SUPPORTING INFORMATION

Zirconium (IV) compounds as efficient catalysts for synthesis of α-aminophosphonates

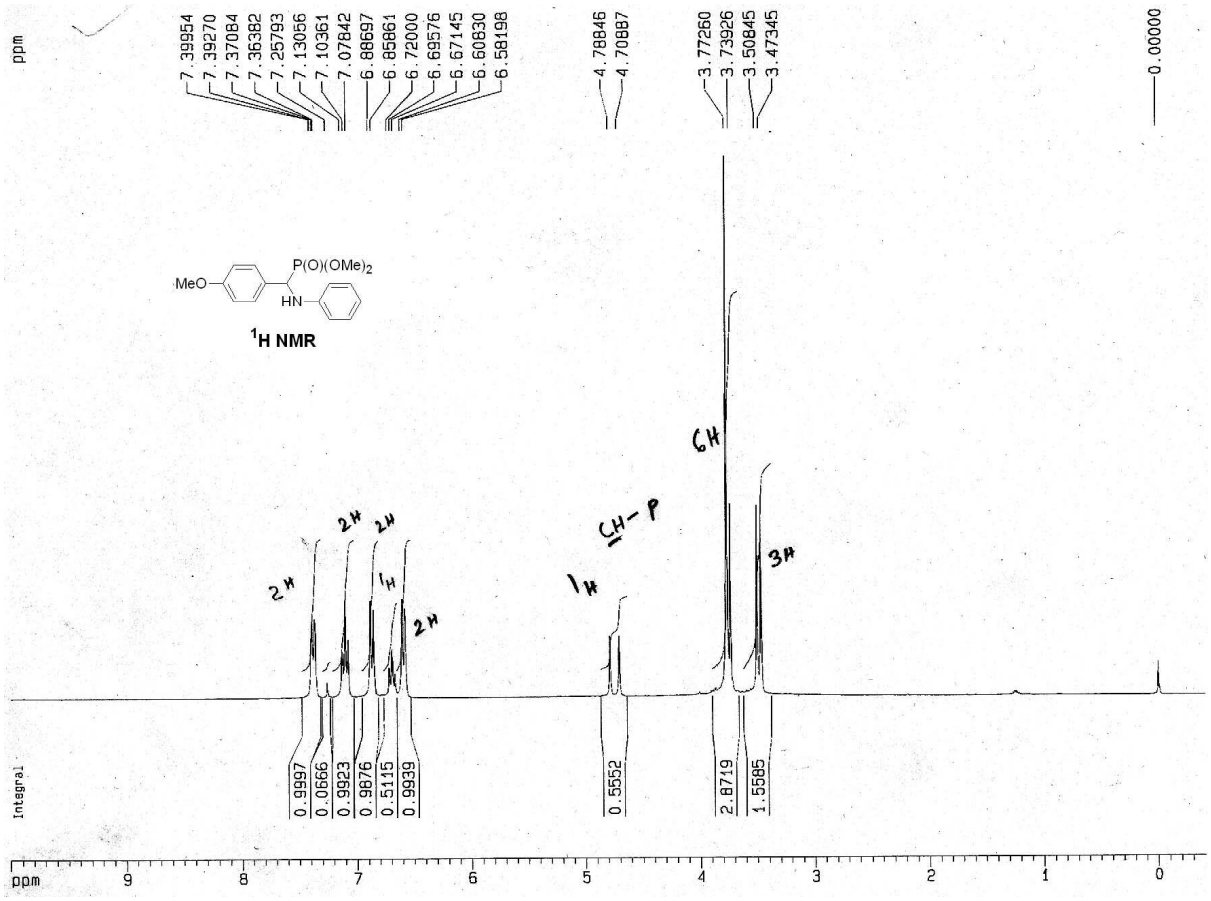
Srikant Bhagat and Asit K. Chakraborti*

Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S. A. S. Nagar, Punjab 160 062, India

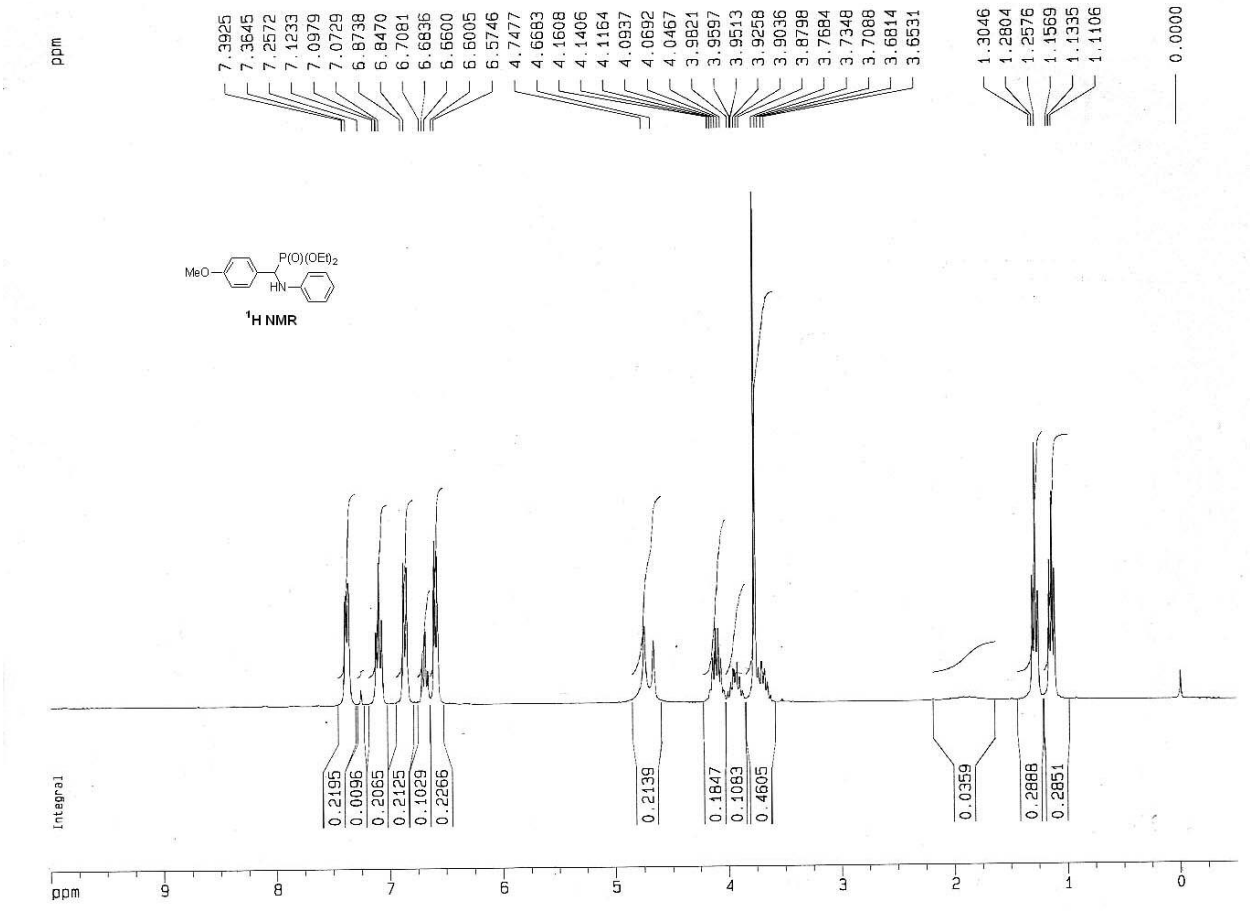
Corresponding Author: akchakraborti@niper.ac.in

