*Supporting Information*

# Rh-Catalyzed Asymmetric Hydrogenation of α- and β-Enamido Phosphonates: Highly Enantioselective Access to Amino Phosphonic Acids

Hong-Quan Du[a,b]*

[a]Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China
[b]University of Chinese Academy of Sciences, Beijing 100049, China
E-mail: dhquan@dicp.ac.cn

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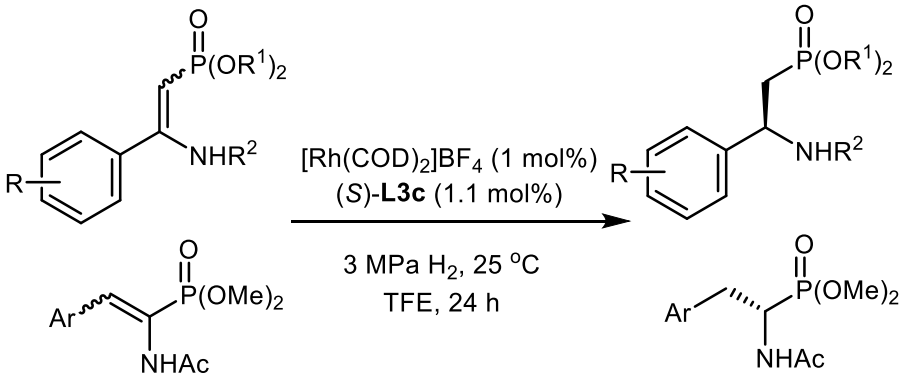
## I. General Information

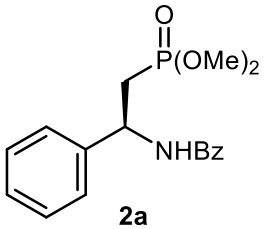
All reactions were carried out under a nitrogen atmosphere. Solvents were purified by standard procedure before use. Commercial reagents were used without further purification. Flash chromatography was performed on silica gel 60 (40-63μm, 60Å). Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 with F254 indicator. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on a Bruker 400 MHz spectrometer. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$= δ 7.26). Carbon nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded on a Bruker 100 MHz spectrometer. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.07). Phosphorus nuclear magnetic resonance ($^{31}$P NMR) spectra were recorded on a Bruker 162 MHz spectrometer. Chemical shifts for phosphorus are reported in parts per million downfield from the external 85% $H_3PO_4$ signal at 0.0 ppm as a standard. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t= triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz) integration. Enantiomeric ratios were determined by chiral HPLC with *n*-hexane and *i*-PrOH as solvents. Optical rotations were recorded on a JASCO P-1020 polarimeter. ESI HRMS spectra were recorded on Bio TOFQ. Conversions were determined by GC. β-enamido phosphonates[1-4] and β-substituted α-enamido phosphonates[5] were prepared according to the literatures.

## II. General Procedure for Asymmetric Hydrogenation of the Substrates



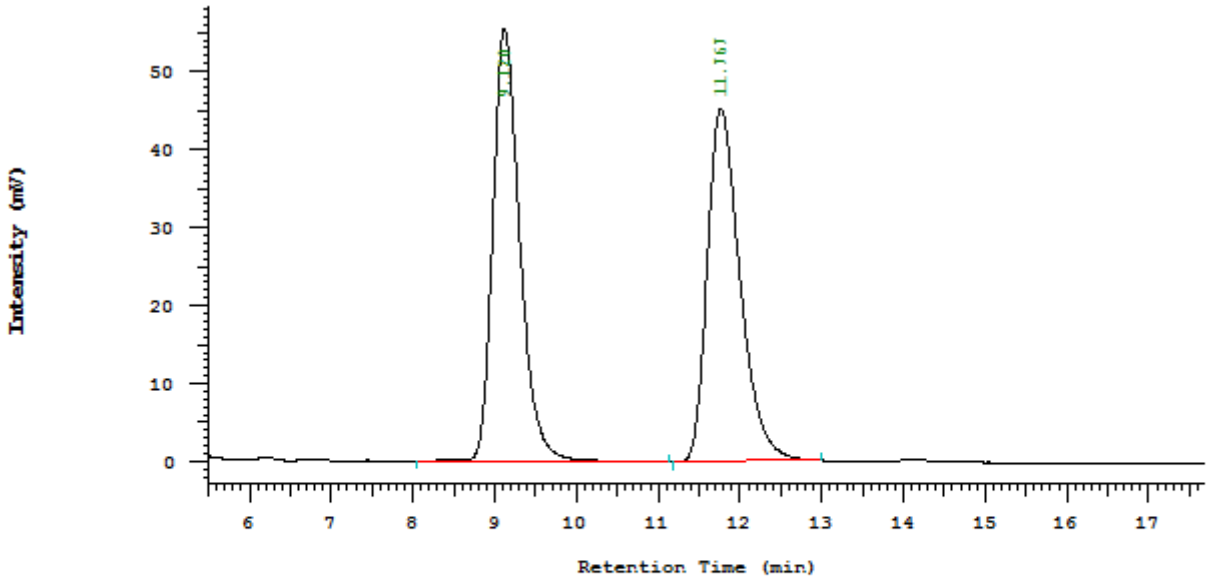

In a nitrogen-filled glovebox, a stainless steel autoclave was charged with $[Rh(COD)_2]BF_4$ (0.00125mmol, 0.01 equiv), (S)-**L3c** (0.001375mmol, 0.011 equiv) in 1.0 mL of a degassed TFE. After stirring for 60 min at room temperature, the reaction mixture was added to a mixture of the substrate (**1a-l, 3a-j**) (0.125 mmol, 1 equiv) in 1.0 mL of the same solvent, and the hydrogenation was performed at 25 ℃ under H2 pressure of 3 MPa for 24 h. The solvent was then evaporated, and the residue was purified by flash

column chromatography to give the corresponding hydrogenation product (**2a-l, 4a-j**).




**2a**

**dimethyl (*S*)-(2-benzamido-2-phenylethyl)phosphonate (2a).** [6] 41.7 mg (99% yield) of **2a** was obtained as a white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 9.2 min, $t_R$ (minor) = 11.8 min. $[\alpha]_D^{20}$ = -23.5 (*c* 1.2, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.4 Hz, 1H), 7.94 – 7.92 (m, 2H), 7.51 – 7.31 (m, 7H), 7.27 – 7.23 (m, 1H), 5.61 (ddd, *J* = 26.1, 12.9, 7.0 Hz, 1H), 3.69 (d, *J* = 11.0 Hz, 3H), 3.39 (d, *J* = 11.1 Hz, 3H), 2.54 – 2.36 (m, 2H); $^{13}$C NMR (176 MHz, $CDCl_3$) δ 166.4, 141.2 (d, $J_{C-p}$ = 8.3 Hz), 134.0, 131.6, 128.7, 128.6, 127.6, 127.2, 126.0, 52.5 (d, $J_{C-p}$ = 6.5 Hz), 52.4 (d, $J_{C-p}$ = 6.7 Hz), 48.7 (d, $J_{C-p}$ = 5.5 Hz), 31.6 (d, $J_{C-p}$ = 138.1 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.7.




| No. | RT | Area | Conc 1 |
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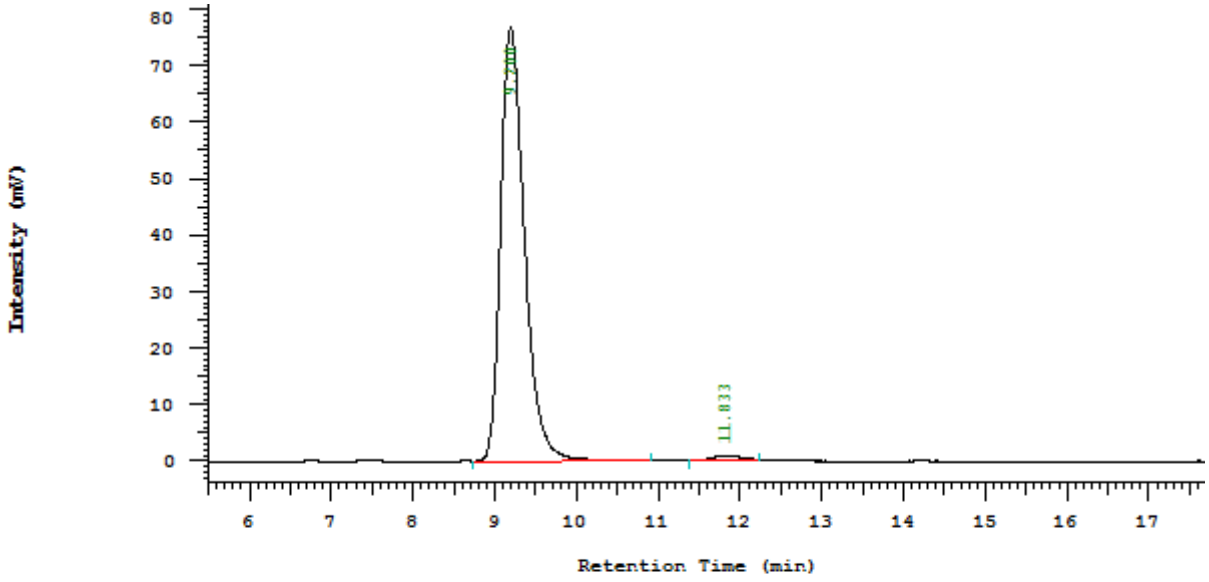
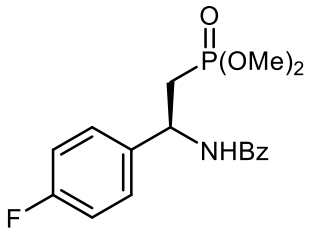
| 2 | 11.767 | 1262622 | 49.526 |
| | | 2549395 | 100.000 |

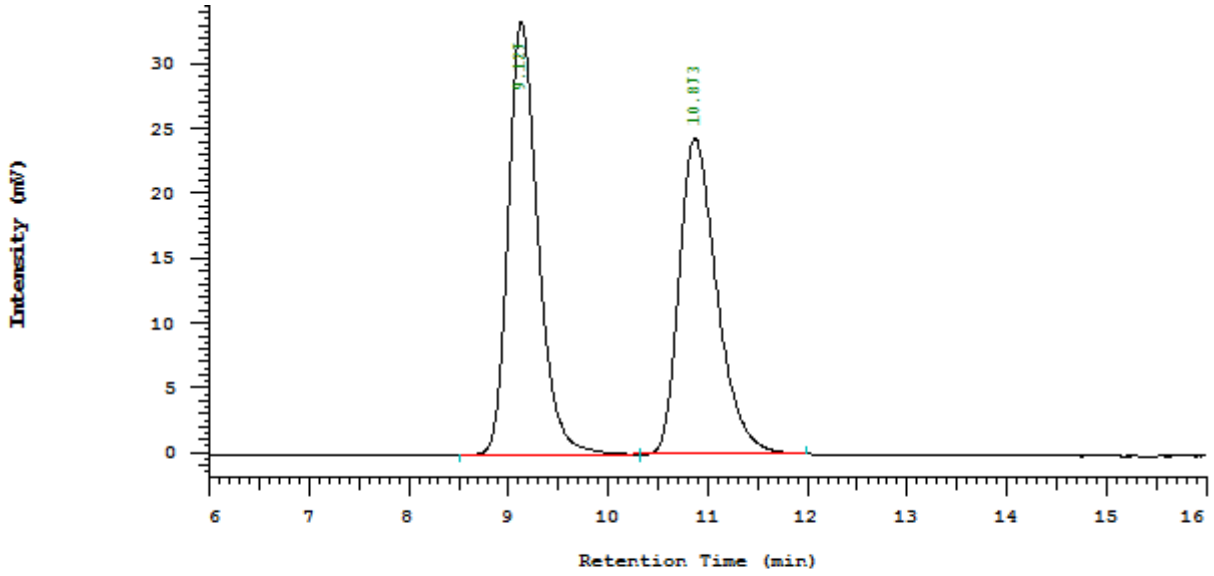



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 9.200 | 1553242 | 98.624 |
| 2 | 11.833 | 21667 | 1.376 |
| | | 1574909 | 100.000 |

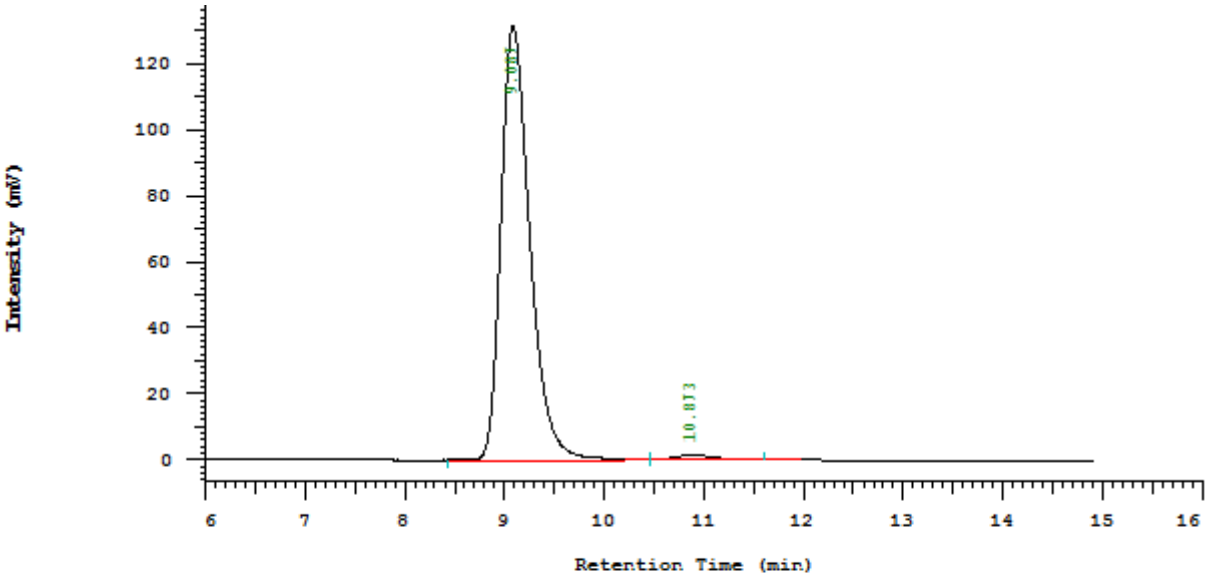



**2b**

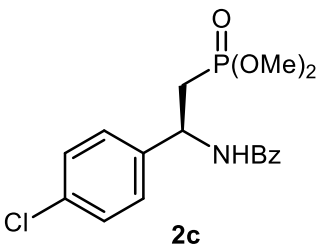
**dimethyl (*S*)-(2-benzamido-2-(4-fluorophenyl)ethyl)phosphonate (2b).** 43.6 mg (99% yield) of **2b** was obtained as white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). M.P.: 114 – 116 °C. 97% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 9.1 min, $t_R$ (minor) = 10.9 min. $[\alpha]_D^{20}$ = -19.2 (*c* 0.9, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.0 Hz, 1H), 7.93 (d, *J* = 7.7 Hz, 2H), 7.52 – 7.43 (m, 3H), 7.38 – 7.34 (m, 2H), 7.03 (t, *J* = 8.4 Hz, 2H), 5.58 (ddd, *J* = 26.9, 12.9, 6.4 Hz, 1H), 3.72 (d, *J* = 11.0 Hz, 3H), 3.45 (d, *J* = 11.1 Hz, 3H), 2.49 – 2.34 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.4, 162.1 (d, $J_{C-f}$ = 245.9 Hz), 137.0 (dd, *J* = 9.8, 4.6 Hz), 133.8, 131.8, 128.7, 127.7 (d, *J* = 8.1 Hz), 127.2, 115.5 (d, *J* = 21.6 Hz), 52.6 (d, $J_{C-p}$ = 6.6 Hz), 52.4 (d, $J_{C-p}$ = 6.7 Hz), 48.2 (d, $J_{C-p}$ = 5.6 Hz), 31.5 (d, $J_{C-p}$ = 138.3 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.6. HRMS calc. for $C_{17}H_{20}FNO_4P$ $[M+H]^+$: 352.1108, found: 352.1114.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 9.127 | 695886 | 51.889 |
| 2 | 10.873 | 645223 | 48.111 |
| | | 1341109 | 100.000 |



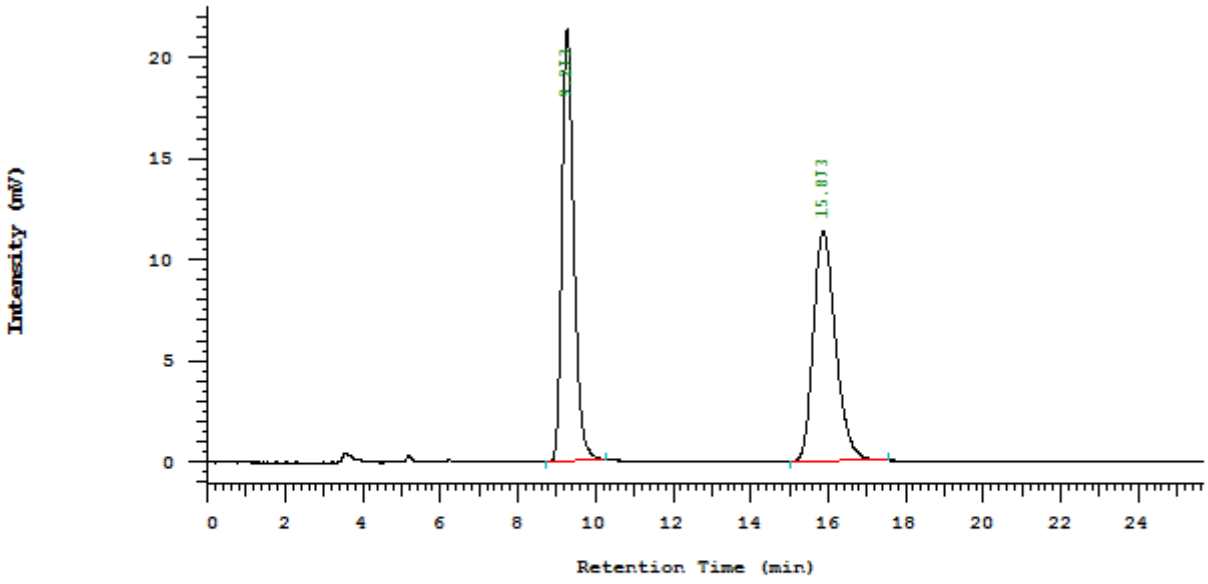

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 9.087 | 2651467 | 98.591 |
| 2 | 10.873 | 37887 | 1.409 |
| | | 2689354 | 100.000 |




**2c**

**dimethyl (*S*)-(2-benzamido-2-(4-chlorophenyl)ethyl)phosphonate (2c).** [6] 45.7

mg (99% yield) of **2c** was obtained as white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). M.P.: 184 – 186 ℃. 96% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 9.2 min, $t_R$ (minor) = 15.9 min. $[\alpha]_D^{20}$ = -22.4 (*c* 1.3, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.0 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 2H), 7.52 – 7.44 (m, 3H), 7.34 – 7.30 (m, 4H), 5.56 (ddd, *J* = 26.7, 12.9, 6.4 Hz, 1H), 3.72 (d, *J* = 11.0 Hz, 3H), 3.46 (d, *J* = 11.1 Hz, 3H), 2.41 (dd, *J* = 16.3, 5.6 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.4, 139.8 (d, $J_{C\text{-}p}$ = 8.4 Hz), 133.7, 133.3, 131.8, 128.8, 128.7, 127.4, 127.2, 52.6 (d, $J_{C\text{-}p}$ = 6.6 Hz), 52.4 (d, $J_{C\text{-}p}$ = 6.7 Hz), 48.3 (d, $J_{C\text{-}p}$ = 5.8 Hz), 31.4 (d, $J_{C\text{-}p}$ = 138.2 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.4.




| No. | RT | Area | Conc 1 |
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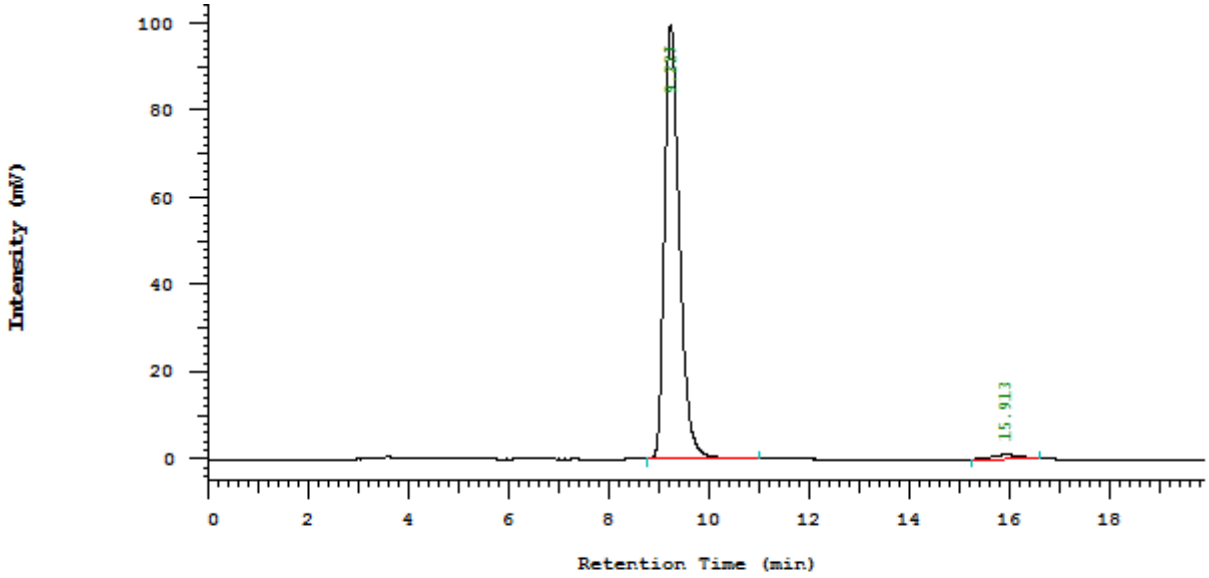
| 1 | 9.273 | 451014 | 49.990 |
| 2 | 15.873 | 451192 | 50.010 |
| | | 902206 | 100.000 |




| No. | RT | Area | Conc 1 |
|---|---|---|---|
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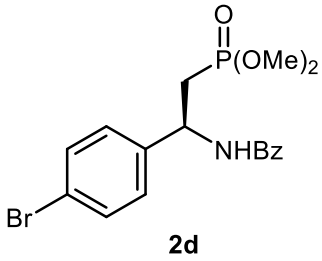
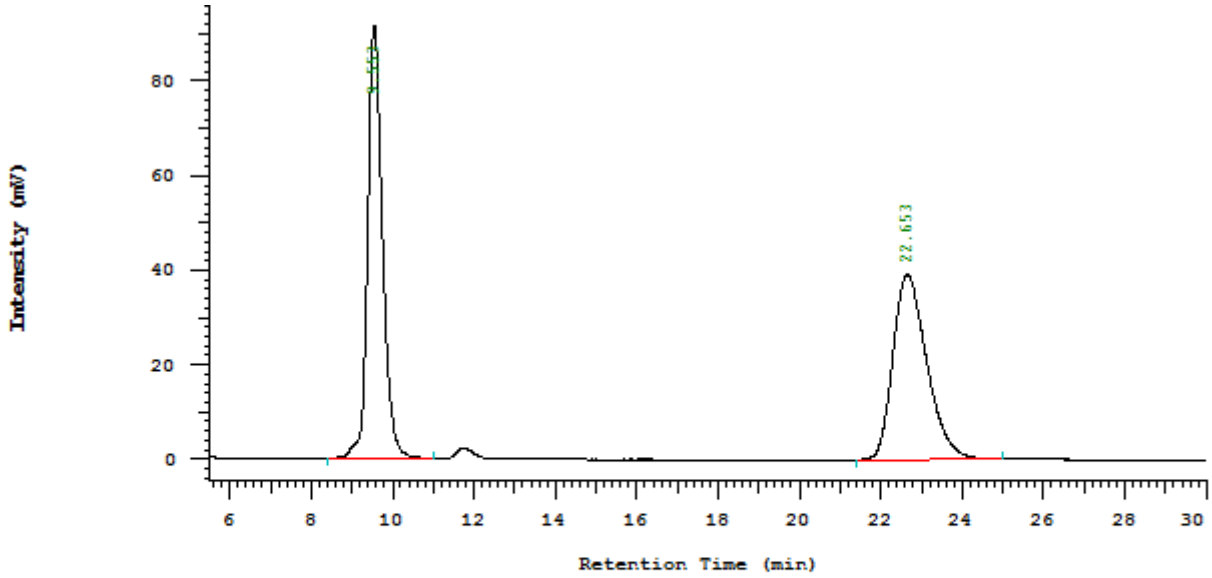
| 2 | 15.913 | 37901 | 1.787 |
| | | 2121129 | 100.000 |

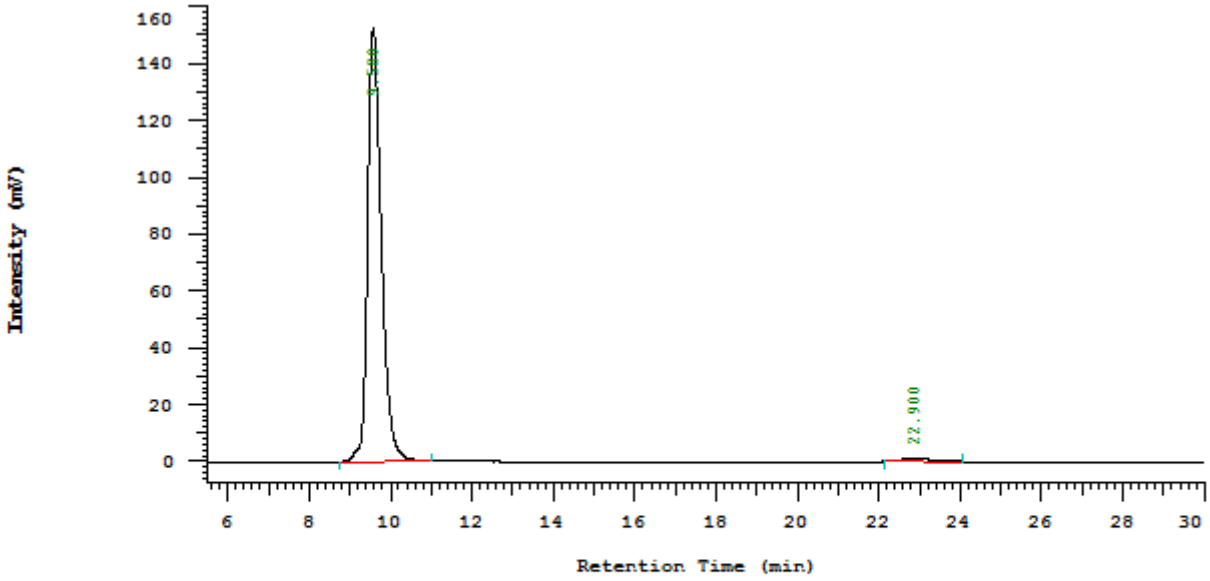



**2d**

**dimethyl (*S*)-(2-benzamido-2-(4-bromophenyl)ethyl)phosphonate (2d).** [6] 51.1 mg (99% yield) of **2d** was obtained as white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). M.p.: 92 – 94 °C. 97% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 9.6 min, $t_R$ (minor) = 22.9 min. $[\alpha]_D^{20}$ = -16.8 (*c* 0.8, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 6.9 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 2H), 7.54 – 7.44 (m, 5H), 7.28 – 7.25 (m, 2H), 5.54 (dq, *J* = 26.8, 6.5 Hz, 1H), 3.73 (d, *J* = 11.0 Hz, 3H), 3.46 (d, *J* = 11.1 Hz, 3H), 2.40 (dd, *J* = 16.6, 6.0 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.4, 140.4 (d, $J_{C-p}$ = 8.6 Hz), 133.7, 131.8, 131.8, 128.7, 127.8, 127.2, 121.4, 52.6 (d, $J_{C-p}$ = 6.6 Hz), 52.5 (d, $J_{C-p}$ = 6.7 Hz), 48.4 (d, $J_{C-p}$ = 5.8 Hz), 31.3 (d, $J_{C-p}$ = 138.5 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.4.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 9.553 | 2335339 | 50.862 |
| 2 | 22.653 | 2256174 | 49.138 |
| | | 4591513 | 100.000 |




| No. | RT | Area | Conc 1 |
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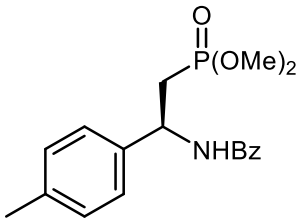
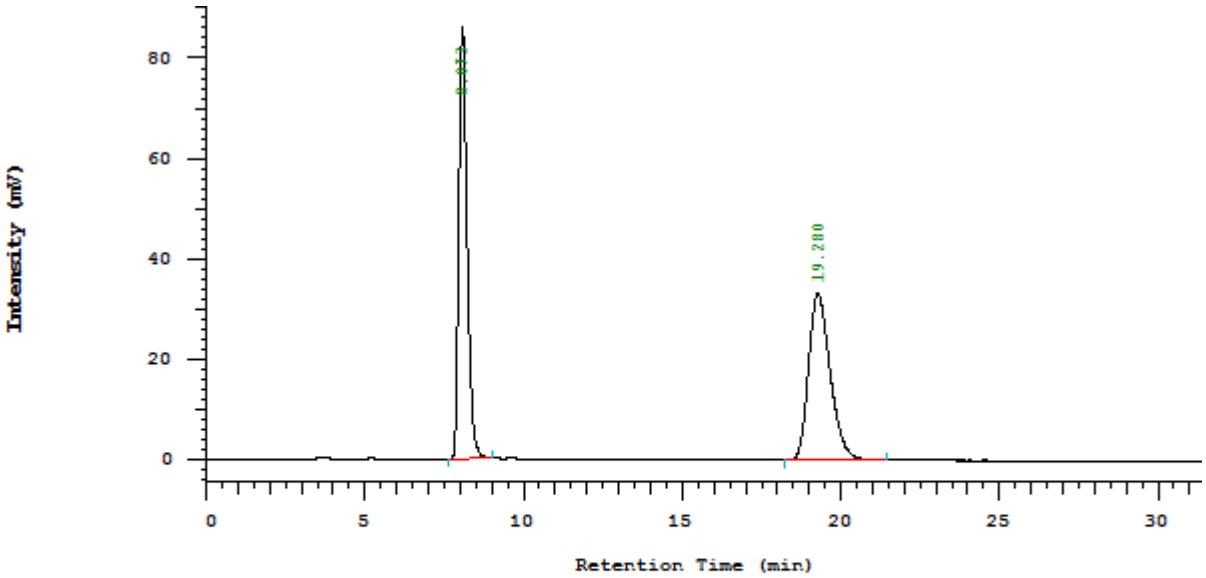
| 1 | 9.580 | 3584987 | 98.471 |
| 2 | 22.900 | 55651 | 1.529 |
| | | 3640638 | 100.000 |

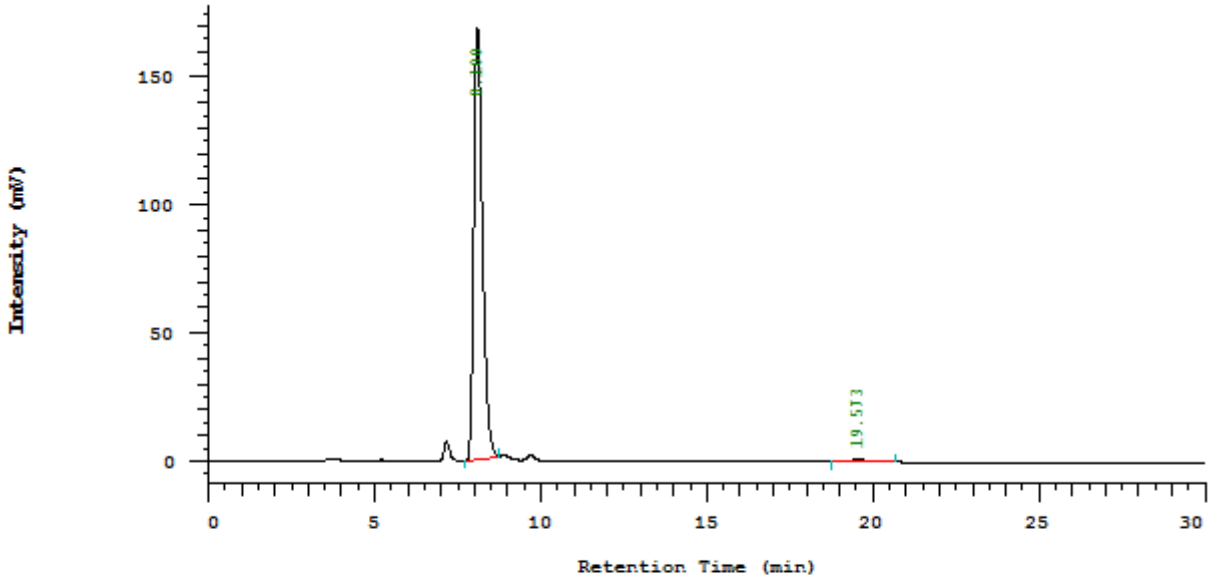



**2e**

**dimethyl (*S*)-(2-benzamido-2-(p-tolyl)ethyl)phosphonate (2e).** [6] 43.1 mg (>99% yield) of **2e** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 8.1 min, $t_R$ (minor) = 19.6 min. $[\alpha]_D^{20}$ = -24.5 (*c* 3.2, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.3 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.50 – 7.39 (m, 3H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 5.55 (ddd, *J* = 24.4, 13.1, 6.8 Hz, 1H), 3.69 (d, *J* = 10.9 Hz, 3H), 3.42 (d, *J* = 11.0 Hz, 3H), 2.53 – 2.37 (m, 2H), 2.31 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.4, 138.3 (d, $J_{C-p}$ = 8.7 Hz), 137.2, 134.1, 131.5, 129.3, 128. 6, 127.2, 126.0, 52.5 (d, $J_{C-p}$ = 6.6 Hz), 52.4 (d, $J_{C-p}$ = 6.6 Hz), 48.6 (d, $J_{C-p}$ = 5.3 Hz), 31.6 (d, $J_{C-p}$ = 137.8 Hz), 21.1; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.8.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 8. 073 | 1564528 | 49. 905 |
| 2 | 19. 280 | 1570464 | 50. 095 |
| | | 3134992 | 100. 000 |




| No. | RT | Area | Conc 1 |
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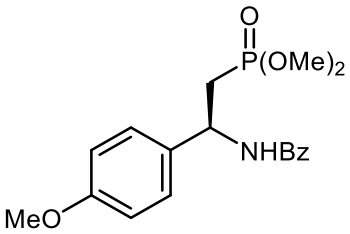
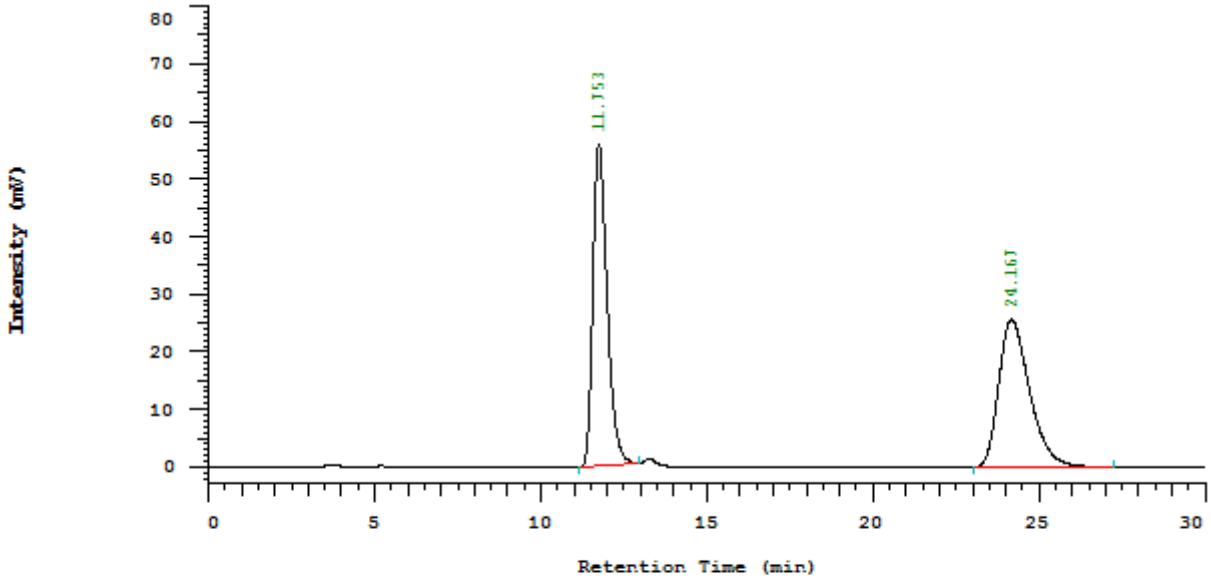
| 2 | 19.573 | 40642 | 1.312 |
| | | 3096882 | 100.000 |




**2f**

**dimethyl (*S*)-(2-benzamido-2-(4-methoxyphenyl)ethyl)phosphonate (2f).** [6] 45.2 mg (>99% yield) of **2f** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 $^{o}$C): $t_R$ (major) = 11.7 min, $t_R$ (minor) = 24.4 min. $[\alpha]_D^{20}$ = -22.5 (*c* 0.8, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.3 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 2H), 7.47 (dt, *J* = 25.1, 7.4 Hz, 3H), 7.31 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.1 Hz, 2H), 5.55 (ddd, *J* = 25.7, 13.0, 6.5 Hz, 1H), 3.78 (s, 3H), 3.70 (d, *J* = 10.9 Hz, 3H), 3.44 (d, *J* = 11.0 Hz, 3H), 2.52 – 2.35 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.4, 159.0, 134.0, 133.3 (d, $J_{C-p}$ = 8.2 Hz), 131.6, 128.6, 127.2, 127.2, 114.1, 55.3, 52.5, 52.5 (d, $J_{C-p}$ = 3.6 Hz), 52.4 (d, $J_{C-p}$ = 3.6 Hz), 48.3 (d, $J_{C-p}$ = 5.4 Hz), 31.6 (d, $J_{C-p}$ = 137.6 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.9.




| No. | RT | Area | Conc 1 |
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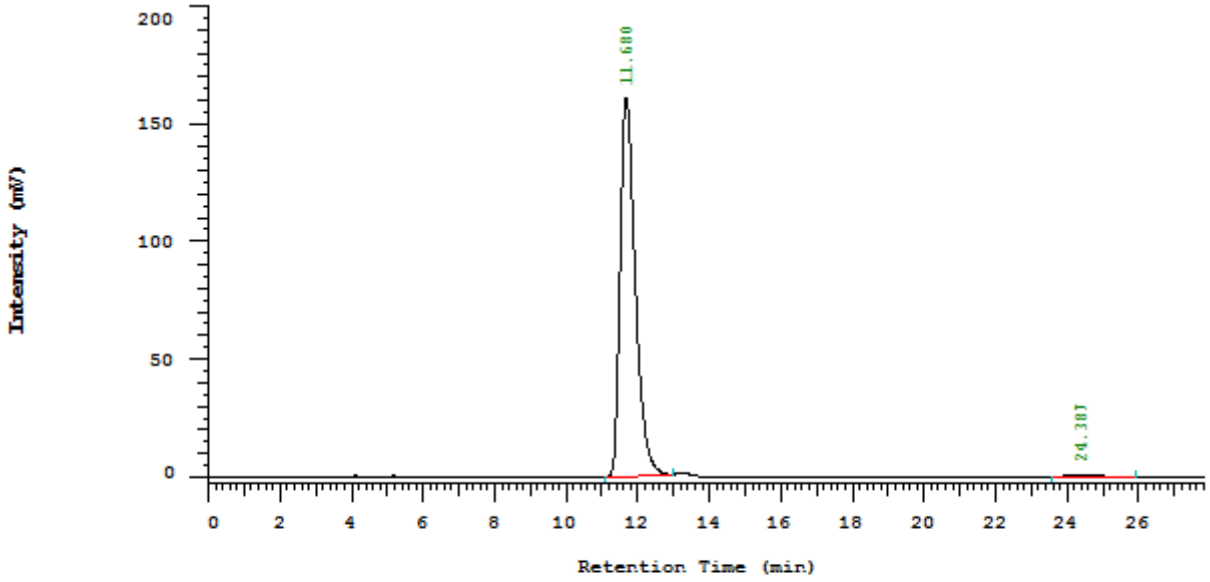
| 1 | 11.753 | 1652668 | 49.823 |
| 2 | 24.167 | 1664389 | 50.177 |
| | | 3317057 | 100.000 |




| No. | RT | Area | Conc 1 |
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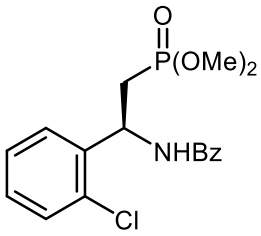
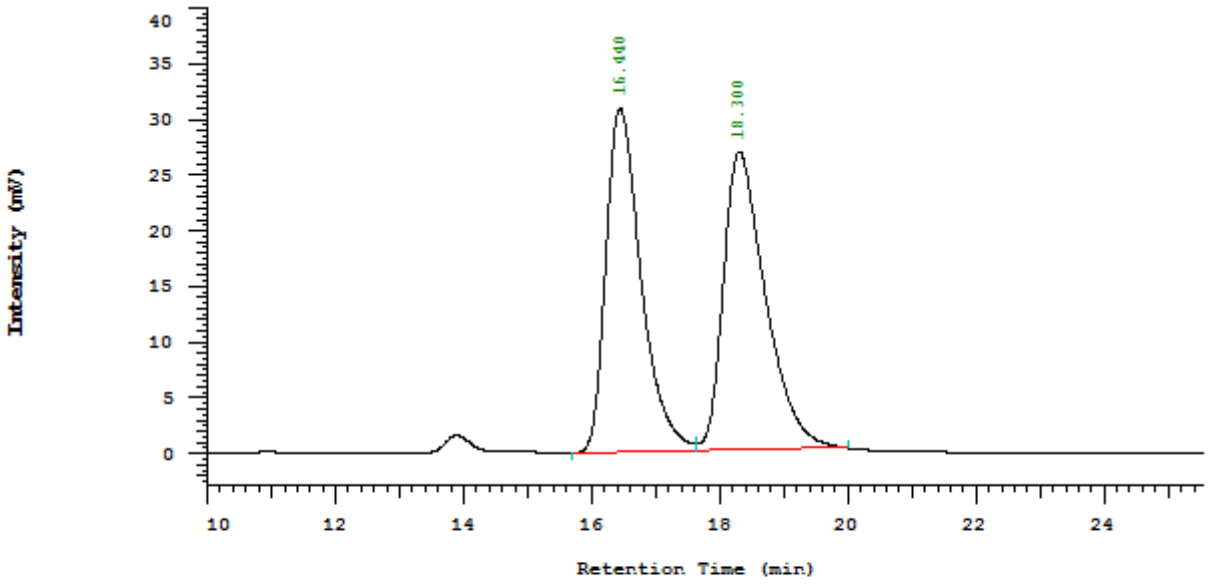
| 2 | 24.387 | 68870 | 1.442 |
| | | 4775969 | 100.000 |

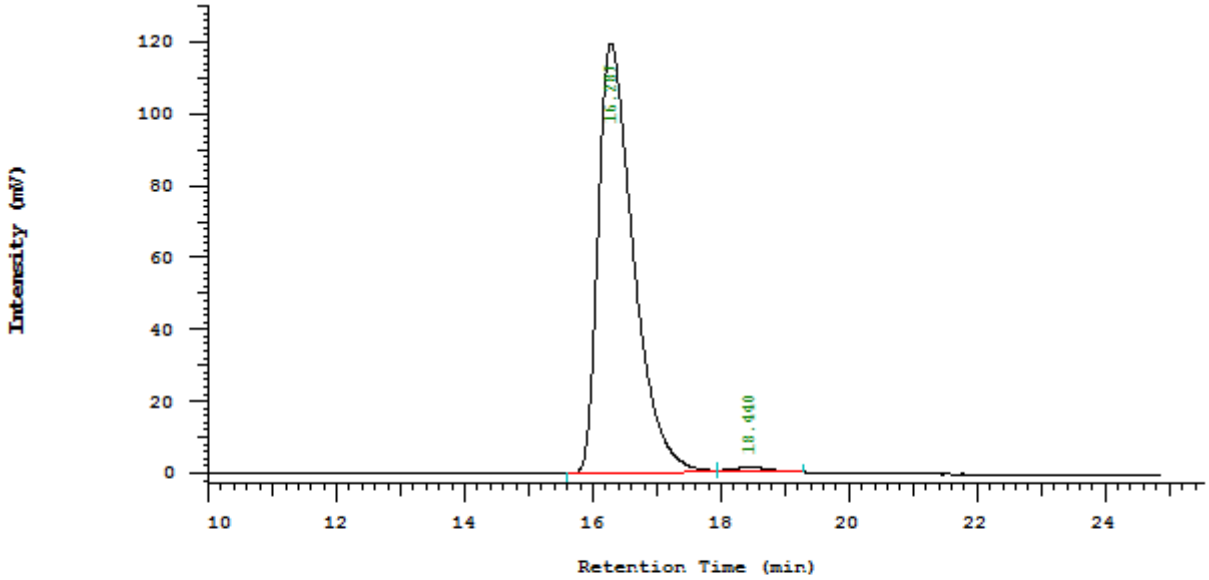



**2g**

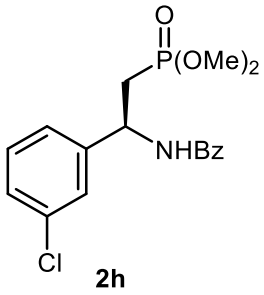
**dimethyl (*S*)-(2-benzamido-2-(2-chlorophenyl)ethyl)phosphonate (2g).** [6] 44.6 mg (>99% yield) of **2g** was obtained as white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). M.P.: 106 – 108 °C. 98% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90/10, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 16.3 min, $t_R$ (minor) = 18.4 min. $[\alpha]_D^{20}$ = -74.1 (*c* 3.4, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 7.0 Hz, 1H), 7.95 (d, *J* = 7.7 Hz, 2H), 7.53 – 7.43 (m, 4H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.25 – 7.18 (m, 2H), 5.86 (ddd, *J* = 26.7, 12.5, 6.7 Hz, 1H), 3.73 (d, *J* = 11.0 Hz, 3H), 3.43 (d, *J* = 11.1 Hz, 3H), 2.64 – 2.39 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.1, 138.5 (d, $J_{C-p}$ = 8.4 Hz), 133.7, 132.2, 131.7, 129.9, 128.8, 128.7, 127.4, 127.2, 127.1, 52.6 (d, $J_{C-p}$ = 6.6 Hz), 52.3 (d, $J_{C-p}$ = 6.8 Hz), 46.8 (d, $J_{C-p}$ = 5.9 Hz), 28.7 (d, $J_{C-p}$ = 137.9 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.7.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 16.440 | 1176046 | 49.012 |
| 2 | 18.300 | 1223468 | 50.988 |
| | | 2399514 | 100.000 |

