MICHAEL ADDITION OF HETEROAROMATIC COMPOUNDS TO α,β-UNSATURATED PHOSPHONATES AND THEIR REACTIONS

HETEROAROMATİK BİLEŞİKLERİN α,β-DOYMAMIŞ FOSFONATLARA MICHAEL KATILMASI VE TEPKİMELERİ

DİLEK IŞIK TAŞGIN

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This is to certify that we have read this thesis and that in our opinion it is fully adequate, in scope and quality, as a thesis for degree of **Doctor of Philosophy** in **Chemistry**.

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MICHAEL ADDITION OF HETEROAROMATIC COMPOUNDS TO α,β-UNSATURATED PHOSPHONATES AND THEIR REACTIONS

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ABSTRACT

Organophosphorus compounds are synthetic targets of interest because of their value for a variety of industrial, biological and chemical uses. Therefore new or improved methods for the synthesis of phosphonates continue to attract considerable attention.

In this study; it was aimed to synthesize novel heteroaromatics substituted phosphonate analogues by the Michael reaction in the presence of metal trifluorometanesulfonates (triflates) and novel phosphono-pyrrolizine derivatives by an intramolecular cyclization reaction.

In the first part of the study; different vinylphosphonates were synthesized by the Knoevenagel reaction of active methylene compounds and aldehydes.

In the second part of the study; vinylphosphonates including ester, ketone and cyano functional groups were used in the addition reactions of heteroaromatics in the presence of metal triflates as catalysts. The effects of solvent, temperature, catalyst type and substituents on the addition reactions were investigated and optimum reaction conditions were determined. Heteroaromatics substituted new phosphonate analogues which are important precursors for the synthesis of pyrrolizines were obtained regioselectively with Michael addition.

In the last part of the study; the reaction of pyrrole substituted addition products with NaH were investigated to obtain phosphono-pyrrolizine compounds. Phosphono-pyrrolizines were obtained in high yields with ester functionalized pyrrole addition products by the intramolecular cyclization reaction. Ketone and cyano functionalized pyrrole addition products gave novel *N*-phosphono-substituted rearrangement products instead of cyclization products.

Synthesized compounds were purified by chromatographic methods and their structures were identified by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques.

Keywords: Phosphonates, Pyrrolizines, Michael addition, Vinylphosphonates, Metal triflates.

Advisor: Prof. Dr. Canan Unaleroglu, Hacettepe University, Faculty of Science, Department of Chemistry, Organic Chemistry Division.

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ÖZ

Organofosfor bileşikleri çeşitli endüstriyel, biyolojik ve kimyasal kullanım değerlerinden dolayı sentetik hedefler olarak ilgi çekicidirler. Bu nedenle fosfonatların sentezi için yeni ve gelişmiş metodlar dikkat çekmeye devam etmektedir.

Bu çalışmada; yeni heteroaromatikler içeren fosfonat bileşiklerinin metal triflatlar varlığında Michael katılmasıyla ve yeni fosfono-pirolizin türevlerinin moleküliçi halkalaşma tepkimeleriyle sentezlenmeleri hedeflenmiştir.

Çalışmanın birinci bölümünde; aktif metilen bileşiklerinin ve aldehitlerin Knoevenagel kondenzasyon tepkimelerinden değişik vinilfosfonatlar sentezlendi.

Çalışmanın ikinci bölümünde; ester, keton ve siyano fonksiyonel gruplarını içeren vinilfosfonatlar, heteroaromatiklerin metal triflatlar katalizörlüğündeki katılma tepkimelerinde kullanılmıştır. Katılma tepkimesi üzerine çözücü, sıcaklık, katalizör türü ve substitüent etkileri araştırılmış ve optimum tepkime koşulları saptanmıştır. Pirolizinlerin sentezinde önemli başlangıç maddeleri olan heteroaromatikler içeren yeni fosfonat bileşikleri yer seçimli olarak Michael katılması ile elde edilmiştir.

Çalışmanın son bölümünde; fosfono-pirolizin bileşiklerini elde etmek için pirol substitüye katılma ürünlerinin NaH ile tepkimeleri incelenmiştir. Fosfono-pirolizin bileşikleri ester grubu içeren pirol katılma ürünlerinin moleküliçi halkalaşma tepkimelerinden elde edilmiştir. Keton ve siyano grubu içeren pirol katılma ürünleri halkalaşma ürünleri yerine moleküliçi düzenlenme tepkimesiyle yeni *N*-fosfono-substitüye yerdeğiştirme ürünlerini vermiştir.

Sentezlenen bileşikler kromatografik yöntemlerle saflaştırılmış ve yapıları ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR ve HRMS teknikleriyle aydınlatılmıştır.

Anahtar Kelimeler: Fosfonatlar, Pirolizinler, Michael katılması, Vinilfosfonatlar, Metal triflatlar.

Danışman: Prof. Dr. Canan Ünaleroğlu, Hacettepe Üniversitesi, Fen Fakültesi, Kimya Bölümü, Organik Kimya Anabilim Dalı.

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1. INTRODUCTION

Synthesis of phosphonate analogues continues to attract considerable interest because of their biologically important properties and synthetic aspects (Cohen et al., 2003). Phosphonate derivatives have activities as insecticides, herbicides, fungicides, planth growth regulators and drugs to treat bone disorders and also effective transition-state analogue inhibitors for a variety of enzymes. The Michael addition of various nucleophiles to α,β-unsaturated phosphonates is a versatile tool for the synthesis of phosphonate-functionalized molecules.

Vinylphosphonates have found a wide application in organic synthesis. In recent years substituted vinylphosphonates were beside their pharmacological activity, extensively used in polymer sciences as well as in organic synthesis, in particular, for preparing carbon- and heterocycles compounds (Brunner et al., 2000).

Heterocyclic compounds are important structural units in medicinal chemistry and valuable as organic building blocks.

Pyrrolizine alkaloids constitute a very large family of natural products having a wide range of biological activities and are isolated from a variety of natural sources. Derivatives of pyrrolizines are used for antiinflammation and analgesia, as aromatase and tumor inhibitors. In view of intense interest in these compounds, a number of new methodologies and strategies have been developing for their synthesis.

Metal trifluoromethanesulfonates (triflates) are new type of Lewis acids which are different from conventional Lewis acids. Metal triflates are water compatible Lewis acids. Many useful reactions are catalyzed by metal triflate in aqueous media. Only catalytic amounts of the triflates are enough to complete the reactions and they can be recovered easily after reactions and reused without loss of activity.

In this study; it was aimed to synthesize heteroaromatic substituted phosphonate analogues by the addition reaction of heteroaromatics to functionalized vinylphosphonates and their cyclization reactions. Substituted α,β-unsaturated

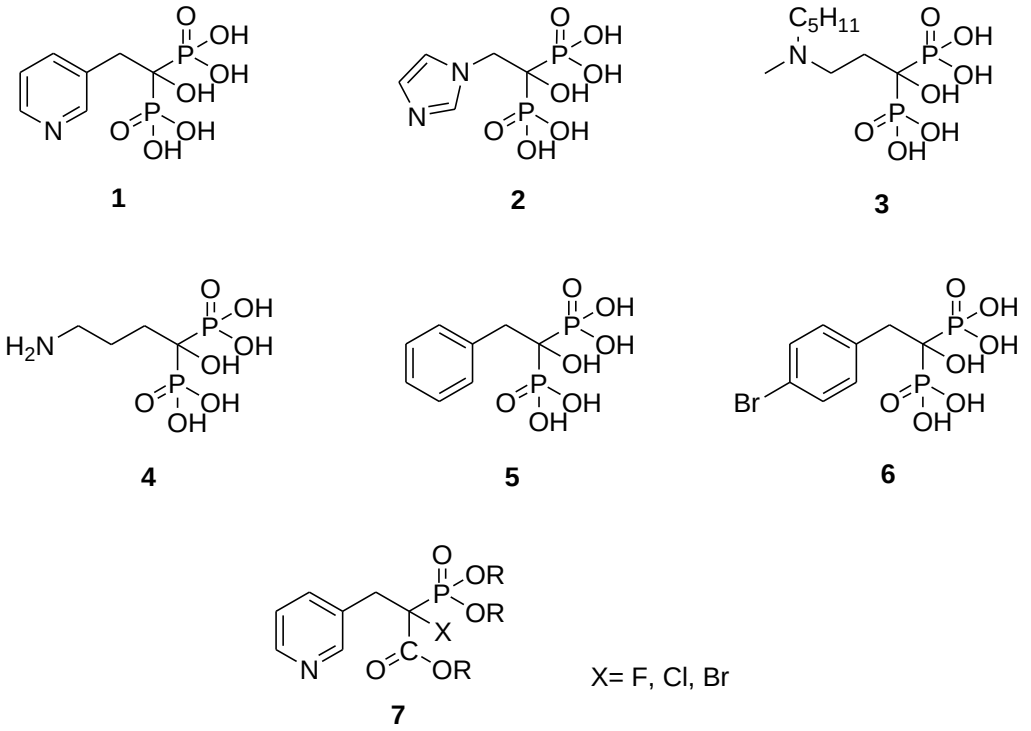
phosphonates which were prepared from active methylene compounds and aldehydes, were used as Michael acceptors in the addition of heteroaromatic compounds. The effects of solvent, temperature, catalyst type, amount of catalyst and substituents on the addition reactions were investigated. The obtained Michael addition products are valuable precursors for the synthesis of pyrrolizine ring structures. Therefore the cyclization reactions of these products were also investigated to obtain the pyrrolizine ring structures in the presence of NaH.

2. GENERAL INFORMATION

2.1. Importance of Phosphonates

Phosphorus is an essential structural constituent of many biomolecules and plays a crucial role in energy conservation and metabolic regulation (Guo et al., 2009). Organophosphorus compounds are important substrates in the study of biochemical processes. Therefore, tetracordinated pentavalent phosphorus compounds, which include at least a phosphonic acid ($P(O)(OH)_2$), phosphinic acid (P(O)(OH)R) (in which R may be H, alkyl or aryl), or a phosphonate group ($P(O)(OR)_2$), are widely used as biologically active compounds (Engel, 1977; Palacios et al., 2005).

Phosphonates are not very abundant in nature. However, they have attracted considerable synthetic and pharmacological interest because of their diverse bioactivities. They have found widespread use as enzyme inhibitors, antibacterial agents, anti-HIV agents, plant growth regulators and drugs to treat bone disorders (Peng et al., 2008). Bisphosphonates are the very well-known type of phosphonates. They are widely used drugs for the treatment and prevention of osteoporosis, Paget's disease, tumor-induced osteolysis and hypercalcemia and have also been found to have antiparasitic, antibacterial, herbicidal and anticancer properties (Zhang et al., 2006). The most potencially used bisphosphonates are nitrogen-containing bisphosphonates such as; risedronate (**1**), zoledronate (**2**), ibandronate (**3**) and alendronate (**4**). Another type of bisphosphonates are non-nitrogen-containing bisphosphonates which are deaza analogues of risedronate (**5** and **6**) have also biological activities. Phosphonocarboxylate analogues of risedronate (**7**) were also found as active to reduce bone mineral affinity and can inhibit tumor cell invasion within bone (Scheme 2.1) (Marma et al., 2007).



Scheme 2.1. Examples of phosphonate analogues.

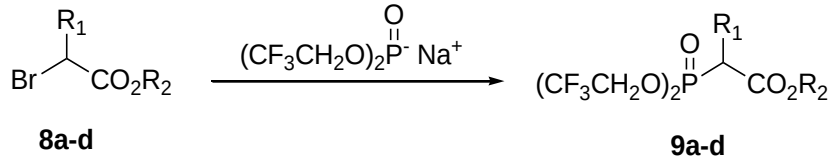
2.2. Synthesis of Phosphonate Analogues

Synthesis of phosphonate analogues is a growing field in organic chemistry because of their important biological activities. There are many different reactions for the synthesis of phosphonate analogues. The most often used reactions are the carbon-phosphorus (C-P), carbon-carbon (C-C), carbon-nitrogen (C-N) and carbon-oxygen (C-O) bond formation processes (Palacios et al., 2005).

2.2.1. Carbon-Phosphorus (C-P) Bond Formation

The first method for the generation of a carbon-phosphorus (C-P) bond is Michaelis-Becker reaction. This method involves the nucleophilic phosphorylation of a saturated carbon by the salts of dialkylphosphites. In this reaction, the salts of dialkylphosphites were obtained by the reaction between a dialkylphosphite and a strong base (Eymery et al., 1999; Rodrigues et al., 2002). The Michaelis-Becker reaction is a well known method for the synthesis of phosphonates but the yields of the obtained phosphono esters are low.

Michaelis-Becker reaction was used by Ciszewski et al. (1999) to prepare *bis*(2,2,2-trifluoroethyl)phosphono esters **9a-d**. In this reaction, the anion of *bis*(2,2,2-trifluoroethyl)phosphite is a nucleophile toward bromo esters **8a-d**. The best results were obtained with unhindered bromo ester **8a**, which was converted to the corresponding phosphonate **9a** in 30% yield. With the secondary bromo esters **8b-d**, lower yields for **9a-d** were obtained (Scheme 2.2).

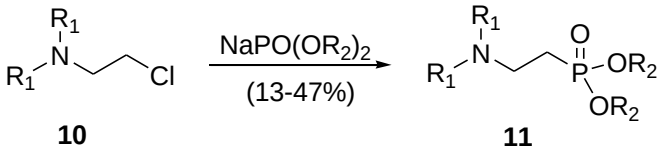


8a-d **9a-d**

a) R_1 = H, R_2 = CH_2CH_3, **b**) R_1 = CH_3, R_2 = CH_2CH_3
c) R_1 = CH_2CH_3, R_2 = CH_2CH_3, **d**) R_1 = CH_3, R_2 = Cl

Scheme 2.2. Synthesis of *bis*(2,2,2-trifluoroethyl)phosphono esters **9a-d** with Michaelis-Becker reaction.

Xu et al. (1990) used Michaelis-Becker reaction for the synthesis of β-aminophosphonates. They synthesized *N*,*N*-disubstituted dialkyl 2-aminoethyl-phosphonates **11** and their derivatives by the reaction of dialkyl (2-chloroethyl)-amines **10** with the sodium salt of dialkylphosphonate (Scheme 2.3). This method gave the products with low yields.



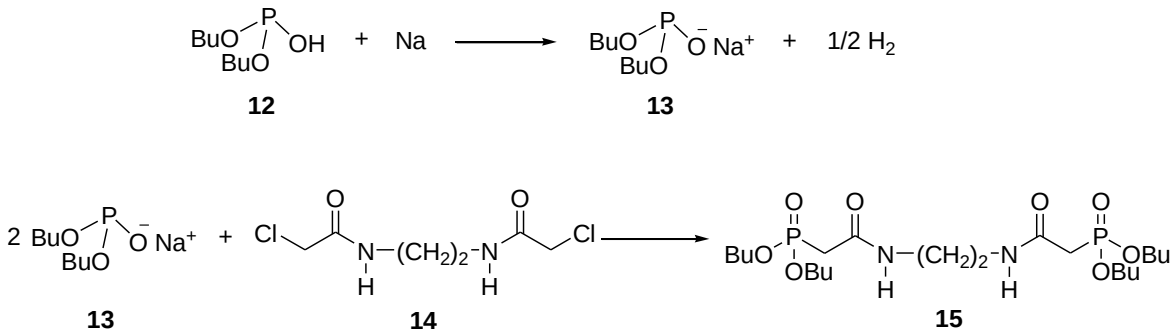
10 **11**

R_1 = Bu, $^nC_8H_{17}$
R_2 = Et, Bu, $^nC_8H_{17}$

Scheme 2.3. Synthesis of *N*,*N*-disubstituted dialkyl 2-aminoethylphosphonates **11** with Michaelis-Becker reaction.

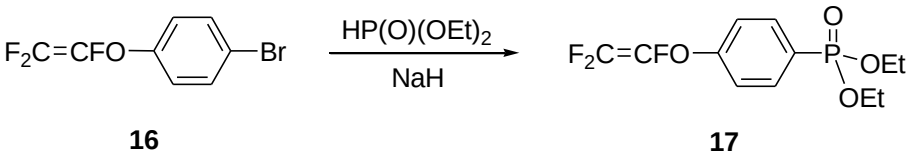
For the synthesis of symmetrical bisphosphonates the Michaelis-Becker reaction was used by Rodrigues et al. (2002). Firstly, sodium salt of dibutylphosphite **13**

was prepared from dibutylphosphite **12** and metallic sodium at room temperature. Then *N*,*N'*-bis(chloroacetyl)ethylenediamine **14** was added to this reaction mixture and *N*,*N'*-bis(dibutylphosphonoacetyl)ethylenediamine **15** was obtained with 25% yield (Scheme 2.4).



Scheme 2.4. Synthesis of symmetrical bisphosphonates with Michaelis-Becker reaction.

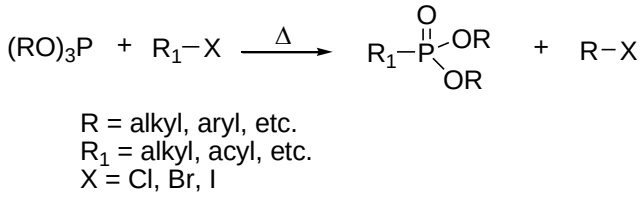
Aromatic trifluorovinyl ethers are good monomers for obtaining thermoplastic and thermoset polymers. Synthesis of fluoropolymers incorporating aromatic or aliphatic monomers and including sulphonic and phosphonic acid functionalities have a growing interest because of their potential applications in proton exchange membranes for fuel cells and ionic membranes. Souzy et al. (2004) used Michaelis-Becker reaction to obtain new aromatic perfluorovinyl ether monomers containing phosphonic acid functionalities. The product 4-[(α,β,β-trifluorovinyl)oxy]-benzene diethylphosphonate **17** was obtained in 12% yield from the reaction of 4-[(α,β,β-trifluorovinyl)oxy]bromo benzene **16** with the phosphonic salt (Scheme 2.5).



Scheme 2.5. Synthesis of 4-[(α,β,β-trifluorovinyl)oxy]benzene diethylphosphonate **17**.

A second method for generation of a carbon-phosphorus (C-P) bond is Michaelis-Arbuzov reaction. Classical Michaelis-Arbuzov reaction is the nucleophilic

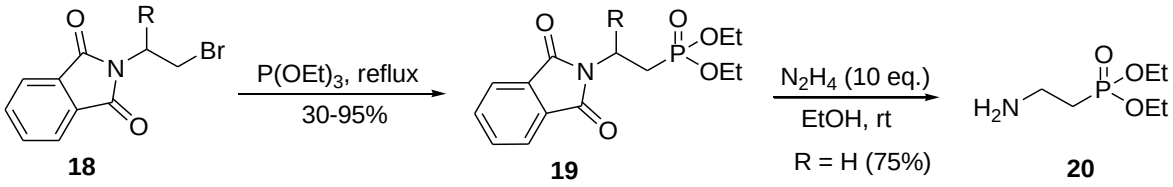
phosphorylation of a saturated carbon by reaction of an ester of trivalent phosphorus with an alkyl halide. This reaction is the most useful transformation of this type and widely employed for the synthesis of phosphonates (Scheme 2.6) (Bhattacharya et al., 1981; Eymery et al., 1999).



Scheme 2.6. General reaction pathway for the Michaelis-Arbuzov reaction.

In Michaelis-Arbuzov reaction, the variation of the products depends on the choice of phosphites and alkyl halides and this reaction generally proceeds without the help of catalysts. However, in some cases to use catalysts are necessary. The reaction is limited only by the availability of the phosphites and alkyl halides.

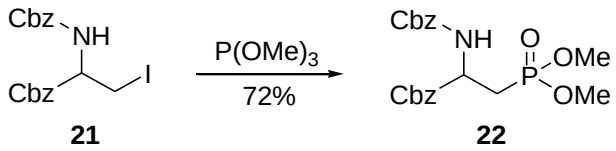
Gali et al. (2000) synthesized phthaloylaminophosphonates **19** in good yields from *N*-(bromoethyl)phthalimides **18** and triethyl phosphite by the Michaelis-Arbuzov reaction. The *N*-substituted phthaloyl-β-aminophosphonate **19** was dephthaloylated to β-aminoethylphosphonate **20** with hydrazine at room temperature (Scheme 2.7).



Scheme 2.7. Synthesis of phthaloylaminophosphonates **19** and β-aminoethyl phosphonate **20**.

Brachwitz et al. (1997) synthesized the free aminophosphonic acids or their derivatives by the Michaelis-Arbuzov reaction from *N*-protected aminoalkylhalides. Compound **21** was converted to the dimethylphosphonate **22** by treatment with

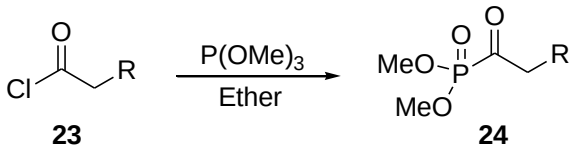
trimethylphosphite (Scheme 2.8). Then, the blocking groups were removed to give the free aminophosphonic acids.



21 **22**

Scheme 2.8. Synthesis of dimethylphosphonate **22** with Michaelis-Arbuzov reaction.

Michaelis-Arbuzov reaction was also used for the synthesis of α-ketophosphonates using acyl halides instead of alkyl halides. Afarinkia et al. (1997) were synthesized α-ketophosphonates **24** with the reaction of a phosphite and an acid chloride **23** under relatively mild conditions (Scheme 2.9).

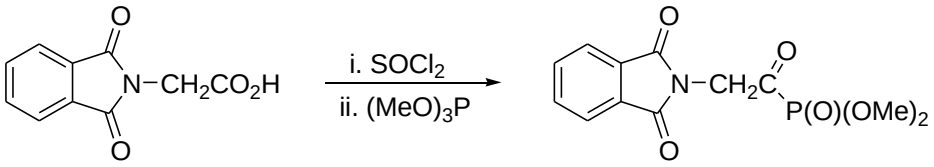


23 **24**

R = H, Me, Et, ^{i}Pr, C_8H_{17},
4-$MeOC_6H_4$, Ph, 2-thiophenyl

Scheme 2.9. Synthesis of α-ketophosphonates **24** with Michaelis-Arbuzov reaction.

Griffiths et al. (1997) used the Michaelis-Arbuzov reaction for the synthesis of α-ketophosphonates. Treatment of *N*-phthaloylglycine **25** with thionyl chloride gave the corresponding acid chloride and α-ketophosphonate **26** was obtained with the subsequent reaction of acid chloride with trimethylphosphite (Scheme 2.10).

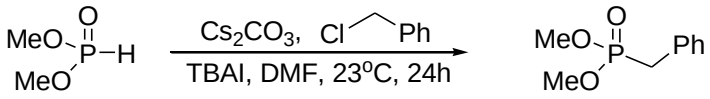


25 **26**

Scheme 2.10. Michaelis-Arbuzov reaction for the synthesis of α-ketophosphonate **26**.

Although the Michaelis-Becker and Michaelis-Arbuzov reactions are traditional methods for obtaining organophosphonate esters, these reactions have some major drawbacks. In Michaelis-Arbuzov reaction; the requirement of elevated temperature limits the scope of the substrate suitable for the reaction and very long reaction times lead to a complicated mixture of side products. In Michaelis-Becker reaction; the use of strong anhydrous base and also longer reaction times result in poor yield of phosphonates.

To improve new methods for obtaining phosphonates, Cohen et al. (2003) used various alkali metal carbonates. They found that cesium carbonate was the most successful base. They performed the reaction with dimethylphosphite **27** and benzyl chloride in the presence of TBAI at 23°C. They obtained dimethyl benzylphosphonate **28** in 97 % yield with Cs_2CO_3 (Scheme 2.11). They employed this procedure to various dialkylphosphites and alkyl halides and they obtained the products in good yields.

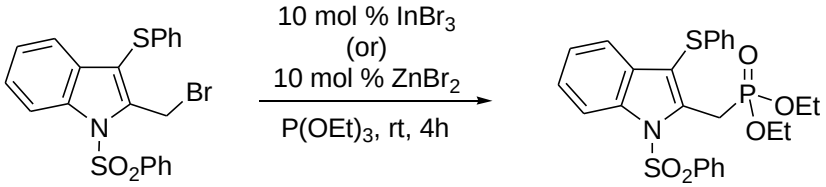


27 **28**

Scheme 2.11. Synthesis of dimethyl benzylphosphonate **28** in the presence of Cs_2CO_3.

With similar reasons Rajeshwaran et al. (2011) performed the Michaelis-Arbuzov reaction with Lewis acids at room temperature. When the reaction of

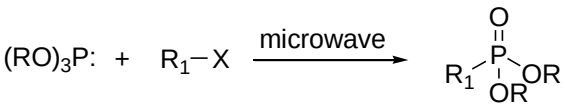
bromomethylindole **29** was performed with triethylphosphite in the presence of 10 mol % of $InBr_3$ at room temperature and phosphonate ester **30** was obtained in 80% yield (Scheme 2.12). They found that $ZnBr_2$ is also a suitable catalyst for this reaction. They performed the Lewis acid-mediated Michaelis-Arbuzov reaction successfully with a wide variety of aryl and heteroarylmethyl bromides to afford the corresponding phosphonates in good yields.



29 **30**

Scheme 2.12. Lewis acid-mediated Michaelis-Arbuzov reaction between bromomethylindole **29** and triethylphosphite.

Microwave irradiation is an applicable method for the synthesis of phosphonates. This method allows the synthesis of phosphonates using considerably shorter times at elevated temperatures. Kiddle et al. (2000) used microwave irradiation for the synthesis of alkylphosphonates **33** from phosphites **31** and alkyl halides **32** (Scheme 2.13). They obtained the corresponding phosphonates in good yields.

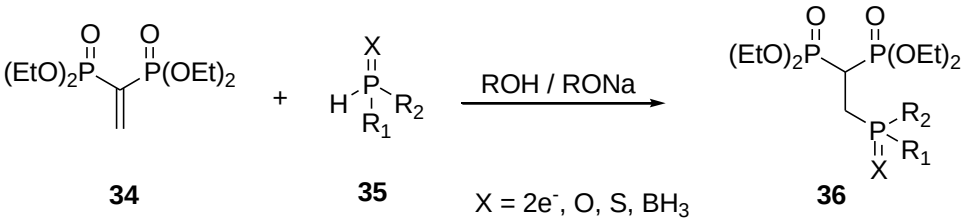


31 **32** **33**

R = CH_3, C_2H_5, $CH(CH_3)_2$, $(CH_3)_3Si$
R1 = CH_3, CH_3CH_2, $CH_3CH_2CH_2$, $CH_3CH_2CH_2CH_2$
X = I

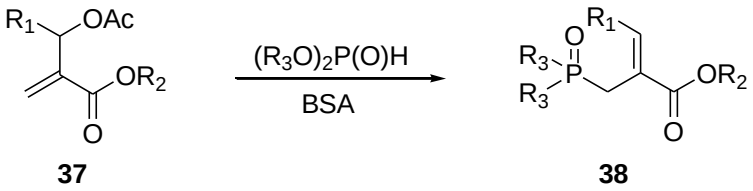
Scheme 2.13. Microwave irradiated Michaelis-Arbuzov reaction.

Delain-Biotin et al. (2005) used Michael addition for forming C-P bonds. They used tetraethyl ethylidenediphosphonate (**34**) as a Michael acceptor for the addition of phosphites **35**. Addition of phosphites **35** to tetraethyl ethylidenediphosphonate (**34**) gave the addition products **36** in 67-93% yields (Scheme 2.14).



Scheme 2.14. Michael addition of phosphites **35** to tetraethyl ethylidenedi-phosphonate (**34**).

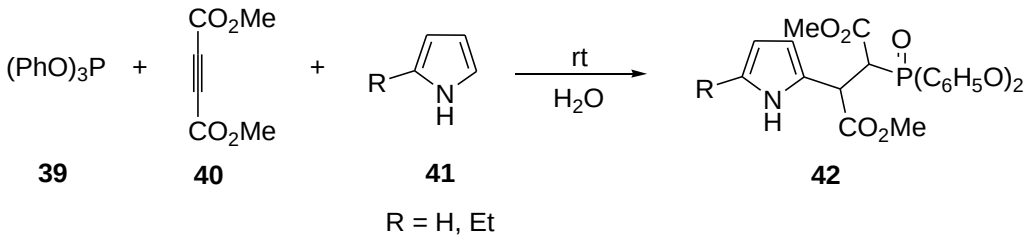
Badkar et al. (2007) synthesized the phosphono unsaturated esters by the addition of dialkyl phosphites to the allylic acetates **37**. They obtained phosphono unsaturated esters **38** with good yields except with benzyl phosphate (Scheme 2.15).



R_1 = Ph, 2-furyl, *p*-MeO-C_6H_4, *p*-Cl-C_6H_4, *p*-F-C_6H_4, *p*-Br-C_6H_4, Me
R_2 = Me, *t*-Bu
R_3 = Me, Et, Bn, *i*-Pr

Scheme 2.15. Addition of dialkyl phosphites to the allylic acetates **37**.

Pyrrole phosphonate esters **42** were synthesized from the reaction of triphenylphosphite **39** and dimethyl acetylenedicarboxylate **40** in the presence of pyrrole **41** by Maghsoodlou et al. (2006) (Scheme 2.16). They reported an efficient one-pot synthesis in aqueous media of pyrrole phosphonate esters.

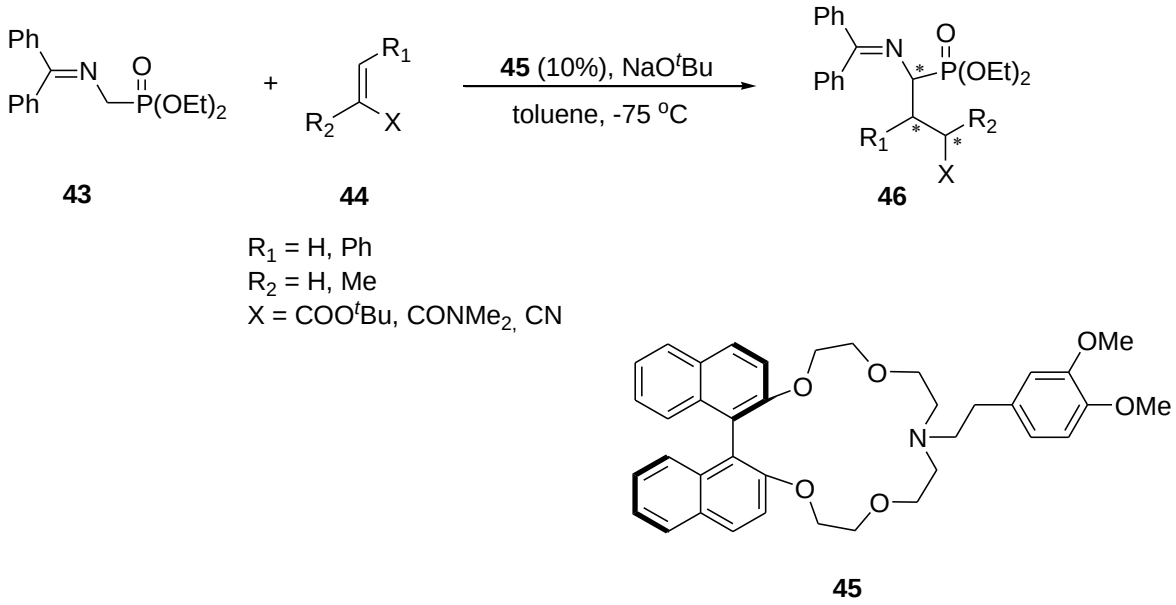


Scheme 2.16. Synthesis of pyrrole phosphonate esters **42**.

2.2.2. Carbon-Carbon (C-C) Bond Formation

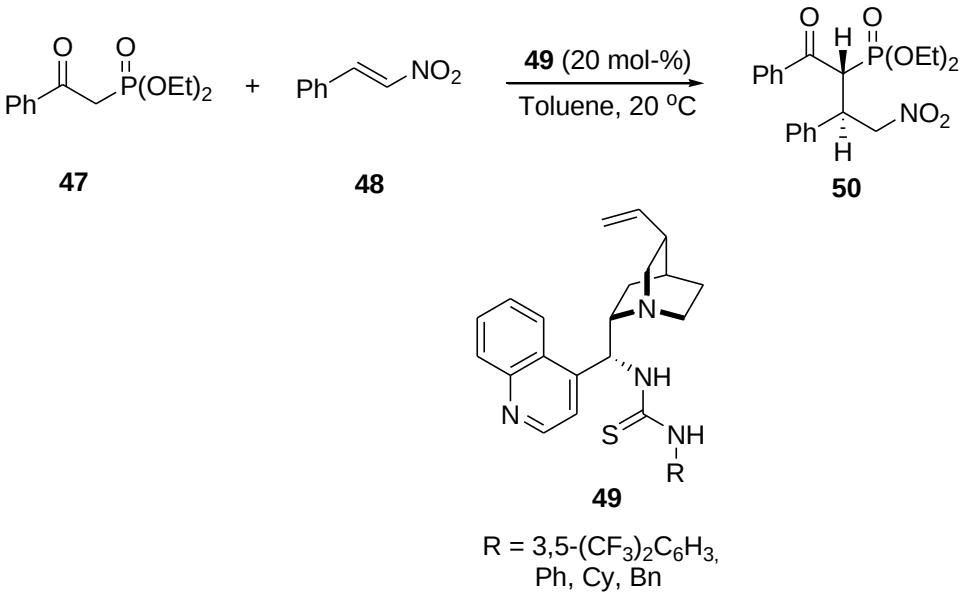
Carbon-carbon (C-C) bond forming transformations are versatile tools in organic chemistry. Among the different methods applied for the synthesis of phosphonate analogues the most often used carbon-carbon bond forming reaction is the Michael addition. Addition to acrylic acid derivatives, nitro olefins, imines and vinylphosphonates are some important examples of achieving the phosphonate analogues in literature.

Pham et al. (2011) reported the asymmetric synthesis of α-aminophosphonates **46** by the Michael addition of *N*-protected aminomethylenephosphonate **43** onto acrylonitriles **44** in the presence of azacrowns **45** as catalysts (Scheme 2.17). They found that these macrocycles catalyzed the addition of aminomethylenephosphonate to a wide range of Michael acceptors, although the stereoselectivity was only good in cases where the Michael acceptor possessed cyano group.



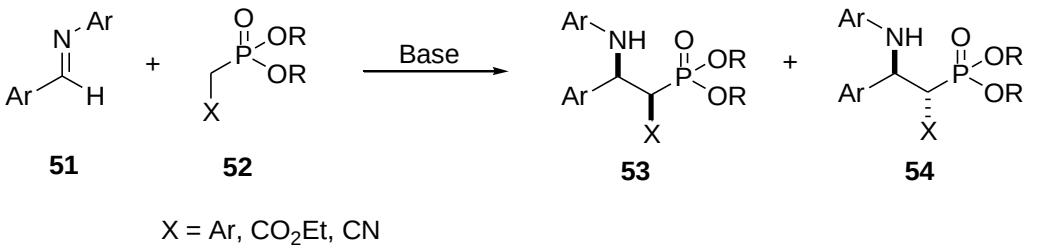
Scheme 2.17. Michael addition of *N*-protected aminomethylenephosphonate **43** onto acrylonitriles **44** in the presence of azacrowns **45** as catalysts.

The first organocatalyzed asymmetric Michael addition of simple β-oxo phosphonates **47** to nitro olefins **48** was reported by Hu et al. (2011). They obtained valuable α-substituted β-oxo phosphonates **50** in satisfactory yields with good to excellent enantioselectivities with chiral thiourea catalysts **49** (Scheme 2.18).



Scheme 2.18. Synthesis of α-substituted β-oxo phosphonates **50** with chiral thiourea catalysts **49**.

Michael addition of carbanions derived from phosphonates to imines **51** was studied by Kirilov et al. (1980) for the preparation of α-aryl-substituted β-aminophosphonates **53** and **54**. Thus, addition of α-phosphonate carbanions, generated from phosphonates **52** using 0.5 equiv of $NaNH_2$, to imines **51** in ether or liquid ammonia afforded syn- **53** and anti-α-aryl-β-aminophosphonates **54** (Scheme 2.19).



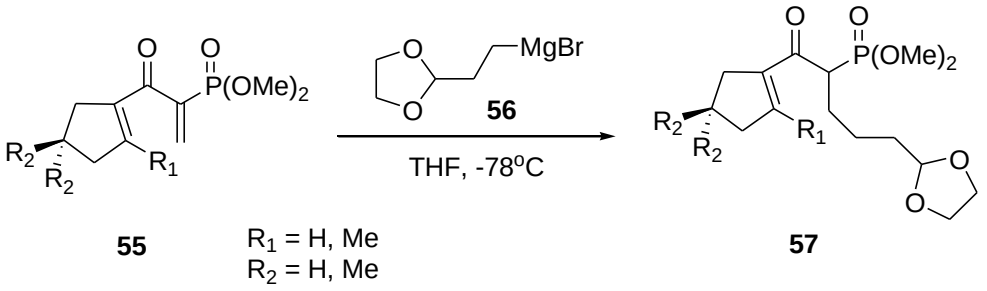
51 **52** **53** **54**

X = Ar, CO_2Et, CN

Scheme 2.19. Michael addition of phosphonates **52** to imines **51**.

Vinylphosphonates containing electron-withdrawing groups at the α-position, such as alkoxycarbonyl, carbonyl, cyano, sulfinyl, sulfonyl or phosphoryl groups are valuable Michael acceptors (Janecki et al., 2009). There are many studies on the Michael addition to vinylphosphonates in literature for obtaining functionalized phosphonates (Minami et al., 1992).

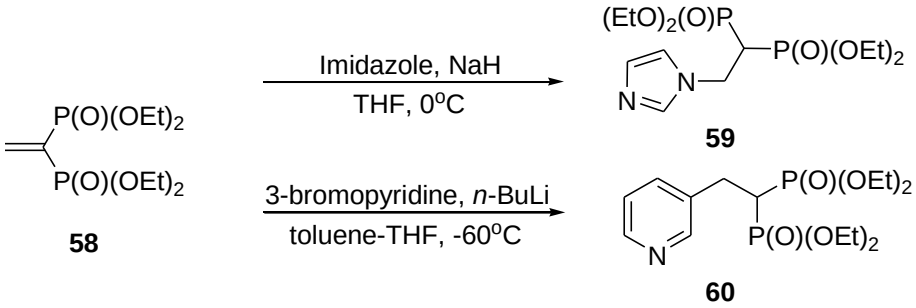
Minami et al. (1992, 1993) have synthesized 1-(cyclopent-1-enylcarbonyl) vinylphosphonates **55** and used it in the Michael addition of (1,3-dioxolan-2-yl)-ethylmagnesium bromide (**56**) (Scheme 2.20). They have proved that the produced Michael adducts **57** are useful for the construction of triguinane ring systems.



55 R_1 = H, Me; R_2 = H, Me **57**

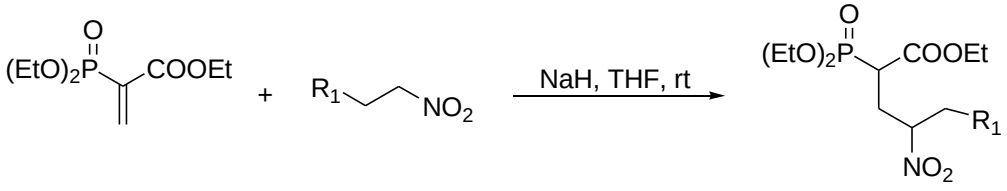
Scheme 2.20. Michael addition of (1,3-dioxolan-2-yl)- ethylmagnesium bromide (**56**) to 1-(cyclopent-1-enyl- carbonyl)vinylphosphonates **55**.

Inoue et al. (2003) studied the Michael addition of imidazole and 3-bromopyridine to bis(phosphono)ethylene (**58**) (Scheme 2.21) and then worked on the halogenations of the addition products **59**, **60**.



Scheme 2.21. Michael addition of imidazole and 3-bromopyridine to bis-(phosphono)ethylene.

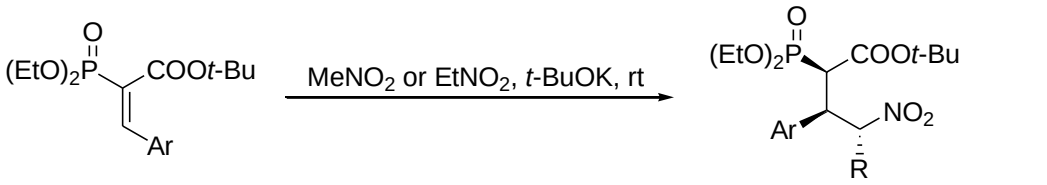
Krawczyk and Blaszczyk et al. performed the Michael addition of nitroalkanes **62** to ethyl (2-diethylphosphoryl)acrylate (**61**) and to *tert*-butyl acrylates (**64**) (Scheme 2.22 and Scheme 2.23).



61 **62** **63**

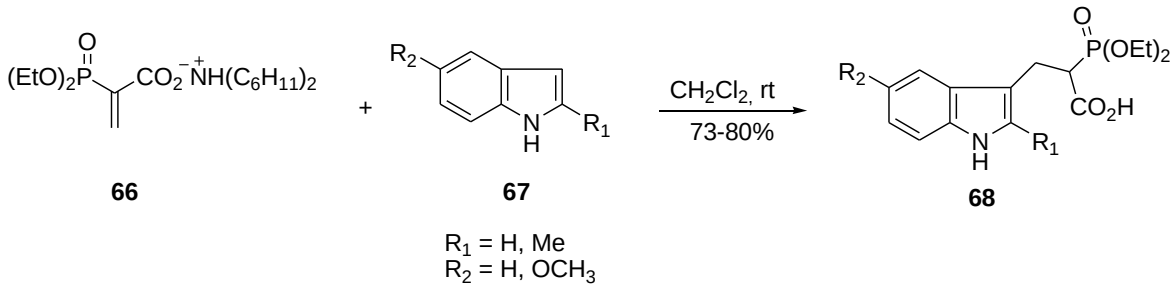
R_1 = H, Me, n-Bu, Ph, 1,2-OCH_3-4-$CH_3C_6H_3$, *p*-$NO_2C_6H_4$

Scheme 2.22. Michael addition of nitroalkanes **62** to ethyl (2-diethylphosphoryl)-acrylate (**61**)



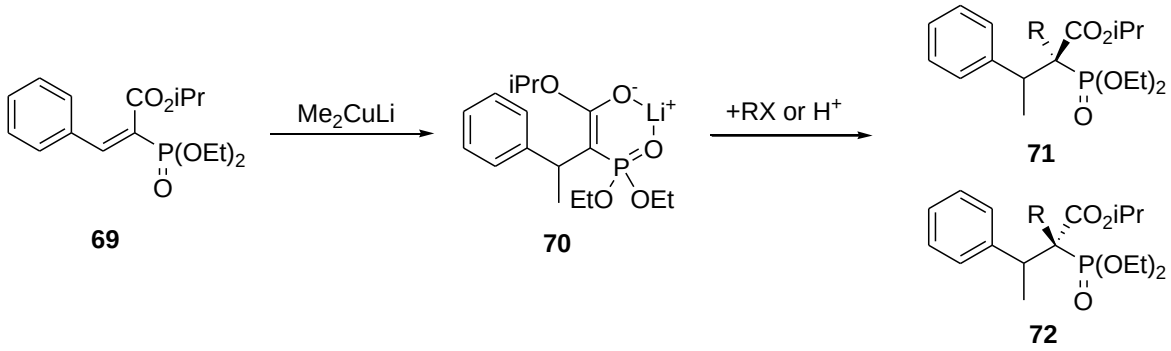
Scheme 2.23. Michael addition of nitromethane or nitroethane to *tert*-butyl acrylates (**64**).

Krawczyk et al. (2002) also performed the Michael addition of indole **67** to dicyclohexylammonium 2-(diethylphosphoryl)acrylate (**66**) that provides 2-(diethoxyphosphoryl)-3-(1*H*-indol-3-yl)propionates **68** (Scheme 2.24). These adducts are useful synthons for the constructions of biologically active and medicinally attractive amino phosphonic acids.



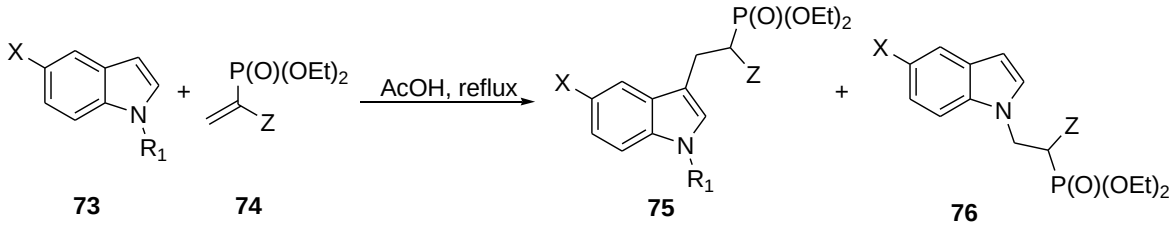
Scheme 2.24. Michael addition of indole **67** to dicyclo hexylammonium 2-(diethylphosphoryl)acrylate (**66**).

Vieth et al. (1997) used α-phosphonocinnamate (**69**) as a Michael acceptor for the alkylation reaction with alkylhalogens. They obtained the addition products **71** and **72** with good yields as a diastereomeric mixture (Scheme 2.25).



Scheme 2.25. For the alkylation reaction with Me2CuLi and trapping of the addition intermediate with an alkyl halide.

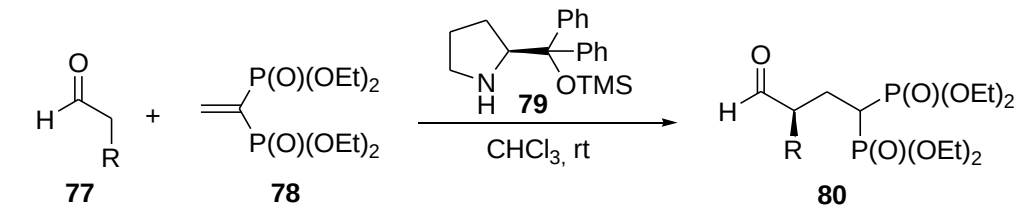
The Michael addition of indoles **73** to α,β-unsaturated phosphorus molecules **74** was studied by Couthan-Govrues et al. (2006). They synthesized novel diethyl indolylphosphonates (**75** and **76**) and tetraethyl indolyl-1,1-bisphosphonates (**75** and **76**) in glacial acetic acid. They obtained a mixture of *C*- and *N*-substituted indoles **75** and **76** with tetraethyl ethylidene-1,1-bisphosphonate (Scheme 2.26). Electron-donating substituents at C-5 increased the proportion of **75**.



R_1 = H, CH_3; Z = $P(O)(OEt)_2$, CO_2Et; X = H, F, Cl, Br, OCH_3, NO_2

Scheme 2.26. The Michael addition of indoles **73** to α,β-unsaturated phosphonates **74**.

The first catalytic enantioselective organocatalytic Michael addition of aldehydes **77** to vinyl phosphonates **78** was performed by Sulzer-Mosse et al. (2007). They used chiral amines **79** to catalyze the Michael addition of aldehydes to vinyl phosphonates. They obtained chiral γ-geminal phosphonate aldehydes **80** in high yields and with enantioselectivities up to 97% ee (Scheme 2.27).

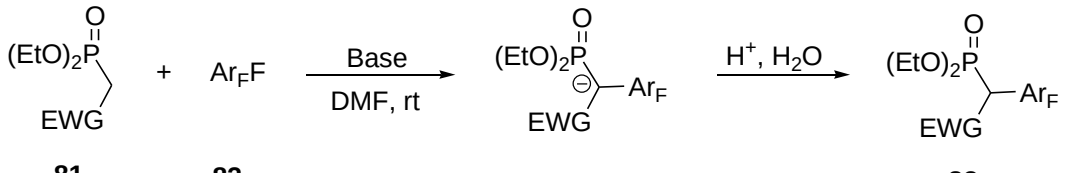


R = *i*-Pr, *t*-Bu, *n*-Pr, Bn, Me, allyl

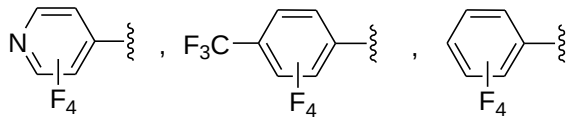
Scheme 2.27. Michael addition of aldehyde enolates to vinyl phosphonates **78**.

Some other carbon-carbon bond forming reactions in literature for the synthesis of phosphonates are nucleophilic aromatic substitution and Heck reactions.

Artamkina et al. (1998) showed the synthesis of perhaloaromatic diethyl methylphosphonates **83** using nucleophilic aromatic substitution. These compounds can be obtained by the reaction of perhaloarenes **82** with carbanions of diethyl methylphosphonates **81**. Reactions were carried out in solid-liquid system using CsF, NaH or K_2CO_3 as a base in the presence of $Et_3BnN^+Cl^-$ (TEBA) as a phase transfer agent (Scheme 2.28).



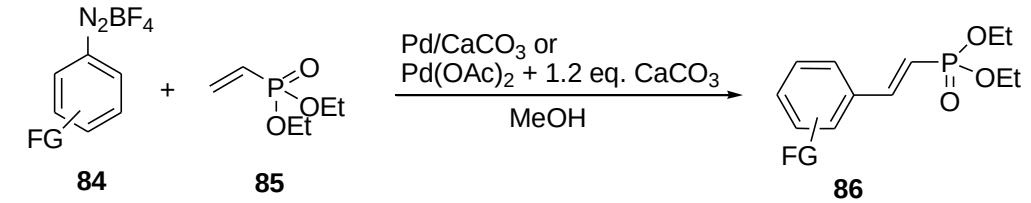
EWG = CN, CO_2Et, P(O)(OEt)$_2$

Ar_F = 

Scheme 2.28. Synthesis of perhaloaromatic diethyl methylphosphonates **83** using nucleophilic aromatic substitution.

Brunner et al. (2000) reported the synthesis of phosphonic derivatives **86** by Heck reaction of aryldiazonium salts **84** bearing electron-withdrawing or donating groups with vinylphosphonates **85**. Pd/$CaCO_3$ and Pd(OAc)$_2$/$CaCO_3$ catalytic systems

were used for the preparation of aryl vinylphosphonates **86** and high yields were obtained (Scheme 2.29) .



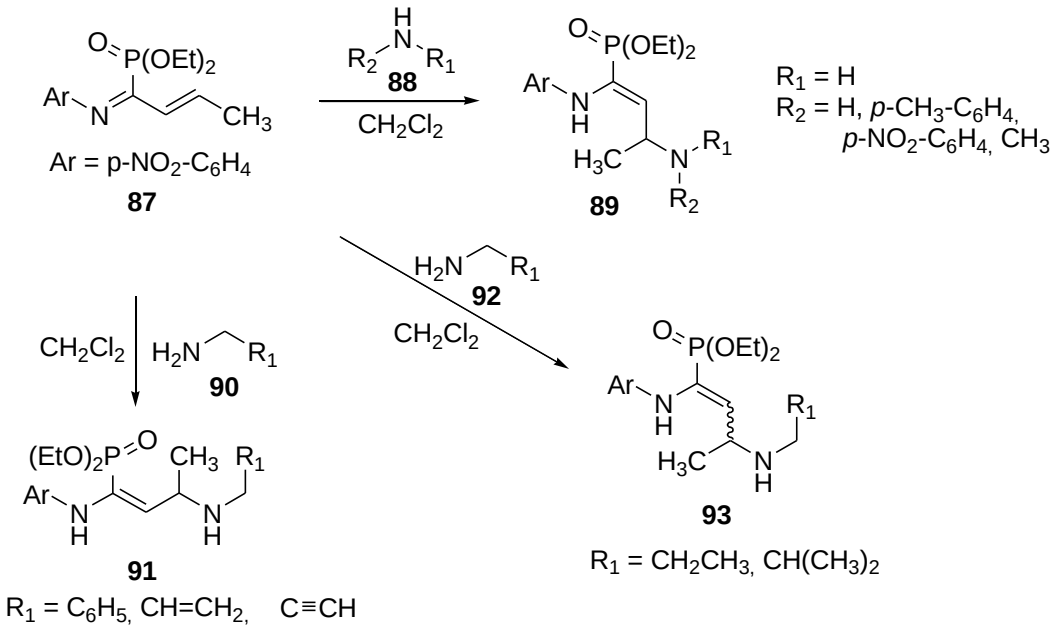
FG = *p*-MeO, 4-Cl-3-MeO, 4-F-3-NO_2,
3,4,5-tri-MeO, *o*-Br, *p*-I, *o*-COOEt

Scheme 2.29. Heck reaction of aryldiazonium salts **84** with vinylphosphonates **85**.

2.2.3. Carbon-Nitrogen (C-N) Bond Formation

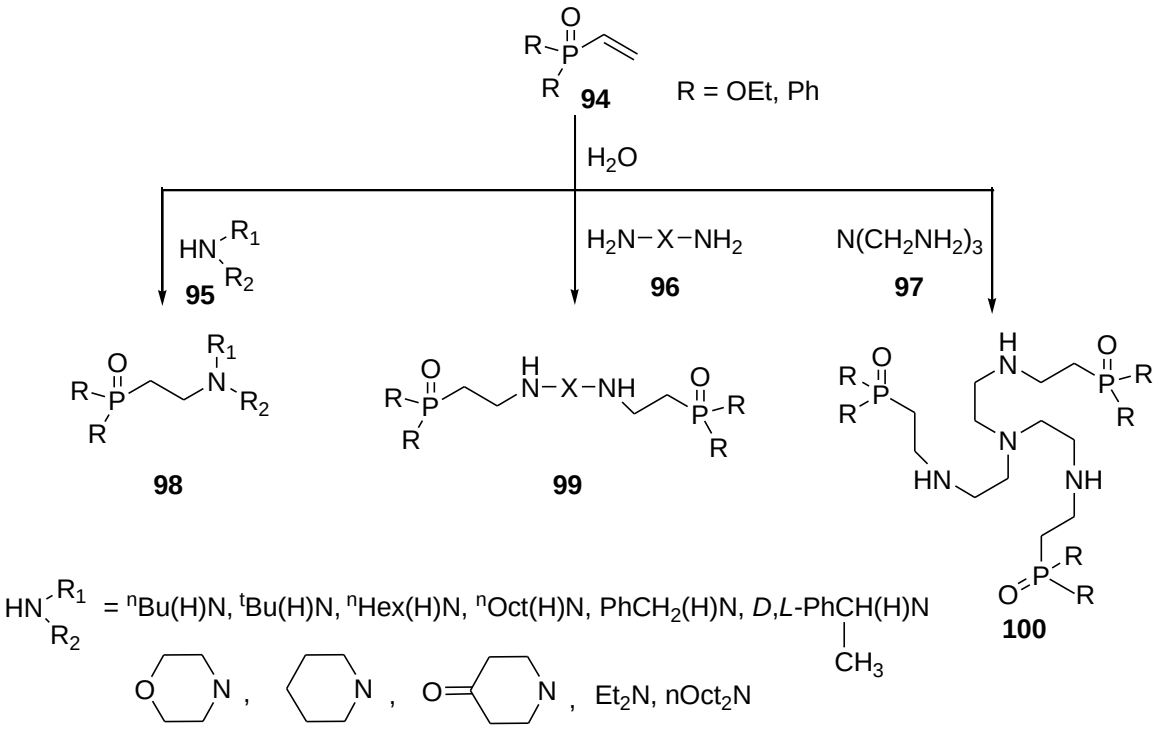
The aza-Michael reaction is one of the most general and widely used method for the formation of new carbon-nitrogen (C-N) bonds. The simplicity of the method makes it the most appropriate alternative for the preparation of functionalized amino compounds. Generally addition of nitrogen nucleophiles to Michael acceptors proceeds without catalyst, but, very often the conjugated system was activated with acids or organocatalysts.

Vicario et al. (2009) studied the conjugate addition of amines to an α,β-unsaturated imine **87** derived from α-aminophosphonate. Conjugate addition of amines **88**, **90**, **92** to α,β-unsaturated imine **87** was performed in CH_2Cl_2 under mild conditions without using any catalyst. γ-Amino-α-dehydroaminophosphonates **89**, **91** were obtained stereoselectively with good yields. When aliphatic amines were treated with α,β-unsaturated imine **87** mixtures of *E*- and *Z*-enamines **93** were obtained in high yields(Scheme 2.30).



Scheme 2.30. Conjugate addition of amines **88**, **90**, **92** to α,β-unsaturated imine **87**.

A practical and efficient green synthesis of β-aminophosphoryl compounds **98**, **99**, **100** via the aza-Michael addition reaction were performed by Matveeva et al. (2011). They applied water as a solvent in the aza-Michael reaction of diethyl vinylphosphonate and diphenylvinylphosphine oxide (**94**) with a wide range of *N*-nucleophiles **95**, **96**, **97**. β-aminophosphoryl compounds **98**, **99**, **100** were isolated after lyophilization with >95% yields (Scheme 2.31).

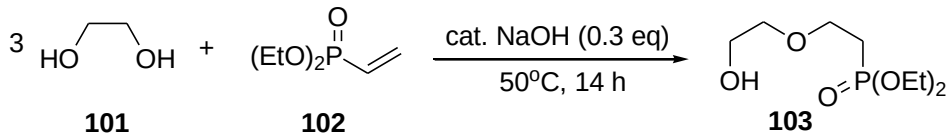


Scheme 2.31. Green synthesis of β-aminophosphoryl compounds **98**, **99**, **100** *via* the aza-Michael addition reaction.

2.2.4. Carbon-Oxygen (C-O) Bond Formation

Oxa-Michael addition to vinylphosphonates scarcely described in literature due to the reversibility of the reaction and low reactivity of alcohols, requiring harsh conditions and thus limiting the synthetic scope of the reaction (Köhler et al., 2011). Therefore, there are some examples on this subject oxa-Michael addition to vinylphosphonates is an ongoing interest in organic chemistry.

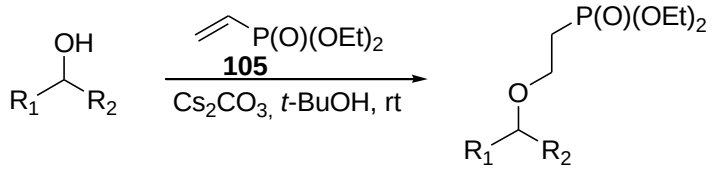
Cristau et al. (1999) studied the reaction of a vinylic phosphorus compound with an alcohol in basic catalytic conditions. They synthesized diethyl 5-hydroxy-3-oxapentylphosphonate (**103**) by the reaction of diethyl vinylphosphonate (**102**) with an excess of ethyleneglycol (**101**) and catalytic amount of NaOH and isolated the compound **103** in 61% yield (Scheme 2.32).



101 **102** **103**

Scheme 2.32. Oxa-Michael reaction of diethyl vinylphosphonate (**102**) with ethyleneglycol (**101**).

The first efficient oxa-Michael reaction of secondary and sterically hindered primary alcohols **104** with diethyl vinylphosphonate (**105**) is reported by Baszczynski et al. (2012) under very mild reaction conditions. They performed the oxa-Michael addition of various alcohols to diethyl vinylphosphonate with Cs_2CO_3, in *t*-BuOH, at rt. They obtained the corresponding products **106** in moderate to high yields (Scheme 2.33).



104 **106**

Scheme 2.33. Oxa-Michael reaction of alcohols **104** with diethyl vinylphosphonate (**105**).

2.3. Addition Reactions of Heteroaromatics

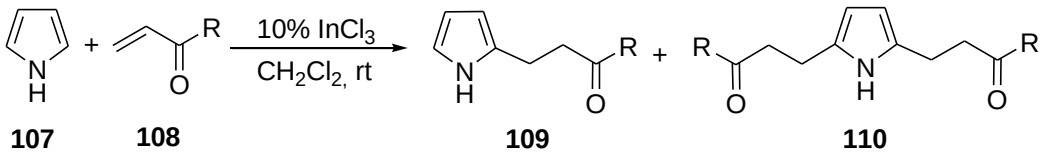
2.3.1. Addition of Pyrrole

Pyrrole and *C*-alkylated pyrroles are important building blocks in various biologically active molecules (Kusurkar et al., 2006). Thus the synthesis and reactions of pyrroles have attracted much research interest over a century. 2-Alkyl or 2-acyl pyrroles are useful precursors for the synthesis of pyrrole derivatives. Generally *C*-alkyl pyrroles are synthesized by the reduction of 2-formyl or 2-acetyl pyrroles. Isomerization of *N*-alkyl pyrroles by thermal rearrangement at high temperature to obtain 2- and 3-alkyl pyrroles is another method. Alternatively, 2- and 3-alkyl pyrroles are prepared using pyrrolylmagnesium halides. However,

these indirect methods involve the drawbacks of multistep reactions and of polymerization under many reaction conditions.

The direct synthesis of 2-alkyl pyrroles is a challenge for the synthetic chemists because of their sensitivity to air and acids which lead to polymerization. Acid-catalyzed reactions of pyrrole are limited and require careful control of acidity to prevent side reactions (Yadav et al., 2001). Because of these reasons, Michael addition of pyrroles to α,β-unsaturated compounds is an ongoing interest for organic chemists.

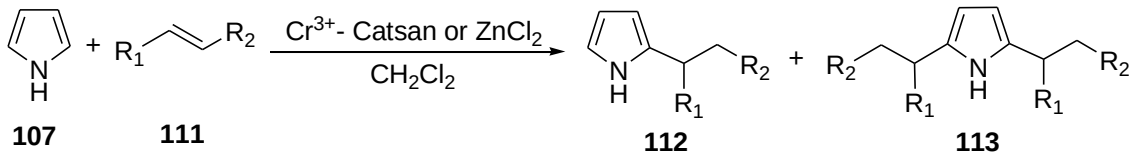
Yadav et al. (2001) reported a simple and direct method for the synthesis of 2-alkyl pyrroles **109** by using $InCl_3$ (Scheme 2.34). Treatment of pyrrole (**107**) with various α,β-unsaturated carbonyl compounds **108** in the presence of a catalytic amount of $InCl_3$ gave the corresponding 2-alkylated products **109** in high yields. 2,5-dialkylated products **110** could be obtained by increasing reaction time and changing the molar ratio.



107 **108** **109** **110**

Scheme 2.34. Synthesis of 2-alkyl pyrroles **109** by using $InCl_3$ as catalyst.

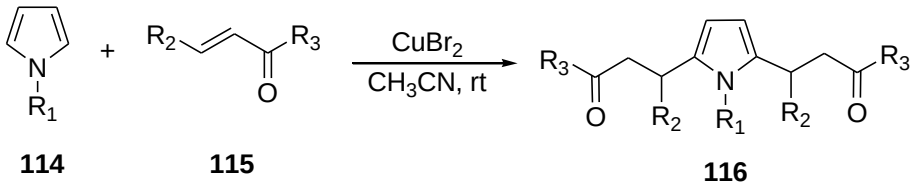
Zhang et al. (2006) used Cr^{3+}- Catsan and $ZnCl_2$ as Lewis acid catalysts in the Michael addition of pyrrole (**107**) to conjugated alkenes **111**. They found that Cr^{3+}-Catsan and $ZnCl_2$ are effective and selective catalysts for the addition of pyrrole to conjugated alkenes **111**. 2-Alkyl **112** and 2,5-dialkyl pyrrole **113** derivatives could be obtained selectively with Cr^{3+}- Catsan and $ZnCl_2$ catalyst, respectively (Scheme 2.35).



R_1 = H, Ph, 4-Me-Ph
R_2 = PhCO, COMe, 4-Me-PhCO,
PhCH=CHCO, NO_2, CN, CO_2Et

Scheme 2.35. Michael addition of pyrrole (**107**) to conjugated alkenes **111**.

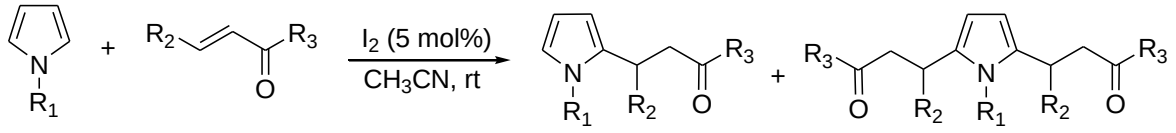
An efficient method has been developed using copper bromide as a catalyst for the dialkylation of pyrroles **114** by Kusurkar et al. (2006). Dialkylation product **116** was achieved selectively when the reaction was carried out in excess amount of enone **115** (Scheme 2.36). However, the use of equimolar amounts of pyrrole and enones resulted in fast reactions with less selectivity, forming both mono- and dialkylated products.



R_1 = H, Me
R_2 = Ph, 4-Cl-Ph
R_3 = Ph, Me

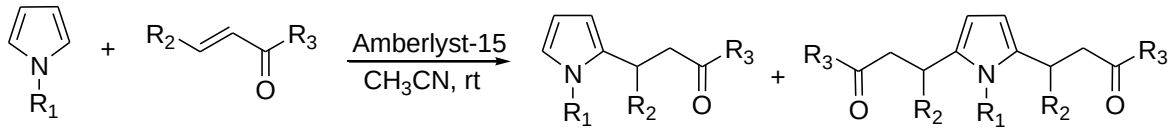
Scheme 2.36. Dialkylation of pyrroles **114** using copper bromide as catalyst.

Das and coworkers (2007) used iodine and Amberlyst-15 as catalysts in the addition reaction of pyrroles **117** to α,β-unsaturated ketones **118** (Scheme 2.37). Different α,β-unsaturated ketones were reacted with pyrrole at room temperature to give the corresponding 2-alkyl **119** and 2,5-dialkyl pyrroles **120** in various ratios. When *N*-methyl and *N*-benzoyl pyrroles were used for alkylation, *N*-benzoyl pyrrole afforded only monoalkylated products in low yields.



117 **118** **119** **120**

R_1 = H, Me, COPh
R_2 = Ph, 4-Cl-Ph, p-OMe-Ph
R_3 = Ph, Me, Et

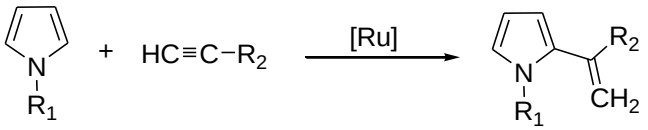


117 **118** **119** **120**

R_1 = H, Me, COPh
R_2 = Ph, 4-Cl-Ph, p-OMe-Ph
R_3 = Ph, Me, Et

Scheme 2.37. Addition reaction of pyrroles **117** to α,β-unsaturated ketones **118** with iodine and Amberlyst-15 as catalysts.

Dinuclear ruthenium (II) complex was used for the functionalization of pyrroles by Tan et al. (2012). The addition of pyrroles **121** onto alkynes **122** has been catalyzed by $Ru_2(CO)_4(PPh_3)Br_4$, resulting in the formation of 2-vinylpyrroles **123** in high yields under mild conditions (Scheme 2.38).



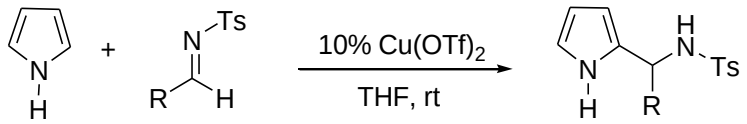
121 **122** **123**

R_1 = H, Me, Ph
R_2 = phenyl or alkyl

Scheme 2.38. Addition of pyrroles **121** onto terminal alkynes **122** catalyzed by a dinuclear ruthenium (II) complex.

Unaleroglu et al. used metal triflates for the alkylation of pyrrole with *N*-tosyl imines **124** and α,β-unsaturated carbonyl compounds **126** and **128**. They performed the addition of pyrrole to *N*-tosyl imines **124** with $Cu(OTf)_2$. The addition reactions of

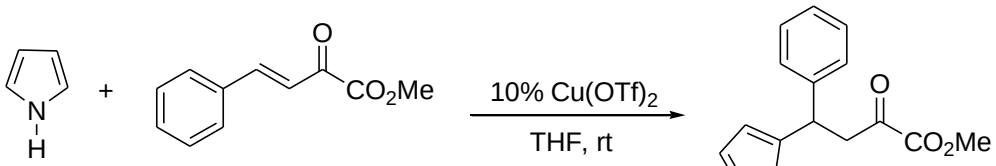
pyrrole to *N*-tosyl imines occur regioselectively at the 2-position of pyrrole and the new pyrrole derivatives **125** were obtained in high yields.



107 **124** **125**

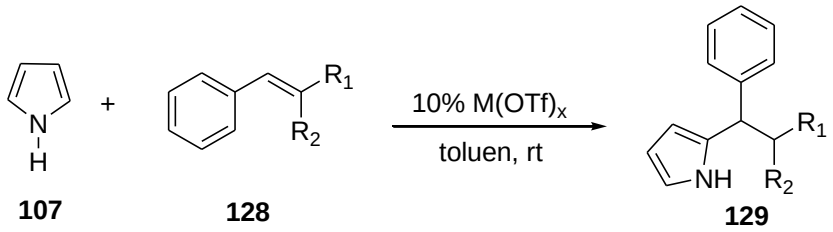
Scheme 2.39. Alkylation of pyrrole with *N*-tosyl imines **124** in the presence of $Cu(OTf)_2$.

The addition of pyrrole to α,β-unsaturated carbonyl compounds **126** and **128** is also performed in the presence of metal triflates. Ketone, cyano and ester functionalized α,β-unsaturated compounds are good Michael acceptors and addition of pyrrole to these compounds were performed successfully with metal triflates. In all cases, the addition products **127** and **129** were obtained regioselectively in high yields (Scheme 2.40 and Scheme 2.41).



107 **126** **127**

Scheme 2.40. Addition of pyrrole to keton functionalized α,β-unsaturated compounds **126**.



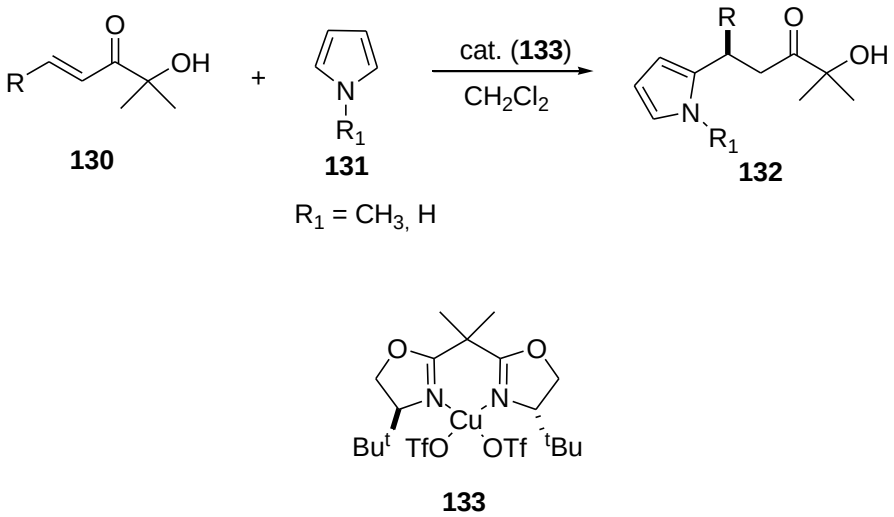
107 **128** **129**

R_1= CO_2CH_3, CN
R_2= CO_2CH_3, CN

Scheme 2.41. Addition of pyrrole to cyano and ester functionalized α,β-unsaturated compounds **128**.

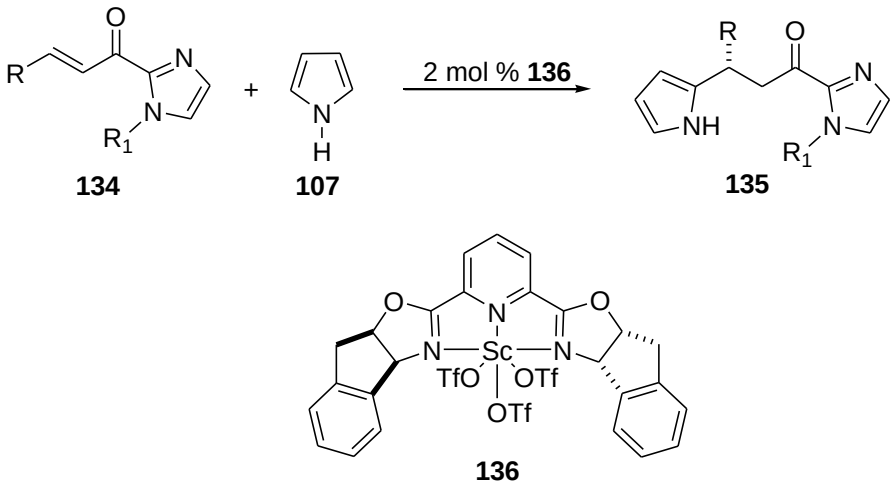
Enantioselective alkylation of pyrrole under the catalysis of metal triflate complexes was also studied. $Cu(OTf)_2$, $Sc(OTf)_3$ and $In(OTf)_3$ are the most effective triflates used for these systems.

Palomo et al. (2005) were used Cu(II)-simple bis(oxazoline) catalyst **133** for the addition of pyrrole **131** to α'-hydroxy enones **130**. The addition products **132** were obtained in high yields with high enantioselectivities (Scheme 2.42).



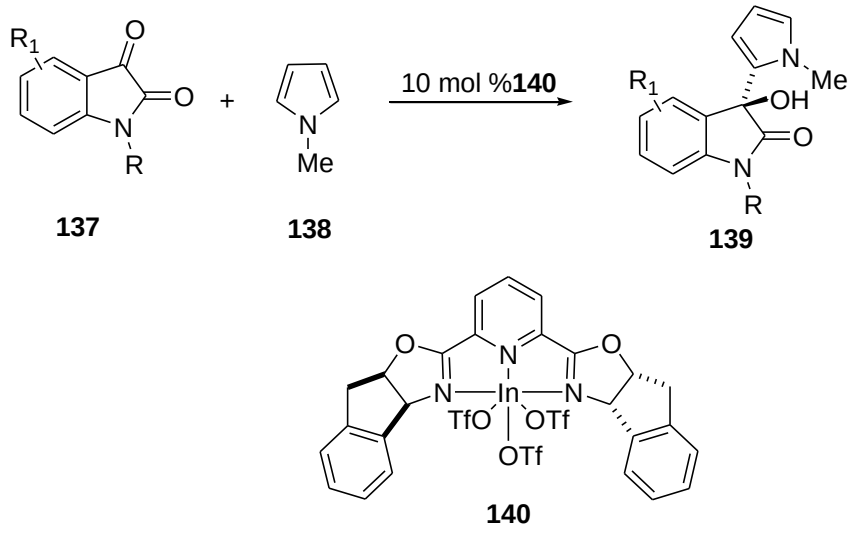
Scheme 2.42. Enantioselective addition of pyrrole **131** to α'-hydroxy enones **130**.

Evans et al. (2006) have been accomplished enantioselective additions of pyrrole **107** to α,β-unsaturated 2-acyl imidazoles **134** with the bis(oxazolinyl)pyridine-scandium (III) triflate complex **136** as catalyst (Scheme 2.43).



Scheme 2.43. Bis(oxazolinyl)pyridine-scandium (III) triflate **136** catalyzed addition of pyrrole **107** to α,β-unsaturated 2-acyl imidazoles **134**.

The indium (III) **140** catalyzed enantioselective and regioselective addition of pyrroles **138** to isatins **137** is described by Gutierrez et al. (2011). High enantioselectivity and regioselectivity was observed with various *N*-alkylated isatins **137** (Scheme 2.44).

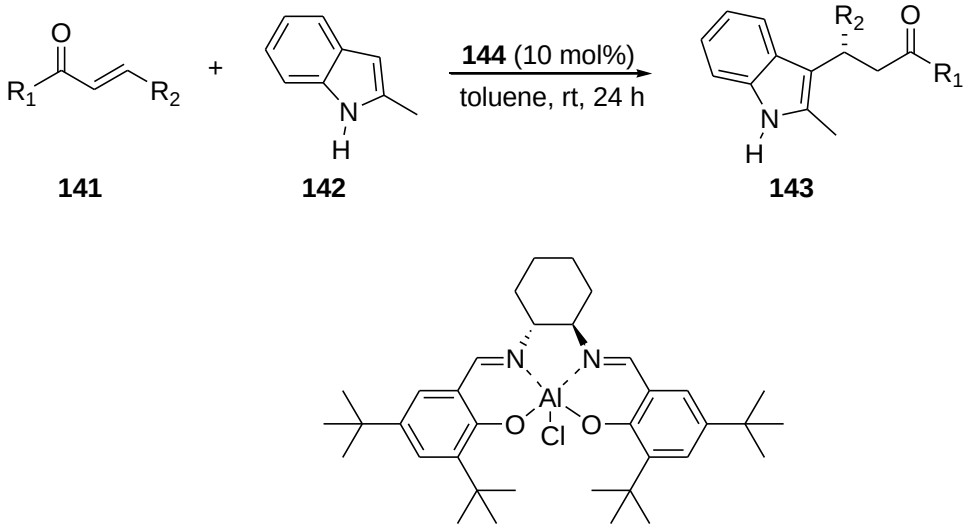


Scheme 2.44. The indium (III) **140** catalyzed enantioselective addition of pyrroles **138** to isatins **137**.

2.3.2. Addition of Indole

The indole framework represents a privileged structure motif in a large number of biologically active alkaloids and pharmaceutical agents. In this regard, the development of effective routes to indole architecture has attracted much attention from synthetic chemists (Bartoli et al., 2007). Since the 3-position of indole is the preferred site for the electrophilic substitution reaction, the introduction of functionalized alkyl frameworks at this position constitutes a well established strategy. Therefore, Friedel-Crafts alkylation has become a powerful strategy for the construction of indole architectures. Among the Friedel-Crafts reactions, Michael type Friedel-Crafts reactions of indoles with α,β-unsaturated carbonyl compounds have been widely investigated (Blay et al., 2007).

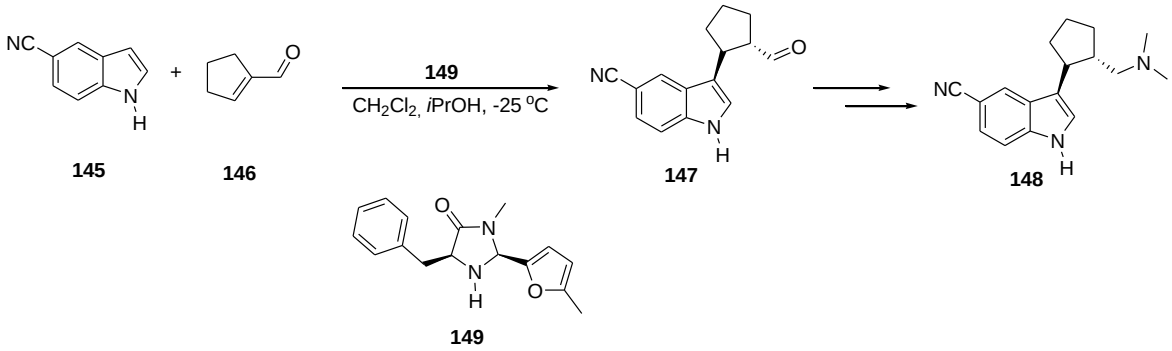
Bandini et al. (2003) employed chiral (*R*,*R*)-[Al(salen)Cl] complex **144** as catalyst for the conjugate addition of indoles **142** to α,β-unsaturated ketones **141**. This process provides functionalized β-indolyl ketones **143** possessing a stereocentre in the β-position in excellent yields and high enantiomeric excesses (Scheme 2.45).



(*R*,*R*)-[Al(salen)Cl] **144**

Scheme 2.45. Asymmetric conjugate addition reaction of indoles catalyzed by (*R*,*R*)-[Al(salen)Cl] complex **144**.

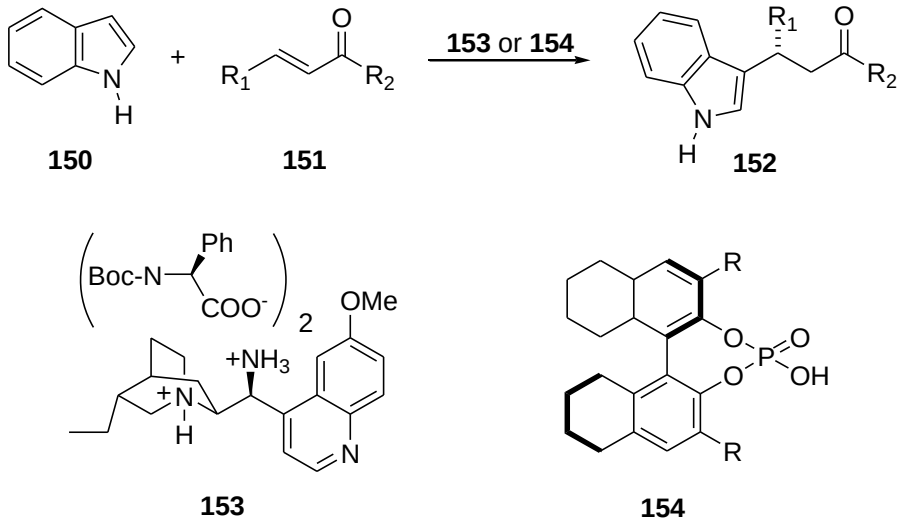
The synthesis of a highly potent and selective serotonin reuptake inhibitor (BMS-594726) **148** is described by King et al. (2005). Imidazolidinone catalyst **149** was applied for the alkylation of indoles **145** with an α,β-disubstituted α,β-unsaturated aldehyde **146** which is key step in the construction of serotonin reuptake inhibitor (Scheme 2.46). By this method they have developed a very efficient synthesis of this inhibitor **148**.



145 **146** **147** **148** **149**

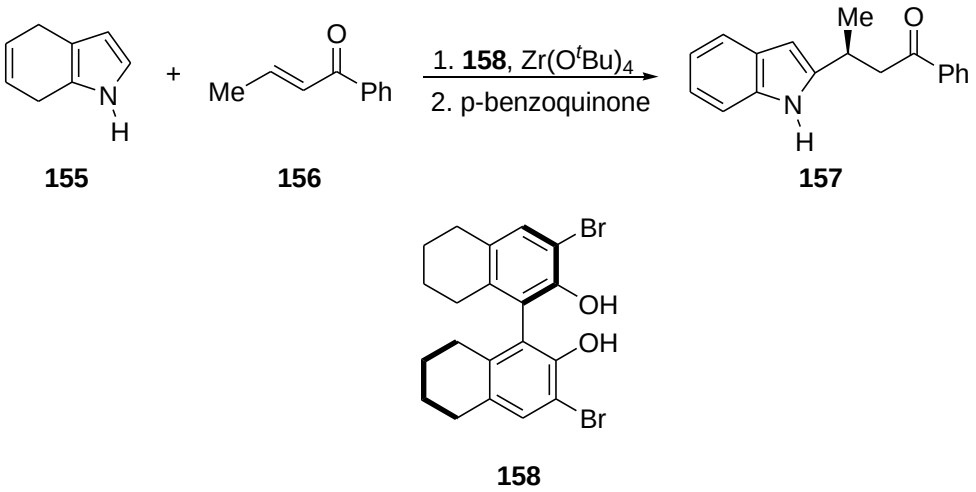
Scheme 2.46. Alkylation of indoles **145** with an α,β-disubstituted α,β-unsaturated aldehyde **146** in the presence of imidazolidinone catalyst **149**.

Friedel-Crafts alkylation of indoles **150** with simple α,β-unsaturated ketones **151** was performed with organocatalysts by Bartoli et al. (2007) and Tang et al. (2008). Bartoli et al. employed an amine salt catalyst **153**, in which both the cation and the anion are chiral. Tang et al. studied a chiral H_8-BINOL-based phosphoric acid catalyst **154** on the alkylation of indoles with simple α,β-unsaturated ketones. While chiral amine salt catalyst **153** exhibits high reactivity and selectivity, chiral H_8-BINOL-based phosphoric acid **154** catalyzed the reaction in good yields but only moderate selectivities (Scheme 2.47).



Scheme 2.47. Friedel-Crafts alkylation of indoles with α,β-unsaturated ketones in the presence of amine salt or phosphoric acid as catalysts.

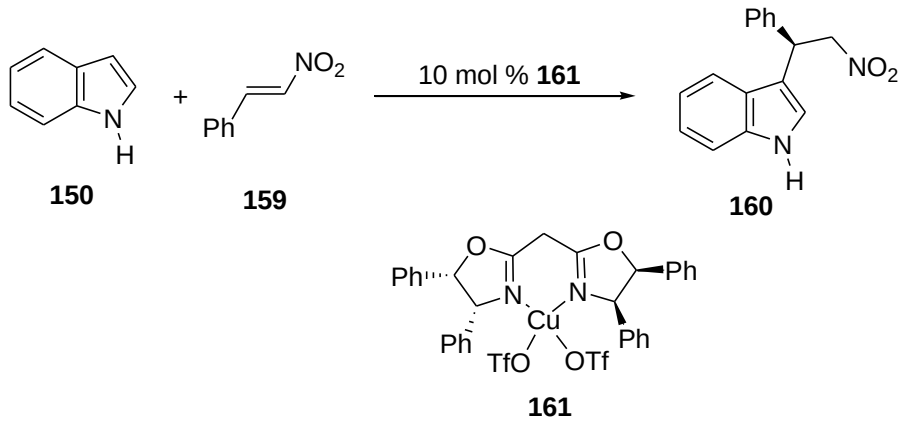
In case the less reactivity of 2-position of indole, Blay et al. (2007) showed the Friedel-Crafts alkylation of indole at the 2-position with enones. They have performed the enantioselective Friedel-Crafts reaction of α,β-unsaturated ketones **156** with 4,7-dihydroindole (**155**) catalyzed by a chiral BINOL-zirconium(IV) *tert*-butoxide complex **158**, followed by a p-benzoquinone oxidation (Scheme 2.48). The reaction proceeded in good yield and moderate enantioselectivities.



Scheme 2.48. Friedel-Crafts alkylation of 4,7-dihydroindole (**155**) at the 2-position with α,β-unsaturated ketones **156**.

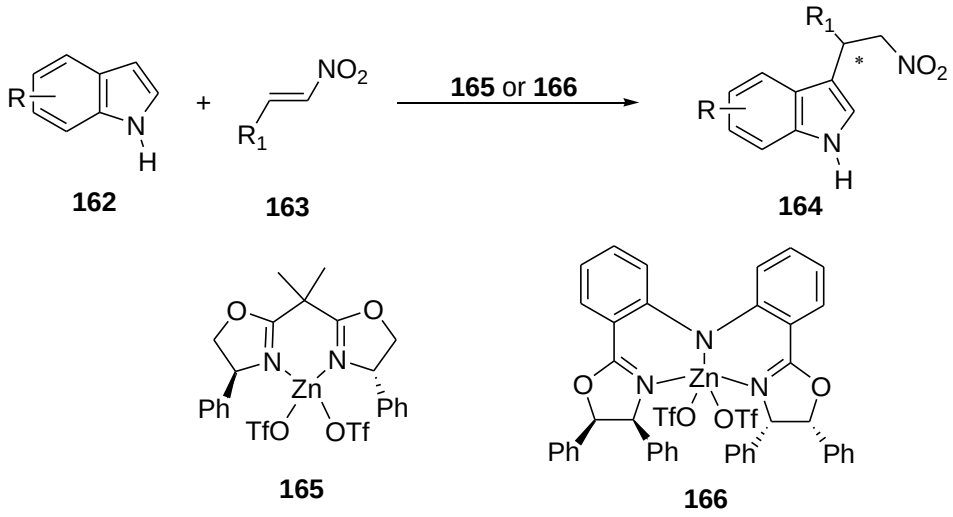
Nitroalkenes are very attractive Michael acceptors because the nitro group is the strongest electron-withdrawing group known and it can easily transformed into a range of different functionalities. Many research groups were employed nitroalkenes in the Friedel-Crafts alkylation of indoles in the presence of chiral catalysts.

Bis(oxazoline)-Cu(II) **161** and –Zn(II) complexes were used in the enantioselective Friedel-Crafts alkylation of indoles with nitroalkenes. Singh et al. (2007) prepared chiral Cu(II)-bis(oxazoline) complex **161** and employed in the Friedel-Crafts reaction of indole **150** with nitroalkene **159**. The reaction furnished nitroalkylated indole **160** in good to excellent yield with high enantioselectivity (Scheme 2.49).



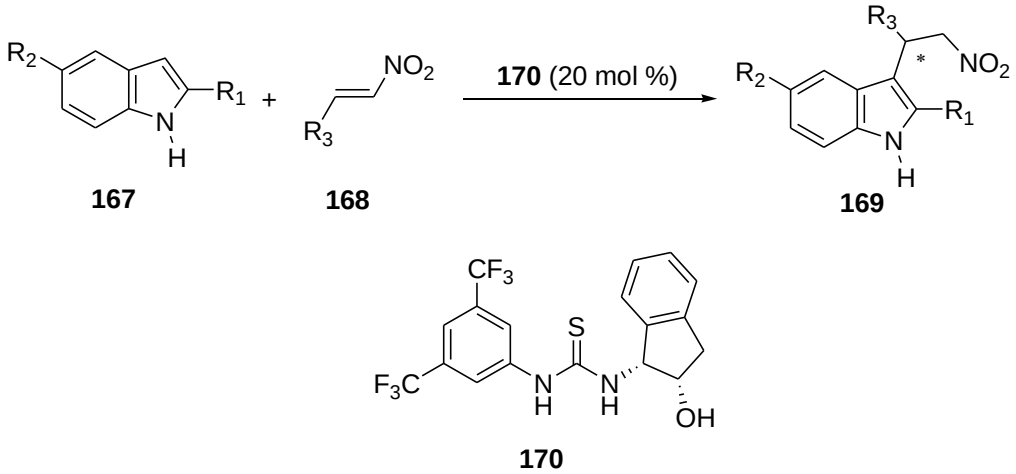
Scheme 2.49. Friedel-Crafts reaction of indole **150** with nitroalkenes **159** in the presence of bis(oxazoline)-Cu(II) complex **161**.

Similarly, Jia et al. (2006) and Lu et al. (2006) performed the Friedel-Crafts alkylation of indoles **162** with nitroalkenes **163** by bidentate and tridentate bis(oxazoline)-Zn(II) complexes **165** and **166**, respectively. In both cases various types of the nitroalkylated indoles **164** were obtained successfully (Scheme 2.50).



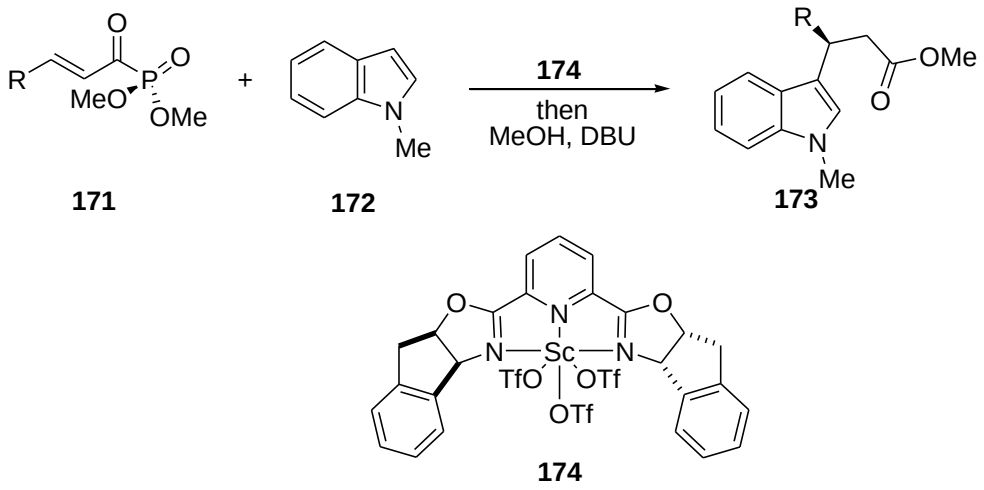
Scheme 2.50. Bidentate and tridentate bis(oxazoline)-Zn(II) complexes **165** and **166** in the Friedel-Crafts alkylation of indoles with nitroalkenes.

Thiourea-based organocatalysts **170** were found effective catalysts in the alkylation of indoles **167** by Herrera et al. (2005). Friedel-Crafts alkylation of indoles with nitroalkenes **168** provided optically active 2-indolyl-1-nitro derivatives **169** in fairly good yields and enantioselectivities (Scheme 2.51).



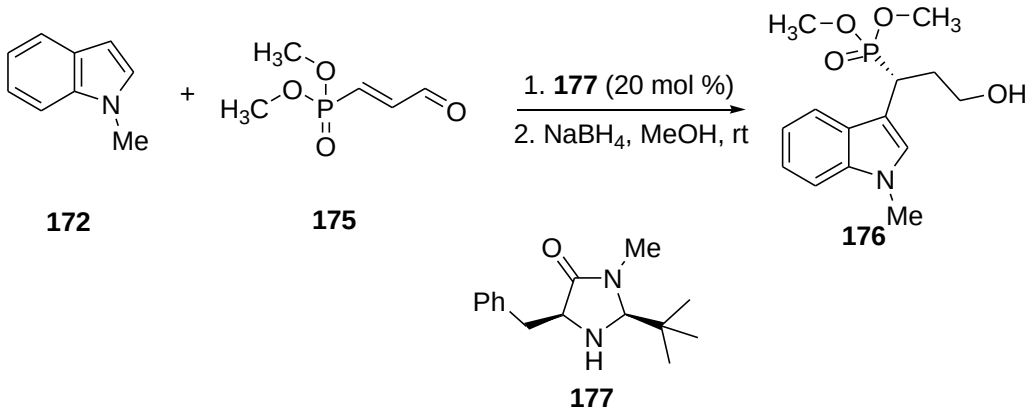
Scheme 2.51. Friedel-Crafts alkylation of indoles with nitroalkenes in the presence of thiourea-based organocatalyst **170**.

Bis(oxazolinyl)pyridine-scandium(III) triflate complexes **174** were found efficient catalysts for the Friedel-Crafts additions of indoles **172** to α,β-unsaturated acyl phosphonates **171** by Evans et al. (2003) (Scheme 2.52). The obtained acyl phosphonates **173** are effective active esters that may be employed in subsequent acyl-transfer reactions.



Scheme 2.52. Friedel-Crafts additions of indoles to α,β-unsaturated acyl phosphonates **171**.

Guo et al. (2009) reported highly enantioselective synthesis of α-indolyl phosphonates **176** via Friedel-Crafts alkylation of substituted indoles **172** with (*E*)-dialkyl 3-oxo-prop-1-enylphosphonate **175** using imidazolidinone catalyst **177** (Scheme 2.53). The incorporation of indolyl group at the α-position of phosphonates is useful for further functionalizations, and should exhibit diverse biological activities.



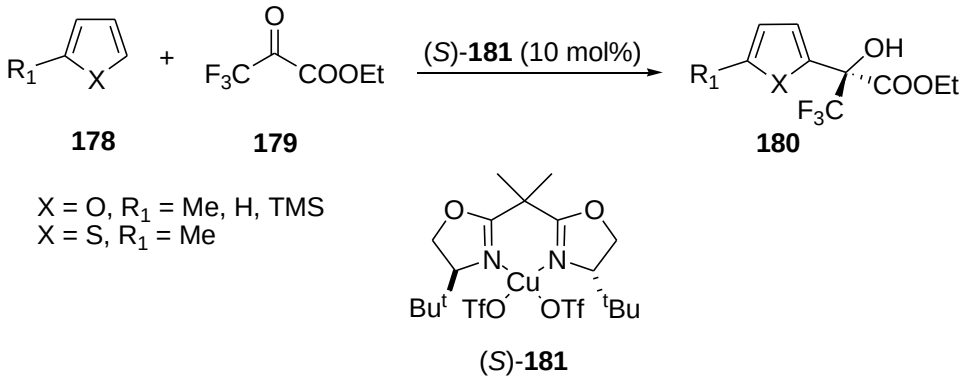
172 **175** **176** **177**

Scheme 2.53. Imidazolidinone **177** catalyzed Friedel-Crafts alkylation of substituted indoles.

2.3.3. Addition of Furan and Thiophene

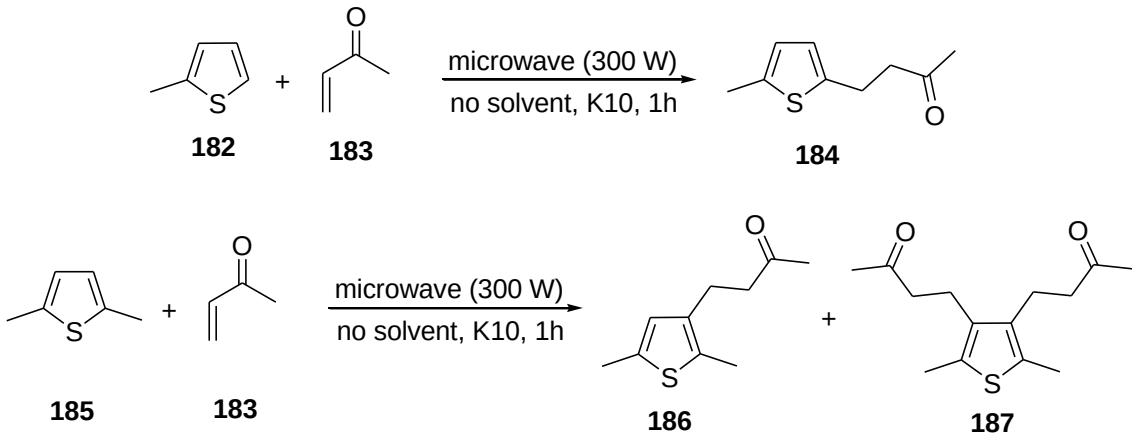
Furan and thiophene derivatives are important structural fragment in many pharmaceutical and chemical compounds. Furan and thiophene compounds have been found to show nematocidal, insecticidal, antibacterial, antifungal, antiviral and antioxidant activity. Despite their low reactivity against Friedel-Crafts reaction, some examples existed in literature.

Zhuang et al. (2001) studied the catalytic and enantioselective Friedel-Crafts reactions of aromatic and heteroaromatic compounds to trifluoropyruvate **179**. They aimed to synthesize optically active hydroxyl trifluoromethyl esters. Beside pyrrole, indole and aromatic compounds, they performed the Friedel-Crafts addition reactions also with furans and 2-methylthiophene **178** in the presence of (*S*)-*t*-Bu-BOX-Cu(OTf)$_2$ (*S*)-**181** (Scheme 2.54). The isolated yields were low, however the enantioselectivities were good.



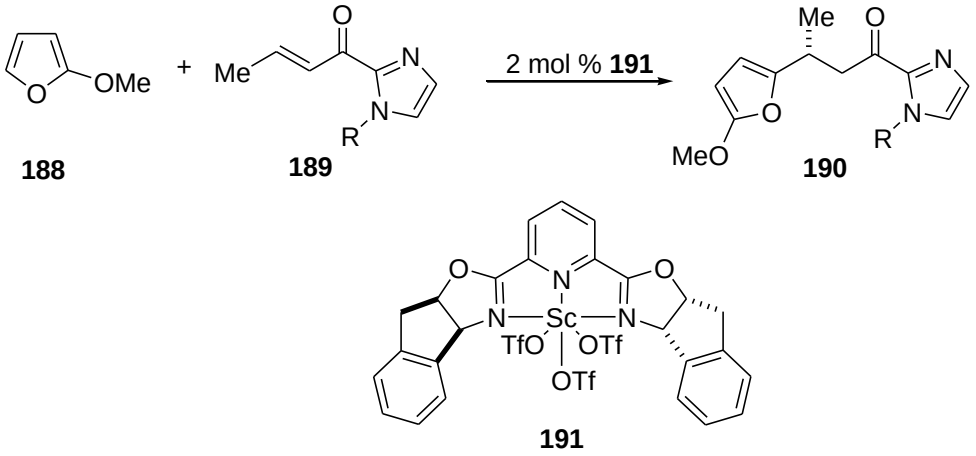
Scheme 2.54. Friedel-Crafts addition reactions with furans and 2-methylthiophene to trifluoropyruvate (**179**).

Avalos et al. (2001) performed the conjugate addition of thiophene to methyl vinyl ketone (**183**) with Montmorillonite K-10 catalyst under microwave irradiation. When they used 2-methythiophene (**182**) in the Friedel-Crafts addition reaction 5-substituted alkylation product **184** was obtained in 85% yield but when they used 2,5-dimethylthiophene (**185**) both monoalkylated **186** and dialkylated products **187** were obtained (Scheme 2.55).



Scheme 2.55. Conjugate addition of thiophene to methyl vinyl ketone (**183**) with Montmorillonite K-10 catalyst under microwave irradiation.

Evans et al. (2005) gave an example to enantioselective Friedel-Crafts alkylation of α,β-unsaturated 2-acyl imidazoles **189** with 2-methoxyfuran (**188**) by bis(oxazolinyl)- pyridine-scandium(III) triflate complex **191** (Scheme 2.56).



Scheme 2.56. Enantioselective Friedel-Crafts alkylation of α,β-unsaturated 2-acyl imidazoles **189** with 2-methoxyfuran **188**.

2.4. Pyrrolizines

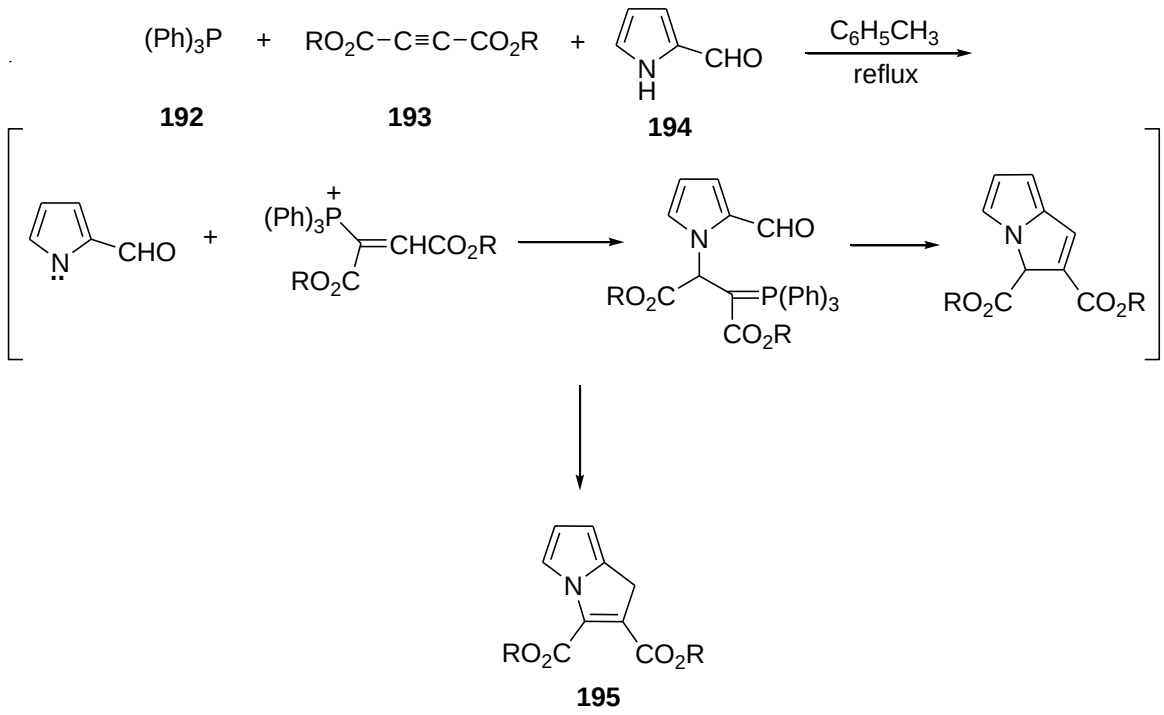
Bridgehead nitrogen heterocycles are of interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activity. Among these heterocycles pyrrolizine derivatives have attracted considerable attention since they are used for antiinflammation and analgesia, as aromatase and tumor inhibitors (Kalantari et al., 2006). Although pyrrolizines can be isolated from a wide variety of plants, insects, animals, marine organisms and microbes, there has been an ongoing interest in the synthesis of pyrrolizine derivatives (Sobenina et al., 2005).

2.4.1. Synthesis of Pyrrolizines

In literature there are different approaches for the construction of pyrrolizine ring structure. They can be synthesized from *N*-alkyl or *C*-alkyl pyrrole derivatives.

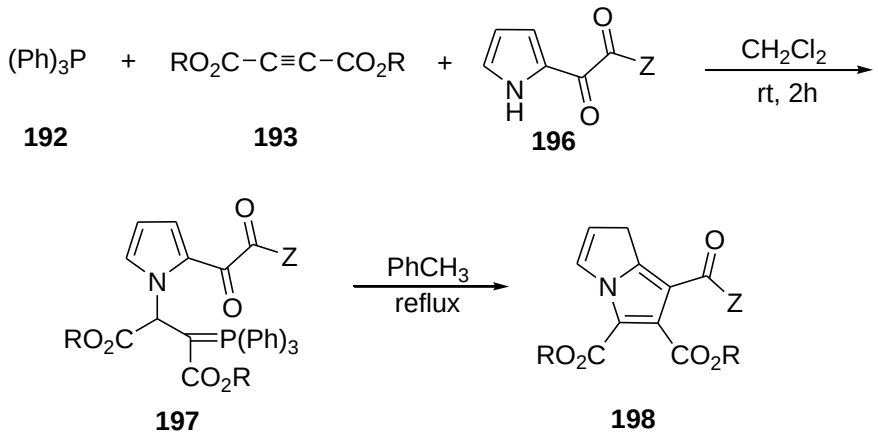
Yavari et al. (1999) have described the synthesis of functionalized 1*H*-pyrrolizine derivatives **195** from the reaction of triphenylphosphine (**192**), dialkyl acetylenedicarboxylates **193** and pyrrole-2-carboxyaldehyde (**194**) using an intramolecular Wittig reaction (Scheme 2.57). Performing the reaction under

neutral conditions and not using any catalyst for activation are the advantages of this method.



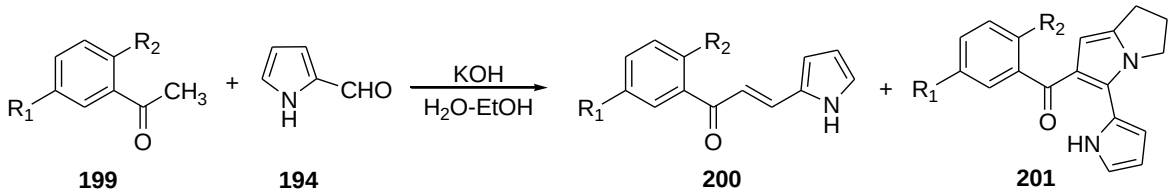
Scheme 2.57. Synthesis of functionalized 1H-pyrrolizine derivatives by an intramolecular Wittig reaction.

Same group (2001) also synthesized the 4-substituted 1*H*-pyrrolizines **198** by Wittig reaction. In this case they firstly obtained phosphorus ylides **197** by the reaction of dialkyl acetylenedicarboxylates **193** and triphenylphosphine (**192**) in quantitative yields and then refluxed them in toluene to obtain the 1*H*-pyrrolizines **198** (Scheme 2.58).



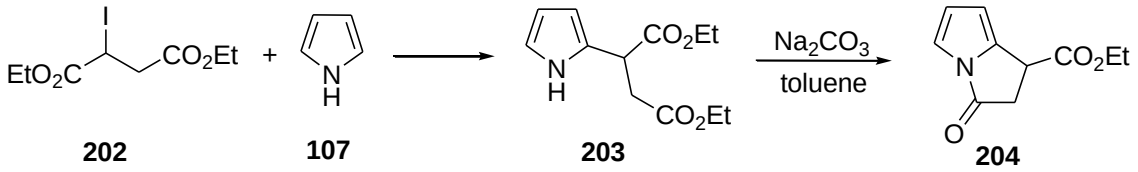
Scheme 2.58. Synthesis of 4-substituted 1*H*-pyrrolizines **198** from phosphorus ylides **197**.

Base-catalyzed condensation of pyrrole-2-aldehyde (**194**) with methyl ketones **199** is another method employed by Mallik et al. (2002). They obtained two products **200** and **201** after the acidification of the reaction mixture followed by the usual work-up and separation. One of the products was the usual condensation product **200** and the other was the 3*H*-pyrrolizine **201** which was formed by condensation of two molecules of **194** with one molecule of **199** (Scheme 2.59).



Scheme 2.59. Synthesis of 3*H*-pyrrolizine **201** by base-catalyzed condensation.

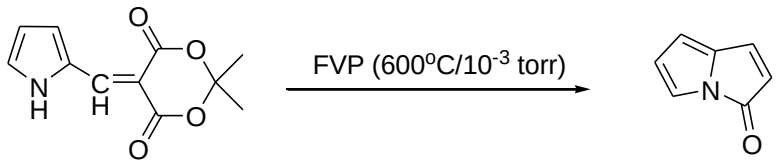
Byers et al. (2004) synthesized the pyrrolizine ring structure from *C*-alkylated pyrroles. For the synthesis of *C*-alkyl pyrrole **203** they used aromatic substitution with alkyl iodides **202**. The substitution product **203** is capable of undergoing intramolecular cyclization with Na_2CO_3 to form pyrrolizine ring structure **204** (Scheme 2.60).



202 **107** **203** **204**

Scheme 2.60. Synthesis of the pyrrolizine ring from *C*-alkylated pyrrole with Na_2CO_3.

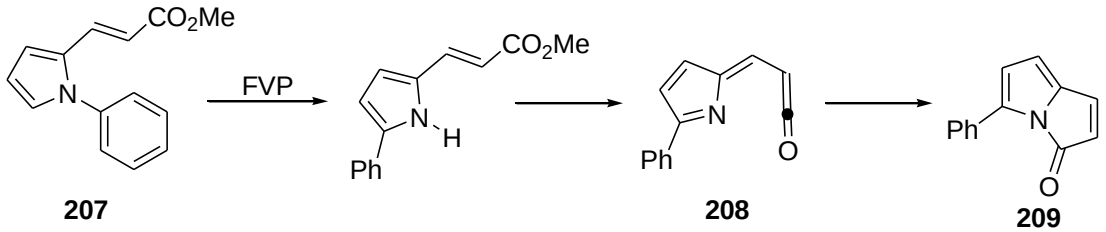
Flash vacuum pyrolysis (FVP) is another important method used for the synthesis of pyrrolizine ring structures. Firstly, McNab (1981) used this method for the synthesis of pyrrolizin-3-one **206** from the condensation product **205** of pyrrole-2-carbaldehyde and Meldrum's acid (Scheme 2.61).



205 **206**

Scheme 2.61. Flash vacuum pyrolysis of Meldrum's acid derivative.

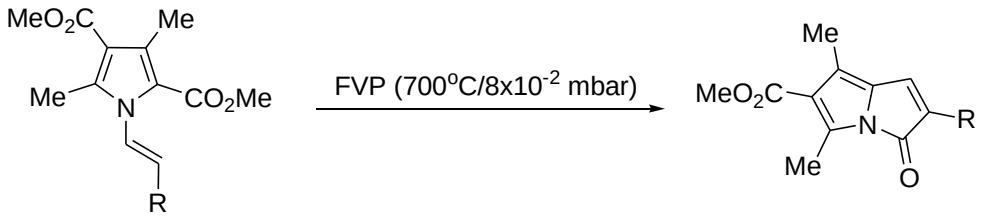
McNab et al. (2007) also employed flash vacuum pyrolysis method for the synthesis of pyrrolizine-3-one **209** from pyrrolylcinnamate derivative **207**. In the pyrolysis experiment of the pyrrolylcinnamate derivative **207**, a 1,5-sigmatropic shift of the phenyl group takes place and then elimination of methanol to generates the ketene **208** and electrocyclisation of the ketene gives to the pyrrolizinone **209** (Scheme 2.62).



207 **208** **209**

Scheme 2.62. Synthesis of pyrrolizine-3-one **209** by flash vacuum pyrolysis.

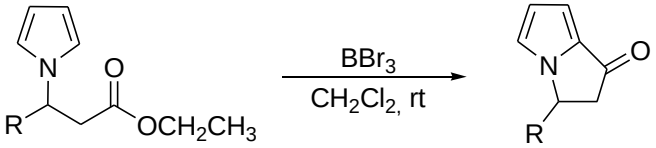
Another example for the synthesis of pyrrolizines by flash vacuum pyrolysis was studied by Pinho e Melo et al. (2005). They were synthesized 5-oxo-5*H*-pyrrolizines **211** by flash vacuum pyrolysis of *N*-alkylated pyrrole derivatives **210** (Scheme 2.63).



210 **211**

Scheme 2.63. Flash vacuum pyrolysis (FVP) of *N*-alkylated pyrrole derivatives **210**.

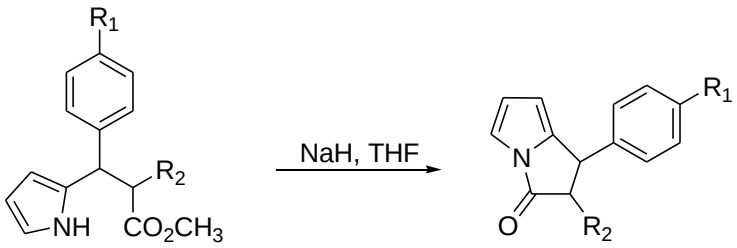
Sonnet et al. (2000) reported some aryl-substituted pyrrolizine derivatives from *N*-alkylpyrrole derivatives. They synthesised pyrrolizinones **213** from ethyl arylpyrrolylpropionates **212** in the presence of boron tribromide (BBr_3) as a catalyst (Scheme 2.64).



212 **213**

Scheme 2.64. Synthesis of aryl-substituted pyrrolizine derivatives from *N*-alkylpyrrole derivatives by BBr_3.

Unaleroglu et al. (2007, 2009) synthesized the 2-alkylated pyrrole derivatives **214** and employed them in the synthesis of pyrrolizine ring structures. *C*-alkylated pyrroles afforded pyrrolizin-3-ones **215** in good to high yields and with high diastereoselective ratio by an intramolecular cyclization reaction with NaH (Scheme 2.65).



214 **215**

Scheme 2.65. Synthesis of pyrrolizin-3-ones **215** from 2-alkylated pyrrole derivatives **214**

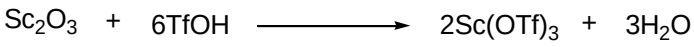
2.5. Metal Triflates

Lewis-acid catalyzed reactions are of great interest because of their unique reactivities and selectivities. A wide variety of reactions using Lewis acids have been developed, and they have been applied to the synthesis of natural and unnatural compounds. Traditionally, Lewis acids such as $AlCl_3$, BF_3, $TiCl_4$, $SnCl_4$, etc., have been employed in these reactions; however, more than stoichiometric amounts of the Lewis acids are needed in many cases. Moreover, these Lewisacids are moisture sensitive and easily decomposed or deactivated in the presence of even a small amount of water. Furthermore, these Lewis acids cannot be recovered and reused after the reactions are completed. In 1991, the first report on water-compatible Lewis acids Metal triflates appeared. Lanthanide triflates were literature-known compounds at that time, but their use in organic synthesis was limited.

The most characteristic feature of metal triflates is that they are stable and work as Lewis acids in water. Many useful reactions are catalyzed by rare-earth metaltriflates in aqueous media. Only catalytic amounts of the triflates are enough to complete the reactions in most cases. Furthermore, rare-earth metal triflates can be recovered easily after reactions and reused without loss of activity. Rare earth metal triflates are available not only in aquoeus media but also in many organic solvents. The triflates are still active in the coexistence of many Lewis bases containing nitrogen, oxygen, phosphorus and sulfur atoms. In almost all

cases, catalytic use, recovery, and reuse of triflates are possible. While large amounts of conventional Lewis acids are required and treatment of the residues of the Lewis acids after reactions may induce some serious environmental problems, metal triflate-catalysed reactions are clean and the triflates are regarded as environmentally friendly catalysts (Kobayashi et al., 2002).

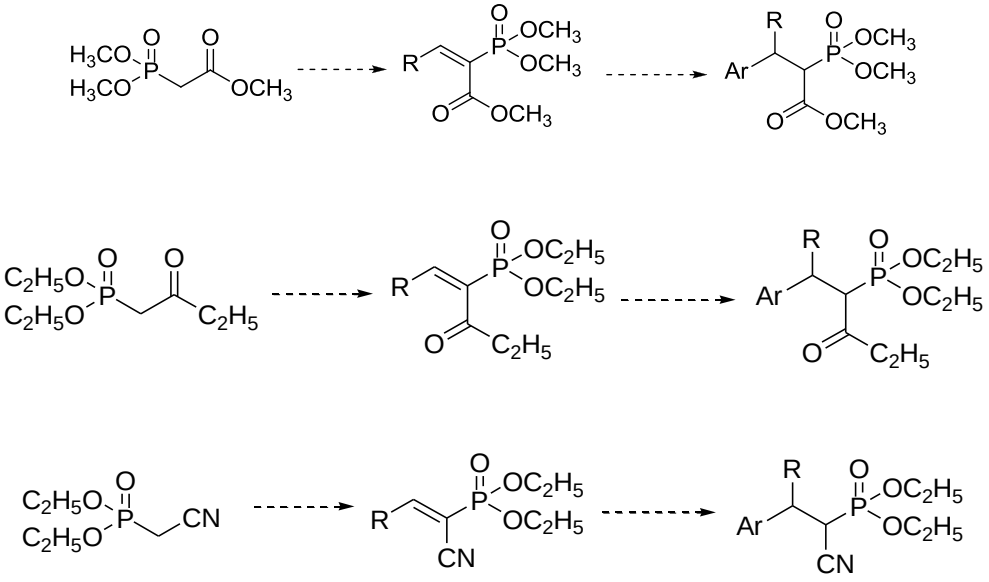
Metal triflates are readily prepared by heating the corresponding metal oxides or chlorides in an aqueous trifluoromethanesulfonic acid (TfOH) solution (Scheme 2.66). They are also prepared by the reaction of aqueous solutions of the corresponding metal halides with silver triflate. Typically, eight or nine molecules of water are contained in the triflates after removal of water at room temperature. Unhydrous samples are obtained after drying at elevated temperature under high vacuum.



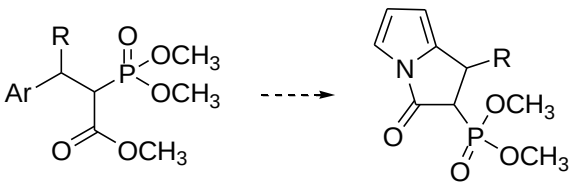
Scheme 2.66. Synthesis of Scandium triflate.

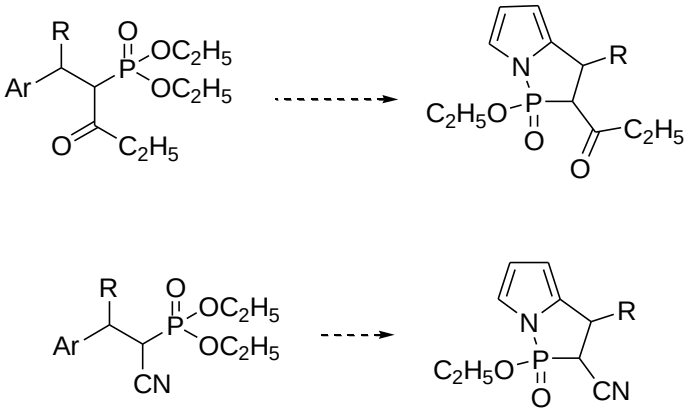
3. AIM OF THE WORK

In this study; it is aimed to synthesize heteroaromatics substituted phosphonate analogues *via* carbon-carbon bond formation process. For this purpose; trimethylphosphonoacetate, diethyl 2-oxobutylphosphonate and diethyl cyanomethylphosphonate are chosen as starting compounds for the Knoevenagel condensation reactions to produce α,β-unsaturated phosphonates. The synthesis of novel phosphanate derivatives by Michael addition reactions of heteroaromatics to α,β-unsaturated phosphonates is one of the main scope of this thesis.



Obtained Michael addition products are valuable precursors for the synthesis of pyrrolizine ring structures. In the second part of the study; the cyclization reaction of Michael adducts will be investigated to obtain novel pyrrolizine derivatives.





It is also aimed to examine the mechanisms and the effects of different parameters (solvent, temperature, catalyst type and amount, substituents) on these reactions.

4. EXPERIMENTAL

4.1. General Procedures

All chemicals were purchased from Aldrich and Sigma. Solvents were either reagent or technical grade and when necessary they were purified and dried by distillation from an appropriate desiccant. Concentrations of solutions after reactions and extractions were achieved using a rotary evaporator at reduced pressure. Organic extracts were dried over anhydrous magnesium sulfate and calcium chloride.

Reactions were monitored by Thin Layer Chromatography (TLC) using precoated silica plates (Kieselgel 60, F254, E.Merck), visualized with UV light. Flash column chromatography was performed by using silica gel (0.05-0.63 mm, 230-400 mesh ASTM, E.Merck).

^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{31}P NMR (162 MHz) spectra were recorded using $SiMe_4$ and H_3PO_4 as an internal reference with Bruker DPX-400, ultra shield, 400 MHz high performance digital FT-NMR spectrometer. Data for ^{1}H NMR are reported as follows: chemical shift (ppm) and multiplicity (s=singlet, d=doublet, t=triplet, dd=doublet of doublet, dt=doublet of triplet, dq=doublet of quartet, m=multiplet, br s=broad singlet). Data for ^{13}C NMR are reported as: chemical shift (ppm) and multiplicity (d=doublet, q=quartet). Coupling constants are expressed as *J* values in hertz. Peaks that represent both the major and minor diastereomers are donated by $^{<*>}$. Square brackets indicate peaks arising from the minor diastereomer, where applicable.

Infrared spectra were taken by ATR (Nicolet İS10) and are reported in cm^{-1}.

All melting points were measured in sealed tubes using an electrothermal digital melting-point apparatus (Gallenkamp).

High resolution mass spectra were recorded on a Agilent (1200/6210) TOF LC/MS spectrometer.

4.2. Synthesis of α,β-unsaturated phosphonates

4.2.1. General Procedure for the Synthesis of Vinylphosphonates from Trimethylphosphonoacetate and Aldehydes

Trimethylphosphonoacetate (2.08 mmol) and aldehyde (2.35 mmol) were dissolved in toluene (10 mL) and piperidine (0.062 mmol) and acetic acid (0.033 mmol) were added to this solution. The resulting mixture was refluxed under a Dean-Stark trap for 8 h (TLC monitoring). After the completion of the reaction the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1 or EtOAc-hexane, 4:1).

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (217):** Colorless viscous oil; yield: 309 mg (55 %); *E*:*Z* 95:5; R_f = 0.20 (1:1, EtOAc-hexane). IR (ATR): 3007, 2956, 2854, 1743, 1613, 1566, 1436, 1255, 1211, 1006, 861,746 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.60 (s, 3H, OCH_3, *Z*), 3.63 (s, 3H, OCH_3, *Z*), 3.82 (s, 3H, OCH_3, *E*), 3.84 (s, 3H, OCH_3, *E*), 3.87 (s, 3H, OCH_3, *E*), 3.91 (s, 3H, OCH_3, *Z*), 7.37-7.45 (m, 8H, Ar*H*, *E* and *Z*), 7.61-7.65 (m, 2H, Ar*H*, *Z*), 7.70 (d, $^{3}J_{P,H}$ = 24.2 Hz, 1H, C*H*=C, *E*), 8.28 (d, $^{3}J_{P,H}$ = 44.1 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.4 (*E* and *Z*), 52.9 (*E* and *Z*), 53.0 (*E* and *Z*), 122.6 (d, $^{1}J_{P,C}$ = 180.0 Hz, *E* and *Z*), 128.5 (*E* and *Z*), 128.9 (*E* and *Z*), 130.4 (*E* and *Z*), 133.2 (d, $^{3}J_{P,C}$ = 19.8 Hz, *E* and *Z*), 149.0 (d, $^{2}J_{P,C}$ = 6.2 Hz, *E* and *Z*), 166.5 (d, $^{2}J_{P,C}$ = 12.6 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.7 (*Z*), 17.1 (*E*). HRMS (ESI): *m/z* calcd for $C_{12}H_{16}O_5P$ $[M+H]^+$: 271.0735; found: 271.0705.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-(4-(trifluoromethyl)phenyl) acrylate (218):** Light yellow viscous oil; yield: 281 mg (40 %); *E*:*Z* 89:11; R_f = 0.29 (1:1, EtOAc-hexane). IR (ATR): 3011, 2952, 1718, 1610, 1579, 1438, 1411, 1323, 1251, 1212, 1169, 1126, 1034, 849, 745 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.53 (s, 3H, OCH_3, *Z*), 3.56 (s, 3H, OCH_3, *Z*), 3.72 (s, 3H, OCH_3, *E*), 3.75 (s, 3H, OCH_3, *E*), 3.78 (s, 3H, OCH_3, *E*), 3.83 (s, 3H, OCH_3, *Z*), 7.44 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2H, Ar*H*, *E*), 7.58 (d, $^{3}J_{H,H}$ = 8.0 Hz, 4H, Ar*H*, *E* and *Z*), 7.60 (d, $^{3}J_{P,H}$ = 26.8 Hz, 1H, C*H*=C, *E*), 7.62 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*, *Z*), 8.13 (d, $^{3}J_{P,H}$ = 43.6 Hz, 1H, C*H*=C,

Z). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.6 (*E*), 52.7 (*Z*), 52.8 (*Z*), 52.9 (*Z*), 53.0 (*E*), 53.1 (*E*), 123.6 (q, $^1J_{F,C}$ = 270.6 Hz, *E* and *Z*), 124.9 (q, $^3J_{F,C}$ = 3.7 Hz, *Z*), 125.6 (q, $^3J_{F,C}$ = 3.7 Hz, *E*), 126.0 (d, $^1J_{P,C}$ = 178.8 Hz, *E*), 126.1 (d, $^1J_{P,C}$ = 187.6 Hz, *Z*), 129.2 (*E*), 129.9 (*Z*), 132.1 (q, $^2J_{F,C}$ = 32.6 Hz, *E* and *Z*), 137.0 (d, $^3J_{P,C}$ = 20.3 Hz, *E*), 137.5 (d, $^3J_{P,C}$ = 6.1 Hz, *Z*), 147.2 (d, $^2J_{P,C}$ = 6.3 Hz, *E*), 153.0 (d, $^2J_{P,C}$ = 4.0 Hz, *Z*), 165.7 (d, $^2J_{P,C}$ = 14.2 Hz, *Z*), 165.8 (d, $^2J_{P,C}$ = 12.1 Hz, *E*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.5 (*Z*), 15.9 (*E*). HRMS (ESI): *m/z* calcd for $C_{13}H_{15}F_3O_5P$ $[M+H]^+$: 339.0609; found: 339.0591.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-*p*-tolylacrylate (219):** Light yellow viscous oil; yield: 384 mg (65 %); *E*:*Z* 95:5; R_f = 0.15 (1:1, EtOAc-hexane). IR (ATR): 3005, 2952, 2866, 1725, 1616, 1508, 1433, 1368, 1314, 1257, 1222, 1176, 1015, 960, 832, 777 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.18 (s, 3H, C*H*$_3$, *E*), 2.19 (s, 3H, C*H*$_3$, *Z*), 3.40 (s, 3H, OC*H*$_3$, *Z*), 3.43 (s, 3H, OC*H*$_3$, *Z*), 3.60 (s, 6H, 2 OC*H*$_3$, *E*), 3.62 (s, 3H, OC*H*$_3$, *E*), 3.67 (s, 3H, OC*H*$_3$, *Z*), 6.97 (d, $^3J_{H,H}$ = 7.9 Hz, 4H, Ar*H*, *E* and *Z*), 7.09 (d, $^3J_{H,H}$ = 7.9 Hz, 4H, Ar*H*, *E* and *Z*), 7.40 (d, $^3J_{P,H}$ = 24.3 Hz, 1H, C*H*=C, *E*), 7.97 (d, $^3J_{P,H}$ = 44.1 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (*E*), 21.1 (*Z*), 51.9 (*E*), 52.0 (*Z*), 52.3 (*Z*), 52.3 (*Z*), 52.4 (*E*), 52.5 (*E*), 121.2 (d, $^1J_{P,C}$ = 180.3 Hz, *E* and *Z*), 128.3 (*Z*), 128.9 (*E*), 129.0 (*E*), 130.1 (*Z*), 130.3 (d, $^3J_{P,C}$ = 20.1 Hz, *E* and *Z*), 140.4 (*Z*), 140.5 (*E*), 148.5 (d, $^2J_{P,C}$ = 6.3 Hz, *E*), 155.0 (d, $^2J_{P,C}$ = 5.0 Hz, *Z*), 166.2 (d, $^2J_{P,C}$ = 12.8 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.9 (*Z*), 17.4 (*E*). HRMS (ESI): *m/z* calcd for $C_{13}H_{18}O_5P$ $[M+H]^+$: 285.0891; found: 285.0860.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-(4-methoxyphenyl)acrylate (220):** Light yellow viscous oil; yield: 218 mg (35 %); *E*:*Z* 88:12; R_f = 0.23 (1:1, EtOAc-hexane). IR (ATR): 3005, 2956, 2850, 1712, 1597, 1499, 1428, 1369, 1314, 1251, 1223, 1184, 1030, 971, 821, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.55 (s, 3H, OC*H*$_3$, *Z*), 3.56 (s, 3H, OC*H*$_3$, *Z*), 3.70 (s, 3H, OC*H*$_3$, *E*), 3.72 (s, 3H, OC*H*$_3$, *E*), 3.73 (s, 3H, OC*H*$_3$, *E*), 3.74 (s, 3H, OC*H*$_3$, *Z*), 3.74 (s, 3H, OC*H*$_3$, *E*), 3.75 (s, 3H, OC*H*$_3$, *Z*), 6.80 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, Ar*H*, *E*), 6.82 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, Ar*H*, *Z*), 7.30 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, Ar*H*, *E*), 7.50 (d, $^3J_{P,H}$ = 24.4 Hz, 1H, C*H*=C, *E*), 7.59 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, Ar*H*, *Z*), 8.08 (d, $^3J_{P,H}$=44.0 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.3 (*E*), 52.4 (*Z*), 52.7 (*E*), 52.7 (*Z*), 52.8 (*Z*),

52.9 (*E*), 55.1 (*E* and *Z*), 113.5 (*Z*), 114.1 (*E*), 119.4 (d, $^{1}J_{P,C}$ = 181.7 Hz, *E*), 119.5 (d, $^{1}J_{P,C}$ = 189.5 Hz, *Z*), 126.0 (d, $^{3}J_{P,C}$ = 20.4 Hz, *E* and *Z*), 131.4 (*E*), 133.0 (*Z*), 149.0 (d, $^{2}J_{P,C}$ = 6.6 Hz, *E*), 155.2 (d, $^{2}J_{P,C}$ = 5.0 Hz, *Z*), 161.6 (*E*), 161.8 (*Z*), 166.7 (d, $^{2}J_{P,C}$ = 15.3 Hz, *Z*), 166.8 (d, $^{2}J_{P,C}$ = 12.9 Hz, *E*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.2 (*Z*), 18.2 (*E*). HRMS (ESI): *m/z* calcd for $C_{13}H_{18}O_6P$ $[M+H]^+$: 301.0841; found: 301.0827.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-(4-fluorophenyl)acrylate (221):** Light yellow viscous oil; yield: 300 mg (50 %); *E*:*Z* 87:13; R_f = 0.49 (EtOAc). IR (ATR): 3153, 3015, 2954, 2854, 1720, 1596, 1453, 1375, 1205, 1173, 1024, 837, 796, 752 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.61 (s, 3H, OC*H*$_3$, *Z*), 3.64 (s, 3H, OC*H*$_3$, *Z*), 3.79 (s, 3H, OC*H*$_3$, *E*), 3.80 (s, 3H, OC*H*$_3$, *E*), 3.83 (s, 3H, OC*H*$_3$, *E*), 3.88 (s, 3H, OC*H*$_3$, *Z*), 7.04-7.09 (m, 4H, Ar*H*, *E* and *Z*), 7.39-7.43 (m, 4H, Ar*H*, *E* and *Z*), 7.61 (d, $^{3}J_{P,H}$ = 24.2 Hz, 1H, C*H*=C, *E*), 8.15 (d, $^{3}J_{P,H}$ = 40.0 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.3 (*Z*), 52.6 (*E*), 52.8 (*Z*), 52.9 (*Z*), 53.0 (*E*), 53.1 (*E*), 115.3 (d, $^{2}J_{F,C}$ = 21.8 Hz, *Z*), 116.0 (d, $^{2}J_{F,C}$ = 21.7 Hz, *E*), 122.8 (d, $^{1}J_{P,C}$ = 180.0 Hz, *E*), 127.3 (d, $^{1}J_{P,C}$ = 181.0 Hz, *Z*), 129.7 (d, $^{3}J_{F,C}$ = 3.4 Hz, *E* and *Z*), 130.0 (d, $^{3}J_{F,C}$ = 3.2 Hz, *E* and *Z*), 131.5 (d, $^{3}J_{P,C}$ = 8.7 Hz, *E*), 132.7 (d, $^{3}J_{P,C}$ = 7.5 Hz, *Z*), 148.0 (d, $^{2}J_{P,C}$ = 6.6 Hz, *E*), 153.9 (d, $^{2}J_{P,C}$ = 4.4 Hz, *Z*), 164.0 (d, $^{1}J_{F,C}$ = 251.7 Hz, *E* and *Z*), 166.3 (d, $^{2}J_{P,C}$ = 12.4 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.5 (*Z*), 17.1 (*E*). HRMS (ESI): *m/z* calcd for $C_{12}H_{15}FO_5P$ $[M+H]^+$: 289.0641; found: 289.0650.

***E*- and *Z*-methyl 3-(4-chlorophenyl)-2-(dimethoxyphosphoryl)acrylate (222):** Light yellow viscous oil; yield: 285 mg (45 %); *E*:*Z* 92:8; R_f = 0.39 (EtOAc). IR (ATR): 3010, 2954, 2850, 1723, 1613, 1590, 1491, 1253, 1219, 1022, 833, 770 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.60 (d, $^{3}J_{P,H}$ = 2.4 Hz, 3H, OC*H*$_3$, *Z*), 3.63 (d, $^{3}J_{P,H}$ = 2.4 Hz, 3H, OC*H*$_3$, *Z*), 3.79 (d, $^{3}J_{P,H}$ = 2.4 Hz, 3H, OC*H*$_3$, *E*), 3.80 (d, $^{3}J_{P,H}$ = 2.4 Hz, 3H, OC*H*$_3$, *E*), 3.83 (d, $^{3}J_{P,H}$ = 2.4 Hz, 3H, OC*H*$_3$, *E*), 3.87 (d, $^{3}J_{P,H}$ = 2.5 Hz, 3H, OC*H*$_3$, *Z*), 7.26-7.37 (m, 8H, Ar*H*, *E* and *Z*), 7.62 (d, $^{3}J_{P,H}$ = 24.1 Hz, 1H, C*H*=C, *E*), 8.15 (d, $^{3}J_{P,H}$ = 43.7 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.7 (*E*), 52.8 (*Z*), 53.0 (*Z*), 53.1 (*Z*), 53.2 (*E*), 53.3 (*E*), 123.4 (d, $^{1}J_{P,C}$ = 180.2 Hz, *E*), 123.6 (d, $^{1}J_{P,C}$ = 188.2 Hz, *Z*), 128.3 (*Z*), 129.0 (*E*), 130.4 (E), 131.5 (*Z*), 131.9 (d, $^{3}J_{P,C}$ = 20.4 Hz, *E*), 132.1 (d, $^{3}J_{P,C}$ = 6.5 Hz, *Z*), 136.6 (*Z*),

136.7 (*E*), 147.9 (d, $^{2}J_{P,C}$ = 6.5 Hz, *E*), 153.9 (d, $^{2}J_{P,C}$ = 4.4 Hz, *Z*), 166.4 (d, $^{2}J_{P,C}$ = 12.5 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.4 (*Z*), 16.9 (*E*). HRMS (ESI): *m/z* calcd for $C_{12}H_{15}ClO_5P$ $[M+H]^+$: 305.0345; found: 305.0327.

***E*- and *Z*-methyl 3-(4-bromophenyl)-2-(dimethoxyphosphoryl)acrylate (223):** Light yellow viscous oil; yield: 363 mg (50 %); *E*:*Z* 93:7; R_f = 0.35 (1:1, EtOAc-hexane). IR (ATR): 3015, 2940, 2842, 1712, 1605, 1589, 1491, 1432, 1357, 1262, 1223, 1030, 746 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.55 (s, 3H, OC*H*$_3$, *Z*), 3.58 (s, 3H, OC*H*$_3$, *Z*), 3.72 (s, 3H, OC*H*$_3$, *E*), 3.74 (s, 3H, OC*H*$_3$, *E*), 3.77 (s, 3H, OC*H*$_3$, *E*), 3.82 (s, 3H, OC*H*$_3$, *Z*), 7.20 (d, $^{3}J_{H,H}$ = 8.3 Hz, 4H, Ar*H*, *E* and *Z*), 7.45 (d, $^{3}J_{H,H}$ = 8.4 Hz, 4H, Ar*H*, *E* and *Z*), 7.51 (d, $^{3}J_{P,H}$ = 24.1 Hz, 1H, C*H*=C, *E*), 8.04 (d, $^{3}J_{P,H}$ = 43.6 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.6 (*E*), 52.7 (*Z*), 52.8 (*Z*), 52.9 (*Z*), 53.0 (*E*), 53.1 (*E*), 123.8 (d, $^{1}J_{P,C}$ = 179.7 Hz, *E*), 124.1 (d, $^{1}J_{P,C}$ = 188.1 Hz, *Z*), 125.0 (*Z*), 125.1 (*E*), 130.6 (*E*), 131.3 (*Z*), 131.6 (*Z*), 132.0 (*E*), 132.5 (d, $^{3}J_{P,C}$ = 20.4 Hz, *E* and *Z*), 147.7 (d, $^{2}J_{P,C}$ = 6.5 Hz, *E*), 153.6 (d, $^{2}J_{P,C}$ = 4.4 Hz, *Z*), 166.1 (d, $^{2}J_{P,C}$ = 12.4 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.2 (*Z*), 16.7 (*E*). HRMS (ESI): *m/z* calcd for $C_{12}H_{15}BrO_5P$ $[M+H]^+$: 348.9840; found: 348.9814.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-(4-hydroxyphenyl)acrylate (224):** Light yellow viscous oil; yield: 511 mg (86 %); *E*:*Z* 86:14; R_f = 0.39 (EtOAc). IR (ATR): 3005, 2952, 2925, 2854, 1719, 1601, 1507, 1436, 1377, 1290, 1223, 1026, 912, 833, 790 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.63 (s, 3H, OC*H*$_3$, *Z*), 3.67 (s, 3H, OC*H*$_3$, *Z*), 3.81 (s, 6H, 2 OC*H*$_3$, *E*), 3.84 (s, 3H, OC*H*$_3$, *E*), 3.85 (s, 3H, OC*H*$_3$, *Z*), 6.85 (d, $^{3}J_{H,H}$ = 10.9 Hz, 4H, Ar*H*, *E* and *Z*), 7.29 (d, $^{3}J_{H,H}$ = 8.6 Hz, 4H, Ar*H*, *E* and *Z*), 7.56 (d, $^{3}J_{P,H}$ = 24.7 Hz, 1H, C*H*=C, *E*), 8.24 (d, $^{3}J_{P,H}$ = 45.2 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.6 (*E*), 52.7 (*Z*), 52.8 (*Z*), 52.9 (*Z*), 53.0 (*E*), 53.1 (*E*), 115.2 (*Z*), 115.4 (*Z*), 115.9 (*E*), 116.1 (*E*), 122.8 (d, $^{1}J_{P,C}$ = 180.3 Hz, *E* and *Z*), 129.6 (*Z*), 130.0 (*Z*), 131.4 (*E*), 131.5 (*E*), 132.7 (d, $^{3}J_{P,C}$ = 8.6 Hz, *E* and *Z*), 147.9 (d, $^{2}J_{P,C}$ = 6.5 Hz, *E*), 153.9 (d, $^{2}J_{P,C}$ = 4.8 Hz, *Z*), 162.7 (*E* and *Z*), 166.3 (d, $^{2}J_{P,C}$ = 12.3 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.5 (*Z*), 17.0 (*E*). HRMS (ESI): *m/z* calcd for $C_{12}H_{14}O_6P$ $[M-H]^-$: 285.0528; found: 285.0556.

***E*- and *Z*-methyl 3-(4-cyanophenyl)-2-(dimethoxyphosphoryl)acrylate (225):** Light yellow viscous oil; yield: 221 mg (36 %); *E*:*Z* 89:11; R_f = 0.43 (EtOAc). IR (ATR): 3004, 2956, 2850, 2229, 1726, 1605, 1503, 1436, 1357, 1257, 1223, 1027, 750 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.56 (d, $^3J_{P,H}$ = 3.1 Hz, 3H, OCH_3, *Z*), 3.59 (d, $^3J_{P,H}$ = 3.1 Hz, 3H, OCH_3, *Z*), 3.73 (d, $^3J_{P,H}$ = 7.8 Hz, 3H, OCH_3, *E*), 3.77 (d, $^3J_{P,H}$ = 3.1 Hz, 3H, OCH_3, *E*), 3.80 (d, $^3J_{P,H}$ = 3.2 Hz, 3H, OCH_3, *E*), 3.85 (d, $^3J_{P,H}$ = 3.4 Hz, 3H, OCH_3, *Z*), 7.44 (d, $^3J_{H,H}$ = 10.1 Hz, 4H, Ar*H*, *E* and *Z*), 7.62 (d, $^3J_{H,H}$ = 10.5 Hz, 4H, Ar*H*, *E* and *Z*), 7.63 (d, $^3J_{P,H}$ = 23.8 Hz, 1H, C*H*=C, *E*), 8.16 (d, $^3J_{P,H}$ = 43.1 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.7 (*E*), 52.8 (*Z*), 52.9 (*Z*), 53.0 (*Z*), 53.2 (*E*), 53.3 (*E*), 113.2 (*Z*), 113.5 (*E*), 117.9 (*E*), 118.1 (*Z*), 126.5 (d, $^1J_{P,C}$ = 187.0 Hz, *Z*), 126.6 (d, $^1J_{P,C}$ = 178.9 Hz, *E*), 129.2 (*E*), 129.9 (*Z*), 131.5 (*Z*), 132.2 (*E*), 137.9 (d, $^3J_{P,C}$ = 20.3 Hz, *E*), 138.4 (d, $^3J_{P,C}$ = 7.0 Hz, *Z*), 146.8 (d, $^2J_{P,C}$ = 6.4 Hz, *E*), 152.5 (d, $^2J_{P,C}$ = 4.0 Hz, *Z*), 165.8 (d, $^2J_{P,C}$ = 12.2 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.3 (*Z*), 15.6 (*E*). HRMS (ESI): *m/z* calcd for $C_{13}H_{15}NO_5P$ $[M+H]^+$: 296.0687; found: 296.0657.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-(4-nitrophenyl)acrylate (226):** Orange powder; mp 103.5-105.3 °C; yield: 197 mg (30 %); *E*:*Z* 87:13; R_f = 0.47 (EtOAc). IR (ATR): 3008, 2956, 2850, 1724, 1593, 1520, 1345, 1252, 1026, 856, 784, 764 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.59 (s, 3H, OCH_3, *Z*), 3.63 (s, 3H, OCH_3, *Z*), 3.79 (s, 3H, OCH_3, *E*), 3.84 (s, 3H, OCH_3, *E*), 3.86 (s, 3H, OCH_3, *E*), 3.90 (s, 3H, OCH_3, *Z*), 7.54 (d, $^3J_{H,H}$ = 8.8 Hz, 4H, Ar*H*, *E* and *Z*), 7.74 (d, $^3J_{P,H}$ = 23.8 Hz, 1H, C*H*=C, *E*), 8.23 (d, $^3J_{H,H}$ = 9.0 Hz, 4H, Ar*H*, *E* and *Z*), 8.24 (d, $^3J_{P,H}$ = 44.0 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 53.0 (*E*), 53.1 (*Z*), 53.2 (*Z*), 53.3 (*Z*), 53.4 (*E*), 53.5 (*E*), 123.0 (*Z*), 123.9 (*E*), 127.3 (d, $^1J_{P,C}$ = 178.9 Hz, *E* and *Z*), 129.6 (*E*), 130.3 (*Z*), 139.7 (d, $^3J_{P,C}$ = 20.3 Hz, *E*), 140.4 (d, $^3J_{P,C}$ = 7.0 Hz, *Z*), 146.6 (d, $^2J_{P,C}$ = 6.5 Hz, *E*), 148.3 (*Z*), 148.4 (*E*), 152.3 (d, $^2J_{P,C}$ = 2.6 Hz, *Z*), 165.7 (d, $^2J_{P,C}$ = 11.8 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.1 (*Z*), 15.5 (*E*). HRMS (ESI): *m/z* calcd for $C_{12}H_{15}NO_7P$ $[M+H]^+$: 316.0586; found: 316.0559.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-mesitylacrylate (227):** Light yellow viscous oil; yield: 130 mg (20 %); *E*:*Z* 75:25; R_f = 0.21 (1:1, EtOAc-hexane). IR (ATR): 3008, 2954, 2917, 2850, 1724, 1614, 1435, 1338, 1252, 1220, 1024, 834, 781, 733 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.02 (s, 3H, CH_3, *Z*), 2.12 (s,

3H, CH_3, *Z*), 2.15 (s, 3H, CH_3, *E*), 2.17 (s, 3H, CH_3, *E*), 2.25 (s, 3H, CH_3, *E*), 2.38 (s, 3H, CH_3, *Z*), 3.41 (s, 3H, OCH_3, *Z*), 3.44 (s, 3H, OCH_3, *Z*), 3.56 (s, 3H, OCH_3, *E*), 3.83 (s, 3H, OCH_3, *E*), 3.86 (s, 3H, OCH_3, *E*), 3.89 (s, 3H, OCH_3, *Z*), 6.83 (s, 2H, Ar*H*, *E*), 6.84 (s, 2H, Ar*H*, *Z*), 7.92 (d, $^3J_{P,H}$ = 22.6 Hz, 1H, C*H*=C, *E*), 8.30 (d, $^3J_{P,H}$ = 45.2 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.9 (*E*), 20.1 (*Z*), 20.9 (*Z*), 21.0 (*E*), 52.1 (*E*), 52.7 (*Z*), 52.8 (*Z*), 52.8 (*Z*), 53.1 (*E*), 53.2 (*E*), 126.8 (d, $^1J_{P,C}$ = 181.5 Hz, *E*), 127.3 (d, $^1J_{P,C}$ = 191.4 Hz, *Z*), 127.8 (*Z*), 128.0 (*E*), 131.3 (d, $^3J_{P,C}$ = 17.7 Hz, *E*), 131.5 (d, $^3J_{P,C}$ = 5.7 Hz, *Z*), 134.2 (*E*), 134.3 (*Z*), 137.6 (*Z*), 137.8 (*E*), 154.7 (d, $^2J_{P,C}$ = 6.1 Hz, *E*), 156.6 (d, $^2J_{P,C}$ = 5.3 Hz, *Z*), 164.9 (d, $^2J_{P,C}$ = 15.1 Hz, *E*), 165.4 (d, $^2J_{P,C}$ = 17.0 Hz, *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.9 (*Z*), 15.9 (*E*). HRMS (ESI): *m/z* calcd for $C_{15}H_{22}O_5P$ $[M+H]^+$: 313.1205; found: 313.1220.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)acrylate (228): *E* isomer:** Brown viscous oil; yield: 127 mg (24 %); R_f = 0.21 (1:1, EtOAc-hexane). IR (ATR): 3283, 2937, 2838, 1696, 1576, 1517, 1453, 1413, 1348, 1221, 1132, 1020, 955, 834, 758 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.65 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 6.26 (br s, 1H, $H_{pyrrole}$), 6.73 (br s, 1H, $H_{pyrrole}$), 7.07 (br s, 1H, $H_{pyrrole}$), 7.78 (d, $^3J_{P,H}$ = 20.0 Hz, 1H, C*H*=C), 12.09 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.4, 52.9, 53.0, 104.4 (d, $^1J_{P,C}$ = 191.0 Hz), 111.9, 125.1, 127.1, 128.5 (d, $^3J_{P,C}$ = 15.0 Hz), 146.3 (d, $^2J_{P,C}$ = 10.0 Hz), 167.9 (d, $^2J_{P,C}$ = 13.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.2.

***Z* isomer:** Brown viscous oil; yield: 286 mg (53 %); R_f = 0.68 (1:1, EtOAc-hexane). IR(ATR): 3283, 2937, 2838, 1696, 1576, 1517, 1453, 1413, 1348, 1221, 1132, 1020, 955, 834, 758 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 3.68 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 6.23 (br s, 1H, $H_{pyrrole}$), 6.71 (br s, 1H, $H_{pyrrole}$), 7.08 (br s, 1H, $H_{pyrrole}$), 8.18 (d, $^3J_{P,H}$ = 44.0 Hz, 1H, C*H*=C), 13.10 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.1, 52.8, 53.0, 102.4 (d, $^1J_{P,C}$ = 193.2 Hz), 111.3, 126.0, 127.1 (d, $^3J_{P,C}$ = 8.4 Hz), 128.5, 146.4 (d, $^2J_{P,C}$ = 10.0 Hz), 167.1 (d, $^2J_{P,C}$ = 14.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 21.9. HRMS (ESI): *m/z* calcd for $C_{10}H_{15}NO_5P$ $[M+H]^+$: 260.0687; found: 260.0668.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl-)3-(furan-2-yl)acrylate (229):** Light brown viscous oil; yield: 379 mg (70 %); *E*:*Z* 93:7; R_f = 0.15 (1:1, EtOAc-hexane).

IR (ATR): 2960, 2862, 1723, 1625, 1467, 1436, 1333, 1239, 1211, 1026, 924, 829, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.71 (s, 3H, OCH_3, *Z*), 3.72 (s, 3H, OCH_3, *E*), 3.74 (s, 3H, OCH_3, *Z*), 3.75 (s, 3H, OCH_3, *E*), 3.78 (s, 3H, OCH_3, *Z*), 3.82 (s, 3H, OCH_3, *E*), 6.43-6.45 (m, 1H, H_{furan}, *E*), 6.50 (br s, 1H, H_{furan}, *Z*), 6.83 (d, $^{3}J_{H,H}$ = 3.6 Hz, 1H, H_{furan}, *E*), 7.46 (br s, 1H, H_{furan}, *E*), 7.57 (br s, 1H, H_{furan}, *Z*), 7.62 (d, $^{3}J_{H,H}$ = 3.6 Hz, 1H, H_{furan}, *Z*), 7.35 (d, $^{3}J_{P,H}$ = 24.0 Hz, 1H, C*H*=C, *E*), 7.98 (d, $^{3}J_{P,H}$ = 42.0 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.6 (*E*), 51.7 (*Z*), 51.8 (*Z*), 52.0 (*Z*), 52.1 (*E*), 52.2 (*E*), 111.5 (*E*), 112.5 (*Z*), 115.8 (d, $^{1}J_{P,C}$ = 183.7 Hz, *E* and *Z*), 117.3 (*E*), 120.4 (*Z*), 134.0 (d, $^{3}J_{P,C}$ = 7.9 Hz, *E*), 140.3 (d, $^{3}J_{P,C}$ = 4.3 Hz, *Z*), 145.2 (*E*), 145.9 (*Z*), 148.3 (d, $^{2}J_{P,C}$ = 23.3 Hz, *E* and *Z*), 165.3 (d, $^{2}J_{P,C}$ = 11.7 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 15.3 (*Z*), 18.1 (*E*). HRMS (ESI): *m/z* calcd for $C_{10}H_{14}O_6P$ $[M+H]^+$: 261.0528; found: 261.0511.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl-)3-(thiophen-2-yl)acrylate (230):** Light brown viscous oil; yield: 287 mg (50 %); *E*:*Z* 91:9; R_f = 0.24 (1:1, EtOAc-hexane). IR (ATR): 2948, 2921, 2862, 1715, 1598, 1436, 1333, 1266, 1201, 1022, 837, 782 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.78 (s, 3H, OCH_3, *Z*), 3.80 (s, 3H, OCH_3, *E*), 3.81 (s, 3H, OCH_3, *Z*), 3.83 (s, 3H, OCH_3, *E*), 3.87 (s, 3H, OCH_3, *Z*), 3.91 (s, 3H, OCH_3, *E*), 7.10-7.12 (m, 2H, 2 $H_{thiophene}$, *E* and *Z*), 7.48 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, $H_{thiophene}$, *E*), 7.63 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, $H_{thiophene}$, *E*), 7.70 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, $H_{thiophene}$, *Z*), 7.76 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, $H_{thiophene}$, *Z*), 7.97 (d, $^{3}J_{P,H}$ = 24.0 Hz, 1H, C*H*=C, *E*), 8.35 (d, $^{3}J_{P,H}$ = 44.0 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.0 (*E*), 52.2 (*Z*), 52.5 (*Z*), 52.6 (*E* and *Z*), 52.7 (*E*), 115.7 (d, $^{1}J_{P,C}$ = 184.7 Hz, *E* and *Z*), 127.1 (*E*), 127.4 (*Z*), 133.3 (*E*), 134.8 (*Z*), 136.5 (d, $^{3}J_{P,C}$ = 22.5 Hz, *E* and *Z*), 136.9 (*E*), 137.9 (*Z*), 144.4 (d, $^{2}J_{P,C}$ = 9.2 Hz, *E*), 147.7 (d, $^{2}J_{P,C}$ = 5.2 Hz, *Z*), 165.4 (d, $^{2}J_{P,C}$ = 12.4 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 15.4 (*Z*), 19.1 (*E*). HRMS (ESI): *m/z* calcd for $C_{10}H_{14}O_5PS$ $[M+H]^+$: 277.0299; found: 277.0280.

***E*- and *Z*-methyl 3-cyclohexyl-2-(dimethoxyphosphoryl)acrylate (231):** Colorless viscous oil; yield: 75 mg (15 %); *E*:*Z* 93:7; R_f = 0.20 (1:1, EtOAc-hexane). IR (ATR): 2924, 2854, 1722, 1460, 1366, 1266, 1213, 1033, 841, 794 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14-1.30 (m, 12H, CH_2, *E* and *Z*), 1.65-1.74 (m, 8H, CH_2, *E* and *Z*), 2.76-2.79 (m, 2H, C*H*, *E* and *Z*), 3.71 (s, 3H, OCH_3, *E*),

3.74 (s, 6H, OCH_3, *E* and *Z*), 3.75 (s, 3H, OCH_3, *Z*), 3.76 (s, 3H, OCH_3, *Z*), 3.78 (s, 3H, OCH_3, *E*), 6.89 (dd, $^3J_{H,H}$ = 10.1 Hz, $^3J_{P,H}$ = 23.2 Hz, 1H, C*H*=C, *E*), 7.29 (dd, $^3J_{H,H}$ = 10.7 Hz, $^3J_{P,H}$ = 46.5 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2 (*E* and *Z*), 25.7 (*E* and *Z*), 31.7 (*E* and *Z*), 39.9 (d, $^3J_{P,C}$ = 15.3 Hz, *E* and *Z*), 52.0 (*E* and *Z*), 52.8 (d, $^3J_{P,C}$ = 5.5 Hz, *E* and *Z*), 121.4 (d, $^1J_{P,C}$ = 182.7 Hz, *E* and *Z*), 165.0 (d, $^2J_{P,C}$ = 15.2 Hz, *E* and *Z*), 165.2 (d, $^2J_{P,C}$ = 4.6 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 15.9 (*Z*), 17.9 (*E*). HRMS (ESI): *m/z* calcd for $C_{12}H_{22}O_5P$ $[M+H]^+$: 277.1199; found: 277.1245.

***E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-4-methylpent-2-enoate (232):** Colorless viscous oil; yield: 39 mg (10 %); *E*:*Z* 83:17; R_f = 0.29 (1:1, EtOAc-hexane). IR (ATR): 2954, 2877, 2854, 1725, 1622, 1472, 1442, 1372, 1325, 1260, 1042, 906, 788 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (d, $^3J_{H,H}$ = 6.4 Hz, 6H, CH_3, *Z*), 1.09 (d, $^3J_{H,H}$ = 6.6 Hz, 6H, CH_3, *E*), 3.05-3.14 (m, 2H, C*H*, *E* and *Z*), 3.75 (s, 3H, OCH_3, *E*), 3.77 (s, 3H, OCH_3, *Z*), 3.78 (s, 3H, OCH_3, *E*), 3.79 (s, 6H, OCH_3, *Z*), 3.81 (s, 3H, OCH_3, *E*), 6.90 (dd, $^3J_{H,H}$ = 10.2 Hz, $^3J_{P,H}$ = 23.1 Hz, 1H, C*H*=C, *E*), 7.28 (dd, $^3J_{H,H}$ = 10.8 Hz, $^3J_{P,H}$ = 46.2 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.9 (*E*), 22.0 (*Z*), 29.1 (*Z*), 30.2 (d, $^3J_{P,C}$ = 15.9 Hz, *E*), 52.1 (*E*), 52.3 (*Z*), 52.6 (d, $^3J_{P,C}$ = 5.9 Hz, Z), 52.8 (d, $^3J_{P,C}$ = 5.6 Hz, *E*), 121.3 (d, $^1J_{P,C}$ = 183.2 Hz, *E* and *Z*), 164.9 (d, $^2J_{P,C}$ = 15.1 Hz, *Z*), 166.4 (d, $^2J_{P,C}$ = 4.3 Hz, *E*), 170.0 (d, $^2J_{P,C}$ = 8.8 Hz, *E* and *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 15.8 (*Z*), 17.8 (*E*). HRMS (ESI): *m/z* calcd for $C_9H_{18}O_5P$ $[M+H]^+$: 237.0886; found: 237.0925.

4.2.2. General Procedure for the Synthesis of Vinylphosphonates from Diethyl 2-oxobutylphosphonate and Aldehydes

Diethyl 2-oxobutylphosphonate (1.56 mmol) and aldehyde (1.75 mmol) were dissolved in toluene (10 mL) and piperidine (0.046 mmol) and acetic acid (0.025 mmol) were added to this solution. The resulting mixture was refluxed under a Dean-Stark trap for 8 h (TLC monitoring). After the completion of the reaction the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1 or EtOAc-hexane, 4:1).

***E*-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (234):** Yellow viscous oil; yield: 435 mg (95 %); R_f = 0.53 (EtOAc). IR (ATR): 2980, 2936, 2907, 1698, 1646, 1606, 1448, 1391, 1248, 1016, 963, 794, 757 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.37 (t, $^3J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3), 2.51 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.19 (dq, $^3J_{P,H}$ = 7.5 Hz, $^3J_{H,H}$ = 7.1 Hz, 4H, OCH_2CH_3), 7.30-7.32 (m, 2H, Ar*H*), 7.36-7.39 (m, 3H, Ar*H*), 7.59 (d, $^3J_{P,H}$ = 25.6 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.7, 16.2 (d, $^3J_{P,C}$ = 6.6 Hz), 36.7 (d, $^3J_{P,C}$ = 2.0 Hz), 62.5 (d, $^2J_{P,C}$ = 5.6 Hz), 128.8, 129.1, 130.1, 133.9 (d, $^3J_{P,C}$ = 21.3 Hz), 134.0 (d, $^1J_{P,C}$ = 168.8 Hz), 144.7 (d, $^2J_{P,C}$ = 5.9 Hz), 205.8 (d, $^2J_{P,C}$ = 8.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.5. HRMS (ESI): *m/z* calcd for $C_{15}H_{22}O_4P$ $[M+H]^+$: 297.1250; found: 297.1271.

***E*-diethyl 3-oxo-1-(4-(trifluoromethyl)phenyl)pent-1-en-2-ylphosphonate (235):** Yellow viscous oil; yield: 540 mg (96 %); R_f = 0.35 (1:1, EtOAc-hexane). IR (ATR): 2989, 2936, 2907, 1699, 1610, 1323, 1254, 1166, 1125, 1015, 964, 835, 798 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.38 (t, $^3J_{H,H}$ = 7.2 Hz, 6H, OCH_2CH_3), 2.51 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.21 (dq, $^3J_{P,H}$ = 8.8 Hz, $^3J_{H,H}$ = 7.2 Hz, 4H, OCH_2CH_3), 7.42 (d, $^3J_{H,H}$ = 7.2 Hz, 2H, Ar*H*), 7.57 (d, $^3J_{P,H}$ = 26.0 Hz, 1H, C*H*=C), 7.62 (d, $^3J_{H,H}$ = 8.0 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 16.3 (d, $^3J_{P,C}$ = 6.5 Hz), 36.9 (d, $^3J_{P,C}$ = 1.1 Hz), 62.9 (d, $^2J_{P,C}$ = 5.7 Hz), 123.7 (q, $^1J_{F,C}$ = 270.8 Hz), 125.8 (q, $^3J_{F,C}$ = 3.6 Hz), 129.3, 131.8 (q, $^2J_{F,C}$ = 32.7 Hz), 136.9 (d, $^1J_{P,C}$ = 167.8 Hz), 137.3 (d, $^3J_{P,C}$ = 21.9 Hz), 142.7 (d, $^2J_{P,C}$ = 5.9 Hz), 205.6 (d, $^2J_{P,C}$ = 8.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.3. HRMS (ESI): *m/z* calcd for $C_{16}H_{21}F_3O_4P$ $[M+H]^+$: 365.1130; found: 365.1175.

***E*-diethyl 3-oxo-1-*p*-tolylpent-1-en-2-ylphosphonate (236):** Yellow viscous oil; yield: 470 mg (98 %); R_f = 0.54 (EtOAc). IR (ATR): 2979, 2939, 2904, 1697, 1606, 1511, 1456, 1251, 1129, 1017, 958, 814, 771 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, CH_2CH_3), 1.36 (t, $^3J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 2.36 (s, 3H, CH_3), 2.52 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.17 (dq, $^3J_{P,H}$ = 7.5 Hz, $^3J_{H,H}$ = 7.1 Hz, 4H, OCH_2CH_3), 7.19 (q, $^3J_{H,H}$ = 8.1 Hz, 4H, Ar*H*), 7.55 (d, $^3J_{P,H}$ = 25.6 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.8, 16.3 (d, $^3J_{P,C}$ = 6.6 Hz), 21.4, 36.8 (d, $^3J_{P,C}$ = 2.0 Hz), 62.6 (d, $^2J_{P,C}$ = 5.5 Hz), 129.3, 129.6, 131.1 (d, $^3J_{P,C}$ = 21.7 Hz), 132.6 (d, $^1J_{P,C}$ = 169.6 Hz), 140.8, 145.1 (d, $^2J_{P,C}$ = 5.9 Hz), 206.5 (d,

$^{2}J_{P,C}$ = 8.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.7. HRMS (ESI): *m/z* calcd for $C_{16}H_{24}O_4P$ $[M+H]^+$: 311.1412; found: 311.1449.

***E*-diethyl 1-(4-methoxyphenyl)-3-oxopent-1-en-2-ylphosphonate (237):** Yellow viscous oil; yield: 494 mg (98 %); R_f = 0.56 (EtOAc). IR (ATR): 2983, 2936, 2901, 1696, 1602, 1510, 1460, 1300, 1250, 1178, 1017, 958, 831, 792, 769 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.36 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H, OCH_2CH_3), 2.55 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 3.83 (s, 3H, OCH_3), 4.17 (dq, $^{3}J_{P,H}$ = 7.6 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 4H, OCH_2CH_3), 6.89 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.27 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.52 (d, $^{3}J_{P,H}$ = 25.6 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.8, 16.2 (d, $^{3}J_{P,C}$ = 6.6 Hz), 36.8 (d, $^{3}J_{P,C}$ = 1.8 Hz), 55.4, 62.5 (d, $^{2}J_{P,C}$ = 5.6 Hz), 114.3, 126.4 (d, $^{3}J_{P,C}$ = 21.8 Hz), 131.0 (d, $^{1}J_{P,C}$ = 170.7 Hz), 131.2, 144.8 (d, $^{2}J_{P,C}$ = 6.1 Hz), 161.3, 206.7 (d, $^{2}J_{P,C}$ = 8.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 15.1. HRMS (ESI): *m/z* calcd for $C_{16}H_{24}O_5P$ $[M+H]^+$: 327.1361; found: 327.1404.

***E*-diethyl 1-(4-fluorophenyl)-3-oxopent-1-en-2-ylphosphonate (238):** Yellow viscous oil; yield: 481 mg (99 %); R_f = 0.23 (EtOAc). IR (ATR): 2983, 2936, 2904, 1698, 1601, 1508, 1457, 1392, 1231, 1162, 1030, 1016, 961, 836, 774 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.37 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 2.50 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.17 (dq, $^{3}J_{P,H}$ = 7.5 Hz, $^{3}J_{H,H}$ = 7.0 Hz, 4H, OCH_2CH_3), 7.05 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.29 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.49 (d, $^{3}J_{P,H}$ = 25.6 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 16.2 (d, $^{3}J_{P,C}$ = 6.5 Hz), 36.6 (d, $^{3}J_{P,C}$ = 1.3 Hz), 62.4 (d, $^{2}J_{P,C}$ = 5.5 Hz), 115.9 (d, $^{2}J_{F,C}$ = 21.7 Hz), 130.1 (d, $^{3}J_{P,C}$ = 21.9 Hz), 131.1 (d, $^{3}J_{F,C}$ = 8.8 Hz), 133.9 (d, $^{1}J_{P,C}$ = 170.7 Hz), 143.1 (d, $^{2}J_{P,C}$ = 6.1 Hz), 163.6 (d, $^{1}J_{F,C}$ = 251.2 Hz), 205.3 (d, $^{2}J_{P,C}$ = 8.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.6. HRMS (ESI): *m/z* calcd for $C_{15}H_{21}FO_4P$ $[M+H]^+$: 315.1156; found: 315.1180.

***E*-diethyl 1-(4-chlorophenyl)-3-oxopent-1-en-2-ylphosphonate (239):** Yellow viscous oil; yield: 506 mg (98 %); R_f = 0.51 (EtOAc). IR (ATR): 2983, 2939, 2907, 1738, 1698, 1607, 1409, 1372, 1250, 1163, 1130, 1013, 962, 823, 794, 759 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.37 (t, $^{3}J_{H,H}$ = 6.8 Hz, 6H, OCH_2CH_3), 2.51 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.18 (dq, $^{3}J_{P,H}$ = 7.4

Hz, $^{3}J_{H,H}$ = 7.2 Hz, 4H, OC*H*$_2$CH$_3$), 7.25 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.34 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.51 (d, $^{3}J_{P,H}$ = 25.6 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.7, 16.3 (d, $^{3}J_{P,C}$ = 6.6 Hz), 36.9 (d, $^{3}J_{P,C}$ = 1.8 Hz), 62.8 (d, $^{2}J_{P,C}$ = 5.6 Hz), 129.2, 130.4, 132.3 (d, $^{3}J_{P,C}$ = 21.9 Hz), 134.7 (d, $^{1}J_{P,C}$ = 168.8 Hz), 143.3 (d, $^{2}J_{P,C}$ = 6.1 Hz), 206.0 (d, $^{2}J_{P,C}$ = 8.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.9. HRMS (ESI): *m/z* calcd for $C_{15}H_{21}ClO_4P$ $[M+H]^+$: 331.0866; found: 331.0905.

***E*-diethyl 1-(4-bromophenyl)-3-oxopent-1-en-2-ylphosphonate (240):** Yellow viscous oil; yield: 568 mg (98 %); R_f = 0.51 (EtOAc). IR (ATR): 2980, 2945, 2904, 1698, 1606, 1586, 1487, 1457, 1393, 1251, 1163, 1129, 1009, 960, 819, 793, 756 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH$_2$C*H*$_3$), 1.37 (t, $^{3}J_{H,H}$ = 6.8 Hz, 6H, OCH$_2$C*H*$_3$), 2.51 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, C*H*$_2$CH$_3$), 4.17 (dq, $^{3}J_{P,H}$ = 7.2 Hz, $^{3}J_{H,H}$ = 6.8 Hz, 4H, OC*H*$_2$CH$_3$), 7.18 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.49 (d, $^{3}J_{P,H}$ = 25.6 Hz, 1H, C*H*=C), 7.50 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.7, 16.3 (d, $^{3}J_{P,C}$ = 6.6 Hz), 36.9, 62.8 (d, $^{2}J_{P,C}$ = 5.7 Hz), 124.8, 130.6, 132.2, 132.8 (d, $^{3}J_{P,C}$ = 21.9 Hz), 134.9 (d, $^{1}J_{P,C}$ = 168.7 Hz), 143.3 (d, $^{2}J_{P,C}$ = 5.9 Hz), 206.0 (d, $^{2}J_{P,C}$ = 8.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.9. HRMS (ESI): *m/z* calcd for $C_{15}H_{21}BrO_4P$ $[M+H]^+$: 375.0361; found: 375.0416.

***E*-diethyl 1-(4-cyanophenyl)-3-oxopent-1-en-2-ylphosphonate (241):** Yellow viscous oil; yield: 491 mg (99 %); R_f = 0.41 (EtOAc). IR (ATR): 2986, 2939, 2910, 2232, 1734, 1699, 1602, 1501, 1445, 1395, 1372, 1251, 1163, 1015, 964, 834, 792, 761 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH$_2$C*H*$_3$), 1.38 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH$_2$C*H*$_3$), 2.48 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, C*H*$_2$CH$_3$), 4.18 (dq, $^{3}J_{P,H}$ = 8.0 Hz, $^{3}J_{H,H}$ = 7.1 Hz, 4H, OC*H*$_2$CH$_3$), 7.41 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H, Ar*H*), 7.50 (d, $^{3}J_{P,H}$ = 25.5 Hz, 1H, C*H*=C), 7.66 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.5, 16.2 (d, $^{3}J_{P,C}$ = 6.5 Hz), 36.8, 62.7 (d, $^{2}J_{P,C}$ = 5.7 Hz), 113.7, 117.5, 129.3, 132.3, 137.9 (d, $^{1}J_{P,C}$ = 166.9 Hz), 138.0 (d, $^{3}J_{P,C}$ = 21.8 Hz), 141.7 (d, $^{2}J_{P,C}$ = 6.0 Hz), 204.5 (d, $^{2}J_{P,C}$ = 8.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 12.8. HRMS (ESI): *m/z* calcd for $C_{16}H_{21}NO_4P$ $[M+H]^+$: 322.1203; found: 322.1238.

***E*-diethyl 1-(4-nitrophenyl)-3-oxopent-1-en-2-ylphosphonate (242):** Yellow powder; mp 61.9-62.9 °C; yield: 456 mg (86 %); R_f = 0.51 (EtOAc). IR (ATR):

3098, 3063, 2992, 2939, 1699, 1596, 1516, 1448, 1401, 1343, 1248, 1165, 1040, 1012, 970, 948, 862 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.39 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3), 2.50 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.19 (dq, $^{3}J_{P,H}$ = 8.7 Hz, $^{3}J_{H,H}$ = 7.1 Hz, 4H, OCH_2CH_3), 7.48 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar*H*), 7.54 (d, $^{3}J_{P,H}$ = 25.5 Hz, 1H, C*H*=C), 8.23 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 16.3 (d, $^{3}J_{P,C}$ = 6.5 Hz), 36.9, 62.8 (d, $^{2}J_{P,C}$ = 5.6 Hz), 124.0, 129.7, 138.7 (d, $^{1}J_{P,C}$ = 166.7 Hz), 140.0 (d, $^{3}J_{P,C}$ = 21.8 Hz), 141.3 (d, $^{2}J_{P,C}$ = 5.9 Hz), 148.4, 204.6 (d, $^{2}J_{P,C}$ = 7.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 12.6. HRMS (ESI): *m/z* calcd for $C_{15}H_{21}NO_6P$ $[M+H]^+$: 342.1101; found: 342.1162.

***E*- and *Z*-diethyl 1-mesityl-3-oxopent-1-en-2-ylphosphonate (243):** Yellow viscous oil; yield: 314 mg (60 %); *E*:*Z* 54:46; R_f = 0.56 (EtOAc). IR (ATR): 2979, 2925, 2869, 1695, 1614, 1457, 1378, 1246, 1163, 1134, 1019, 964, 850, 790 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, CH_2CH_3, *E*), 1.08 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3, *Z*), 1.19 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3, *Z*), 1.38 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3, *E*), 2.17 (s, 6H, CH_3, *E* and *Z*), 2.20 (s, 6H, CH_3, *E* and *Z*), 2.27 (s, 6H, CH_3, *E* and *Z*), 2.29-2.35 (m, 2H, CH_2CH_3, *E*), 2.92 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3, *Z*), 3.67-3.74 (m, 2H, OCH_2CH_3, *Z*), 3.90-3.96 (m, 2H, OCH_2CH_3, *Z*), 4.18-4.22 (m, 4H, OCH_2CH_3, *E*), 6.85 (s, 4H, Ar*H*, *E* and *Z*), 7.77 (d, $^{3}J_{P,H}$ = 24.2 Hz, 1H, C*H*=C, *E*), 7.90 (d, $^{3}J_{P,H}$ = 46.7 Hz, 1H, C*H*=C, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6 (*E*), 8.2 (*Z*), 16.1 (d, $^{3}J_{P,C}$ = 6.5 Hz, *Z*), 16.3 (d, $^{3}J_{P,C}$ = 6.5 Hz, *E*), 20.3 (*E*), 20.3 (*Z*), 21.0 (*Z*), 21.1 (*E*), 34.2 (*E*), 35.8 (d, $^{3}J_{P,C}$ = 2.9 Hz, *Z*), 62.0 (d, $^{2}J_{P,C}$ = 6.3 Hz, *Z*), 62.6 (d, $^{2}J_{P,C}$ = 5.6 Hz, *E*), 127.8 (*Z*), 128.5 (*E*), 131.3 (d, $^{3}J_{P,C}$ = 19.5 Hz, *E*), 132.0 (d, $^{3}J_{P,C}$ = 6.3 Hz, *Z*), 134.5 (*Z*), 134.9 (*E*), 136.9 (d, $^{1}J_{P,C}$ = 167.3 Hz, *E*), 137.1 (d, $^{1}J_{P,C}$ = 178.9 Hz, *Z*), 137.4 (*E*), 138.3 (*Z*), 148.1 (d, $^{2}J_{P,C}$ = 5.9 Hz, *E*), 151.8 (d, $^{2}J_{P,C}$ = 5.7 Hz, *Z*), 201.0 (d, $^{2}J_{P,C}$ = 14.4 Hz, *Z*), 204.0 (d, $^{2}J_{P,C}$ = 9.5 Hz, *E*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.3 (*Z*), 14.0 (*E*). HRMS (ESI): *m/z* calcd for $C_{18}H_{28}O_4P$ $[M+H]^+$: 339.1720; found: 339.1756.

***E*- and *Z*-diethyl 3-oxo-1-(1*H*-pyrrol-2-yl)pent-1-en-2-ylphosphonate (244):** Brown viscous oil; yield: 397 mg (90 %); *E*:*Z* 36:64; R_f = 0.42 (*Z*), 0.79 (*E*) (EtOAc). IR (ATR): 2978, 2936, 2913, 1661, 1568, 1506, 1460, 1393, 1340, 1313, 1292, 1213, 1123, 1015, 959, 749 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (t,

$^{3}J_{H,H}$ = 7.2 Hz, 6H, CH_2CH_3, *E* and *Z*), 1.32-1.38 (m, 12H, OCH_2CH_3, *E* and *Z*), 2.82 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3, *Z*), 2.95 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3, *E*), 4.06-4.19 (m, 8H, OCH_2CH_3, *E* and *Z*), 6.31-6.33 (m, 1H, $H_{pyrrole}$, *Z*), 6.39-6.41 (m, 1H, $H_{pyrrole}$, *E*), 6.79 (br s, 1H, $H_{pyrrole}$, *Z*), 6.85 (br s, 1H, $H_{pyrrole}$, *E*), 7.15 (br s, 2H, $H_{pyrrole}$, *E* and *Z*), 7.78 (d, $^{3}J_{P,H}$ = 24.3 Hz, 1H, C*H*=C, *E*), 8.01 (d, $^{3}J_{P,H}$ = 45.1 Hz, 1H, C*H*=C, *Z*), 12.4 (br s, 1H, N*H*, *E*), 13.2 (br s, 1H, N*H*, *Z*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.4 (*Z*), 8.8 (*E*), 16.3 (d, $^{3}J_{P,C}$ = 4.4 Hz, *Z*), 16.4 (d, $^{3}J_{P,C}$ = 4.5 Hz, *E*), 33.2 (*E*), 35.5 (d, $^{3}J_{P,C}$ = 2.4 Hz, *Z*), 62.2 (d, $^{2}J_{P,C}$ = 5.5 Hz, *E*), 62.5 (d, $^{2}J_{P,C}$ = 5.4 Hz, *Z*), 111.4 (Z), 112.5 (E), 114.2 (d, $^{1}J_{P,C}$ = 181.5 Hz, Z), 114.5 (d, $^{1}J_{P,C}$ = 178.3 Hz, E), 125.7 (Z), 125.9 (E), 126.4 (E), 127.3 (d, $^{3}J_{P,C}$ = 9.0 Hz, *E*), 128.2 (Z), 129.3 (d, $^{3}J_{P,C}$ = 21.3 Hz, *Z*), 143.9 (d, $^{2}J_{P,C}$ = 11.1 Hz, *Z*), 144.1 (d, $^{2}J_{P,C}$ = 11.4 Hz, *E*), 199.9 (d, $^{2}J_{P,C}$ = 13.1 Hz, *E*), 201.9 (d, $^{2}J_{P,C}$ = 19.6 Hz, *Z*). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 20.7 (*E*), 23.3 (*Z*). HRMS (ESI): *m/z* calcd for $C_{13}H_{21}NO_4P$ $[M+H]^+$: 286.1203; found: 286.1241.

***E*-diethyl 1-(furan-2-yl)-3-oxopent-1-en-2-ylphosphonate (245):** Brown viscous oil; yield: 407 mg (92 %); R_f = 0.22 (1:1 EtOAc-hexane). IR (ATR): 2981, 2939, 2907, 1701, 1617, 1545, 1474, 1391, 1352, 1243, 1155, 1124, 1015, 961, 756 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.34 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 2.73 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.15 (dq, $^{3}J_{P,H}$ = 7.4 Hz, $^{3}J_{H,H}$ = 7.1 Hz, 4H, OCH_2CH_3), 6.46-6.44 (br s, 1H, H_{furan}), 6.64 (d, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H_{furan}), 7.19 (d, $^{3}J_{P,H}$ = 25.2 Hz, 1H, C*H*=C), 7.46 (br s, 1H, H_{furan}). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.5, 16.2 (d, $^{3}J_{P,C}$ = 6.7 Hz), 36.9, 62.6 (d, $^{2}J_{P,C}$ = 5.3 Hz), 112.4, 116.6, 128.8 (d, $^{1}J_{P,C}$ = 172.3 Hz), 130.1 (d, $^{2}J_{P,C}$ = 7.2 Hz), 145.7, 149.5 (d, $^{3}J_{P,C}$ = 24.2 Hz), 204.9 (d, $^{2}J_{P,C}$ = 8.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.9. HRMS (ESI): *m/z* calcd for $C_{13}H_{20}O_5P$ $[M+H]^+$: 287.1043; found: 287.1079.

***E*-diethyl 3-oxo-1-(thiophen-2-yl)pent-1-en-2-ylphosphonate (246):** Yellow viscous oil; yield: 444 mg (95 %); R_f = 0.29 (1:1 EtOAc-hexane). IR (ATR): 3101, 3069, 2989, 2945, 2904, 1699, 1596, 1517, 1407, 1344, 1292, 1248, 1166, 1130, 1040, 1012, 969, 949, 857 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.36 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 2.78 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2CH_3), 4.17 (dq, $^{3}J_{P,H}$ = 7.5 Hz, $^{3}J_{H,H}$ = 7.1 Hz, 4H, OCH_2CH_3), 7.06-7.08 (m, 1H, $H_{thiophene}$), 7.27-7.29 (m, 1H, $H_{thiophene}$), 7.49 (d, $^{3}J_{H,H}$ = 5.0 Hz, 1H,

$H_{thiophene}$), 7.65 (d, $^{3}J_{P,H}$ = 25.0 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.8, 16.2 (d, $^{3}J_{P,C}$ = 6.6 Hz), 36.6, 62.6 (d, $^{2}J_{P,C}$ = 5.5 Hz), 127.8, 128.8 (d, $^{1}J_{P,C}$ = 172.5 Hz), 131.4, 134.2, 136.8 (d, $^{3}J_{P,C}$ = 24.1 Hz), 138.4 (d, $^{2}J_{P,C}$ = 8.0 Hz), 204.8 (d, $^{2}J_{P,C}$ = 10.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 15.7. HRMS (ESI): *m/z* calcd for $C_{13}H_{20}O_4PS$ $[M+H]^+$: 303.0814; found: 303.0853.

4.2.3. General Procedure for the Synthesis of Vinylphosphonates from Diethyl cyanomethylphosphonate and Aldehydes

Diethyl cyanomethylphosphonate (1.85 mmol) and aldehyde (2.09 mmol) were dissolved in toluene (10 mL) and piperidine (0.18 mmol) was added to this solution. The resulting mixture was refluxed under a Dean-Stark trap for 8 h (TLC monitoring). After the completion of the reaction the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1).

***E*-diethyl 1-cyano-2-phenylvinylphosphonate (248):** Yellow viscous oil; yield: 486 mg (93 %); R_f = 0.28 (1:1 EtOAc-hexane). IR (ATR): 2988, 2914, 2212, 1595, 1571, 1450, 1393, 1259, 1211, 1163, 1014, 974, 791, 760 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H, OCH_2CH_3), 4.15-4.27 (m, 4H, OCH_2CH_3), 7.48-7.56 (m, 3H, Ar*H*), 7.97 (d, $^{3}J_{H,H}$ = 7.2 Hz, 2H, Ar*H*), 8.02 (d, $^{3}J_{P,H}$ = 21.2 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.3 Hz), 63.4 (d, $^{2}J_{P,C}$ = 5.8 Hz), 100.2 (d, $^{1}J_{P,C}$ = 195.9 Hz), 115.2 (d, $^{2}J_{P,C}$ = 10.0 Hz), 129.1, 130.4, 132.4 (d, $^{3}J_{P,C}$ = 17.7 Hz), 132.9, 158.6 (d, $^{2}J_{P,C}$ = 7.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 10.8. HRMS (ESI): *m/z* calcd for $C_{13}H_{17}NO_3P$ $[M+H]^+$: 266.0941; found: 266.0992.

***E*-diethyl 1-cyano-2-(4-(trifluoromethyl)phenyl)vinylphosphonate (249):** Light yellow viscous oil; yield: 609 mg (99 %); R_f = 0.44 (1:1, EtOAc-hexane). IR (ATR): 2980, 2935, 2903, 2214, 1601, 1416, 1322, 1263, 1168, 1133, 1069, 1014, 975, 837, 789 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 4.19-4.29 (m, 4H, OCH_2CH_3), 7.76 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2H, Ar*H*), 8.02 (d, $^{3}J_{P,H}$ = 21.6 Hz, 1H, C*H*=C), 8.06 (d, $^{3}J_{H,H}$ = 8.5 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.3 Hz), 63.6 (d, $^{2}J_{P,C}$ = 5.9 Hz), 103.9 (d, $^{1}J_{P,C}$ =

194.3 Hz), 114.5 (d, $^{2}J_{P,C}$ = 9.4 Hz), 123.2 (q, $^{1}J_{F,C}$ = 271.1 Hz), 126.0 (q, $^{3}J_{F,C}$ = 3.7 Hz), 130.4, 134.0 (q, $^{2}J_{F,C}$ = 32.8 Hz), 135.4 (d, $^{3}J_{P,C}$ = 18.1 Hz), 156.3 (d, $^{2}J_{P,C}$ = 7.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 10.1. HRMS (ESI): *m/z* calcd for $C_{14}H_{16}F_3NO_3P$ $[M+H]^+$: 334.0814; found: 334.0876.

***E*-diethyl 1-cyano-2-*p*-tolylvinylphosphonate (250):** Yellow viscous oil; yield: 510 mg (99 %); R_f = 0.34 (1:1 EtOAc-hexane). IR (ATR): 2980, 2905, 2208, 1593, 1562, 1507, 1444, 1392, 1259, 1188, 1160, 1014, 971, 845, 794 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3), 2.44 (s, 3H, CH_3), 4.16-4.26 (m, 4H, OCH_2CH_3), 7.29 (d, $^{3}J_{H,H}$ = 7.9 Hz, 2H, Ar*H*), 7.86 (d, $^{3}J_{H,H}$ = 7.7 Hz, 2H, Ar*H*), 7.94 (d, $^{3}J_{P,H}$ = 21.4 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.4 Hz), 21.7, 63.2 (d, $^{2}J_{P,C}$ = 5.8 Hz), 98.5 (d, $^{1}J_{P,C}$ = 196.8 Hz), 114.5, 115.3 (d, $^{2}J_{P,C}$ = 10.1 Hz), 129.8, 129.9 (d, $^{3}J_{P,C}$ = 17.9 Hz), 130.6, 143.8, 158.5 (d, $^{2}J_{P,C}$ = 7.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 12.1. HRMS (ESI): *m/z* calcd for $C_{14}H_{19}NO_3P$ $[M+H]^+$: 280.1097; found: 280.1149.

***E*-diethyl 1-cyano-2-(4-methoxyphenyl)vinylphosphonate (251):** Yellow viscous oil; yield: 540 mg (99 %); R_f = 0.21 (1:1 EtOAc-hexane). IR (ATR): 2984, 2933, 2909, 2842, 2212, 1586, 1558, 1511, 1424, 1369, 1306, 1259, 1180, 1097, 1014, 971, 833, 794 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3), 3.89 (s, 3H, OCH_3), 4.15-4.25 (m, 4H, OCH_2CH_3), 6.97 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, Ar*H*), 7.89 (d, $^{3}J_{P,H}$ = 21.3 Hz, 1H, C*H*=C), 7.96 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.2 Hz), 55.3, 63.1 (d, $^{2}J_{P,C}$ = 5.6 Hz), 95.9 (d, $^{1}J_{P,C}$ = 198.4 Hz), 114.5, 115.7 (d, $^{2}J_{P,C}$ = 10.1 Hz), 125.5 (d, $^{3}J_{P,C}$ = 18.1 Hz), 132.8, 158.0 (d, $^{2}J_{P,C}$ = 7.7 Hz), 163.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 12.8. HRMS (ESI): *m/z* calcd for $C_{14}H_{19}NO_4P$ $[M+H]^+$: 296.1046; found: 296.1103.

***E*-diethyl 1-cyano-2-(4-fluorophenyl)vinylphosphonate (252):** Yellow viscous oil; yield: 518 mg (99 %); R_f = 0.30 (1:1 EtOAc-hexane). IR (ATR): 2964, 2908, 2212, 1597, 1507, 1416, 1259, 1160, 1066, 1014, 971, 837, 790 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H, OCH_2CH_3), 4.18-4.28 (m, 4H, OCH_2CH_3), 7.20 (t, $^{3}J_{H,H}$ = 8.0 Hz, 2H, Ar*H*), 7.96 (d, $^{3}J_{P,H}$ = 21.2 Hz, 1H, C*H*=C), 7.99-8.03 (m, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.4 Hz),

63.4 (d, $^{2}J_{P,C}$ = 5.8 Hz), 99.8 (d, $^{1}J_{P,C}$ = 195.5 Hz), 115.0 (d, $^{2}J_{P,C}$ = 9.9 Hz), 116.5 (d, $^{2}J_{F,C}$ = 21.9 Hz), 128.9, 132.9 (d, $^{3}J_{F,C}$ = 8.8 Hz), 157.0 (d, $^{2}J_{P,C}$ = 7.3 Hz), 165.1 (d, $^{1}J_{F,C}$ = 255.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 11.0. HRMS (ESI): *m/z* calcd for $C_{13}H_{16}FNO_3P$ $[M+H]^+$: 284.0846; found: 284.0901.

***E*-diethyl 2-(4-chlorophenyl)-1-cyanovinylphosphonate (253):** Yellow viscous oil; yield: 548 mg (99 %); R_f = 0.47 (1:1 EtOAc-hexane). IR (ATR): 2984, 2933, 2909, 2212, 1589, 1558, 1491, 1408, 1255, 1211, 1160, 1097, 1010, 975, 829, 786 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H, OCH_2CH_3), 4.17-4.27 (m, 4H, OCH_2CH_3), 7.47 (d, $^{3}J_{H,H}$ = 7.2 Hz, 2H, Ar*H*), 7.91 (d, $^{3}J_{H,H}$ = 7.6 Hz, 2H, Ar*H*), 7.93 (d, $^{3}J_{P,H}$ = 20.4 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3 (d, $^{3}J_{P,C}$ = 6.3 Hz), 63.5 (d, $^{2}J_{P,C}$ = 5.8 Hz), 101.0 (d, $^{1}J_{P,C}$ = 196.1 Hz), 115.0 (d, $^{2}J_{P,C}$ = 9.8 Hz), 129.6, 130.9 (d, $^{3}J_{P,C}$ = 18.2 Hz), 131.6, 139.3, 156.9 (d, $^{2}J_{P,C}$ = 7.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 11.0. HRMS (ESI): *m/z* calcd for $C_{13}H_{16}ClNO_3P$ $[M+H]^+$: 300.0551; found: 300.0604.

***E*-diethyl 2-(4-bromophenyl)-1-cyanovinylphosphonate (254):** Yellow viscous oil; yield: 623 mg (98 %); R_f = 0.44 (1:1 EtOAc-hexane). IR (ATR): 2988, 2911, 2216, 1597, 1586, 1554, 1487, 1404, 1255, 1164, 1046, 1006, 979, 821, 790 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H, OCH_2CH_3), 4.18-4.27 (m, 4H, OCH_2CH_3), 7.64 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.83 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.92 (d, $^{3}J_{P,H}$ = 21.2 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.3 Hz), 63.4 (d, $^{2}J_{P,C}$ = 5.9 Hz), 101.1 (d, $^{1}J_{P,C}$ = 195.7 Hz), 114.9 (d, $^{2}J_{P,C}$ = 9.6 Hz), 127.8, 131.2 (d, $^{3}J_{P,C}$ = 18.2 Hz), 131.6, 132.5, 156.9 (d, $^{2}J_{P,C}$ = 7.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 11.0. HRMS (ESI): *m/z* calcd for $C_{13}H_{16}BrNO_3P$ $[M+H]^+$: 344.0046; found: 344.0102.

***E*-diethyl 1-cyano-2-(4-hydroxyphenyl)vinylphosphonate (255):** Light yellow powder; mp 123.2-123.8 °C; yield: 467 mg (90 %); R_f = 0.18 (1:1 EtOAc-hexane). IR (ATR): 3130, 2996, 2901, 2212, 1601, 1589, 1574, 1515, 1440, 1361, 1298, 1215, 1164, 1018, 975, 908, 786, 727 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3), 4.18-4.30 (m, 4H, OCH_2CH_3), 6.98 (d, $^{3}J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), 7.83 (d, $^{3}J_{P,H}$ = 21.2 Hz, 1H, C*H*=C), 7.87 (d, $^{3}J_{H,H}$ = 8.5 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.4 Hz), 63.7 (d, $^{2}J_{P,C}$ = 5.9

Hz), 93.3 (d, $^{1}J_{P,C}$ = 202.8 Hz), 115.8 (d, $^{2}J_{P,C}$ = 10.9 Hz), 116.5, 124.4 (d, $^{3}J_{P,C}$ = 18.2 Hz), 133.5, 159.0 (d, $^{2}J_{P,C}$ = 7.5 Hz), 162.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 13.7. HRMS (ESI): *m/z* calcd for $C_{13}H_{17}NO_4P$ $[M+H]^+$: 282.0890; found: 282.0942.

***E*-diethyl 1-cyano-2-(4-cyanophenyl)vinylphosphonate (256):** Light yellow powder; mp 60.6-61.8 °C; yield: 434 mg (81 %); R_f = 0.28 (1:1 EtOAc-hexane). IR (ATR): 2992, 2937, 2909, 2239, 2212, 1597, 1499, 1389, 1259, 1168, 1011, 975, 861, 794 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 4.18-4.32 (m, 4H, OCH_2CH_3), 7.80 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 8.00 (d, $^{3}J_{P,H}$ = 21.2 Hz, 1H, C*H*=C), 8.04 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3 (d, $^{3}J_{P,C}$ = 6.1 Hz), 63.8 (d, $^{2}J_{P,C}$ = 5.9 Hz), 105.0 (d, $^{1}J_{P,C}$ = 193.7 Hz), 114.4 (d, $^{2}J_{P,C}$ = 9.3 Hz), 116.0, 117.4, 130.5, 132.8, 136.0 (d, $^{3}J_{P,C}$ = 18.1 Hz), 155.7 (d, $^{2}J_{P,C}$ = 7.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 9.6. HRMS (ESI): *m/z* calcd for $C_{14}H_{16}N_2O_3P$ $[M+H]^+$: 291.0893; found: 291.0919.

***E*-diethyl 1-cyano-2-(4-nitrophenyl)vinylphosphonate (257):** Yellow powder; mp 107.8-108.1 °C; yield: 470 mg (82 %); R_f = 0.30 (1:1 EtOAc-hexane). IR (ATR): 2995, 2972, 2911, 1597, 1514, 1435, 1353, 1251, 1152, 1045, 1006, 971, 869, 786 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3), 4.20-4.31 (m, 4H, OCH_2CH_3), 8.04 (d, $^{3}J_{P,H}$ = 21.0 Hz, 1H, C*H*=C), 8.11 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, Ar*H*), 8.35 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.2 Hz), 63.8 (d, $^{2}J_{P,C}$ = 6.1 Hz), 105.7 (d, $^{1}J_{P,C}$ = 193.4 Hz), 114.2 (d, $^{2}J_{P,C}$ = 9.2 Hz), 124.2, 130.9, 137.6 (d, $^{3}J_{P,C}$ = 18.0 Hz), 149.6, 155.1 (d, $^{2}J_{P,C}$ = 7.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 9.4. HRMS (ESI): *m/z* calcd for $C_{13}H_{16}N_2O_5P$ $[M+H]^+$: 311.0791; found: 311.0821.

***E*-diethyl 1-cyano-2-mesitylvinylphosphonate (258):** White powder; mp 77.0-77.5 °C; yield: 340 mg (60 %); R_f = 0.49 (1:1 EtOAc-hexane). IR (ATR): 2988, 2913, 2216, 1593, 1440, 1392, 1259, 1164, 1077, 1018, 975, 912, 786, 727 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 2.28 (s, 6H, CH_3), 2.30 (s, 3H, CH_3), 4.18-4.31 (m, 4H, OCH_2CH_3), 6.87 (s, 2H, Ar*H*), 8.22 (d, $^{3}J_{P,H}$ = 19.5 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^{3}J_{P,C}$ = 6.2 Hz), 20.1, 21.1, 63.3 (d, $^{2}J_{P,C}$ = 5.8 Hz), 108.9 (d, $^{1}J_{P,C}$ = 192.9 Hz), 114.1 (d, $^{2}J_{P,C}$ = 12.5 Hz), 128.8, 129.7 (d, $^{3}J_{P,C}$ = 16.0 Hz), 135.3, 139.5, 161.9 (d, $^{2}J_{P,C}$ = 6.5

Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 9.5. HRMS (ESI): *m/z* calcd for $C_{16}H_{23}NO_3P$ $[M+H]^+$: 308.1410; found: 308.1467.

***E*-diethyl 1-cyano-2-(1*H*-pyrrol-2-yl)vinylphosphonate (259):** Brown solid; mp 77.7-78.6 °C; yield: 422 mg (90 %); R_f = 0.14 (1:1 EtOAc-hexane). IR (ATR): 3197, 3078, 2992, 2976, 2212, 1586, 1432, 1396, 1341, 1231, 1144, 1018, 967, 782, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 4.14-4.22 (m, 4H, OCH_2CH_3), 6.42 (s, 1H, $H_{pyrrole}$), 7.13 (s, 1H, $H_{pyrrole}$), 7.38 (br s, 1H, $H_{pyrrole}$), 7.96 (d, $^3J_{P,H}$ = 19.8 Hz, 1H, C*H*=C), 11.3 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d, $^3J_{P,C}$ = 6.6 Hz), 63.1 (d, $^2J_{P,C}$ = 5.7 Hz), 85.5 (d, $^1J_{P,C}$ = 207.4 Hz), 112.7, 116.9 (d, $^2J_{P,C}$ = 11.3 Hz), 126.2, 127.9, 128.1, 147.6 (d, $^2J_{P,C}$ = 8.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 14.9. HRMS (ESI): *m/z* calcd for $C_{11}H_{16}N_2O_3P$ $[M+H]^+$: 255.0893; found: 255.0941.

***E*-diethyl 1-cyano-2-(furan-2-yl)vinylphosphonate (260):** Brown viscous oil; yield: 433 mg (92 %); R_f = 0.26 (1:1 EtOAc-hexane). IR (ATR): 2984, 2905, 2204, 1609, 1585, 1542, 1455, 1385, 1251, 1164, 1042, 1018, 971, 790, 739 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, $^3J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 4.16-4.25 (m, 4H, OCH_2CH_3), 6.63 (br s, 1H, H_{furan}), 7.28 (br s, 1H, H_{furan}), 7.72 (br s, 1H, H_{furan}), 7.76 (d, $^3J_{P,H}$ = 20.2 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3 (d, $^3J_{P,C}$ = 6.3 Hz), 63.3 (d, $^2J_{P,C}$ = 5.7 Hz), 95.5 (d, $^1J_{P,C}$ = 200.0 Hz), 113.4, 115.1 (d, $^2J_{P,C}$ = 9.3 Hz), 120.3, 143.3 (d, $^2J_{P,C}$ = 8.5 Hz), 147.4, 149.4 (d, $^3J_{P,C}$ = 21.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 11.7. HRMS (ESI): *m/z* calcd for $C_{11}H_{15}NO_4P$ $[M+H]^+$: 256.0733; found: 256.0783.

***E*-diethyl 1-cyano-2-(thiophen-2-yl)vinylphosphonate (261):** Light yellow viscous oil; yield: 507 mg (95 %); R_f = 0.26 (1:1 EtOAc-hexane). IR (ATR): 2987, 2876, 2209, 1581, 1413, 1392, 1362, 1259, 1238, 1164, 1046, 1013, 973, 787 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, $^3J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3), 4.14-4.22 (m, 4H, OCH_2CH_3), 7.17-7.20 (m, 1H, $H_{thiophene}$), 7.70 (d, $^3J_{H,H}$ = 5.0 Hz, 1H, $H_{thiophene}$), 7.76 (d, $^3J_{H,H}$ = 3.6 Hz, 1H, $H_{thiophene}$), 8.05 (d, $^3J_{P,H}$ = 19.8 Hz, 1H, C*H*=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3 (d, $^3J_{P,C}$ = 6.3 Hz), 63.2 (d, $^2J_{P,C}$ = 5.7 Hz), 96.2 (d, $^1J_{P,C}$ = 199.6 Hz), 115.2 (d, $^2J_{P,C}$ = 9.7 Hz), 128.2, 133.9, 135.8, 137.2 (d, $^3J_{P,C}$ = 20.0 Hz), 150.2 (d, $^2J_{P,C}$ = 8.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ

= 11.8. HRMS (ESI): *m/z* calcd for $C_{11}H_{15}NO_4P$ $[M+H]^+$: 272.0505; found: 272.0549.

4.3. Michael Addition Reactions of Heteroaromatics to Vinylphosphonates

4.3.1. General Procedure for the Michael Addition of Heteroaromatics to Ester Functionalized Vinylphosphonates

To a solution of ester functionalized vinylphosphonates (**217-232**) (0.093 mmol) in toluene (2mL) was added 10 mol % of Metal triflate (0.0093 mmol) and the reaction mixture was stirred for 0.5 h at room temperature. Pyrrole (0.93 mmol) was added to the reaction mixture instantly *via* syringe pump. The resulting mixture was stirred at room temperature for 48 h (TLC monitoring). Metal triflate was removed from the reaction medium by subjecting the mixture to a short flash column chromatography (silica gel, EtOAc). The eluent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1 or 4:1).

Methyl 2-(dimethoxyphosphoryl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (262): Light brown powder; mp 173.8-174.8 °C; yield: 31 mg (98 %); dr 55:45; R_f = 0.13 (1:1, EtOAc-hexane). IR (ATR): 3260, 3007, 2948, 2849, 1731, 1570, 1495, 1439, 1264, 1234, 1209, 1030, 805, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.33-3.42 (m, 12H, 4 OC*H*$_3$)*, 3.56 (s, 3H, OC*H*$_3$), [3.65 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OC*H*$_3$)], 3.75 (dd, $^2J_{P,H}$ = 21.3 Hz, $^3J_{H,H}$ = 6.2 Hz, 1H, C*H*), [3.77 (dd, $^2J_{P,H}$ = 21.7 Hz, $^3J_{H,H}$ = 5.2 Hz, 1H, C*H*)], 4.57-4.73 (m, 2H, 2 C*H*)*, [5.80 (br s, 1H, $H_{pyrrole}$)], 5.97-6.08 (m, 3H, 3 $H_{pyrrole}$)*, 6.60 (br s, 2H, 2 $H_{pyrrole}$)*, 7.12-7.25 (m, 10H, Ar*H*)*, 8.66 (br s, 1H, N*H*), [9.17 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.2 (d, $^2J_{P,C}$ = 2.6 Hz), [43.8 (d, $^2J_{P,C}$ = 3.0 Hz)], 51.2 (d, $^1J_{P,C}$ = 131.5 Hz), [52.2 (d, $^1J_{P,C}$ = 132.3 Hz)], 52.4, [52.8], 53.0 (d, $^2J_{P,C}$ = 6.6 Hz), [53.2], 53.3, [53.6 (d, $^2J_{P,C}$ = 7.1 Hz)], 106.7, [107.5], 108.1, [108.4], [117.3], 117.7, [127.1], 127.2, 127.9*, 128.3*, 128.5*, 130.1, [130.7 (d, $^3J_{P,C}$ = 8.3 Hz)], 140.3 (d, $^3J_{P,C}$ = 4.0 Hz), [140.5], [168.0 (d, $^2J_{P,C}$ = 4.8 Hz)], 169.3 (d, $^2J_{P,C}$ = 4.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.5, [25.5]. HRMS (ESI): *m/z* calcd for $C_{16}H_{21}NO_5P$ $[M+H]^+$: 338.1152; found: 338.1127.

Methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)-3-(4-(trifluoromethyl)-phenyl)propanoate (263): Light brown powder; mp 167.5-168 °C; yield: 37 mg (98 %); dr 61:39; R_f = 0.13 (1:1, EtOAc-hexane). IR (ATR): 3277, 2963, 2923, 2848, 1732, 1616, 1438, 1326, 1251, 1171, 1128, 1068, 1032, 929, 770, 726 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.43-3.51 (m, 12H, 4 OCH_3)*, 3.67 (s, 3H, OCH_3), [3.73 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3)], [3.82 (dd, $^2J_{P,H}$ = 20.3 Hz, $^3J_{H,H}$ = 7.7 Hz, 1H, C*H*)], 3.83 (dd, $^2J_{P,H}$ = 22.0 Hz, $^3J_{H,H}$ = 9.0 Hz, 1H, C*H*), 4.82-4.88 (m, 2H, 2 C*H*)*, [5.81 (br s, 1H, $H_{pyrrole}$)], 6.05-6.11 (m, 3H, 3 $H_{pyrrole}$)*, 6.70-6.72 (m, 2H, 2 $H_{pyrrole}$)*, 7.42-7.45 (m, 4H, Ar*H*)*, 7.52-7.57 (m, 4H, Ar*H*)*, 8.86 (br s, 1H, N*H*), [9.31 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.9 (d, $^2J_{P,C}$ = 2.7 Hz), [43.5 (d, $^2J_{P,C}$ = 2.7 Hz)], 50.8 (d, $^1J_{P,C}$ = 131.6 Hz), [51.9 (d, $^1J_{P,C}$ = 132.9 Hz)], [52.6], 53.0, 53.0 (d, $^2J_{P,C}$ = 6.6 Hz), [53.3 (d, $^2J_{P,C}$ = 6.9 Hz)], 53.4 (d, $^2J_{P,C}$ = 7.0 Hz), [53.8 (d, $^2J_{P,C}$ = 7.2 Hz)], 107.2, [107.8], 108.3, [108.7], [117.7], 118.1, 124.1 (q, $^1J_{F,C}$ = 273.4 Hz)*, 125.4 (q, $^3J_{F,C}$ = 3.7 Hz), [125.6 (q, $^3J_{F,C}$ = 3.8 Hz)], [128.3], 128.7, 129.4 (q, $^2J_{F,C}$ = 32.4 Hz)*, 129.7, [130.1], 144.5, [144.6], [167.8 (d, $^2J_{P,C}$ = 4.7 Hz)], 169.1 (d, $^2J_{P,C}$ = 4.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.9, [25.0]. HRMS (ESI): *m/z* calcd for $C_{17}H_{20}F_3NO_5P$ $[M+H]^+$: 406.1026; found: 406.0986.

Methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)-3-*p*-tolylpropanoate (264): Light orange powder; mp 145.3-146.9 °C; yield: 30 mg (92 %); dr 51:49; R_f = 0.28 (1:1, EtOAc-hexane). IR (ATR): 3273, 2959, 2852, 1732, 1517, 1434, 1259, 1239, 1187, 1156, 1032, 925, 802, 758 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = [2.28 (s, 3H, CH_3)], 2.29 (s, 3H, CH_3), 3.37-3.50 (m, 12H, 4 OCH_3)*, 3.64 (s, 3H, OCH_3), [3.70 (d, $^3J_{P,H}$ = 3.4 Hz, 3H, OCH_3)], 3.85 (dd, $^2J_{P,H}$ = 21.2 Hz, $^3J_{H,H}$ = 9.6 Hz, 2H, 2 C*H*)*, 4.72-4.78 (m, 2H, 2 C*H*)*, [5.91 (br s, 1H, $H_{pyrrole}$)], 6.03-6.09 (m, 3H, 3 $H_{pyrrole}$)*, 6.64-6.65 (br s, 2H, 2 $H_{pyrrole}$)*, 7.08 (t, $^3J_{H,H}$ = 8.0 Hz, 4H, Ar*H*)*, 7.21 (d, $^3J_{H,H}$ = 8.0 Hz, 4H, Ar*H*)*, 8.70 (br s, 1H, N*H*), [9.16 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0*, 42.9, [43.4 (d, $^2J_{P,C}$ = 3.1 Hz)], 51.2 (d, $^1J_{P,C}$ = 131.2 Hz), [52.2 (d, $^1J_{P,C}$ = 131.7 Hz)], [52.4], 52.8, 53.0 (d, $^2J_{P,C}$ = 6.6 Hz), 53.2 (d, $^2J_{P,C}$ = 6.7 Hz), [53.3 (d, $^2J_{P,C}$ = 6.8 Hz)], [53.5 (d, $^2J_{P,C}$ = 7.2 Hz)], [106.3], 107.1, 107.9, [108.3], [117.2], 117.6, 127.7, [128.2], 129.1, [129.2], 130.9 (d, $^3J_{P,C}$ = 1.3 Hz), [131.2 (d, $^3J_{P,C}$ = 16.0 Hz)], [136.6], 136.7, 137.3 (d, $^3J_{P,C}$ = 5.8 Hz), [137.6 (d, $^3J_{P,C}$ = 13.9 Hz)], [168.1 (d, $^2J_{P,C}$ = 4.7 Hz)], 169.4 (d, $^2J_{P,C}$ = 4.2 Hz). ^{31}P NMR (162

MHz, $CDCl_3$): *δ* 23.6, [25.7]. HRMS (ESI): *m/z* calcd for $C_{17}H_{23}NO_5P$ $[M+H]^+$: 352.1308; found: 352.1282.

Methyl 2-(dimethoxyphosphoryl)-3-(4-methoxyphenyl)-3-(1*H*-pyrrol-2-yl)propanoate (265): Brown powder; mp 151.4-152.0 °C; yield: 29 mg (84 %); dr 55:45; R_f = 0.19 (1:1, EtOAc-hexane). IR (ATR): 3285, 2967, 2919, 2852, 1736, 1608, 1513, 1469, 1438, 1255, 1183, 1032, 929, 810, 758 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.45 (s, 3H, OCH_3), 3.48 (s, 6H, 2 OCH_3)*, [3.51 (s, 3H, OCH_3)], [3.66 (s, 3H, OCH_3)], 3.72 (d, $^3J_{P,H}$ = 10.9 Hz, 3H, OCH_3)], 3.77 (s, 6H, 2 OCH_3)*, 3.77-3.85 (m, 2H, 2 C*H*)*, 4.69-4.77 (m, 2H, 2 C*H*)*, 5.86 (br s, 1H, $H_{pyrrole}$), [6.02 (br s, 1H, $H_{pyrrole}$)], 6.06 (br s, 2H, 2 $H_{pyrrole}$)*, 6.67 (br s, 2H, 2 $H_{pyrrole}$)*, 6.81-6.84 (m, 4H, Ar*H*)*, 7.23 (d, $^3J_{H,H}$ = 7.1 Hz, 4H, Ar*H*)*, [8.68 (br s, 1H, N*H*)], 9.20 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.2 (d, $^2J_{P,C}$ = 2.7 Hz), [42.8 (d, $^2J_{P,C}$ = 3.1 Hz)], [51.1 (d, $^1J_{P,C}$ = 131.3 Hz)], 52.2 (d, $^1J_{P,C}$ = 125.2 Hz)], [52.2], 52.6, [52.9], 53.0 (d, $^2J_{P,C}$ = 2.6 Hz), 53.1 (d, $^2J_{P,C}$ = 2.2 Hz), [53.4 (d, $^2J_{P,C}$ = 7.1 Hz)], [55.0], 55.0, 106.3, [107.1], 107.9, [108.2], [113.6], 113.7, 116.9, [117.3], 128.8, [129.2], 130.9, [131.1], 132.2 (d, $^3J_{P,C}$ = 6.0 Hz), [132.4], 158.3, [158.4], [167.9], 169.2 (d, $^2J_{P,C}$ = 4.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.6, [25.7]. HRMS (ESI): *m/z* calcd for $C_{17}H_{23}NO_6P$ $[M+H]^+$: 368.1258; found: 368.1222.

Methyl 2-(dimethoxyphosphoryl)-3-(4-fluorophenyl)-3-(1*H*-pyrrol-2-yl)propanoate (266): Yellow powder; mp 186.8-188.4 °C; yield: 20 mg (62 %); dr 65:35; R_f = 0.44 (EtOAc). IR (ATR): 2952, 2920, 2846, 1738, 1508, 1233, 1164, 1033, 727 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.47-3.54 (m, 12H, 4 OCH_3)*, 3.69 (s, 3H, OCH_3), [3.75 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3)], 3.78-3.87 (m, 2H, 2 C*H*)*, 4.77-4.84 (m, 2H, 2 C*H*)*, [5.88 (br s, 1H, $H_{pyrrole}$)], 6.06 (br s, 1H, $H_{pyrrole}$), 6.10 (br s, 2H, 2 $H_{pyrrole}$)*, 6.71 (br s, 2H, 2 $H_{pyrrole}$)*, 6.99-7.03 (m, 4H, Ar*H*)*, 7.30-7.34 (m, 4H, Ar*H*)*, 8.85 (br s, 1H, N*H*), [9.37 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.5 (d, $^2J_{P,C}$ = 2.5 Hz), [43.1], 51.3 (d, $^1J_{P,C}$ = 131.5 Hz), [52.3 (d, $^1J_{P,C}$ = 132.4 Hz)], [52.5], 52.8, 53.0 (d, $^2J_{P,C}$ = 6.8 Hz), [53.2], 53.3 (d, $^2J_{P,C}$ = 6.7 Hz), [53.7 (d, $^2J_{P,C}$ = 6.9 Hz)], 106.7, [107.5], 108.2, [108.5], 115.3 (d, $^2J_{F,C}$ = 21.4 Hz), [115.4 (d, $^2J_{F,C}$ = 21.4 Hz)], [117.4], 117.8, [129.6 (d, $^3J_{F,C}$ = 8.0 Hz)], 130.0 (d, $^3J_{F,C}$ = 8.0 Hz), [130.5], 130.7 (d, $^3J_{P,C}$ = 15.2 Hz), 136.2 (d, $^3J_{P,C}$ = 9.6 Hz), [136.4], [161.8 (d, $^1J_{F,C}$ = 244.4 Hz)], 161.9 (d, $^1J_{F,C}$ = 244.5 Hz), [167.9 (d, $^2J_{P,C}$ = 4.8 Hz)], 169.2

(d, $^{2}J_{P,C}$ = 4.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.3, [25.3]. HRMS (ESI): *m/z* calcd for $C_{16}H_{20}FNO_5P$ $[M+H]^+$: 356.1063; found: 356.1057.