Table of Contents

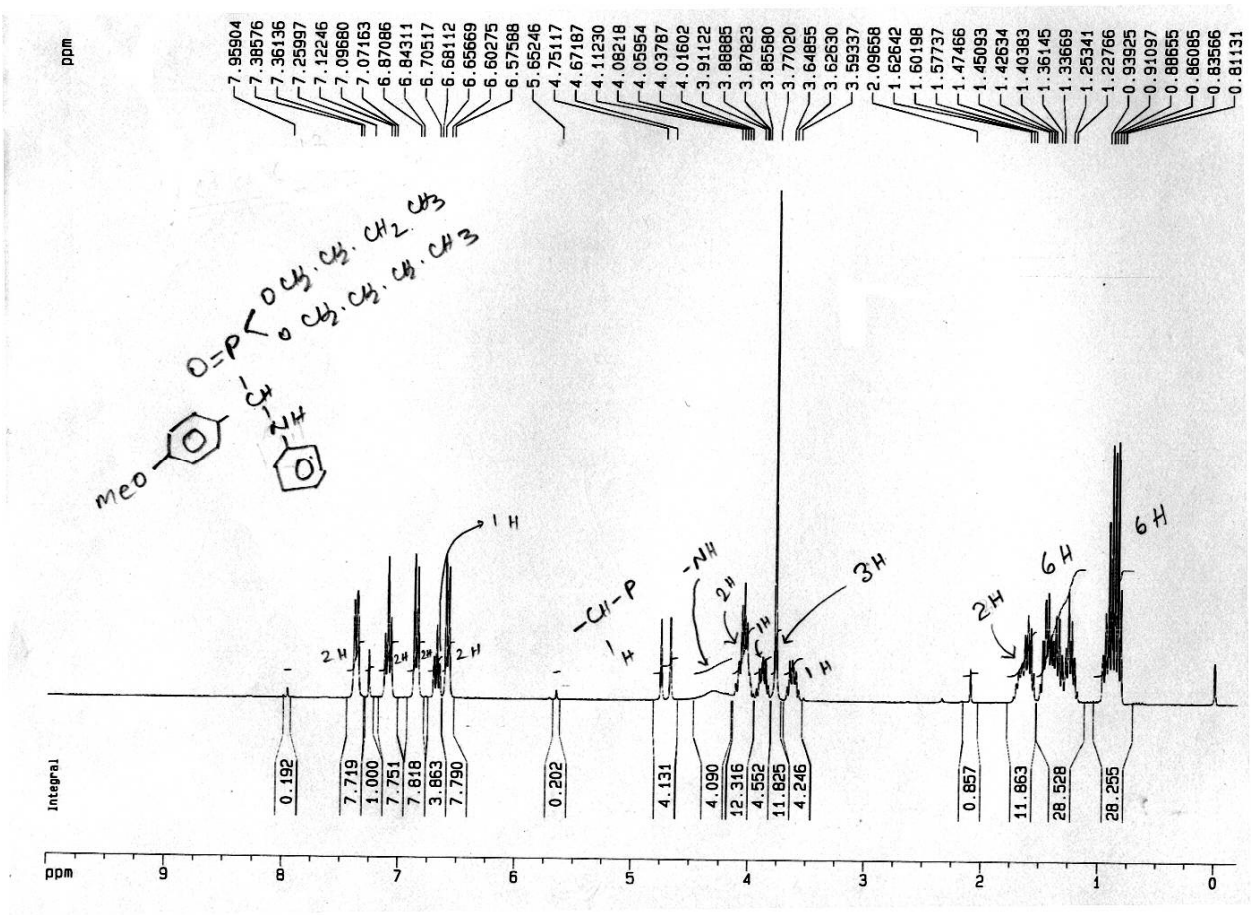
Entry 1, Table 2, ^{1}H NMR



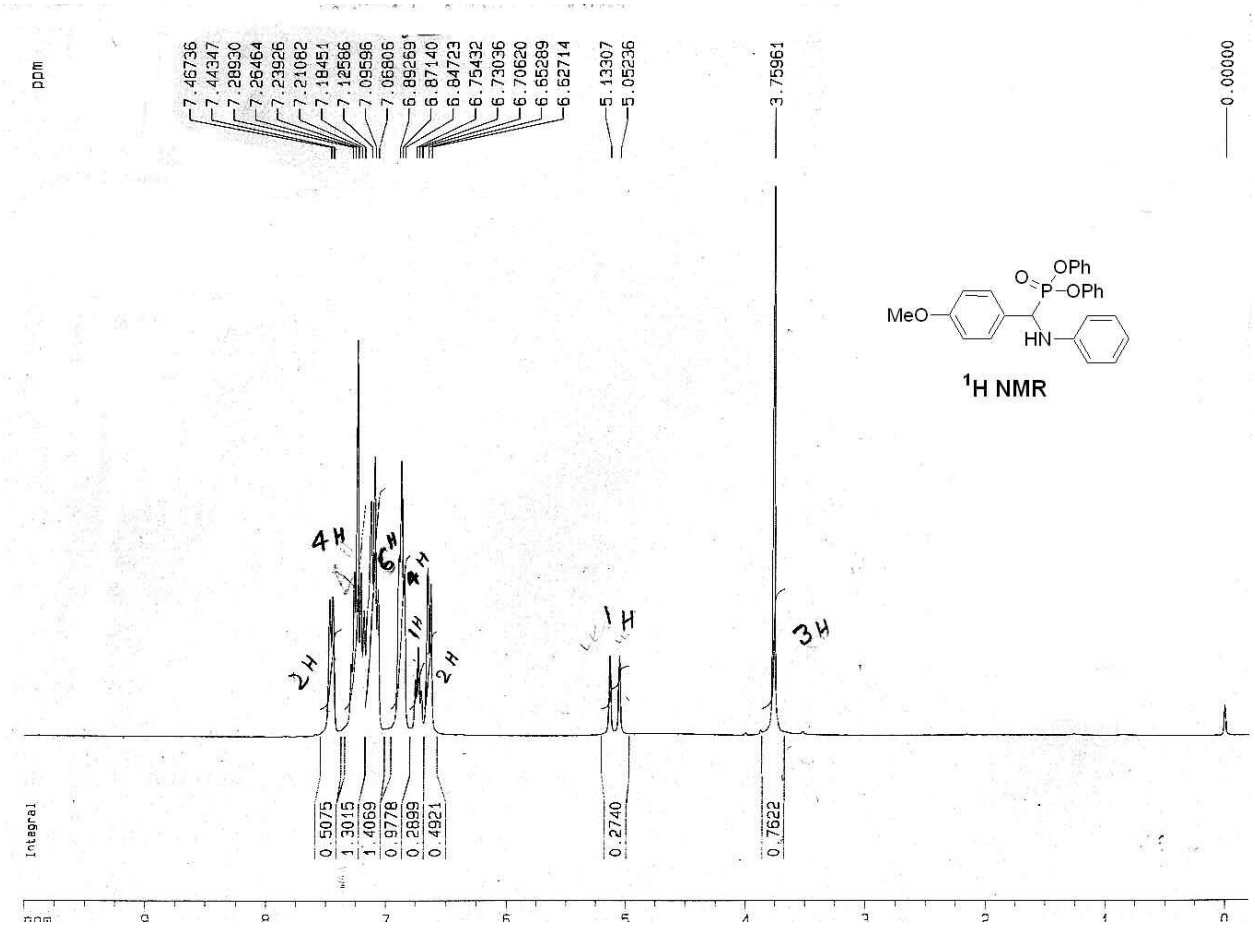
Entry 2, Table 2, ^{1}H NMR



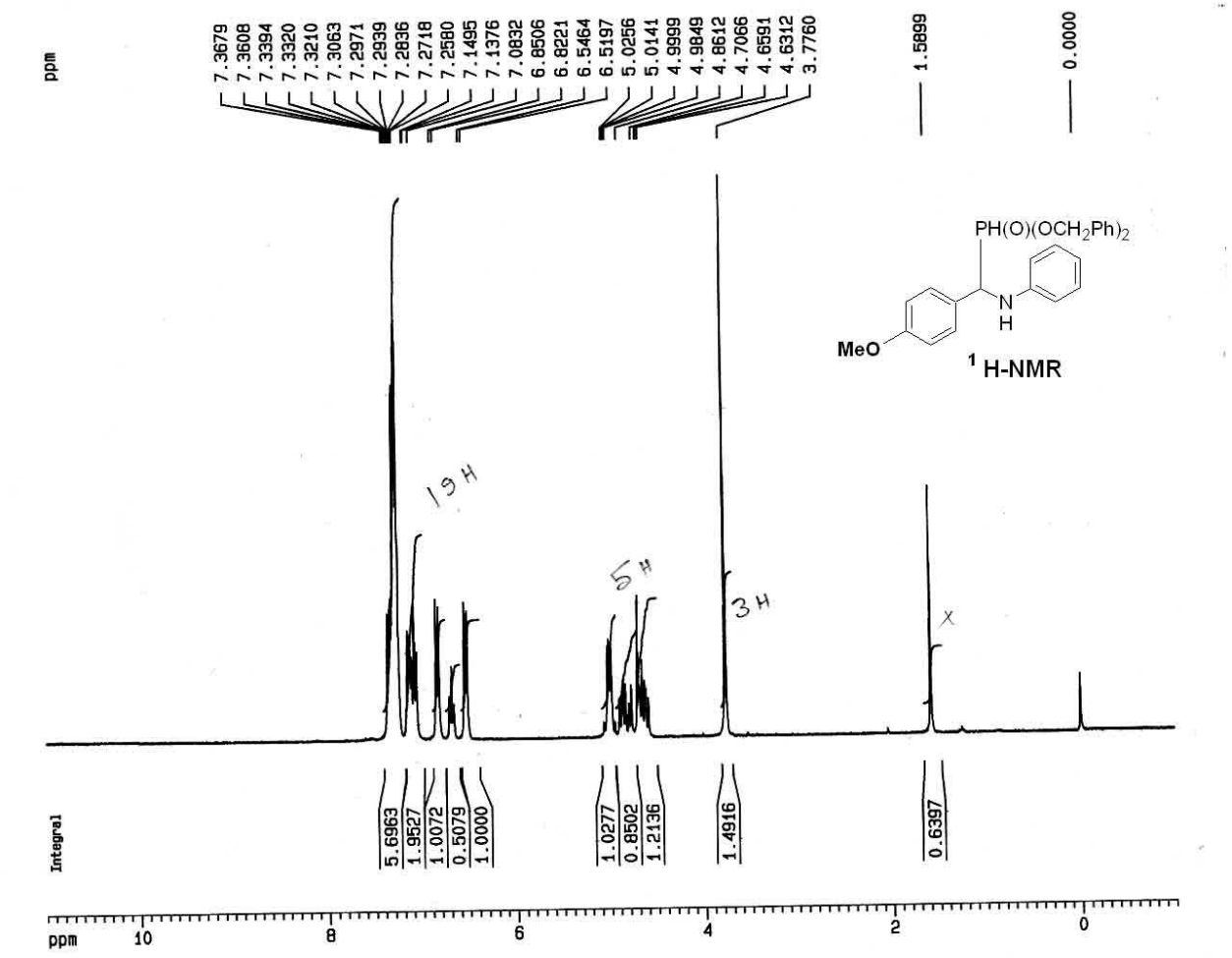
Entry 3, Table 2, ^{1}H NMR



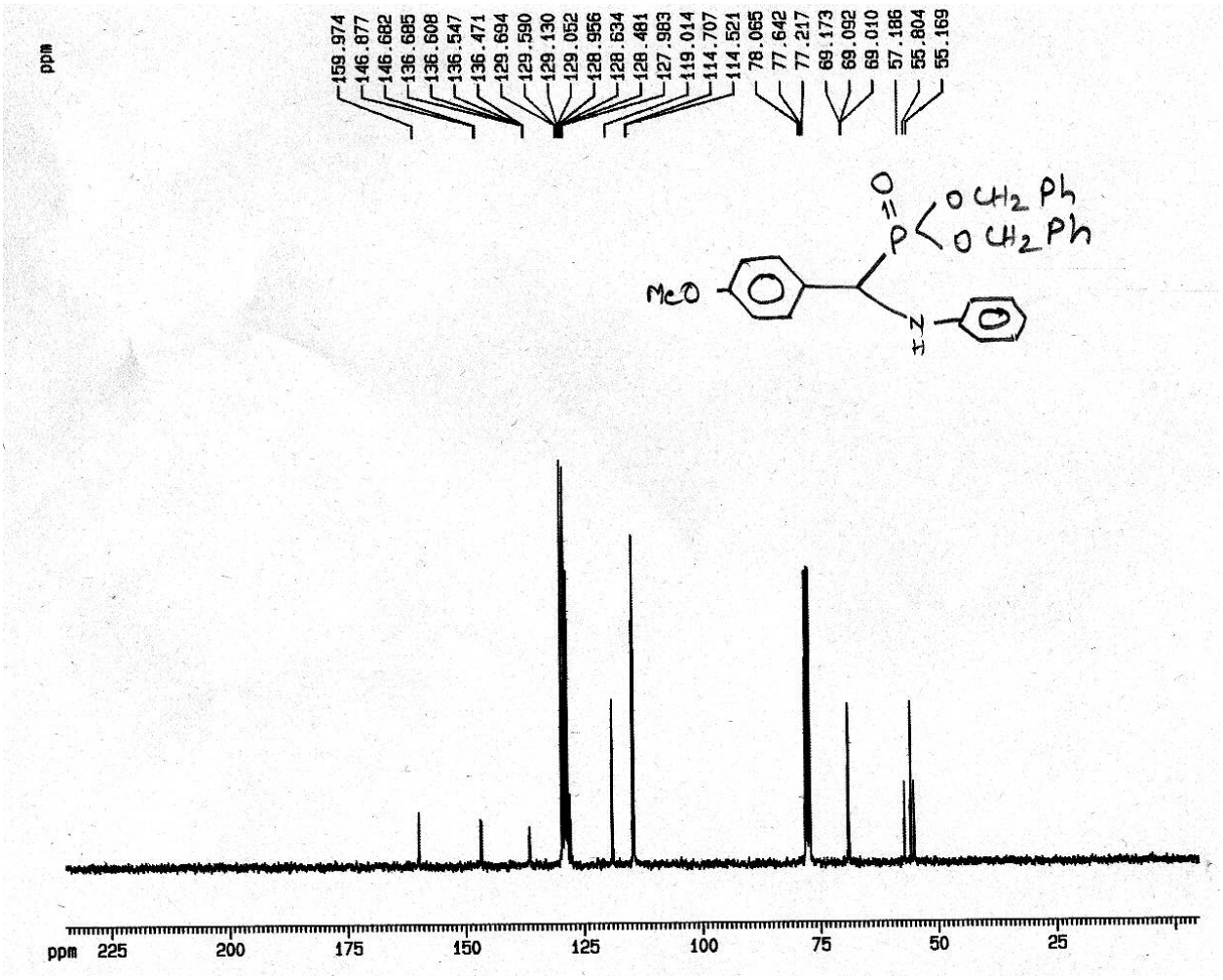
Entry 4, Table 2, ^{1}H NMR



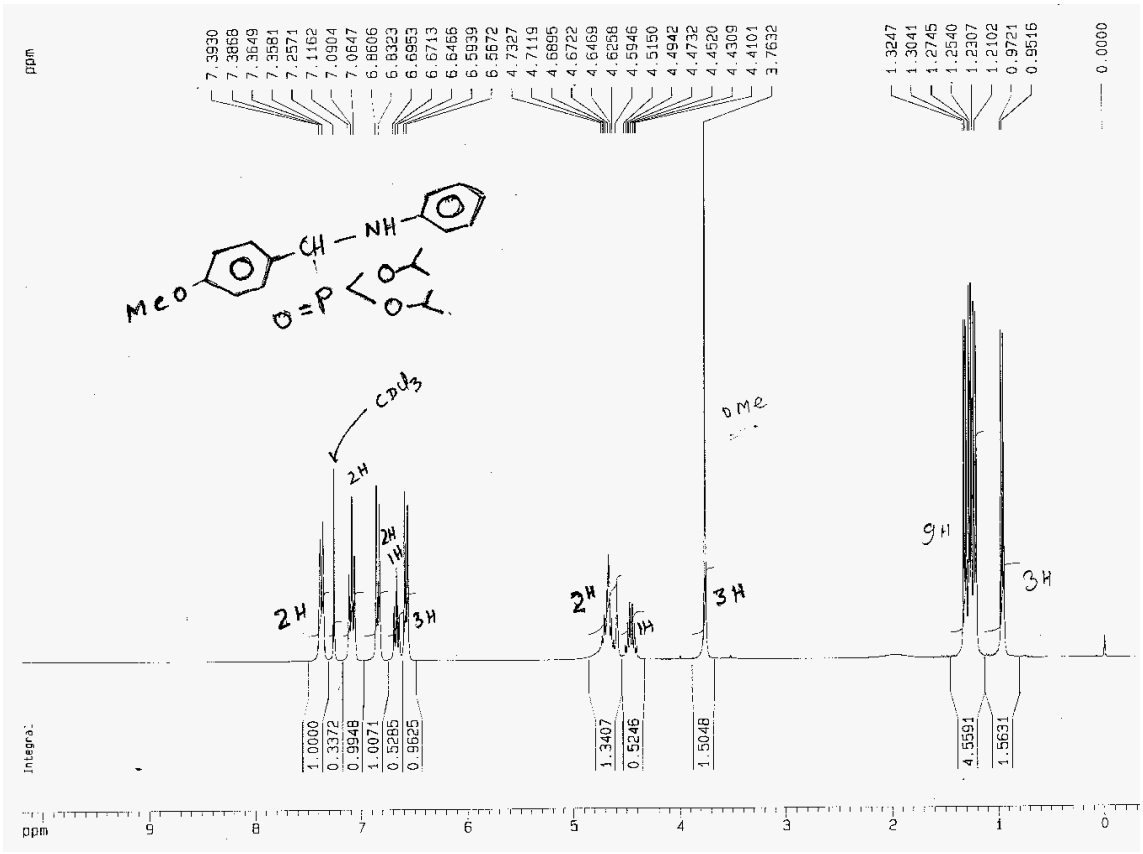
Entry 5, Table 2, ^{1}H NMR



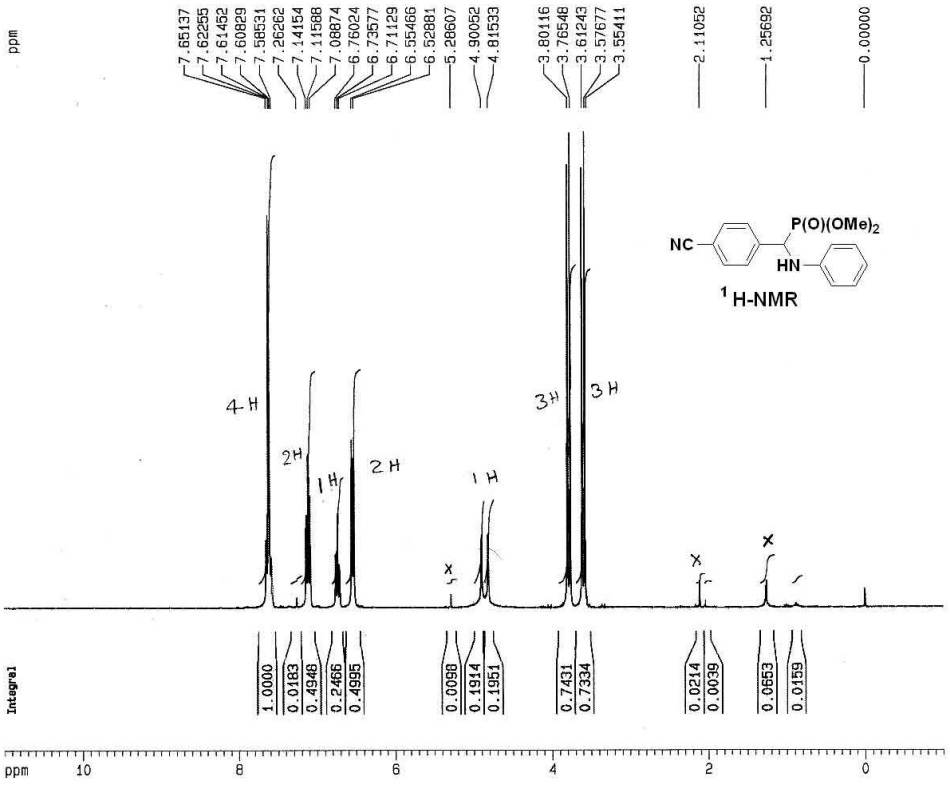
Entry 5, Table 2, ^{13}C NMR



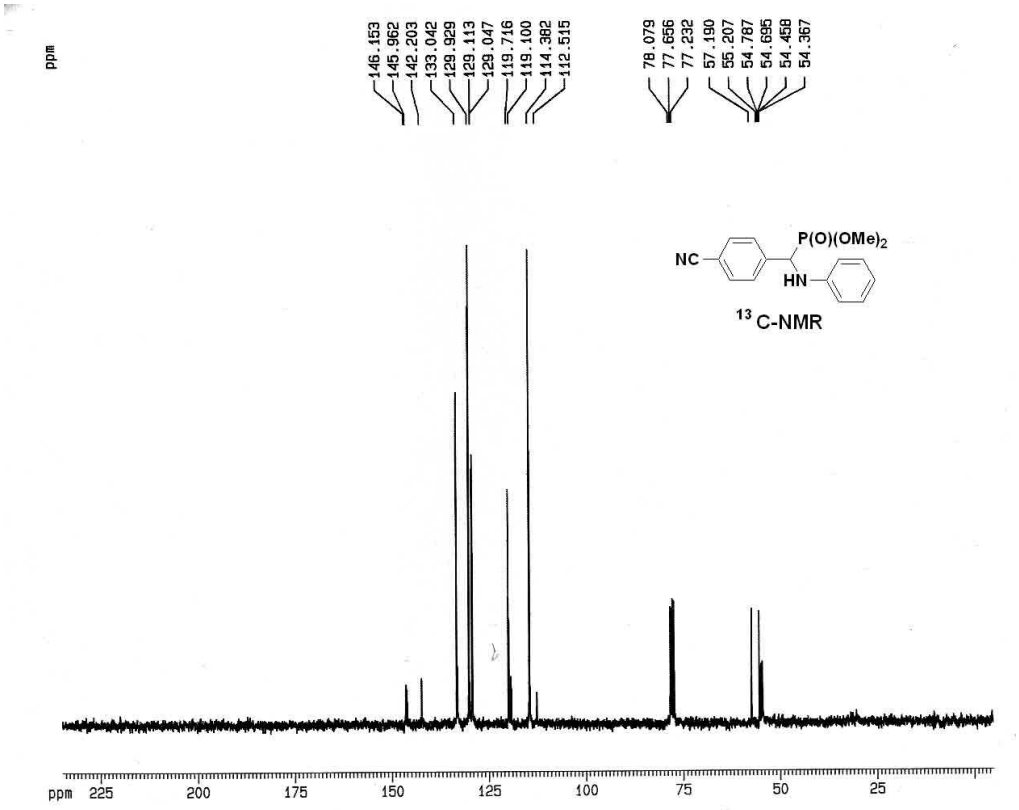
Entry 8, Table 2, ^{1}H NMR



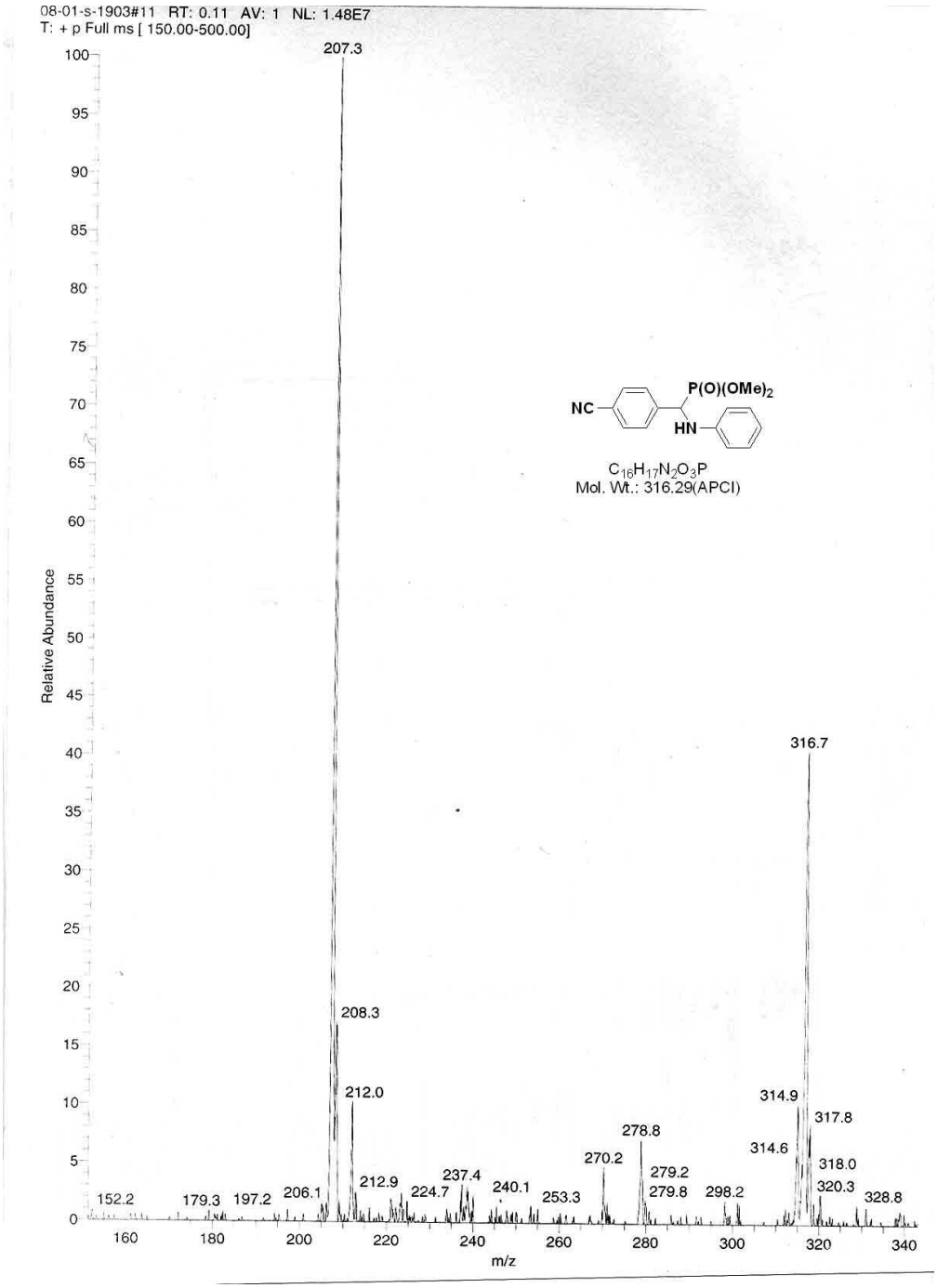
Entry 4, Table 3, ^{1}H NMR



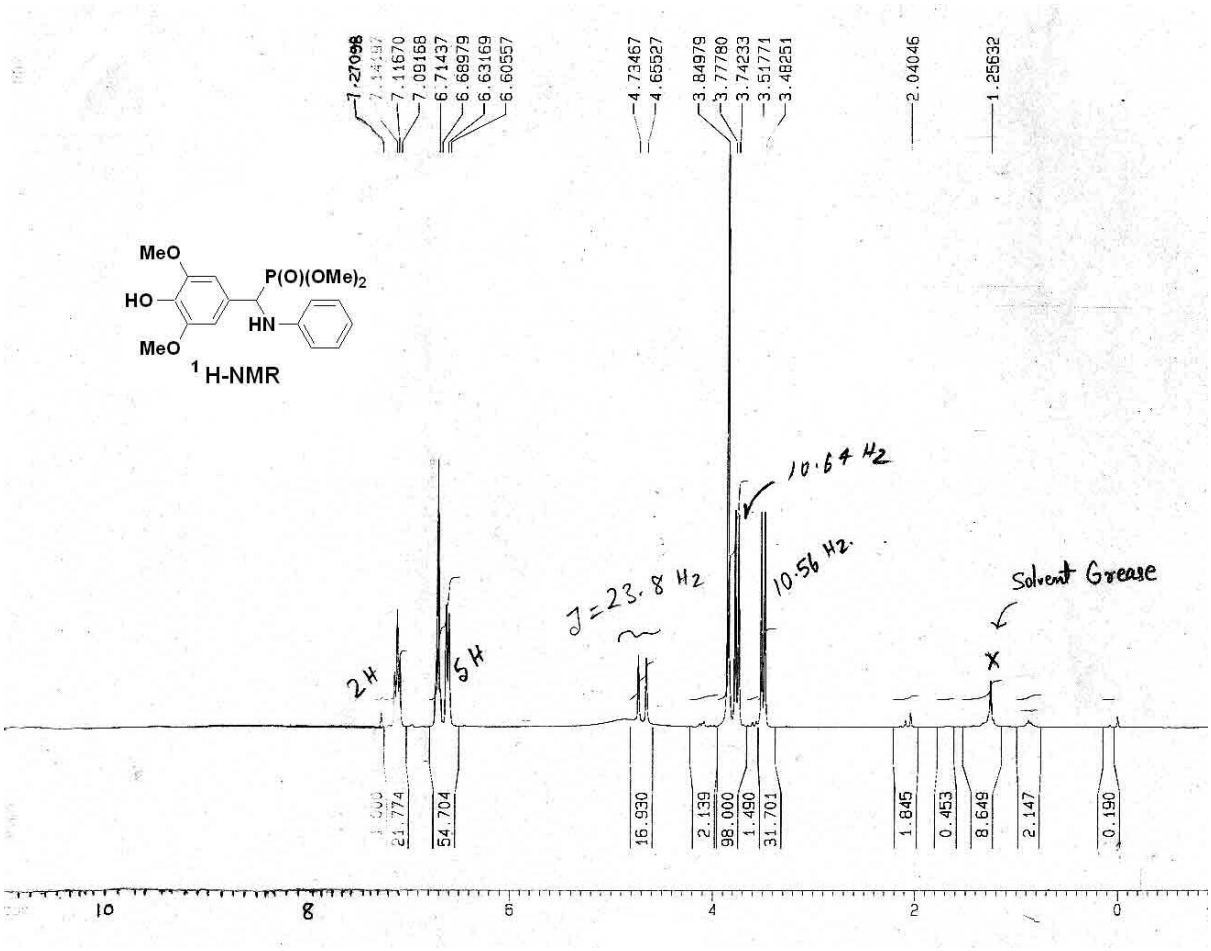
Entry 4, Table 3, ^{13}C NMR



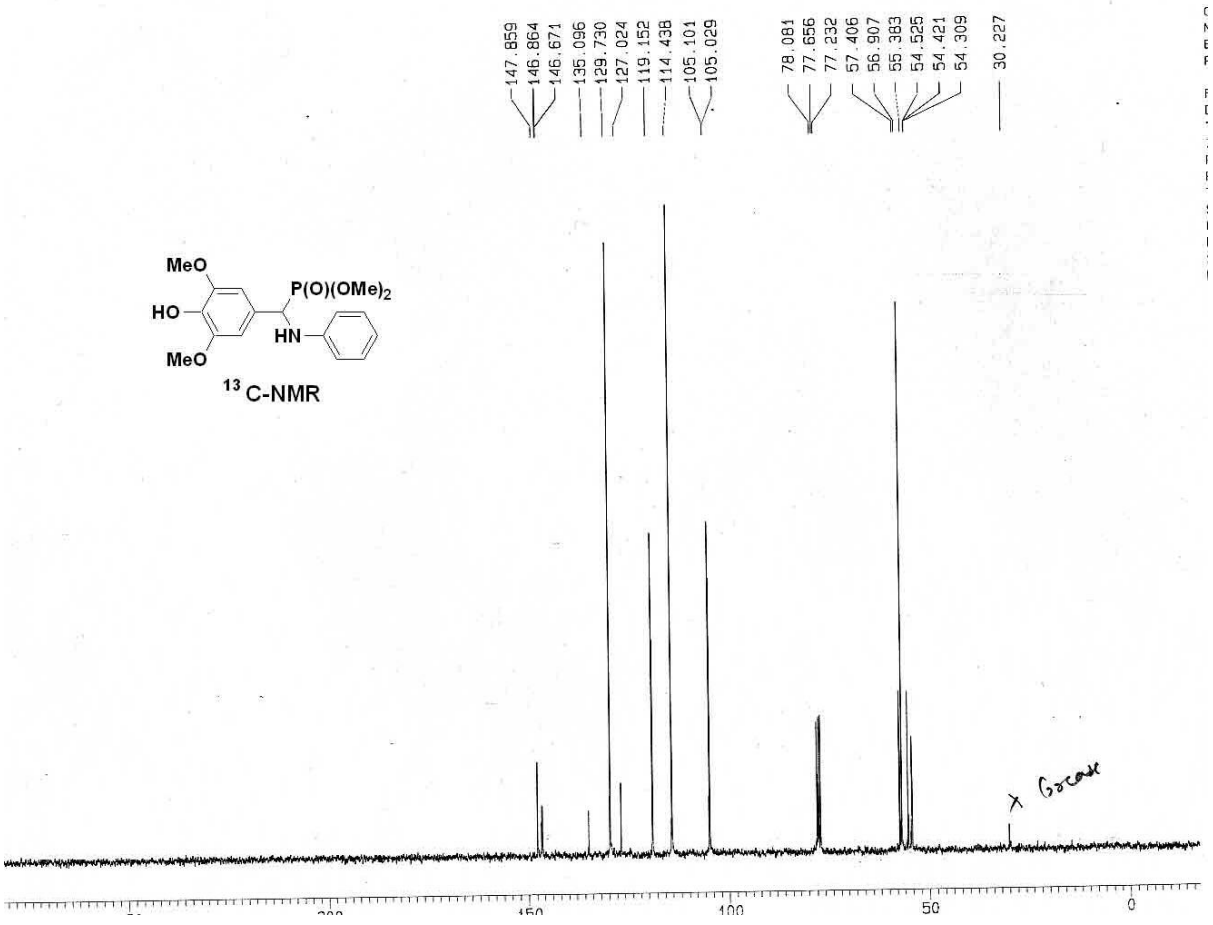
Entry 4, Table 3, Mass (APCI)



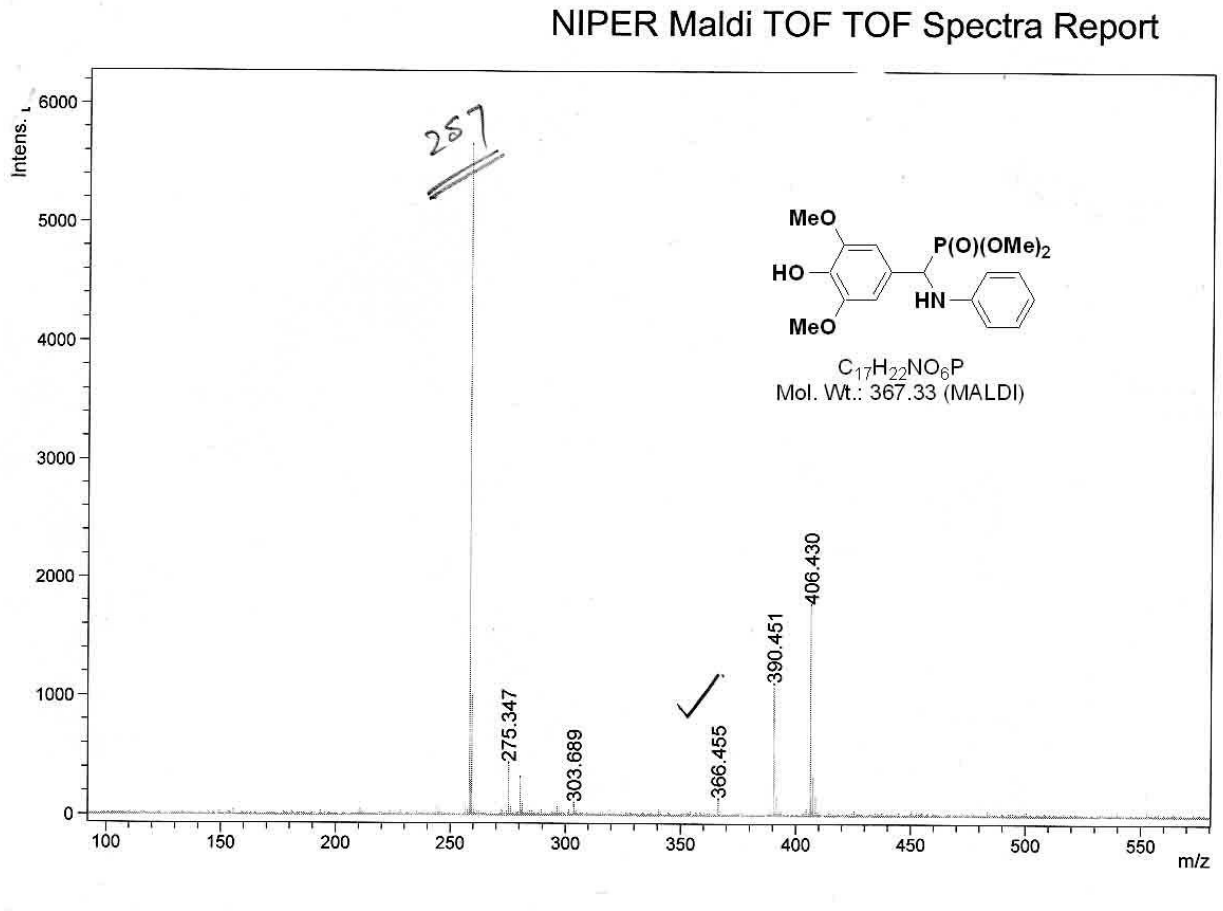
Entry 6, Table 3, ^{1}H NMR



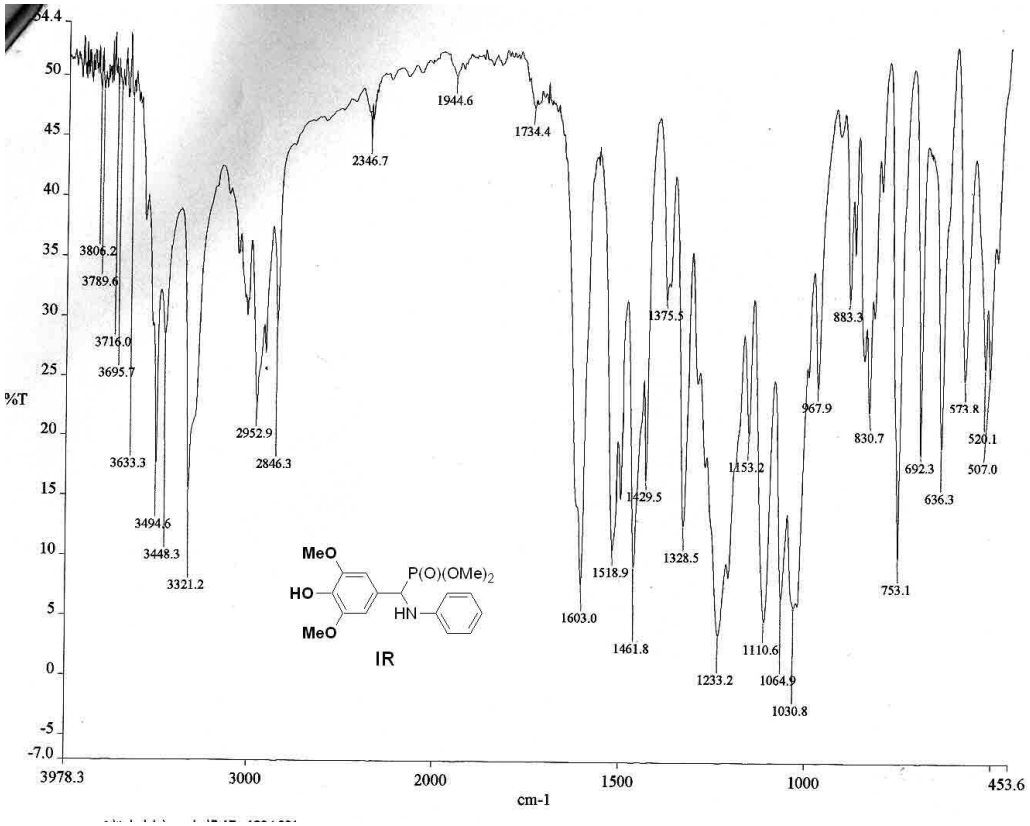
Entry 6, Table 3, ^{13}C NMR



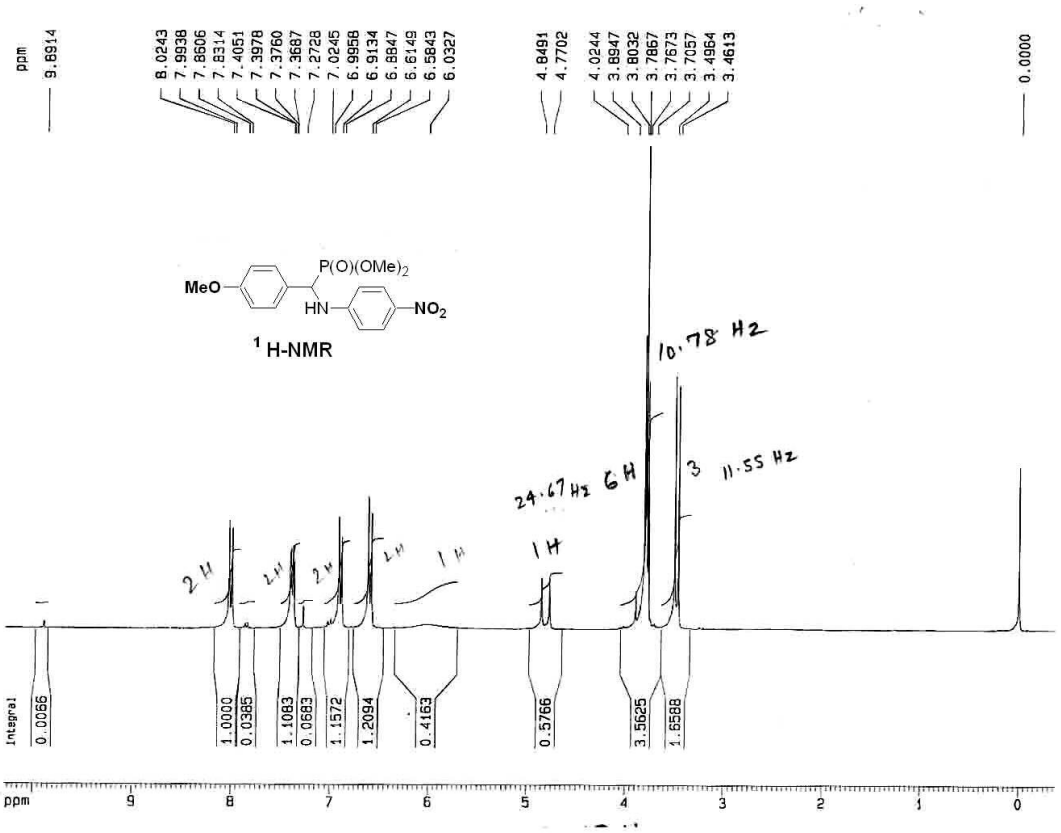
Entry 6, Table 3, Mass Spectra (MALDI, ESI)