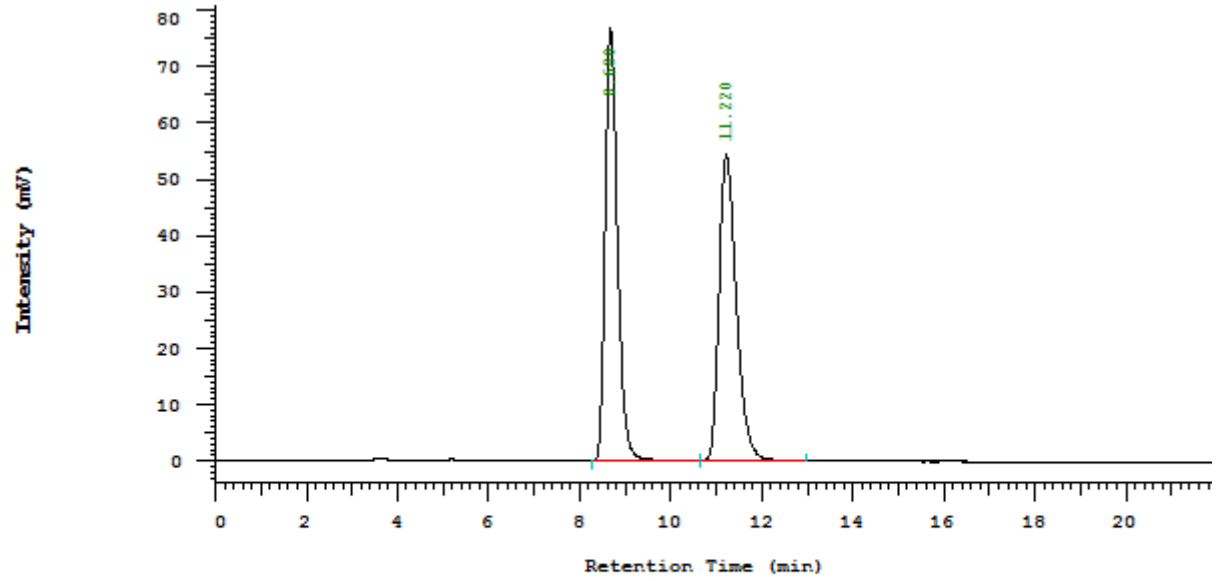



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 16.287 | 4618621 | 99.144 |
| 2 | 18.440 | 39879 | 0.856 |
| | | 4658500 | 100.000 |

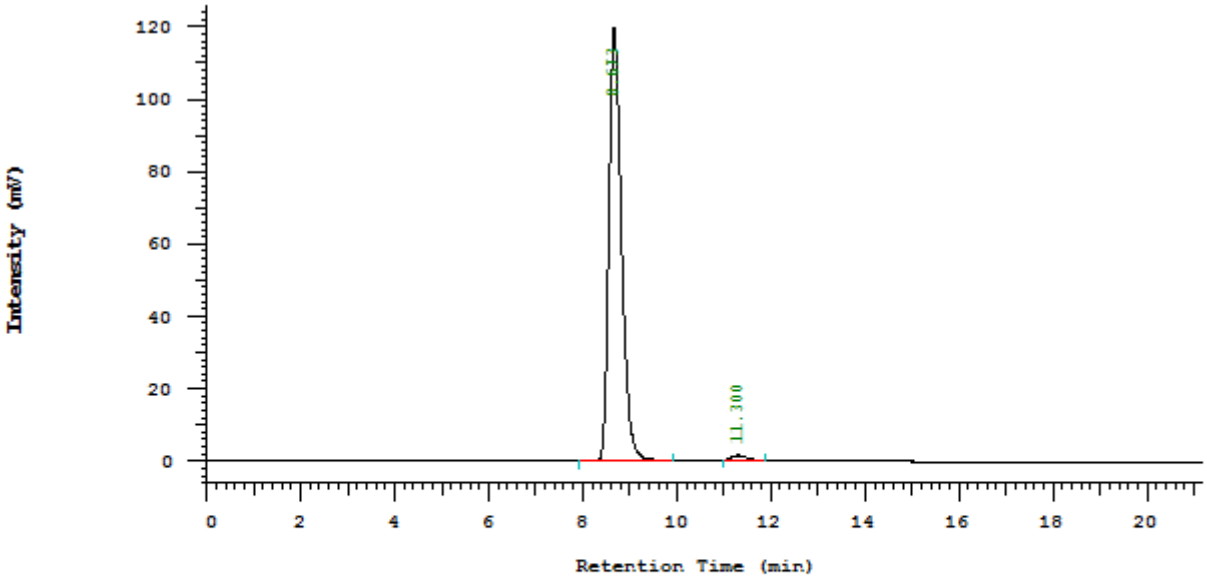



**2h**

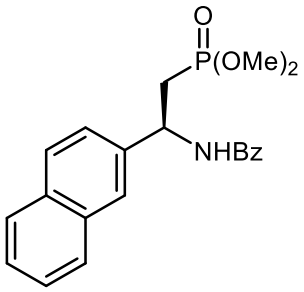
**dimethyl (*S*)-(2-benzamido-2-(3-chlorophenyl)ethyl)phosphonate (2h).** 45.4 mg (99% yield) of **2h** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 8.7 min, $t_R$ (minor) = 11.3 min. $[\alpha]_D^{20}$ = -29.5 (*c* 1.1, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 6.9 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 2H), 7.54 – 7.37 (m, 4H), 7.28 – 7.24 (m, 3H), 5.56 (ddd, *J* = 26.5, 12.9, 6.4 Hz, 1H), 3.73 (d, *J* = 11.0 Hz, 3H), 3.47 (d, *J* = 11.1 Hz, 3H), 2.44 – 2.38 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.5, 143.5 (d, $J_{C-p}$ = 8.7 Hz), 134.6, 133.7, 131.8, 130.0, 128.7, 127.8, 127.2, 126.2, 124.3, 52.6 (d, $J_{C-p}$ = 6.6 Hz), 52.5 (d, $J_{C-p}$ = 6.8 Hz), 48.4 (d, $J_{C-p}$ = 5.8 Hz), 31.4 (d, $J_{C-p}$ = 138.7 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.3. HRMS calc. for $C_{17}H_{20}ClNO_4P$ $[M+H]^+$: 368.0813, found: 368.0821.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 8.680 | 1454019 | 50.172 |
| 2 | 11.220 | 1444037 | 49.828 |
| | | 2898056 | 100.000 |

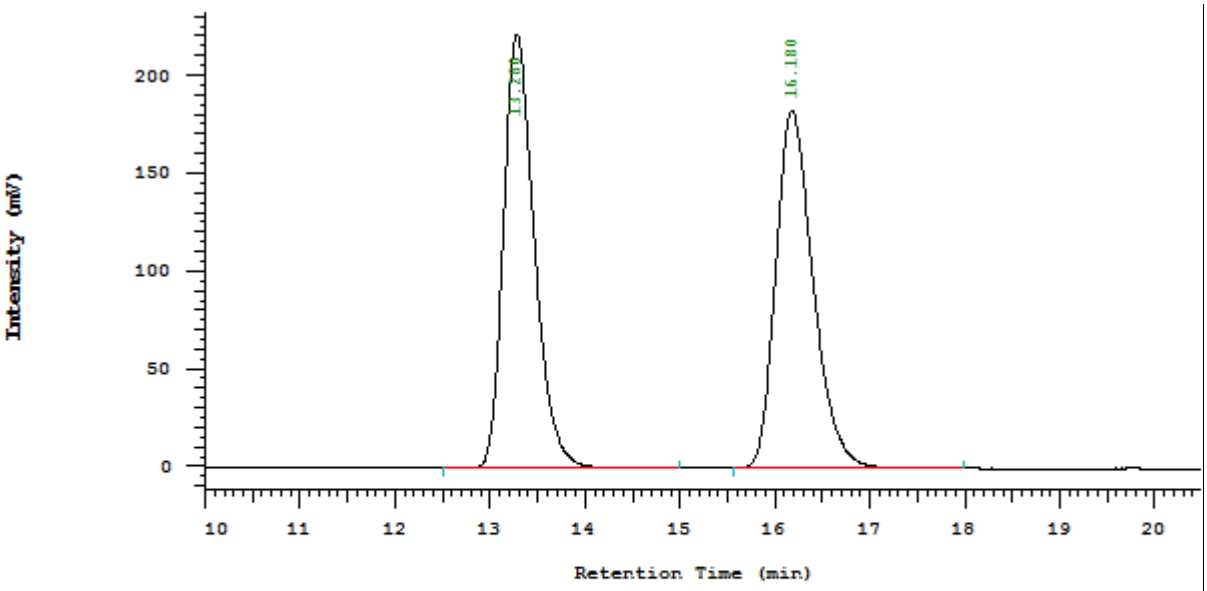



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 8.673 | 2243062 | 98.447 |
| 2 | 11.300 | 35377 | 1.553 |
| | | 2278439 | 100.000 |

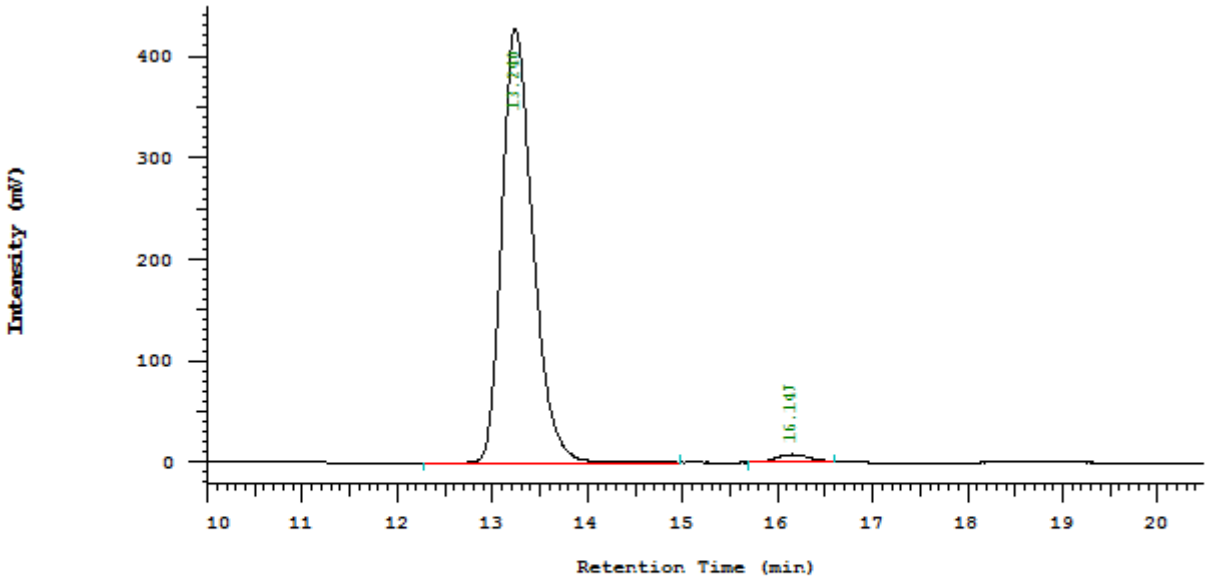



**2i**

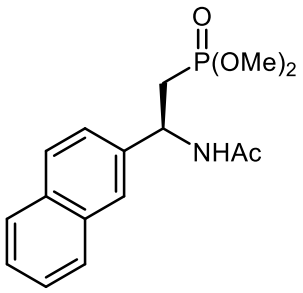
**dimethyl (*S*)-(2-benzamido-2-(naphthalen-2-yl)ethyl)phosphonate (2i).** 47.6 mg (99% yield) of **2i** was obtained as white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). M.P.: 138 – 140 $^{o}$C. 96% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 $^{o}$C): $t_R$ (major) = 13.2 min, $t_R$ (minor) = 16.1 min. $[\alpha]_D^{20}$ = -32.9 (*c* 4.2, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.5 Hz, 1H), 7.96 – 7.94 (m, 2H), 7.83 – 7.76 (m, 4H), 7.51 – 7.41 (m, 6H), 5.75 (ddd, *J* = 25.3, 12.8, 7.1 Hz, 1H), 3.69 (d, *J* = 11.0 Hz, 3H), 3.33 (d, *J* = 11.1 Hz, 3H), 2.62 – 2.41 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.5, 138.7 (d, $J_{C-p}$ = 8.7 Hz), 134.0, 133.3, 132.8, 131.7, 128.6, 128.6, 128.0, 127.6, 127.3, 126.30, 126.0, 124.7, 124.3, 52.5 (d, $J_{C-p}$ = 6.6 Hz), 52.4 (d, $J_{C-p}$ = 6.7 Hz), 48.9 (d, $J_{C-p}$ = 5.5 Hz), 31.5 (d, $J_{C-p}$ = 138.2 Hz); $^{31}$P NMR (162 MHz, $CDCl_3$) δ 31.7. HRMS calc. for $C_{21}H_{23}NO_4P$ $[M+H]^+$: 384.1359, found: 384.1354.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 13.280 | 5009552 | 50.018 |
| 2 | 16.180 | 5006034 | 49.982 |
| | | 10015586 | 100.000 |

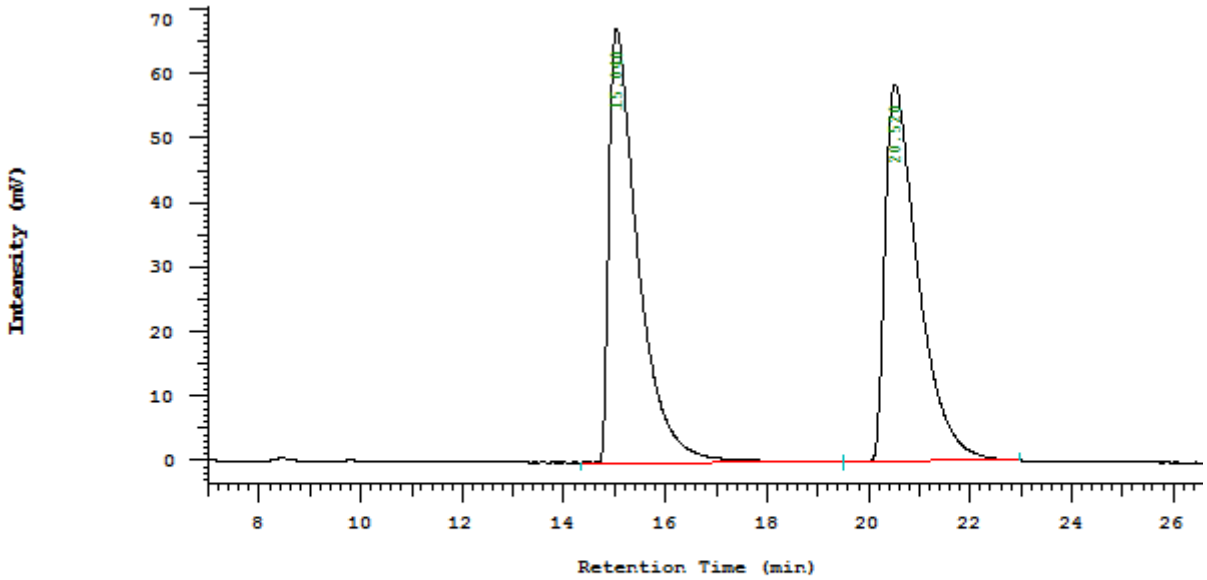



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 13.240 | 9706539 | 98.174 |
| 2 | 16.147 | 180556 | 1.826 |
| | | 9887095 | 100.000 |

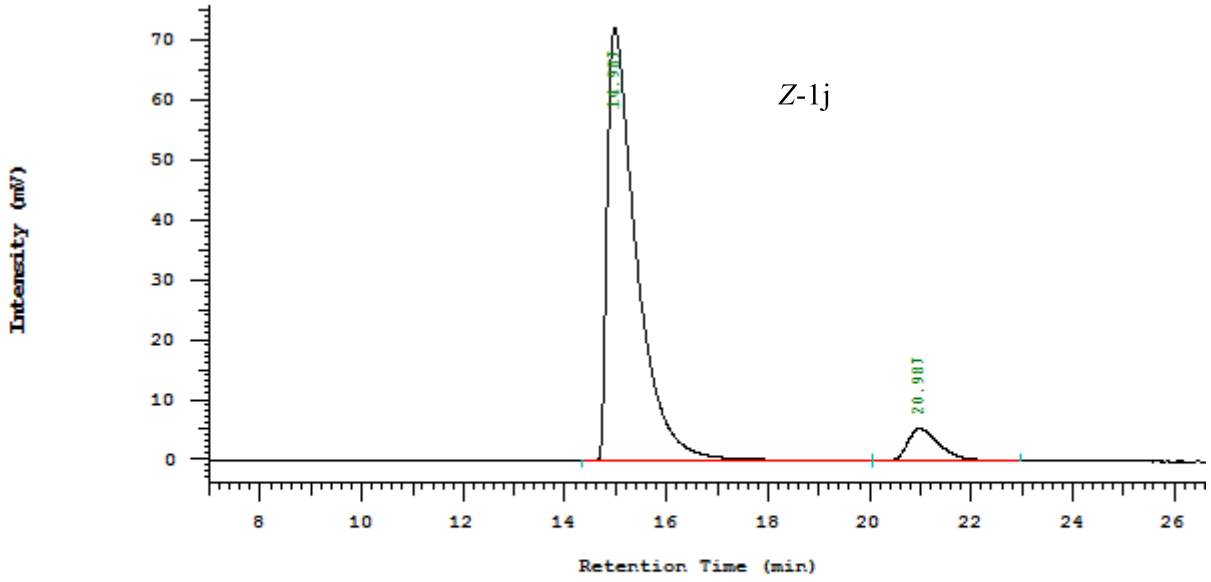



**2j**

**dimethyl (*S*)-(2-acetamido-2-(naphthalen-2-yl)ethyl)phosphonate (2j).** 39.2 mg (99% yield) of **2j** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.3). 85% ee (*Z*-1j) and 15% ee (*E*-1j) were determined by chiral HPLC (Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 85/15, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 15.0 min, $t_R$ (minor) = 21.0 min. $[\alpha]_D^{20}$ = 17.8 (*c* 1.0, $CHCl_3$), (*Z*-1j) ; $[\alpha]_D^{20}$ = 0.8 (*c* 0.8, $CHCl_3$), (*E*-1j). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 4H), 7.50 – 7.41 (m, 3H), 7.15 (d, *J* = 7.9 Hz, 1H), 5.64 – 5.54 (m, 1H), 3.70 (d, *J* = 11.0 Hz, 3H), 3.31 (d, *J* = 11.0 Hz, 3H), 2.54 – 2.34 (m, 2H), 2.09 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.6, 138.4 (d, $J_{C-p}$ = 8.3 Hz), 133.3, 132.8, 128.5, 128.0, 127.6, 126.4, 126.1, 124.8, 124.3, 52.5 (d, $J_{C-p}$ = 6.7 Hz), 52.3 (d, $J_{C-p}$ = 6.8 Hz), 48.4, 31.5 (d, $J_{C-p}$ = 138.6 Hz), 23.5; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.3. HRMS calc. for $C_{16}H_{21}NO_4P$ $[M+H]^+$: 322.1203, found: 322.1209.

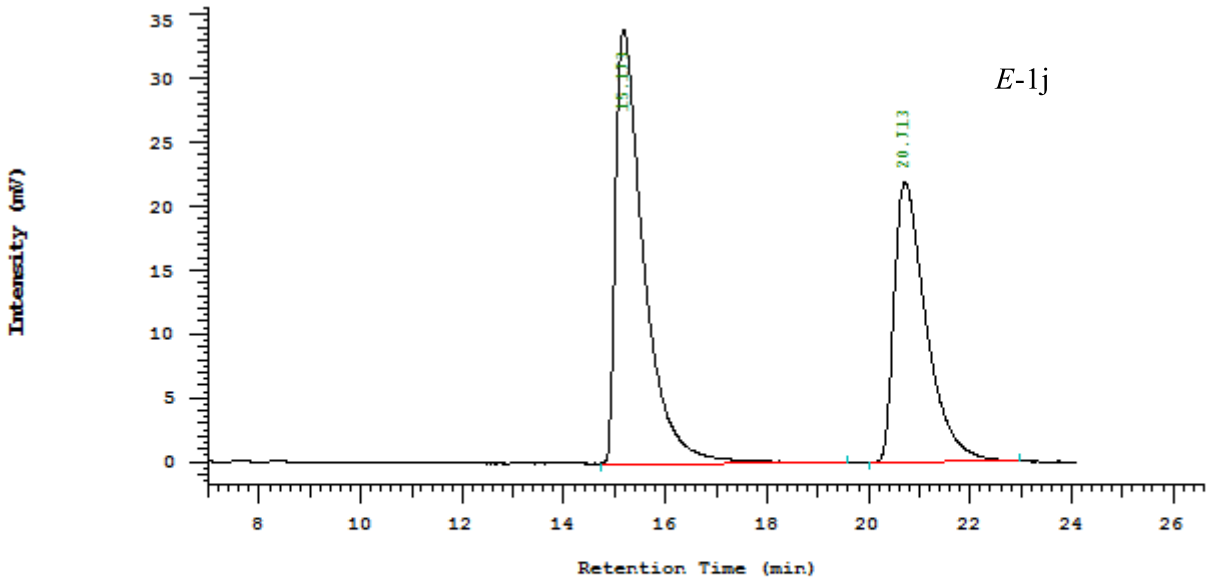



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 15.040 | 2704776 | 50.363 |
| 2 | 20.520 | 2665826 | 49.637 |
| | | 5370602 | 100.000 |

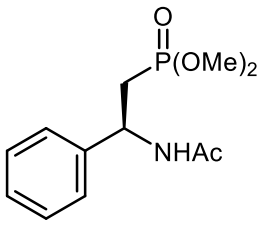



*Z*-1j

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 14.987 | 2895255 | 92.373 |
| 2 | 20.987 | 239045 | 7.627 |
| | | 3134300 | 100.000 |

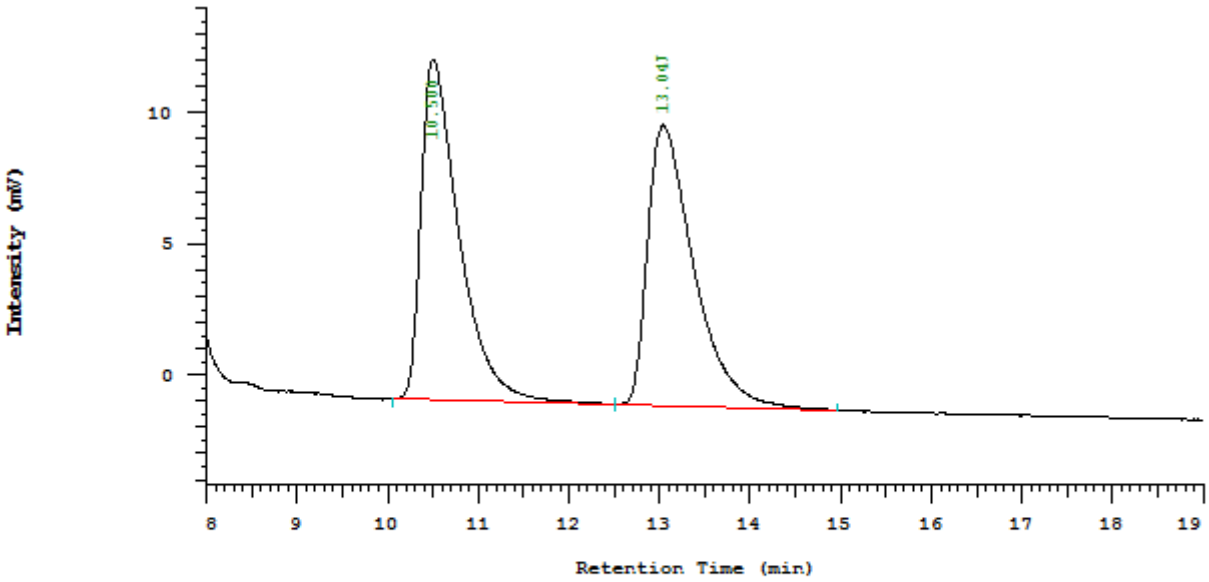



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 15.173 | 1311067 | 57.593 |
| 2 | 20.713 | 965357 | 42.407 |
| | | 2276424 | 100.000 |

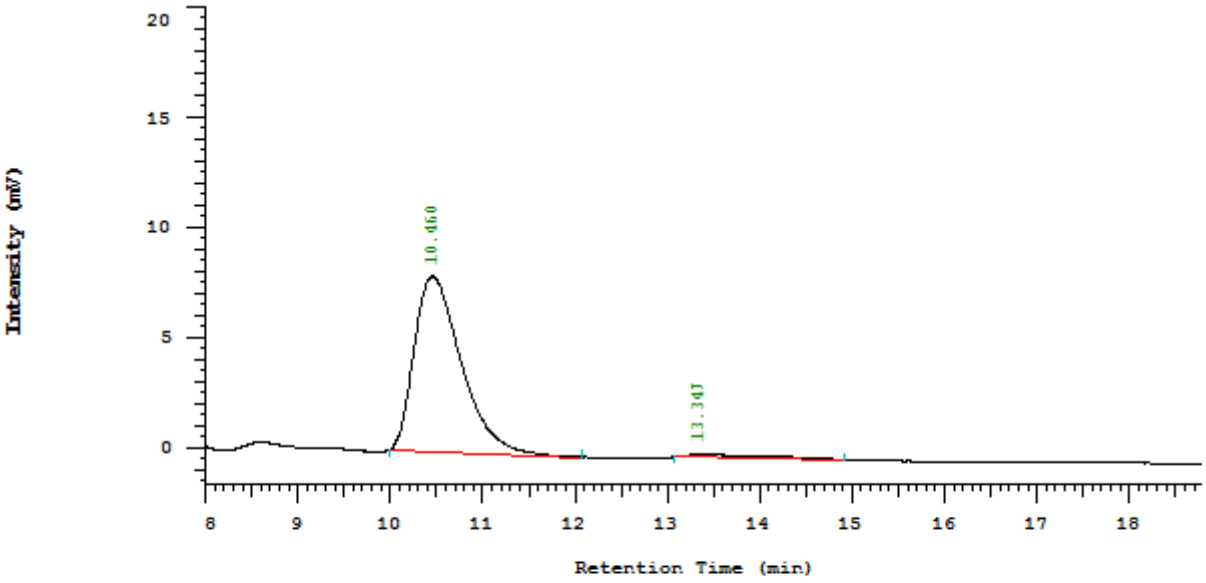



**2k**

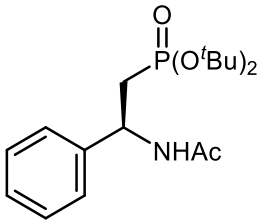
**dimethyl (*S*)-(2-acetamido-2-phenylethyl)phosphonate (2k).**[7] 51.0 mg (>99% yield) of **2k** was obtained as white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 2/1/0.5). M.P.: 132 – 134 °C. 94% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 85/15, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 10.5 min, $t_R$ (minor) = 13.3 min. $[\alpha]_D^{30}$ = 25.1 (*c* 1.6, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.32 (m, 4H), 7.29 – 7.21 (m, 2H), 5.45 – 5.34 (m, 1H), 3.68 (d, *J* = 10.9 Hz, 3H), 3.39 (d, *J* = 11.0 Hz, 3H), 2.40 – 2.28 (m, 2H), 2.02 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.5, 141.1 (d, $J_{C-p}$ = 8.4 Hz), 128.6, 127.5, 126.1, 52.4 (d, $J_{C-p}$ = 6.6 Hz), 52.2 (d, $J_{C-p}$ = 6.6 Hz), 48.3 (d, $J_{C-p}$ = 4.7 Hz), 31.6 (d, $J_{C-p}$ = 138.6 Hz), 23.3; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 30.2.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 10.500 | 381027 | 50.057 |
| 2 | 13.047 | 380158 | 49.943 |
| | | 761185 | 100.000 |

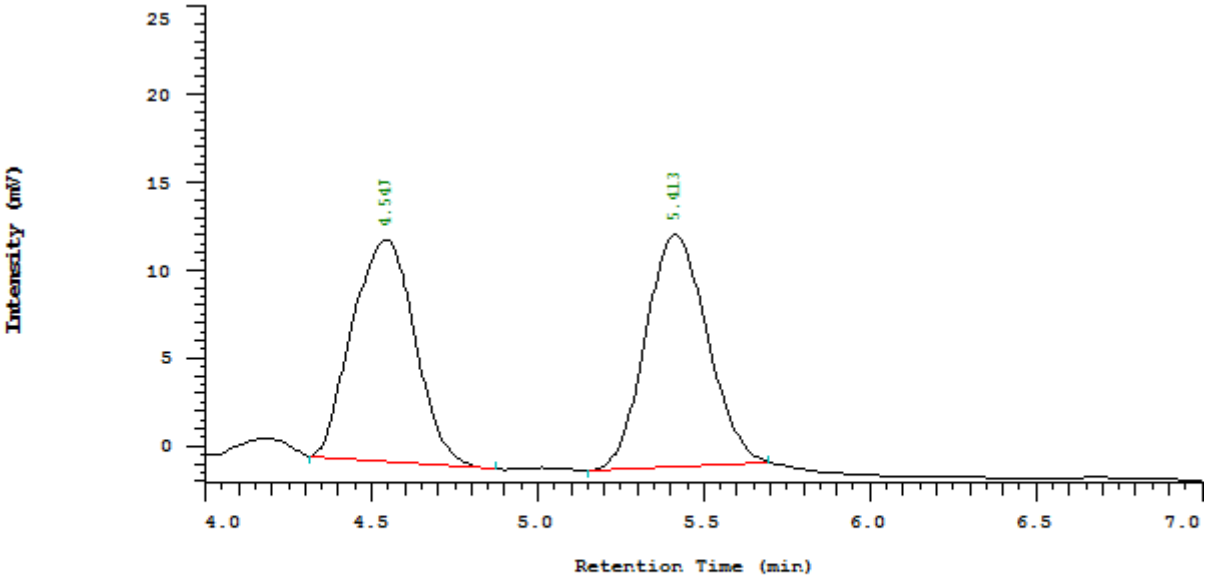



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 10.460 | 279035 | 97.002 |
| 2 | 13.347 | 8624 | 2.998 |
| | | 287659 | 100.000 |

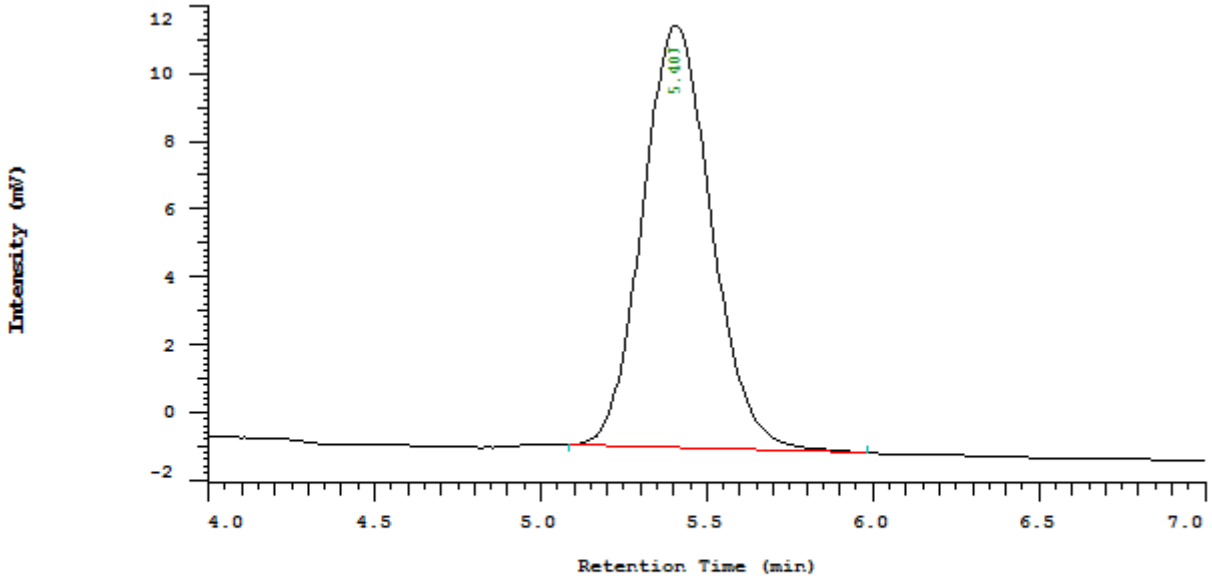



**2l**

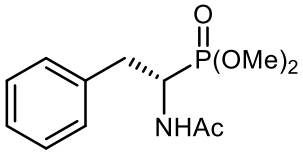
**di-*tert*-butyl (*S*)-(2-acetamido-2-phenylethyl)phosphonate (2l).** 43.9 mg (99% yield) of **2l** was obtained as a white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 2/1/0.1). M.p.: 148 – 150 $^{o}$C. >99% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 85/15, 0.8 mL/min, 254 nm, 40 $^{o}$C): $t_R$ (major) = 5.4 min, $t_R$ (minor) = 4.5 min. $[\alpha]_D^{30}$ = 30.9 (*c* 1.8, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 4H), 7.25 – 7.20 (m, 1H), 7.18– 7.16 (m, 1H), 1H), 5.29 – 5.19 (m, 1H), 2.18 (dd, *J* = 16.9, 6.7 Hz, 2H), 2.03 (s, 3H), 1.51 (s, 9H), 1.32 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.5, 142.0 (d, $J_{C\text{-}p}$ = 9.9 Hz), 128.5, 127.1, 126.1, 82.9 (d, $J_{C\text{-}p}$ = 8.8 Hz), 82.5 (d, $J_{C\text{-}p}$ = 8.9 Hz), 49.7 (d, $J_{C\text{-}p}$ = 5.8 Hz), 36.6 (d, $J_{C\text{-}p}$ = 142.1 Hz), 30.4 (d, $J_{C\text{-}p}$ = 4.0 Hz), 30.2 (d, $J_{C\text{-}p}$ = 4.0 Hz), 23.3; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 19.1. HRMS calc. for $C_{18}H_{31}NO_4P$ $[M+H]^+$: 356.1995, found: 356.1995.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 4.547 | 165306 | 49.388 |
| 2 | 5.413 | 169405 | 50.612 |

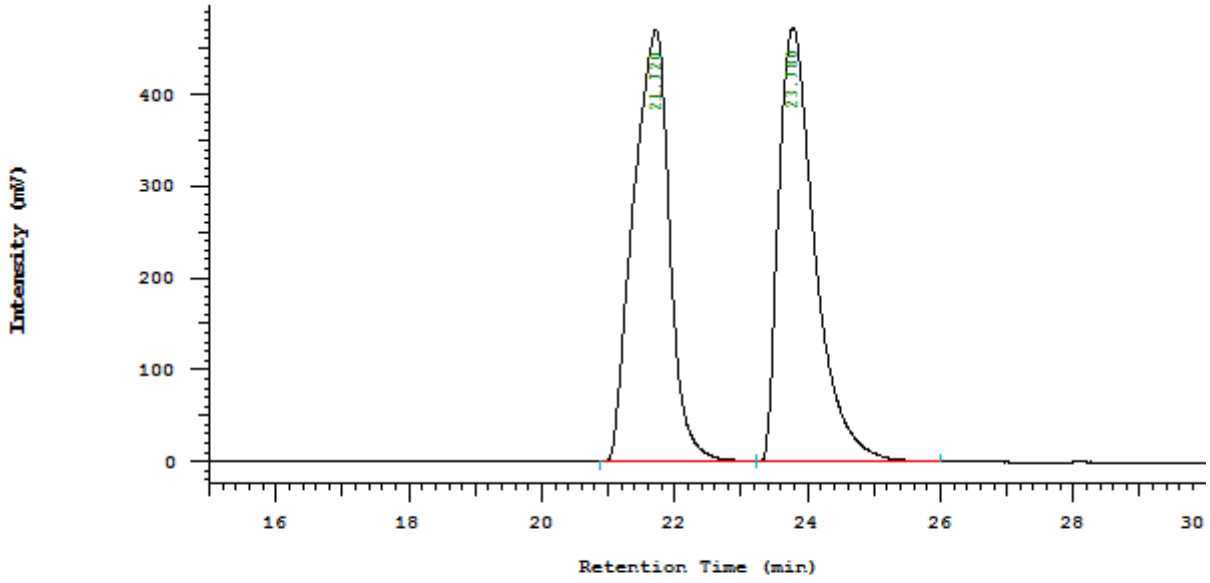



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 5.407 | 180742 | 100.000 |
| | | 180742 | 100.000 |

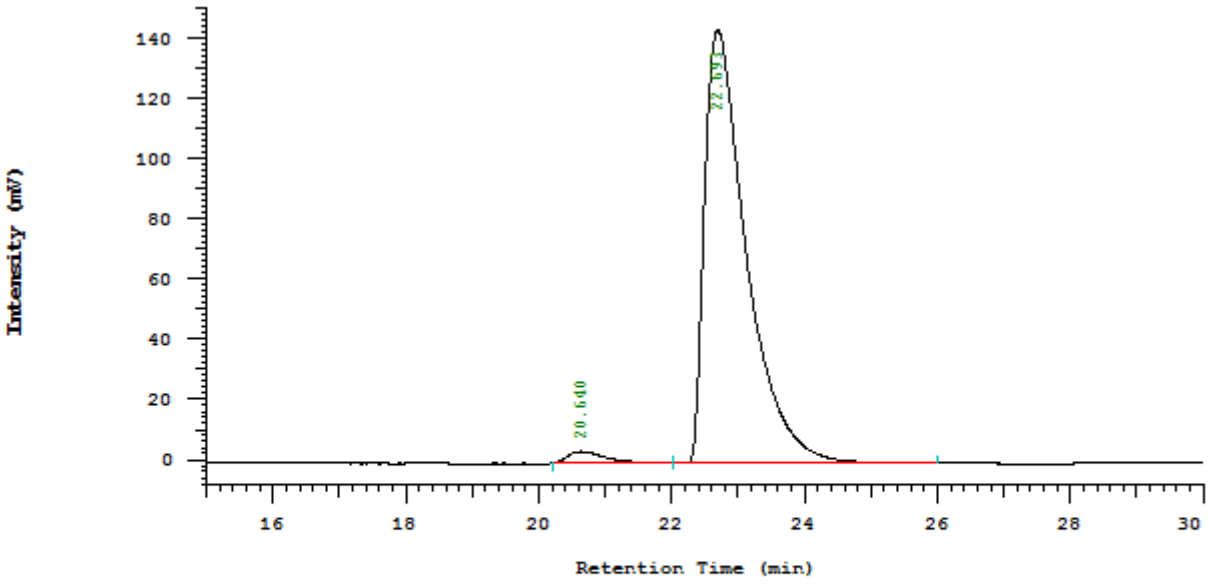



**4a**

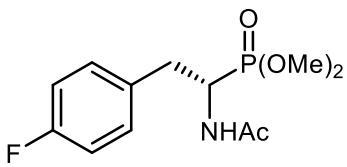
**dimethyl (*S*)-(1-acetamido-2-phenylethyl)phosphonate (4a).**[4] 33.5 mg (99% yield) of **4a** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.2). >95% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 22.7 min, $t_R$ (minor) = 20.6 min. $[\alpha]_D^{20}$ = 13.8 (*c* 1.2, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.19 (m, 5H), 6.65 (d, *J* = 9.8 Hz, 1H), 4.86 – 4.72 (m, 1H), 3.75 (d, *J* = 10.7 Hz, 6H), 3.25 – 3.10 (m, 1H), 2.98 – 2.89 (m, 1H), 1.89 (d, *J* = 0.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.8 (d, $J_{C\text{-}p}$ = 4.9 Hz), 136.5 (d, $J_{C\text{-}p}$ = 13.3 Hz), 129.1, 128.4, 126.9, 53.5 (d, $J_{C\text{-}p}$ = 6.9 Hz), 52.9 (d, $J_{C\text{-}p}$ = 6.9 Hz), 45.7 (d, $J_{C\text{-}p}$ = 156.3 Hz), 35.5 (d, *J* = 3.3 Hz), 22.8; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.8.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 21.720 | 17840172 | 49.872 |
| 2 | 23.780 | 17931500 | 50.128 |
| | | 35771672 | 100.000 |



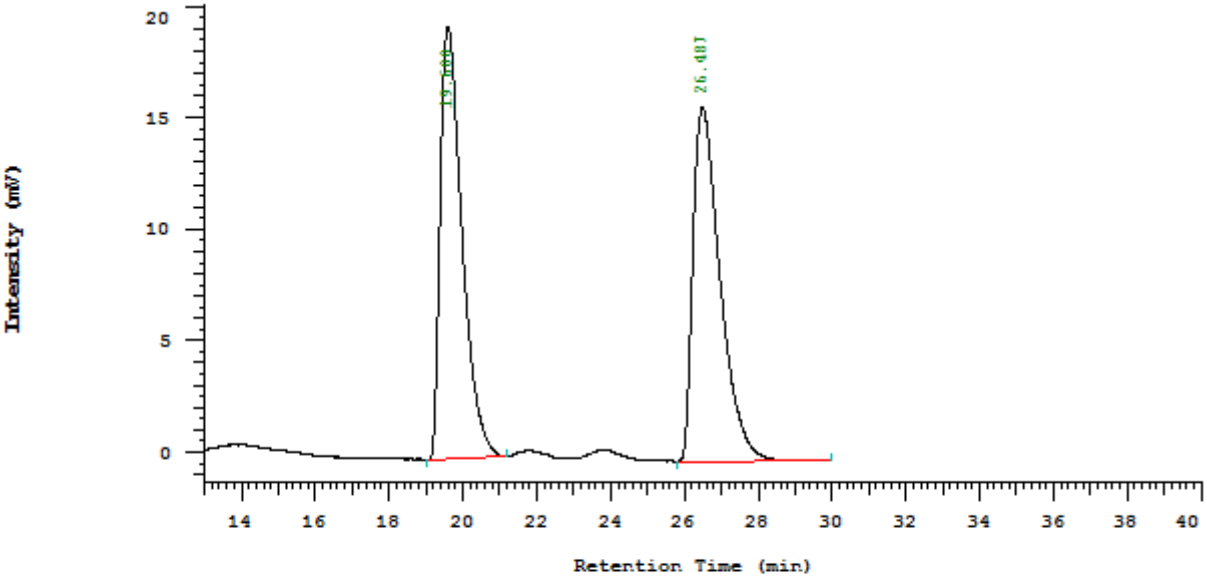

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 20.640 | 157852 | 2.447 |
| 2 | 22.693 | 6294001 | 97.553 |
| | | 6451853 | 100.000 |



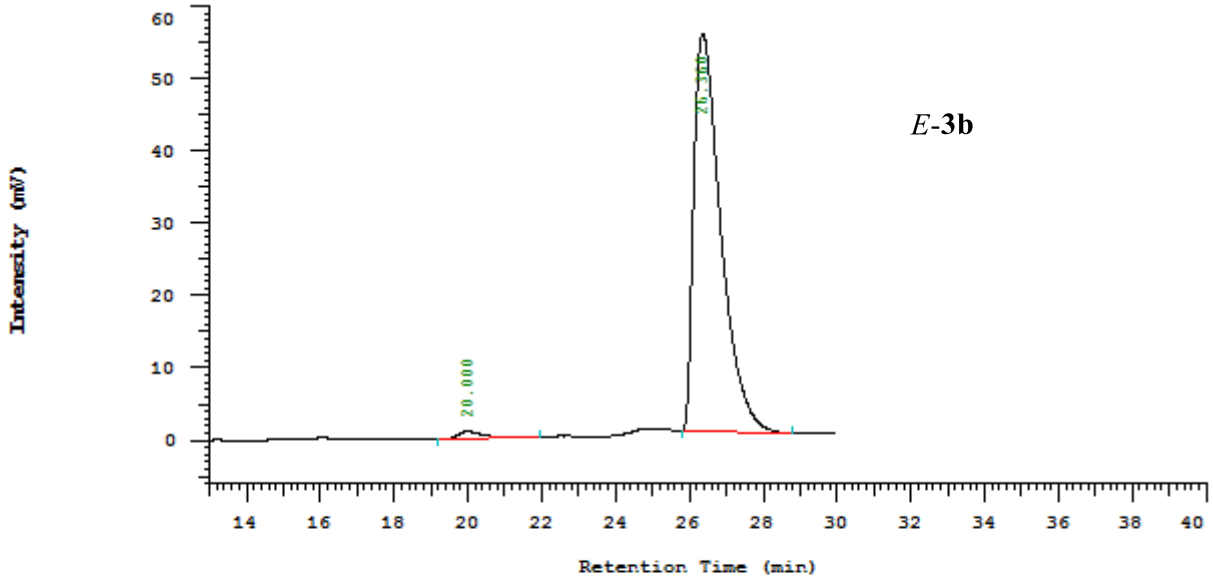

**4b**

**dimethyl (*S*)-(1-acetamido-2-(4-fluorophenyl)ethyl)phosphonate (4b).** >35.8 mg (>99% yield) of **4b** was obtained as colorless oil after purification with column chromatography on silica

gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee (*E*-**3b**), 35% ee (*Z*-**3b**), 92% ee (*E*-**3b**/*Z*-**3b** = 10/1) and 35% ee (*E*-**3b**/*Z*-**3b** = 1/1) were determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 26.4 min, $t_R$ (minor) = 20.0 min. $[\alpha]_D^{20}$ = 28.6 (*c* 3.5, $CH_2Cl_2$) (*E*-**3b**); $[\alpha]_D^{20}$ = -0.2 (*c* 3.3, $CH_2Cl_2$) (*Z*-**3b**); $[\alpha]_D^{30}$ = 26.5 (*c* 3.7, $CH_2Cl_2$) (*E*-**3b**/*Z*-**3b** = 10/1); $[\alpha]_D^{30}$ = 1.2 (*c* 3.2, $CH_2Cl_2$) (*E*-**3b**/*Z*-**3b** = 1/1). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.18 (m, 2H), 7.00 – 6.95 (m, 2H), 6.78 (d, *J* = 9.9 Hz, 1H), 4.80 – 4.70 (m, 1H), 3.76 (dd, *J* = 10.7, 3.5 Hz, 6H), 3.19 – 3.12 (m, 1H), 2.95 – 2.86 (m, 1H), 1.90 (d, *J* = 1.0 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.9 (d, *J* = 5.1 Hz), 161.8 (d, $J_{C-f}$ = 245.0 Hz), 132.2 (dd, *J* = 13.6, 3.3 Hz), 130.6 (d, *J* = 8.0 Hz), 115.3 (d, *J* = 21.3 Hz), 53.6 (d, $J_{C-p}$ = 6.9 Hz), 52.9 (d, $J_{C-p}$ = 7.0 Hz), 45.7 (d, $J_{C-p}$ = 156.2 Hz), 34.7 (d, $J_{C-p}$ = 3.4 Hz), 22.7; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.6. HRMS calc. for $C_{12}H_{18}FNO_4P$ $[M+H]^+$: 290.0952, found: 290.0956.

