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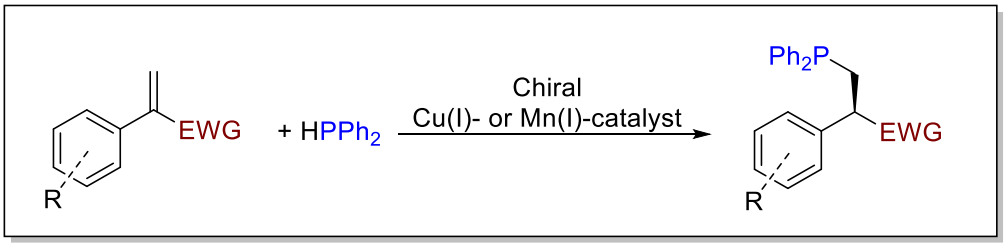
Copper(I)- and Manganese(I)-catalysed asymmetric hydrophosphination of α-substituted Michael acceptors



Master Thesis by

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Abstract

Homogeneous, asymmetric catalysis traditionally heavily relied on scarce, expensive and toxic noble metal complexes containing chiral phosphine ligands, which require lengthy synthesis procedures. Our group has tackled both these issues by developing a Mn(I)-catalysed asymmetric hydrophosphination whereof the products can be easily transformed into chiral phosphine ligands. The scope of the previous research was largely based on β-substituted Michael acceptors containing a nitrile functionality. This work expands the scope of α-substituted Michael acceptors (**18**). A variety of Michael acceptors was attempted to synthesize. However, due to the inability to prepare the α-substituted α,β-unsaturated nitro- and thioester substrates and the rapid polymerisation of the aromatic α-substituted α,β-unsaturated nitriles, the scope was limited to Michael acceptors containing an ester (**18c**) or carboxamide (**18e**) functionality. High enantioselectivity was obtained for the asymmetric hydrophosphination of the α,β-unsaturated carboxamides, presenting three examples with an enantiomeric excess (e.e.) of 92-96%. Interestingly, when the α,β-unsaturated esters were assessed, it was observed that the electronic effect of the substituent on the aromatic ring plays a large role in the enantioselectivity of the reaction. Electron-donating substituents, such as *p*-MeO and *o*-MeO have a positive effect on the selectivity and present an e.e. of 92% and 95% respectively, whereas an electron-withdrawing substituent decreases the e.e., down to 6% for *p*-CF_3. Furthermore, this work gives us access to chiral phosphine products that can be transformed into ligands with structures unlike any previously reported. Using a procedure developed by our group, a demonstration is given where a nitrile substrate is asymmetrically hydrophosphinated with 96% e.e. and subsequently transformed in three steps into a chiral PNN ligand **L8**. The Mn(I)-**L8** complex was then employed as catalyst in a hydrophosphination of an α,β-unsaturated ester substrate resulting in the addition product with 42% e.e. Finally, as the Mn(I)-catalysed hydrophosphination is suggested to follow a mechanism which is based on metal-ligand cooperation (MLC), we explored how it compares to Cu(I)-catalysed hydrophosphination, which does not follow this mechanism. A variety of commercially available bidentate ligands were screened, whereof (*S*,S_p)-Taniaphos **L13** presented the highest e.e. of 58%. Although Cu(I)-catalysis remains to have high potential in asymmetric hydrophosphination, for the α-substituted α,β-unsaturated esters **18c** it is inferior to Mn(I)-catalysis, due to the required presence of a large amount of base which catalysis the racemic base-catalysed side reaction.

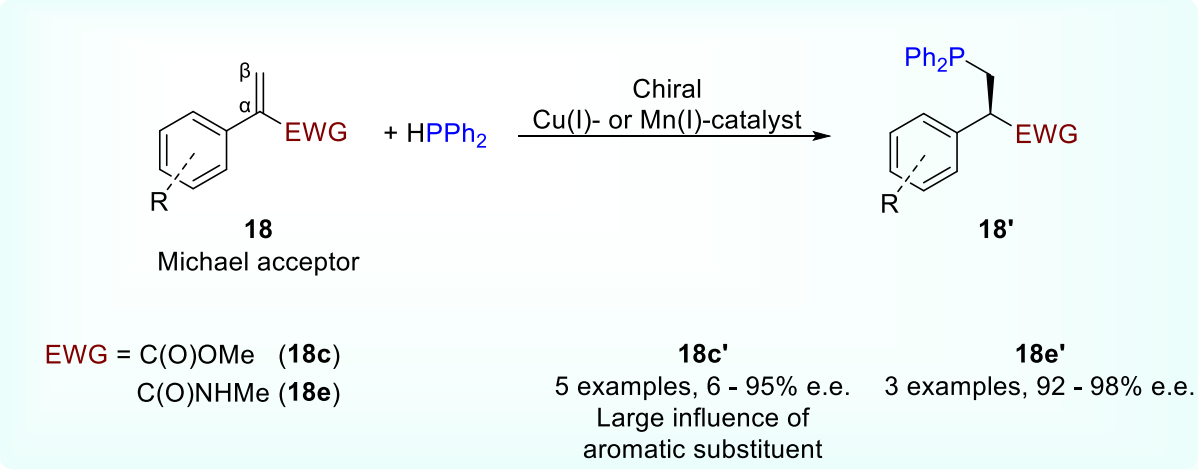


Figure 1. This work on asymmetric Cu(I)- or Mn(I)-catalysed hydrophosphination of α-substituted Michael acceptors

Abbreviations

°C	- Degrees Celsius
Ar	- aromatic
BDPP	- 1,3-Dimethyl-1,3-propanediyl]bis[diphenylphosphine]
Boc_2O	- Di-*tert*-butyl dicarbonate
conv.	- conversion
Cy	- Cyclohexyl
DBU	- Diazabycycloundecene
DCC	- N,N'-Dicyclohexylcarbodiimide
DCM	- Dichloromethane
DMAP	- 4-Dimethylaminopyridine
DTBM	- 3,5-di-*tert*-butyl
e.e.	- enantiomeric excess
eq	- equivalents
Et_2O	- Diethyl ether
EtOAc	- Ethyl acetate
EWG	- Electron withdrawing group
g	- gram
h	- hours
HATU	- (1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate
HRMS	- High Resolution Mass Spectrometry
Hz	- Hertz
^{i}Pr	- isopropyl
mg	- milligram
MHz	- Megahertz
mL	- millilitre
MLC	- Metal-Ligand Cooperation
NMR	- Nuclear Magnetic Resonance
ON	- Overnight
Ph	- Phenyl
ppm	- parts per million
PTFE	- Polytetrafluoroethylene
RT	- Room temperature
SFC	- Supercritical Fluid Chromatography
T	- Temperature
TBAI	- Tetra-n-butylammonium iodide
^{t}Bu	- *tert*-Butyl
TM	- Transition Metal
t-PentOK	- Potassium *tert*-pentoxide

Contents

1. Introduction

Organometallic chemistry has provided us with powerful synthetic tools that are widely applicable to many areas of both the synthetic chemistry and the chemical industry [1]. An increasing amount of asymmetric transformations have been made possible by the development of chiral homogeneous catalysts. Traditionally, these catalysts were based on precious and scarce noble metals, such as iridium, palladium, rhodium and ruthenium [2], which demonstrated to have high catalytic efficiency and wide versatility for many areas of asymmetric transformations [3] [4]. However, these 4d and 5d transition metals (TM) lose appeal to be employed in industrial processes, not only because of the scarcity and high cost of the metal, but also due to its high toxicity [5].

In scope of Green Chemistry and sustainability, industrial processes based on noble metal catalysis are obligated to be substituted by more earth-abundant [6] and 'greener' first row TM's such as nickel, manganese and copper. These first row TM's are more biocompatible as they function inside the human body to catalyse various biochemical processes [7]. As a result, these metals are much less toxic for human health. A pharmaceutical drug has an allowed concentration of 10 ppm for noble metals, such as iridium, palladium, rhodium and ruthenium, compared to 15 ppm for nickel and up to 250 ppm for manganese and copper [8] [9]. A pharmaceutical process which is catalysed by a first row TM, rather than a noble metal, allows for a higher amount of residual in the product and subsequently less costly purification methods need to be applied.

A prominent reaction in the chemical industry and pharmaceutical chemistry and a reaction that traditionally relied heavily on noble metal catalysis is a (de)hydrogenation reaction [10]. However, in the last few years it has been shown that manganese can efficiently catalyse this reaction [11]. In 2016, Beller et al. presented the first example of a Mn(I)-pincer catalyst **1** (Figure 2) that was able to perform hydrogenation on a wide range of functional groups [12]. A year later, the same group extended this to asymmetric hydrogenation of ketones. Chiral PNP pincer complex **2** was able to catalyse the asymmetric transformation with up to 94% enantiomeric excess (e.e.) [13]. In the same year, 2017, Kirchner et al. described an unsymmetrical ferrocene-based PNP Mn(I)-complex **3** that was able to catalyse transfer hydrogenation of ketones with up to 96% conversion and 86% e.e. [14]. Moreover, also in 2017, a chiral tridentate PNN Mn(I)-complex **4** was reported by Clarke et al. that was able to catalyse asymmetric hydrogenation of both esters and ketones with up to 97% e.e. [15]. The (R_c,S_p)-Clarke catalyst **4** showed to be highly effective as only low catalyst loadings, down to 0.1 mol%, were required to get high selectivity. The work of the last decade on non-noble metal catalysed hydrogenation proved that a first row TM, such as manganese, can also effectively catalyse a reaction which was previously only achievable with noble metals.

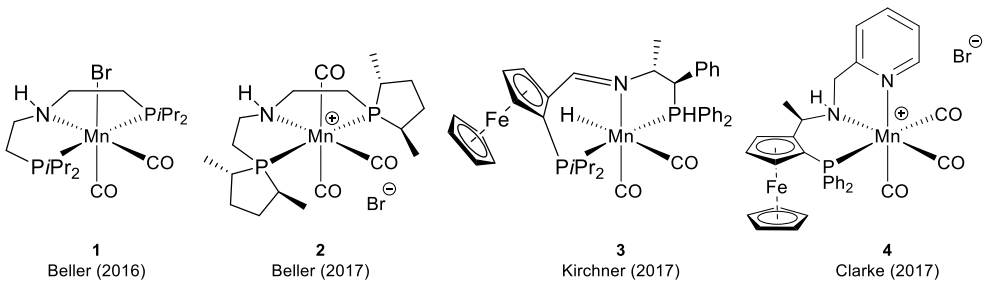
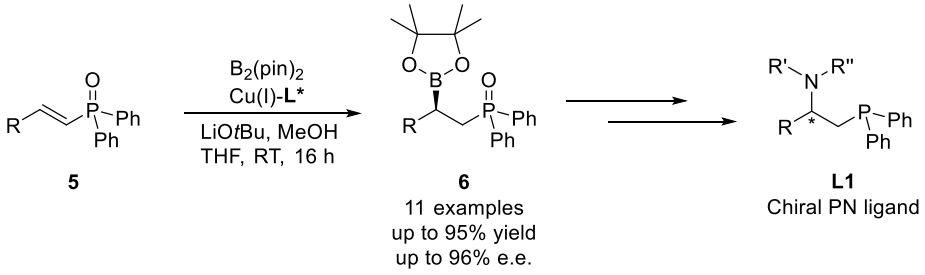


Figure 2. Published Mn(I)-complexes that show high catalytic effectivity in hydrogenation [12] [13] [14] [15]

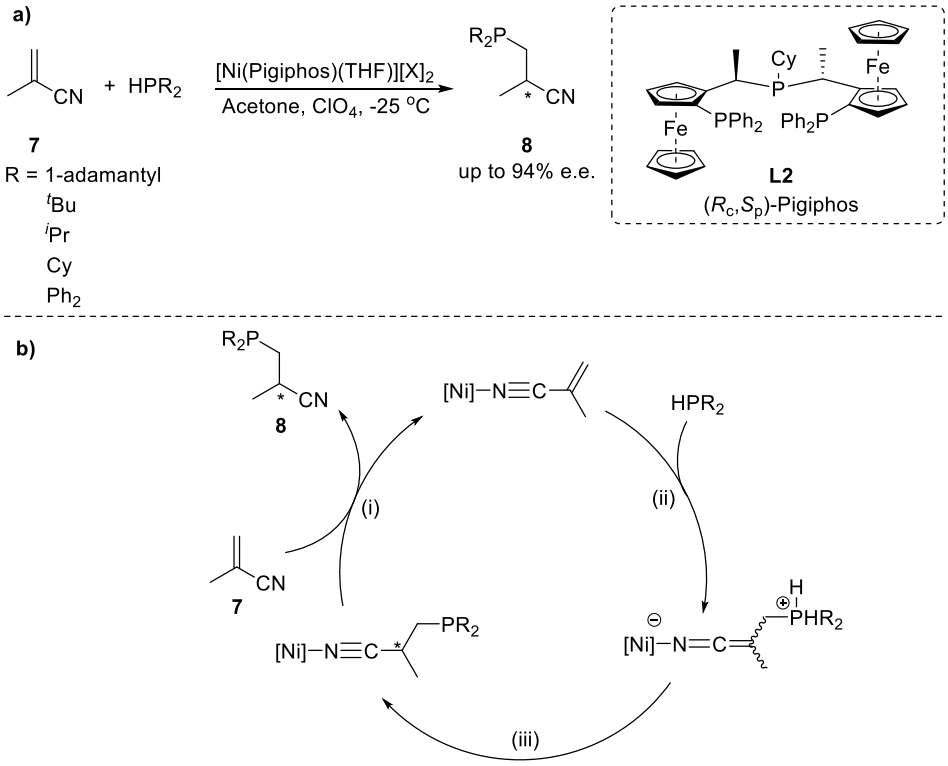
Having access to cheaper TM's as asymmetric catalysts has potential to greatly reduce the cost of a process. However, another factor contributes significantly to the price of an asymmetric catalyst, the chiral phosphine ligand. Synthetic methods to produce chiral ligands can be rather lengthy, time consuming, proceed with low yield or the preparation results in a ligand with low optic purity which requires burdensome purification [3] [16]. This results in chiral ligands that are more expensive than the metal itself or have no commercial availability at all.

Chiral phosphine ligands can be prepared in a large number of ways [17] [18]. Simply an interaction between a phosphinechloride and a Grignard or organolithium reagent that contains a chiral centre elsewhere in the structure can result in a chiral ligand [19] or diastereomers can be separated using chiral resolution [20]. A chiral ligand can also be prepared by utilizing asymmetric synthetic methods, such as employing chiral auxiliaries [21], diastereoselective synthesis [22] or trough catalytic asymmetric addition to an unsaturated compound. For example, in 2015, Feringa et al. reported a method to perform asymmetric copper-catalysed boronation of α,β-unsaturated phosphine oxides **5** (Scheme 1) [23], producing phosphine boronates **6** that could be utilized as precursors to chiral, phosphorus containing ligands. The boronate functional group is able to undergo stereospecific substitution to form a C-N [24] or C-C [25] bond, with the former having potential to be transformed into chiral ligand scaffold **L1**. However, this method requires the substrate to contain a phosphine moiety, limiting the substrate choice for the preparation of a chiral ligand.



Scheme 1. Chiral PN ligand synthesis through a phosphine boronate intermediate [23] [24]

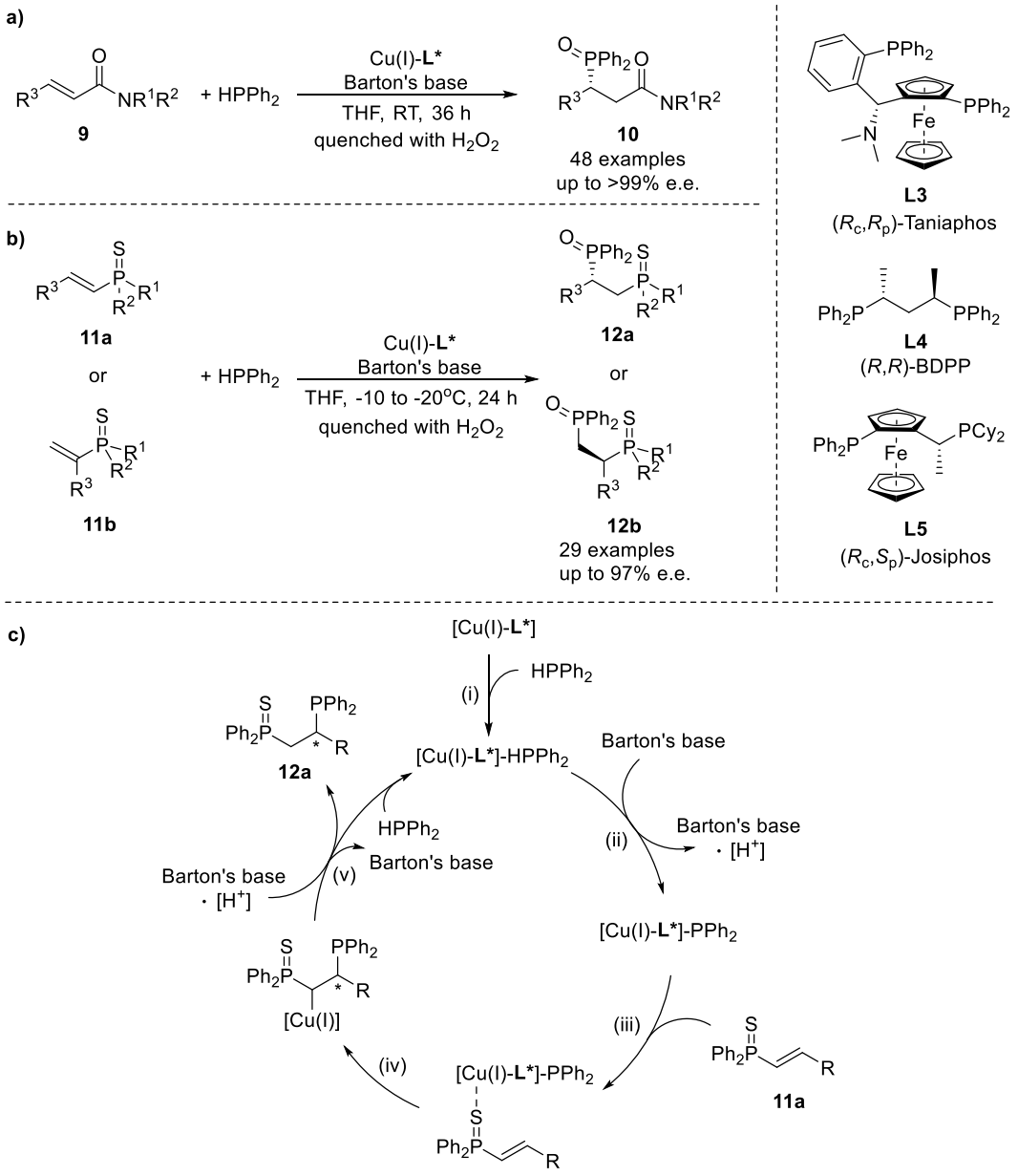
Another technique to prepare a chiral, phosphine ligand and a reaction that is highly atom-efficient is asymmetric hydrophosphination. This procedure is an excellent synthetic procedure to introduce both a stereocentre as well as a phosphorus atom to a ligand. Traditionally, this transformation heavily relied on noble metal catalysis [26]. In 2004, the first non-noble metal asymmetric hydrophosphination was reported with a nickel(II) catalyst containing a (R_C,S_p)-Pigiphos **L2** ligand (Scheme 2a) [27]. Even though the scope of the research was limited to methyl acrylonitrile **7**, the catalyst allowed a variety of secondary phosphine nucleophiles to be used as nucleophile. The highest selectivity was observed when bulky and aliphatic phosphines were used. For example, with di-1-adamantylphosphine as nucleophile the phosphinated product was obtained with 95% yield and 94% e.e. When an aromatic phosphine, diphenylphosphine, was used, the reaction still proceeded but with drastic reduction of both the yield (10% yield) and enantioselectivity (32% e.e.). In the proposed catalytic cycle (see Scheme 2b), first the nitrogen atom of methyl acrylonitrile **7** coordinates to the nickel centre (i), followed by a 1,4-conjugate addition of the phosphine nucleophile (ii). A final stereospecific proton transfer from the phosphonium to the α-carbon induces the chiral centre in the product **8** (iii).



Scheme 2. Ni(II)-catalysed hydrophosphination of methyl acrylonitrile, showing the a) scope of the reaction and b) the proposed catalytic cycle [27]

More recently, in 2020, the first asymmetric hydrophosphination was reported with a copper(I) catalyst (Scheme 3a) [28], an even more biocompatible metal than nickel. Whereas the optimal yield and selectivity were obtained with aliphatic phosphines in the case of nickel catalysed hydrophosphination, for copper catalysed hydrophosphination great selectivity was obtained with diphenylphosphine as nucleophile. The substrate scope is based on Michael acceptors with an amide functionality **9**. Although, no α-substituted substrates are presented, the scope contains a large amount of both β-substituted- and unsubstituted α,β-unsaturated amides. Especially, great selectivity is obtained using aromatic β-substituted substrates, with an e.e. of 91-99%. An aliphatic substituent at the β-position of the substrate reduces the enantioselectivity marginally to 84-98% e.e. The same group expanded the scope later to α,β-unsaturated phosphine sulphides **11** (Scheme 3b) [29]. The product, a chiral 1,2-bisphosphine derivative **12**, can be further modified to form chiral 1,2-bisphosphine ligands. Furthermore, the substrate scope was also extended to α-substituted phosphine sulphide substrates **11b**. Both substrates show excellent e.e. up to 97%. The choice of ligand shows to be dependent on the position of the substituent on the substrate. For the α-substituted α,β-unsaturated phosphine sulphides **11b**, the highest selectivity was obtained with (*R,R*)-BDPP **L4** as ligand, while a racemic product was obtained when this ligand was employed for the β-substituted α,β-unsaturated phosphine sulphides **11a**. Instead the ideal ligand was found to be (R_c,R_p)-Taniaphos **L3**, as was the case for the β-substituted α,β-unsaturated amides **9**. A mechanism is proposed for both the copper catalysed hydrophosphination of α,β-unsaturated amides **9** and phosphine sulphides **11** (see Scheme 3c) where the catalytic cycle is initiated by coordination of the phosphine to the metal centre (i). This is opposed to nickel catalysed hydrophosphination where first the Michael acceptor coordinates to the metal. In addition, the mechanism of copper catalysed hydrophosphination also requires the presence of a base to deprotonate the coordinated diphenylphosphine. The increased acidity of the proton allows for facile deprotonation by Barton's base (ii). Next, when an α,β-

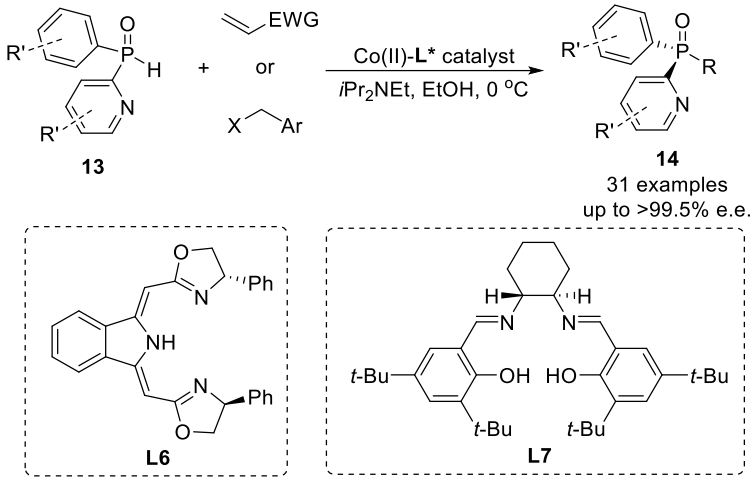
unsaturated phosphine sulphide **11** is used as substrate, it can coordinate to the metal centre through ''soft-soft'' interaction between copper and sulphur (iii). After nucleophilic attack of the phosphorus to install the chirality in the product (iv), the intermediate is protonated and released to give the phosphinated product **12** (v).



Scheme 3. Cu(I)-catalysed hydrophosphination of a) α,β-unsaturated amides [28] and b) α,β-unsaturated phosphine sulphides c) with the proposed catalytic cycle for hydrophosphination of the phosphine sulphides [29]

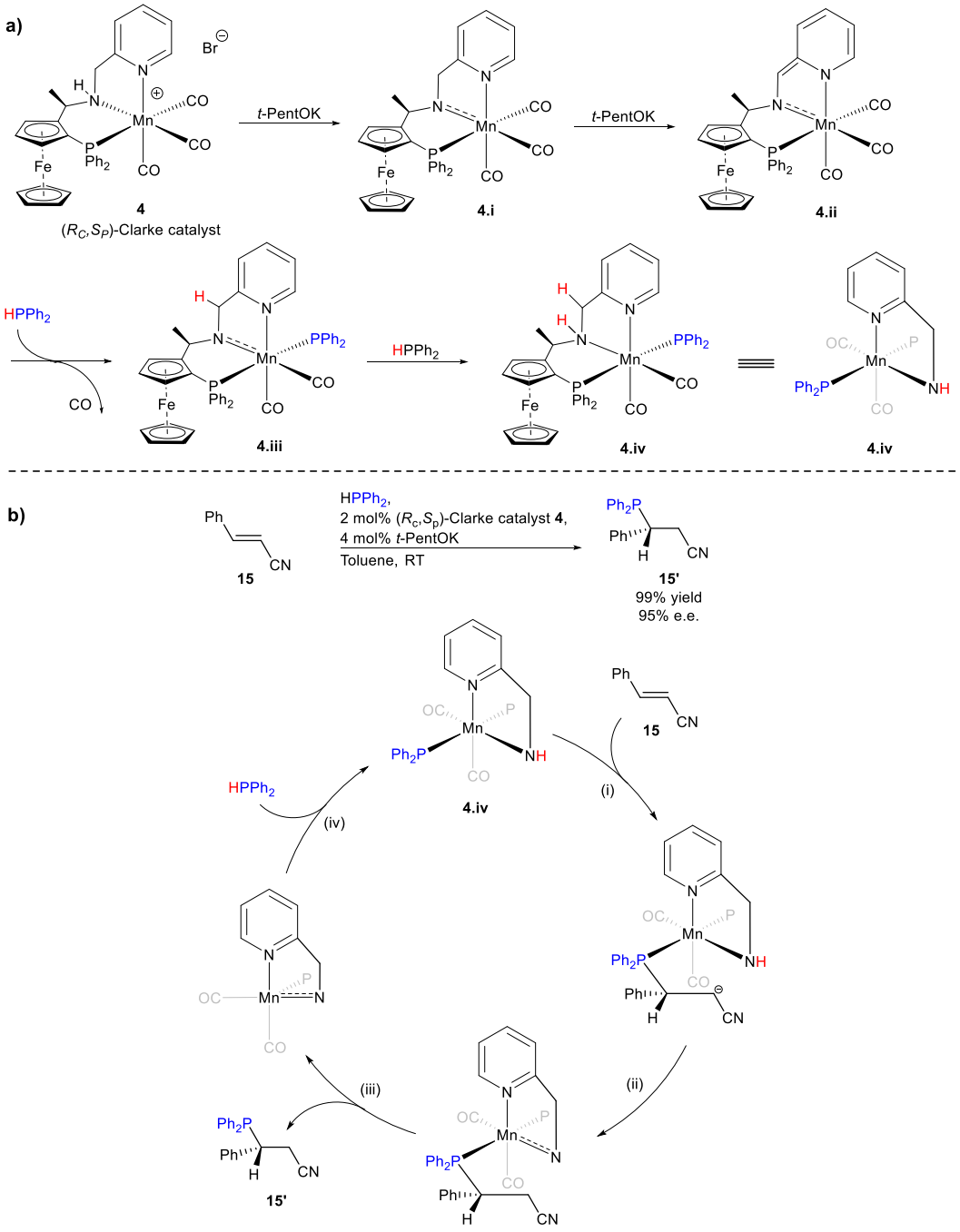
Next to nickel and copper, another first row TM has been described to catalyse asymmetric hydrophosphination. One procedure has been reported that makes use of a cobalt(II)-complex to couple a secondary phosphine oxide **13** to a Michael acceptor or a benzyl halide (Scheme 4) [30]. Whereas previous described methods prepare phosphine ligands with a chiral carbon, this method constructs a *P*-stereogenic phosphine **14**. One of the aryl-rings has been substituted by a 2-pyridinyl moiety in order to form a chiral product. The 2-pyridinyl-moiety allows for the phosphine oxide to

coordinate to the metal catalyst in a bidentate chelating fashion, which promotes high stereoselectivity control. Phosphine ligands containing such 2-pyridinyl-moieties have shown to have great potential in catalysis [31] [32] [33]. The ligand used for Co(II)-catalysed hydrophosphination is a chiral NNN pincer ligand **L6** and some examples of hydrophosphination are presented of a cobalt(II)-complex with quadridentate ligand **L7**. The catalyst allows coupling of the phosphine oxide to a wide variety of Michael acceptors, with 86 to >99.5% e.e. In addition, the catalyst allows the phosphine oxide to be coupled to a benzyl halide substrate, obtaining 90 to >99.5% e.e.



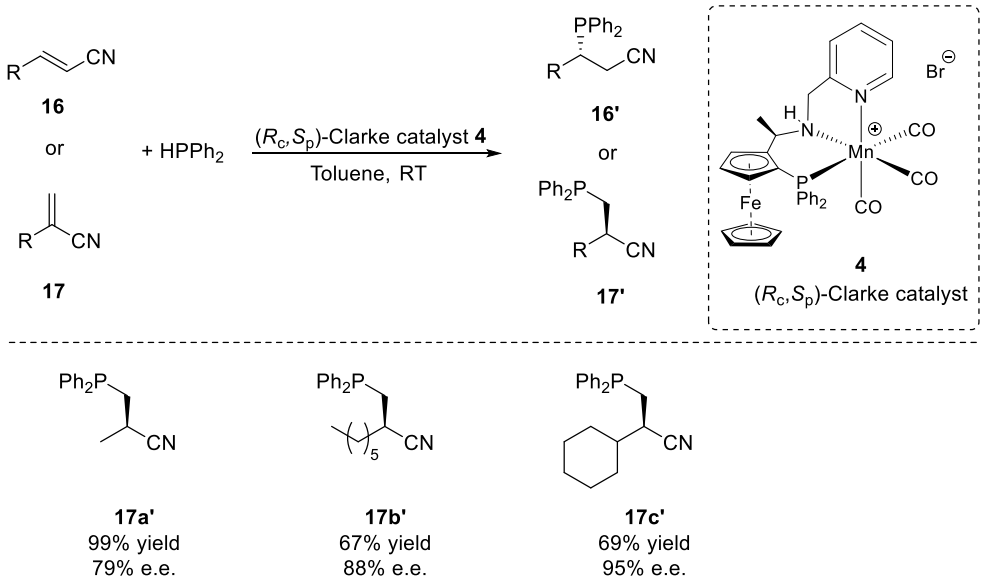
Scheme 4. Co(II)-catalysed asymmetric hydrophosphination with a phosphine oxide [30]

Our group was the first to report manganese(I) catalysed asymmetric hydrophosphination [34]. Manganese is the third most abundant TM in earth's crust (after iron and titanium) [6] and one of the 'greener' metals [8], thus the preferred alternative in terms of sustainable chemistry. Inspired by the success of the (R_c,S_p)-Clarke catalyst **4** in the activation of the H-H bond in a hydrogenation reaction [15], our group showed that it is similarly possible to activate a H-P bond. A distinctive feature of the (R_c,S_p)-Clarke catalysed hydrophosphination is the participation of the ligand in the reaction. Whereas the ligands in aforementioned hydrophosphinations function only as a bulky steric factor surrounding the metal centre, here the ligand undergoes a chemical transformation and actively participates in the reaction. This involvement is also known as metal-ligand cooperation (MLC). Computational studies were conducted in order to propose a mechanism for MLC assisted hydrophosphination (Scheme 5a). To activate the ligand, the amine-moiety first has to be deprotonated to form a metal-amide (**4.i**). Next, the ligand is deprotonated a second time at the α-position with respect to the amine, which dearomatizes the pyridine moiety (**4.ii**). After release of a carbonyl ligand, $HPPh_2$ can bind to the metal and re-protonate the ligand (**4.iii**). A final protonation of an additional $HPPh_2$ generates the active catalyst (**4.iv**). During activation of the ligand, the metal centre does not change in oxidation state. The requirement for double deprotonation was also confirmed experimentally. When a 1:1 ratio of catalyst to base was used, the ligand could not be properly activated and <5% conversion was observed. Full conversion was obtained by increasing the ratio to 1:2. Computational studies were conducted in order to propose a catalytic cycle, see Scheme 5b. For this purpose, cinnamonitrile **15** was used as substrate. In the first step, the metal-complex is stereospecifically approached by the substrate **15**. The phosphide moiety of **4.iv** performs a nucleophilic attack on the electron deficient β-carbon of the substrate (i). Subsequently, this first step induces the chirality of the final product. The amine protonates the carbanion (ii) and the product **15'** is released (iii). Finally, the active catalyst is regenerated by addition of $HPPh_2$ (iv).



*Scheme 5. Computational data on the a) deprotonation of the ligand to generate the active catalyst **4.iv** b) proposed catalytic cycle of Mn(I)-catalysed asymmetric hydrophosphination through MLC [34]. Parts of the ligand are omitted for clarity.*

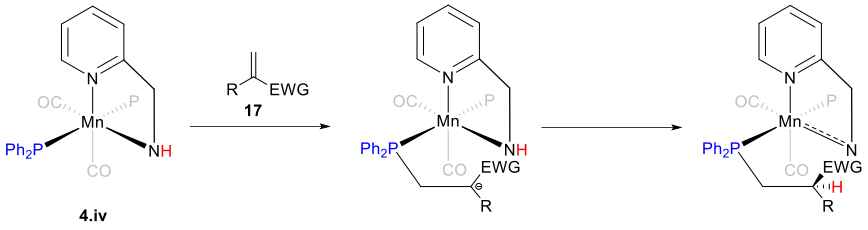
Previously the scope of the reaction consisted of Michael acceptors with a nitrile functionality (Scheme 6). The majority of the substrates were based on β-substituted Michael acceptors **16**, presenting 16 examples with excellent e.e. up to >99%. Both aromatic and aliphatic R-substituted substrates were examined. The best selectivity was obtained for substrates with aromatic substituents, giving 85-99% e.e., whereas aliphatic substrates proceeded with a small reduction in selectivity (80-85% e.e.). The α-substituted Michael acceptors **17** were previously less thoroughly explored. Only three examples of aliphatic R-substituted α,β-unsaturated-nitriles were presented, with a varying e.e. of 79-95%.



*Scheme 6. Scope of Mn(I)-catalysed hydrophosphination of α-substituted substrates **17** [34]*

2. Outline of this project

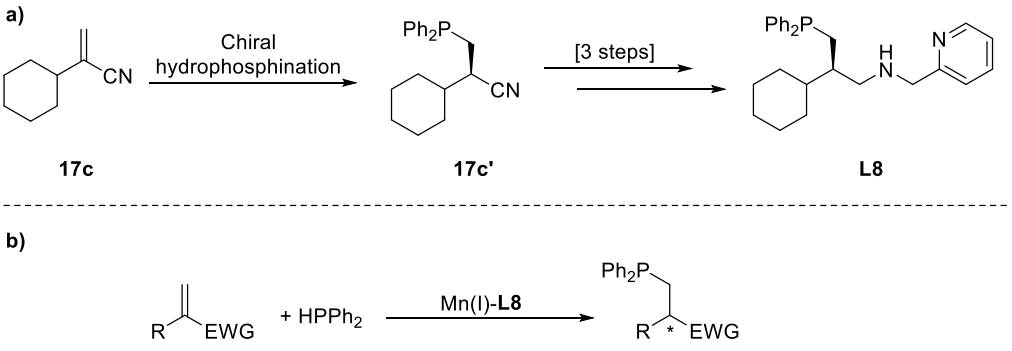
This work will further expand the substrate scope of α-substituted Michael acceptors in the (R_c,S_p)-Clarke **4** catalysed hydrophosphination. These substrates are sterically less obstructed and more reactive than their β-substituted counterparts. Furthermore, the introduction of chirality to the product differs for these two types of substrates. Whereas chirality is introduced by addition of the phosphorus to the double bond for the β-substituted substrates, see Scheme 5b step (i), in the case for the α-substituted substrates the stereogenic centre formed after protonation, see Scheme 7.



*Scheme 7. Addition of **17** to activated catalyst **4.iv** and the induction of chirality*

In light of the previous success of our group with Michael acceptors containing a nitrile functionality [34], the scope will be further extended to substrates based on other Michael acceptors. A wide variety of electron-withdrawing groups can be used in order to construct a Michael acceptor. For this purpose, a series is selected based on either a nitrile, nitro, ester, thioester or amide electron-withdrawing group **18a-e**. Preparation of the substrates will be discussed in chapter 3.1. Whereas chapter 3.2 focuses on the (R_c,S_p)-Clarke **4** catalysed asymmetric hydrophosphination.

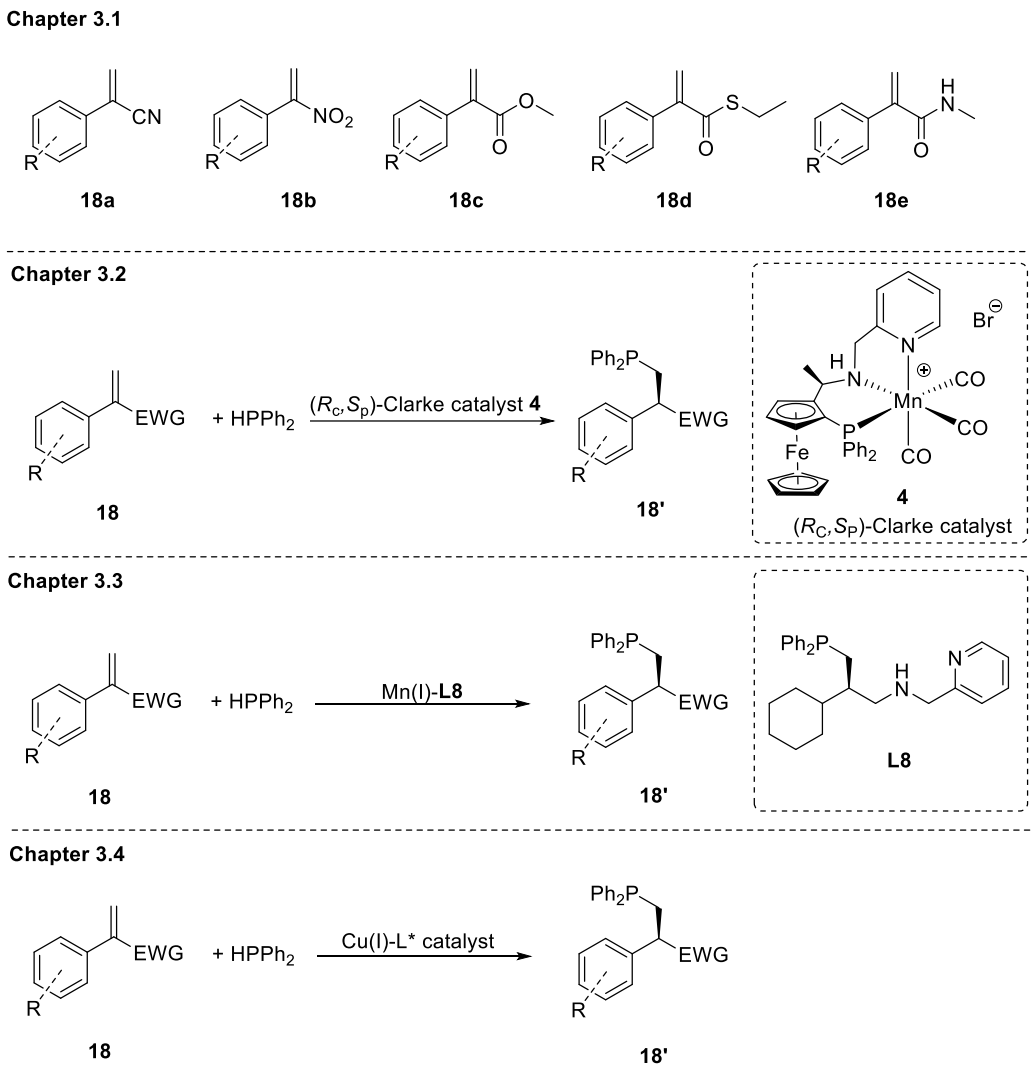
Furthermore, this work now gives us access to chiral phosphine products that have potential to be transformed into chiral ligands. To illustrate this, in chapter 3.3, chiral product **17c'** is transformed into ligand **L8** in three steps following a procedure developed by our group, see Scheme 8a. Subsequently, an example is presented of asymmetric hydrophosphination catalysed by Mn(I)-**L8**, see Scheme 8b.



*Scheme 8. a) Preparation of a chiral, tridentate ligand following a method previously reported by our group [34], followed by b) an illustration of asymmetric hydrophosphination catalysed by Mn(I)-**L8***

Finally, Mn(I)-catalysed hydrophosphination follows a unique mechanism which is based on MLC. We were interested in understanding how this mechanism compares to Cu(I)-catalysed hydrophosphination, using the same ester substrates **18c**. Although previous examples have been presented of Cu(I)-catalysed asymmetric hydrophosphination of α,β-unsaturated amides and phosphine sulphides, there are no reports of Cu(I)-catalysed hydrophosphination of esters. In chapter

3.4, a series of commercially available bidentate PP ligands are screened in Cu(I)-catalysed hydrophosphination.

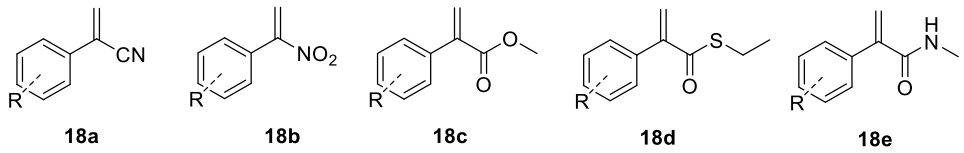


Scheme 9. This work on asymmetric hydrophosphination on α-substituted Michael acceptors

3. Results and discussion

3.1. Synthesis of Michael acceptor substrates

A variety of electron-withdrawing groups are selected to construct the α-substituted Michael acceptor substrates **18a-e**. This includes the nitrile **18a** substrate of which examples were previously presented by our group. However, the nitrile scope was limited to aliphatic nitriles and this work aims to expand the scope to aromatic nitriles. The resulting phosphinated product is an interesting compound to further transform into a chiral ligand. Furthermore, the goal is to expand the scope of α-substituted Michael acceptors with an electron-withdrawing group such as nitro **18b**, ester **18c**, thioester **18d** and carboxamide **18e** of which no previous examples are presented.



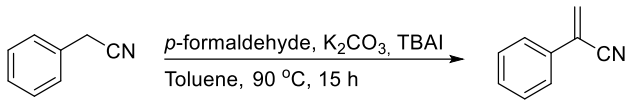
18a **18b** **18c** **18d** **18e**

Figure 3. Targeted substrates

Synthesis of α-substituted Michael acceptors is generally not so straightforward. The activated and sterically unhindered alkenes are prone to polymerisation. The tendency to polymerise is enhanced the stronger the electron withdrawing group is and with electron withdrawing substituents on the aromatic ring.

3.1.1. Nitrile substrates

The scope of reported nitriles is mainly based on aliphatic nitriles, though expanding the scope to aromatic nitriles will allow for substrates that are potentially very interesting for ligands. Multiple procedures are known to synthesize the nitrile-substituted substrate, such as the installation of *p*-formaldehyde on phenyl acetonitrile **19** [35].