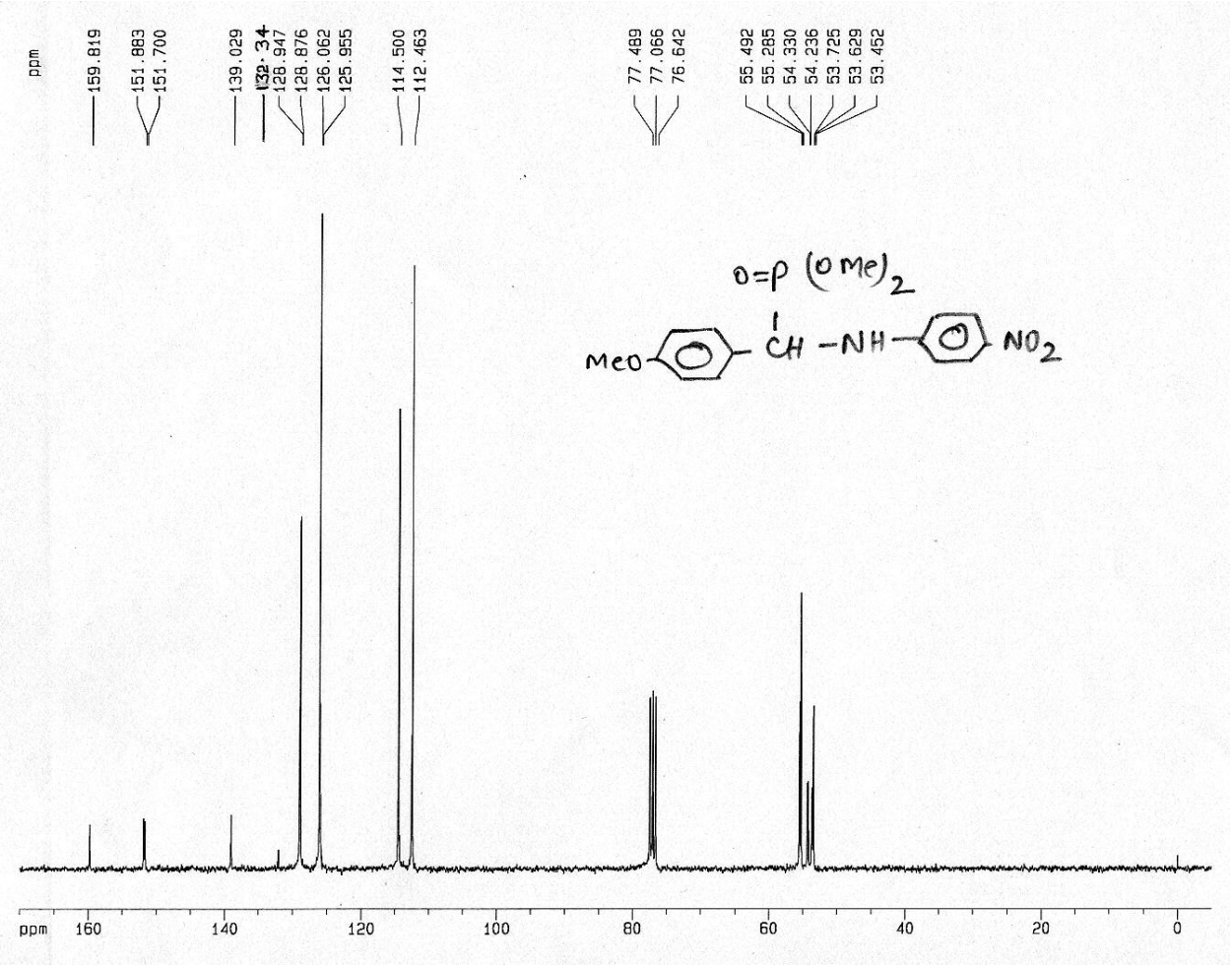
Entry 6, Table 3, IR



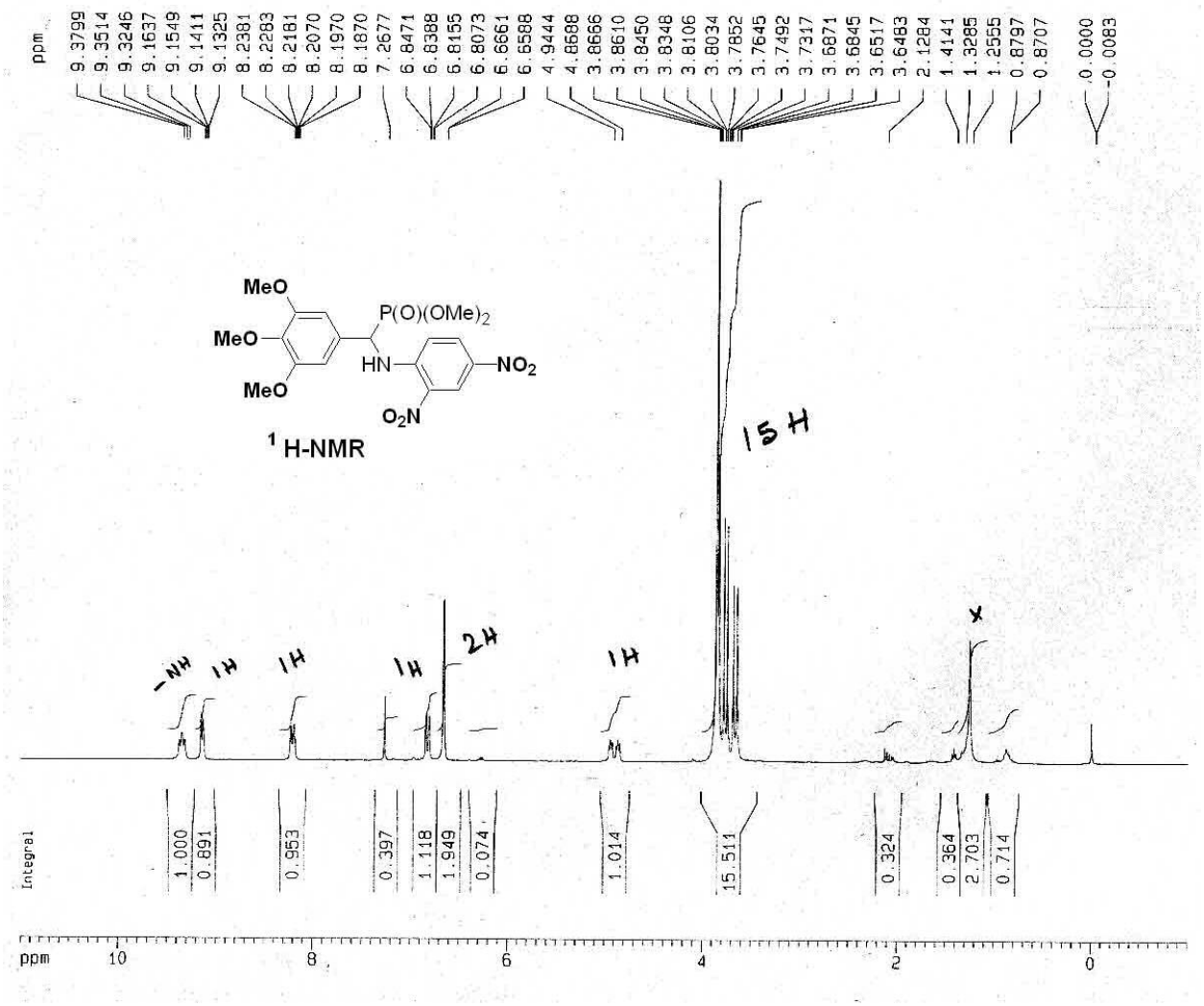
Entry 7, Table 3, ^{1}H NMR



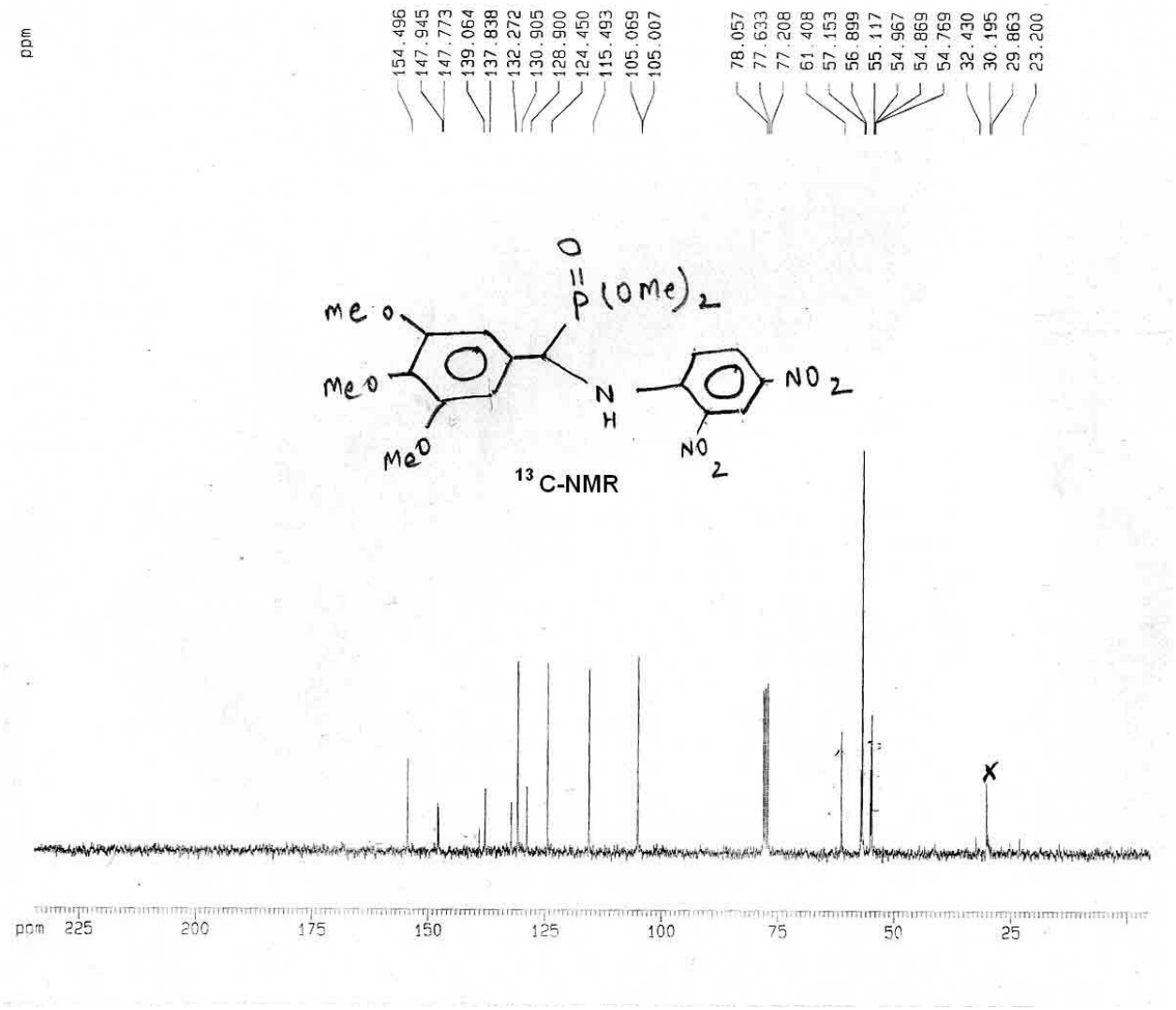
Entry 7, Table 3, ^{13}C NMR



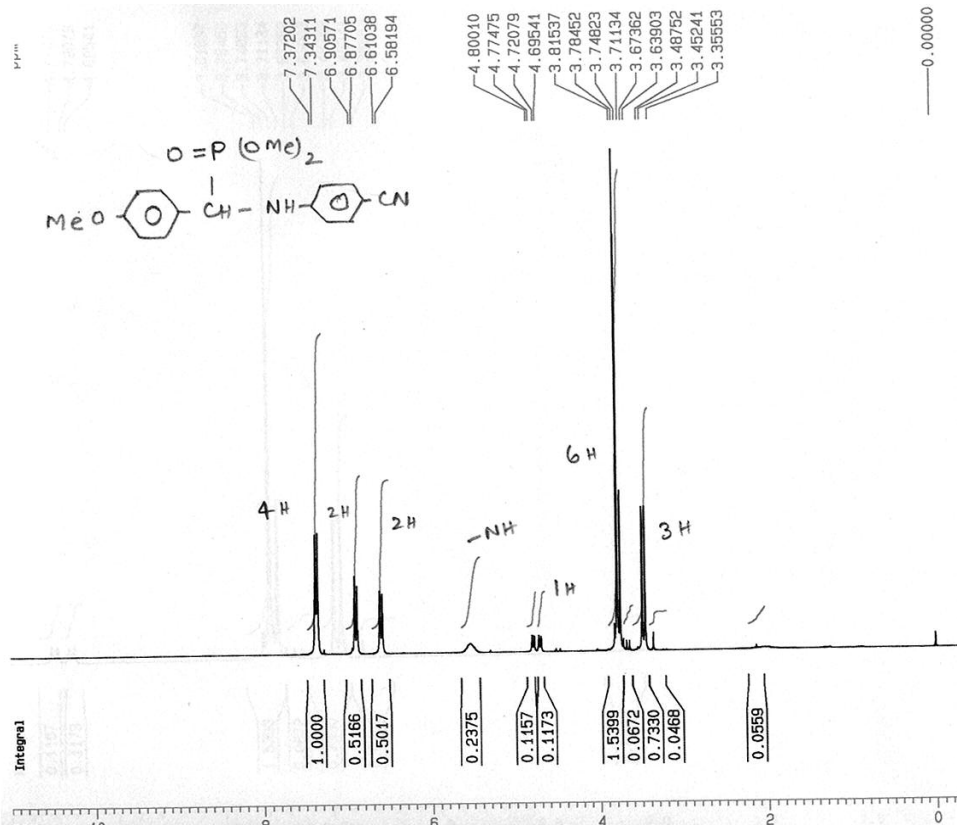
Entry 13, Table 3, ^{1}H NMR



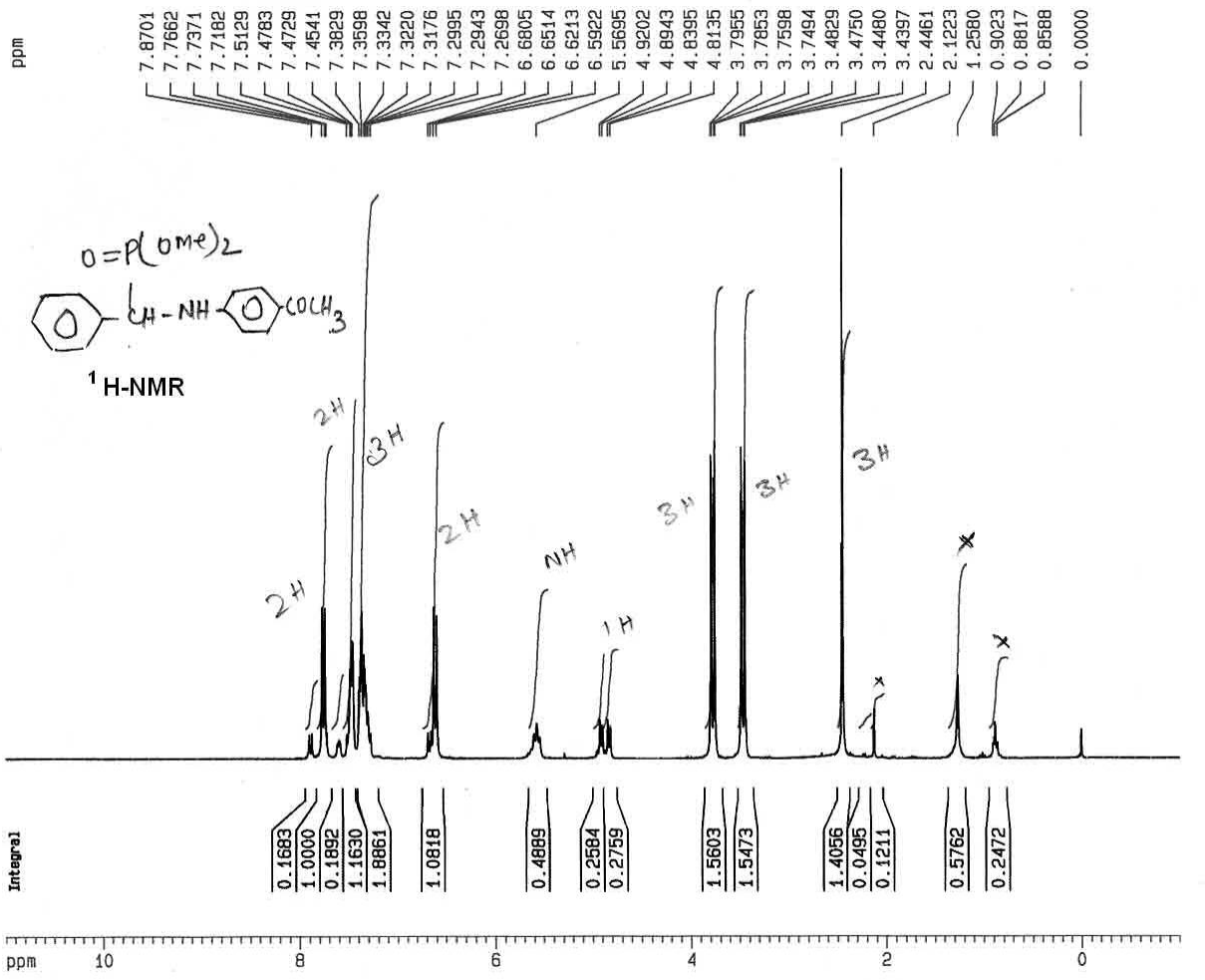
Entry 13, Table 3, ^{13}C NMR



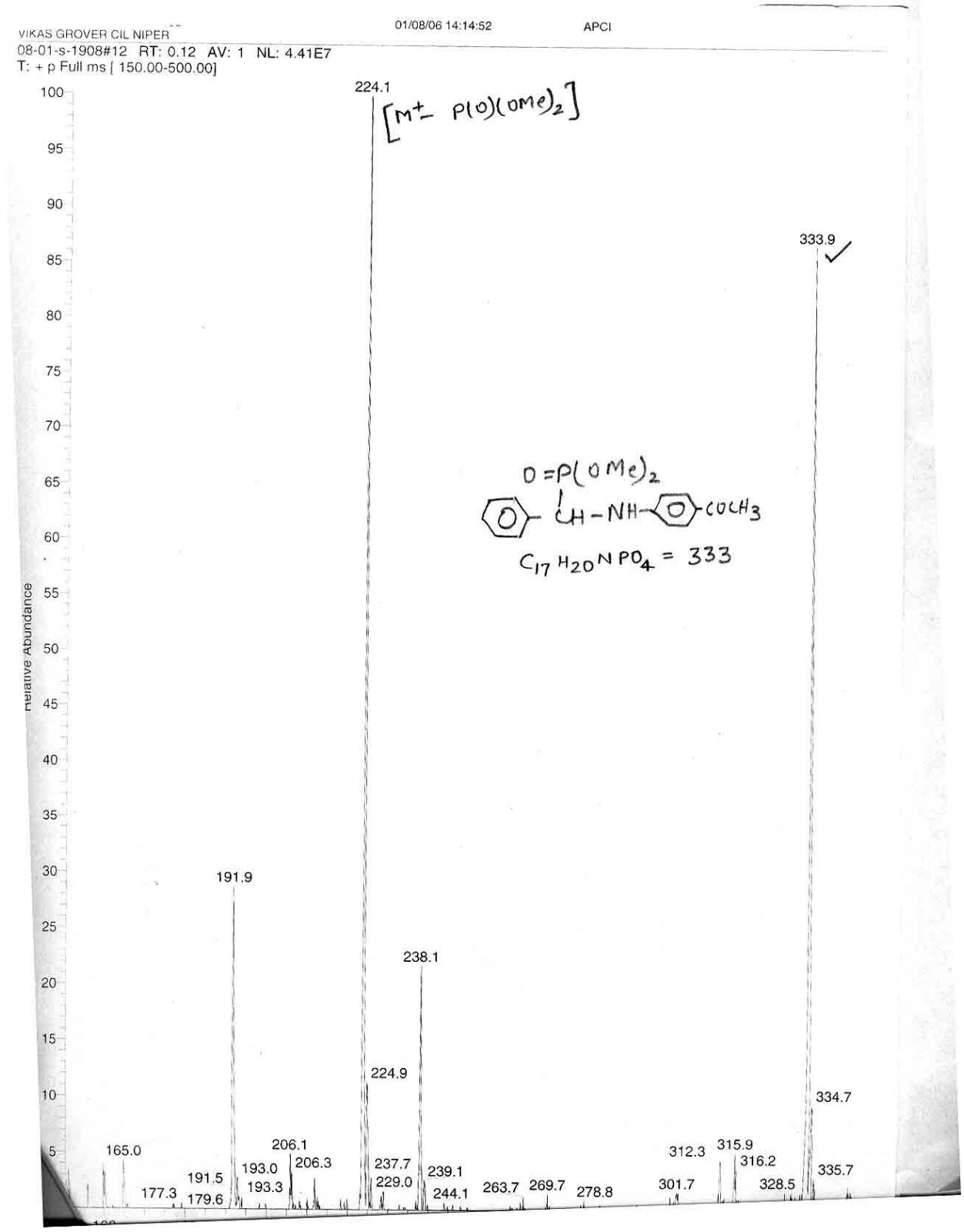
Entry 14, Table 3, ^{1}H NMR



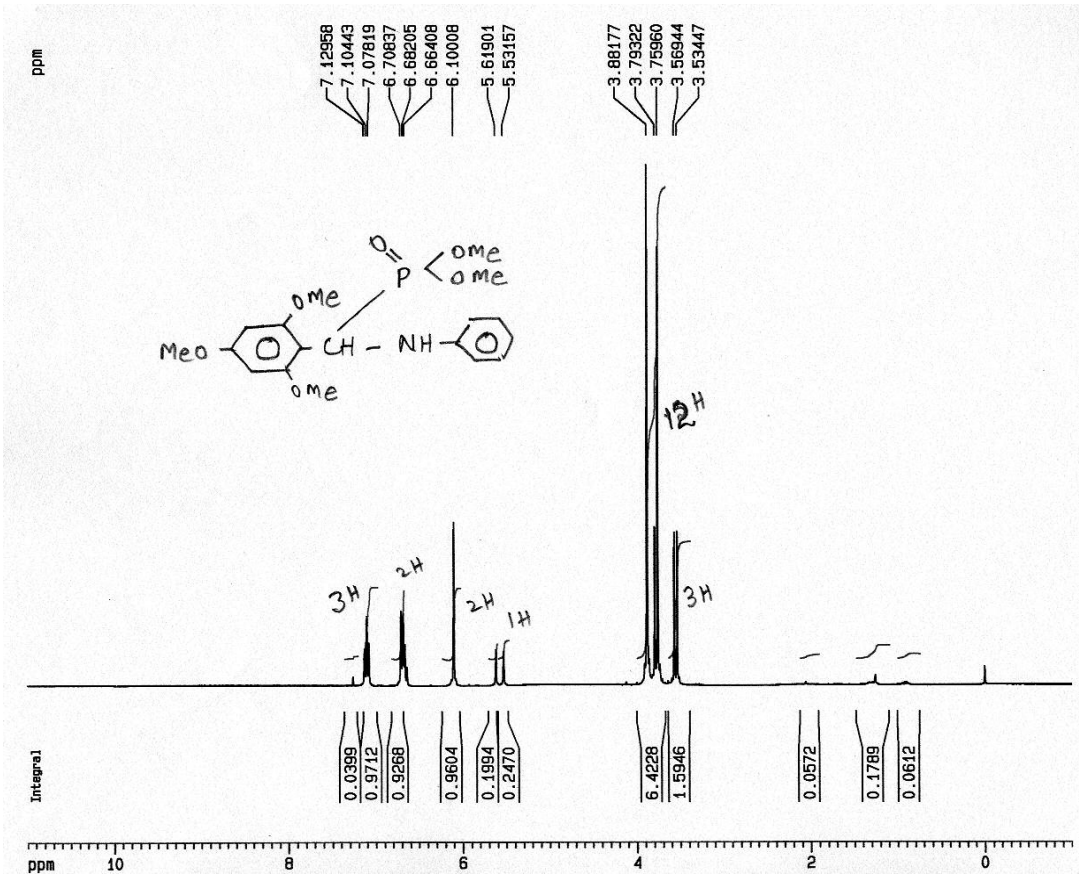
Entry 15, Table 3, ^{1}H NMR



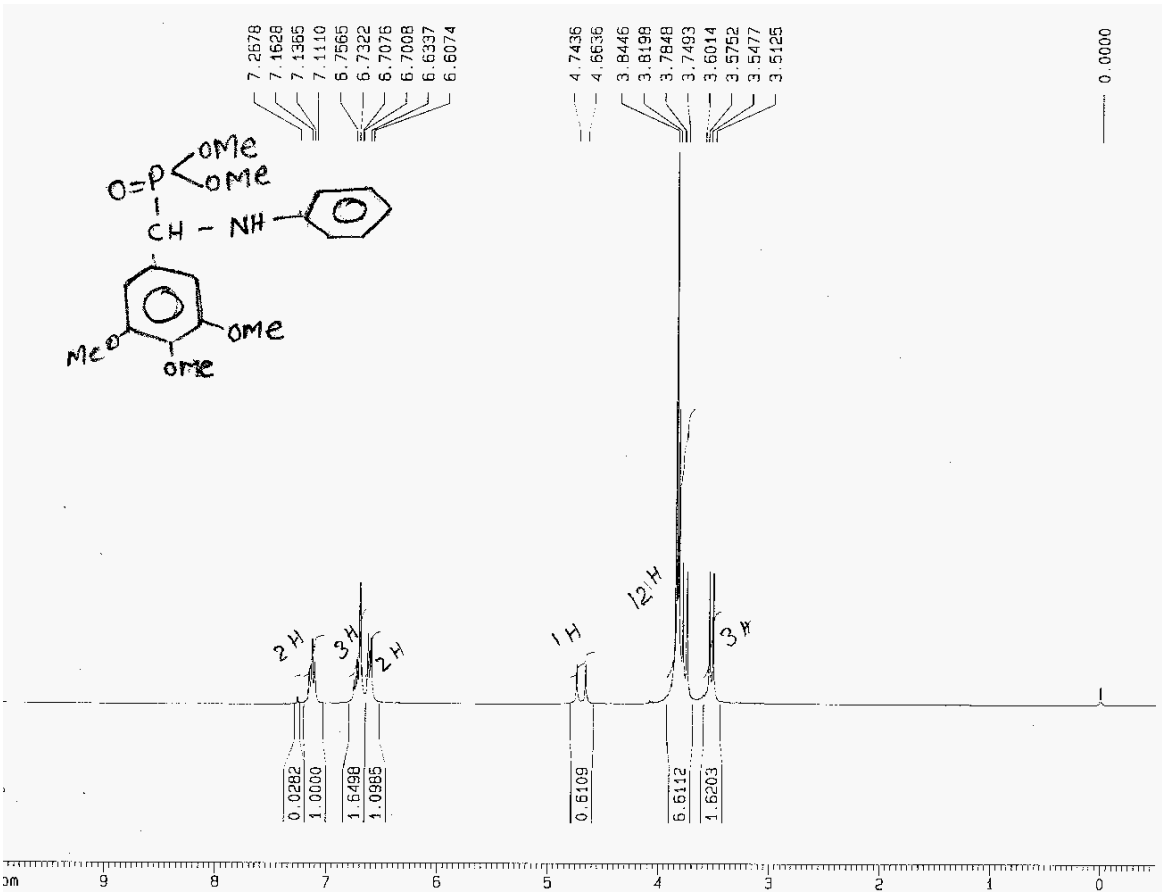
Entry 15, Table 3, Mass (APCI)



