

Base Accelerated Enantioselective Substitution of Morita-Baylis-Hillman Carbonates with Dialkyl Phosphine Oxides

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Index:

General Methods	S2
General Procedure for the Synthesis of 3a	S3
Spectral Data for the Products 3a	S3
General Procedure for the Synthesis of 4	S4
Spectral Data for the Products 4	S4-S11
HPLC Analytic Conditions	S12-S13
Copies of HPLC data	S14-S27
Copies of ^1H , ^{13}C and ^{31}P NMR Spectra	S28-S72

General Methods:

Unless stated otherwise, all reactions were carried out in flamedried glassware. All solvents were purified and dried according to standard methods prior to use. Morita-Baylis-Hillman carbonates **1** were prepared according to the literature.¹ Dialkyl phosphine oxides **2** were prepared according to the literature.² ^1H , ^{13}C and ^{31}P NMR spectra were recorded on a Varian instrument (300, 75 and 121 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for ^1H NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet or unresolved, coupling constant(s) in Hz, integration). Data for ^{13}C and ^{31}P NMR are reported in terms of chemical shift (δ , ppm). IR spectra were recorded on a FT-IR spectrometer and only major peaks were reported in cm^{-1} . Optical rotations were reported as follows: $[\alpha]_{\text{D}}^{25}$ (c: g/100 mL, in solvent). Highresolution mass spectra (HRMS) were obtained by the ESI ionization sources. The ee value determination was carried out using chiral HPLC with Daicel Chiracel OD-H or AD column on Waters with a 996 UV-detector.

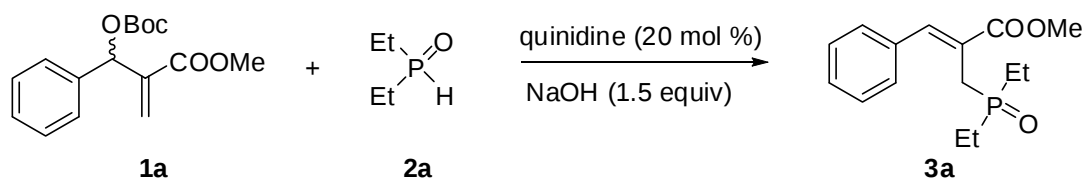
[1] J. Feng, X. Lu, A. Kong, X. Han, *Tetrahedron*. **2007**, 63, 6035.

[2] H. R. Hays, *J. Org. Chem.* **1968**, 33, 3690;

G. Aksnes, P. Majewski, *Phosphorous and Sulfur*, **1986**, 26, 261.

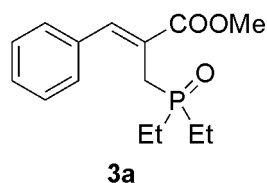
Experimental Procedures and Characterizations:

General Procedure A: Synthesis of **3a**.



To a solution of MBH carbonate **1a** (0.20 mmol), quinidine (0.04 mmol) and NaOH (0.30 mmol) in toluene (1.0 mL), diethyl phosphine oxide **2a** (0.50 mmol) was added at room temperature and stirred for 48 h. The reaction mixture was directly purified by silica gel chromatography without work up and fractions were collected and concentrated in vacuo to provide the pure desired product **3a**.

(Z)-methyl 2-((diethylphosphoryl)methyl)-3-phenylacrylate (**3a**)



3a was isolated by column chromatography using silica gel in 78% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.95 (d, *J* = 4.2 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.45-7.29 (m, 3H), 3.85 (s, 3H), 3.17 (s, 1H), 3.12 (s, 1H) 1.77-1.70 (m, 4H), 1.13 (dt, *J* = 7.8 Hz, *J* = 16.5 Hz, 6H);

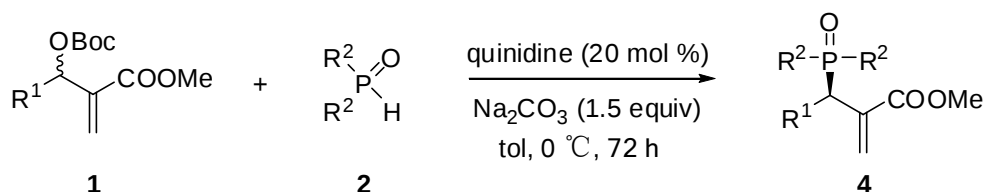
¹³C NMR (75 MHz, CDCl₃): δ 168.2, 143.0 (*J* = 7.5 Hz), 134.7 (*J* = 3.0 Hz), 129.3 (*J* = 1.5 Hz), 128.6, 123.6 (*J* = 9.0 Hz), 52.3, 27.3 (*J* = 59.25 Hz), 21.0 (*J* = 66.0 Hz), 5.6, 5.5;

³¹P NMR (121 MHz, CDCl₃): δ 50.7;

IR: 3417, 2946, 1709, 1441, 1271, 1154, 1074, 765, 704 cm⁻¹;

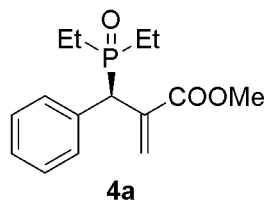
HRMS (ESI): C₁₅H₂₁O₃P+H, Calc: 281.1301, Found: 281.1296;

General Procedure B: Synthesis of 4.



To a solution of MBH carbonate **1** (0.20 mmol), quinidine (0.04 mmol) and Na_2CO_3 (0.30 mmol) in toluene (1.0 mL), dialkyl phosphine oxide **2** (0.50 mmol) was added at 0 °C and stirred for 72 h. The reaction mixture was directly purified by silica gel chromatography without work up and fractions were collected and concentrated in vacuo to provide the pure desired product **4**.

(R)-methyl-2-((diethylphosphoryl)(phenyl)methyl)acrylate (4a)



4a was isolated by column chromatography using silica gel in 73% yield;

^1H NMR (300 MHz, CDCl_3): δ 7.52 (d, J = 2.1 Hz, 1H), 7.50 (d, J = 1.5 Hz, 1H), 7.36-7.24 (m, 3H), 6.80 (d, J = 2.4 Hz, 1H), 6.55 (d, J = 2.4 Hz, 1H), 4.28 (d, J = 7.8 Hz, 1H), 3.75 (s, 3H), 1.93-1.73 (m, 2H), 1.72-1.43 (m, 2H), 1.14 (dt, J = 7.8 Hz, J = 15.6 Hz, 3H), 0.99 (dt, J = 9.0 Hz, J = 16.8 Hz, 3H);

^{13}C NMR (75 MHz, CDCl_3): δ 167.0 (J = 8.25 Hz), 136.4 (J = 3.0 Hz), 136.1 (J = 5.25 Hz), 129.9 (J = 5.25 Hz), 129.5 (J = 6.0 Hz), 128.8 (J = 1.5 Hz), 127.4 (J = 1.5 Hz), 52.5, 43.5 (J = 60.0 Hz), 19.5 (J = 64.5 Hz), 19.3 (J = 67.5 Hz), 6.4 (J = 4.5 Hz), 5.8 (J = 4.5 Hz);

^{31}P NMR (121 MHz, CDCl_3): δ 52.3;

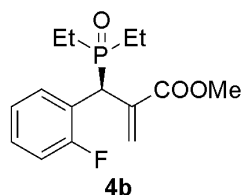
IR: 3424, 2945, 1716, 1454, 1241, 1165, 1131, 703 cm^{-1} ;

HRMS (ESI): $\text{C}_{15}\text{H}_{21}\text{O}_3\text{P}+\text{H}$, Calc: 281.1301, Found: 281.1307;

$[\alpha]_{\text{D}}^{25}$ = - 48 (c = 1.08, CHCl_3);

HPLC: DAICEL CHIRALCEL AD, Hexane/ i PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 8.0, t_{minor} = 10.1, 95% ee.

(S)-methyl 2-((diethylphosphoryl)(2-fluorophenyl)methyl)acrylate (4b)



4b was isolated by column chromatography using silica gel in 66% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.75 (t, *J* = 7.5 Hz, 1H), 7.25 (t, *J* = 6.6 Hz, 1H), 7.16 (dt, *J* = 0.9 Hz, *J* = 7.5 Hz, 1H), 7.06 (t, *J* = 9.0 Hz, 1H), 6.80 (d, *J* = 2.4 Hz, 1H), 6.62 (d, *J* = 2.1 Hz, 1H), 4.77 (d, *J* = 7.8 Hz, 1H), 3.76 (s, 3H), 1.99-1.76 (m, 2H), 1.63-1.51 (m, 2H), 1.15 (dt, *J* = 7.8 Hz, *J* = 16.8 Hz, 3H), 0.98 (dt, *J* = 7.8 Hz, *J* = 16.5 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 166.6 (*J* = 8.25 Hz), 160.1 (*J* = 6.0 Hz, *J* = 243.75 Hz), 135.8 (*J* = 3.0 Hz), 131.0 (*J* = 3.0 Hz), 130.9 (*J* = 5.25 Hz, *J* = 10.5 Hz), 129.6 (*J* = 2.25 Hz, *J* = 8.25 Hz), 124.6 (*J* = 1.5 Hz, *J* = 3.75 Hz), 122.8 (*J* = 4.5 Hz, *J* = 15.0 Hz), 115.2 (*J* = 21.0 Hz), 52.0, 34.5 (*J* = 3.0 Hz, *J* = 60.8 Hz), 19.6 (*J* = 64.5 Hz), 19.1 (*J* = 67.5 Hz), 6.4 (*J* = 3.8 Hz), 5.5 (*J* = 4.5 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 52.8 (*J* = 2.4 Hz);

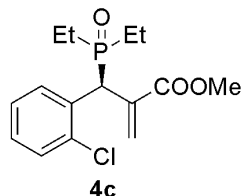
IR: 3432, 2947, 1719, 1489, 1231, 1172, 1133, 1035, 762 cm⁻¹;

HRMS (ESI): C₁₅H₂₀FO₃P+H, Calc: 299.1207, Found: 299.1203;

[α]_D^{rt} = - 48 (c = 1.09, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 9.4, t_{minor} = 12.3, 91% ee.

(S)-methyl 2-((2-chlorophenyl)(diethylphosphoryl)methyl)acrylate (4c)



4c was isolated by column chromatography using silica gel in 63% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.87 (dt, *J* = 1.8 Hz, *J* = 7.2 Hz, 1H), 7.39 (dd, *J* = 0.6 Hz, *J* = 7.8 Hz, 1H), 7.32-7.19 (m, 2H), 6.75 (d, *J* = 2.4 Hz, 1H), 6.62 (d, *J* = 2.1 Hz, 1H), 5.02 (d, *J* = 8.1 Hz, 1H), 3.77 (s, 3H), 1.96-1.82 (m, 2H), 1.67-1.53 (m, 2H), 1.16 (dt, *J* = 7.8 Hz, *J* = 17.1 Hz, 3H), 0.96 (dt, *J* = 7.8 Hz, *J* = 16.8 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 166.7 (*J* = 7.5 Hz), 135.8 (*J* = 3.75 Hz), 134.1 (*J* = 6.75 Hz), 133.7 (*J* = 4.5 Hz), 131.2 (*J* = 4.5 Hz), 131.0 (*J* = 6.0 Hz), 129.6, 128.6 (*J* = 2.25 Hz), 127.4 (*J* = 0.75 Hz), 52.5, 39.0 (*J* = 60.0 Hz), 19.7 (*J* = 65.25 Hz), 19.0 (*J* = 66.75 Hz), 6.4 (*J* = 4.5 Hz), 5.4 (*J* = 4.5 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 54.1;

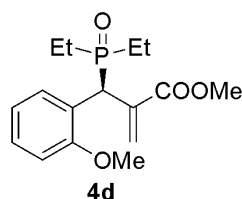
IR: 3425, 2946, 1720, 1439, 1239, 1166, 1133, 1035, 763 cm⁻¹;

HRMS (ESI): C₁₅H₂₀ClO₃P+H, Calc: 315.0911, Found: 315.0914;

[α]_D^{rt} = - 25 (c = 1.18, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 8.2, t_{minor} = 10.4, 95% ee.

(R)-methyl 2-((diethylphosphoryl)(2-methoxyphenyl)methyl)acrylate (4d)



4d was isolated by column chromatography using silica gel in 61% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.70 (t, *J* = 1.5 Hz, 1H), 7.28-7.21 (m, 1H), 6.97 (dt, *J* = 0.9 Hz, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 2.7 Hz, 1H), 6.57 (d, *J* = 2.4 Hz, 1H), 5.02 (d, *J* = 8.1 Hz, 1H), 3.86 (s, 3H), 3.74 (s, 3H), 1.90-1.76 (m, 2H), 1.61-1.49 (m, 2H), 1.15 (dt, *J* = 7.8 Hz, *J* = 16.8 Hz, 3H), 0.94 (dt, *J* = 7.8 Hz, *J* = 19.5 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 167.1 (*J* = 8.3 Hz), 156.5 (*J* = 6.0 Hz), 136.5 (*J* = 3.8 Hz), 130.5 (*J* = 6.0 Hz), 130.4, 128.4 (*J* = 1.5 Hz), 124.3 (*J* = 4.5 Hz), 121.1 (*J* = 1.5 Hz), 110.7, 55.8, 52.3, 34.7 (*J* = 61.5 Hz), 19.8 (*J* = 64.5 Hz), 19.0 (*J* = 66.8 Hz), 6.4 (*J* = 3.8 Hz), 5.6 (*J* = 3.8 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 53.2;

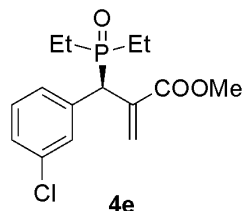
IR: 3424, 2945, 1719, 1491, 1246, 1166, 1133, 1028, 759 cm⁻¹;

HRMS (ESI): C₁₆H₂₃O₄P+H, Calc: 311.1407, Found: 311.1404;

[α]_D^{rt} = - 27 (c = 0.74, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: *t*_{major} = 12.3, *t*_{minor} = 17.2, 90% ee.

(R)-methyl 2-((3-chlorophenyl)(diethylphosphoryl)methyl)acrylate (4e)



4e was isolated by column chromatography using silica gel in 80% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.40 (s, 2H), 7.20 (t, *J* = 4.5 Hz, 2H), 6.72 (s, 1H), 6.50 (s, 1H), 4.17 (d, *J* = 7.5 Hz, 1H), 3.69 (s, 3H), 1.83-1.67 (m, 2H), 1.56-1.41 (m, 2H), 1.06 (dt, *J* = 7.8 Hz, *J* = 16.8 Hz, 3H), 0.91 (dt, *J* = 7.8 Hz, *J* = 16.5 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 166.8 (*J* = 7.5 Hz), 138.1 (*J* = 5.3 Hz), 136.0 (*J* = 3.8 Hz), 134.4, 130.3, 130.2, 130.0, 129.5 (*J* = 6.0 Hz), 127.6 (*J* = 6.0 Hz), 52.5, 43.1 (*J* = 59.3 Hz), 19.4 (*J* = 62.3 Hz), 19.3 (*J* = 66.8 Hz), 6.3 (*J* = 3.8 Hz), 5.8 (*J* = 5.3 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 52.0;

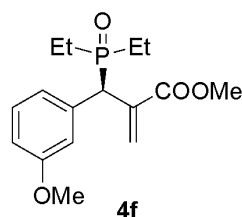
IR: 3423, 2946, 1718, 1240, 1165, 1131, 1035, 763, 696 cm⁻¹;

HRMS (ESI): C₁₅H₂₀ClO₃P+H, Calc: 315.0911, Found: 315.0919;

[α]_D^{rt} = - 33 (c = 0.99, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: *t*_{major} = 7.7, *t*_{minor} = 9.1, 94% ee.