Methyl 3-(4-chlorophenyl)-2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)propanoate (267): Yellow powder; mp 172.3-173.9 °C; yield: 27 mg (78 %); dr 53:47; R_f = 0.46 (EtOAc). IR (ATR): 3248, 3141, 2999, 2956, 2849, 1735, 1491, 1432, 1266, 1227, 1050, 1026, 1014, 853, 770, 716 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$), [3.43 (d, $^{3}J_{P,H}$ = 7.9 Hz, 3H, OC*H*$_3$)], 3.44 (s, 3H, OC*H*$_3$), [3.47 (d, $^{3}J_{P,H}$ = 5.5 Hz, 3H, OC*H*$_3$)], [3.66 (s, 3H, OC*H*$_3$)], 3.72 (d, $^{3}J_{P,H}$ = 11.0 Hz, 3H, OC*H*$_3$), 3.75-3.84 (m, 2H, 2 C*H*)*, 4.09-4.15 (m, 2H, 2 C*H*)*, 5.84 (br s, 1H, $H_{pyrrole}$), [6.02 (br s, 1H, $H_{pyrrole}$)], 6.06-6.09 (m, 2H, 2 $H_{pyrrole}$)*, 6.68 (br s, 2H, 2 $H_{pyrrole}$)*, 7.17-7.23 (m, 8H, Ar*H*)*, [8.84 (br s, 1H, N*H*)], 9.32 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [42.6 (d, $^{2}J_{P,C}$ = 2.6 Hz)], 43.2 (d, $^{2}J_{P,C}$ = 2.9 Hz), [51.0 (d, $^{1}J_{P,C}$ = 131.3 Hz)], 52.1 (d, $^{1}J_{P,C}$ = 132.4 Hz), [52.5], 52.9, [53.0 (d, $^{2}J_{P,C}$ = 6.6 Hz)], 53.3 (d, $^{2}J_{P,C}$ = 7.3 Hz), 53.4 (d, $^{2}J_{P,C}$ = 7.3 Hz), [53.7 (d, $^{2}J_{P,C}$ = 6.9 Hz)], [106.9], [107.6], 108.2, 108.5, 117.5, [117.9], 128.6, [128.7], [129.0], 129.3, 130.2, [130.3 (d, $^{3}J_{P,C}$ = 14.8 Hz)], 132.9, [133.0], 139.0, [139.2], 167.9 (d, $^{2}J_{P,C}$ = 4.7 Hz), [169.2 (d, $^{2}J_{P,C}$ = 4.4 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.2, [25.2]. HRMS (ESI): *m/z* calcd for $C_{16}H_{20}ClNO_5P$ $[M+H]^+$: 372.0767; found: 372.0755.

Methyl 3-(4-bromophenyl)-2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)propanoate (268): Light brown powder; mp 158.9-159.4 °C; yield: 33 mg (86 %); dr 51:49; R_f = 0.28 (1:1, EtOAc-hexane). IR (ATR): 3285, 2999, 2959, 2856, 1736, 1481, 1446, 1402, 1259, 1235, 1036, 929, 802, 750 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.45-3.53 (m, 12H, 4 OC*H*$_3$)*, [3.68 (s, 3H, OC*H*$_3$)], [3.73 (d, $^{3}J_{P,H}$ = 10.8 Hz, 3H, OC*H*$_3$)], [3.81 (dd, $^{2}J_{P,H}$ = 21.6 Hz, $^{3}J_{H,H}$ = 3.2 Hz, 1H, C*H*)], 3.83 (dd, $^{3}J_{H,H}$ = 5.6 Hz, $^{2}J_{P,H}$ = 22.0 Hz, 1H, C*H*), 4.75-4.81 (m, 2H, 2 C*H*)*, 5.87 (br s, 1H, $H_{pyrrole}$), [6.05 (br s, 1H, $H_{pyrrole}$)], 6.09 (br s, 2H, 2 $H_{pyrrole}$)*, 6.70 (br s, 2H, 2 $H_{pyrrole}$)*, [7.21 (d, $^{3}J_{H,H}$ = 2.8 Hz, 2H, Ar*H*)], 7.23 (d, $^{3}J_{H,H}$ = 2.8 Hz, 2H, Ar*H*), 7.42 (d, $^{3}J_{H,H}$ = 2.4 Hz, 2H, Ar*H*), [7.44 (d, $^{3}J_{H,H}$ = 2.4 Hz, 2H, Ar*H*)], [8.94 (br s, 1H, N*H*)], 9.42 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.7, [43.2 (d, $^{2}J_{P,C}$ = 3.0 Hz)], 50.9 (d, $^{1}J_{P,C}$ = 131.5 Hz), [51.9 (d, $^{1}J_{P,C}$ = 132.3 Hz)], [52.5], 52.9, [53.0 (d, $^{2}J_{P,C}$ = 6.7 Hz)], [53.3 (d, $^{2}J_{P,C}$ = 6.7 Hz)], 53.3 (d, $^{2}J_{P,C}$ = 5.1 Hz), 53.7 (d, $^{2}J_{P,C}$ = 7.1 Hz), 106.8, [107.4], [108.1], 108.5, 117.5, [117.9], 121.0, [121.1], 129.6,

[130.1], 130.2, [130.3], [131.5], 131.6, 139.5 (d, $^{3}J_{P,C}$ = 10.5 Hz), [139.6 (d, $^{3}J_{P,C}$ = 20.0 Hz)], 167.9 (d, $^{2}J_{P,C}$ = 4.8 Hz), [169.1 (d, $^{2}J_{P,C}$ = 4.4 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.1, [25.2]. HRMS (ESI): *m/z* calcd for $C_{16}H_{20}BrNO_5P$ $[M+H]^+$: 416.0257; found: 416.0218.

Methyl 2-(dimethoxyphosphoryl)-3-(4-hydroxyphenyl)-3-(1*H*-pyrrol-2-yl)propanoate (269): Light yellow viscous oil; yield: 28 mg (85 %); dr 56:44; R_f = 0.37 (EtOAc). IR (ATR): 3011, 2956, 2846, 1724, 1597, 1514, 1436, 1373, 1215, 1032, 840, 749 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), [3.47 (s, 3H, OCH_3)], [3.55 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OCH_3)], 3.66 (s, 3H, OCH_3), [3.71 (d, $^{3}J_{P,H}$ = 11.0 Hz, 3H, OCH_3)], 3.77-3.87 (m, 2H, 2 C*H*)*, 4.66-4.74 (m, 2H, 2 C*H*)*, [5.92 (br s, 1H, $H_{pyrrole}$)], 6.01 (br s, 1H, $H_{pyrrole}$), 6.05-6.08 (m, 2H, 2 $H_{pyrrole}$)*, 6.63 (br s, 1H, $H_{pyrrole}$), [6.66 (br s, 1H, $H_{pyrrole}$)], 6.73 (d, $^{3}J_{H,H}$ = 8.5 Hz, 4H, Ar*H*)*, 7.16 (d, $^{3}J_{H,H}$ = 8.4 Hz, 4H, Ar*H*)*, 8.46 (br s, 1H, N*H*), [9.13 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.7 (d, $^{2}J_{P,C}$ = 2.4 Hz), [43.0 (d, $^{2}J_{P,C}$ = 3.2 Hz)], 51.4 (d, $^{1}J_{P,C}$ = 132.0 Hz), [52.4 (d, $^{1}J_{P,C}$ = 132.1 Hz)], [52.5], 52.9, 53.2, [53.3], 53.4 (d, $^{2}J_{P,C}$ = 6.9 Hz), [53.6 (d, $^{2}J_{P,C}$ = 7.2 Hz)], 106.0, [107.1], 108.1, [108.4], [115.4], 115.5, [117.2], 117.6, [129.1], 129.6, [131.0], 131.4 (d, $^{3}J_{P,C}$ = 4.8 Hz), [131.5], 131.9, [155.0], 155.4, [168.2 (d, $^{2}J_{P,C}$ = 4.4 Hz)], 169.2 (d, $^{2}J_{P,C}$ = 4.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): *δ* 23.6, [25.5]. HRMS (ESI): *m/z* calcd for $C_{16}H_{21}NO_6P$ $[M+H]^+$: 354.1107; found: 354.1106.

Methyl 3-(4-cyanophenyl)-2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)propanoate (270): Light yellow powder; mp 173.5-174.4 °C; yield: 24 mg (72 %); dr 54:46; R_f = 0.51 (EtOAc). IR (ATR): 2957, 2924, 2855, 2224, 1725, 1605, 1457, 1259, 1030, 804 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [3.46 (d, $^{3}J_{P,H}$ = 11.4 Hz, 3H, OCH_3)], [3.47 (s, 3H, OCH_3)], 3.49 (d, $^{3}J_{P,H}$ = 5.2 Hz, 3H, OCH_3), 3.53 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OCH_3), 3.67 (s, 3H, OCH_3), [3.69 (d, $^{3}J_{P,H}$ = 11.1 Hz, 3H, OCH_3)], 3.77-3.86 (m, 2H, 2 C*H*)*, 4.82-4.88 (m, 2H, 2 C*H*)*, [5.80 (br s, 1H, $H_{pyrrole}$)], 6.04 (br s, 1H, $H_{pyrrole}$), 6.08-6.10 (m, 2H, 2 $H_{pyrrole}$)*, 6.71 (br s, 2H, 2 $H_{pyrrole}$)*, 7.42 (m, 4H, Ar*H*)*, 7.58-7.60 (m, 4H, Ar*H*)*, 8.94 (br s, 1H, N*H*), [9.39 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.1 (d, $^{2}J_{P,C}$ = 2.7 Hz), [43.8 (d, $^{2}J_{P,C}$ = 2.8 Hz)], 50.7 (d, $^{1}J_{P,C}$ = 131.5 Hz), [51.7 (d, $^{1}J_{P,C}$ = 133.1 Hz)], [52.7], 53.0, 53.1, [53.3 (d, $^{2}J_{P,C}$ = 6.8 Hz)], 53.5 (d, $^{2}J_{P,C}$ = 6.9 Hz), [53.9 (d, $^{2}J_{P,C}$ = 7.1 Hz)], 107.4, [107.9], 108.4,

[108.7], 111.0, [111.1], [117.9], 118.3, [118.6], 118.7, [128.8], [129.1], 129.2, 129.3, 132.2, [132.4], [145.9], 146.0 (d, $^{3}J_{P,C}$ = 6.7 Hz), [167.7 (d, $^{2}J_{P,C}$ = 4.9 Hz)], 168.9 (d, $^{2}J_{P,C}$ = 4.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.7, [24.7]. HRMS (ESI): *m/z* calcd for $C_{17}H_{20}N_2O_5P$ $[M+H]^+$: 363.1109; found: 363.1085.

Methyl 2-(dimethoxyphosphoryl)-3-(4-nitrophenyl)-3-(1*H*-pyrrol-2-yl)propanoate (271): Yellow powder; mp 172.2-174.6 °C; yield: 14 mg (40 %); dr 52:48; R_f = 0.39 (EtOAc). IR (ATR): 3252, 2960, 2830, 1735, 1641, 1519, 1444, 1353, 1223, 1117, 1022 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [3.48 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$)], [3.53 (s, 3H, OC*H*$_3$)], 3.54 (d, $^{3}J_{P,H}$ = 10.2 Hz, 3H, OC*H*$_3$), 3.57 (d, $^{3}J_{P,H}$ = 11.7 Hz, 3H, OC*H*$_3$), 3.70 (s, 3H, OC*H*$_3$), [3.76 (d, $^{3}J_{P,H}$ = 11.1 Hz, 3H, OC*H*$_3$)], 3.90 (dd, $^{2}J_{P,H}$ = 22.0, $^{3}J_{H,H}$ = 9.3 Hz, 1H, C*H*), [3.92 (dd, $^{2}J_{P,H}$ = 20.4, $^{3}J_{H,H}$ = 11.4 Hz, 1H, C*H*)], 4.94-5.00 (m, 2H, 2 C*H*)*, [5.89 (br s, 1H, $H_{pyrrole}$)], 6.09 (br s, 1H, $H_{pyrrole}$), 6.13 (br s, 2H, 2 $H_{pyrrole}$)*, 6.74 (br s, 2H, 2 $H_{pyrrole}$)*, 7.52-7.55 (m, 4H, Ar*H*)*, 8.17-8.19 (m, 4H, Ar*H*)*, 9.11 (br s, 1H, N*H*), [9.56 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.9 (d, $^{2}J_{P,C}$ = 2.7 Hz), [43.5 (d, $^{2}J_{P,C}$ = 2.7 Hz)], 50.6 (d, $^{1}J_{P,C}$ = 131.4 Hz), [51.6 (d, $^{1}J_{P,C}$ = 133.1 Hz)], [52.7], 53.0, 53.1 (d, $^{2}J_{P,C}$ = 6.0 Hz), [53.4 (d, $^{2}J_{P,C}$ = 6.7 Hz)], 53.6 (d, $^{2}J_{P,C}$ = 7.0 Hz), [53.8 (d, $^{2}J_{P,C}$ = 7.2 Hz)], 107.3, [107.7], 108.4, [108.8], [117.9], 118.4, 123.6, [123.9], [128.8], 128.9 (d, $^{3}J_{P,C}$ = 1.6 Hz), [129.1], 129.3, 146.9, [147.9], 148.0 (d, $^{3}J_{P,C}$ = 4.2 Hz), [148.2], [167.8 (d, $^{2}J_{P,C}$ = 4.7 Hz)], 168.9 (d, $^{2}J_{P,C}$ = 4.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.3, [24.6]. HRMS (ESI): *m/z* calcd for $C_{16}H_{20}N_2O_7P$ $[M+H]^+$: 383.1008; found: 383.0993.

Methyl 3-cyclohexyl-2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)propanoate (275): Light yellow viscous oil; yield: 22 mg (69 %); dr 61:39; R_f = 0.15 (1:1, EtOAc-hexane). IR (ATR): 3272, 2924, 2868, 1737, 1684, 1445, 1248, 1189, 1151, 1030, 906, 827, 794 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08-1.75 (m, 22H, C*H*$_2$, C*H*)*, 3.07 (q, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{P,H}$ = 6.5 Hz, 1H, C*H*), 3.30 (d, $^{3}J_{P,H}$ = 10.3 Hz, 3H, OC*H*$_3$), [3.27-3.31 (m, 1H, C*H*)], [3.38 (d, $^{3}J_{P,H}$ = 11.1 Hz, 3H, OC*H*$_3$)], [3.49 (dd, $^{2}J_{P,H}$ = 19.6 Hz, $^{3}J_{H,H}$ = 11.1 Hz, 1H, C*H*)], 3.59 (dd, $^{2}J_{P,H}$ = 22.0 Hz, $^{3}J_{H,H}$ = 6.0 Hz, 1H, C*H*), [3.61 (d, $^{3}J_{P,H}$ = 10.9 Hz, 3H, OC*H*$_3$)], [3.68 (s, 3H, OC*H*$_3$)], 3.70 (d, $^{3}J_{P,H}$ = 12.0 Hz, 3H, OC*H*$_3$), 3.71 (s, 3H, OC*H*$_3$), [5.87 (br s, 1H, $H_{pyrrole}$)], 5.96 (br s, 1H, $H_{pyrrole}$), 5.99 (br s, 1H, $H_{pyrrole}$), [6.04 (d, $^{3}J_{H,H}$ = 2.7 Hz,

1H, $H_{pyrrole}$)], [6.63 (br s, 1H, $H_{pyrrole}$)], 6.66 (br s, 1H, $H_{pyrrole}$), [9.01 (br s, 1H, N*H*)], 9.33 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1, 26.2, 26.3, [26.4], [26.5], [28.5], [29.7], 30.8, 31.7, [32.1], 40.1 (d, $^3J_{P,C}$ = 10.8 Hz), [40.9 (d, $^3J_{P,C}$ = 10.9 Hz)], 43.0 (d, $^2J_{P,C}$ = 3.0 Hz), [44.2 (d, $^2J_{P,C}$ = 5.4 Hz)], 46.6 (d, $^1J_{P,C}$ = 131.4 Hz), [48.9 (d, $^1J_{P,C}$ = 137.4 Hz)], [52.3], 52.4 (d, $^2J_{P,C}$ = 6.6 Hz), 52.5, [52.6 (d, $^2J_{P,C}$ = 6.9 Hz)], [53.3 (d, $^2J_{P,C}$ = 7.1 Hz)], 53.4 (d, $^2J_{P,C}$ = 6.4 Hz), 107.4, [107.9], [108.0], 109.4, [116.7], 117.0, [128.3 (d, $^3J_{P,C}$ = 2.6 Hz)], 129.2 (d, $^3J_{P,C}$ = 7.2 Hz), [169.0 (d, $^2J_{P,C}$ = 4.7 Hz)], 170.0 (d, $^2J_{P,C}$ = 4.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.6, [26.7]. HRMS (ESI): *m/z* calcd for $C_{16}H_{26}NO_5P$ $[M+H]^+$: 344.1621; found: 344.1685.

Methyl 2-(dimethoxyphosphoryl)-4-methyl-3-(1*H*-pyrrol-2-yl)pentanoate (276): Light yellow viscous oil; yield: 22 mg (77 %); dr 67:33; R_f = 0.12 (1:1, EtOAc-hexane). IR (ATR): 3275, 2923, 2869, 1735, 1681, 1447, 1250, 1191, 1150, 1033, 908, 825, 796 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [0.76 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, C*H*$_3$)], 0.81 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, C*H*$_3$), 0.87 (d, $^3J_{H,H}$ = 6.8 Hz, 3H, C*H*$_3$), [0.94 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, C*H*$_3$)], 1.84-1.92 (m, 1H, C*H*), [2.00-2.07 (m, 1H, C*H*)], 3.07 (q, $^3J_{H,H}$ = 6.9 Hz, $^3J_{P,H}$ = 6.9 Hz, 1H, C*H*), 3.32 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OC*H*$_3$), 3.37 (d, $^3J_{P,H}$ = 11.0 Hz, 3H, OC*H*$_3$), [3.38 (m, 1H, C*H*)], 3.50 (dd, $^2J_{P,H}$ = 19.5 Hz, $^3J_{H,H}$ = 10.9 Hz, 1H, C*H*), [3.59 (dd, $^2J_{P,H}$ = 24.8 Hz, $^3J_{H,H}$ = 6.6 Hz, 1H, C*H*)], 3.60 (d, $^3J_{P,H}$ = 11.0 Hz, 3H, OC*H*$_3$), [3.69 (s, 3H, OC*H*$_3$)], [3.72 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OC*H*$_3$)], 3.74 (s, 3H, OC*H*$_3$), 5.93 (br s, 1H, $H_{pyrrole}$), [5.97 (br s, 1H, $H_{pyrrole}$)], [6.00 (q, $^3J_{H,H}$ = 2.9 Hz, 1H, $H_{pyrrole}$)], 6.07 (q, $^3J_{H,H}$ = 2.8 Hz, 1H, $H_{pyrrole}$), 6.65 (q, $^3J_{H,H}$ = 1.4 Hz, 1H, $H_{pyrrole}$), [6.67 (q, $^3J_{H,H}$ = 1.6 Hz, 1H, $H_{pyrrole}$)], 9.05 (br s, 1H, N*H*), [9.31 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.4, [20.3], [21.5], 21.6, 30.7 (d, $^3J_{P,C}$ = 12.9 Hz), [30.9 (d, $^3J_{P,C}$ = 10.4 Hz)], 44.1 (d, $^2J_{P,C}$ = 4.1 Hz), [44.2 (d, $^3J_{P,C}$ = 3.6 Hz)], [47.5 (d, $^1J_{P,C}$ = 131.6 Hz)], 49.9 (d, $^1J_{P,C}$ = 135.8 Hz), 52.4, [52.5 (d, $^2J_{P,C}$ = 6.4 Hz)], [52.6], 52.9 (d, $^2J_{P,C}$ = 6.6 Hz), 53.0 (d, $^2J_{P,C}$ = 7.0 Hz), [53.5 (d, $^2J_{P,C}$ = 6.6 Hz)], [107.5], 107.9, 108.0, [109.0], 116.6, [117.0], 127.6 (d, $^3J_{P,C}$ = 2.3 Hz), [129.2 (d, $^3J_{P,C}$ = 8.3 Hz)], 169.1 (d, $^2J_{P,C}$ = 4.3 Hz), [169.9 (d, $^2J_{P,C}$ = 4.5 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [24.5], 26.3. HRMS (ESI): *m/z* calcd for $C_{13}H_{22}NO_5P$ $[M+H]^+$: 304.1308; found: 304.1362.

Methyl 2-(dimethoxyphosphoryl)-3-(1-methyl-1*H*-pyrrol-2-yl)-3-phenylpropanoate (277): Yellow viscous oil; yield: 19 mg (58 %); dr 57:43; R_f = 0.09 (1:1, EtOAc-hexane). IR (ATR): 3012, 2945, 2852, 1730, 1572, 1496, 1437, 1265, 1236, 1031, 808, 695 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.22 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3), [3.35 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3)], 3.40 (s, 3H, CH_3), [3.43 (s, 3H, CH_3)], 3.55 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3), [3.62 (s, 3H, OCH_3)], [3.63 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3)], 3.65 (s, 3H, OCH_3), 3.76 (dd, $^2J_{P,H}$ = 20.6 Hz, $^3J_{H,H}$ = 12.2 Hz, 1H, C*H*), [3.82 (dd, $^2J_{P,H}$ = 19.1 Hz, $^3J_{H,H}$ = 12.0 Hz, 1H, C*H*)], 4.67-4.74 (m, 2H, 2 C*H*)*, 5.97 (t, $^3J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), [6.03 (t, $^3J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$)], 6.13-6.14 (m, 1H, $H_{pyrrole}$), [6.20-6.22 (m, 1H, $H_{pyrrole}$)], 6.39 (br s, 1H, $H_{pyrrole}$), [6.43 (br s, 1H, $H_{pyrrole}$)], 7.15-7.35 (m, 10H, Ar*H*)*. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.7, [33.9], [41.6 (d, $^2J_{P,C}$ = 3.4 Hz)], 42.1 (d, $^2J_{P,C}$ = 2.0 Hz), 51.6 (d, $^1J_{P,C}$ = 132.3 Hz), [52.0], [52.5 (d, $^1J_{P,C}$ = 132.1 Hz)], 52.5, 52.6, 52.7, [52.7 (d, $^2J_{P,C}$ = 4.9 Hz)], [53.4 (d, $^2J_{P,C}$ = 6.5 Hz)], 105.2, 106.6, [106.9], [107.0], [121.7], 122.0, [126.8], 126.9, [128.1], 128.2, [128.3], 129.2, [131.2], 132.6 (d, $^3J_{P,C}$ = 23.0 Hz), [139.2 (d, $^3J_{P,C}$ = 1.2 Hz)], 140.3 (d, $^3J_{P,C}$ = 16.2 Hz), [167.8 (d, $^2J_{P,C}$ = 4.7 Hz)], 168.4 (d, $^2J_{P,C}$ = 4.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.6, [24.9]. HRMS (ESI): *m/z* calcd for $C_{17}H_{23}NO_5P$ $[M+H]^+$: 352.1308; found: 352.1291.

Methyl 2-(dimethoxyphosphoryl)-3-(1*H*-indol-3-yl)-3-phenylpropanoate (278): Light yellow powder; mp 164.8-166.2 °C; yield: 31 mg (99 %); dr 60:40; R_f = 0.10 (1:1, EtOAc-hexane). IR (ATR): 3007, 2951, 2852, 1734, 1489, 1456, 1435, 1242, 1151, 1036, 933, 834, 804, 746, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.28 (d, $^3J_{P,H}$ = 10.8 Hz, 3H, OCH_3), [3.37 (d, $^3J_{P,H}$ = 11.2 Hz, 3H, OCH_3)], [3.47 (d, $^3J_{P,H}$ = 11.2 Hz, 3H, OCH_3)], [3.52 (s, 3H, OCH_3)], 3.54 (s, 3H, OCH_3), 3.57 (d, $^3J_{P,H}$ = 11.2 Hz, 3H, OCH_3), 3.96 (dd, $^2J_{P,H}$ = 20.0 Hz, $^3J_{H,H}$ = 12.0 Hz, 1H, C*H*), [4.13 (dd, $^2J_{P,H}$ = 20.0 Hz, $^3J_{H,H}$ = 12.4 Hz, 1H, C*H*)], 5.00-5.09 (m, 2H, 2 C*H*)*, 7.00-7.35 (m, 4 H, Ar*H*)*, [7.39 (d, $^3J_{H,H}$ = 7.6 Hz, 2H, Ar*H*)], 7.46 (d, $^3J_{H,H}$ = 7.2 Hz, 2H, Ar*H*), 7.56 (d, $^3J_{H,H}$ = 8.0 Hz, 1H, Ar*H*), [7.67 (d, $^3J_{H,H}$ = 8.0 Hz, 1H, Ar*H*)], 8.12 (br s, 1H, N*H*), [8.29 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.9 (d, $^2J_{P,C}$ = 2.7 Hz), [42.0 (d, $^2J_{P,C}$ = 3.6 Hz)], [51.5 (d, $^1J_{P,C}$ = 132.0 Hz)], 52.2 (d, $^1J_{P,C}$ = 126.6 Hz), [52.4], 52.7, 52.9, [53.1 (d, $^2J_{P,C}$ = 5.1 Hz)], 53.1 (d, $^2J_{P,C}$ = 6.5 Hz), [53.3 (d, $^2J_{P,C}$ = 6.8 Hz)], 111.0, [111.3], 115.6, [117.7 (d, $^3J_{P,C}$ = 18.7 Hz)], [119.1], 119.2, 119.4, [119.5], 120.4, [122.0], 122.2, [122.6], 126.3, [126.4], [126.7], 126.8,

[127.7], 128.3, [128.4], 128.8, 136.1*, 141.2, [142.0 (d, $^{3}J_{P,C}$ = 16.8 Hz)], [168.7 (d, $^{2}J_{P,C}$ = 5.0 Hz)], 168.9 (d, $^{2}J_{P,C}$ = 4.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.1, [24.4]. HRMS (ESI): *m/z* calcd for $C_{20}H_{23}NO_5P$ $[M+H]^+$: 388.1308; found: 388.1281.

Methyl 2-(dimethoxyphosphoryl)-3-(3,5-dimethyl-1*H*-pyrrol-2-yl)-3-phenylpropanoate (279): Light brown powder; mp 146.4-146.8 °C; yield: 34 mg (99 %); dr 58:42; R_f = 0.49 (EtOAc). IR (ATR): 3282, 2949, 1745, 1736, 1688, 1455, 1432, 1233, 1200, 1159, 1031, 820, 785, 759 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [1.97 (s, 3H, C*H*$_3$)], 1.99 (s, 3H, C*H*$_3$), 2.14 (s, 3H, C*H*$_3$), [2.20 (s, 3H, C*H*$_3$)], [3.30 (d, $^{3}J_{P,H}$ = 10.8 Hz, 3H, OC*H*$_3$)], 3.36 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$), 3.48 (s, 3H, OC*H*$_3$), [3.53 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$)], [3.57 (s, 3H, OC*H*$_3$)], 3.61 (d, $^{3}J_{P,H}$ = 10.8 Hz, 3H, OC*H*$_3$), 3.87-3.97 (m, 2H, 2 C*H*)*, 4.75-4.82 (m, 2H, 2 C*H*)*, 5.53 (br s, 1H, *H*$_{pyrrole}$), [5.58 (br s, 1H, *H*$_{pyrrole}$)], 7.09-7.25 (m, 10 H, Ar*H*)*, 8.44 (br s, 1H, N*H*), [9.12 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = [11.0], 11.2, 13.0, [13.2], [39.9 (d, $^{2}J_{P,C}$ = 2.7 Hz)], 41.6 (d, $^{2}J_{P,C}$ = 3.2 Hz), 50.6 (d, $^{1}J_{P,C}$ = 134.6 Hz), [50.7 (d, $^{1}J_{P,C}$ = 130.8 Hz)], 52.5, [52.8], [52.8 (d, $^{2}J_{P,C}$ = 7.8 Hz)], 53.2 (d, $^{2}J_{P,C}$ = 6.8 Hz), 53.3 (d, $^{2}J_{P,C}$ = 6.5 Hz), [53.4 (d, $^{2}J_{P,C}$ = 7.8 Hz)], [107.6], 108.1, 115.9, [116.8], [123.3 (d, $^{3}J_{P,C}$ = 8.1 Hz)], 123.9 (d, $^{3}J_{P,C}$ = 2.1 Hz), [126.6], 126.7, 126.7, [126.8], 127.4, [127.6], [128.5], 128.6, [141.0 (d, $^{3}J_{P,C}$ = 10.9 Hz)], 141.1 (d, $^{3}J_{P,C}$ = 14.6 Hz), 168.6 (d, $^{2}J_{P,C}$ = 4.2 Hz), [169.9 (d, $^{2}J_{P,C}$ = 4.2 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [23.4], 24.9. HRMS (ESI): *m/z* calcd for $C_{18}H_{25}NO_5P$ $[M+H]^+$: 366.1465; found: 366.1481.

Methyl 2-(dimethoxyphosphoryl)-3-(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)-3-phenylpropanoate (280): Brown viscous oil; yield: 36 mg (99 %); dr 94:6; R_f = 0.58 (EtOAc). IR (ATR): 3264, 2955, 1674, 1452, 1379, 1229, 1158, 1030, 821, 768 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, $^{3}J_{H,H}$ = 7.6 Hz, 3H, CH_2CH_3), [1.15 (t, $^{3}J_{H,H}$ = 7.6 Hz, 3H, CH_2CH_3)], [1.93 (s, 3H, C*H*$_3$)], 1.97 (s, 3H, C*H*$_3$), 2.08 (s, 3H, C*H*$_3$), [2.14 (s, 3H, C*H*$_3$)], 2.26 (q, $^{3}J_{H,H}$ = 7.6 Hz, 4H, 2 CH_2CH_3)*, [3.25 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$)], 3.31 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$), 3.47 (s, 3H, OC*H*$_3$), [3.53 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$)], [3.56 (s, 3H, OC*H*$_3$)], 3.58 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$), 3.83 (dd, $^{2}J_{P,H}$ = 20.8 Hz, $^{3}J_{H,H}$ = 11.6 Hz, 2H, 2 C*H*)*, 4.80 (dd, $^{3}J_{H,H}$ = 11.6 Hz, $^{3}J_{P,H}$ = 11.6 Hz, 2H, 2 C*H*)*, [7.09-7.13 (m, 5 H, Ar*H*)], 7.19-

7.23 (m, 5H, Ar*H*), 7.84 (br s, 1H, N*H*), [8.84 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = [9.1], 9.3, 11.1, [11.2], 15.7, [15.9], 17.7*, 41.6 (d, $^2J_{P,C}$ = 3.1 Hz)*, 50.8 (d, $^1J_{P,C}$ = 134.6 Hz)*, 52.7*, 53.0 (d, $^2J_{P,C}$ = 7.0 Hz)*, 53.2 (d, $^2J_{P,C}$ = 6.5 Hz)*, 114.9, [115.5], [120.2], 120.7, [122.3], 122.5, 122.9*, 126.6, [127.0], 127.3, [127.6], [128.0], 128.5 (d, $^3J_{P,C}$ = 11.6 Hz)*, 128.6, 141.2 (d, $^3J_{P,C}$ = 14.8 Hz)*, 168.5 (d, $^2J_{P,C}$ = 4.4 Hz)*. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [23.6], 24.8. HRMS (ESI): *m/z* calcd for $C_{20}H_{29}NO_5P$ $[M+H]^+$: 394.1778; found: 394.1756.

4.3.2. General Procedure for TFA (trifluoroacetic acid) and Montmorillonite K-10 Catalyzed Addition of Pyrrole to Pyrrolyl, Furyl and Thiophenyl Substituted Ester Functionalized Vinylphosphonates

Ester functionalized vinylphosphonates (**228-230**) (0.093 mmol) was dissolved in excess pyrrole (3.72 mmol) and catalyst (TFA (0.0093 mmol) or Montmorillonite K-10 (0.093 g)) was added to the reaction mixture at room temperature. The resulting mixture was stirred at room temperature for 48 h (TLC monitoring). The catalyst was removed from the reaction medium by subjecting the mixture to a short flash column chromatography (silica gel, EtOAc). The eluent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 4:1).

Methyl 2-(dimethoxyphosphoryl)-3,3-di(1*H*-pyrrol-2-yl)propanoate (272): Light yellow powder; mp 168.5-169.7 °C; yield: 14 mg (45 %); R_f = 0.44 (EtOAc). IR (ATR): 3255, 2968, 2836, 1737, 1638, 1520, 1443, 1358, 1226, 1120, 1025 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.21 (d, $^3J_{P,H}$ = 10.8 Hz, 3H, OCH_3), 3.43 (s, 3H, OCH_3), 3.47 (d, $^3J_{P,H}$ = 10.8 Hz, 3H, OCH_3), 4.03 (dd, $^2J_{P,H}$ = 19.6 Hz, $^3J_{H,H}$ = 12.4 Hz, 1H, C*H*), 4.63 (dd, $^3J_{P,H}$ = 12.0 Hz, $^3J_{H,H}$ = 10.0 Hz, 1H, C*H*), 5.80 (br s, 1H, $H_{pyrrole}$), 5.84 (br s, 1H, $H_{pyrrole}$), 5.89 (br s, 1H, $H_{pyrrole}$), 5.96 (br s, 1H, $H_{pyrrole}$), 6.50 (br s, 1H, $H_{pyrrole}$), 6.60 (br s, 1H, $H_{pyrrole}$), 10.49 (br s, 1H, N*H*), 10.55 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 37.1, 50.7 (d, $^1J_{P,C}$ = 129.2 Hz), 52.5, 52.9 (d, $^2J_{P,C}$ = 6.7 Hz), 53.2 (d, $^2J_{P,C}$ = 6.4 Hz), 104.7, 106.4, 107.3, 107.4, 116.9, 117.5, 132.0, 132.2, 168.5 (d, $^2J_{P,C}$ = 4.3 Hz). ^{31}P NMR (162 MHz, DMSO-d_6): δ = 24.1. HRMS (ESI): *m/z* calcd for $C_{14}H_{20}N_2O_5P$ $[M+H]^+$: 327.1109; found: 327.1116.

Methyl 2-(dimethoxyphosphoryl)-3-(furan-2-yl)-3-(1*H*-pyrrol-2-yl)propanoate (273): Brown viscous oil; yield: 8 mg (25 %); dr 81:19; R_f = 0.48 (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.51 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3), 3.64 (d, $^3J_{P,H}$ = 9.6 Hz, 3H, OCH_3), 3.65 (s, 3H, OCH_3), [3.79 (s, 3H, OCH_3)], [3.82 (s, 3H, OCH_3)], [3.89 (s, 3H, OCH_3)], 3.76-3.92 (m, 2H, 2 C*H*)*, 4.85-4.89 (m, 2H, 2 C*H*)*, 6.06-6.08 (m, 3H, $H_{pyrrole}$, H_{furan})*, 6.14 (br s, 3H, $H_{pyrrole}$, H_{furan})*, 6.28-6.30 (m, 2H, H_{furan})*, 6.71 (br s, 2H, $H_{pyrrole}$)*, 7.37 (br s, 2H, H_{furan})*, [8.60 (br s, 1H, N*H*)], 9.02 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [36.6], 37.0 (d, $^2J_{P,C}$ = 3.4 Hz), 49.8 (d, $^1J_{P,C}$ = 131.0 Hz)*, [52.6], [52.7 (d, $^2J_{P,C}$ = 3.6 Hz)], 52.8, [53.0 (d, $^2J_{P,C}$ = 6.7 Hz)], 53.2 (d, $^2J_{P,C}$ = 6.5 Hz), 53.4 (d, $^2J_{P,C}$ = 6.8 Hz), [105.8], 107.4*, 107.8, 108.0*, [108.4], 110.5, 118.0, [118.3], 127.8 (d, $^3J_{P,C}$ = 12.4 Hz), [128.6], 141.9*, 152.7 (d, $^3J_{P,C}$ = 7.3 Hz)*, 168.7 (d, $^2J_{P,C}$ = 4.3 Hz)*. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [18.2], 22.8. HRMS (ESI): *m/z* calcd for $C_{14}H_{19}NO_6P$ $[M+H]^+$: 328.0950; found: 328.0934.

Methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)-3-(thiophen-2-yl)propanoate (274): Brown viscous oil; yield: 10 mg (30 %); dr 66:34; R_f = 0.35 (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43 (d, $^3J_{P,H}$ = 11.2 Hz, 3H, OCH_3), [3.44 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3)], 3.60 (s, 3H, OCH_3), [3.62 (d, $^3J_{P,H}$ = 12.2 Hz, 3H, OCH_3)], 3.67 (d, $^3J_{P,H}$ = 11.0 Hz, 3H, OCH_3), [3.67 (s, 3H, OCH_3)], 3.72-3.88 (m, 2H, 2 C*H*)*, 5.06-5.13 (m, 2H, 2 C*H*)*, 6.07-6.11 (m, 4H, $H_{pyrrole}$)*, 6.69 (br s, 1H, $H_{pyrrole}$), [6.73 (br s, 1H, $H_{pyrrole}$)], 6.87-6.91 (m, 3H, $H_{thiophene}$)*, 6.96 (br s, 1H, $H_{thiophene}$), 7.16 (br s, 2H, $H_{thiophene}$)*, 9.14 (br s, 1H, N*H*), [9.37 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.3*, 51.8 (d, $^1J_{P,C}$ = 130.9 Hz)*, 52.6, [52.7], 53.0 (d, $^2J_{P,C}$ = 5.9 Hz)*, 53.3 (d, $^2J_{P,C}$ = 6.7 Hz)*, 107.6, [107.8], [107.9], 108.5, 117.4, [118.0], 124.6, [124.7], 125.3, [125.6], 126.5, [126.6], [129.9 (d, $^3J_{P,C}$ = 10.2 Hz)], 130.0, 143.8 (d, $^3J_{P,C}$ = 17.6 Hz), [144.6 (d, $^3J_{P,C}$ = 14.5 Hz)], 167.9 (d, $^2J_{P,C}$ = 4.2 Hz), [169.2]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [22.7], 24.1. HRMS (ESI): *m/z* calcd for $C_{14}H_{19}NO_5PS$ $[M+H]^+$: 344.0721; found: 344.0687.

4.3.3. General Procedure for the Michael Addition of Pyrrole to Ketone Functionalized Vinylphosphonates

To a solution of ketone functionalized vinylphosphonates (**234-246**) (0.384 mmol) in toluene (2 mL) was added 10 mol % of Metal triflate (0.0384 mmol) and the

reaction mixture was stirred for 0.5 h at room temperature. Pyrrole (3.84 mmol) was added to the reaction mixture instantly *via* syringe pump and the resulting mixture was stirred at 50°C for 15 min (TLC monitoring). Metal triflate was removed from the reaction medium by subjecting the mixture to a short flash column chromatography (silica gel, EtOAc). The eluent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:2).

Diethyl 3-oxo-1-phenyl-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (281): Brown powder; mp 83.4-84.1 °C; yield: 56 mg (40 %); dr 74:26; R_f = 0.33 (1:1, EtOAc-hexane). IR (ATR): 3251, 2981, 2931, 1715, 1454, 1365, 1218, 1160, 1095, 1014, 961, 787, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.75 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), [0.90 (t, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_2CH_3)], [1.11 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], [1.13 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 1.16 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.25 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.13 (dq, $^2J_{H,H}$ = 18.0 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.25 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.40 (dq, $^2J_{H,H}$ = 18.0 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.65 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 3.60-3.70 (m, 2H, OCH_2CH_3), [3.76-3.89 (m, 3H, OCH_2CH_3, C*H* (major))], 3.94-4.03 (m, 5H, 2 OCH_2CH_3, C*H* (minor))*, 4.77 (dd, $^3J_{H,H}$ = 11.1, $^3J_{P,H}$ = 11.1 Hz, 2H, 2 C*H*)*, 5.79 (br s, 1H, $H_{pyrrole}$), [5.92 (br s, 1H, $H_{pyrrole}$)], 5.98-6.01 (m, 2H, 2 $H_{pyrrole}$)*, 6.61 (br s, 2H, 2 $H_{pyrrole}$)*, [7.14-7.18 (m, 5H, Ar*H*)], 7.23-7.29 (m, 5H, Ar*H*), [8.94 (br s, 1H, N*H*)], 9.46 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.3, [7.4], 16.1 (d, $^3J_{P,C}$ = 6.1 Hz)*, 37.4, [38.2], [43.3 (d, $^2J_{P,C}$ = 2.9 Hz)], 43.6 (d, $^2J_{P,C}$ = 3.2 Hz), [58.1 (d, $^1J_{P,C}$ = 125.3 Hz)], 58.8 (d, $^1J_{P,C}$ = 127.6 Hz), [61.9 (d, $^2J_{P,C}$ = 6.9 Hz)], [62.0 (d, $^2J_{P,C}$ = 7.0 Hz)], 62.2 (d, $^2J_{P,C}$ = 6.8 Hz), 62.5 (d, $^2J_{P,C}$ = 7.0 Hz), [106.7], 107.4, [108.1], 108.2, 116.8, [117.1], [126.7], 126.8, 128.0, [128.2], [128.3], 128.4, [130.7 (d, $^3J_{P,C}$ = 15.5 Hz)], 130.7 (d, $^3J_{P,C}$ = 1.9 Hz), 140.9 (d, $^3J_{P,C}$ = 16.5 Hz), [140.8 (d, $^3J_{P,C}$ = 8.2 Hz)], 204.4 (d, $^2J_{P,C}$ = 4.6 Hz), [206.7 (d, $^2J_{P,C}$ = 4.3 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [20.2], 23.0. HRMS (ESI): *m/z* calcd for $C_{19}H_{27}NO_4P$ $[M+H]^+$: 364.1672; found: 364.1664.

Diethyl 3-oxo-1-(1*H*-pyrrol-2-yl)-1-(4-(trifluoromethyl)phenyl)pentan-2-ylphosphonate (282): Light yellow powder; mp 179.3-179.8 °C; yield: 75 mg (45 %); dr 50:50; R_f = 0.29 (1:1, EtOAc-hexane). IR (ATR): 3271, 2982, 2904, 1715, 1619,

1572, 1446, 1421, 1326, 1217, 1160, 1123, 1068, 1049, 1014, 974, 949, 857, 801, 719 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_2CH_3), 0.93 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_2CH_3), 1.09 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.11 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.16 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.24 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.18 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.36 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.53 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.74 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.63-3.75 (m, 3H, OCH_2CH_3), 3.84-3.90 (m, 3H, OCH_2CH_3), 3.98-4.09 (m, 2H, OCH_2CH_3), 4.08 (dd, $^{2}J_{P,H}$ = 21.8 Hz, $^{3}J_{H,H}$ = 10.2, 1H, C*H*), 4.10 (dd, $^{2}J_{P,H}$ = 20.6 Hz, $^{3}J_{H,H}$ = 11.5, 1H, C*H*), 4.91 (dd, $^{3}J_{H,H}$ = 10.4, $^{3}J_{P,H}$ = 10.4 Hz, 1H, C*H*), 4.94 (dd, $^{3}J_{H,H}$ = 11.3, $^{3}J_{P,H}$ = 11.3 Hz, 1H, C*H*), 5.86 (br s, 1H, $H_{pyrrole}$), 6.00 (br s, 1H, $H_{pyrrole}$), 6.05-6.07 (m, 2H, 2 $H_{pyrrole}$), 6.64 (br s, 1H, $H_{pyrrole}$), 6.67 (br s, 1H, $H_{pyrrole}$), 7.43-7.52 (m, 8H, Ar*H*), 9.03 (br s, 1H, N*H*), 9.61 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.4, 7.5, 16.0 (d, $^{3}J_{P,C}$ = 2.7 Hz), 16.1 (d, $^{3}J_{P,C}$ = 2.8 Hz), 16.2 (d, $^{3}J_{P,C}$ = 6.2 Hz), 38.1, 38.4, 43.4 (d, $^{2}J_{P,C}$ = 2.8 Hz), 43.5 (d, $^{2}J_{P,C}$ = 2.9 Hz), 57.9 (d, $^{1}J_{P,C}$ = 125.7 Hz), 58.4 (d, $^{1}J_{P,C}$ = 127.6 Hz), 62.5 (d, $^{2}J_{P,C}$ = 6.8 Hz), 62.6 (d, $^{2}J_{P,C}$ = 7.0 Hz), 62.8 (d, $^{2}J_{P,C}$ = 6.9 Hz), 63.0 (d, $^{2}J_{P,C}$ = 7.1 Hz), 106.4, 107.4, 108.4, 108.5, 117.5, 117.7, 124.1 (q, $^{1}J_{F,C}$ = 278.6 Hz), 124.1 (q, $^{1}J_{F,C}$ = 262.2 Hz), 125.3 (q, $^{3}J_{F,C}$ = 3.6 Hz), 125.6 (q, $^{3}J_{F,C}$ = 3.6 Hz), 128.4, 129.0, 129.1 (q, $^{2}J_{F,C}$ = 32.1 Hz)*, 130.0 (d, $^{3}J_{P,C}$ = 1.5 Hz), 130.5 (d, $^{3}J_{P,C}$ = 17.2 Hz), 144.9 (d, $^{3}J_{P,C}$ = 3.9 Hz), 145.3 (d, $^{3}J_{P,C}$ = 17.3 Hz), 205.1 (d, $^{2}J_{P,C}$ = 4.9 Hz), 206.8 (d, $^{2}J_{P,C}$ = 4.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 20.6, 23.0. HRMS (ESI): *m/z* calcd for $C_{20}H_{26}F_3NO_4P$ $[M+H]^+$: 432.1546; found: 432.1596.

Diethyl 3-oxo-1-(1*H*-pyrrol-2-yl)-1-*p*-tolylpentan-2-ylphosphonate (283): Light yellow powder; mp 150.6-151.2 °C; yield: 72 mg (50 %); dr 51:49; R_f = 0.21 (1:1, EtOAc-hexane). IR (ATR): 3257, 2983, 2935, 1716, 1515, 1446, 1353, 1217, 1161, 1129, 1096, 1052, 1019, 973, 797, 714 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.77 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), [0.90 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3)], [1.12 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], [1.14 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 1.15 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.24 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.16 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.23 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.40 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.65 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 3.60-3.71 (m, 3H, OCH_2CH_3)*,

3.73-3.88 (m, 3H, OCH_2CH$_3$)*, 3.90-4.05 (m, 4H, OCH_2CH$_3$, 2 CH)*, 4.70-4.75 (m, 2H, 2 CH)*, 5.76 (br s, 1H, $H_{pyrrole}$), [5.90 (br s, 1H, $H_{pyrrole}$)], 5.97-6.00 (m, 2H, 2 $H_{pyrrole}$)*, 6.61 (br s, 2H, 2 $H_{pyrrole}$)*, 7.05 (d, $^3J_{H,H}$ = 7.7 Hz, 4H, ArH)*, 7.14 (d, $^3J_{H,H}$ = 8.1 Hz, 2H, ArH), [7.15 (d, $^3J_{H,H}$ = 8.0 Hz, 2H, ArH)], [8.90 (br s, 1H, NH)], 9.38 (br s, 1H, NH). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 7.3, [7.4], 16.2 (d, $^3J_{P,C}$ = 5.8 Hz)*, 21.0*, 37.4, [38.3], [42.9 (d, $^2J_{P,C}$ = 2.9 Hz)], 43.2 (d, $^2J_{P,C}$ = 3.2 Hz), [58.1 (d, $^1J_{P,C}$ = 125.4 Hz)], 58.9 (d, $^1J_{P,C}$ = 126.6 Hz), [61.9 (d, $^2J_{P,C}$ = 9.3 Hz)], [62.1 (d, $^2J_{P,C}$ = 7.4 Hz)], 62.3 (d, $^2J_{P,C}$ = 6.0 Hz), 62.5 (d, $^2J_{P,C}$ = 7.0 Hz), [106.7], 107.3, [108.1], 108.2, 116.7, [117.1], 127.9, [128.1], [128.9], 129.1, [131.0], 130.1 (d, $^3J_{P,C}$ = 1.6 Hz), [136.1], 136.2, 137.7 (d, $^3J_{P,C}$ = 5.4 Hz), [137.8 (d, $^3J_{P,C}$ = 4.3 Hz)], 204.7 (d, $^2J_{P,C}$ = 4.6 Hz), [206.9 (d, $^2J_{P,C}$ = 3.5 Hz)]. ^{31}P NMR (162 MHz, CDCl$_3$): δ = [21.0], 23.7. HRMS (ESI): *m/z* calcd for $C_{20}H_{29}NO_4P$ [M+H]$^+$: 378.1829; found: 378.1883.

Diethyl 1-(4-methoxyphenyl)-3-oxo-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (284): Light brown powder; mp 116.5-117.0 °C; yield: 79 mg (52 %); dr 58:42; R_f = 0.11 (1:1, EtOAc-hexane). IR (ATR): 3264, 2976, 2917, 2848, 1716, 1610, 1512, 1457, 1290, 1247, 1222, 1178, 1096, 1018, 969, 843, 726 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.78 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, CH$_2$CH_3), [0.90 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, CH$_2$CH_3)], [1.13 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH$_2$CH_3)], 1.15 (t, $^3J_{H,H}$ = 7.0 Hz, 6H, OCH$_2$CH_3)*, 1.25 (t, $^3J_{H,H}$ = 6.9 Hz, 3H, OCH$_2$CH_3), 2.14 (dq, $^2J_{H,H}$ = 18.2 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH$_3$), [2.25 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH$_3$)], 2.40 (dq, $^2J_{H,H}$ = 18.2 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH$_3$), [2.65 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH$_3$)], 3.60-3.71 (m, 2H, OCH_2CH$_3$)*, 3.75 (s, 3H, OCH_3), [3.76 (s, 3H, OCH_3)], 3.79-3.89 (m, 5H, 2 OCH_2CH$_3$, CH)*, 3.92-4.02 (m, 3H, OCH_2CH$_3$, CH)*, 4.68-4.74 (m, 2H, CH)*, [5.76 (br s, 1H, $H_{pyrrole}$)], 5.89 (br s, 1H, $H_{pyrrole}$), 5.99 (br s, 2H, 2 $H_{pyrrole}$)*, 6.61 (br s, 2H, 2 $H_{pyrrole}$)*, 6.77 (d, $^3J_{H,H}$ = 8.4 Hz, 4H, ArH)*, 7.16 (d, $^3J_{H,H}$ = 9.6 Hz, 4H, ArH)*, 8.89 (br s, 1H, NH), [9.40 (br s, 1H, NH)]. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 7.5, [7.6], [16.2 (d, $^3J_{P,C}$ = 1.9 Hz)], 16.3 (d, $^3J_{P,C}$ = 1.8 Hz), 37.5, [38.3], [42.6 (d, $^2J_{P,C}$ = 2.9 Hz)], 42.9 (d, $^2J_{P,C}$ = 3.3 Hz), 54.9, [55.0], [58.4 (d, $^1J_{P,C}$ = 124.9 Hz)], 59.2 (d, $^1J_{P,C}$ = 126.6 Hz), [62.0 (d, $^2J_{P,C}$ = 7.0 Hz)], [62.1 (d, $^2J_{P,C}$ = 6.9 Hz)], 62.2 (d, $^2J_{P,C}$ = 6.7 Hz), 62.6 (d, $^2J_{P,C}$ = 7.0 Hz), [106.7], 107.4, [108.2], 108.3, [113.6], 113.8, 116.8, [117.1], 129.2, [129.4], [131.1], 131.3 (d, $^3J_{P,C}$ = 5.0 Hz)], 133.0 (d, $^3J_{P,C}$ = 9.3 Hz), [133.1], 158.3, [158.4], 204.5 (d, $^2J_{P,C}$ = 4.4 Hz), [206.8 (d, $^2J_{P,C}$ = 4.4 Hz)]. ^{31}P NMR (162 MHz, CDCl$_3$): δ

= [20.5], 23.9. HRMS (ESI): *m/z* calcd for $C_{20}H_{28}NO_5P$ [M+H] $^+$: 394.1778; found: 394.1832.

Diethyl 1-(4-fluorophenyl)-3-oxo-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (285): Light yellow powder; yield: 40 mg (27 %); dr 58:42; R_f = 0.26 (1:1, EtOAc-hexane). IR (ATR): 3269, 2977, 2907, 1715, 1604, 1510, 1456, 1345, 1288, 1219, 1161, 1096, 1014, 945, 850, 762, 725 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79 (t, $^3J_{H,H}$ = 7.6 Hz, 3H, CH_2CH_3), [0.91 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3)], [1.12 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3)], [1.15 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 1.16 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.24 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.15 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.30 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.47 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.69 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 3.64-3.78 (m, 3H, OCH_2CH_3)*, 3.79-3.91 (m, 3H, OCH_2CH_3)*, 3.93-4.07 (m, 4H, OCH_2CH_3, 2 C*H*)*, 4.77-4.83 (m, 2H, CH)*, 5.81 (br s, 1H, $H_{pyrrole}$), [5.95 (br s, 1H, $H_{pyrrole}$)], 6.05 (q, $^3J_{H,H}$ = 3.0 Hz, 2H, 2 $H_{pyrrole}$)*, [6.64 (br s, 1H, $H_{pyrrole}$)], 6.67 (br s, 1H, $H_{pyrrole}$), 6.96 (t, $^3J_{H,H}$ = 8.6 Hz, 4H, Ar*H*)*, 7.25-7.30 (m, 4H, Ar*H*)*, [8.84 (br s, 1H, N*H*)], 9.45 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.3, [7.5], 16.2 (d, $^3J_{P,C}$ = 2.7 Hz), [16.3 (d, $^3J_{P,C}$ = 2.2 Hz)], 37.9, [38.5], [42.8 (d, $^2J_{P,C}$ = 2.9 Hz)], 43.0 (d, $^2J_{P,C}$ = 3.1 Hz), [58.3 (d, $^1J_{P,C}$ = 125.5 Hz)], 59.0 (d, $^1J_{P,C}$ = 127.3 Hz), [62.4 (d, $^2J_{P,C}$ = 7.9 Hz)], [62.5 (d, $^2J_{P,C}$ = 7.2 Hz)], 62.6 (d, $^2J_{P,C}$ = 7.0 Hz), 63.0 (d, $^2J_{P,C}$ = 7.1 Hz), [106.5], 107.4, [108.3], 108.4, [115.1 (d, $^2J_{F,C}$ = 21.2 Hz)], 115.5 (d, $^2J_{F,C}$ = 21.3 Hz), 117.2, [117.5], 129.7 (d, $^3J_{F,C}$ = 7.9 Hz), 129.8, [130.0 (d, $^3J_{F,C}$ = 8.0 Hz)], [130.9], 136.7 (d, $^3J_{P,C}$ = 3.5 Hz), [136.9 (d, $^3J_{P,C}$ = 3.4 Hz)], 161.7 (d, $^1J_{F,C}$ = 244.3 Hz), [161.8 (d, $^1J_{F,C}$ = 244.1 Hz)], 205.2 (d, $^2J_{P,C}$ = 4.6 Hz), [207.2 (d, $^2J_{P,C}$ = 4.3 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [20.7], 23.3. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}FNO_4P$ [M+H] $^+$: 382.1578; found: 382.1647.

Diethyl 1-(4-chlorophenyl)-3-oxo-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (286): Light yellow powder; yield: 83 mg (54 %); dr 52:48; R_f = 0.24 (1:1, EtOAc-hexane). IR (ATR): 3272, 2978, 2935, 2854, 1715, 1493, 1447, 1410, 1353, 1217, 1092, 1048, 1013, 946, 847, 800, 717 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [0.80 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3)], 0.92 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.12 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), [1.16 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3)], 1.17 (t, $^3J_{H,H}$ =

7.0 Hz, 3H, OCH_2CH_3), [1.24 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], [2.16 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.29 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.48 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.71 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.64-3.74 (m, 2H, OCH_2CH_3)*, 3.75-4.06 (m, 8H, 3 OCH_2CH_3, 2 CH)*, 4.74-4.81 (m, 2H, 2 CH)*, [5.78 (br s, 1H, $H_{pyrrole}$)], 5.95 (br s, 1H, $H_{pyrrole}$), 6.04-6.07 (m, 2H, 2 $H_{pyrrole}$)*, 6.64-6.66 (m, 1H, $H_{pyrrole}$), [6.66-6.68 (m, 1H, $H_{pyrrole}$)], 7.24 (br s, 8H, ArH)*, 8.77 (br s, 1H, NH), [9.37 (br s, 1H, NH)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.4, [7.5], [16.2 (d, $^3J_{P,C}$ = 4.4 Hz)], 16.3 (d, $^3J_{P,C}$ = 3.8 Hz), 38.0, [38.5], 42.9 (d, $^2J_{P,C}$ = 2.9 Hz), [43.1 (d, $^2J_{P,C}$ = 3.0 Hz)], 58.1 (d, $^1J_{P,C}$ = 125.4 Hz), [58.8 (d, $^1J_{P,C}$ = 127.1 Hz)], [62.4 (d, $^2J_{P,C}$ = 6.5 Hz)], [62.5 (d, $^2J_{P,C}$ = 6.5 Hz)], 62.6 (d, $^2J_{P,C}$ = 6.9 Hz), 63.0 (d, $^2J_{P,C}$ = 7.0 Hz), [106.7], 107.6, 108.3, [108.4], 117.3, [117.6], [128.5], 128.8, 129.5, [129.8], 130.5 (d, $^3J_{P,C}$ = 2.1 Hz), [130.7 (d, $^3J_{P,C}$ = 15.8 Hz)], [131.7], 132.8, [139.3 (d, $^3J_{P,C}$ = 5.9 Hz)], 139.5 (d, $^3J_{P,C}$ = 16.7 Hz), [205.1 (d, $^2J_{P,C}$ = 4.8 Hz)], 207.1 (d, $^2J_{P,C}$ = 4.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 20.5, [23.2]. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}ClNO_4P$ $[M+H]^+$: 398.1282; found: 398.1335.

Diethyl 1-(4-bromophenyl)-3-oxo-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (287): Light brown powder; mp 176.7-177.2 °C; yield: 124 mg (73 %); dr 55:45; R_f = 0.20 (1:1, EtOAc-hexane). IR (ATR): 3265, 2982, 2938, 1716, 1488, 1456, 1407, 1260, 1218, 1159, 1095, 1049, 1009, 975, 850, 797 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [0.81 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, CH_2CH_3)], 0.92 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, CH_2CH_3), 1.12 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), [1.16 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 1.17 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), [1.24 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3)], [2.17 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.30 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.48 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.71 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.64-3.74 (m, 2H, OCH_2CH_3)*, 3.75-3.92 (m, 4H, 2 OCH_2CH_3)*, 3.95-4.06 (m, 4H, OCH_2CH_3, 2 CH)*, 4.73-4.80 (m, 2H, 2 CH)*, [5.78 (br s, 1H, $H_{pyrrole}$)], 5.95 (br s, 1H, $H_{pyrrole}$), 6.04-6.06 (m, 2H, 2 $H_{pyrrole}$)*, 6.64 (br s, 1H, $H_{pyrrole}$), [6.67 (br s, 1H, $H_{pyrrole}$)], 7.17-7.19 (m, 4H, ArH)*, 7.39-7.41 (m, 4H, ArH)*, 8.79 (br s, 1H, NH), [9.38 (br s, 1H, NH)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = [7.4], 7.5, [16.2 (d, $^3J_{P,C}$ = 5.3 Hz)], 16.3 (d, $^3J_{P,C}$ = 3.7 Hz), [38.0], 38.5, 42.9 (d, $^2J_{P,C}$ = 2.9 Hz), [43.1 (d, $^2J_{P,C}$ = 2.9 Hz)], 58.0 (d, $^1J_{P,C}$ = 125.3 Hz), [58.7 (d, $^1J_{P,C}$ = 127.2 Hz)], 62.4 (d, $^2J_{P,C}$ = 4.9 Hz), 62.5 (d,

$^{2}J_{P,C}$ = 5.0 Hz), [62.6 (d, $^{2}J_{P,C}$ = 7.0 Hz)], [63.0 (d, $^{2}J_{P,C}$ = 7.0 Hz)], 106.7, [107.6], 108.3, [108.4], 117.3, [117.6], 120.8, [120.9], [129.8], 130.2, [130.4 (d, $^{3}J_{P,C}$ = 1.9 Hz)], 130.6 (d, $^{3}J_{P,C}$ = 15.8 Hz), 131.4, [131.8], 139.8 (d, $^{3}J_{P,C}$ = 5.9 Hz), [140.1 (d, $^{3}J_{P,C}$ = 16.8 Hz)], [205.1 (d, $^{2}J_{P,C}$ = 4.6 Hz)], 207.1 (d, $^{2}J_{P,C}$ = 4.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 20.5, [23.1]. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}BrNO_4P$ $[M+H]^+$: 442.0777; found: 442.0819.

Diethyl 1-(4-cyanophenyl)-3-oxo-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (288): Brown viscous oil; yield: 60 mg (40 %); dr 54:46; R_f = 0.19 (1:1, EtOAc-hexane). IR (ATR): 3244, 2983, 2935, 2227, 1715, 1607, 1443, 1232, 1096, 1047, 1023, 970, 851, 792 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [0.81 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3)], 0.93 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_2CH_3), 1.11 (t, $^{3}J_{H,H}$ = 7.3 Hz, 3H, OCH_2CH_3), [1.13 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3)], 1.17 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), [1.24 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 2.13 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.37 (dq, $^{2}J_{H,H}$ = 18.5 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], [2.56 (dq, $^{2}J_{H,H}$ = 18.5 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.72 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.70-3.90 (m, 3H, 2 OCH_2CH_3)*, 3.94-4.23 (m, 7H, 2 OCH_2CH_3, 2 C*H*)*, 4.94-5.01 (m, 2H, 2 C*H*)*, [5.91 (br s, 1H, $H_{pyrrole}$)], 5.97 (br s, 1H, $H_{pyrrole}$), 6.01-6.04 (m, 2H, 2 $H_{pyrrole}$)*, 6.58 (br s, 1H, $H_{pyrrole}$), [6.62 (br s, 1H, $H_{pyrrole}$)], 7.46 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H, Ar*H*), 7.51-7.56 (m, 6H, Ar*H*)*, 9.50 (br s, 1H, N*H*), [9.95 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = [7.3], 7.4, 16.1, [16.2], [38.0], 38.2, 43.4*, 57.3 (d, $^{1}J_{P,C}$ = 126.1 Hz), [57.8 (d, $^{1}J_{P,C}$ = 127.8 Hz)], [62.1 (d, $^{2}J_{P,C}$ = 7.0 Hz)], 62.5 (d, $^{2}J_{P,C}$ = 7.2 Hz), [62.6 (d, $^{2}J_{P,C}$ = 8.3 Hz)], 62.7 (d, $^{2}J_{P,C}$ = 5.4 Hz), [105.9], 106.8, [108.3], 108.4, 110.5, [110.7], [117.4], 117.5, [118.2], 118.3, [128.7], 129.5, 130.0 (d, $^{3}J_{P,C}$ = 18.2 Hz), [131.7], [132.0], 132.1, 146.3 (d, $^{3}J_{P,C}$ = 3.8 Hz), [146.9 (d, $^{3}J_{P,C}$ = 17.5 Hz)], [204.4 (d, $^{2}J_{P,C}$ = 4.9 Hz)], 205.8 (d, $^{2}J_{P,C}$ = 4.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = [20.9], 22.7. HRMS (ESI): *m/z* calcd for $C_{20}H_{26}N_2O_4P$ $[M+H]^+$: 389.1625; found: 389.1678.

Diethyl 1-(4-nitrophenyl)-3-oxo-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (289): Light brown powder; yield: 39 mg (25 %); dr 59:41; R_f = 0.19 (1:1, EtOAc-hexane). IR (ATR): 3266, 2983, 2939, 2907, 1714, 1596, 1510, 1460, 1393, 1345, 1291, 1221, 1136, 1105, 1046, 1015, 971, 909, 861, 784, 732 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [0.82 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3)], 0.93 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H,

CH_2CH_3), [1.11 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 1.13 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), [1.17 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 1.26 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), [2.15 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.38 (dq, $^2J_{H,H}$ = 18.5 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.60 (dq, $^2J_{H,H}$ = 18.3 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.75 (dq, $^2J_{H,H}$ = 18.5 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.53-3.63 (m, 1H, OCH_2CH_3), 3.65-3.78 (m, 2H, OCH_2CH_3)*, 3.79-3.89 (m, 3H, OCH_2CH_3)*, 3.95-4.05 (m, 2H, OCH_2CH_3)*, 4.13 (dd, $^2J_{P,H}$ = 21.3 Hz, $^3J_{H,H}$ = 10.4, 1H, CH), [4.19 (dd, $^2J_{P,H}$ = 21.9 Hz, $^3J_{H,H}$ = 11.8, 1H, CH)], 5.03 (dd, $^3J_{H,H}$ = 10.3, $^3J_{P,H}$ = 10.3 Hz, 1H, CH), [5.07 (dd, $^3J_{H,H}$ = 11.3, $^3J_{P,H}$ = 11.3 Hz, 1H, CH)], [5.92 (br s, 1H, $H_{pyrrole}$)], 5.99 (br s, 1H, $H_{pyrrole}$), 6.02-6.06 (m, 2H, 2 $H_{pyrrole}$)*, 6.59 (br s, 1H, $H_{pyrrole}$), [6.63 (br s, 1H, $H_{pyrrole}$)], [7.53 (d, $^3J_{H,H}$ = 8.7 Hz, 2H, ArH)], 7.58 (d, $^3J_{H,H}$ = 8.7 Hz, 2H, ArH), 8.10 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, ArH), [8.11 (d, $^3J_{H,H}$ = 8.6 Hz, 2H, ArH)], 9.50 (br s, 1H, NH), [9.97 (br s, 1H, NH)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.3, [7.4], 16.1 (d, $^3J_{P,C}$ = 5.8 Hz), [16.2 (d, $^3J_{P,C}$ = 5.4 Hz)], 38.1, [38.4], [43.1 (d, $^2J_{P,C}$ = 2.9 Hz)], 43.2 (d, $^2J_{P,C}$ = 2.7 Hz), [57.5 (d, $^1J_{P,C}$ = 125.8 Hz)], 58.0 (d, $^1J_{P,C}$ = 127.9 Hz), [62.2 (d, $^2J_{P,C}$ = 6.8 Hz)], [62.5 (d, $^2J_{P,C}$ = 6.9 Hz)], 62.6 (d, $^2J_{P,C}$ = 6.5 Hz), 62.7 (d, $^2J_{P,C}$ = 6.9 Hz), [106.4], 107.2, [108.5], 108.6, 117.4, [117.7], [123.2], 123.6, 128.7, 129.0 (d, $^3J_{P,C}$ = 1.9 Hz), [129.4], [129.6 (d, $^3J_{P,C}$ = 16.7 Hz)], 146.6, [146.7], [148.2 (d, $^3J_{P,C}$ = 4.9 Hz)], 148.7 (d, $^3J_{P,C}$ = 17.4 Hz), 204.2 (d, $^2J_{P,C}$ = 5.0 Hz), [206.0 (d, $^2J_{P,C}$ = 4.5 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [20.5], 22.7. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}N_2O_6P$ $[M+H]^+$: 409.1523; found: 409.1587.

Diethyl 3-oxo-1,1-di(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (290): Brown powder; yield: 20 mg (15 %); R_f = 0.28 (1:1, EtOAc-hexane). IR (ATR): 3293, 2995, 2927, 1717, 1569, 1460, 1345, 1292, 1263, 1210, 1101, 1062, 1033, 907, 730 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.13 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.23 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.38 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.74 (dq, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.47-3.53 (m, 1H, OCH_2CH_3), 3.72-3.93 (m, 3H, OCH_2CH_3), 3.97 (dd, $^2J_{P,H}$ = 23.6 Hz, $^3J_{H,H}$ = 6.2, 1H, CH), 4.88 (dd, $^2J_{P,H}$ = 17.6 Hz, $^3J_{H,H}$ = 6.2, 1H, CH)], 5.86 (br s, 1H, $H_{pyrrole}$), 5.97 (br s, 1H, $H_{pyrrole}$), 5.99-6.03 (m, 2H, 2 $H_{pyrrole}$), 6.61 (br s, 1H, $H_{pyrrole}$), 6.66 (br s, 1H, $H_{pyrrole}$), 9.33 (br s, 1H, NH), 10.03 (br s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.7, 16.2 (d, $^3J_{P,C}$ = 6.1 Hz), 16.3 (d, $^3J_{P,C}$ = 4.8 Hz), 36.3 (d, $^2J_{P,C}$ = 3.1 Hz), 37.8, 58.5 (d, $^1J_{P,C}$ = 125.9 Hz), 62.3 (d,

$^{2}J_{P,C}$ = 6.8 Hz), 62.9 (d, $^{2}J_{P,C}$ = 6.8 Hz), 106.7, 107.0, 107.7, 108.1, 116.8, 117.6, 130.5 (d, $^{3}J_{P,C}$ = 8.7 Hz), 130.6 (d, $^{3}J_{P,C}$ = 7.9 Hz), 207.9 (d, $^{2}J_{P,C}$ = 4.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.1. HRMS (ESI): *m/z* calcd for $C_{17}H_{26}N_2O_4P$ $[M+H]^+$: 353.1625; found: 353.1681.

Diethyl 1-(furan-2-yl)-3-oxo-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (291): Brown viscous oil; yield: 52 mg (38 %); dr 77:23; R_f = 0.21 (1:1, EtOAc-hexane). IR (ATR): 3260, 2986, 2918, 2851, 1713, 1633, 1444, 1392, 1217, 1162, 1097, 1048, 1015, 960, 884, 724 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H, 2 CH_2CH_3)*, 1.16 (t, $^{3}J_{H,H}$ = 7.1 Hz, 6H, 2 OCH_2CH_3)*, [1.22 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3)], 1.24 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.21 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), [2.26 (dq, $^{2}J_{H,H}$ = 18.2 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], [2.51 (dq, $^{2}J_{H,H}$ = 18.2 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3)], 2.66 (dq, $^{2}J_{H,H}$ = 18.3 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.59-3.76 (m, 2H, OCH_2CH_3)*, 3.81-3.91 (m, 2H, OCH_2CH_3)*, 3.93-4.00 (m, 5H, 2 OCH_2CH_3, C*H*)*, 4.11 (dd, $^{2}J_{P,H}$ = 22.0 Hz, $^{3}J_{H,H}$ = 9.0 Hz, 1H, C*H*), 4.81 (dd, $^{3}J_{H,H}$ = 8.7 Hz, $^{3}J_{P,H}$ = 8.7 Hz, 1H, C*H*), [4.88 (dd, $^{3}J_{H,H}$ = 11.0 Hz, $^{3}J_{P,H}$ = 11.0 Hz, 1H, C*H*)], 5.99-6.03 (m, 5H, 3 $H_{pyrrole}$, 2 H_{furan})*, [6.05 (br s, 1H, $H_{pyrrole}$)], 6.22-6.26 (m, 2H, 2 H_{furan})*, 6.64-6.66 (m, 2H, 2 $H_{pyrrole}$)*, [7.30 (br s, 1H, H_{furan})], 7.32 (br s, 1H, H_{furan}), 9.16 (br s, 1H, N*H*), [9.22 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = [7.3], 7.4, [16.1 (d, $^{3}J_{P,C}$ = 3.6 Hz)], 16.2 (d, $^{3}J_{P,C}$ = 3.6 Hz), 36.9 (d, $^{2}J_{P,C}$ = 3.3 Hz), [37.1], [37.3 (d, $^{2}J_{P,C}$ = 2.6 Hz)], 38.2, 56.0 (d, $^{1}J_{P,C}$ = 126.2 Hz), [57.1 (d, $^{1}J_{P,C}$ = 129.8 Hz)], 62.1 (d, $^{2}J_{P,C}$ = 6.7 Hz), 62.2 (d, $^{2}J_{P,C}$ = 6.7 Hz)*, [62.3 (d, $^{2}J_{P,C}$ = 7.1 Hz)], [106.7], 107.1, [107.5], 107.8, 107.9, [108.2], 110.4*, [117.0], 117.4, 127.8 (d, $^{3}J_{P,C}$ = 12.7 Hz), [128.0 (d, $^{3}J_{P,C}$ = 2.2 Hz)], 141.1, [141.2], 153.4 (d, $^{3}J_{P,C}$ = 7.5 Hz), [153.5], [204.5 (d, $^{2}J_{P,C}$ = 4.6 Hz)], 206.3 (d, $^{2}J_{P,C}$ = 4.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = [19.9], 21.9. HRMS (ESI): *m/z* calcd for $C_{17}H_{25}N_2O_5P$ $[M+H]^+$: 354.1465; found: 354.1525.

Diethyl 3-oxo-1-(1*H*-pyrrol-2-yl)-1-(thiophen-2-yl)pentan-2-ylphosphonate (292): Brown powder; yield: 88 mg (62 %); dr 60:40; R_f = 0.26 (1:1, EtOAc-hexane). IR (ATR): 3257, 2976, 2935, 1714, 1572, 1446, 1411, 1388, 1368, 1350, 1219, 1162, 1102, 1051, 1017, 965, 846, 795 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [0.86 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3)], 0.93 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_2CH_3), 1.13 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), [1.15 (t, $^{3}J_{H,H}$ = 6.7 Hz, 3H, OCH_2CH_3)], 1.21 (t,

$^{3}J_{H,H}$ = 7.1 Hz, 6H, 2 OCH$_2$C*H*$_3$)*, [2.23 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, C*H*$_2$CH$_3$)], 2.27 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, C*H*$_2$CH$_3$), [2.54 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, C*H*$_2$CH$_3$)], 2.74 (dq, $^{2}J_{H,H}$ = 18.4 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, C*H*$_2$CH$_3$), 3.52-3.65 (m, 2H, OC*H*$_2$CH$_3$)*, 3.76-3.87 (m, 2H, OC*H*$_2$CH$_3$)*, 3.89-4.00 (m, 5H, 2 OC*H*$_2$CH$_3$, C*H*)*, 4.05 (dd, $^{2}J_{P,H}$ = 23.4 Hz, $^{3}J_{H,H}$ = 8.1 Hz, 1H, C*H*), 5.07 (dd, $^{3}J_{H,H}$ = 8.3 Hz, $^{3}J_{P,H}$ = 8.3 Hz, 1H, C*H*), [5.13 (dd, $^{3}J_{H,H}$ = 10.6 Hz, $^{3}J_{P,H}$ = 10.6 Hz, 1H, C*H*)], 6.01-6.04 (m, 4H, 4 $H_{pyrrole}$)*, [6.62 (br s, 1H, $H_{pyrrole}$)], 6.66 (br s, 1H, $H_{pyrrole}$), 6.81-6.87 (m, 4H, 4 $H_{thiophene}$)*, 7.08-7.11 (m, 2H, 2 $H_{thiophene}$)*, [9.48 (br s, 1H, N*H*)], 9.55 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [7.3], 7.5, [16.1 (d, $^{3}J_{P,C}$ = 3.3 Hz)], 16.2 (d, $^{3}J_{P,C}$ = 5.7 Hz), [37.7], 38.2, 38.5 (d, $^{2}J_{P,C}$ = 3.0 Hz), [38.9 (d, $^{2}J_{P,C}$ = 2.5 Hz)], 59.0 (d, $^{1}J_{P,C}$ = 125.4 Hz), [59.8 (d, $^{1}J_{P,C}$ = 127.5 Hz)], 62.0 (d, $^{2}J_{P,C}$ = 6.8 Hz), 62.3 (d, $^{2}J_{P,C}$ = 6.3 Hz)*, [62.4 (d, $^{2}J_{P,C}$ = 6.8 Hz)], [107.1], 107.2, 107.9, [108.2], [116.9], 117.4, [124.0], 124.1, [125.4], 125.5, 126.2, [126.3], 130.1 (d, $^{3}J_{P,C}$ = 12.0 Hz), [130.2 (d, $^{3}J_{P,C}$ = 2.1 Hz)], [144.7 (d, $^{3}J_{P,C}$ = 19.4 Hz)], 145.0 (d, $^{3}J_{P,C}$ = 9.3 Hz), [204.6 (d, $^{2}J_{P,C}$ = 4.7 Hz)], 206.3 (d, $^{2}J_{P,C}$ = 4.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 20.3, [21.1]. HRMS (ESI): *m/z* calcd for $C_{17}H_{25}NO_4PS$ $[M+H]^+$: 370.1236; found: 370.1300.

4.3.4. General procedure for the synthesis of pyrrolizines from ketone functionalized vinylphosphonates

To a solution of ketone functionalized vinylphosphonates (**234-246**) (0.384 mmol) in toluene (2 mL) was added 10 mol % of Metal triflate (0.0384 mmol) and the reaction mixture was stirred for 0.5 h at room temperature. Pyrrole (3.84 mmol) was added to the reaction mixture instantly *via* syringe pump and the resulting mixture was stirred at 50°C for 6 h (TLC monitoring). Metal triflate was removed from the reaction medium by subjecting the mixture to a short flash column chromatography (silica gel, EtOAc). The eluent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:2).

Diethyl 3-ethyl-1-phenyl-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-yl-phosphonate (293): Brown powder; yield: 79 mg (50 %); R_f = 0.31 (1:1, EtOAc-hexane). IR (ATR): 3257, 2965, 2927, 1711, 1496, 1393, 1291, 1260, 1234, 1216,

1130, 1102, 1015, 964, 795, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.68 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), 0.94 (t, $^{3}J_{H,H}$ = 7.4 Hz, 3H, OCH_2CH_3), 1.00 (t, $^{3}J_{H,H}$ = 7.4 Hz, 3H, CH_2CH_3), 2.47 (dq, $^{2}J_{H,H}$ = 14.7 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 2.67 (dq, $^{2}J_{H,H}$ = 14.7 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 3.11 (dd, $^{2}J_{P,H}$ = 17.5 Hz, $^{3}J_{H,H}$ = 10.4 Hz, 1H, C*H*), 3.31-3.46 (m, 2H, OCH_2CH_3), 3.56-3.62 (m, 1H, OCH_2CH_3), 3.63-3.71 (m, 1H, OCH_2CH_3), 4.41 (dd, $^{3}J_{H,H}$ = 10.4 Hz, $^{3}J_{P,H}$ = 10.4 Hz, 1H, C*H*), 5.27 (br s, 1H, $H_{pyrrole}$), 5.59 (br s, 1H, $H_{pyrrole}$), 5.94 (dt, $^{4}J_{H,H}$ = 3.0 Hz, $^{3}J_{H,H}$ = 2.7 Hz, 1H, $H_{pyrrole}$), 6.22 (dt, $^{4}J_{H,H}$ = 2.2 Hz, $^{3}J_{H,H}$ = 2.8 Hz, 1H, $H_{pyrrole}$), 6.55 (br d, , $^{3}J_{H,H}$ = 1.7 Hz, 1H, $H_{pyrrole}$), 6.63 (d, , $^{3}J_{H,H}$ = 2.6 Hz, 1H, $H_{pyrrole}$), 7.20-7.27 (m, 5H, Ar*H*), 8.98 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2, 15.6 (d, $^{3}J_{P,C}$ = 6.8 Hz), 16.1 (d, $^{3}J_{P,C}$ = 6.7 Hz), 30.5, 44.8 (d, $^{2}J_{P,C}$ = 2.3 Hz), 56.7 (d, $^{1}J_{P,C}$ = 147.4 Hz), 61.2 (d, $^{2}J_{P,C}$ = 6.1 Hz), 61.7 (d, $^{2}J_{P,C}$ = 6.7 Hz), 67.1 (d, $^{2}J_{P,C}$ = 6.5 Hz), 99.6, 107.1, 107.8, 112.6, 112.7 (d, $^{4}J_{P,C}$ = 2.2 Hz), 117.9, 127.1, 128.2, 128.7, 133.0 (d, $^{3}J_{P,C}$ = 3.2 Hz), 139.1 (d, $^{3}J_{P,C}$ = 15.3 Hz), 141.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.8. HRMS (ESI): *m/z* calcd for $C_{23}H_{30}N_2O_3P$ $[M+H]^+$: 413.1989; found: 413.2049.

Diethyl 3-ethyl-3-(1*H*-pyrrol-2-yl)-1-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (294): Brown powder; yield: 50 mg (27 %); R_f = 0.53 (1:1, EtOAc-hexane). IR (ATR): 2974, 2939, 1655, 1568, 1507, 1456, 1393, 1340, 1291, 1214, 1162, 1124, 1017, 965, 881, 764 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.06 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.07 (t, $^{3}J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 2.50 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.68 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.14 (dd, $^{2}J_{P,H}$ = 17.5 Hz, $^{3}J_{H,H}$ = 10.5 Hz, 1H, C*H*), 3.42-3.56 (m, 2H, OCH_2CH_3), 3.65-3.73 (m, 1H, OCH_2CH_3), 3.77-3.85 (m, 1H, OCH_2CH_3), 4.49 (dd, $^{3}J_{H,H}$ = 10.7 Hz, $^{3}J_{P,H}$ = 10.7 Hz, 1H, C*H*), 5.31 (t, $^{3}J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), 5.66 (br d, $^{3}J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), 6.02 (dt, $^{4}J_{H,H}$ = 3.2 Hz, $^{3}J_{H,H}$ = 2.7 Hz, 1H, $H_{pyrrole}$), 6.31 (dt, $^{3}J_{H,H}$ = 2.8 Hz, $^{4}J_{H,H}$ = 2.6 Hz, 1H, $H_{pyrrole}$), 6.65 (br d, $^{3}J_{H,H}$ = 2.2 Hz, 1H, $H_{pyrrole}$), 6.72 (dt, $^{3}J_{H,H}$ = 2.6 Hz, $^{4}J_{H,H}$ = 1.7 Hz, 1H, $H_{pyrrole}$), 7.42 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H, Ar*H*), 7.56 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2H, Ar*H*), 8.97 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2, 15.5 (d, $^{3}J_{P,C}$ = 7.0 Hz), 16.2 (d, $^{3}J_{P,C}$ = 6.6 Hz), 30.4, 44.7 (d, $^{2}J_{P,C}$ = 8.6 Hz), 56.8 (d, $^{1}J_{P,C}$ = 148.1 Hz), 61.2 (d, $^{2}J_{P,C}$ = 6.3 Hz), 62.0 (d, $^{2}J_{P,C}$ = 6.6 Hz), 67.2 (d, $^{2}J_{P,C}$ = 7.0 Hz), 99.8, 107.2, 107.9, 112.9 (d, $^{4}J_{P,C}$ = 2.2 Hz), 113.0, 118.1, 124.2

(q, $^{1}J_{F,C}$ = 270.4 Hz), 125.2 (q, $^{3}J_{F,C}$ = 3.7 Hz), 129.1, 129.5 (q, $^{2}J_{F,C}$ = 31.9 Hz), 132.6 (d, $^{3}J_{P,C}$ = 3.1 Hz), 138.0 (d, $^{3}J_{P,C}$ = 14.7 Hz), 145.6 (d, $^{3}J_{P,C}$ = 1.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.8. HRMS (ESI): *m/z* calcd for $C_{24}H_{29}F_3N_2O_3P$ $[M+H]^+$: 481.1862; found: 481.1911.

Diethyl 3-ethyl-3-(1*H*-pyrrol-2-yl)-1-*p*-tolyl-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (295): Brown powder; yield: 103 mg (63 %); R_f = 0.42 (1:1, EtOAc-hexane). IR (ATR): 3272, 3098, 2977, 2921, 1559, 1515, 1456, 1393,1289, 1233, 1161, 1105, 1026, 957, 828, 794, 716 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.05 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), 1.07 (t, $^{3}J_{H,H}$ = 7.6 Hz, 3H, CH_2CH_3), 2.33 (s, 3H, CH_3), 2.47 (dq, $^{2}J_{H,H}$ = 14.7 Hz, $^{3}J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.65 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 3.12 (dd, $^{2}J_{P,H}$ = 17.5 Hz, $^{3}J_{H,H}$ = 10.4 Hz, 1H, CH), 3.38-3.49 (m, 2H, OCH_2CH_3), 3.63-3.71 (m, 1H, OCH_2CH_3), 3.72-3.79 (m, 1H, OCH_2CH_3), 4.38 (dd, $^{3}J_{H,H}$ = 10.8 Hz, $^{3}J_{P,H}$ = 10.8 Hz, 1H, CH), 5.29 (br s, 1H, $H_{pyrrole}$), 5.60 (br d, 1H, $^{3}J_{H,H}$ = 3.0 Hz, $H_{pyrrole}$), 5.95 (dt, $^{4}J_{H,H}$ = 2.8 Hz, $^{3}J_{H,H}$ = 2.6 Hz, 1H, $H_{pyrrole}$), 6.24 (dt, $^{3}J_{H,H}$ = 2.6 Hz, $^{4}J_{H,H}$ = 2.4 Hz, 1H, $H_{pyrrole}$), 6.57 (br s, 1H, $H_{pyrrole}$), 6.65 (br s, 1H, $H_{pyrrole}$), 7.07 (d, $^{3}J_{H,H}$ = 7.9 Hz, 2H, ArH), 7.15 (d, $^{3}J_{H,H}$ = 7.9 Hz, 2H, ArH), 8.99 (br s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2, 15.6 (d, $^{3}J_{P,C}$ = 6.8 Hz), 16.2 (d, $^{3}J_{P,C}$ = 6.8 Hz), 21.2, 30.5, 44.4 (d, $^{2}J_{P,C}$ = 1.9 Hz), 56.6 (d, $^{1}J_{P,C}$ = 147.1 Hz), 61.0 (d, $^{2}J_{P,C}$ = 5.9 Hz), 61.6 (d, $^{2}J_{P,C}$ = 6.7 Hz), 67.0 (d, $^{2}J_{P,C}$ = 6.6 Hz), 99.6, 107.2, 107.8, 112.4, 112.9 (d, $^{4}J_{P,C}$ = 1.9 Hz), 117.7, 128.6, 128.8, 132.9 (d, $^{3}J_{P,C}$ = 3.0 Hz), 136.4, 138.4, 139.0 (d, $^{3}J_{P,C}$ = 1.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.6. HRMS (ESI): *m/z* calcd for $C_{24}H_{32}N_2O_3P$ $[M+H]^+$: 427.2145; found: 427.2214.

Diethyl 3-ethyl-1-(4-methoxyphenyl)-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1H-pyrrolizin-2-ylphosphonate (296): Brown powder; yield: 68 mg (40 %); R_f = 0.39 (1:1, EtOAc-hexane). IR (ATR): 3266, 2972, 2939, 2907, 2842, 1613, 1501, 1463, 1236, 1186, 1107, 1030, 980, 800, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.06 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.07 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 2.46 (dq, $^{2}J_{H,H}$ = 14.6 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 2.65 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 3.09 (dd, $^{2}J_{P,H}$ = 17.5 Hz, $^{3}J_{H,H}$ = 10.4 Hz, 1H, CH), 3.41-3.50 (m, 2H, OCH_2CH_3), 3.65-3.73 (m, 1H, OCH_2CH_3), 3.74-3.82 (m, 1H, OCH_2CH_3), 3.79 (s, 3H, OCH_3), 4.37 (dd, $^{3}J_{H,H}$ =

10.8 Hz, $^{3}J_{P,H}$ = 10.8 Hz, 1H, C*H*), 5.29 (br s, 1H, $H_{pyrrole}$), 5.60 (br d, $^{3}J_{H,H}$ = 3.2 Hz, 1H, $H_{pyrrole}$), 5.96 (dt, $^{4}J_{H,H}$ = 3.0 Hz, $^{3}J_{H,H}$ = 2.6 Hz, 1H, $H_{pyrrole}$), 6.25 (dt, $^{3}J_{H,H}$ = 2.8 Hz, $^{4}J_{H,H}$ = 2.3 Hz, 1H, $H_{pyrrole}$), 6.58 (br s, 1H, $H_{pyrrole}$), 6.66 (dt, $^{3}J_{H,H}$ = 2.4 Hz, $^{4}J_{H,H}$ = 1.6 Hz, 1H, $H_{pyrrole}$), 6.81 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar*H*), 7.19 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar*H*), 8.95 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.1, 15.6 (d, $^{3}J_{P,C}$ = 6.7 Hz), 16.1 (d, $^{3}J_{P,C}$ = 6.9 Hz), 30.3, 43.9 (d, $^{2}J_{P,C}$ = 2.1 Hz), 55.0, 56.6 (d, $^{1}J_{P,C}$ = 147.1 Hz), 60.9 (d, $^{2}J_{P,C}$ = 6.2 Hz), 61.4 (d, $^{2}J_{P,C}$ = 6.7 Hz), 66.8 (d, $^{2}J_{P,C}$ = 6.6 Hz), 99.5, 107.1, 107.7, 112.3, 112.7 (d, $^{4}J_{P,C}$ = 2.0 Hz), 113.4, 117.6, 129.5, 132.8 (d, $^{3}J_{P,C}$ = 3.4 Hz), 133.2, 138.9 (d, $^{3}J_{P,C}$ = 15.3 Hz), 158.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.7. HRMS (ESI): *m/z* calcd for $C_{24}H_{32}N_2O_4P$ $[M+H]^+$: 443.2094; found: 443.2163.

Diethyl 3-ethyl-1-(4-fluorophenyl)-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (297): Light brown powder; yield: 93 mg (56 %); R_f = 0.50 (1:1, EtOAc-hexane). IR (ATR): 3269, 2975, 1718, 1606, 1508, 1456, 1392, 1292, 1224, 1158, 1128, 1096, 1023, 958, 841, 786 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.06 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.07 (t, $^{3}J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 2.47 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.65 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.05 (dd, $^{2}J_{P,H}$ = 17.4 Hz, $^{3}J_{H,H}$ = 10.4 Hz, 1H, C*H*), 3.38-3.53 (m, 2H, OCH_2CH_3), 3.65-3.81 (m, 2H, OCH_2CH_3), 4.39 (dd, $^{3}J_{H,H}$ = 10.7 Hz, $^{3}J_{P,H}$ = 10.7 Hz, 1H, C*H*), 5.25 (br t, $^{3}J_{H,H}$ = 3.7 Hz, 1H, $H_{pyrrole}$), 5.58 (br d, $^{3}J_{H,H}$ = 3.3 Hz, 1H, $H_{pyrrole}$), 5.94 (dt, $^{4}J_{H,H}$ = 3.0 Hz, $^{3}J_{H,H}$ = 2.8 Hz, 1H, $H_{pyrrole}$), 6.23 (dt, $^{3}J_{H,H}$ = 2.9 Hz, $^{4}J_{H,H}$ = 2.4 Hz, 1H, $H_{pyrrole}$), 6.57 (br d, $^{3}J_{H,H}$ = 2.1 Hz, 1H, $H_{pyrrole}$), 6.66 (dt, $^{3}J_{H,H}$ = 2.4 Hz, $^{4}J_{H,H}$ = 1.6 Hz, 1H, $H_{pyrrole}$), 6.97 (t, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar*H*), 7.24 (t, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar*H*), 8.95 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.1, 15.6 (d, $^{3}J_{P,C}$ = 6.7 Hz), 16.0 (d, $^{3}J_{P,C}$ = 6.6 Hz), 30.3, 44.0 (d, $^{2}J_{P,C}$ = 2.2 Hz), 56.7 (d, $^{1}J_{P,C}$ = 146.9 Hz), 60.8 (d, $^{2}J_{P,C}$ = 6.0 Hz), 61.5 (d, $^{2}J_{P,C}$ = 6.7 Hz), 66.8 (d, $^{2}J_{P,C}$ = 6.8 Hz), 99.6, 107.2, 107.8, 112.5, 112.8 (d, $^{4}J_{P,C}$ = 2.1 Hz), 114.8 (d, $^{2}J_{F,C}$ = 21.1 Hz), 117.6, 130.0 (d, $^{3}J_{F,C}$ = 7.9 Hz), 132.4 (d, $^{3}J_{P,C}$ = 3.2 Hz), 136.9 (d, $^{3}J_{P,C}$ = 3.1 Hz), 138.2 (d, $^{3}J_{P,C}$ = 15.2 Hz), 161.8 (d, $^{3}J_{F,C}$ = 244.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.4. HRMS (ESI): *m/z* calcd for $C_{23}H_{29}FN_2O_3P$ $[M+H]^+$: 431.1894; found: 431.1958.

Diethyl 1-(4-chlorophenyl)-3-ethyl-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (298): Light yellow powder; yield: 76 mg (44 %); R_f = 0.45 (1:1, EtOAc-hexane). IR (ATR): 3264, 2974, 2850, 1489, 1461, 1407, 1392, 1233, 1132, 1104, 1012, 983, 957, 907, 791, 724 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.05 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.06 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 2.47 (dq, $^2J_{H,H}$ = 14.8 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.66 (dq, $^2J_{H,H}$ = 14.8 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.09 (dd, $^2J_{P,H}$ = 17.5 Hz, $^3J_{H,H}$ = 10.5 Hz, 1H, C*H*), 3.39-3.55 (m, 2H, OCH_2CH_3), 3.67-3.80 (m, 2H, OCH_2CH_3), 4.39 (dd, $^3J_{H,H}$ = 10.8 Hz, $^3J_{P,H}$ = 10.8 Hz, 1H, C*H*), 5.26 (br s, 1H, $H_{pyrrole}$), 5.60 (br d, $^3J_{H,H}$ = 2.5 Hz, 1H, $H_{pyrrole}$), 5.96 (dt, $^4J_{H,H}$ = 2.7 Hz, $^3J_{H,H}$ = 2.5 Hz, 1H, $H_{pyrrole}$), 6.25 (dt, $^3J_{H,H}$ = 2.6 Hz, $^4J_{H,H}$ = 2.3 Hz, 1H, $H_{pyrrole}$), 6.59 (br s, 1H, $H_{pyrrole}$), 6.67 (br s, 1H, $H_{pyrrole}$), 7.23 (t, $^3J_{H,H}$ = 8.5 Hz, 2H, Ar*H*), 7.25 (t, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 9.00 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2, 15.7 (d, $^3J_{P,C}$ = 6.6 Hz), 16.2 (d, $^3J_{P,C}$ = 6.6 Hz), 30.4, 44.3 (d, $^2J_{P,C}$ = 2.1 Hz), 56.8 (d, $^1J_{P,C}$ = 147.7 Hz), 61.1 (d, $^2J_{P,C}$ = 6.1 Hz), 61.8 (d, $^2J_{P,C}$ = 6.6 Hz), 67.1 (d, $^2J_{P,C}$ = 6.7 Hz), 99.8, 107.3, 107.9, 112.7, 113.0 (d, $^4J_{P,C}$ = 2.0 Hz), 117.9, 128.3, 130.1, 132.5 (d, $^3J_{P,C}$ = 3.1 Hz), 132.9, 138.2 (d, $^3J_{P,C}$ = 15.2 Hz), 140.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.1. HRMS (ESI): *m/z* calcd for $C_{23}H_{29}ClN_2O_3P$ $[M+H]^+$: 447.1599; found: 447.1628.

Diethyl 1-(4-bromophenyl)-3-ethyl-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (299): Brown powder; yield: 38 mg (20 %); R_f = 0.45 (1:1, EtOAc-hexane). IR (ATR): 3272, 2989, 2919, 1484, 1454, 1227, 1124, 1110, 1030, 974, 830, 797, 724 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.06 (t, $^3J_{H,H}$ = 7.2 Hz, 6H, OCH_2CH_3, CH_2CH_3), 2.47 (dq, $^2J_{H,H}$ = 14.8 Hz, $^3J_{H,H}$ = 7.1 Hz, 1H, CH_2CH_3), 2.65 (dq, $^2J_{H,H}$ = 14.7 Hz, $^3J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 3.06 (dd, $^2J_{P,H}$ = 17.5 Hz, $^3J_{H,H}$ = 10.5 Hz, 1H, C*H*), 3.39-3.56 (m, 2H, OCH_2CH_3), 3.67-3.82 (m, 2H, OCH_2CH_3), 4.38 (dd, $^3J_{H,H}$ = 10.8 Hz, $^3J_{P,H}$ = 10.8 Hz, 1H, C*H*), 5.26 (br s, 1H, $H_{pyrrole}$), 5.61 (br s, 1H, $H_{pyrrole}$), 5.96 (br s, 1H, $H_{pyrrole}$), 6.26 (br s, 1H, $H_{pyrrole}$), 6.59 (br s, 1H, $H_{pyrrole}$), 6.67 (br s, 1H, $H_{pyrrole}$), 7.12 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.41 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 8.97 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.1, 15.6 (d, $^3J_{P,C}$ = 6.7 Hz), 16.0 (d, $^3J_{P,C}$ = 6.6 Hz), 30.3, 44.3 (d, $^2J_{P,C}$ = 2.2 Hz), 56.6 (d, $^1J_{P,C}$ = 147.9 Hz), 61.2 (d, $^2J_{P,C}$ = 6.1 Hz), 61.8 (d, $^2J_{P,C}$ = 6.8 Hz), 67.0 (d, $^2J_{P,C}$ = 6.6 Hz), 99.7, 107.1, 107.8, 112.7,

112.8 (d, $^{4}J_{P,C}$ = 2.0 Hz), 117.9, 120.9, 130.4, 131.2, 132.6 (d, $^{3}J_{P,C}$ = 2.9 Hz), 138.1 (d, $^{3}J_{P,C}$ = 15.2 Hz), 140.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.1. HRMS (ESI): *m/z* calcd for $C_{23}H_{29}BrN_2O_3P$ $[M+H]^+$: 491.1094; found: 491.1067.

Diethyl 1-(4-cyanophenyl)-3-ethyl-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (300): Brown viscous oil; yield: 22 mg (13 %); R_f = 0.44 (1:1, EtOAc-hexane). IR (ATR): 3329, 2993, 2227, 1611, 1559, 1507, 1460, 1399, 1285, 1234, 1159, 1104, 1022, 975, 841, 788, 726 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.07 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3, CH_2CH_3), 2.49 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.66 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 3.08 (dd, $^{2}J_{P,H}$ = 17.4 Hz, $^{3}J_{H,H}$ = 10.5 Hz, 1H, C*H*), 3.39-3.49 (m, 1H, OCH_2CH_3), 3.51-3.58 (m, 1H, OCH_2CH_3), 3.66-3.82 (m, 2H, OCH_2CH_3), 4.47 (dd, $^{3}J_{H,H}$ = 10.7 Hz, $^{3}J_{P,H}$ = 10.7 Hz, 1H, C*H*), 5.25 (br s, 1H, $H_{pyrrole}$), 5.60 (br d, $^{3}J_{H,H}$ = 3.3 Hz, 1H, $H_{pyrrole}$), 5.97 (dt, $^{4}J_{H,H}$ = 3.0 Hz, $^{3}J_{H,H}$ = 2.7 Hz, 1H, $H_{pyrrole}$), 6.27 (dt, $^{3}J_{H,H}$ = 2.8 Hz, $^{4}J_{H,H}$ = 2.6 Hz, 1H, $H_{pyrrole}$), 6.61 (br s, 1H, $H_{pyrrole}$), 6.68 (br s, 1H, $H_{pyrrole}$), 7.41 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2H, Ar*H*), 7.60 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H, Ar*H*), 8.99 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.1, 15.7 (d, $^{3}J_{P,C}$ = 6.5 Hz), 16.1 (d, $^{3}J_{P,C}$ = 6.6 Hz), 30.2, 44.8 (d, $^{2}J_{P,C}$ = 2.2 Hz), 56.7 (d, $^{1}J_{P,C}$ = 148.3 Hz), 61.1 (d, $^{2}J_{P,C}$ = 6.3 Hz), 61.9 (d, $^{2}J_{P,C}$ = 6.7 Hz), 67.1 (d, $^{2}J_{P,C}$ = 6.7 Hz), 99.9, 107.2, 107.9, 111.1, 113.0, 113.1 (d, $^{4}J_{P,C}$ = 1.9 Hz), 118.0, 118.4, 129.5, 131.9, 132.1 (d, $^{3}J_{P,C}$ = 3.2 Hz), 137.2 (d, $^{3}J_{P,C}$ = 14.6 Hz), 147.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.3. HRMS (ESI): *m/z* calcd for $C_{24}H_{29}N_3O_3P$ $[M+H]^+$: 438.1941; found: 438.2021.

Diethyl 3-ethyl-1-(4-nitrophenyl)-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (301): Brown powder; yield: 24 mg (15 %); R_f = 0.31 (1:1, EtOAc-hexane). IR (ATR): 3267, 2930, 2860, 1599, 1521, 1460, 1392, 1347, 1289, 1234, 1101, 1054, 1025, 974, 784, 761 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.08 (t, $^{3}J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3, CH_2CH_3), 2.50 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 2.67 (dq, $^{2}J_{H,H}$ = 14.9 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 3.10 (dd, $^{2}J_{P,H}$ = 17.4 Hz, $^{3}J_{H,H}$ = 10.5 Hz, 1H, C*H*), 3.39-3.49 (m, 1H, OCH_2CH_3), 3.51-3.60 (m, 1H, OCH_2CH_3), 3.67-3.83 (m, 2H, OCH_2CH_3), 4.52 (dd, $^{3}J_{H,H}$ = 10.8 Hz, $^{3}J_{P,H}$ = 10.8 Hz, 1H, C*H*), 5.25 (br s, 1H, $H_{pyrrole}$), 5.60 (br d, $^{3}J_{H,H}$ = 3.3 Hz, 1H, $H_{pyrrole}$), 5.98 (dt, $^{4}J_{H,H}$ = 2.7 Hz, $^{3}J_{H,H}$ =

2.6 Hz, 1H, $H_{pyrrole}$), 6.27 (dt, $^{3}J_{H,H}$ = 2.7 Hz, $^{4}J_{H,H}$ = 2.2 Hz, 1H, $H_{pyrrole}$), 6.62 (br s, 1H, $H_{pyrrole}$), 6.69 (br d, $^{3}J_{H,H}$ = 1.4 Hz, 1H, $H_{pyrrole}$), 7.47 (d, $^{3}J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), 8.17 (d, $^{3}J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), 8.96 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2, 15.8 (d, $^{3}J_{P,C}$ = 6.4 Hz), 16.2 (d, $^{3}J_{P,C}$ = 6.5 Hz), 30.4, 44.7 (d, $^{2}J_{P,C}$ = 2.4 Hz), 56.9 (d, $^{1}J_{P,C}$ = 148.7 Hz), 61.2 (d, $^{2}J_{P,C}$ = 6.3 Hz), 62.0 (d, $^{2}J_{P,C}$ = 6.5 Hz), 67.2 (d, $^{2}J_{P,C}$ = 6.7 Hz), 100.1, 107.4, 108.0, 113.1, 113.3 (d, $^{4}J_{P,C}$ = 2.0 Hz), 118.1, 123.3, 129.6, 132.1 (d, $^{3}J_{P,C}$ = 3.0 Hz), 137.2 (d, $^{3}J_{P,C}$ = 14.6 Hz), 147.3, 149.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.3. HRMS (ESI): *m/z* calcd for $C_{23}H_{29}N_3O_5P$ $[M+H]^+$: 458.1839; found: 458.1929.

Diethyl 3-ethyl-1-(furan-2-yl)-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-yl-phosphonate (302): Black powder; yield: 20 mg (13 %); R_f = 0.35 (1:1, EtOAc-hexane). IR (ATR): 3369, 3123, 2967, 2938, 2904, 1510, 1461, 1393, 1342, 1260, 1228, 1149, 1100, 1064, 1021, 983, 954, 795, 738 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.04 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), 1.06 (t, $^{3}J_{H,H}$ = 7.4 Hz, 3H, CH_2CH_3), 2.46 (dq, $^{2}J_{H,H}$ = 14.9 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 2.64 (dq, $^{2}J_{H,H}$ = 14.8 Hz, $^{3}J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 3.41-3.49 (m, 2H, C*H*, OCH_2CH_3), 3.68-3.79 (m, 2H, OCH_2CH_3), 3.81-3.89 (m, 1H, OCH_2CH_3), 4.54 (dd, $^{3}J_{H,H}$ = 10.9 Hz, $^{3}J_{P,H}$ = 10.9 Hz, 1H, C*H*), 5.26 (br s, 1H, $H_{pyrrole}$), 5.69 (br d, $^{3}J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), 5.94 (dt, $^{4}J_{H,H}$ = 3.2 Hz, $^{3}J_{H,H}$ = 2.7 Hz, 1H, $H_{pyrrole}$), 6.21-6.24 (m, 2H, $H_{pyrrole,}$ H_{furan}), 6.29-6.31 (m, 1H, $H_{pyrrole}$), 6.56 (br d, 1H, $^{3}J_{H,H}$ = 2.3 Hz, H_{furan}), 6.65 (dt, $^{3}J_{H,H}$ = 2.5 Hz, $^{4}J_{H,H}$ = 1.7 Hz, 1H, $H_{pyrrole}$), 7.33 (br d, 1H, $^{3}J_{H,H}$ = 1.0 Hz, H_{furan}), 8.92 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.0, 14.9 (d, $^{3}J_{P,C}$ = 6.6 Hz), 15.0 (d, $^{3}J_{P,C}$ = 6.7 Hz), 29.6, 37.1 (d, $^{2}J_{P,C}$ = 2.8 Hz), 51.7 (d, $^{1}J_{P,C}$ = 148.5 Hz), 60.1 (d, $^{2}J_{P,C}$ = 6.3 Hz), 60.5 (d, $^{2}J_{P,C}$ = 6.6 Hz), 65.6 (d, $^{2}J_{P,C}$ = 6.2 Hz), 98.4, 106.1, 106.2, 106.8, 109.1, 111.6, 111.7 (d, $^{4}J_{P,C}$ = 2.1 Hz), 116.7, 131.4 (d, $^{3}J_{P,C}$ = 3.0 Hz), 134.4 (d, $^{3}J_{P,C}$ = 14.7 Hz), 140.4, 152.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.1. HRMS (ESI): *m/z* calcd for $C_{21}H_{28}N_2O_4P$ $[M+H]^+$: 403.1781; found: 403.1782.

Diethyl 3-ethyl-3-(1*H*-pyrrol-2-yl)-1-(thiophen-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (303): Brown powder; yield: 50 mg (31 %); R_f = 0.49 (1:1, EtOAc-hexane). IR (ATR): 2976, 1458, 1393, 1260, 1231, 1160, 1101, 1025, 977, 800, 752, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, $^{3}J_{H,H}$ = 6.8 Hz, 3H,

OCH_2CH_3), 1.05 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.07 (t, $^3J_{H,H}$ = 6.7 Hz, 3H, OCH_2CH_3), 2.47 (dq, $^2J_{H,H}$ = 14.9 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.66 (dq, $^2J_{H,H}$ = 14.8 Hz, $^3J_{H,H}$ = 7.0 Hz, 1H, CH_2CH_3), 3.23 (dd, $^2J_{P,H}$ = 17.3 Hz, $^3J_{H,H}$ = 10.3 Hz, 1H, CH), 3.46-3.56 (m, 1H, OCH_2CH_3), 3.58-3.68 (m, 1H, OCH_2CH_3), 3.77-3.86 (m, 2H, OCH_2CH_3), 4.79 (dd, $^3J_{H,H}$ = 10.5 Hz, $^3J_{P,H}$ = 10.5 Hz, 1H, CH), 5.30 (br t, $^3J_{H,H}$ = 4.0 Hz, 1H, $H_{pyrrole}$), 5.82 (dt, $^4J_{H,H}$ = 3.4 Hz, $^3J_{H,H}$ = 1.2 Hz, 1H, $H_{pyrrole}$), 6.01 (dt, $^3J_{H,H}$ = 3.2 Hz, $^4J_{H,H}$ = 2.7 Hz, 1H, $H_{pyrrole}$), 6.31 (dt, $^3J_{H,H}$ = 2.7 Hz, $^4J_{H,H}$ = 2.6 Hz, 1H, $H_{pyrrole}$), 6.62 (br s, 1H, $H_{pyrrole}$), 6.72 (dt, $^3J_{H,H}$ = 2.6 Hz, $^4J_{H,H}$ = 1.6 Hz, 1H, $H_{pyrrole}$), 6.94 (dd, $^3J_{H,H}$ = 5.1 Hz, $^3J_{H,H}$ = 3.5 Hz, 1H, $H_{thiophene}$), 7.02 (d, $^3J_{H,H}$ = 3.4 Hz, 1H, $H_{thiophene}$), 7.21 (d, $^3J_{H,H}$ = 4.6 Hz, 1H, $H_{thiophene}$), 9.04 (br s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.1, 15.8 (d, $^3J_{P,C}$ = 6.8 Hz), 16.1 (d, $^3J_{P,C}$ = 6.6 Hz), 30.5, 40.2 (d, $^2J_{P,C}$ = 2.7 Hz), 57.3 (d, $^1J_{P,C}$ = 147.5 Hz), 61.5 (d, $^2J_{P,C}$ = 6.0 Hz), 61.8 (d, $^2J_{P,C}$ = 6.7 Hz), 67.1 (d, $^2J_{P,C}$ = 6.4 Hz), 100.1, 107.2, 107.8, 112.7 (d, $^4J_{P,C}$ = 2.0 Hz), 112.8, 118.0, 124.3, 126.9, 132.7 (d, $^3J_{P,C}$ = 2.9 Hz), 138.3 (d, $^3J_{P,C}$ = 14.8 Hz), 144.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.0. HRMS (ESI): *m/z* calcd for $C_{21}H_{28}N_2O_3PS$ $[M+H]^+$: 419.1553; found: 419.1555.

4.3.5. General Procedure for the Michael Addition of Pyrrole to Cyano Functionalized Vinylphosphonates

To a solution of cyano functionalized vinylphosphonates (**234-246**) (0.384 mmol) in excess pyrrole (3.84 mmol) was added 10 mol % of Metal triflate (0.0384 mmol) and the reaction mixture was stirred for 48 h at room temperature (TLC monitoring). Metal triflate was removed from the reaction medium by subjecting the mixture to a short flash column chromatography (silica gel, EtOAc). The eluent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:2).

Diethyl 1-cyano-2-phenyl-2-(1*H*-pyrrol-2-yl)ethylphosphonate (304): Brown powder; yield: 119 mg (93 %); dr 56:44; R_f = 0.38 (1:1, EtOAc-hexane). IR (ATR): 3286, 2984, 2902, 2225, 1715, 1455, 1393, 1368, 1228, 1162, 1096, 1014, 792, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [1.14 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.24 (t, $^3J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3)*, 1.33 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 3.54 (dd, $^2J_{P,H}$ = 25.0 Hz, $^3J_{H,H}$ = 3.2 Hz, 1H, CH), 3.74-3.87 (m, 3H, OCH_2CH_3, CH

(minor)), [3.90-3.99 (m, 2H, OC*H*$_2$CH$_3$)], [4.00-4.11 (m, 2H, OC*H*$_2$CH$_3$)], 4.13-4.16 (m, 2H, OCH$_2$CH$_3$), 4.65-4.71 (m, 2H, C*H*)*, 6.01 (br s, 1H, *H*$_{pyrrole}$), 6.07 (t, $^3J_{H,H}$ = 2.4 Hz, 3H, *H*$_{pyrrole}$)*, [6.63 (br s, 1H, *H*$_{pyrrole}$)], 6.72 (br s, 1H, *H*$_{pyrrole}$), 7.26-7.36 (m, 6H, Ar*H*), 7.39 (d, $^3J_{H,H}$ = 7.5 Hz, 1H, Ar*H*), [7.46 (d, $^3J_{H,H}$ = 7.2 Hz, 1H, Ar*H*), [8.96 (br s, 1H, N*H*)], 9.65 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, CDCl$_3$): δ = [16.0 (d, $^3J_{P,C}$ = 6.4 Hz)], [16.1 (d, $^3J_{P,C}$ = 6.5 Hz)], 16.2 (d, $^3J_{P,C}$ = 2.1 Hz), 16.3 (d, $^3J_{P,C}$ = 2.2 Hz), [36.2 (d, $^1J_{P,C}$ = 140.6 Hz)], 37.2 (d, $^1J_{P,C}$ = 140.1 Hz), 42.0 (d, $^2J_{P,C}$ = 2.0 Hz), [42.5 (d, $^2J_{P,C}$ = 3.7 Hz)], 63.3 (d, $^2J_{P,C}$ = 7.0 Hz), [63.4 (d, $^2J_{P,C}$ = 7.0 Hz)], [64.1 (d, $^2J_{P,C}$ = 7.1 Hz)], 64.8 (d, $^2J_{P,C}$ = 6.9 Hz), [107.1], 108.1, [108.4], 109.2, [115.1 (d, $^2J_{P,C}$ = 8.9 Hz)], 115.2 (d, $^2J_{P,C}$ = 8.4 Hz), [117.9], 118.4, 127.6, 127.7, [128.0], [128.6], 128.8, [129.0], 129.8 (d, $^3J_{P,C}$ = 12.2 Hz), [130.4], [138.2 (d, $^3J_{P,C}$ = 5.4 Hz)], 140.3 (d, $^3J_{P,C}$ = 12.1 Hz). ^{31}P NMR (162 MHz, CDCl$_3$): δ = [16.8], 18.1. HRMS (ESI): *m/z* calcd for $C_{17}H_{22}N_2O_3P$ $[M+H]^+$: 333.1363; found: 333.1423.

Diethyl 1-cyano-2-(1*H*-pyrrol-2-yl)-2-(4-(trifluoromethyl)phenyl)ethylphosphonate (305): Brown powder; yield: 148 mg (96 %); dr 51:49; R_f = 0.26 (1:1, EtOAc-hexane). IR (ATR): 3275, 2992, 2889, 2235, 1617, 1329, 1247, 1172, 1129, 1006, 913, 774, 735 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = [1.15 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH$_2$C*H*$_3$), 1.24 (t, $^3J_{H,H}$ = 7.0 Hz, 6H, OCH$_2$C*H*$_3$)*, 1.31 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH$_2$C*H*$_3$), 3.60 (dd, $^2J_{P,H}$ = 24.8 Hz, $^3J_{H,H}$ = 3.8 Hz, 1H, C*H*), 3.87-4.16 (m, 9H, 4 OC*H*$_2$CH$_3$, C*H* (minor))*, 4.77-4.83 (m, 2H, C*H*)*, [6.07 (br s, 1H, *H*$_{pyrrole}$)], 6.14 (br s, 3H, *H*$_{pyrrole}$)*, 6.69 (br s, 1H, *H*$_{pyrrole}$), [6.72 (br s, 1H, *H*$_{pyrrole}$)], 7.53-7.63 (m, 10H, Ar*H*), [9.10 (br s, 1H, N*H*)], 9.72 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 16.0 (d, $^3J_{P,C}$ = 6.2 Hz), [16.1 (d, $^3J_{P,C}$ = 7.5 Hz)], [16.2], 16.3, [36.0 (d, $^1J_{P,C}$ = 140.5 Hz)], 37.0 (d, $^1J_{P,C}$ = 140.6 Hz), 42.1, [42.4], 63.8 (d, $^2J_{P,C}$ = 7.2 Hz), [64.1 (d, $^2J_{P,C}$ = 7.0 Hz)], 64.4 (d, $^2J_{P,C}$ = 7.3 Hz), [65.1 (d, $^2J_{P,C}$ = 6.9 Hz)], [107.3], 108.5, 108.6, [108.9], [115.3 (d, $^2J_{P,C}$ = 9.1 Hz)], 115.4 (d, $^2J_{P,C}$ = 8.5 Hz), [118.4], 118.6, 123.9 (q, $^1J_{F,C}$ = 270.5 Hz), [124.0 (q, $^1J_{F,C}$ = 270.5 Hz)], [125.6 (q, $^3J_{F,C}$ = 3.7 Hz)], 125.8 (q, $^3J_{F,C}$ = 3.7 Hz), 127.7 (d, $^3J_{P,C}$ = 3.8 Hz), 128.3, [129.2 (d, $^3J_{P,C}$ = 12.0 Hz)], [129.5], 130.0 (q, $^2J_{F,C}$ = 20.4 Hz), [130.3 (q, $^2J_{F,C}$ = 20.3 Hz)], [142.5 (d, $^3J_{P,C}$ = 4.8 Hz)], 144.1 (d, $^3J_{P,C}$ = 11.3 Hz). ^{31}P NMR (162 MHz, CDCl$_3$): δ = [16.2], 17.2. HRMS (ESI): *m/z* calcd for $C_{18}H_{21}F_3N_2O_3P$ $[M+H]^+$: 401.1236; found: 401.1308.

Diethyl 1-cyano-2-(1*H*-pyrrol-2-yl)-2-*p*-tolylethylphosphonate (306): Brown powder; yield: 92 mg (69 %); dr 57:43; R_f = 0.24 (1:1, EtOAc-hexane). IR (ATR): 3283, 2980, 2905, 2239, 1589, 1515, 1444, 1392, 1365, 1243, 1164, 1018, 979, 727 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = [1.17 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.26 (t, $^3J_{H,H}$ = 7.0 Hz, 6H, OCH_2CH_3)*, 1.35 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.34 (s, 6H, CH_3)*, 3.50 (dd, $^2J_{P,H}$ = 25.2 Hz, $^3J_{H,H}$ = 2.9 Hz, 1H, C*H*), 3.73-3.91 (m, 3H, OCH_2CH_3, C*H* (minor)), 3.93-4.24 (m, 6H, 3 OCH_2CH_3)*, 4.61-4.66 (m, 2H, C*H*)*, 5.96 (br s, 1H, $H_{pyrrole}$), 6.04-6.08 (m, 3H, $H_{pyrrole}$)*, [6.63 (br s, 1H, $H_{pyrrole}$)], 6.73 (br s, 1H, $H_{pyrrole}$), [7.14 (d, $^3J_{H,H}$ = 7.7 Hz, 2H, Ar*H*)], 7.15 (d, $^3J_{H,H}$ = 8.0 Hz, 2H, Ar*H*), 7.27 (d, $^3J_{H,H}$ = 8.0 Hz, 2H, Ar*H*), [7.33 (d, $^3J_{H,H}$ = 7.9 Hz, 1H, Ar*H*), [8.79 (br s, 1H, N*H*)], 9.58 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [16.0 (d, $^3J_{P,C}$ = 7.2 Hz)], 16.2 (d, $^3J_{P,C}$ = 6.0 Hz), 20.9, [21.0], [36.3 (d, $^1J_{P,C}$ = 140.4 Hz)], 37.3 (d, $^1J_{P,C}$ = 139.7 Hz), 41.7, [42.1], 63.2 (d, $^2J_{P,C}$ = 8.3 Hz), [63.3 (d, $^2J_{P,C}$ = 7.3 Hz)], [64.0 (d, $^2J_{P,C}$ = 7.0 Hz)], 64.7 (d, $^2J_{P,C}$ = 6.8 Hz), [107.0], 108.1, [108.4], 109.0, [115.1 (d, $^2J_{P,C}$ = 9.8 Hz)], 115.2 (d, $^2J_{P,C}$ = 9.8 Hz), [117.7], 118.1, 127.5, 128.6, [128.8], [129.2], 129.4, [129.8], 130.1 (d, $^3J_{P,C}$ = 11.9 Hz), [130.6], [135.3 (d, $^3J_{P,C}$ = 6.7 Hz)], 137.2, [137.3], 137.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [17.0], 18.1. HRMS (ESI): *m/z* calcd for $C_{18}H_{24}N_2O_3P$ $[M+H]^+$: 347.1519; found: 347.1586.

Diethyl 1-cyano-2-(4-methoxyphenyl)-2-(1*H*-pyrrol-2-yl)ethylphosphonate (307): Brown powder; yield: 21 mg (15 %); dr 55:45; R_f = 0.17 (1:1, EtOAc-hexane). IR (ATR): 3285, 2981, 2903, 2227, 1584, 1518, 1436, 1341, 1246, 1168, 1013, 980, 729 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = [1.20 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.29 (t, $^3J_{H,H}$ = 7.1 Hz, 6H, OCH_2CH_3)*, 1.43 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 3.47-3.54 (m, 2H, C*H*)*, 3.81 (s, 3H, OCH_3), [3.90 (s, 3H, OCH_3)], 3.98-4.13 (m, 4H, 2 OCH_2CH_3)*, 4.14-4.27 (m, 4H, 2 OCH_2CH_3)*, 4.63-4.68 (m, 2H, C*H*)*, 5.96 (br s, 1H, $H_{pyrrole}$), 6.08-6.11 (m, 3H, $H_{pyrrole}$)*, [6.67 (br s, 1H, $H_{pyrrole}$)], 6.77 (br s, 1H, $H_{pyrrole}$), [6.88 (d, $^3J_{H,H}$ = 6.7 Hz, 2H, Ar*H*)], 6.90 (d, $^3J_{H,H}$ = 6.6 Hz, 2H, Ar*H*), 7.33 (d, $^3J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), [7.38 (d, $^3J_{H,H}$ = 8.7 Hz, 1H, Ar*H*), [8.59 (br s, 1H, N*H*)], 9.60 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [16.1 (d, $^3J_{P,C}$ = 6.0 Hz)], 16.2 (d, $^3J_{P,C}$ = 6.3 Hz), [36.3 (d, $^1J_{P,C}$ = 140.5 Hz)], 37.4 (d, $^1J_{P,C}$ = 139.6 Hz), 41.3 (d, $^2J_{P,C}$ = 2.0 Hz), [41.6 (d, $^2J_{P,C}$ = 1.7 Hz)], 55.1, [55.4], 63.2 (d, $^2J_{P,C}$ = 5.7 Hz), [63.3 (d, $^2J_{P,C}$ = 7.0 Hz)], [64.1 (d, $^2J_{P,C}$ = 7.2 Hz)], 64.8 (d, $^2J_{P,C}$ = 6.9 Hz), [106.8], 108.1, [108.4], 109.0, [113.9], 114.1, 115.3 (d, $^2J_{P,C}$ = 8.2

Hz), [115.8 (d, $^{2}J_{P,C}$ = 10.3 Hz)], [117.8], 118.3, 128.7, [130.1], 132.4 (d, $^{3}J_{P,C}$ = 12.3 Hz)*, 133.9*, 159.0, [159.3]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = [16.9], 18.2. HRMS (ESI): *m/z* calcd for $C_{18}H_{24}N_2O_4P$ $[M+H]^+$: 363.1468; found: 363.1534.

Diethyl 1-cyano-2-(4-fluorophenyl)-2-(1*H*-pyrrol-2-yl)ethylphosphonate (308): Brown powder; yield: 98 mg (73 %); dr 50:50; R_f = 0.20 (1:1, EtOAc-hexane). IR (ATR): 3279, 2972, 2913, 2239, 1609, 1515, 1408, 1223, 1156, 1014, 912, 849, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.24-1.28 (m, 6H, OCH_2CH_3), 1.35 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 3.50 (dd, $^{2}J_{P,H}$ = 25.0 Hz, $^{3}J_{H,H}$ = 3.2 Hz, 1H, C*H*), 3.77-3.90 (m, 3H, OCH_2CH_3, C*H*), 3.96-4.18 (m, 6H, OCH_2CH_3), 4.66-4.70 (m, 2H, C*H*), 5.99 (br s, 1H, $H_{pyrrole}$), 6.06-6.09 (m, 3H, $H_{pyrrole}$), 6.64 (br s, 1H, $H_{pyrrole}$), 6.73 (br s, 1H, $H_{pyrrole}$), 7.00-7.06 (m, 4H, Ar*H*), 7.35-7.45 (m, 4H, Ar*H*), 8.96 (br s, 1H, N*H*), 9.68 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.1, 16.2 (d, $^{3}J_{P,C}$ = 3.2 Hz), 16.3 (d, $^{3}J_{P,C}$ = 2.6 Hz), 16.3 (d, $^{3}J_{P,C}$ = 2.7 Hz), 36.4 (d, $^{1}J_{P,C}$ = 140.3 Hz), 37.4 (d, $^{1}J_{P,C}$ = 140.1 Hz), 41.6, 41.9, 63.4 (d, $^{2}J_{P,C}$ = 6.9 Hz), 63.7 (d, $^{2}J_{P,C}$ = 6.9 Hz), 64.2 (d, $^{2}J_{P,C}$ = 7.1 Hz), 64.9 (d, $^{2}J_{P,C}$ = 6.6 Hz), 107.2, 108.4, 108.6, 109.0, 115.1 (d, $^{2}J_{P,C}$ = 9.0 Hz), 115.2 (d, $^{2}J_{P,C}$ = 8.3 Hz), 115.5 (d, $^{2}J_{F,C}$ = 18.9 Hz), 115.7 (d, $^{2}J_{F,C}$ = 18.9 Hz), 118.1, 118.4, 128.2 (d, $^{3}J_{P,C}$ = 2.6 Hz), 129.5 (d, $^{3}J_{F,C}$ = 8.0 Hz), 129.8 (d, $^{3}J_{P,C}$ = 12.1 Hz), 130.8 (d, $^{3}J_{F,C}$ = 8.0 Hz), 134.3, 136.2 (d, $^{3}J_{P,C}$ = 12.0 Hz), 162.2 (d, $^{1}J_{F,C}$ = 245.9 Hz), 162.4 (q, $^{1}J_{F,C}$ = 246.2 Hz)]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 16.7, 17.8. HRMS (ESI): *m/z* calcd for $C_{17}H_{21}FN_2O_3P$ $[M+H]^+$: 351.1268; found: 351.1336.

Diethyl 2-(4-chlorophenyl)-1-cyano-2-(1*H*-pyrrol-2-yl)ethylphosphonate (309): Brown powder; yield: 113 mg (80 %); dr 53:47; R_f = 0.23 (1:1, EtOAc-hexane). IR (ATR): 3279, 2988, 2905, 2243, 1589, 1495, 1400, 1239, 1101, 1018, 979, 782, 723 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [1.20 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3)], 1.24-1.28 (m, 6H, OCH_2CH_3)*, 1.35 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 3.49 (dd, $^{2}J_{P,H}$ = 25.0 Hz, $^{3}J_{H,H}$ = 3.1 Hz, 1H, C*H*), 3.75-4.19 (m, 9H, 4 OCH_2CH_3, C*H*)*, 4.64-4.69 (m, 2H, C*H*)*, 5.98 (br s, 1H, $H_{pyrrole}$), 6.06-6.09 (m, 3H, $H_{pyrrole}$)*, [6.65 (br s, 1H, $H_{pyrrole}$)], 6.74 (br s, 1H, $H_{pyrrole}$), 7.30-7.40 (m, 8H, Ar*H*)*, [8.93 (br s, 1H, N*H*)], 9.65 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [16.1], 16.2 (d, $^{3}J_{P,C}$ = 3.3 Hz), 16.3 (d, $^{3}J_{P,C}$ = 2.5 Hz), [16.3 (d, $^{3}J_{P,C}$ = 2.6 Hz)], [36.2 (d, $^{1}J_{P,C}$ = 140.0 Hz)], 37.2 (d, $^{1}J_{P,C}$ = 140.3 Hz), 41.7, [42.0], 63.5 (d, $^{2}J_{P,C}$ = 7.0 Hz), [63.7 (d, $^{2}J_{P,C}$ = 7.2

Hz)], [64.3 (d, $^{2}J_{P,C}$ = 7.5 Hz)], 65.0 (d, $^{2}J_{P,C}$ = 6.9 Hz)], [107.3], 108.5, 108.6, [109.1], [115.0 (d, $^{2}J_{P,C}$ = 9.2 Hz)], 115.2 (d, $^{2}J_{P,C}$ = 8.6 Hz), [118.2], 118.5, 127.8 (d, $^{3}J_{P,C}$ = 2.8 Hz), [128.8], [129.0], 129.2, [129.5 (d, $^{3}J_{P,C}$ =11.9 Hz)], 130.4, 133.8, [134.0], [137.0 (d, $^{3}J_{P,C}$ = 5.6 Hz)], 138.8 (d, $^{3}J_{P,C}$ = 12.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = [16.3], 17.3. HRMS (ESI): *m/z* calcd for $C_{17}H_{21}ClN_2O_3P$ $[M+H]^+$: 367.0973; found: 367.1042.

Diethyl 2-(4-bromophenyl)-1-cyano-2-(1*H*-pyrrol-2-yl)ethylphosphonate (310): Brown powder; yield: 133 mg (84 %); dr 59:41; R_f = 0.23 (1:1, EtOAc-hexane). IR (ATR): 3256, 2985, 2903, 2236, 1491, 1259, 1160, 1022, 908, 778, 758, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), [1.26 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3)], 1.27 (t, $^{3}J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), [1.36 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], [3.47 (dd, $^{2}J_{P,H}$ = 25.2 Hz, $^{3}J_{H,H}$ = 2.8 Hz, 1H, C*H*)], 3.72 (dd, $^{2}J_{P,H}$ = 24.0 Hz, $^{3}J_{H,H}$ = 6.0 Hz, 1H, C*H*), 3.84-4.20 (m, 8H, 4 OCH_2CH_3)*, 4.62-4.67 (m, 2H, C*H*)*, [5.93 (br s, 1H, $H_{pyrrole}$)], 6.05 (br s, 1H, $H_{pyrrole}$), 6.07-6.10 (m, 2H, $H_{pyrrole}$)*, 6.66 (dt, $^{3}J_{H,H}$ = 2.6 Hz, $^{4}J_{H,H}$ = 1.4 Hz, 1H, $H_{pyrrole}$), [6.66 (dt, $^{3}J_{H,H}$ = 2.6 Hz, $^{4}J_{H,H}$ = 1.5 Hz, 1H, $H_{pyrrole}$)], 7.27-7.33 (m, 4H, Ar*H*)*, 7.47-7.50 (m, 4H, Ar*H*)*, 8.73 (br s, 1H, N*H*), [9.65 (br s, 1H, N*H*)]. ^{13}C NMR (100 MHz, $CDCl_3$): δ = [16.0], 16.1 (d, $^{3}J_{P,C}$ = 8.3 Hz), 16.2, [16.3], 36.0 (d, $^{1}J_{P,C}$ = 140.8 Hz), [37.0 (d, $^{1}J_{P,C}$ = 140.1 Hz)], [41.6], 42.0, [63.4 (d, $^{2}J_{P,C}$ = 7.2 Hz)], 63.5 (d, $^{2}J_{P,C}$ = 6.3 Hz), 64.3 (d, $^{2}J_{P,C}$ = 7.0 Hz), [64.9 (d, $^{2}J_{P,C}$ = 6.4 Hz)], 107.3, [108.3], 108.6, [109.2], 114.7 (d, $^{2}J_{P,C}$ = 7.1 Hz), [115.0 (d, $^{2}J_{P,C}$ = 8.0 Hz)], 118.2, [118.6], [121.8], 122.1, [127.7 (d, $^{3}J_{P,C}$ = 2.1 Hz)], 129.2 (d, $^{3}J_{P,C}$ = 11.8 Hz), [129.4], 130.6, 131.7, [131.9], 137.2, [137.3]. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 16.6, [17.8]. HRMS (ESI): *m/z* calcd for $C_{17}H_{21}BrN_2O_3P$ $[M+H]^+$: 411.0468; found: 411.0543.

Diethyl 1-cyano-2-(4-cyanophenyl)-2-(1*H*-pyrrol-2-yl)ethylphosphonate (311): Brown powder; yield: 132 mg (96 %); dr 55:45; R_f = 0.08 (1:1, EtOAc-hexane). IR (ATR): 3275, 2980, 2909, 2866, 2228, 1601, 1503, 1440, 1392, 1247, 1160, 1097, 1014, 979, 782, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = [1.21 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 1.26 (t, $^{3}J_{H,H}$ = 7.2 Hz, 6H, 2 OCH_2CH_3)*, 1.34 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 3.56 (dd, $^{2}J_{P,H}$ = 24.8 Hz, $^{3}J_{H,H}$ = 3.2 Hz, 1H, C*H*), [3.84 (dd, $^{2}J_{P,H}$ = 23.8 Hz, $^{3}J_{H,H}$ = 6.2 Hz, 1H, C*H*)], 3.91-4.18 (m, 8H, 4 OCH_2CH_3)*, 4.73-4.79 (m, 2H, C*H*)*, 6.05 (br s, 2H, $H_{pyrrole}$)*, 6.09-6.12 (m, 2H, $H_{pyrrole}$)*, [6.66 (br s, 1H,

H$_{pyrrole}$)], 6.75 (br s, 1H, *H*$_{pyrrole}$), 7.53 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H, Ar*H*), [7.56 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2H, Ar*H*)], 7.63 (d, $^{3}J_{H,H}$ = 8.1 Hz, 4H, Ar*H*)*, [9.16 (br s, 1H, N*H*)], 9.69 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [16.1 (d, $^{3}J_{P,C}$ = 6.1 Hz)], 16.2 (d, $^{3}J_{P,C}$ = 4.4 Hz), [16.2], 16.3 (d, $^{3}J_{P,C}$ = 3.0 Hz), [36.0 (d, $^{1}J_{P,C}$ = 140.3 Hz)], 36.8 (d, $^{1}J_{P,C}$ = 140.7 Hz), 42.2 (d, $^{2}J_{P,C}$ = 1.6 Hz), [42.6 (d, $^{3}J_{P,C}$ = 1.9 Hz)], 63.6 (d, $^{2}J_{P,C}$ = 7.1 Hz), [63.9 (d, $^{2}J_{P,C}$ = 6.9 Hz)], [64.5 (d, $^{2}J_{P,C}$ = 7.4 Hz)], 65.0 (d, $^{2}J_{P,C}$ = 6.9 Hz), [107.6], 108.7, [108.8], 109.1, 111.9, [112.1], [114.8 (d, $^{2}J_{P,C}$ = 9.0 Hz)], 114.9 (d, $^{2}J_{P,C}$ = 8.6 Hz), 118.0, [118.1], [118.4], 118.6, 126.9 (d, $^{3}J_{P,C}$ = 3.1 Hz), [128.5 (d, $^{3}J_{P,C}$ = 10.7 Hz)], 128.7, [129.8], [132.3], 132.5, [143.9 (d, $^{3}J_{P,C}$ = 6.2 Hz)], 145.3 (d, $^{3}J_{P,C}$ = 11.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = [16.3], 16.9. HRMS (ESI): *m/z* calcd for $C_{18}H_{21}N_3O_3P$ $[M+H]^+$: 358.1315; found: 358.1385.

Diethyl 1-cyano-2-(4-nitrophenyl)-2-(1*H*-pyrrol-2-yl)ethylphosphonate (312): Brown powder; yield: 133 mg (92 %); dr 51:49; R_f = 0.11 (1:1, EtOAc-hexane). IR (ATR): 3265, 2982, 2911, 2863, 2225, 1603, 1505, 1437, 1395, 1240, 1162, 1095, 1012, 980, 785 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21-1.28 (m, 9H, 3 OCH_2CH_3), [1.35 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3)], 3.56 (dd, $^{2}J_{P,H}$ = 24.9 Hz, $^{3}J_{H,H}$ = 3.6 Hz, 1H, C*H*), 3.82-4.21 (m, 9H, 4 OCH_2CH_3, C*H* (minor))*, 4.80-4.85 (m, 2H, C*H*)*, [6.03 (br s, 1H, *H*$_{pyrrole}$)], 6.07 (br s, 1H, *H*$_{pyrrole}$), 6.10-6.13 (m, 2H, *H*$_{pyrrole}$), [6.67 (br s, 1H, *H*$_{pyrrole}$)], 6.76 (br s, 1H, *H*$_{pyrrole}$), [7.59 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, Ar*H*)], 7.61 (d, $^{3}J_{H,H}$ = 9.0 Hz, 2H, Ar*H*), 8.20 (d, $^{3}J_{H,H}$ = 8.8 Hz, 4H, Ar*H*)*, [9.18 (br s, 1H, N*H*)], 9.71 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = [16.0 (d, $^{3}J_{P,C}$ = 6.2 Hz)], 16.1 (d, $^{3}J_{P,C}$ = 7.2 Hz), [16.1], 16.2 (d, $^{3}J_{P,C}$ = 3.1 Hz), [35.8 (d, $^{1}J_{P,C}$ = 140.3 Hz)], 36.7 (d, $^{1}J_{P,C}$ = 140.6 Hz), 41.9 (d, $^{2}J_{P,C}$ = 1.3 Hz), [42.3 (d, $^{3}J_{P,C}$ = 1.8 Hz)], 63.6 (d, $^{2}J_{P,C}$ = 7.0 Hz), [63.9 (d, $^{2}J_{P,C}$ = 6.9 Hz)], [64.5 (d, $^{2}J_{P,C}$ = 7.2 Hz)], 65.0 (d, $^{2}J_{P,C}$ = 7.0 Hz), [107.5], 108.7, [108.8], 109.0, [114.7 (d, $^{2}J_{P,C}$ = 9.0 Hz)], 114.8 (d, $^{2}J_{P,C}$ = 8.7 Hz), [118.4], 118.6, [123.6], 123.8, 126.7 (d, $^{3}J_{P,C}$ = 3.4 Hz), [128.2 (d, $^{3}J_{P,C}$ = 10.3 Hz)], 128.7, [129.7], 145.7, [145.8], [147.1 (d, $^{3}J_{P,C}$ = 11.9 Hz)], 147.4 (d, $^{3}J_{P,C}$ = 12.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = [16.3], 16.9. HRMS (ESI): *m/z* calcd for $C_{17}H_{21}N_3O_5P$ $[M+H]^+$: 378.1213; found: 378.1286.

4.4. Reactions of Pyrrole Addition Products with NaH

4.4.1. General procedure for the intramolecular cyclization reaction of the ester functionalized pyrrole addition products

Pyrrole addition products (**262-276,279-280**) (0.074 mmol) was dissolved in THF (2 mL) and NaH (0.111 mmol) was added to the solution at 0 °C. The resultant mixture was stirred at room temperature for 2 h (TLC monitoring). After completion of the reaction pH 7 phosphate buffer (5 mL) was added to the reaction mixture and the product was extracted with EtOAc (3x10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1).

Dimethyl 3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (316): Light yellow powder; mp 71.2-72.1 °C; yield: 18 mg (81 %); R_f = 0.27 (1:1, EtOAc-hexane). IR (ATR): 2952, 2925, 2893, 2838, 1751, 1593, 1558, 1499, 1479, 1389, 1286, 1251, 1192, 1026, 888, 829, 810, 687, 601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.45 (dd, $^2J_{P,H}$ = 24.8 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, C*H*), 3.75 (d, $^3J_{P,H}$ = 10.5 Hz, 3H, OCH_3), 3.78 (d, $^3J_{P,H}$ = 10.4 Hz, 3H, OCH_3), 4.79 (dd, $^3J_{P,H}$ = 16.8 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, C*H*), 5.90-5.91 (m, 1H, $H_{pyrrole}$), 6.46 (t, $^3J_{H,H}$ = 3.2 Hz, 1H, $H_{pyrrole}$), 7.05 (d, $^3J_{H,H}$ = 3.2 Hz, 1H, $H_{pyrrole}$), 7.15-7.28 (m, 5H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.1 (d, $^2J_{P,C}$ = 1.4 Hz), 52.3 (d, $^2J_{P,C}$ = 6.7 Hz), 53.1 (d, $^2J_{P,C}$ = 6.5 Hz), 54.6 (d, $^1J_{P,C}$ = 137.5 Hz), 105.3, 110.8, 118.9, 126.2, 126.8, 128.0, 139.5 (d, $^3J_{P,C}$ = 7.0 Hz), 140.0 (d, $^3J_{P,C}$ = 4.0 Hz), 164.5 (d, $^2J_{P,C}$ = 3.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.4. HRMS (ESI): *m/z* calcd for $C_{15}H_{17}NO_4P$ $[M+H]^+$: 306.0890; found: 306.0885.

Dimethyl 3-oxo-1-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-pyrrolizin-2-yl-phosphonate (317): Brown viscous oil; yield: 27 mg (99 %); R_f = 0.18 (1:1, EtOAc-hexane). IR (ATR): 2955, 2915, 2848, 1736, 1465, 1336, 1235, 1171, 1120, 1064, 1040, 854, 762 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.48 (dd, $^2J_{P,H}$ = 24.8 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, C*H*), 3.85 (d, $^3J_{P,H}$ = 8.2 Hz, 3H, OCH_3), 3.87 (d, $^3J_{P,H}$ = 8.0 Hz, 3H, OCH_3), 4.93 (dd, $^3J_{P,H}$ = 16.7 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, C*H*), 6.0 (br s, 1H, $H_{pyrrole}$), 6.56 (t, $^3J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.15 (d, $^3J_{H,H}$ = 3.0 Hz, 1H, $H_{pyrrole}$),

7.38 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H, Ar*H*), 7.60 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.7, 53.4 (d, $^{2}J_{P,C}$ = 6.6 Hz), 54.2 (d, $^{2}J_{P,C}$ = 6.7 Hz), 55.1 (d, $^{1}J_{P,C}$ = 138.5 Hz), 106.6, 112.2, 120.1, 126.0 (q, $^{3}J_{F,C}$ = 3.6 Hz), 126.6 (q, $^{1}J_{F,C}$ = 270.0 Hz), 127.8, 130.1 (q, $^{2}J_{F,C}$ = 32.5 Hz), 139.5 (d, $^{3}J_{P,C}$ = 6.9 Hz), 144.9, 165.1 (d, $^{2}J_{P,C}$ = 3.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.7. HRMS (ESI): *m/z* calcd for $C_{16}H_{16}F_3NO_4P$ $[M+H]^+$: 374.0764; found: 374.0746.

Dimethyl 3-oxo-1-*p*-tolyl-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (318): Brown viscous oil; yield: 23 mg (98 %); R_f = 0.29 (1:1, EtOAc-hexane). IR (ATR): 3007, 2956, 2921, 2846, 1782, 1747, 1719, 1609, 1570, 1400, 1294, 1243, 1180, 1121, 1028, 908, 833, 750, 668 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 3H, C*H*$_3$), 3.43 (dd, $^{2}J_{P,H}$ = 24.8 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, C*H*), 3.82 (d, $^{3}J_{P,H}$ = 11.3 Hz, 3H, OC*H*$_3$), 3.85 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OC*H*$_3$), 4.79 (dd, $^{3}J_{P,H}$ = 16.6 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, C*H*), 5.92 (br s, 1H, $H_{pyrrole}$), 6.50 (t, $^{3}J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.08 (br s, 1H, $H_{pyrrole}$), 7.10 (s, 4H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 40.6 (d, $^{2}J_{P,C}$ = 1.5 Hz), 52.9 (d, $^{2}J_{P,C}$ = 6.6 Hz), 53.9 (d, $^{2}J_{P,C}$ = 6.5 Hz), 55.4 (d, $^{1}J_{P,C}$ = 137.4 Hz), 105.9, 111.5, 119.6, 127.0, 129.5, 137.0, 138.0 (d, $^{3}J_{P,C}$ = 4.3 Hz), 140.6 (d, $^{3}J_{P,C}$ = 7.1 Hz), 165.1 (d, $^{2}J_{P,C}$ = 3.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.7. HRMS (ESI): *m/z* calcd for $C_{16}H_{19}NO_4P$ $[M+H]^+$: 320.1046; found: 320.1043.

Dimethyl 1-(4-methoxyphenyl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (319): Brown viscous oil; yield: 24 mg (98 %); R_f = 0.13 (1:1, EtOAc-hexane). IR (ATR): 2959, 1749, 1720, 1607, 1514, 1465, 1401, 1294, 1252, 1181, 1030, 836, 760 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.47 (dd, $^{2}J_{P,H}$ = 24.9 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, C*H*), 3.79 (s, 3H, OC*H*$_3$), 3.82 (d, $^{3}J_{P,H}$ = 11.1 Hz, 3H, OC*H*$_3$), 3.85 (d, $^{3}J_{P,H}$ = 11.0 Hz, 3H, OC*H*$_3$), 4.82 (dd, $^{3}J_{P,H}$ = 16.4 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, C*H*), 5.96 (br s, 1H, $H_{pyrrole}$), 6.52 (t, $^{3}J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 6.85 (d, $^{3}J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), 7.11 (br s, 1H, $H_{pyrrole}$), 7.15 (d, $^{3}J_{H,H}$ = 8.7 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.2, 52.9 (d, $^{2}J_{P,C}$ = 6.8 Hz), 53.9 (d, $^{2}J_{P,C}$ = 6.6 Hz), 54.9, 55.5 (d, $^{1}J_{P,C}$ = 137.1 Hz), 105.9, 111.5, 114.2, 119.6, 128.2, 132.9 (d, $^{3}J_{P,C}$ = 4.2 Hz), 140.7 (d, $^{3}J_{P,C}$ = 7.1 Hz), 159.0, 165.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.2. HRMS (ESI): *m/z* calcd for $C_{16}H_{19}NO_5P$ $[M+H]^+$: 336.0995; found: 336.0983.

Dimethyl 1-(4-fluorophenyl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (320): Brown viscous oil; yield: 18 mg (74 %); R_f = 0.43 (EtOAc). IR (ATR): 2964, 2854, 1739, 1605, 1573, 1511, 1463, 1396, 1290, 1259, 1087, 908, 723 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.47 (dd, $^2J_{P,H}$ = 24.0 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, C*H*), 3.83 (d, $^3J_{P,H}$ = 8.0 Hz, 3H, OCH_3), 3.86 (d, $^3J_{P,H}$ = 8.0 Hz, 3H, OCH_3), 4.86 (dd, $^3J_{P,H}$ = 16.0 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, C*H*), 5.98 (br s, 1H, $H_{pyrrole}$), 6.54 (t, $^3J_{H,H}$ = 4.0 Hz, 1H, $H_{pyrrole}$), 6.99-7.04 (m, 2H, Ar*H*), 7.13 (d, $^3J_{H,H}$ = 4.0 Hz, 1H, $H_{pyrrole}$), 7.20-7.24 (m, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.4, 53.4 (d, $^2J_{P,C}$ = 6.7 Hz), 54.2 (d, $^2J_{P,C}$ = 6.6 Hz), 55.5 (d, $^1J_{P,C}$ = 138.1 Hz), 106.4, 112.0, 115.9 (d, $^2J_{F,C}$ = 21.6 Hz), 119.9, 129.0 (d, $^3J_{F,C}$ = 8.1 Hz), 136.7 (d, $^3J_{P,C}$ = 3.7 Hz), 140.3 (d, $^3J_{P,C}$ = 6.9 Hz), 162.2 (d, $^1J_{F,C}$ = 245.3 Hz), 165.3 (d, $^2J_{P,C}$ = 3.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.0. HRMS (ESI): *m/z* calcd for $C_{15}H_{16}FNO_4P$ $[M+H]^+$: 324.0801; found: 324.0776.

Dimethyl 1-(4-chlorophenyl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (321): Brown viscous oil; yield: 22 mg (88 %); R_f = 0.56 (EtOAc). IR (ATR): 2964, 2929, 2854, 1747, 1712, 1569, 1499, 1400, 1286, 1255, 1038, 900, 825, 743 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 3.45 (dd, $^2J_{P,H}$ = 25.2 Hz, $^3J_{H,H}$ = 4.4 Hz, 1H, C*H*), 3.83 (d, $^3J_{P,H}$ = 8.8 Hz, 3H, OCH_3), 3.86 (d, $^3J_{P,H}$ = 8.8 Hz, 3H, OCH_3), 4.84 (dd, $^3J_{P,H}$ = 16.4 Hz, $^3J_{H,H}$ = 4.4 Hz, 1H, C*H*), 5.97 (br s, 1H, $H_{pyrrole}$), 6.54 (t, $^3J_{H,H}$ = 3.2 Hz, 1H, $H_{pyrrole}$), 7.12 (d, $^3J_{H,H}$ = 2.8 Hz, 1H, $H_{pyrrole}$), 7.19 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.31 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.5, 53.4 (d, $^2J_{P,C}$ = 6.6 Hz), 54.2 (d, $^2J_{P,C}$ = 6.6 Hz), 55.3 (d, $^1J_{P,C}$ = 138.0 Hz), 106.5, 112.0, 120.0, 128.7, 129.2, 133.7, 139.4 (d, $^3J_{P,C}$ = 4.2 Hz), 139.9 (d, $^3J_{P,C}$ = 7.1 Hz), 165.2 (d, $^2J_{P,C}$ = 3.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.8. HRMS (ESI): *m/z* calcd for $C_{15}H_{16}ClNO_4P$ $[M+H]^+$: 340.0505; found: 340.0461.

Dimethyl 1-(4-bromophenyl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (322): Brown viscous oil; yield: 28 mg (99 %); R_f = 0.18 (1:1, EtOAc-hexane). IR (ATR): 2959, 2919, 2852, 1787, 1724, 1489, 1453, 1406, 1243, 1183, 1040, 1005, 834, 758 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.44 (dd, $^2J_{P,H}$ = 24.8 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, C*H*), 3.83 (d, $^3J_{P,H}$ = 9.7 Hz, 3H, OCH_3), 3.86 (d, $^3J_{P,H}$ = 9.7 Hz, 3H, OCH_3), 4.83 (dd, $^3J_{P,H}$ = 16.8 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, C*H*), 5.97 (br s, 1H, $H_{pyrrole}$), 6.54 (t, $^3J_{H,H}$ = 3.0 Hz, 1H, $H_{pyrrole}$), 7.12 (br s, 1H, $H_{pyrrole}$), 7.13 (d, $^3J_{H,H}$ =

8.2 Hz, 2H, Ar*H*), 7.45 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.4, 53.0 (d, $^{2}J_{P,C}$ = 6.7 Hz), 53.9 (d, $^{2}J_{P,C}$ = 6.5 Hz), 55.1 (d, $^{1}J_{P,C}$ = 137.8 Hz), 106.2, 111.9, 119.7, 121.7, 128.9, 132.0, 139.6 (d, $^{3}J_{P,C}$ = 7.0 Hz), 139.8 (d, $^{3}J_{P,C}$ = 4.2 Hz), 164.6 (d, $^{2}J_{P,C}$ = 3.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.8. HRMS (ESI): *m/z* calcd for $C_{15}H_{16}BrNO_4P$ $[M+H]^+$: 383.9995; found: 383.9973.

Dimethyl 1-(4-hydroxyphenyl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (323): Brown viscous oil; yield: 10 mg (44 %); R_f = 0.51 (EtOAc). IR(ATR): 3259, 2960, 2858, 1747, 1621, 1519, 1467, 1408, 1306, 1211, 1108, 912, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.48 (dd, $^{2}J_{P,H}$ = 25.0 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, C*H*), 3.85 (d, $^{3}J_{P,H}$ = 11.0 Hz, 3H, OCH_3), 3.89 (d, $^{3}J_{P,H}$ = 11.0 Hz, 3H, OCH_3), 4.79 (dd, $^{3}J_{P,H}$ = 16.6 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, C*H*), 5.97 (br s, 1H, $H_{pyrrole}$), 6.55 (br s, 1H, $H_{pyrrole}$), 6.78 (d, $^{3}J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.08 (d, $^{3}J_{H,H}$ = 8.8 Hz, 2H, Ar*H*), 7.12 (br s, 1H, $H_{pyrrole}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.5, 53.7 (d, $^{2}J_{P,C}$ = 6.7 Hz), 54.0 (d, $^{2}J_{P,C}$ = 6.9 Hz), 55.4 (d, $^{1}J_{P,C}$ = 138.3 Hz), 106.2, 111.8, 116.0, 120.0, 128.5, 132.3 (d, $^{3}J_{P,C}$ = 4.0 Hz), 140.9 (d, $^{3}J_{P,C}$ = 7.6 Hz), 155.9, 165.4 (d, $^{2}J_{P,C}$ = 3.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.2. HRMS (ESI): *m/z* calcd for $C_{15}H_{17}NO_5P$ $[M+H]^+$: 322.0844; found: 322.0816.

Dimethyl 1-(4-cyanophenyl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (324): Brown viscous oil; yield: 21 mg (87 %); R_f = 0.47 (EtOAc). IR (ATR): 2968, 2929, 2862, 2231, 1747, 1613, 1582, 1463, 1408, 1298, 1262, 1168, 1030, 908, 853, 723 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.45 (dd, $^{2}J_{P,H}$ = 24.8 Hz, $^{3}J_{H,H}$ = 4.1 Hz, 1H, C*H*), 3.85 (d, $^{3}J_{P,H}$ = 4.9 Hz, 3H, OCH_3), 3.87 (d, $^{3}J_{P,H}$ = 4.2 Hz, 3H, OCH_3), 4.92 (dd, $^{3}J_{P,H}$ = 16.7 Hz, $^{3}J_{H,H}$ = 4.1 Hz, 1H, C*H*), 6.00 (br s, 1H, $H_{pyrrole}$), 6.56 (t, $^{3}J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.14 (d, $^{3}J_{H,H}$ = 3.0 Hz, 1H, $H_{pyrrole}$), 7.39 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H, Ar*H*), 7.64 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.9 (d, $^{2}J_{P,C}$ = 1.3 Hz), 53.5 (d, $^{2}J_{P,C}$ = 6.8 Hz), 54.3 (d, $^{2}J_{P,C}$ = 6.5 Hz), 55.0 (d, $^{1}J_{P,C}$ = 138.8 Hz), 106.9, 111.9, 112.4, 118.4, 120.1, 128.2, 132.9, 138.8 (d, $^{3}J_{P,C}$ = 6.8 Hz), 146.1 (d, $^{3}J_{P,C}$ = 4.3 Hz), 164.7 (d, $^{2}J_{P,C}$ = 4.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.2. HRMS (ESI): *m/z* calcd for $C_{16}H_{16}N_2O_4P$ $[M+H]^+$: 331.0847; found: 331.0819.

Dimethyl 1-(4-nitrophenyl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (325): Brown viscous oil; yield: 12 mg (45 %); R_f = 0.46 (EtOAc). IR (ATR): 2960, 2901, 2846, 1751, 1515, 1463, 1412, 1337, 1294, 1259, 1034, 904, 731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.39 (dd, $^2J_{P,H}$ = 24.8 Hz, $^3J_{H,H}$ = 4.2 Hz, 1H, C*H*), 3.74 (d, $^3J_{P,H}$ = 11.4 Hz, 3H, OCH_3), 3.79 (d, $^3J_{P,H}$ = 11.2 Hz, 3H, OCH_3), 4.90 (dd, $^3J_{P,H}$ = 16.6 Hz, $^3J_{H,H}$ = 4.2 Hz, 1H, C*H*), 5.95 (br s, 1H, $H_{pyrrole}$), 6.49-6.51 (m,1H, $H_{pyrrole}$), 7.09 (d, $^3J_{H,H}$ = 3.2 Hz, 1H, $H_{pyrrole}$), 7.38 (d, $^3J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), 8.13 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.7 (d, $^2J_{P,C}$ = 1.4 Hz), 53.5 (d, $^2J_{P,C}$ = 6.6 Hz), 54.3 (d, $^2J_{P,C}$ = 6.7 Hz), 54.9 (d, $^1J_{P,C}$ = 138.9 Hz), 106.9, 112.5, 120.1, 124.3, 128.4, 138.8 (d, $^3J_{P,C}$ = 6.7 Hz), 147.5, 148.0 (d, $^3J_{P,C}$ = 4.0 Hz), 164.7 (d, $^2J_{P,C}$ = 3.8 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.4. HRMS (ESI): *m/z* calcd for $C_{15}H_{16}N_2O_6P$ $[M+H]^+$: 351.0746; found: 351.0725.

Dimethyl 3-oxo-1-(1H-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (326): Brown viscous oil; yield: 22 mg (99 %); R_f = 0.51 (EtOAc). IR (ATR): 2956, 2913, 2862, 1751, 1463, 1412, 1365, 1302, 1259, 1026, 904, 786, 731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.57 (dd, $^2J_{P,H}$ = 24.0 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, C*H*), 3.88 (d, $^3J_{P,H}$ = 12.0 Hz, 3H, OCH_3), 3.95 (d, $^3J_{P,H}$ = 11.8 Hz, 3H, OCH_3), 4.94 (dd, $^3J_{P,H}$ = 15.9 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, C*H*), 6.09-6.13 (m, 2H, 2 $H_{pyrrole}$), 6.26-6.28 (m, 1H, $H_{pyrrole}$), 6.57 (t, $^3J_{H,H}$ = 3.7 Hz, 1H, $H_{pyrrole}$), 6.79-6.81 (m, 1H, $H_{pyrrole}$), 7.11 (d, $^3J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), 9.38 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.4, 53.2 (d, $^1J_{P,C}$ = 141.8 Hz), 53.9 (d, $^2J_{P,C}$ = 7.5 Hz), 54.1 (d, $^2J_{P,C}$ = 6.3 Hz), 105.3, 106.9, 107.8, 112.0, 118.9, 119.7, 129.0, 137.6 (d, $^3J_{P,C}$ = 9.3 Hz), 164.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 23.7. HRMS (ESI): *m/z* calcd for $C_{13}H_{16}N_2O_4P$ $[M+H]^+$: 295.0847; found: 295.0817.

Dimethyl 1-(furan-2-yl)-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (327): Brown viscous oil; yield: 20 mg (92 %); R_f = 0.53 (EtOAc). IR (ATR): 3122, 2964, 2850, 1743, 1574, 1467, 1400, 1290, 1251, 1030, 880, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.76 (dd, $^2J_{P,H}$ = 24.4 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, C*H*), 3.84 (d, $^3J_{P,H}$ = 11.2 Hz, 3H, OCH_3), 3.88 (d, $^3J_{P,H}$ = 11.0 Hz, 3H, OCH_3), 4.92 (dd, $^3J_{P,H}$ = 16.2 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, C*H*), 6.08 (br s, 1H, $H_{pyrrole}$), 6.21 (d, $^3J_{H,H}$ = 3.2 Hz, 1H, H_{furan}), 6.31-6.33 (m, 1H, $H_{pyrrole}$), 6.50 (t, $^3J_{H,H}$ = 3.2 Hz, 1H, H_{furan}), 7.09 (d, $^3J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.36 (br s, 1H, H_{furan}). ^{13}C NMR (100 MHz, $CDCl_3$): δ =

34.9, 51.7 (d, $^{1}J_{P,C}$ = 139.1 Hz), 53.5 (d, $^{2}J_{P,C}$ = 6.8 Hz), 54.2 (d, $^{2}J_{P,C}$ = 6.5 Hz), 106.2, 106.9, 110.5, 112.1, 119.7, 137.7 (d, $^{3}J_{P,C}$ = 7.1 Hz), 142.7, 151.9 (d, $^{3}J_{P,C}$ = 4.9 Hz), 165.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.6. HRMS (ESI): *m/z* calcd for $C_{13}H_{15}NO_5P$ $[M+H]^+$: 296.0687; found: 296.0728.

Dimethyl 3-oxo-1-(thiophen-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (328): Brown viscous oil; yield: 22 mg (96 %); R_f = 0.42 (EtOAc). IR (ATR): 3102, 2960, 2893, 1751, 1570, 1459, 1396, 1286, 1251, 1184, 1022, 880, 833, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.61 (dd, $^{2}J_{P,H}$ = 24.7 Hz, $^{3}J_{H,H}$ = 4.2 Hz, 1H, C*H*), 3.86 (d, $^{3}J_{P,H}$ = 11.2 Hz, 3H, OCH_3), 3.89 (d, $^{3}J_{P,H}$ = 11.0 Hz, 3H, OCH_3), 5.14 (dd, $^{3}J_{P,H}$ = 16.0 Hz, $^{3}J_{H,H}$ = 4.2 Hz, 1H, C*H*), 6.13 (br s, 1H, $H_{pyrrole}$), 6.53 (d, $^{3}J_{H,H}$ = 3.2 Hz, 1H, $H_{pyrrole}$), 6.94-6.97 (m, 1H, $H_{thiophene}$), 7.02 (d, $^{3}J_{H,H}$ = 3.4 Hz, 1H, $H_{thiophene}$), 7.11 (d, $^{3}J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.22 (d, $^{3}J_{H,H}$ = 5.1 Hz, 1H, $H_{thiophene}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.4, 53.4 (d, $^{2}J_{P,C}$ = 6.7 Hz), 54.2 (d, $^{2}J_{P,C}$ = 6.5 Hz), 55.7 (d, $^{1}J_{P,C}$ = 138.7 Hz), 106.7, 112.1, 119.8, 125.0, 125.6, 127.1, 139.7 (d, $^{3}J_{P,C}$ = 7.2 Hz), 143.6 (d, $^{3}J_{P,C}$ = 4.4 Hz), 164.9 (d, $^{2}J_{P,C}$ = 3.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.6. HRMS (ESI): *m/z* calcd for $C_{13}H_{14}NNaO_4PS$ $[M+Na]^+$: 334.0279; found: 334.0316.

Dimethyl 1-cyclohexyl-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (329): Yellow viscous oil; yield: 23 mg (99 %); R_f = 0.26 (1:1, EtOAc-hexane). IR (ATR): 3005, 2921, 2854, 1743, 1563, 1466, 1451, 1407, 1292, 1251, 1186, 1068, 1039, 827, 791 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09-1.25 (m, 4H, CH_2), 1.55-1.79 (m, 7H, CH_2, C*H*), 3.31 (dd, $^{2}J_{P,H}$ = 25.5 Hz, $^{3}J_{H,H}$ = 2.8 Hz, 1H, C*H*), 3.49 (br d, $^{3}J_{P,H}$ = 16.4 Hz, 1H, C*H*), 3.77 (d, $^{3}J_{P,H}$ = 10.9 Hz, 3H, OCH_3), 3.85 (d, $^{3}J_{P,H}$ = 11.1 Hz, 3H, OCH_3), 5.97 (d, $^{3}J_{H,H}$ = 3.0 Hz, 1H, $H_{pyrrole}$), 6.42 (t, $^{3}J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.26 (d, $^{3}J_{H,H}$ = 2.3 Hz, 1H, $H_{pyrrole}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 266.1, 28.4, 30.3, 41.4 (d, $^{3}J_{P,C}$ = 2.1 Hz), 42.2 (d, $^{2}J_{P,C}$ = 5.6 Hz), 49.5 (d, $^{1}J_{P,C}$ = 136.2 Hz), 53.0 (d, $^{2}J_{P,C}$ = 6.6 Hz), 53.7 (d, $^{2}J_{P,C}$ = 6.6 Hz), 105.8, 111.2, 118.9, 139.8 (d, $^{3}J_{P,C}$ = 4.7 Hz), 165.6 (d, $^{2}J_{P,C}$ = 4.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.3. HRMS (ESI): *m/z* calcd for $C_{15}H_{22}NO_4P$ $[M+H]^+$: 312.1359; found: 312.1407.

Dimethyl 1-isopropyl-3-oxo-2,3-dihydro-1H-pyrrolizin-2-ylphosphonate (330): Yellow viscous oil; yield: 13 mg (65 %); R_f = 0.31 (2:1, EtOAc-hexane). IR (ATR): 3003, 2923, 2857, 1740, 1569, 1468, 1455, 1408, 1296, 1250, 1185, 1067, 1036, 829, 793 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3), 1.00 (d, $^3J_{P,H}$ = 6.8 Hz, 3H, CH_3), 1.93-2.04 (m, 1H, C*H*), 3.30 (dd, $^2J_{P,H}$ = 25.6 Hz, $^3J_{H,H}$ = 2.9 Hz, 1H, C*H*), 3.58 (br d, $^3J_{P,H}$ = 17.1 Hz, 1H, C*H*), 3.80 (d, $^3J_{P,H}$ = 10.9 Hz, 3H, OCH_3), 3.85 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3), 6.02 (d, $^3J_{H,H}$ = 3.0 Hz, 1H, $H_{pyrrole}$), 6.46 (t, $^3J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.02 (d, $^3J_{H,H}$ = 3.0 Hz, 1H, $H_{pyrrole}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9, 19.8, 32.4 (d, $^3J_{P,C}$ = 5.5 Hz), 42.2 (d, $^2J_{P,C}$ = 1.9 Hz), 50.0 (d, $^1J_{P,C}$ = 136.7 Hz), 53.3 (d, $^2J_{P,C}$ = 6.8 Hz), 54.0 (d, $^2J_{P,C}$ = 6.5 Hz), 106.0, 111.5, 119.2, 140.0 (d, $^3J_{P,C}$ = 4.9 Hz), 166.2 (d, $^2J_{P,C}$ = 5.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 24.0. HRMS (ESI): *m/z* calcd for $C_{12}H_{18}NO_4P$ $[M+H]^+$: 272.1046; found: 272.1054.

4.4.2. General procedure for the synthesis of dimethyl 1-(4-bromophenyl)-2-methyl-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (331)

Methyl 3-(4-bromophenyl)-2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)propanoate (**268**) (0.074 mmol) was dissolved in THF (2 mL) and MeI (0.081 mmol) was added. Then NaH (0.111 mmol) was added to this solution at 0 °C. The resultant mixture was stirred at room temperature for 1 h (TLC monitoring). After completion of the reaction pH 7 phosphate buffer (5 mL) was added to the reaction mixture and the product was extracted with EtOAc (3x10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1).

Dimethyl 1-(4-bromophenyl)-2-methyl-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (331): Light yellow viscous oil; yield: 14 mg (60 %); R_f = 0.57 (2:1, EtOAc-hexane). IR (ATR): 2954, 2923, 2890, 1752, 1595, 1557, 1493, 1477, 1387, 1285, 1190, 1023, 889, 687, cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.81 (d, $^3J_{P,H}$ = 15.6 Hz, 3H, CH_3), 3.25 (d, $^3J_{P,H}$ = 11.1 Hz, 3H, OCH_3), 3.63 (d, $^3J_{P,H}$ = 9.0 Hz, 3H, OCH_3), 4.37 (d, $^3J_{P,H}$ = 17.1 Hz, 1H, C*H*), 5.97 (br s, 1H, $H_{pyrrole}$), 6.55 (t, $^3J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.14 (d, $^3J_{H,H}$ = 3.1 Hz, 1H, $H_{pyrrole}$), 7.33 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.45 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ =

20.2 (d, $^{3}J_{P,C}$ = 4.9 Hz), 50.7, 52.5 (d, $^{2}J_{P,C}$ = 7.2 Hz), 54.1 (d, $^{2}J_{P,C}$ = 7.0 Hz), 58.6 (d, $^{1}J_{P,C}$ = 137.7 Hz), 106.0, 112.2, 119.5, 122.0, 129.6, 131.8, 135.4 (d, $^{3}J_{P,C}$ = 5.4 Hz), 138.5 (d, $^{3}J_{P,C}$ = 2.0 Hz), 169.5 (d, $^{2}J_{P,C}$ = 3.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ = 22.6. HRMS (ESI): *m/z* calcd for $C_{16}H_{18}BrNO_4P$ $[M+H]^+$: 398.0151; found: 398.0154.

4.4.3. General procedure for the reaction of ketone functionalized pyrrole addition products with NaH

Ketone functionalized pyrrole addition products (**281-292**) (0.074 mmol) was dissolved in THF (2 mL) and NaH (0.111 mmol) was added to this solution at 0 °C. The resultant mixture was stirred at room temperature for 2 h (TLC monitoring). After completion of the reaction pH 7 phosphate buffer (5 mL) was added to the reaction mixture and the product was extracted with EtOAc (3x10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1).

Diethyl 2-(3-oxo-1-phenylpentyl)-1*H*-pyrrol-1-ylphosphonate (332): Light brown viscous oil; yield: 19 mg (70 %); R_f = 0.80 (1:1, EtOAc-hexane). IR (ATR): 3257, 2965, 2927, 1711, 1453, 1393, 1260, 1234, 1101, 1015, 964, 795, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, $^{3}J_{H,H}$ = 7.8 Hz, 3H, OCH_2CH_3), 0.97 (t, $^{3}J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.29 (t, $^{3}J_{H,H}$ = 7.9 Hz, 3H, OCH_2CH_3), 2.29 (dq, $^{2}J_{H,H}$ = 17.6 Hz, $^{3}J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.37 (dq, $^{2}J_{H,H}$ = 17.6 Hz, $^{3}J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.85 (dd, $^{2}J_{H,H}$ = 16.5 Hz, $^{3}J_{H,H}$ = 6.6 Hz, 1H, CH_2), 3.10 (dd, $^{2}J_{H,H}$ = 16.5 Hz, $^{3}J_{H,H}$ = 8.7 Hz, 1H, CH_2), 3.30-3.40 (m, 1H, OCH_2CH_3), 3.83-4.06 (m, 3H, OCH_2CH_3), 5.00 (t, $^{3}J_{H,H}$ = 8.3 Hz, 1H, C*H*), 6.19-6.22 (m, 1H, $H_{pyrrole}$), 7.04-7.06 (m, 2H, $H_{pyrrole}$), 7.13-7.24 (m, 5H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.5, 15.5 (d, $^{3}J_{P,C}$ = 7.0 Hz), 15.8 (d, $^{3}J_{P,C}$ = 7.2 Hz), 36.3, 38.6, 50.4, 63.4 (d, $^{2}J_{P,C}$ = 4.7 Hz), 63.7 (d, $^{2}J_{P,C}$ = 4.8 Hz), 110.5 (d, $^{3}J_{P,C}$ = 10.5 Hz), 111.3 (d, $^{3}J_{P,C}$ = 11.0 Hz), 124.8 (d, $^{2}J_{P,C}$ = 5.7 Hz), 126.2, 127.7, 128.2, 137.1 (d, $^{2}J_{P,C}$ = 5.7 Hz), 143.5, 208.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -3.3. HRMS (ESI): *m/z* calcd for $C_{19}H_{27}NO_4P$ $[M+H]^+$: 364.1672; found: 364.1664.

Diethyl 2-(3-oxo-1-(4-(trifluoromethyl)phenyl)pentyl)-1*H*-pyrrol-1-ylphosphonate (345): Light brown viscous oil; yield: 11 mg (35 %); R_f = 0.67 (1:1, EtOAc-hexane). IR (ATR): 3254, 2921, 1708, 1419, 1324, 1215, 1167, 1127, 1068, 1017, 752 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 0.99 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.26 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.30 (dq, $^2J_{H,H}$ = 17.6 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.40 (dq, $^2J_{H,H}$ = 17.6 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.84 (dd, $^2J_{H,H}$ = 16.8 Hz, $^3J_{H,H}$ = 8.4 Hz, 1H, CH_2), 3.13 (dd, $^2J_{H,H}$ = 16.8 Hz, $^3J_{H,H}$ = 8.4 Hz, 1H, CH_2), 3.46-3.56 (m, 1H, OCH_2CH_3), 3.87-4.00 (m, 3H, OCH_2CH_3), 5.13 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, C*H*), 6.19-6.22 (m, 2H, $H_{pyrrole}$), 7.01 (br s, 1H, $H_{pyrrole}$), 7.29 (d, $^3J_{H,H}$ = 8.1 Hz, 2H, Ar*H*), 7.49 (d, $^3J_{H,H}$ = 8.2 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.5 (d, $^3J_{P,C}$ = 7.0 Hz), 15.8 (d, $^3J_{P,C}$ = 7.2 Hz), 36.3, 38.2, 49.9, 63.5 (d, $^2J_{P,C}$ = 4.7 Hz), 63.8 (d, $^2J_{P,C}$ = 4.8 Hz), 110.8 (d, $^3J_{P,C}$ = 10.3 Hz), 111.4 (d, $^3J_{P,C}$ = 11.0 Hz), 124.1 (q, $^1J_{F,C}$ = 270.4 Hz), 125.0 (d, $^2J_{P,C}$ = 6.5 Hz), 125.1 (q, $^3J_{F,C}$ = 3.7 Hz), 128.3, 128.8 (q, $^2J_{F,C}$ = 32.3 Hz), 136.6 (d, $^2J_{P,C}$ = 5.9 Hz), 147.8, 207.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.8. HRMS (ESI): *m/z* calcd for $C_{20}H_{26}F_3NO_4P$ $[M+H]^+$: 432.1546; found: 432.1520.

Diethyl 2-(3-oxo-1-*p*-tolylpentyl)-1*H*-pyrrol-1-ylphosphonate (346): Brown viscous oil; yield: 21 mg (76 %); R_f = 0.64 (1:1, EtOAc-hexane). IR (ATR): 2975, 2938, 1715, 1513, 1455, 1369, 1256, 1169, 1109, 1016, 815, 728 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 0.96 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.30 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.27 (s, 3H, CH_3), 2.27 (dq, $^2J_{H,H}$ = 17.6 Hz, $^3J_{H,H}$ = 7.1 Hz, 1H, CH_2CH_3), 2.40 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.81 (dd, $^2J_{H,H}$ = 16.4 Hz, $^3J_{H,H}$ = 6.7 Hz, 1H, CH_2), 3.07 (dd, $^2J_{H,H}$ = 16.4 Hz, $^3J_{H,H}$ = 8.6 Hz, 1H, CH_2), 3.31-3.41 (m, 1H, OCH_2CH_3), 3.83-4.06 (m, 3H, OCH_2CH_3), 4.94 (t, $^3J_{H,H}$ = 7.0 Hz, 1H, C*H*), 6.15-6.18 (m, 2H, $H_{pyrrole}$), 6.99-7.03 (m, 5H, Ar*H*, $H_{pyrrole}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.5, 15.4 (d, $^3J_{P,C}$ = 7.1 Hz), 15.7 (d, $^3J_{P,C}$ = 7.2 Hz), 20.9, 36.2, 38.1, 50.5, 63.3 (d, $^2J_{P,C}$ = 4.8 Hz), 63.5 (d, $^2J_{P,C}$ = 4.7 Hz), 110.4 (d, $^3J_{P,C}$ = 10.6 Hz), 111.1 (d, $^3J_{P,C}$ = 11.0 Hz), 124.7 (d, $^2J_{P,C}$ = 6.6 Hz), 127.5, 128.7, 135.4, 137.4 (d, $^2J_{P,C}$ = 5.7 Hz), 140.4, 207.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.6. HRMS (ESI): *m/z* calcd for $C_{20}H_{29}NO_4P$ $[M+H]^+$: 378.1829; found: 378.1787.

Diethyl 2-(1-(4-methoxyphenyl)-3-oxopentyl)-1*H*-pyrrol-1-ylphosphonate (347): Brown viscous oil; yield: 22 mg (77 %); R_f = 0.56 (1:1, EtOAc-hexane). IR (ATR): 2973, 2936, 1712, 1515, 1456, 1370, 1240, 1162, 1113, 1014, 817, 730 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.00 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.29 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.26 (dq, $^2J_{H,H}$ = 17.6 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.37 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.82 (dd, $^2J_{H,H}$ = 16.3 Hz, $^3J_{H,H}$ = 6.9 Hz, 1H, CH_2), 3.06 (dd, $^2J_{H,H}$ = 16.4 Hz, $^3J_{H,H}$ = 8.4 Hz, 1H, CH_2), 3.38-3.44 (m, 1H, OCH_2CH_3), 3.74 (s, 3H, OCH_3), 3.87-4.04 (m, 3H, OCH_2CH_3), 4.94 (t, $^3J_{H,H}$ = 7.8 Hz, 1H, C*H*), 6.17-6.19 (m, 2H, $H_{pyrrole}$), 6.74 (d, $^3J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), 7.02 (dt, $^3J_{H,H}$ = 2.6 Hz, $^4J_{H,H}$ = 2.1 Hz, 1H, $H_{pyrrole}$), 7.06 (d, $^3J_{H,H}$ = 8.6 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.6 (d, $^3J_{P,C}$ = 6.8 Hz), 15.9 (d, $^3J_{P,C}$ = 7.2 Hz), 36.4, 37.9, 50.6, 55.0, 63.5 (d, $^2J_{P,C}$ = 4.8 Hz), 63.7 (d, $^2J_{P,C}$ = 4.9 Hz), 110.6 (d, $^3J_{P,C}$ = 10.6 Hz), 111.1 (d, $^3J_{P,C}$ = 11.0 Hz), 113.5, 124.7 (d, $^2J_{P,C}$ = 6.7 Hz), 128.7, 135.6, 137.8 (d, $^2J_{P,C}$ = 5.9 Hz), 158.1, 208.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.9. HRMS (ESI): *m/z* calcd for $C_{20}H_{29}NO_5P$ $[M+H]^+$: 394.1778; found: 394.1730.

Diethyl 2-(1-(4-fluorophenyl)-3-oxopentyl)-1*H*-pyrrol-1-ylphosphonate (348): Yellow viscous oil; yield: 16 mg (57 %); R_f = 0.64 (1:1, EtOAc-hexane). IR (ATR): 2980, 2938, 1716, 1603, 1507, 1479, 1370, 1274, 1222, 1170, 1019, 908, 810, 729 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.02 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.26 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.28 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.40 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.87 (dd, $^2J_{H,H}$ = 16.6 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2), 3.10 (dd, $^2J_{H,H}$ = 16.5 Hz, $^3J_{H,H}$ = 8.0 Hz, 1H, CH_2), 3.47-3.57 (m, 1H, OCH_2CH_3), 3.87-4.04 (m, 3H, OCH_2CH_3), 5.05 (t, $^3J_{H,H}$ = 7.6 Hz, 1H, C*H*), 6.21-6.25 (m, 2H, $H_{pyrrole}$), 6.92 (t, $^3J_{H,H}$ = 8.7 Hz, 2H, Ar*H*), 7.05 (dt, $^3J_{H,H}$ = 2.7 Hz, $^4J_{H,H}$ = 2.0 Hz, 1H, $H_{pyrrole}$), 7.13-7.18 (m, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.6 (d, $^3J_{P,C}$ = 7.0 Hz), 15.8 (d, $^3J_{P,C}$ = 7.2 Hz), 36.4, 37.9, 50.4, 63.7 (d, $^2J_{P,C}$ = 4.6 Hz), 63.9 (d, $^2J_{P,C}$ = 5.0 Hz), 110.8 (d, $^3J_{P,C}$ = 10.4 Hz), 111.3 (d, $^3J_{P,C}$ = 11.0 Hz), 115.0 (d, $^2J_{F,C}$ = 21.1 Hz), 124.8 (d, $^2J_{P,C}$ = 6.5 Hz), 129.4 (d, $^3J_{F,C}$ = 7.7 Hz), 137.6 (d, $^2J_{P,C}$ = 6.0 Hz), 139.2, 161.5 (d, $^1J_{F,C}$ = 243.3 Hz), 208.6. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.9. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}FNO_4P$ $[M+H]^+$: 382.1578; found: 382.1577.

Diethyl 2-(1-(4-chlorophenyl)-3-oxopentyl)-1*H*-pyrrol-1-ylphosphonate (349): Yellow viscous oil; yield: 19 mg (65 %); R_f = 0.57 (1:1, EtOAc-hexane). IR (ATR): 2981, 2936, 1714, 1489, 1414, 1370, 1278, 1171, 1091, 1013, 981, 815, 799, 733 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.02 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.26 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.29 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.40 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.86 (dd, $^2J_{H,H}$ = 16.6 Hz, $^3J_{H,H}$ = 7.1 Hz, 1H, CH_2), 3.11 (dd, $^2J_{H,H}$ = 16.7 Hz, $^3J_{H,H}$ = 8.1 Hz, 1H, CH_2), 3.48-3.58 (m, 1H, OCH_2CH_3), 3.88-4.05 (m, 3H, OCH_2CH_3), 5.04 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, C*H*), 6.21-6.24 (m, 2H, $H_{pyrrole}$), 7.05 (dt, $^3J_{H,H}$ = 2.5 Hz, $^4J_{H,H}$ = 2.2 Hz, 1H, $H_{pyrrole}$), 7.12 (d, $^3J_{H,H}$ = 8.5 Hz, 2H, Ar*H*), 7.21 (d, $^3J_{H,H}$ = 8.5 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.6 (d, $^3J_{P,C}$ = 6.8 Hz), 15.8 (d, $^3J_{P,C}$ = 7.2 Hz), 36.4, 38.0, 50.1, 63.8 (d, $^2J_{P,C}$ = 4.8 Hz), 64.0 (d, $^2J_{P,C}$ = 5.0 Hz), 110.8 (d, $^3J_{P,C}$ = 10.6 Hz), 111.5 (d, $^3J_{P,C}$ = 11.1 Hz), 124.9 (d, $^2J_{P,C}$ = 6.6 Hz), 128.3, 129.3, 132.1, 137.2 (d, $^2J_{P,C}$ = 5.9 Hz), 142.1, 208.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.6. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}ClNO_4P$ $[M+H]^+$: 398.1282; found: 398.1282.

Diethyl 2-(1-(4-bromophenyl)-3-oxopentyl)-1*H*-pyrrol-1-ylphosphonate (350): Brown viscous oil; yield: 28 mg (85 %); R_f = 0.64 (1:1, EtOAc-hexane). IR (ATR): 2982, 2916, 1714, 1488, 1370, 1242, 1164, 1099, 1009, 817 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_2CH_3), 1.02 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.28 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.28 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.38 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.81 (dd, $^2J_{H,H}$ = 16.6 Hz, $^3J_{H,H}$ = 6.8 Hz, 1H, CH_2), 3.08 (dd, $^2J_{H,H}$ = 16.6 Hz, $^3J_{H,H}$ = 8.3 Hz, 1H, CH_2), 3.45-3.55 (m, 1H, OCH_2CH_3), 3.87-4.04 (m, 3H, OCH_2CH_3), 5.00 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, C*H*), 6.17-6.19 (m, 2H, $H_{pyrrole}$), 7.01 (dt, $^4J_{H,H}$ = 2.4 Hz, $^3J_{H,H}$ = 2.3 Hz, 1H, $H_{pyrrole}$), 7.04 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*), 7.34 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.6 (d, $^3J_{P,C}$ = 6.8 Hz), 15.9 (d, $^3J_{P,C}$ = 7.2 Hz), 36.4, 38.0, 50.1, 63.6 (d, $^2J_{P,C}$ = 4.6 Hz), 63.8 (d, $^2J_{P,C}$ = 4.9 Hz), 110.7 (d, $^3J_{P,C}$ = 10.5 Hz), 111.2 (d, $^3J_{P,C}$ = 11.0 Hz), 120.1, 124.9 (d, $^2J_{P,C}$ = 6.6 Hz), 129.7, 131.2, 136.9 (d, $^2J_{P,C}$ = 5.9 Hz), 142.6, 207.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.7. HRMS (ESI): *m/z* calcd for $C_{19}H_{26}BrNO_4P$ $[M+H]^+$: 442.0777; found: 442.0703.

Diethyl 2-(1-(4-cyanophenyl)-3-oxopentyl)-1*H*-pyrrol-1-ylphosphonate (351): Yellow viscous oil; yield: 11 mg (38 %); R_f = 0.56 (1:1, EtOAc-hexane). IR (ATR): 2986, 2253, 2234, 1716, 1608, 1275, 1168, 1109, 1018, 908, 839, 727 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.04 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.24 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.31 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.42 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.4 Hz, 1H, CH_2CH_3), 2.88 (dd, $^2J_{H,H}$ = 17.0 Hz, $^3J_{H,H}$ = 7.0 Hz, 1H, CH_2), 3.15 (dd, $^2J_{H,H}$ = 17.0 Hz, $^3J_{H,H}$ = 8.0 Hz, 1H, CH_2), 3.57-3.67 (m, 1H, OCH_2CH_3), 3.86-4.03 (m, 3H, OCH_2CH_3), 5.17 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, C*H*), 6.23-6.27 (m, 2H, $H_{pyrrole}$), 7.04 (dt, $^3J_{H,H}$ = 2.6 Hz, $^4J_{H,H}$ = 2.1 Hz, 1H, $H_{pyrrole}$), 7.32 (d, $^3J_{H,H}$ = 8.2 Hz, 2H, Ar*H*), 7.54 (d, $^3J_{H,H}$ = 8.4 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.7 (d, $^3J_{P,C}$ = 6.7 Hz), 15.8 (d, $^3J_{P,C}$ = 6.9 Hz), 36.4, 38.5, 49.6, 63.9 (d, $^2J_{P,C}$ = 5.0 Hz), 64.1 (d, $^2J_{P,C}$ = 5.1 Hz), 110.1, 111.0 (d, $^3J_{P,C}$ = 10.4 Hz), 111.7 (d, $^3J_{P,C}$ = 11.0 Hz), 118.9, 124.9 (d, $^2J_{P,C}$ = 6.3 Hz), 128.9, 132.1, 136.2 (d, $^2J_{P,C}$ = 6.0 Hz), 149.3, 207.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -3.1. HRMS (ESI): *m/z* calcd for $C_{20}H_{26}N_2O_4P$ $[M+H]^+$: 389.1625; found: 389.1635.

Diethyl 2-(1-(4-nitrophenyl)-3-oxopentyl)-1*H*-pyrrol-1-ylphosphonate (352): Light brown viscous oil; yield: 16 mg (53 %); R_f = 0.65 (1:1, EtOAc-hexane). IR (ATR): 2981, 2935, 1716, 1596, 1519, 1479, 1396, 1345, 1277, 1170, 1109, 1014, 983, 856, 730 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.06 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.24 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.33 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.42 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 2.91 (dd, $^2J_{H,H}$ = 17.0 Hz, $^3J_{H,H}$ = 7.1 Hz, 1H, CH_2), 3.18 (dd, $^2J_{H,H}$ = 17.0 Hz, $^3J_{H,H}$ = 7.9 Hz, 1H, CH_2), 3.62-3.72 (m, 1H, OCH_2CH_3), 3.87-4.05 (m, 3H, OCH_2CH_3), 5.23 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, C*H*), 6.24-6.27 (m, 2H, $H_{pyrrole}$), 7.05 (dt, $^3J_{H,H}$ = 2.6 Hz, $^4J_{H,H}$ = 1.9 Hz, 1H, $H_{pyrrole}$), 7.38 (d, $^3J_{H,H}$ = 8.8 Hz, 2H, Ar*H*), 8.11 (d, $^3J_{H,H}$ = 8.7 Hz, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.7 (d, $^3J_{P,C}$ = 6.7 Hz), 15.8 (d, $^3J_{P,C}$ = 7.0 Hz), 36.4, 38.3, 49.6, 64.0 (d, $^2J_{P,C}$ = 4.9 Hz), 64.1 (d, $^2J_{P,C}$ = 5.1 Hz), 111.1 (d, $^3J_{P,C}$ = 10.5 Hz), 111.7 (d, $^3J_{P,C}$ = 10.9 Hz), 123.5, 124.9 (d, $^2J_{P,C}$ = 6.3 Hz), 128.9, 136.3 (d, $^2J_{P,C}$ = 6.2 Hz), 146.5, 151.3, 207.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -3.2. HRMS (ESI): *m/z* calcd for $C_{20}H_{26}N_2O_4P$ $[M+H]^+$: 409.1523; found: 409.1531.

Diethyl 2-(3-oxo-1-(1*H*-pyrrol-2-yl)pentyl)-1*H*-pyrrol-1-ylphosphonate (353): Light brown viscous oil; yield: 5 mg (20 %); R_f = 0.68 (1:1, EtOAc-hexane). IR (ATR): 3252, 2983, 2937, 1598, 1520, 1476, 1395, 1342, 1278, 1156, 1108, 987, 854, 733 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.01 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.20 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.29 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 2.40 (q, $^3J_{H,H}$ = 7.3 Hz, 2H, CH_2CH_3), 3.11 (dd, $^2J_{H,H}$ = 17.2 Hz, $^3J_{H,H}$ = 7.8 Hz, 1H, CH_2), 3.19 (dd, $^2J_{H,H}$ = 17.2 Hz, $^3J_{H,H}$ = 7.0 Hz, 1H, CH_2), 3.77-3.86 (m, 1H, OCH_2CH_3), 3.93-4.03 (m, 1H, OCH_2CH_3), 4.05-4.15 (m, 2H, OCH_2CH_3), 5.07 (t, $^3J_{H,H}$ = 7.3 Hz, 1H, C*H*), 5.76 (br s, 1H, $H_{pyrrole}$), 6.02 (q, $^3J_{H,H}$ = 2.8 Hz, 1H, $H_{pyrrole}$), 6.15-6.21 (m, 2H, $H_{pyrrole}$), 6.58 (dt, $^3J_{H,H}$ = 2.6 Hz, $^4J_{H,H}$ = 1.5 Hz, 1H, $H_{pyrrole}$), 6.93 (br s, 1H, $H_{pyrrole}$), 9.08 (br s, 1H, N*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.7, 15.8 (d, $^3J_{P,C}$ = 7.0 Hz), 15.9 (d, $^3J_{P,C}$ = 6.9 Hz), 31.3, 36.3, 48.3, 64.2 (d, $^2J_{P,C}$ = 4.8 Hz), 64.3 (d, $^2J_{P,C}$ = 5.4 Hz), 103.9, 107.8, 110.3 (d, $^3J_{P,C}$ = 11.1 Hz), 111.4 (d, $^3J_{P,C}$ = 10.6 Hz), 116.2, 123.4 (d, $^2J_{P,C}$ = 6.2 Hz), 134.1, 209.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.4. HRMS (ESI): *m/z* calcd for $C_{17}H_{26}N_2O_4P$ $[M+H]^+$: 354.1703; found: 354.1724.

Diethyl 2-(1-(furan-2-yl)-3-oxopentyl)-1*H*-pyrrol-1-ylphosphonate (354): Light brown viscous oil; yield: 17 mg (66 %); R_f = 0.76 (1:1, EtOAc-hexane). IR (ATR): 2980, 2938, 1716, 1506, 1476, 1412, 1370, 1274, 1169, 1111, 1016, 982, 800, 729 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.00 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.19 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.33 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.39 (q, $^3J_{H,H}$ = 7.3 Hz, 2H, CH_2CH_3), 3.02 (dd, $^2J_{H,H}$ = 16.5 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2), 3.08 (dd, $^2J_{H,H}$ = 16.2 Hz, $^3J_{H,H}$ = 7.4 Hz, 1H, CH_2), 3.81-3.91 (m, 1H, OCH_2CH_3), 4.05-4.21 (m, 3H, OCH_2CH_3), 5.11 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, C*H*), 5.91 (d, $^3J_{H,H}$ = 3.2 Hz, 1H, H_{furan}), 6.15-6.17 (m, 1H, $H_{pyrrole}$), 6.20 (q, $^3J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), 6.23 (dd, $^3J_{H,H}$ = 3.2 Hz, $^3J_{H,H}$ = 1.9 Hz, 1H, H_{furan}), 7.05-7.07 (m, 1H, $H_{pyrrole}$), 7.28 (dd, $^3J_{H,H}$ = 1.8 Hz, $^3J_{H,H}$ = 0.8 Hz, 1H, H_{furan}). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.7, 15.8 (d, $^3J_{P,C}$ = 7.2 Hz), 15.9 (d, $^3J_{P,C}$ = 7.0 Hz), 32.7, 36.1, 47.6, 64.1 (d, $^2J_{P,C}$ = 5.0 Hz), 64.2 (d, $^2J_{P,C}$ = 5.1 Hz), 105.8, 110.2, 111.1 (d, $^3J_{P,C}$ = 10.7 Hz), 111.7 (d, $^3J_{P,C}$ = 10.8 Hz), 124.3 (d, $^2J_{P,C}$ = 6.6 Hz), 135.8 (d, $^2J_{P,C}$ = 6.2 Hz), 141.3, 156.0, 208.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.9. HRMS (ESI): *m/z* calcd for $C_{17}H_{25}NO_5P$ $[M+H]^+$: 354.1465; found: 354.1462.

Diethyl 2-(3-oxo-1-(thiophen-2-yl)pentyl)-1*H*-pyrrol-1-ylphosphonate (355): Light brown viscous oil; yield: 16 mg (60 %); R_f = 0.59 (1:1, EtOAc-hexane). IR (ATR): 2985, 2936, 1713, 1507, 1472, 1418, 1376, 1278, 1165, 1114, 1012, 983, 805, 730 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.00 (t, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_2CH_3), 1.09 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 1.30 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.34 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, CH_2CH_3), 2.42 (dq, $^2J_{H,H}$ = 17.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, CH_2CH_3), 3.04 (dd, $^2J_{H,H}$ = 16.6 Hz, $^3J_{H,H}$ = 7.5 Hz, 1H, CH_2), 3.08 (dd, $^2J_{H,H}$ = 16.6 Hz, $^3J_{H,H}$ = 7.4 Hz, 1H, CH_2), 3.59-3.69 (m, 1H, OCH_2CH_3), 3.96-4.14 (m, 3H, OCH_2CH_3), 5.32 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, C*H*), 6.21-6.25 (m, 2H, $H_{pyrrole}$), 6.75 (d, $^3J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), 6.85 (dd, $^3J_{H,H}$ = 5.1 Hz, $^3J_{H,H}$ =3.5 Hz, 1H, $H_{thiophene}$), 7.06-7.10 (m, 2H, $H_{thiophene}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.6, 15.7 (d, $^3J_{P,C}$ = 7.3 Hz), 15.9 (d, $^3J_{P,C}$ = 6.8 Hz), 33.9, 36.4, 51.0, 64.0 (d, $^2J_{P,C}$ = 5.1 Hz), 64.1 (d, $^2J_{P,C}$ = 5.1 Hz), 110.9 (d, $^3J_{P,C}$ = 10.5 Hz), 111.1 (d, $^3J_{P,C}$ = 10.9 Hz), 123.7, 124.4, 124.6 (d, $^2J_{P,C}$ = 7.0 Hz), 126.6, 137.9, 148.0, 208.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -3.0. HRMS (ESI): *m/z* calcd for $C_{17}H_{25}NO_4PS$ $[M+H]^+$: 370.1236; found: 370.1205.

4.4.4. General procedure for the reaction of cyano functionalized pyrrole addition product with NaH

Cyano functionalized pyrrole addition product (**304**) (0.074 mmol) was dissolved in THF (2 mL) and NaH (0.222 mmol) was added to this solution at 0 °C. The resultant mixture was stirred at room temperature for 24 h (TLC monitoring). After completion of the reaction pH 7 phosphate buffer (5 mL) was added to the reaction mixture and the product was extracted with EtOAc (3x10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc-hexane, 1:1).

Diethyl 2-(2-cyano-1-phenylethyl)-1*H*-pyrrol-1-ylphosphonate (358): Brown viscous oil; yield: 5 mg (20 %); R_f = 0.22 (1:1, EtOAc-hexane). IR (ATR): 2968, 2924, 2228, 1456, 1395, 1266, 1231, 1108, 1017, 961, 790, 705 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.08 (t, $^3J_{H,H}$ = 7.0 Hz, 3H, OCH_2CH_3), 1.18 (t, $^3J_{H,H}$ = 7.1 Hz, 3H, OCH_2CH_3), 2.86 (dd, $^2J_{H,H}$ = 16.7 Hz, $^3J_{H,H}$ = 7.0 Hz, 1H, CH_2), 2.94 (dd, $^2J_{H,H}$ = 16.6 Hz, $^3J_{H,H}$ = 8.3 Hz, 1H, CH_2), 3.55-3.65 (m, 1H, OCH_2CH_3), 3.72-3.82 (m, 1H, OCH_2CH_3), 3.84-3.93 (m, 1H, OCH_2CH_3), 3.95-4.04 (m, 1H, OCH_2CH_3),

4.90 (t, $^{3}J_{H,H}$ = 7.6 Hz, 1H, C*H*), 6.27-6.30 (m, 1H, $H_{pyrrole}$), 6.37 (br d, $^{3}J_{H,H}$ = 3.4 Hz, 1H, $H_{pyrrole}$), 7.03 (br s, 1H, $H_{pyrrole}$), 7.20-7.31 (m, 5H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.6 (d, $^{3}J_{P,C}$ = 6.8 Hz), 15.7 (d, $^{3}J_{P,C}$ = 6.9 Hz), 25.5, 40.0, 63.7 (d, $^{2}J_{P,C}$ = 6.0 Hz), 63.8 (d, $^{2}J_{P,C}$ = 5.3 Hz), 111.2 (d, $^{3}J_{P,C}$ = 10.3 Hz), 112.2 (d, $^{3}J_{P,C}$ = 10.8 Hz), 117.6, 124.8 (d, $^{2}J_{P,C}$ = 6.3 Hz), 127.3, 127.6, 128.5, 134.8 (d, $^{2}J_{P,C}$ = 6.1 Hz), 140.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ = -2.9. HRMS (ESI): *m/z* calcd for $C_{17}H_{22}N_2O_3P$ $[M+H]^+$: 333.1363; found: 333.1312.

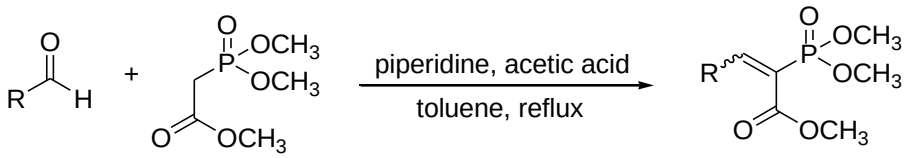
5. EXPERIMENTAL RESULTS AND DISCUSSION

5.1. Synthesis of α,β-Unsaturated Phosphonates

5.1.1. Synthesis of α,β-unsaturated phosphonates from trimethylphosphonoacetate and aldehydes

The Knoevenagel condensation has been an important tool for constructing the α,β-unsaturated structure unit from a carbonyl and an active methylene compound. The Knoevenagel reaction is generally carried out in the presence of weak bases such as ethylenediamine and piperidine and their corresponding ammonium salts, potassium fluoride, or amino acids such as glycine, β-alanine and L-proline under homogeneous conditions (Wada and Suzuki, 2003). Recently, using inorganic solid supports such as alumina, Al_2O_3-$AlPO_4$, xonotlite/tert-butoxide, cation-exchanged zeolites, calcite or fluorite and also some basic solid catalysts under heterogeneous conditions have been reported as suitable methods for the Knoevenagel condensation (Balalaie and Bararjanian, 2006).

In this study; piperidine and acetic acid were used as catalysts according to literature procedure reported by Patai and Schwartz (1960) for phosphonoacetates. The α,β-unsaturated phosphonates were synthesized by the Knoevenagel condensation of trimethylphosphonoacetate (**216**) and aldehydes in toluene in the presence of piperidine and acetic acid (Scheme 5.1). The condensation products **217-232** were obtained in 10-86% yields (Table 5.1).



216 **217-232**

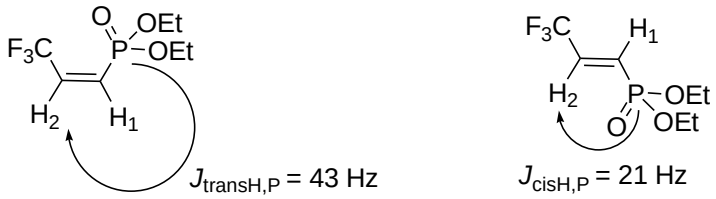
Scheme 5.1. Synthesis of α,β-unsaturated phosphonates from trimethylphosphonoacetate (**216**) and aldehydes.

Table 5.1. Knoevenagel condensation products of trimethylphosphonoacetate (**216**) and aldehydes

Compound	R	*E*:*Z*[a]	Yield (%)[b]
217	phenyl[c]	95:5	55
218	*p*-CF_3-phenyl	89:11	40
219	*p*-CH_3-phenyl	95:5	65
220	*p*-OCH_3-phenyl	88:12	35
221	*p*-F-phenyl	87:13	50
222	*p*-Cl-phenyl[d]	92:8	45
223	*p*-Br-phenyl	93:7	50
224	*p*-OH-phenyl	86:14	86
225	*p*-CN-phenyl	89:11	36
226	*p*-NO_2-phenyl	87:13	30
227	2,4,6-trimethylphenyl	75:25	20
228	2-pyrrolyl	31:69	77
229	2-furyl	93:7	70
230	2-thiophenyl	91:9	50
231	cyclohexyl	93:7	15
232	isobutyl	83:17	10

[a]*E*:*Z* ratios are determined from NMR spectra.
[b]yield refers to pure product after column chromatography.
[c,d]These compounds are synthesized by Chiba et al. (2008), Snider et al. (1983) and Chiefari et al. (1987).

Characterization of Knoevenagel condensation products were carried out by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. The configurational assignment of the compounds **217-232** were based on the values of vicinal coupling constant $^{3}J_{H,P}$ of olefinic proton and phosphorus atom. Nickson reported $^{3}J_{H,P}$ values of *E*- and *Z*-diethyl(3,3,3-trifluoro-1-propenyl)phosphonate as 21 Hz for $^{3}J_{cis,H,P}$ and 43 Hz for $^{3}J_{trans,H,P}$ (Scheme 5.2). In our case, $^{3}J_{H,P}$ value of the major isomer is in the range of 22.6-26.8 Hz except methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)acrylate (**228**). The $^{3}J_{H,P}$ value of major isomer of **228** equals to 44.0 Hz. According to these values, configurations of the **217-227,229-232** are assigned as mainly *E*, and **228** as mainly *Z*. These Knoevenagel condensation products were used as mixture of *E*- and *Z*-isomers for further reactions.



***Z*-isomer** ***E*-isomer**

Scheme 5.2. $^{3}J_{H,P}$ values of *E*- and *Z*-diethyl(3,3,3-trifluoro-1-propenyl)phosphonate.

E- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**) was obtained in 55% yield as colorless viscous oil. The ^{1}H NMR spectrum of methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate is in agreement with the structure. The signals of methoxy protons for *Z* isomer appeared at 3.60 ppm, 3.63 ppm and 3.91 ppm as singlet. The singlets appeared at 3.82 ppm, 3.84 ppm and 3.87 ppm belong to methoxy protons of *E* isomer. The multiplets between 7.37-7.45 ppm and 7.61-7.65 ppm belong to phenyl protons of *E* and *Z* isomers. The doublets at 7.70 ppm and 8.28 ppm belong to vinyl protons of *E* and *Z* isomers, respectively. The ^{13}C NMR spectrum is also in agreement with the structure. The signals at 52.4 ppm, 52.9 ppm and 53.0 ppm belong to methoxy carbons of *E* and *Z* isomers. The signal of vinyl carbons appear at 122.6 ppm for both isomers. The aromatic carbons appeared at 128.5 ppm, 128.9 ppm, 130.4 ppm and 149.0 ppm. The signal for the CH carbon appeared at 133.2 ppm. The signal of carbonyl carbons appeared at 166.5 ppm for *E* and *Z* isomers. In the ^{31}P NMR spectrum signals at 14.7 ppm and 17.1 ppm belong to *Z* and *E* isomers, respectively.

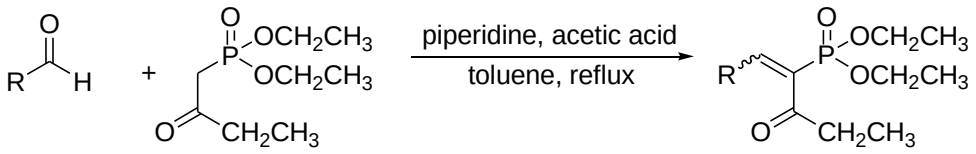
The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-OH, *p*-CN, *p*-NO_2, 2,4,6-trimethyl, 2-pyrrolyl, 2-furyl, 2-thiophenyl, cyclohexyl and isobutyl substituted α,β-unsaturated phosphonates are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of synthesized α,β-unsaturated phosphonates **217-232** are given in Figure A.1-A.51 (page 180-205). Chemical shift values and coupling constants of characteristic vinyl protons of these compounds are summarized in Table 5.2.

Table 5.2. Chemical shift values in ppm and coupling constants of vinyl protons of *E* and *Z* isomers.

Compound	C*H*=C (*E* isomer)	C*H*=C (*Z* isomer)
217	7.70 (d, $^3J_{P,H}$ = 24.2 Hz)	8.28 (d, $^3J_{P,H}$ = 44.1 Hz)
218	7.60 (d, $^3J_{P,H}$ = 26.8 Hz)	8.13 (d, $^3J_{P,H}$ = 43.6 Hz)
219	7.40 (d, $^3J_{P,H}$ = 24.3 Hz)	7.97 (d, $^3J_{P,H}$ = 44.1 Hz)
220	7.50 (d, $^3J_{P,H}$ = 24.4 Hz)	8.08 (d, $^3J_{P,H}$ = 44.0 Hz)
221	7.61 (d, $^3J_{P,H}$ = 24.2 Hz)	8.15 (d, $^3J_{P,H}$ = 40.0 Hz)
222	7.62 (d, $^3J_{P,H}$ = 24.1 Hz)	8.15 (d, $^3J_{P,H}$ = 43.7 Hz)
223	7.51 (d, $^3J_{P,H}$ = 24.1 Hz)	8.04 (d, $^3J_{P,H}$ = 43.6 Hz)
224	7.56 (d, $^3J_{P,H}$ = 24.7 Hz)	8.24 (d, $^3J_{P,H}$ = 45.2 Hz)
225	7.63 (d, $^3J_{P,H}$ = 23.8 Hz)	8.16 (d, $^3J_{P,H}$ = 43.1 Hz)
226	7.74 (d, $^3J_{P,H}$ = 23.8 Hz)	8.24 (d, $^3J_{P,H}$ = 44.0 Hz)
227	7.92 (d, $^3J_{P,H}$ = 22.6 Hz)	8.30 (d, $^3J_{P,H}$ = 45.2 Hz)
228	7.78 (d, $^3J_{P,H}$ = 20.0 Hz)	8.18 (d, $^3J_{P,H}$ = 44.0 Hz)
229	7.35 (d, $^3J_{P,H}$ = 24.0 Hz)	7.98 (d, $^3J_{P,H}$ = 42.0 Hz)
230	7.97 (d, $^3J_{P,H}$ = 24.0 Hz)	8.35 (d, $^3J_{P,H}$ = 44.0 Hz)
231	6.89 (dd, $^3J_{H,H}$ = 10.1Hz, $^3J_{P,H}$ = 23.2 Hz)	7.29 (dd, $^3J_{H,H}$ = 10.7 Hz, $^3J_{P,H}$ = 46.5 Hz)
232	6.90 (dd, $^3J_{H,H}$= 10.2 Hz, $^3J_{P,H}$ = 23.1 Hz)	7.28 (dd, $^3J_{H,H}$ = 10.8 Hz, $^3J_{P,H}$ = 46.2 Hz)

5.1.2. Synthesis of α,β-unsaturated phosphonates from diethyl 2-oxo-butylphosphonate and aldehydes

The same experimental procedure was carried out in Knoevenagel reaction of diethyl 2-oxobutylphosphonate and aldehydes (Scheme 5.3). The condensation products **234-246** were obtained in 99-60% yields (Table 5.3). The products **234-242,245-246** were obtained as *E* isomer but the products **243-244** were obtained as a mixture of *E* and *Z* isomers. Characterization of Knoevenagel condensation products were carried out by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques.



233 **234-246**

Scheme 5.3. Synthesis of α,β-unsaturated phosphonates from diethyl 2-oxobutylphosphonate (**233**) and aldehydes.

Table 5.3. Knoevenagel condensation products of diethyl 2-oxobutylphosphonate (**233**) and aldehydes

Compound	R	Yield (%)[a]
234	phenyl	95
235	*p*-CF_3-phenyl	96
236	*p*-CH_3-phenyl	98
237	*p*-OCH_3-phenyl	98
238	*p*-F-phenyl	99
239	*p*-Cl-phenyl	98
240	*p*-Br-phenyl	98
241	*p*-CN-phenyl	99
242	*p*-NO_2-phenyl	86
243	2,4,6-trimethylphenyl	60[b]
244	2-pyrrolyl	90[b]
245	2-furyl	92
246	2-thiophenyl	95

[a]yield refers to pure product after column chromatography.

[b]compounds were obtained in 54:46 and 36:64 *E*:*Z* ratios, respectively.

E-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**) was obtained in 95% yield as yellow viscous oil. The ^{1}H NMR spectrum of diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**) is in agreement with the structure. The signals of methyl protons appeared at 1.05 ppm and 1.37 ppm as triplets. The quartet appeared at 2.51 ppm belong to methylene protons. The doublet of quartet at 4.19 ppm belongs to methylene protons of ethoxy group. The multiplets between 7.30-7.32 ppm and 7.36-7.39 ppm belong to phenyl protons. The doublet at 7.59 ppm belongs to vinyl proton of *E* isomer. The ^{13}C NMR spectrum is also in agreement

with the structure. The signal at 7.7 ppm belongs to methyl carbon. The doublet appeared at 16.2 ppm belongs to methyl carbons of ethoxy groups. The doublet signal at 36.7 ppm belongs to methylene carbon. The methylene carbons of ethoxy groups appeared at 62.5 ppm as doublet. The aromatic carbons appeared at 128.8 ppm, 129.1 ppm, 130.1 ppm and 133.9 ppm. The signal of vinyl carbon appeared at 134.0 ppm. The signal for the CH carbon appeared at 144.7 ppm. The signal of carbonyl carbon appeared at 205.8 ppm. The signal at 13.5 ppm in the ^{31}P NMR spectrum belongs to the phosphorus atom in the structure.

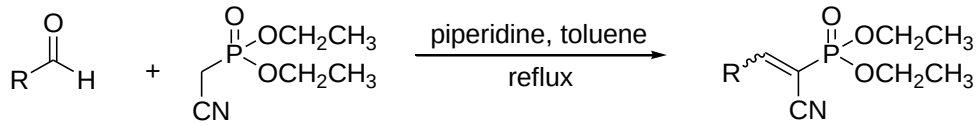
The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN, *p*-NO_2, 2,4,6-trimethyl, 2-pyrrolyl, 2-furyl and 2-thiophenyl substituted α,β-unsaturated phosphonates are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of synthesized α,β-unsaturated phosphonates **234-246** are given in Figure A.52-A.90 (page 205-224). In Table 5.4, chemical shift values and coupling constants of characteristic vinyl protons of compounds **234-246** are summarized.

Table 5.4. Chemical shift values and coupling constants of vinyl protons of *E* and *Z* isomers in ppm

Compound	C*H*=C (*E* isomer)	C*H*=C (*Z* isomer)
234	7.59 (d, $^{3}J_{P,H}$ = 25.6 Hz)	-
235	7.57 (d, $^{3}J_{P,H}$ = 26.0 Hz)	-
236	7.55 (d, $^{3}J_{P,H}$ = 25.6 Hz)	-
237	7.52 (d, $^{3}J_{P,H}$ = 25.6 Hz)	-
238	7.49 (d, $^{3}J_{P,H}$ = 25.6 Hz)	-
239	7.51 (d, $^{3}J_{P,H}$ = 25.6 Hz)	-
240	7.49 (d, $^{3}J_{P,H}$ = 25.6 Hz)	-
241	7.50 (d, $^{3}J_{P,H}$ = 25.5 Hz)	-
242	7.54 (d, $^{3}J_{P,H}$ = 25.5 Hz)	-
243	7.77 (d, $^{3}J_{P,H}$ = 24.2 Hz)	7.90 (d, $^{3}J_{P,H}$ = 46.7 Hz)
244	7.78 (d, $^{3}J_{P,H}$ = 24.3 Hz)	8.01 (d, $^{3}J_{P,H}$ = 45.1 Hz)
245	7.19 (d, $^{3}J_{P,H}$ = 25.2 Hz)	-
246	7.65 (d, $^{3}J_{P,H}$ = 25.0 Hz)	-

5.1.3. Synthesis of α,β-unsaturated phosphonates from diethyl cyanomethylphosphonate and aldehydes

The cyano functionalized α,β-unsaturated phosphonates were synthesized by the Knoevenagel condensation of diethyl cyanomethylphosphonate and aldehydes in toluene in the presence of piperidine (Scheme 5.4). The condensation products **248-261** were obtained in 99-60% yields (Table 5.5). The configurations of the condensation products were assigned as *E* according to their vicinal coupling constants $^{3}J_{H,P}$ of the olefinic protons and phosphorus atom. Characterization of Knoevenagel condensation products were carried out by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques.



247 **248-261**

Scheme 5.4. Synthesis of α,β-unsaturated phosphonates from diethyl cyano-methylphosphonate (**247**) and aldehydes.

Table 5.5. Knoevenagel condensation products of diethyl cyanomethyl-phosphonate (**247**) with aldehydes

Compound No	R[a]	Yield (%)[b]
248	Phenyl	93
249	*p*-CF_3-phenyl	99
250	*p*-CH_3-phenyl	99
251	*p*-OCH_3-phenyl	99
252	*p*-F-phenyl	99
253	*p*-Cl-phenyl	99
254	*p*-Br-phenyl	98
255	*p*-OH-phenyl	90
256	*p*-CN-phenyl	81
257	*p*-NO_2-phenyl	82
258	2,4,6-trimethylphenyl	60
259	2-pyrrolyl	90
260	2-furyl	92
261	2-thiophenyl	95

[a]These compounds are synthesized by Robinson et al. (1987), Shen et al. (2000).

[b]yield refers to pure product after column chromatography.

E-diethyl 1-cyano-2-phenylvinylphosphonate (**248**) was obtained in 93% yield as yellow viscous oil. The ^{1}H NMR spectrum of *E*-diethyl 1-cyano-2-phenylvinyl-phosphonate (**248**) is in agreement with the structure. The triplet appeared at 1.42 ppm belongs to methyl protons. The methylene protons of ethoxy group appeared at 4.15-4.27 ppm as multiplet. The signals of the aromatic protons appeared between 7.48-7.56 ppm as multiplet and at 7.97 ppm as dublet. The characteristic signal of vinyl proton appeared at 8.02 ppm. The ^{13}C NMR spectrum is also in agreement with the structure. The dublet signal at 16.2 ppm belongs to methyl carbon. The doublet appeared at 63.4 ppm belongs to methylene carbons of ethoxy groups. The signal of vinyl carbon appeared at 100.2 ppm. The doublet signal at 115.2 ppm belongs to cyano group. The aromatic carbons appeared at 129.1 ppm, 130.4 ppm, 132.4 ppm and 132.9 ppm. The signal for the CH carbon appeared at 158.6 ppm. The signal at 10.8 ppm in the ^{31}P NMR spectrum shows the phosphorus atom in the structure.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectrums of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-OH, *p*-CN, *p*-NO_2, 2,4,6-trimethyl, 2-pyrrolyl, 2-furyl and 2-thiophenyl substituted α,β-unsaturated phosphonates are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of synthesized α,β-unsaturated phosphonates **248-261** are given in Figure A.91-A.132 (page 225-245). In Table 5.6 chemical shift values and coupling constants of characteristic vinyl protons of compounds **248-261** are summarized.

