(8)	19.7(6)	1.6(7)	1.7(6)	6.7(5)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
H13	54(9)	52(9)	48(11)	27(5)	26(7)	35(7)
C14	31.4(8)	37.4(10)	18.8(6)	-3.1(7)	1.3(6)	6.0(6)
H14	41(11)	61(9)	41(8)	12(7)	15(6)	28(5)
C15	29.6(8)	37.0(9)	20.2(6)	-2.8(7)	1.0(6)	-5.3(6)
H15	49(8)	60(13)	44(9)	2(6)	23(4)	2(7)
C16	27.5(8)	27.4(8)	30.2(7)	1.0(7)	0.3(6)	-7.1(6)
H16	51(10)	50(9)	62(13)	25(5)	17(7)	9(7)
C17	27.7(8)	20.4(7)	24.9(6)	1.6(6)	-1.7(6)	-0.8(5)
H17	53(12)	31(7)	33(8)	4(6)	0(6)	8(4)
O1	26.2(5)	22.7(5)	18.8(4)	3.9(4)	0.1(4)	-0.1(4)
O2	26.4(6)	21.0(5)	18.3(4)	3.2(4)	-3.0(4)	2.5(4)
O3	38.4(6)	26.4(6)	22.7(5)	-16.8(5)	1.0(5)	0.3(4)
P1	20.4(5)	13.0(5)	13.0(5)	-3.7(5)	-0.1(4)	0.2(4)

Table 7: Bond Lengths in Å for **4.39b**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Br1	C7	1.8961(13)	C10	H10b	1.04(2)
C1	C2	1.5504(18)	C10	H10c	1.04(2)
C1	C3	1.5195(18)	C10	O1	1.4415(17)
C1	C4	1.4993(18)	C11	H11a	1.11(2)
C1	P1	1.7876(15)	C11	H11b	1.080(19)
C2	H2	1.105(18)	C11	H11c	1.04(2)
C2	C3	1.505(2)	C11	O2	1.4378(19)
C2	C12	1.4867(19)	C12	C13	1.3959(18)
C3	H3a	1.093(18)	C12	C17	1.391(2)
C3	H3b	1.071(17)	C13	H13	1.093(19)
C4	C5	1.3949(18)	C13	C14	1.394(2)
C4	C9	1.3971(19)	C14	H14	1.090(18)
C5	H5	1.077(17)	C14	C15	1.389(2)
C5	C6	1.395(2)	C15	H15	1.093(18)
C6	H6	1.094(16)	C15	C16	1.390(2)
C6	C7	1.391(2)	C16	H16	1.07(2)
C7	C8	1.3893(18)	C16	C17	1.392(2)
C8	H8	1.081(16)	C17	H17	1.109(17)
C8	C9	1.3931(19)	O1	P1	1.5736(13)
C9	H9	1.076(17)	O2	P1	1.5798(13)
C10	H10a	1.08(2)	O3	P1	1.4708(13)

Table 8: Bond Angles in ° for **4.39b**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	C1	C2	58.71(9)	C12	C2	H2	114.3(10)
C4	C1	C2	120.02(11)	C12	C2	C3	123.35(12)
C4	C1	C3	120.18(11)	C2	C3	C1	61.67(9)
P1	C1	C2	113.97(10)	H3a	C3	C1	118.6(9)
P1	C1	C3	113.98(10)	H3a	C3	C2	116.9(9)
P1	C1	C4	117.09(9)	H3b	C3	C1	116.0(9)
H2	C2	C1	112.7(9)	H3b	C3	C2	118.0(10)
C3	C2	C1	59.62(9)	H3b	C3	H3a	115.2(14)
C3	C2	H2	115.0(10)	C5	C4	C1	120.76(12)
C12	C2	C1	120.92(12)	C9	C4	C1	120.39(12)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C9	C4	C5	118.82(13)	O2	C11	H11c	110.7(12)
H5	C5	C4	119.2(10)	C13	C12	C2	123.11(14)
C6	C5	C4	120.87(13)	C17	C12	C2	118.67(12)
C6	C5	H5	119.9(10)	C17	C12	C13	118.21(13)
H6	C6	C5	119.7(9)	H13	C13	C12	119.5(9)
C7	C6	C5	119.26(12)	C14	C13	C12	120.59(15)
C7	C6	H6	121.0(9)	C14	C13	H13	119.9(9)
C6	C7	Br1	119.93(10)	H14	C14	C13	120.5(10)
C8	C7	Br1	119.17(10)	C15	C14	C13	120.67(14)
C8	C7	C6	120.80(12)	C15	C14	H14	118.7(10)
H8	C8	C7	120.7(8)	H15	C15	C14	120.2(11)
C9	C8	C7	119.35(12)	C16	C15	C14	119.09(15)
C9	C8	H8	119.8(8)	C16	C15	H15	120.7(11)
C8	C9	C4	120.89(13)	H16	C16	C15	119.2(11)
H9	C9	C4	118.6(10)	C17	C16	C15	120.10(16)
H9	C9	C8	120.5(10)	C17	C16	H16	120.7(11)
H10b	C10	H10a	110.2(18)	C16	C17	C12	121.35(14)
H10c	C10	H10a	107.9(19)	H17	C17	C12	119.0(11)
H10c	C10	H10b	107.2(18)	H17	C17	C16	119.6(11)
O1	C10	H10a	110.7(11)	P1	O1	C10	120.48(10)
O1	C10	H10b	111.1(13)	P1	O2	C11	121.52(11)
O1	C10	H10c	109.6(12)	O1	P1	C1	101.73(7)
H11b	C11	H11a	108.6(16)	O2	P1	C1	108.46(7)
H11c	C11	H11a	111.5(17)	O2	P1	O1	101.86(7)
H11c	C11	H11b	106.8(17)	O3	P1	C1	113.37(7)
O2	C11	H11a	108.8(11)	O3	P1	O1	115.78(8)
O2	C11	H11b	110.5(10)	O3	P1	O2	114.32(8)

Table 9: Torsion Angles in ° for **4.39b**.

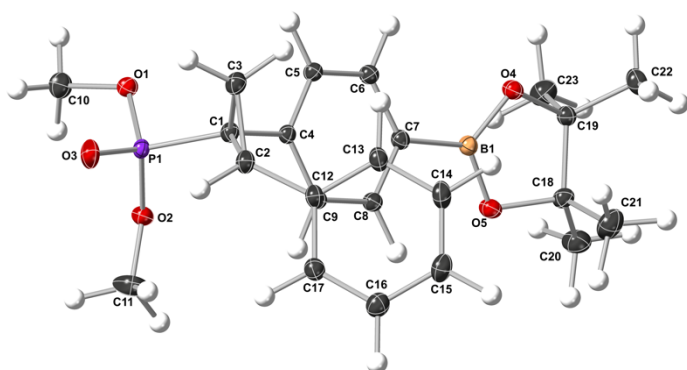
Atom	Atom	Atom	Atom	Angle/°
Br1	C7	C6	C5	175.48(10)
Br1	C7	C8	C9	-175.33(10)
C1	C2	C12	C13	66.32(15)
C1	C2	C12	C17	-114.15(14)
C1	C3	C2	C12	109.10(10)
C1	C4	C5	C6	-176.56(11)
C1	C4	C9	C8	176.75(12)
C1	P1	O1	C10	-166.00(11)
C1	P1	O2	C11	91.79(11)
C2	C12	C13	C14	179.22(13)
C2	C12	C17	C16	-179.49(13)
C4	C5	C6	C7	-0.26(15)
C4	C9	C8	C7	-0.10(15)
C5	C6	C7	C8	-0.88(15)
C6	C7	C8	C9	1.05(14)
C10	O1	P1	O2	82.04(12)
C10	O1	P1	O3	-42.62(13)
C11	O2	P1	O1	-161.40(11)
C11	O2	P1	O3	-35.77(12)
C12	C13	C14	C15	0.23(17)
C12	C17	C16	C15	0.28(17)
C13	C14	C15	C16	0.11(18)
C14	C15	C16	C17	-0.36(17)

Table 10: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **4.39b**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
H2	6490(30)	6580(20)	6514(6)	32(4)
H3a	9440(30)	4910(19)	6551(6)	32(4)
H3b	7970(30)	3590(19)	6896(6)	32(4)
H5	7220(30)	1500(19)	6425(7)	40(5)
H6	4940(30)	-630(18)	6354(7)	41(5)
H8	-10(30)	2214(17)	5957(7)	33(5)
H9	2320(30)	4315(18)	6044(7)	40(5)
H10a	10870(30)	4340(30)	5107(7)	66(6)
H10b	8700(40)	4380(30)	4748(8)	70(6)
H10c	9800(40)	2790(20)	4881(7)	63(6)
H11a	2710(30)	6530(20)	5544(8)	53(5)
H11b	3840(40)	6970(20)	4983(7)	55(5)
H11c	5090(40)	7460(20)	5496(8)	67(6)
H13	5470(30)	3430(20)	7348(7)	51(6)
H14	2650(30)	3460(20)	7952(7)	48(6)
H15	-20(30)	5350(20)	7926(7)	51(6)
H16	250(40)	7300(20)	7326(7)	55(6)
H17	3080(30)	7350(20)	6729(6)	39(5)

$R_1 = 1.08\%$ Submitted by: **Yasir Naeem, Davies Group**Solved by: **John Bacsá**

Crystal Data and Experimental



Experimental. Single colorless needle-shaped crystals of **4.39f** were crystallised from ethyl acetate by slow evaporation. A suitable crystal with dimensions $0.18 \times 0.14 \times 0.10 \text{ mm}^3$ was selected and mounted on a loop with paratone on a XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was kept at a steady $T = 100.0(1) \text{ K}$ during data collection. The structure was solved with the ShelXT 2018/2 (Sheldrick, 2018) solution program and by using Olex2 1.5-alpha (Dolomanov et al., 2009) as the graphical interface. The model was refined with olex2.refine 1.5-alpha (Bourhis et al., 2015) using full matrix least squares minimisation on F^2 .

