The Synthesis and use of Trifluoroethyl Vinyl Phosphates as Electrophiles in the Suzuki Coupling Reaction

by

Agozie N. Oyeamalu

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Agozie N. Oyeamalu — 5/3/02

Agozie N. Oyeamalu — Date

Approvals:

5-3-02

Dr. John A. Jackson — Date
Thesis Advisor

05/01/02

Dr. Sherri Lovelace-Cameron — Date
Committee Member

May 1 '02

Dr. Jeff A. Smiley — Date
Committee Member

5/6/02

Dr. Peter J. Kasvinsky — Date
Dean of Graduate Studies

Abstract

The focus of the research presented here is the synthesis and use of trifluoroethyl vinyl phosphates as electrophiles in the Suzuki coupling reaction. The first step involves the synthesis of vinyl phosphates with the bis(2,2,2-trifluoroethoxy)phosphinyl group. The cross-coupling reaction of vinyl phosphates with arylboronic acids, using catalytic amounts of Ni(0) and K_3PO_4, in anhydrous toluene provides new methods for the synthesis of aryl-substituted olefins.

Acknowledgements

I would gladly like to thank Dr. John Jackson for not only being my research adviser, but also for his support during this research project and writing of this thesis. I would like to thank and acknowledge my committee members Dr. Lovelace and Dr. Smiley for their time and contributions in this thesis review. My thanks also go out to my parents Mr. and Mrs. Rufus Oyeamalu and my sister Chioma for their love and support throughout my educational pursuits. I would also like to thank the Onyebeke family for their support. Last but not least, I would like to thank Youngstown State University for giving me the opportunity to pursue my Masters degree.

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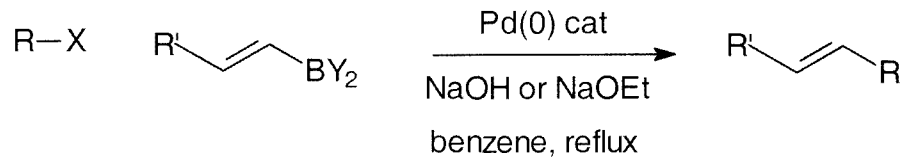
List of Abbreviations

Abbreviation	Description
bipy	bipyridine
d	doublet
DMA	*N,N*-Dimethylacetamide
DME	dimethoxyethane
dppb	1,4'-Bis(diphenylphosphino)butane
dppe	1,2'-Bis(diphenylphosphino)ethane
dppf	1,1'-Bis(diphenylphosphino)ferrocene
dppp	1,5'-Bis(diphenylphosphino)pentane
dq	doublet of quartets
g	gram
J	coupling constant (in Hz)
LDA	lithium diisopropylamide
m	multiplet
mmol	millimole
n-Bu	*n*-butyl
$NiCl_2$(dppf)	1,1'-Bis(diphenylphosphino)-ferrocene]dichloronickel(II)
NMR	nuclear magnetic resonance
ppm	parts per million
s	singlet
Sia_2BH	disiamylborane
THF	tetrahydrofuran

TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine

Chapter 1: Introduction

The nickel or palladium-catalyzed cross-coupling of organoboron reagents with aryl halides, vinyl halides, and triflates or related electrophiles, which is known as the Suzuki coupling, has found many uses in organic synthesis.[1] A general scheme of the Suzuki coupling is shown in Scheme 1.

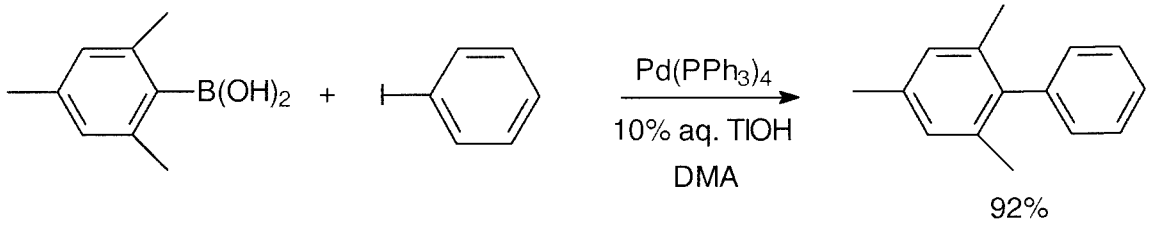


R = vinyl, aryl
X = I, Br, OTf
Y = OH, OR

Scheme 1

By using a palladium(0) catalyst with a base such as sodium hydroxide, the Suzuki reaction can accomplish a cross-coupling of a 1-alkenyl boron compound with an organic electrophile to produce the coupling product.

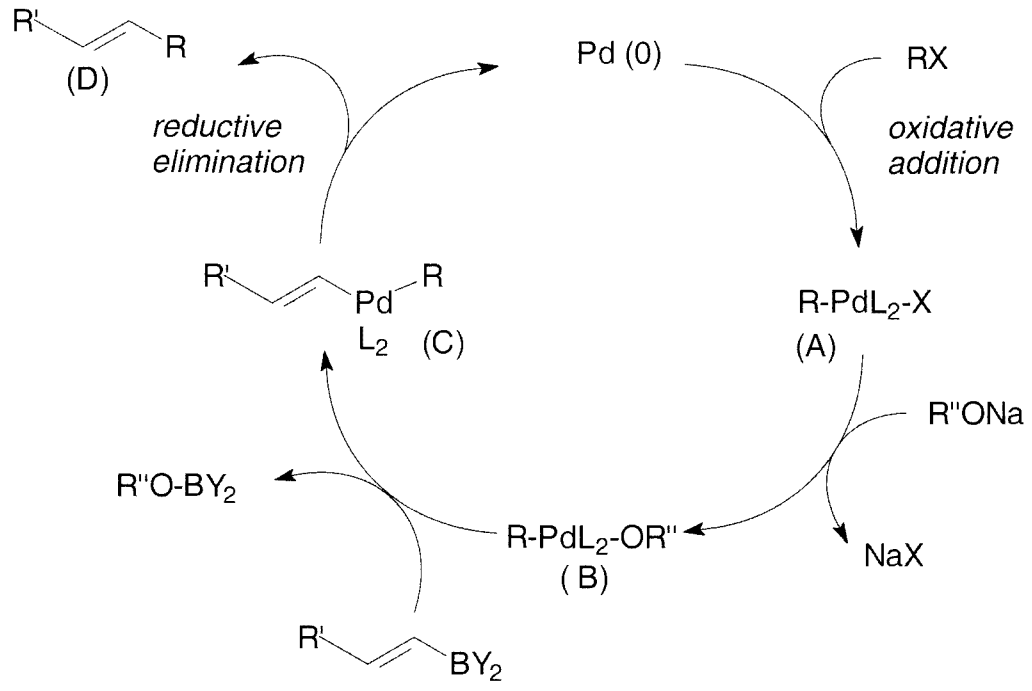
A specific example of the Suzuki reaction is shown in Scheme 2. In this reaction, mesityl boronic acid is coupled with an aromatic halide with aqueous thallium hydroxide to produce a sterically hindered unsymmetrical biphenyl derivative.[2]



Scheme 2

The most effective halides that are used in the Suzuki reaction are bromides and iodides.

Suzuki couplings are subjected to mild reaction conditions and they are not water sensitive.[2] Suzuki reaction byproducts are relatively nontoxic and easy to remove from the reaction mixture.[3] Suzuki couplings are compatible with a wide array of functional groups present such as alcohols, ethers, aldehydes, ketones and esters, which makes them suitable for use at both laboratory and industrial scales.[3] Scheme 3 shows the entire catalytic cycle for the cross-coupling reaction, which includes the oxidative addition and reductive elimination reactions.[1]

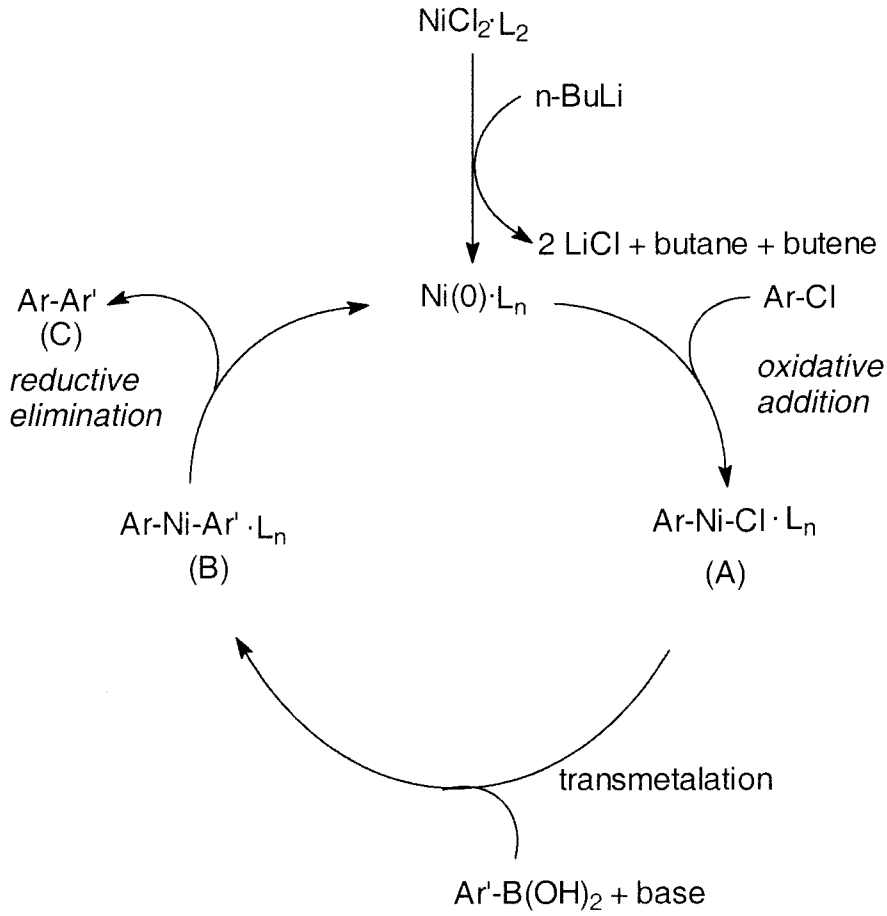


Scheme 3

The most common catalyst used in the Suzuki coupling reaction is tetrakis (triphenylphosphine) palladium(0). Oxidative addition, often characterized as the rate determining step in any organometallic catalytic cycle, involves the addition of the aryl halide to the Pd(0) catalyst, forming organopalladium[1] species **A**. It is believed that a hydroxide or an alkoxide base is necessary to displace the halide from the complex **A**, which forms a stable alkoxopalladium(II) complex **B**. The palladium complex **B** reacts

with the alkenylborane to produce the diorganopalladium complex **C**. After this has been achieved, the final step would be the reductive elimination of **C** in order to produce the final product **D** and regenerate the palladium(0) catalyst.

Nickel complexes have been used as catalysts in the Suzuki coupling reaction.[4] Ni(II) complexes have been found to be highly favorable as compared to Ni(0) complexes due to their greater stability.

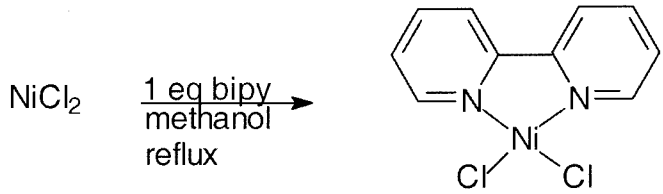


Scheme 4

The catalytic cycle begins with a nickel(0) catalyst.[4] In this particular cycle, a dichloronickel(II) species with an additional ligand is reduced to a Ni(0) species with *n*-butyllithium. After the addition of the arylhalide to the nickel(0) catalyst, an organonickel

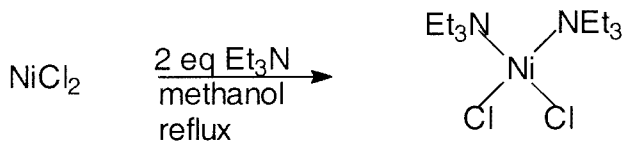
chloride species **A** is formed. An aryl boronic acid is then added to species **A** to get a diarylnickel(0) complex **B**. The final step would be the reductive elimination to produce the coupling product **C**, and regenerate the nickel (0) catalyst (Scheme 4).[4]

Phosphine-free nickel complexes in the Suzuki cross-coupling reaction have been examined.[5] Examples of phosphine-free nickel complexes include the use of 2,2'-bipyridine (bipy) and triethylamine as ligands on the Ni(II) species. After $NiCl_2$ reacts with one equivalent of 2,2'-bipyridine (bipy) in methanol under reflux, the nickel(II) complex of $NiCl_2$(bipy) is produced (Scheme 5).[6]



Scheme 5

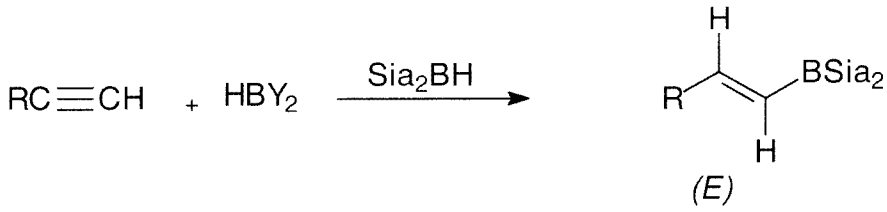
Nickel chloride reacts with 2 equivalents of triethylamine in methanol under reflux after a few minutes to generate the catalyst $NiCl_2(Et_3N)_2$.[7] Triethylamine acts as a monodentate ligand.



Scheme 6

Results show that solely changing the catalyst to a phosphine-free catalyst does not increase the yield of the Suzuki coupling product. Using phosphine-free catalyst to attain great yields of products is a function of the base, catalyst concentration, solvent and reaction time.

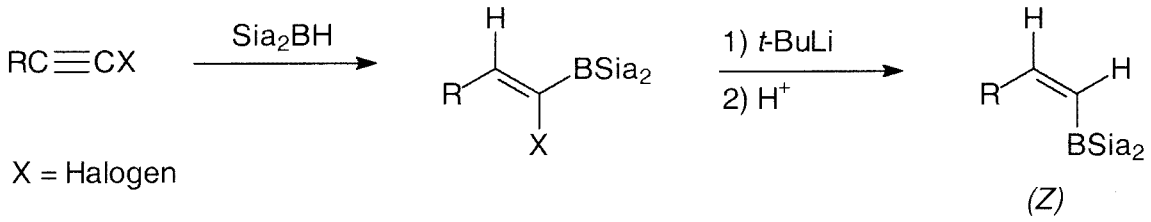
Another useful feature of the palladium or nickel-catalyzed Suzuki coupling is the construction of conjugated dienes and trienes from vinylboranes. Examples of the formation of the *E* and *Z* vinylboranes using disiamylborane (Sia_2BH) are depicted in schemes 7 and 8.



Scheme 7

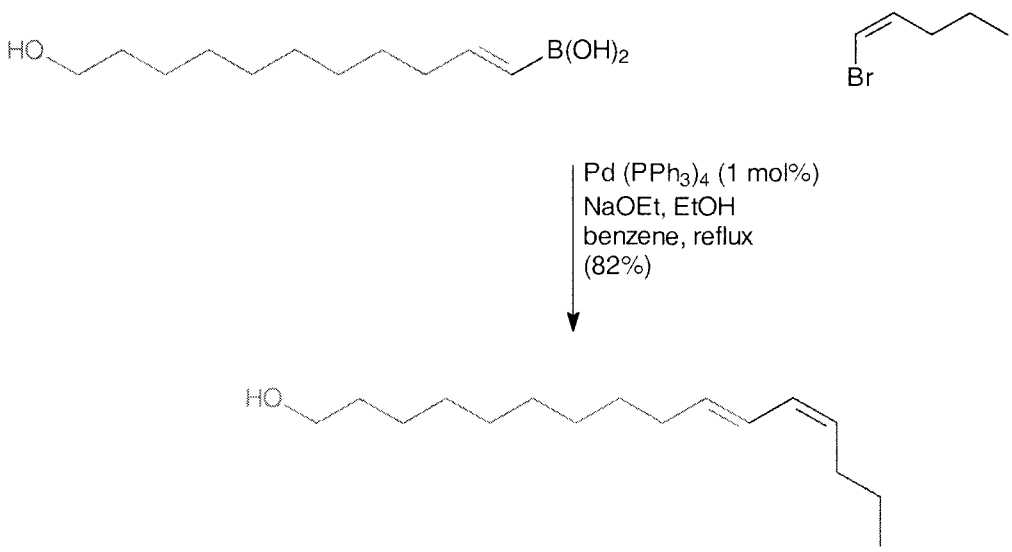
E-Vinylboranes may be prepared by hydroboration of the terminal alkynes with disiamylborane or other reagents such as 9-borabicyclo[3.3.1]nonane (Scheme 7).

Treatment of terminal haloalkynes with disiamylborane affords the (*E*)-vinylborane, which undergoes halogen-metal exchange with *t*-BuLi, and rearrangement followed by protonation to produce the (*Z*)-vinylborane (Scheme 8).[1]



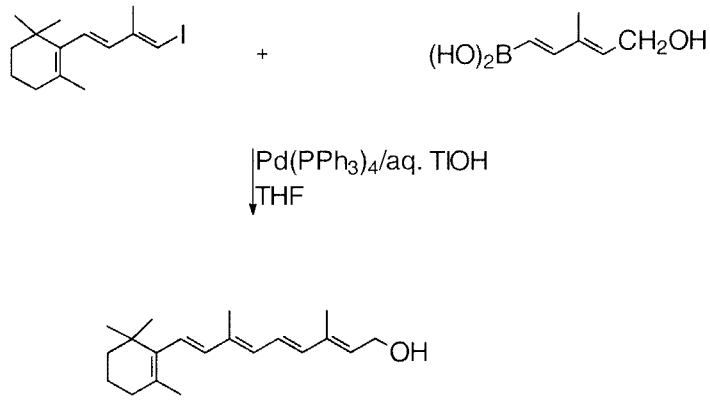
Scheme 8

The synthesis of the insect pheromone bombykol illustrates the application of the Suzuki coupling reaction to produce conjugated dienes. In the synthesis of bombykol, an (*E*)-vinylboronic acid is coupled with a (*Z*)-1-bromo-1-alkene to generate the coupling product in high yield.[10,13]



Scheme 9

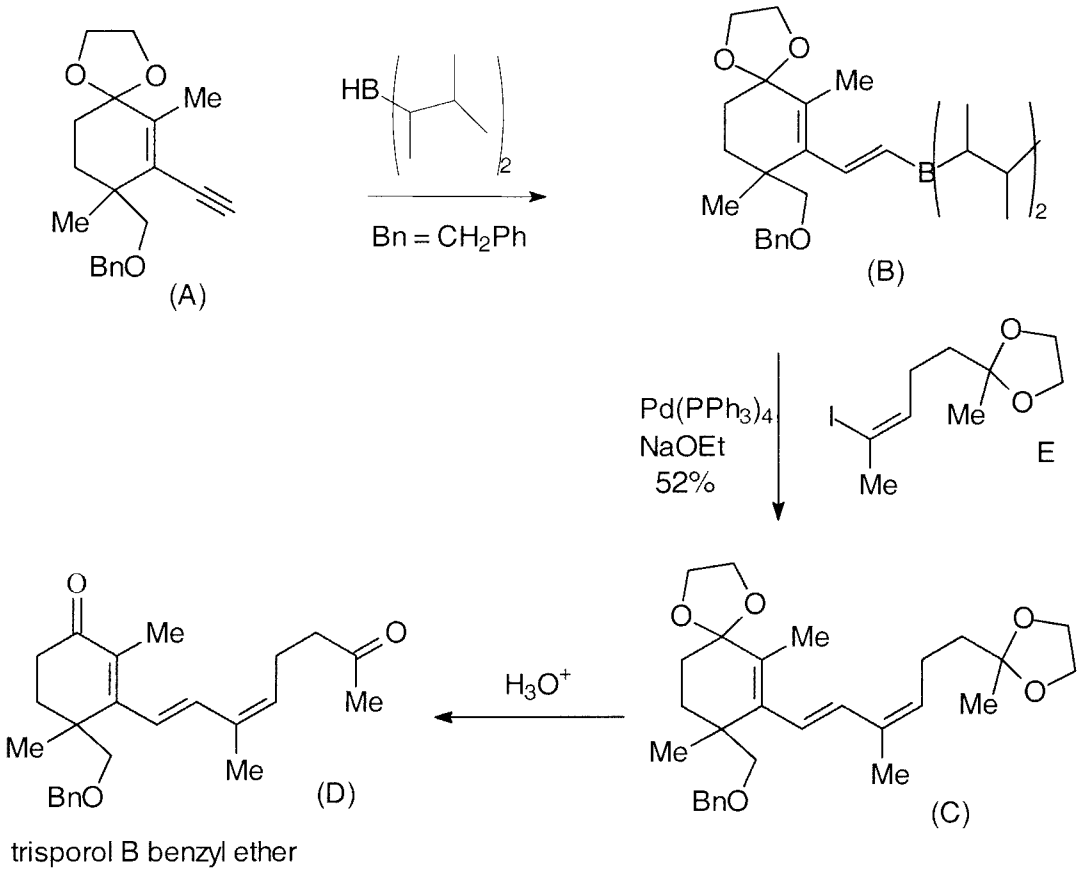
Vitamin A is another compound which has been synthesized via the Suzuki coupling reaction.[2] Complete stereochemical control was achieved in the coupling of the (*E*)-vinyliodide and the (*E*)-vinylboronic acid catalyzed by $Pd(PPh_3)_4$ in the presence of thallium hydroxide (Scheme 10).[2]



Scheme 10

Another example which demonstrates the stereospecificity of the Suzuki coupling is shown in the synthesis of trisporol B benzyl ether (Scheme 11). Hydroboration of conjugated ene-yne **A** with Sia_2BH results in formation of the (*E*)-vinyl borane derivative **B**. The (*E*)-vinylborane was stereospecifically coupled with the vinyl iodide **E** to produce

a conjugated triene **C**. Acid-induced hydrolysis is then applied to the dioxolane ketal to generate the trisporol B benzyl ether **D**. [10,13]

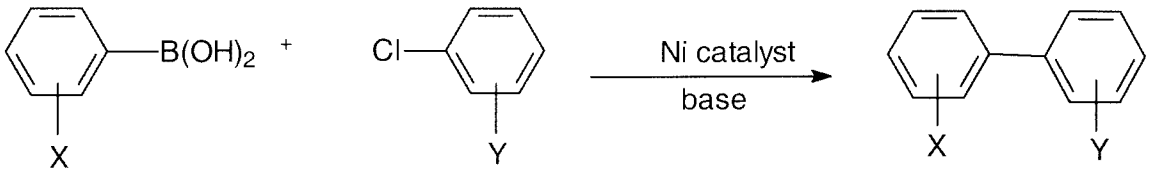


Scheme 11

Scope and Limitations of the Suzuki Coupling.