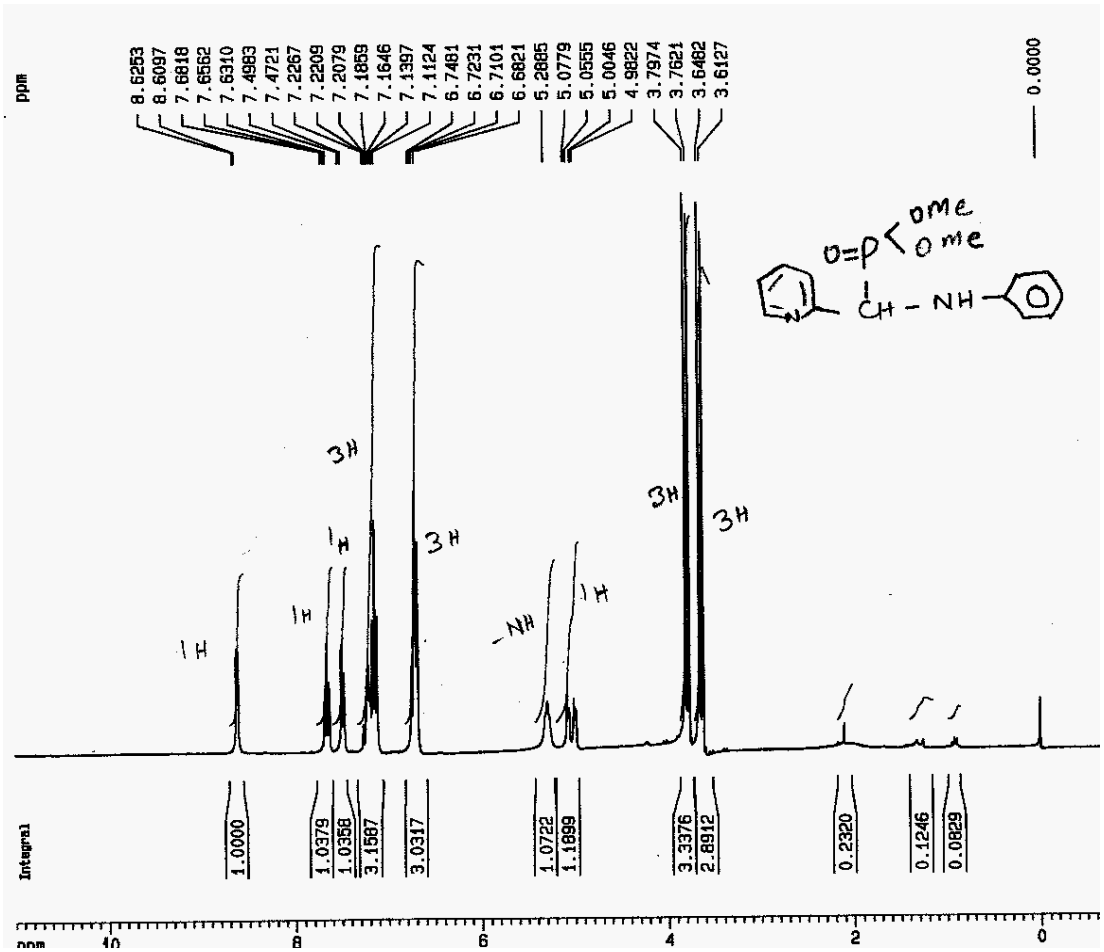
Entry 22, Table 3, ^{1}H NMR



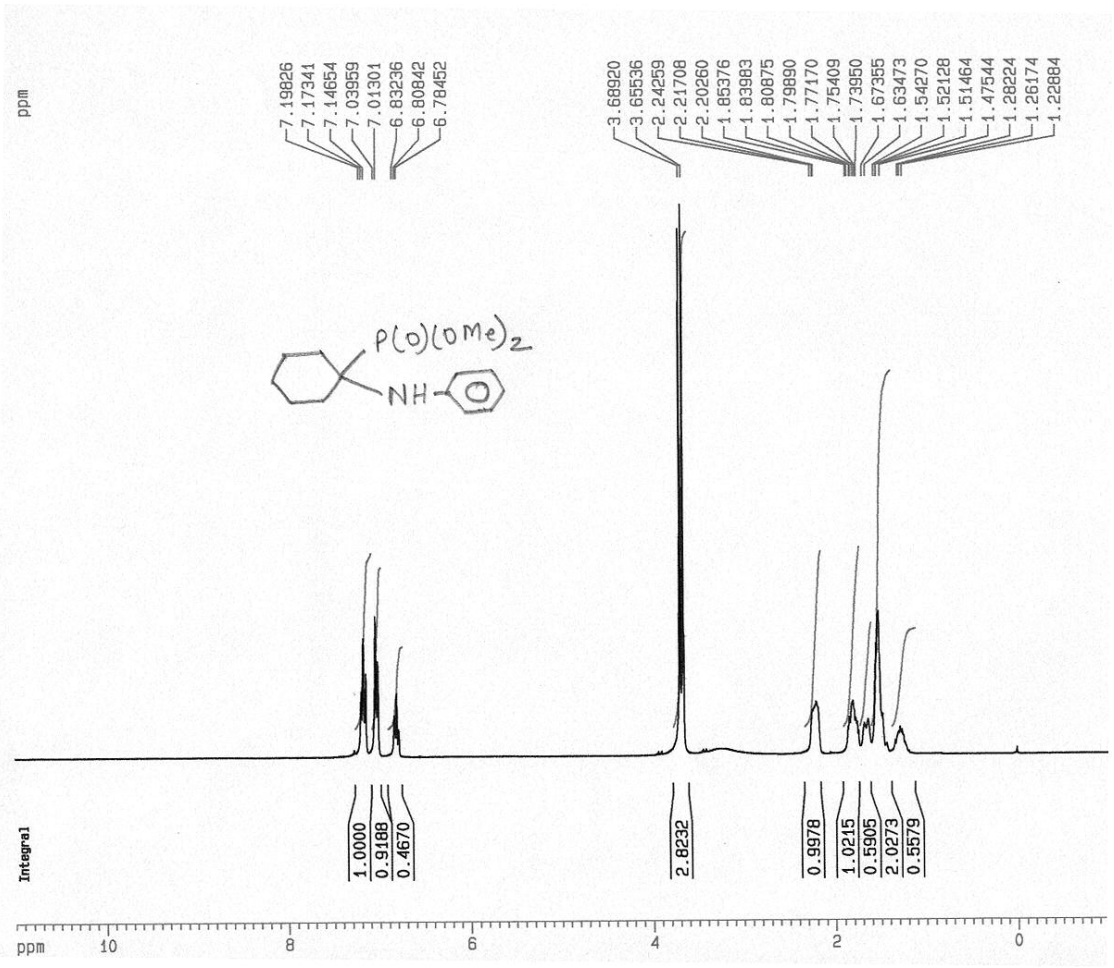
Entry 23, Table 3, ^{1}H NMR



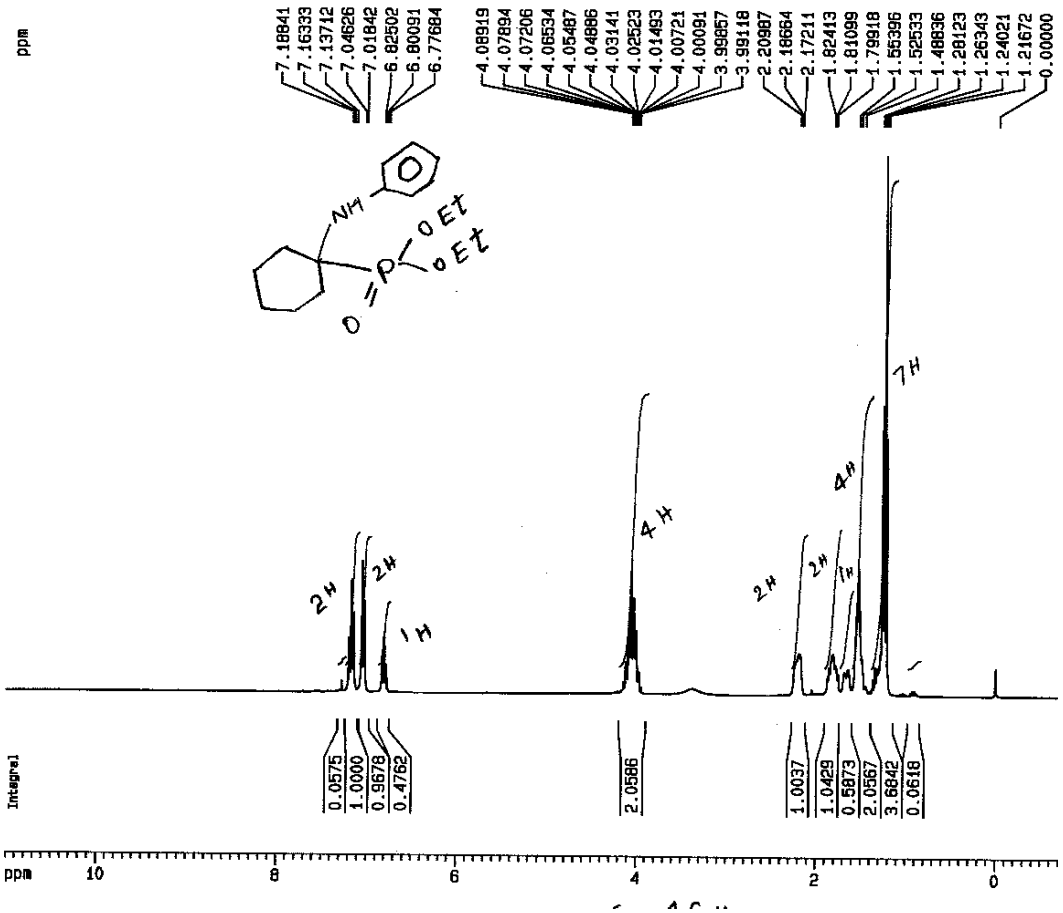
Entry 31, Table 3, ^{1}H NMR



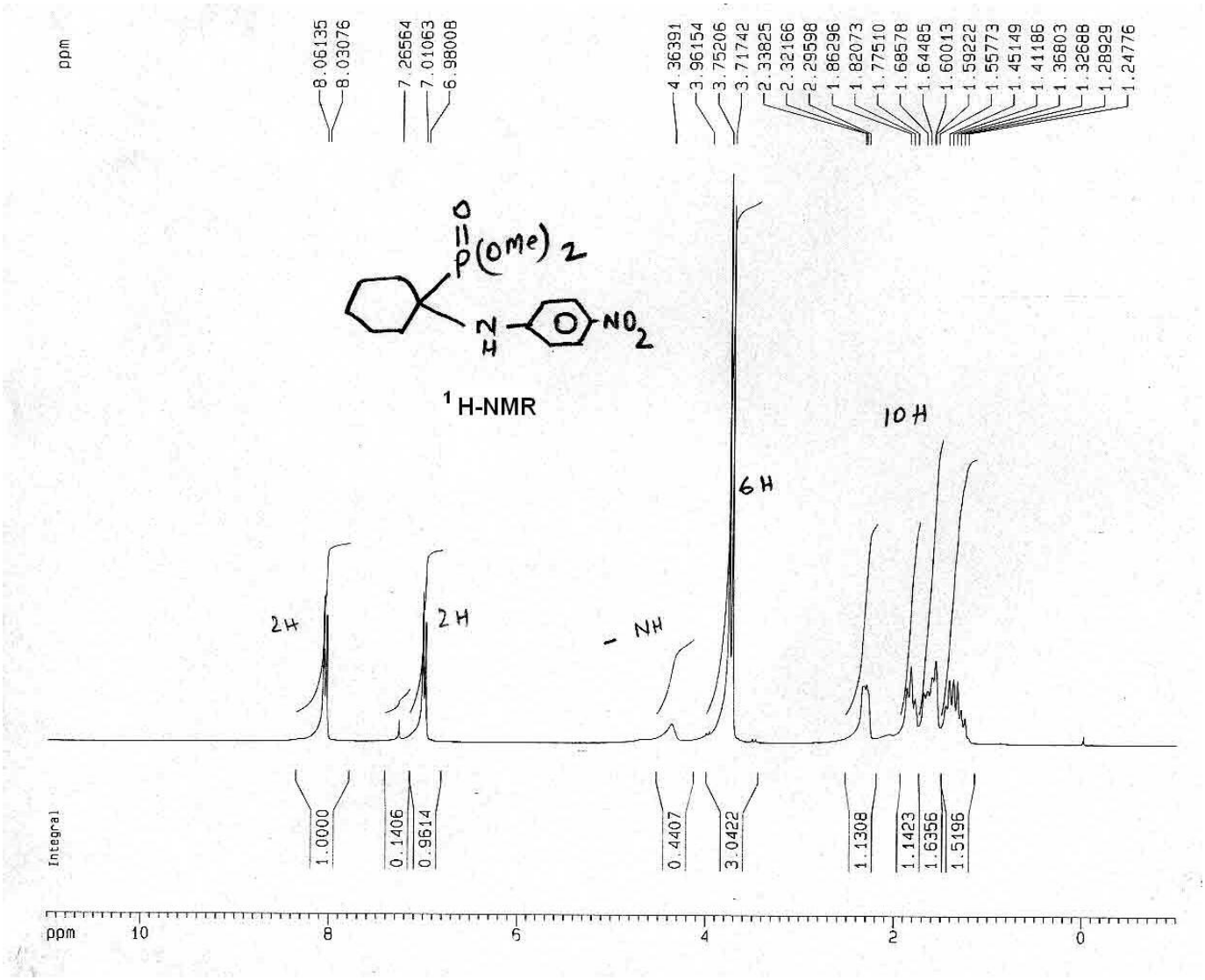
Entry 36, Table 3, ^{1}H NMR



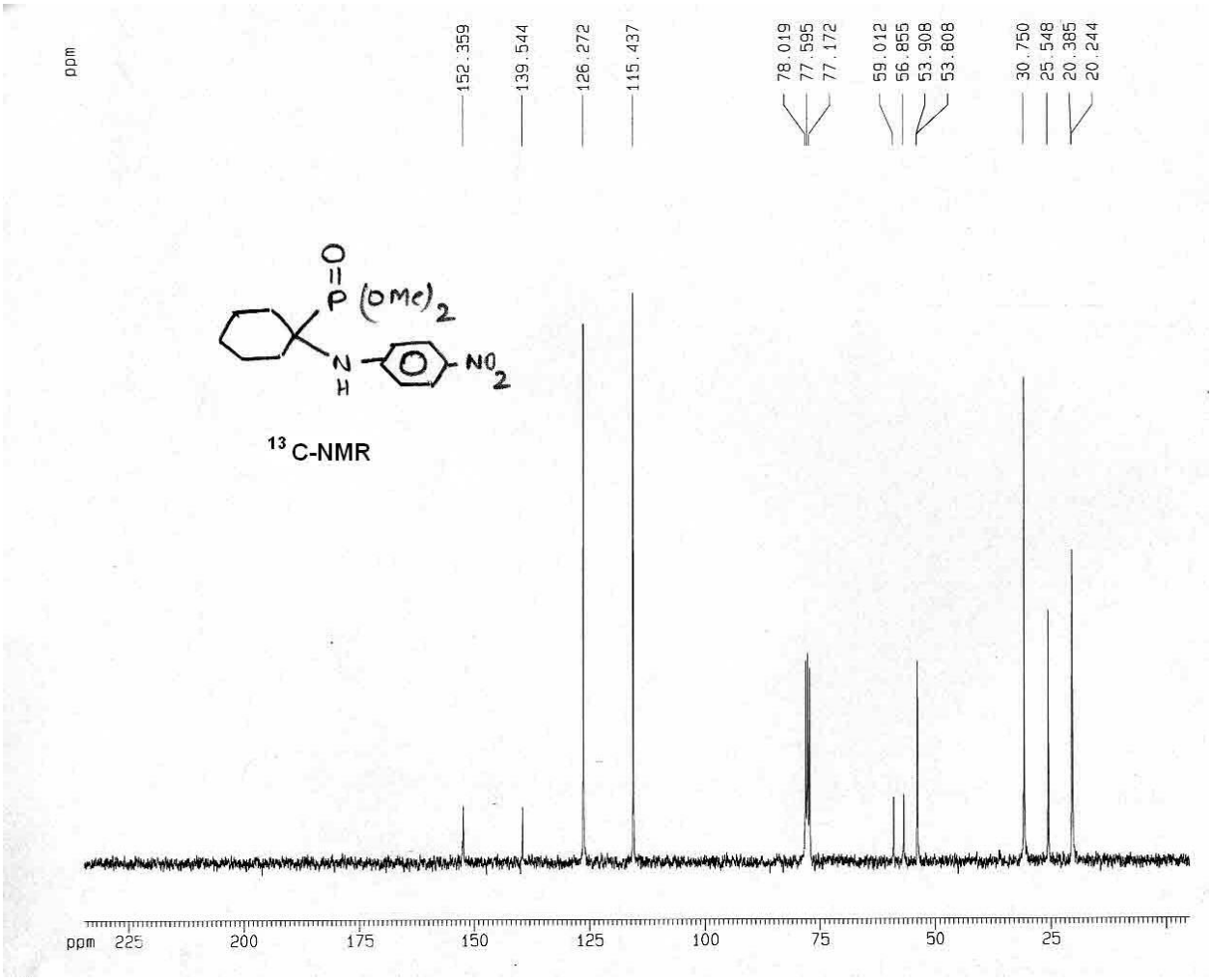
Entry 37, Table 3, ^{1}H NMR



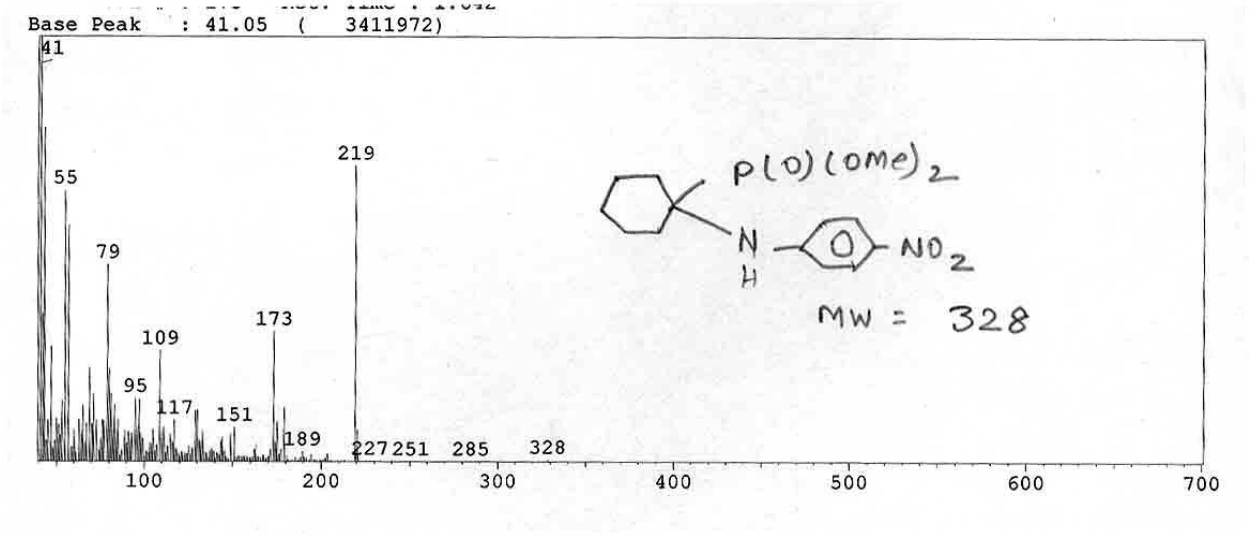
Entry 38, Table 3, ^{1}H NMR



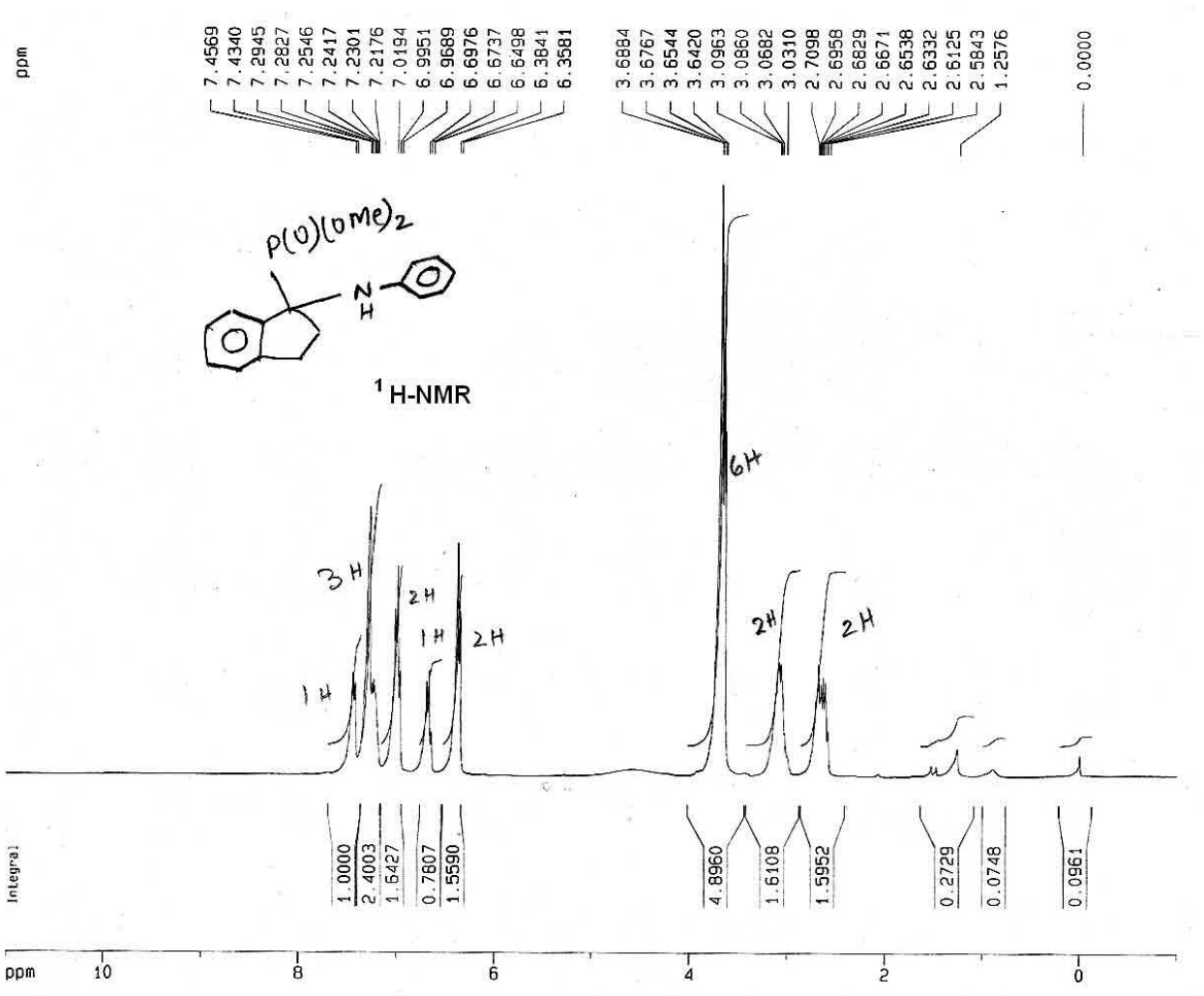
Entry 38, Table 3, ^{13}C NMR