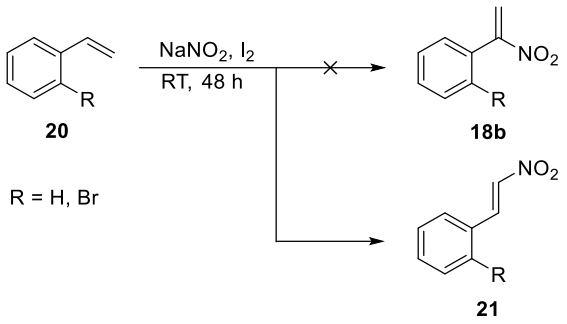
19 **18a1**

*Scheme 10. Synthesis of substrate **18a***

Unfortunately, during the work up of the reaction it was noted that the compound rapidly polymerises, which is a common characteristic of α-substituted Michael acceptors. Further attempts to prepare the product **18a**, through different synthesis methods, are not explored due to the difficulty of handling of the product.

3.1.2. Nitro substrates

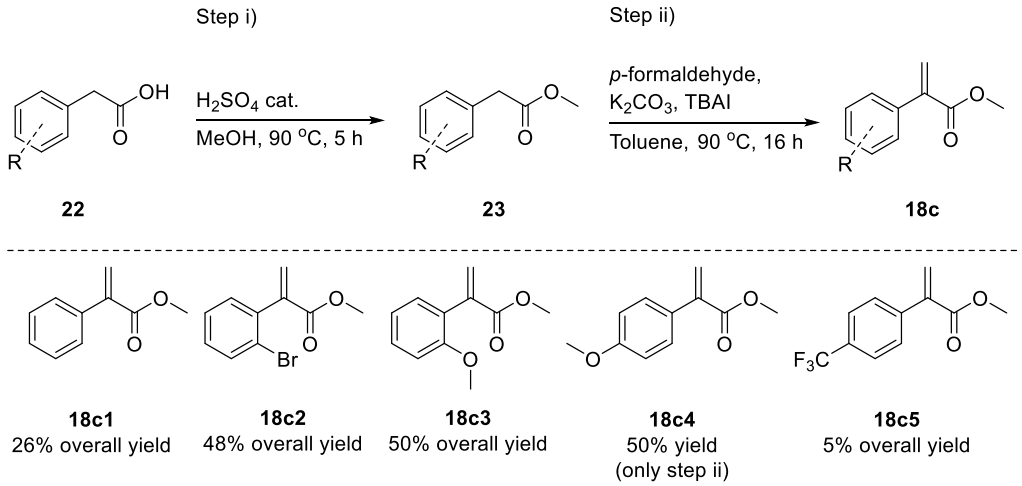
Preparation of the nitro substrate **18b** was performed as described in a previously reported procedure [36], starting from a styrene (derivative) **20.** Although the ^{1}H NMR spectrum of the product was in accordance with the reported spectrum, no doublet was observed between 5.5 to 6.5 ppm, which is expected for the β-protons. Further analysis by APT-NMR show the compounds contains two quaternary (or secondary) carbons giving a negative signal. For the desired (bromo-substituted) product four need to be observed. Furthermore, the HSQC-spectrum indicates the two protons from the double bond are attached to different carbons, revealing that β-addition has occurred to form trans-product **21**. See appendix B for the NMR spectra. There are no other examples presented in literature for the synthesis of substrate **18b**.



*Scheme 11. Synthesis of substrate **18b***

3.1.3. Ester substrates

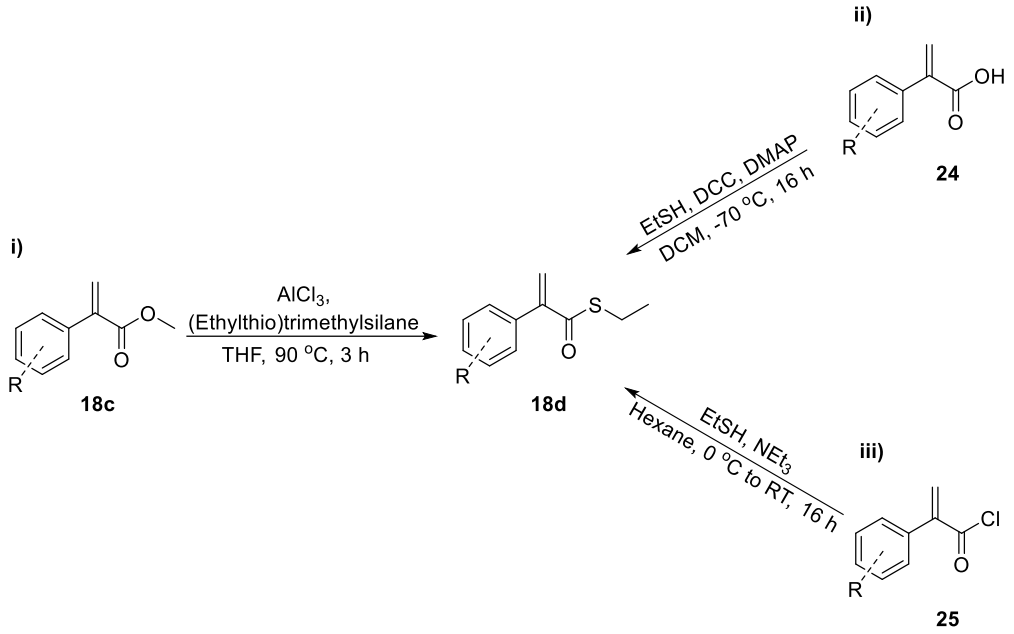
The ester α,β-unsaturated substrates **18c** were prepared following a known procedure [37], performing an esterification on phenylacetic acid derivatives **22**, followed by an aldol condensation with *p*-formaldehyde.



*Scheme 12. Synthesis of substrates **18c1-18c5***

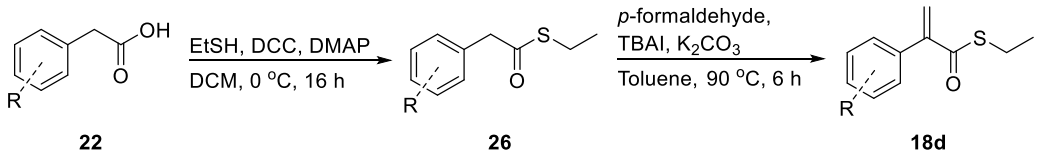
3.1.4. Thioester substrates

Procedures for the synthesis of the α-substituted thioester substrates **18d** have not yet been reported. However, synthesis of the β-substituted substrate is well reported [38]. Varying starting material can be selected, such as an i) ester, ii) acid or iii) acyl chloride derivative, see Scheme 13.



*Scheme 13. Different synthetic methods to produce substrate **18d**, starting from the i) ester, ii) carboxylic acid or iii) acyl chloride derivative. Methods based on the synthesis of β-substituted α,β-unsaturated thioesters*

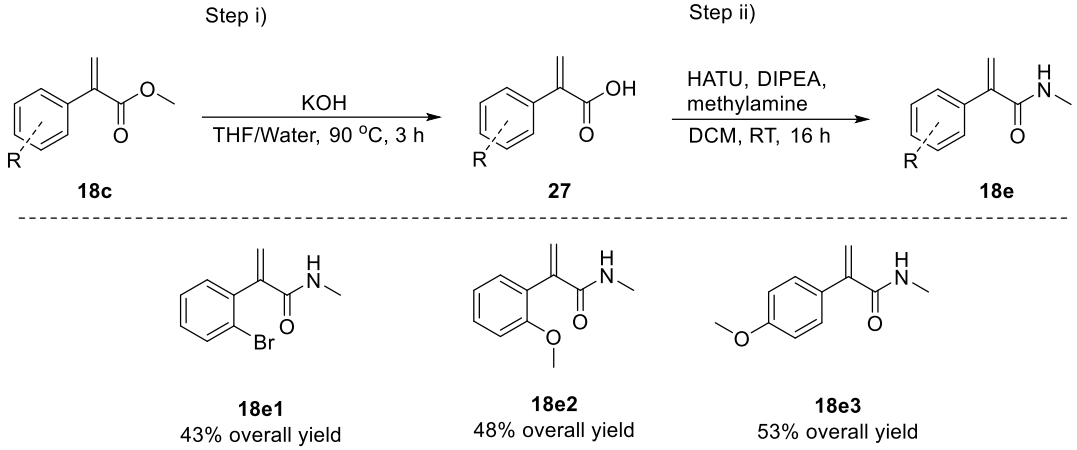
Although these procedures work well for β-substituted substrates, the desired product **18d** was formed as the minor product (< 5% yield) for all instances. The major product that formed resulted from nucleophilic addition of the thiol to the double bond, as the thiol is a sufficiently strong nucleophile to prefer addition to the double bond in fashion of a 1,4-addition over 1,2 addition (appendix B). In order to prevent the thiol to add to the double bond, a different order of synthesis can be used where first the thiol **26** is prepared and subsequently the aldol condensation with *p*-formaldehyde is performed. Although this is an efficient method to produce the ester substrates **18c** and even though the α-hydrogens of a thioester are more acidic, no conversion was observed.



*Scheme 14. Attempted preparation of substrate **18d** through a similar procedure as the ester substrate*

3.1.5. Carboxamide substrates

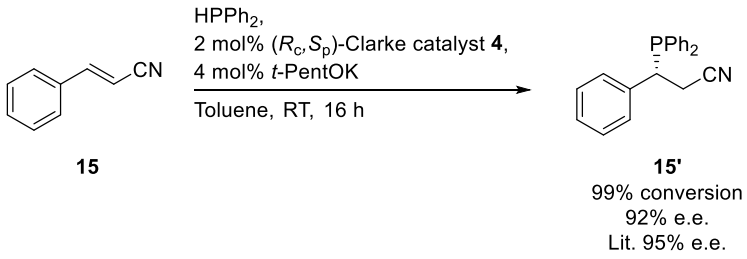
The carboxamide substrate **18e** was prepared from the ester derivative **18c**, following a known procedure, in which first the ester is hydrolysed [37], followed by a peptide coupling with HATU [39].



*Scheme 15. Synthesis of substrates **18c1-18c5***

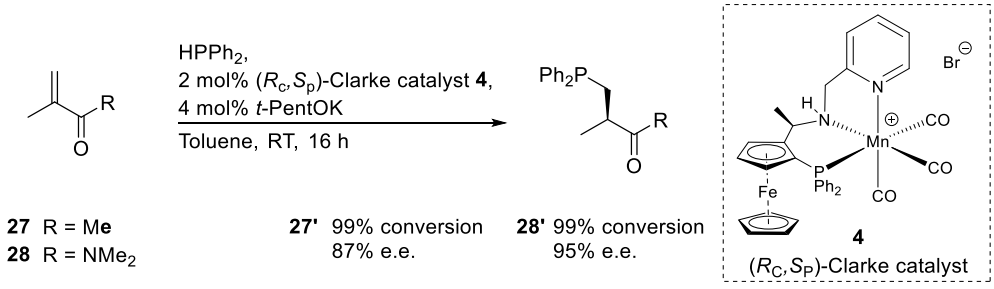
3.2. (R_c,S_p)-Clarke catalysed hydrophosphination

The investigation on asymmetric hydrophosphination was initiated by performing the reaction on cinnamonitrile **15**, a commercially available β-substituted nitrile. This substrate was previously well studied by our group [34]. Under standardized conditions, the reaction proceeded to full conversion and gave 92% e.e., showing a comparable result to the reported e.e. of 95%.



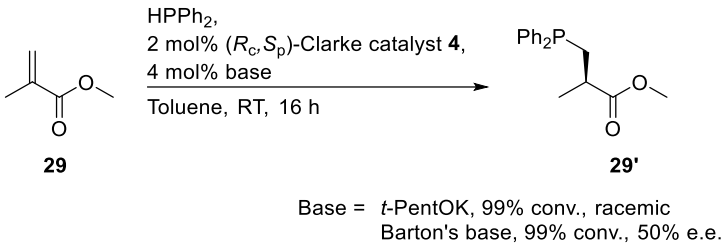
*Scheme 16. Asymmetric hydrophosphination of cinnamonitrile **15** [34]*

Next, the work was moved on to α-substituted Michael acceptors, which is more in line with the rest of this research. Both the methyl α-substituted 3-methylbut-3-en-2-one **27** and N,N-dimethylmethacrylamide **28** are commercially available. Under the same conditions as the above reaction, the ketone **27** proceeded with 87% e.e. and the amide **28** with 95% e.e.



*Scheme 17. Asymmetric hydrophosphination of 3-methylbut-3-en-2-one **27** and N,N-dimethylmethacrylamide **28***

With having various ester substrates synthesized, we were curious to see how methyl methacrylate **29**, the ester analogue of **27** and **28**, would perform in the reaction. As the reactivity of an ester is between a ketone and amide, we expected the reaction to proceed with an e.e. between 87-95%. Surprisingly, when the reaction with methyl methacrylate **29** was performed under the same standard conditions no enantioselectivity was obtained. A base that previously showed to be highly effective in catalysing asymmetric hydrophosphination is Barton's base [28] [29] [34]. When the reaction was performed with Barton's base instead of *t*-PentOK, the reaction proceeded with 50% e.e. Barton's base is a weaker base than *t*-PentOK, thus the rate of the racemic base-catalysed side reaction is reduced.

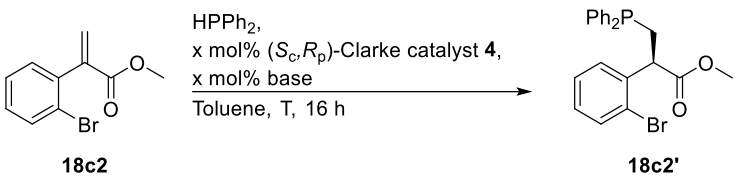


*Scheme 18. Asymmetric hydrophosphination of methyl methacrylate **29***

3.2.1. Conditions screening

Noting that esters do not behave as expected, some alternative conditions were screened. Optimization of the conditions for (R_c,S_p)-Clarke **4** catalysed hydrophosphination was done using methyl 2-(2-bromophenyl)acrylate **18c2** as substrate, see table 1. First, the reaction was performed under standard hydrophosphination conditions from literature (entry 1) [34], using *t*-PentOK as base. When the temperature was lowered to 0 °C (entry 2), the conversion decreased to 85% and the e.e. decreased from 66% to 42%. Next, when the reaction was performed at room temperature with Barton's base, a minor increase in stereoselectivity of the reaction was observed, 70% e.e. (entry 3). Next, a slight excess of catalyst compared to the base (2 mol% catalyst to 3.8 mol% base) was used to reduce the amount of free base is present to a minimum, as the deprotonation of the catalyst is in equilibrium. As was stated earlier, 2 equivalents of base are required to deprotonate the catalyst and generate the active species **4.iv** (see Scheme 5). Any excess of free base can potentially catalyse the racemic base-catalysed reaction. However, the same e.e. is obtained as with the standard loadings (entry 4). Increasing the catalyst and base loading by a factor of 2 gives a minor decrease in selectivity (entry 5). Lowering the temperature again (entry 6 & 7), gave rise to similar results as when *t*-PentOK was used as a base, a counterintuitive decrease in stereoselectivity was observed. However, full conversion was still obtained at -50 °C. Generally for asymmetric catalysis, lowering the temperature increases the stereoselectivity of the reaction. By reducing the amount of energy a substrate has, through lowering the temperature, it also reduces the likelihood of the substrate to approach the metal-complex with the energetically unfavoured orientation. For this instance, the transition state of the interaction between the metal-complex and a substrate **18c** with *pro-S* orientation has a higher activation energy barrier than for *pro-R*, which makes it harder to overcome at reduced temperatures. Theoretically, this should result in increased optic purity of the product. Although, lowering the temperature can also lead to a change of mechanism. Sufficiently lowering the temperature decreases the rate of both the *pro-R* and *pro-S* pathways and instead the racemic base-catalysed reaction is the predominant pathway. The control reactions in entry 8 and 9 indicate that the reaction can indeed proceed without presence of the metal catalyst and even without presence of a base. Noting the trend that the stereoselectivity goes down with temperature a logical step would be to increase the

temperature, however due to the instability of the (S_c,R_p)-Clarke catalyst **4** at elevated temperature, this is not explored.



18c2 **18c2'**

table 1. Effects of the base, temperature and loadings on the (R_c,S_p)-Clarke-catalysed hydrophosphination

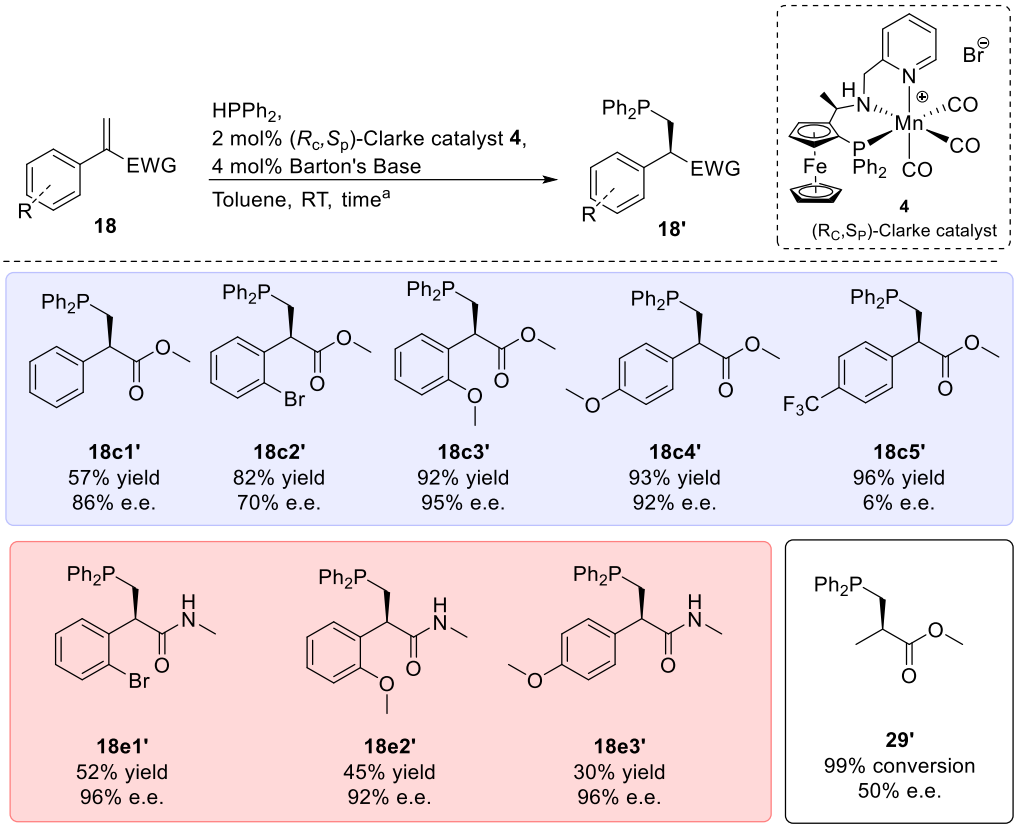
Entry	*mol% catalyst*	*Base*	*mol% base*	*Temperature (°C)*	*Conversion (%)*	*Isolated yield (%)*	*e.e. (%)*
1	2	*t*-PentOK	4	RT	99	63	66
2	2	*t*-PentOK	4	0	85	68	42
3	**2**	**Barton's base**	**4**	**RT**	**99**	**82**	**70**
4	2	Barton's base	3.8	RT	96	96[a]	70
5	4	Barton's base	8	RT	99	84	66
6	2	Barton's base	4	0	99	73	62
7	2	Barton's base	4	-50	99	98[a]	63
8[b]	0	-	0	RT	19	-	-
9	0	Barton's base	4	RT	80	-	-

[a] purified over PTFE filter, [b] with 3 days reaction time

3.2.2. Substrate scope

The optimized reaction conditions found for methyl 2-(2-bromophenyl)acrylate **18c2** were 2 mol% (R_c,S_p)-Clarke catalyst **4** and 4 mol% Barton's at room temperature, see table 1 entry 3. The hydrophosphination of the prepared substrates were performed under these conditions. Going from the unsubstituted ester substrate **18c1'** to the *o*-bromo-substrate **18c2'**, a significant decline in enantioselectivity is observed, the e.e. drops from 86% to 70%. When an electron-donating substituent is introduced, such as *o*-MeO (**18c3'**) and *p*-MeO (**18c4'**), the e.e. increases to 95% and 92% respectively. This shows that both the electronic and steric effect of the substituent play a large role on the enantioselectivity. An electron-donating substituents increases the enantioselectivity, whereas a decrease of selectivity is observed for withdrawing substituents. Also, the *ortho*-substituted **18c3'** has a slightly higher e.e. compared to the *para*-substituted **18c4'**, indicating that an increased steric effect also plays a positive effect on the enantioselectivity. Though the influence of the electronic effect outweighs the steric effect. This is confirmed when a strongly electron-withdrawing group, such as CF_3, is located at the *para*-position. An almost racemic product is obtained for product **18c5'**. The strongly withdrawing effect of the ester-group combined with the withdrawing effect of the substituted aromatic ring greatly reduces the electron density at the olefinic β-position. The trend that the e.e. reduces for strongly electrophilic substrates was noted all throughout this research, starting with the observation that the methyl R-substituted ketone **27** had a lower e.e. than the amide analogue **28**, 87% to 95% respectively. This trend can be explained by the poor enantiodiscrimination of the catalyst for the more electrophilic substrates. If these substrates approach the catalyst, it has a high tendency to react with the catalyst-bound phosphine nucleophile regardless of the orientation (*pro-R* or *pro-S*), thus reducing the enantioselectivity of the reaction. In the case of the carboxamides (**18e1'-18e3'**), the carboxamide nitrogen easily donates its lone pair in the C-N bond, causing the electron

withdrawing nature of the carboxamide to be less significant than that of an ester. Subsequently, the double bond is less activated towards nucleophilic attack of the phosphine and higher enantioselectivity is obtained. Furthermore, the trend that the aromatic substituent increases the selectivity for electron donating substituents and decreases for electron withdrawing substituents is not observed, which is also a consequence of the notably less withdrawing nature of the carboxamide functionality.



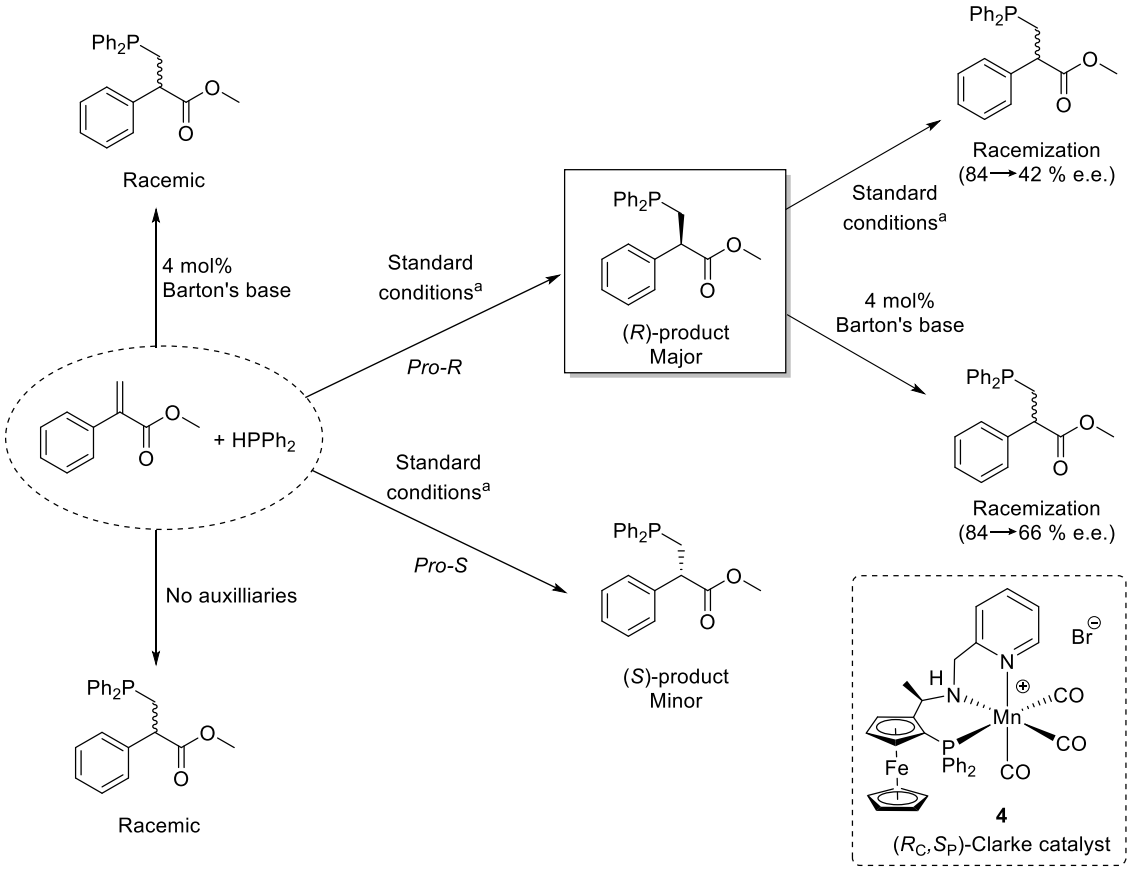
*Scheme 19. Substrate scope of Clarke **4** catalysed hydrophosphination under optimized conditions (see table 1, entry 3), [a] 16 hour reaction time for esters and 3 day reaction time for carboxamides*

3.2.3. Racemization studies

To investigate the configurational stability of the ester products **18c'**, various racemization experiments were conducted. First, the product **18c1'** with known e.e. (84%) was mixed with Barton's base and stirred for 2 hours. A substantial decrease in e.e. was observed, from 84% to 66%. The second racemization experiment was conducted by activating 2 mol% (R_c,S_p)-Clarke catalyst **4** with 4 mol% base and then addition of the substrate. Here, an even more significant drop of e.e. was observed from 84% down to 42%.

The racemization is thought to go through a deprotonation, re-protonation mechanism, as the α-proton with respect to the electron withdrawing group is rather acidic. For the product **18c2'**, the conjugate base is not only stabilized by the electron withdrawing ester, but also through resonance with the electron deficient aromatic ring. The magnitude of racemization should be less severe for the carboxamide scope and for a product with an electron donating aromatic substituent, such as MeO. Though, to confirm this mechanism α-deuterium labelling experiments should be conducted.

The competing pathways that can take place are illustrated in Scheme 20. As was discussed in the previous section, the substrate can react with the phosphine without the presence of base. When Barton's base is added to the mixture the rate of the reaction is significantly accelerated. Furthermore, under standard reaction conditions the substrate can approach the activated, phosphinated catalyst **4.iv** with two orientations, *Pro-S* and *Pro-R*. With the latter being the product with the predominant stereoselectivity. Subsequently, if such a product has formed there are two competing pathways that can racemize it. This indicates the difficulty in getting optically pure ester products.

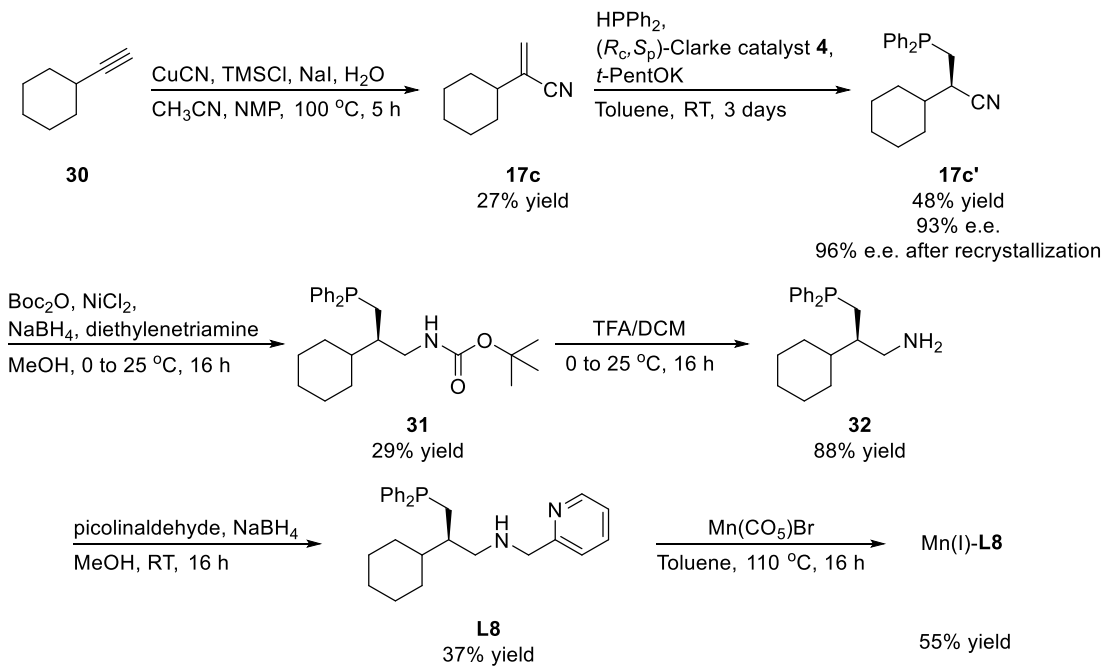


*Scheme 20. Competing pathways for hydrophosphination of the ester substrate **18c**. [a]Standard reaction conditions: 2 mol% (R_C,S_P)-Clarke catalyst **4**, 4 mol% Barton's base, Toluene (0.1 mmol/mL), at RT*

3.3. Mn(I)-L8 hydrophosphination

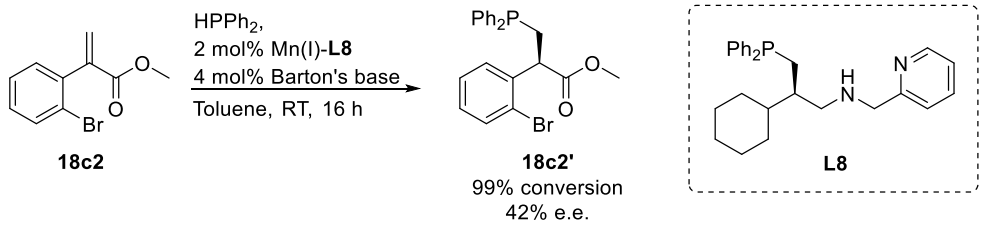
To demonstrate that this procedure of preparing chiral phosphinated products can be further extended to preparing chiral tridentate phosphine ligands, which has a unique type of structure that has not been reported before. The synthesis route was previously reported by our group [34] and the full experimental details are described in Appendix A-III.

The substrate for the asymmetric hydrophosphination, 2-cyclohexylacrylonitrile **17c,** is prepared by nucleophilic attack of copper cyanide to cyclohexylacetylene **30**. Next, the asymmetric hydrophosphination was performed under standardized conditions with *t*-PentOK as base, giving 93% e.e. Though, since this substrate is further used to prepare a chiral ligand, a recrystallization is performed to increase the e.e. Next, a boc-protecting reduction is performed, followed by the cleavage of the boc-group to generate the free amine **32**. Finally, a reductive amination with picolinaldehyde forms the chiral ligand **L8.**



*Scheme 21. Synthesis of chiral catalyst Mn(I)-**L8** following a previously reported procedure [34]. Full experimental details are described in appendix A-III.*

To illustrate the effectiveness of the Mn(I)-**L8** catalyst in asymmetric hydrophosphination, the catalyst is employed in a hydrophosphination of substrate **18c2** (Scheme 22). Although, the catalyst was obtained as a mixture of multiple configurations, as indicated by multiple peaks in the ^{31}P NMR spectrum (see appendix B), it did show to be capable of catalysing the reaction and achieve an e.e. of 42%. Compared to the (R_c,S_p)-Clarke catalyst **4**, which reached 70% e.e., Mn(I)-**L8** does not catalyse it as efficiently, however this is merely an indication that this class of non-ferrocene ligands have high potential in asymmetric hydrophosphination.

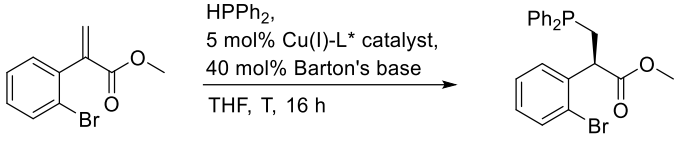


*Scheme 22. Asymmetric hydrophosphination catalysed by Mn(I)-**L8***

3.4. Cu(I)-catalysed hydrophosphination

Previous research showed that asymmetric hydrophosphination can also be achieved by applying chiral copper(I) bidentate complexes, allowing a variety of bidentate ligands [28] [29]. Though, research has been mainly performed using α,β-unsaturated amides and phosphine sulphides as substrates. These substrates showed, however, to be highly effective in the reaction, giving e.e. of 84-98%. So far no work has been performed on Cu(I)-catalysed asymmetric hydrophosphination of α,β-unsaturated esters. To compare how Mn(I)-catalysed asymmetric hydrophosphination compares to Cu(I)-catalysed hydrophosphination, the ester substrate **18c2** is selected and evaluated for its ability to undergo Cu(I)-catalysed hydrophosphination, screening commercially available PP ligands that have previously shown to be effective in the reaction.

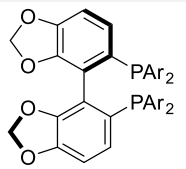
Results of Cu(I)-catalysed asymmetric hydrophosphination are presented in table 2. Two ligands show to be able to catalyse the reaction with fair selectivity, those are the two ferrocene based ligands (R,S_p)-Josiphos **L10** and (S,S_p)-Taniaphos **L13**, entry 2 and 5 respectively. With (S,S_p)-Taniaphos **L13** having marginally better enantioselectivity. When the temperature was increased (entry 6) or decreased (entry 7), a decrease in e.e. was observed, showing an optimal reaction temperature at -20 °C.



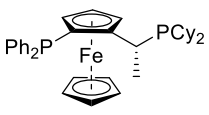
18c2 **18c2'**

table 2. Ligand and temperature screening for Cu(I)-catalyzed hydrophosphination

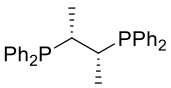
Entry	*Ligand*	*Temperature (°C)*	*Conversion (%)*	*Isolated yield (%)*	*e.e. (%)*
1	(*R*)-DTBM-Segphos	-20	99	82	9
2	(R,S_p)-Josiphos	-20	99	70	44
3	(*R,R*)-Chiraphos	-20	99	73	6
4	(*R,R*)-BDPP	-20	99	68	9
5	**(S,S_p)-Taniaphos**	**-20**	**99**	**75**	**58**
6	(S,S_p)-Taniaphos	-10	99	75	37
7	(S,S_p)-Taniaphos	-50	99	80	33



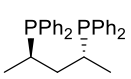
L9
(*R*)-DTBM-Segphos



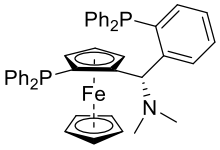
L10
(R,S_p)-Josiphos



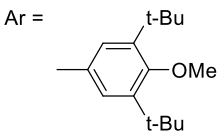
L11
(*R,R*)-Chiraphos



L12
(*R,R*)-BDPP



L13
(S,S_p)-Taniaphos



Under the screened reaction conditions, Mn(I) shows to be more effective at catalysing asymmetric hydrophosphination of the α,β-unsaturated ester substrate **18c2**. The advantage of Mn(I)-catalysis is presumed to lie in the mechanism of catalysis. Due to the principle of MLC, where the ligand is

deprotonated, no large excess of free base is present in the reaction mixture. Effectively, the ligand acts as the base. MLC does not play a role in copper catalysis, the ligand is merely a bulky, steric factor. A large excess of base is used in the Cu(I)-catalysed hydrophosphination which promotes the racemic base catalysed reaction. For the previously reported substrates, α,β-unsaturated amides and phosphine sulphides, the magnitude of the electron withdrawing effect is less severe. The conjugated double bond in carboxamides is less reactive, especially for β-substituted substrates, towards nucleophilic attack. Therefore the base catalysed reaction is less of a competing factor and a higher selectivity can be obtained than for the α,β-unsaturated ester substrates.

Nevertheless, Cu(I) remains to have high potential as catalyst for asymmetric hydrophosphination. Even though there is competition of the racemic side reaction, a significant selectivity can be obtained with a Cu(I)-catalyst (58% e.e. with (*S,S*$_p$)-Taniaphos **L13**). An advantage of Cu(I)-catalysis is the ease of preparing a Cu(I)-complex *in situ*, as such, a large amount of commercially available PP ligands can be rapidly screened. As was reported before, a ligand that shows to be highly selective for one substrate can have no selectivity for a similar substrate. Furthermore, base optimization (with bases such as K_2CO_3, Cs_2CO_3 and DBU and the base loading) may also substantially affect the selectivity of the reaction for the more reactive substrates, as the competing base catalysed reaction has a significant impact on the e.e. Finally, it would be interesting to investigate how less reactive substrates perform in this reaction, such as the prepared α,β-unsaturated amides **18e** and α,β-unsaturated esters which have either an electron-donation aromatic substituent (**18c3**-**18c4**) or which are instead β-substituted.

4. Conclusion

The goal of this work was to extend previous research on Mn(I)-catalysed asymmetric hydrophosphination further to α-substituted Michael acceptors. To achieve this, first the α-substituted Michael acceptor substrates were synthesized, though this proved more difficult than initially anticipated. Due to the enhanced electron deficiency of the double bond, these substrates are more prone to polymerisation. Nonetheless, several α,β-unsaturated esters **18c** and amides **18e** were prepared according to literature precedents.

The (R_c,S_p)-Clarke **4** catalysed asymmetric hydrophosphination was performed on the substrate library. Interestingly, data showed that the electronic effect of the aromatic substituent showed to have a high influence on the selectivity of the reaction. Whereas electron withdrawing aromatic substituents have a negative impact on the stereoselectivity, electron donating aromatic substituents increase the selectivity. However, this trend was only observed for the α,β-unsaturated ester substrates. The α,β-unsaturated carboxamides performed well in the reaction, with an e.e. of 92-96%. Due, to the less withdrawing effect of carboxamides, the β-carbon is less prone to nucleophilic attack of the phosphine.

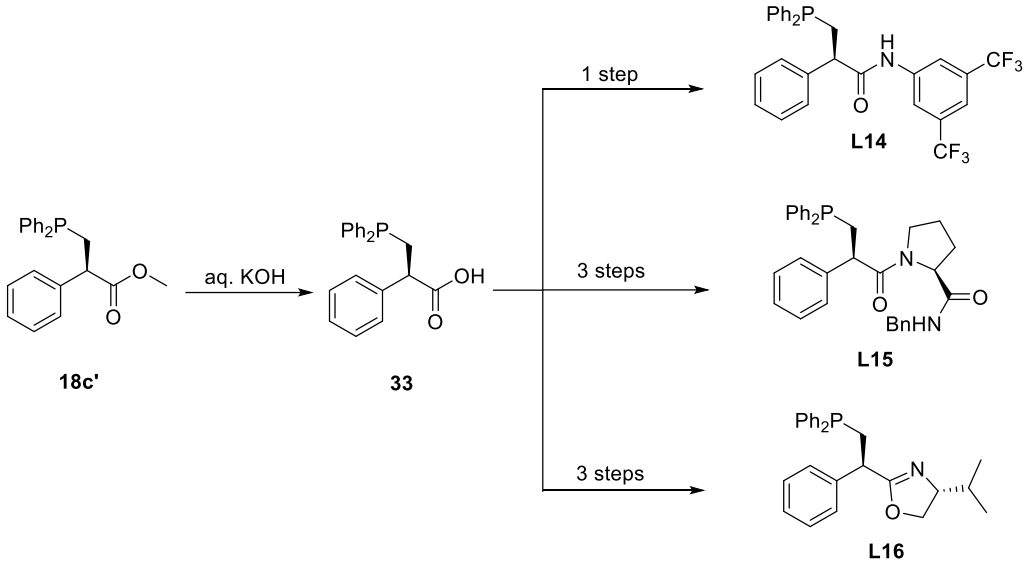
To illustrate that this work can be used further to synthesize chiral phosphine ligands, the synthesis of such ligand was achieved from phosphinated substrate **17c'** to chiral PNN ligand **L8** in three steps. Furthermore, using Mn(I)-**L8** in as catalyst in asymmetric hydrophosphination showed that the catalyst is capable of catalysing the reaction, though with reduced selectivity compared to the (R_c,S_p)-Clarke catalyst **4**.

Finally, the ester substrate was evaluated in Cu(I)-catalysed hydrophosphination, screening a variety of commercially available bidentate ligands. Under the screened conditions, a fair stereoselectivity could be obtained (up to 58% e.e.). However, the results of Cu(I)-catalysed hydrophosphination are inferior to Mn(I)-catalysed hydrophosphination. The culprit is presumed to be the free base that is present in the mixture, which catalysis the racemic base-catalysed reaction. The advantage of Mn(I) is the participation of the ligand in MLC fashion, thus not having the presence of a large excess of free base.

5. Future prospects

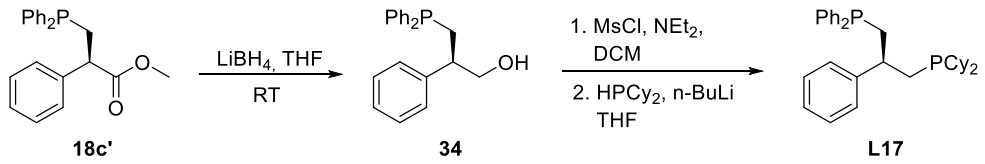
Mechanistic studies can shine light on the behaviour of the α-substituted α,β-unsaturated ester substrate in the Mn(I)-catalysed hydrophosphination. For these studies, a substrate which contains an electron withdrawing substituent on the aromatic ring, such as **18c2**, should be selected, as they can give the most information about the factors that are negatively influencing the reaction. First of all, the conversion should be followed over time in order to determine the optimal reaction time, which is a factor that is still eligible for optimisation. Parallel, the e.e. can be followed over time. This can give insight on how the optic purity of the product behaves. Whether the product initially forms with high enantioselectivity and then racemizes over time, or whether the catalyst shows poor enantiodiscrimination for the electron poor substrates.

Furthermore, the prepared ester products **18c'** can be further utilized for the synthesis of chiral ligands. A variety of procedures are described to prepare chiral phosphine ligands that are used in Pd-catalysed allylic alkylation reactions [40]. After hydrolysis of the chiral ester substrate **18c'** to form compound **33**, chiral PO-ligand **L14** can be prepared in one step [40]. In addition, from compound **33**, PO-ligand **L15** and phosphino oxazoline ligand **L16** can be prepared in an additional three steps [41] [42].



Scheme 23. Proposed synthesis of bidentate ligands for Pd-catalysed allylic alkylation [40] [41] [42].

Preparation of a PP-ligand **L17** can also be achieved starting from chiral ester compound **18c'**. By reducing the ester moiety to an alcohol and then a nucleophilic substitution with a phosphine, such as dicyclohexylphosphine **L17** can be obtained [40]. Thus, a variety of chiral phosphine ligands can be quickly accessed through asymmetric hydrophosphination of an α-substituted α,β-unsaturated ester substrate.



Scheme 24. Future prospect for the ester substrates [40].

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Appendix A – Experimental

General remarks

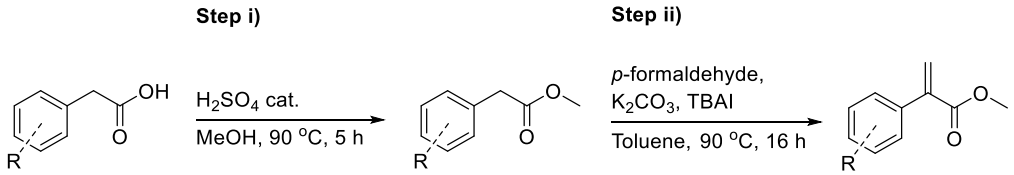
All hydrophosphination reactions were performed inside a glovebox under nitrogen atmosphere, using oven-dried vials or Schlenk flasks and using deoxygenated solvents. Supplementary oxygen- and/or moisture sensitive reactions were carried out under (P_2O_5) dried nitrogen and in oven dried glassware and using standard Schlenk techniques. When indicated, purification of the products was performed by flash column chromatography using Merck 60 Å 230-400 mesh silica gel. NMR analysis was performed on a Varian MercuryPlus (^{1}H at 400 MHz; ^{13}C at 101 MHz; ^{31}P at 162 MHz) equipped with a 400 Autosw probe or a Bruker NEO (^{1}H at 600 MHz; ^{13}C at 151 MHz; ^{31}P at 243 MHz), equipped with a SmartProbe BBFO. Chemical shifts are reported in parts per million (ppm) relative to residual solvent peak: $CDCl_3$: ^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm. Exact mass spectra were recorded on a LTQ Orbitrap XL apparatus with ESI ionization. Enantiomeric excess (e.e.) were determined by chiral SFC analysis with UV detection, using, unless noted otherwise, a Chiracel OJ-3 column.