Crystal Data. $\text{C}_{23}\text{H}_{30}\text{BO}_5\text{P}$, $M_r = 428.290$, orthorhombic, $P2_12_12_1$ (No. 19), $a = 6.64621(3) \text{ \AA}$, $b = 13.47483(7) \text{ \AA}$, $c = 25.47104(11) \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$, $V = 2281.100(18) \text{ \AA}^3$, $T = 100.00(10) \text{ K}$, $Z = 4$, $Z' = 1$, $\mu(\text{Cu K}\alpha) = 1.320$, 68237 reflections measured, 4751 unique ($R_{\text{int}} = 0.0403$) which were used in all calculations. The final wR_2 was 0.0242 (all data) and R_1 was 0.0108 ($I \geq 2 \sigma(I)$).

Compound	4.39f
Formula	$\text{C}_{23}\text{H}_{30}\text{BO}_5\text{P}$
$D_{\text{calc.}} / \text{g cm}^{-3}$	1.247
μ / mm^{-1}	1.320
Formula Weight	428.290
Colour	colourless
Shape	needle-shaped
Size/ mm^3	$0.18 \times 0.14 \times 0.10$
T / K	100.00(10)
Crystal System	orthorhombic
Flack Parameter	0.004(4)
Hooft Parameter	0.004(4)
Space Group	$P2_12_12_1$
$a / \text{\AA}$	6.64621(3)
$b / \text{\AA}$	13.47483(7)
$c / \text{\AA}$	25.47104(11)
$\alpha / ^\circ$	90
$\beta / ^\circ$	90
$\gamma / ^\circ$	90
$V / \text{\AA}^3$	2281.100(18)
Z	4
Z'	1
Wavelength/ $\text{\AA}$	1.54184
Radiation type	Cu $K\alpha$
$\theta_{\text{min}} / ^\circ$	3.47
$\theta_{\text{max}} / ^\circ$	77.23
Measured Refl's.	68237
Indep't Refl's	4751
Refl's $I \geq 2 \sigma(I)$	4662
R_{int}	0.0403
Parameters	566
Restraints	387
Largest Peak	0.0916
Deepest Hole	-0.0722
GooF	1.1258
wR_2 (all data)	0.0242
wR_2	0.0241
R_1 (all data)	0.0112
R_1	0.0108

Structure Quality Indicators

Reflections:	d min (CuK α) 2 Θ =154.5°	0.79	I/ σ (I)	67.3	Rint m=14.24	4.03%	Full 135.4° 98% to 154.5°	98.6
	Shift	0.000	Max Peak	0.1	Min Peak	-0.1	GooF	1.126
Refinement:							Hoof	.004(4)

A colourless needle-shaped crystal with dimensions $0.18 \times 0.14 \times 0.10$ mm³ was mounted on a loop with paratone. Data were collected using a XtaLAB Synergy, Dualflex, HyPix diffractometer operating at $T = 100.00(10)$ K.

Data were measured using ω scans with Cu K α radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlisPro system (CCD 43.128a 64-bit (release 20-06-2024)). The maximum resolution that was achieved was $\Theta = 77.23^\circ$ (0.79 Å).

The unit cell was refined using CrysAlisPro 1.171.43.121a (Rigaku OD, 2024) on 52224 reflections, 77% of the observed reflections. Data reduction, scaling and absorption corrections were performed using CrysAlisPro 1.171.43.121a (Rigaku OD, 2024). The final completeness is 99.50 % out to 77.23° in Θ . A numerical absorption correction based on gaussian integration over a multifaceted crystal model was performed using CrysAlisPro 1.171.42.74a (Rigaku Oxford Diffraction, 2022). An empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm was also applied. The absorption coefficient μ of this material is 1.320 mm⁻¹ at this wavelength ($\lambda = 1.54184$ Å) and the minimum and maximum transmissions are 0.825 and 1.000.

The structure was solved and the space group $P2_12_12_1$ (# 19) determined by the ShelXT 2018/2 (Sheldrick, 2018) structure solution program and refined by full matrix least squares minimisation on F^2 using version of olex2.refine 1.5-alpha (Bourhis et al., 2015). Hydrogen atom positions were located from the electron densities and freely refined using Hirshfeld scattering factors. Refinement was by using NoSpherA2, an implementation of non-spherical atom-form-factors (F. Kleemiss, H. Puschmann, O. Dolomanov, S. Grabowsky - <https://doi.org/10.1039/D0SC05526C> – 2020). NoSpherA2 implementation of HAR makes use of tailor-made aspherical atomic form factors calculated from a Hirshfeld-partitioned electron density (ED) not from spherical-atom form factors. The ED was calculated from a Gaussian basis set single determinant SCF wavefunction from DFT using selected functionals for a fragment of this crystal. This fragment was embedded in an electrostatic crystal field by employing cluster charges. The following options were used: SOFTWARE: ORCA 5.0 PARTITIONING: NoSpherA2 INT ACCURACY: Normal METHOD: PBE0 BASIS SET: def2-TZVP CHARGE: 0 MULTIPLICITY: 1 SOLVATION: Acetone DATE: 2024-09-22_18-05-39

There is a single formula unit in the asymmetric unit, which is represented by the reported sum formula. In other words: Z is 4 and Z' is 1. The moiety formula is C₂₃ H₃₀ B O₅ P.

The Flack parameter was refined to 0.004(4). Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2 results in 0.004(4). The chiral atoms in this structure are: C1(S), C2(R). Note: The Flack parameter is used to determine chirality of the crystal studied, the value should be near 0, a value of 1 means that the stereochemistry is wrong and the model should be inverted. A value of 0.5 means that the crystal consists of a racemic mixture of the two enantiomers.

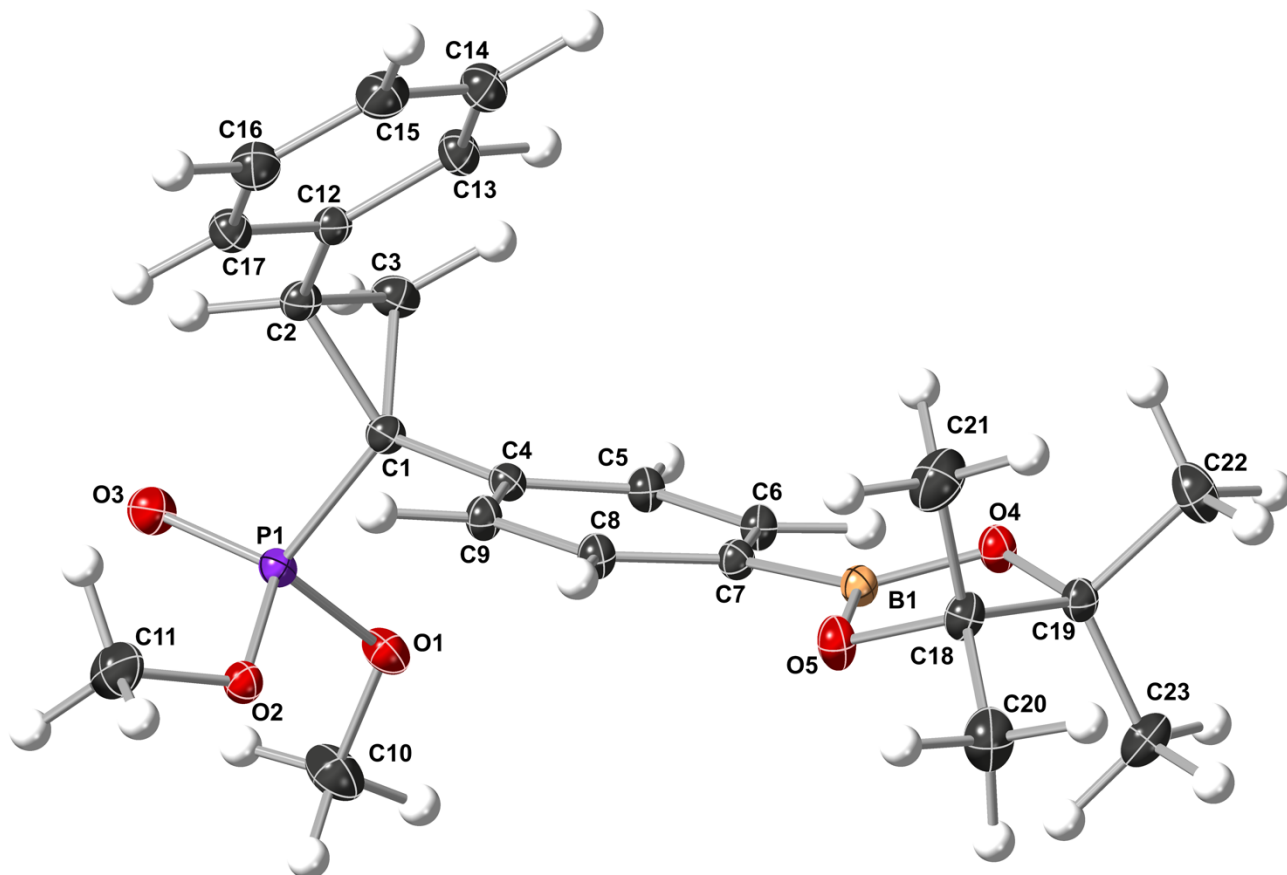


Figure 7 Thermal ellipsoidal representation (50% probability for all atoms, including hydrogens) of the molecular structure in the crystal. The chiral atoms in this structure are: C1(S), C2(R).

