Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Organocatalytic Access to 3-Pyridylphosphonates from Vinyl Phosphonates and Aldehydes

Ram Subhawan Verma, Anil Kumar Khatana, Deepika Verma, and Bhoopendra Tiwari*

Department of Biological and Synthetic Chemistry, Centre of Biomedical Research, SGPGIMS-Campus, Raebareli Road, Lucknow 226014, India

E-mail: btiwari@cbmr.res.in

Table of Content

General Information: Aldehydes and other reagents were purchased from a commercial supplier and used without further purification. All reactions were performed in oven-dried glasswares. The Arylacetadehydes[1] **1** and vinylphosphonates[2] **2** were prepared by following literature known methods. Solvents were dried and distilled following the standard procedures; TLC was carried out on pre-coated plates (Merck silica gel 60, f_{254}), and the spots were visualized with UV light or by charring the plates dipped in PMA charring solution. Flash chromatography was performed using silica gel (100-200 mess) with distilled solvents. ^{1}H, $^{13}C\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR for compounds were recorded at 400 MHz, 100 MHz and 162 MHz instrument respectively using $CDCl_3$ or DMSO-d_6 as the solvent. $^{31}P\{^{1}H\}$ NMR was recorded by using 98% PPh_3 as an external standard. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), etc. High-resolution mass spectral analysis (HRMS) was performed on Q-TOF Premier mass spectrometer. The melting points were recorded on Buchi M-560 melting point apparatus and are uncorrected.

General catalytic procedure for the synthesis of 3-pyridylphosphonates 3: To an oven-dried Schlenk tube equipped with a magnetic stir bar, aldehyde **1** (2.0-5.0 equiv.), vinylphosphonate **2** (0.1 mmol, 1.0 equiv.), pyrrolidine (20 mol %) and $CHCl_3$ (1.0 mL) were added under argon atmosphere and the reaction mixture was stirred for 12 h at room temperature. NH_4OAc (15.0 equiv.) and AcOH (20.0 equiv.) was added to this reaction mixture and stirred further at 50 ^{o}C for 12 h. After completion of the reaction, the reaction mixture was quenched with an aqueous saturated solution of $NaHCO_3$, and extracted with CH_2Cl_2 (3 x 5 ml). The combined organic layers were dried over anhydrous Na_2SO_4, evaporated under reduced pressure and the crude product was purified by flash column chromatography on silica gel using 60% EtOAc in hexane to obtain the pure desired product **3**.

*The preparation of **3a** on gram scale:* The product **3a** was obtained in 91% yield (870 mg) when the reaction was run using **1a** (670 mg, 3.75 mmol) and **2a** (670 mg, 2.5 mmol) under the optimized reaction condition.

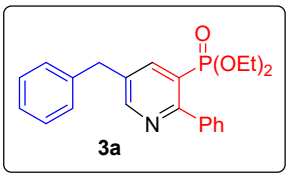
Synthesis of 5: To an oven-dried Schlenk tube equipped with a magnetic stir bar, aldehyde **1a** (27 mg, 0.2 mmol), vinylphosphonate **2a** (27 mg, 0.10 mmol), pyrrolidine (1.6 µL, 0.02 mmol) was added in $CHCl_3$ (1.0 mL) under argon atmosphere and the reaction mixture was stirred for 12 h at room temperature. After the completion, the reaction mixure was concentrated under reduced pressure and the crude product was purified by flash column chromatography on silica gel using 60% EtOAc in hexane to obtain the intermediate **5** in 95% yield (38 mg).

Synthesis of the 3-pyridylphosphonic acid-hydrogen bromide 4: 3-Pyridylphosphonic acid-hydrogen bromide was prepared following a literature known procedure.[3] 3-Pyridylphosphonate **3a** (445 mg, 1.16 mmol) and TMSBr (307 µL, 2.33 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 16 h. After completion of the reaction, the solvent was removed under a reduced

pressure and the crude reaction mass was dissolved in MeOH (10 mL) and stirred for an additional 30 min. Methanol was removed under a reduced pressure to obtain 3-pyrdiylphosphonic acid-hydrogen bromide **4** as white crystalline solid in 96% yield (517 mg).

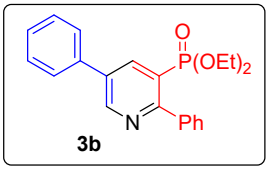
Characterization of the Products:

Diethyl (5-benzyl-2-phenylpyridin-3-yl)phosphonate (3a): 95% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (6H, t, J = 7.2 Hz), 3.74-3.98 (4H, m), 4.05 (2H, s), 7.17-7.26 (3H, m), 7.28-7.36 (2H, m), 7.37-7.47 (3H, m), 7.58-7.68 (2H, m), 8.13 (1H, dd, J = 14.8, 2.0 Hz), 8.66 (1H, t, J = 2.4 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.8 (d, $J_{C\text{-}P}$ = 7.0 Hz), 38.4, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 123.0 (d, $J_{C\text{-}P}$ = 186.0 Hz), 126.6, 127.5, 128.4, 128.7, 128.8, 129.0, 134.4 (d, $J_{C\text{-}P}$ = 11.0 Hz), 138.9, 140.4, 142.3 (d, $J_{C\text{-}P}$ = 9.0 Hz), 152.0 (d, $J_{C\text{-}P}$ = 1.0 Hz), 160.1 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}NO_3PNa^+$ 404.1386, found: 404.1385.



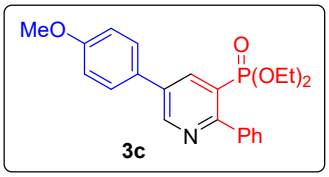
3a

Diethyl (2,5-diphenylpyridin-3-yl)phosphonate (3b): 94% yield (35 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (6H, t, J = 6.8 Hz), 3.83-4.08 (4H, m), 7.39-7.59 (6H, m), 7.61-7.77 (4H, m), 8.56 (1H, dd, J = 15.2, 2.4 Hz), 9.03 (1H, t, J = 2.0 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 123.3 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.1, 127.7, 128.5, 128.6, 129.1, 129.2, 134.3 (d, $J_{C\text{-}P}$ = 11.0 Hz), 136.4, 140.3, 140.6 (d, $J_{C\text{-}P}$ = 9.0 Hz), 150.1 (d, $J_{C\text{-}P}$ = 2.0 Hz), 160.7 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{21}H_{22}NO_3PNa^+$ 390.1230, found: 390.1232.



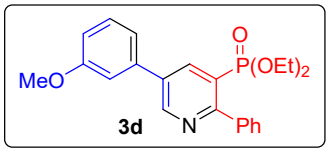
3b

Diethyl (5-(4-methoxyphenyl)-2-phenylpyridin-3-yl)phosphonate (3c): 89% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07 (6H, t, J = 7.2 Hz), 3.76-3.99 (7H, m), 6.97 (2H, d, J = 8.4 Hz), 7.31-7.44 (3H, m), 7.53 (2H, d, J = 8.4 Hz), 7.58-7.68 (2H, m), 8.44 (1H, dd, J = 14.8, 1.6 Hz), 8.91 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0, 55.4, 62.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 114.7, 123.2 (d, $J_{C\text{-}P}$ = 185.0 Hz), 127.7, 128.3, 128.6, 128.8, 129.2, 134.0 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 140.5, 149.7 (d, $J_{C\text{-}P}$ = 1.0 Hz), 160.1, 160.2; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}NO_4PNa^+$ 420.1336, found: 420.1331.



3c

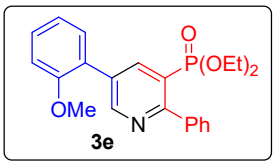
Diethyl (5-(3-methoxyphenyl)-2-phenylpyridin-3-yl)phosphonate (3d): 91% yield (37 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (6H, t, J = 7.2 Hz), 3.77-4.07 (7H, m), 6.96-7.02 (1H, m), 7.18 (1H, s), 7.24 (1H, d, J = 7.6 Hz), 7.39-7.51 (4H, m), 7.66-7.74 (2H, m), 8.55 (1H, dd, J = 14.8, 2.0 Hz), 9.0 (1H, s);



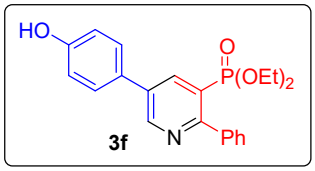
3d

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 55.4, 62.4 (d, $J_{C\text{-}P}$ = 7.0 Hz), 112.9, 113.9, 119.6, 123.2 (d, $J_{C\text{-}P}$ = 187.0 Hz), 127.7, 128.7, 129.2, 130.3, 134.3 (d, $J_{C\text{-}P}$ = 11.0 Hz), 137.9, 140.4, 140.7 (d, $J_{C\text{-}P}$ = 8.0 Hz), 150.2, 160.2, 160.9 (d, $J_{C\text{-}P}$ = 11.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 16.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{22}H_{24}NO_4PH^+$ 398.1516, found: 398.1514.

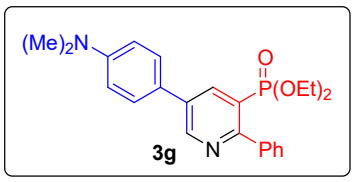
Diethyl (5-(2-methoxyphenyl)-2-phenylpyridin-3-yl)phosphonate (3e): 87% yield (35 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (6H, t, J = 7.2 Hz), 3.81-4.07 (7H, m), 7.03 (1H, d, J = 8.4 Hz), 7.09 (1H, t, J = 7.6 Hz), 7.35-7.51 (5H, m), 7.68-7.77 (2H, m), 7.24 (1H, d, J = 7.6 Hz), 7.39-7.51 (4H, m), 7.66-7.74 (2H, m), 8.50 (1H, dd, J = 14.8, 1.6 Hz), 8.97 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 6.0 Hz), 55.5, 62.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 111.2, 121.1, 122.6 (d, $J_{C\text{-}P}$ = 187.0 Hz), 125.7, 127.7, 128.5, 129.2, 130.0, 130.6, 133.0 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.6, 142.7 (d, $J_{C\text{-}P}$ = 9.0 Hz), 152.2 (d, $J_{C\text{-}P}$ = 1.0 Hz), 156.6, 160.2 (d, $J_{C\text{-}P}$ = 12.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 16.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{22}H_{24}NO_4PH^+$ 398.1516, found: 398.1513.



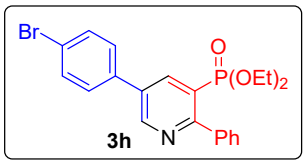
Diethyl (5-(4-hydroxyphenyl)-2-phenylpyridin-3-yl)phosphonate (3f): 80% yield (31 mg), pale yellow gummy liquid, eluent: 70% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (6H, t, J = 6.8 Hz), 3.86-4.13 (4H, m), 7.06 (2H, d, J = 8.4 Hz), 7.41-7.49 (3H, m), 7.52 (2H, d, J = 8.4 Hz), 7.60-7.69 (2H, m), 8.64 (1H, dd, J = 15.2, 1.6 Hz), 9.01 (1H, s), 9.11 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 15.9 (d, $J_{C\text{-}P}$ = 6.0 Hz), 62.8 (d, $J_{C\text{-}P}$ = 6.0 Hz), 116.5, 122.4 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.2, 127.7, 128.2, 128.7, 129.1, 134.5 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.2, 140.5 (d, $J_{C\text{-}P}$ = 10.0 Hz), 149.7, 158.2, 159.7 (d, $J_{C\text{-}P}$ = 11.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 16.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{22}NO_4PH^+$ 384.1360, found: 384.1357.



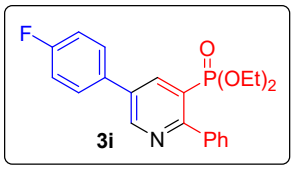
Diethyl (5-(4-(dimethylamino)phenyl)-2-phenylpyridin-3-yl)phosphonate (3g): 75% yield (31 mg), pale yellow gummy liquid, eluent: 70% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14 (6H, t, J = 6.8 Hz), 3.02 (6H, s), 3.79-4.09 (4H, m), 6.83 (2H, d, J = 8.4 Hz), 7.38-7.50 (3H, m), 7.58 (2H, d, J = 8.4 Hz), 7.65-7.74 (2H, m), 8.50 (1H, dd, J = 14.8, 1.6 Hz), 8.99 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 40.3, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 112.7, 123.0 (d, $J_{C\text{-}P}$ = 186.0 Hz), 123.7, 127.6, 127.7, 128.4, 129.2, 134.3 (d, $J_{C\text{-}P}$ = 11.0 Hz), 139.3 (d, $J_{C\text{-}P}$ = 9.0 Hz), 140.6, 149.3, 150.6, 159.2 (d, $J_{C\text{-}P}$ = 11.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 16.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{23}H_{27}N_2O_3PH^+$ 411.1833, found: 411.1831.



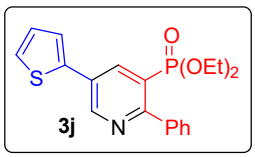
Diethyl (5-(4-bromophenyl)-2-phenylpyridin-3-yl)phosphonate (3h): 94% yield (42 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (6H, t, J = 7.2 Hz), 3.83-4.08 (4H, m), 7.41-7.49 (3H, m), 7.53 (2H, d, J = 8.4 Hz), 7.61-7.74 (4H, m), 8.53 (1H, dd, J = 14.8, 2.0 Hz), 8.98 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 5.0 Hz), 62.5 (d, $J_{C\text{-}P}$ = 6.0 Hz), 123.1, 123.6 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.7, 128.7, 128.8, 129.2, 132.4, 133.3 (d, $J_{C\text{-}P}$ = 11.0 Hz), 135.4, 140.3, 140.5 (d, $J_{C\text{-}P}$ = 9.0 Hz), 149.8, 161.2 (d, $J_{C\text{-}P}$ = 12.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 15.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{21}BrNO_3PH^+$ 446.0516, found: 446.0513.



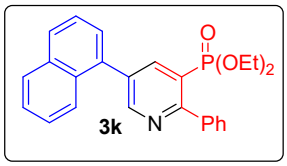
Diethyl (5-(4-fluorophenyl)-2-phenylpyridin-3-yl)phosphonate (3i): 92% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (6H, t, J = 7.2 Hz), 3.83-4.08 (4H, m), 7.21 (2H, t, J = 8.4 Hz), 7.38-7.53 (3H, m), 7.56-7.77 (4H, m), 8.52 (1H, dd, J = 14.8, 2.0 Hz), 8.98 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.9 (d, $J_{C\text{-}P}$ = 6.0 Hz), 62.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 116.2 (d, $J_{C\text{-}F}$ = 22.0 Hz), 123.4 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.7, 128.7, 128.8 (d, $J_{C\text{-}F}$ = 8.0 Hz), 129.1, 132.5 (d, $J_{C\text{-}F}$ = 4.0 Hz), 133.4 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.2, 140.5 (d, $J_{C\text{-}P}$ = 9.0 Hz), 149.9, 160.8 (d, $J_{C\text{-}P}$ = 12.0 Hz), 163.1 (d, $J_{C\text{-}F}$ = 247.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{21}FNO_3PH^+$ 386.1316, found: 386.1316.

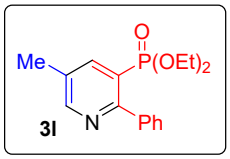


Diethyl (2-phenyl-5-(thiophen-2-yl)pyridin-3-yl)phosphonate (3j): 78% yield (29 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (6H, t, J = 6.8 Hz), 3.76-4.00 (4H, m), 7.09 (1H, t, J = 4.8 Hz), 7.31-7.44 (5H, m), 7.55-7.66 (2H, m), 8.45 (1H, dd, J = 14.8, 2.0 Hz), 8.95 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 123.5 (d, $J_{C\text{-}P}$ = 186.0 Hz), 124.9, 126.6, 127.7, 128.3 (d, $J_{C\text{-}P}$ = 11.0 Hz), 128.4, 128.7, 129.1, 139.0, 139.2 (d, $J_{C\text{-}P}$ = 9.0 Hz), 140.2, 148.6, 160.6 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 15.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{19}H_{20}NO_3PSNa^+$ 396.0794, found: 396.0794.

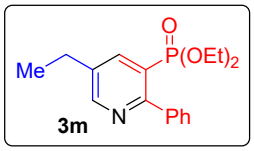


Diethyl (5-(naphthalen-1-yl)-2-phenylpyridin-3-yl)phosphonate (3k): 83% yield (35 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14 (6H, t, J = 7.2 Hz), 3.81-4.08 (4H, m), 7.42-7.64 (7H, m), 7.79 (2H, d, J = 6.8 Hz), 7.86 (1H, d, J = 8.0 Hz), 7.95 (2H, d, J = 8.0 Hz), 8.47 (1H, dd, J = 14.8, 2.0 Hz), 8.94 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.5 (d, $J_{C\text{-}P}$ = 6.0 Hz), 123.3 (d, $J_{C\text{-}P}$ = 187.0 Hz), 125.0, 125.4, 126.2, 126.8, 127.6, 127.8, 128.5, 128.7, 128.9, 129.3, 131.3, 133.8, 134.1 (d, $J_{C\text{-}P}$ = 11.0 Hz), 135.1, 140.5, 143.2 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.5, 161.0 (d, $J_{C\text{-}P}$ = 12.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 15.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{25}H_{24}NO_3PH^+$ 418.1567, found: 418.1565.

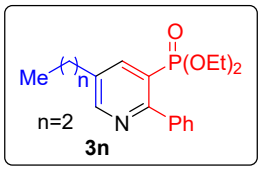


Diethyl (5-methyl-2-phenylpyridin-3-yl)phosphonate (3l): 72% yield (22 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. 

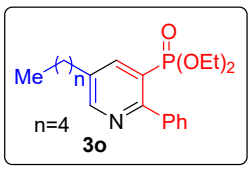
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (6H, t, J = 6.8 Hz), 2.43 (3H, s), 3.78-4.04 (4H, m), 7.36-7.48 (3H, m), 7.56-7.67 (2H, m), 8.18 (1H, d, J = 14.4 Hz), 8.62 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 17.9, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.7 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.6, 128.4, 128.5, 129.1, 131.1 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.6, 142.7 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.4 (d, $J_{C\text{-}P}$ = 2.0 Hz), 159.5 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.6; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{16}H_{20}NO_3PNa^+$ 328.1073, found: 328.1071.

Diethyl (5-ethyl-2-phenylpyridin-3-yl)phosphonate (3m): 75% yield (24 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. 

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (6H, t, J = 7.2 Hz), 1.33 (3H, t, J = 7.6 Hz), 2.65-2.83 (2H, m), 3.76-4.05 (4H, m), 7.35-7.50 (3H, m), 7.55-7.68 (2H, m), 8.19 (1H, dd, J = 14.8, 2.0 Hz), 8.64 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.07, 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 25.6, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.8 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.6, 128.4, 129.1, 137.1 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.7, 141.6 (d, $J_{C\text{-}P}$ = 8.0 Hz), 151.7 (d, $J_{C\text{-}P}$ = 2.0 Hz), 159.8 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{17}H_{22}NO_3PNa^+$ 342.1230, found: 342.1230.

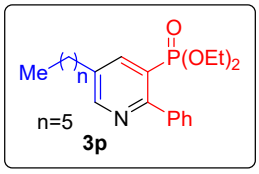
Diethyl (2-phenyl-5-propylpyridin-3-yl)phosphonate (3n): 72% yield (24 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. 

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00 (3H, t, J = 7.6 Hz), 1.13 (6H, t, J = 7.2 Hz), 1.64-1.80 (2H, m), 2.68 (2H, t, J = 8.0 Hz), 3.76-4.06 (4H, m), 7.35-7.50 (3H, m), 7.57-7.71 (2H, m), 8.17 (1H, d, J = 14.4 Hz), 8.62 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 13.6, 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 24.1, 34.5, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.8 (d, $J_{C\text{-}P}$ = 185.0 Hz), 127.6, 128.3, 129.1, 135.6 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.7, 142.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.1 (d, $J_{C\text{-}P}$ = 2.0 Hz), 159.8 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{18}H_{24}NO_3PNa^+$ 356.1386, found: 356.1387.

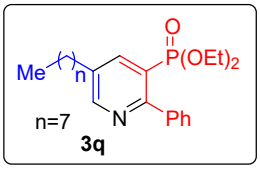
Diethyl (5-pentyl-2-phenylpyridin-3-yl)phosphonate (3o): 78% yield (29 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. 

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (3H, t, J = 6.8 Hz), 1.13 (6H, t, J = 7.2 Hz), 1.32-1.42 (4H, m), 1.62-1.76 (2H, m), 2.70 (2H, t, J = 8.0 Hz), 3.78-4.05 (4H, m), 7.35-7.50 (3H, m), 7.56-7.70 (2H, m), 8.17 (1H, d, J = 14.4, 1.6 Hz), 8.62 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 13.9, 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 22.4, 30.6, 31.3, 32.5, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.8 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.6, 128.4, 129.1, 135.9 (d, $J_{C\text{-}P}$ = 11.0 Hz), 140.6, 142.1 (d, $J_{C\text{-}P}$ = 9.0 Hz), 152.0, 159.7 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{28}NO_3PNa^+$ 384.1699, found: 384.1698.

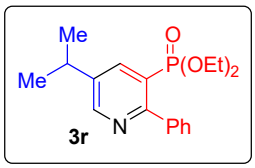
Diethyl (5-hexyl-2-phenylpyridin-3-yl)phosphonate (3p): 74% yield (28 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (3H, t, J = 6.8 Hz), 1.08 (6H, t, J = 7.2 Hz), 1.19-1.38 (6H, m), 1.58-1.70 (2H, m), 2.65 (2H, t, J = 7.6 Hz), 3.72-3.98 (4H, m), 7.29-7.41 (3H, m), 7.51-7.62 (2H, m), 8.10 (1H, d, J = 14.8, 2.0 Hz), 8.55 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 14.0, 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 22.5, 28.8, 30.9, 31.5, 32.5, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.7 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.6, 128.4, 129.1, 135.9 (d, $J_{C\text{-}P}$ = 10.0 Hz), 140.6, 142.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.0, 159.7 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{30}NO_3PH^+$ 376.2037, found: 376.2035.



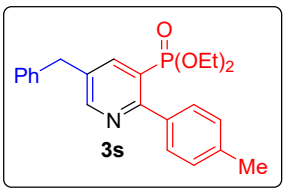
Diethyl (5-octyl-2-phenylpyridin-3-yl)phosphonate (3q): 70% yield (29 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, J = 6.8 Hz), 1.11 (6H, t, J = 7.2 Hz), 1.20-1.38 (10H, m), 1.60-1.75 (2H, m), 2.68 (2H, t, J = 7.6 Hz), 3.76-4.04 (4H, m), 7.35-7.46 (3H, m), 7.56-7.66 (2H, m), 8.15 (1H, d, J = 14.8, 1.2 Hz), 8.60 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 14.0, 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 22.6, 29.1, 29.2, 29.3, 31.0, 31.8, 32.5, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.7 (d, $J_{C\text{-}P}$ = 185.0 Hz), 127.6, 128.3, 129.1, 135.9 (d, $J_{C\text{-}P}$ = 10.0 Hz), 140.6, 142.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.0 (d, $J_{C\text{-}P}$ = 2.0 Hz), 159.7 (d, $J_{C\text{-}P}$ = 12.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{23}H_{34}NO_3PNa^+$ 426.2169, found: 426.2165.



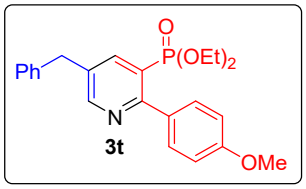
Diethyl (5-isopropyl-2-phenylpyridin-3-yl)phosphonate (3r): 86% yield (29 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (6H, t, J = 7.2 Hz), 1.35 (6H, d, J = 6.8 Hz), 2.96-2.13 (1H, m), 3.77-4.05 (4H, m), 7.35-7.49 (3H, m), 7.56-7.68 (2H, m), 8.22 (1H, dd, J = 15.2, 2.0 Hz), 8.67 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 23.5, 31.4, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.8 (d, $J_{C\text{-}P}$ = 186.0 Hz), 127.6, 128.3, 129.1, 140.1 (d, $J_{C\text{-}P}$ = 9.0 Hz), 140.6, 141.4 (d, $J_{C\text{-}P}$ = 11.0 Hz), 150.7, 159.9 (d, $J_{C\text{-}P}$ = 12.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{18}H_{24}NO_3PNa^+$ 356.1386, found: 356.1383.



Diethyl (5-benzyl-2-(p-tolyl)pyridin-3-yl)phosphonate (3s): 93% yield (37 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (6H, t, J = 7.2 Hz), 2.38 (3H, s), 3.75-3.98 (4H, m), 4.03 (2H, s), 7.21 (5H, t, J = 8.0 Hz), 7.30 (2H, t, J = 7.2 Hz), 7.55 (2H, d, J = 7.6 Hz), 8.11 (1H, dd, J = 14.8, 2.0 Hz), 8.64 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.6 (d, $J_{C\text{-}P}$ = 6.0 Hz), 21.0, 38.2, 61.9 (d, $J_{C\text{-}P}$ = 6.0 Hz), 122.6 (d, $J_{C\text{-}P}$ = 186.0 Hz), 126.4, 128.0, 128.5, 128.6, 128.8, 133.9 (d, $J_{C\text{-}P}$ = 10.0 Hz), 137.4, 138.0, 138.8, 142.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 151.9 (d, $J_{C\text{-}P}$ = 1.0 Hz), 160.0 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.5; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{23}H_{26}NO_3PNa^+$ 418.1543, found: 418.1541.

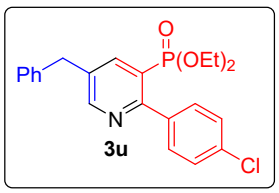


Diethyl (5-benzyl-2-(4-methoxyphenyl)pyridin-3-yl)phosphonate (3t): 92% yield (38 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (6H, t, J = 8.4 Hz), 3.65-3.89 (7H, m), 3.94 (2H, s), 6.86 (2H, d, J = 8.4 Hz), 7.07-7.17 (3H, m), 7.17-7.26 (2H, m), 7.54 (2H, d, J = 8.4 Hz), 8.00 (1H, d, J = 15.2 Hz), 8.55 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 38.5, 55.3, 62.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 113.1, 122.7 (d, $J_{C\text{-}P}$ = 186.0 Hz), 126.7, 128.8, 128.9, 130.7, 133.1, 134.1 (d, $J_{C\text{-}P}$ = 10.0 Hz), 139.1, 142.5 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.2, 159.9 (d, $J_{C\text{-}P}$ = 11.0 Hz), 160.0; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{23}H_{26}NO_4PH^+$ 412.1673, found: 412.1670.



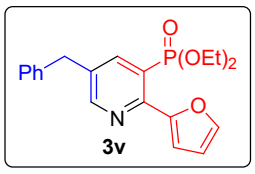
3t

Diethyl (5-benzyl-2-(4-chlorophenyl)pyridin-3-yl)phosphonate (3u): 94% yield (49 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (6H, t, J = 7.2 Hz), 3.80-4.00 (4H, m), 4.05 (2H, s), 7.17-7.27 (3H, m), 7.28-7.35 (2H, m), 7.40 (2H, d, J = 8.4 Hz), 7.61 (2H, d, J = 8.4 Hz), 8.11 (1H, dd, J = 14.8, 2.0 Hz), 8.65 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.8 (d, $J_{C\text{-}P}$ = 7.0 Hz), 38.3, 62.2 (d, $J_{C\text{-}P}$ = 6.0 Hz), 123.0 (d, $J_{C\text{-}P}$ = 186.0 Hz), 126.6, 127.6, 128.6, 128.7, 130.5, 134.5, 134.6 (d, $J_{C\text{-}P}$ = 11.0 Hz), 138.7, 138.8, 142.2 (d, $J_{C\text{-}P}$ = 9.0 Hz), 152.1 (d, $J_{C\text{-}P}$ = 2.0 Hz), 158.7 (d, $J_{C\text{-}P}$ = 11.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 16.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{22}H_{23}ClNO_3PH^+$ 416.1177, found: 416.1176.



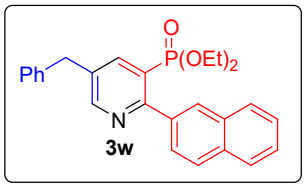
3u

Diethyl (5-benzyl-2-(furan-2-yl)pyridin-3-yl)phosphonate (3v): 91% yield (34 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (6H, t, J = 7.2 Hz), 3.96-4.18 (6H, m), 6.48-6.56 (1H, m), 7.08-7.37 (6H, m), 7.59 (1H, s), 8.14 (1H, dd, J = 15.2, 2.0 Hz), 8.64 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.9 (d, $J_{C\text{-}P}$ = 7.0 Hz), 38.3, 62.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 111.5, 112.8, 120.4 (d, $J_{C\text{-}P}$ = 184.0 Hz), 126.5, 128.6, 128.6, 134.2 (d, $J_{C\text{-}P}$ = 10.0 Hz), 138.7, 143.0 (d, $J_{C\text{-}P}$ = 8.0 Hz), 143.6, 148.9 (d, $J_{C\text{-}P}$ = 10.0 Hz), 151.5, 152.2 (d, $J_{C\text{-}P}$ = 2.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 15.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{22}NO_4PNa^+$ 394.1179, found: 394.1179.



3v

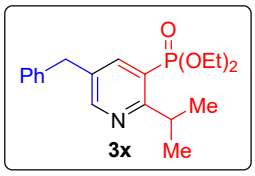
Diethyl (5-benzyl-2-(naphthalen-2-yl)pyridin-3-yl)phosphonate (3w): 93% yield (40 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (6H, t, J = 6.8 Hz), 3.72-3.95 (4H, m), 4.05 (2H, s), 7.16-7.25 (3H, m), 7.27-7.34 (2H, m), 7.42-7.51 (2H, m), 7.78 (1H, d, J = 8.4 Hz), 7.81-7.94 (3H, m), 8.13-823 (2H, m), 8.70 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 15.6 (d, $J_{C\text{-}P}$ = 7.0 Hz), 38.3, 62.0 (d, $J_{C\text{-}P}$ = 6.0 Hz), 123.1 (d, $J_{C\text{-}P}$ = 186.0 Hz), 125.9, 126.1, 126.4, 126.6, 127.1, 127.3, 128.2, 128.5, 128.6, 132.4, 132.9, 134.2 (d, $J_{C\text{-}P}$ = 10.0 Hz), 137.6, 138.8, 142.3 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.0



3w

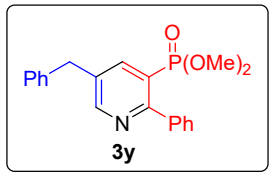
(d, $J_{C\text{-}P}$ = 1.0 Hz), 159.9 (d, $J_{C\text{-}P}$ = 11.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 16.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{26}H_{26}NO_3PH^+$ 432.1724, found: 432.1723.

Diethyl (5-benzyl-2-isopropylpyridin-3-yl)phosphonate (3x): 94% yield (33 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24-1.34 (12H, m), 3.58-3.71 (1H, m), 3.97 (2H, s), 4.01-4.23 (4H, m), 7.14-7.26 (3H, m), 7.26-7.35 (2H, m), 8.00 (1H, dd, J = 14.8, 2.0 Hz), 8.57 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 16.2 (d, $J_{C\text{-}P}$ = 7.0 Hz), 22.4, 33.4, 38.6, 62.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 121.5 (d, $J_{C\text{-}P}$ = 184.0 Hz), 126.6, 128.8, 128.9, 133.3 (d, $J_{C\text{-}P}$ = 11.0 Hz), 139.4, 142.1 (d, $J_{C\text{-}P}$ = 10.0 Hz), 152.8 (d, $J_{C\text{-}P}$ = 2.0 Hz), 167.8 (d, $J_{C\text{-}P}$ = 13.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 18.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{19}H_{26}NO_3PH^+$ 348.1724, found: 348.1722.



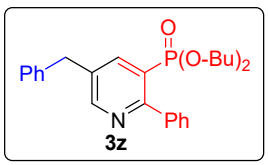
3x

Dimethyl (5-benzyl-2-phenylpyridin-3-yl)phosphonate (3y): 92% yield (32 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.47 (6H, d, J = 11.2 Hz), 4.04 (2H, s), 7.16-7.26 (3H, m), 7.26-7.35 (2H, m), 7.36-7.47 (3H, m), 7.62 (2H, d, J = 6.8 Hz), 8.13 (1H, dd, J = 14.8, 1.6 Hz), 8.67 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 38.2, 52.4 (d, $J_{C\text{-}P}$ = 6.0 Hz), 121.8 (d, $J_{C\text{-}P}$ = 187.0 Hz), 126.4, 127.4, 128.3, 128.5, 128.6, 134.2 (d, $J_{C\text{-}P}$ = 11.0 Hz), 138.7, 140.0, 142.2 (d, $J_{C\text{-}P}$ = 8.0 Hz), 152.1 (d, $J_{C\text{-}P}$ = 1.0 Hz), 159.9 (d, $J_{C\text{-}P}$ = 12.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 19.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{20}NO_3PH^+$ 354.1254, found: 354.1255.



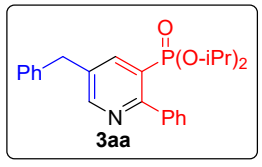
3y

Dibutyl (5-benzyl-2-phenylpyridin-3-yl)phosphonate (3z): 91% yield (40 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82 (6H, t, J = 7.2 Hz), 1.12-1.27 (4H, m), 1.32-1.47 (4H, m), 3.69-3.80 (2H, m), 3.81-3.91 (2H, m), 4.03 (2H, s), 7.16-7.26 (3H, m), 7.27-7.35 (2H, m), 7.36-7.46 (3H, m), 7.60-7.71 (2H, m), 8.12 (1H, dd, J = 14.8, 1.6 Hz), 8.66 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 13.2, 18.3, 31.8 (d, $J_{C\text{-}P}$ = 7.0 Hz), 38.2, 65.7 (d, $J_{C\text{-}P}$ = 7.0 Hz), 122.9 (d, $J_{C\text{-}P}$ = 187.0 Hz), 126.4, 127.4, 128.2, 128.5, 128.6, 128.9, 134.1 (d, $J_{C\text{-}P}$ = 11.0 Hz), 138.8, 140.3, 142.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 151.8 (d, $J_{C\text{-}P}$ = 1.0 Hz), 159.8 (d, $J_{C\text{-}P}$ = 12.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 16.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{26}H_{32}NO_3PH^+$ 438.2193, found: 438.2193.



3z

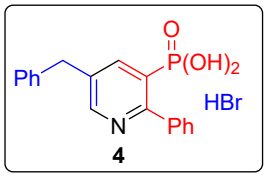
Diisopropyl (5-benzyl-2-phenylpyridin-3-yl)phosphonate (3aa): 92% yield (38 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (6H, d, J = 6.4 Hz), 1.16 (6H, d, J = 6.0 Hz), 4.04 (2H, s), 4.48-4.62 (2H, m), 7.17-7.26 (3H, m), 7.27-7.34 (2H, m), 7.35-7.43 (3H, m), 7.62-7.71 (2H, m), 8.16 (1H, dd, J = 14.8, 1.6 Hz), 8.64 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 23.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 23.5 (d, $J_{C\text{-}P}$ = 4.0 Hz), 38.3, 71.1 (d, $J_{C\text{-}P}$ = 7.0 Hz), 124.3 (d, $J_{C\text{-}P}$ = 188.0 Hz), 126.4, 127.3, 128.1, 128.6, 128.7, 129.3,



3aa

134.1 (d, $J_{C\text{-}P}$ = 11.0 Hz), 138.9, 140.5, 142.0 (d, $J_{C\text{-}P}$ = 9.0 Hz), 151.6 (d, $J_{C\text{-}P}$ = 1.0 Hz), 159.9 (d, $J_{C\text{-}P}$ = 11.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{24}H_{28}NO_3PNa^+$ 432.1699, found: 432.1698.

(5-Benzyl-2-phenylpyridin-3-yl)phosphonic acid hydrogen bromide (4): 96% yield (517 mg), white crystalline solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.04 (2H, s), 7.16-7.43 (8H, m), 7.66 (2H, d, J = 3.2 Hz), 8.01 (1H, d, J = 14.0), 8.67 (1H, s); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ 37.9, 126.9, 127.4, 127.7, 128.4, 129., 129.3, 129.9, 135.1 (d, $J_{C\text{-}P}$ = 10.0 Hz), 140.6, 141.3, 141.9 (d, $J_{C\text{-}P}$ = 8.0 Hz), 150.9, 158.8 (d, $J_{C\text{-}P}$ = 11.0 Hz); $^{31}P\{^{1}H\}$ NMR (162 MHz, DMSO-d_6): δ 10.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{18}H_{16}NO_3PH^+$ 326.0941, found: 326.0943.



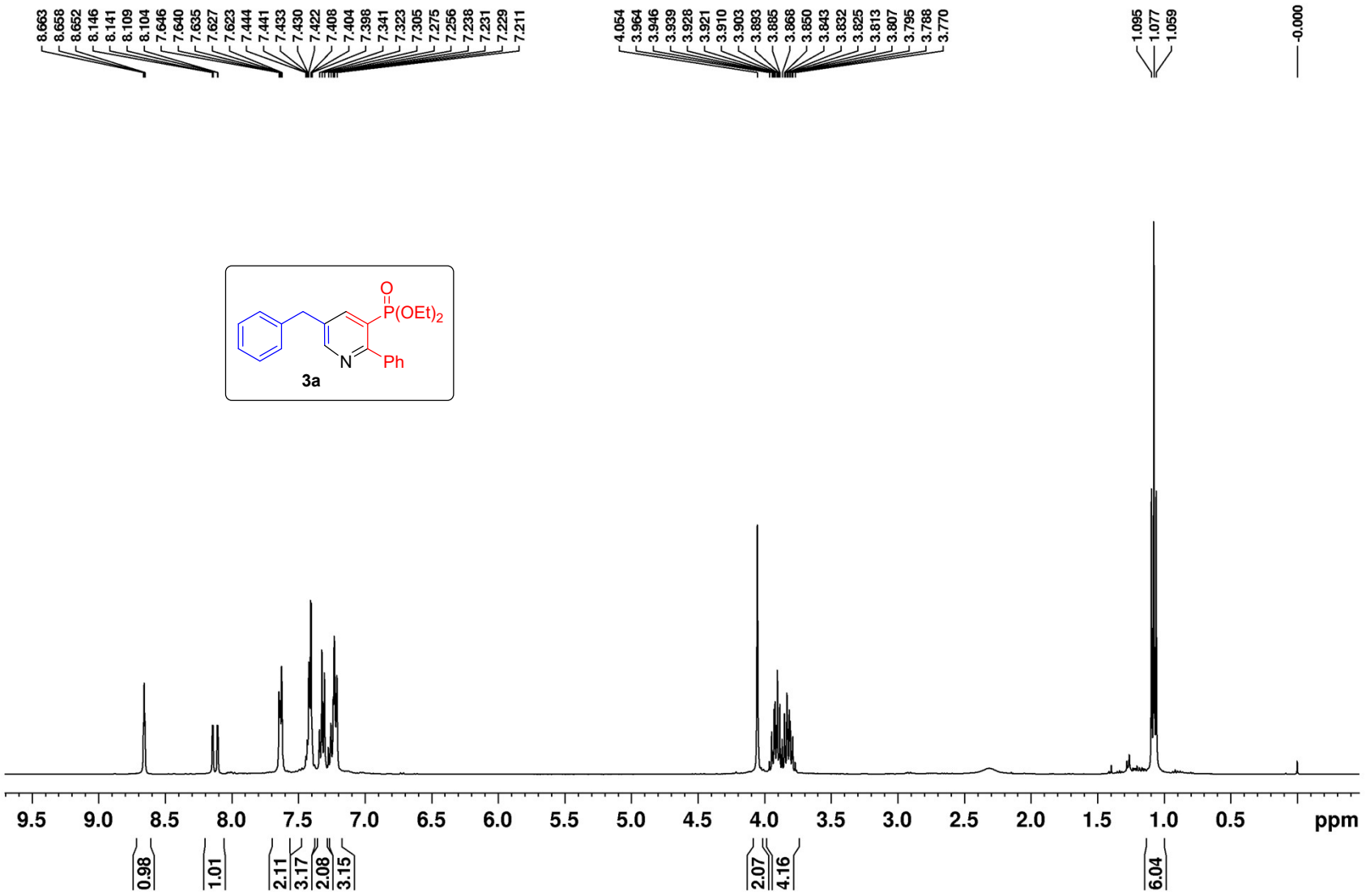
4

References

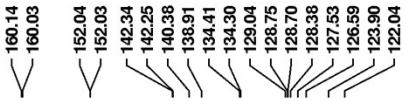
1. a) Hostier, T.; Neouchy, Z.; Ferey, V.; Gomez Pardo, D.; Cossy, J. *Org. Lett.* **2018**, *20*, 1815-1818. b) Ermolat'ev, D. S.; Bariwal, J. B.; Steenackers, H. P.; De Keersmaecker, S. C.; Van der Eycken, E. V. *Angew. Chem. Int. Ed.* **2010**, *49*, 9465-9468.
2. a) Zhang, J.; Dong, K.; Wang, Z.; Ding, K. *Org. Biomol. Chem.,* **2012**, *10*, 1598-1601. b) De Fusco, C.; Fuoco, T.; Croce, G.; Lattanzi, A. *Org. Lett.* **2012,** *14*, 4078-4081.
3. Ayyappan, P.; Evans, O. R.; Foxman, B. M.; Wheeler, K. A.; Warren, T. H.; Lin, W. *Inorg. Chem.* **2001**, *40*, 5954-5961.