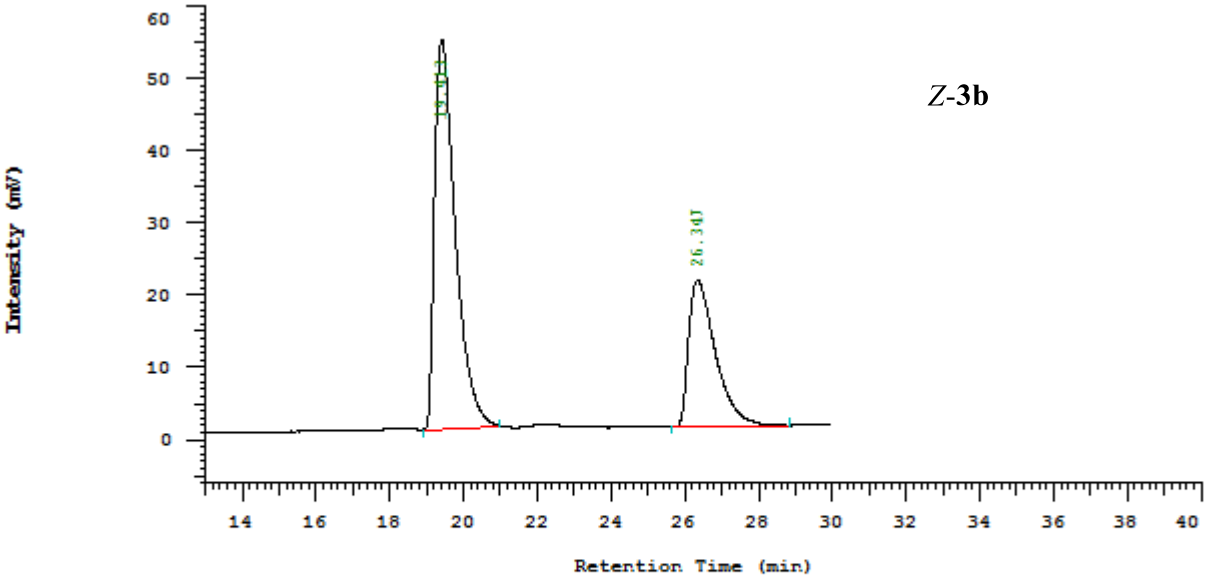



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 19.600 | 795448 | 49.532 |
| 2 | 26.487 | 810464 | 50.468 |
| | | 1605912 | 100.000 |



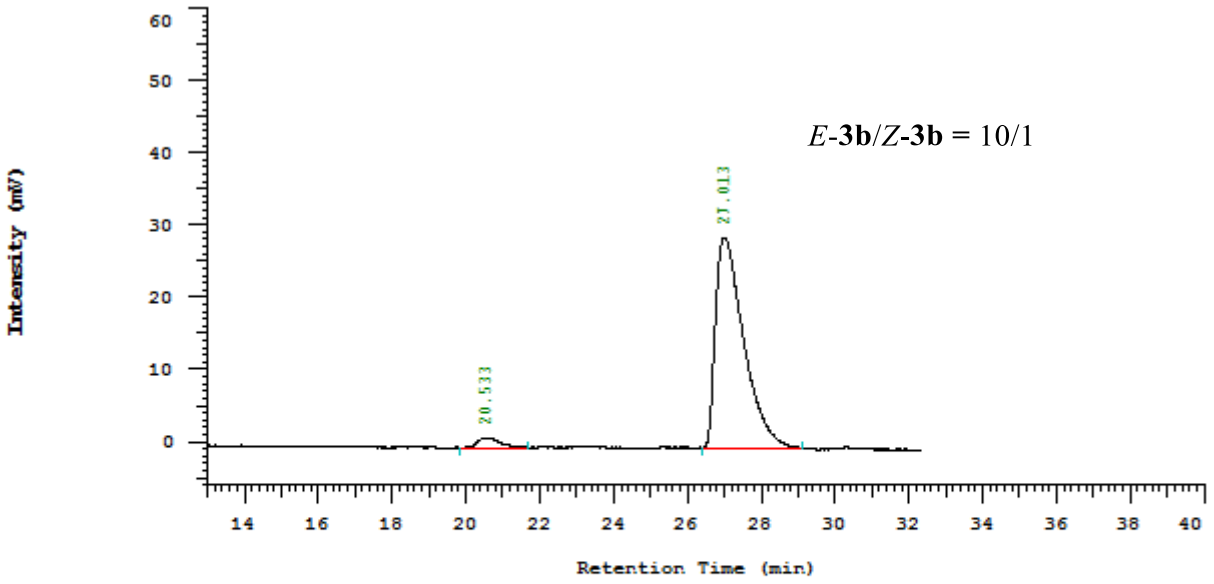

*E*-**3b**

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 20.000 | 46220 | 1.623 |
| 2 | 26.360 | 2801795 | 98.377 |
| | | 2848015 | 100.000 |



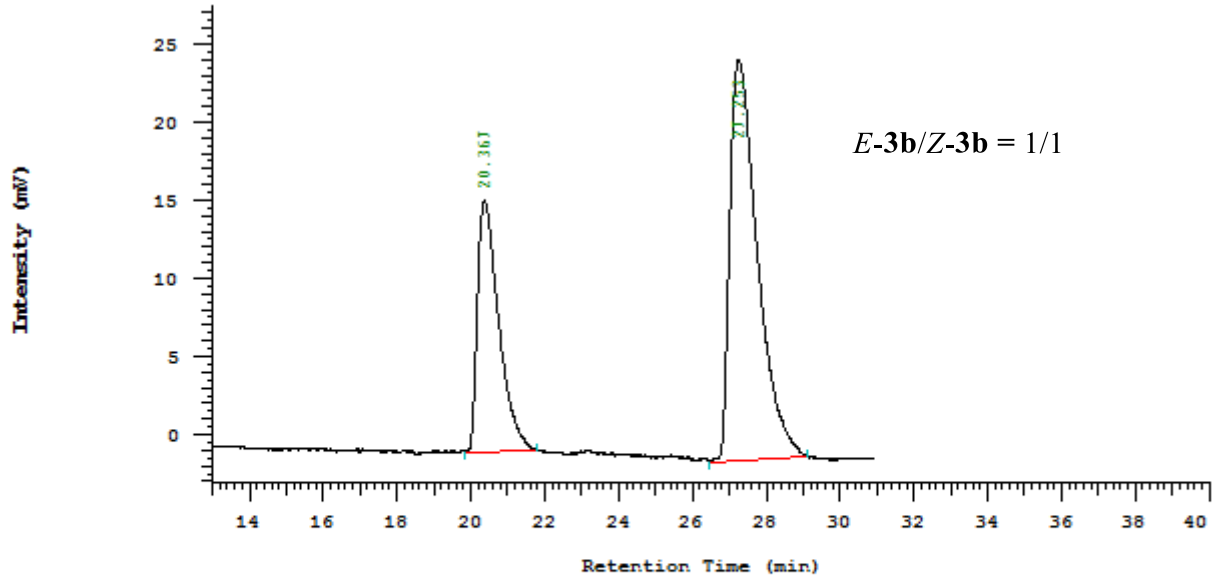

*Z*-**3b**

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 19.413 | 2098356 | 67.277 |
| 2 | 26.347 | 1020617 | 32.723 |
| | | 3118973 | 100.000 |



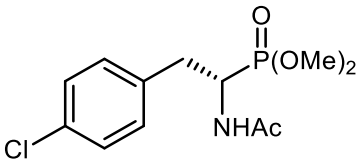

*E*-**3b**/*Z*-**3b** = 10/1

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 20.533 | 61942 | 3.839 |
| 2 | 27.013 | 1551640 | 96.161 |
| | | 1613582 | 100.000 |



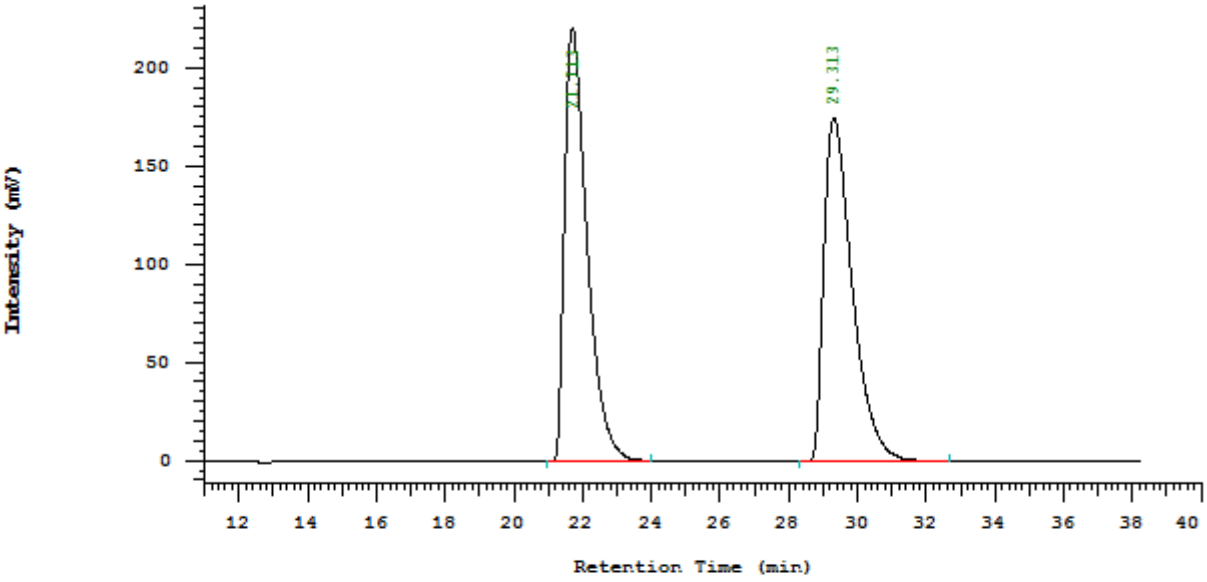

*E*-**3b**/*Z*-**3b** = 1/1

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 20.367 | 644990 | 32.654 |
| 2 | 27.253 | 1330250 | 67.346 |
| | | 1975240 | 100.000 |

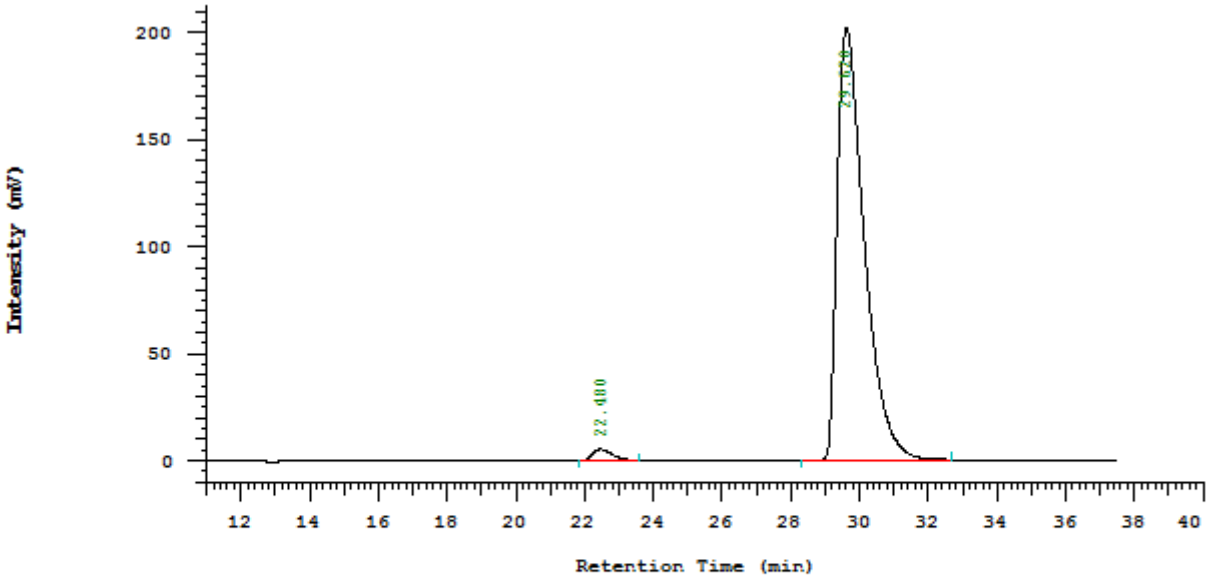



**4c**

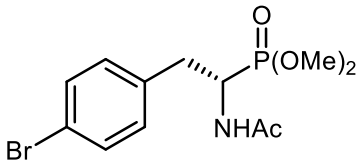
**dimethyl (*S*)-(1-acetamido-2-(4-chlorophenyl)ethyl)phosphonate (4c).** 38.1 mg (99% yield) of **4c** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 29.6 min, $t_R$ (minor) = 22.5 min. $[\alpha]_D^{20}$ = 22.6 (*c* 1.5, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.24 (m, 2H), 7.18 – 7.15 (m, 2H), 6.39 (d, *J* = 9.9 Hz, 1H), 4.82 – 4.71 (m, 1H), 3.76 (dd, *J* = 10.7, 5.3 Hz, 6H), 3.20 – 3.13 (m, 1H), 2.94 – 2.85 (m, 1H), 1.90 (d, *J* = 0.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.7 (d, $J_{C-p}$ = 5.0 Hz), 135.0 (d, $J_{C-p}$ = 13.3 Hz), 132.8, 130.4, 128.6, 53.5 (d, $J_{C-p}$ = 6.9 Hz), 52.9 (d, $J_{C-p}$ = 6.9 Hz), 45.4 (d, $J_{C-p}$ = 156.4 Hz), 34.9 (d, $J_{C-p}$ = 3.5 Hz), 22.8; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.4. HRMS calc. for $C_{12}H_{18}ClNO_4P$ $[M+H]^+$: 306.0656, found: 306.0661.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 21.713 | 10010366 | 49.925 |
| 2 | 29.313 | 10040403 | 50.075 |
| | | 20050769 | 100.000 |

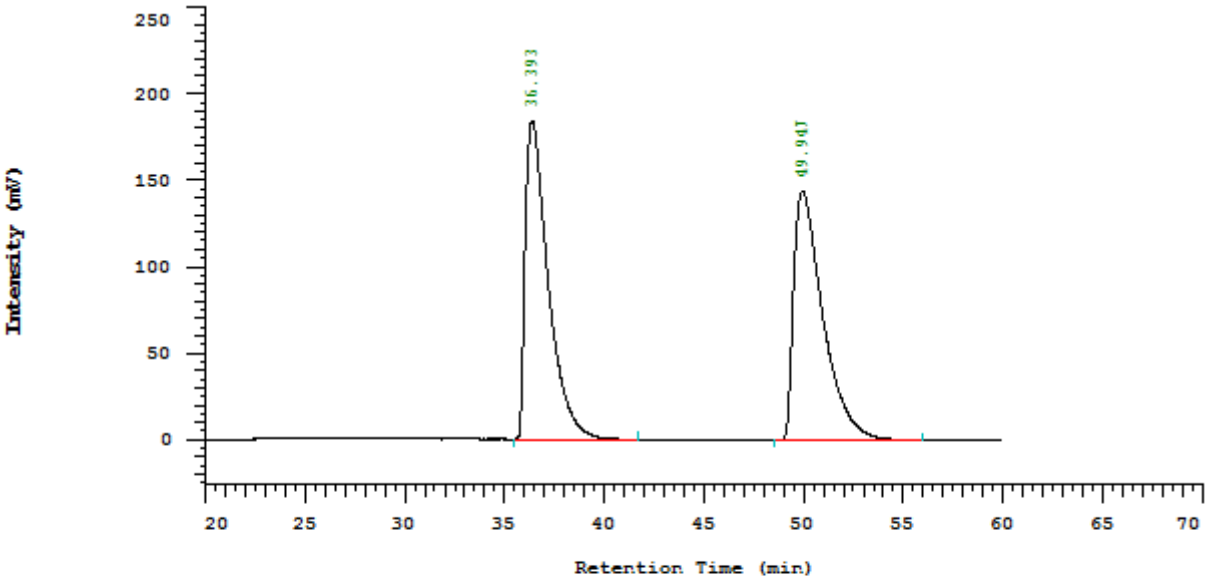



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 22.480 | 222705 | 1.973 |
| 2 | 29.620 | 11062199 | 98.027 |
| | | 11284904 | 100.000 |

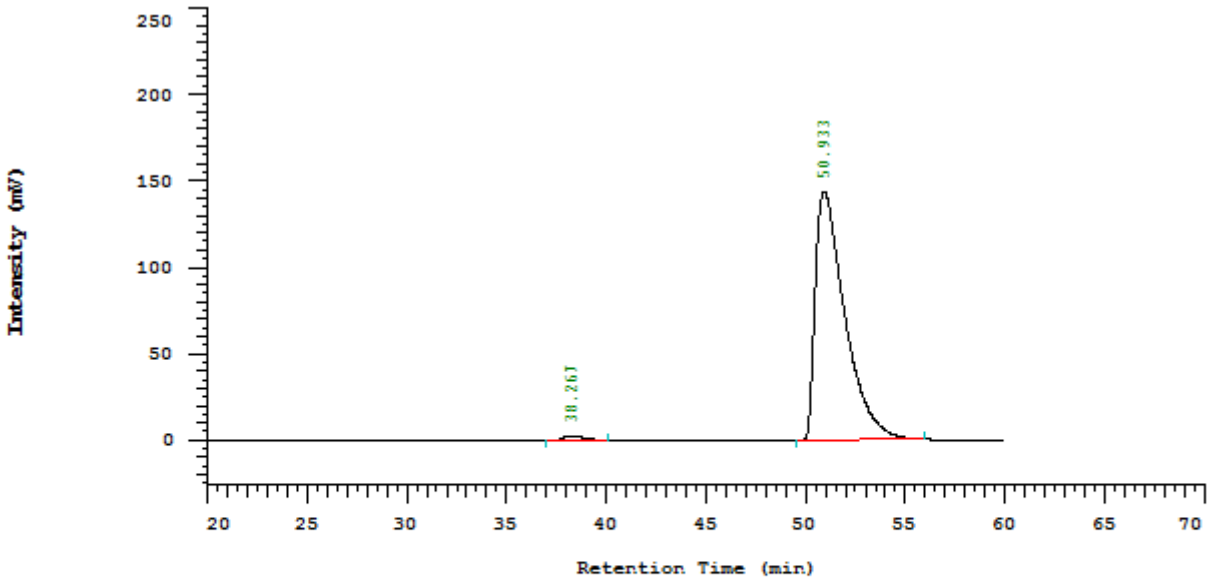



**4d**

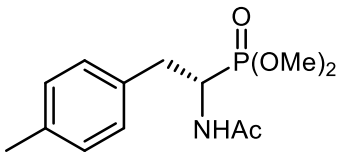
**dimethyl (*S*)-(1-acetamido-2-(4-bromophenyl)ethyl)phosphonate (4d).** 43.3 mg (>99% yield) of **4d** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 50.9 min, $t_R$ (minor) = 38.3 min. $[\alpha]_D^{20}$ = 27.0 (*c* 1.0, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.45 (d, *J* = 9.9 Hz, 1H), 4.81 – 4.71 (m, 1H), 3.76 (dd, *J* = 10.7, 5.5 Hz, 6H), 3.18 – 3.11 (m, 1H), 2.92 – 2.84 (m, 1H), 1.91 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.7 (d, $J_{C\text{-}p}$ = 4.9 Hz), 135.5 (d, $J_{C\text{-}p}$ = 13.3 Hz), 131.5, 130.8, 120.9, 53.5 (d, $J_{C\text{-}p}$ = 7.0 Hz), 52.9 (d, $J_{C\text{-}p}$ = 6.8 Hz), 45.3 (d, $J_{C\text{-}p}$ = 156.5 Hz), 35.0 (d, $J_{C\text{-}p}$ = 3.4 Hz), 22.8; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.4. HRMS calc. for $C_{12}H_{18}BrNO_4P$ $[M+H]^+$: 350.0151, found: 350.0156.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 36.393 | 14619170 | 50.110 |
| 2 | 49.947 | 14554735 | 49.890 |
| | | 29173905 | 100.000 |

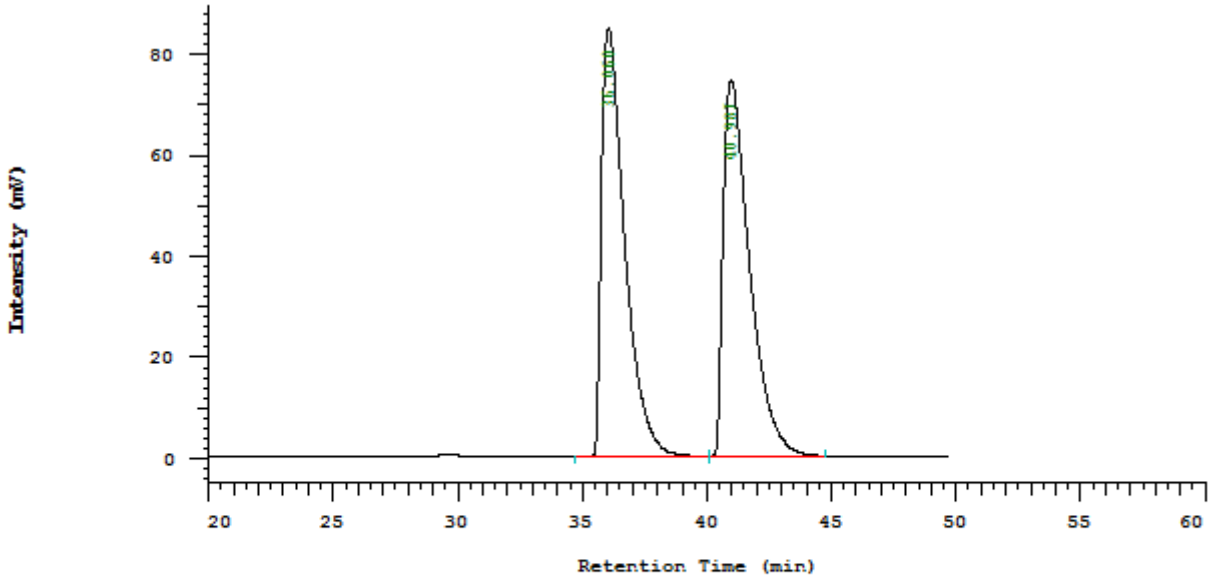



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 38.267 | 213050 | 1.427 |
| 2 | 50.933 | 14713550 | 98.573 |
| | | 14926600 | 100.000 |

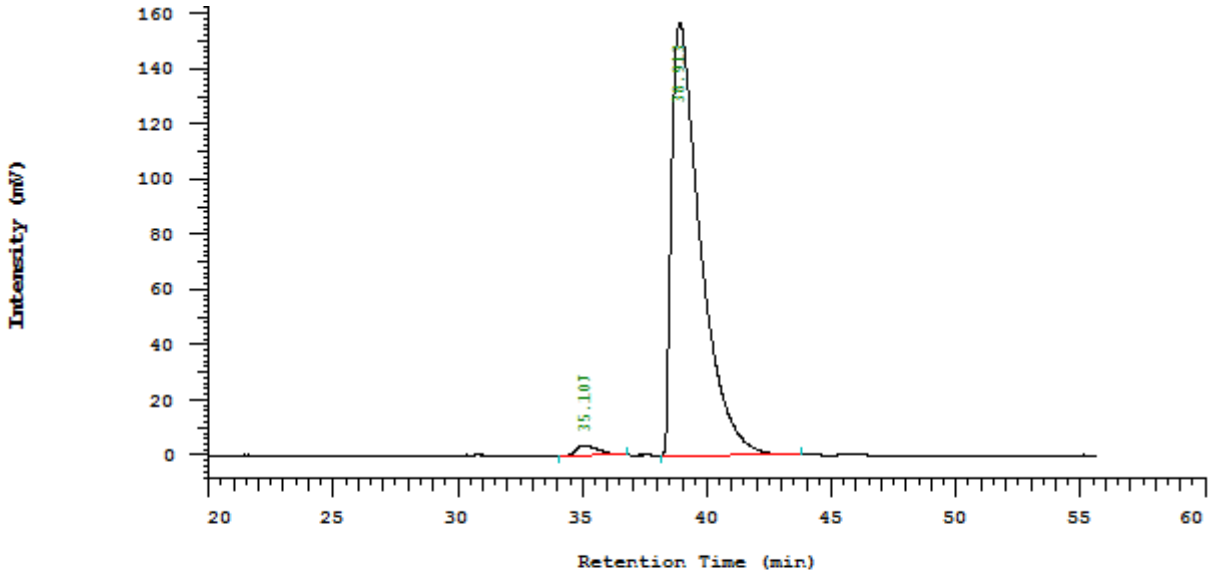



**4e**

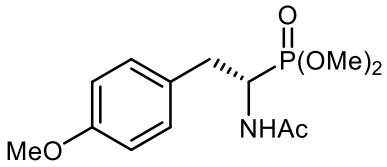
**dimethyl (*S*)-(1-acetamido-2-(p-tolyl)ethyl)phosphonate (4e).** 35.5 mg (>99% yield) of **4e** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 38.9 min, $t_R$ (minor) = 35.1 min. $[\alpha]_D^{20}$ = 29.3 (*c* 2.1, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.12 – 7.07 (m, 4H), 6.30 (d, *J* = 9.8 Hz, 1H), 4.82 – 4.72 (m, 1H), 3.75 (dd, *J* = 10.6, 3.0 Hz, 6H), 3.20 – 3.13 (m, 1H), 2.92 – 2.83 (m, 1H), 2.30 (s, 3H), 1.89 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.7 (d, $J_{C-p}$ = 4.9 Hz), 133.3 (d, $J_{C-p}$ = 13.2 Hz), 136.4, 129.2, 128.9, 53.4 (d, $J_{C-p}$ = 7.0 Hz), 52.9 (d, $J_{C-p}$ = 6.9 Hz), 45.7 (d, $J_{C-p}$ = 155.8 Hz), 35.1 (d, $J_{C-p}$ = 3.2 Hz), 22.9, 21.1; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.9. HRMS calc. for $C_{13}H_{21}NO_4P$ $[M+H]^+$: 286.1203, found: 286.1206.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 36.060 | 5484764 | 50.079 |
| 2 | 40.987 | 5467480 | 49.921 |
| | | 10952244 | 100.000 |

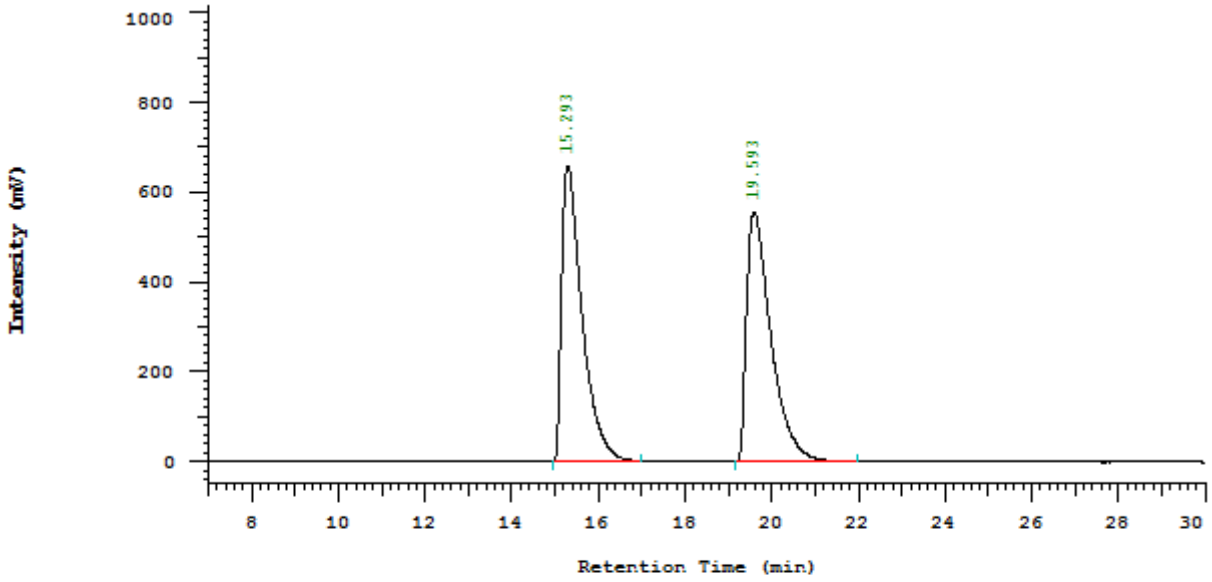



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 35.107 | 226529 | 1.768 |
| 2 | 38.913 | 12585378 | 98.232 |
| | | 12811907 | 100.000 |

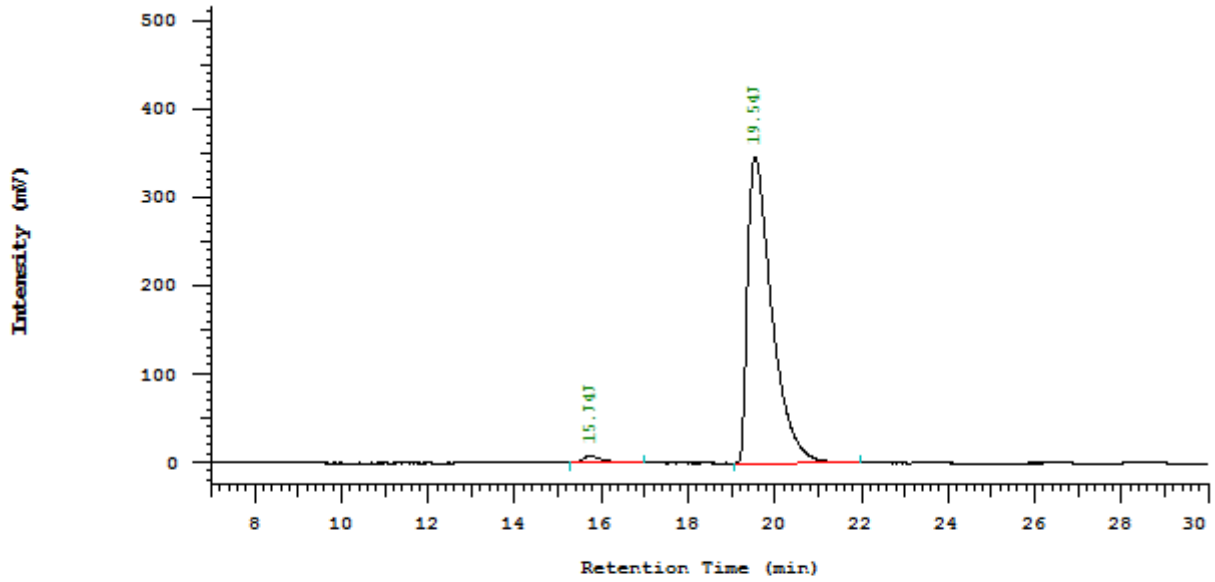



**4f**

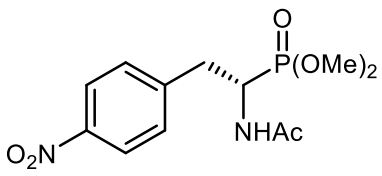
**dimethyl (*S*)-(1-acetamido-2-(4-methoxyphenyl)ethyl)phosphonate (4f).** 34.5 mg (99% yield) of **4f** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 19.5 min, $t_R$ (minor) = 15.7 min. $[\alpha]_D^{20}$ = 26.8 (*c* 1.7, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 6.25 (d, *J* = 9.9 Hz, 1H), 4.80 – 4.70 (m, 1H), 3.78 (s, 3H), 3.75 (dd, *J* = 10.7, 3.5 Hz, 6H), 3.18 – 3.11 (m, 1H), 2.91 – 2.82 (m, 1H), 1.90 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.6 (d, $J_{C\text{-}p}$ = 5.0 Hz), 158.5, 130.1, 128.3 (d, $J_{C\text{-}p}$ = 13.1 Hz), 113.9, 55.2, 53.4 (d, $J_{C\text{-}p}$ = 7.0 Hz), 52.9 (d, $J_{C\text{-}p}$ = 6.8 Hz), 45.8 (d, $J_{C\text{-}p}$ = 155.5 Hz), 34.7 (d, $J_{C\text{-}p}$ = 3.2 Hz), 22.9; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.9. HRMS calc. for $C_{13}H_{21}NO_5P$ $[M+H]^+$: 302.1152, found: 302.1158.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 15.293 | 21667425 | 49.848 |
| 2 | 19.593 | 21799559 | 50.152 |
| | | 43466984 | 100.000 |



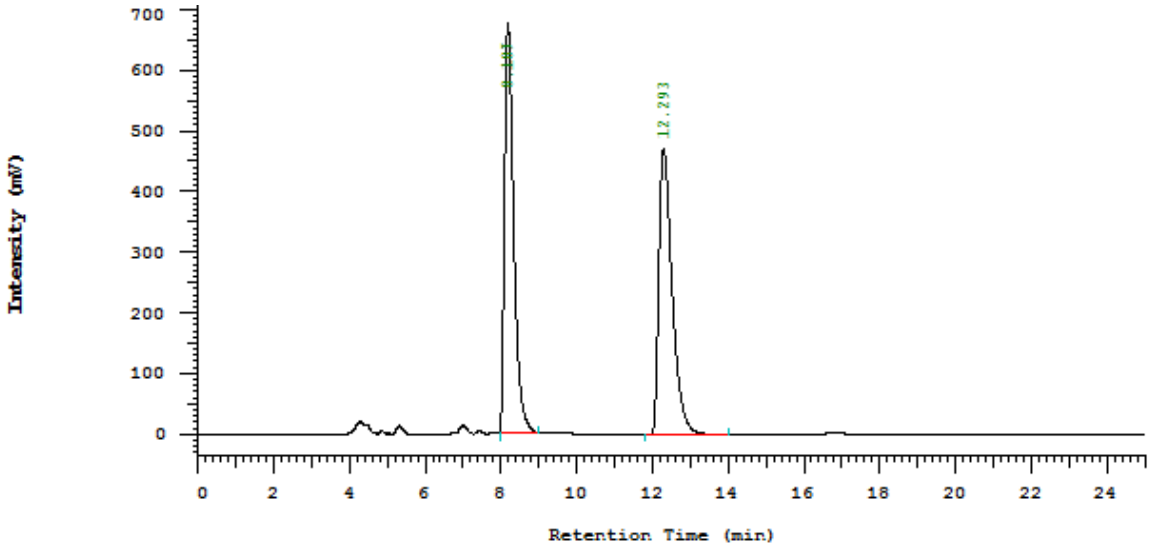

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 15.747 | 244220 | 1.783 |
| 2 | 19.547 | 13450058 | 98.217 |
| | | 13694278 | 100.000 |



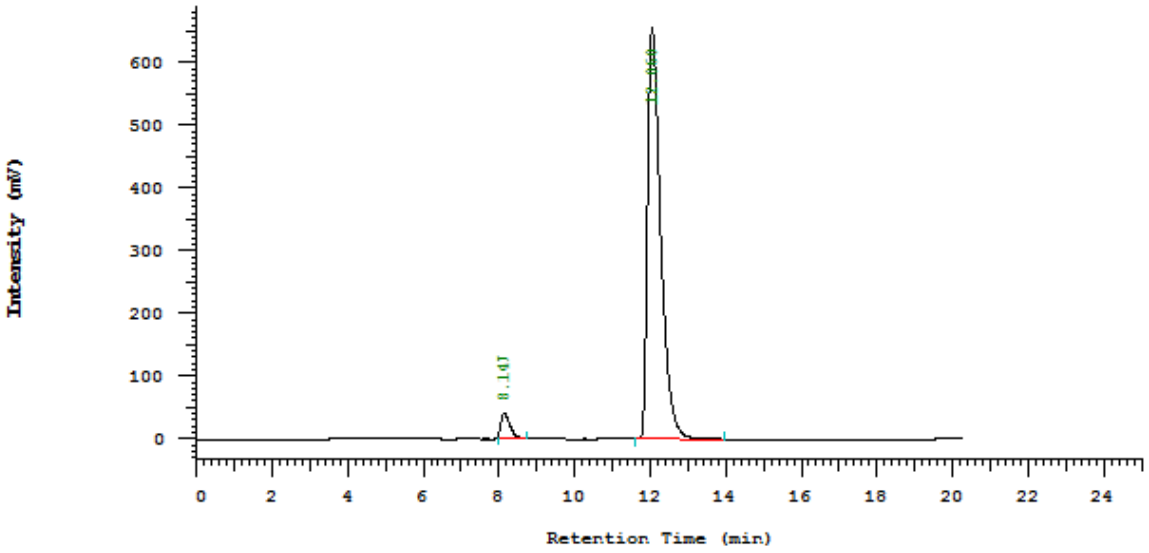

**4g**

**dimethyl (*S*)-(1-acetamido-2-(4-nitrophenyl)ethyl)phosphonate (4g).** 37.7 mg (96% yield) of **4g** was obtained as a white solid after purification with column chromatography on silica

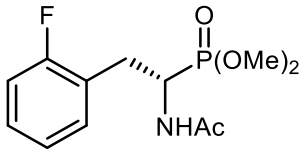
gel (hexanes/EtOAc/methanol, 1/1/0.1). M.p.: 146 – 148 ℃. >92% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 12.1 min, $t_R$ (minor) = 8.1 min. $[\alpha]_D^{20}$ = 37.9 (*c* 1.3, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 6.69 (d, *J* = 9.8 Hz, 1H), 4.88 – 4.78 (m, 1H), 3.79 (t, *J* = 11.0 Hz, 6H), 3.32 – 3.25 (m, 1H), 3.08 – 2.99 (m, 1H), 1.91 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.8 (d, $J_{C\text{-}p}$ = 5.1 Hz), 147.1, 144.4 (d, $J_{C\text{-}p}$ = 13.8 Hz), 130.0, 123.6, 53.8 (d, $J_{C\text{-}p}$ = 7.0 Hz), 53.0 (d, $J_{C\text{-}p}$ = 7.1 Hz), 45.2 (d, $J_{C\text{-}p}$ = 157.4 Hz), 35.5 (d, $J_{C\text{-}p}$ = 3.7 Hz), 22.8; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 25.8. HRMS calc. for $C_{12}H_{18}N_2O_6P$ $[M+H]^+$: 317.0897, found: 317.0899.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 8.187 | 11400752 | 49.779 |
| 2 | 12.293 | 11501806 | 50.221 |
| | | 22902558 | 100.000 |

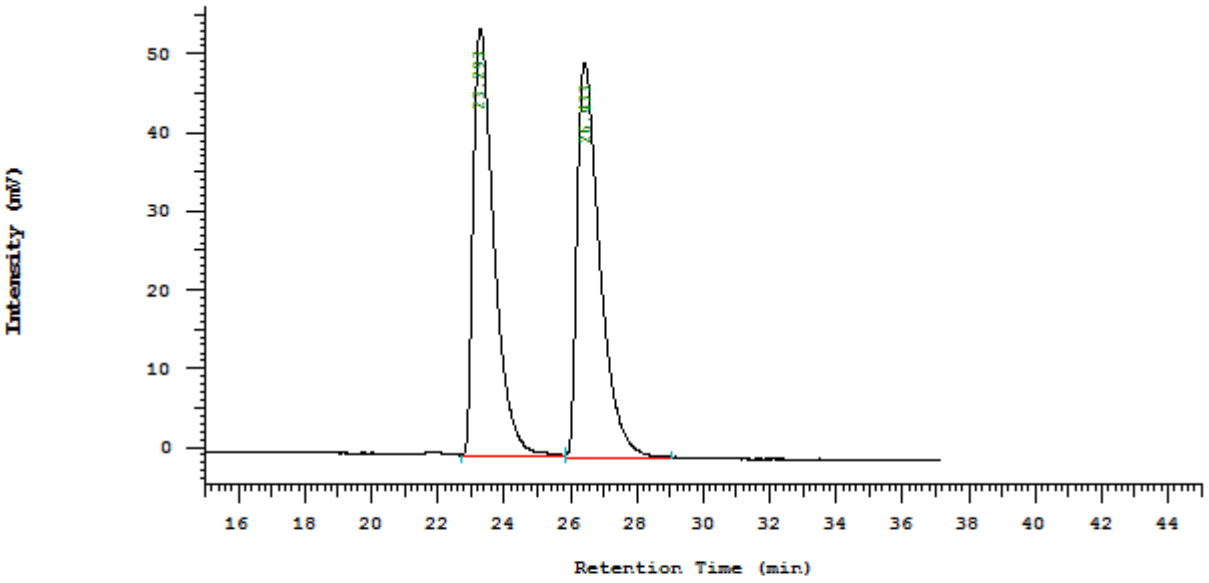



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 8.147 | 651047 | 3.961 |
| 2 | 12.060 | 15786295 | 96.039 |
| | | 16437342 | 100.000 |

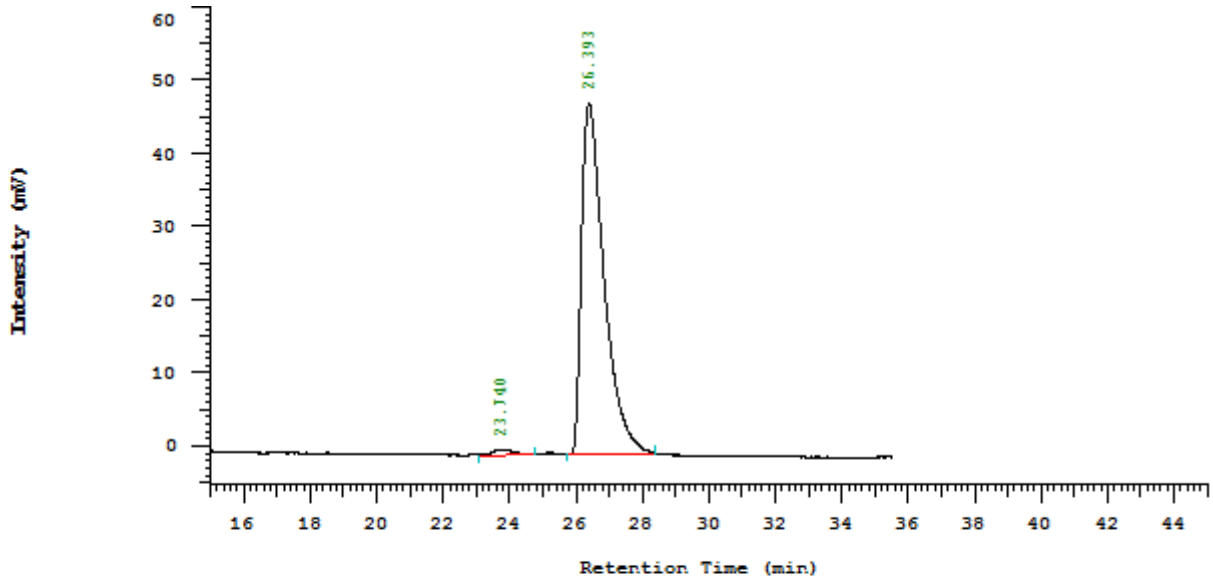



**4h**

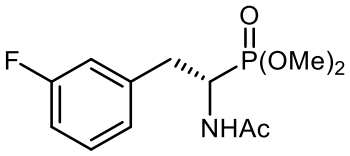
**dimethyl (*S*)-(1-acetamido-2-(2-fluorophenyl)ethyl)phosphonate (4h).** 35.9 mg (99% yield) of **4h** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 26.4 min, $t_R$ (minor) = 23.7 min. $[\alpha]_D^{20}$ = 25.6 (*c* 1.7, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.19 (m, 2H), 7.09 – 6.99 (m, 2H), 6.34 (d, *J* = 9.8 Hz, 1H), 4.83 – 4.72 (m, 1H), 3.78 (dd, *J* = 10.6, 8.4 Hz, 6H), 3.22 – 3.16 (m, 1H), 3.04 – 2.95 (m, 1H), 1.89 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.6 (d, $J_{C-p}$ = 4.9 Hz), 161.3 (d, $J_{C-f}$ = 244.7 Hz), 131.3 (d, *J* = 4.3 Hz), 128.8 (d, *J* = 8.2 Hz), 124.2 (d, *J* = 3.5 Hz), 123.9 – 123.3 (m), 115.2 (d, *J* = 22.2 Hz), 53.5 (d, $J_{C-p}$ = 7.0 Hz), 53.0 (d, $J_{C-p}$ = 6.8 Hz), 45.1 (d, $J_{C-p}$ = 156.4 Hz), 28.9 (dd, *J* = 4.0, 1.7 Hz). 22.8; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.2. HRMS calc. for $C_{12}H_{18}FNO_4P$ $[M+H]^+$: 290.0952, found: 290.0959.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 23.293 | 2373859 | 49.980 |
| 2 | 26.433 | 2375728 | 50.020 |
| | | 4749587 | 100.000 |



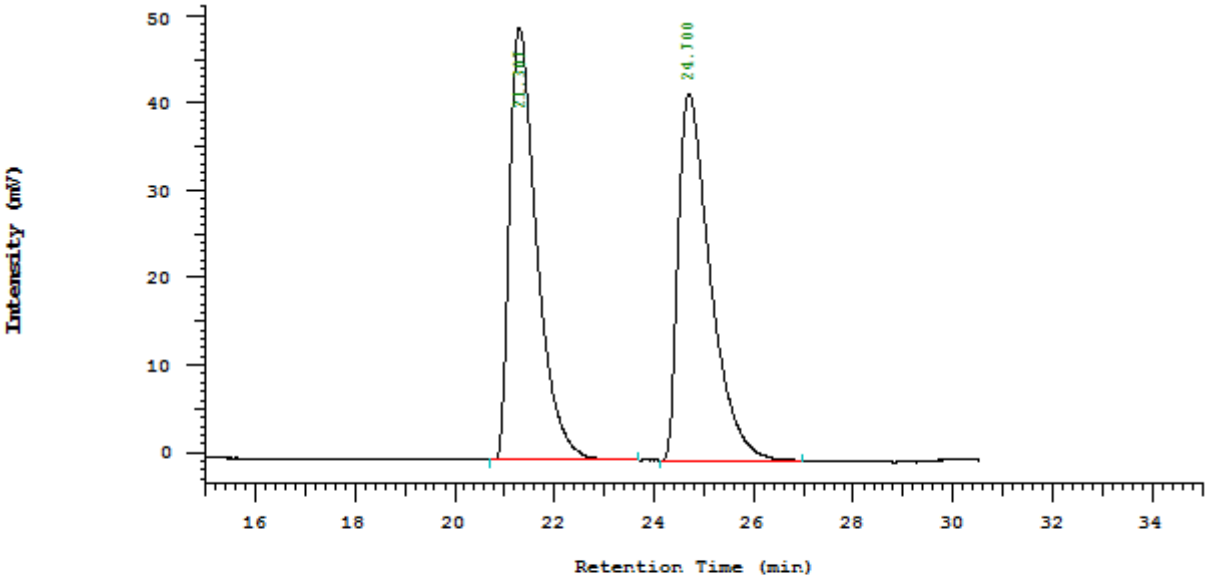

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 23.740 | 31439 | 1.377 |
| 2 | 26.393 | 2251619 | 98.623 |
| | | 2283058 | 100.000 |