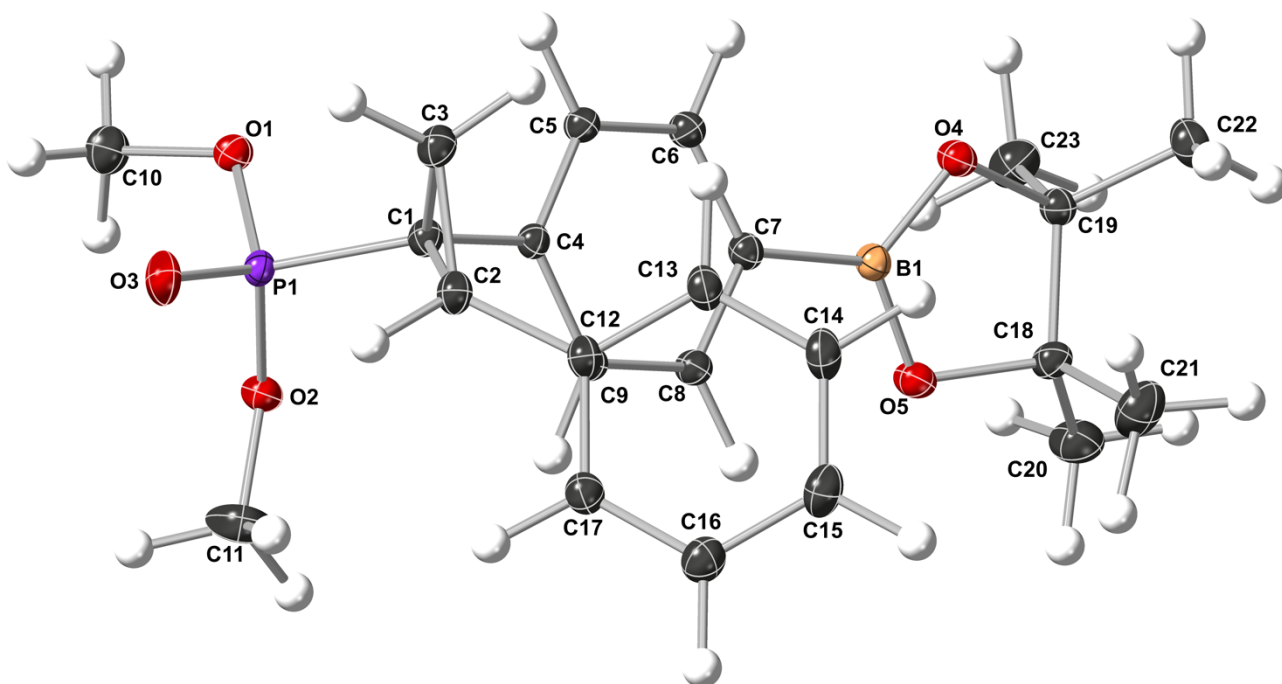
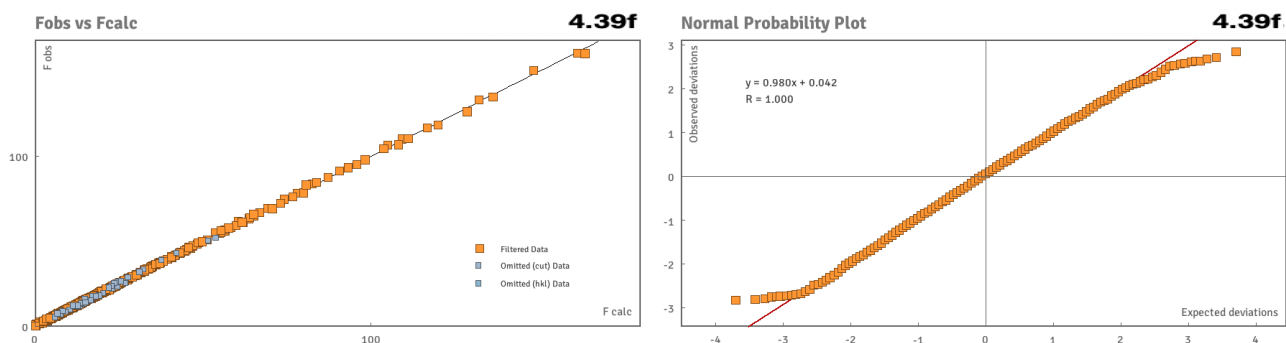


Figure 8 Thermal ellipsoidal representation (50% probability for all atoms, including hydrogens) of the

Data Plots: Diffraction Data



Data Plots: Refinement and Data



Reflection Statistics

Total reflections (after filtering)	67648	Unique reflections	4751
Completeness	0.982	Mean I/ σ	51.11
hkl _{max} collected	(8, 16, 32)	hkl _{min} collected	(-8, -17, -31)
hkl _{max} used	(8, 17, 32)	hkl _{min} used	(-8, 0, 0)
Lim d _{max} collected	100.0	Lim d _{min} collected	0.77
d _{max} used	12.74	d _{min} used	0.79
Friedel pairs	6117	Friedel pairs merged	0
Inconsistent equivalents	0	R _{int}	0.0402
R _{sigma}	0.0149	Intensity transformed	0
Omitted reflections	589	Omitted by user (OMIT hkl)	8
Multiplicity	(3365, 2687, 2025, 1479, 982, 1040, 796, 686, 567, 504, 342, 250, 169, 160, 79, 62, 47, 33, 15, 5)	Maximum multiplicity	37
Removed systematic absences	0	Filtered off (Shel/OMIT)	0



Table 11: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **4.39f**. U_{eq} is defined as $1/3$ of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
B1	3814.6(8)	2266.0(4)	6881.6(2)	14.78(10)
C1	1281.9(7)	5711.6(4)	5633.10(17)	14.47(9)
C2	1694.1(8)	5632.5(4)	5035.51(18)	16.27(9)
C3	-419.0(8)	5577.6(4)	5239.86(19)	18.49(10)
C4	1897.6(7)	4872.4(3)	5983.53(17)	13.21(9)
C5	489.4(8)	4348.4(4)	6283.25(19)	15.40(9)
C6	1079.1(8)	3537.4(4)	6587.18(19)	15.89(10)
C7	3096.3(7)	3232.1(4)	6602.05(17)	14.61(10)
C8	4504.5(8)	3782.2(4)	6313.57(19)	15.87(10)
C9	3920.4(7)	4588.9(4)	6009.14(19)	15.55(10)
C10	46.1(10)	7833.2(5)	6690.9(3)	30.27(13)

Atom	x	y	z	U_{eq}
C11	5381.5(9)	7363.4(6)	5842.8(3)	32.22(13)
C12	2806.2(8)	4770.2(4)	4814.65(18)	15.36(10)
C13	2047.1(8)	3805.6(4)	4810.4(2)	19.46(11)
C14	3188.7(9)	3024.8(4)	4609.93(19)	23.22(11)
C15	5107.4(9)	3200.3(4)	4410.3(2)	23.70(11)
C16	5864.3(9)	4163.1(4)	4406.8(2)	22.75(11)
C17	4722.3(8)	4943.1(4)	4605.49(19)	18.69(10)
C18	5947.4(7)	1021.7(4)	7107.00(19)	17.42(10)
C19	3782.2(7)	785.1(4)	7308.77(19)	15.61(10)
C20	7591.4(9)	875.0(5)	7512.1(3)	28.67(13)
C21	6484.4(11)	489.7(5)	6599.5(2)	31.19(13)
C22	3020.4(9)	-245.4(4)	7174.1(3)	27.77(13)
C23	3504.5(9)	984.2(4)	7891.0(2)	24.53(11)
O1	134.6(5)	6946.1(3)	6376.96(14)	19.76(8)
O2	3693.5(5)	7025.7(3)	6142.42(12)	16.64(7)
O3	1131.0(6)	7714.5(3)	5486.53(15)	22.65(8)
O4	2558.3(5)	1513.4(3)	7030.05(14)	17.35(8)
O5	5800.1(5)	2072.6(3)	6979.01(14)	20.19(8)
P1	1546.8(5)	6942.0(3)	5879.47(13)	13.25(10)