Table 5.6. Chemical shift values and coupling constants of vinyl protons of *E* isomer in ppm

Compound	C*H*=C (*E* isomer)
248	8.02 (d, $^{3}J_{P,H}$ = 21.2 Hz)
249	8.02 (d, $^{3}J_{P,H}$ = 21.6 Hz)
250	7.94 (d, $^{3}J_{P,H}$ = 21.4 Hz)
251	7.89 (d, $^{3}J_{P,H}$ = 21.3 Hz)
252	7.96 (d, $^{3}J_{P,H}$ = 21.2 Hz)
253	7.93 (d, $^{3}J_{P,H}$ = 20.4 Hz)
254	7.92 (d, $^{3}J_{P,H}$ = 21.2 Hz)
255	7.83 (d, $^{3}J_{P,H}$ = 21.2 Hz)
256	8.00 (d, $^{3}J_{P,H}$ = 21.2 Hz)
257	8.04 (d, $^{3}J_{P,H}$ = 21.0 Hz)
258	8.22 (d, $^{3}J_{P,H}$ = 19.5 Hz)
259	7.96 (d, $^{3}J_{P,H}$ = 19.8 Hz)
260	7.76 (d, $^{3}J_{P,H}$ = 20.2 Hz)
261	8.05 (d, $^{3}J_{P,H}$ = 19.8 Hz)

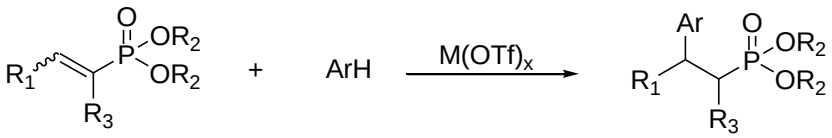
5.2. Michael Addition Reactions of Heteroaromatics to Vinylphosphonates

Michael reaction is the most often used carbon-carbon bond forming reaction in organic synthesis. Vinylphosphonates containing electron-withdrawing groups at the α-position are valuable Michael acceptors and suitable precursors for the synthesis of functionalized phosphonates by Michael reaction (Minami and Motoyoshiya, 1992 and Janecki et al., 2009). In literature, Michael addition to vinylphosphonates was exemplified with indole (Couthon-Gourves et al., 2006),

pyridine, imidazole (Inoue et al.,2003), aldehydes, nitroalkanes (Krawczyk et al., 2002, 2006 and Blaszcyk et al., 2004) and alkylhalogens (Vieth et al., 1997) in the presence of acids or bases such as AcOH, NaH or *t*-BuOK.

In the last decades, metal triflates have attracted great deal of attention as water-tolerent and reusable Lewis acid catalysts. They were used in carbon-carbon bond forming reactions such as; Aldol, Michael, Diels-Alder and Friedel-Crafts alkylation and acylations (Kobayashi et al., 2002).

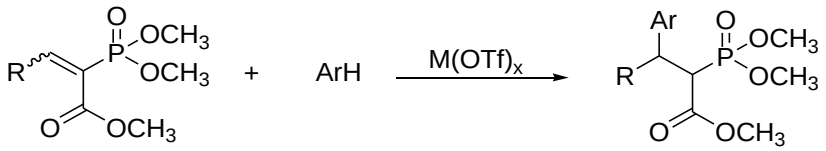
In the second part of the study; we searched the Michael reaction of heteroaromatics to vinylphosphonates in the presence of metal triflates (Scheme 5.5). To our knowledge; there is no example of such an addition reaction of heteroaromatics to vinylphosphonates catalyzed with metal triflates.



Scheme 5.5. General Michael addition reaction to vinylphosphonates with metal triflates.

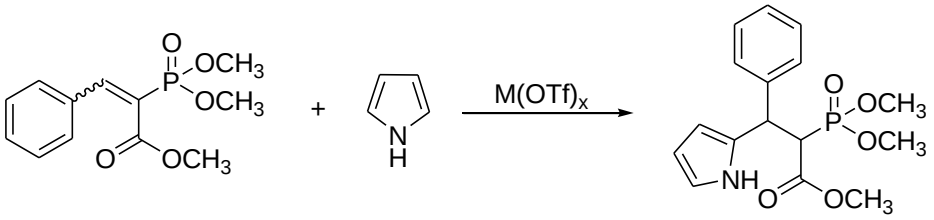
5.2.1. Michael addition reactions of heteroaromatics to ester functionalized vinylphosphonates

We focused on the metal triflates catalyzed additions of heteroaromatics to ester functionalized vinylphosphonates (Scheme 5.6).



Scheme 5.6. Michael addition reaction to ester functionalized vinylphosphonates with metal triflates.

The addition of pyrrole to *E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-phenyl-acrylate (**217**) was chosen as a model reaction to optimize the reaction conditions (Scheme 5.7). Firstly, *E*- and *Z*-methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**) and metal triflate were mixed for 30 minutes in toluene at room temperature to activate vinylphosphonate. Then the pyrrole was added instantly to the reaction mixture. The reaction was monitored by TLC and completed in 48 h.



217 **262**

Scheme 5.7. The model reaction to optimize the conditions of addition reaction of pyrrole to ester functionalized vinylphosphonates.

The addition product methyl 2-(dimethoxyphosphoryl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (**262**) was obtained in 98% yield with $Sc(OTf)_3$ after screening a wide number of metal triflates. $Zn(OTf)_2$, $Gd(OTf)_3$, $Yb(OTf)_3$, $Nd(OTf)_3$, $Er(OTf)_3$, $Pr(OTf)_3$, $La(OTf)_3$ and $Ce(OTf)_3$ are not very effective catalysts for this reaction. These metal triflates gave the addition product **262** in 10-63% yields while $Cu(OTf)_2$ didn't give the addition product. Performing the reaction with $Y(OTf)_3$ and $Dy(OTf)_3$ increased the yield of the product to 86% and 91%, respectively. But the highest yield was obtained as 98% with $Sc(OTf)_3$ in toluene at room temperature (Table 5.7).

Table 5.7. Effect of metal triflates on Michael reaction of pyrrole with methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**)

Entry	$M(OTf)_x$	Yield (%)[a]
1	$Cu(OTf)_2$	-
2	$Zn(OTf)_2$	10
3	$Gd(OTf)_3$	65
4	$Y(OTf)_3$	86
5	$Yb(OTf)_3$	63
6	$Dy(OTf)_3$	91
7	$Nd(OTf)_3$	25
8	$Sc(OTf)_3$	98
9	$Er(OTf)_3$	48
10	$Pr(OTf)_3$	22
11	$La(OTf)_3$	30
12	$Ce(OTf)_3$	45

[a]yield refers to pure product after column chromatography.

The effect of solvent was investigated on the model addition reaction in the presence of 10 mol % of $Sc(OTf)_3$ at room temperature. When the reaction was performed in different solvents, the product **262** formed with lower yields in tetrahydrofuran, dichloromethane and acetonitrile and not formed in acetone. The highest yield was obtained in toluene (Table 5.8).

Table 5.8. Effect of solvent on Michael reaction of pyrrole with methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**)

Entry	Solvent	Yield (%)[a]
1	Toluene	98
2	THF	25
3	DCM	70
4	Acetonitrile	15
5	Acetone	-

[a]yield refers to pure product after column chromatography.

After determination of effects of solvent and catalyst, the effect of amount of catalyst on the Michael reaction was investigated. The reaction was repeated with 5, 10, 15, 20 mol % $Sc(OTf)_3$ in toluene (Table 5.9). The highest yield was obtained with 10 mol % $Sc(OTf)_3$ as 98%.

Table 5.9. Effect of amount of catalyst on Michael reaction of pyrrole with methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**)

Entry	**Mol % $Sc(OTf)_3$**	**Yield (%)[a]**
1	5	69
2	10	98
3	15	65
4	20	30

[a]yield refers to pure product after column chromatography.

Characterization of the compound methyl 2-(dimethoxyphosphoryl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (**262**) was achieved by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. Figure 5.1 shows the ^{1}H NMR spectrum of **262**. As it is seen in the spectrum the addition product **262** was obtained as a mixture of diastereoisomers. Methoxy protons of major and minor isomers appeared in the 3.33 ppm and 3.65 ppm region. The doublet of doublets at 3.75 ppm and 3.77 ppm belong to methine protons attached to phosphonate group of major and minor isomers, respectively. The benzylic methine protons observed between 4.57-4.73 ppm as multiplet for both isomers. The signals of pyrrole ring protons appeared at 5.80 ppm as broad singlet, 5.97-6.08 ppm as multiplet and 6.60 ppm as broad singlet for both isomers. Aromatic protons of phenyl ring can be seen as multiplet between 7.12-7.25 ppm for both isomers. The NH protons of major and minor isomer were observed as broad singlets at 8.66 ppm and 9.17 ppm, respectively.

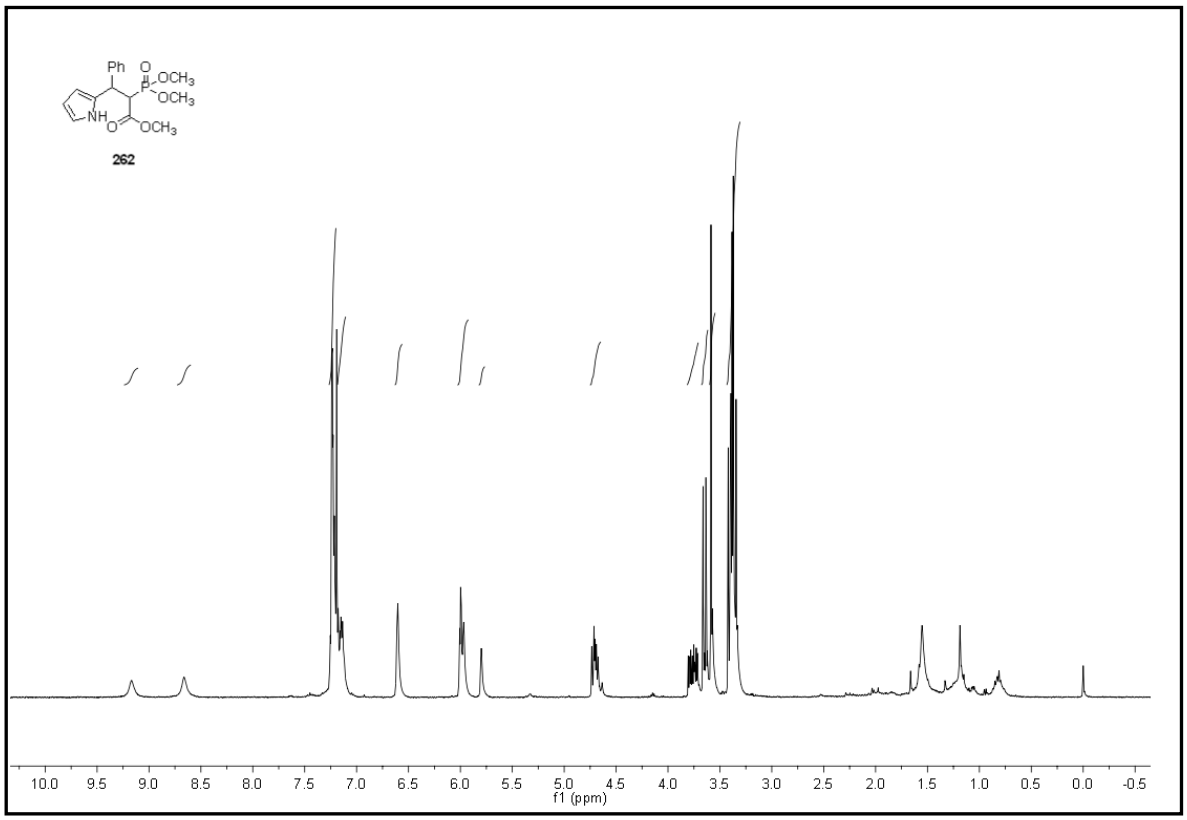


Figure 5.1. ^{1}H NMR spectrum of **262**

^{13}C NMR spectrum also confirms the suggested structure (Figure 5.2). The doublets appeared at 43.2 ppm and 43.8 ppm belongs to benzylic carbons of major and minor isomers, respectively. The methine carbons attached to phosphonate group appeared at 51.2 ppm and 52.2 ppm as doublets. The methoxy carbons of major and minor isomers appeared at 52.4 ppm, 52.8 ppm, 53.0 ppm, 53.2 ppm, 53.3 ppm and 53.6 ppm. The characteristic carbons of pyrrole ring apperared at 106.7 ppm, 107.5 ppm, 108.1 ppm, 108.4 ppm, 117.3 ppm and 117.7 ppm. The aromatic carbons of the phenyl ring observed at 127.1 ppm, 127.2 ppm, 127.9 ppm, 128.3 ppm and 128.5 ppm for both isomers. The peaks at 130.1 ppm and 130.7 ppm belong to quaternary carbons of the pyrrole rings of major and minor isomers, respectively. The quaternary carbons of the phenyl rings appeared at 140.3 ppm and 140.5 ppm for major and minor isomers. The peaks at 168.0 ppm and 169.3 ppm belong to the carbonyl groups of the minor and major isomers, respectively.

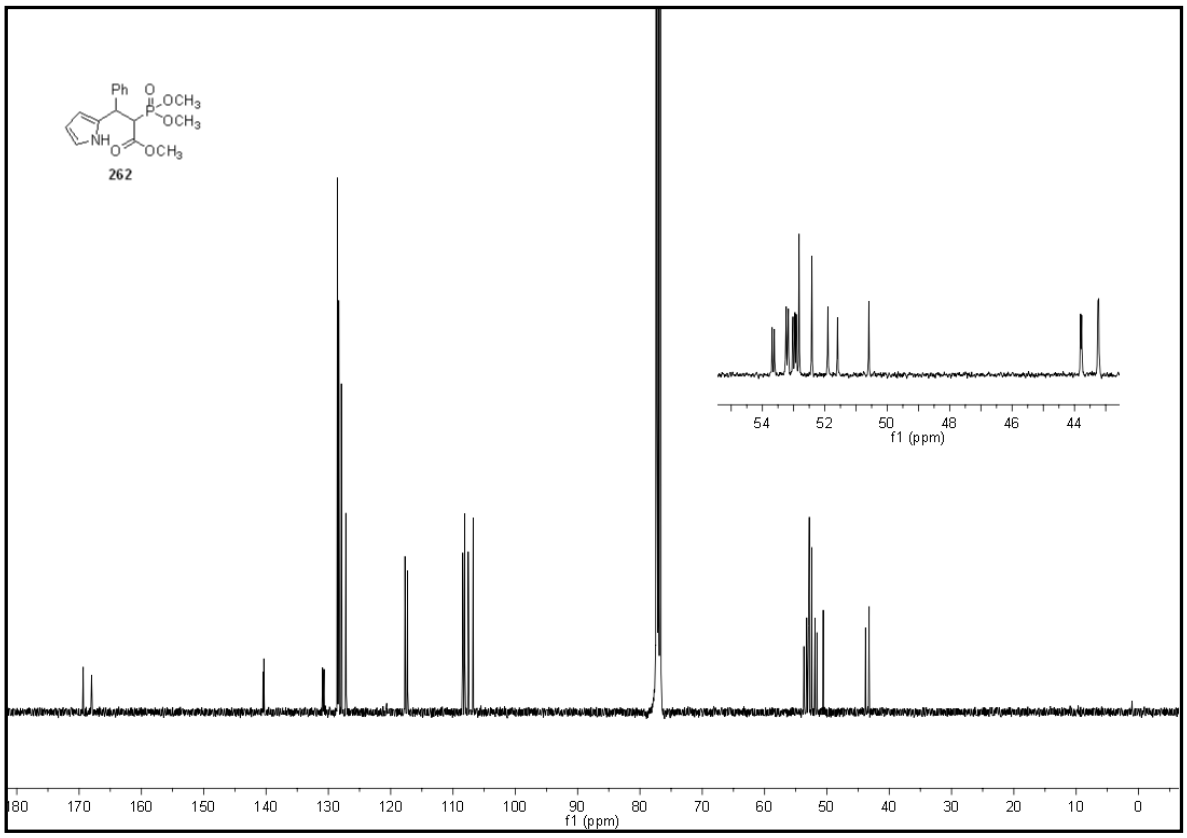


Figure 5.2. ^{13}C NMR spectrum of **262**

The two peaks at 23.5 ppm and 25.5 ppm in the ^{31}P NMR spectrum belong to the phosphorus atom in the addition products for major and minor isomers (Figure 5.3).

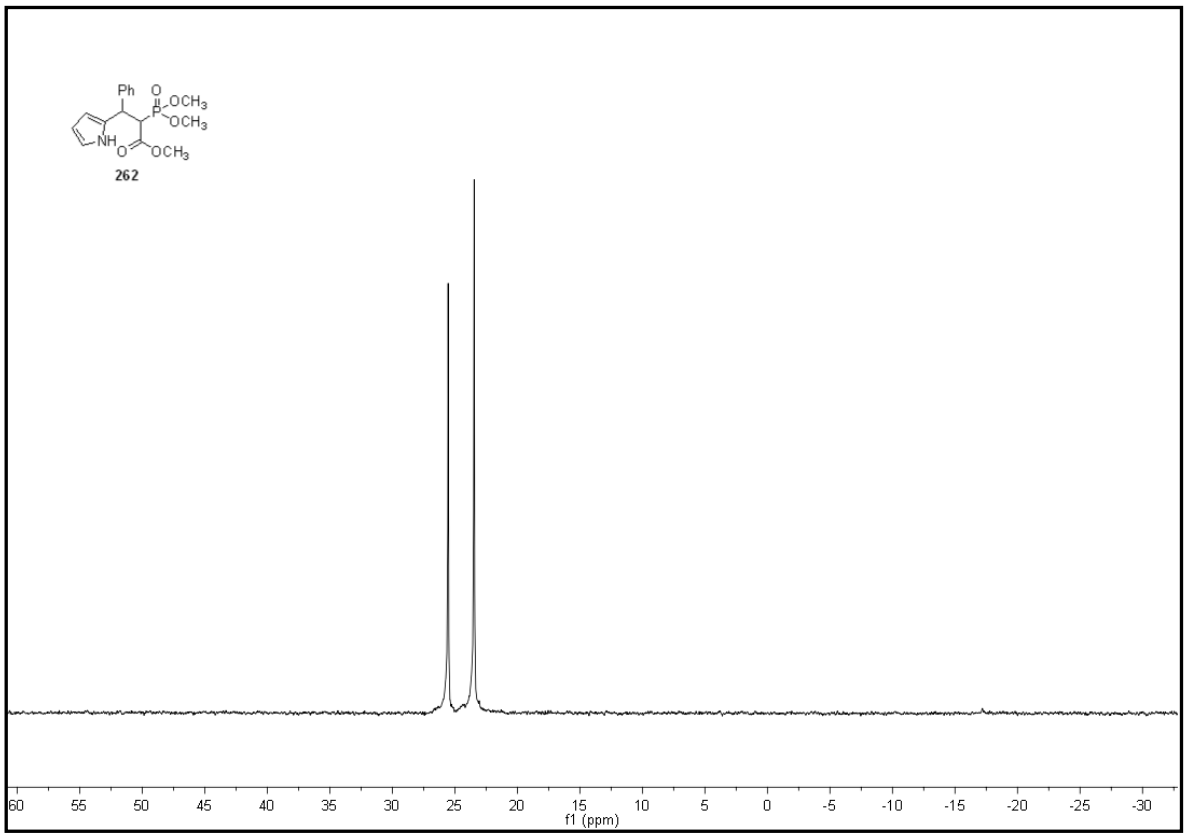
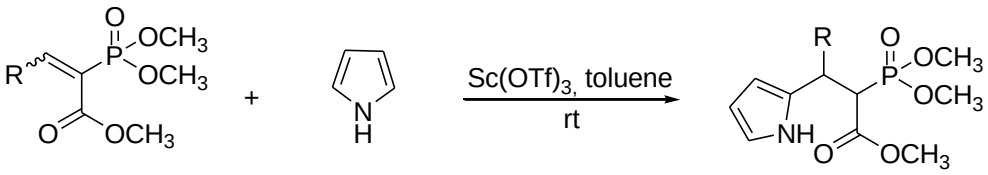


Figure 5.3. ^{31}P NMR sectrum of **262**

With the optimized conditions in hand, we performed the addition reaction of pyrrole to ester functionalized vinylphosphonates that have *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-OH, *p*-CN, *p*-NO_2, 2,4,6-trimethyl substituted phenyl ring, 2-pyrrolyl, 2-furyl, 2-thiophenyl, cyclohexyl and isobutyl substituents. The results are summarized in Table 5.10. The addition of pyrrole to *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-OH, *p*-CN and *p*-NO_2 substituted vinylphosphonates (**218-226**) gave the addition products **263-271** in 40-98% yields. An electron-withdrawing *p*-CF_3 substituent didn't affect the performance of the reaction and 98% yield was obtained. On the other hand, an electron-donating *p*-OCH_3 and *p*-OH substituents lowered the yield and gave the addition products **265** and **269** in 84% and 85% yields, respectively. The *p*-CH_3, *p*-F, *p*-Cl, *p*-Br and *p*-CN substituents gave the products **264**, **266**, **267**, **268** and **270** in 62-92% yields. The *p*-NO_2 substituted addition product **271** was obtained with lowest yield as 40%. Sterically hindered 2,4,6-trimethyl substituted vinylphosphonate **227** didn't give the addition product. The addition reactions of pyrrole to pyrrolyl, furyl and thiophenyl substituted vinylphosphonates **228-230** were also performed. Attempts at the addition of

pyrrole to these vinylphosphonates were disappointing under the optimized conditions. The starting materials were recovered in all cases and no addition product was observed. Aliphatic substituents on the vinylphosphonates are also successful in the addition reaction of pyrrole with $Sc(OTf)_3$. Cyclohexyl and isobutyl substituted vinylphosphonates gave the corresponding addition products **275** and **276** in 69% and 77% yields, respectively.

Table 5.10. Addition reaction of pyrrole to ester functionalized substituted vinylphosphonates (**217-232**)



217-232 **262-276**

Entry	R	Product	dr[a]	Yield (%)[b]
1	Phenyl	**262**	55:45	98
2	*p*-CF_3-phenyl	**263**	61:39	98
3	*p*-CH_3-phenyl	**264**	51:49	92
4	*p*-OCH_3-phenyl	**265**	55:45	84
5	*p*-F-phenyl	**266**	65:35	62
6	*p*-Cl-phenyl	**267**	53:47	78
7	*p*-Br-phenyl	**268**	51:49	86
8	*p*-OH-phenyl	**269**	56:44	85
9	*p*-CN-phenyl	**270**	54:46	72
10	*p*-NO_2-phenyl	**271**	52:48	40
11	2,4,6-trimethylphenyl	**-**	-	-
12	2-pyrrolyl	**272**	-	-
13	2-furyl	**273**	-	-
14	2-thiophenyl	**274**	-	-
15	cyclohexyl	**275**	61:39	69
16	isobutyl	**276**	65:35	77

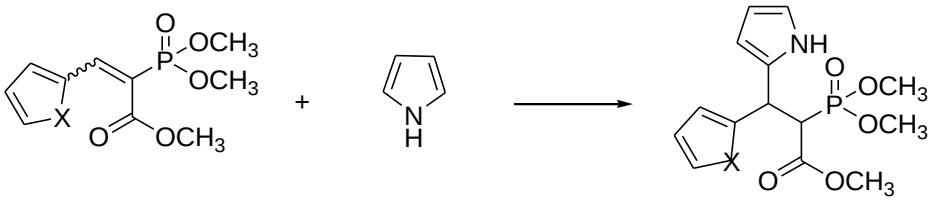
[a]diastereomeric ratios are determined from NMR spectra.
[b]yield refers to pure product after column chromatography.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-OH, *p*-CN, *p*-NO_2, cyclohexyl and isobutyl substituted addition products **263-271,275-276** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of these addition products are given in Figure A.133-A.159, A.169-A.174 (page 246-259,264-266).

To obtain the addition products **272-274**; the catalytic activities of $InCl_3$, TFA, HCl, Montmorillonite K-10 and Montmorillonite KSF were searched beside $Sc(OTf)_3$ and $Cu(OTf)_2$, on the addition reaction of pyrrole to pyrrolyl, furyl and thiophenyl substituted vinylphosphonates **228-230** (Table 5.11). $Cu(OTf)_2$ and TFA catalyzed the addition reaction of pyrrole to methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)acrylate (**228**) and the addition product methyl 2-(dimethoxy- phosphoryl)-3,3-di(1*H*-pyrrol-2-yl)propanoate (**272**) was obtained in 15% and 45% yields, respectively. $Sc(OTf)_3$, $InCl_3$, HCl, Montmorillonite K-10 and Montmorillonite KSF didn't catalyze the addition reaction of pyrrole to methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)acrylate (**228**). The addition reactions of pyrrole to furyl and thiophenyl substituted vinylphosphonates (**229-230**) were catalyzed by Montmorillonite K-10 in 25% and 30% yields. But the addition products methyl 2-(dimethoxyphosphoryl)-3-(furan-2-yl)-3-(1*H*-pyrrol-2-yl)propanoate (**273**) and methyl 2-(dimethoxyphosphoryl)-3-(1*H*-pyrrol-2-yl)-3-(thiophen-2-yl)propanoate (**274**) couldn't be obtained as pure compounds because of the same R_f values with the starting materials (**229-230**).

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of 2-pyrrolyl, 2-furyl and 2-thiophenyl substituted addition products **272-274** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of these addition products are given in Figure A.160-A.168 (page 259-263).

Table 5.11. Addition reactions of pyrrole to pyrrolyl, furyl and thiophenyl substituted vinylphosphonates **228-230**



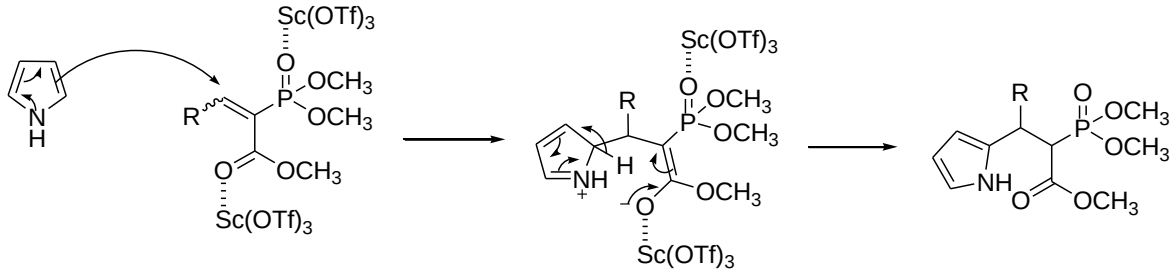
X = NH (**228**)
X = O (**229**)
X = S (**230**)

X = NH (**272**)
X = O (**273**)
X = S (**274**)

Entry	Catalyst	Solvent	272	273	274
1	$Sc(OTf)_3$	Toluene	-	-	-
2	$Cu(OTf)_2$	Toluene	-	-	-
3	$InCl_3$	Toluene	-	-	-
4	TFA	Toluene	-	-	-
5	HCl	Toluene	-	-	-
6	Mont. K-10	Toluene	-	-	-
7	Mont. KSF	Toluene	-	-	-
8	$Sc(OTf)_3$	Pyrrole	-	-	-
9	$Cu(OTf)_2$	Pyrrole	15[a]	-	-
10	$InCl_3$	Pyrrole	-	-	-
11	TFA	Pyrrole	45[a]	-	-
12	HCl	Pyrrole	-	-	-
13	Mont. K-10	Pyrrole	-	25[b]	30[b]
14	Mont. KSF	Pyrrole	-	-	-

[a]yields refer to pure product after column chromatography.
[b]yields are determined from NMR spectra.

The proposed reaction mechanism for the metal triflate catalyzed reaction of ester vinylphosphonate with pyrrole is given in Scheme 5.8. In the first step, vinylphosphonate is activated by the coordination of metal triflate to carbonyl and phosphonate oxygen. The addition of pyrrole to the activated vinylphosphonate affords the addition products.

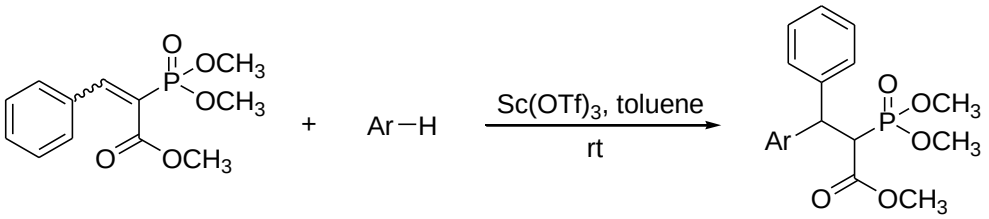


Scheme 5.8. The proposed reaction mechanism for the $Sc(OTf)_3$ catalyzed reaction of vinylphosphonate with pyrrole.

When the addition reaction of pyrrole to **217** was performed without using the $Sc(OTf)_3$, addition product **262** did not form. This result indicated that $Sc(OTf)_3$ has a crucial role for the activation of double bond in the molecule.

The Michael addition of indole, furan, thiophene and substituted pyrroles to methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**) were searched. When *N*-methylpyrrole was employed, a sharp decrease was observed in the yield of the addition product. With *N*-phenylpyrrole, no addition product was observed even after 96 hours. These results showed us that substituents on pyrrole nitrogen complicated the reaction. On the indole side, the addition product **278** was obtained with 99% yield as a diastereomeric mixture. However the addition reactions of furan and thiophene to methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**) didn't give the desired products under the optimized conditions. Addition reactions to methyl 2-(dimethoxyphosphoryl)-3-phenylacrylate (**217**) were performed with substituted pyrroles that have electron-donating and electron-withdrawing substituents. Electron-donating 2,4-dimethyl and 2,4-dimethyl-3-ethyl on pyrrole ring gave the addition products **279** and **280** in 99% yields. Electron-withdrawing substituents cyano, formyl and acetyl on the 2-position of pyrrole didn't give the expected addition products.

Table 5.12. Addition reaction of heteroaromatics to methyl 2-(dimethoxy-phosphoryl)-3-phenylacrylate (**217**)



217 **277-280**

Entry	Ar	Product	dr[a]	Yield (%)[b]
1	*N*-methylpyrrolyl	**277**	57:43	58
2	*N*-phenylpyrrolyl	**-**	-	-
3	indolyl	**278**	60:40	99
4	furyl	**-**	-	-
5	thiophenyl	**-**	-	-
6	2,4-dimethylpyrrolyl	**279**	58:42	99
7	2,4-dimethyl-3-ethylpyrrolyl	**280**	94:6	99
8	2-cyanopyrrolyl	**-**	-	-
9	2-formylpyrrolyl	**-**	-	-
10	2-acetylpyrrolyl	**-**	-	-

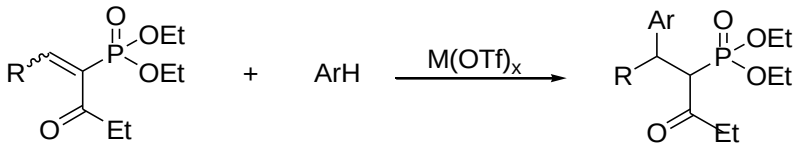
[a]diastereomeric ratios are determined from NMR spectra.
[b]yield refers to pure product after column chromatography.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *N*-methylpyrrolyl, indolyl, 2,4-dimethylpyrrolyl and 2,4-dimethyl-3-ethylpyrrolyl substituted addition products **277-280** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of these addition products are given in Figure A.175-A.186 (page 275-280).

As they are seen in the NMR spectra, the addition products **262-280** were obtained as mixture of diastereomers. To determine the kinetic or thermodynamic control on these diastereomers, several experiments were carried out at different temperatures. We performed the addition reaction of pyrrole to **223** and the addition product **268** were obtained with 40:60, 48:52, 49:51 ratios at -70 °C, rt, 100 °C, respectively. These results indicated that temperature change has no clear effect on diastereoselectivity and formation of the addition product is thermodynamically controlled.

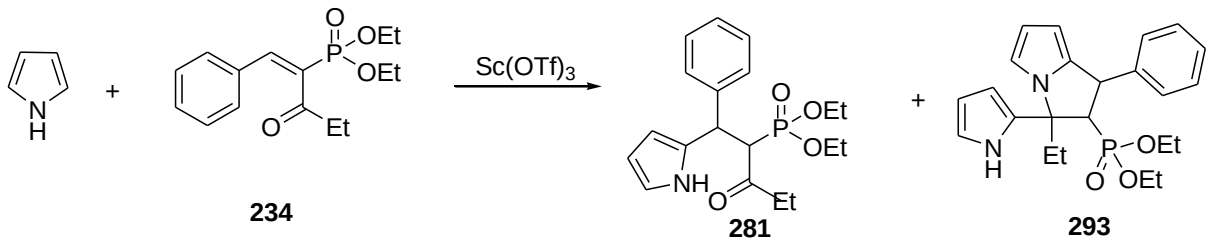
5.2.2. Michael addition reactions of heteroaromatics to ketone functionalized vinylphosphonates

Ketone functionalized vinylphosphonates were used as Michael acceptors in this part of the work. Metal triflates were employed as catalysts in the additions of heteroaromatics to ketone functionalized vinylphosphonates (Scheme 5.9).



Scheme 5.9. Michael addition reaction to ketone functionalized vinylphosphonates with metal triflates.

The addition of pyrrole to *E*-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**) was chosen as a model reaction to optimize the reaction conditions (Scheme 5.10). Firstly the addition reaction of pyrrole to *E*-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**) was performed by using 10 equivalent of pyrrole with 10 mol % $Sc(OTf)_3$ in toluene at room temperature in order to obtain the addition product **281**. However, we obtained the cyclization product **293** as major product and the expected addition product **281** was formed as minor product.

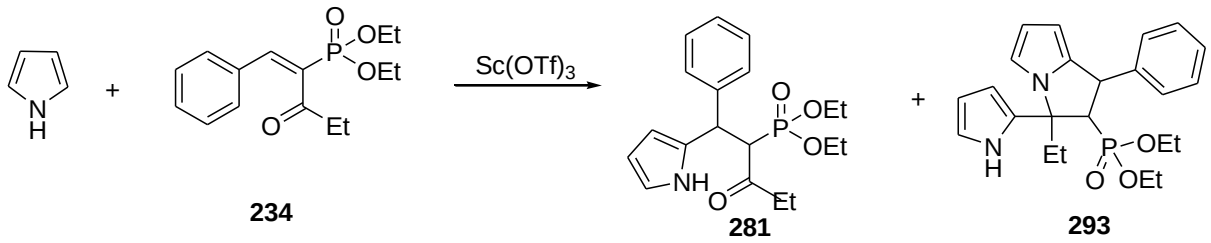


Scheme 5.10. The model reaction to optimize the conditions of addition reaction of pyrrole to ketone functionalized vinylphosphonates.

After this examination, we focused on obtaining the addition product **281** as the major product from the reaction of pyrrole and *E*-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**). We performed the reaction of pyrrole with **234** by using different pyrrole/**234** ratios (1, 2, 5, 10 and 40) in the presence of $Sc(OTf)_3$ (10 mol

%) at rt. These results showed that the addition product **281** was obtained as a minor product in 24h at rt in all ratios. By increasing the temperature to 50 °C and performing the reaction with 10 mole % $Sc(OTf)_3$, only **281** was obtained in 40% yield after 15 min. At longer reaction times the yield of the addition product **281** decreases while the cyclization product **293** increases. Neither the addition product nor the cyclization product was obtained when the reaction was performed at reflux. Performing the reaction in THF, chloroform and acetonitrile afforded the **281** in 18%, 33% and 38% yields, respectively (Table 5.13).

Table 5.13. Optimization of the reaction conditions for the addition of pyrrole to *E*-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**)

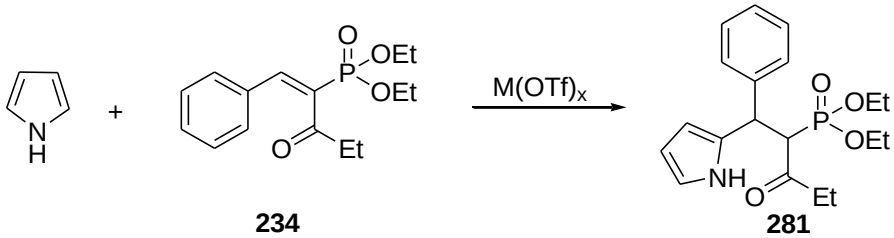


Entry	Solvent	Mole ratio Pyrrole/234	Temperature	Time	Yield (%) 281[a]	Yield (%) 293[a]
1	Toluene	1	rt	24h	10	12
2	Toluene	2	rt	24h	14	19
3	Toluene	5	rt	24h	20	30
4	Toluene	10	rt	24h	23	36
5	Toluene	40	rt	24h	5	40
6	Toluene	10	50 °C	15min	40	-
7	Toluene	10	50 °C	30min	38	5
8	Toluene	10	50 °C	45min	30	12
9	Toluene	10	50 °C	3h	20	40
10	Toluene	10	50 °C	6h	12	50
11	-[b]	40	50 °C	15min	38	5
12	Toluene	1	reflux	15min	-	-
13	THF	10	50 °C	15min	18	-
14	Chloroform	10	50 °C	15min	33	-
15	Acetonitrile	10	50 °C	15min	38	-

[a]yield refers to pure product after column chromatography.
[b]reaction was carried out in excess pyrrole as solvent.

To investigate the effects of metal triflates, the reactions of pyrrole and *E*-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**) were carried out in the presence of metal triflates with 10 mol % pyrrole at 50 °C in 15 min. Among the tested metal triflates, $Sc(OTf)_3$ gave the highest yield of diethyl 3-oxo-1-phenyl-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (**281**) (Table 5.14).

Table 5.14. Effect of metal triflates on Michael reaction of pyrrole with *E*-diethyl 3-oxo-1-phenylpent-1-en-2-ylphosphonate (**234**)



234 **281**

Entry	$M(OTf)_x$	Yield (%)[a]
1	$Sc(OTf)_3$	40
2	$Gd(OTf)_3$	9
3	$Dy(OTf)_3$	4
4	$Y(OTf)_3$	5

[a]yield refers to pure product after column chromatography.

Identification of the compound **281** was achieved by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. Figure 5.4 shows the ^{1}H NMR spectrum of diethyl 3-oxo-1-phenyl-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (**281**). Methyl protons of ethyl group appeared as triplet at 0.75 ppm and 0.90 ppm for major and minor isomers, respectively. Methyl protons of ethoxy groups appeared as triplets at 1.11 ppm and 1.13 ppm for minor isomer and at 1.16 ppm and 1.25 ppm for major isomer. Methylene protons of ethyl group gave doublet of quartets at 2.13 ppm and 2.40 ppm for major isomer and at 2.25 and 2.65 for minor isomer. Multiplets between 3.60-3.70 ppm, 3.76-3.89 ppm and 3.94-4.03 ppm belong to methylene protons of ethoxy groups and methine protons attached to phosphonate group in major and minor isomers. The benzylic methine protons observed at 4.77 ppm as doublet of doublet for both isomers. Pyrrole ring protons gave broad singlets at 5.79 ppm and 5.92 ppm for major and minor isomers and multiplets between 5.98-

6.01 ppm and 6.61-6.63 ppm for both isomers. The multiplets between 7.14-7.18 ppm and 7.23-7.29 ppm belong to aromatic protons of phenyl ring for both isomers. The NH protons of major and minor isomers appeared as broad singlets at 8.94 ppm and 9.46 ppm, respectively.

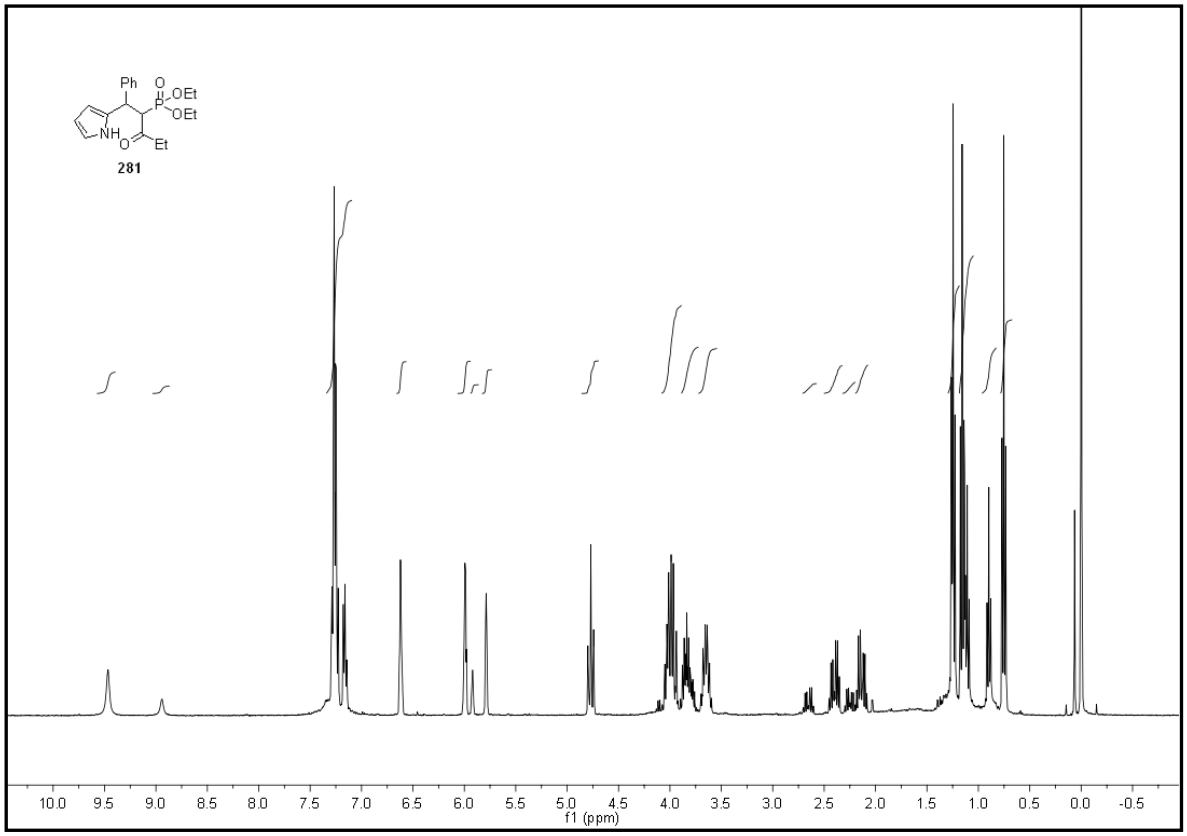


Figure 5.4. ^{1}H NMR spectrum of **281**

^{13}C NMR spectrum is also in agreement with the structure (Figure 5.5). Methyl carbons of ethyl group appeared at 7.3 ppm and 7.4 ppm for major and minor isomers, respectively. Methyl carbons of ethoxy groups appeared at 16.1 ppm as dublet for both isomers. Methylene carbons of ethyl group appeared at 37.4 ppm and 38.2 ppm for major and minor isomers, respectively. The benzylic carbon of minor and major isomers appeared at 43.3 ppm and 43.6 ppm as dublet. The doublets appeared at 58.1 ppm and 58.8 ppm belong to methine carbons attached to phosphonate group of minor and major isomers, respectively. The methylene carbons of ethoxy groups appeared at 61.9 ppm, 62.0 ppm, 62.2 ppm and 62.5 ppm. The characteristic carbons of pyrrole ring appeared at 106.7 ppm, 107.4 ppm, 108.1 ppm, 108.2 ppm 116.8 ppm and 117.1 ppm. The aromatic carbons of

the phenyl ring observed at 126.7 ppm, 126.8 ppm, 128.0 ppm, 128.2 ppm, 128.3 ppm and 128.4 ppm for both isomers. The peaks at 130.7 ppm and 130.7 ppm belong to quaternary carbons of the pyrrole rings of minor and major isomers, respectively. The quaternary carbons of the phenyl rings appeared at 140.8 ppm and 140.9 ppm for minor and major isomers. The peaks at 204.4 ppm and 206.7 ppm belong to the carbonyl groups of the major and minor isomers, respectively.

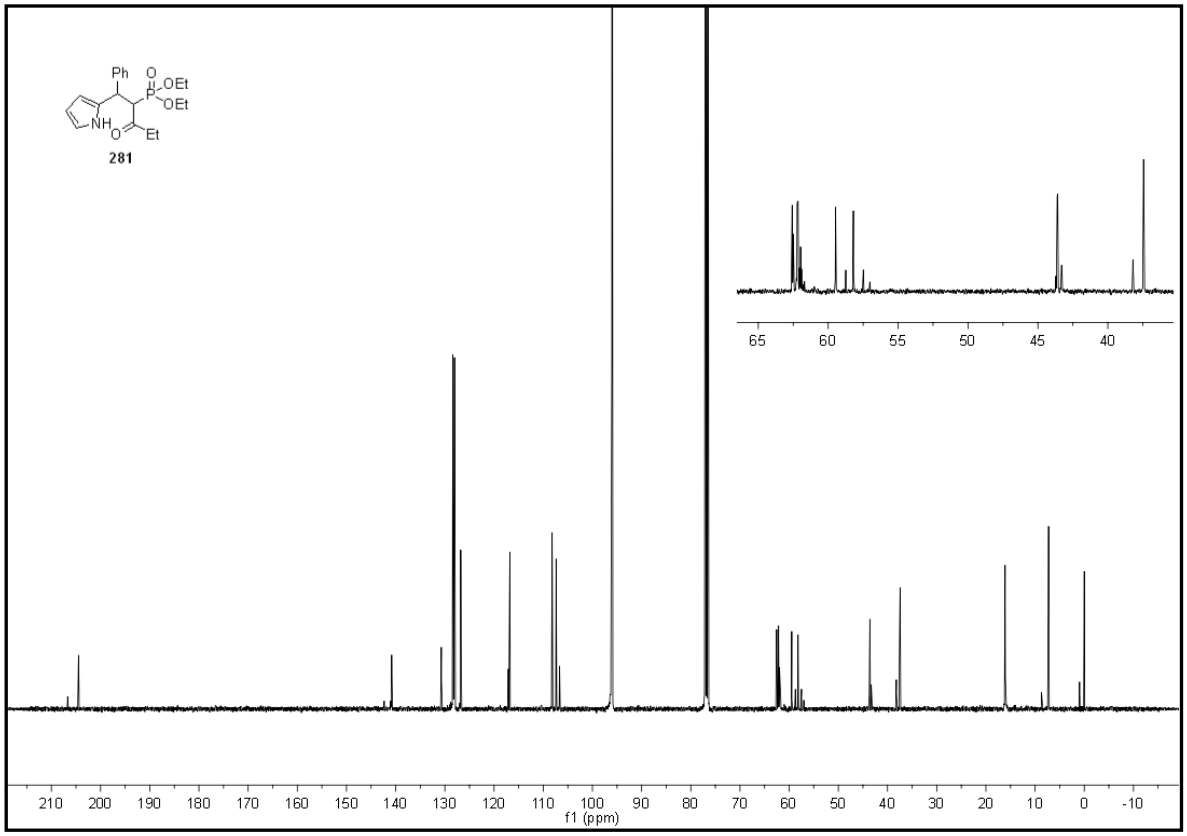


Figure 5.5. ^{13}C NMR spectrum of **281**

The two peaks appeared at 20.2 ppm and 23.0 ppm in the ^{31}P NMR spectrum of **281** indicate the phosphorus atoms in the addition products for minor and major isomers (Figure 5.6).

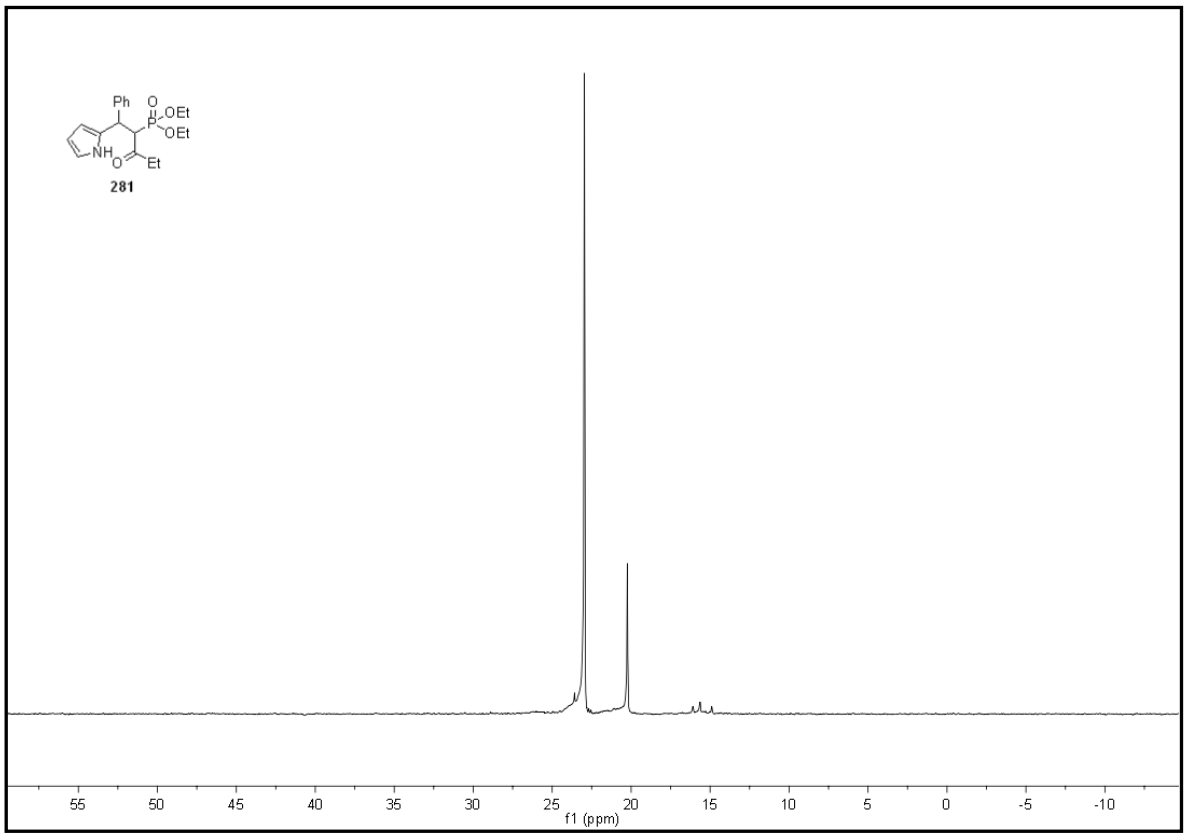


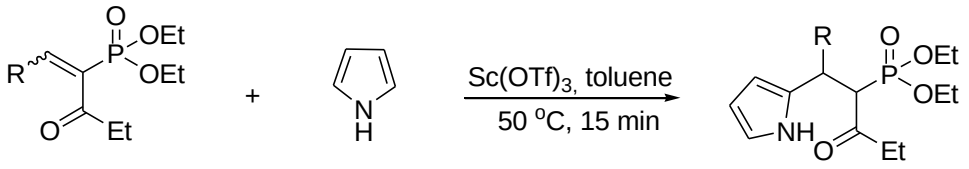
Figure 5.6. ^{31}P NMR spectrum of **281**

We continued to study the effect of substituents on the reaction of pyrrole with the ketone functionalized vinylphosphonates using $Sc(OTf)_3$ in toluene at 50 °C in 15 min. Reactions of ketone functionalized phosphonates **234-246** and pyrrole with $Sc(OTf)_3$ gave 2-alkylated pyrrole derivatives **281-292** in 15-73% yields (Table 5.15). The highest yield was obtained with p-Br-phenyl substituted vinylphosphonate (**239**) as 73%. Electron-withdrawing substituents *p*-CF_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN and *p*-NO_2 on phenyl ring gave the corresponding addition products in 25-73% yields. Electron-donating substituents *p*-CH_3 and *p*-OCH_3 on phenyl ring produced the addition products in 50% and 52% yields. Sterically hindered 2,4,6-trimethyphenyl substituted vinylphosphonate didn't give the expected product. With 2-pyrrolyl, 2-furyl and 2-thiophenyl substituted vinylphosphonates, 15%, 38% and 62% yields are observed, respectively.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN, *p*-NO_2, 2-pyrrolyl, 2-furyl and 2-thiophenyl substituted addition products **282-292** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P

NMR spectra of these addition products are given in Figure A.187-A.219 (page 273-289).

Table 5.15. Addition reaction of pyrrole to ketone functionalized substituted vinylphosphonates (**234-246**).



234-246 **281-292**

Entry	R	Product	dr[a]	Yield (%)[b]
1	Phenyl	**281**	74:26	40
2	*p*-CF_3-phenyl	**282**	50:50	45
3	*p*-CH_3-phenyl	**283**	51:49	50
4	*p*-OCH_3-phenyl	**284**	58:42	52
5	*p*-F-phenyl	**285**	58:42	27
6	*p*-Cl-phenyl	**286**	52:48	54
7	*p*-Br-phenyl	**287**	55:45	73
8	*p*-CN-phenyl	**288**	54:46	40
9	*p*-NO_2-phenyl	**289**	59:41	25
10	2,4,6-trimethylphenyl	**-**	-	-
11	2-pyrrolyl	**290**	-	15
12	2-furyl	**291**	78:22	38
13	2-thiophenyl	**292**	60:40	62

[a]diastereomeric ratios are determined from NMR spectra.
[b]yield refers to pure product after column chromatography.

We next turned our attention to the cyclization product which was obtained in the addition reaction. We have planned to synthesize the pyrrolizine structures from the cyclization reaction of addition products. However, we obtain pyrrole substituted pyrrolizine beside addition products. The reaction didn't stop at the addition step in longer reaction times. Ketone moiety on addition product gave the reaction with pyrrole nitrogen and with second pyrrole molecule. The cyclization product diethyl 3-ethyl-1-phenyl-3-(1H-pyrrol-2-yl)-2,3-dihydro-1H-pyrrolizin-2-ylphosphonate (**293**) was obtained in 50% yield at 50 °C in 6h with a small amount of addition product **281**.

Characterization of the cyclization product diethyl 3-ethyl-1-phenyl-3-(1*H*-pyrrol-2-yl)-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (**293**) was performed by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. Figure 5.7 shows the ^{1}H NMR spectrum of diethyl 3-ethyl-1-phenyl-3-(1H-pyrrol-2-yl)-2,3-dihydro-1H-pyrrolizin-2-ylphosphonate (**293**). Methyl protons of ethoxy groups appeared as triplets at 0.68 ppm and 0.94 ppm. Methyl protons of ethyl group appeared as triplet at 1.00 ppm. Methylene protons of ethyl group gave doublet of quartets at 2.47 ppm and 2.67 ppm. Methine proton attached to phosphonate group appeared at 3.11 ppm as doublet of doublet. Multiplets between 3.31-3.46 ppm, 3.56-3.62 ppm and 3.63-3.71 ppm belong to methylene protons of ethoxy groups. The benzylic methine proton observed at 4.41 ppm as doublet of doublet. Pyrrole ring protons gave broad singlets at 5.27 ppm, 5.59 ppm, doublet of triplets at 5.94 ppm, 6.22 ppm, 6.63 ppm and a broad doublet at 6.55 ppm. The multiplet between 7.20-7.27 ppm belong to aromatic protons of phenyl ring. The NH proton appeared as broad singlet at 8.98 ppm.

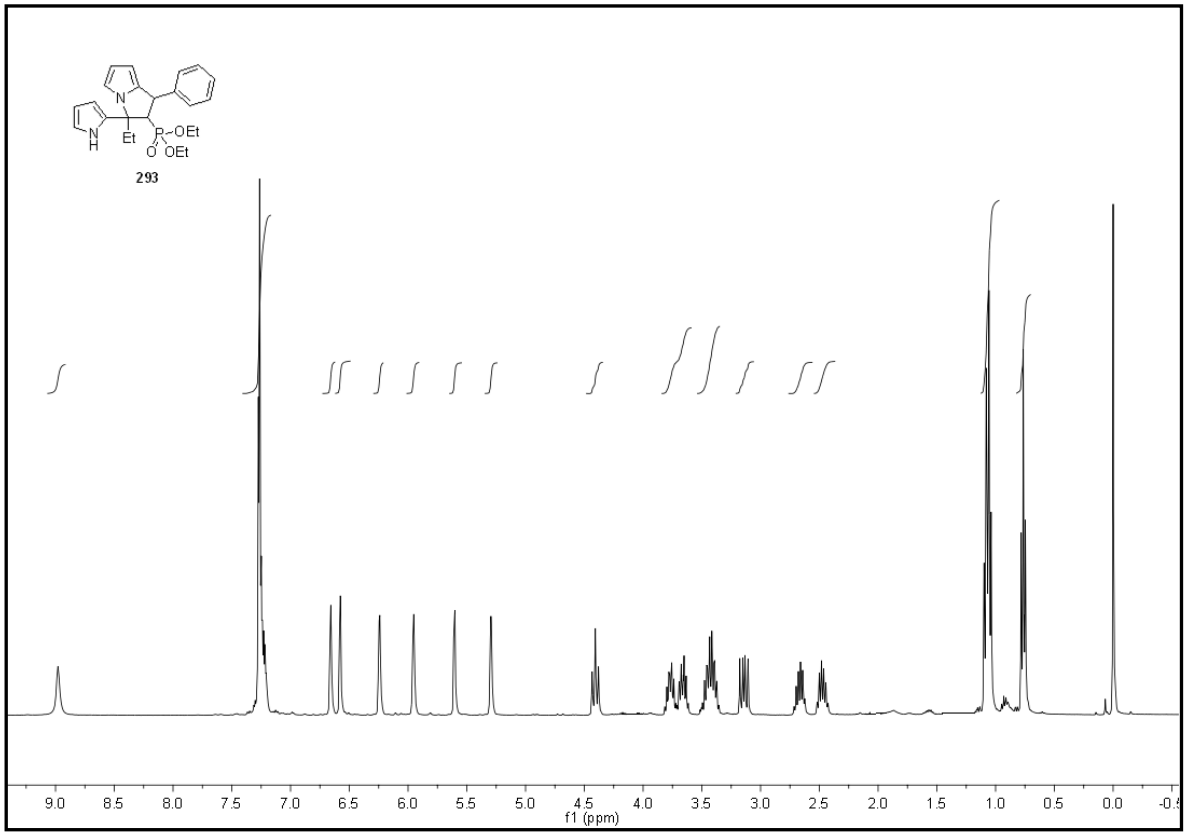


Figure 5.7. ^{1}H NMR spectrum of **293**

^{13}C NMR spectrum is also in agreement with the structure (Figure 5.8). Methyl carbon of ethyl group appeared at 8.2 ppm. Methyl carbons of ethoxy groups appeared at 15.6 ppm and 16.1 ppm as doublets. Methylene carbon of ethyl group appeared at 30.5 ppm. The benzylic carbon was appeared at 44.8 ppm as doublet. The doublet appeared at 56.7 ppm belong to methine carbon attached to phosphonate group. The methylene carbons of ethoxy groups appeared at 61.2 ppm and 61.7 ppm as doublets. The quaternary carbon attached to both pyrrole ring and ethyl group appeared at 67.1 ppm. Pyrrole ring carbons appeared at 99.6 ppm, 107.1 ppm, 107.8 ppm, 112.6 ppm, 112.7 ppm and 117.9 ppm. The aromatic carbons of the phenyl ring observed at 127.1 ppm, 128.2 ppm, 128.7 ppm. The doublet peaks at 133.0 ppm and 139.1 ppm belong to quaternary carbons of the pyrrole rings. The quaternary carbon of the phenyl ring appeared at 141.4 ppm.

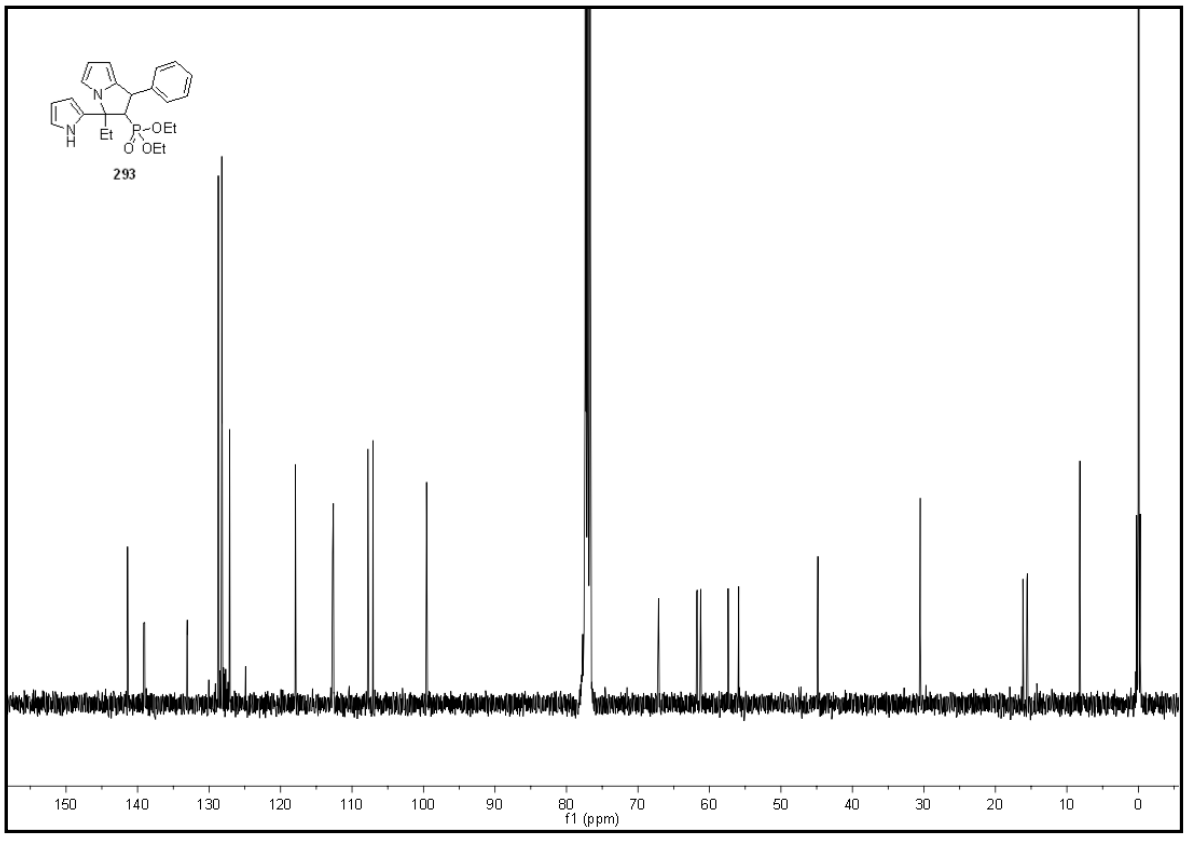


Figure 5.8. ^{13}C NMR spectrum of **293**

The phosphorus atom in the structure **293** appeared at 23.8 ppm in the ^{31}P NMR spectrum (Figure 5.9).

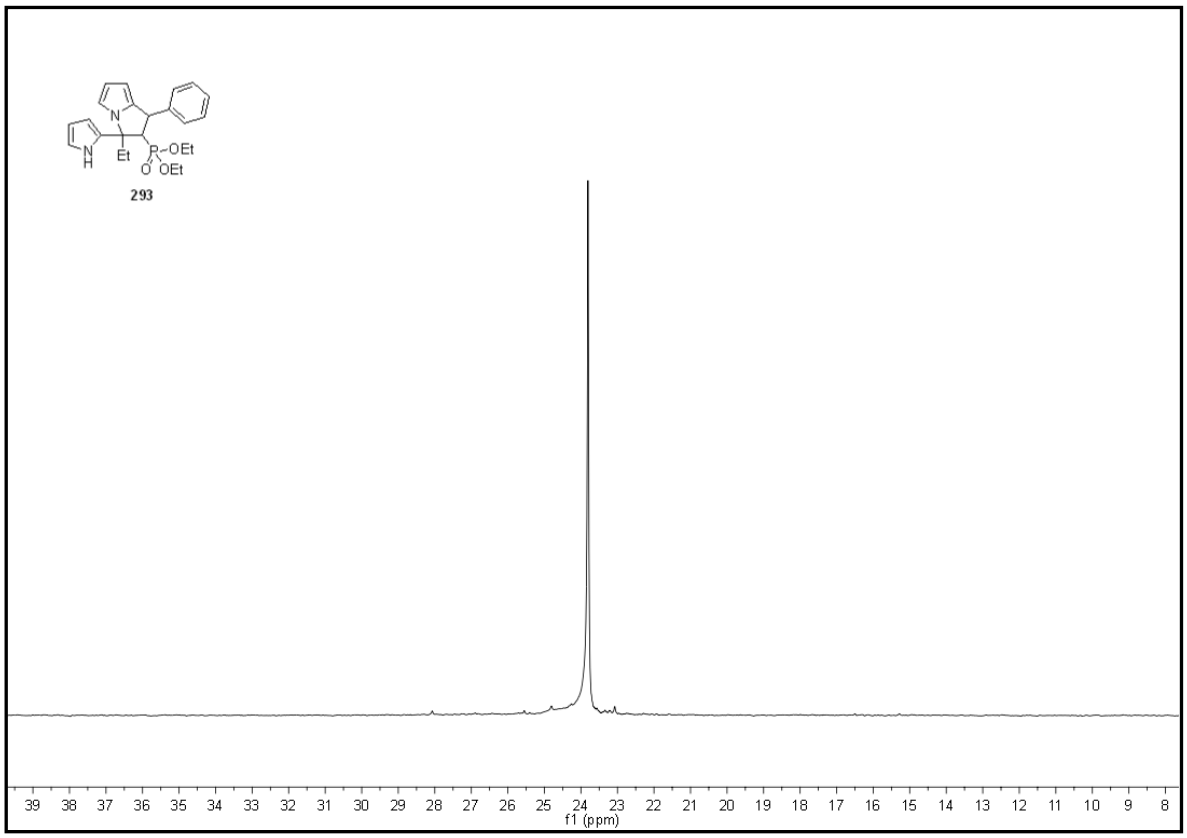
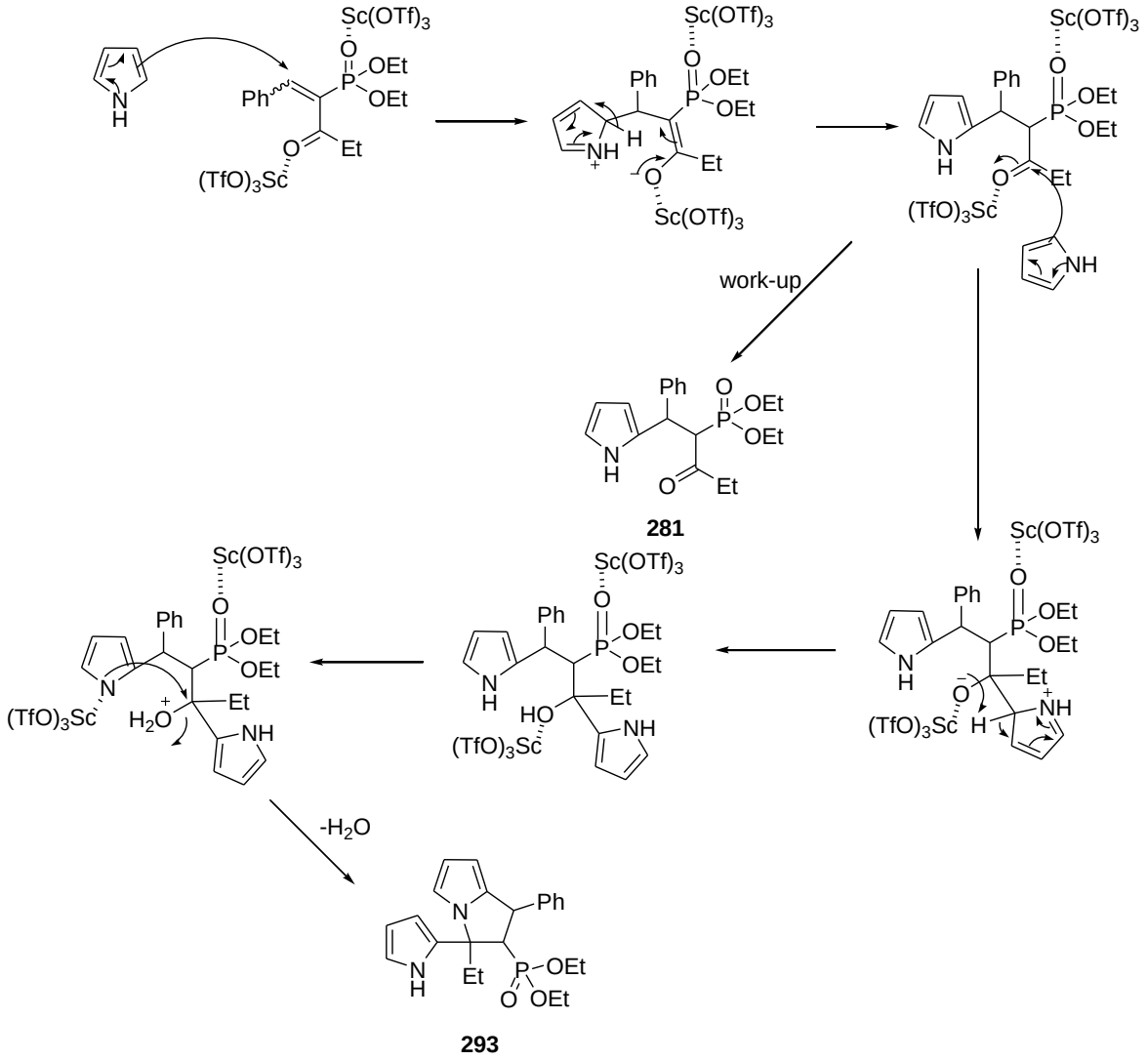


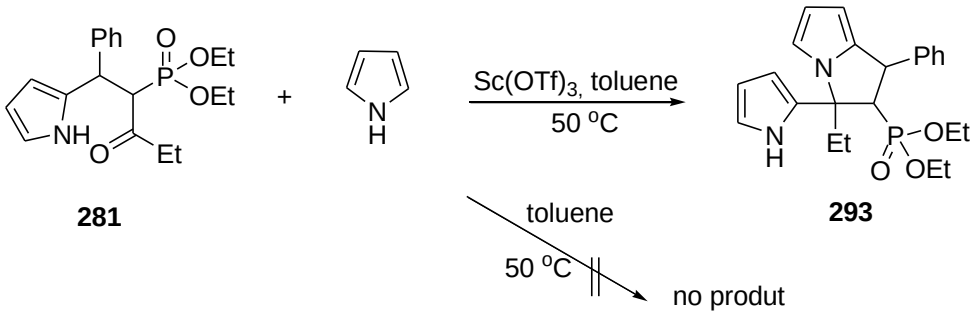
Figure 5.9. ^{31}P NMR spectrum of **293**

The proposed reaction mechanism for the metal triflate catalyzed reaction of ketone vinylphosphonate with pyrrole is given in Scheme 5.11. In the first step, vinylphosphonate is activated by $Sc(OTf)_3$. The addition of pyrrole to the activated vinylphosphonate complex yielded only addition product **281** if the reaction was stopped at 15 min. If we didn't stop the reaction in 15 min, second pyrrole molecule adds to carbonyl carbon of activated addition product and subsequent intramolecular substitution reaction gives the cyclization product **293** (Scheme 5.11).



Scheme 5.11. Proposed mechanism for the formation of addition (**281**) and cyclization (**293**) products by the reaction of vinylphosphonate and pyrrole.

To support this mechanism some experiments were done (Scheme 5.12). Firstly; the isolated addition product **281** reacted with pyrrole under the same reaction conditions. Formation of the cyclization product **293** was observed after 6h. Then, the same reaction was performed without using $Sc(OTf)_3$ and cyclization product **293** was not obtained.

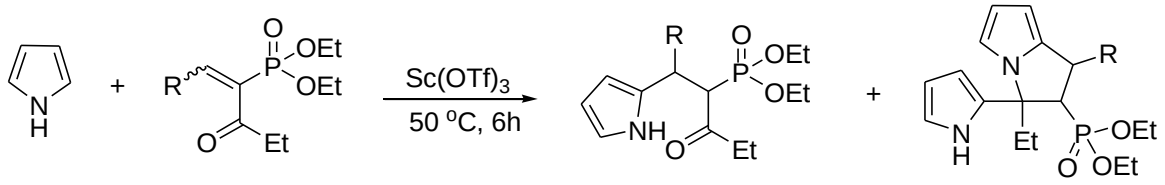


Scheme 5.12. Reaction of pyrrole with **281** in the presence of $Sc(OTf)_3$ and in the absence of $Sc(OTf)_3$.

We employed the reaction conditions to the substituted ketone functionalized vinylphosphonates (Table 5.16). Reactions of ketone functionalized phosphonates **234-246** and pyrrole were performed in the presence of $Sc(OTf)_3$ at 50 °C in 6h. The cyclization products **293-303** were obtained in 13-63% yields. The highest yield was obtained with electron-donating *p*-CH_3-phenyl substituted vinylphosphonate as 63%. The lowest yields were obtained as 13% with electron-withdrawing *p*-CN-phenyl vinylphosphonate and 2-furyl substituted vinylphosphonate. 2,4,6-trimethylphenyl substituted vinylphosphonate didn't give corresponding the addition and cyclization products.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN, *p*-NO_2, 2-pyrrolyl, 2-furyl and 2-thiophenyl substituted cyclization products **294-303** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of these addition products are given in Figure A.220-A.249 (page 289-304).

Table 5.16. Reaction of pyrrole with ketone functionalized substituted vinylphosphonates (**234-246**)



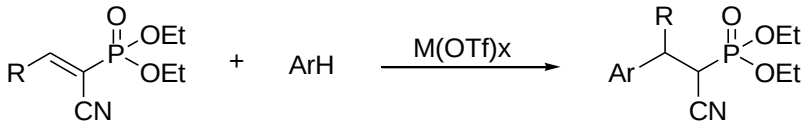
234-246 **281-292** **293-303**

Entry	R	Addition/ Cyclization	Yield (%)[a]
1	Phenyl	**281/293**	12/50
2	*p*-CF_3-phenyl	**282/294**	30/27
3	*p*-CH_3-phenyl	**283/295**	5/63
4	*p*-OCH_3-phenyl	**284/296**	7/40
5	*p*-F-phenyl	**285/297**	10/56
6	*p*-Cl-phenyl	**286/298**	15/44
7	*p*-Br-phenyl	**287/299**	35/20
8	*p*-CN-phenyl	**288/300**	15/13
9	*p*-NO_2-phenyl	**289/301**	65/15
10	2,4,6-trimethylphenyl	**-**	-
11	2-pyrrolyl	**-**	-[b]
12	2-furyl	**291/302**	25/13
13	2-thiophenyl	**292/303**	27/31

[a]yield refers to pure product after column chromatography.
[b]Both of the products decomposed and couldn't be isolated in column chromatography.

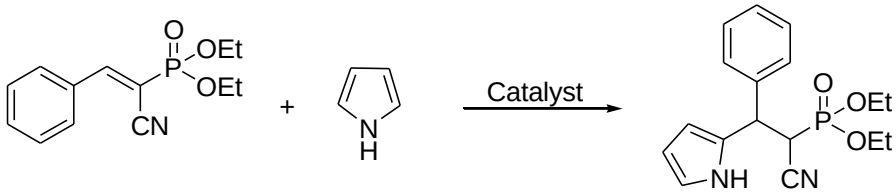
5.2.3. Michael addition reactions of heteroaromatics to cyano functionalized vinylphosphonates

Cyano functionalized vinylphosphonates are the last Michael acceptors to be worked. They were employed in the addition reaction of heteroaromatics to obtain different phosphonate analogues (Scheme 5.13).



Scheme 5.13. Michael addition reaction to cyano functionalized vinylphosphonates with metal triflates.

The addition of pyrrole to *E*-diethyl 1-cyano-2-phenylvinylphosphonate (**248**) was chosen as a model reaction to optimize the reaction conditions (Scheme 5.14).



248 **304**

Scheme 5.14. The model reaction to optimize the conditions of addition reaction of pyrrole to cyano functionalized vinylphosphonates.

The addition of pyrrole to *E*-diethyl 1-cyano-2-phenylvinylphosphonate (**248**) was performed firstly in the presence of $Sc(OTf)_3$ as it is known as the active metal triflate for vinylphosphonates. However, $Sc(OTf)_3$ gave the expected addition product **304** only in 18% yield in toluene with 10 mol % pyrrole at rt. To increase the yield of the reaction, we searched a significant number of different catalysts such as; metal triflates, metal chlorides, acids and clays (Table 5.17). Among the tested catalysts $Sc(OTf)_3$, TFA and Mont. K-10 gave the addition products in very low yields as 18%, 15% and 10%, respectively. When we performed the reaction at 50 °C, the yield of the addition product increased to 45%.

Table 5.17. Effect of catalyst on Michael reaction of pyrrole with diethyl 1-cyano-2-phenylvinylphosphonate (**248**)

Entry	Catalyst	Yield (%)[a]
1	$Sc(OTf)_3$	18
2	$Sc(OTf)_3$	45[b]
3	$Cu(OTf)_2$	-
4	$Gd(OTf)_3$	-
5	$Y(OTf)_3$	-
6	$Yb(OTf)_3$	-
7	$Dy(OTf)_3$	-
8	$AlCl_3$	-
9	$FeCl_3$	-
10	$InCl_3$	-
11	TFA	15
12	HCl	-
13	PTSA	-
14	Mont. KSF	-
15	Mont. K-10	10
16	Propionic acid	-

[a]yield refers to pure product after column chromatography.

[b]reaction was performed at 50°C.

To improve the yields of the addition product **304**, the addition reaction of pyrrole to *E*-diethyl 1-cyano-2-phenylvinylphosphonate (**248**) was carried out at rt in different solvents (Table 5.18). THF, dichloromethane and acetonitrile didn't obviously increase the yield and acetone didn't give the addition product **304**. When pyrrole was used as a solvent, the yield of the reaction increased to 93%.

Table 5.18. Effect of solvent on Michael reaction of pyrrole with diethyl 1-cyano-2-phenylvinylphosphonate (**248**)

Entry	Solvent	Yield (%)[a]
1	Toluene	18
2	THF	42
3	DCM	37
4	Acetonitrile	27
5	Acetone	-
6	Pyrrole	93

[a]yield refers to pure product after column chromatography.

After examination of the solvent as pyrrole, the effect of the amount of catalyst was searched on the reaction (Table 5.19). The highest yield was obtained with 10 mol % of $Sc(OTf)_3$ in pyrrole at room temperature.

Table 5.19. Effect of amount of catalyst on Michael reaction of pyrrole with diethyl 1-cyano-2-phenylvinylphosphonate (**248**)

Entry	Mol % $Sc(OTf)_3$	Yield (%)[a]
1	5	38
2	10	93
3	15	70
4	20	83

[a]yield refers to pure product after column chromatography.

Identification of the compound diethyl 1-cyano-2-phenyl-2-(1*H*-pyrrol-2-yl)ethylphosphonate (**304**) was performed by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. Figure 5.10 shows the ^{1}H NMR spectrum of diethyl 1-cyano-2-phenyl-2-(1*H*-pyrrol-2-yl)ethylphosphonate (**304**). Methyl protons of ethoxy groups appeared at 1.14 ppm, 1.24 ppm and 1.33 ppm as triplets for both isomers. The doublet of doublet at 3.54 ppm belongs to methine proton attached to phosphonate group of major isomer. Methylene protons of ethoxy groups appeared as multiplets between the regions 3.74-3.87 ppm, 3.90-3.99 ppm, 4.00-4.11 ppm and 4.13-4.16 ppm. The benzylic methine protons observed between 4.65-4.71 ppm as multiplet for both isomers. The signals of pyrrole ring protons

appeared at 6.01 ppm as broad singlet, 6.07 ppm as triplet, 6.63 ppm and 6.72 ppm as broad singlets for both isomers. Aromatic protons of phenyl rings appeared between 7.26-7.36 ppm as multiplet and as doublets at 7.39 ppm and 7.46 ppm for major and minor isomers. The NH protons of minor and major isomers were observed as broad singlets at 8.96 ppm and 9.17 ppm, respectively.

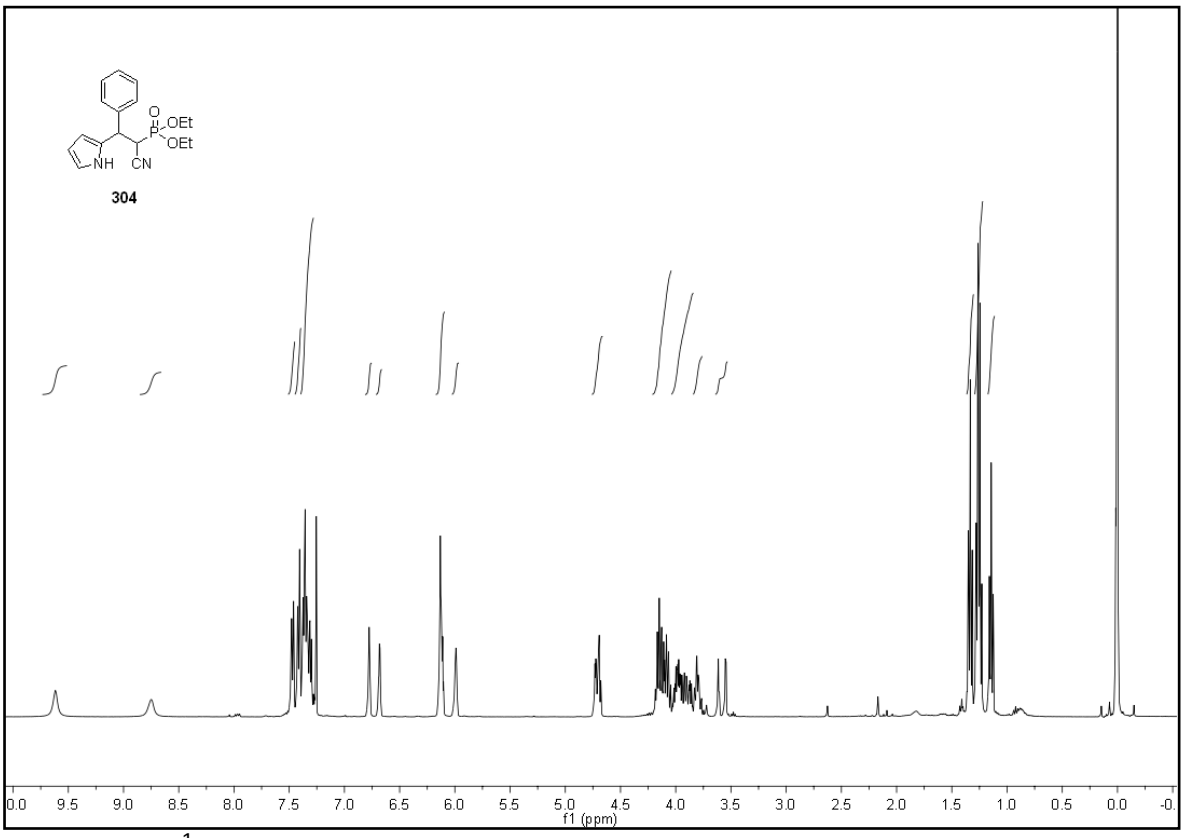


Figure 5.10. ^{1}H NMR spectrum of **304**

^{13}C NMR spectrum is also in agreement with the structure (Figure 5.11). The methyl carbons of ethoxy groups appeared at 16.0 ppm, 16.1 ppm, 16.2 ppm and 16.3 ppm as doublets for minor and major isomer, respectively. The methine carbons attached to phosphonate group appeared at 36.2 ppm and 37.2 ppm as doublets. The doublets appeared at 42.0 ppm and 42.5 ppm belongs to benzylic carbons. The methylene carbons of ethoxy group appeared at 63.3 ppm, 63.4 ppm, 64.1 ppm and 64.8 ppm as doublets. The characteristic carbons of pyrrole ring appeared at 107.1 ppm, 108.1 ppm, 108.4 ppm, 109.2 ppm, 117.9 ppm and 118.4 ppm for both isomers. CN group was observed at 115.1 ppm and 115.2 ppm as doublets for minor and major isomers, respectively. The peaks at 127.6 ppm, 127.7 ppm, 128.0 ppm, 128.6 ppm, 128.8 ppm and 129.0 ppm belong to phenyl

ring carbons. The quaternary carbons of the pyrrole ring appeared at 129.8 ppm and 130.4 ppm. The doublet peaks at 138.2 ppm and 140.3 ppm belong to quaternary carbons of phenyl ring of minor and major isomers, respectively.

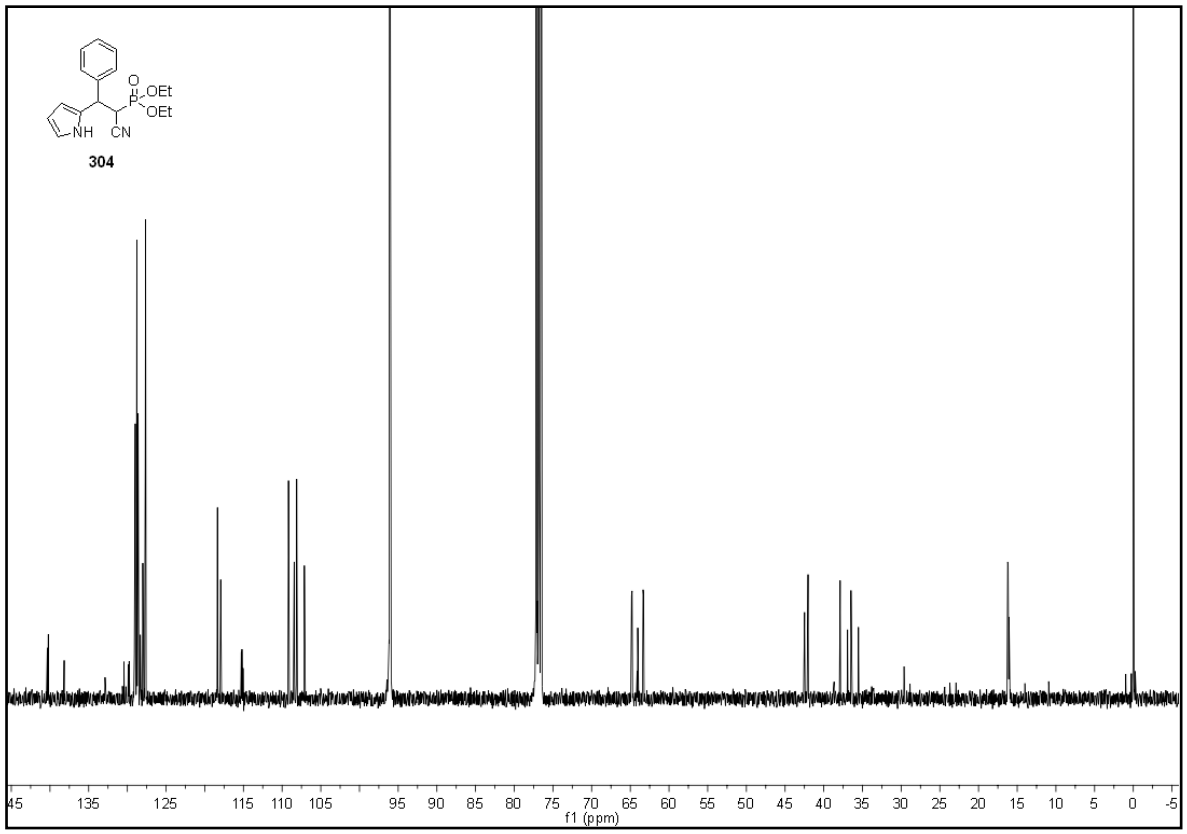


Figure 5.11. ^{13}C NMR spectrum of **304**

In the ^{31}P NMR spectrum of diethyl 1-cyano-2-phenyl-2-(1H-pyrrol-2-yl)ethylphosphonate (**304**), two peaks were observed at 16.8 ppm and 18.1 ppm for the minor and major isomers, respectively (Figure 5.12).

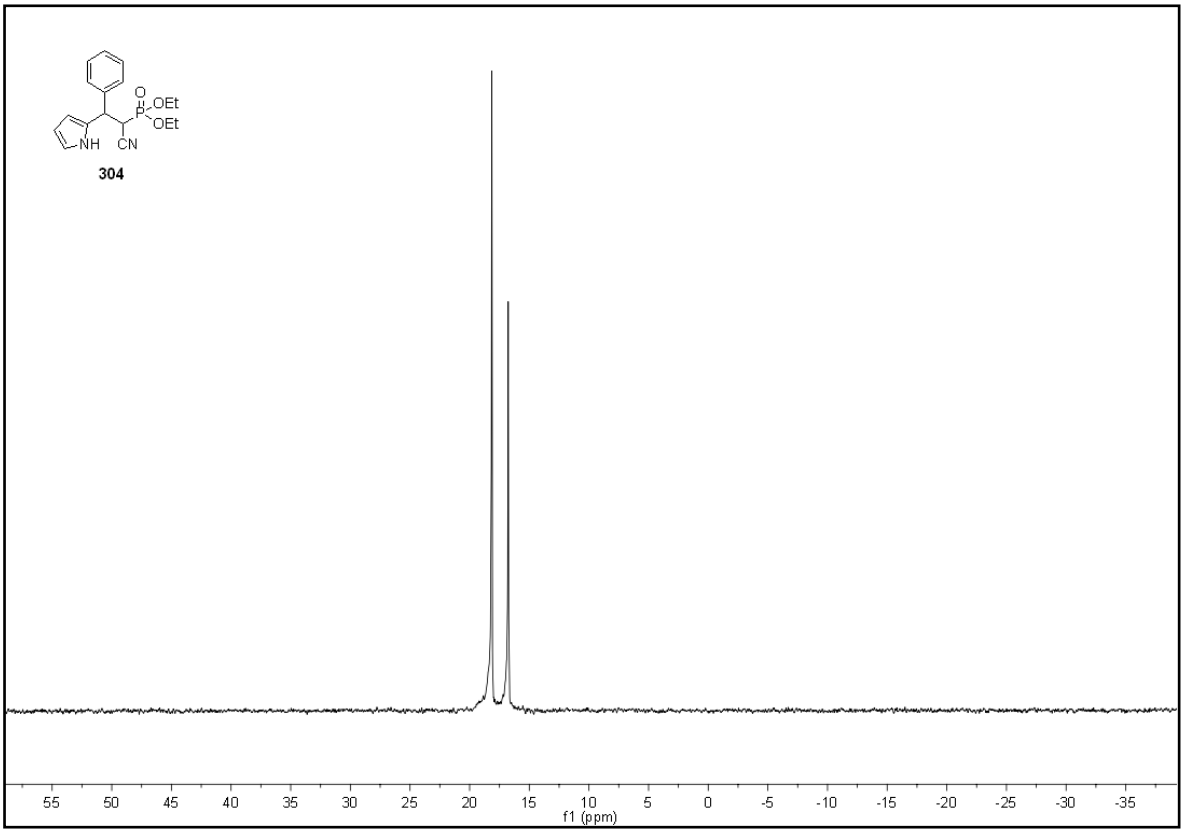
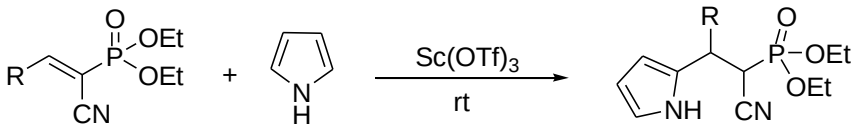


Figure 5.12. ^{31}P NMR spectrum of **304**

After optimization of the reaction conditions, the effects of substituents were searched with the substituted vinylphosphonates. The results are summarized in Table 5.20. Strong electron-withdrawing groups *p*-CF_3, *p*-NO_2 and *p*-CN on the phenyl ring gave the corresponding addition products **305,311-312** in high yields. *p*-F, *p*-Cl and *p*-Br substituents lowered the yield of the addition products **308-310**. Electron-donating *p*-CH_3 substituent gave the addition product **306** in moderate yield. Strongly electron-donating *p*-OCH_3 substituent gave the addition product **307** in very low yield. *p*-OH substituent, sterically hindered 2,4,6-trimethylphenyl substituent and heteroaromatics substituted vinylphosphonates did not give the corresponding addition products.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN and *p*-NO_2 substituted addition products **305-312** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of these addition products are given in Figure A.250-A.273 (page 304-316).

Table 5.20. Addition reaction of pyrrole to cyano functionalized substituted vinylphosphonates (**248-261**)

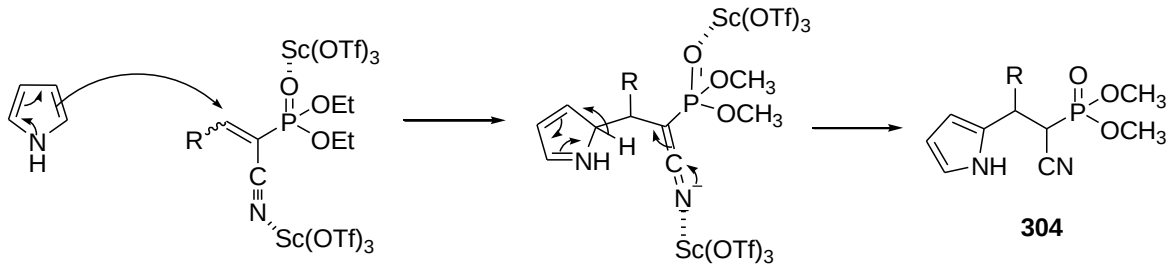


248-261 **304-312**

Entry	R	Product	dr[a]	Yield (%)[b]
1	phenyl	**304**	56:44	93
2	*p*-CF_3-phenyl	**305**	51:49	96
3	*p*-CH_3-phenyl	**306**	57:43	69
4	*p*-OCH_3-phenyl	**307**	55:45	15
5	*p*-F-phenyl	**308**	50:50	73
6	*p*-Cl-phenyl	**309**	53:47	80
7	*p*-Br-phenyl	**310**	59:41	84
8	*p*-OH-phenyl	**-**	-	-
9	*p*-CN-phenyl	**311**	55:45	96
10	*p*-NO_2-phenyl	**312**	51:49	92
11	2,4,6-trimethylphenyl	**-**	-	-
12	2-pyrrolyl	**-**	-	-
13	2-furyl	**-**	-	-
14	2-thiophenyl	**-**	-	-

[a]diastereomeric ratios are determined from NMR spectra.
[b]yield refers to pure product after column chromatography.

The proposed reaction mechanism for the metal triflate catalyzed reaction of cyano vinylphosphonate with pyrrole is given in Scheme 5.15. In the first step, vinylphosphonate is activated by the coordination of metal triflate to cyano group and phosphonate. The addition of pyrrole to the activated vinylphosphonate affords the addition products.



Scheme 5.15. The proposed reaction mechanism for the $Sc(OTf)_3$ catalyzed reaction of cyano vinylphosphonate with pyrrole.

When the addition reaction of pyrrole to **248** was performed without using the $Sc(OTf)_3$, addition product **304** did not form. This result indicated that $Sc(OTf)_3$ has a crucial role for the activation of double bond in the molecule.

5.3. Reactions of Addition Products with NaH

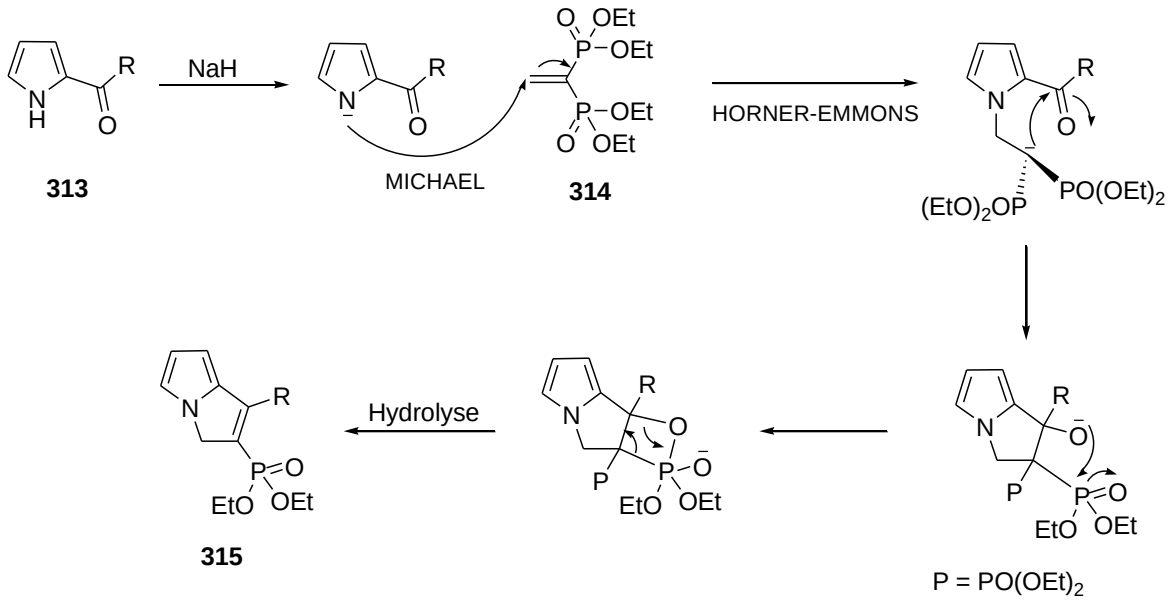
The phosphonate substituted pyrrole addition products are valuable precursors for the synthesis of pyrrolizines. In this study; it was aimed to obtain phosphonate substituted pyrrolizine ring structures from the obtained pyrrole addition products.

Pyrrolizines are compounds generally associated with pharmaceutical activities such as; anti-inflammatory and anti-tumor agents. Access to structural analogues and synthesis of diversely substituted derivatives would be an important target for research in medicinal chemistry. There are some methods reported describing the preparation of such compounds. These methods involve the intramolecular cyclization of the *N*- or *C*-substituted pyrrole derivatives.

Phosphonic acids with heteroatoms in the α- or β-positions have attracted considerable interest because of their use as inhibitors, as agents affecting the growth of plants or haptens in the development of catalytic antibodies.

To the best of our knowledge; there is only one example on the synthesis of phosphonate substituted pyrrolizines.

Loussouarn et al. (1996) synthesized the diethylphosphoryl substituted 3*H*-pyrrolizines **314** by Michael-Horner-Emmons reaction between 2-acylpyrrole derivatives **313** and tetraethyl ethylidene gem-bisphosphonate (**314**) in the presence of NaH (Scheme 5.16).

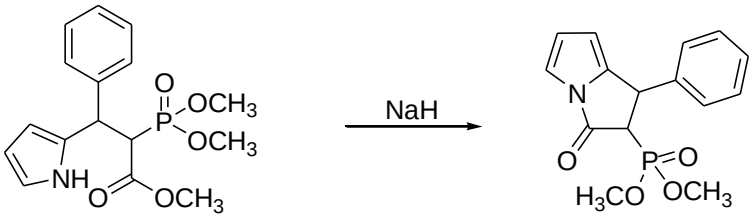


Scheme 5.16. Synthesis of diethylphosphoryl substituted 3*H*-pyrrolizines **314** by Michael-Horner-Emmons reaction.

In the last part of the study, reactions of addition products were investigated in the presence of NaH to obtain pyrrolizine ring structures.

5.3.1. Reactions of ester functionalized addition products with NaH

Reactions of ester functionalized addition products **262-276** were searched in the presence of NaH. We expect to obtain phosphoryl substituted pyrrolizine ring structures from these addition products. The reaction of methyl 2-(dimethoxyphosphoryl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (**262**) with NaH was chosen as a model reaction to optimize the reaction conditions (Scheme 5.17).



262 **316**

Scheme 5.17. The model reaction to optimize the conditions of intramolecular cyclization reaction of **262** with NaH.

The reaction was carried out in the presence of NaH in dry THF under nitrogen atmosphere and monitored by TLC. After 2 hours 10 mL of phosphate buffer (pH 7.0) was added to the reaction mixture. The aqueous solution was extracted with ethyl acetate. Combined organic layers were removed under reduced pressure and the residue was purified by flash column chromatography.

The intramolecular cyclization product dimethyl 3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (**316**) was obtained in 55% yield at 0 °C. To increase the yield of the cyclization product **316** the effects of temperature were searched. When the reaction was performed at room temperature, the yield of the cyclization product was obtained in 81% yield. However, increasing the temperature to 50 °C decreased the yield of the product to 33% (Table 5.21).

Table 5.21. Effect of temperature on the cyclization reaction of methyl 2-(dimethoxyphosphoryl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (**262**)

Entry	Temperature	Yield (%)[a]
1	0 °C	55
2	rt	81
3	50 °C	33

[a]yield refers to pure product after column chromatography.

Another parameter for the optimization of the reaction conditions is the amount of NaH. The model reaction was repeated with 1.0, 1.5 and 2.0 equivalents of NaH.

The highest yield was obtained with 1.5 equivalent of NaH at room temperature (Table 5.22).

Table 5.22. Effect of amount of NaH on the cyclization reaction of methyl 2-(dimethoxyphosphoryl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (**262**)

Entry	Mole ratio 262/NaH	Yield (%)[a]
1	1:1	39
2	1:1.5	81
3	1:2	78

[a]yield refers to pure product after column chromatography.

We continued searching solvent effect on the reaction parameters. Effects of toluene and DCM were searched beside THF. When the reaction was performed in toluene or DCM, the yield of the cyclization product decreased. The best yield was obtained in THF with 1.5 equivalent of NaH at room temperature (Table 5.23).

Table 5.23. Effect of solvent on the cyclization reaction of methyl 2-(dimethoxyphosphoryl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (**262**)

Entry	Solvent	Yield (%)[a]
1	THF	81
2	Toluene	57
3	DCM	49

[a]yield refers to pure product after column chromatography.

Characterization of the compound dimethyl 3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (**316**) was achieved by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. Figure 5.13 shows the ^{1}H NMR spectrum of dimethyl 3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (**316**). The doublet of doublet signal at 3.45 ppm belongs to methine proton attached to phosphonate group. The methoxy protons appeared at 3.75 ppm and 3.78 ppm as doublets. The benzylic methine proton appeared at 4.79 ppm as doublet of doublet. The pyrrole ring protons appeared between 5.90-5.91 ppm as multiplet, at 6.46 ppm as

triplet and 7.05 ppm as doublet. The multiplet between 7.15-7.28 ppm belongs to phenyl ring protons.

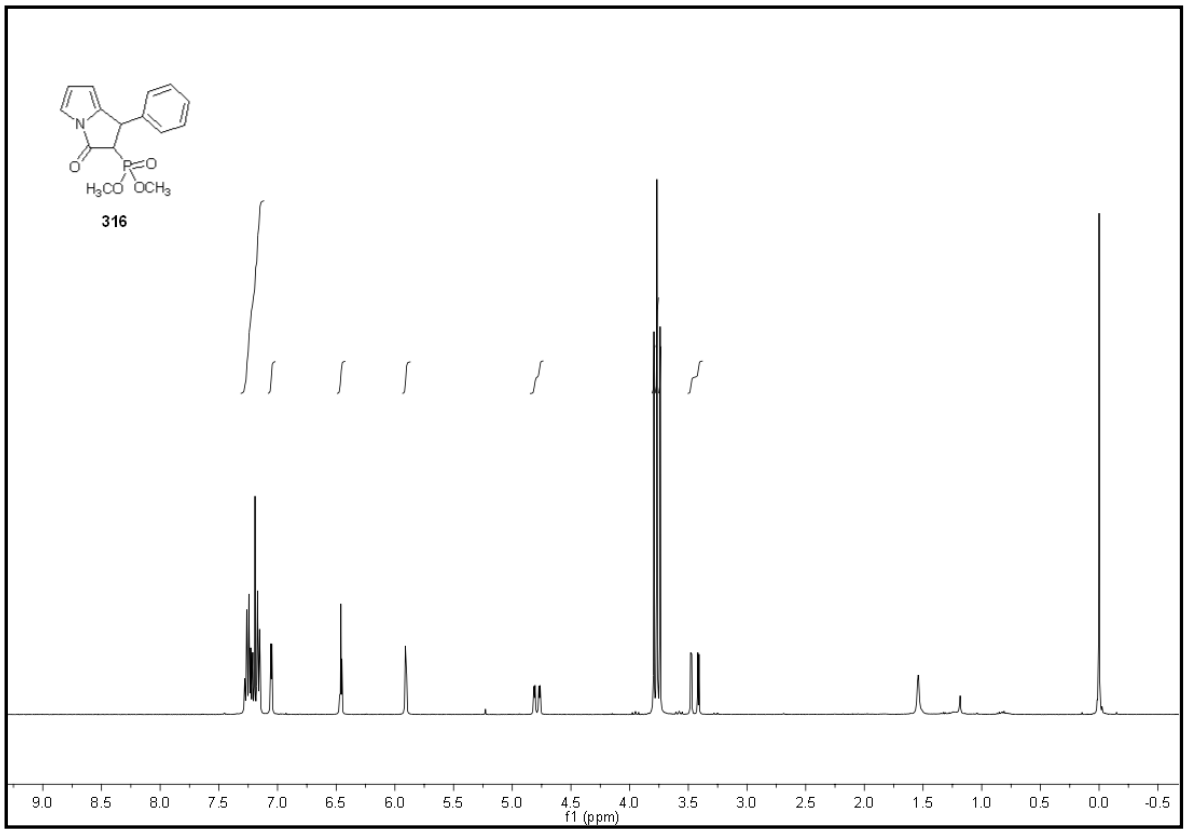


Figure 5.13. ^{1}H NMR spectrum of **316**

^{13}C NMR spectrum is also in agreement with the structure (Figure 5.14). The benzylic carbon appeared at 40.1 ppm as doublet. Methoxy carbons appeared at 52.3 ppm and 53.1 ppm as doublets. The doublet signal at 54.6 ppm belongs to methine carbon attached to phosphonate group. The pyrrole ring carbons appeared at 105.3 ppm, 110.8 ppm, 118.9 ppm and 139.5 ppm. The phenyl ring carbons appeared at 126.2 ppm, 126.8 ppm, 128.0 ppm and 140.0 ppm. The carbonyl carbon appeared at 164.5 ppm as doublet.

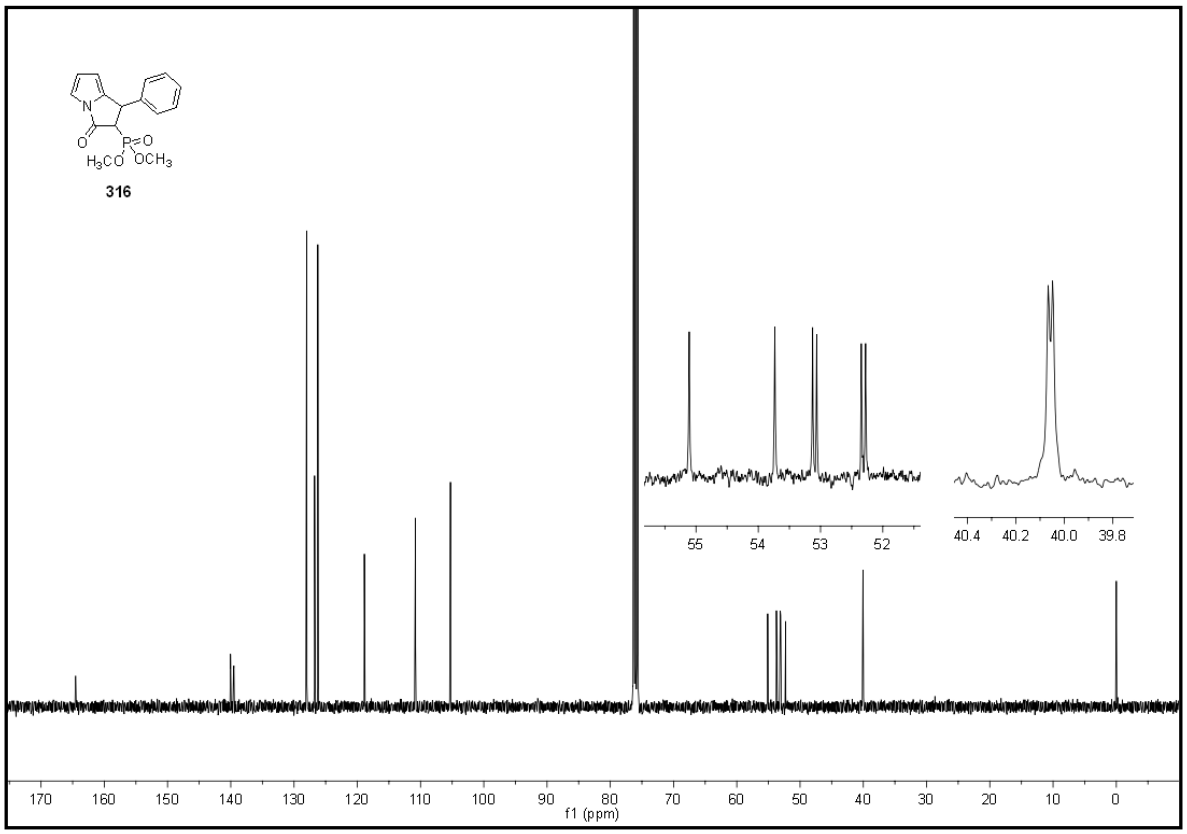


Figure 5.14. ^{13}C NMR spectrum of **316**

In the ^{31}P NMR spectrum of dimethyl 3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (**316**) the peak at 22.4 ppm belongs to phosphorus atom in the structure (Figure 5.15).

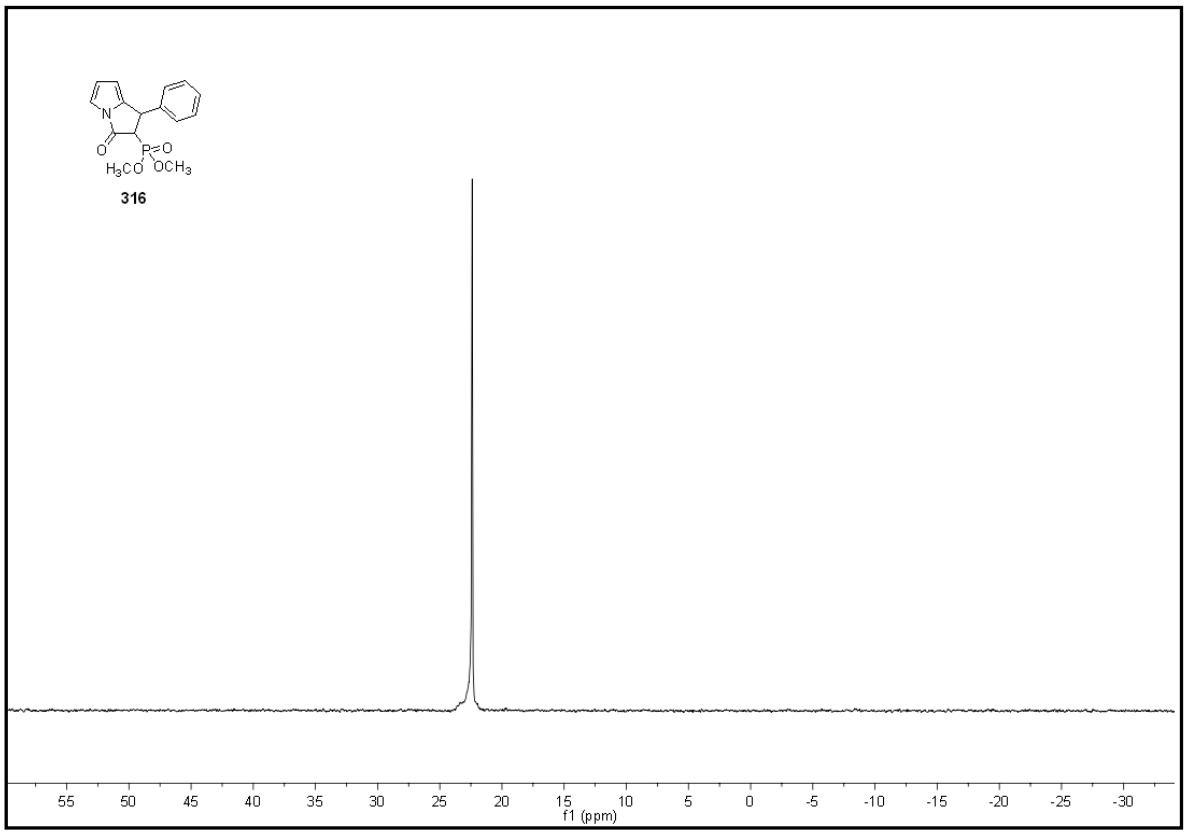
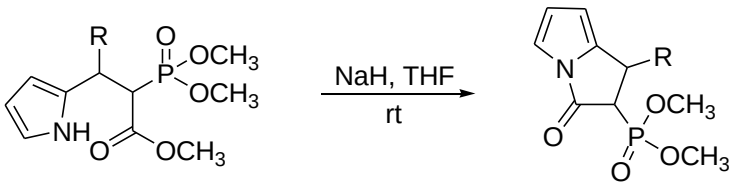


Figure 5.15. ^{31}P NMR spectrum of **316**

The optimum conditions of the model reaction were applied to the cyclization reactions of the substituted ester functionalized addition products to obtain pyrrolizine ring structures. The intramolecular cyclization reactions of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN-phenyl, pyrrolyl, furyl, thiophenyl and cyclohexyl substituted addition products **263-268,270,272-275** gave the cyclization products **317-322,324,326-329** in 74-99% yields. *p*-OH and *p*-NO_2 substituents on the phenyl ring and isobutyl substituent lowered the yield of the cyclization products **323,325** and **330** to 44%, 45% and 65%, respectively.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-OH, *p*-CN, *p*-NO_2-phenyl, 2-pyrrolyl, 2-furyl, 2-thiophenyl, cyclohexyl and isobutyl substituted cyclization products **317-330** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of these addition products are given in Figure A.274-A.315 (page 316-337).

Table 5.24. Intramolecular cyclization reaction of substituted addition products (**262-276,279-280**)



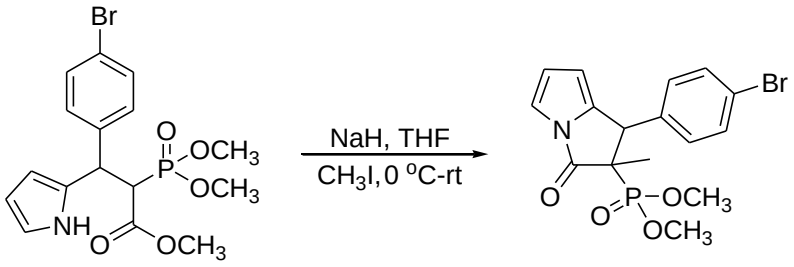
262-276,279-280 **316-330**

Entry	R	Product	Yield (%)[a]
1	Phenyl	**316**	81
2	*p*-CF_3-phenyl	**317**	99
3	*p*-CH_3-phenyl	**318**	98
4	*p*-OCH_3-phenyl	**319**	98
5	*p*-F-phenyl	**320**	74
6	*p*-Cl-phenyl	**321**	88
7	*p*-Br-phenyl	**322**	99
8	*p*-OH-phenyl	**323**	44
9	*p*-CN-phenyl	**324**	87
10	*p*-NO_2-phenyl	**325**	45
11	2-pyrrolyl	**326**	99
12	2-furyl	**327**	92
13	2-thiophenyl	**328**	96
14	cyclohexyl	**329**	99
15	isobutyl	**330**	65
16	2,4-dimethylpyrrolyl	**-**	-
17	2,4-dimethyl-3-ethylpyrrolyl	**-**	-

[a]yield refers to pure product after column chromatography.

Cyclization products **316-330** were obtained as single diastereomers. Configurational assignment of the cyclization products could be done from their $^3J_{H\text{-}H}$ values. In our previous study; we showed that *trans* isomer of the 3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolizine-2-carbonitrile has vicinal coupling constants between 4.8-6.4 Hz and *cis* isomer has between 8.2-8.8 Hz. In this case; the vicinal coupling constants of the hydrogens of **316-330** are in the range of 2.8-4.4 Hz. These novel phosphoryl pyrrolizones can be assigned as *trans* because the vicinal coupling constants are in agreement with the previous ones (Unaleroglu et al., 2009). We designed an experiment to understand why only one diastereoisomer is formed in all cases. In this experiment, the reaction of **268** with

NaH in the presence of methyl iodide in THF was investigated (Scheme 5.18). Substitution of methyl group to C-2 atom in dimethyl 1-(4-bromophenyl)-2-methyl-3-oxo-2,3-dihydro-1*H*-pyrrolizin-2-ylphosphonate (**331**) indicated that epimerization took place under the applied reaction conditions. As a result of epimerization the thermodynamically more stable *trans* products **316-330** formed.

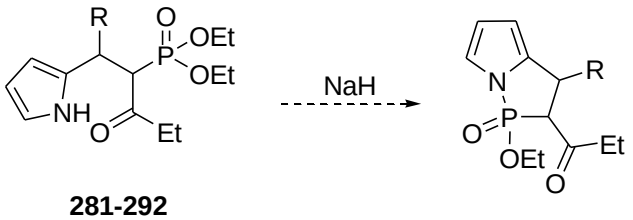


268 **331**

Scheme 5.18. The reaction of **268** with NaH in the presence of methyl iodide.

5.3.2. Reactions of ketone functionalized addition products with NaH

The reactions of ketone functionalized addition products with NaH were also investigated. We have obtained the pyrrole substituted pyrrolizines **293-303** in the addition of pyrrole to ketone vinylphosphonates **234-246** with $Sc(OTf)_3$. At this time; we aimed to obtain pyrrolizine rings from the reaction of ketone functionalized addition products **281-292** with NaH (Scheme 5.19).

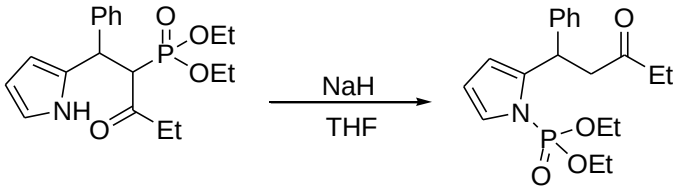


281-292

Scheme 5.19. Synthetic pathway for the pyrrolizine rings from ketone functionalized addition products **281-292**.

The reaction of diethyl 3-oxo-1-phenyl-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (**281**) with NaH was chosen as a model reaction. When we performed the reaction of **281** in the presence of 1.5 equivalents of NaH in THF at room temperature, we

didn’t obtain the expected cyclization product. Instead of this cyclization product we obtained the *N*-phosphoryl substituted pyrrole derivative **332** by the migration of phosphonate group (Scheme 5.20).



281-292 **332**

Scheme 5.20. The reaction of diethyl 3-oxo-1-phenyl-1-(1*H*-pyrrol-2-yl)pentan-2-ylphosphonate (**281**) with NaH.

Characterization of the compound diethyl 2-(3-oxo-1-phenylpentyl)-1*H*-pyrrol-1-ylphosphonate (**332**) was achieved by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. Figure 5.16 shows the ^{1}H NMR spectrum of diethyl 2-(3-oxo-1-phenylpentyl)-1*H*-pyrrol-1-ylphosphonate (**332**). Methyl protons of ethyl group appeared as triplet at 0.97 ppm. Methyl protons of ethoxy groups appeared as triplets at 0.94 ppm and 1.29 ppm. Methylene protons of ethyl group gave doublet of quartets at 2.29 ppm and 2.37 ppm. The doublet of doublets at 2.85 ppm and 3.10 ppm belong to methylene protons. Multiplets between 3.30-3.40 ppm and 3.83-4.06 ppm belong to methylene protons of ethoxy groups. The benzylic methine proton observed at 5.00 ppm as triplet. Pyrrole ring protons observed between 6.19-6.22 ppm and 7.04-7.06 ppm as multiplet. The multiplet between 7.13-7.24 ppm belong to aromatic protons of phenyl ring.

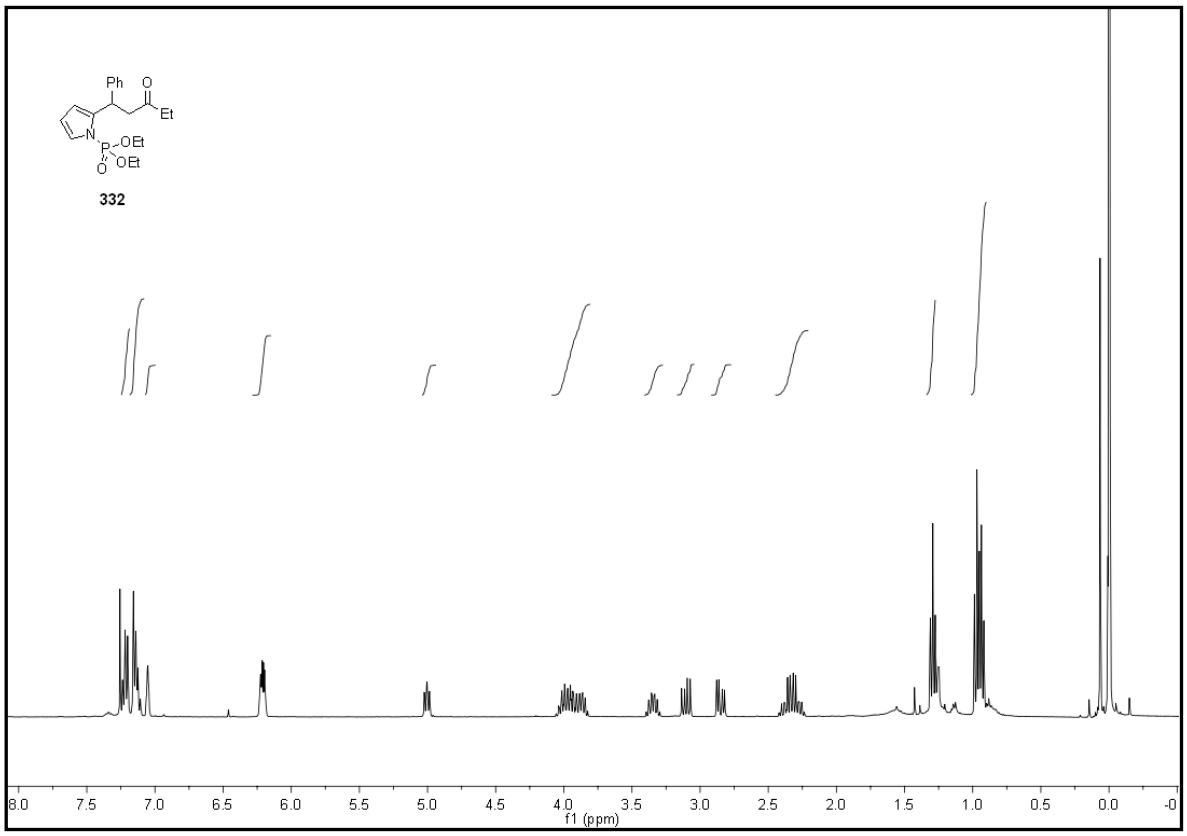


Figure 5.16. ^{1}H NMR spectrum of **332**

^{13}C NMR spectrum is also in agreement with the structure (Figure 5.17). Methyl carbon of ethyl group appeared at 7.5 ppm. Methyl carbons of ethoxy groups appeared at 15.5 ppm and 15.8 ppm as doublet for both groups. The singlet at 36.3 ppm belongs to benzylic carbon attached to phenyl ring. Methylene carbon of ethyl group appeared at 38.6 ppm. The methylene carbon attached to carbonyl group appeared at 50.4 ppm. The doublets appeared at 63.4 ppm and 63.7 ppm belong to methylene carbons of ethoxy groups. The characteristic carbons of pyrrole ring appeared at 110.5 ppm, 111.3 ppm, 124.8 and 137.1 ppm as doublets. The aromatic carbons of the phenyl ring observed at 126.2 ppm, 127.7 ppm, 128.2 ppm and 143.5 ppm. The peak at 208.0 ppm belongs to the carbonyl group.

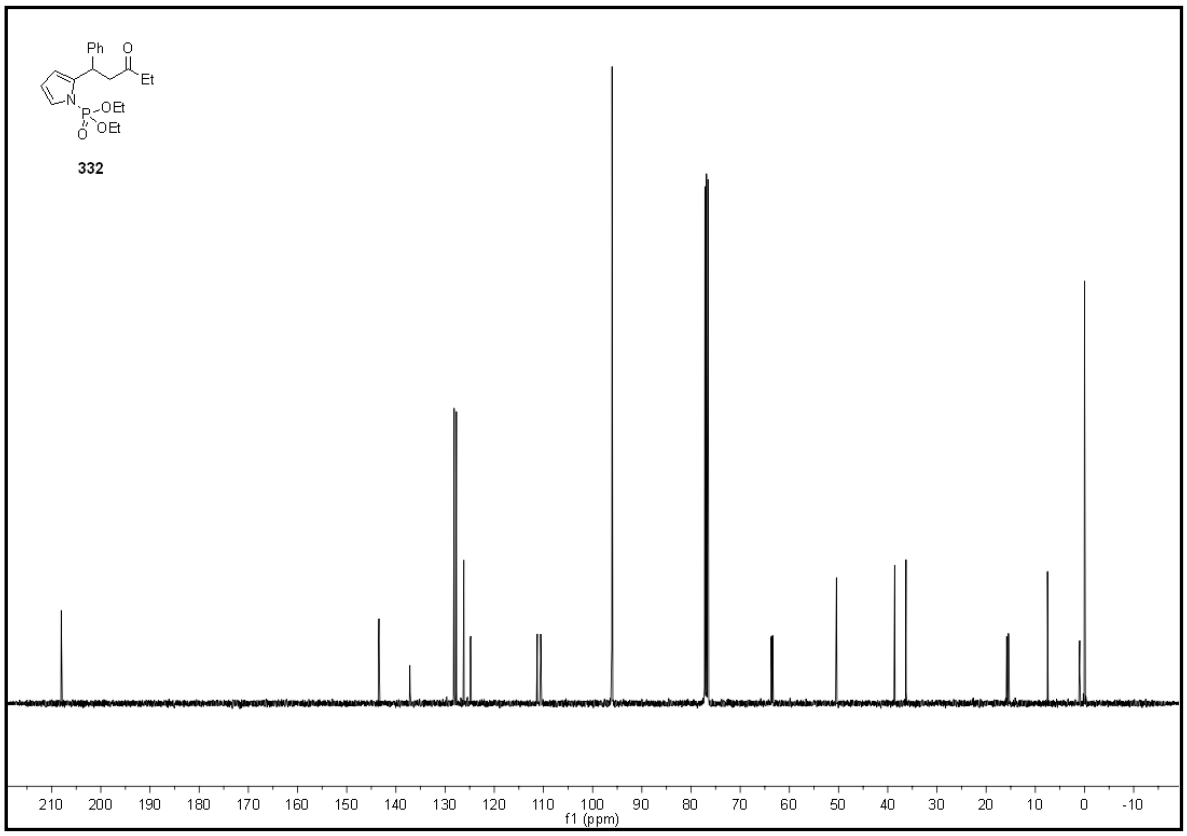


Figure 5.17. ^{13}C NMR spectrum of **332**

The phosphorus atom in the structure **332** appeared at -3.3 ppm in the ^{31}P NMR spectrum (Figure 5.18).

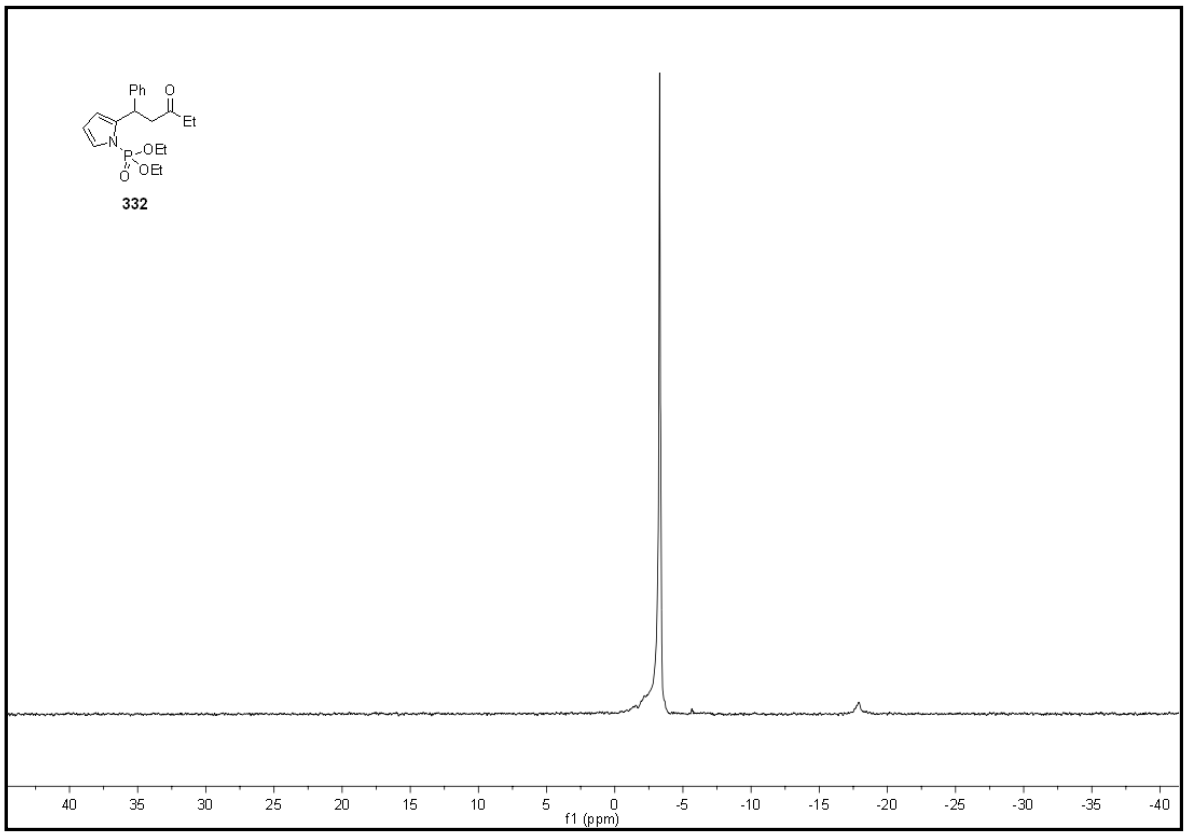
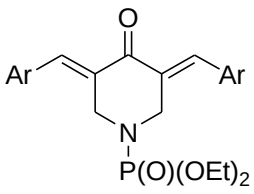


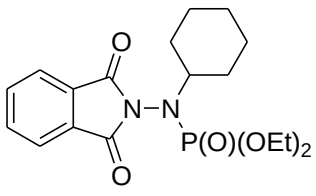
Figure 5.18. ^{31}P NMR spectrum of **332**

This unexpected result attracted our attention to *N*-phosphoryl substituted heterocycles. We know from literature that there are many compounds which have bioactivities among phosphoric acid derivatives. The diethylphosphoryl derivatives are valuable intermediates in synthetic organic chemistry, or used as medicine or agrochemicals (Milen et al., 2012). The two *N*-phosphoryl derivatives **333** and **334** shown below have activities as antitumor (Leonova et al., 2010 and Das et al., 2010) and antimicrobial drug (Gupta et al., 2007) (Scheme 5.21).



333

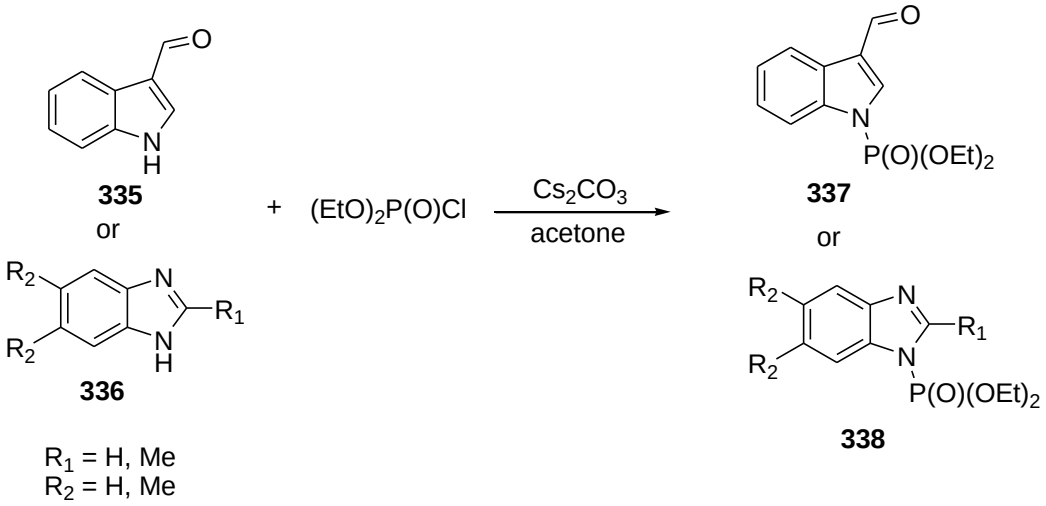
Ar = aryl, hetaryl



334

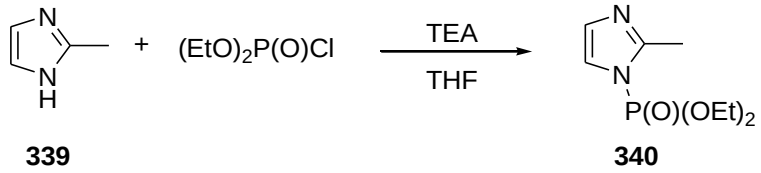
Scheme 5.21. Examples to *N*-phosphoryl derivatives.

The phosphorylation of *N*-heterocycles generally performed by dialkyl chlorophosphate and a base. Milen et al. (2012) performed the *N*-phosphorylation of *N*-heterocycles by diethyl chlorophosphate using alkali carbonate or triethylamine as the base. Indolecarbaldehyde (**335**) and substituted benzimidazoles (**336**) gave the phosphorylation reaction in the presence of Cs_2CO_3 in acetone (Scheme 5.22).



Scheme 5.22. *N*-phosphorylation of indolecarbaldehyde (**335**) and substituted benzimidazoles (**336**) by diethyl chlorophosphate with Cs_2CO_3.

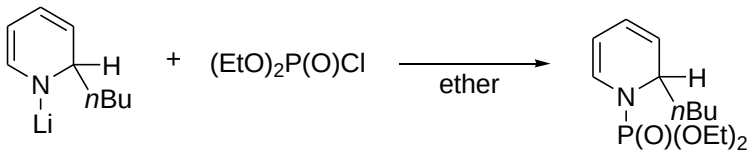
When methylimidazole (**339**) was employed in the phosphorylation reaction the highest yield was observed for **340** in THF in the presence of triethylamine (Scheme 5.23).



Scheme 5.23. *N*-phosphorylation of methylimidazole (**339**) by diethyl chlorophosphate with TEA.

Ondrus et al. (1978) gave an example on the *N*-phosphorylation of pyridine with diethyl chlorophosphate. Treatment of *N*-lithio-2-*n*-butyl-1,2-dihydropyridine (**341**)

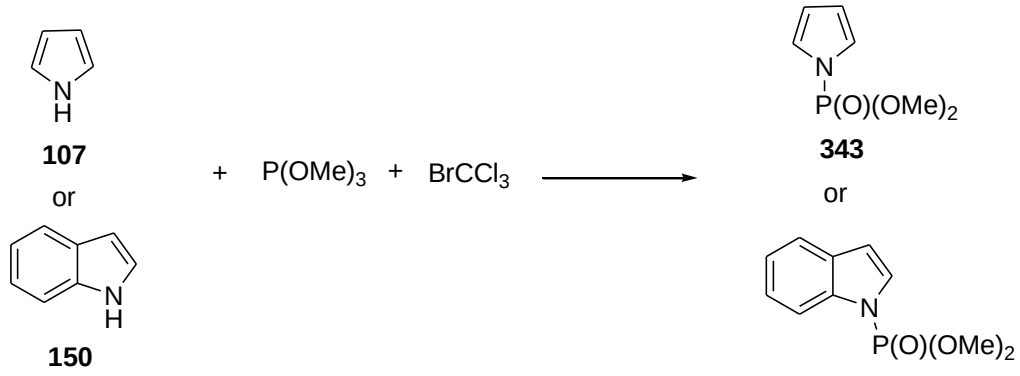
afforded *N*-diethylphosphoryl-2-*n*-butyl-1,2-dihydropyridine (**342**) in 68% yield (Scheme 5.24).



341 **342**

Scheme 5.24. *N*-phosphorylation of *N*-lithio-2-*n*-butyl-1,2-dihydropyridine (**341**) by diethyl chlorophosphate.

Napier R.P. (1977) patented a one-step process for *N*-phosphorylation of heterocyclic amines with bromotrichloromethane and trialkylphosphite. This process generally relates to acidic amines such as pyrrole (**107**) and indole (**150**). The reaction was performed by the dropwise addition of the trialkylphosphite to the solution of heterocyclic amine in the bromotrichloromethane. *N*-phosphorylated pyrrole **343** and indole **344** were obtained in 68% and 85% yields, respectively (Scheme 5.25).



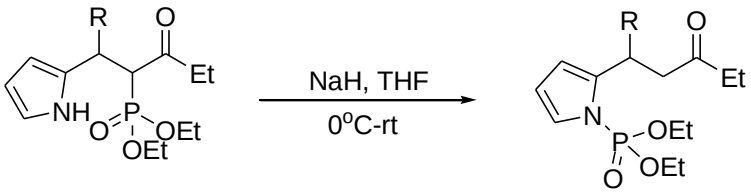
Scheme 5.25. *N*-phosphorylation of pyrrole (**107**) and indole (**150**) with bromotrichloromethane and trialkylphosphite.

The literature search showed that the synthesis of the *N*-phosphorylated compounds have importance because of their biological activities. We turned our attention to the synthesis of *N*-phosphoryl substituted pyrrole derivatives and the

reactions of substituted ketone functionalized addition products **282-292** were performed with NaH. The reactions of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN-phenyl, pyrrolyl, furyl and thiophenyl substituted addition products **282-292** with NaH gave the *N*-phosphoryl substituted pyrrole derivatives **345-355** in 35-85% yields (Table 5.25). The electron-withdrawing *p*-CF_3, *p*-CN and *p*-NO_2 substituents on the phenyl ring lowered the yield of the corresponding products **345,351-352** to 35%, 38% and 53%, respectively. The highest yield was obtained with *p*-Br-phenyl substituent as 85%.

The ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of *p*-CF_3, *p*-CH_3, *p*-OCH_3, *p*-F, *p*-Cl, *p*-Br, *p*-CN, *p*-NO_2-phenyl, 2-pyrrolyl, 2-furyl and 2-thiophenyl substituted *N*-phosphorylation products **345-355** are in agreement with the structures. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra of these addition products are given in Figure A.319-A.351 (page 339-355).

Table 5.25. Reactions of substituted ketone functionalized addition products **282-292** with NaH

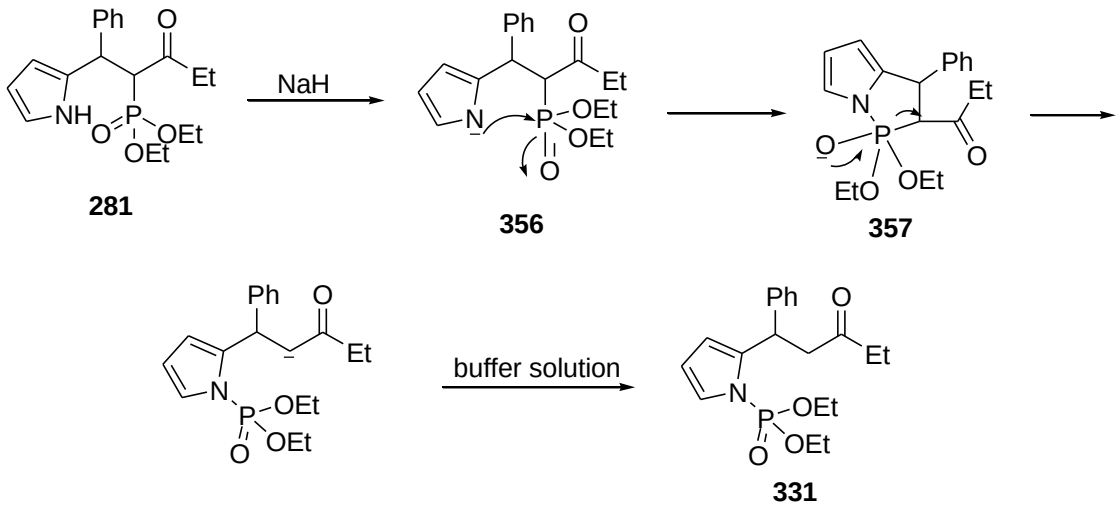


281-292 **332,345-355**

Entry	R	Product	Yield (%)[a]
1	Phenyl	**332**	70
2	*p*-CF_3-phenyl	**345**	35
3	*p*-CH_3-phenyl	**346**	76
4	*p*-OCH_3-phenyl	**347**	77
5	*p*-F-phenyl	**348**	57
6	*p*-Cl-phenyl	**349**	65
7	*p*-Br-phenyl	**350**	85
8	*p*-CN-phenyl	**351**	38
9	*p*-NO_2-phenyl	**352**	53
10	2-pyrrolyl	**353**	20
11	2-furyl	**354**	66
12	2-thiophenyl	**355**	60

[a]yield refers to pure product after column chromatography.

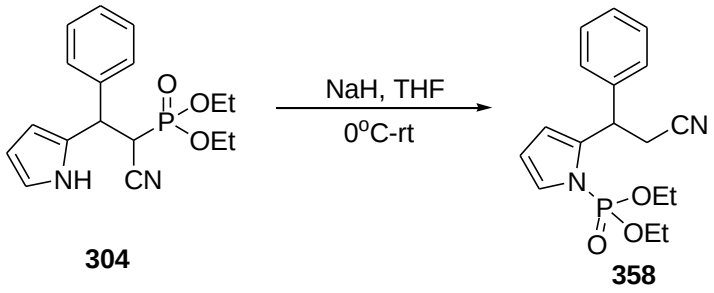
The proposed reaction mechanism for the synthesis of *N*-phosphorylated pyrrole derivatives is given in Scheme 5.26. Firstly, hydride ion took the acidic hydrogen of the pyrrole and formed an anion **356** at the pyrrole nitrogen. The attack of the resulted anion to the phosphonate group generated a five-membered intermediate **357**. Cleavage of the P-C bond and subsequent reaction gave *N*-phosphorylated pyrrole derivatives.



Scheme 5.26. Proposed reaction mechanism for the synthesis of *N*-phosphorylated pyrrole derivatives

5.3.3. Reactions of cyano functionalized addition products with NaH

In this part; the reactions of cyano functionalized addition products with NaH were investigated. The reactions of ketone functionalized addition products gave the *N*-phosphorylated pyrrole derivatives. Therefore; we expect to obtain *N*-phosphorylated pyrrole derivatives from the reaction of cyano functionalized addition products with NaH because of the similarity of the structures. When the reaction of diethyl 1-cyano-2-phenyl-2-(1*H*-pyrrol-2-yl)ethylphosphonate (**304**) was performed with 3.0 equiv of NaH, the phosphorylated product diethyl 2-(2-cyano-1-phenylethyl)-1*H*-pyrrol-1-ylphosphonate (**358**) was obtained in 20 % yield in 24 h (Scheme 5.27). The ketone functionalized addition products produced the corresponding rearrangement products easily however; the cyano functionalized addition product **304** gave the *N*-phosphorylated product **358** reluctantly.



304 **358**

Scheme 5.27. The reaction of diethyl 2-(2-cyano-1-phenylethyl)-1*H*-pyrrol-1-ylphosphonate (**358**) with NaH.

Characterization of the compound diethyl 2-(2-cyano-1-phenylethyl)-1*H*-pyrrol-1-ylphosphonate (**358**) was achieved by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR and HRMS techniques. Figure 5.19 shows the ^{1}H NMR spectrum of diethyl 2-(2-cyano-1-phenylethyl)-1H-pyrrol-1-ylphosphonate (**358**). Methyl protons of ethoxy groups appeared as triplets at 1.08 ppm and 1.18 ppm. The doublet of doublets at 2.86 ppm and 2.84 ppm belong to methylene protons. Multiplets between 3.55-3.65 ppm, 3.72-3.82 ppm, 3.84-3.93 ppm and 3.95-4.04 ppm belong to methylene protons of ethoxy groups. The benzylic methine proton observed at 4.90 ppm as triplet. Pyrrole ring protons observed between 6.27-6.30 ppm as multiplet, at 6.37 ppm as broad doublet and 7.03 ppm as broad singlet. The multiplet between 7.20-7.31 ppm belong to aromatic protons of phenyl ring.

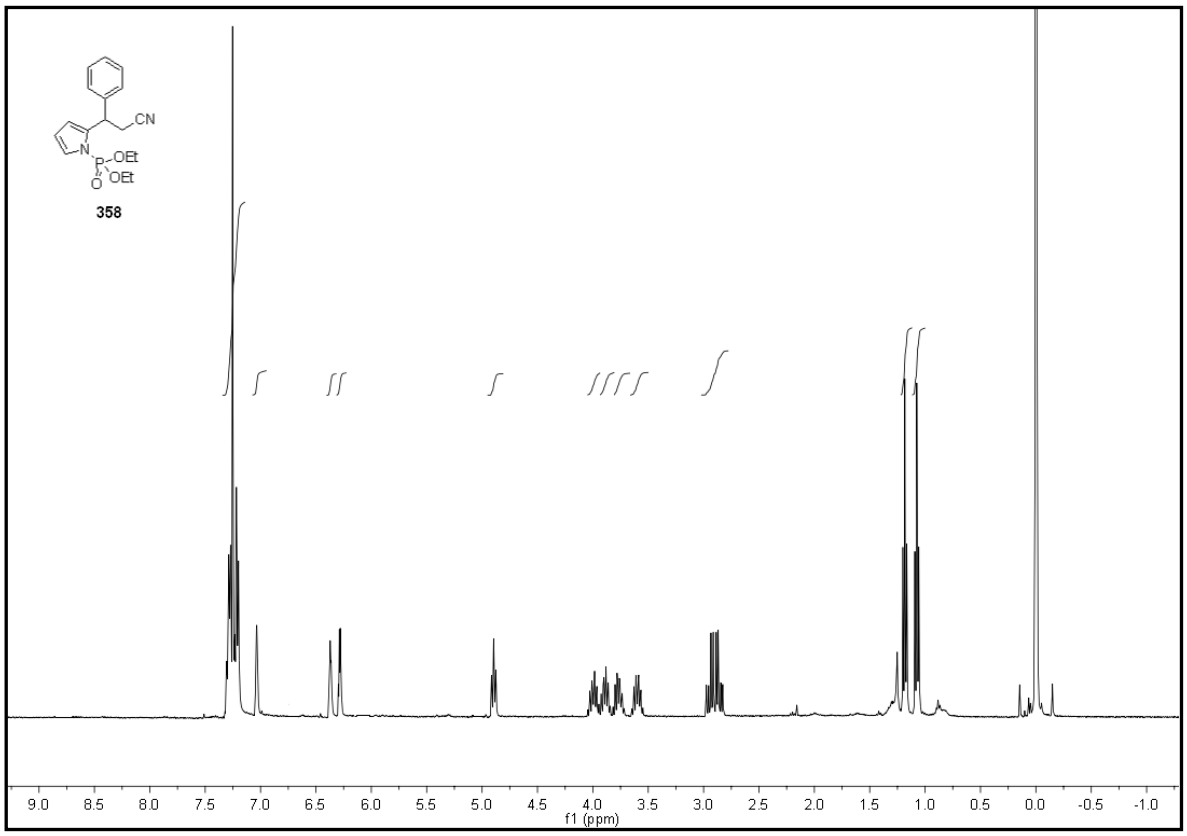


Figure 5.19. ^{1}H NMR spectrum of **358**

^{13}C NMR spectrum is also in agreement with the structure (Figure 5.20). Methyl carbons of ethoxy groups appeared at 15.6 ppm and 15.7 ppm as doublet for both groups. The methylene carbon attached to cyano group appeared at 25.5 ppm. The singlet at 40.0 ppm belongs to benzylic carbon. The doublets appeared at 63.7 ppm and 63.8 ppm belong to methylene carbons of ethoxy groups. The characteristic carbons of pyrrole ring appeared at 111.2 ppm, 112.2 ppm, 124.8 and 134.8 ppm as doublets. The peak at 117.6 ppm belongs to cyano group. The aromatic carbons of the phenyl ring observed at 127.3 ppm, 127.6 ppm, 128.5 ppm and 140.8 ppm.

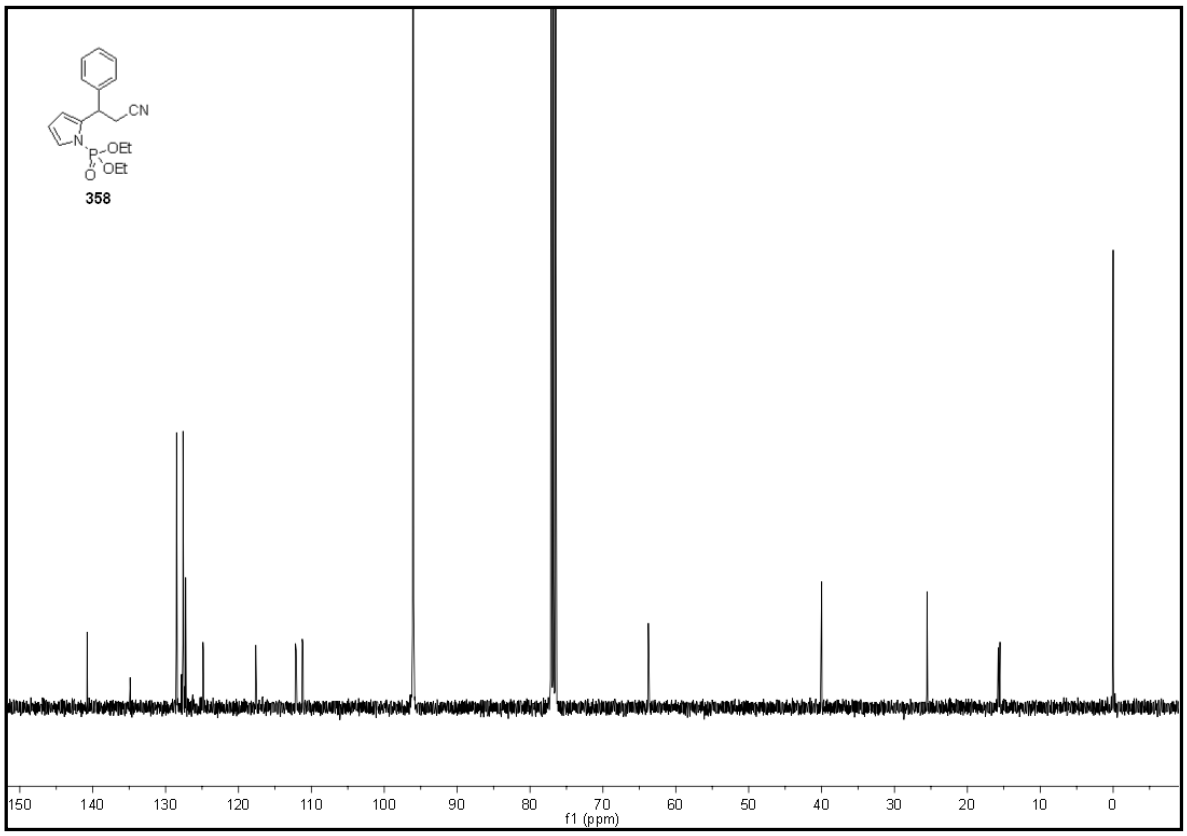


Figure 5.20. ^{13}C NMR spectrum of **358**

The phosphorus atom in the structure **358** appeared at -2.9 ppm in the ^{31}P NMR spectrum (Figure 5.21).

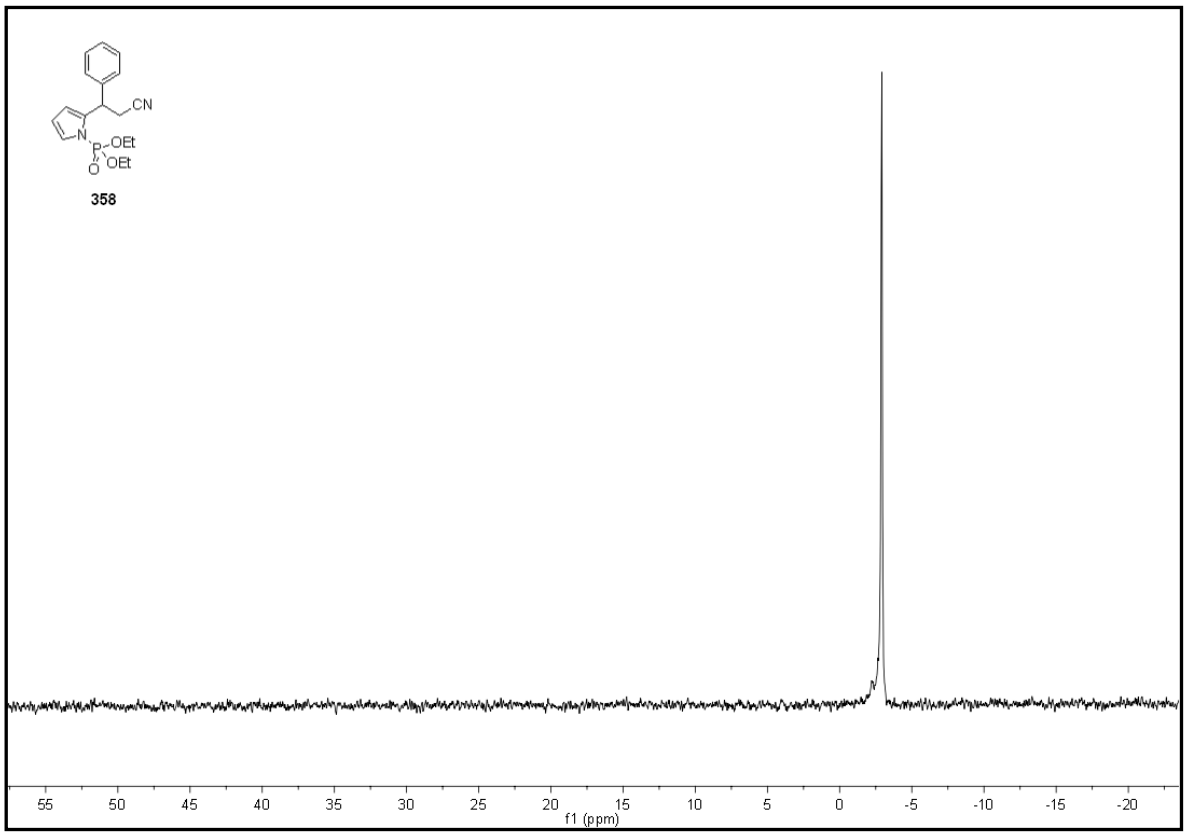
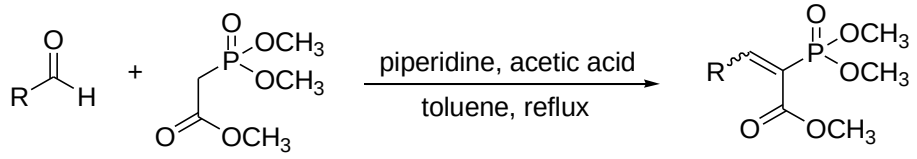


Figure 5.20. ^{31}P NMR spectrum of **358**

The phosphorylation reaction was searched with the substituted addition products. However; when the reaction was performed with *p*-CF_3, *p*-CH_3, *p*-OCH_3 and p-Br-phenyl substituted cyano functionalized addition products **305-307,310** with 3.0 equiv of NaH in THF at rt, the starting materials were recovered after 48 h. These results indicate that the migration of the phosphonate groups to nitrogen for these molecules is difficult under these reaction conditions.

6. CONCLUSIONS

In the first part, a conventional method was employed for the synthesis of ester, ketone and cyano vinylphosphonates. Vinylphosphonates were synthesized by the Knoevenagel reaction of active methylene compounds with substituted aldehydes. Ester vinylphosphonates were synthesized by the Knoevenagel reaction of trimethylphosphonoacetate (**216**) and substituted aldehydes in the presence of piperidine and acetic acid as catalysts. Synthesized ester vinylphosphonates **217**-**232** were obtained in 10-86% yields.



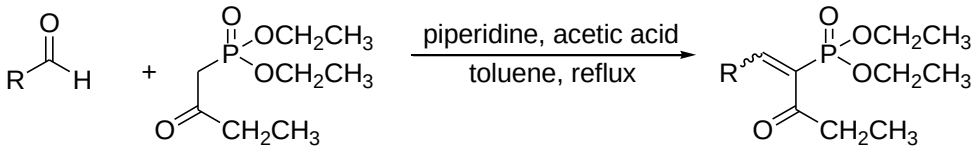
216 **217-232**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4, *p*-Cl-C_6H_4 (**217-222**)

R = *p*-Br-C_6H_4, *p*-HO-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4, mesityl (**223-227**)

R = 2-pyrrolyl, 2-furyl, 2-thiophenyl, cyclohexyl, *iso*-butyl (**228-232**)

Ketone vinylphosphonates were synthesized by the Knoevenagel reaction of diethyl 2-oxobutylphosphonate (**233**) and substituted aldehydes in the presence of piperidine and acetic acid as catalysts. Synthesized ketone vinylphosphonates **234**-**246** were obtained in 60-99% yields.

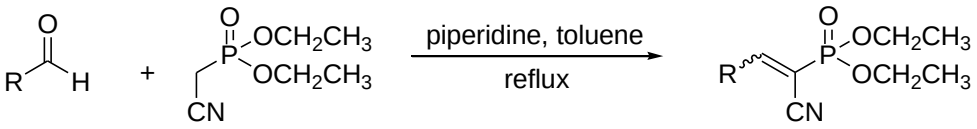


233 **234-246**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4, *p*-Cl-C_6H_4 (**234-239**)

R = *p*-Br-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4, mesityl, 2-pyrrolyl, 2-furyl, 2-thiophenyl (**240-246**)

Cyano vinylphosphonates were synthesized by the Knoevenagel reaction of diethyl cyanomethylphosphonate (**247**) and substituted aldehydes in the presence of piperidine as catalyst. Synthesized cyano vinylphosphonates **248**-**261** were obtained in 81-99% yields.



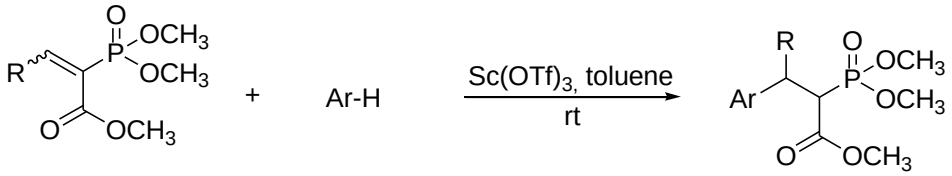
247 **248-261**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4, *p*-Cl-C_6H_4, *p*-Br-C_6H_4 (**248-254**)

R = *p*-OH-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4, mesityl, 2-pyrrolyl, 2-furyl, 2-thiophenyl (**255-261**)

In the second part; synthesized vinylphosphonates have been used in metal triflates catalyzed Michael addition reaction of heteroaromatics. The effects of different reaction parameters (solvent, catalyst, amount of catalyst and temperature) were investigated and optimum conditions have been determined for each type of vinylphosphonate.

Michael additions of heteroaromatics to ester functionalized vinylphosphonates were performed with $Sc(OTf)_3$ in toluene at rt. The ester functionalized novel phosphonate analogues **262-271,275-280** were obtained in 40-99% yields.



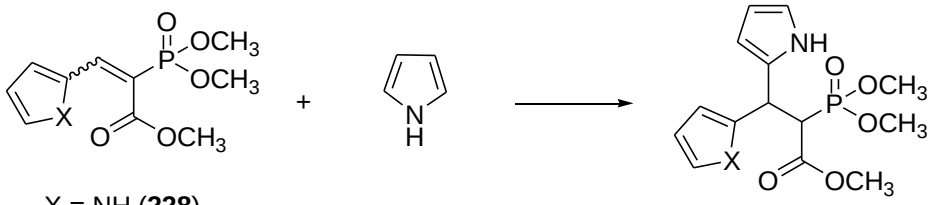
217-232 **262-271,275-280**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4, *p*-Cl-C_6H_4 (**262-267**)

R = *p*-Br-C_6H_4, *p*-HO-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4, cyclohexyl, *iso*-butyl (**268-271, 275-276**)

Ar = *N*-methylpyrrolyl, indolyl, 2,4-dimethylpyrrolyl, 2,4-dimethyl-3-ethylpyrrolyl (**277-280**)

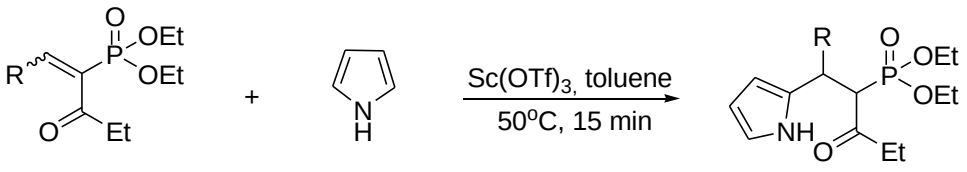
Pyrrolyl-substituted vinylphosphonate gave the corresponding addition product with TFA and furyl and thiophenyl-substituted vinylphosphonates gave the addition products with Mont. K-10. The pyrrolyl, furyl and thiophenyl-substituted novel phosphonate analogues **272-274** were obtained in 25-45% yields.



X = NH (**228**)
X = O (**229**)
X = S (**230**)

X = NH (**272**)
X = O (**273**)
X = S (**274**)

Michael addition of pyrrole to ketone functionalized vinylphosphonates were performed with $Sc(OTf)_3$ in toluene at 50°C in 15 min. The novel phosphonate analogues (**281-292**) were obtained in 15-73% yields.

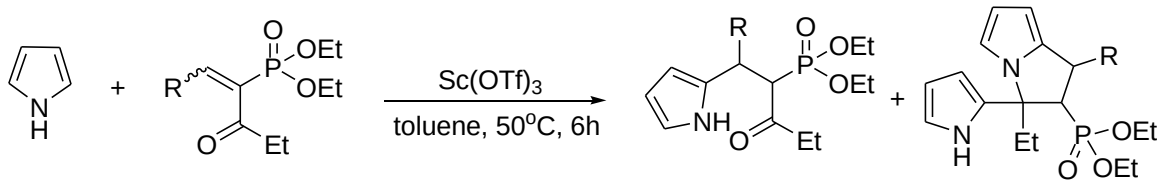


234-246 **281-292**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4, *p*-Cl-C_6H_4 (**281-286**)

R = *p*-Br-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4, 2-pyrrolyl, 2-furyl, 2-thiophenyl (**287-292**)

Michael addition of pyrrole to ketone functionalized vinylphosphonates with $Sc(OTf)_3$ in toluene at 50°C gave pyrrole substituted pyrrolizine ring structures **293-303** besides addition products. The novel pyrrole substituted pyrrolizine rings were obtained in 13-63% yields.

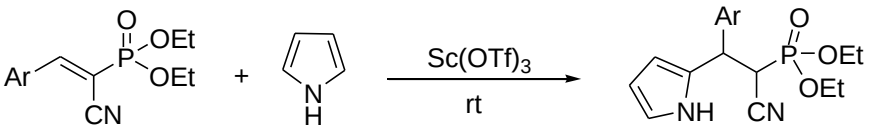


234-246 **281-292** **293-303**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4, *p*-Cl-C_6H_4 (**293-298**)

R = *p*-Br-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4, 2-furyl, 2-thiophenyl (**299-303**)

Michael additions of pyrrole to cyano functionalized vinylphosphonates with $Sc(OTf)_3$ in excess pyrrole at rt produced novel phosphonate analogues **304-312** in 15-96% yields.



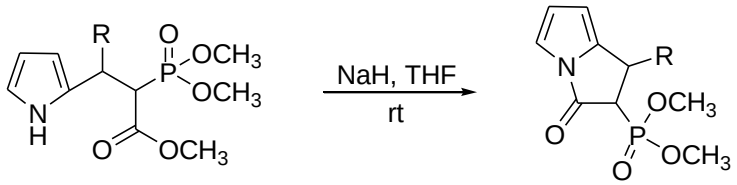
248-261 **304-312**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4 (**304-308**)

R = *p*-Cl-C_6H_4, *p*-Br-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4 (**309-312**)

$Sc(OTf)_3$ was found as the effective catalyst for the Michael addition of heteroaromatics to ester, ketone and cyano functionalized vinylphosphonates. $Sc(OTf)_3$ is also effective for the synthesis of pyrrole substituted pyrrolizines by the addition of pyrrole to the ketone vinylphosphonates.

In the last part of the study; pyrrole addition products have been used in the synthesis of pyrrolizines with an intramolecular cyclization reaction. Reactions of ester functionalized pyrrole addition products with NaH were performed in THF at rt. The novel phosphoryl pyrrolizines **316-330** were obtained in 44-99% yields as a single diastereomer.



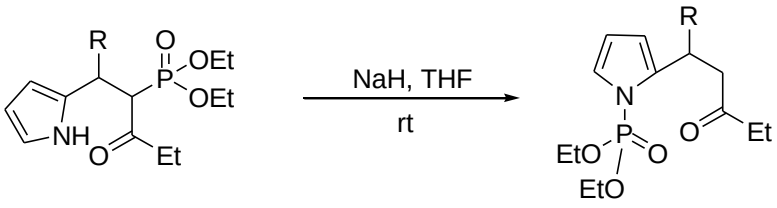
262-276,279-280 **316-330**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4 (**316-320**)

R =*p*-Cl-C_6H_4, *p*-Br-C_6H_4, *p*-HO-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4 (**321-325**)

R = 2-pyrrolyl, 2-furyl, 2-thiophenyl, cyclohexyl, *iso*-butyl (**326-330**)

Reactions of ketone functionalized pyrrole addition products with NaH in THF at rt did not gave the expected pyrrolizine ring structures. Novel *N*-phosphorylated pyrrole derivatives were obtained instead of pyrrolizines under these reaction conditions. The novel *N*-phosphorylated pyrrole derivatives **331,345-355** were obtained in 20-85% yields. Synthesis of *N*-phosphorylated pyrrole derivatives by the migration of phosphonate group is a novel method.

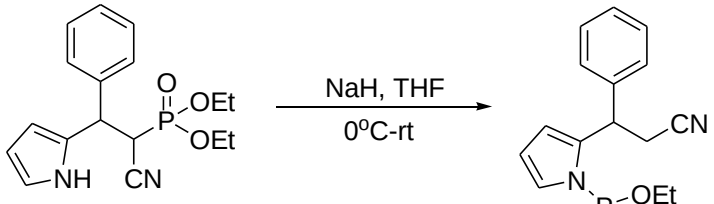


281-292 **331,345-355**

R = C_6H_5, *p*-CF_3-C_6H_4, *p*-CH_3-C_6H_4, *p*-H_3CO-C_6H_4, *p*-F-C_6H_4, *p*-Cl-C_6H_4 (**331, 345-349**)

R = *p*-Br-C_6H_4, *p*-CN-C_6H_4, *p*-NO_2-C_6H_4, 2-pyrrolyl, 2-furyl, 2-thiophenyl (**350-355**)

Reactions of cyano functionalized pyrrole addition products with NaH gave *N*-phosphorylated pyrrole derivative **356** in 20% yield.