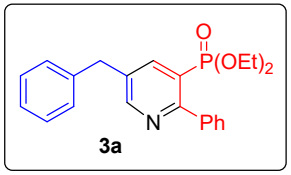
^{1}H, $^{13}C\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR Spectra

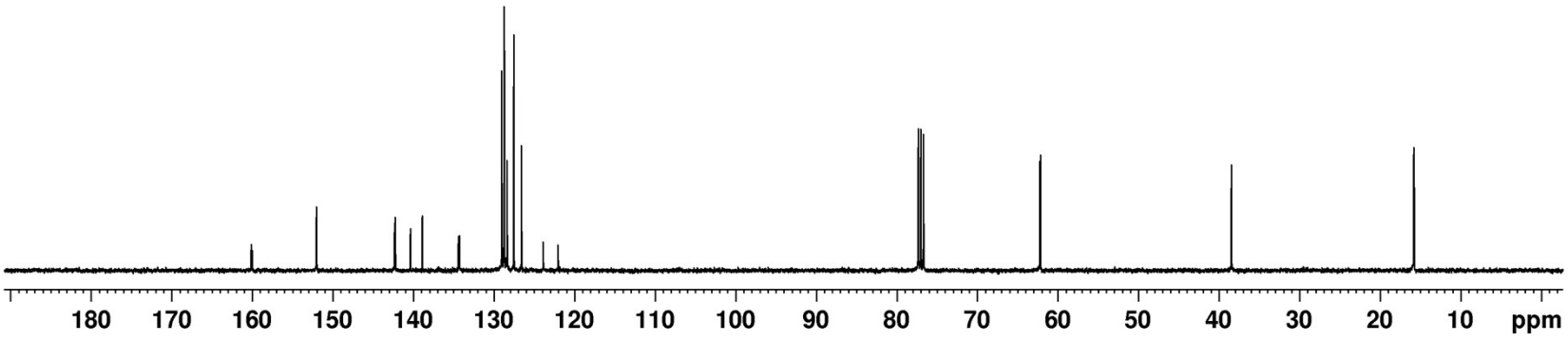
^{1}H NMR of compound **3a** (400 MHz/$CDCl_3$)



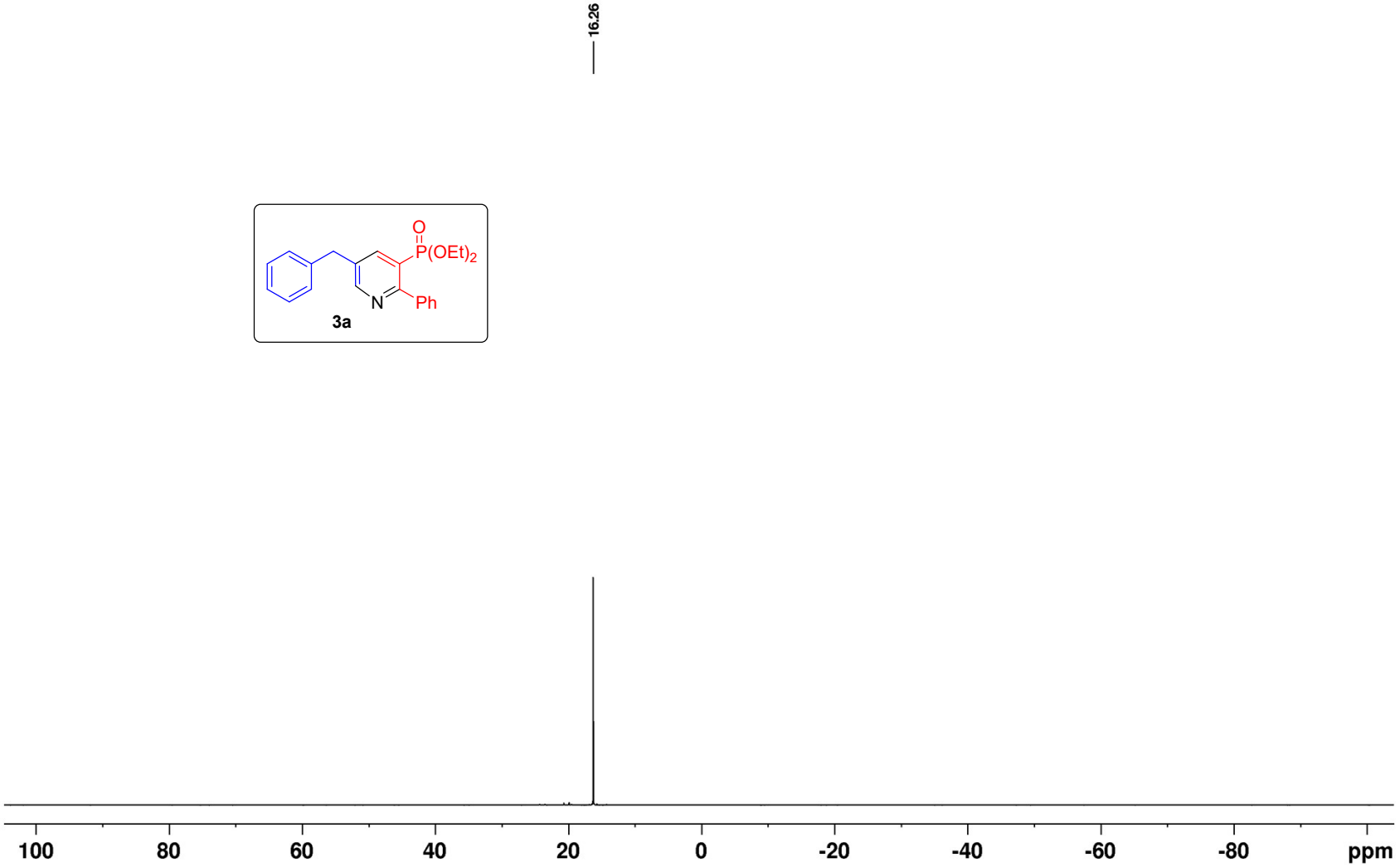
$^{13}C\{^{1}H\}$ NMR of compound **3a** (100 MHz/$CDCl_3$)



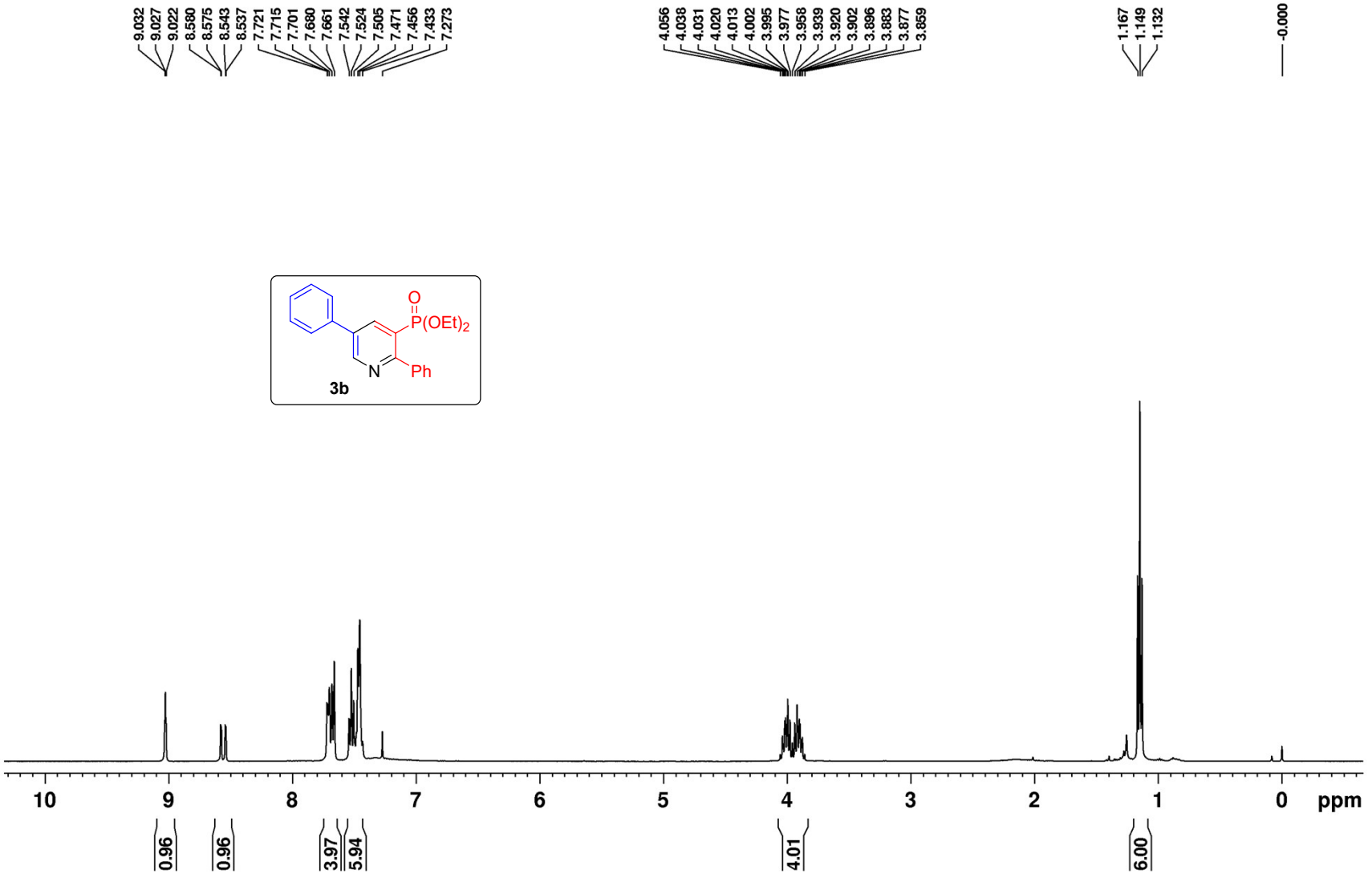




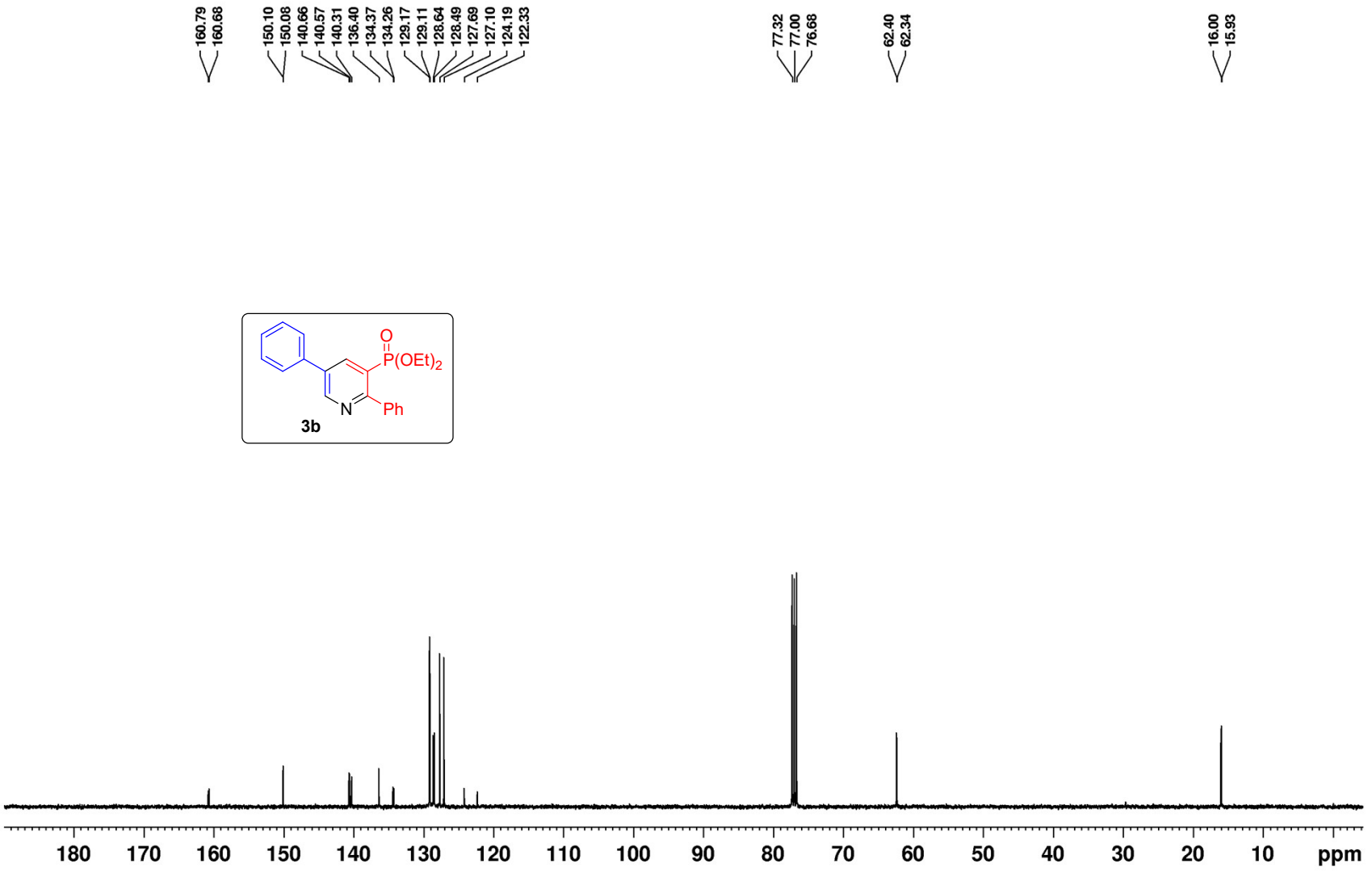
$^{31}P\{^{1}H\}$ NMR of compound **3a** (162 MHz/CDCl3)



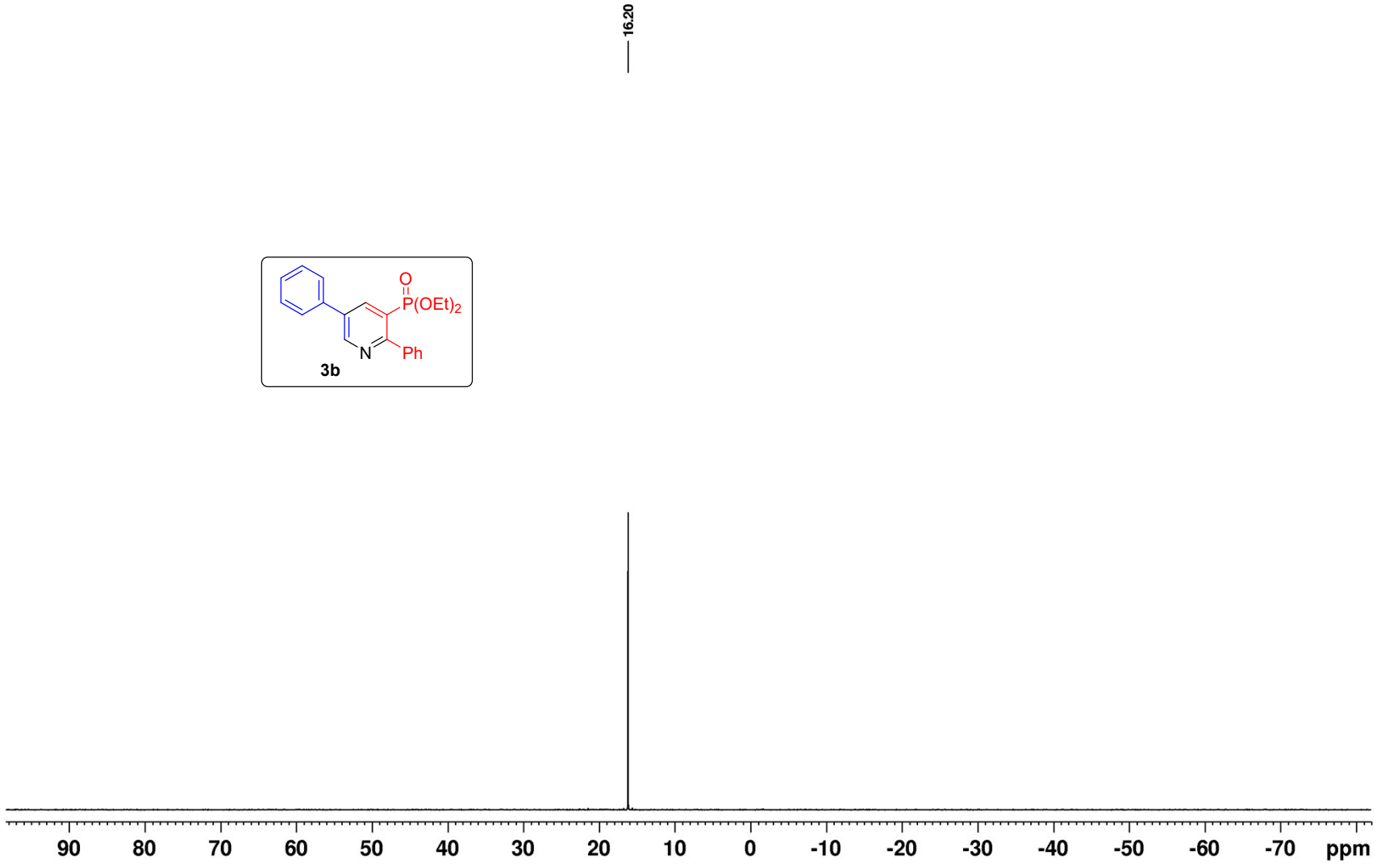
^{1}H NMR of compound **3b** (400 MHz/$CDCl_3$)



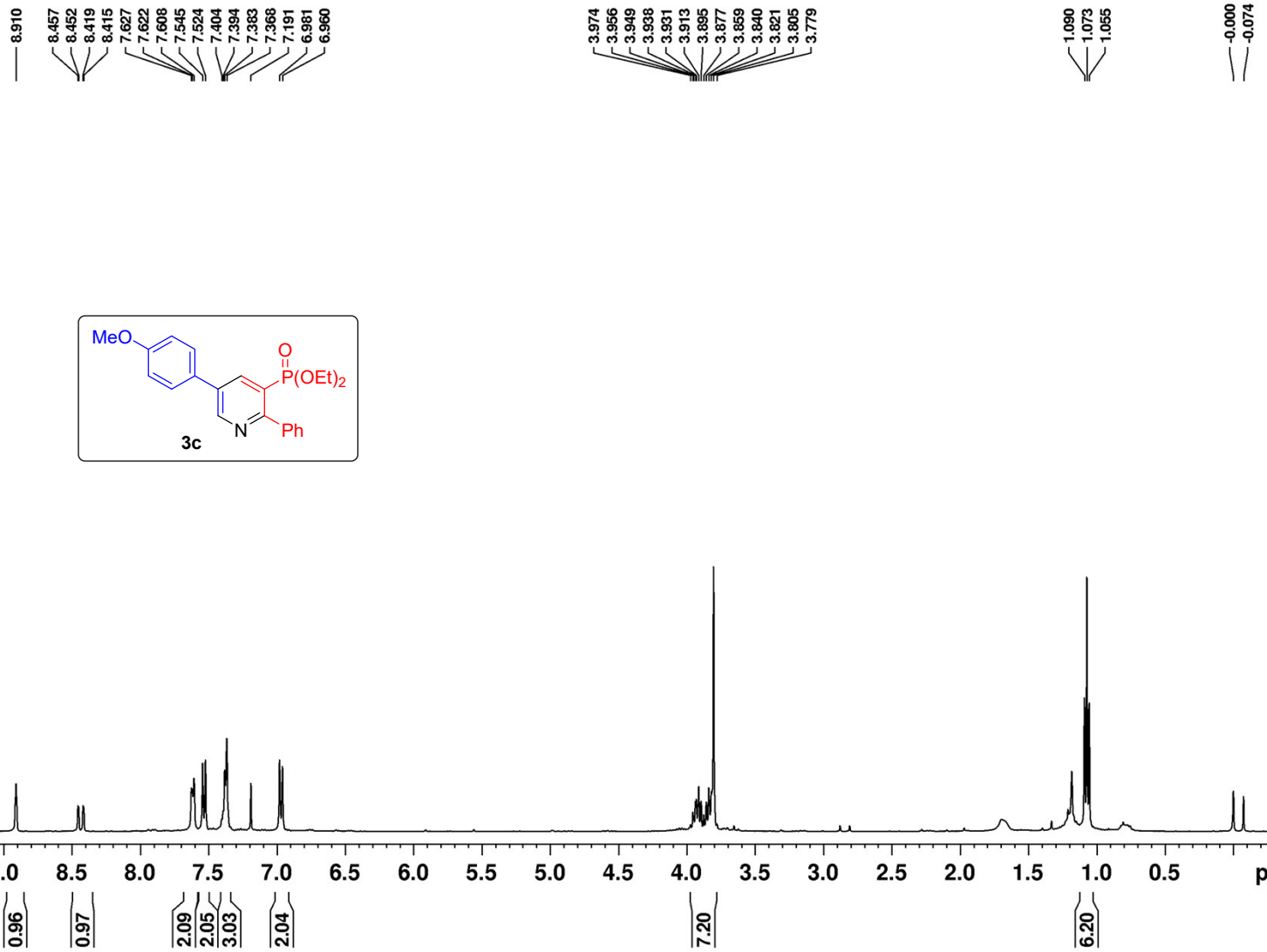
$^{13}C\{^{1}H\}$ NMR of compound **3b** (100 MHz/$CDCl_3$)



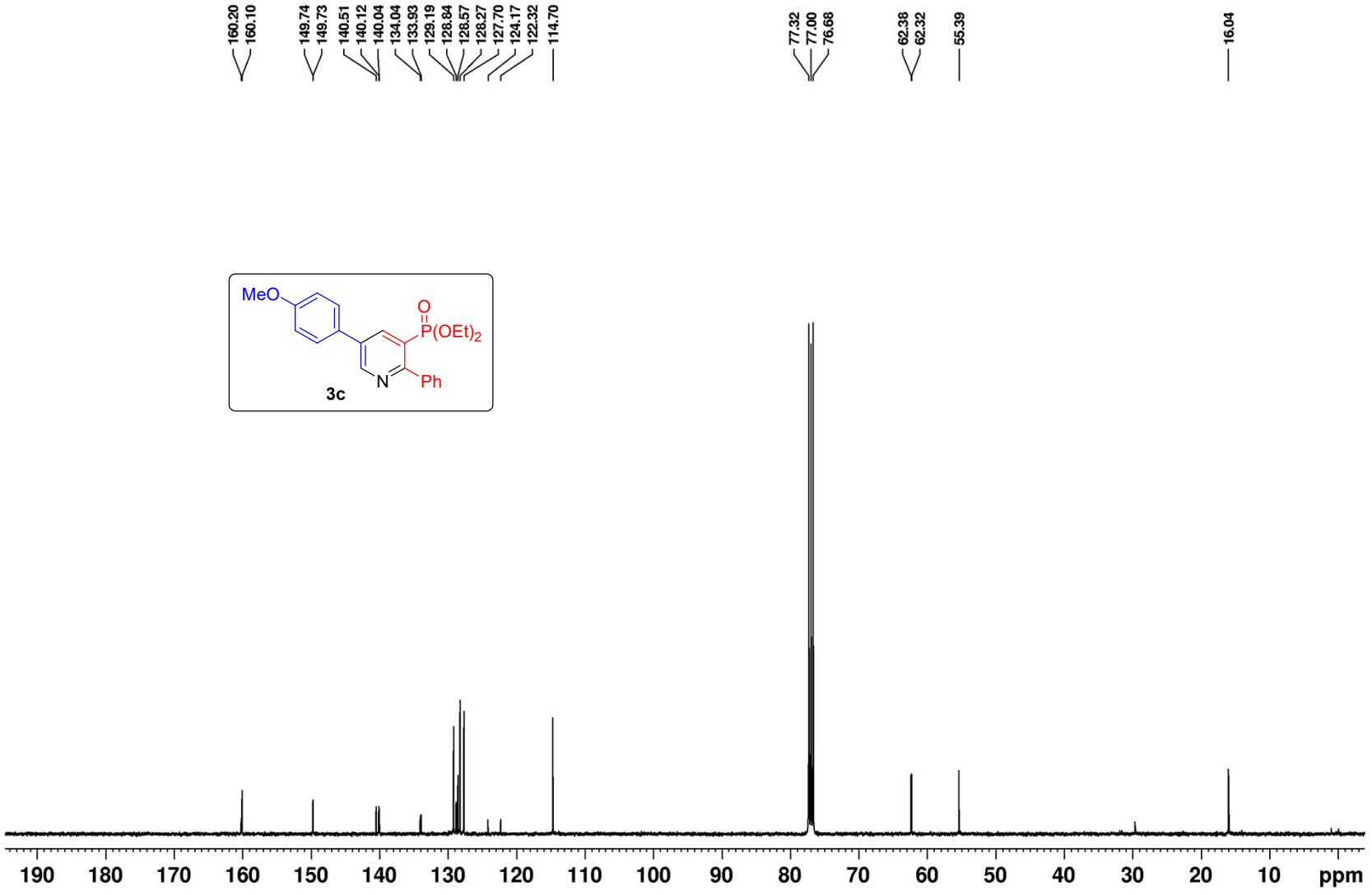
$^{31}P\{^{1}H\}$ NMR of compound **3b** (162 MHz/$CDCl_3$)



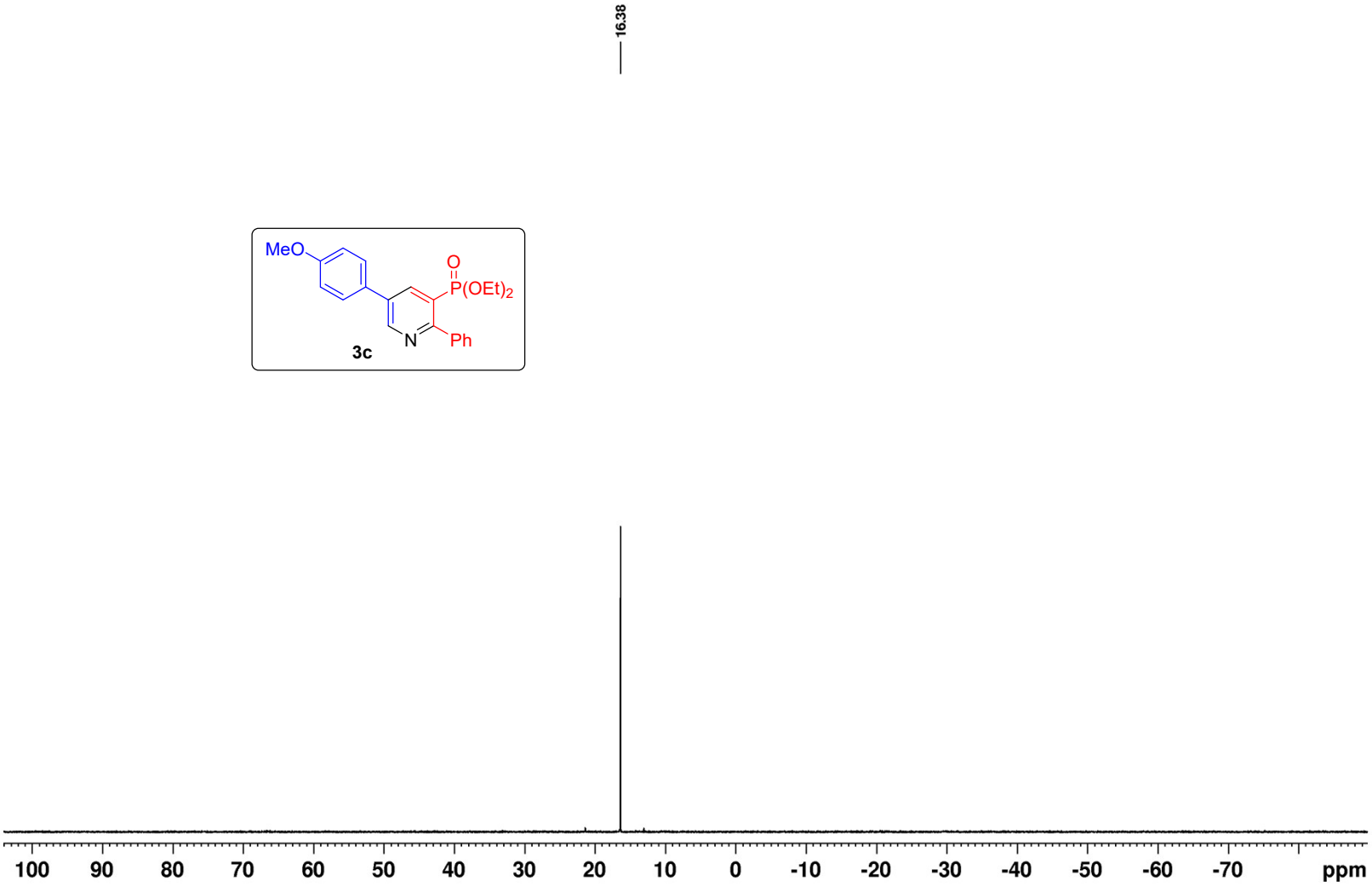
^{1}H NMR of compound **3c** (400 MHz/$CDCl_3$)



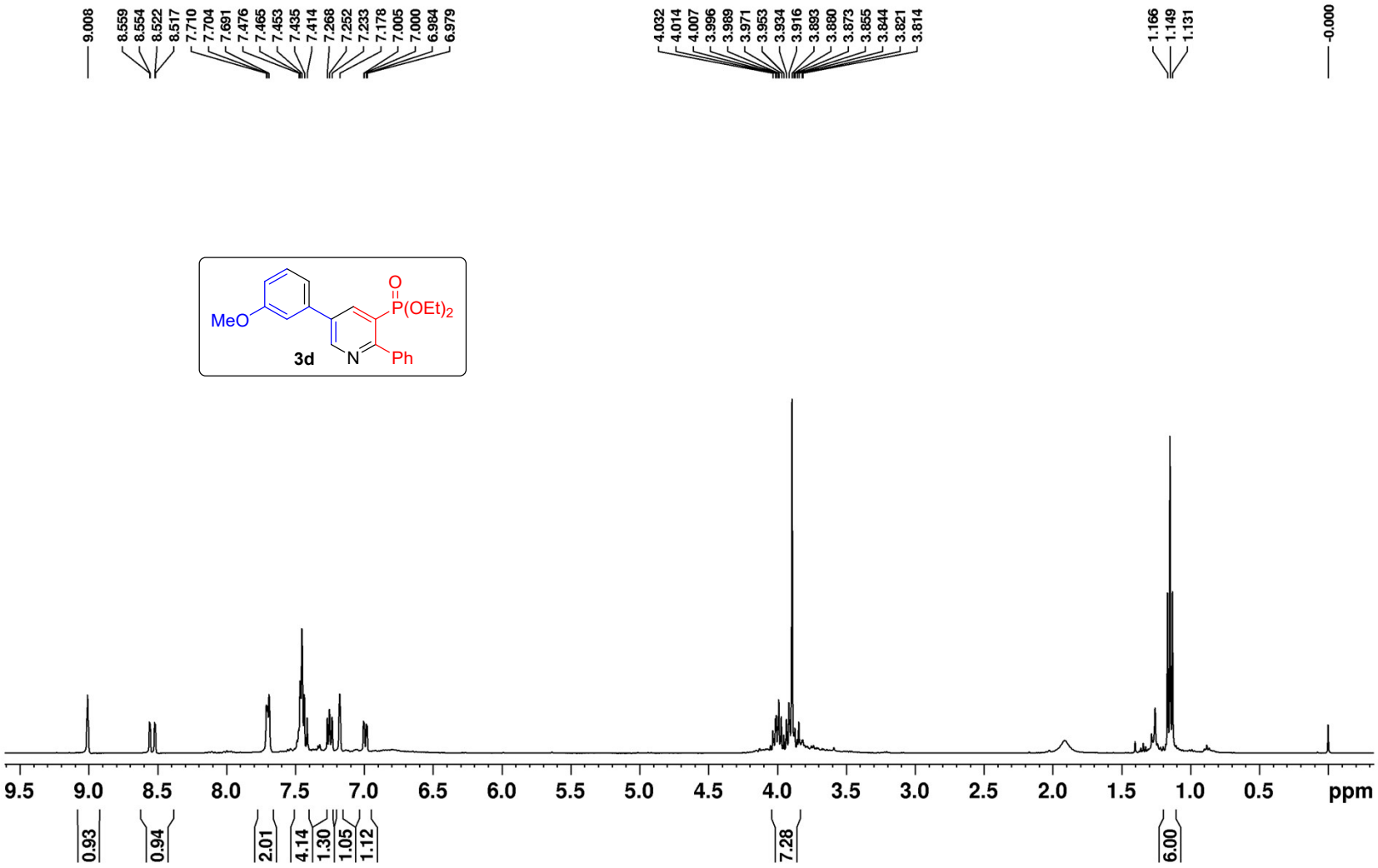
$^{13}C\{^{1}H\}$ NMR of compound **3c** (100 MHz/$CDCl_3$)



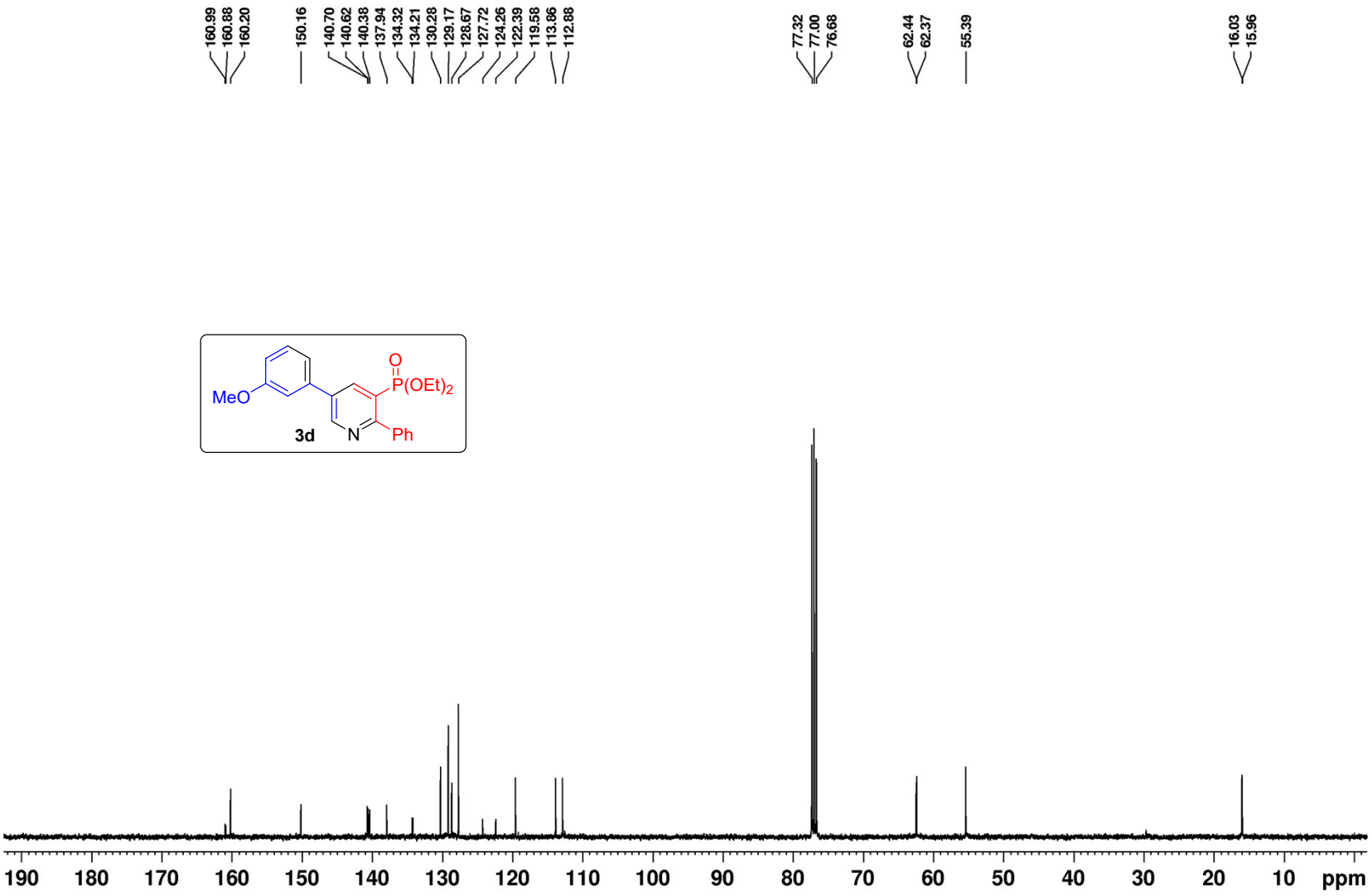
$^{31}P\{^{1}H\}$ NMR of compound **3c** (162 MHz/$CDCl_3$)



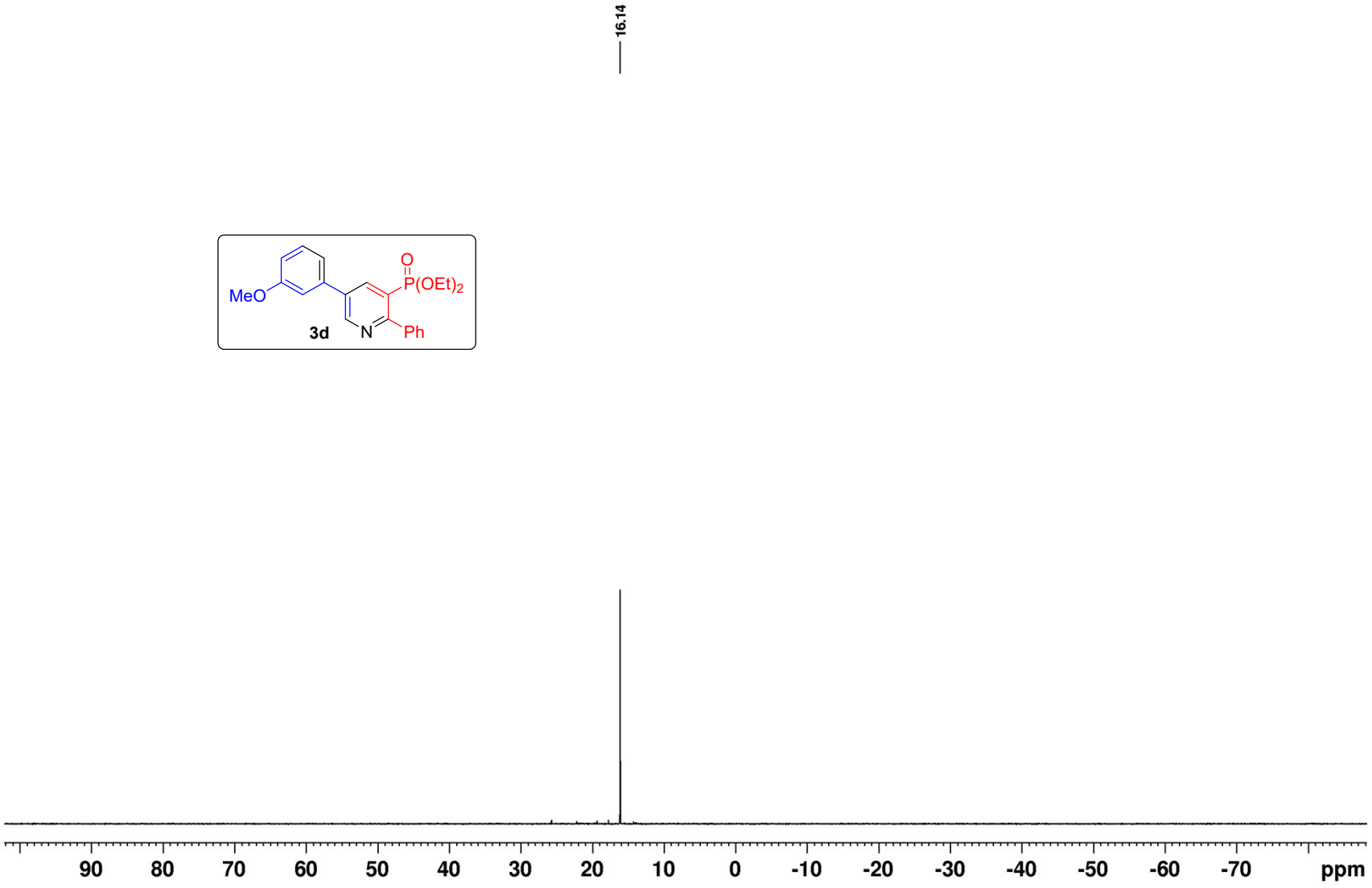
^{1}H NMR of compound **3d** (400 MHz/$CDCl_3$)



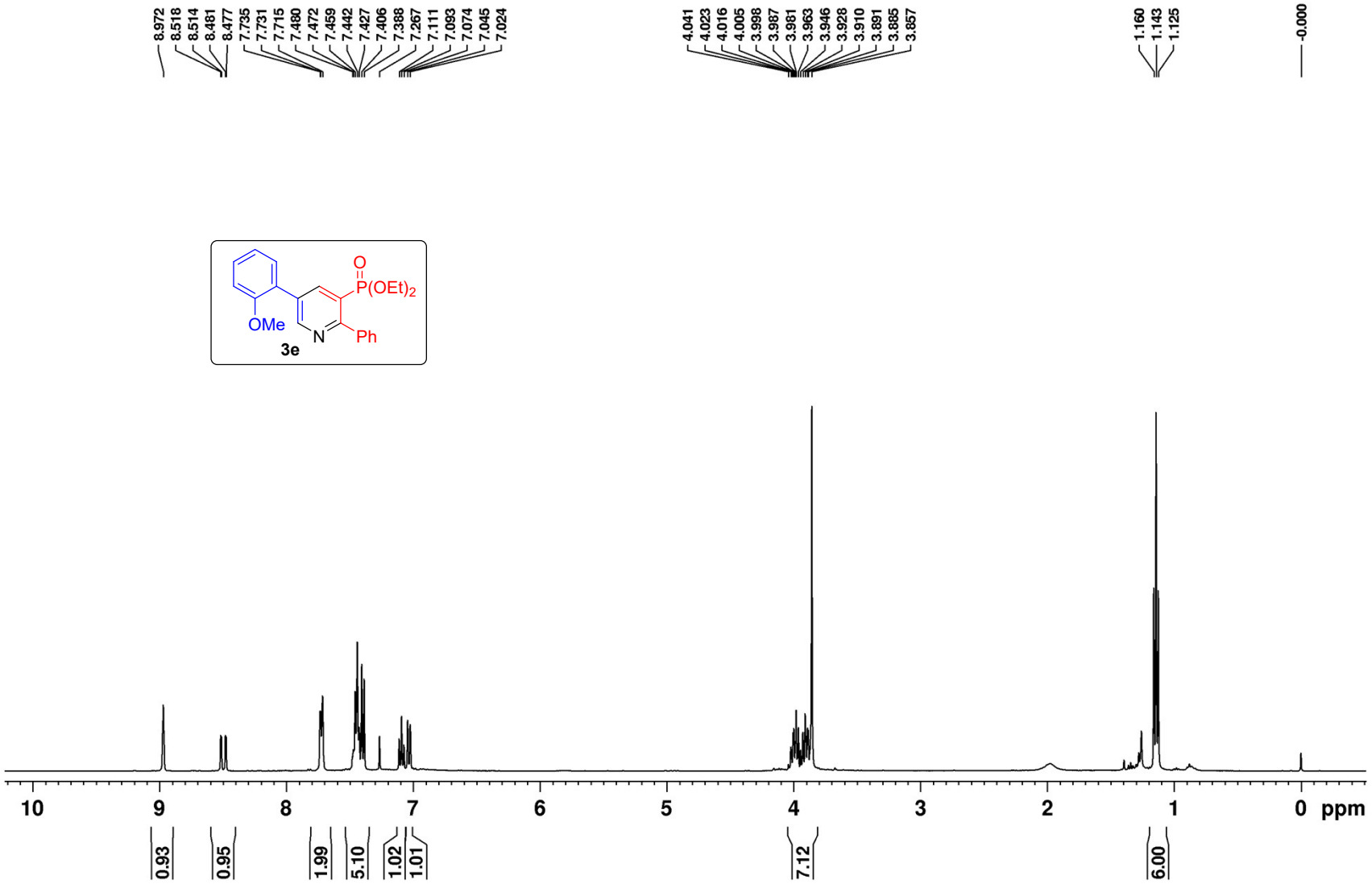
$^{13}C\{^{1}H\}$ NMR of compound **3d** (100 MHz/$CDCl_3$)