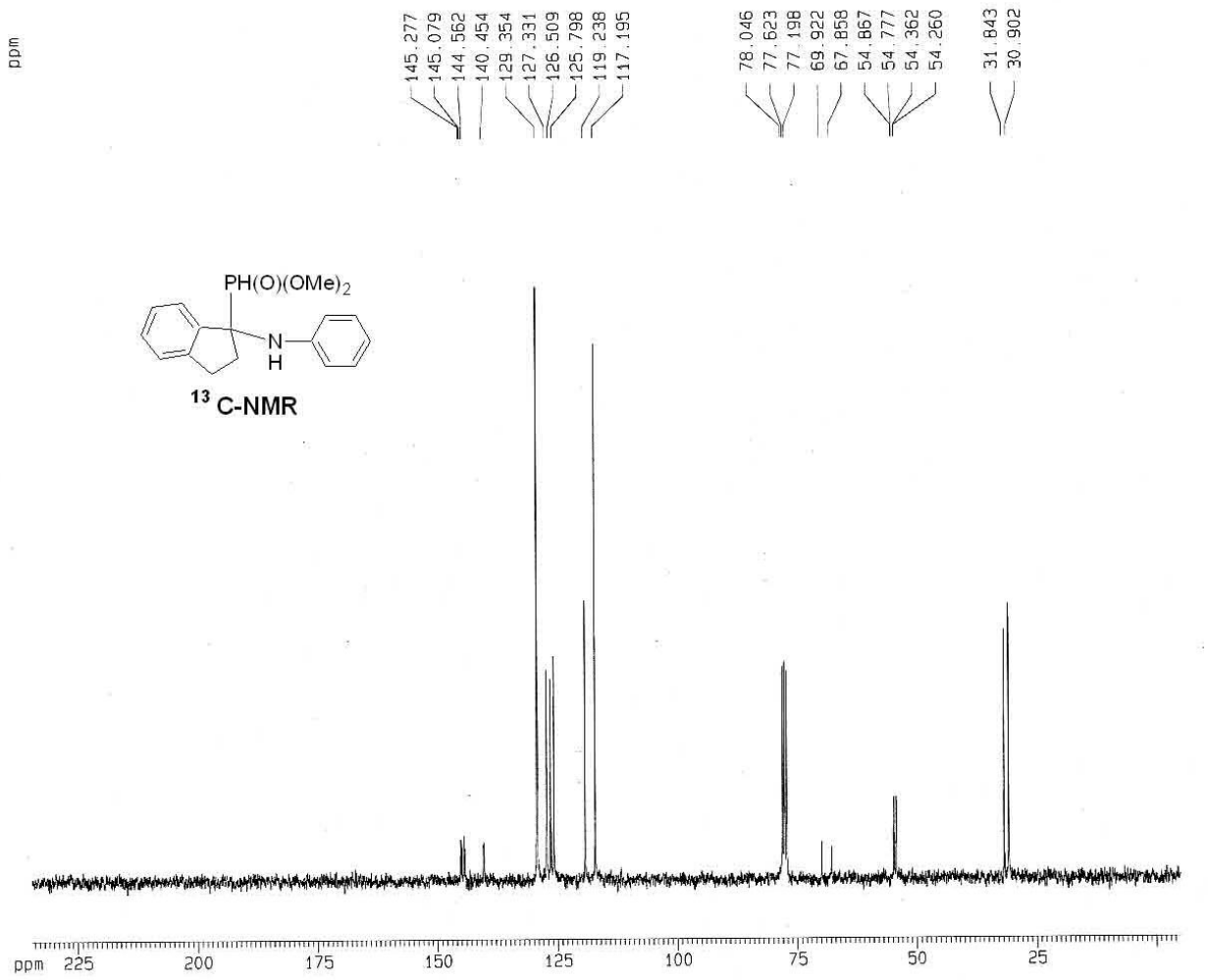
Entry 38, Table 3, Mass (EI)



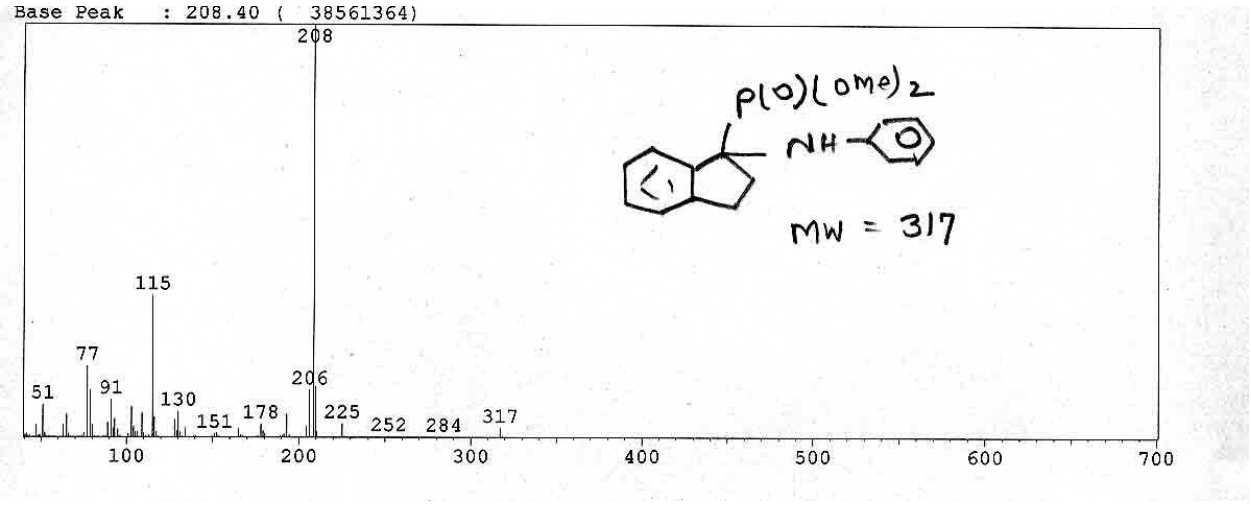
Entry 39, Table 3, ^{1}H NMR



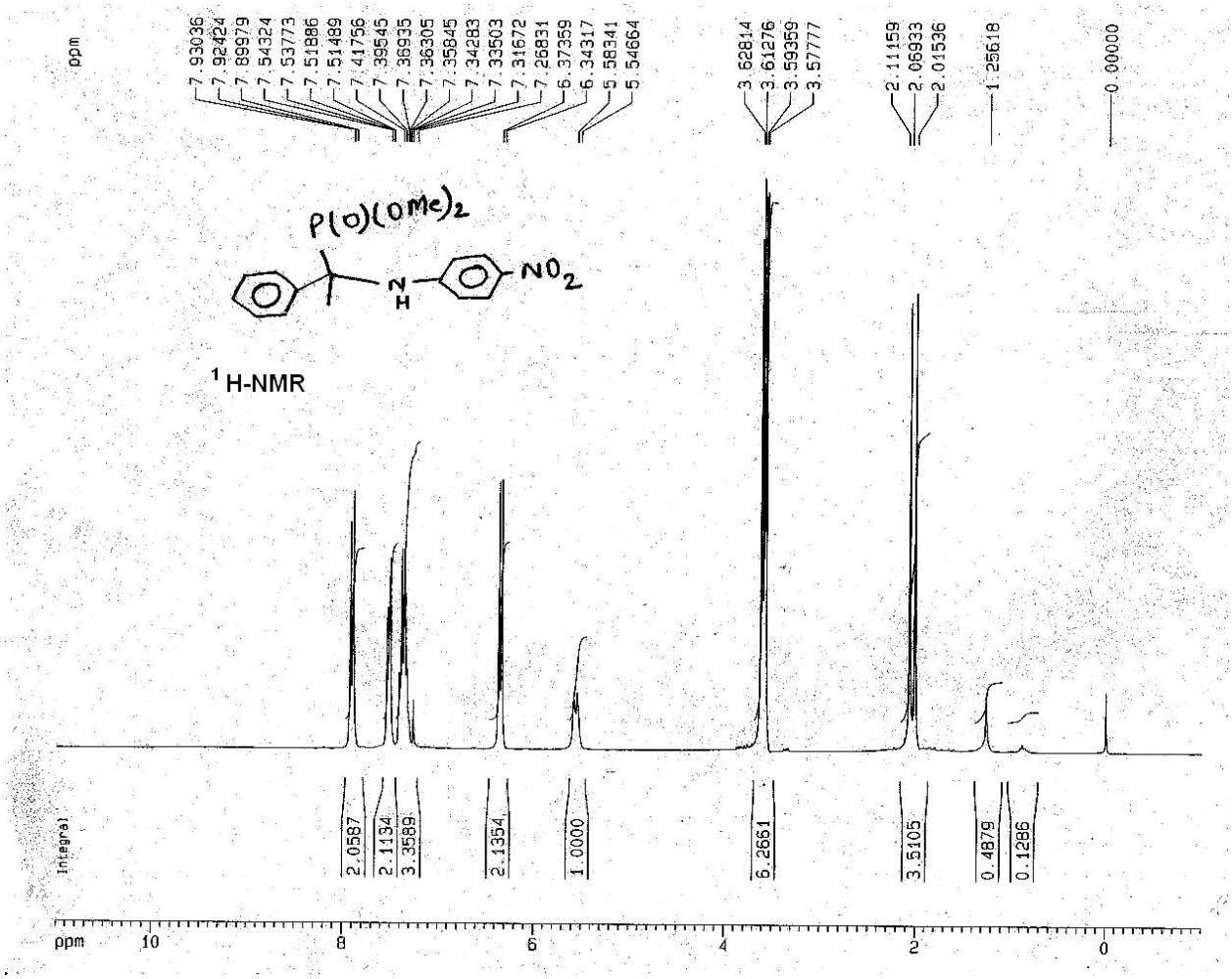
Entry 39, Table 3, ^{13}C NMR



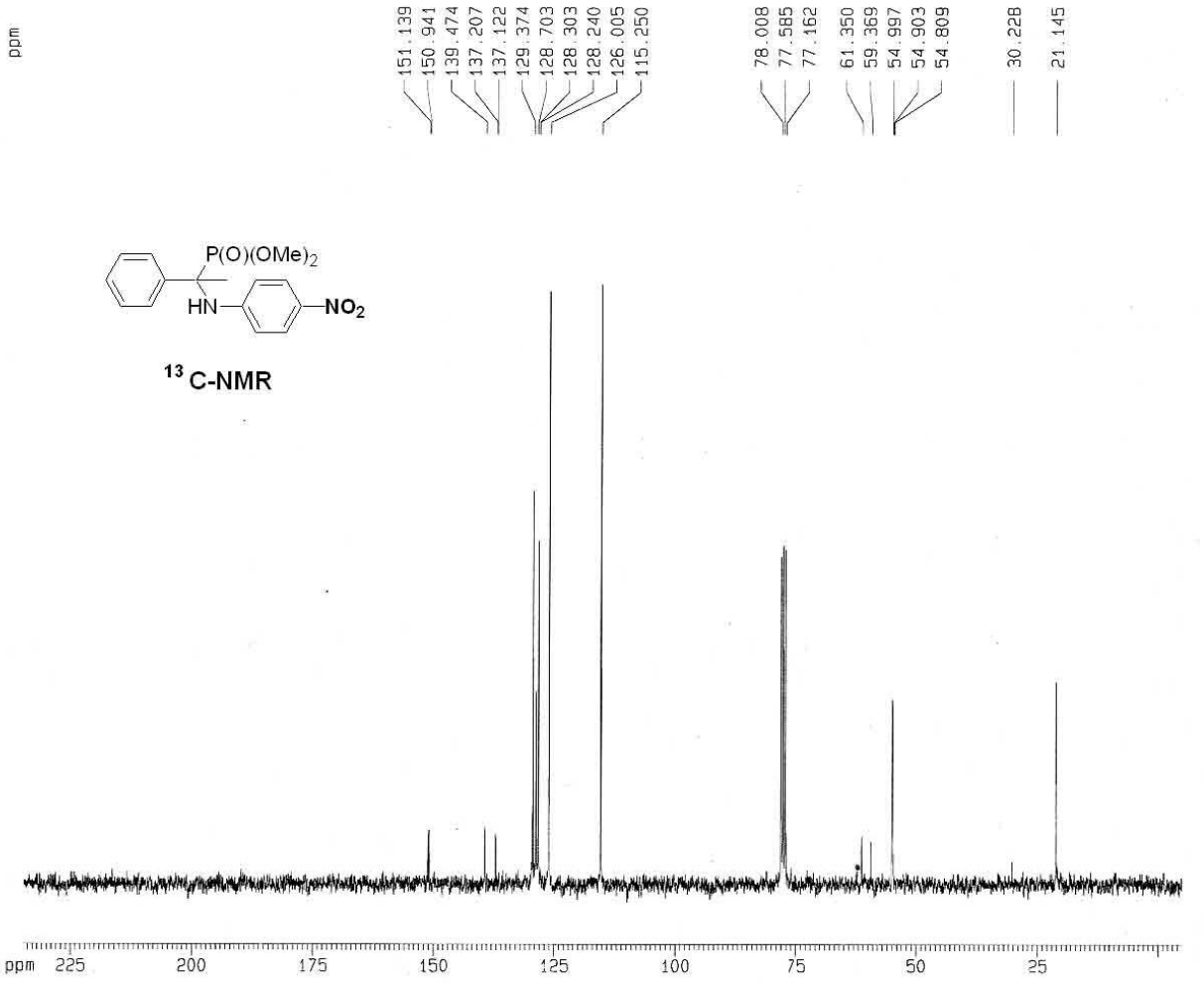
Entry 39, Table 3, Mass (EI)



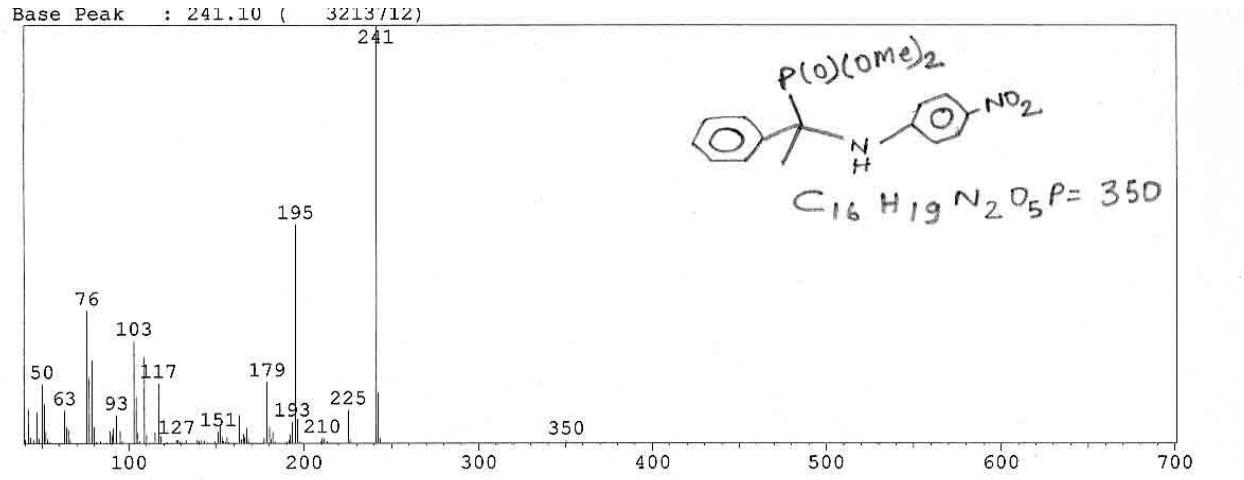
Entry 42, Table 3, ^{1}H NMR



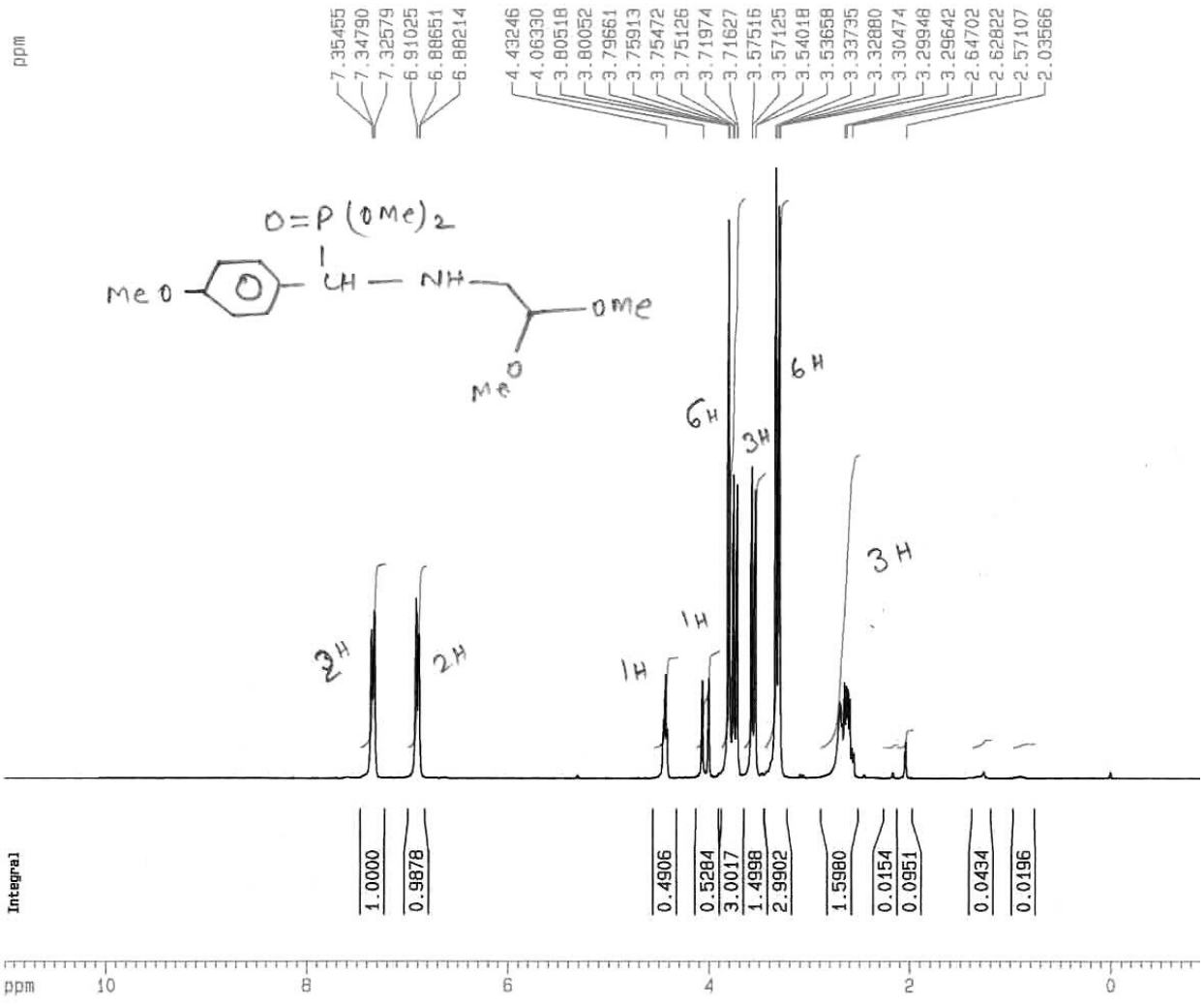
Entry 42, Table 3, ^{13}C NMR



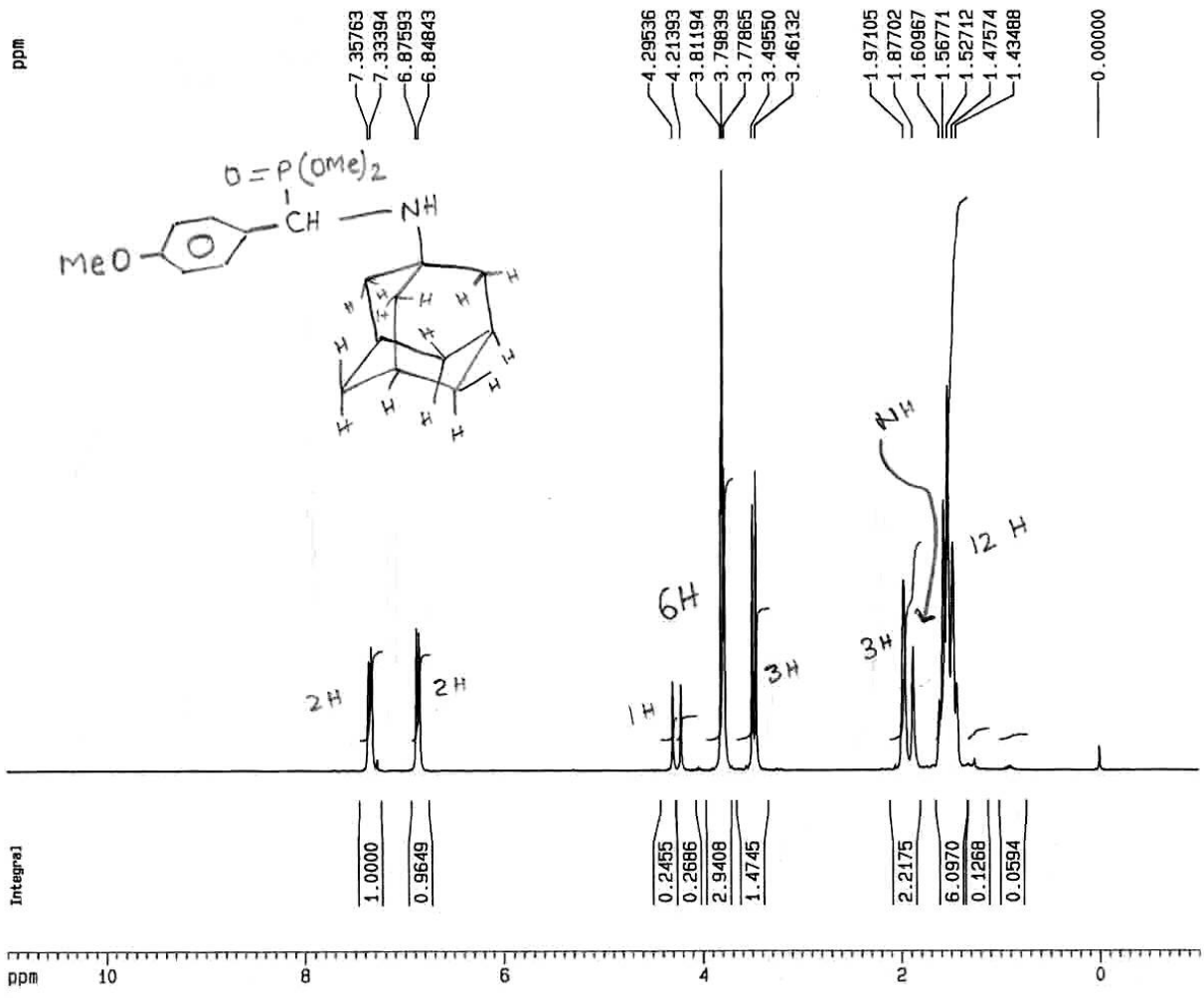
Entry 42, Table 3, Mass (EI)