Various arylboronic acids can be used in the cross-coupling reaction. Recent studies have shown that chloroarenes are suitable substrates for the Suzuki coupling, when $NiCl_2(dppf)$ is utilized as the catalyst.[8,14] $NiCl_2(dppf)$ plus an additional ligand gives a better yield of biaryls, but when $Ni(PPh_3)_4$ was employed, it is not active enough to complete the coupling reaction. The catalytic activities depend on the ligand, 1,1'-bis(diphenylphosphino)ferrocene (dppf) > 1,5'-bis(diphenylphosphino)pentane (dppp) >

1,2'-bis(diphenylphosphino)ethane (dppe) > 1,4'-bis(diphenylphosphino) butane (dppb).[4] In order to generate the Ni(0) complex, dppf as a ligand has to react with $NiCl_2$ to form $NiCl_2$(dppf) followed by reduction to finally produce the Ni(0) complex.[4] Base, solvent, reducing agent, time, and reaction temperature dictates if trace amounts of products or high yields are obtained in the Suzuki coupling.[11,12]



X= CH_3

Y= OCH_3

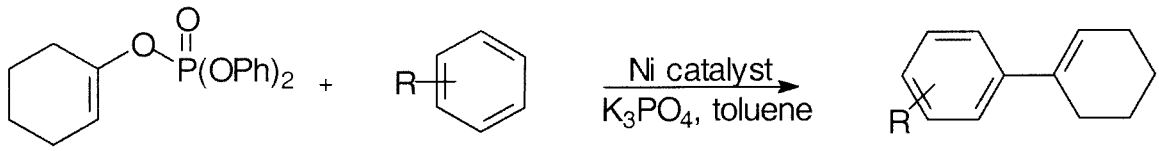
Scheme 12

Steric hindrance plays a vital role in both the nickel and palladium-catalyzed cross-coupling. For the coupling of chloroarenes with arylboronic acids, nickel-catalyzed cross-coupling reactions are more sensitive to steric hindrance than are palladium-catalyzed couplings.[4]

Palladium-catalyzed Suzuki cross-coupling has been employed in the synthesis of biaryls. Aryl chlorides are not readily reactive with the palladium catalysts, unless they are used with an electron-withdrawing group. Palladium-catalyzed cross-coupling reactions of bromides, iodides or triflates are usually carried out with aqueous base such as potassium phosphate or sodium carbonate.[4] However, since the transmetalation step of the catalytic cycle is sometimes water sensitive, the use of aqueous bases with the catalyst species should be avoided.

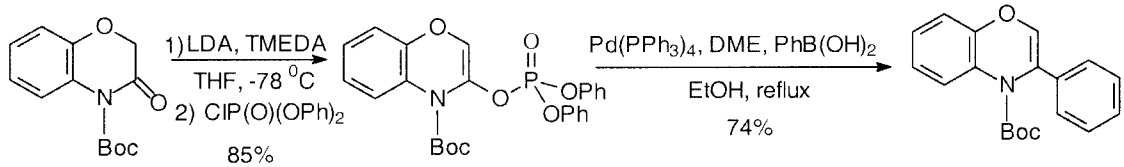
The use of diphenyl vinyl phosphates as electrophiles in the Suzuki reaction.

The most recent modification in the Suzuki reaction has been the use of diphenyl vinyl phosphates, which act as good electrophiles for the Suzuki coupling reaction. However, when palladium catalysts were employed, little or no coupling was observed. The second modification was to use a nickel complex rather then a palladium complex.[8,14] Diphenyl vinyl phosphates, which act as stable and available substrates, undergo nickel(0)-catalyzed coupling with arylboronic acids (Scheme 13).



Scheme 13

Another application of the use of diphenyl vinyl phosphates as electrophiles in the Suzuki reaction is the synthesis of nitrogen-containing heterocycles.[9] Scheme 14 shows an example of the synthesis of a nitrogen-containing heterocycle.

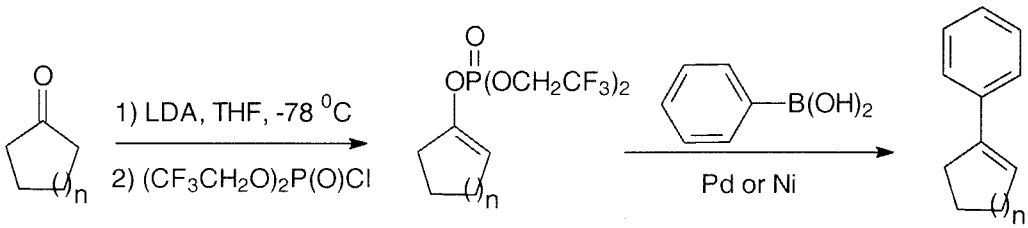


Scheme 14

The-*N*-Boc lactam reacts with a solution of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) and tetramethylethylenediamine (TMEDA) at –78 ^{0}C to form an enolate, which after the addition of the diphenyl chlorophosphate, is trapped as a vinylphosphate.[9] After the addition of the tetrakis(triphenylphosphine)palladium(0) in DME, and arylboronic acid in ethanol under reflux, the Suzuki coupling product was obtained.[9]

Chapter 2: Results and Discussion

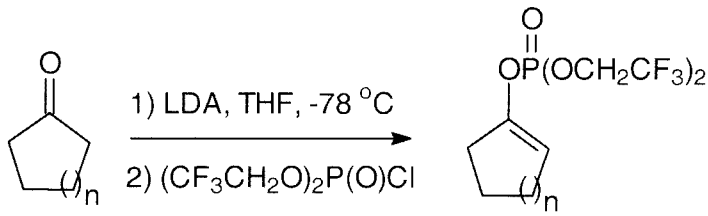
The main focus of this research was the synthesis and use of trifluoroethyl vinyl phosphates as electrophiles in the Suzuki coupling reaction (Scheme 15). Prior to the Suzuki coupling reaction, the vinyl phosphates derived from commercially available ketones with the bis(2,2,2-trifluoroethoxy) phosphinyl group had to be synthesized.[15]



n = 1, 2, 3, ...

Scheme 15

The first step in the general procedure for the synthesis of the vinyl phosphates was the formation of an enolate by the reaction of lithium diisopropylamide (LDA) and a ketone in tetrahydrofuran (THF) at –78 °C. After thirty minutes, the lithium enolate was trapped with bis(2,2,2-trifluoroethyl) phosphorochloridate to generate the corresponding vinyl phosphates during a 24 hour reaction period [15] (Scheme 16).



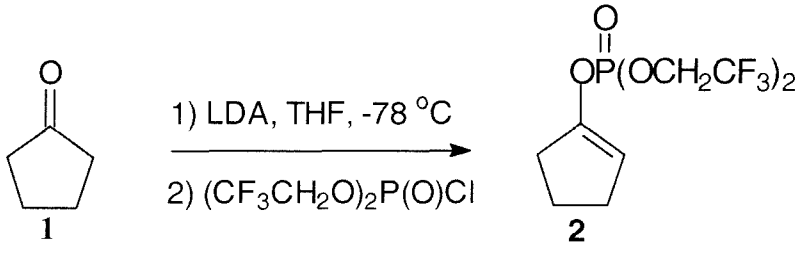
n = 1, 2, 3, ...

Scheme 16

The first compound synthesized with the electrophile, bis(2,2,2-trifluoroethyl) phosphorochloridate was vinyl phosphate **2**. After standard aqueous workup and purification by flash column chromatography, a 65% yield of compound **2** was isolated.

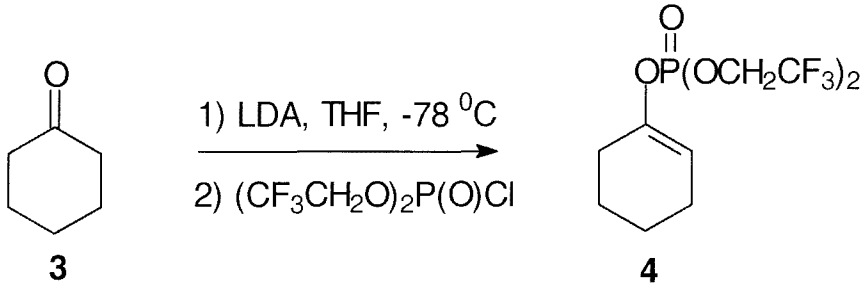
Analysis by ^{31}P NMR of compound **2**, (Fig 4) showed only one peak at – 6.82 ppm indicating a pure compound. ^{13}C NMR of vinyl phosphate **2**, (Fig 3) showed a doublet of quartets for the CF_3 carbon group at 122.01 ppm, and another doublet of quartets for the CH_2 group was noted at 64.18 ppm. This was due to the coupling with fluorine and phosphorus. The C-F and C-P coupling constants for the CH_2 carbon were also noted at 38.1 and 4.6 Hz. The C-F and C-P coupling constants for the CF_3 carbon atom were 276.9 and 9.9 Hz, respectively. The vinylic carbons were observed as doublets at 148.91 ppm and 111.34 ppm, while their corresponding coupling constants were noted at 9.1 and 5.3 Hz. In the methylene signals of the five membered ring, the homoallylic carbon signal was observed as a singlet at 20.94 ppm while the allylic methylene carbons were observed as a doublet at 31.2 ppm and as a singlet at 28.33 ppm.

In the ^{1}H NMR of compound **2**, (Fig 2) the vinylic proton was observed as a multiplet at 5.35-5.31 ppm, while the methylene group of the phosphorus ester appeared as a multiplet at 4.47-4.38 ppm. The four allylic protons appeared as multiplets at 2.51-2.32 ppm, while the homoallylic protons also appeared as a multiplet at 2.01-1.92 ppm.



Scheme 17

Vinyl phosphates **4, 6,** and **8** where synthesized in the same manner as compound **2** using the ketones cyclohexanone, cycloheptanone, and α-tetralone. Results of these reactions are summarized in Table 1. Analysis by ^{13}C NMR of vinyl phosphate **4**, (Fig 7) shows doublets for the vinylic carbons at 147.20 ppm adjacent to the phosphate group and 112.40 ppm for the unsubstituted one with coupling constants of 9.9 and 5.3 Hz respectively. For the CF_3 carbon of vinyl phosphate **4**, a doublet of quartets was noted at 122.10 ppm with coupling constants of 276.9 and 9.9 Hz. The other doublet of quartet for the CH_2 group was noted at 64.09 ppm with the corresponding coupling constants of 38.1 and 4.6 Hz. The four allylic and homoallylic carbons were observed at 27.42-21.41 ppm. In the ^1H NMR of compound **4**, (Fig 6) the CH_2 of the trifluoroethyl group was observed as a multiplet with a chemical shift of 4.44-4.36 ppm. The vinylic proton was observed at 5.55-5.52 ppm as a multiplet. The allylic and homoallylic protons were observed at 2.21-1.52 ppm. ^{31}P NMR of compound **4**, showed one peak at –6.64 ppm. (Scheme 18).

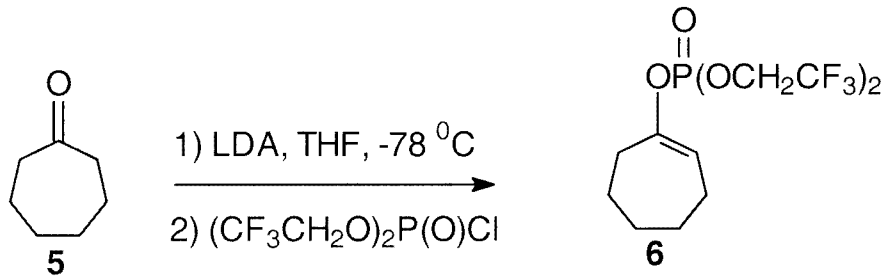


3 **4**

Scheme 18

After aqueous workup, and purification by flash column chromatography, compound **6** was obtained in a 64% yield as a light yellow oil. In the ^1H NMR of compound **6**, the vinylic proton was observed as a multiplet at 5.70-5.66 ppm. The CH_2 signal of the trifluoroethyl group was observed as a multiplet at 4.44-4.36 ppm. The allylic and homoallylic protons appeared as multiplets at 2.42-1.56 ppm. ^{13}C NMR of

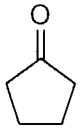
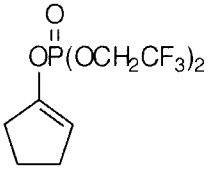
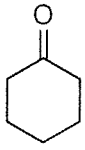
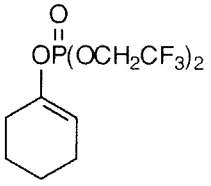
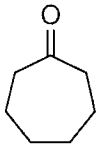
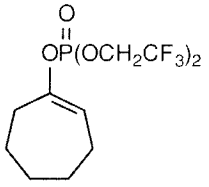
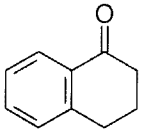
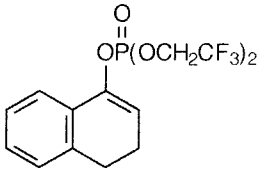
vinyl phosphate **6**, (Fig 11) showed doublet of quartets for the carbon atoms of the CF_3 group at 122.12 ppm. The C-F and C-P coupling constants for the CF_3 carbon atom were 276.7 and 9.9 Hz respectively, while the CH_2 group has a chemical shift of 64.07 ppm with coupling constants of 38.1 and 4.6 Hz. The vinylic carbons were observed as doublets at 151.41 ppm and 117.18 ppm with coupling constants of 9.9 and 5.3 Hz respectively. The allylic and homoallylic carbons were observed at 33-25 ppm. Three of them appeared as singlets while the other two carbons appeared as doublets with coupling constants of 3.1 and 1.5 Hz respectively. The ^{31}P NMR signal of compound **6**, (Fig 12) appeared as a singlet at –6.50 ppm.



Scheme 19

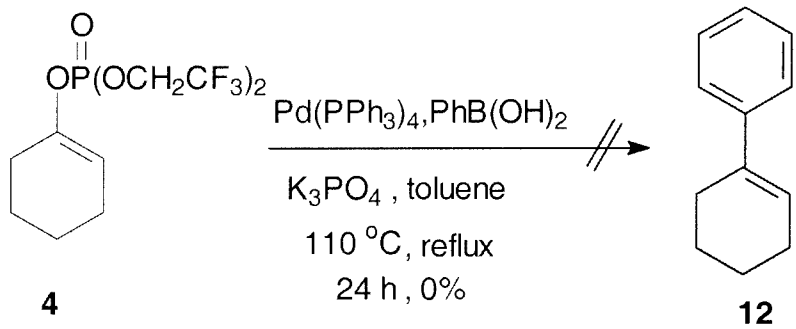
In the ^{13}C NMR for compound **8**, the CF_3 group was observed as a doublet of quartets with a chemical shift of 122.03 ppm and coupling constants of 276.9 and 9.9 Hz. The CH_2 group was also noted as a doublet of quartets at 64.34 ppm with coupling constants of 38.1 and 4.4 Hz. The vinylic carbons were observed as doublets at chemical shifts of 129.23 and 112.09 ppm with coupling constants of 6.2 and 3.8 ppm respectively. The benzylic and allylic carbons appeared as singlets at 27.24 and 22.04 ppm. ^{31}P NMR showed a single peak for compound **8** at –6.09 ppm, (Fig 16). In the ^{1}H NMR, the vinylic protons were observed as multiplets. The methylene groups of the phosphorus ester also appeared as multiplets, as were the signals for the allylic and benzylic ring protons.

Table 1. Yields of Vinyl Phosphates

Ketone	Vinyl Phosphate	Yield
 **1**	 **2**	65%
 **3**	 **4**	72%
 **5**	 **6**	64%
 **7**	 **8**	75%

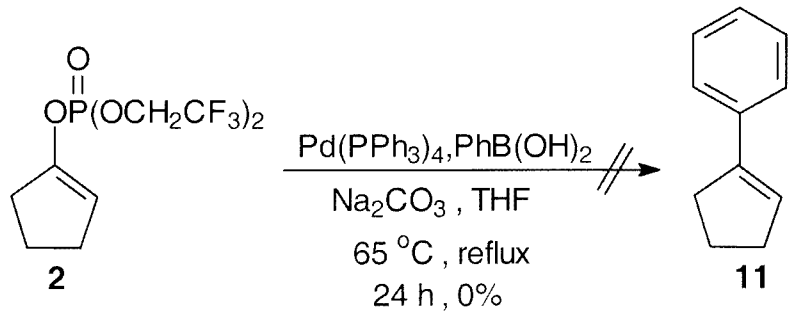
Having synthesized a number of vinyl phosphates, the next step in the project was to utilize them as the electrophile in the Suzuki coupling reaction. The initial plan was to first attempt the Suzuki couplings of these vinyl phosphates under standard conditions, utilizing a palladium catalyst. However, since we were aware of the fact that the Suzuki couplings of the diphenyl vinyl phosphates were unsuccessful with a palladium catalyst, we also had plans to utilize nickel catalysts in later studies.

The first set of reactions were attempted under standard Suzuki coupling conditions. In the attempted synthesis of compound **12** under reflux, the purified vinyl phosphate **4** was added to the palladium(0) catalyst. In the next step of the reaction, potassium phosphate and phenylboronic acid were added to the reaction mixture. The solvent used was anhydrous toluene. The final step in the reaction process was the reductive elimination. No traces of coupling product could be detected after a 24 h period (Scheme 20).



Scheme 20

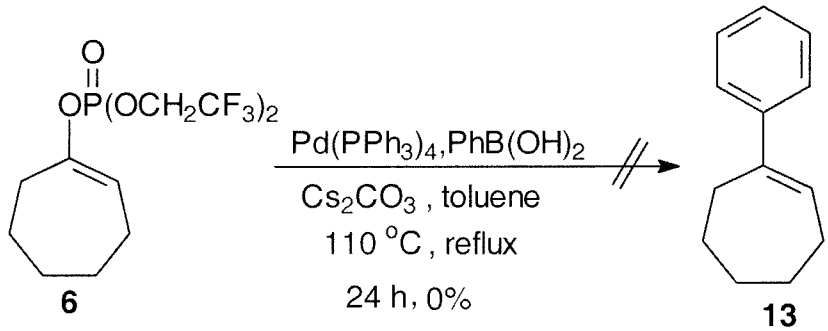
The next Suzuki coupling was attempted with phenylboronic acid, and aqueous sodium carbonate in THF in the presence of $Pd(PPh_3)_4$, the mixture was refluxed with vinyl phosphate **2** at 65 °C for 24 h. Coupling product **11** was not produced (Scheme 21).