304 **356**

APPENDIX A

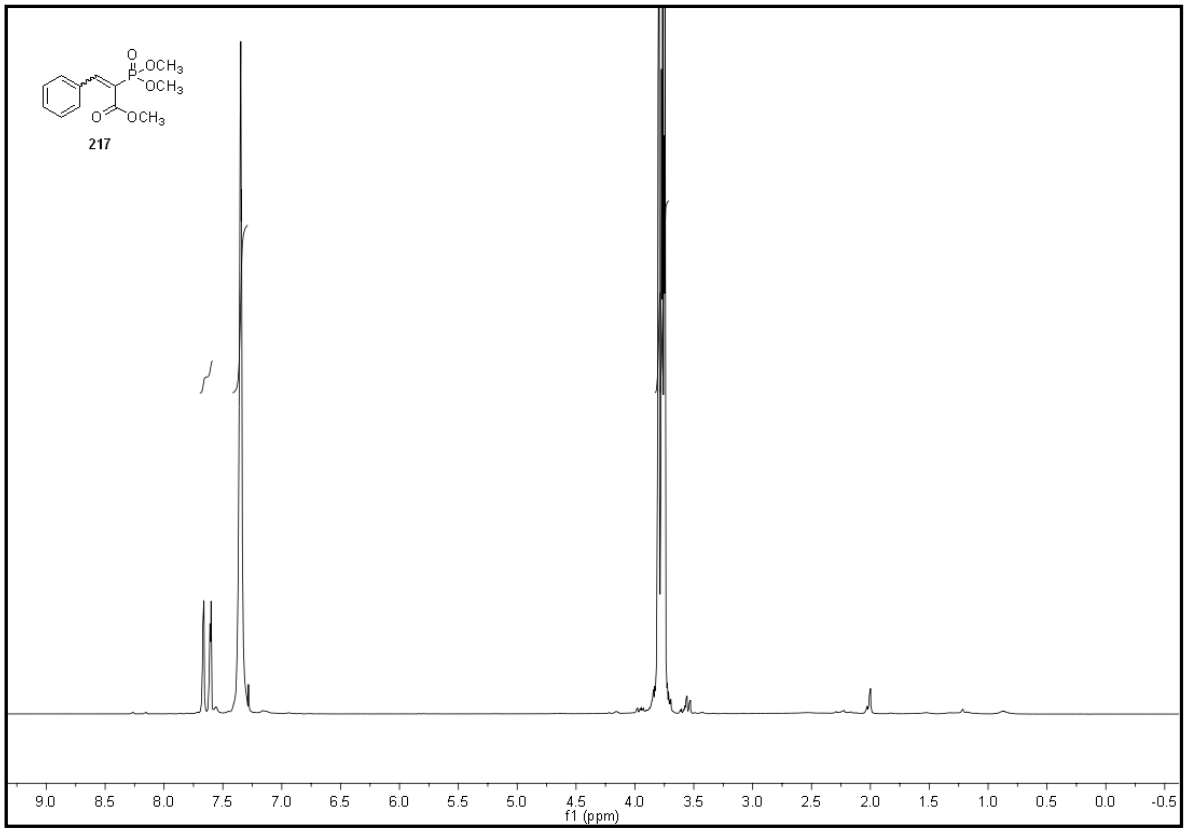


Figure A.1. ^{1}H NMR spectrum of compound **217**

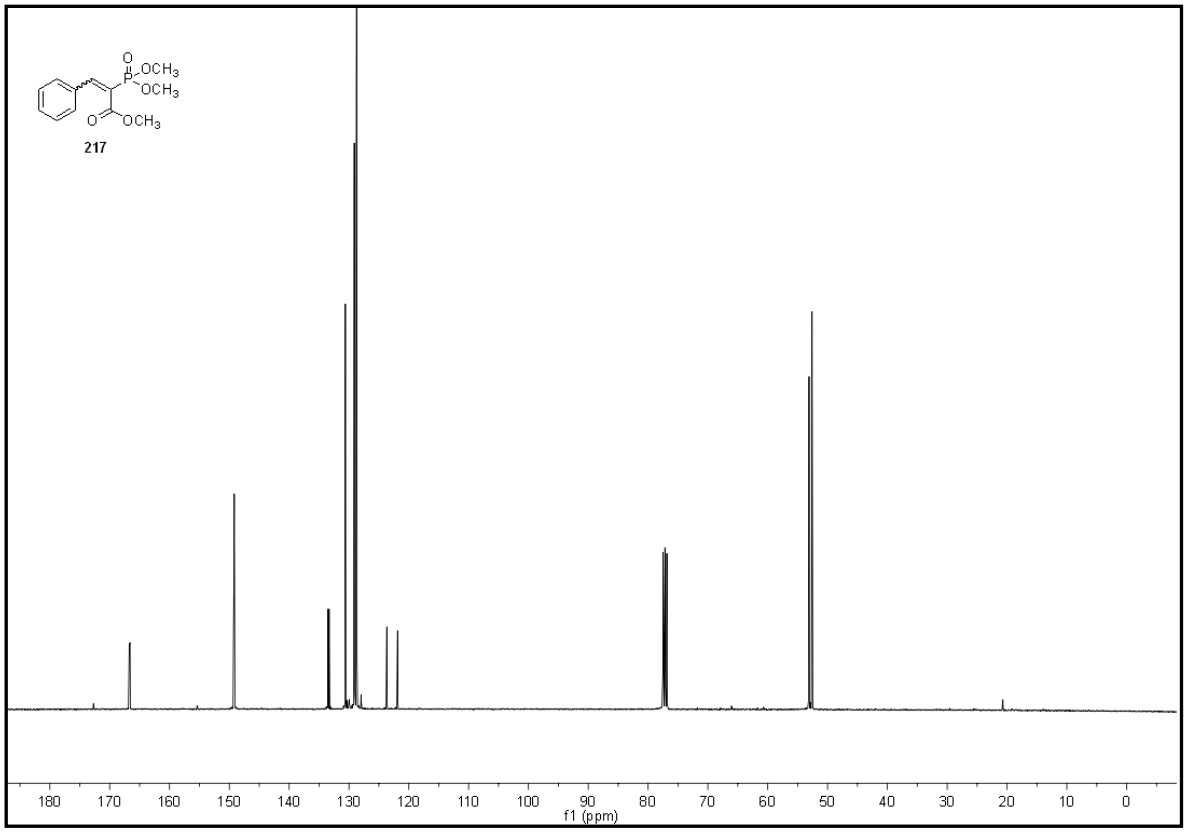


Figure A.2. ^{13}C NMR spectrum of compound **217**

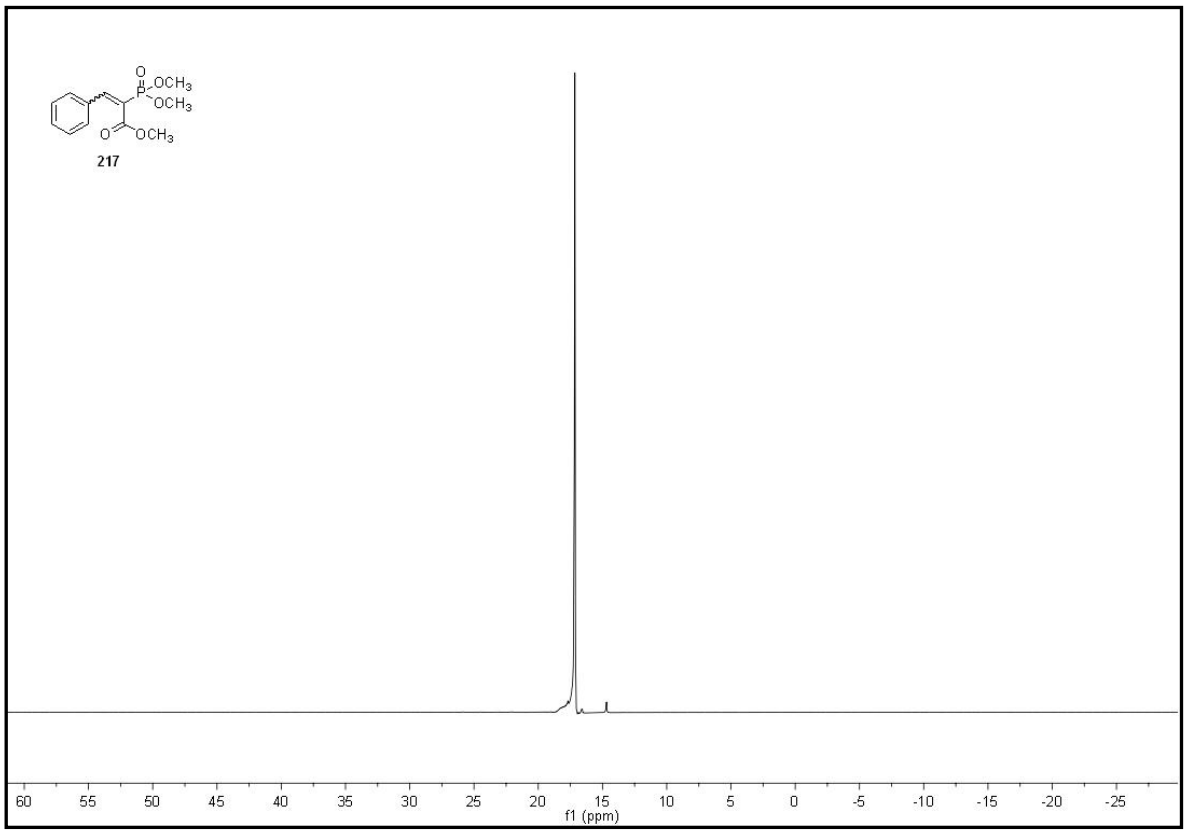


Figure A.3. ^{31}P NMR spectrum of compound **217**

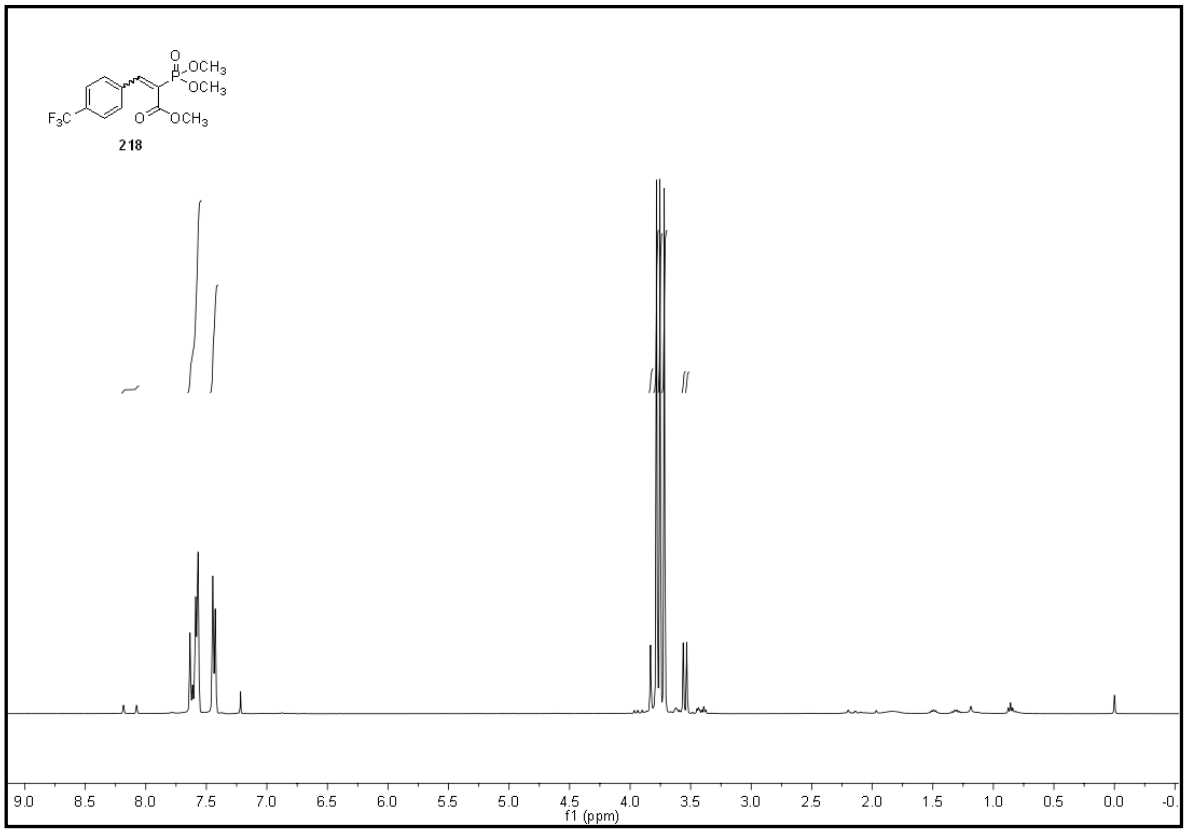


Figure A.4. ^{1}H NMR spectrum of compound **218**

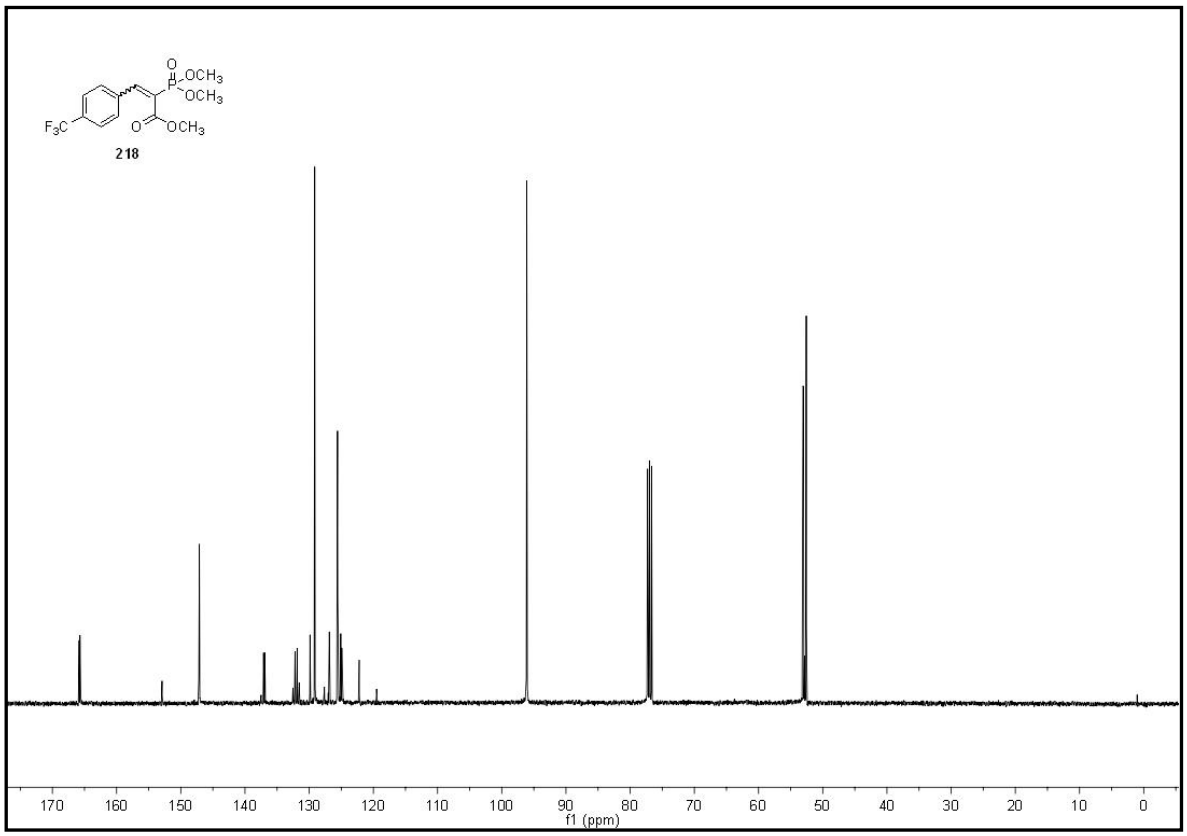


Figure A.5. ^{13}C NMR spectrum of compound **218**

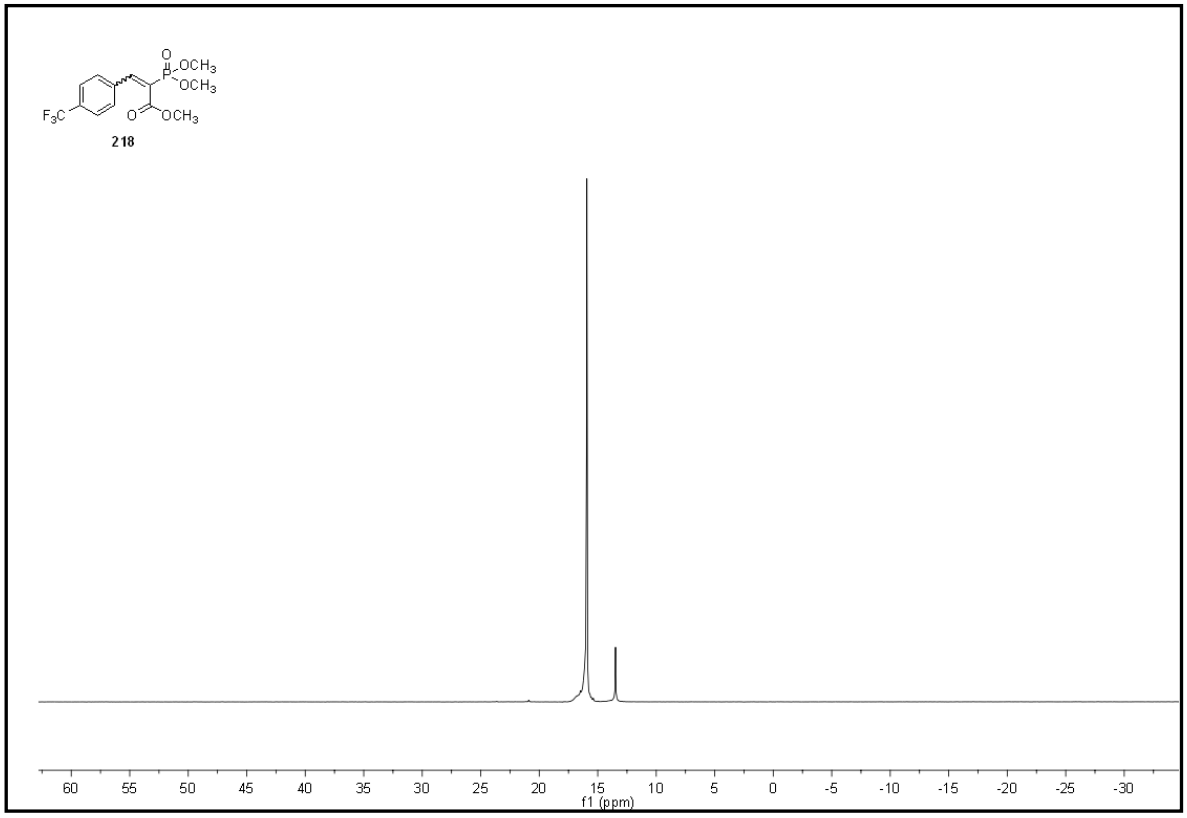


Figure A.6. ^{31}P NMR spectrum of compound **218**

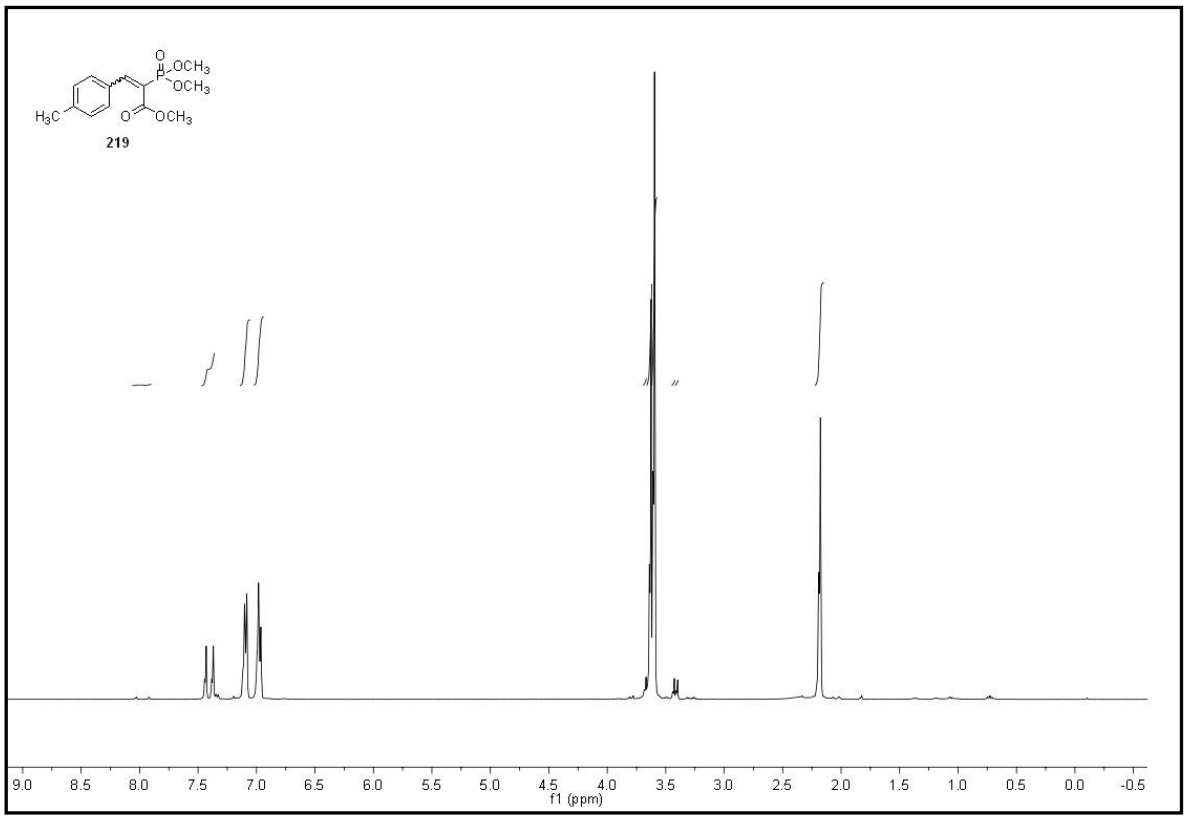


Figure A.7. ^{1}H NMR spectrum of compound **219**

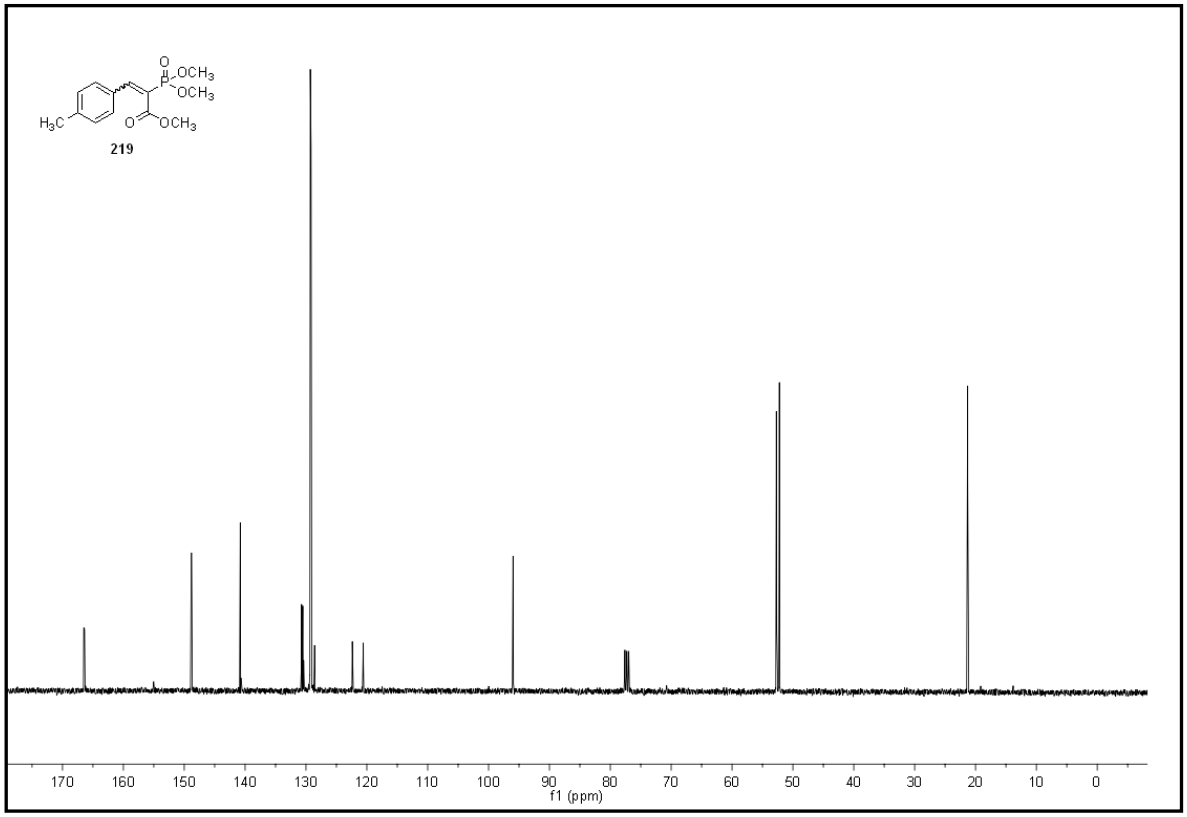


Figure A.8. ^{13}C NMR spectrum of compound **219**

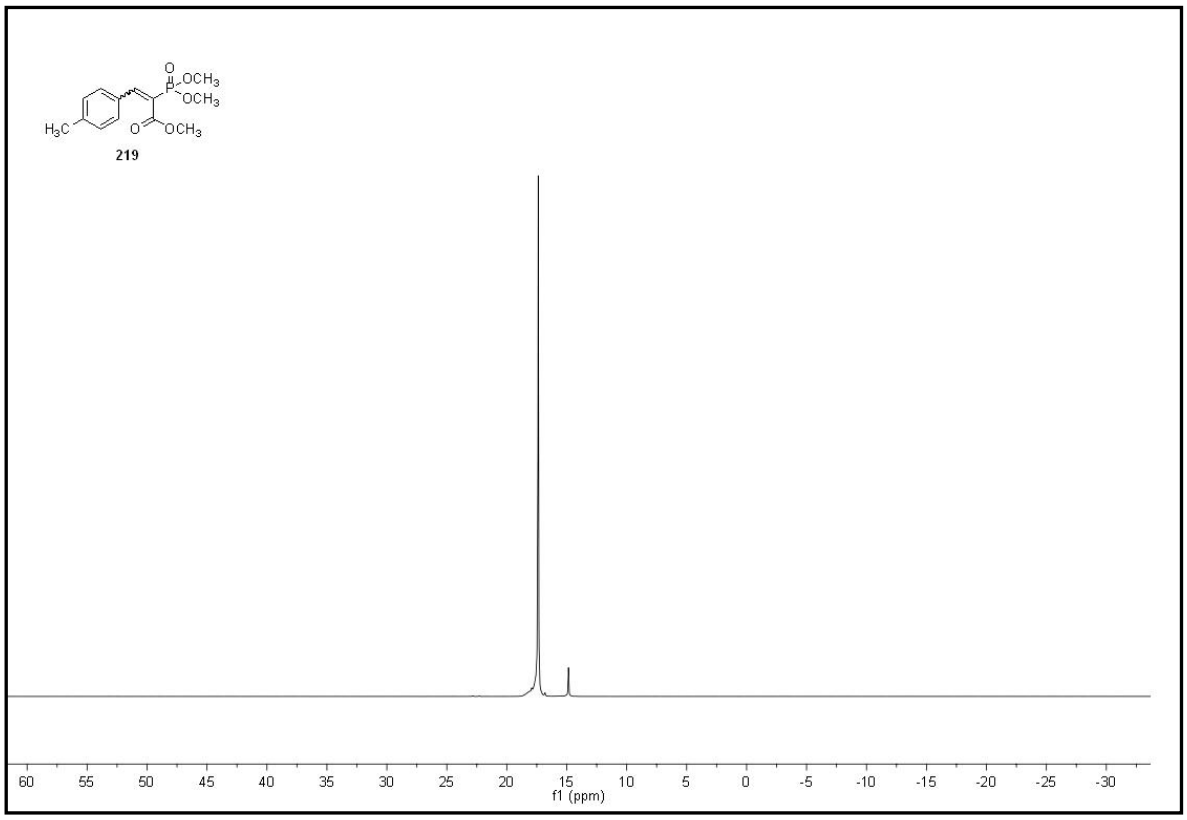


Figure A.9. ^{31}P NMR spectrum of compound **219**

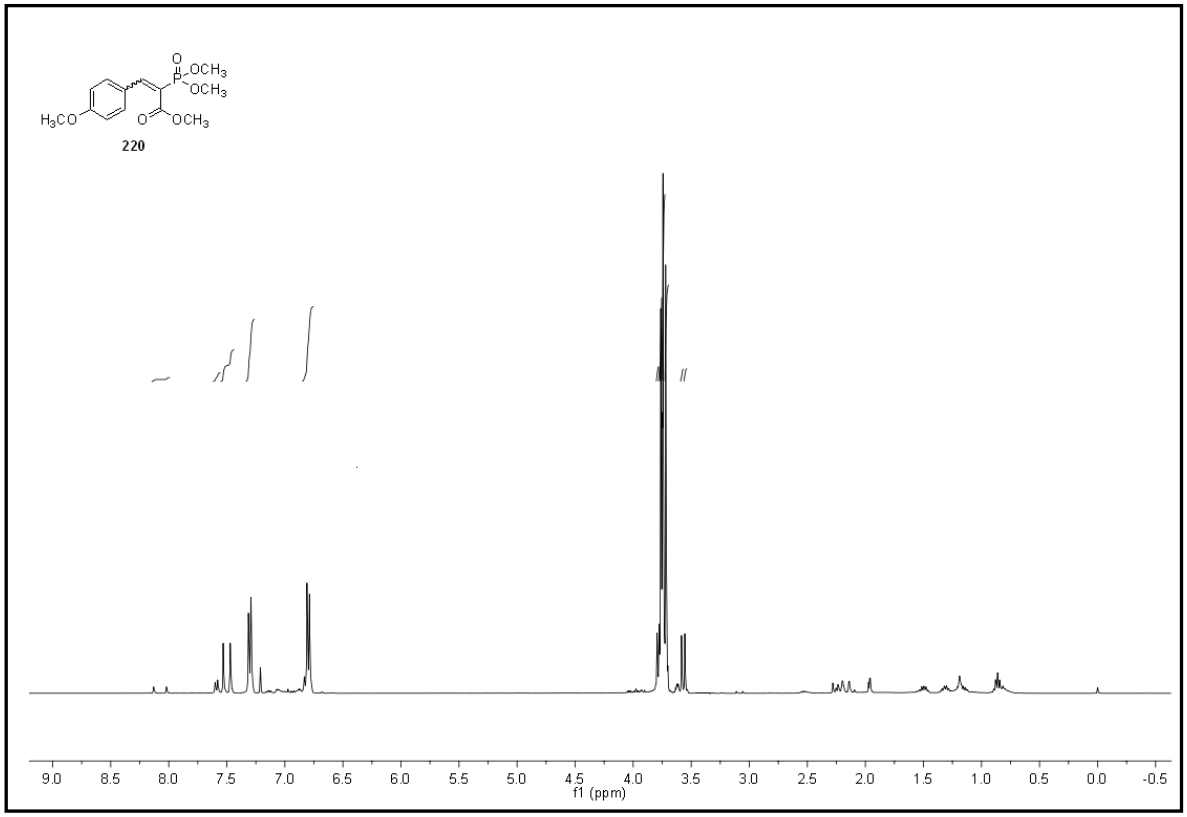


Figure A.10. ^{1}H NMR spectrum of compound **220**

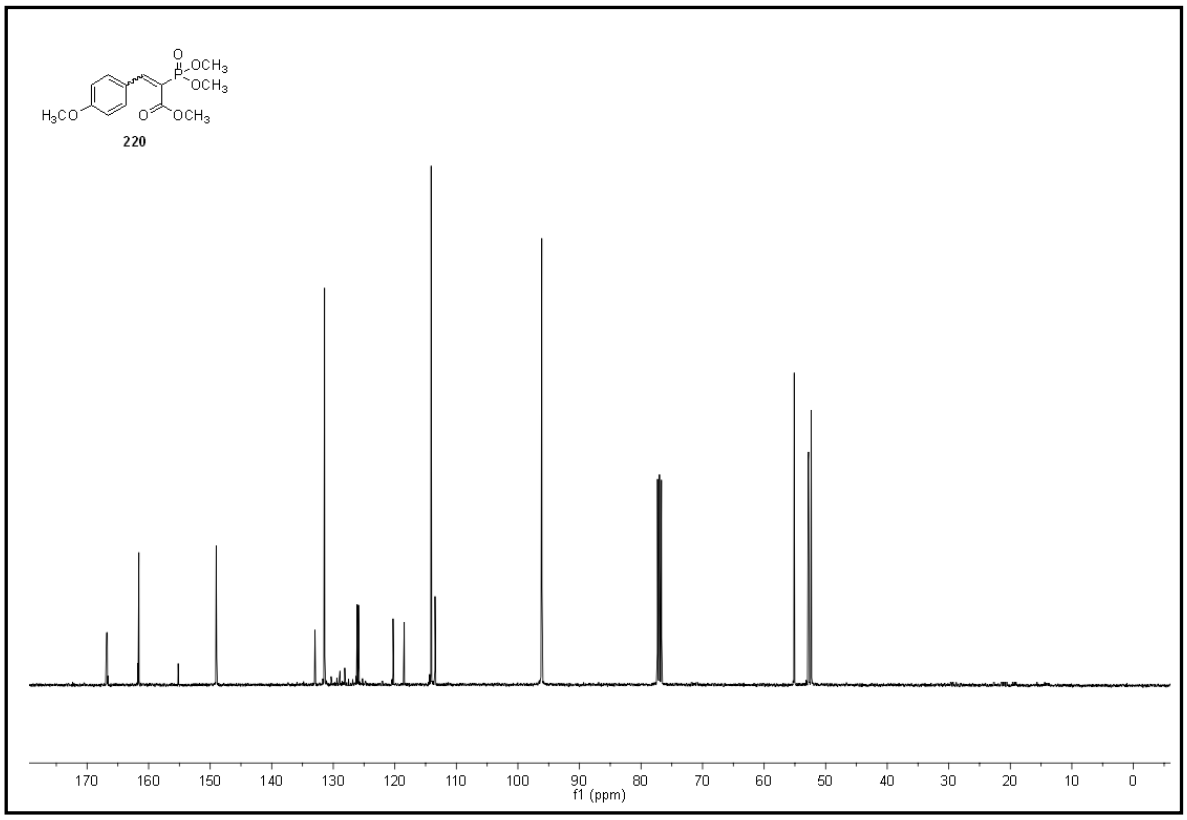


Figure A.11. ^{13}C NMR spectrum of compound **220**

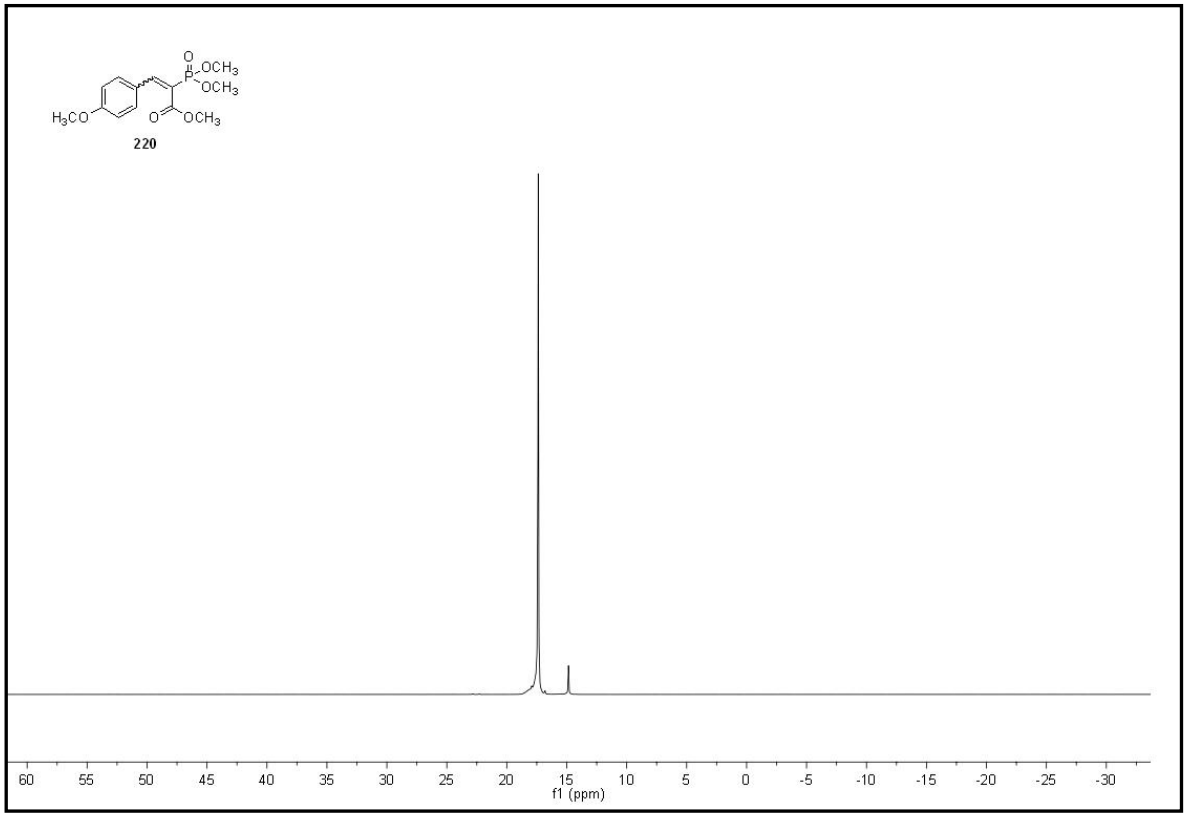


Figure A.12. ^{31}P NMR spectrum of compound **220**

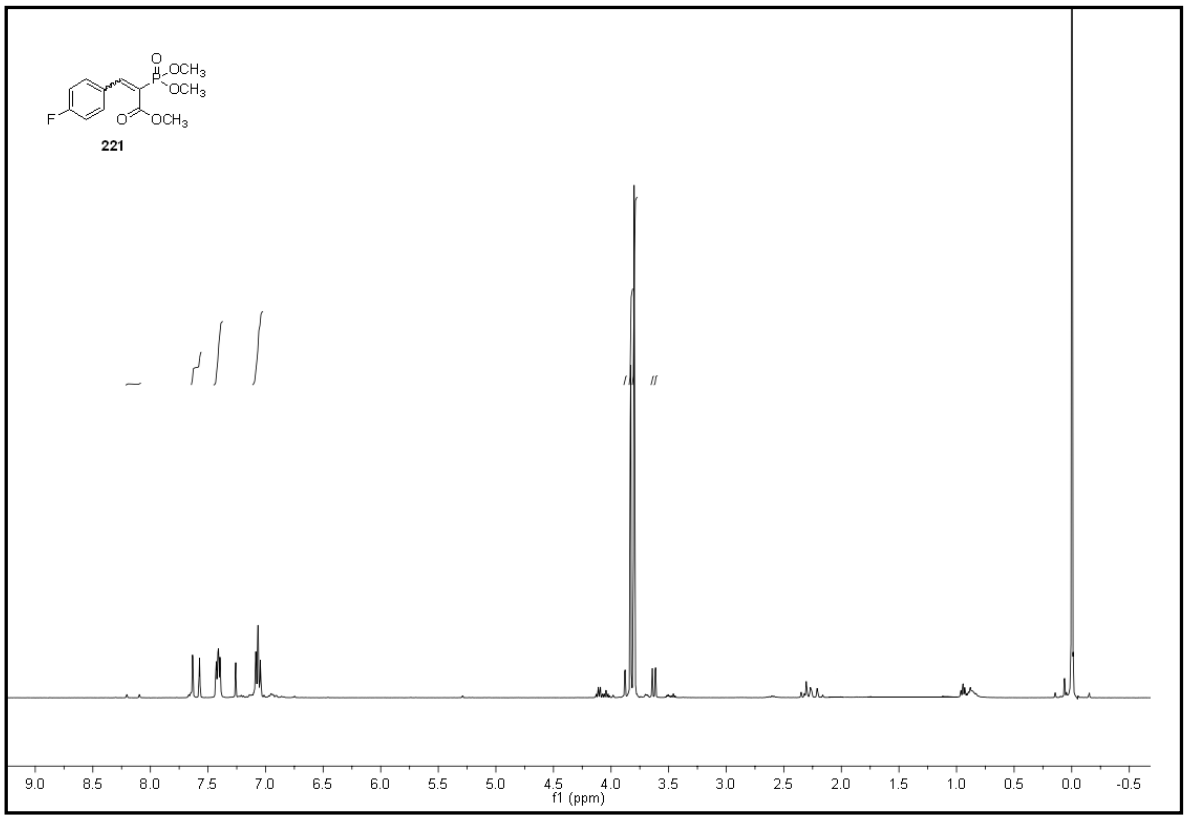


Figure A.13. ^{1}H NMR spectrum of compound **221**

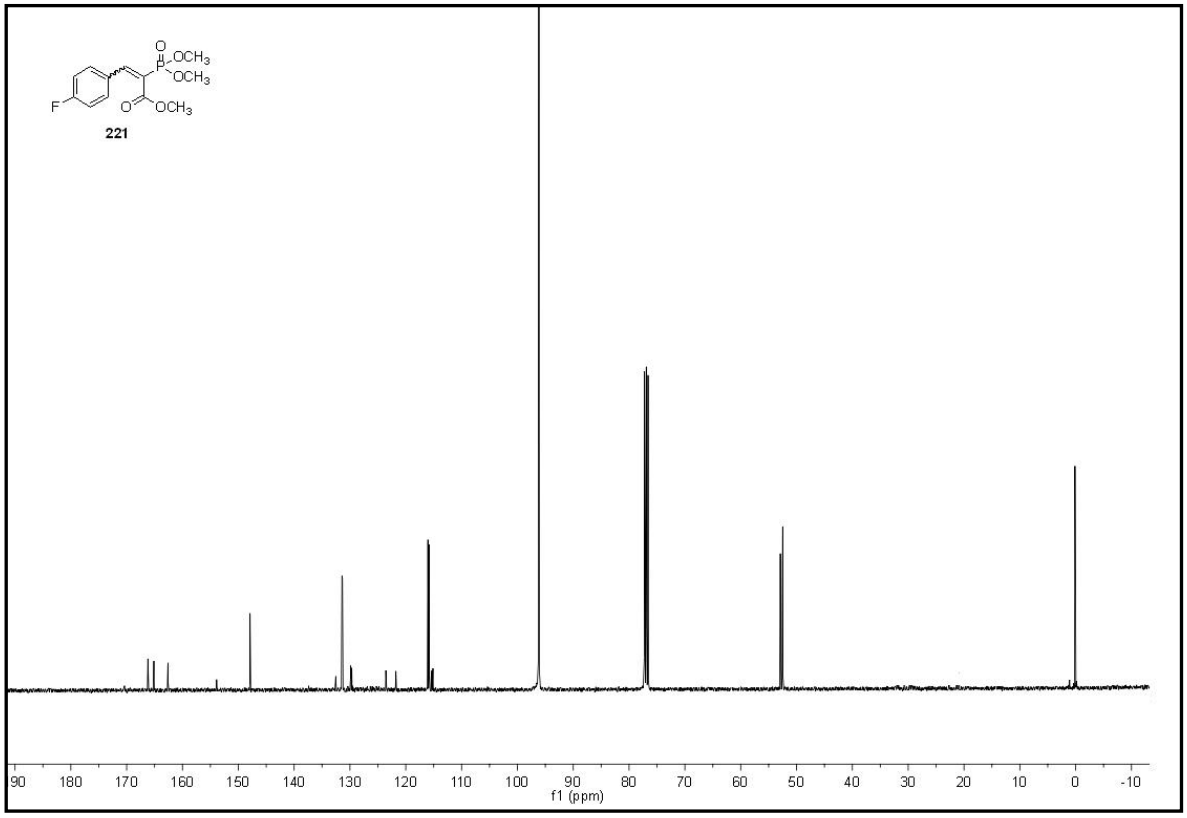


Figure A.14. ^{13}C NMR spectrum of compound **221**

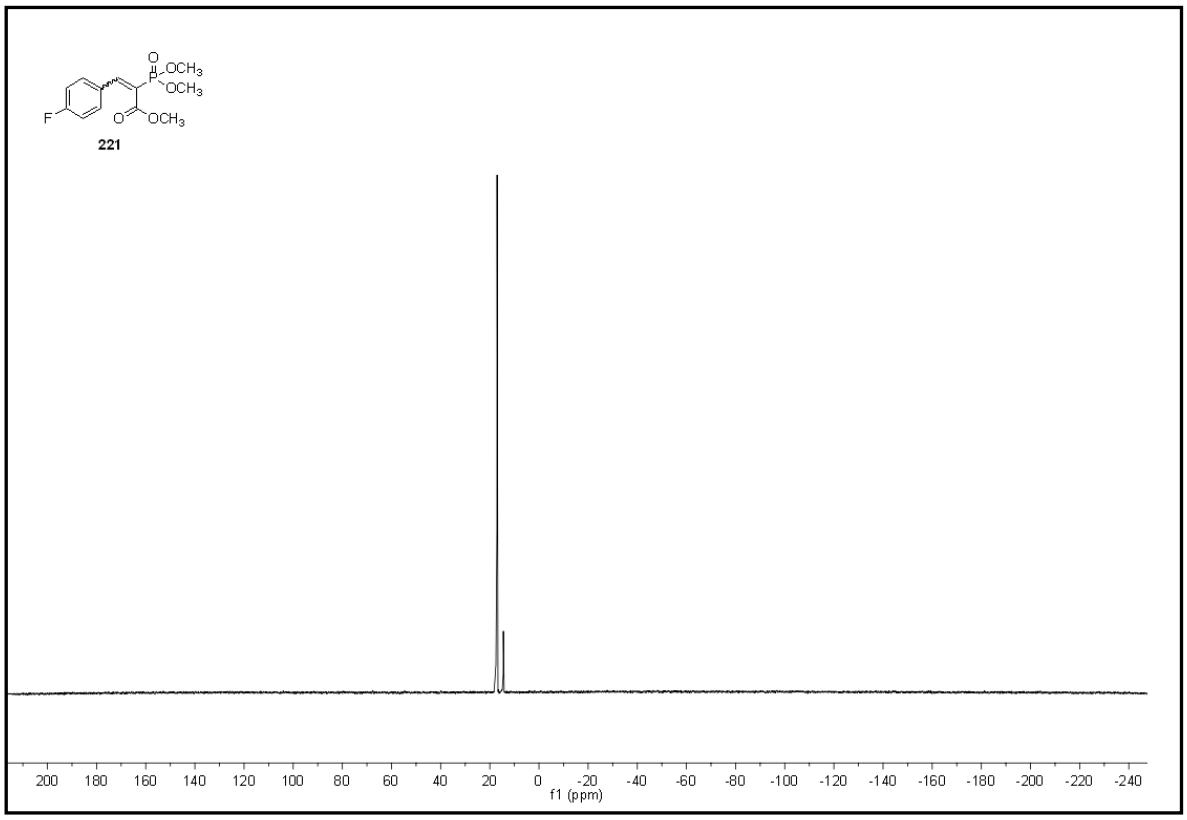


Figure A.15. ^{31}P NMR spectrum of compound **221**

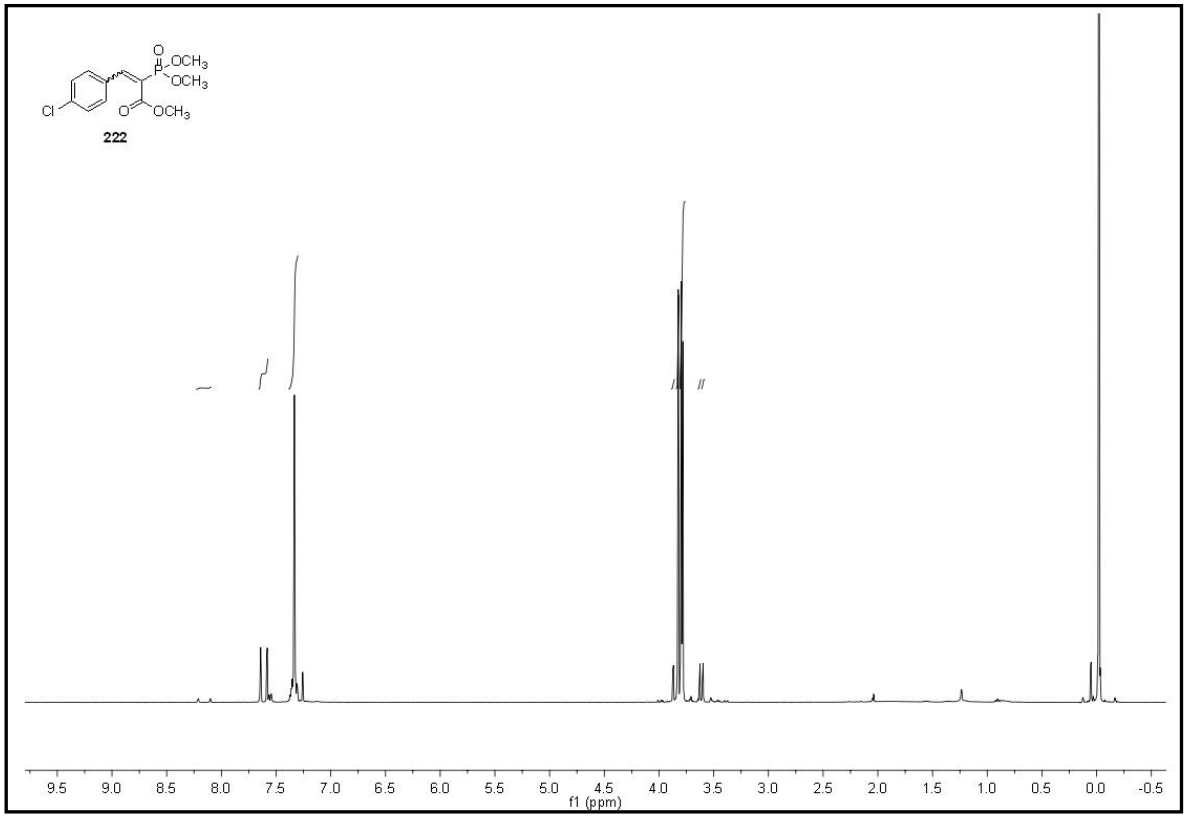


Figure A.16. ^{1}H NMR spectrum of compound **222**

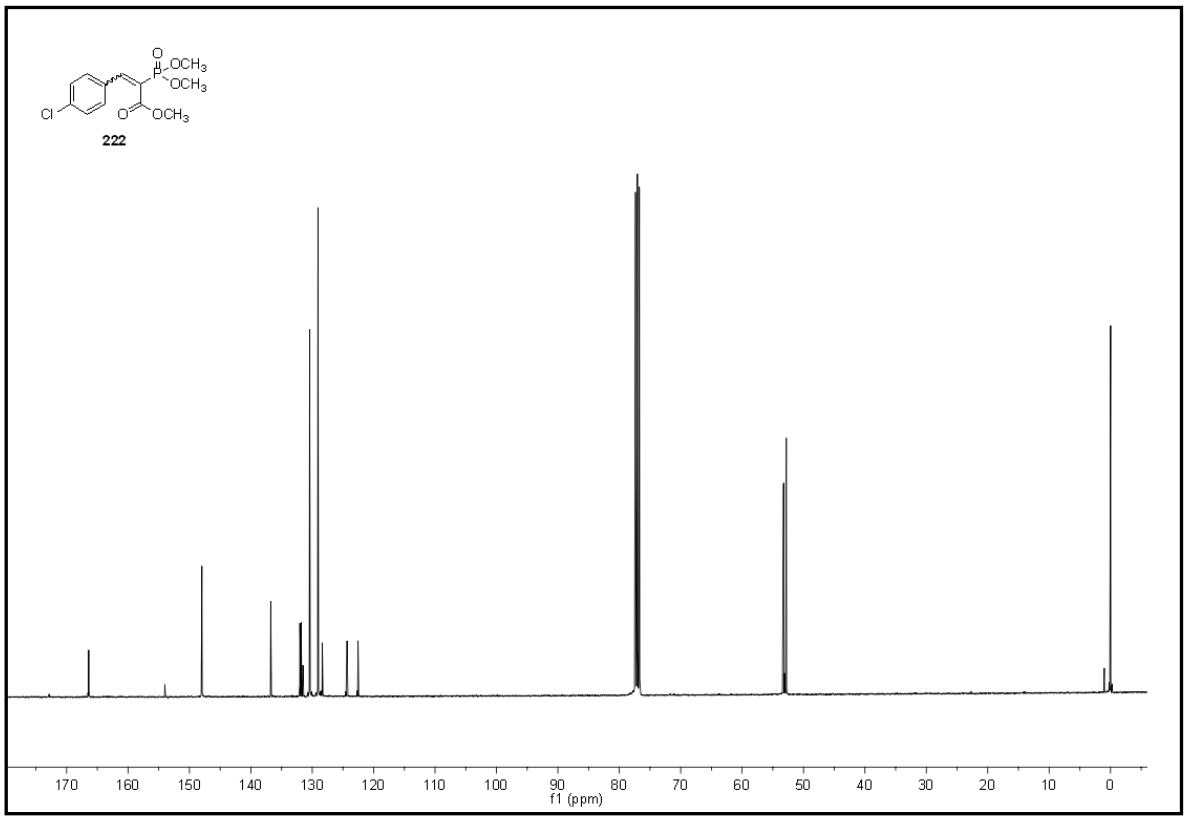


Figure A.17. ^{13}C NMR spectrum of compound **222**

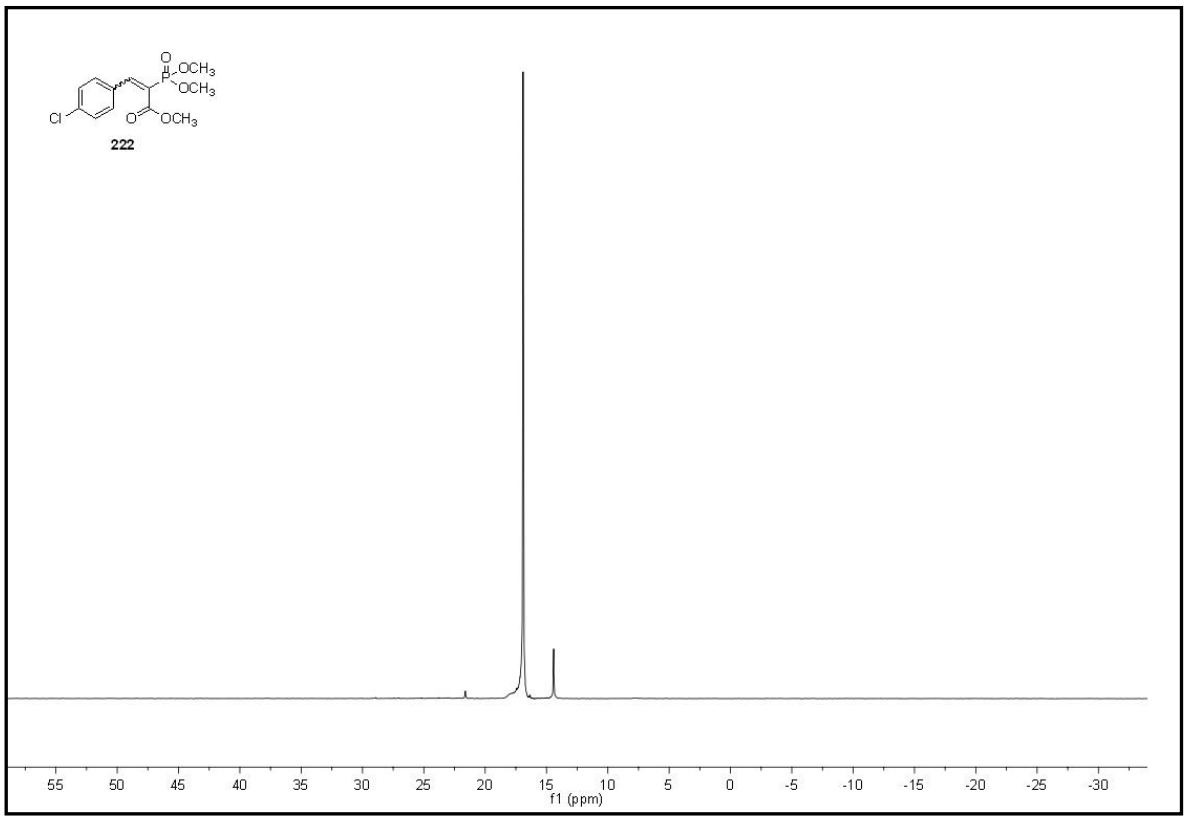


Figure A.18. ^{31}P NMR spectrum of compound **222**

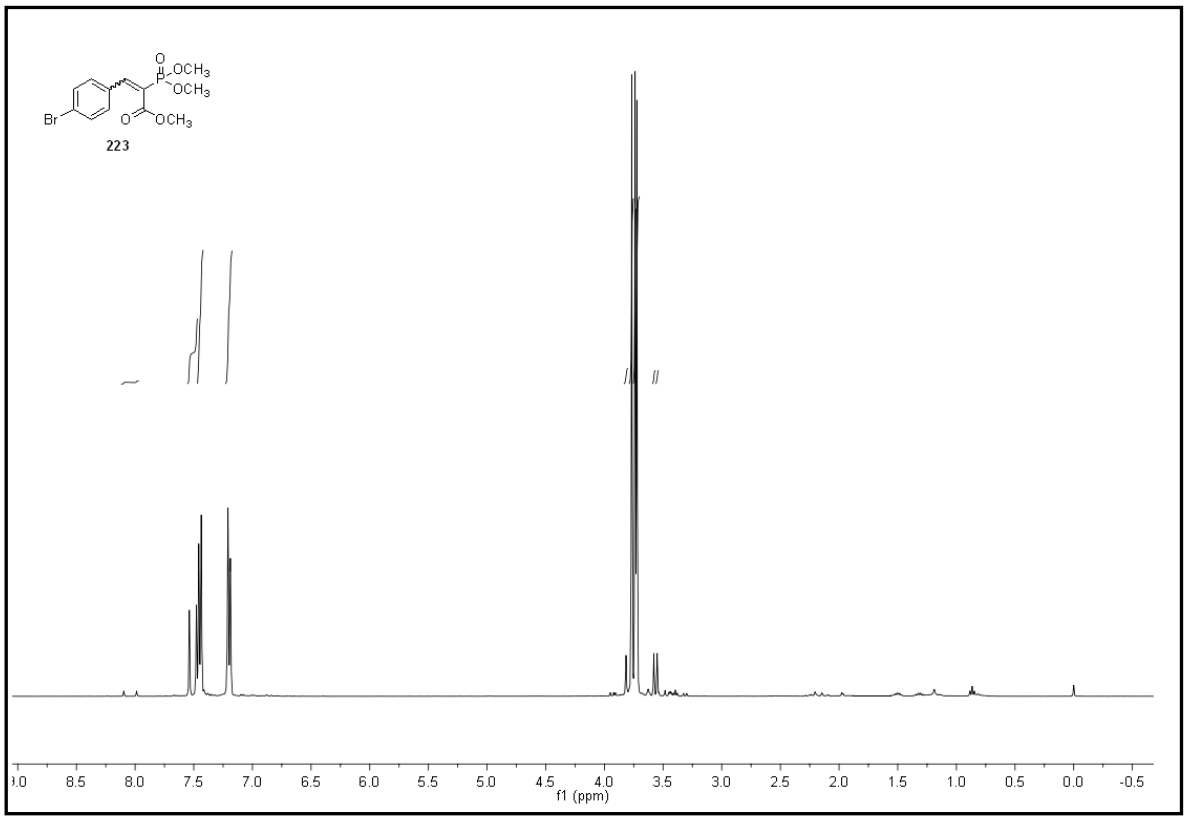


Figure A.19. ^{1}H NMR spectrum of compound **223**

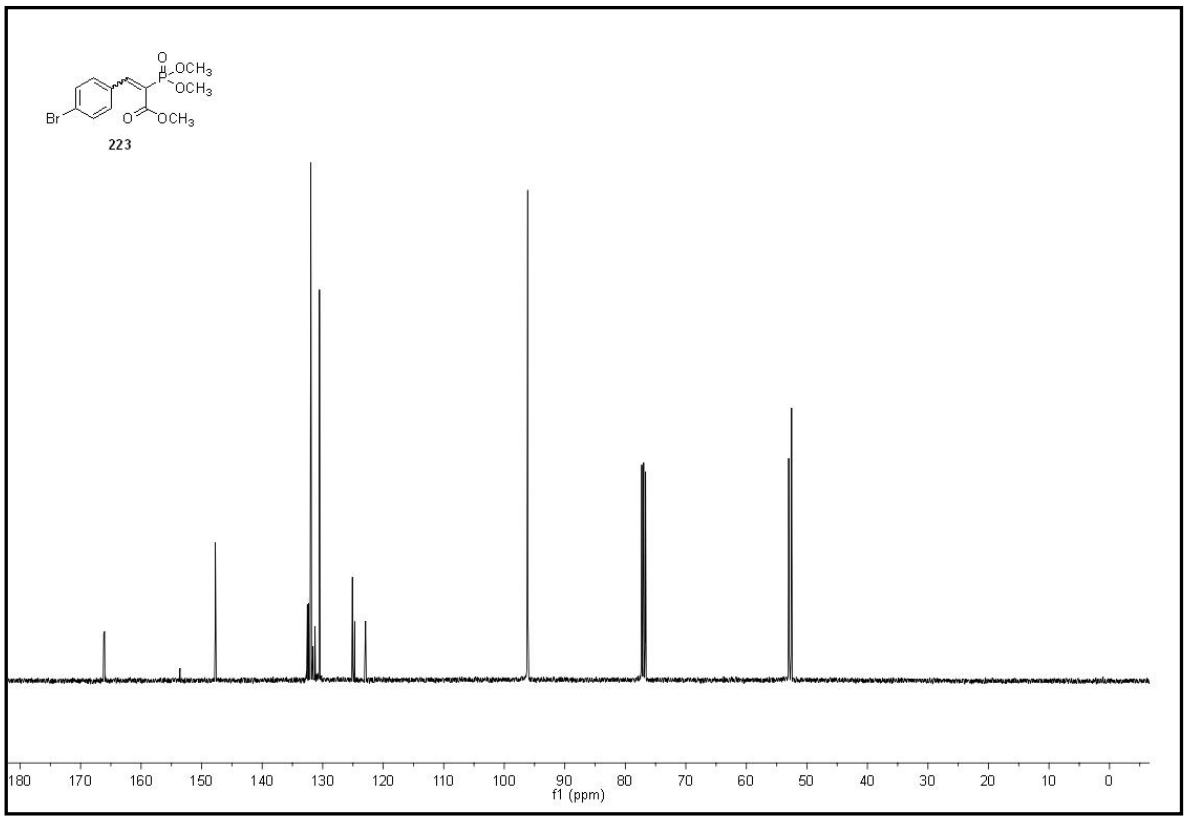


Figure A.20. ^{13}C NMR spectrum of compound **223**

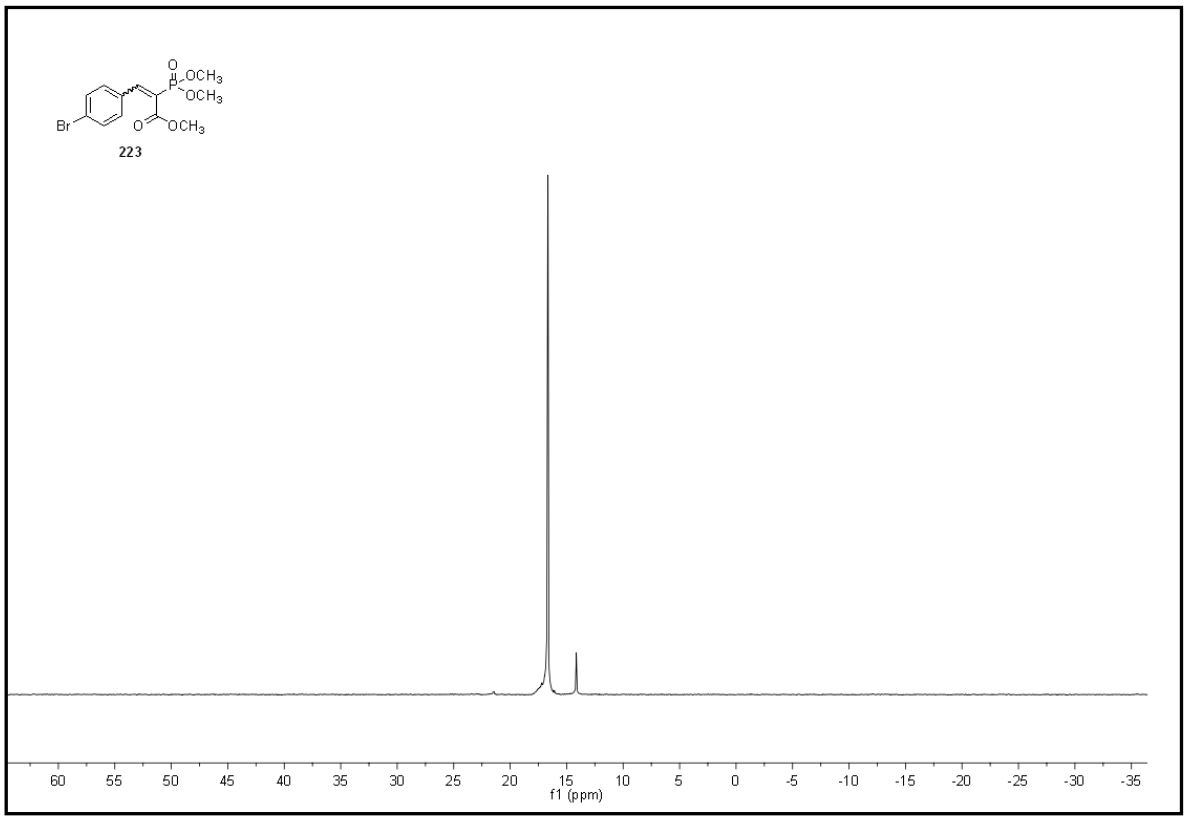


Figure A.21. ^{31}P NMR spectrum of compound **223**

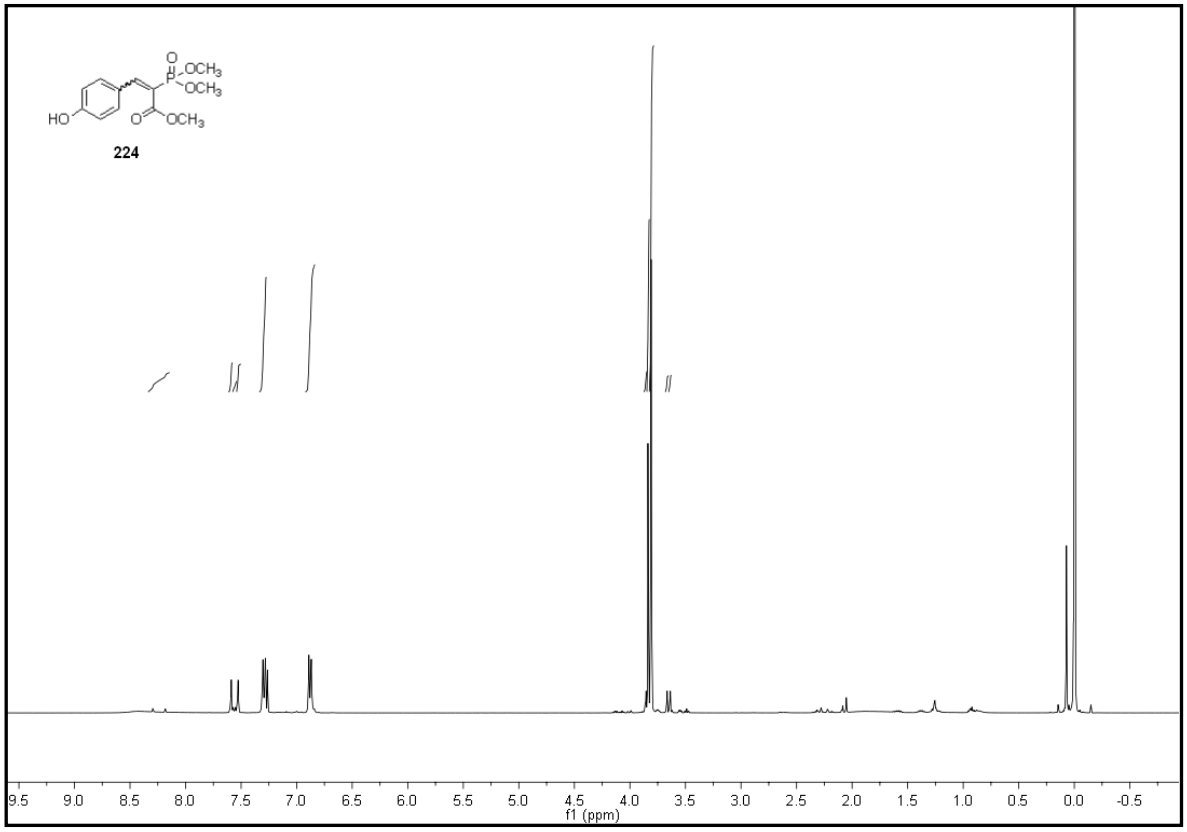


Figure A.22. ^{1}H NMR spectrum of compound **224**

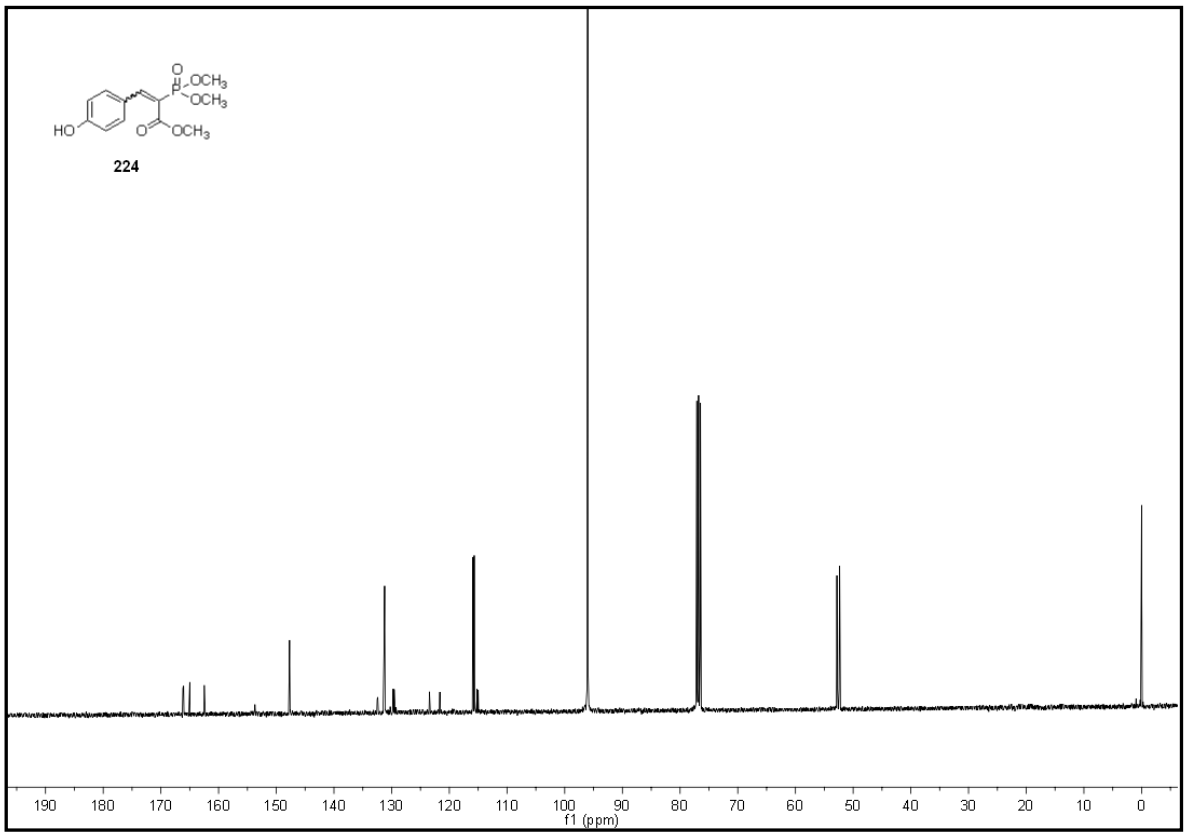


Figure A.23. ^{13}C NMR spectrum of compound **224**

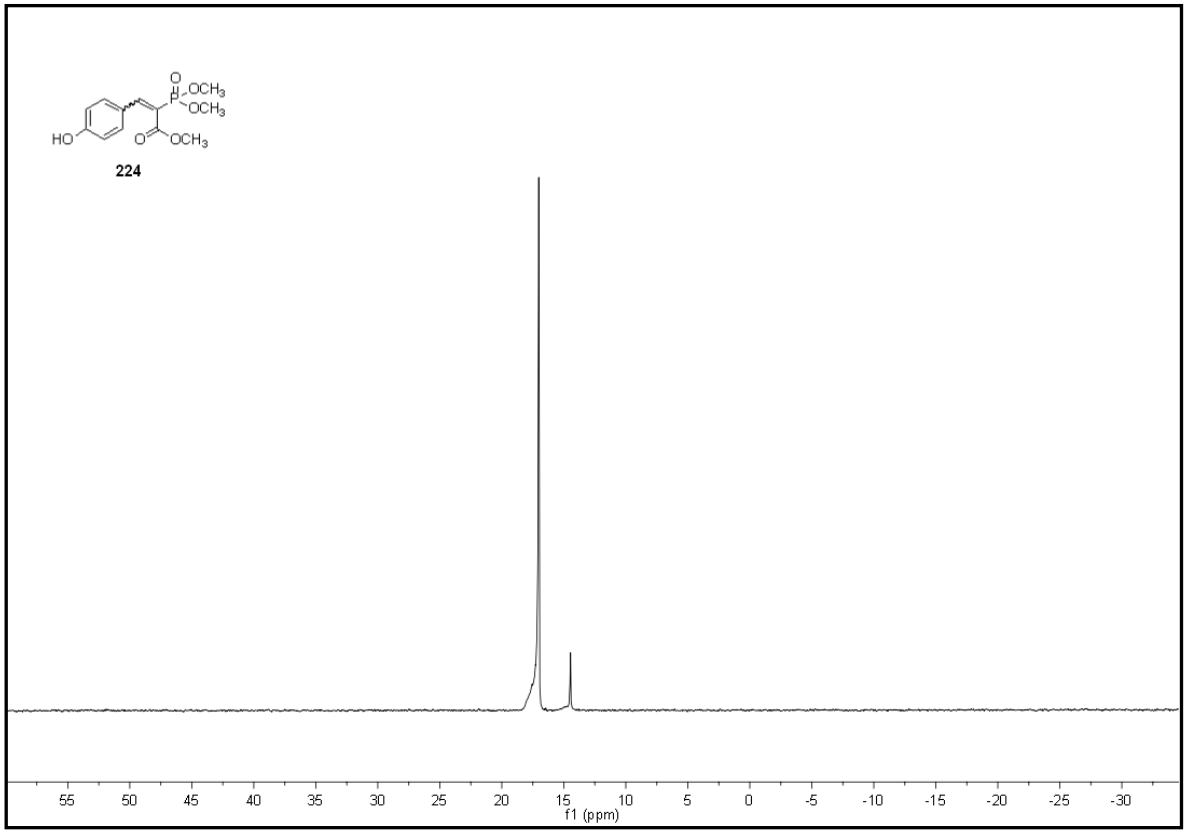


Figure A.24. ^{31}P NMR spectrum of compound **224**

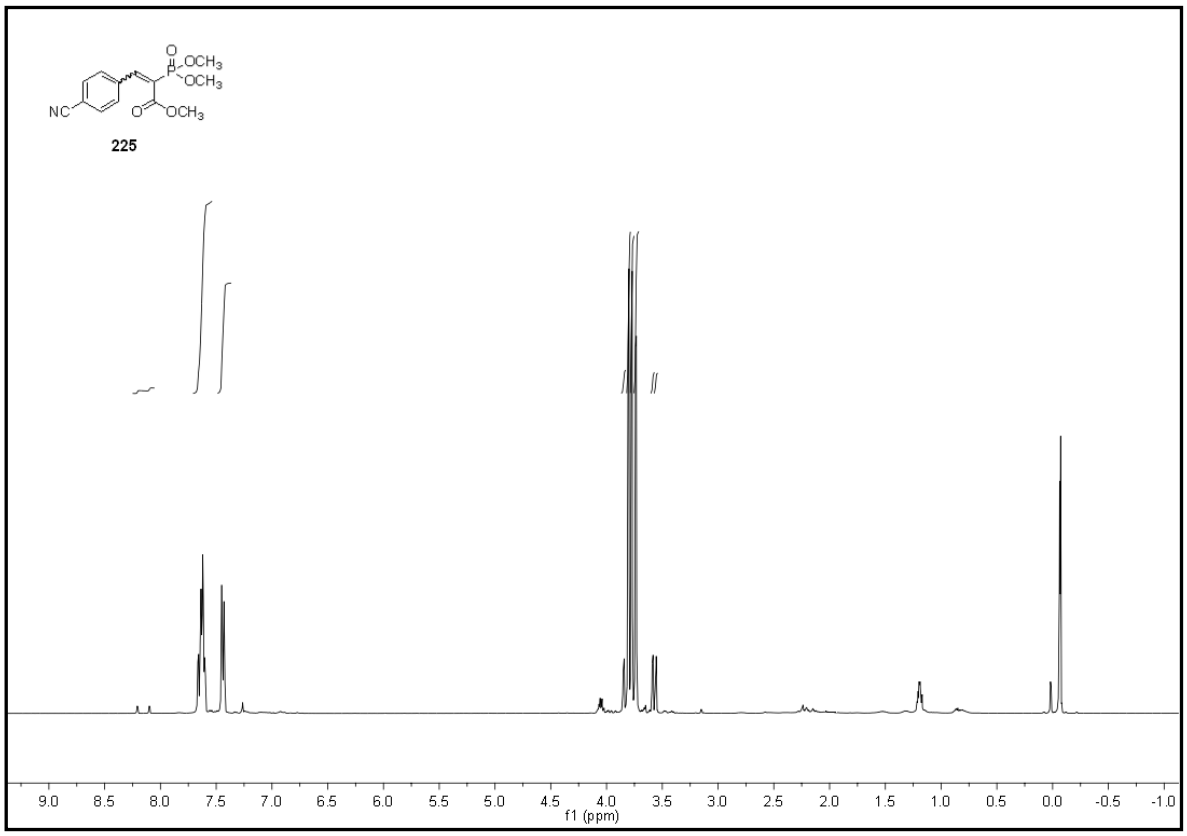


Figure A.25. ^{1}H NMR spectrum of compound **225**

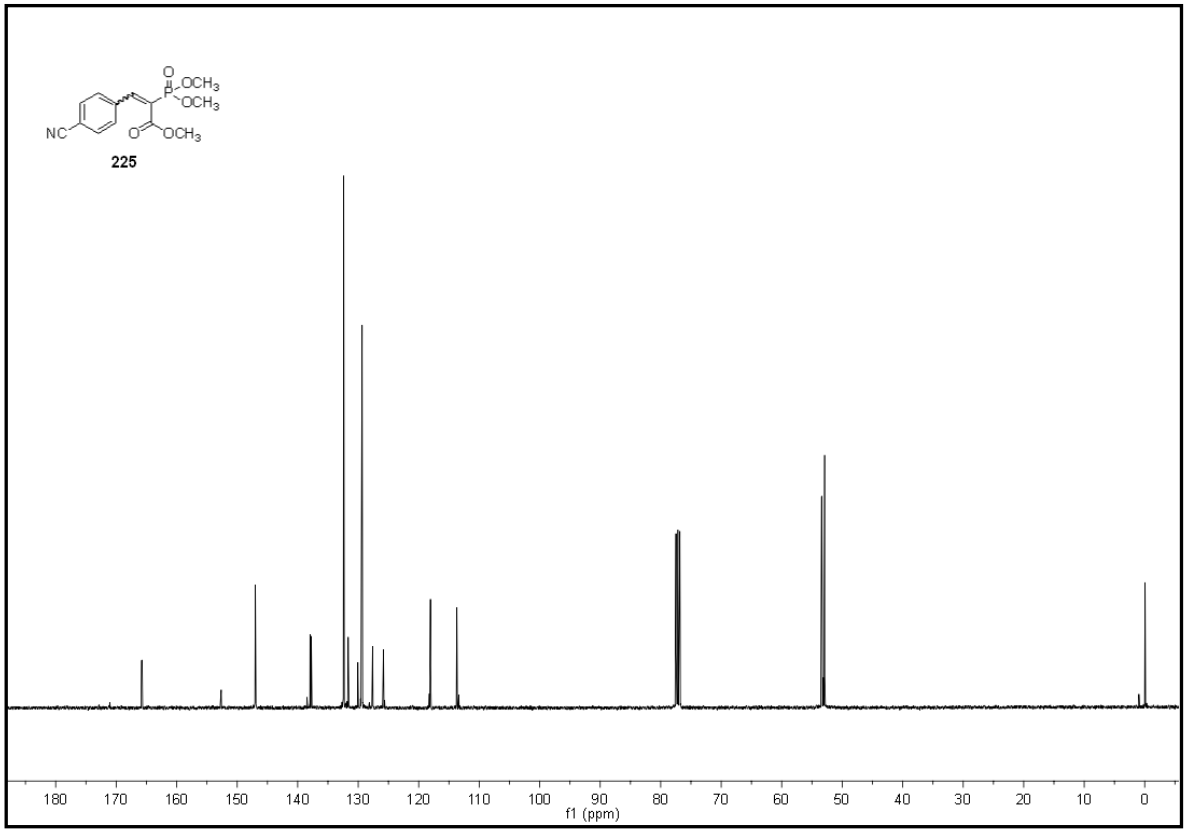


Figure A.26. ^{13}C NMR spectrum of compound **225**

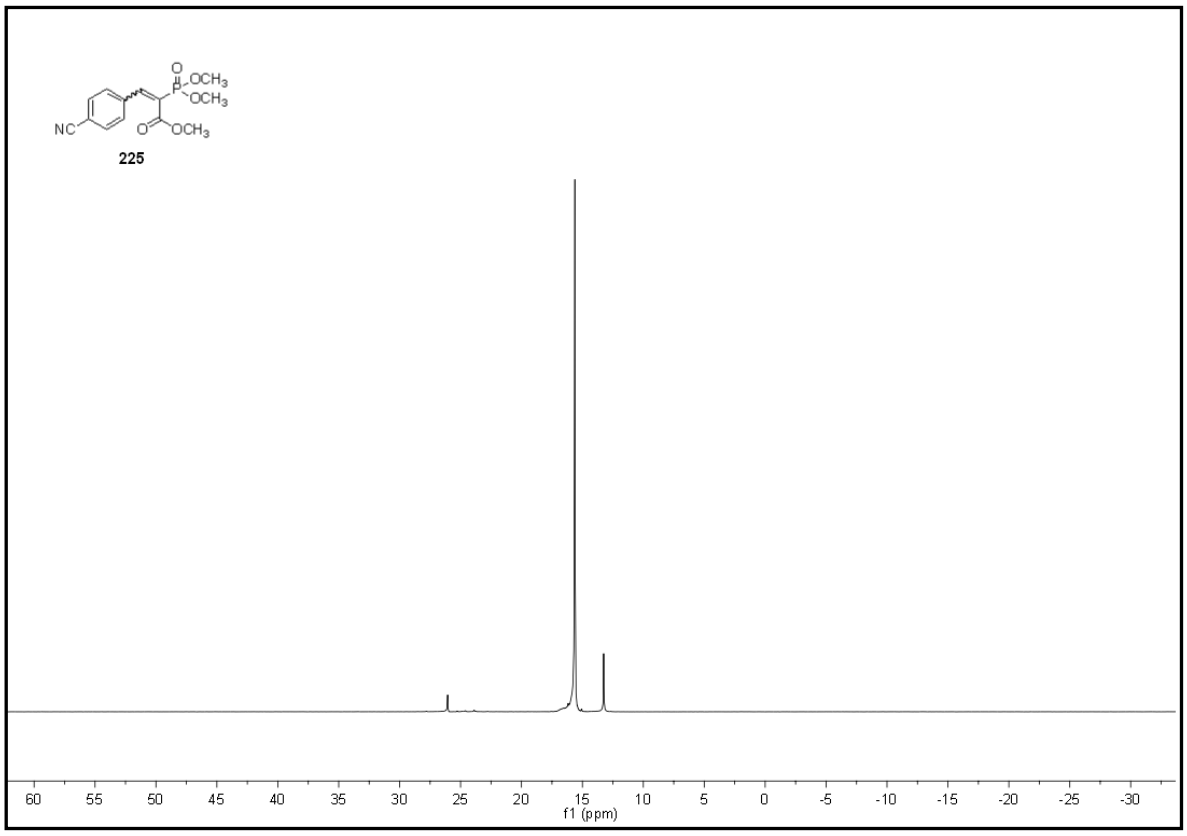


Figure A.27. ^{31}P NMR spectrum of compound **225**

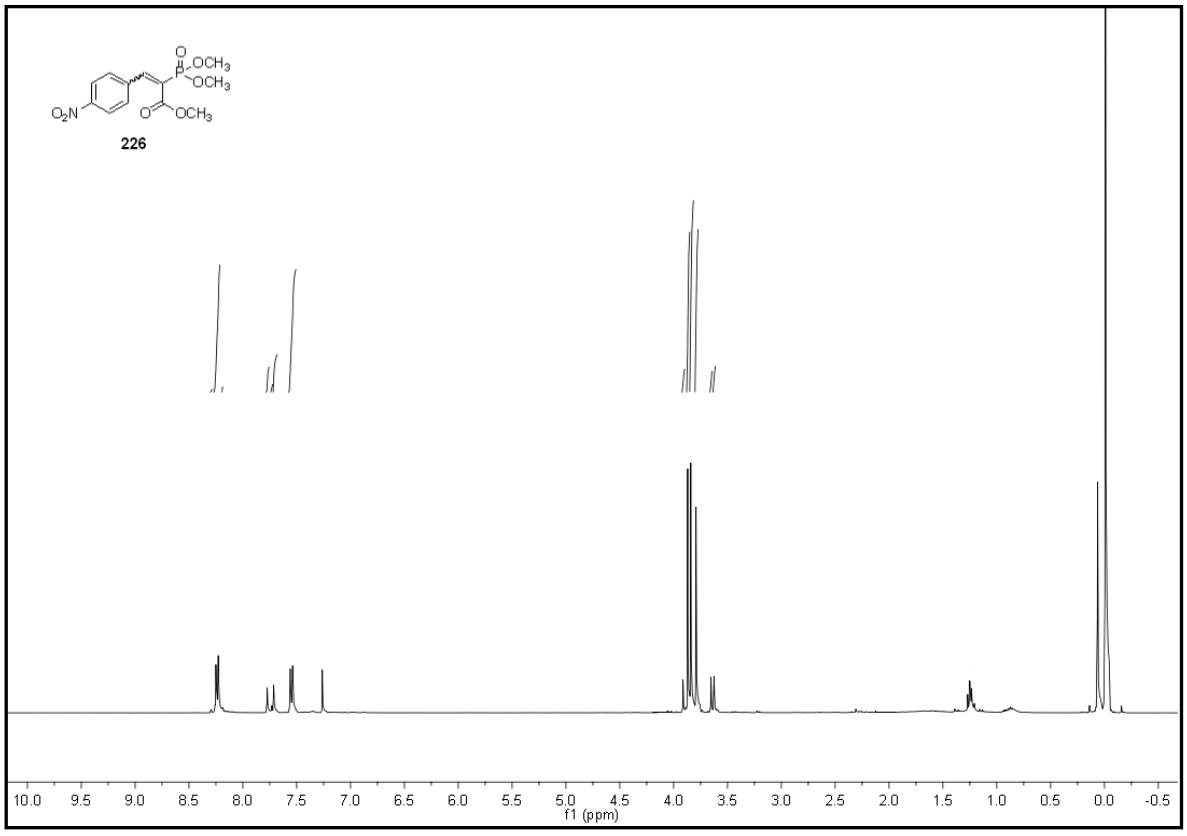


Figure A.28. ^{1}H NMR spectrum of compound **226**

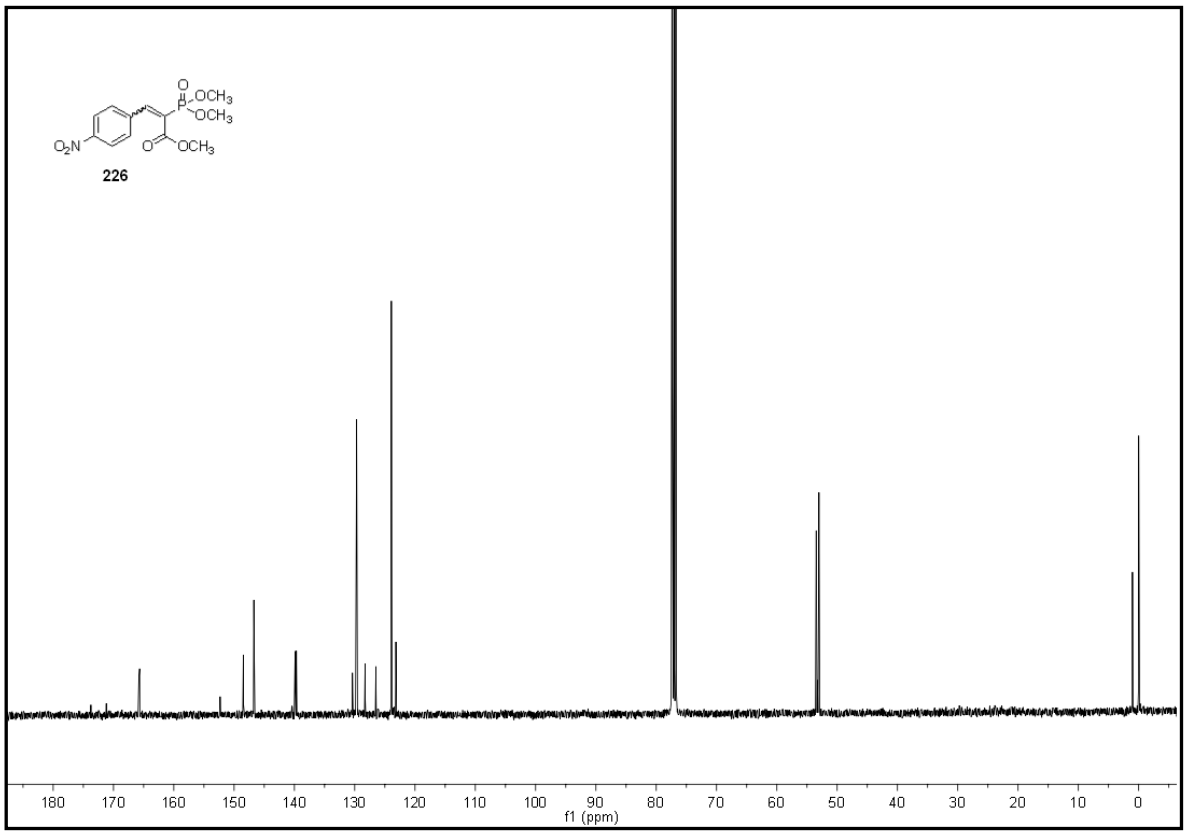


Figure A.29. ^{13}C NMR spectrum of compound **226**

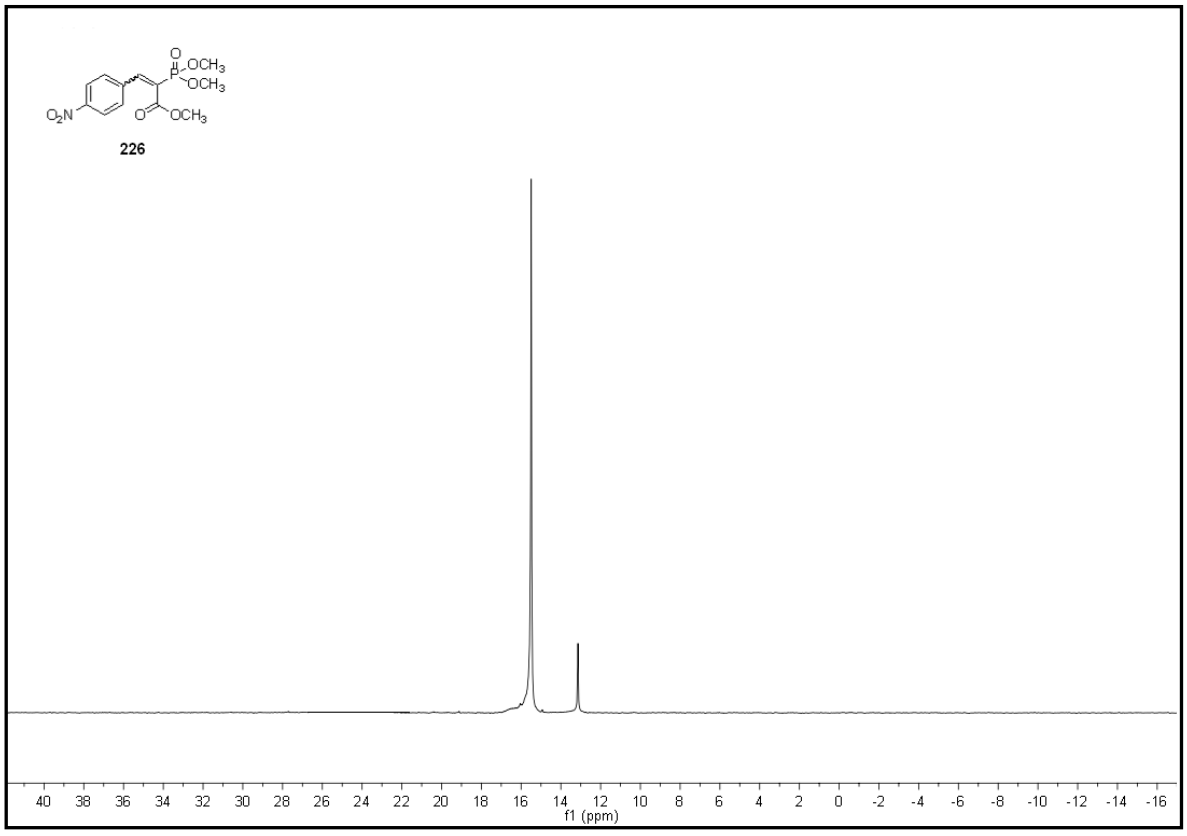


Figure A.30. ^{31}P NMR spectrum of compound **226**

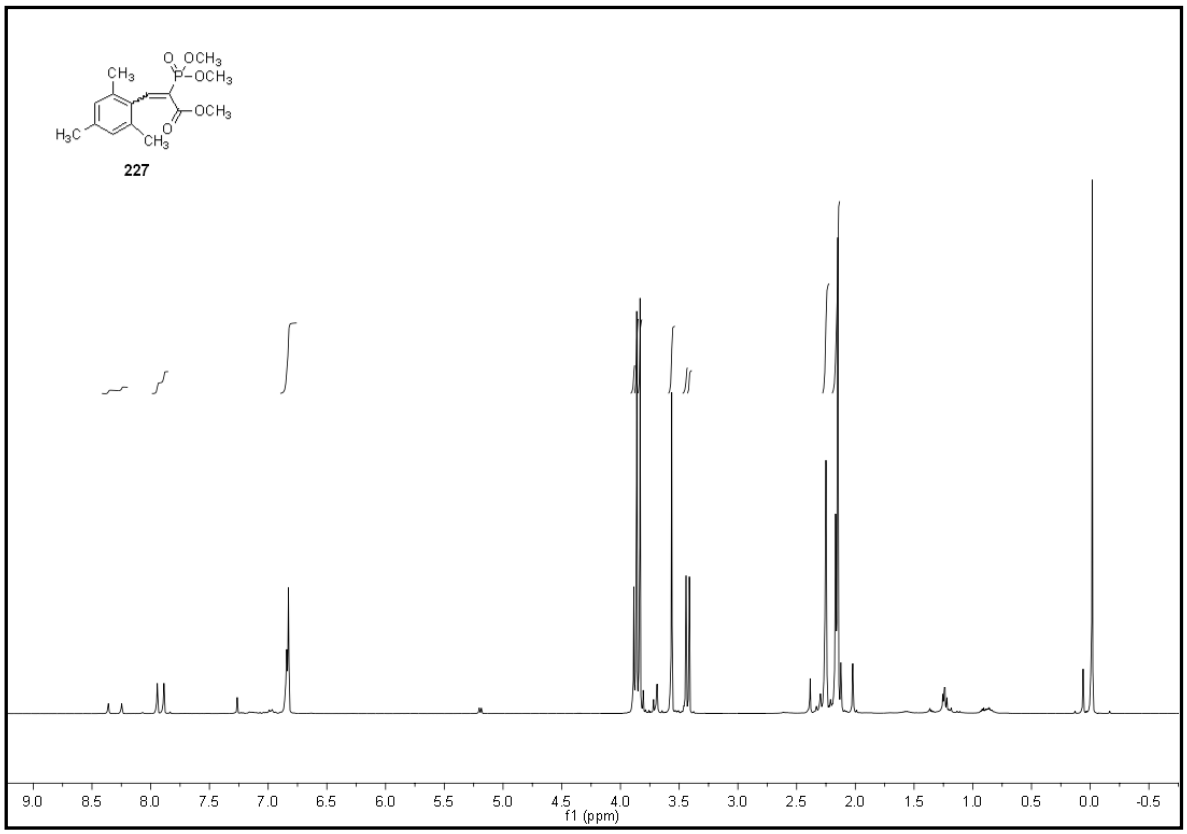


Figure A.31. ^{1}H NMR spectrum of compound **227**

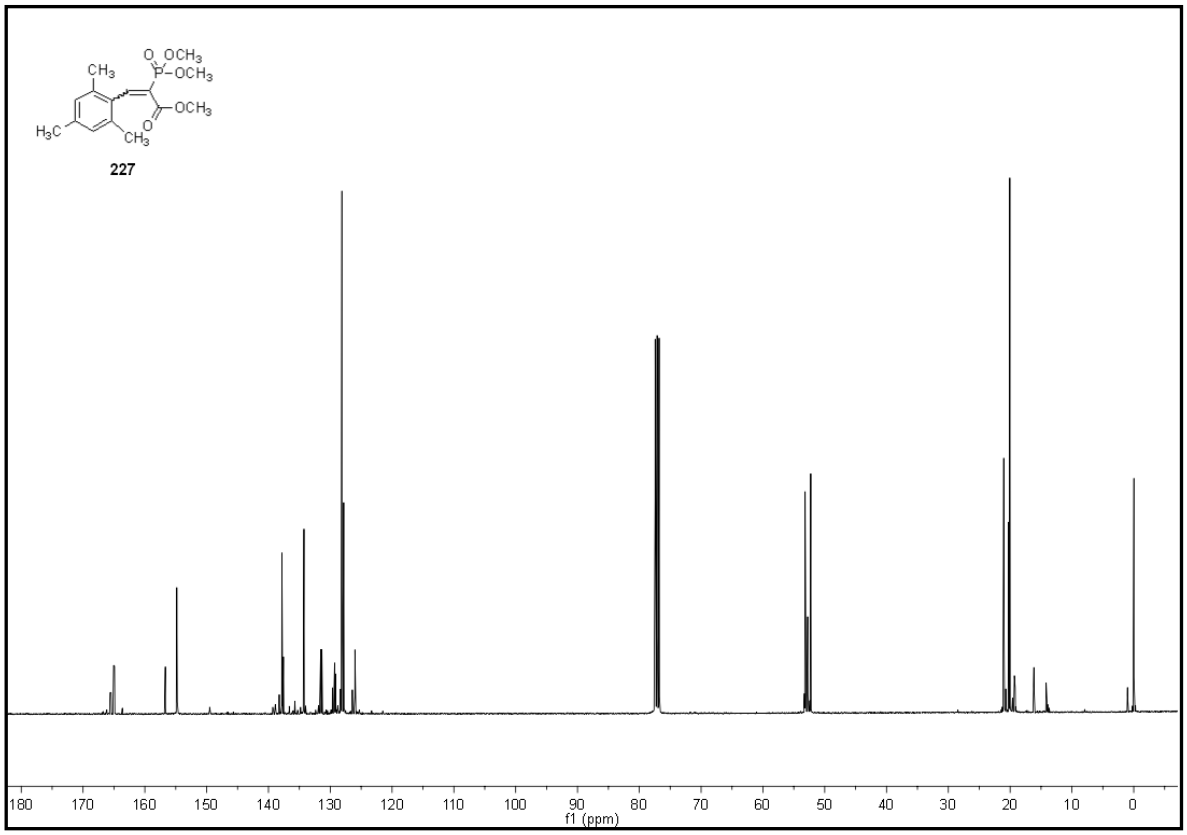


Figure A.32. ^{13}C NMR spectrum of compound **227**

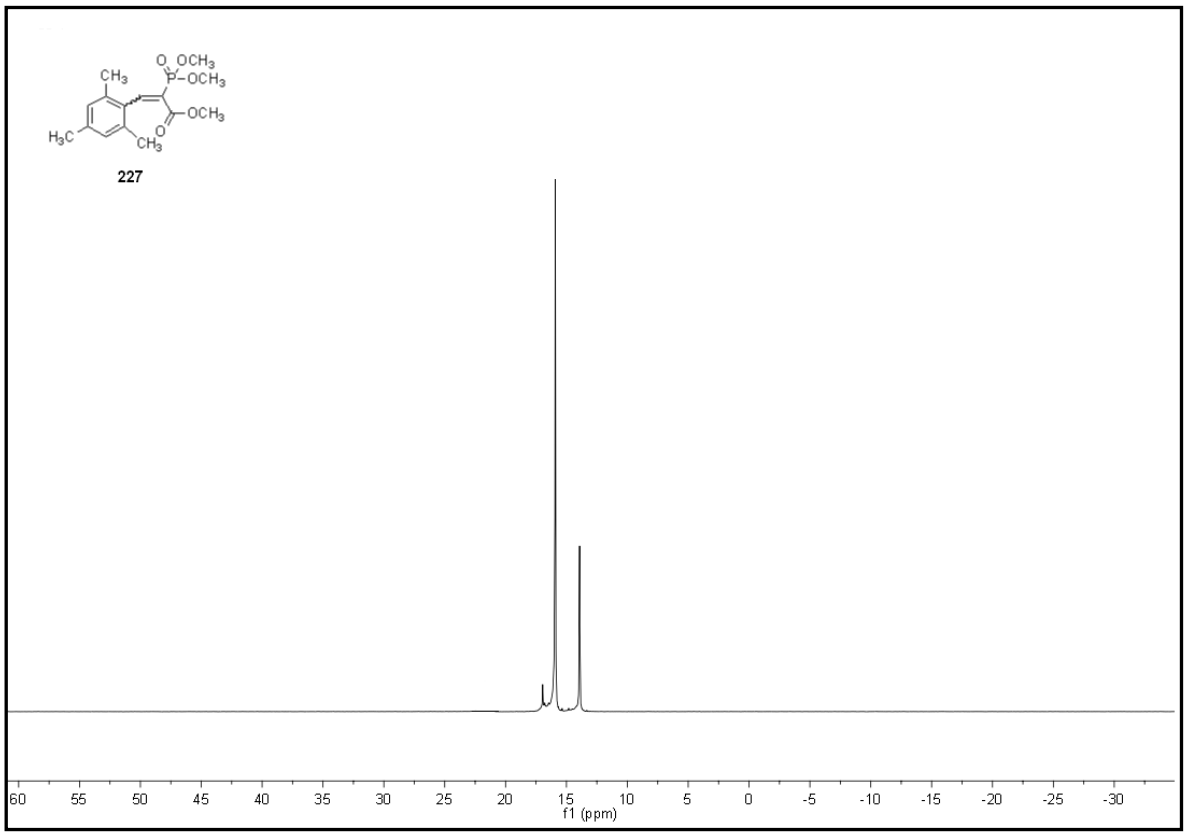


Figure A.33. ^{31}P NMR spectrum of compound **227**

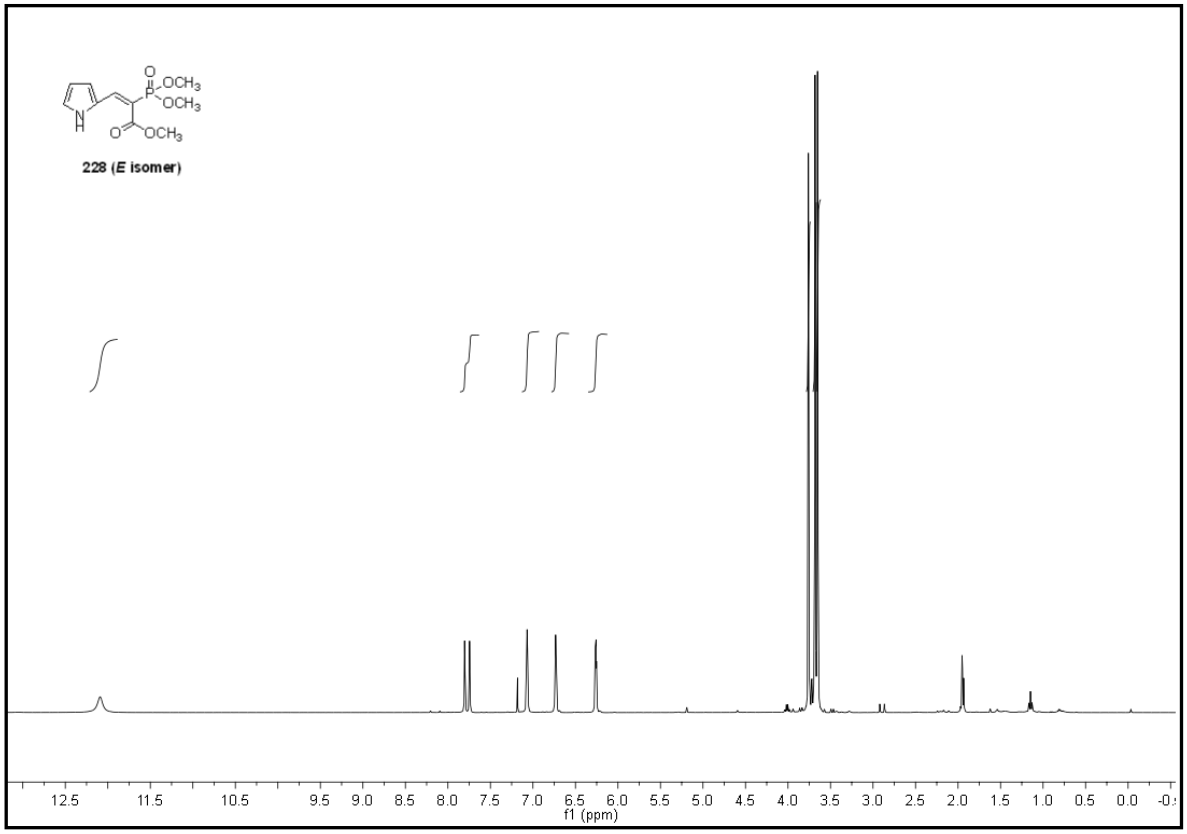


Figure A.34. ^{1}H NMR spectrum of E isomer of compound **228**

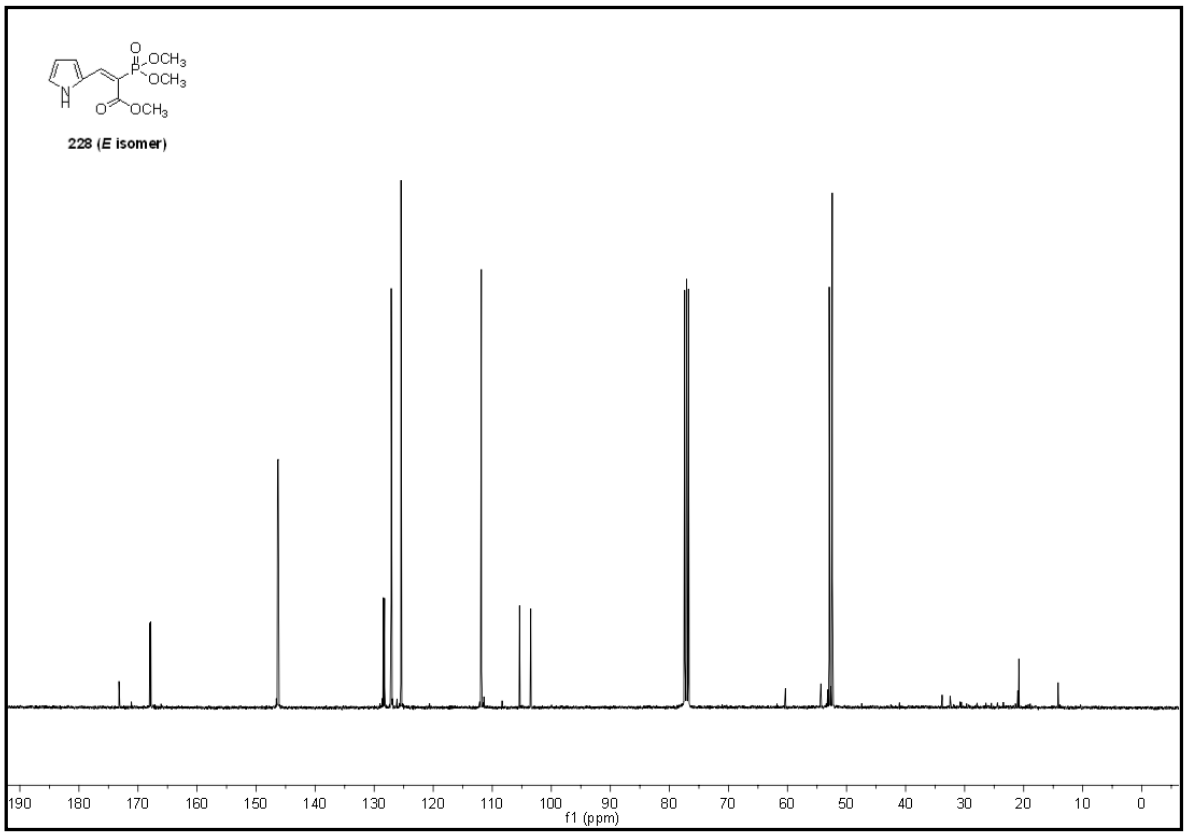


Figure A.35. ^{13}C NMR spectrum of E isomer of compound **228**

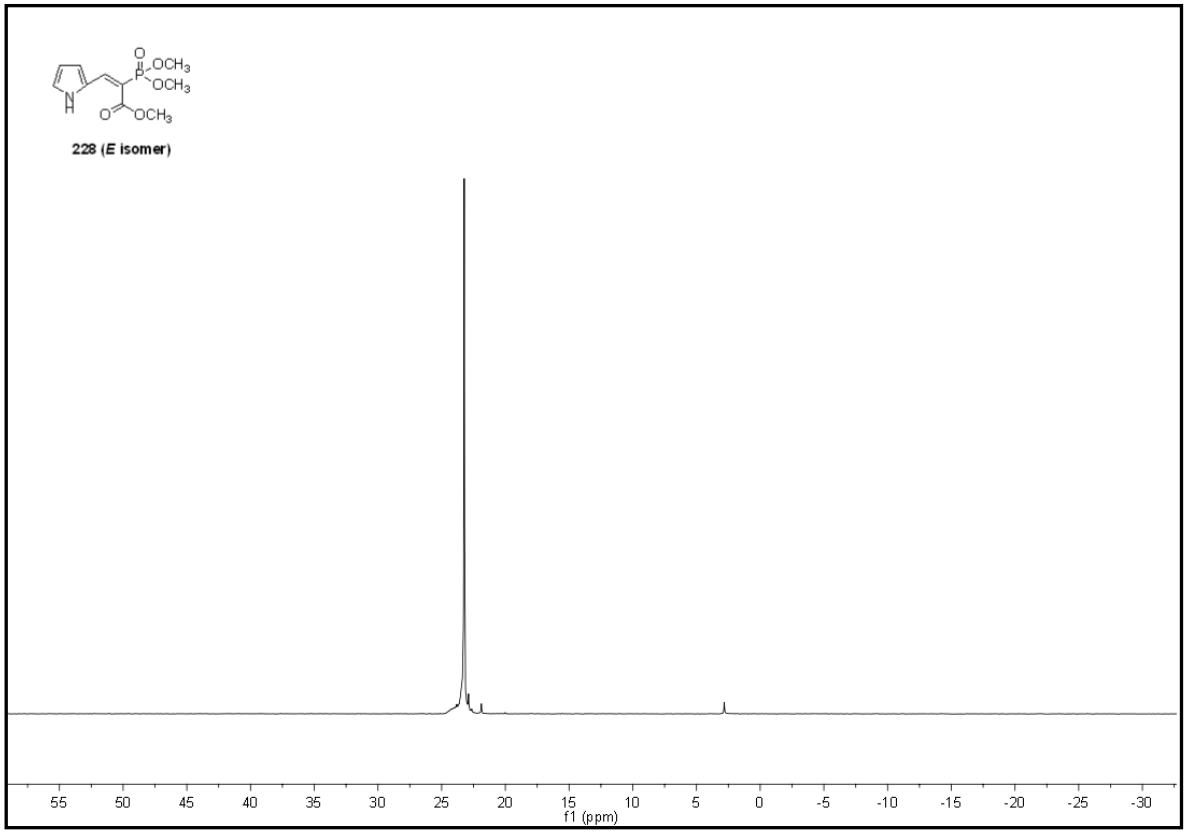


Figure A.36. ^{31}P NMR spectrum of E isomer of compound **228**

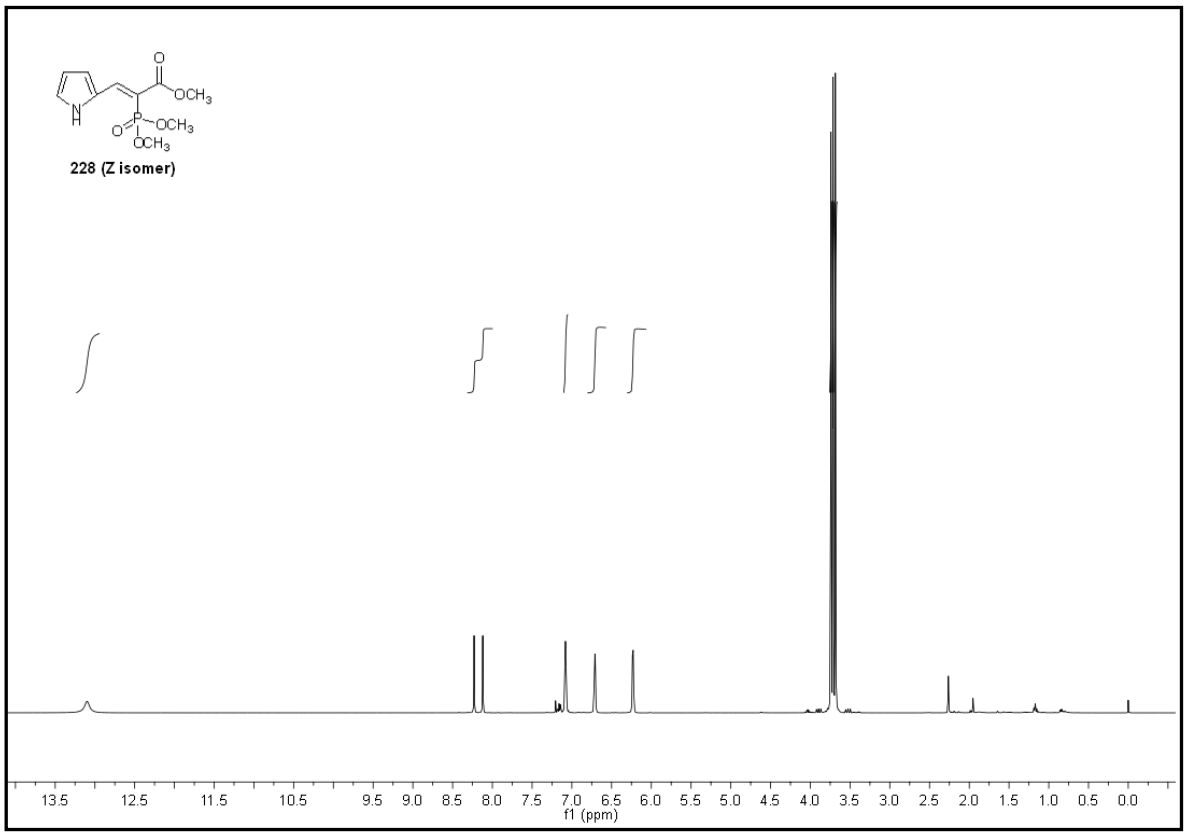


Figure A.37. ^{1}H NMR spectrum of Z isomer of compound **228**

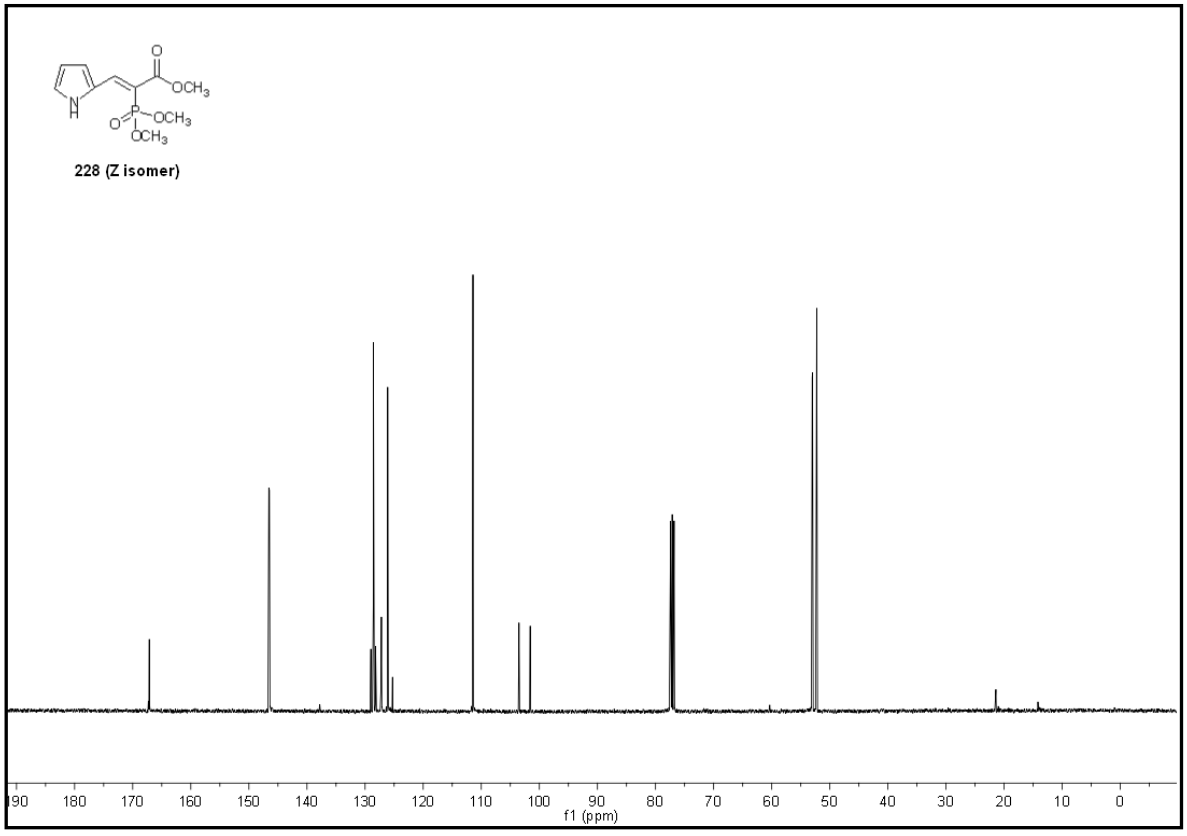


Figure A.38. ^{13}C NMR spectrum of Z isomer of compound **228**

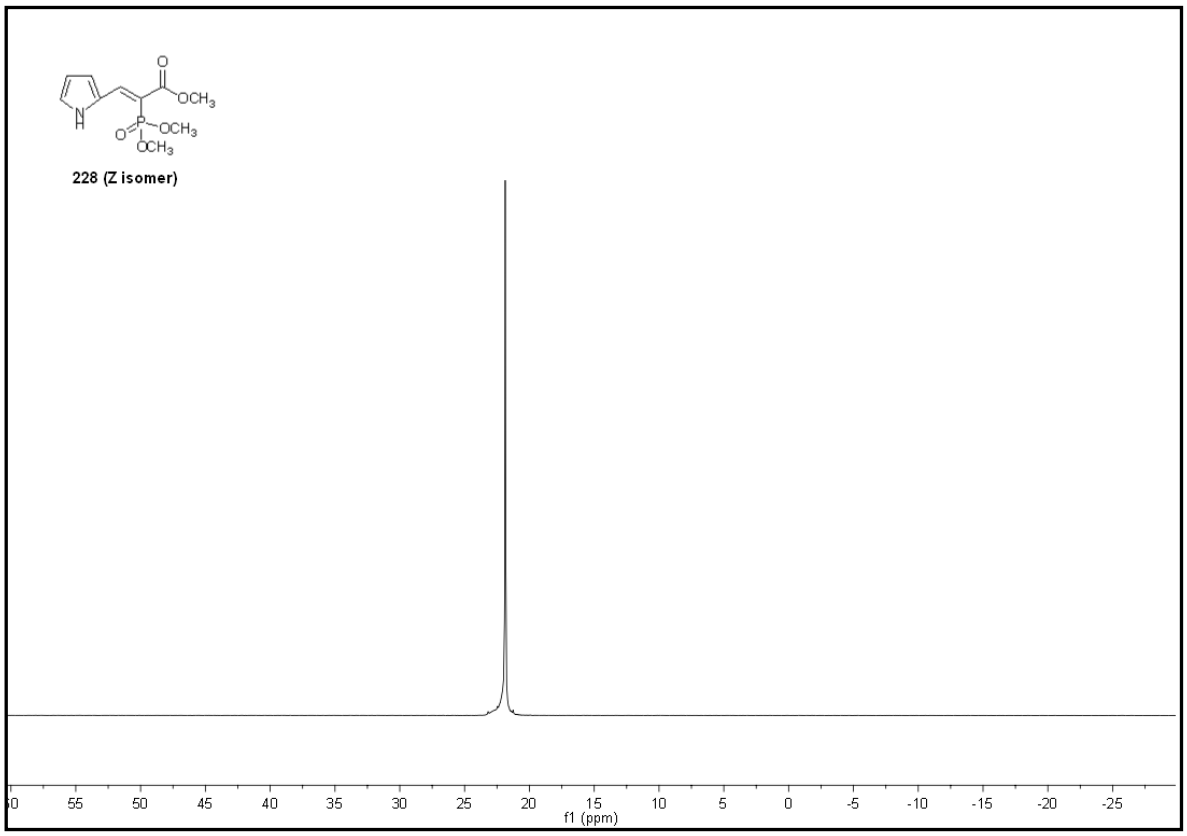


Figure A.39. ^{31}P NMR spectrum of Z isomer of compound **228**

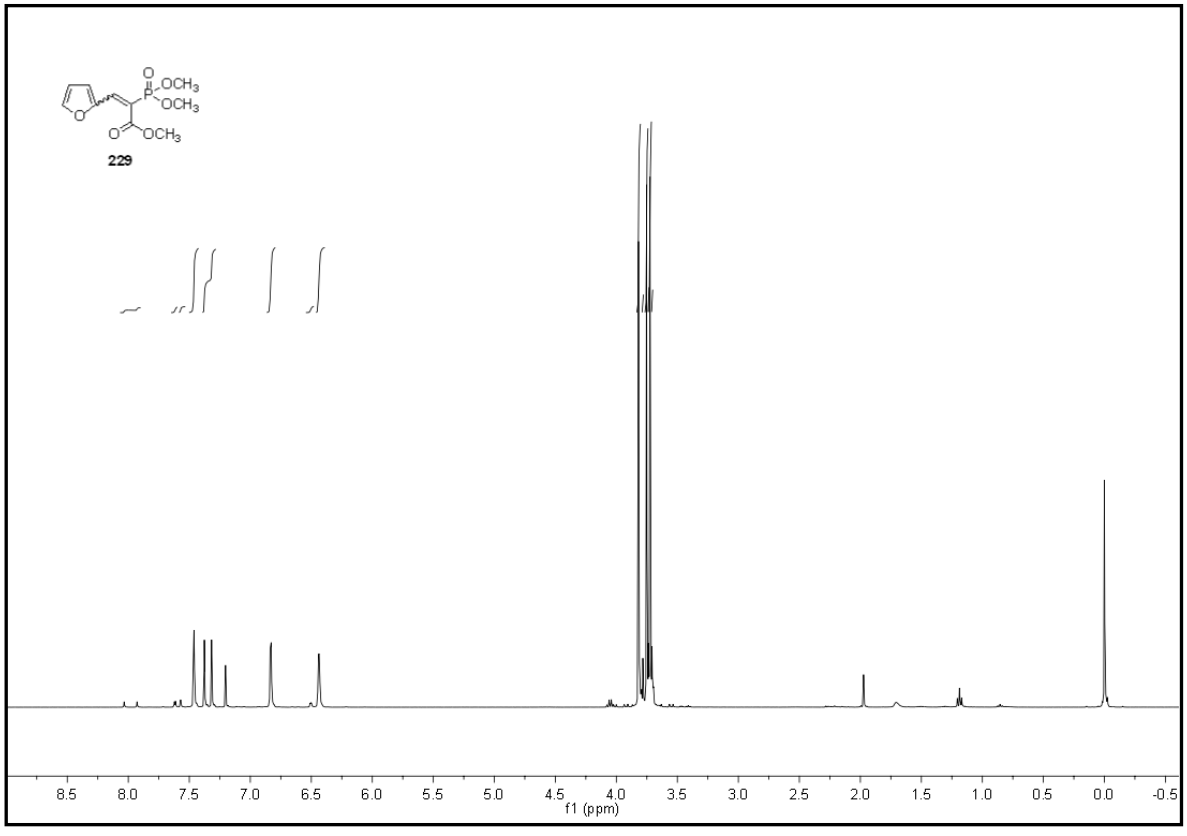


Figure A.40. ^{1}H NMR spectrum of compound **229**

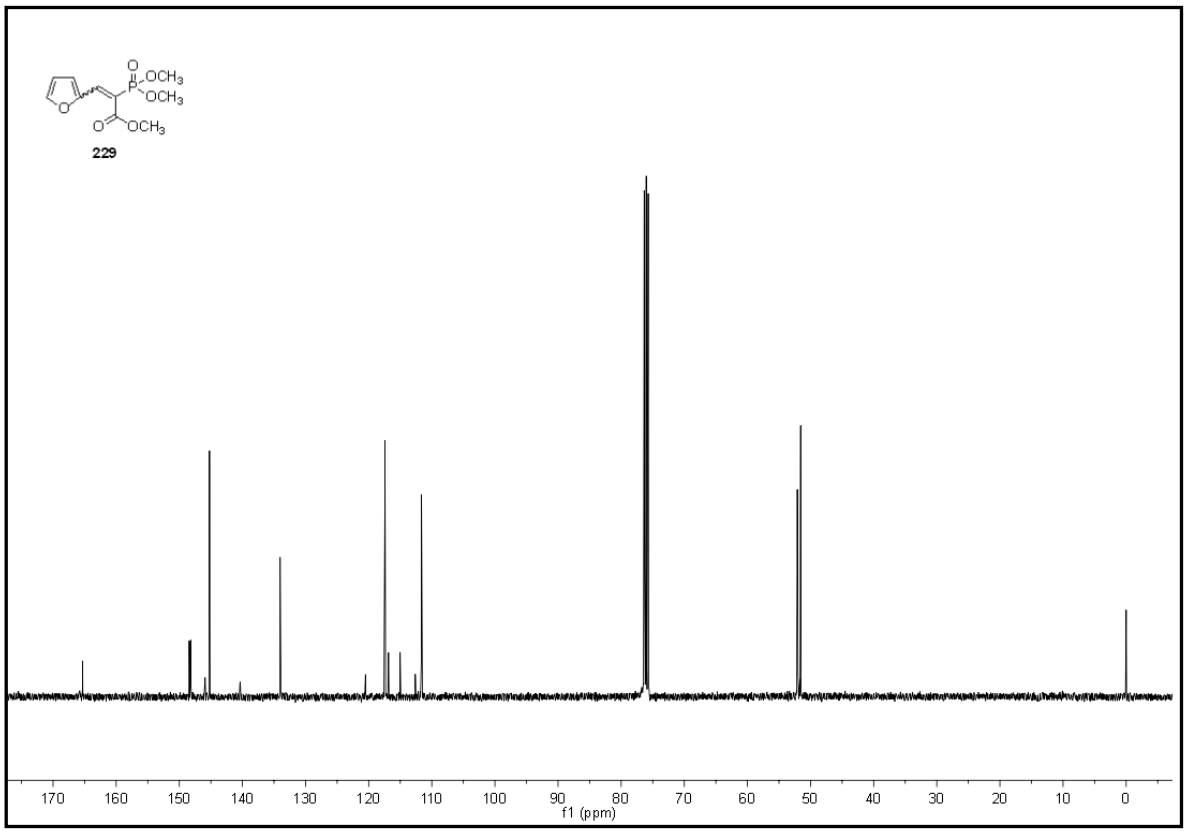


Figure A.41. ^{13}C NMR spectrum of compound **229**

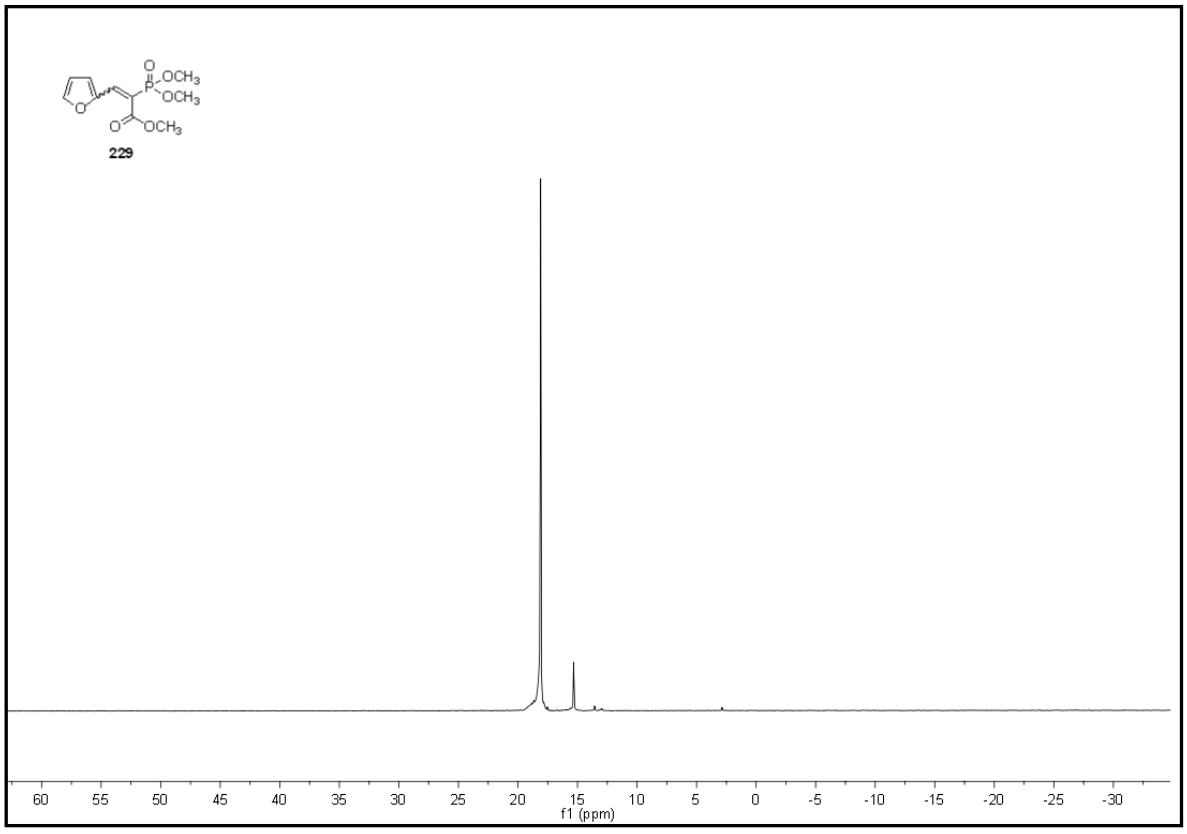


Figure A.42. ^{31}P NMR spectrum of compound **229**

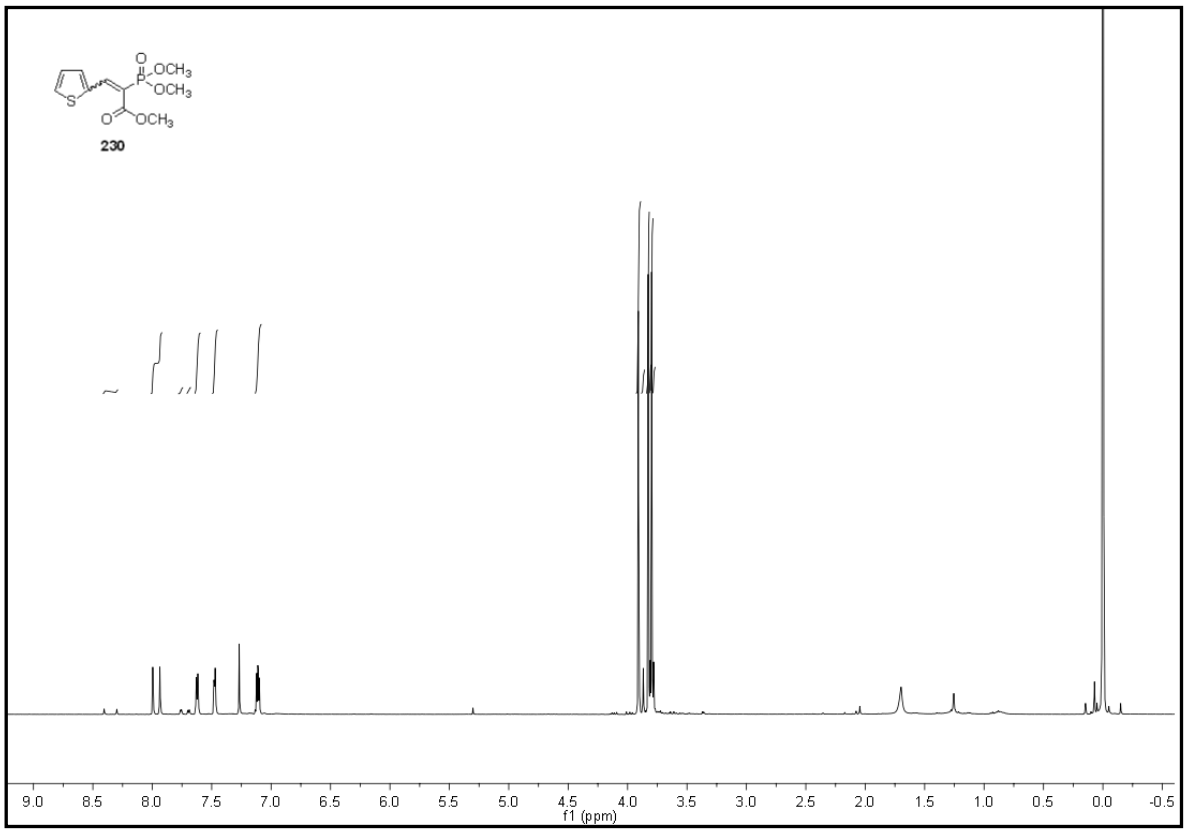


Figure A.43. ^{1}H NMR spectrum of compound **230**

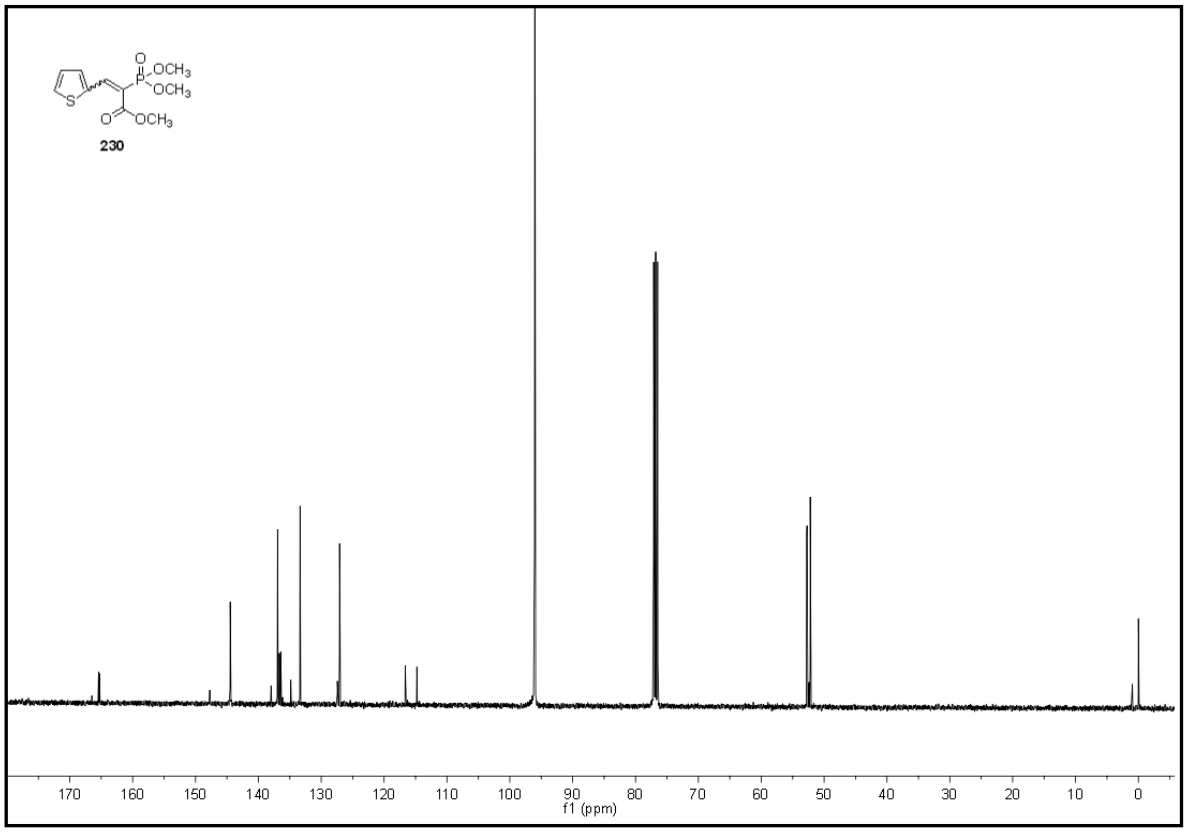


Figure A.44. ^{13}C NMR spectrum of compound **230**

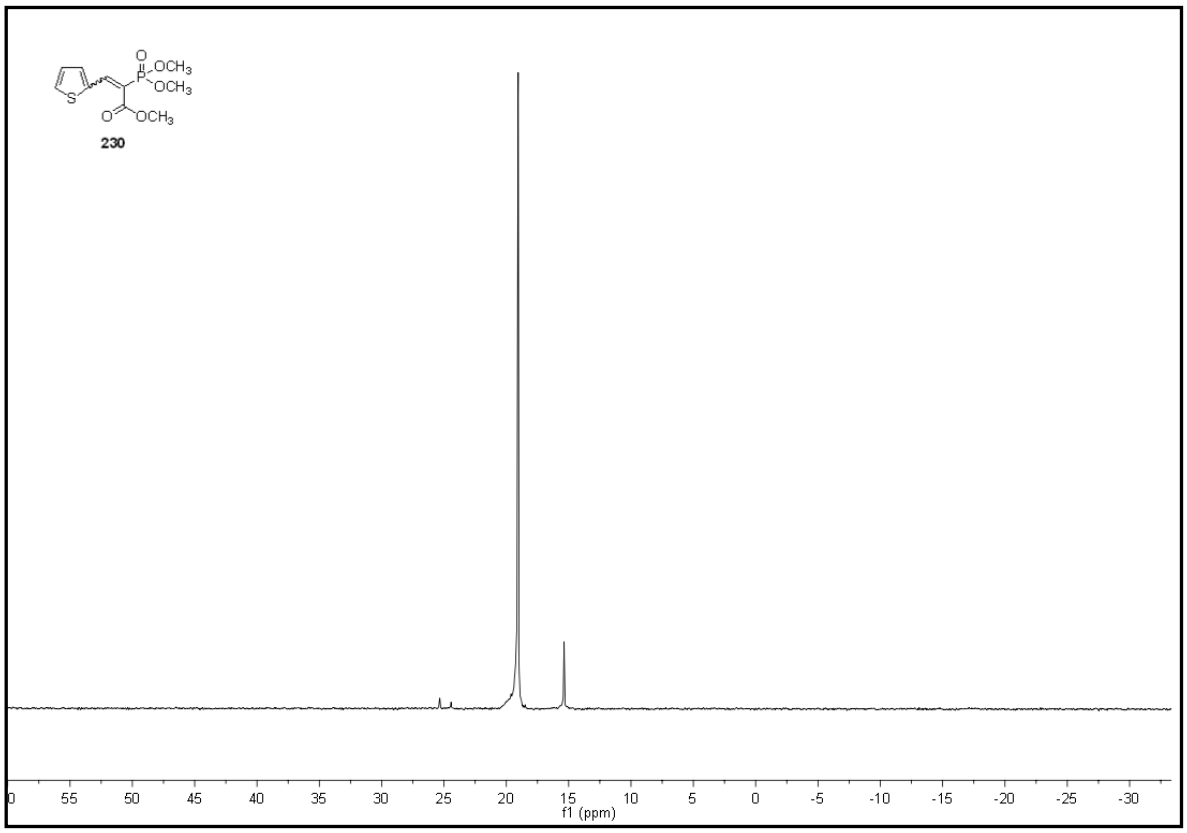


Figure A.45. ^{31}P NMR spectrum of compound **230**

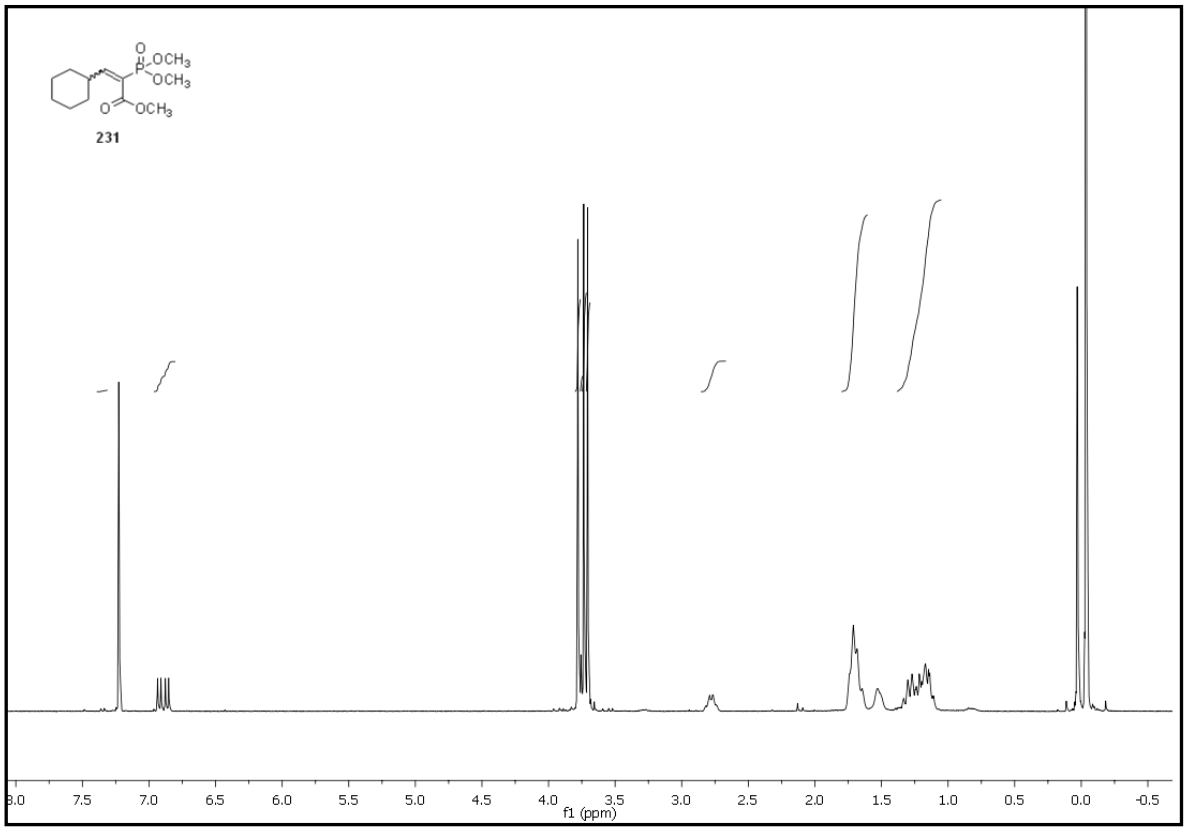


Figure A.46. ^{1}H NMR spectrum of compound **231**

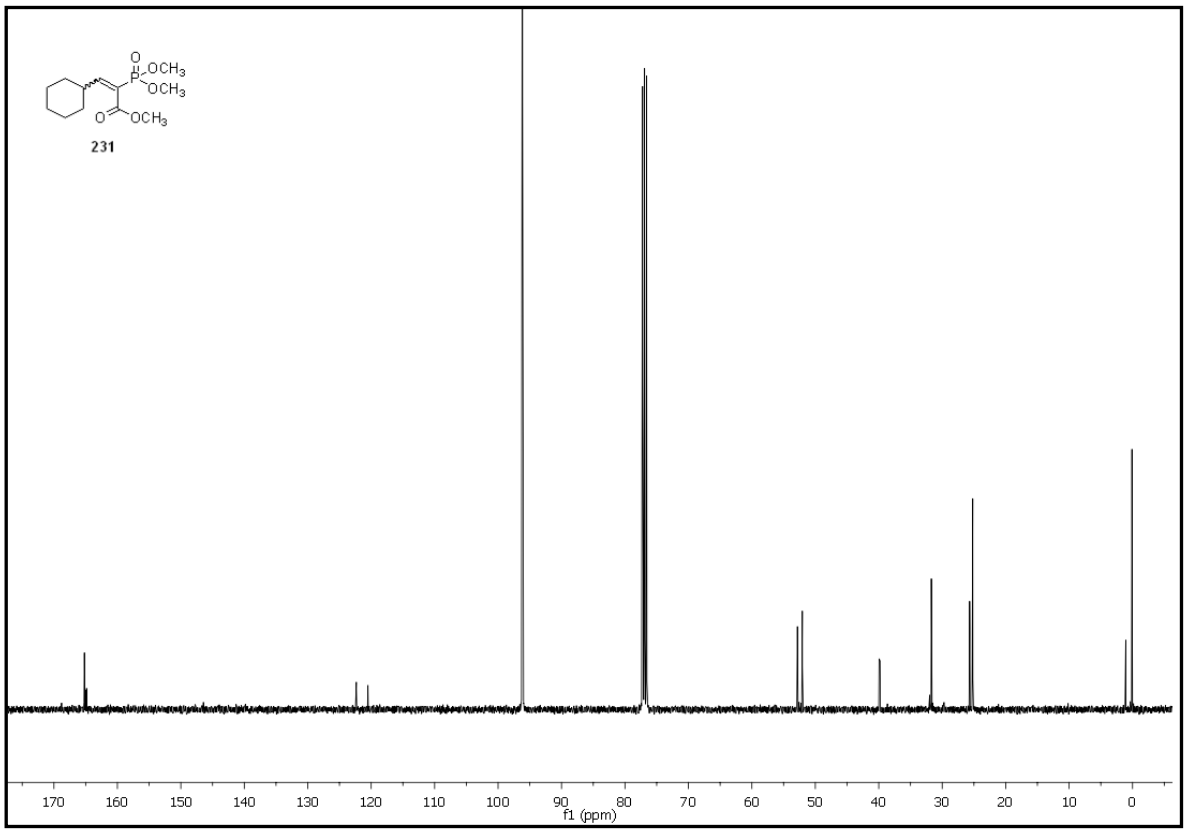


Figure A.47. ^{13}C NMR spectrum of compound **231**

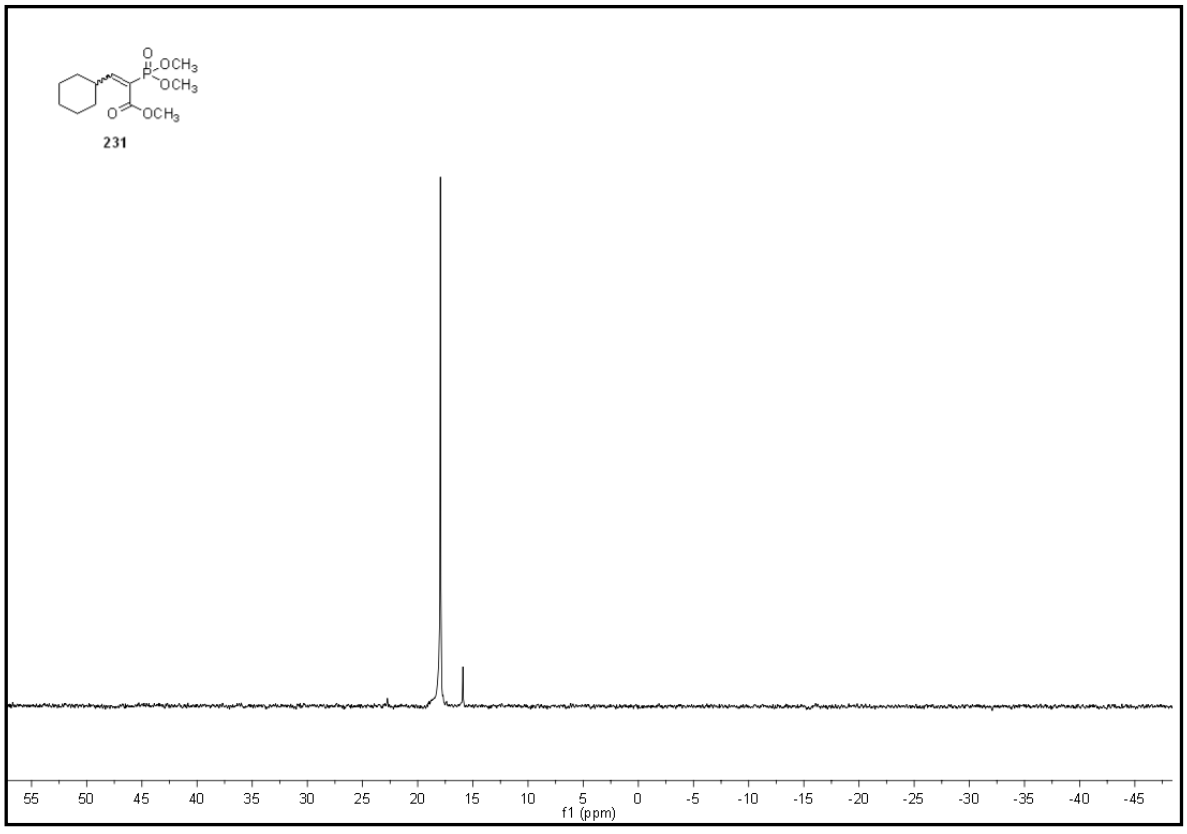


Figure A.48. ^{31}P NMR spectrum of compound **231**

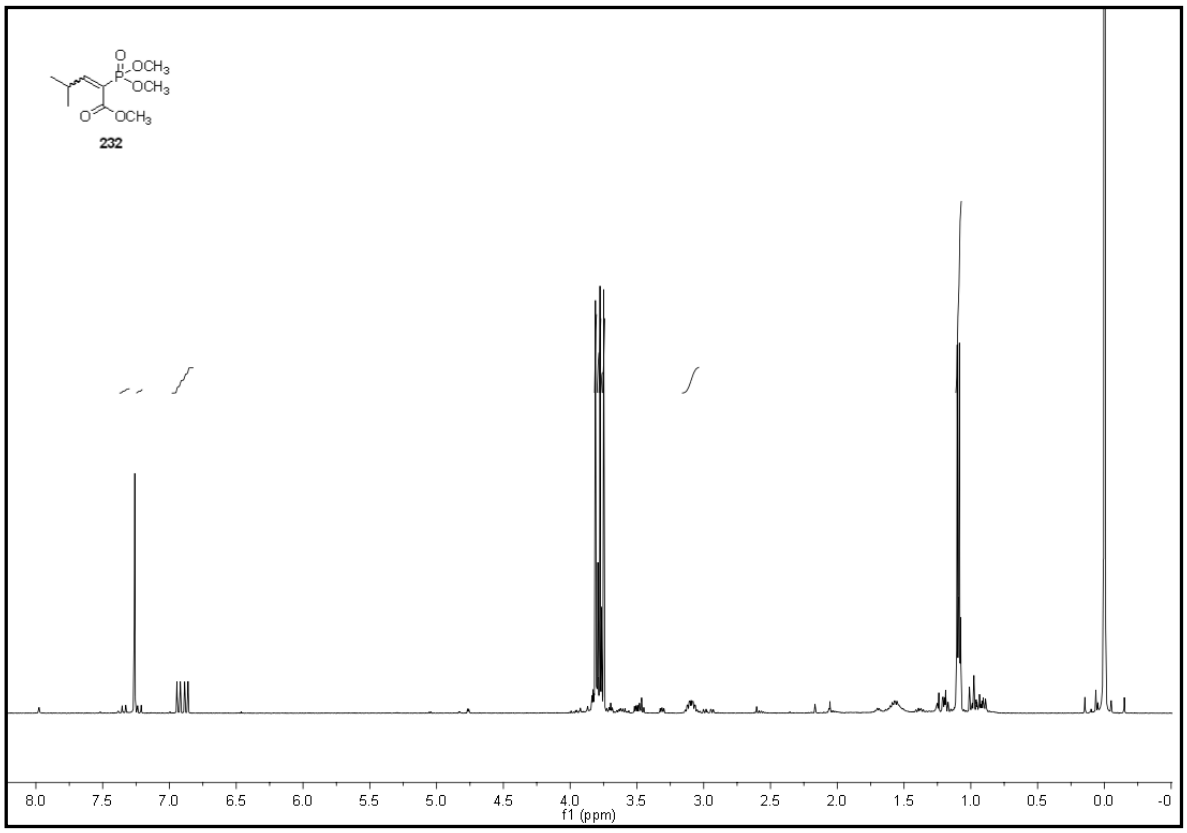


Figure A.49. ^{1}H NMR spectrum of compound **232**

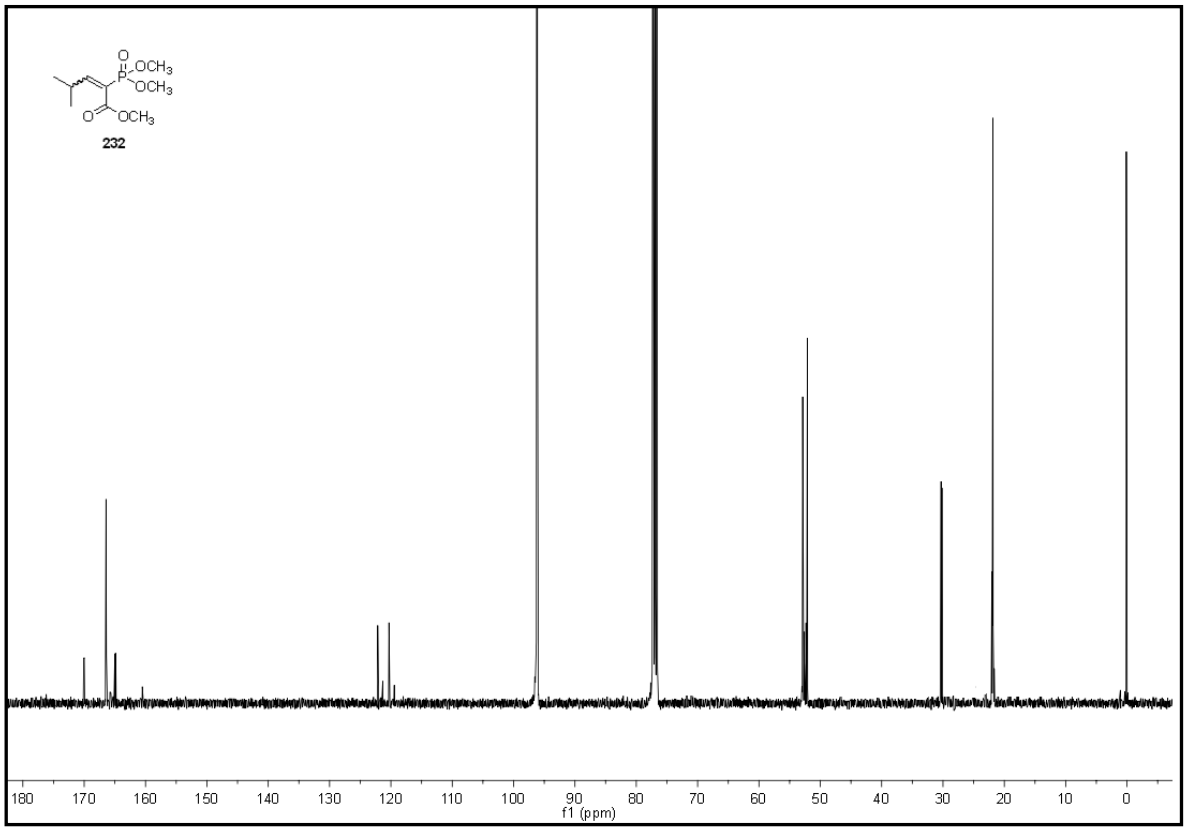


Figure A.50. ^{13}C NMR spectrum of compound **232**

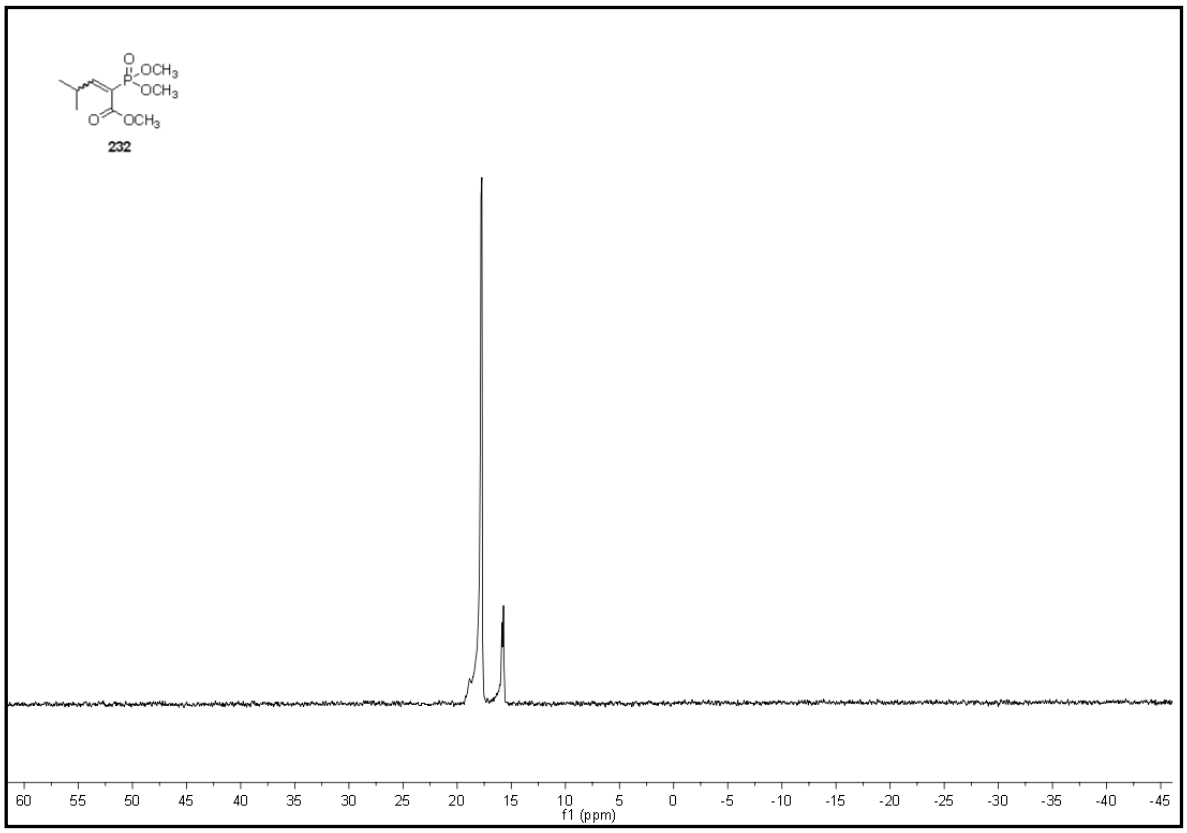


Figure A.51. ^{31}P NMR spectrum of compound **232**

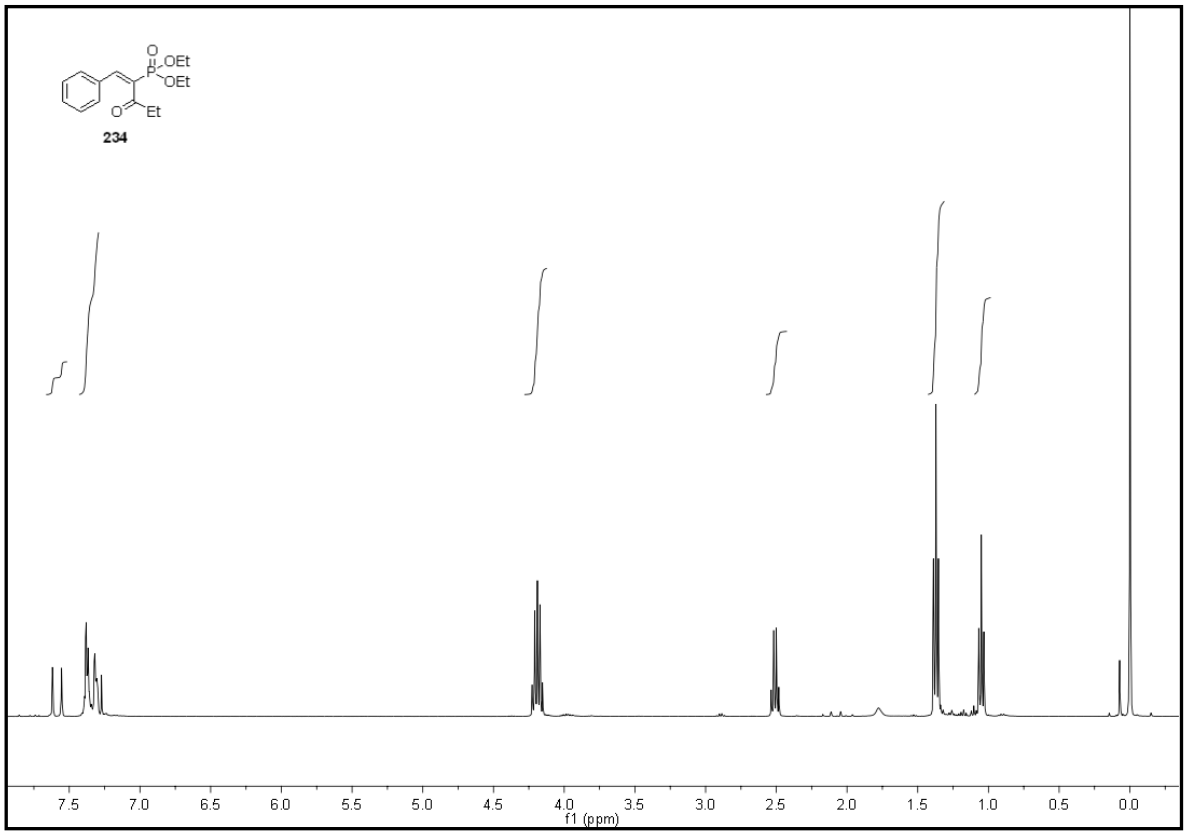


Figure A.52. ^{1}H NMR spectrum of compound **234**

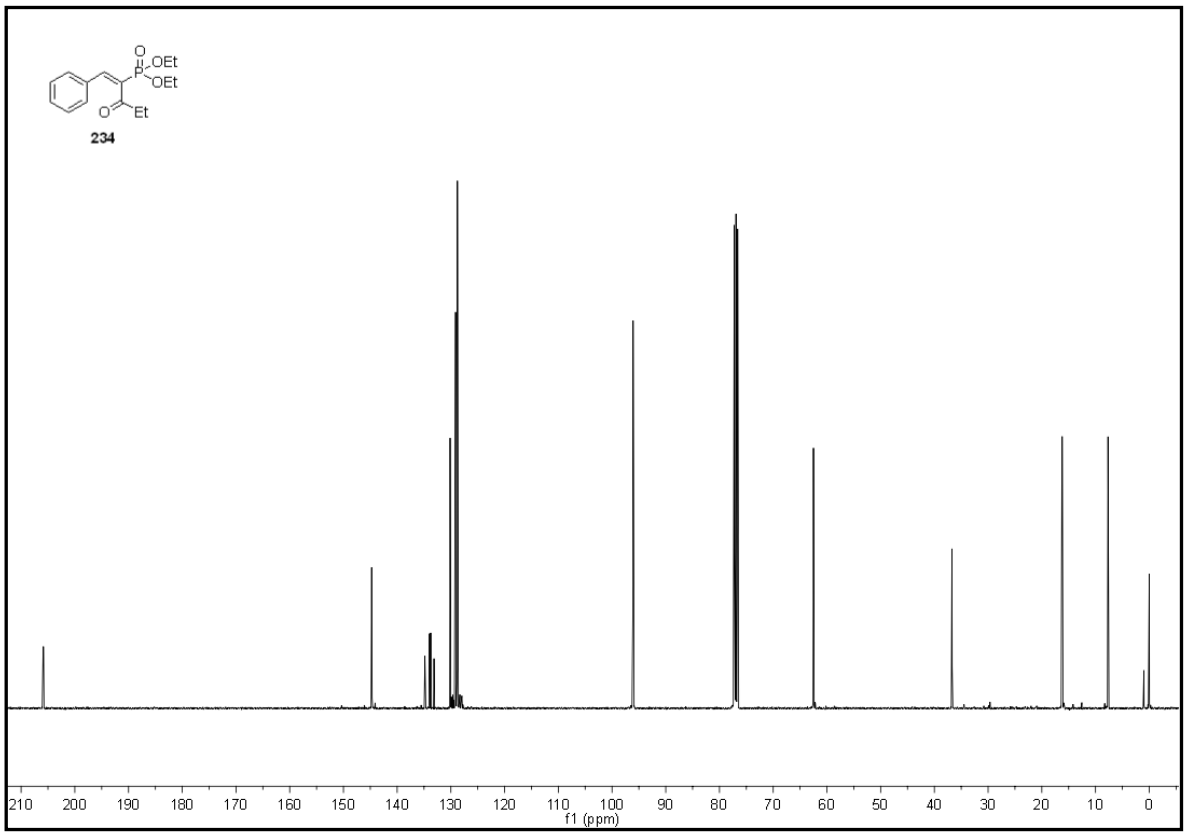


Figure A.53. ^{13}C NMR spectrum of compound **234**

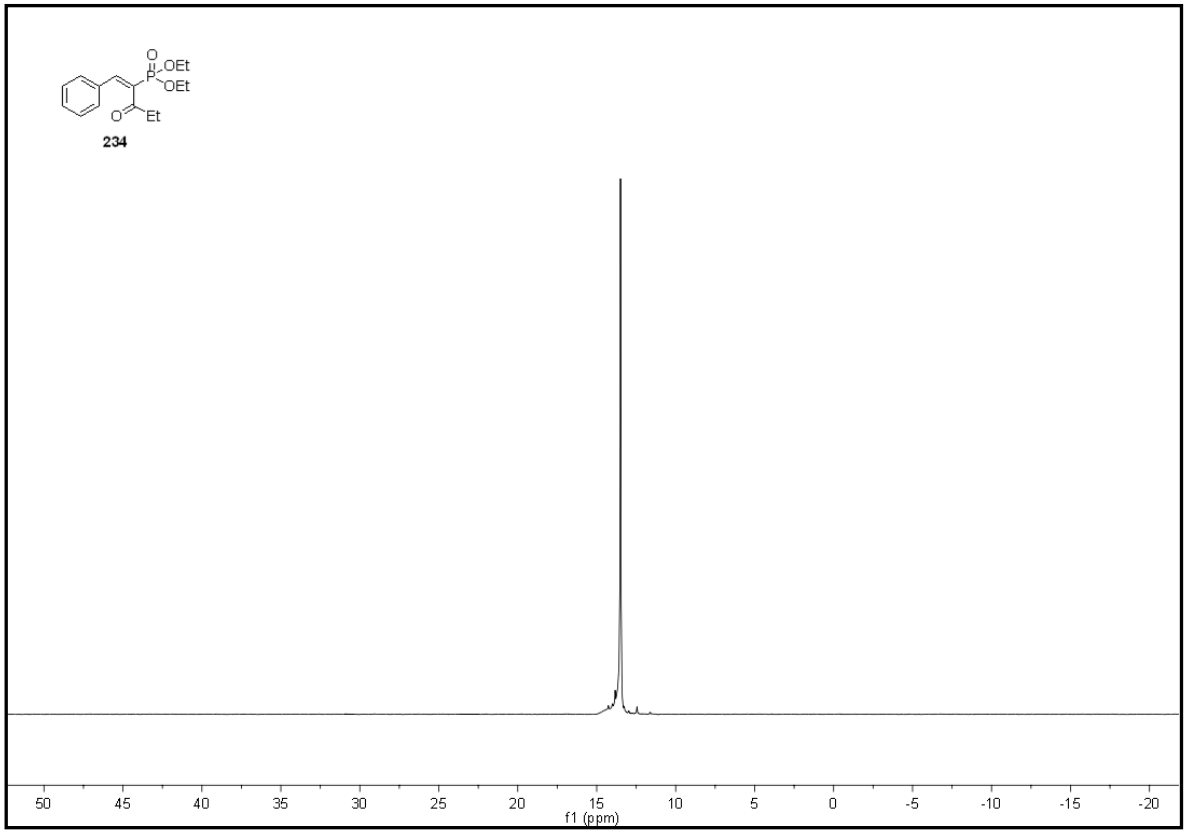


Figure A.54. ^{31}P NMR spectrum of compound **234**

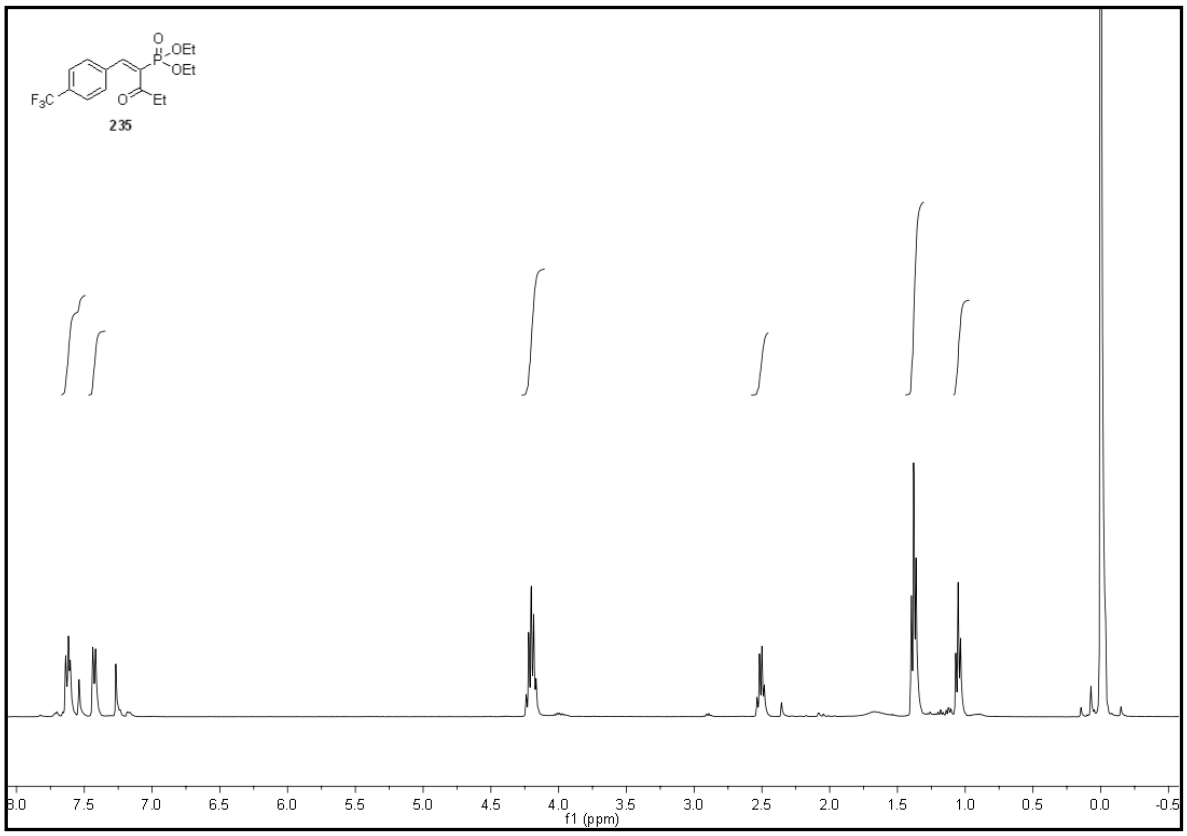


Figure A.55. ^{1}H NMR spectrum of compound **235**

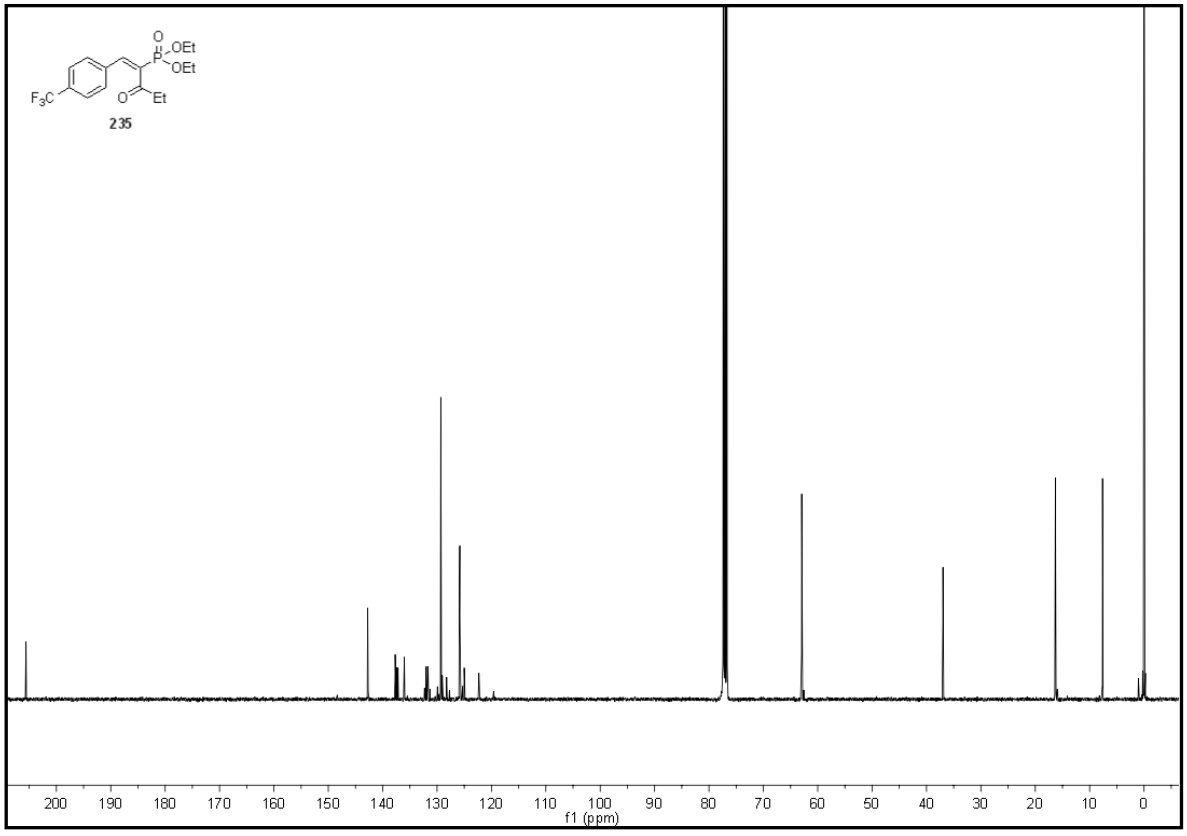


Figure A.56. ^{13}C NMR spectrum of compound **235**

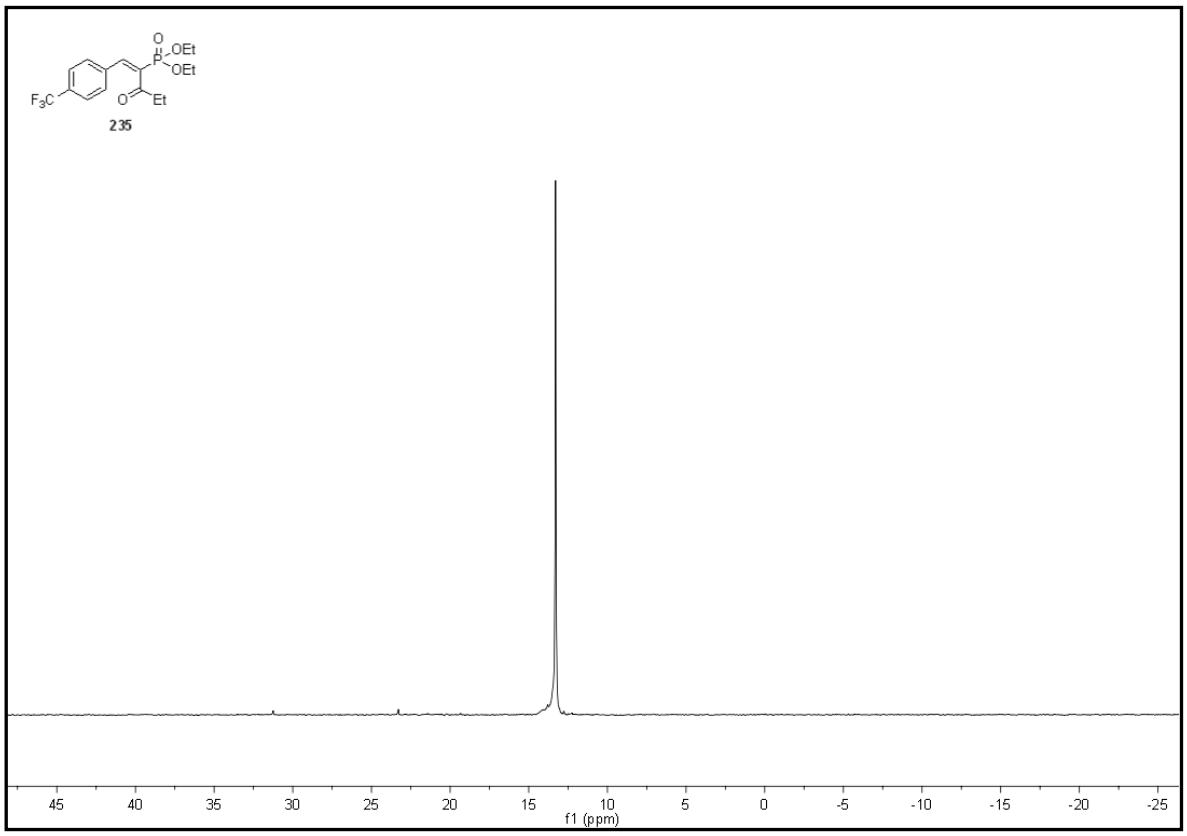


Figure A.57. ^{31}P NMR spectrum of compound **235**

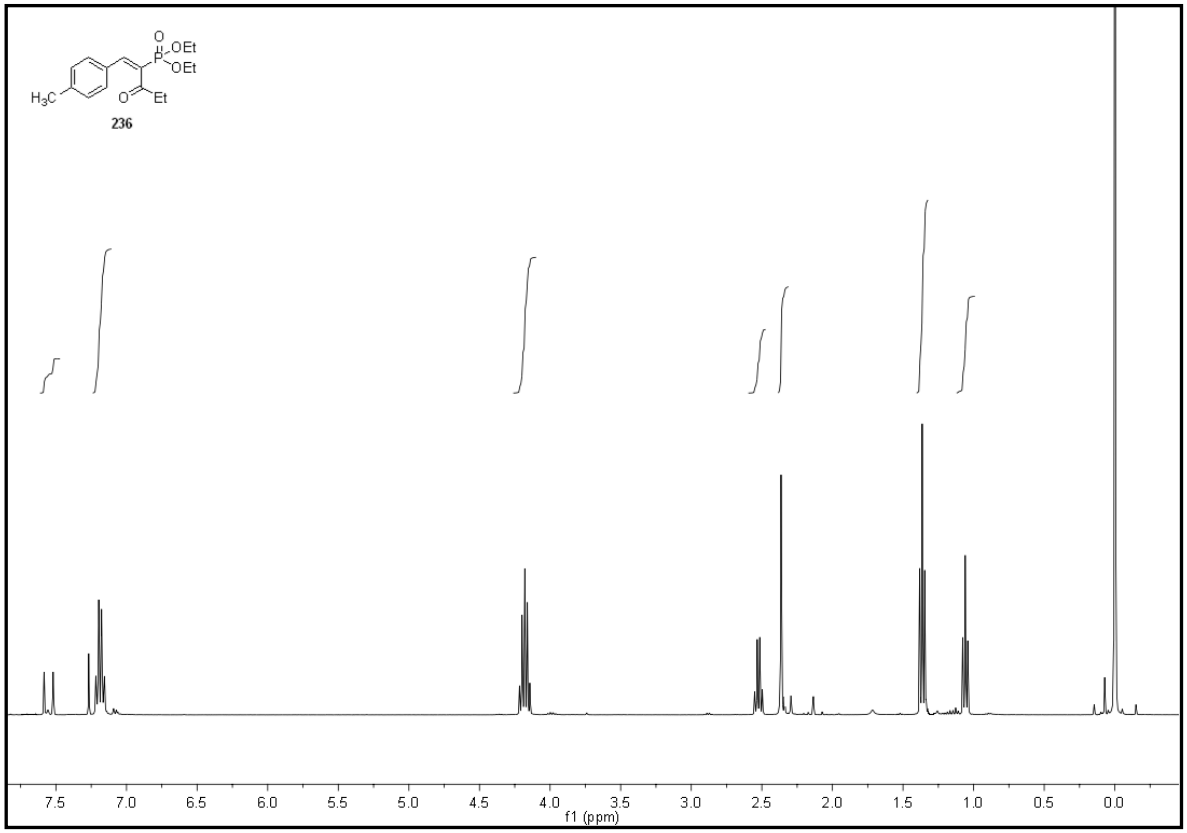


Figure A.58. ^{1}H NMR spectrum of compound **236**

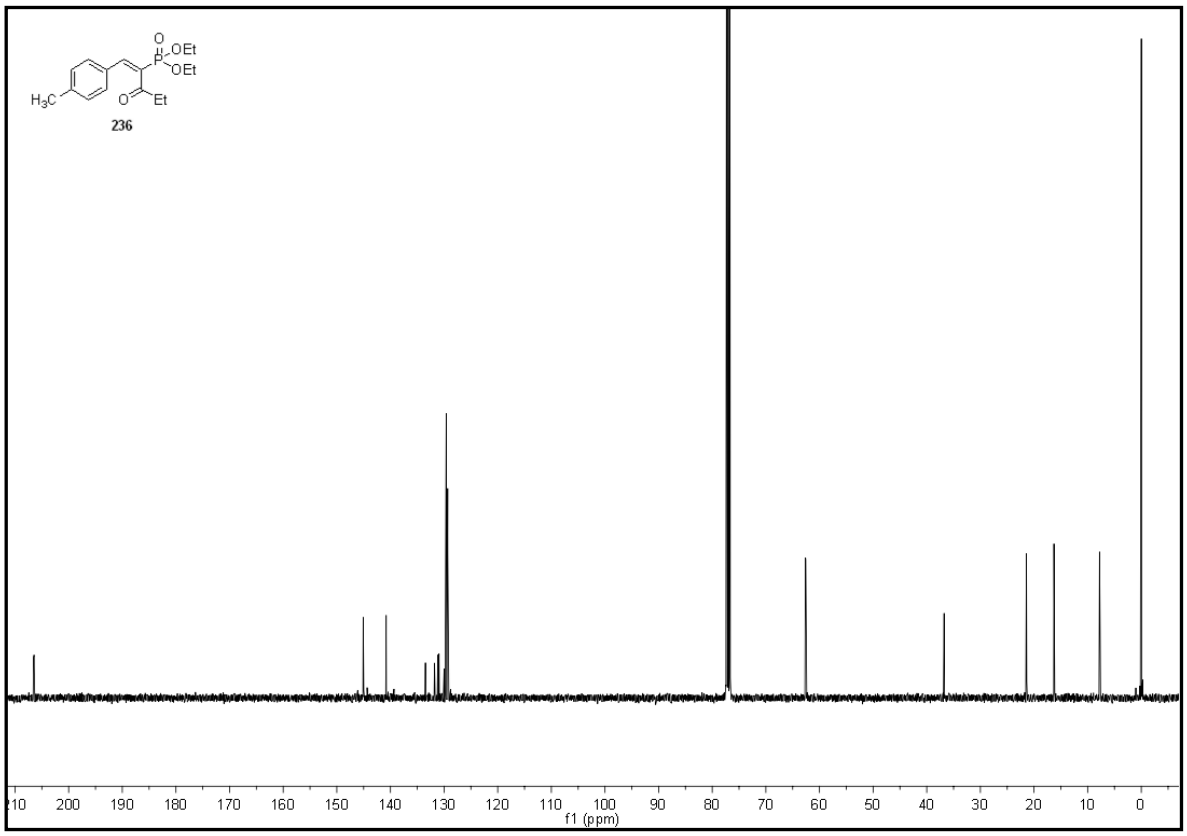


Figure A.59. ^{13}C NMR spectrum of compound **236**

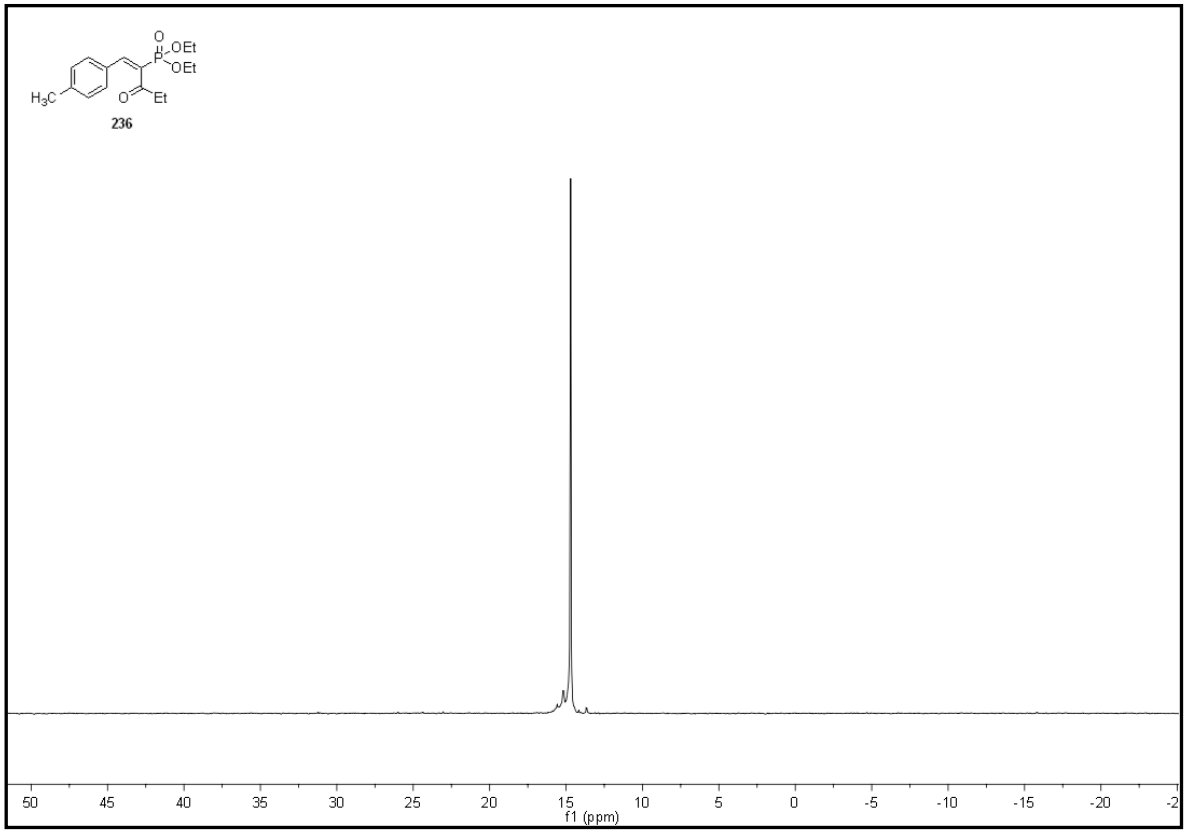


Figure A.60. ^{31}P NMR spectrum of compound **236**

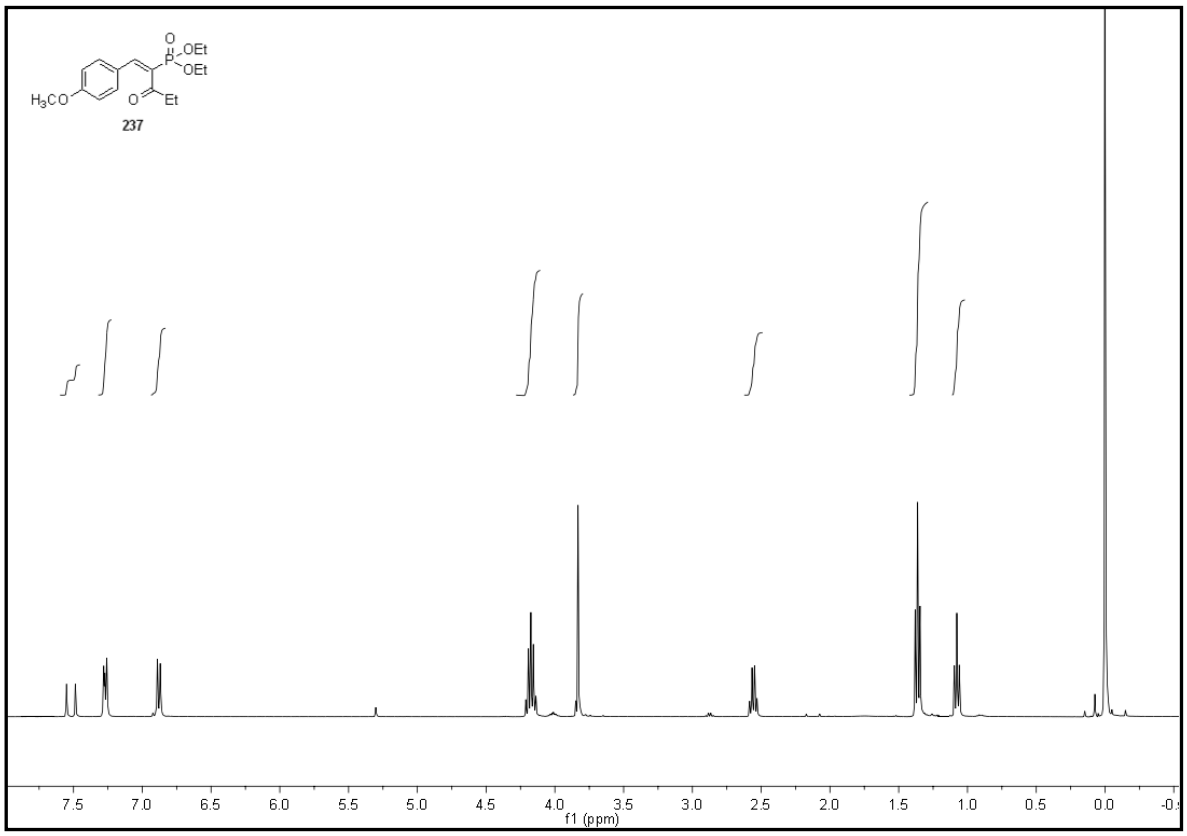


Figure A.61. ^{1}H NMR spectrum of compound **237**

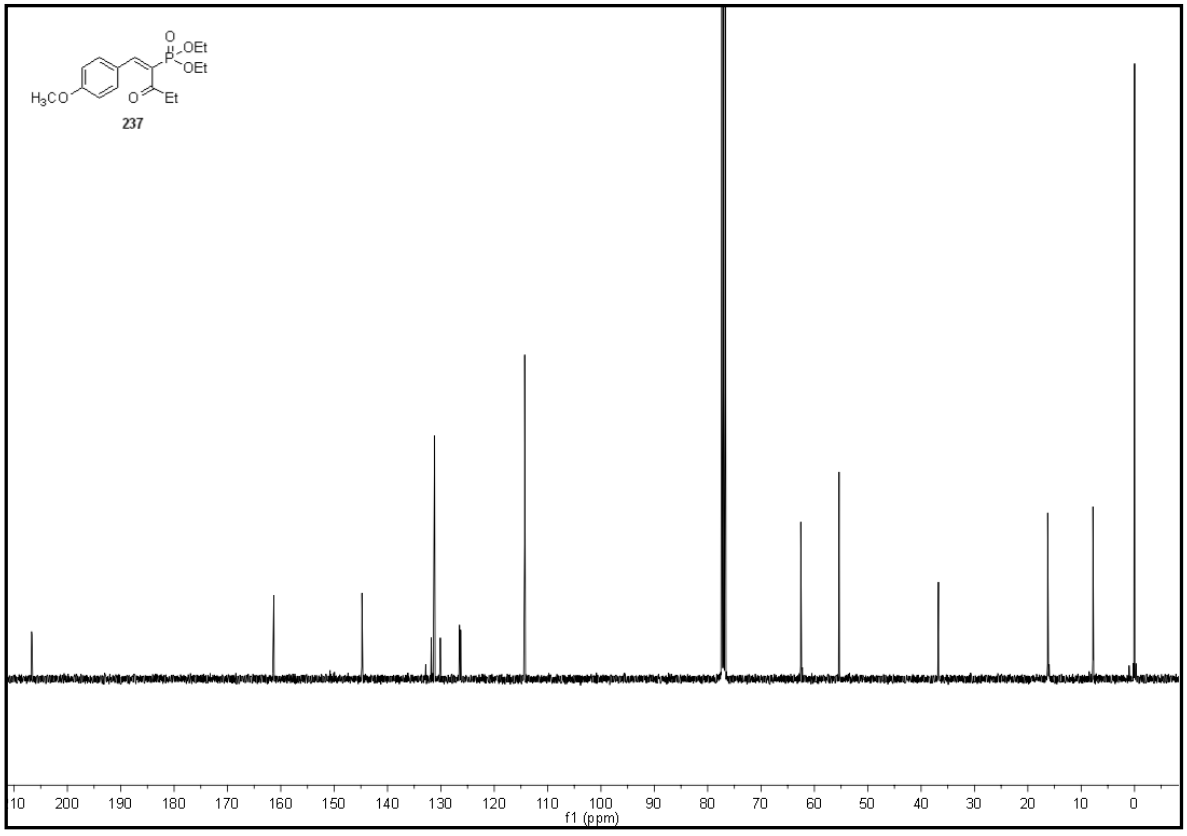


Figure A.62. ^{13}C NMR spectrum of compound **237**

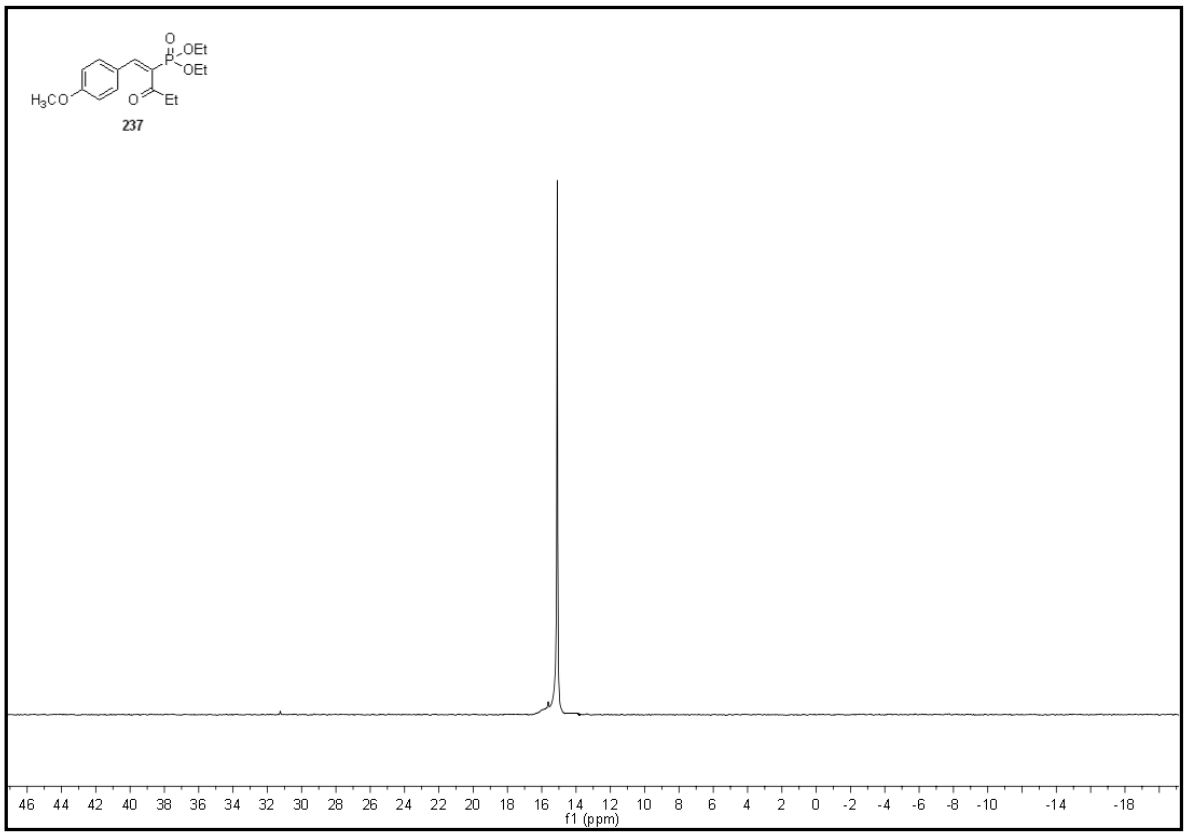


Figure A.63. ^{31}P NMR spectrum of compound **237**

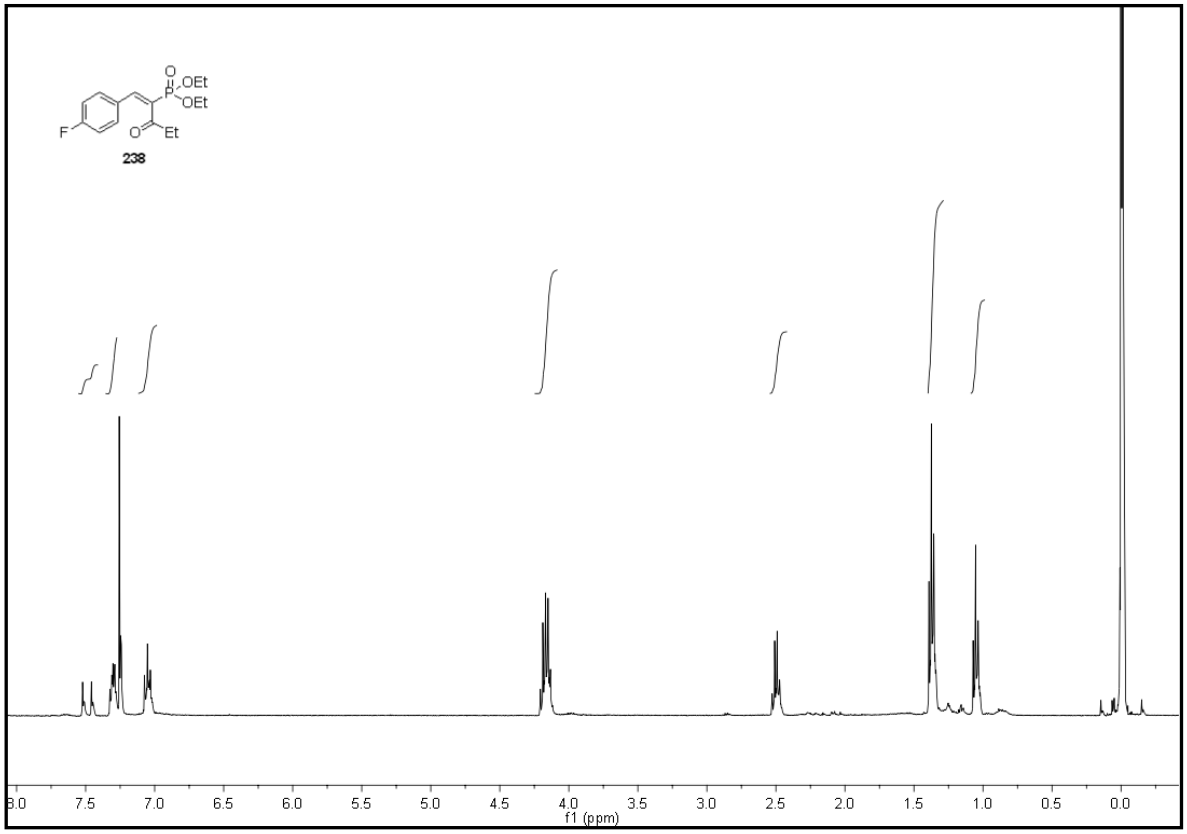


Figure A.64. ^{1}H NMR spectrum of compound **238**

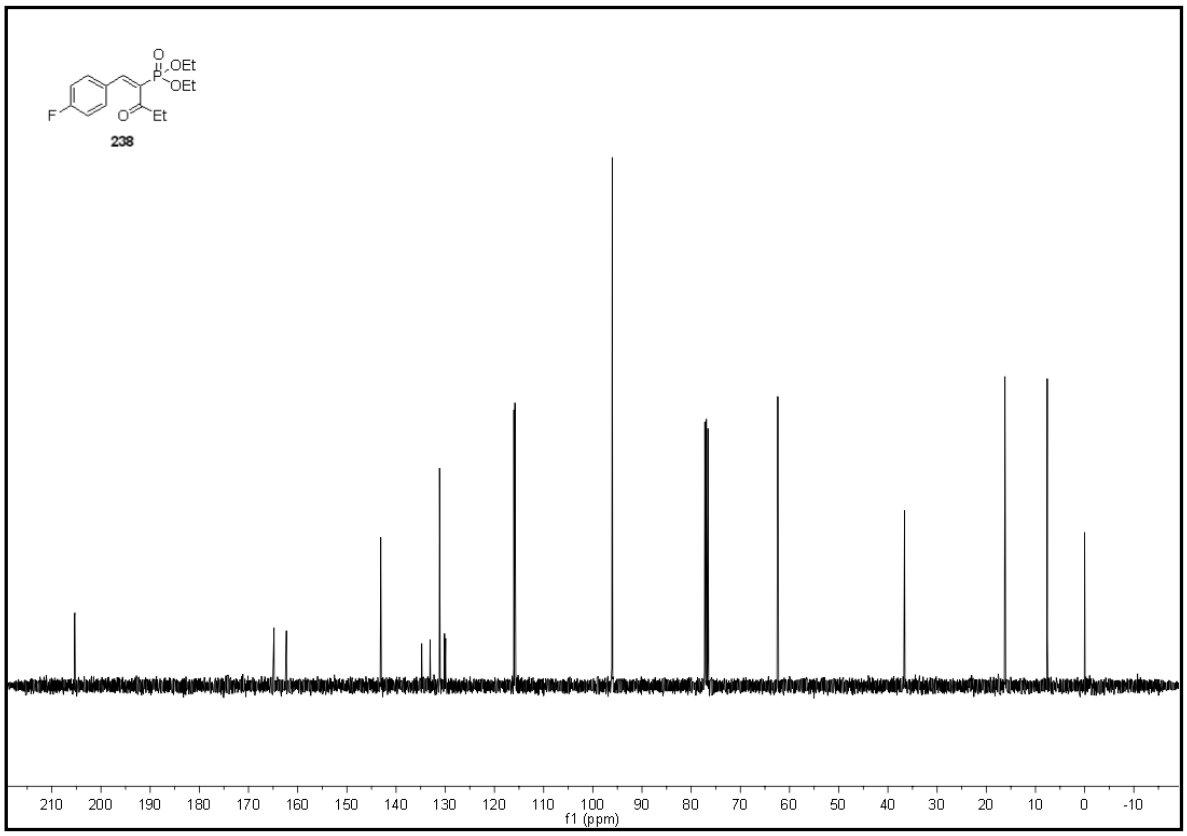


Figure A.65. ^{13}C NMR spectrum of compound **238**

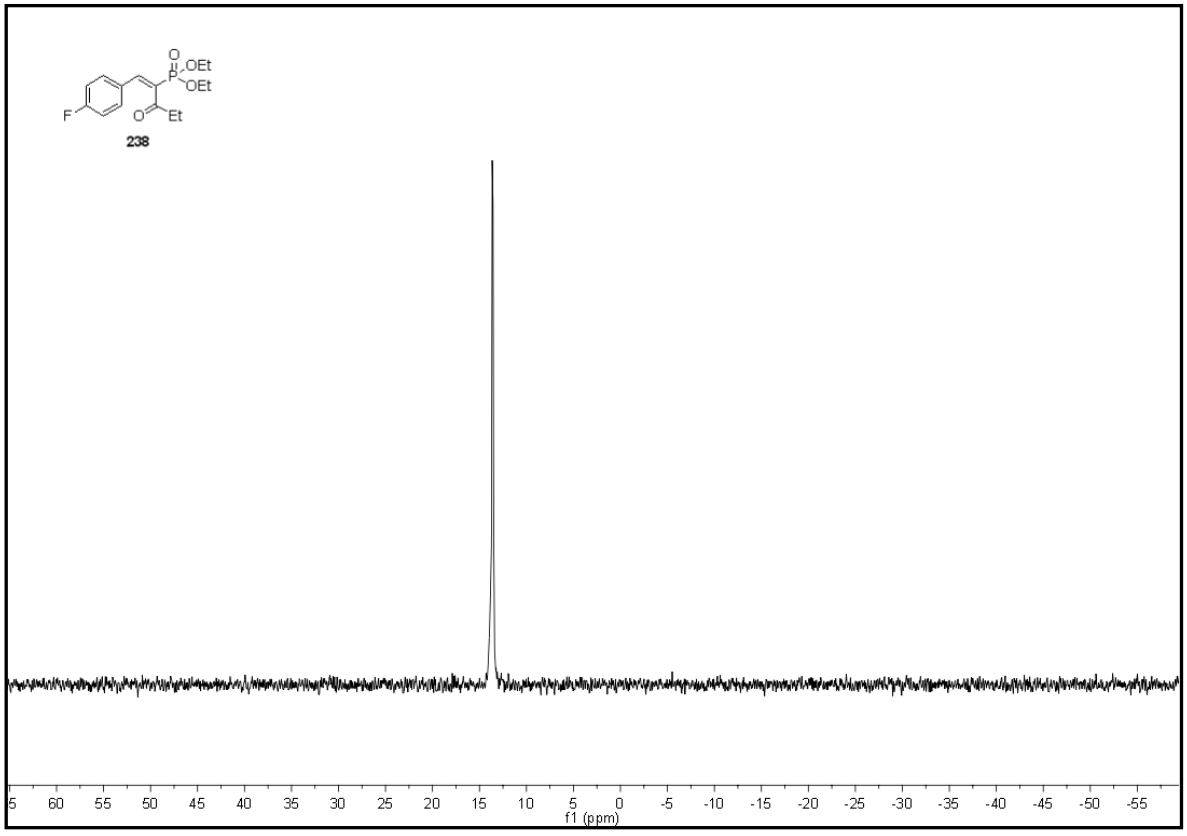


Figure A.66. ^{31}P NMR spectrum of compound **238**

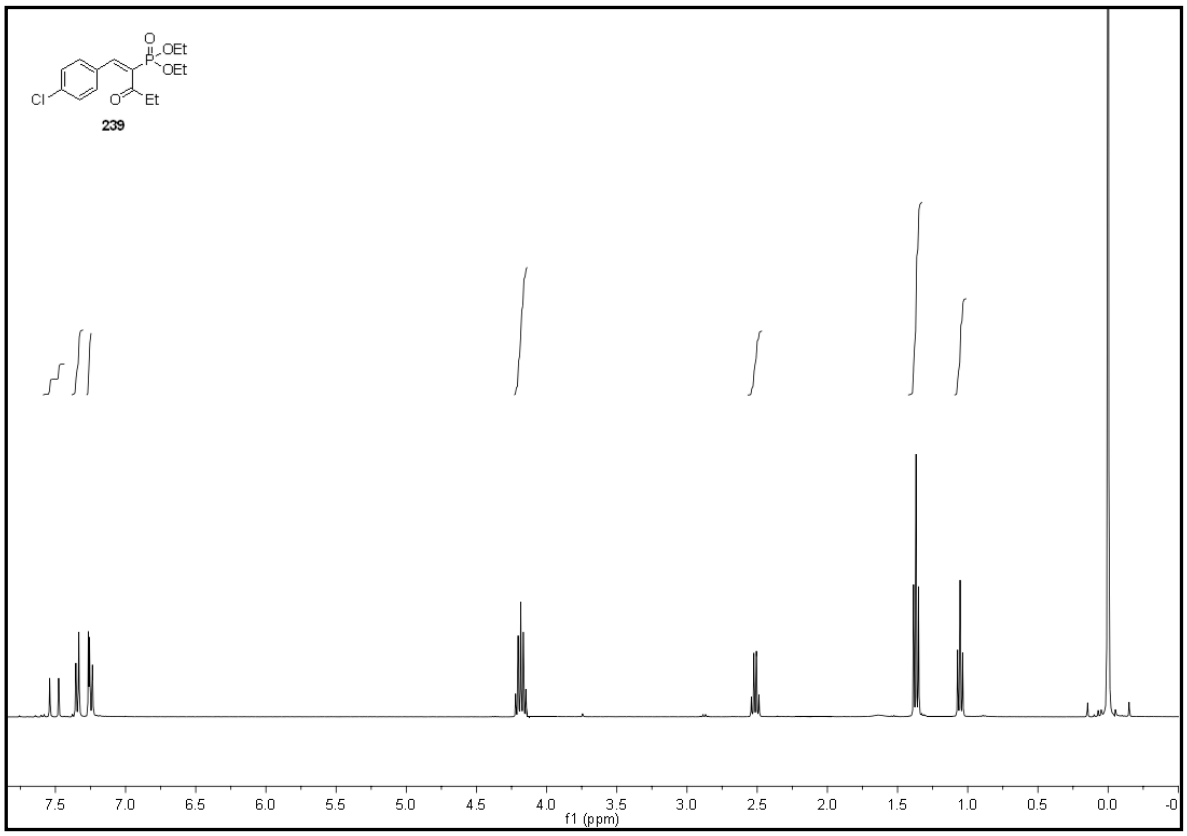


Figure A.67. ^{1}H NMR spectrum of compound **239**

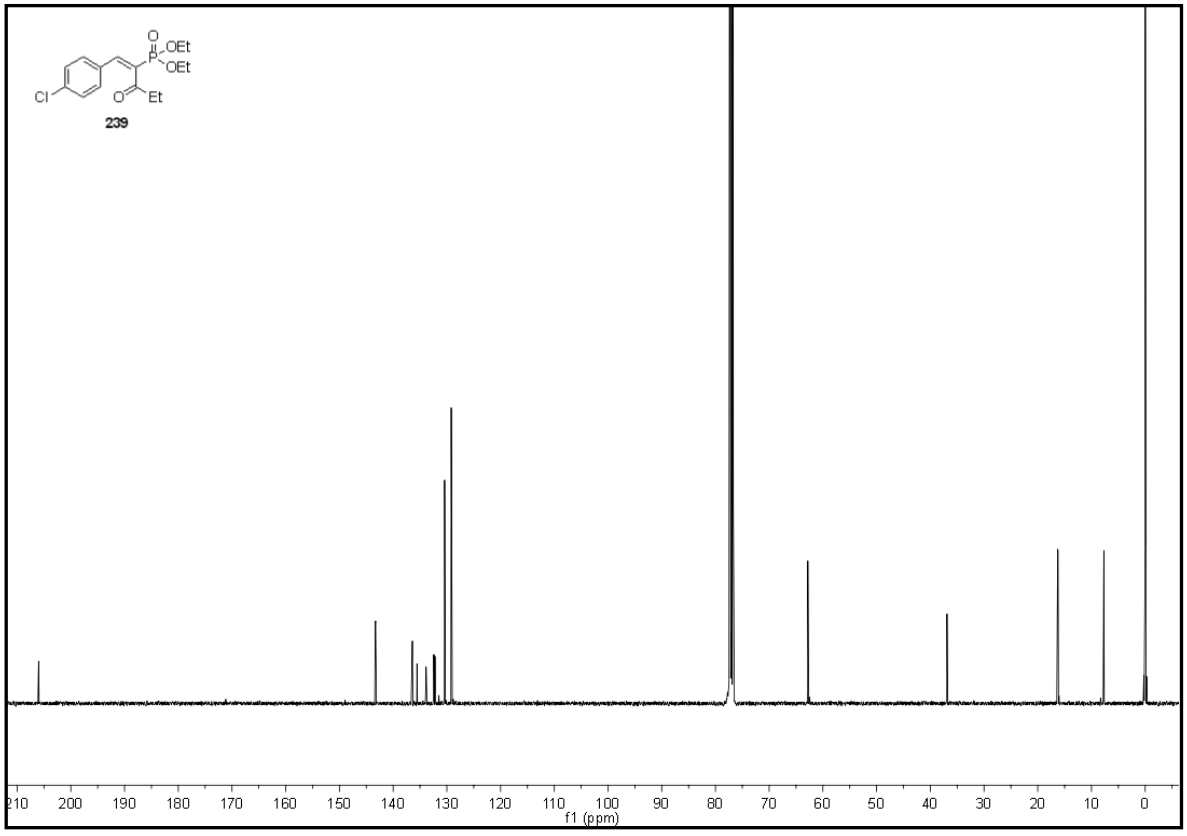


Figure A.68. ^{13}C NMR spectrum of compound **239**

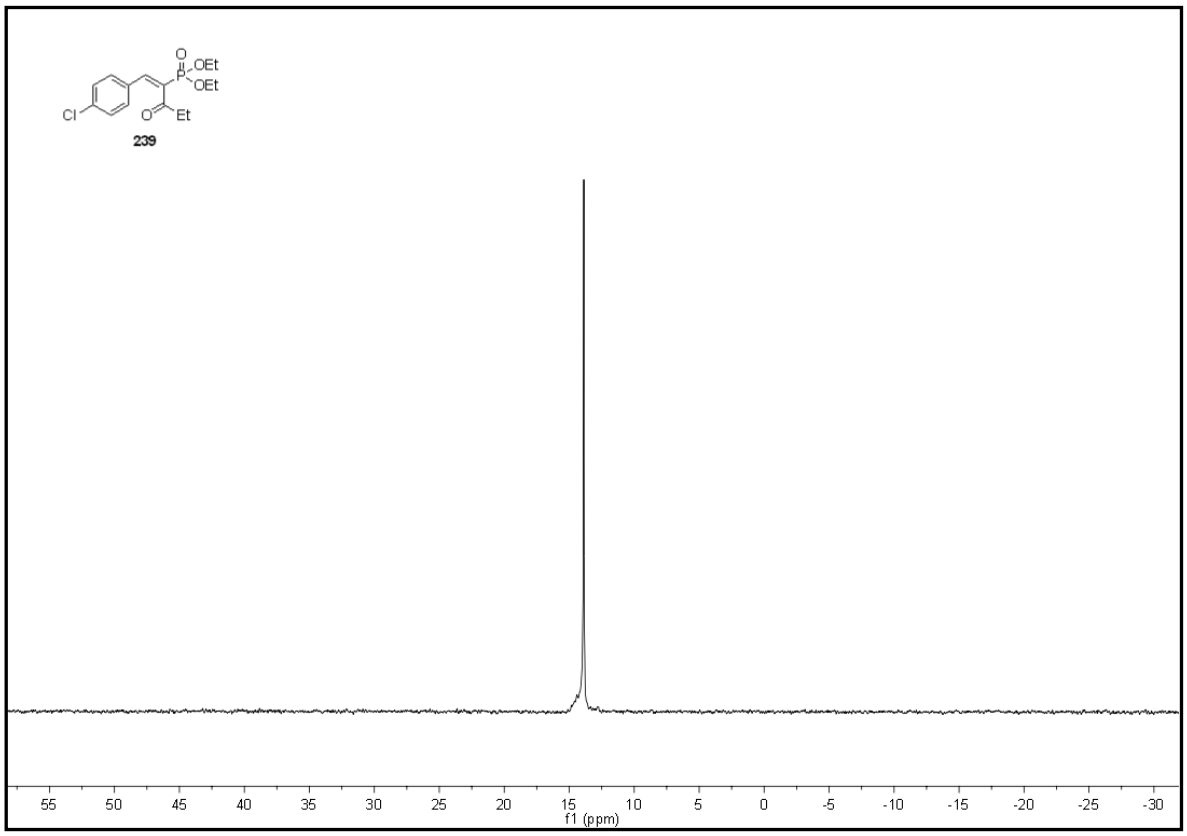


Figure A.69. ^{31}P NMR spectrum of compound **239**

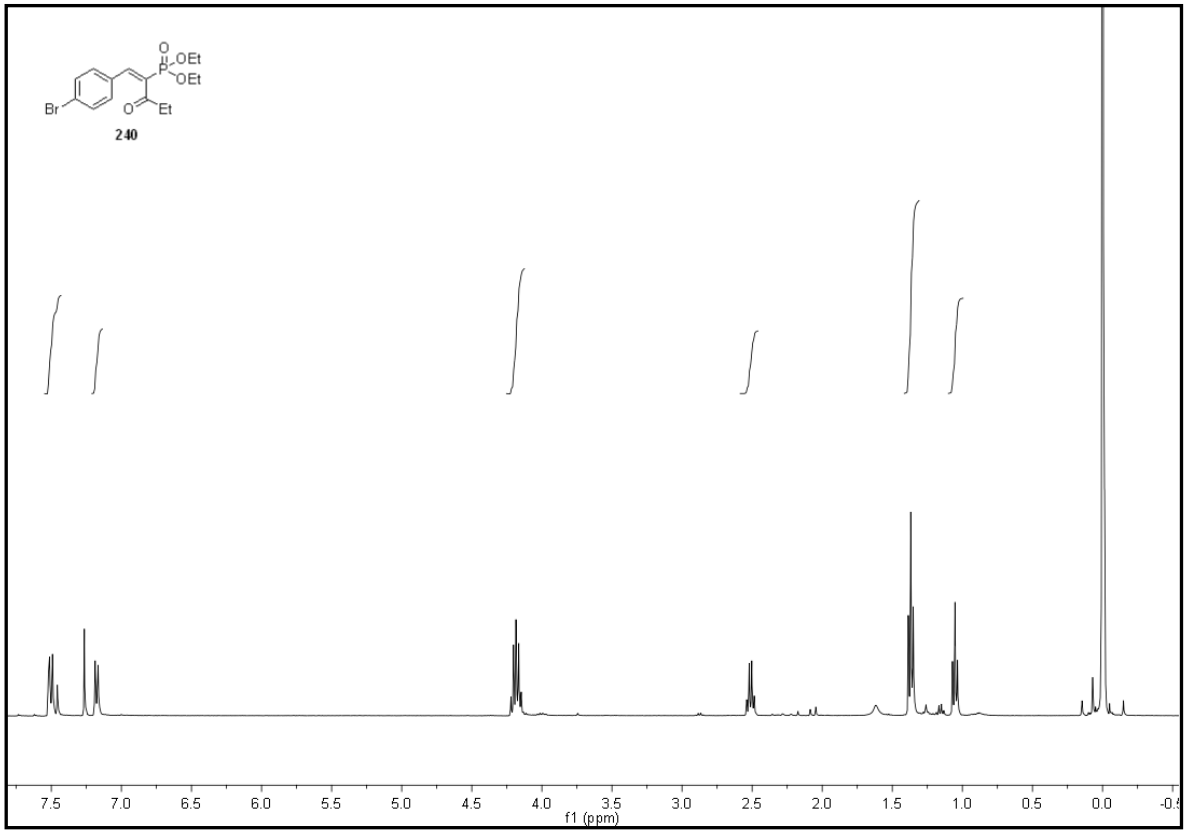


Figure A.70. ^{1}H NMR spectrum of compound **240**