(R)-methyl 2-((diethylphosphoryl)(3-methoxyphenyl)methyl)acrylate (4f)



4f was isolated by column chromatography using silica gel in 87% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.24 (d, *J* = 7.8 Hz, 1H), 7.11 (dd, *J* = 1.2 Hz, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 1.2 Hz, 1H), 6.82 (dt, *J* = 1.2 Hz, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 2.4 Hz, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 4.26 (d, *J* = 7.8 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 1.91-1.70 (m, 2H), 1.67-1.47 (m, 2H), 1.14 (dt, *J* = 7.8 Hz, *J* = 16.5 Hz, 3H), 0.98 (dt, *J* = 7.8 Hz, *J* = 16.8 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 167.0 (*J* = 8.25 Hz), 159.6, 137.5 (*J* = 4.5 Hz), 136.2 (*J* = 3.0 Hz), 129.9 (*J* = 5.3 Hz), 129.7, 121.8 (*J* = 6.0 Hz), 115.1 (*J* = 6.0 Hz), 112.8 (*J* = 1.5 Hz), 55.1, 52.4, 43.4 (*J* = 60.0 Hz), 19.5 (*J* = 65.3 Hz), 19.3 (*J* = 66.8 Hz), 6.3 (*J* = 3.8 Hz), 5.9 (*J* = 4.5 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 52.0;

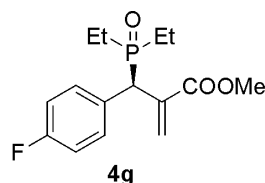
IR: 3423, 2946, 1716, 1600, 1489, 1235, 1164, 1131, 1040, 760, 704 cm⁻¹;

HRMS (ESI): C₁₆H₂₃O₄P+H, Calc: 311.1407, Found: 311.1400;

[α]_D^{rt} = -29 (c = 1.04, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 95/5, flow rate = 0.7 mL/min, retention time: t_{major} = 32.7, t_{minor} = 35.0, 95% ee.

(R)-methyl 2-((diethylphosphoryl)(4-fluorophenyl)methyl)acrylate (4g)



4g was isolated by column chromatography using silica gel in 75% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.52-7.45 (m, 2H), 7.02 (t, *J* = 8.1 Hz, 2H), 6.77 (d, *J* = 2.4 Hz, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 4.26 (d, *J* = 7.5 Hz, 1H), 3.76 (s, 3H), 1.91-1.71 (m, 2H), 1.61-1.46 (m, 2H), 1.14 (dt, *J* = 7.8 Hz, *J* = 16.8 Hz, 3H), 0.97 (dt, *J* = 7.8 Hz, *J* = 16.5 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 166.9 (*J* = 9 Hz), 162.2 (*J* = 247.5 Hz), 136.5 (*J* = 3.0 Hz), 131.9 (*J* = 3.75 Hz, *J* = 6 Hz), 131.1 (*J* = 6 Hz, *J* = 8.25 Hz), 129.9 (*J* = 5.25 Hz), 115.7 (*J* = 21 Hz), 52.5, 42.6 (*J* = 60 Hz), 19.5 (*J* = 64.5 Hz), 19.3 (*J* = 67.5 Hz), 6.3 (*J* = 4.5 Hz), 5.8 (*J* = 4.5 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 52.3;

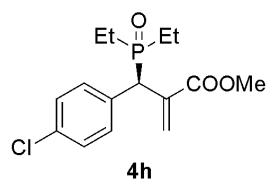
IR: 3417, 2948, 1718, 1508, 1241, 1161, 1132 cm⁻¹;

HRMS (ESI): C₁₅H₂₀FO₃P+H, Calc: 299.1207, Found: 299.1205;

[α]_D^{rt} = -41 (c = 0.83, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 7.9, t_{minor} = 10.8, 92% ee.

(R)-methyl 2-((4-chlorophenyl)(diethylphosphoryl)methyl)acrylate (4h)



4h was isolated by column chromatography using silica gel in 78% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.46 (d, *J* = 7.2 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 2.1 Hz, 1H), 6.55 (d, *J* = 1.8 Hz, 1H), 4.25 (d, *J* = 7.5 Hz, 1H), 3.76 (s, 3H), 1.91-1.74 (m, 2H), 1.59-1.46 (m, 2H), 1.13 (dt, *J* = 7.8 Hz, *J* = 16.8 Hz, 3H), 0.97 (dt, *J* = 7.8 Hz, *J* = 16.5 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 166.8 (*J* = 9 Hz), 136.3 (*J* = 3.0 Hz), 134.7 (*J* = 5.25 Hz), 133.5 (*J* = 1.5 Hz), 130.8 (*J* = 5.25 Hz), 130.0 (*J* = 5.25 Hz), 128.9, 52.5, 42.8 (*J* = 59.25 Hz), 19.5 (*J* = 64.5 Hz), 19.3 (*J* = 66.75 Hz), 6.3 (*J* = 4.5 Hz), 5.8 (*J* = 4.5 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 52.2;

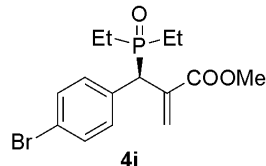
IR: 3421, 2947, 1718, 1490, 1240, 1164, 1131, 762 cm⁻¹;

HRMS (ESI): C₁₅H₂₀ClO₃P+H, Calc: 315.0911, Found: 315.0905;

[α]_D^{rt} = - 49 (c = 0.94, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: *t*_{major} = 7.7, *t*_{minor} = 11.8, 96% ee.

(R)-methyl 2-((4-bromophenyl)(diethylphosphoryl)methyl)acrylate (4i)



4i was isolated by column chromatography using silica gel in 76% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.48-7.38 (m, 4H), 6.76 (d, *J* = 2.4 Hz, 1H), 6.55 (d, *J* = 2.1 Hz, 1H), 4.23 (d, *J* = 7.5 Hz, 1H), 3.76 (s, 3H), 1.94-1.64 (m, 2H), 1.62-1.46 (m, 2H), 1.33 (dt, *J* = 7.5 Hz, *J* = 17.1 Hz, 3H), 0.94 (dt, *J* = 7.8 Hz, *J* = 15.6 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 166.8 (*J* = 8.3 Hz), 136.2 (*J* = 2.3 Hz), 135.2 (*J* = 5.3 Hz), 131.9, 131.2 (*J* = 6.0 Hz), 130.0 (*J* = 5.3 Hz), 121.6 (*J* = 2.3 Hz), 52.5, 42.9 (*J* = 60.0 Hz), 19.4 (*J* = 64.5 Hz), 19.3 (*J* = 66.8 Hz), 6.3 (*J* = 4.5 Hz), 5.8 (*J* = 4.5 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 52.2;

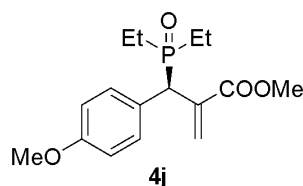
IR: 3423, 2946, 1717, 1486, 1239, 1164, 1131, 762 cm⁻¹;

HRMS (ESI): C₁₅H₂₀BrO₃P+H, Calc: 359.0406, Found: 359.0412;

[α]_D^{rt} = - 43 (c = 0.93, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: *t*_{major} = 8.2, *t*_{minor} = 13.0, 95% ee.

(R)-methyl 2-((diethylphosphoryl)(4-methoxyphenyl)methyl)acrylate (4j)



4j was isolated by column chromatography using silica gel in 83% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.42 (dd, *J* = 1.5 Hz, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 2.1 Hz, 1H), 6.85 (d, *J* = 1.8 Hz, 1H), 6.75 (d, *J* = 2.4 Hz, 1H), 6.53 (d, *J* = 2.1 Hz, 1H), 4.22 (d, *J* = 7.8 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 1.92-1.71 (m, 2H), 1.64-1.43 (m, 2H), 1.13 (dt, *J* = 7.8 Hz, *J* = 16.5 Hz, 3H), 0.96 (dt, *J* = 7.5 Hz, *J* = 16.5 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 167.1 (*J* = 8.25 Hz), 158.9 (*J* = 1.5 Hz), 136.7 (*J* = 3.0 Hz), 130.6 (*J* = 5.25 Hz), 129.5 (*J* = 6.0 Hz), 127.9 (*J* = 5.25 Hz), 114.2, 55.2, 52.4, 42.6 (*J* = 61.5 Hz), 19.5 (*J* = 63.75 Hz), 19.2 (*J* = 67.5 Hz), 6.4 (*J* = 4.5 Hz), 5.8 (*J* = 4.5 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 52.8;

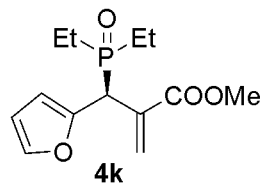
IR: 3417, 2946, 1716, 1510, 1252, 1163, 11321, 1033, 762 cm⁻¹;

HRMS (ESI): C₁₆H₂₃O₄P+H, Calc: 311.1407, Found: 311.1413;

[α]_D^{rt} = - 47 (c = 1.00, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: *t*_{major} = 9.7, *t*_{minor} = 14.3, 96% ee.

(S)-methyl 2-((diethylphosphoryl)(furan-2-yl)methyl)acrylate (4k)



4k was isolated by column chromatography using silica gel in 48% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.38(s, 1H), 6.62 (d, *J* = 3.3 Hz, 1H), 6.51 (d, *J* = 3.0 Hz, 1H), 6.40 (t, *J* = 2.7 Hz, 1H), 6.35 (t, *J* = 2.7 Hz, 1H), 4.65 (d, *J* = 10.8 Hz, 1H), 3.81 (s, 3H), 1.80-1.64 (m, 4H), 1.20-1.00 (m, 6H);

¹³C NMR (75 MHz, CDCl₃): δ 166.8 (*J* = 5.3 Hz), 149.2 (*J* = 6.0 Hz), 142.3 (*J* = 1.5 Hz), 133.3 (*J* = 3.8 Hz), 131.3 (*J* = 6.0 Hz), 110.8 (*J* = 1.5 Hz), 108.8 (*J* = 4.5 Hz), 52.6, 38.3 (*J* = 57.8 Hz), 19.5 (*J* = 65.3 Hz), 19.4 (*J* = 66.0 Hz), 5.9 (*J* = 2.3 Hz), 5.8 (*J* = 2.3 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 51.4;

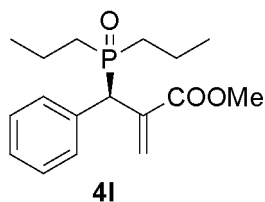
IR: 3427, 2947, 1716, 1273, 1210, 1173, 1132, 759 cm⁻¹;

HRMS (ESI): C₁₃H₁₉O₄P+H, Calc: 271.1094, Found: 271.1097;

[α]_D^{rt} = + 15 (c = 1.02, CHCl₃);

HPLC: DAICEL CHIRALCEL OD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: *t*_{major} = 9.3, *t*_{minor} = 11.6, 71% ee.

(R)-methyl-2-((dipropylphosphoryl)(phenyl)methyl)acrylate (4l)



4l was isolated by column chromatography using silica gel in 81% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.49 (d, *J* = 7.8 Hz, 2H), 7.35-7.27 (m, 3H), 6.79 (d, *J* = 2.1 Hz, 1H), 6.54 (d, *J* = 1.8 Hz, 1H), 4.23 (d, *J* = 7.8 Hz, 1H), 3.75 (s, 3H), 1.85-1.71 (m, 2H), 1.61-1.35 (m, 6H), 1.03 (t, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 167.0 (*J* = 9.0 Hz), 136.5 (*J* = 3.8 Hz), 136.1 (*J* = 5.3 Hz), 129.8 (*J* = 6.0 Hz), 129.5 (*J* = 6.0 Hz), 128.8 (*J* = 1.5 Hz), 127.4 (*J* = 1.5 Hz), 52.5, 44.4 (*J* = 60.0 Hz), 29.5 (*J* = 63.0 Hz), 29.2 (*J* = 66.0 Hz), 16.0 (*J* = 3.8 Hz), 15.9 (*J* = 15.0 Hz), 15.7 (*J* = 14.3 Hz), 15.5 (*J* = 3.8 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 49.0;

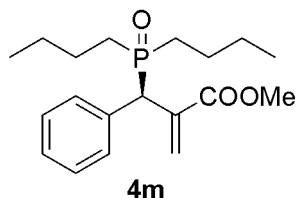
IR: 3425, 2962, 1717, 1455, 1242, 1163, 1131, 704 cm⁻¹;

HRMS (ESI): C₁₇H₂₅O₃P+H, Calc: 309.1604, Found: 309.1620;

[α]_D^{rt} = - 44 (c = 0.93, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 7.5, t_{minor} = 11.2, 90% ee.

(R)-methyl-2-((dibutylphosphoryl)(phenyl)methyl)acrylate (4m)



4m was isolated by column chromatography using silica gel in 63% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.50 (*J* = 1.2 Hz, *J* = 6.9 Hz, 2H), 7.36-7.27 (m, 3H), 6.79 (d, *J* = 2.4 Hz, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 4.24 (d, *J* = 7.5 Hz, 1H), 3.75 (s, 3H), 1.89-1.67 (m, 2H), 1.61-1.17 (m, 10H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.78 (t, *J* = 7.2 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 167.0 (*J* = 9.0 Hz), 136.4 (*J* = 3.75 Hz), 136.0 (*J* = 5.25 Hz), 129.9 (*J* = 5.25 Hz), 129.5 (*J* = 6.0 Hz), 128.7, 127.4 (*J* = 1.5 Hz), 52.4, 44.3 (*J* = 60.0 Hz), 26.9 (*J* = 63.8 Hz), 26.6 (*J* = 66.0 Hz), 24.2 (*J* = 3.8 Hz), 24.2, 23.9, 23.8 (*J* = 3.8 Hz), 13.5, 13.4;

³¹P NMR (121 MHz, CDCl₃): δ 49.9;

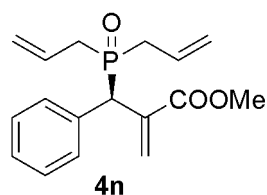
IR: 3418, 2957, 1718, 1455, 1240, 1162, 1132, 703 cm⁻¹;

HRMS (ESI): C₁₉H₂₉O₃P+H, Calc: 337.1927, Found: 337.1929;

[α]_D^{rt} = - 44 (c = 0.95, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 9.2, t_{minor} = 18.4, 98% ee.