2 11

Scheme 21

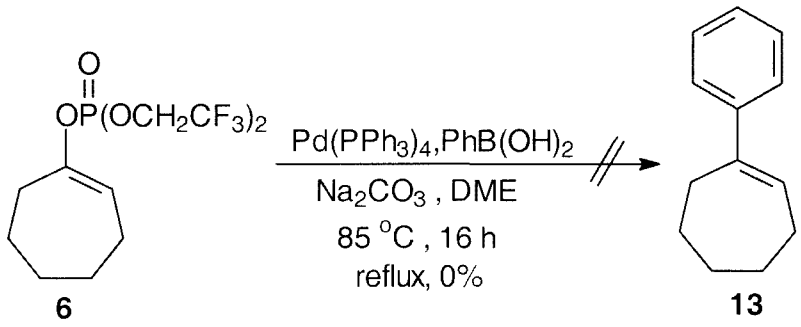
In the next attempted synthesis, cesium carbonate was used as the base. It was added to vinyl phosphate **6** in anhydrous toluene with heating at 110 °C for 24 h (Scheme 22). Again, no trace of coupling product was observed.



6 13

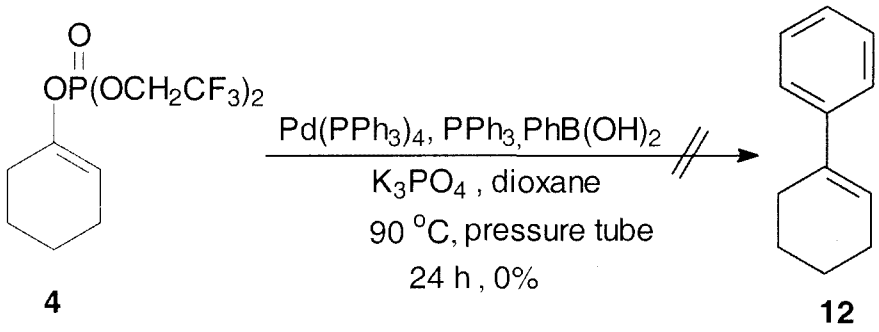
Scheme 22

Treatment of vinyl phosphate **6** with catalytic amounts of $Pd(PPh_3)_4$ followed by the addition of Na_2CO_3 in DME at 85 °C was carried out under standard Suzuki coupling reaction conditions in an attempt to produce compound **13**. After 16 h of reaction time, no traces of coupling product **13** could be detected (Scheme 23).



Scheme 23

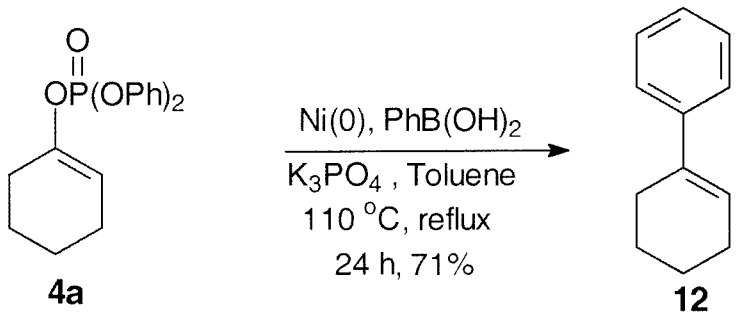
Since the use of the $Pd(PPh_3)_4$ catalyst with the vinyl phosphates were unsuccessful under reflux, the next variation was to conduct the coupling under a different solvent system. Dioxane was used as the solvent. To stabilize the catalyst, an additional ligand, triphenylphosphine was added. Also, rather than performing the coupling in a round bottom flask under reflux, the reaction was conducted in a pressure tube (Scheme 24). Results for the attempted preparative of coupling product **12** showed no trace of the product.



Scheme 24

Since the use of the $Pd(PPh_3)_4$ catalyst was unsuccessful, the next approach in the cross-coupling reaction was to utilize a nickel catalyst to see if a coupling product would form. Before conducting the Ni(0) catalyzed Suzuki coupling on a trifluoroethyl vinyl

phosphate, we decided to reproduce the literature procedure with a diphenyl vinyl phosphate **4a**, (Scheme 25).[8]

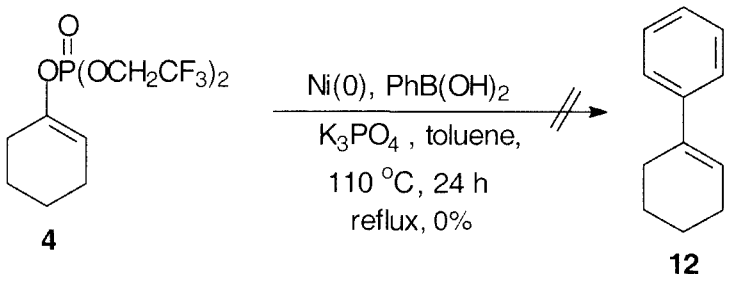


4a **12**

Scheme 25

After attempting the Suzuki coupling reaction utilizing the nickel catalyst from the literature, coupling product **12** was obtained. This meant that the diphenyl vinyl phosphate underwent the Ni(0) catalyzed cross-coupling reaction readily with phenylboronic acid to generate the aryl-substituted species. In order for the reaction to take place, the Ni(0) catalyst had to be prepared by reducing $NiCl_2$(dppf) in anhydrous toluene with *n*-butyllithium. The ligand used was 1,1'-Bis(diphenylphosphino)ferrocene dppf. The formation of the coupling product **12** was synthesized under reflux at 110 °C for 24 h. It was shown that during a 24 hour period, compound **12** was produced with a good yield of 71%.

The Ni(0)-catalyzed Suzuki coupling was then attempted utilizing the literature method with a trifluoroethyl vinyl phosphate. The first step we took was to synthesize compound **12** under the same conditions as the literature (Scheme 26). This included the addition of phenylboronic acid in anhydrous toluene with anhydrous potassium phosphate under reflux at 110 °C for 24 h in a three necked flask. No coupling product was formed.



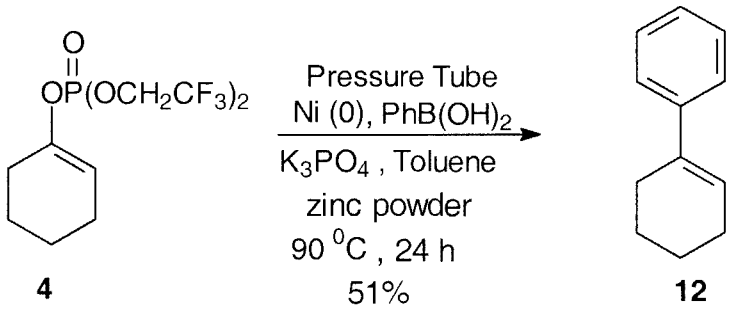
Scheme 26

This prompted us to make appropriate synthetic adjustments. The use of a pressure tube was used again as opposed to reflux with a three-necked flask. Catalytic amounts of zinc powder were also employed. It was noted that when catalytic amounts of zinc powder was present in the reaction mixture, the coupling was successful, but when zinc powder was absent, no coupling product was noticed.

The results of the nickel(0)-catalyzed cross-coupling reaction of phenylboronic acid with trifluoroethyl vinyl phosphate derivatives are summarized in Table 2. The reaction with vinyl phosphates having the trifluoroethyl group gave moderate yields for the aryl-substituted olefins. In general, the cross-coupling reaction took place when the reaction mixture was heated in an oil bath in a pressure tube at 90 °C for at least 24 h. It was important that the reaction mixture was degassed with argon for thirty minutes before the reaction took place and sealed tightly. For all the coupling reactions conducted, the Ni(0) catalyst which incorporated the dppf as its ligand was an effective catalyst in the cross-coupling process. Various solvents were investigated in the cross-coupling reaction. These solvents included THF, anhydrous toluene, anhydrous dioxane and DME. As a result of trying these different solvent systems, anhydrous toluene was the best choice. Potassium phosphate was the most effective base in the Suzuki coupling

reaction probably because it was more soluble than some of the other bases that were used such as sodium carbonate. After washing twice with 1.0 ml water and 1.0 ml brine, the organic layer appeared as a yellowish liquid. The mixture was then dried over sodium sulfate and filtered. After purification by flash chromatography, compound **12** was obtained in 51% yield (Scheme 27).

The formation of product **12** was confirmed by ^{1}H NMR and ^{13}C NMR. The vinylic proton of compound **12**, (Fig 20) appeared as a multiplet at 6.16-6.13 ppm. The four allylic protons appeared as multiplets at 2.45-2.41 ppm and 2.24-2.21 ppm, while the other four homoallylic protons appeared at 1.82-1.77 and 1.71-1.67 ppm as multiplets. The aromatic protons were observed in the region of 7.41-7.32 ppm.

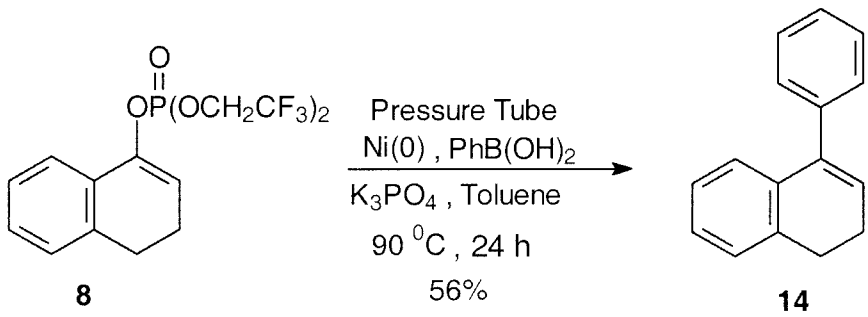


Scheme 27

In the ^{13}C NMR of compound **12**, (Fig 21) the vinylic carbons were observed with chemical shifts of 125.81 and 137.55 ppm as singlets while the allylic and homoallylic carbons showed signals at 28.65, 27.16, 24.35 and 22.46 ppm. The ipso carbon atom of the aromatic ring was observed at 143.66 ppm. The other aromatic carbons were observed in the region of 129.20-125.81 ppm.

In the synthesis of compound **14** from vinyl phosphate **8**, total consumption of the substrate was observed by TLC. The coupling reaction was run in an oil bath for a 24 h period at 90 ^{0}C. After purification by flash chromatography, compound **14** was obtained

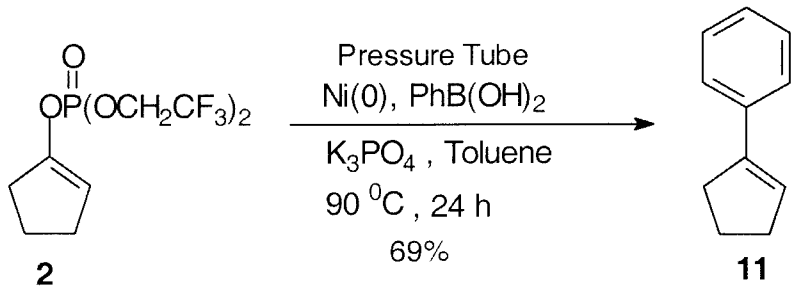
in 56% yield. Formation of compound **14** (Scheme 28) was confirmed by ^{1}H NMR, and ^{13}C NMR. In the ^{1}H NMR of compound **14**, (Fig 24) the aromatic protons were observed as multiplets at 7.43-7.02 ppm. The allylic and benzylic protons showed signals at 2.89-2.85 and 2.45-2.40 ppm. The vinylic proton was observed as a multiplet at 6.12-6.10 ppm. For the ^{13}C NMR of compound **14**, (Fig 25) the vinylic carbons were observed as singlets at 140.84 and 127.22 ppm, while the ipso carbon of the aromatic ring was observed at a chemical shift at 141.74 ppm. The allylic and benzylic carbons were also observed as singlets at 29.56 and 24.81 ppm. The aromatic carbon rings were observed as singlets in the region of 129.76-126.46 ppm.



Scheme 28

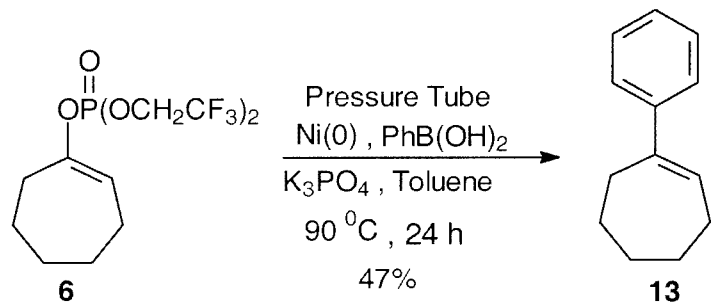
The next coupling product synthesized was 1-phenylcyclopentene **11**. After purification, coupling product **11** was obtained in a 69% yield as a light yellow oil (Scheme 29). In the ^{1}H NMR of compound **11**, (Fig 18) a multiplet was observed for the aromatic group at a chemical shift of 7.47-7.33 ppm. The vinylic proton was noted as a multiplet at 6.20-6.18 ppm. The four allylic protons were observed at 2.73-2.36 ppm, while the homoallylic protons were observed at 2.05-2.00 ppm. In the ^{13}C NMR of compound **11**, (Fig 19) the two vinylic carbons were observed at 137.55 and 126.55 ppm. The ipso carbon of the aromatic ring of compound **11** had a chemical shift of 143.66 ppm. The two allylic carbons were observed at 28.65 and 27.16 ppm, while the

homoallylic carbon had a chemical shift at 22.76 ppm. The other aromatic carbons were observed at 129.27-125.81 ppm.



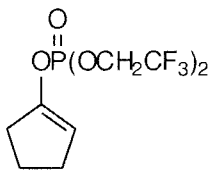
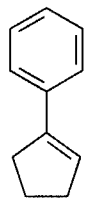
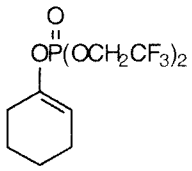
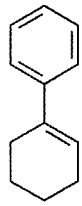
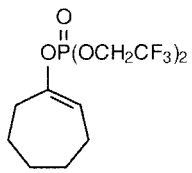
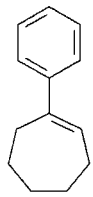
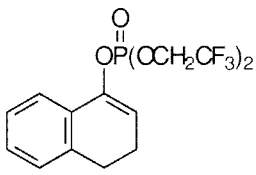
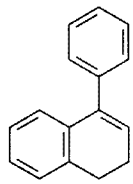
Scheme 29

After purification by flash column chromatography, compound **13** was obtained in a 47% yield (Scheme 30). Formation of coupling product **13** was confirmed by carbon and proton NMR. For the ^{1}H NMR of compound **13**, (Fig 22) the aromatic protons appeared at 7.60-7.30 ppm as multiplets. The vinylic proton was observed as a multiplet at 6.10-6.07 ppm. The homoallylic and allylic protons also appeared as multiplets at 2.62-1.54 ppm. In the ^{13}C NMR analysis of compound **13**, (Fig 23) the vinylic carbons were observed as singlets at 142.19 and 127.24 ppm. The ipso carbon of the aromatic ring was noted at a chemical shift of 145.91 ppm. The aromatic carbons were observed at 129.43-126.64 ppm. The homoallylic and allylic carbons were noted at regions 34.00-28.04 ppm.



Scheme 30

Table 2. Yields of Suzuki Coupling Product

Vinyl phosphate	Coupling Product	Yield
 **2**	 **11**	69%
 **4**	 **12**	51%
 **6**	 **13**	47%
 **8**	 **14**	56%

Chapter 3: Conclusion

In conclusion, several synthetic procedures were attempted for the Suzuki coupling reaction in order to produce aryl-substituted olefins. We have developed a new method for the Suzuki coupling of bis(2,2,2-trifluoroethyl) vinyl phosphates with phenylboronic acid using catalytic amounts of Ni(0) in the presence of zinc powder with an additional ligand, dppf. The air-sensitive Ni(0) complex was prepared from $NiCl_2$(dppf) and used as the catalyst upon reduction and activation with *n*-butyllithium. All coupling products were attempted under an inert argon atmosphere in a pressure tube.

Chapter 4: Experimental

General methods. All the reactions were conducted under a positive argon pressure. All solvents were dried by standard techniques. Flash chromatography was conducted with Merck grade 9385, 230-400 mesh silica. Analytical thin layer chromatography (TLC) was conducted on aluminum-backed silica plates. Visualization was accomplished with an ultraviolet lamp and/or staining with 5% phosphomolybdic acid (PMA) in ethanol with heating.

NMR spectra (^{1}H, ^{13}C and ^{31}P) were recorded with a Varian Gemini 2000, 400 MHz spectrometer, with $CDCl_3$ as the solvent. The ^{1}H and ^{13}C chemical shifts are reported in parts per million downfield from $(CH_3)_4Si$. ^{31}P chemical shifts are reported in parts per million downfield from H_3PO_4 (external standard). Coupling constants are reported in Hertz.

A. General procedure for the preparation of bis (2,2,2-trifluoroethyl) vinyl phosphates.

1-[[Bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cyclopentene (2).

To a solution of LDA [5.5 mmol, prepared *in situ* from diisopropylamine (0.77 mL, 5 mmol) and *n*-butyllithium (3.40 mL, 5.44 mmol, 1.6 M in hexane)] in anhydrous THF (25 mL) at –78 ^{0}C was added dropwise *via* syringe cyclopentanone (0.49 mL, 5.5 mmol). After 30 minutes, a solution of bis(2,2,2-trifluororethoxy) phosphochloridate (1.13 mL, 6.5 mmol) was added dropwise *via* syringe to the ketone enolate. The mixture was allowed to warm gradually to room temperature and was then stirred overnight. The reaction was diluted with 100 mL of diethyl ether, and then quenched by slow addition of

saturated aqueous NH_4Cl. The organic layer was washed with saturated sodium chloride, dried over anhydrous $MgSO_4$, and filtered. After removal of the solvent by rotary evaporation, the crude product was purified by flash chromatography (silica gel, 90% hexane, 10% EtOAc) to produce compound **2** (1.12 g, 65%) as a light yellow oil.

^{1}H NMR δ 5.35-5.31 (1H, m), 4.47-4.38 (4H, m), 2.51-2.43 (2H, m), 2.38-2.32 (2H, m), 2.01-1.92 (2H, m).

^{13}C NMR δ 148.91 (d, *J*=9.1 Hz), 122.01 (2, dq, *J*=276.9, 9.9 Hz), 111.34 (d, *J*=5.3 Hz), 64.18 (2, dq, *J*=38.1, 4.6 Hz), 31.20 (d, *J*=4.6 Hz), 28.33 (s), 20.94 (s).

^{31}P NMR δ -6.82.

1-[[Bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cyclohexene (4).

Cyclohexanone (0.62 mL, 6.0 mmol) was added dropwise *via* syringe to a solution of LDA [6.0 mmol, prepared *in situ* from diisopropylamine (0.84 mL, 6.0 mmol) and *n*-butyllithium (3.75 mL, 6.0 mmol in 1.6 M hexane), in anhydrous THF (20 mL) at – 78 ^{0}C]. After 30 minutes, a solution of bis(2,2,2-trifluororethoxy) phosphochloridate (1.13 mL, 6.5 mmol) was added dropwise *via* syringe to the ketone enolate. The mixture was allowed to warm gradually to room temperature and was then stirred overnight. The reaction was diluted with 100 mL of ether and quenched by slow addition of saturated NH_4Cl. The organic layer was washed with brine, dryed over anhydrous magnesium sulfate and filtered. Final purification by flash chromatography (silica gel, 90% hexane, 10% EtOAc) produced compound **4** (1.31 g, 72%).

^{1}H NMR δ 5.55-5.52 (1H, m), 4.44-4.36 (4H, m), 2.21-2.17 (2H, m), 2.10-2.06 (2H, m), 1.76-1.69 (2H, m), 1.58-1.52 (2H, m).

^{13}C NMR δ 147.20 (d, *J*=9.9 Hz), 122.10 (2, dq, *J*=276.9, 9.9 Hz), 112.40 (d, *J*=5.3 Hz), 64.09 (2, dq, *J*=38.1, 4.6 Hz), 27.42 (d, *J*=3.1 Hz), 23.62 (s), 22.65 (s), 21.41 (s).

^{31}P NMR δ -6.64.

1-[[Bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cycloheptene (6).