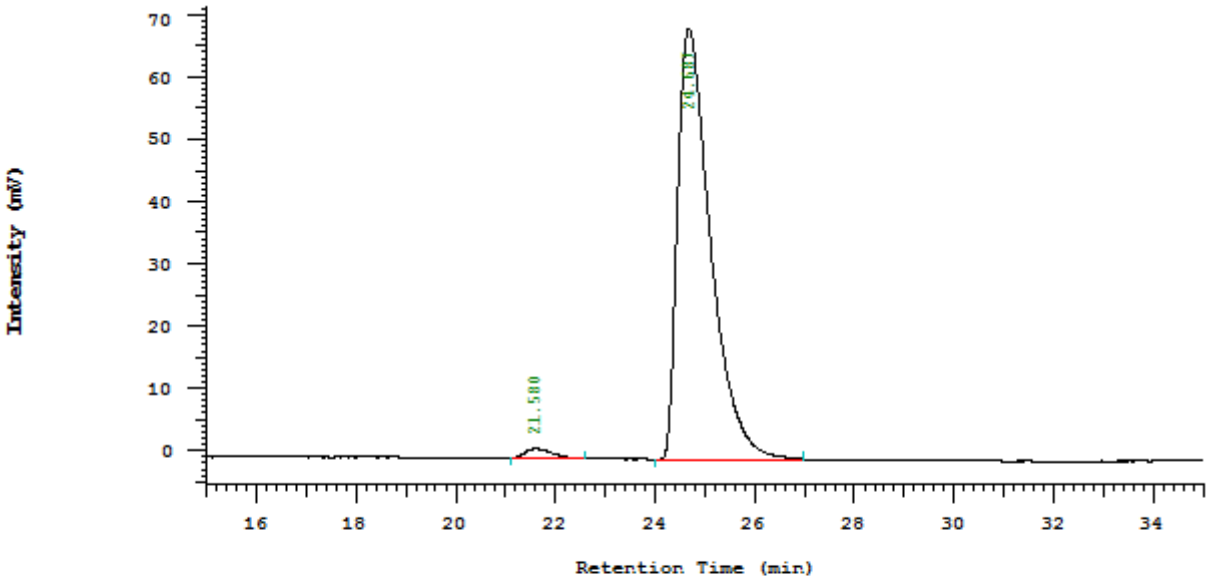

**4i**

**dimethyl (*S*)-(1-acetamido-2-(3-fluorophenyl)ethyl)phosphonate (4i).** 35.8 mg (99% yield) of **4i** was obtained as colorless oil after purification with column chromatography on silica

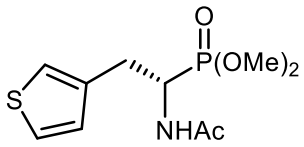
gel (hexanes/EtOAc/methanol, 1/1/0.1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 24.7 min, $t_R$ (minor) = 21.6 min. $[\alpha]_D^{20}$ = 29.9 (*c* 2.0, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 1H), 7.03 – 6.90 (m, 3H), 6.63 (d, *J* = 9.8 Hz, 1H), 4.82 – 4.72 (m, 1H), 3.77 (dd, *J* = 10.7, 8.3 Hz, 6H), 3.22 – 3.15 (m, 1H), 2.97 – 2.88 (m, 1H), 1.91 (d, *J* = 0.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.8 (d, $J_{C-p}$ = 5.0 Hz), 162.7 (d, $J_{C-f}$ = 245.8 Hz), 139.1 (dd, *J* = 13.7, 7.4 Hz), 129.9 (d, *J* = 8.3 Hz), 124.7 (d, *J* = 2.8 Hz), 116.2 (d, *J* = 21.4 Hz), 113.8 (d, *J* = 21.0 Hz), 53.6 (d, $J_{C-p}$ = 7.0 Hz), 52.9 (d, *J* = 6.9 Hz), 45.5 (d, $J_{C-p}$ = 156.7 Hz), 35.3, 22.8; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.3. HRMS calc. for $C_{12}H_{18}FNO_4P$ $[M+H]^+$: 290.0952, found: 290.0951.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 21.307 | 1879968 | 49.918 |
| 2 | 24.700 | 1886151 | 50.082 |
| | | 3766119 | 100.000 |

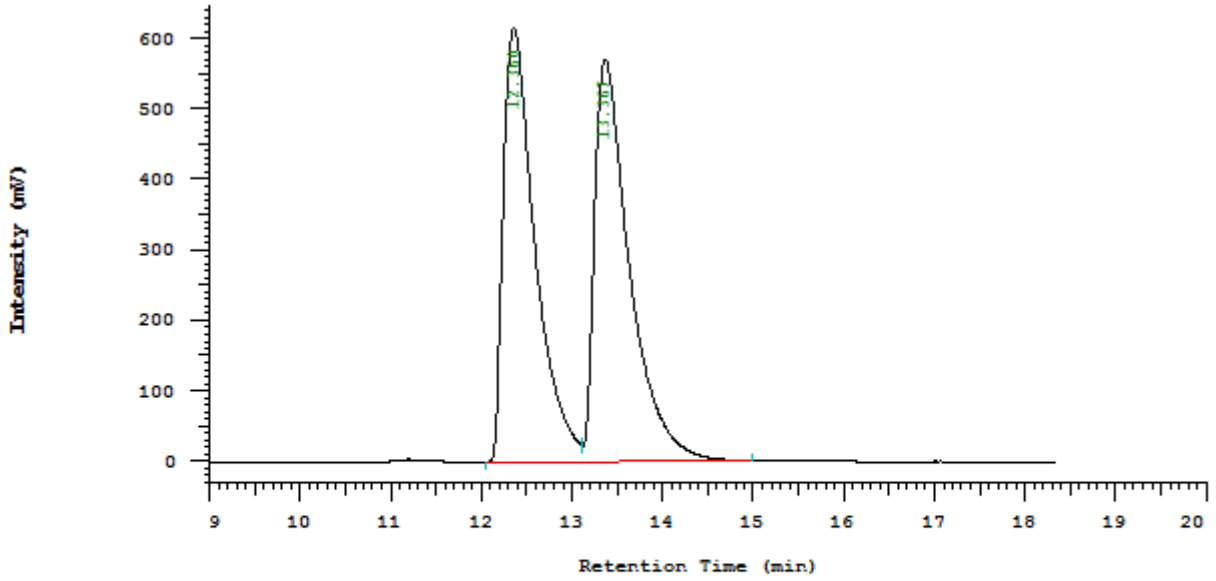



| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 21.580 | 61272 | 1.889 |
| 2 | 24.687 | 3183118 | 98.111 |
| | | 3244390 | 100.000 |

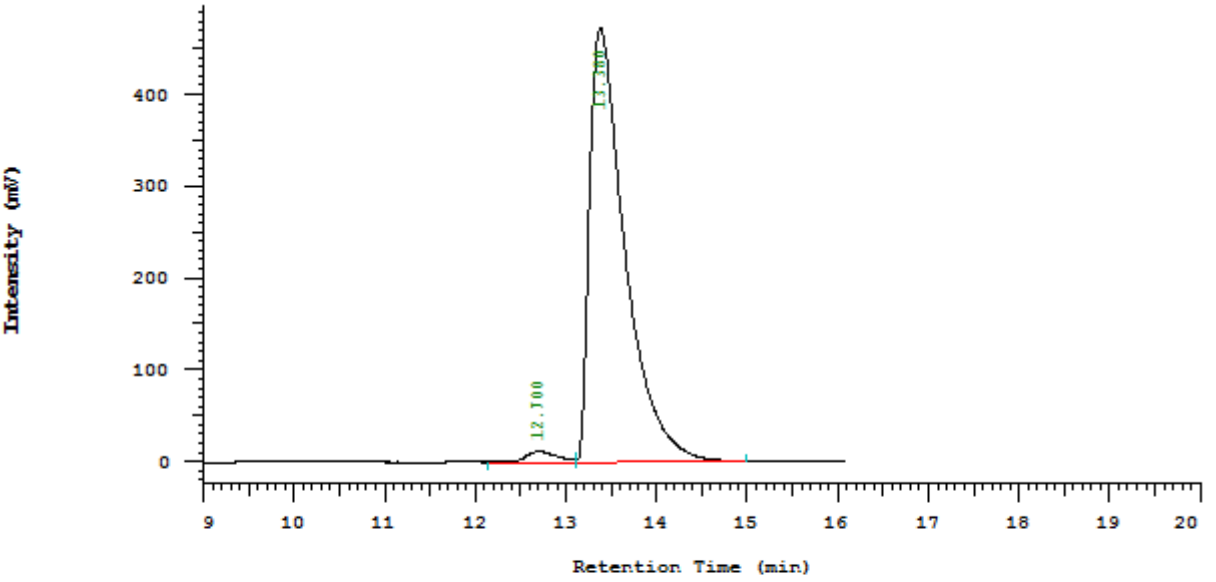



**4j**

**dimethyl (*S*)-(1-acetamido-2-(thiophen-3-yl)ethyl)phosphonate (4j).** 33.7 mg (99% yield) of **4j** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 13.4 min, $t_R$ (minor) = 12.7 min. $[\alpha]_D^{20}$ = 19.8 (*c* 1.6, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.25 (m, 1H), 7.07 (d, *J* = 1.7 Hz, 1H), 6.97 (d, *J* = 4.9 Hz, 1H), 6.39 (d, *J* = 9.7 Hz, 1H), 4.84 – 4.74 (m, 1H), 3.75 (dd, *J* = 10.7, 3.6 Hz, 6H), 3.22 – 3.15 (m, 1H), 3.05 – 2.96 (m, 1H), 1.93 (d, *J* = 0.5 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.8 (d, $J_{C-p}$ = 4.9 Hz), 136.6 (d, $J_{C-p}$ = 13.9 Hz), 128.3, 125.8, 122.3, 53.5 (d, $J_{C-p}$ = 7.0 Hz), 52.9 (d, $J_{C-p}$ = 6.9 Hz), 45.1 (d, $J_{C-p}$ = 156.5 Hz), 30.2 (d, $J_{C-p}$ = 3.6 Hz), 22.9; $^{31}$P NMR (162 MHz, $CDCl_3$) δ 26.6. HRMS calc. for $C_{10}H_{17}NO_4PS$ $[M+H]^+$: 278.0610, found: 278.0615.



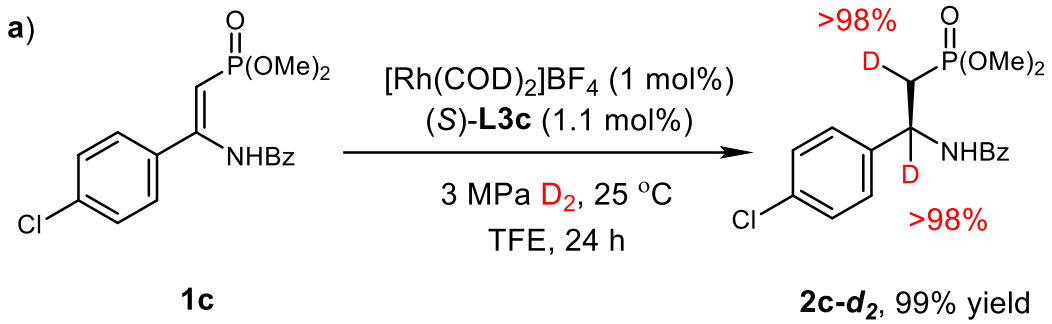

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 12.360 | 14938968 | 49.351 |
| 2 | 13.367 | 15331816 | 50.649 |
| | | 30270784 | 100.000 |




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 12.700 | 268212 | 2.041 |
| 2 | 13.380 | 12871025 | 97.959 |
| | | 13139237 | 100.000 |

## III. Deuterium Labelling Experiments

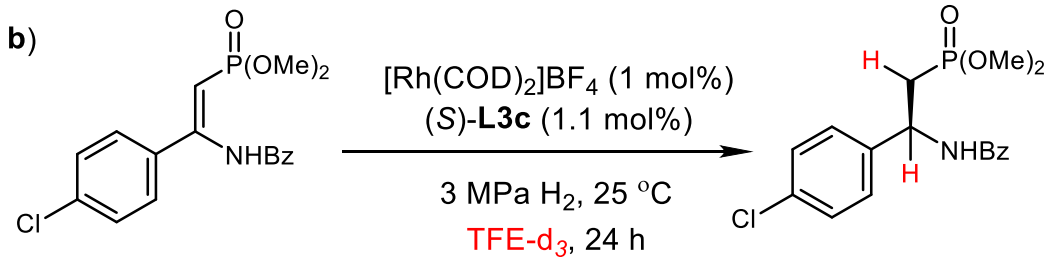
The reactions were conducted according to the general asymmetric hydrogenation procedure.




**1c** **2c-*d*$_2$**, 99% yield

The reactions using $D_2$ as hydrogen source was conducted, and fully deuterated product was observed.

**dimethyl ((1*S*)-2-benzamido-2-(4-chlorophenyl) ethyl-1,2-*d2*) phosphonate** (**2c-*d*$_2$**). 45.8 mg (99% yield) of **2c-*d*$_2$** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). $^1$H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.53 – 7.29 (m, 7H), 3.72 (d, *J* = 10.8 Hz, 3H), 3.46 (d, *J* = 10.9 Hz, 3H), 2.40 (d, *J* = 17.5 Hz, 1H).



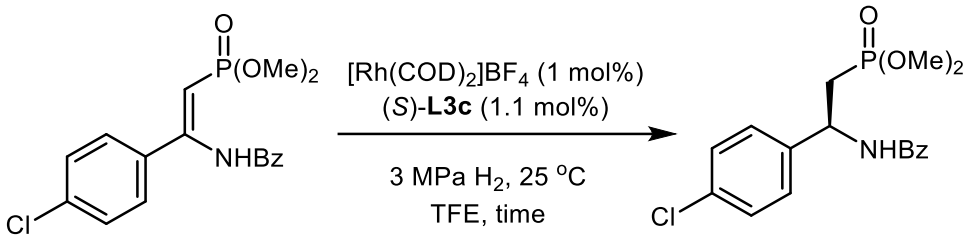

**1c** **2c**, 99% yield

The reactions using TFE-*d*$_3$ as solvent was conducted, and no deuterated product was observed.

**dimethyl (*S*)-(2-benzamido-2-(4-chlorophenyl)ethyl)phosphonate (2c)**. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.3 Hz, 1H), 7.93 – 7.91 (m, 2H), 7.53 – 7.42 (m, 3H), 7.33 – 7.31 (m, 4H), 5.55 (dq, *J* = 26.3, 6.6 Hz, 1H), 3.72 (d, *J* = 11.0 Hz, 3H), 3.46 (d, *J* = 11.1 Hz, 3H), 2.40 (dt, *J* = 17.2, 6.0 Hz, 2H).

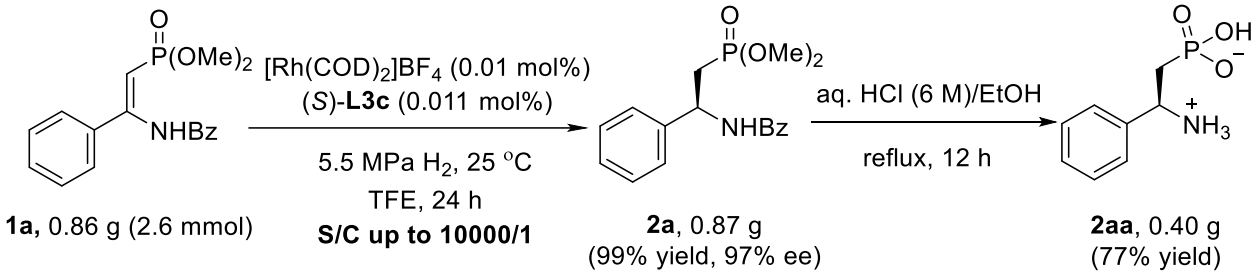
## IV. Monitoring the Ees along with the Reaction Process

In a nitrogen-filled glovebox, a stainless steel autoclave was charged with $[Rh(COD)_2]BF_4$ (0.00125mmol, 0.01 equiv), (S)-**L3c** (0.001375mmol, 0.011 equiv) in 1.0 mL of a degassed TFE. After stirring for 60 min at room temperature, the reaction mixture was added to a mixture of the substrate (**1c**) (0.125 mmol, 1 equiv) in 1.0 mL of the same solvent, and the hydrogenation was performed at 25 ℃ under $H_2$ pressure of 3 MPa for indicated time. After indicated time, the hydrogen was slowly released and the reaction solvent was evaporated. The residue was purified by flash column chromatography to determine the yields and ee values of the product **2c**.

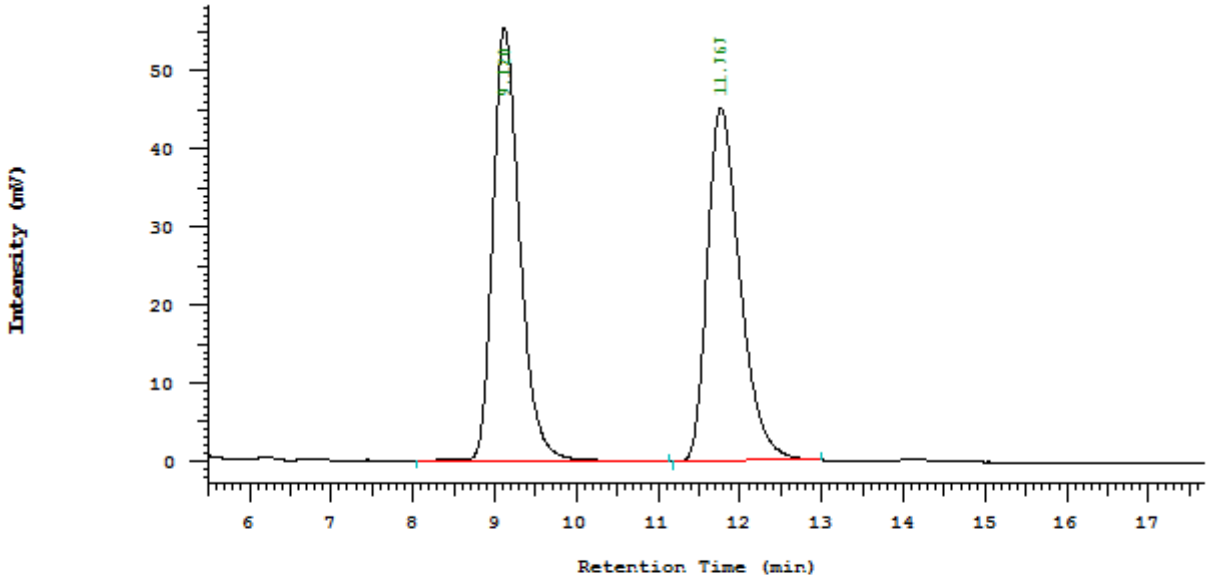



| Time (h) | Yield (%) | Ee (%) |
|---|---|---|
| 0.5 | 6 | 96 |
| 1.5 | 20 | 96 |
| 3 | 38 | 96 |
| 5 | 56 | 96 |
| 9 | 85 | 96 |
| 12 | 94 | 96 |
| 16 | 99 | 96 |
| 20 | 99 | 96 |
| 24 | 99 | 96 |

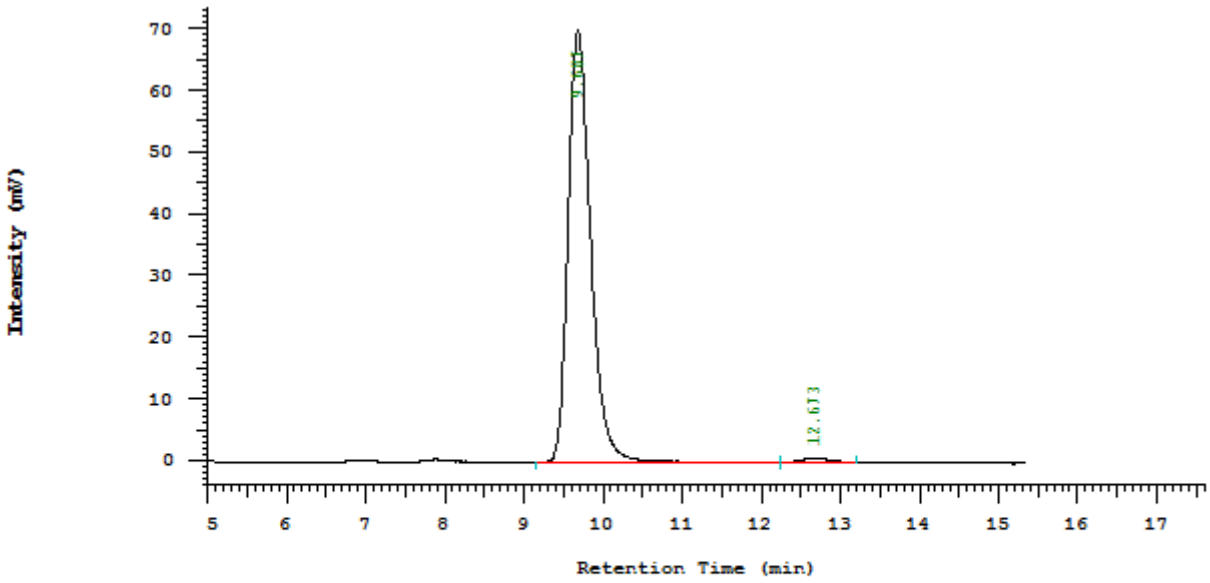
## V. Gram-scale Reaction and Synthetic Transformations




In a nitrogen-filled glovebox, a stainless steel autoclave was charged with $[Rh(COD)_2]BF_4$ (0.0026mmol, 1.0 mg), (S)-**L3c** (0.00286mmol, 2.0 mg) in 1.0 mL of a degassed TFE. After stirring for 60 min at room temperature, 0.1 ml of the reaction mixture was added to the substrate **1a** (2.60 mmol, 0.86 g) in 1.9 mL of the same solvent, and the hydrogenation was performed at 25 ℃ under $H_2$ pressure of 5.5 MPa for 24 h. Then the hydrogen was slowly released and the reaction solvent was evaporated. 0.87 g (99% yield) of **2a** was obtained as a white solid after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 97% ee was determined by chiral HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80/20, 0.8 mL/min, 254 nm, 40 °C): $t_R$ (major) = 9.7 min, $t_R$ (minor) = 12.7 min.



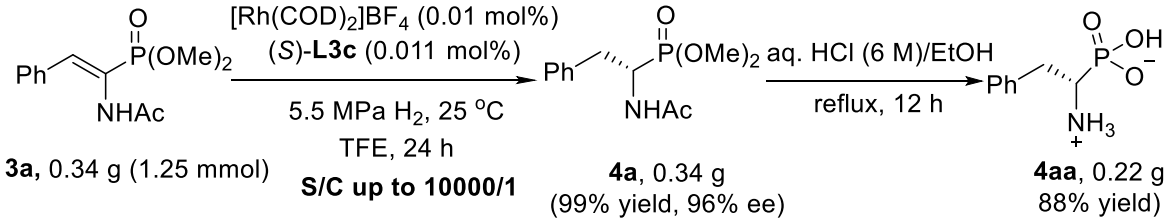

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 9.120 | 1286773 | 50.474 |
| 2 | 11.767 | 1262622 | 49.526 |
| | | 2549395 | 100.000 |



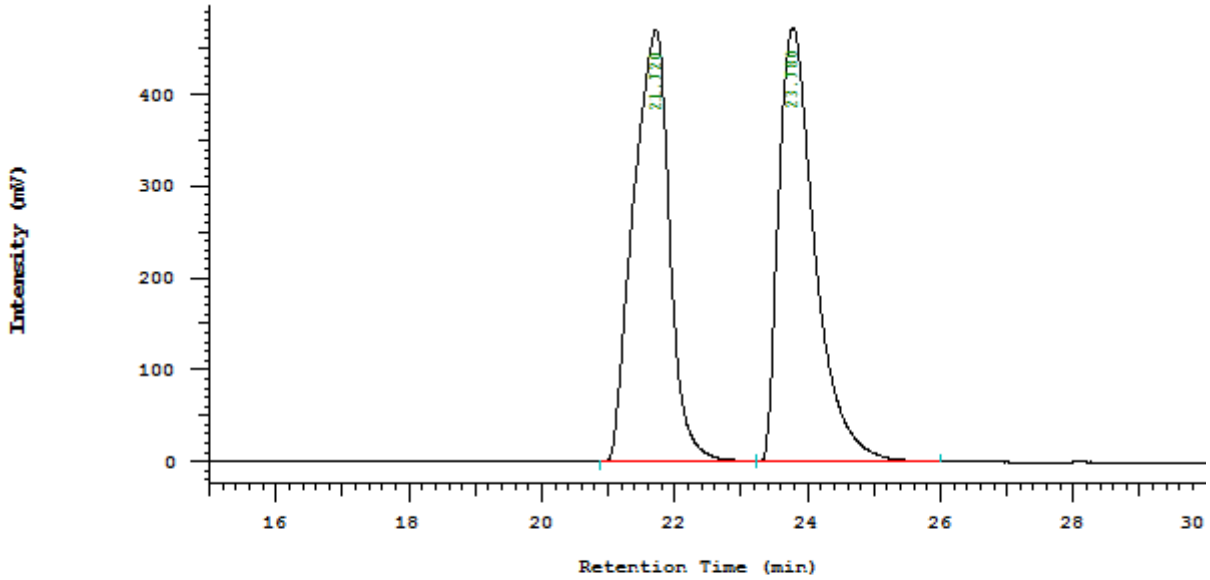

| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 9.687 | 1390440 | 98.687 |
| 2 | 12.673 | 18495 | 1.313 |
| | | 1408935 | 100.000 |

The above hydrogenated product **4a** (0.87 g, 2.6 mmol) was added to 20 mL of a mixed solution of hydrochloric acid (6 M) and ethanol (v/v = 1/1), and then placed in an oil bath at 110 °C for heating and refluxing for 12 hours. After the completion of the reaction was monitored by TLC, the reaction solution was cooled to room temperature, and ethanol and part of hydrogen chloride were removed under reduced pressure. To the aqueous solution of the product, 10 mL of ethyl acetate was added to extract organic

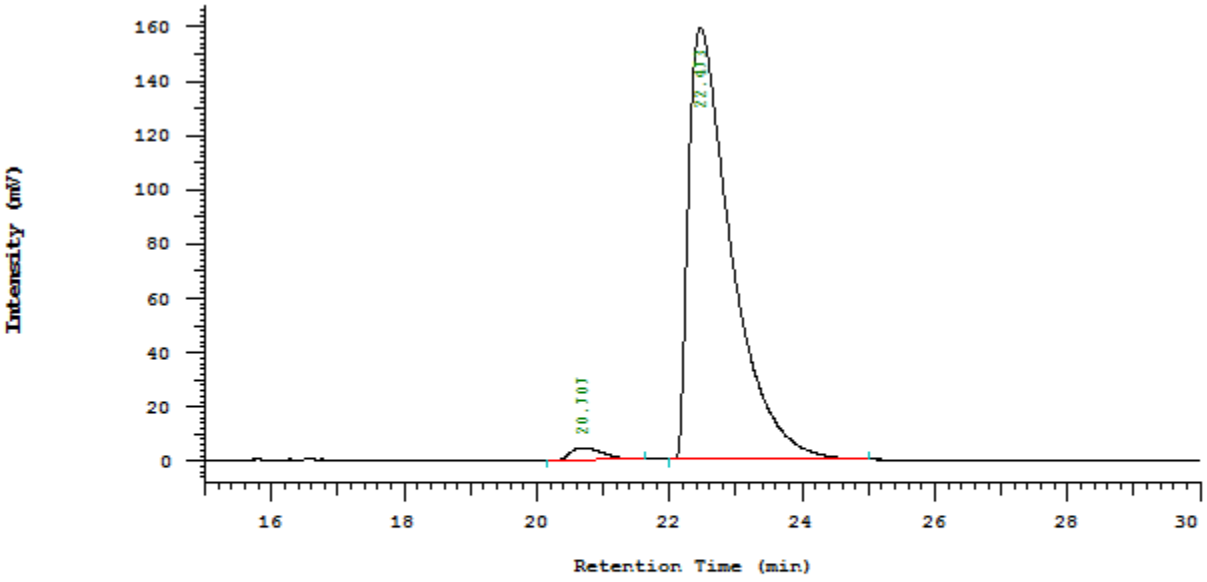
impurities, and the aqueous phase was retained (the hydrolyzed product was slightly soluble in ethyl acetate). The extraction and purification were repeated three times, and the water was removed by a rotary evaporator to obtain a white solid. The resulting solid hydrogenated product was placed in an oven at 105°C for 12 hours to remove excess impurities. Finally, pure chiral aminophosphonic acid compounds **2aa** was obtained. **(*S*)-hydrogen (2-ammonio-2-phenylethyl) phosphonate** (**2aa**)[8] 0.40 g (77% yield) of **2aa** was obtained as a white solid without further purification. M.p.: 178 – 180 °C. $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 8.92 – 8.91 (m, 1H), 7.91 – 7.89 (m, 1H), 7.58 – 7.22 (m, 7H), 5.37 – 5.32 (m, 1H), 2.49 – 2.27 (m, 1H), 2.07 – 1.97 (m, 1H); $^{31}$P NMR (162 MHz, DMSO-$d_6$) δ 22.1.




In a nitrogen-filled glovebox, a stainless steel autoclave was charged with $[Rh(COD)_2]BF_4$ (0.00125mmol, 0.5 mg), (S)-**L3c** (0.001375mmol, 1.0 mg) in 1.0 mL of a degassed TFE. After stirring for 60 min at room temperature, 0.1 ml of the reaction mixture was added to the substrate **3a** (1.25 mmol, 0.34 g) in 1.9 mL of the same solvent, and the hydrogenation was performed at 25 ℃ under $H_2$ pressure of 5.5 MPa for 24 h. Then the hydrogen was slowly released and the reaction solvent was evaporated. 0.34 g (99% yield) of **4a** was obtained as colorless oil after purification with column chromatography on silica gel (hexanes/EtOAc/methanol, 1/1/0.1). 96% ee was determined by chiral HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, 0.8 mL/min, 220 nm, 40 °C): $t_R$ (major) = 22.5 min, $t_R$ (minor) = 20.7 min.




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 21.720 | 17840172 | 49.872 |
| 2 | 23.780 | 17931500 | 50.128 |
| | | 35771672 | 100.000 |




| No. | RT | Area | Conc 1 |
|---|---|---|---|
| 1 | 20.707 | 156706 | 2.158 |
| 2 | 22.473 | 7106197 | 97.842 |
| | | 7262903 | 100.000 |

The above hydrogenated product **4a** (0.34 g, 1.25 mmol) was added to 20 mL of a mixed solution of hydrochloric acid (6 M) and ethanol (v/v = 1/1), and then placed in an oil bath at 110 °C for heating and refluxing for 12 hours. After the completion of the reaction was monitored by TLC, the reaction solution was cooled to room temperature, and ethanol and part of hydrogen chloride were removed under reduced

pressure. To the aqueous solution of the product, 10 mL of ethyl acetate was added to extract organic impurities, and the aqueous phase was retained (the hydrolyzed product was slightly soluble in ethyl acetate). The extraction and purification were repeated three times, and the water was removed by a rotary evaporator to obtain a white solid. The resulting solid hydrogenated product was placed in an oven at 105℃ for 12 hours to remove excess impurities. Finally, pure chiral aminophosphonic acid compounds **4aa** was obtained. **(*S*)-hydrogen (1-ammonio-2-phenylethyl) phosphonate** (**4aa**).[9] 0.22 g (88% yield) of **4aa** was obtained as a white solid without further purification. M.p.: 186 – 188 ºC. $[\alpha]_D^{20}$ = 35.0 (*c* 2.0, 1 M aq. NaOH). $^1$H NMR (400 MHz, Deuterium Oxide with 1 drop 30%NaOD) δ 7.42 – 7.02 (m, 5H), 3.13 (ddd, *J* = 14.0, 5.3, 2.6 Hz, 1H), 2.78 (td, *J* = 11.7, 2.6 Hz, 1H), 2.52 – 2.31 (m, 1H); $^{13}$C NMR (101 MHz, Deuterium Oxide with 1 drop 30%NaOD) δ 141.2 (d, *J* = 15.3 Hz), 129.3, 128.5, 126.1, 52.1 (d, *J* = 138.5 Hz), 38.1; $^{31}$P NMR (162 MHz, Deuterium Oxide with 1 drop 30%NaOD) δ 20.3.

## VI. References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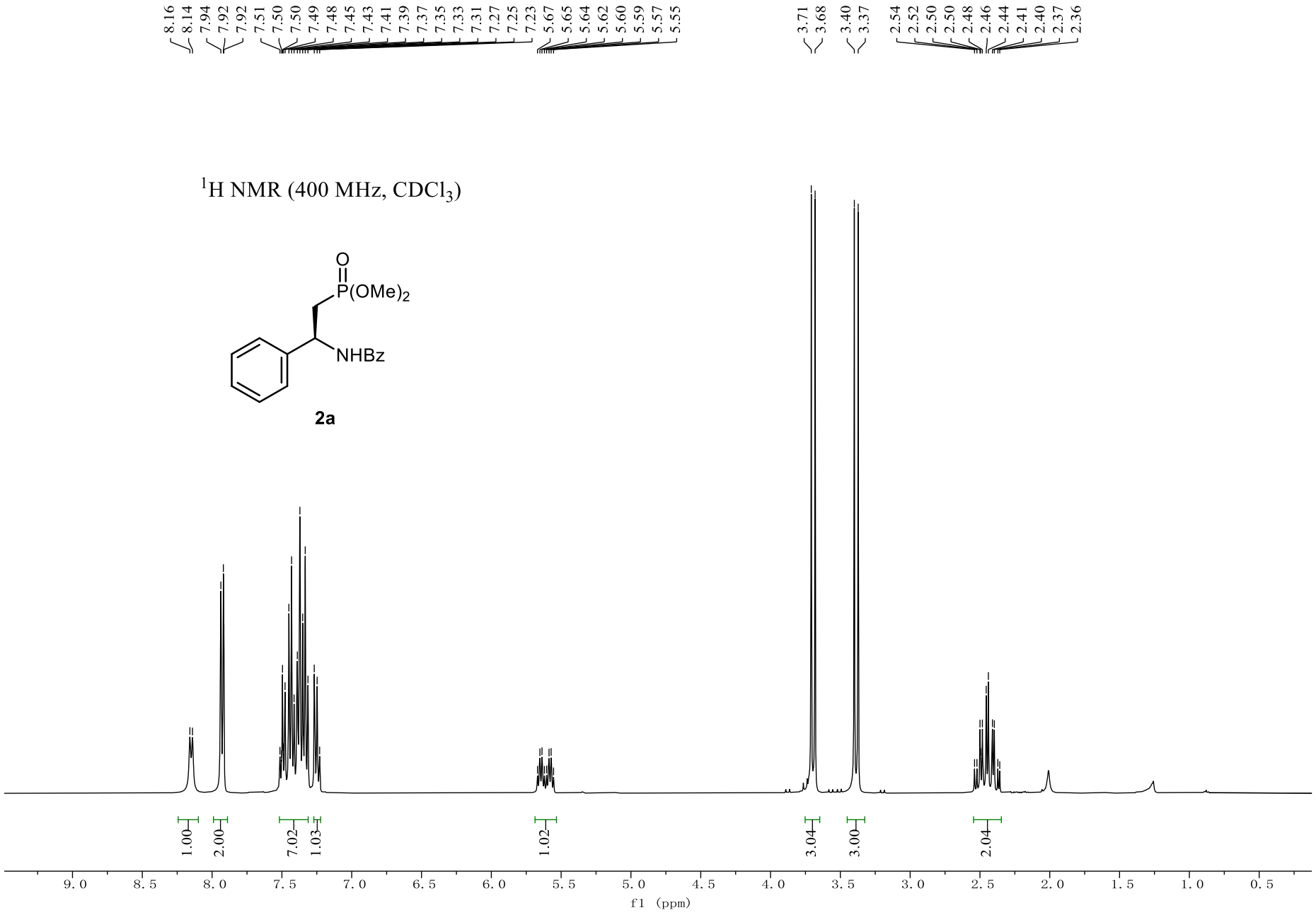
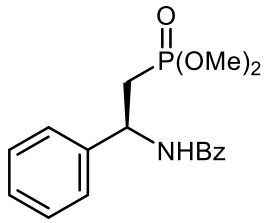
## VII. NMR Spectra


8.16
8.14
7.94
7.92
7.92
7.51
7.50
7.50
7.49
7.48
7.45
7.43
7.41
7.39
7.37
7.35
7.33
7.31
7.27
7.25
7.23
5.67
5.65
5.64
5.62
5.60
5.59
5.57
5.55
3.71
3.68
3.40
3.37
2.54
2.52
2.50
2.50
2.48
2.46
2.44
2.41
2.40
2.37
2.36
$^1$H NMR (400 MHz, $CDCl_3$)
O
P(OMe)2
NHBz
2a
1.00
2.00
7.02
1.03
1.02
3.04
3.00
2.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

166.43
141.21
141.16
133.98
131.63
128.68
128.62
127.55
127.19
126.03
52.47
52.43
52.38
52.35
48.70
48.67
31.99
31.20

$^{13}$C NMR (176 MHz, $CDCl_{3)}$

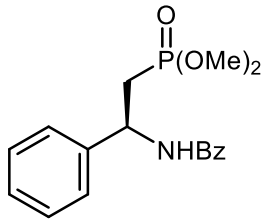



**2a**

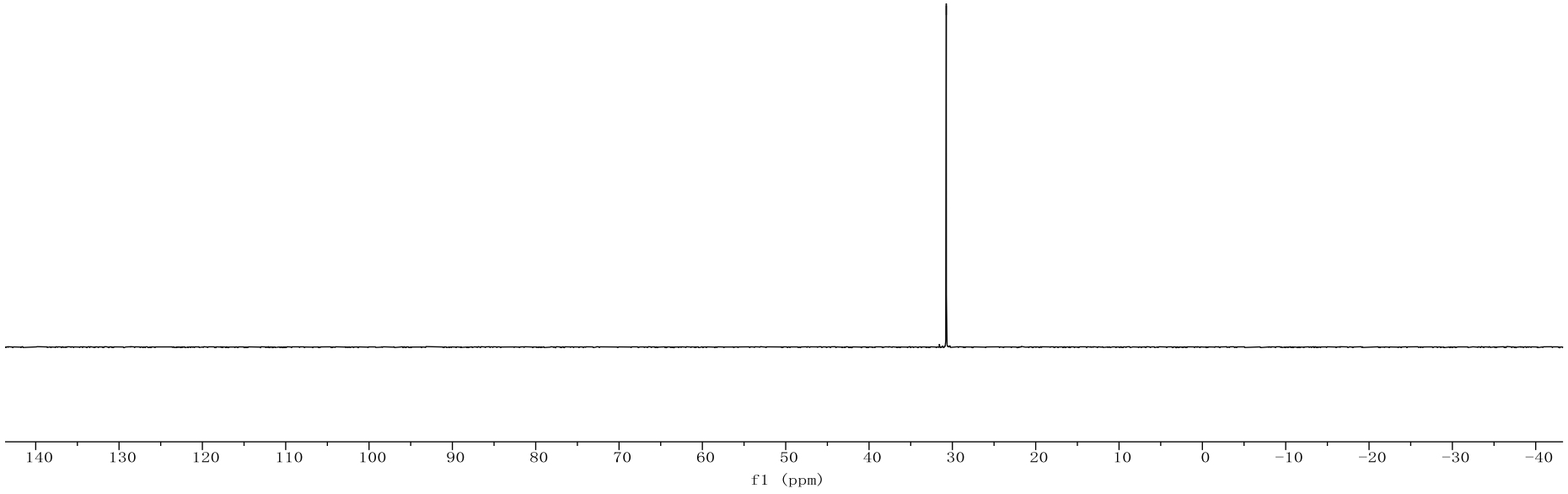


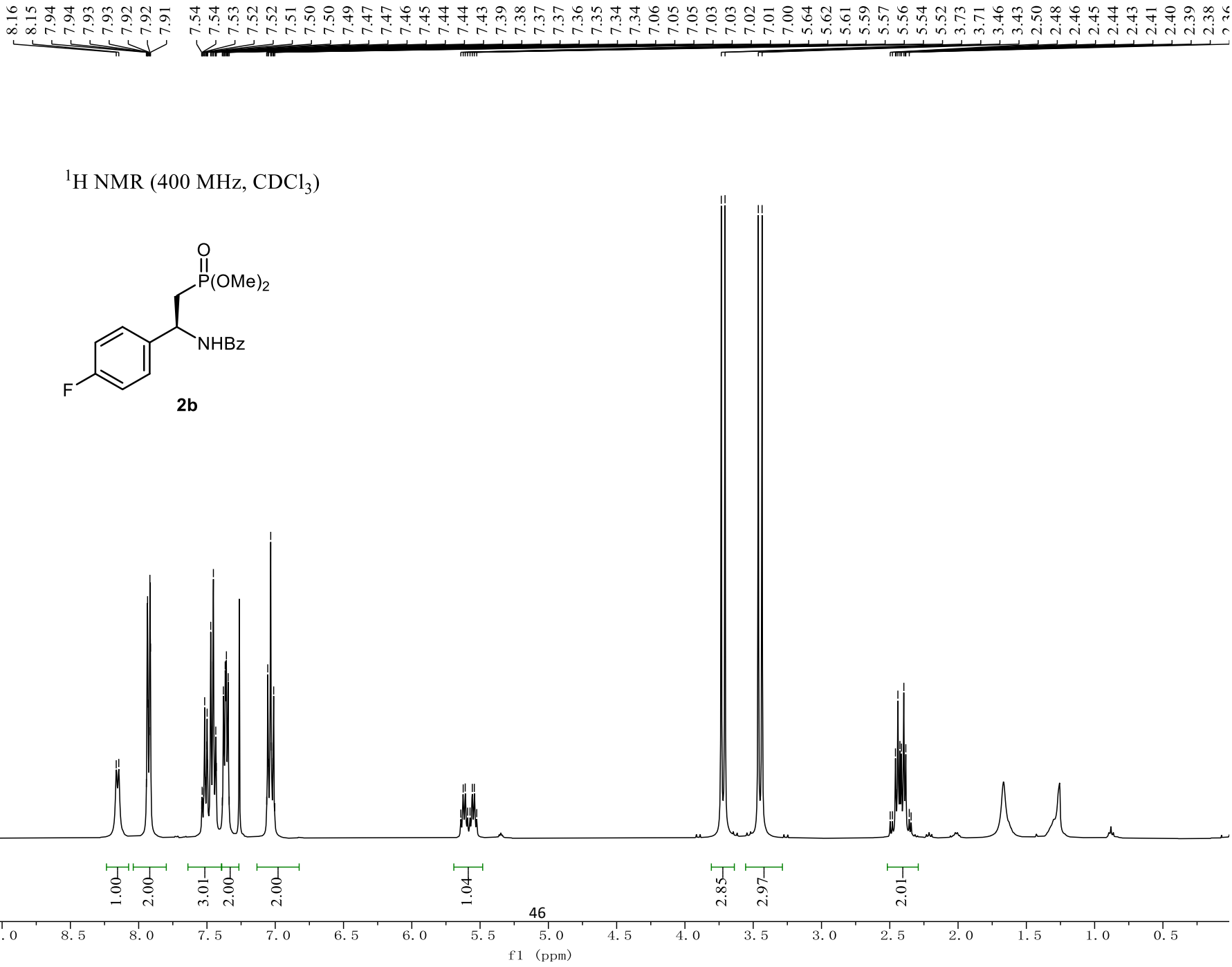
f1 (ppm)

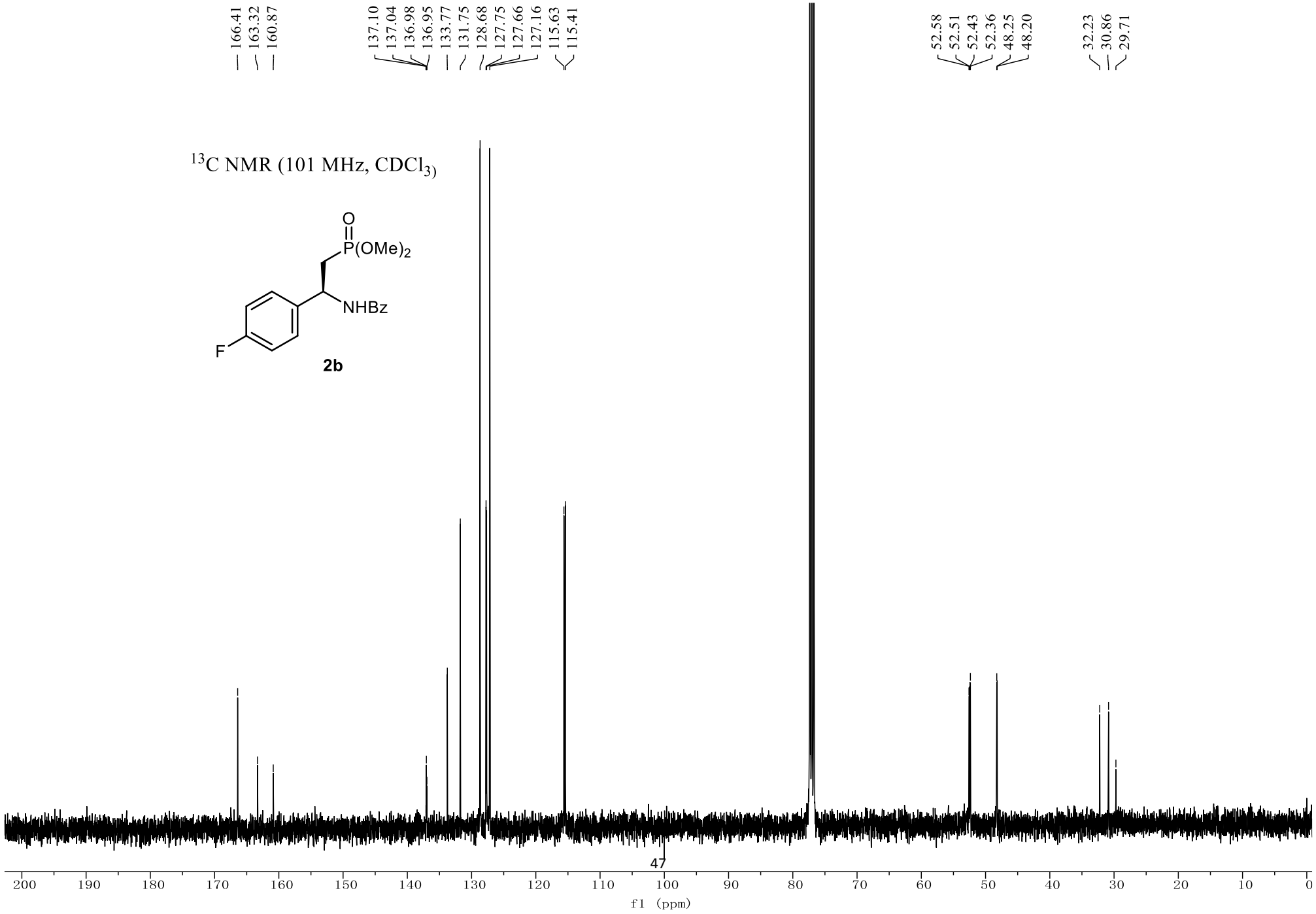
$^{31}$P NMR (162 MHz, $CDCl_3$)