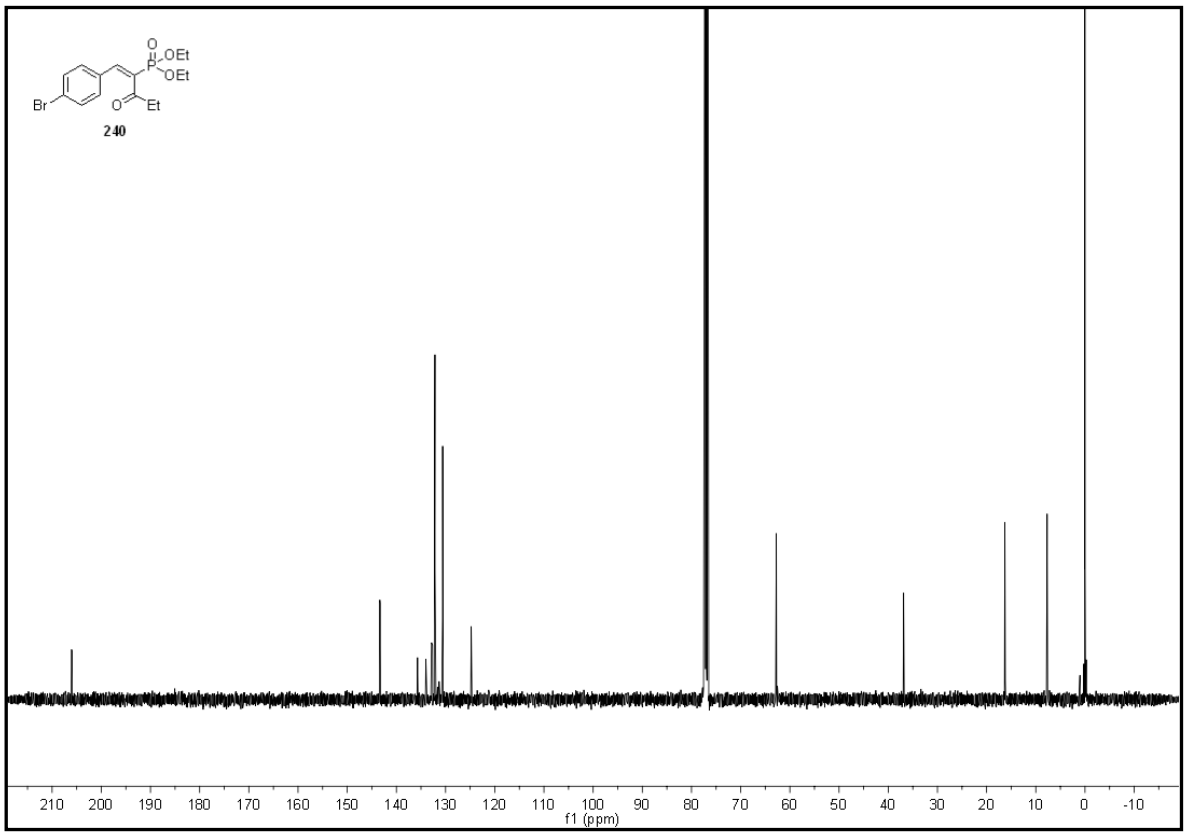


Figure A.71. ^{13}C NMR spectrum of compound **240**

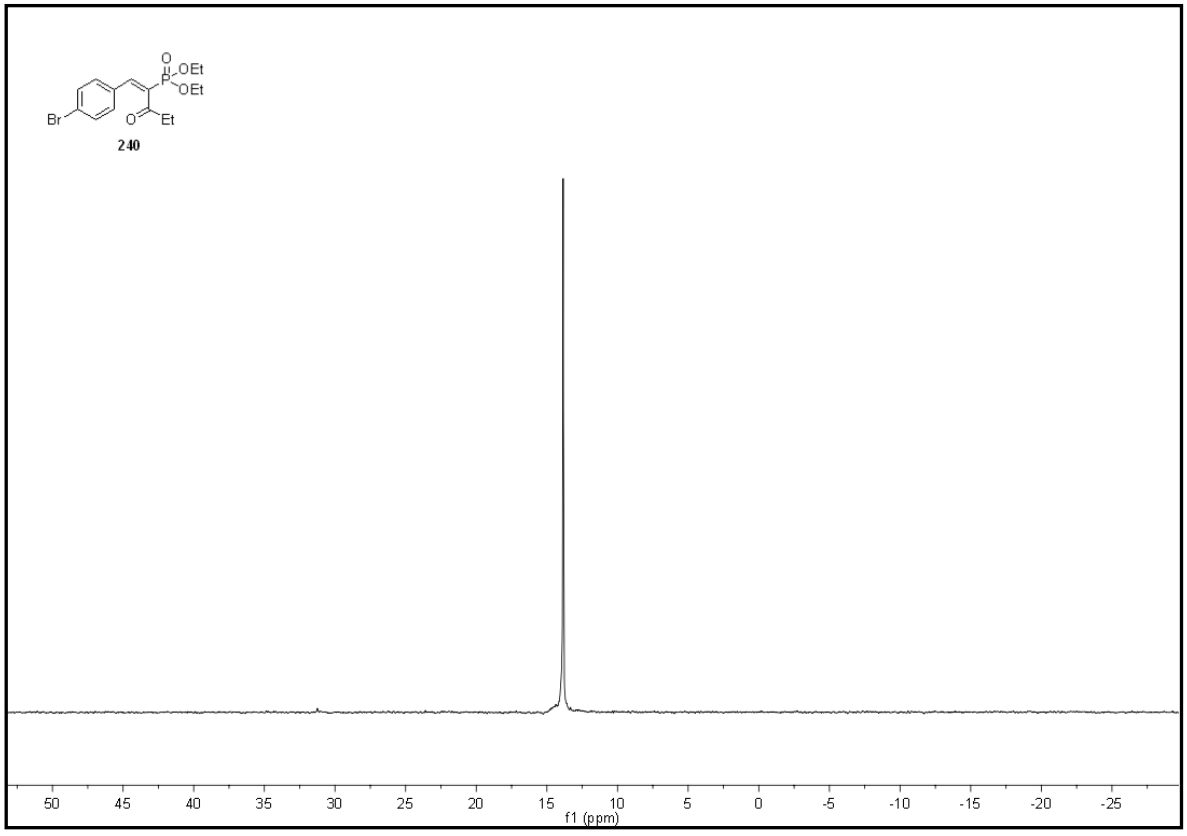


Figure A.72. ^{31}P NMR spectrum of compound **240**

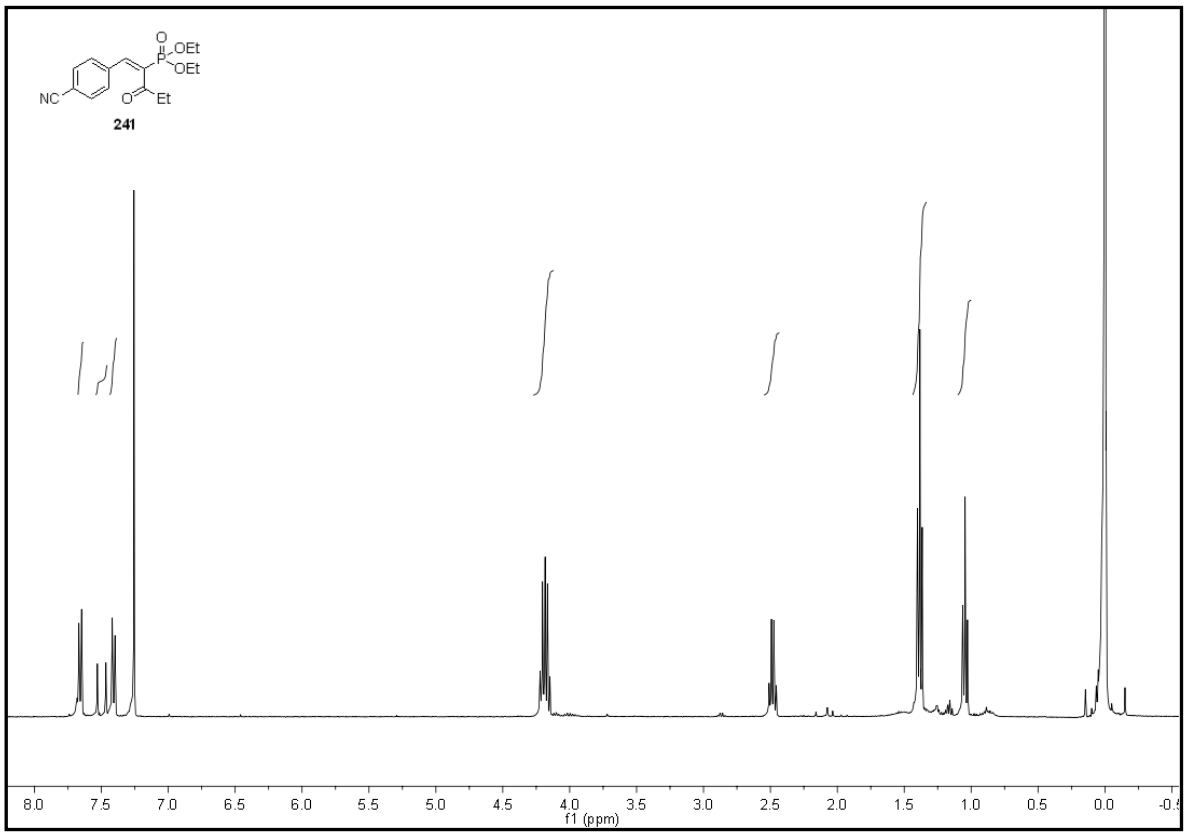


Figure A.73. ^{1}H NMR spectrum of compound **241**

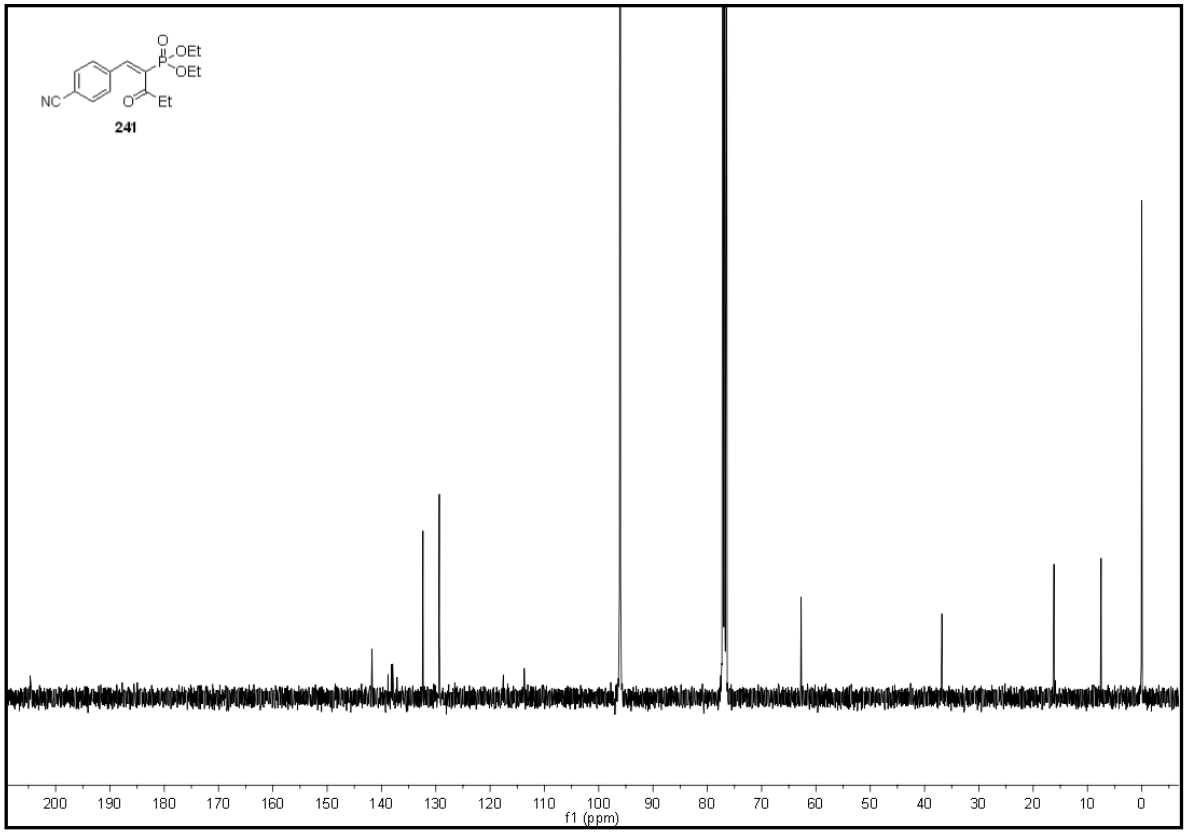


Figure A.74. ^{13}C NMR spectrum of compound **241**

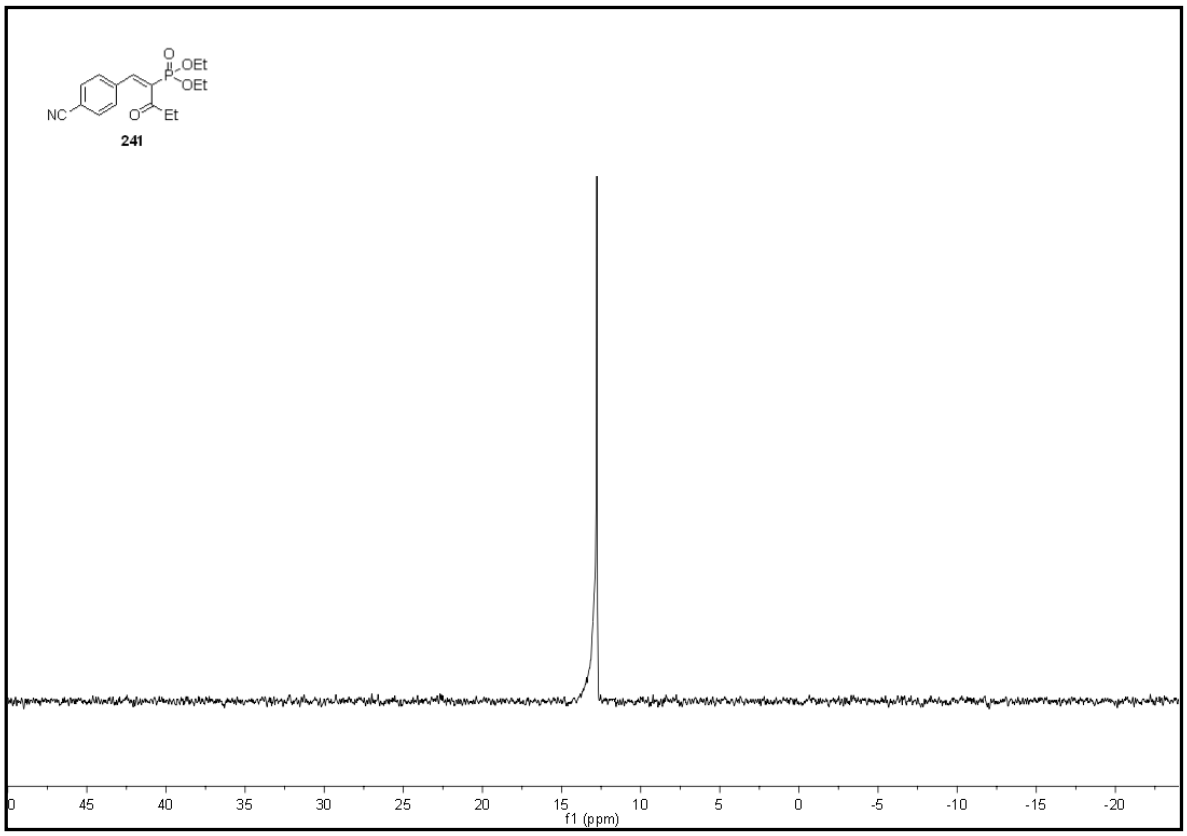


Figure A.75. ^{31}P NMR spectrum of compound **241**

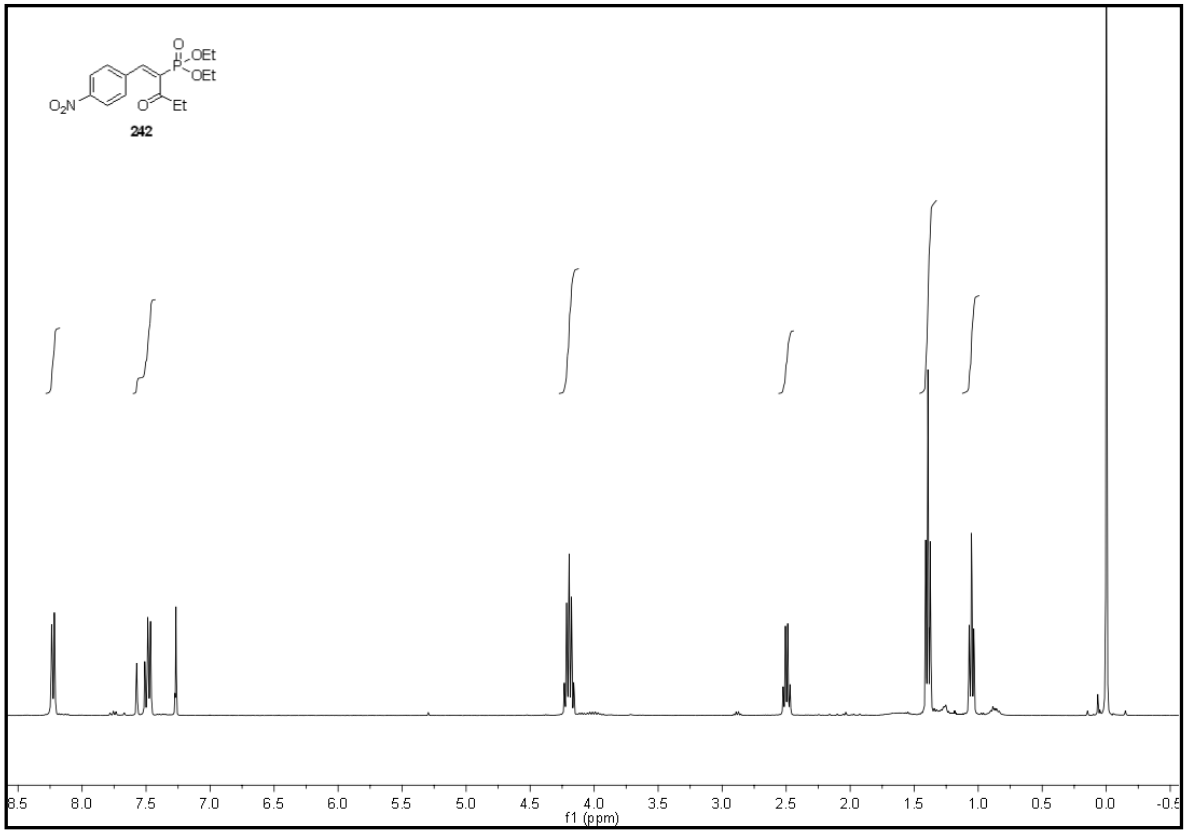


Figure A.76. ^{1}H NMR spectrum of compound **242**

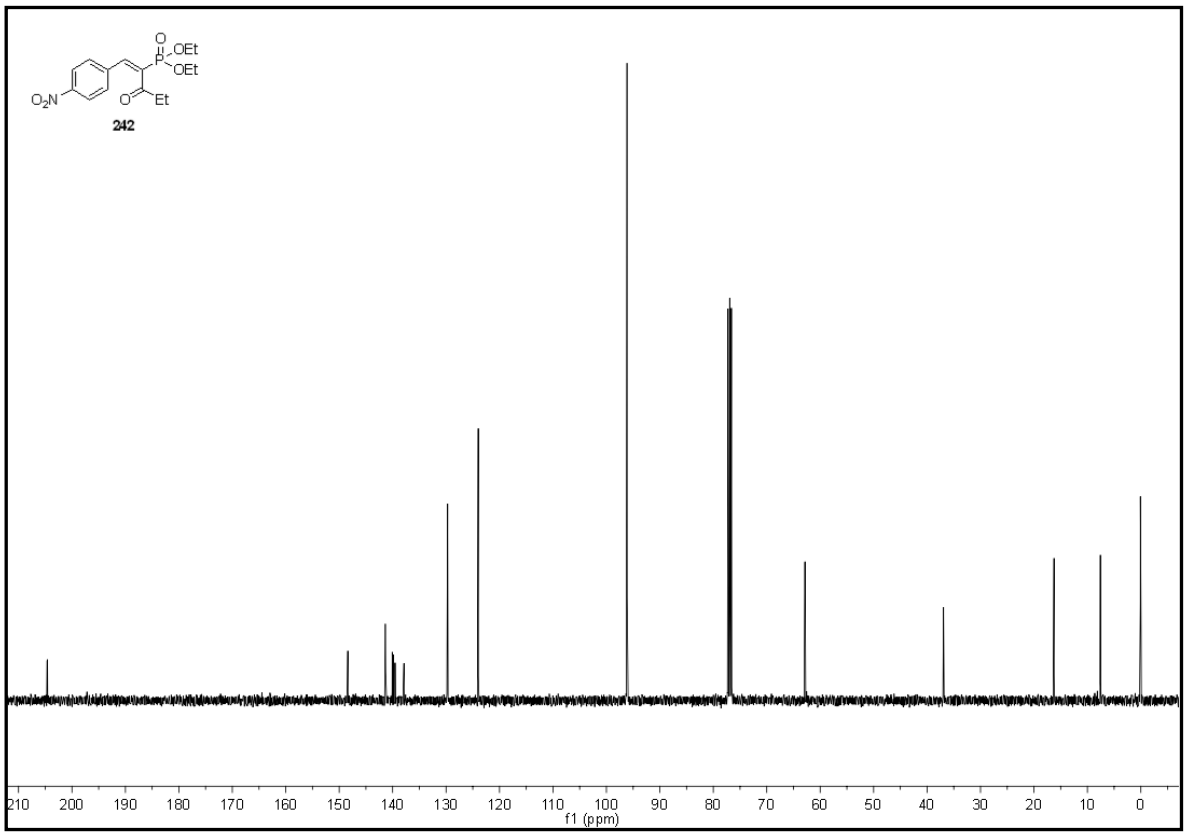


Figure A.77. ^{13}C NMR spectrum of compound **242**

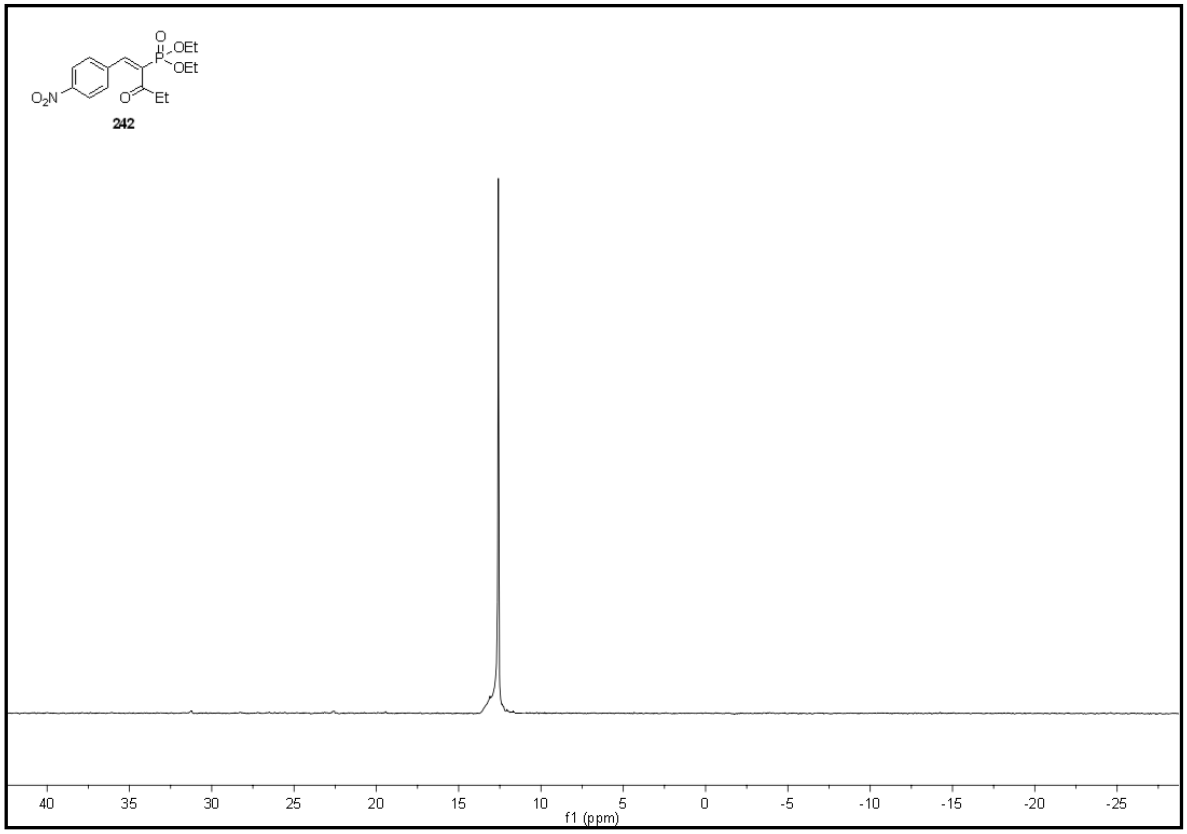


Figure A.78. ^{31}P NMR spectrum of compound **242**

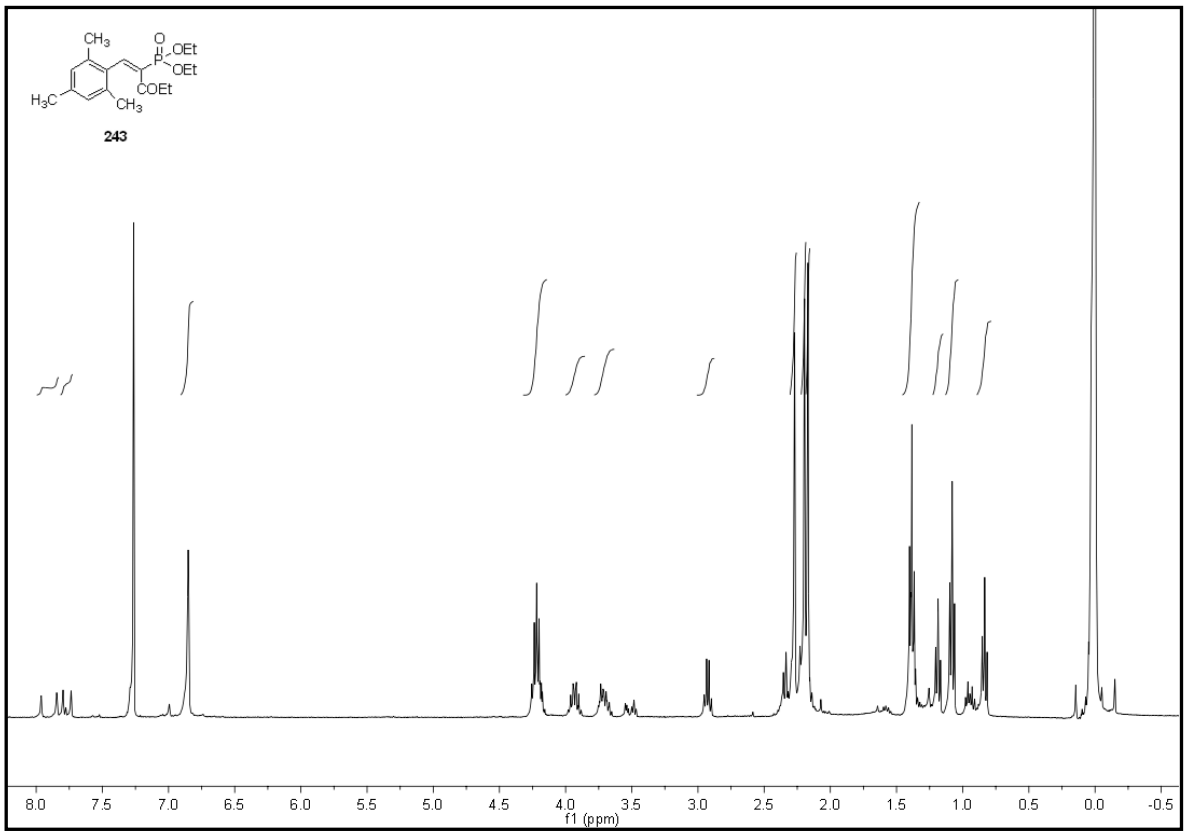


Figure A.79. ^{1}H NMR spectrum of compound **243**

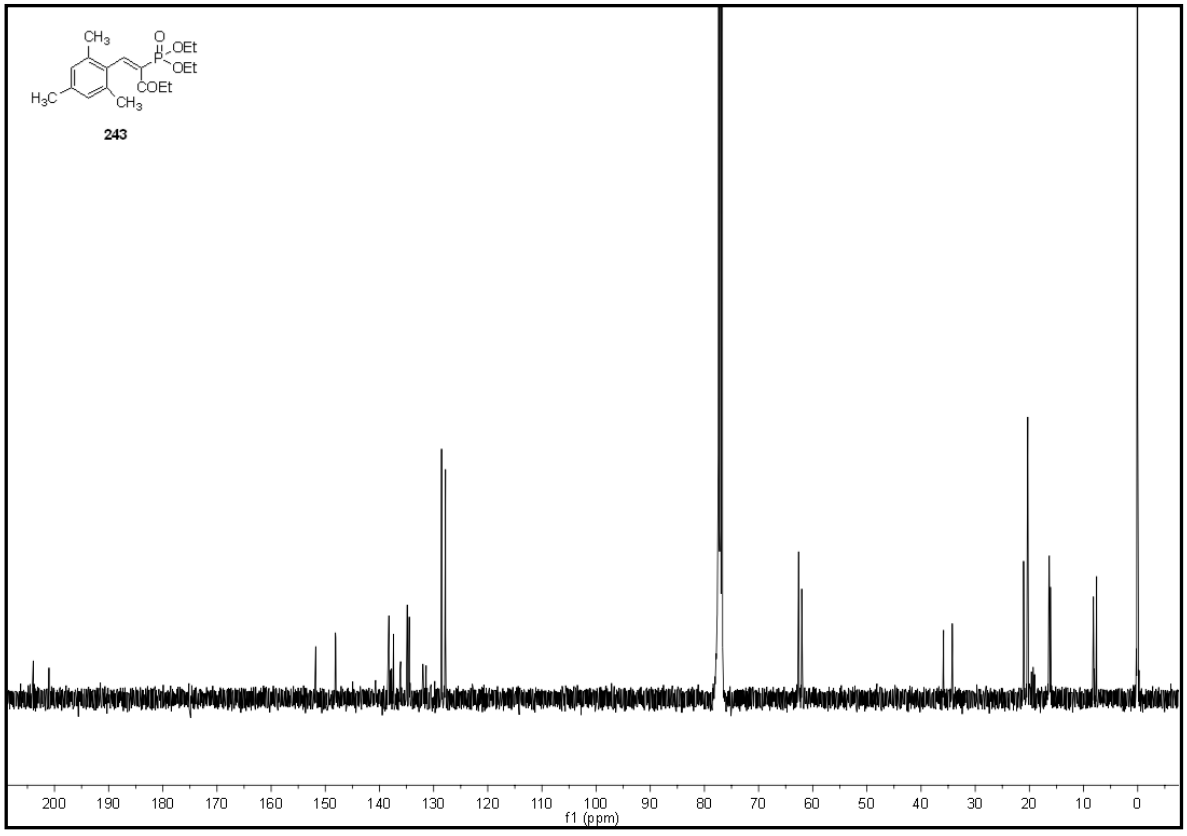


Figure A.80. ^{13}C NMR spectrum of compound **243**

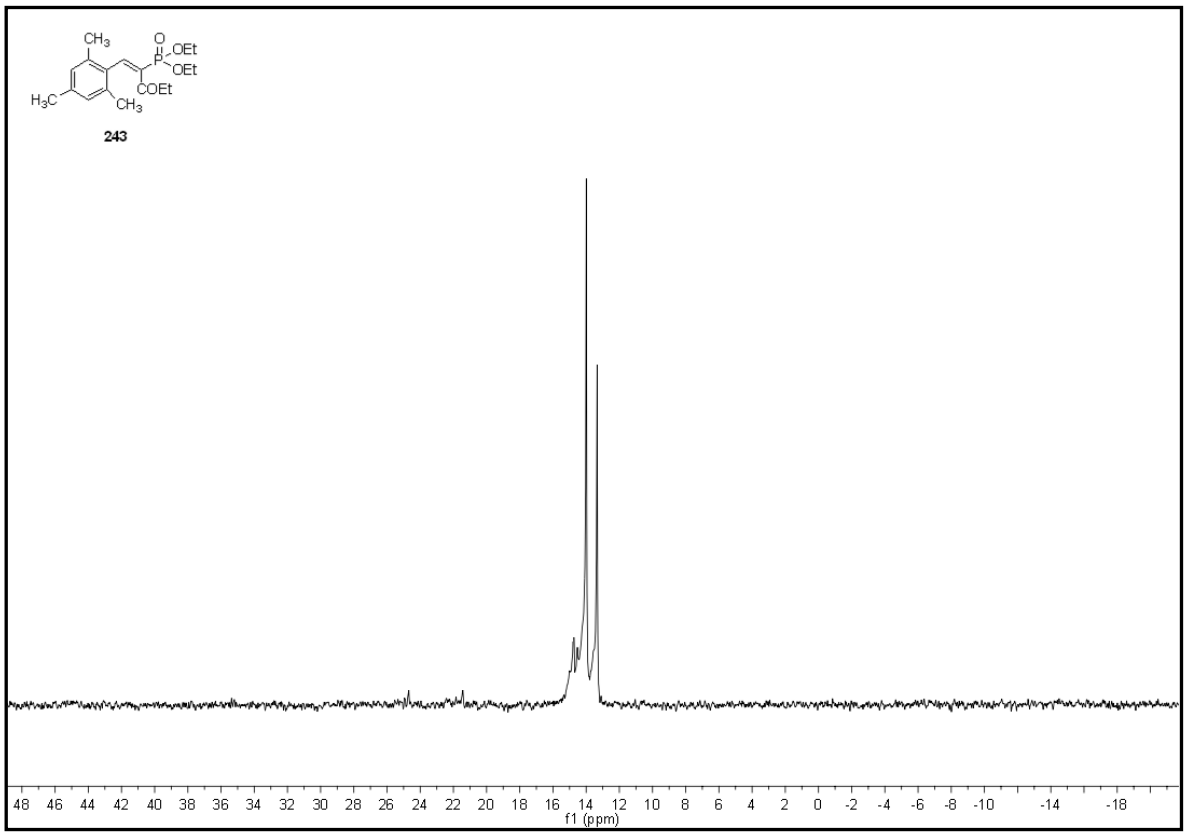


Figure A.81. ^{31}P NMR spectrum of compound **243**

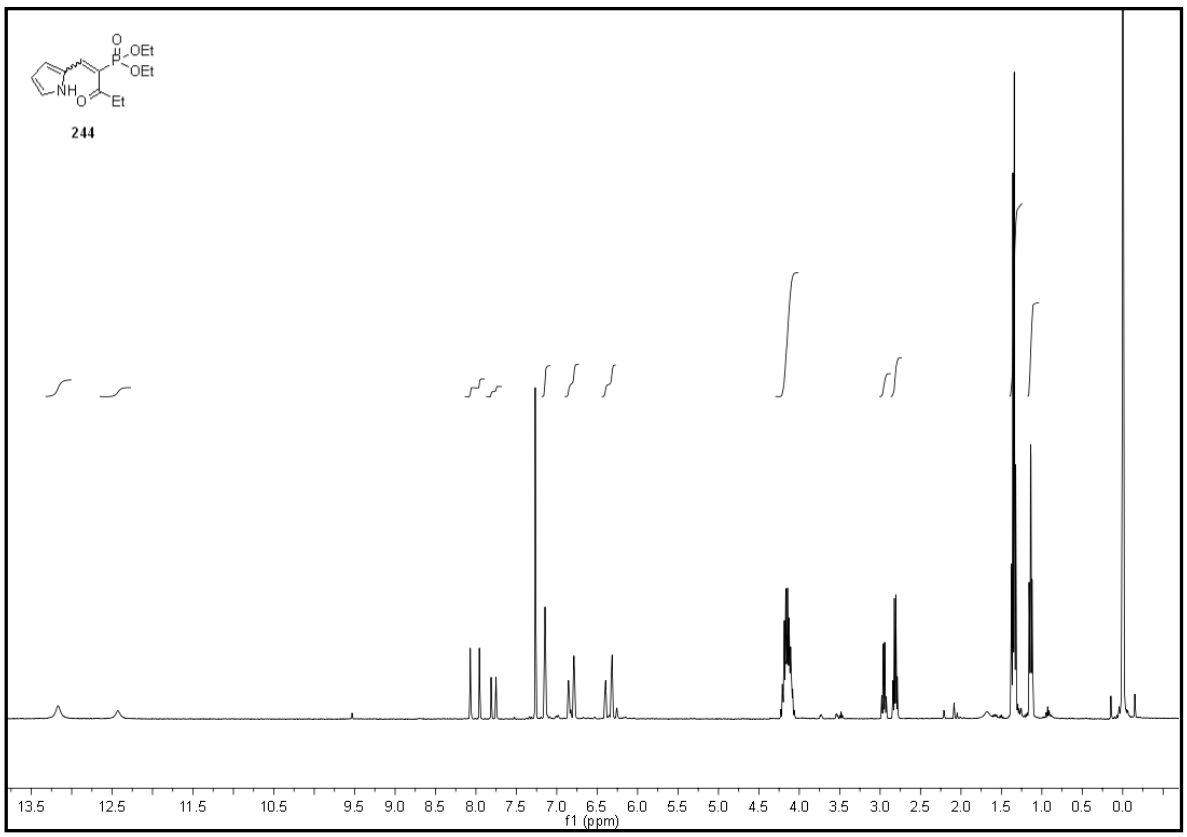


Figure A.82. ^{1}H NMR spectrum of compound **244**

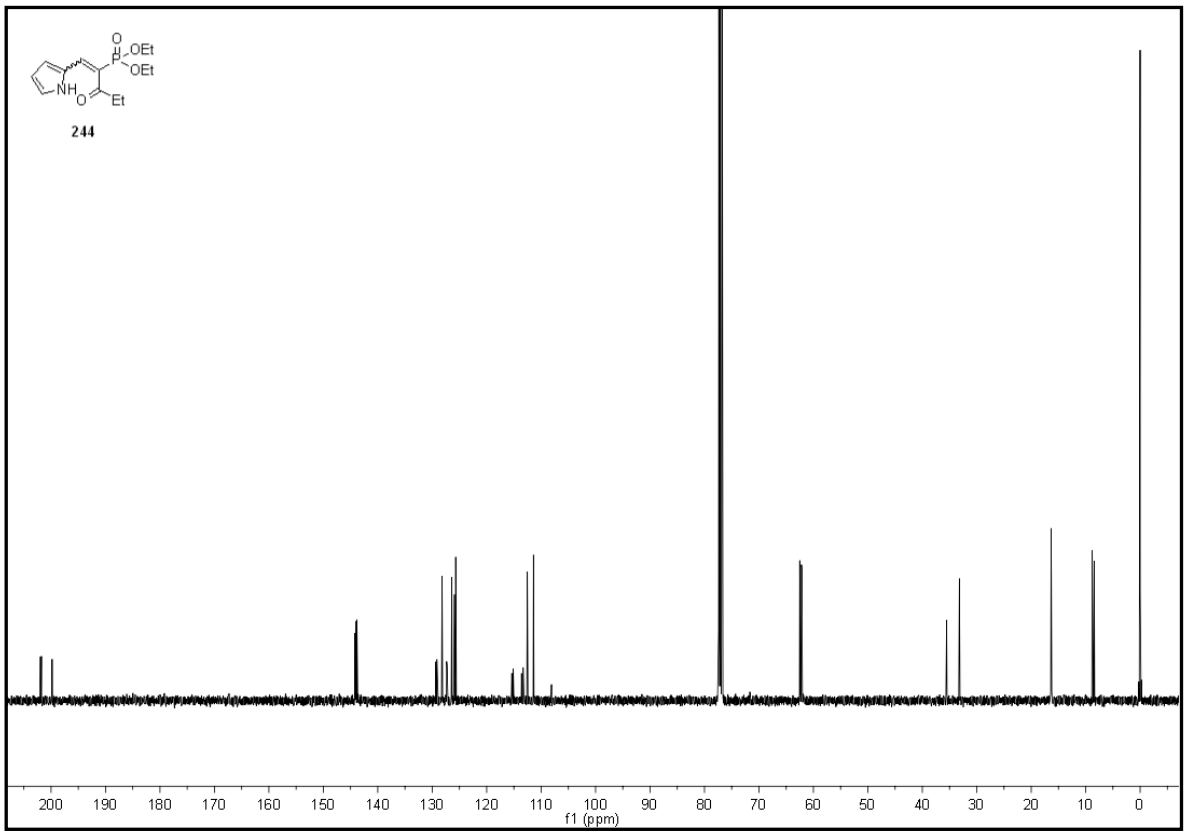


Figure A.83. ^{13}C NMR spectrum of compound **244**

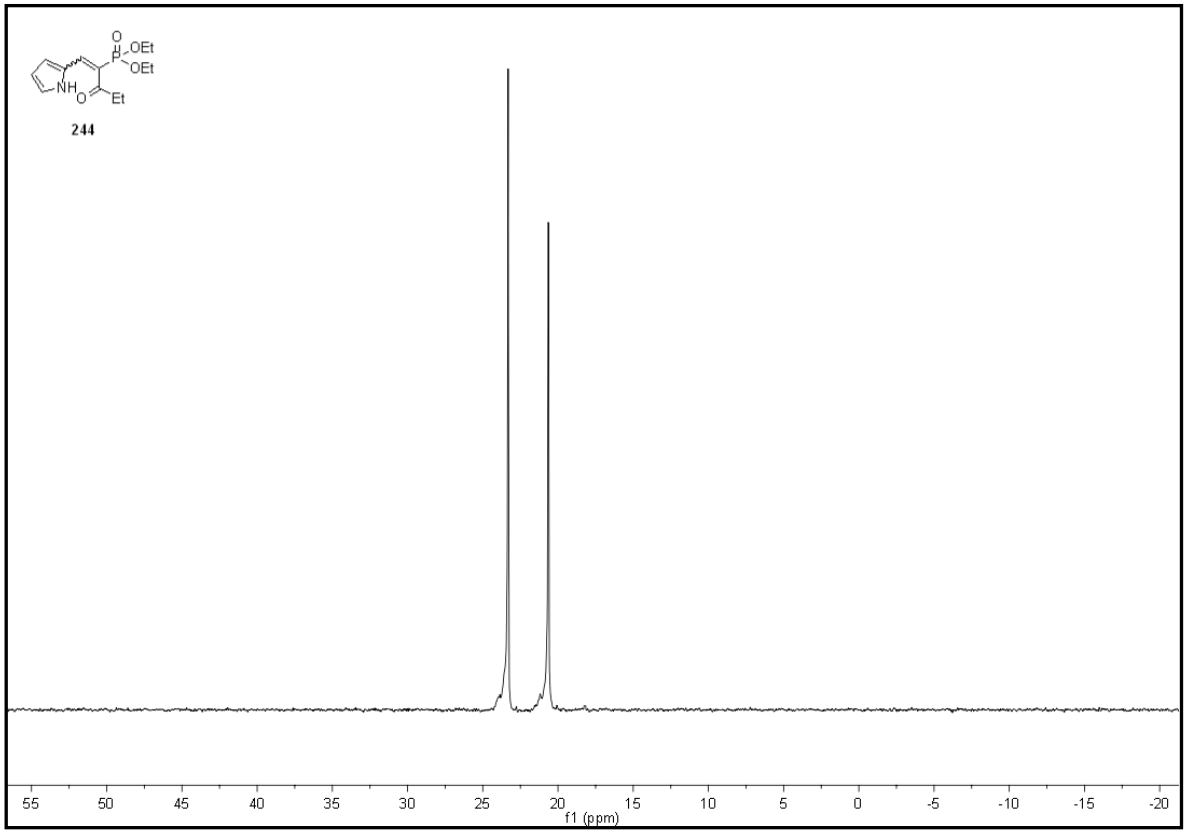


Figure A.84. ^{31}P NMR spectrum of compound **244**

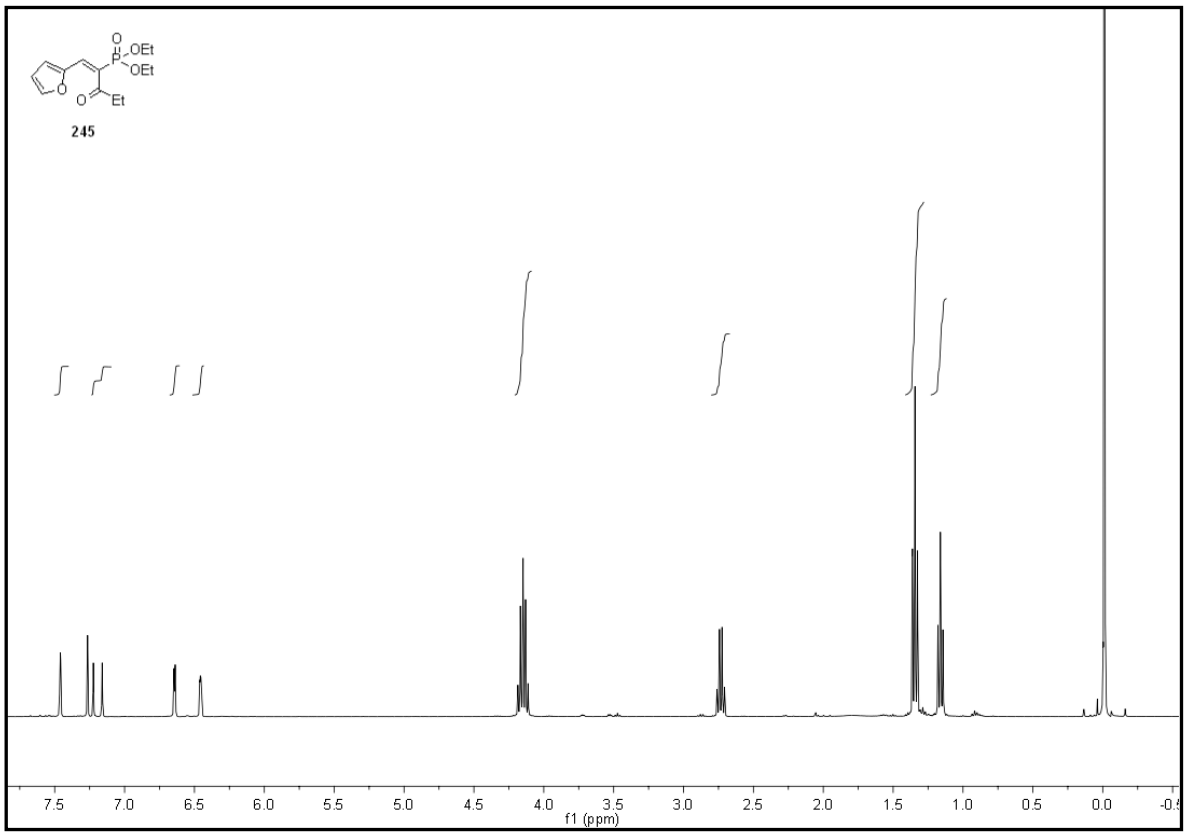


Figure A.85. ^{1}H NMR spectrum of compound **245**

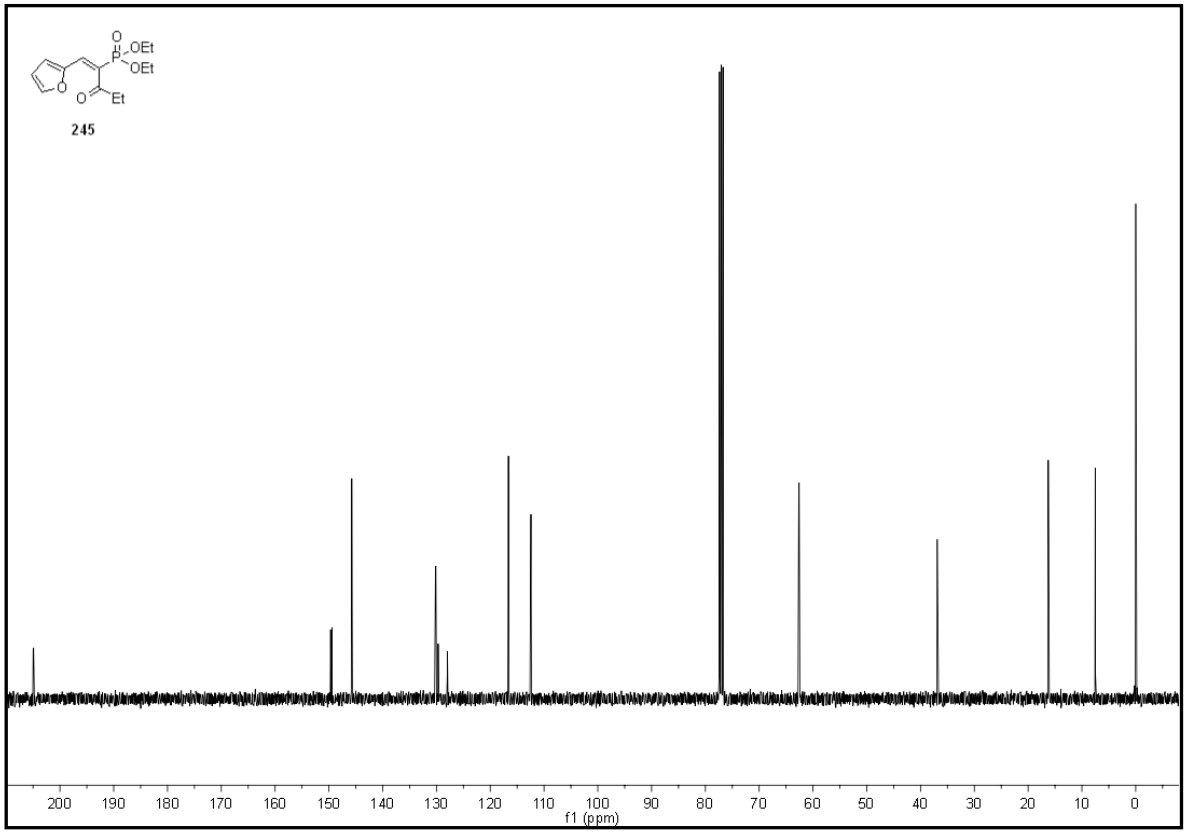


Figure A.86. ^{13}C NMR spectrum of compound **245**

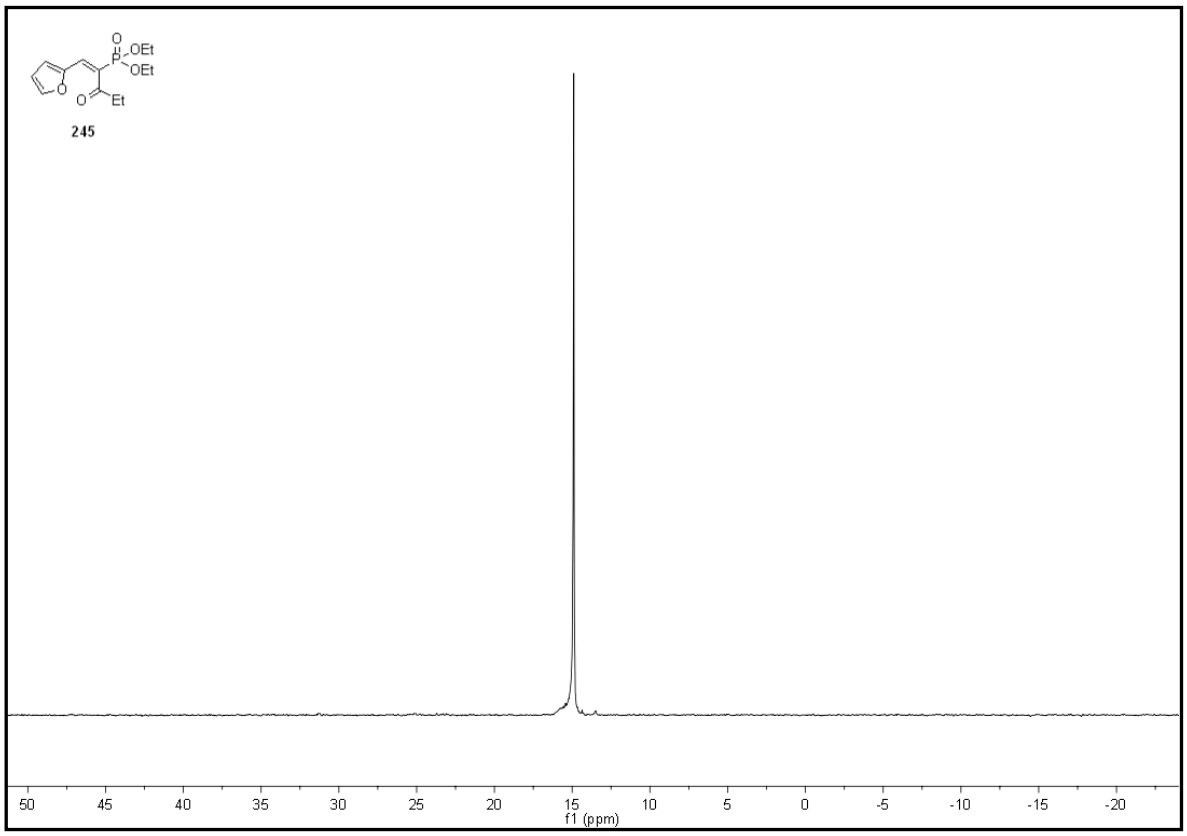


Figure A.87. ^{31}P NMR spectrum of compound **245**

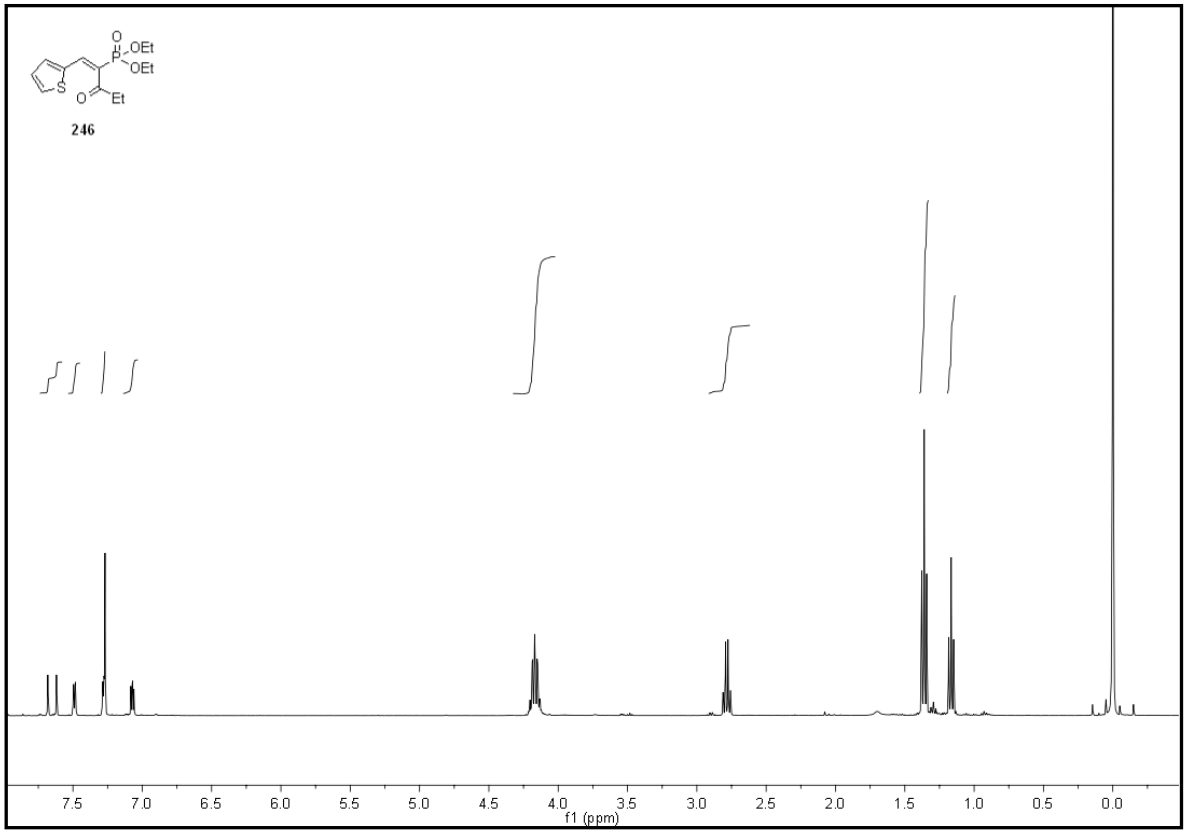


Figure A.88. ^{1}H NMR spectrum of compound **246**

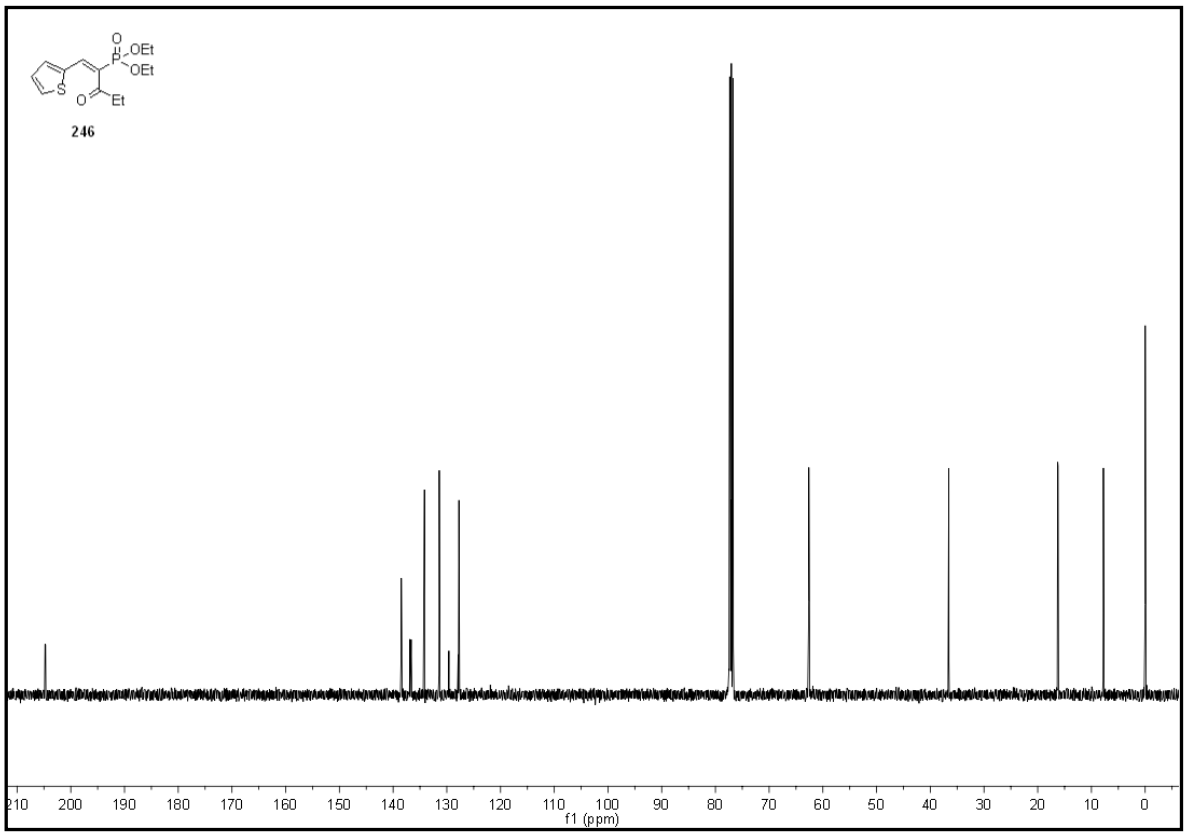


Figure A.89. ^{13}C NMR spectrum of compound **246**

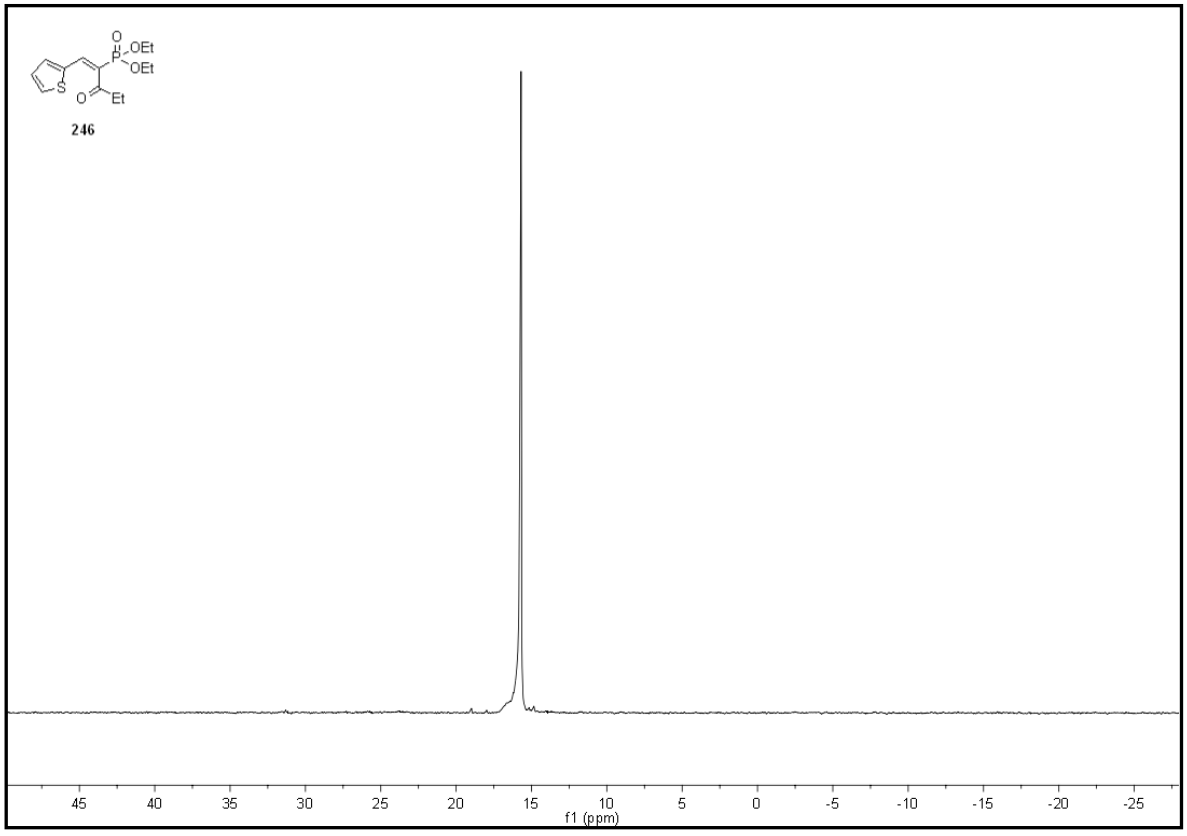


Figure A.90. ^{31}P NMR spectrum of compound **246**

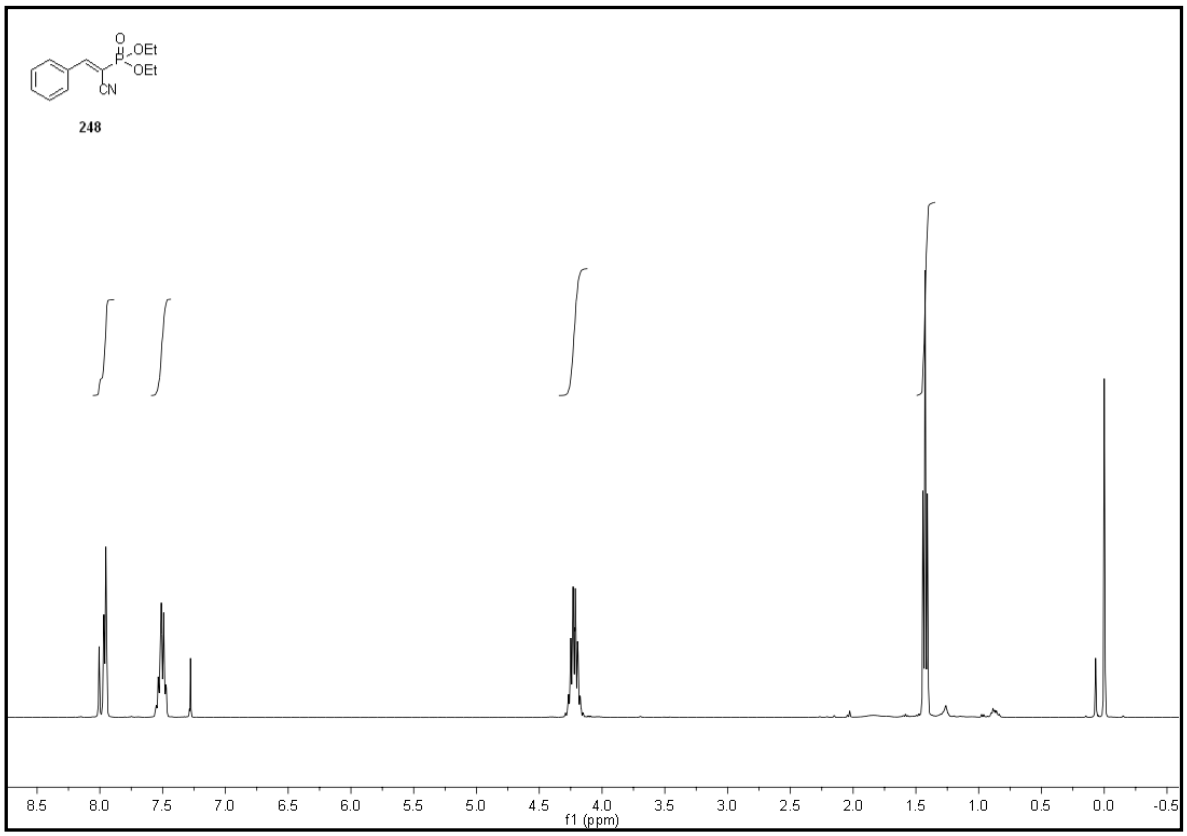


Figure A.91. ^{1}H NMR spectrum of compound **248**

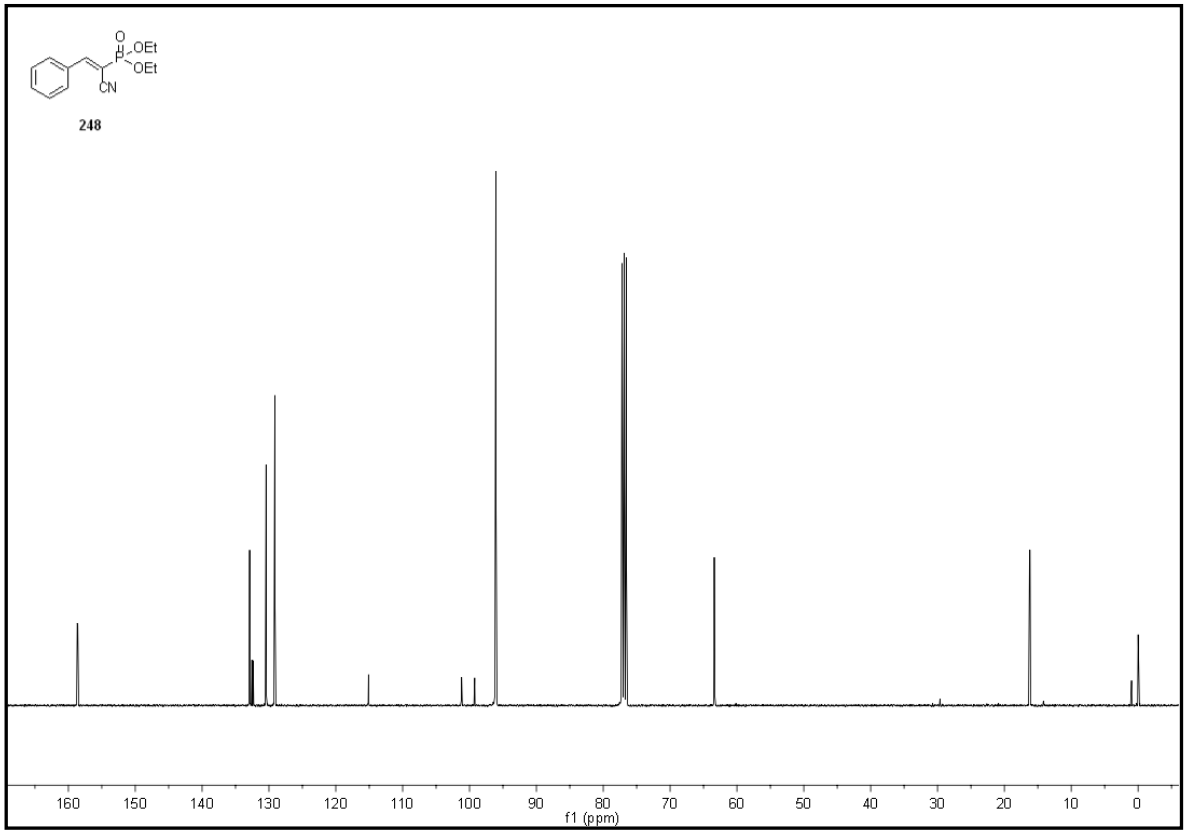


Figure A.92. ^{13}C NMR spectrum of compound **248**

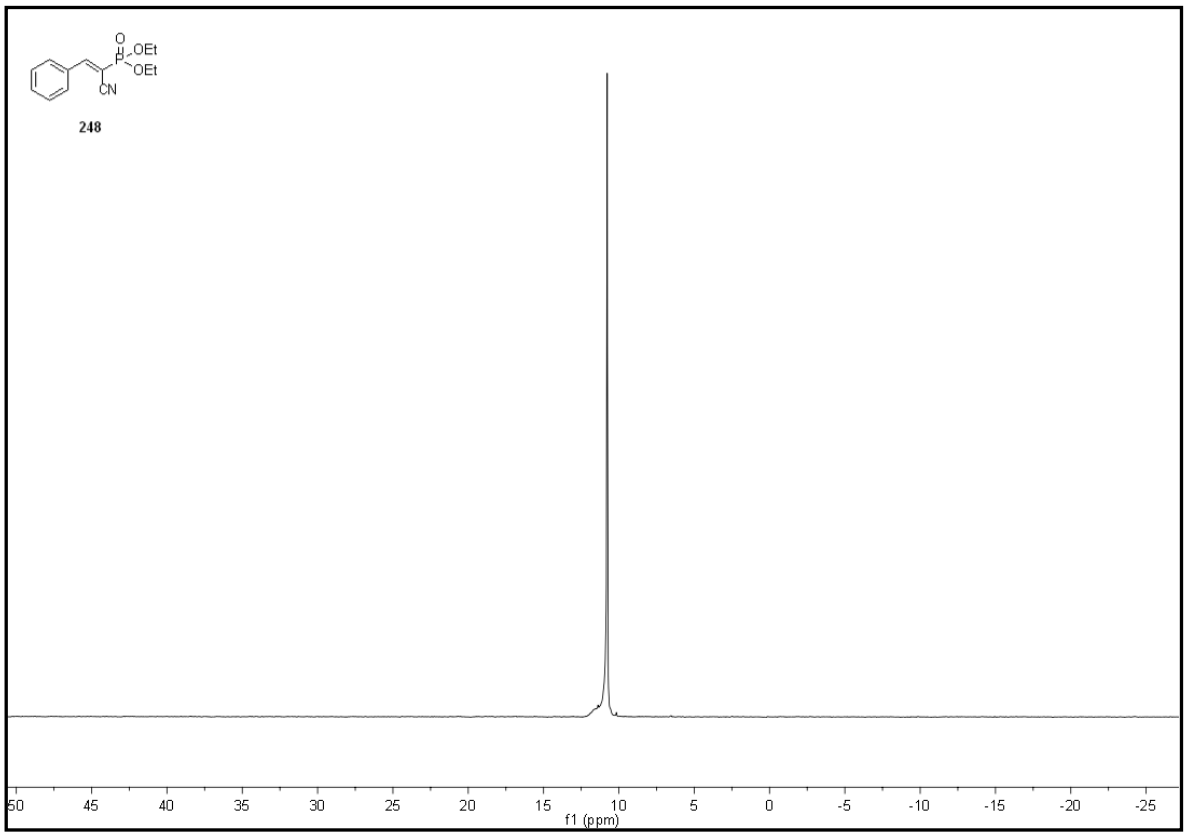


Figure A.93. ^{31}P NMR spectrum of compound **248**

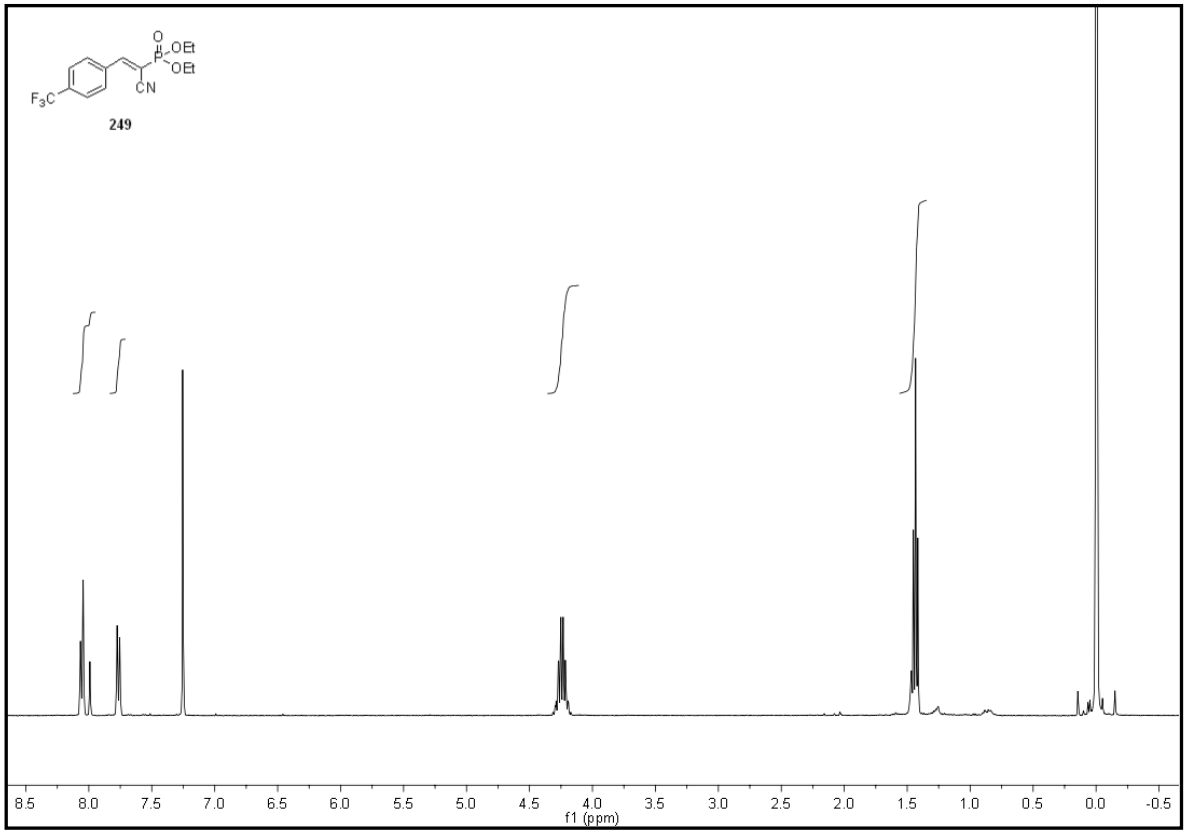


Figure A.94. ^{1}H NMR spectrum of compound **249**

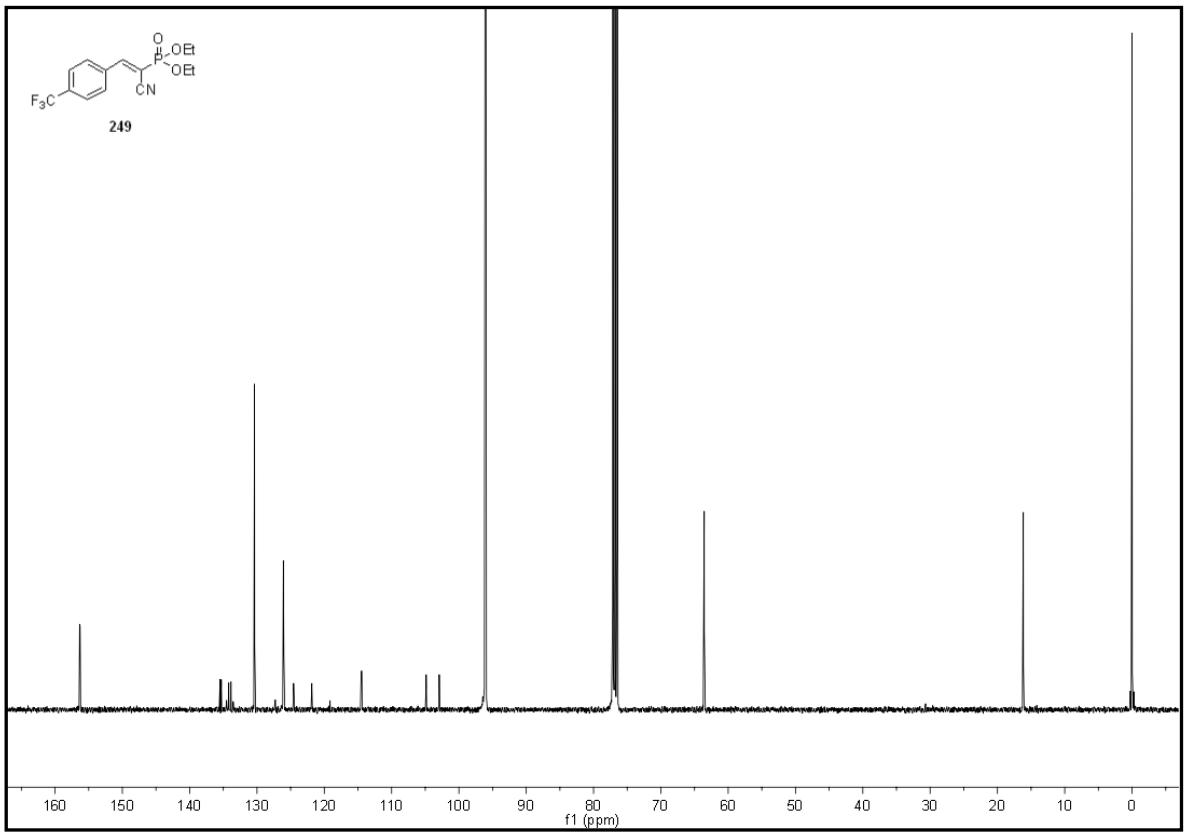


Figure A.95. ^{13}C NMR spectrum of compound **249**

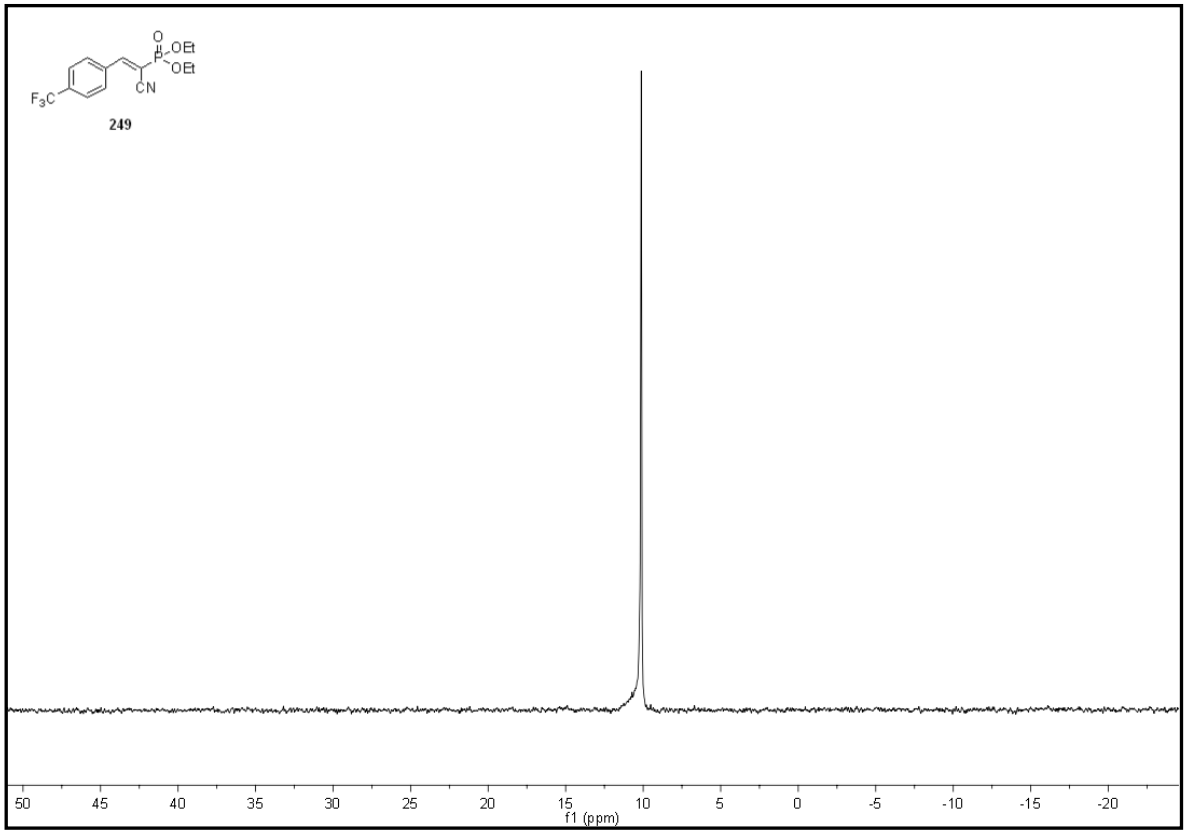


Figure A.96. ^{31}P NMR spectrum of compound **249**

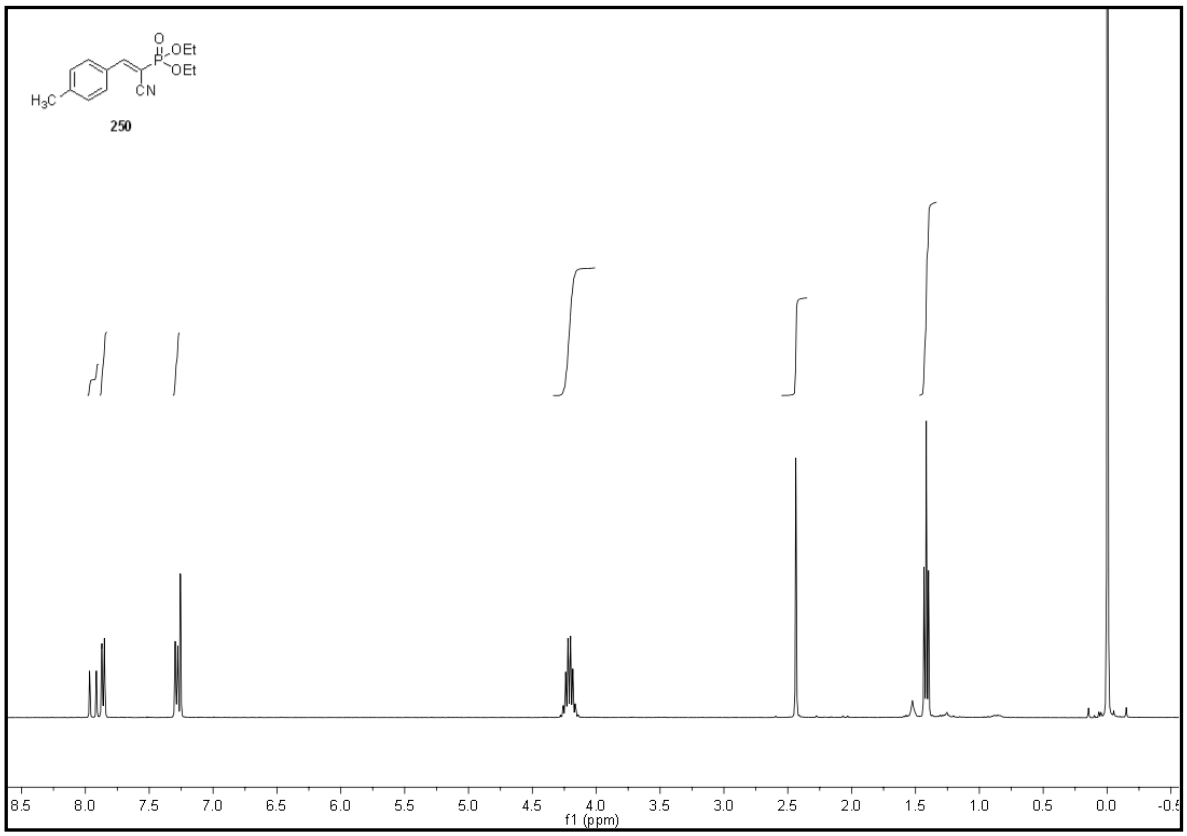


Figure A.97. ^{1}H NMR spectrum of compound **250**

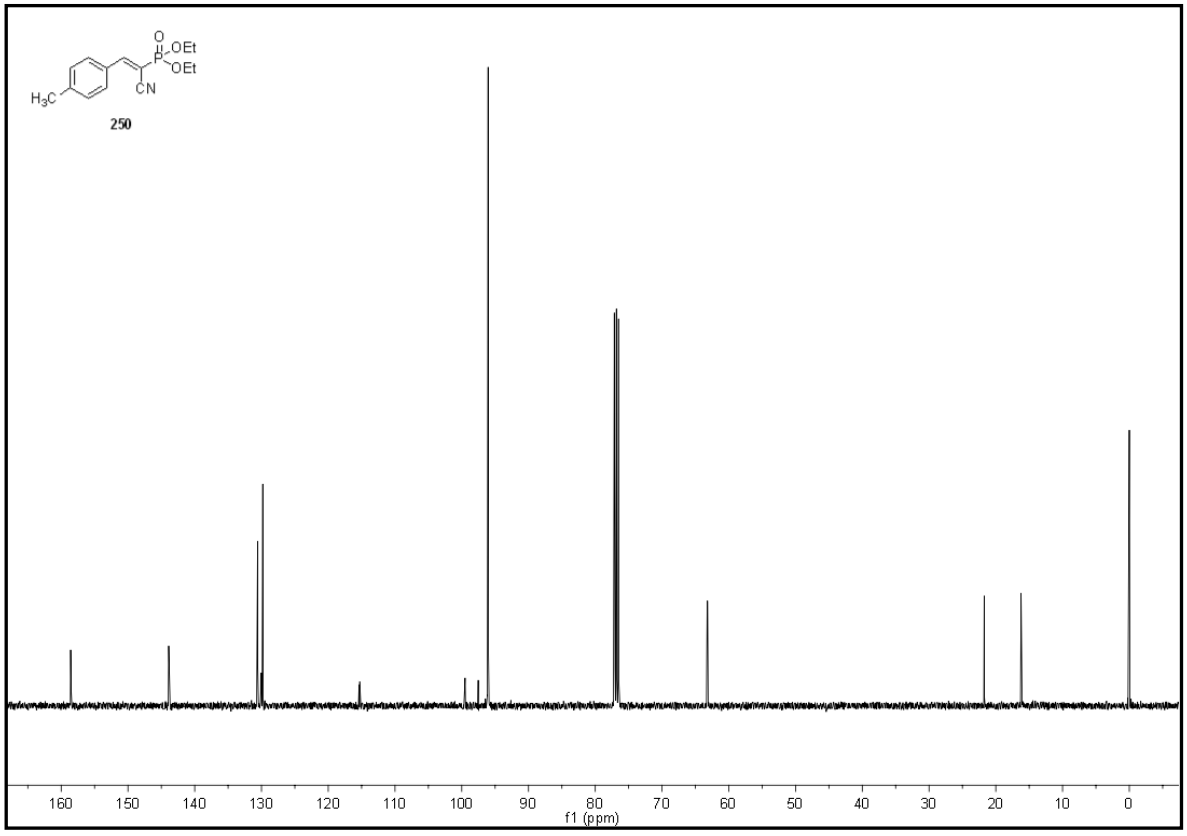


Figure A.98. ^{13}C NMR spectrum of compound **250**

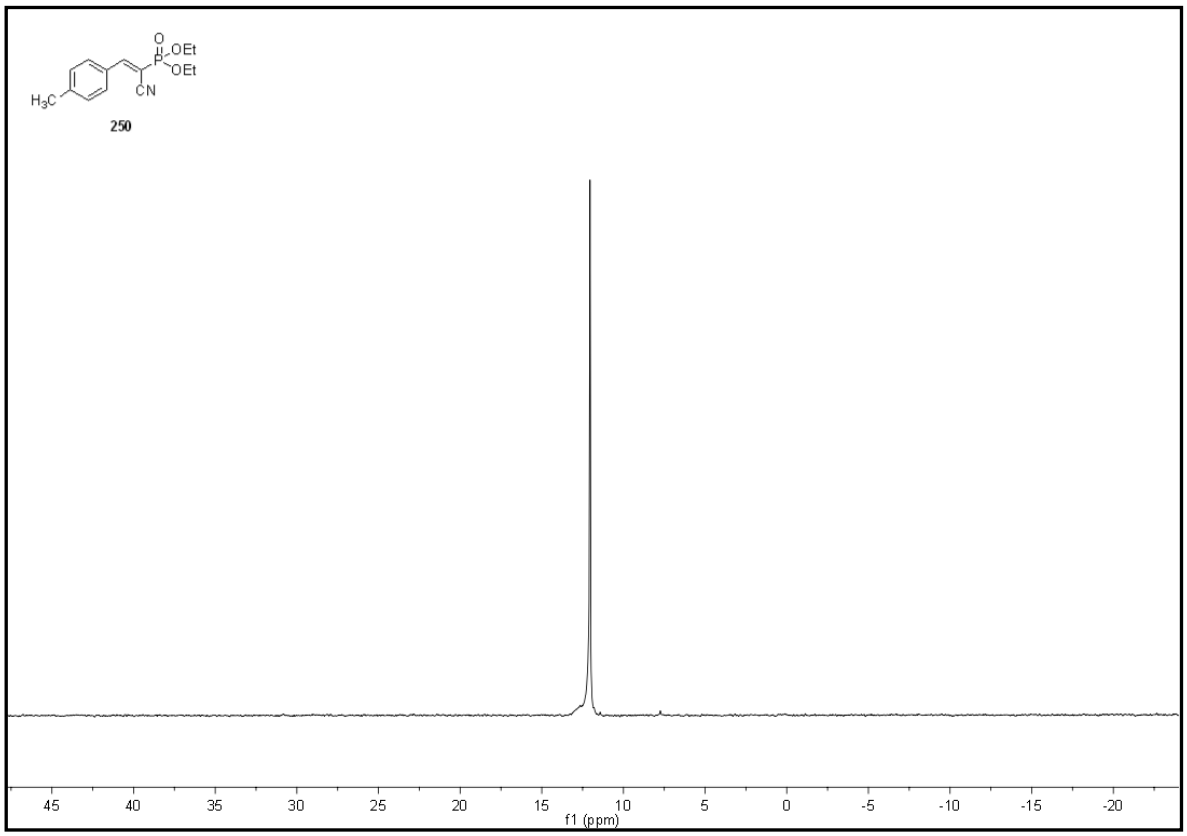


Figure A.99. ^{31}P NMR spectrum of compound **250**

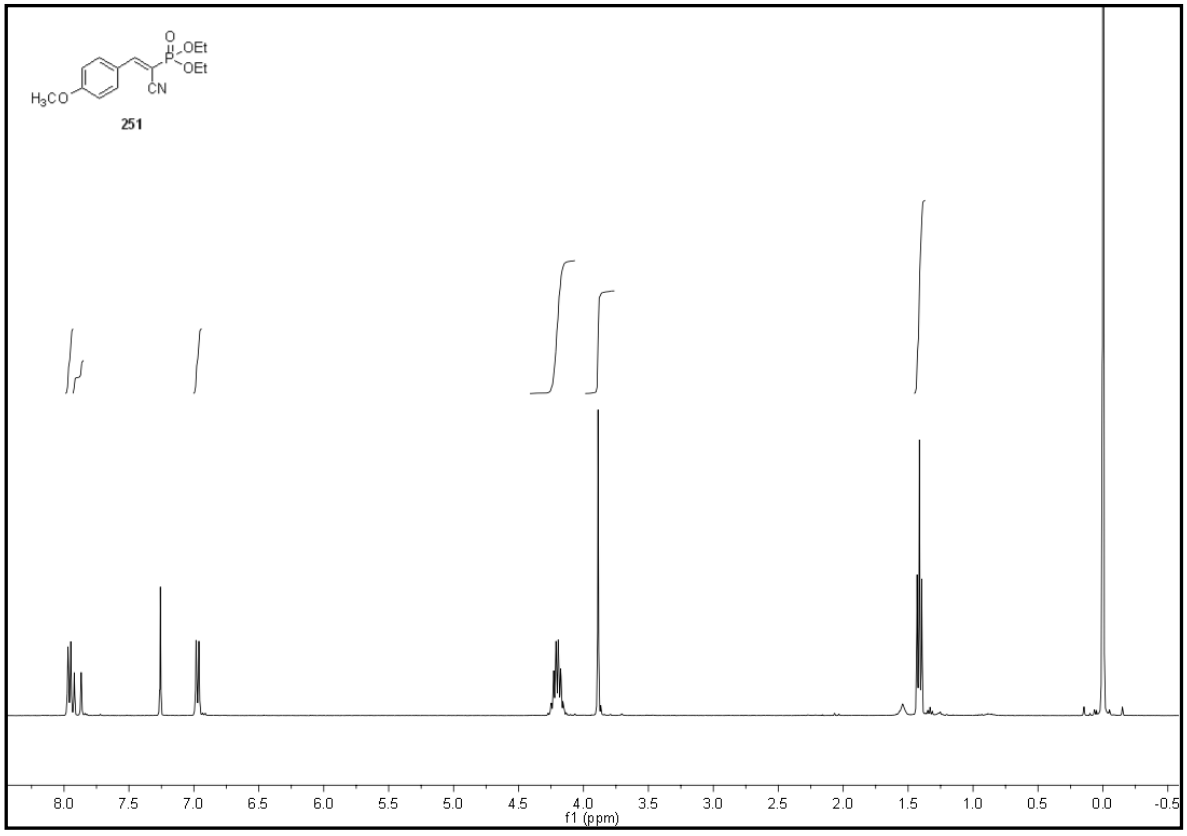


Figure A.100. ^{1}H NMR spectrum of compound **251**

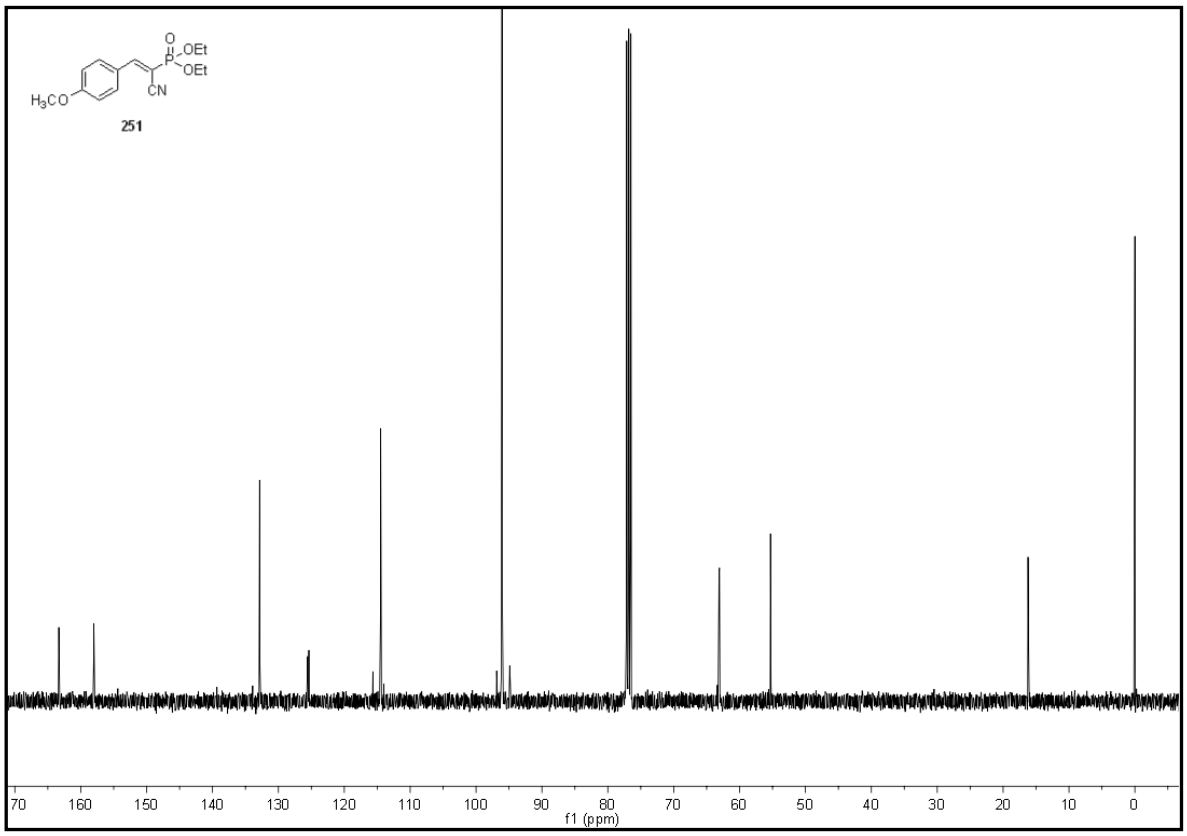


Figure A.101. ^{13}C NMR spectrum of compound **251**

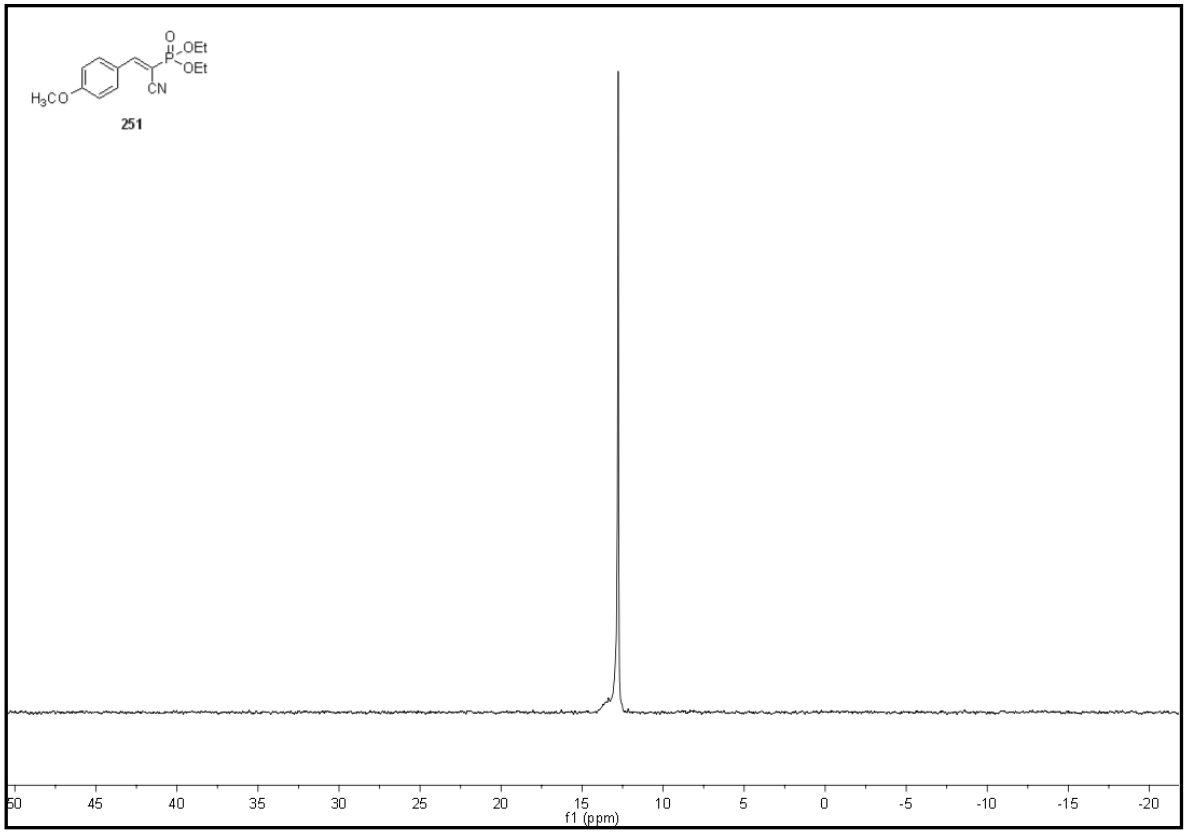


Figure A.102. ^{31}P NMR spectrum of compound **251**

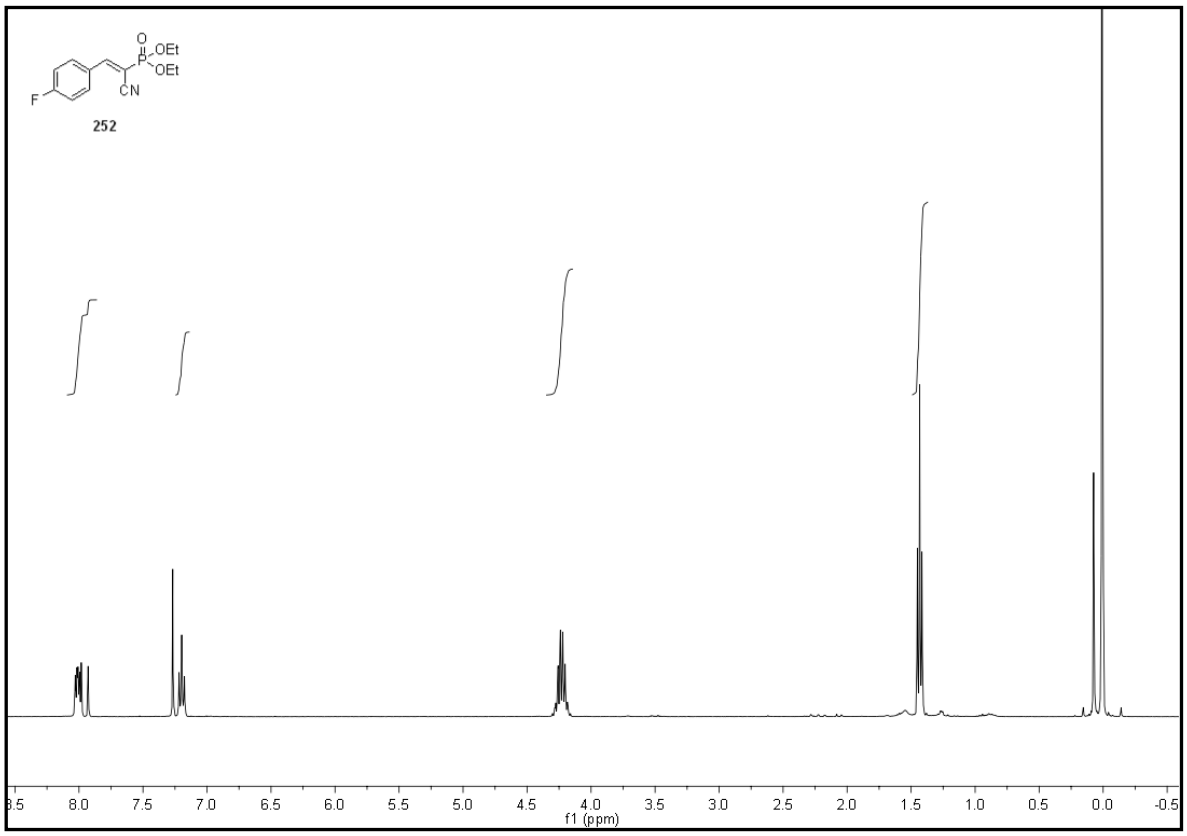


Figure A.103. ^{1}H NMR spectrum of compound **252**

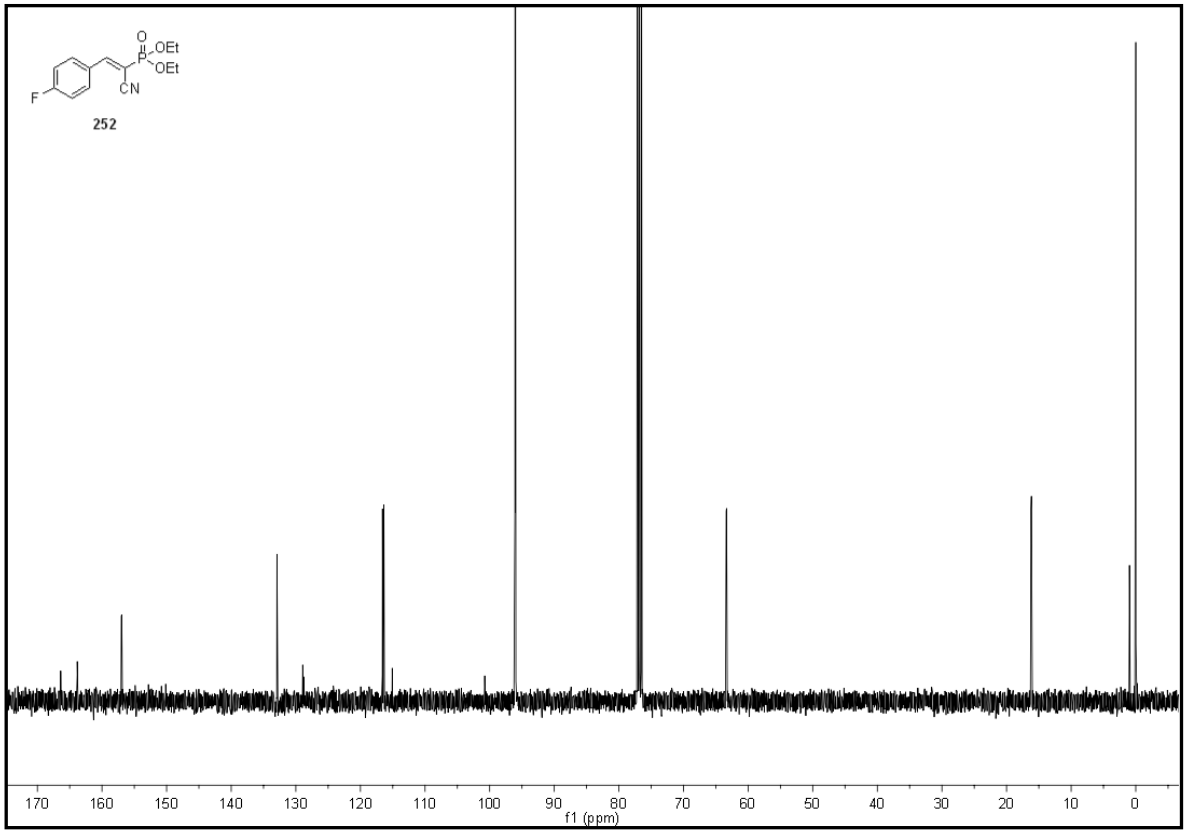


Figure A.104. ^{13}C NMR spectrum of compound **252**

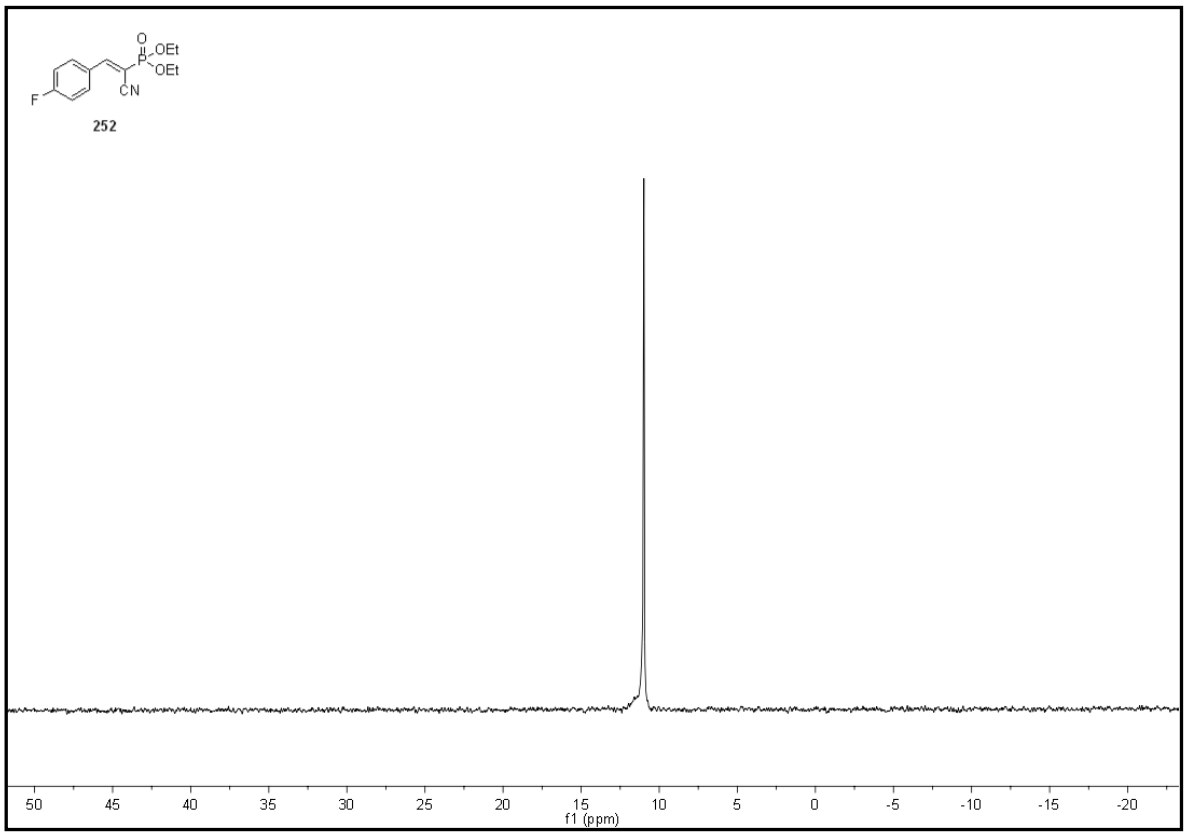


Figure A.105. ^{31}P NMR spectrum of compound **252**

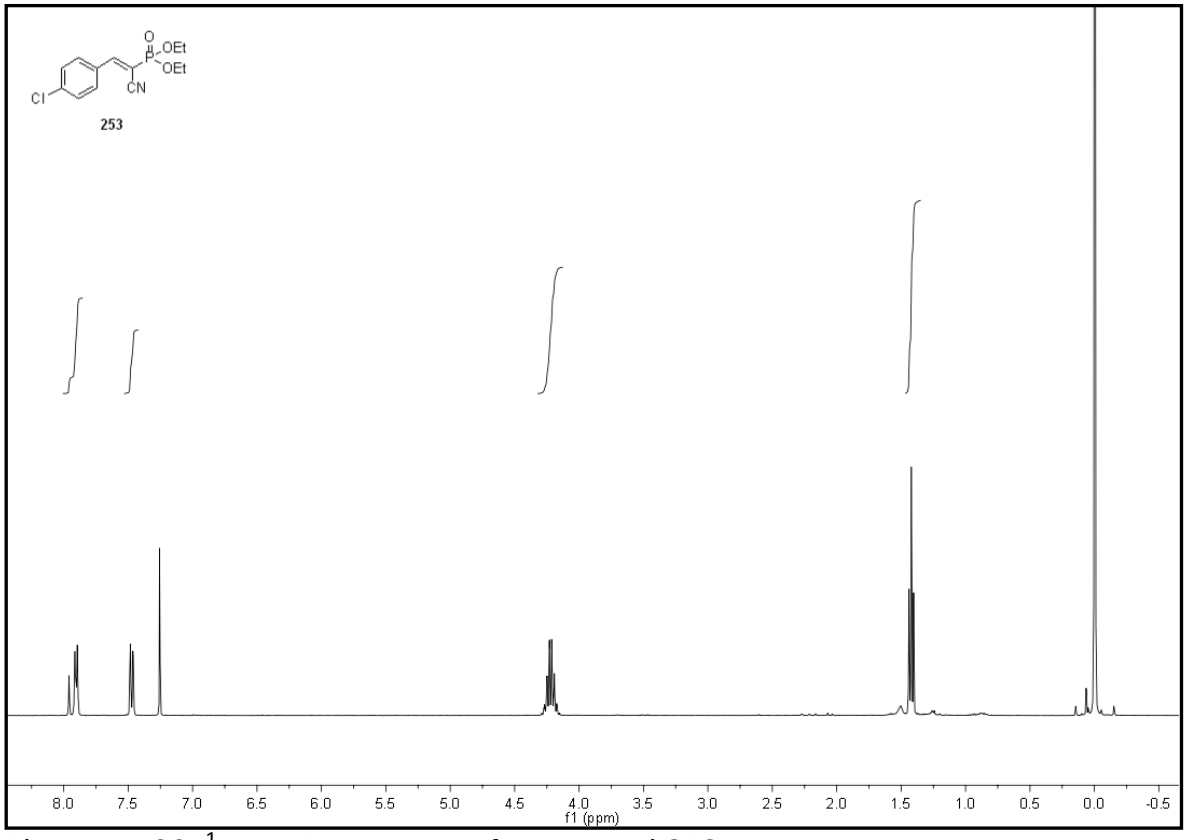


Figure A.106. ^{1}H NMR spectrum of compound **253**

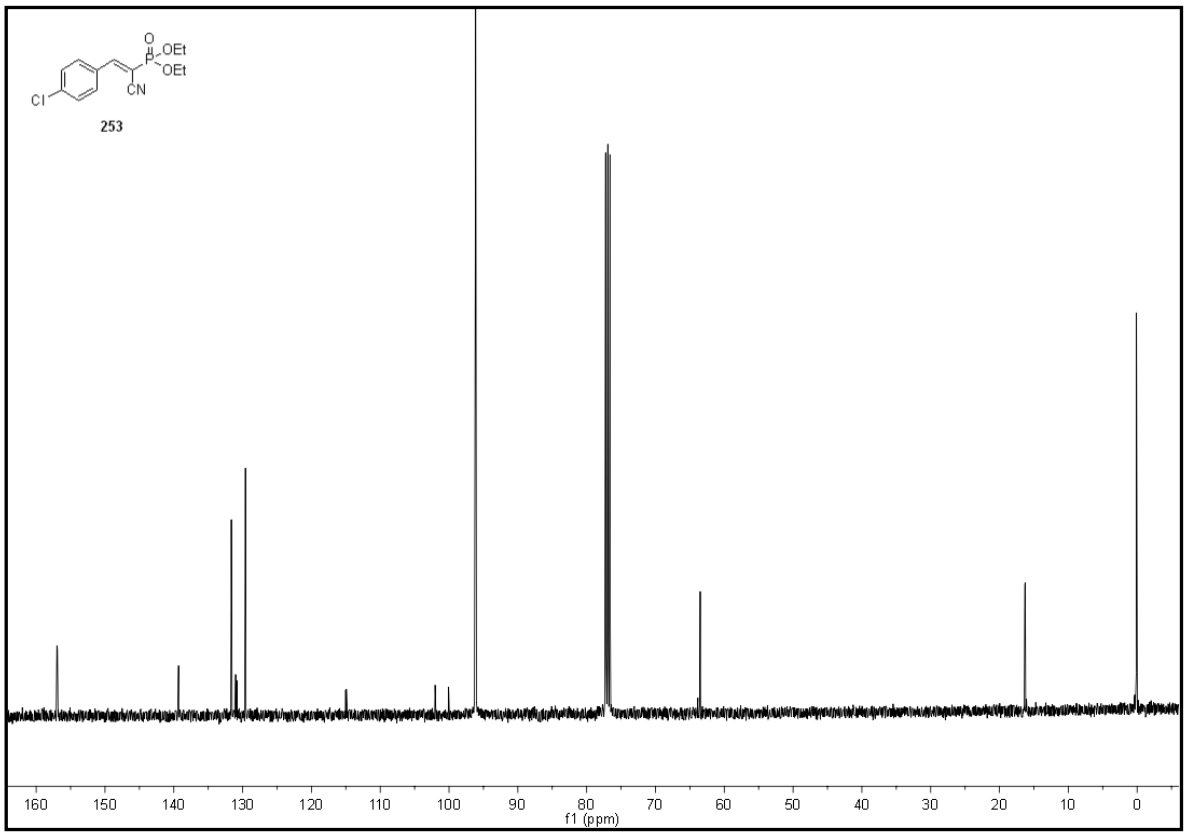


Figure A.107. ^{13}C NMR spectrum of compound **253**

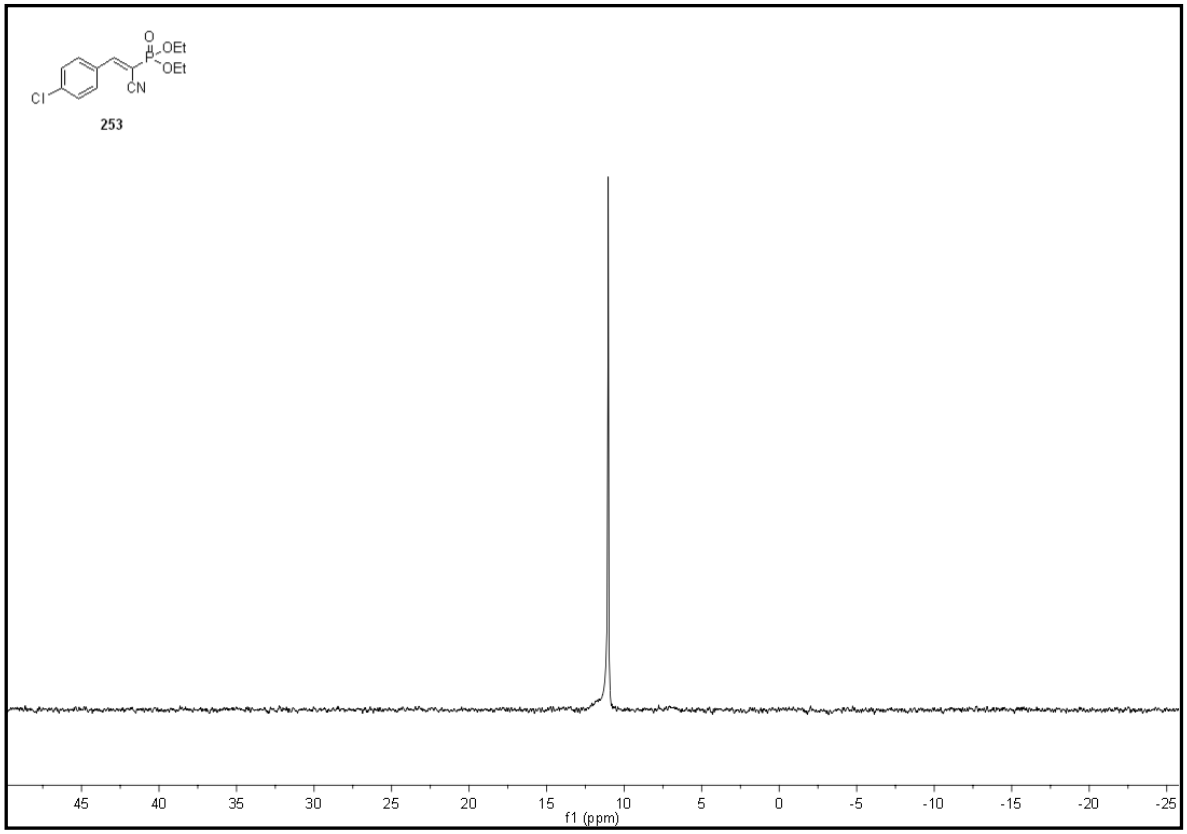


Figure A.108. ^{31}P NMR spectrum of compound **253**

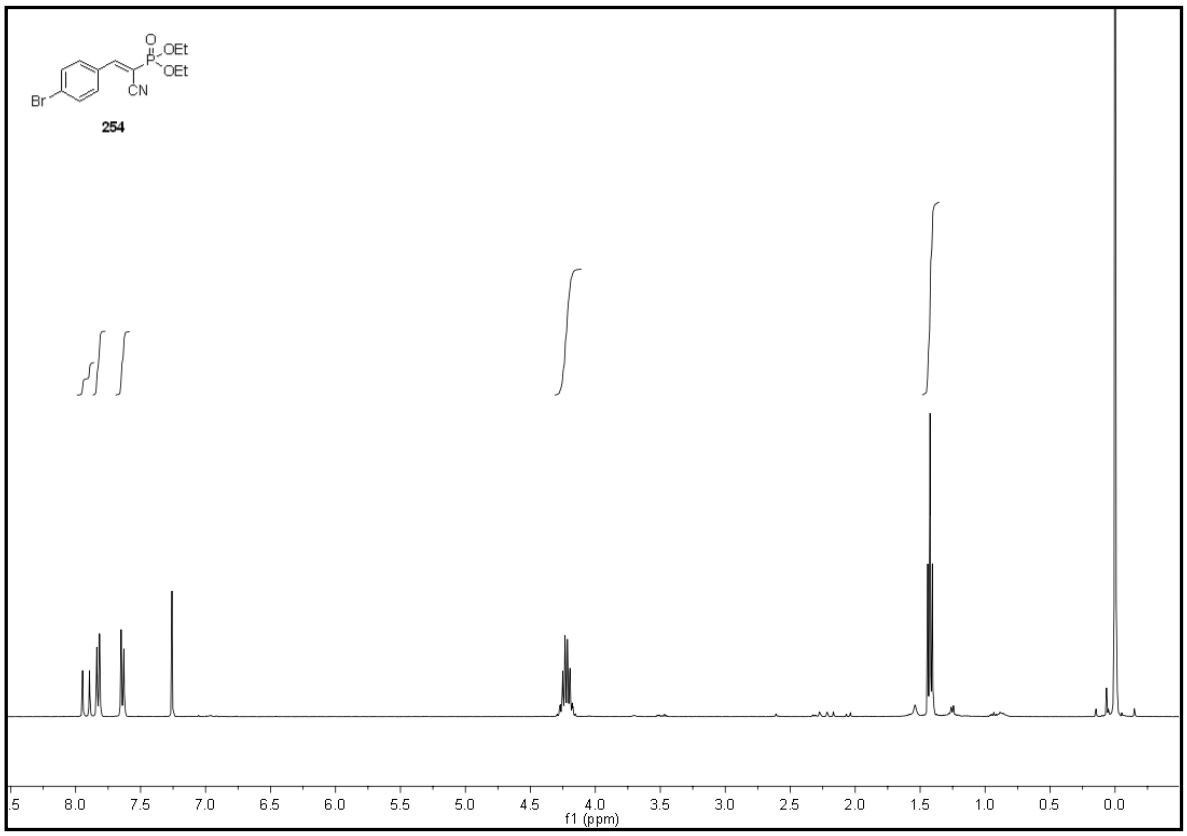


Figure A.109. ^{1}H NMR spectrum of compound **254**

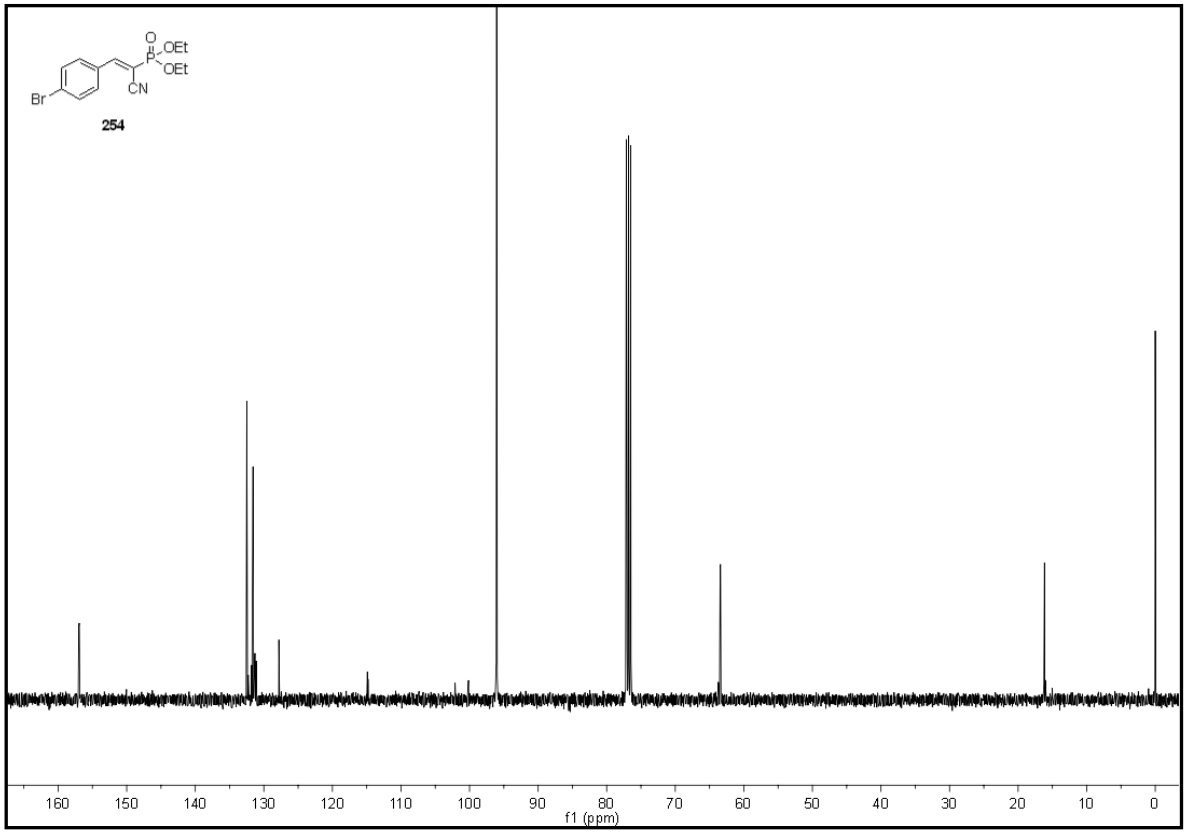


Figure A.110. ^{13}C NMR spectrum of compound **254**

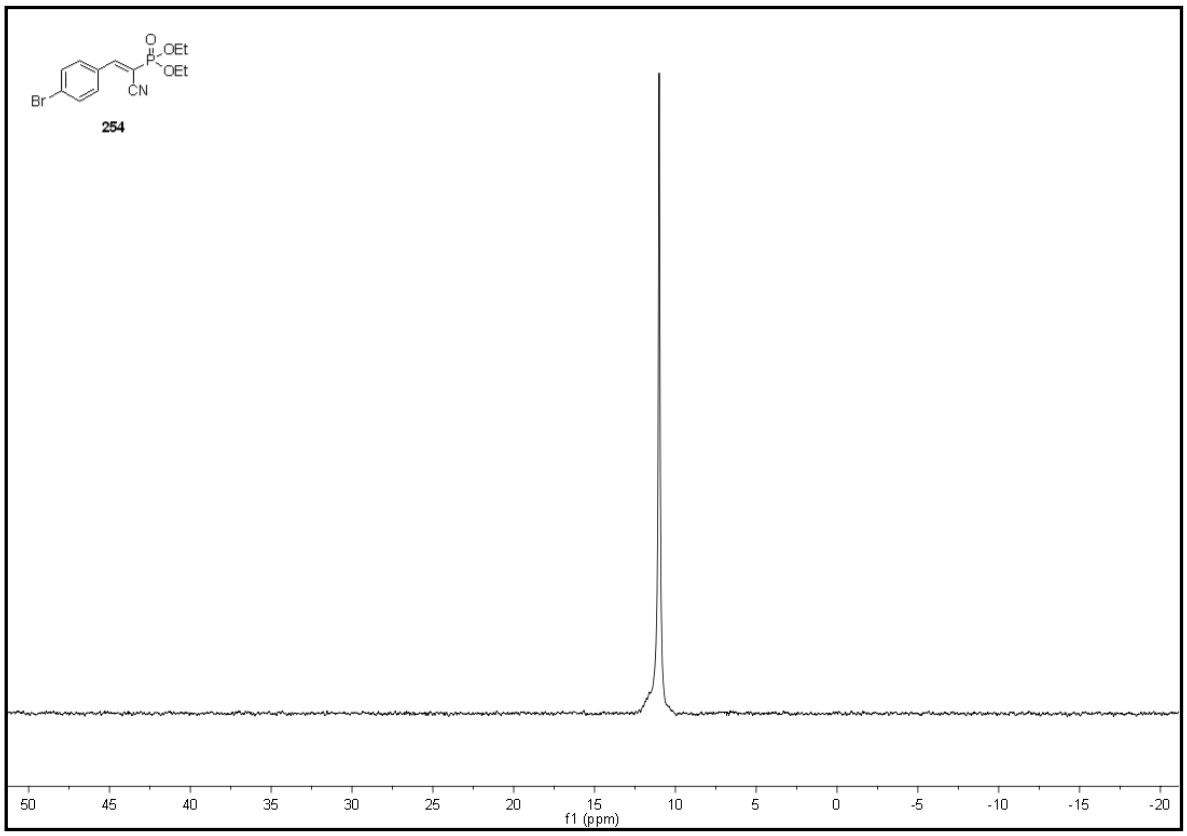


Figure A.111. ^{31}P NMR spectrum of compound **254**

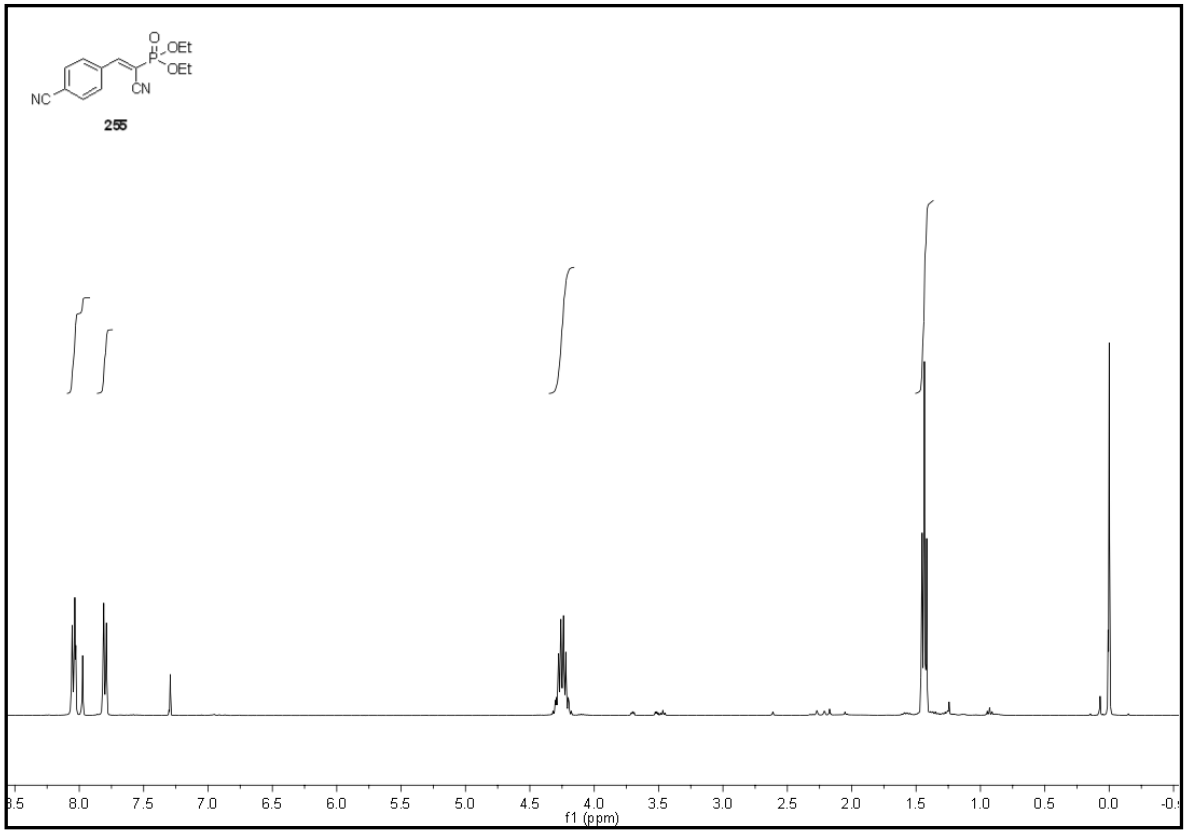


Figure A.112. ^{1}H NMR spectrum of compound **255**

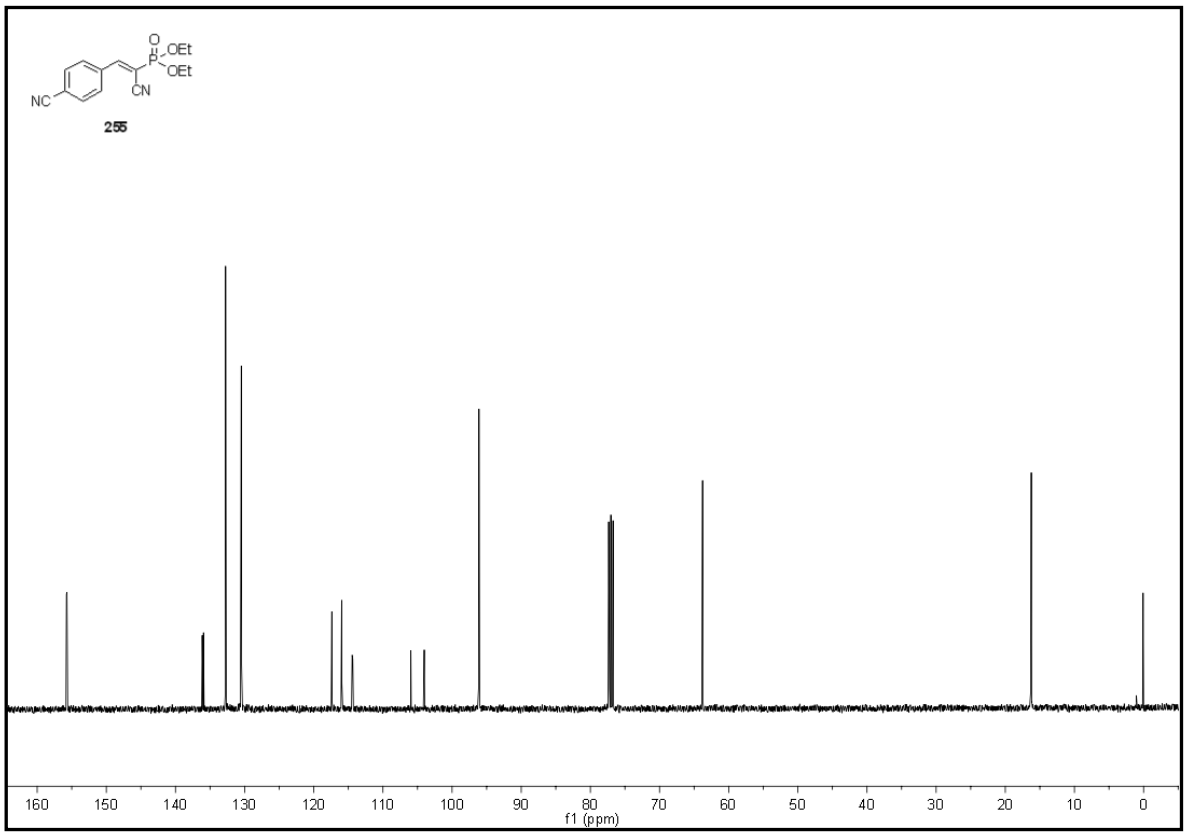


Figure A.113. ^{13}C NMR spectrum of compound **255**

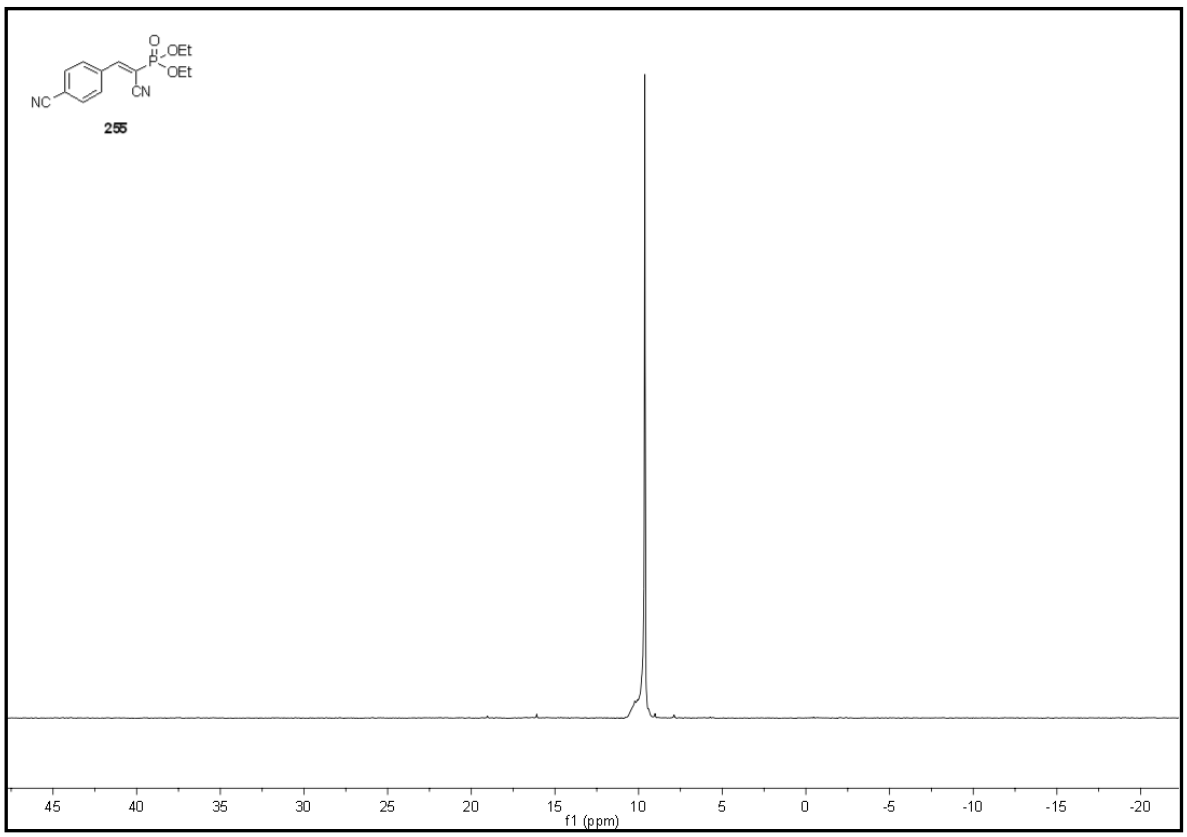


Figure A.114. ^{31}P NMR spectrum of compound **255**

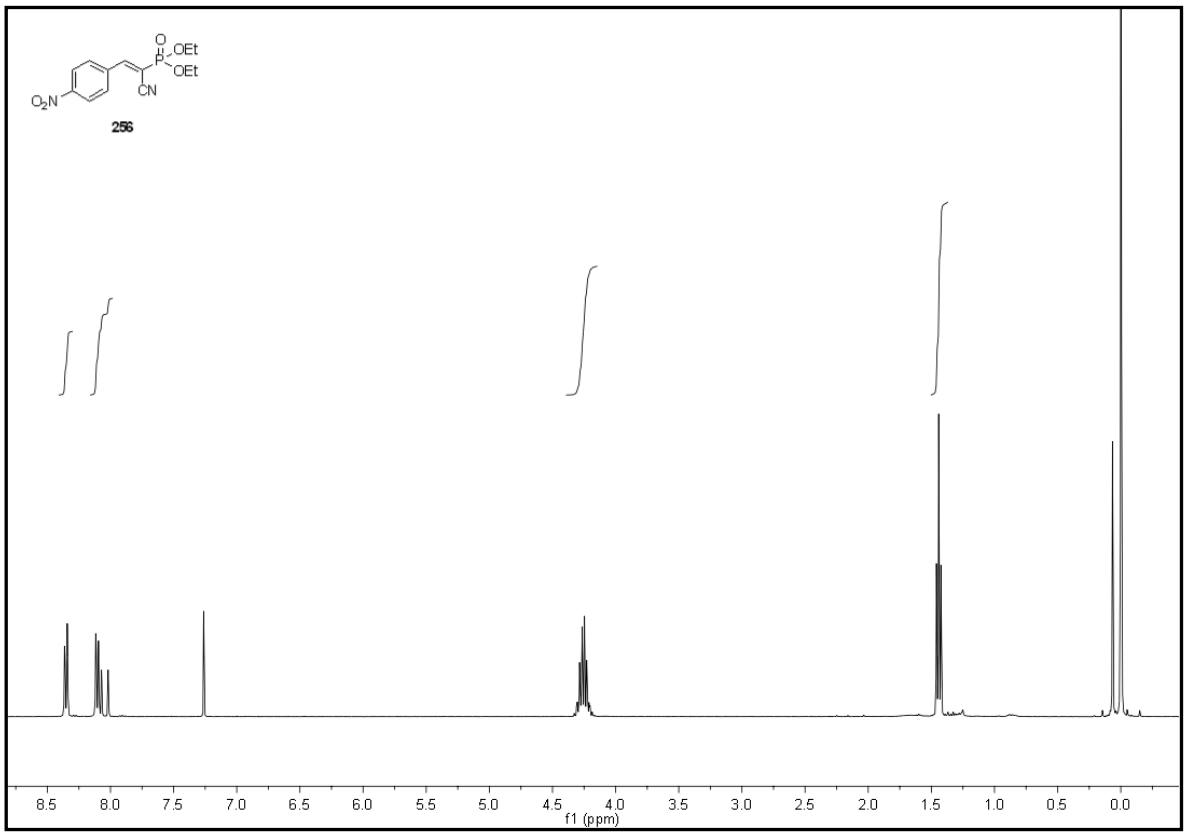


Figure A.115. ^{1}H NMR spectrum of compound **256**

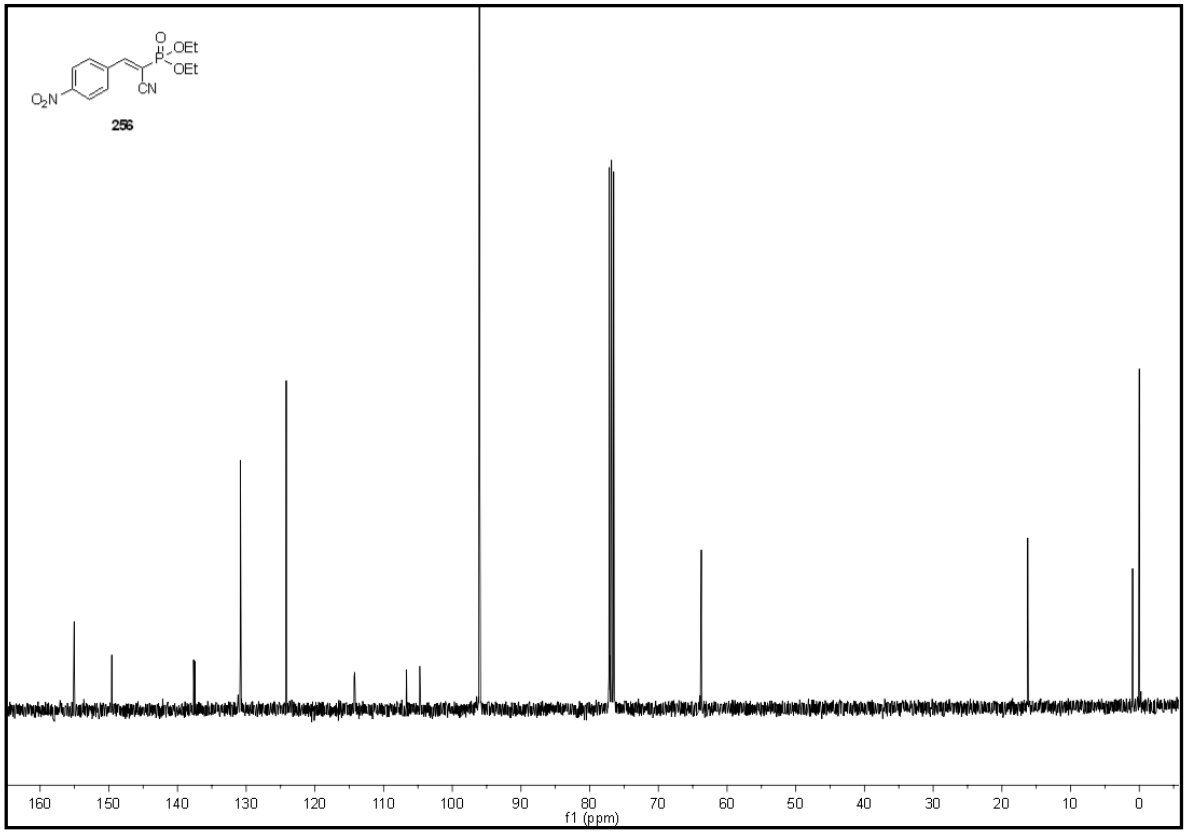


Figure A.116. ^{13}C NMR spectrum of compound **256**

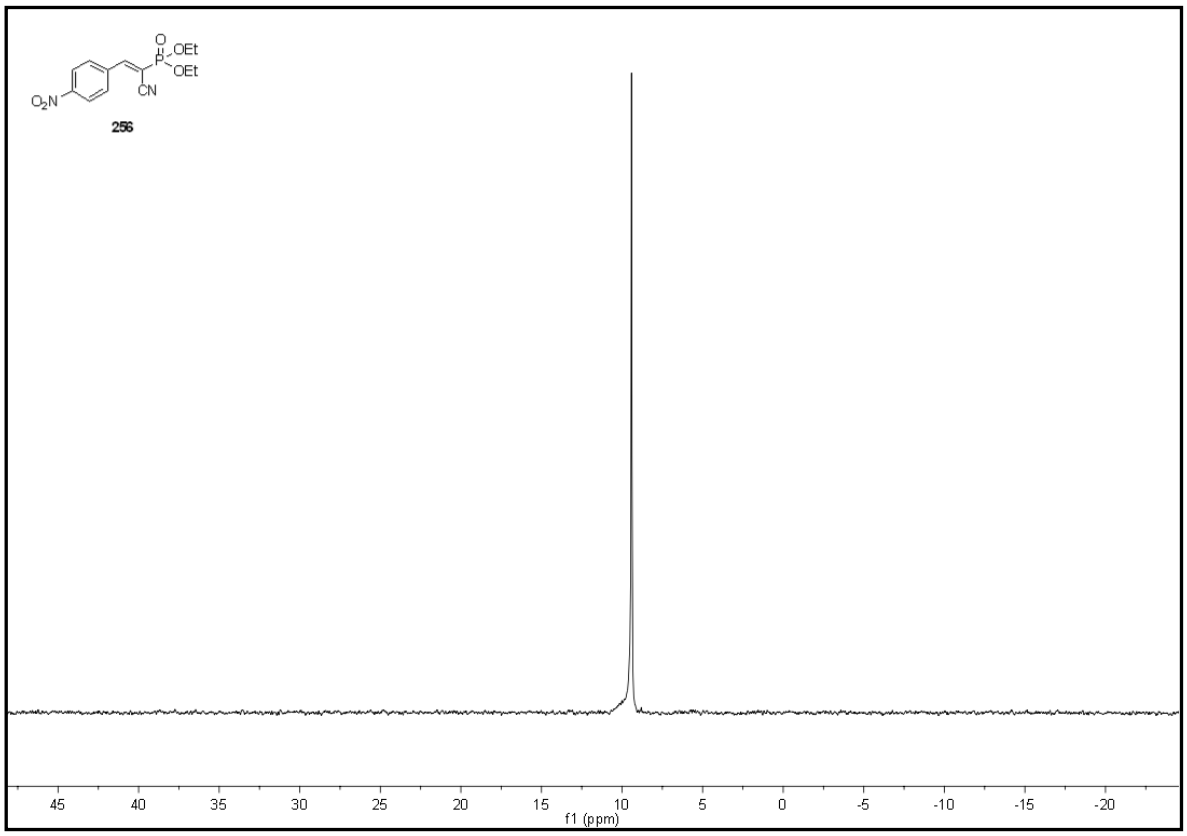


Figure A.117. ^{31}P NMR spectrum of compound **256**

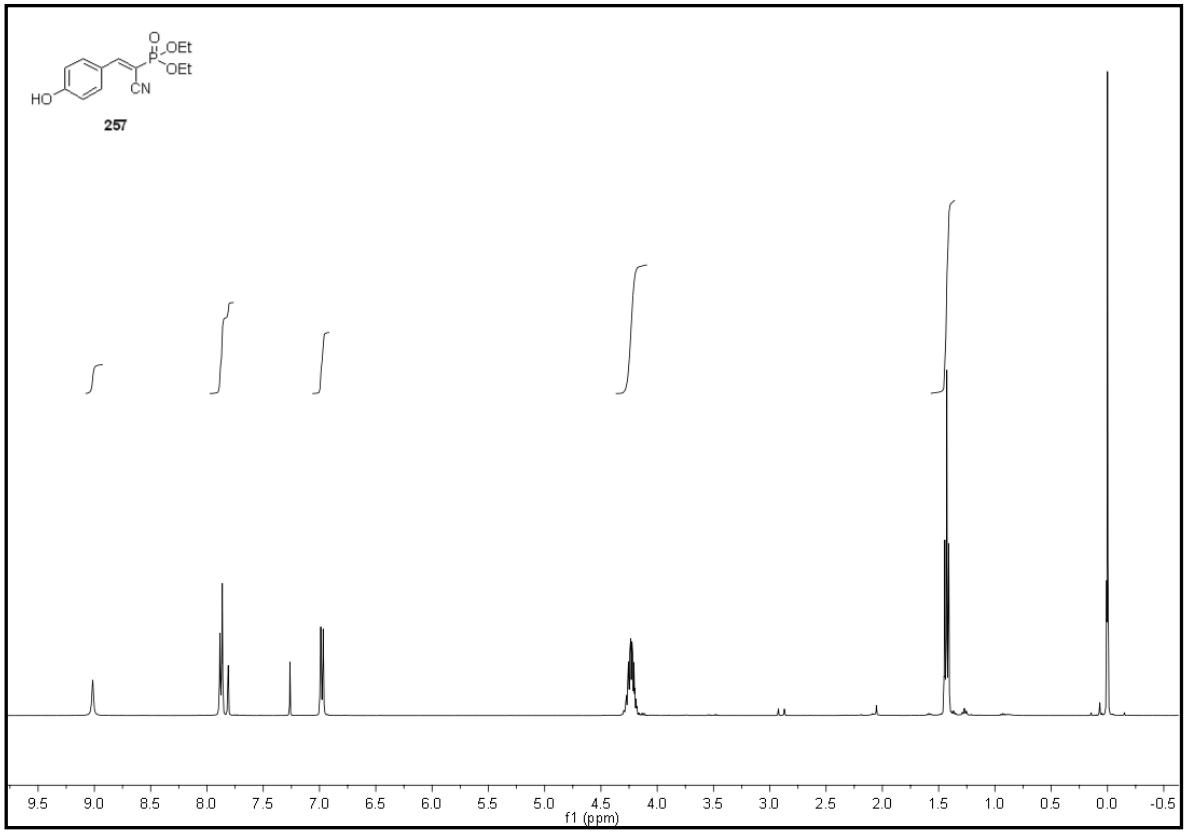


Figure A.118. ^{1}H NMR spectrum of compound **257**

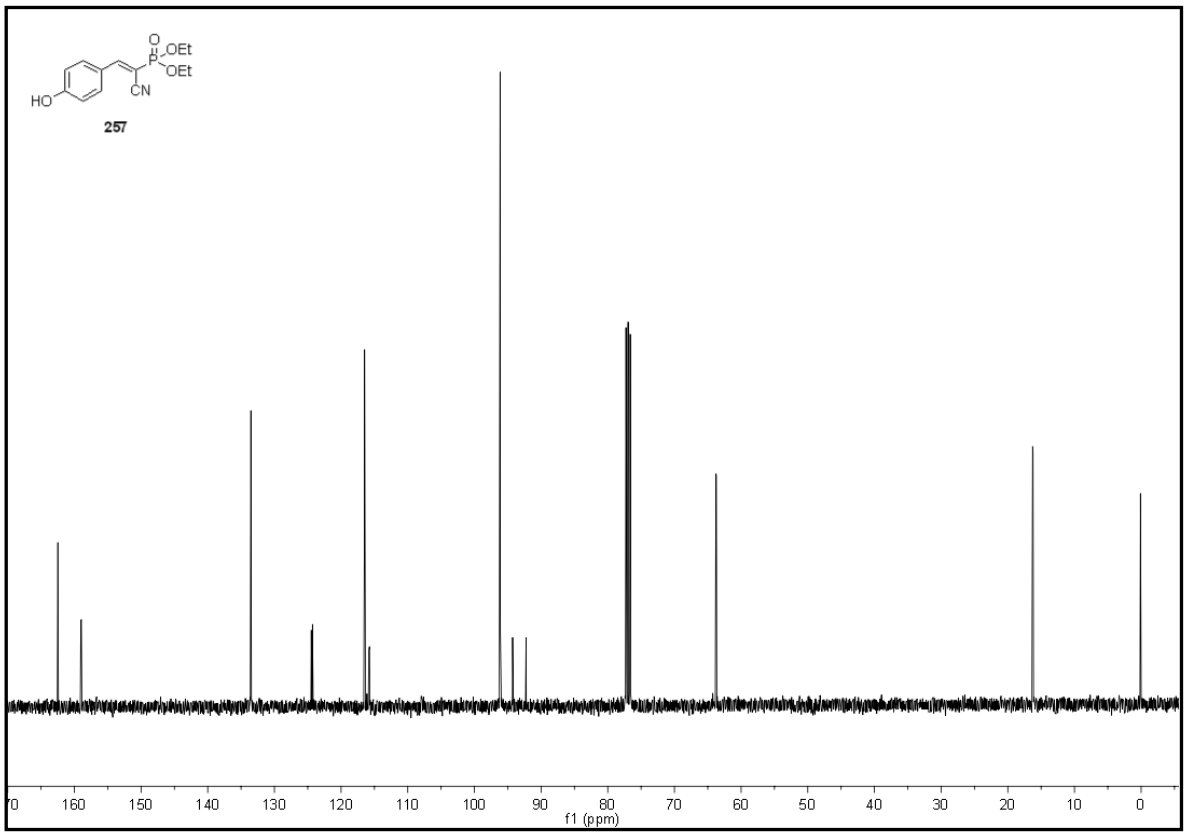


Figure A.119. ^{13}C NMR spectrum of compound **257**

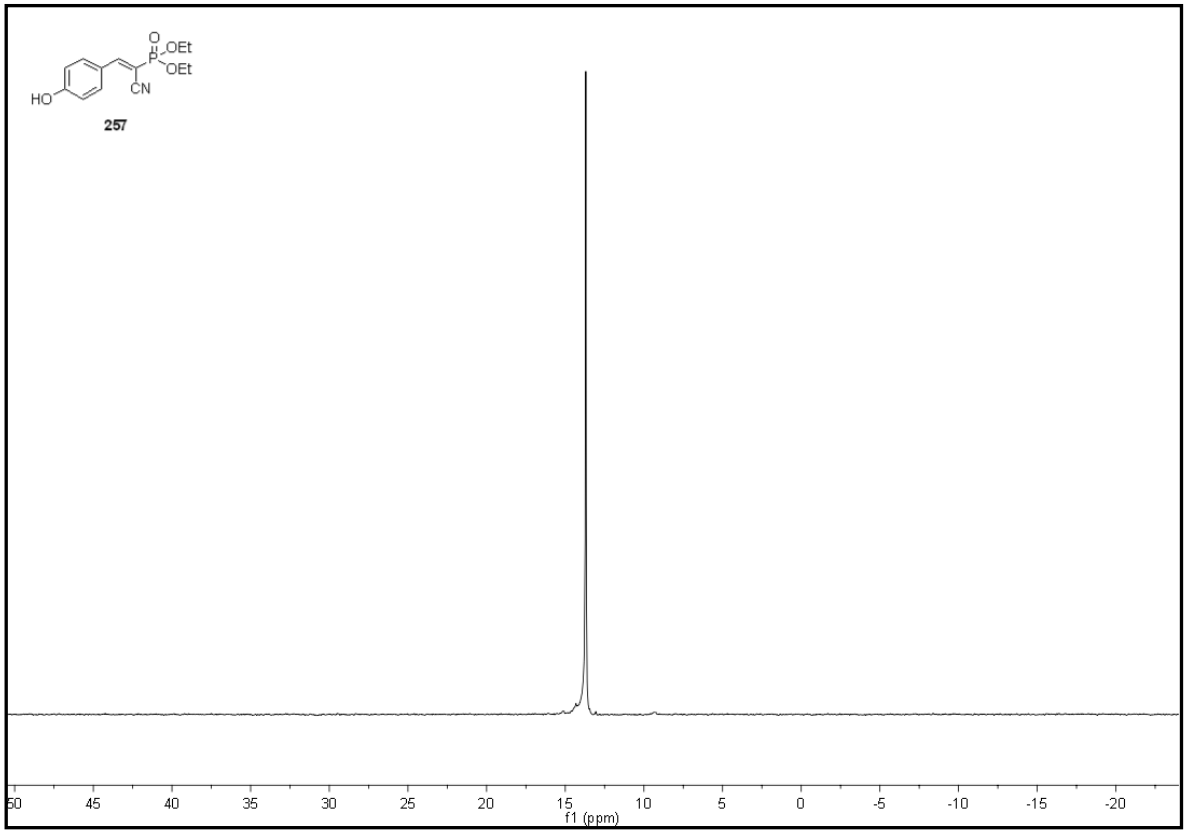


Figure A.120. ^{31}P NMR spectrum of compound **257**

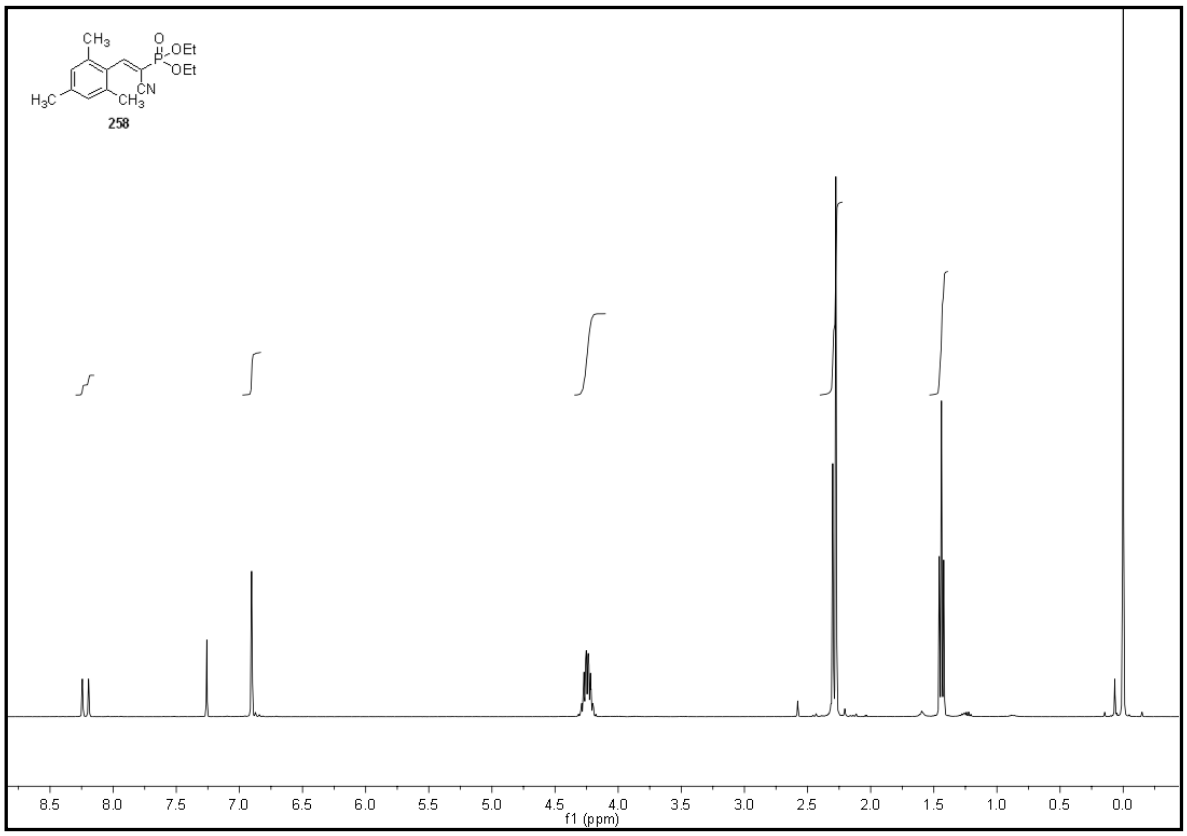


Figure A.121. ^{1}H NMR spectrum of compound **258**

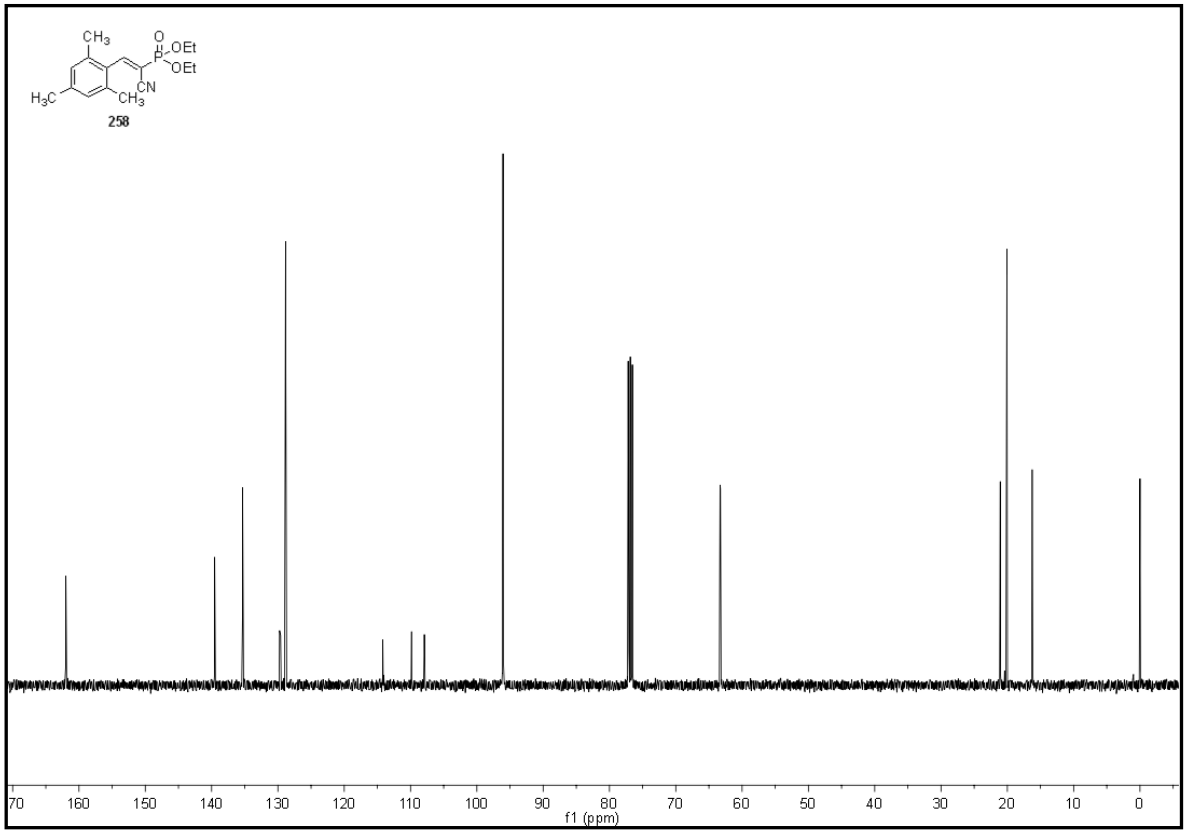


Figure A.122. ^{13}C NMR spectrum of compound **258**

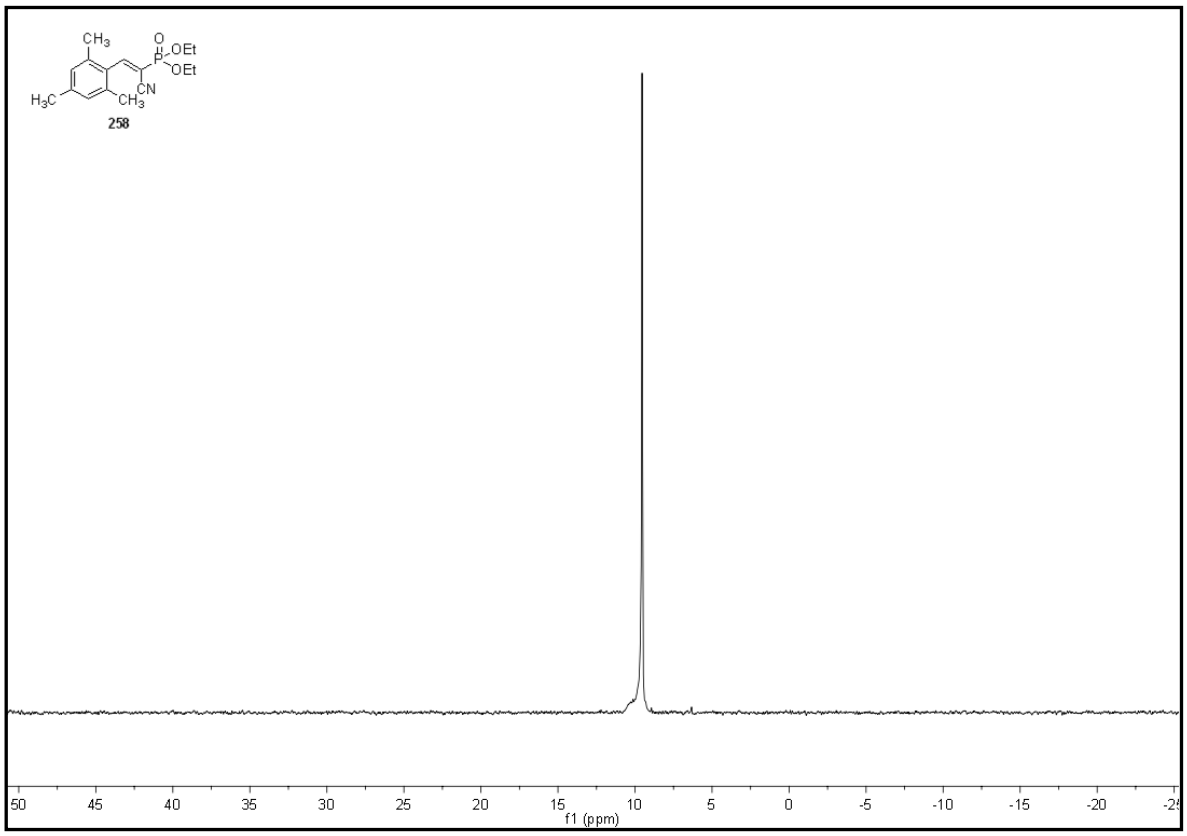


Figure A.123. ^{31}P NMR spectrum of compound **258**

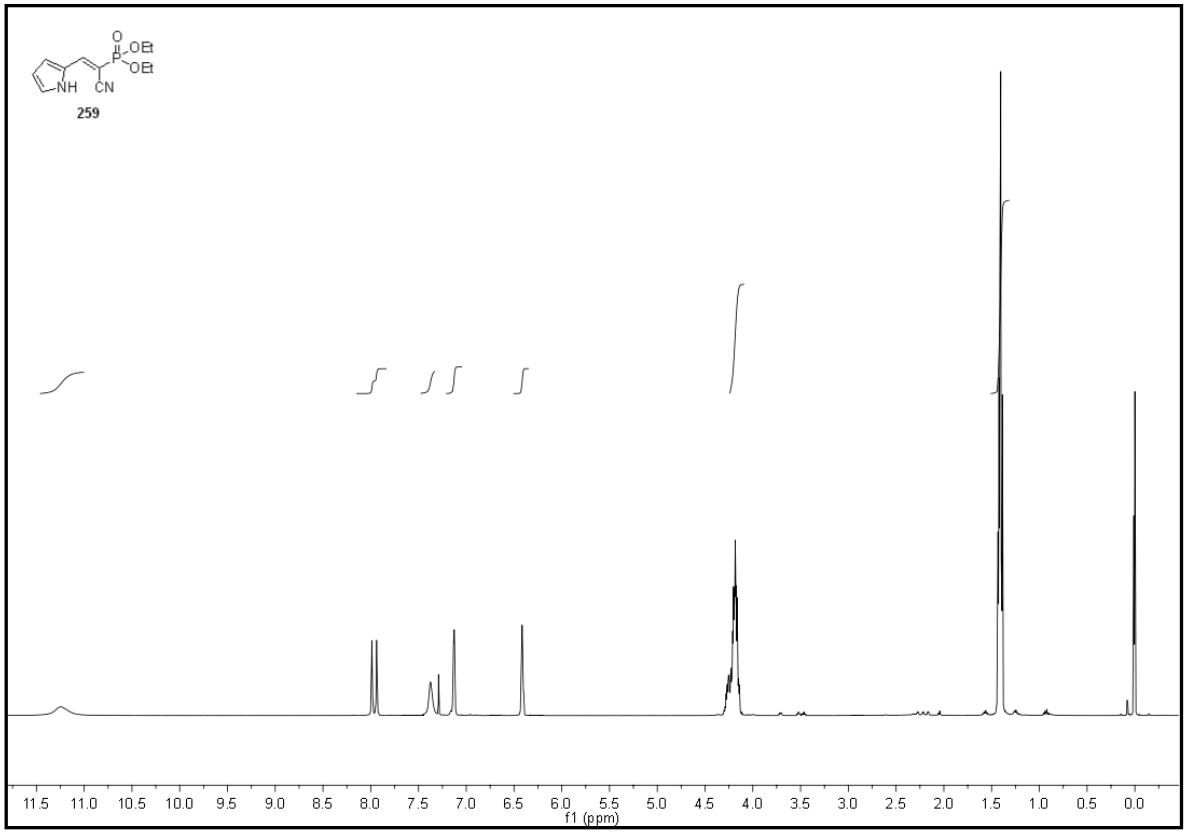


Figure A.124. ^{1}H NMR spectrum of compound **259**

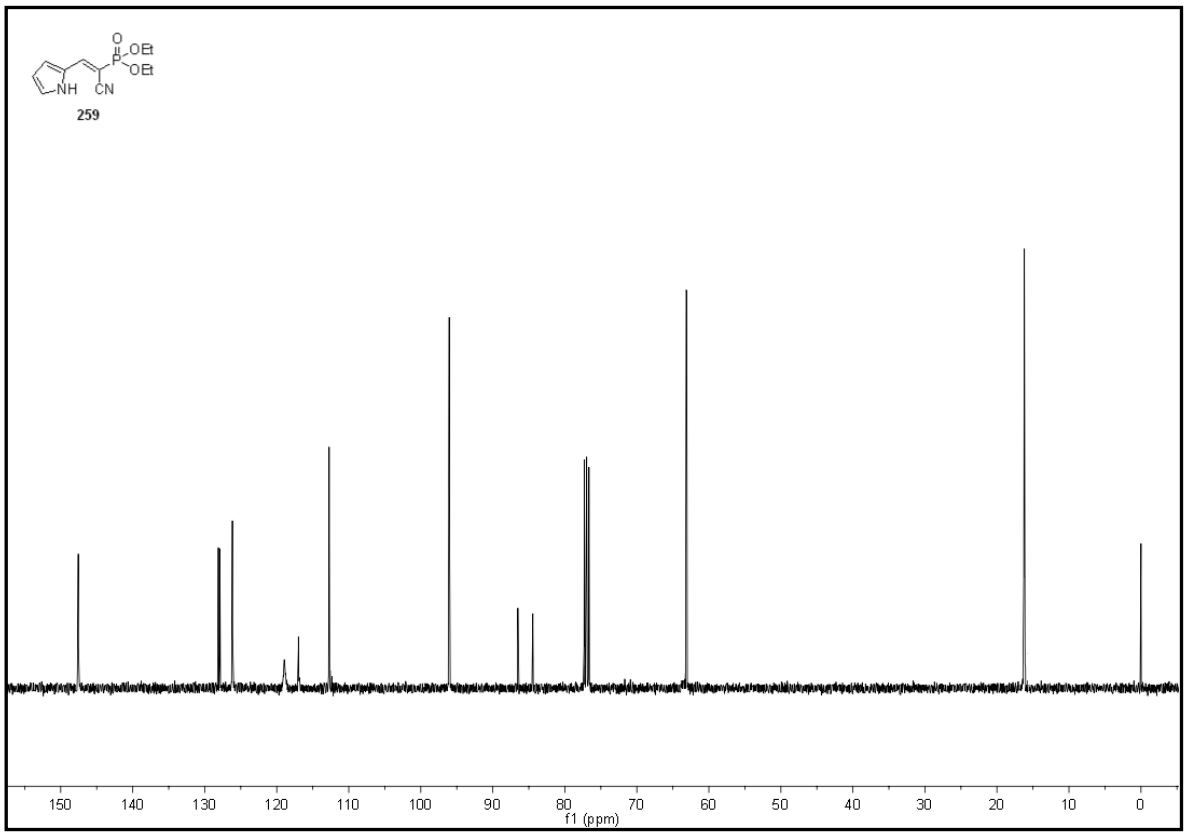


Figure A.125. ^{13}C NMR spectrum of compound **259**

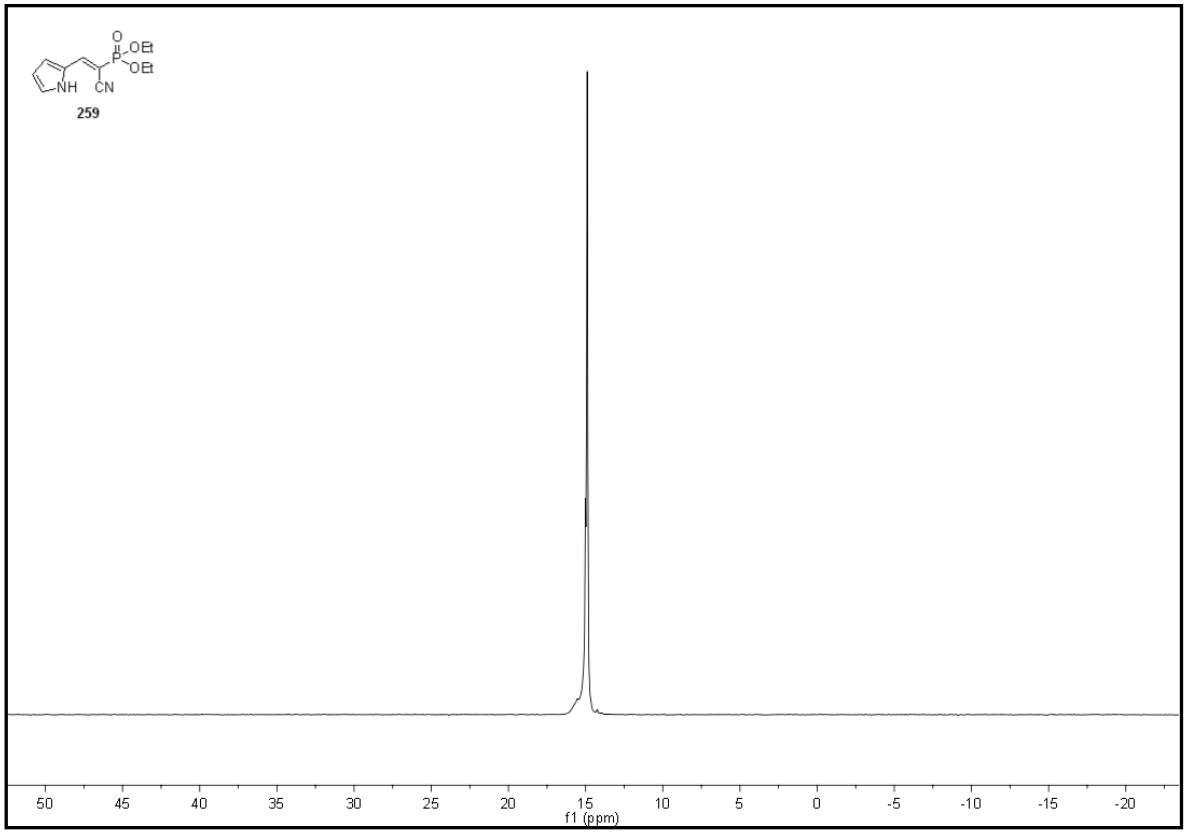


Figure A.126. ^{31}P NMR spectrum of compound **259**

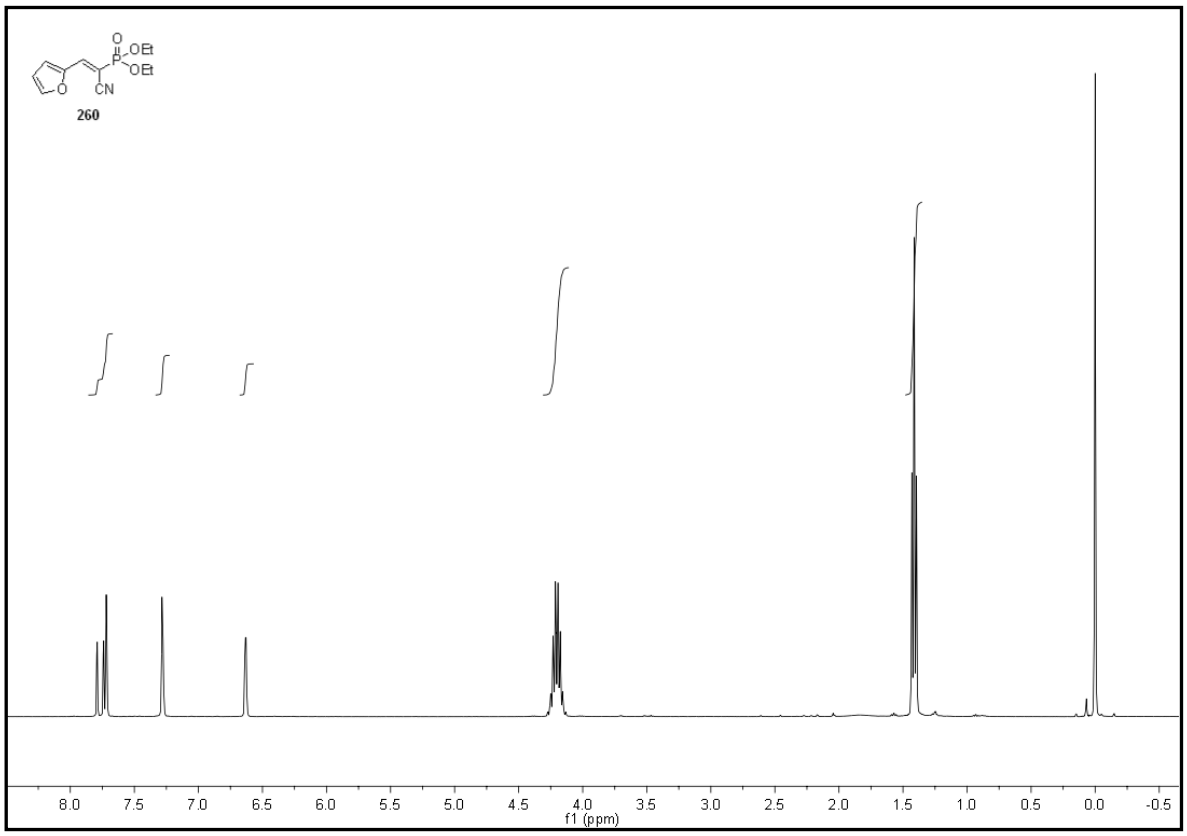


Figure A.127. ^{1}H NMR spectrum of compound **260**

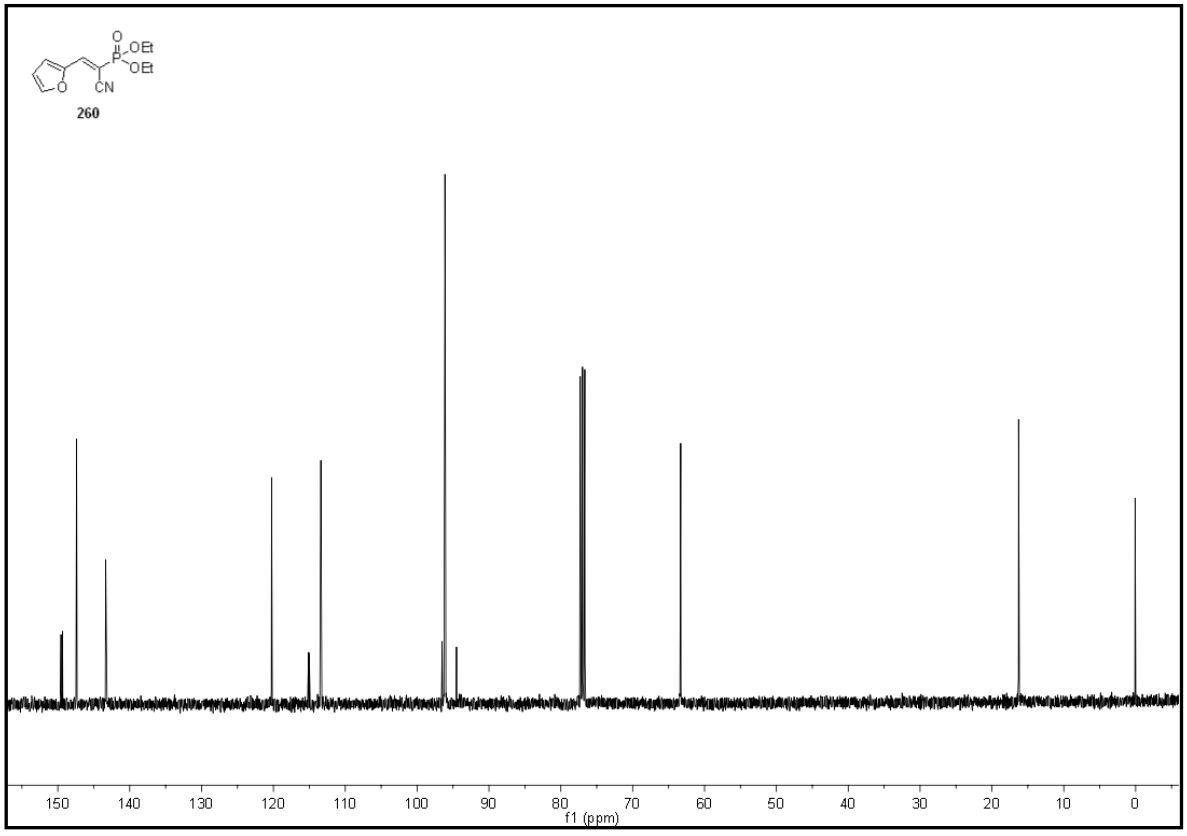


Figure A.128. ^{13}C NMR spectrum of compound **260**

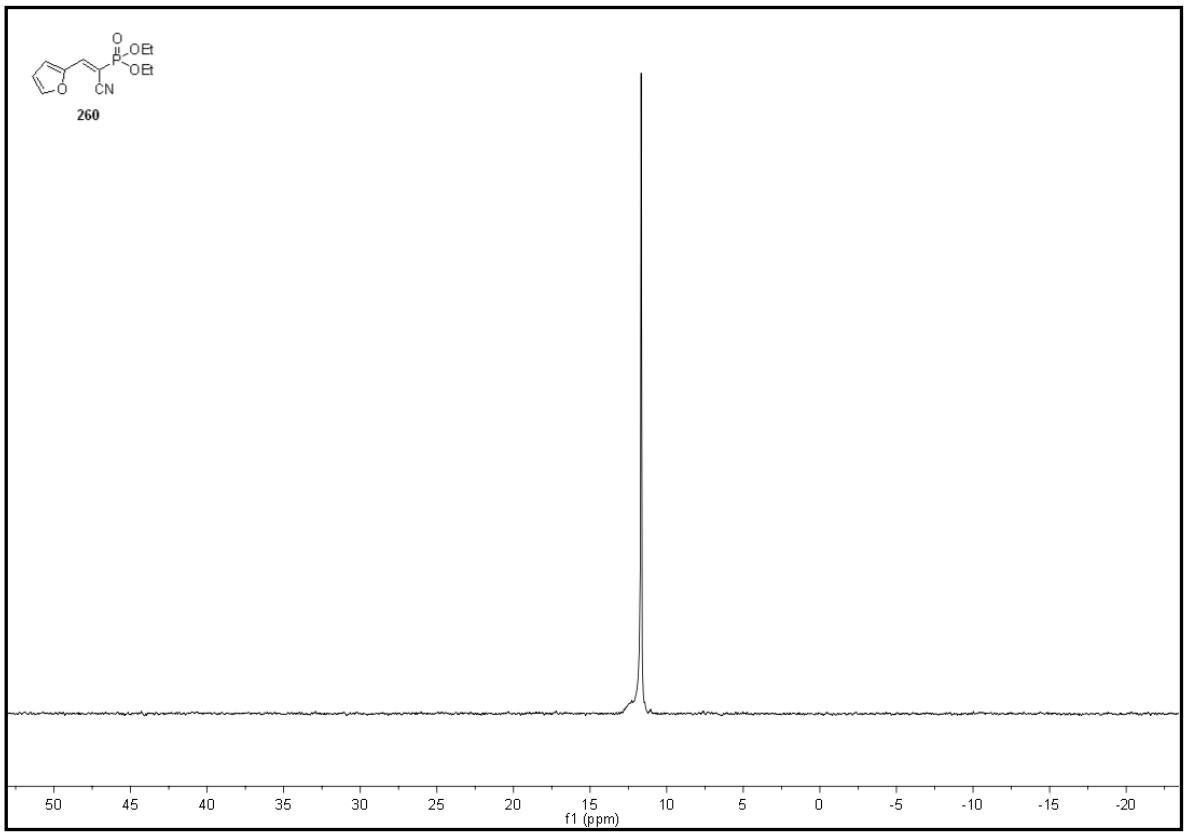


Figure A.129. ^{31}P NMR spectrum of compound **260**

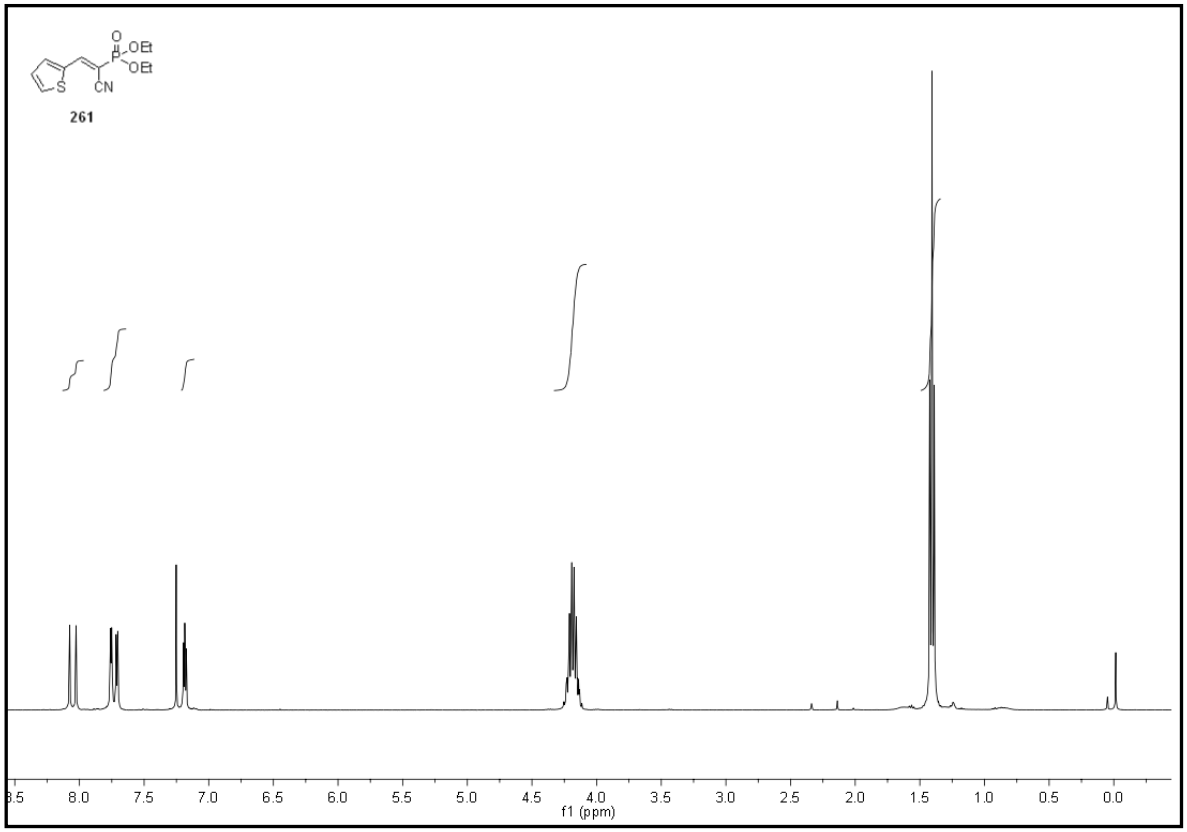


Figure A.130. ^{1}H NMR spectrum of compound **261**

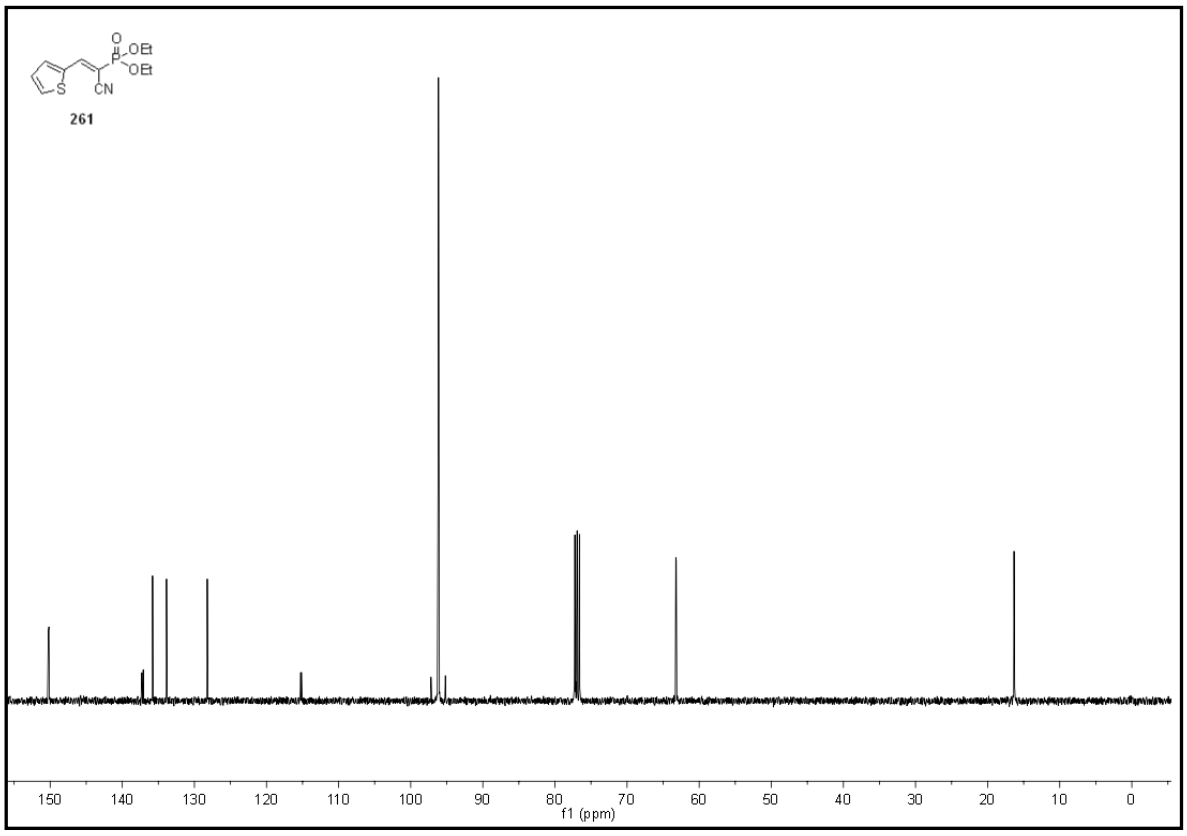


Figure A.131. ^{13}C NMR spectrum of compound **261**

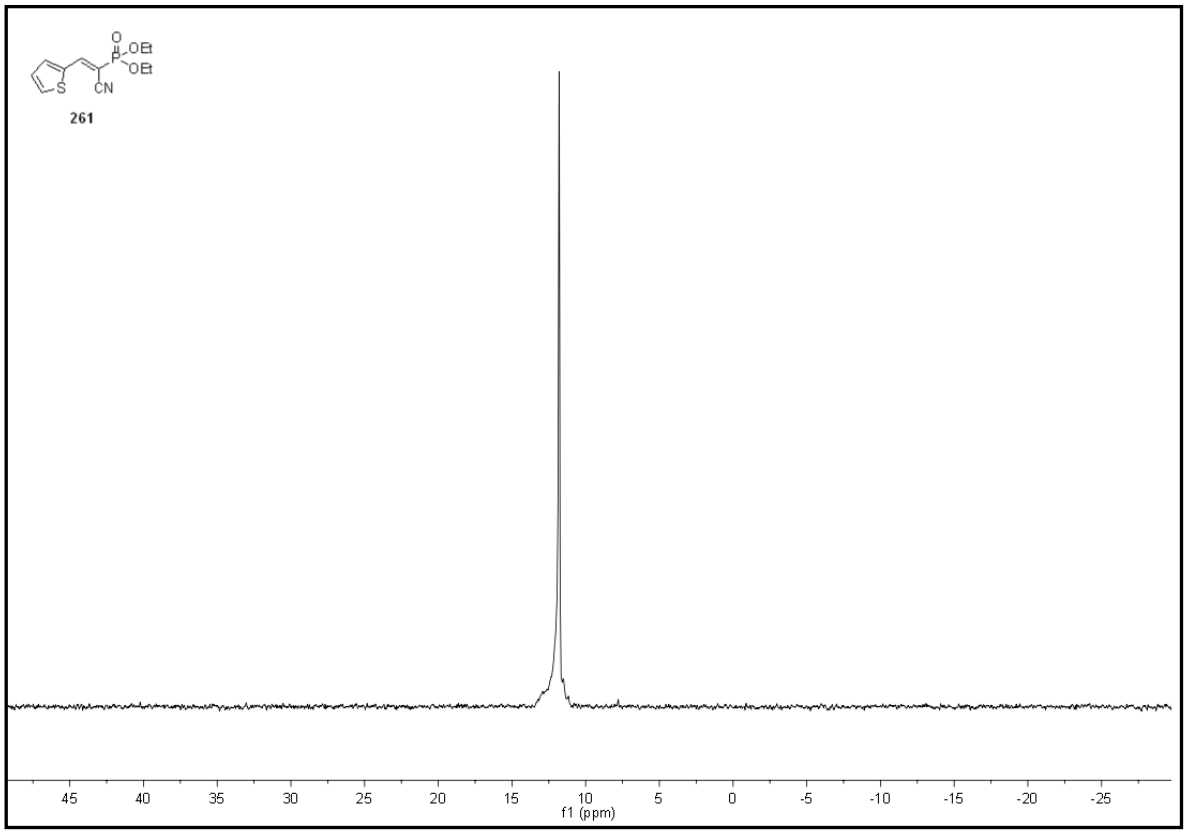


Figure A.132. ^{31}P NMR spectrum of compound **261**

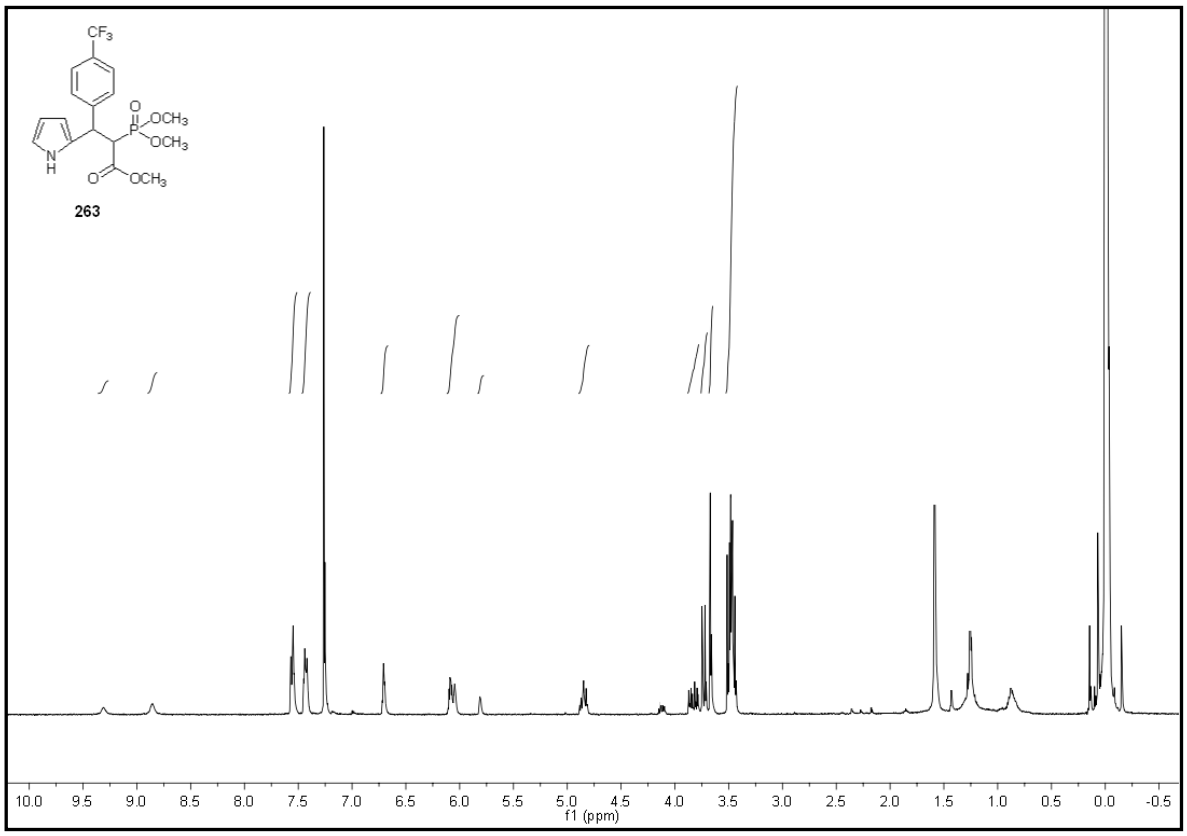


Figure A.133. ^{1}H NMR spectrum of compound **263**

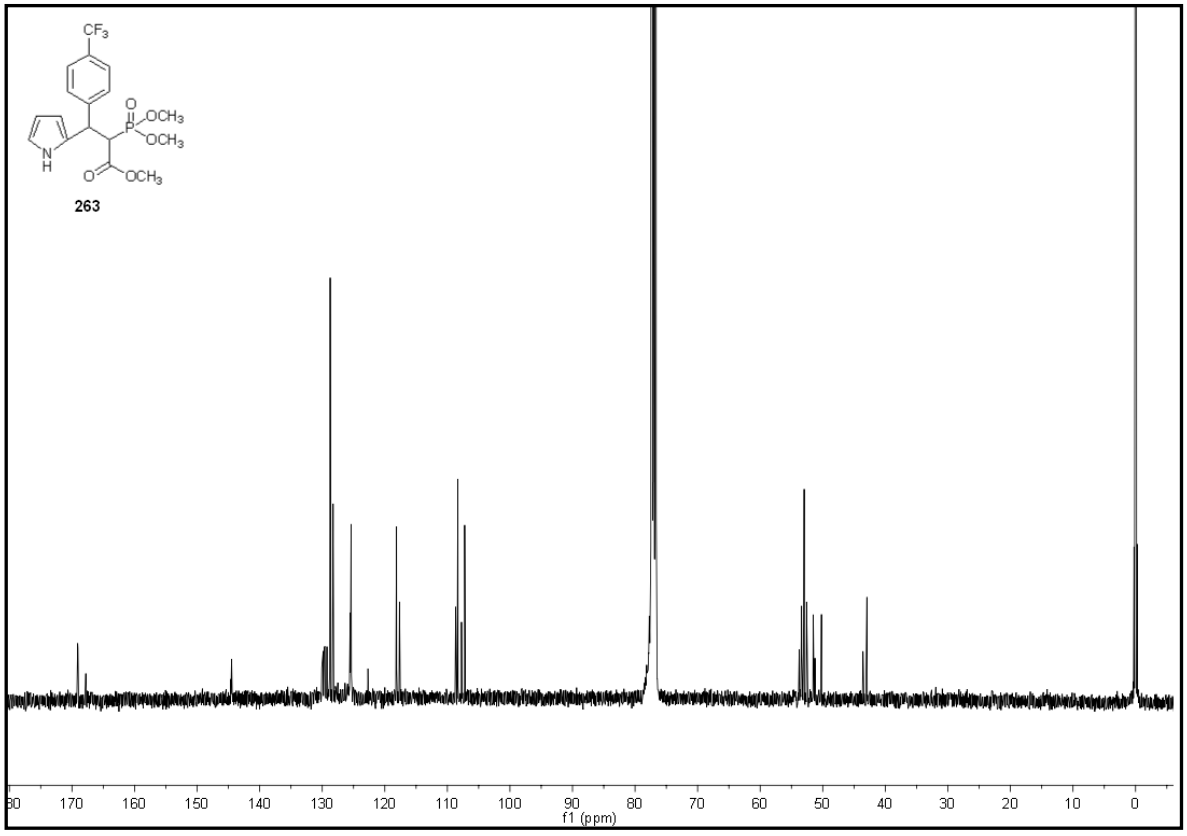


Figure A.134. ^{13}C NMR spectrum of compound **263**

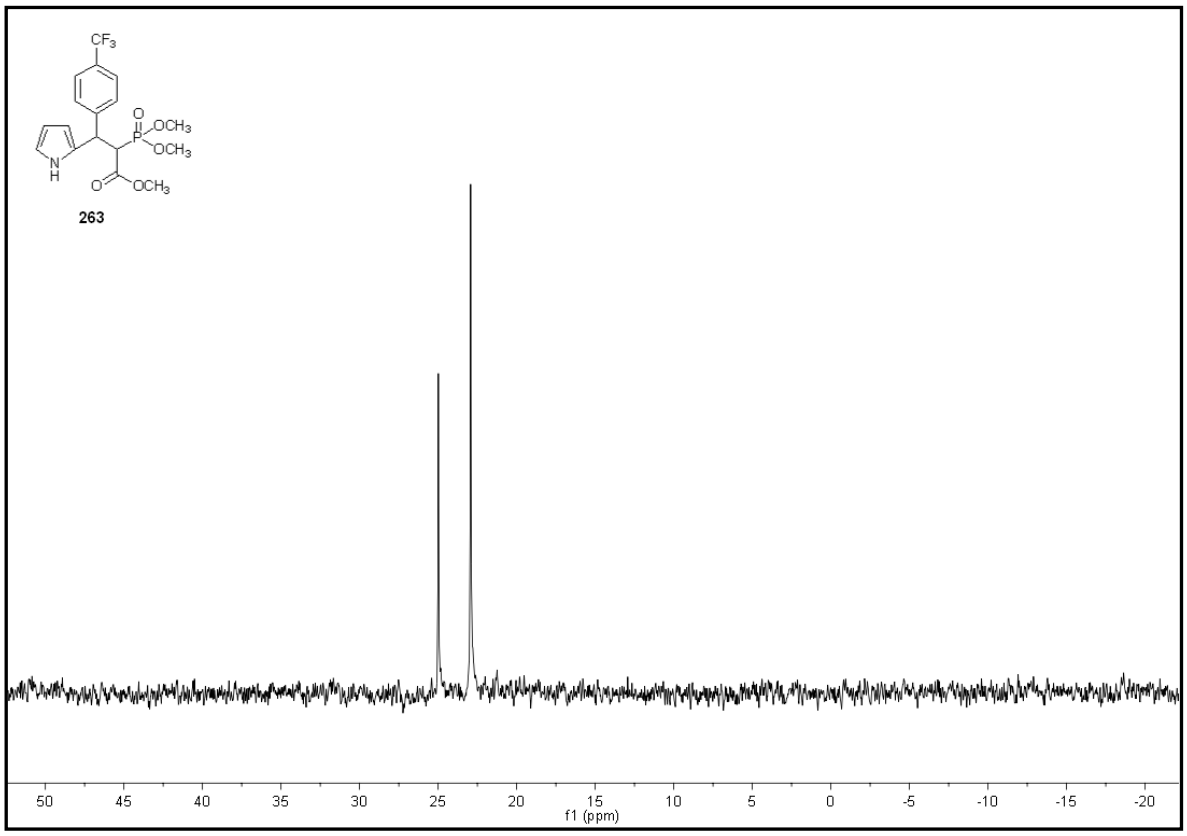


Figure A.135. ^{31}P NMR spectrum of compound **263**

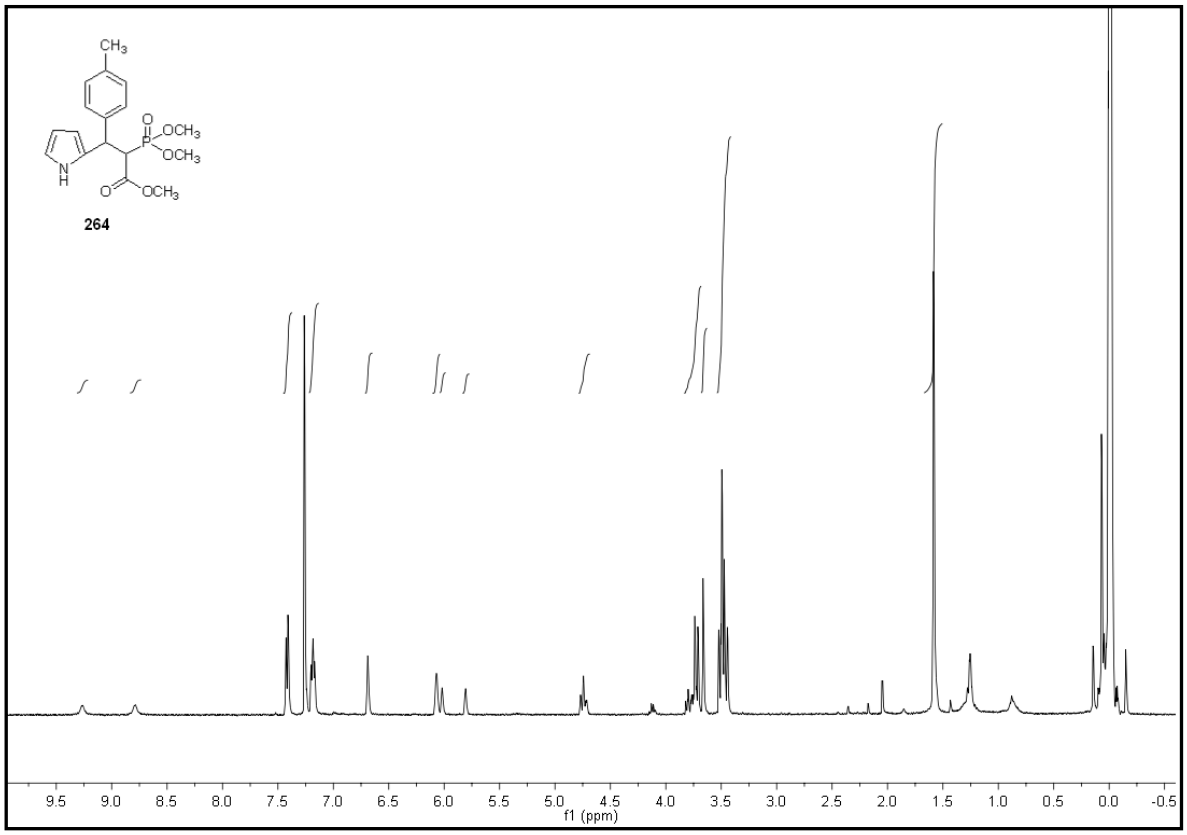


Figure A.136. ^{1}H NMR spectrum of compound **264**

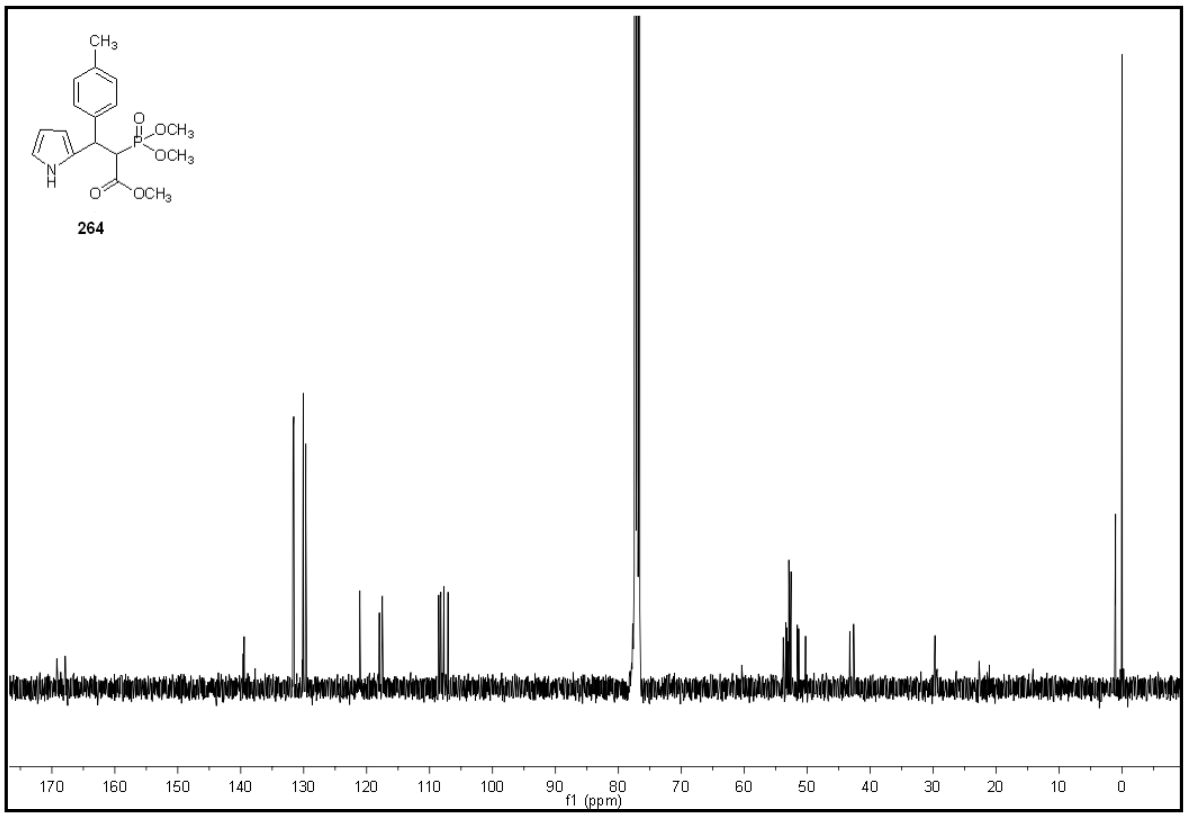


Figure A.137. ^{13}C NMR spectrum of compound **264**

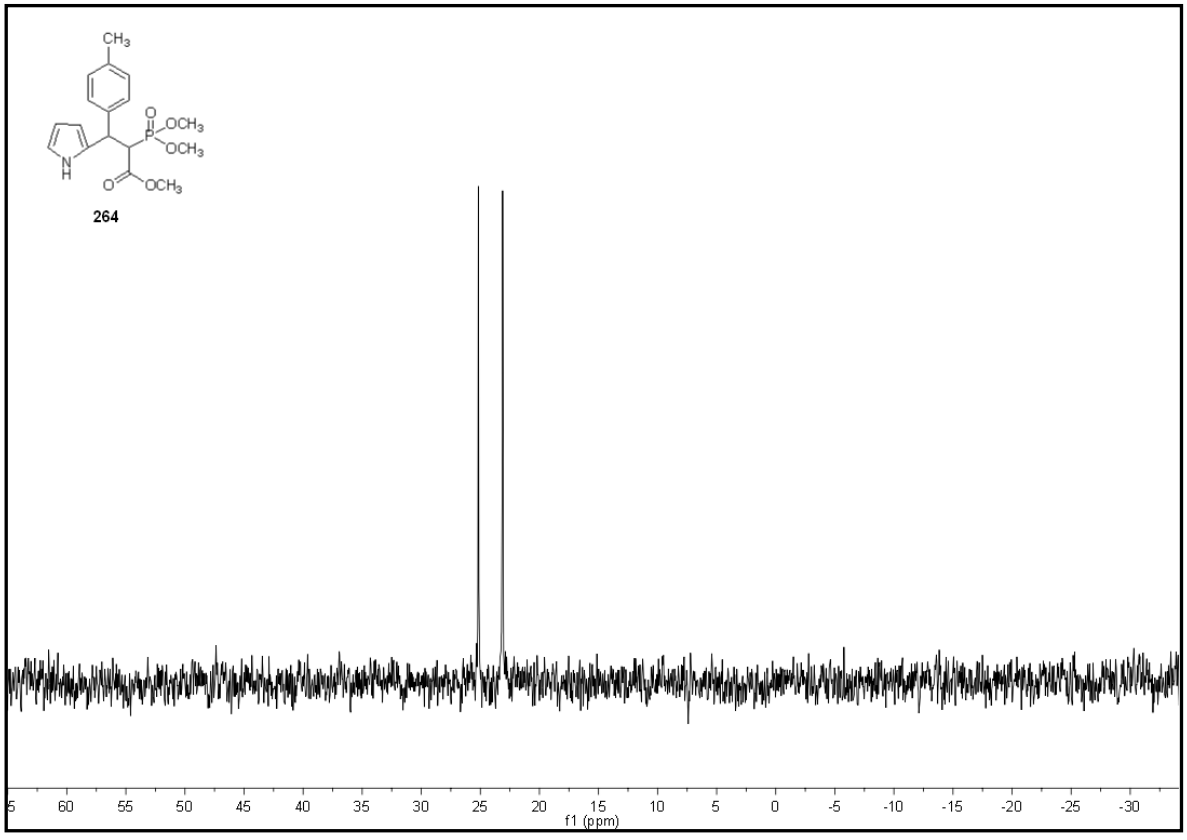


Figure A.138. ^{31}P NMR spectrum of compound **264**

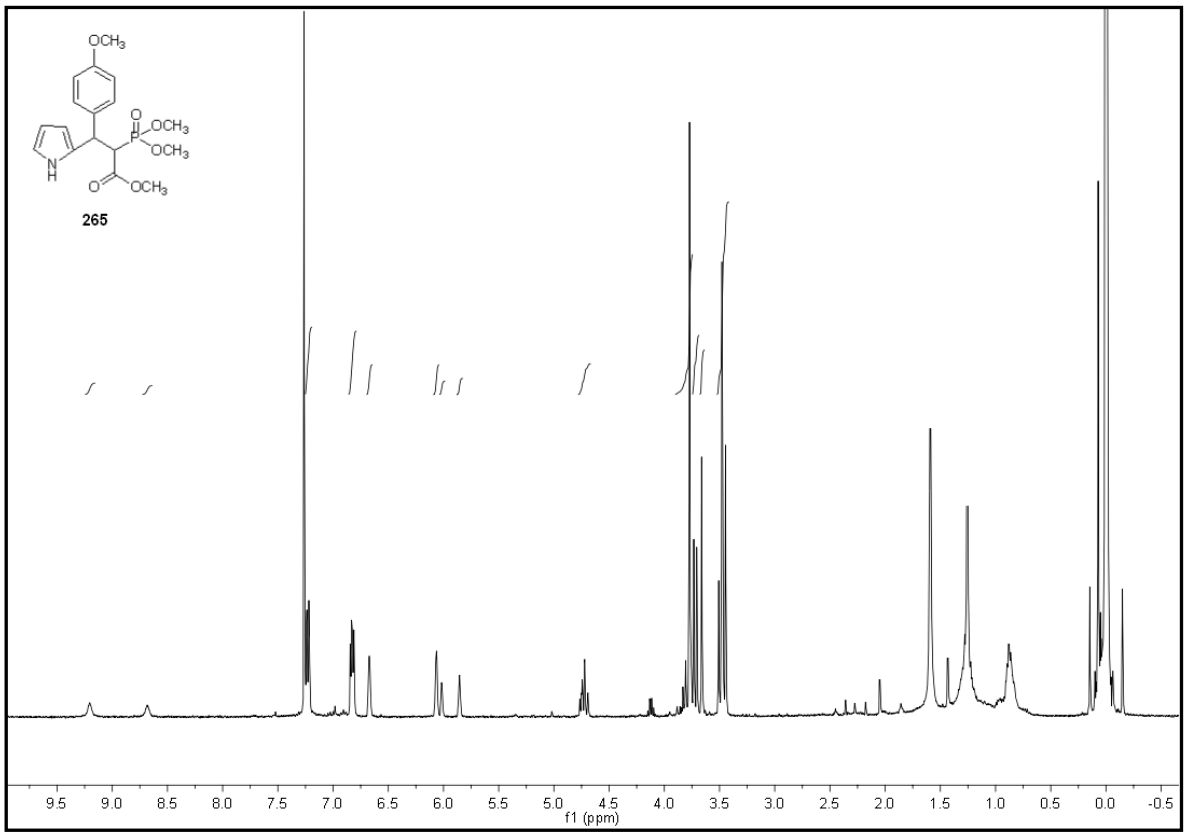


Figure A.139. ^{1}H NMR spectrum of compound **265**

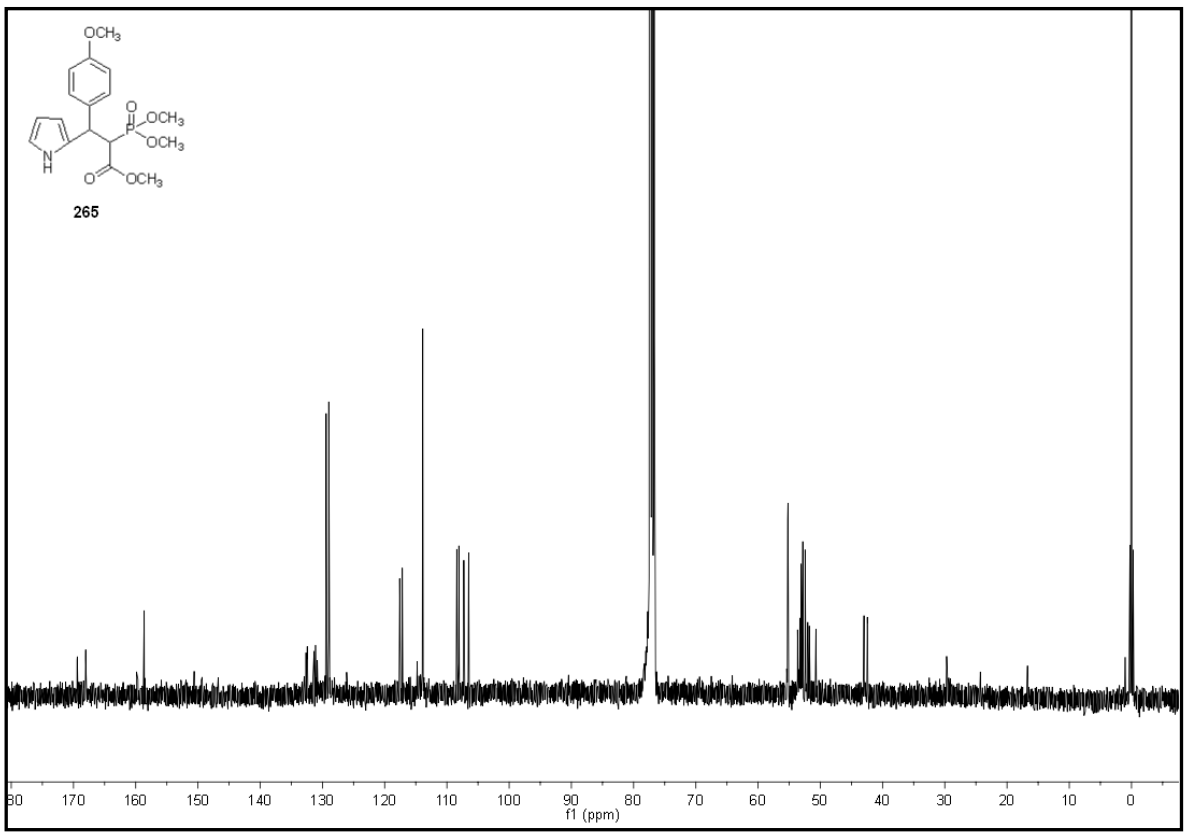


Figure A.140. ^{13}C NMR spectrum of compound **265**

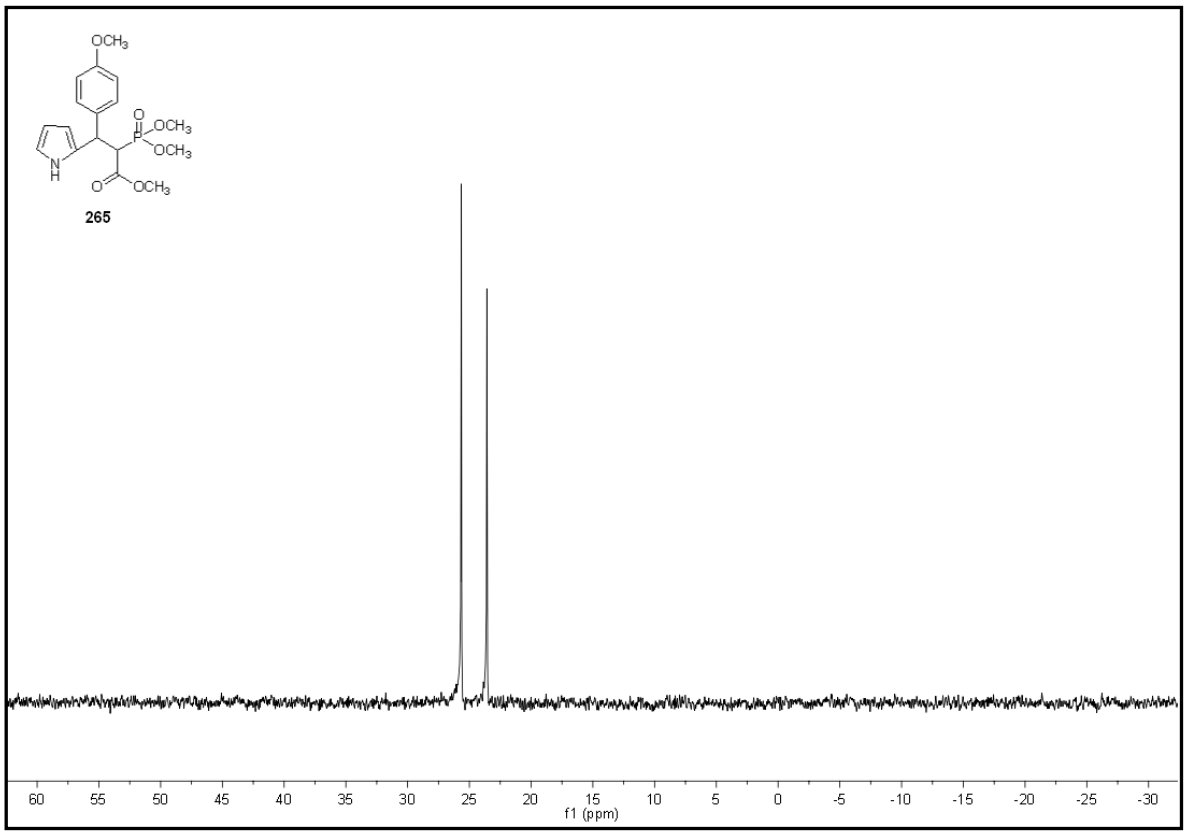