To a solution of LDA [5.0 mmol, prepared *in situ* from diisopropylamine (0.70 mL, 5.0 mmol) and *n*-butyllithium (3.10 mL, 4.96 mmol in 1.6 M hexane), in anhydrous THF (20 mL) at –78 ^{0}C was added dropwise *via* syringe cycloheptanone (0.65 mL, 5.5 mmol)]. After 30 minutes, bis(2,2,2-trifluororethoxy) phosphochloridate (1.13 mL, 6.5 mmol) was added dropwise *via* syringe to the ketone enolate. The mixture was allowed to warm gradually to room temperature and was then stirred overnight. The reaction was diluted with 100 mL of ether and quenched by slow addition of saturated NH_4Cl (2 x 50 mL). The organic layer was washed with saturated sodium chloride (2 x 50mL), dried over anhydrous $MgSO_4$, and filtered. Final purification by flash chromatography (silica gel, 90% hexane, 10% EtOAc), produced compound **6** (1.13 g, 64%) as a yellow oil.

^{1}H NMR δ 5.70-5.66 (1H, m), 4.44-4.36 (4H, m), 2.42-2.39 (2H, m), 2.10-2.05 (2H, m), 1.71-1.56 (6H, m).

^{13}C NMR δ 151.41 (d, *J*=9.9 Hz), 122.12 (2, dq, *J*=276.7, 9.9 Hz), 117.18 (d, *J*=5.3 Hz), 64.07 (2, dq, *J*=38.1, 4.6 Hz), 33.08 (d, *J*=3.1 Hz), 30.32 (s), 26.78 (d, *J*=1.5 Hz), 24.96 (s), 24.72 (s).

^{31}P NMR δ -6.50.

7-[[Bis(2,2,2-trifluoroethoxy)phosphinyl]oxy]bicyclo[4.4.0]-1,3,5,7-decatetraene (8).

A solution of α-tetralone (0.73 mL, 5.5 mmol) was added *via* syringe to a solution of LDA [5.5 mmol, prepared *in situ* from diisopropylamine (0.77 mL, 5.5 mmol) and *n*-butyllithium (3.30 mL, 5.28 mmol 1.6 M in hexane)] in anhydrous THF (20 mL) at –78 ^{0}C]. After 30 minutes, bis(2,2,2-trifluororethoxy) phosphochloridate (1.13 mL, 6.5 mmol) was added dropwise *via* syringe to the ketone enolate. The reaction mixture was allowed to warm gradually to room temperature and was then stirred overnight. The mixture was diluted with diethyl ether and quenched with NH_4Cl (2 x 50 mL). The organic layer was washed with brine (2 x 50 ml) , dried over anhydrous $MgSO_4$ and filtered. The resulting product was purified by flash chromatography (silica gel, 90% hexane, 10% EtOAc) to produce compound **8** (1.46 g 75%) as a white solid.

^{1}H NMR δ 7.35-7.30 (1H, m), 7.26-7.22 (2H, m), 7.16-7.14 (1H, m), 5.90-5.87 (1H, m), 4.50-4.40 (4H, m), 2.84-2.80 (2H, m), 2.46-2.40 (2H, m).

^{13}C NMR δ 144.75 (d, *J*=8.4 Hz), 136.38 (s), 129.23 (d, *J*=6.2 Hz), 128.50 (s), 127.42 (s), 126.49 (s), 122.03 (2, dq, *J*=276.9, 9.9 Hz), 120.60 (s), 112.09 (d, *J*=3.8 Hz), 64.34 (2, dq, *J*=38.1, 4.4 Hz), 27.24 (s), 22.04 (s).

^{31}P NMR δ -6.09.

B. General procedure for the Suzuki coupling catalyzed by Ni(0) in a pressure tube.

1-Phenylcyclopentene (11).

In a 50 mL round bottom flask under an inert argon atmosphere, $NiCl_2$(dppf){1,1'-Bis (diphenylphosphino)-ferrocene] dichloronickel(II)} (34 mg, 0.049 mmol) was added. The catalyst was dissolved in anhydrous toluene (8 mL) and then reduced with *n*-butyllithium (0.75 mmol, 0.30 mL, 2.5 M in hexane) with stirring at room

temperature to give a red solution of the Ni(0) complex. After being stirred for 30 min, 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cyclopentene (330 mg, 1.0 mmol), anhydrous K_3PO_4 (630 mg, 2.9 mmol), [1,1'-bis(diphenylphosphino)ferrocene] (58 mg, 0.1 mmol), phenylboronic acid (280 mg, 2.3 mmol), anhydrous toluene (2 mL) and zinc powder (200 mg, 3.1 mmol) were added to a pressure tube. The catalyst solution in the 50 mL round bottom flask was carefully cannulated into the pressure tube, which was purged with argon for 30 min and sealed. The reaction was stirred in an oil bath with heating at 90 ^{0}C for 24 h. Upon cooling, the reaction mixture was extracted with water (2 x 1.0 mL), brine (1 x 1.0 mL), dried over Na_2SO_4 and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash chromatography (silica gel, hexanes:ethyl acetate 10:1) to produce compound **11** (100 mg, 69%) as a light yellow oil.

^{1}H NMR ($CDCl_3$): δ (ppm) 7.47-7.33 (m, 5H), 6.20-6.18 (m, 1H), 2.73-2.69 (m, 2H), 2.53-2.36 (m, 2H), 2.05-2.00 (m, 2H).

^{13}C NMR ($CDCl_3$): δ (ppm) 143.66, 137.55, 129.27, 126.55, 126.32, 125.81, 28.65, 27.16, 22.76.

1-Phenylcyclohexene (12).

A solution of *n*-butyllithium (1.30 mmol, 0.52 mL, 2.5 M in hexane) was added to a solution of $NiCl_2$(dppf) (60 mg, 0.1 mmol) in anhydrous toluene (8 mL) at room temperature to produce the Ni(0) catalyst. Phenylboronic acid (330 mg, 2.5 mmol), anhydrous K_3PO_4 (530 mg, 2.9 mmol), dppf (60 mg, 0.1 mmol), zinc powder (400 mg, 6.1 mmol) and 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cyclohexene (200 mg, 1.3 mmol), were added to a pressure tube according to the general procedure. After addition of the catalyst solution, the reaction was stirred in an oil bath with heating at 90 ^{0}C for 24

h. The crude product was subjected to standard aqueous workup and purification by column chromatography (silica gel, hexanes:ethyl acetate 10:1) to produce compound **12** as a colorless oil. (47 mg, 51%).

^{1}H NMR ($CDCl_3$): δ (ppm) 7.41-7.32 (m, 5H), 6.14-6.13 (m, 1H), 2.45-2.41(m, 2H), 2.24-2.21 (m, 2H), 1.82-1.77 (m, 2H), 1.71-1.67 (m, 2H).

^{13}C NMR ($CDCl_3$): δ (ppm) 143.66, 137.55, 129.20, 127.53, 125.95, 125.81, 28.65, 27.16, 24.35, 22.46.

1-Phenylcycloheptene (13).

In a pressure tube, 1-[[bis(2,2,2trifluoroethoxy)phosphinyl]oxy]cycloheptene (250 mg, 1.5 mmol), phenylboronic acid (350 mg, 2.9 mmol), anhydrous K_3PO_4 (630 mg, 2.9 mmol), dppf (58 mg, 0.1 mmol) and zinc powder (100 mg, 1.5 mmol) was added. $NiCl_2$ (dppf) (34 mg, 0.049 mmol) was dissolved in anhydrous toluene, (10 mL) followed by reduction with *n*-butyllithium (0.75 mmol, 0.30 mL, 2.5 M in hexane) to give the nickel(0) species. After stirring for 30 minutes, the nickel(0) catalyst was cannulated into the pressure tube, which was purged with argon for 30 min and sealed. The reaction was stirred in an oil bath with heating at 90 ^{0}C for a 24 h period. The crude product was subjected to standard aqueous workup and isolation by flash column chromatography (silica gel, hexanes:ethyl acetate 10:1) to produce compound **13** as a light yellow oil (57 mg, 47%).

^{1}H NMR ($CDCl_3$): δ (ppm) 7.60-7.30 (m, 5H), 6.10-6.07 (m, 1H), 2.62-2.60 (m, 2H), 2.29-2.26 (m, 2H), 1.84-1.84 (m, 2H), 1.65-1.63 (m, 2H), 1.56-1.54 (m, 2H).

^{13}C NMR ($CDCl_3$): δ (ppm) 145.93, 142.19, 129.12, 128.27, 127.25, 126.66, 34.09, 34.03, 30.15, 28.20, 28.08 .

1-Phenyl-3,4-dihydronaphthalene (14).

After the addition of the $NiCl_2$(dppf) (65 mg, 0.1 mmol) to a solution of *n*-butyllithium (0.75 mmol, 0.30 mL, 2.5 M in hexane) in anhydrous toluene (8 mL), with stirring for 30 min, the Ni(0) catalyst was formed. Anhydrous K_3PO_4 (450 mg, 2.9 mmol), 7-[[bis(2,2,2-triflouroethoxy)phosphinyl]oxo]bicyclo[4.4.0]-1,3,5,7-decatetraene (150 mg, 0.7 mmol), zinc powder (200 mg, 3.1 mmol), dppf (65 mg, 0.1mmol) and phenylboronic acid (280 mg, 2.3 mmol) were added to a pressure tube with anhydrous toluene (3 mL). After 30 min of stirring, the nickel(0) species was cannulated into the pressure tube, purged with argon for 30 min and sealed. The reaction was stirred in an oil bath with heating at 90 ^{0}C for 24 h. Upon cooling, the reaction mixture was extracted with water (2 x 1.0 mL), brine (1 x 1.0 mL), dried over Na_2SO_4 and filtered. The solvent was removed by rotary evaporation. The crude product was purified by flash chromatography (silica gel, hexanes:ethyl acetate 10:1) to produce compound **14** (44 mg, 56%).

^{1}H NMR ($CDCl_3$): δ (ppm) 7.43-7.20 (m, 5H), 7.19-7.16 (m, 2H), 7.14-7.02 (m, 2H), 6.12-6.10 (m, 1H), 2.89-2.85 (m, 2H), 2.45-2.40 (m, 2H).

^{13}C NMR ($CDCl_3$): δ (ppm) 141.74, 140.84, 137.78, 136.08, 129.76, 129.24, 128.71, 128.57, 128.10, 128.00, 127.22, 126.46, 29.56, 24.81.

C. Attempted Suzuki Couplings with a Palladium catalyst at 1 Atm.

1-Phenylcyclopentene (11).

A 50 mL flask charged with $Pd(PPh_3)_4$ (250 mg, 0.22 mmol) in 10 mL THF and 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy]cyclopentene (330 mg, 1.0 mmol) was purged with argon with stirring at room temperature for 30 min. Phenylboronic acid (914 mg, 75

mmol), ethanol (3 mL) and aqueous Na_2CO_3 (500 mg in 10 mL H_2O) were added to the flask. The reaction mixture was refluxed for 24 h at 65 ^{0}C. After cooling, the reaction mixture was washed with water (2 x 50 mL), saturated sodium chloride (2 x 50 mL), and dried over magnesium sulfate. After removal of the solvent *via* rotary evaporation, examination of the crude reaction mixture by ^{1}H NMR indicated there were no traces of coupling product.

1-Phenylcyclohexene (12).

To a mixture of phenylboronic acid (714 mg, 5.9 mmol) and anhydrous potassium phosphate (661 mg, 0.31 mmol) in anhydrous toluene (8 mL) under argon, was added tetrakis(triphenylphosphine)palladium(0) (25 mg, 0.021 mmol) followed by 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cyclohexene (350 mg, 0.102 mmol). The mixture was stirred, degassed with argon for 10 min and refluxed for 24 h at 110 ^{0}C. The solution was allowed to cool and the reaction mixture was washed with water (2 x 50 mL), saturated sodium chloride (2 x 50 mL) and dried over magnesium sulfate. The resulting mixture was filtered through a 2 cm layer of florisil (60-120 mesh). After removing the solvent by rotary evaporation, and analysis by NMR (^{1}H, ^{13}C), and GC-MS, no coupling product was observed.

1-Phenylcycloheptene (13).

A mixture of 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy]cycloheptene (850 mg, 2.4 mmol), anhydrous cesium carbonate (600 mg, 1.8 mmol), and anhydrous toluene was added to a 50 mL flask. Phenylboronic acid (500 mg, 4.1 mmol), $Pd(PPh_3)_4$ (5 mg, 0.0043 mmol) were also added to the flask. The reaction mixture was degassed with argon for 30 min. and then refluxed at 110 ^{0}C for 24 h. After cooling, the reaction

mixture was washed with water (2 x 50 mL), saturated sodium chloride (2 x 50 mL) and dried over sodium sulfate. No coupling product was detected by spectroscopic analysis.

1-Phenylcycloheptene (13).

In a 50 mL flask containing $Pd(PPh_3)_4$ (4 mg, 0.0034 mmol) suspended in DME (3 mL) was added phenylboronic acid (140 mg, 1.14 mmol), 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cycloheptene (237 mg, 0.665 mmol) and sodium carbonate (370 mg, 3.48 mmol). The reaction mixture was degassed with argon for 30 min, and then was refluxed at 85 ^{0}C for 16 h. After cooling, the organic layer was washed with water (2 x 50 mL), saturated sodium chloride (2 x 50 mL) and dried under magnesium sulfate. The solvent was removed *via* rotary evaporation and the crude mixture was analyzed by ^{1}H NMR revealing no trace of the coupling product.

1-Phenylcyclohexene (12).

After the addition of $Pd(PPh_3)_4$ (34 mg, 0.029 mmol) to a solution of 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cyclohexene (340 mg, 0.99 mmol), phenylboronic acid (280 mg, 2.3 mmol), anhydrous potassium phosphate (637 mg, 3.0 mmol), triphenylphosphine (70 mg, 0.266 mmol) and anhydrous dioxane (8 mL) in a pressure tube, the reaction mixture was degassed with argon for 20 min and then sealed. The mixture was stirred in an oil bath with heating at 90 ^{0}C for 24 hr. After cooling, the reaction mixture was extracted with water (2 x 1.0 mL), saturated sodium chloride (1 x 1.0 mL), dried over Na_2SO_4 and filtered. After the solvent was removed *via* rotary evaporation, dried on the pump there were no traces of coupling product observed upon analysis of the crude mixture by GC-MS and NMR (^{1}H, ^{13}C).

D. Attempted Suzuki couplings with Nickel catalyst at 1 Atm.

1-Phenylcyclopentene (11).

A solution of $NiCl_2$(dppf) (33 mg, 0.048 mmol) was reduced to Ni(0) with *n*-butyllithium (0.3 mL, 0.75 mmol, 2.5 M in hexane) and stirred for 20 min. Dppf{1,1'-Bis(diphenylphosphino)-ferrocene] dichloronickel(II) (58 mg, 0.014 mmol), phenylboronic acid (280 mg, 2.3 mmol), 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy]cyclopentene (440 mg, 1.3 mmol), and sodium carbonate (637 mg, 3.0 mmol) were added into a pressure tube, with a minimum of 2.0 mL anhydrous toluene. The Ni(0) catalyst was carefully cannulated into the pressure tube and degassed with argon for 30 min and then sealed. The reaction mixture was heated at 110 ^{0}C for 24 h. After cooling, the mixture was extracted with water (2 x 1.0 mL), saturated sodium chloride (2 x 1.0 mL) and filtered. No coupling product was observed after analysis by GC-MS and NMR.

3-(Isopropenyl-6-methyl-cyclohexa-1,5-dienyl)-benzene (15).

In a 50 mL flask containing $NiCl_2$(dppf) (40 mg, 0.034 mmol) was added *n*-butyllithium (0.5 mL, 1.25 mmol, 2.5 M in hexane). The mixture was stirred at room temperature for 20 min. Phenylboronic acid (140 mg, 1.14 mmol), 2-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy]-3-methyl-6-isopropenyl-1,3-cyclohexadiene (237 mg, 0.665 mmol) and anhydrous cesium carbonate (370 mg, 3.48 mmol) were added to the flask with 8 mL of DME, and the mixture was degassed with argon for 30 min. The reaction mixture was refluxed at 64 ^{0}C for 24 h. After cooling, the organic layer was washed with water (2 x 50 mL), saturated sodium chloride (2 x 50 mL) and dried under

anhydrous sodium sulfate. The solvent was removed *via* rotary evaporation and the crude mixture was analyzed by ^{1}H NMR revealing no trace of the coupling product.

1-Phenylcyclohexene (12).

A solution of *n*-butyllithium (0.5 mL, 1.25 mmol, 2.5 M in hexane) was added to a solution of $NiCl_2$(dppf) (60 mg, 0.1 mmol) in anhydrous toluene (8 mL) at room temperature to produce the Ni(0) catalyst. A separate flask containing phenylboronic acid (330 mg, 2.5 mmol), anhydrous K_3PO_4 (530 mg, 2.9 mmol), dppf (60 mg, 0.1 mmol), and 1-[[bis(2,2,2-trifluoroethoxy)phosphinyl]oxy] cyclohexene (200 mg, 1.3 mmol), in 0.3 mL anhydrous toluene was degassed with argon for 20 min. The Ni catalyst solution was added to the degassed vinyl phosphate solution, and the resultant mixture was refluxed at 110 ^{0}C for 24 h. After standard aqueous workup and analysis by ^{1}H, ^{13}C NMR and GC-MS, no coupling product was observed.

1-Phenylcycloheptene (13).

A solution of nickel(0) catalyst (prepared from the addition of *n*-butyllithium (0.5 mL, 1.25 mmol, 2.5 M in hexane) to a suspension of $NiCl_2$(dppf) (60 mg, 0.1 mmol) in toluene (8 mL) at room temperature was added *via* cannulation to the degassed solution of 1-[[bis(2,2,2trifluoroethoxy)phosphinyl]oxy]cycloheptene (250 mg, 1.5 mmol), phenylboronic acid (350 mg, 2.9 mmol), anhydrous K_3PO_4 (630 mg, 2.9 mmol), in 10 mL anhydrous toluene. The reaction mixture was refluxed for 24 h. After standard aqueous workup, there were no traces of coupling product upon analysis by GC-MS and NMR (^{1}H, ^{13}C).