Chemicals

Reagents and solvents were purchased from commercial sources and used without further purification. Dry solvents were collected from a dry solvent purification system and were additionally dried over molecular sieves prior to use. Hydrophosphination reactions were performed in solvents that were deoxygenated, by freeze-pump-thaw procedure. All reported products of esterification were characterized by ^{1}H-NMR and used without further purification. All other reported compounds were characterised by ^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR (when applicable) and compared with literature data when available.

I. Substrate synthesis

General procedure A – Ester synthesis



22 **23** **18c**

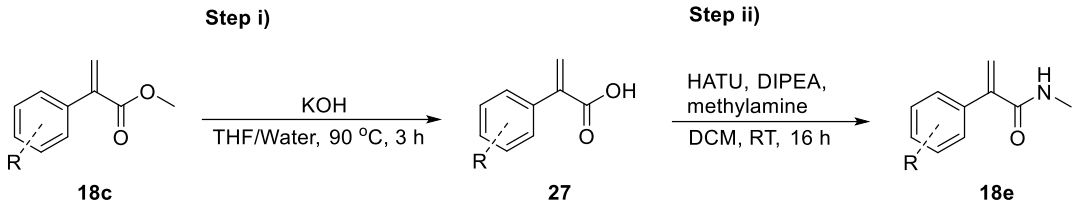
Step i)

Phenylacetic acid derivative **22** was added to a round bottom flask equipped with a magnetic stirring bar. The substrate was dissolved in dry methanol (1 M) and a catalytic amount of concentrated sulphuric acid was added. The mixture was heated at 90 °C for 5 hours. After that, the reaction mixture was allowed to cool down to room temperature. After the methanol was removed by rotary evaporation, the residue was diluted with ethyl acetate and treated with saturated sodium bicarbonate solution and brine. The organic layer was dried over anhydrous sodium sulphate and concentrated *in vacuo* to afford the corresponding methyl 2-phenylacetate derivatives **23** [37].

Step ii)

To a solution of prepared methyl 2-phenylacetate derivative **23** (1 eq) in anhydrous toluene (5 mL/g), potassium carbonate (2.0 eq), tetrabutylammonium iodide (0.4 eq), and p-formaldehyde (2.0 eq) were added. The reaction mixture was heated at 90 °C for 16 hours, quenched with water, and extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulphate and concentrated *in vacuo*. The residue was purified on silica gel column chromatography by using pentane/EA as the eluent to afford methyl 2-phenylacrylate derivatives **18c** [37].

General procedure B – Amide synthesis



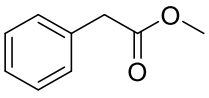
Step i)

To a solution of prepared methyl 2-phenylacrylate derivatives **18c** (1 eq) in THF (2 M), a solution of potassium hydrate (4.0 eq) in water (2 M) was added. The reaction mixture was heated at reflux for 3 hours and then cooled to 0 °C. Addition of concentrated hydrochloric acid resulted in precipitation of a white solid, which was extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulphate and concentrated *in vacuo* to afford 2-phenylacrylic acid derivatives **27**, which was used without further purification in the following step [37].

Step ii)

A solution of 2-phenylacrylic acid derivatives **27** (1 eq) in dichloromethane (8 M), peptide coupling reagent HATU (1.1 eq) was added at room temperature. Next, diisopropylethylamine (1.2 eq) and methylamine (1 eq) in THF (1 M) were added subsequently. The reaction mixture was stirred overnight at room temperature. The mixture was combined with DCM and water and the organic layer was separated, washed with saturated $NaHCO_3$, and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* to afford the crude residue as a colorless oil, which was purified by flash chromatography with pentane/EA yielding the α-substituted acrylamides **18e** [43].

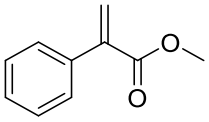
Methyl 2-phenylacetate (23a)



The title compound **23a** was prepared in line with general procedure **A**, step i. The product was obtained as a clear oil with 86% yield. NMR data in accordance with literature precedents [44].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 6.88 (m, 5H, ArH), 3.69 (s, 3H, CH_3), 3.63 (s, 2H, CH_2) ppm.

Methyl 2-phenylacrylate (18c1)



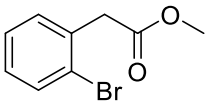
The title compound **18c1** was prepared in line with general procedure **A**, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 10:1 and obtained as a clear oil with 30% yield. This compound polymerises slowly (over approx. 2 weeks) at room temperature, though can be stored below 0 °C for extended time (>2 months) without significant polymerisation.

Compound **15c1** was also prepared by esterification of atropic acid following step i of general procedure **A**, and obtained as a clear oil with 78% yield without further purification. NMR data in accordance with literature precedents [45].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.30 (m, 5H, ArH), 6.37 (d, J = 1.3 Hz, 1H, CH_2), 5.90 (d, J = 1.3 Hz, 1H, CH_2), 3.83 (s, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 144.0, 139.4, 131.0, 130.9, 130.8, 129.5, 54.8 ppm.

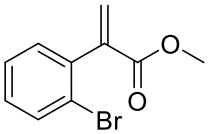
Methyl 2-(2-bromophenyl)acetate (23b)



The title compound was prepared in line with general procedure **A**, step i. Compound **23b** was obtained as a clear oil with 85% yield. NMR data in accordance with literature precedents [46].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dt, J = 8.2, 1.4 Hz, 1H, ArH), 7.37 – 7.21 (m, 2H, ArH), 7.14 (tdd, J = 8.1, 4.1, 2.3 Hz, 1H, ArH), 3.80 (s, 2H, CH_2), 3.71 (s, 3H, CH_3).

Methyl 2-(2-bromophenyl)acrylate (18c2)



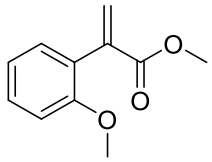
The title compound **18c2** was prepared in line with general procedure **A**, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 10:1 and obtained as a clear oil with 67% yield. NMR data in accordance with literature precedents [47].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.45 (m, 1H, ArH), 7.46 – 7.01 (m, 3H, ArH), 6.53 (d, J = 1.3 Hz, 1H, CH_2), 5.76 (d, J = 1.3 Hz, 1H, CH_2), 3.77 (s, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 141.8, 138.6, 132.5, 130.9, 129.6, 129.1, 127.4, 123.3, 52.4 ppm.

HRMS (ESI+, m/z) calc. for $C_{10}H_9BrO_3Na$ (oxidized product): $[M+H]^+$ = 278.9627, found $[M+H]^+$ = 278.9630.

Methyl 2-(2-methoxyphenyl)acrylate (18c3)

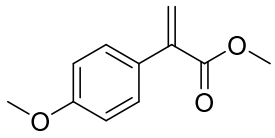


The title compound **18c3** was prepared in line with general procedure **A**, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 10:1 and obtained as a yellowish oil with 50% yield. NMR data in accordance with literature precedents [47].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (ddd, J = 8.2, 7.5, 1.8 Hz, 1H, ArH), 7.22 (dd, J = 7.5, 1.8 Hz, 1H, ArH), 6.97 (td, J = 7.5, 1.0 Hz, 1H, ArH), 6.90 (dd, J = 8.3, 1.0 Hz, 1H, ArH), 6.29 (d, J = 1.5 Hz, 1H, CH_2), 5.74 (d, J = 1.5 Hz, 1H, CH_2), 3.80 (s, 3H, CH_3), 3.76 (s, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 156.9, 139.9, 130.0, 129.8, 127.0, 126.4, 120.7, 110.8, 55.6, 52.0 ppm.

Methyl 2-(4-methoxyphenyl)acrylate (18c4)



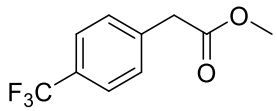
The title compound **18c4** was prepared in line with general procedure **A**, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 10:1 and obtained as a clear oil with 18% yield. NMR data in accordance with literature precedents [48].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.9 Hz, 2H, ArH), 6.89 (d, J = 8.9 Hz, 2H, ArH), 6.27 (s, 1H, CH_2), 5.83 (s, 1H, CH_2), 3.82 (d, 6H, 2x CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 129.5, 129.1, 125.4, 125.4, 113.5, 99.9, 55.3, 52.2 ppm.

HRMS (ESI+, m/z) calc. for $C_{11}H_{12}O_4Na$ (oxidized product): $[M+H]^+$ = 231.0628, found $[M+H]^+$ = 231.0628.

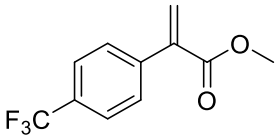
Methyl 2-(4-(trifluoromethyl)phenyl)acetate (23e)



The title compound **23e** was prepared in line with general procedure **A**, step i. The product was obtained as a clear oil with 95% yield. NMR data in accordance with literature precedents [49].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.0 Hz, 2H, ArH), 7.40 (d, J = 8.0 Hz, 2H, ArH), 3.71 (s, 3H, CH_3), 3.69 (s, 2H, CH_2) ppm.

Methyl 2-(4-(trifluoromethyl)phenyl)acrylate (18c5)

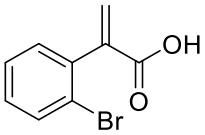


The title compound **18c5** was prepared in line with general procedure **A**, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 15:1 and obtained as a clear oil with 5% yield. A significant amount of product polymerised during the reaction, though can be stored below 0 °C for over 2 weeks without significant polymerisation.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H, ArH), 7.56 – 7.50 (m, 2H, ArH), 6.48 (d, J = 1.0 Hz, 1H, CH_2), 5.97 (d, J = 1.0 Hz, 1H, CH_2), 3.84 (s, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 140.2, 128.7, 128.7, 125.1, 125.1, 52.4 ppm. Due to splitting and a low concentration of the sample the CF_3 carbon (approx. 123.7 ppm) and adjacent aromatic carbon (approx. 133.0 ppm) were not found.

2-(2-Bromophenyl)acrylic acid (27a)



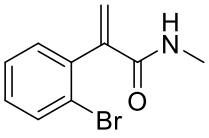
The title compound **27a** was prepared in line with general procedure **B**, step i. The product was obtained as a white solid with 96% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.0, 1.3 Hz, 1H, ArH), 7.43 – 7.12 (m, 3H, ArH), 6.66 (d, J = 1.2 Hz, 1H, CH_2), 5.90 (d, J = 1.2 Hz, 1H, CH_2) ppm.

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.1, 141.0, 137.9, 132.6, 131.3, 131.0, 129.8, 127.4, 123.3 ppm.

HRMS (ESI+, m/z) calc. for $C_9H_6BrO_2$: $[M+H]^+$ = 224.9557, found $[M+H]^+$ = 224.9556

2-(2-Bromophenyl)-N-methylacrylamide (18e1)

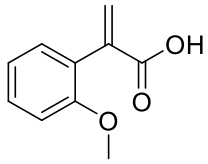


The title compound **18e1** was prepared in line with general procedure B, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 1:1 and obtained as a yellow-white solid with 47% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.0, 1.2 Hz, 1H, ArH), 7.40 – 7.12 (m, 3H, ArH), 6.43 (d, J = 1.5 Hz, 1H, CH_2), 5.49 (d, J = 1.5 Hz, 1H, CH_2), 5.46 (bs, 1H, NH), 2.81 (d, J = 4.9 Hz, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 143.8, 138.5, 133.1, 131.5, 130.1, 127.8, 125.7, 123.5, 26.8 ppm.

2-(2-Methoxyphenyl)acrylic acid (27b)

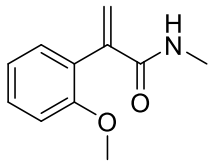


The title compound **27b** was prepared in line with general procedure **B**, step i. The product was obtained as a white solid with 92% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.14 (m, 2H, ArH), 7.12 – 6.79 (m, 2H, ArH), 6.44 (d, J = 1.8 Hz, 1H, CH_2), 5.86 (d, J = 2.0 Hz, 1H, CH_2), 3.81 (s, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 139.3, 130.2, 130.0, 129.8, 128.6, 126.5, 120.7, 110.9, 55.7 ppm.

2-(2-Methoxyphenyl)-N-methylacrylamide (18e2)

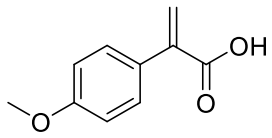


The title compound **18e2** was prepared in line with general procedure B, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 1:1 and obtained as a yellow-white solid with 53% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 1H, ArH), 7.20 (dd, J = 7.5, 1.7 Hz, 1H, ArH), 6.96 (td, J = 7.5, 1.0 Hz, 1H, ArH), 6.91 (dd, J = 8.3, 1.1 Hz, 1H, ArH), 6.25 (d, J = 1.7 Hz, 1H, CH_2), 5.60 (s, 1H, NH), 5.48 (d, J = 1.7 Hz, 1H, CH_2), 3.78 (s, 3H, CH_3), 2.81 (d, J = 4.9 Hz, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 156.9, 142.0, 131.0, 130.2, 126.8, 123.8, 120.8, 111.1, 55.7, 26.6 ppm.

2-(4-Methoxyphenyl)acrylic acid (27c)

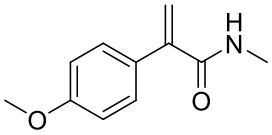


The title compound **27c** was prepared in line with general procedure **B**, step i. The product was obtained as a white solid with 90% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H, ArH), 6.93 – 6.86 (m, 2H, ArH), 6.46 (s, 1H, CH_2), 5.97 (s, 1H, CH_2), 3.83 (s, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 159.7, 139.8, 129.7, 128.5, 128.0, 113.6, 55.3 ppm.

2-(4-Methoxyphenyl)-N-methylacrylamide (18e3)



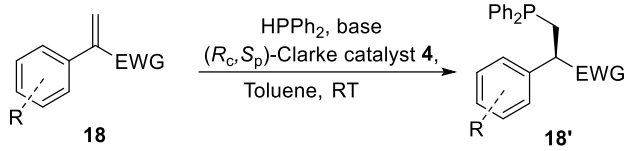
The title compound **18e3** was prepared in line with general procedure B, step ii. The product was purified by silica flash chromatography eluting with pentane:EA 1:1 and obtained as a yellow-white solid with 59% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.16 (m, 2H, ArH), 7.04 – 6.79 (m, 2H, ArH), 6.06 (s, 1H, CH_2), 5.70 (s, 1H, NH), 5.53 (s, 1H, CH_2), 3.83 (s, 3H, CH_3), 2.88 (d, J = 4.9 Hz, 3H, CH_3) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 159.8, 144.2, 129.5, 120.9, 114.1, 55.3, 26.6 ppm. Due to a low concentration of the sample the Michael acceptor substituted aromatic carbon (approx. 125.8 ppm) was not found.

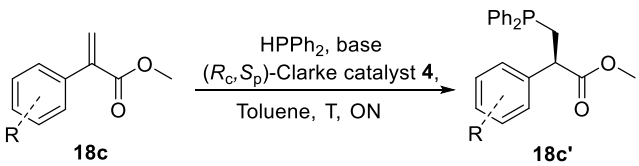
II. Hydrophosphination reactions

General procedure C – (R_c,S_p)-Clarke catalysed hydrophosphination



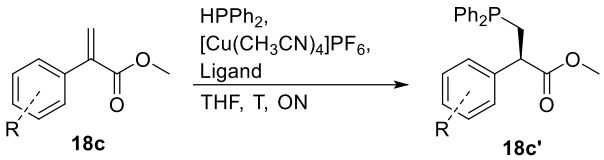
The hydrophosphination reactions were performed inside a glovebox to ensure inert reaction conditions. An oven-dried 4 mL vial was equipped with a magnetic stirring bar and (R_c,S_p)-Clarke catalyst **4** (2 mol%). The catalyst was dissolved in dry, deoxygenated toluene (1 mL), then the base (4 mol%) was added and the mixture was stirred for 15 min. Next, the α,β-unsaturated substrate **18** (0.1 mmol, 1.0 eq) was added, followed by the addition of diphenylphosphine (0.1 mmol, 1.0 eq). The mixture was stirred at room temperature overnight when an ester was used as substrate and 3 days for amides and nitriles. The solvent was then evaporated and the residue was purified by silica flash column chromatography [34].

General procedure D – Cooled hydrophosphination



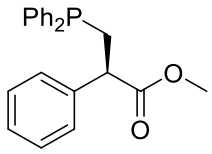
An oven-dried Schlenk flask was equipped with a magnetic stirring bar and (R_c,S_p)-Clarke catalyst **4** (2 mol%). Inside a glovebox, the catalyst was dissolved in dry, deoxygenated toluene (1 mL). Then the base (4 mol%) was added and the mixture was stirred for 15 min. The α,β-unsaturated substrate **18c** (0.1 mmol, 1.0 eq) was added and the Schlenk flask was removed from the glovebox to a cryostat and cooled to the desired temperature. Then, diphenylphosphine (0.1 mmol, 1.0 eq) was added and the mixture was stirred overnight. The mixture was allowed to warm up to room temperature before the solvent was evaporated and the residual was purified by silica flash column chromatography [34].

General procedure E – Cu(I) catalysed hydrophosphination



An oven-dried Schlenk flask was equipped with a magnetic stirring bar and charged with $[Cu(CH_3CN)_4]PF_6$ (5 mol%) and the specified chiral PP ligand (5 mol%). Inside a glovebox dry, deoxygenated THF (1 mL) was added. The mixture was stirred at room temperature for 15 minutes to give a yellow catalyst solution. Diphenylphosphine (0.1 mmol, 1 eq) and the α,β-unsaturated ester **18c** (0.1 mmol, 1.0 eq) were added sequentially. The Schlenk flask was removed from the glovebox and cooled in a cryostat at the specified temperature. Then, Barton's Base (8 µL, 0.04 mmol, 0.40 eq) was added and the resulting reaction mixture was stirred overnight. The mixture was allowed to warm up to RT and the solvent was removed under reduced pressure. The residue was purified by silica flash column chromatography [29].

Methyl (*R*)-3-(diphenylphosphaneyl)-2-phenylpropanoate (18c1')



The title compound **18c1'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA:MeOH 10:1:0.1 as eluent to give compound **18c1'** as a clear oil with 57% yield and 86% e.e.

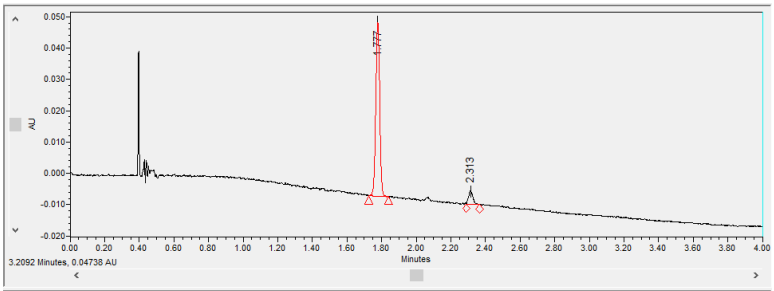
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.20 (m, 15H, ArH), 3.58 (s, 3H, CH_3), 3.63 – 3.51 (m, 1H, CH), 2.87 (dd, J = 13.6, 8.9 Hz, 1H, CH_2), 2.51 (dd, J = 13.7, 6.5 Hz, 1H, CH_2) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.5, 141.8, 135.6 (d, J = 7.4 Hz), 135.4 (d, J = 7.6 Hz), 131.4 (d, J = 3.9 Hz), 131.4, 131.1 (dd, J = 6.7, 1.8 Hz), 130.5, 130.2, 54.8, 51.2 (d, J = 19.2 Hz), 35.4 (d, J = 13.9 Hz) ppm.

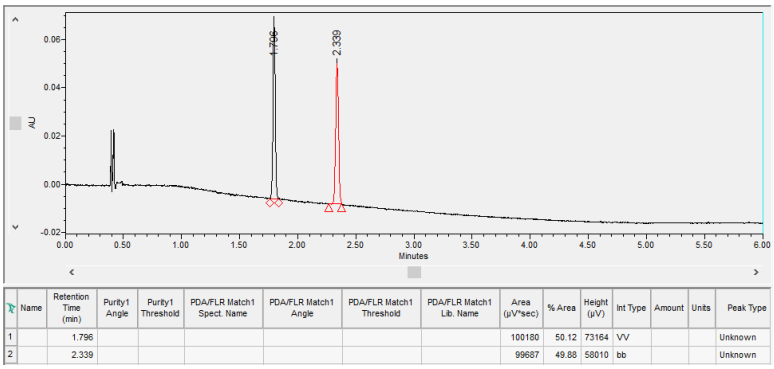
^{31}P NMR (162 MHz, $CDCl_3$) δ -22.5 ppm.

HRMS (ESI+, m/z) calc. for $C_{22}H_{21}O_2P$: $[M+H]^+$ = 349.1352, found $[M+H]^+$ = 349.1355

SFC (254 nm, Chiracel OJ-3) t_R = 1.8 min (major), t_R 2.3 min (minor)

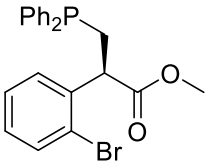


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		1.777							86943	92.16	55450	Bb			Unknown
2		2.313							7397	7.84	4240	VV			Unknown



	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		1.796							100180	50.12	73164	VV			Unknown
2		2.339							99687	49.88	58010	bb			Unknown

Methyl (*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)propanoate (18c2')



The title compound **18c2'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA:MeOH 10:1:0.1 as eluent to give compound **18c2'** as a clear oil with 82% yield and 70% e.e.

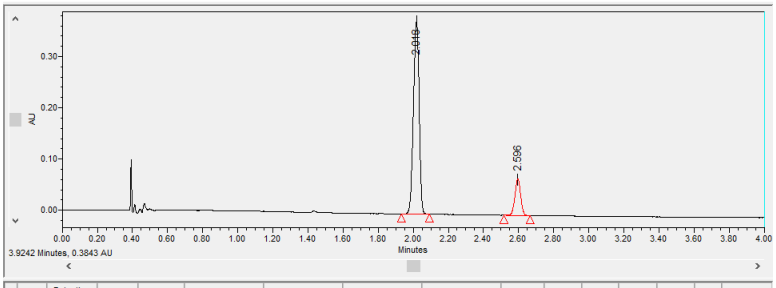
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.21 (m, 13H, ArH), 7.09 (ddd, J = 8.1, 7.3, 1.7 Hz, 1H, ArH), 4.19 (td, J = 8.6, 6.6 Hz, 1H, CH), 3.65 (s, 3H, CH_3), 2.86 (dd, J = 13.7, 8.7 Hz, 1H, CH_2), 2.51 (dd, J = 13.6, 6.5 Hz, 1H, CH_2) ppm.

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.4 (d, J = 5.7 Hz), 138.8 (d, J = 7.8 Hz), 137.8 (d, J = 12.8 Hz), 133.2, 133.1 – 132.7 (m), 129.1, 128.9 (d, J = 3.2 Hz), 128.8, 128.5 (dd, J = 7.0, 4.5 Hz), 127.8, 124.4, 52.4, 47.3 (d, J = 20.1 Hz), 32.5 (d, J = 14.7 Hz) ppm.

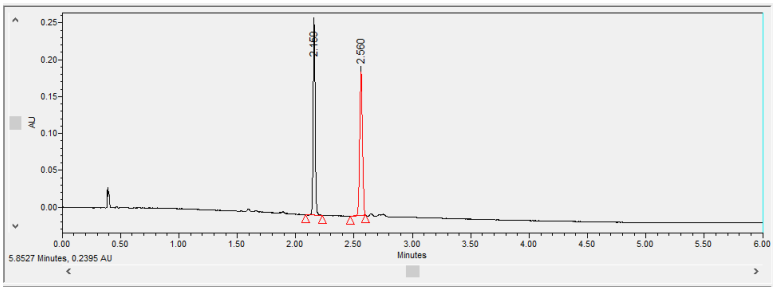
^{31}P NMR (162 MHz, $CDCl_3$) δ -19.4 ppm.

HRMS (ESI+, m/z) calc. for $C_{22}H_{20}BrO_2P$: $[M+H]^+$ = 427.0457, found $[M+H]^+$ = 427.0461

SFC (254 nm, Chiracel OJ-3) t_R = 2.0 min (major), t_R 2.6 min (minor)

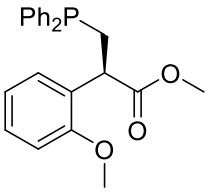


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		2.018							856069	84.15	375727	bb			Unknown
2		2.596							161303	15.85	71182	bb			Unknown



	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		2.159							316008	49.66	260418	bB			Unknown
2		2.560							320389	50.34	194672	bb			Unknown

Methyl (*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)propanoate (18c3')



The title compound **18c3'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA:MeOH 10:1:0.1 as eluent to give compound **18c3'** as a clear oil with 92% yield and 95% e.e.

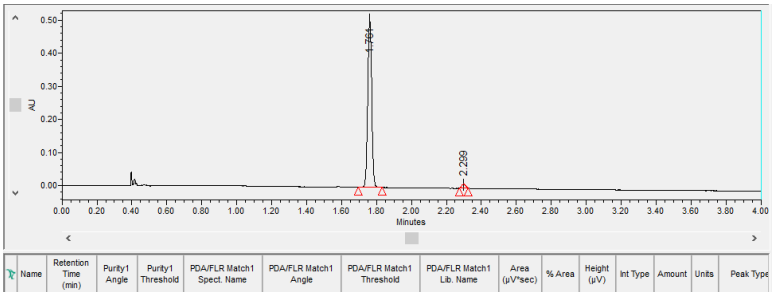
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.16 (m, 12H, ArH), 6.91 (td, J = 7.5, 1.1 Hz, 1H, ArH), 6.81 (dd, J = 8.6, 1.0 Hz, 1H, ArH), 4.05 (q, J = 8.0 Hz, 1H, CH), 3.71 (s, 3H, CH_3), 3.63 (s, 3H, CH_3), 2.84 (dd, J = 13.7, 8.0 Hz, 1H, CH_2), 2.54 (dd, J = 13.7, 7.2 Hz, 1H, CH_2) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4 (d, J = 6.7 Hz), 156.5, 138.4 (d, J = 13.2 Hz), 132.9 (d, J = 18.8 Hz), 128.6 (d, J = 3.1 Hz), 128.5 (d, J = 2.3 Hz), 128.4 (d, J = 6.8 Hz), 128.3 (d, J = 6.7 Hz), 128.0 (d, J = 7.4 Hz), 120.7, 110.7, 55.3, 52.1, 42.0 (d, J = 19.2 Hz), 31.6 (d, J = 13.1 Hz) ppm.

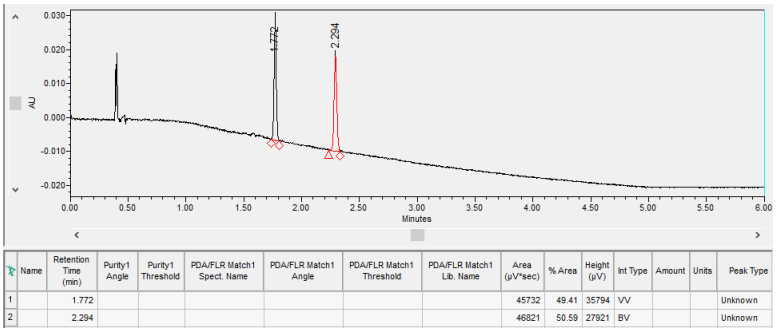
^{31}P NMR (162 MHz, $CDCl_3$) δ -19.3 ppm.

HRMS (ESI+, m/z) calc. for $C_{23}H_{24}O_3P$: $[M+H]^+$ = 379.1458, found $[M+H]^+$ = 379.1458

SFC (254 nm, Chiracel OJ-3) t_R = 1.8 min (major), t_R 2.3 min (minor)

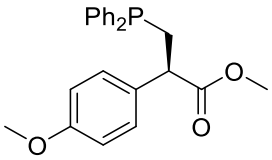


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		1.761							795772	97.83	507974	bb			Unknown
2		2.299							17653	2.17	11231	bb			Unknown



	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		1.772							45732	49.41	35794	VV			Unknown
2		2.294							46821	50.59	27921	BV			Unknown

Methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)propanoate (18c4')



The title compound **18c4'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA:MeOH 10:1:0.1 as eluent to give compound **18c4'** as a clear oil with 93% yield and 92% e.e.

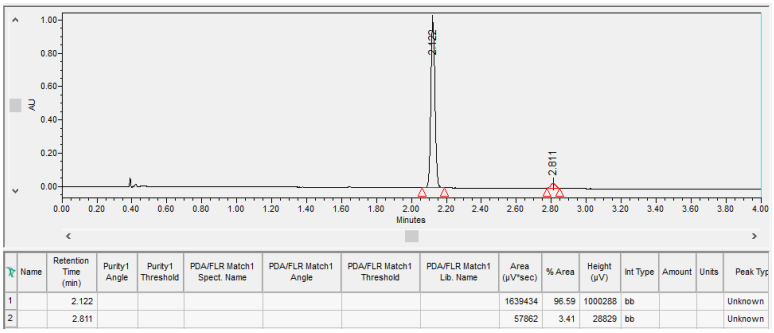
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.27 (m, 10H, ArH), 7.18 (d, J = 8.7 Hz, 2H, ArH), 6.83 (d, J = 8.6 Hz, 2H, ArH), 3.78 (s, 3H, CH_3), 3.60 (s, 3H, CH_3), 3.54 (q, J = 8.1 Hz, 1H, CH), 2.86 (dd, J = 13.6, 8.5 Hz, 1H, CH_2), 2.53 (dd, J = 13.6, 7.1 Hz, 1H, CH_2) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2 (d, J = 5.9 Hz), 159.0, 137.9 (dd, J = 19.4, 12.8 Hz), 132.9 (dd, J = 19.1, 17.8 Hz), 131.2 (d, J = 8.0 Hz), 128.9, 128.8 (d, J = 13.1 Hz), 128.5 (dd, J = 6.8, 5.4 Hz), 114.1, 55.2, 52.1, 47.7 (d, J = 19.1 Hz), 32.8 (d, J = 13.5 Hz) ppm.

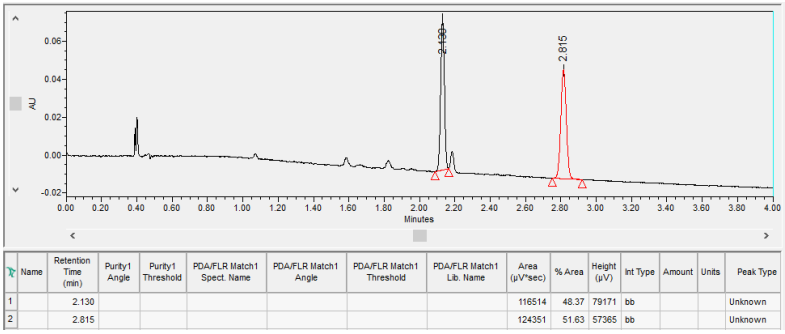
^{31}P NMR (162 MHz, $CDCl_3$) δ -19.9 ppm.

HRMS (ESI+, m/z) calc. for $C_{23}H_{24}O_3P$: $[M+H]^+$ = 379.1458, found $[M+H]^+$ = 379.1460

SFC (254 nm, Chiracel OJ-3) t_R = 1.8 min (major), t_R 2.3 min (minor)

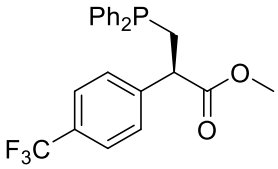


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Typ
1		2.122							1639434	96.59	1000288	bb			Unknown
2		2.811							57862	3.41	28829	bb			Unknown



	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		2.130							116514	48.37	79171	bb			Unknown
2		2.815							124351	51.63	57365	bb			Unknown

Methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-(trifluoromethyl)phenyl)propanoate (18c5')



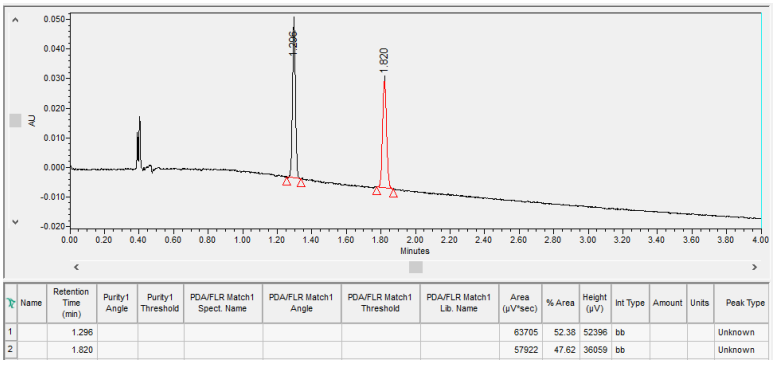
The title compound **18c5'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA 10:1 as eluent to give compound **18c4'** as a clear oil with 96% yield and 6% e.e.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.1 Hz, 2H, ArH), 7.45 – 7.27 (m, 12H, ArH), 3.66 (q, J = 8.0 Hz, 1H, CH), 3.61 (s, 3H, CH_3), 2.88 (ddd, J = 13.7, 8.1, 1.0 Hz, 1H, CH_2), 2.54 (ddd, J = 13.7, 7.3, 1.0 Hz, 1H, CH_2) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 132.9 (d, J = 1.5 Hz), 132.7 (d, J = 1.3 Hz), 128.9 (d, J = 2.4 Hz), 128.6, 128.6 (d, J = 1.2 Hz), 128.5, 128.4, 125.6 (d, J = 3.8 Hz), 52.4, 48.5 (d, J = 19.7 Hz), 32.6 (d, J = 14.3 Hz) ppm.

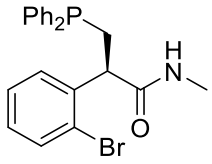
^{31}P NMR (162 MHz, $CDCl_3$) δ -19.8 ppm.

SFC (254 nm, Chiracel OJ-3) t_R = 1.3 min (major), t_R 1.8 min (minor)



	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		1.296							63705	52.38	52396	bb			Unknown
2		1.820							57922	47.62	36059	bb			Unknown

(*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)-N-methylpropanamide (18e1')



The title compound **18e1'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA:MeOH 10:1:0.1 to 10:10:0.1 as eluent to give compound **18e1'** as a yellow oil with 52% yield and 96% e.e.

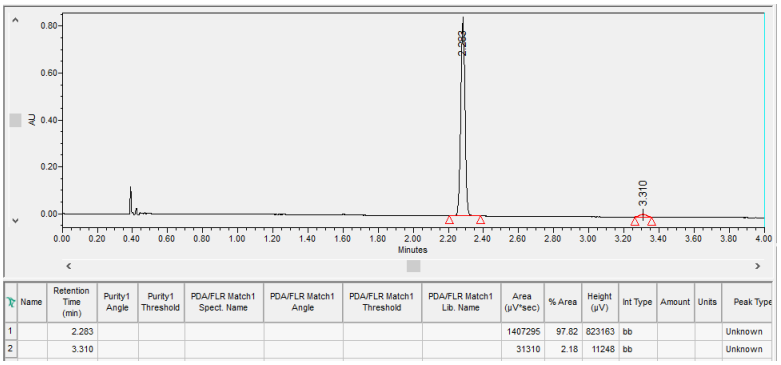
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (ddd, J = 21.2, 7.9, 1.4 Hz, 2H, ArH), 7.48 – 7.38 (m, 4H, ArH), 7.35 – 7.23 (m, 7H, ArH), 7.13 – 7.05 (m, 1H, ArH), 5.47 (d, J = 5.9 Hz, 1H, NH), 3.92 (q, J = 7.9 Hz, 1H, CH), 2.99 (dd, J = 13.7, 8.1 Hz, 1H, CH_2), 2.72 (d, J = 4.9 Hz, 3H, CH_3), 2.53 (dd, J = 13.6, 6.9 Hz, 1H, CH_2) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3 (d, J = 5.5 Hz), 139.3 (d, J = 7.6 Hz), 138.0 (d, J = 20.9 Hz), 133.0 (d, J = 7.0 Hz), 132.8 (d, J = 7.0 Hz), 129.4, 128.9, 128.7 (d, J = 5.5 Hz), 128.4 (d, J = 6.7 Hz), 128.1, 124.3, 48.0 (d, J = 19.6 Hz), 32.0 (d, J = 13.4 Hz), 26.6 ppm.

^{31}P NMR (162 MHz, $CDCl_3$) δ -19.6 ppm.

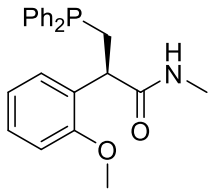
HRMS (ESI+, m/z) calc. for $C_{22}H_{22}BrNOP$: $[M+H]^+$ = 426.0617, found $[M+H]^+$ = 426.0610

SFC (254 nm, Chiracel OJ-3) t_R = 2.3 min (major), t_R 3.3 min (minor)



	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		2.283							1407295	97.82	823163	bb			Unknown
2		3.310							31310	2.18	11248	bb			Unknown

(*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)-N-methylpropanamide (18e2')



The title compound **18e2'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA:MeOH 10:1:0.1 to 10:10:0.1 as eluent to give compound **18e2'** as a yellow oil with 90% yield and 92% e.e.

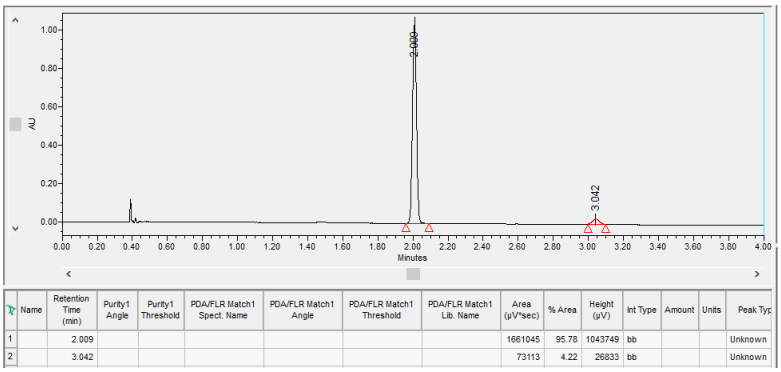
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.14 (m, 12H, ArH), 6.93 (t, J = 7.5 Hz, 1H, ArH), 6.82 (d, J = 8.2 Hz, 1H, ArH), 5.55 (s, 1H, NH), 3.84 (q, J = 8.1 Hz, 1H, CH), 3.72 (d, J = 0.9 Hz, 3H, CH_3), 2.98 (dd, J = 13.7, 7.4 Hz, 1H, CH_2), 2.69 (d, J = 4.8 Hz, 3H, CH_3), 2.56 (dd, J = 13.7, 8.0 Hz, 1H, CH_2) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (d, J = 6.8 Hz), 156.4, 138.6 (d, J = 12.6 Hz), 133.0 (d, J = 12.9 Hz), 132.8 (d, J = 12.9 Hz), 128.8, 128.5, 128.4 (d, J = 2.1 Hz), 128.3 – 128.1 (m), 121.2, 110.7, 55.4, 42.1 (d, J = 19.1 Hz), 30.4 (d, J = 11.8 Hz), 26.5 ppm.

^{31}P NMR (162 MHz, $CDCl_3$) δ -19.1 ppm.

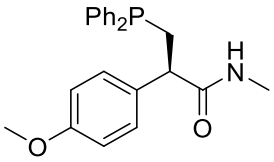
HRMS (ESI+, m/z) calc. for $C_{23}H_{25}NO_2P$: $[M+H]^+$ = 378.1617, found $[M+H]^+$ = 378.1608

SFC (254 nm, Chiracel OJ-3) t_R = 2.0 min (major), t_R 3.0 min (minor)



	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		2.009							1661045	95.78	1043749	bb			Unknown
2		3.042							73113	4.22	26833	bb			Unknown

(*R*)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)-N-methylpropanamide (18e3')



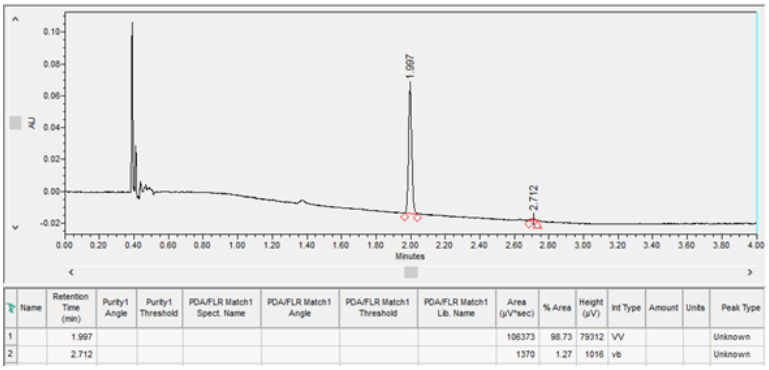
The title compound **18e3'** was prepared in line with general procedure **C**. Purification by silica flash column chromatography with pentane:EA:MeOH 10:1:0.1 to 10:10:0.1 as eluent to give compound **18e3'** as a yellow oil with 30% yield and 96% e.e.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.27 (m, 10H, ArH), 7.14 (d, J = 8.6 Hz, 2H, ArH), 6.83 (d, J = 8.4 Hz, 2H, ArH), 5.29 (s, 1H, NH), 3.78 (s, 3H, CH_3), 3.24 (q, J = 8.2 Hz, 1H, CH), 3.11 – 2.97 (m, 1H, CH_2), 2.70 (d, J = 4.9 Hz, 3H, CH_3), 2.53 – 2.42 (m, 1H, CH_2) ppm.

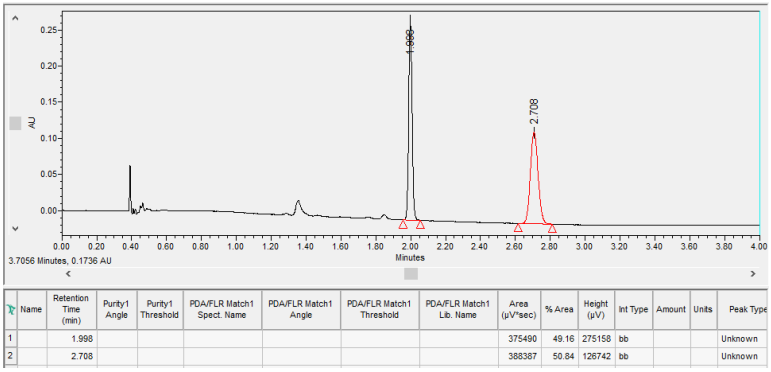
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.78, 158.9, 133.2, 133.0, 132.7 (d, J = 18.9 Hz), 129.2, 128.8, 128.5, 114.3, 55.3, 49.3 (d, J = 17.4 Hz), 32.3, 26.6 ppm.

^{31}P NMR (162 MHz, $CDCl_3$) δ -20.0 ppm.