Figure A.141. ^{31}P NMR spectrum of compound **265**

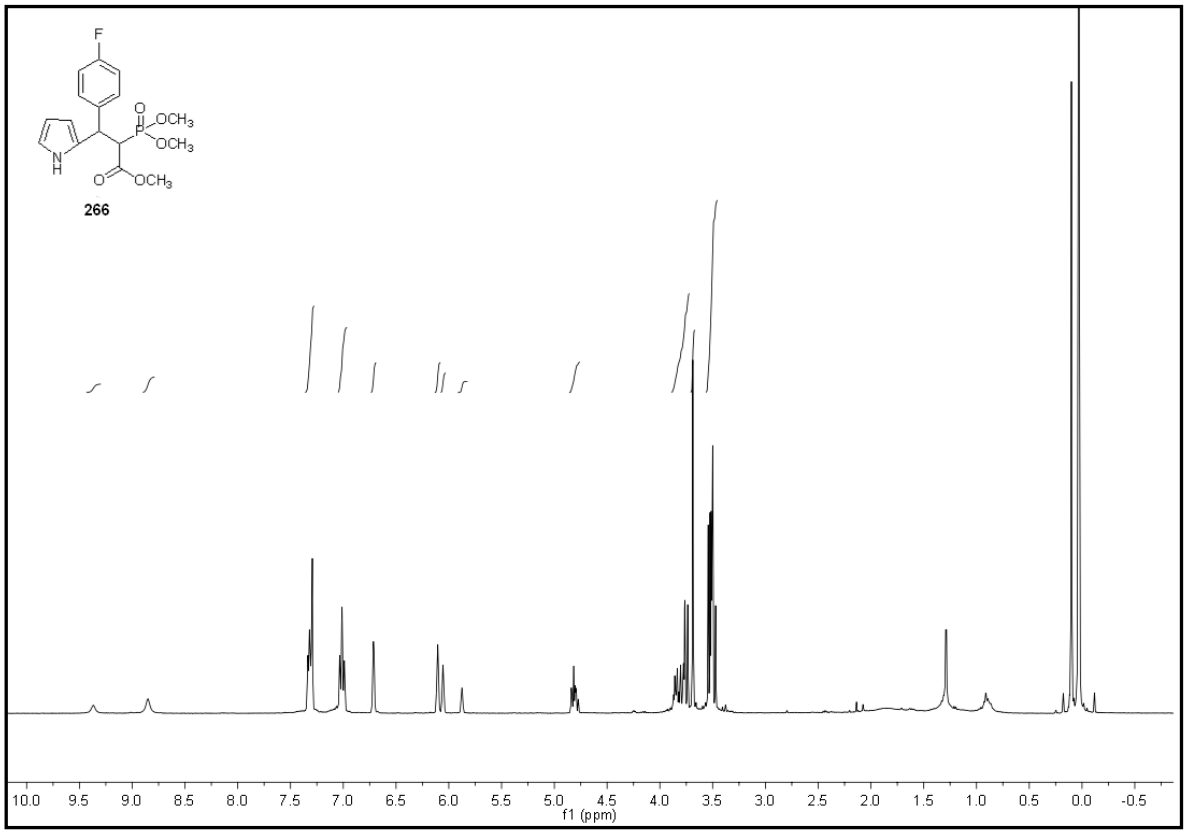


Figure A.142. ^{1}H NMR spectrum of compound **266**

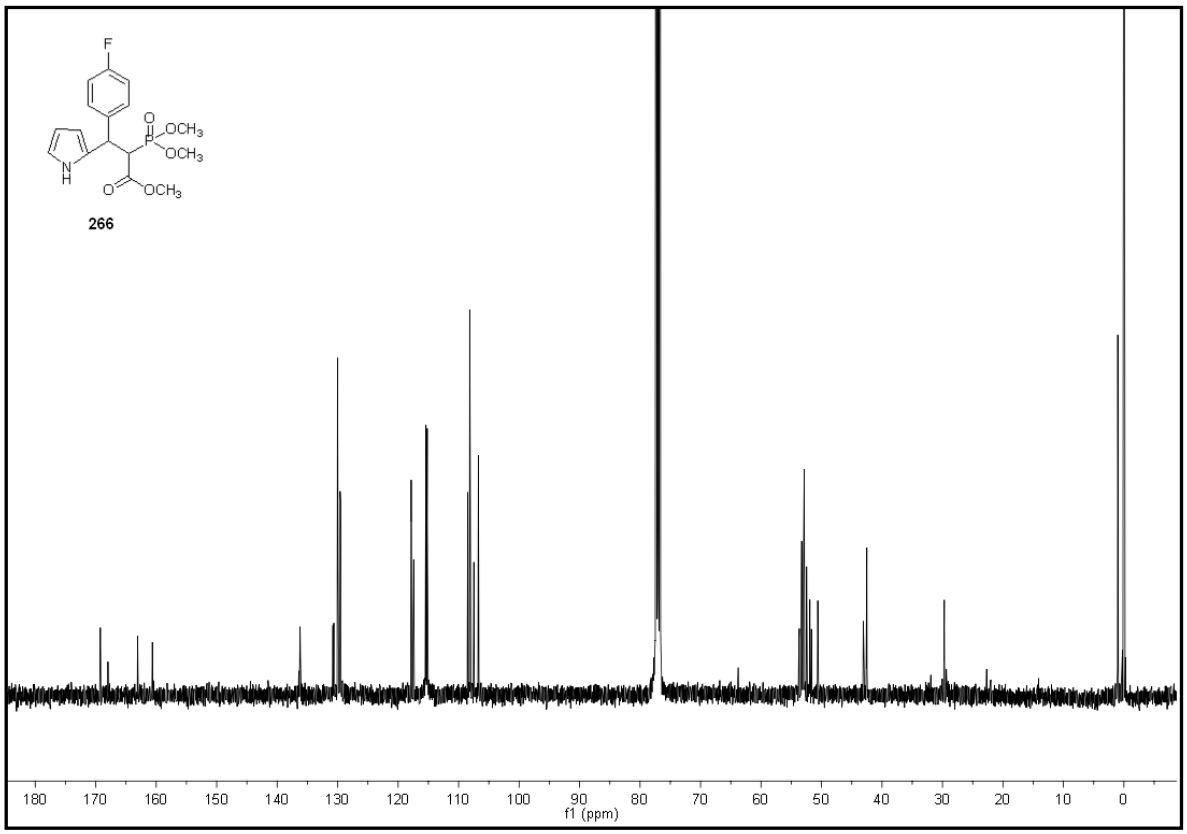


Figure A.143. ^{13}C NMR spectrum of compound **266**

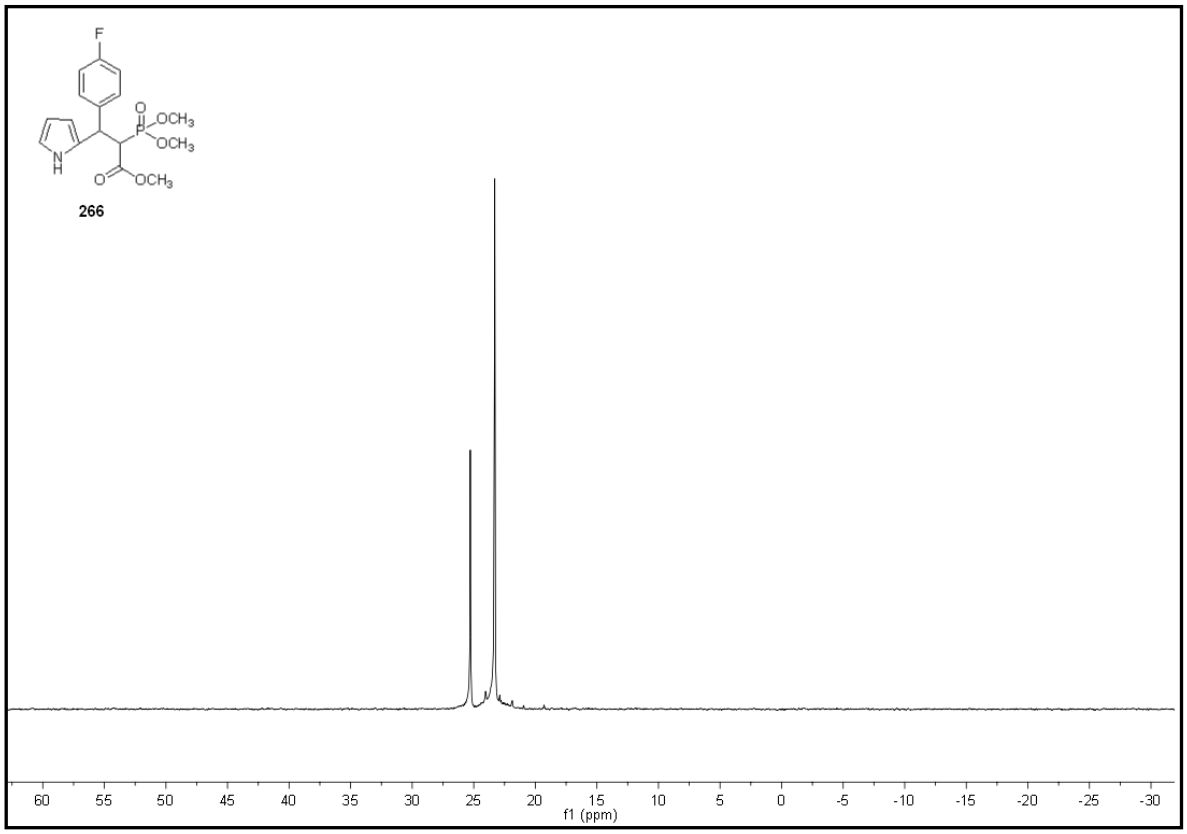


Figure A.144. ^{31}P NMR spectrum of compound **266**

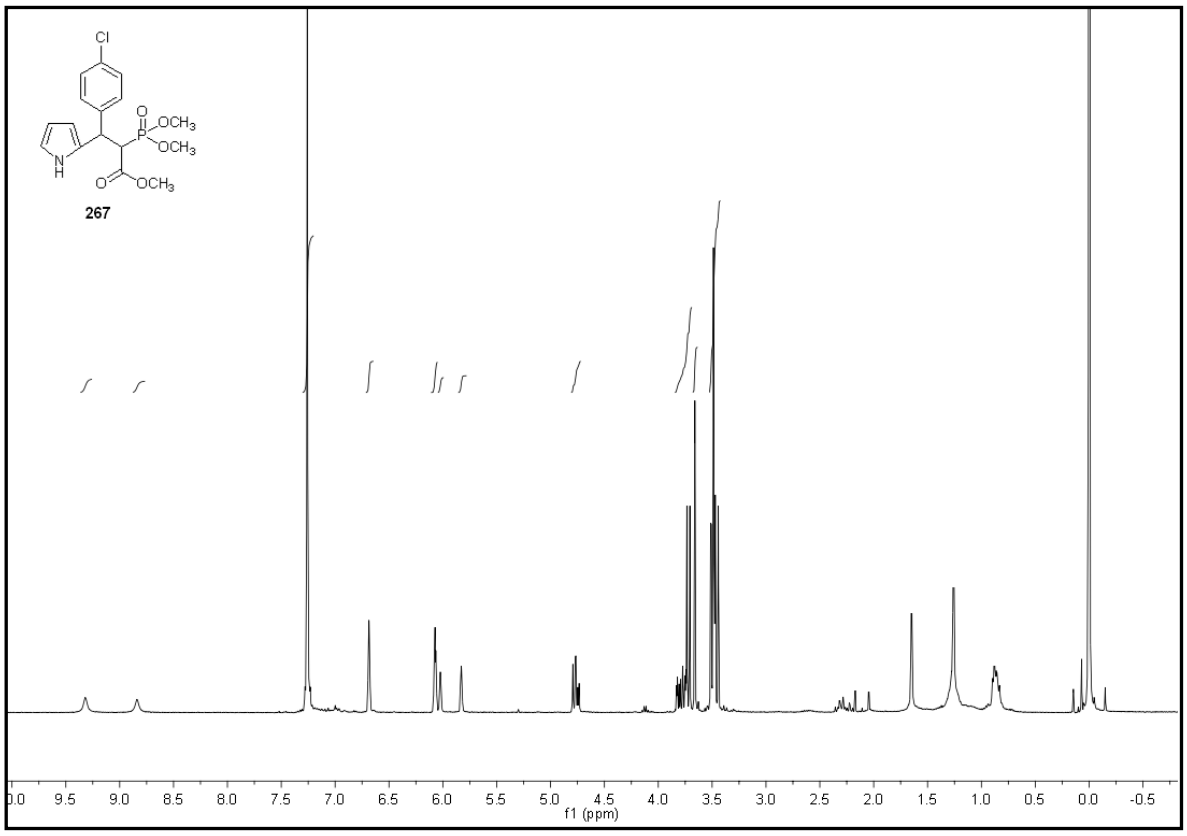


Figure A.145. ^{1}H NMR spectrum of compound **267**

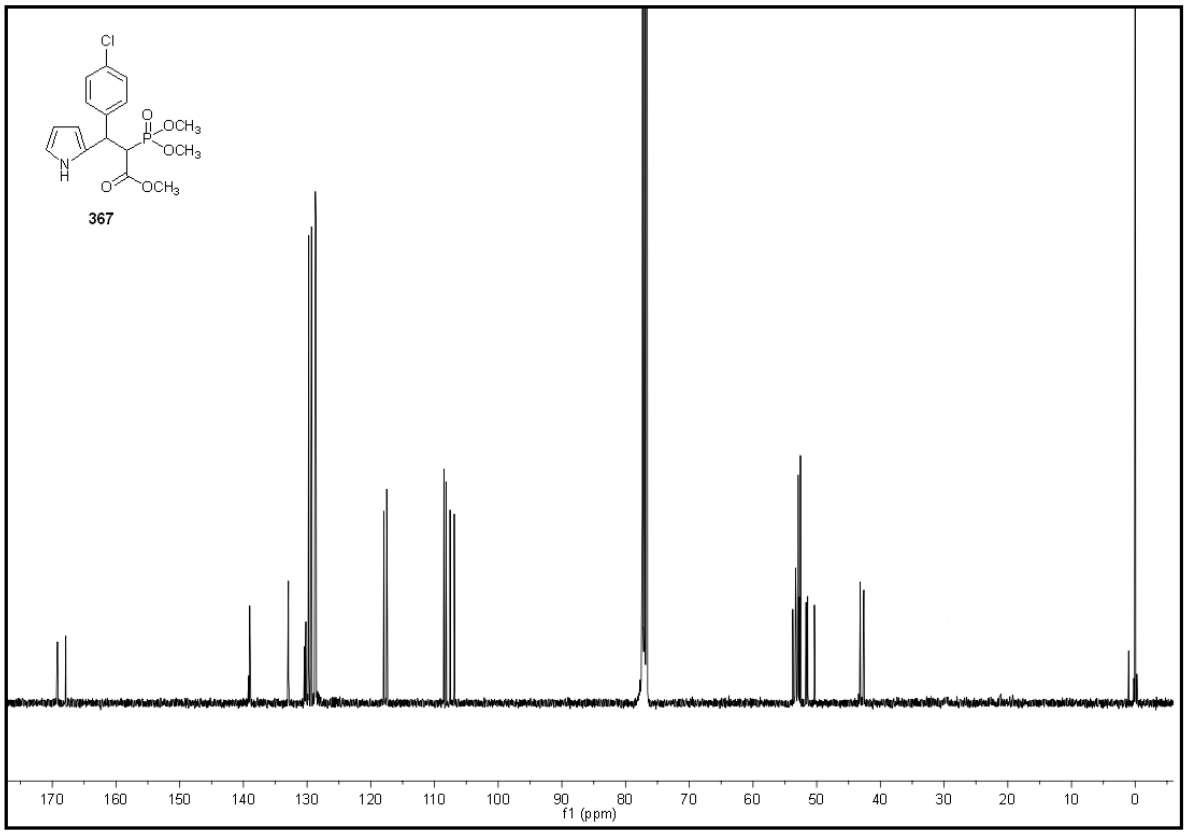


Figure A.146. ^{13}C NMR spectrum of compound **267**

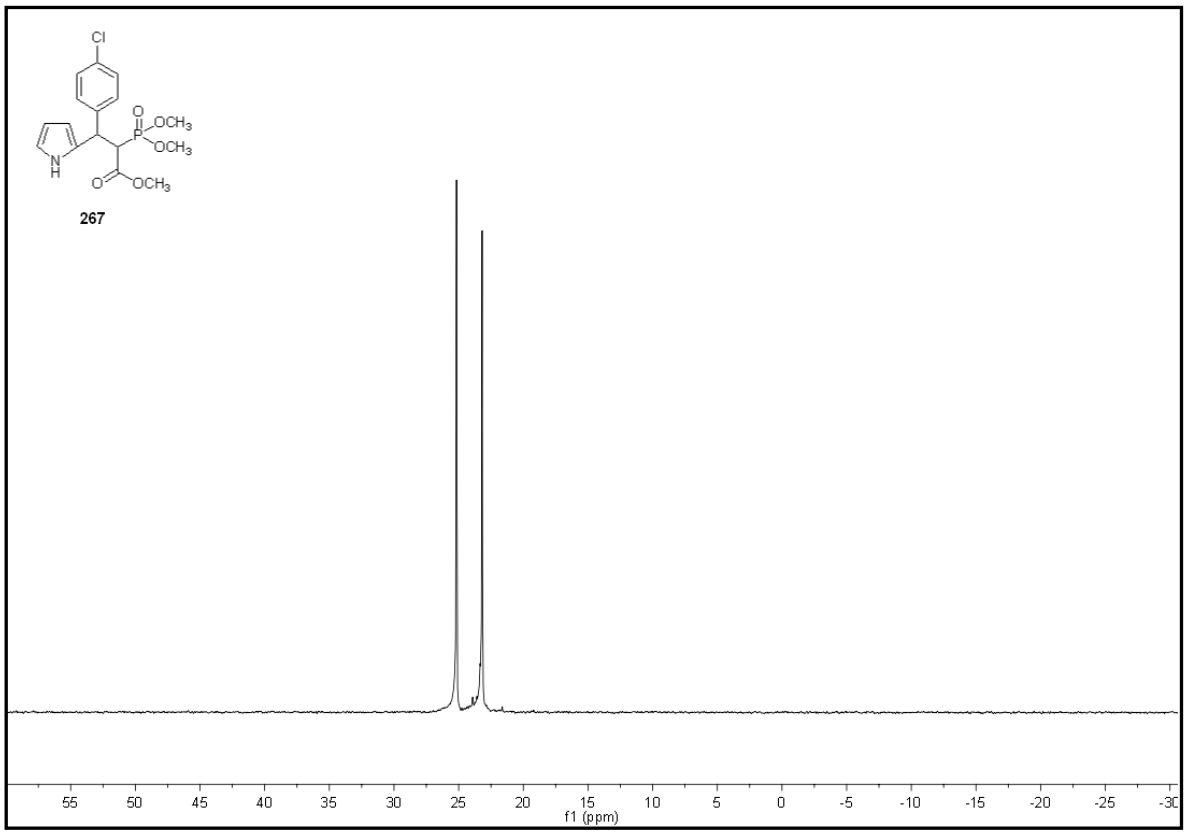


Figure A.147. ^{31}P NMR spectrum of compound **267**

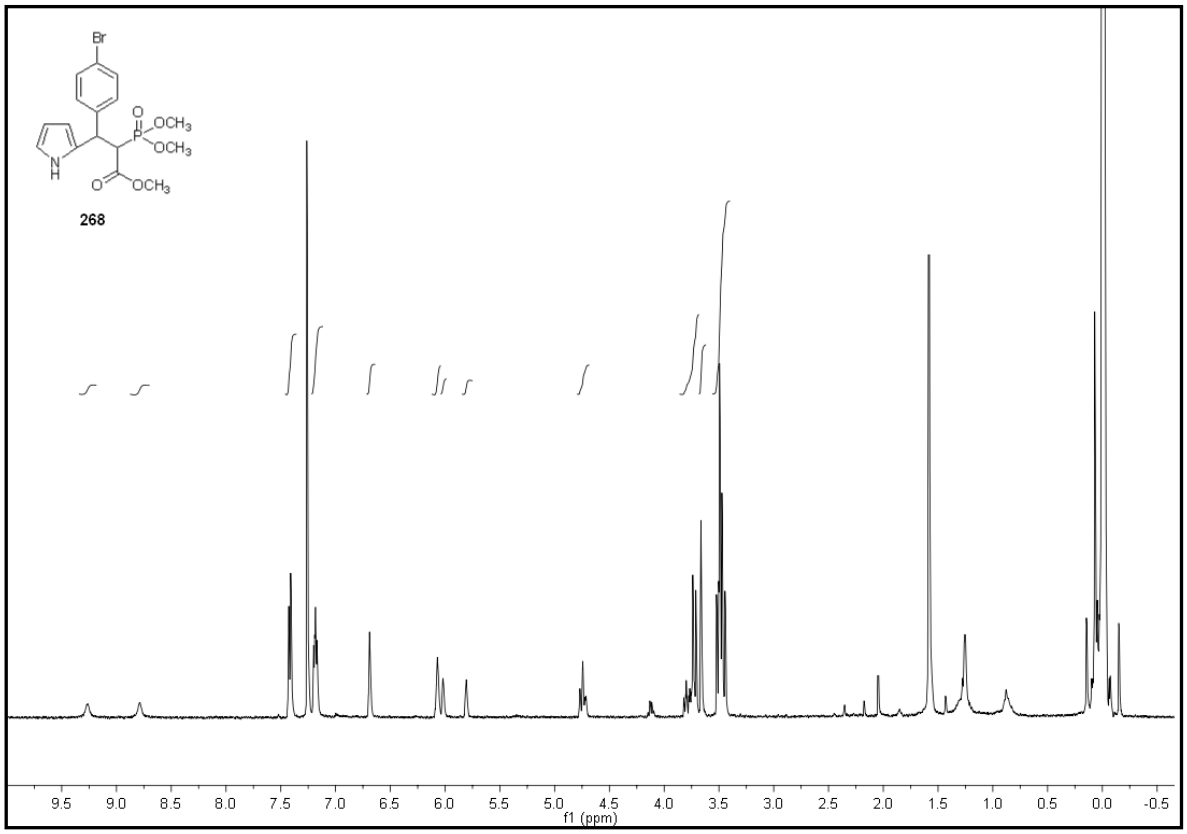


Figure A.148. ^{1}H NMR spectrum of compound **268**

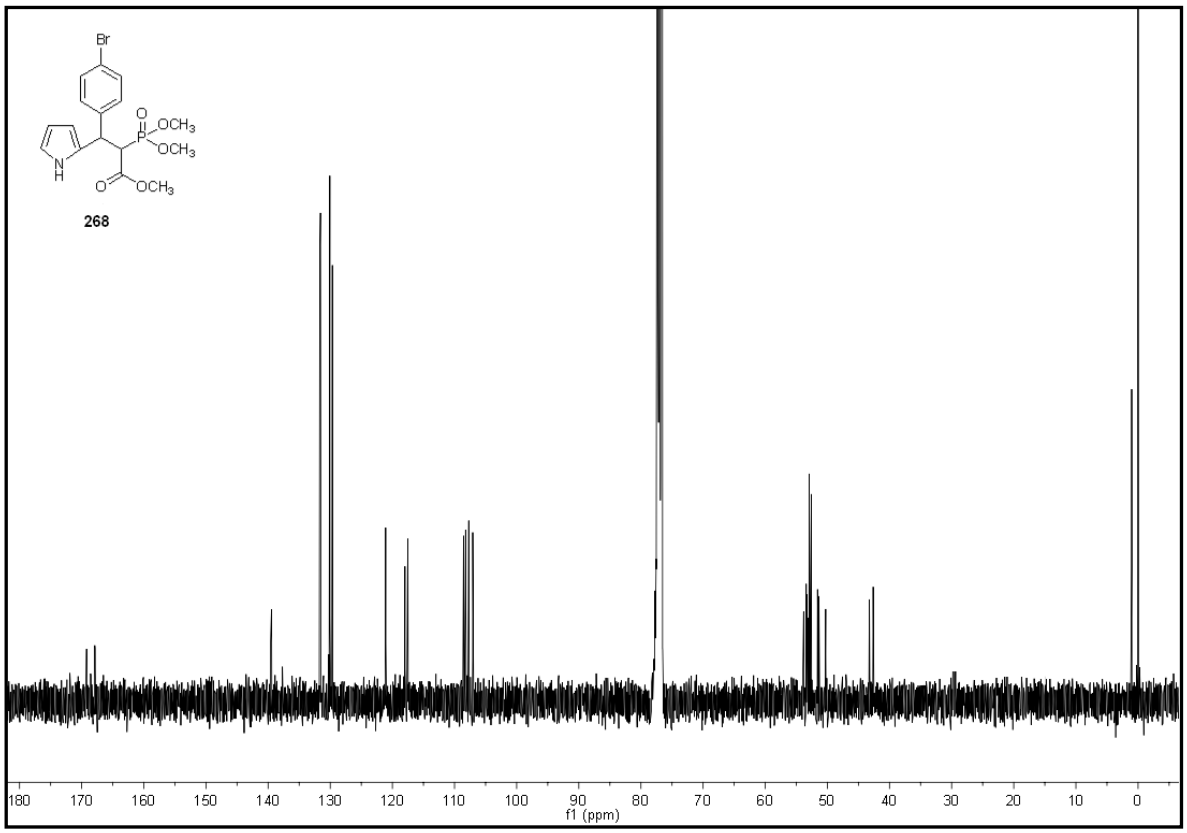


Figure A.149. ^{13}C NMR spectrum of compound **268**

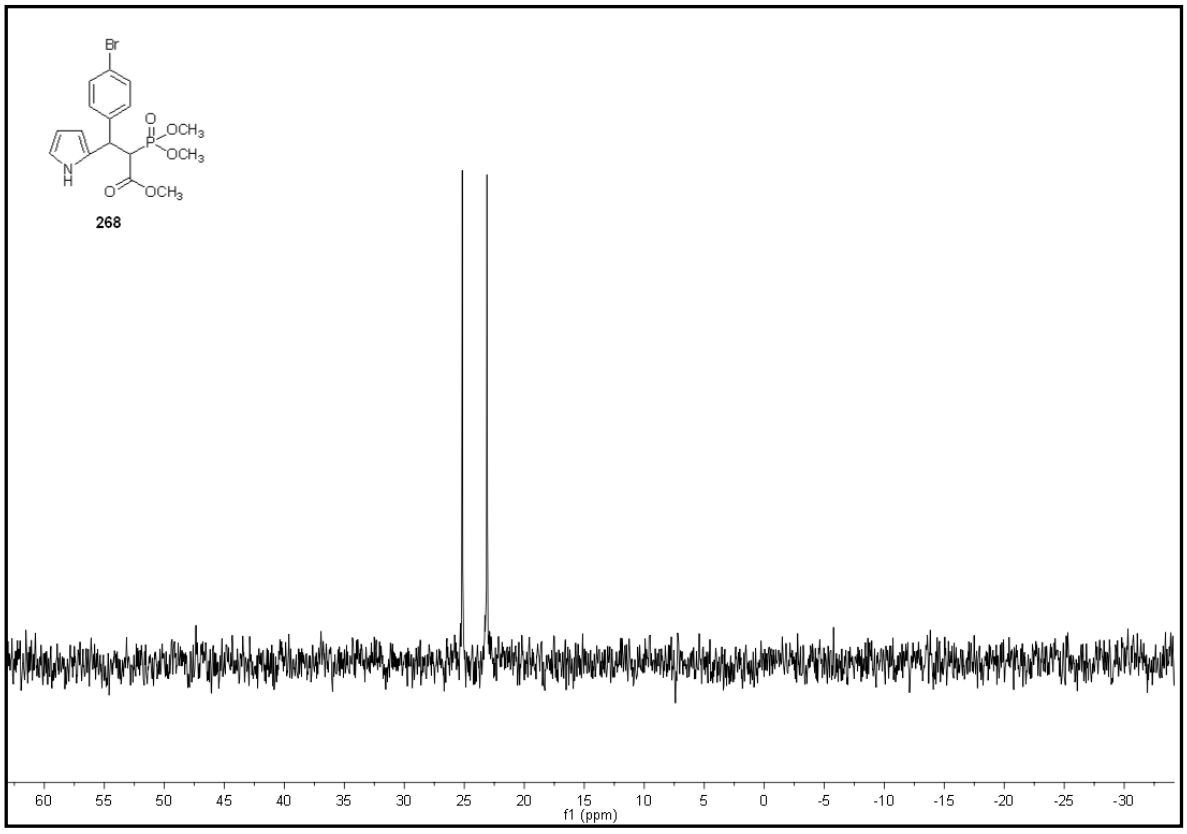


Figure A.150. ^{31}P NMR spectrum of compound **268**

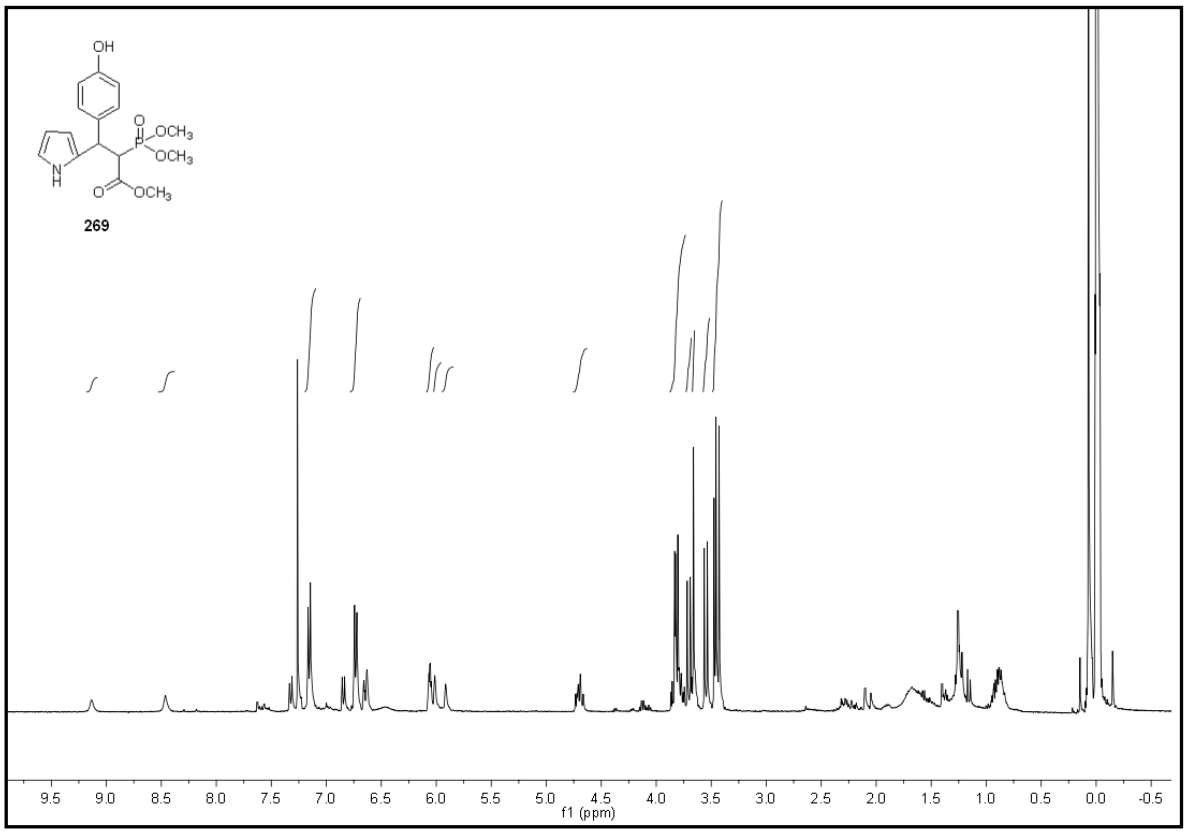


Figure A.151. ^{1}H NMR spectrum of compound **269**

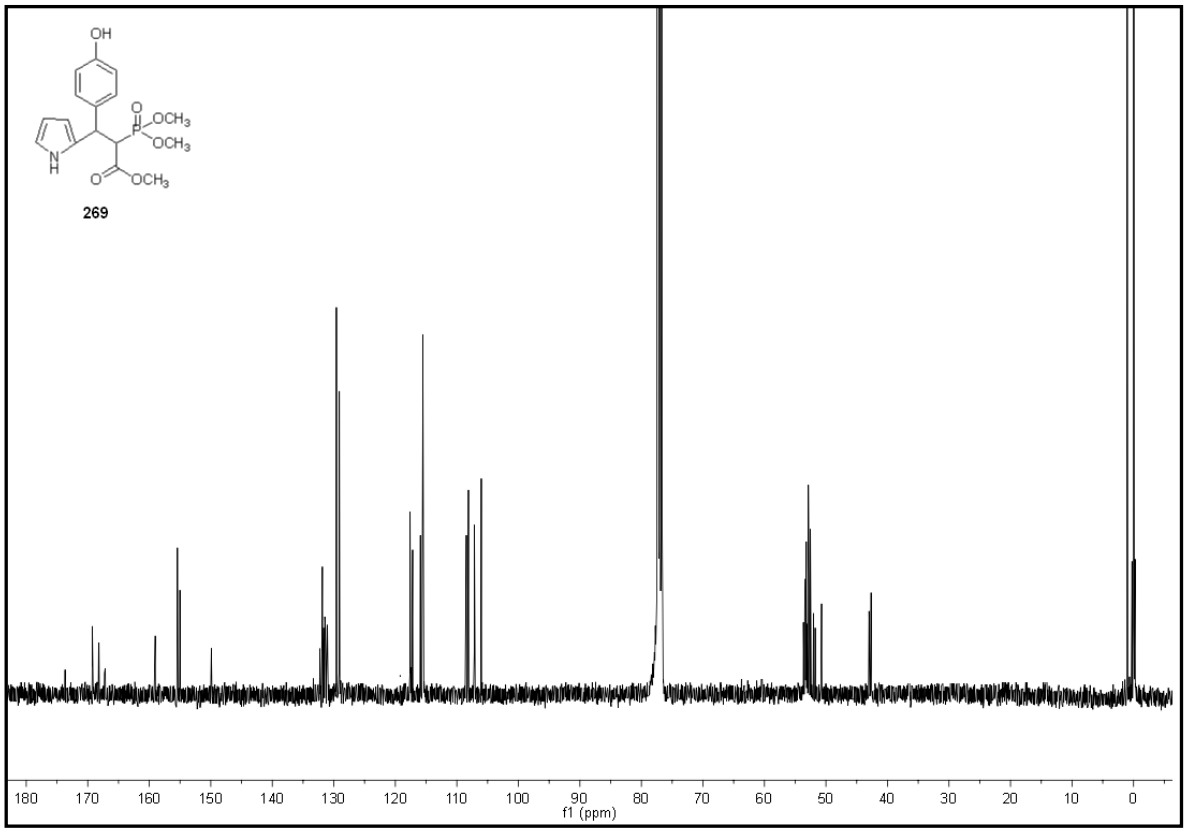


Figure A.152. ^{13}C NMR spectrum of compound **269**

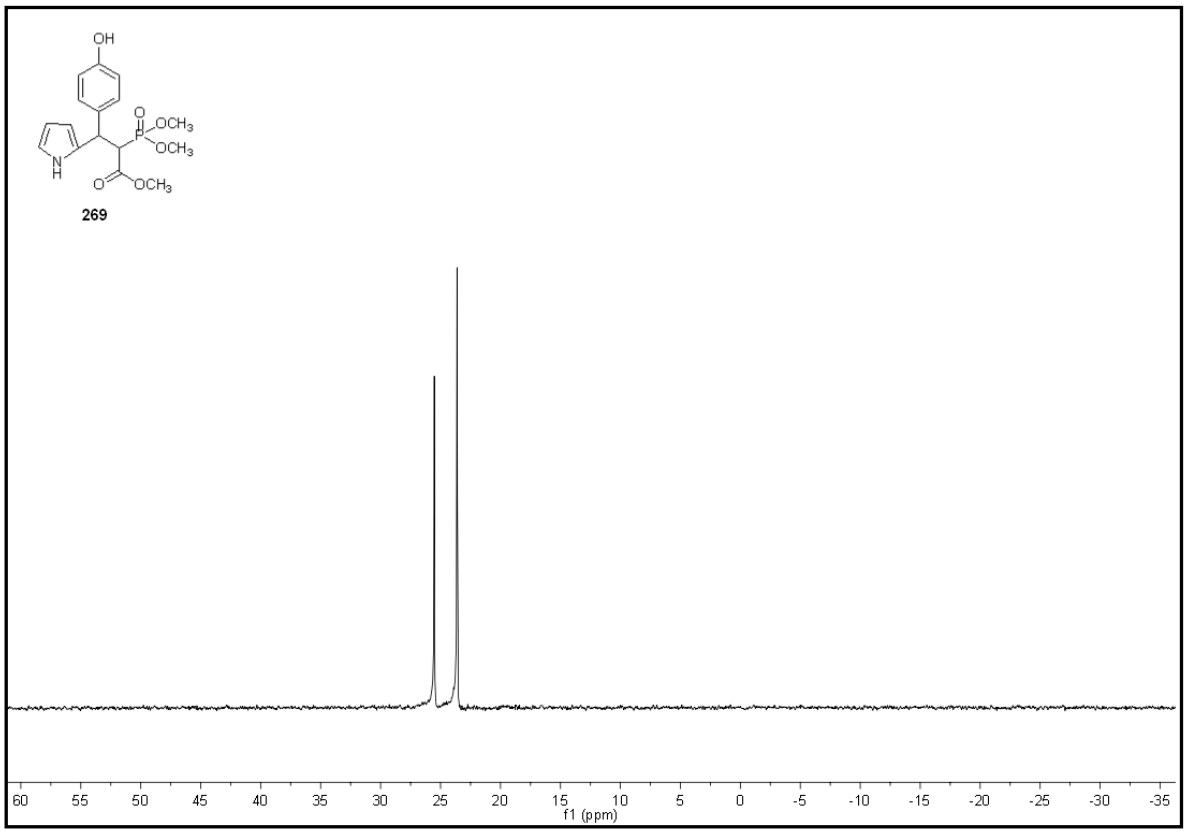


Figure A.153. ^{31}P NMR spectrum of compound **269**

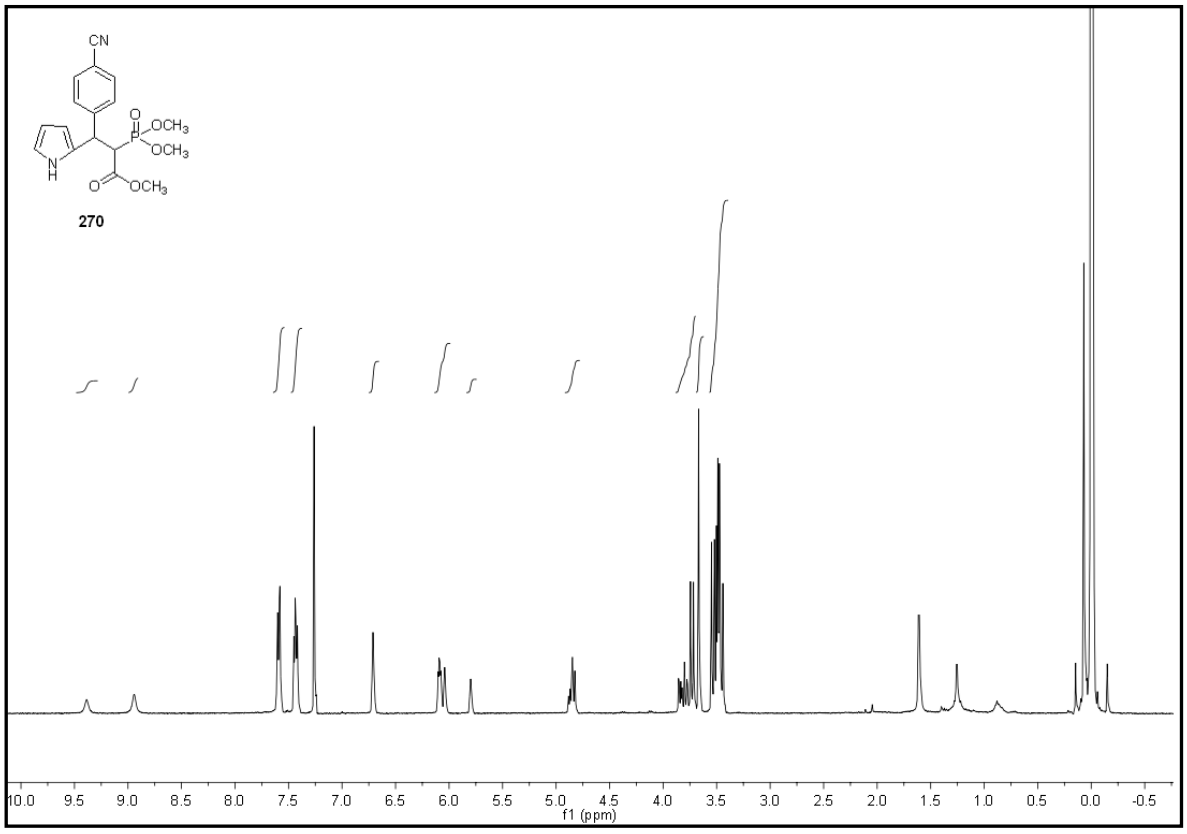


Figure A.154. ^{1}H NMR spectrum of compound **270**

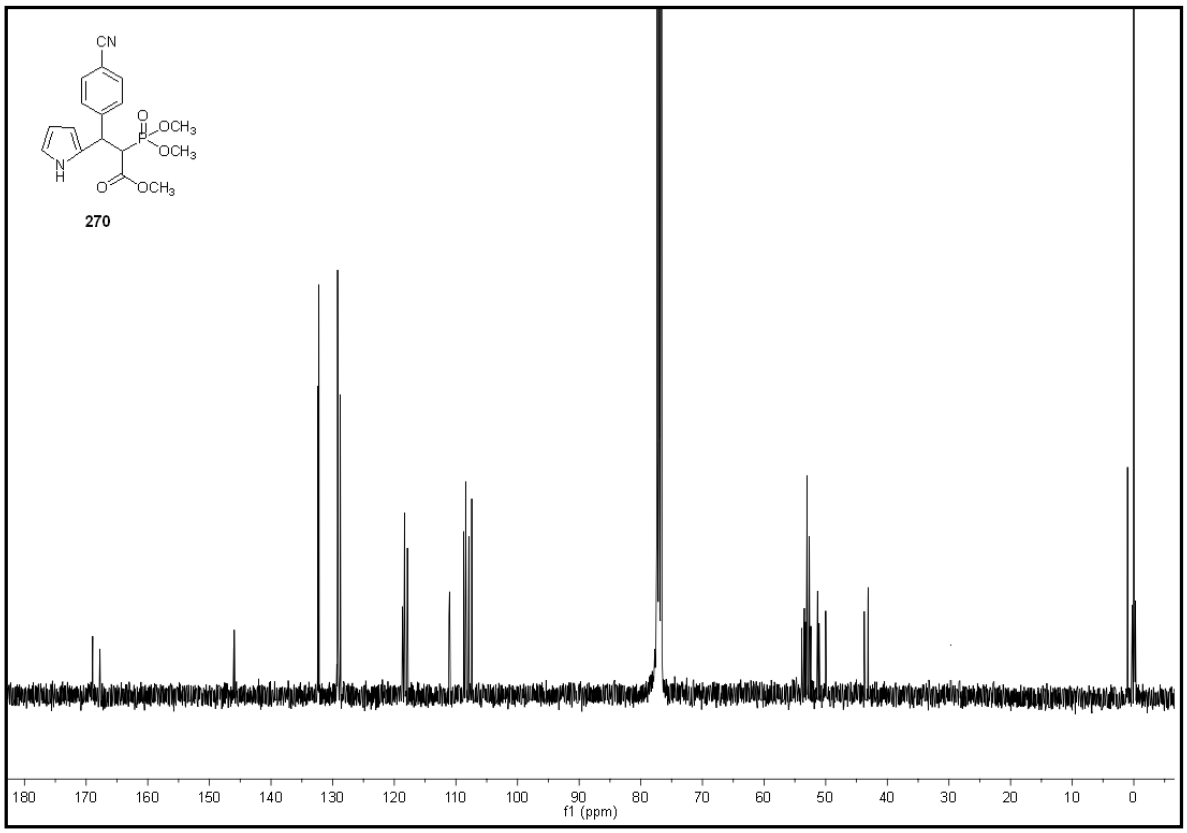


Figure A.155. ^{13}C NMR spectrum of compound **270**

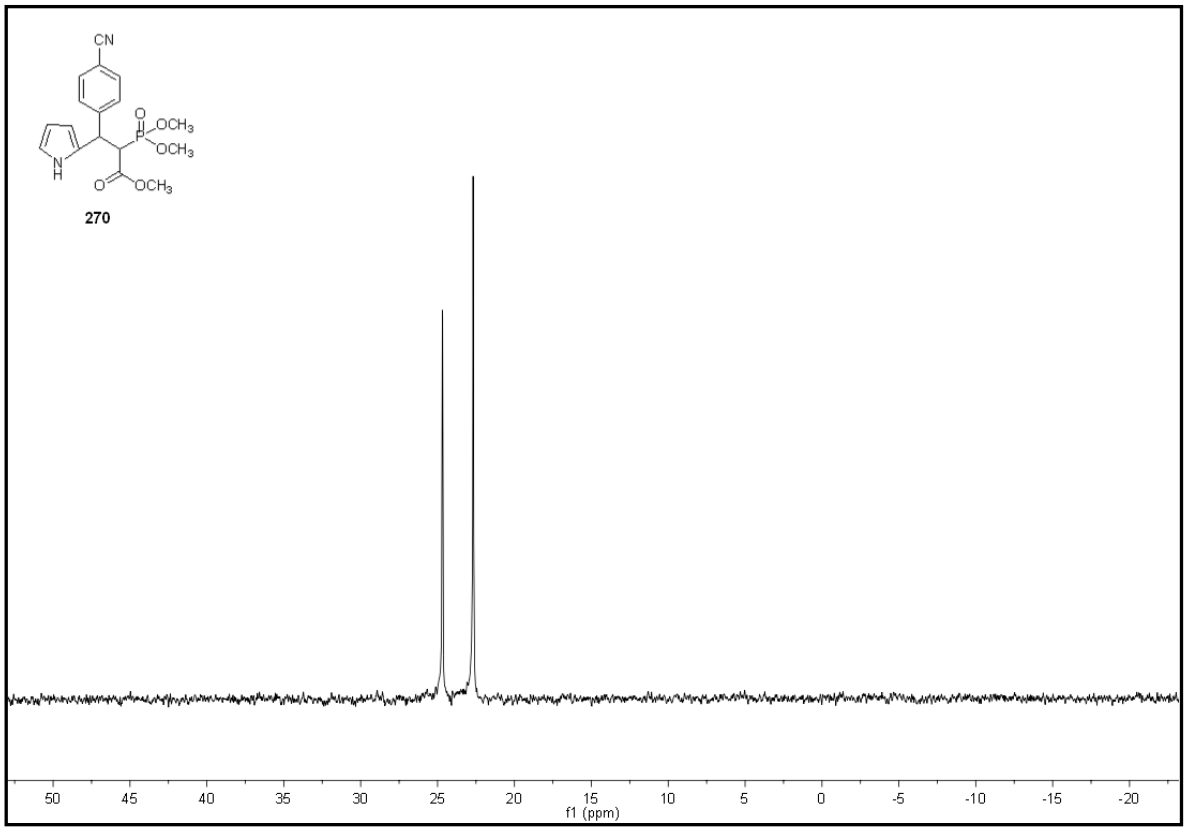


Figure A.156. ^{31}P NMR spectrum of compound **270**

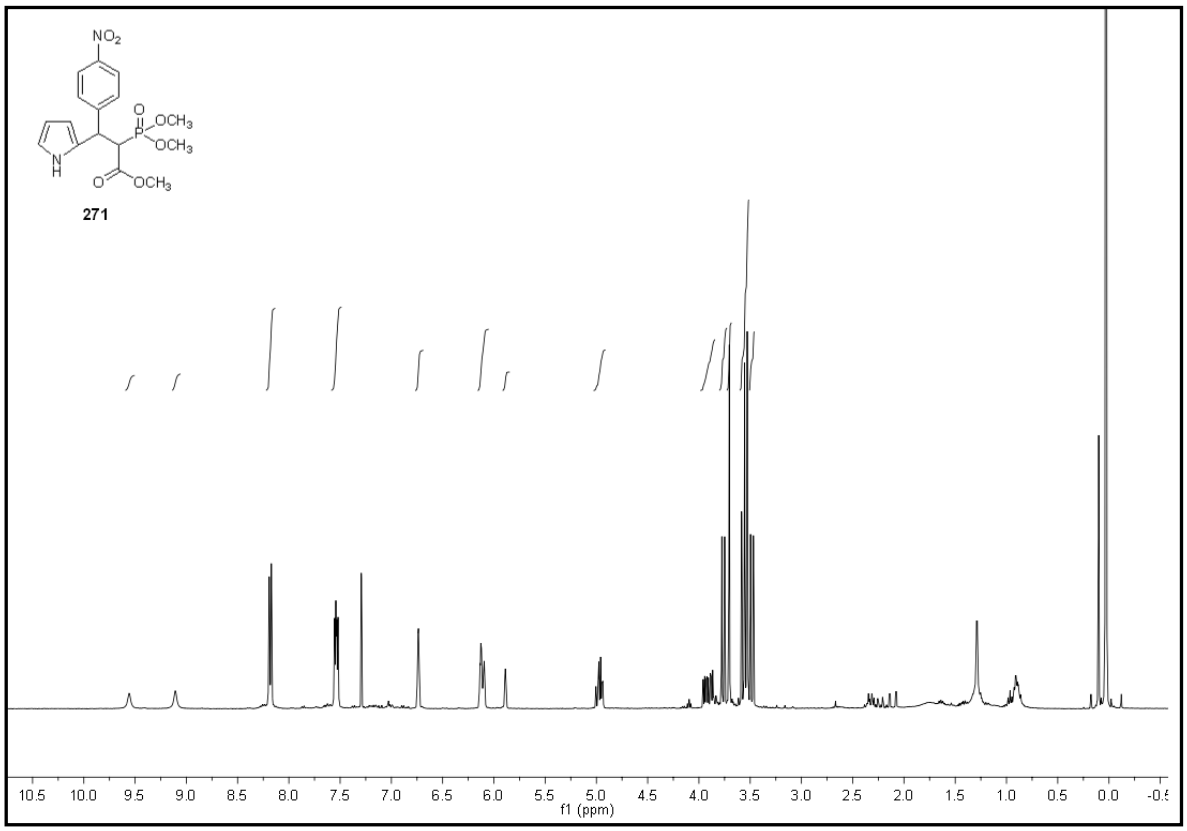


Figure A.157. ^{1}H NMR spectrum of compound **271**

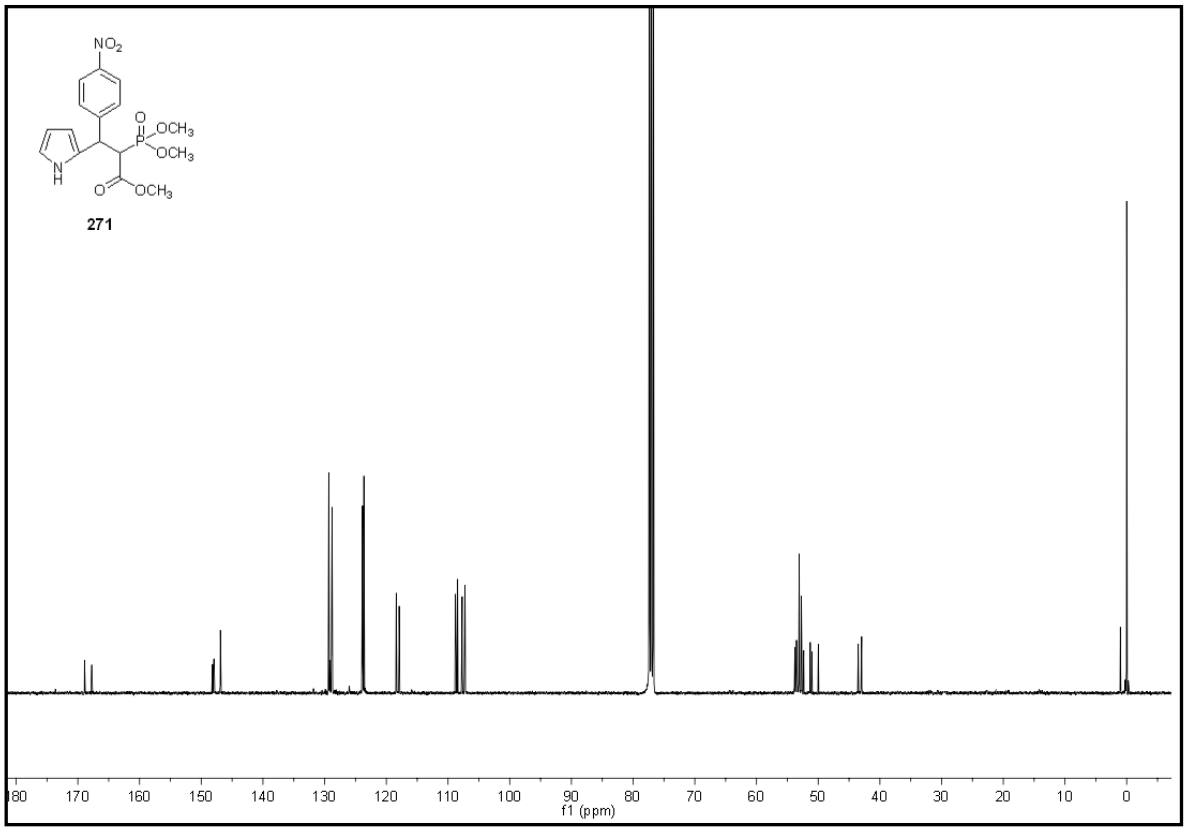


Figure A.158. ^{13}C NMR spectrum of compound **271**

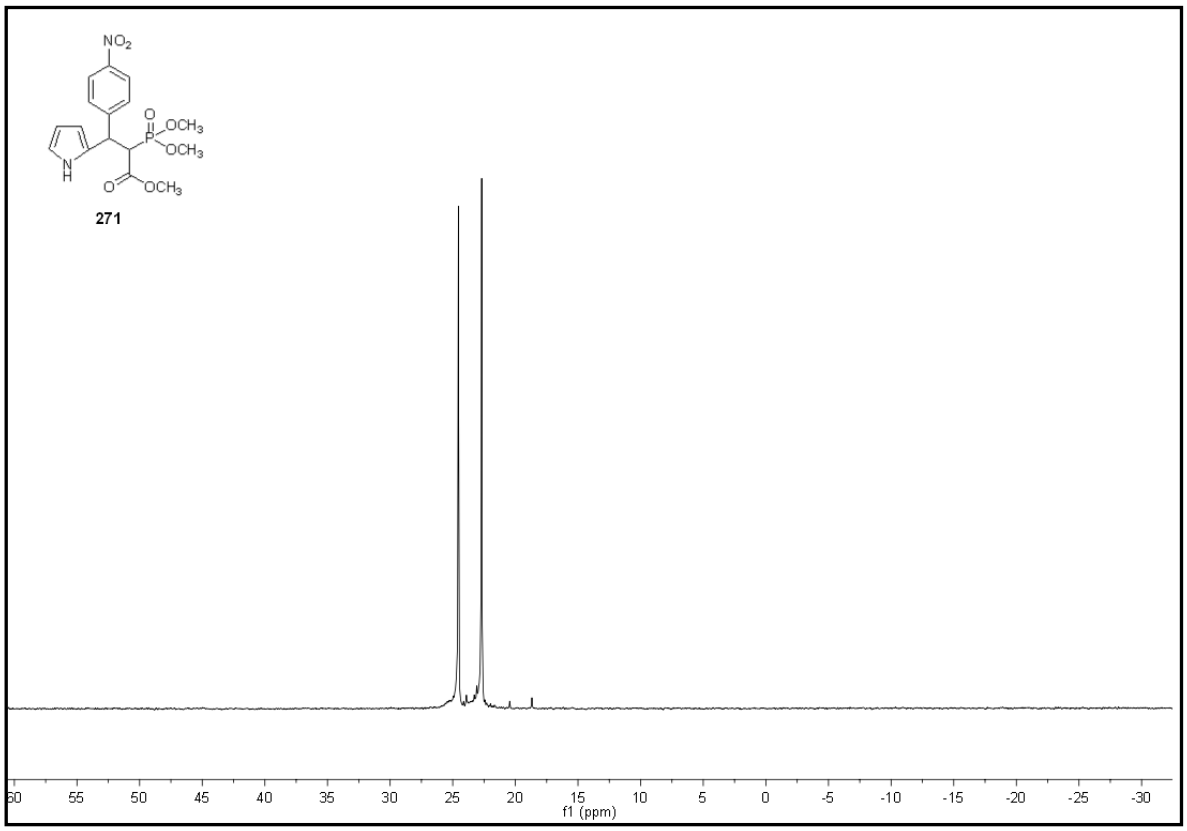


Figure A.159. ^{31}P NMR spectrum of compound **271**

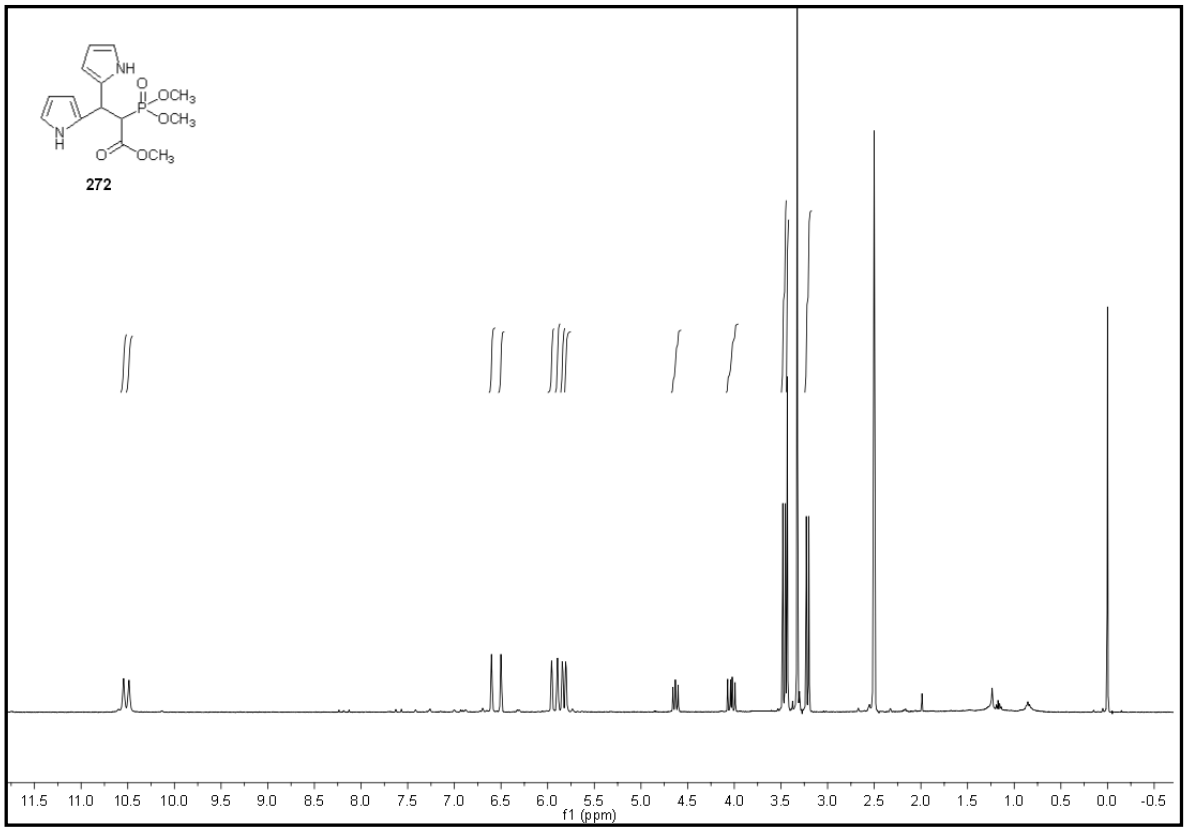


Figure A.160. ^{1}H NMR spectrum of compound **272**

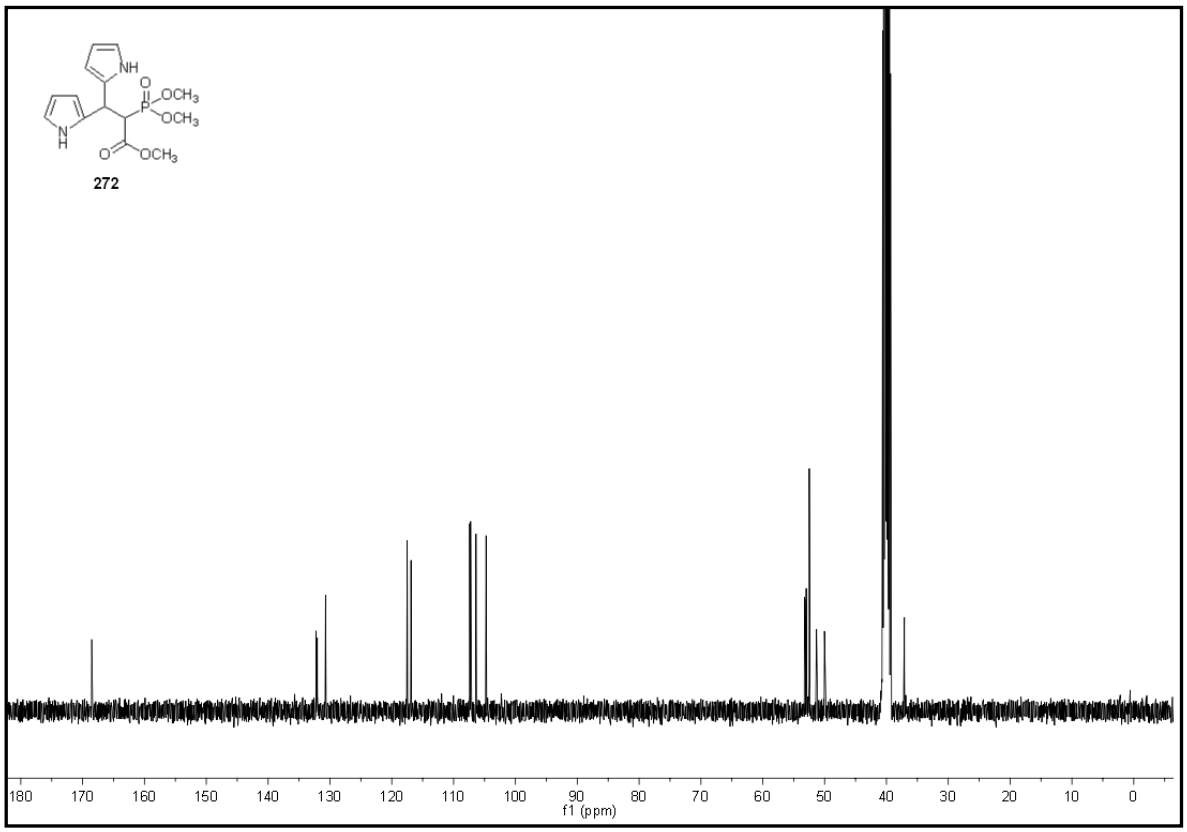


Figure A.161. ^{13}C NMR spectrum of compound **272**

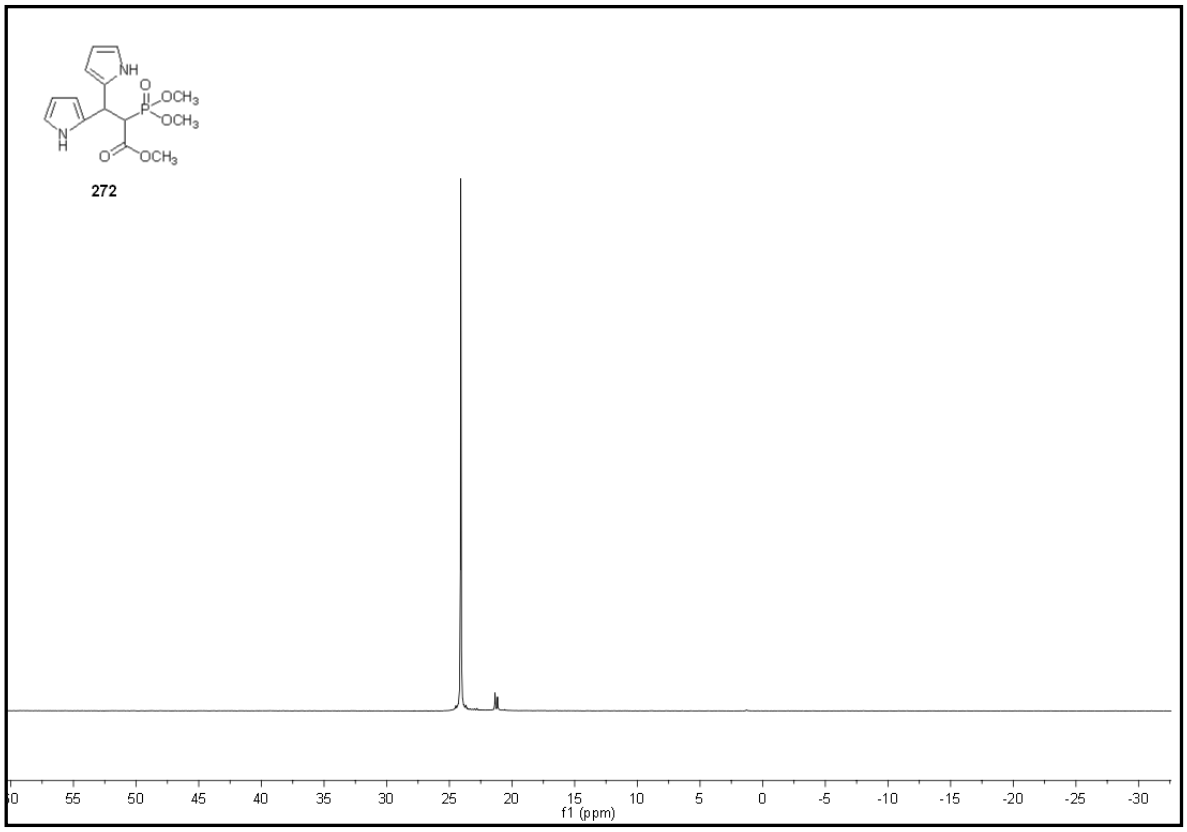


Figure A.162. ^{31}P NMR spectrum of compound **272**

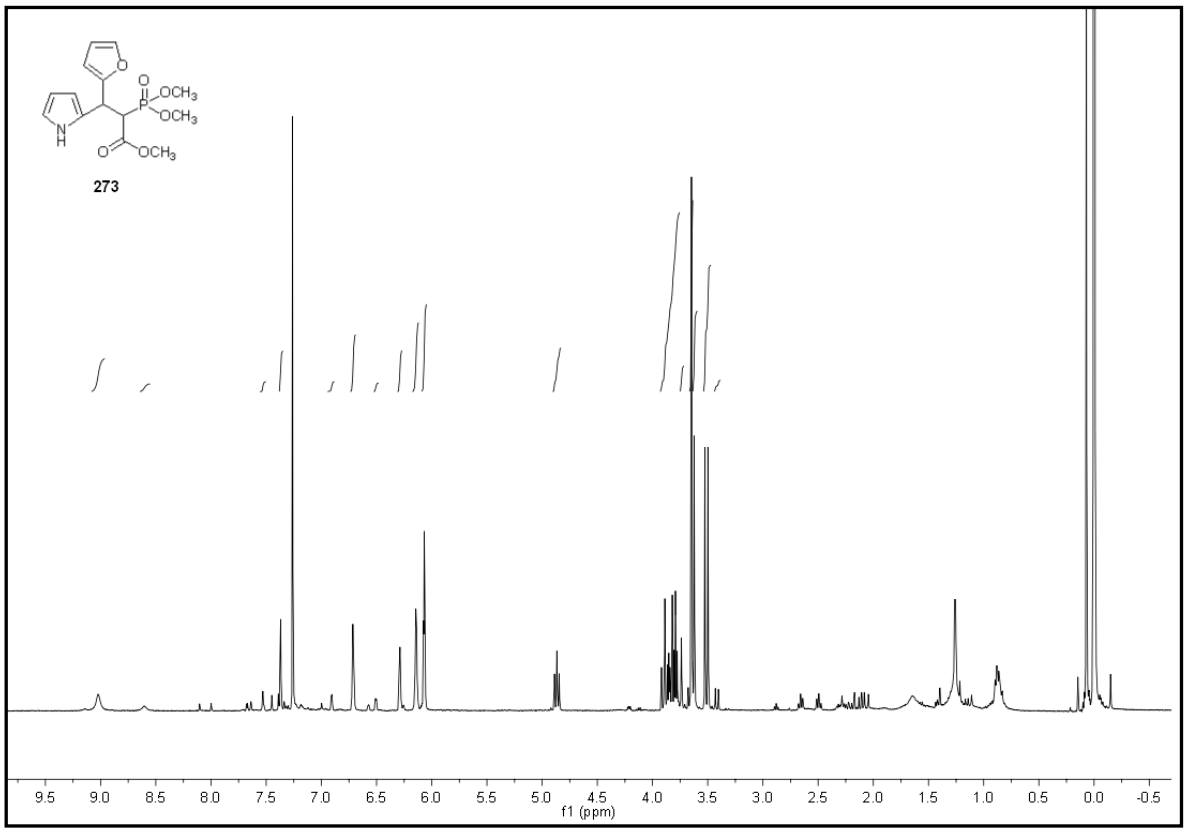


Figure A.163. ^{1}H NMR spectrum of compound **273**

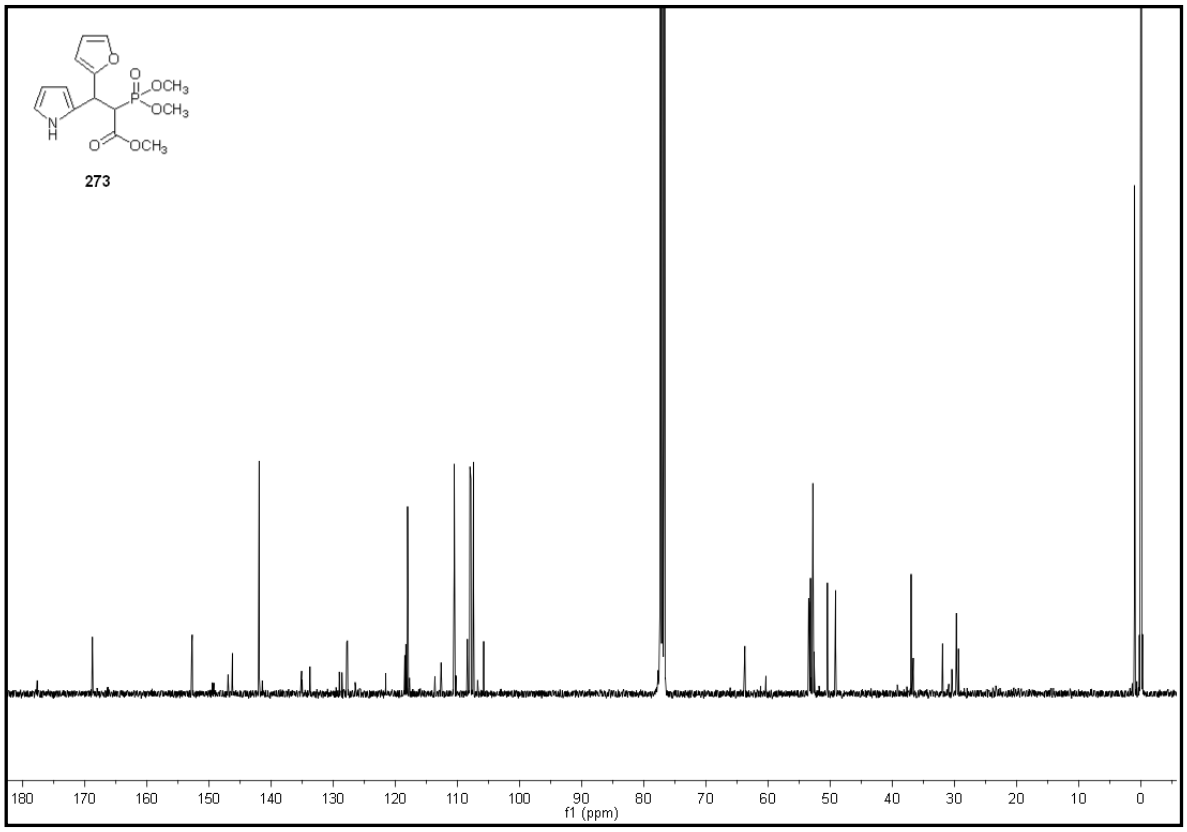


Figure A.164. ^{13}C NMR spectrum of compound **273**

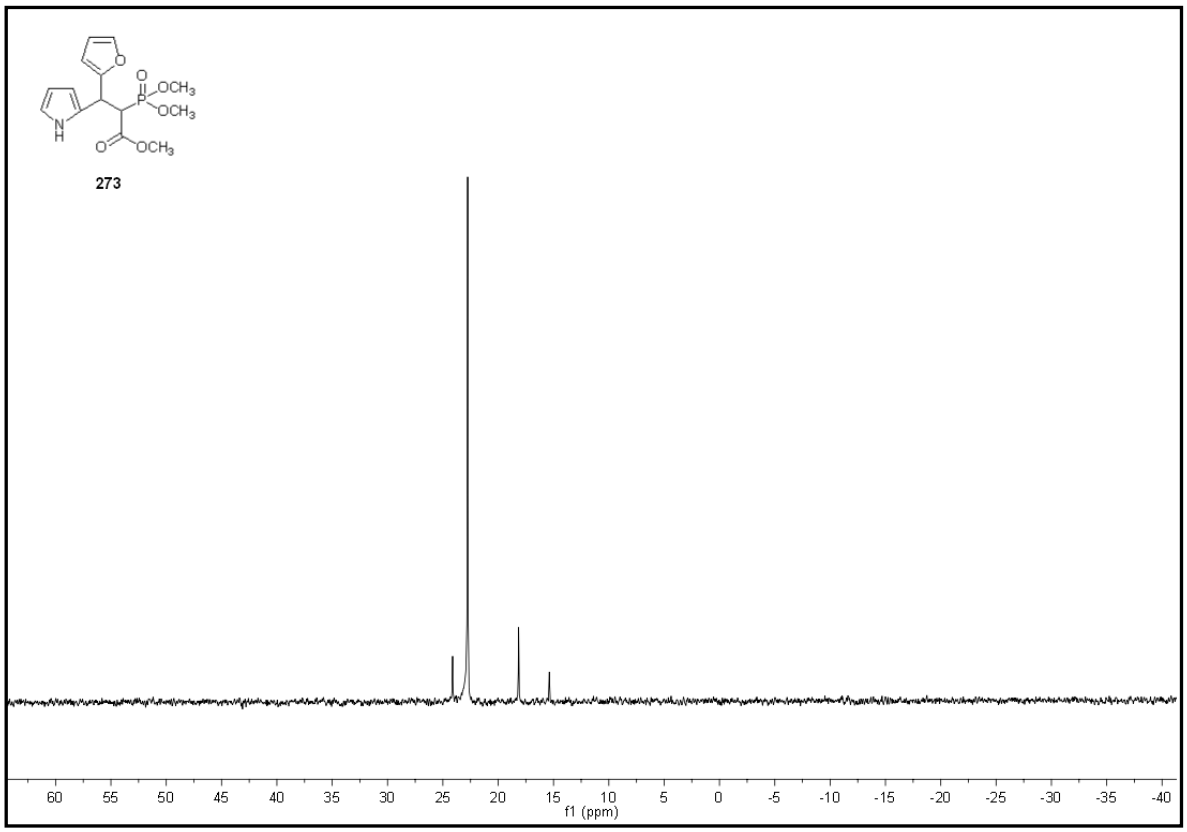


Figure A.165. ^{31}P NMR spectrum of compound **273**

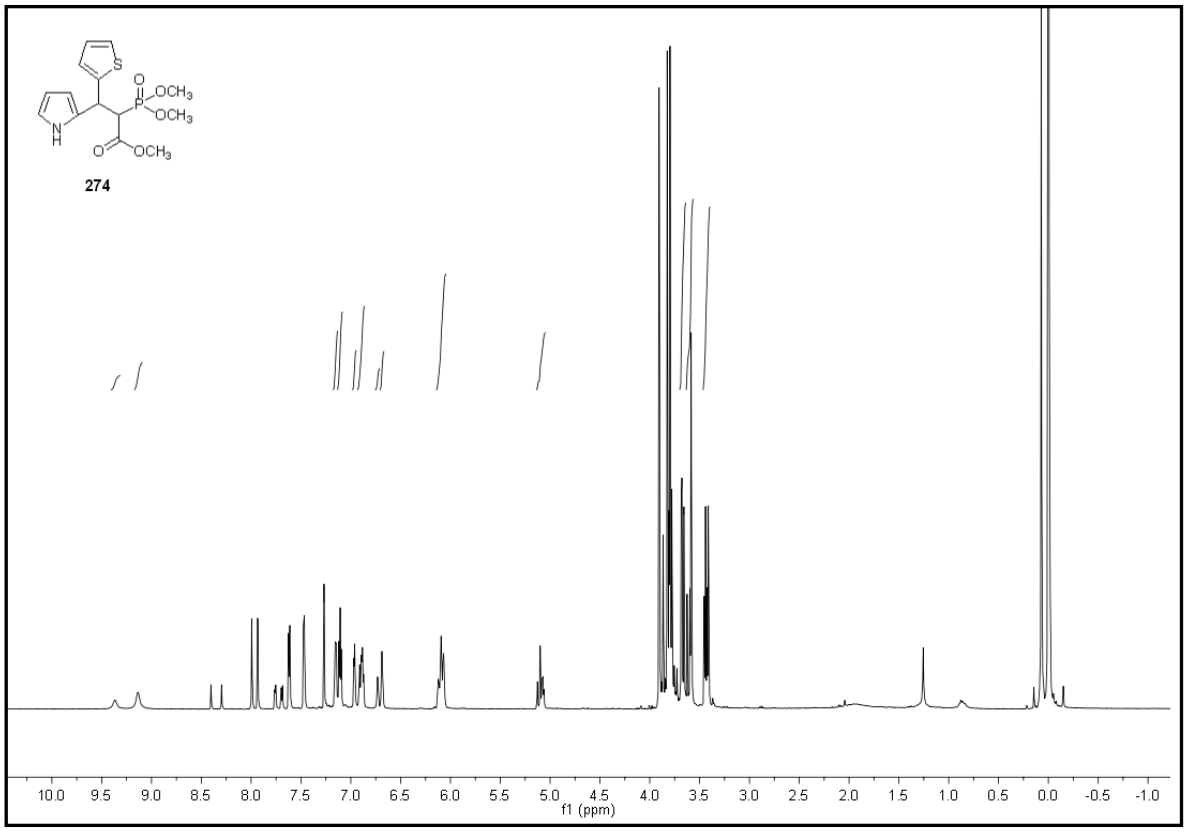


Figure A.166. ^{1}H NMR spectrum of compound **274**

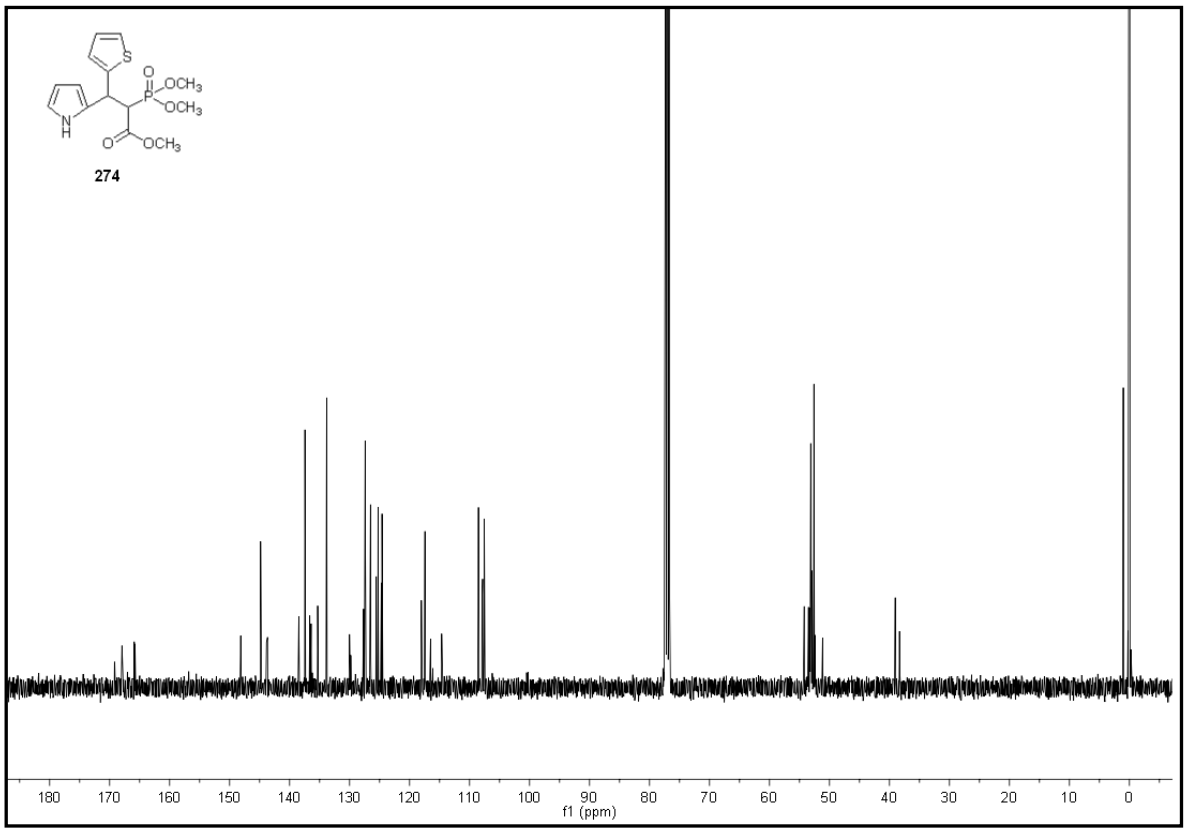


Figure A.167. ^{13}C NMR spectrum of compound **274**

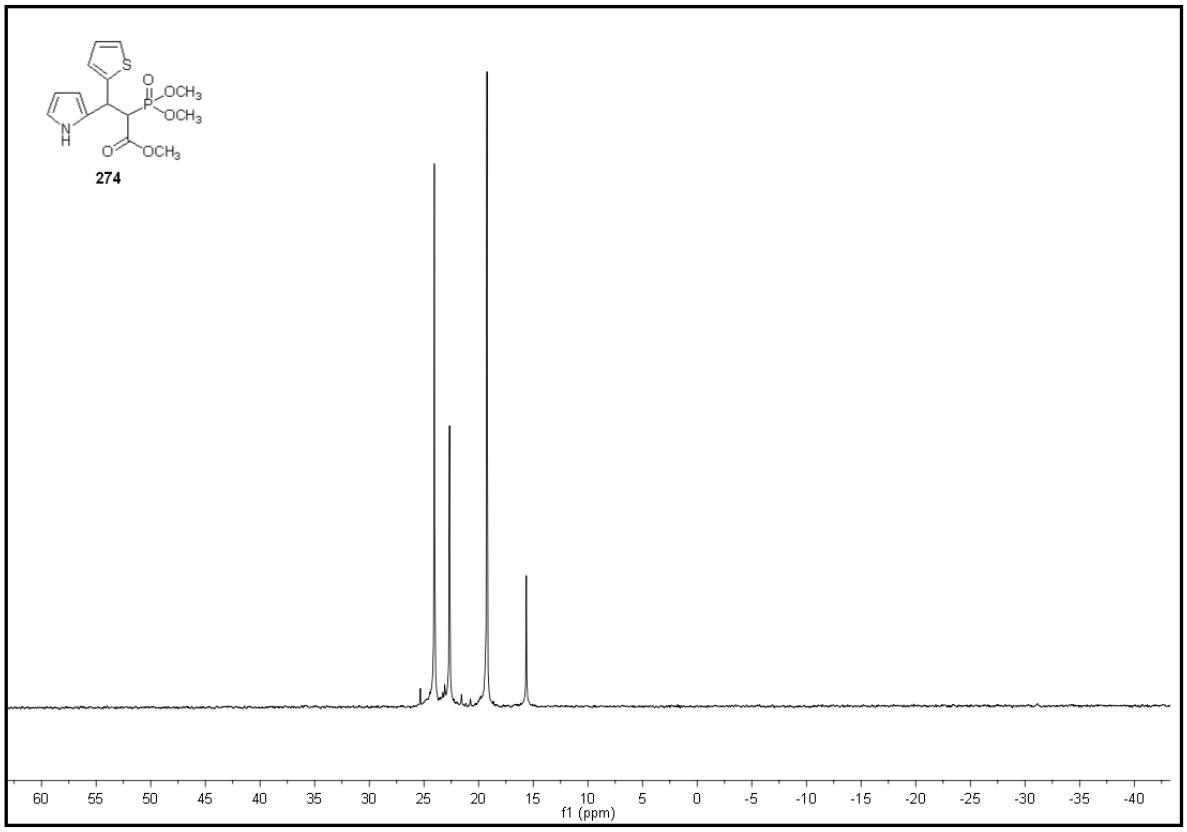


Figure A.168. ^{31}P NMR spectrum of compound **274**

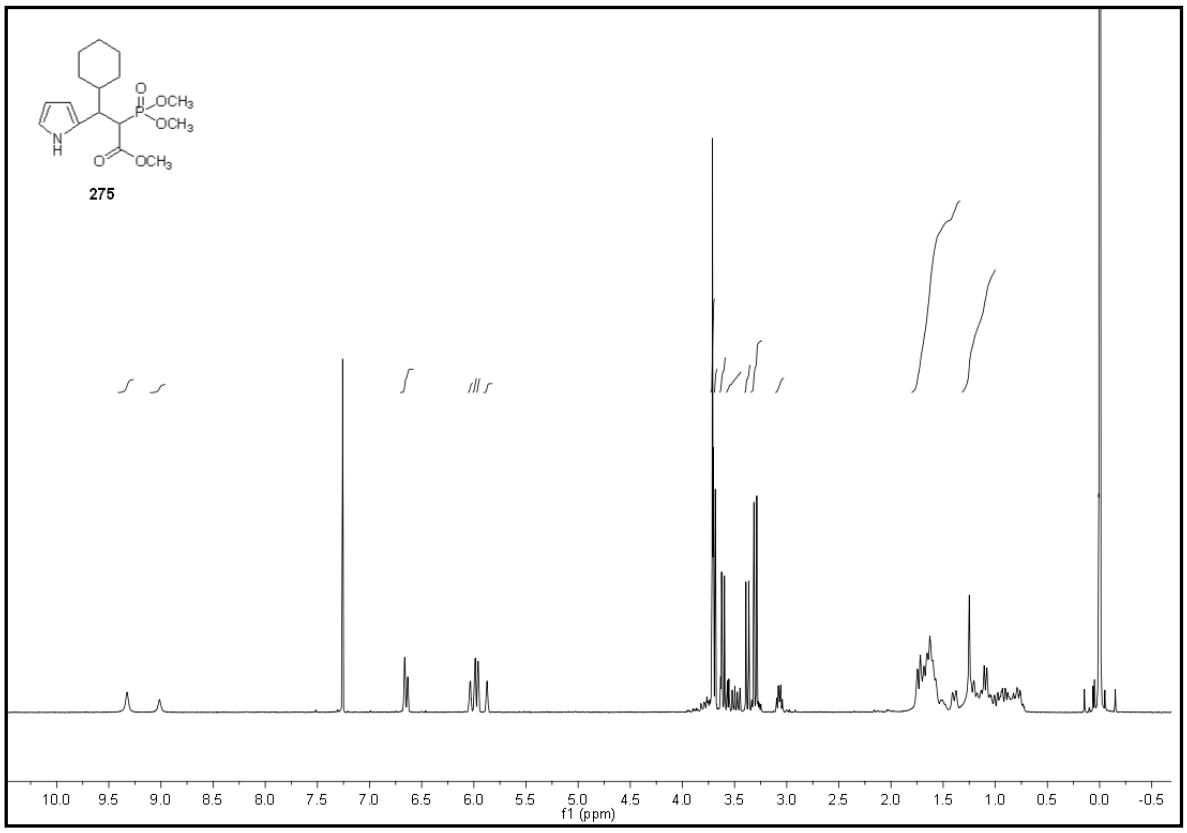


Figure A.169. ^{1}H NMR spectrum of compound **275**

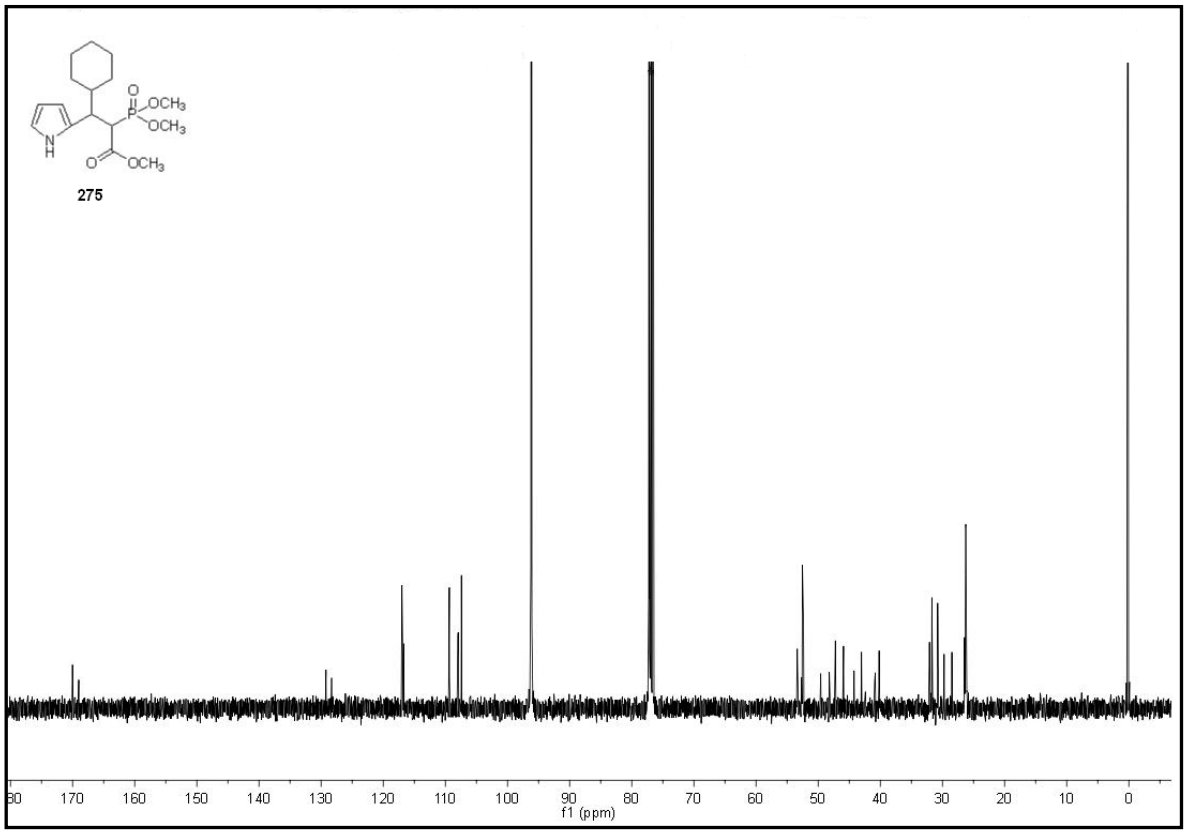


Figure A.170. ^{13}C NMR spectrum of compound **275**

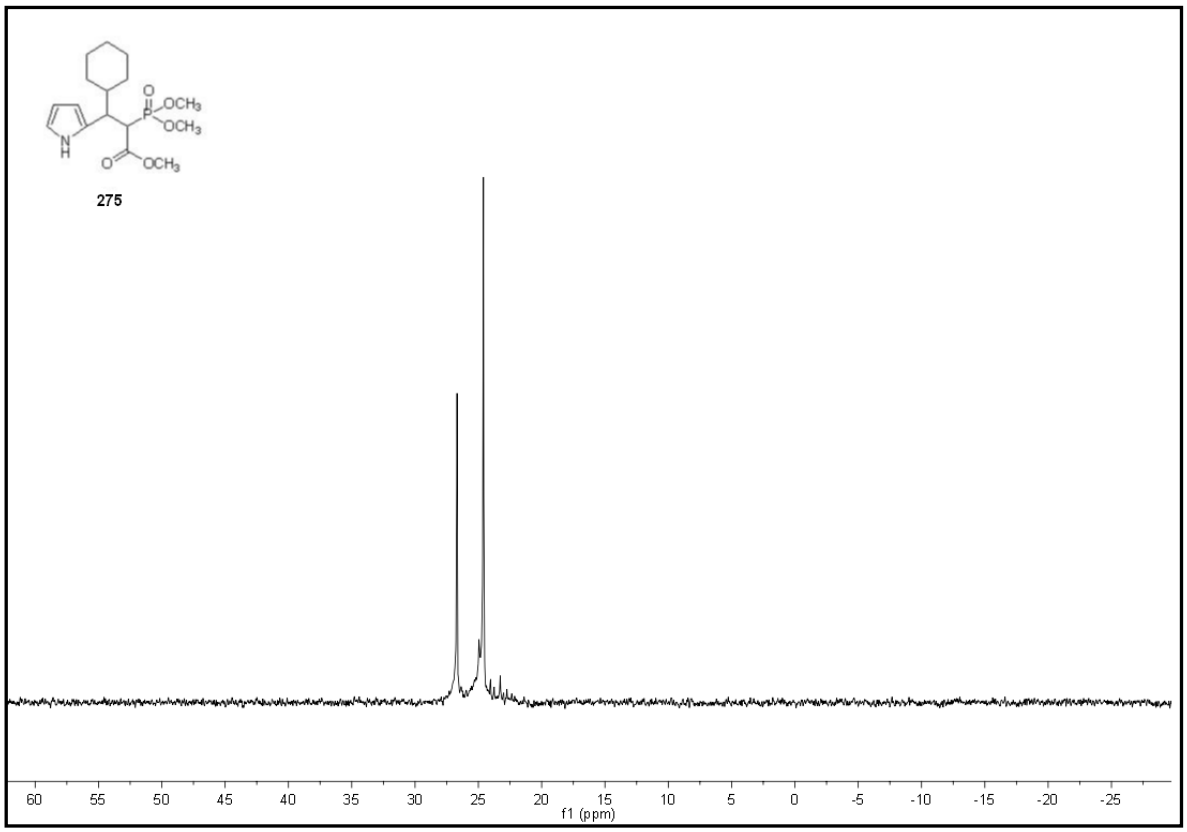


Figure A.171. ^{31}P NMR spectrum of compound **275**

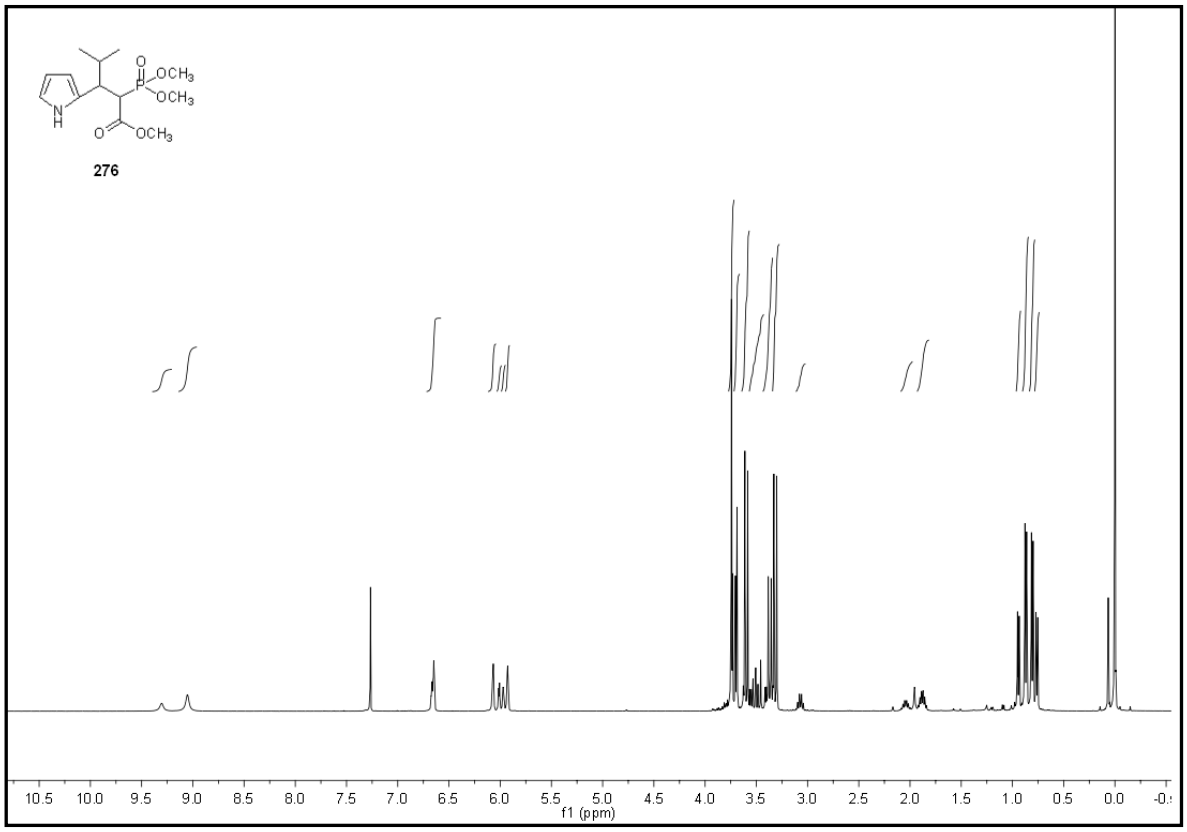


Figure A.172. ^{1}H NMR spectrum of compound **276**

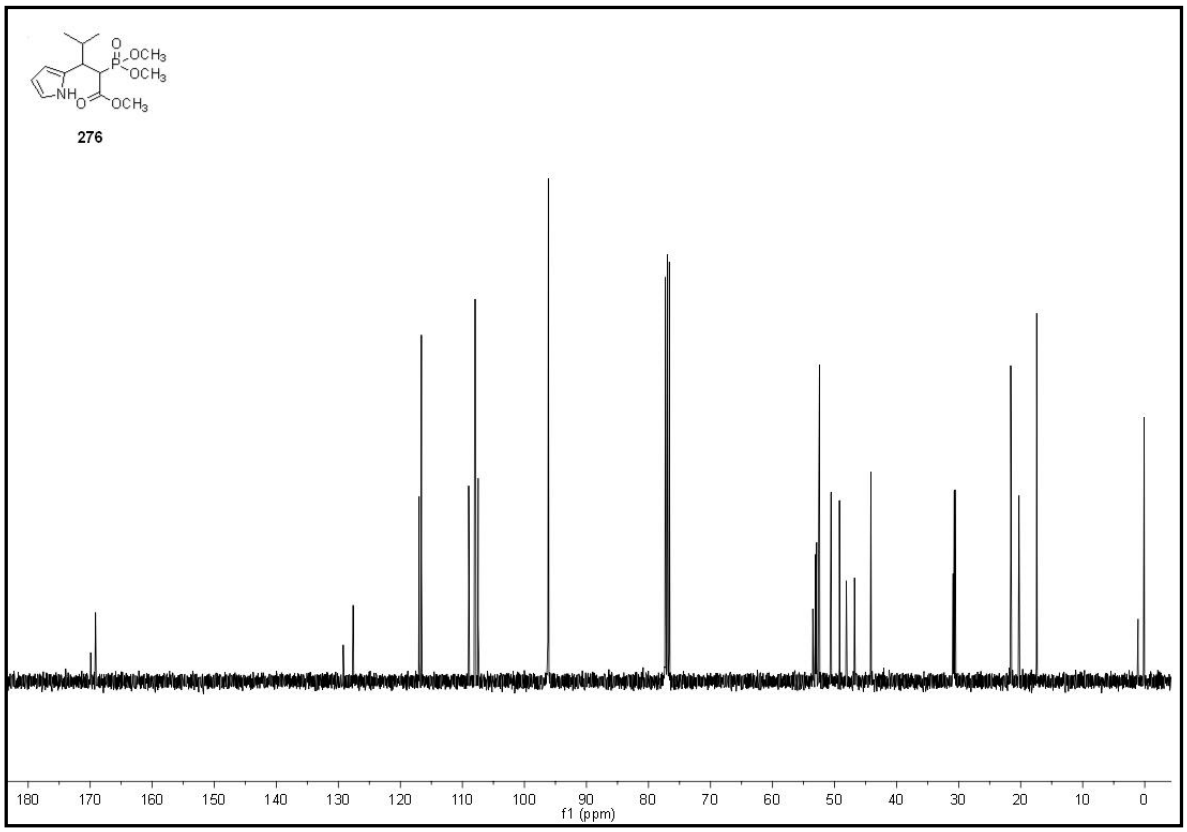


Figure A.173. ^{13}C NMR spectrum of compound **276**

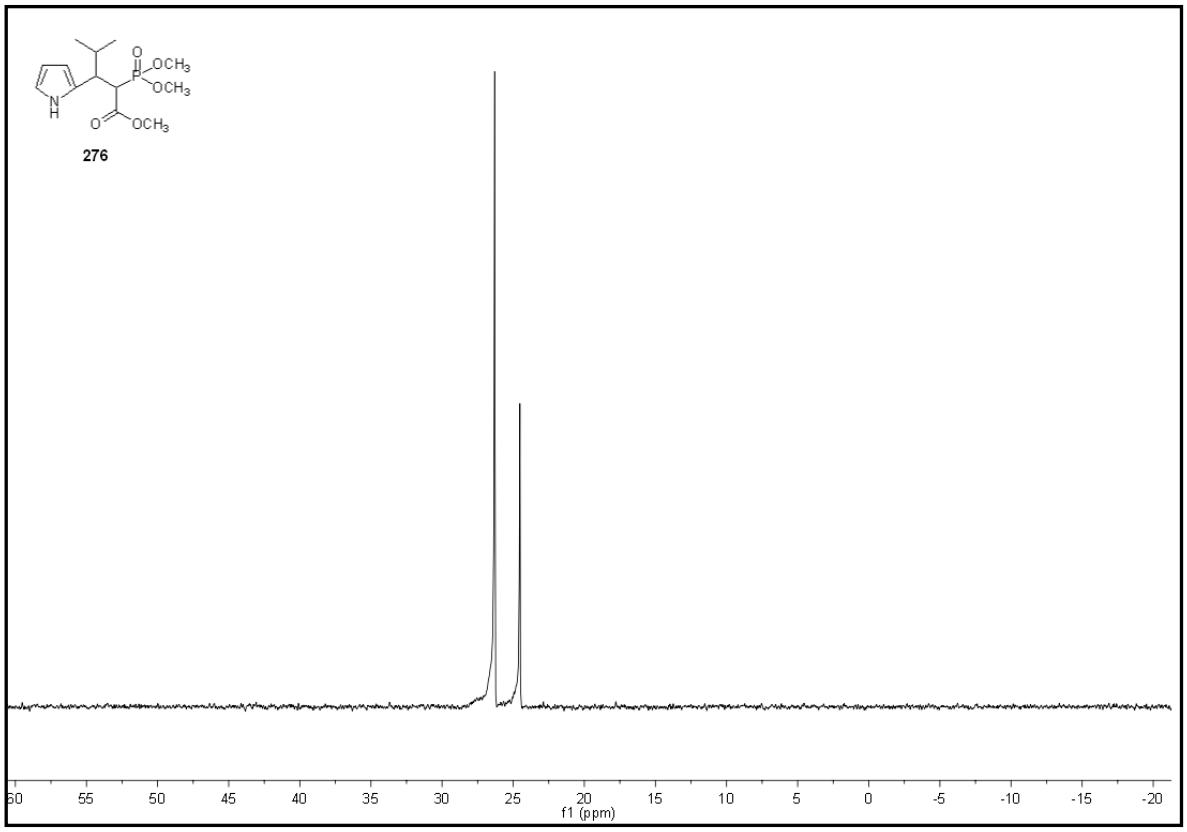


Figure A.174. ^{31}P NMR spectrum of compound **276**

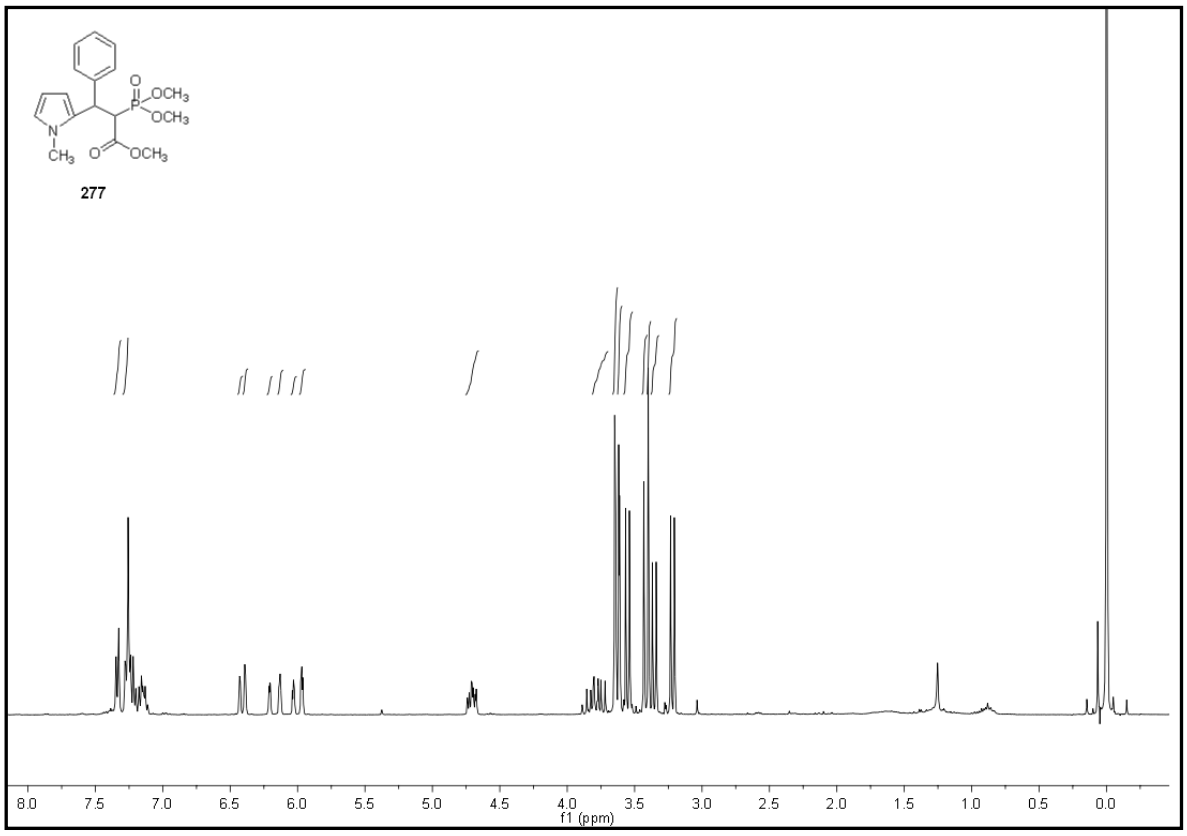


Figure A.175. ^{1}H NMR spectrum of compound **277**

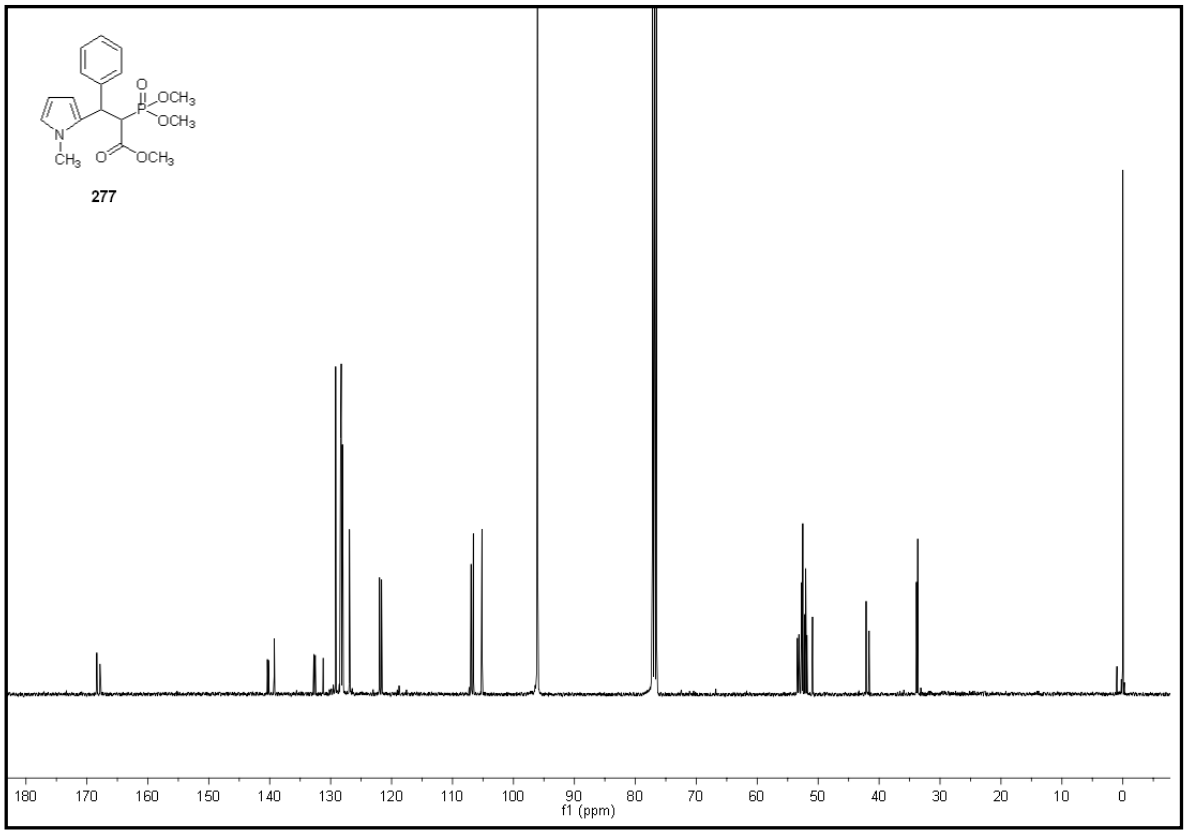


Figure A.176. ^{13}C NMR spectrum of compound **277**

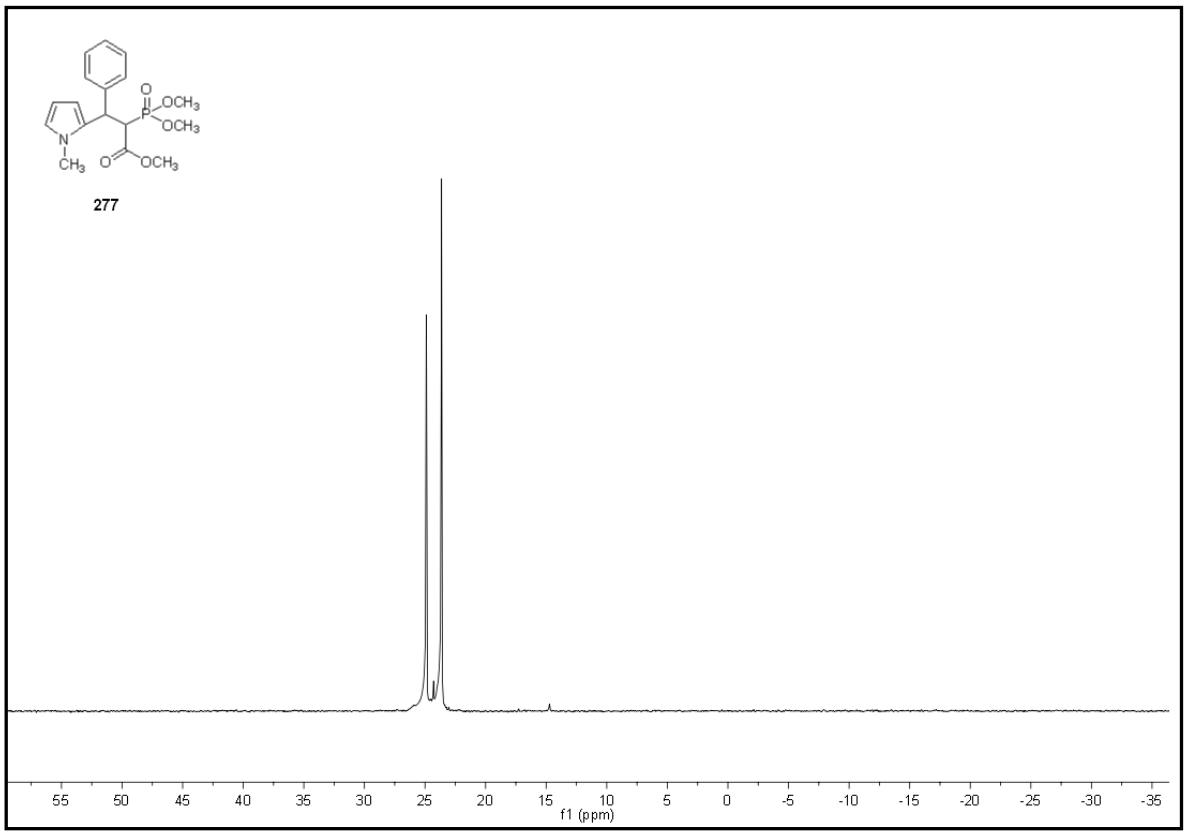


Figure A.177. ^{31}P NMR spectrum of compound **277**

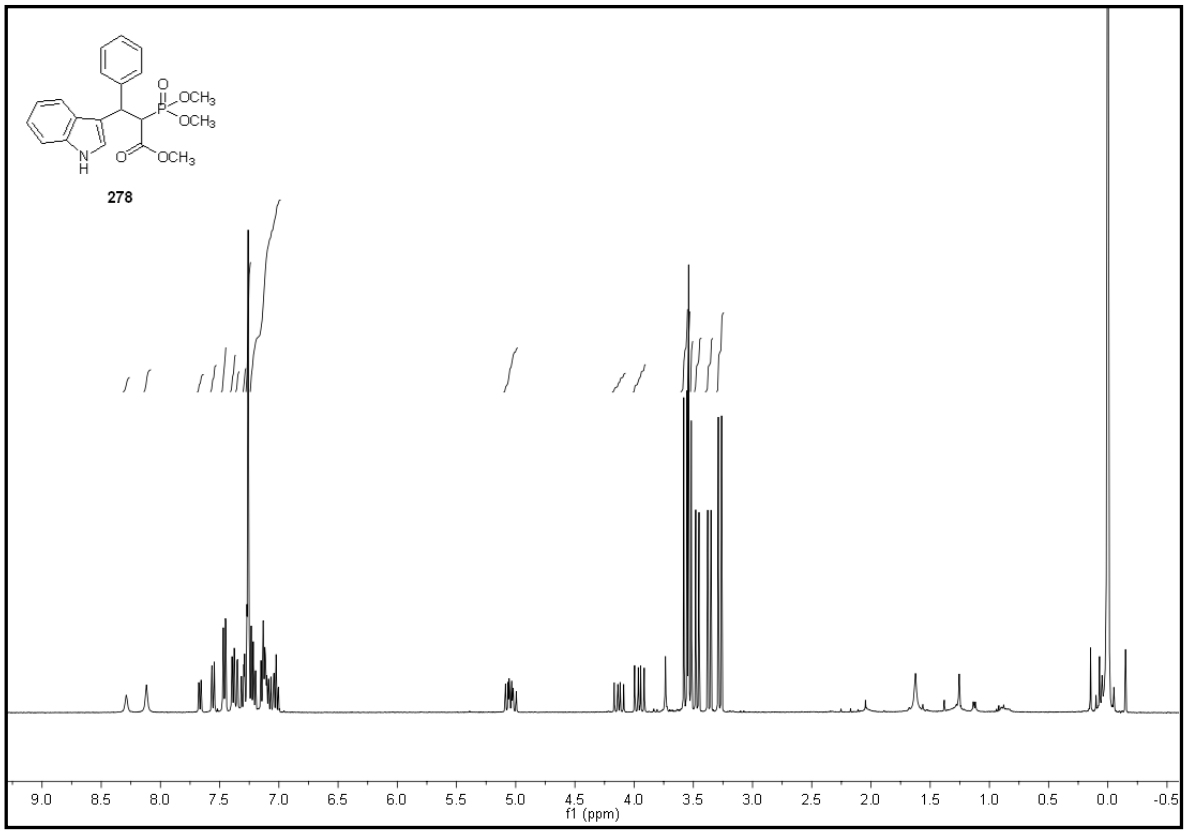


Figure A.178. ^{1}H NMR spectrum of compound **278**

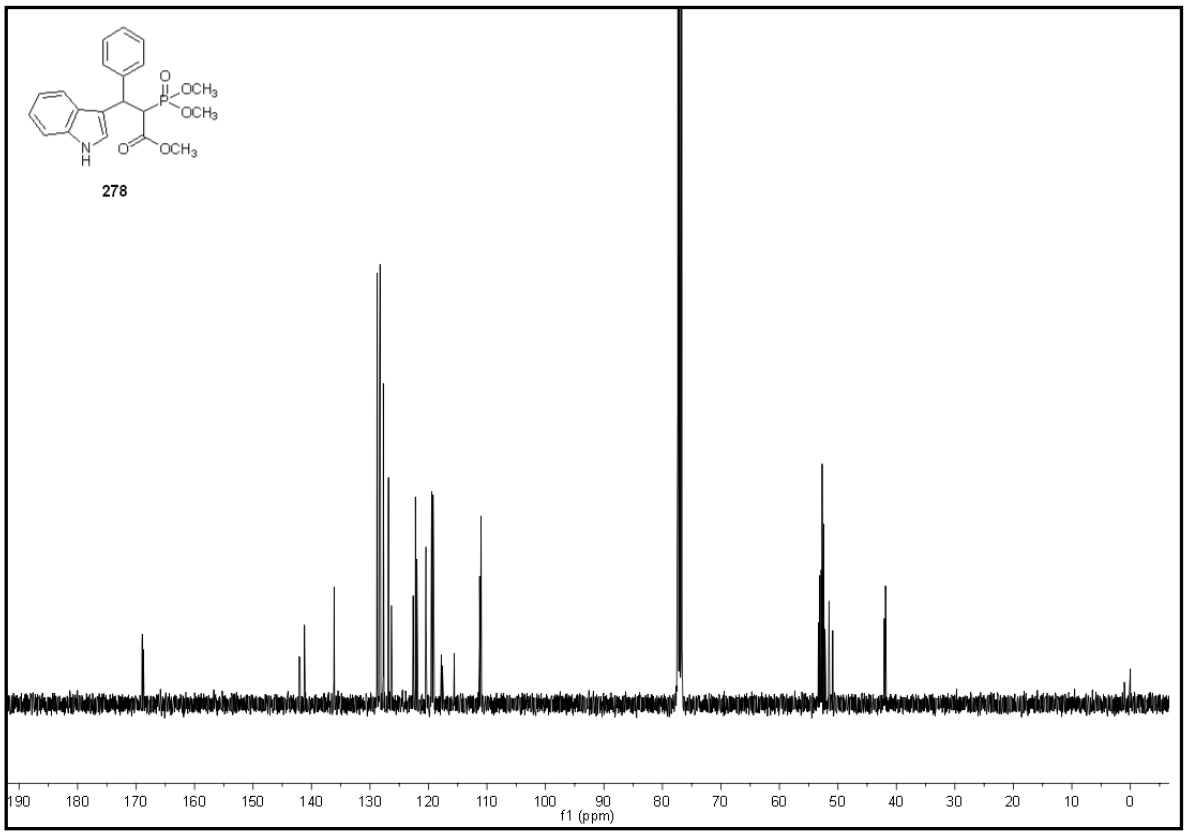


Figure A.179. ^{13}C NMR spectrum of compound **278**

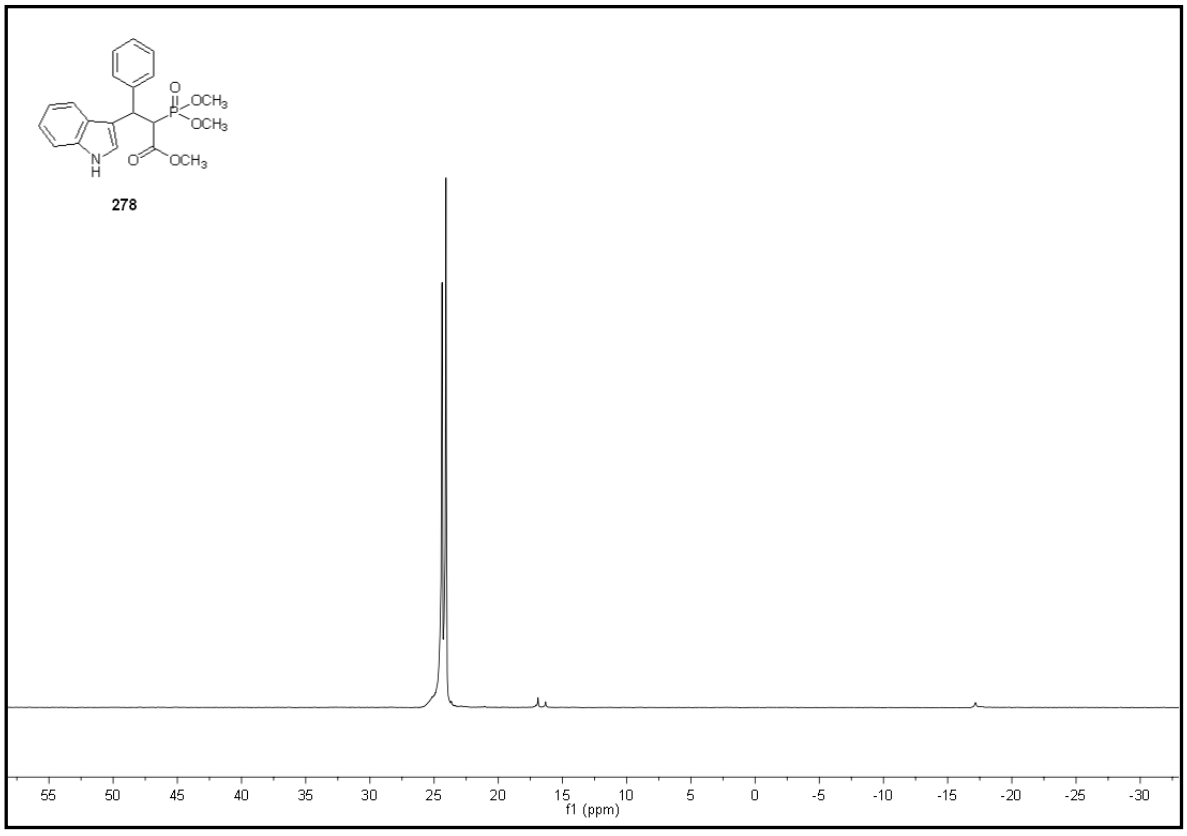


Figure A.180. ^{31}P NMR spectrum of compound **278**

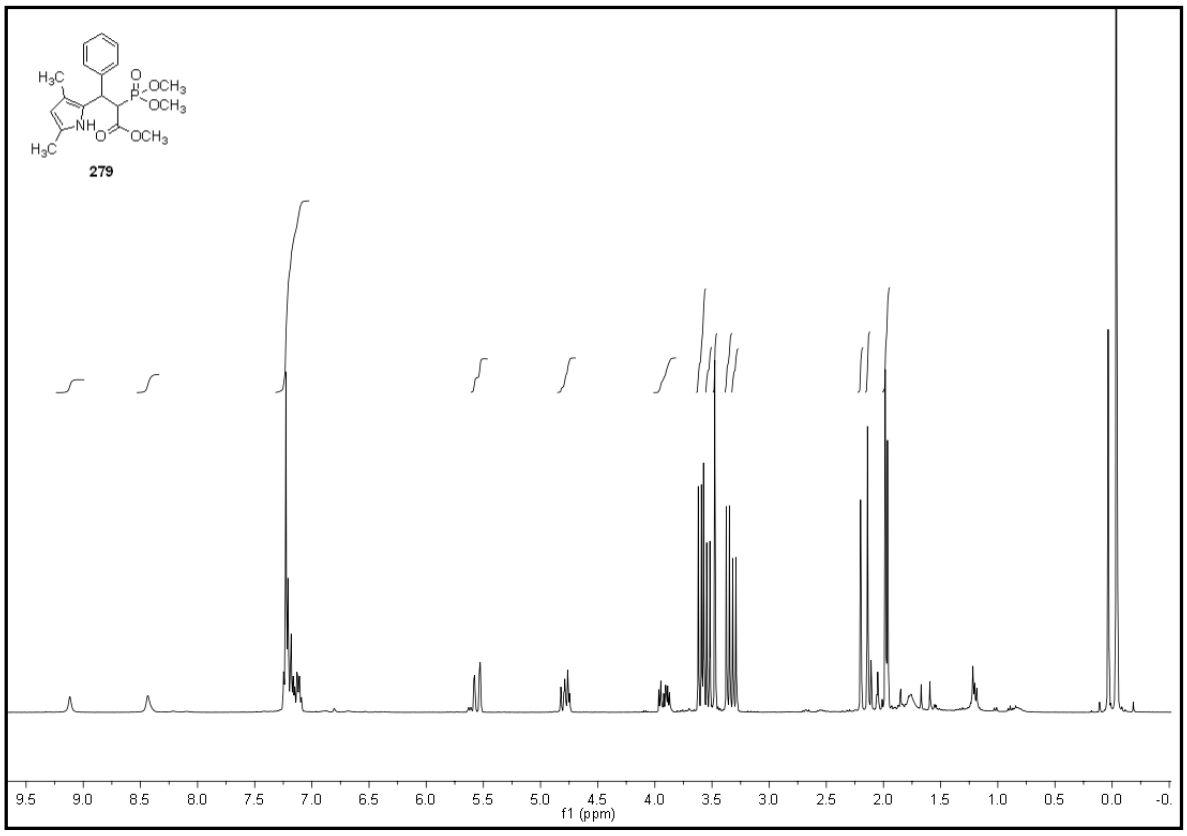


Figure A.181. ^{1}H NMR spectrum of compound **279**

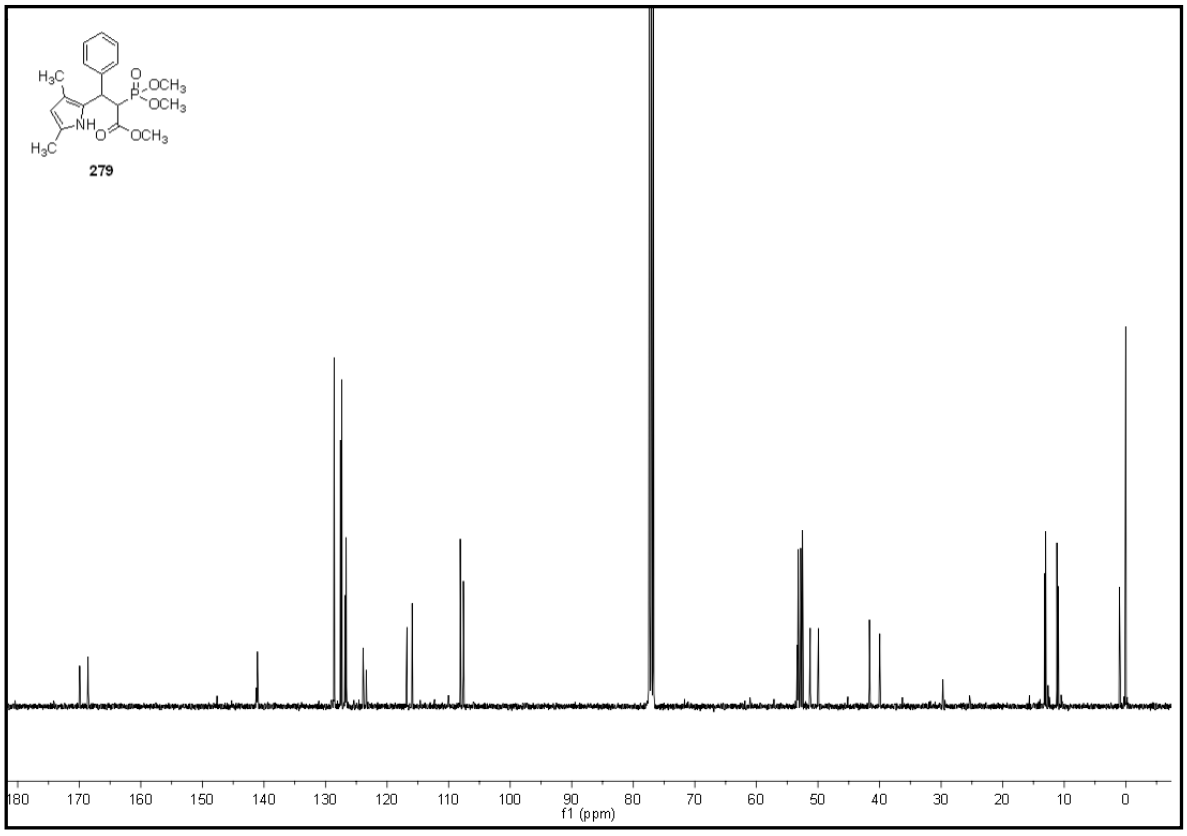


Figure A.182. ^{13}C NMR spectrum of compound **279**

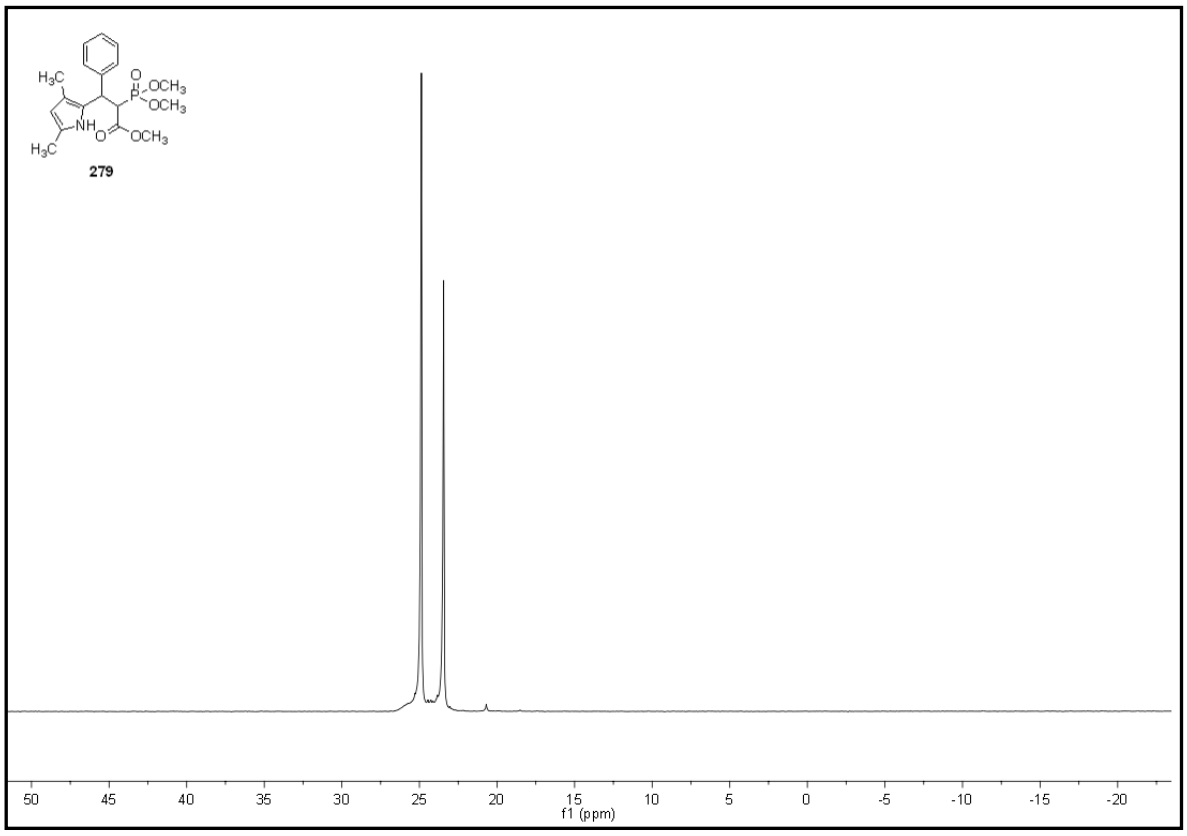


Figure A.183. ^{31}P NMR spectrum of compound **279**

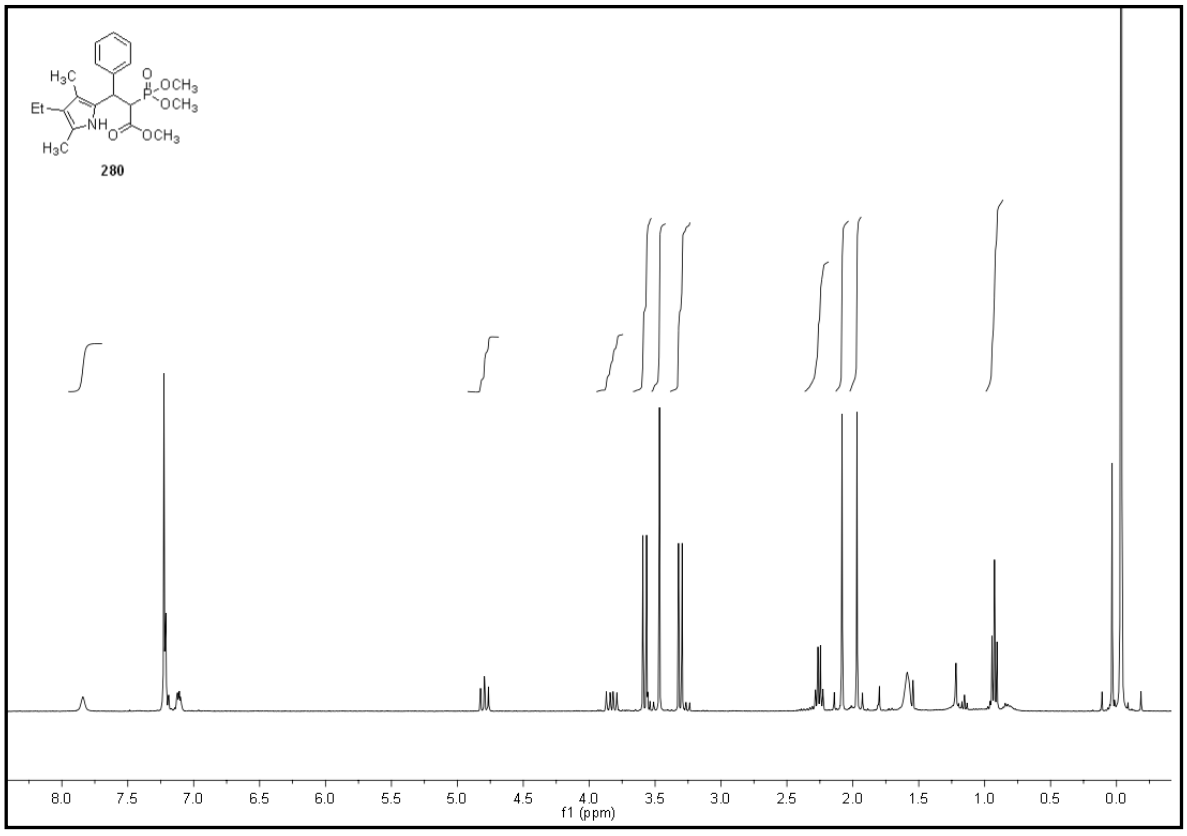


Figure A.184. ^{1}H NMR spectrum of compound **280**

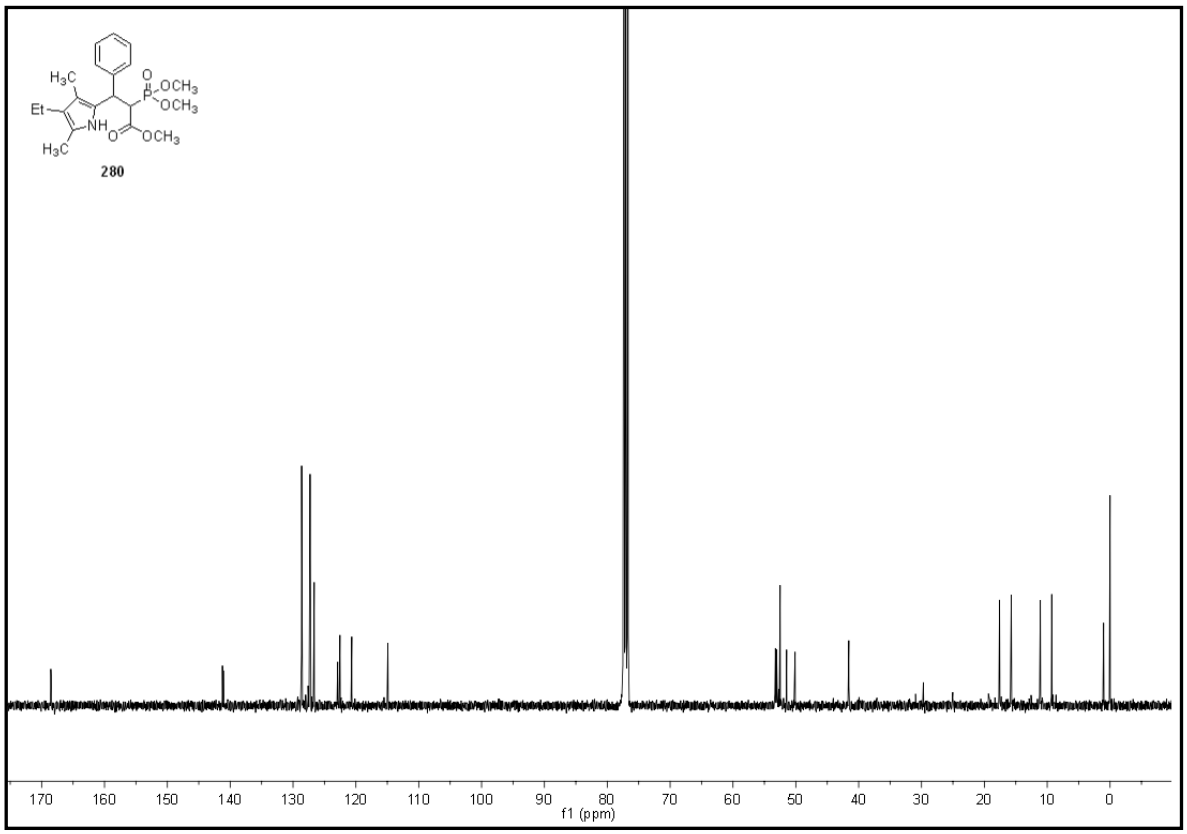


Figure A.185. ^{13}C NMR spectrum of compound **280**

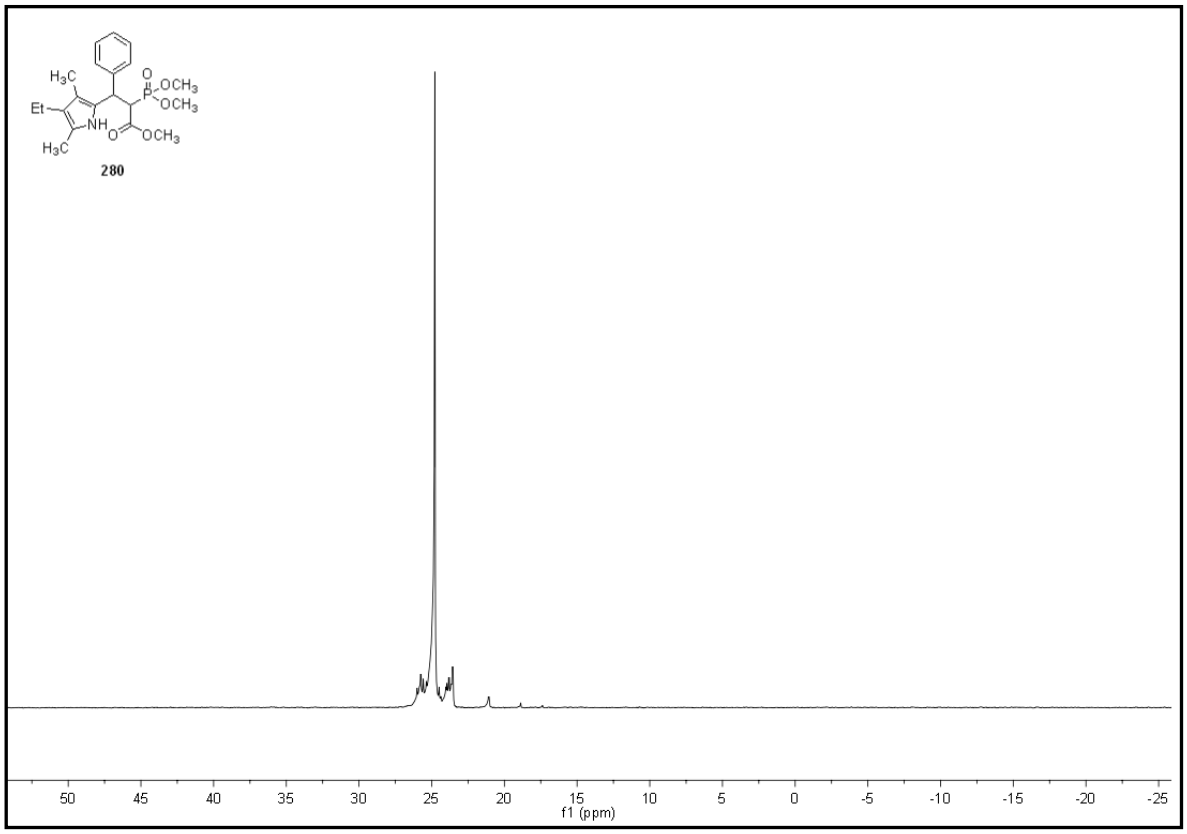


Figure A.186. ^{31}P NMR spectrum of compound **280**

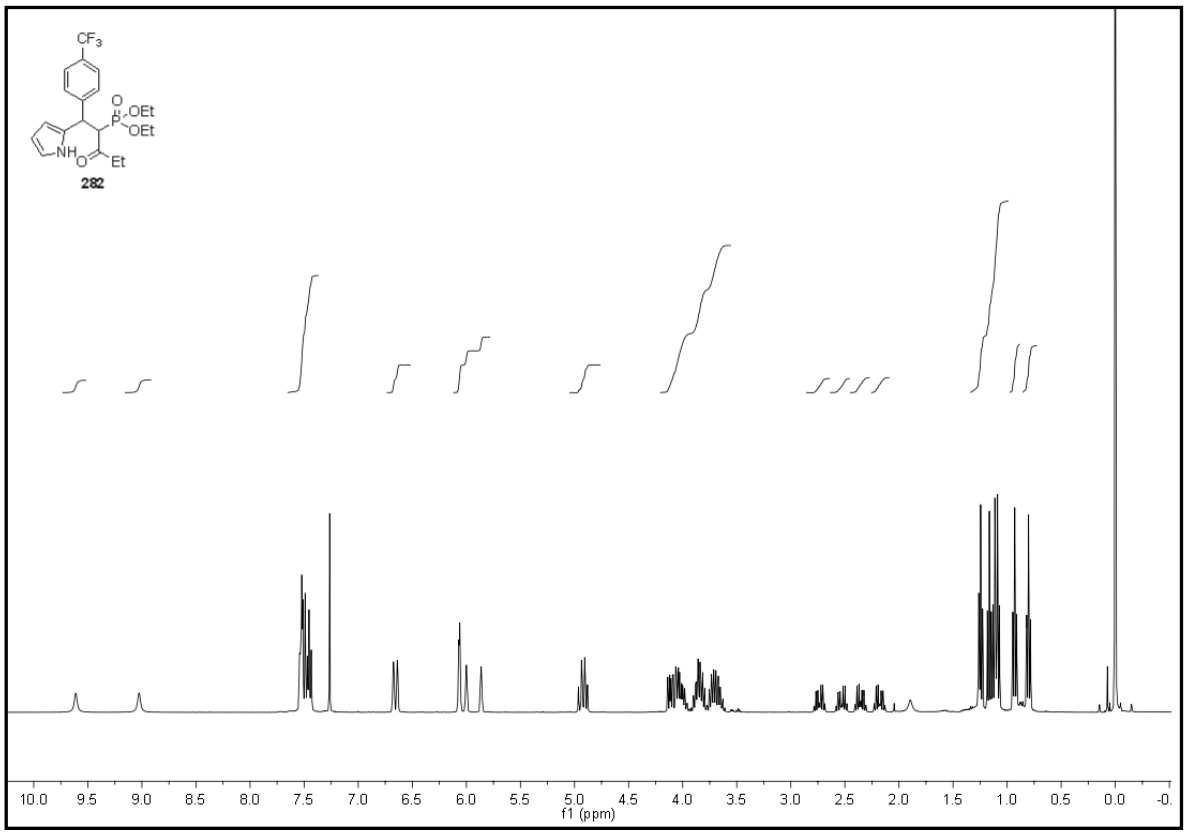


Figure A.187. ^{1}H NMR spectrum of compound **282**

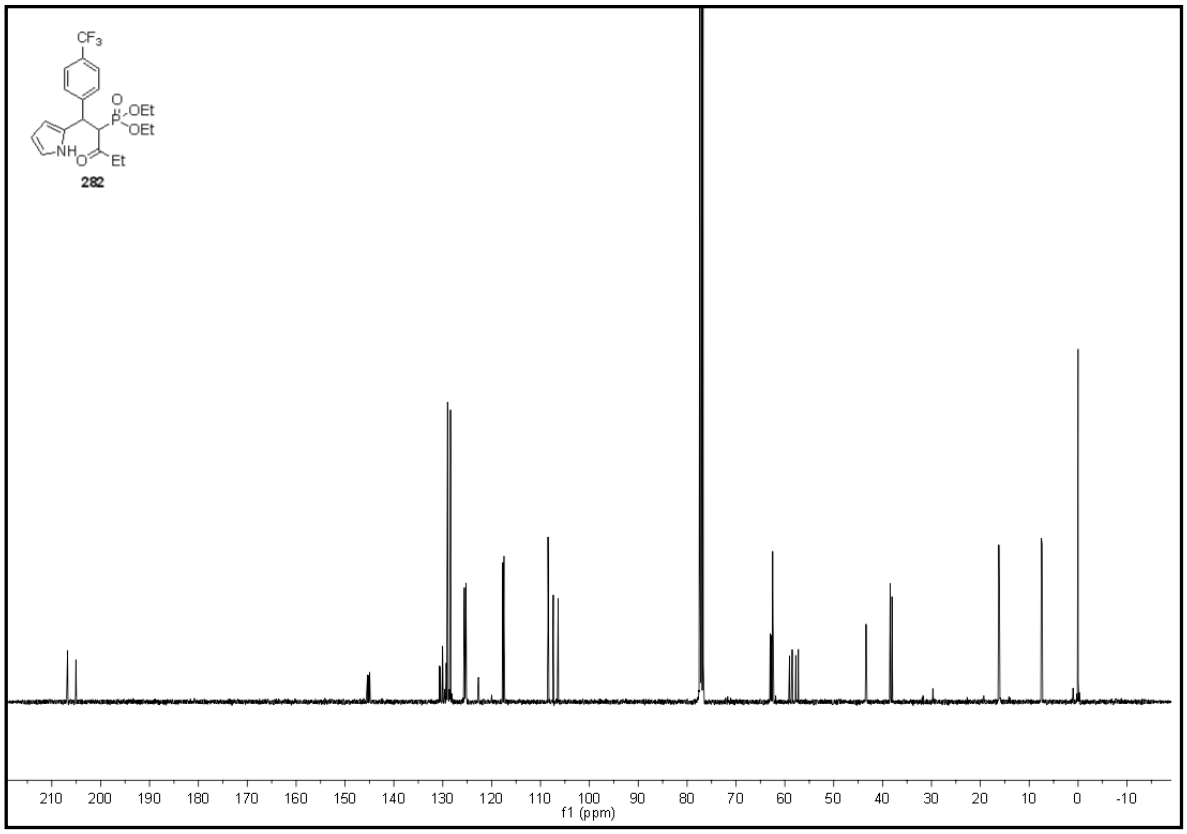


Figure A.188. ^{13}C NMR spectrum of compound **282**

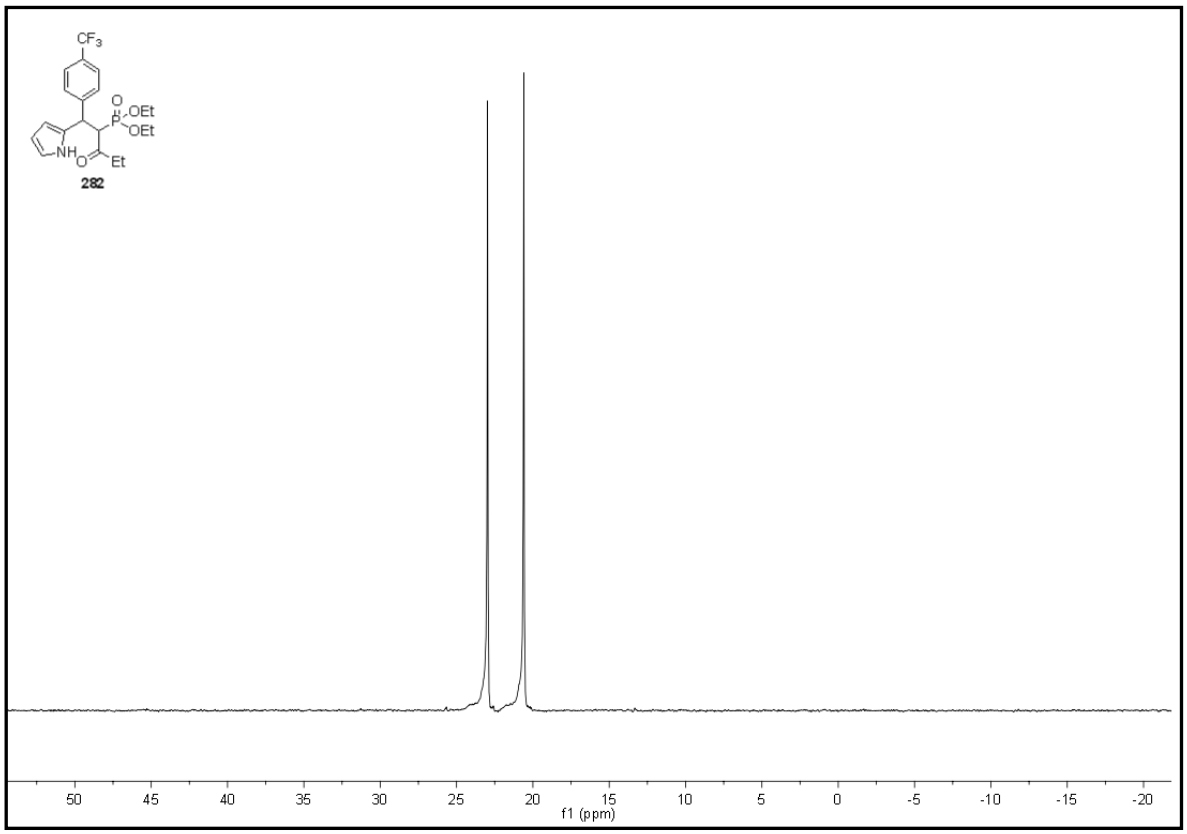


Figure A.189. ^{31}P NMR spectrum of compound **282**

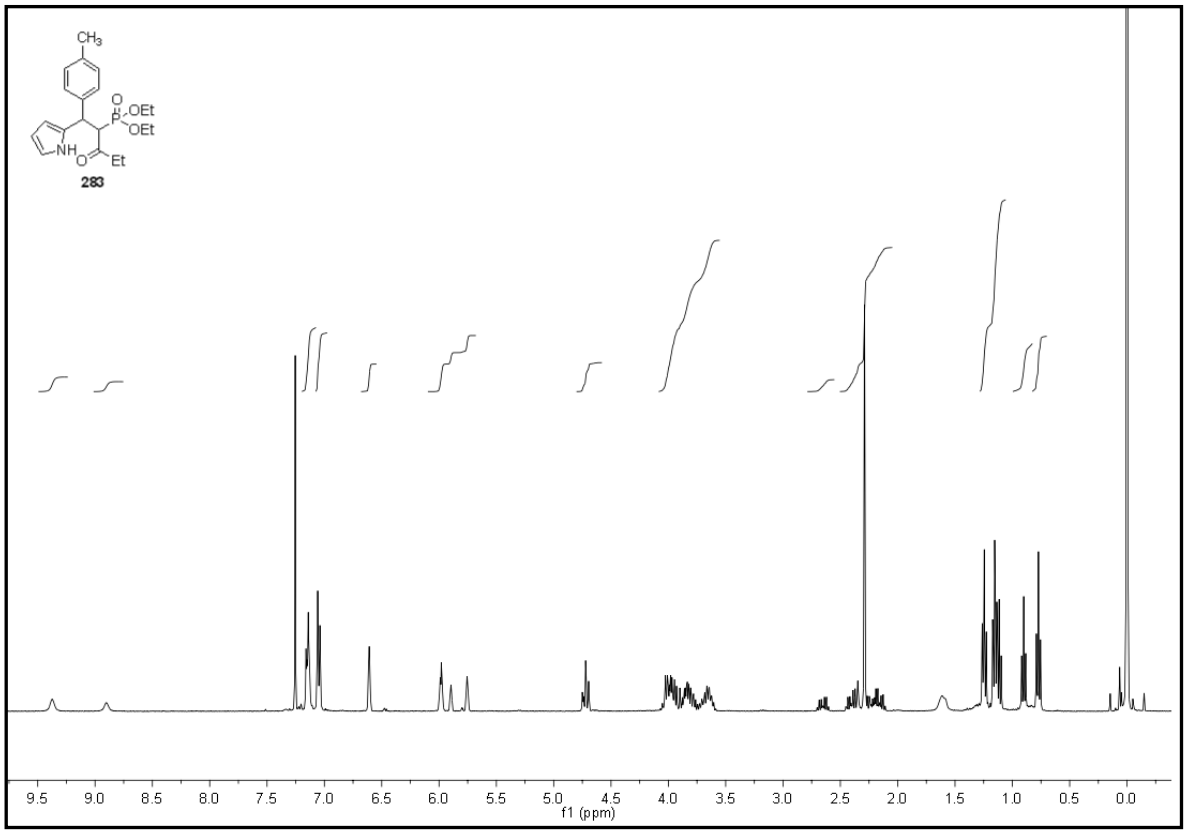


Figure A.190. ^{1}H NMR spectrum of compound **283**

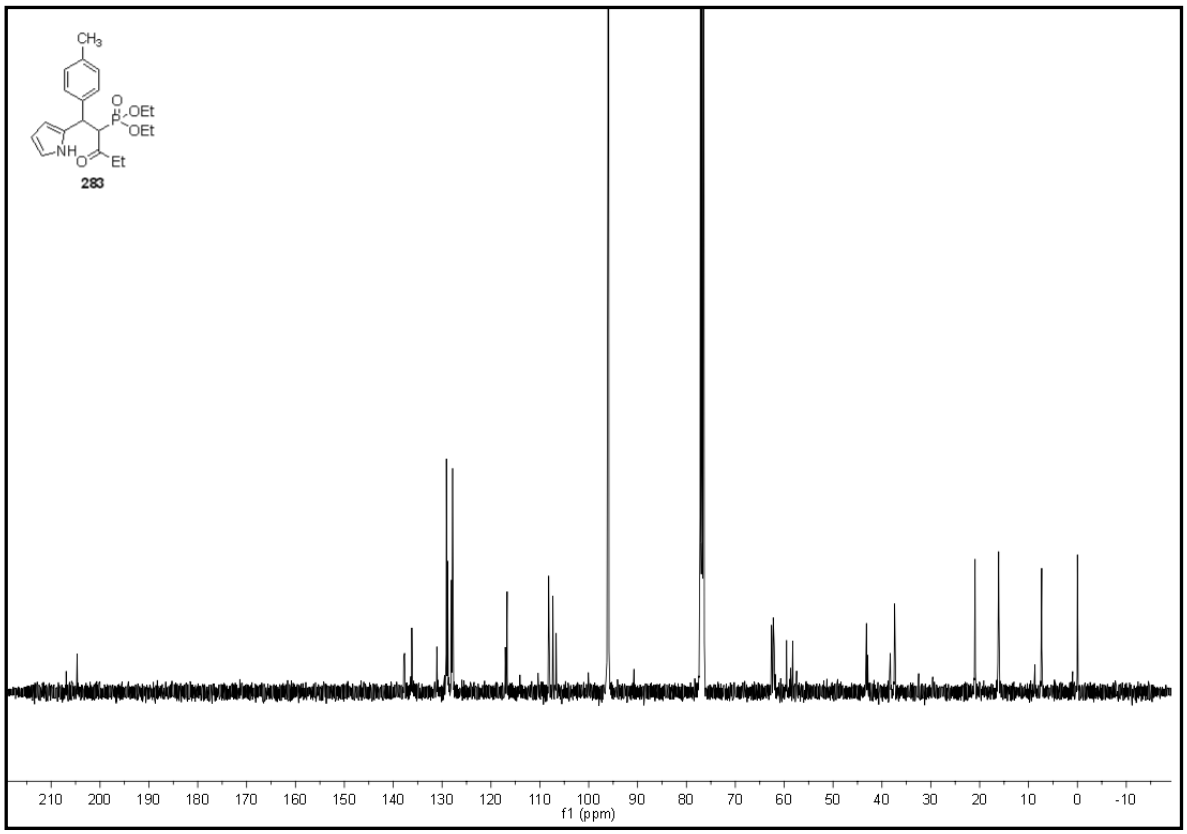


Figure A.191. ^{13}C NMR spectrum of compound **283**

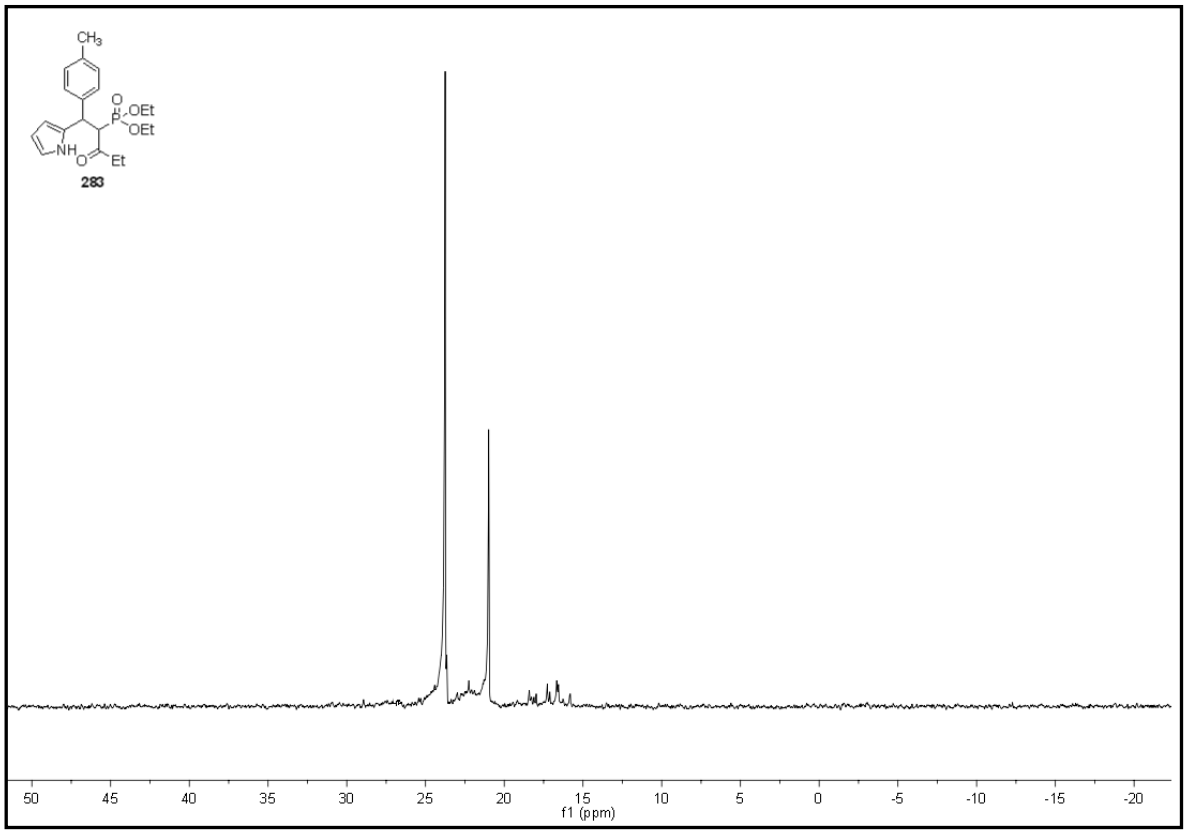


Figure A.192. ^{31}P NMR spectrum of compound **283**

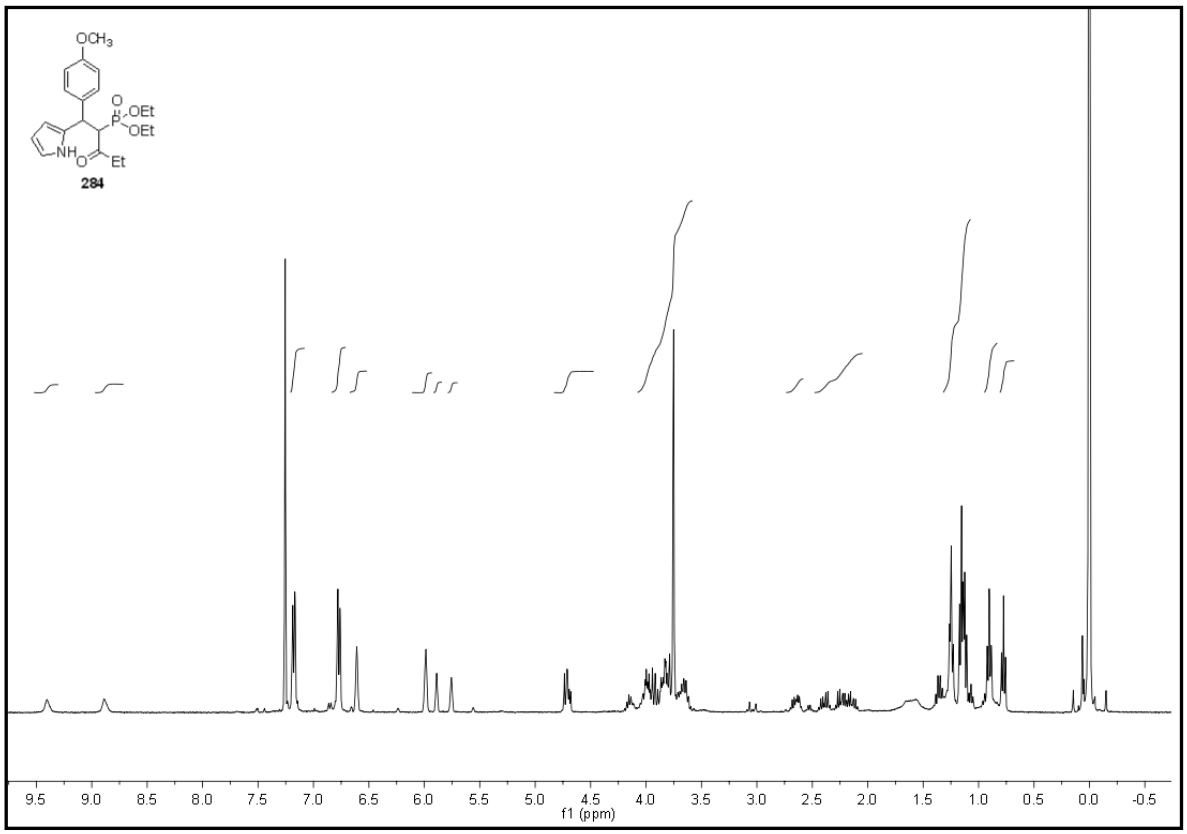


Figure A.193. ^{1}H NMR spectrum of compound **284**

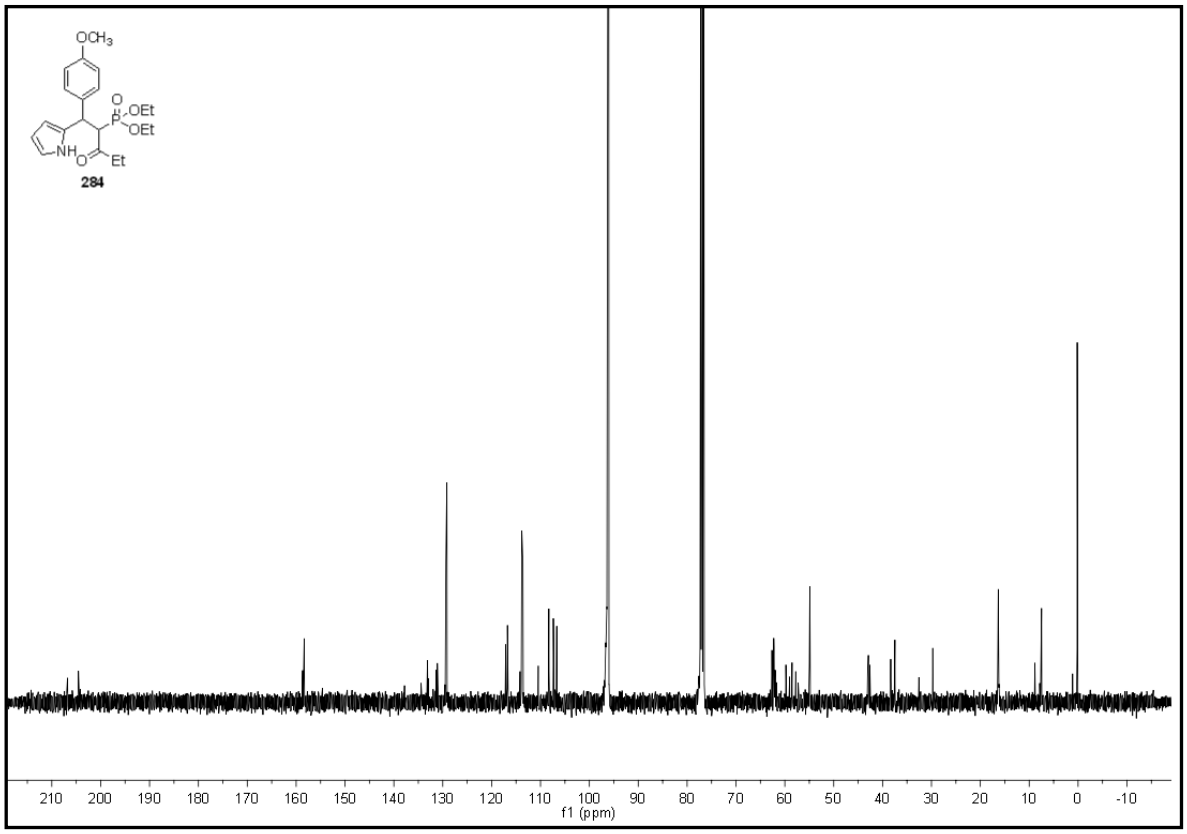


Figure A.194. ^{13}C NMR spectrum of compound **284**

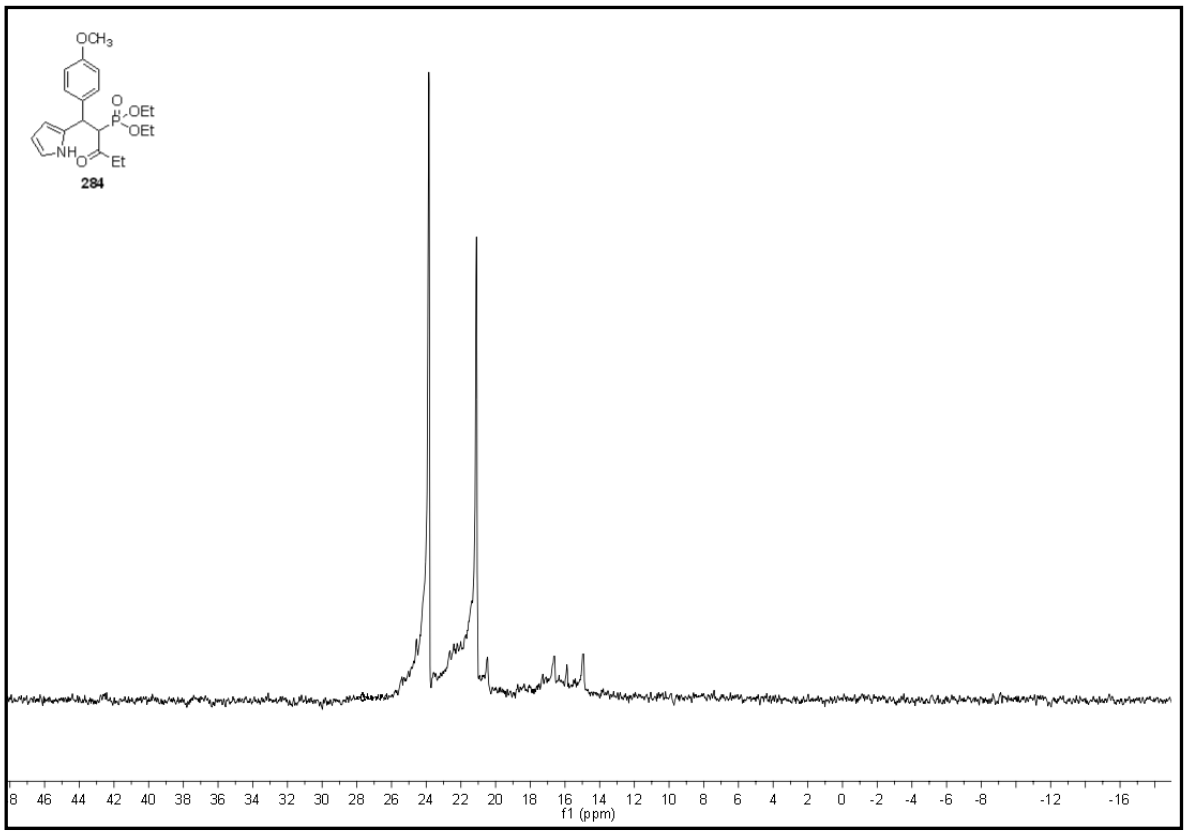


Figure A.195. ^{31}P NMR spectrum of compound **284**

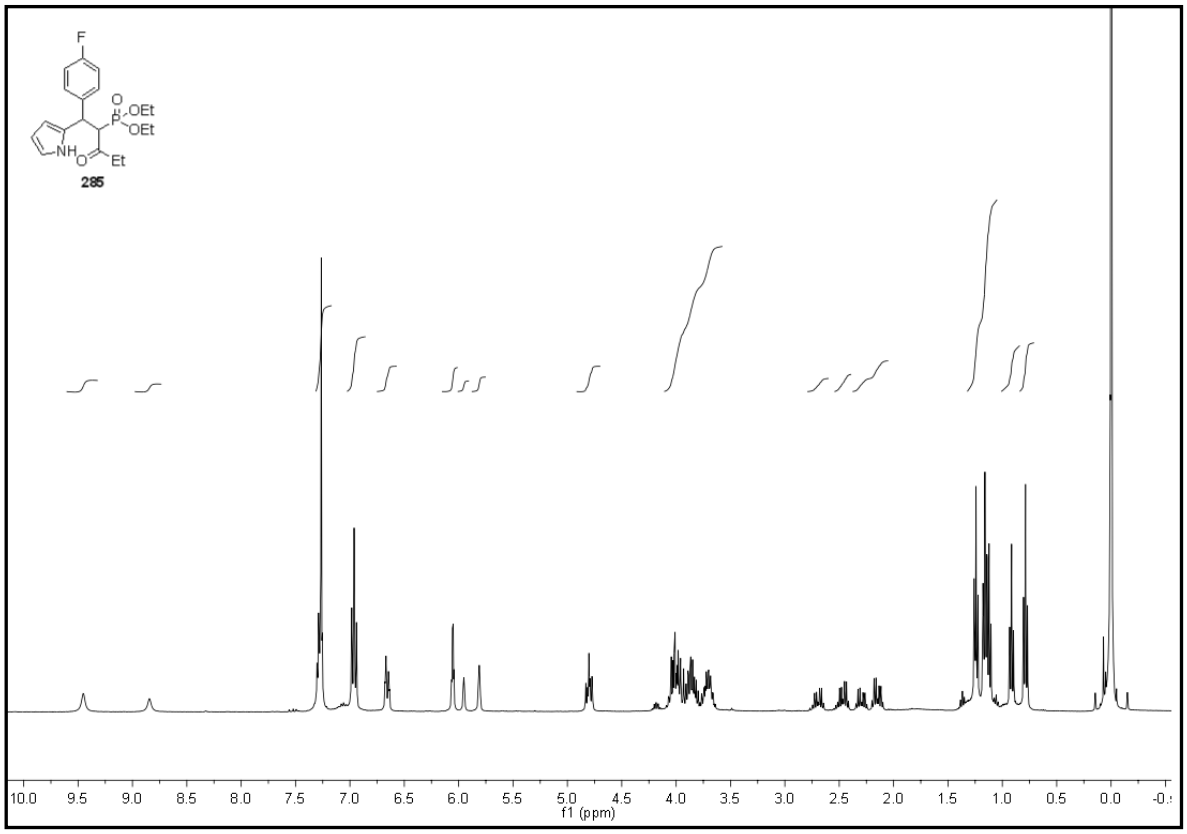


Figure A.196. ^{1}H NMR spectrum of compound **285**

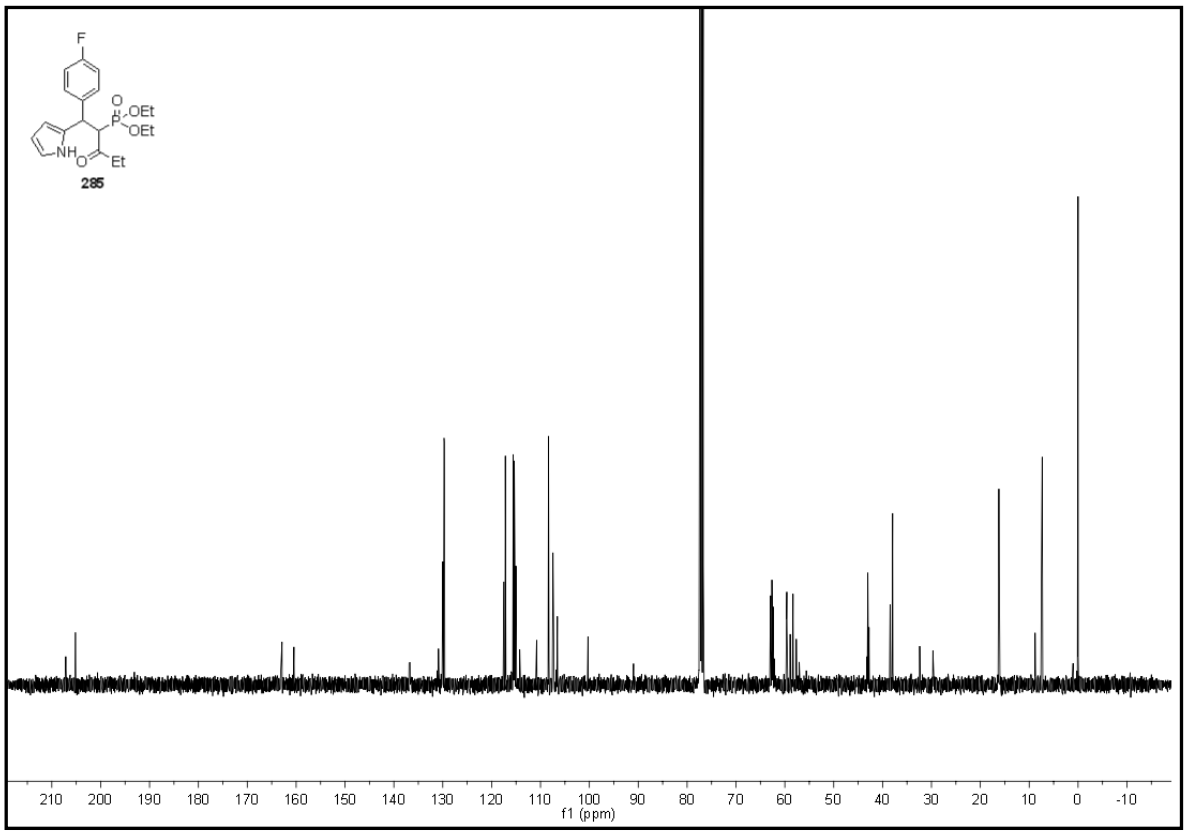


Figure A.197. ^{13}C NMR spectrum of compound **285**

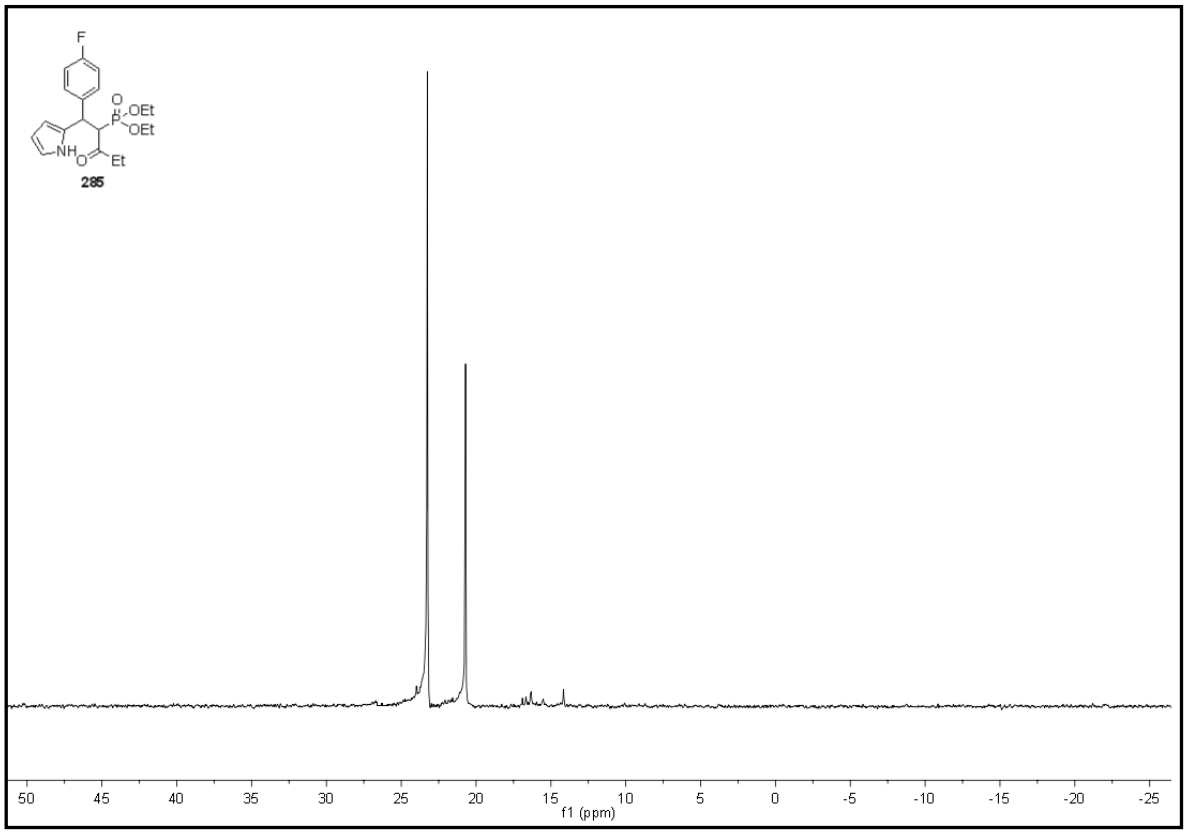


Figure A.198. ^{31}P NMR spectrum of compound **285**

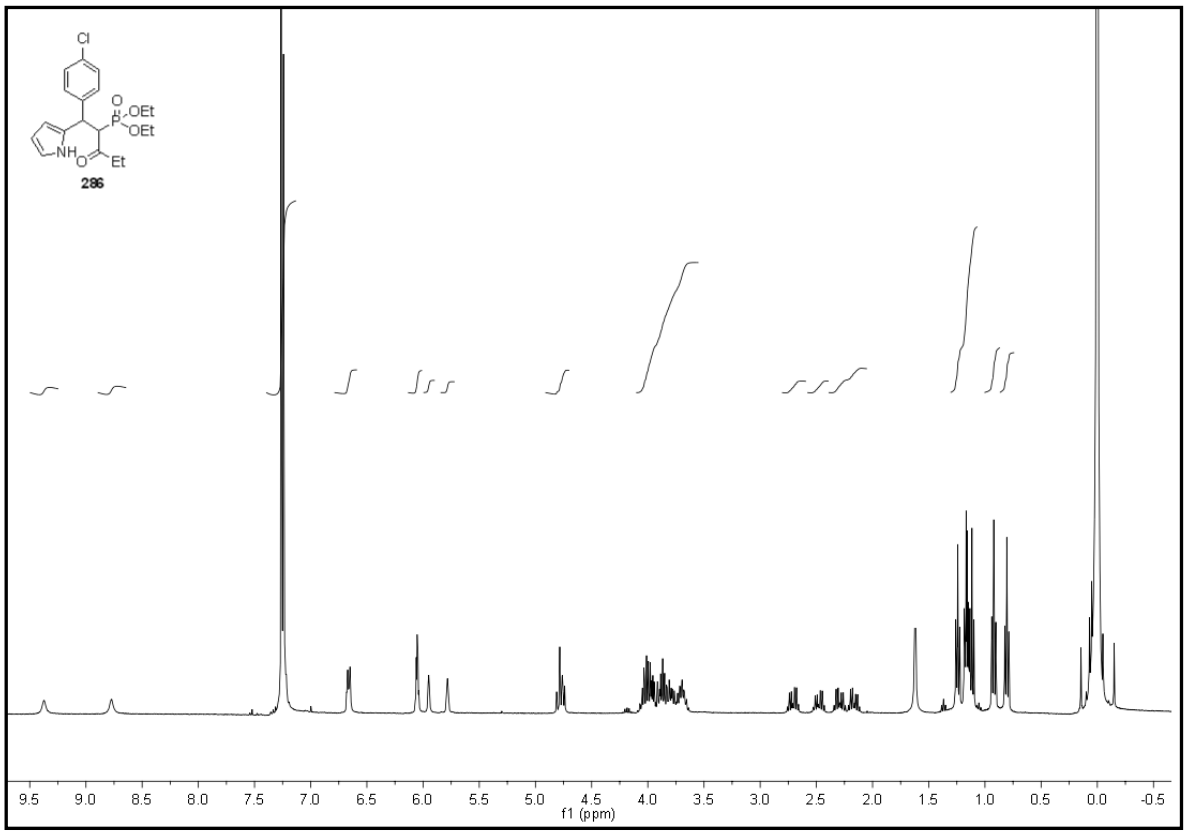


Figure A.199. ^{1}H NMR spectrum of compound **286**

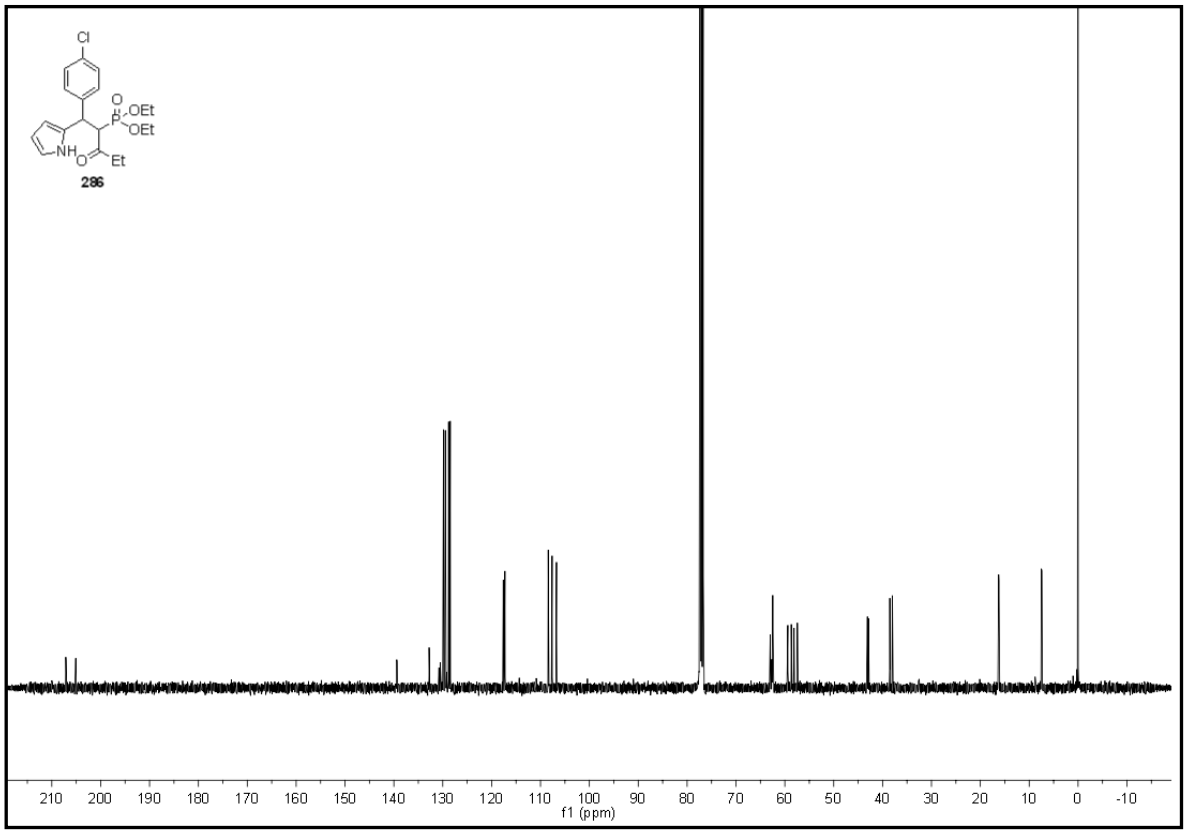


Figure A.200. ^{13}C NMR spectrum of compound **286**

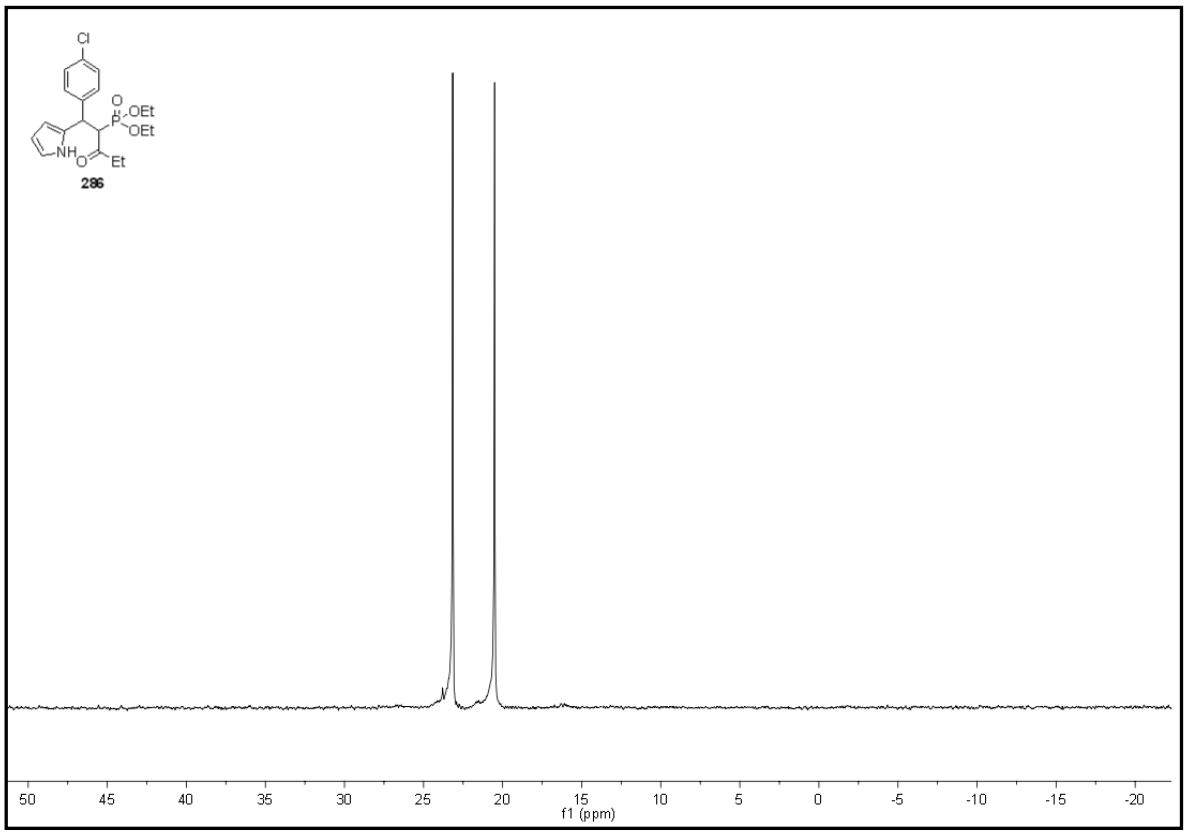


Figure A.201. ^{31}P NMR spectrum of compound **286**

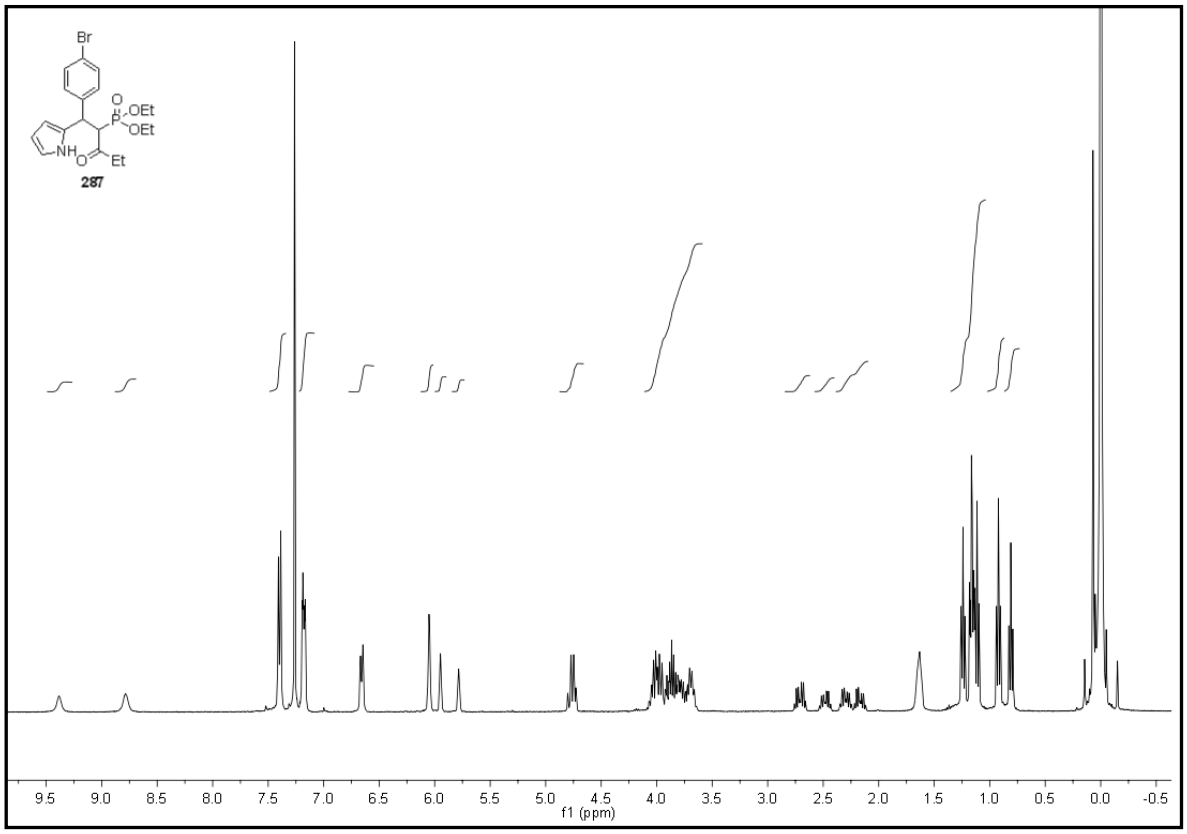


Figure A.202. ^{1}H NMR spectrum of compound **287**

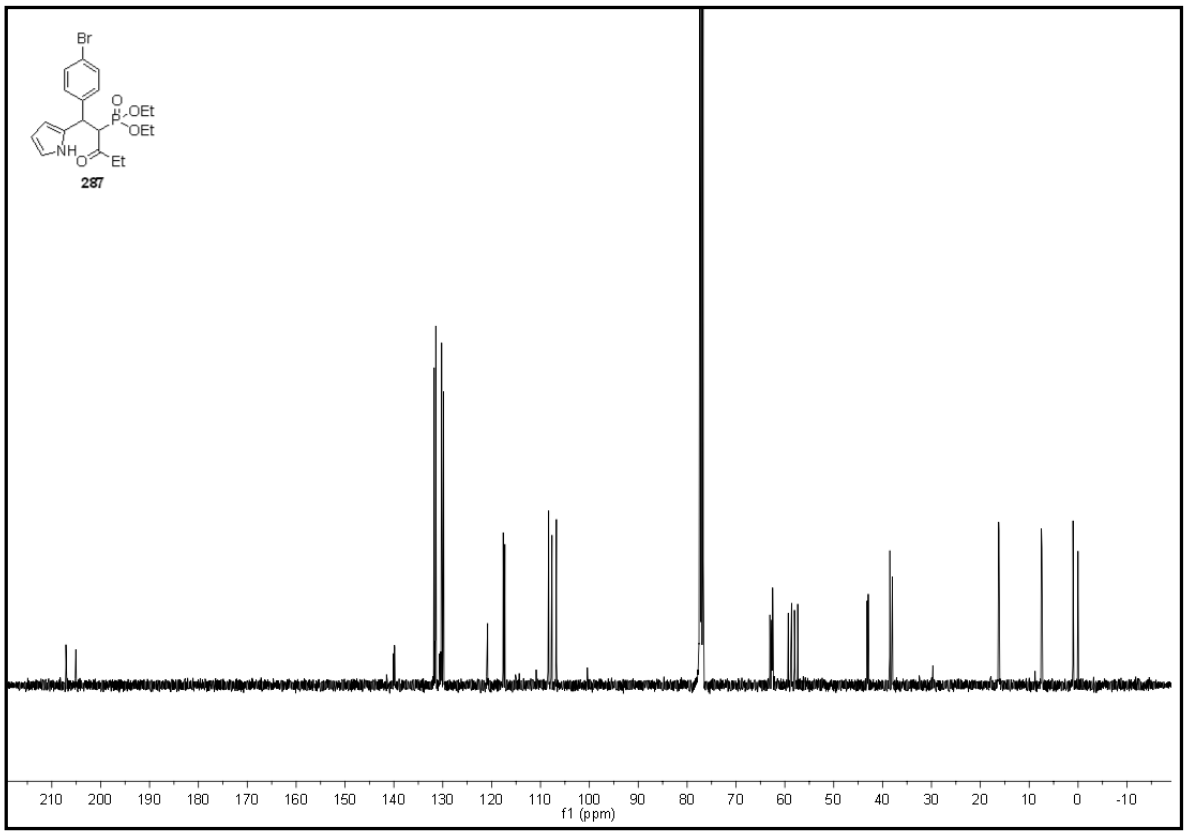


Figure A.203. ^{13}C NMR spectrum of compound **287**

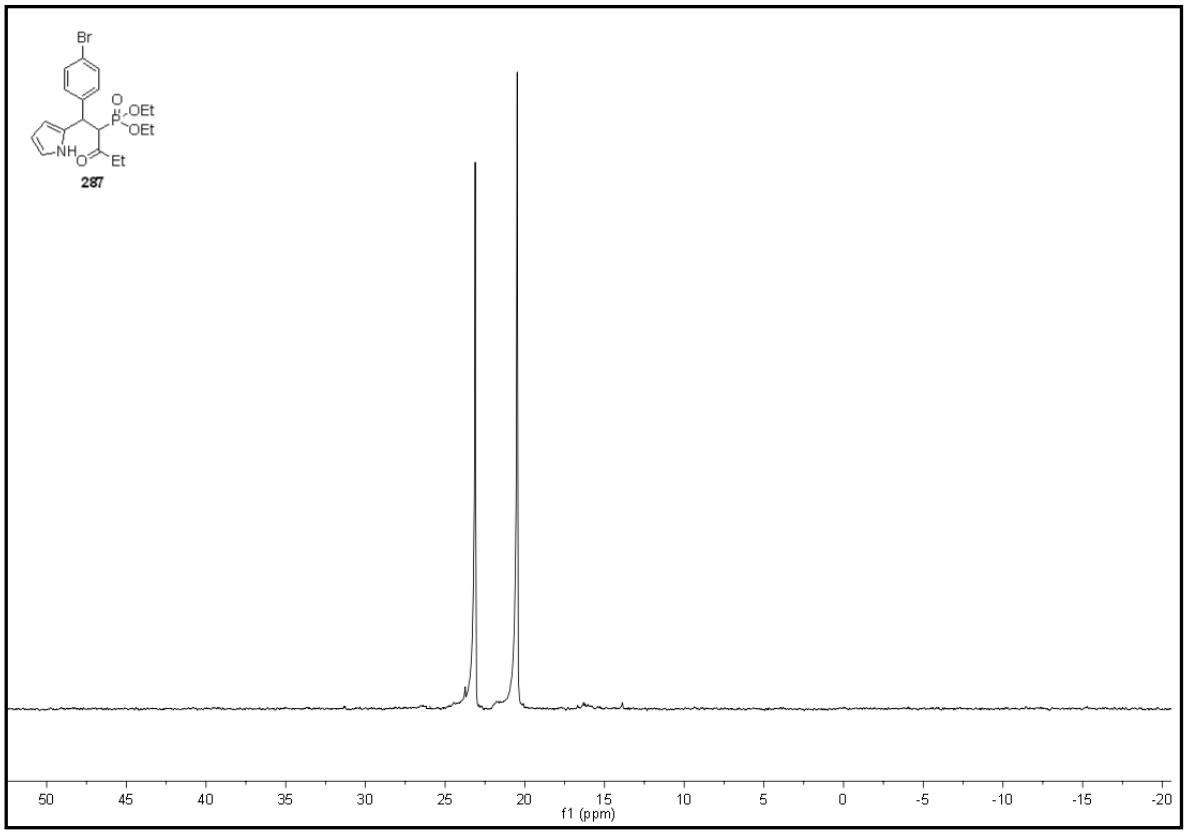


Figure A.204. ^{31}P NMR spectrum of compound **287**

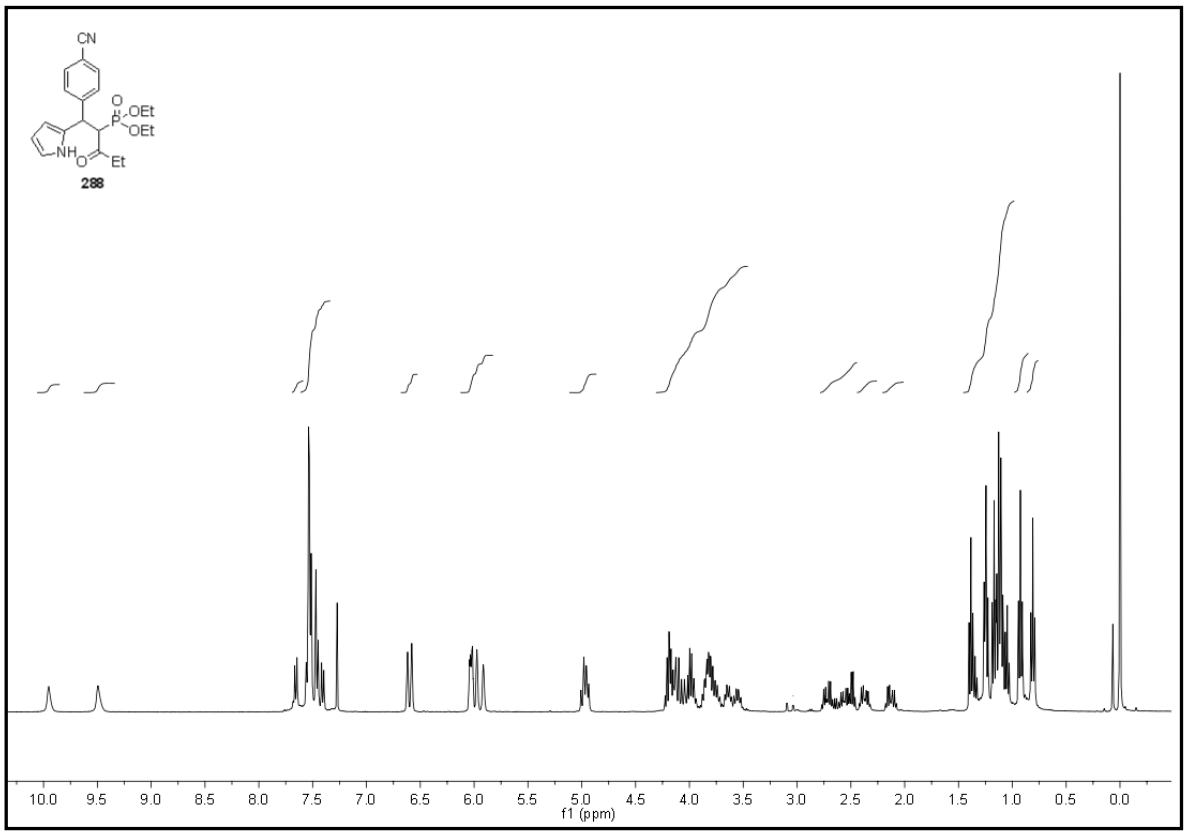


Figure A.205. ^{1}H NMR spectrum of compound **288**

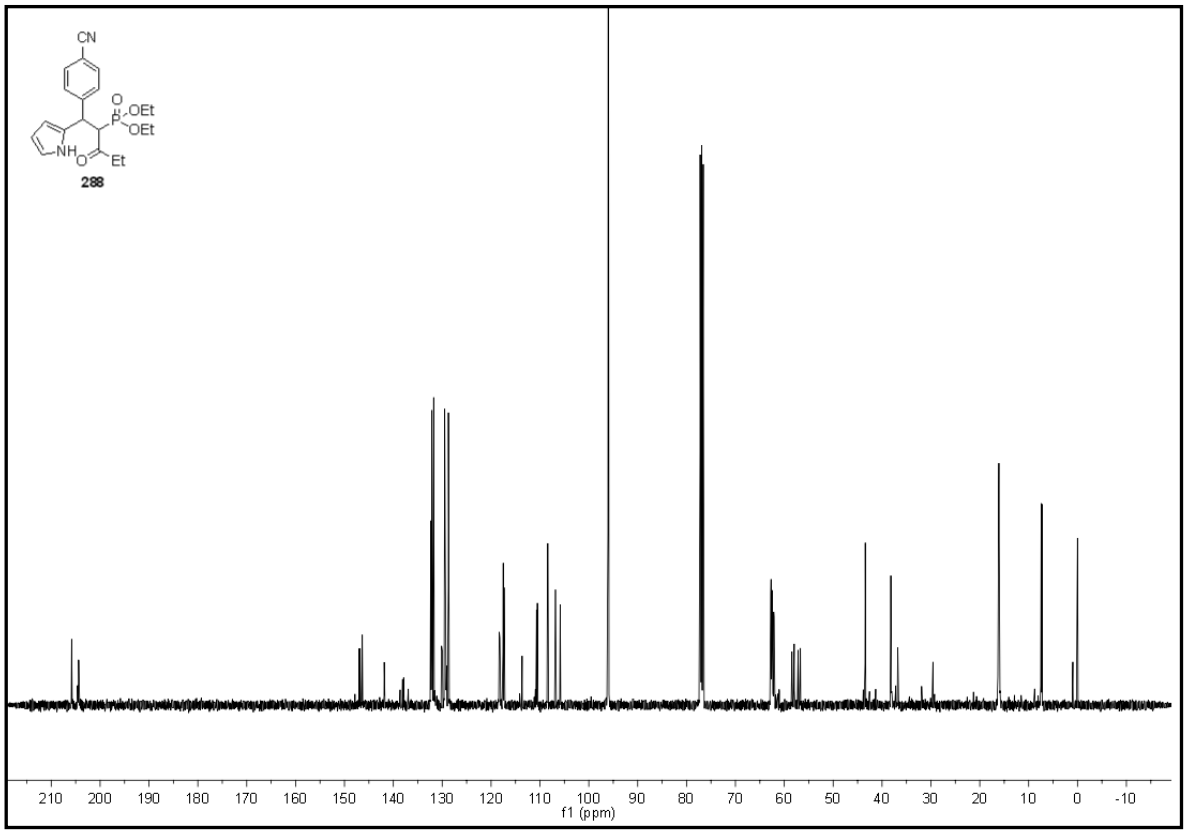


Figure A.206. ^{13}C NMR spectrum of compound **288**

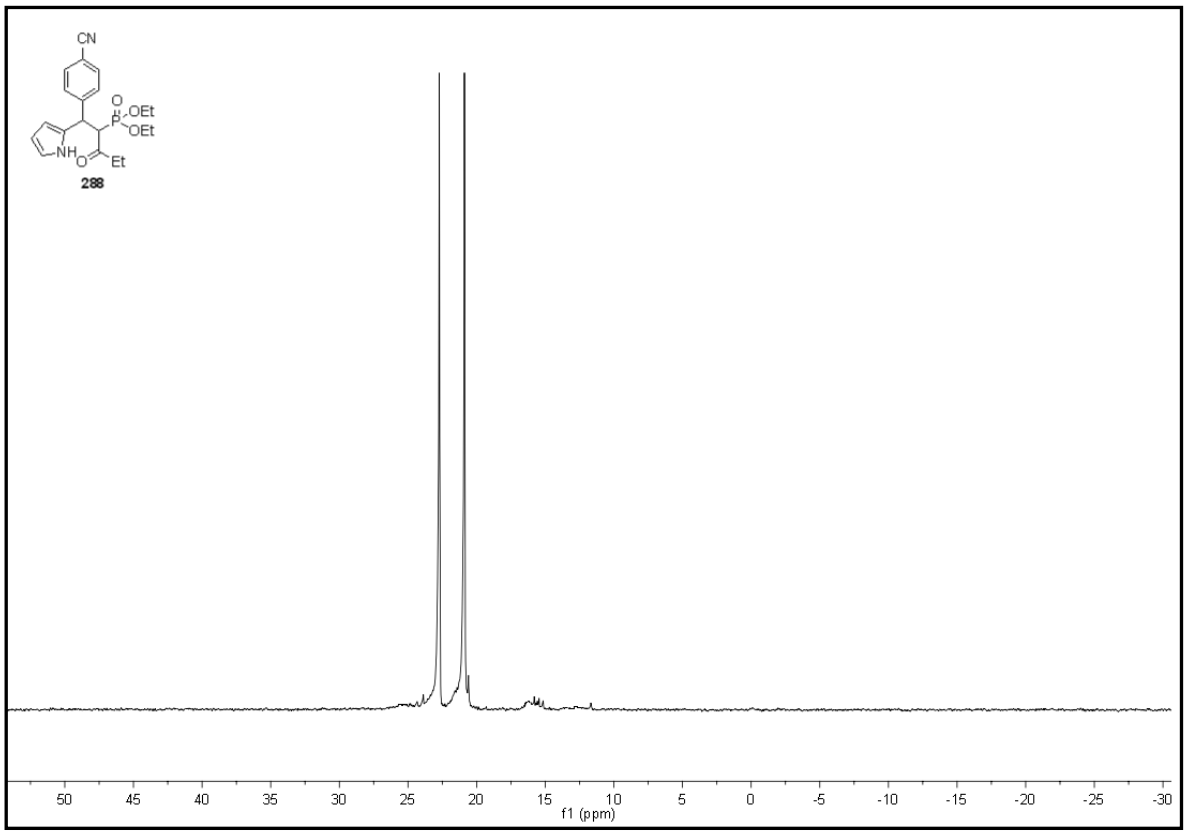


Figure A.207. ^{31}P NMR spectrum of compound **288**

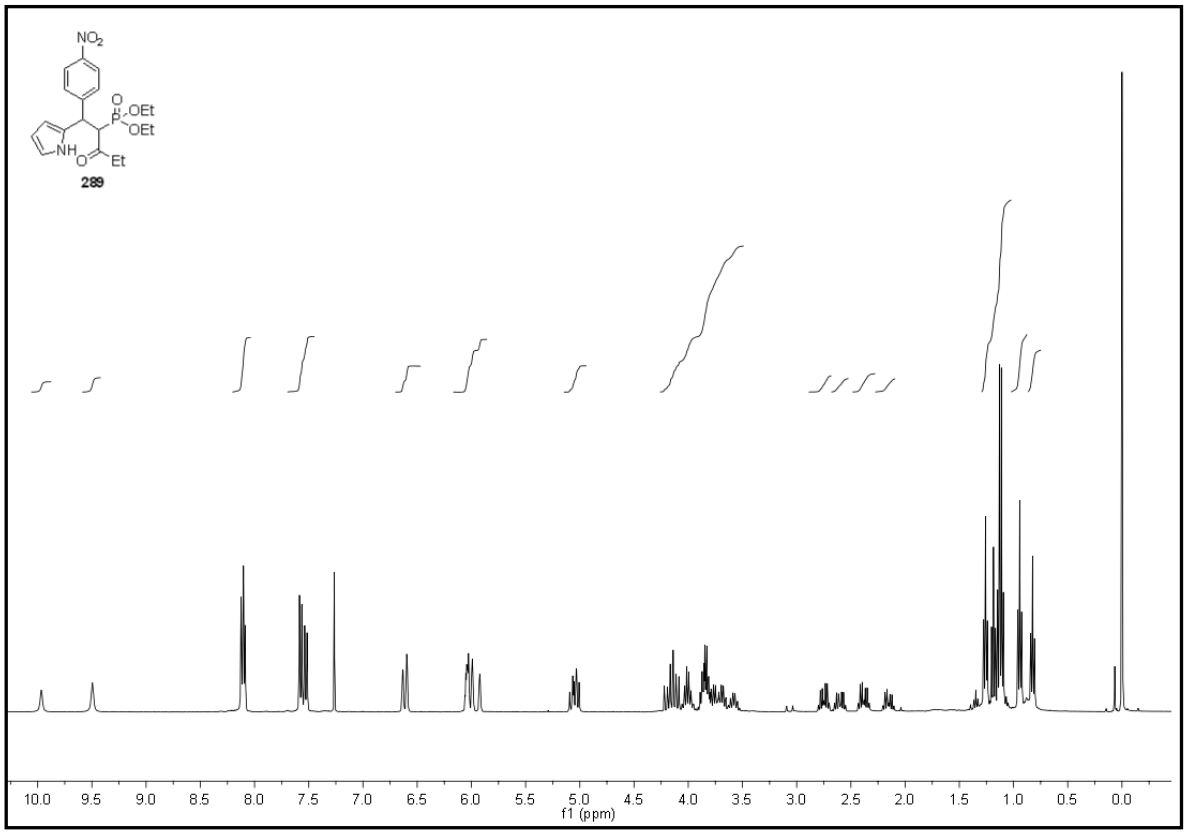


Figure A.208. ^{1}H NMR spectrum of compound **289**

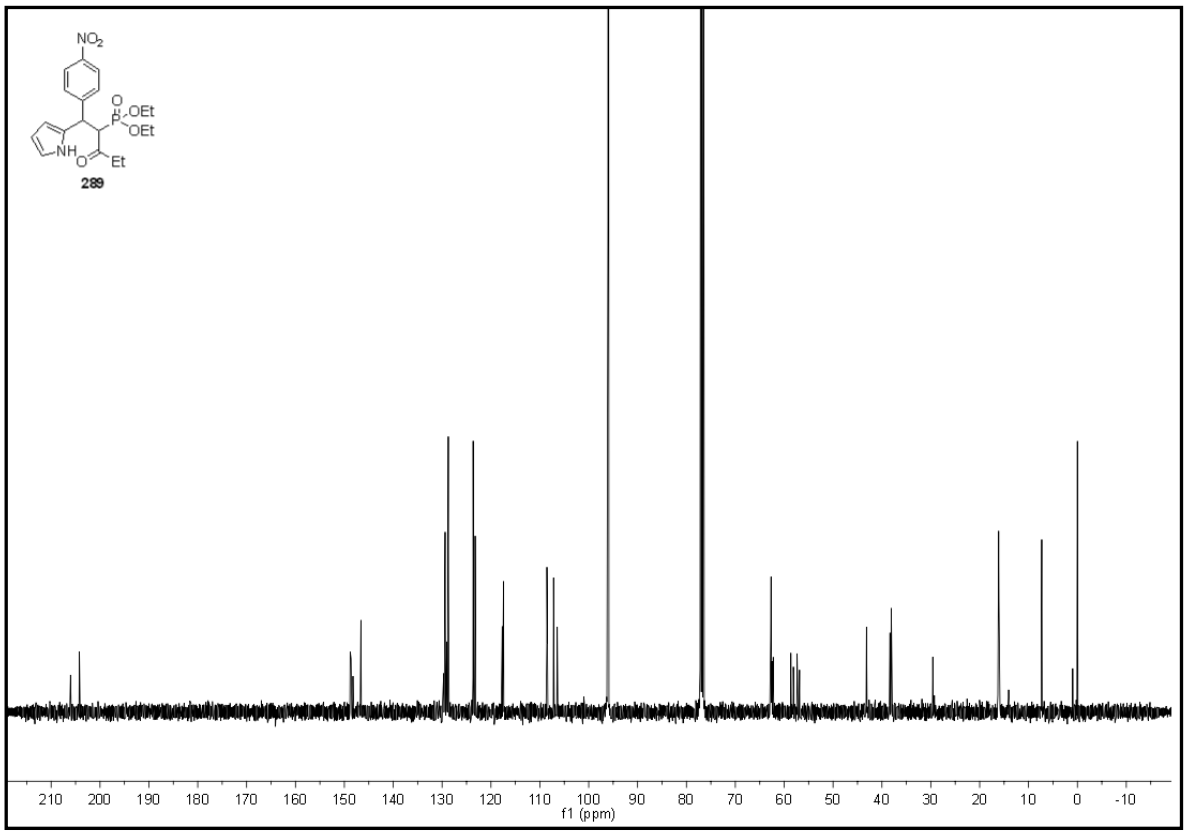


Figure A.209. ^{13}C NMR spectrum of compound **289**

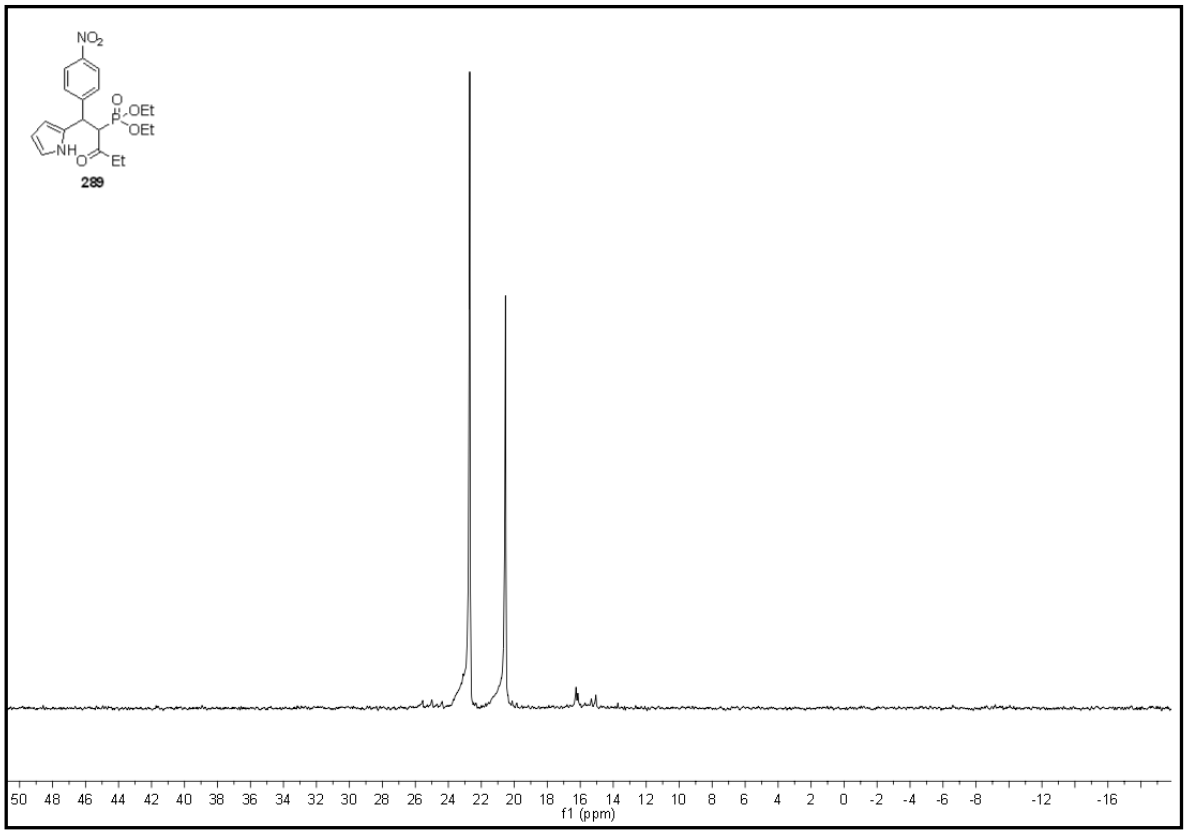


Figure A.210. ^{31}P NMR spectrum of compound **289**

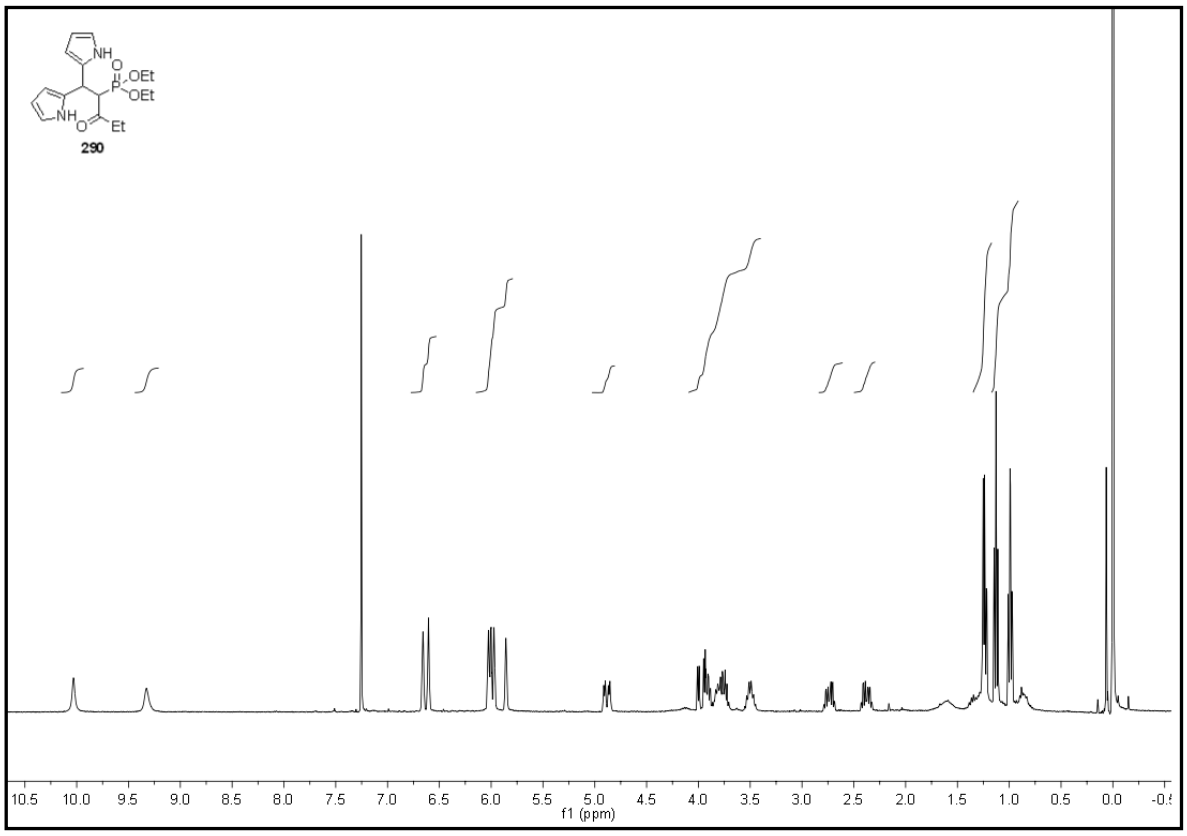


Figure A.211. ^{1}H NMR spectrum of compound **290**