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Figure **1** ^{1}H NMR of Compound **2**

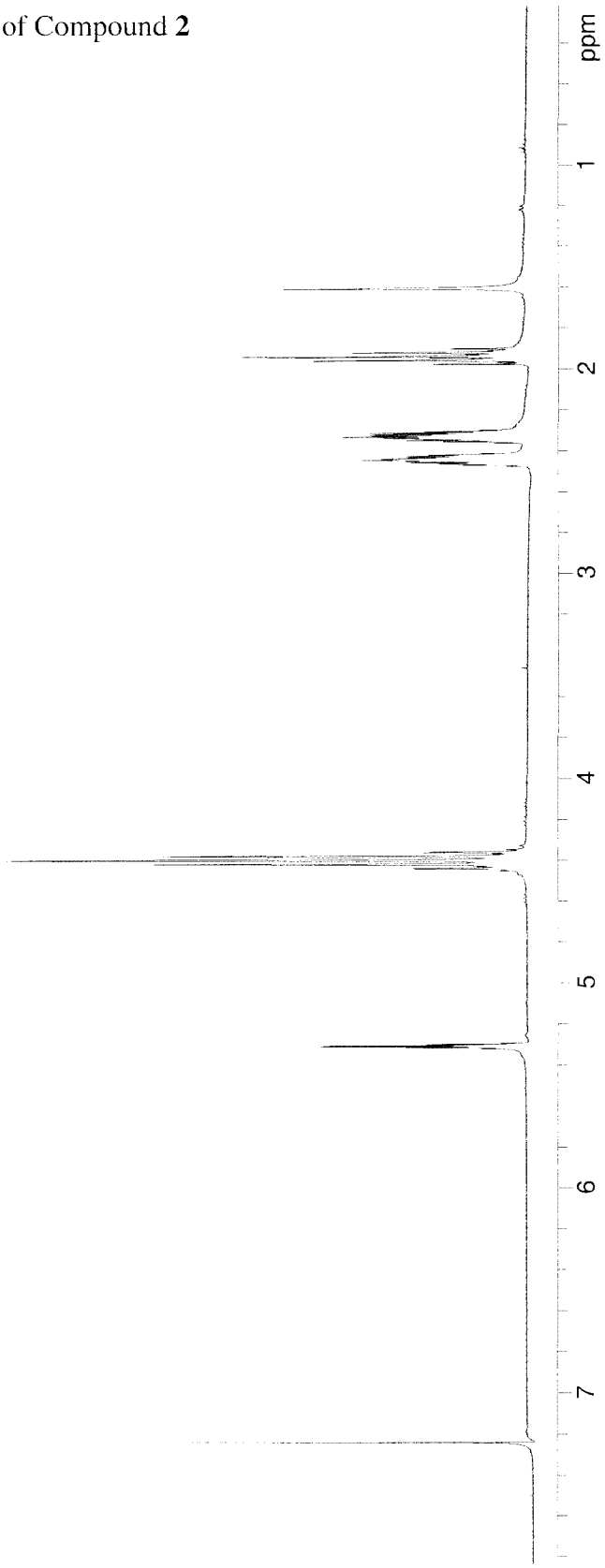

Figure **2** Expanded ^{1}H NMR of Compound **2**

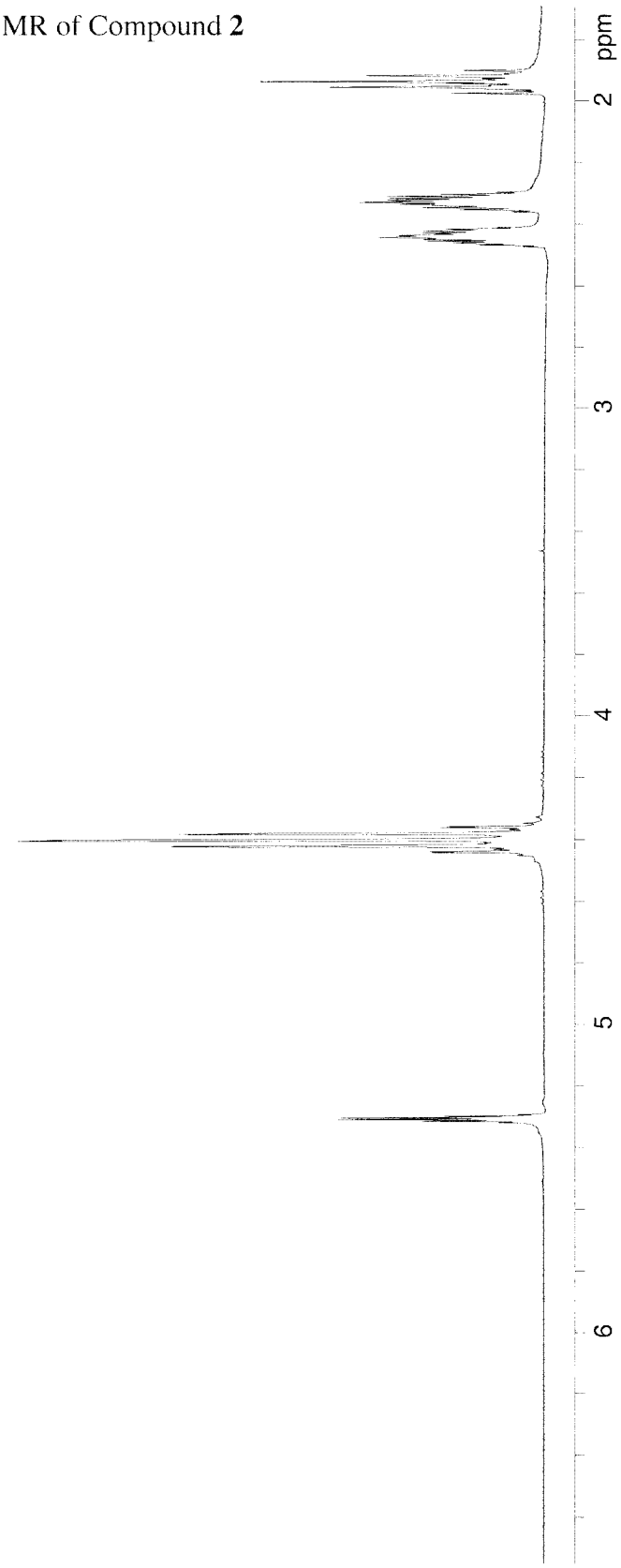

Figure **3** ^{13}C NMR of Compound **2**

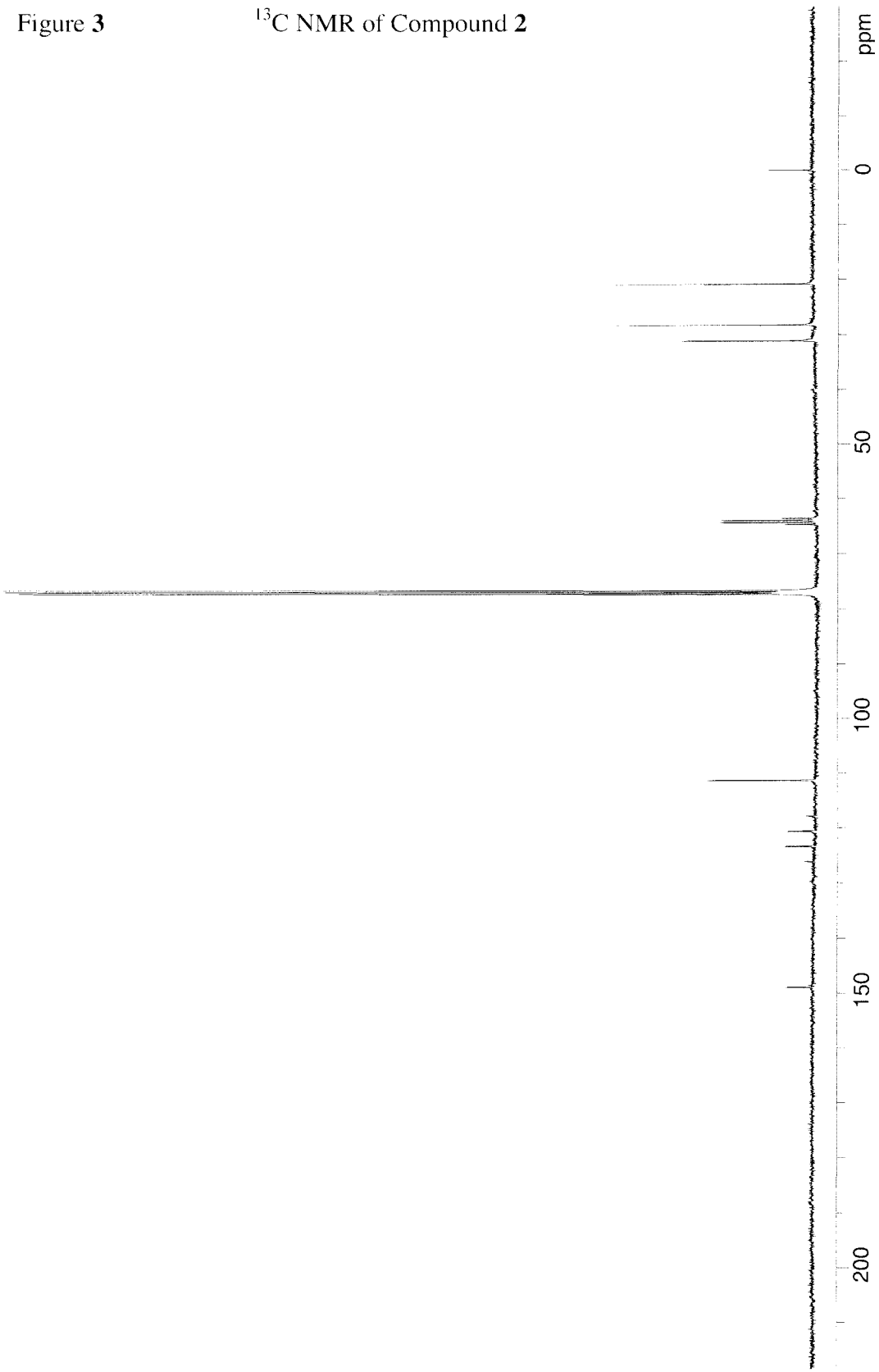

Figure **4** ^{31}P NMR of Compound **2**

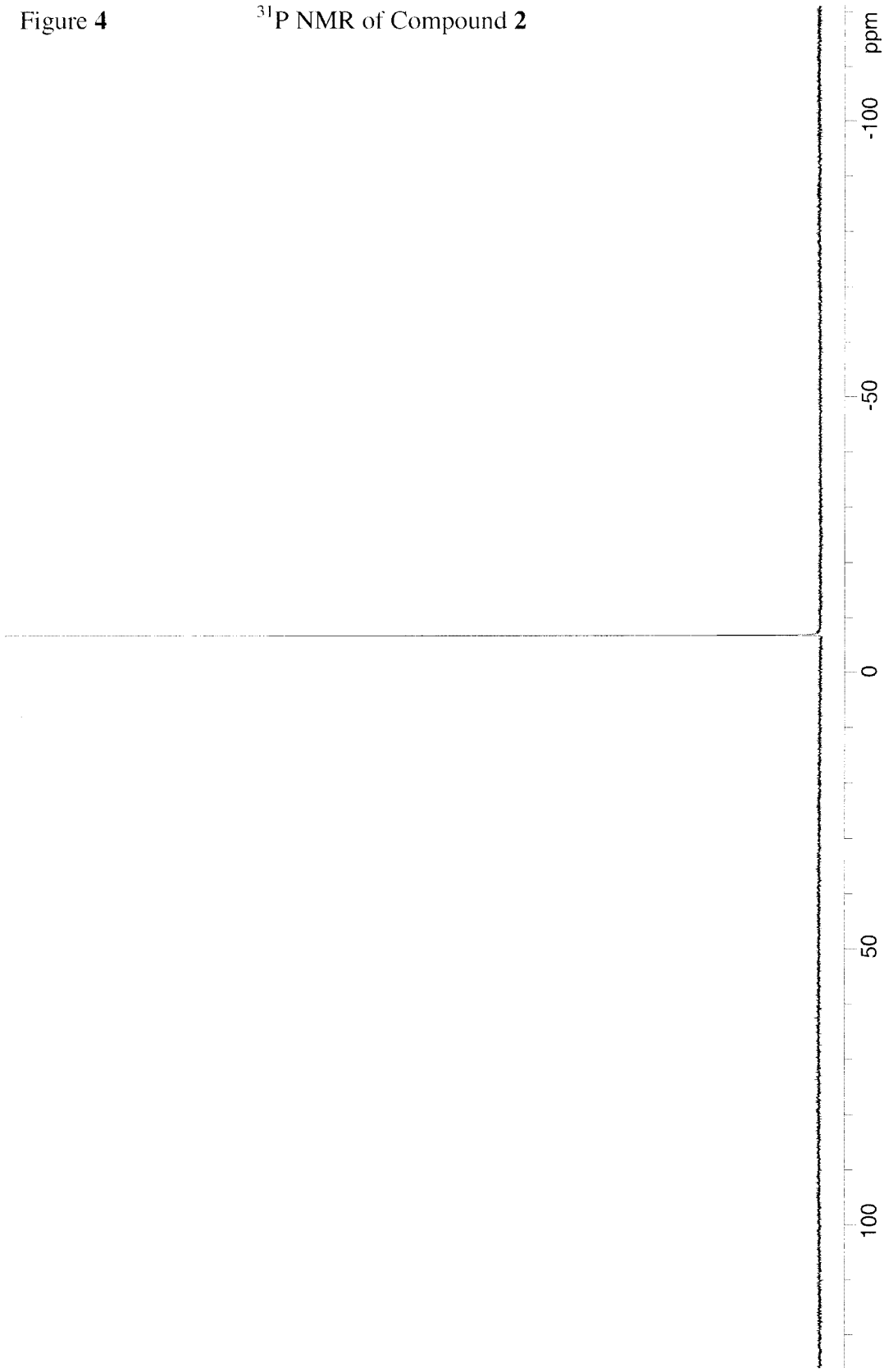

Figure **5** ^{1}H NMR of Compound **4**

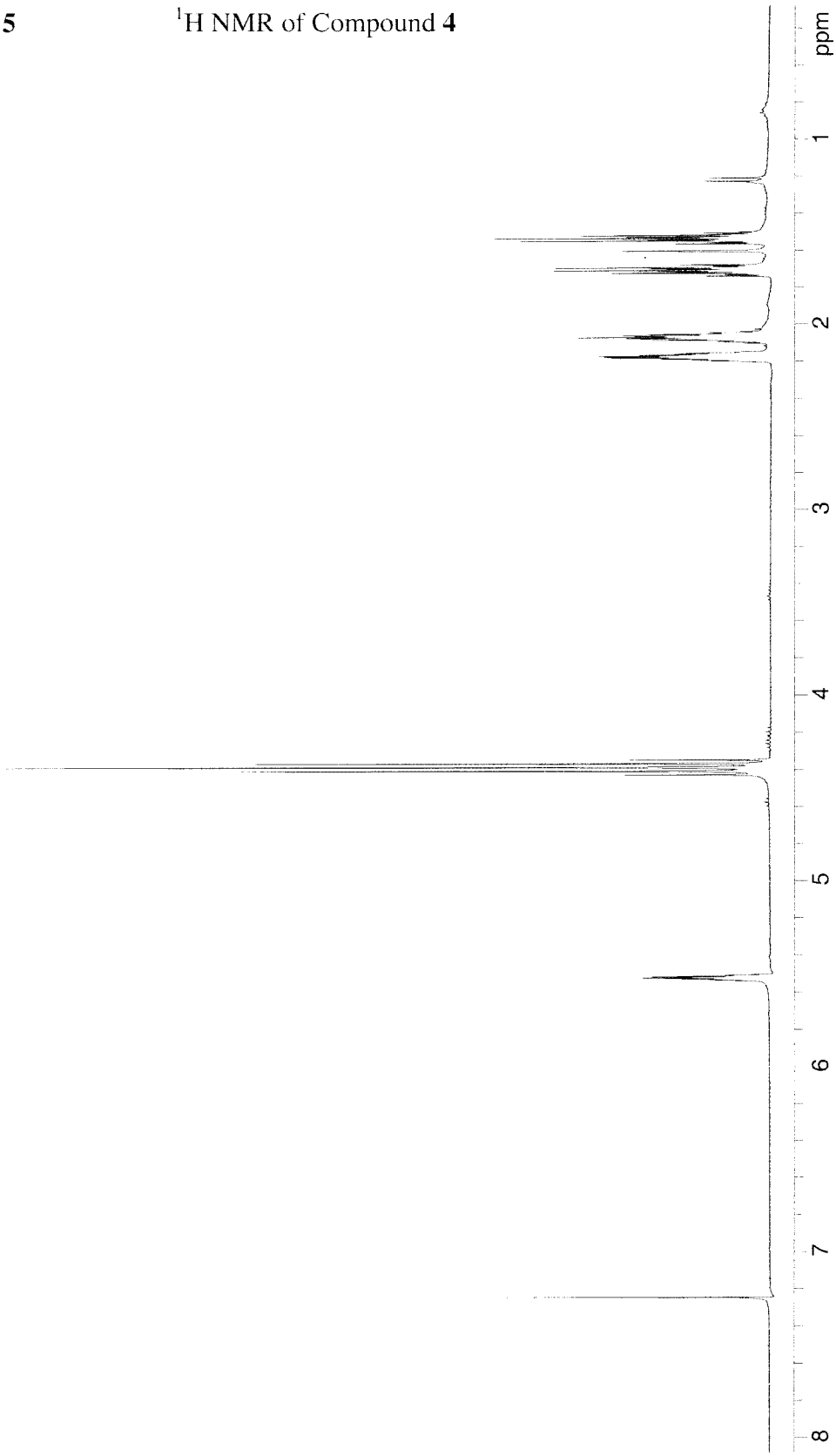

Figure **6** Expanded ^{1}H NMR of Compound **4**