(R)-methyl-2-((diallylphosphoryl)(phenyl)methyl)acrylate (4n)



4n was isolated by column chromatography using silica gel in 92% yield;

¹H NMR (300 MHz, CDCl₃): δ 7.51 (dd, *J* = 1.2 Hz, *J* = 6.9 Hz, 2H), 7.37-7.28 (m, 3H), 6.80 (d, *J* = 2.4 Hz, 1H), 6.57 (d, *J* = 2.4 Hz, 1H), 5.87-5.75 (m, 1H), 5.71-5.59 (m, 1H), 5.27-5.16 (m, 3H), 5.10-5.03 (m, 1H), 4.32 (d, *J* = 7.5 Hz, 1H), 3.75 (s, 3H), 2.84-2.61 (m, 2H), 2.53-2.30 (m, 2H);

¹³C NMR (75 MHz, CDCl₃): δ 166.7 (*J* = 9.0 Hz), 136.2 (*J* = 3.0 Hz), 135.5 (*J* = 5.3 Hz), 130.2 (*J* = 5.3 Hz), 129.6 (*J* = 6.0 Hz), 128.8 (*J* = 0.8 Hz), 127.7 (*J* = 8.3 Hz), 127.6 (*J* = 2.3 Hz), 127.3 (*J* = 8.3 Hz), 120.8 (*J* = 4.5 Hz), 120.6 (*J* = 4.5 Hz), 52.5, 43.5 (*J* = 60.8 Hz), 32.7 (*J* = 61.5 Hz), 32.5 (*J* = 63.8 Hz);

³¹P NMR (121 MHz, CDCl₃): δ 45.3;

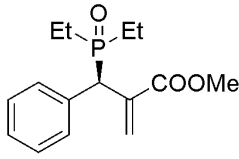
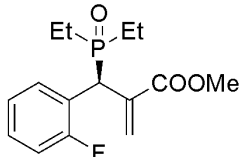
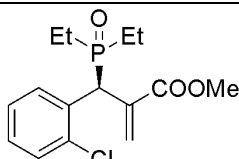
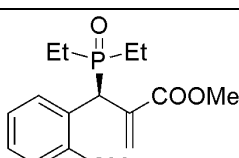
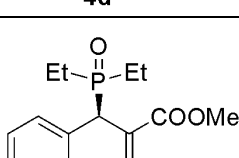
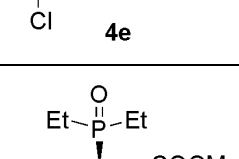
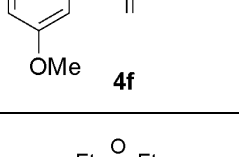
IR: 3430, 2951, 1717, 1634, 1439, 1240, 1165, 1132, 920, 704, 600 cm⁻¹;

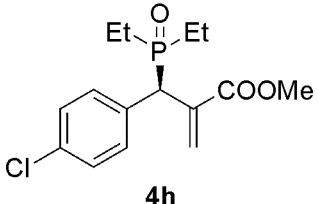
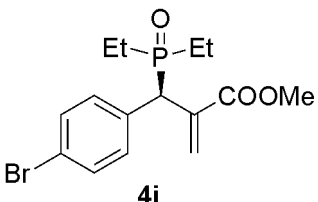
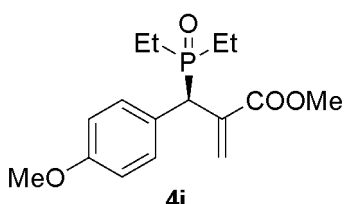
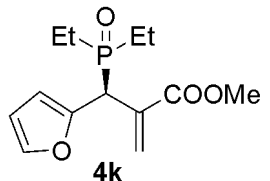
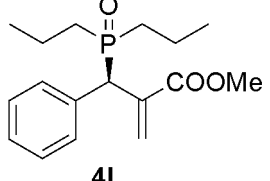
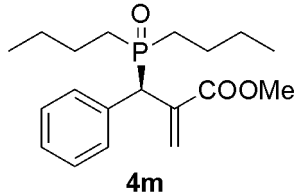
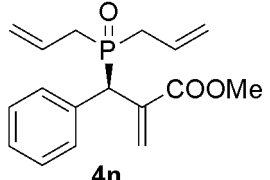
HRMS (ESI): C₁₇H₂₁O₃P+H, Calc: 305.1301, Found: 305.1303;

[α]_D^{rt} = - 60 (*c* = 1.09, CHCl₃);

HPLC: DAICEL CHIRALCEL AD, Hexane/iPrOH = 90/10, flow rate = 1.0 mL/min, retention time: *t*_{major} = 8.3, *t*_{minor} = 10.7, 90% ee.

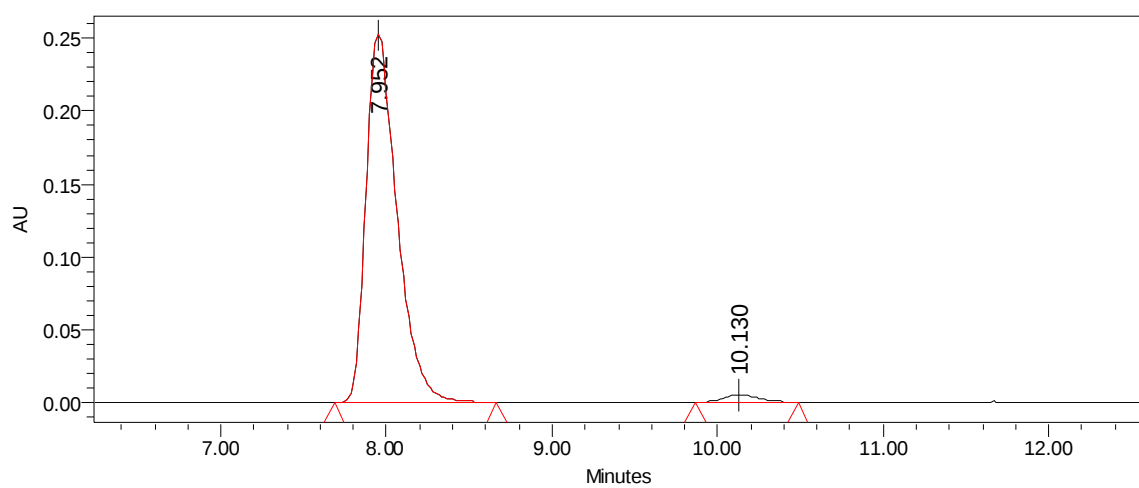
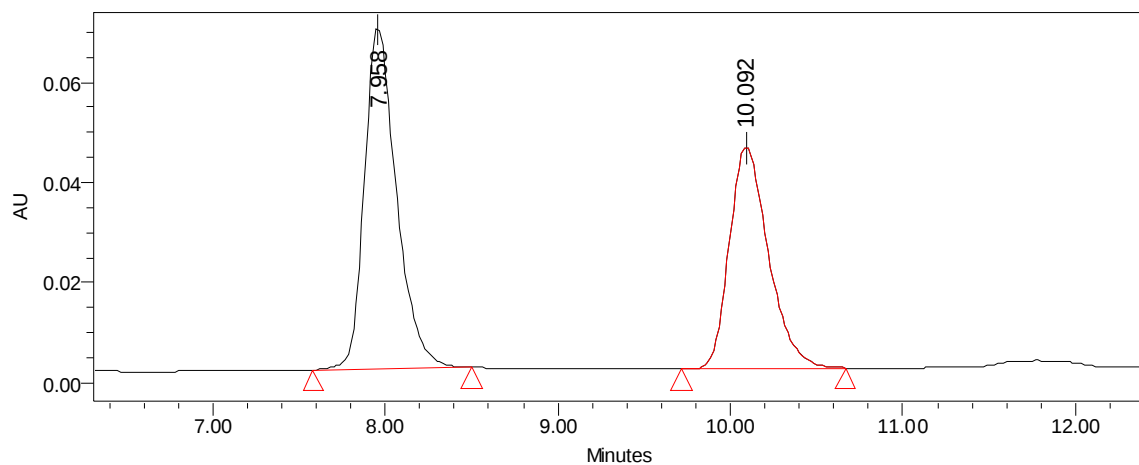
HPLC Analytic Conditions:

Entry	Product	Chiralcel column	Fluent phase Hexane/iPrOH	Flow rate	Retention time	ee (%)
1	 4a	AD	90:10	1.0	$t_{\text{major}} = 8.0$ $t_{\text{minor}} = 10.1$	95
2	 4b	AD	90:10	1.0	$t_{\text{major}} = 9.4$ $t_{\text{minor}} = 12.3$	91
3	 4c	AD	90:10	1.0	$t_{\text{major}} = 8.2$ $t_{\text{minor}} = 10.4$	95
4	 4d	AD	90:10	1.0	$t_{\text{major}} = 12.3$ $t_{\text{minor}} = 17.2$	90
5	 4e	AD	90:10	1.0	$t_{\text{major}} = 7.7$ $t_{\text{minor}} = 9.1$	94
6	 4f	AD	95:5	0.7	$t_{\text{major}} = 32.7$ $t_{\text{minor}} = 35.0$	95
7	 4g	AD	90:10	1.0	$t_{\text{major}} = 7.9$ $t_{\text{minor}} = 10.8$	92

8	 4h	AD	90:10	1.0	$t_{\text{major}} = 7.7$ $t_{\text{minor}} = 11.8$	96
9	 4i	AD	90:10	1.0	$t_{\text{major}} = 8.2$ $t_{\text{minor}} = 13.0$	95
10	 4j	AD	90:10	1.0	$t_{\text{major}} = 9.7$ $t_{\text{minor}} = 14.3$	96
11	 4k	OD-H	90:10	1.0	$t_{\text{major}} = 11.6$ $t_{\text{minor}} = 9.3$	71
12	 4l	AD	90:10	1.0	$t_{\text{major}} = 7.5$ $t_{\text{minor}} = 11.2$	90
13	 4m	AD	90:10	1.0	$t_{\text{major}} = 9.2$ $t_{\text{minor}} = 18.4$	98
14	 4n	AD	90:10	1.0	$t_{\text{major}} = 8.3$ $t_{\text{minor}} = 10.7$	90

(*R*)-methyl-2-((diethylphosphoryl)(phenyl)methyl)acrylate (4a)

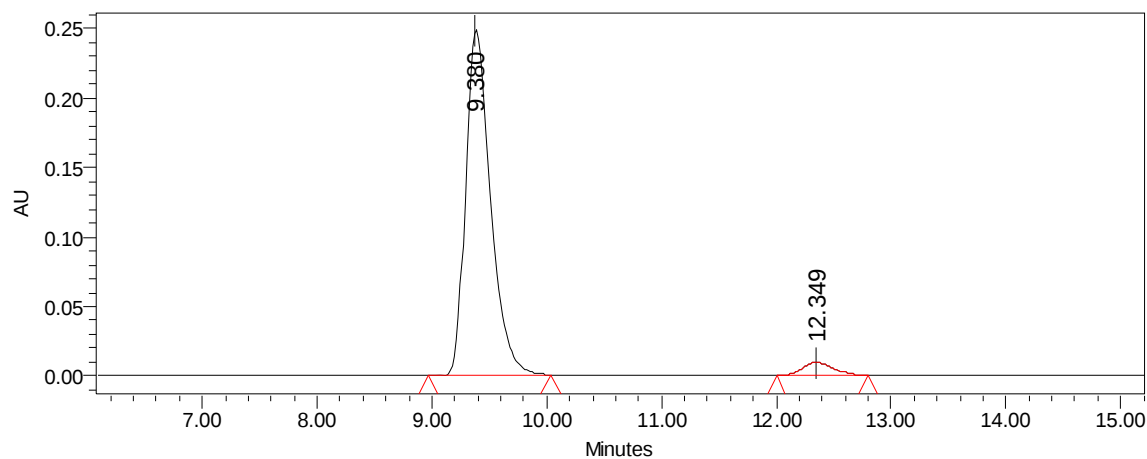
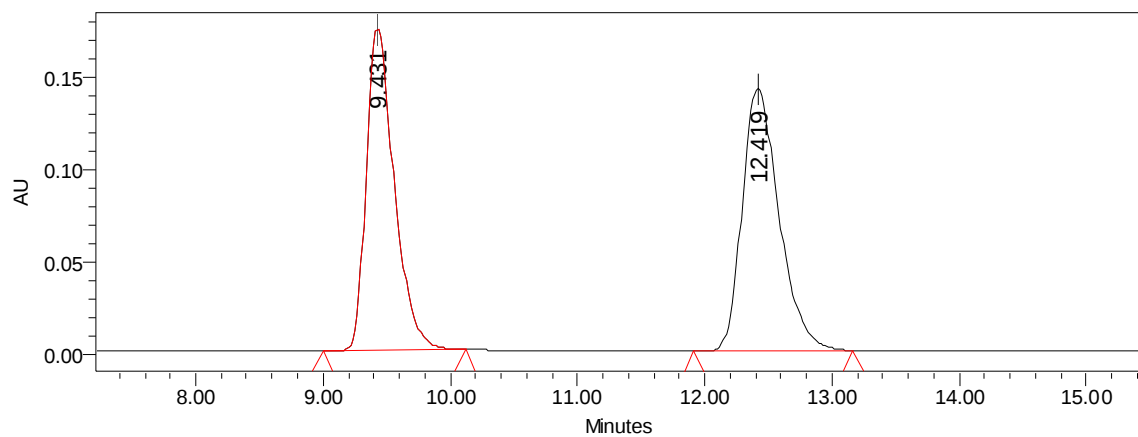
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	7.952	3255639	97.72	251627
2	10.130	75908	2.28	4912

(R)-methyl-2-((diethylphosphoryl)(4-fluorophenyl)methyl)acrylate (4b)

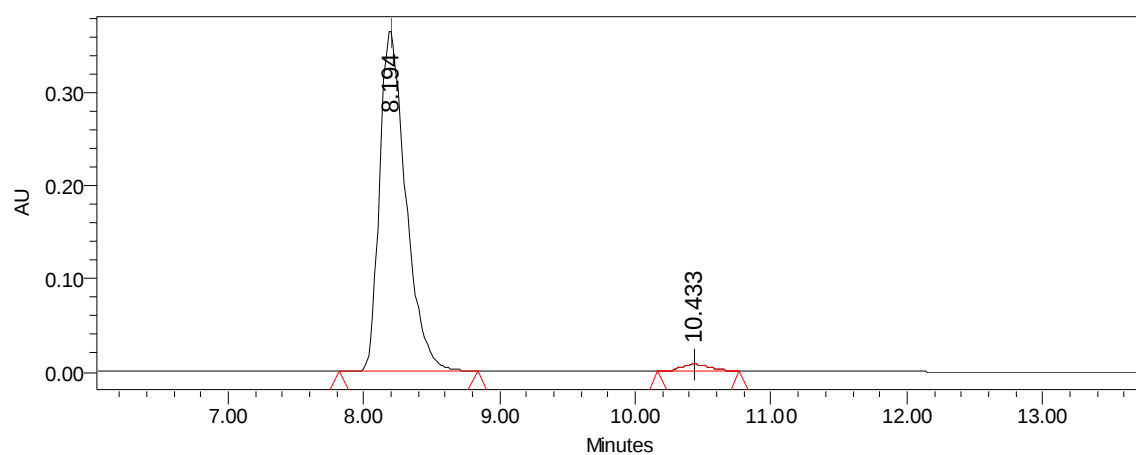
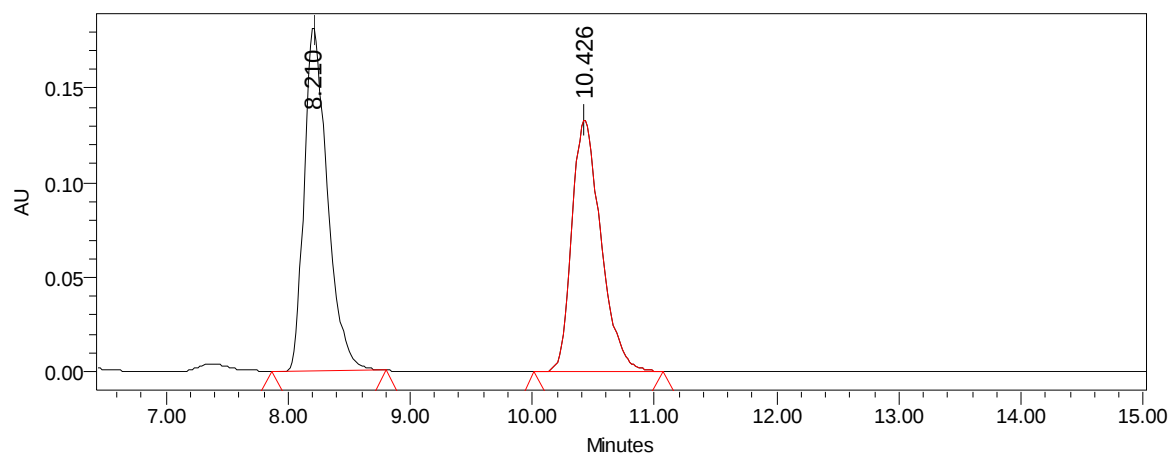
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	9.380	3759359	95.47	248245
2	12.349	178315	4.53	9380