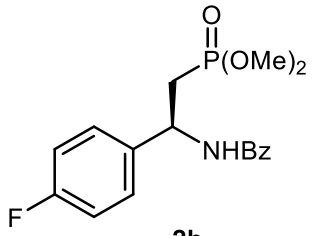

**2a**



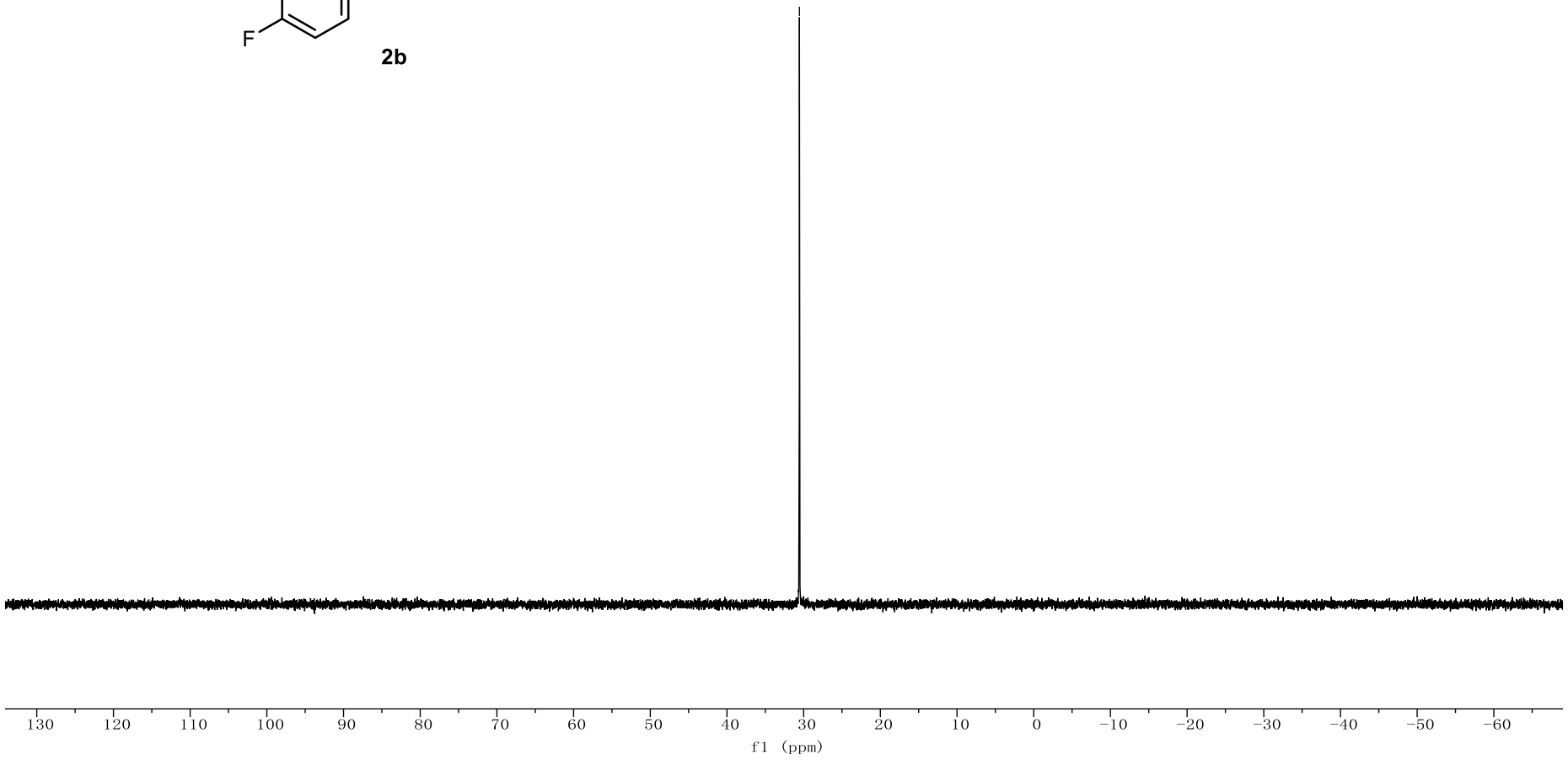

8.16 8.15 7.94 7.94 7.93 7.93 7.92 7.92 7.91
7.54 7.54 7.53 7.52 7.52 7.51 7.50 7.50 7.49 7.47 7.47 7.46 7.45 7.44 7.44 7.43 7.39 7.38 7.37 7.37 7.36 7.35 7.34 7.34 7.06 7.05 7.05 7.03 7.03 7.02 7.01 7.00 5.64 5.62 5.61 5.59 5.57 5.56 5.54 5.52 3.73 3.71 3.46 3.43 2.50 2.48 2.46 2.45 2.44 2.43 2.41 2.40 2.39 2.38
1H NMR (400 MHz, CDCl3)
O
P(OMe)2
NHBz
F
2b
1.00 2.00 3.01 2.00 2.00 1.04 2.85 2.97 2.01
46
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

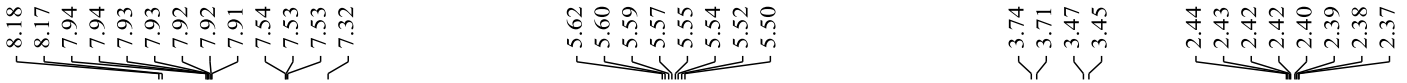

166.41
163.32
160.87
137.10
137.04
136.98
136.95
133.77
131.75
128.68
127.75
127.66
127.16
115.63
115.41
52.58
52.51
52.43
52.36
48.25
48.20
32.23
30.86
29.71
$^{13}$C NMR (101 MHz, CDCl$_3$)
O
P(OMe)$_2$
NHBz
F
2b
47
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)

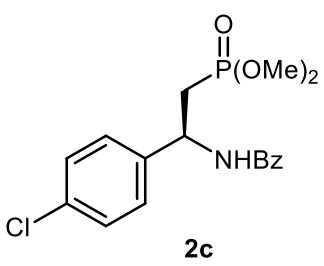



**2b**

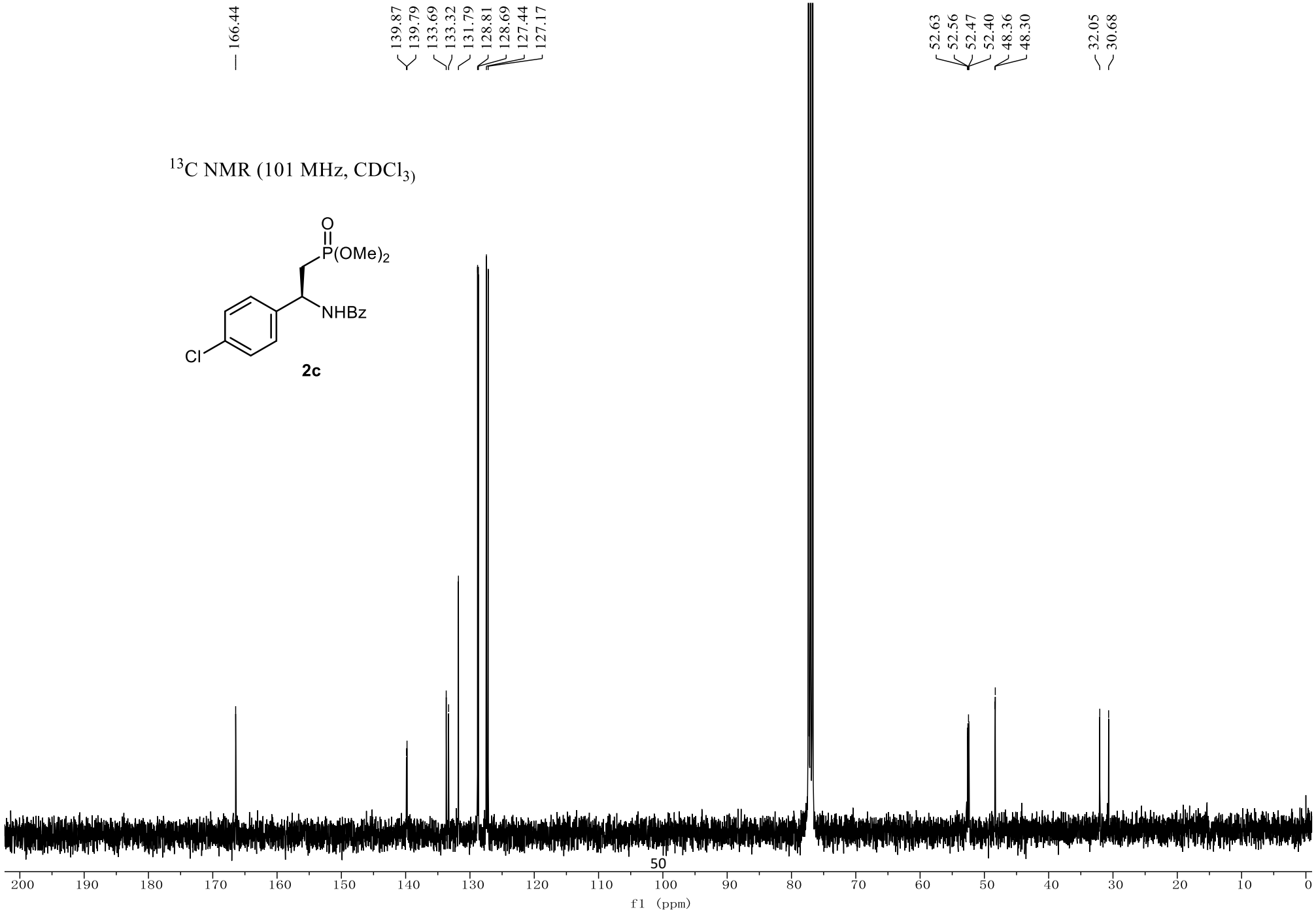




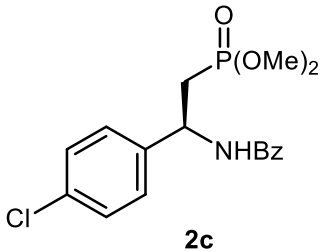

$^1$H NMR (400 MHz, $CDCl_3$)



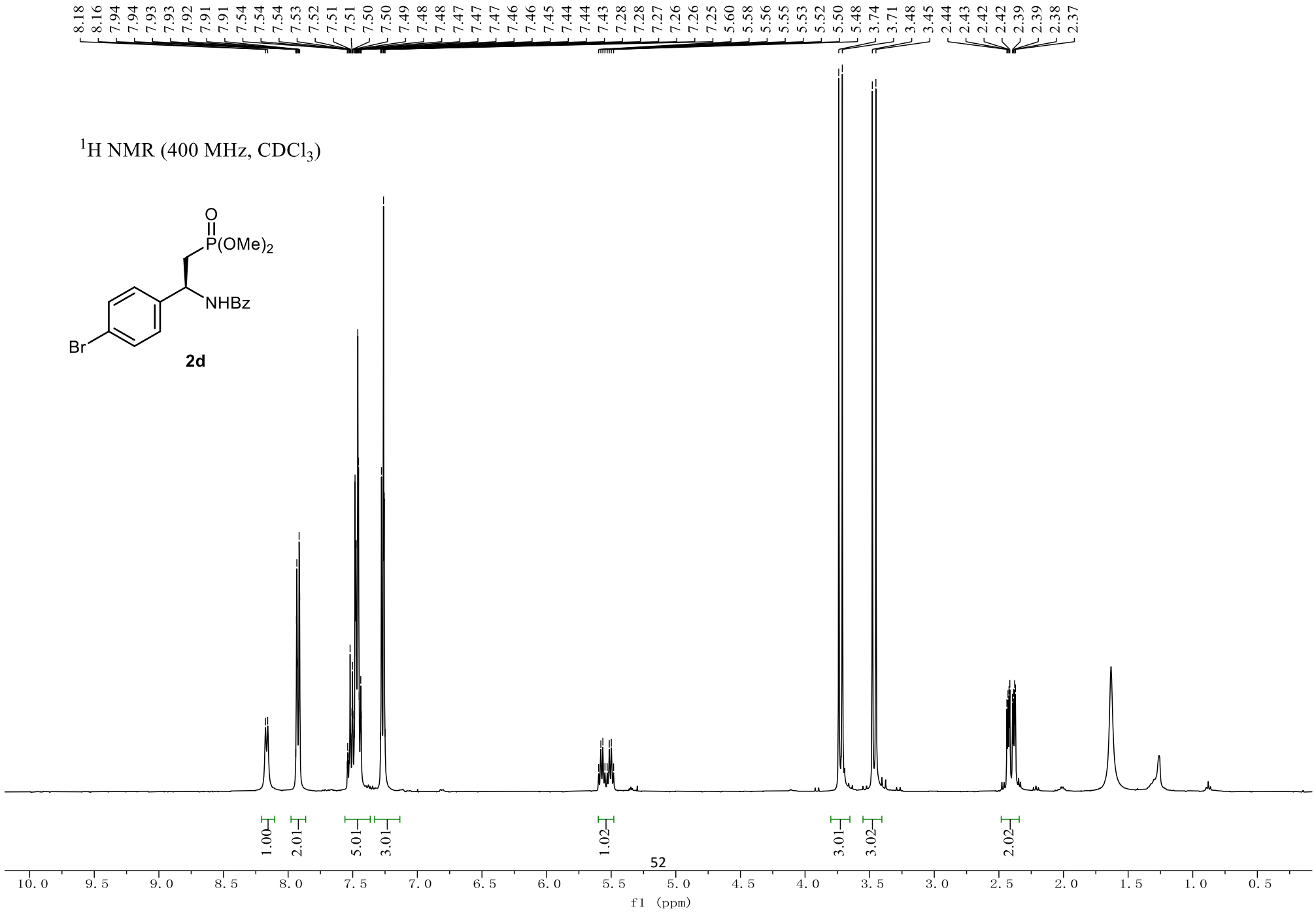

**2c**

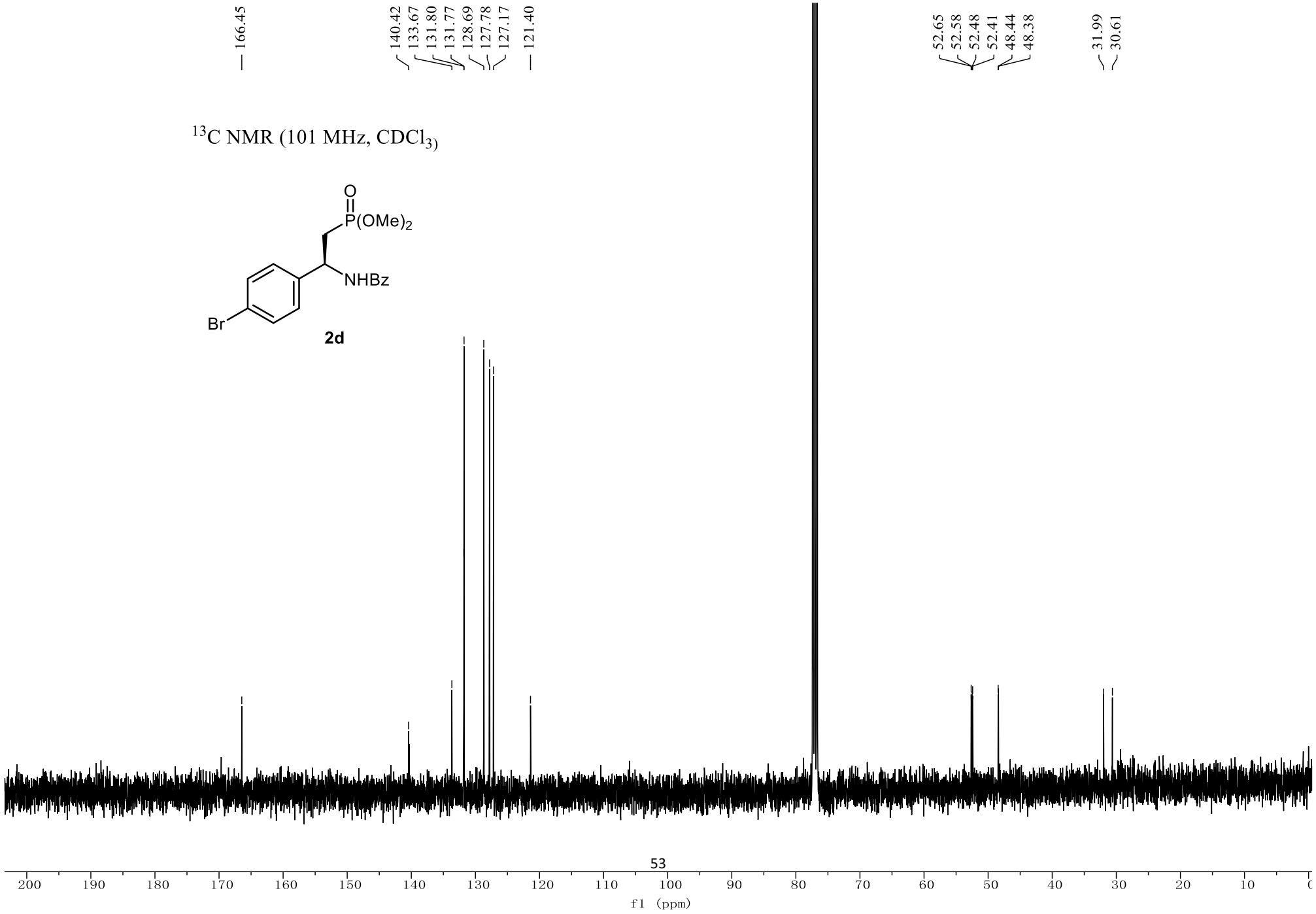

166.44
139.87
139.79
133.69
133.32
131.79
128.81
128.69
127.44
127.17
52.63
52.56
52.47
52.40
48.36
48.30
32.05
30.68
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHBz
Cl
2c
50
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)

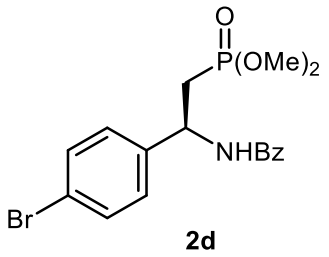



**2c**

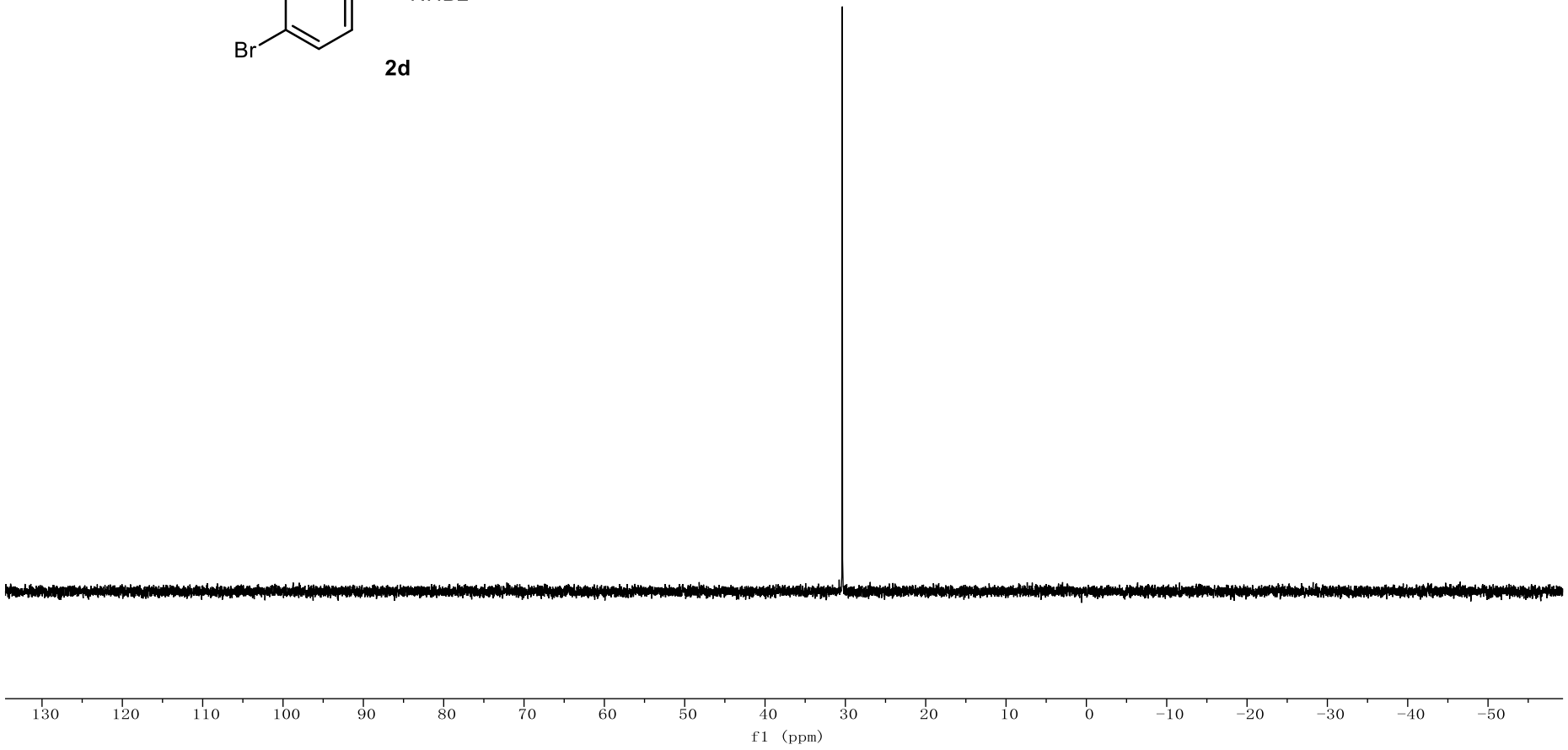

8.18 8.16 7.94 7.94 7.93 7.93 7.92 7.91 7.91 7.54 7.54 7.54 7.53 7.52 7.51 7.51 7.50 7.50 7.49 7.48 7.48 7.47 7.47 7.47 7.46 7.46 7.45 7.44 7.44 7.43 7.28 7.28 7.27 7.26 7.26 7.25 5.60 5.58 5.56 5.55 5.53 5.52 5.50 5.48 3.74 3.71 3.48 3.45 2.44 2.43 2.42 2.42 2.39 2.39 2.38 2.37
1H NMR (400 MHz, CDCl3)
O
P(OMe)2
NHBz
Br
2d
1.00 2.01 5.01 3.01 1.02 3.01 3.02 2.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

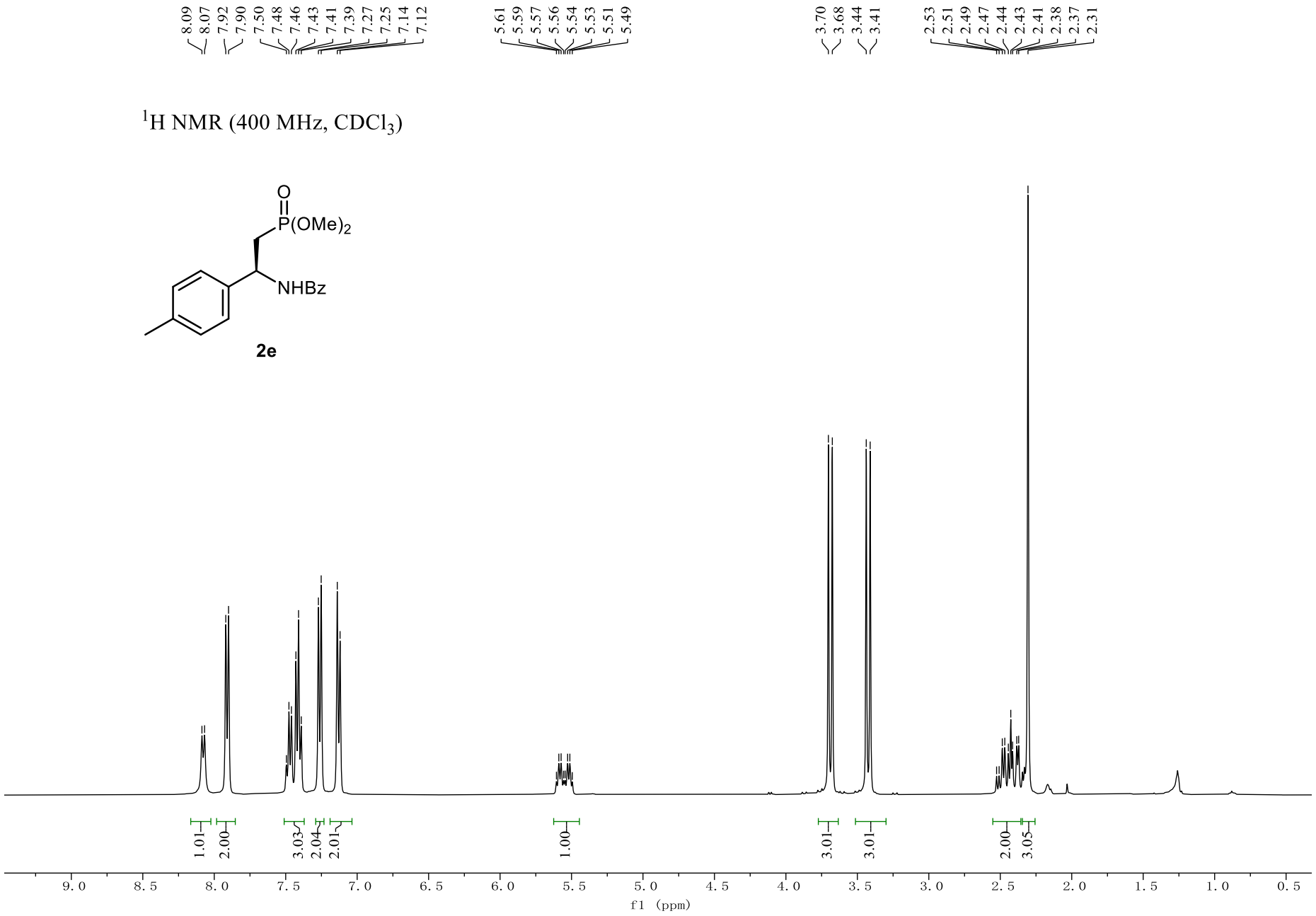

166.45
140.42
133.67
131.80
131.77
128.69
127.78
127.17
121.40
52.65
52.58
52.48
52.41
48.44
48.38
31.99
30.61
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHBz
Br
2d
53
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)




**2d**

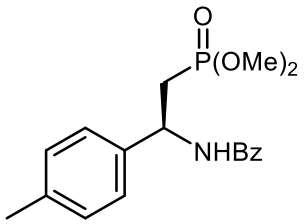





$^1$H NMR (400 MHz, $CDCl_3$)

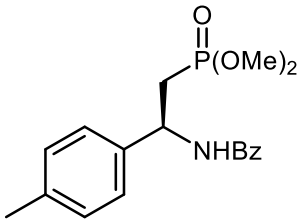
166.39
138.34
138.25
137.16
134.09
131.54
129.32
128.56
127.19
125.97
52.49
52.42
52.39
52.32
48.58
48.52
32.28
30.91
21.06

$^{13}C$ NMR (101 MHz, $CDCl_{3)}$

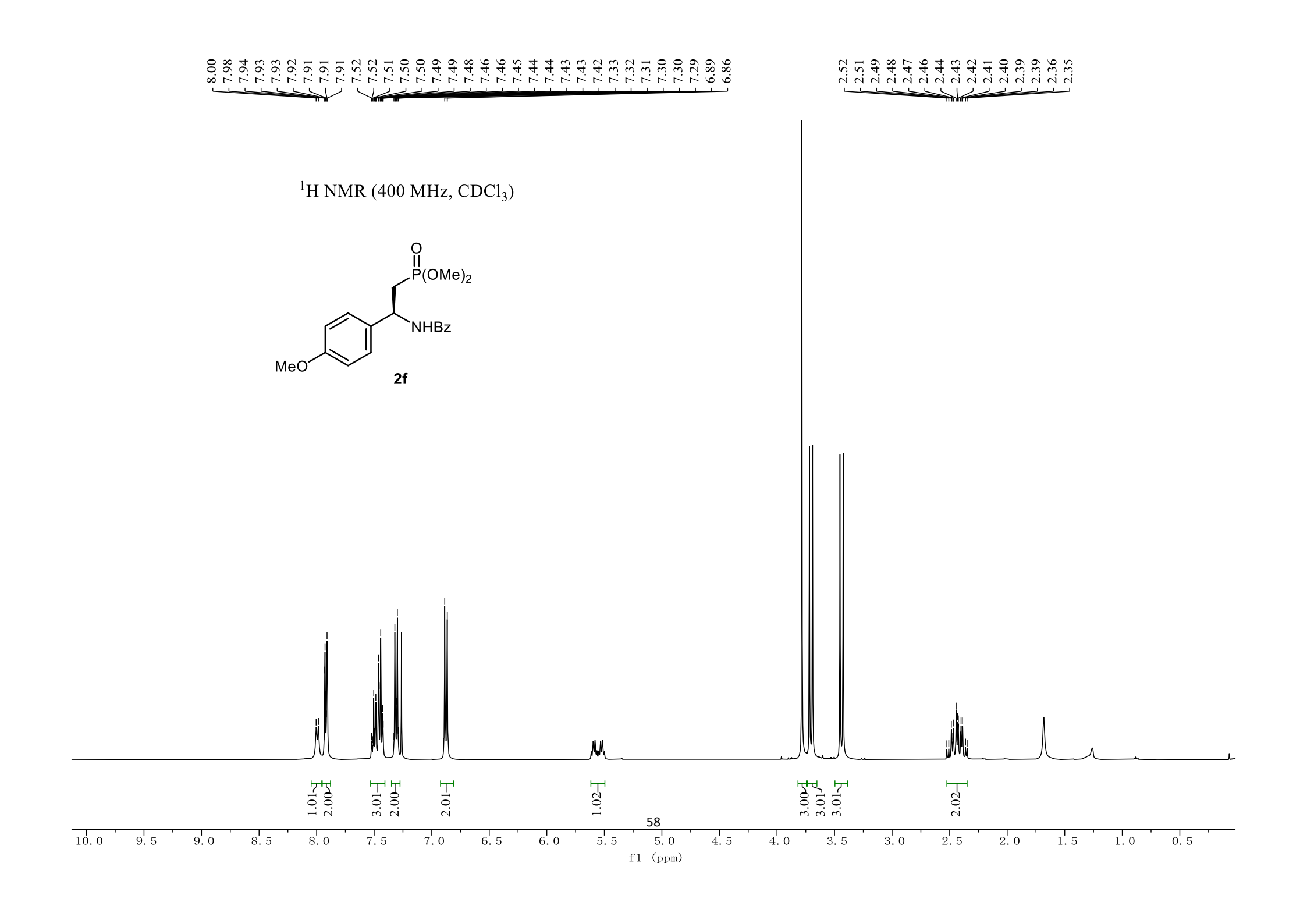


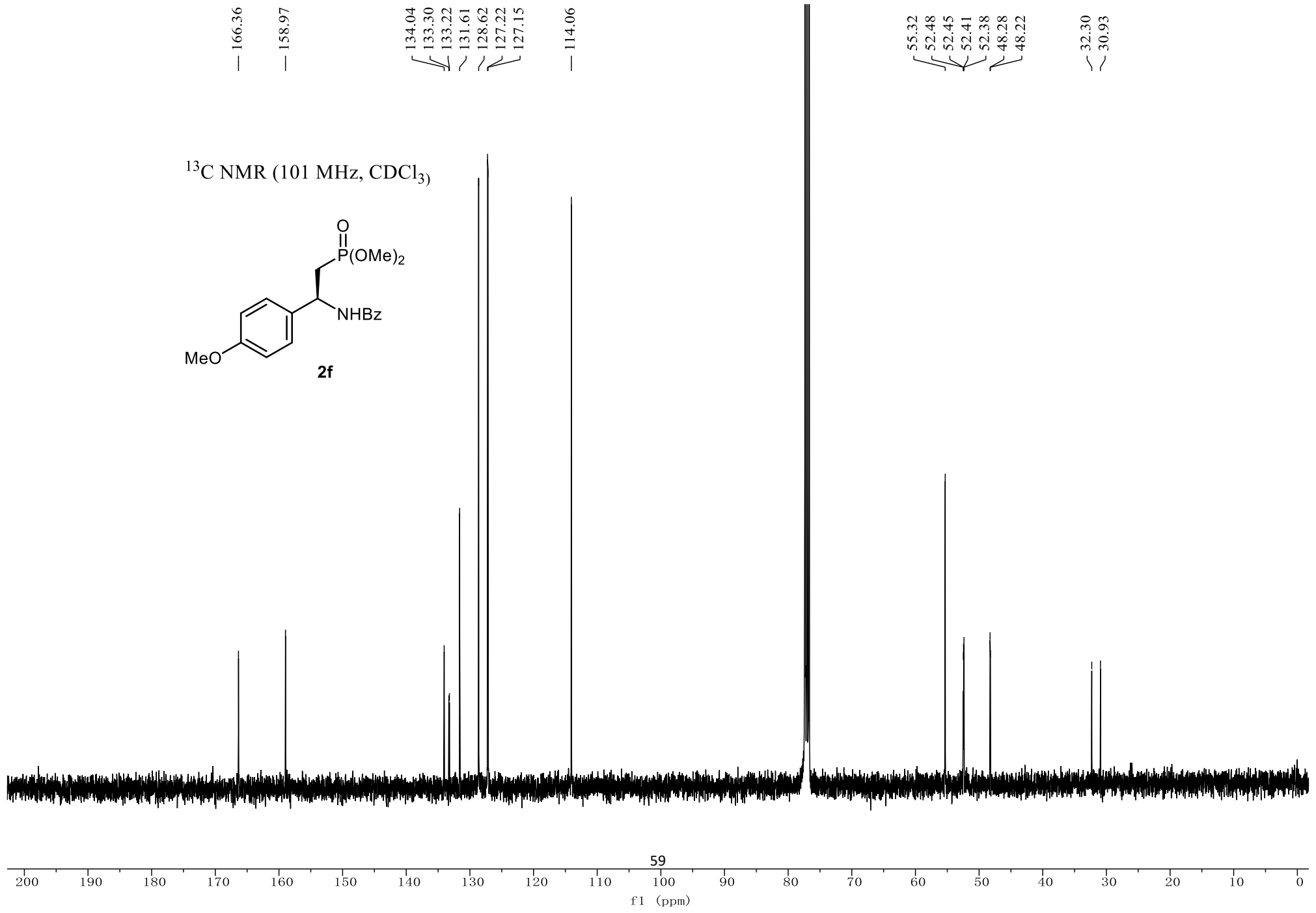

**2e**

$^{31}$P NMR (162 MHz, $CDCl_3$)

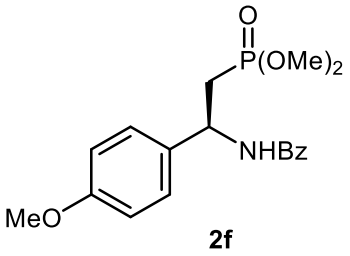



**2e**

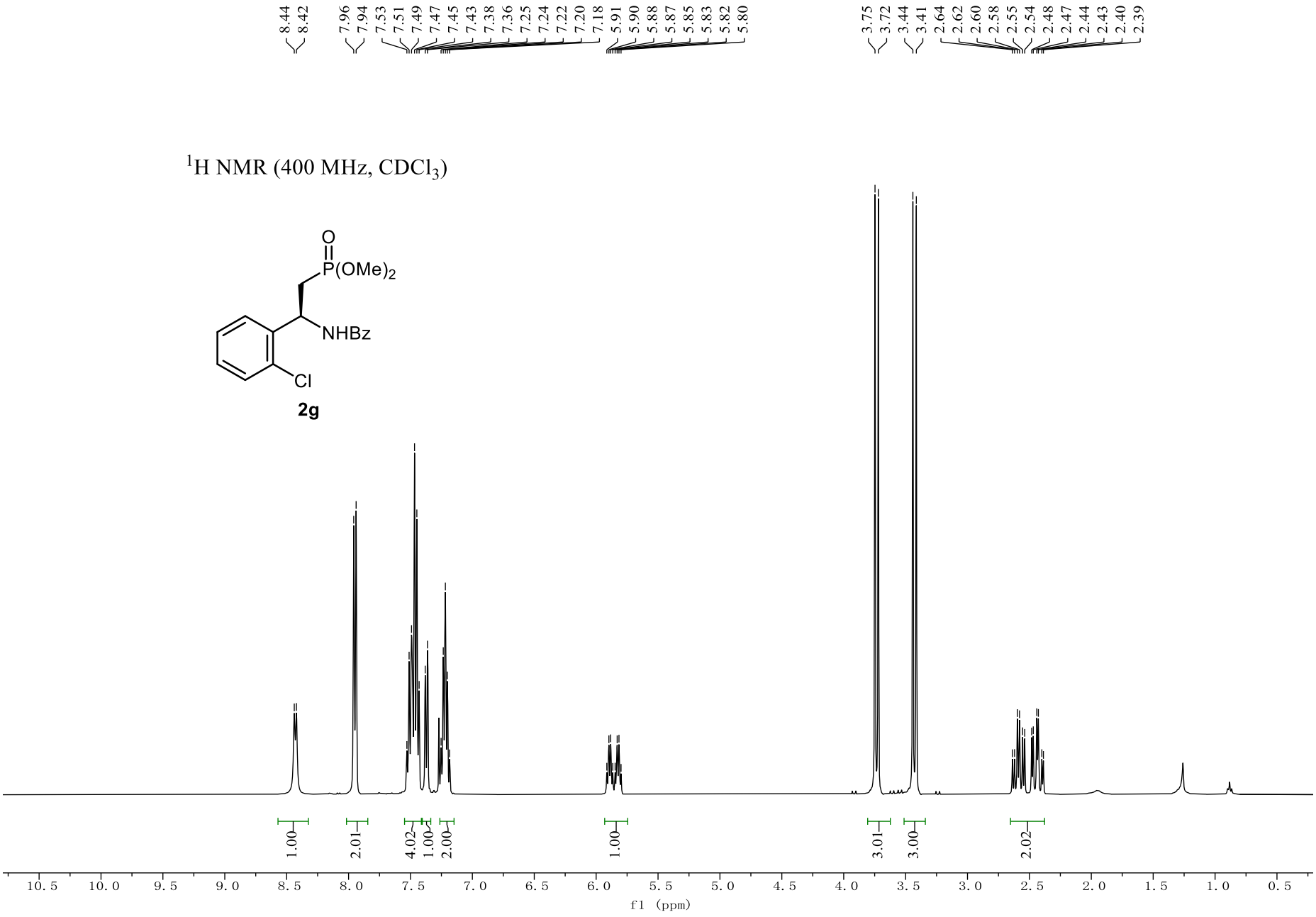

8.00
7.98
7.94
7.93
7.93
7.92
7.91
7.91
7.91
7.52
7.52
7.51
7.50
7.50
7.49
7.49
7.48
7.46
7.46
7.45
7.44
7.44
7.43
7.43
7.42
7.33
7.32
7.31
7.30
7.30
7.29
6.89
6.86
2.52
2.51
2.49
2.48
2.47
2.46
2.44
2.43
2.42
2.41
2.40
2.39
2.39
2.36
2.35
$^1$H NMR (400 MHz, $CDCl_3$)
O
P(OMe)2
NHBz
MeO
2f
1.01
2.00
3.01
2.00
2.01
1.02
3.00
3.01
3.01
2.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

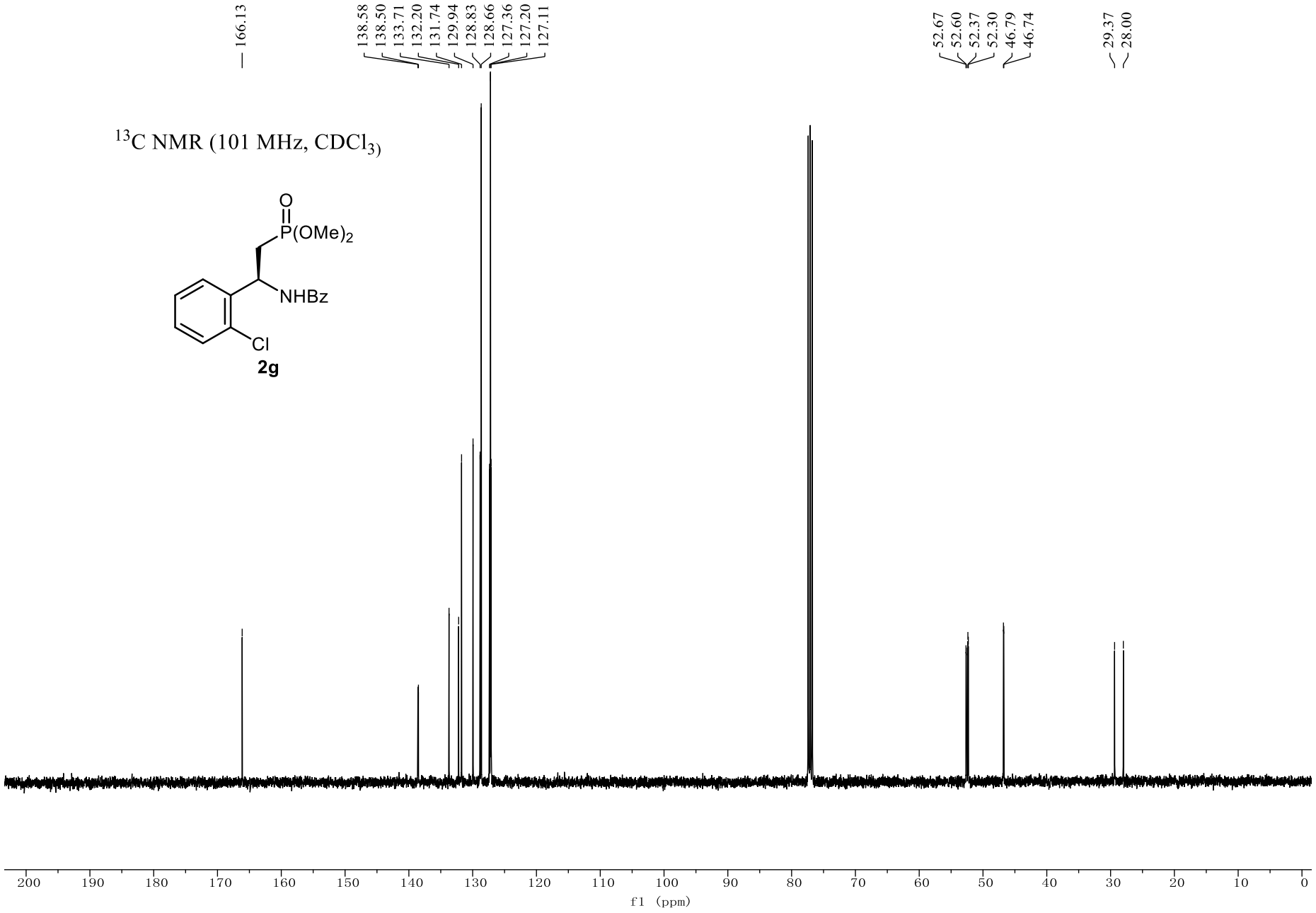

166.36
158.97
134.04
133.30
133.22
131.61
128.62
127.22
127.15
114.06
55.32
52.48
52.45
52.41
52.38
48.28
48.22
32.30
30.93
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHBz
MeO
2f
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)

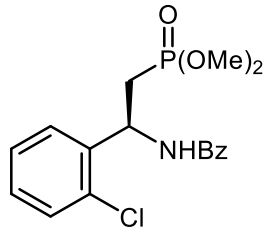



**2f**

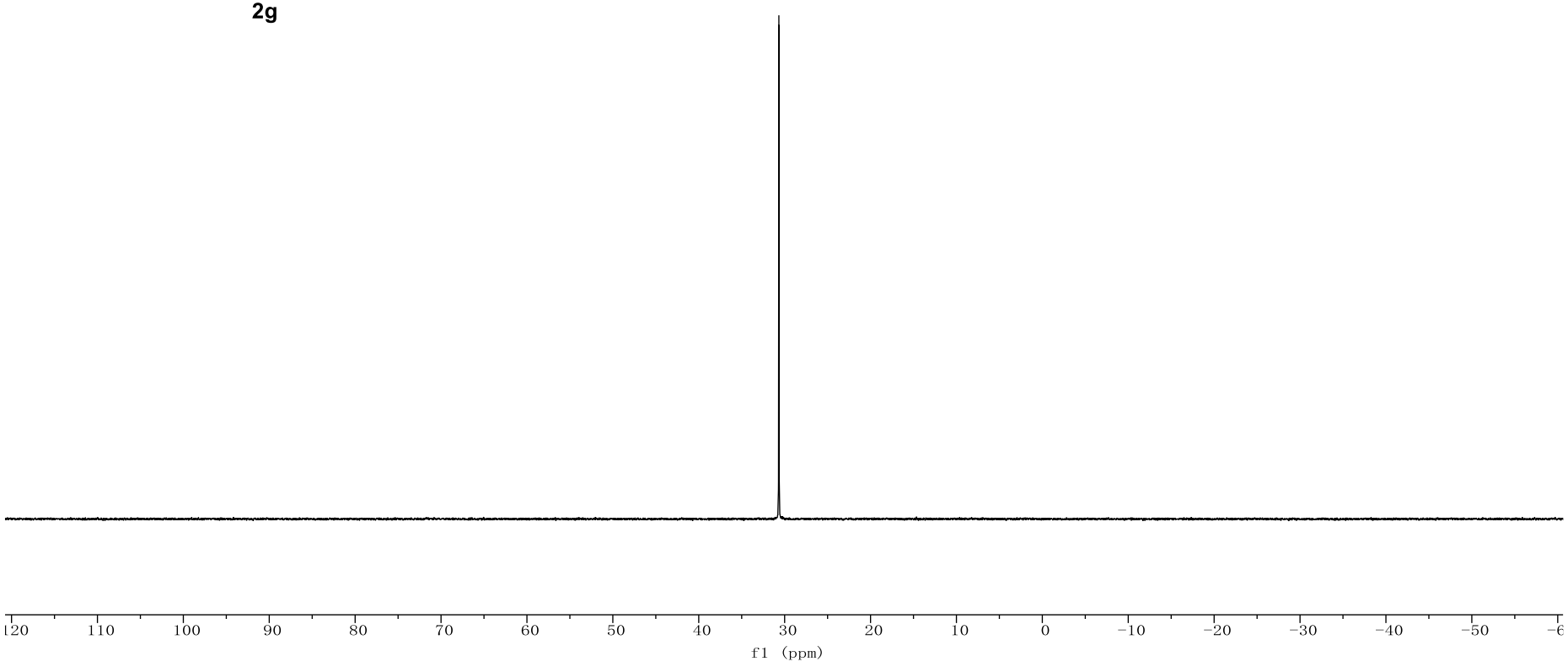

8.44
8.42
7.96
7.94
7.53
7.51
7.49
7.47
7.45
7.43
7.38
7.36
7.25
7.24
7.22
7.20
7.18
5.91
5.90
5.88
5.87
5.85
5.83
5.82
5.80
3.75
3.72
3.44
3.41
2.64
2.62
2.60
2.58
2.55
2.54
2.48
2.47
2.44
2.43
2.40
2.39
$^1$H NMR (400 MHz, $CDCl_3$)
O
P(OMe)2
NHBz
Cl
2g
1.00
2.01
4.02
1.00
2.00
1.00
3.01
3.00
2.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

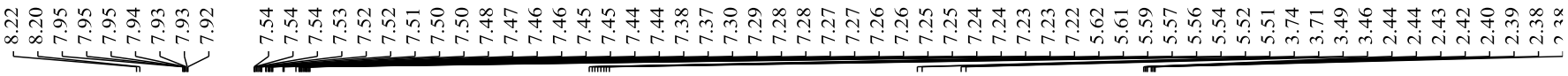

166.13
138.58
138.50
133.71
132.20
131.74
129.94
128.83
128.66
127.36
127.20
127.11
52.67
52.60
52.37
52.30
46.79
46.74
29.37
28.00
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHBz
Cl
2g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)