SFC (254 nm, Chiracel OJ-3) t_R = 2.0 min (major), t_R 2.7 min (minor)

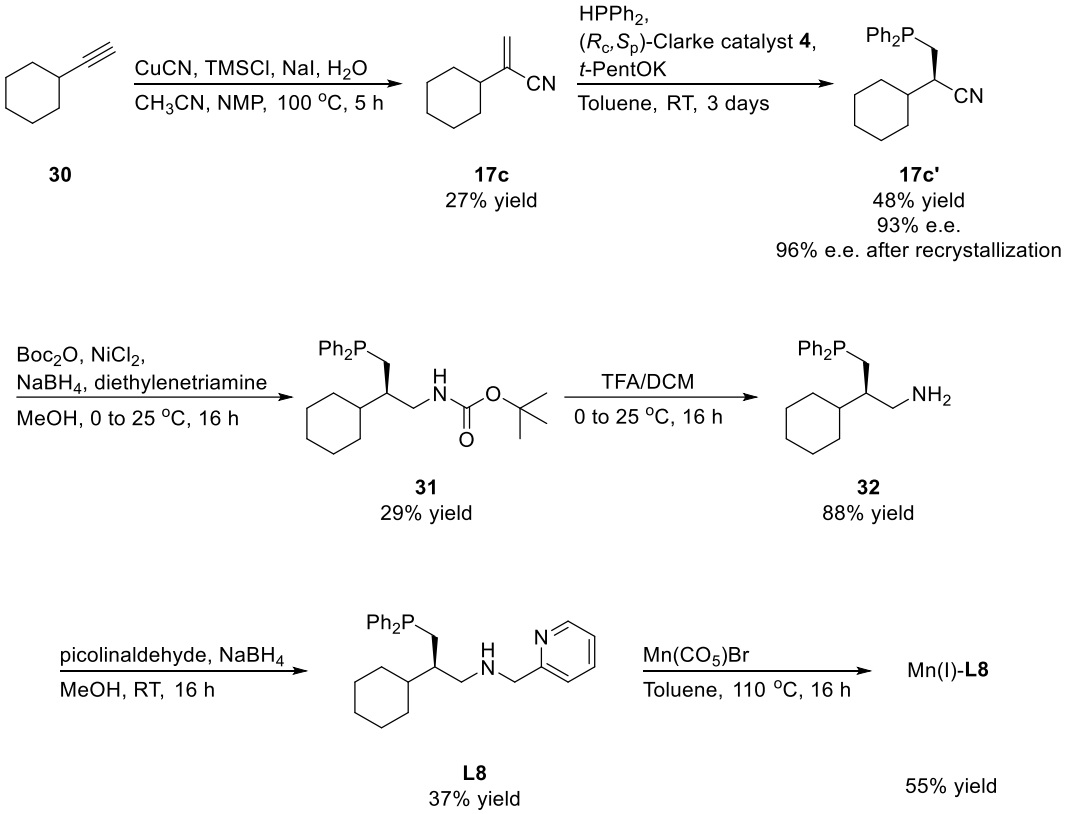


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		1.997							106373	98.73	79312	VV			Unknown
2		2.712							1370	1.27	1016	vb			Unknown

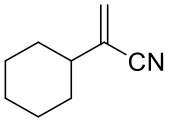


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA/FLR Match1 Spect. Name	PDA/FLR Match1 Angle	PDA/FLR Match1 Threshold	PDA/FLR Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		1.998							375490	49.16	275158	bb			Unknown
2		2.708							388387	50.84	126742	bb			Unknown

III. Synthesis of Mn(I)-L8



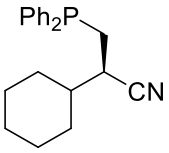
2-Cyclohexylacrylonitrile (17c)



Compound **17c** was prepared following a procedure reported in literature [50]. CH_3CN (5 ml), TMSCl (0.635 mL, 5 mmol), H_2O (45 µL, 2.5 mmol) and cyclohexylacetylene **30** (0.541 g, 5 mmol) were sequentially added to an oven-dried dry Schlenk flask containing NaI (0.749 g, 5 mmol) under a nitrogen atmosphere at room temperature. After 0.5 h dry CuCN (1.791 g, 20 mmol) and dry N-methyl-2-pyrrolidinon (NMP, 15 mL) were added to the reaction mixture at room temperature. The reaction mixture was then heated under a nitrogen atmosphere at 100 °C for 5 hours. After being cooled to RT, the mixture was stirred while first ether was added and then a large amount of water to quench the reaction. The mixture was vacuum filtered and the organic layer was washed with brine (3x), dried over $MgSO_4$ and concentrated *in vacuo.* The residual was purified by silica flash column chromatography with pentane:EA 100:0 to 20:1 to give 184 mg of a colorless liquid (27% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (s, 1H, $=CH_2$), 5.68 (dd, J = 1.3, 0.6 Hz, 1H, $=CH_2$), 2.20 – 2.09 (m, 1H, CH), 1.89 – 1.77 (m, 4H, 2x CH_2), 1.70 (dtt, J = 12.5, 3.2, 1.5 Hz, 2H, CH_2), 1.38 – 1.10 (m, 5H, 2x CH_2 and CH) ppm.

(*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)propanenitrile (17*c*')

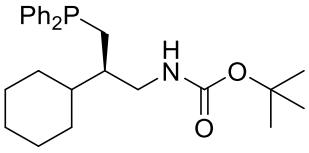


Compound **17c'** was prepared following general procedure **C**, using *t*-PentOK as a base and 3 days reaction time. Purification by silica flash column chromatography eluting with pentane:EA 25:1 to give 290 mg of a clear liquid, which crystallized overnight. The compound was recrystallized by first adding 0.5 mL ether and then 5 mL pentane to increase the optic purity from 93% e.e. to 96%, resulting in 193 mg of clouded crystals (48% yield). NMR data in accordance with literature precedents [34].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.32 (m, 10H, ArH), 2.43 – 2.27 (m, 3H, CH and CH_2P), 1.90 – 1.59 (m, 6H, 3x CH_2), 1.27 – 1.11 (m, 5H, 2x CH_2 and CH) ppm.

^{31}P NMR (162 MHz, $CDCl_3$) δ -20.4 ppm.

***Tert*-butyl (*R*)-(2-cyclohexyl-3-(diphenylphosphaneyl)propyl)carbamate (31)**

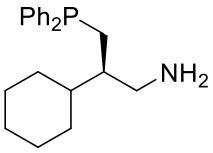


Compound **31** was prepared following a procedure reported in literature [51]. To a solution of nitrile **17c'** (190 mg, 0.591 mmol, 1.0 eq) in dry methanol (5.9 mL), at 0 °C, Boc_2O (2.0 eq) and $NiCl_2$ (1.0 eq) were added. After that, $NaBH_4$ (7.0 eq) was added in small portions. The resulting reaction mixture was allowed to warm to room temperature and stirred for an additional 16 h. Diethylenetriamine (1.6 eq) was added and the mixture was stirred for 30 min before concentrating it. The residue was dissolved in EtOAc (5 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (3 x 5 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica flash column chromatography eluting with pentane:EA 10:1 to give 73 mg of a clear sticky oil (29% yield). NMR data in accordance with literature precedents [34].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.37 (m, 5H, ArH), 7.36 – 7.26 (m, 5H, ArH), 4.50 (s, 1H, NH), 3.34 – 3.23 (m, 1H, CH_2N), 3.15 (dt, J = 13.4, 6.5 Hz, 1H, CH_2N), 2.16 (dd, J = 13.9, 5.7 Hz, 1H, CH_2P), 1.90 (dd, J = 13.8, 8.0 Hz, 1H, CH_2P), 1.75 – 1.57 (m, 4H, 2x CH_2), 1.51 – 1.47 (m, 2H, 2x CH), 1.42 (s, 9H, 3x CH_3), 1.22 – 0.92 (m, 6H, 3x CH_2) ppm.

^{31}P NMR (162 MHz, $CDCl_3$) δ -19.4 ppm.

(*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)propan-1-amine (32)



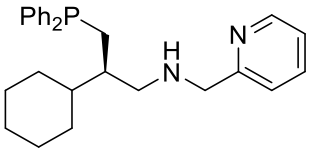
Compound **32** was prepared following a procedure reported in literature [52]. In a sealed Schlenk flask Boc-protected amine **31** (73 mg, 0.59 mmol, 1.0 eq) was kept under nitrogen and dissolved in 12 mL deoxygenated DCM/TFA (2:1). After stirring at room temperature for 2 h, a deoxygenated aqueous saturated $NaHCO_3$ solution (30 mL) was added to the reaction mixture. The aqueous phase was extracted with DCM. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford the product **32** as a clear oil (49 mg, 88% yield). NMR data in accordance with literature precedents [34].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 5H, ArH), 7.30 – 7.21 (m, 5H, ArH), 2.82 – 2.70 (m, 2H, CH_2N), 2.13 (ddd, J = 13.7, 5.0, 2.4 Hz, 1H, CH_2P), 1.87 (ddd, J = 13.8, 8.9, 2.1 Hz, 1H, CH_2P), 1.72 – 1.34 (m, 6H, 2x CH_2 and 2x CH), 1.28 – 0.87 (m, 6H, 3x CH_2) ppm.

^{31}P NMR (243 MHz, $CDCl_3$) δ -19.3 ppm.

HRMS (ESI+, m/z) calc. for $C_{21}H_{29}NPO$ (oxidized product): $[M+H]^+$ = 342.1981, found $[M+H]^+$ = 342.1987.

(*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)-N-(pyridin-2-ylmethyl)propan-1-amine (L8)



L8 was prepared following a procedure reported in literature [15]. A mixture of dry, deoxygenated MeOH (1 mL), amine **30** (48 mg, 0.147 mmol, 1.0 eq) and picolinaldehyde (0.162 mmol, 1.1 eq) was stirred at room temperature for 3 h. $NaBH_4$ (0.295 mmol, 2.0 eq) was added to the mixture and the reaction mixture was stirred at 40 °C for 1.5 h. The mixture was then allowed to cool down to RT overnight and concentrated under reduced pressure. The crude product was dissolved in DCM (5 mL) and washed with saturated aqueous $NaHCO_3$ solution (3 x 5 mL). The combined aqueous layers were extracted with DCM (5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The product was purified by silica flash column chromatography, where the silica is treated with NEt_3 and using pentane:EA 5:1 to 0:1 as eluent, yielding 23 mg of **L8** as a colorless oil (37% yield). NMR data in accordance with literature precedents [34].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 4.7 Hz, 1H, ArH), 7.60 (td, J = 7.7, 1.8 Hz, 1H, ArH), 7.48 – 7.20 (m, 11H, ArH), 7.13 (dd, J = 7.5, 5.0 Hz, 1H, ArH), 3.79 (s, 2H, CH_2N), 2.70 (dd, J = 6.2, 3.5 Hz, 2H, CH_2N), 2.17 – 2.09 (m, 1H, CH_2P), 2.00 (dd, J = 13.8, 8.3 Hz, 1H, CH_2P), 1.73 – 1.52 (m, 5H, 2x CH_2 and CH), 1.44 (d, J = 12.9 Hz, 2H, CH_2), 1.30 – 0.88 (m, 5H, 2x CH_2 and CH) ppm.

^{31}P NMR (162 MHz, $CDCl_3$) δ -19.1 ppm.

Mn(I)-**L8** was prepared following a known procedure [15]. **L8** (0.17 mmol, 1.2 eq) and $Mn(CO)_5Br$ (0.15 mmol, 1.0 eq) were combined in an oven-dried round bottom flask. Then, dry deoxygenated toluene (2 mL) was added and the mixture was heated to 110 °C for 16 h. The mixture was allowed to cool down to RT before it was concentrated *in vacuo*. The residual was dissolved in a small amount of DCM and then crashed out by addition of pentane. The solvent was removed and the residual was washed 2x with pentane to yield 16 mg of Mn(I)-**L8** as a yellow solid (55% yield). The metal complex shows multiple configuration in the ^{31}P NMR spectrum, though it is in accordance to literature precedents [34].

^{31}P NMR (243 MHz, $CDCl_3$) δ 69.0 ppm.

Appendix B – NMR spectral data

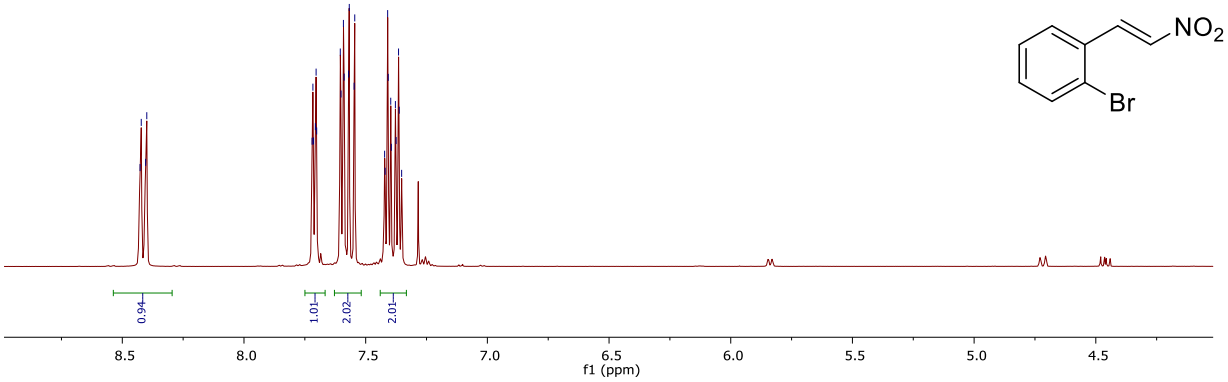


*Figure 4. ^{1}H NMR nitro product **18b** (R=Br)*

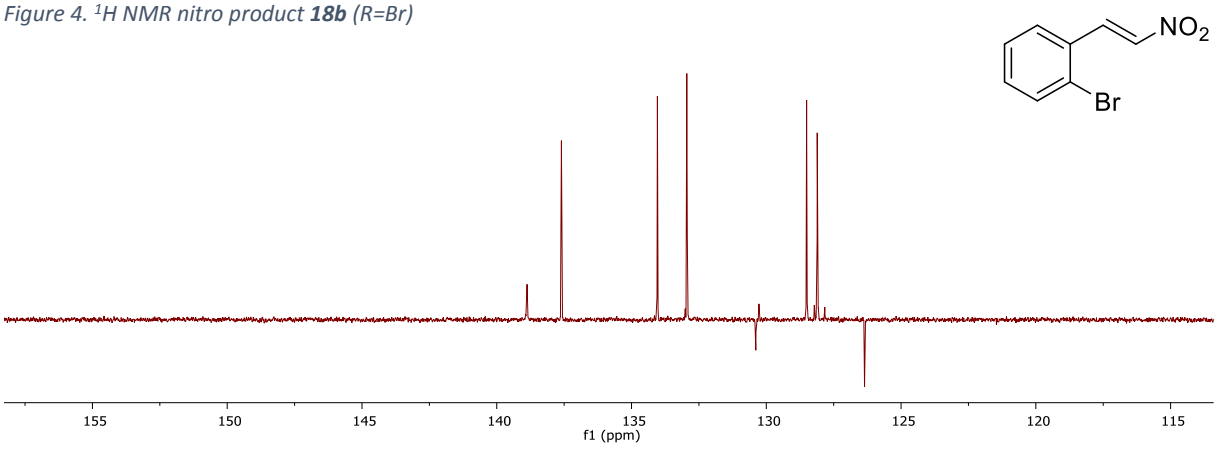


*Figure 5. APT NMR nitro product **18b** (R=Br)*

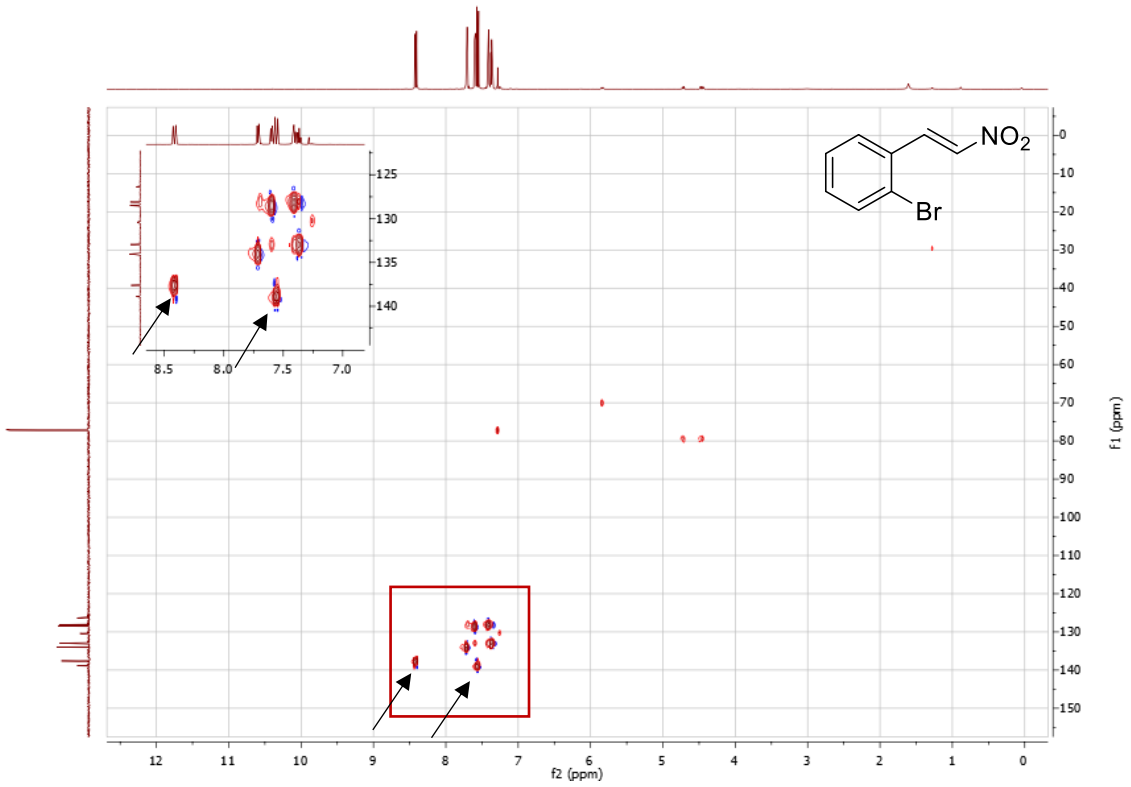
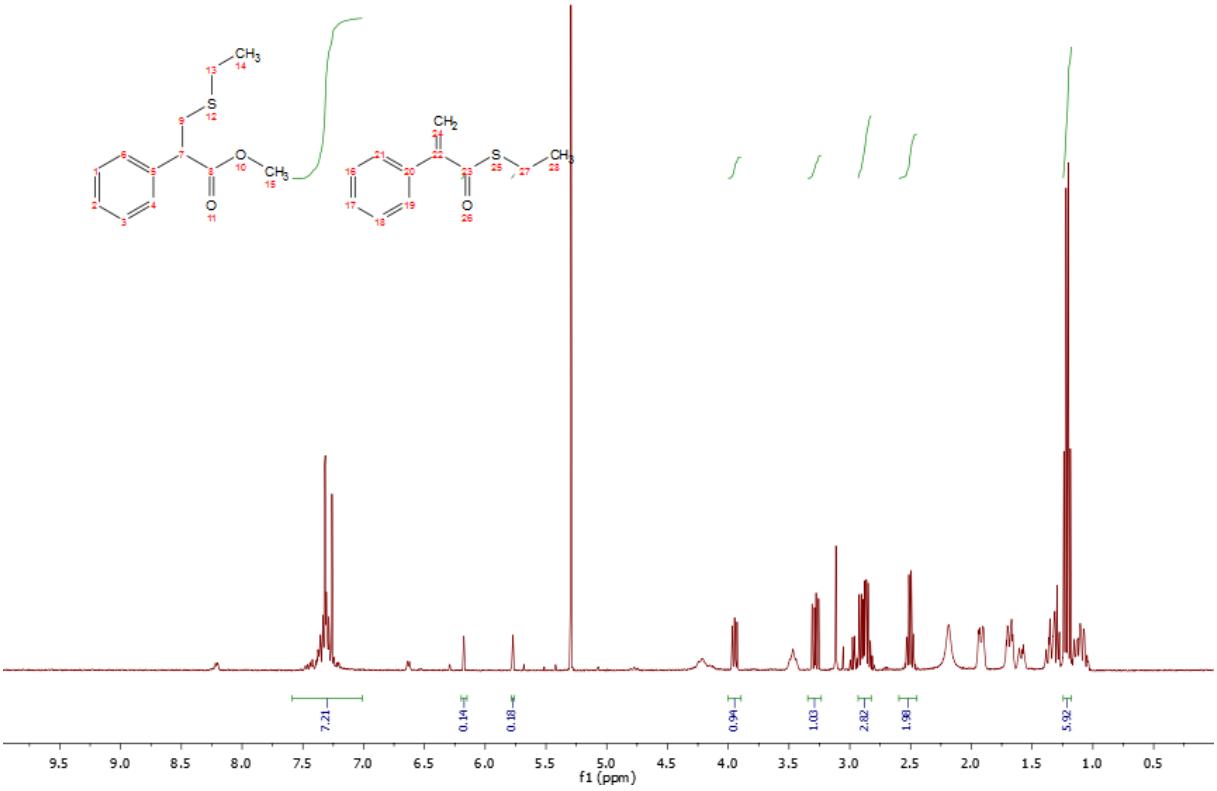
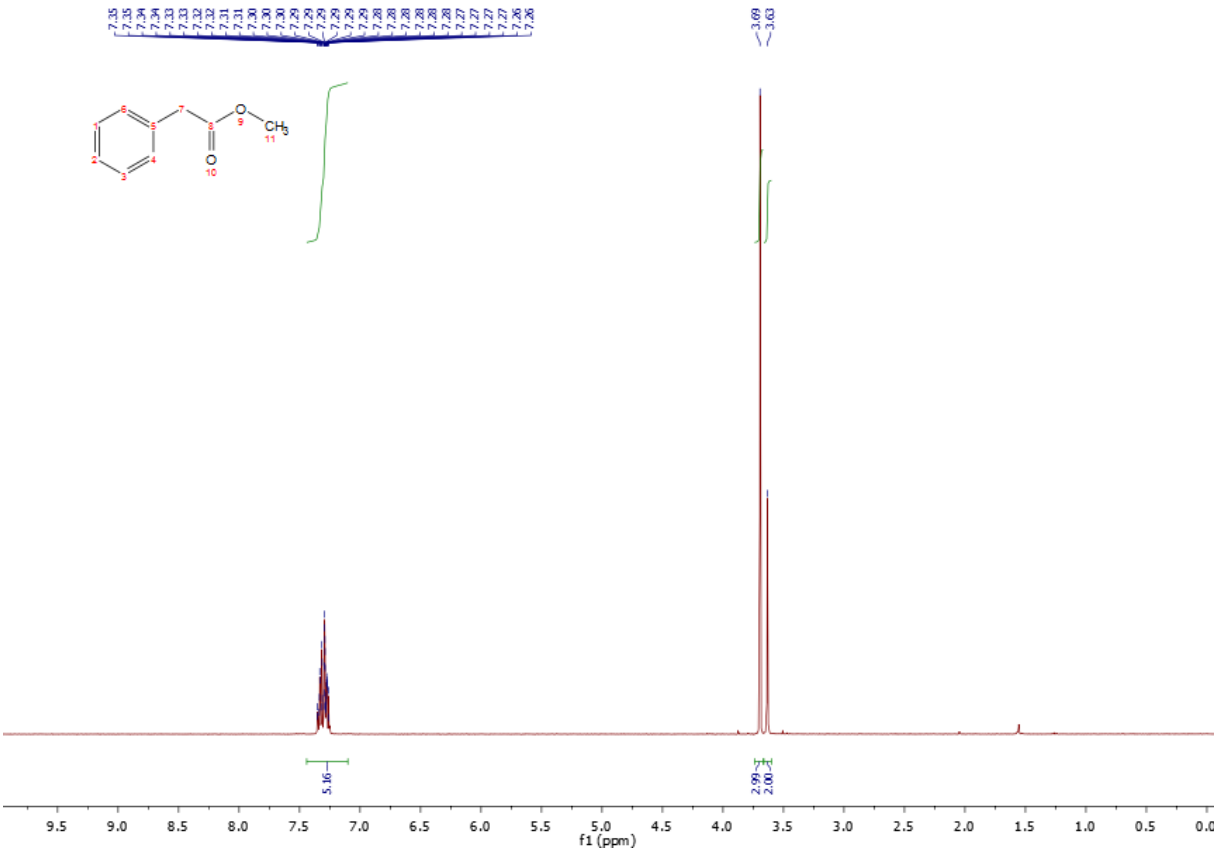


*Figure 6. HSQC-spectrum nitro product **18b** (R=Br), indicating the protons of the double bond by the arrows*

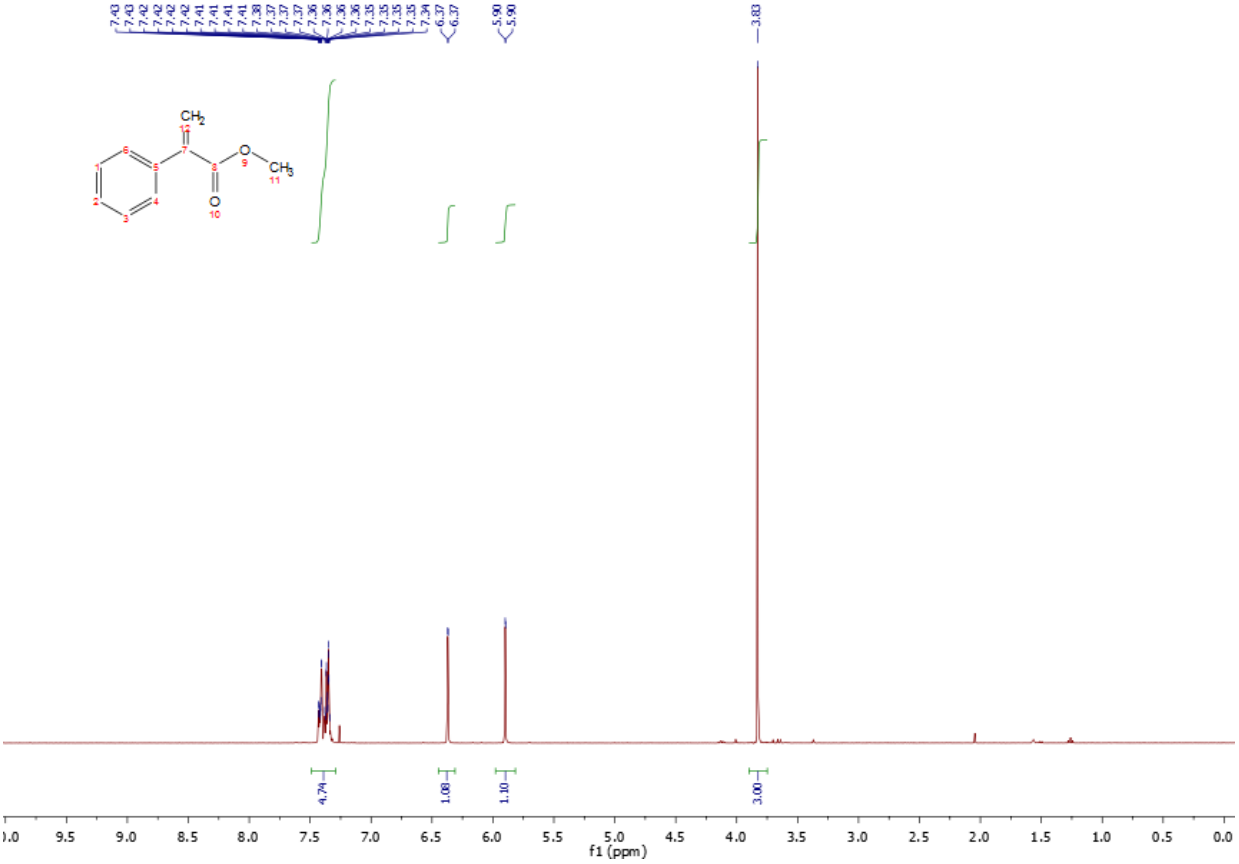
^{1}H NMR for crude mixture of S-ethyl 2-phenylprop-2-enethioate (**18d**) and 1,4-addition product methyl 3-(ethylthio)-2-phenylpropanoate



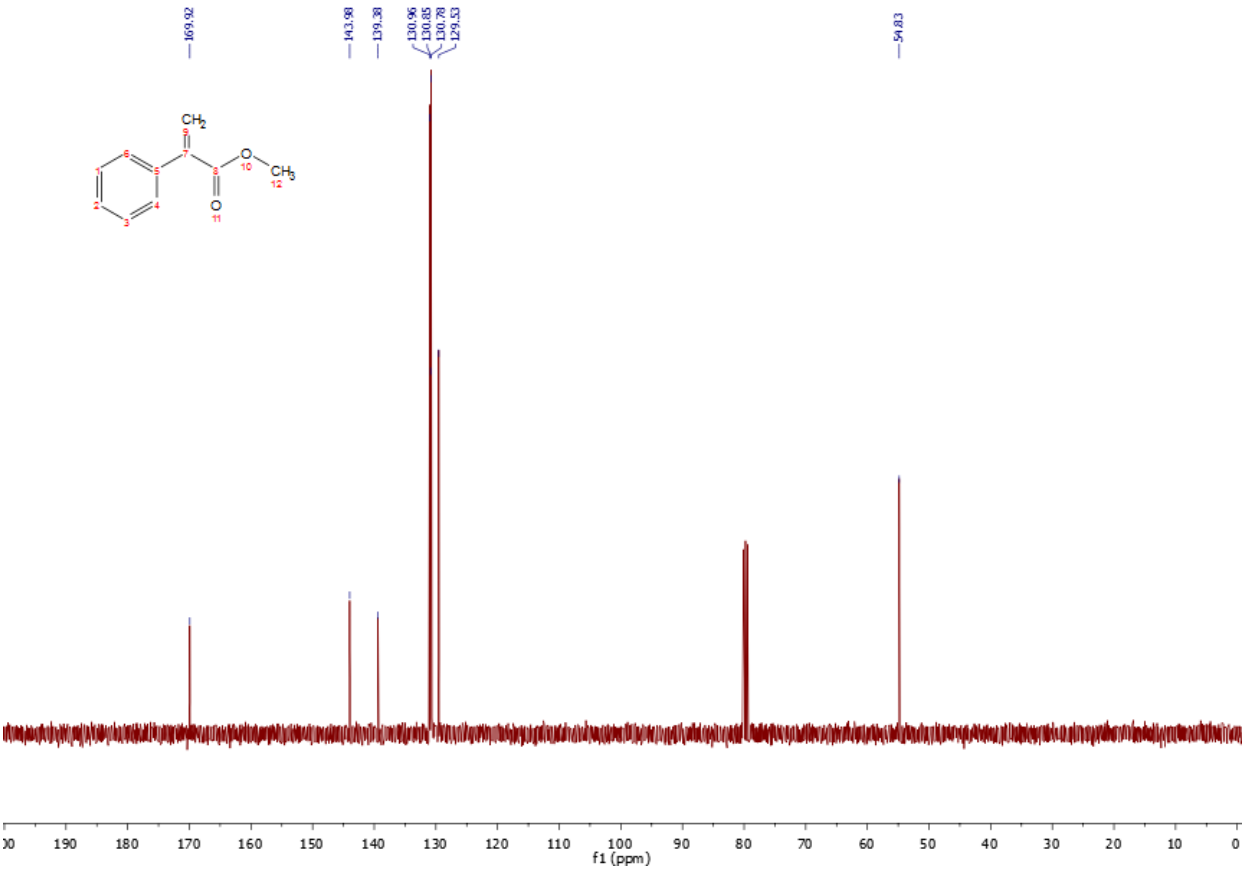
^{1}H NMR for methyl 2-phenylacetate (**23a**)



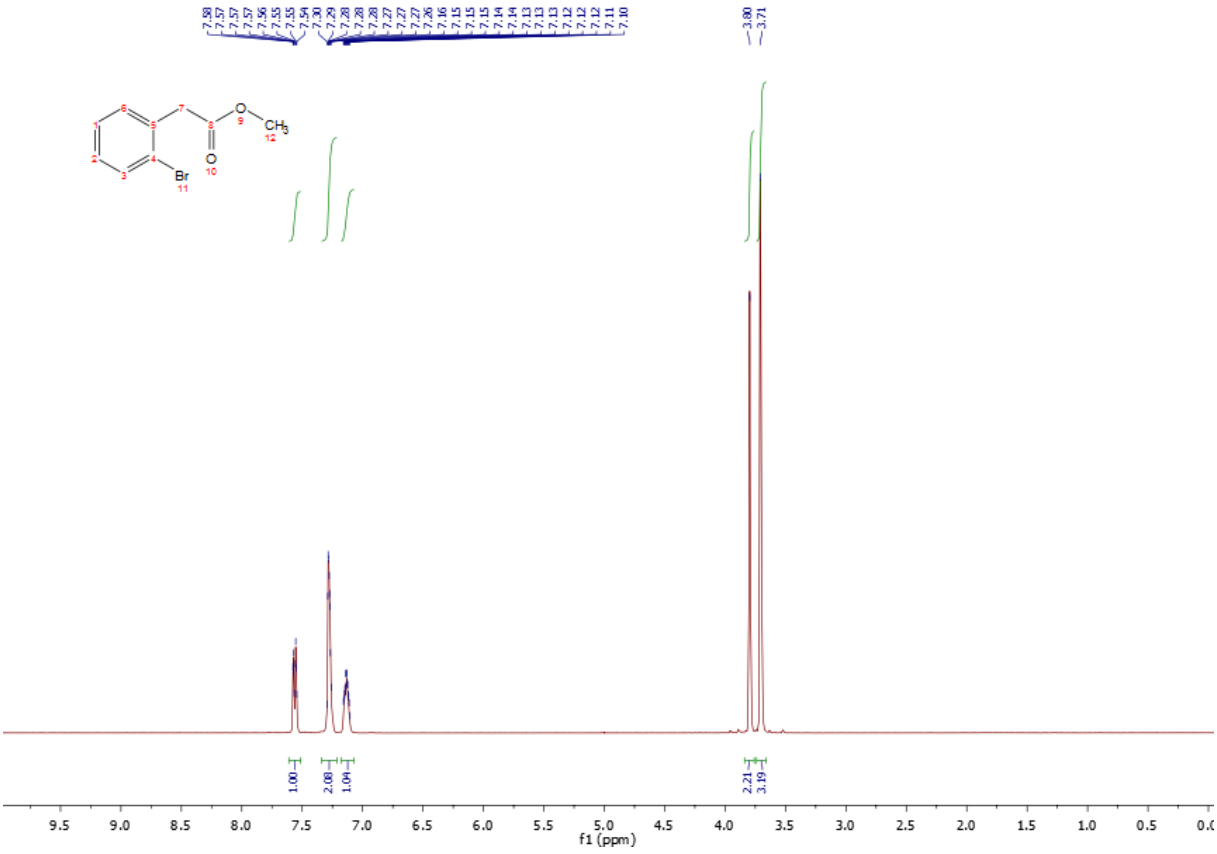
^{1}H NMR for methyl 2-phenylacrylate (**18c1**)



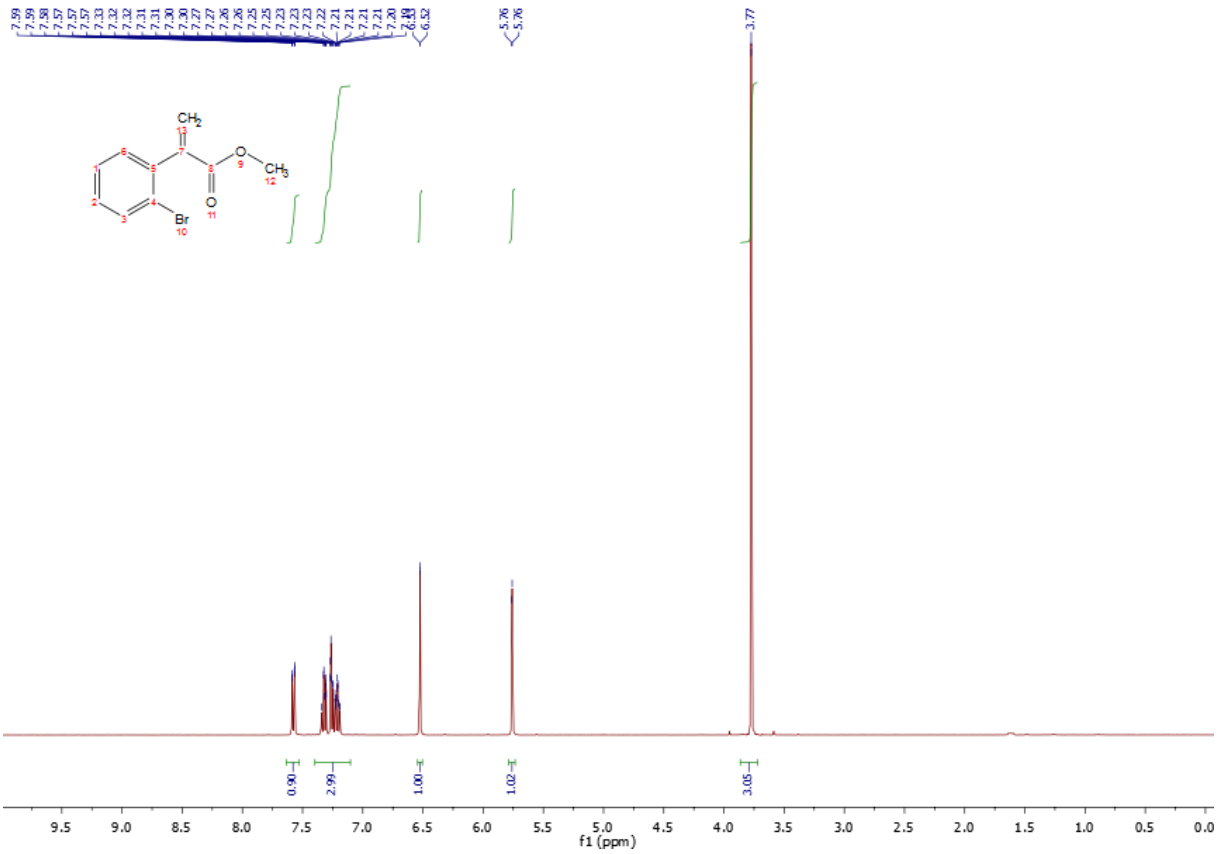
^{13}C NMR for methyl 2-phenylacrylate (**18c1**)



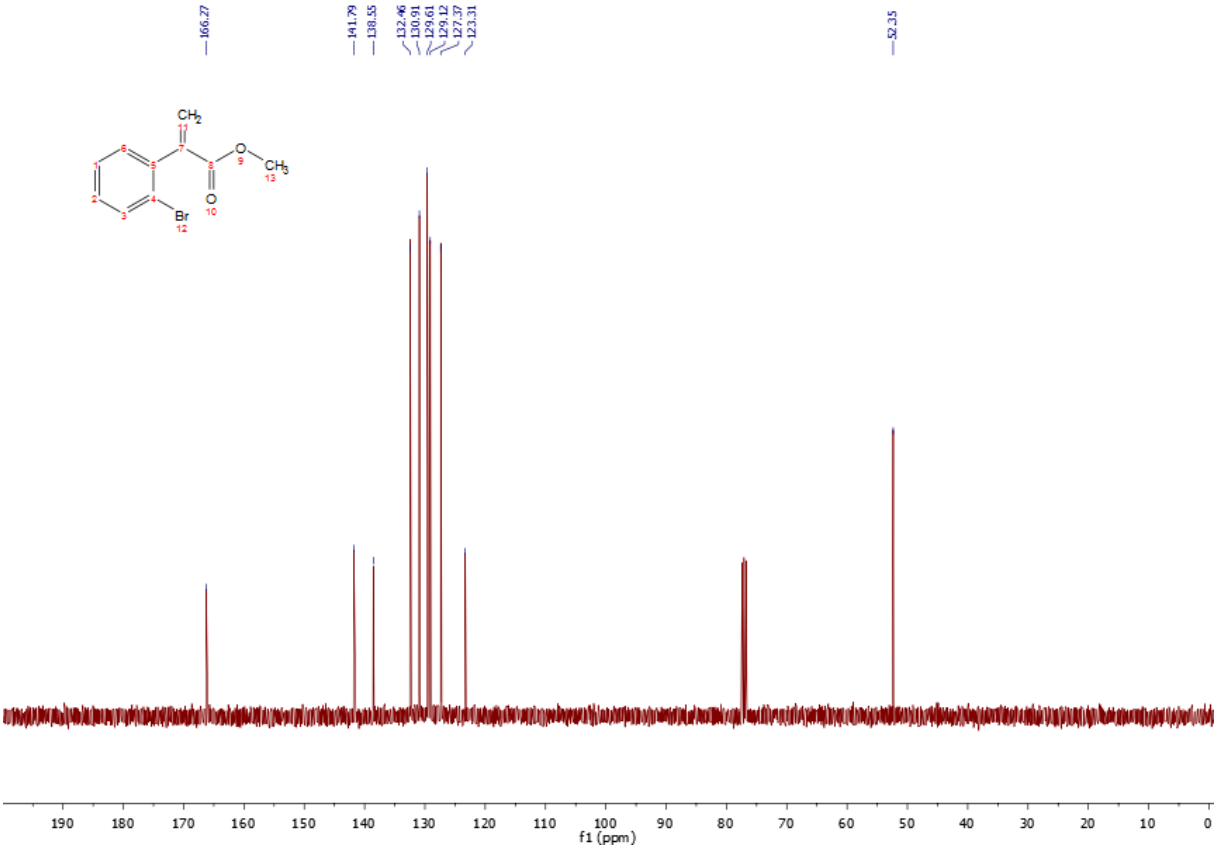
^{1}H NMR for methyl 2-(2-bromophenyl)acetate (**23b**)



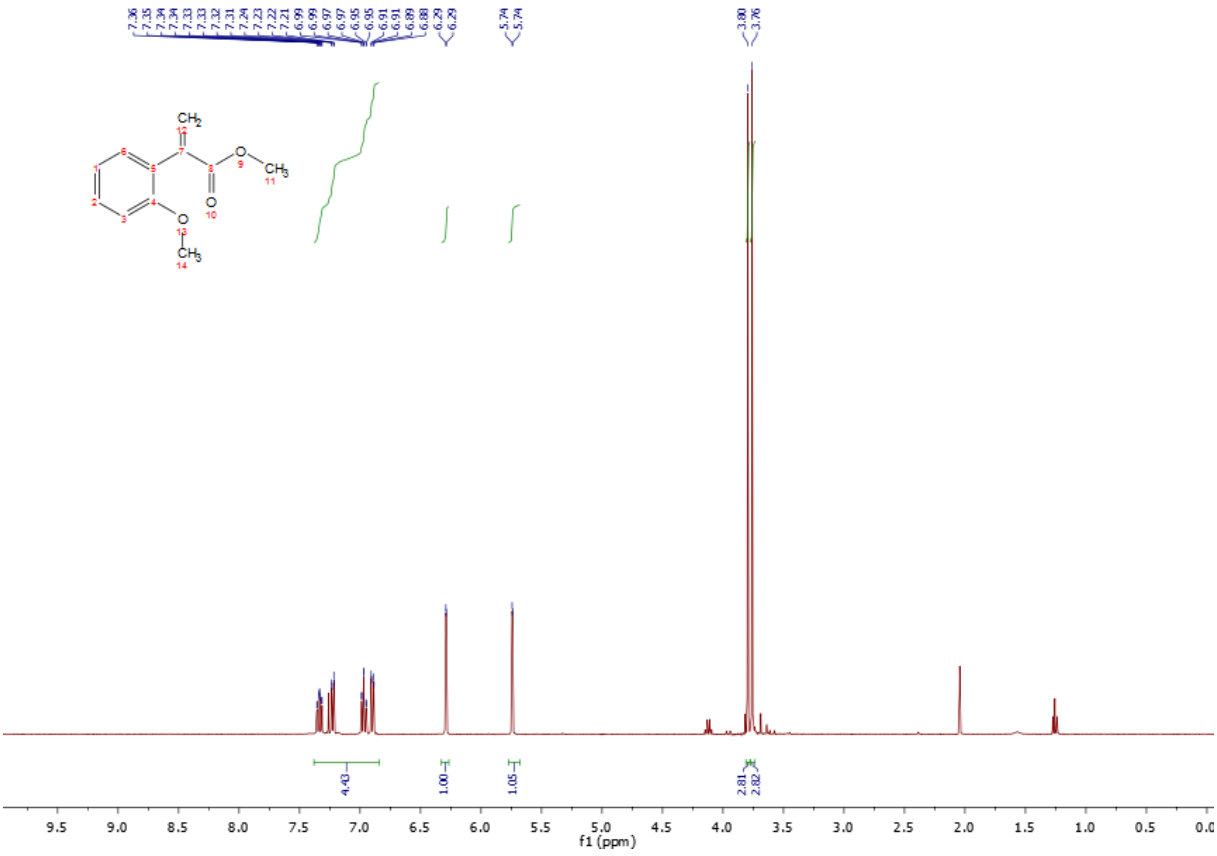
^{1}H NMR for methyl 2-(2-bromophenyl)acrylate (**18c2**)