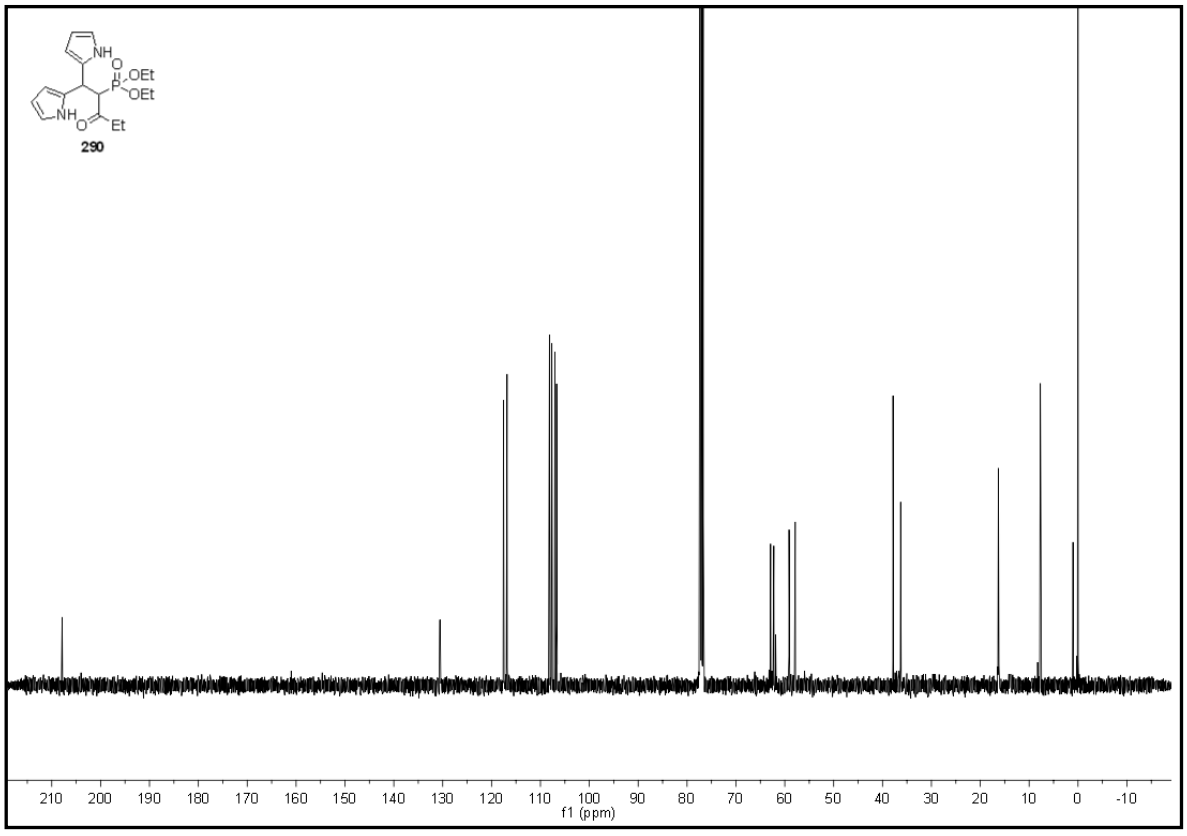


Figure A.212. ^{13}C NMR spectrum of compound **290**

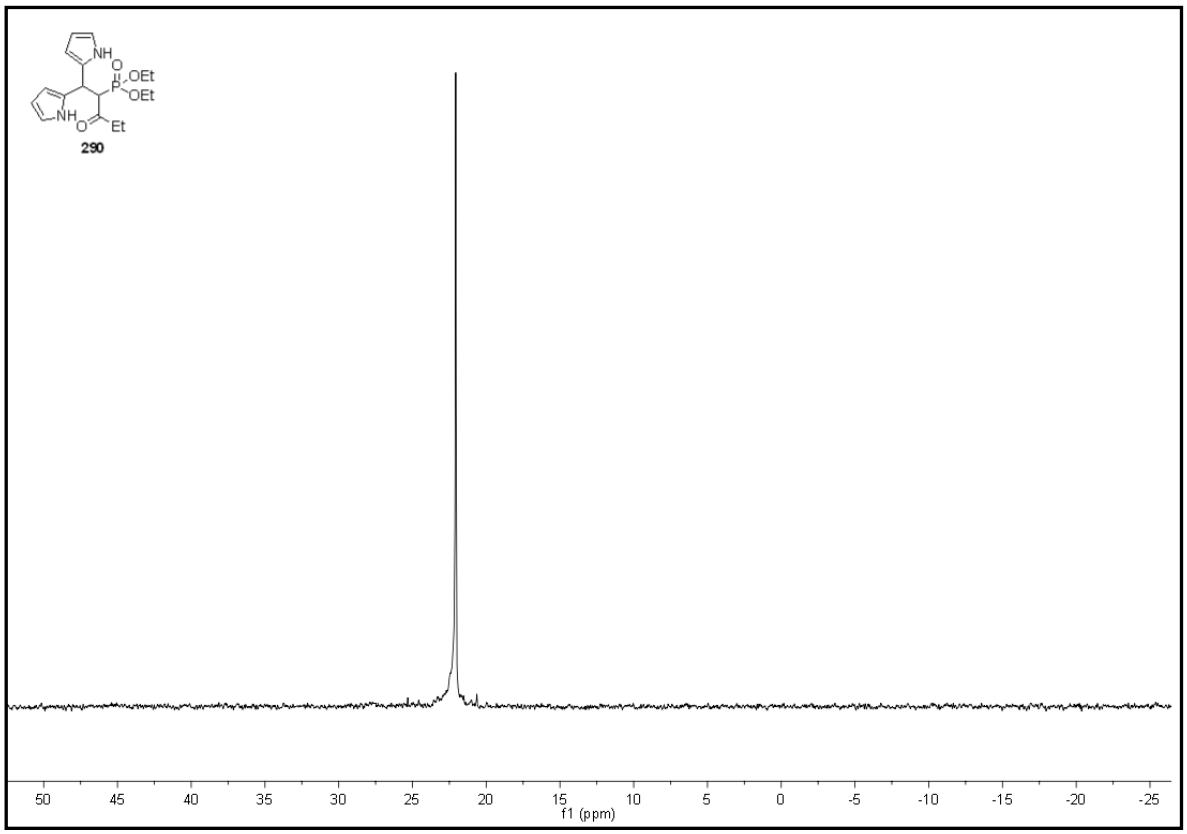


Figure A.213. ^{31}P NMR spectrum of compound **290**

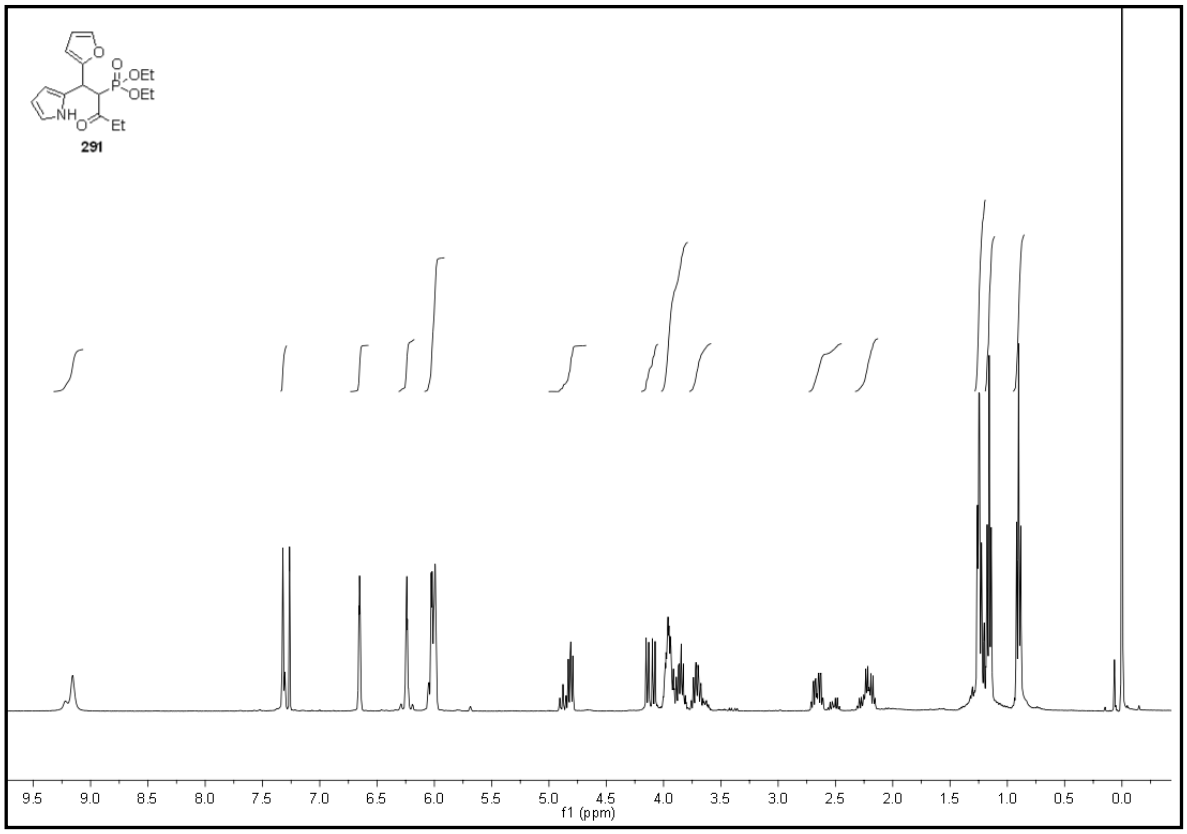


Figure A.214. ^{1}H NMR spectrum of compound **291**

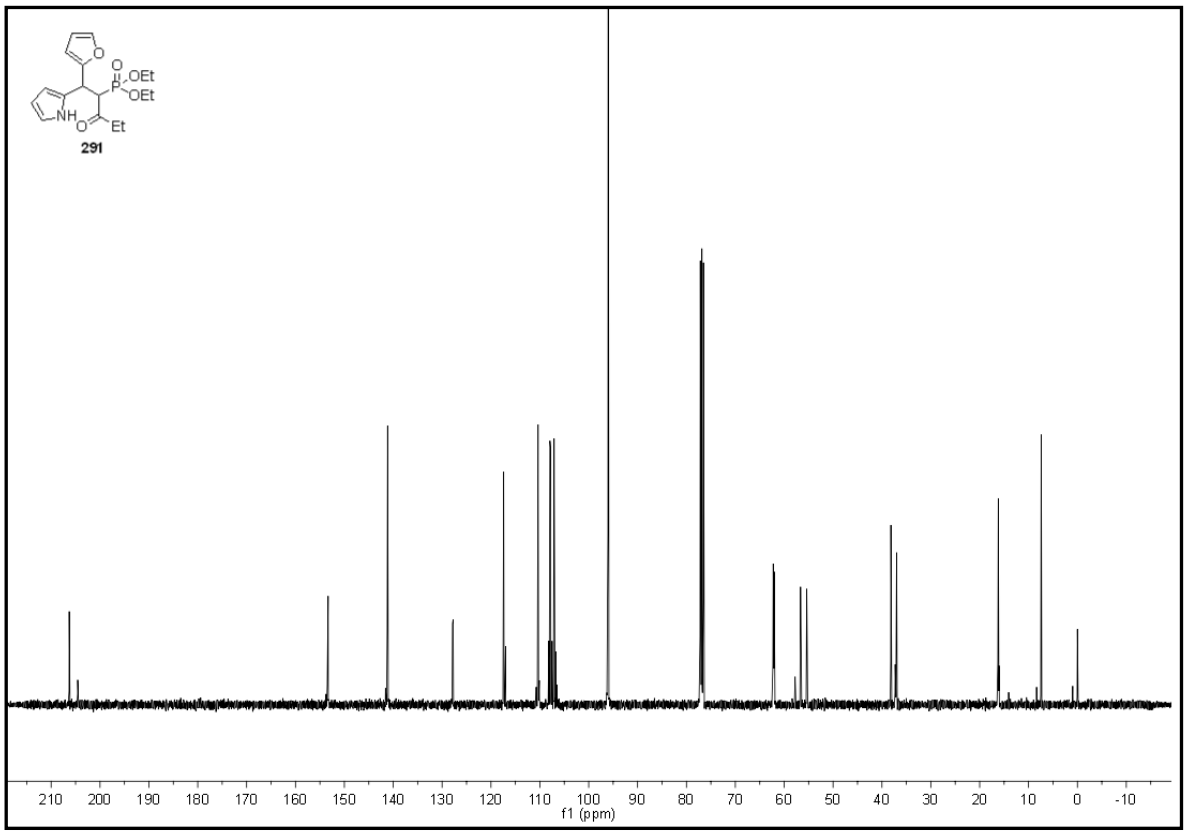


Figure A.215. ^{13}C NMR spectrum of compound **291**

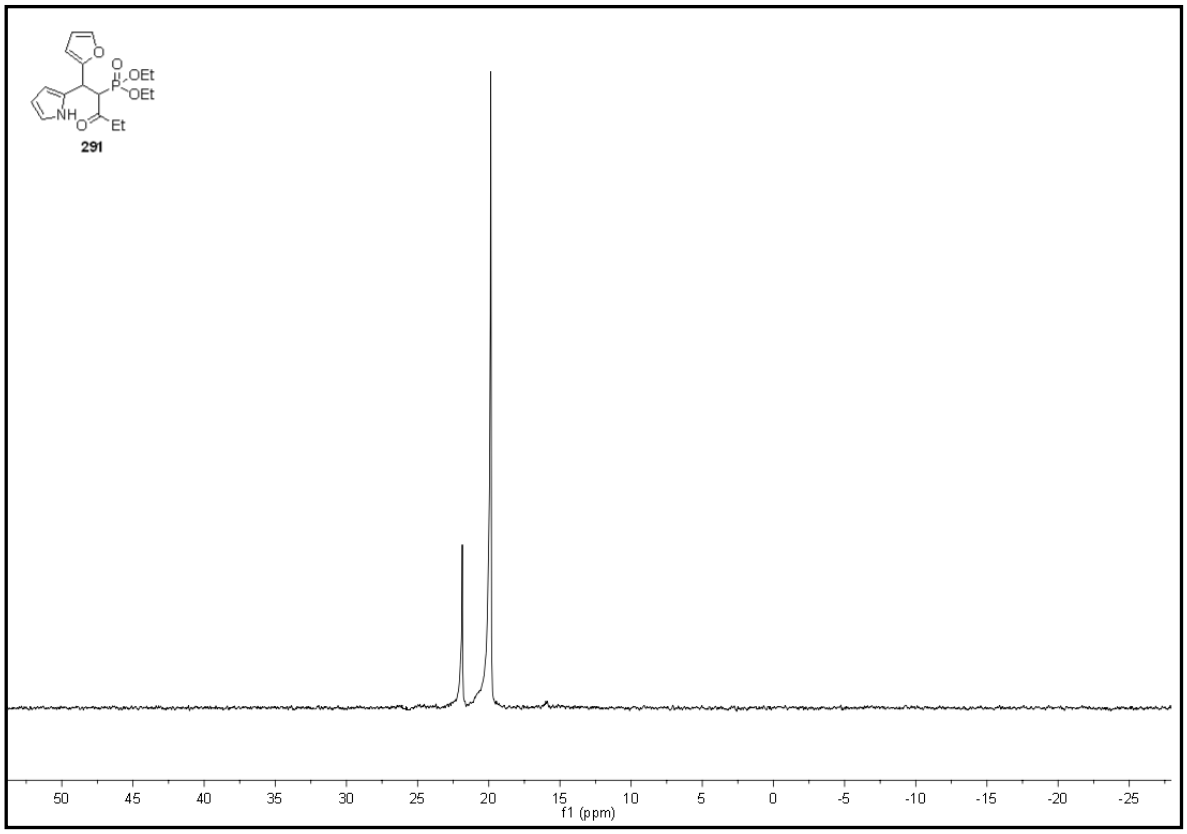


Figure A.216. ^{31}P NMR spectrum of compound **291**

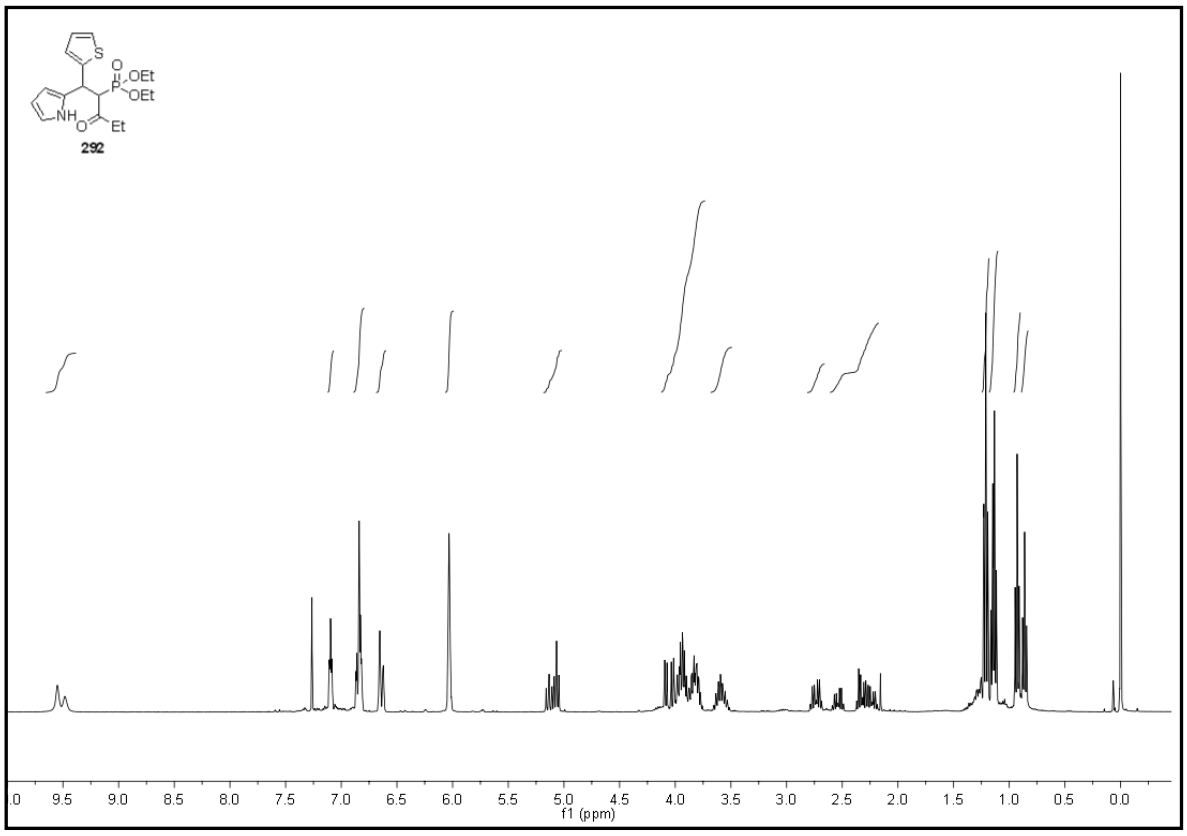


Figure A.217. ^{1}H NMR spectrum of compound **292**

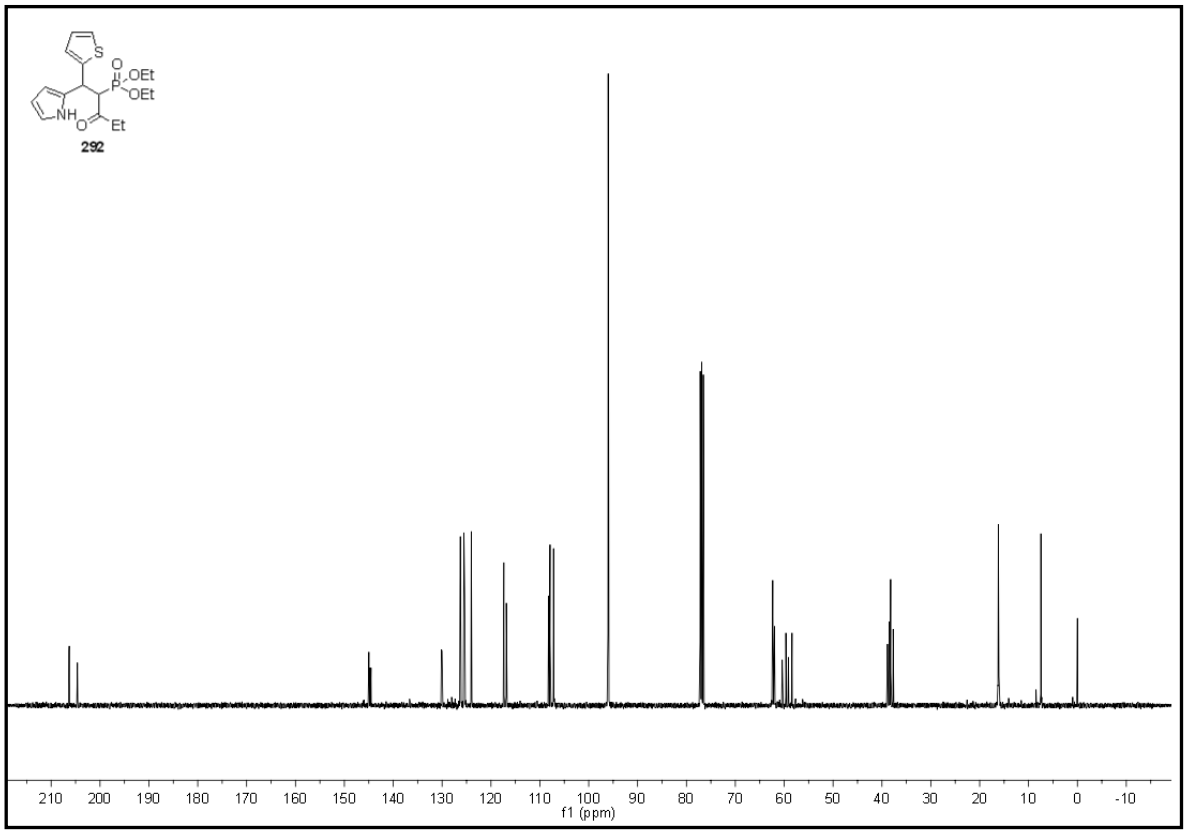


Figure A.218. ^{13}C NMR spectrum of compound **292**

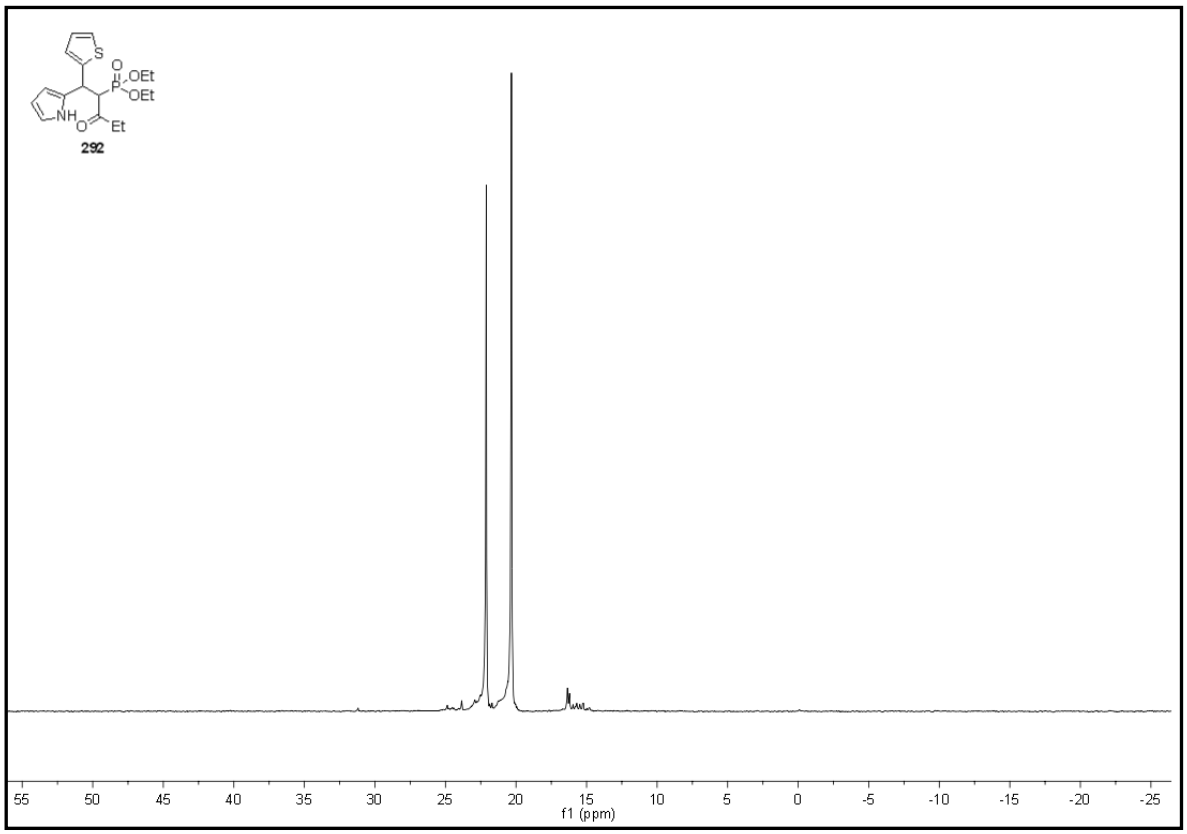


Figure A.219. ^{31}P NMR spectrum of compound **292**

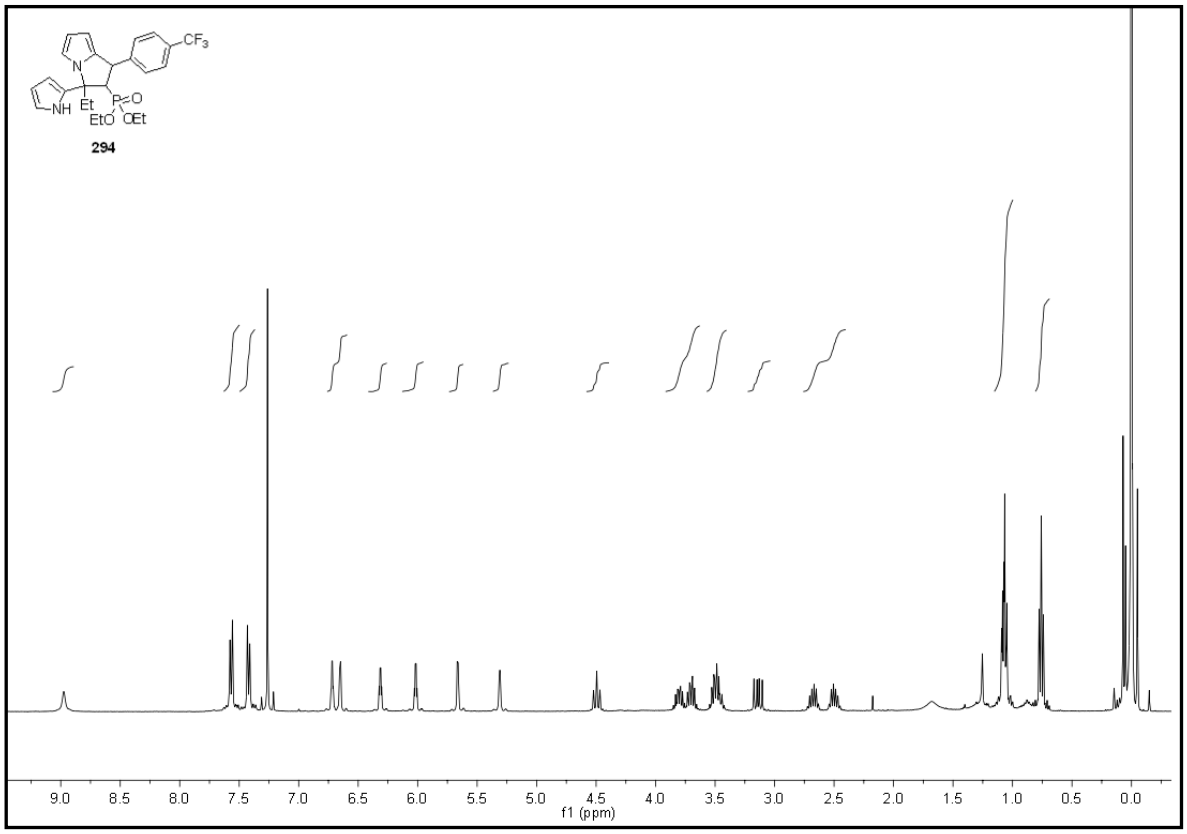


Figure A.220. ^{1}H NMR spectrum of compound **294**

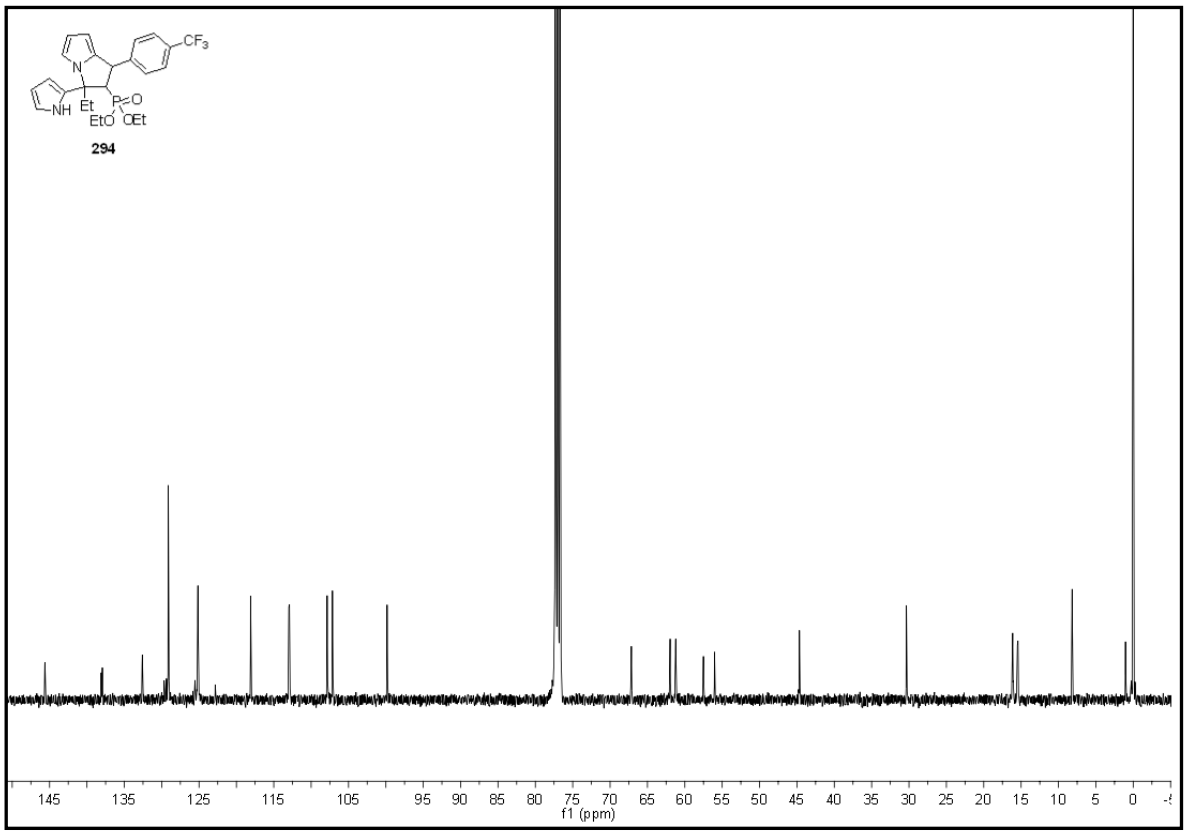


Figure A.221. ^{13}C NMR spectrum of compound **294**

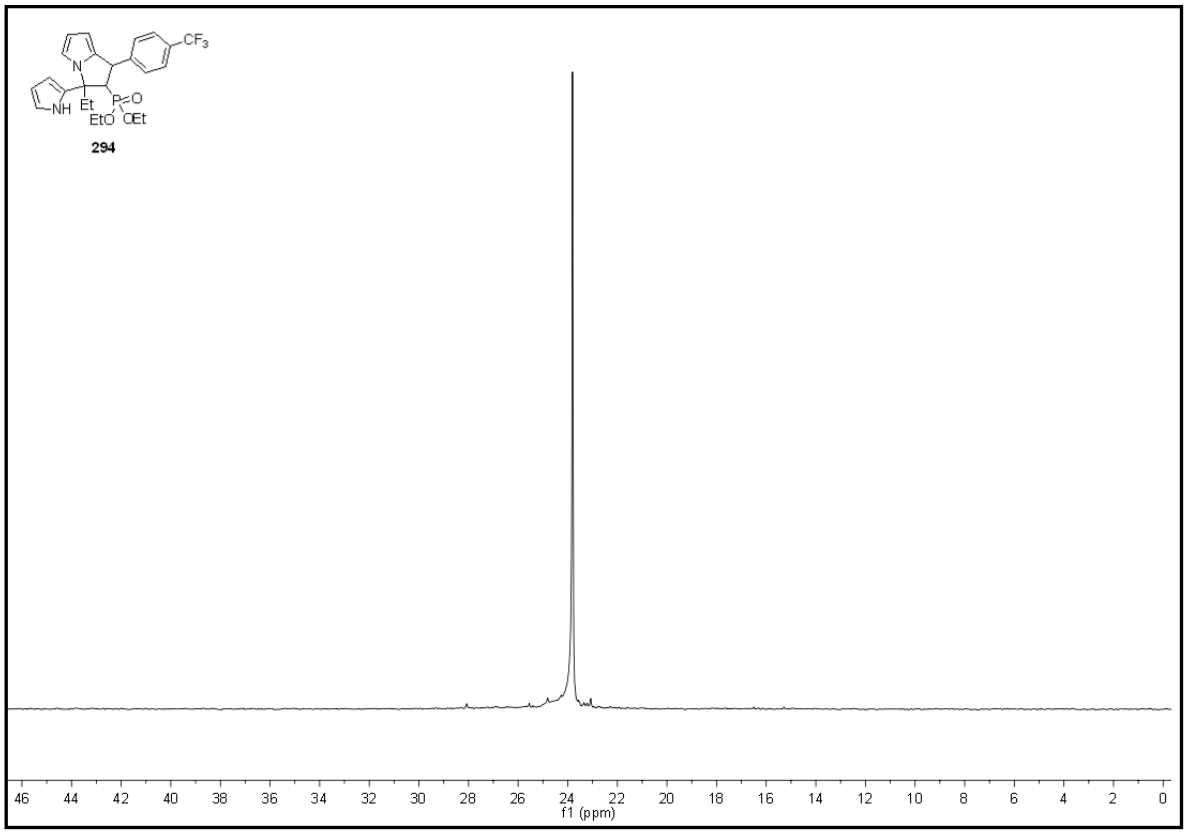


Figure A.222. ^{31}P NMR spectrum of compound **294**

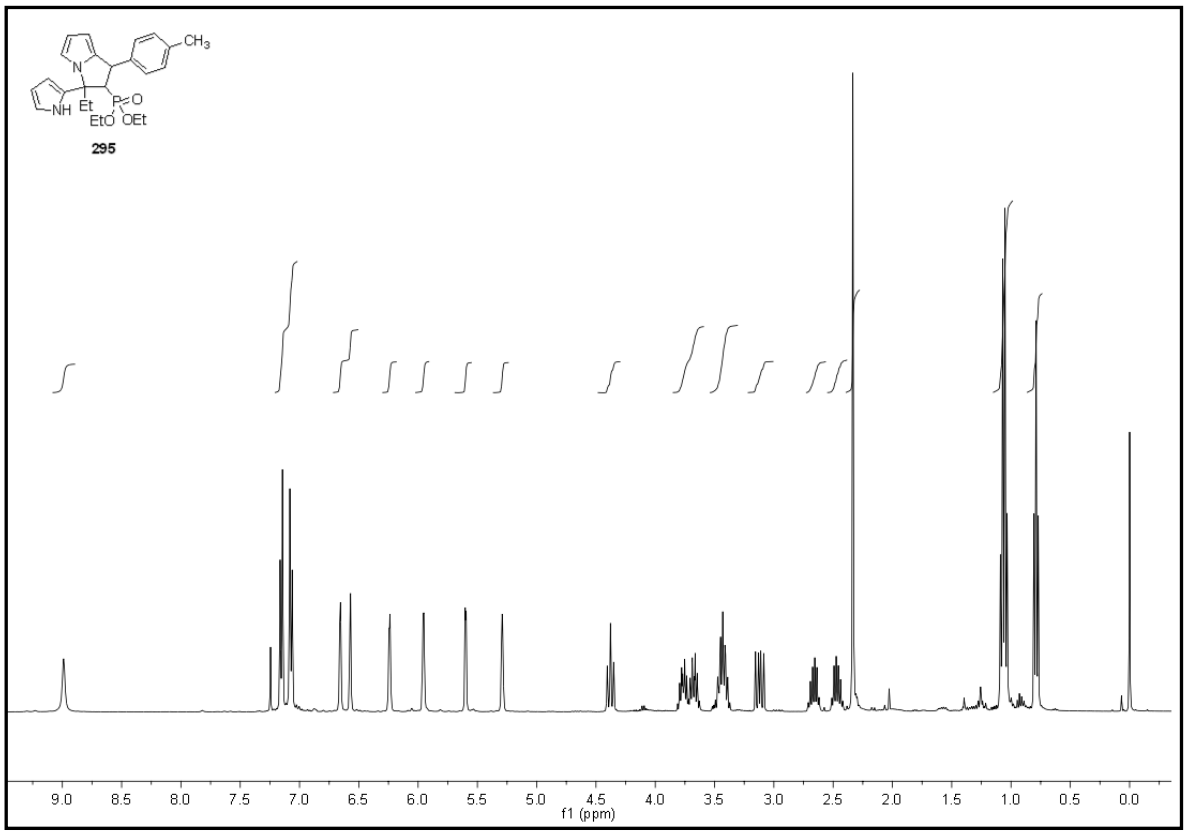


Figure A.223. ^{1}H NMR spectrum of compound **295**

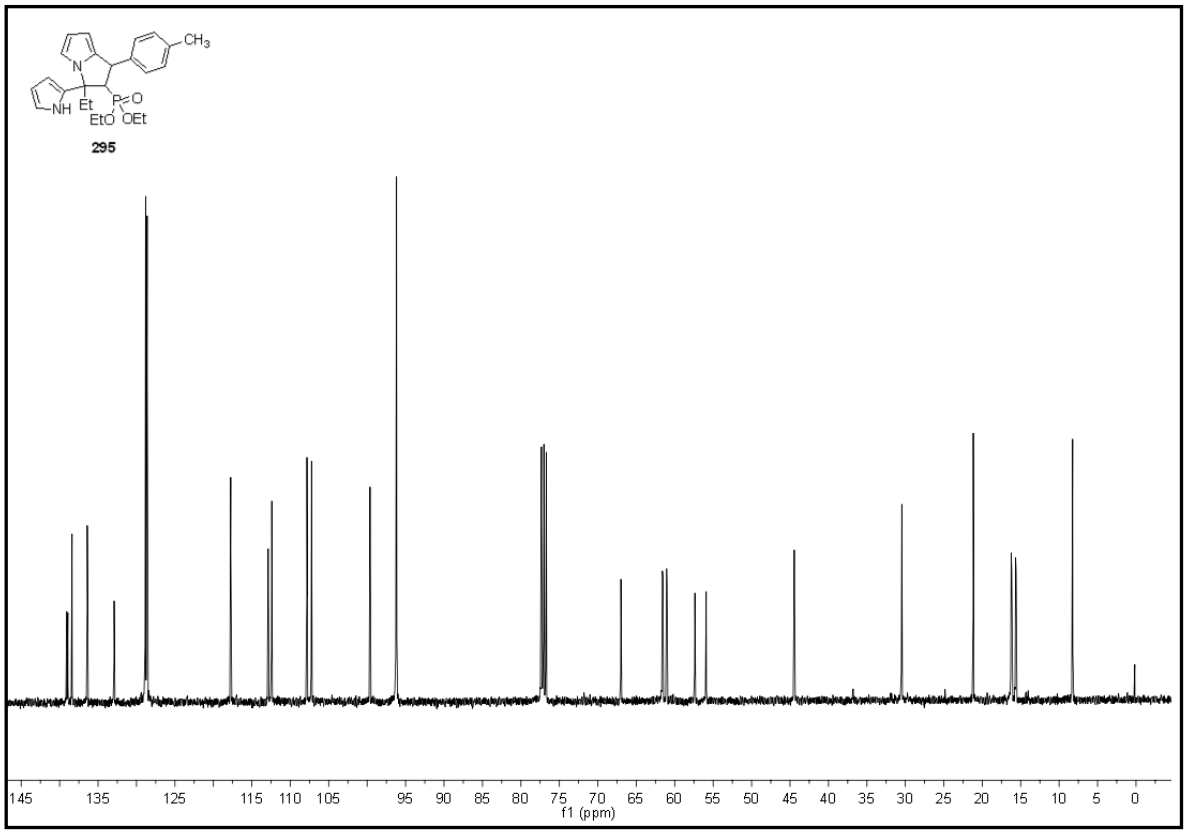


Figure A.224. ^{13}C NMR spectrum of compound **295**

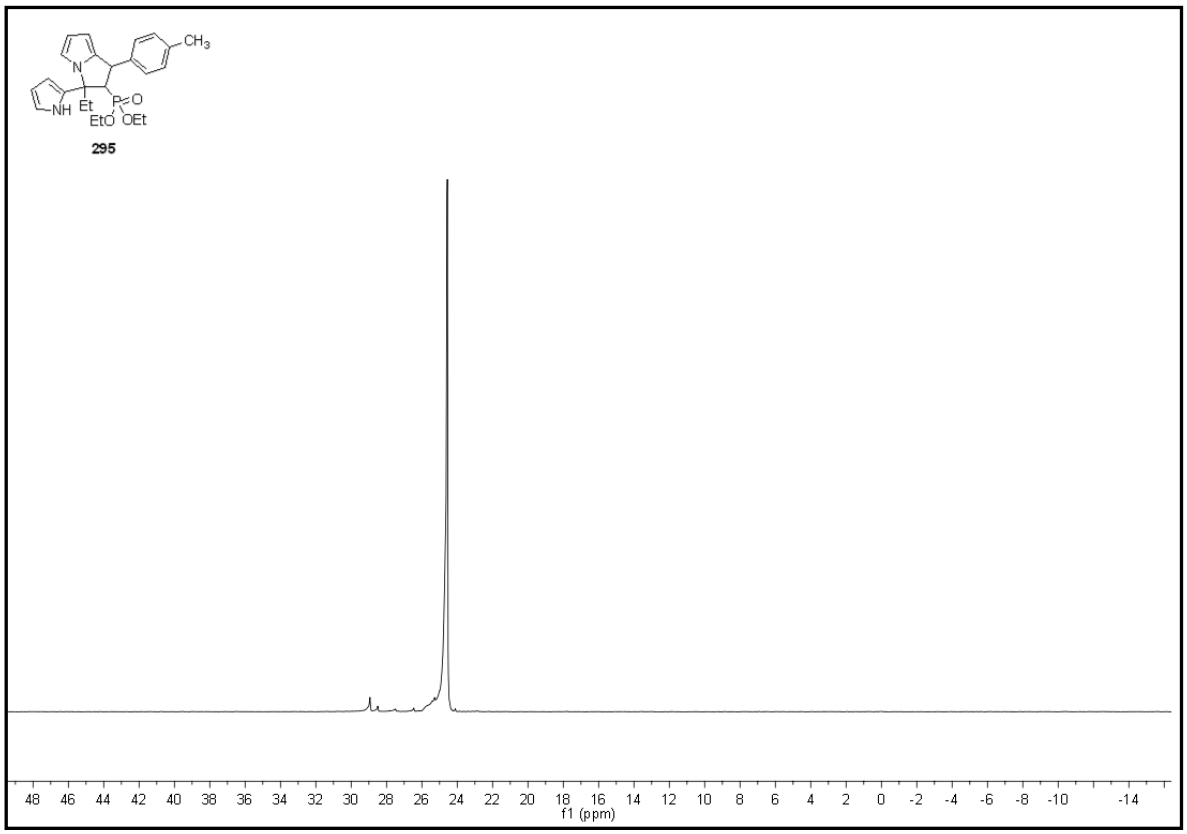


Figure A.225. ^{31}P NMR spectrum of compound **295**

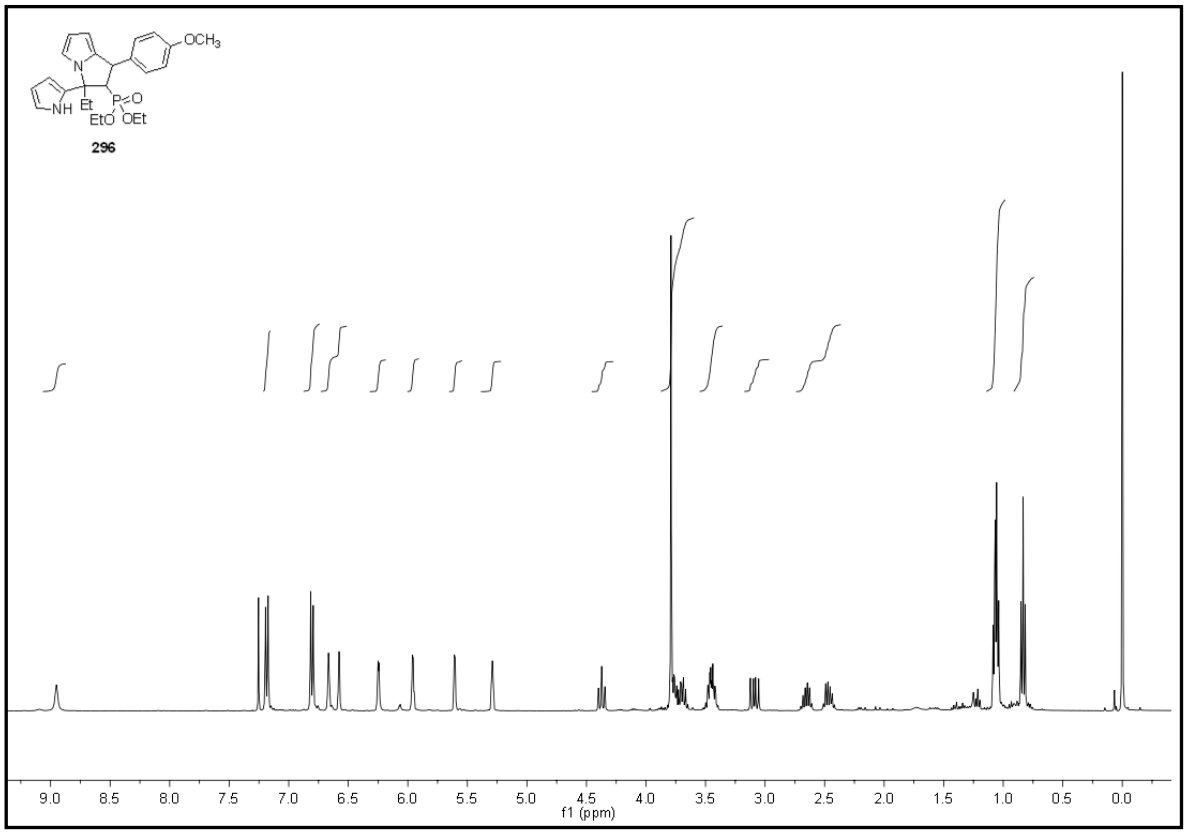


Figure A.226. ^{1}H NMR spectrum of compound **296**

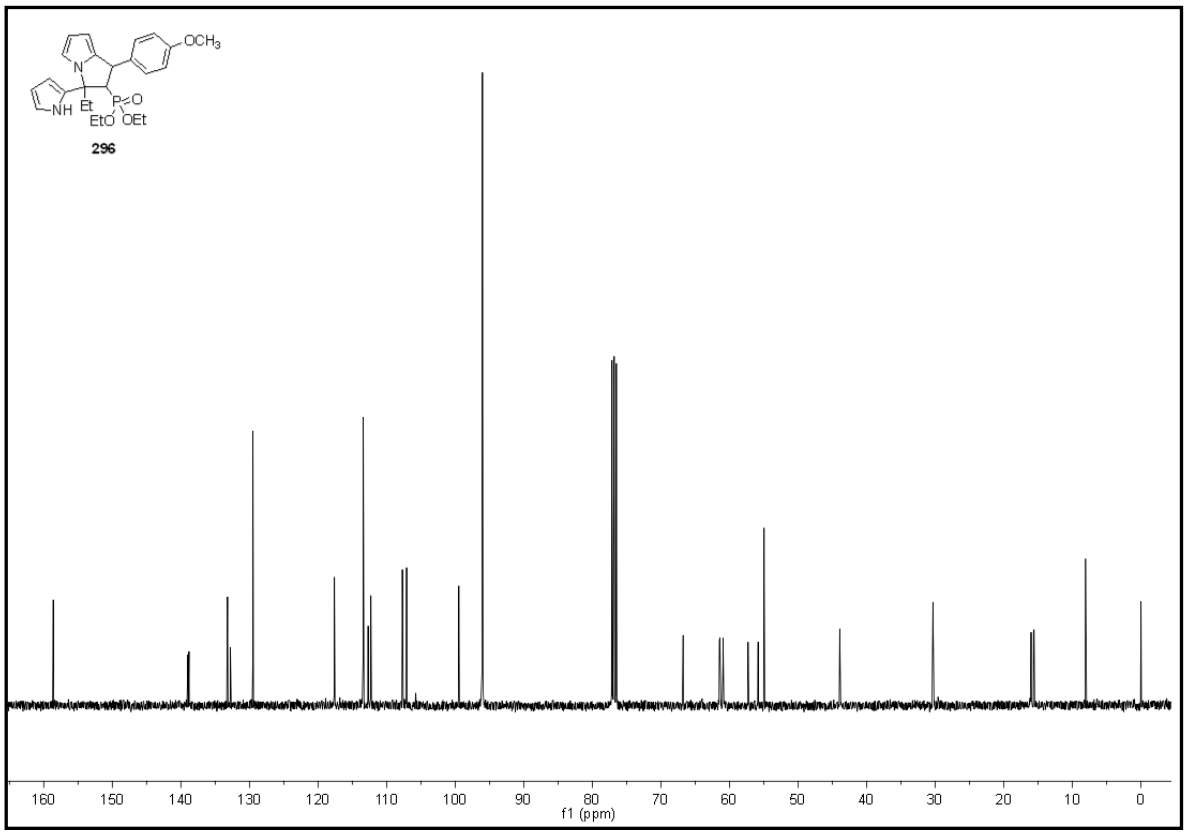


Figure A.227. ^{13}C NMR spectrum of compound **296**

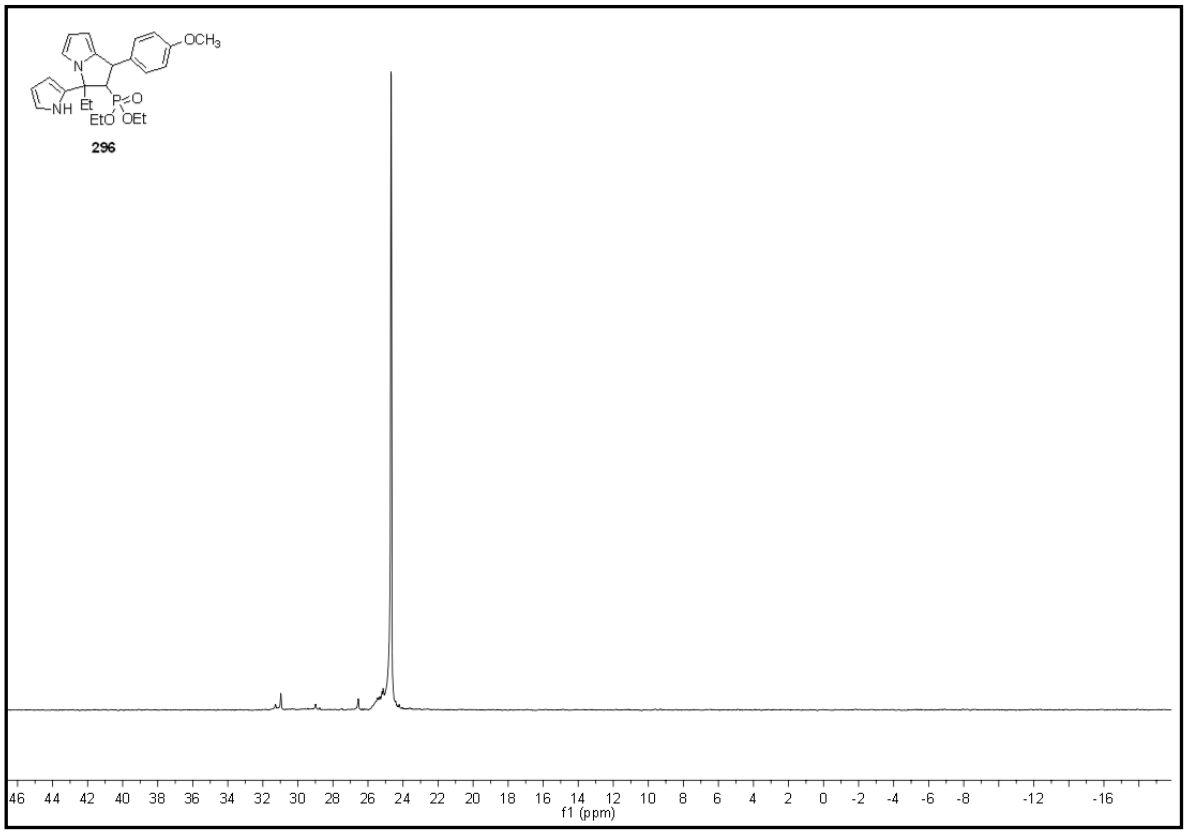


Figure A.228. ^{31}P NMR spectrum of compound **296**

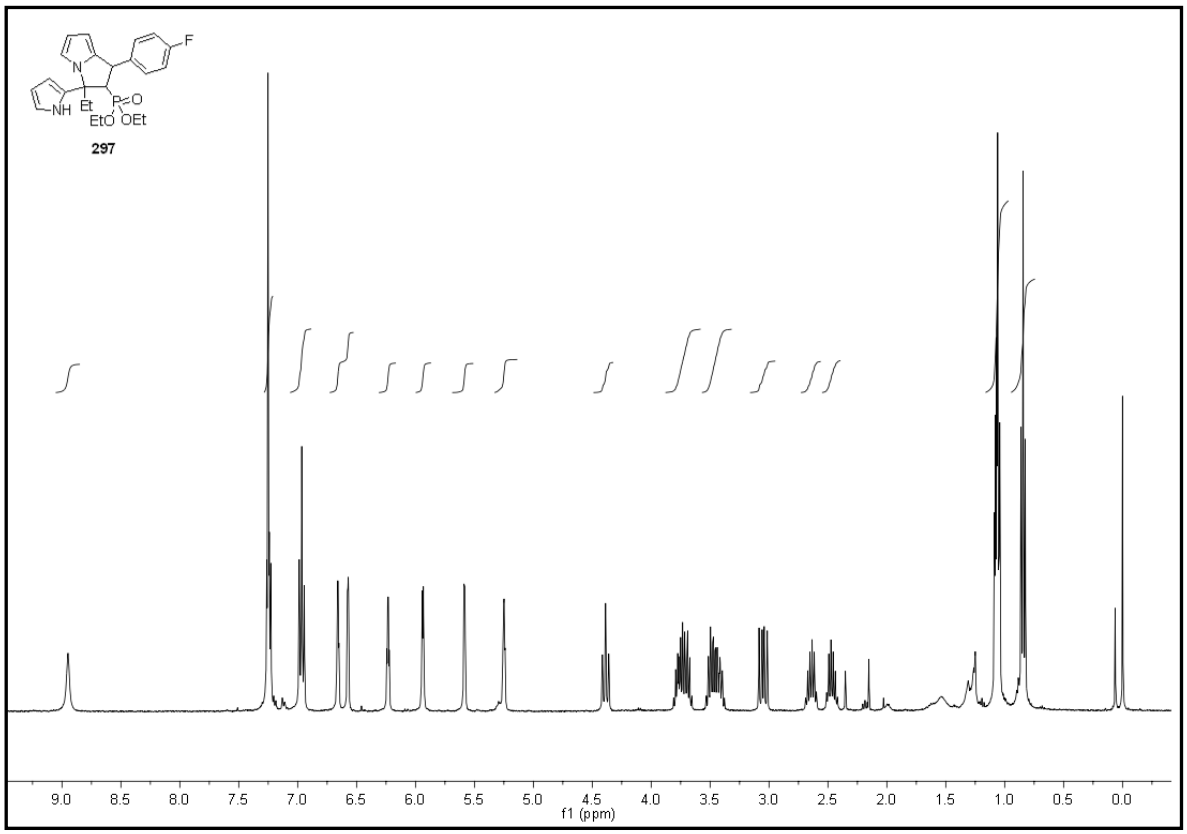


Figure A.229. ^{1}H NMR spectrum of compound **297**

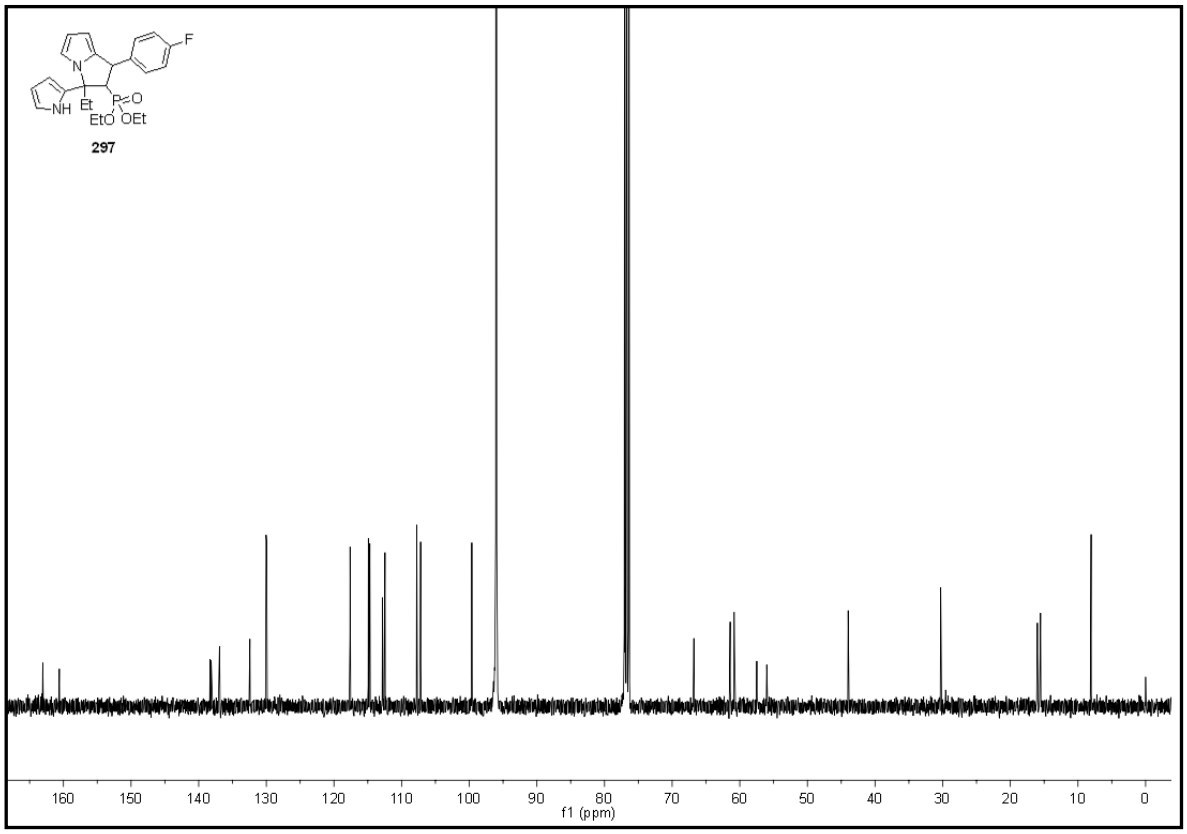


Figure A.230. ^{13}C NMR spectrum of compound **297**

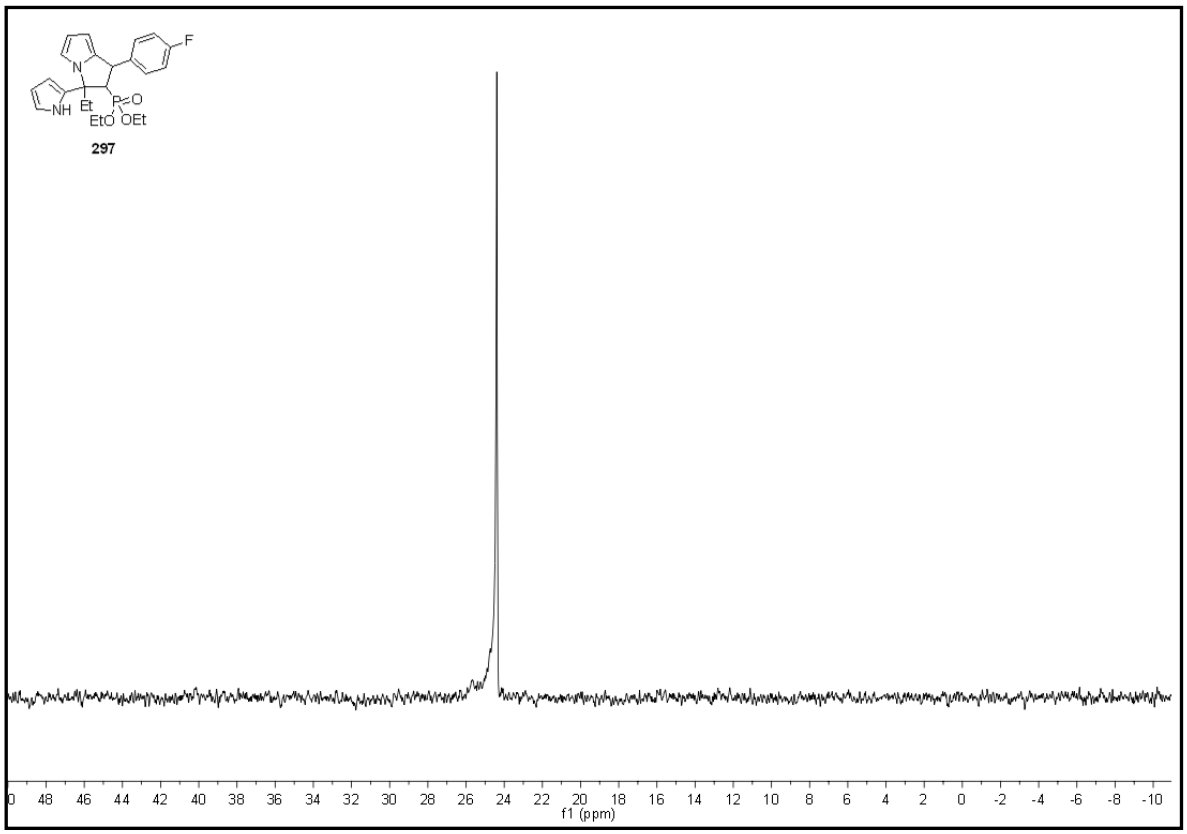


Figure A.231. ^{31}P NMR spectrum of compound **297**

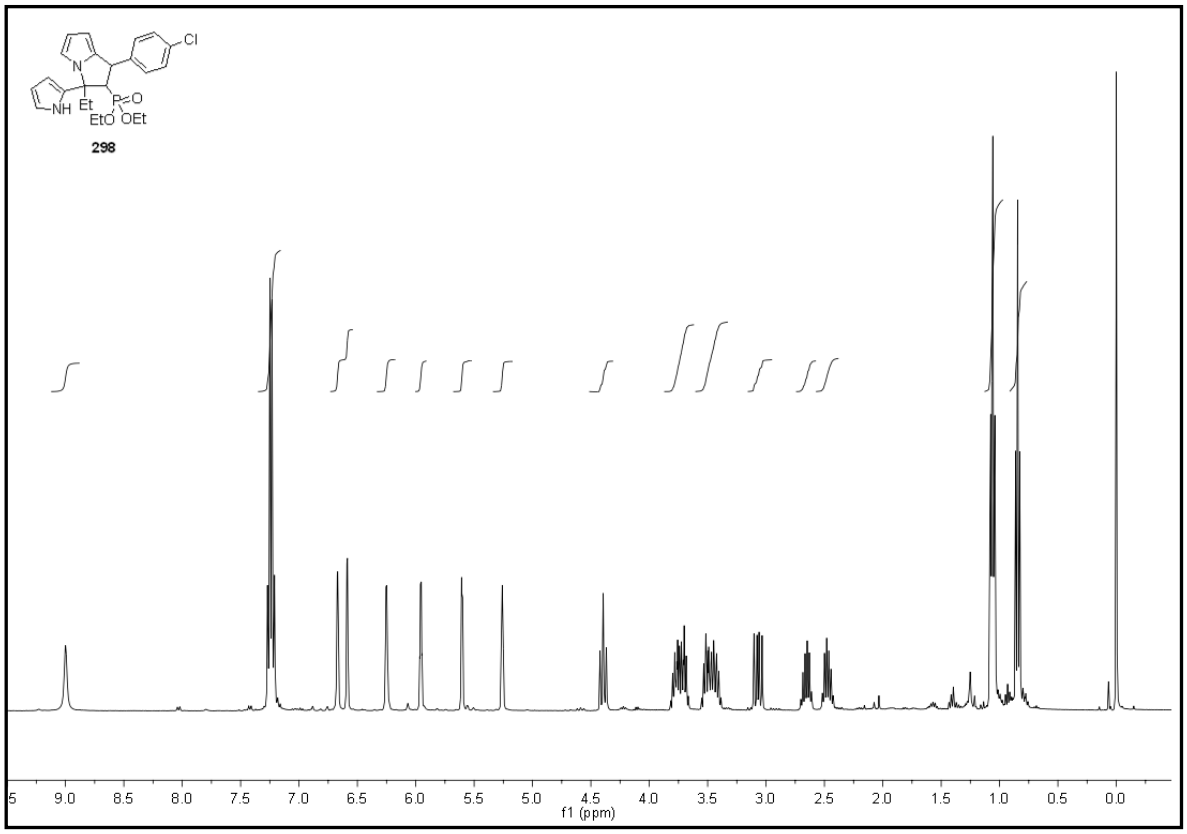


Figure A.232. ^{1}H NMR spectrum of compound **298**

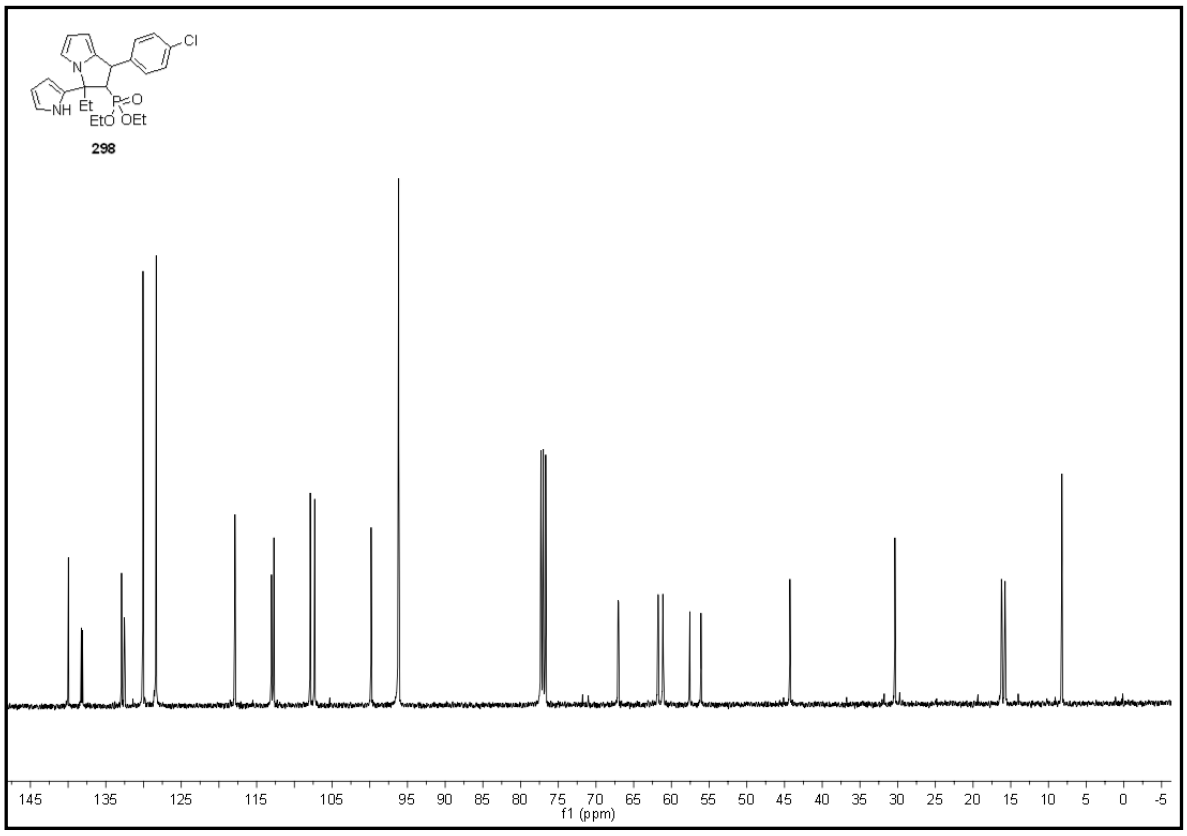


Figure A.233. ^{13}C NMR spectrum of compound **298**

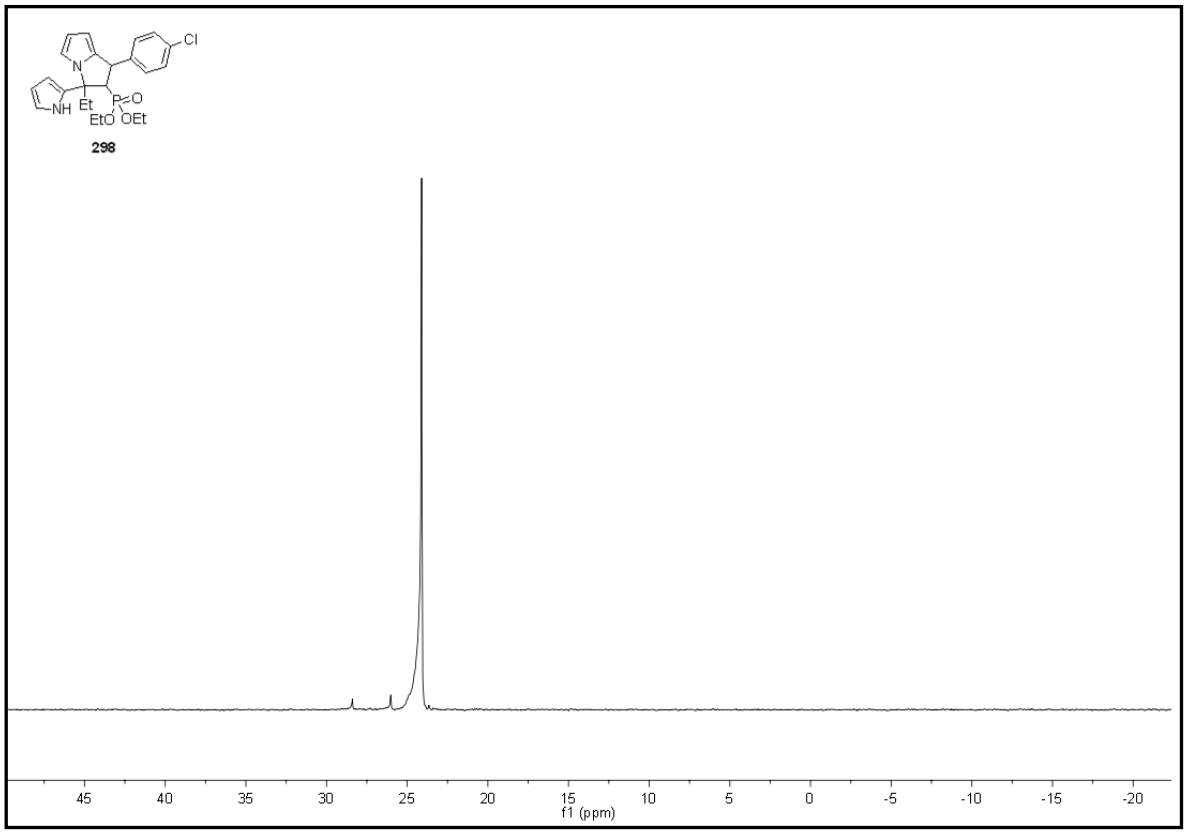


Figure A.234. ^{31}P NMR spectrum of compound **298**

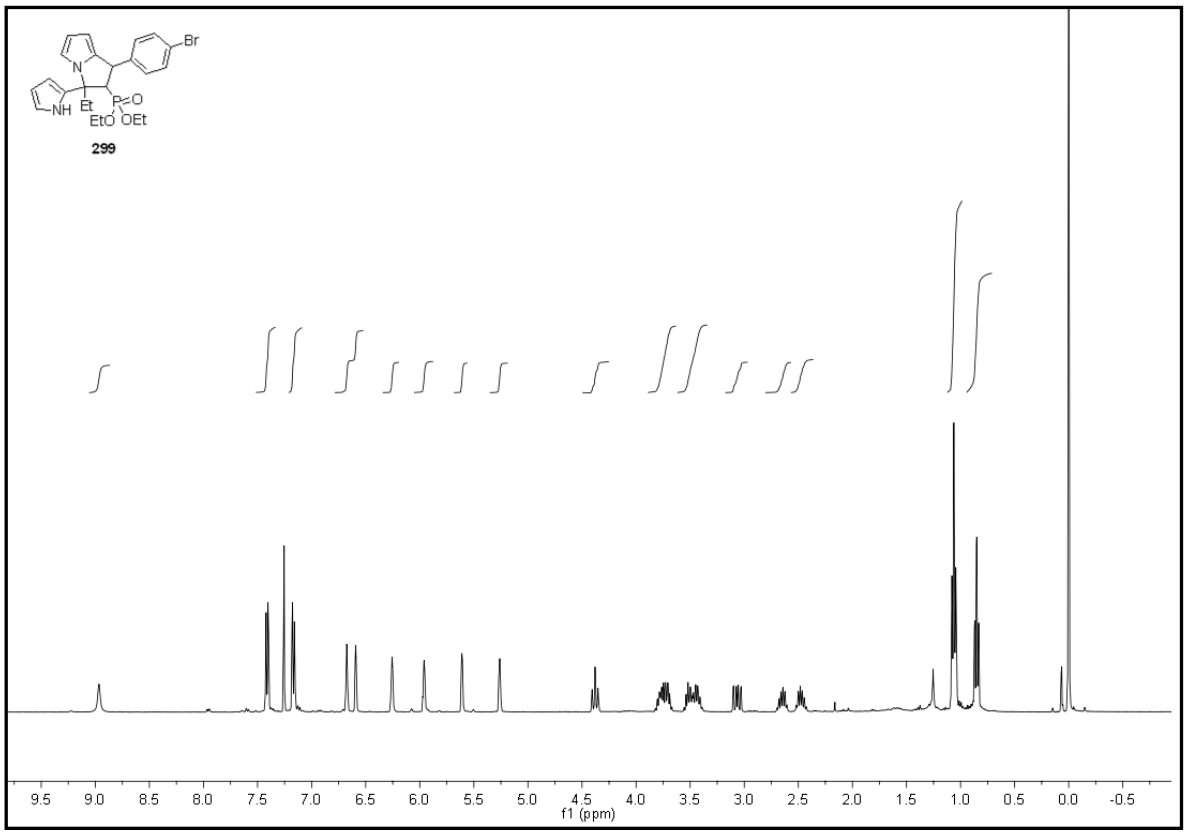


Figure A.235. ^{1}H NMR spectrum of compound **299**

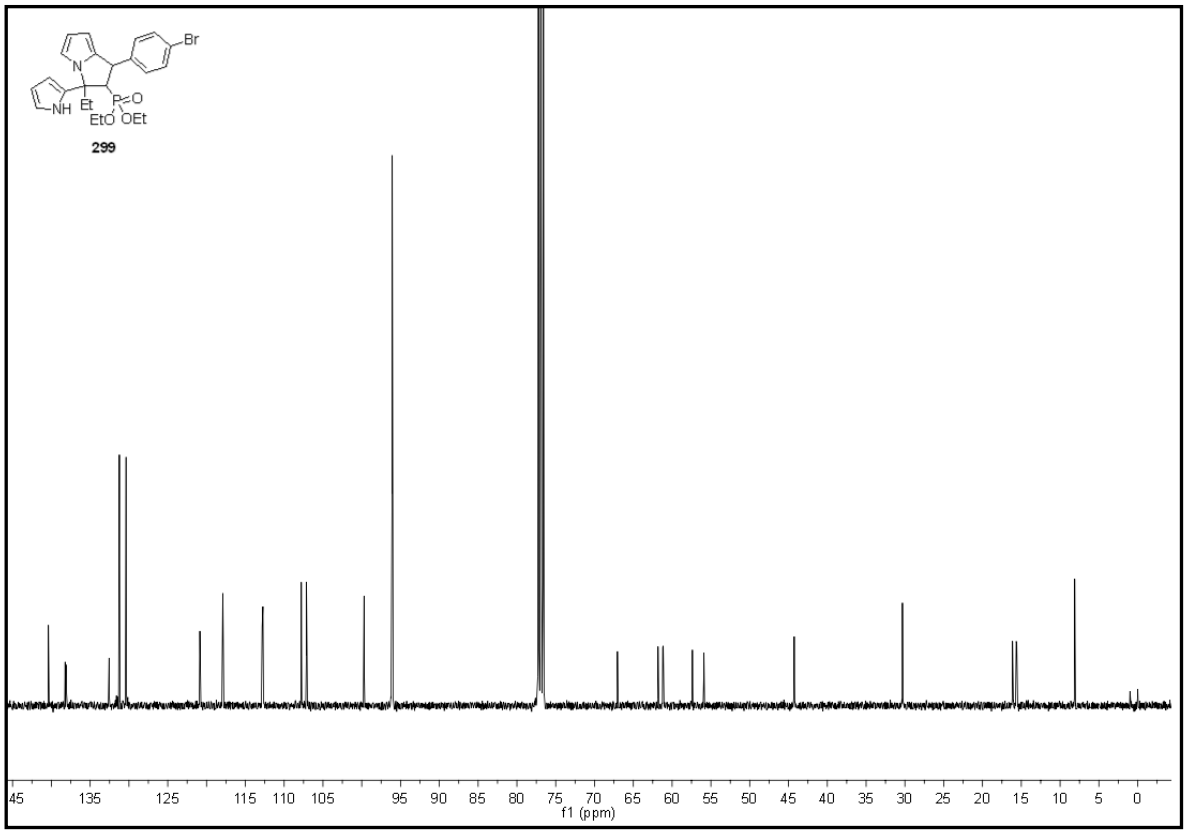


Figure A.236. ^{13}C NMR spectrum of compound **299**

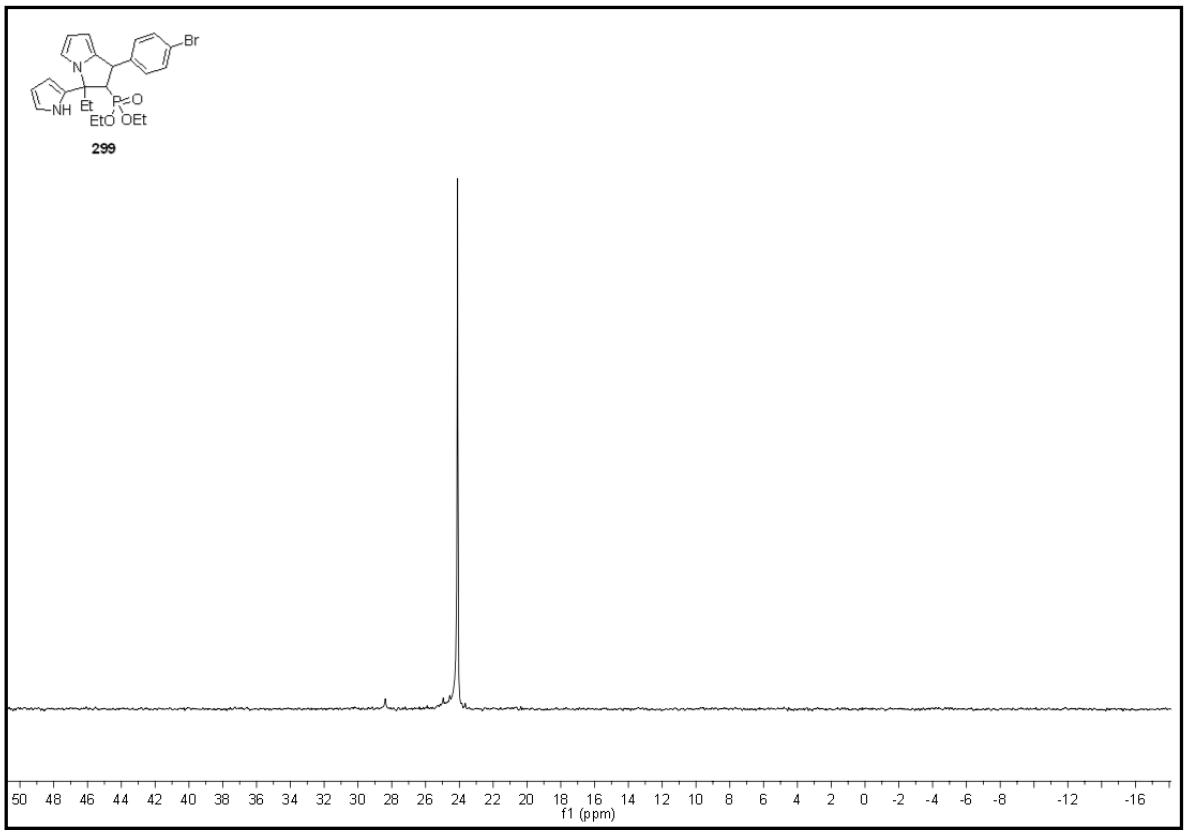


Figure A.237. ^{31}P NMR spectrum of compound **299**

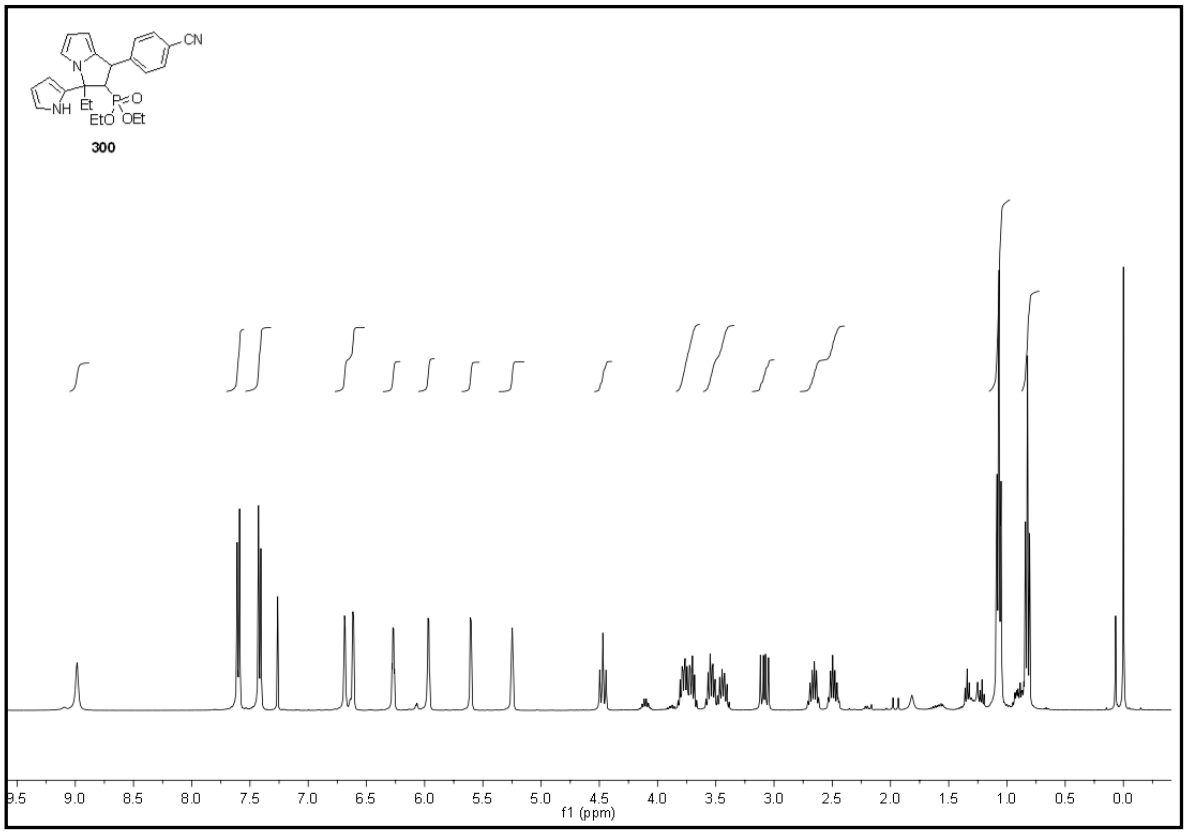


Figure A.236. ^{1}H NMR spectrum of compound **300**

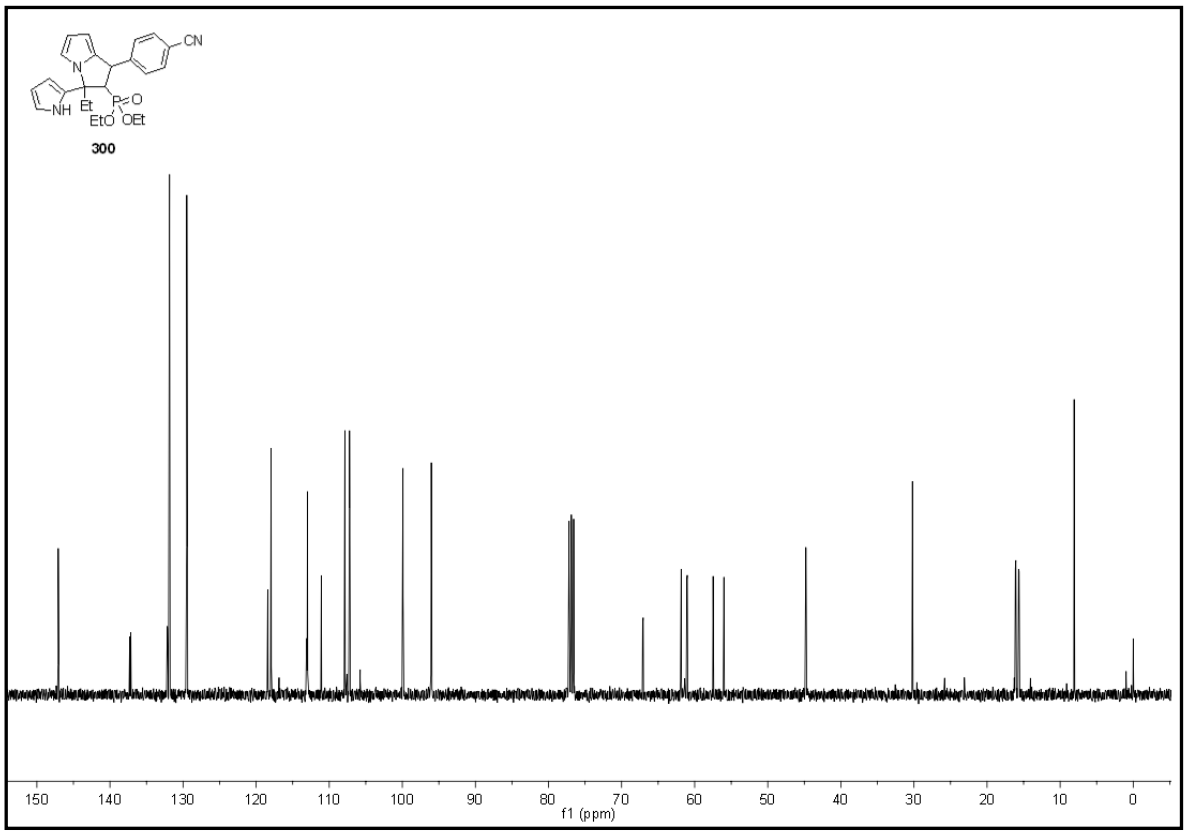


Figure A.239. ^{13}C NMR spectrum of compound **300**

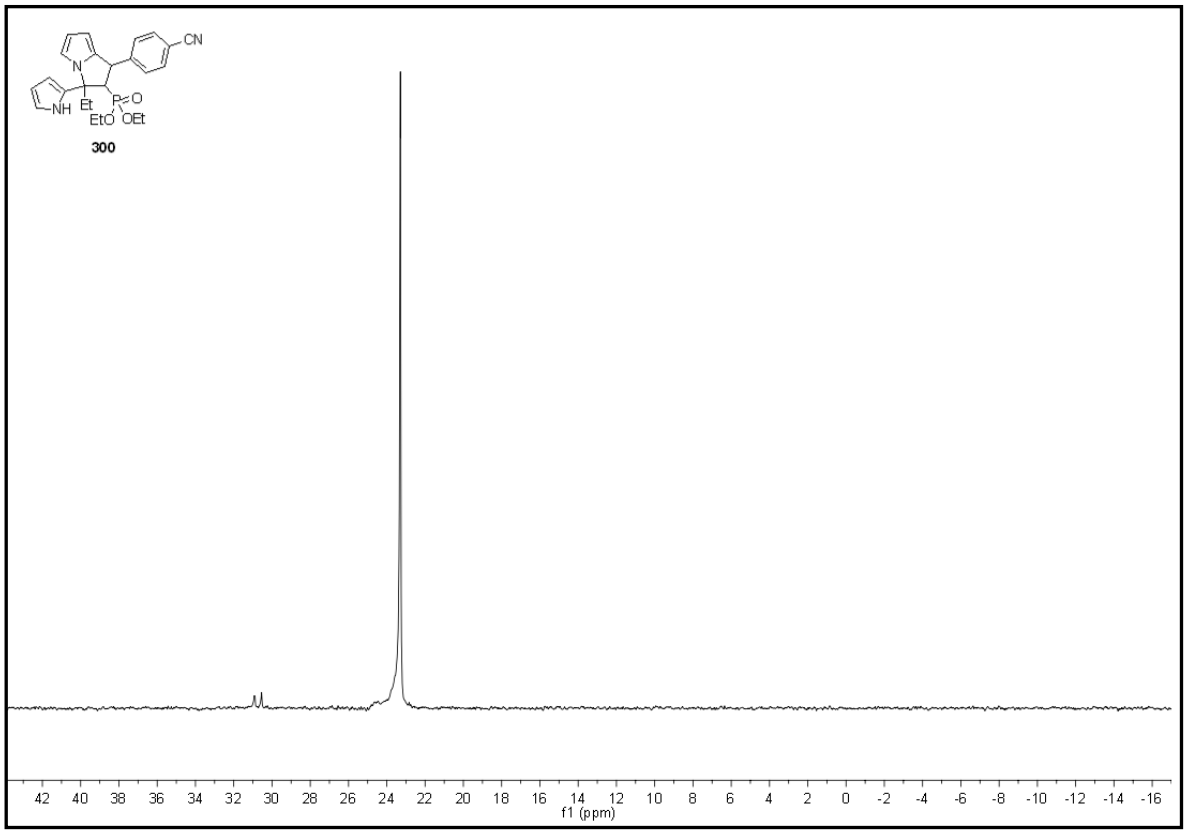


Figure A.240. ^{31}P NMR spectrum of compound **300**

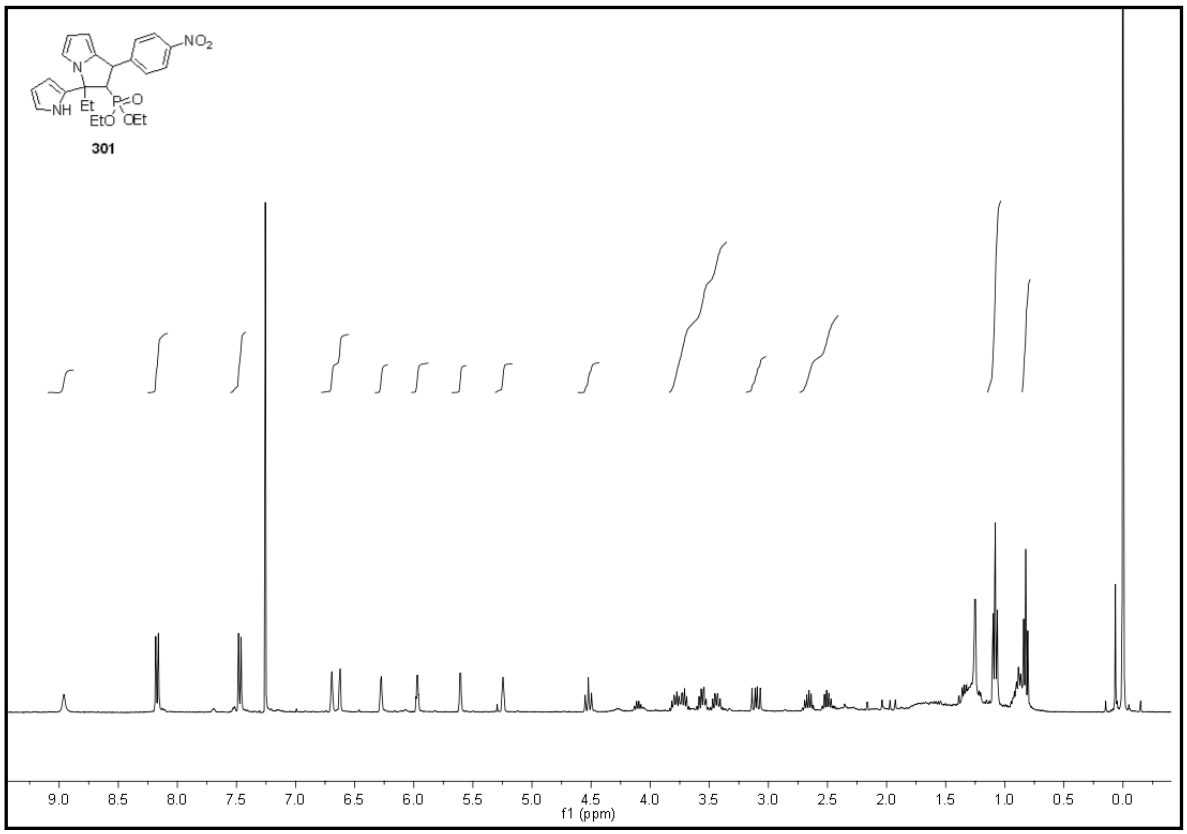


Figure A.241. ^{1}H NMR spectrum of compound **301**

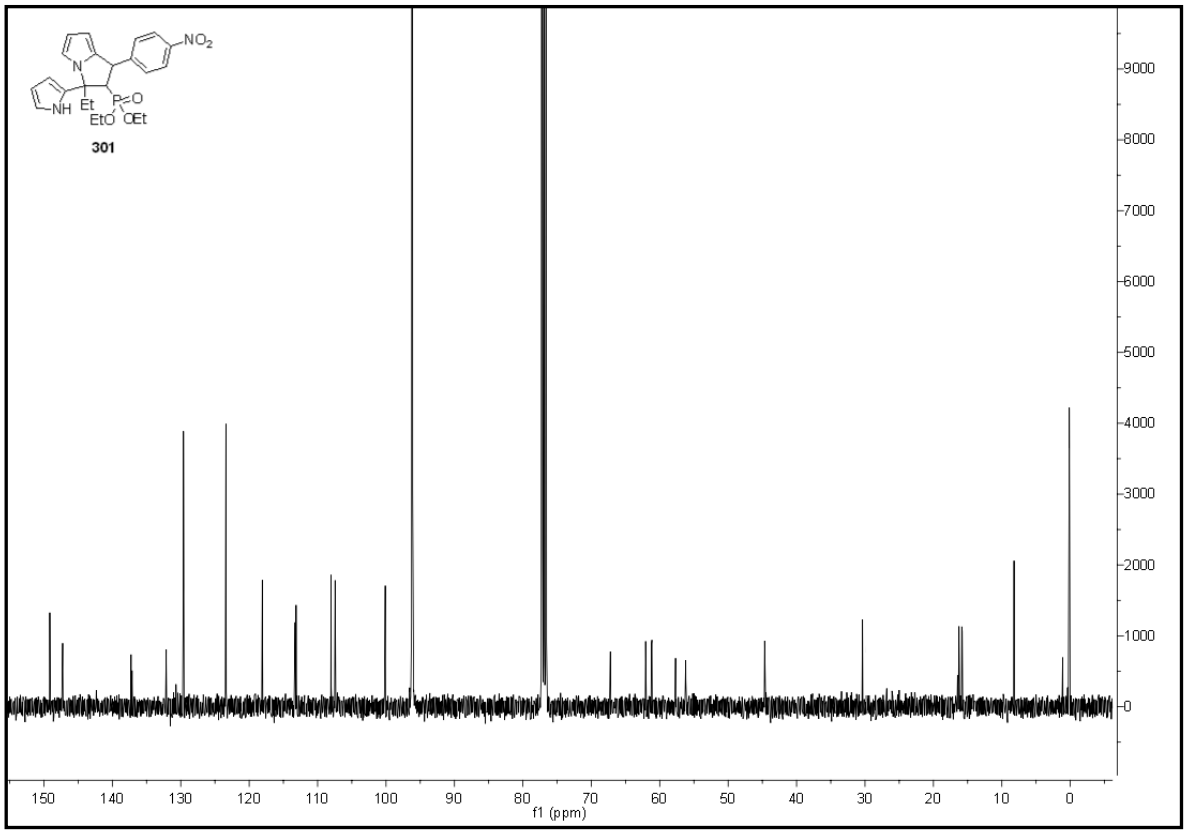


Figure A.242. ^{13}C NMR spectrum of compound **301**

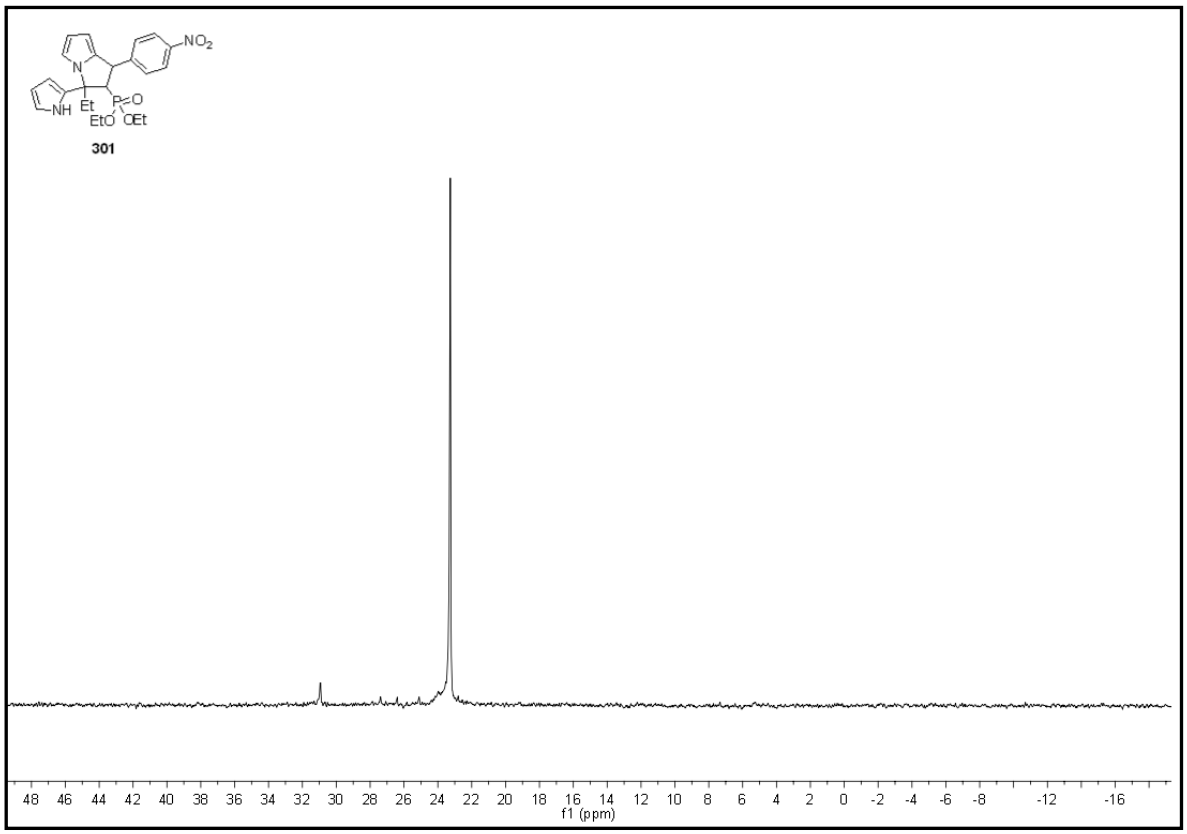


Figure A.243. ^{31}P NMR spectrum of compound **301**

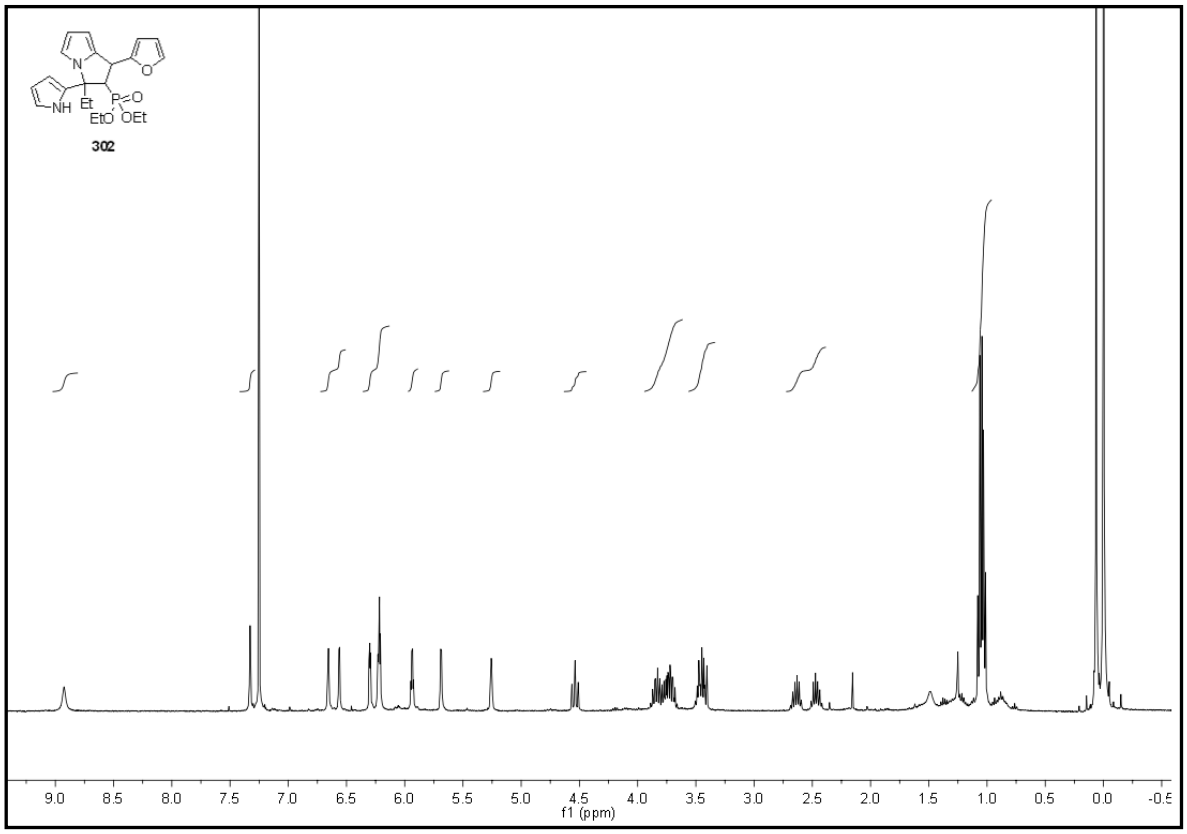


Figure A.244. ^{1}H NMR spectrum of compound **302**

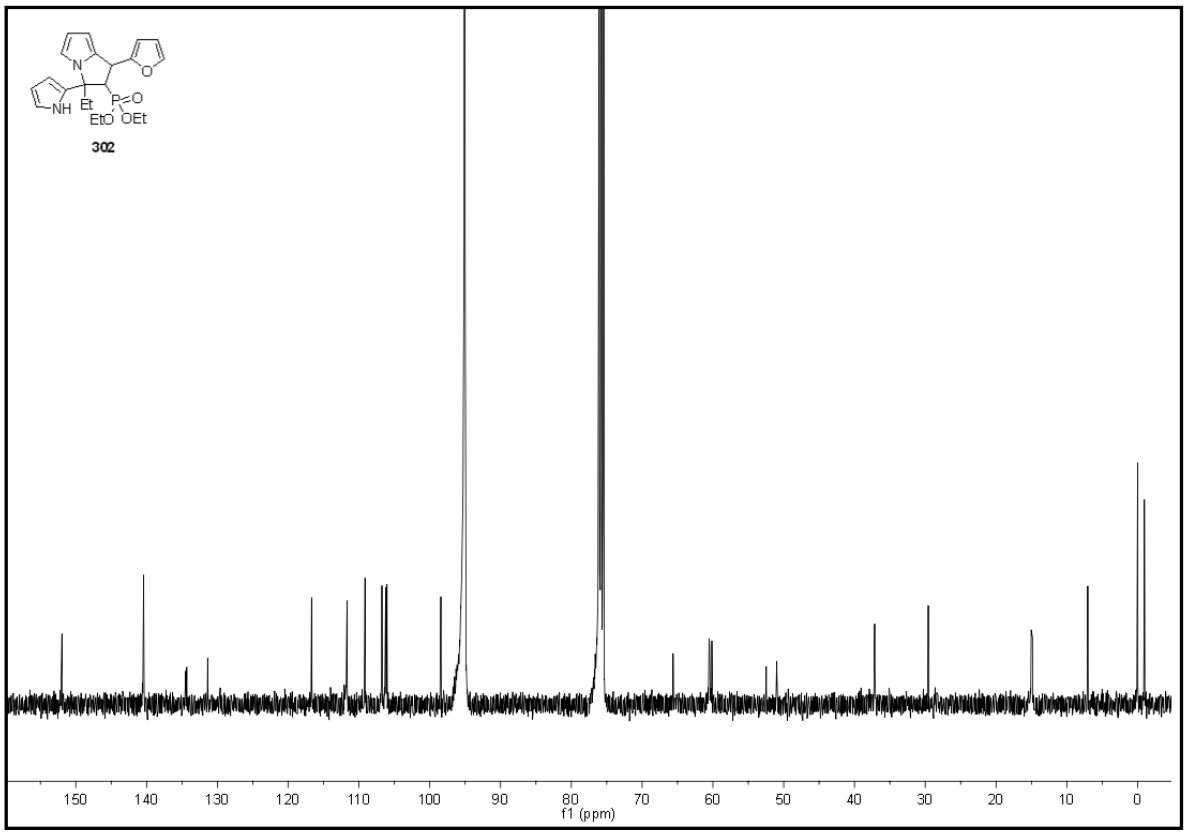


Figure A.245. ^{13}C NMR spectrum of compound **302**

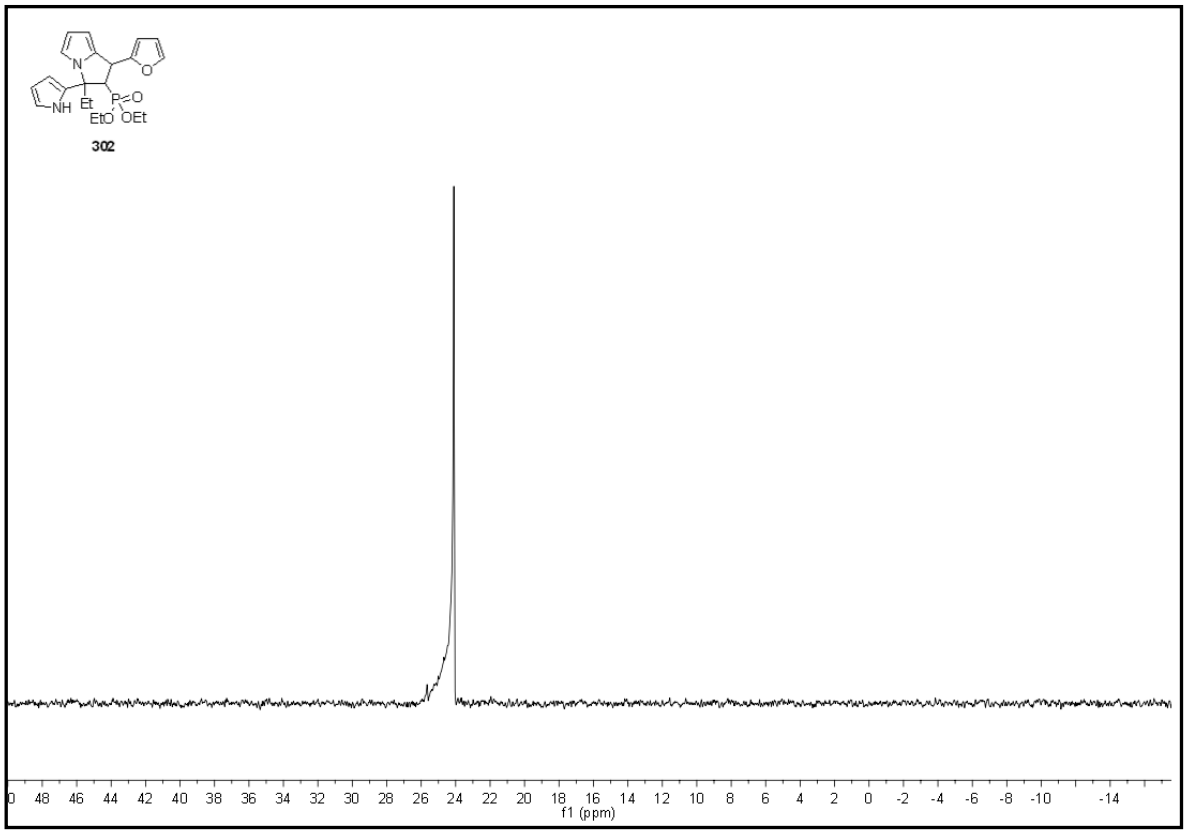


Figure A.246. ^{31}P NMR spectrum of compound **302**

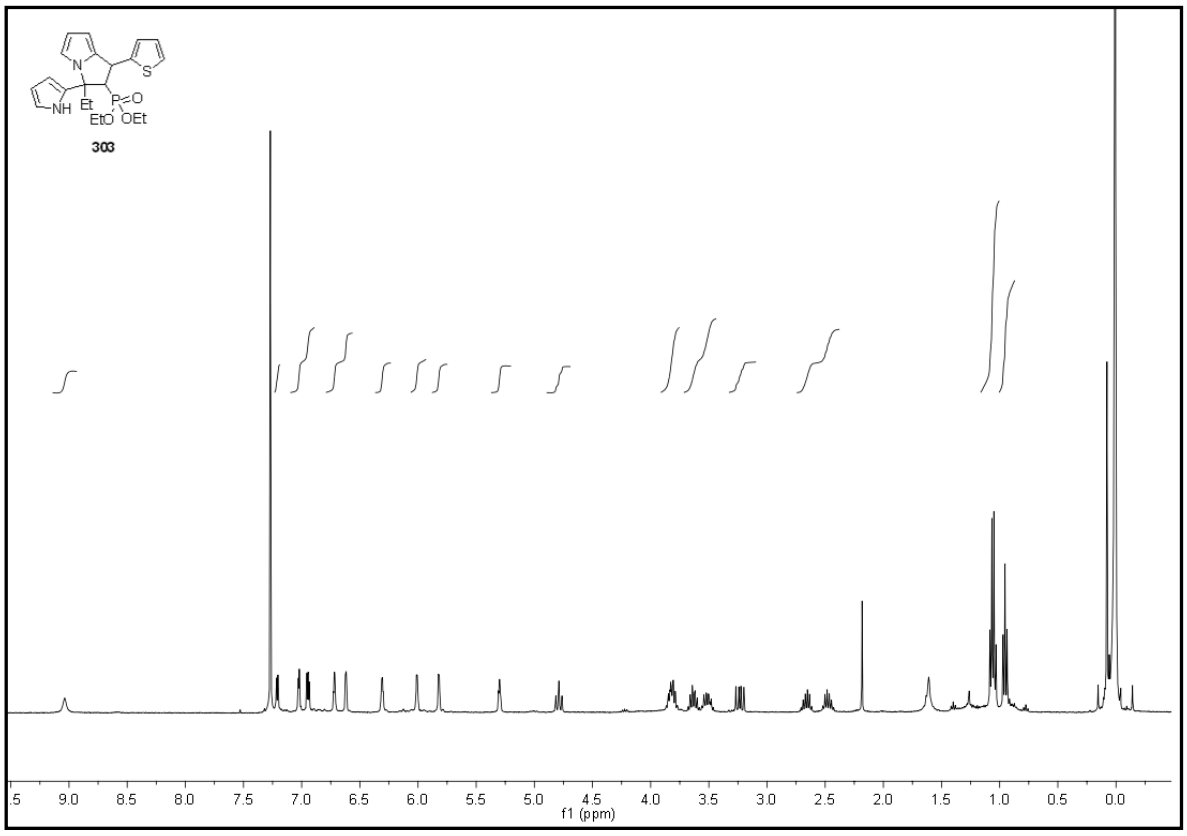


Figure A.247. ^{1}H NMR spectrum of compound **303**

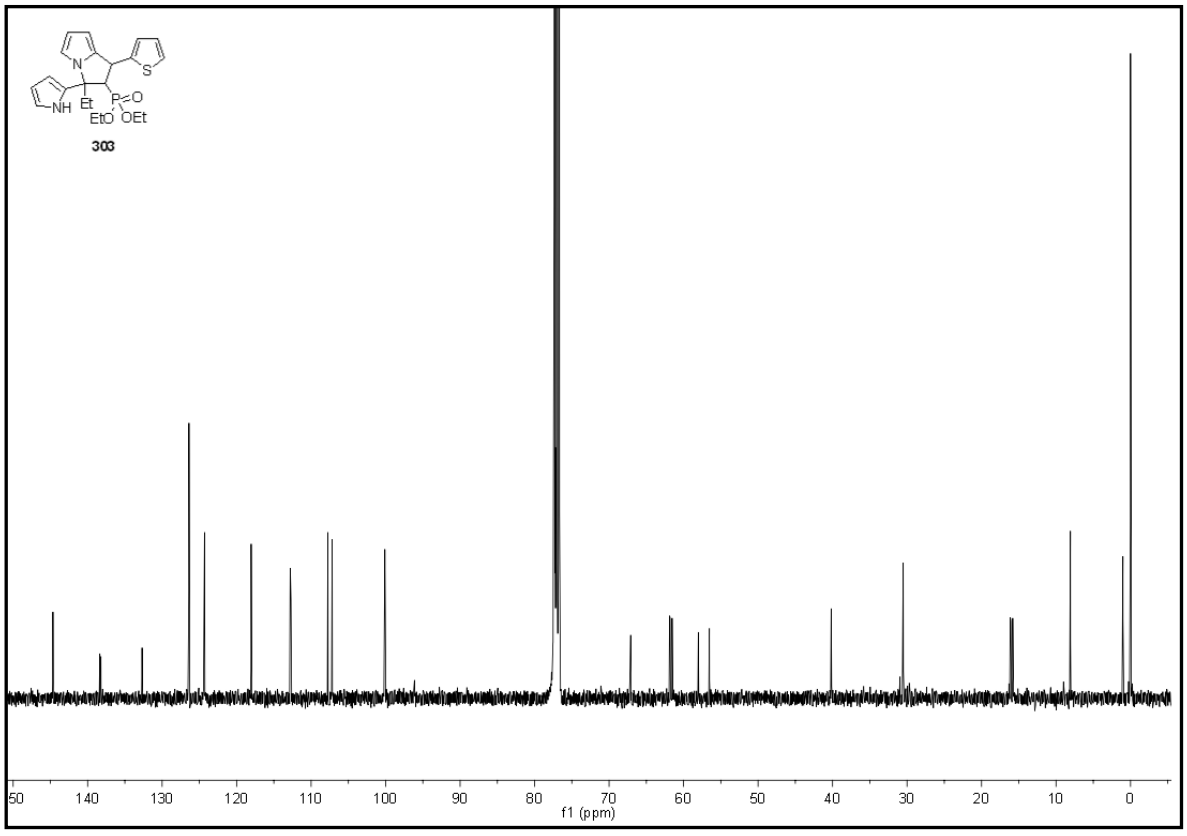


Figure A.248. ^{13}C NMR spectrum of compound **303**

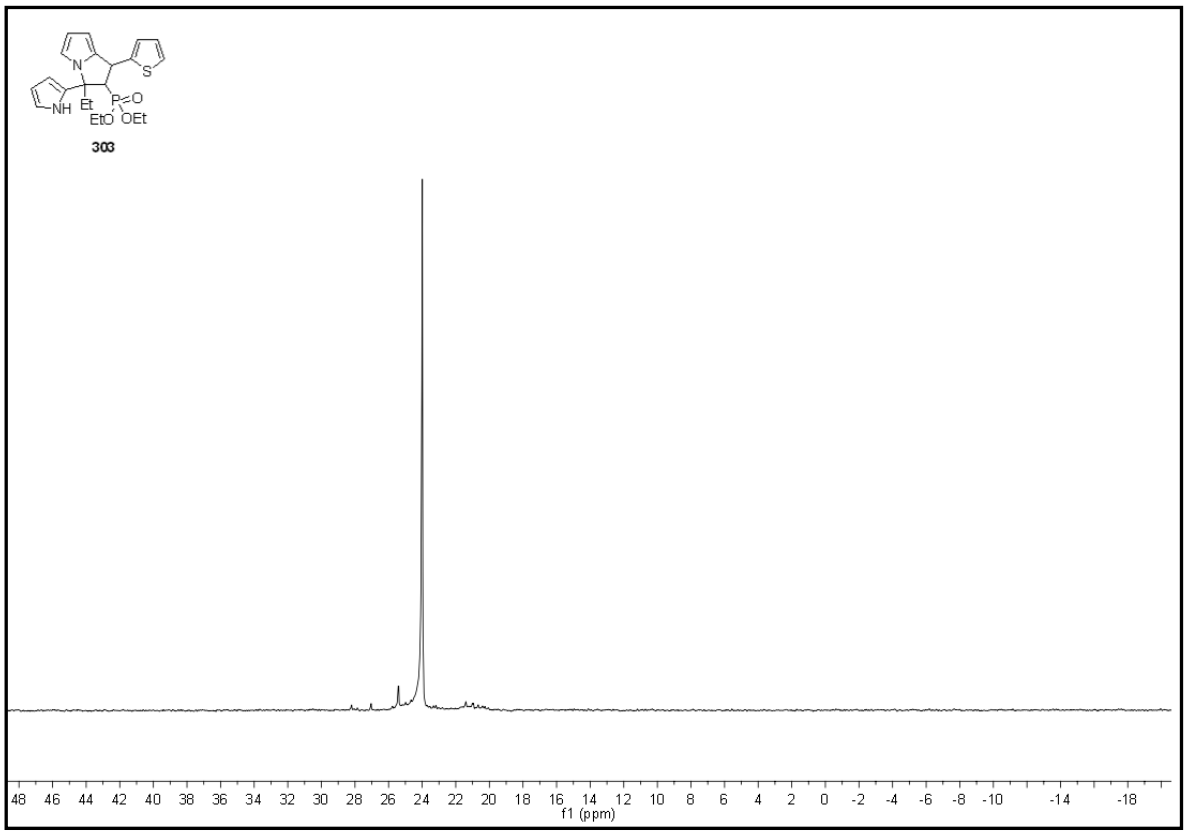


Figure A.249. ^{31}P NMR spectrum of compound **303**

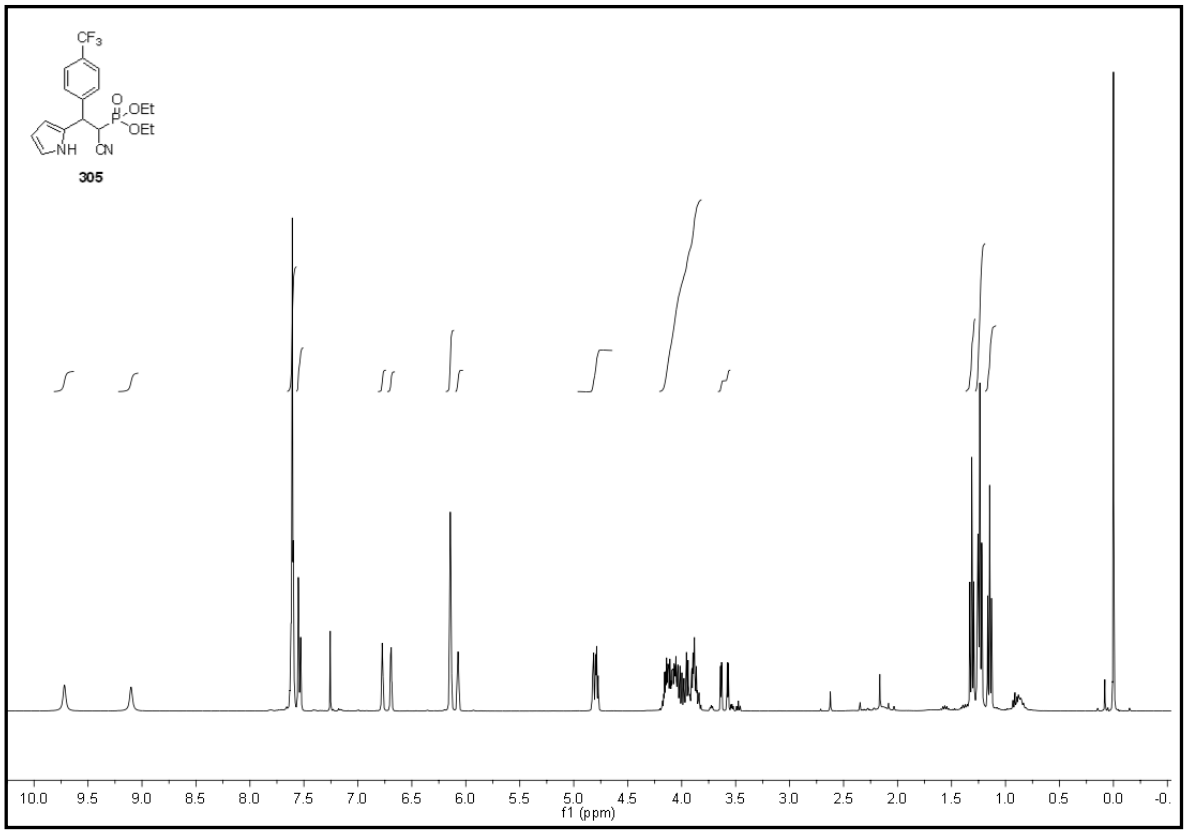


Figure A.250. ^{1}H NMR spectrum of compound **305**

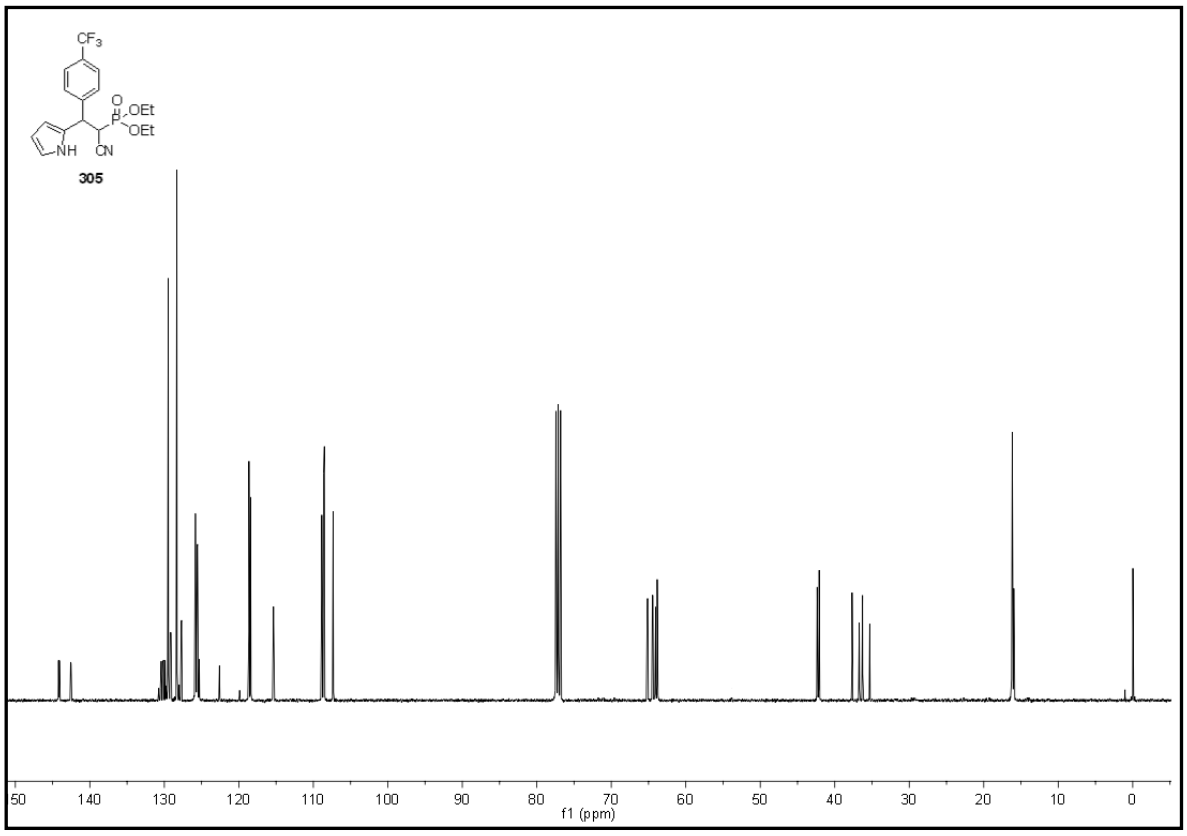


Figure A.251. ^{13}C NMR spectrum of compound **305**

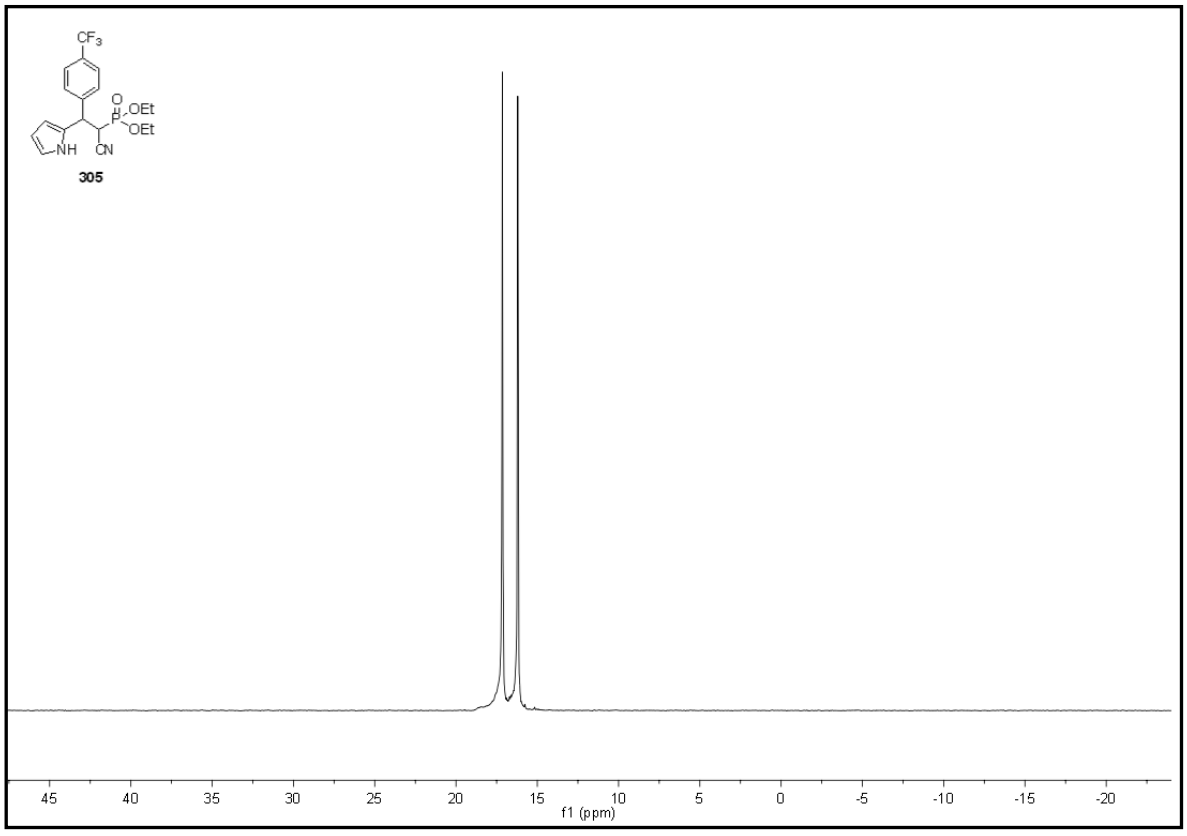


Figure A.252. ^{31}P NMR spectrum of compound **305**

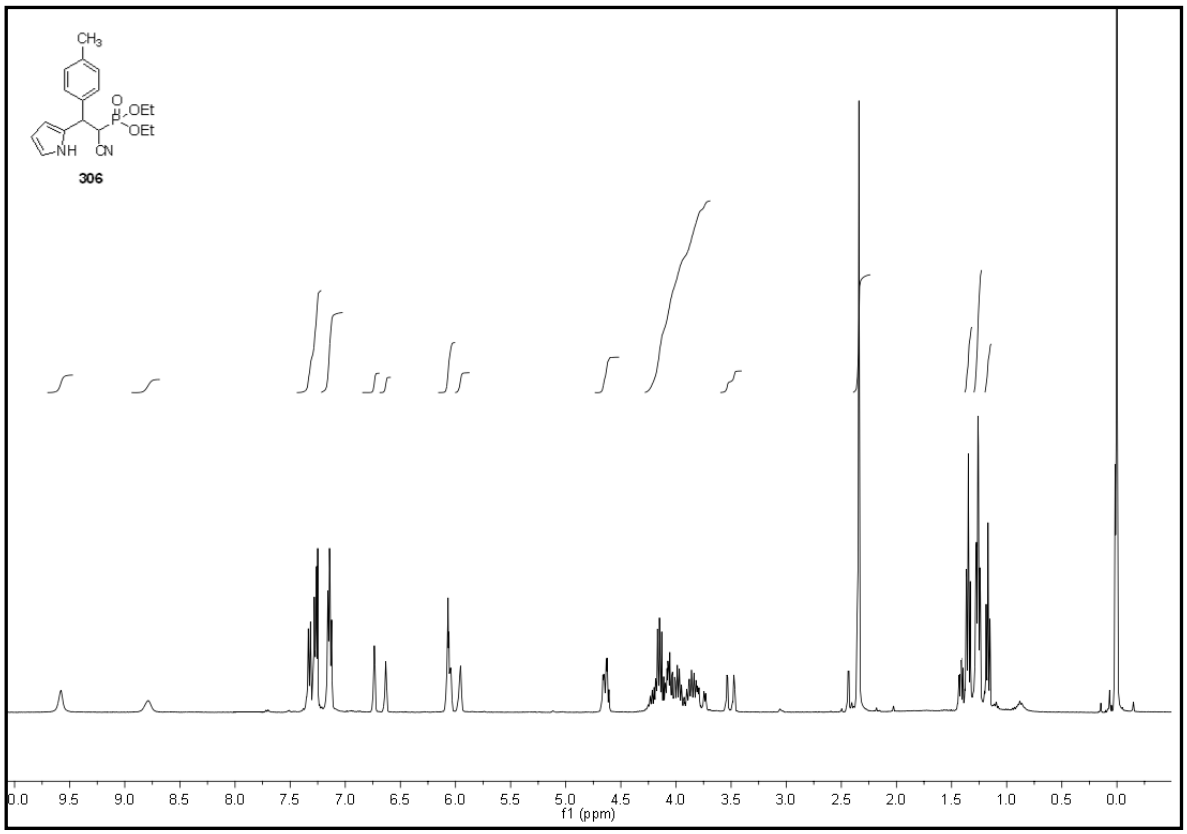


Figure A.253. ^{1}H NMR spectrum of compound **306**

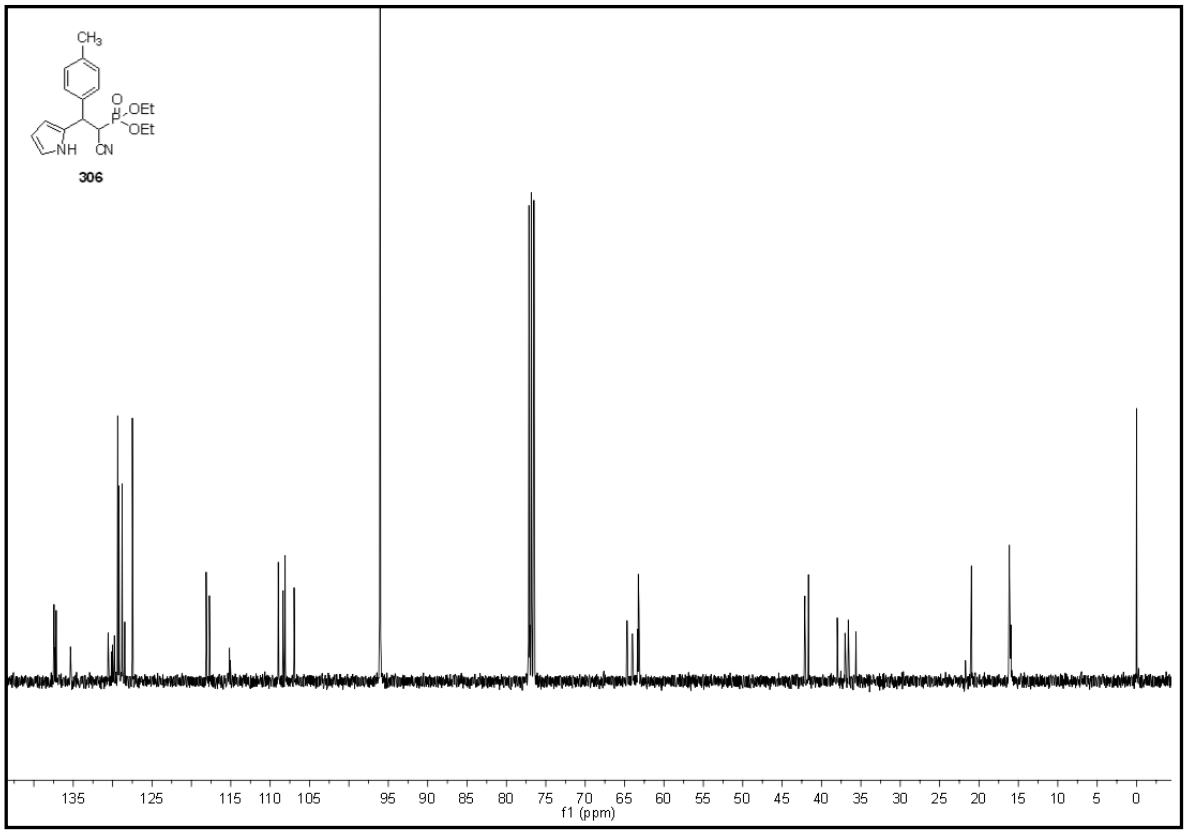


Figure A.254. ^{13}C NMR spectrum of compound **306**

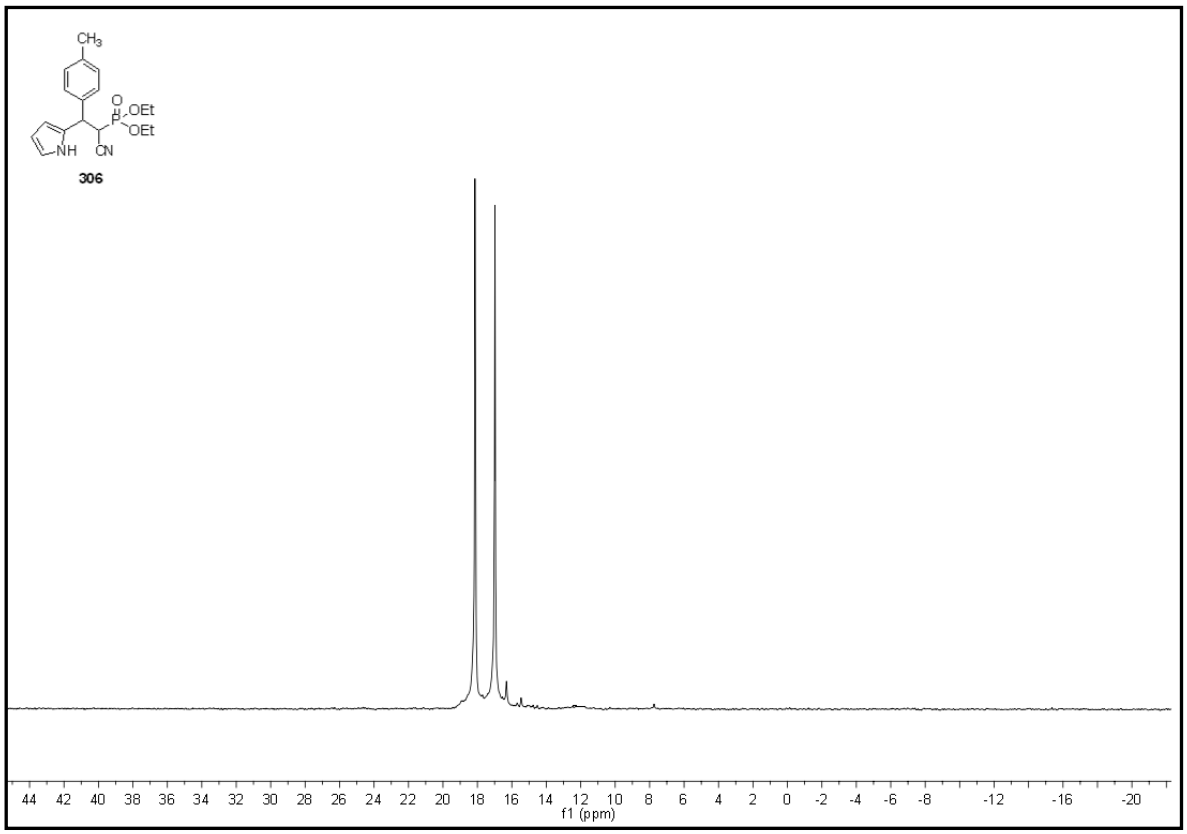


Figure A.255. ^{31}P NMR spectrum of compound **306**

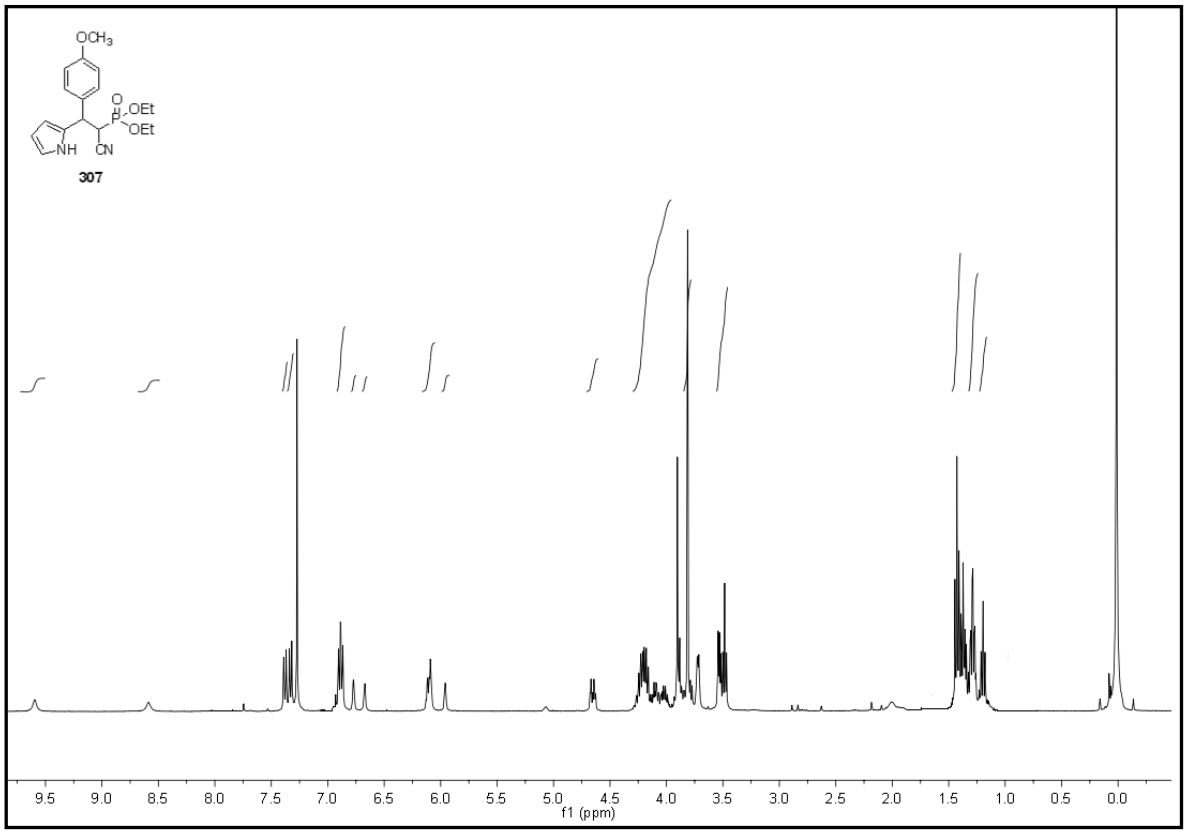


Figure A.256. ^{1}H NMR spectrum of compound **307**

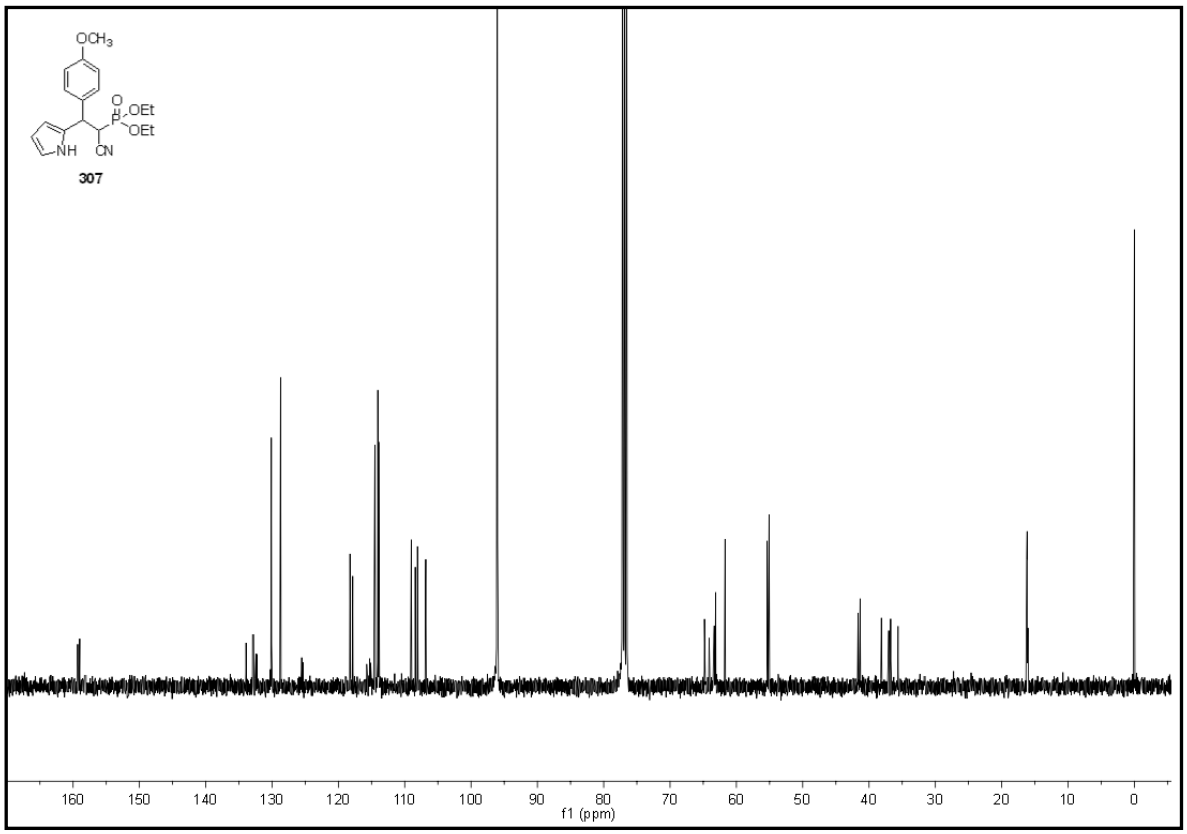


Figure A.257. ^{13}C NMR spectrum of compound **307**

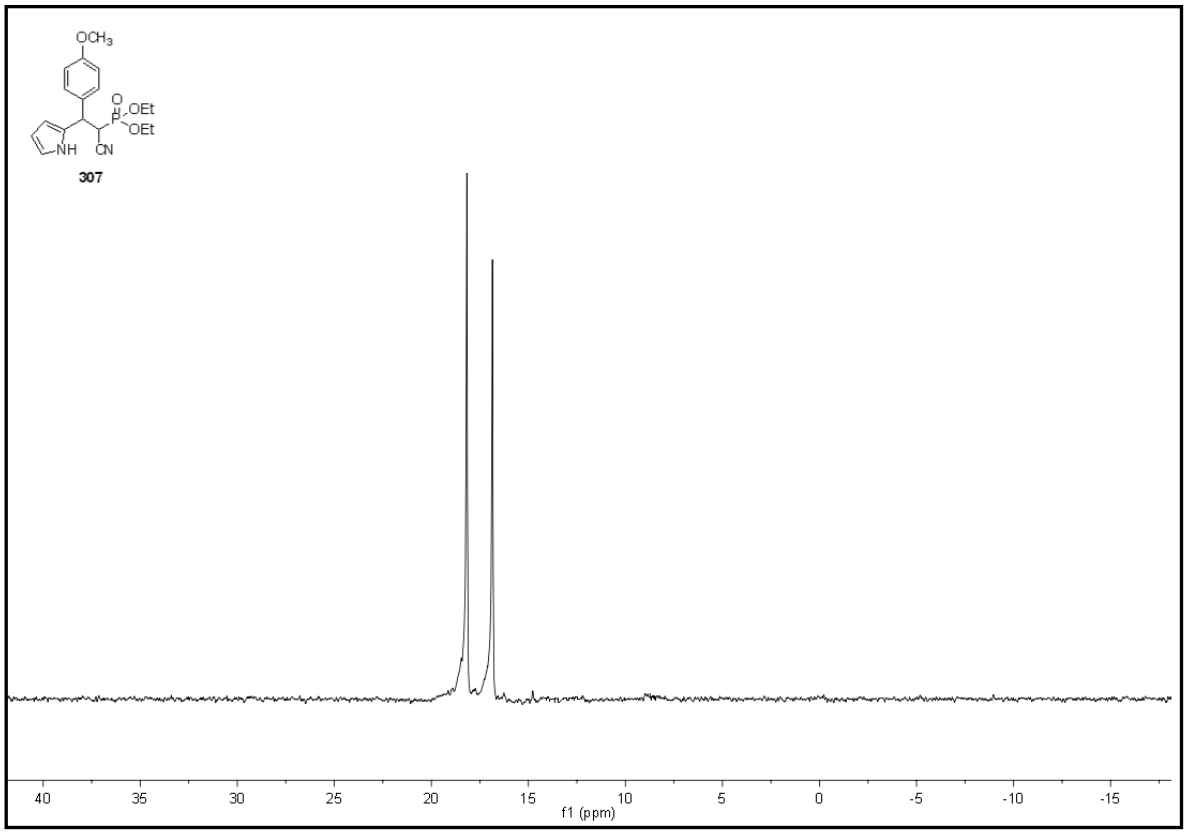


Figure A.258. ^{31}P NMR spectrum of compound **307**

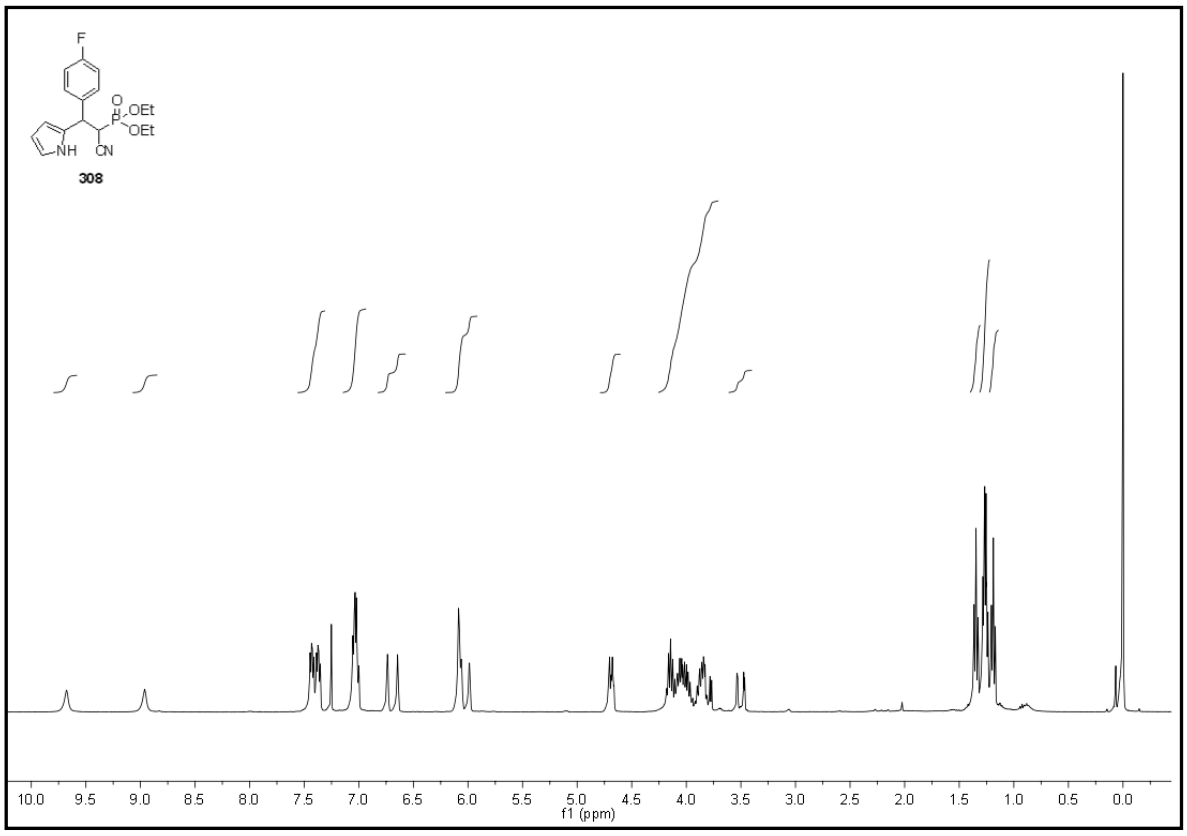


Figure A.259. ^{1}H NMR spectrum of compound **308**

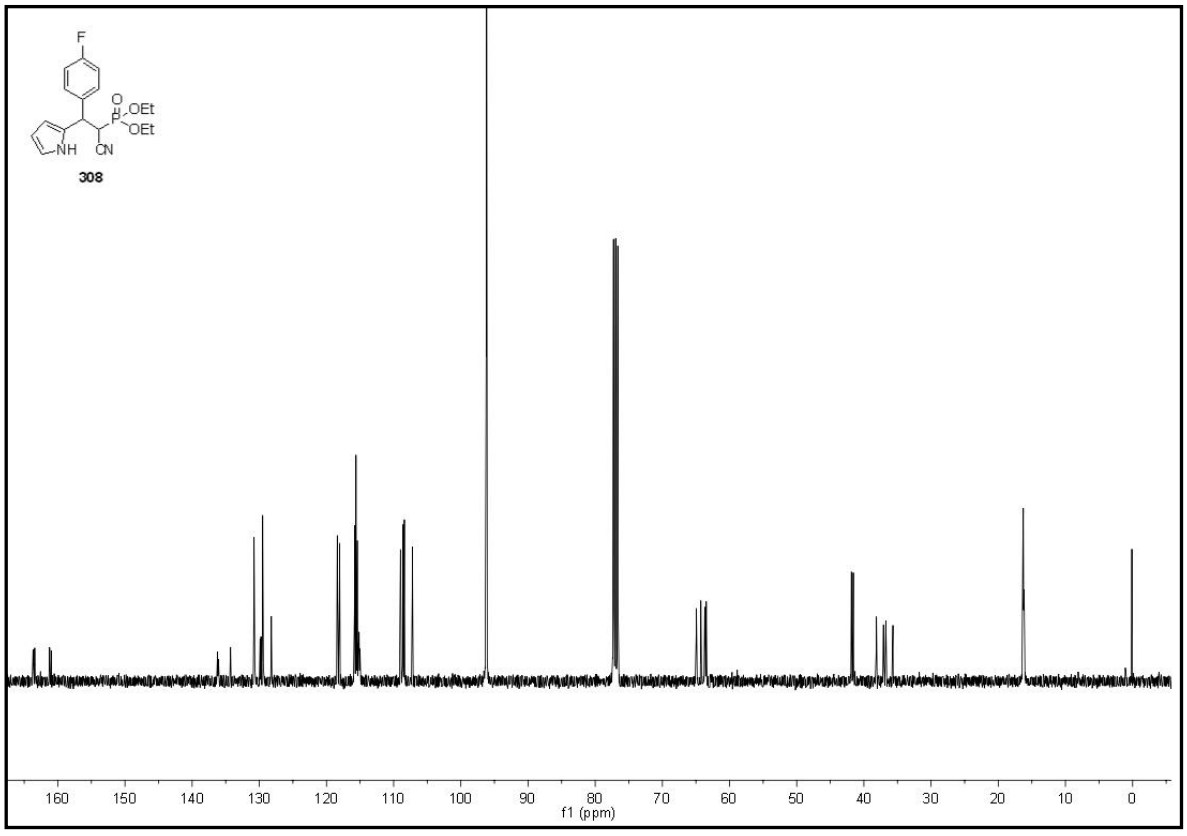


Figure A.260. ^{13}C NMR spectrum of compound **308**

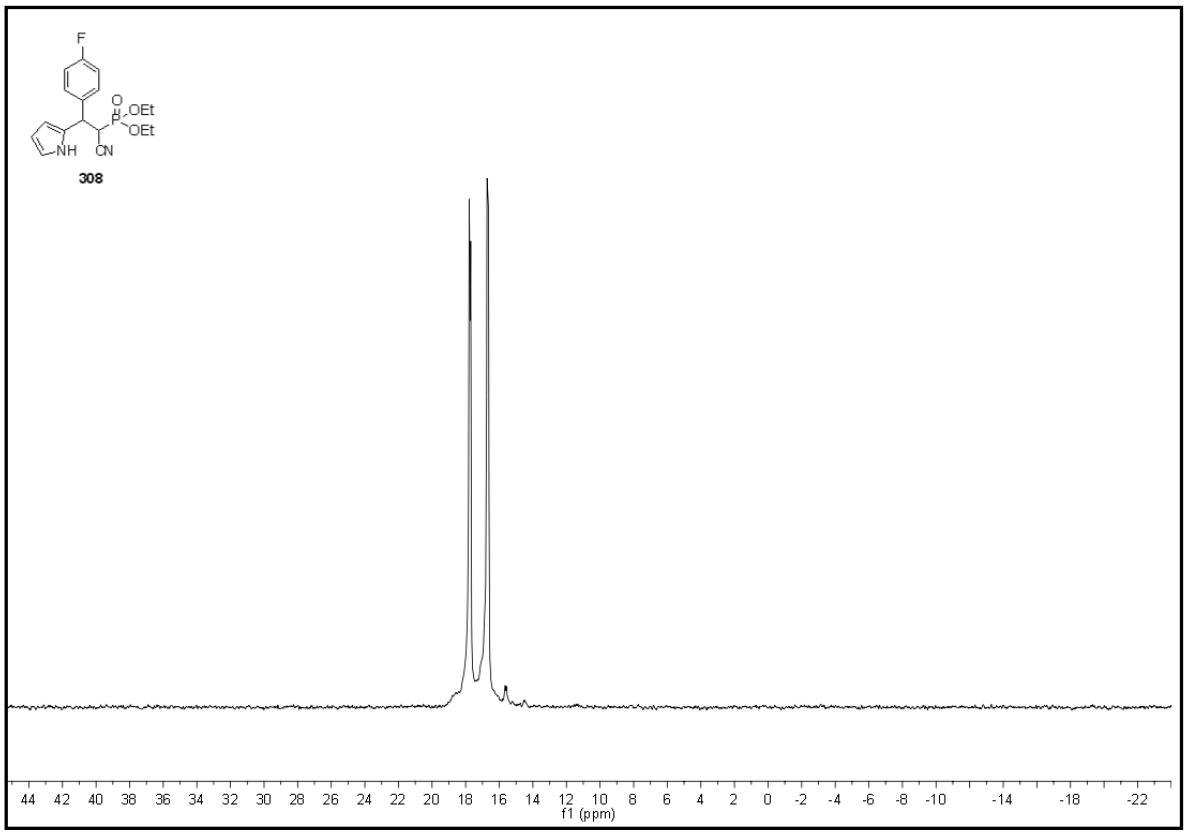


Figure A.261. ^{31}P NMR spectrum of compound **308**

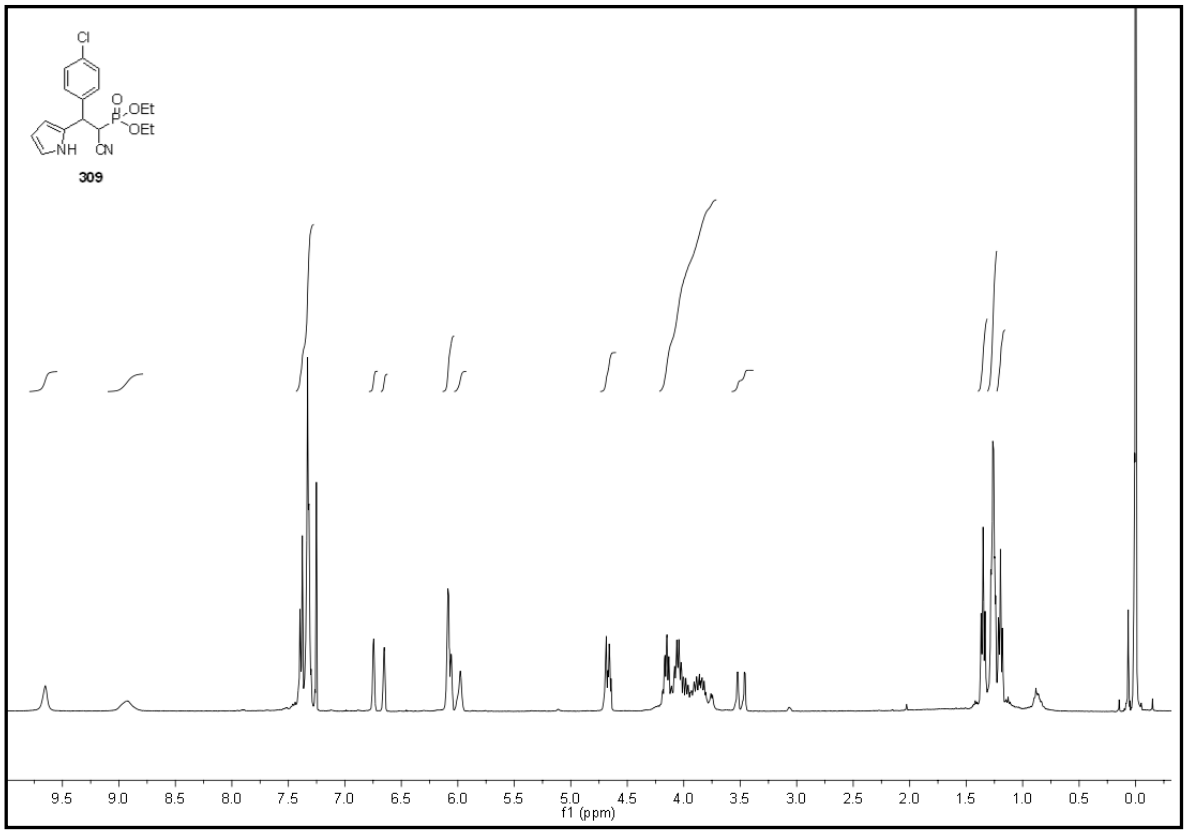


Figure A.262. ^{1}H NMR spectrum of compound **309**

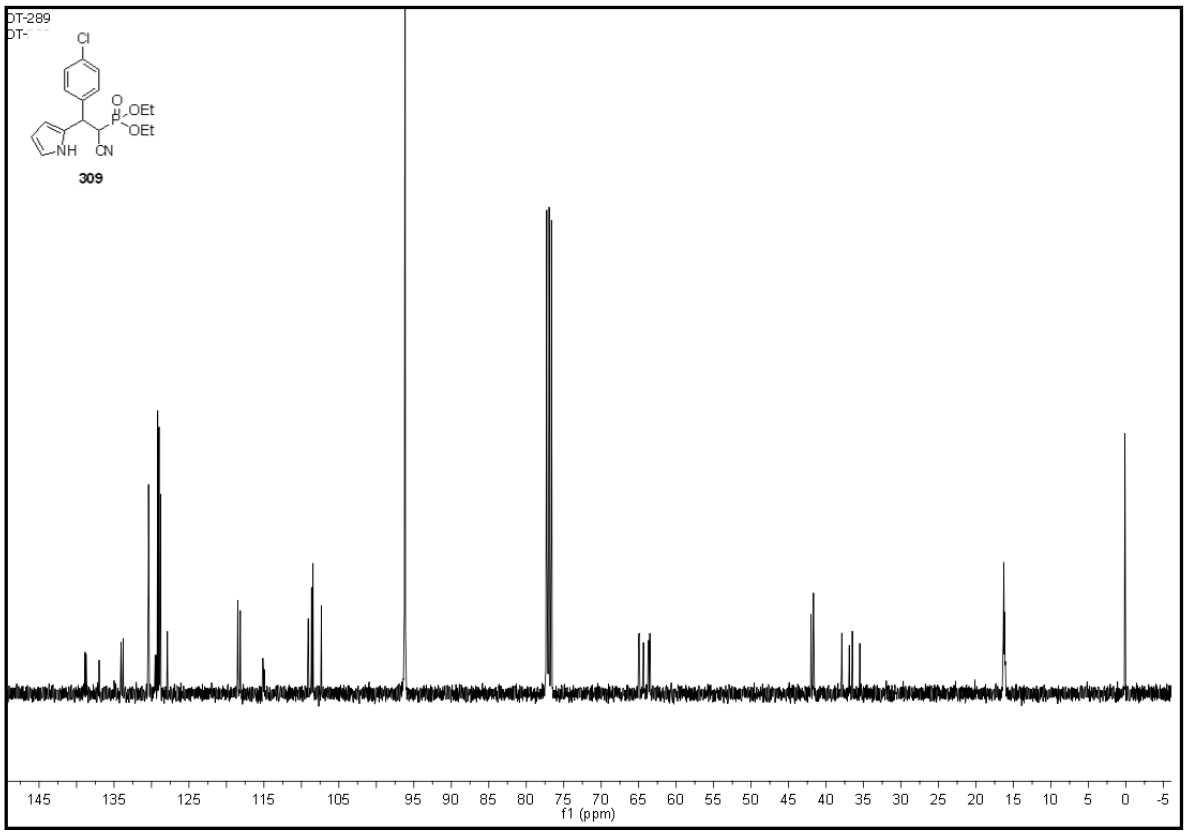


Figure A.263. ^{13}C NMR spectrum of compound **309**

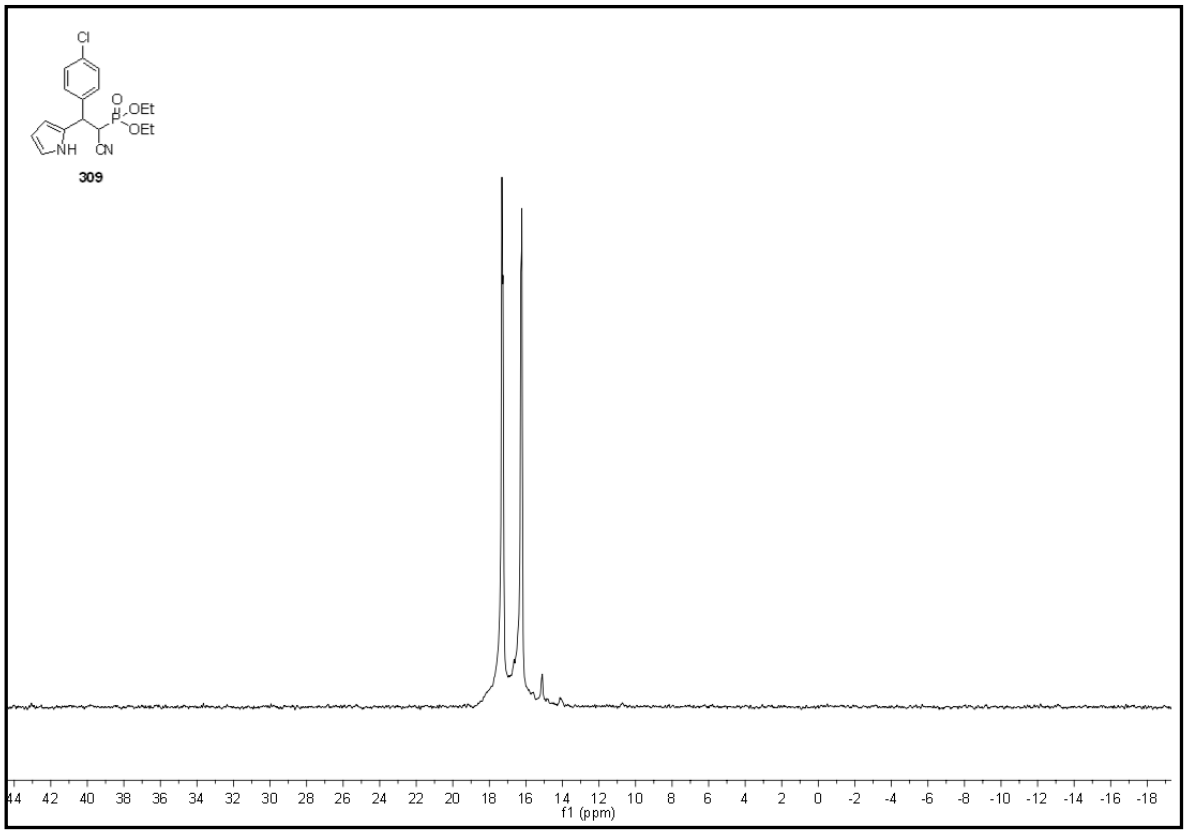


Figure A.264. ^{31}P NMR spectrum of compound **309**

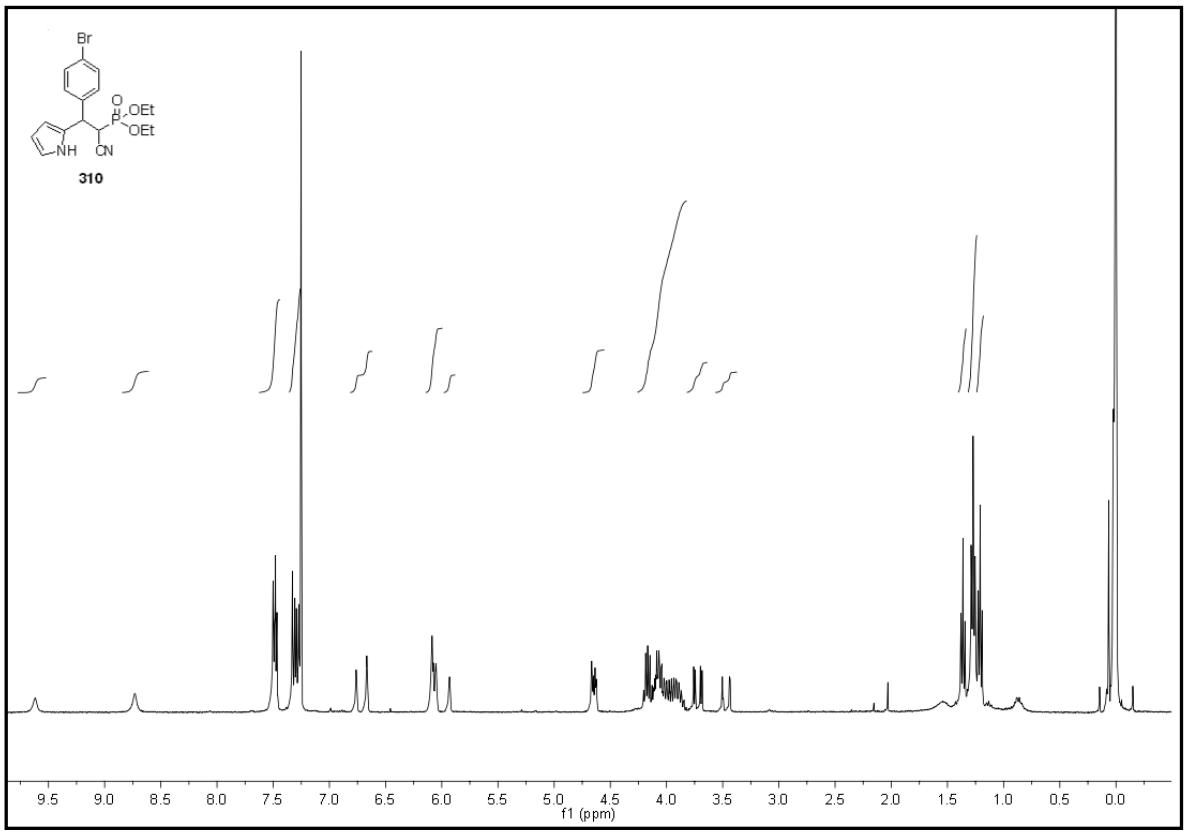


Figure A.265. ^{1}H NMR spectrum of compound **310**

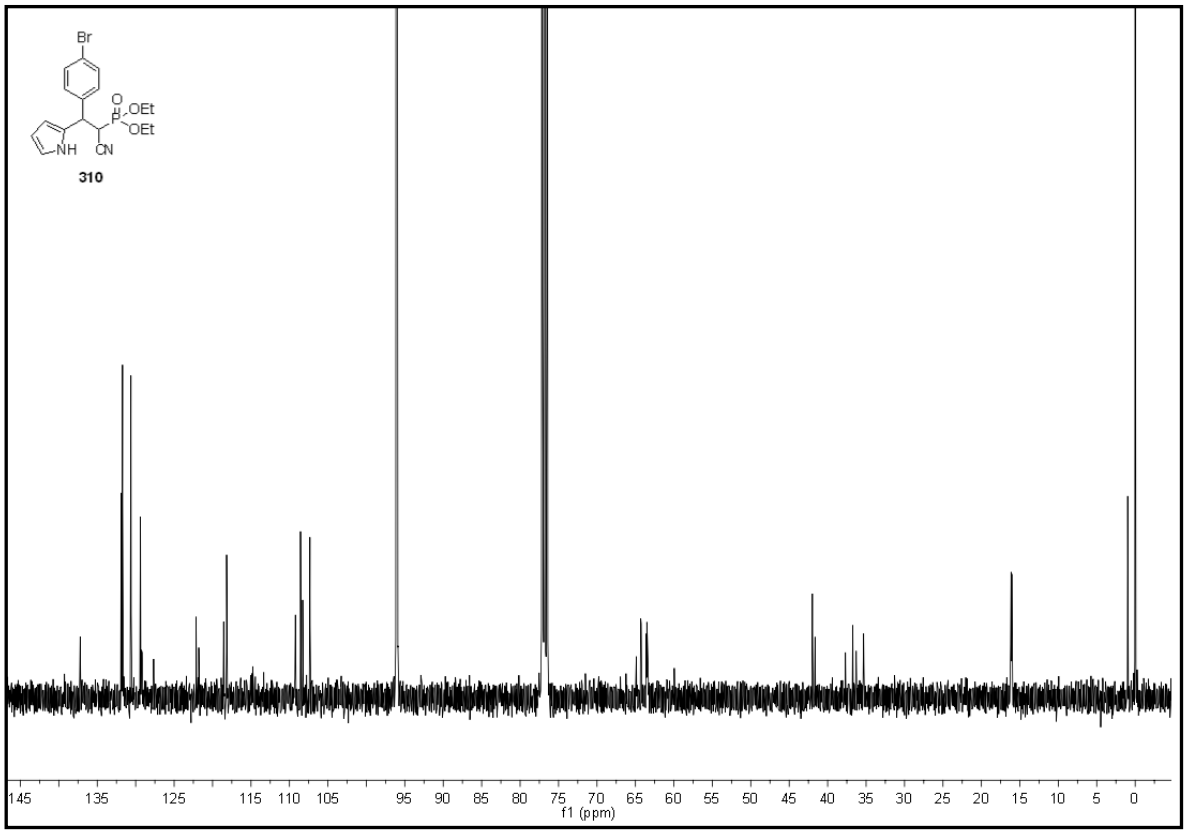


Figure A.266. ^{13}C NMR spectrum of compound **310**

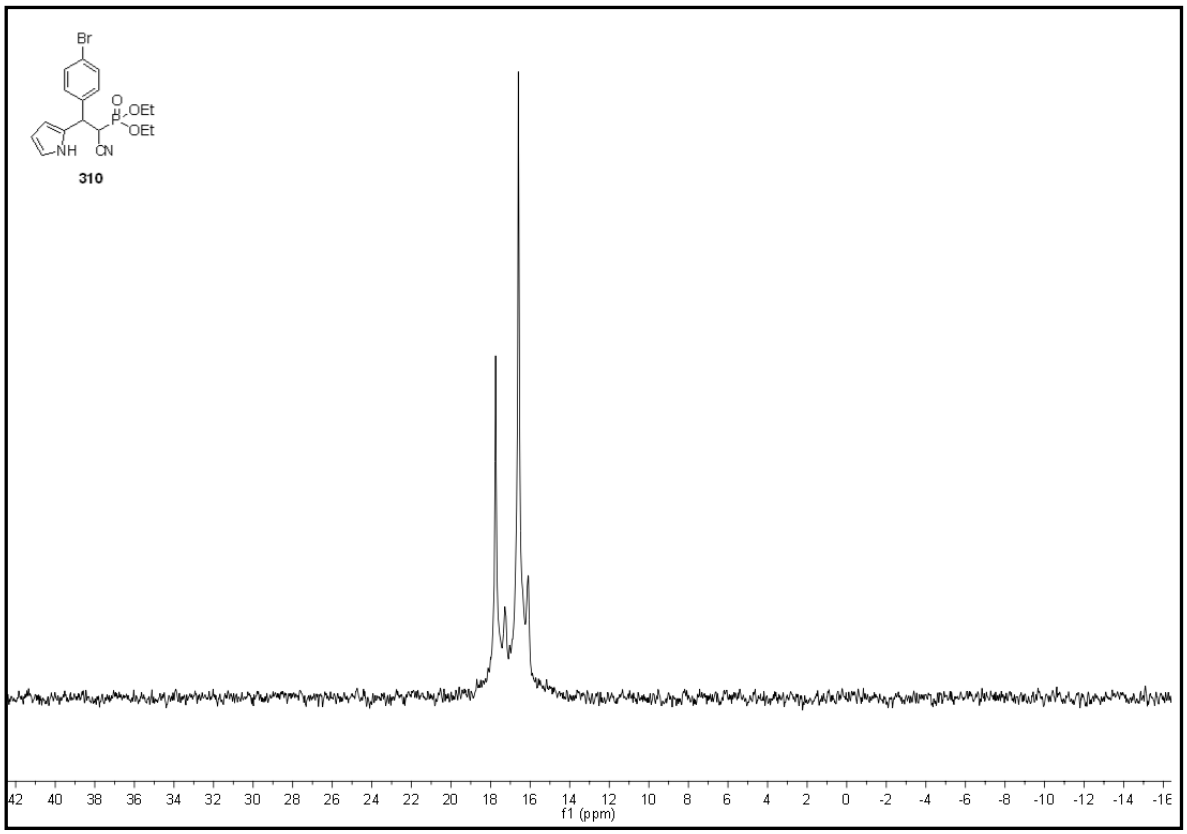


Figure A.267. ^{31}P NMR spectrum of compound **310**

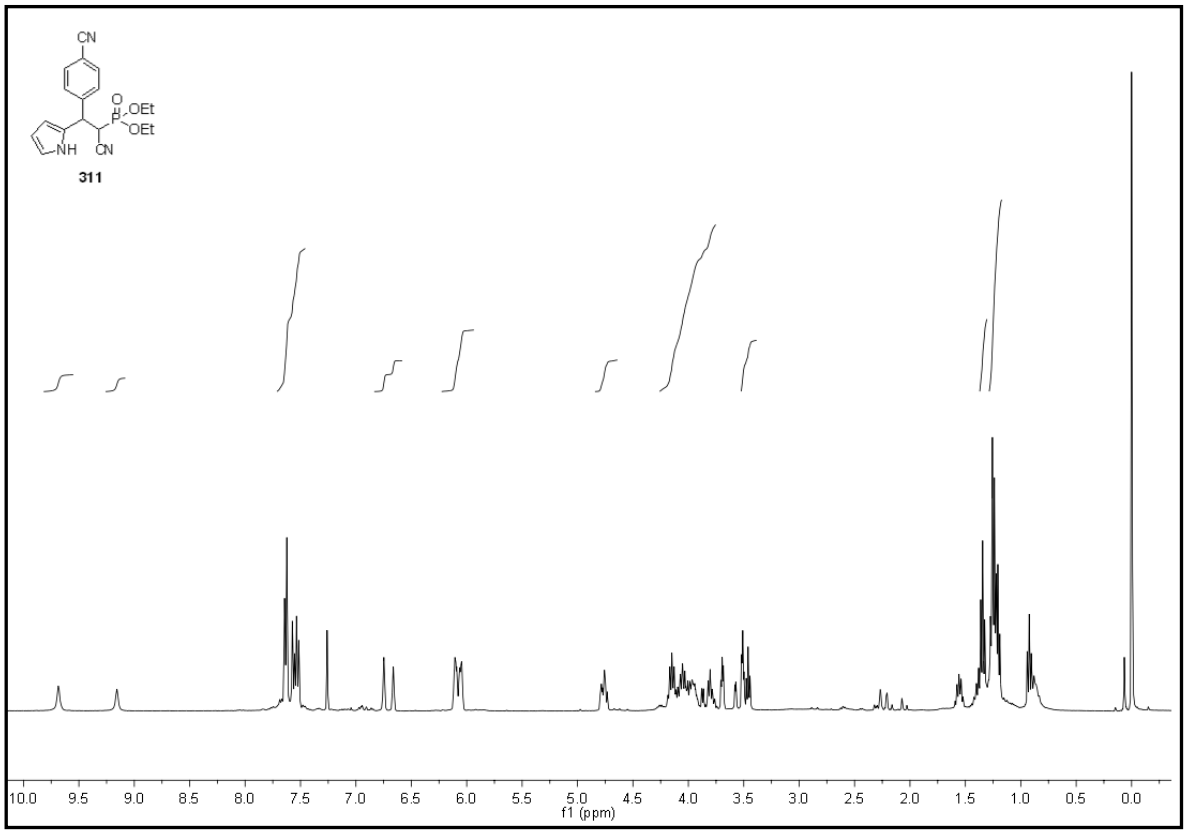


Figure A.268. ^{1}H NMR spectrum of compound **311**

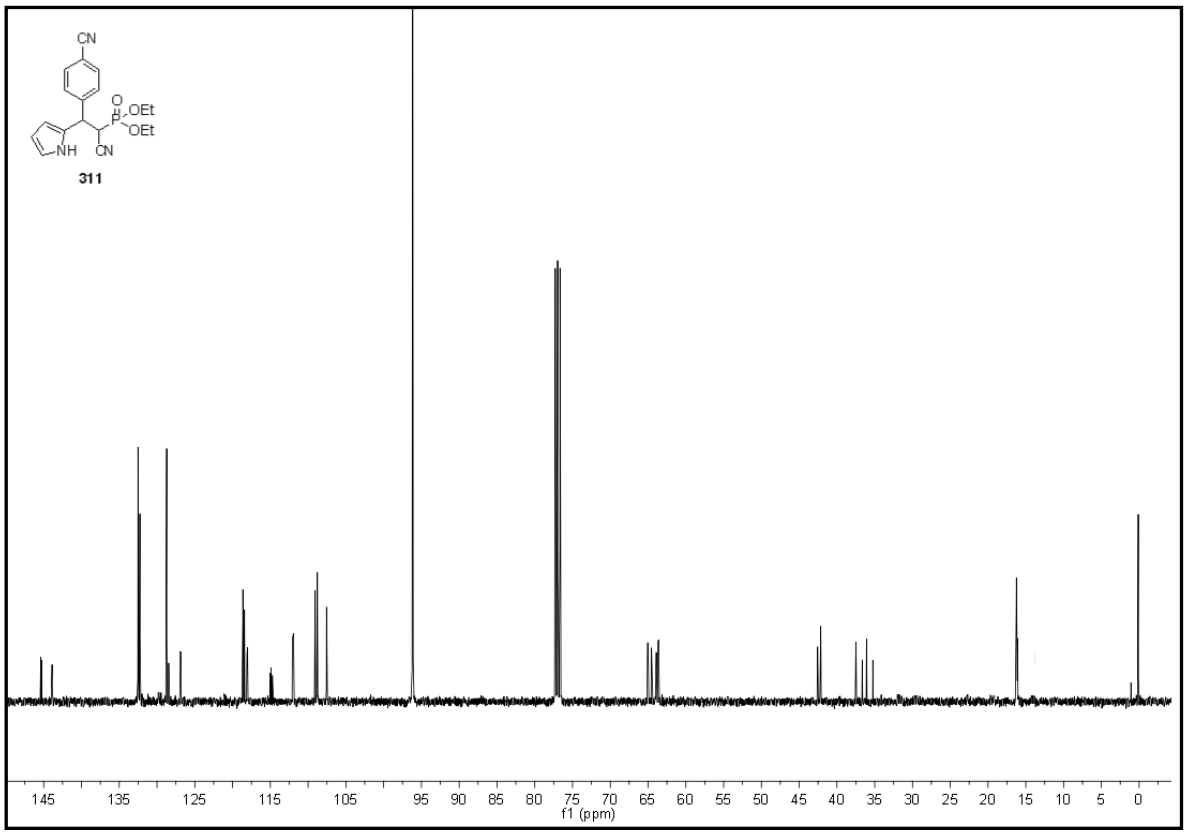


Figure A.269. ^{13}C NMR spectrum of compound **311**

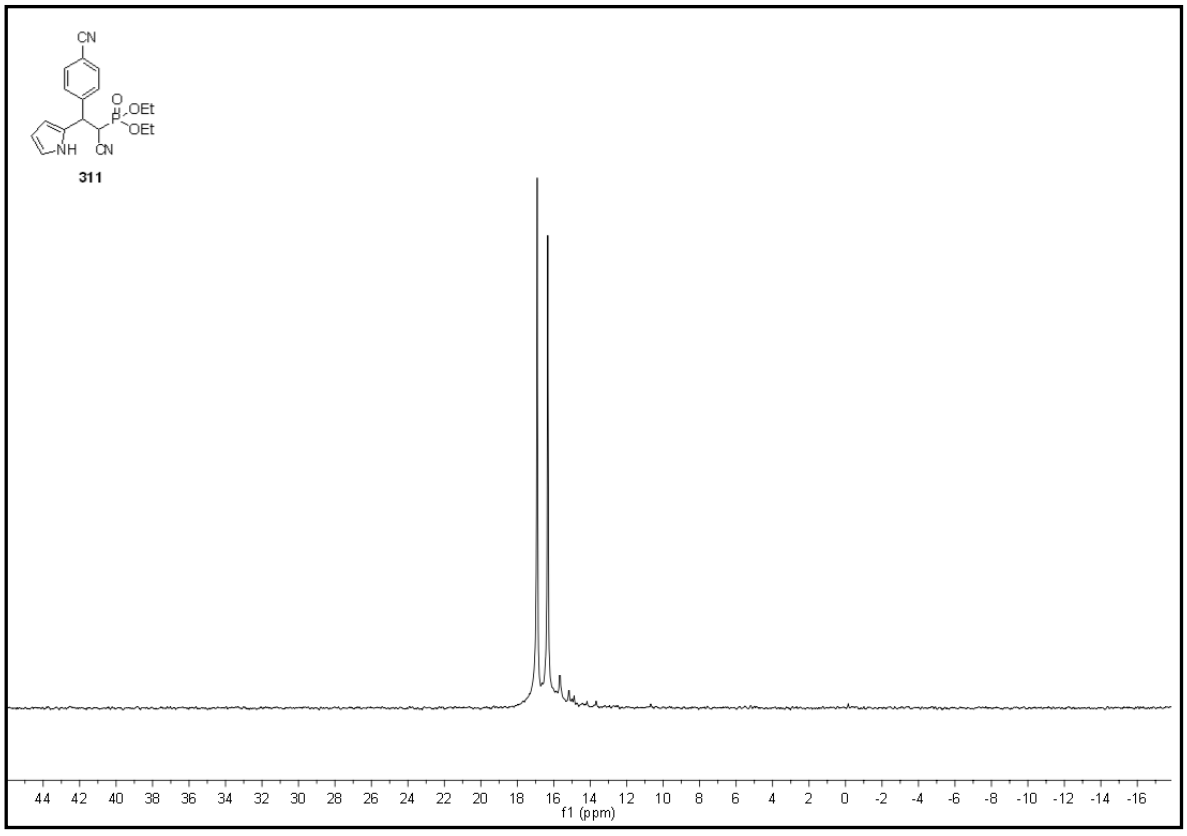


Figure A.270. ^{31}P NMR spectrum of compound **311**

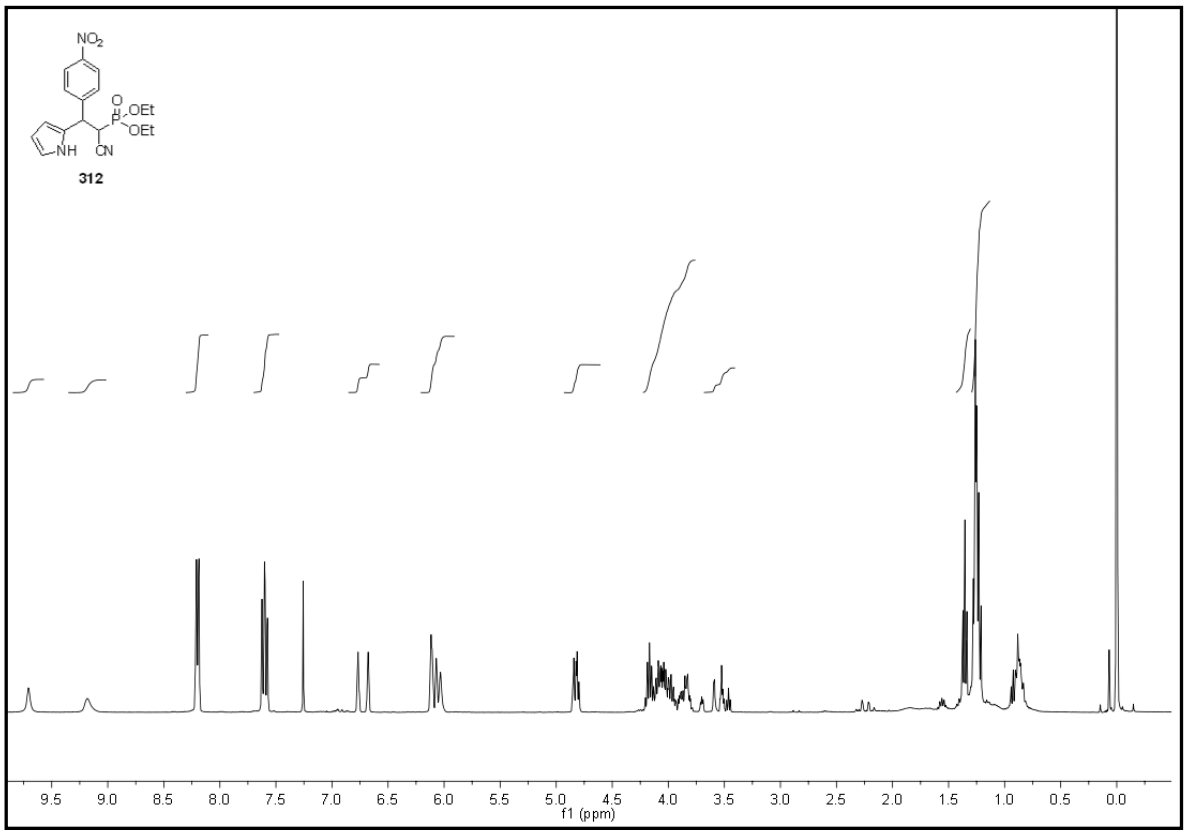


Figure A.271. ^{1}H NMR spectrum of compound **312**

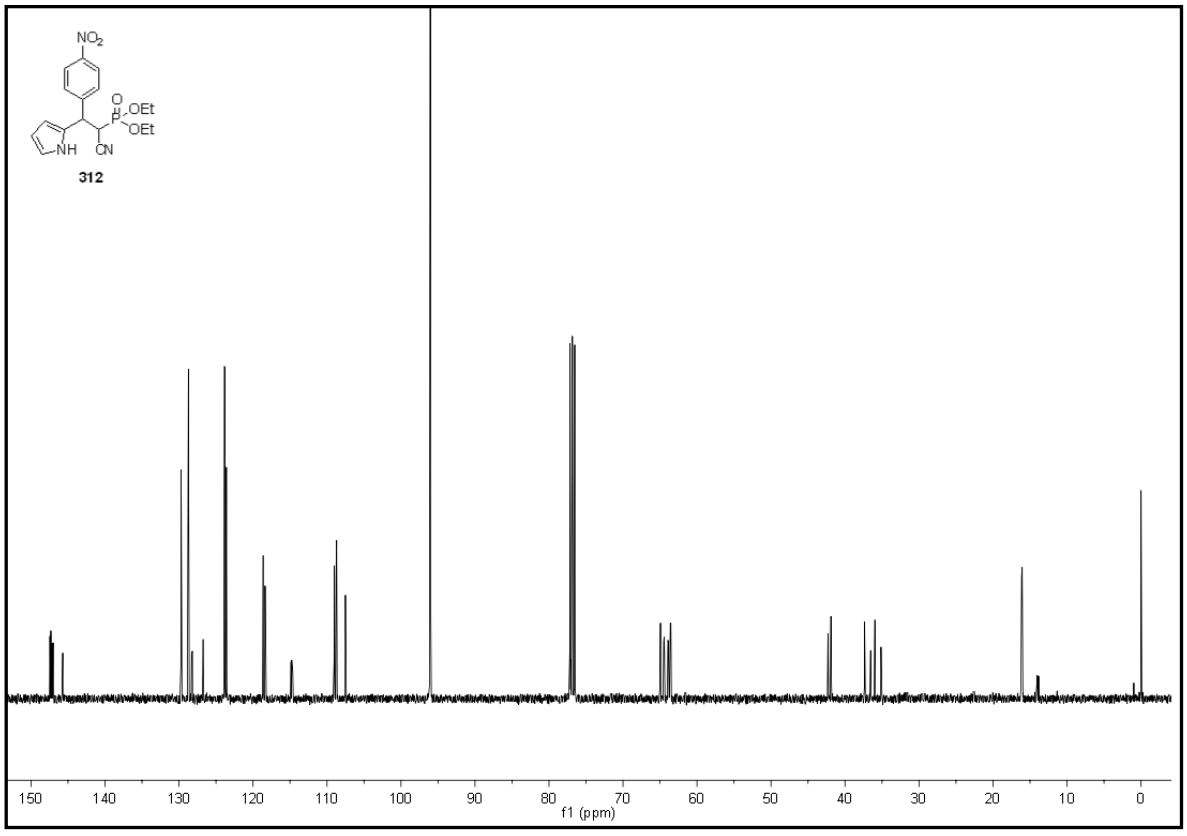


Figure A.272. ^{13}C NMR spectrum of compound **312**

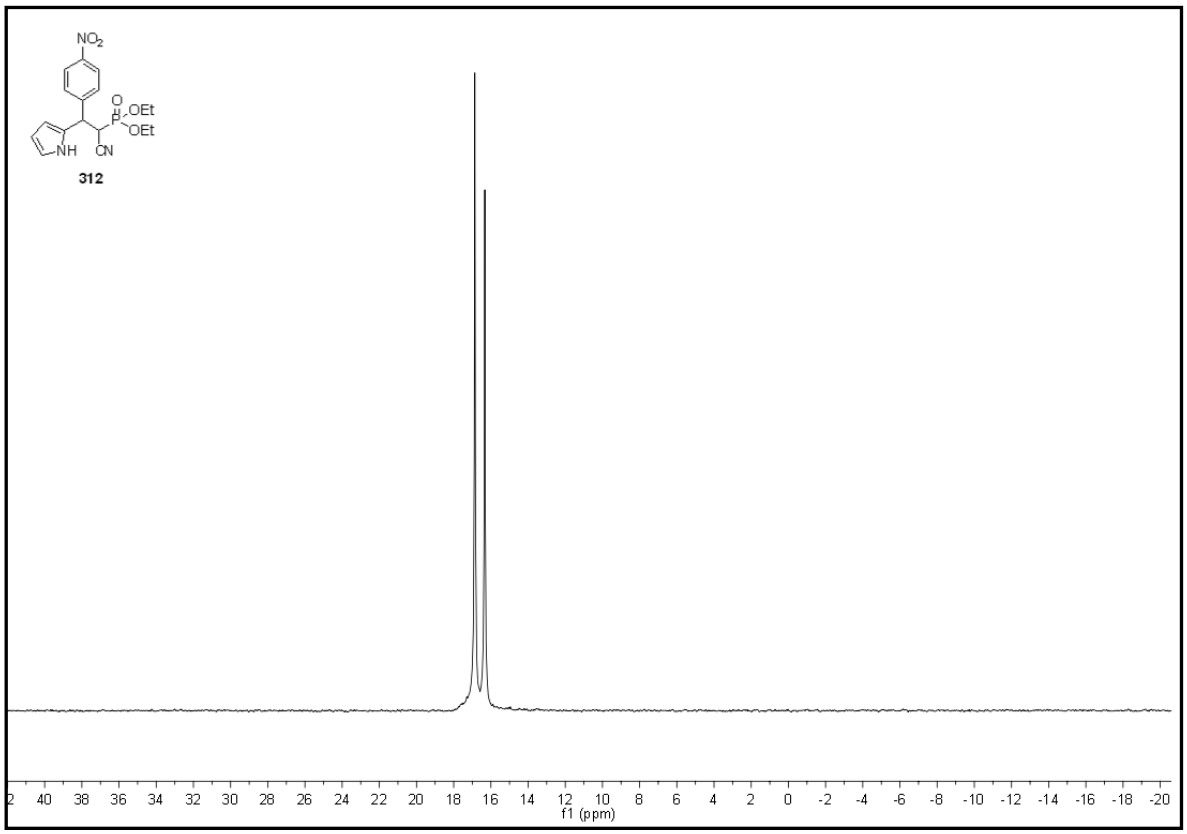


Figure A.273. ^{31}P NMR spectrum of compound **312**

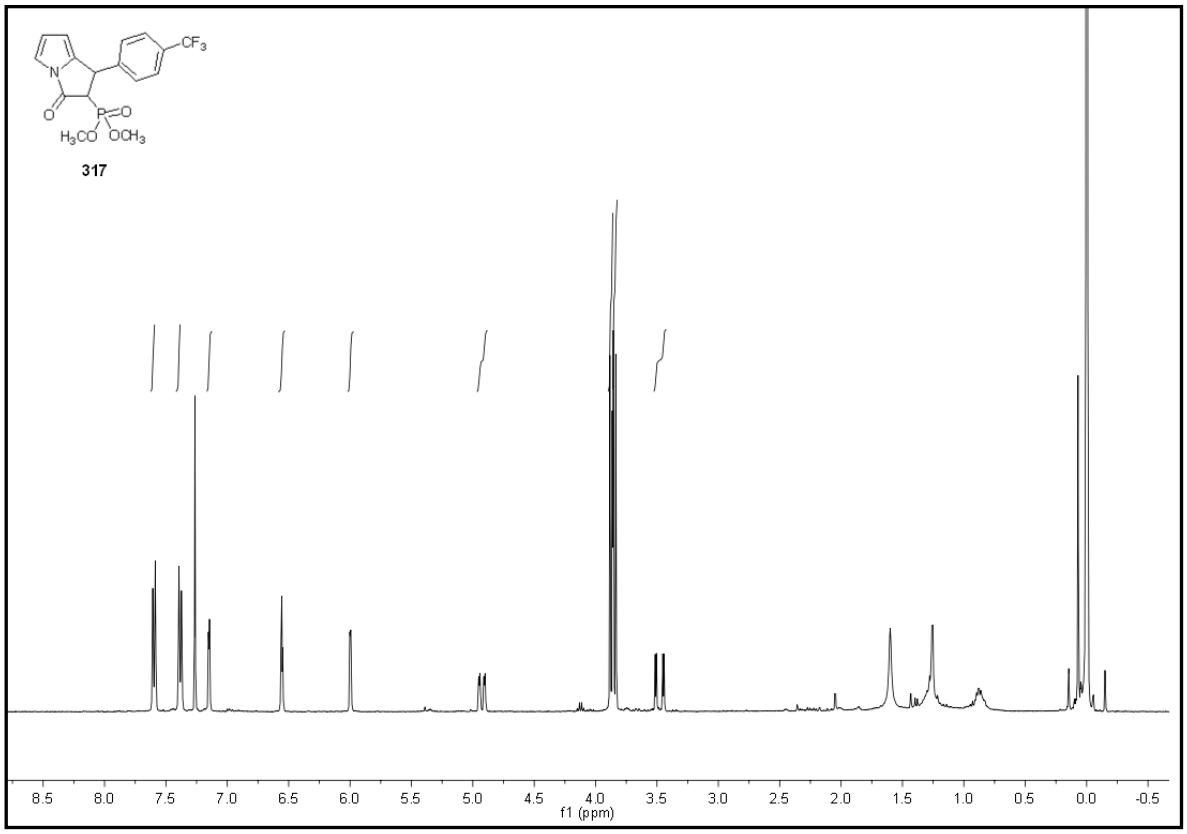


Figure A.274. ^{1}H NMR spectrum of compound **317**

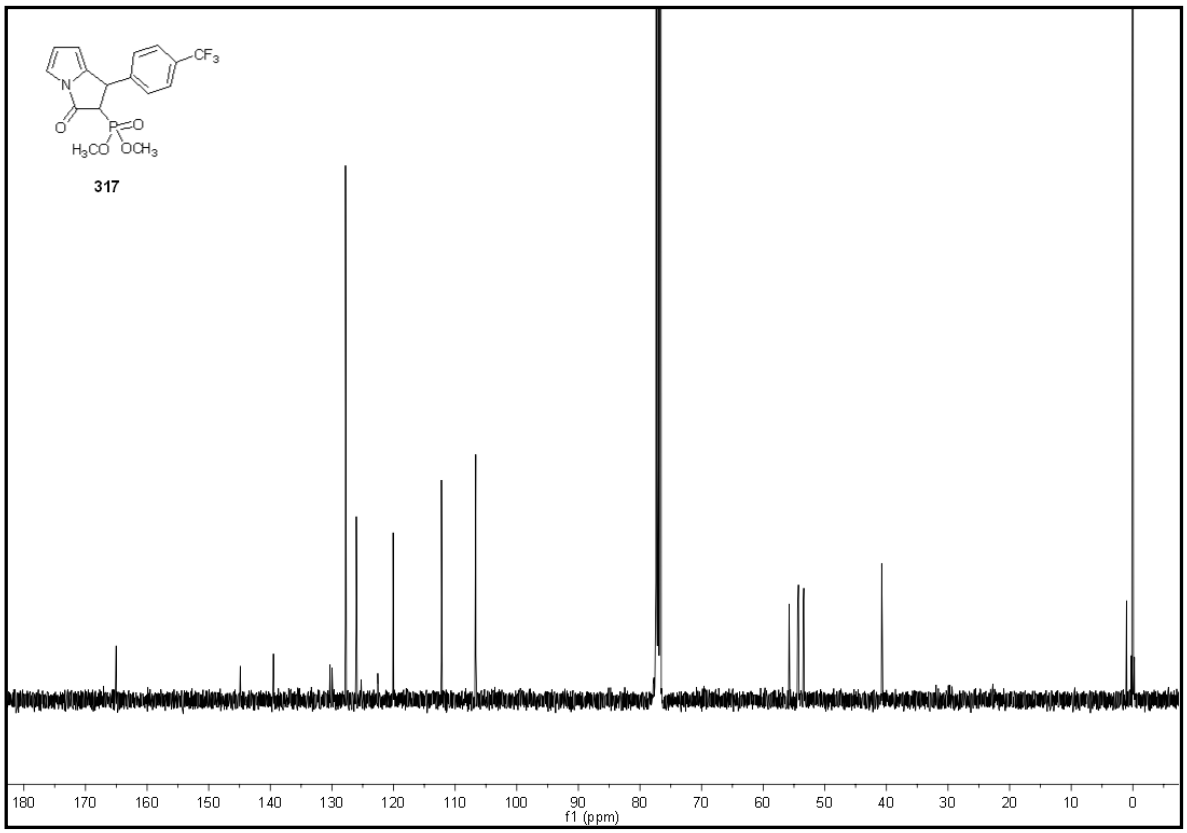


Figure A.275. ^{13}C NMR spectrum of compound **317**

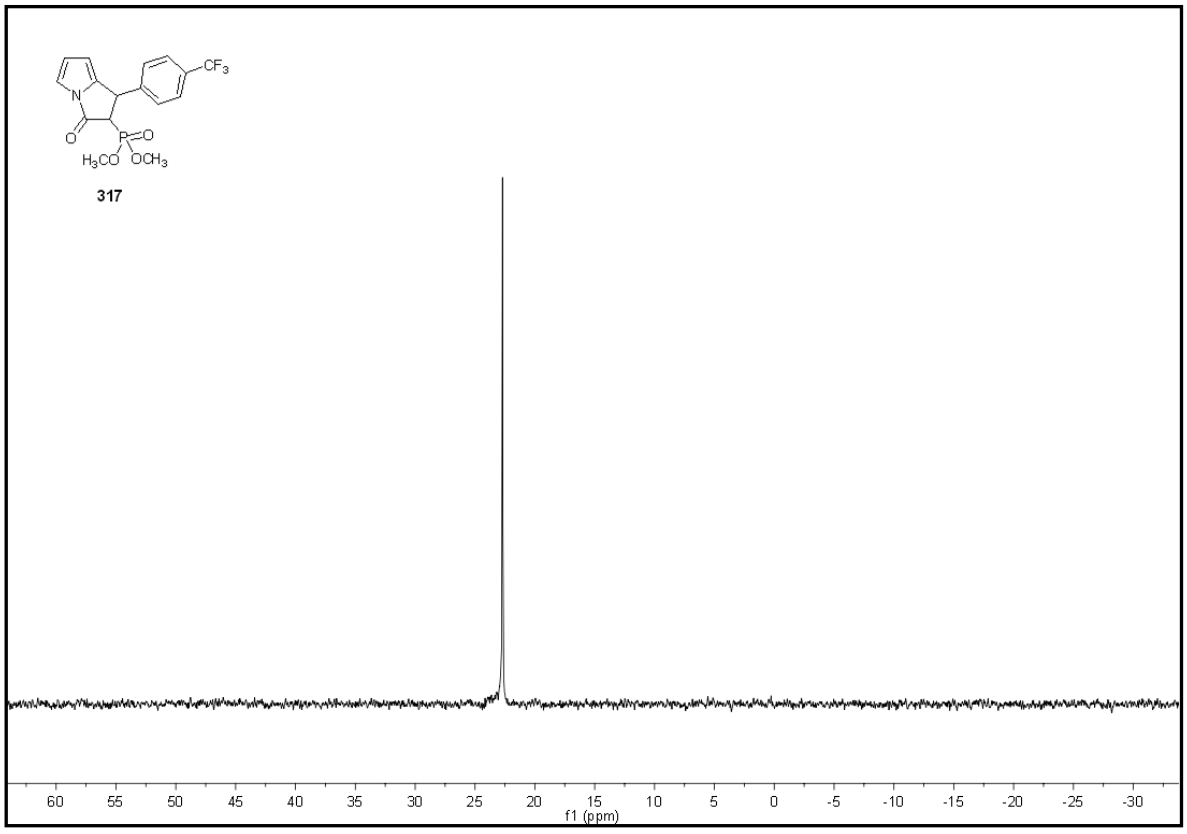


Figure A.276. ^{31}P NMR spectrum of compound **317**

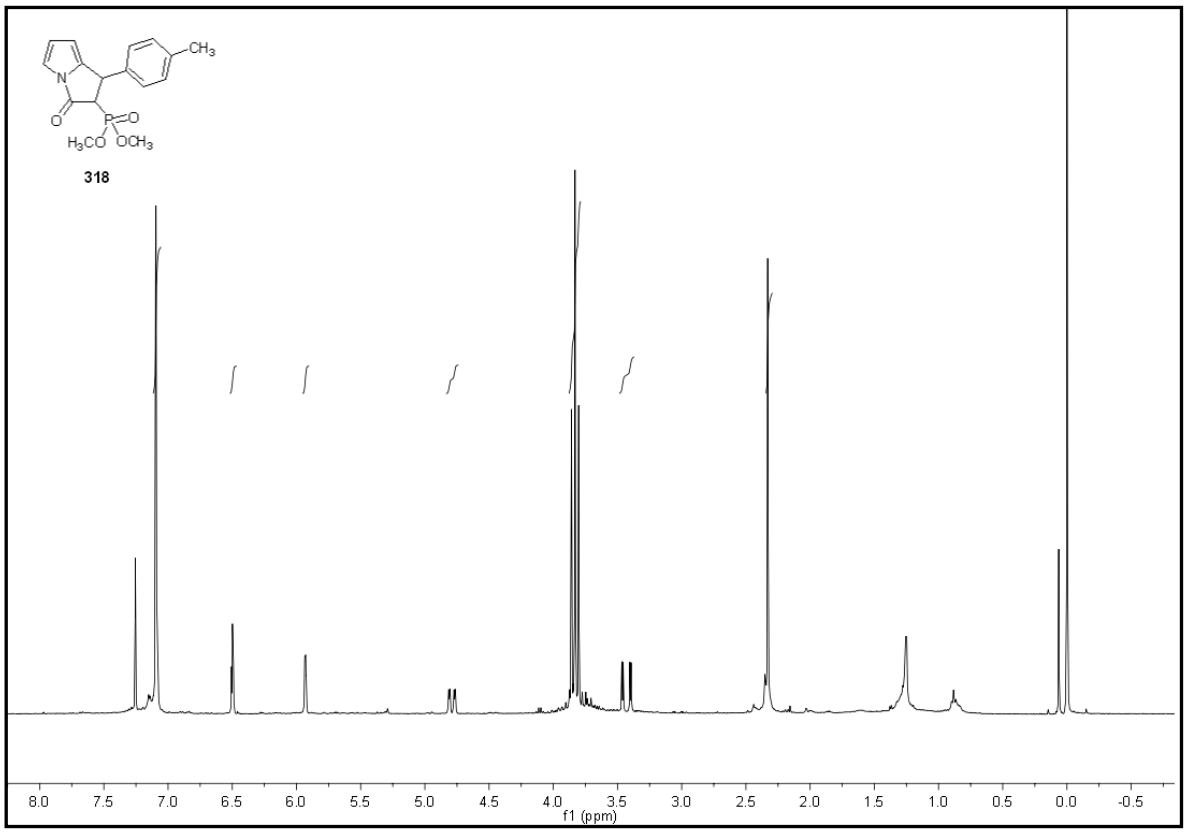


Figure A.277. ^{1}H NMR spectrum of compound **318**

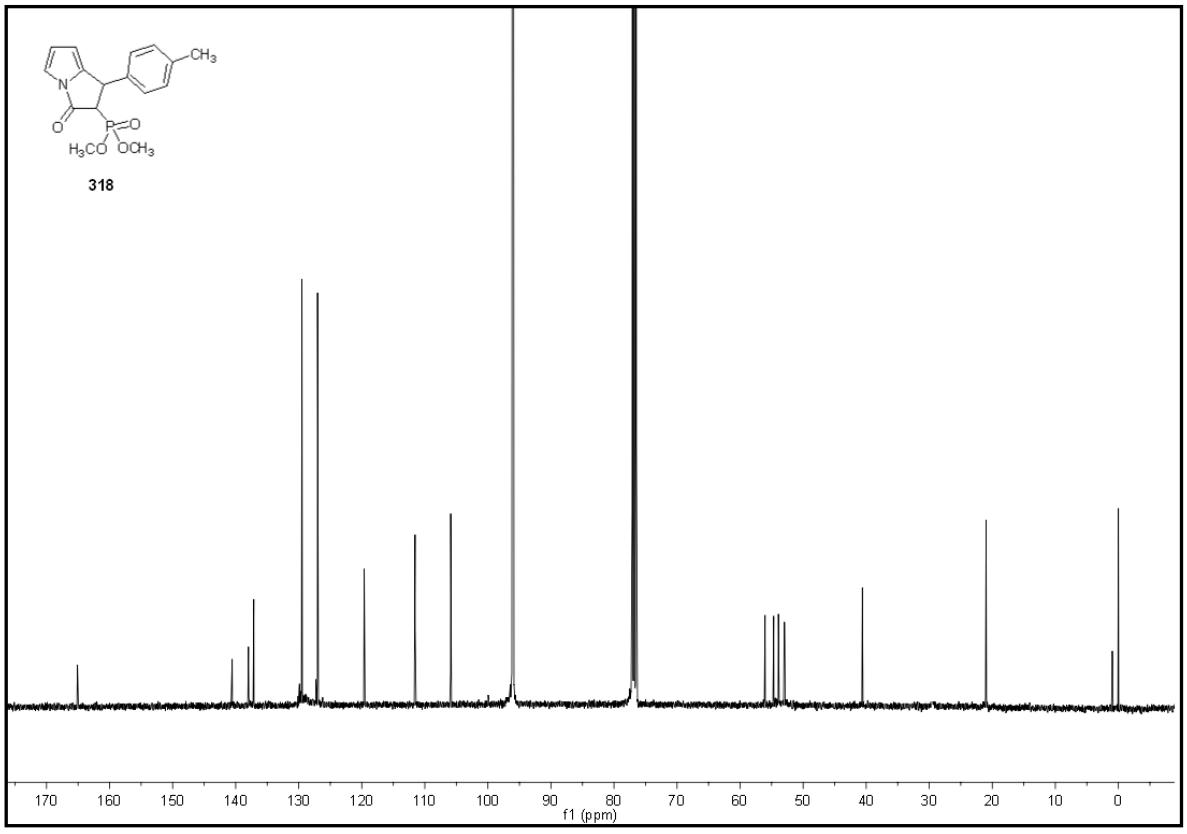


Figure A.278. ^{13}C NMR spectrum of compound **318**

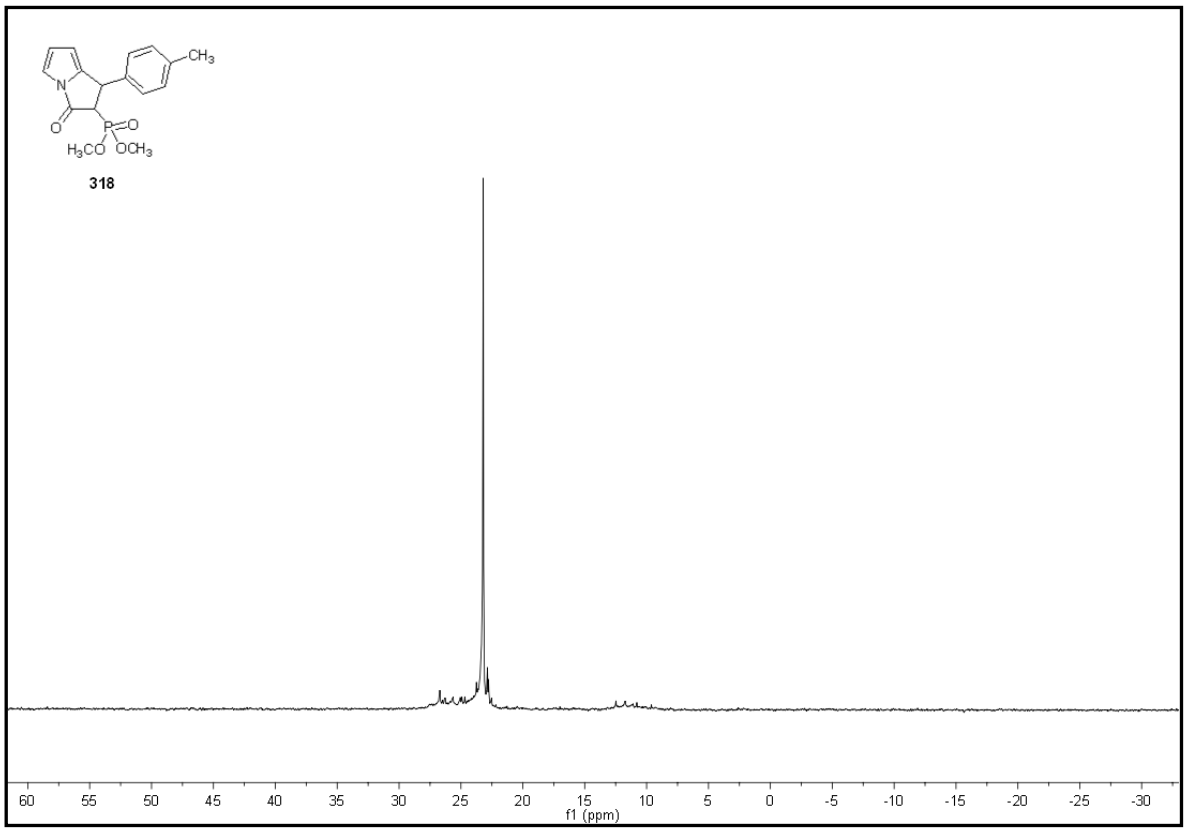


Figure A.279. ^{31}P NMR spectrum of compound **318**

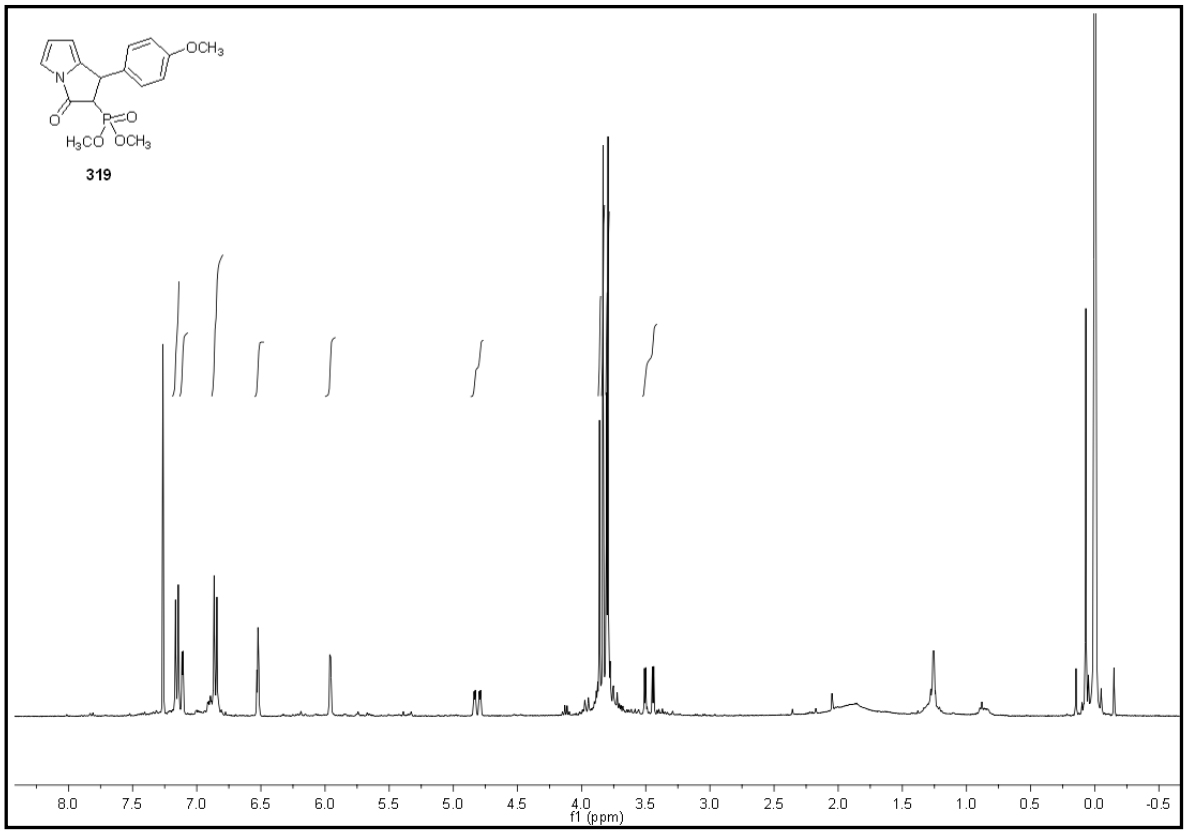


Figure A.280. ^{1}H NMR spectrum of compound **319**

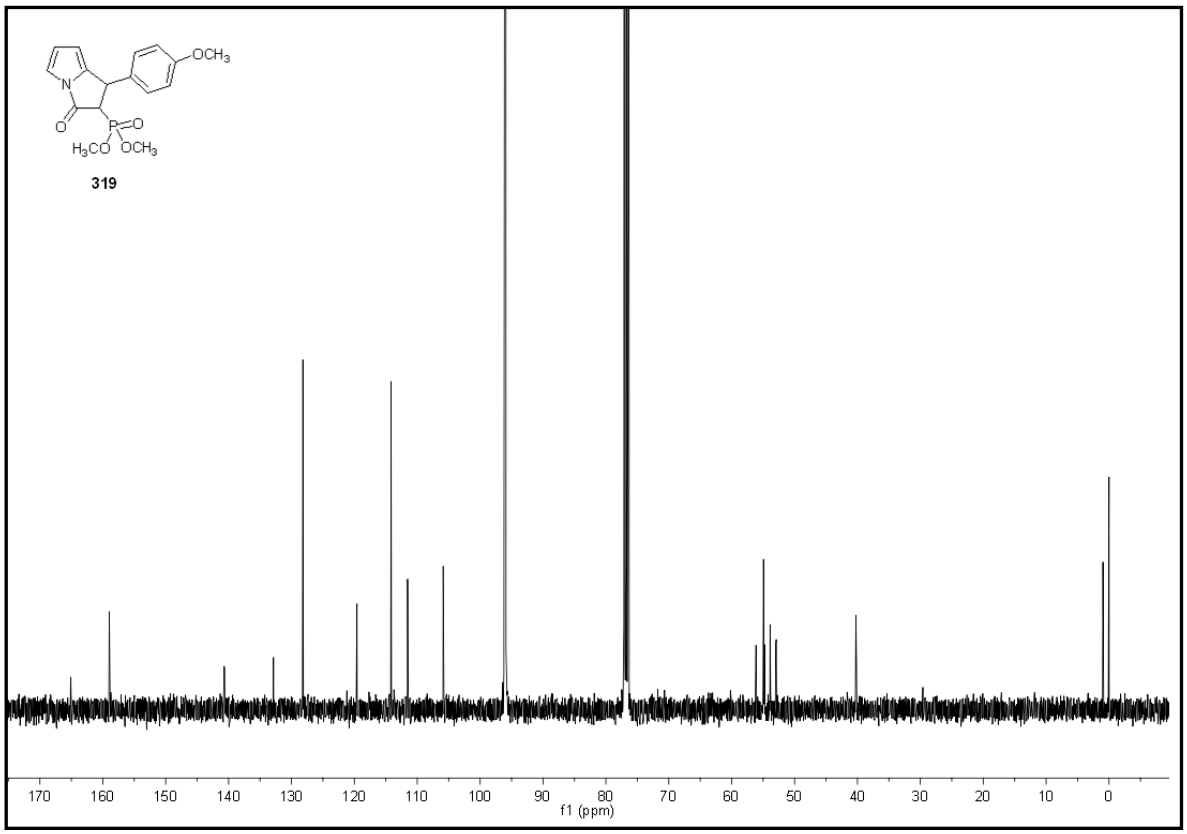


Figure A.281. ^{13}C NMR spectrum of compound **319**

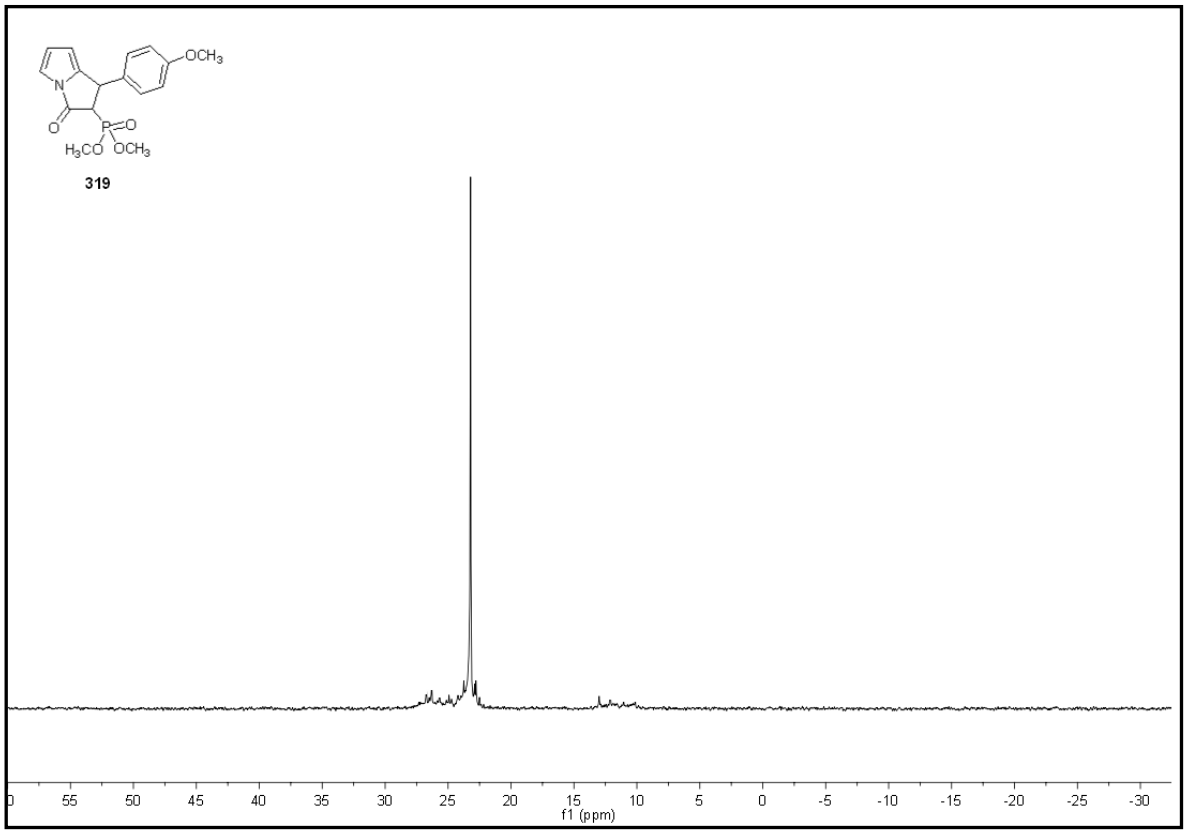