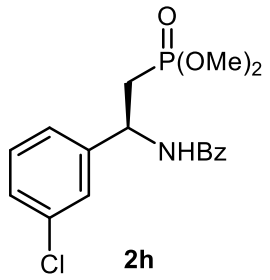



**2g**

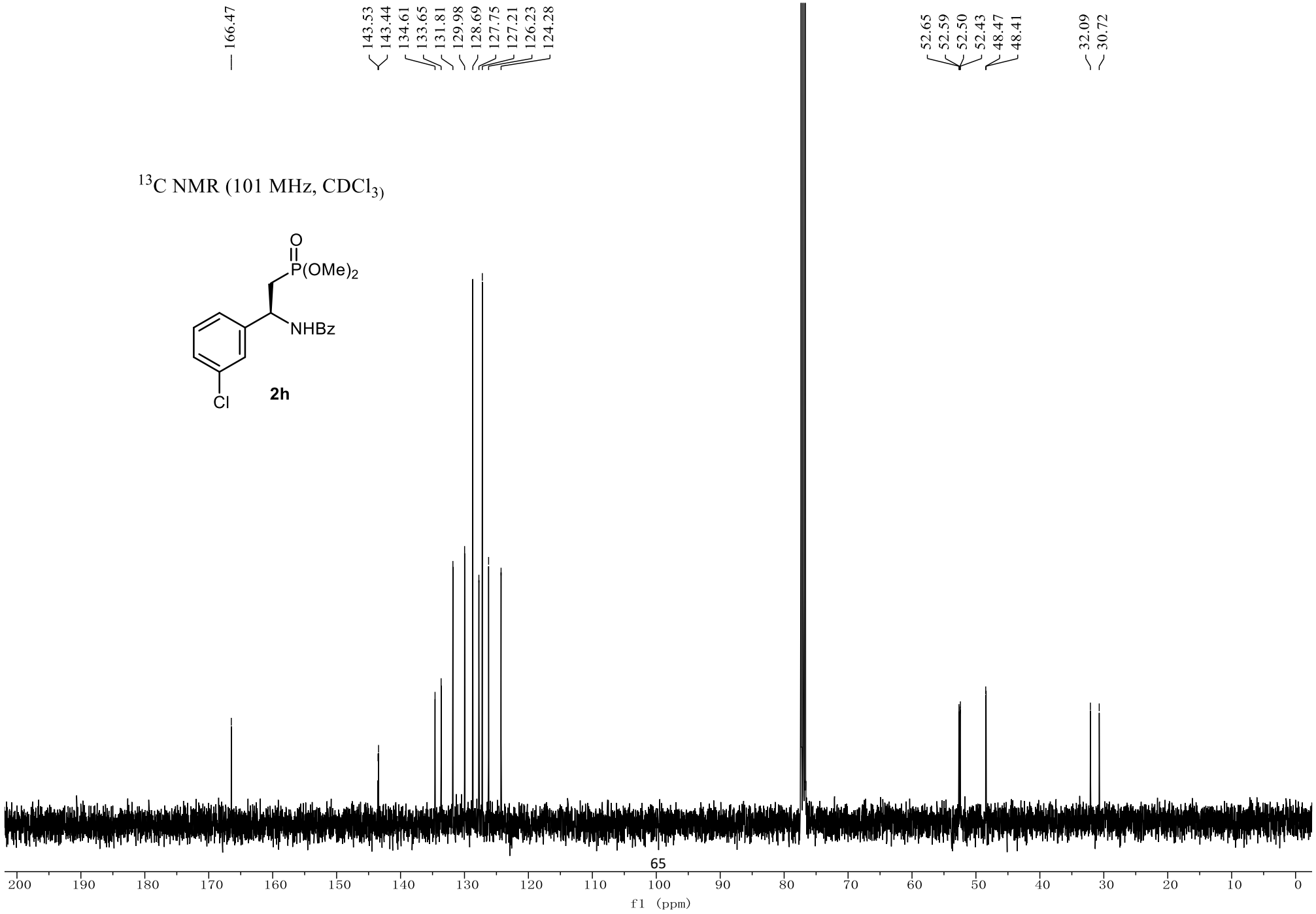




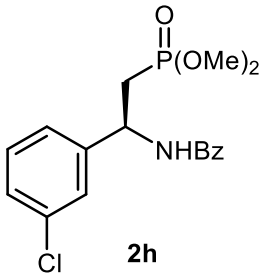

$^1$H NMR (400 MHz, $CDCl_3$)



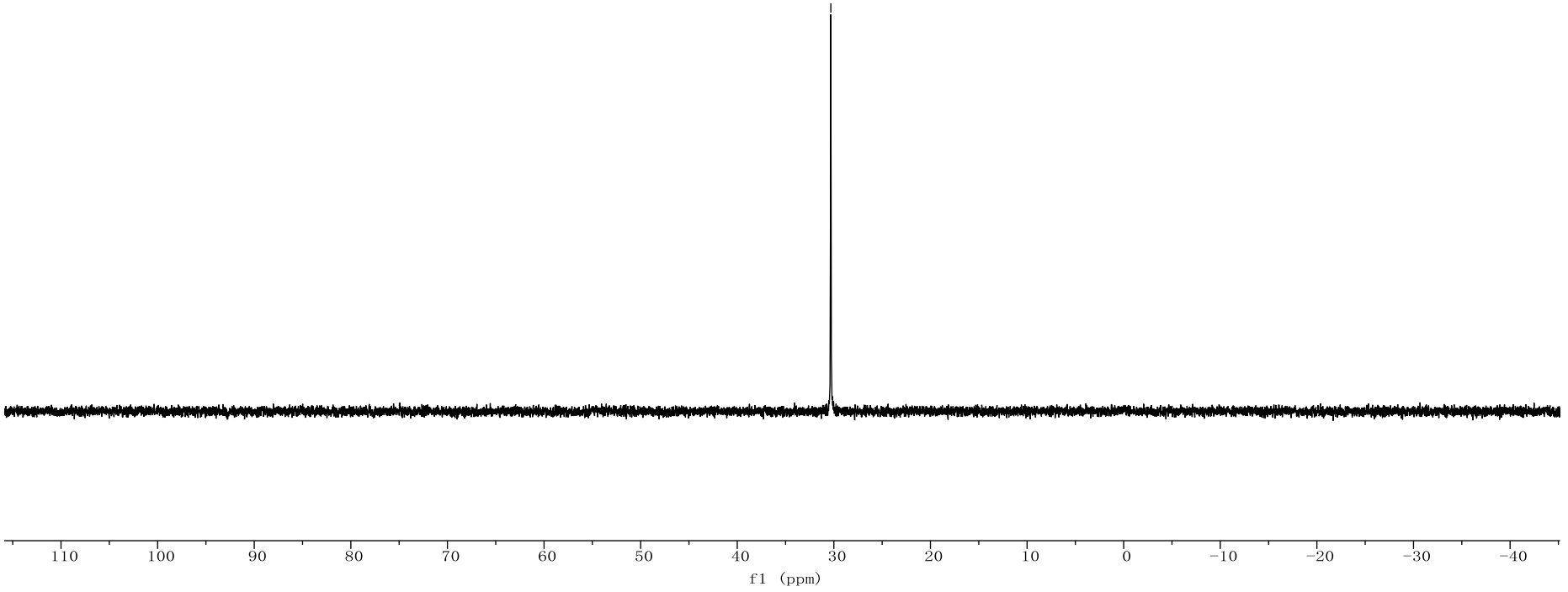

**2h**

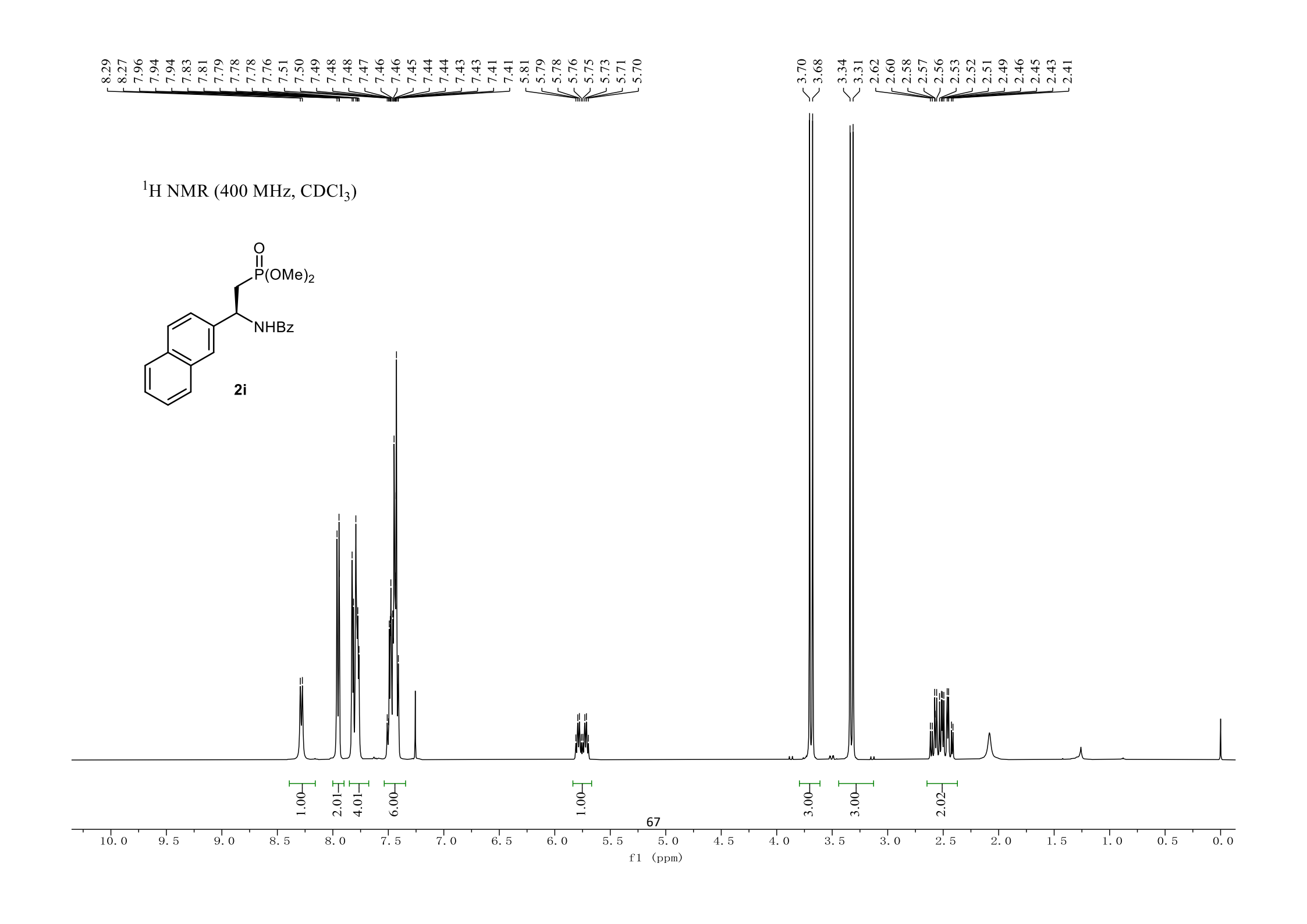

166.47
143.53
143.44
134.61
133.65
131.81
129.98
128.69
127.75
127.21
126.23
124.28
52.65
52.59
52.50
52.43
48.47
48.41
32.09
30.72
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHBz
Cl
2h
65
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)



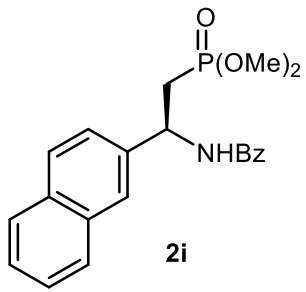

**2h**




8.29
8.27
7.96
7.94
7.94
7.83
7.81
7.79
7.78
7.78
7.76
7.51
7.50
7.49
7.48
7.48
7.47
7.46
7.46
7.45
7.44
7.44
7.43
7.43
7.41
7.41
5.81
5.79
5.78
5.76
5.75
5.73
5.71
5.70
3.70
3.68
3.34
3.31
2.62
2.60
2.58
2.57
2.56
2.53
2.52
2.51
2.49
2.46
2.45
2.43
2.41
1H NMR (400 MHz, CDCl3)
O
P(OMe)2
NHBz
2i
1.00
2.01
4.01
6.00
1.00
3.00
3.00
2.02
67
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

166.53
138.70
138.61
134.00
133.31
132.80
131.67
128.64
128.55
128.02
127.62
127.26
126.30
126.01
124.71
124.25
52.57
52.50
52.43
52.36
48.94
48.89
32.15
30.78

$^{13}C$ NMR (101 MHz, $CDCl_{3)}$



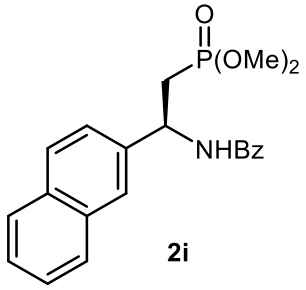

**2i**



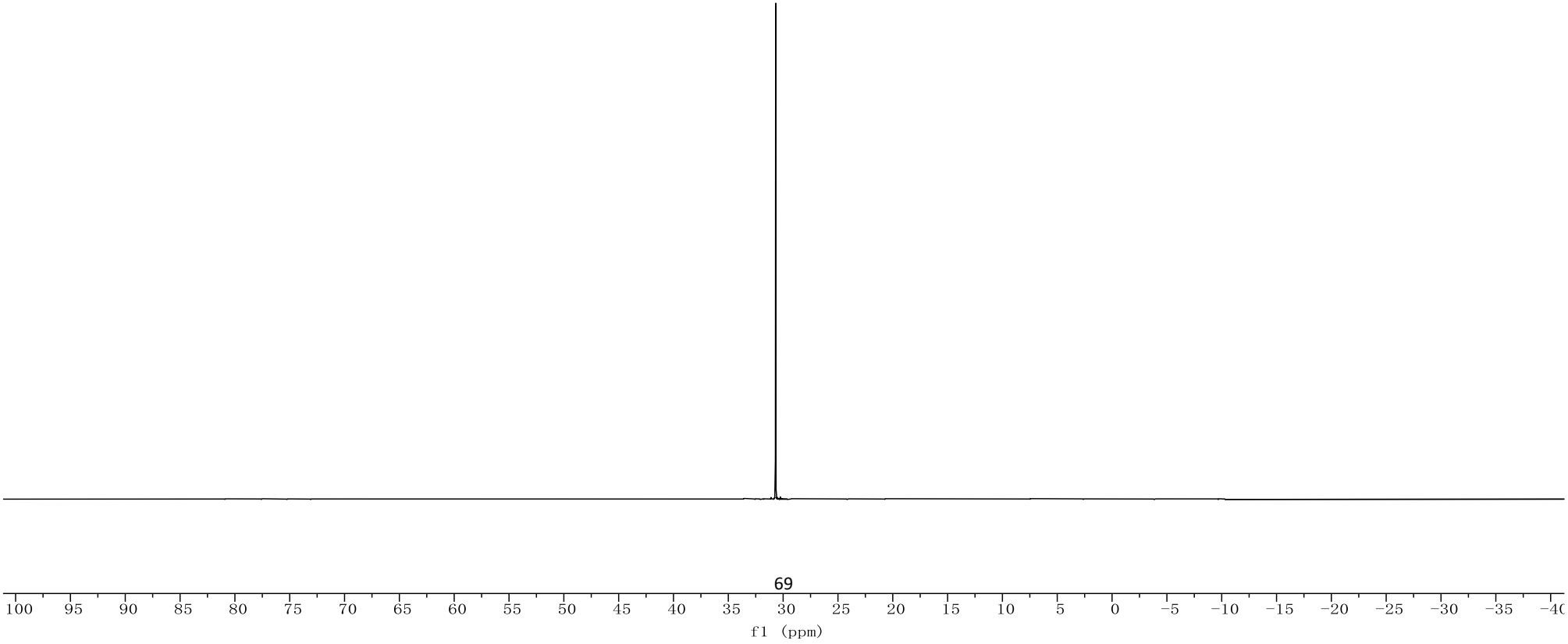
f1 (ppm)

30.68

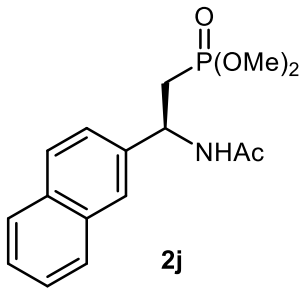
$^{31}$P NMR (162 MHz, $CDCl_3$)



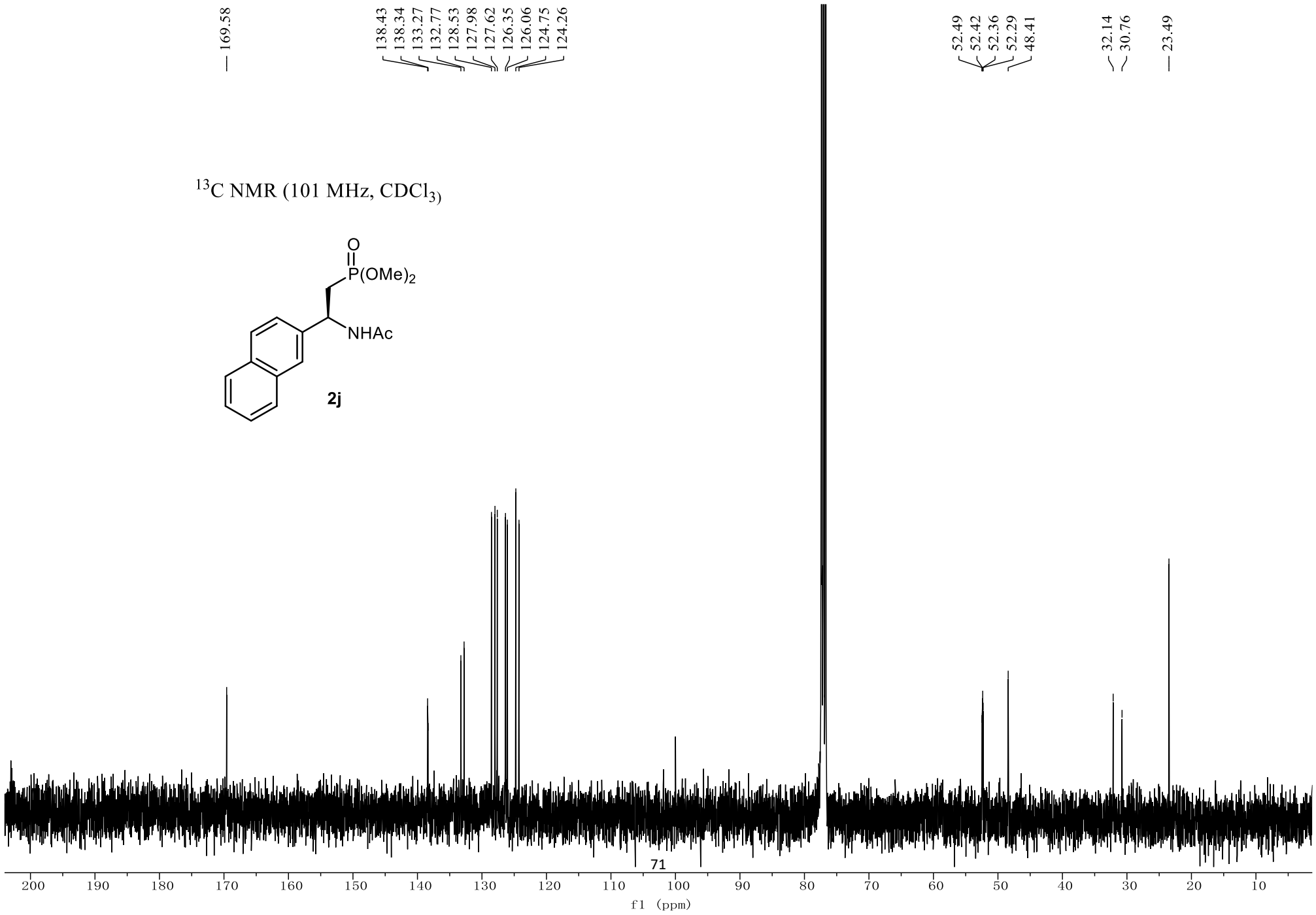

**2i**




$^1$H NMR (400 MHz, $CDCl_3$)

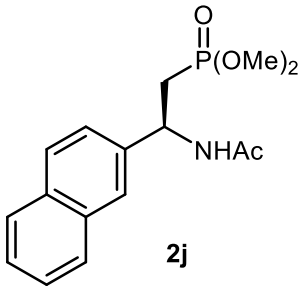



**2j**

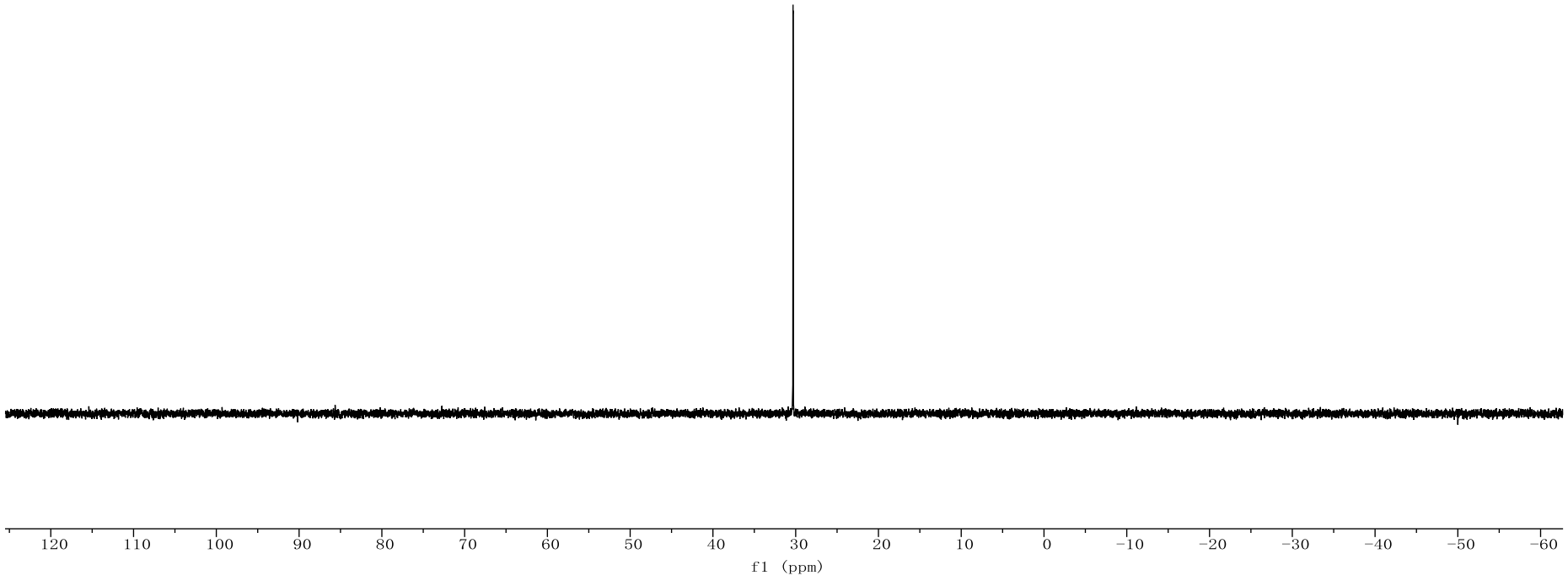

169.58
138.43
138.34
133.27
132.77
128.53
127.98
127.62
126.35
126.06
124.75
124.26
52.49
52.42
52.36
52.29
48.41
32.14
30.76
23.49
$^{13}$C NMR (101 MHz, CDCl$_{3)}$
O
P(OMe)$_2$
NHAc
2j
71
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

— 30.32

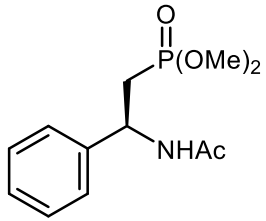
$^{31}$P NMR (162 MHz, $CDCl_3$)



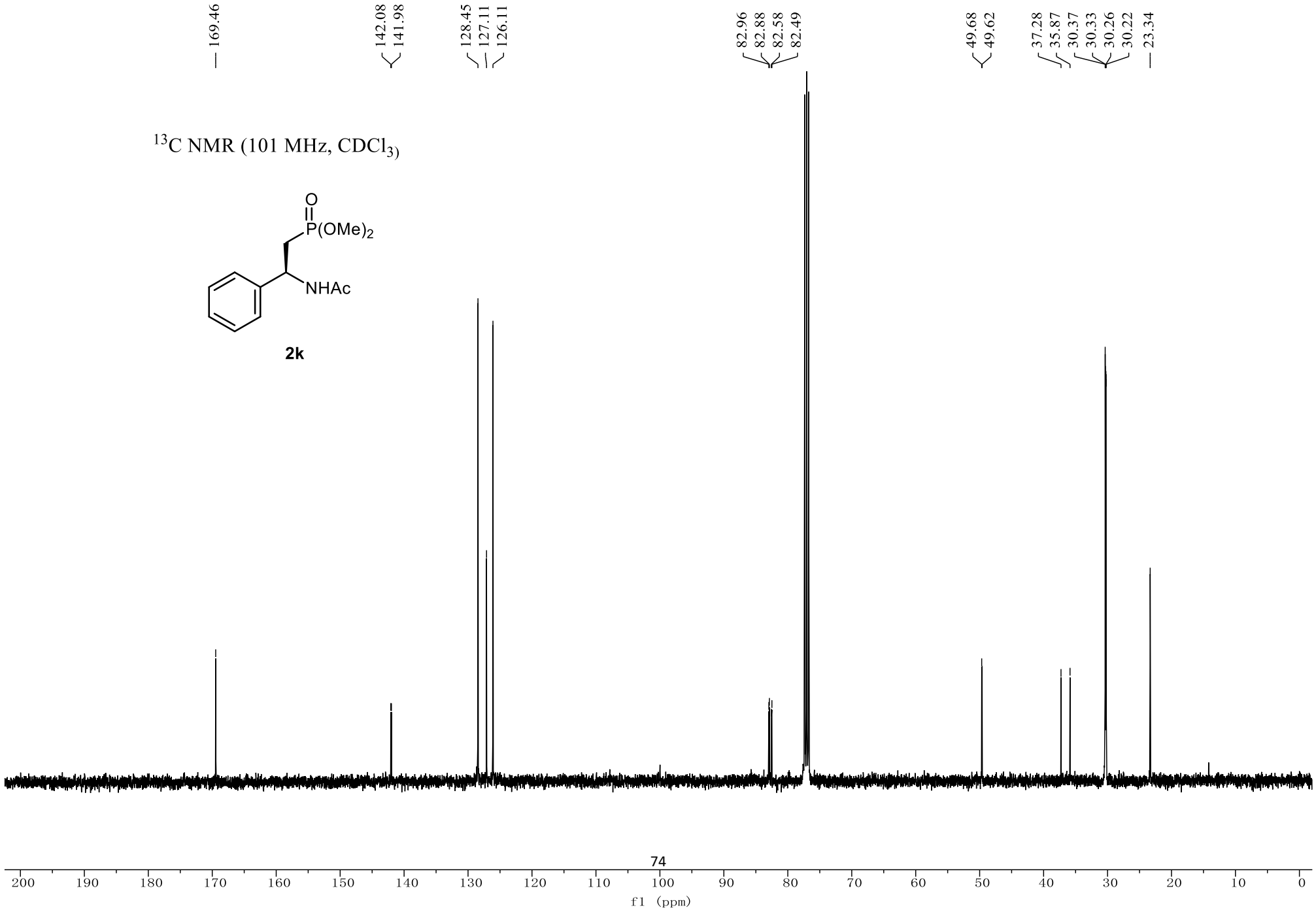

**2j**



$^1$H NMR (400 MHz, $CDCl_3$)

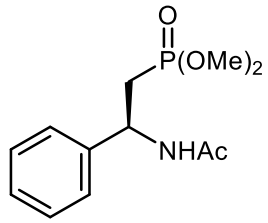



**2k**

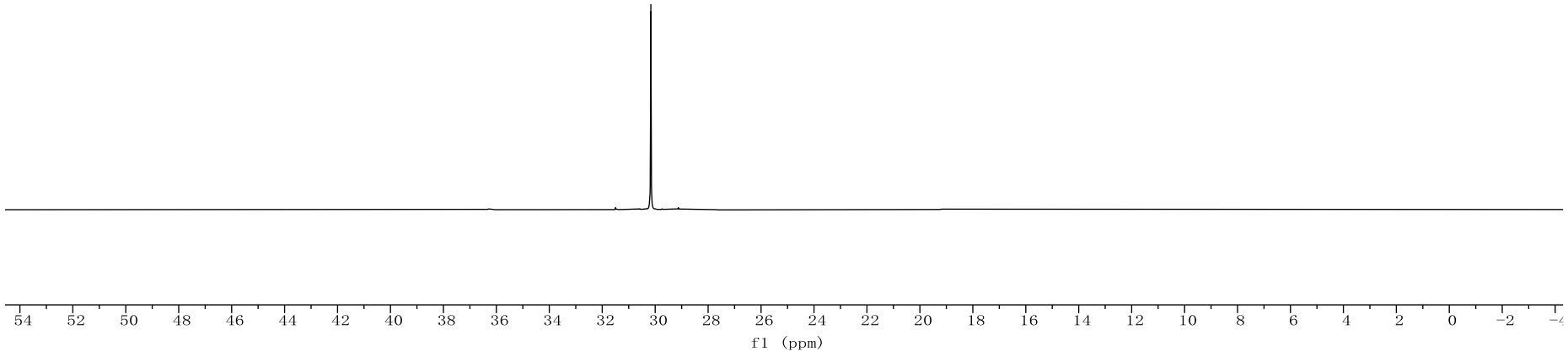

169.46
142.08
141.98
128.45
127.11
126.11
82.96
82.88
82.58
82.49
49.68
49.62
37.28
35.87
30.37
30.33
30.26
30.22
23.34
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHAc
2k
74
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

— 30.16

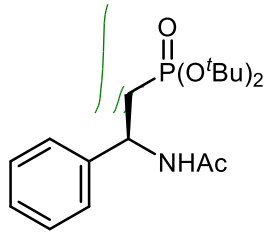
$^{31}P$ NMR (162 MHz, $CDCl_3$)




**2k**



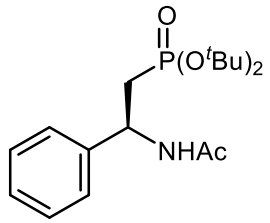
$^1$H NMR (400 MHz, $CDCl_3$)



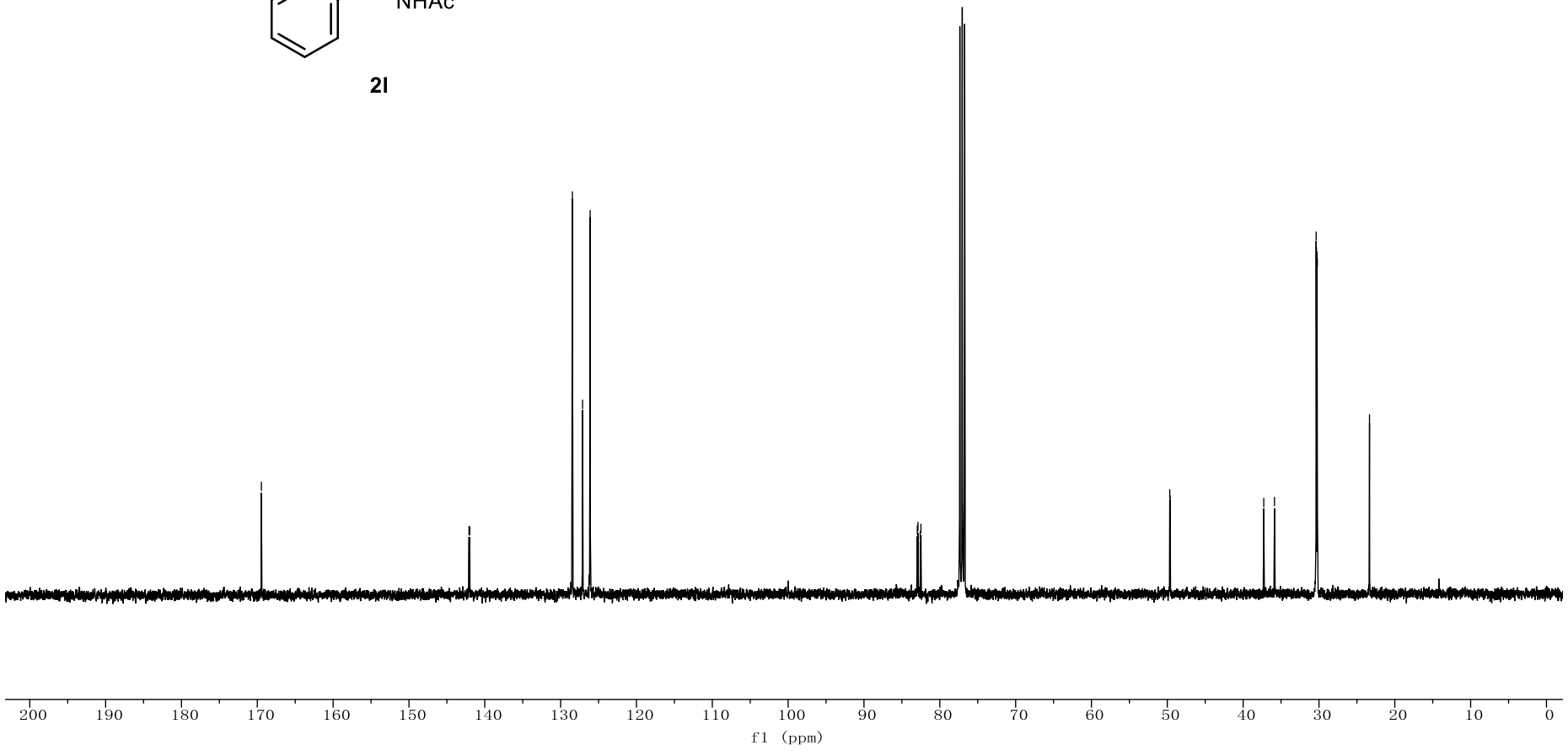

**2l**

169.46
142.08
141.98
128.45
127.11
126.11
82.96
82.88
82.58
82.49
49.68
49.62
37.28
35.87
30.37
30.33
30.26
30.22
23.34

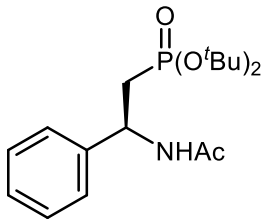
$^{13}C$ NMR (101 MHz, $CDCl_{3)}$



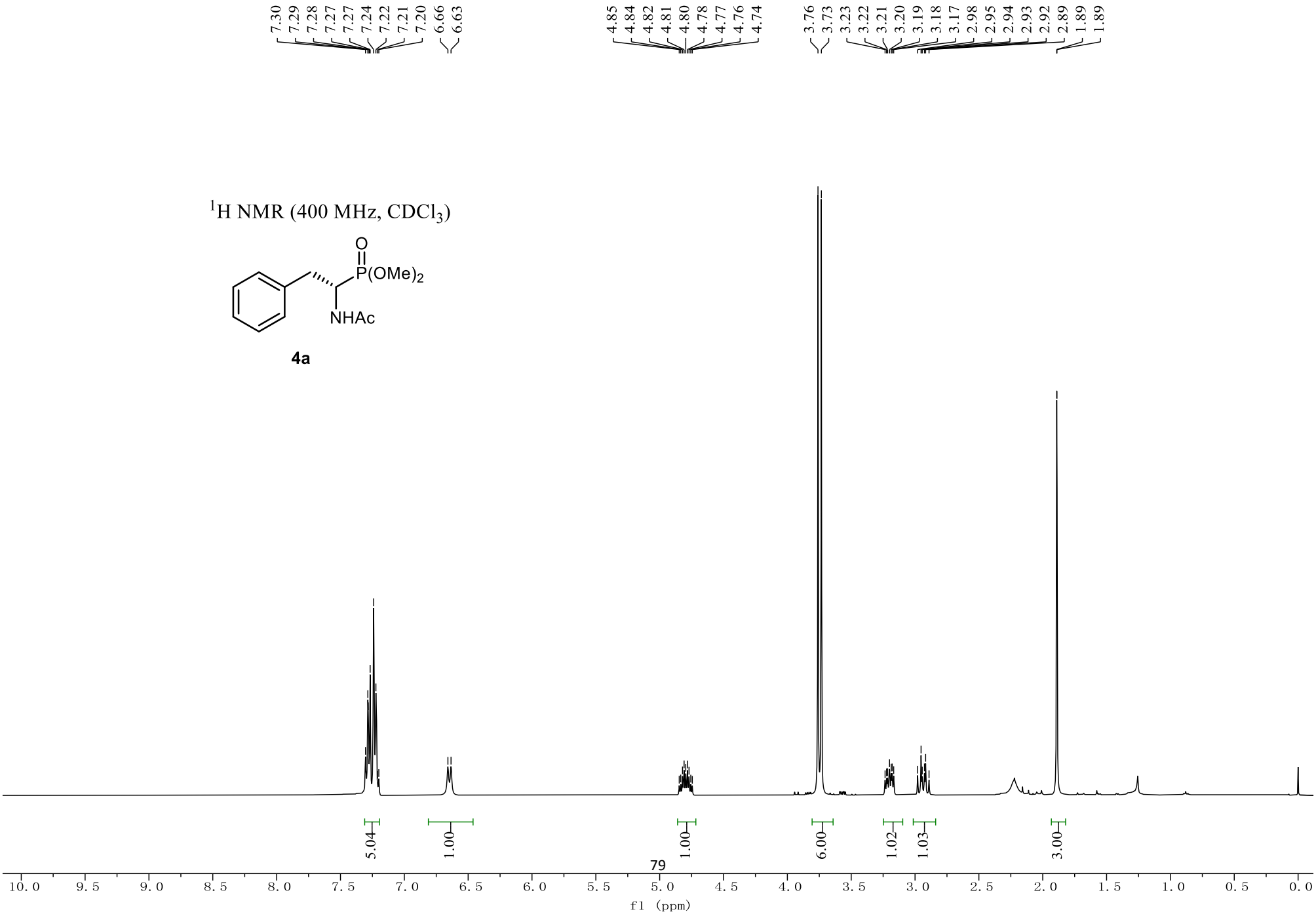

**2l**



$^{31}P$ NMR (162 MHz, $CDCl_3$)

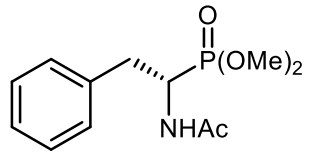



**2l**

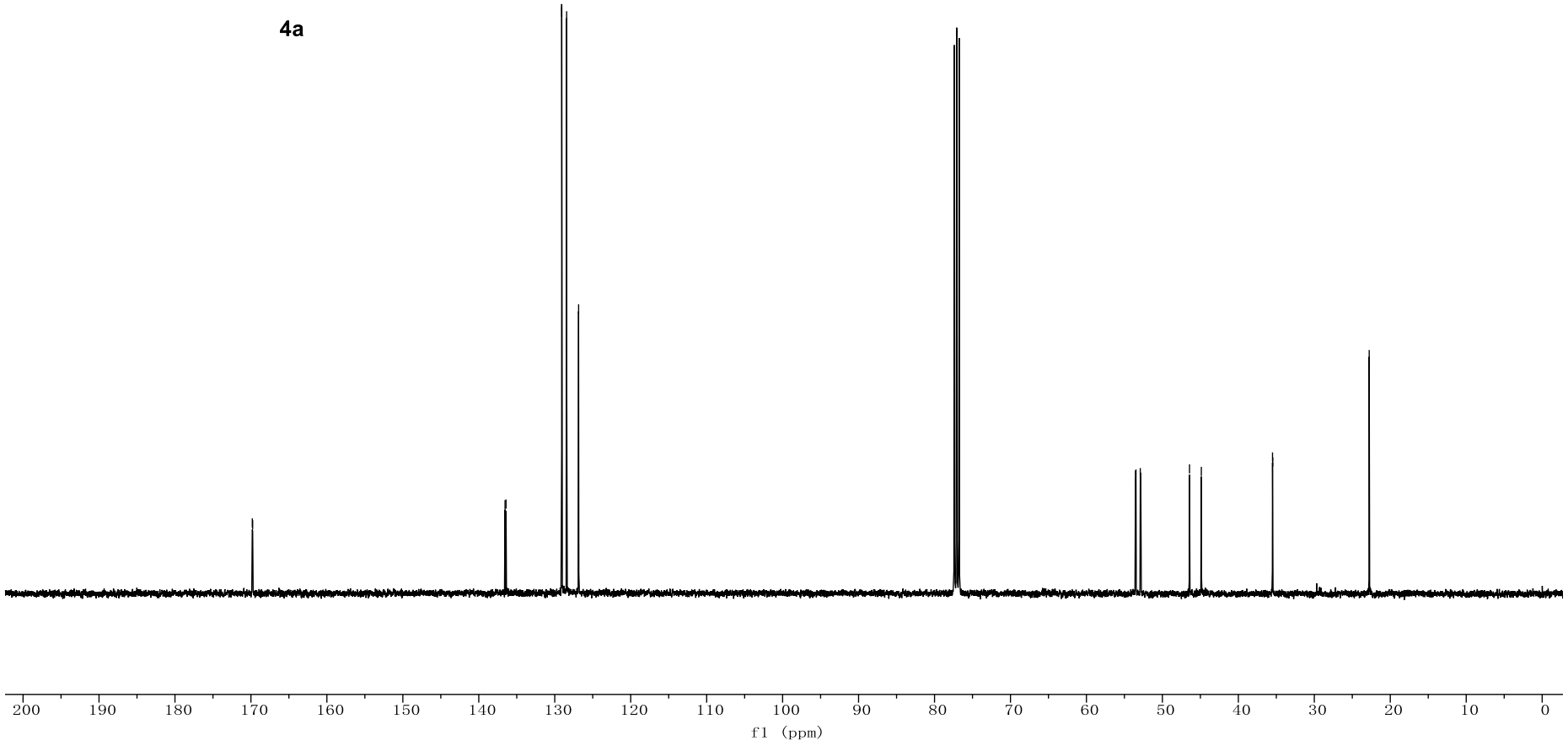

7.30
7.29
7.28
7.27
7.27
7.24
7.22
7.21
7.20
6.66
6.63
4.85
4.84
4.82
4.81
4.80
4.78
4.77
4.76
4.74
3.76
3.73
3.23
3.22
3.21
3.20
3.19
3.18
3.17
2.98
2.95
2.94
2.93
2.92
2.89
1.89
1.89
$^1$H NMR (400 MHz, $CDCl_3$)
O
P(OMe)$_2$
NHAc
4a
5.04
1.00
1.00
6.00
1.02
1.03
3.00
79
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

169.82
169.77
136.54
136.41
129.08
128.44
126.86
53.54
53.48
52.91
52.84
46.43
44.88
35.50
35.47
22.77

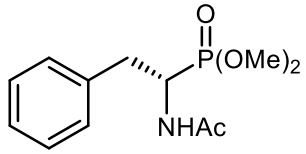
$^{13}$C NMR (101 MHz, $CDCl_3$)