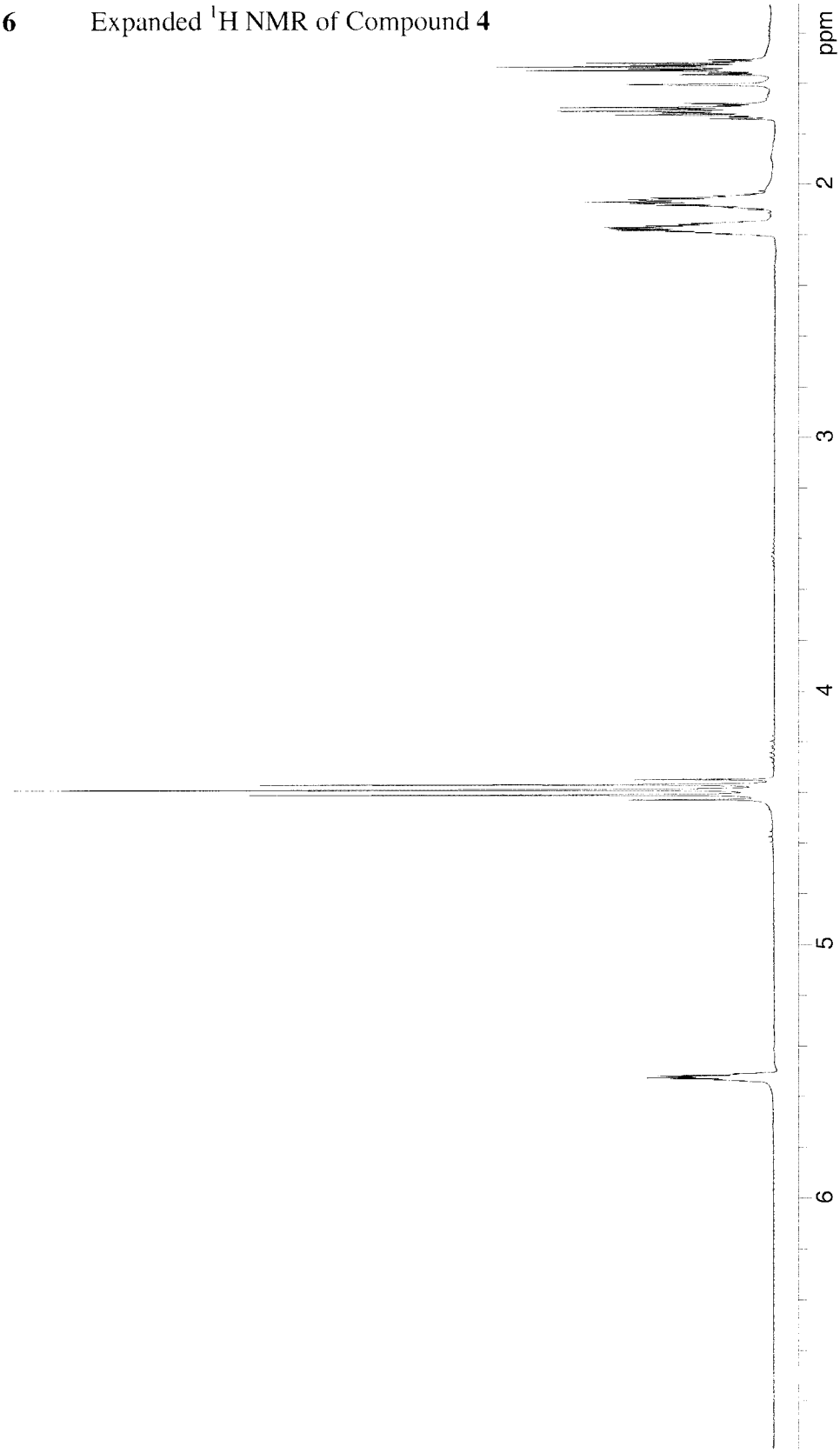

Figure **7** ^{13}C NMR of Compound **4**

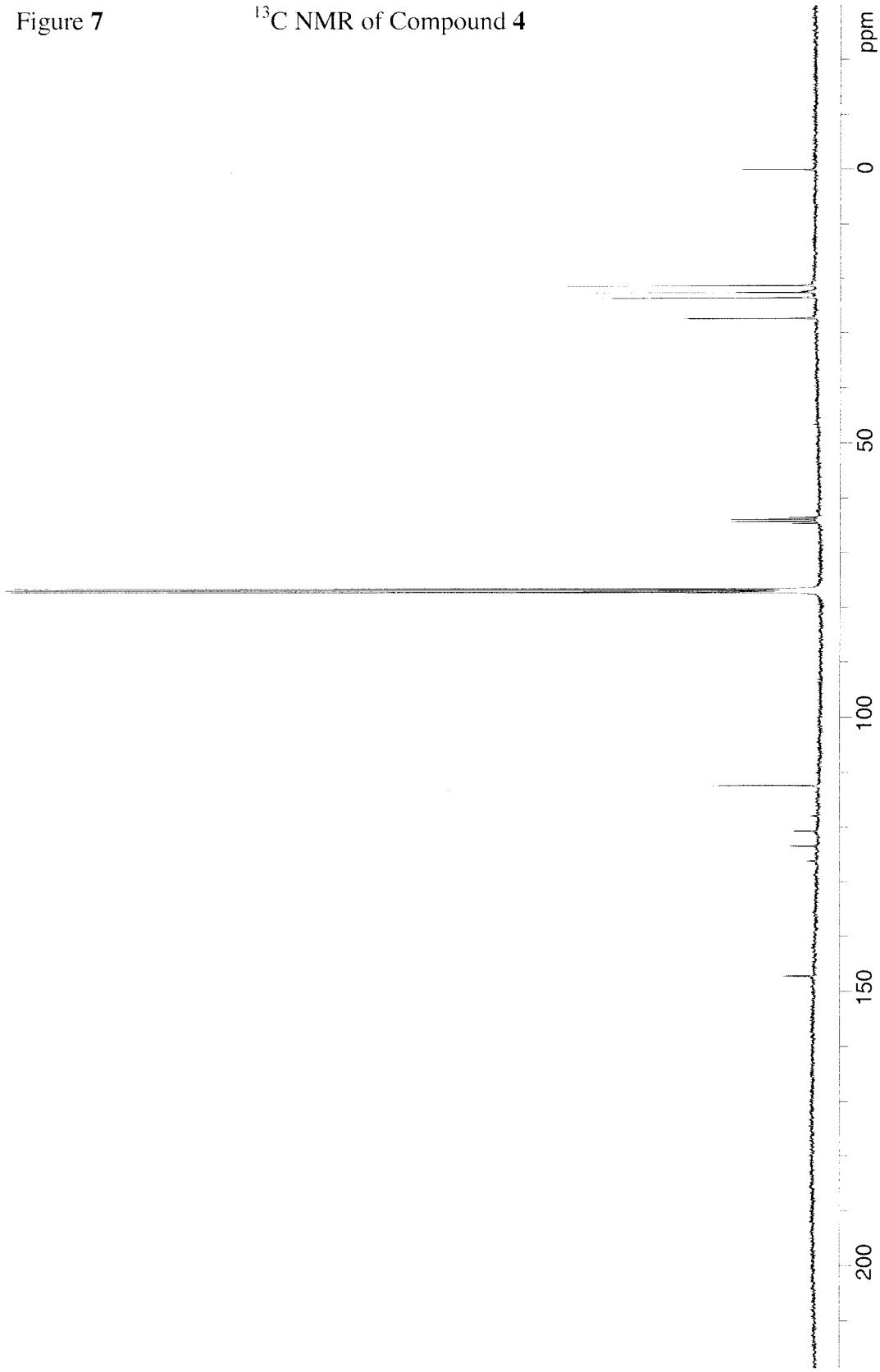

Figure **8** ^{31}P NMR of Compound **4**

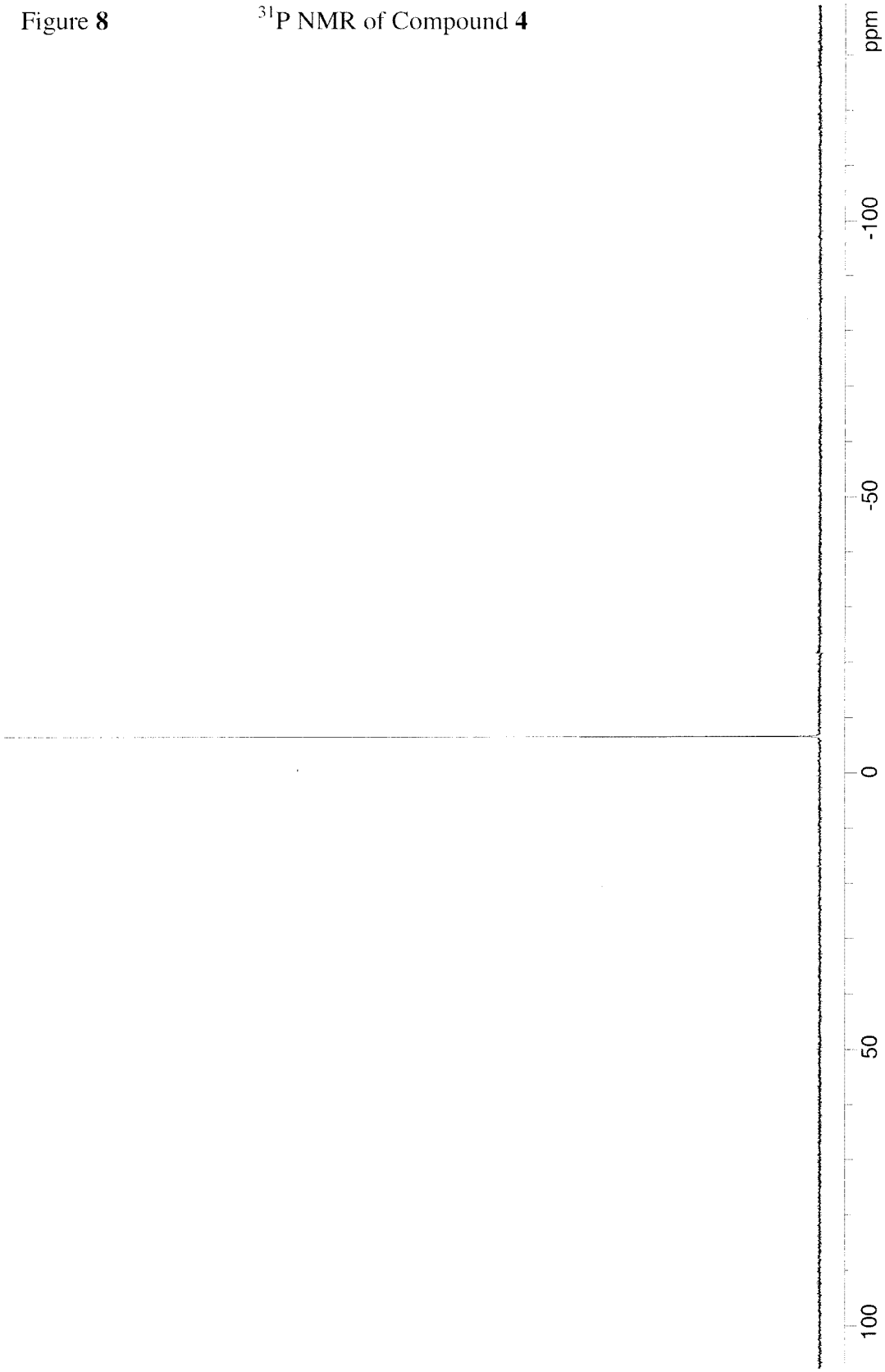

Figure **9** ^{1}H NMR of Compound **6**

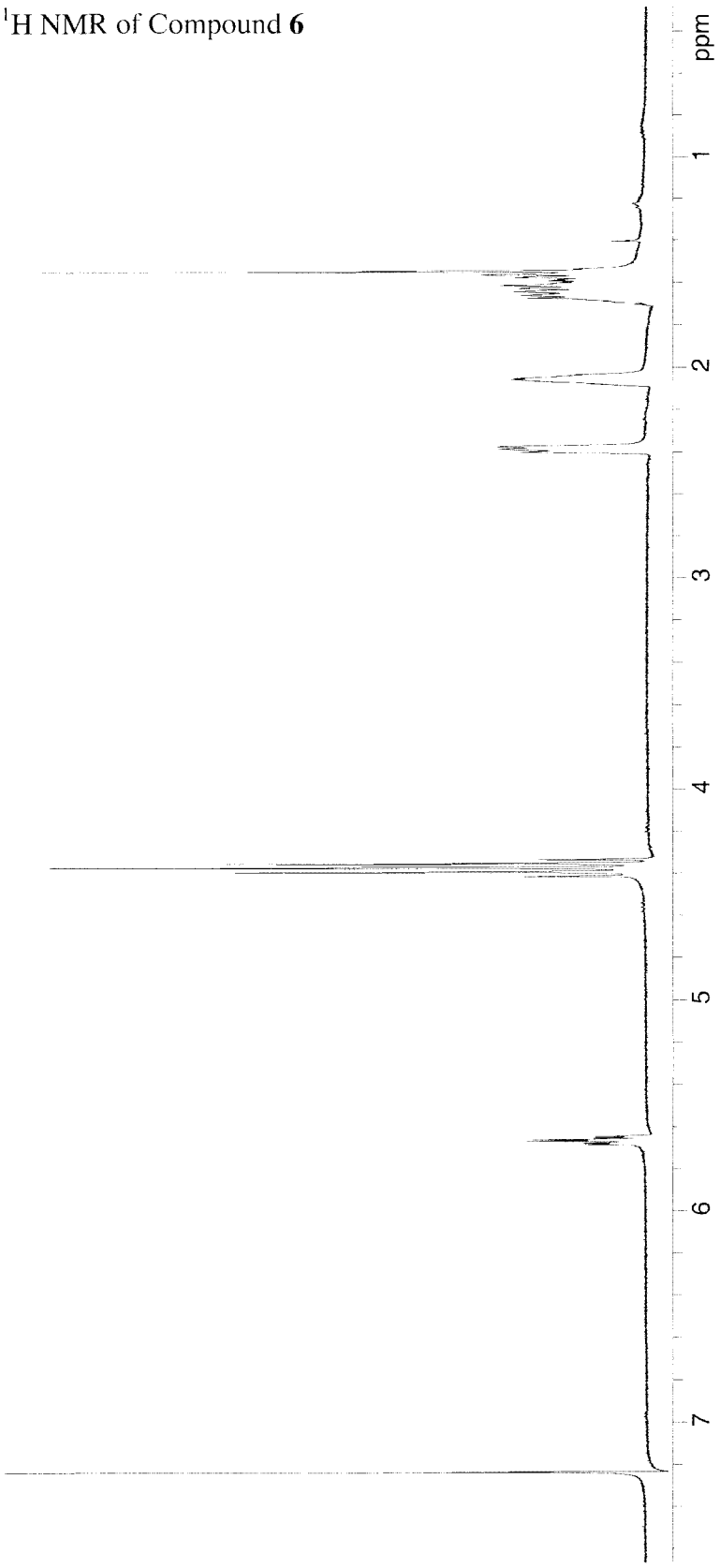

Figure **10** Expanded ^{1}H NMR of Compound **6**

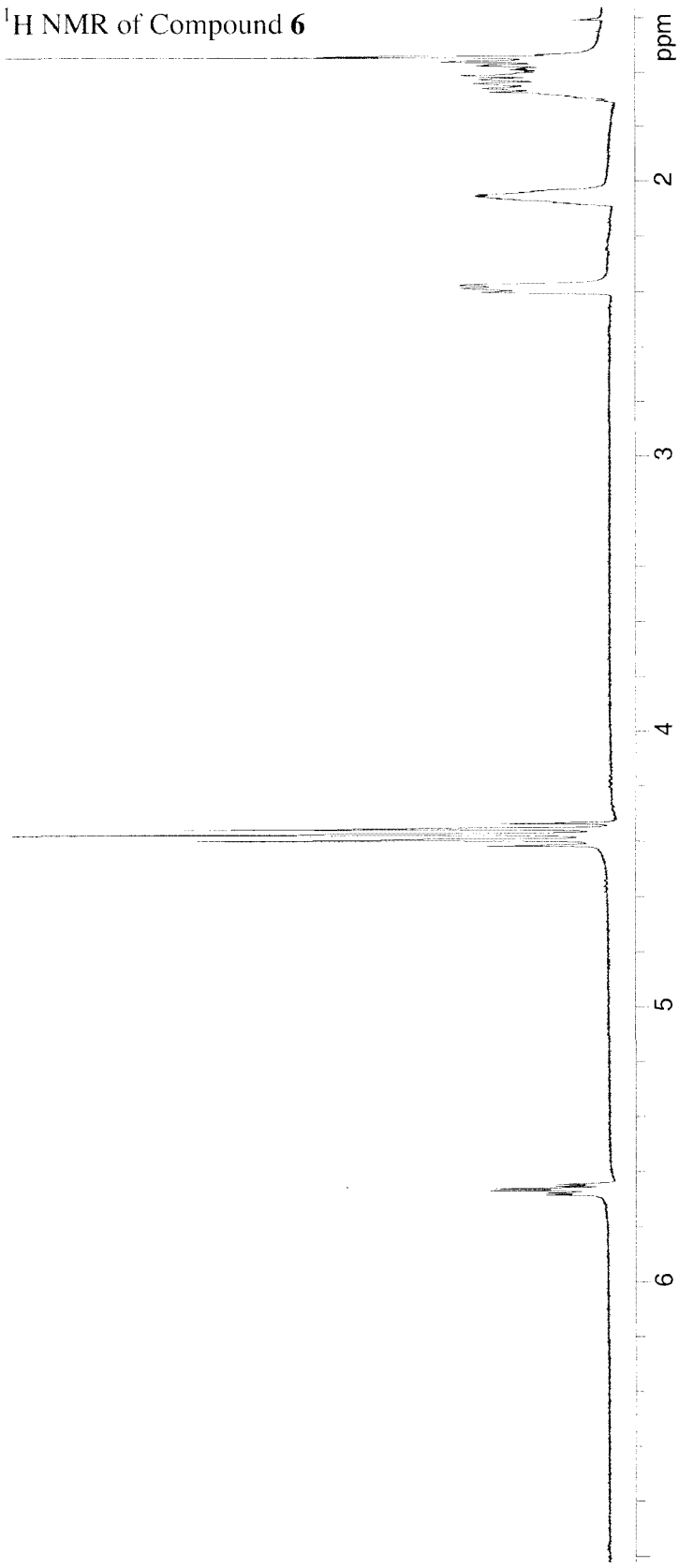

Figure **11** ^{13}C NMR of Compound **6**

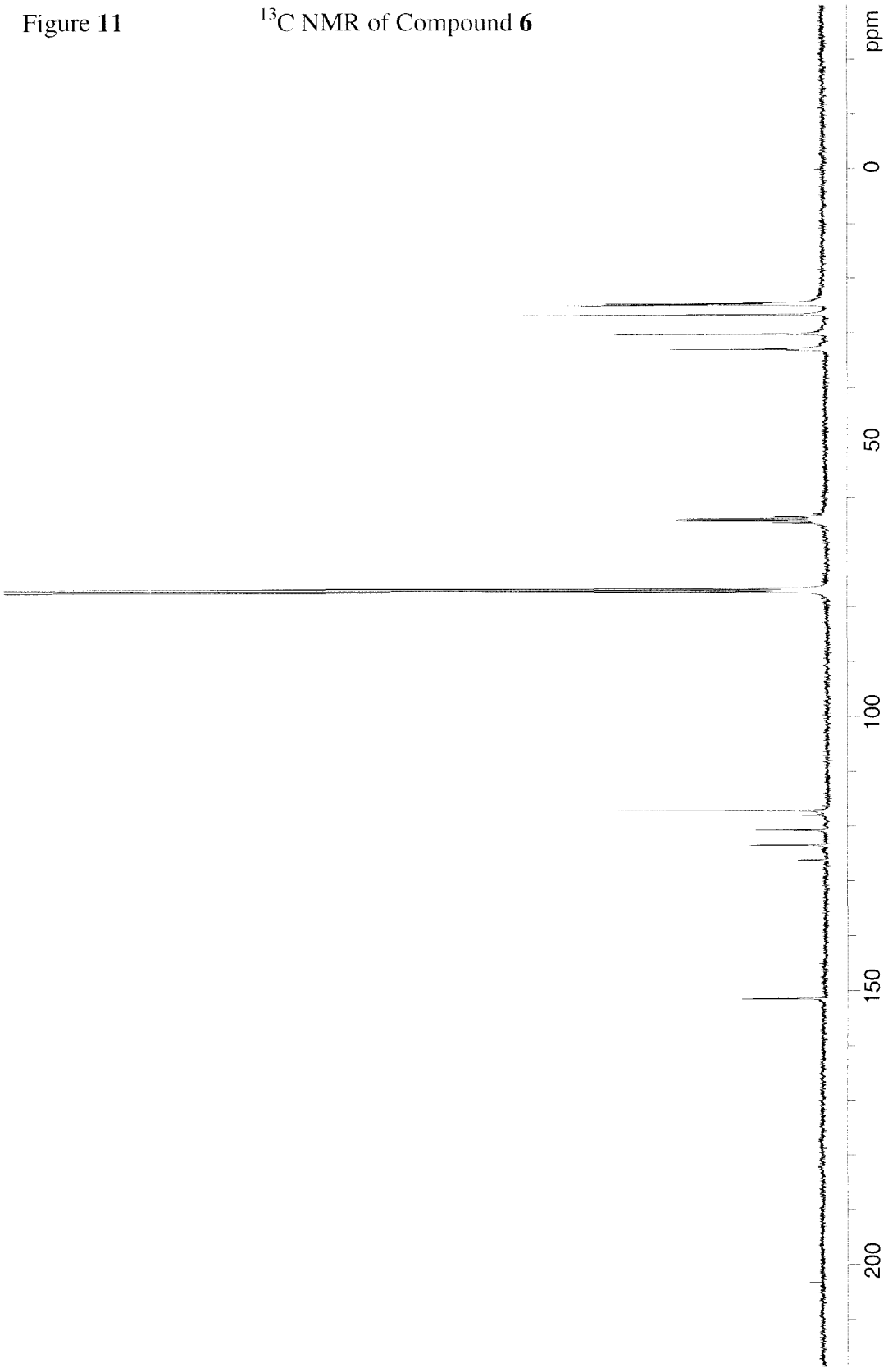

Figure **12** ^{31}P NMR of Compound **6**