(S)-methyl 2-((2-chlorophenyl)(diethylphosphoryl)methyl)acrylate (4c)

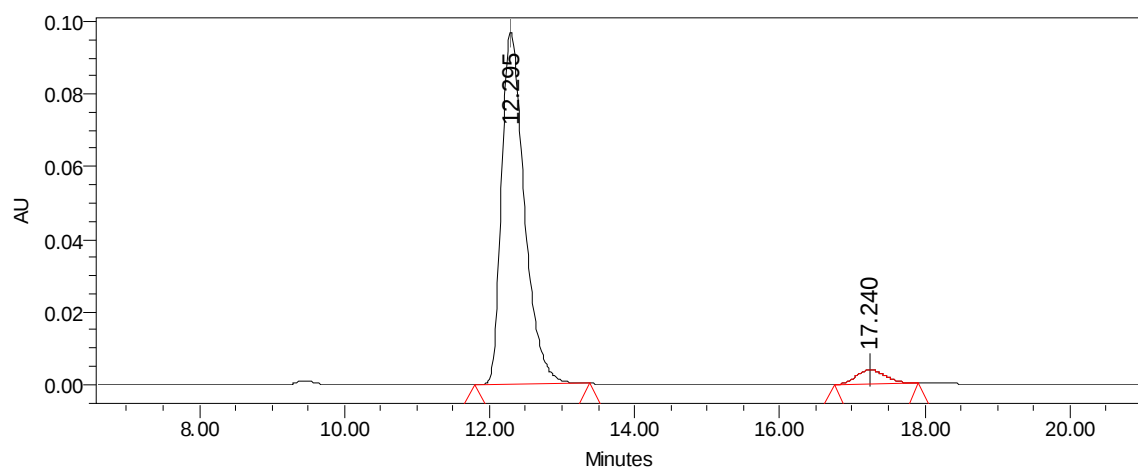
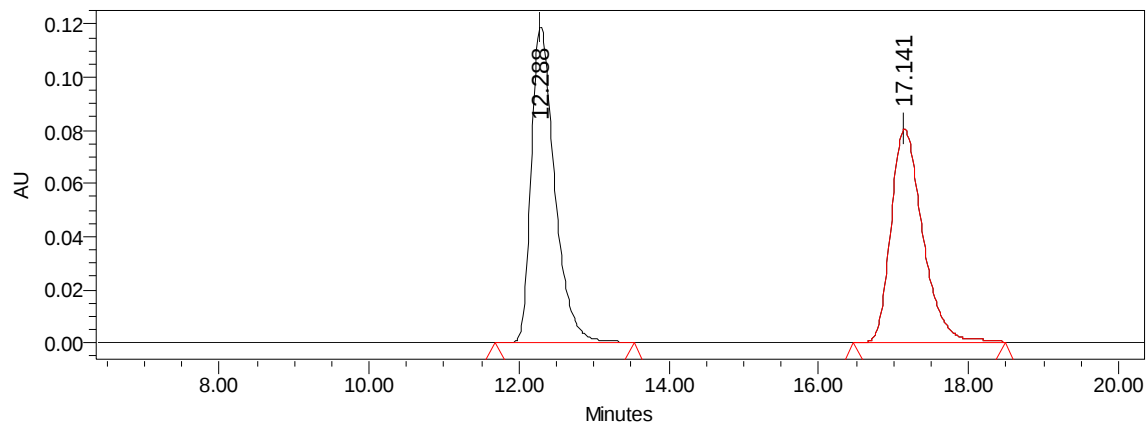
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	8.194	4905054	97.63	366066
2	10.433	118927	2.37	7609

(R)-methyl 2-((diethylphosphoryl)(2-methoxyphenyl)methyl)acrylate (4d)

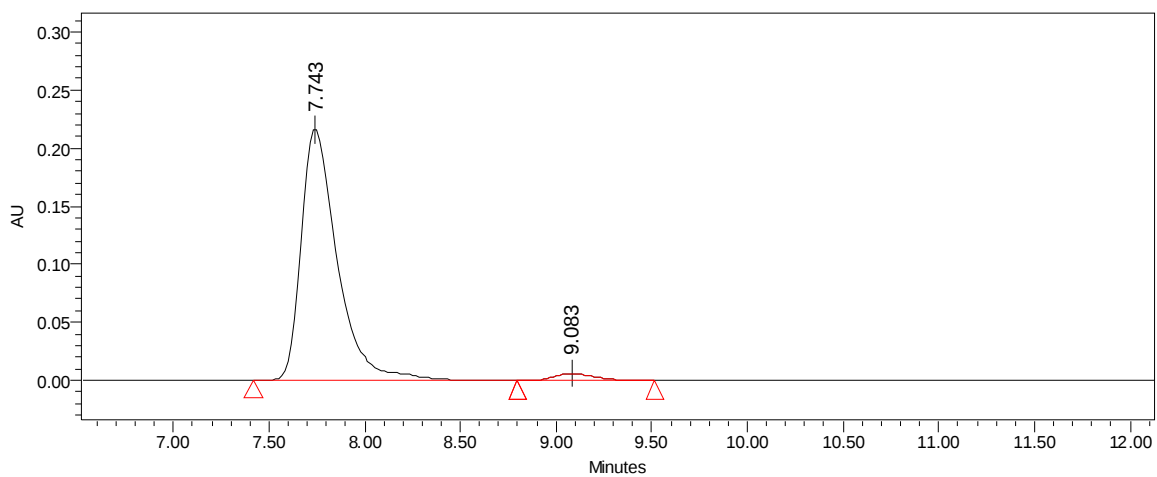
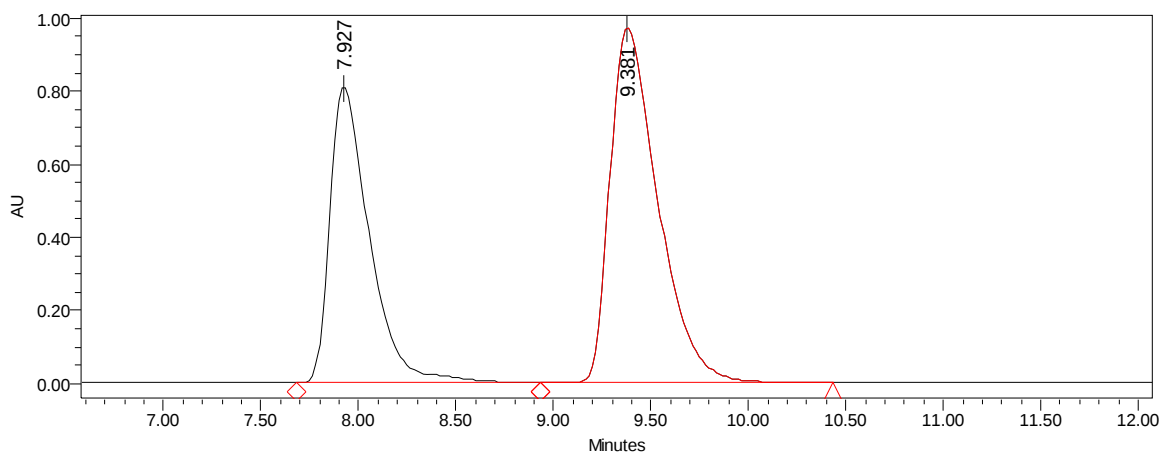
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	12.295	2118894	94.94	97187
2	17.240	112905	5.06	3992

(R)-methyl 2-((3-chlorophenyl)(diethylphosphoryl)methyl)acrylate (4e)

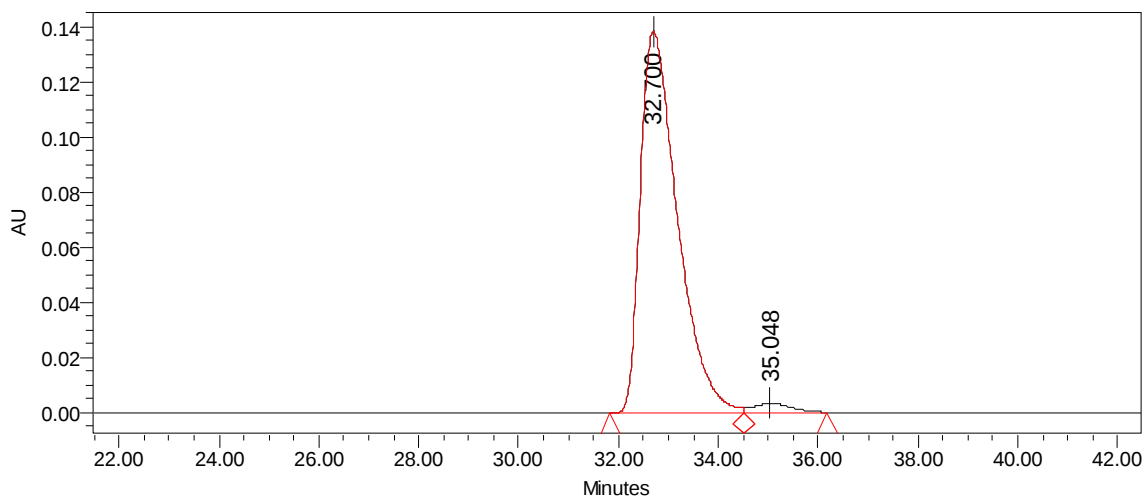
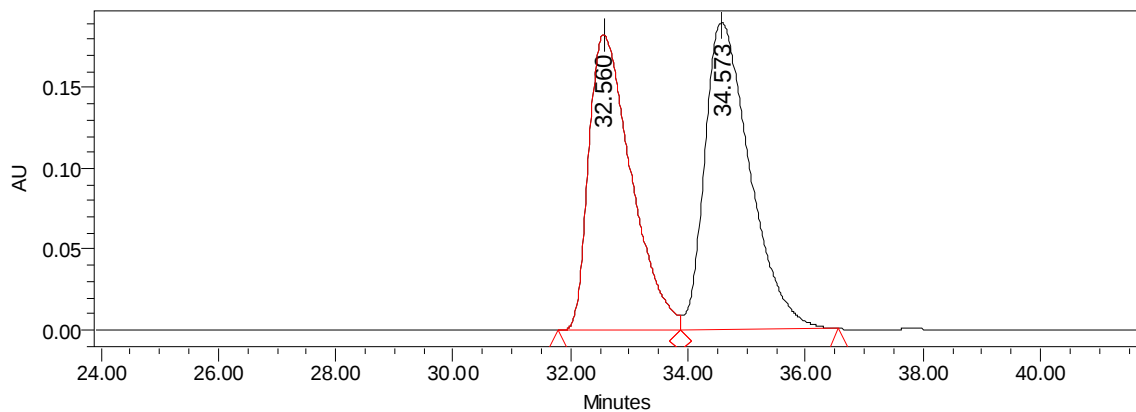
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	7.743	2861172	96.91	216336
2	9.083	91373	3.09	6113

(R)-methyl 2-((diethylphosphoryl)(3-methoxyphenyl)methyl)acrylate (4f)

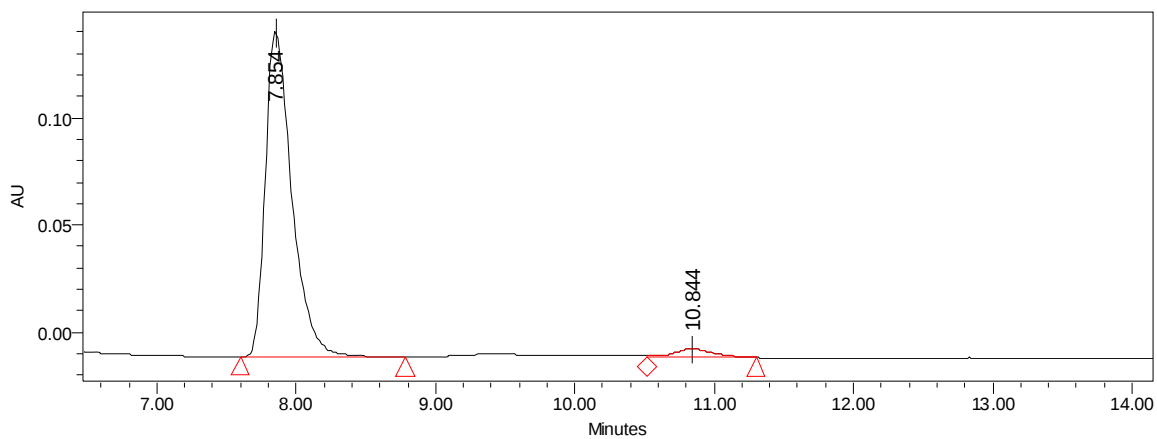
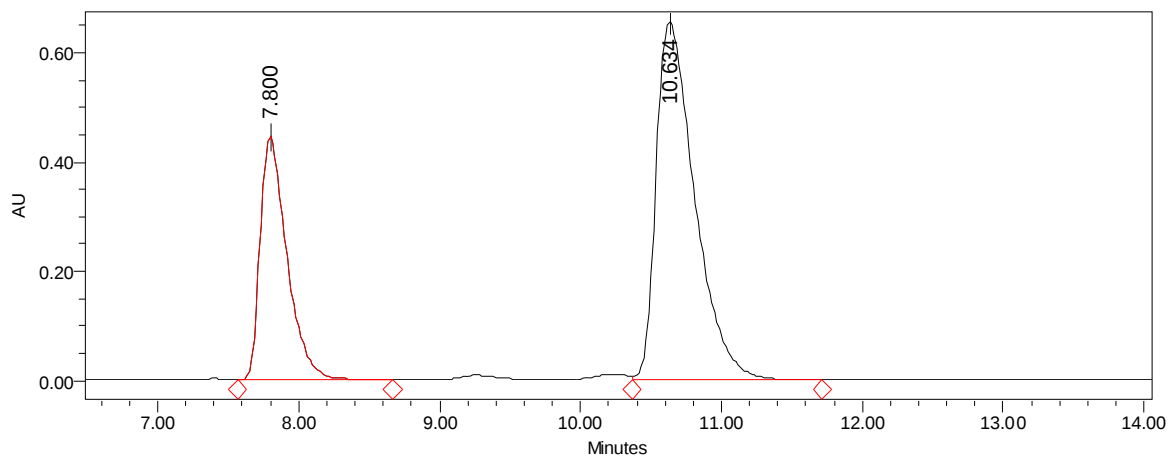
Chiralpak AD column, hexane/iPrOH (95:5), flow rate 0.7 mL/min



	Retention Time	Area	% Area	Height
1	32.700	7188912	97.56	138482
2	35.048	179897	2.44	3311

(R)-methyl-2-((diethylphosphoryl)(4-fluorophenyl)methyl)acrylate (4g)