Table 12: Anisotropic Displacement Parameters ($\times 10^4$) for **4.39f**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \dots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
B1	14.6(3)	13.4(2)	16.3(2)	0.0(2)	-1.86(19)	2.37(19)
C1	14.7(2)	13.1(2)	15.6(2)	1.57(18)	-2.49(18)	0.90(17)
C2	19.7(2)	13.9(2)	15.2(2)	1.95(19)	-2.48(19)	1.11(18)
H2	35(4)	16(3)	29(4)	1(2)	2(3)	3.2(19)
C3	16.6(2)	17.8(3)	21.1(2)	3.1(2)	-5.38(19)	-1.0(2)
H3a	24(4)	24(3)	34(4)	-2.6(18)	-8(3)	1(2)
H3b	30(4)	29(3)	45(4)	13(2)	-7(3)	0(2)
C4	12.9(2)	11.7(2)	15.1(2)	0.74(17)	-1.36(17)	0.29(16)
C5	13.4(2)	14.4(2)	18.4(2)	1.08(18)	0.60(18)	2.09(18)
H5	23(4)	31(4)	46(4)	5(3)	5(3)	5(4)
C6	15.1(2)	14.7(2)	17.8(2)	-0.02(19)	1.44(19)	2.74(18)
H6	31(4)	32(4)	35(4)	1(3)	10(3)	10(3)
C7	14.9(2)	13.1(2)	15.8(2)	0.03(18)	-1.48(18)	2.05(17)
C8	13.0(2)	15.0(2)	19.6(2)	0.64(19)	-1.47(19)	3.97(18)
H8	20(4)	36(4)	46(4)	5(3)	-3(3)	14(4)
C9	13.5(2)	14.7(2)	18.4(2)	0.31(19)	-1.09(19)	4.24(18)
H9	20(4)	28(4)	42(4)	1(3)	3(3)	13(3)
C10	29.3(3)	23.0(3)	38.5(3)	-2.5(2)	9.6(3)	-13.5(3)
H10a	54(4)	52(6)	80(6)	-2(3)	-14(2)	-27(4)
H10b	94(7)	35(4)	74(5)	12(3)	2(4)	-2(2)
H10c	78(5)	56(6)	79(5)	-23(4)	47(3)	-33(4)
C11	20.9(3)	50.6(4)	25.3(3)	-11.5(3)	3.5(2)	4.8(3)
H11a	45(5)	95(7)	31(3)	-5(4)	5(2)	-2(2)
H11b	30(4)	160(9)	66(6)	13(3)	8(3)	39(4)
H11c	111(8)	62(4)	80(6)	-29(2)	34(5)	-3(2)
C12	19.5(2)	12.5(2)	14.1(2)	0.45(18)	-1.58(18)	0.71(17)
C13	23.7(3)	13.3(2)	21.4(2)	-0.9(2)	1.8(2)	-0.52(19)
H13	33(3)	28(4)	49(5)	-3(2)	15(2)	2(3)
C14	31.2(3)	14.0(2)	24.5(2)	0.6(2)	2.0(2)	-2.66(19)
H14	54(5)	18(3)	55(5)	-10(2)	11(4)	-8(2)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C15	30.6(3)	19.3(3)	21.2(2)	5.8(2)	2.1(2)	-3.9(2)
H15	51(5)	27(4)	49(5)	16(2)	6(3)	-9(2)
C16	23.8(3)	22.5(3)	21.9(2)	1.9(2)	3.3(2)	-2.5(2)
H16	32(3)	47(5)	56(5)	2(2)	19(2)	3(4)
C17	20.2(3)	16.6(3)	19.2(2)	-1.0(2)	0.89(19)	-0.78(19)
H17	38(4)	23(3)	44(4)	-10.6(19)	11(3)	-2(2)
C18	15.2(2)	18.3(2)	18.8(2)	2.70(18)	1.52(19)	4.22(19)
C19	15.4(2)	14.2(2)	17.2(2)	0.18(18)	-0.21(18)	2.98(18)
C20	17.7(3)	31.4(3)	37.0(3)	1.3(2)	-5.9(2)	12.5(3)
H20a	40(5)	56(5)	49(4)	5(3)	-6(3)	-6(2)
H20b	49(5)	32(3)	49(5)	4(2)	-13(4)	19(2)
H20c	20(3)	72(6)	71(5)	-2(2)	-1(2)	32(4)
C21	37.5(3)	30.4(3)	25.7(3)	10.4(3)	12.0(3)	1.8(2)
H21a	66(5)	72(6)	24(4)	20(3)	0(2)	-5(3)
H21b	50(4)	62(6)	56(5)	2(3)	27(3)	9(4)
H21c	78(6)	27(3)	48(5)	17(2)	15(4)	0(2)
C22	26.8(3)	15.8(3)	40.6(4)	-2.6(2)	-2.4(3)	2.9(2)
H22a	62(6)	57(6)	39(3)	-5(4)	-6(2)	-3(2)
H22b	49(5)	22(4)	73(5)	6(2)	-11(3)	9(3)
H22c	39(4)	38(5)	82(6)	-10(2)	14(2)	2(4)
C23	26.2(3)	29.5(3)	17.9(2)	5.3(2)	3.3(2)	5.5(2)
H23a	30(3)	64(6)	44(5)	5(2)	16(2)	5(4)
H23b	59(5)	41(4)	31(4)	-8(2)	6(3)	-5(2)
H23c	44(5)	52(5)	46(4)	14(3)	1(3)	21(3)
O1	15.96(17)	17.95(17)	25.35(18)	-1.37(14)	3.73(14)	-6.14(15)
O2	14.89(16)	18.14(17)	16.90(16)	-2.11(14)	-0.40(13)	1.83(13)
O3	29.8(2)	13.78(17)	24.38(18)	4.24(15)	-7.03(16)	2.28(15)
O4	14.08(16)	16.17(18)	21.81(18)	-1.01(13)	-2.07(13)	4.81(14)
O5	14.33(16)	18.55(18)	27.69(18)	-1.11(14)	-1.17(14)	7.54(14)
P1	13.49(19)	10.9(2)	15.38(18)	1.52(15)	-1.38(16)	-0.00(16)

Table 13: Bond Lengths in Å for **4.39f**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
B1	C7	1.5587(7)	C8	C9	1.3905(7)
B1	O4	1.3670(6)	C9	H9	1.092(7)
B1	O5	1.3678(6)	C10	H10a	1.090(9)
C1	C2	1.5502(6)	C10	H10b	1.077(9)
C1	C3	1.5211(7)	C10	H10c	1.066(8)
C1	C4	1.4976(6)	C10	O1	1.4394(6)
C1	P1	1.7815(6)	C11	H11a	1.051(8)
C2	H2	1.082(6)	C11	H11b	1.066(10)
C2	C3	1.4996(7)	C11	H11c	1.104(10)
C2	C12	1.4876(7)	C11	O2	1.4311(6)
C3	H3a	1.084(7)	C12	C13	1.3942(7)
C3	H3b	1.073(7)	C12	C17	1.4000(7)
C4	C5	1.3990(7)	C13	H13	1.087(7)
C4	C9	1.3991(7)	C13	C14	1.3941(7)
C5	H5	1.084(7)	C14	H14	1.084(7)
C5	C6	1.3954(7)	C14	C15	1.3931(8)
C6	H6	1.075(7)	C15	H15	1.084(7)
C6	C7	1.4029(7)	C15	C16	1.3915(8)
C7	C8	1.4019(7)	C16	H16	1.109(7)
C8	H8	1.080(7)	C16	C17	1.3917(8)

Atom	Atom	Length/Å
C17	H17	1.072(7)
C18	C19	1.5610(7)
C18	C20	1.5158(7)
C18	C21	1.5207(7)
C18	O5	1.4563(6)
C19	C22	1.5172(7)
C19	C23	1.5184(7)
C19	O4	1.4590(6)
C20	H20a	1.106(9)
C20	H20b	1.102(7)
C20	H20c	1.081(8)
C21	H21a	1.101(8)

Atom	Atom	Length/Å
C21	H21b	1.097(8)
C21	H21c	1.098(8)
C22	H22a	1.104(8)
C22	H22b	1.082(7)
C22	H22c	1.085(8)
C23	H23a	1.103(7)
C23	H23b	1.094(8)
C23	H23c	1.088(7)
O1	P1	1.5769(5)
O2	P1	1.5801(5)
O3	P1	1.4703(5)

Table 14: Bond Angles in ° for **4.39f**.

Atom	Atom	Atom	Angle/°
O4	B1	C7	123.98(4)
O5	B1	C7	122.51(4)
O5	B1	O4	113.44(4)
C3	C1	C2	58.44(3)
C4	C1	C2	119.01(4)
C4	C1	C3	120.39(4)
P1	C1	C2	113.10(3)
P1	C1	C3	114.57(4)
P1	C1	C4	117.76(3)
H2	C2	C1	112.3(3)
C3	C2	C1	59.81(3)
C3	C2	H2	115.0(4)
C12	C2	C1	120.85(4)
C12	C2	H2	114.0(3)
C12	C2	C3	123.92(4)
C2	C3	C1	61.75(3)
H3a	C3	C1	114.9(3)
H3a	C3	C2	117.4(4)
H3b	C3	C1	117.3(4)
H3b	C3	C2	117.2(4)
H3b	C3	H3a	116.8(5)
C5	C4	C1	121.57(4)
C9	C4	C1	119.77(4)
C9	C4	C5	118.66(4)
H5	C5	C4	118.3(4)
C6	C5	C4	120.67(5)
C6	C5	H5	121.1(4)
H6	C6	C5	119.1(4)
C7	C6	C5	120.87(5)
C7	C6	H6	120.0(4)
C6	C7	B1	123.36(4)
C8	C7	B1	118.46(4)
C8	C7	C6	117.96(4)
H8	C8	C7	119.2(4)
C9	C8	C7	121.28(5)
C9	C8	H8	119.5(4)
C8	C9	C4	120.51(5)
H9	C9	C4	119.4(3)
H9	C9	C8	120.0(3)