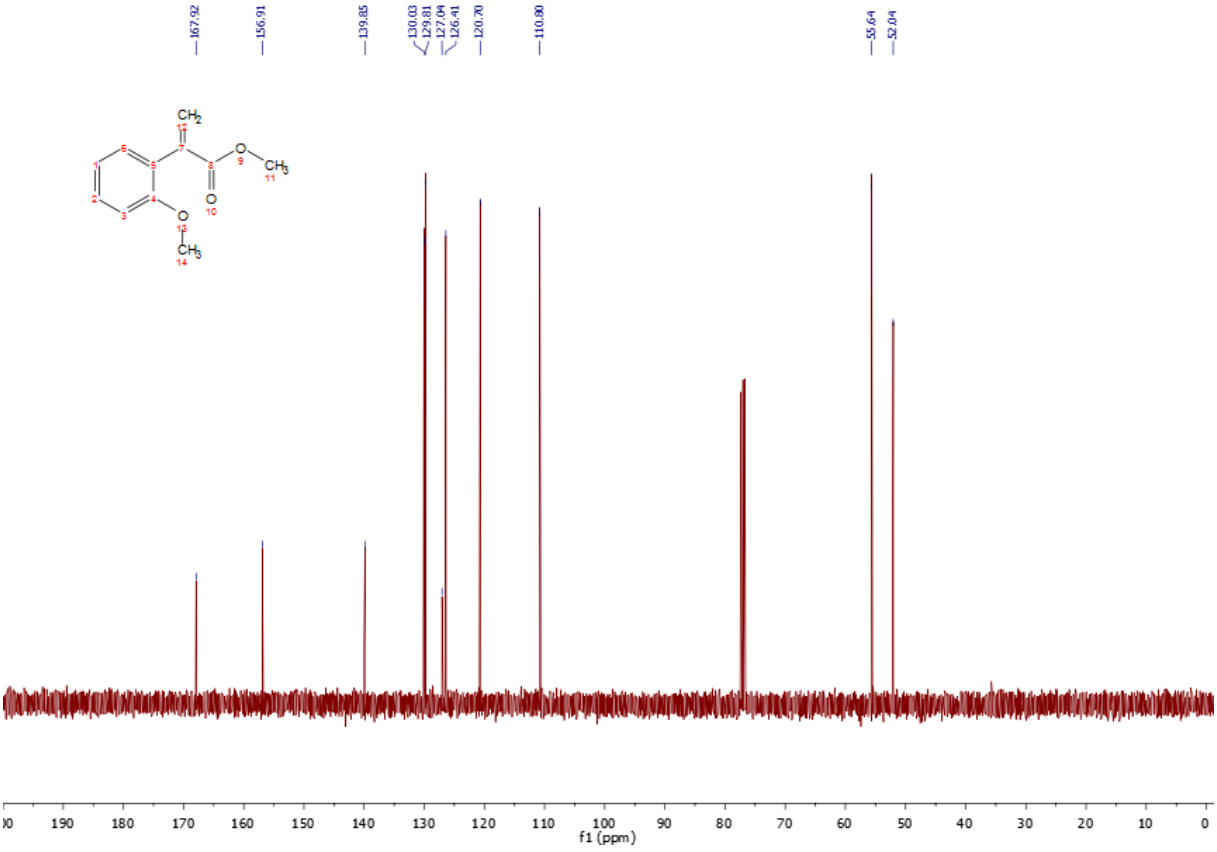
^{13}C NMR for methyl 2-(2-bromophenyl)acrylate (**18c2**)



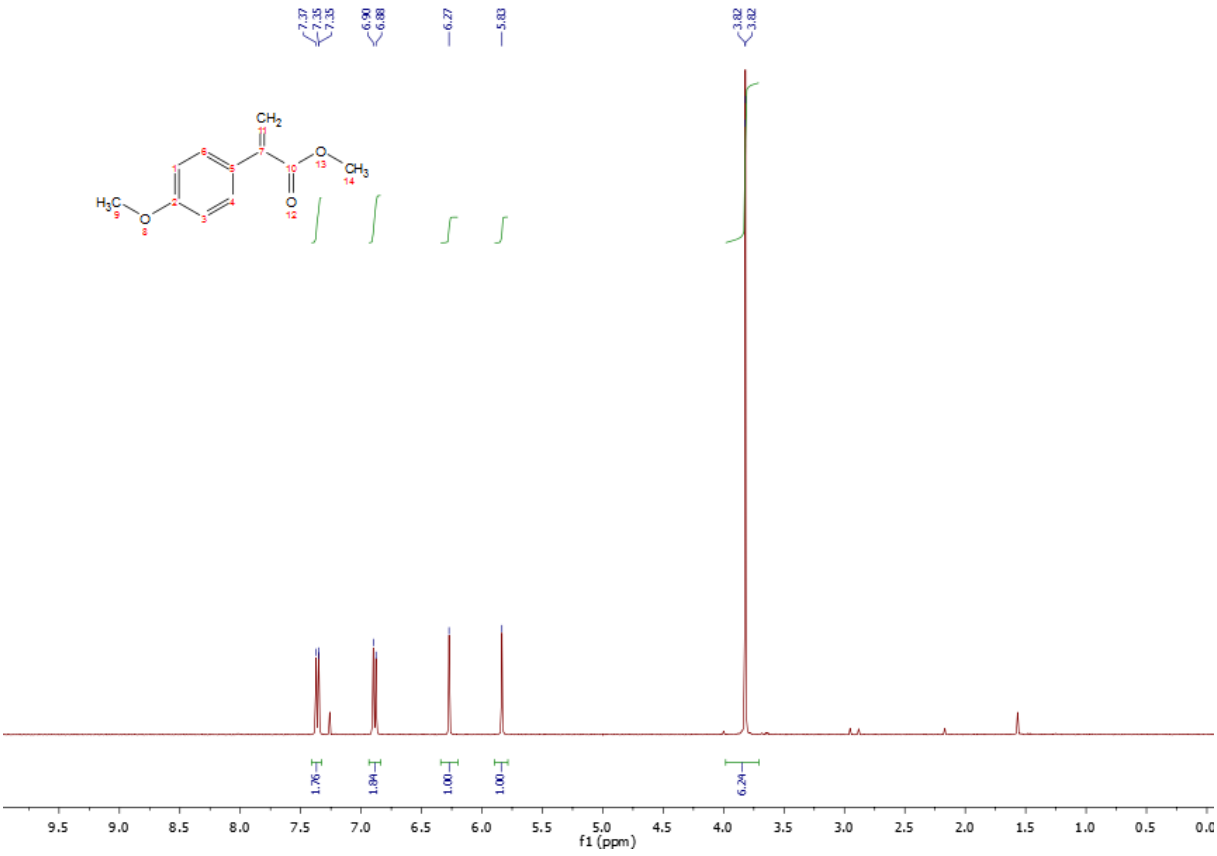
^{1}H NMR for methyl 2-(2-methoxyphenyl)acrylate (**18c3)**



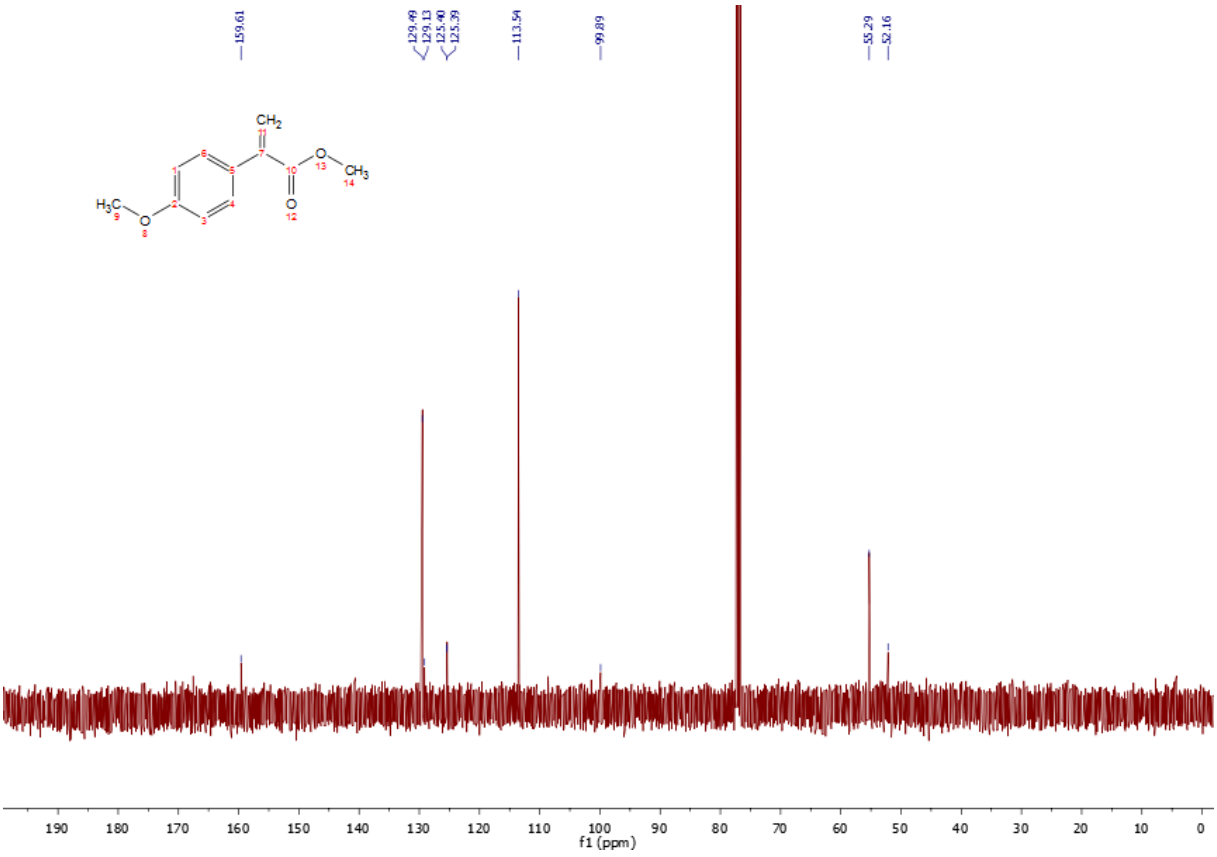
^{13}C NMR for methyl 2-(2-methoxyphenyl)acrylate (**18c3)**



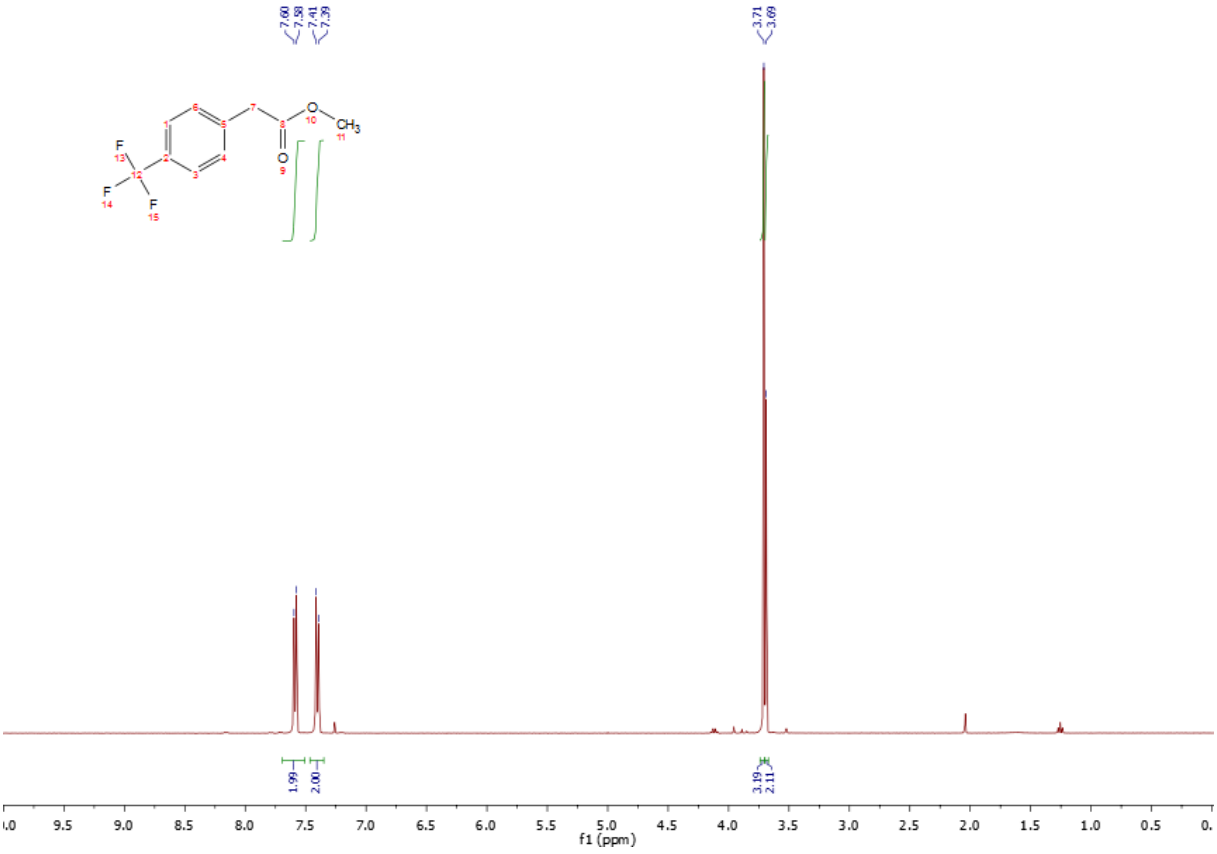
^{1}H NMR for methyl 2-(2-methoxyphenyl)acrylate (**18c4)**



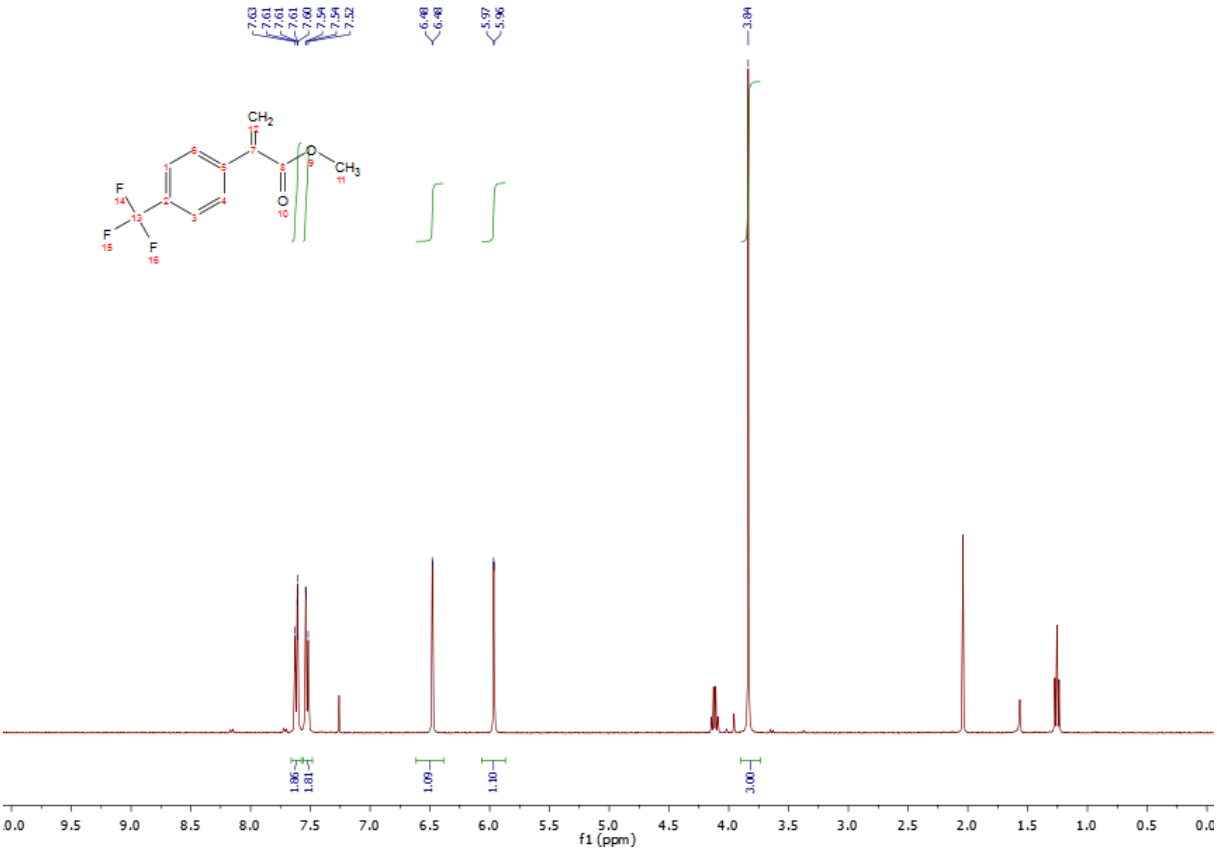
^{13}C NMR for methyl 2-(2-methoxyphenyl)acrylate (**18c4)**



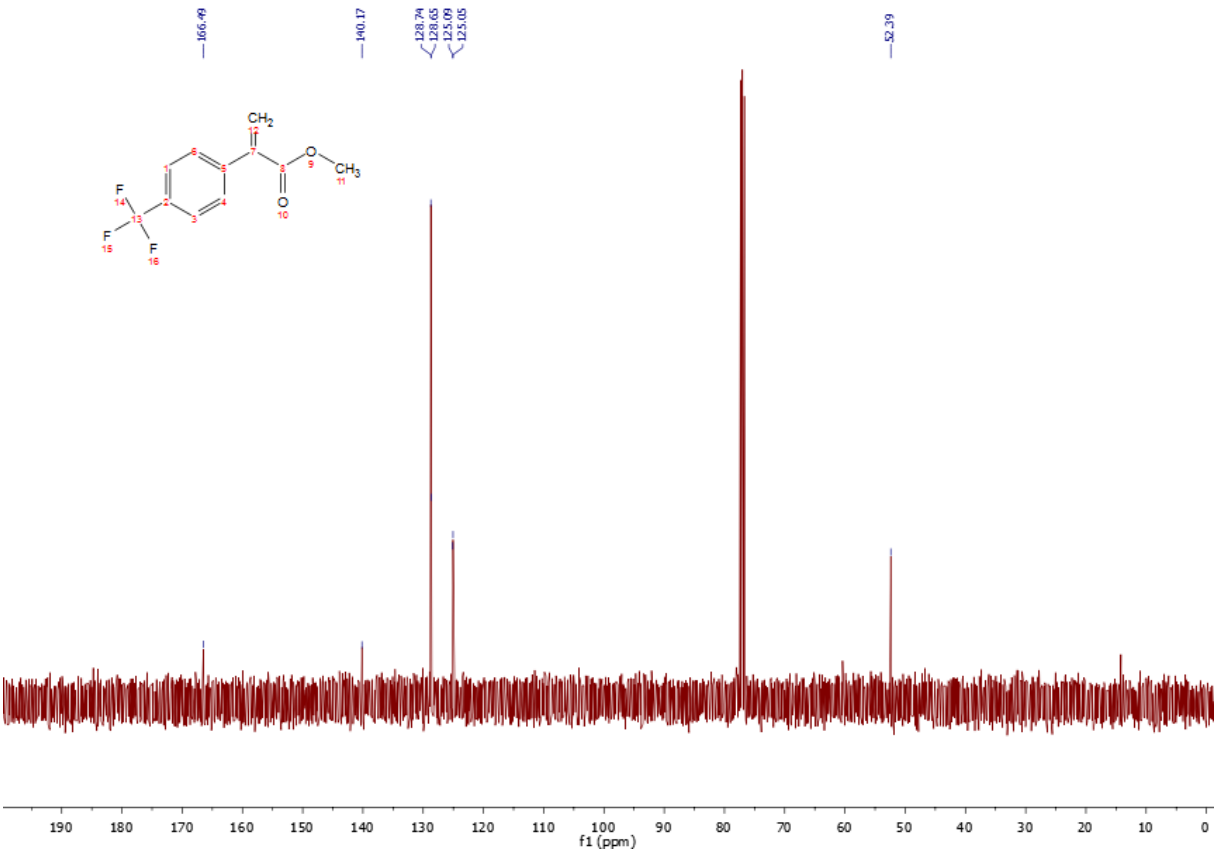
^{1}H NMR for methyl 2-(4-(trifluoromethyl)phenyl)acetate (**23e**)



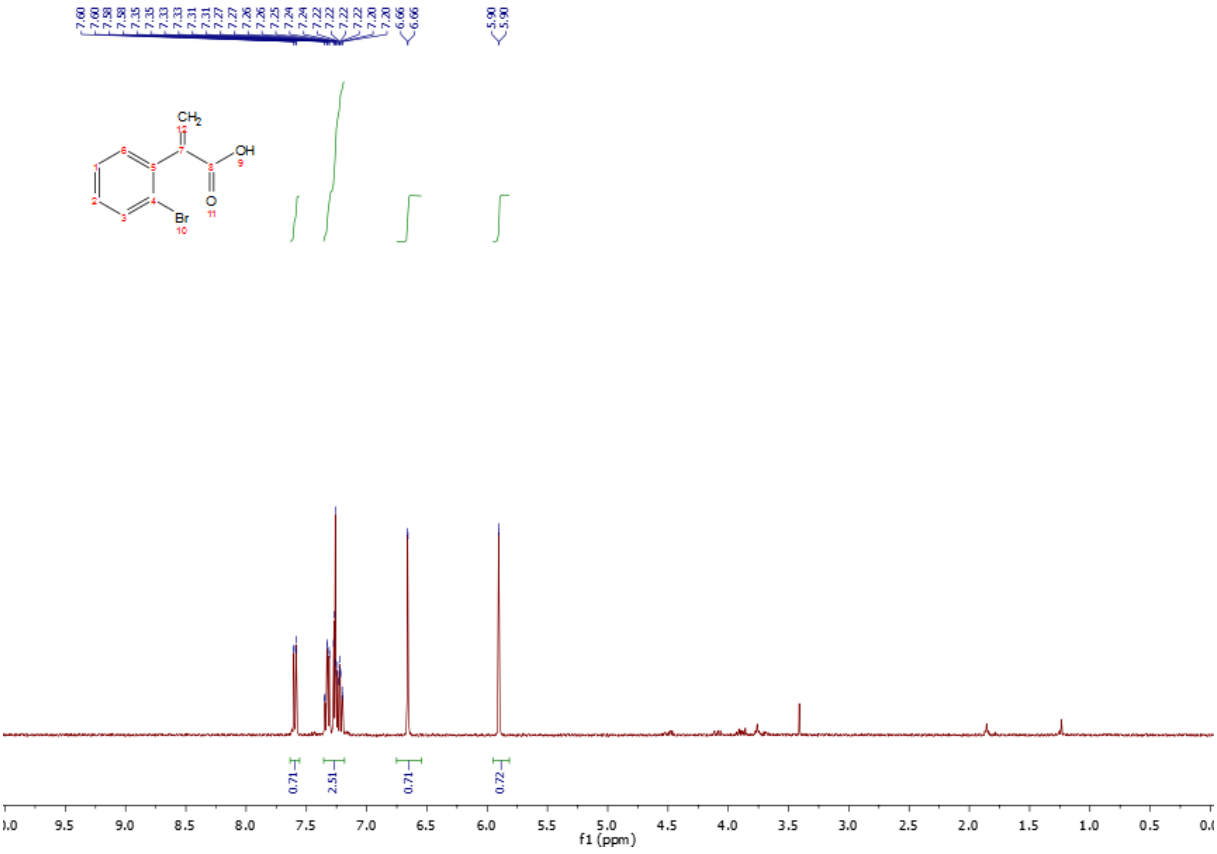
^{1}H NMR methyl 2-(4-(trifluoromethyl)phenyl)acrylate **(18c5)**



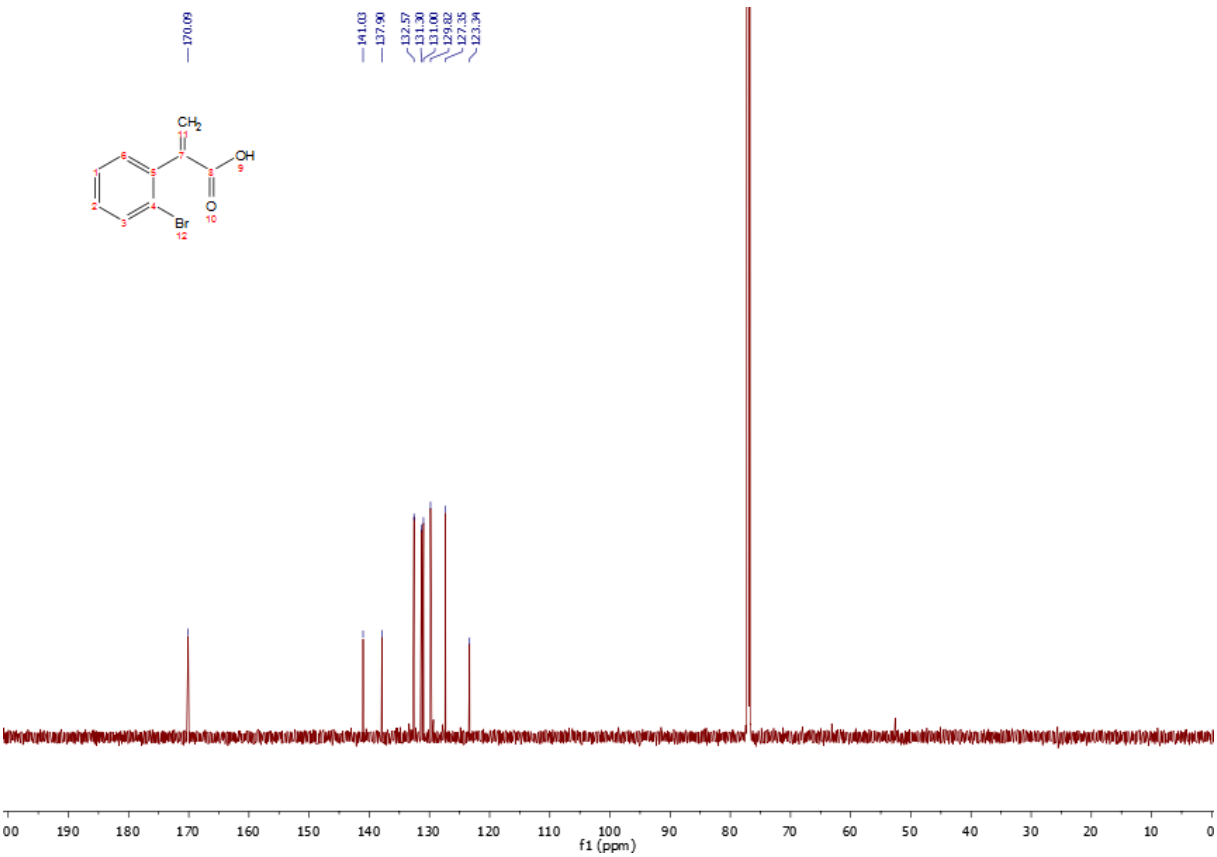
^{13}C NMR methyl 2-(4-(trifluoromethyl)phenyl)acrylate **(18c5)**



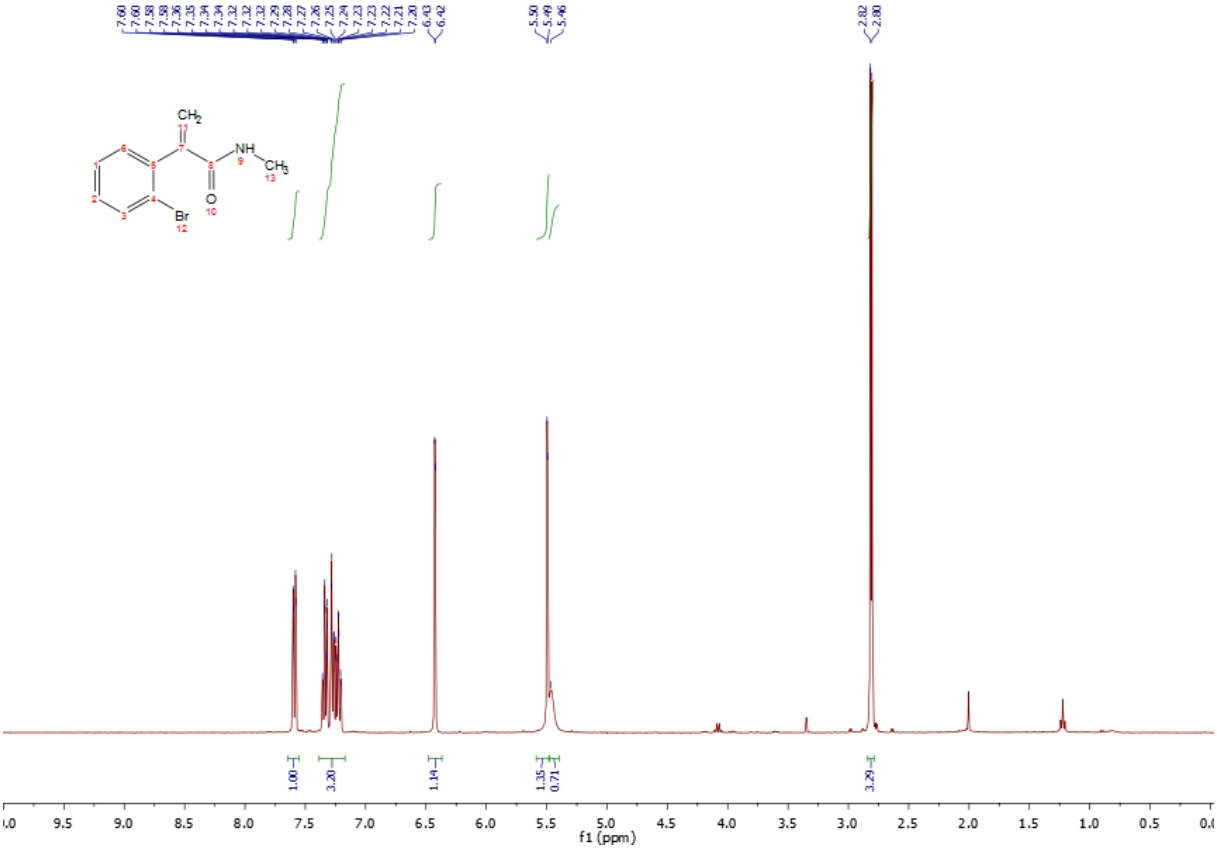
^{1}H NMR for 2-(2-bromophenyl)acrylic acid (**27a**)



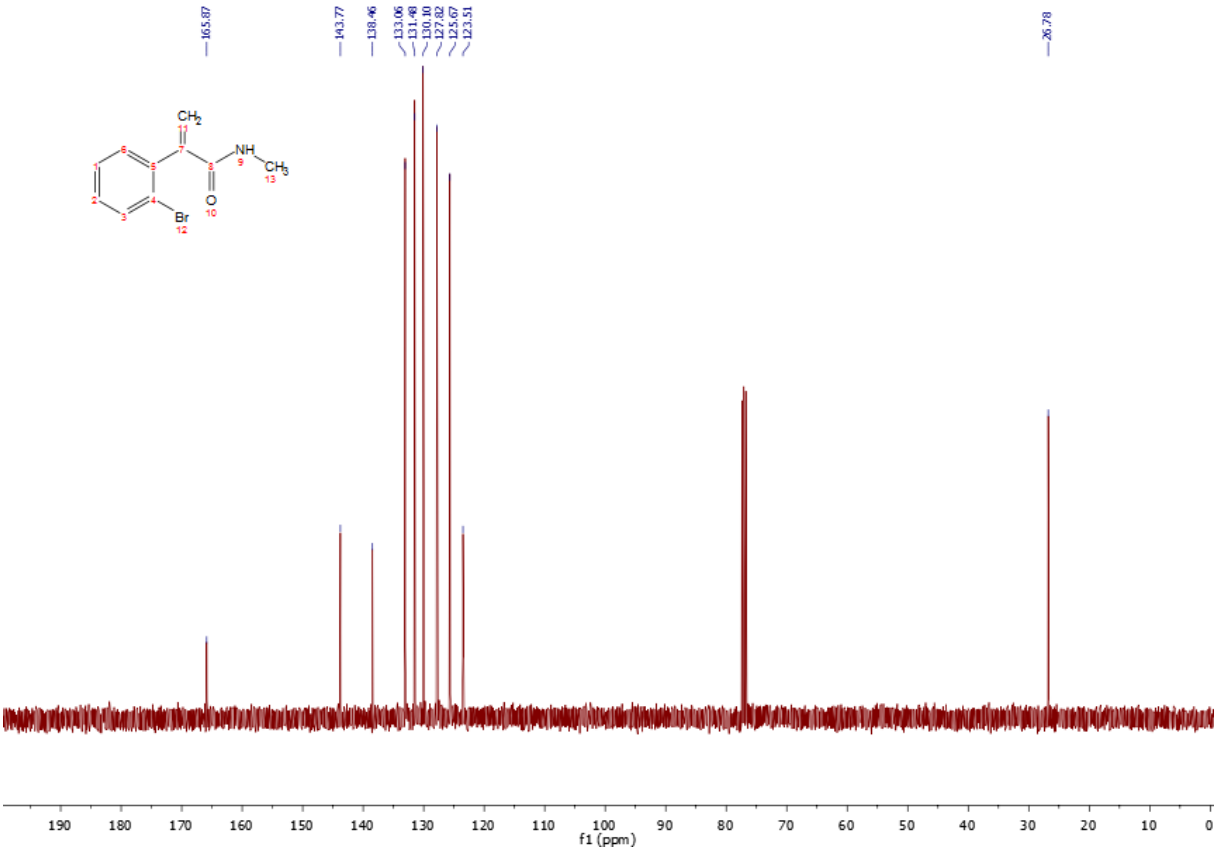
^{13}C NMR for 2-(2-bromophenyl)acrylic acid (**27a**)



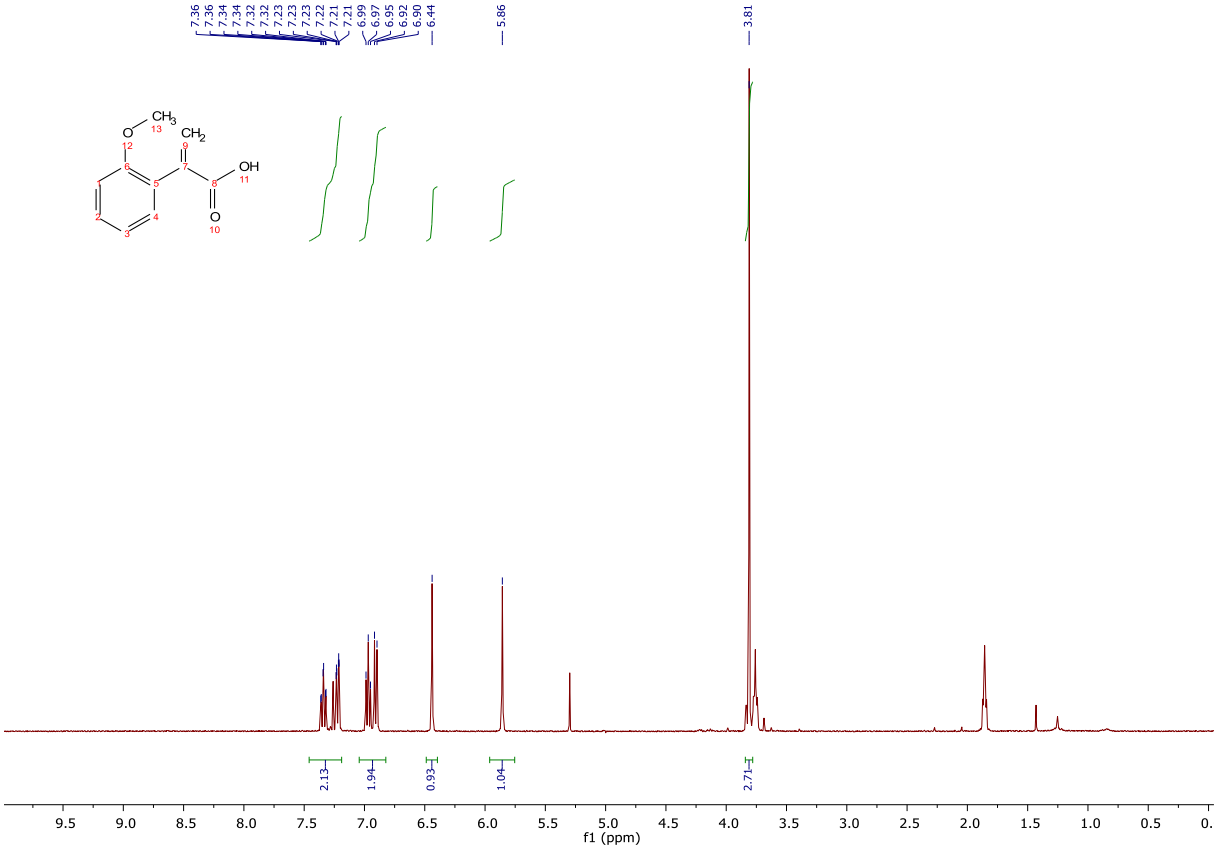
^{1}H NMR for 2-(2-bromophenyl)-N-methylacrylamide **(18e1)**



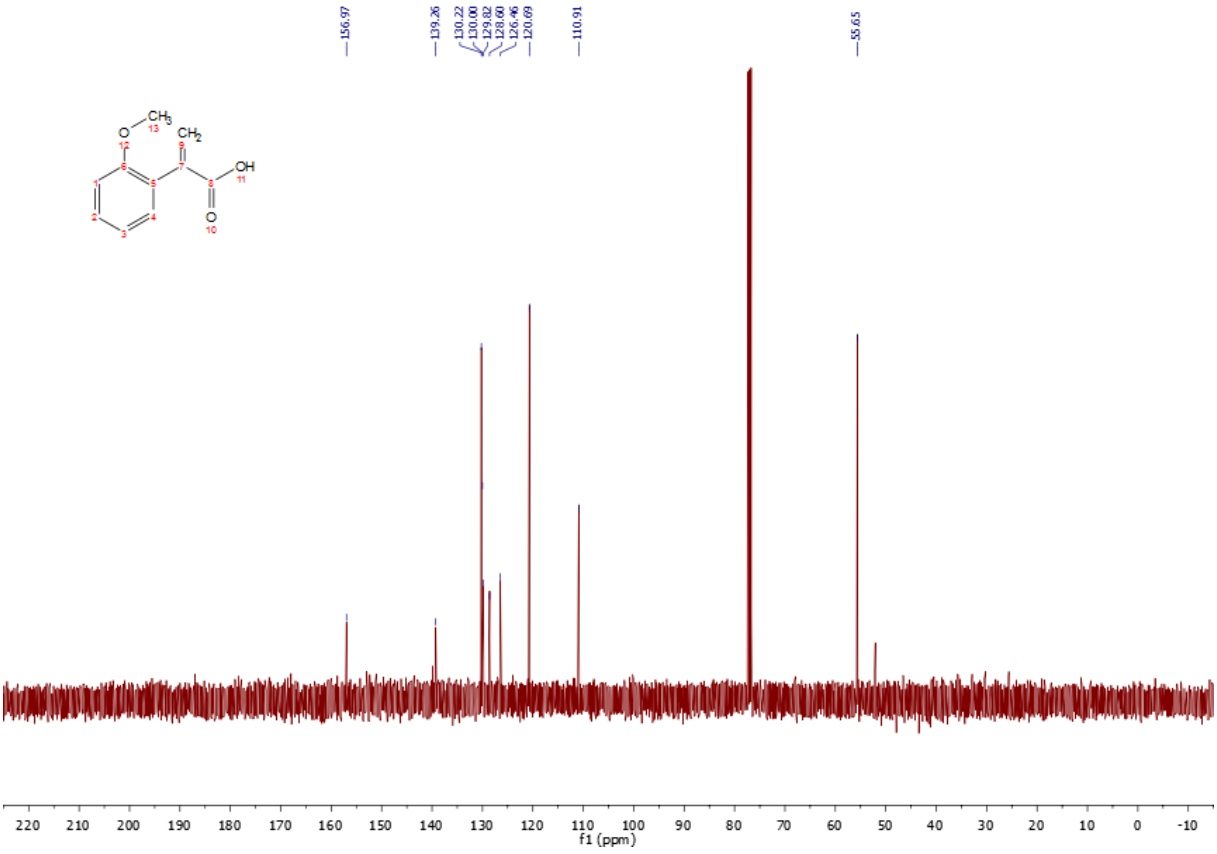
^{13}C NMR for 2-(2-bromophenyl)-N-methylacrylamide **(18e1)**



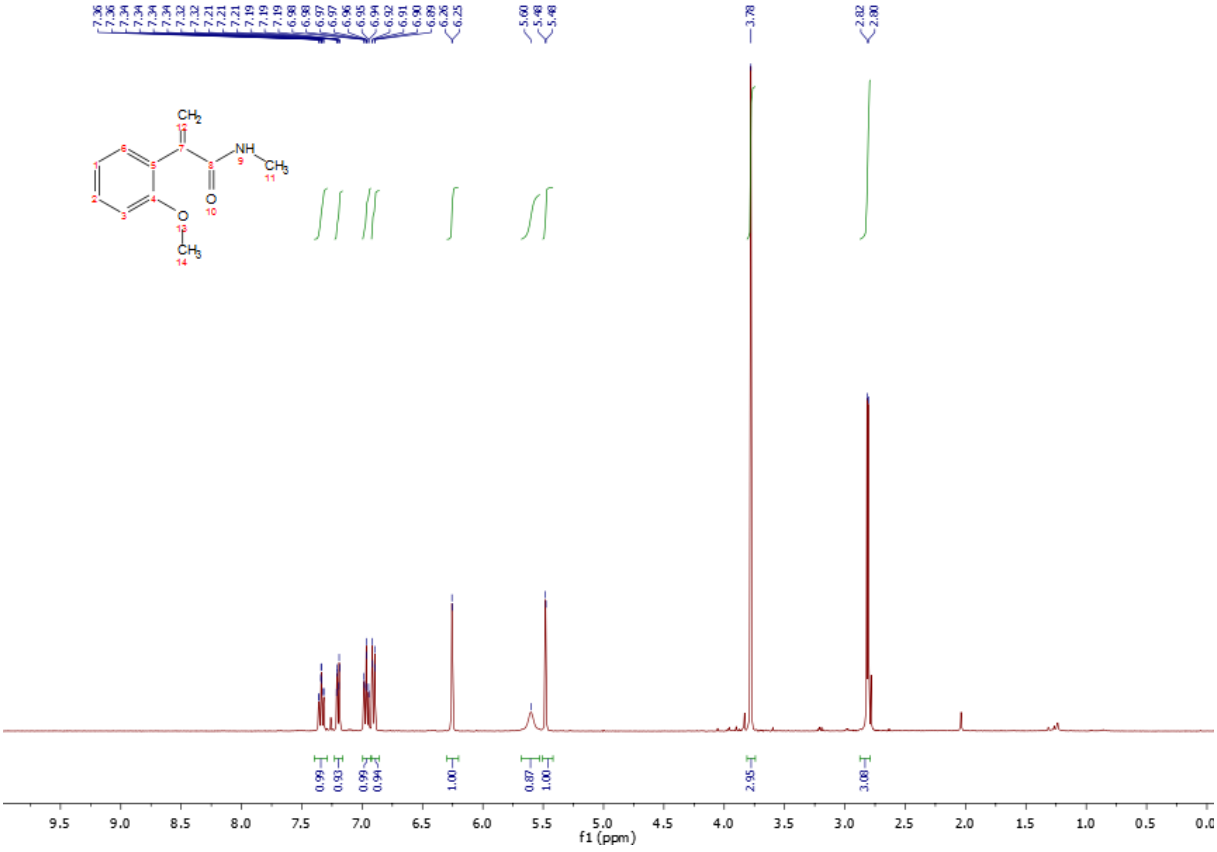
^{1}H NMR for 2-(2-methoxyphenyl)acrylic acid (**27b**)