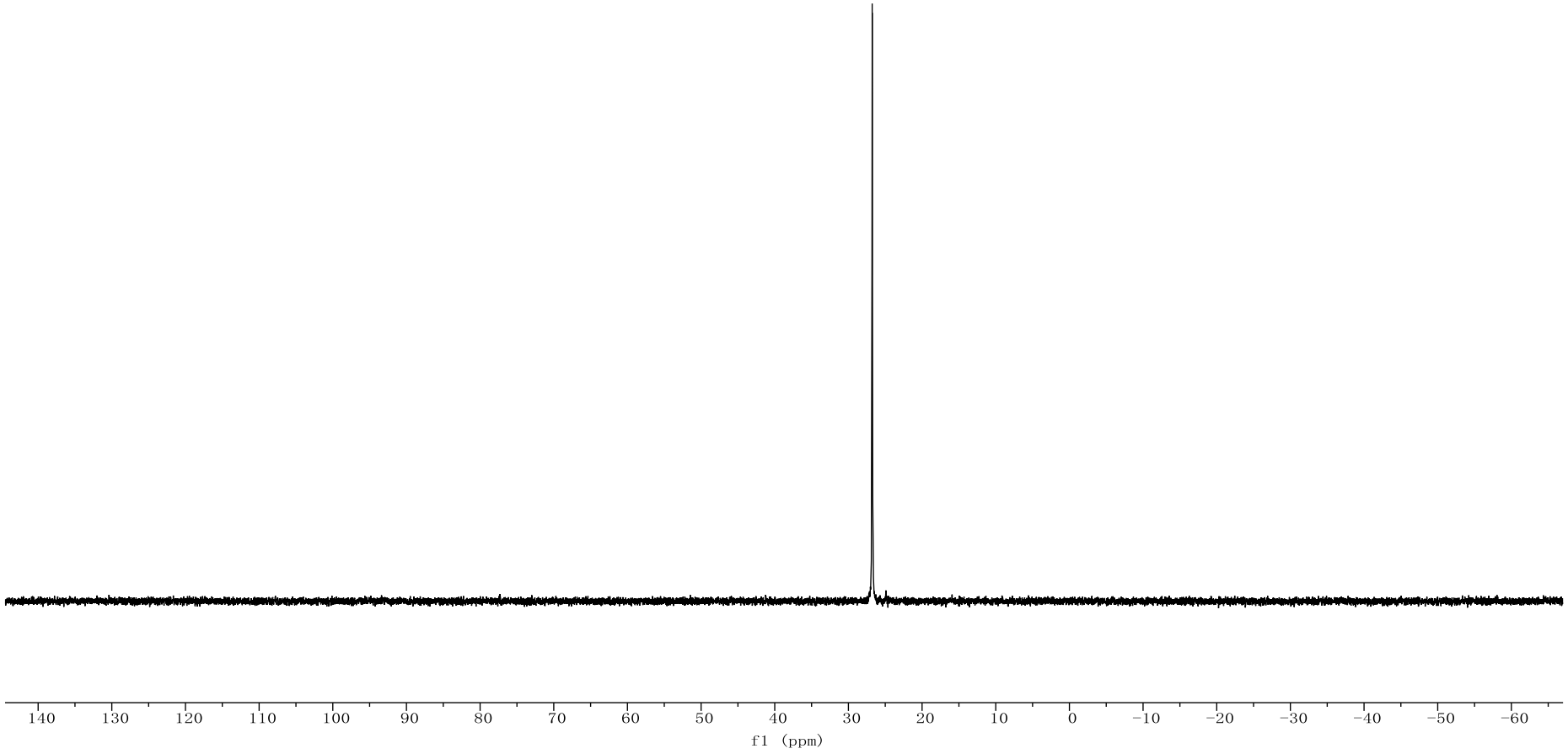

**4a**

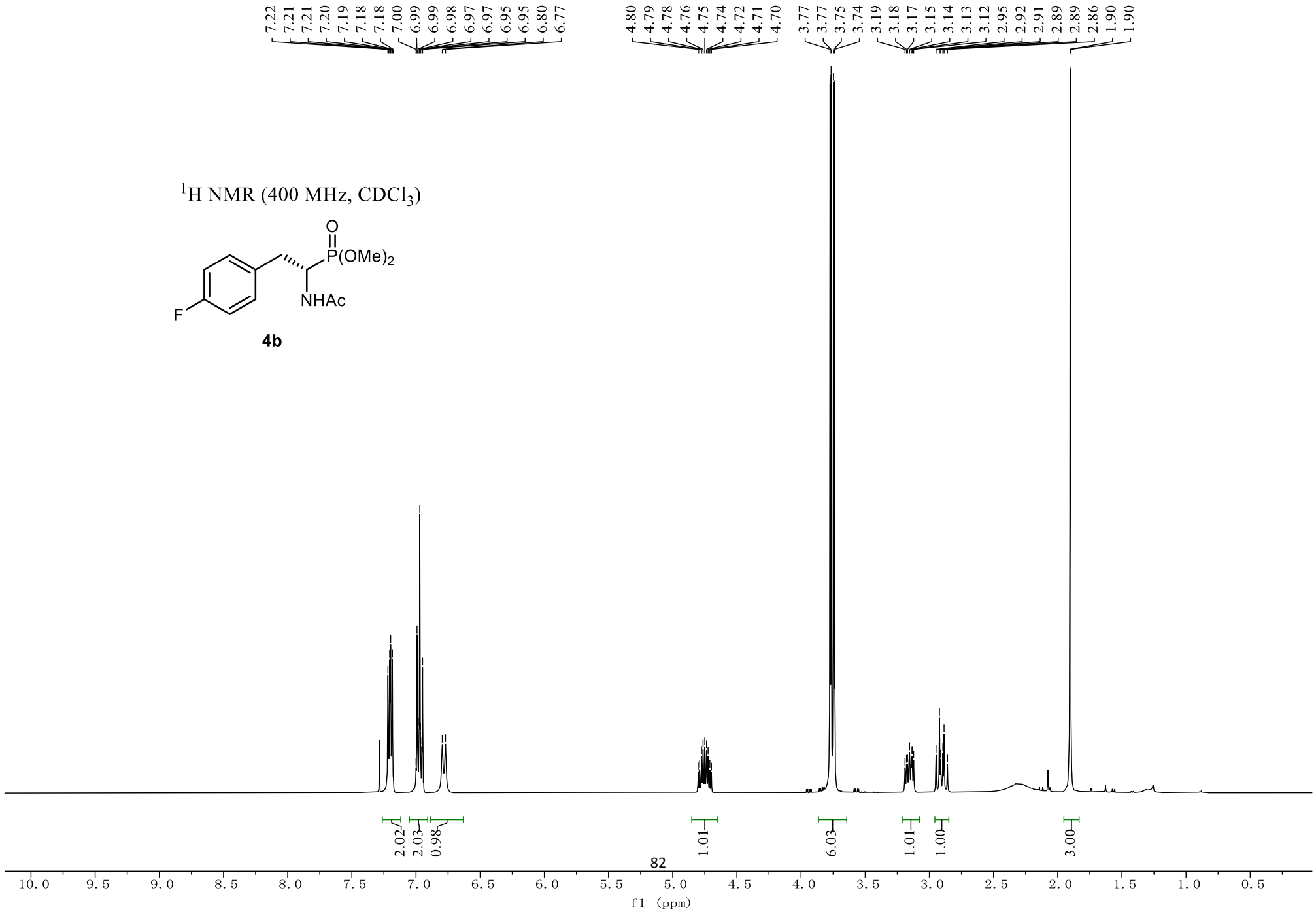


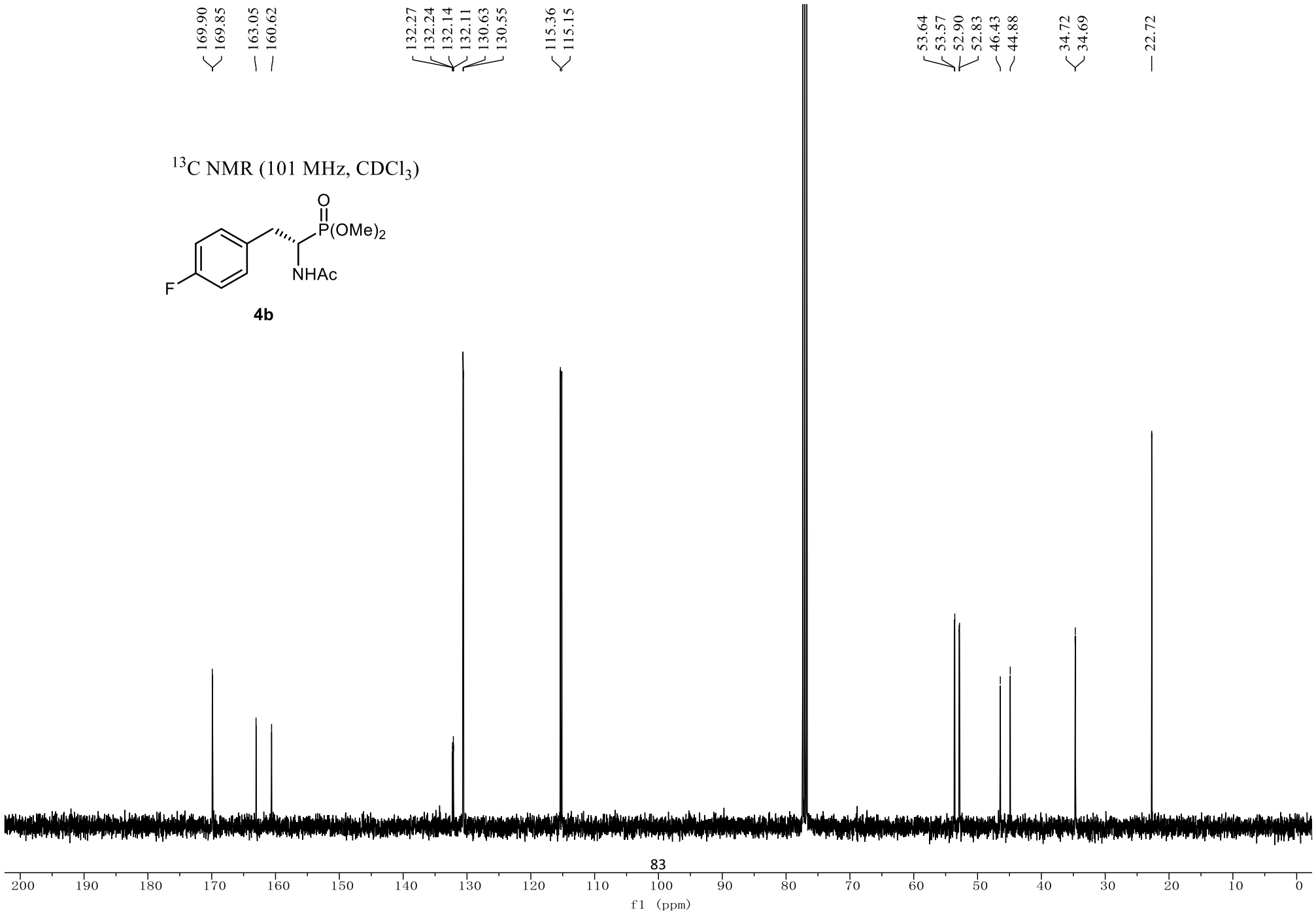
$^{31}$P NMR (162 MHz, $CDCl_3$)



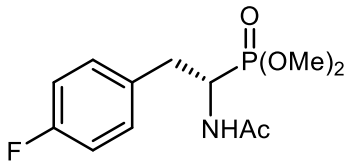

**4a**



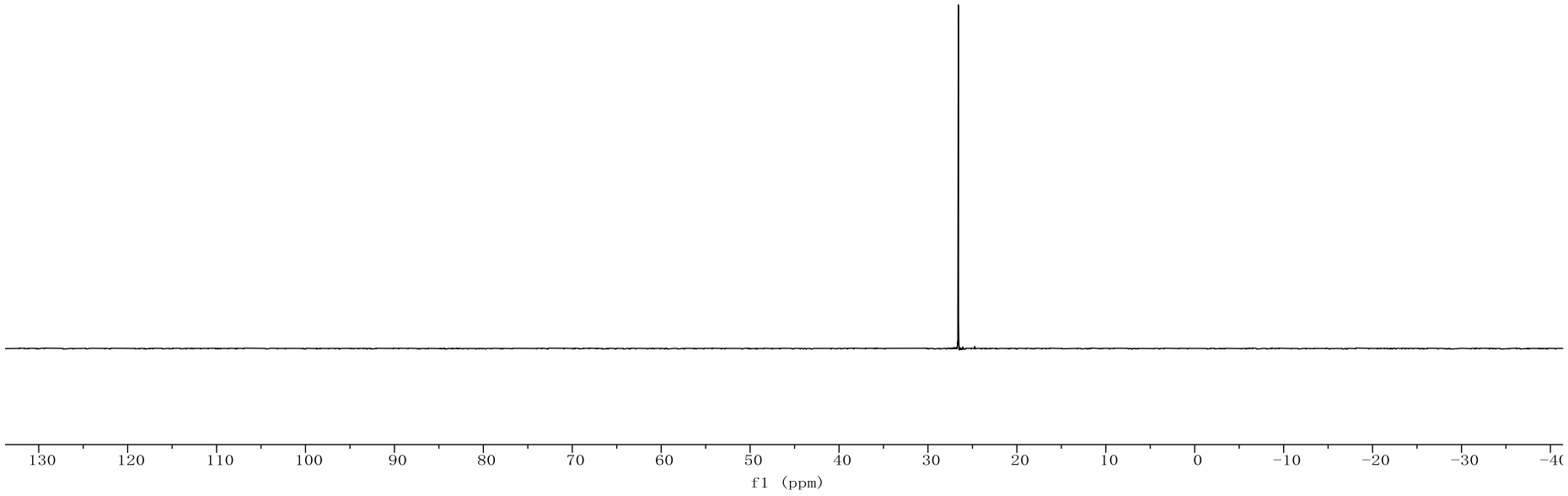

7.22
7.21
7.21
7.20
7.19
7.18
7.18
7.00
6.99
6.99
6.98
6.97
6.97
6.95
6.95
6.80
6.77
4.80
4.79
4.78
4.76
4.75
4.74
4.72
4.71
4.70
3.77
3.77
3.75
3.74
3.19
3.18
3.17
3.15
3.14
3.13
3.12
2.95
2.92
2.91
2.89
2.89
2.86
1.90
1.90
$^1$H NMR (400 MHz, $CDCl_3$)
O
P(OMe)$_2$
NHAc
F
4b
2.02
2.03
0.98
1.01
6.03
1.01
1.00
3.00
82
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


169.90
169.85
163.05
160.62
132.27
132.24
132.14
132.11
130.63
130.55
115.36
115.15
53.64
53.57
52.90
52.83
46.43
44.88
34.72
34.69
22.72
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHAc
F
4b
83
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

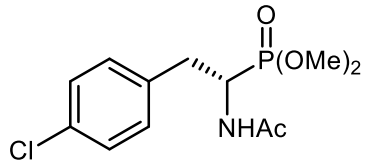
$^{31}$P NMR (162 MHz, $CDCl_3$)



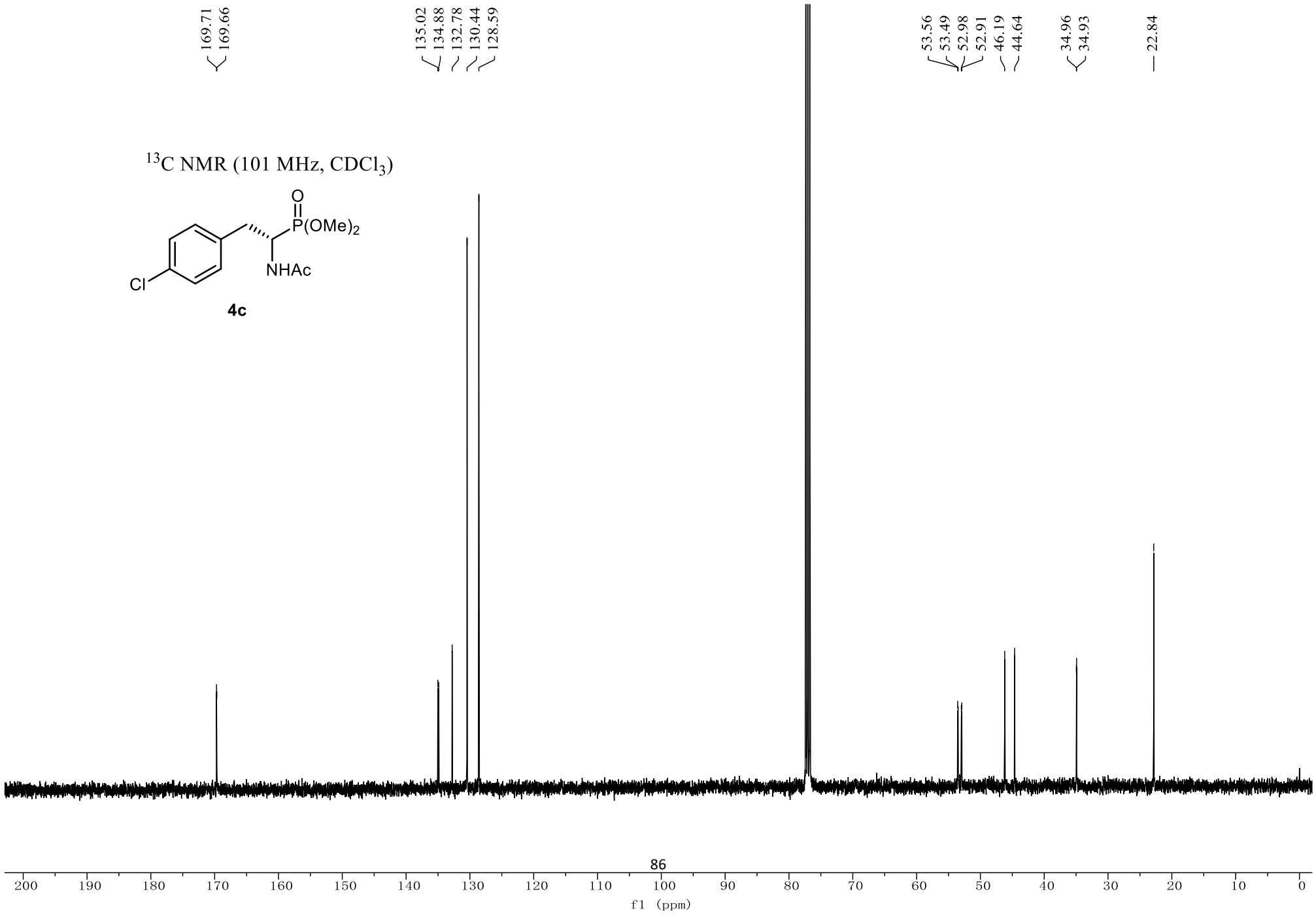

**4b**



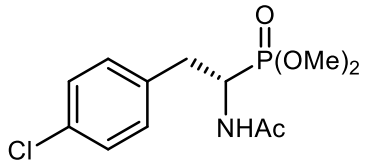
$^1$H NMR (400 MHz, $CDCl_3$)



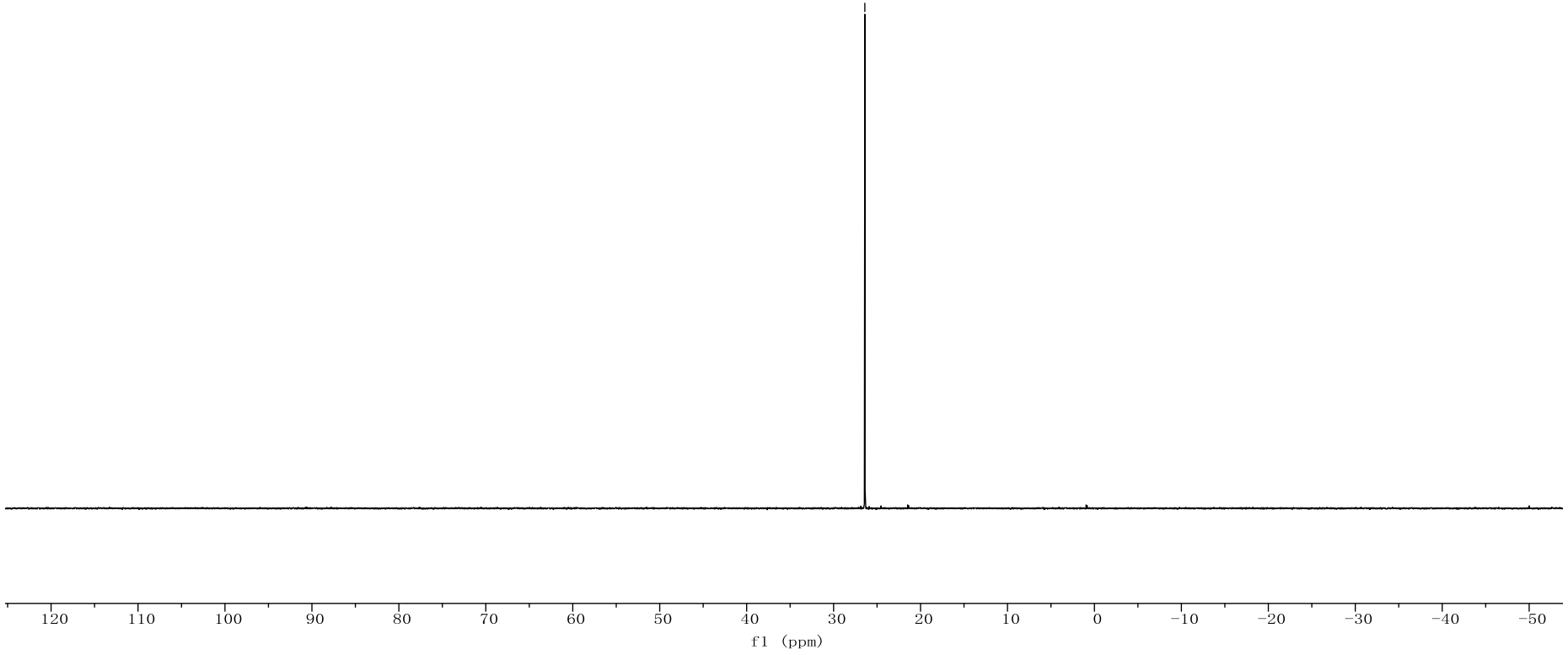

**4c**


169.71
169.66
135.02
134.88
132.78
130.44
128.59
53.56
53.49
52.98
52.91
46.19
44.64
34.96
34.93
22.84
$^{13}$C NMR (101 MHz, CDCl$_3$)
O
P(OMe)$_2$
NHAc
Cl
4c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

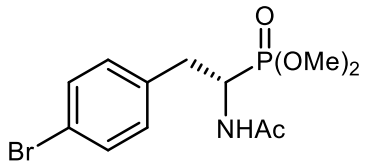
$^{31}$P NMR (162 MHz, $CDCl_3$)



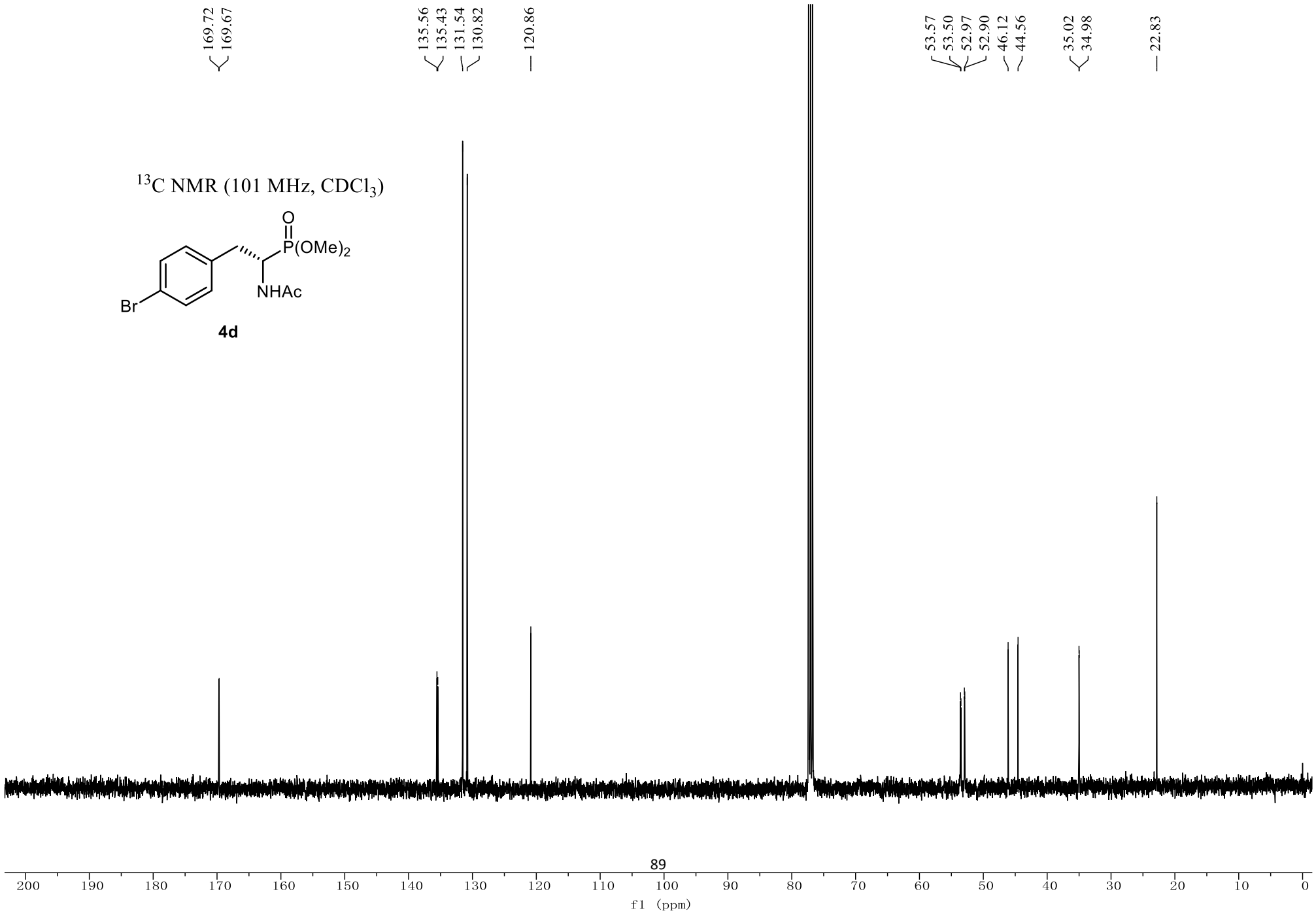

**4c**



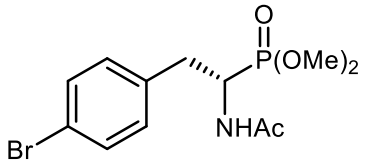
$^1$H NMR (400 MHz, $CDCl_3$)



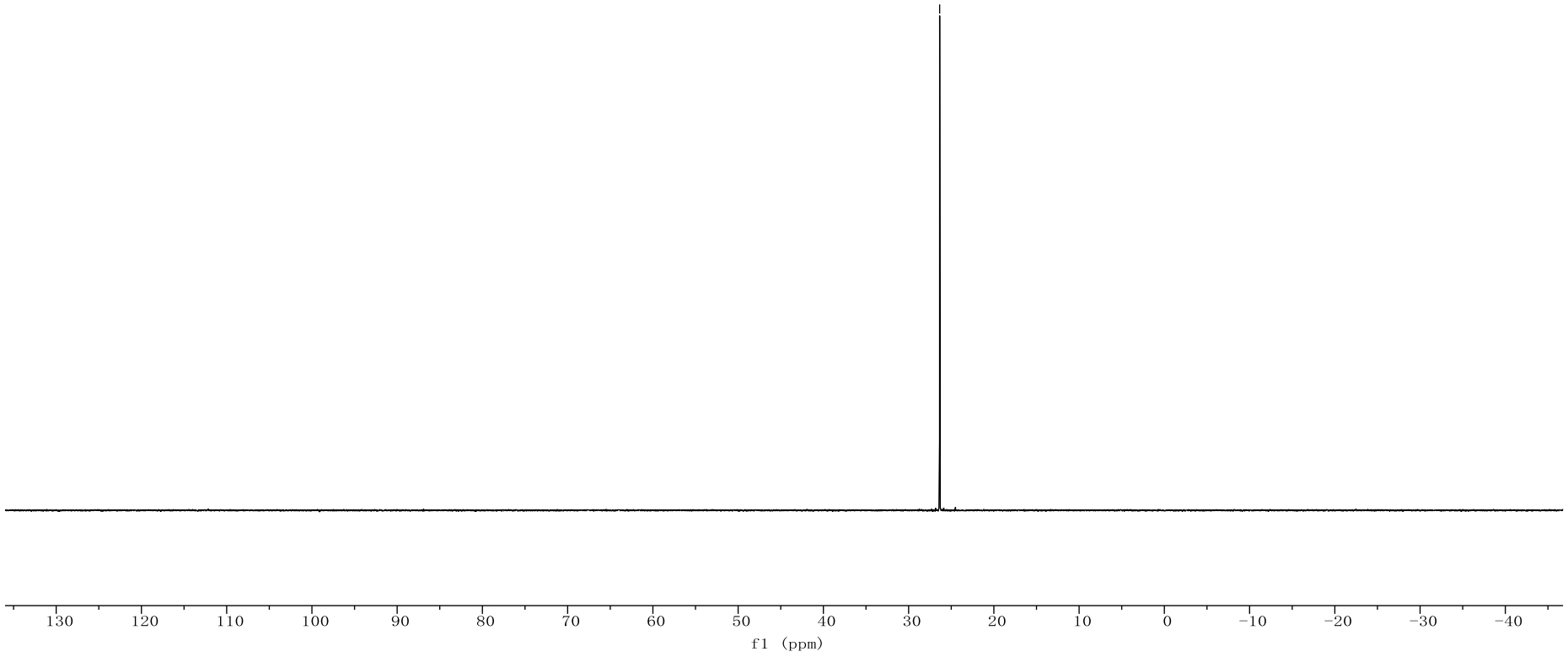

**4d**

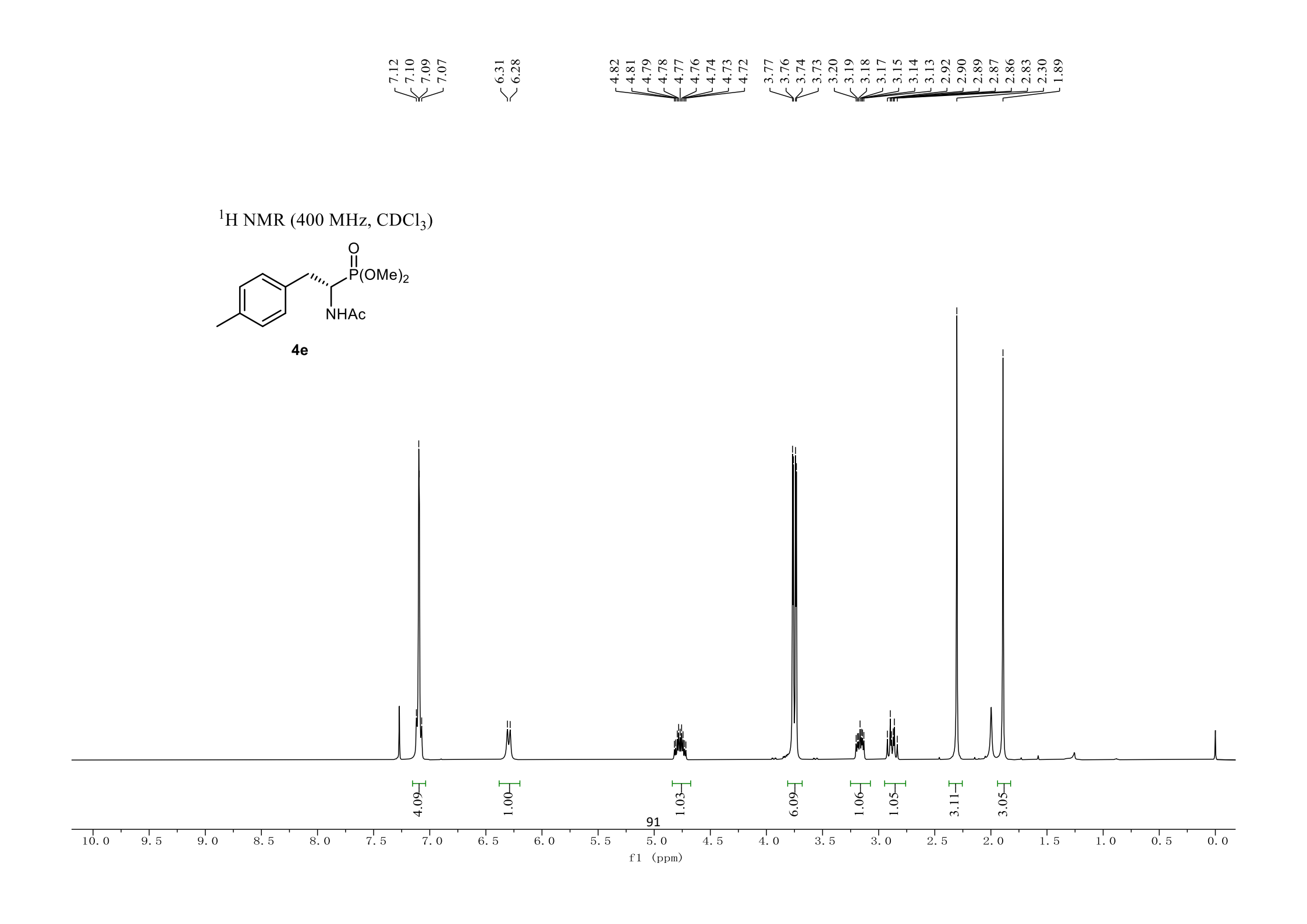

169.72
169.67
135.56
135.43
131.54
130.82
120.86
53.57
53.50
52.97
52.90
46.12
44.56
35.02
34.98
22.83
$^{13}$C NMR (101 MHz, CDCl$_3$)
O
P(OMe)$_2$
NHAc
Br
4d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

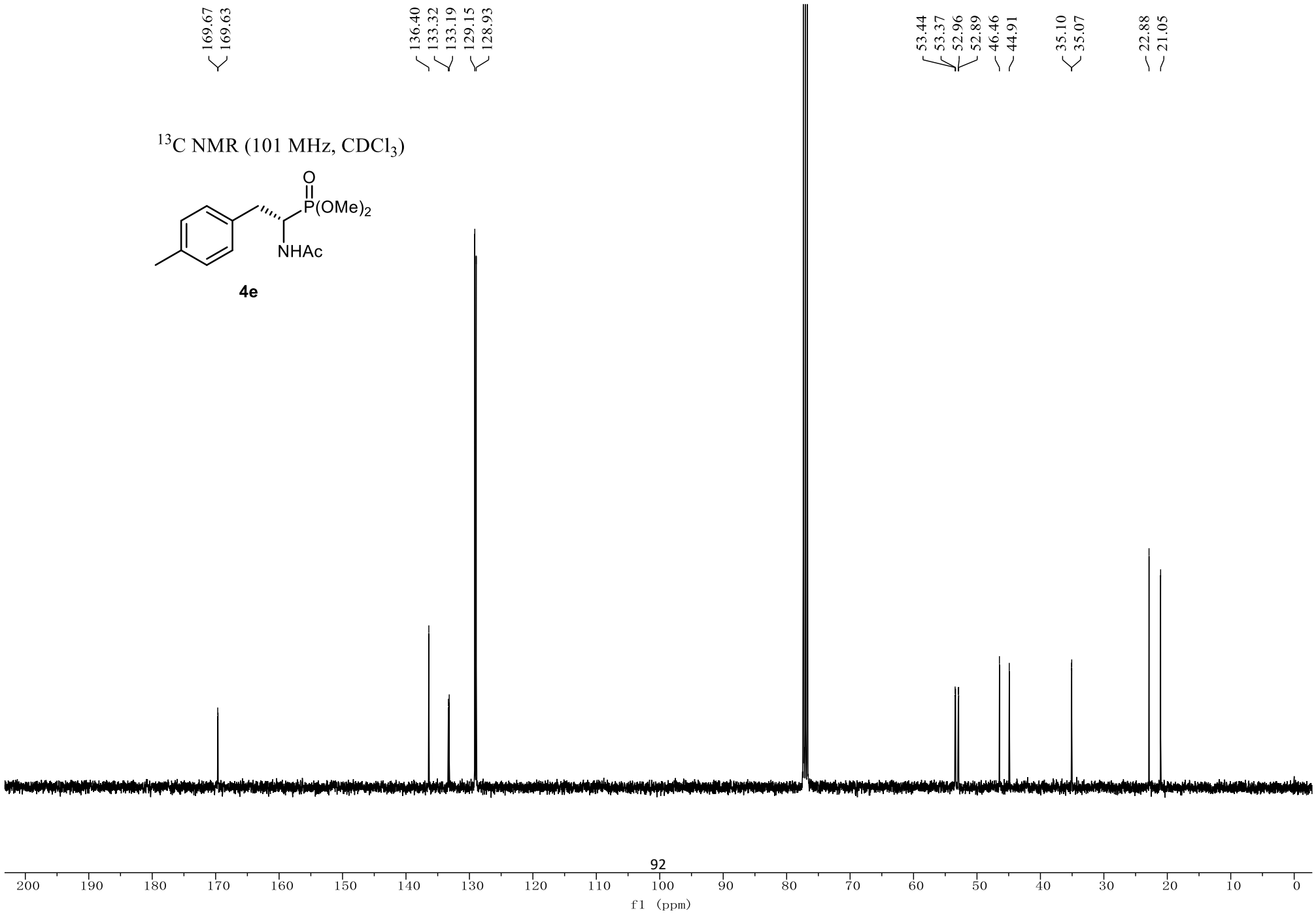
$^{31}$P NMR (162 MHz, $CDCl_3$)




**4d**

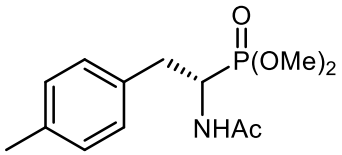



7.12
7.10
7.09
7.07
6.31
6.28
4.82
4.81
4.79
4.78
4.77
4.76
4.74
4.73
4.72
3.77
3.76
3.74
3.73
3.20
3.19
3.18
3.17
3.15
3.14
3.13
2.92
2.90
2.89
2.87
2.86
2.83
2.30
1.89
1H NMR (400 MHz, CDCl3)
O
P(OMe)2
NHAc
4e
4.09
1.00
1.03
6.09
1.06
1.05
3.11
3.05
91
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

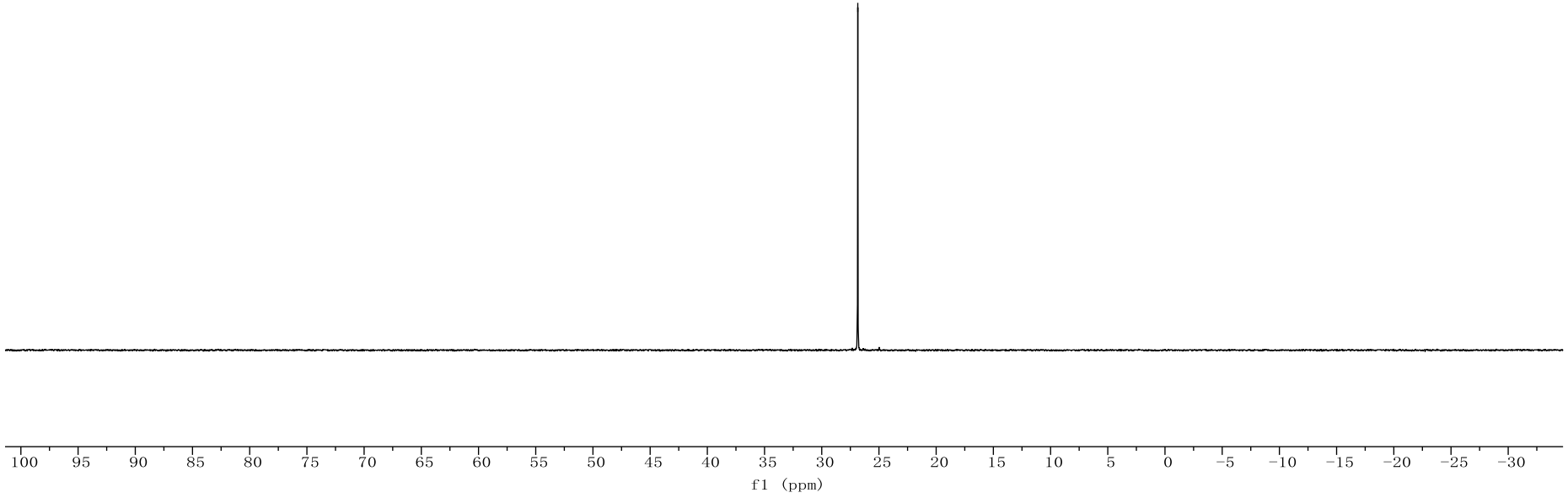

169.67
169.63
136.40
133.32
133.19
129.15
128.93
53.44
53.37
52.96
52.89
46.46
44.91
35.10
35.07
22.88
21.05
13C NMR (101 MHz, CDCl3)
O
P(OMe)2
NHAc
4e
92
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

— 26.85

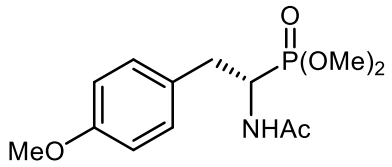
$^{31}$P NMR (162 MHz, $CDCl_3$)



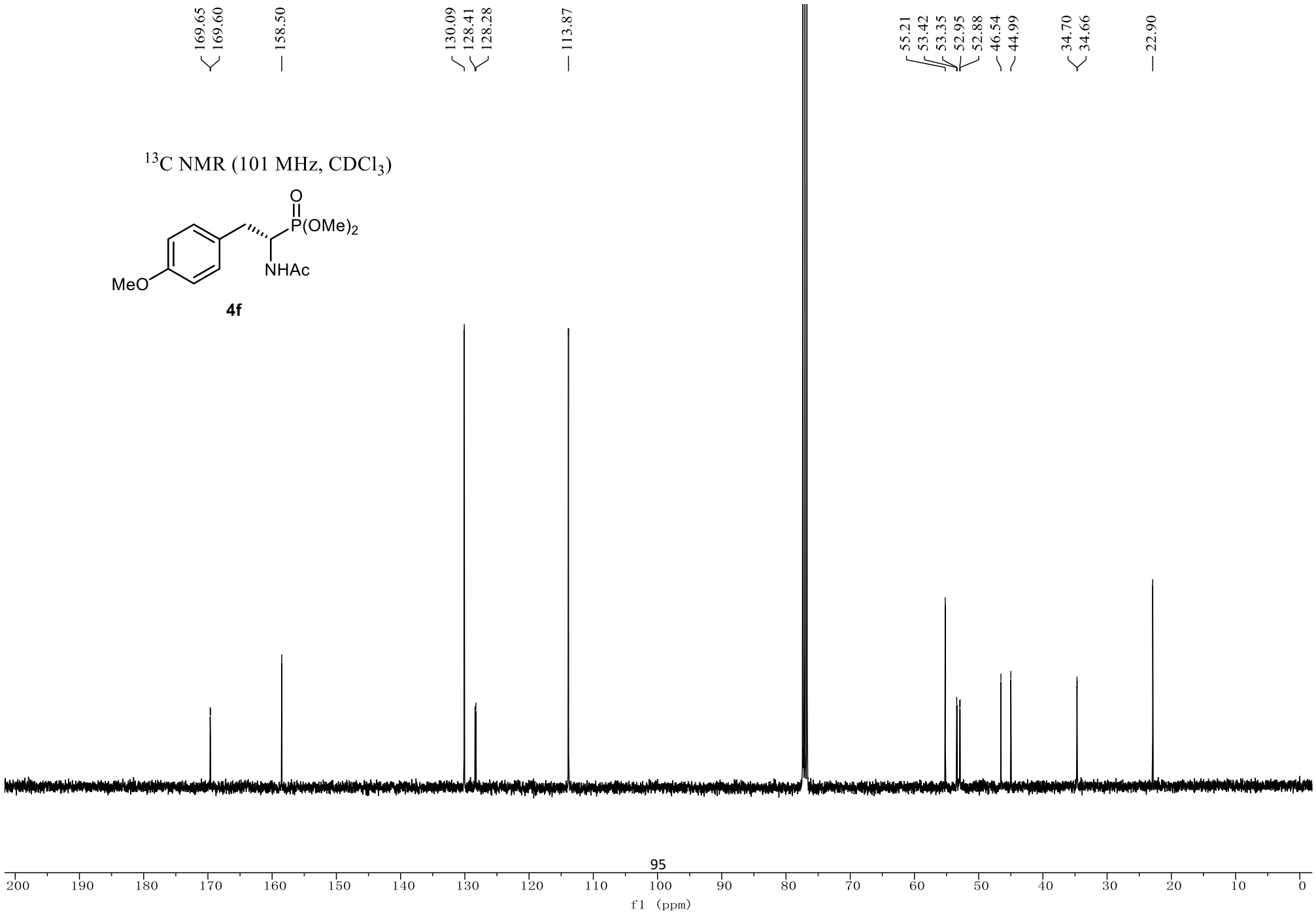

**4e**



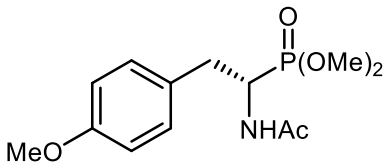
$^1$H NMR (400 MHz, $CDCl_3$)



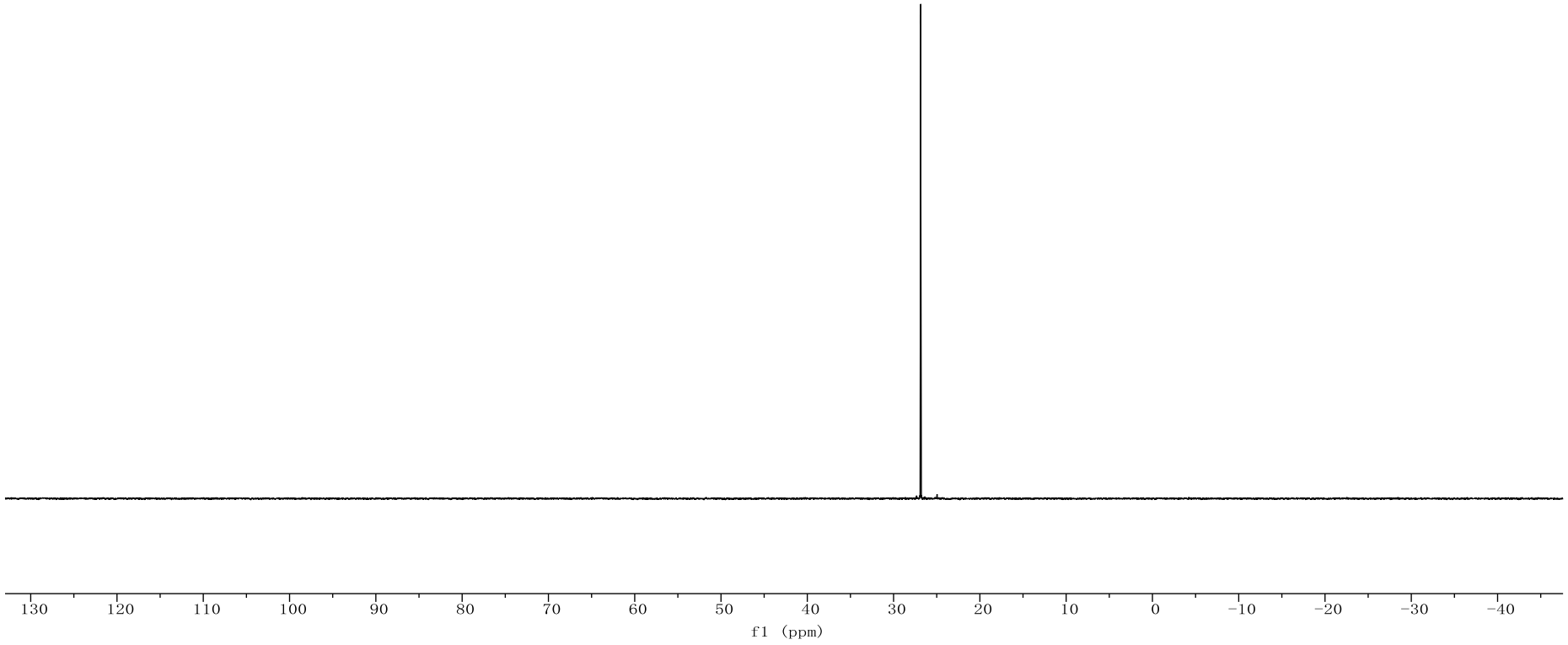

**4f**

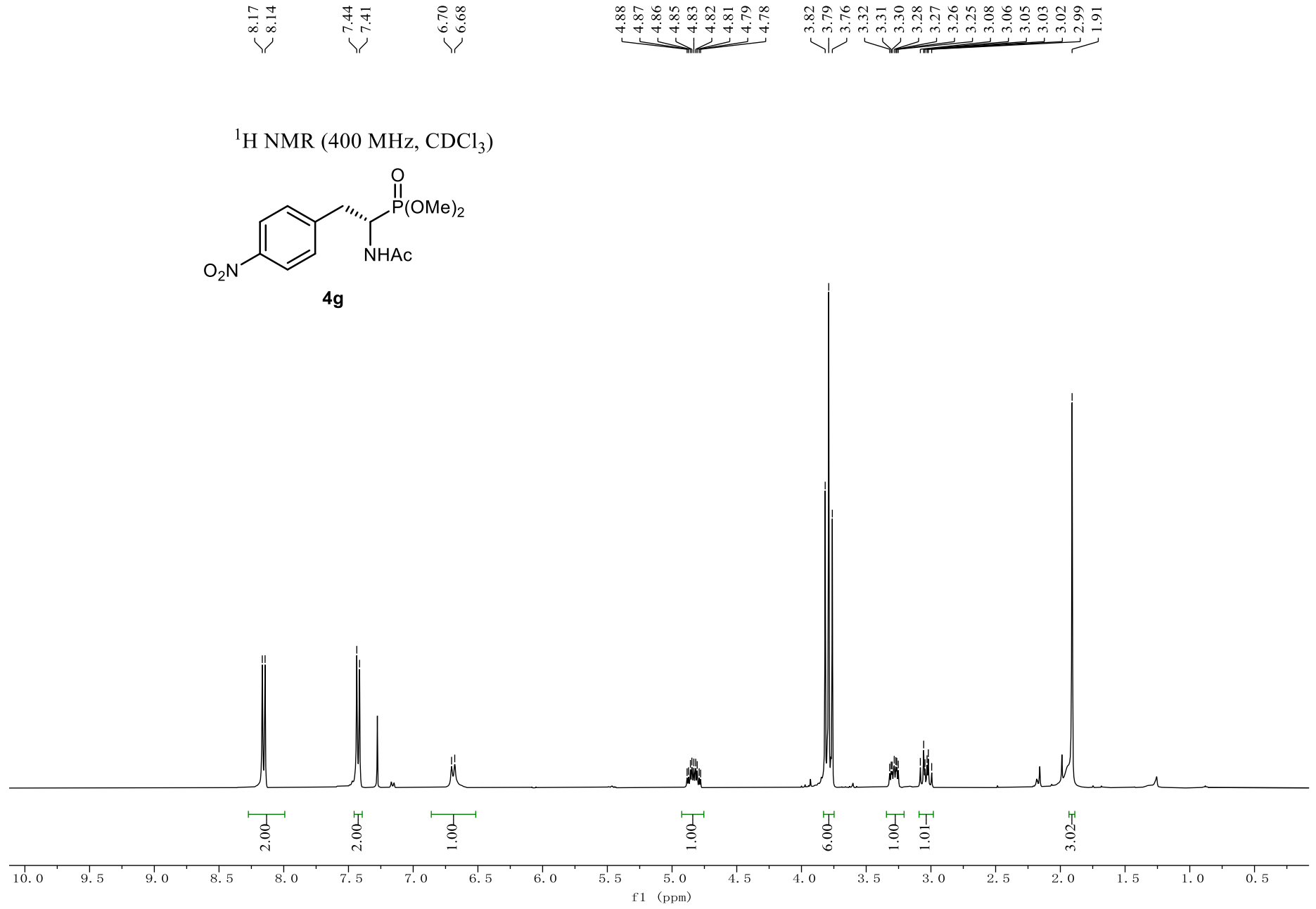

169.65
169.60
158.50
130.09
128.41
128.28
113.87
55.21
53.42
53.35
52.95
52.88
46.54
44.99
34.70
34.66
22.90
$^{13}$C NMR (101 MHz, CDCl$_3$)
O
P(OMe)$_2$
NHAc
MeO
4f
95
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)