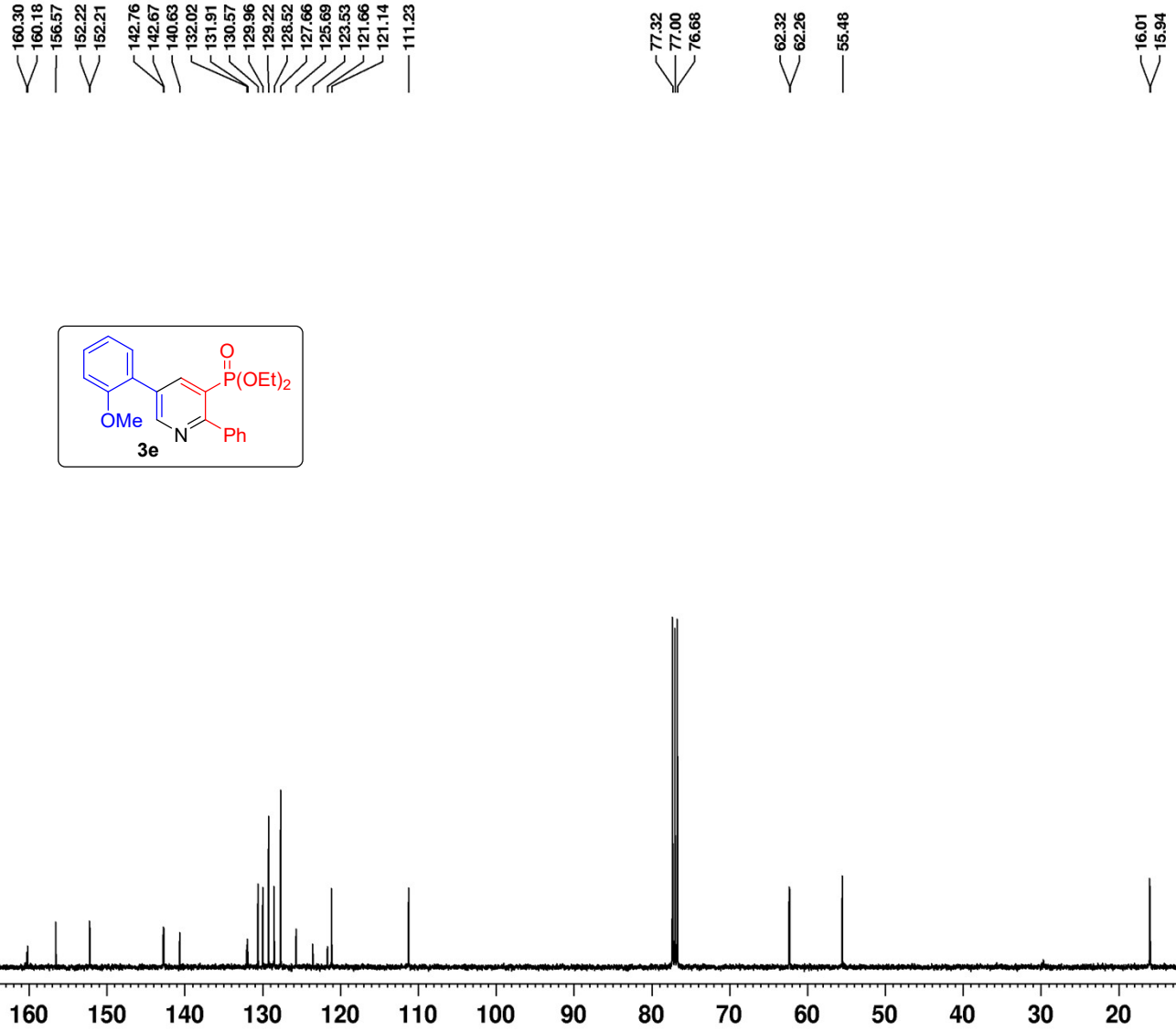
$^{31}P\{^{1}H\}$ NMR of compound **3d** (162MHz/$CDCl_3$)



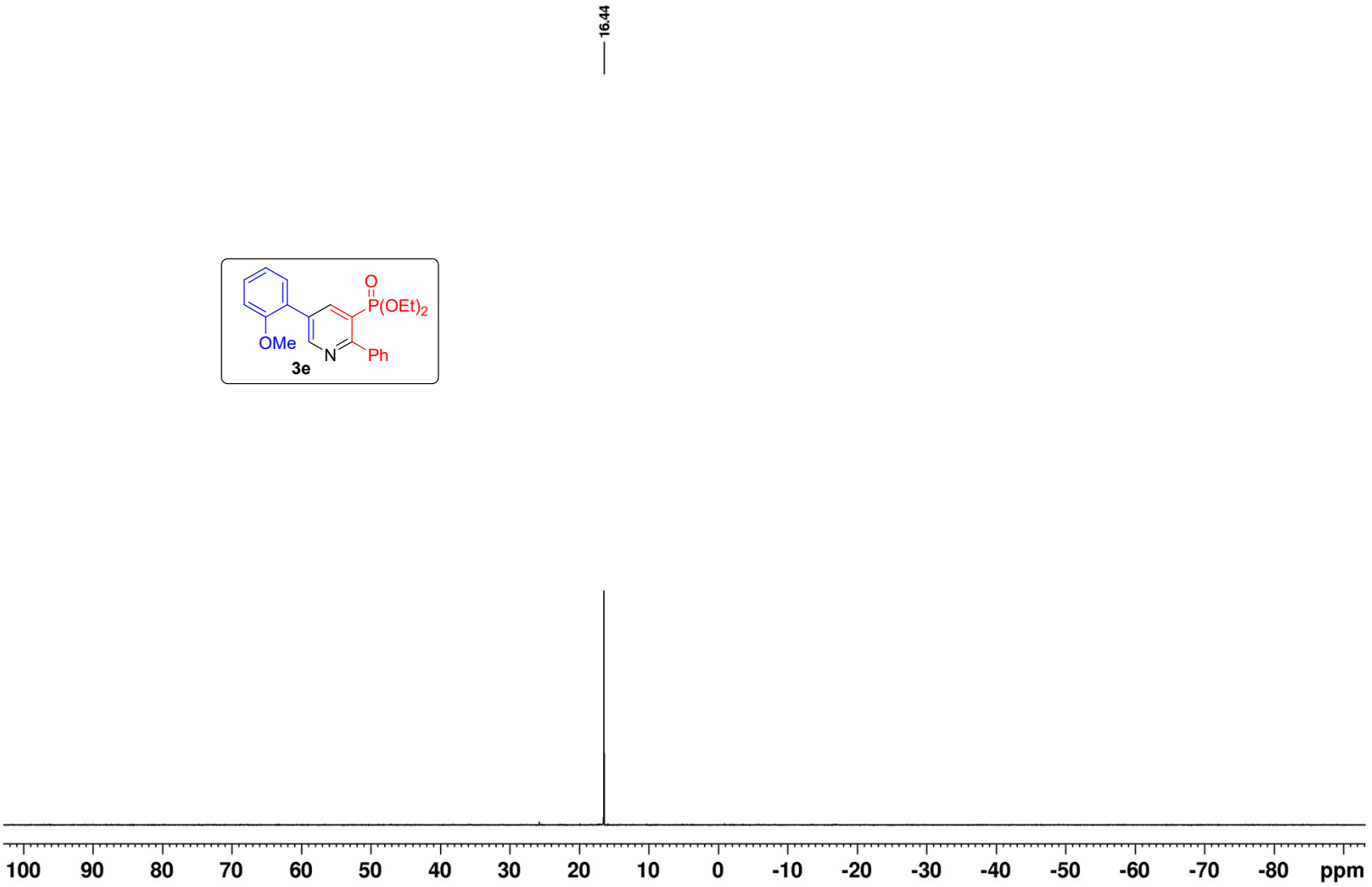
^{1}H NMR of compound **3e** (400MHz/$CDCl_3$)



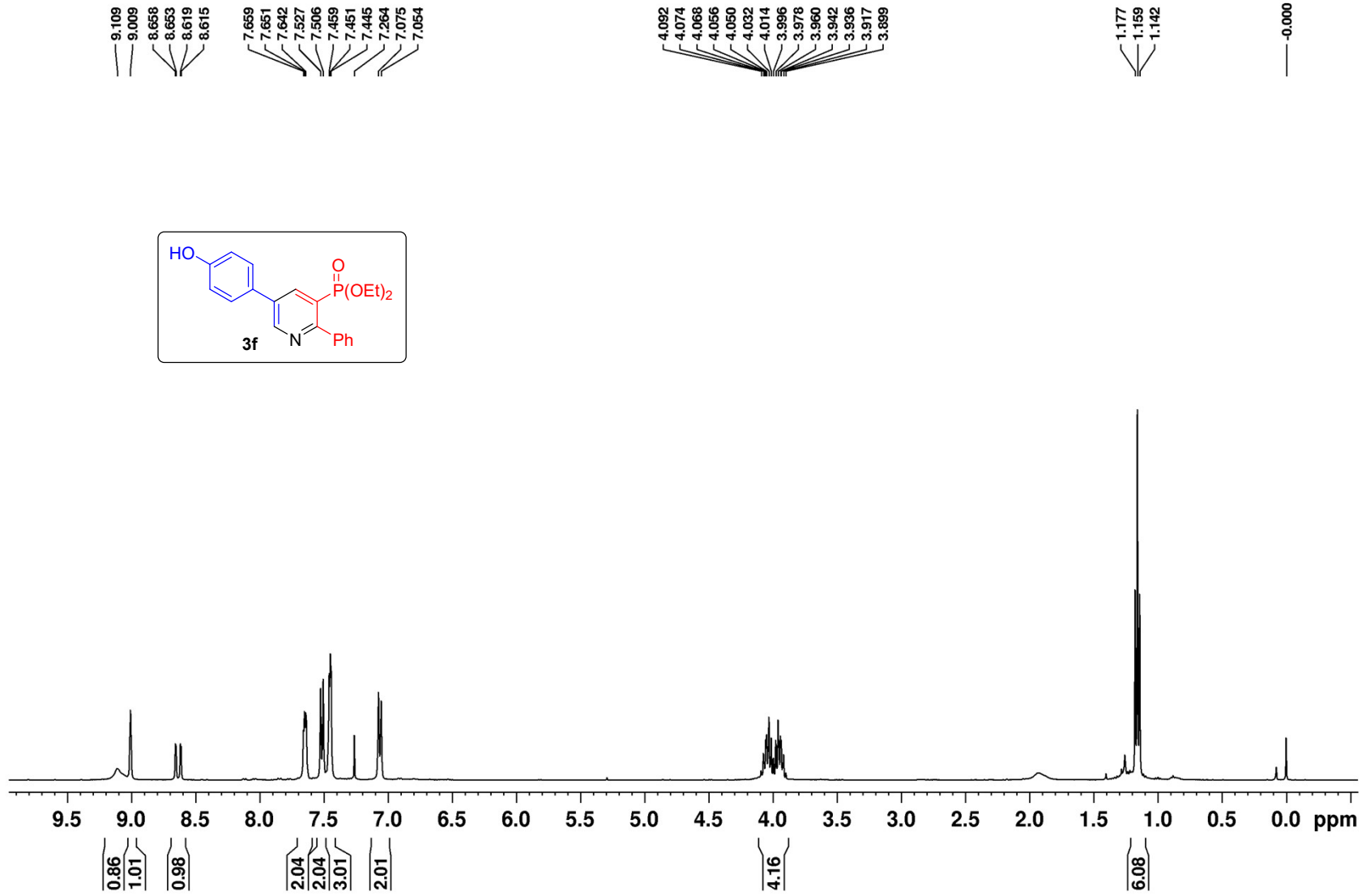
$^{13}C\{^{1}H\}$ NMR of compound **3e** (100MHz/$CDCl_3$)



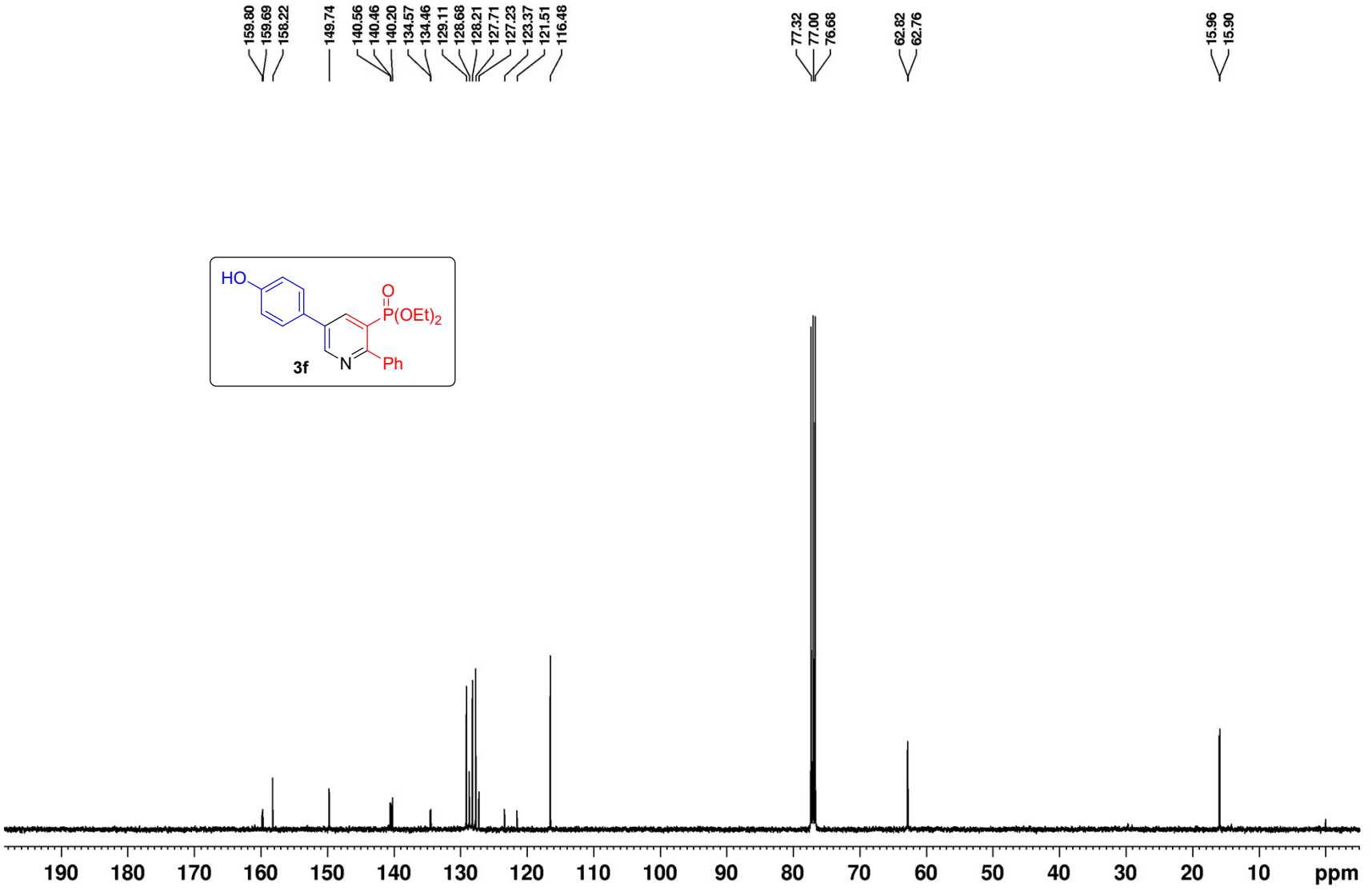
$^{31}P\{^{1}H\}$ NMR of compound **3e** (162MHz/$CDCl_3$)



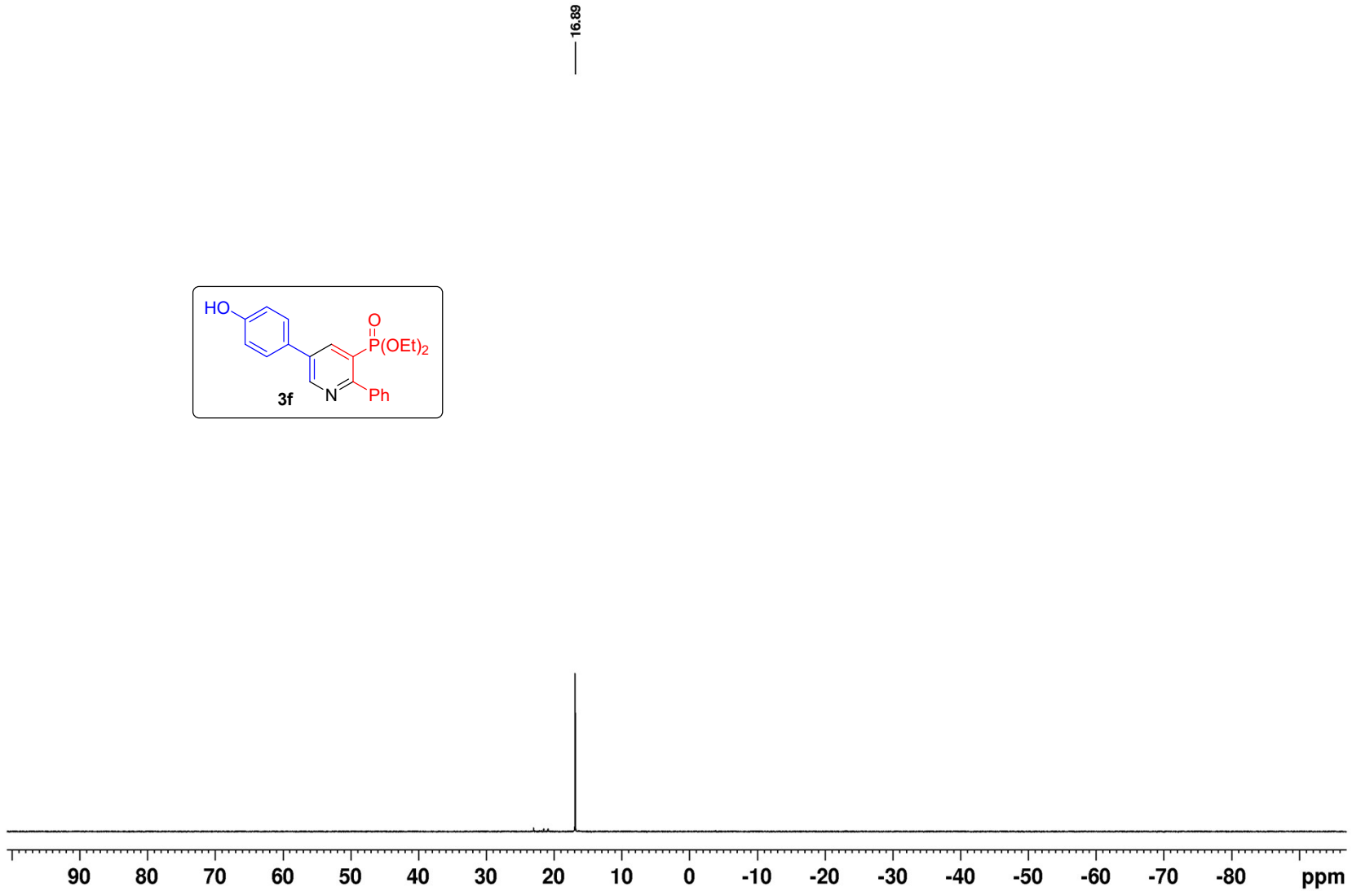
^{1}H NMR of compound **3f** (400MHz/$CDCl_3$)



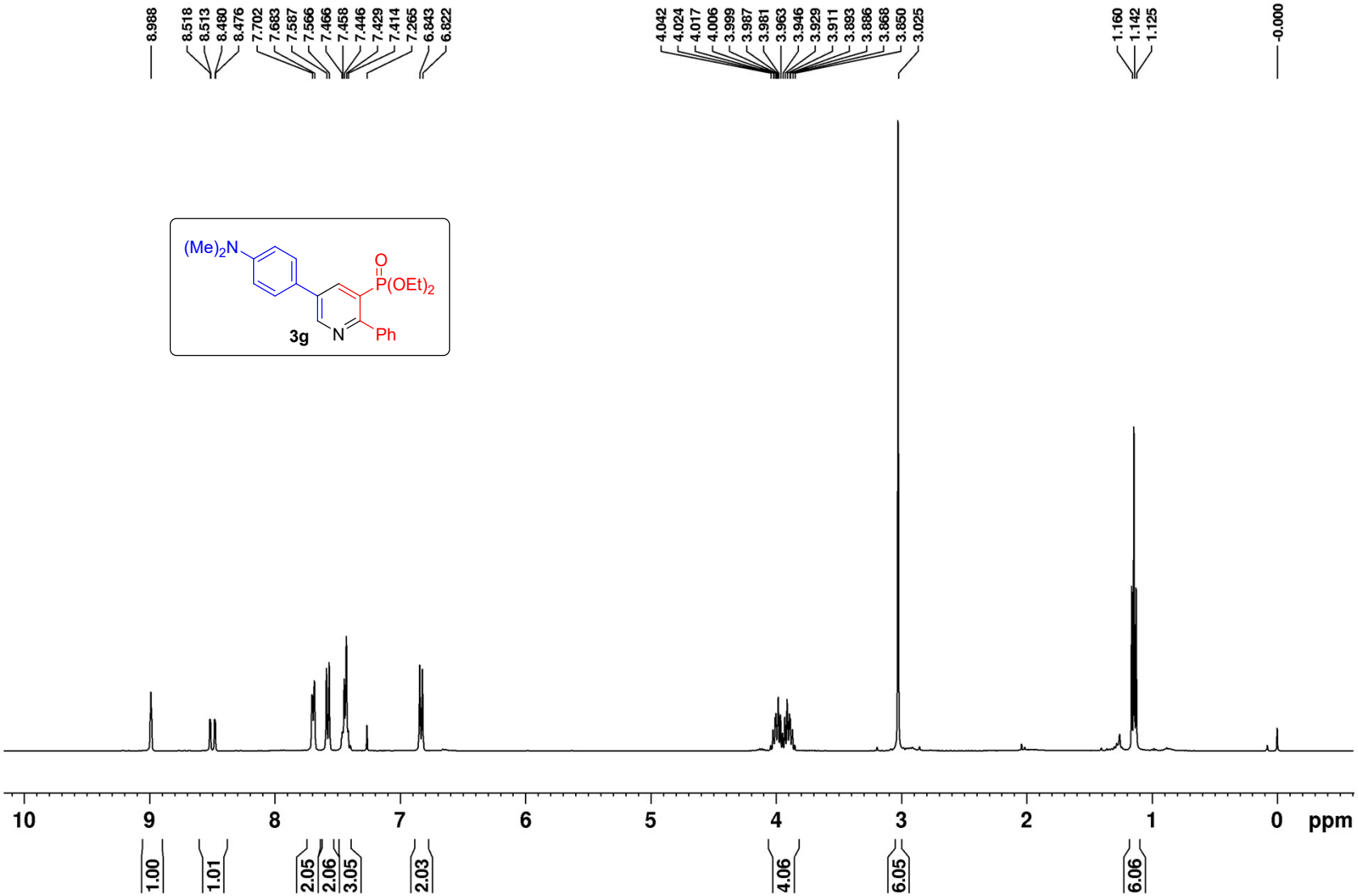
$^{13}C\{^{1}H\}$ NMR of compound **3f** (100MHz/$CDCl_3$)



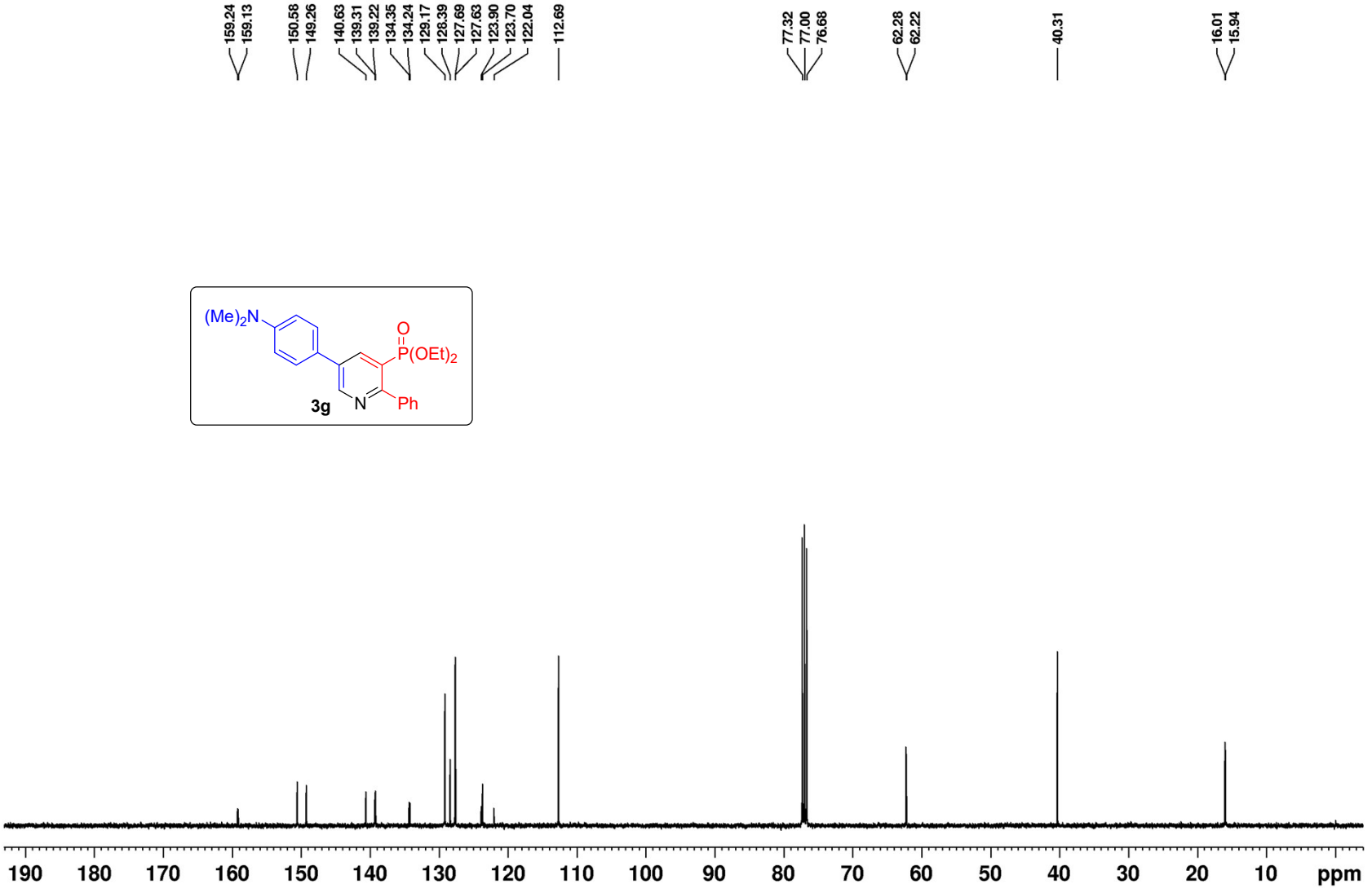
$^{31}P\{^{1}H\}$ NMR of compound **3f** (162MHz/$CDCl_3$)



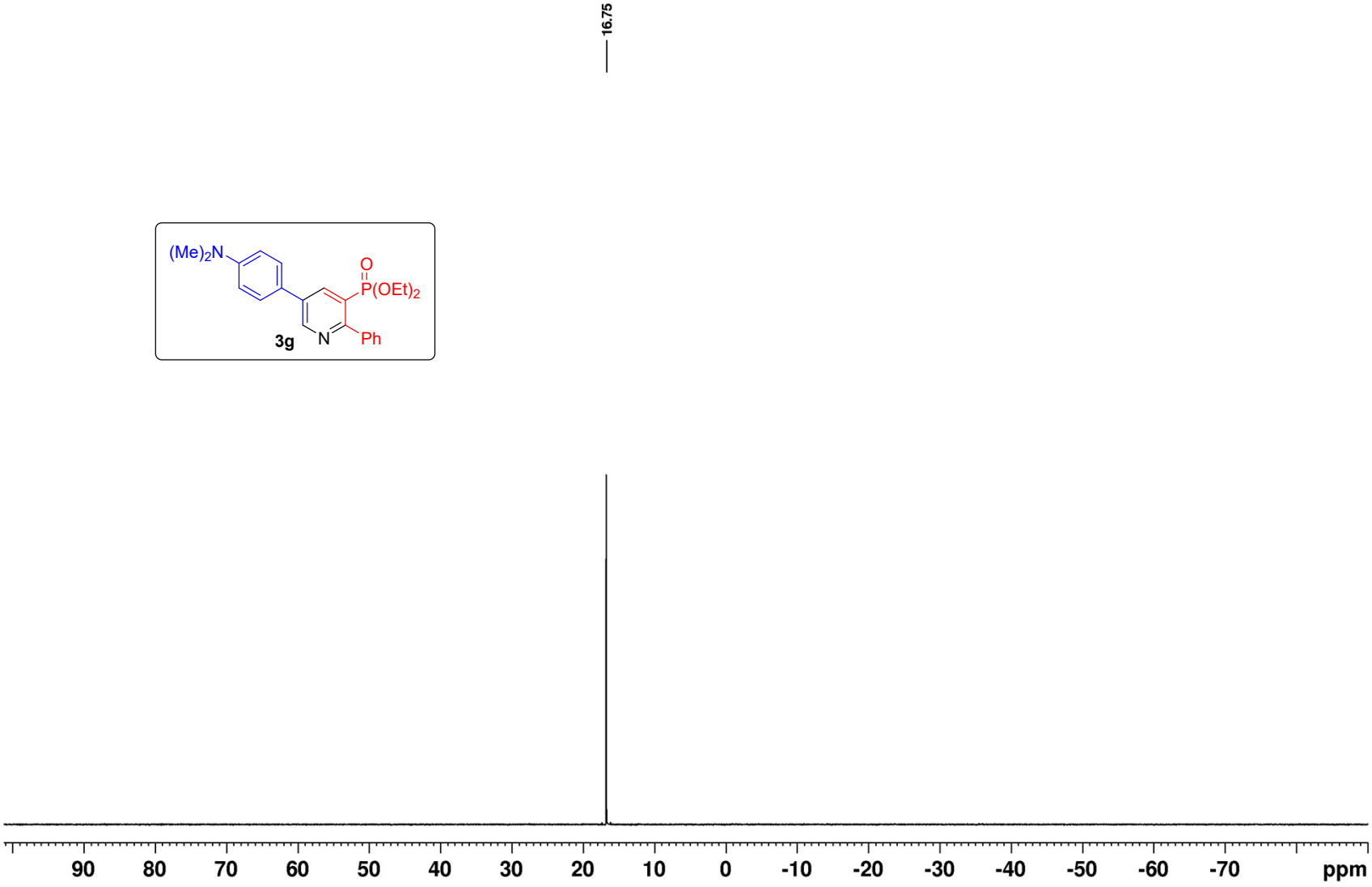
^{1}H NMR of compound **3g** (400MHz/$CDCl_3$)



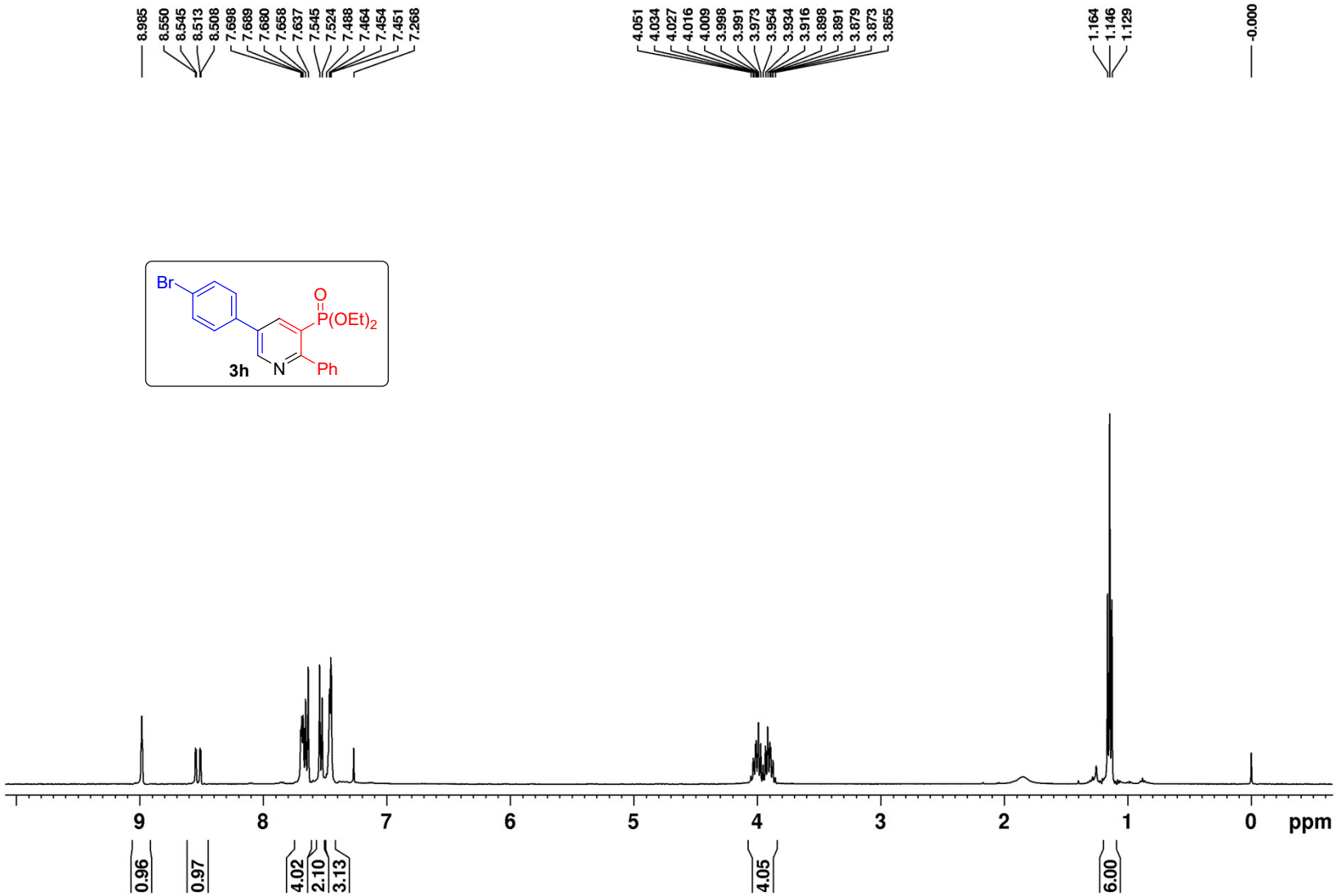
$^{13}C\{^{1}H\}$ NMR of compound **3g** (100MHz/$CDCl_3$)



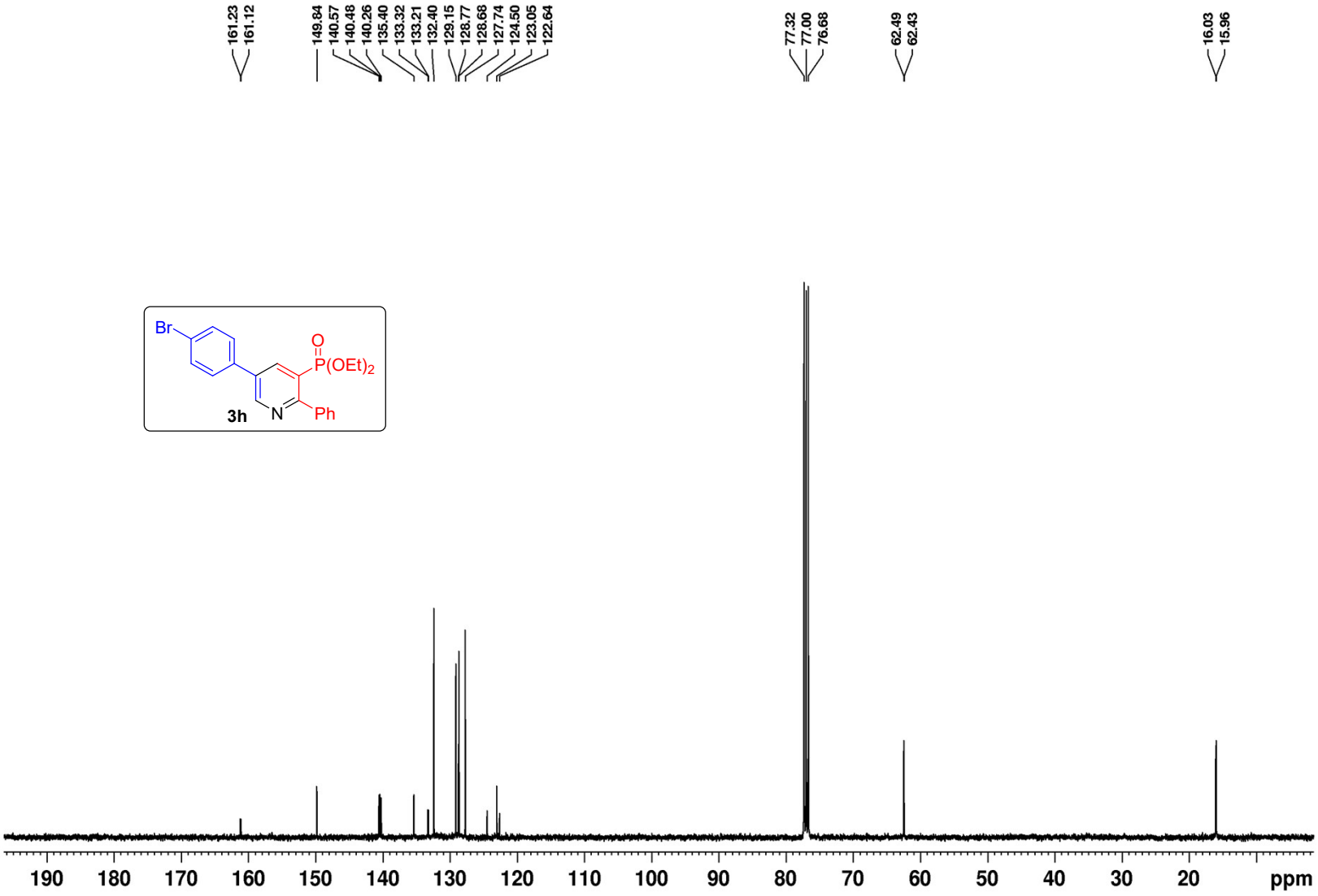
$^{31}P\{^{1}H\}$ NMR of compound **3g** (162MHz/CDCl3)



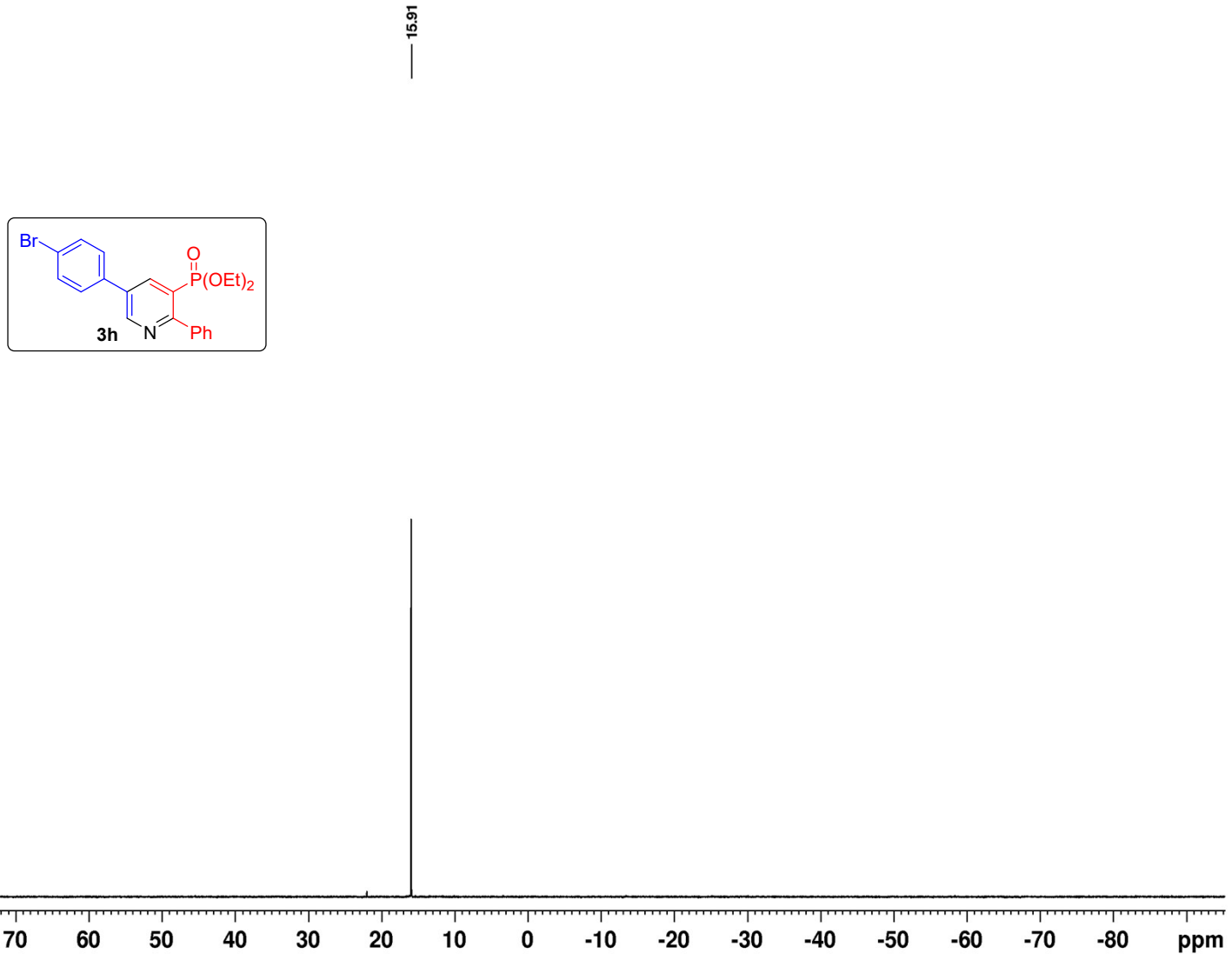
^{1}H NMR of compound **3h** (400MHz/$CDCl_3$)



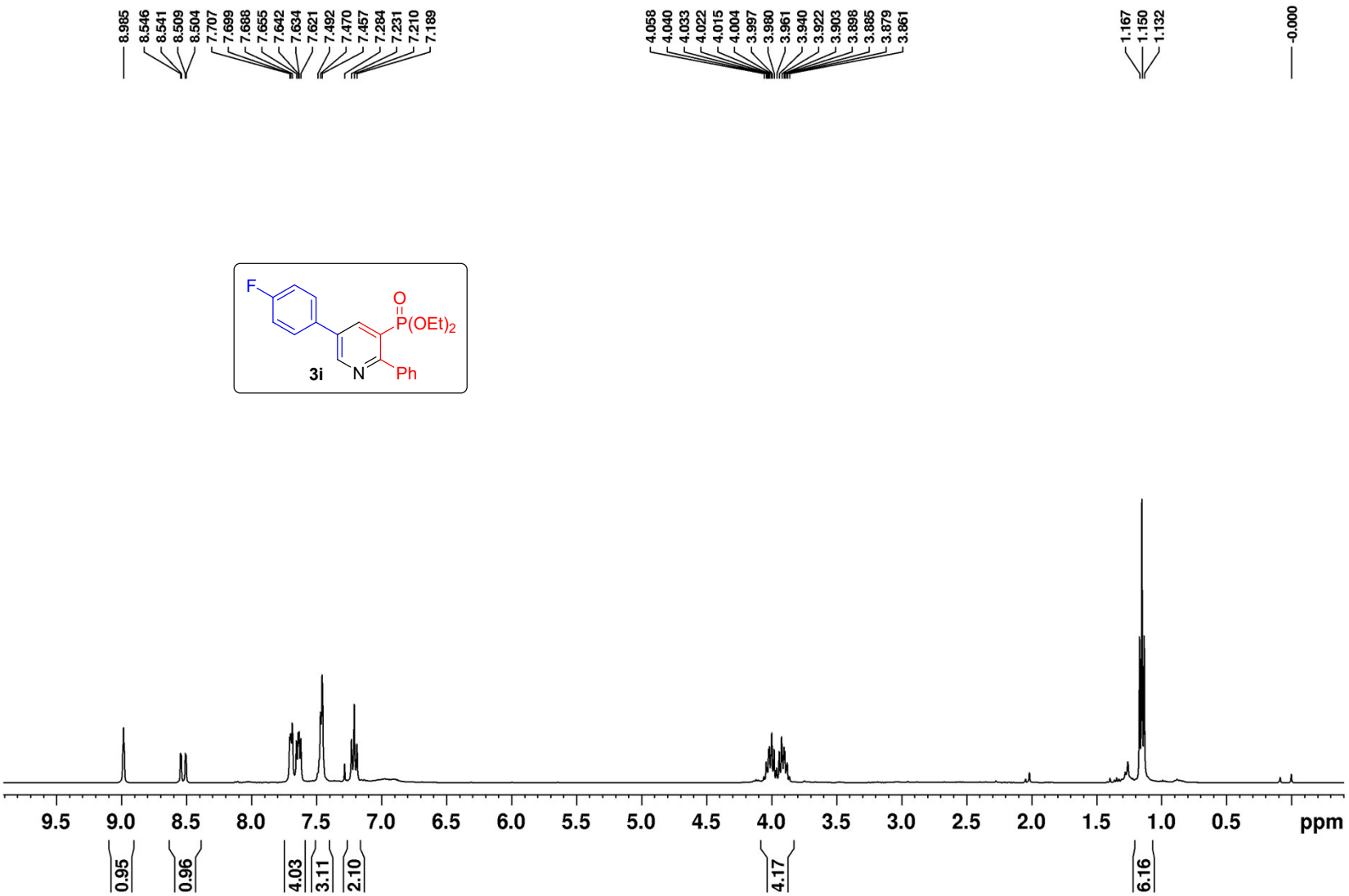
$^{13}C\{^{1}H\}$ NMR of compound **3h** (100MHz/$CDCl_3$)