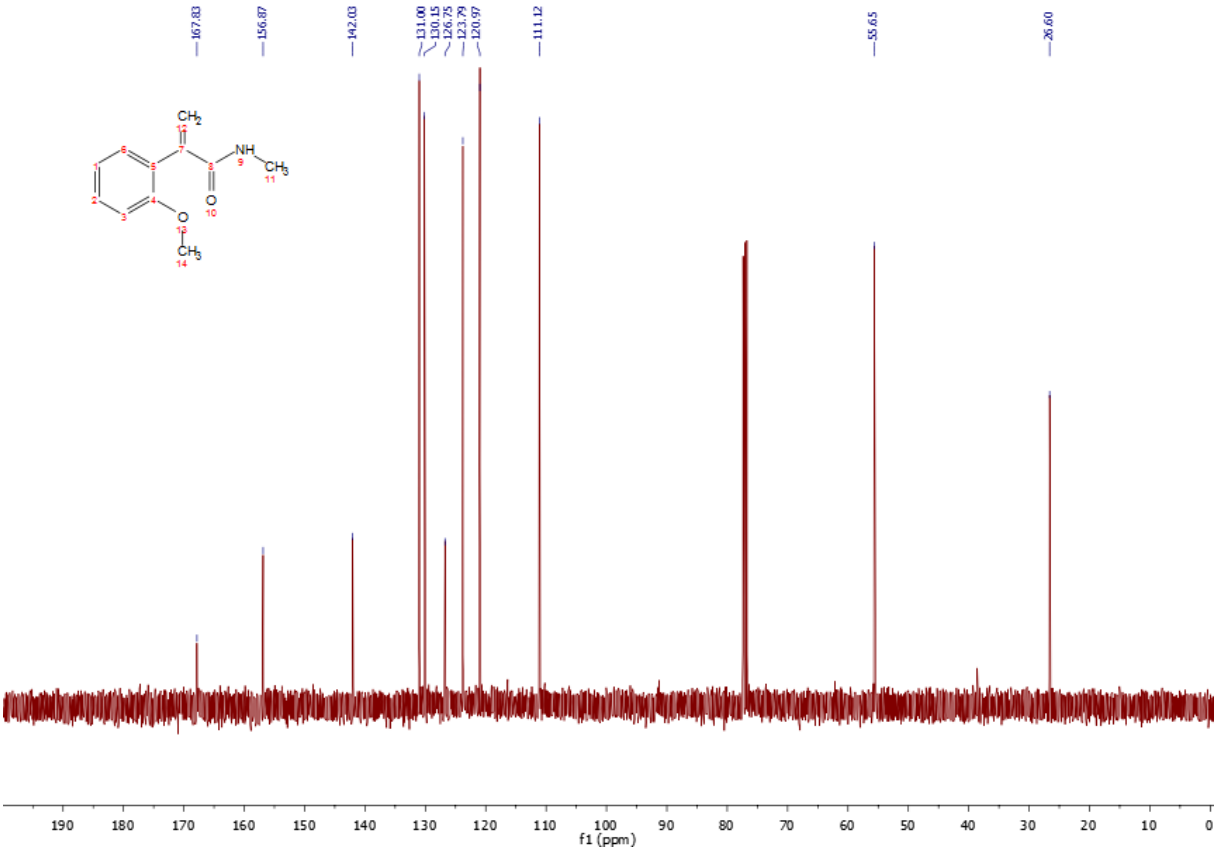
^{13}C NMR for 2-(2-methoxyphenyl)acrylic acid (**27b**)



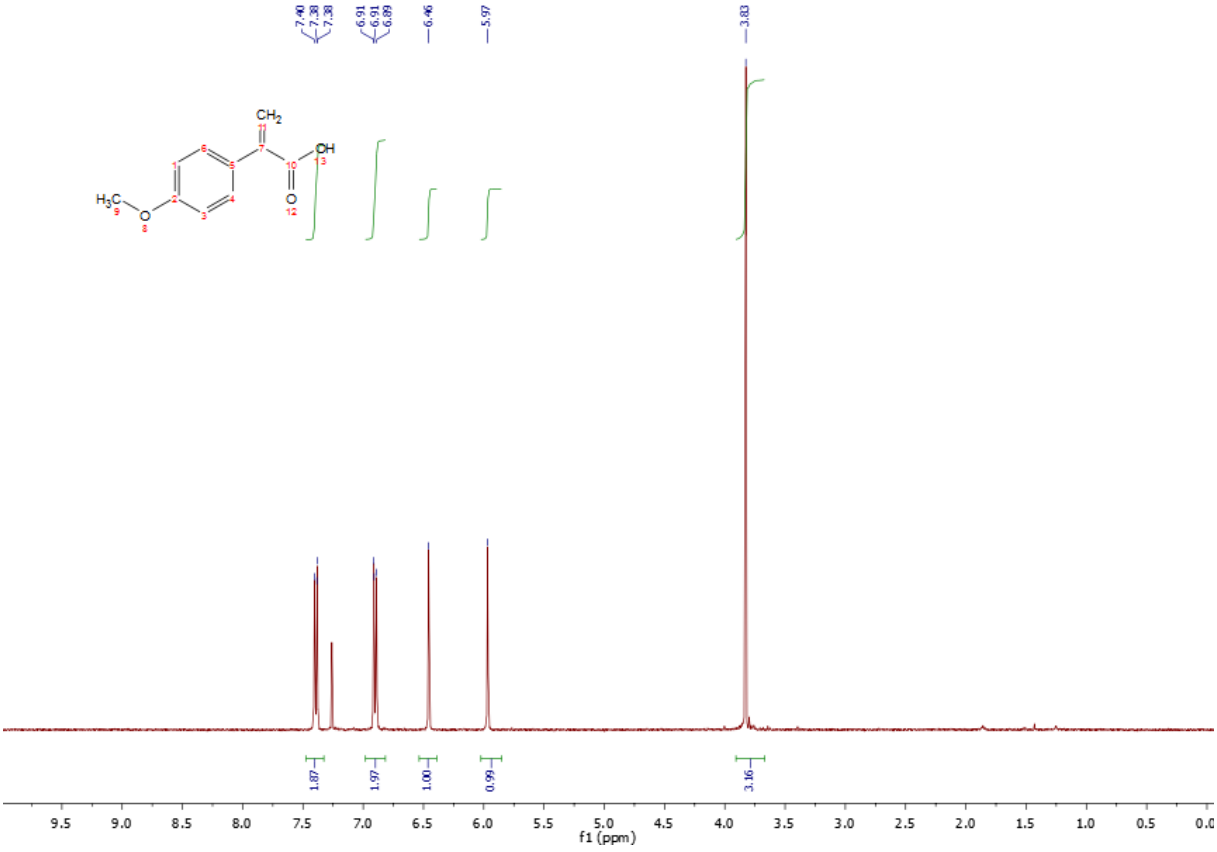
^{1}H NMR for 2-(2-methoxyphenyl)-N-methylacrylamide **(18e2)**



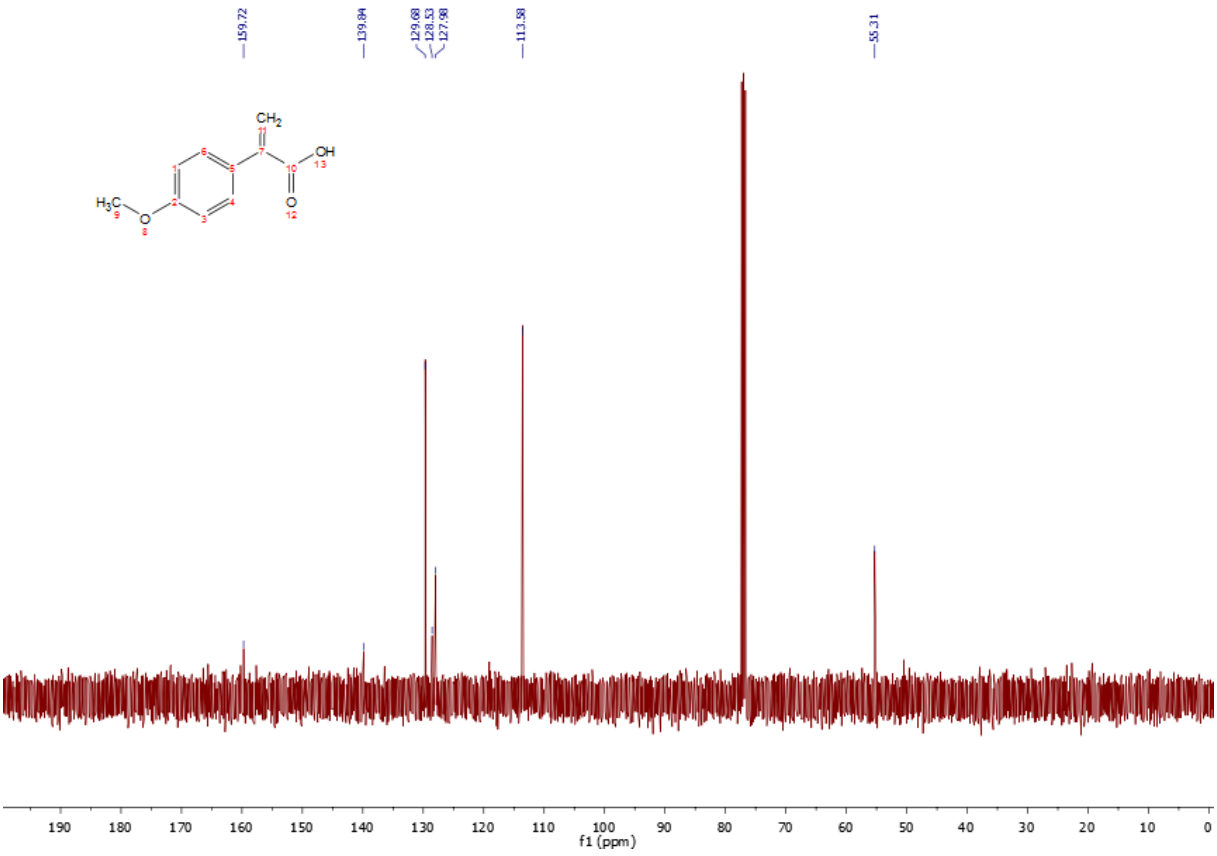
^{13}C NMR for 2-(2-methoxyphenyl)-N-methylacrylamide **(18e2)**



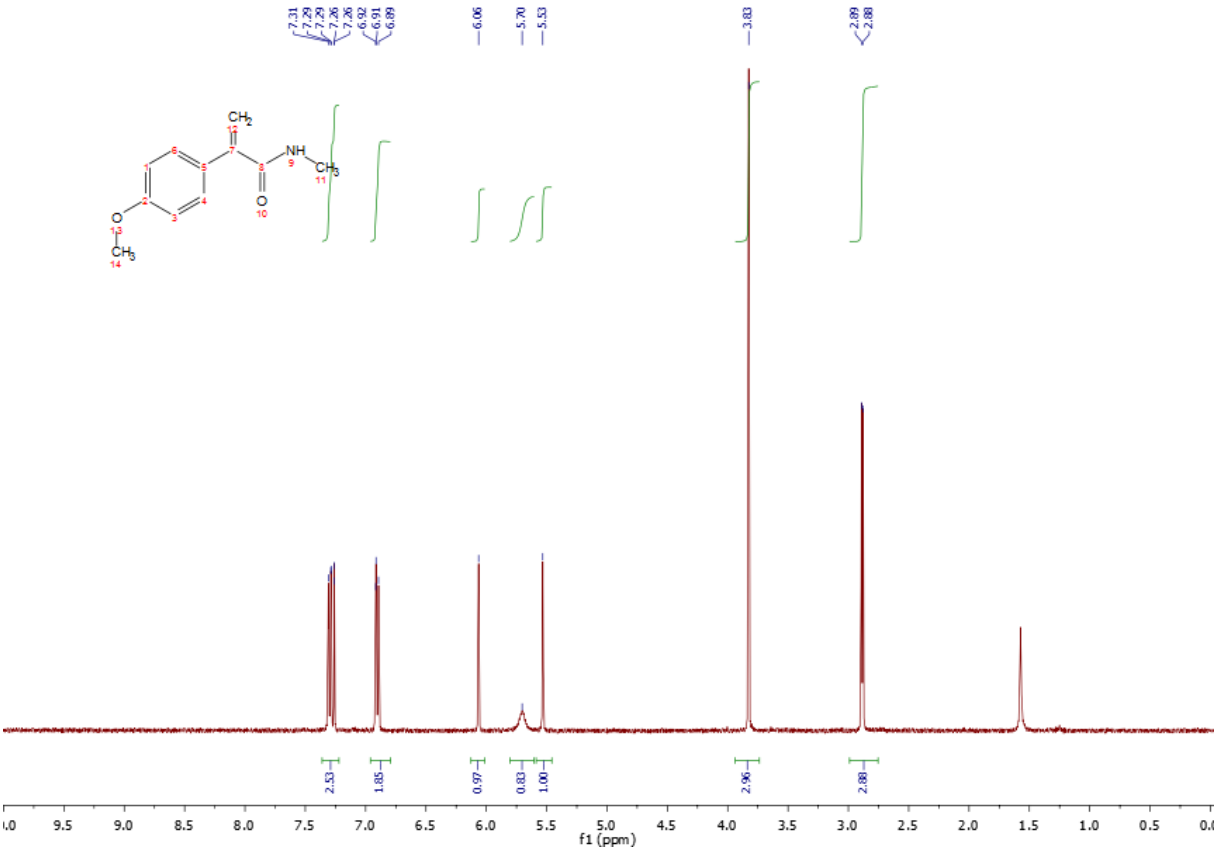
^{1}H NMR for 2-(4-methoxyphenyl)acrylic acid **(27c)**



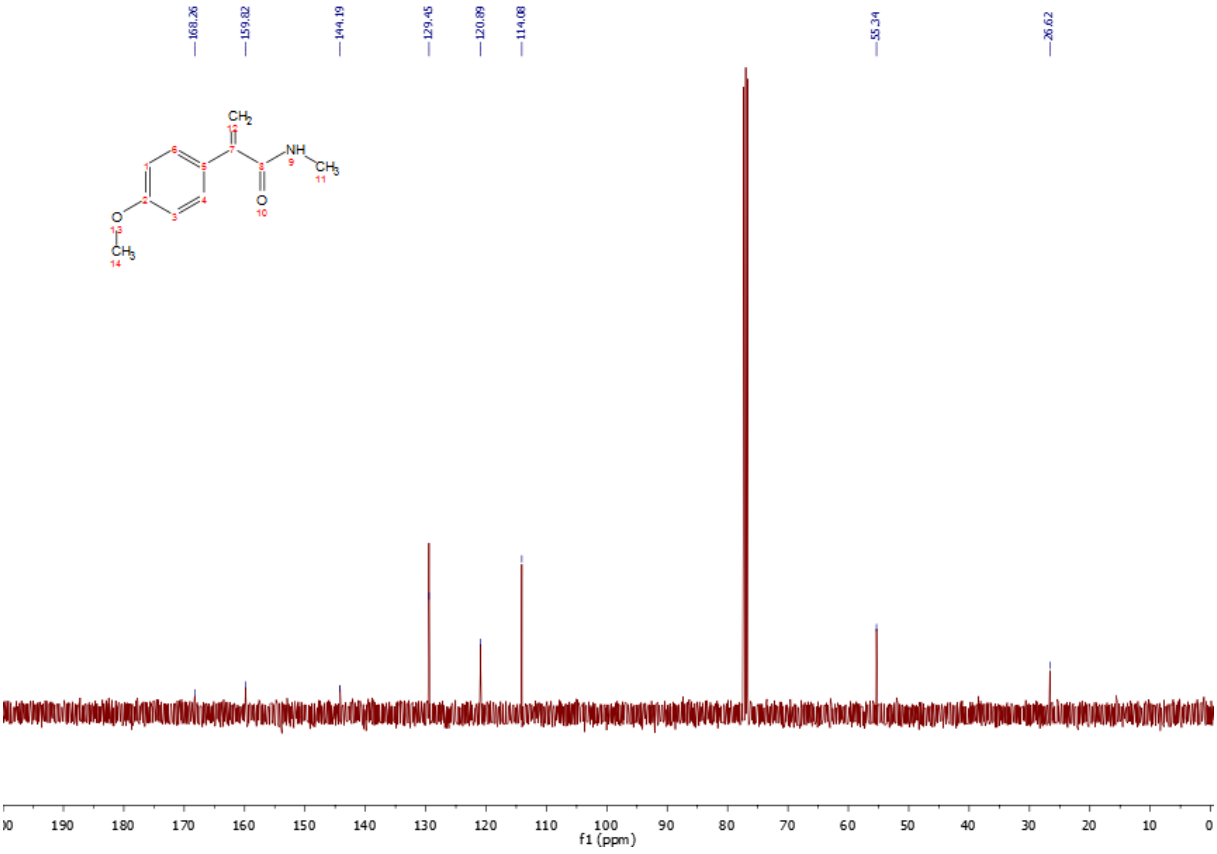
^{13}C NMR for 2-(4-methoxyphenyl)acrylic acid **(27c)**



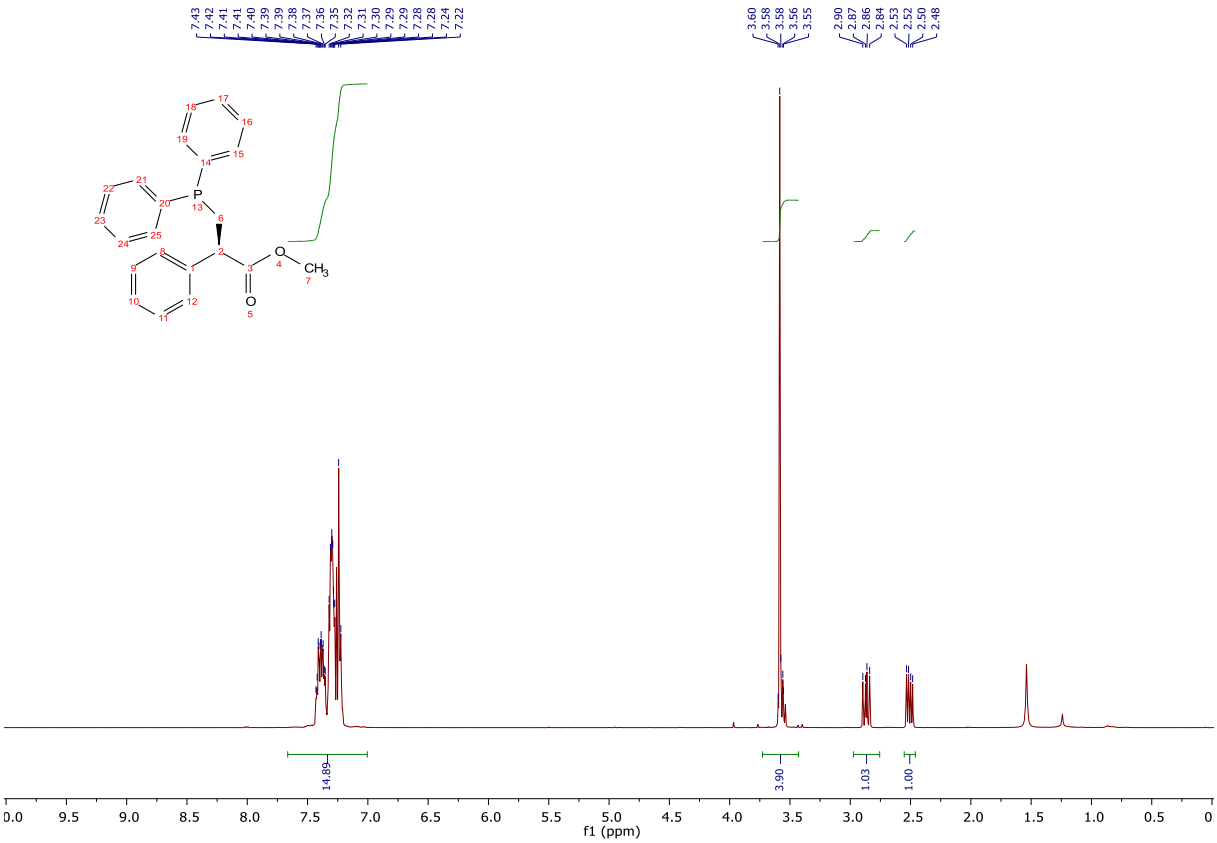
^{1}H NMR for 2-(4-methoxyphenyl)-N-methylacrylamide **(18e3)**



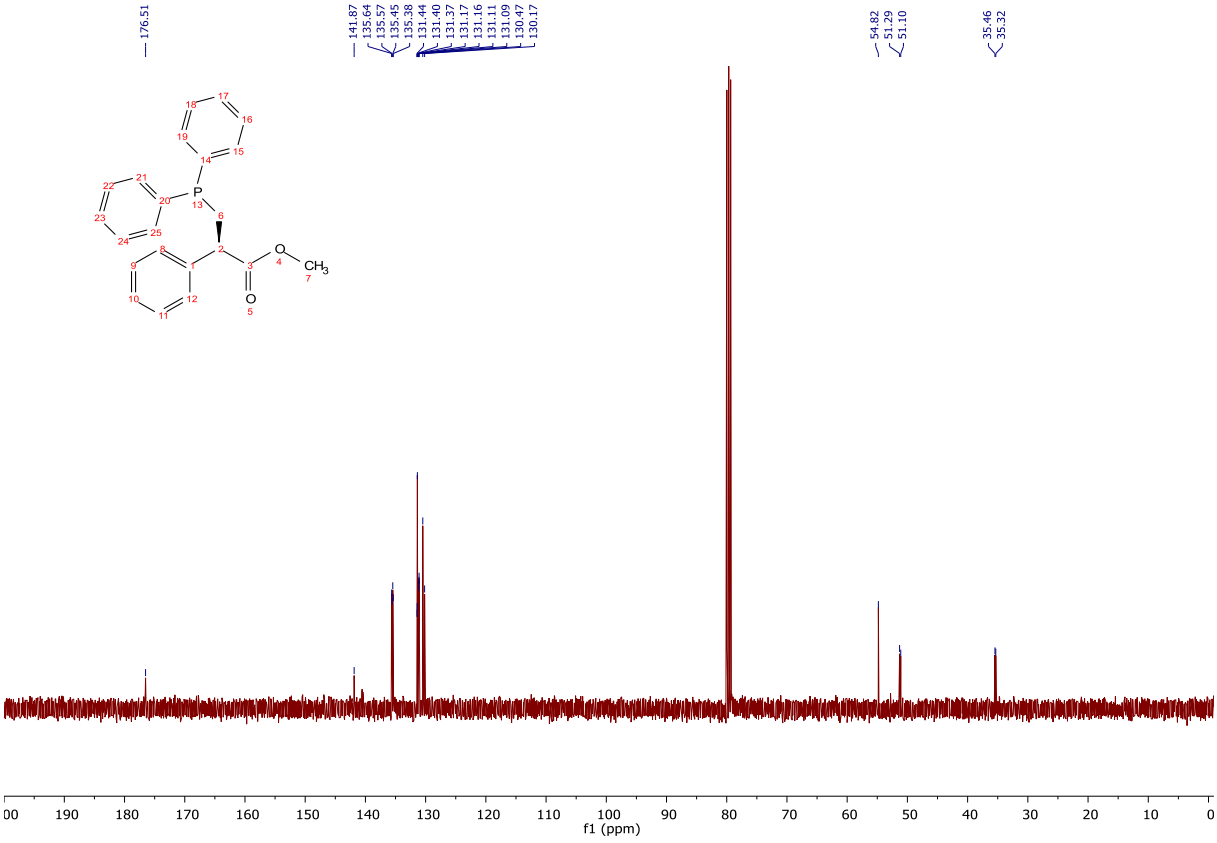
^{13}C NMR for 2-(4-methoxyphenyl)-N-methylacrylamide **(18e3)**



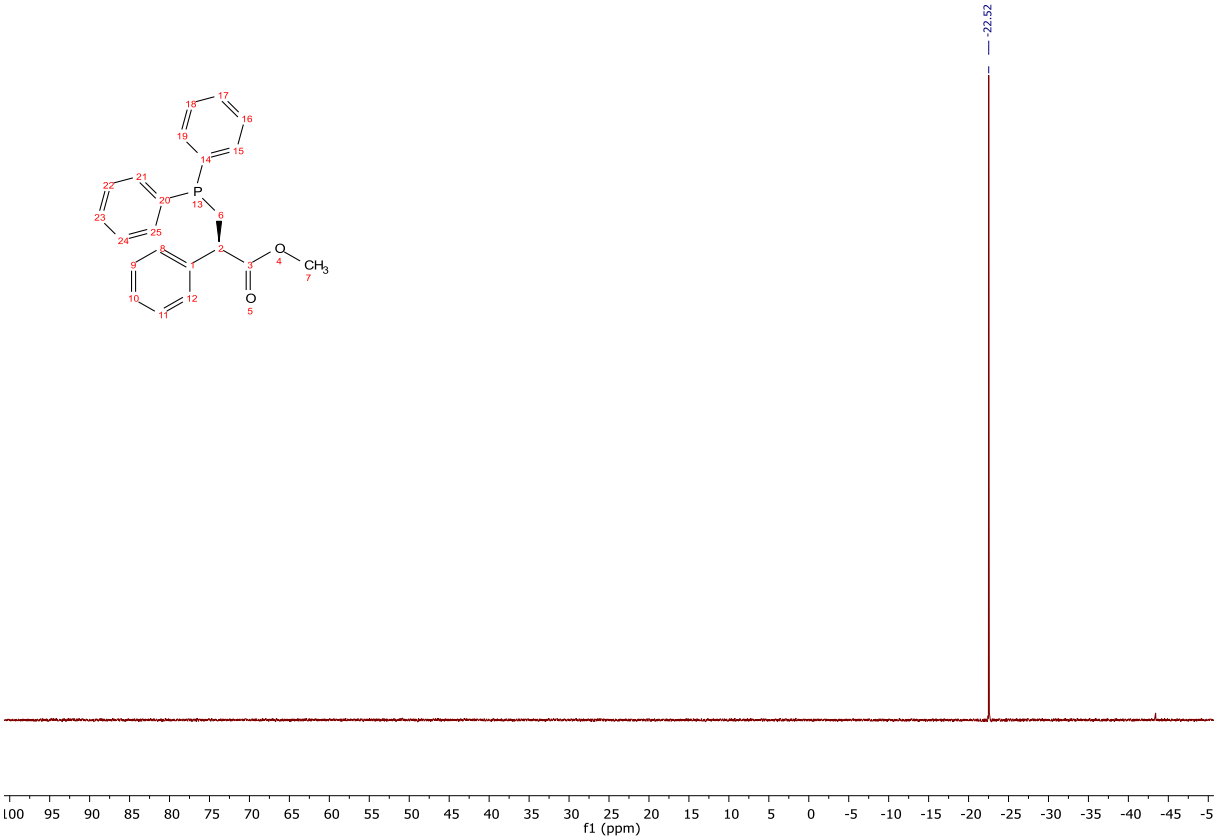
^{1}H NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-phenylpropanoate (**18c1')**



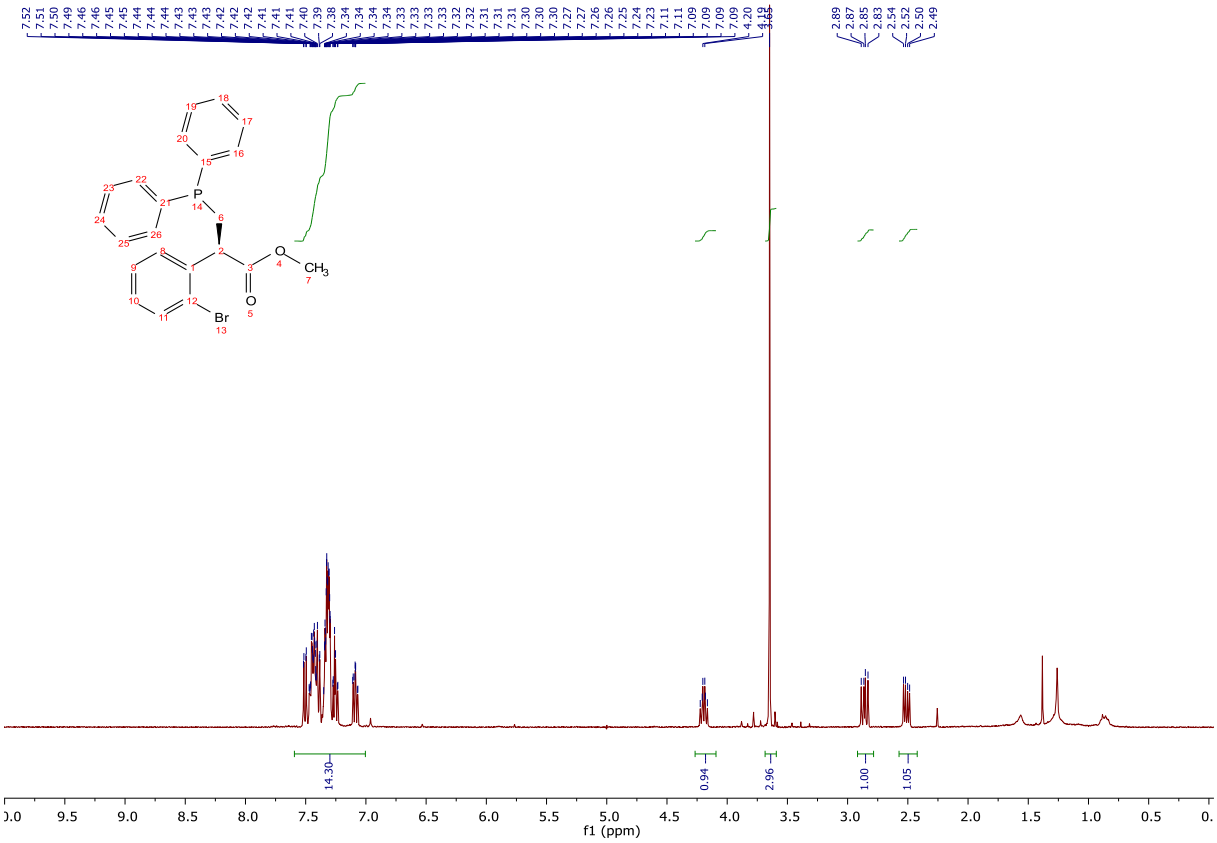
^{13}C NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-phenylpropanoate (**18c1')**



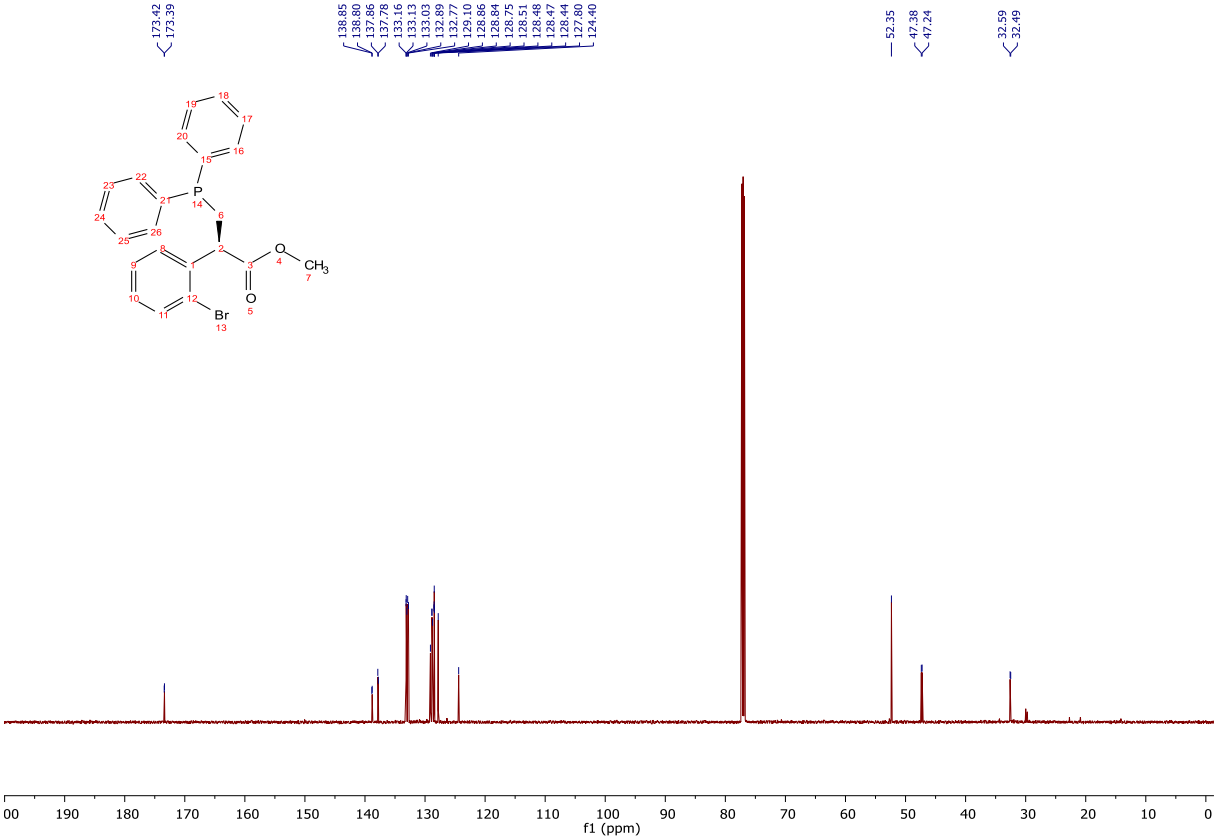
^{31}P NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-phenylpropanoate (**18c1')**



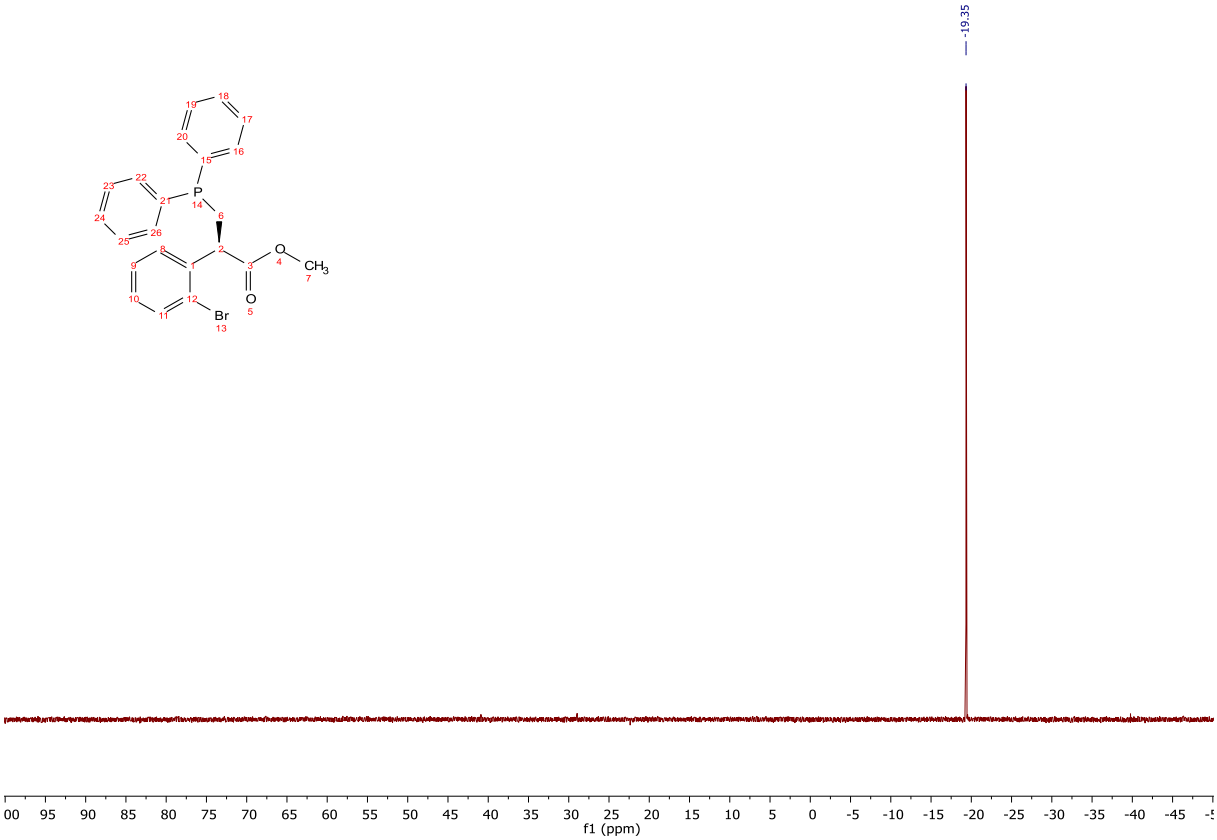
^{1}H NMR for methyl (*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)propanoate **18c2'**



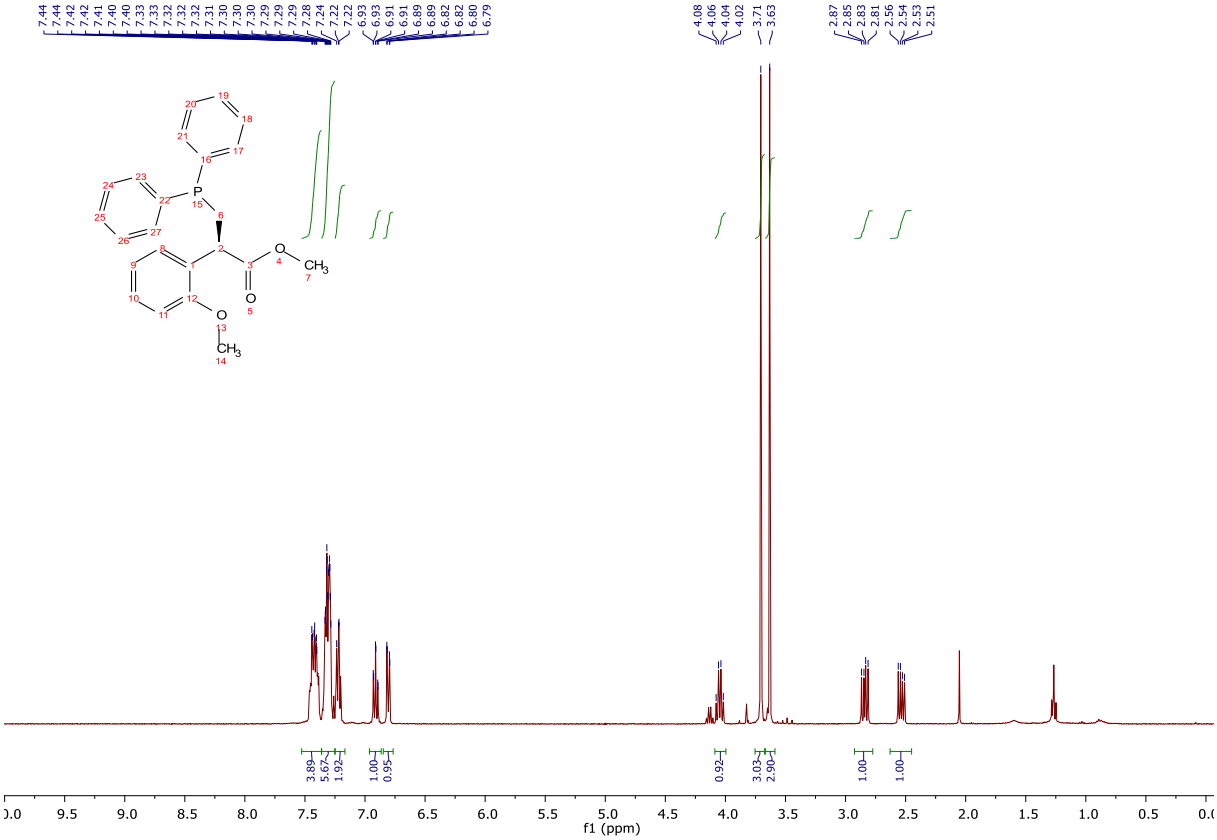
^{13}C NMR for methyl (*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)propanoate **18c2'**



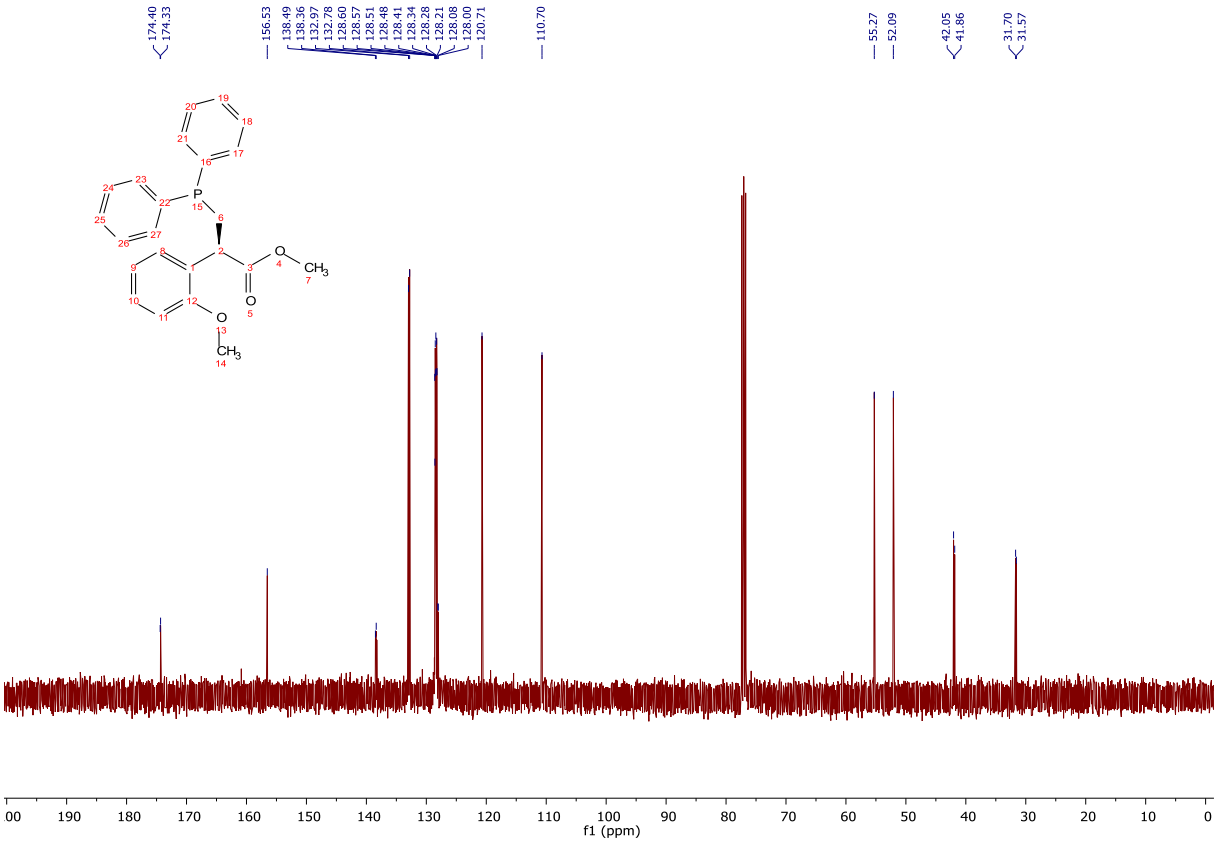
^{31}P NMR for methyl (*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)propanoate **18c2'**