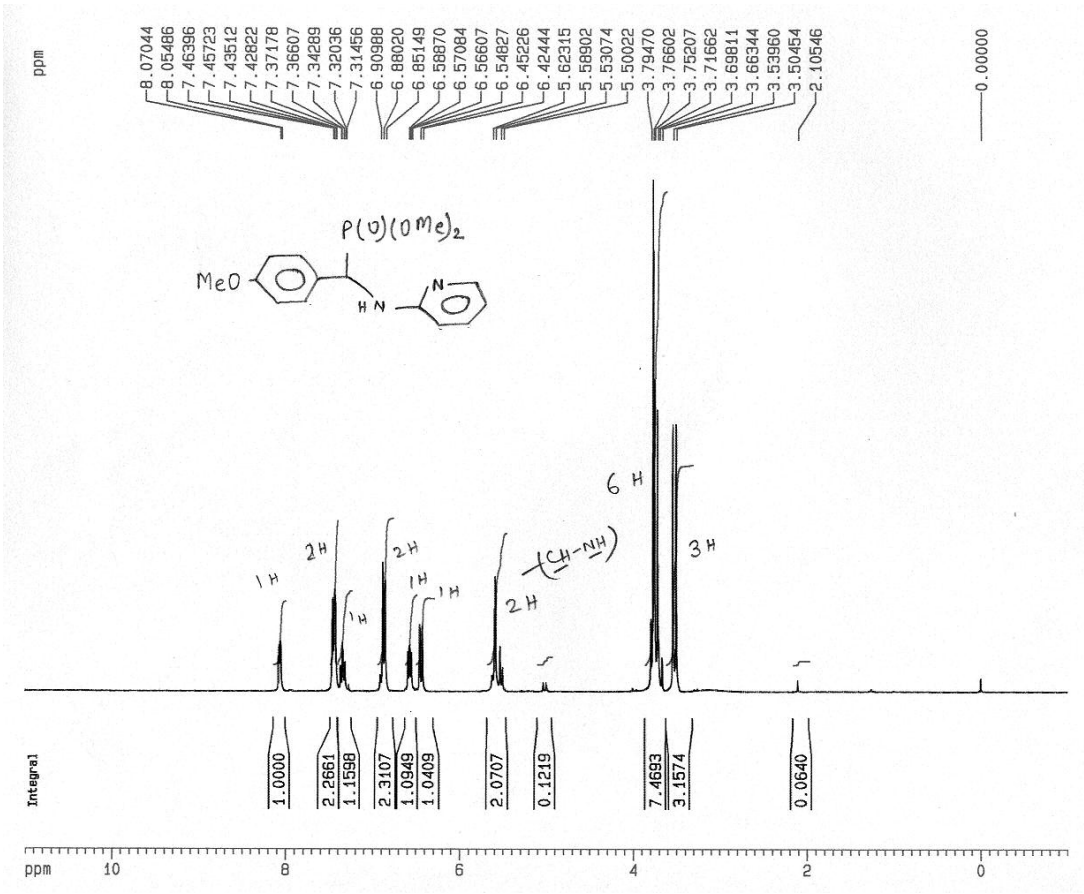
Entry 50, Table 3, ^{1}H NMR



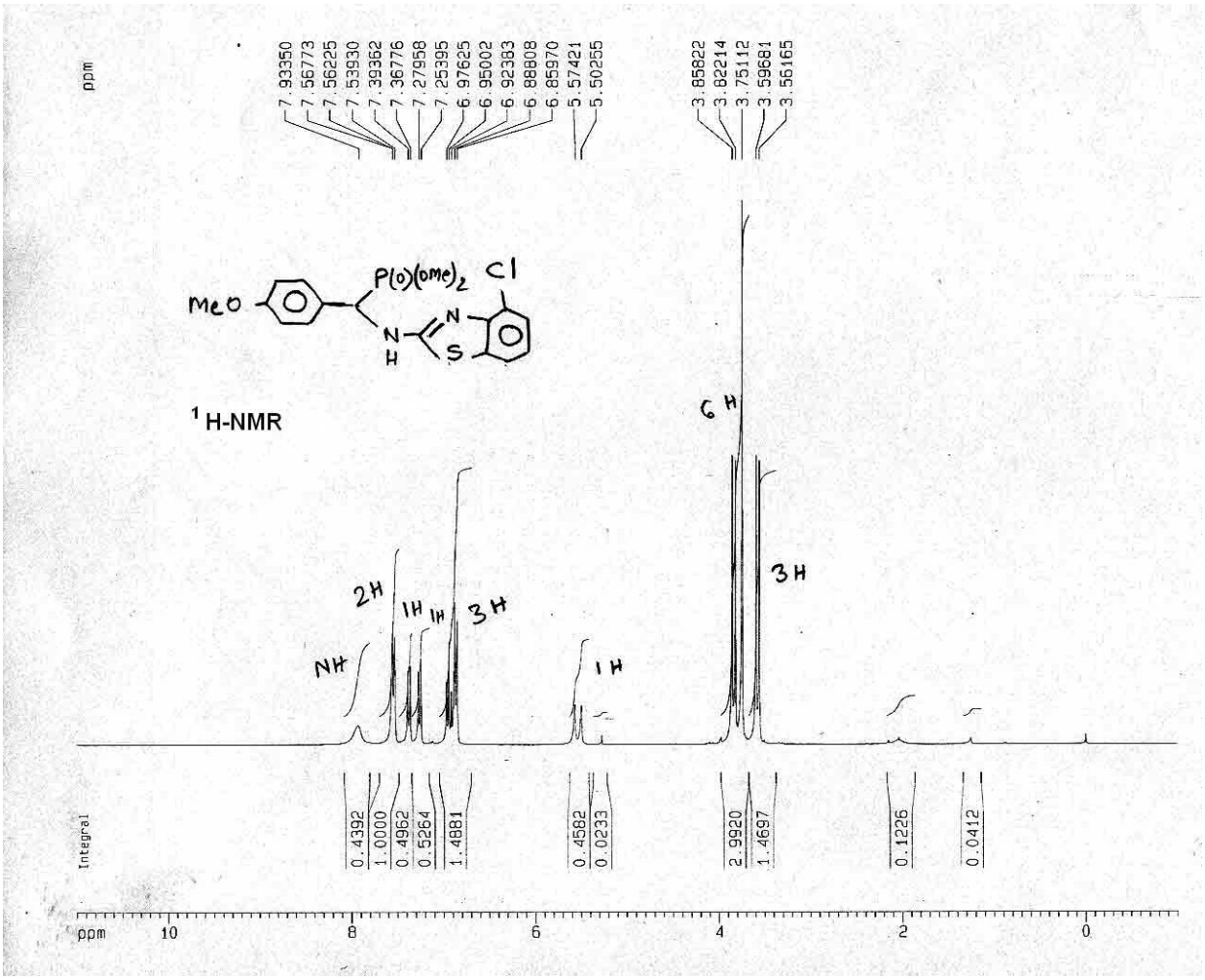
Entry 51, Table 3, ^{1}H NMR



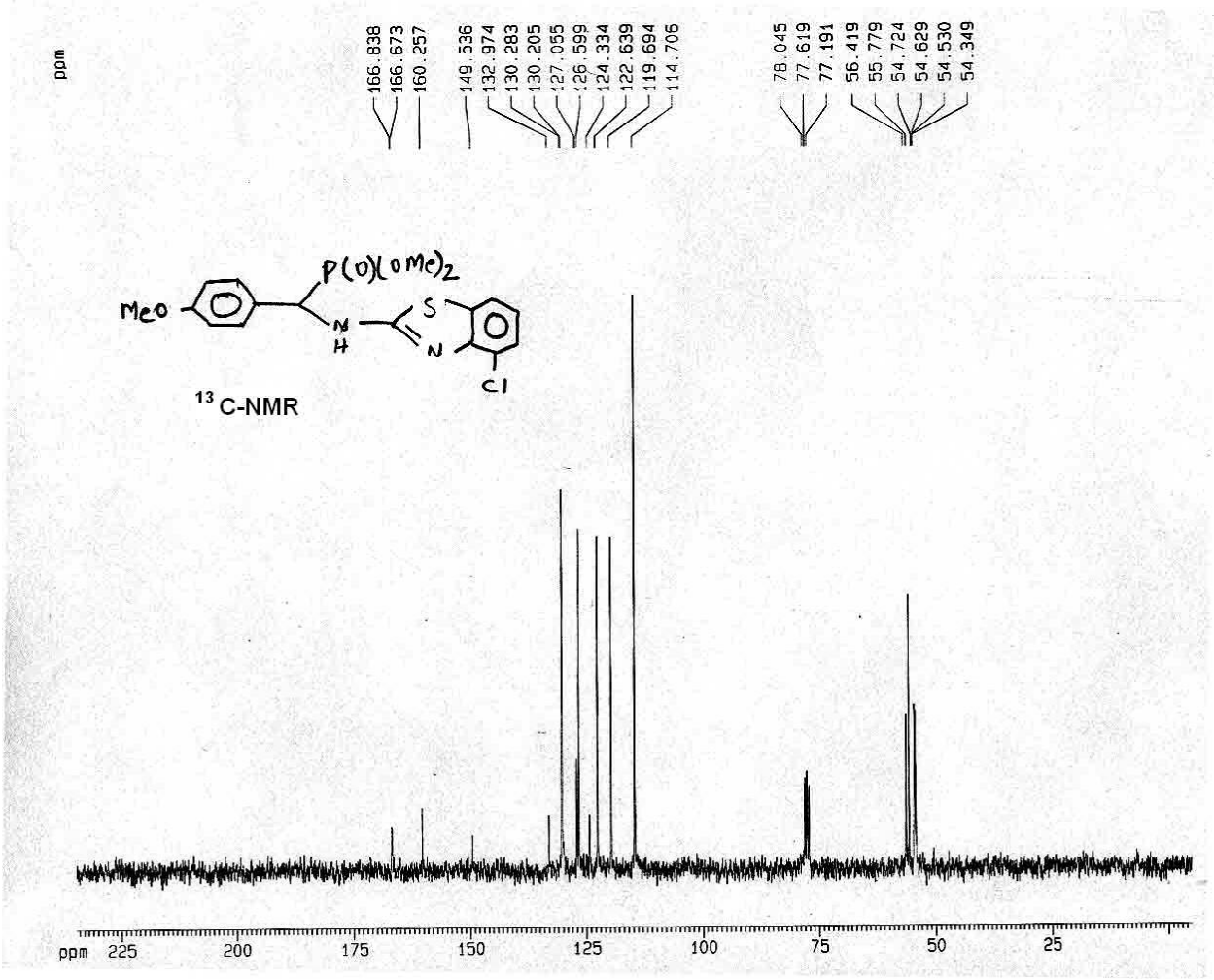
Entry 52, Table 3, ^{1}H NMR



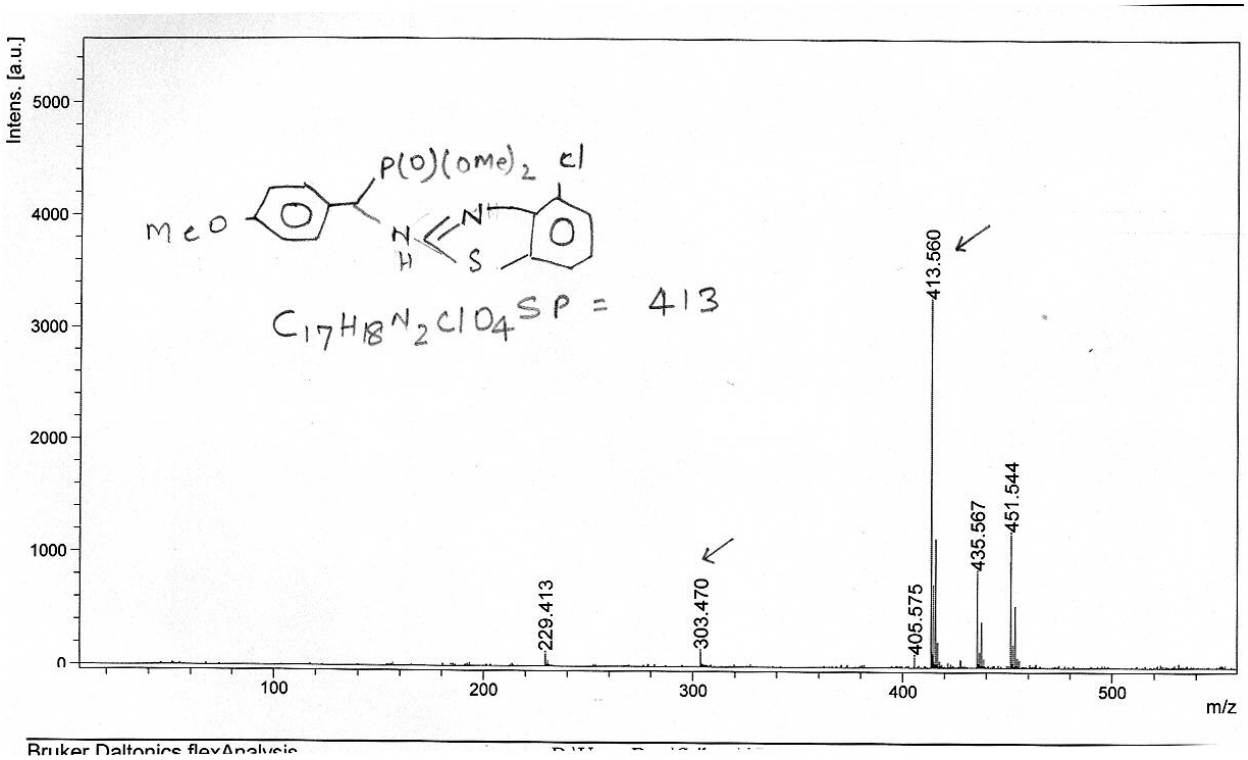
Entry 53, Table 3, ^{1}H NMR



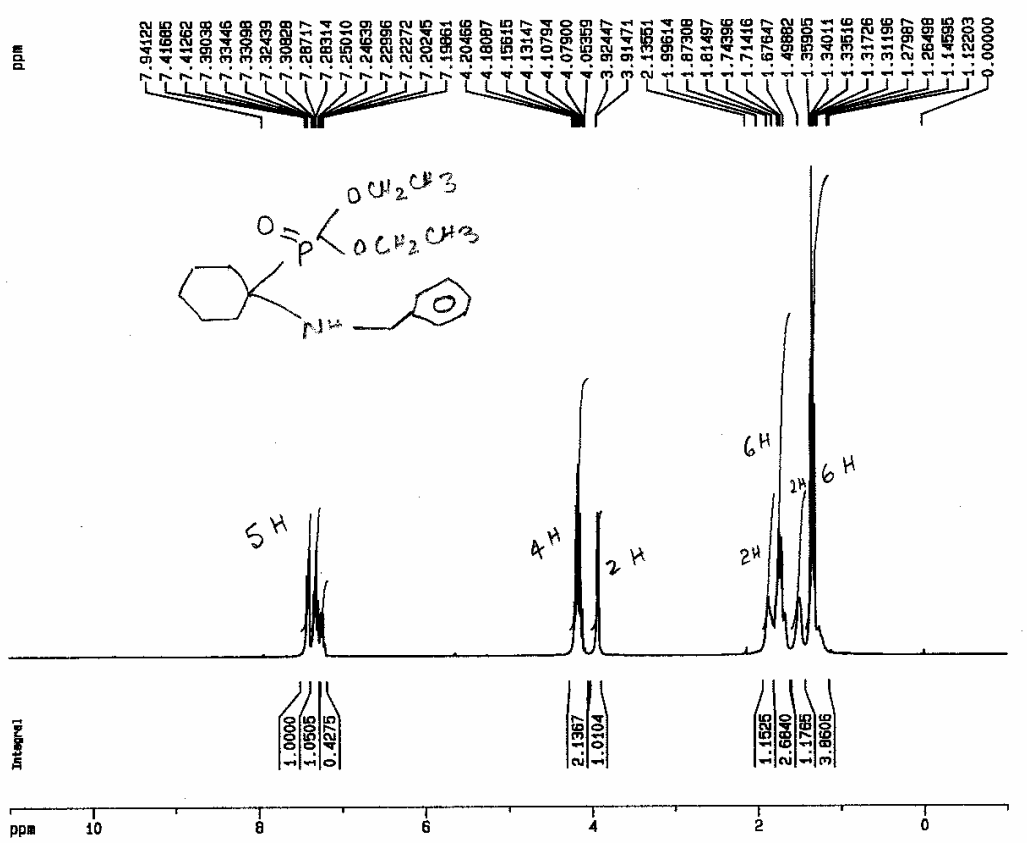
Entry 53, Table 3, ^{13}C NMR



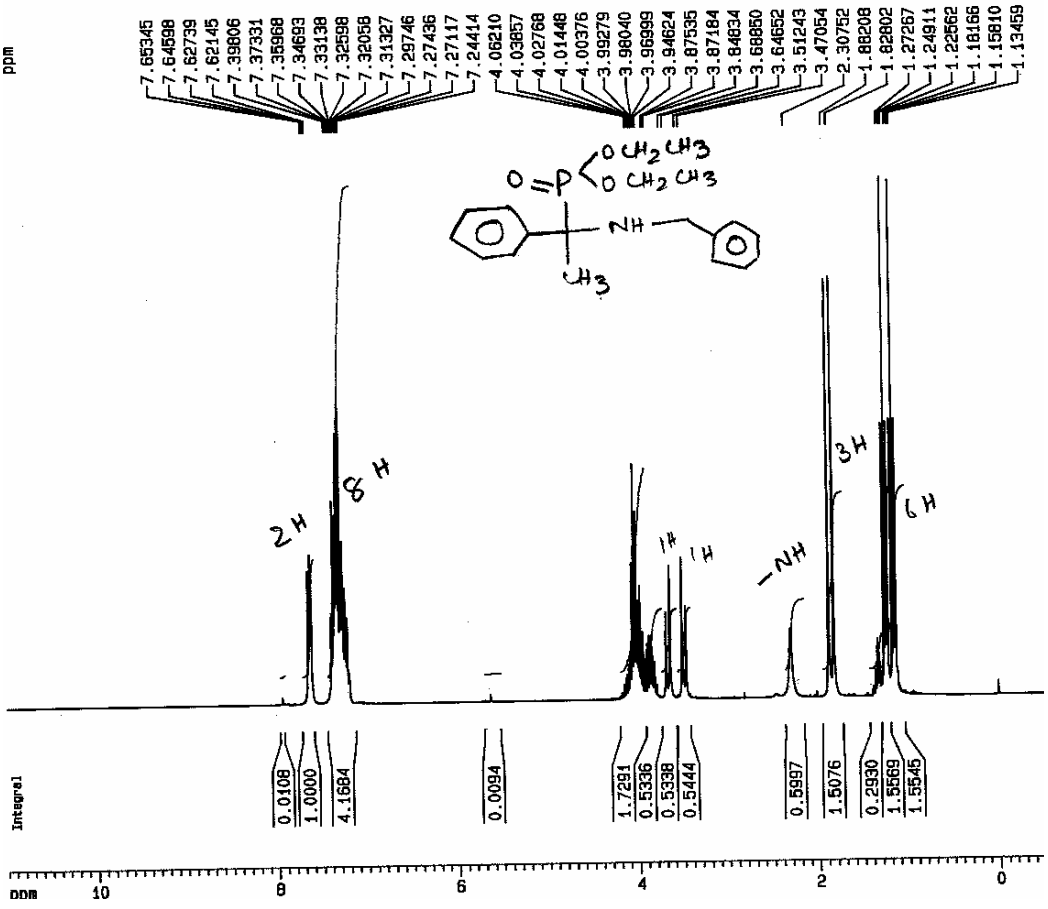
Entry 53, Table 3, Mass (MALDI ESI)



Entry 55, Table 3, ^{1}H NMR



Entry 56, Table 3, ^{1}H NMR



Experimental

General Details

The ^{1}H and ^{13}C NMR spectra were recorded on 300 MHz and 75 MHz spectrometer in $CDCl_3$ using TMS as internal standard. The IR spectra were recorded as KBr pellets for solid samples. MS spectral data were recorded on EI, APCI or MALDI-TOF-TOF. Evaporation of solvents was performed at reduced pressure, using a rotary evaporator. The reactions were monitored by TLC (silica gel-G). Crude samples were purified using flash chromatography.

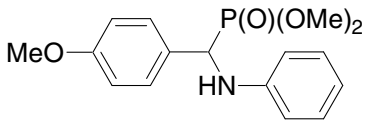
General Procedure:

The mixture of the carbonyl compound (2.5 mmol), amine (2.5 mmol), di/trialkyl/arylphosphite (3 mmol) and $ZrOCl_2 \cdot 8H_2O$ (10 mmol %), in a 25 mL round bottomed flask was magnetically stirring under neat condition at rt or at 80 °C for the required time (tables). After completion of the reaction (TLC), the mixture was extracted with EtOAc (3 × 25 mL). The combined EtOAc extracts were washed with water (2 × 10 mL), dried (Na_2SO_4) and concentrated under vacuum to obtain the crude product. The obtained crude yield was purified by flash chromatography using EtOAc (20-90%) in hexane. For highly polar α-aminophosphonates, the product was eluted with EtOAc or 2-10 % MeOH in EtOAc. Wherever applicable, the solid products were purified by recrystallization (MeOH/DCM/EtOAc). Spectral data of all the known compounds matches well with the reported compounds.

Large Scale Synthesis: The mixture of 4-methoxybenzaldehyde (1.36g, 10 mmol), 4-nitroaniline (1.38 g, 10 mmol), dimethyl phosphite (1.32g, 12 mmol) and $ZrOCl_2 \cdot 8H_2O$ (0.322 g, 10 mol%) were taken in a 50 mL round bottomed flask and stirred magnetically for 40 min at room temperature (TLC). The mixture was extracted with EtOAc (3 × 25 mL) and the combined EtOAc extracts were washed with water (2 × 25 mL), dried with Na_2SO_4 and concentrated under vacuum to obtain the crude product which was further purified by flash chromatography using EtOAc-hexane (70:30) as the eluent to afford the desired α-amino phosphonate as pale yellow solid (3.12 g, 85 %).