Atom	Atom	Atom	Angle/°
H10b	C10	H10a	108.2(8)
H10c	C10	H10a	109.8(7)
H10c	C10	H10b	111.6(8)
O1	C10	H10a	110.0(5)
O1	C10	H10b	110.8(5)
O1	C10	H10c	106.4(4)
H11b	C11	H11a	110.0(7)
H11c	C11	H11a	107.7(8)
H11c	C11	H11b	108.4(9)
O2	C11	H11a	113.9(5)
O2	C11	H11b	107.2(5)
O2	C11	H11c	109.5(6)
C13	C12	C2	123.46(5)
C17	C12	C2	117.77(4)
C17	C12	C13	118.77(5)
H13	C13	C12	120.6(4)
C14	C13	C12	120.63(5)
C14	C13	H13	118.7(4)
H14	C14	C13	119.3(4)
C15	C14	C13	120.25(5)
C15	C14	H14	120.4(4)
H15	C15	C14	119.3(4)
C16	C15	C14	119.44(5)
C16	C15	H15	121.3(4)
H16	C16	C15	120.0(4)
C17	C16	C15	120.31(5)
C17	C16	H16	119.7(4)
C16	C17	C12	120.58(5)
H17	C17	C12	117.4(4)
H17	C17	C16	122.0(4)
C20	C18	C19	114.44(4)
C21	C18	C19	113.57(5)
C21	C18	C20	110.36(5)
O5	C18	C19	102.15(4)
O5	C18	C20	109.13(4)
O5	C18	C21	106.49(4)
C22	C19	C18	114.85(4)
C23	C19	C18	113.42(4)
C23	C19	C22	110.00(4)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O4	C19	C18	102.49(4)	H22c	C22	H22a	110.2(7)
O4	C19	C22	108.63(4)	H22c	C22	H22b	107.2(6)
O4	C19	C23	106.78(4)	H23a	C23	C19	109.4(4)
H20a	C20	C18	111.1(4)	H23b	C23	C19	110.9(4)
H20b	C20	C18	110.4(4)	H23b	C23	H23a	109.8(6)
H20b	C20	H20a	110.4(6)	H23c	C23	C19	110.9(4)
H20c	C20	C18	109.1(4)	H23c	C23	H23a	109.1(6)
H20c	C20	H20a	107.6(7)	H23c	C23	H23b	106.8(6)
H20c	C20	H20b	108.2(6)	P1	O1	C10	118.27(4)
H21a	C21	C18	112.4(4)	P1	O2	C11	120.30(4)
H21b	C21	C18	109.4(5)	C19	O4	B1	107.04(4)
H21b	C21	H21a	107.8(6)	C18	O5	B1	106.90(4)
H21c	C21	C18	111.0(4)	O1	P1	C1	103.15(3)
H21c	C21	H21a	107.6(7)	O2	P1	C1	107.76(3)
H21c	C21	H21b	108.5(7)	O2	P1	O1	101.34(2)
H22a	C22	C19	109.1(5)	O3	P1	C1	113.61(3)
H22b	C22	C19	109.9(4)	O3	P1	O1	115.64(3)
H22b	C22	H22a	110.8(7)	O3	P1	O2	114.06(3)
H22c	C22	C19	109.6(4)				

Table 15: Torsion Angles in ° for **4.39f**.

Atom	Atom	Atom	Atom	Angle/°
B1	C7	C6	C5	-172.89(5)
B1	C7	C8	C9	172.96(4)
B1	O4	C19	C18	-21.39(4)
B1	O4	C19	C22	-143.33(4)
B1	O4	C19	C23	98.08(4)
B1	O5	C18	C19	-24.39(4)
B1	O5	C18	C20	-145.90(4)
B1	O5	C18	C21	94.98(5)
C1	C2	C12	C13	67.43(5)
C1	C2	C12	C17	-111.96(5)
C1	C3	C2	C12	108.89(3)
C1	C4	C5	C6	176.79(4)
C1	C4	C9	C8	-177.00(4)
C1	P1	O1	C10	177.51(4)
C1	P1	O2	C11	92.21(4)
C2	C12	C13	C14	-178.28(5)
C2	C12	C17	C16	178.12(4)
C4	C5	C6	C7	0.39(5)
C4	C9	C8	C7	0.00(6)
C5	C6	C7	C8	1.64(6)
C6	C7	C8	C9	-1.84(5)
C10	O1	P1	O2	66.02(4)
C10	O1	P1	O3	-57.86(5)
C11	O2	P1	O1	-159.87(5)
C11	O2	P1	O3	-34.92(5)
C12	C13	C14	C15	-0.08(6)
C12	C17	C16	C15	0.45(6)
C13	C14	C15	C16	-0.78(6)
C14	C15	C16	C17	0.59(6)

Table 16: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **4.39f**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
H2	2110(10)	6338(5)	4865(3)	26.8(16)
H3a	-1133(10)	4854(5)	5247(3)	27.2(16)
H3b	-1377(11)	6205(5)	5168(3)	34.5(17)
H5	-1073(10)	4577(5)	6265(3)	33.2(17)
H6	-45(11)	3129(5)	6801(3)	32.4(16)
H8	6061(10)	3552(5)	6314(3)	34.0(18)
H9	5035(10)	4991(5)	5777(3)	30.1(17)
H10a	1478(14)	7949(7)	6890(4)	62(2)
H10b	-254(17)	8472(7)	6449(4)	68(3)
H10c	-1114(15)	7717(6)	6973(4)	71(3)
H11a	5282(13)	7202(7)	5440(3)	57(2)
H11b	6690(13)	7025(10)	6005(4)	85(3)
H11c	5528(19)	8175(8)	5884(4)	84(3)
H13	563(11)	3646(5)	4969(3)	36.6(18)
H14	2562(13)	2282(5)	4608(3)	42(2)
H15	5976(12)	2584(5)	4257(3)	42(2)
H16	7374(11)	4313(6)	4239(3)	45(2)
H17	5248(11)	5695(5)	4598(3)	34.9(17)
H20a	7323(12)	1340(6)	7863(3)	48(2)
H20b	7701(13)	87(6)	7624(3)	43(2)
H20c	9016(11)	1098(7)	7345(3)	55(2)
H21a	5325(14)	584(7)	6295(3)	54(2)
H21b	7901(13)	789(7)	6445(3)	56(2)
H21c	6676(15)	-310(6)	6666(3)	51(2)
H22a	2983(13)	-330(7)	6743(3)	53(2)
H22b	3985(12)	-800(6)	7351(3)	48(2)
H22c	1526(13)	-348(6)	7336(4)	53(2)
H23a	1891(11)	942(6)	7990(3)	46(2)
H23b	4092(12)	1715(6)	7997(3)	44(2)
H23c	4325(11)	444(6)	8126(3)	47(2)

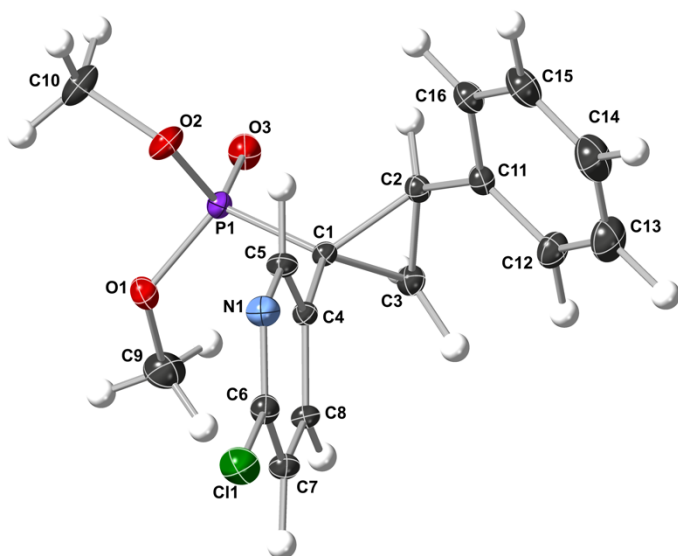
YN-ELN-116-Pg7 (4.39k)

Submitted by: **Yasir Naeem, Davies Group**

Solved by: **John Bacsá**

$R_1 = 3.70\%$

Crystal Data and Experimental



Experimental. Single colorless needle-shaped crystals of **4.39k** were recrystallised from ethyl acetate by slow evaporation. A suitable crystal with dimensions $0.18 \times 0.13 \times 0.04 \text{ mm}^3$ was selected and mounted on a loop with paratone on a XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was kept at a steady $T = 100.0(1) \text{ K}$ during data collection. The structure was solved with the ShelXT 2018/2 (Sheldrick, 2018) solution program and by using Olex2 1.5-alpha (Dolomanov et al., 2009) as the graphical interface. The model was refined with olex2.refine 1.5-alpha (Bourhis et al., 2015) using full matrix least squares minimisation on F^2 .