Figure A.282. ^{31}P NMR spectrum of compound **319**

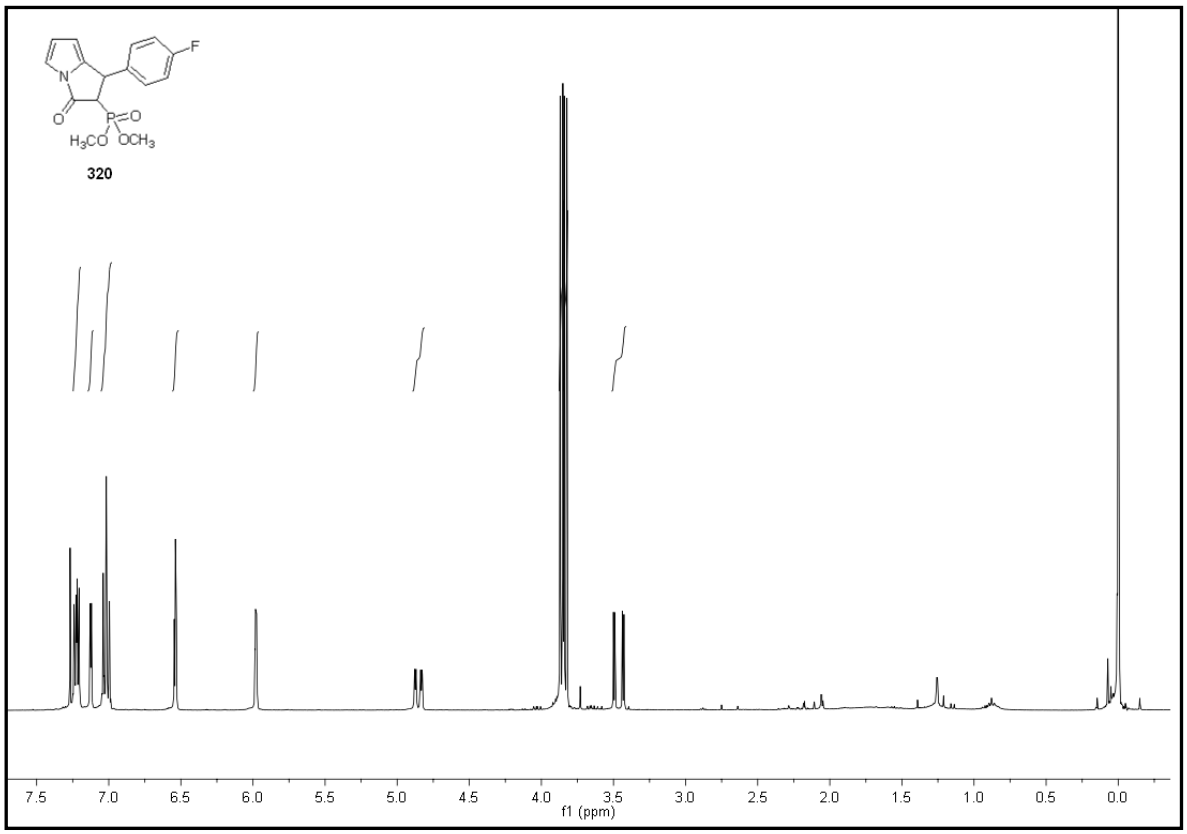


Figure A.283. ^{1}H NMR spectrum of compound **320**

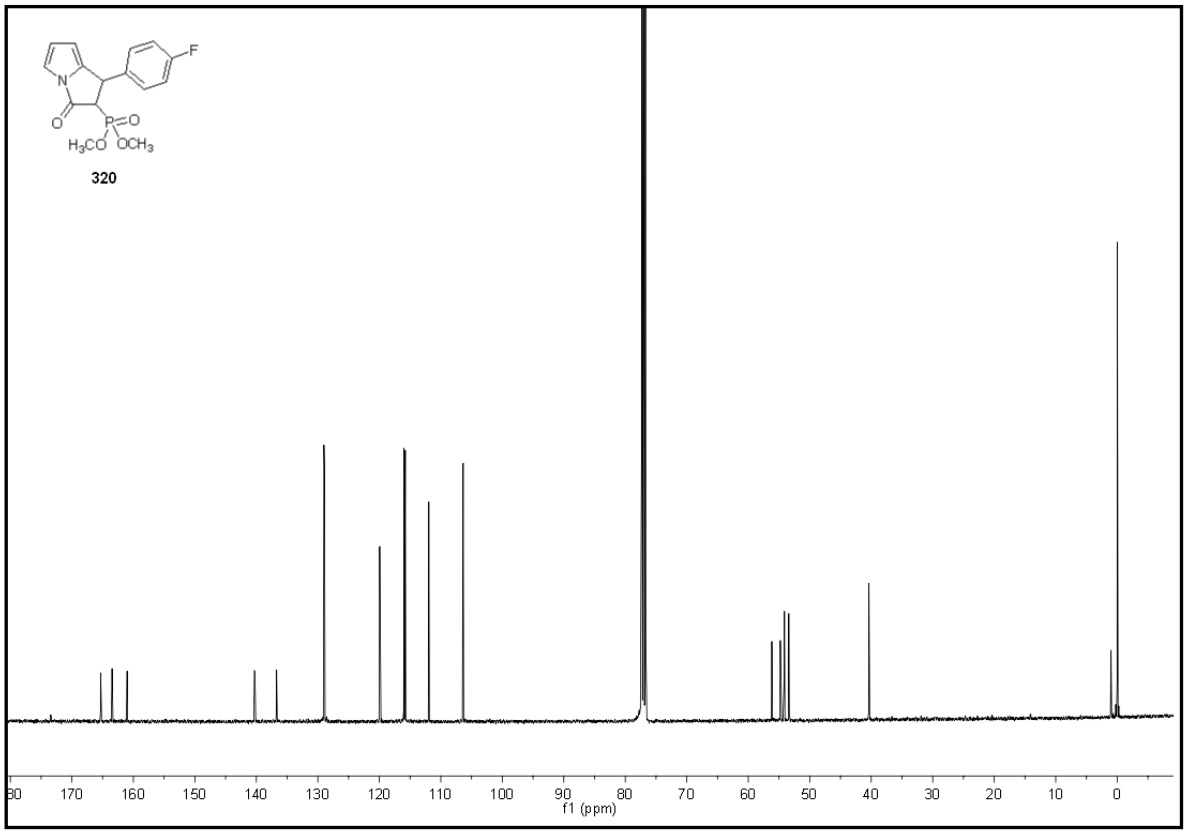


Figure A.284. ^{13}C NMR spectrum of compound **320**

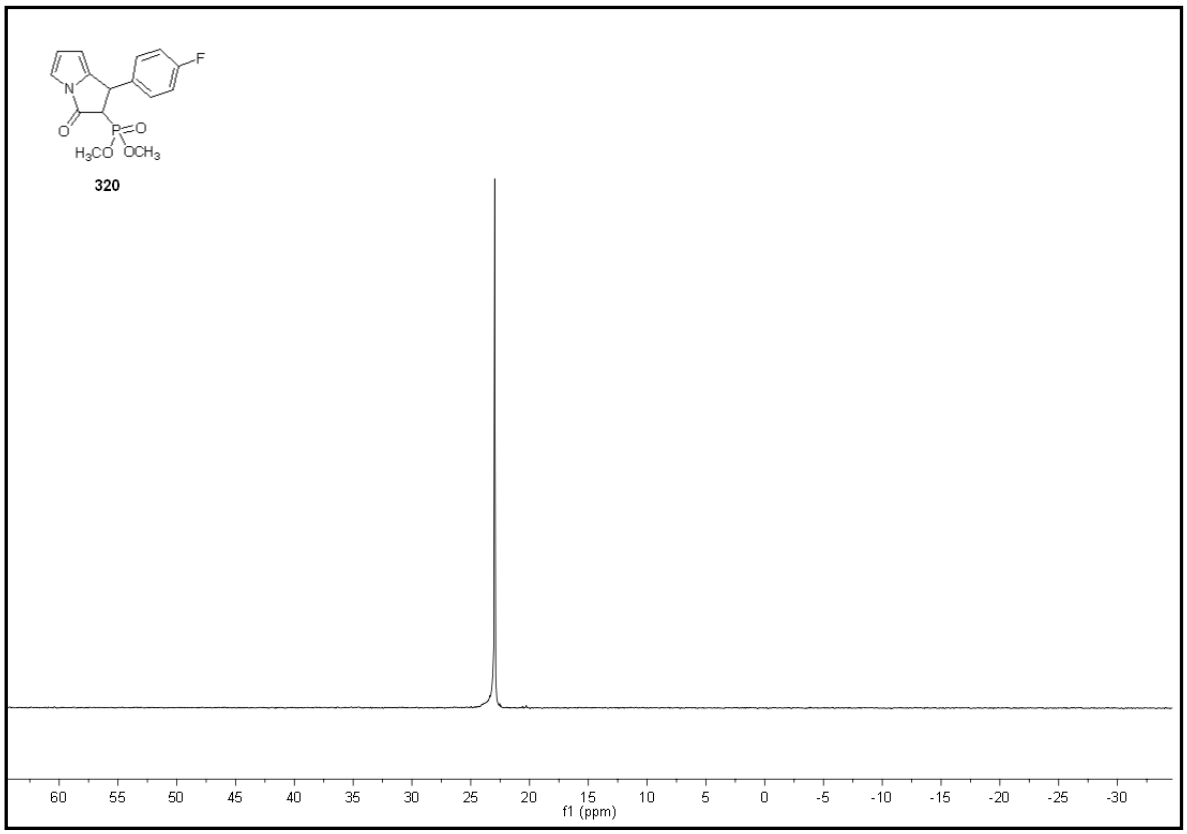


Figure A.285. ^{31}P NMR spectrum of compound **320**

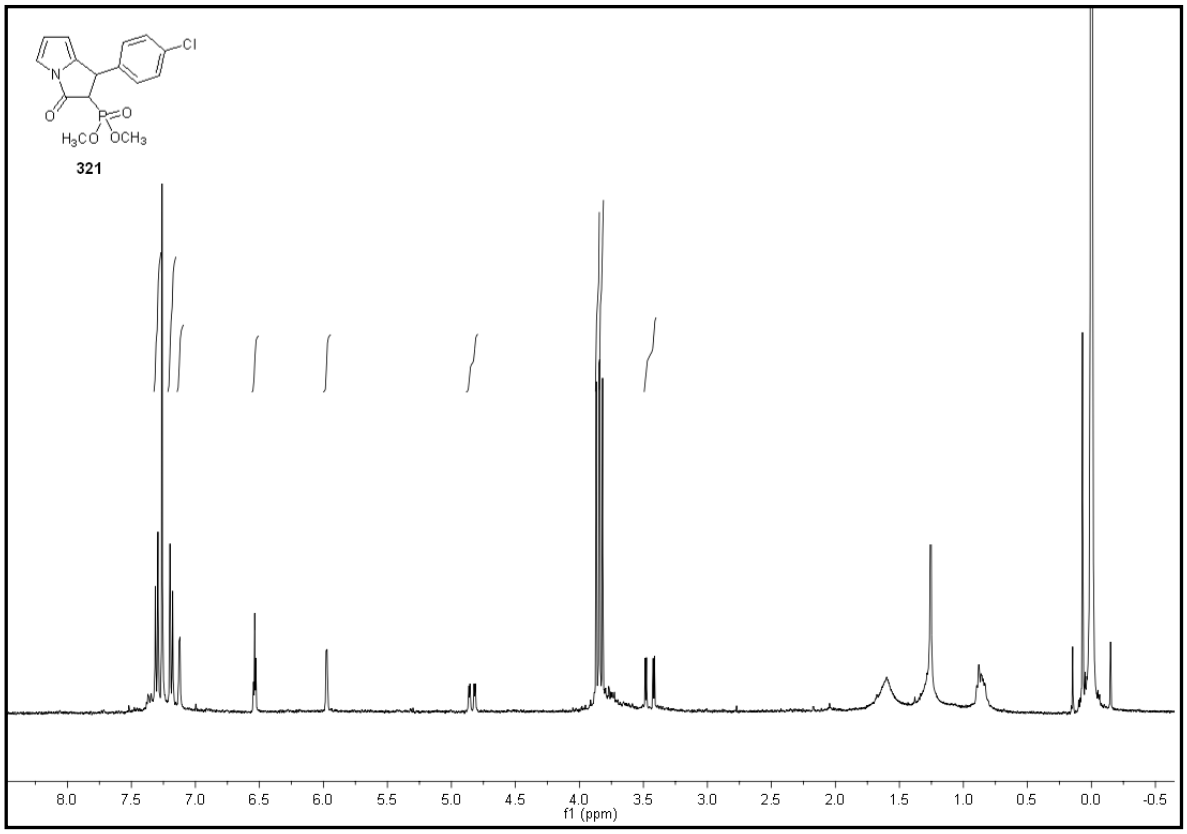


Figure A.286. ^{1}H NMR spectrum of compound **321**

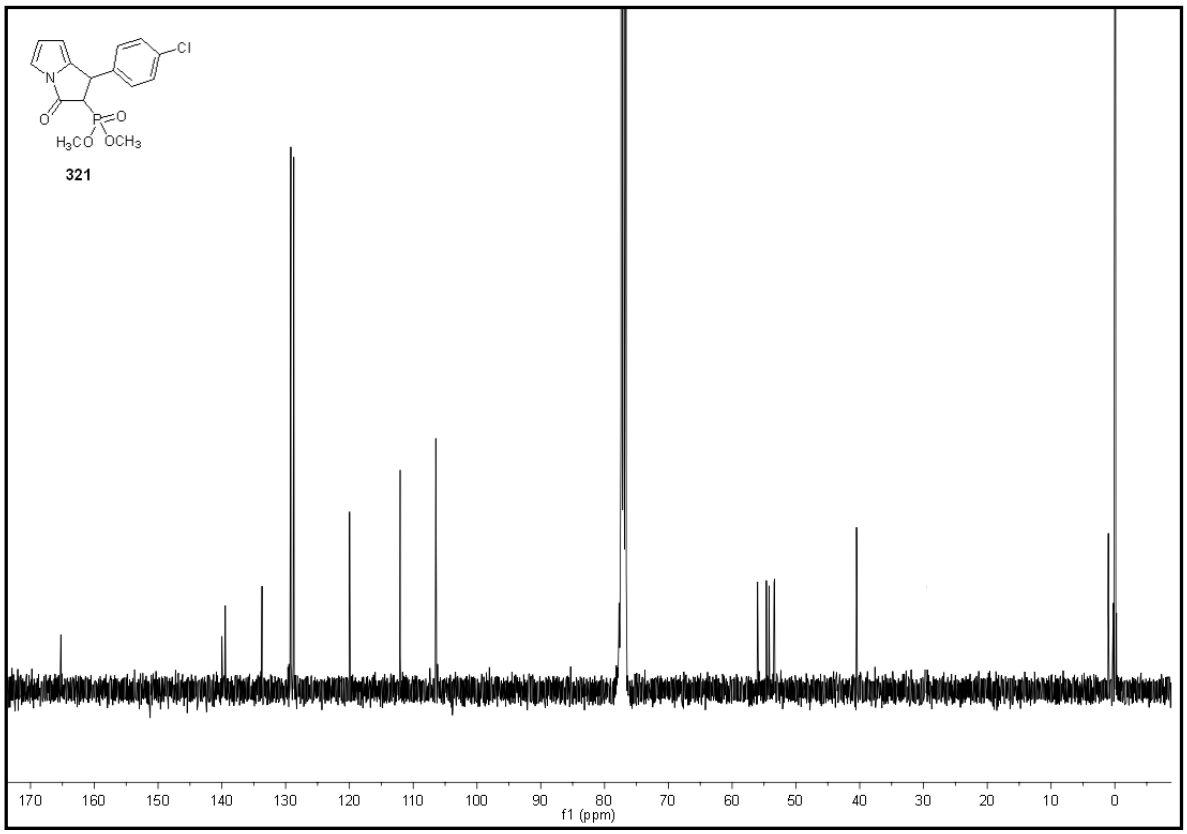


Figure A.287. ^{13}C NMR spectrum of compound **321**

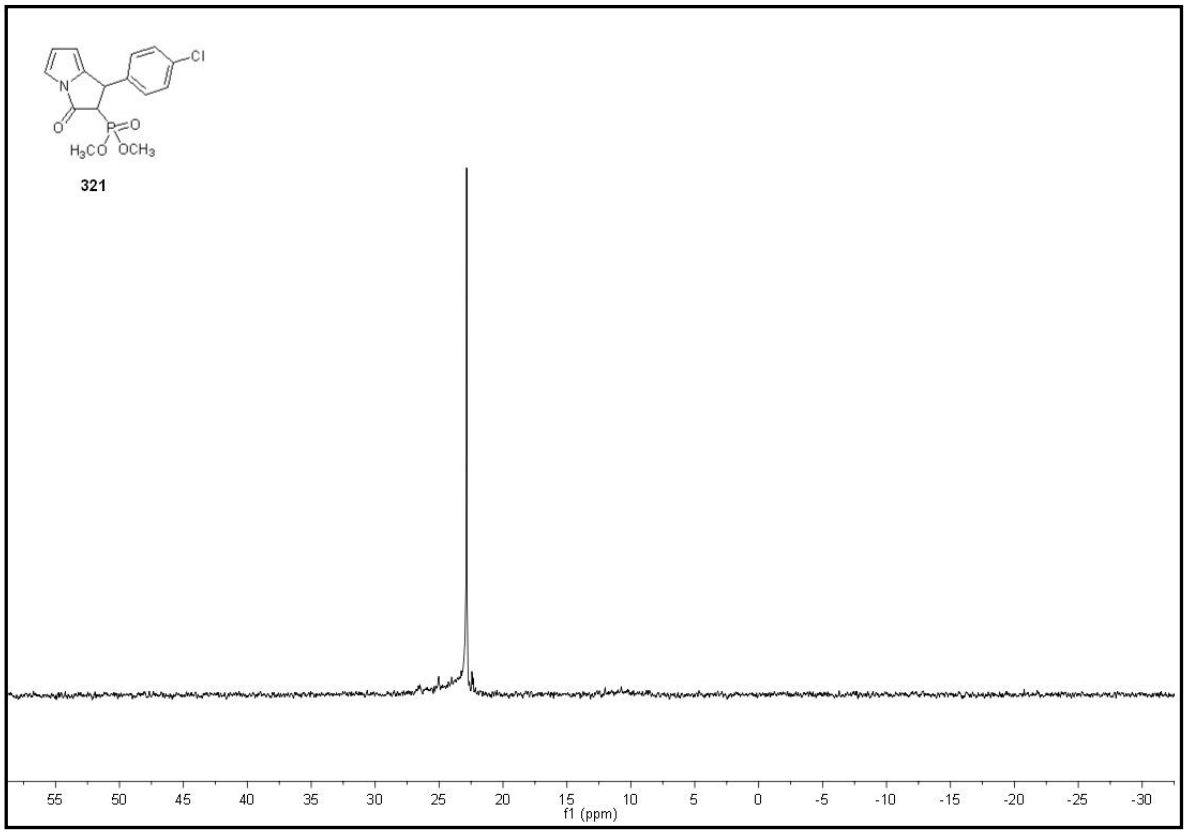


Figure A.288. ^{31}P NMR spectrum of compound **321**

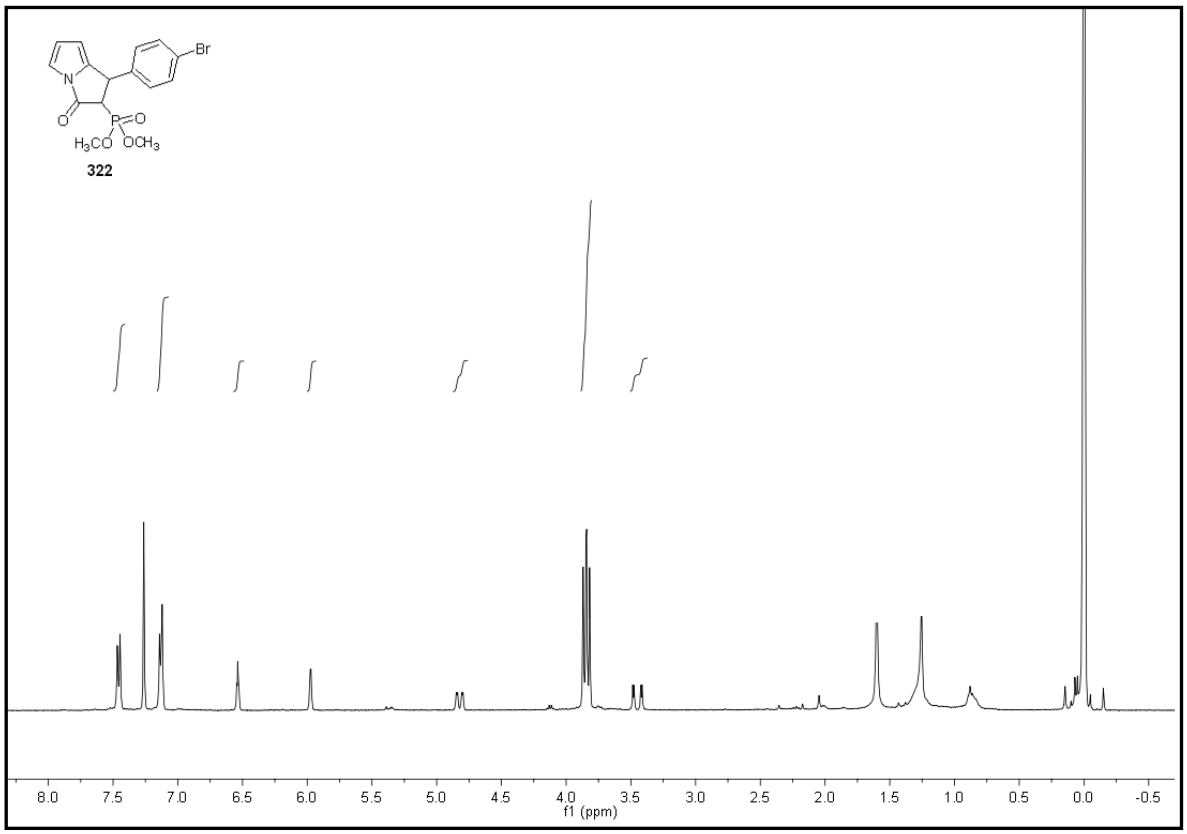


Figure A.289. ^{1}H NMR spectrum of compound **322**

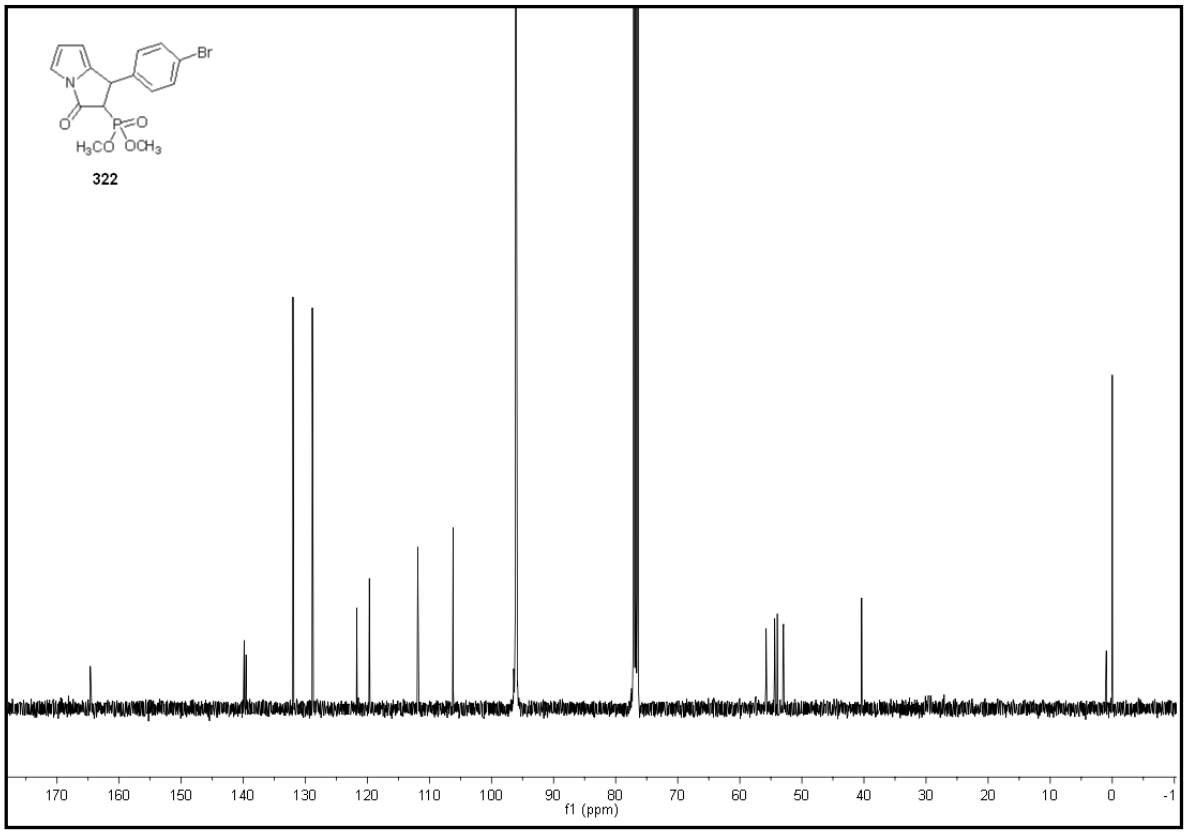


Figure A.290. ^{13}C NMR spectrum of compound **322**

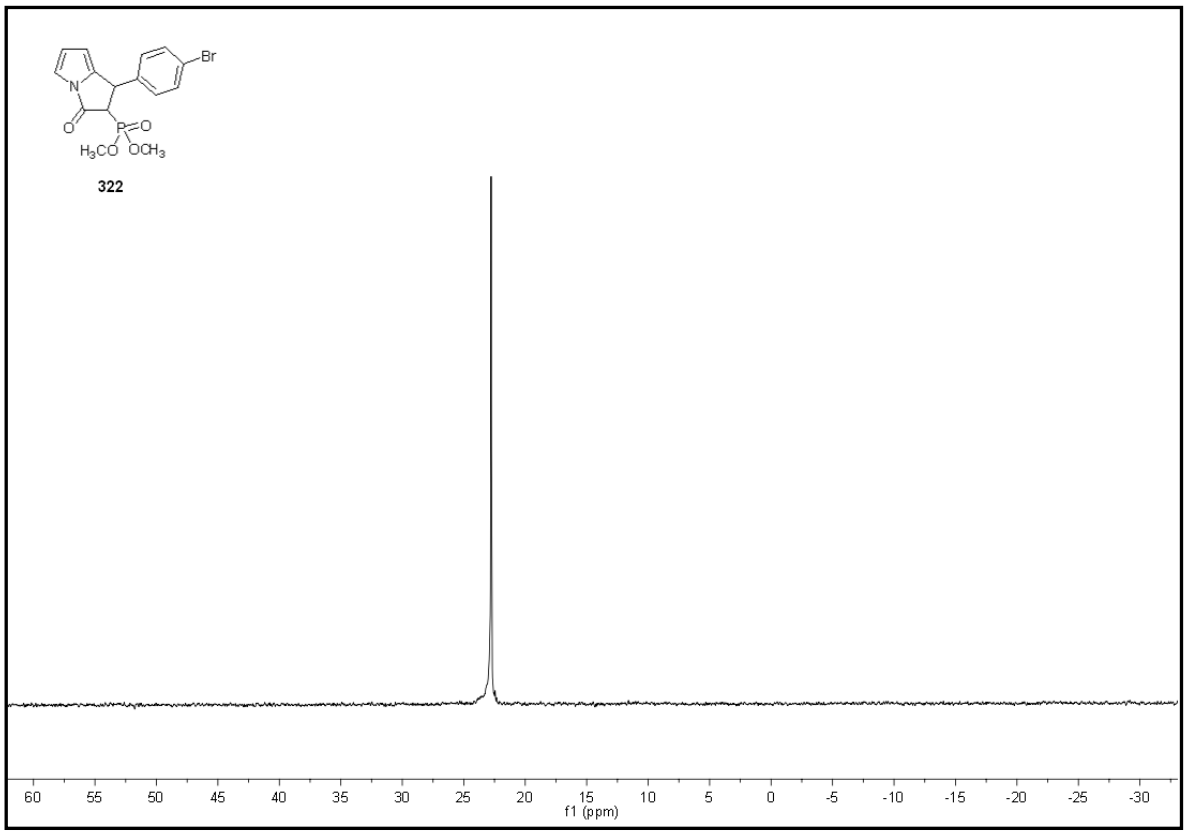


Figure A.291. ^{31}P NMR spectrum of compound **322**

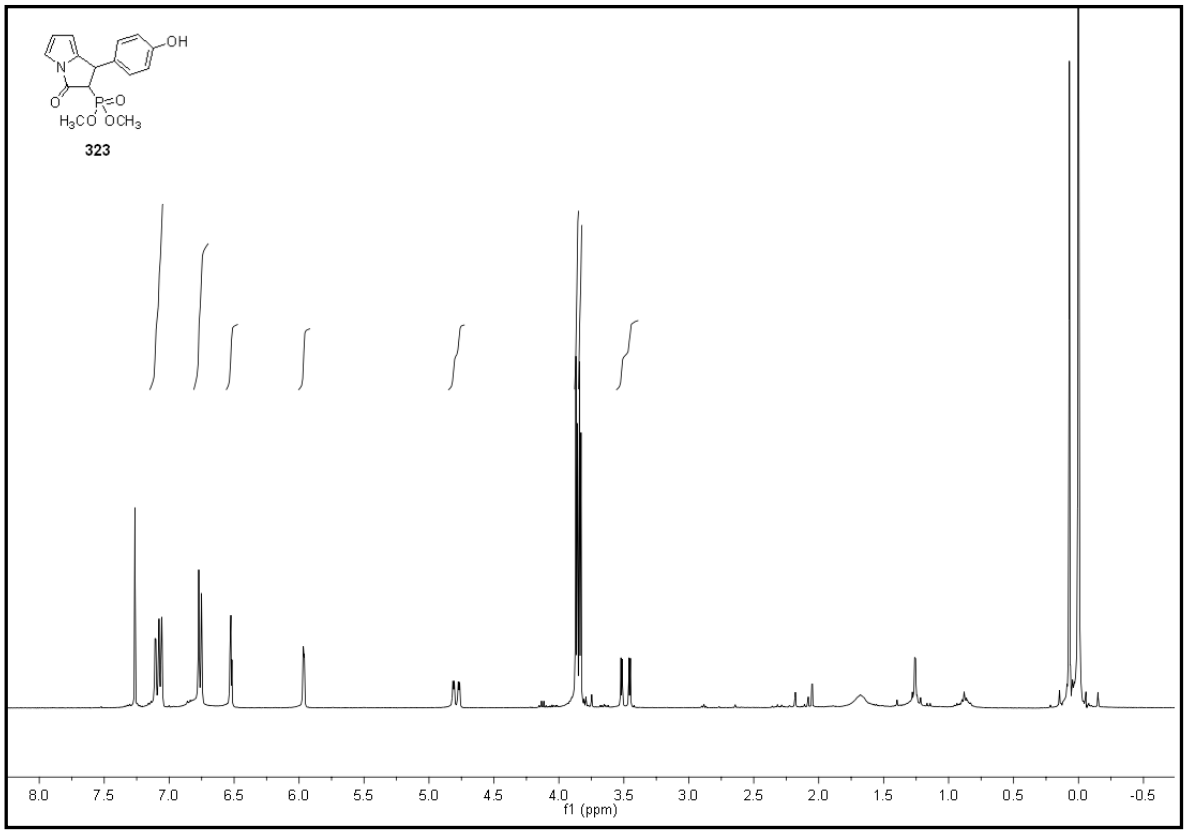


Figure A.292. ^{1}H NMR spectrum of compound **323**

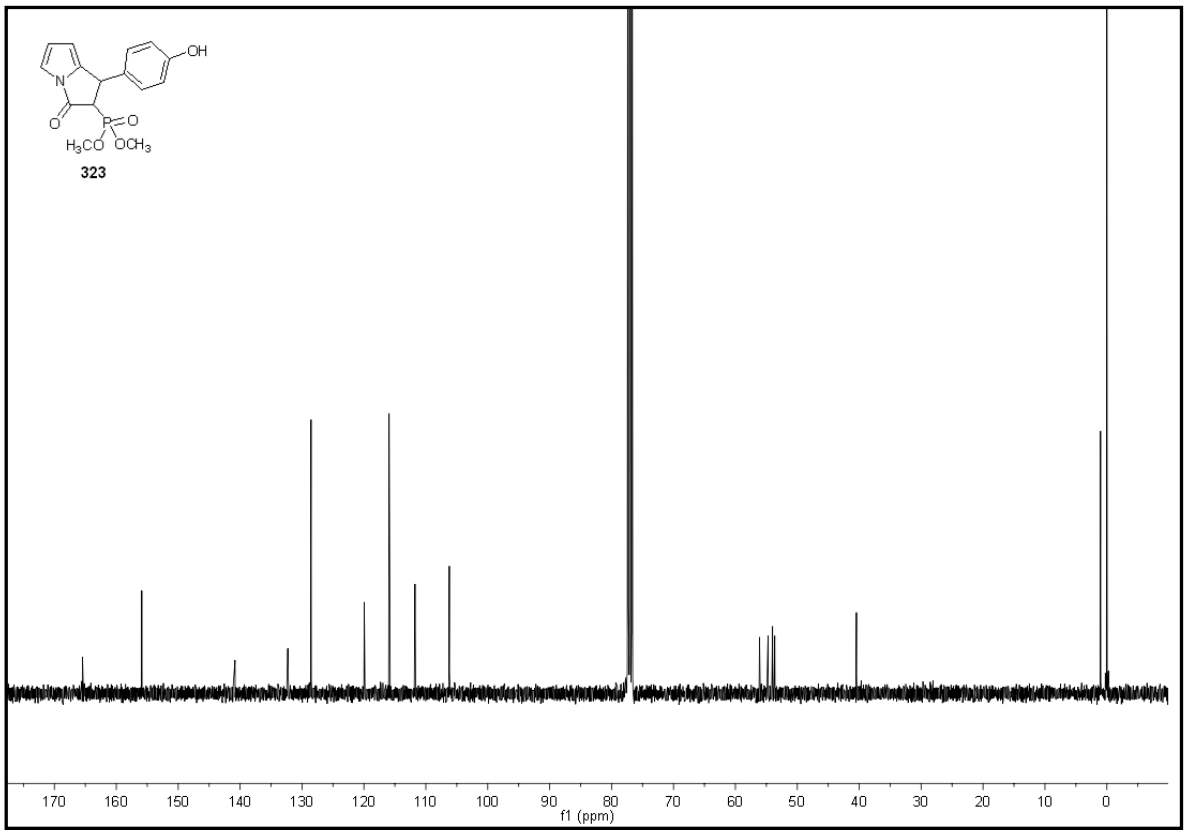


Figure A.293. ^{13}C NMR spectrum of compound **323**

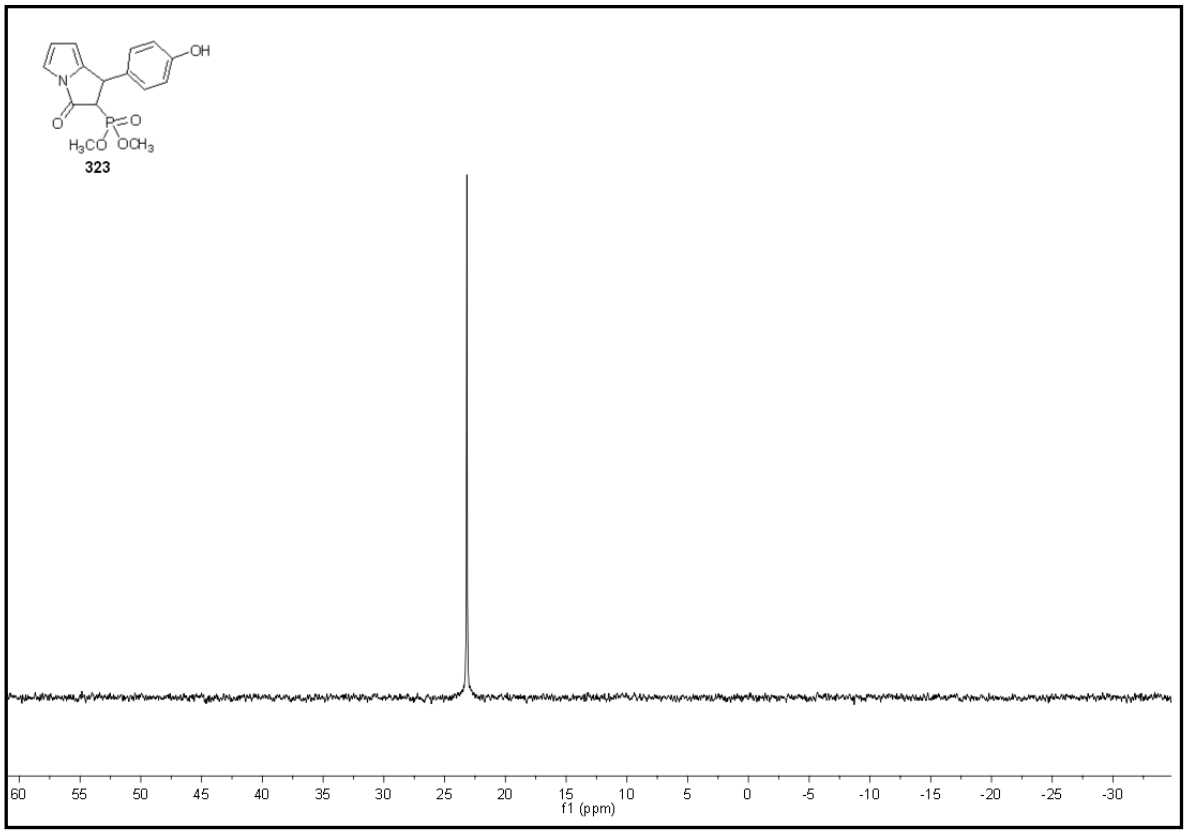


Figure A.294. ^{31}P NMR spectrum of compound **323**

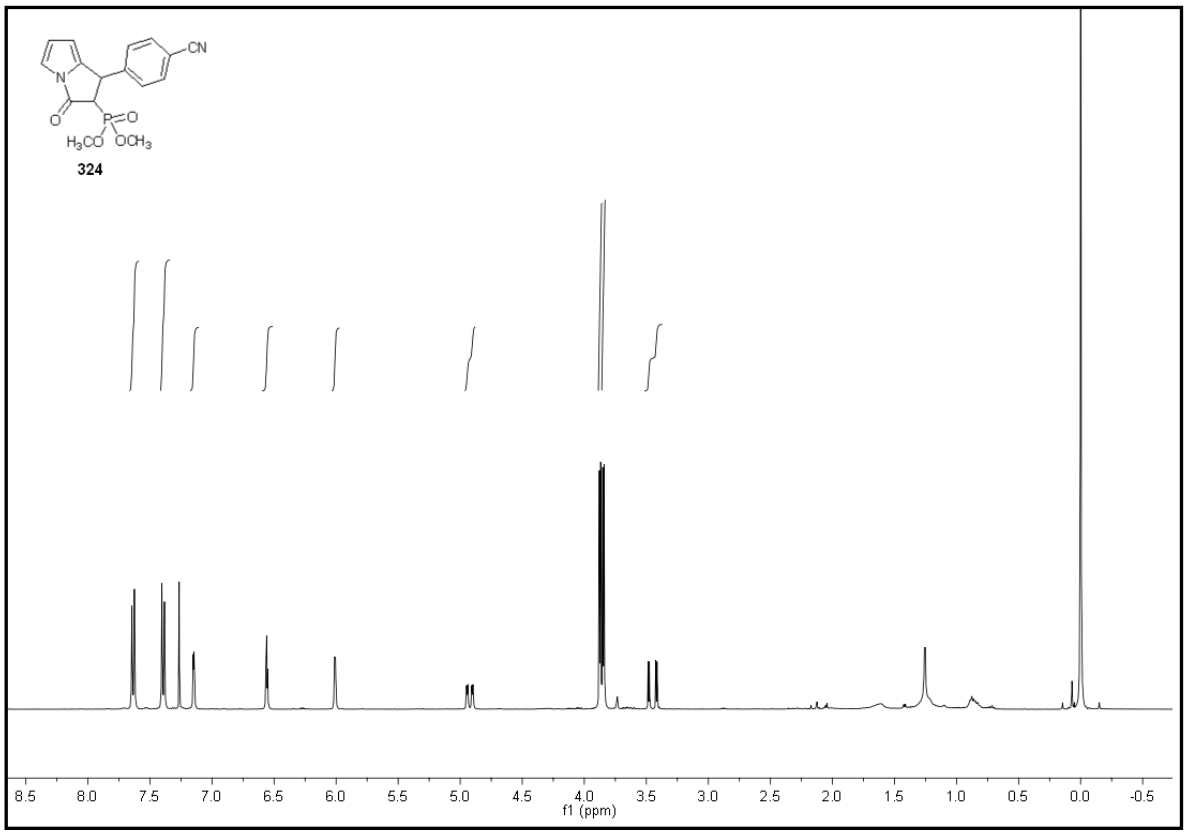


Figure A.295. ^{1}H NMR spectrum of compound **324**

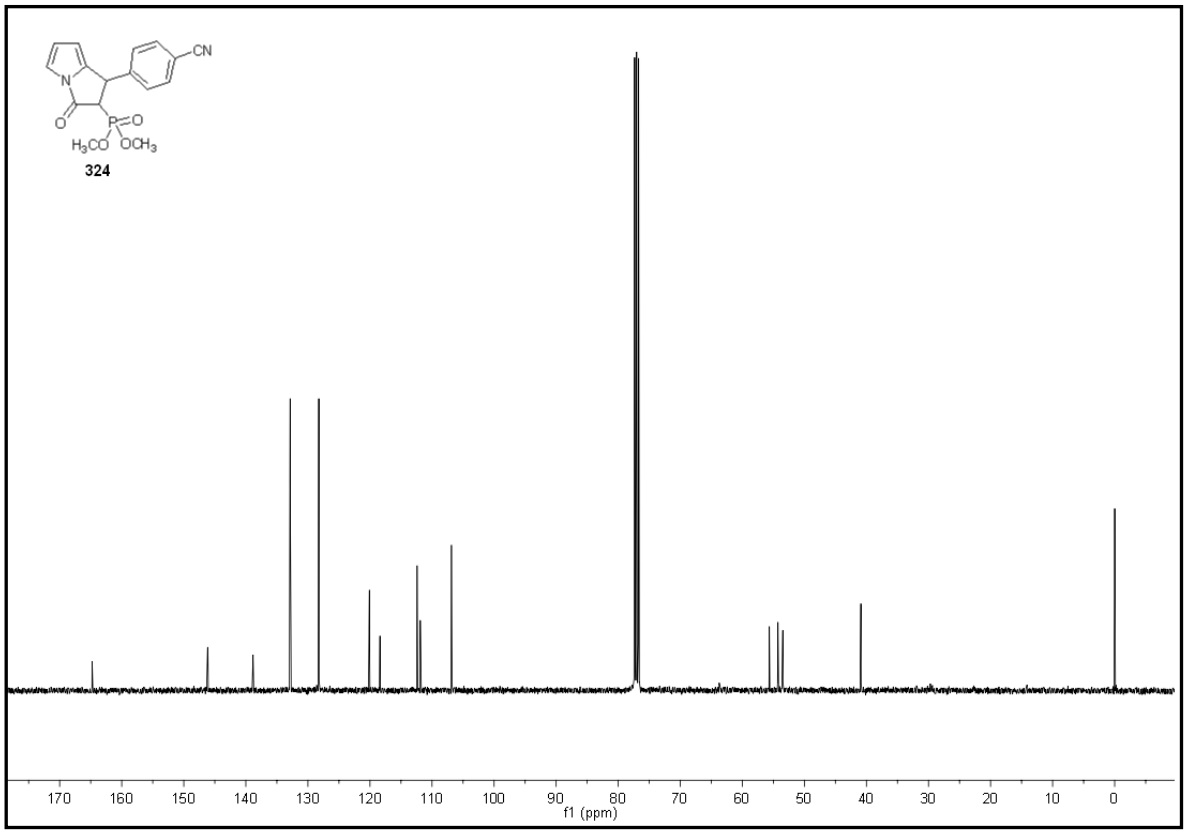


Figure A.296. ^{13}C NMR spectrum of compound **324**

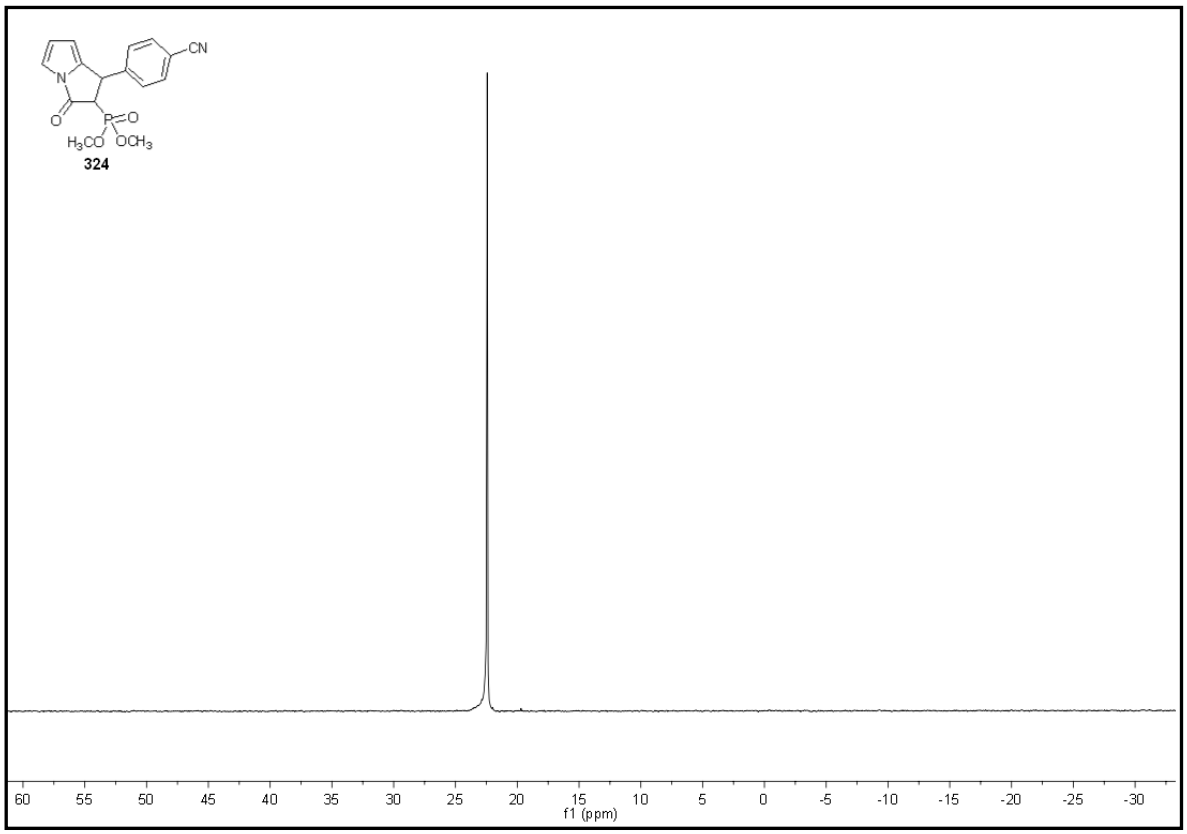


Figure A.297. ^{31}P NMR spectrum of compound **324**

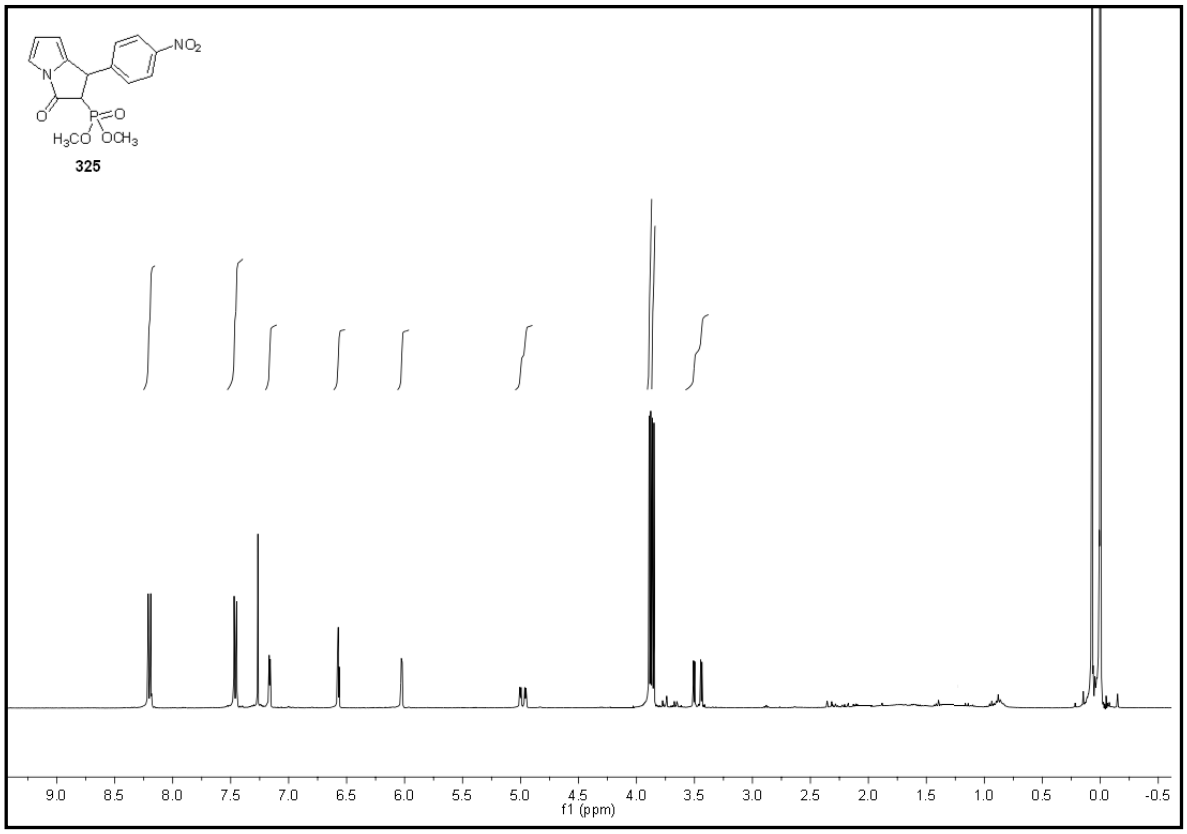


Figure A.298. ^{1}H NMR spectrum of compound **325**

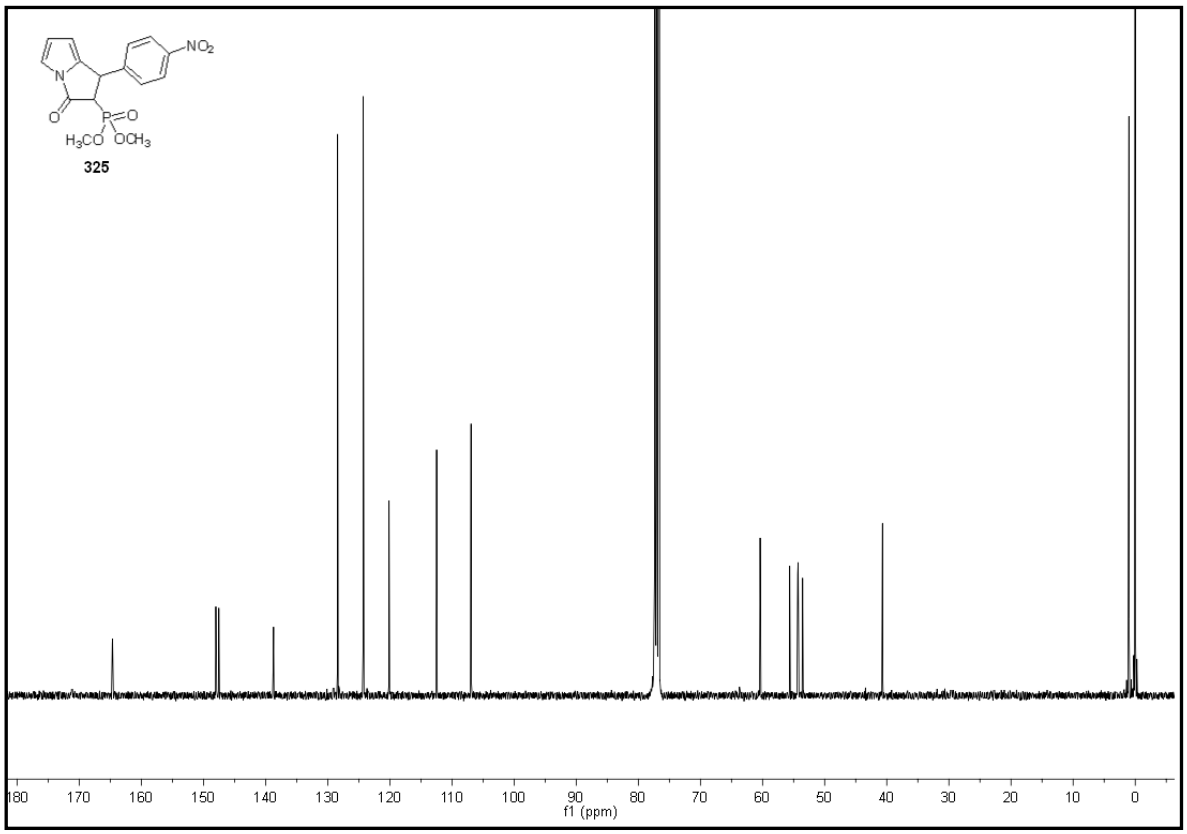


Figure A.299. ^{13}C NMR spectrum of compound **325**

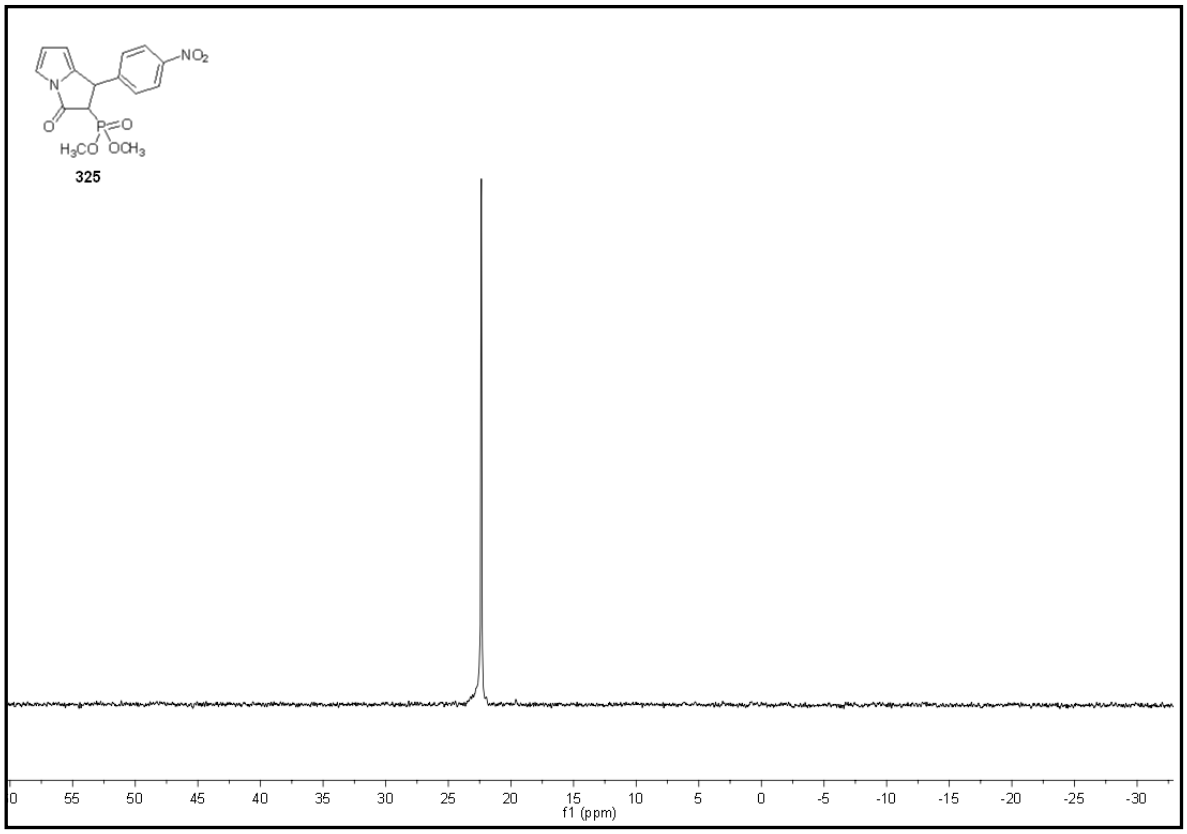


Figure A.300. ^{31}P NMR spectrum of compound **325**

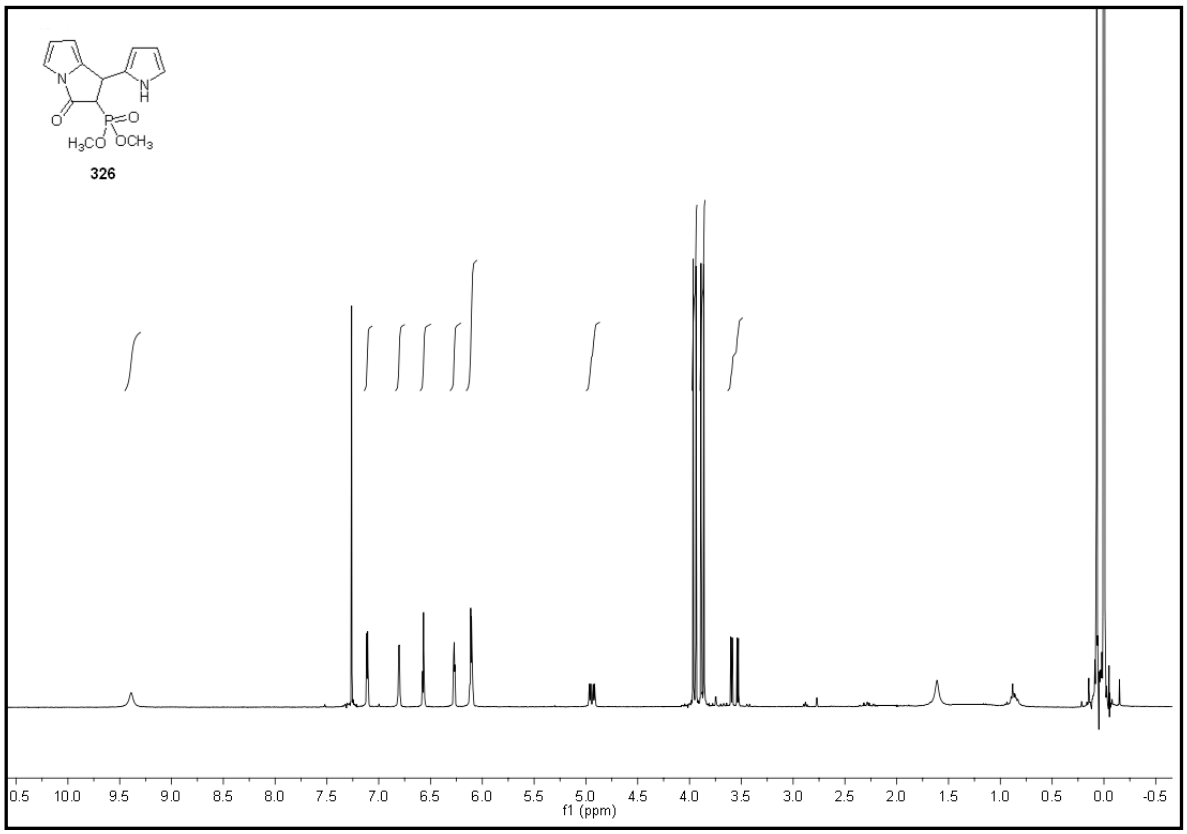


Figure A.301. ^{1}H NMR spectrum of compound **326**

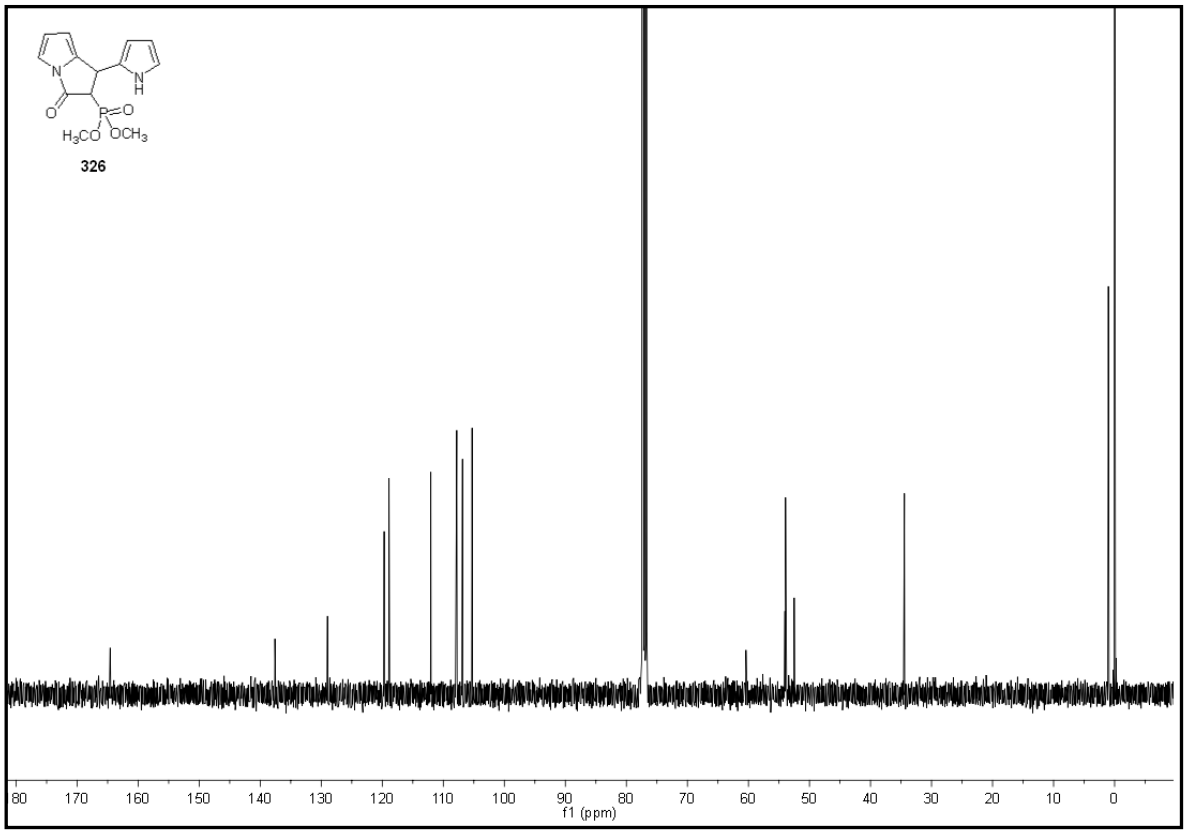


Figure A.302. ^{13}C NMR spectrum of compound **326**

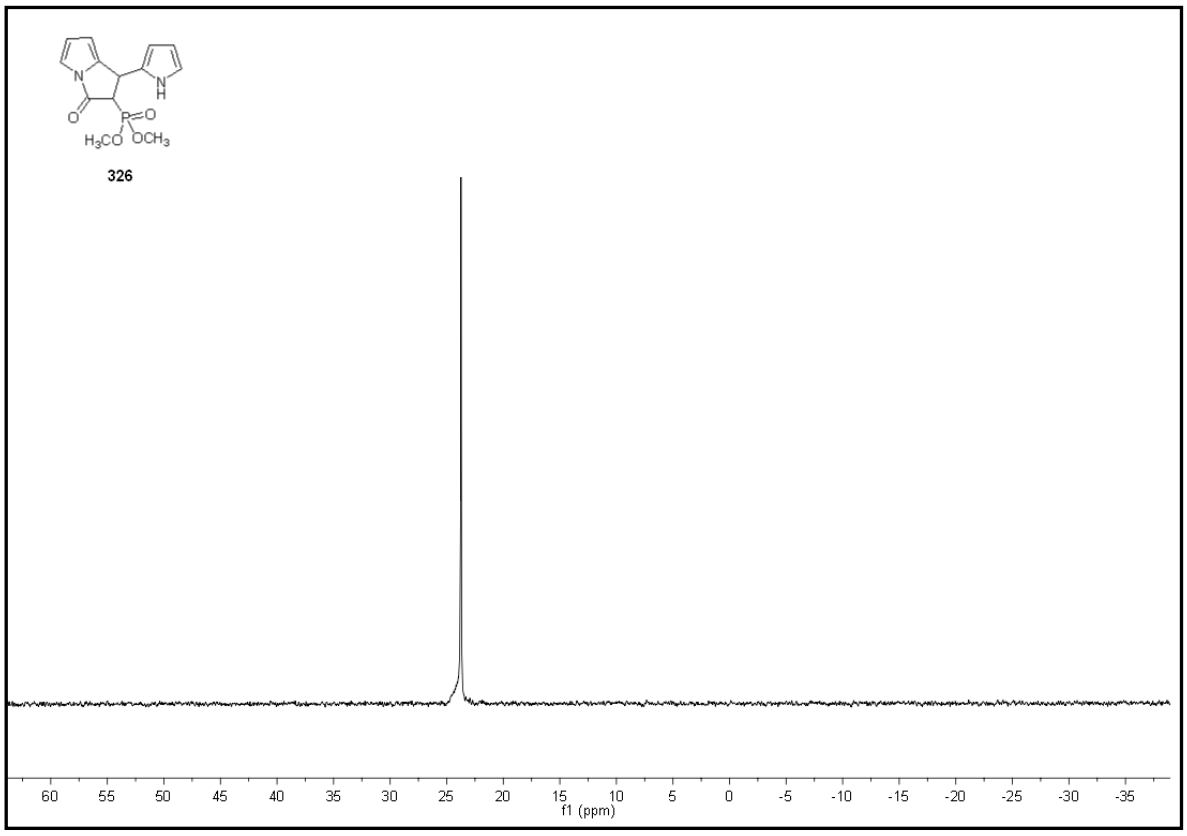


Figure A.303. ^{31}P NMR spectrum of compound **326**

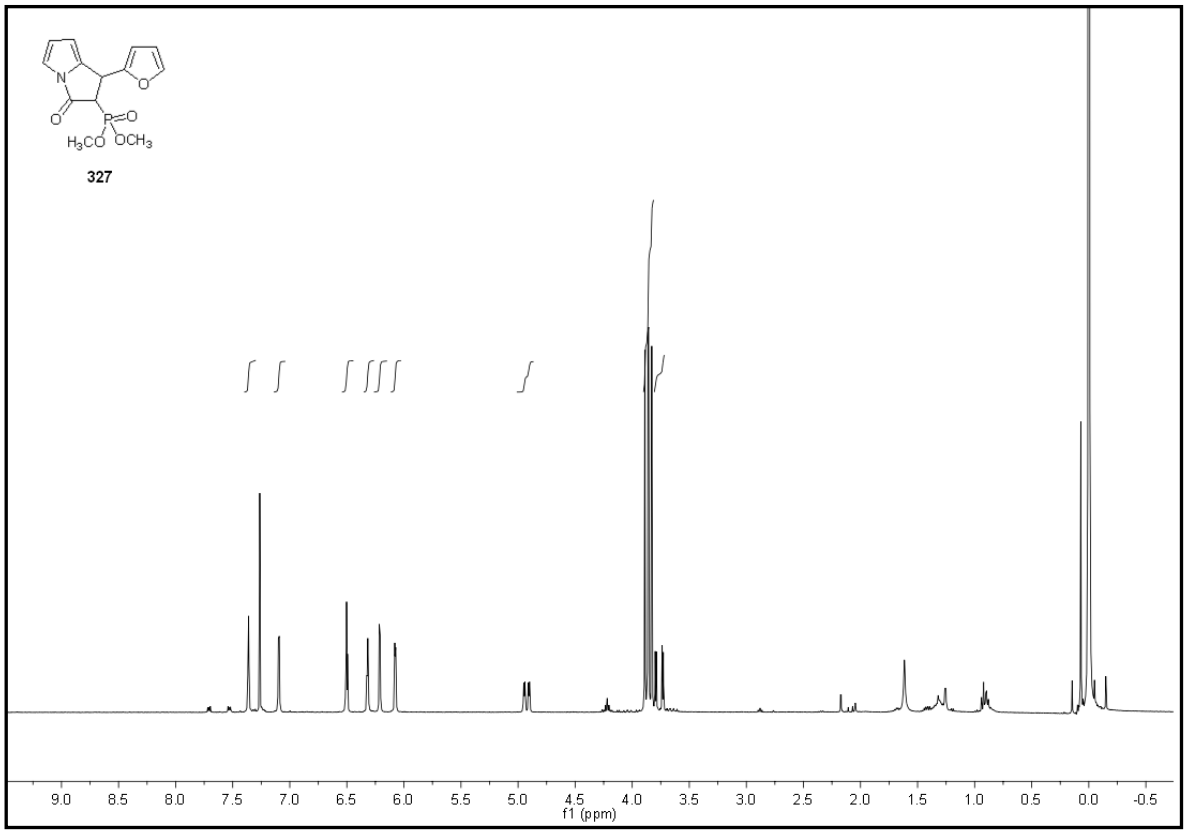


Figure A.304. ^{1}H NMR spectrum of compound **327**

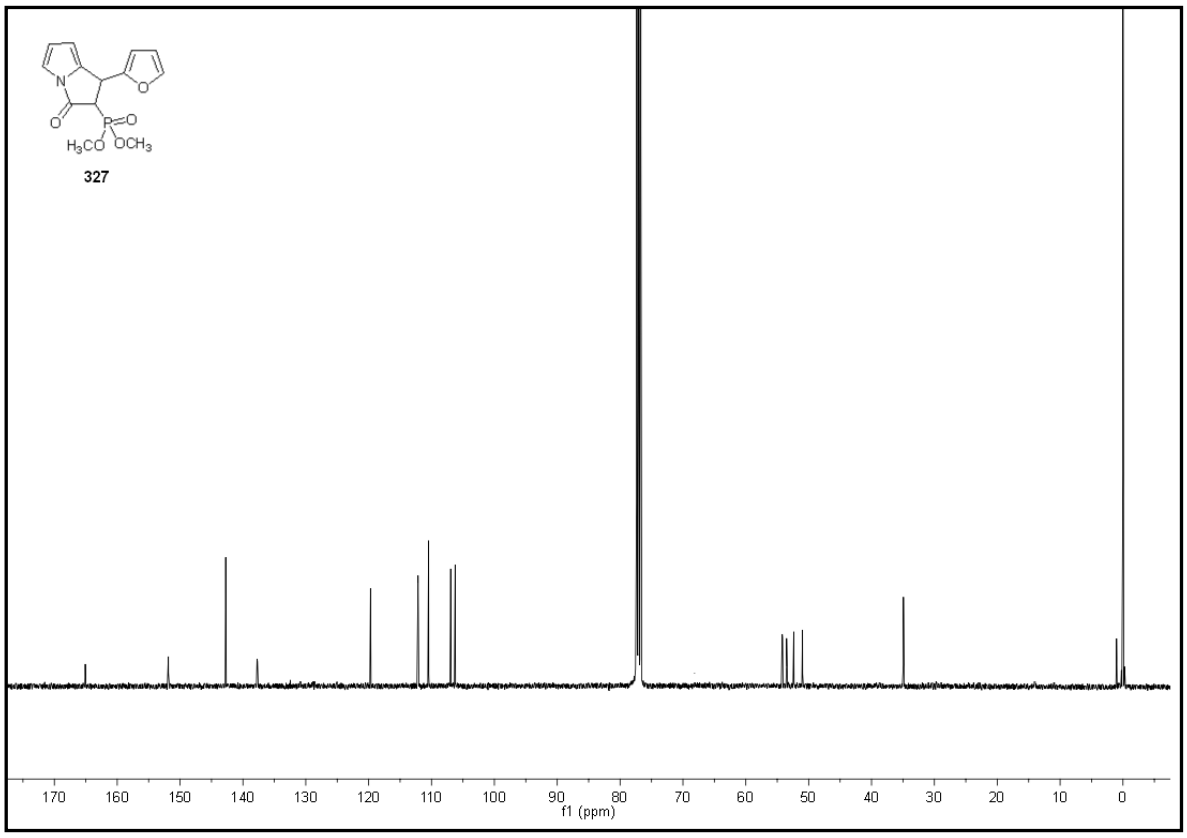


Figure A.305. ^{13}C NMR spectrum of compound **327**

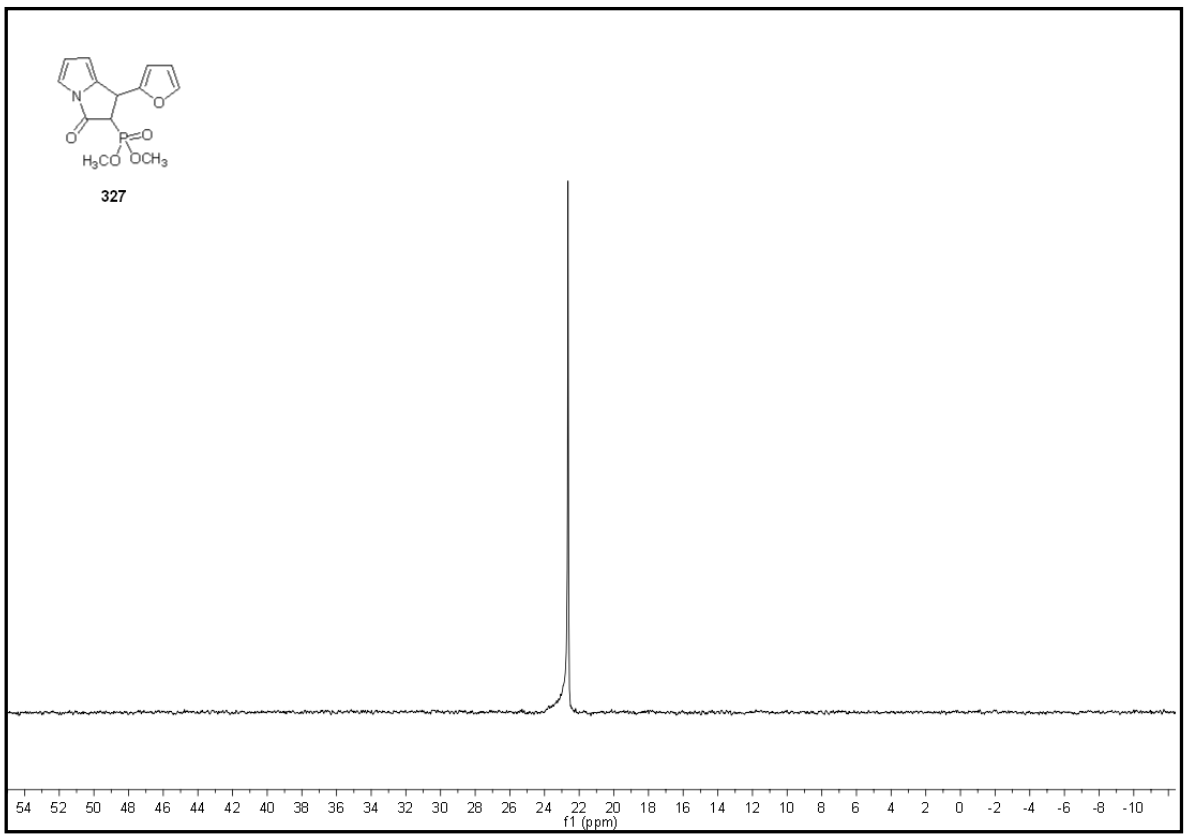


Figure A.306. ^{31}P NMR spectrum of compound **327**

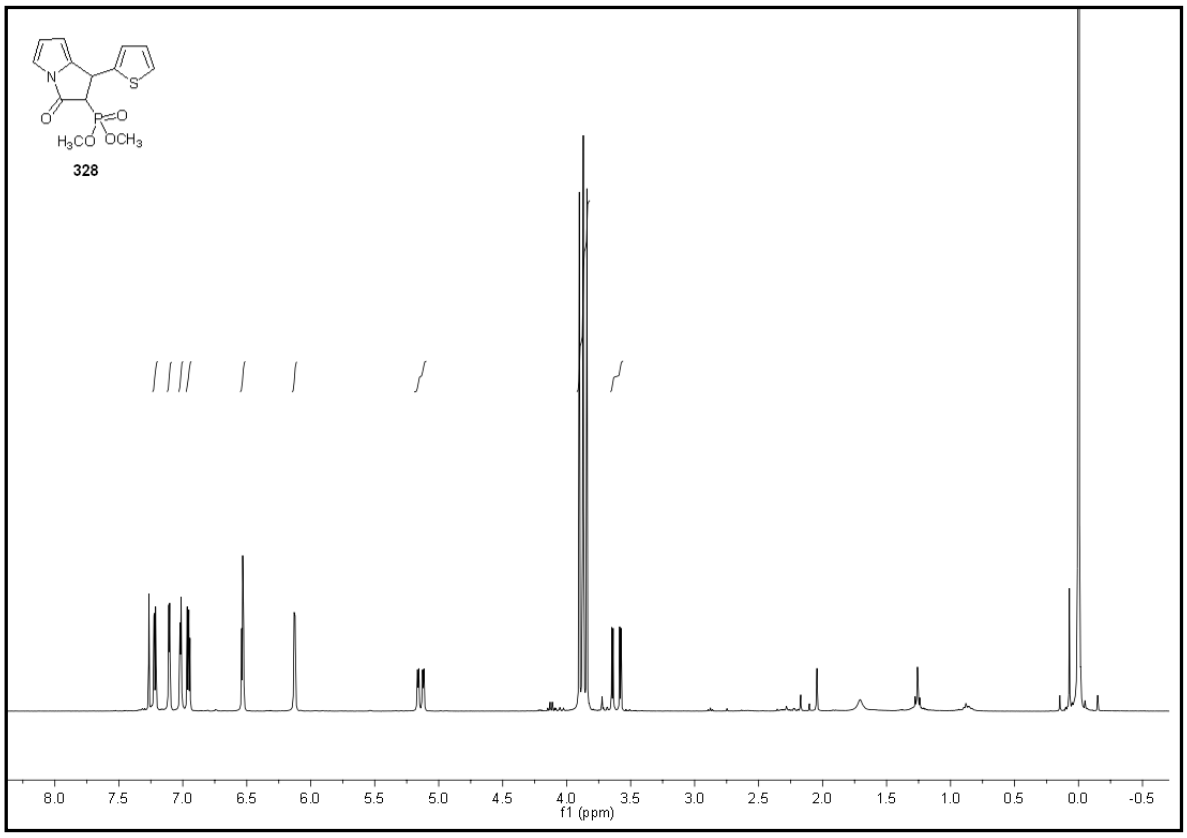


Figure A.307. ^{1}H NMR spectrum of compound **328**

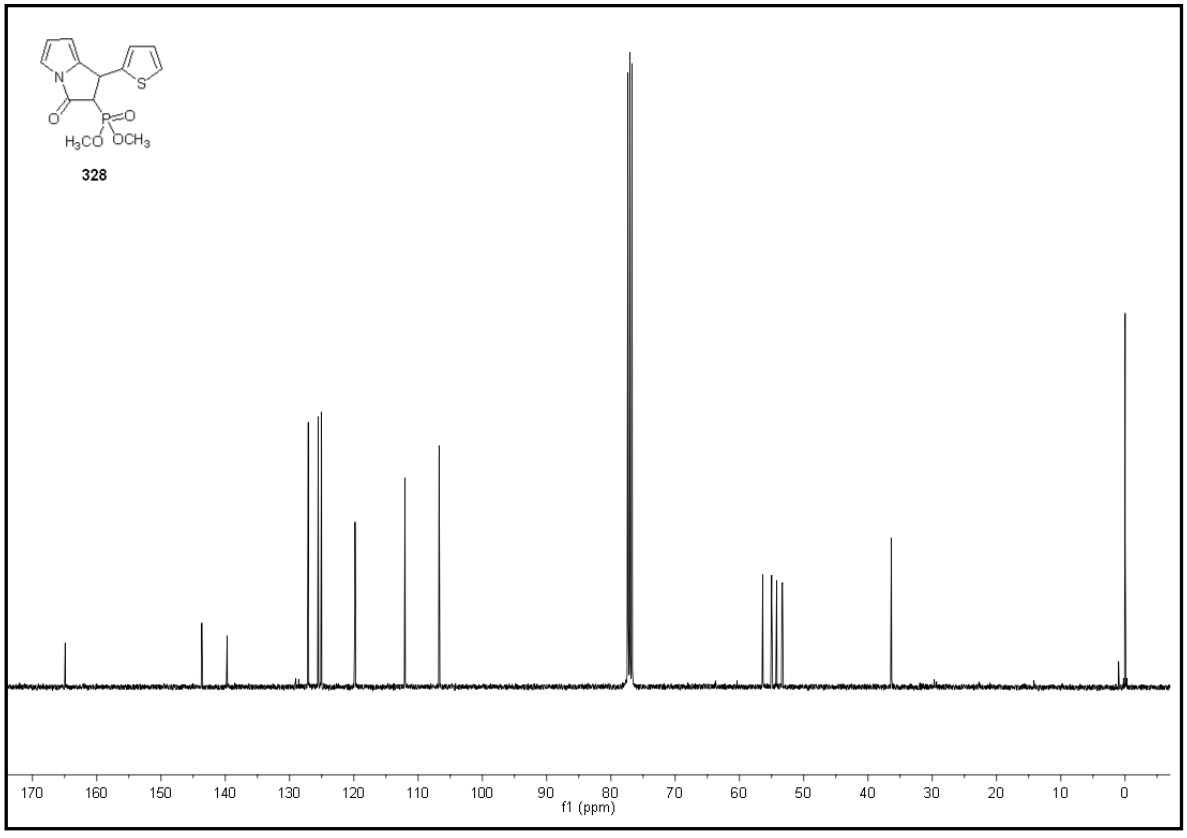


Figure A.308. ^{13}C NMR spectrum of compound **328**

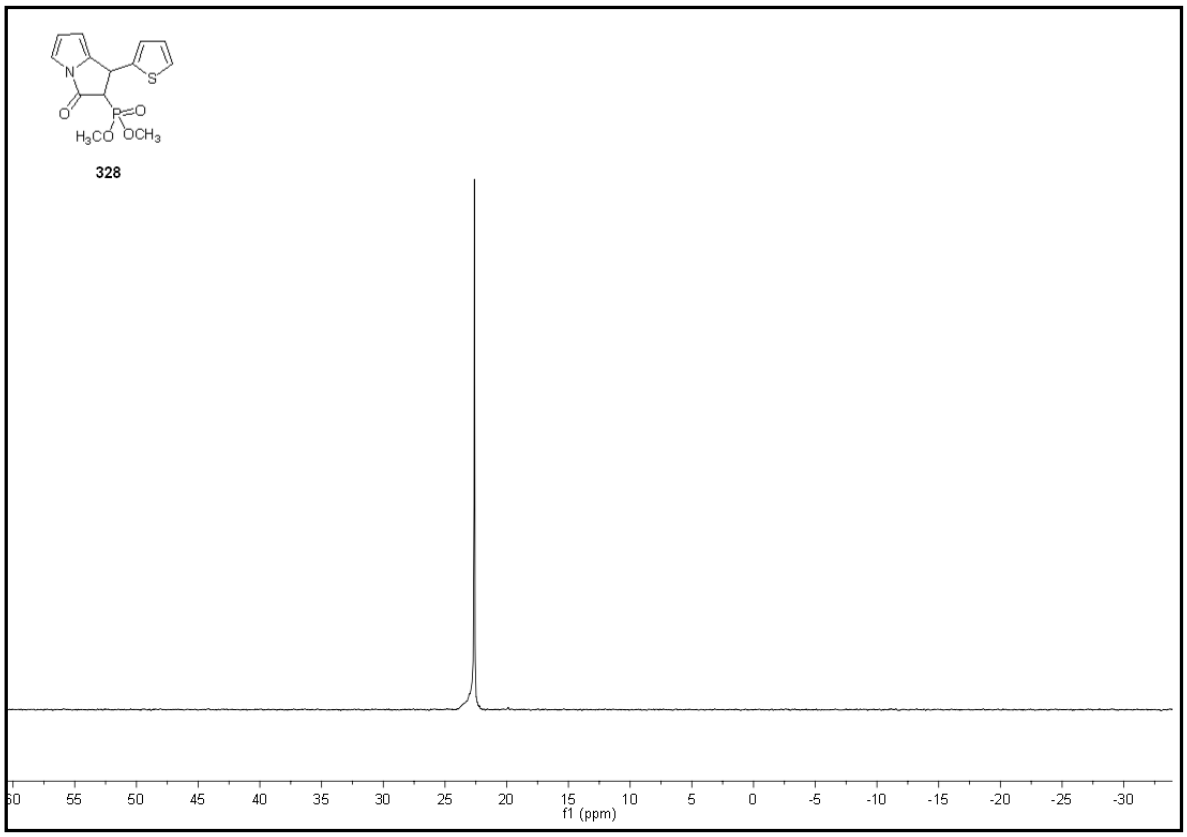


Figure A.309. ^{31}P NMR spectrum of compound **328**

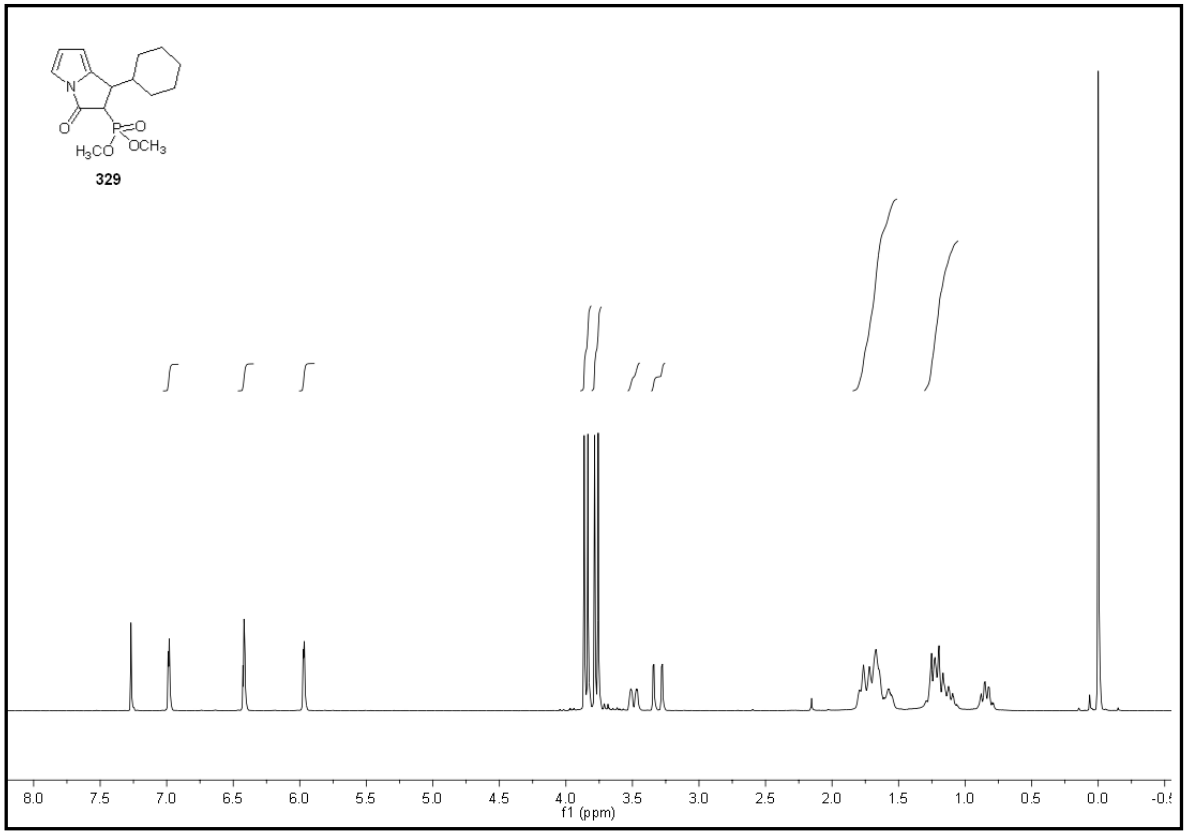


Figure A.310. ^{1}H NMR spectrum of compound **329**

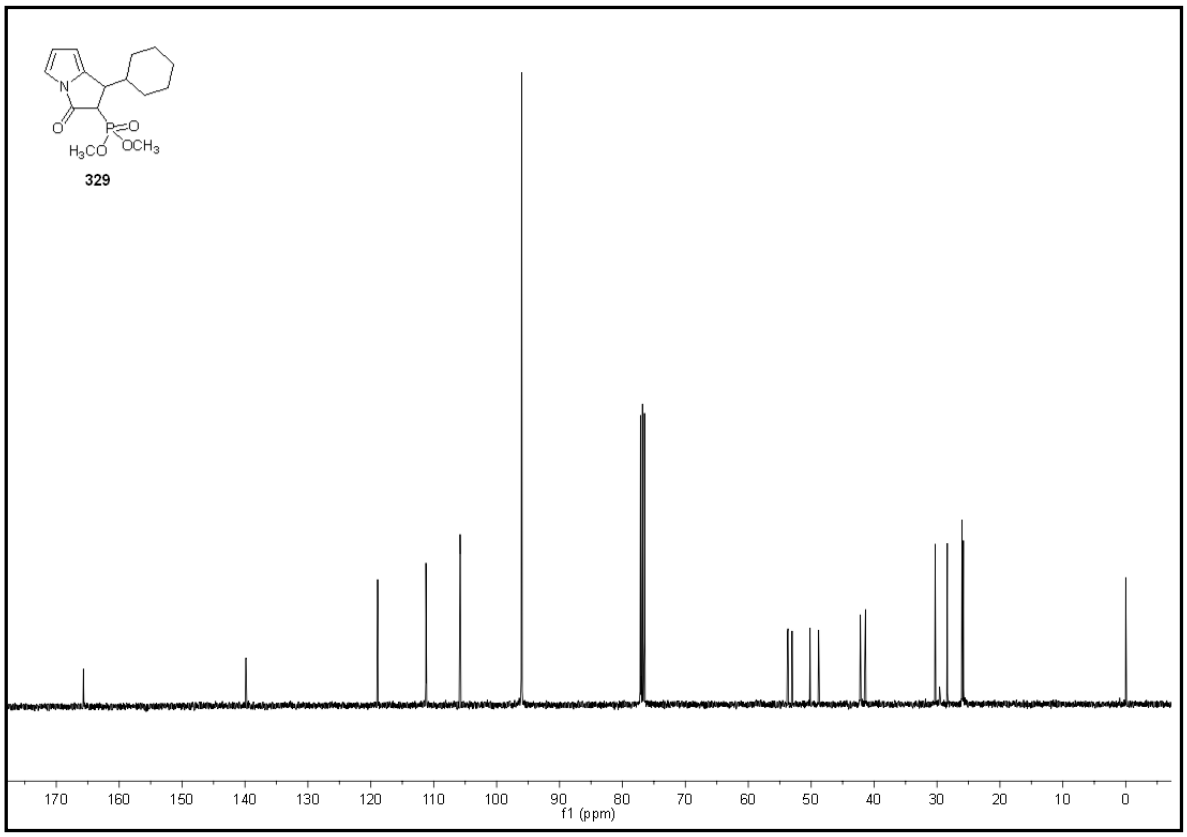


Figure A.311. ^{13}C NMR spectrum of compound **329**

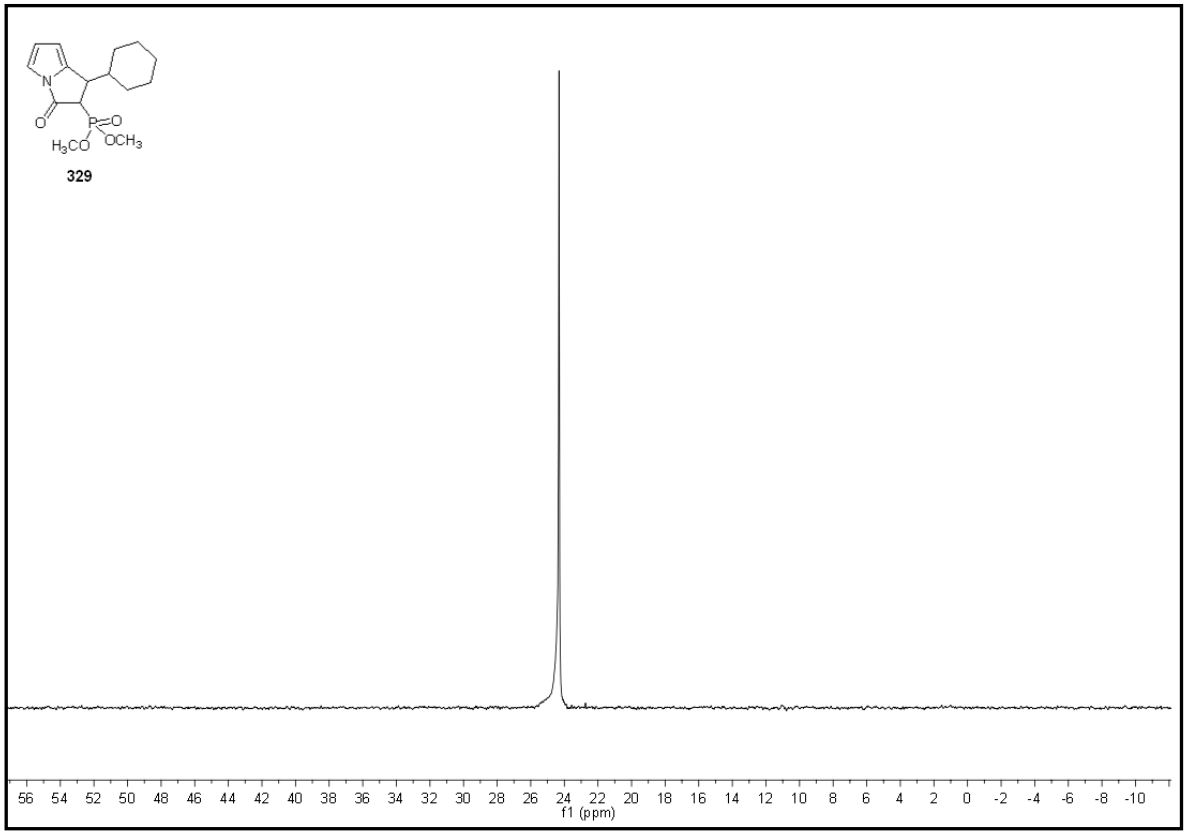


Figure A.312. ^{31}P NMR spectrum of compound **329**

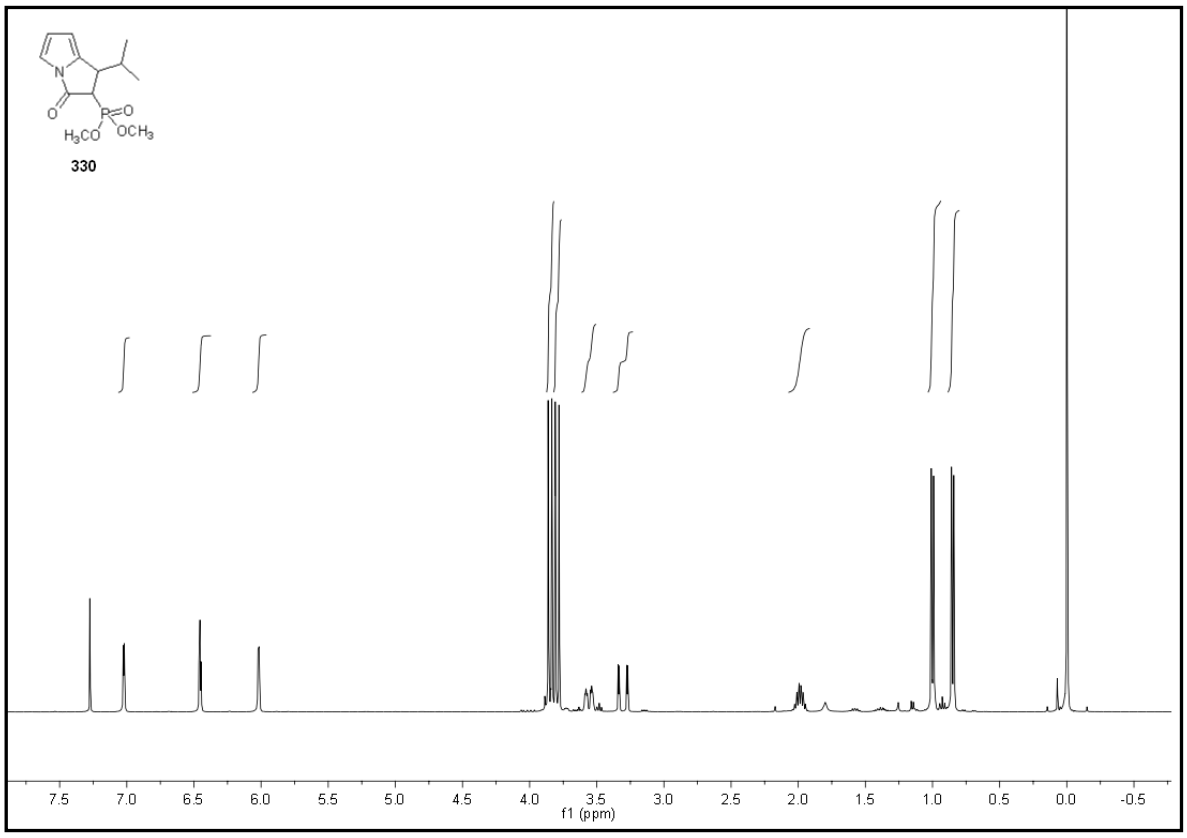


Figure A.313. ^{1}H NMR spectrum of compound **330**

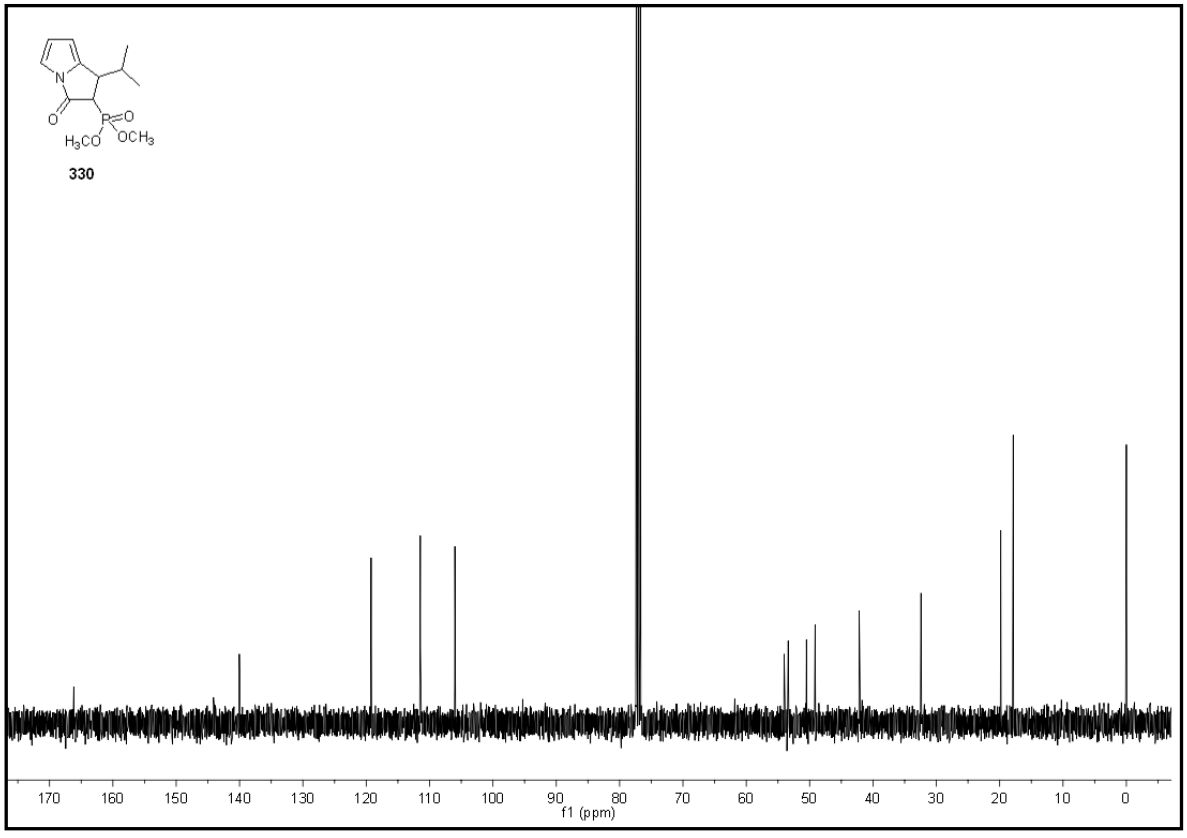


Figure A.314. ^{13}C NMR spectrum of compound **330**

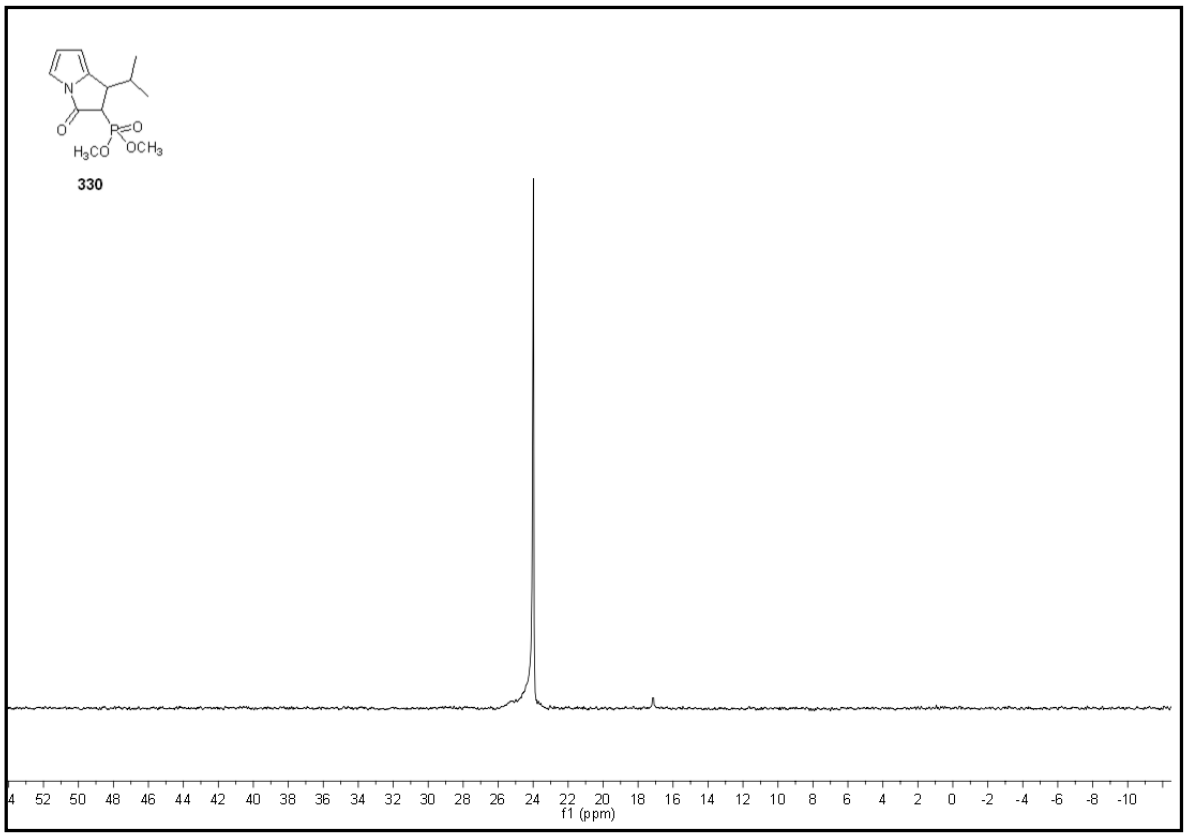


Figure A.315. ^{31}P NMR spectrum of compound **330**

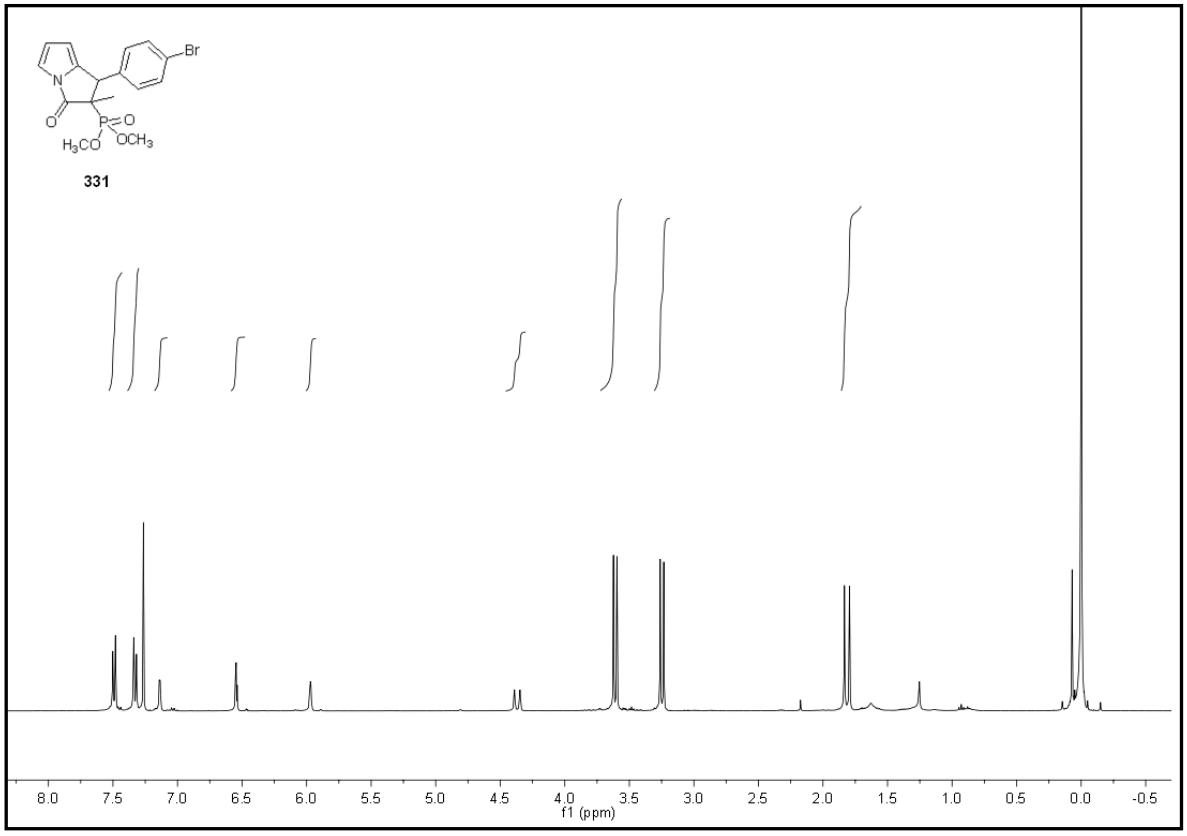


Figure A.316. ^{1}H NMR spectrum of compound **331**

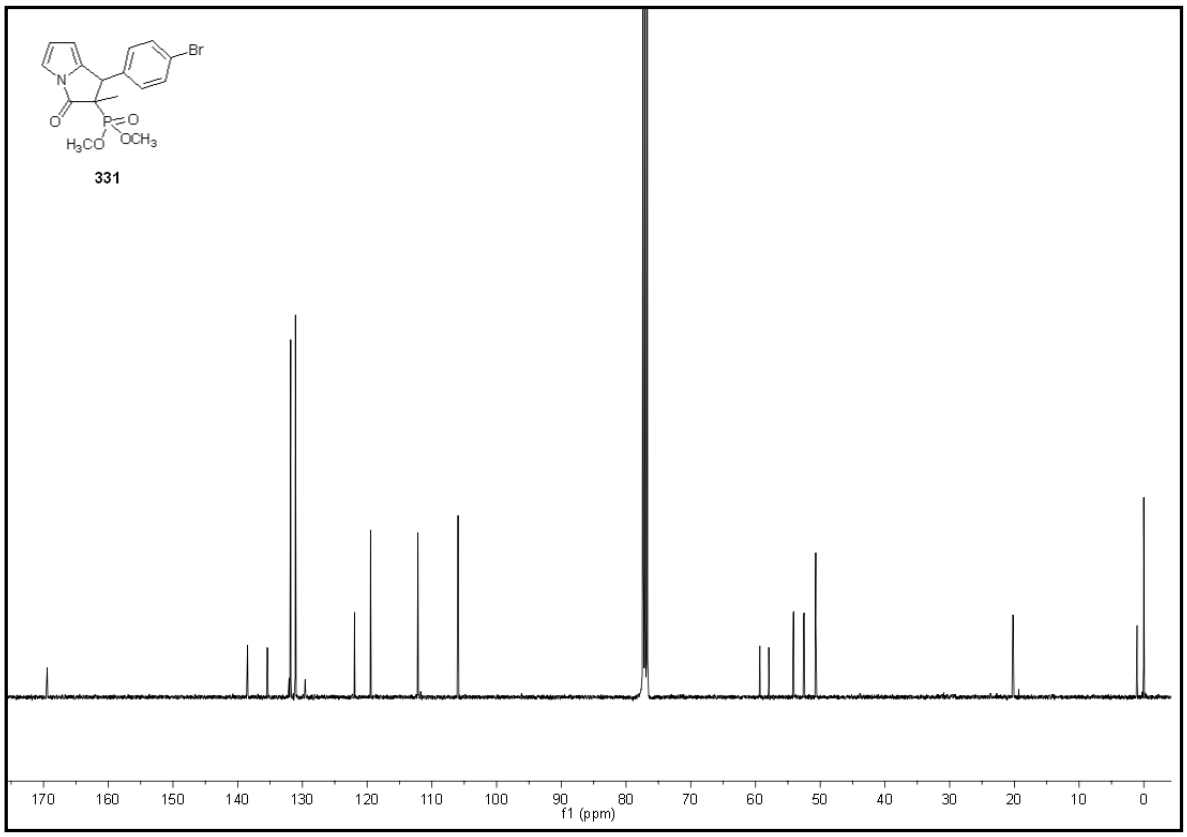


Figure A.317. ^{13}C NMR spectrum of compound **331**

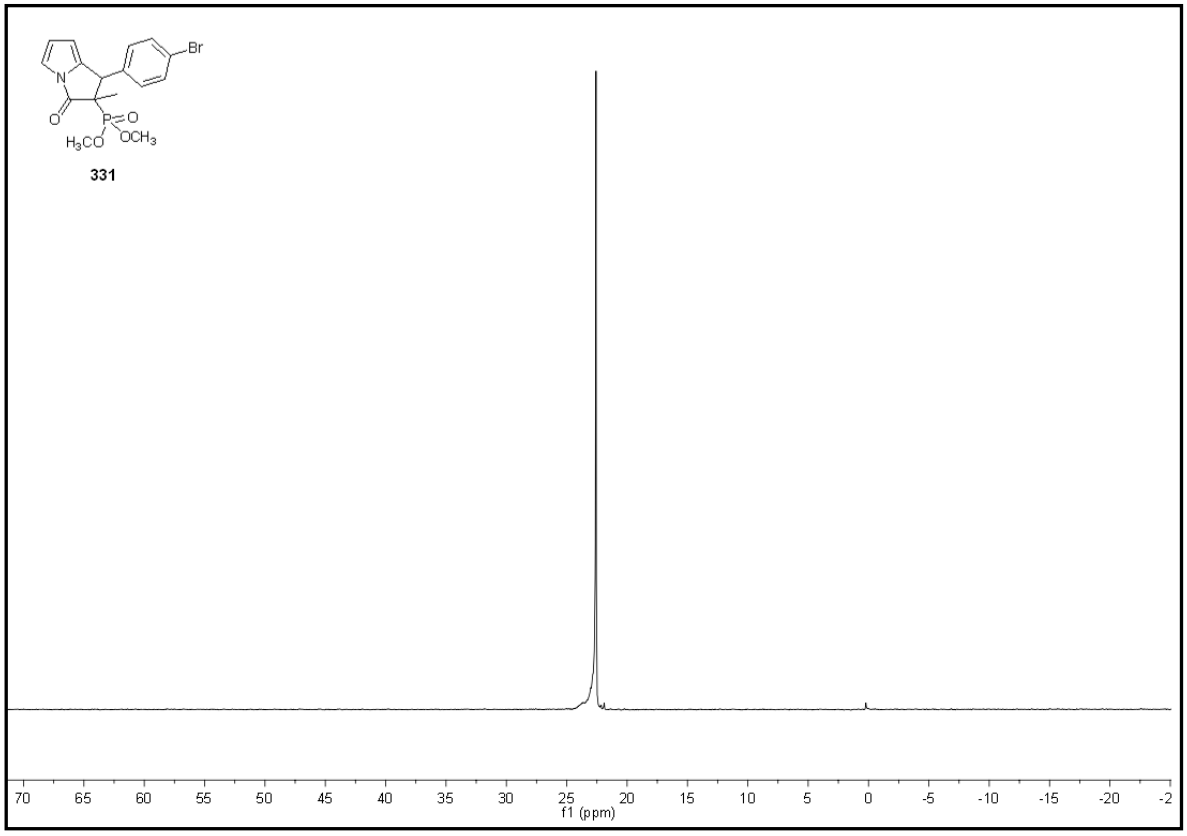


Figure A.318. ^{31}P NMR spectrum of compound **331**

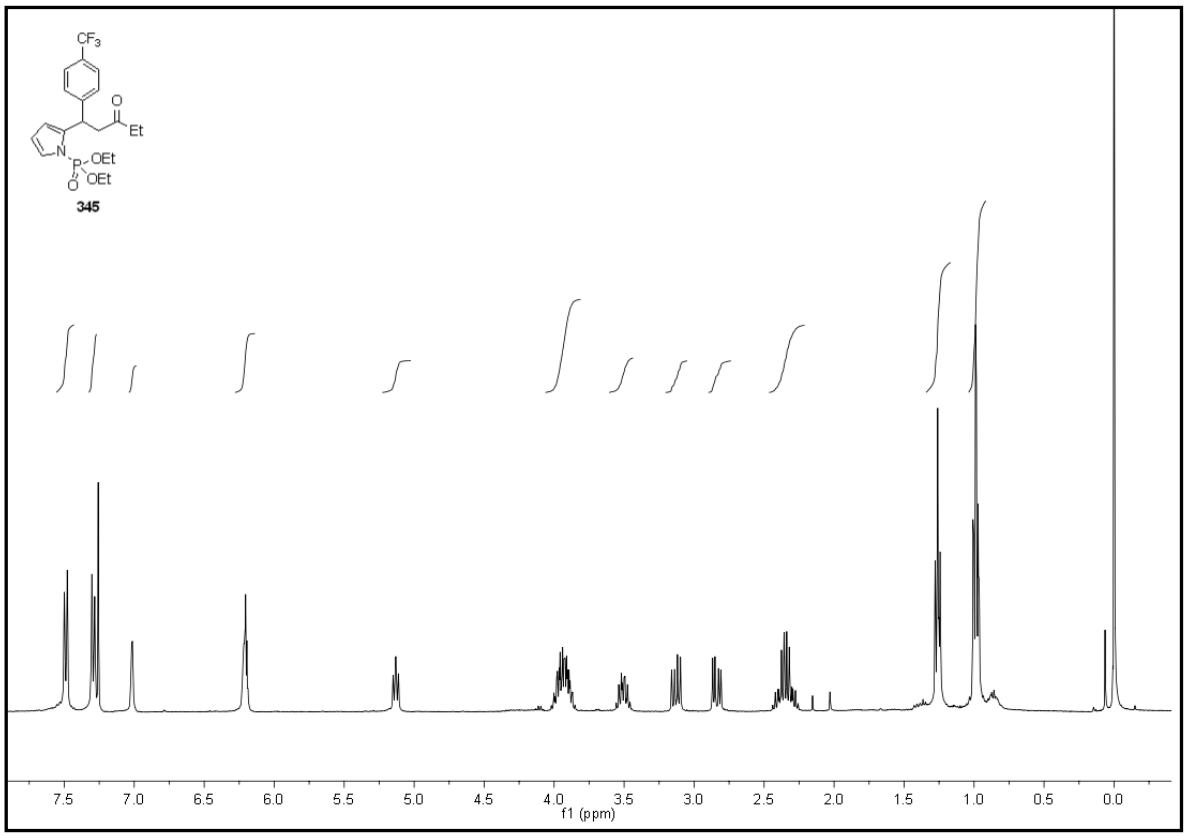


Figure A.319. ^{1}H NMR spectrum of compound **345**

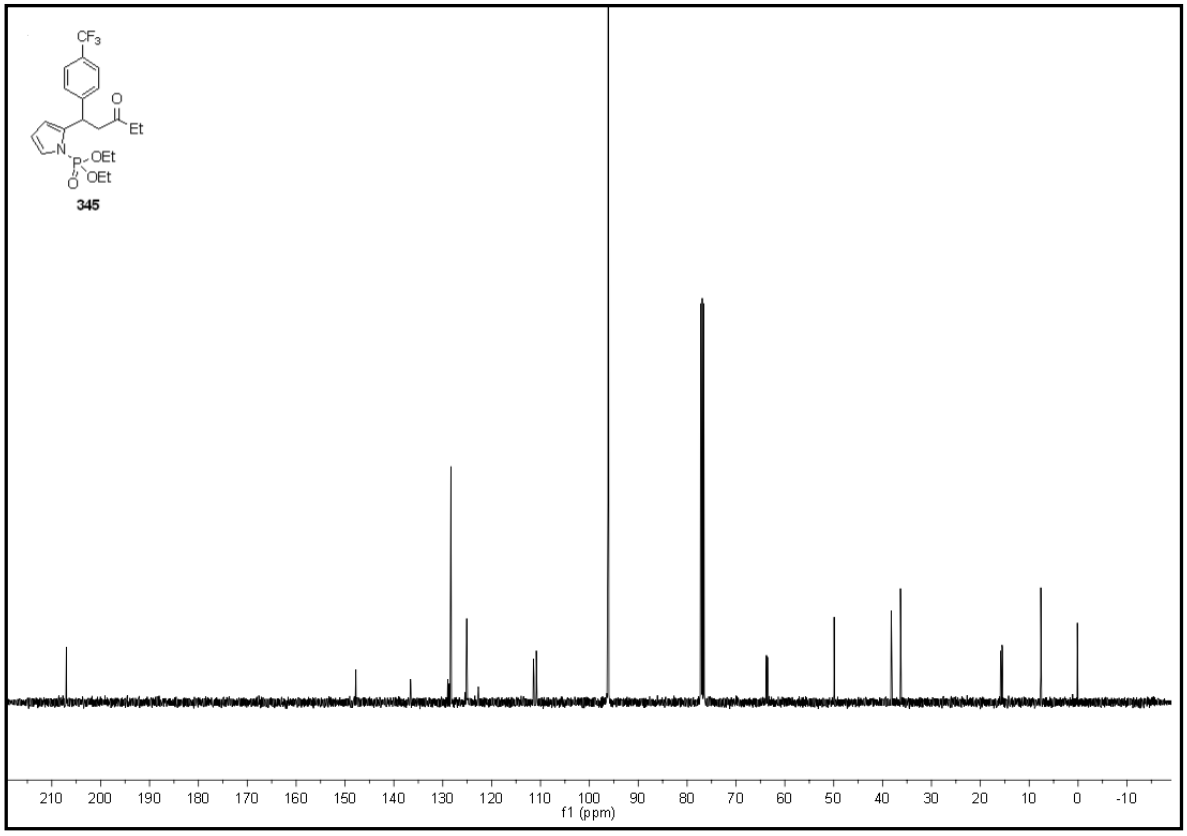


Figure A.320. ^{13}C NMR spectrum of compound **345**

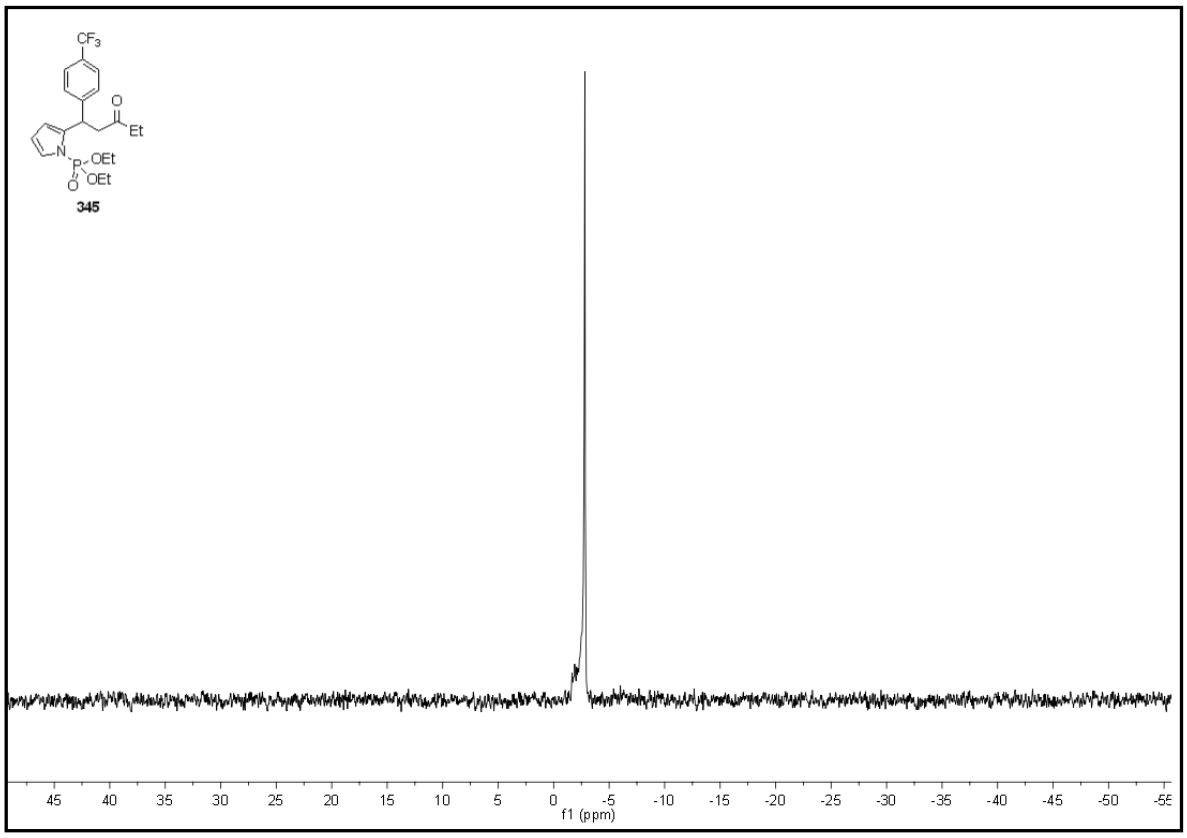


Figure A.321. ^{31}P NMR spectrum of compound **345**

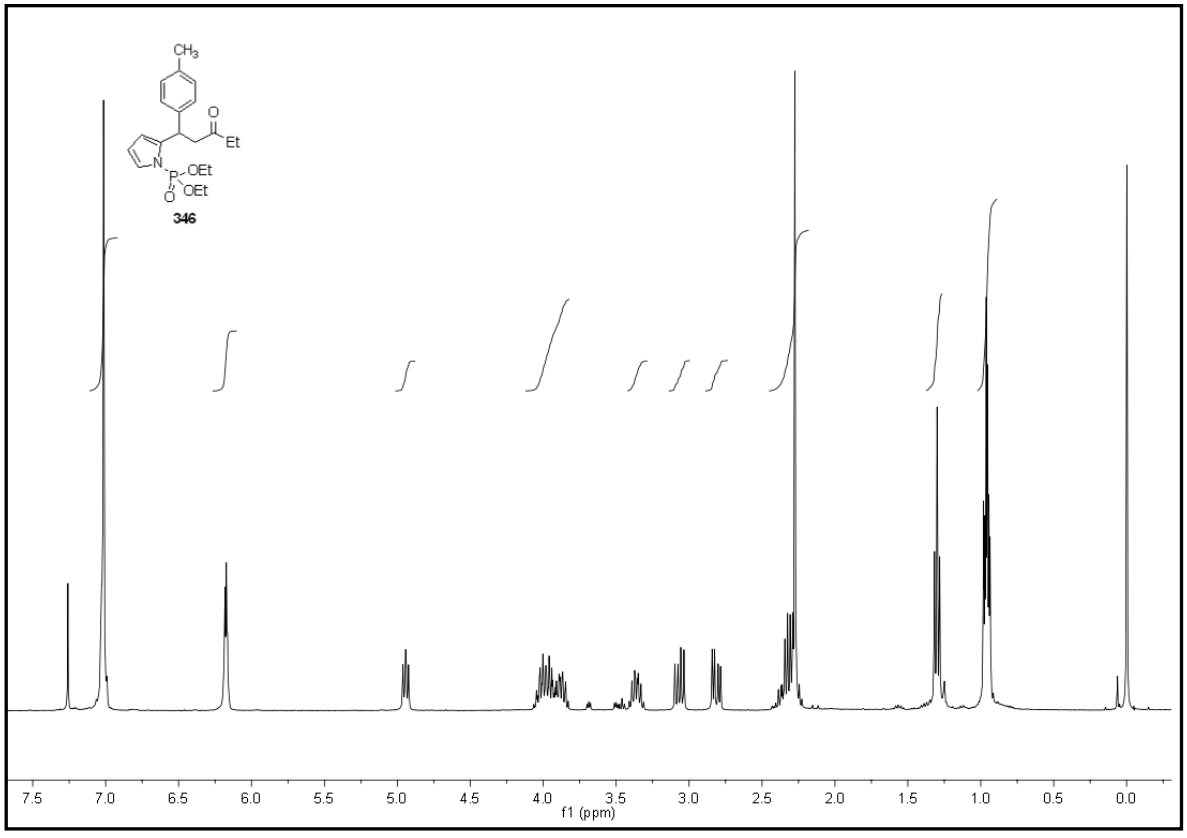


Figure A.322. ^{1}H NMR spectrum of compound **346**

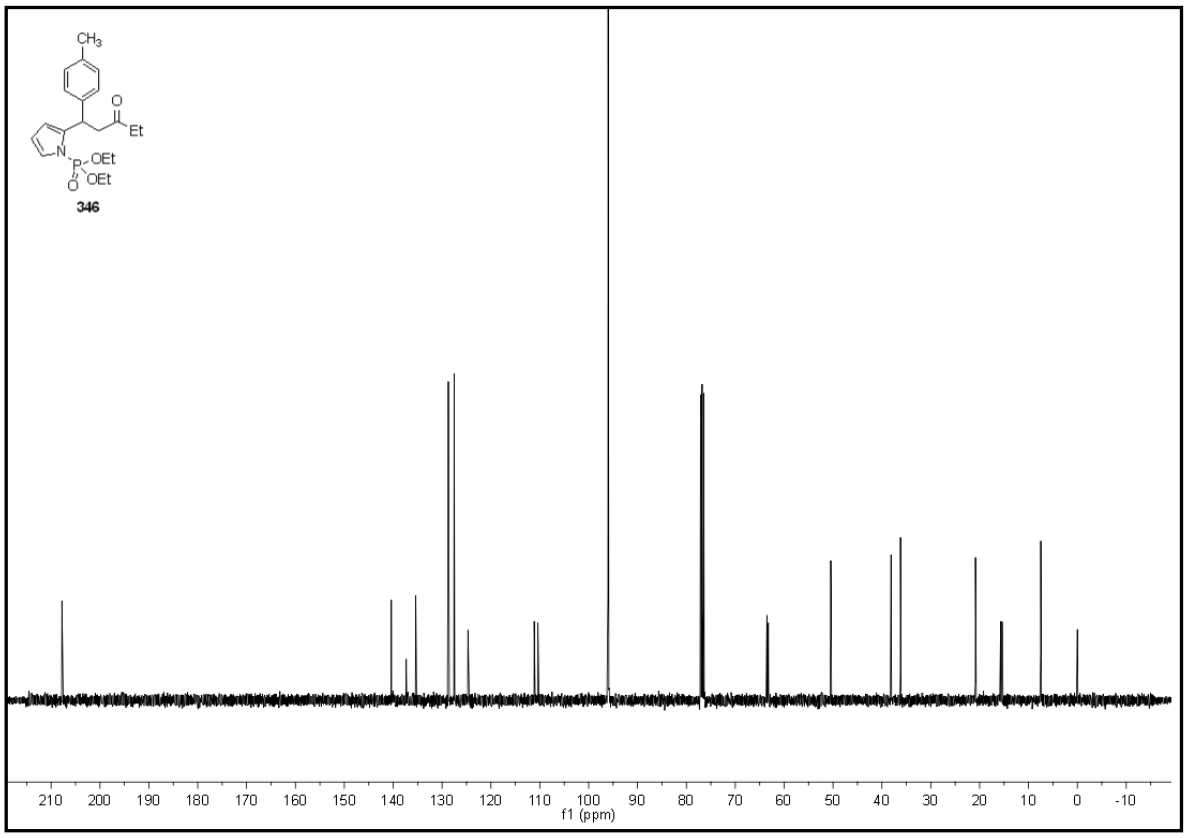


Figure A.323. ^{13}C NMR spectrum of compound **346**

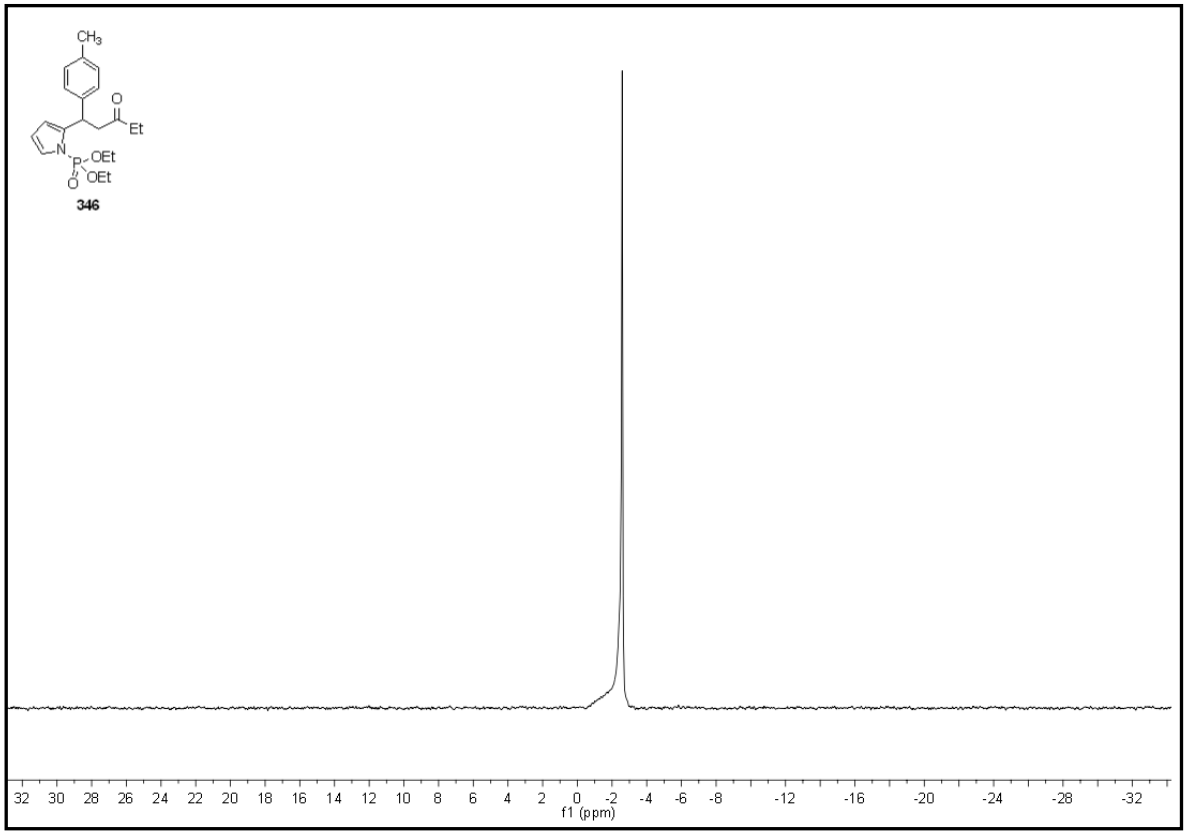


Figure A.324. ^{31}P NMR spectrum of compound **346**

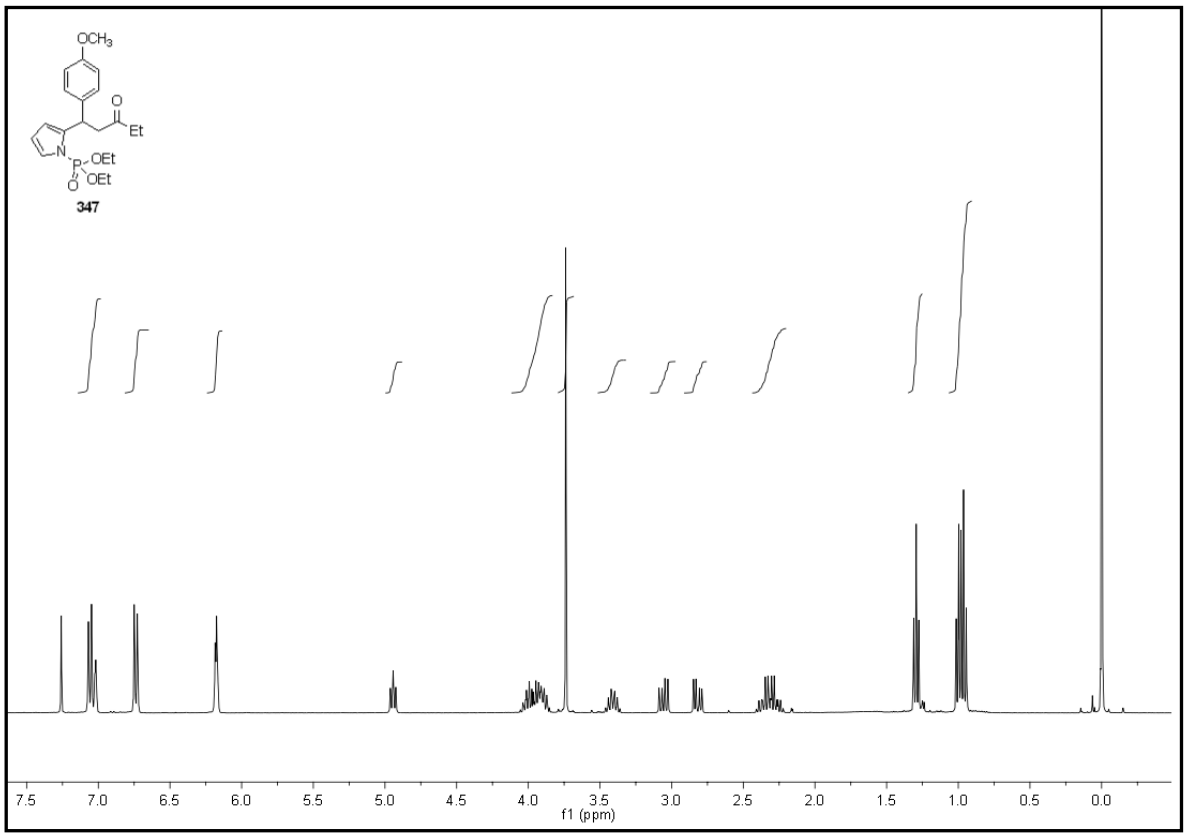


Figure A.325. ^{1}H NMR spectrum of compound **347**

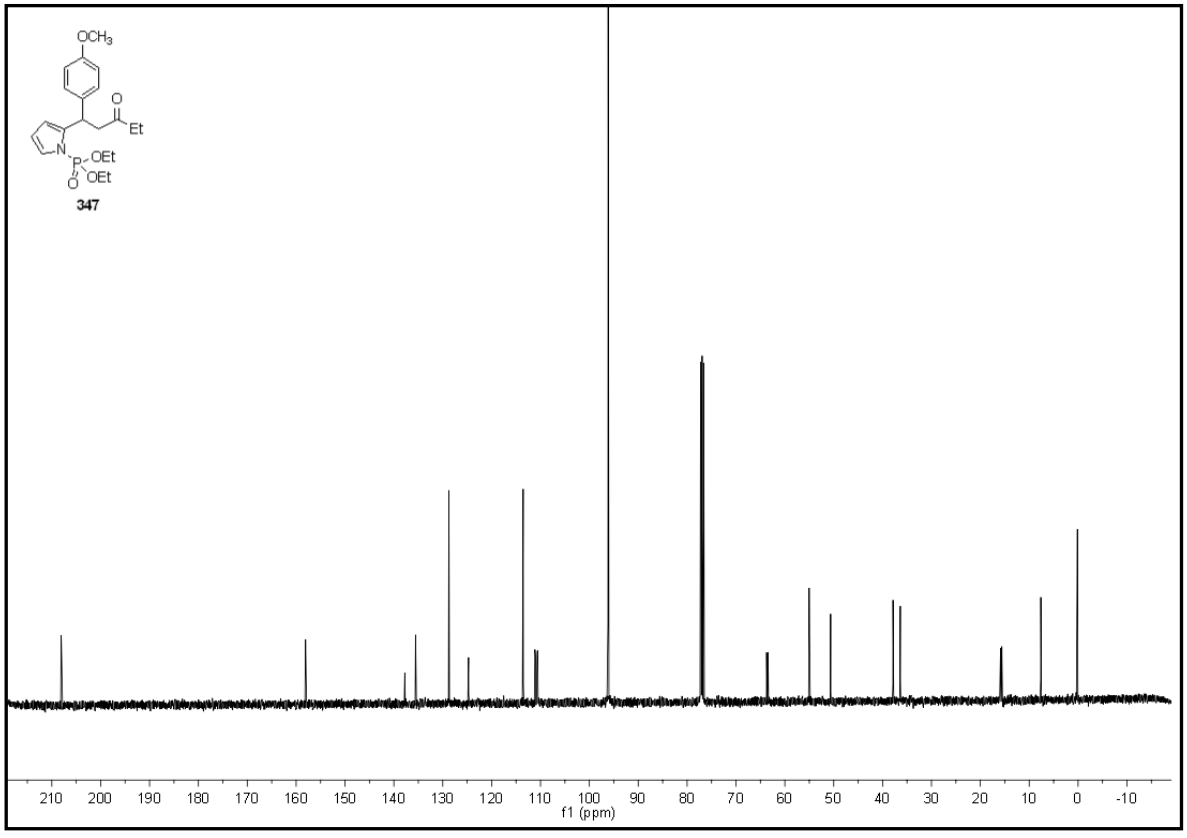


Figure A.326. ^{13}C NMR spectrum of compound **347**

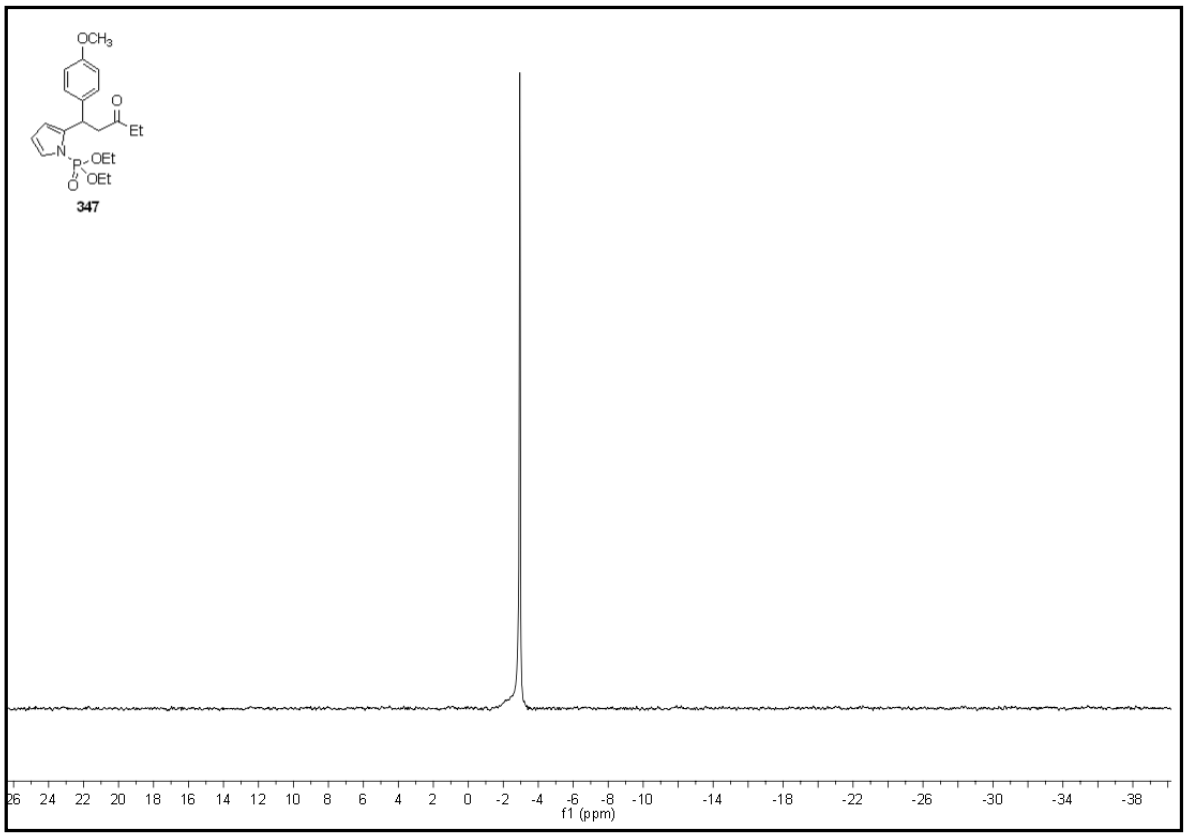


Figure A.327. ^{31}P NMR spectrum of compound **347**

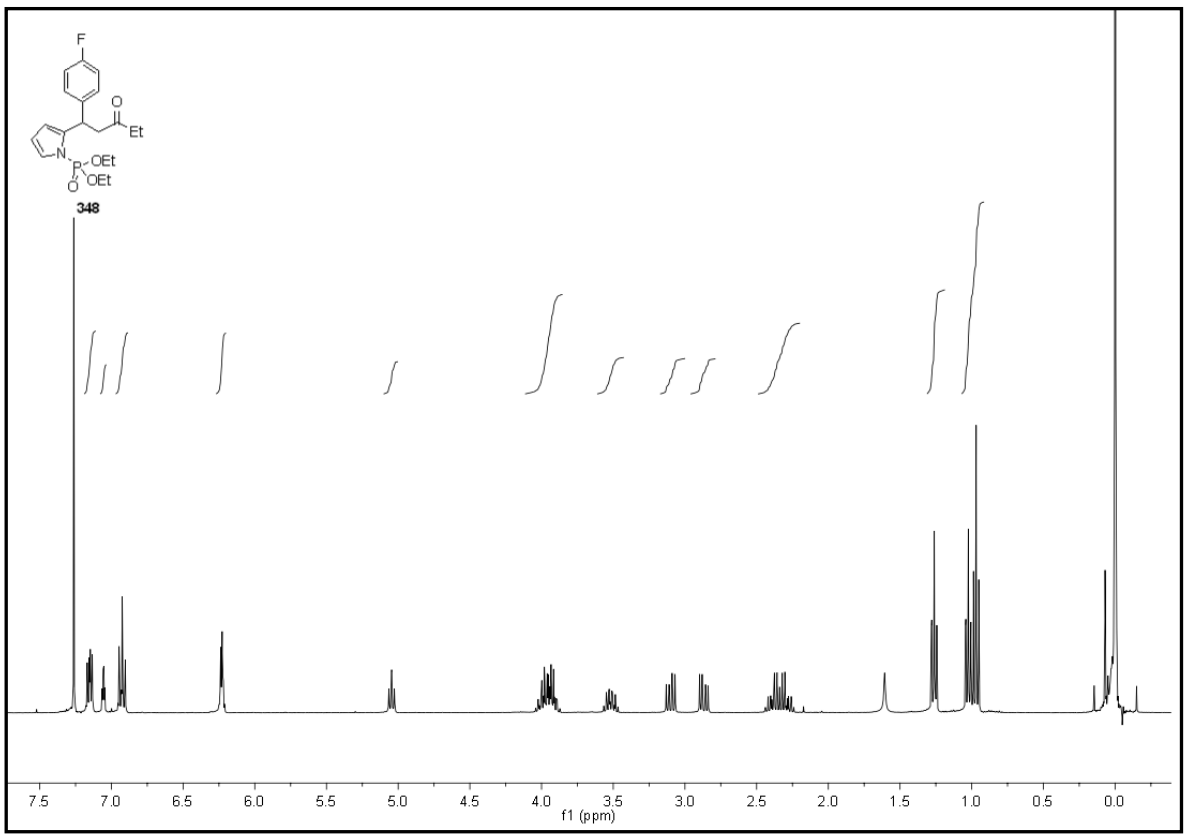


Figure A.328. ^{1}H NMR spectrum of compound **348**

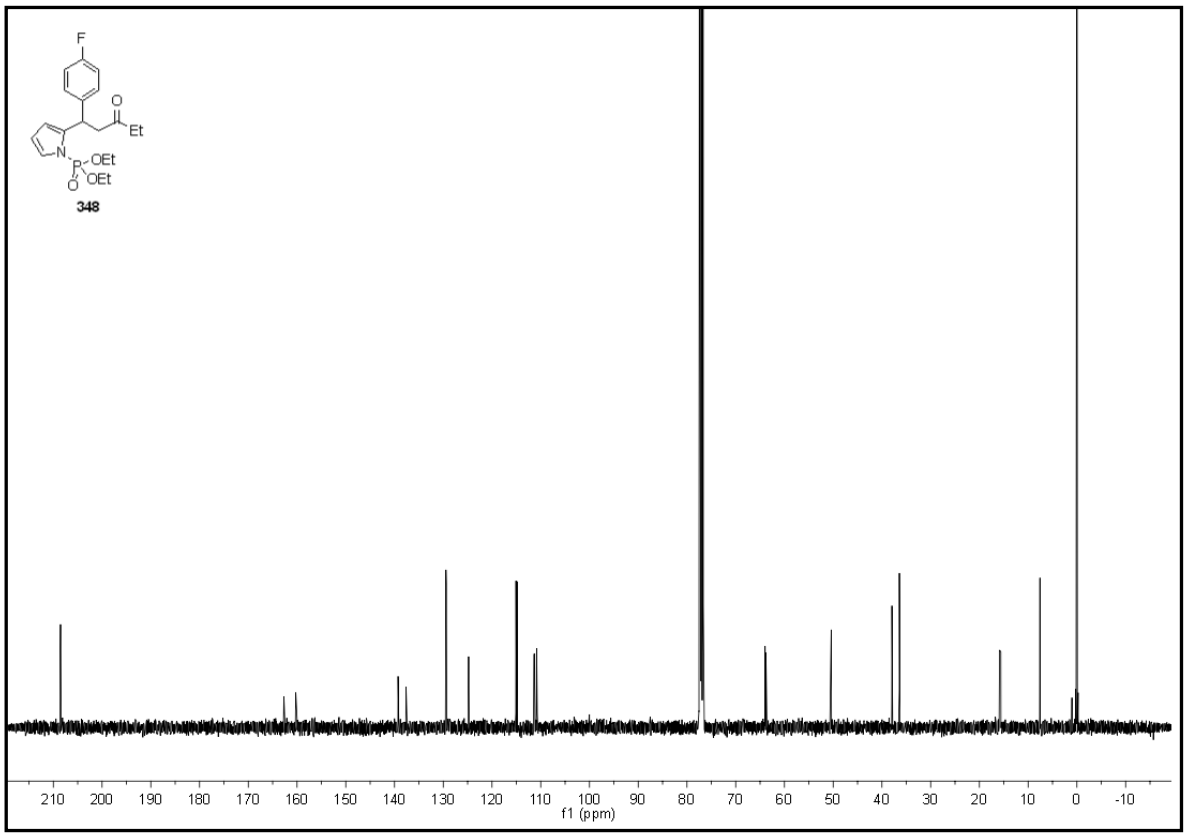


Figure A.329. ^{13}C NMR spectrum of compound **348**

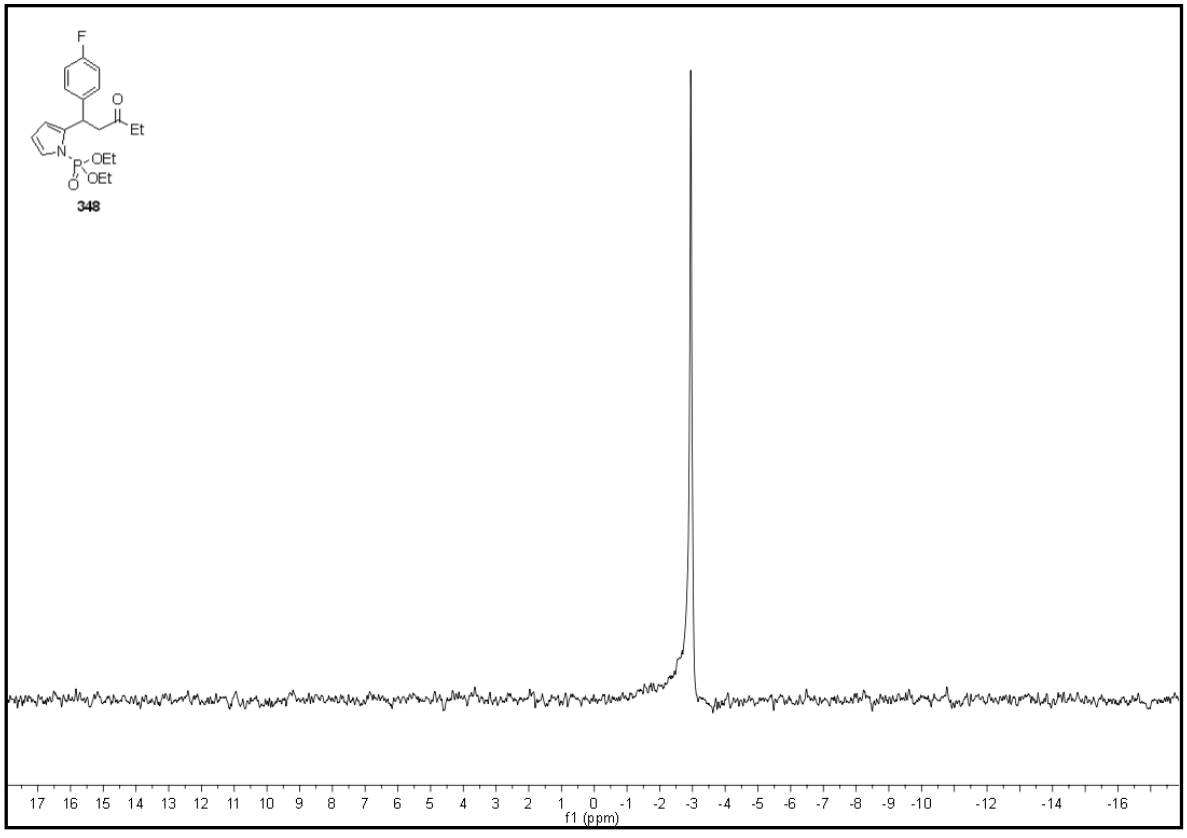


Figure A.330. ^{31}P NMR spectrum of compound **348**

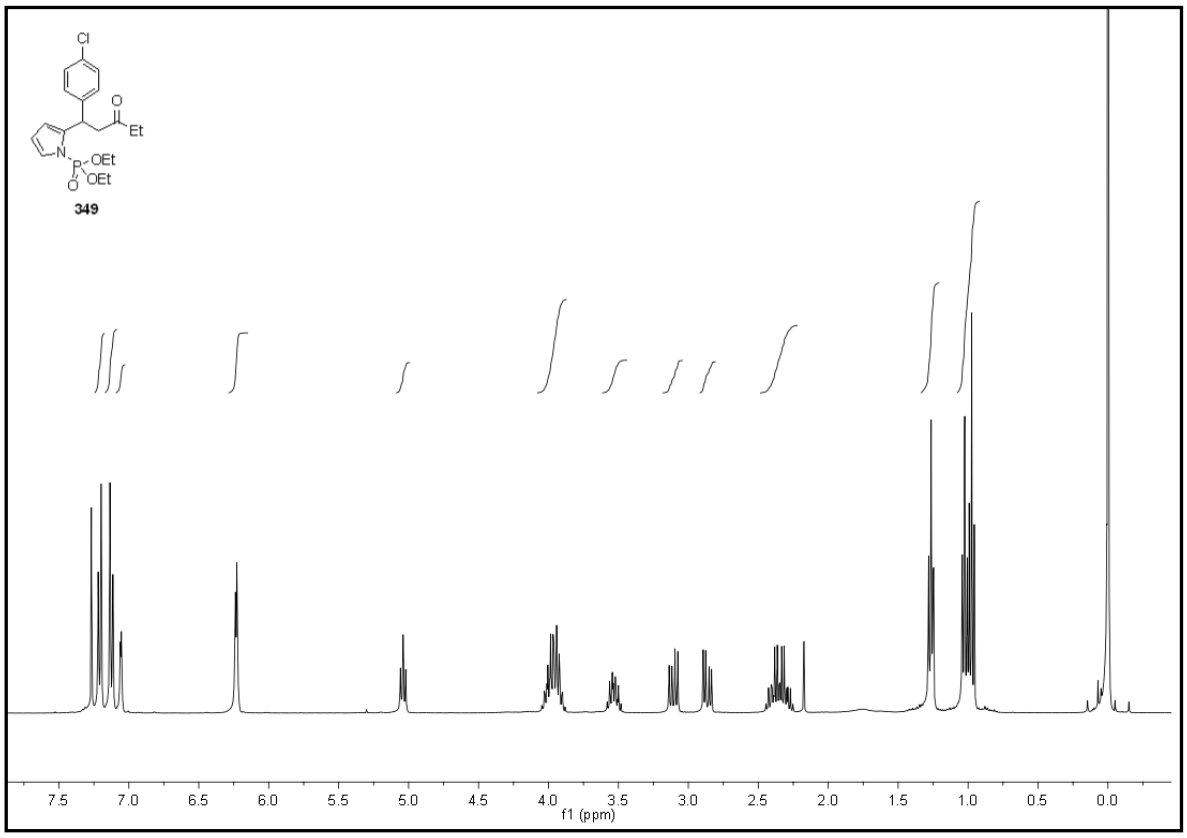


Figure A.331. ^{1}H NMR spectrum of compound **349**

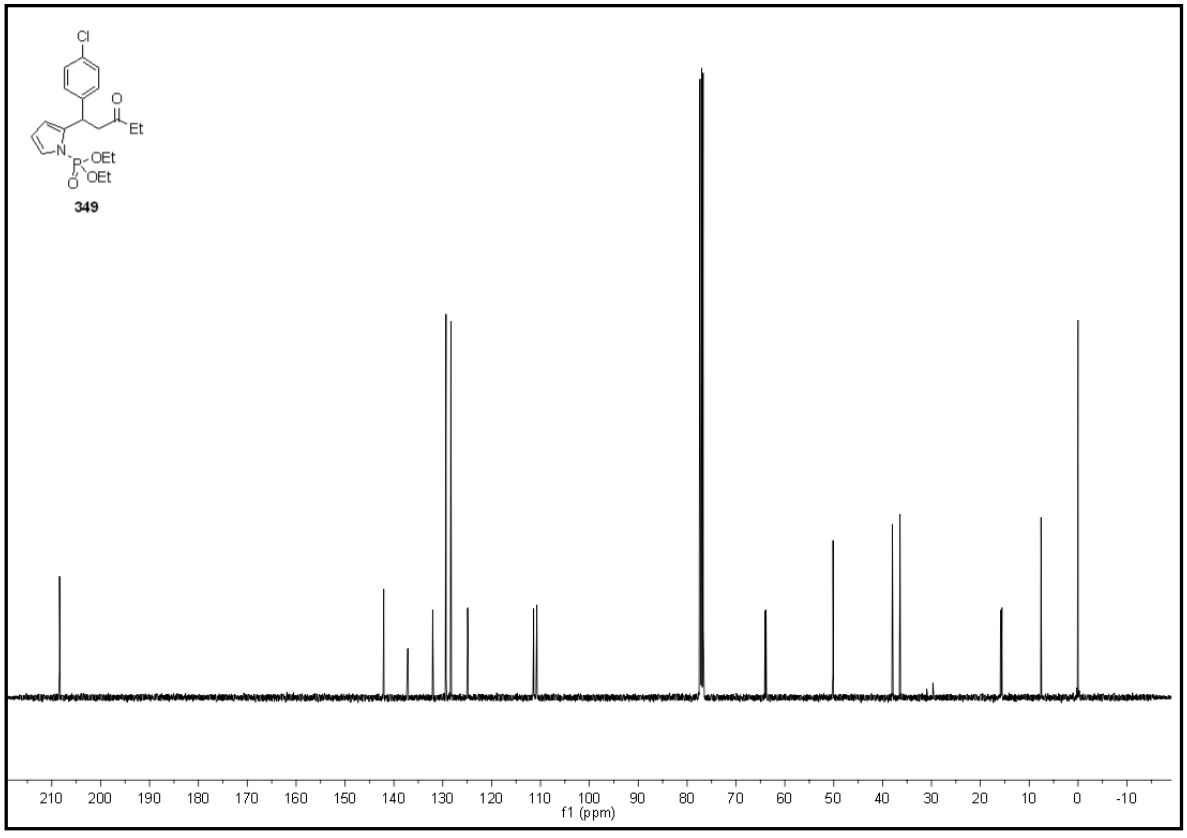


Figure A.332. ^{13}C NMR spectrum of compound **349**

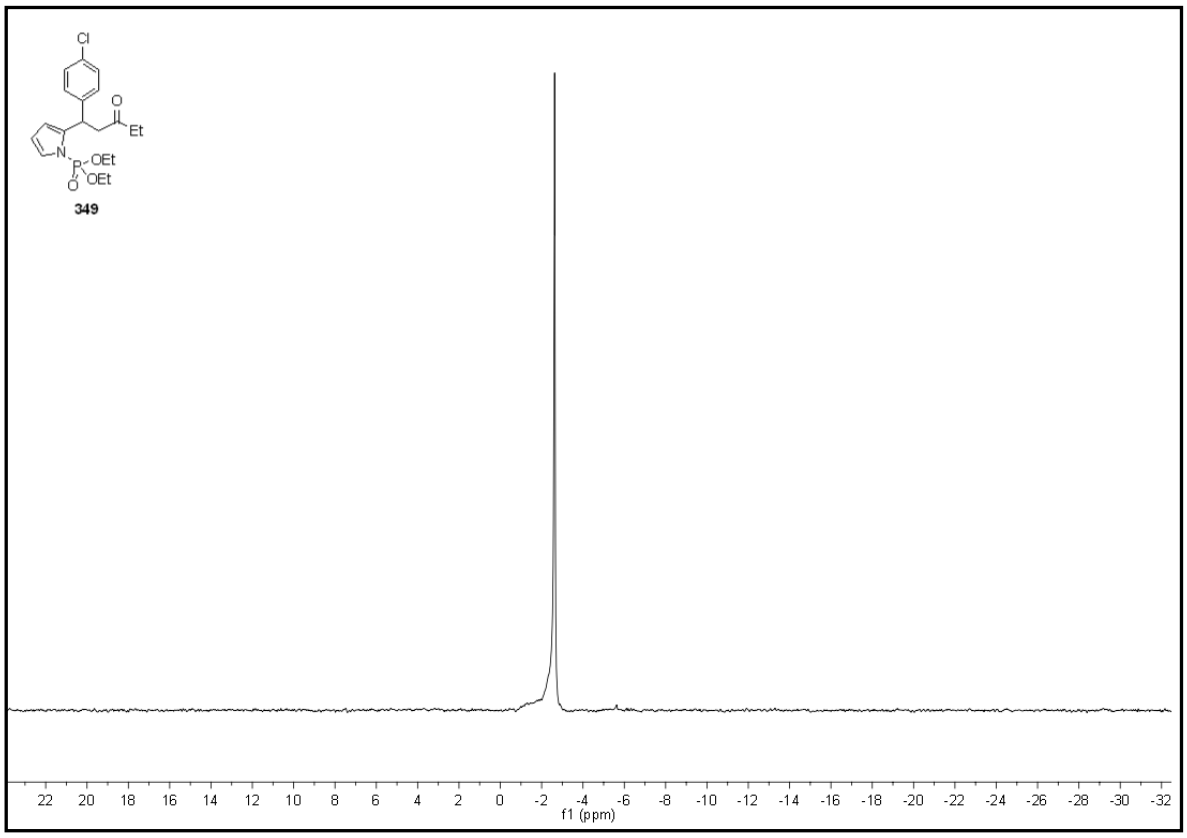


Figure A.333. ^{31}P NMR spectrum of compound **349**

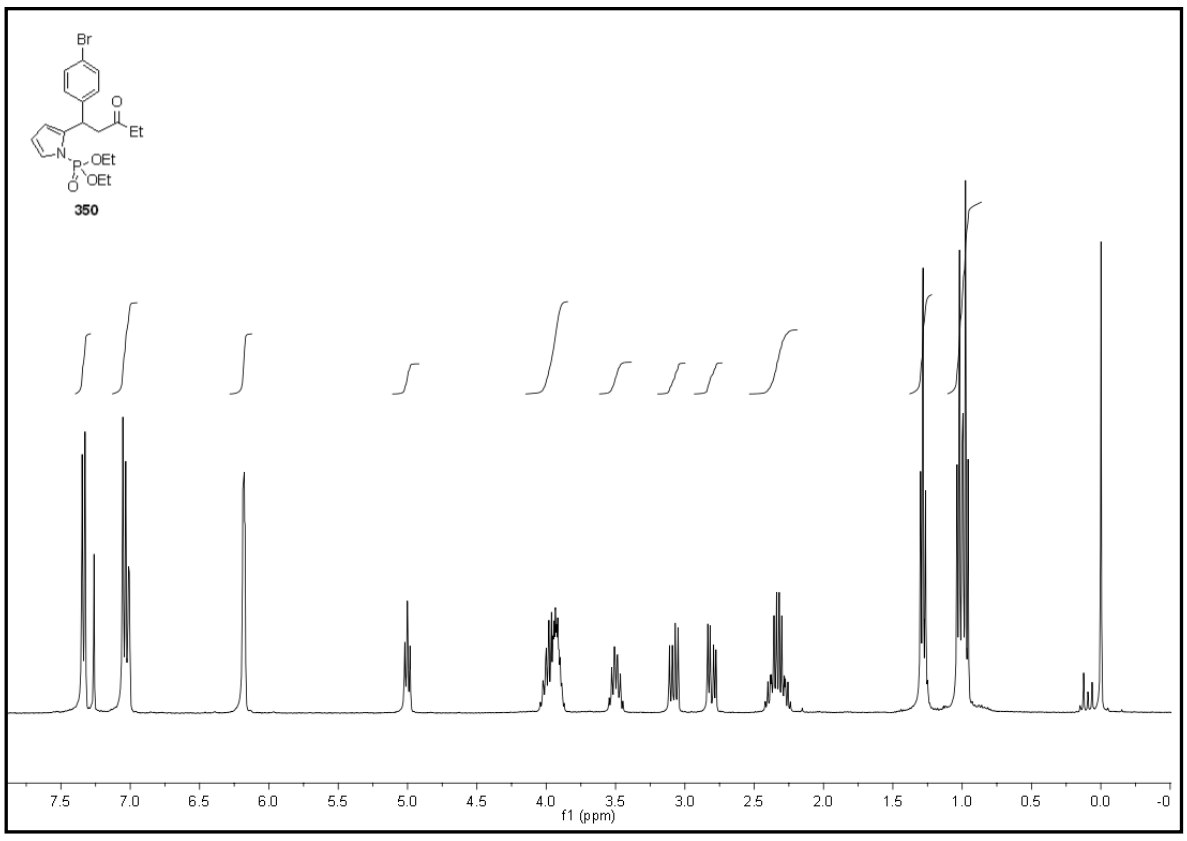


Figure A.334. ^{1}H NMR spectrum of compound **350**

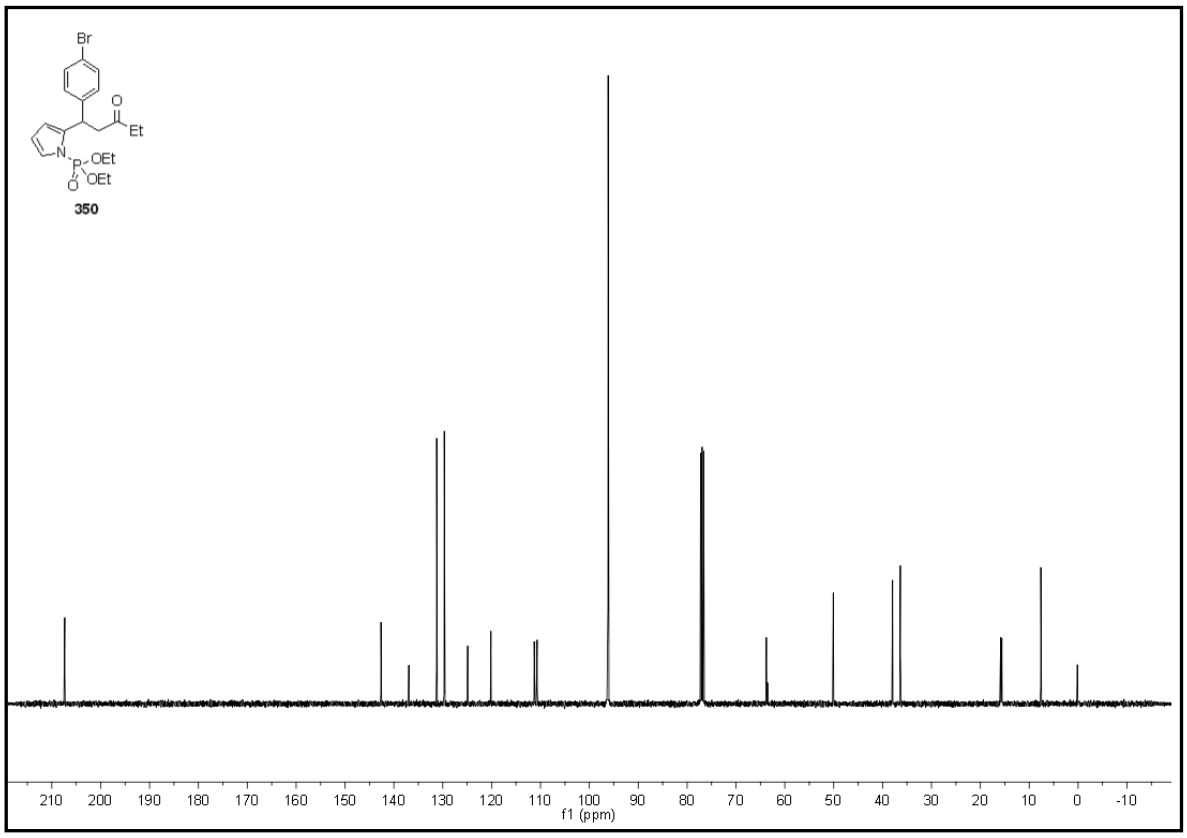


Figure A.335. ^{13}C NMR spectrum of compound **350**

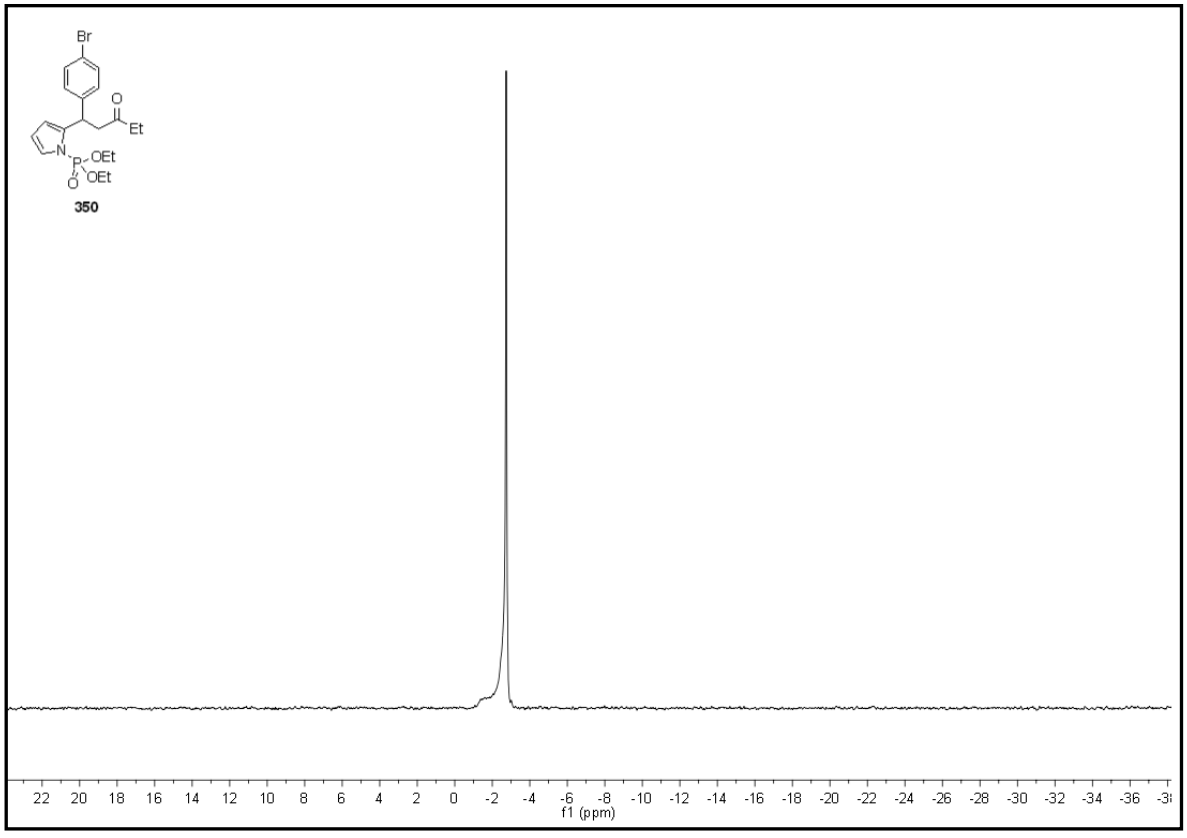


Figure A.336. ^{31}P NMR spectrum of compound **350**

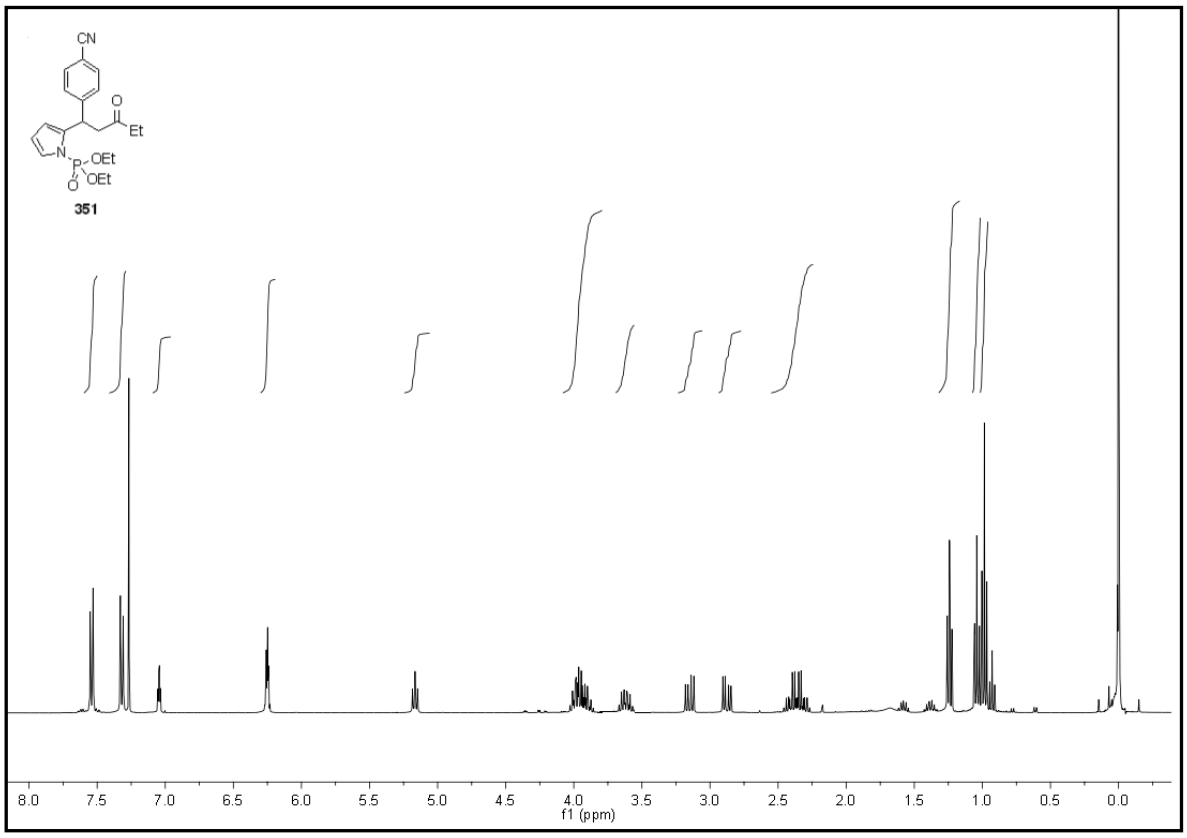


Figure A.337. ^{1}H NMR spectrum of compound **351**

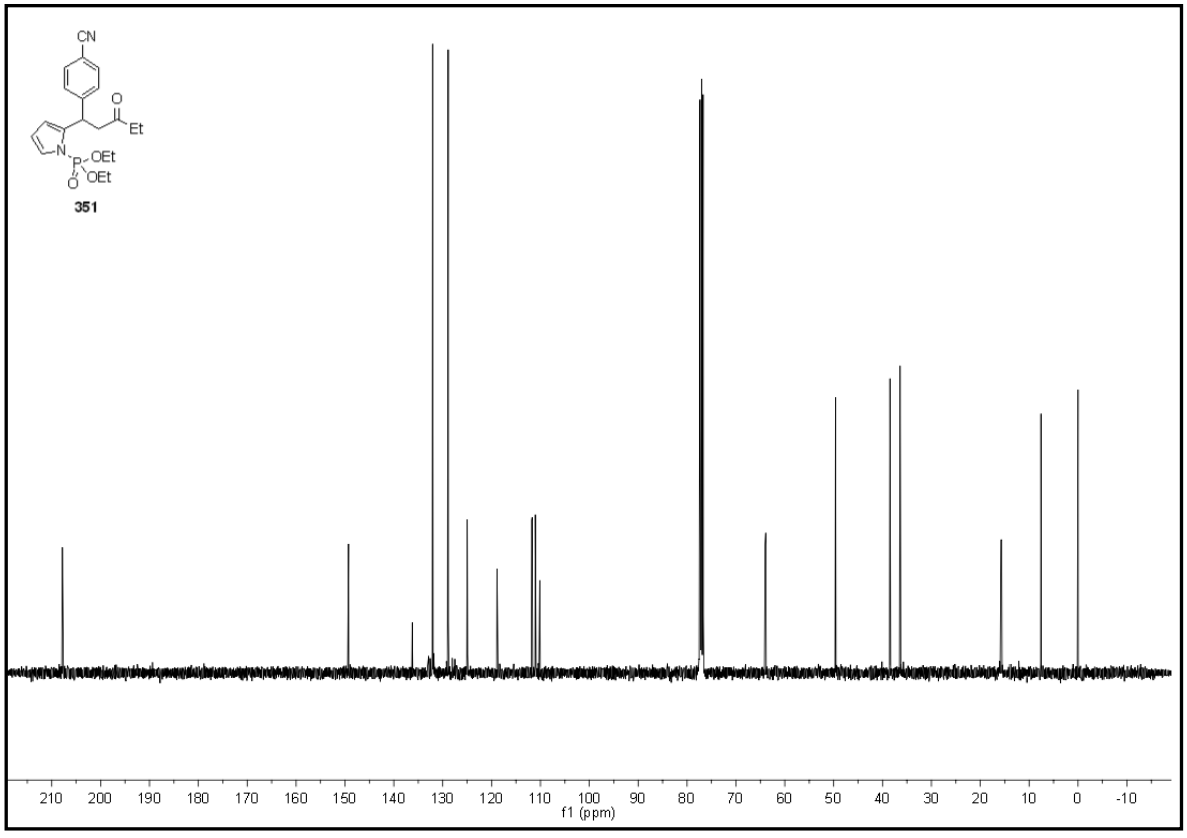


Figure A.338. ^{13}C NMR spectrum of compound **351**

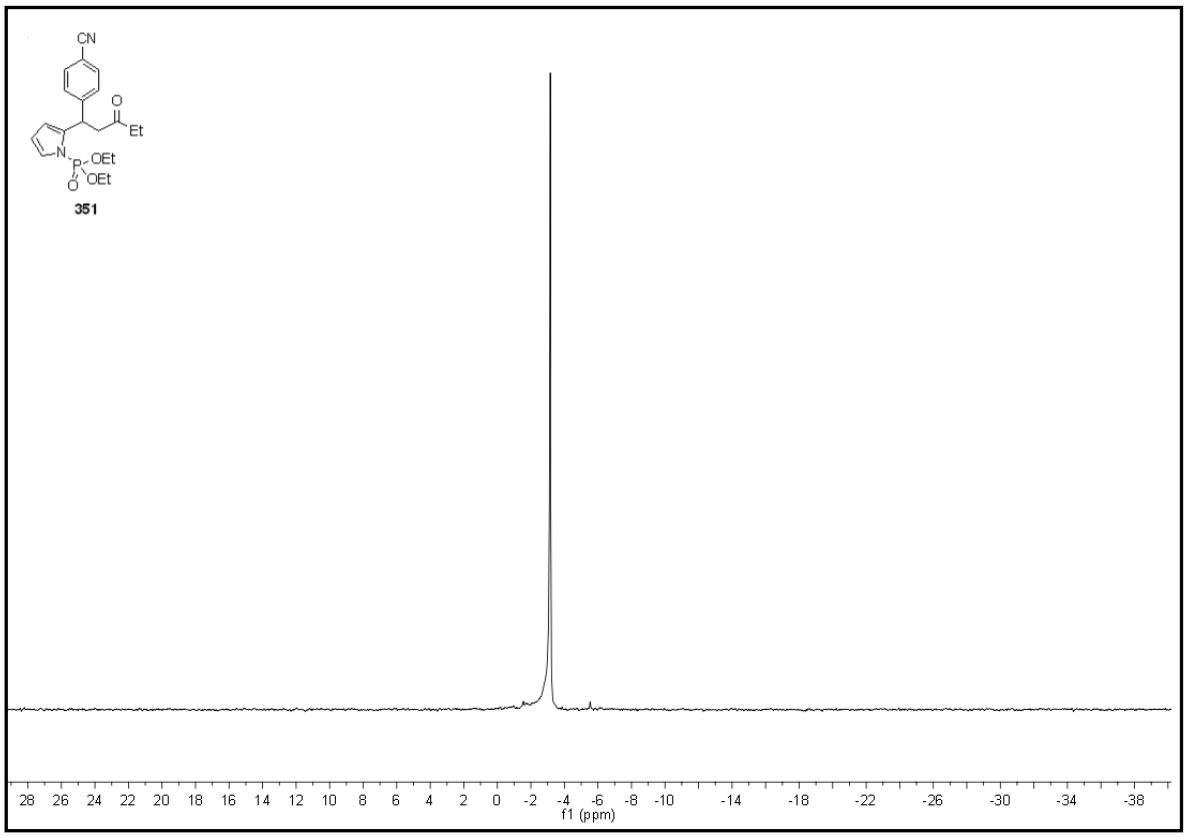


Figure A.339. ^{31}P NMR spectrum of compound **351**

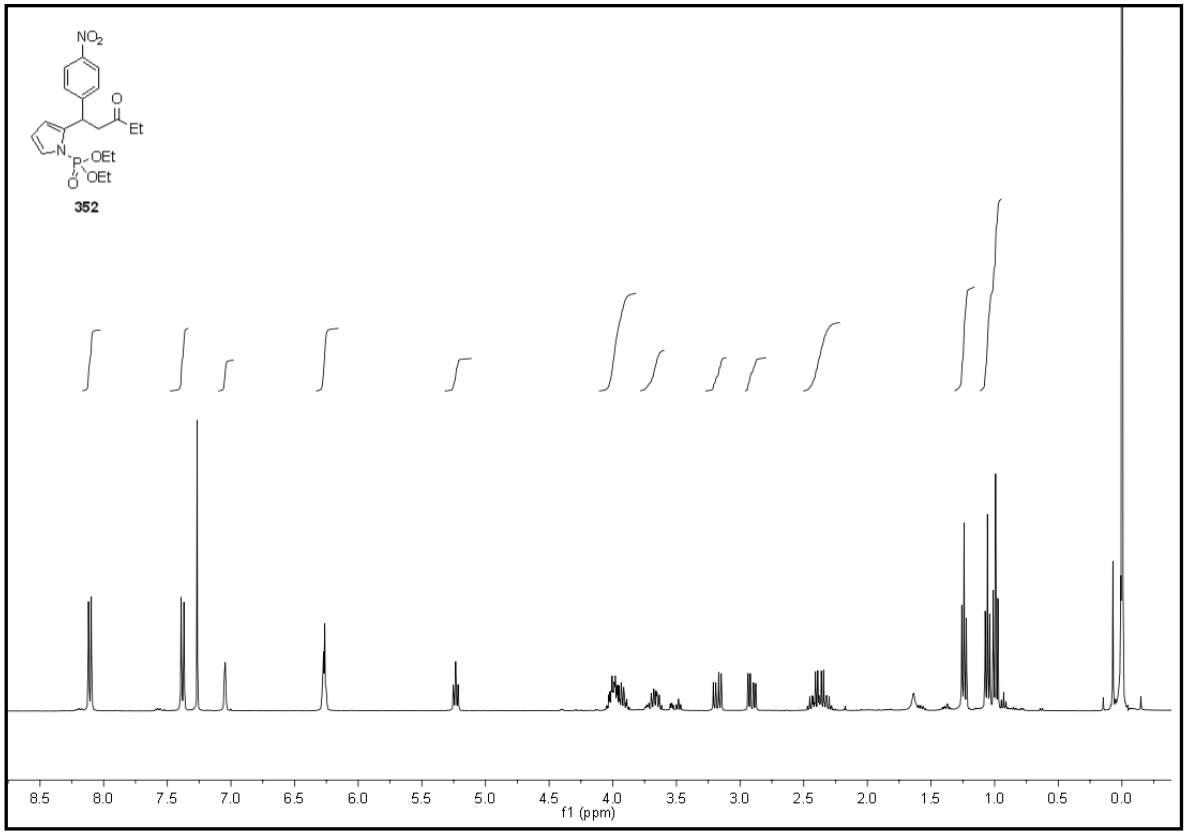


Figure A.340. ^{1}H NMR spectrum of compound **352**

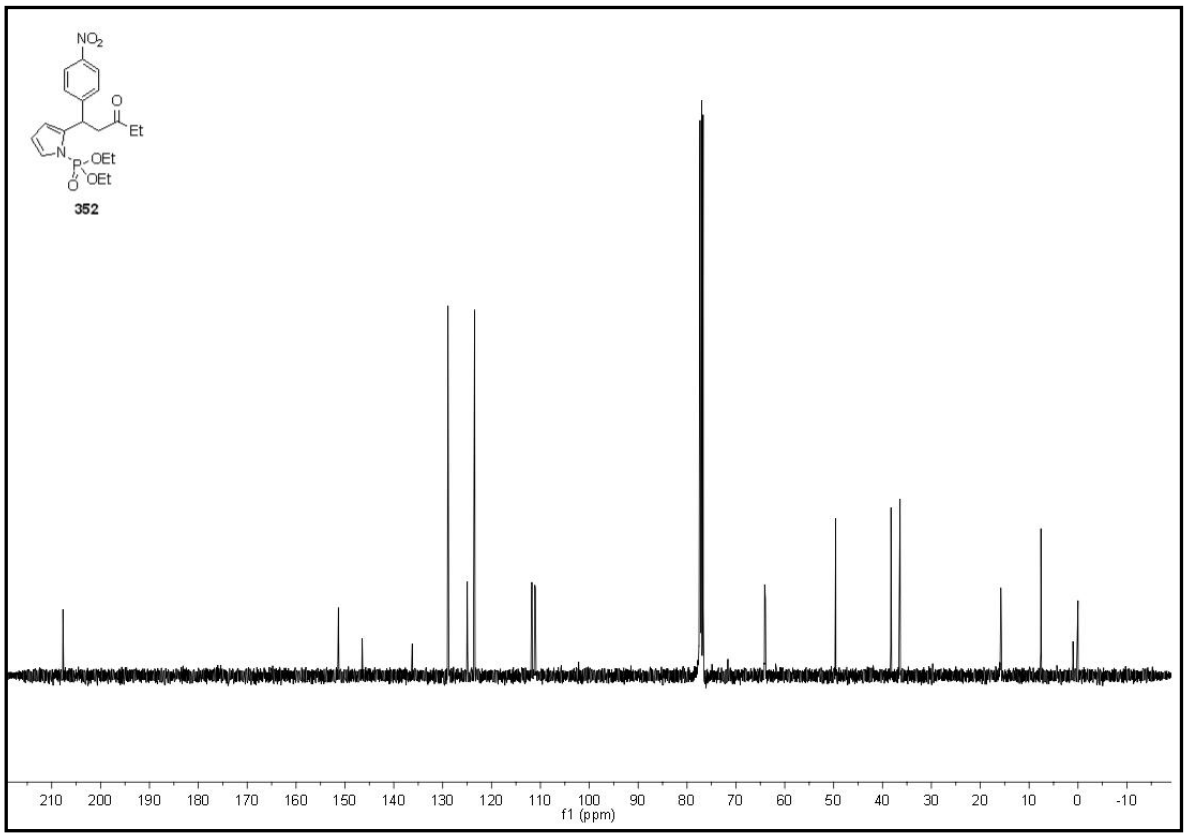


Figure A.341. ^{13}C NMR spectrum of compound **352**

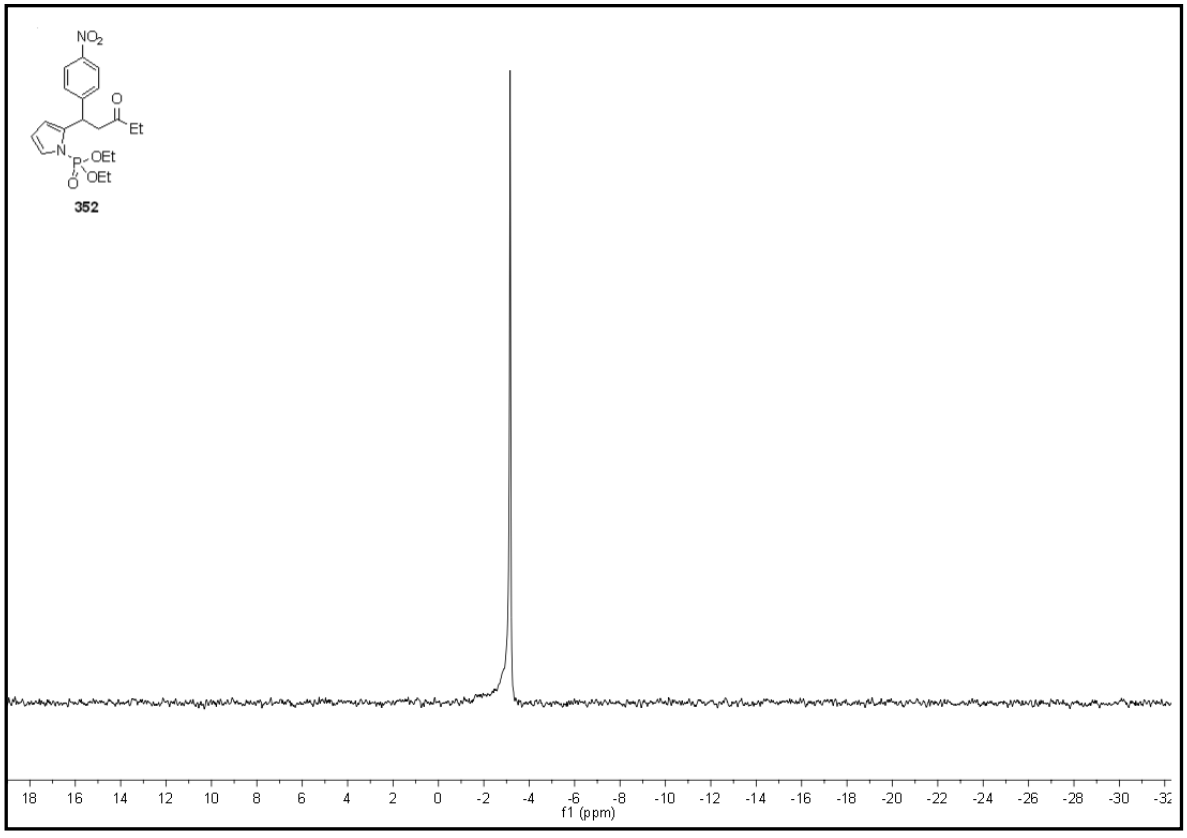


Figure A.342. ^{31}P NMR spectrum of compound **352**

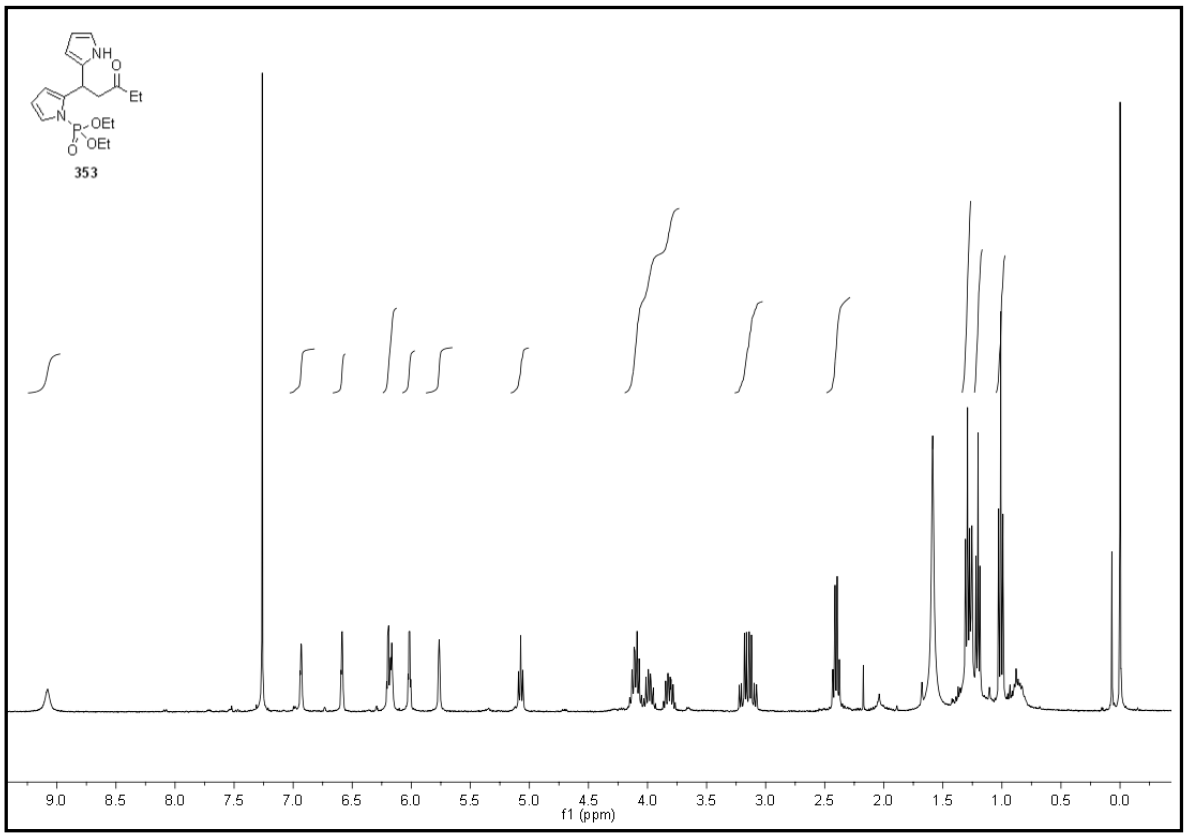


Figure A.343. ^{1}H NMR spectrum of compound **353**

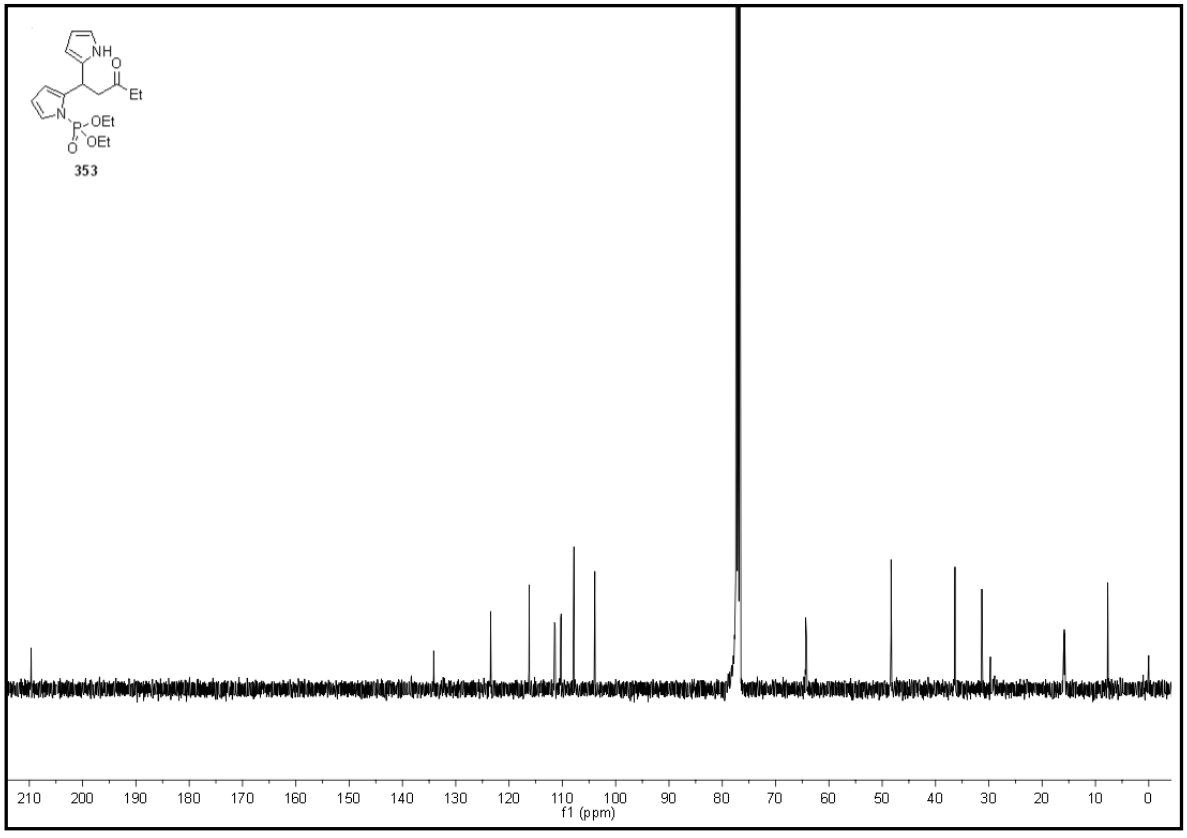


Figure A.344. ^{13}C NMR spectrum of compound **353**

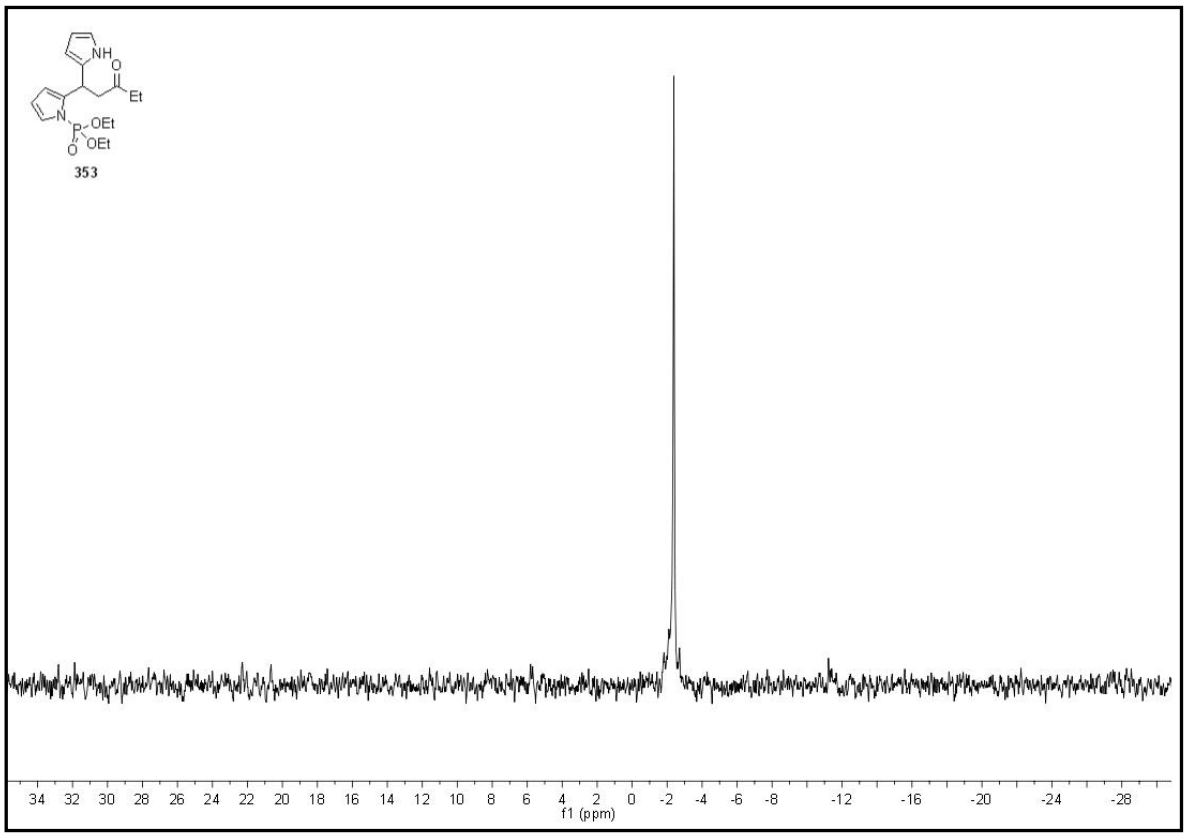


Figure A.345. ^{31}P NMR spectrum of compound **353**

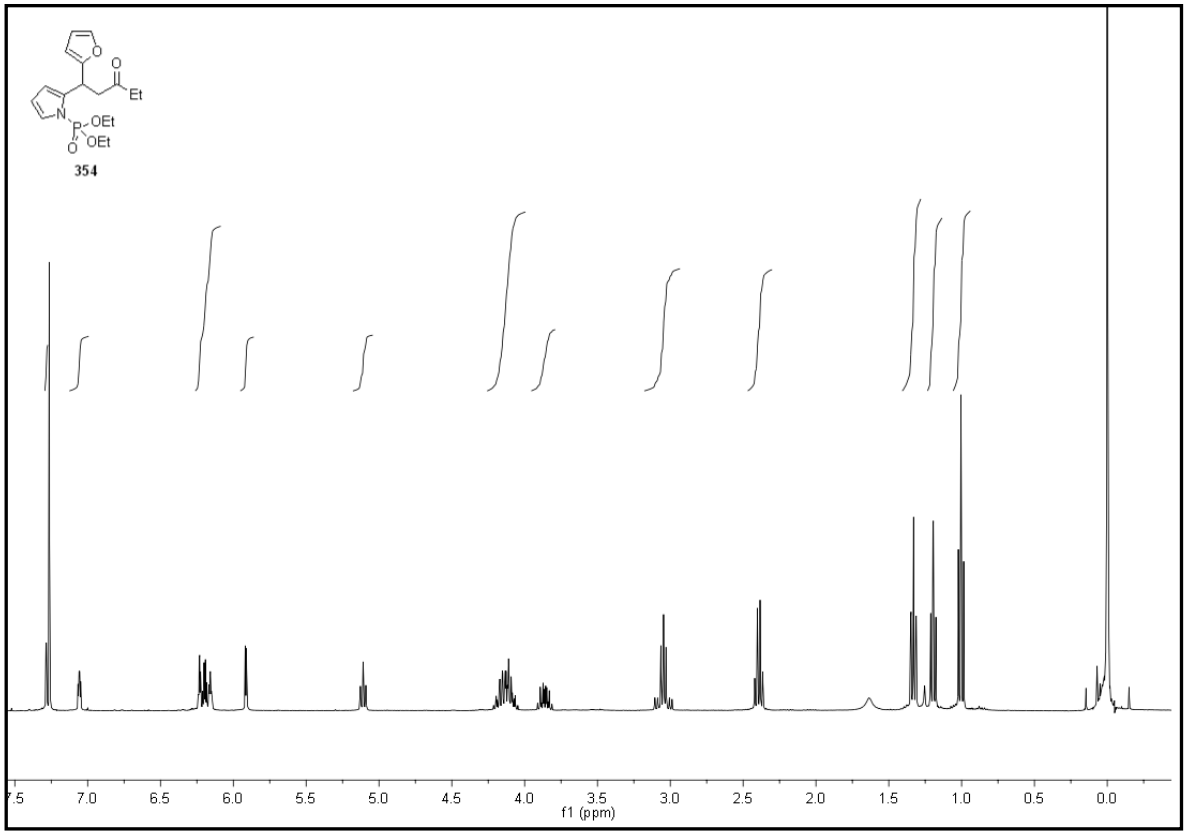


Figure A.346. ^{1}H NMR spectrum of compound **354**

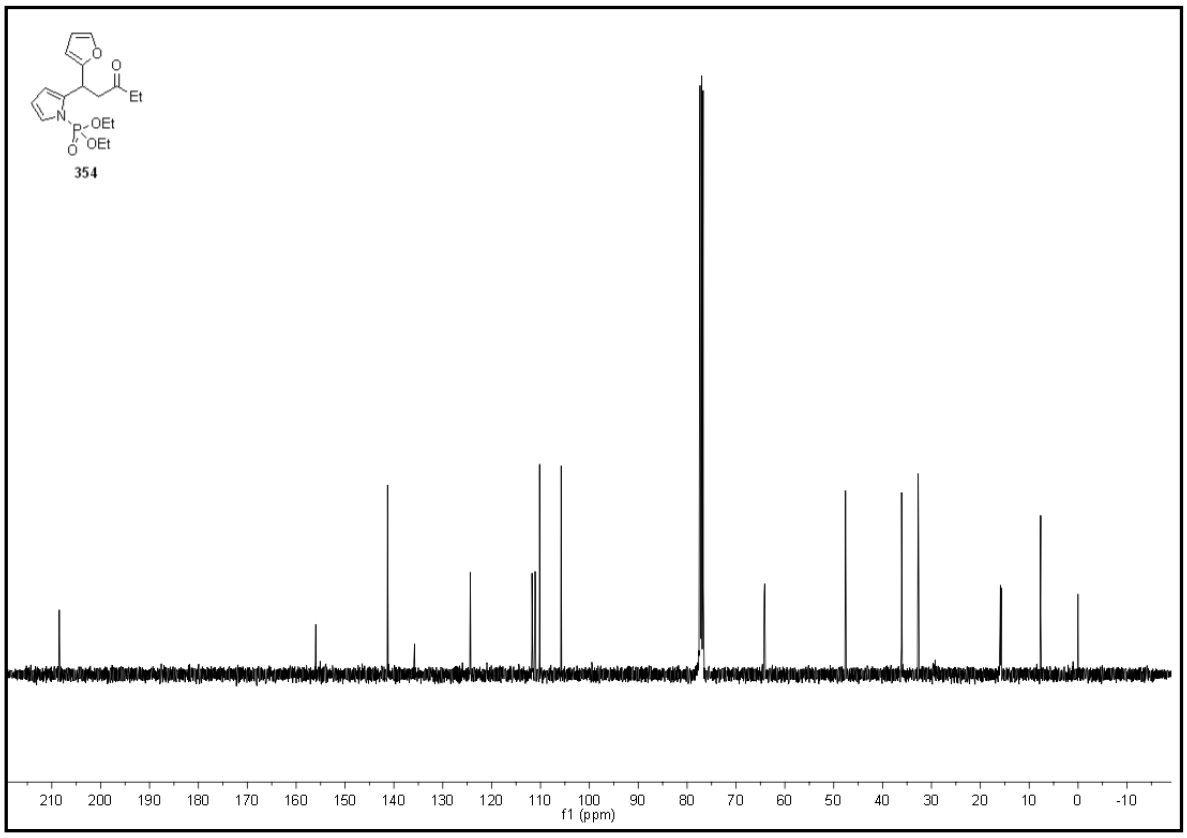


Figure A.347. ^{13}C NMR spectrum of compound **354**

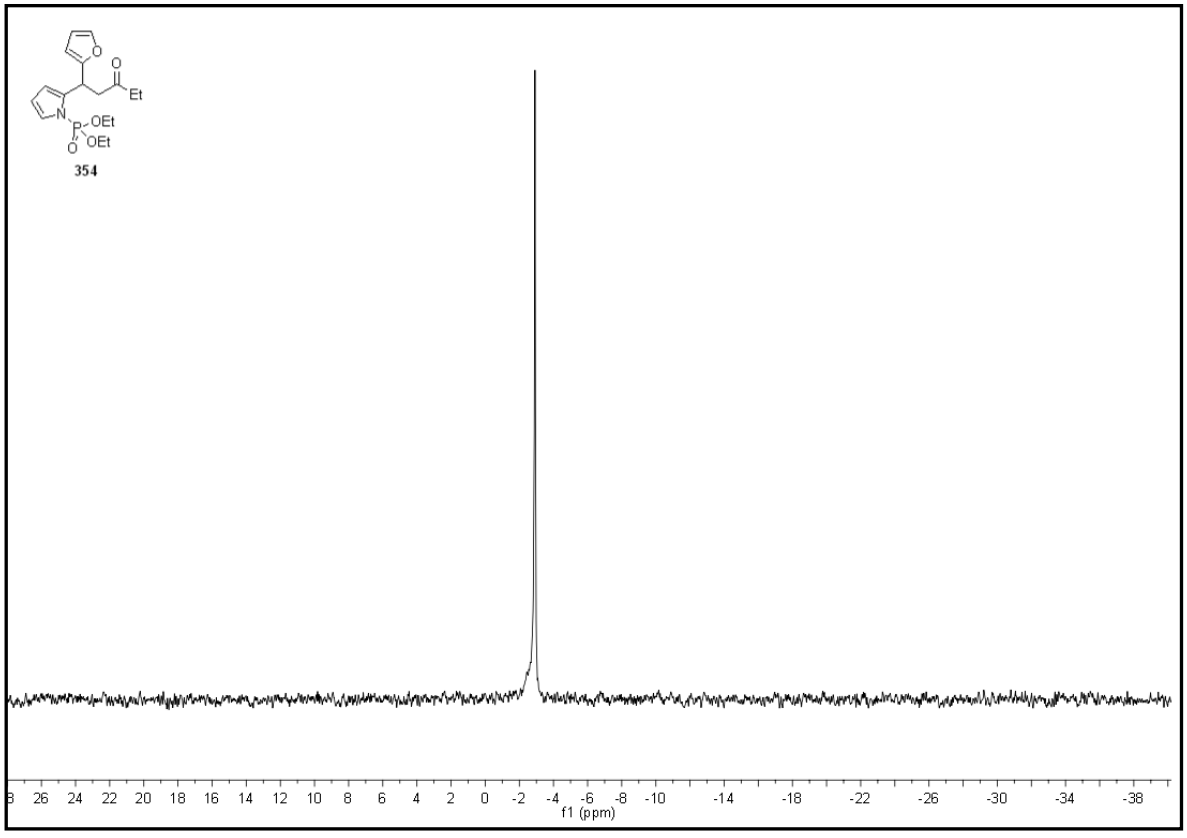


Figure A.348. ^{31}P NMR spectrum of compound **354**

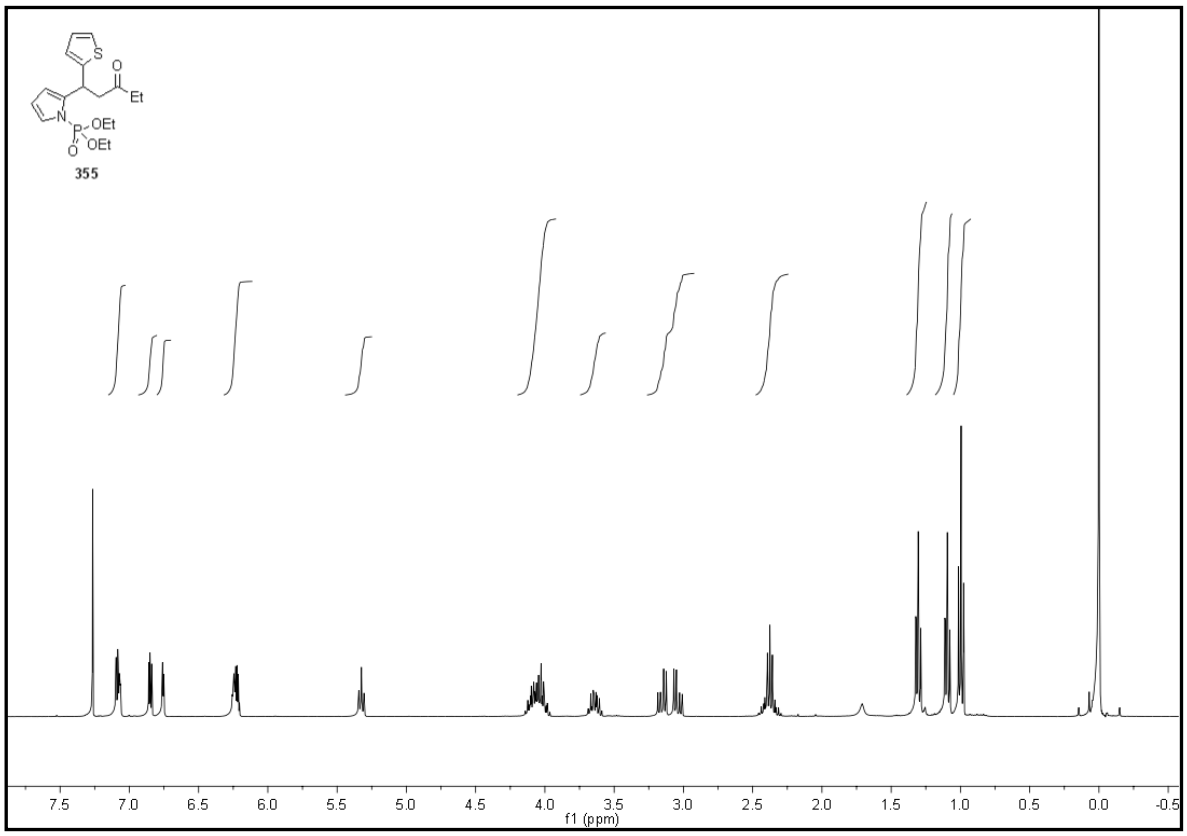


Figure A.349. ^{1}H NMR spectrum of compound **355**

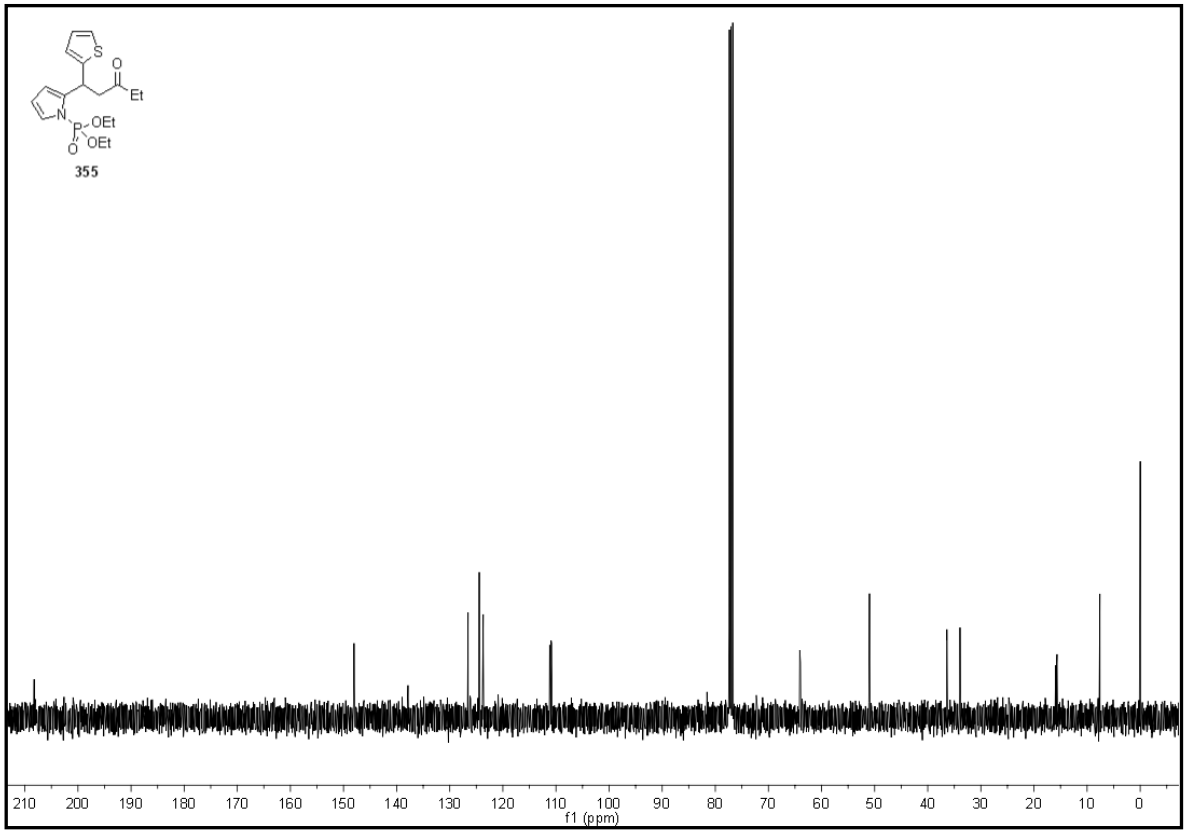


Figure A.350. ^{13}C NMR spectrum of compound **355**

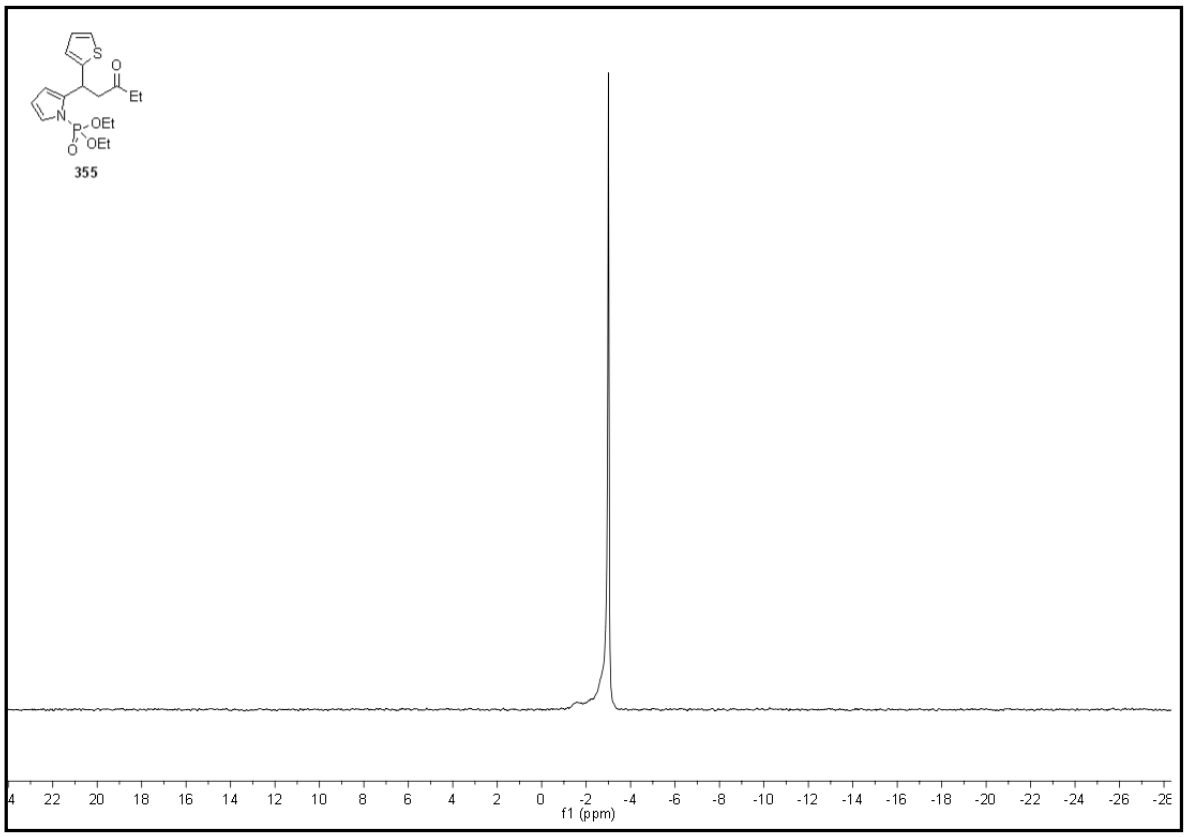


Figure A.351. ^{31}P NMR spectrum of compound **355**

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