The physical data (IR, NMR and MS etc.) of all compounds are follows:

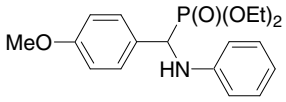
Dimethyl [(4-methoxyphenyl)phenylaminomethyl]phosphonate[1] (Table 2, Entry 1):



Mol. Wt.: 321.31

The crude product on purification by flash chromatography using EtOAc: hexane (60:40) afforded the expected product as greenish blue solid (0.76g, 95%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.47-3.50 (d, 3 H, J = 10.5 Hz), 3.73-3.77 (2 s, 6 H), 4.70-4.78 (d, 1 H, $^1J_{P\text{-}H}$ = 23.88 Hz) 6.58-7.39 (m, 9 H).

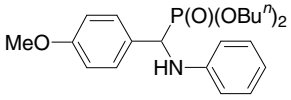
Diethyl [(4-methoxyphenyl)phenylaminomethyl]phosphonate[1](Table 2, Entry 2):



Mol. Wt.: 349.36

Greenish white solid, which on passing through flash chromatography column and elution with EtOAc:hexane (70:30) afforded the desired product (0.78 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.13 (t, 3 H, J = 6.95 Hz), 1.28 (t, 3 H, J = 6.95 Hz), 3.65-4.14 (m, 4 H), 3.77 (s, 3 H), 4.74 (d, 1 H, $^1J_{P\text{-}H}$ = 24.07 Hz), 6.57 (d, 2 H, J = 8.8 Hz), 6.68 (t, 1 H), 6.57-7.39 (m, 9 H).

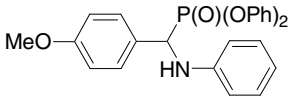
[(4-Methoxyphenyl)phenylaminomethyl]phosphonic acid dibutyl ester[1] (Table 2, Entry 3):



Mol. Wt.: 405.47

The crude product was purified by flash chromatography with EtOAc-hexane (25:75) as eluent to afford the desired product as greenish black solid (0.90 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.81-0.91(m, 6 H), 1.2-1.6 (m, 8 H), 3.59-4.05 (m, 7 H), 4.74 (d, 1 H, $^1J_{P\text{-}H}$ = 22.1 Hz), 6.56-7.38 (m, 9 H).

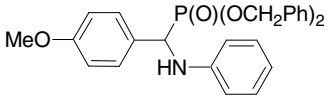
[(4-Methoxyphenyl)phenylaminomethyl]phosphonic acid diphenyl ester[1] (Table 2, Entry 4):



Mol. Wt.: 445.45

The crude reaction mixture was recrystallized from MeOH containing a few drops of DCM to afford the desired product as greenish white amorphous solid (1.06 g, 96 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.75(s, 3 H), 5.05-5.13 (d, 1 H, $^1J_{P\text{-}H}$ = 24.22), 6.62-7.46 (m, 19 H).

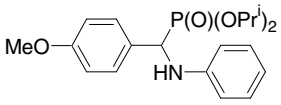
[(4-Methoxyphenyl)phenylaminomethyl]phosphonic acid dibenzyl ester (Table 2, Entry 5):



Mol. Wt.: 473.50

The crude reaction mixture was purified by flash chromatography using EtOAc:hexane (80:20) to afford the desired product as yellowish white solid (0.95 g, 80 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.77 (s, 3 H), 4.63-5.02 (m, 5 H), 6.51-7.36 (m, 19 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 55.2, 55.8, 57.1, 69.1, 114.5, , 114.7, 119.0, 128.0, 128.4, 128.6, 129.0, 129.6, 136.5, 146.7, 159.9; Elem. Anal. Calcd. for $C_{28}H_{28}NO_4P$: C, 65.17; H, 7.95; N, 3.45%. Found: C, 65.14; H, 7.96; N, 3.42.

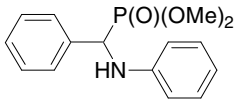
[(4-Methoxyphenyl)phenylaminomethyl]phosphonic acid diisopropyl ester[1] (Table 2, Entry 8)



Mol. Wt.: 377.41

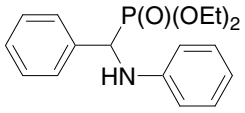
The crude reaction mixture was purified by flash chromatography with EtOAc:hexane (70:30) afforded the desired product as greenish white amorphous solid (0.67g, 70%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.95 (d, 3 H, J = 6.17 Hz), 1.21-1.32 (m, 9 H), 3.76 (s, 3 H), 4.41-4.73 (m, 3 H), 6.56-7.39 (m, 9 H).

Dimethyl (phenylphenylaminomethyl)phosphonate[1] (Table 3, Entry 1):



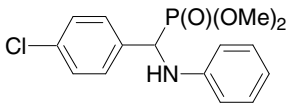
The crude reaction mixture was purified by flash chromatography with EtOAc:hexane (60:40) to afford the desired product as white solid (0.71 g, 98 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.44 (d, 3 H, J = 10.9 Hz), 3.74 (d, 3 H, J = 12.7 Hz), 4.76-4.8 (m, 2 H), 6.58-7.48 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 55.3, 55.4, 55.2, 57.2, 114.4, 119.1, 128.3, 128.6, 129.2, 129.7, 136.1, 146.5, 146.7; MS (APCI) *m/z* 291 $(M)^+$, 182 $[(M\text{-}P(O)(OMe)_2]^+$.

Diethyl (phenylphenylaminomethyl)phosphonate[1](Table 3, Entry 2):



The crude reaction mixture was purified by flash chromatography with EtOAc:hexane (70:30) to afford the desired product as light greenish white amorphous solid (0.79 g, 98 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.08-1.30 (2 t, 6 H), 3.68 (m, 1 H), 3.91 (m, 1 H), 4.07 (m, 2 H), 4.72-4.79 (2 H, PH proton merged with NH proton), 6.57-7.48 (m, 10 H); MS (MALDI) *m/z* 321(M^++2), 183 $[(M - P(O)(OEt)_2]$.

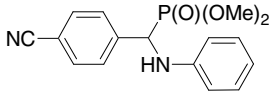
Dimethyl [(4-chlorophenyl)phenylaminomethyl]phosphonate[1] (Table 3, Entry 3):



Mol. Wt.: 325.73

The crude reaction mixture was recrystallized with 1:1 MeOH:EtOAc containing a few drops of DCM to afford the desired product as yellowish green solid (0.73 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.52 (3 H, d, J = 10.6 Hz), 3.75 (3 H, d, J = 10.8 Hz), 4.73-4.81 (d, 1 H, $^1J_{P\text{-}H}$ = 24.5 Hz), 6.45-7.43 (m, 9 H).

[(4-Cyanophenyl)phenylaminomethyl]phosphonic acid dimethyl ester (Table 3, Entry 4)

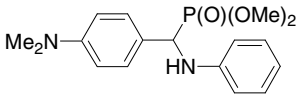


Mol. Wt.: 316.29

The crude reaction mixture was purified by flash chromatography using EtOAc:hexane (70:30) as eluting solvent to afford the desired α-aminophosphonate as fade white solid (0.72g 90 %). ^{1}H

NMR ($CDCl_3$, 300 MHz)δ: 3.57(d, 3 H, J = 10.7 Hz), 3.76 (d, 3 H, J = 10.7 Hz), 4.81-4.90 (d, 1 H, $^1J_{P\text{-}H}$ = 25.56 Hz), 6.52-7.65 (m, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 54.36, 54.69, 55.20, 57.19, 112.51, 114.38, 119.10, 119.71, 129.04, 129.93, 133.04, 142.20, 145.96, 146.15; MS (APCI) *m/z* 316 (M^+), 207 [(M^+-P(O) $(OMe)_2$]; Elem. Anal. Calcd. for $C_{16}H_{17}N_2O_3P$: C, 60.76; H, 5.42; N, 8.86. Found: C, 60.65; H, 5.43; N, 8.84.

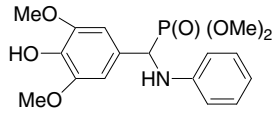
Dimethyl [(4-dimethylaminophenyl)phenylaminomethyl]phosphonate[1] (Table 3, Entry 5):



Mol. Wt.: 334.35

The crude reaction mixture was recrystallized from EtOH to afforded the product as yellowish orange solid, (0.71 g, 85 %), ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.9 (s, 6 H) 3.45 (d, 3 H, J = 10.42 Hz), 3.72 (d, 3 H, J = 10.57 Hz), 4.66-4.74 (d, 1 H, $^1J_{P\text{-}H}$ = 23.52 Hz), 6.59-7.32 (m, 9 H).

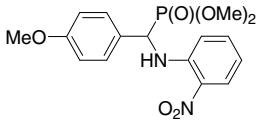
[(4-Hydroxy-3,5-dimethoxy-phenyl)phenylaminomethyl]phosphonic acid dimethyl ester (Table 3, Entry 6)



Mol. Wt.: 367.33

The crude reaction mixture was purified by flash chromatography EtOAc:hexane (80:20) as eluent to afford the desired product as brownish yellow solid (0.83g, 90 %). IR(KBr) ν :1603, 2952, 3321, and 3494.6 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.48 (d, 3 H, J = 10.56 Hz), 3.74 (d, 3 H, J = 10.64 Hz), 3.84 (s, 6 H), 4.65-4.73 (d, 1 H, $^1J_{P\text{-}H}$ = 23.8Hz), 6.60-7.14 (m, 7 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 54.30, 54.52, 55.38, 56.90, 57.40, 105.02, 114.43, 119.15, 127.02, 129.73, 135.09, 146.67, 146.86, 147.85; MS (MALDI TOF-TOF) *m/z* 367(M^+), 257 [(M^+-P(O) $(OMe)_2$]; Elem. Anal. Calcd. for $C_{17}H_{22}NO_6P$: C, 55.58; H, 6.04; N, 3.81. Found: C, 55.52; H, 6.07; N, 3.80.

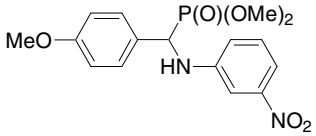
Dimethyl [(4-methoxyphenyl)-(2-nitrophenylamino)methyl]phosphonate[1] (Table 3, Entry 8):



Mol. Wt.: 366.31

The crude reaction mixture was purified by flash chromatography using EtOAc:hexane (70:30) to afford the desired product as yellow solid (0.83 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.64-3.79 (m, 9 H), 4.85-4.95 (dd, 1 H, $^1J_{P\text{-}H}$ = 7.2 & 23.4 Hz), 6.67-8.91 (m, 9 H).

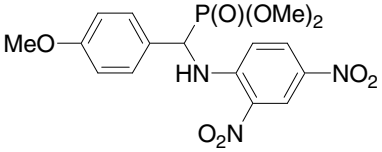
Dimethyl [(4-methoxyphenyl)-(3-nitrophenylamino)methyl]phosphonate[1] (Table 3, Entry 9):



Mol. Wt.: 366.31

The crude reaction mixture was purified by flash chromatography using EtOAc: hexane (60:40) to afford the desired product as yellow solid (0.83 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.47 (d, 3 H, J = 10.53 Hz), 3.78 (d, 6 H, J = 8.9 Hz) 4.74-4.82 (d, 1 H, $^1J_{P\text{-}H}$ = 23.8 Hz), 6.87-7.52 (m, 8 H).

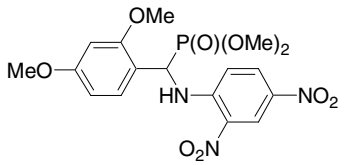
Dimethyl [(2,4-dinitrophenylamino)-(4-methoxyphenyl)methyl]phosphonate[1] (Table 5, Entry 10):



Mol. Wt.: 411.30

The crude reaction mixture was purified by flash chromatography with EtOAc-hexane (80:20) to afford the desired product as yellow solid (0.88 g, 85 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.62 (d, 3 H, J = 10.68 Hz), 3.73 (d, 3 H, J = 10.68 Hz), 3.80 (s, 3 H), 4.90-4.99 (dd, 1 H, $^1J_{P\text{-}H}$ = 7.02 Hz & J = 22.51 Hz). 6.78 (d, 1 H, J = 9.4 Hz), 6.92 (d, 2 H, J = 8.6 Hz), 7.36-7.30 (dd, 2 H, J = 2.2 Hz & 8.7 Hz), 8.14 -8.18 (dd, 1 H, J = 2.5 Hz & 9.4 Hz), 9.13 (d, 1 H, J = 2.3 Hz), 9.36 (m, 1 H).

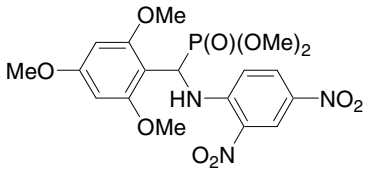
Dimethyl [(2,4-dimethoxyphenyl)-(2,4-dinitrophenylamino)methyl]phosphonate[1] (Table 3, Entry 11):



Mol. Wt.: 441.33

The crude reaction mixture on passing through flash chromatography elution with 1:1 EtOAc-hexane afforded the desired product as yellow yield (0.88 g, 80 %) . ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.6 (d, 3 H, J = 10.73 Hz), 3.77 (d, 3 H, J = 10.55 Hz), 3.80 (s, 3 H), 3.97 (s, 3 H), 5.41-5.52 (dd, 1 H, J = 7.9 & 22.3 Hz), 6.49 (m, 2 H), 6.86 (d, 1 H, J = 9.5 Hz), 7.30-7.33 (dd, 1 H, J = 2.0 & 8.4 Hz), 8.17-8.21 (dd, 1 H, $^1J_{P\text{-}H}$ = 2.3 & 7.4 Hz), 9.1 (d, 1 H, J = 2.3 Hz), 9.48 (m, 1 H).

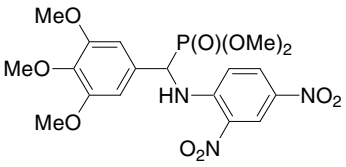
Dimethyl [(2,4-dinitrophenylamino)-(2,4,6-trimethoxyphenyl)methyl]phosphonate[1] (Table 3, Entry 12):



Mol. Wt.: 471.36

The crude reaction mixture was purified by flash chromatography and eluting with 1:1 EtOAc:hexane to afford the desired product as yellow solid (0.94 g, 80 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.67-4.06 (m, 15 H), 5.80-5.90 (dd, 1 H, J = 9.5 & 21.45 Hz), 6.18 (s, 2 H), 7.14 (d, 1 H, J = 9.6 Hz), 8.22 (m, 1 H), 9.10 (s, 1 H), 10.0 (m, 1 H).

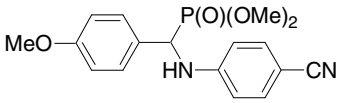
[(2,4-Dinitrophenylamino)-(2,3,4,5-tetramethoxy-phenyl)methyl]phosphonic acid dimethyl ester (Table 3, Entry 13)



Mol. Wt.: 471.36

The crude reaction mixture was purified by flash chromatography using EtOAc:hexane (70:30) to afford the desired product (yellow solid, 0.93 g, 80 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.64-3.86 (m, 15 H), 4.84-4.94 (m, 1 H), 6.65 (s, 2 H), 6.80 (1 H, d, J = 9.4 Hz), 8.18 (m), 8.22 (m, 1 H), 9.13 (m, 1 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 54.8, 55.1, 56.9, 57.2, 61.4, 105.1, 115.5, 124.5, 128.9, 130.9, 132.3, 138.8, 139.1, 147.7, 147.9, 154.5; Elem. Anal. Calcd. for $C_{18}H_{22}N_3O_{10}P$: C, 45.87; H, 4.70; N, 8.91. Found: C, 45.84; H, 4.71; N, 8.88.

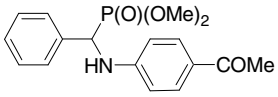
Dimethyl [(4-cyanophenylamino)-(4-methoxyphenyl)methyl]phosphonate[1] (Table 3, Entry 14):



Mol. Wt.: 346.32

The crude reaction mixture was purified by flash chromatography with EtOAc:hexane (70:30) to afford the desired product as fade white solid (0.78 g, 80%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.45 (d, 3 H, J = 10.52 Hz), 3.74-3.78 (2 s, 6 H), 4.69-4.80 (dd, 1 H, $^1J_{P\text{-}H}$ = 7.6 & 23.8 Hz), 5.53 (bs,1 H), 6.58 (d, 2 H, J = 8.5 Hz), 6.87 (d, 2 H, J = 8.6 Hz), 7.34 (d, 4 H, J = 8.7 Hz).

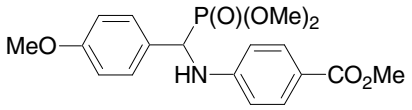
[(4-Acetylphenylamino)phenylmethyl]phosphonic acid diethyl ester (Table 3, Entry 15)



Mol. Wt.: 333.32

The crude reaction mixture was purified by flash chromatography with EtOAc: hexane (40:60) to afford the desired product as yellow semi solid (0.75g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.44 (s, 3 H), 3.44 (d, 3 H, J = 10.6 Hz), 3.75 (d, 3 H, J = 10.7 Hz) 4.81-4.92 (dd, 1 H, $^1J_{P\text{-}H}$ = 7.78 Hz & 22.23 Hz), 5.56 (m, 1 H, NH), 6.59-7.76 (m, 9 H); MS (APCI) *m/z* 333 (M^+), 224 [(M^+-P(O) ($OMe)_2$]; Elem. Anal. Calcd. for $C_{17}H_{20}NO_4P$: C, 61.26; H, 6.05; N, 4.20. Found: C, 61.10; H, 6.09; N, 4.19.

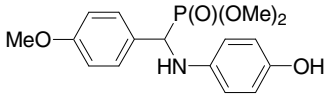
Methyl 4-{[(dimethoxyphosphoryl)-(4-methoxyphenyl)methyl]amino}benzoate[1] (Table 3, Entry 16):



Mol. Wt.: 379.34

The crude reaction mixture was purified by flash chromatography with EtOAc:hexane (1:1) to afford the desired product as fade yellow solid (0.85 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.45 (d, 3 H, J = 10.53 Hz), 3.74-3.80 (m, 9 H), 4.77-4.85 (d, 1 H, $^1J_{P\text{-}H}$ = 23.9 Hz), 5.6 (bs, 1 H), 6.60 (d, 2 H, J = 8.8 Hz), 6.86 (d, 2 H, J = 8.3 Hz), 7.35 (dd, 2 H, J = 2.1 & 8.7 Hz), 7.8 (d, 2 H, J = 8.5 Hz).

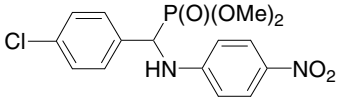
Dimethyl [(4-hydroxyphenylamino)-(4-methoxyphenyl)methyl]phosphonate[1] (Table 3, entry 17):



Mol. Wt.: 337.31

The crude reaction mixture was purified by flash chromatography with EtOAc-hexane (80:20) to afford the desired yield as brown solid (0.76 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.47 (d, 3 H, J = 10.30 Hz), 3.68-3.76 (2 s, 6 H), 4.62-4.70 (d, 1 H, $^1J_{P\text{-}H}$ = 23.5 Hz), 6.45-7.59 (m, 8 H).

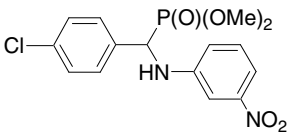
Dimethyl [(4-chlorophenyl)-(4-nitrophenylamino)methyl]phosphonate[1] (Table 3, Entry 18):



Mol. Wt.: 370.72

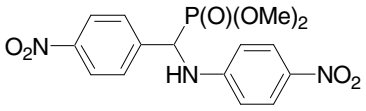
The crude reaction mixture was purified by flash chromatography with EtOAc-hexane (60:40) to afford the desired product as yellow solid (0.8 g, 85 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.51 (d, 3 H, J = 10.7 Hz), 3.75 (d, 3 H, J = 10.6 Hz), 4.65-4.82 (d, 1 H, $^1J_{P\text{-}H}$ = 24.35 Hz), 6.58 (d, 2 H, J = 9.1 Hz), 7.27-7.44 (m, 4 H), 7.98 (d, 2 H, J = 8.8 Hz).

Dimethyl [(4-chlorophenyl)-(3-nitrophenylamino)methyl]phosphonate[1] (Table 3, Entry 19):



The crude reaction mixture was purified by flash chromatography with EtOAc:hexane (60:40) to afford the desired yield as yellow solid (0.81 g, 85 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.55 (d, 3 H, J = 10.7 Hz), 3.80 (d, 3 H J = 10.8 Hz), 4.77-4.88 (dd, 1 H, J = 7.2 Hz & 24.6 Hz), 5.79 (bs, 1 H), 6.84-7.53 (m, 8 H).

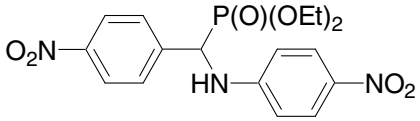
Dimethyl [(4-nitrophenyl)-(4-nitrophenylamino)methyl]phosphonate[1] (Table 3, Entry 20):



Mol. Wt.: 381.28

The crude reaction mixture was purified using flash chromatography with 1:1 EtOAc-hexane to afford the desired product as yellow solid (0.82 g, 86 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.82 (d, 3 H, J = 10.8 Hz), 3.80 (d, 3 H, J = 10.9 Hz), 4.91-5.02 (dd, 1 H, J = 7.4 Hz & 25.1 Hz), 5.76 (bs, 1 H), 6.54 (d, 2 H, J = 9.05 Hz), 7.63 (m, 2 H), 8.01 (d, 2 H, J = 8.9 Hz), 8.23 (d, 2 H, J = 9.4 Hz).

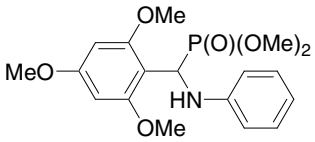
Diethyl [(4-nitrophenyl)-(4-nitrophenylamino)methyl]phosphonate[1] (Table 3, Entry 21):



Mol. Wt.: 409.33

The crude reaction mixture was purified by flash chromatography with (60:40) EtOAc:hexane to afford the desired product as brownish yellow solid (0.85 g, 83 %); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.17-1.35 (m, 6 H), 3.85-4.24 (m, 4 H), 4.92-5.03 (d, 1 H, $^1J_{P\text{-}H}$ = 25.2 Hz), 6.07 (bs, 1 H), 6.56 (d, 2 H, J = 9.1 Hz), 7.65 (d, 2 H, J = 8.6 Hz), 8.0 (d, 2 H, J = 9.1 Hz), 8.21 (d, 2 H, J = 8.5 Hz).

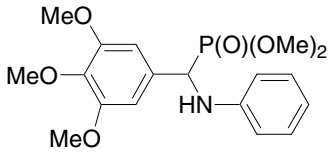
Dimethyl [phenylamino-(2,4,6-trimethoxyphenyl)methyl]phosphonate[1] (Table 3, Entry 22):



Mol. Wt.: 381.36

The crude reaction mixture was purified by flash chromatography with (70:30) EtOAc:hexane to afford the desired product as brownish yellow solid (0.81 g, 85 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.53 (d, 3 H, J = 10.49 Hz), 3.75-3.88 (m, 12 H), 5.53-5.61 (d, 1 H, $^1J_{P\text{-}H}$ = 24.24 Hz), 6.1 (s, 2 H), 6.66-7.12 (m, 5 H).

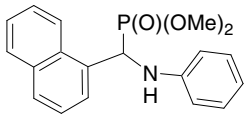
Dimethyl phenylamino-(3, 4, 5-trimethoxyphenyl)methyl]phosphonate[1] (Table 3, Entry 23):



Mol. Wt.: 381.36

The crude yield was subjected to flash chromatography purification with (60:40) EtOAc:hexane to afford the desired product as yellowish green solid (0.80g, 85 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.51 (d, 3 H, J = 10.54 Hz), 3.74 - 3.84 (m, 12 H), 4.66 - 4.74 (d, 1 H, $^1J_{P\text{-}H}$ = 24.0 Hz), 6 .60-7.16 (m, 7 H).

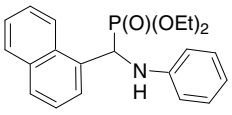
Dimethyl (naphthalen-1-yl-phenylaminomethyl)phosphonate[1] (Table 3, entry 24):



Mol. Wt.: 341.34

The crude reaction mixture was recrystallized from MeOH containing a few drops of EtOAc to afford the desired product as yellow solid (0.77 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.12 (d, 3 H, J = 10.46 Hz), 3.79 (d, 3 H, J =10.75 Hz), 5.62-5.70 (d, 1 H, $^1J_{P\text{-}H}$ = 24.1 Hz), 5.62-8.23 (m, 12 H).