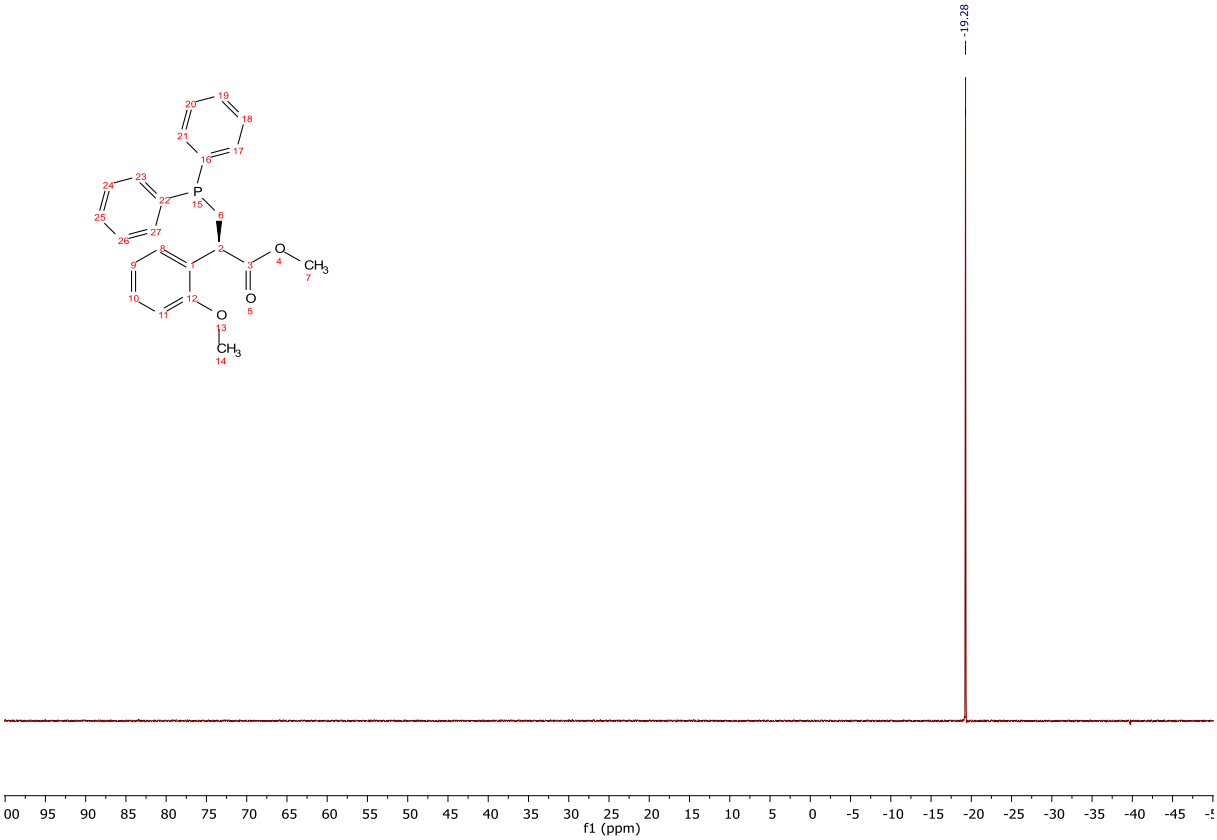
^{1}H NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)propanoate **18c3'**



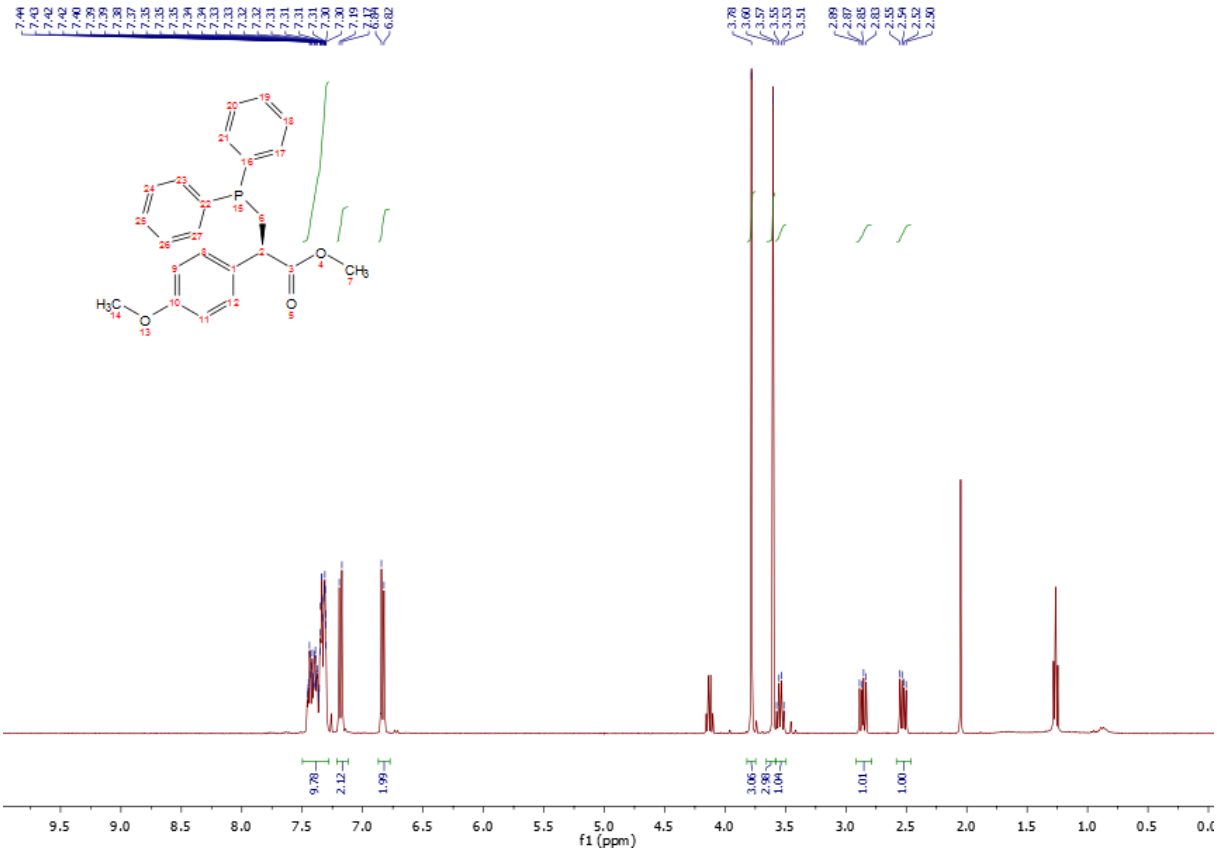
^{13}C NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)propanoate **18c3'**



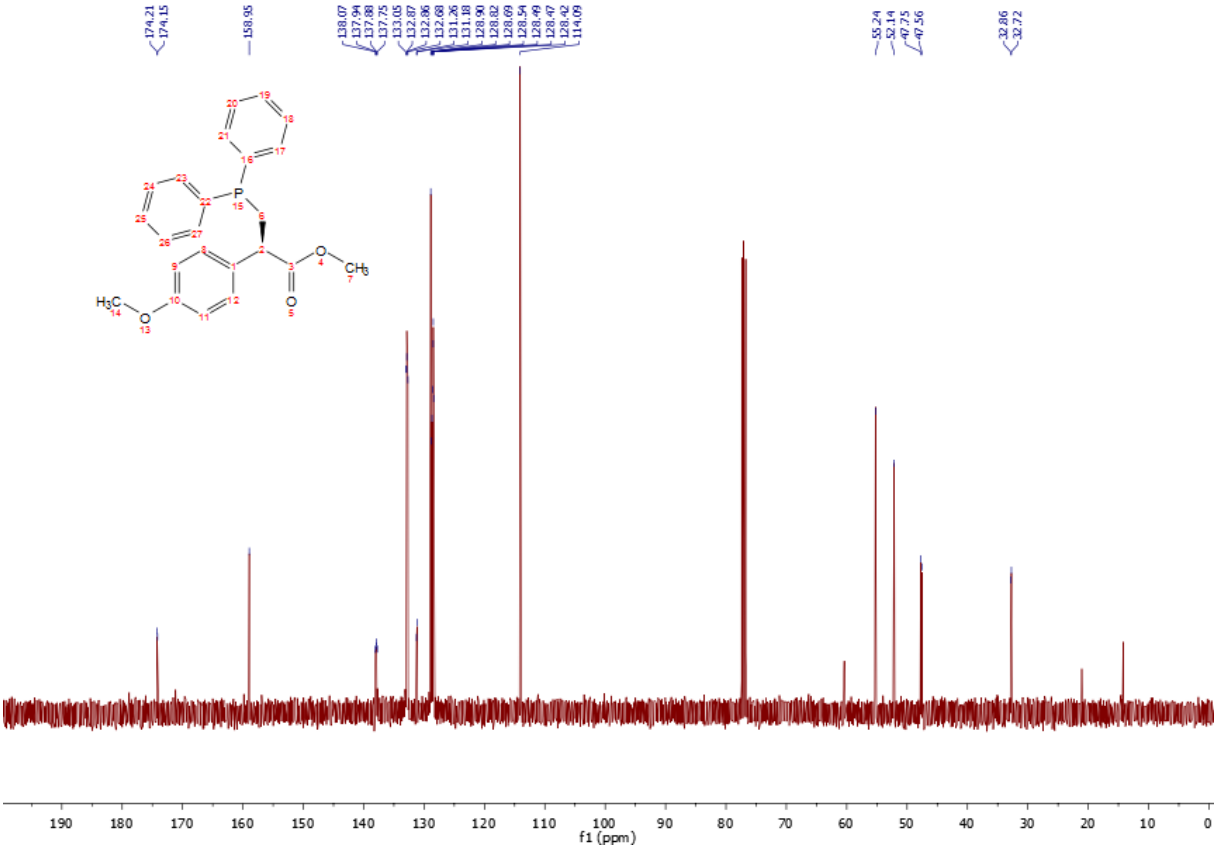
^{31}P NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)propanoate **18c3'**



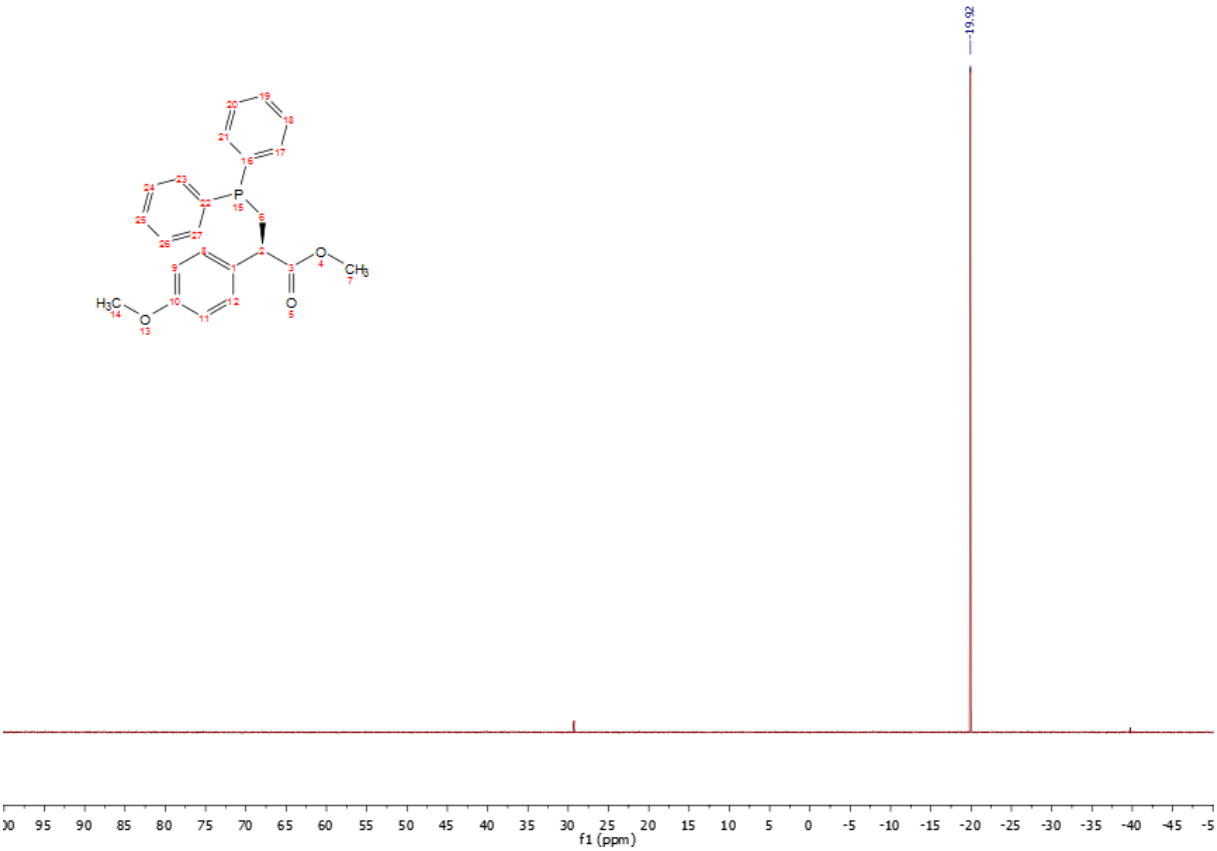
^{1}H NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)propanoate **(18c4')**



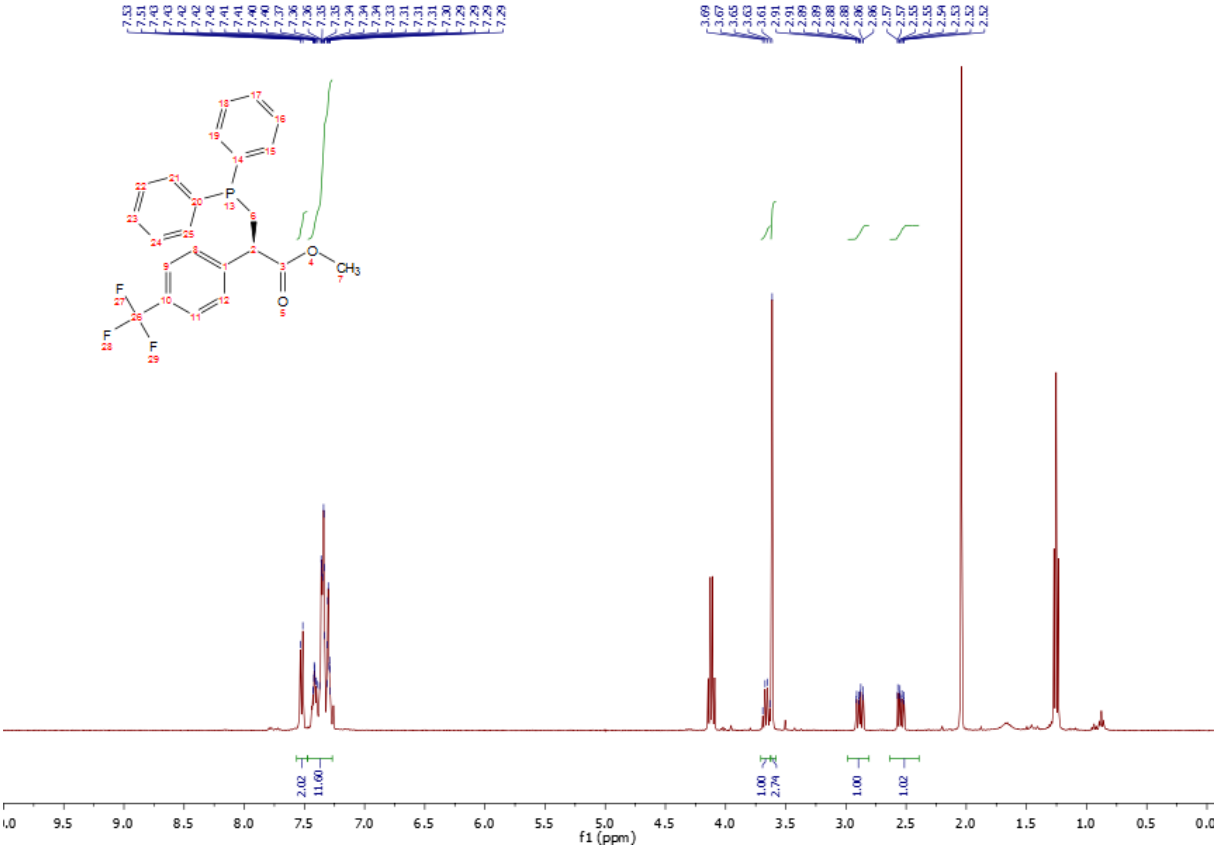
^{13}C NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)propanoate **(18c4')**



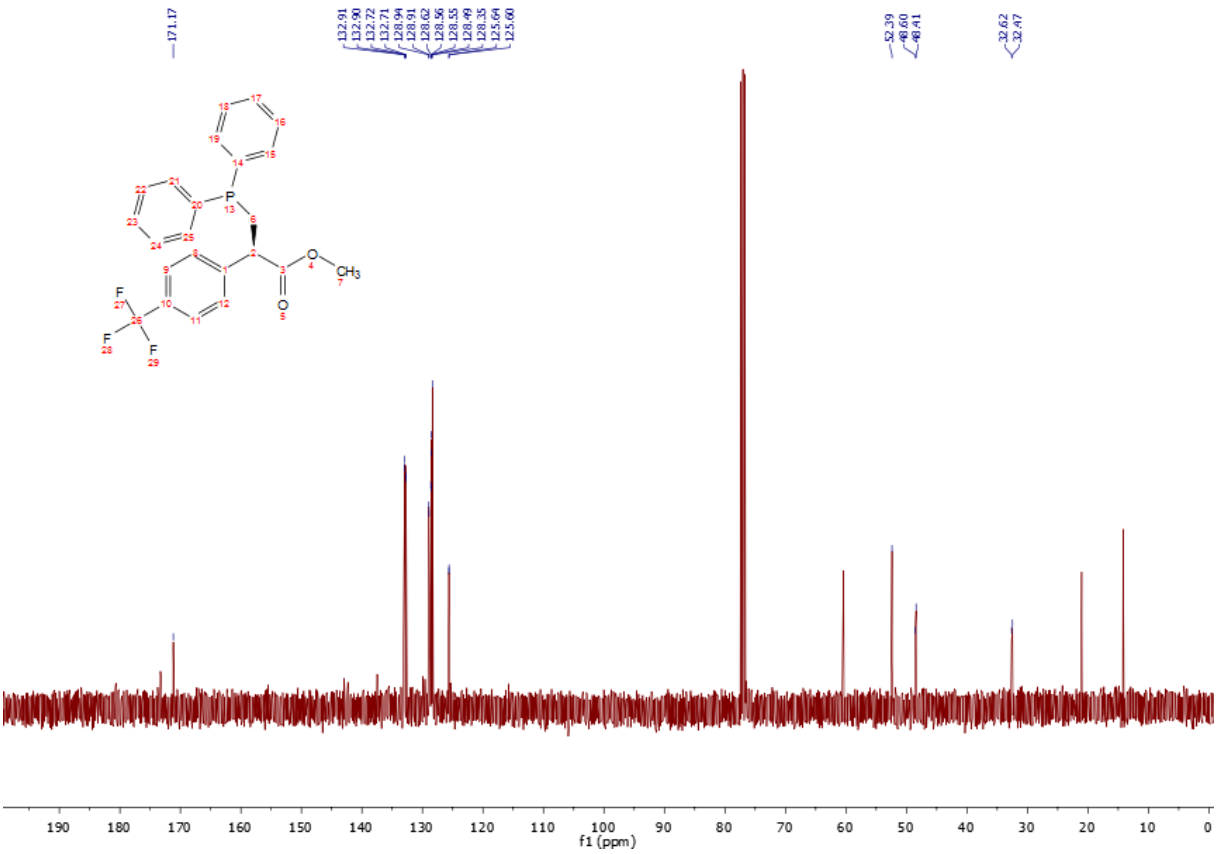
^{31}P NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)propanoate **(18c4')**



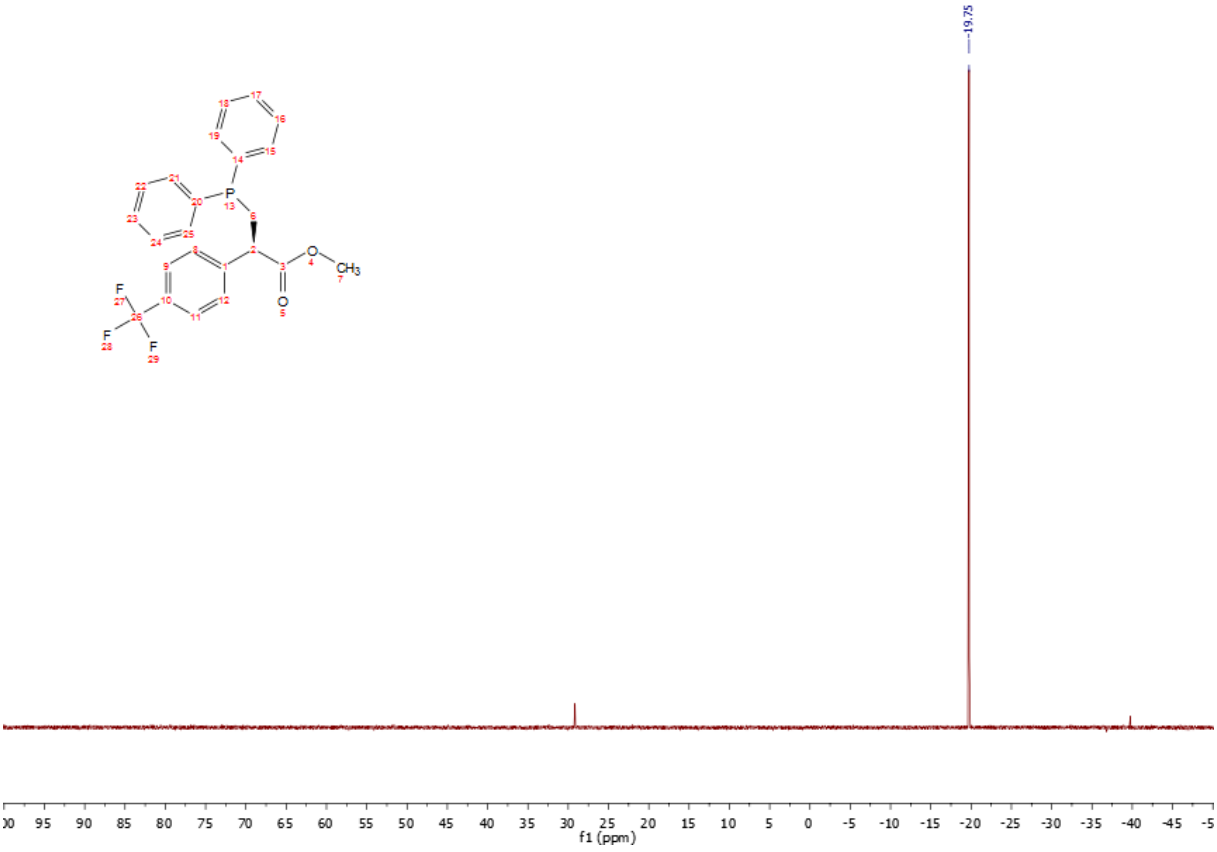
^{1}H NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-(trifluoromethyl)phenyl)propanoate **(18c5')**



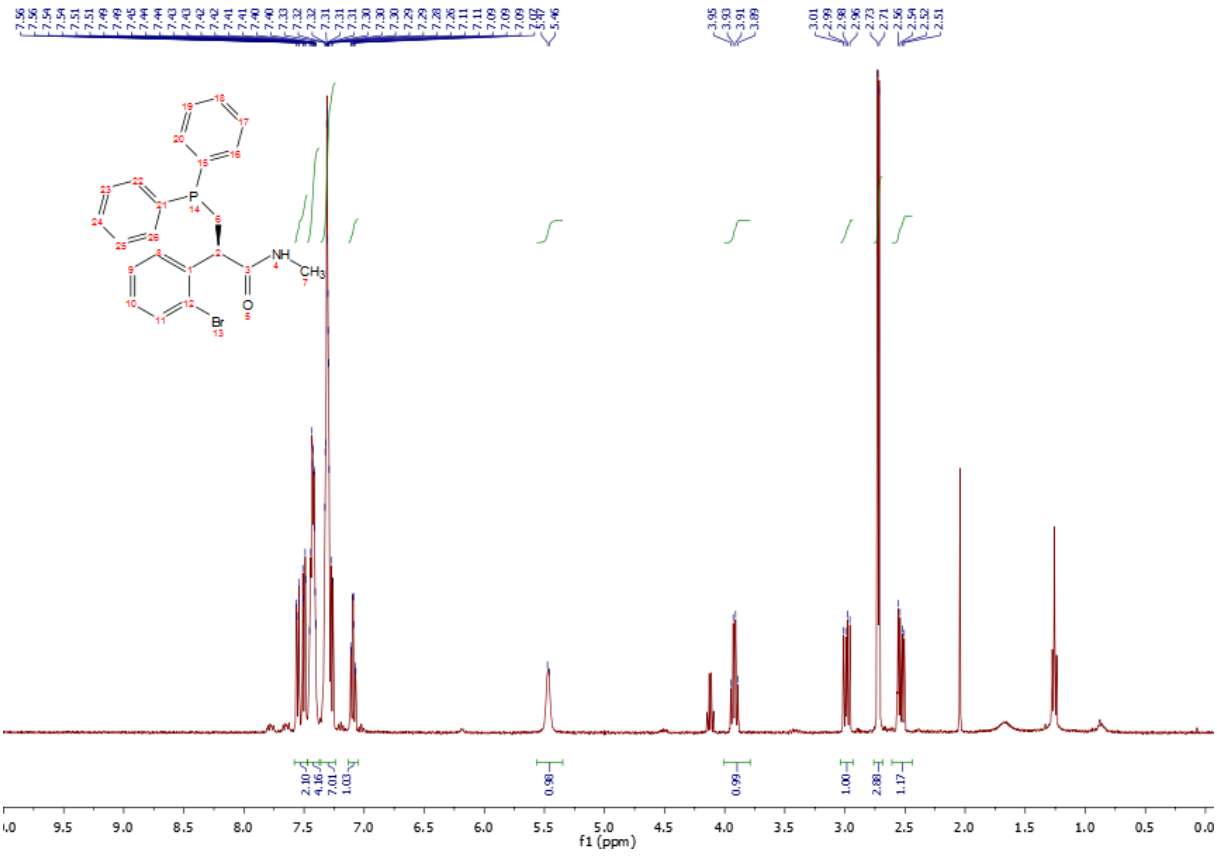
^{13}C NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-(trifluoromethyl)phenyl)propanoate **(18c5')**



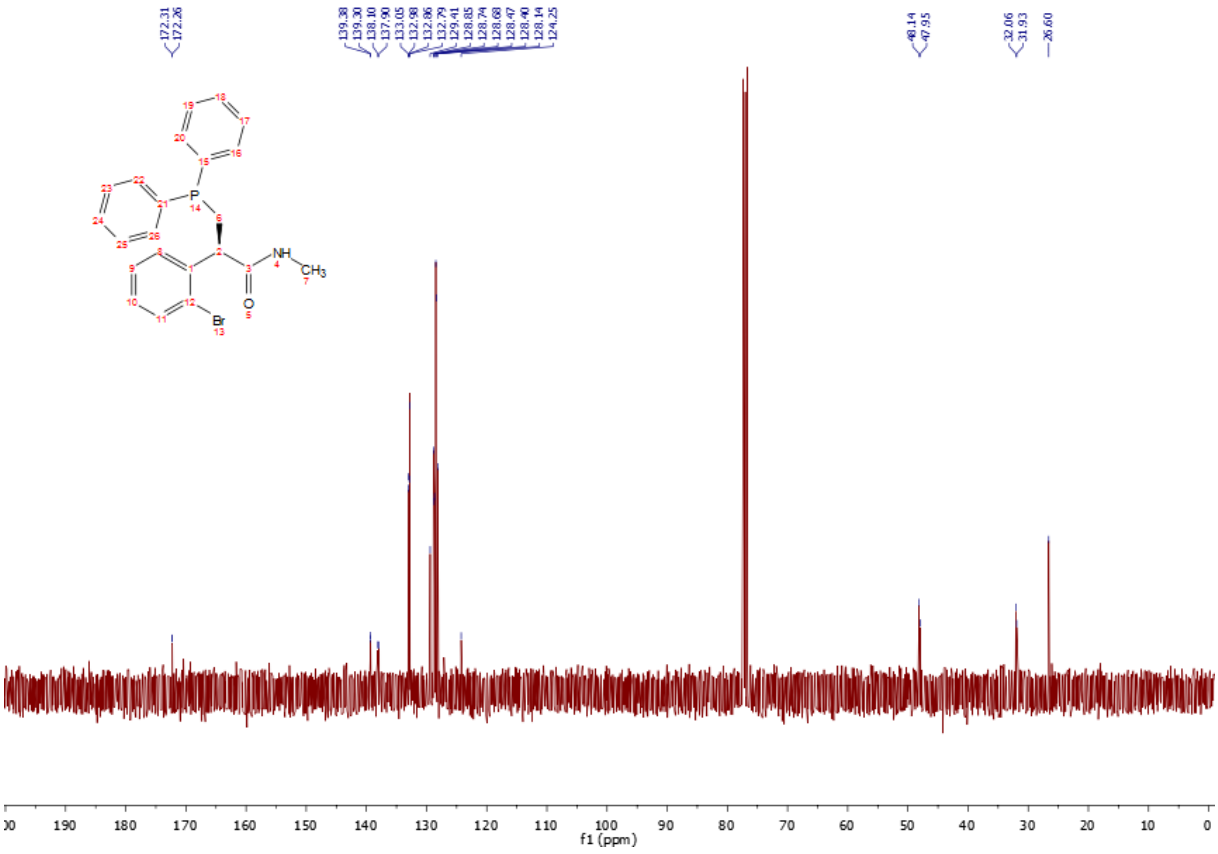
^{31}P NMR for methyl (*R*)-3-(diphenylphosphaneyl)-2-(4-(trifluoromethyl)phenyl)propanoate **(18c5')**



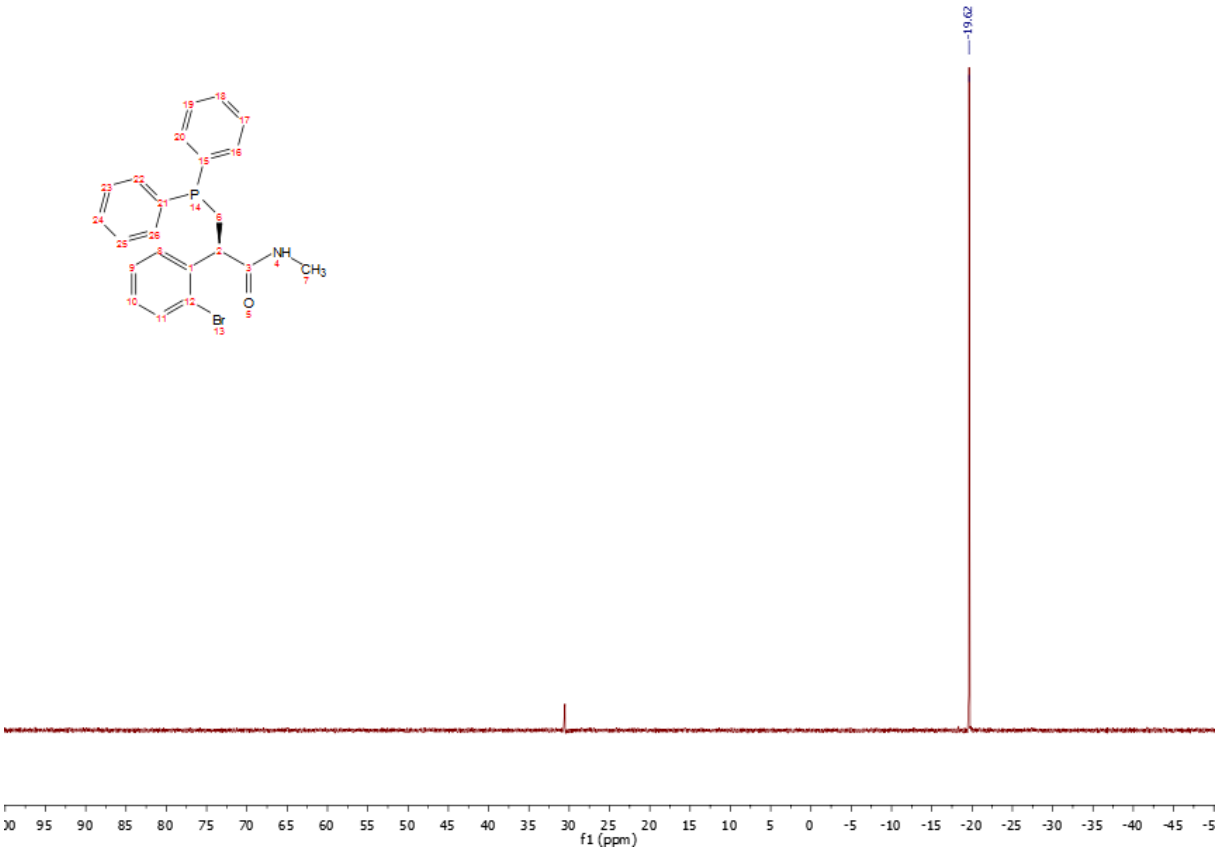
^{1}H NMR for (*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)-N-methylpropanamide **(18e1')**



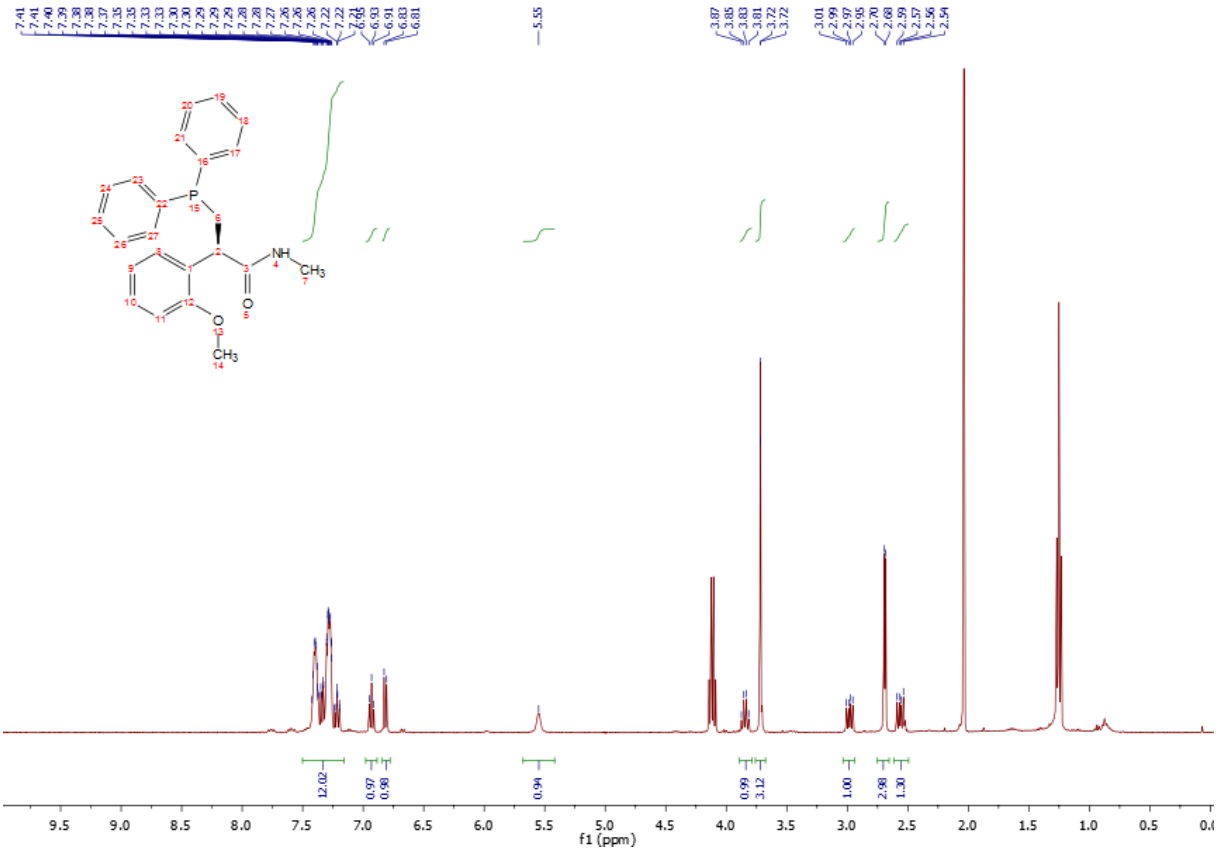
^{13}C NMR for (*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)-N-methylpropanamide **(18e1')**



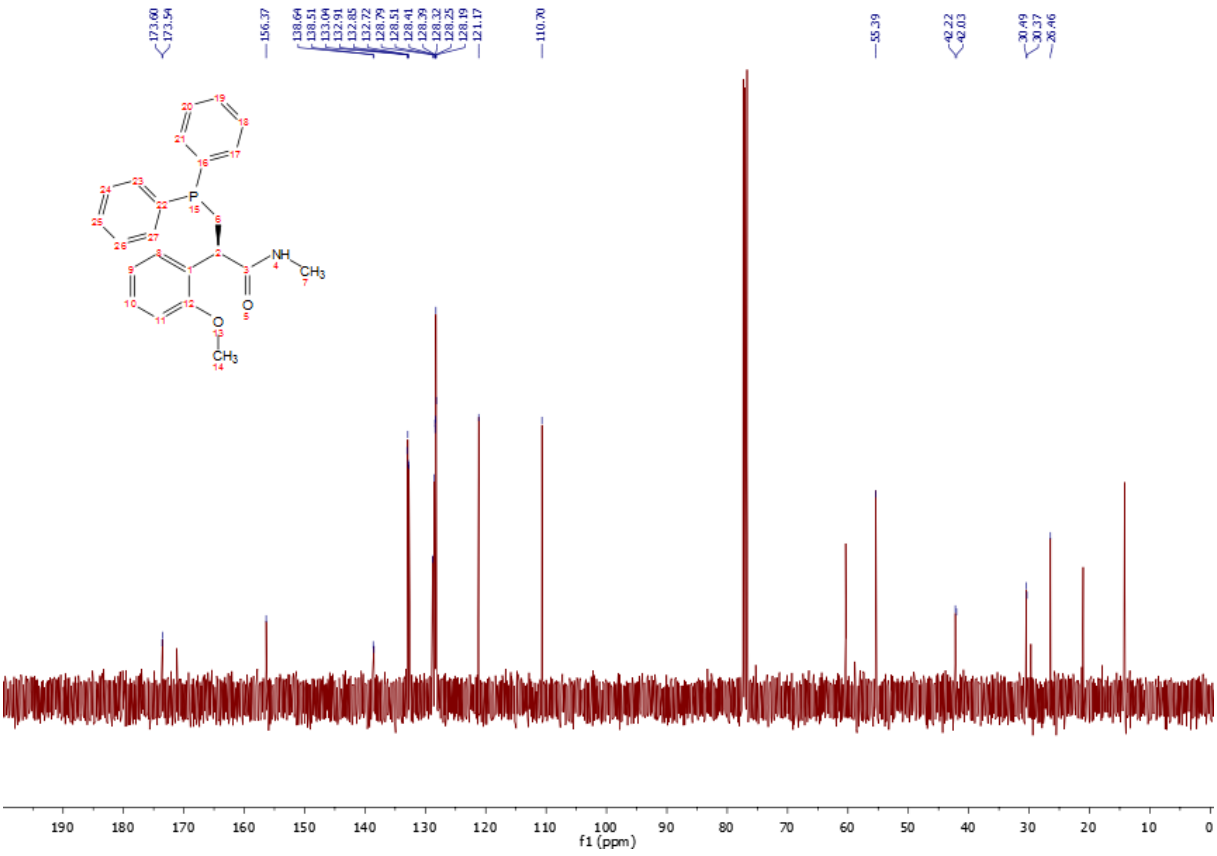
^{31}P NMR for (*R*)-2-(2-bromophenyl)-3-(diphenylphosphaneyl)-N-methylpropanamide **(18e1')**



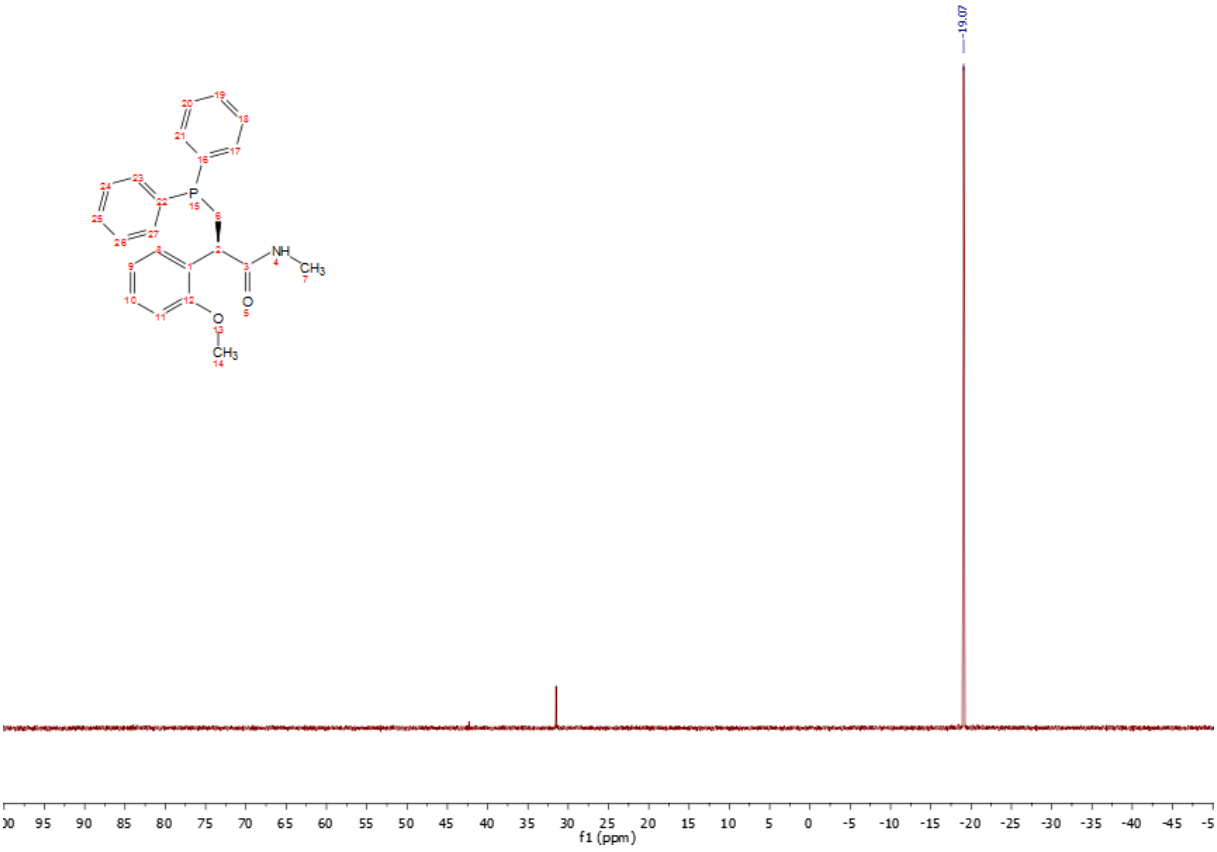
^{1}H NMR for (*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)-N-methylpropanamide **(18e2')**