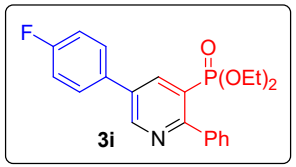
$^{31}P\{^{1}H\}$ NMR of compound **3h** (162MHz/$CDCl_3$)

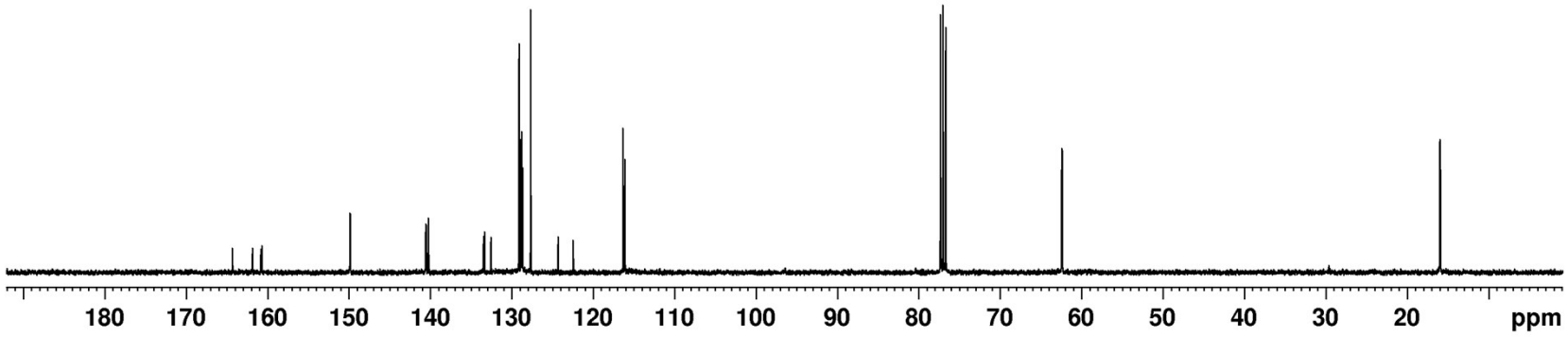


^{1}H NMR of compound **3i** (400MHz/$CDCl_3$)

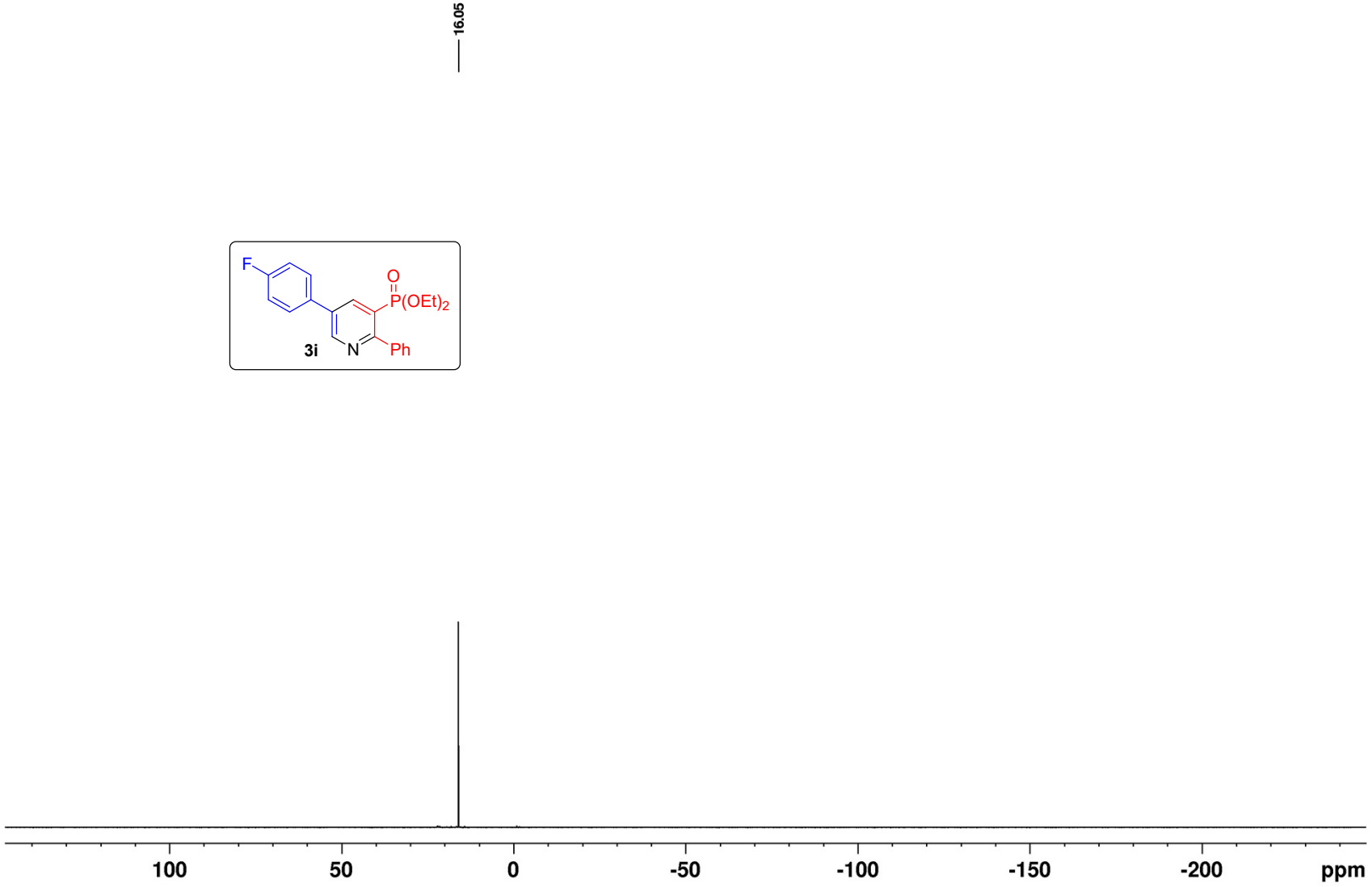


$^{13}C\{^{1}H\}$ NMR of compound **3i** (100MHz/$CDCl_3$)

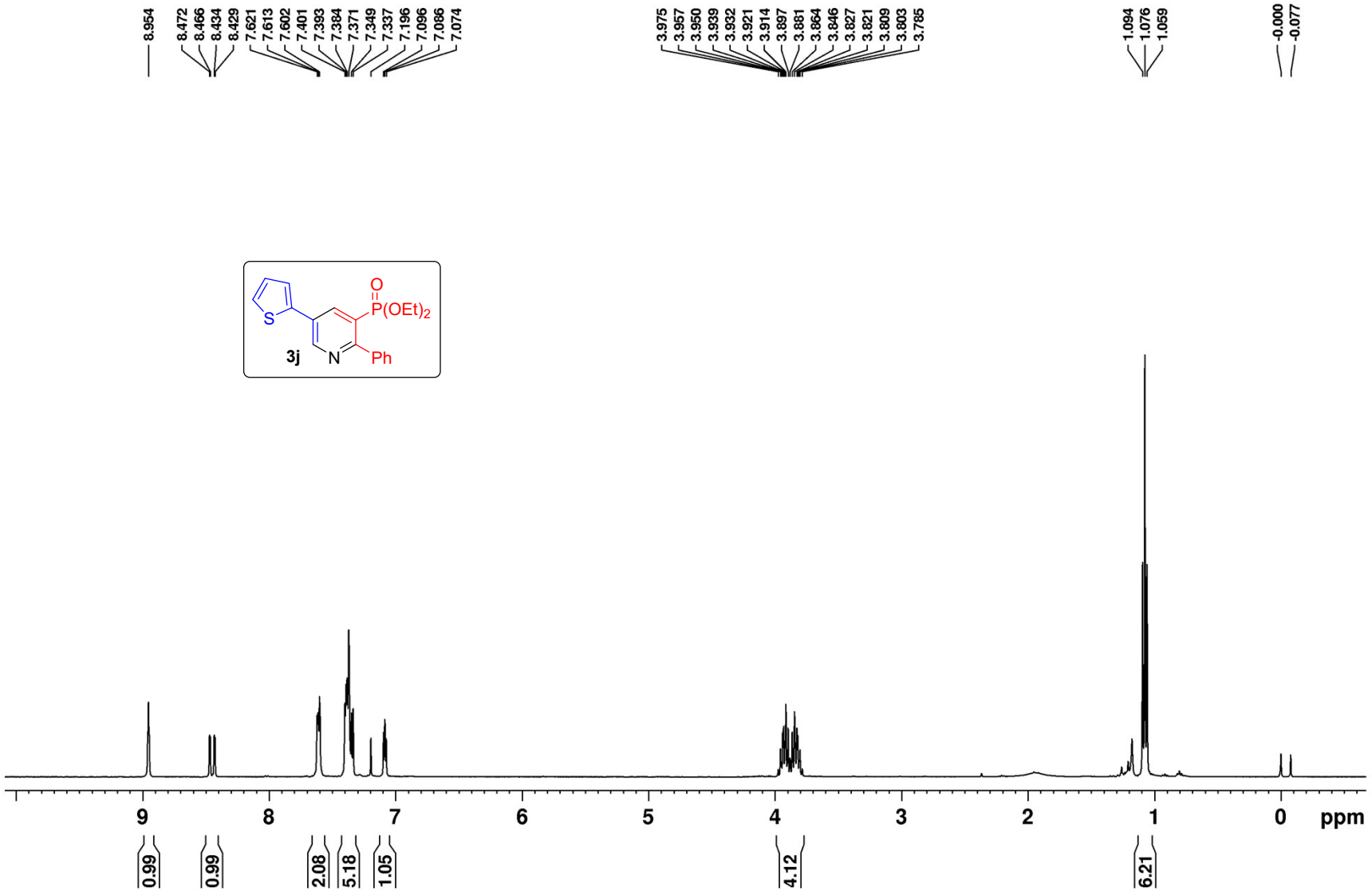




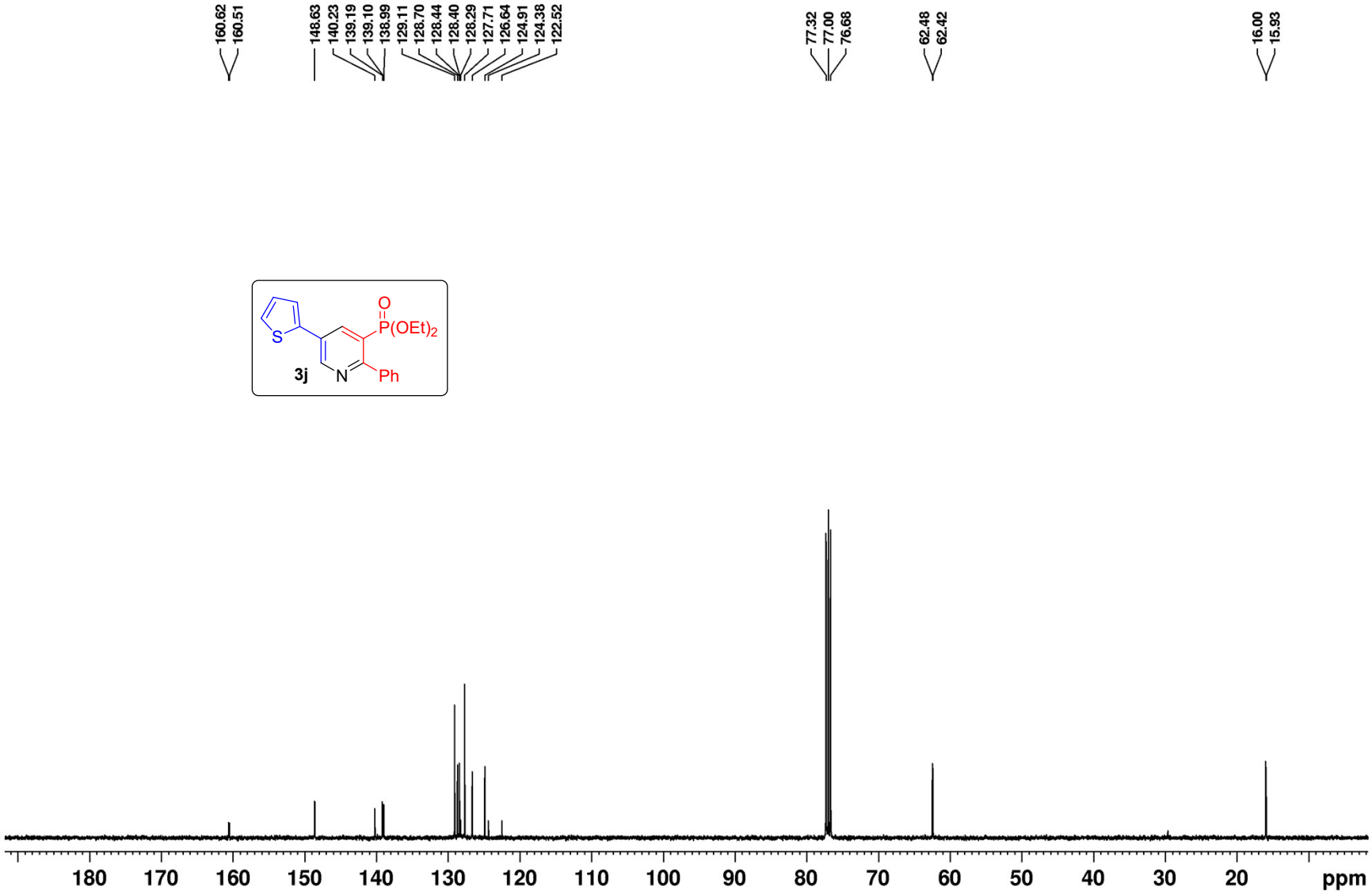
$^{31}P\{^{1}H\}$ NMR of compound **3i** (162MHz/$CDCl_3$)



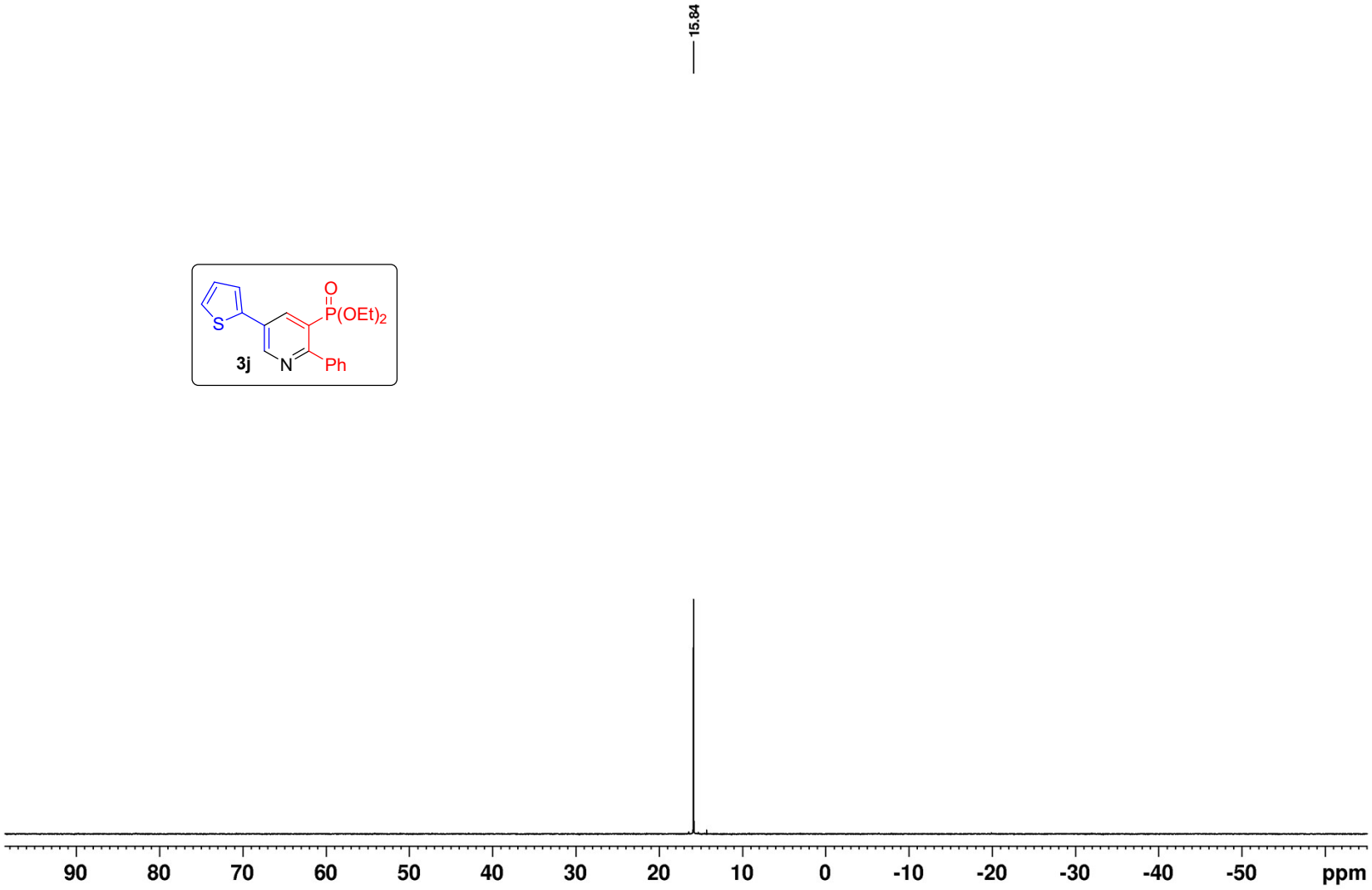
^{1}H NMR of compound **3j** (400MHz/$CDCl_3$)



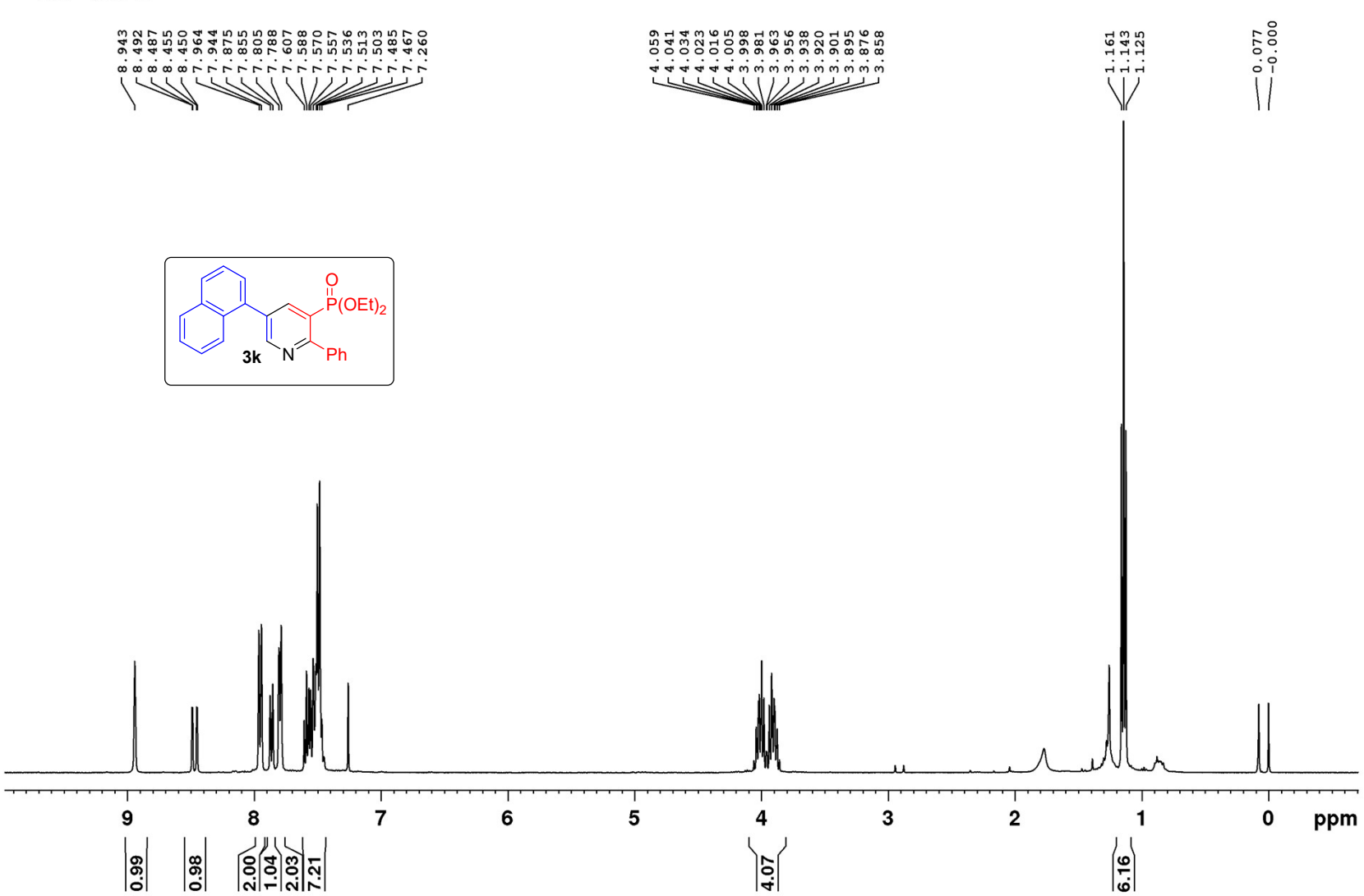
$^{13}C\{^{1}H\}$ NMR of compound **3j** (100MHz/$CDCl_3$)



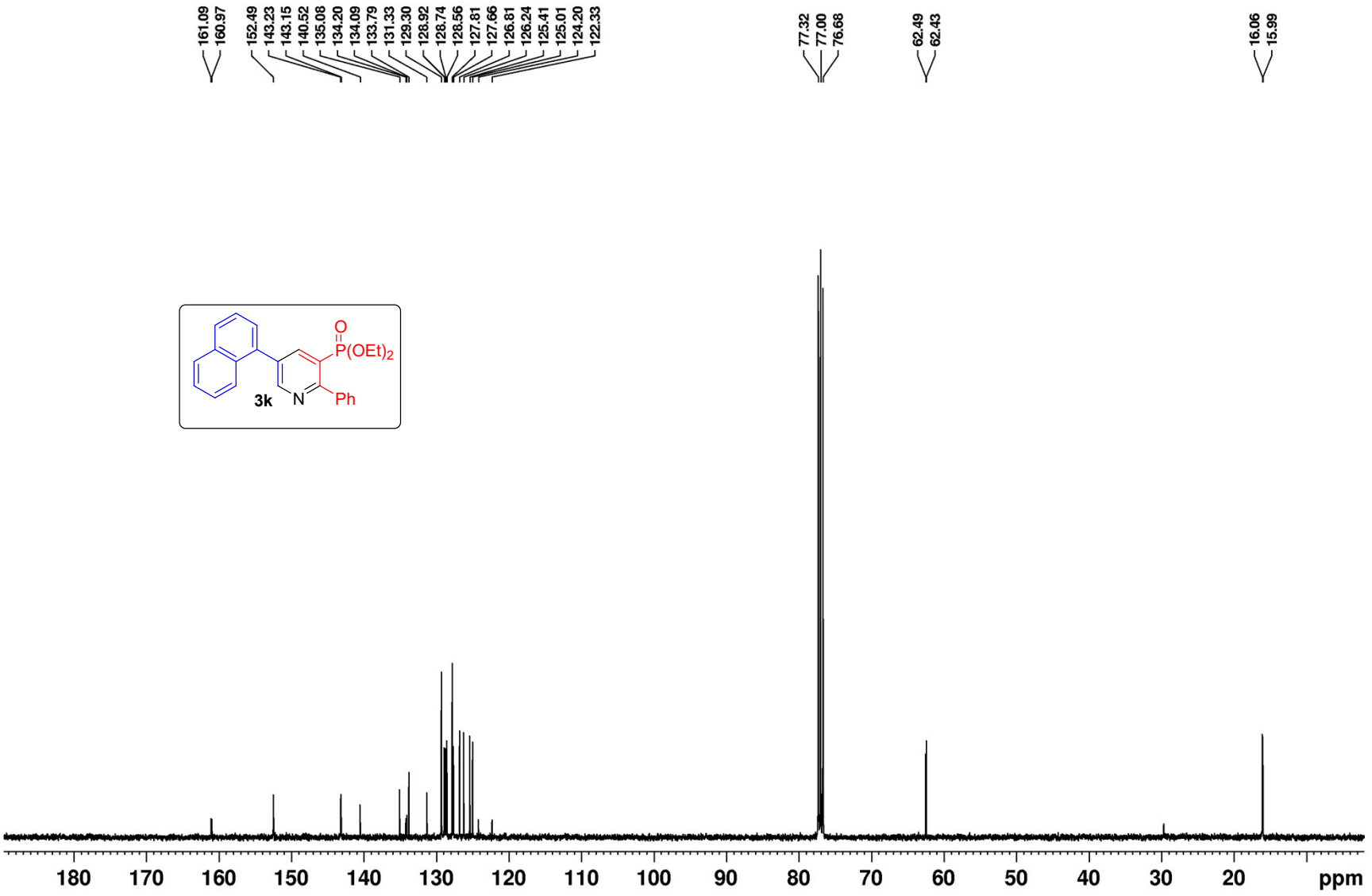
$^{31}P\{^{1}H\}$ NMR of compound **3j** (162MHz/$CDCl_3$)



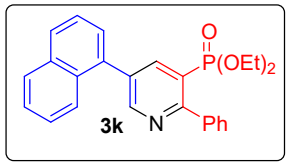
^{1}H NMR of compound **3k** (400MHz/$CDCl_3$)



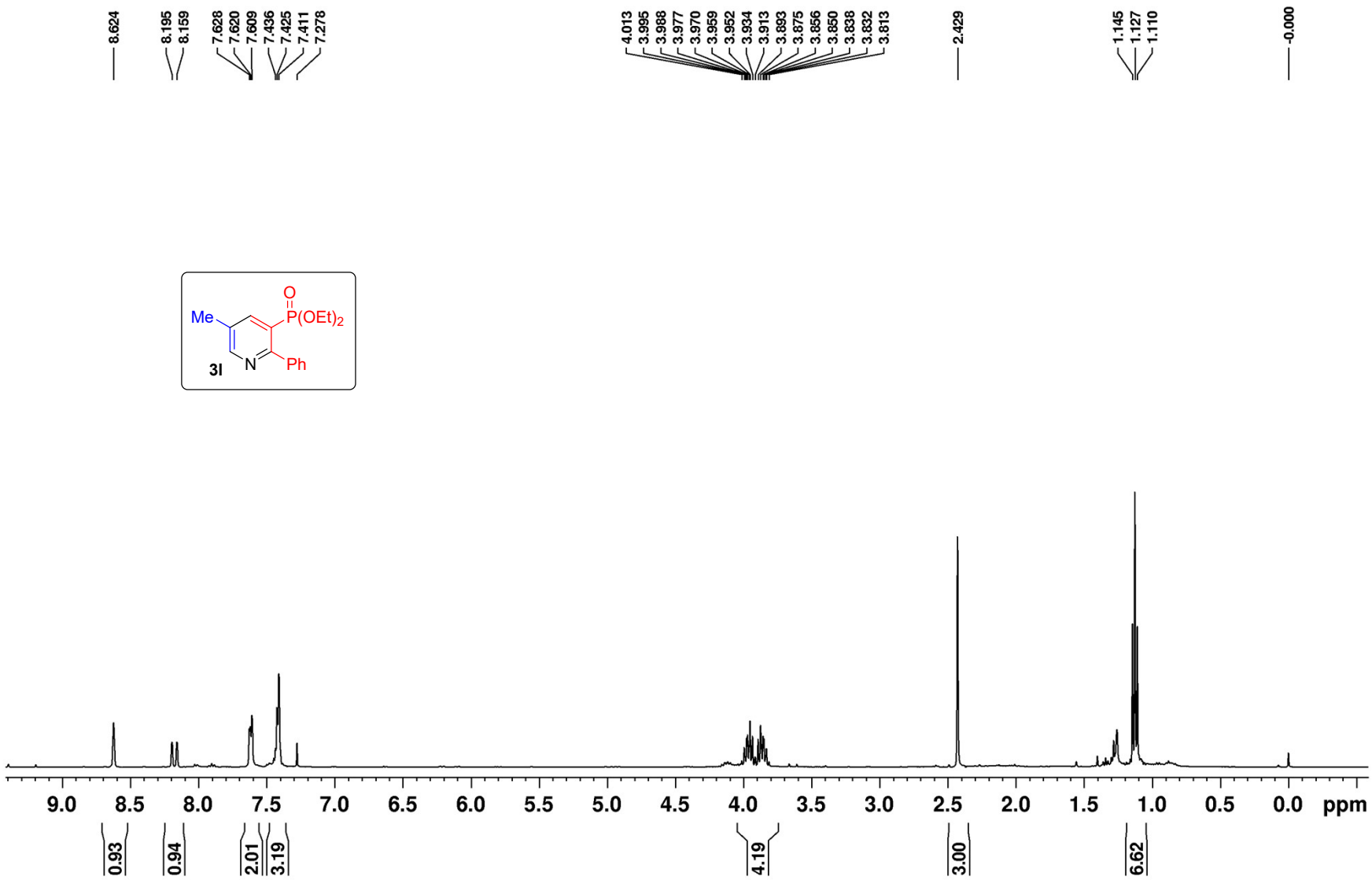
$^{13}C\{^{1}H\}$ NMR of compound **3k** (100MHz/$CDCl_3$)



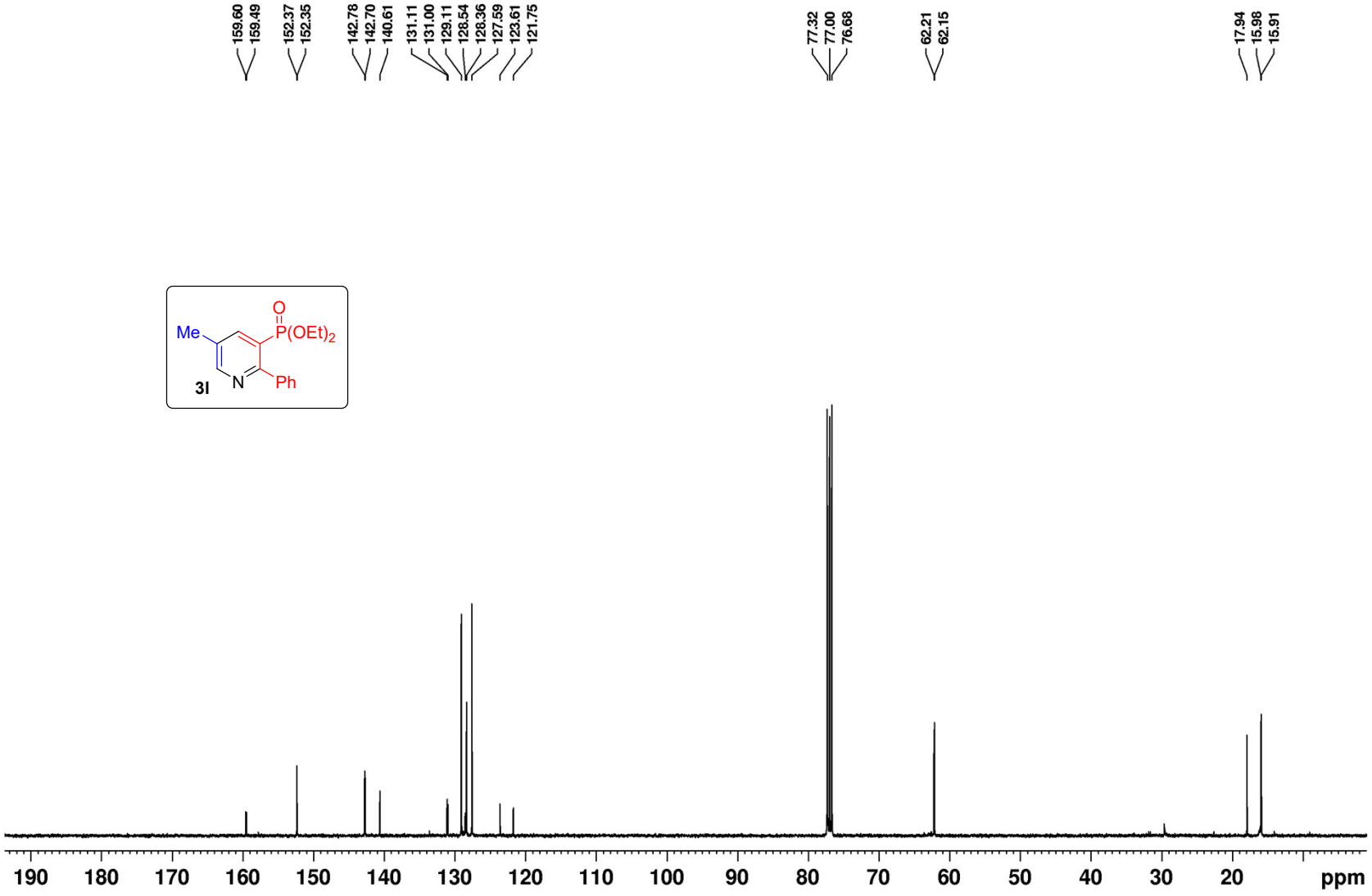
$^{31}P\{^{1}H\}$ NMR of compound **3k** (162MHz/$CDCl_3$)



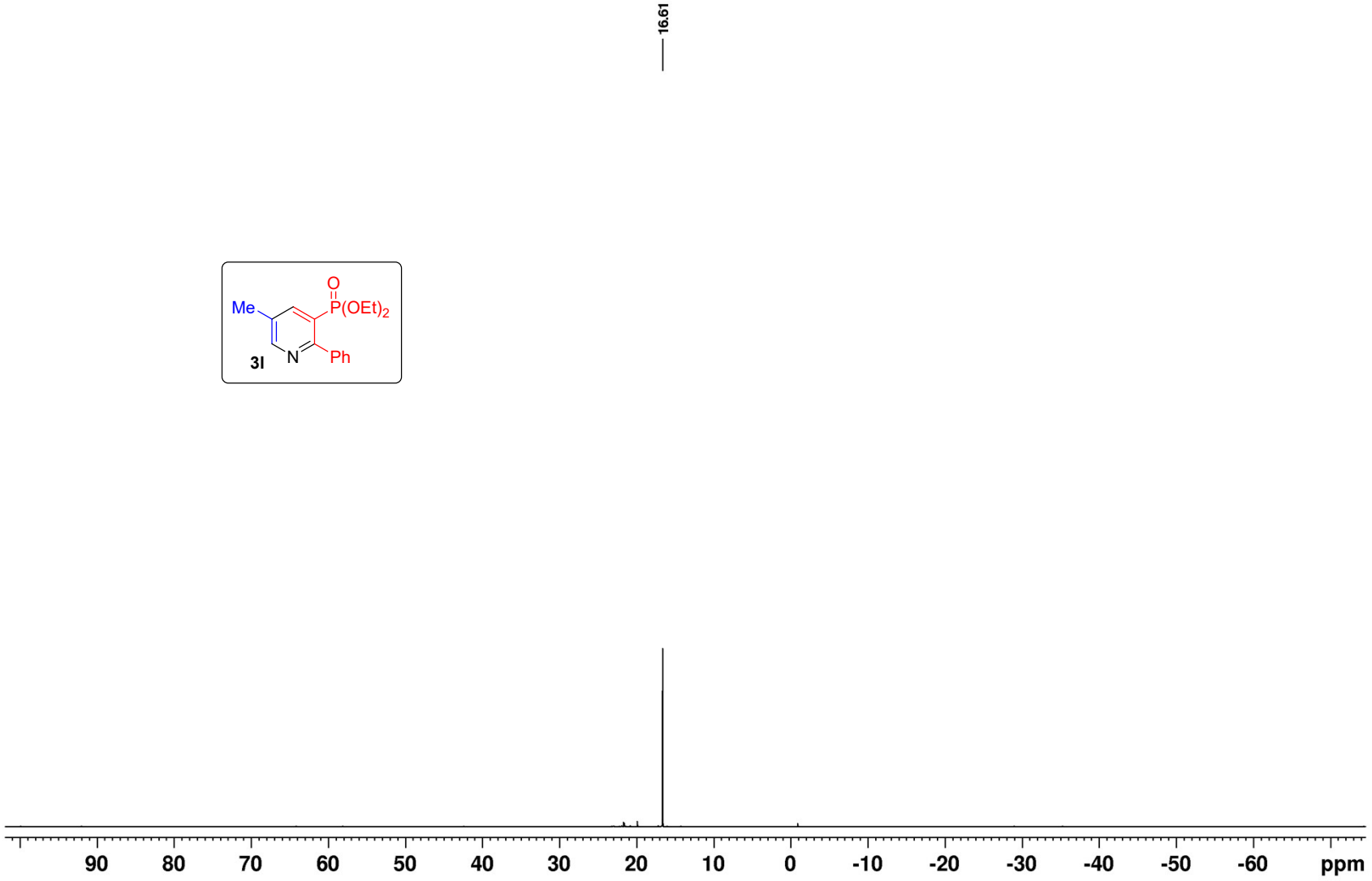
^{1}H NMR of compound **3l** (400MHz/$CDCl_3$)



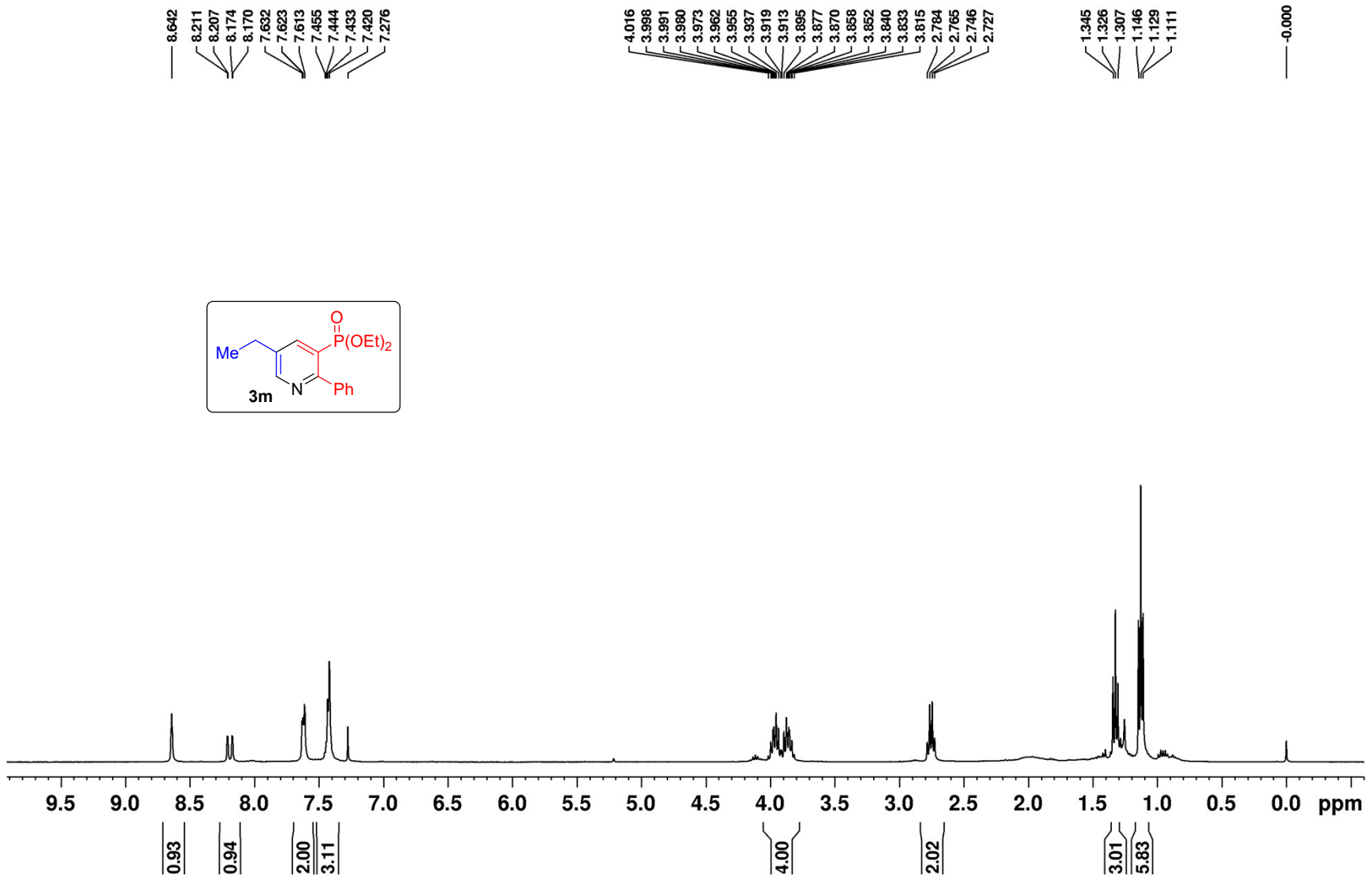
$^{13}C\{^{1}H\}$ NMR of compound **3l** (100MHz/CDCl3)