Crystal Data. $\text{C}_{16}\text{H}_{17}\text{ClNO}_3\text{P}$, $M_r = 337.745$, monoclinic, $P2_1$ (No. 4), $a = 8.7380(3) \text{ \AA}$, $b = 6.4981(2) \text{ \AA}$, $c = 14.2928(4) \text{ \AA}$, $\beta = 98.610(3)^\circ$, $\alpha = \gamma = 90^\circ$, $V = 802.40(4) \text{ \AA}^3$, $T = 100.01(10) \text{ K}$, $Z = 2$, $Z' = 1$, $\mu(\text{Mo K}\alpha) = 0.349$, 33455 reflections measured, 8032 unique ($R_{\text{int}} = 0.0552$) which were used in all calculations. The final wR_2 was 0.0496 (all

Compound

4.39k

Formula	$\text{C}_{16}\text{H}_{17}\text{ClNO}_3\text{P}$
$D_{\text{calc.}} / \text{g cm}^{-3}$	1.398
μ / mm^{-1}	0.349
Formula Weight	337.745
Colour	colourless
Shape	needle-shaped
Size/ mm^3	$0.18 \times 0.13 \times 0.04$
T / K	100.01(10)
Crystal System	monoclinic
Flack Parameter	0.01(3)
Hooft Parameter	0.01(3)
Space Group	$P2_1$
$a / \text{\AA}$	8.7380(3)
$b / \text{\AA}$	6.4981(2)
$c / \text{\AA}$	14.2928(4)
$\alpha / ^\circ$	90
$\beta / ^\circ$	98.610(3)
$\gamma / ^\circ$	90
$V / \text{\AA}^3$	802.40(4)
Z	2
Z'	1
Wavelength/ $\text{\AA}$	0.71073
Radiation type	Mo $K\alpha$
$\Theta_{\text{min}} / ^\circ$	3.44
$\Theta_{\text{max}} / ^\circ$	37.85
Measured Refl's.	33455
Indep't Refl's	8032
Refl's $I \geq 2 \sigma(I)$	6873
R_{int}	0.0552
Parameters	402
Restraints	367
Largest Peak	0.3701
Deepest Hole	-0.3091
GooF	1.0125
wR_2 (all data)	0.0496
wR_2	0.0473
R_1 (all data)	0.0500
R_1	0.0370

data) and R_1 was 0.0370 ($I \geq 2 \sigma(I)$).

Structure Quality Indicators

Reflections:	d min (MoK α) 2 Θ =75.7°	0.58	I/ σ (I)	18.3	R _{int} m=4.15	5.52%	Full 50.5° 95% to 75.7°	98.4
	Shift	0.001	Max Peak	0.4	Min Peak	-0.3	Goof	1.012
Refinement:							Hoof	.01(3)

A colourless needle-shaped crystal with dimensions 0.18 × 0.13 × 0.04 mm³ was mounted on a loop with paratone. Data were collected using a XtaLAB Synergy, Dualflex, HyPix diffractometer operating at $T = 100.01(10)$ K.

Data were measured using ω scans with Mo K α radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program CrysAlisPro system (CCD 43.128a 64-bit (release 20-06-2024)). The maximum resolution that was achieved was $\Theta = 37.85^\circ$ (0.58 Å). The unit cell was refined using CrysAlisPro 1.171.43.121a (Rigaku OD, 2024) on 6897 reflections, 21% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using CrysAlisPro 1.171.43.121a (Rigaku OD, 2024). The final completeness is 99.37 % out to 37.85° in Θ . A numerical absorption correction based on gaussian integration over a multifaceted crystal model was performed using CrysAlisPro 1.171.42.74a (Rigaku Oxford Diffraction, 2022). An empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm was also applied. The absorption coefficient μ of this material is 0.349 mm⁻¹ at this wavelength ($\lambda = 0.71073\text{Å}$) and the minimum and maximum transmissions are 0.806 and 1.000.

The structure was solved and the space group $P2_1$ (# 4) determined by the ShelXT 2018/2 (Sheldrick, 2018) structure solution program and refined by full matrix least squares minimisation on F^2 using version of olex2.refine 1.5-alpha (Bourhis et al., 2015). Hydrogen atom positions were located from the electron densities and freely refined using Hirshfeld scattering factors. Refinement was by using NoSpherA2, an implementation of non-spherical atom-form-factors (F. Kleemiss, H. Puschmann, O. Dolomanov, S. Grabowsky - <https://doi.org/10.1039/D0SC05526C> – 2020). NoSpherA2 implementation of HAR makes use of tailor-made aspherical atomic form factors calculated from a Hirshfeld-partitioned electron density (ED) not from spherical-atom form factors. The ED was calculated from a Gaussian basis set single determinant SCF wavefunction from DFT using selected functionals for a fragment of this crystal. This fragment was embedded in an electrostatic crystal field by employing cluster charges. The following options were used: SOFTWARE: ORCA 5.0 PARTITIONING: NoSpherA2 INT ACCURACY: Normal METHOD: PBE BASIS SET: def2-TZVP CHARGE: 0 MULTIPLICITY: 1 SOLVATION: Ethanol DATE: 2024-09-23_11-01-10

There is a single formula unit in the asymmetric unit, which is represented by the reported sum formula. In other words: Z is 2 and Z' is 1. The moiety formula is C₁₆ H₁₇ Cl N O₃ P.

The Flack parameter was refined to 0.01(3). Determination of absolute structure using Bayesian statistics on Bijvoet differences using the Olex2 results in 0.01(3). The chiral atoms in this structure are: C1(S), C2(R). Note: The Flack parameter is used to determine chirality of the crystal studied, the value should be near 0, a value of 1 means that the stereochemistry is wrong and the model should be inverted. A value of 0.5 means that the crystal consists of a racemic mixture of the two enantiomers.

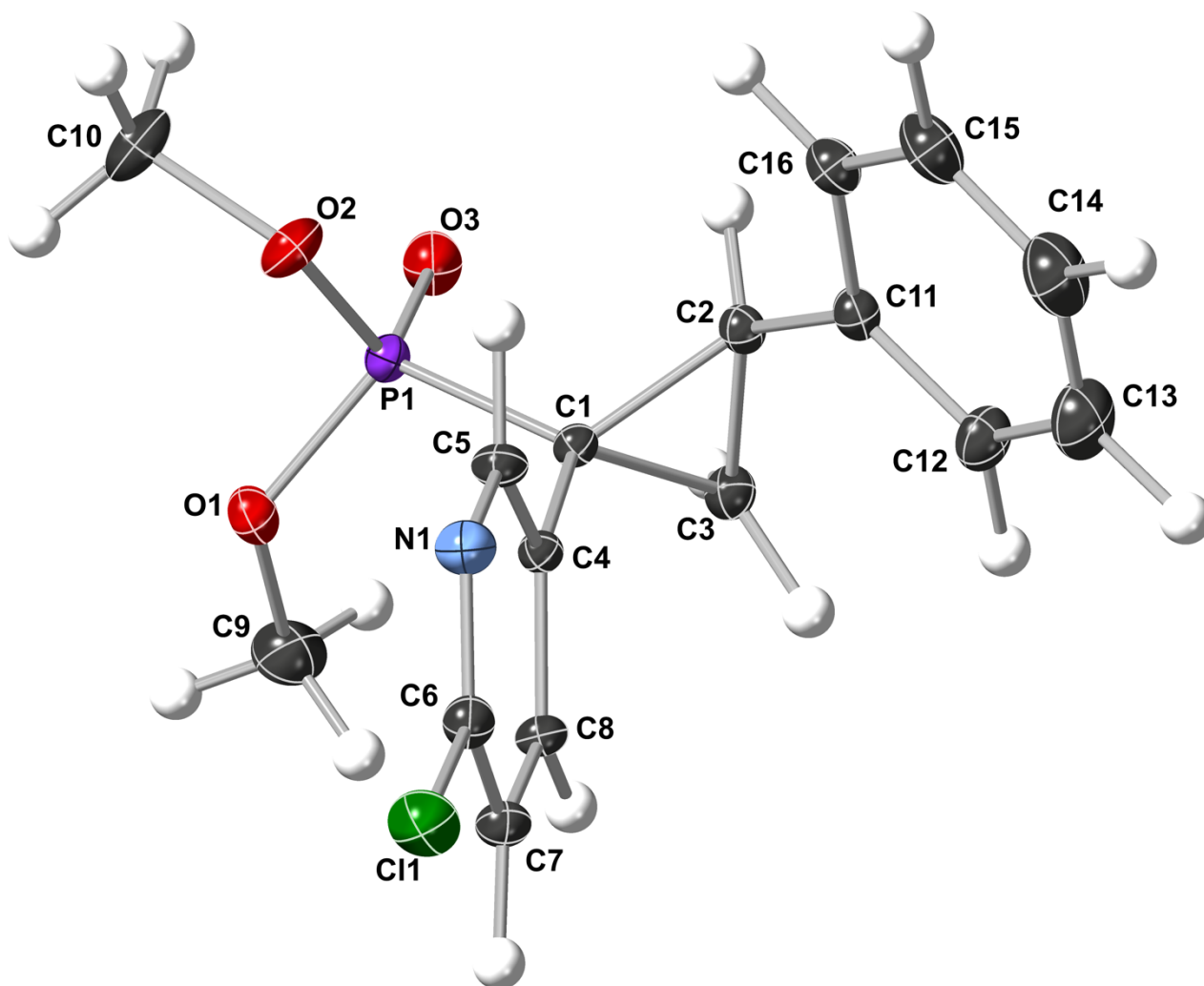
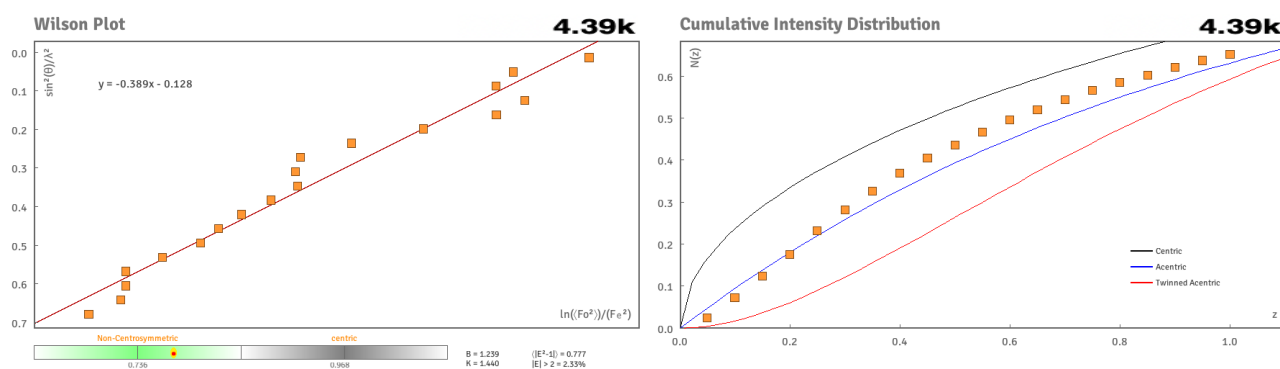
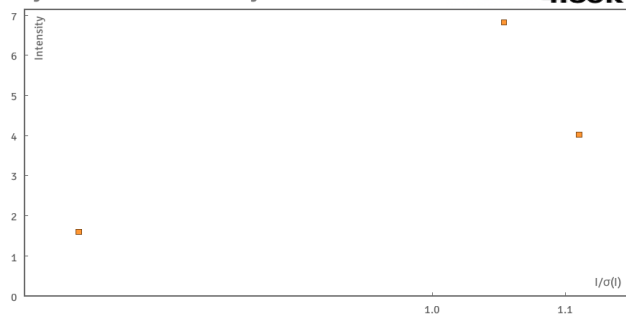