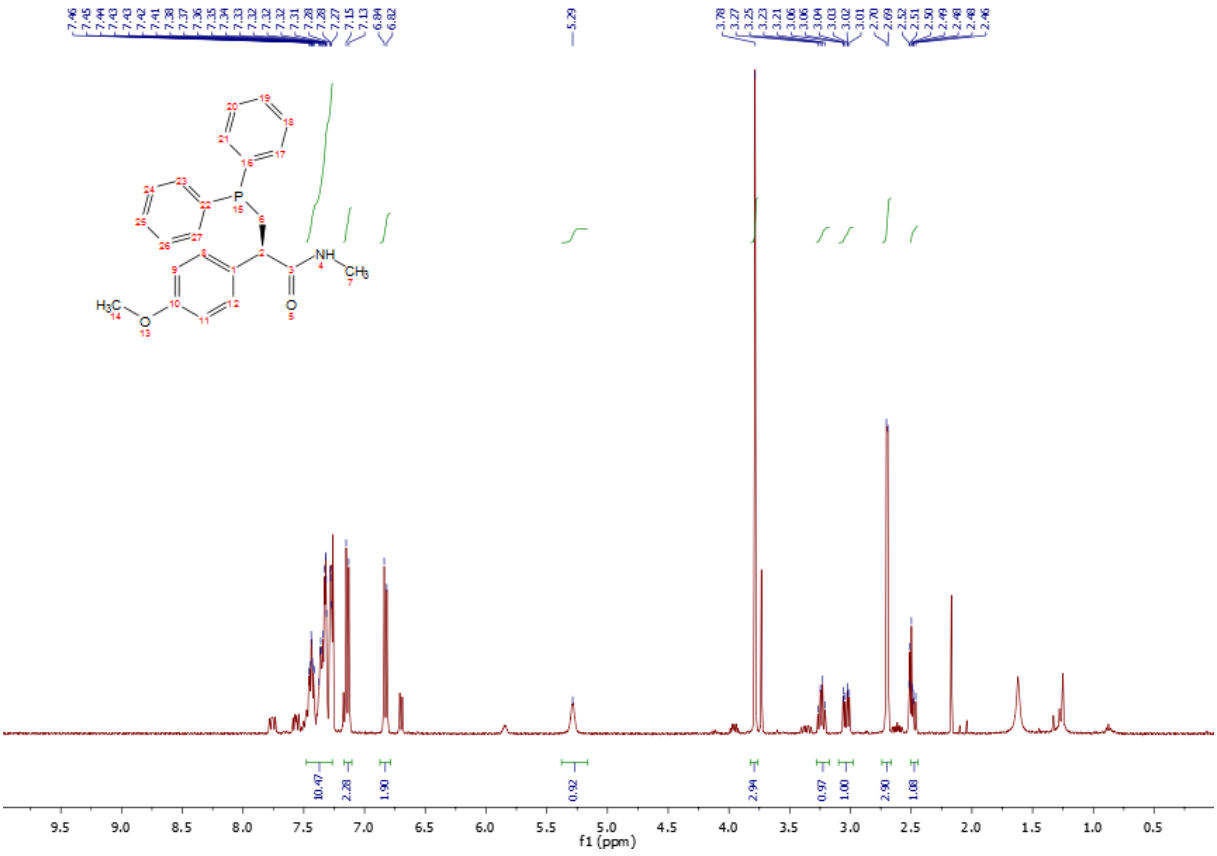
^{13}C NMR for (*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)-N-methylpropanamide **(18e2')**



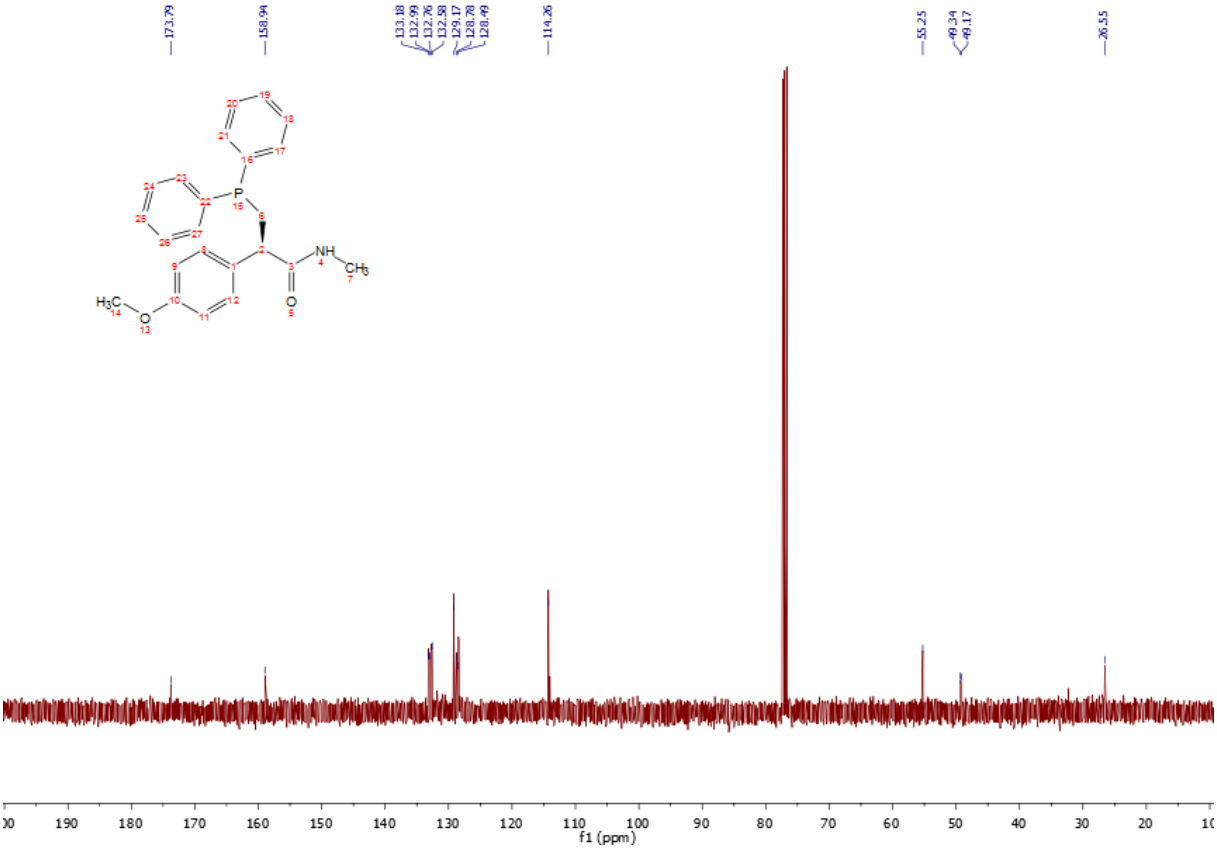
^{31}P NMR for (*R*)-3-(diphenylphosphaneyl)-2-(2-methoxyphenyl)-N-methylpropanamide **(18e2')**



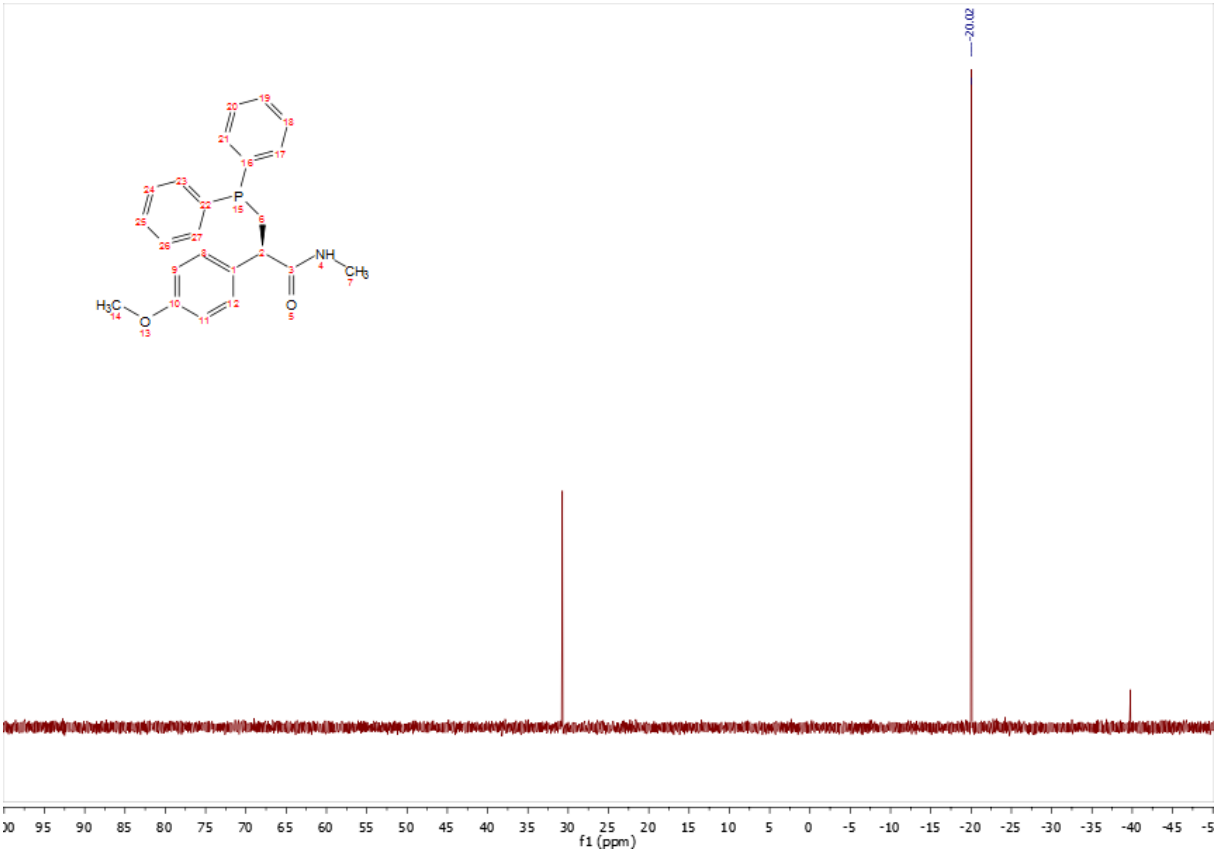
^{1}H NMR for (*R*)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)-N-methylpropanamide **(18e3')**



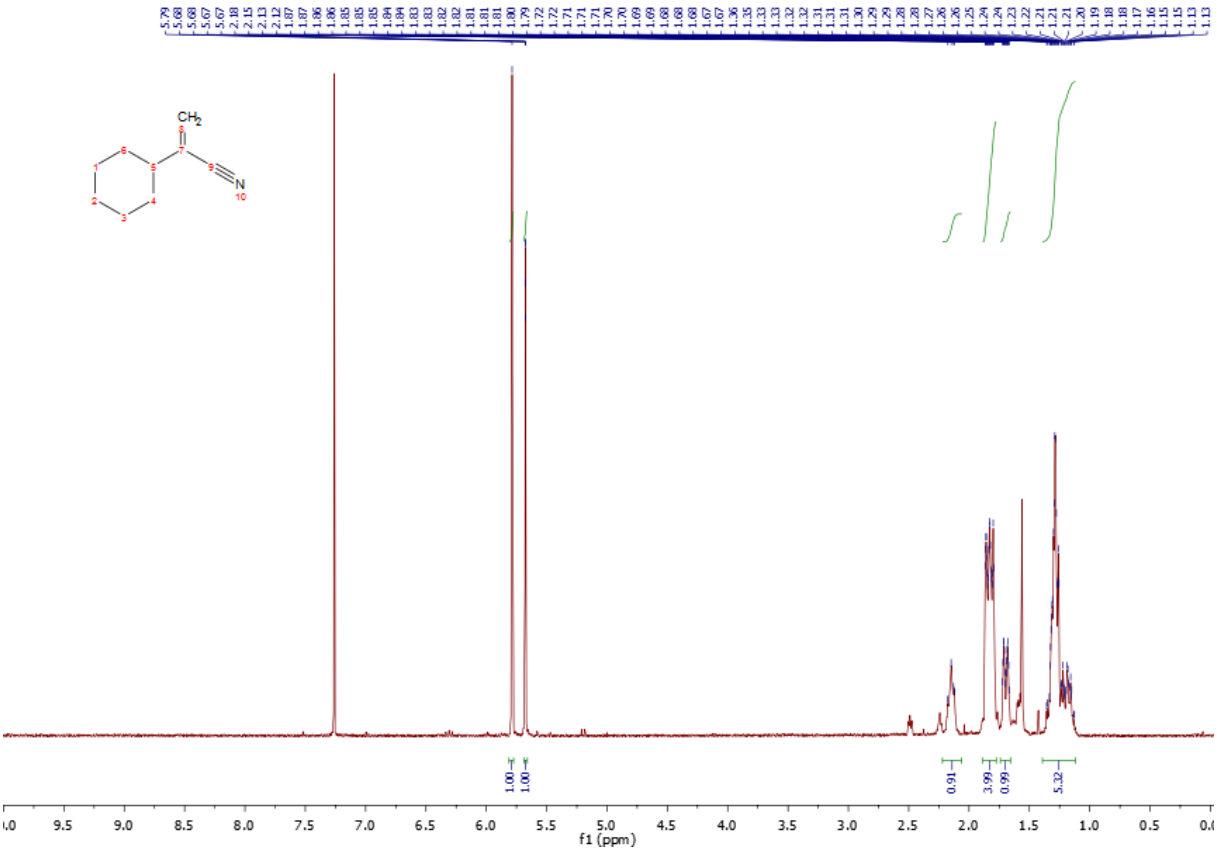
^{13}C NMR for (*R*)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)-N-methylpropanamide **(18e3')**



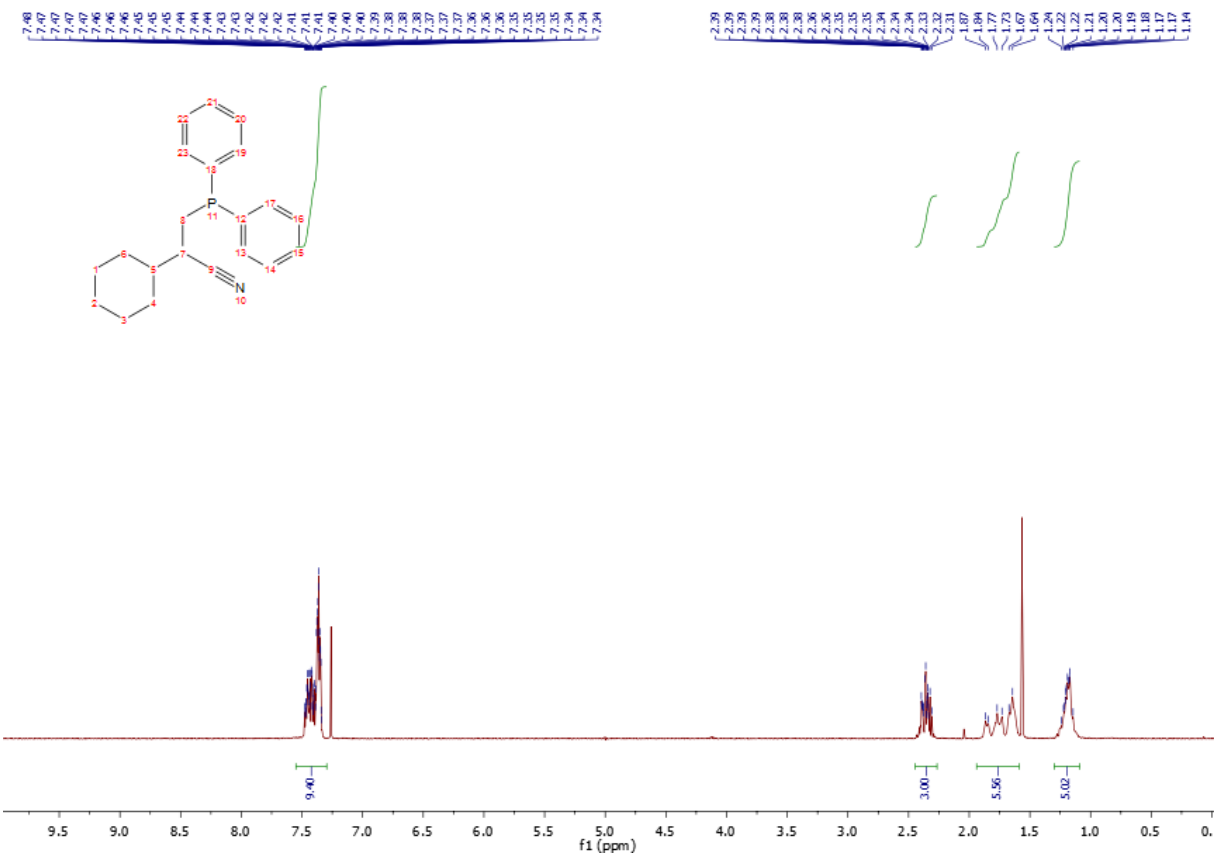
^{31}P NMR for (R)-3-(diphenylphosphaneyl)-2-(4-methoxyphenyl)-N-methylpropanamide **(18e3')**



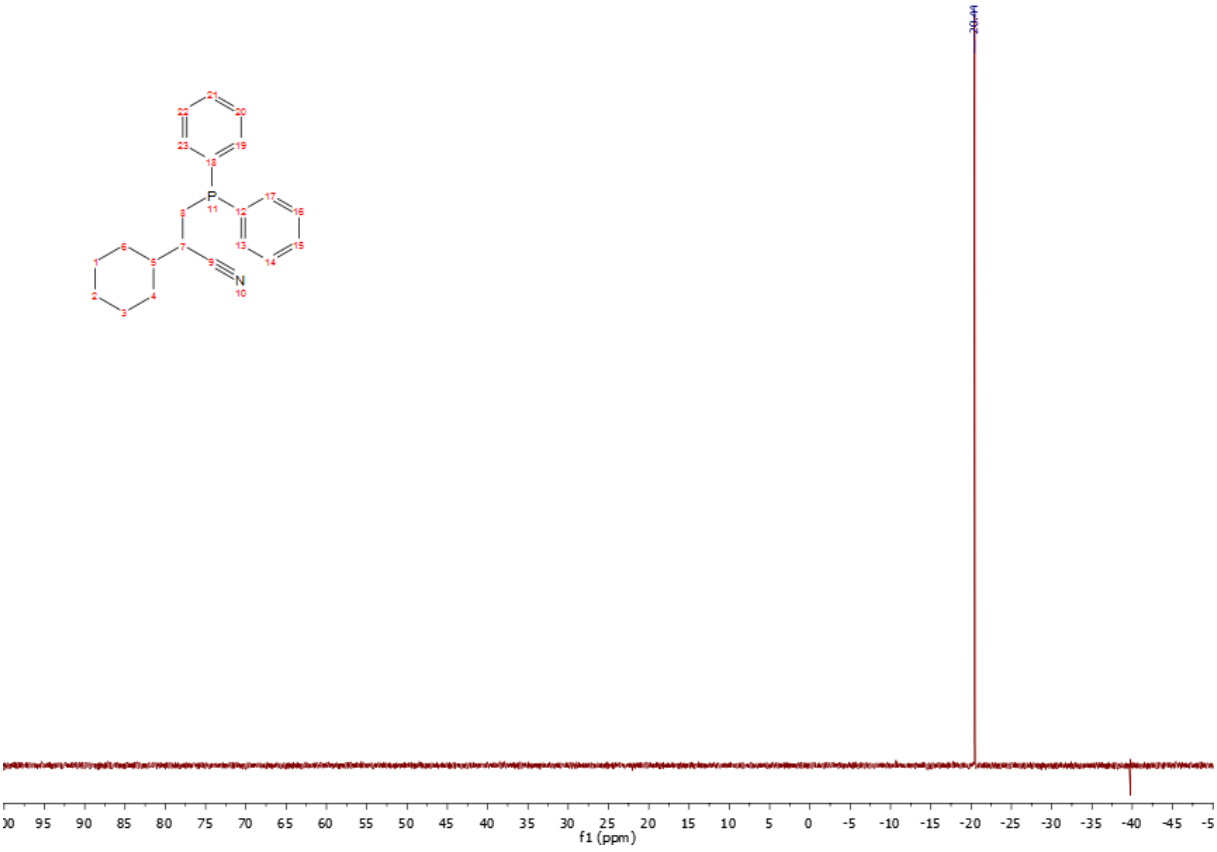
^{1}H NMR for 2-cyclohexylacrylonitrile **(17c)**



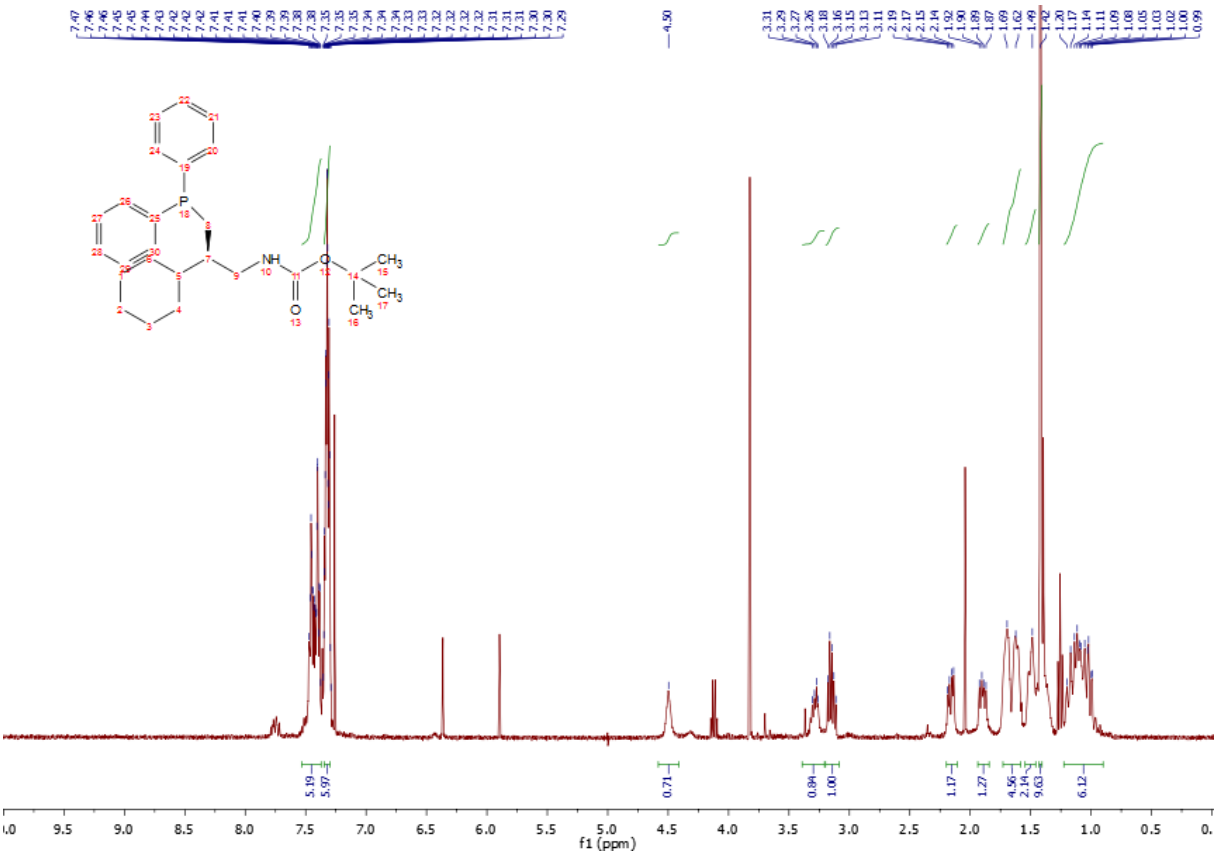
^{1}H NMR for (*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)propanenitrile **(17c')**



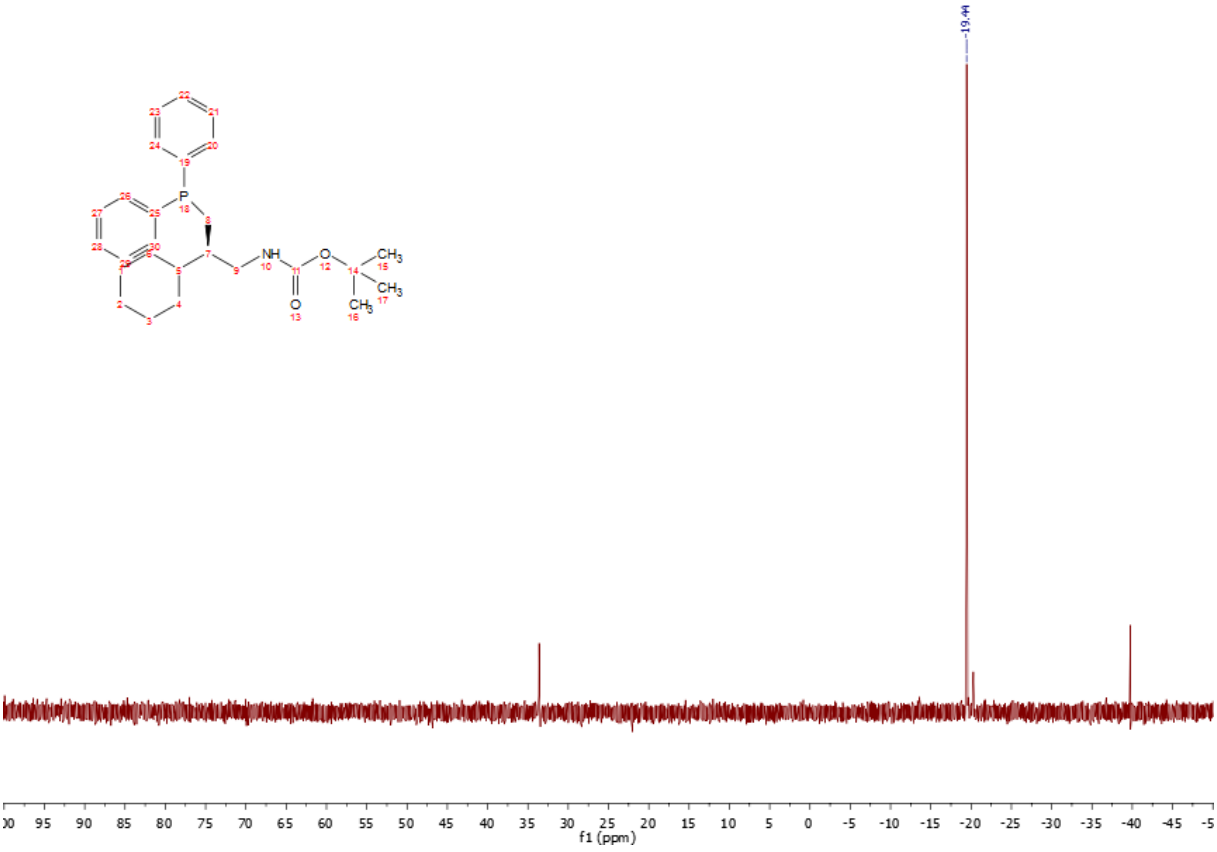
^{31}P NMR for (*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)propanenitrile **(17c')**



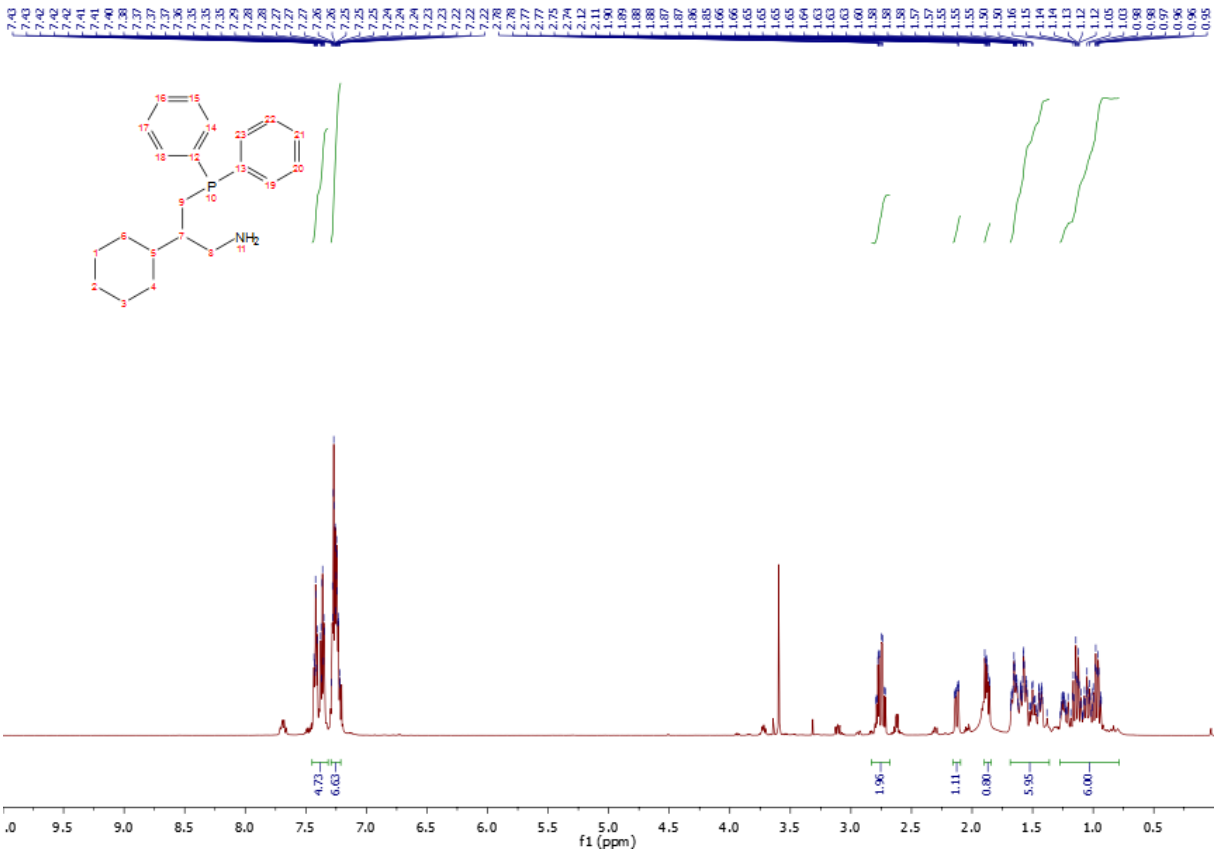
^{1}H NMR for *tert*-butyl (*R*)-(2-cyclohexyl-3-(diphenylphosphaneyl)propyl)carbamate **(29)**



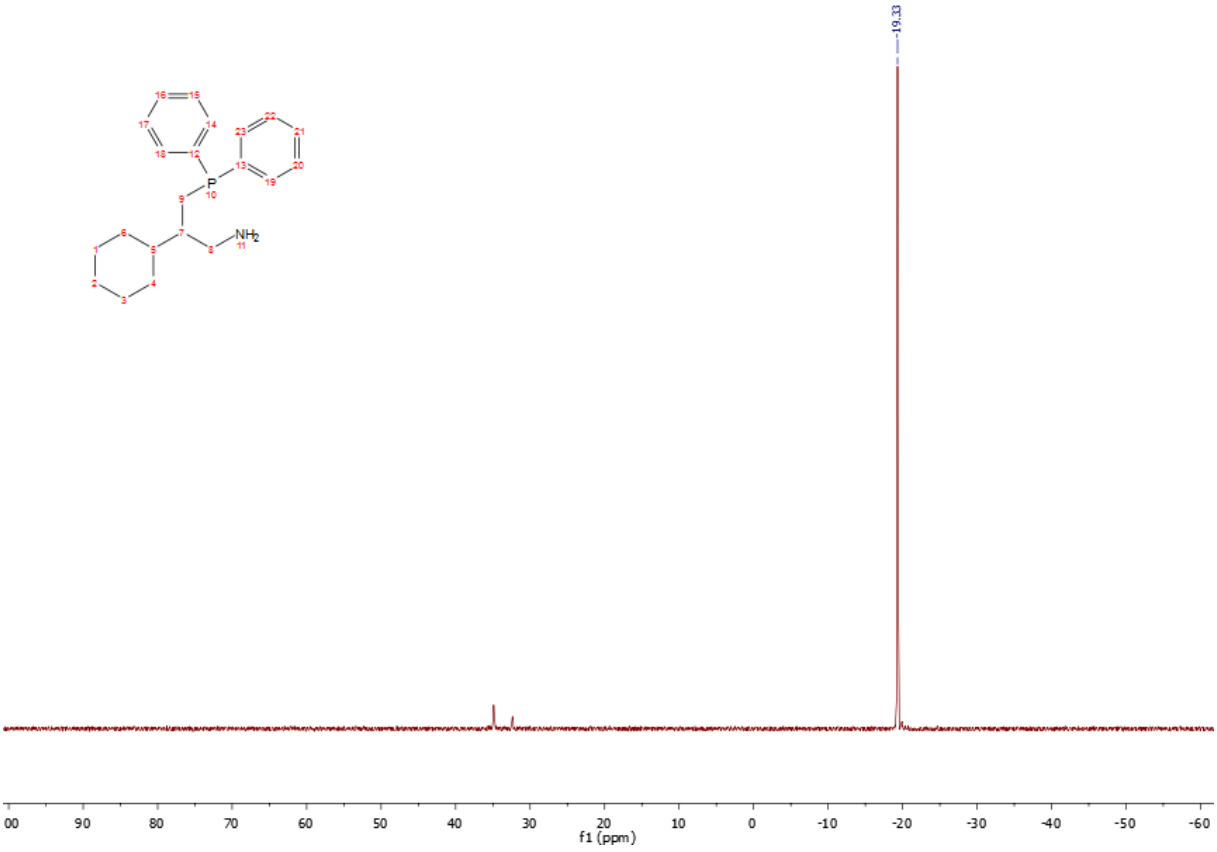
^{31}P NMR for *tert*-butyl (*R*)-(2-cyclohexyl-3-(diphenylphosphaneyl)propyl)carbamate **(29)**



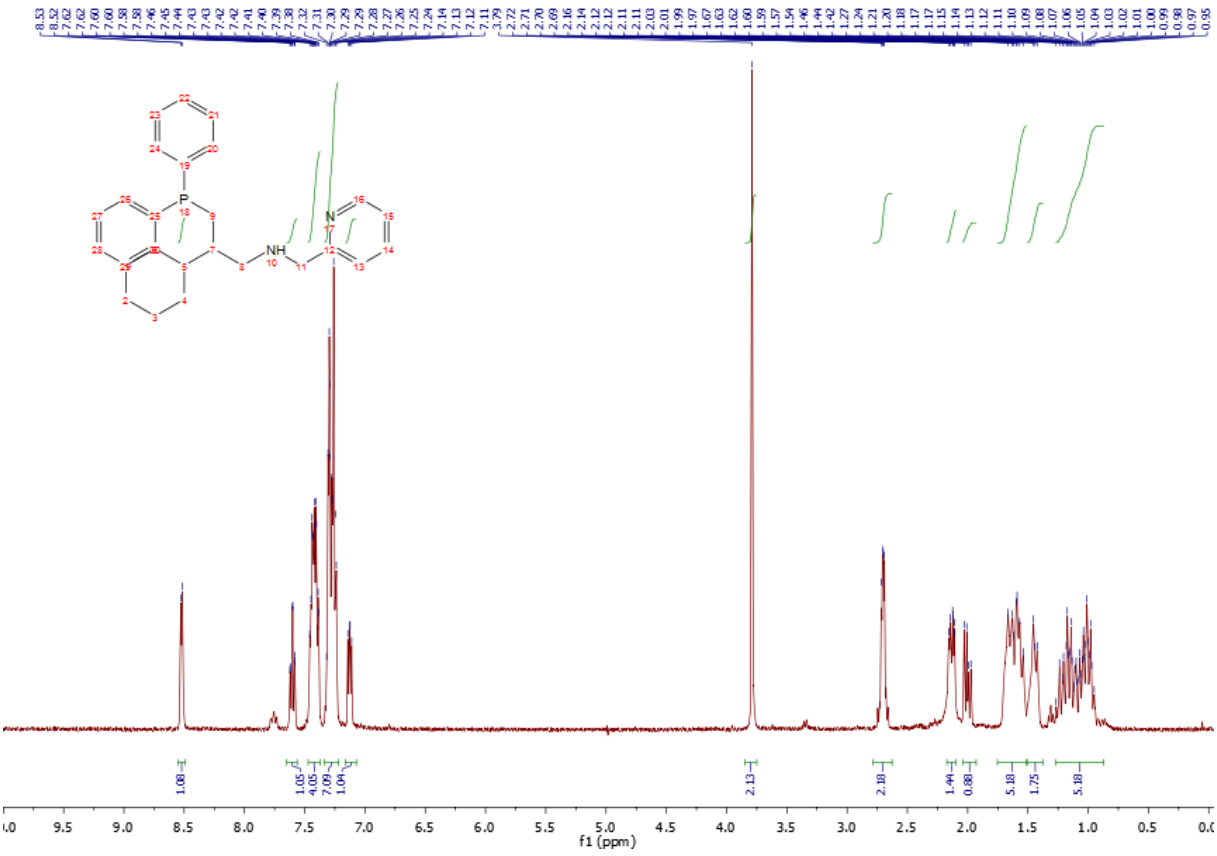
^{1}H NMR for (*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)propan-1-amine **(30)**



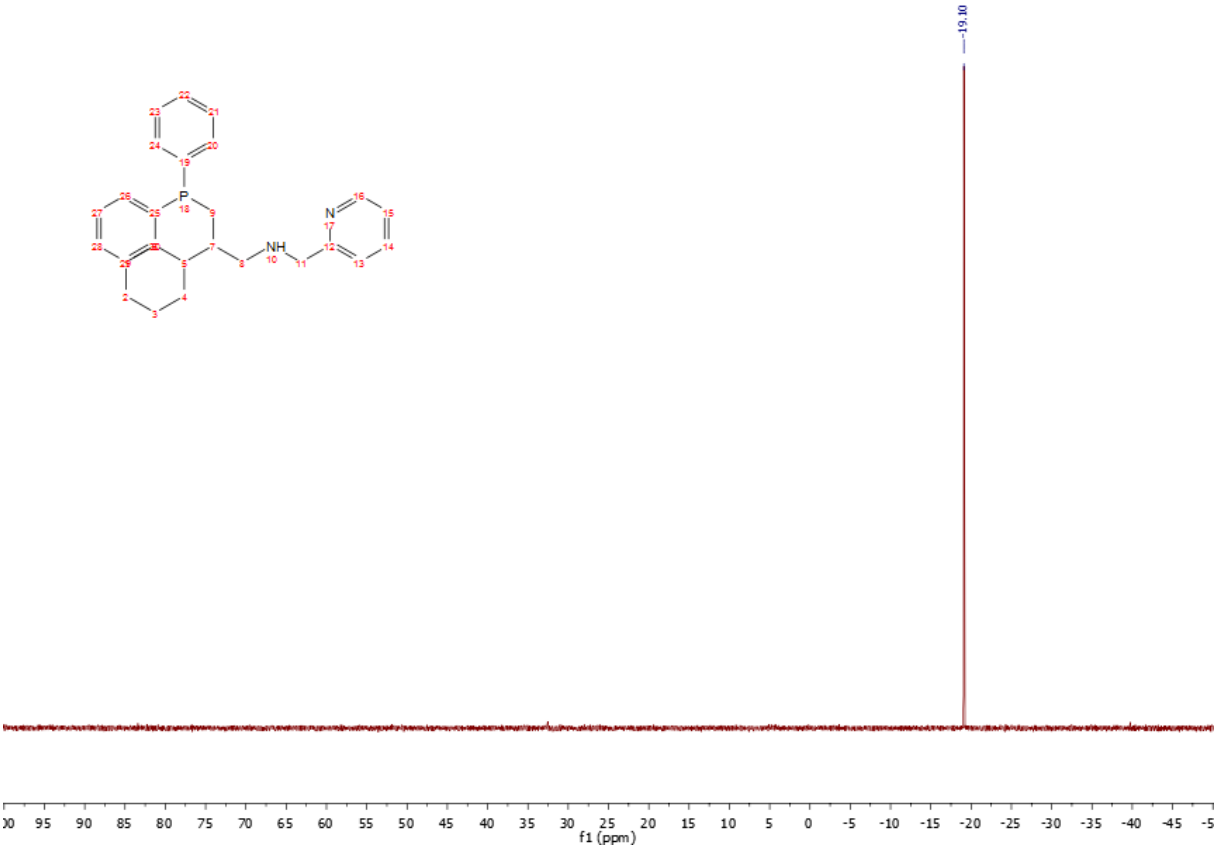
^{31}P NMR for (*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)propan-1-amine **(30)**



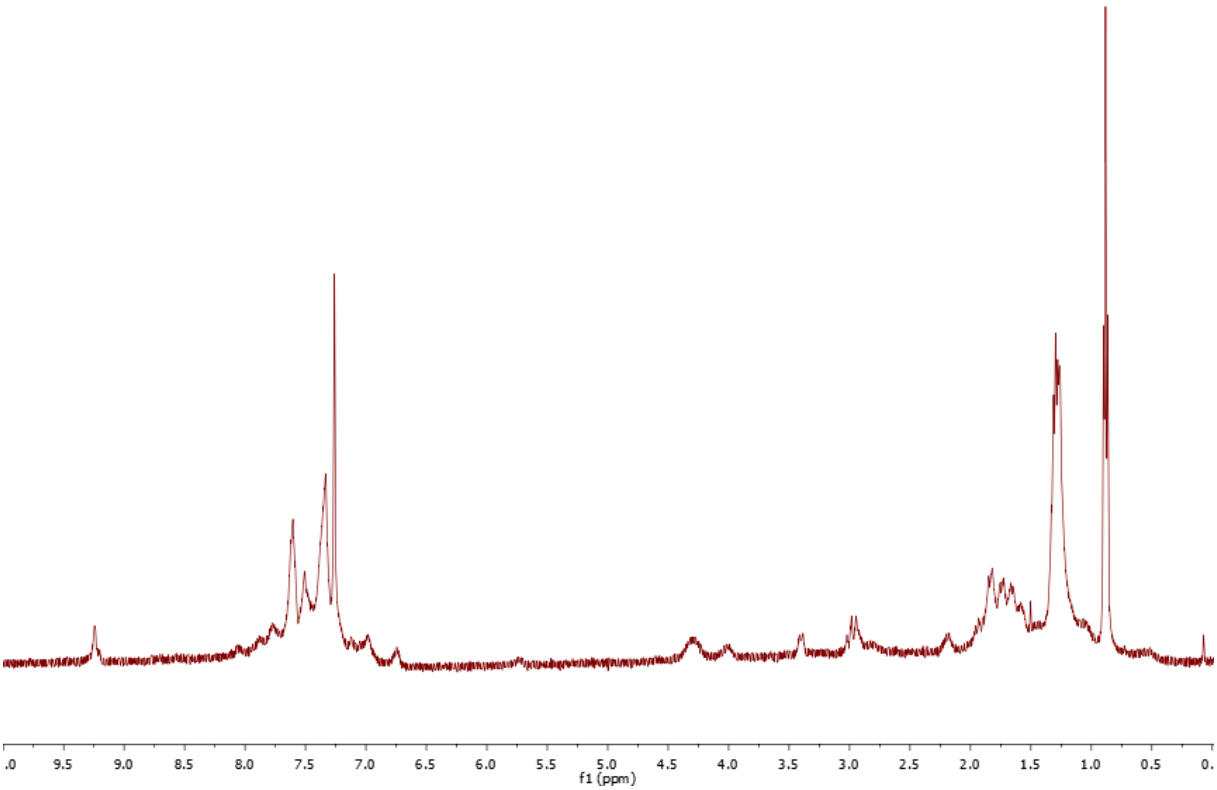
^{1}H NMR for (*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)-N-(pyridin-2-ylmethyl)propan-1-amine **(L8)**



^{31}P NMR for (*R*)-2-cyclohexyl-3-(diphenylphosphaneyl)-N-(pyridin-2-ylmethyl)propan-1-amine **(L8)**



^{1}H NMR for Mn(I)-**L8**



^{31}P NMR for Mn(I)-**L8**