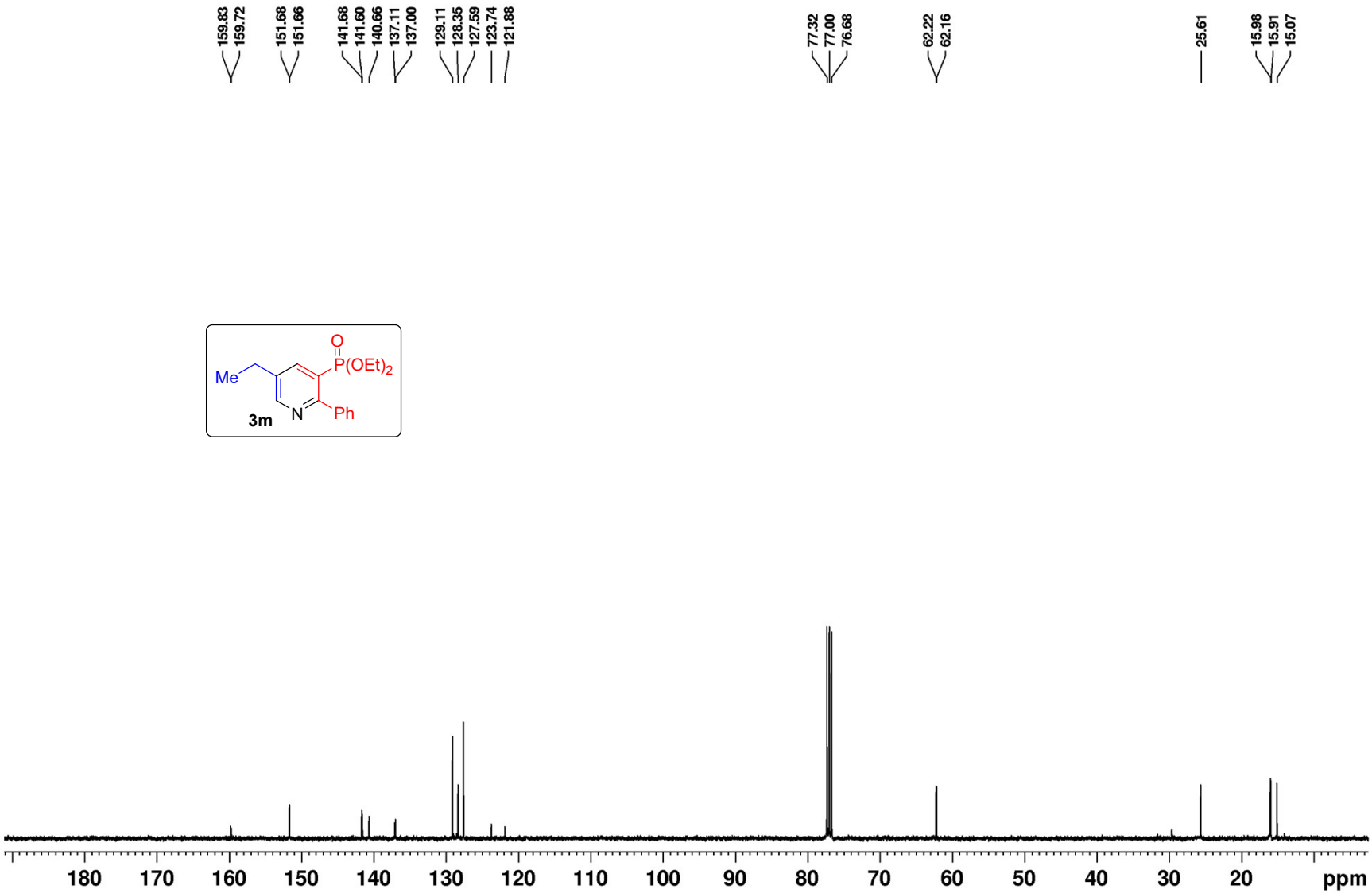
$^{31}P\{^{1}H\}$ NMR of compound **3l** (162MHz/$CDCl_3$)



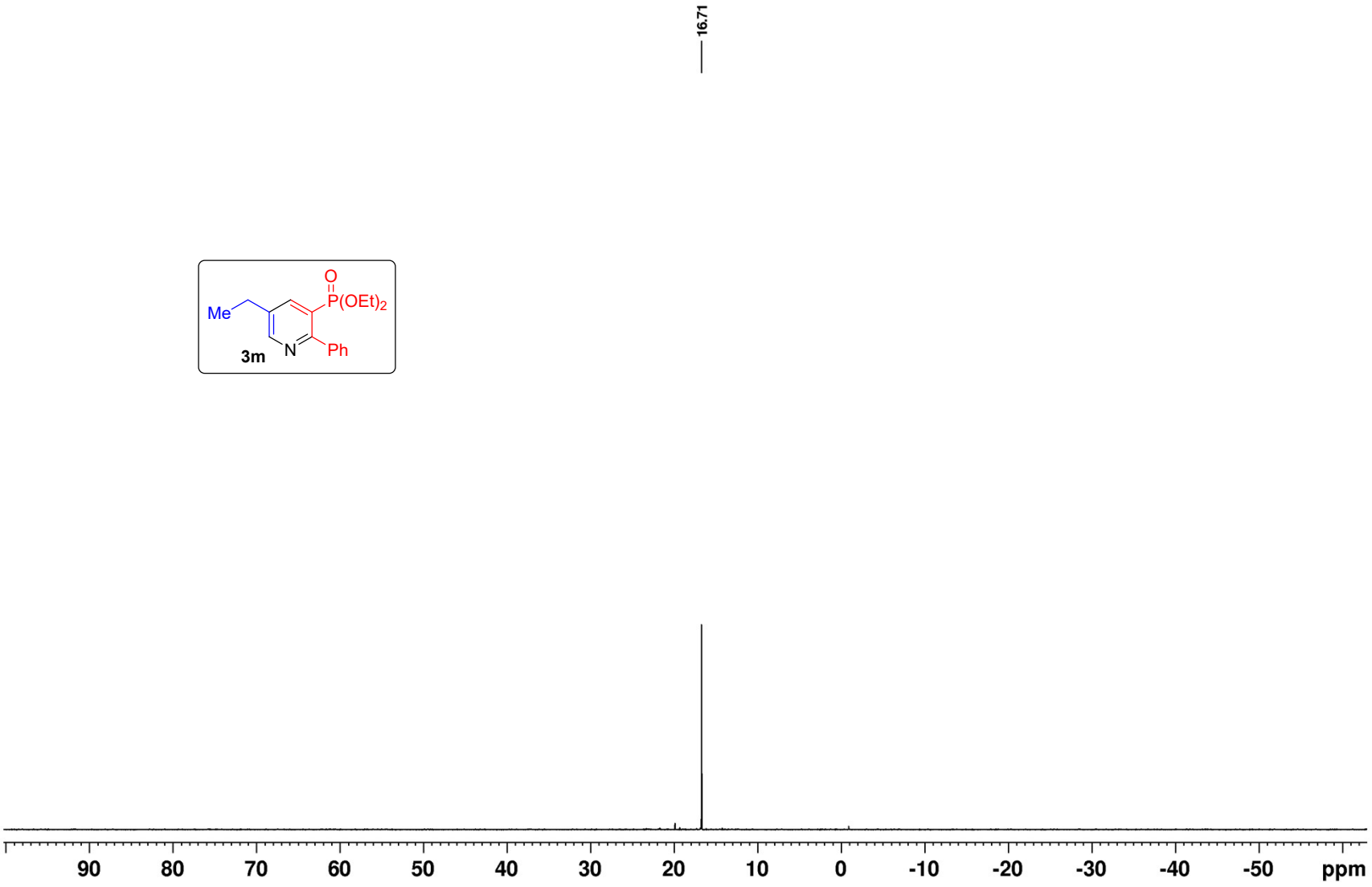
^{1}H NMR of compound **3m** (400MHz/$CDCl_3$)



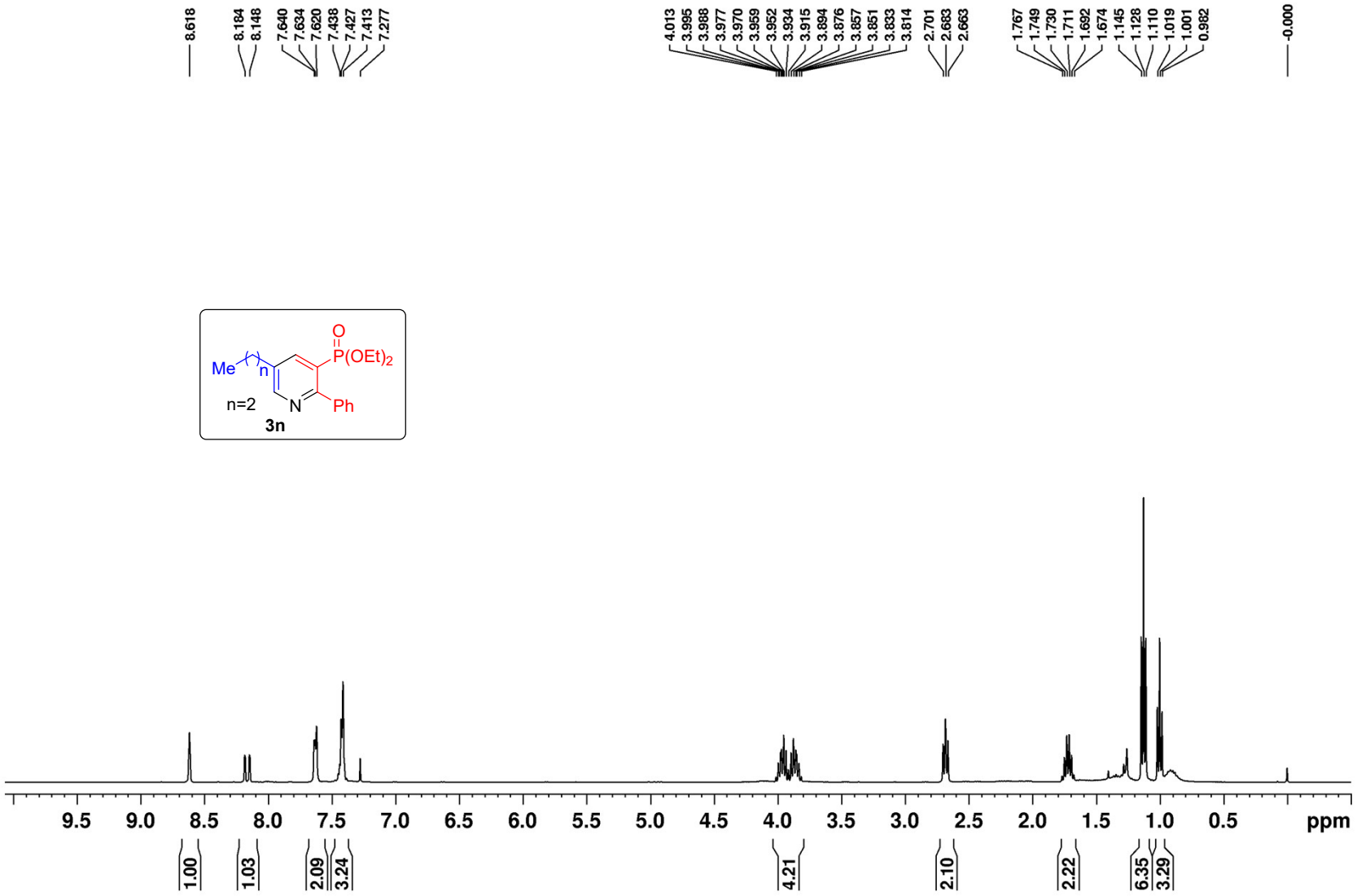
$^{13}C\{^{1}H\}$ NMR of compound **3m** (100MHz/$CDCl_3$)



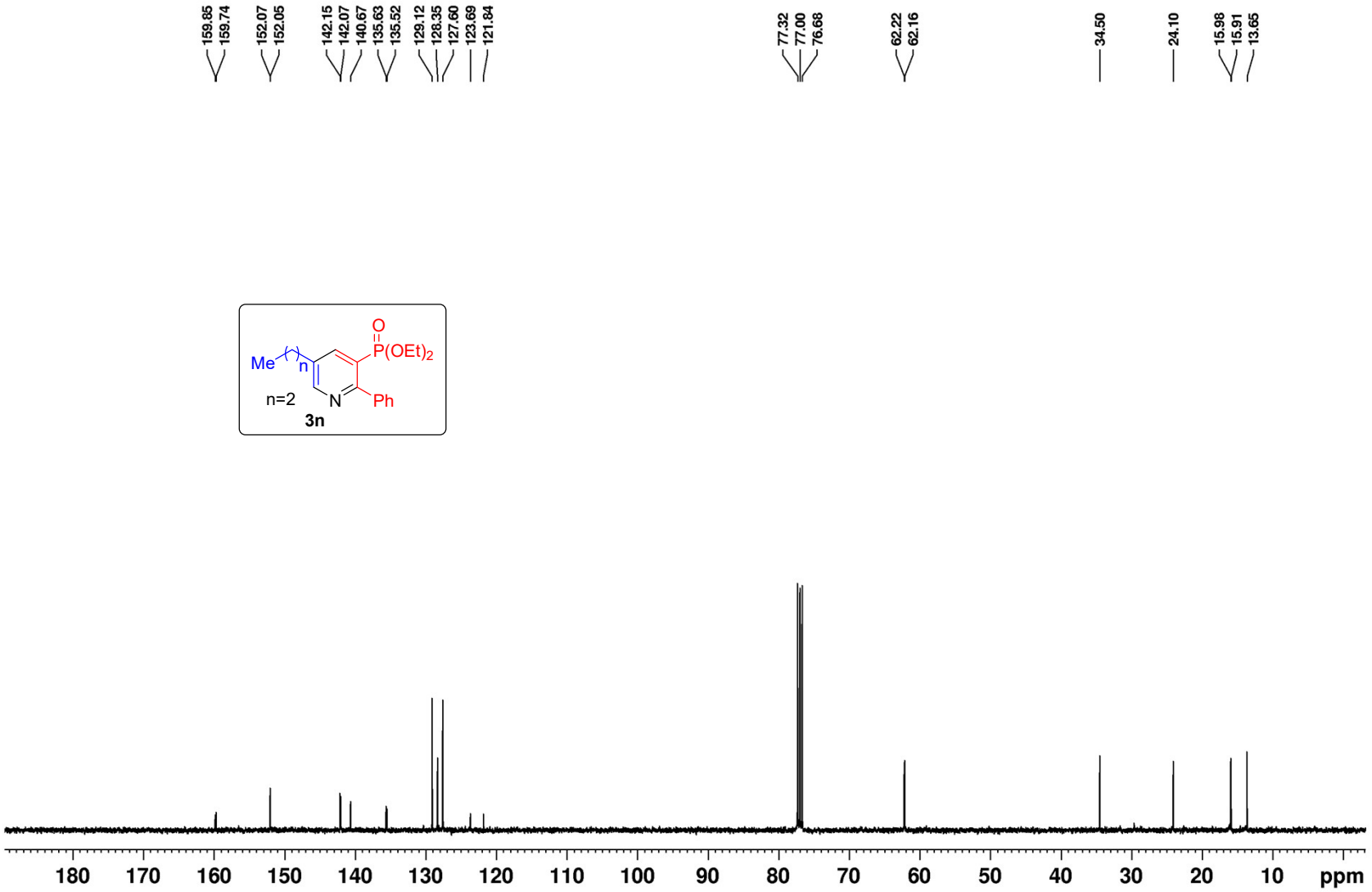
$^{31}P\{^{1}H\}$ NMR of compound **3m** ($162MHz/CDCl_3$)



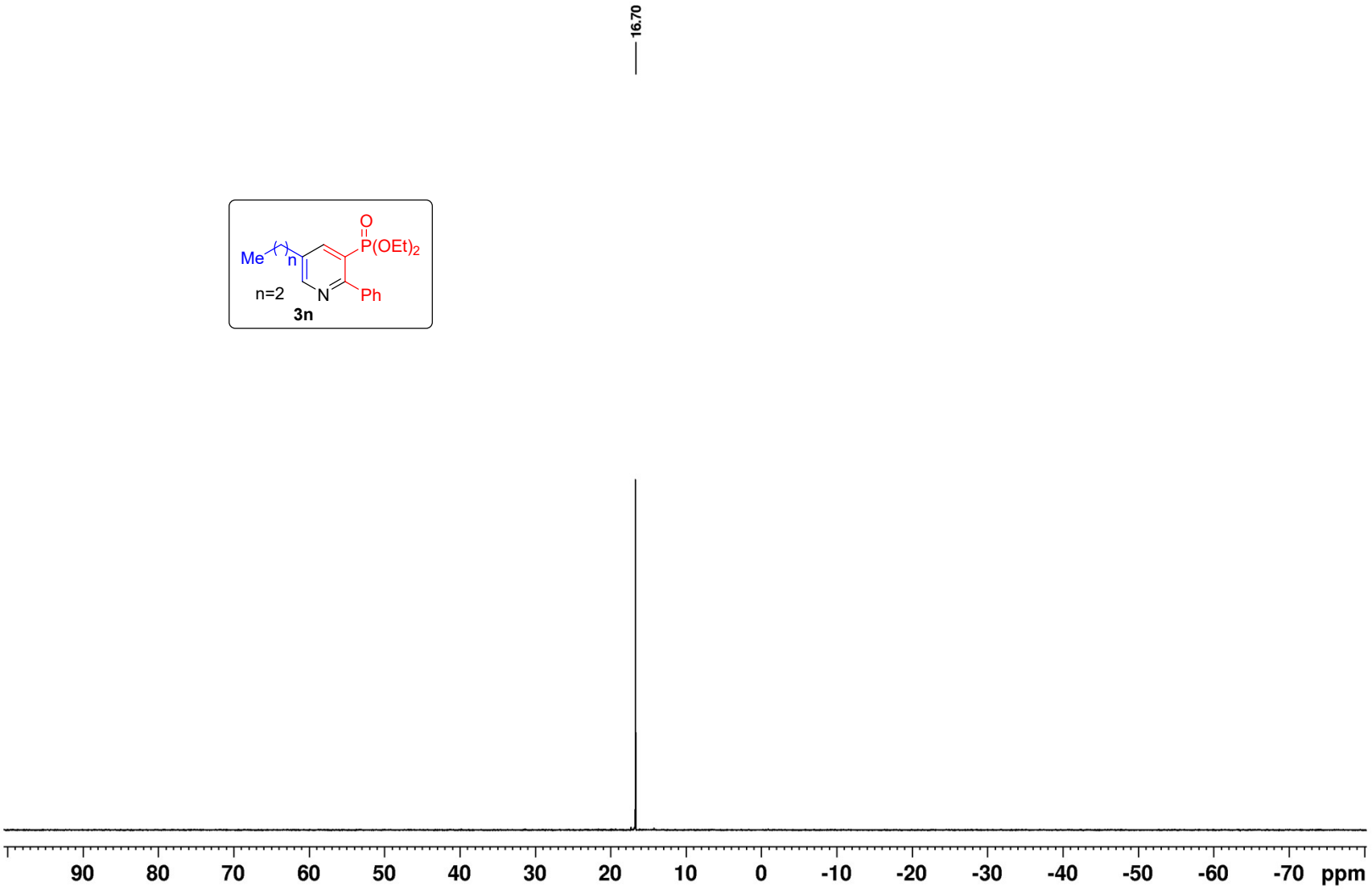
^{1}H NMR of compound **3n** (400MHz/$CDCl_3$)



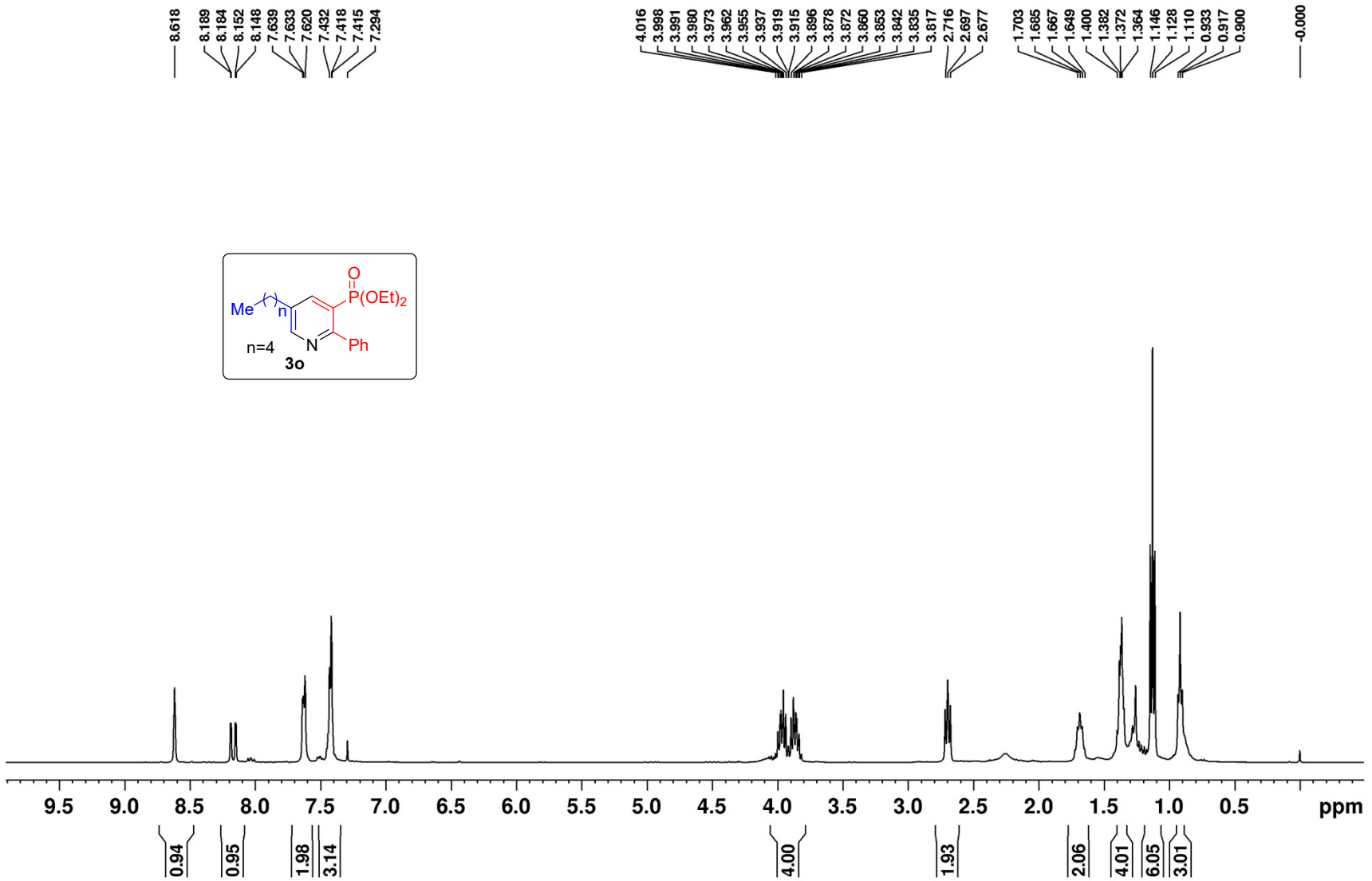
$^{13}C\{^{1}H\}$ NMR of compound **3n** (100MHz/CDCl3)



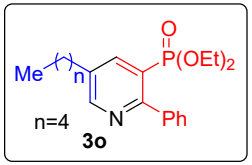
$^{31}P\{^{1}H\}$ NMR of compound **3n** (162MHz/$CDCl_3$)

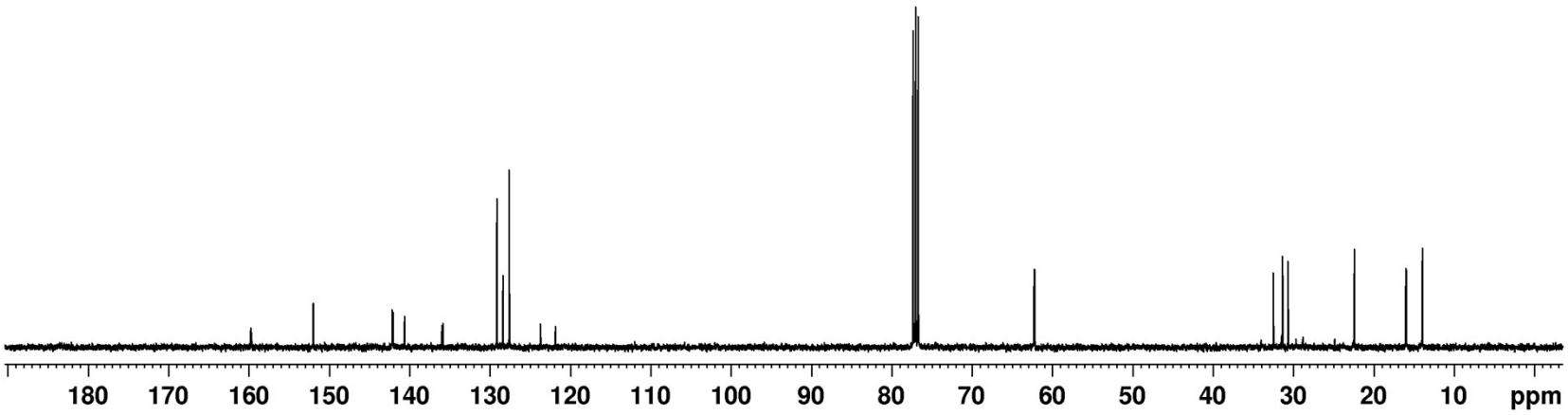


^{1}H NMR of compound **3o** (400MHz/$CDCl_3$)

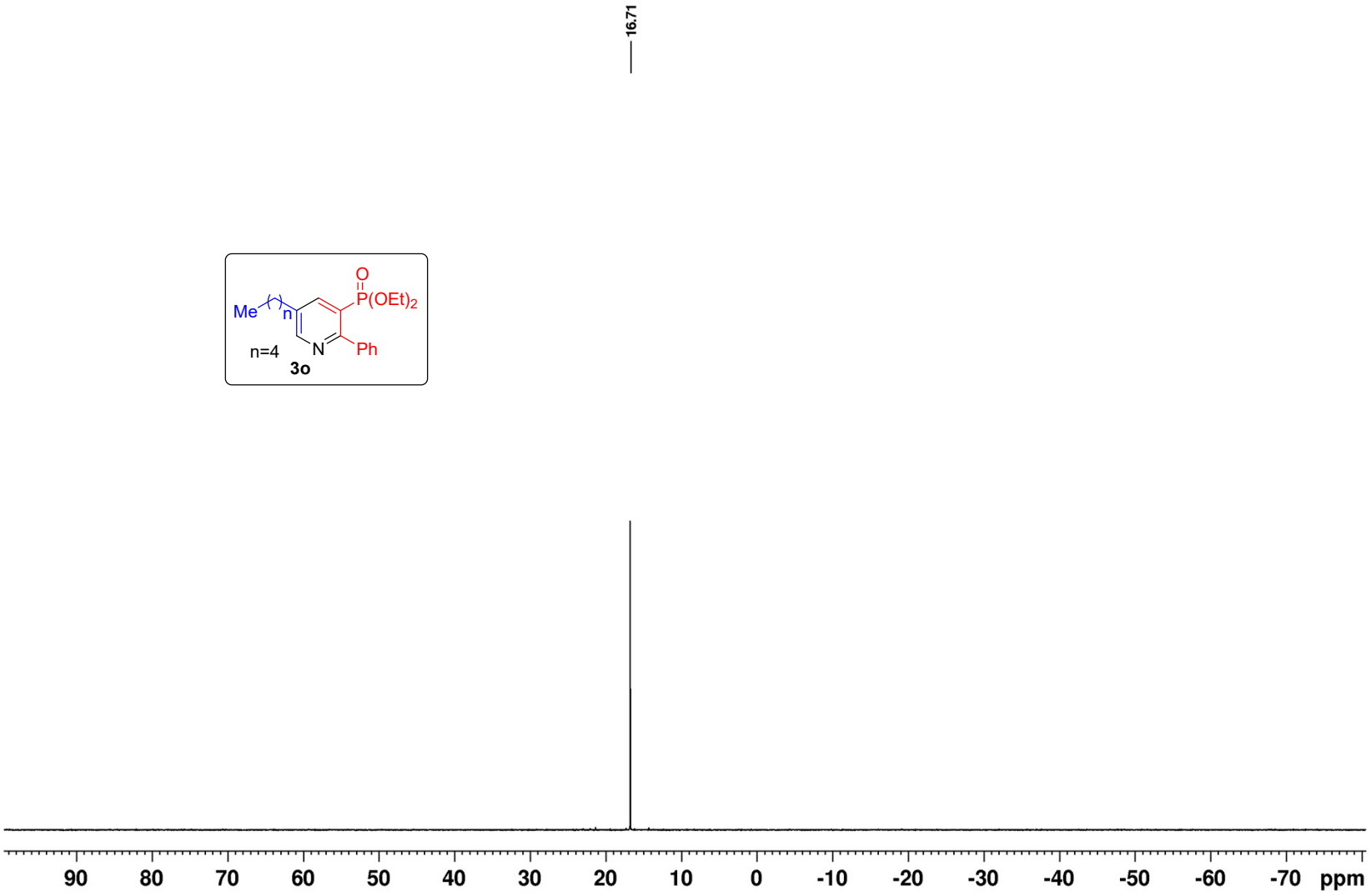


$^{13}C\{^{1}H\}$ NMR of compound **3o** (100MHz/$CDCl_3$)

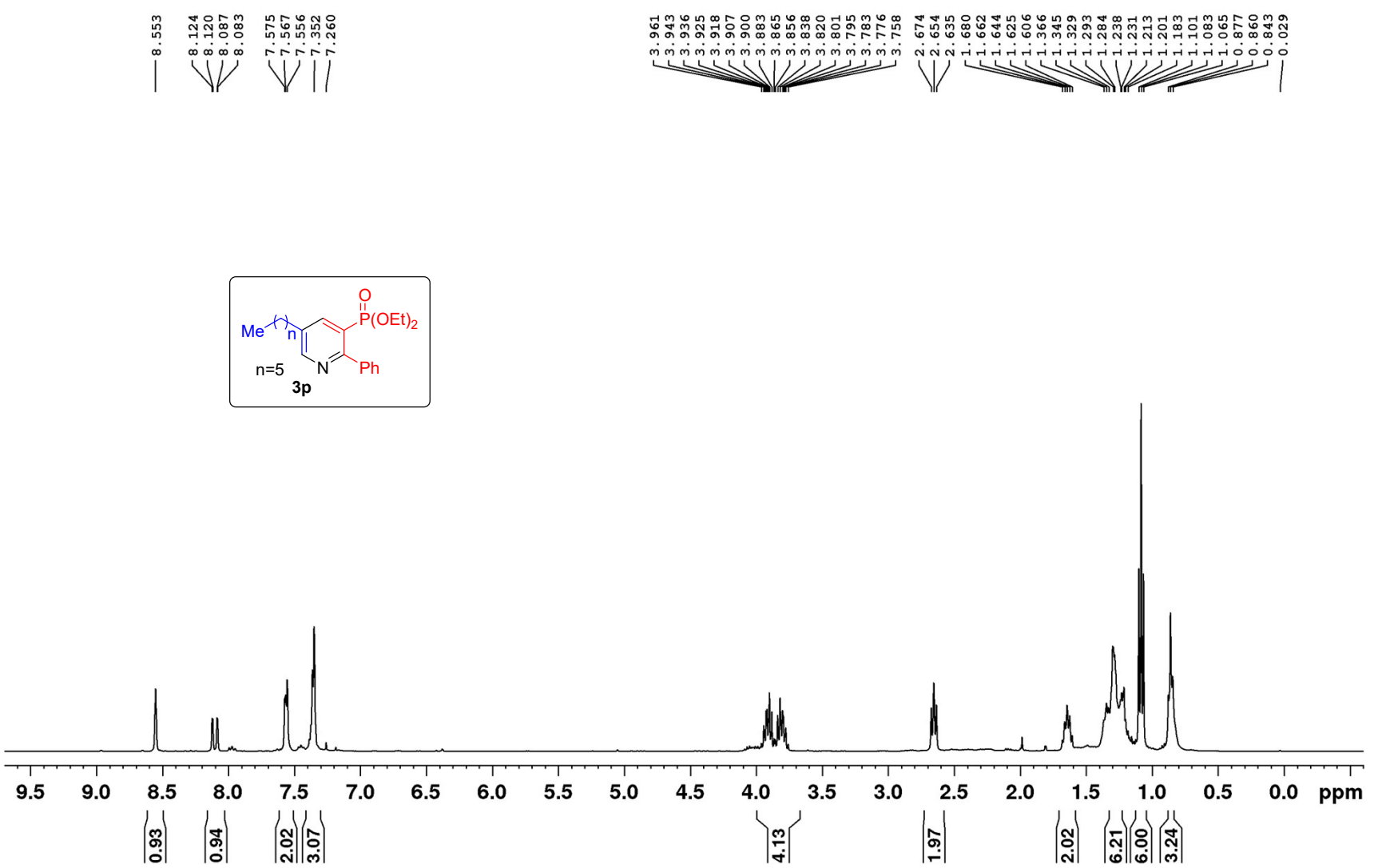




$^{31}P\{^{1}H\}$ NMR of compound **3o** (162MHz/$CDCl_3$)

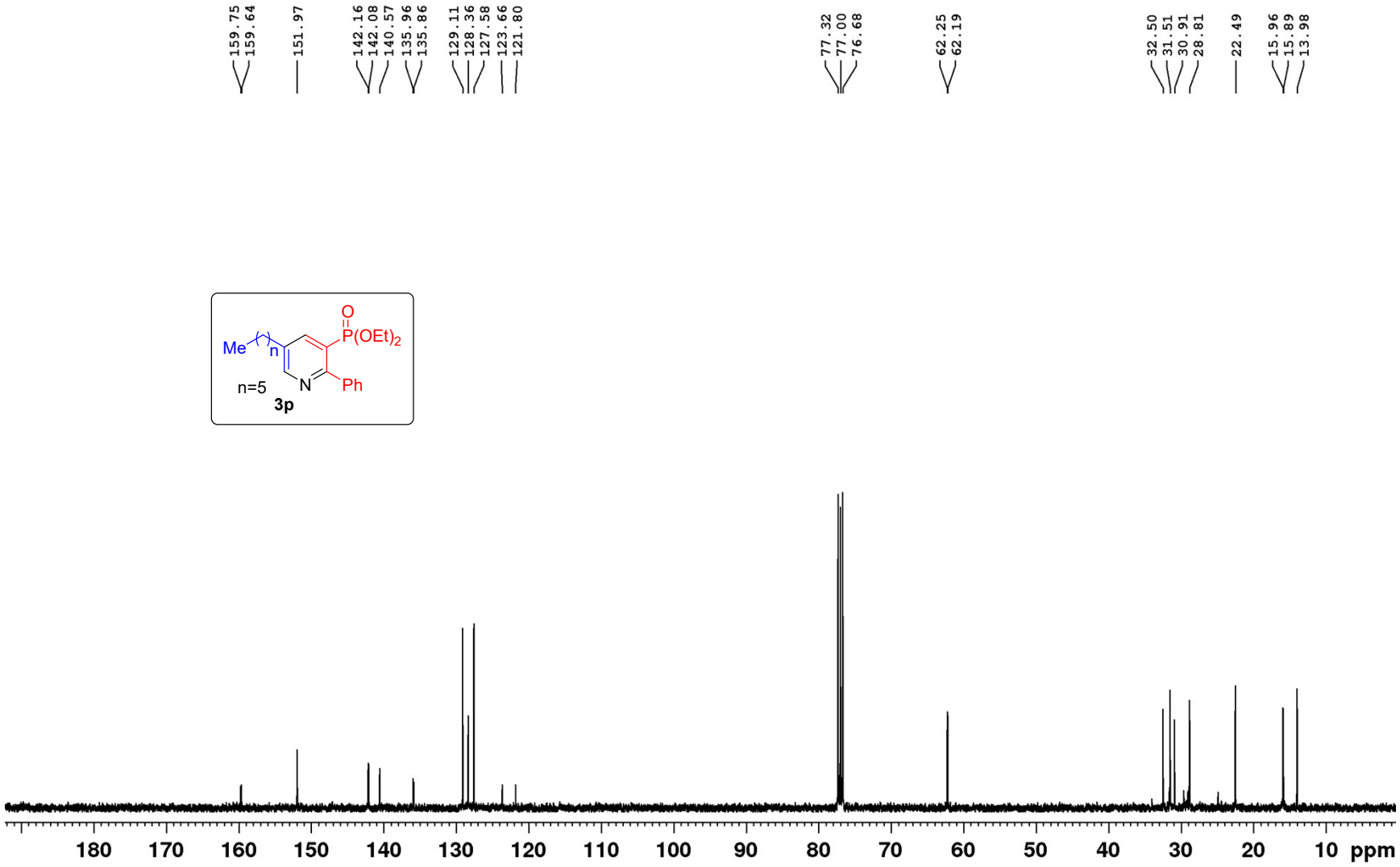


^{1}H NMR of compound **3p** (400MHz/$CDCl_3$)

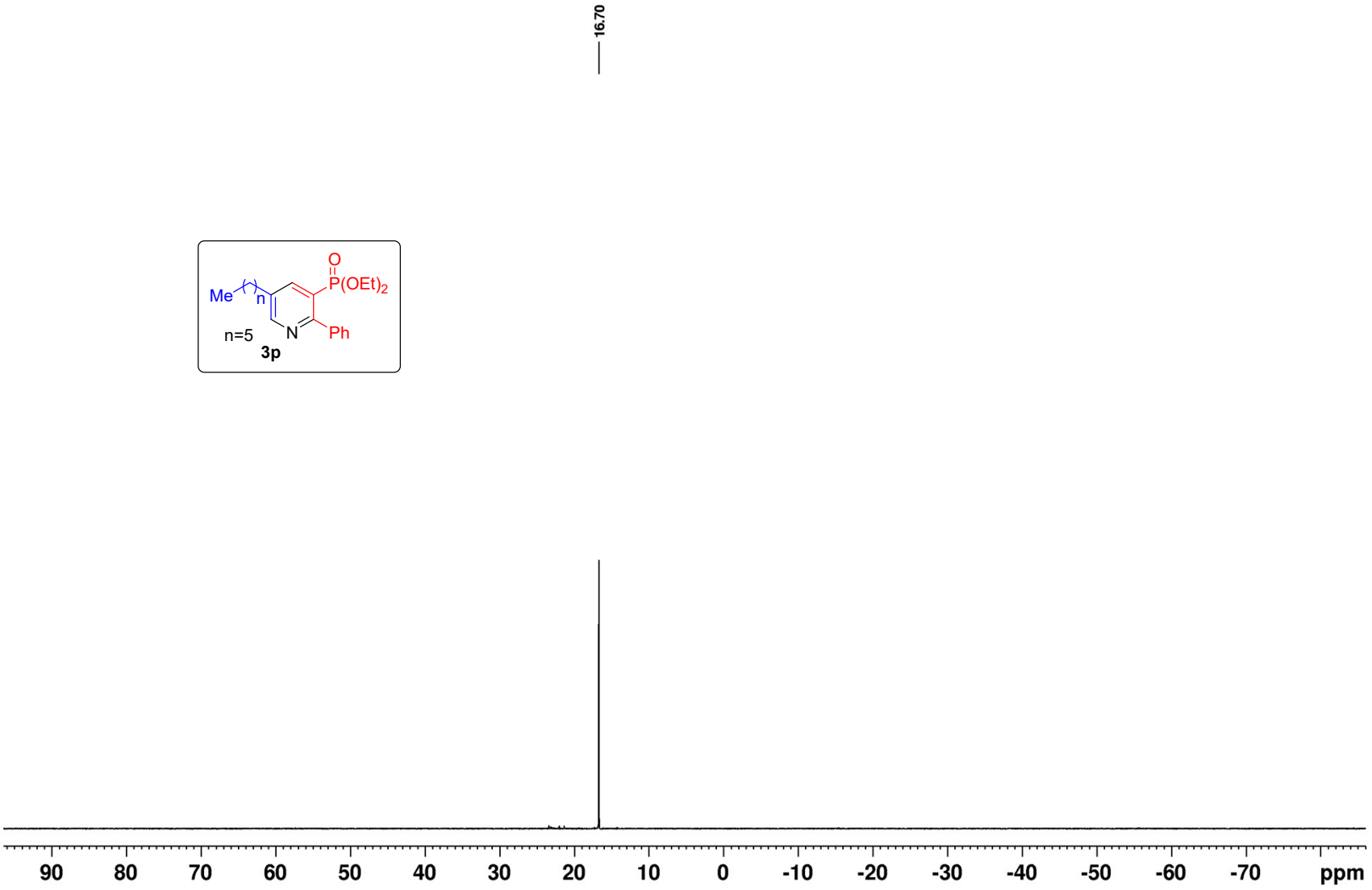


$^{13}C\{^{1}H\}$ NMR of compound **3p** (100MHz/$CDCl_3$)