Figure 9 Thermal ellipsoidal representation (50% probability for all atoms, excluding hydrogens) of the molecular structure in the crystal. The chiral atoms in this structure are: C1(S), C2(R).

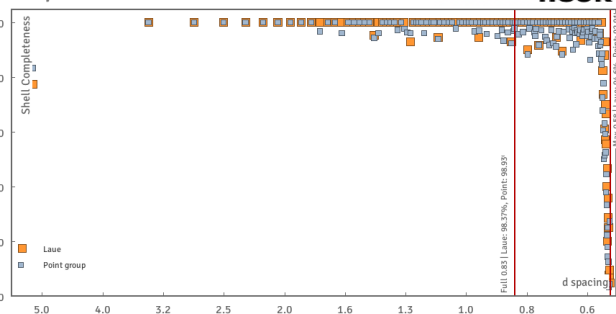
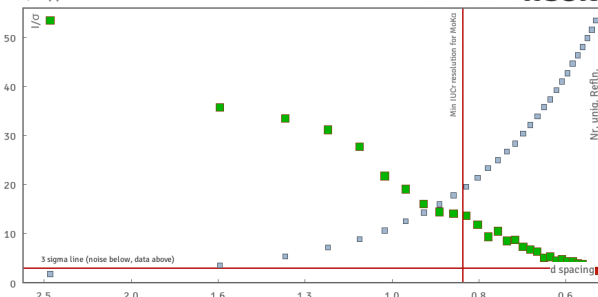
Data Plots: Diffraction Data



Systematic Absences Intensity Distribution

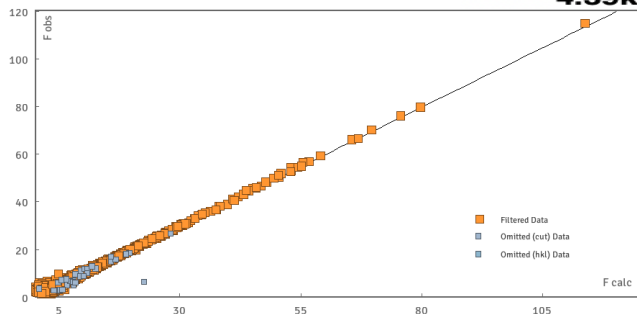


Completeness Plot

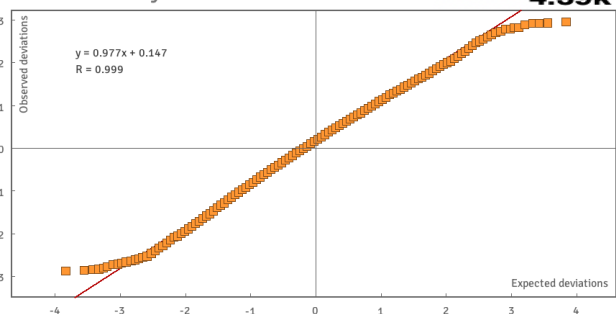
 $I/\sigma(I)$ vs. Resolution

Data Plots: Refinement and Data

Fobs vs Fcalc



Normal Probability Plot



Reflection Statistics

Total reflections (after filtering)	33306	Unique reflections	8032
Completeness	0.929	Mean I/σ	13.77
$hkl_{\max}$ collected	(14, 10, 24)	$hkl_{\min}$ collected	(-14, -11, -23)
$hkl_{\max}$ used	(14, 10, 24)	$hkl_{\min}$ used	(-14, -11, 0)
Lim $d_{\max}$ collected	100.0	Lim $d_{\min}$ collected	0.36
$d_{\max}$ used	5.92	$d_{\min}$ used	0.58
Friedel pairs	6612	Friedel pairs merged	0
Inconsistent equivalents	0	R_{int}	0.0551
R_{sigma}	0.0546	Intensity transformed	0
Omitted reflections	152	Omitted by user (OMIT hkl)	10
Multiplicity	(4069, 4916, 3473, 1403, 494, 117, 33, 12, 3)	Maximum multiplicity	14
Removed systematic absences	3	Filtered off (Shel/OMIT)	0



Table 17: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **4.39k**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
C1	2909.6(8)	3958.4(14)	7660.4(5)	11.82(12)
C2	1737.3(9)	4012.6(15)	6738.3(5)	14.34(14)
C3	2596.1(11)	2074.0(13)	7032.0(7)	16.34(17)
C4	4414.5(9)	5074.0(13)	7703.8(6)	11.88(15)
C5	4415.0(10)	7222.8(13)	7671.7(6)	14.86(16)
C6	7031.1(11)	7378.8(14)	7798.4(6)	16.42(17)
C7	7192.6(10)	5246.6(14)	7862.1(7)	17.00(17)
C8	5845.7(9)	4080.1(15)	7804.3(6)	14.32(15)
C9	3902.6(16)	1089.2(18)	9591.1(9)	32.3(3)
C10	1154.4(15)	6789.0(17)	9769.9(9)	28.9(2)
C11	2074.7(10)	5329.8(13)	5940.3(6)	15.60(16)
C12	3041.6(13)	4716.8(17)	5298.9(8)	23.8(2)
C13	3345.0(14)	6038.1(18)	4582.5(8)	32.9(2)
C14	2694.5(15)	7996.9(18)	4503.3(8)	32.8(2)
C15	1711.5(13)	8613.9(15)	5130.7(7)	26.4(2)
C16	1393.1(11)	7282.0(14)	5840.1(7)	19.53(18)
Cl1	8655.8(5)	8925.7(5)	7843.2(3)	25.91(13)
N1	5692.5(9)	8370.3(11)	7710.0(6)	17.37(15)
O1	3375.0(8)	3186.6(9)	9541.1(5)	19.57(14)
O2	1922.0(8)	6243.5(9)	8973.7(5)	20.48(14)
O3	637.4(8)	2691.2(10)	8632.8(5)	20.99(14)
P1	2069.0(5)	3904.5(6)	8722.5(3)	12.67(11)