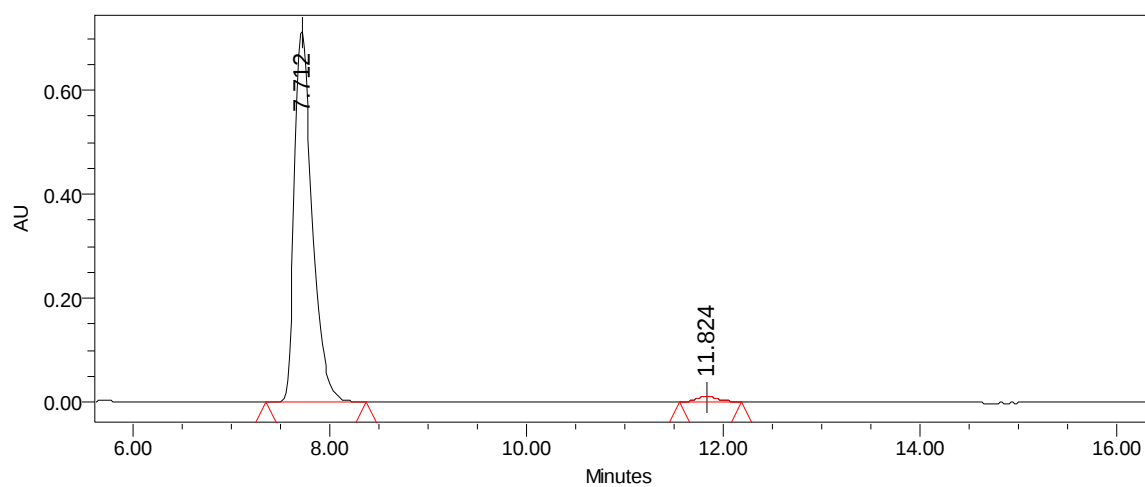
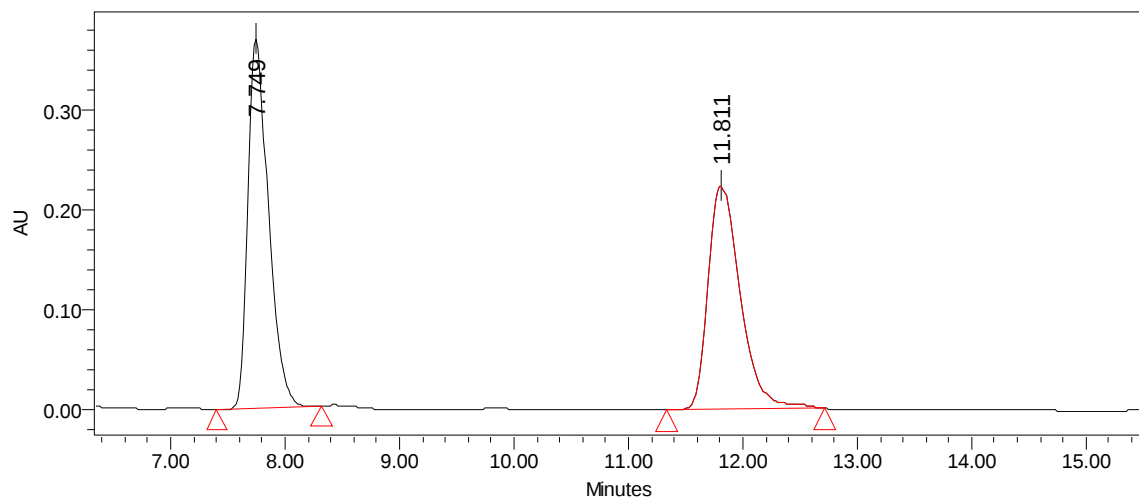
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	7.854	2012787	96.16	151402
2	10.844	80387	3.84	3943

(R)-methyl 2-((4-chlorophenyl)(diethylphosphoryl)methyl)acrylate (4h)

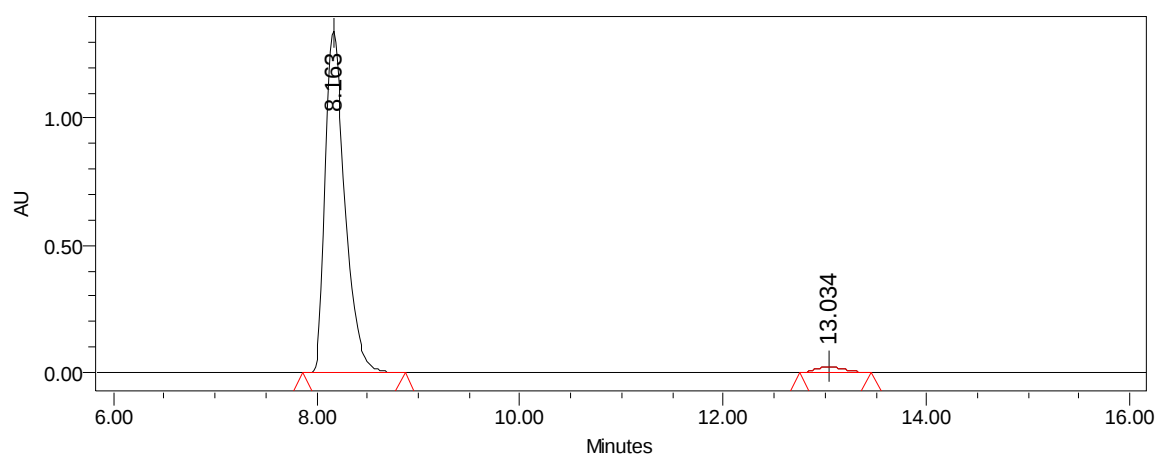
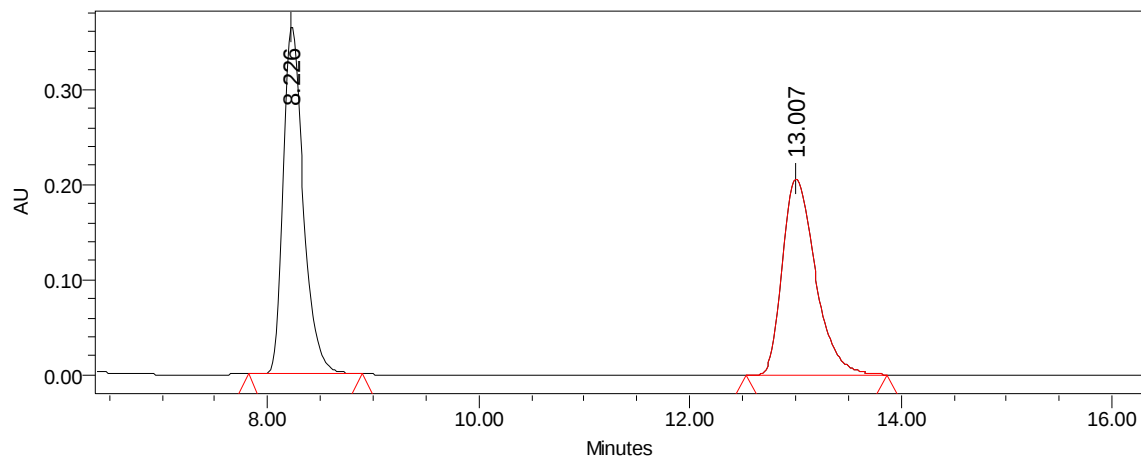
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	7.712	8980306	97.91	713135
2	11.824	191239	2.09	10902

(R)-methyl 2-((4-bromophenyl)(diethylphosphoryl)methyl)acrylate (4i)

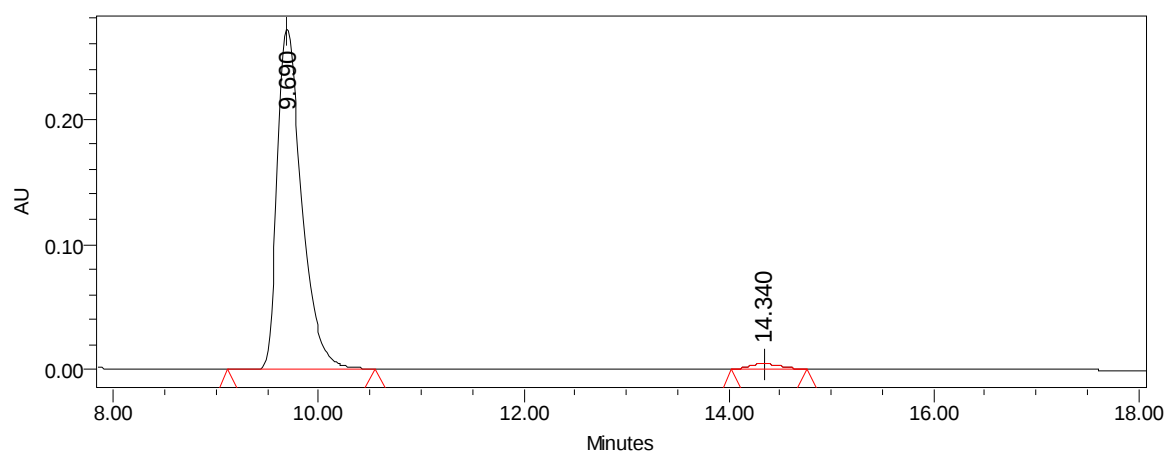
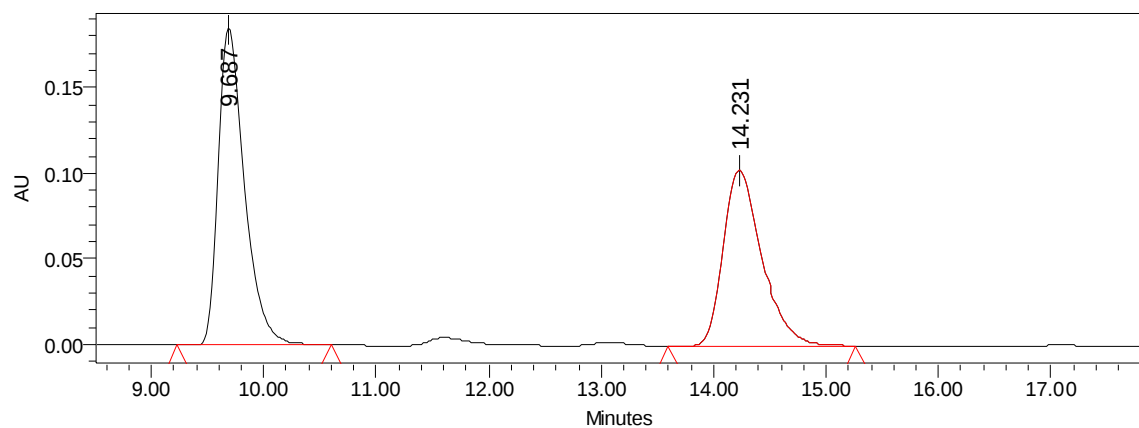
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	8.163	18098438	97.54	1342574
2	13.034	455781	2.46	23596

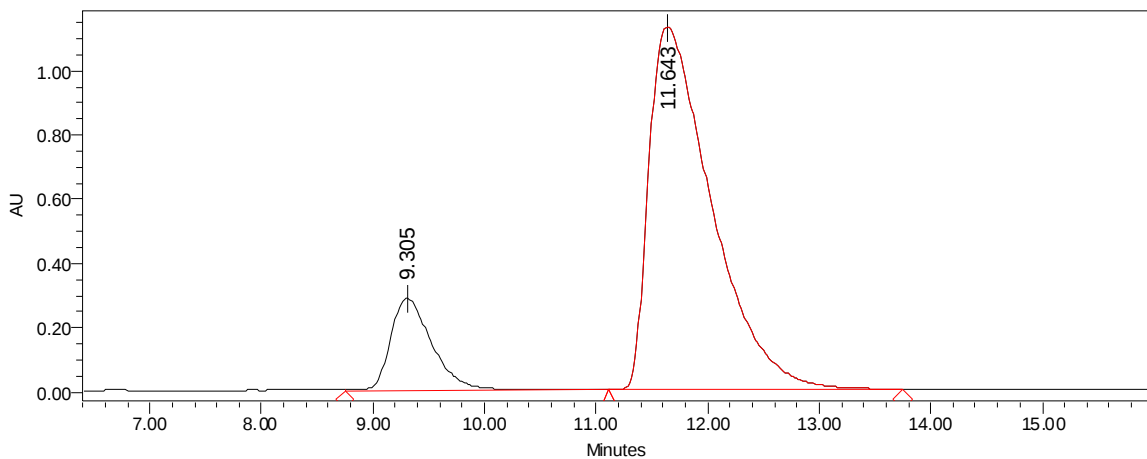
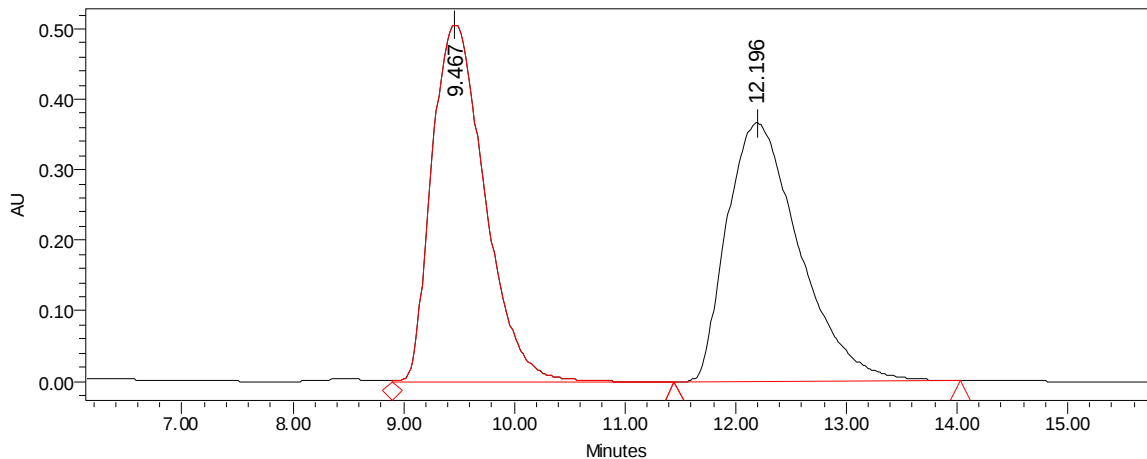
(R)-methyl 2-((diethylphosphoryl)(4-methoxyphenyl)methyl)acrylate (4j)

Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	9.690	4505362	97.97	272268
2	14.340	93401	2.03	4339