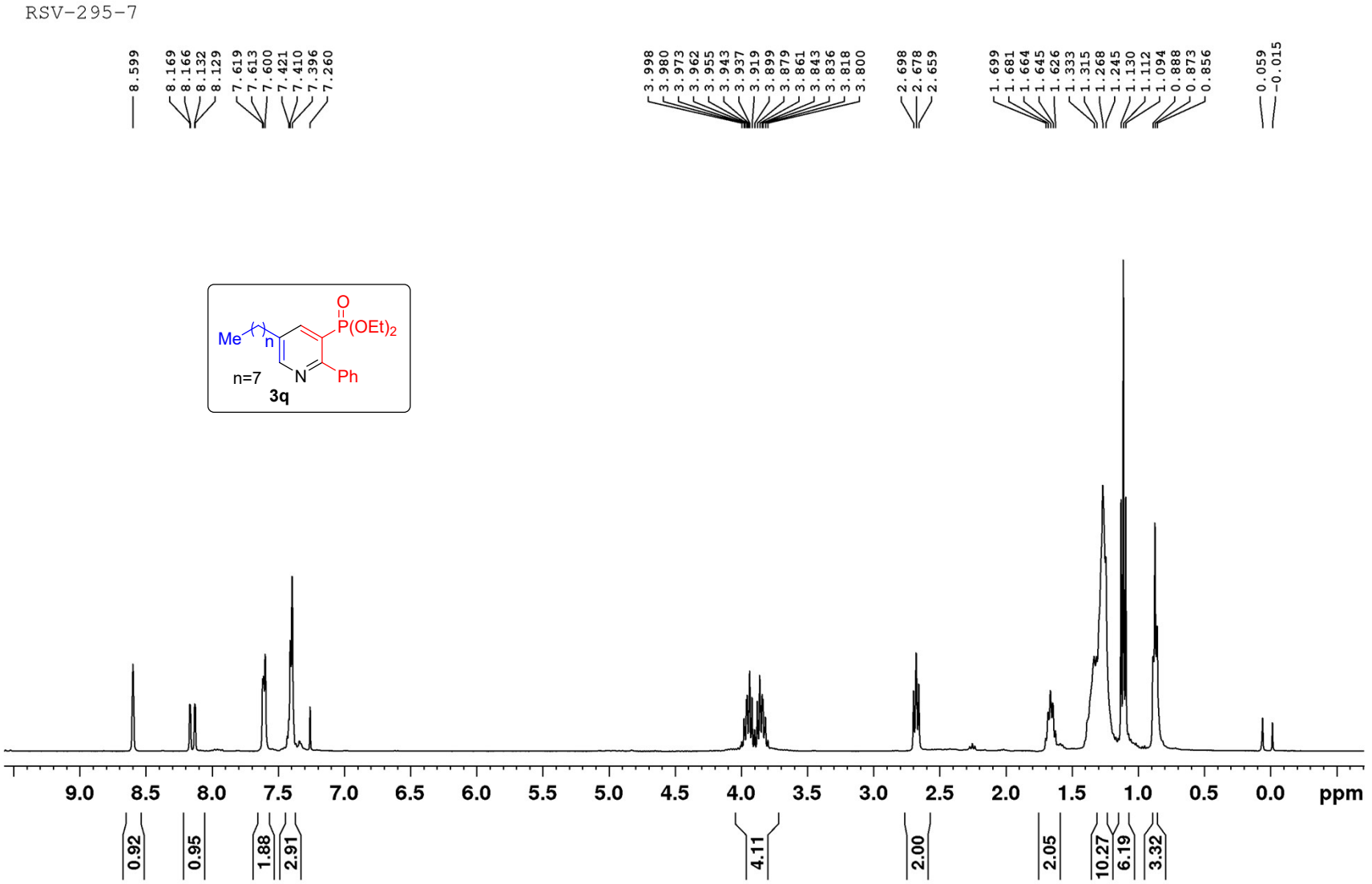
RSV-295-6



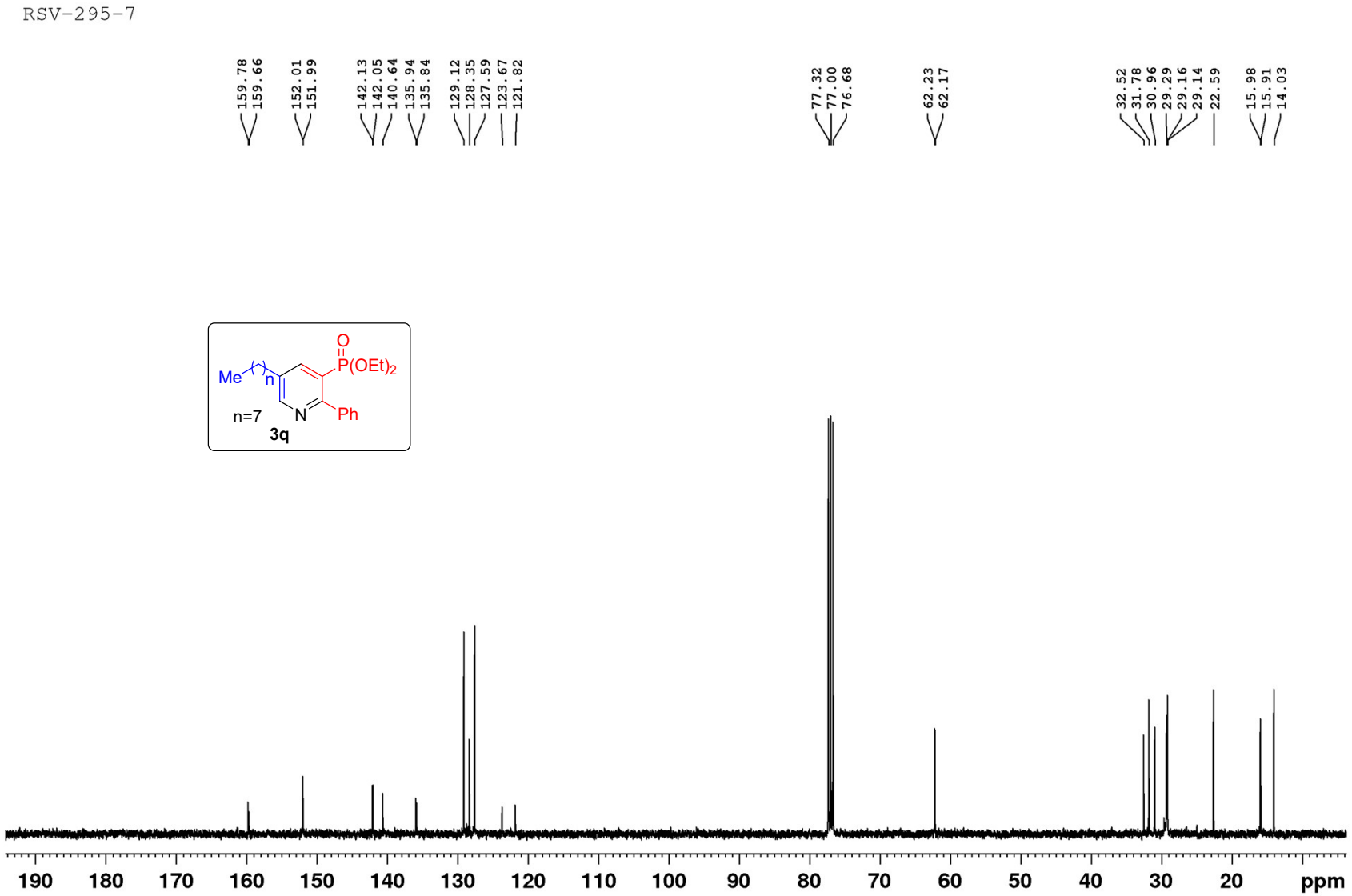
$^{31}P\{^{1}H\}$ NMR of compound **3p** (162MHz/$CDCl_3$)



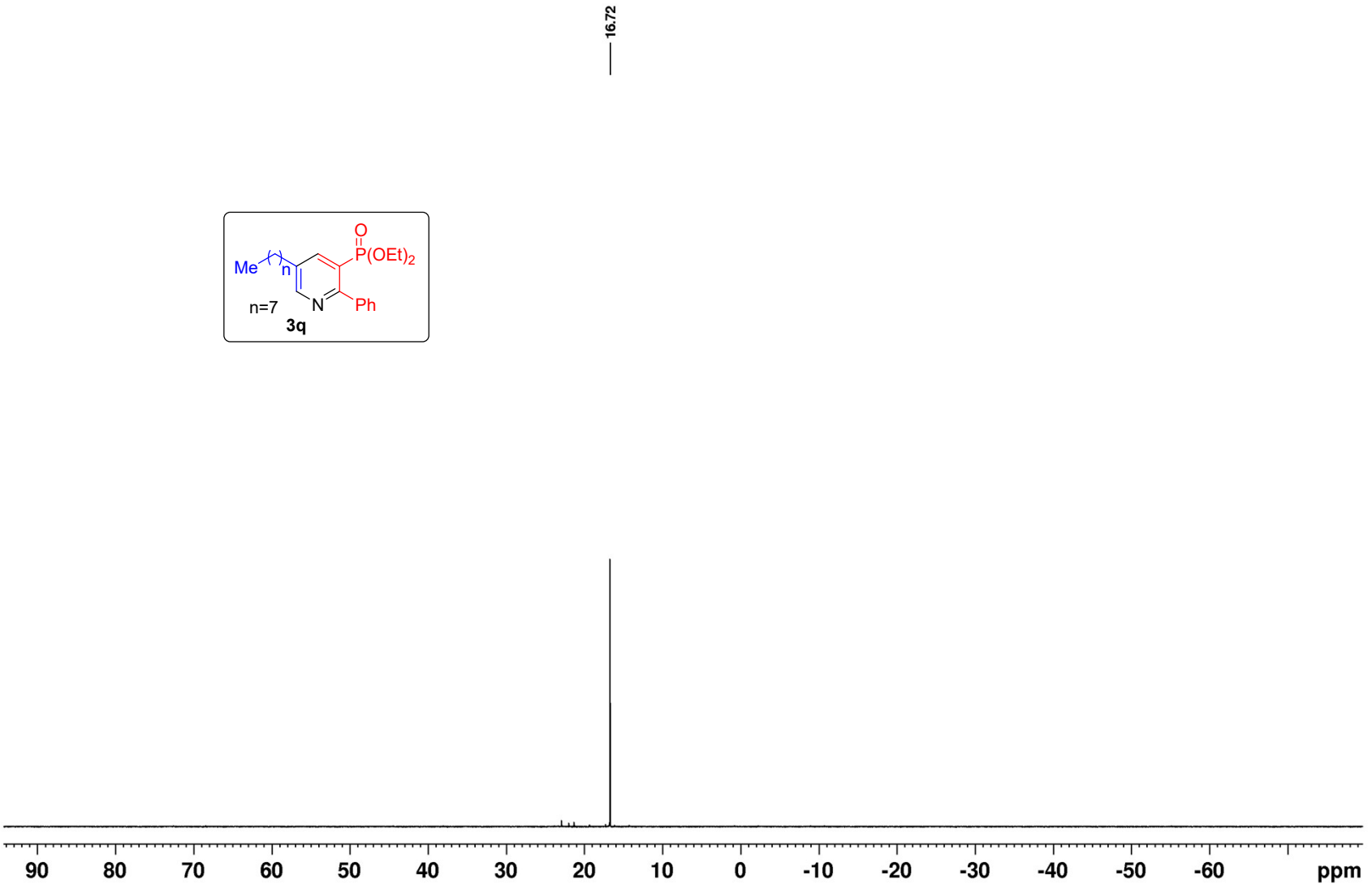
^{1}H NMR of compound **3q** (400MHz/$CDCl_3$)



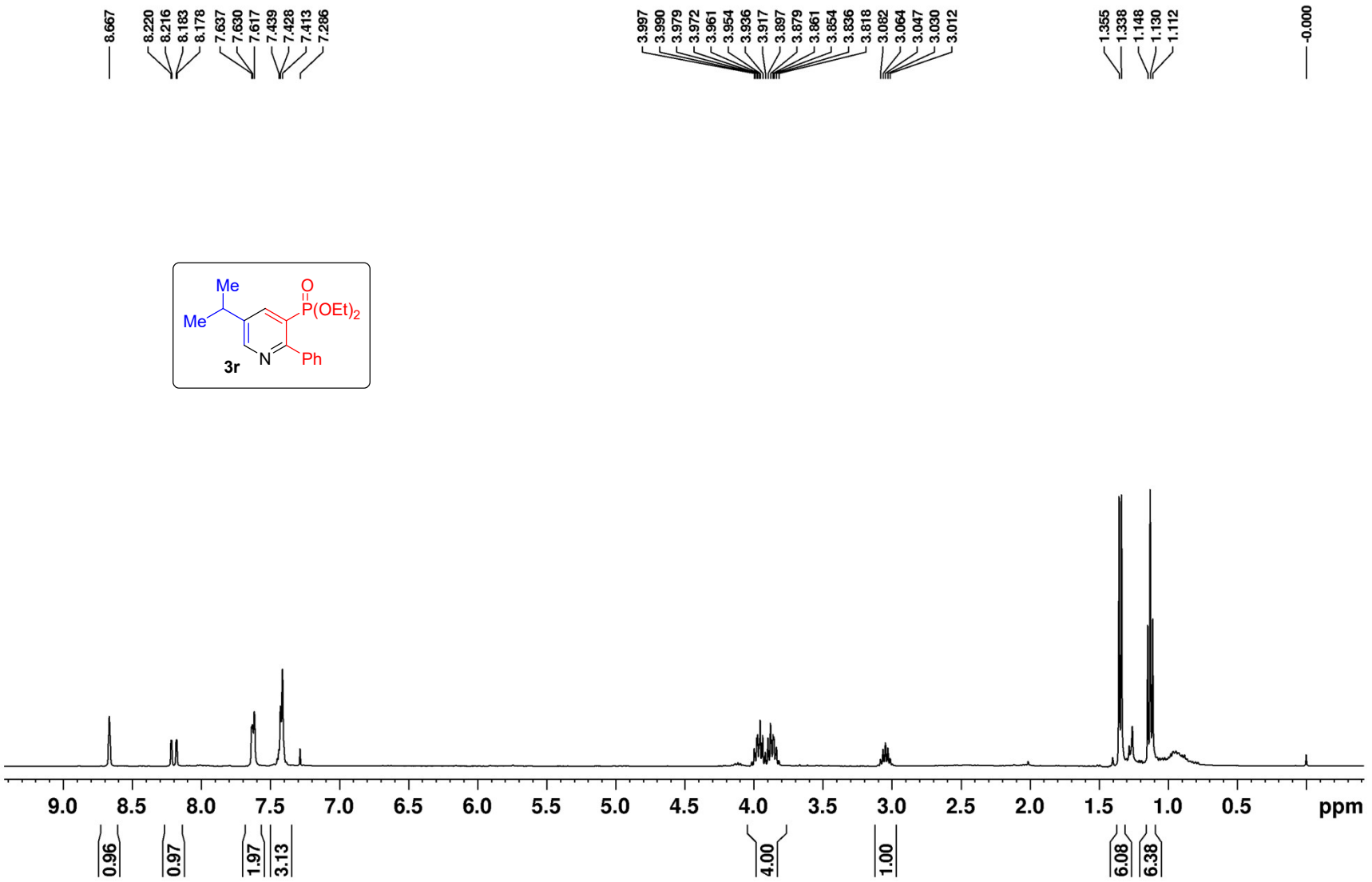
$^{13}C\{^{1}H\}$ NMR of compound **3q** (100MHz/$CDCl_3$)



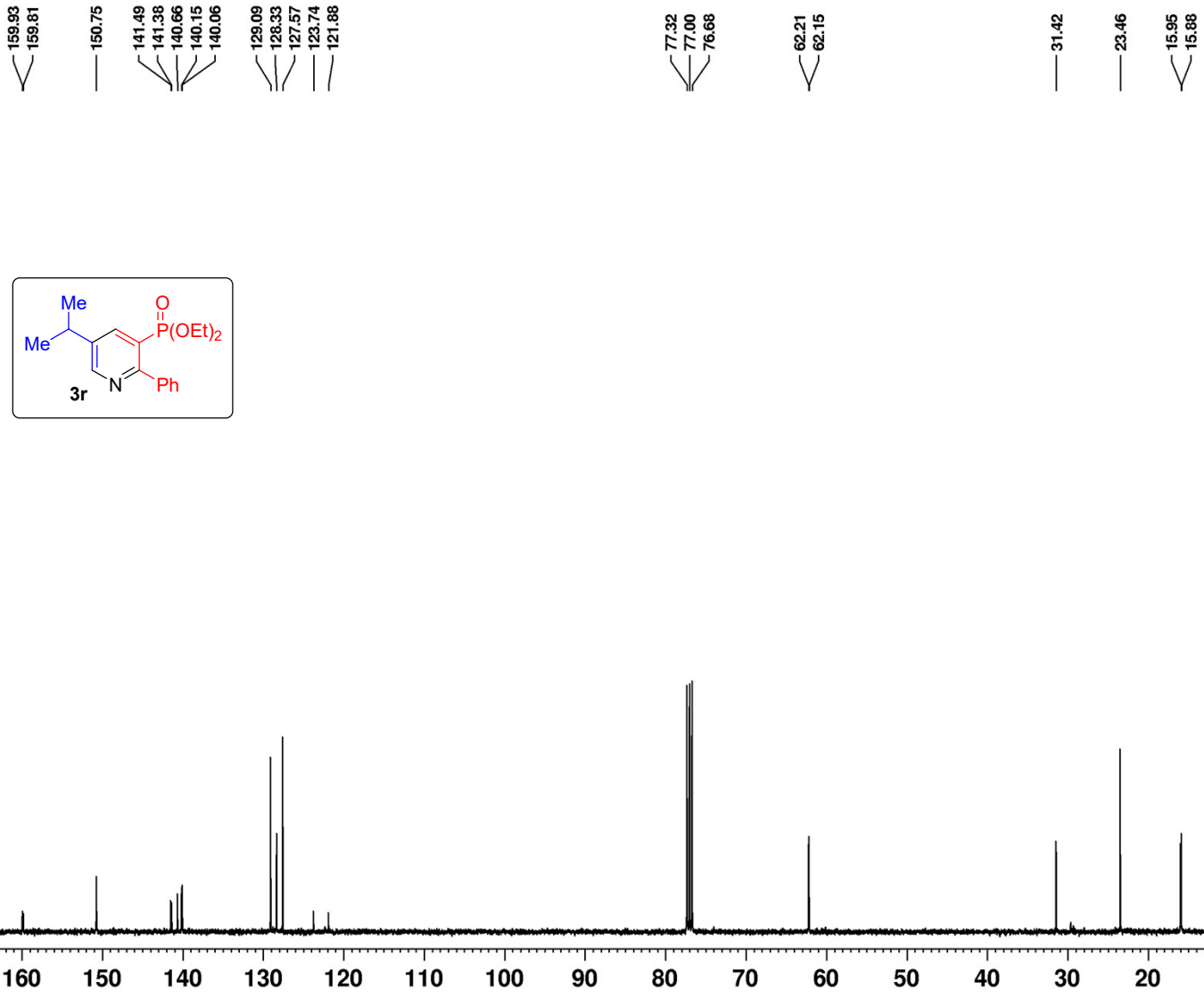
$^{31}P\{^{1}H\}$ NMR of compound **3q** (162MHz/$CDCl_3$)



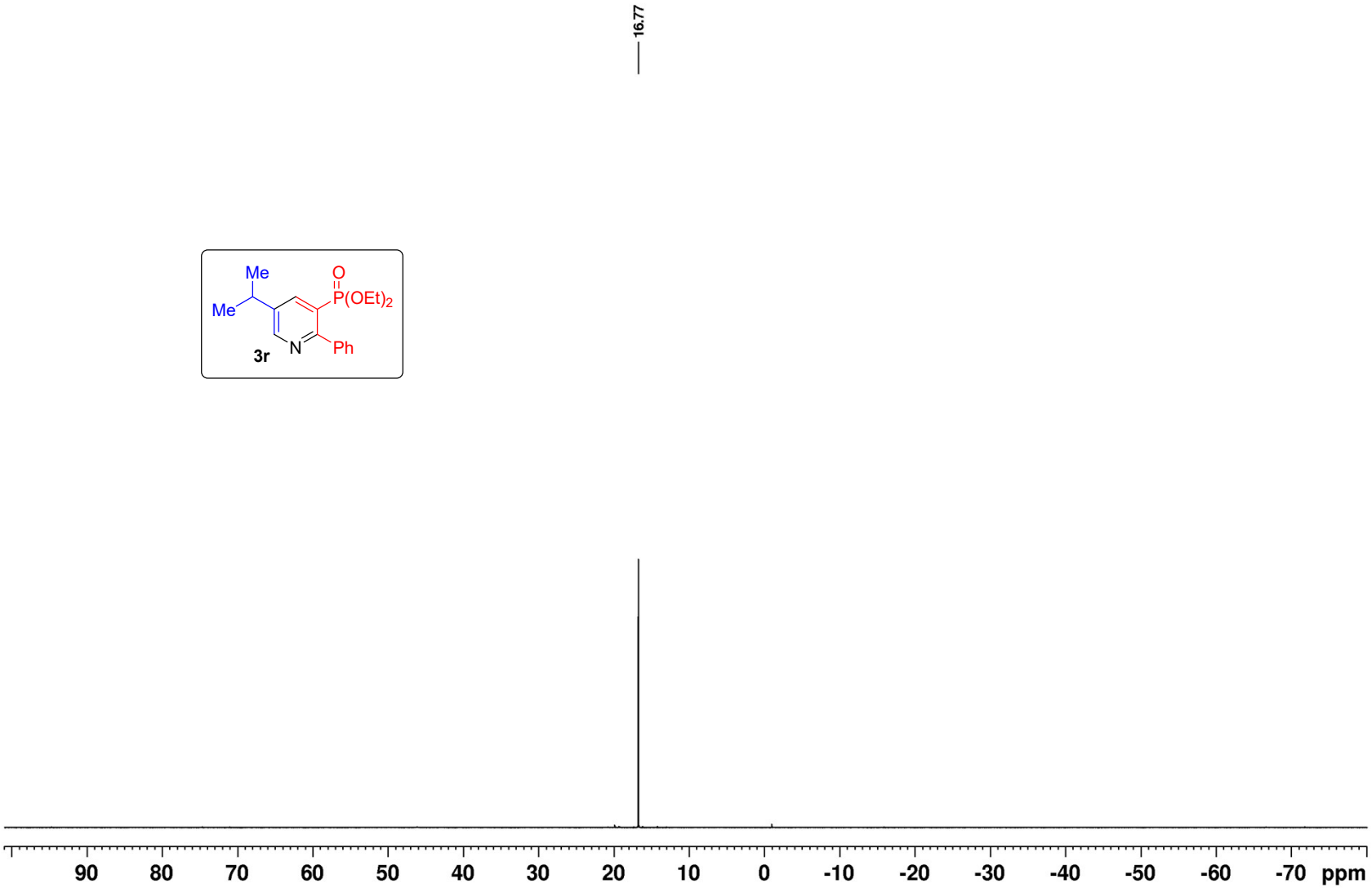
^{1}H NMR of compound **3r** (400MHz/CDCl3)



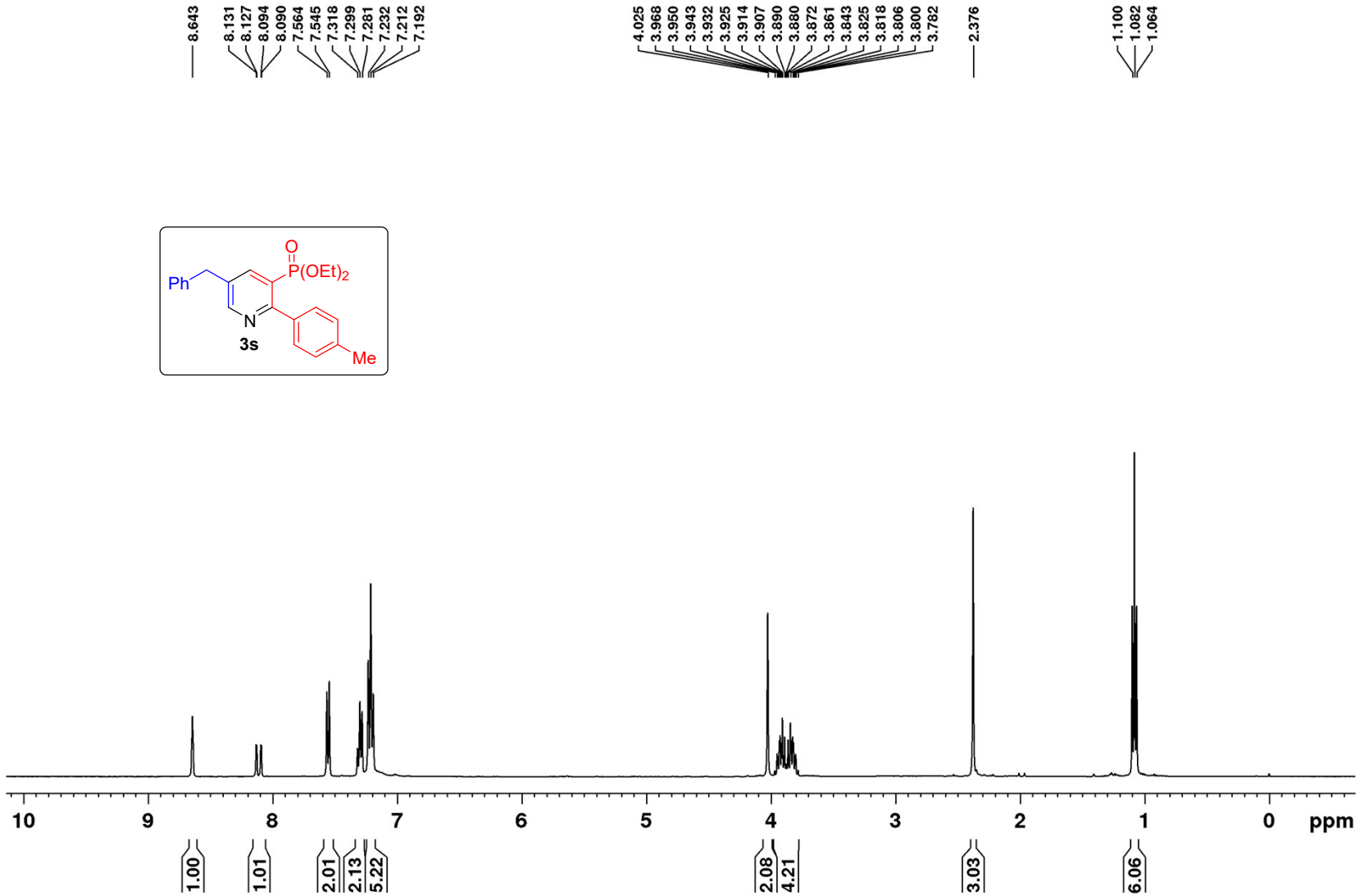
$^{13}C\{^{1}H\}$ NMR of compound **3r** (100MHz/CDCl3)



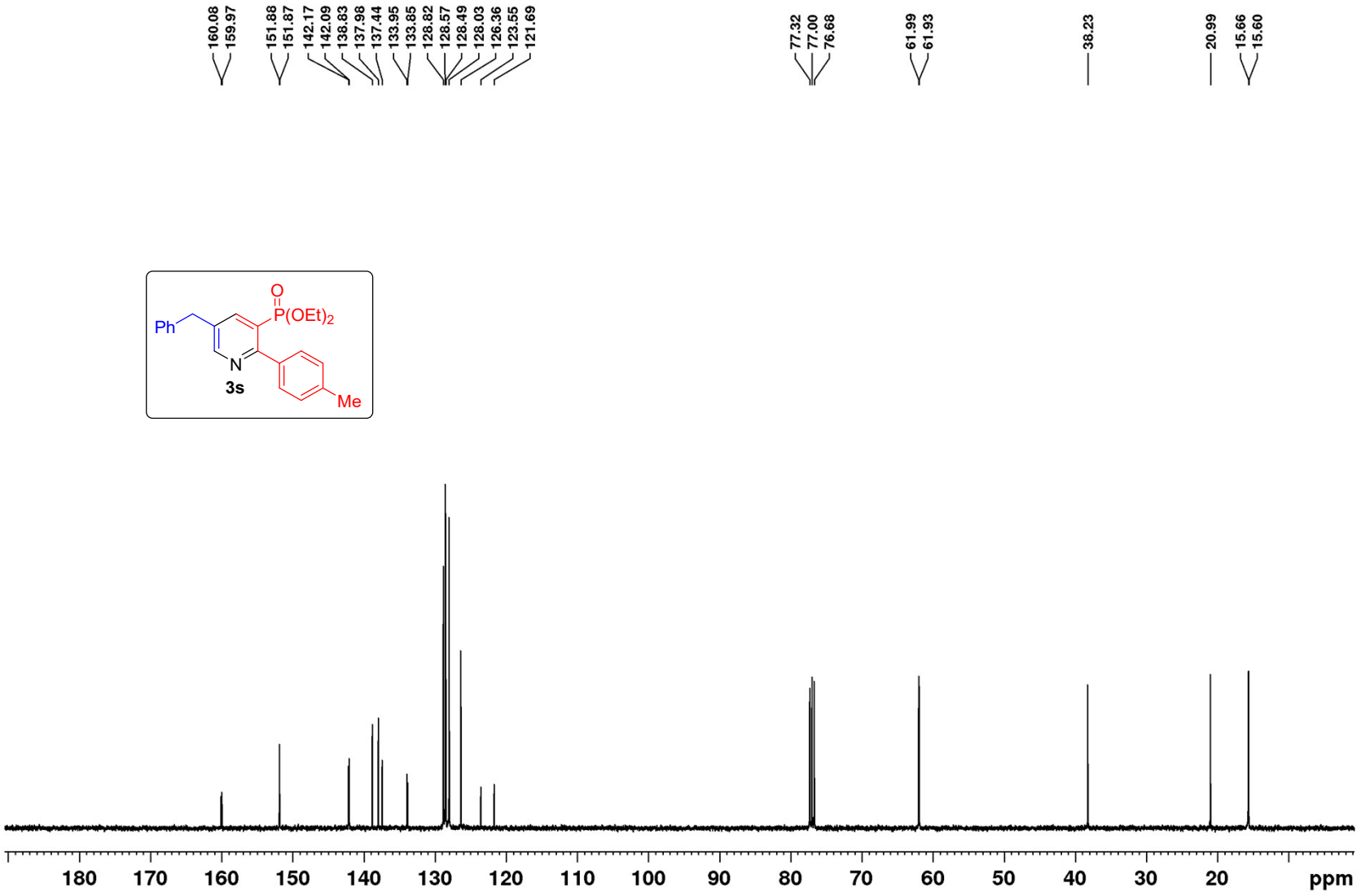
$^{31}P\{^{1}H\}$ NMR of compound **3r** (162MHz/CDCl3)



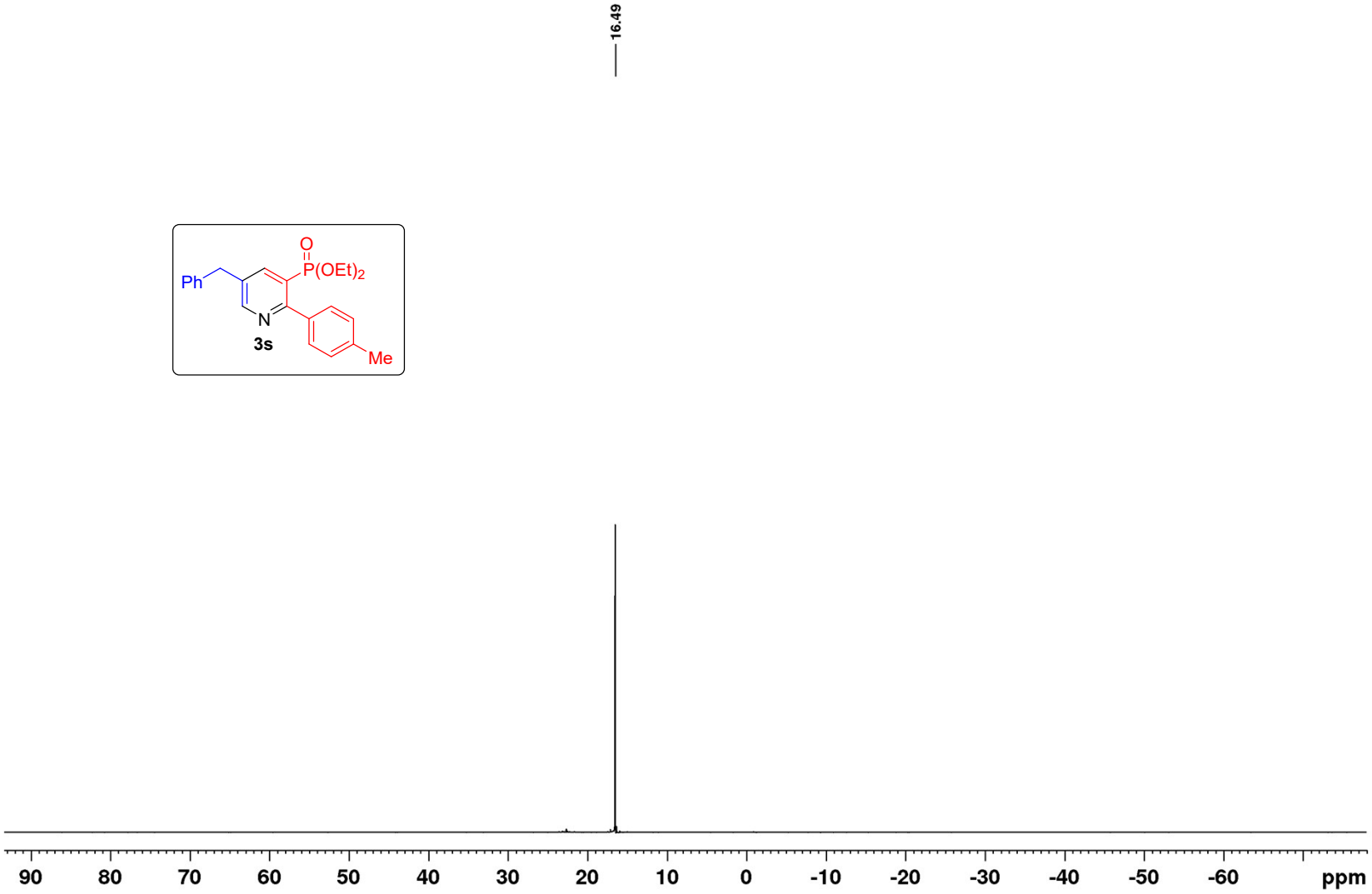
^{1}H NMR of compound **3s** (400MHz/$CDCl_3$)



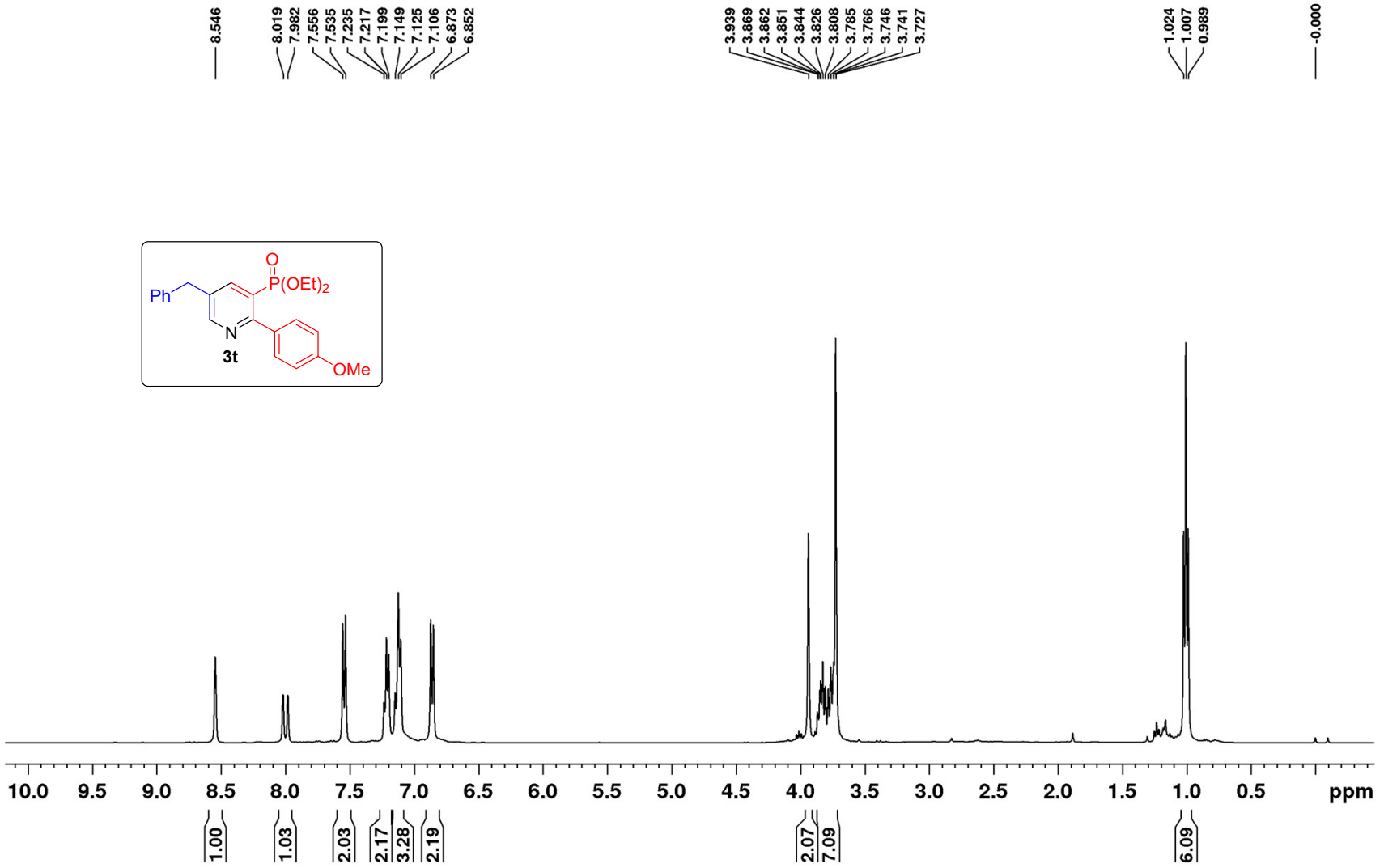
$^{13}C\{^{1}H\}$ NMR of compound **3s** (100MHz/$CDCl_3$)



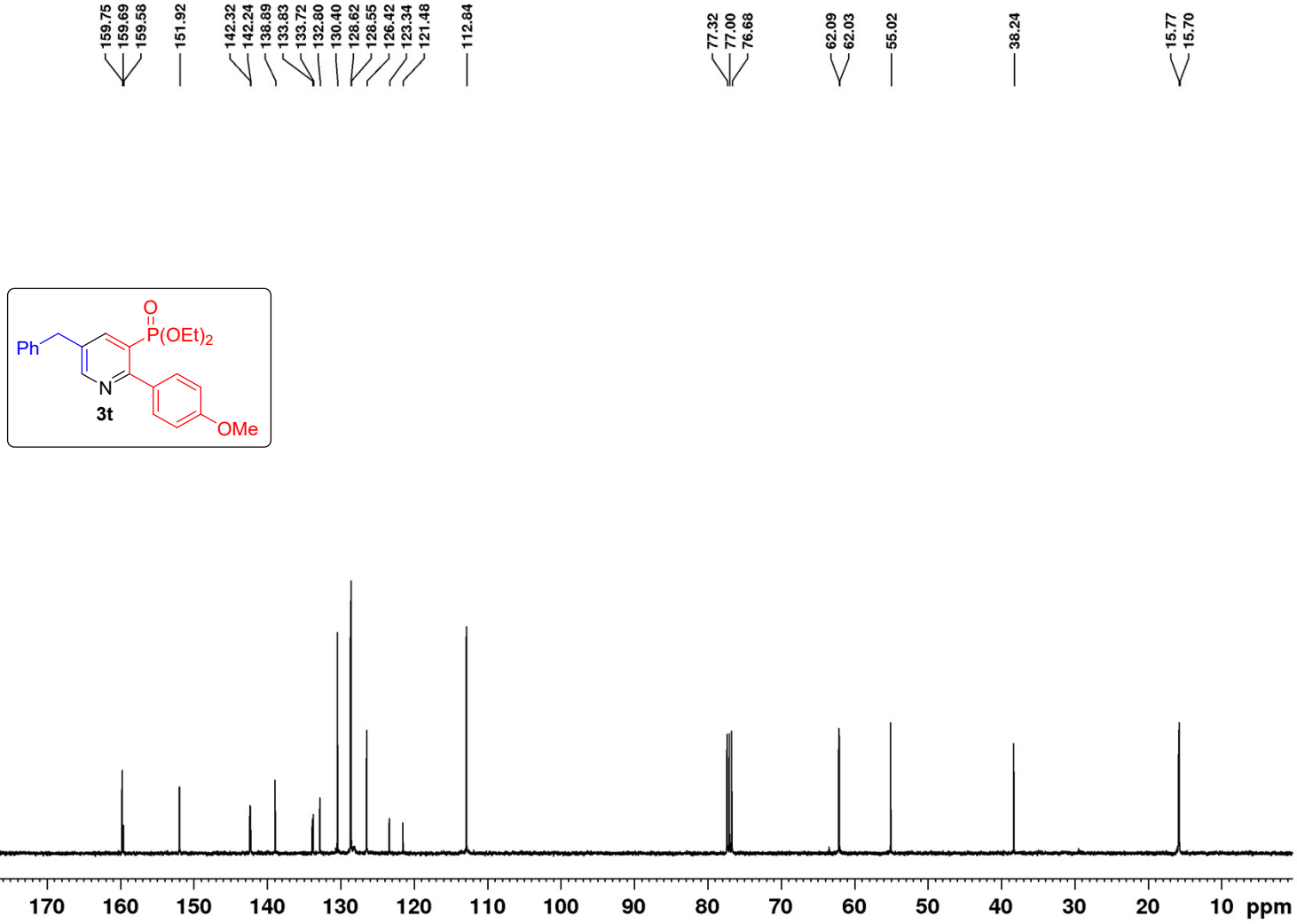
$^{31}P\{^{1}H\}$ NMR of compound **3s** (162MHz/CDCl3)



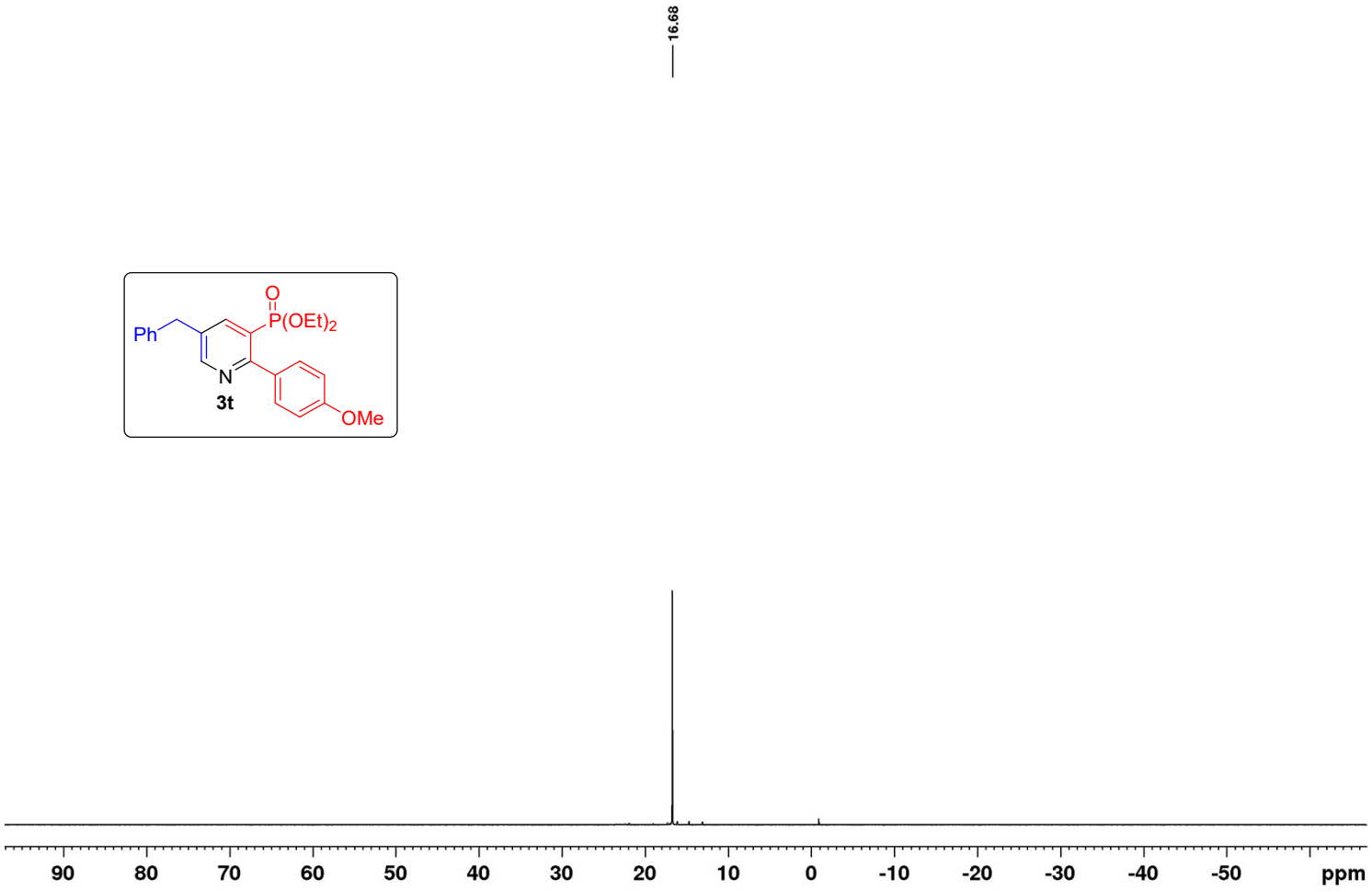
^{1}H NMR of compound **3t** (400 MHz/$CDCl_3$)