Table 18: Anisotropic Displacement Parameters ($\times 10^4$) for 4.39k. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \dots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	11.5(3)	11.3(3)	12.9(3)	-0.6(3)	2.9(2)	-0.7(4)
C2	13.3(3)	16.0(3)	13.5(3)	-1.6(3)	1.4(2)	-0.2(3)
H2	13(4)	40(7)	41(7)	-1(2)	7(2)	10(6)
C3	19.0(4)	12.1(4)	17.7(4)	-1.6(3)	2.2(3)	-2.3(3)
H3a	37(7)	24(5)	45(8)	-10(3)	10(4)	4(3)
H3b	24(5)	27(6)	28(7)	-5(3)	9(3)	-8(4)
C4	10.6(3)	12.2(4)	12.9(4)	-0.5(3)	1.9(3)	-0.5(3)
C5	11.7(4)	12.5(4)	20.4(4)	-0.1(3)	2.2(3)	-0.1(3)
H5	16(4)	18(5)	84(11)	1(2)	13(3)	11(5)
C6	13.0(4)	19.8(4)	17.0(4)	-3.8(3)	3.7(3)	-1.0(3)
C7	11.6(4)	20.5(4)	19.3(4)	0.3(3)	3.7(3)	-0.6(3)
H7	14(4)	38(7)	73(11)	8(2)	3(3)	0(5)
C8	12.1(3)	14.2(4)	17.0(3)	2.1(3)	3.4(3)	-0.3(4)
H8	41(8)	13(4)	57(10)	3(2)	-1(6)	0(2)
C9	37.2(7)	32.4(6)	27.9(6)	12.1(5)	6.8(5)	14.4(5)
H9a	68(7)	79(11)	83(9)	19(5)	43(4)	11(6)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
H9b	141(13)	71(10)	33(4)	39(6)	4(3)	22(3)
H9c	59(7)	44(7)	98(11)	4(3)	-11(4)	6(4)
C10	34.4(6)	26.9(6)	29.4(6)	-0.2(4)	18.3(5)	-8.1(4)
H10a	83(10)	33(4)	79(10)	2(2)	38(7)	-12(2)
H10b	73(9)	110(11)	35(5)	35(5)	16(3)	-1(4)
H10c	44(4)	67(8)	66(10)	-12(3)	23(3)	-12(6)
C11	15.4(4)	17.9(4)	13.2(3)	-2.6(3)	1.3(2)	0.4(2)
C12	25.8(5)	28.6(5)	18.5(5)	-0.1(4)	8.8(4)	-0.2(4)
H12	34(8)	32(4)	33(8)	2(3)	8(5)	-2(3)
C13	37.3(6)	43.4(6)	20.5(5)	-3.7(5)	12.7(4)	4.9(5)
H13	64(9)	72(10)	44(8)	4(6)	36(4)	2(5)
C14	37.3(6)	40.2(6)	20.6(5)	-6.7(5)	3.7(4)	10.7(4)
H14	72(10)	64(7)	44(7)	-4(6)	21(5)	28(4)
C15	29.6(5)	26.2(6)	21.0(4)	-3.5(4)	-3.5(3)	8.7(4)
H15	56(9)	32(4)	54(10)	8(3)	15(6)	20(3)
C16	20.3(4)	20.2(4)	17.1(4)	0.1(3)	-0.2(3)	3.0(3)
H16	35(7)	33(7)	32(6)	10(4)	12(3)	6(4)
Cl1	17.1(2)	28.9(3)	32.1(3)	-9.1(3)	4.7(2)	0.8(3)
N1	15.5(3)	13.6(4)	23.2(4)	-3.0(2)	3.4(3)	0.4(3)
O1	20.2(3)	22.9(3)	14.9(3)	-0.7(3)	0.3(2)	1.7(2)
O2	26.2(4)	14.2(3)	24.1(3)	1.4(3)	13.7(3)	-0.7(3)
O3	16.6(3)	26.1(4)	21.2(3)	-8.7(3)	5.7(3)	-0.8(3)
P1	13.4(2)	12.8(2)	12.4(2)	-1.3(2)	3.75(17)	0.7(2)

Table 19: Bond Lengths in Å for **4.39k**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C2	1.5437(10)	C9	H9c	1.020(15)
C1	C3	1.5191(12)	C9	O1	1.4372(12)
C1	C4	1.4947(11)	C10	H10a	1.075(13)
C1	P1	1.7830(8)	C10	H10b	1.050(15)
C2	H2	1.065(10)	C10	H10c	1.088(15)
C2	C3	1.4939(12)	C10	O2	1.4488(12)
C2	C11	1.4903(12)	C11	C12	1.3946(14)
C3	H3a	1.056(11)	C11	C16	1.3996(12)
C3	H3b	1.124(12)	C12	H12	1.076(12)
C4	C5	1.3970(11)	C12	C13	1.3918(15)
C4	C8	1.3957(11)	C13	H13	1.112(14)
C5	H5	1.063(11)	C13	C14	1.3917(16)
C5	N1	1.3367(11)	C14	H14	1.099(12)
C6	C7	1.3943(12)	C14	C15	1.3904(17)
C6	Cl1	1.7328(10)	C15	H15	1.078(13)
C6	N1	1.3247(12)	C15	C16	1.3925(14)
C7	H7	1.059(12)	C16	H16	1.064(12)
C7	C8	1.3919(12)	O1	P1	1.5776(7)
C8	H8	1.056(11)	O2	P1	1.5714(8)
C9	H9a	1.043(15)	O3	P1	1.4679(8)
C9	H9b	0.990(14)			

Table 20: Bond Angles in ° for **4.39k**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	C1	C2	58.38(6)	C4	C1	C2	119.44(7)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C4	C1	C3	119.68(7)	O1	C9	H9b	108.8(8)
P1	C1	C2	114.96(5)	O1	C9	H9c	109.3(8)
P1	C1	C3	115.26(6)	H10b	C10	H10a	108.2(13)
P1	C1	C4	116.50(6)	H10c	C10	H10a	104.9(12)
H2	C2	C1	115.4(6)	H10c	C10	H10b	115.5(12)
C3	C2	C1	59.98(6)	O2	C10	H10a	107.0(8)
C3	C2	H2	115.7(7)	O2	C10	H10b	108.9(8)
C11	C2	C1	118.98(7)	O2	C10	H10c	111.9(7)
C11	C2	H2	113.3(6)	C12	C11	C2	123.21(8)
C11	C2	C3	123.42(8)	C16	C11	C2	117.97(8)
C2	C3	C1	61.63(5)	C16	C11	C12	118.81(9)
H3a	C3	C1	115.9(7)	H12	C12	C11	119.4(7)
H3a	C3	C2	115.8(7)	C13	C12	C11	120.55(10)
H3b	C3	C1	115.8(6)	C13	C12	H12	120.1(7)
H3b	C3	C2	118.8(6)	H13	C13	C12	119.8(7)
H3b	C3	H3a	117.1(9)	C14	C13	C12	120.24(11)
C5	C4	C1	119.21(8)	C14	C13	H13	120.0(7)
C8	C4	C1	123.30(8)	H14	C14	C13	120.0(9)
C8	C4	C5	117.46(8)	C15	C14	C13	119.70(10)
H5	C5	C4	119.0(6)	C15	C14	H14	120.3(9)
N1	C5	C4	124.10(8)	H15	C15	C14	120.0(7)
N1	C5	H5	116.9(6)	C16	C15	C14	120.03(10)
Cl1	C6	C7	119.98(7)	C16	C15	H15	119.9(8)
N1	C6	C7	124.67(8)	C15	C16	C11	120.63(10)
N1	C6	Cl1	115.35(7)	H16	C16	C11	119.7(6)
H7	C7	C6	119.8(7)	H16	C16	C15	119.7(6)
C8	C7	C6	117.44(8)	C6	N1	C5	116.91(8)
C8	C7	H7	122.7(7)	P1	O1	C9	120.55(7)
C7	C8	C4	119.39(9)	P1	O2	C10	118.65(6)
H8	C8	C4	119.8(7)	O1	P1	C1	107.03(4)
H8	C8	C7	120.8(7)	O2	P1	C1	103.52(4)
H9b	C9	H9a	112.4(13)	O2	P1	O1	101.03(4)
H9c	C9	H9a	107.4(13)	O3	P1	C1	112.98(4)
H9c	C9	H9b	109.4(14)	O3	P1	O1	114.73(4)
O1	C9	H9a	109.6(8)	O3	P1	O2	116.21(5)

Table 21: Torsion Angles in ° for **4.39k**.

Atom	Atom	Atom	Atom	Angle/°
C1	C2	C11	C12	82.11(10)
C1	C2	C11	C16	-97.33(8)
C1	C3	C2	C11	106.81(6)
C1	C4	C5	N1	179.67(8)
C1	C4	C8	C7	-178.40(8)
C1	P1	O1	C9	-71.75(7)
C1	P1	O2	C10	175.01(7)
C2	C11	C12	C13	-178.28(9)
C2	C11	C16	C15	177.51(8)
C4	C5	N1	C6	-1.06(11)
C4	C8	C7	C6	-1.13(9)
C5	N1	C6	C7	-0.63(10)
C5	N1	C6	Cl1	179.90(7)
C9	O1	P1	O2	-179.73(8)
C9	O1	P1	O3	54.45(9)

Atom	Atom	Atom	Atom	Angle/°
C10	O2	P1	O1	-74.28(8)
C10	O2	P1	O3	50.54(9)
C11	C12	C13	C14	0.51(13)
C11	C16	C15	C14	1.08(11)
C12	C13	C14	C15	-1.41(13)
C13	C14	C15	C16	0.61(13)

Table 22: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for **4.39k**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} .

Atom	x	y	z	U_{eq}
H2	550(12)	4034(19)	6831(8)	31(3)
H3a	1943(14)	894(16)	7291(9)	35(3)
H3b	3565(14)	1590(18)	6645(8)	26(3)
H5	3341(14)	8019(16)	7593(10)	39(4)
H7	8311(14)	4579(18)	7955(10)	42(4)
H8	5897(15)	2457(17)	7837(10)	38(4)
H9a	4827(19)	930(20)	9212(12)	73(5)
H9b	4180(20)	700(20)	10265(11)	82(5)
H9c	3034(18)	160(20)	9280(13)	69(5)
H10a	1071(19)	8440(20)	9778(11)	63(4)
H10b	1849(18)	6320(30)	10397(10)	72(5)
H10c	-38(18)	6250(20)	9677(10)	58(4)
H12	3550(15)	3205(18)	5360(9)	33(3)
H13	4103(18)	5520(20)	4069(11)	57(4)
H14	2980(17)	9060(20)	3957(10)	59(4)
H15	1223(16)	10141(19)	5082(10)	47(4)
H16	635(15)	7760(17)	6316(9)	32(3)

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