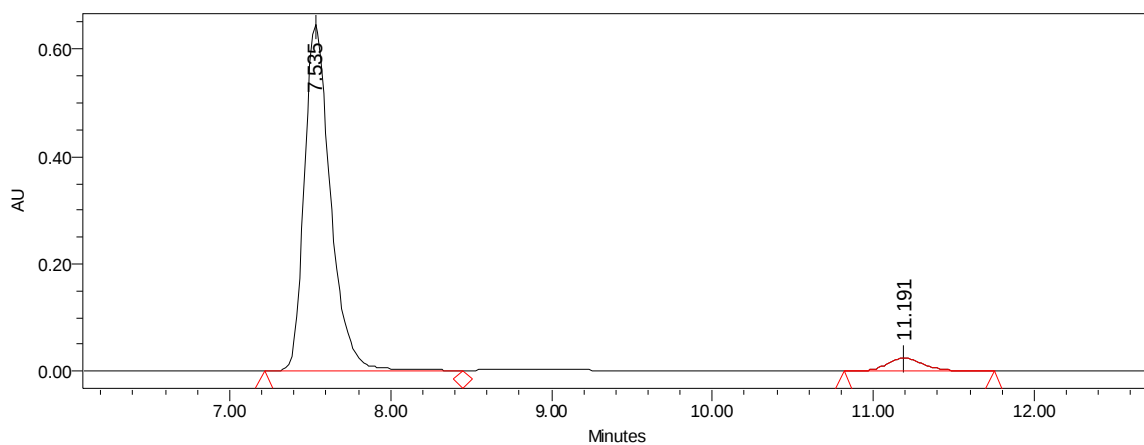
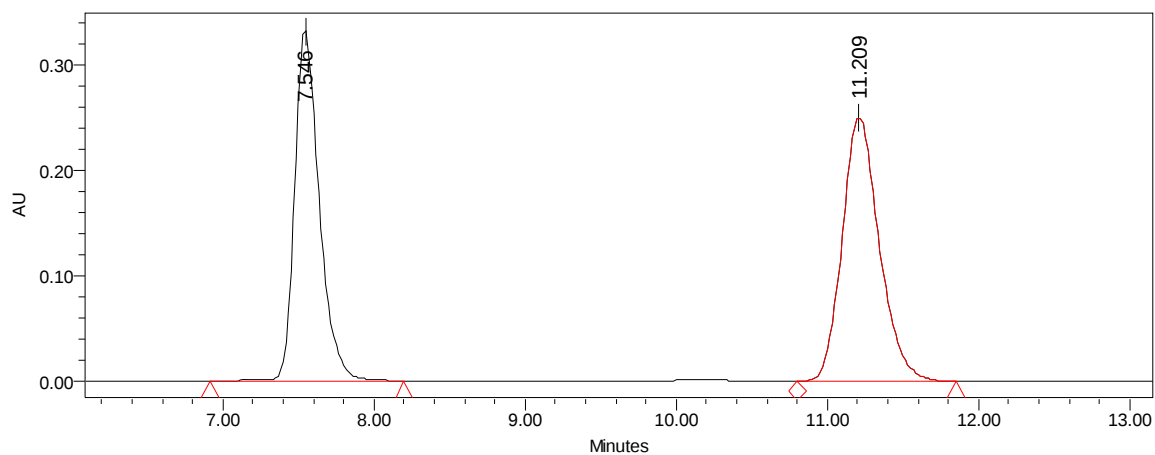
(S)-methyl-2-((diethylphosphoryl)(furan-2-yl)methyl)acrylate (4k)
 Chiralpak OD-H column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	9.305	7425981	14.34	286813
2	11.643	44373719	85.66	1130220

(R)-methyl-2-((dipropylphosphoryl)(phenyl)methyl)acrylate (4l)

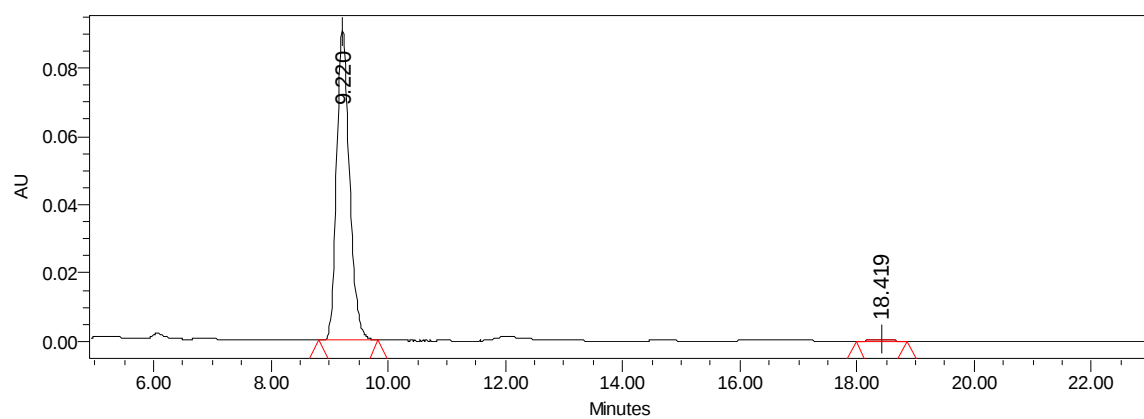
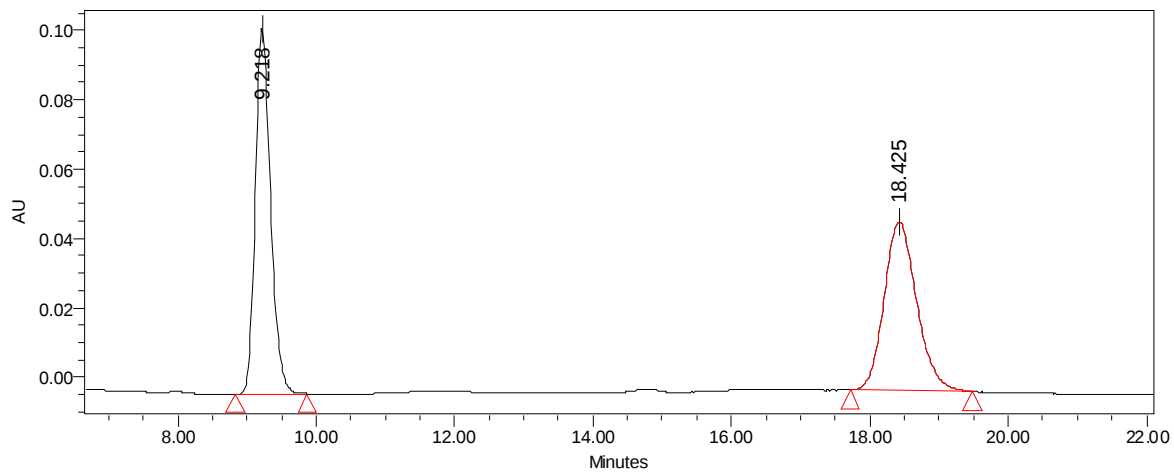
Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	7.535	7301371	94.84	644860
2	11.191	396890	5.16	23916

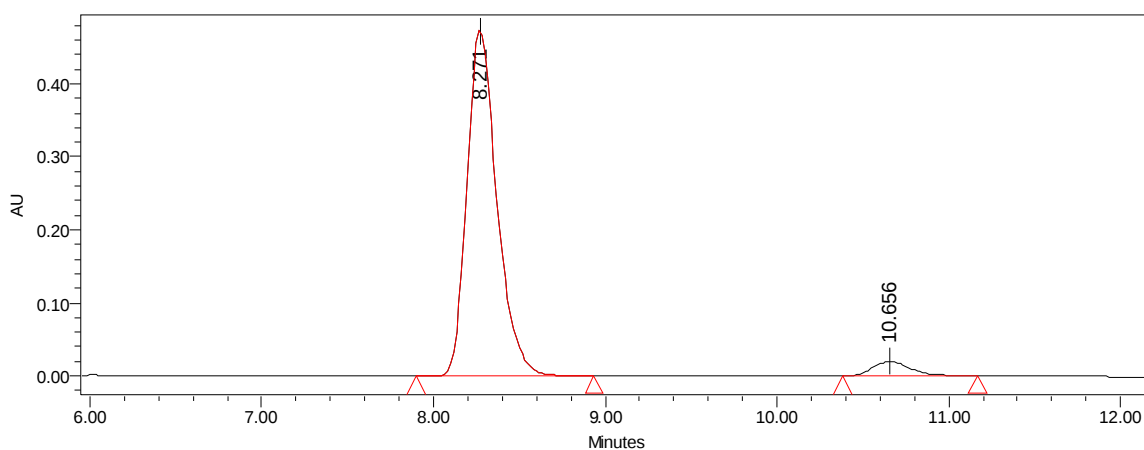
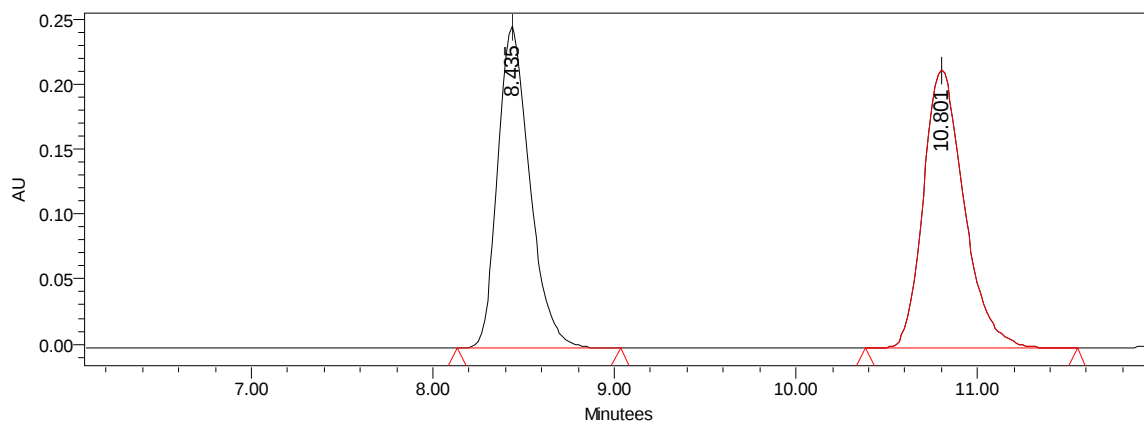
(R)-methyl-2-((dibutylphosphoryl)(phenyl)methyl)acrylate (4m)

Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min

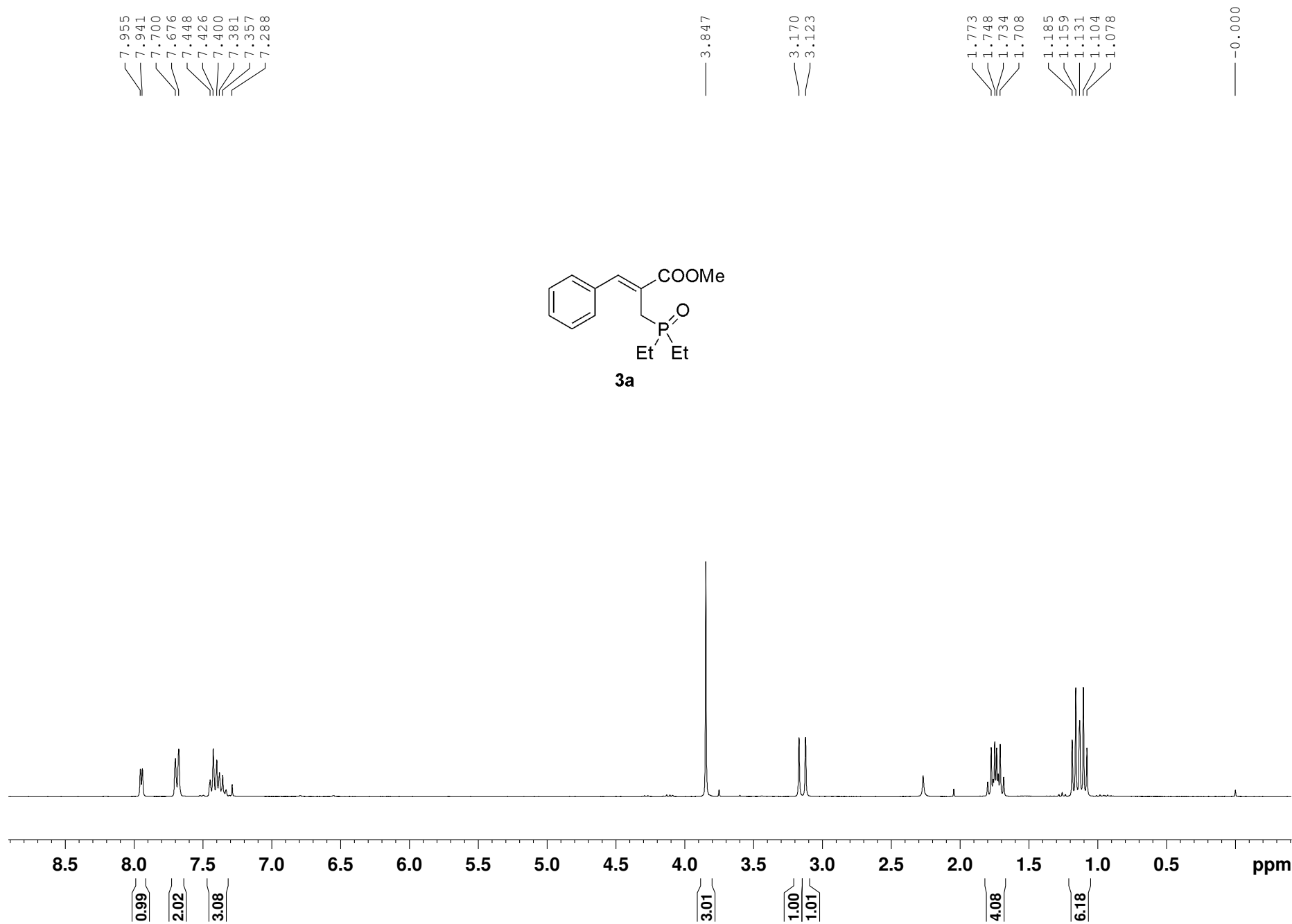


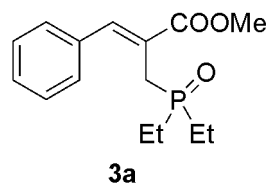
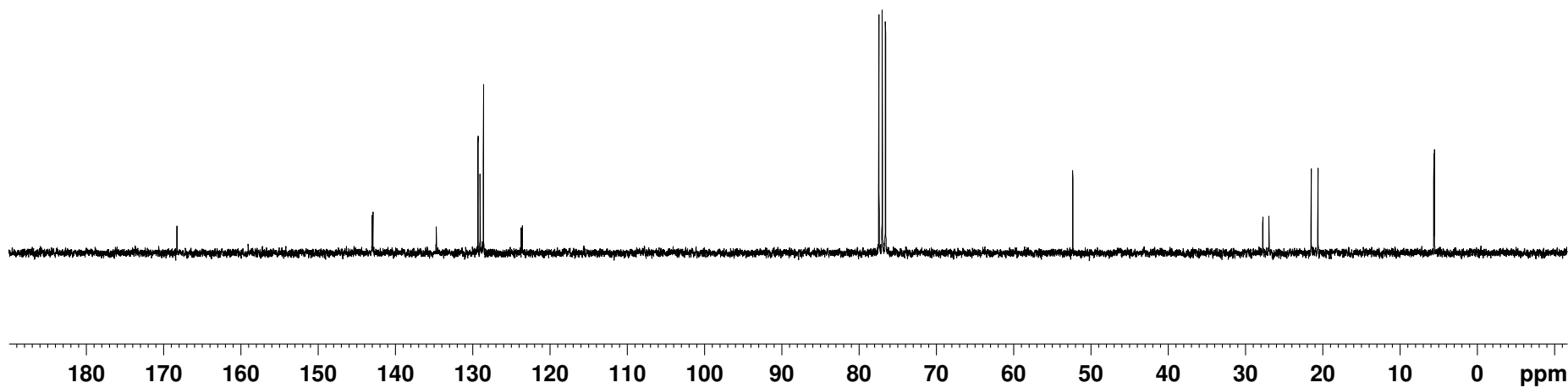
	Retention Time	Area	% Area	Height
1	9.220	1389480	99.08	90530
2	18.419	12905	0.92	506

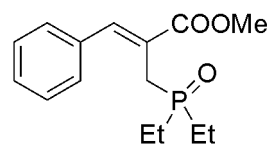
(*R*)-methyl-2-((diallylphosphoryl)(phenyl)methyl)acrylate (4n)
 Chiralpak AD column, hexane/iPrOH (90:10), flow rate 1.0 mL/min



	Retention Time	Area	% Area	Height
1	8.271	5749090	94.85	473815
2	10.656	311964	5.15	20220