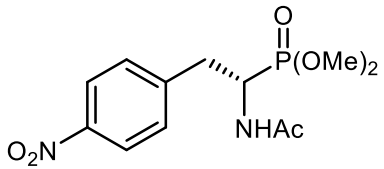

**4f**




8.17
8.14
7.44
7.41
6.70
6.68
4.88
4.87
4.86
4.85
4.83
4.82
4.81
4.79
4.78
3.82
3.79
3.76
3.32
3.31
3.30
3.28
3.27
3.26
3.25
3.08
3.06
3.05
3.03
3.02
2.99
1.91
$^1$H NMR (400 MHz, $CDCl_3$)
O
P(OMe)$_2$
NHAc
$O_2N$
4g
2.00
2.00
1.00
1.00
6.00
1.00
1.01
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

169.82
169.77
147.05
144.48
144.35
130.03
123.63
53.79
53.72
53.07
53.00
45.95
44.39
35.50
35.47
22.75

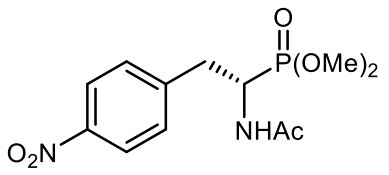
$^{13}C$ NMR (101 MHz, $CDCl_3$)



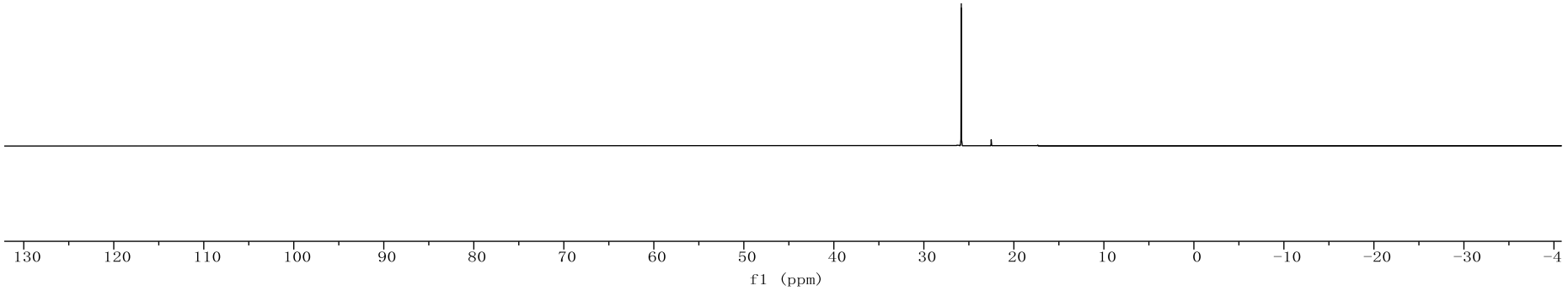

**4g**

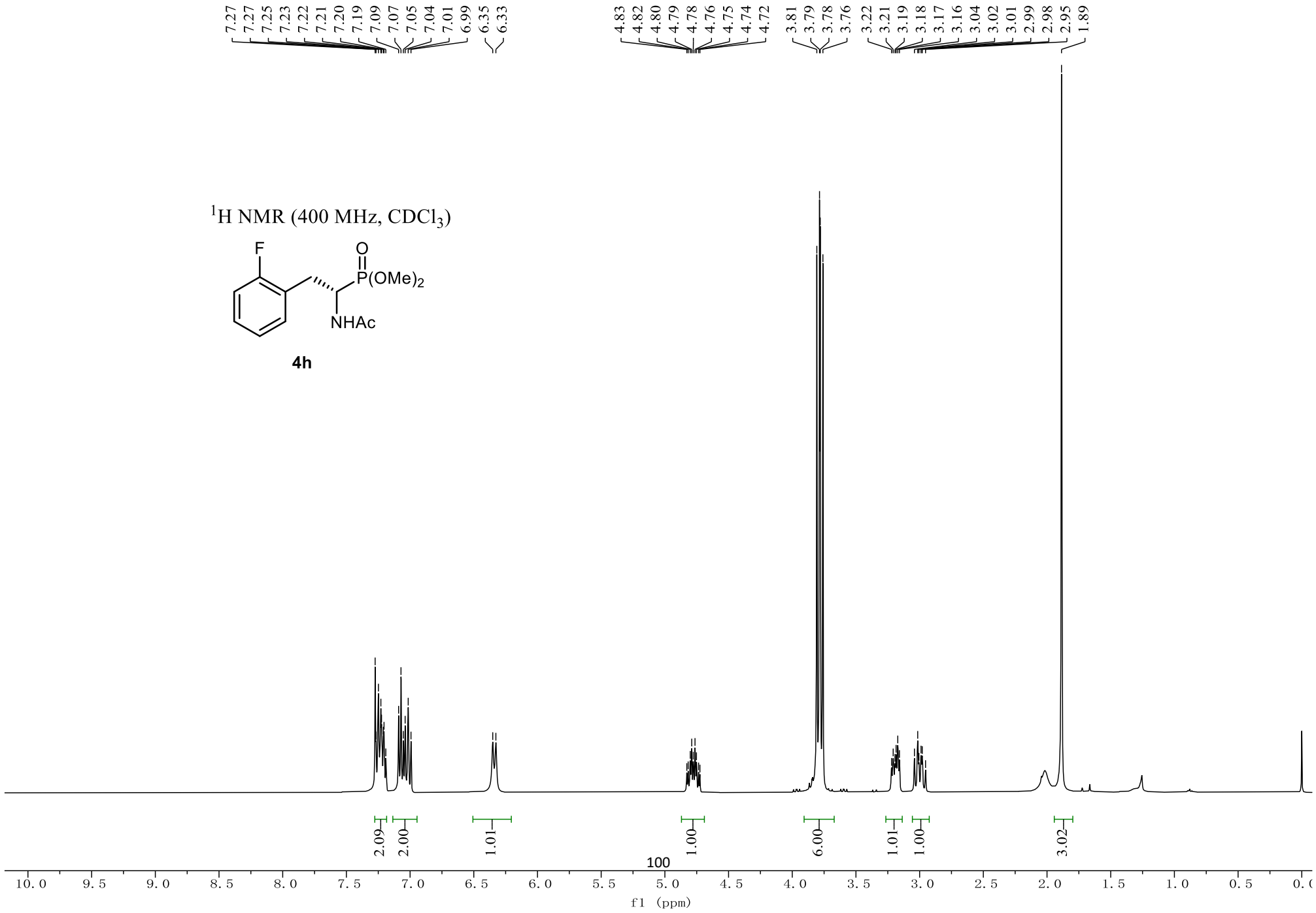
— 25.84

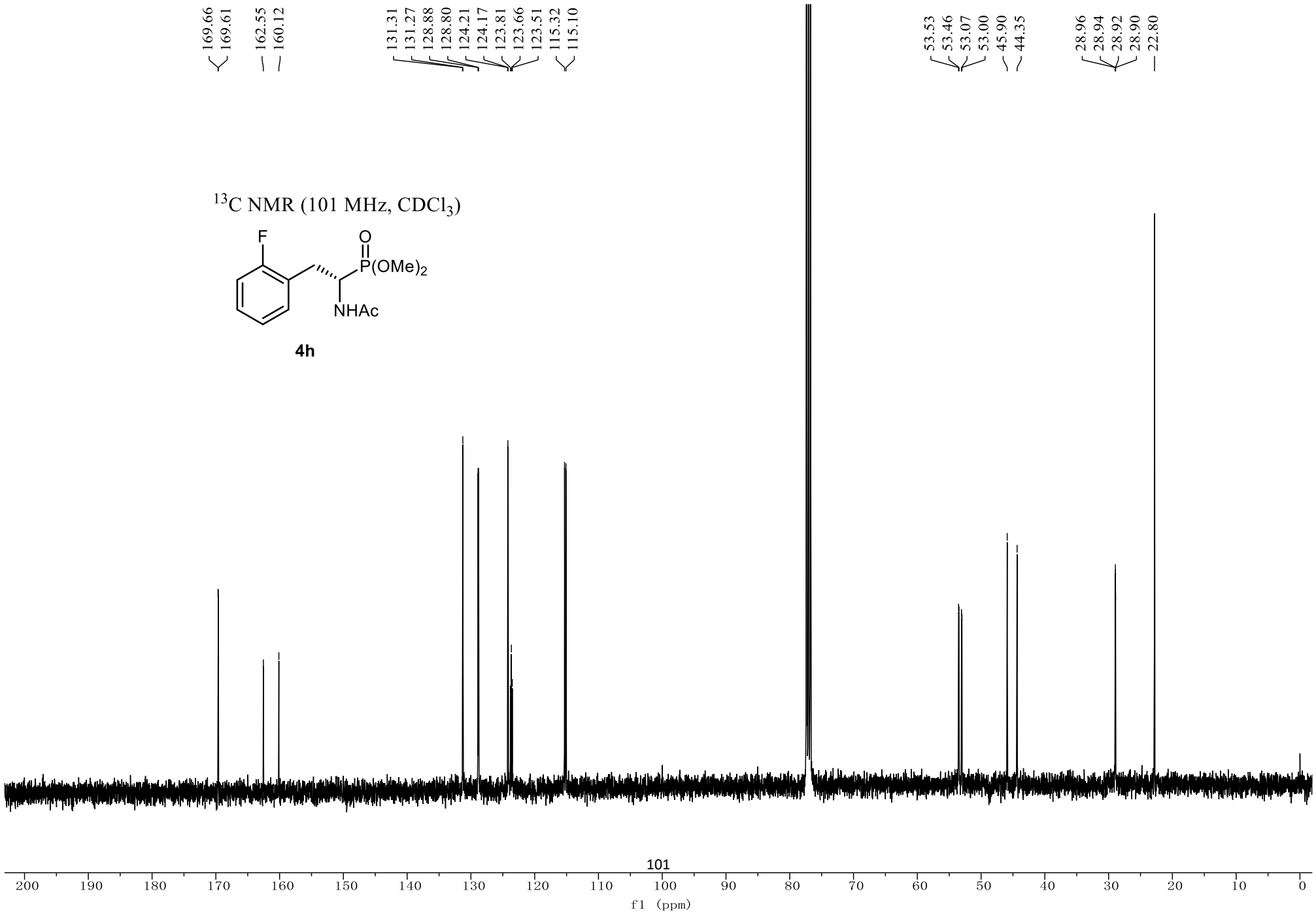
$^{31}$P NMR (162 MHz, $CDCl_3$)




**4g**

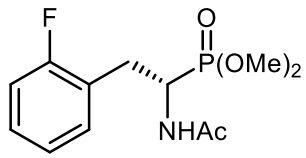



7.27
7.27
7.25
7.23
7.22
7.21
7.20
7.19
7.09
7.07
7.05
7.04
7.01
6.99
6.35
6.33
4.83
4.82
4.80
4.79
4.78
4.76
4.75
4.74
4.72
3.81
3.79
3.78
3.76
3.22
3.21
3.19
3.18
3.17
3.16
3.04
3.02
3.01
2.99
2.98
2.95
1.89
$^1$H NMR (400 MHz, $CDCl_3$)
F
O
P(OMe)$_2$
NHAc
4h
2.09
2.00
1.01
1.00
6.00
1.01
1.00
3.02
100
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

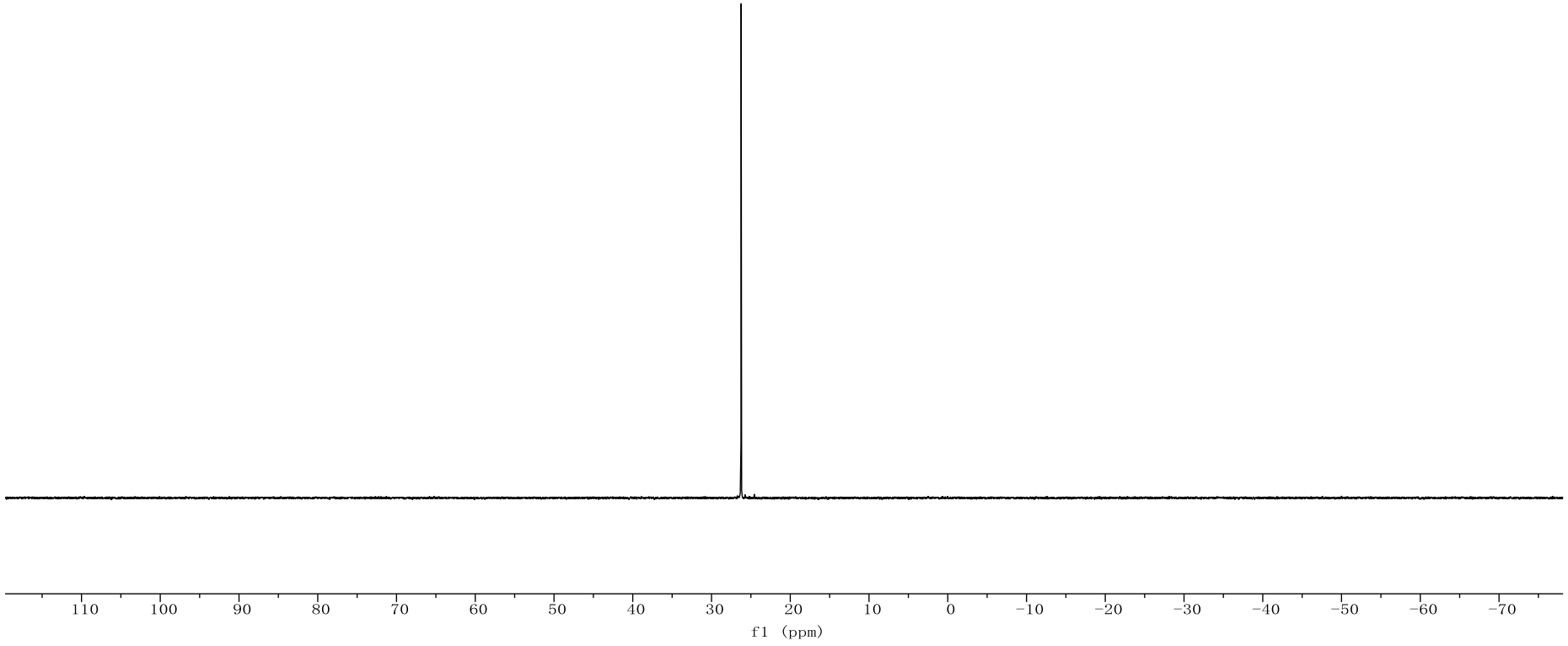

169.66
169.61
162.55
160.12
131.31
131.27
128.88
128.80
124.21
124.17
123.81
123.66
123.51
115.32
115.10
53.53
53.46
53.07
53.00
45.90
44.35
28.96
28.94
28.92
28.90
22.80
$^{13}$C NMR (101 MHz, CDCl$_3$)
F
O
P(OMe)$_2$
NHAc
4h
101
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

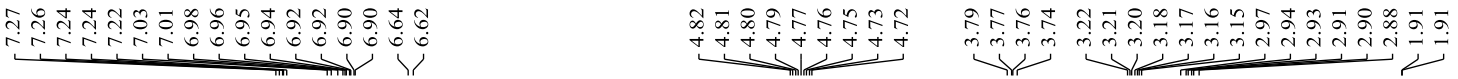
— 26.23

$^{31}$P NMR (162 MHz, $CDCl_3$)

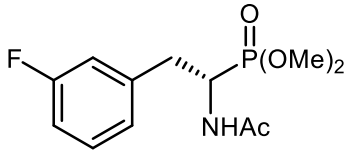



**4h**

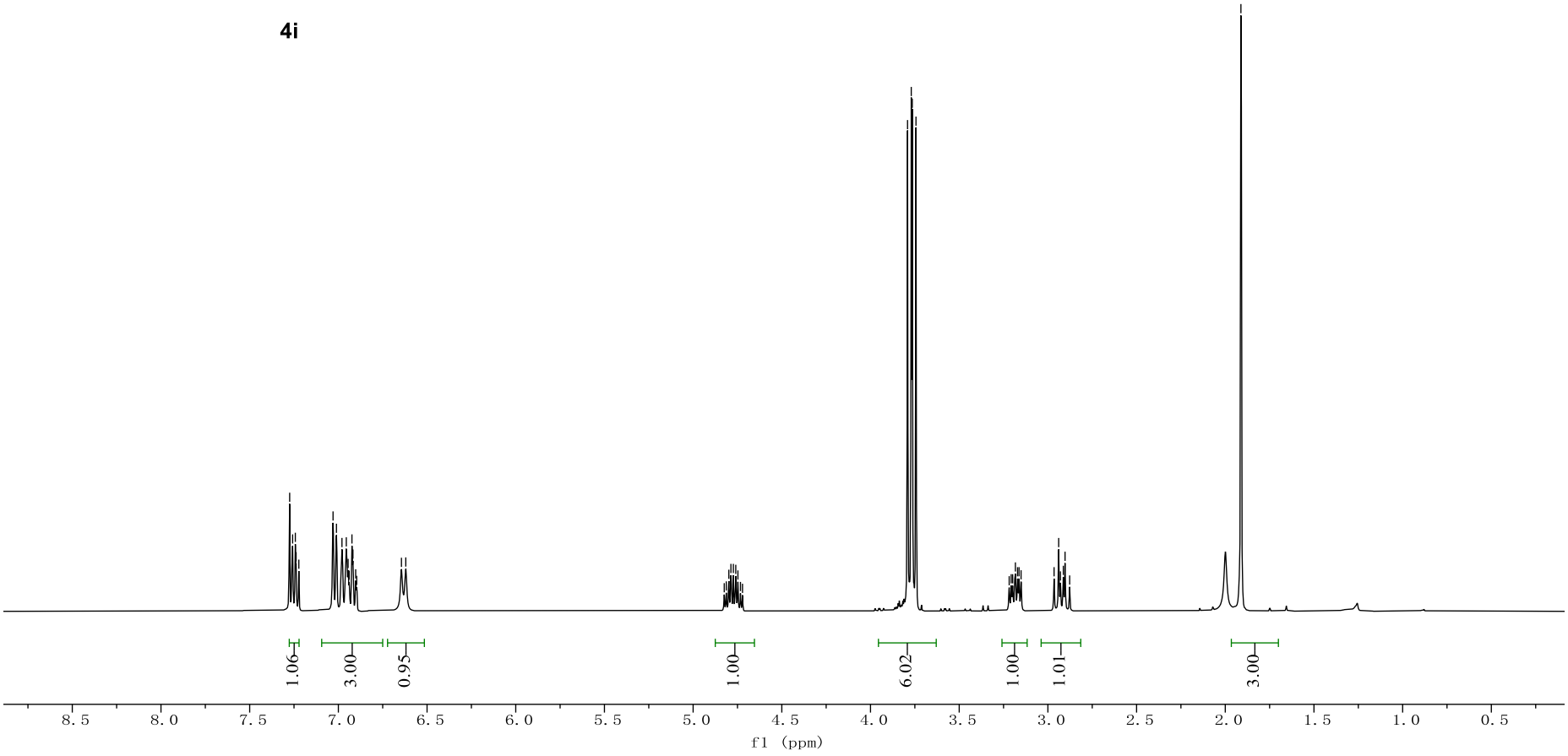


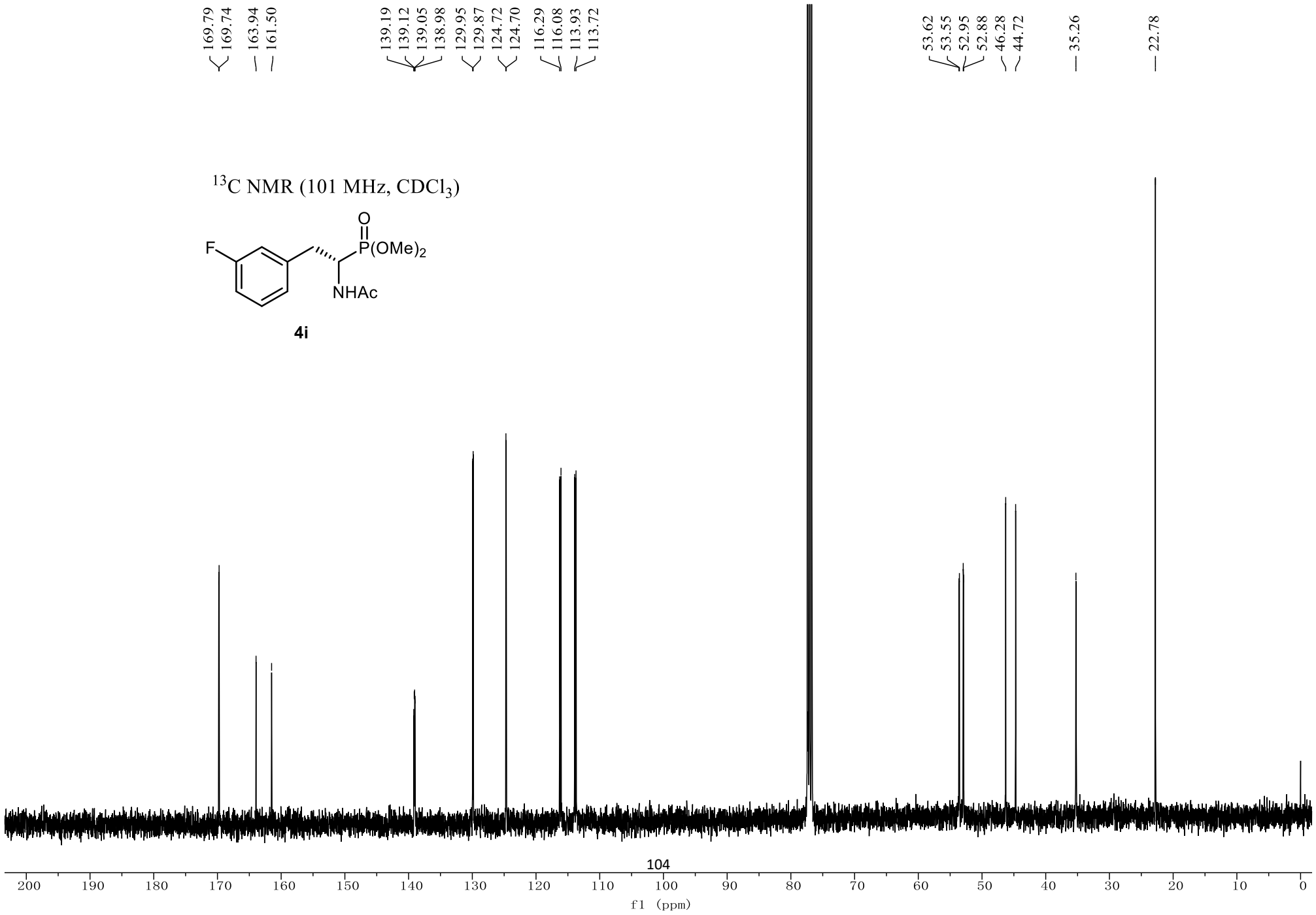



$^1$H NMR (400 MHz, $CDCl_3$)

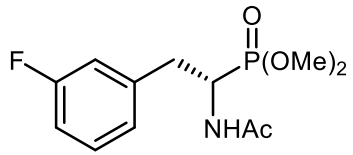



**4i**

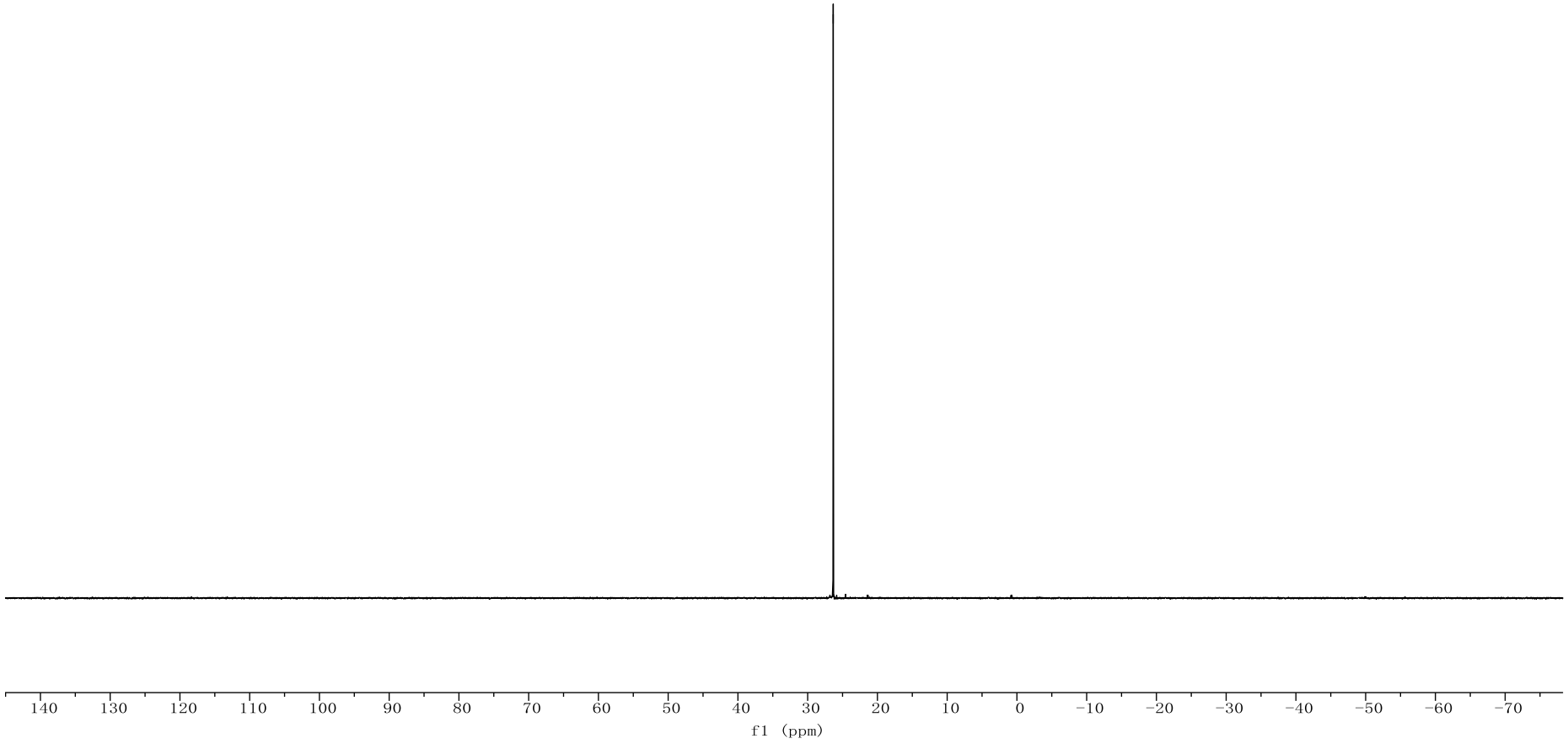


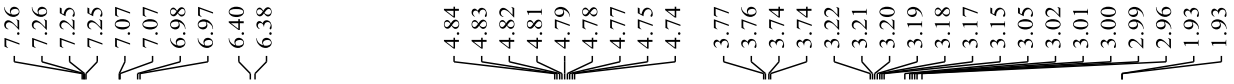

169.79
169.74
163.94
161.50
139.19
139.12
139.05
138.98
129.95
129.87
124.72
124.70
116.29
116.08
113.93
113.72
53.62
53.55
52.95
52.88
46.28
44.72
35.26
22.78
13C NMR (101 MHz, CDCl3)
F
O
P(OMe)2
NHAc
4i
104
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)

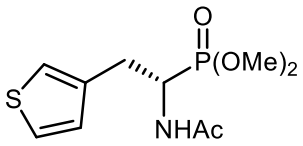



**4i**

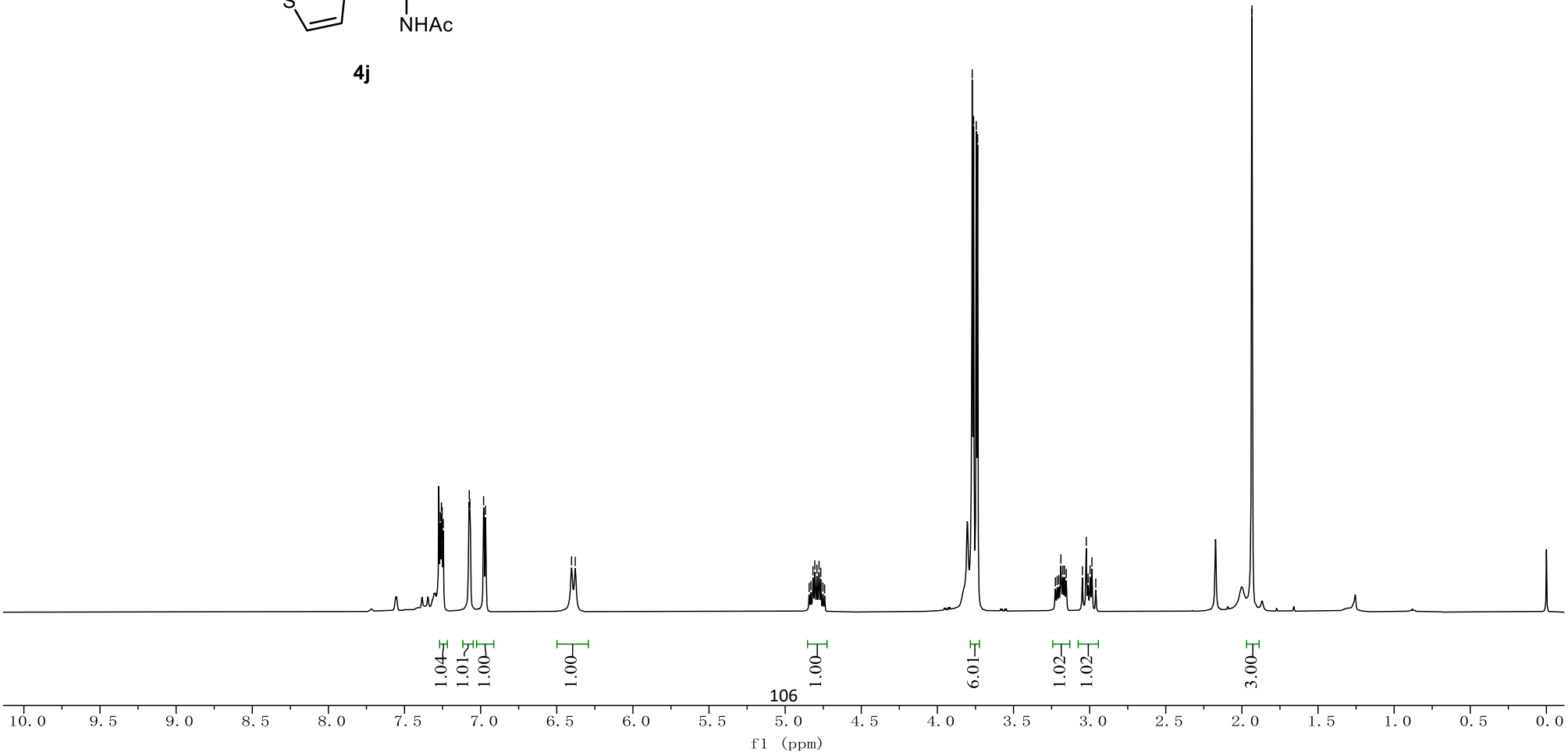


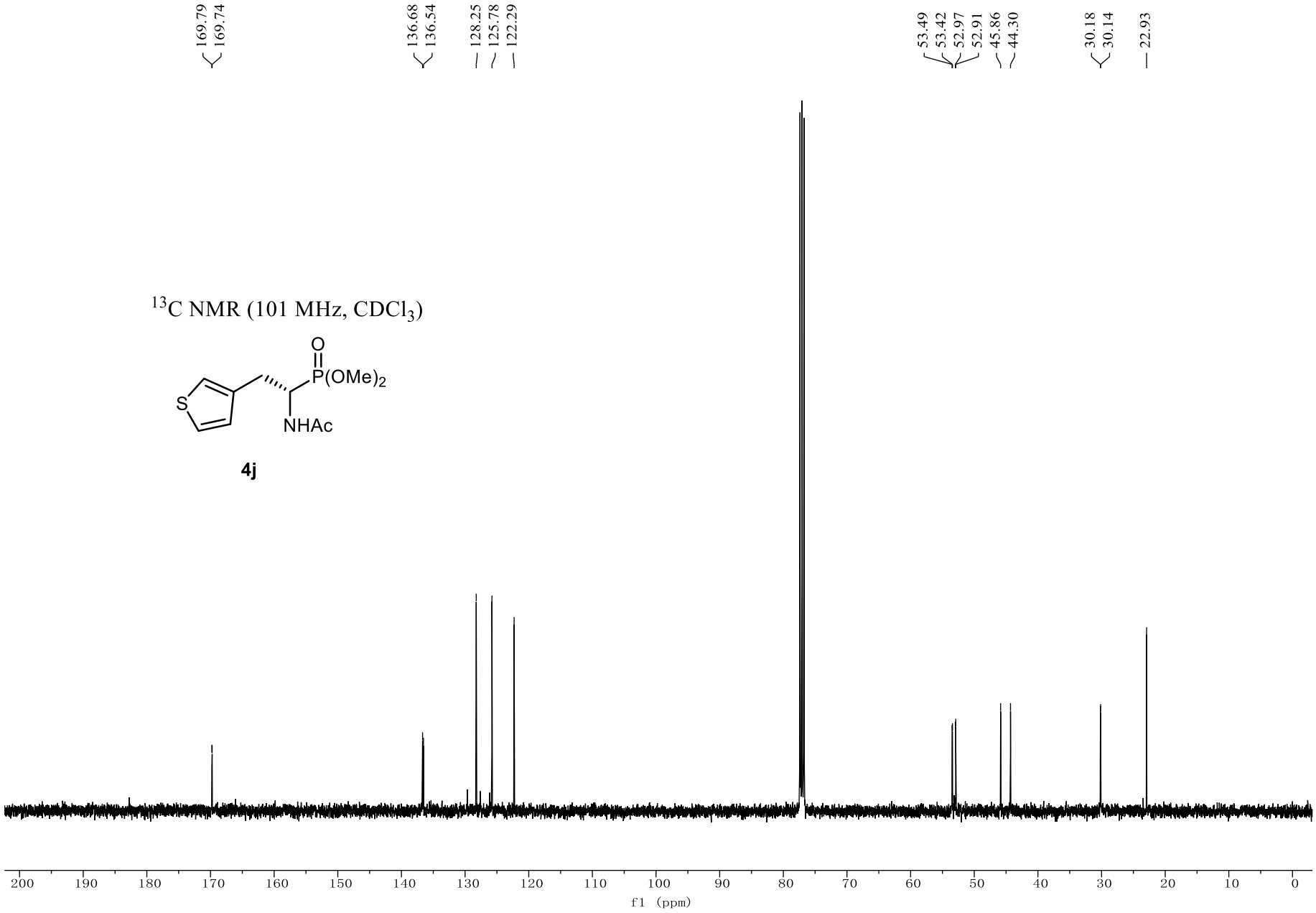



$^1$H NMR (400 MHz, $CDCl_3$)

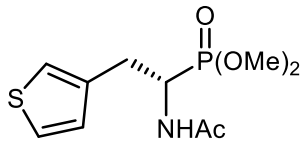



**4j**



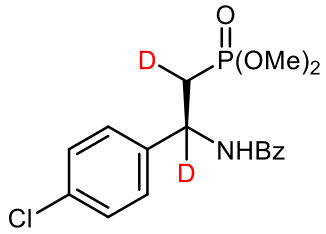

169.79
169.74
136.68
136.54
128.25
125.78
122.29
53.49
53.42
52.97
52.91
45.86
44.30
30.18
30.14
22.93
$^{13}$C NMR (101 MHz, $CDCl_3$)
O
P(OMe)$_2$
S
NHAc
4j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

$^{31}$P NMR (162 MHz, $CDCl_3$)

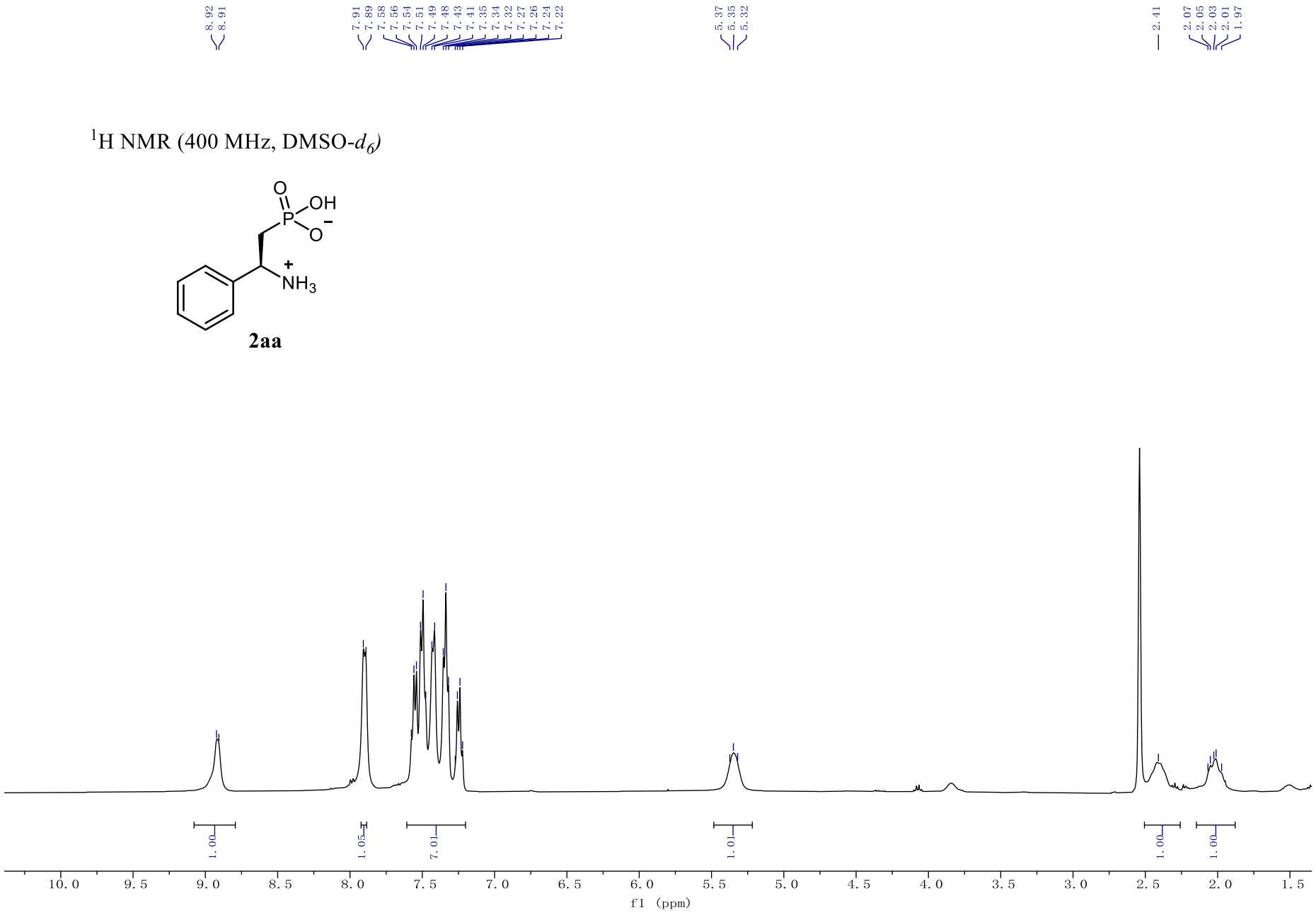



**4j**

$^{1}$H NMR (400 MHz, $CDCl_{3)}$



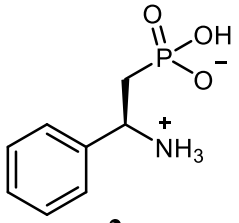

**2c-$d_2$**



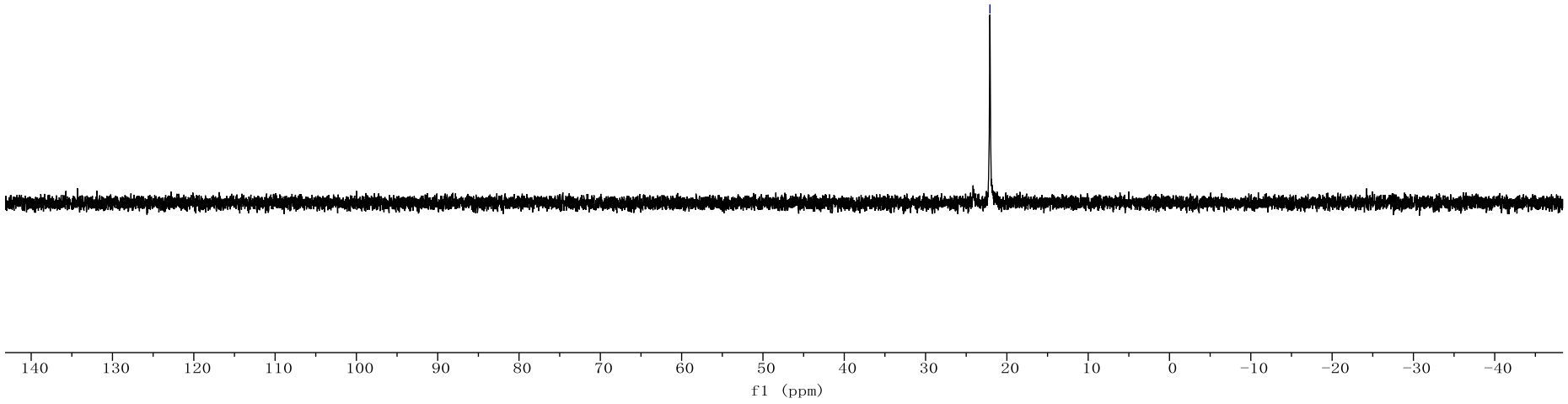

$^1$H NMR (400 MHz, DMSO-$d_6$)

**2aa**

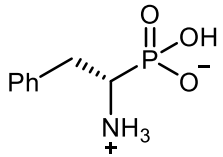
$^{31}$P NMR (162 MHz, DMSO-$d_6$)




**2aa**

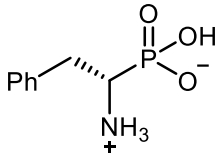


$^{1}$H NMR (400 MHz, Deuterium Oxide with 1 drop 30%NaOD*)*

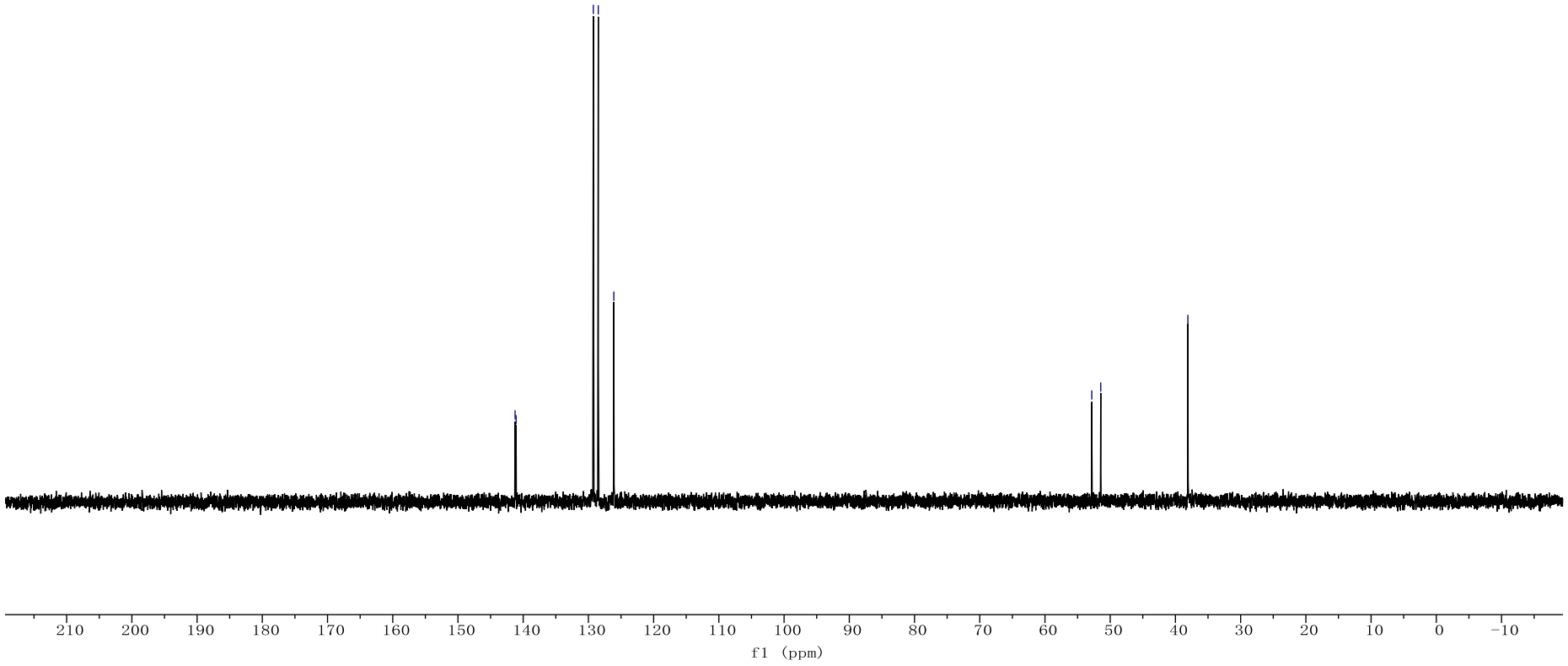



**4aa**

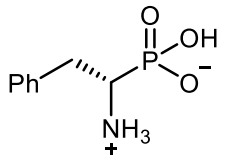
$^{13}$C NMR (101 MHz, Deuterium Oxide with 1 drop 30%NaOD*)*




**4aa**



$^{31}$P NMR (162 MHz, Deuterium Oxide with 1 drop 30%NaOD*)*




**4aa**