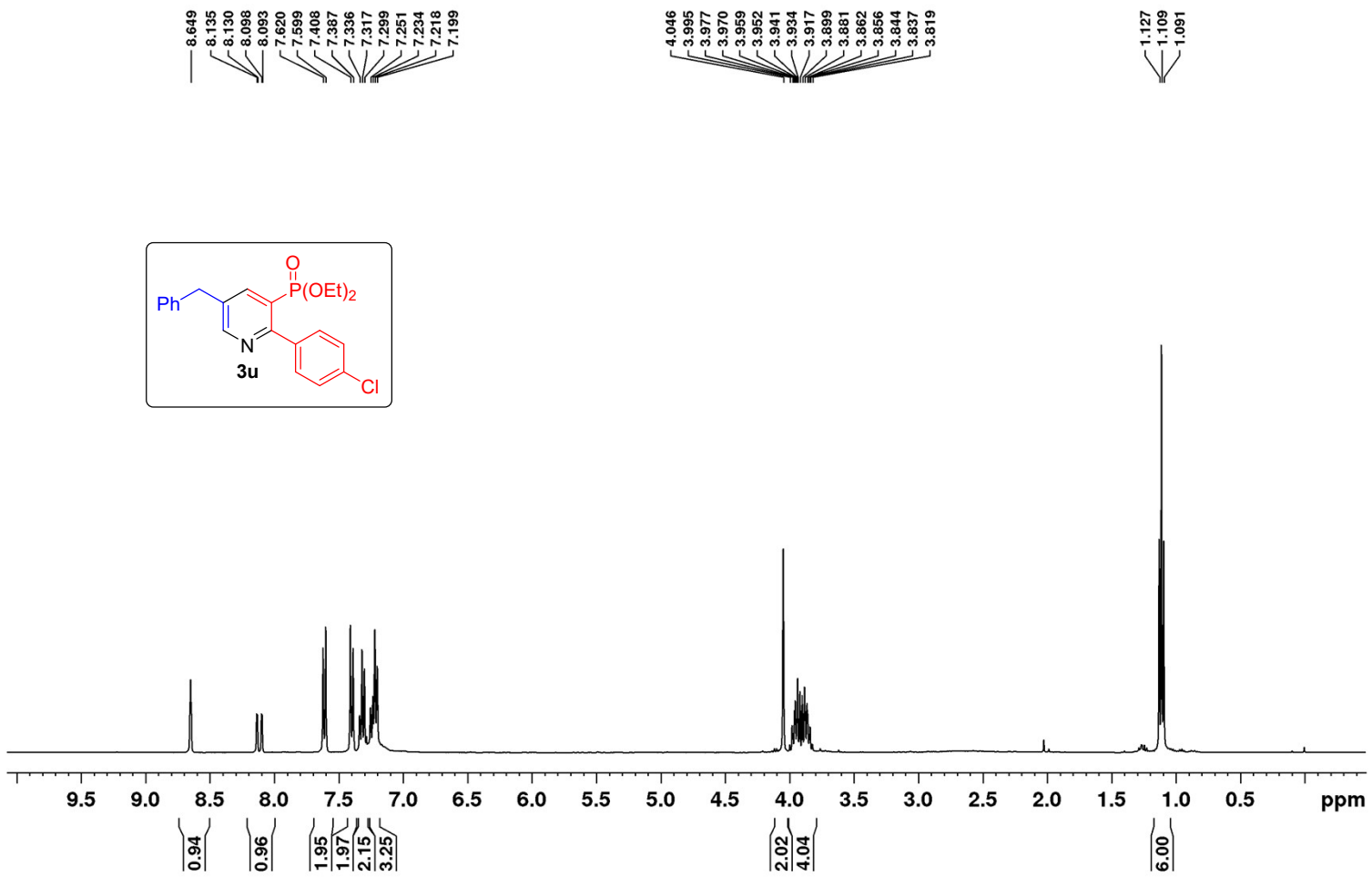
$^{13}C\{^{1}H\}$ NMR of compound **3t** (100MHz/$CDCl_3$)



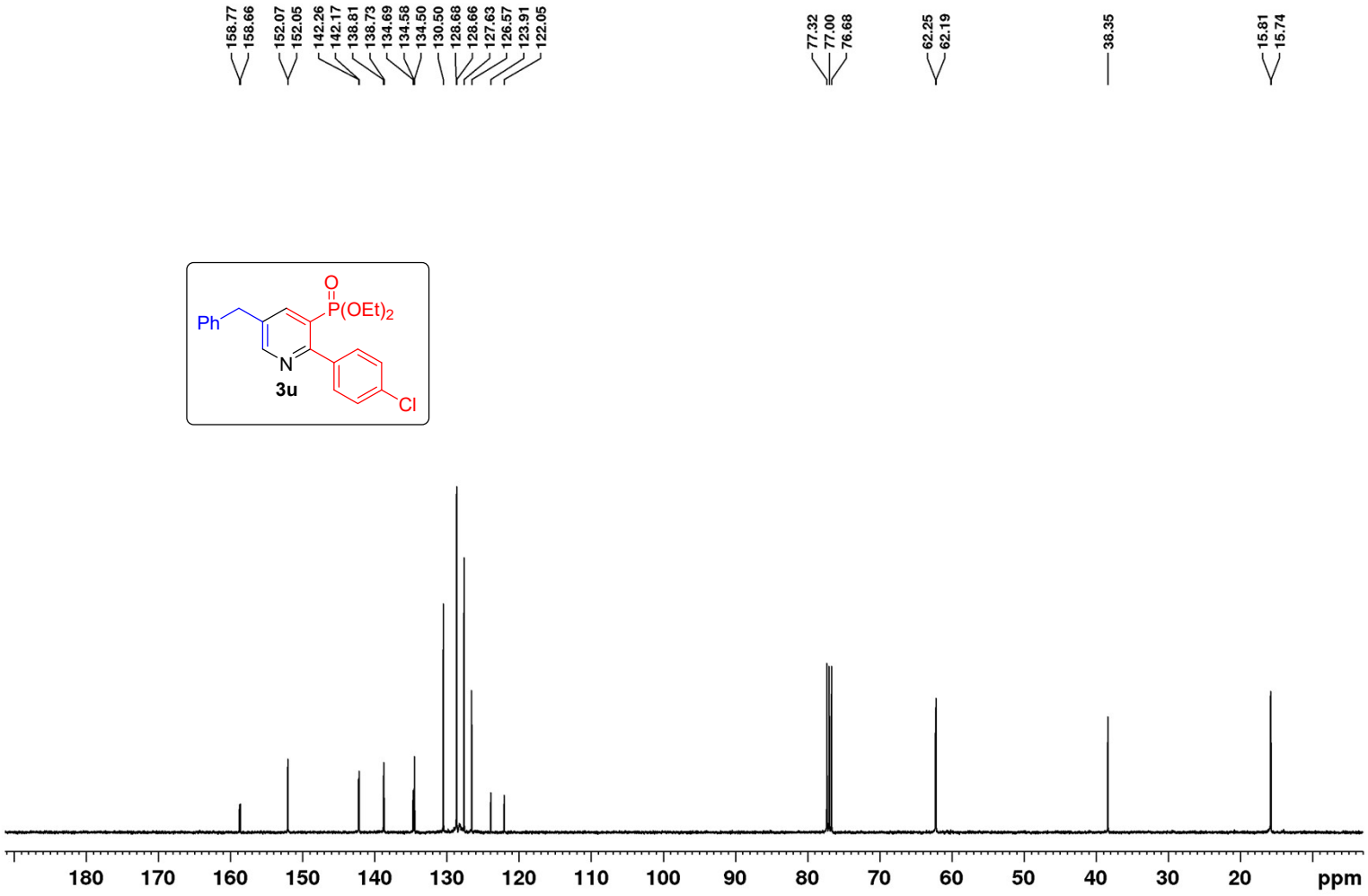
$^{31}P\{^{1}H\}$ NMR of compound **3t** (162MHz/CDCl3)



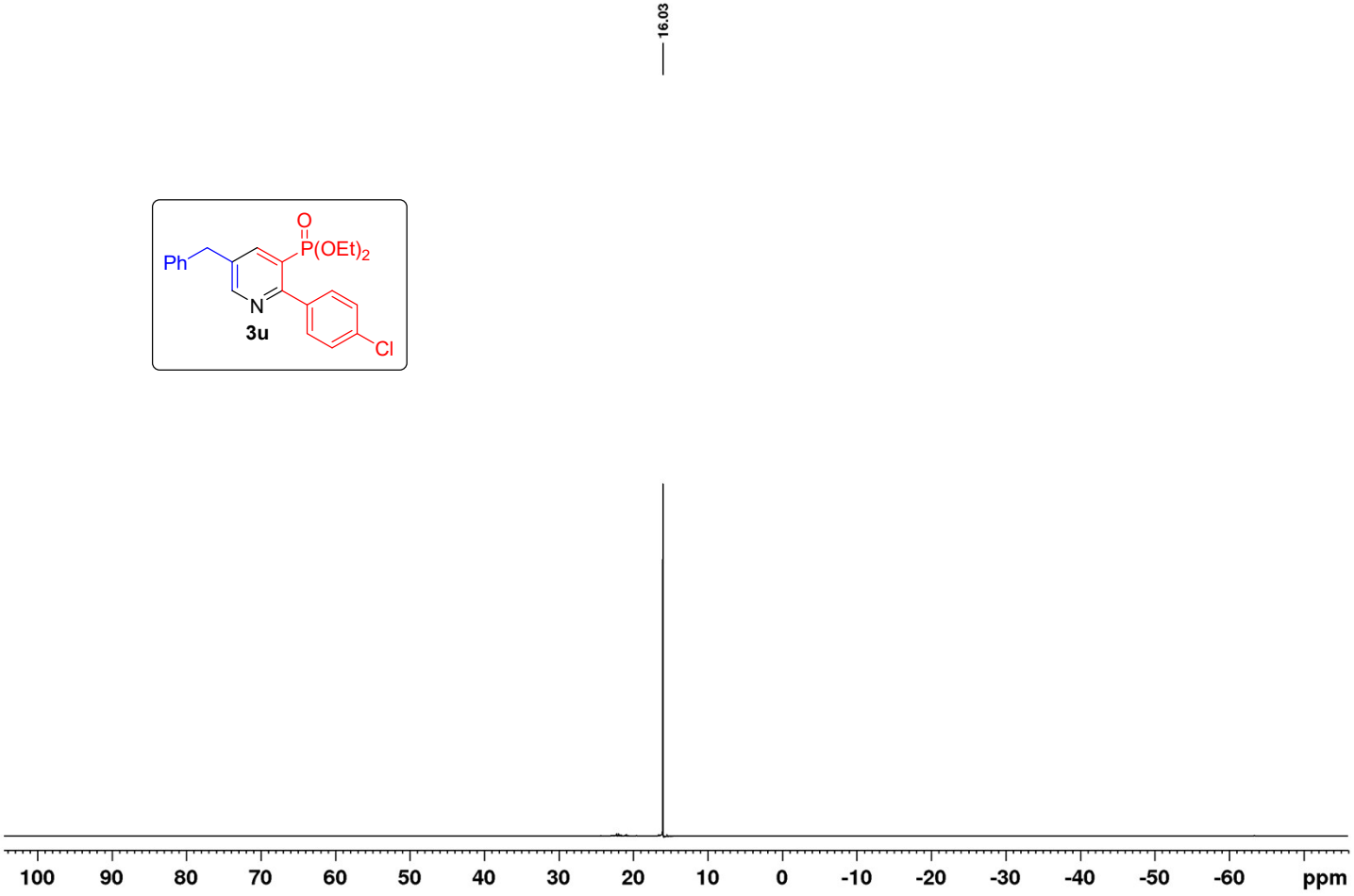
^{1}H NMR of compound **3u** (400 MHz/$CDCl_3$)



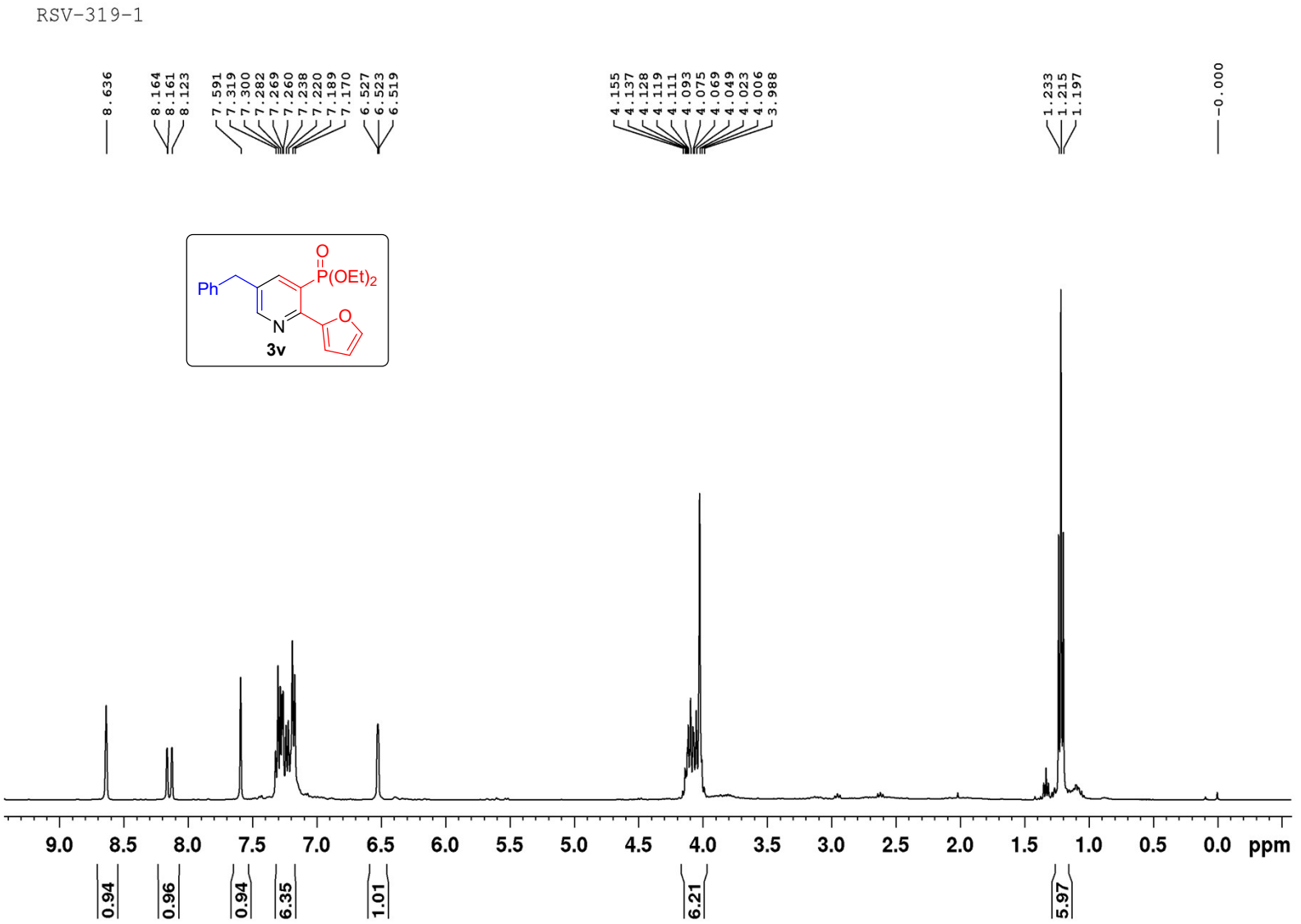
$^{13}C\{^{1}H\}$ NMR of compound **3u** (100MHz/$CDCl_3$)



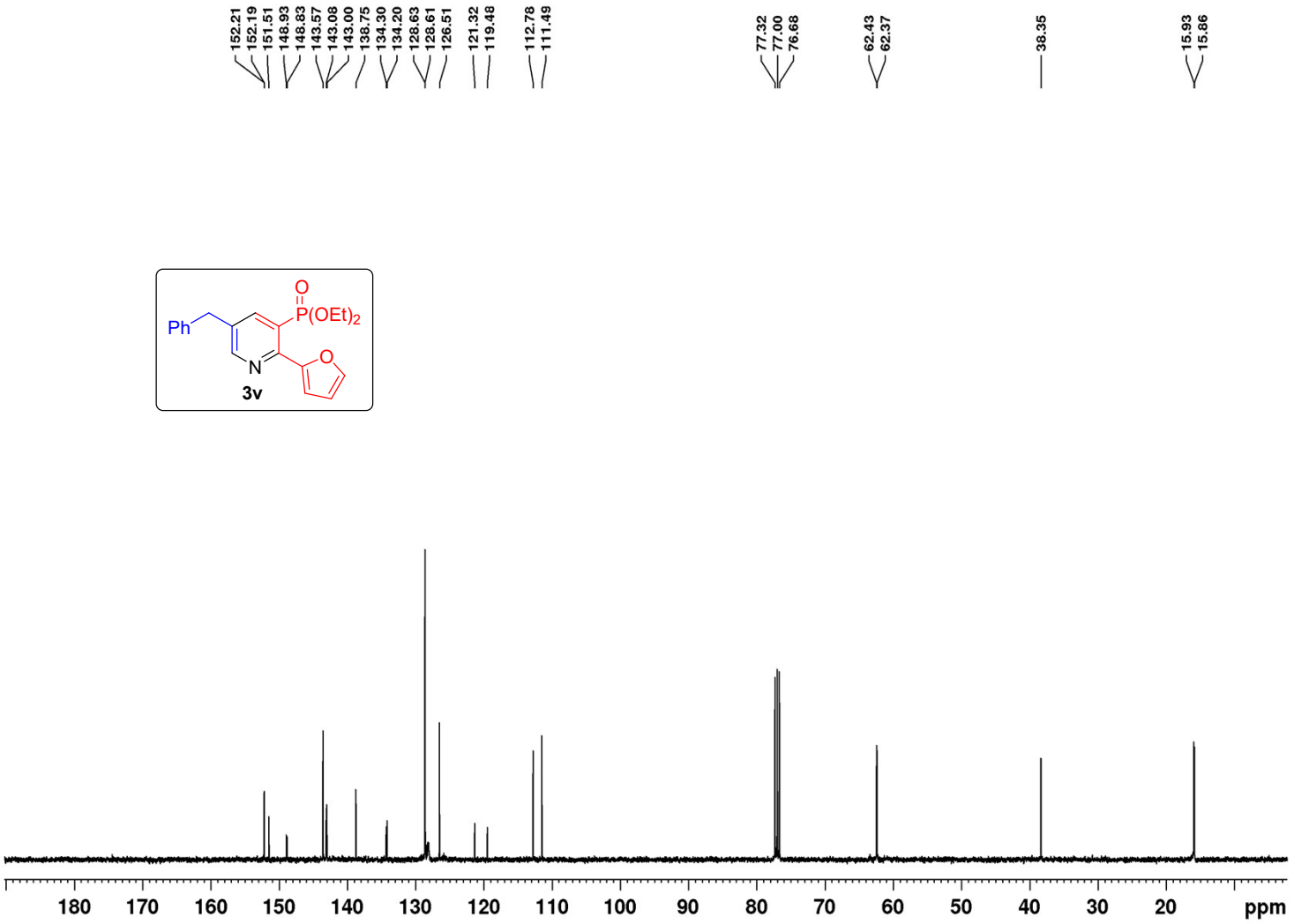
$^{31}P\{^{1}H\}$ NMR of compound **3u** ($162MHz/CDCl_3$)



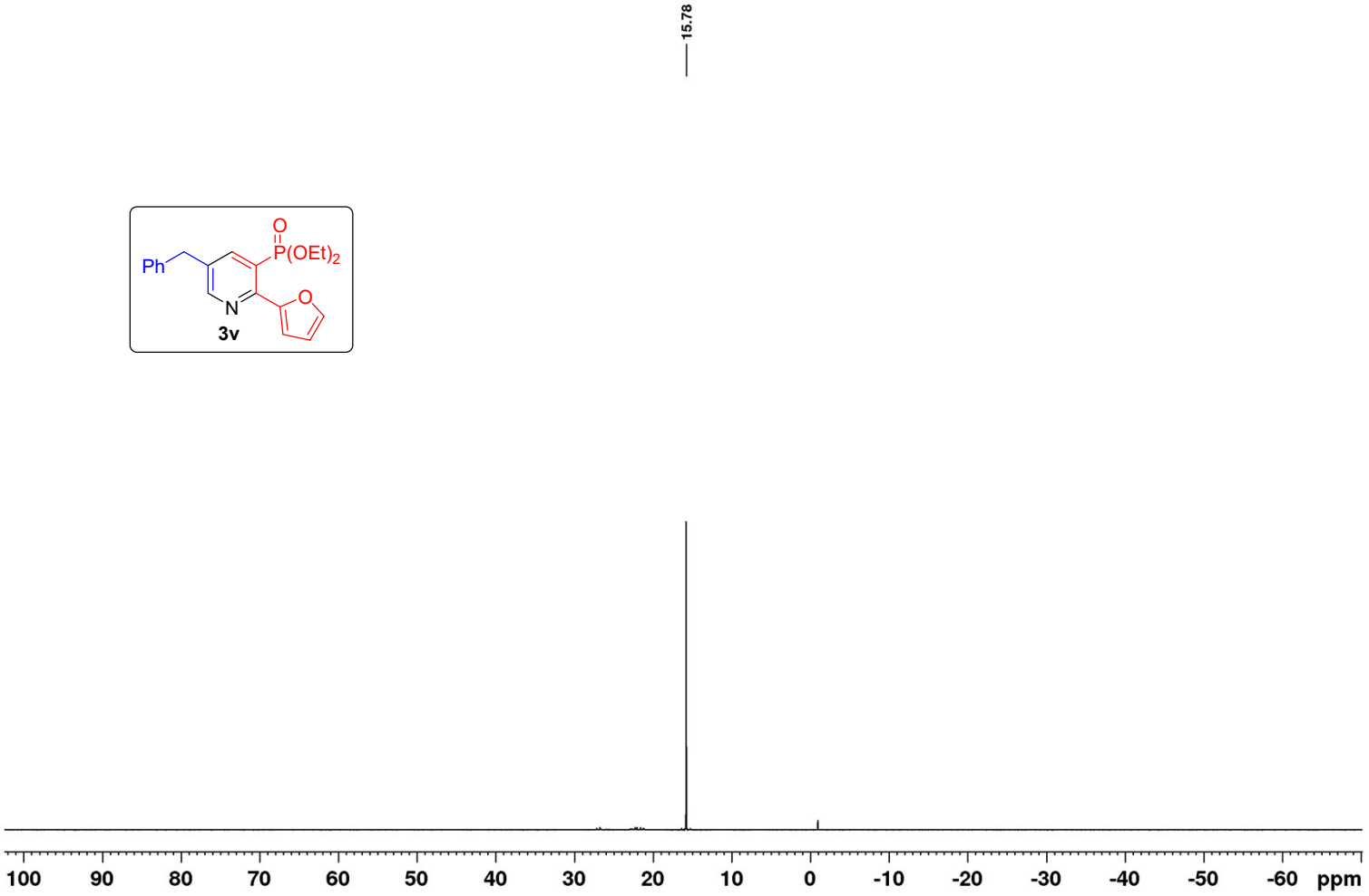
^{1}H NMR of compound **3v** (400 MHz/$CDCl_3$)



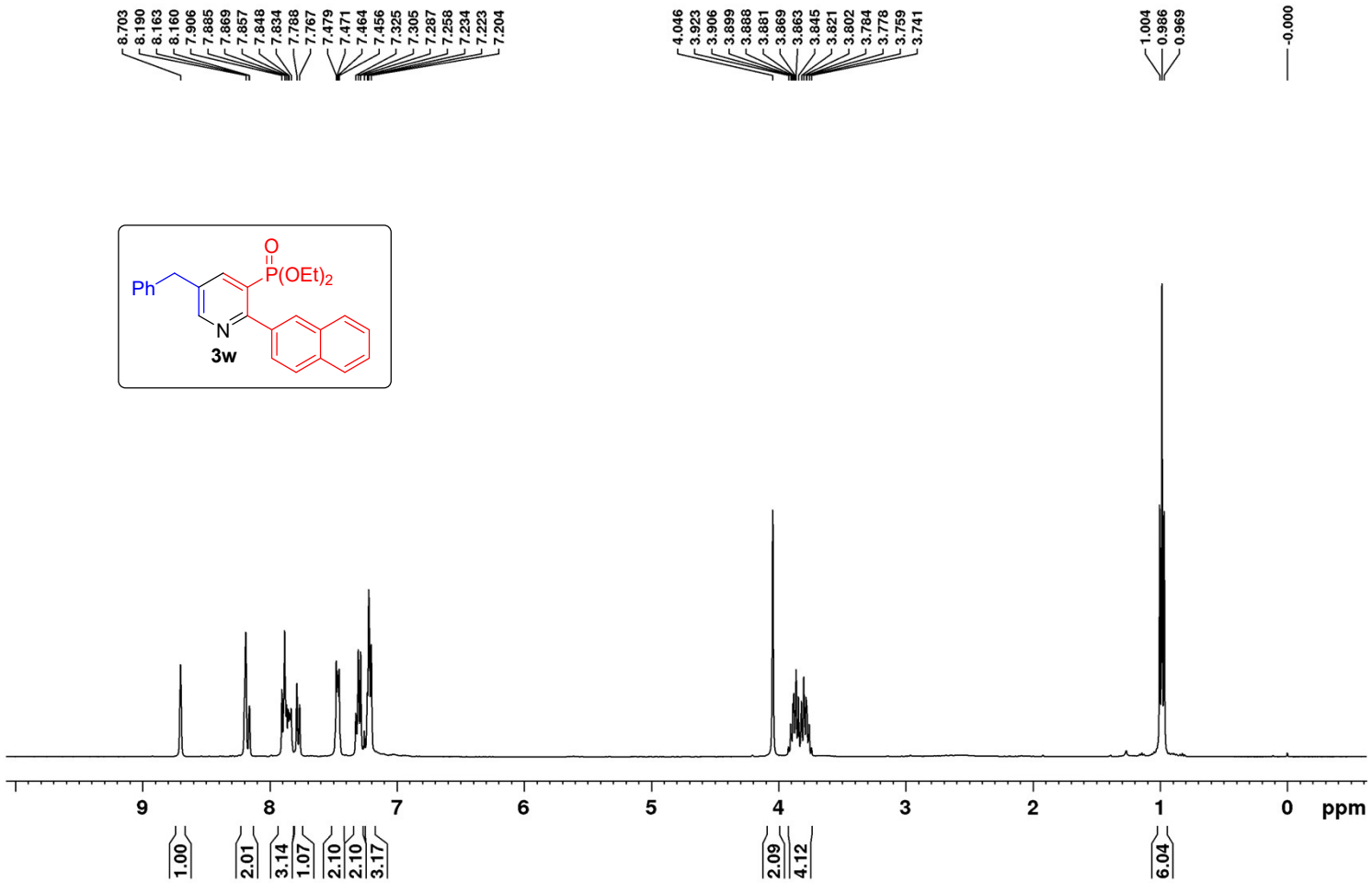
$^{13}C\{^{1}H\}$ NMR of compound **3v** (100MHz/$CDCl_3$)



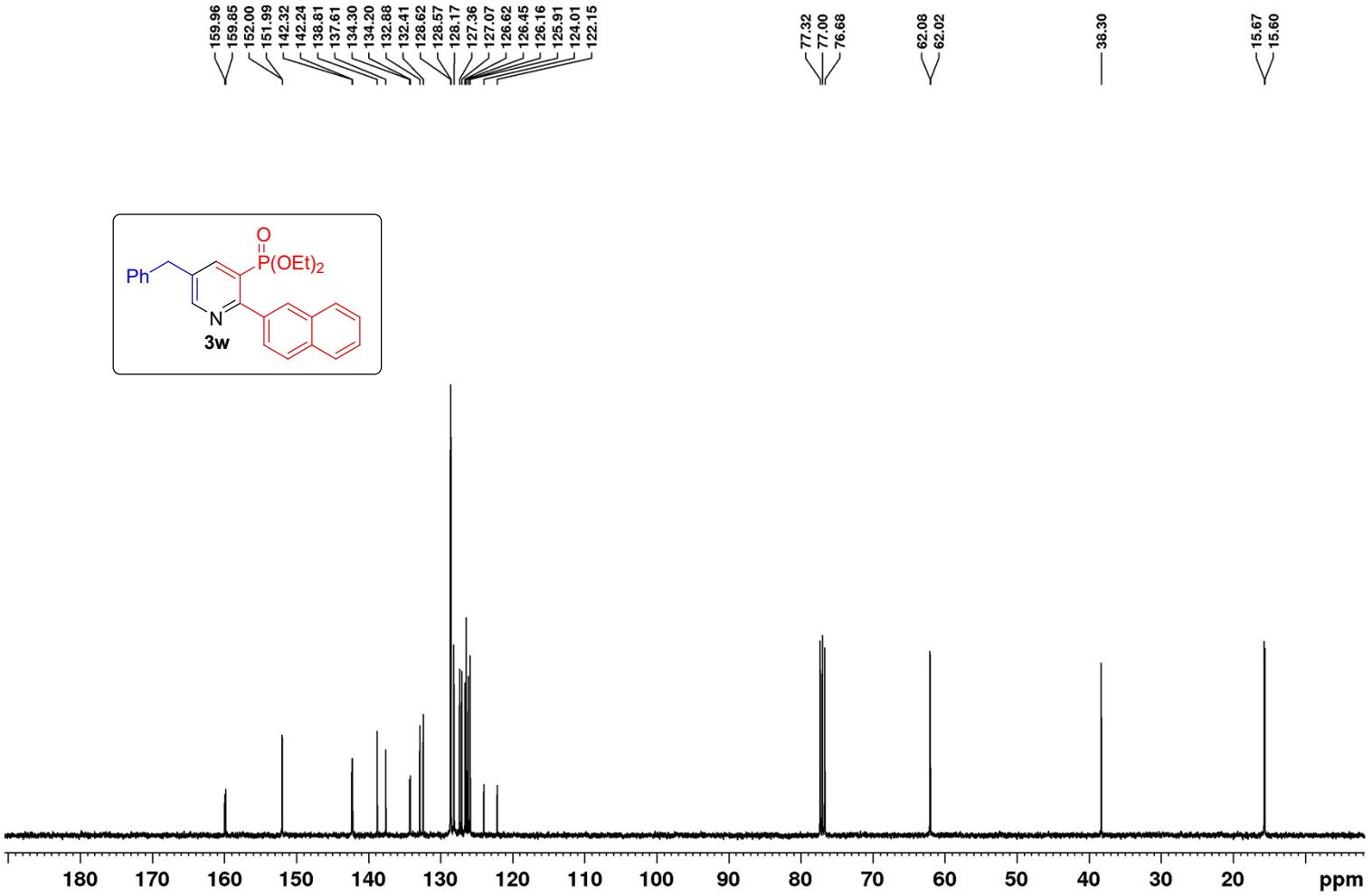
$^{31}P\{^{1}H\}$ NMR of compound **3v** ($162MHz/CDCl_3$)



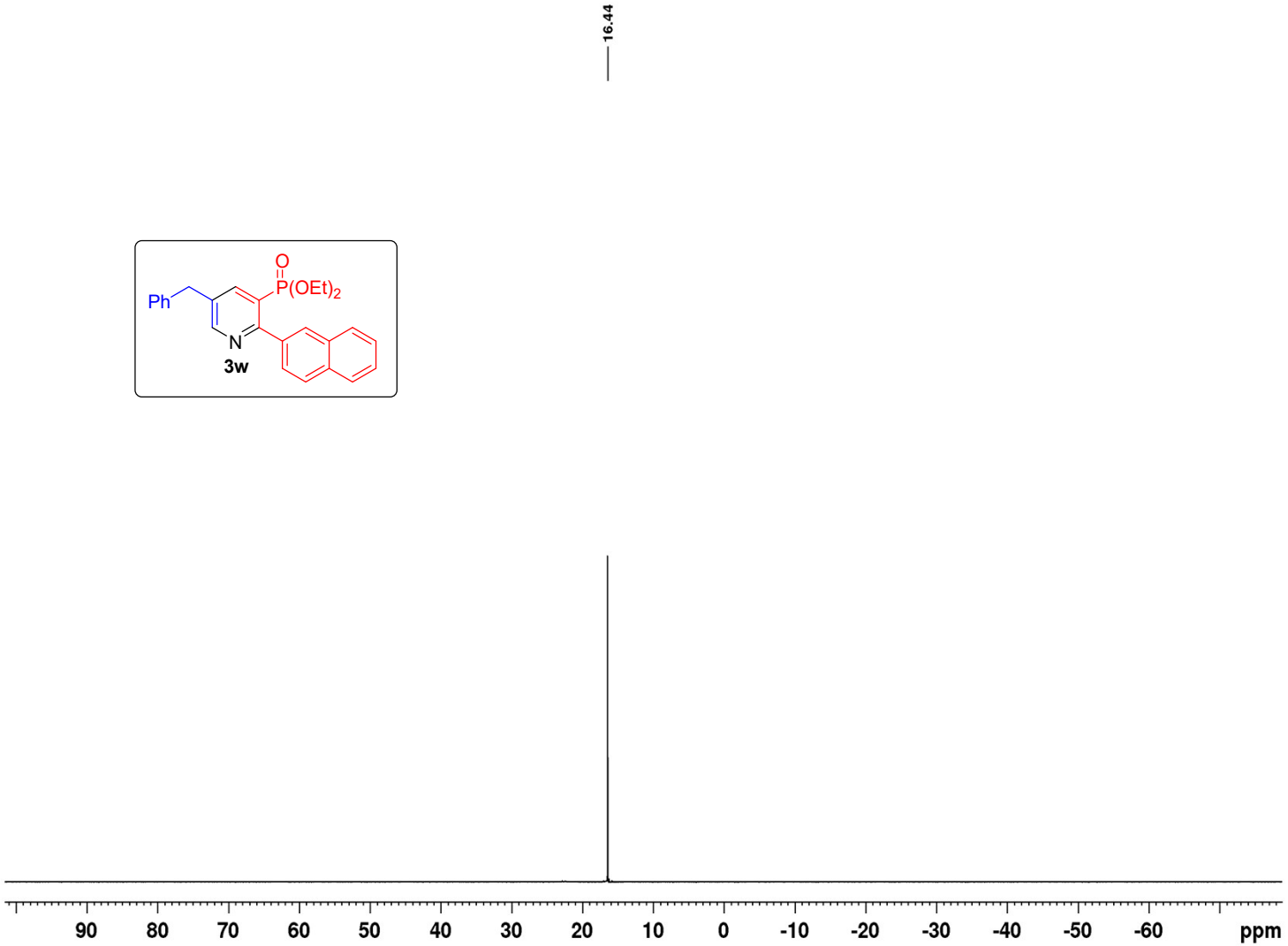
^{1}H NMR of compound **3w** (400 MHz/$CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of compound **3w** (100MHz/$CDCl_3$)

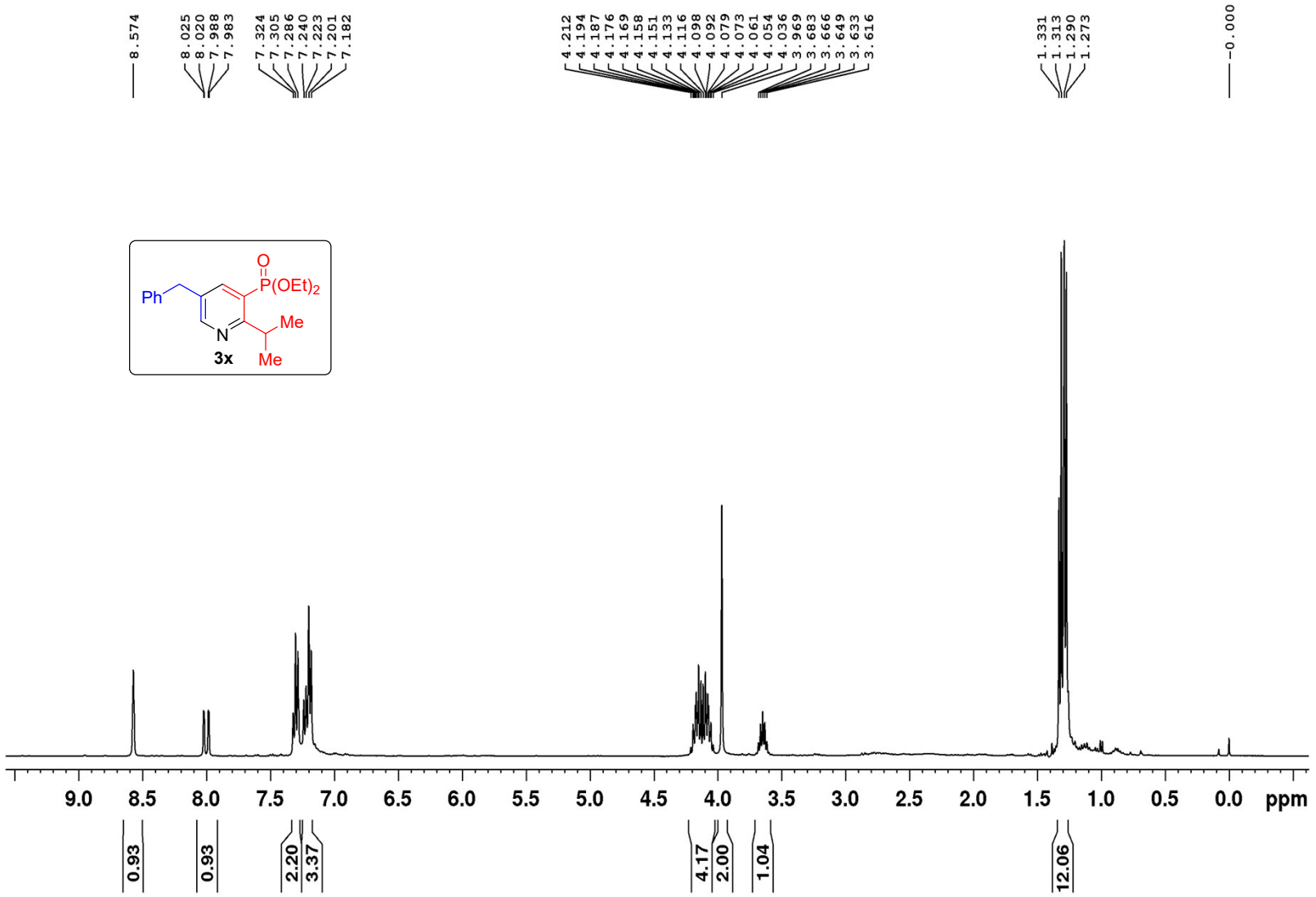


$^{31}P\{^{1}H\}$ NMR of compound **3w** ($162MHz/CDCl_3$)

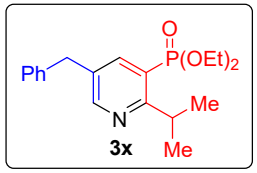


^{1}H NMR of compound **3x** (400 MHz/$CDCl_3$)

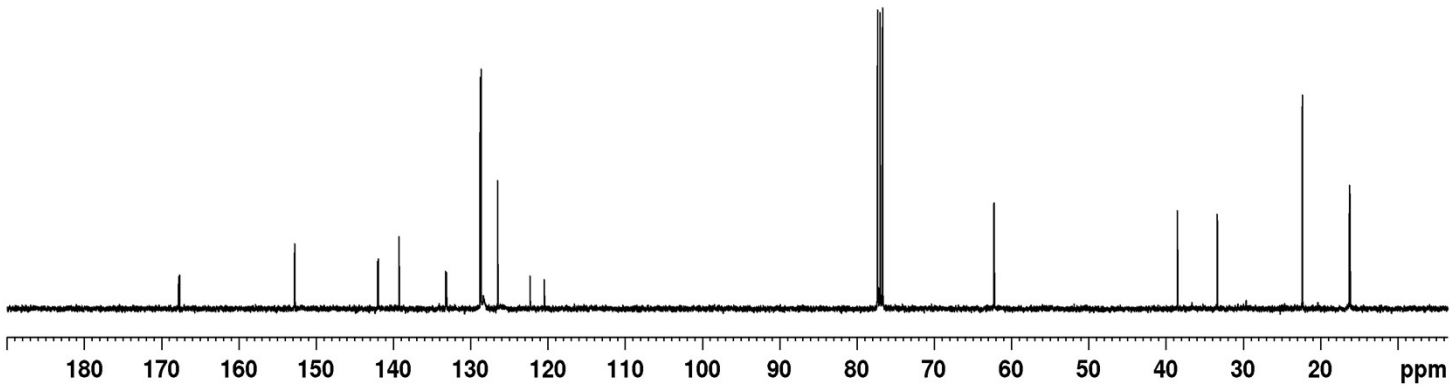
RSV-312-2



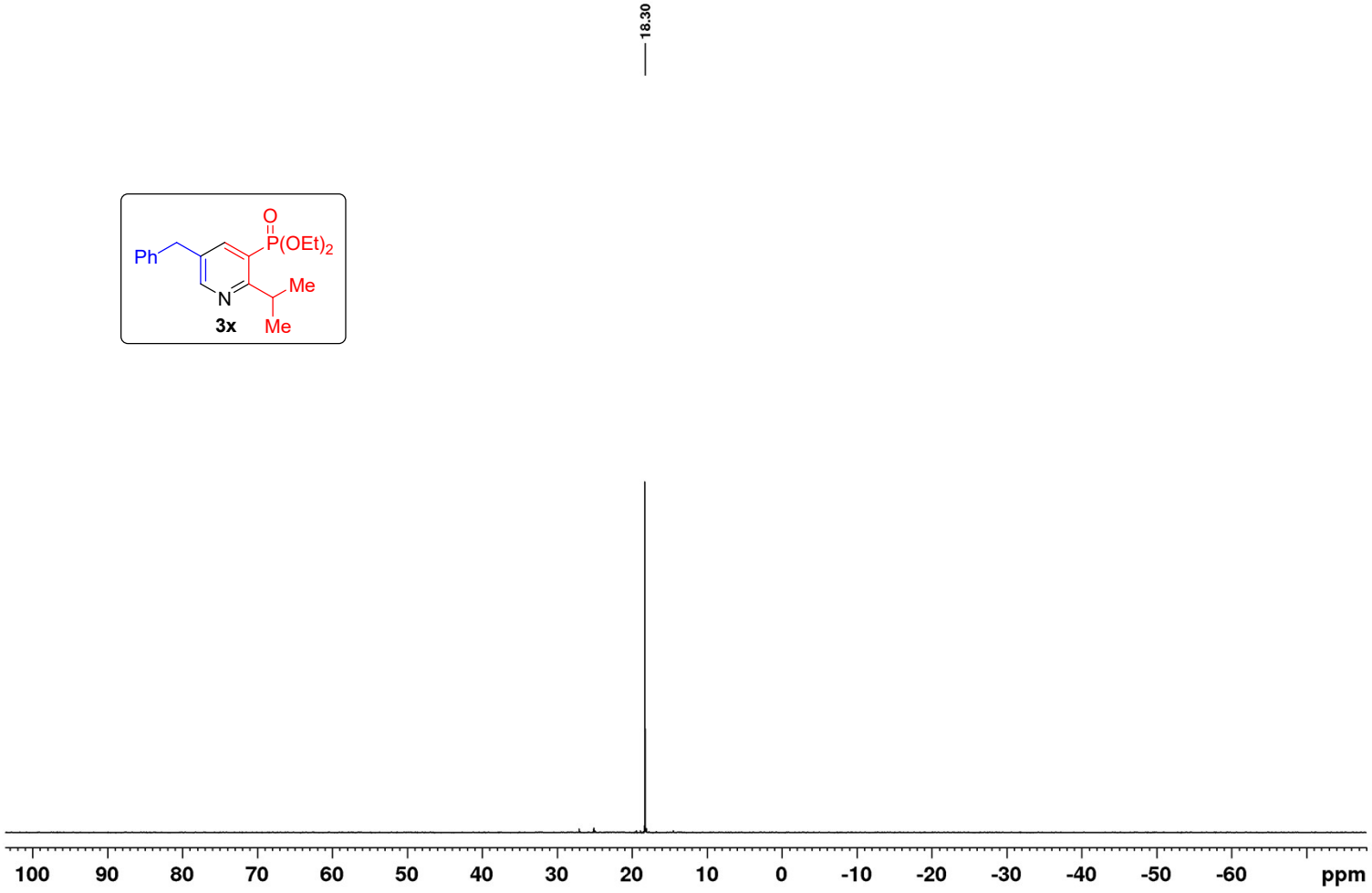
$^{13}C\{^{1}H\}$ NMR of compound **3x** (100MHz/$CDCl_3$)