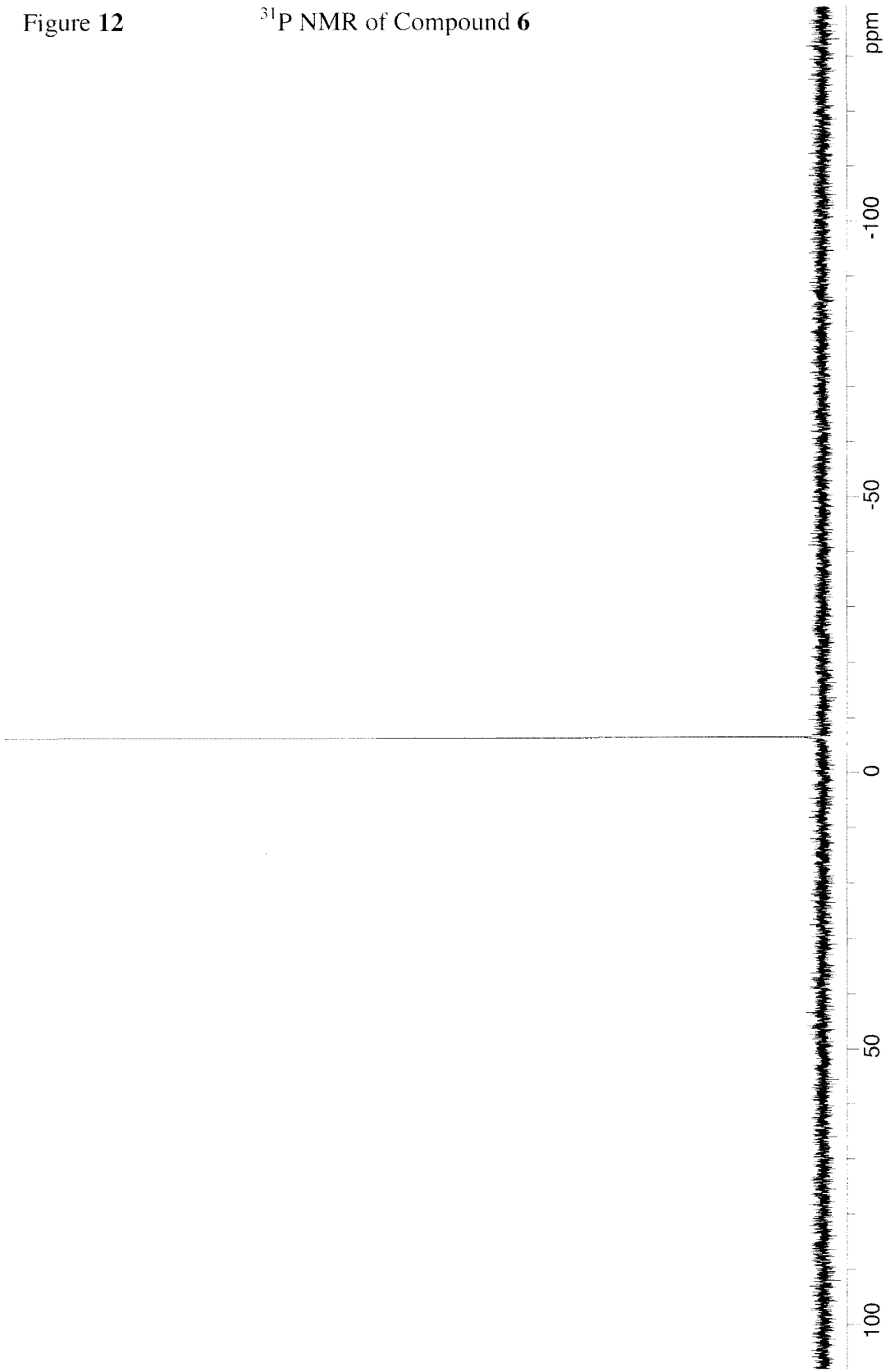

Figure **13** ^{1}H NMR of Compound **8**

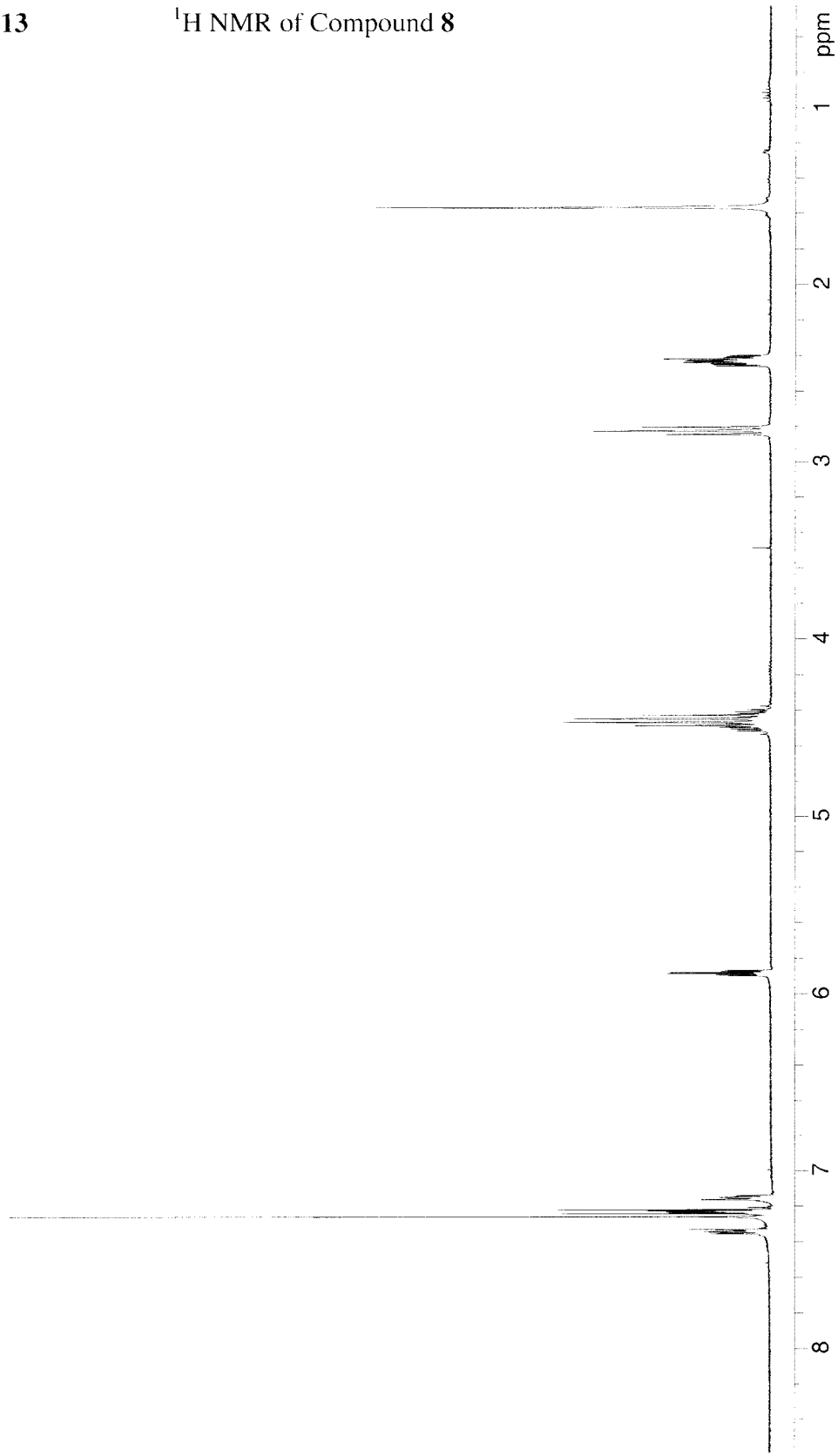

Figure **14** Expanded ^{1}H NMR of Compound **8**

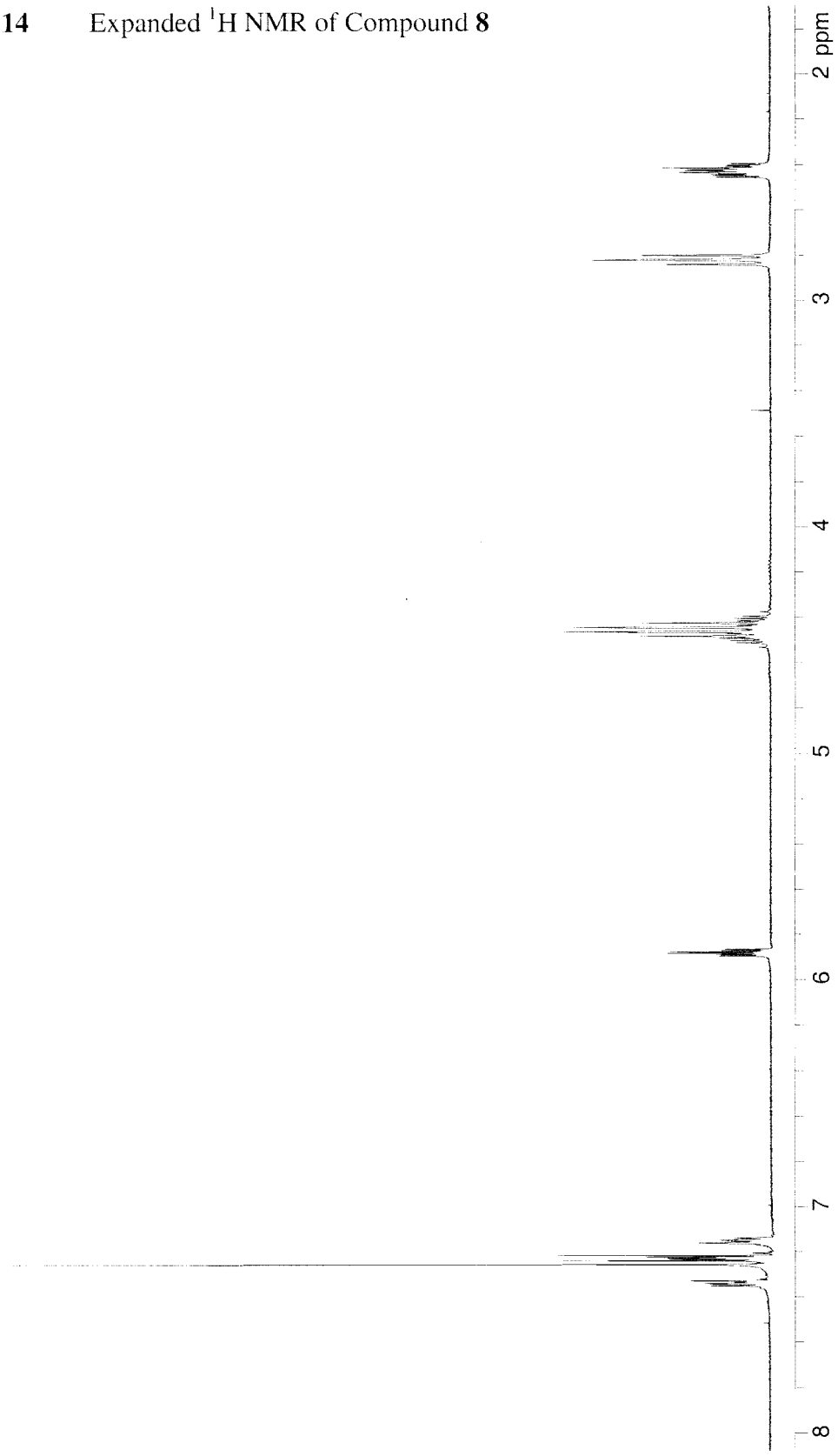

Figure **15** ^{13}C NMR of Compound **8**

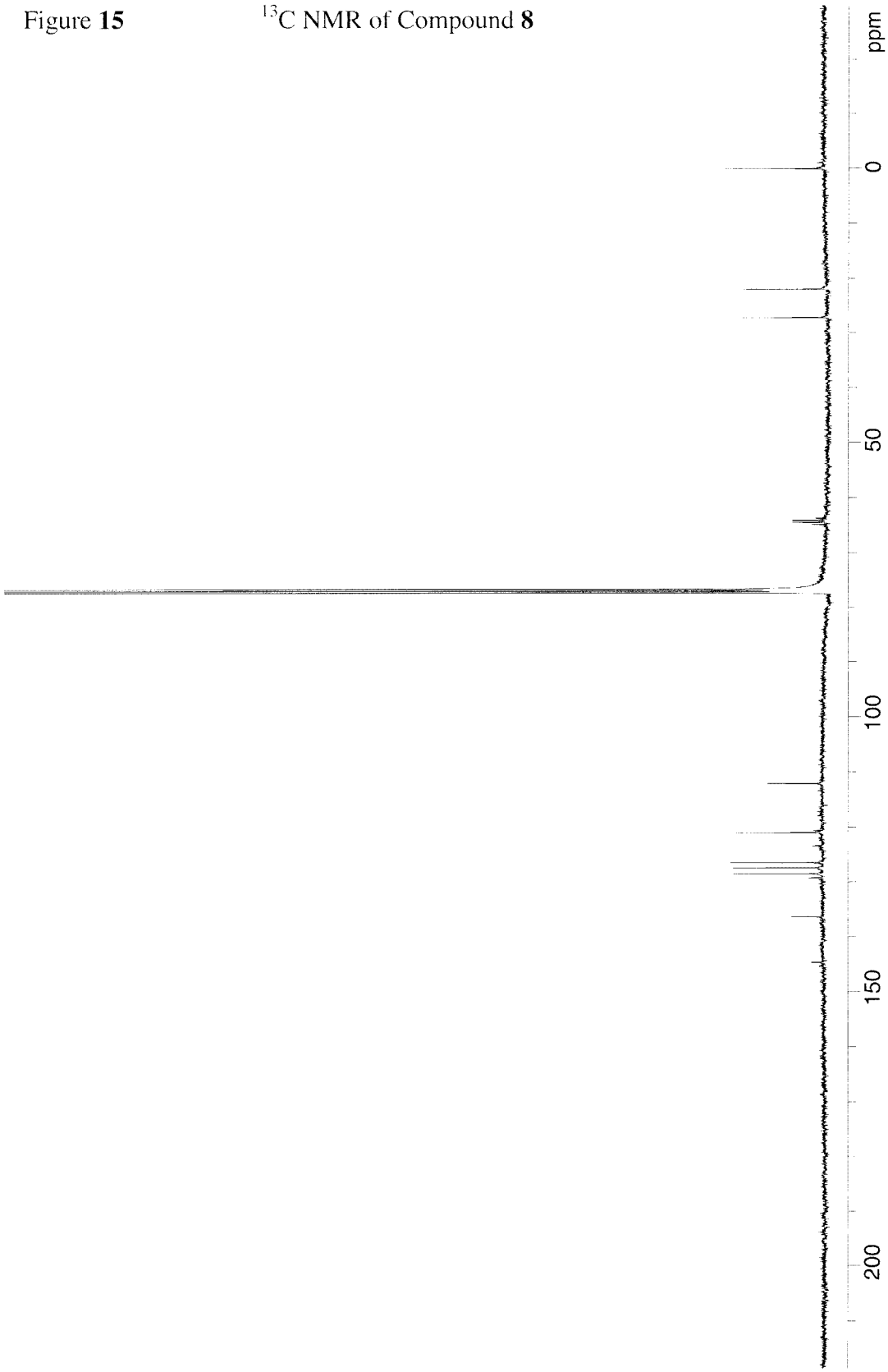

Figure **16** ^{31}P NMR of Compound **8**

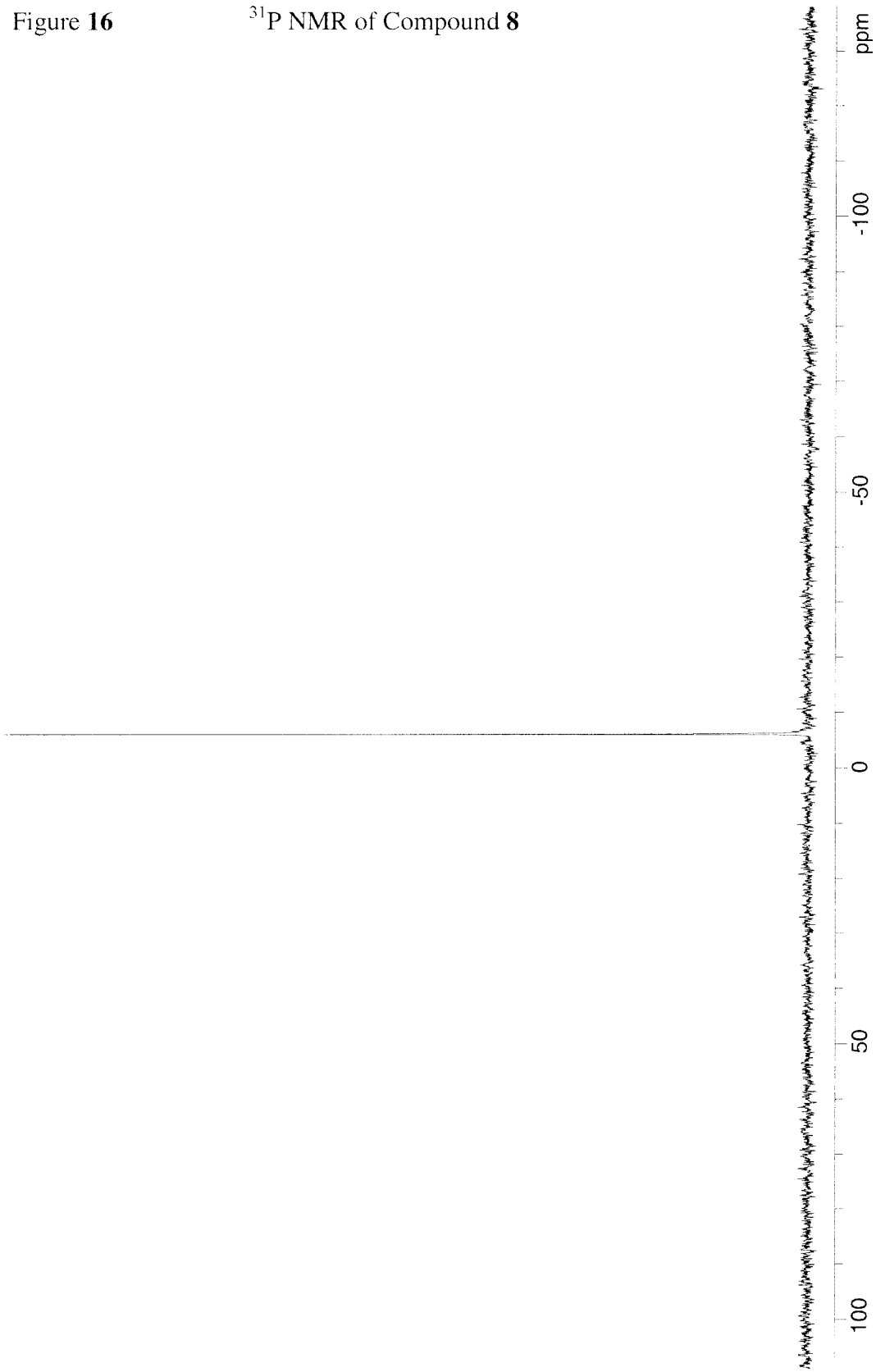

Figure **17** ^{1}H NMR of Compound **11**

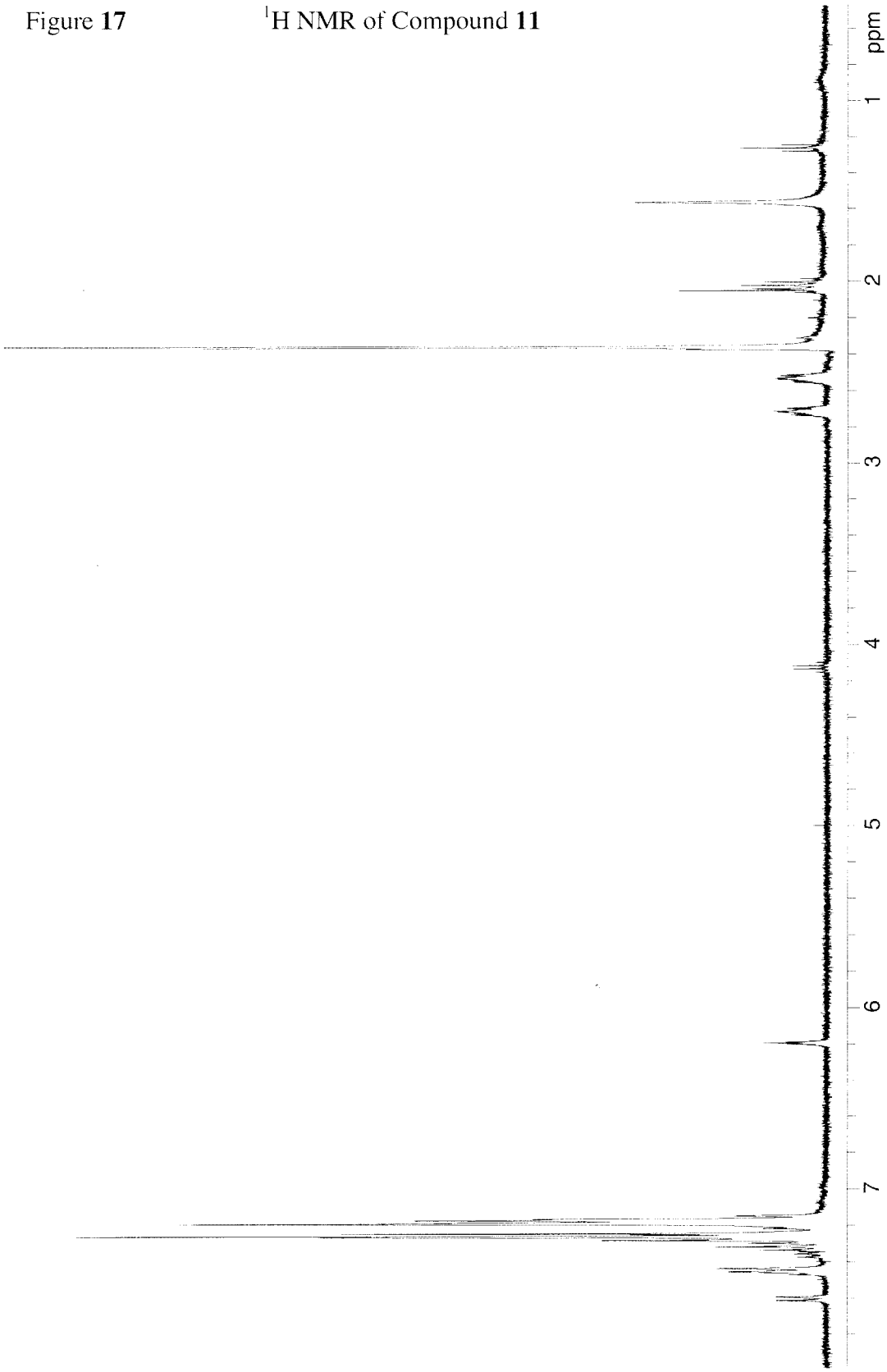

Figure **18** Expanded ^{1}H NMR of Compound **11**

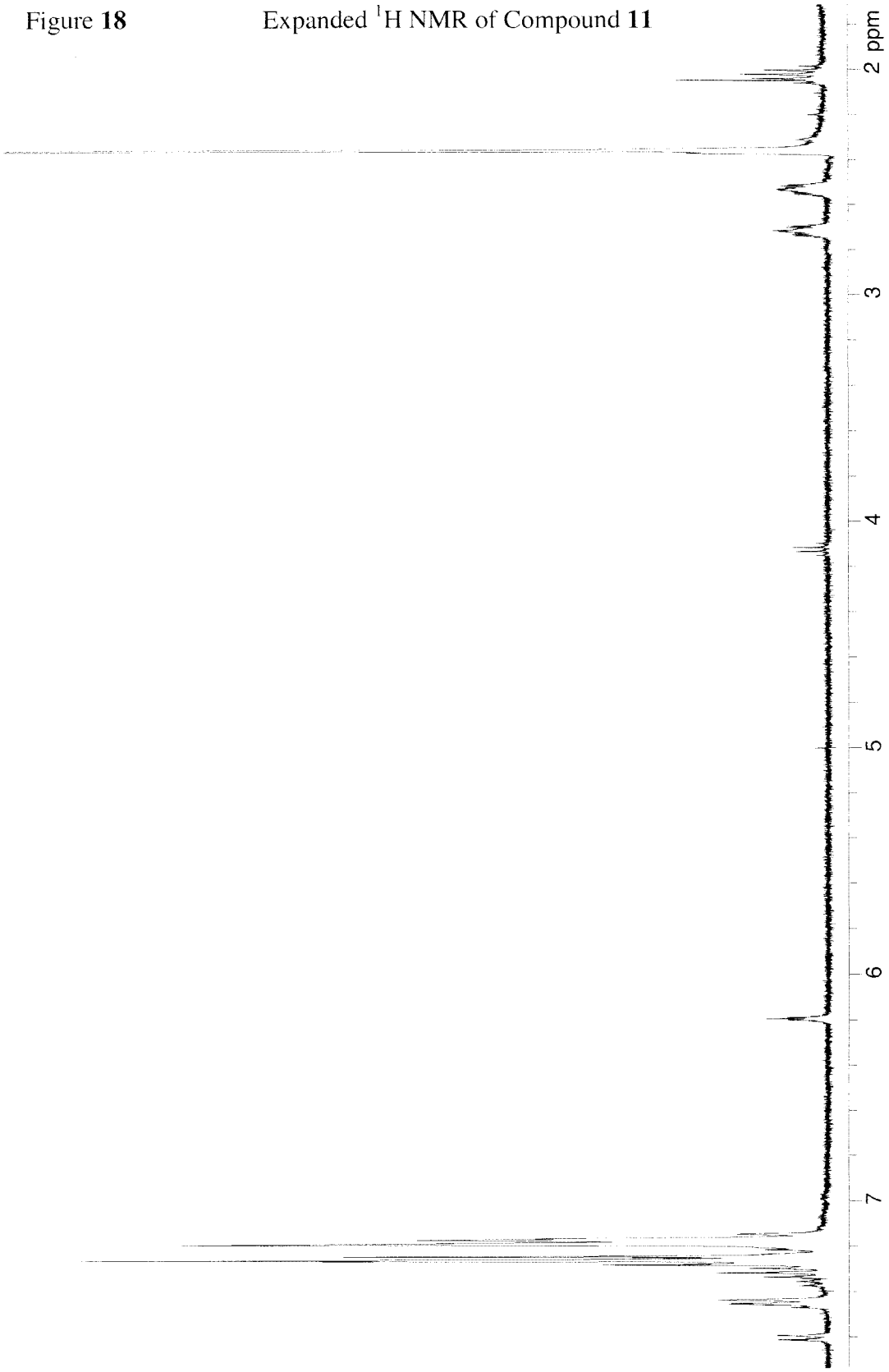