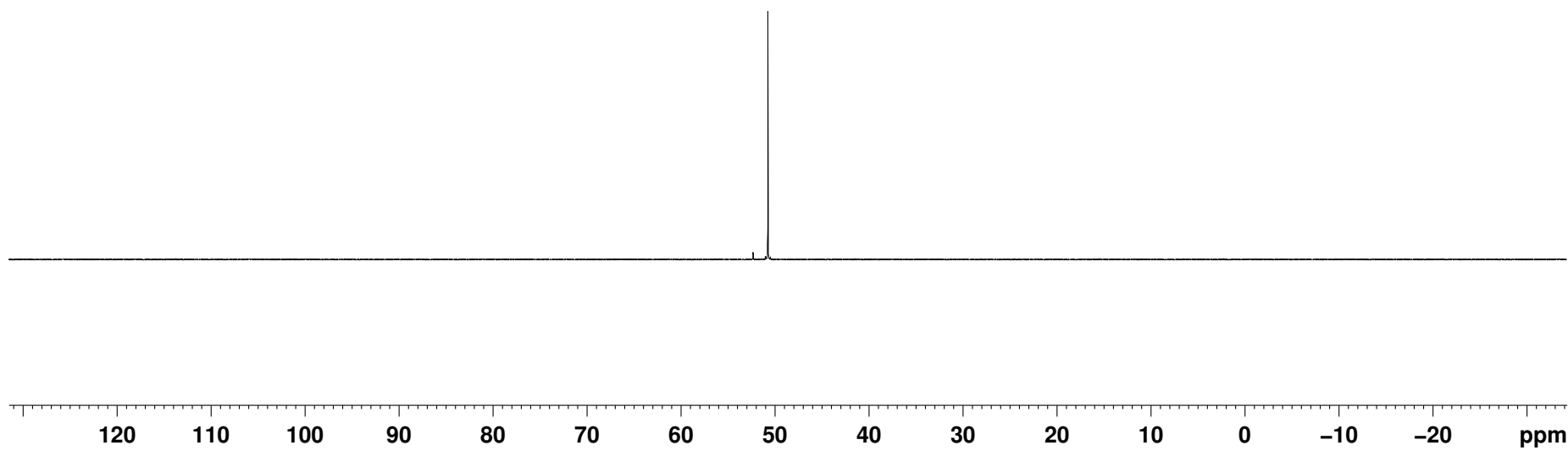


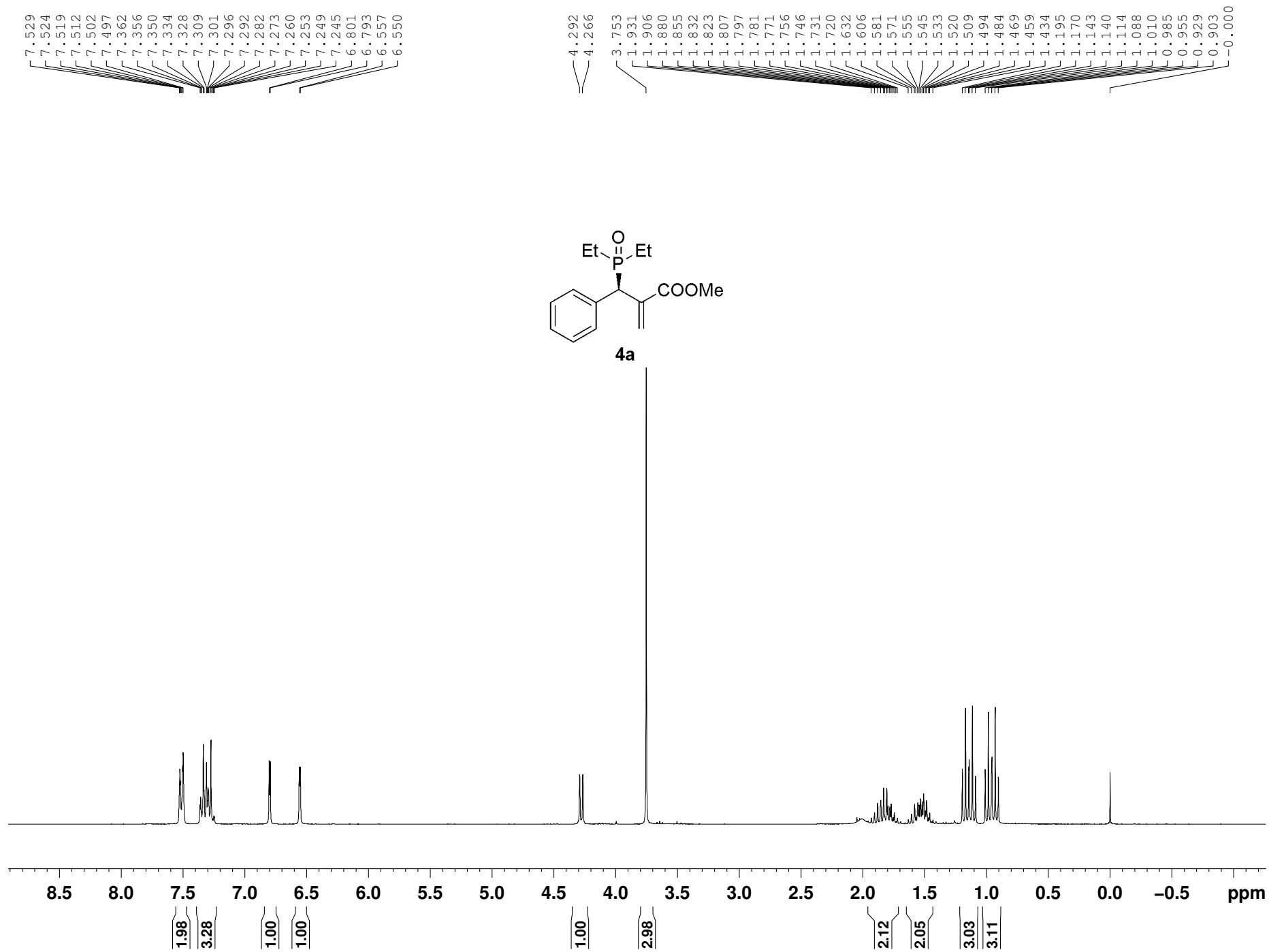


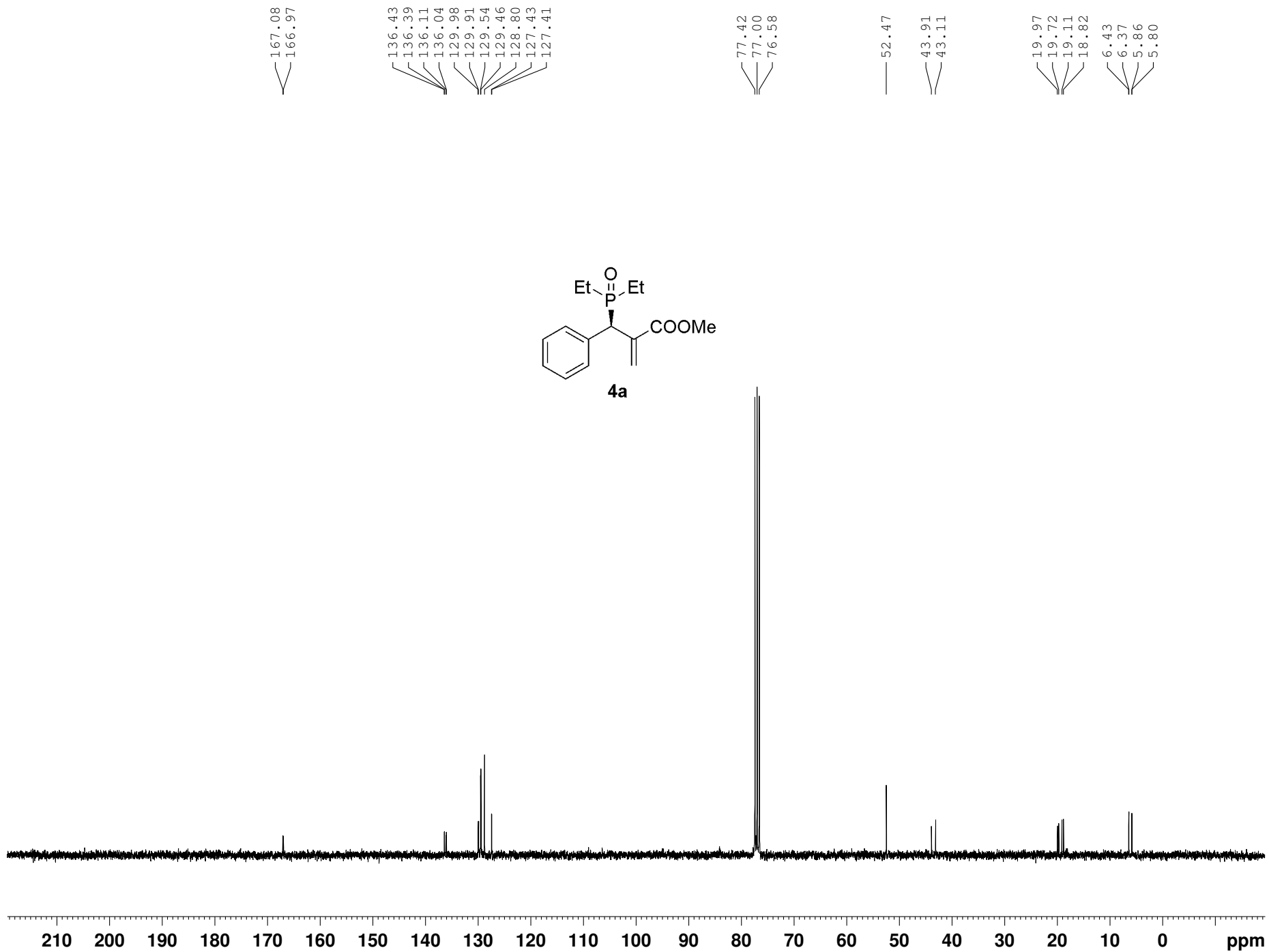


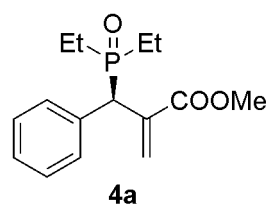
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50.71