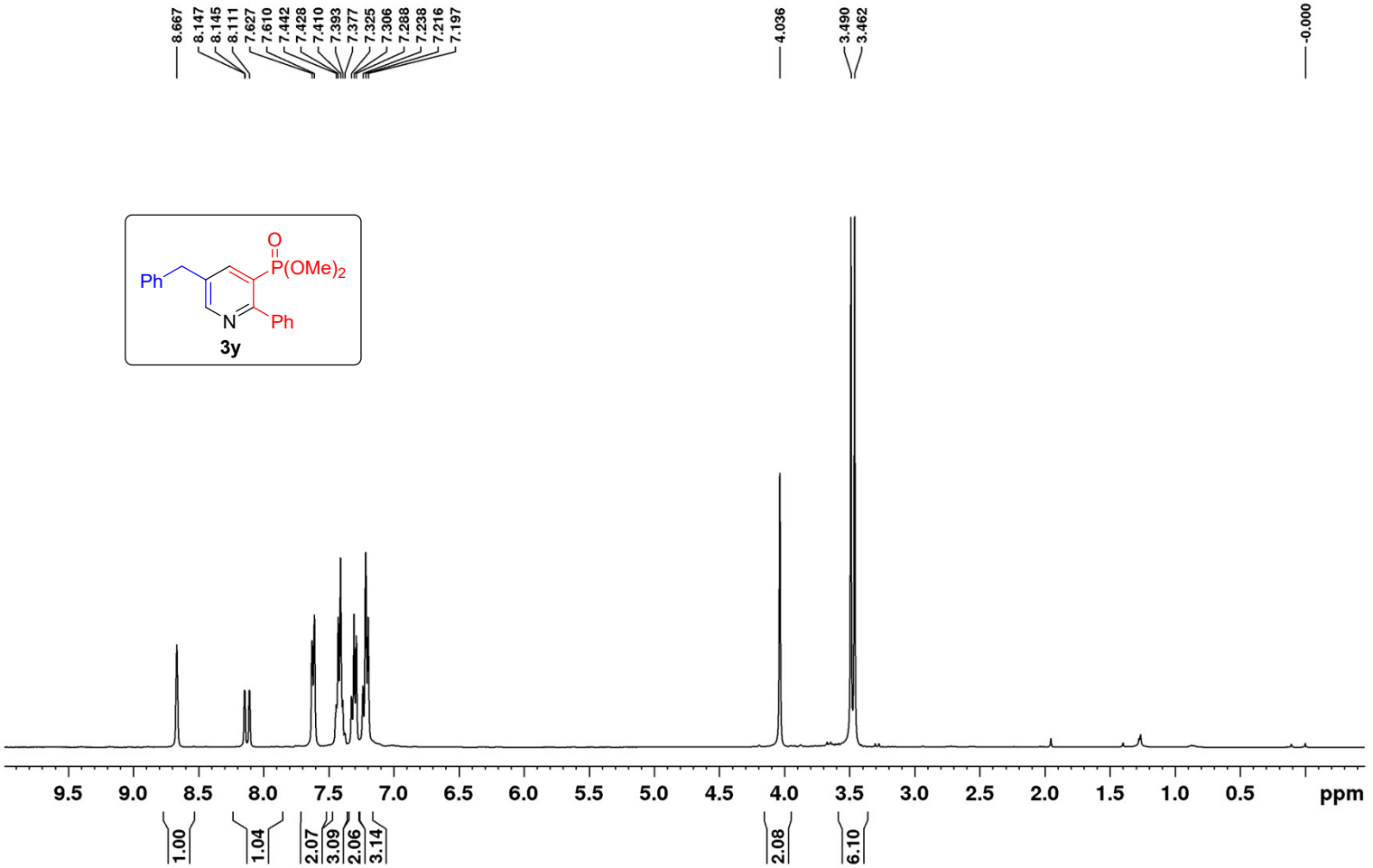
3x



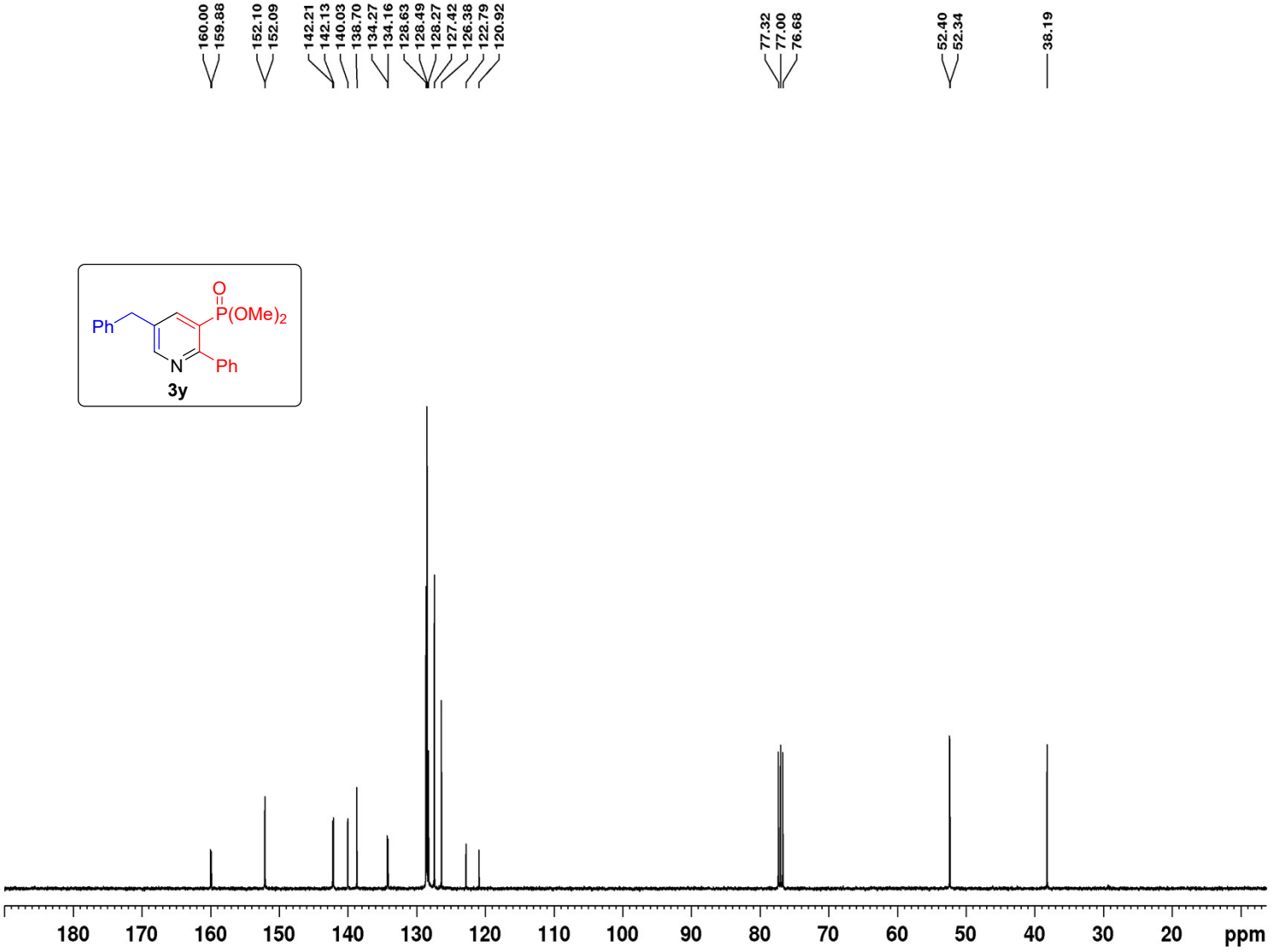
$^{31}P\{^{1}H\}$ NMR of compound **3x** (162MHz/$CDCl_3$)



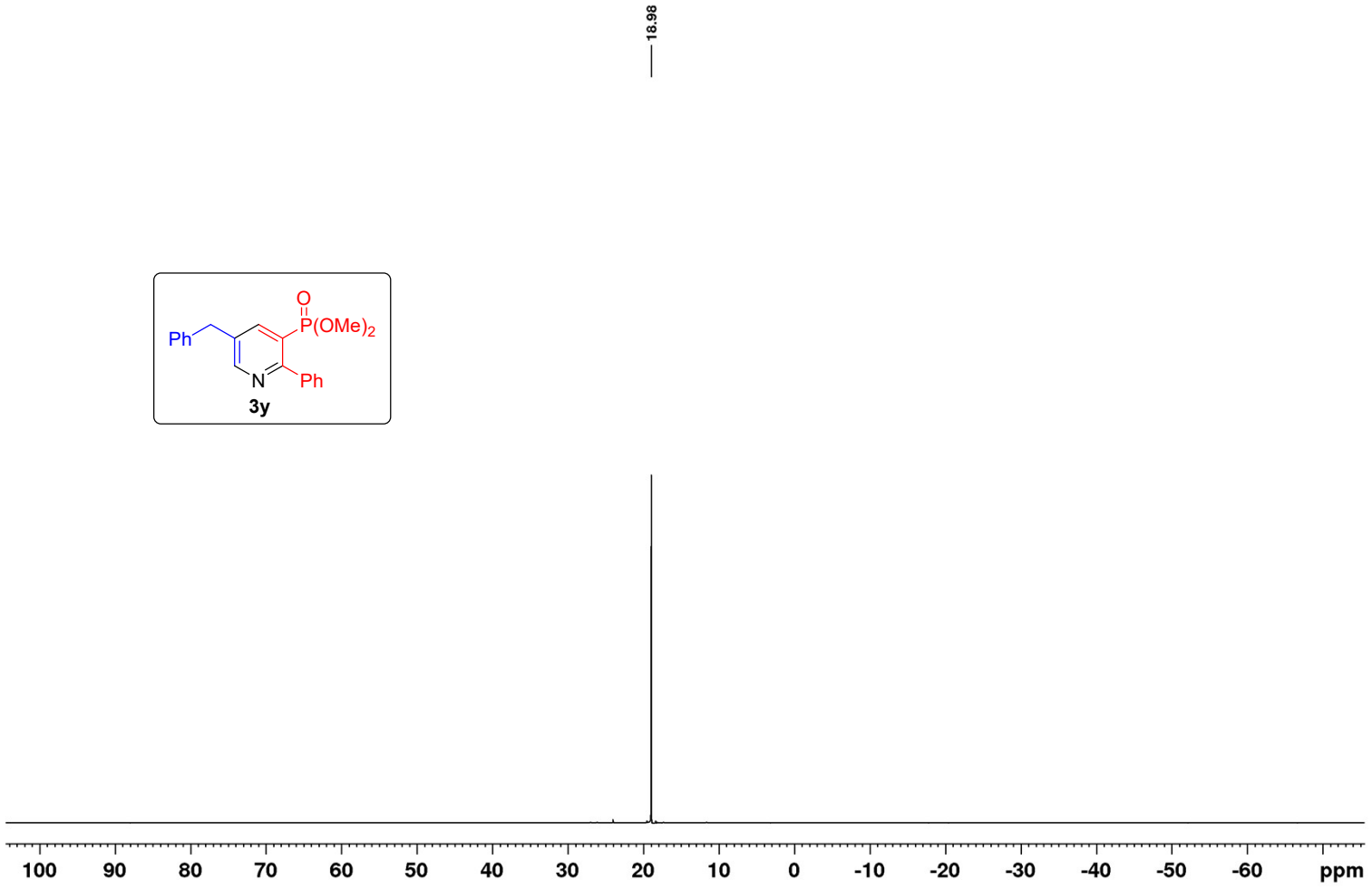
^{1}H NMR of compound **3y** (400 MHz/$CDCl_3$)



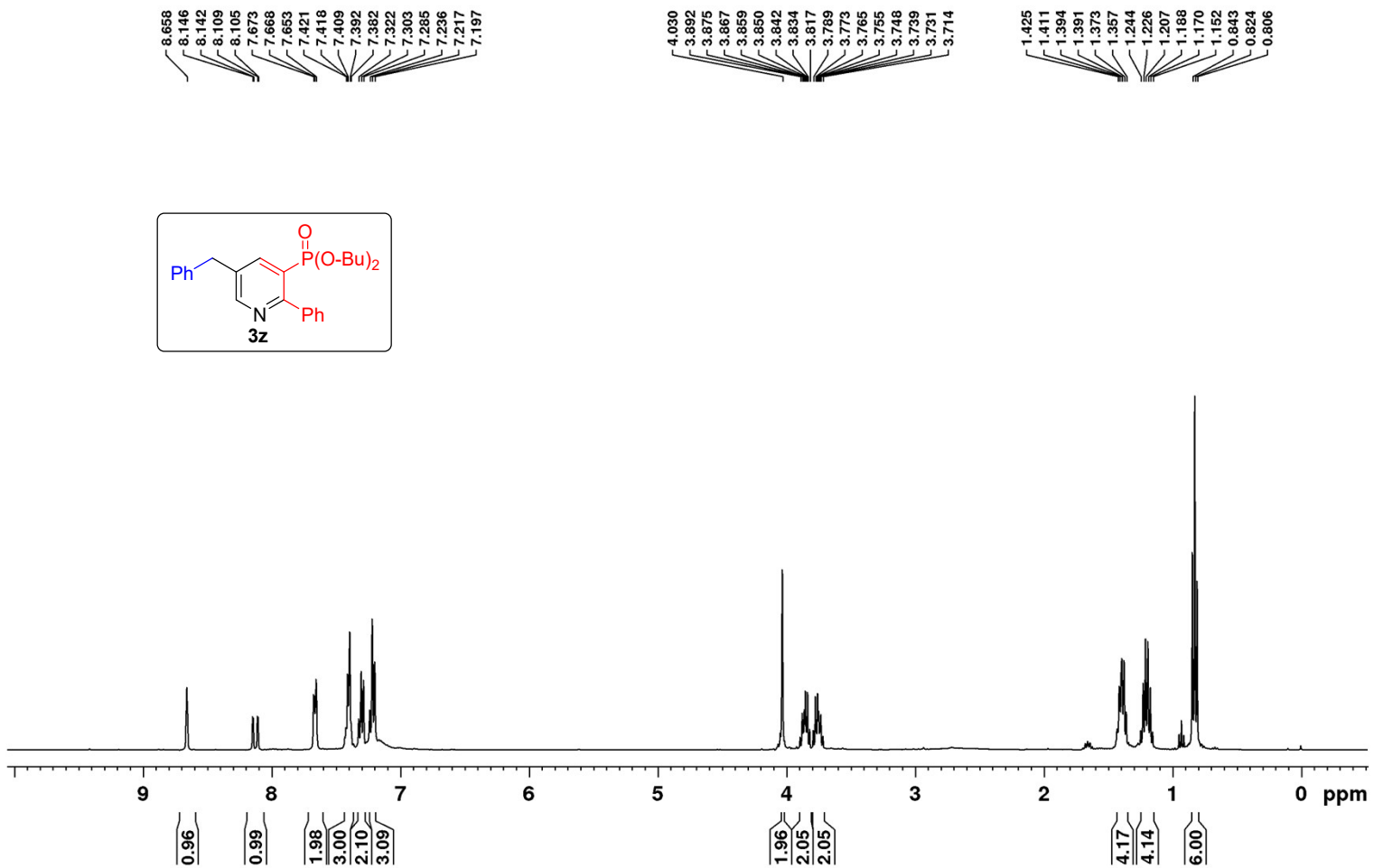
$^{13}C\{^{1}H\}$ NMR of compound **3y** (100MHz/$CDCl_3$)



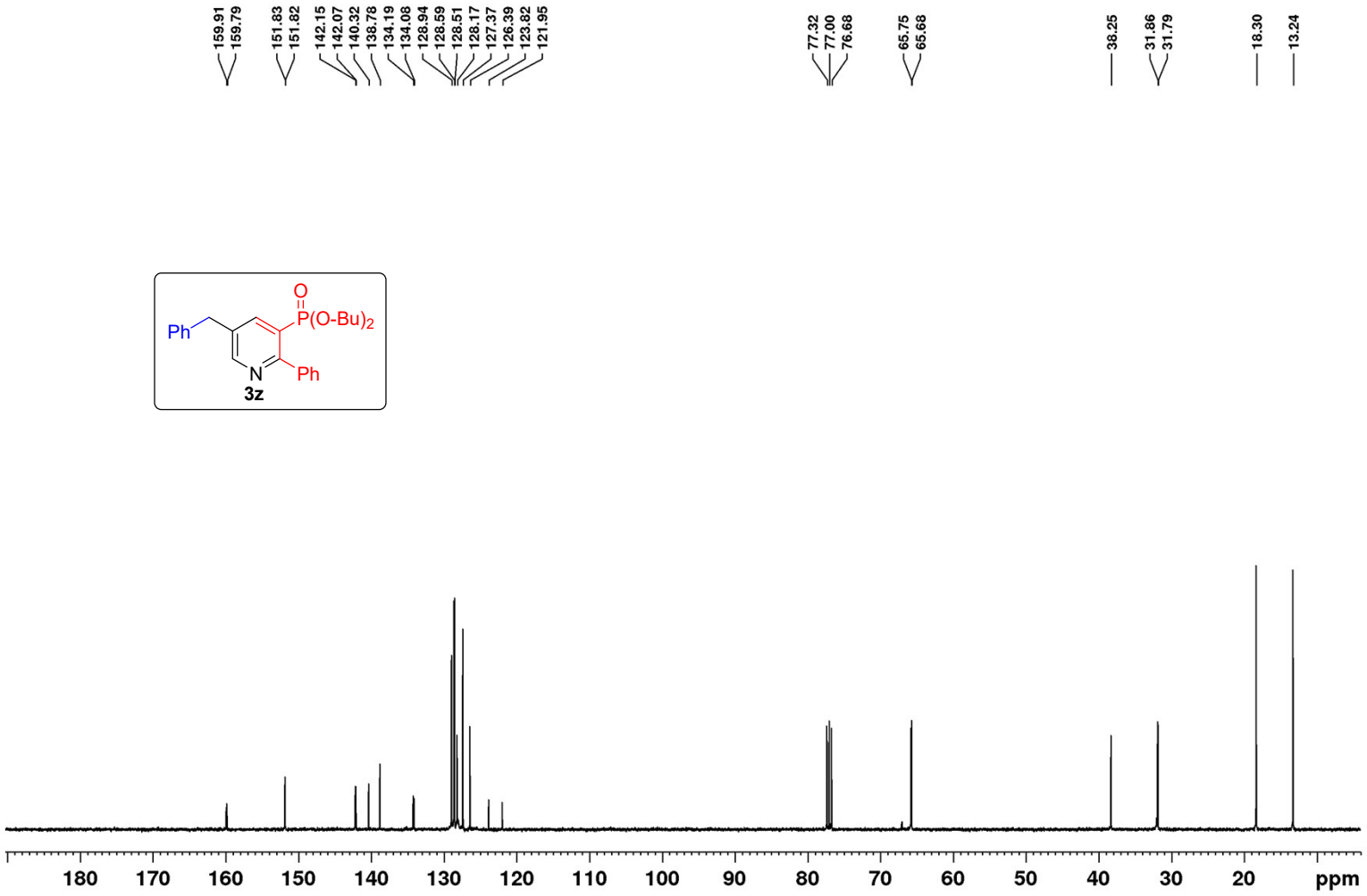
$^{31}P\{^{1}H\}$ NMR of compound **3y** ($162MHz/CDCl_3$)



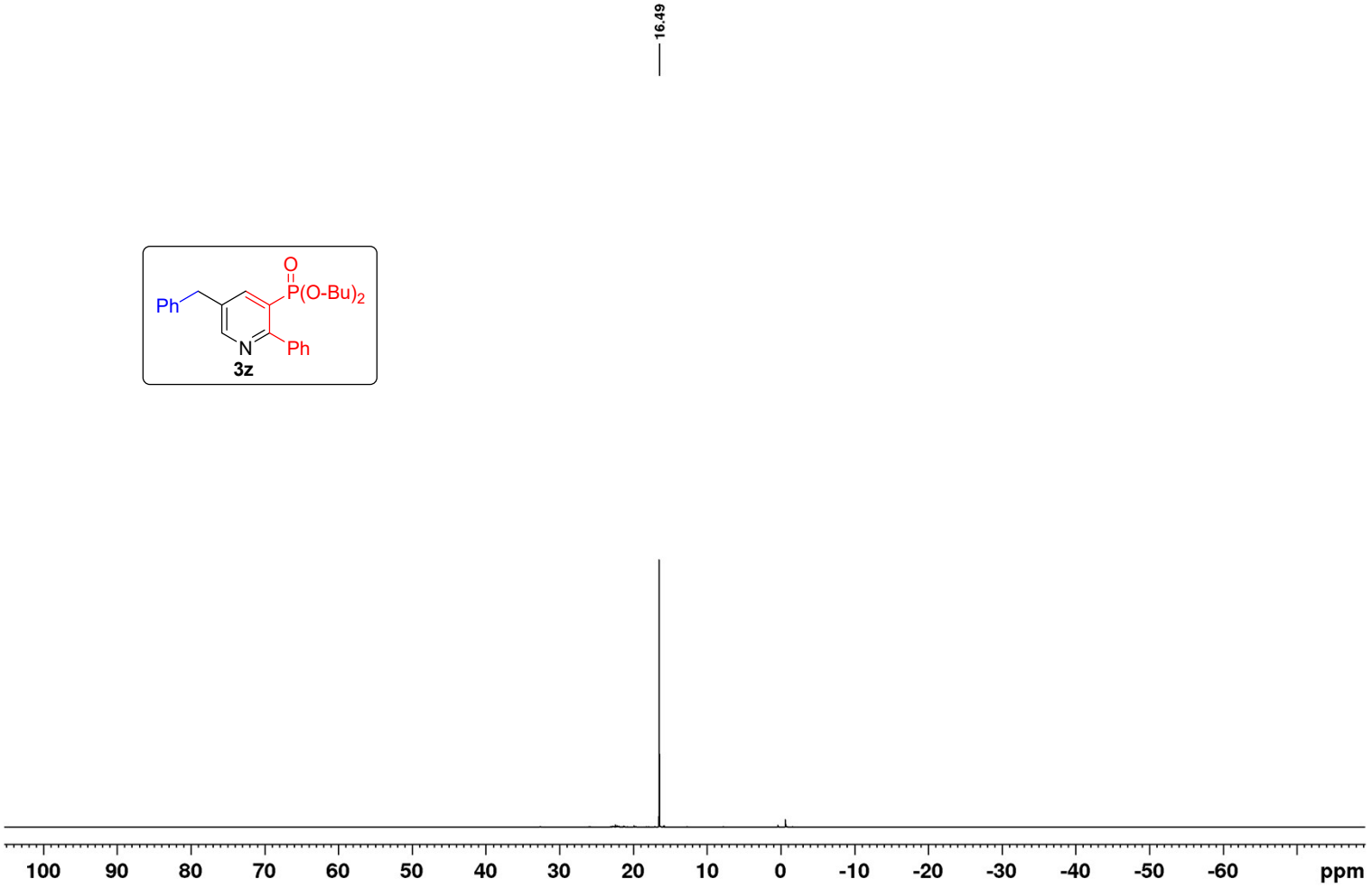
^{1}H NMR of compound **3z** (400 MHz/$CDCl_3$)



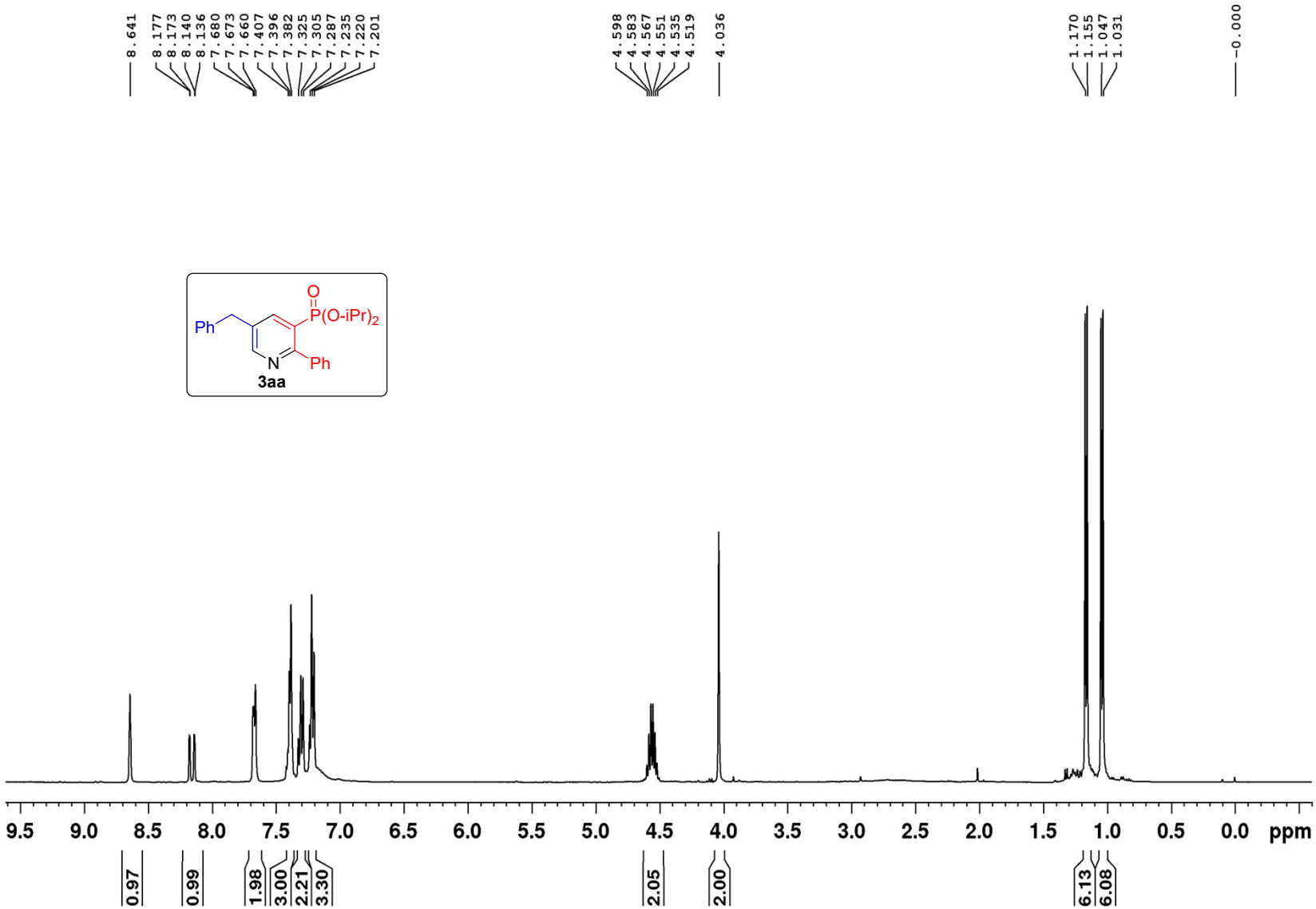
$^{13}C\{^{1}H\}$ NMR of compound **3z** (100MHz/$CDCl_3$)



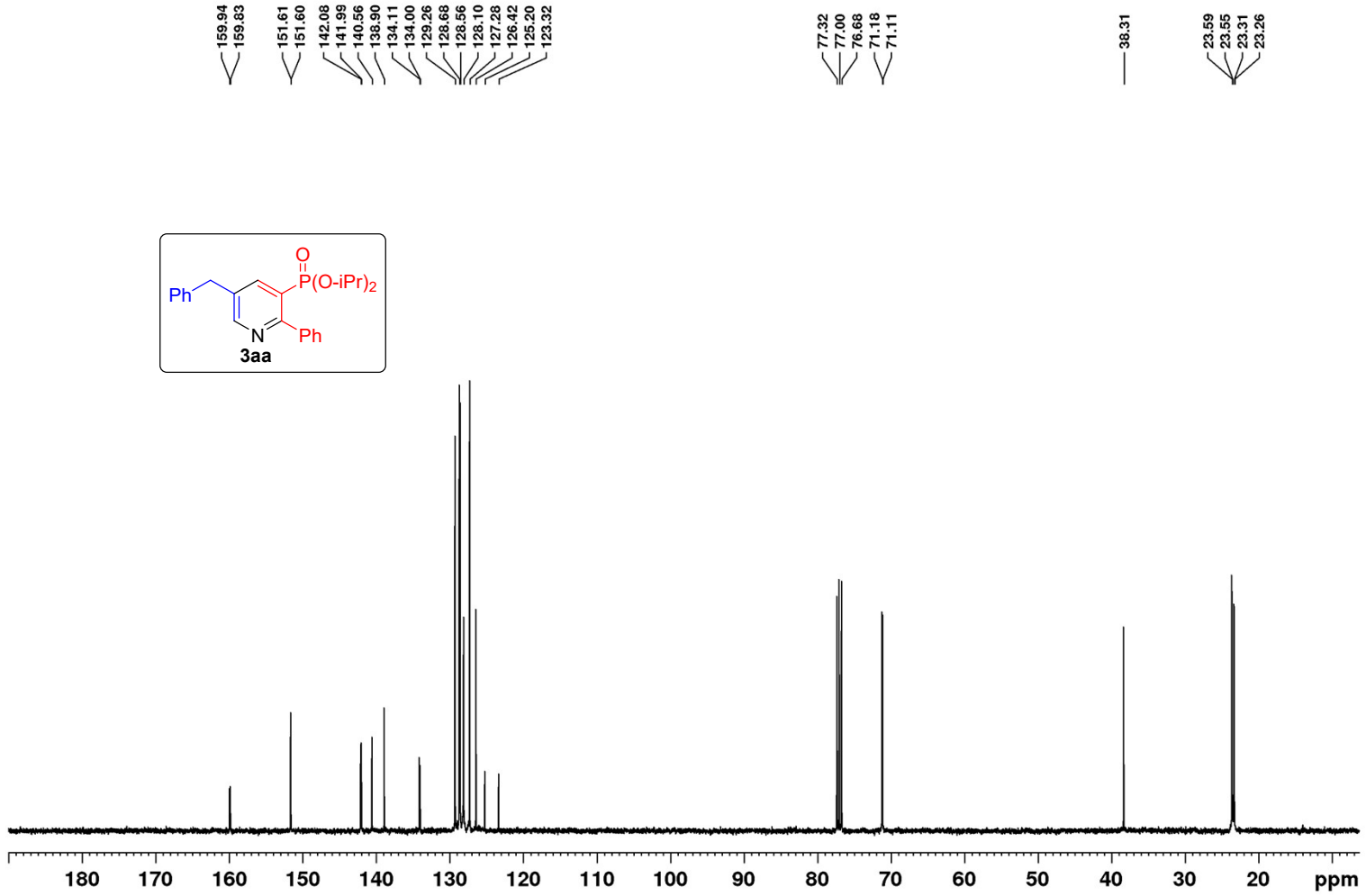
$^{31}P\{^{1}H\}$ NMR of compound **3z** ($162MHz/CDCl_3$)



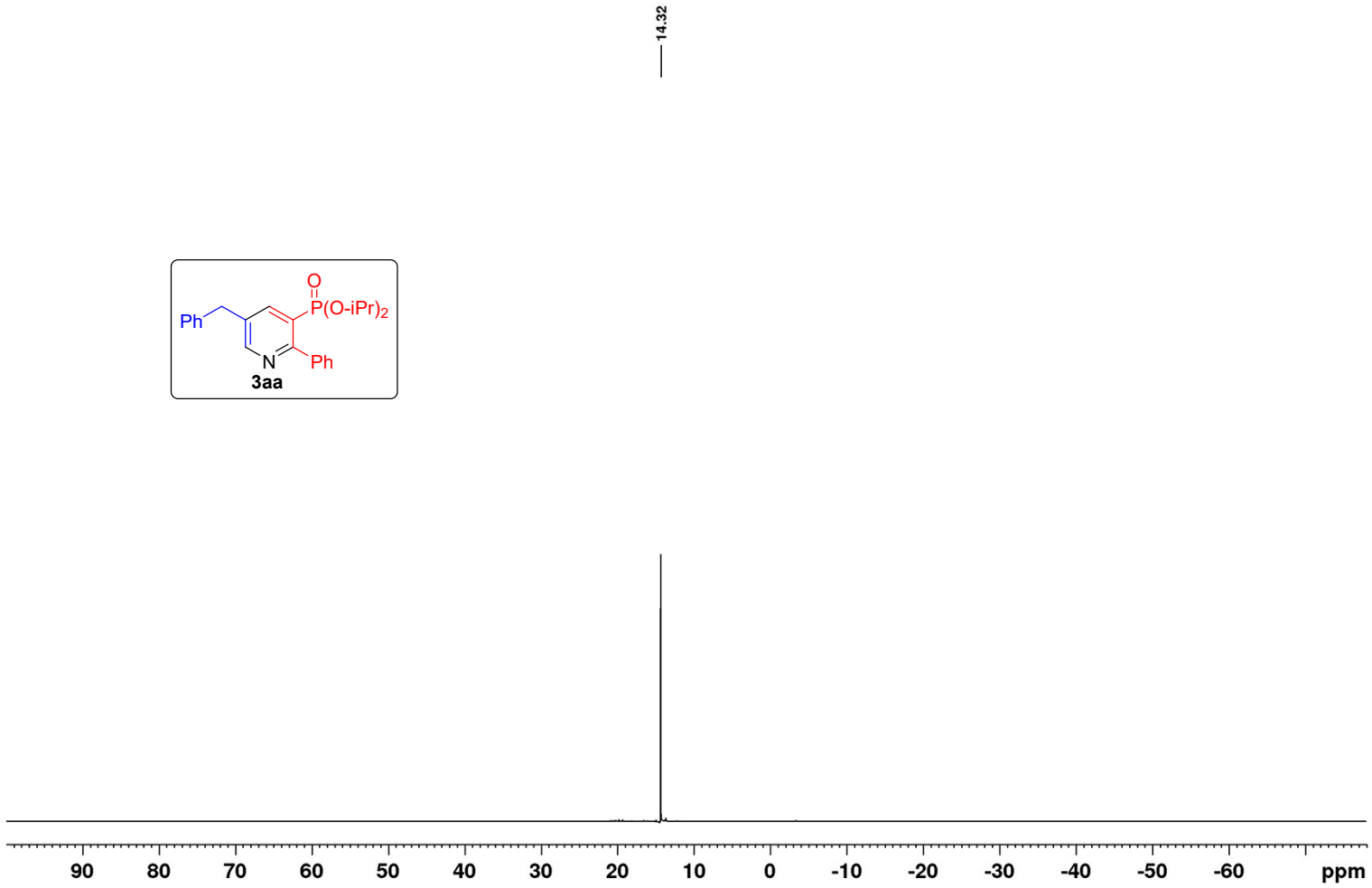
^{1}H NMR of compound **3aa** (400 MHz/$CDCl_3$)



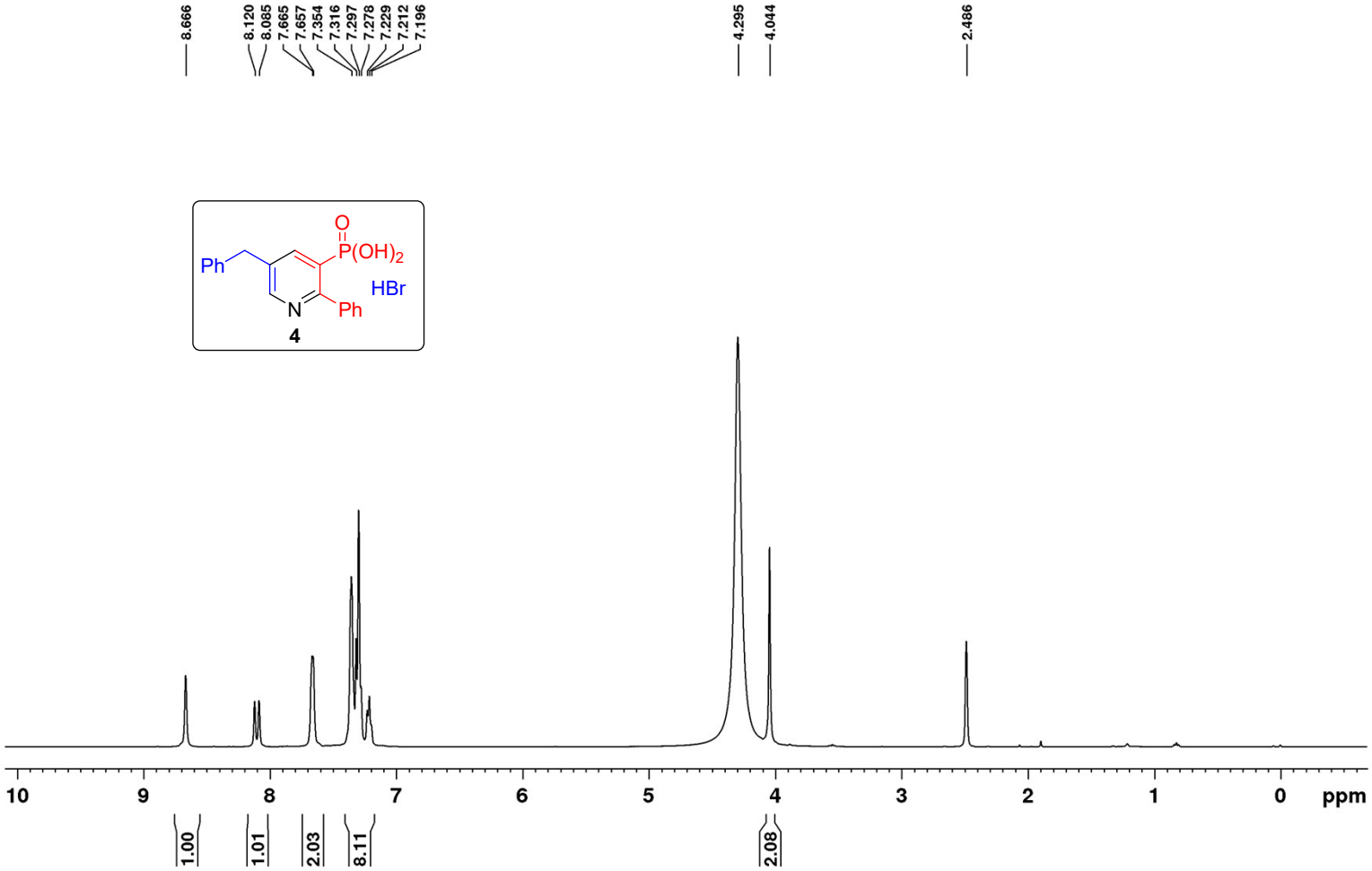
$^{13}C\{^{1}H\}$ NMR of compound **3aa** (100MHz/$CDCL_3$)



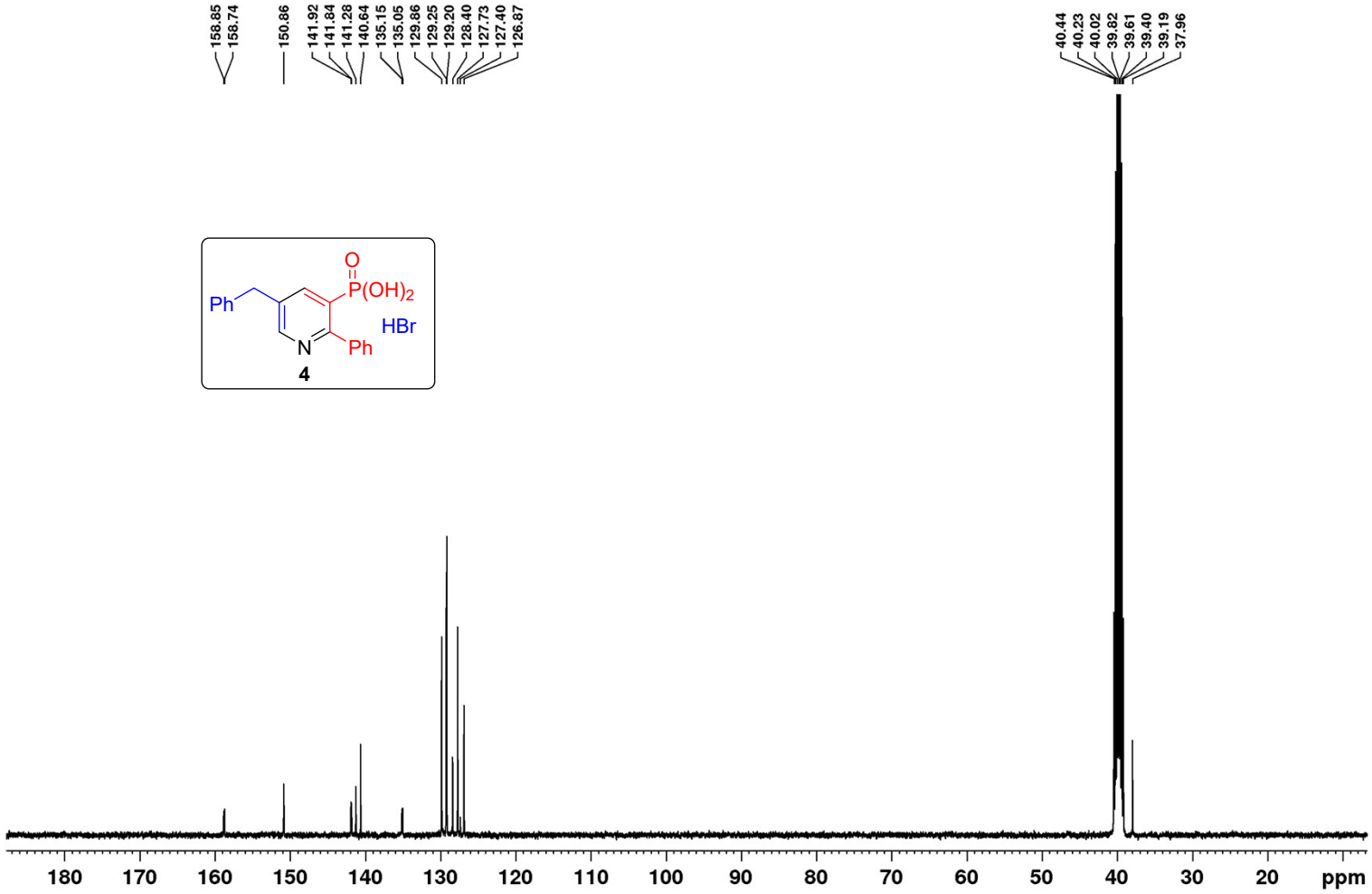
$^{31}P\{^{1}H\}$ NMR of compound **3aa** (162MHz/$CDCl_3$)



^{1}H NMR of compound **4** (400MHz/ DMSO-d_6)



$^{13}C\{^{1}H\}$ NMR of compound **4** (100MHz/ DMSO-d_6)



$^{31}P\{^{1}H\}$ NMR of compound **4** (162MHz/ DMSO-d_6)