Figure **19** ^{13}C NMR of Compound **11**

Figure **20** ^{1}H NMR of Compound **12**

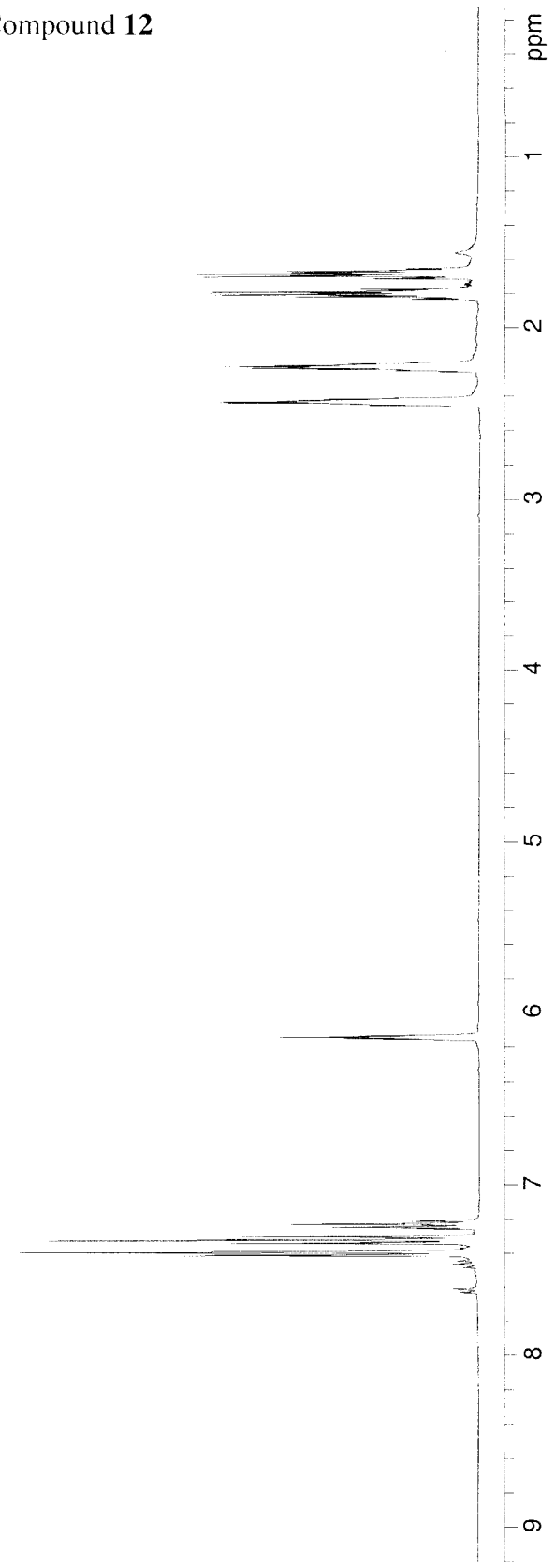

Figure **21** ^{13}C NMR of Compound **12**

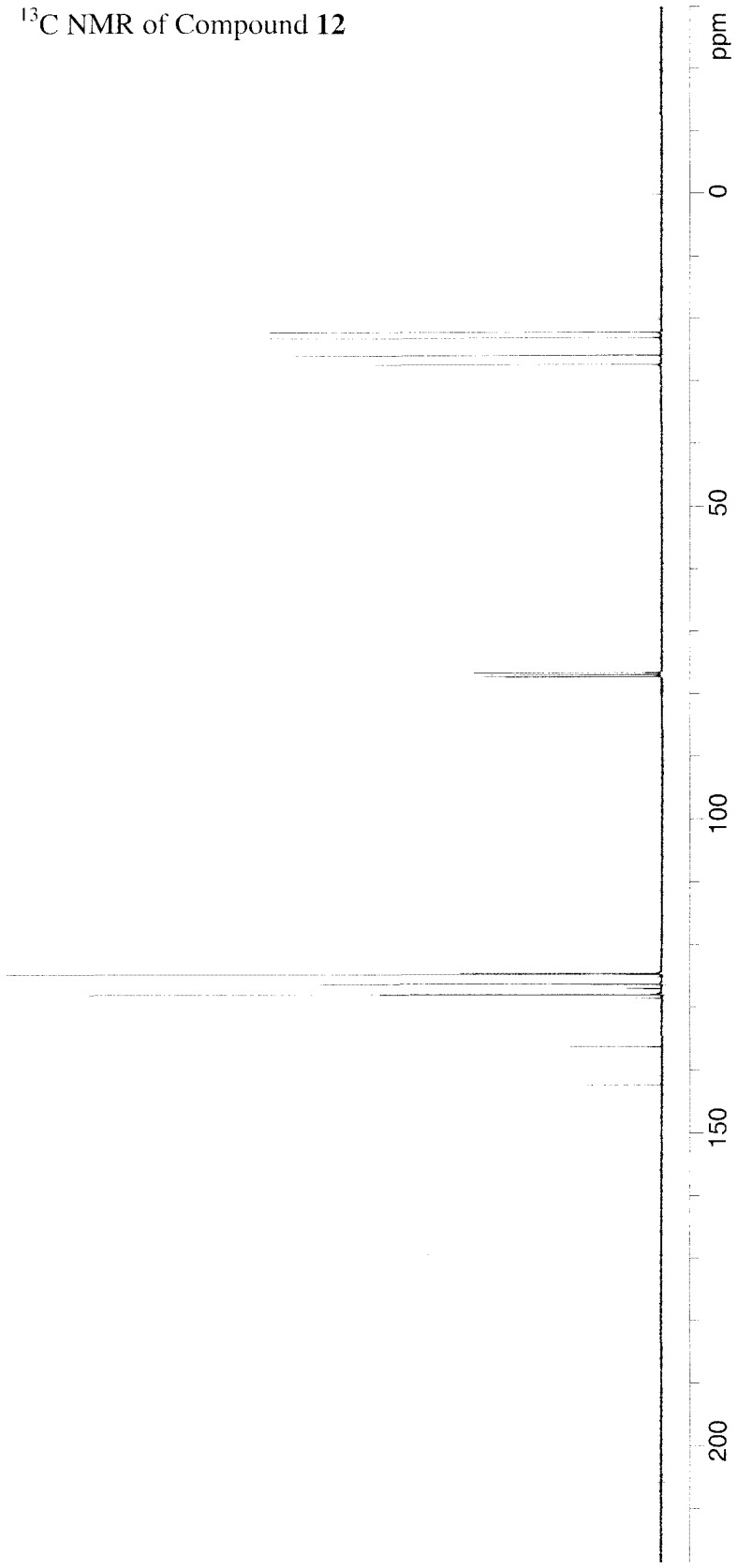

Figure **22** ^{1}H NMR of Compound **13**

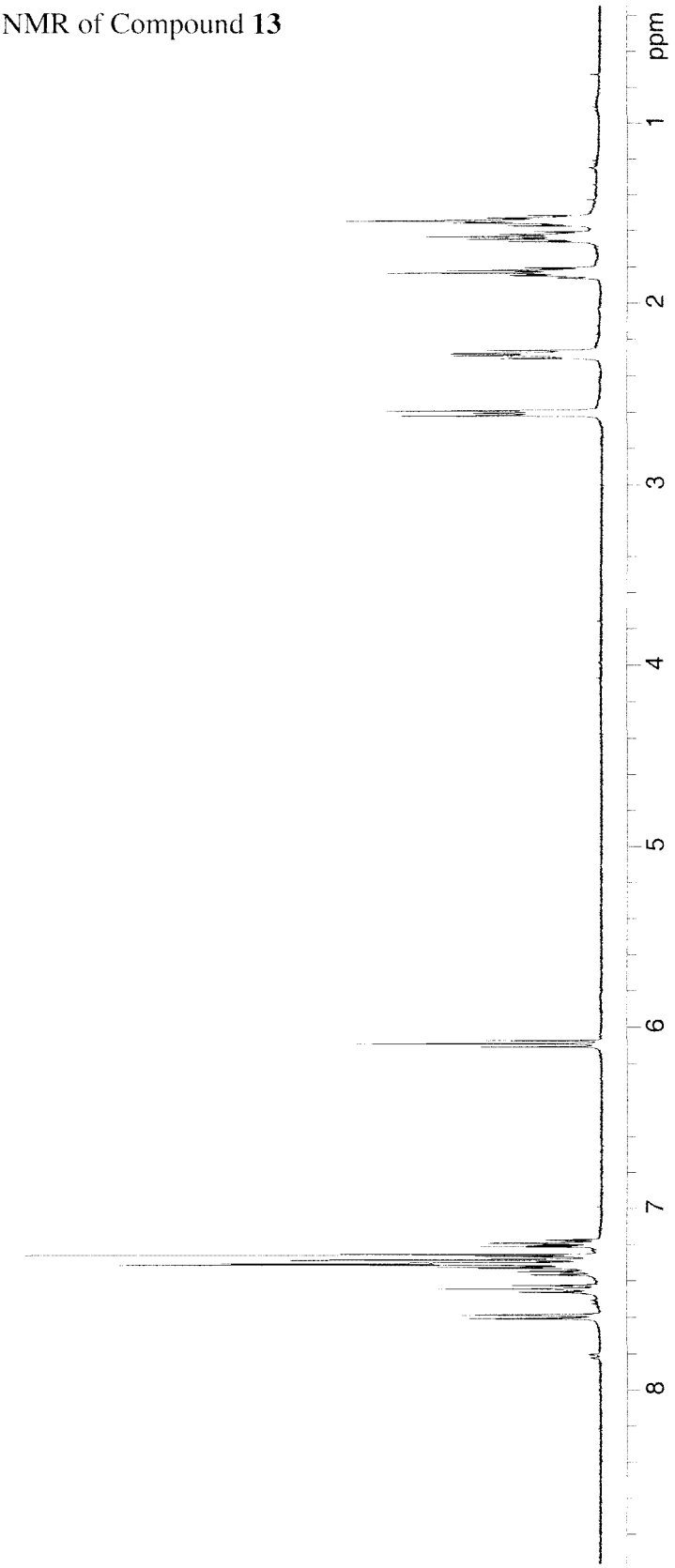

Figure **23** ^{13}C NMR of Compound **13**

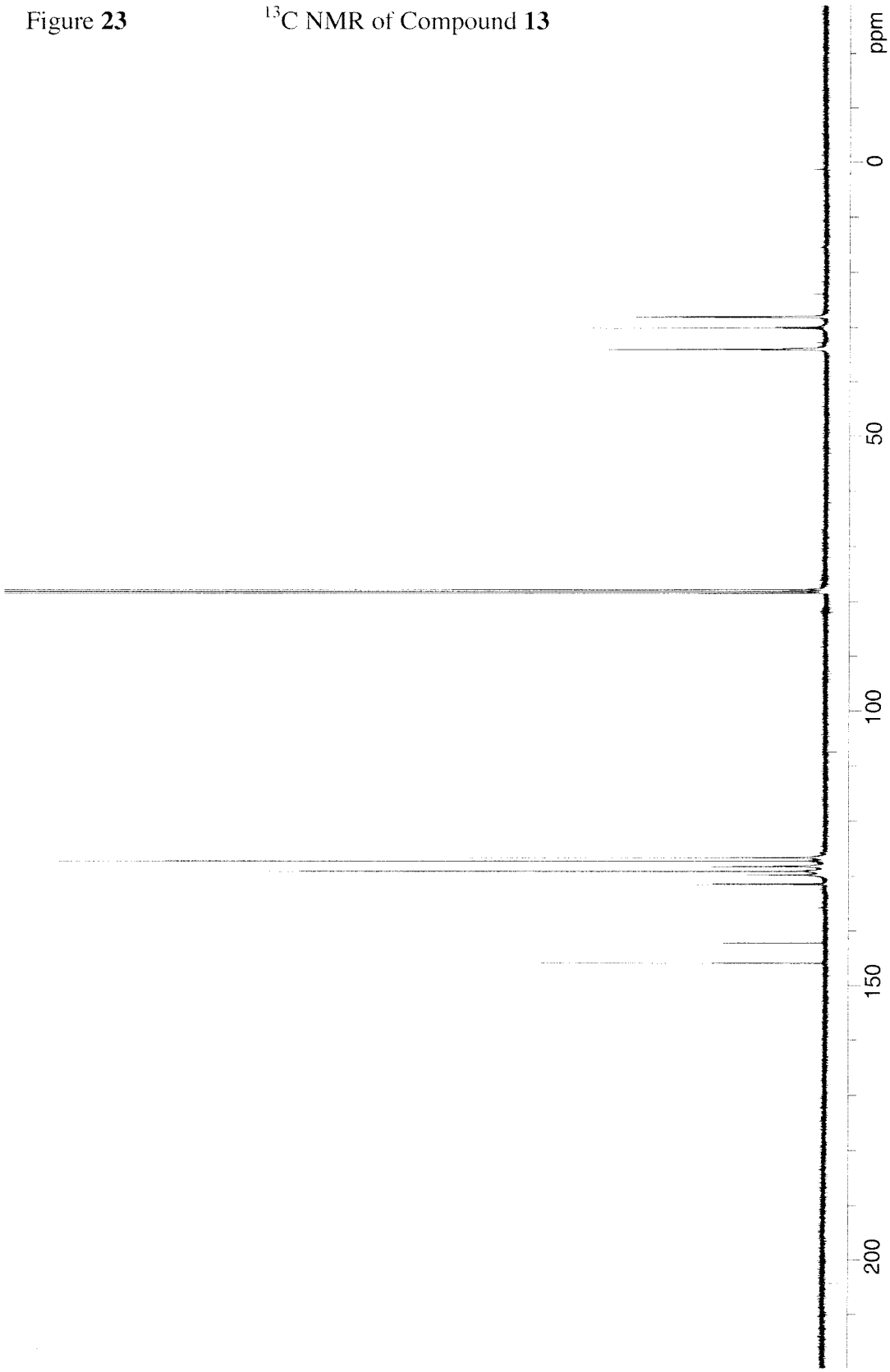

Figure **24** ^{1}H NMR of Compound **14**

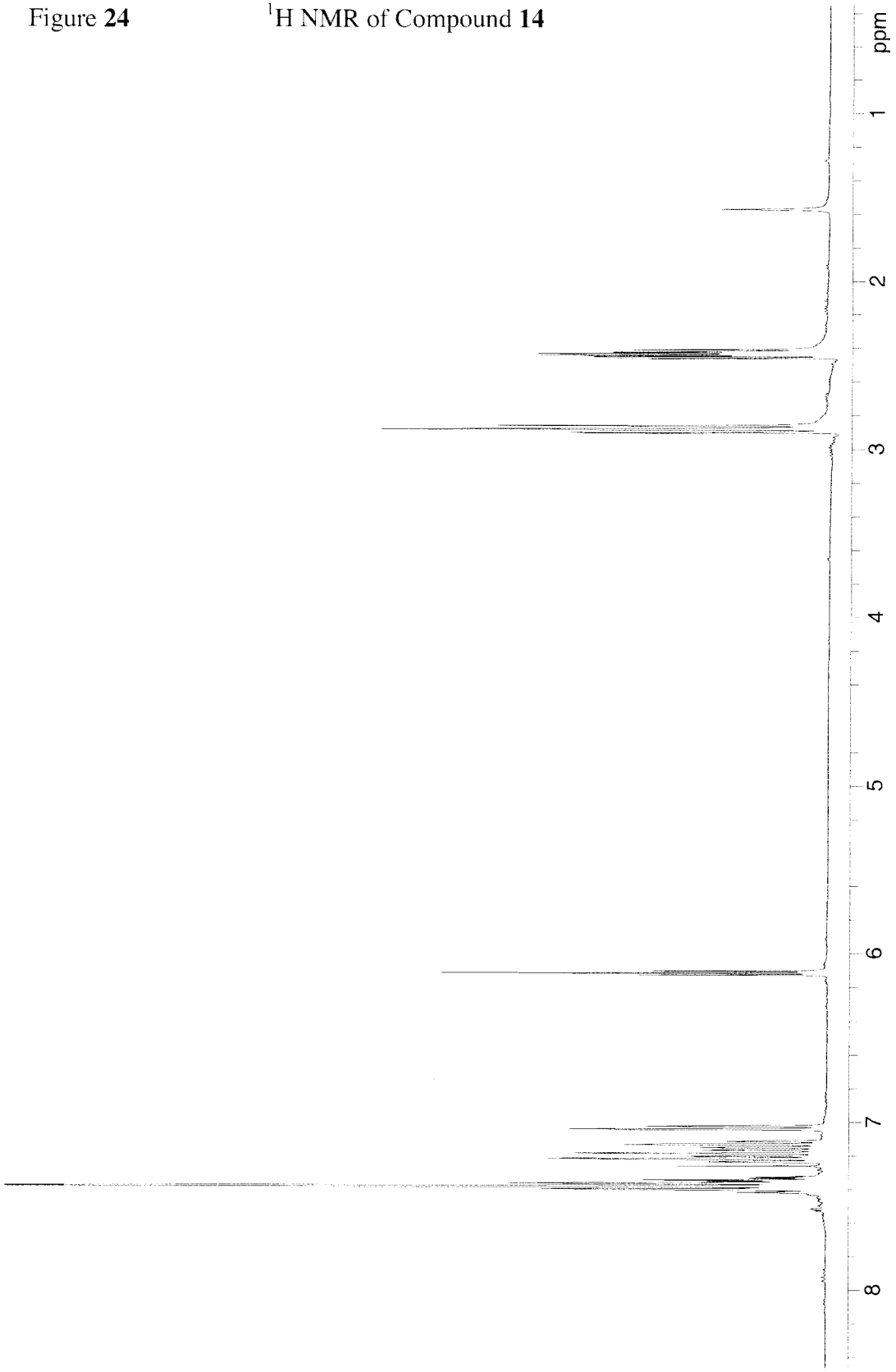

Figure **25** ^{13}C NMR of Compound **14**