Diethyl (naphthalen-1-yl-phenylaminomethyl)phosphonate[1](Table 3, Entry 25):

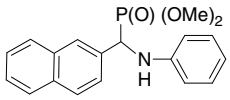


Mol. Wt.: 369.39

The crude reaction mixture was subjected to flash chromatography purification with (60:40) EtOAc-hexane to afford the desired product as yellow solid, (0.78 g, 85 %). ^{1}H NMR ($CDCl_3$,

300 MHz): δ 0.72 (t, 3 H, *J* = 7.0 Hz), 1.32 (s, 3 H, *J* = 7.0 Hz), 3.16-3.24 (m, 1 H), 3.68-3.76 (m, 1 H), 4.13-4.22 (m, 2 H), 5.11 (bs, 1 H), 5.60-5.68 (d, 1 H , $^{1}J_{P\text{-}H}$ = 24.1 Hz), 6.53-8.26 (m, 12 H).

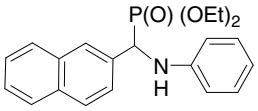
(Naphthalen-2-yl-phenylaminomethyl)phosphonic acid dimethyl ester [2] (Table 3, Entry 26):



Mol. Wt.: 341.34

The crude reaction mixture was purified by recrystallization from EtOAc containing a few drops of DCM to afford the desired product as yellowish green solid, (0.78 g, 92 %). ^{1}H NMR ($CDCl_3$, 300 MHz)*δ*: 3.43 (d, 3 H, *J* = 10.57Hz), 3.74 (d, 3 H, *J* = 10.67Hz), 4.92-5.00 (d, 1 H, $^{1}J_{P\text{-}H}$ = 24.45 Hz), 6.62-7.93 (m, 12 H) ; ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 53.81, 54.90, 56.90, 125.42, 125.47, 126.16, 126.25, 126.86, 126.96, 127.68, 128.01, 128.56, 129.20, 133.13, 133.26, 145.98, 146.18 ; MS (MALDI TOF-TOF) *m/z* 341 (M^+), 232 [(M^+-P(O) ($OMe)_2$].

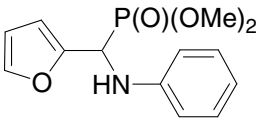
(Naphthalen-2-yl-phenylaminomethyl)phosphonic acid diethyl ester [3] (Table 3, Entry 27):



Mol. Wt.: 369.39

The crude yield was purified by flash chromatography using EtOAc:hexane (40:60) as eluent, afforded the desired yield as liquid, (0.83 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 1.11 (t, 3 H, *J* = 7.0 Hz), 1.30 (t, 3 H, *J* = 7.0 Hz), 3.59-4.15 (m, 4 H), 4.76 (d, 1 H, $^{1}J_{P\text{-}H}$ = 23.6Hz), 6.55-7.91 (m, 12 H).

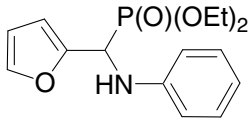
Dimethyl (furan-2-yl-phenylaminomethyl)phosphonate[1] (Table 3, Entry 28):



Mol. Wt.: 281.24

Brownish black crude reaction mixture was recrystallized from MeOH to afforded the desired product as brown solid (0.56 g, 81 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.61 (d, 3 H, J = 10.6 Hz), 3.80 (d, 3 H, J = 10.67 Hz), 4.89-4.96 (d, 1 H, $^1J_{P\text{-}H}$ = 23.92 Hz), 6.37-7.40 (m, 8 H).

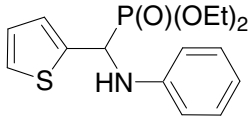
Diethyl (furan-2-yl-phenylaminomethyl)phosphonate[1] (Table 3, Entry 29):



Mol. Wt.: 309.30

The crude reaction mixture was purified by flash chromatography with 1:1 EtOAc:hexane to afford the desired product as deep brown solid (0.60 g, 78%); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.09-1.38 (m, 6 H), 3.86-4.21 (m, 4 H), 4.85-4.93 (d, 1 H, $^1J_{P\text{-}H}$ = 23.8 Hz), 6.32-7.38 (m, 8 H).

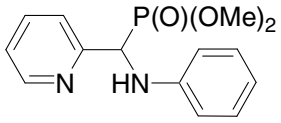
Diethyl (phenylaminothiophen-2-ylmethyl)phosphonate[1] (Table 3, Entry 30):



Mol. Wt.: 325.36

The crude yield was purified by flash chromatography with (70:30) ratio of EtOAc-hexane afforded the desired yield as yellow solid (0.66 g, 81 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.17-1.30 (m, 6 H), 3.82-4.18 (m, 4 H,), 4.6 (bs, 1 H), 4.99-5.09 (dd, 1 H, J = 6.9 & 23. 67 Hz), 6.66-7.22 (m, 8 H).

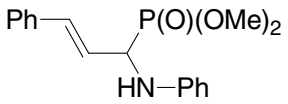
Dimethyl (phenylaminopyridin-2-yl-methyl)phosphonate[1] (Table 3, Entry 31):



Mol. Wt.: 292.27

The crude reaction mixture was purified by flash chromatography with (70:30) EtOAc:hexane to afford the desired product as brownish white amorphous solid (0.60 g, 82 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.61 (d, 3 H, J = 10.6 Hz), 3.76 (d, 3 H, J = 10.6 Hz), 4.98-5.07 (dd, 1 H, $^1J_{P\text{-}H}$ = 6.7 & 22.0 Hz), 5.2 (s,1 H), 3.83 (s, 3 H), 6.68-7.68 (m, 8 H), 8.6 (d, 1 H, J = 4.7 Hz).

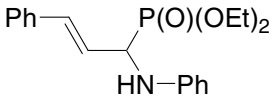
Dimethyl (3-phenyl-1-phenylaminoallyl)phosphonate[1] (Table 3, Entry 32)



Mol. Wt.: 317.32

The crude reaction mixture was purified by flash chromatography with (40:60) EtOAc:hexane to afford the desired product as yellowish brown solid(0.67 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.72-3.83 (m, 6 H), 4.47-4.57 (dd, 1 H, J = 5.8 & 25.46 Hz), 6.21-7.37 (m, 12 H).

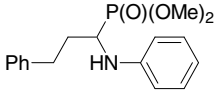
Diethyl (3-phenyl-1-phenylaminoallyl)phosphonate[4] (Table 3, Entry 33)



Mol. Wt.: 345.37

The crude reaction mixture was purified by flash chromatography with (60:40) EtOAc-hexane to afford the desired product as brown solid (0.65 g, 75 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.16-1.33 (m, 6 H), 4.06-4.21 (m, 5 H), 6.13-6.31 (m, 1 H), 6.57-6.77 (m, 4 H), 7.07-7.37 (m, 7 H).

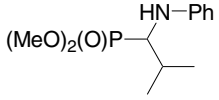
Dimethyl (3-phenyl-1-phenylaminopropyl)phosphonate[1] (Table 3, Entry 34):



Mol. Wt.: 319.34

The crude reaction mixture was purified by flash chromatography with (40:60) EtOAc:hexane to afford the desired product as fade white solid (0.58 g, 75 %).^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.99-2.93 (m, 5 H), 3.63-3.74 (m, 6 H), 6.57-7.28 (m, 10 H).

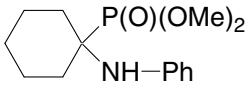
Dimethyl (2-methyl-1-phenylaminopropyl)phosphonate[1] (Table 3, Entry 35):



Mol. Wt.: 257.27

The crude reaction mixture was purified by flash chromatography with (40:60) EtOAc:hexane to afford the desired product as fade white solid (0.45 g, 70 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.05 (m, 6 H), 2.2-2.4 (m, 1 H), 3.6-3.74 (m, 7 H), 3.9 (bs, 1 H), 6.64-7.19 (m, 5 H).

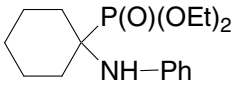
Dimethyl (1-phenylaminocyclohexyl)phosphonate[1] (Table 3, Entry 36):



Mol. Wt.: 283.30

The crude reaction mixture was purified by flash chromatography with 1:1 EtOAc:hexane, to afford the desired product as brown solid (0.56 g, 80 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.22-2.24 (m, 10 H), 3.65 (d, 6 H, J = 10.15 Hz), 6.78-7.2 (m, 5 H).

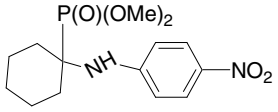
Diethyl (1-phenylaminocyclohexyl)phosphonate [1] (Table 3, Entry 37):



Mol. Wt.: 311.36

The crude reaction mixture was purified by flash chromatography with (60:40) EtOAc-hexane to afford the desired product as brownish white solid (0.54 g, 92 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.21-2.20 (m, 16 H), 3.99-4.08 (m, 4 H), 6.77-7.18 (m, 5 H).

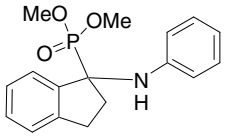
Diethyl (4-nitrophenylaminocyclohexyl)phosphonate (Table 3, Entry 38):



Mol. Wt.: 328.30

The crude reaction mixture was purified using flash chromatography with 70:30 EtOAc:hexane to afford the desired product as yellow solid (0.62 g, 75%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.24-2.34 (m, 10H), 3.71 (d, 6 H, J = 10. 4 Hz), 4.36 (bs, 1 H), 6.98 (d, 2 H, J = 9.16 Hz), 8.03 (d, 2 H, J = 9.18 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.2, 20.4, 25.5, 30.7, 53.8, 56.8, 59.0, 115.4, 126.3, 139.5, 152.4; MS (EI) *m/z* 328 $(M)^+$, 219 $[(M\text{-}P(O)(OMe)_2]^+$; Elem. Anal. Calcd. for $C_{14}H_{21}N_2O_5P$: C, 51.22; H, 6.45; N, 8.53. Found: C, 51.11; H, 6.47; N, 8.56.

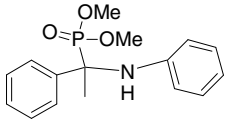
(1-Phenylaminoindan-1-yl)phosphonic acid dimethyl ester (Table 3, Entry 39)



Mol. Wt.: 317.32

The crude reaction mixture (an oil) on passing through flash chromatography column and elution with EtOAc:hexane (60:40) afforded the desired product (0.76 g, 85 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.58-2.70 (m, 2 H), 3.03-3.09 (m, 2 H), 3.64-3.68 (m, 6 H), 6.35-7.45(m, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 30.9, 31.8, 54.3, 54.7, 67.8, 69.9, 117.2, 119.2, 125.8, 126.5, 127.3, 129.3, 140.5, 144.6, 145.1, 145.3; MS (EI) *m/z* 317 $(M)^+$, 208 $[(M\text{-}P(O)(OMe)_2]^+$; Elem. Anal. Calcd. for $C_{17}H_{20}NO_3P$: C, 64.35; H, 6.35; N, 4.41. Found: C, 64.28; H, 6.38 ; N, 4.39.

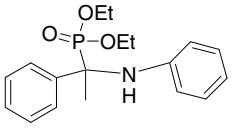
Dimethyl (1-phenyl-1-phenylaminoethyl)phosphonate[1] (Table 3, Entry 40)



Mol. Wt.: 305.31

The flash chromatographic purification of the crude reaction mixture with 1:1 EtOAc:hexane afforded the desired product as brownish yellow solid (0.61 g, 80%).^{1}H NMR (CDCl3, 300 MHz) δ1.97 (d, 3 H, *J*= 16.5 Hz*)* 16.5 Hz), 3.53-3.66 (m, 6 H), 6.38-7.81 (m, 10 H).

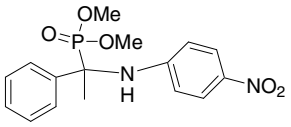
Diethyl (1-phenyl-1-phenylaminoethyl)phosphonate[1] (Table 3, Entry 41)



Mol. Wt.: 333.36

The crude reaction mixture on passing through flash chromatography column and elution with (40:60) EtOAc:hexane afforded the desired product as fade white solid (0.70 g, 80 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.18-1.38 (m, 6 H), 1.96 (d, 3 H, *J* = 16.35 Hz), 3.89-4.03 (m, 4 H), 6.37-7.63 (m, 10 H).

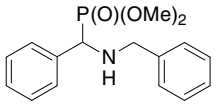
Dimethyl [1-(4-nitrophenylamino)-1-phenylethyl]phosphoate (Table 3, Enrtry 42)



Mol. Wt.: 350.31

The crude reaction mixture on passing through flash chromatography and elution with (60:40) EtOAc:hexane afforded the desired product as yellow solid (0.71 g, 75 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.01 (d, 3 H, J = 16.2 Hz), 3.57-3.62 (m, 4 H), 5.54-7.93 (m, 9 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.1, 54.8, 59.4, 61.4, 115.3, 126.0, 128.2, 128.7, 129.4, 137.1, 139.5, 150.9, 151.2; MS (EI) *m/z* 350 $(M)^+$, 241 $[(M\text{-}P(O)(OMe)_2]^+$; Elem. Anal. Calcd. for $C_{16}H_{19}N_2O_5P$: C, 54.86; H, 5.47; N, 8.0. Found: C, 54.68; H, 5.49; N, 7.91.

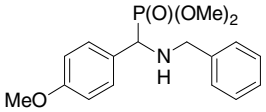
Dimethyl (benzylaminophenylmethyl)phosphonate[1] (Table 3, Entry 43):



Mol. Wt.: 305.31

The crude reaction mixture was purified by flash chromatography with EtOAc to afford the desired product as colorless transparent liquid (0.70 g, 92 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.51-3.82 (m, 8 H), 4.01-4.08 (d, 1 H, $^1J_{P\text{-}H}$ = 20.2 Hz), 7.24-7.44 (m, 10 H).

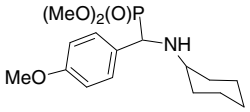
Dimethyl [benzylamino-(4-methoxyphenyl)methyl]phosphonate[1] (Table 3, Entry 44):



Mol. Wt.: 335.33

The crude reaction mixture on passing through flash chromatography column and elution with 90:10 (EtOAc: hexane) afforded the desired product as light yellow transparent liquid (0.76 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.50-3.83 (m, 11 H), 3.96-4.02 (d, 1 H, $^1J_{P\text{-}H}$ = 19.6 Hz), 6.9 (d, 2 H, J = 8.5 Hz), 7.24-7.35 (m, 7 H).

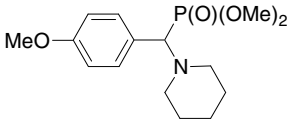
Dimethyl [cyclohexylamino-(4-methoxyphenyl)methyl]phosphonate[1] (Table 3, Entry 45)



Mol. Wt.: 327.36

The crude reaction mixture was passed through flash chromatography column and eluted with 90:10 (EtOAc:hexane) to afford the desired product as colorless transparent liquid (0.78 g, 96 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.079-2.15 (m, 11 H), 2.34 (bs, 1 H), 3.49 (d, 3 H, J = 10.34 Hz), 3.75-3.79 (2 s, 6 H), 4.15-4.22 (d, 1 H, J = 21.7 Hz). 6.87 (d, 2 H, J = 8.2 Hz), 7.31 (d, 2 H, J = 8.0 Hz).

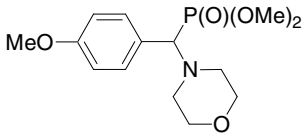
Dimethyl [(4-methoxyphenyl)piperidin-1-yl-methyl]phosphonate[1] (Table 3, Entry 46):



Mol. Wt.: 313.33

The crude reaction mixture on passing through flash chromatography column and elution with 90:10 EtOAc: hexane afforded the desired product as yellow semi-solid (0.70 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.28-1.34 (m, 2 H), 1.55 (d, 4 H, J = 4.2 Hz) 2.35 (d, 2 H, J = 5.2 Hz), 2.78 (t, 2 H, J = 5.44 Hz), 3.46 (d, 3 H, J = 10.44 Hz), 3.80-3.92 (m, 6 H), 6.86 (d, 2 H, J = 8.4 Hz), 7.38 (d, 2 H, J = 8.3 Hz).

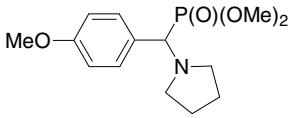
Dimethyl [(4-methoxyphenyl)morpholin-4-yl-methyl]phosphonate (Table 3, Entry 47):



Mol. Wt.: 315.30

The crude reaction mixture on passing through flash chromatography and elution with 90:10 EtOAc:hexane afforded the desired product as light yellow semi-solid (0.71 g, 90 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.47-2.51 (m, 2 H), 2.76-2.82 (m, 2 H), 3.44 (d, 3 H, J = 10.45 Hz), 3.65-3.92 (m, 14 H), 6.88 (d, 2 H, J = 8.4 Hz), 7.37 (d, 2 H, J = 8.4 Hz).

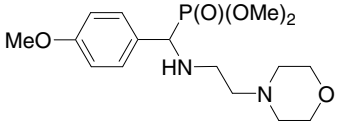
Dimethyl [(4-methoxyphenyl)-pyrrolidin-1-yl-methyl]phosphonate acid dimethyl ester (Table 3, Entry 48):



Mol. Wt.: 299.30

The crude reaction mixture on passing through flash chromatography column and elution with 90:10 EtOAc: hexane afforded the desired product as light yellow semi-solid (0.68 g, 98 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.71 (s, 4 H), 2.6 (s, 4 H), 3.41-3.46(dd, 3 H, J = 2.83 Hz & 10.40 Hz), 3.70-3.79 (m, 7 H), 6.86 (d, 2 H, J = 6.3 Hz), 7.37(d, 2 H, J = 6.7 Hz).

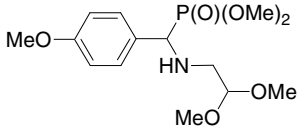
[(4-Methoxy-phenyl)-(2-morpholin-4-yl-ethylamino)methyl]phosphonic acid dimethyl ester[1] (Table 3, Entry 49):



Mol. Wt.: 358.37

The crude liquid reaction mixture on passing through flash chromatography column and elution with 80:20 EtOAc:hexane afforded the desired product as colorless semi-solid (0.72 g, 80 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.34-2.41 (m, 4 H), 248-2.54 (m, 4 H), 3.46-3.87 (m, 13 H), 3.95-4.02 (d, 1 H, $^1J_{P\text{-}H}$ = 20.03 Hz). 6.87 (d, 2 H, J =8.3 Hz), 7.32-7.42 (m, 2 H).

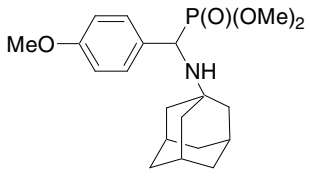
[(2,2-Dimethoxyethylamino)-(4-methoxyphenyl)methyl]phosphonic acid dimethyl ester[1] (Table 3, Entry 50):



Mol. Wt.: 333.32

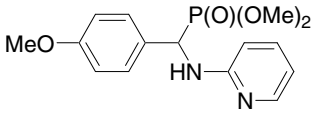
The crude reaction mixture was purified by flash chromatography with EtOAc:hexane (80:20) to afford the desired product as yellow semi-solid (0.79 g, 95 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.57-2.64 (m, 3 H), 3.29 (d, 6 H, J = 11.36 Hz), 3.54 (d, 3 H, J = 10.4 Hz), 3.71 (d, 3 H, J = 10.4 Hz), 3.80 (s, 3 H), 3.00-4.06 (d, 1 H, $^1J_{P\text{-}H}$ = 19.31 Hz), 4.43 (t, 1 H), 6.88 (d, 2 H, J = 8.6 Hz), 7.32 (d, 4 H, J = 8.4 Hz).

Dimethyl [(adamantan-1-ylamino)-(4-methoxyphenyl)methyl]phosphonate[1] (Table 3, Entry 51).



The crude reaction mixture was purified by flash chromatography using EtOAc:hexane (95:5) as eluent to afford the desired product as white solid (0.85 g, 90%). ^{1}H NMR (CDCl3, 300 MHz): δ 1.43- 1.60 (m, 12 H), 1.87 (s, 1 H), 1.97 (s, 2 H), 3.46 (d, 3 H, J) 10.30 Hz), 3.77-3.81 (2 s, 9 H), 4.21-4.29 (1 H, $^1J_{P\text{-}H}$ 24.4 Hz), 6.84 (d, 2 H, J = 8.2 Hz), 7.33 (d, 2 H, J = 7.1 Hz).

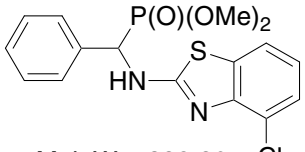
Dimethyl [(4-methoxyphenyl)-(pyridin-2-ylamino)methyl]phosphonate[1] (Table 3, Entry 52):



Mol. Wt.: 322.30

The crude reaction mixture was purified by flash chromatography with (80:20) EtOAc:hexane, to afford the desired product as white solid (0.73 g, 90 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.50 (d, 3 H, J = 10.32 Hz), 3.69-3.76 (m, 6 H), 5.50-5.62 (m, 2 H, NH protons), 6.45-8.07 (m, 8 H).

Dimethyl [(4-chlorobenzothiazol-2-ylamino)(4-methoxyphenyl)methyl] phosphonate (Table 3, Entry 53):

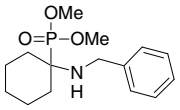


Mol. Wt.: 382.80

The crude reaction mixture was subjected to flash chromatography purification using EtOAc:hexane (80:20) to afford the desired product as yellow solid (0.67 g, 70%). ^{1}H NMR ($CDCl_3$, 300 MHz: δ 3.56 (d, 3 H, J =10.6 Hz), 3.75 (s, 3 H), 3.82 (d, 3 H, J = 10.8 Hz), 5.50 (d, 1 H, $^1J_{P\text{-}H}$ = 21.5Hz), 6.85-7.56 (m, 7 H), 7.9 (bs, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 54.3, 54.5, 54.6, 54.7, 55.7, 56.4, 114.7, 119.7, 122.6, 124.3, 126.6, 127.0, 130.2, 132.9, 149.5,

160.3,166.6, 166.8; MS (MALDI ESI) *m/z* 413(M)$^+$, 303 [(M -P(O)(OMe)$_2$]$^+$; Elem. Anal. Calcd. for $C_{16}H_{16}ClN_2O_3PS$: C, 50.20; H, 4.21; N, 7.32; S, 8.34. Found: C, 50.12; H, 4.24; N, 7.29; S, 8.32.

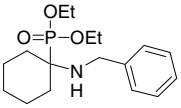
(1-Benzylaminocyclohexyl)phosphonic acid dimethyl ester[1] (Table 3, Entry 54):



Mol. Wt.: 297.33

The crude reaction mixture is subjected to flash chromatography purification using EtOAc:hexane (70:30) to afford the desired product as an oil (0.67 g, 90 %.). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.50-1.87 (m, 10 H), 3.89 (d, 2 H, *J* = 2.5 Hz), 7.20-7.4 (m, 5 H).

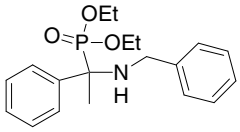
(1-Benzylaminocyclohexyl)phosphonic acid diethyl ester[1] (Table 3, Entry 55):



Mol. Wt.: 325.38

The crude reaction mixture was subjected to flash chromatography purification using EtOAc:hexane (1:1) to afford the desired product as an oil (0.74 g, 91 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.12-1.99 (m, 16 H) 3.91 (d, 2 H, *J* = 3.9 Hz), 4.05-4.20 (m, 4 H), 7.19-7.94 (m, 5 H).

(1-Benzylamino-1-phenyl-ethyl)phosphonic acid diethyl ester[1] (Table 3, Entry 56):



The crude reaction mixture was subjected to flash chromatography purification using EtOAc: hexane (40: 60) to afford the desired product as an oil (0.70 g, 80 %); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.13-1.27 (2 t, 6 H), 1.82 (d, 3 H, *J* = 16.22 Hz), 2.3 (bs, 1 H), 3.47-3.68 (dd, 2 H, *J* = 12.57 Hz, 52.81 Hz), 3.84-4.06 (m, 4 H), 7.24-7.65 (m, 10 H).

References:

1) Bhagat, S.; Chakraborti, A. K.; *J. Org. Chem.* **2007,** *72*, 1263-70.

2) Azizi, N.; Saidi, M. R. *E. J. Org. Chem.* **2003**, *2,* 4630-4633.
3) Firouzabadi H.; Iranpoor, N.; Sobhani, S. *Synthesis* **2004**, 2692-2696.
4) Ambica, Kumar, S.; Taneja, S. C.; Hundal, M. S.; Kapoor, K. K. *Tetrahedron Lett.* **2008,** 49, 2208-2212.