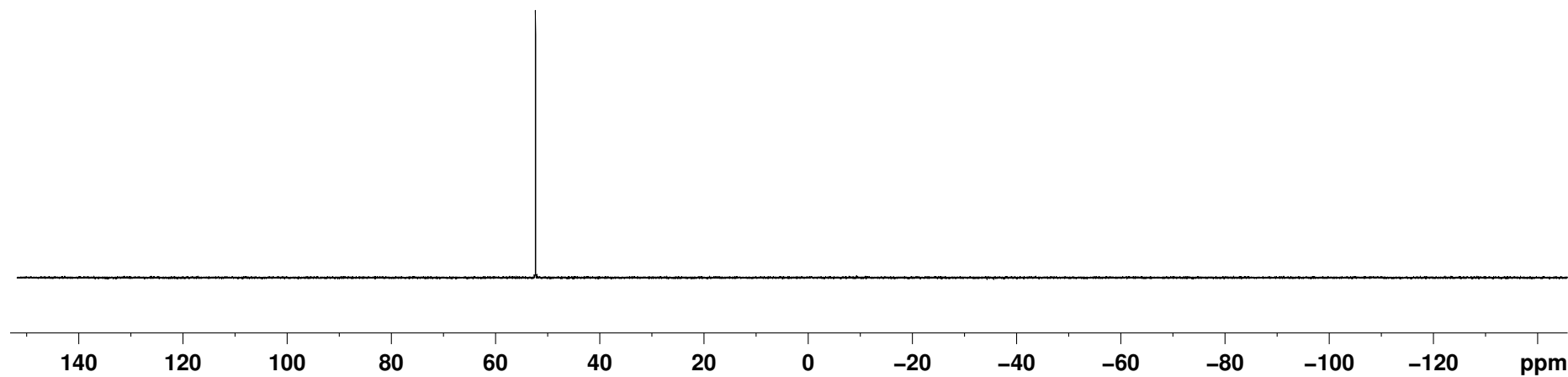


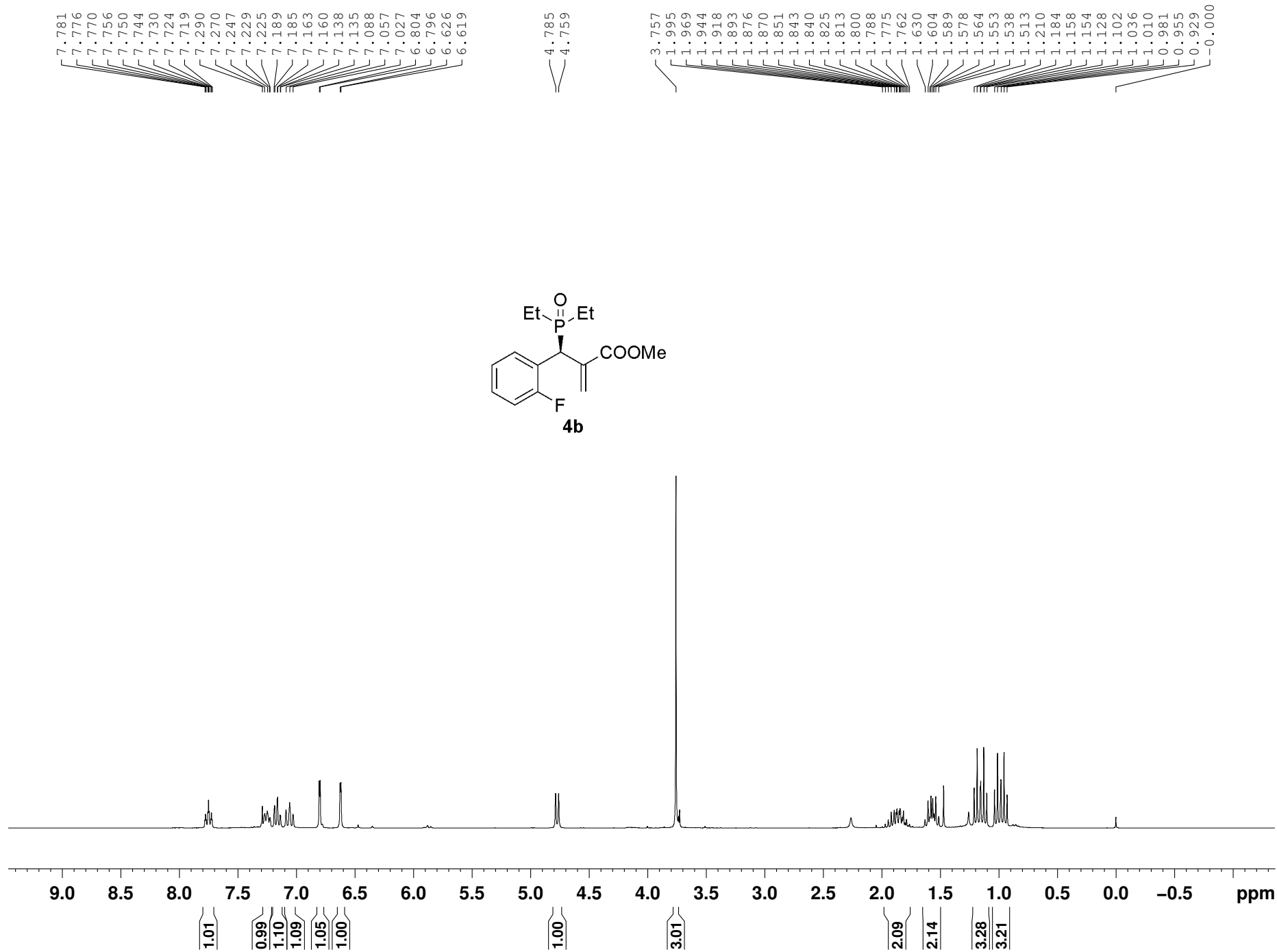


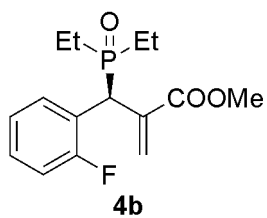
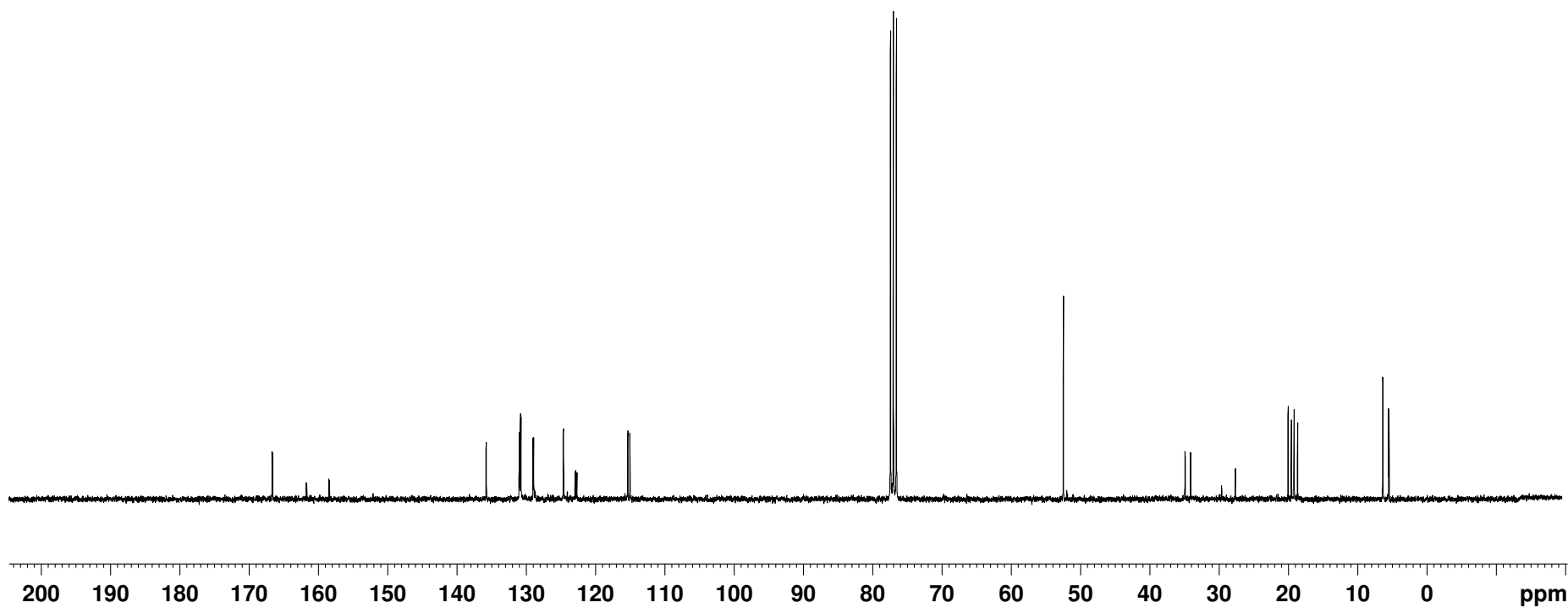


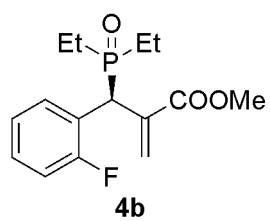


— 52.260

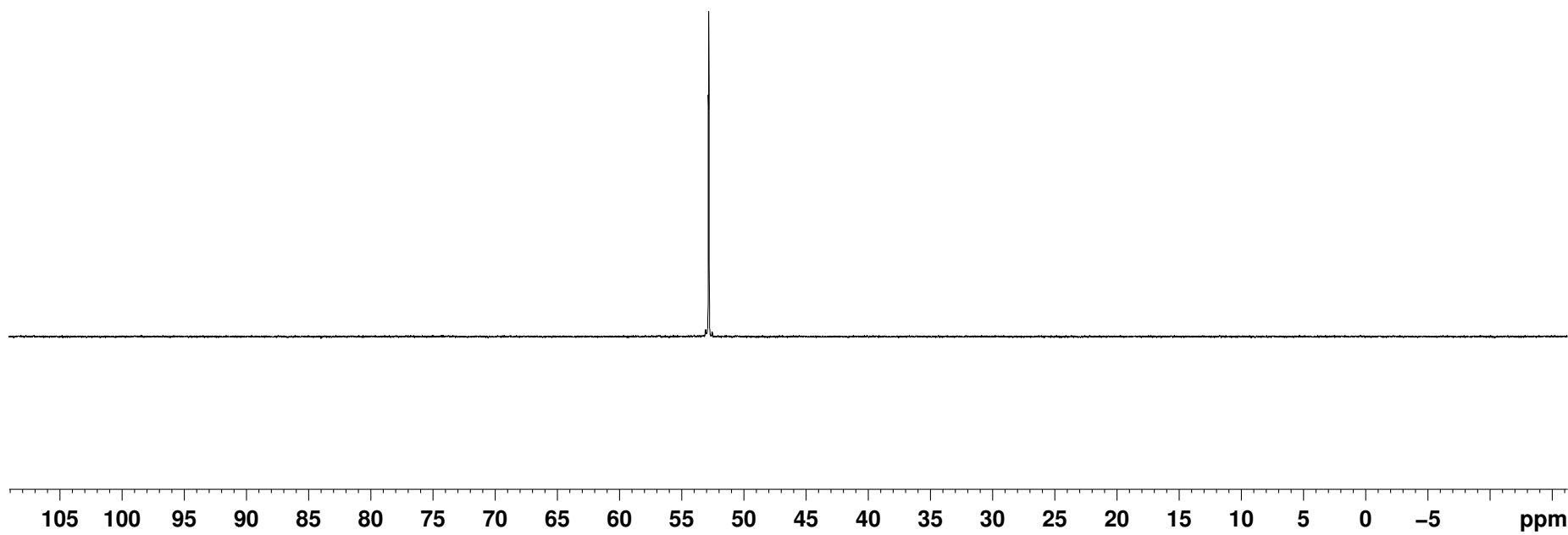


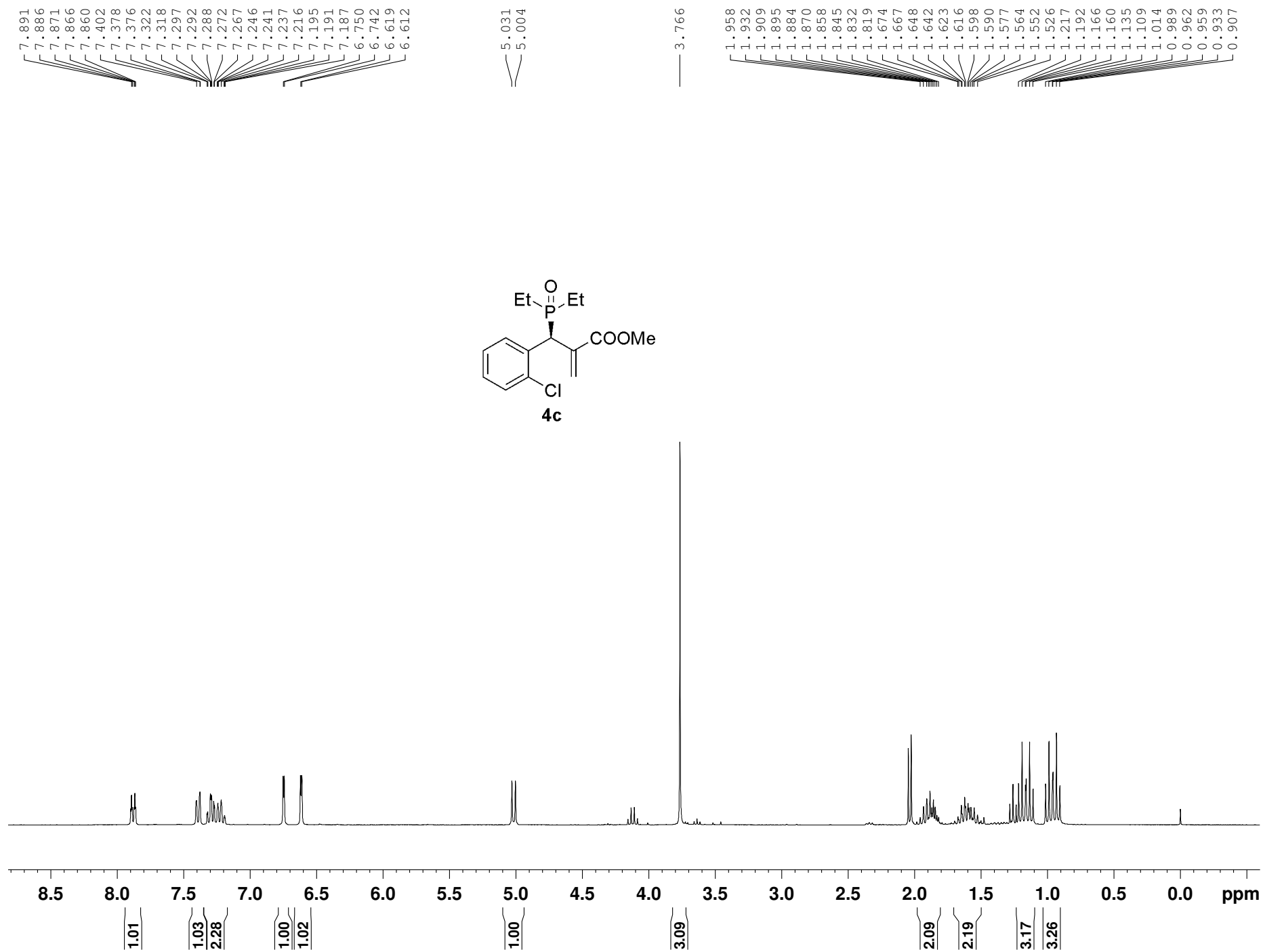
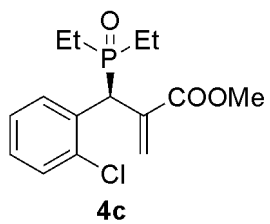


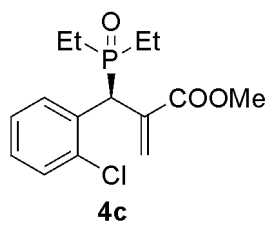
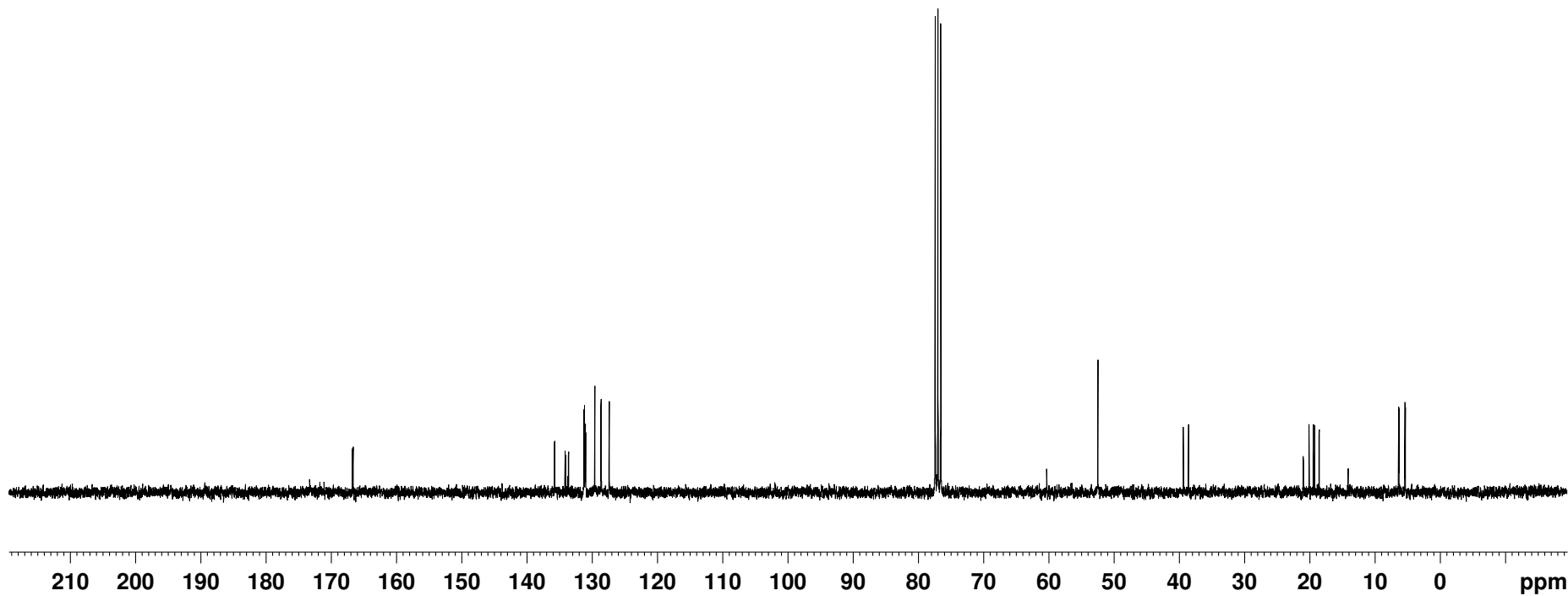


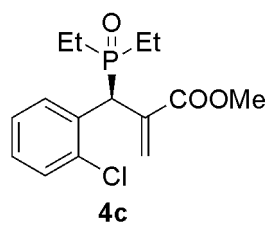


52.83
52.81

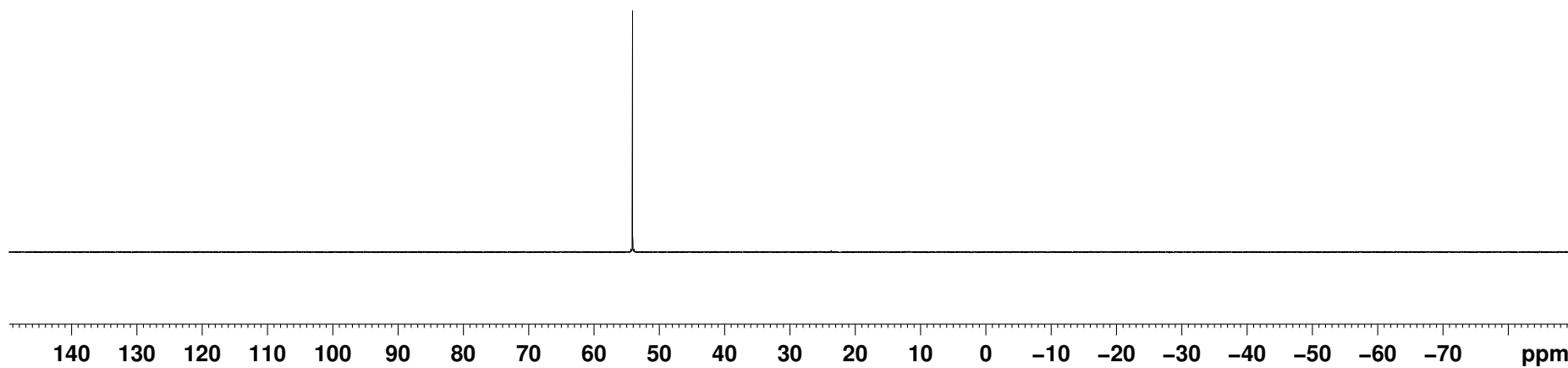


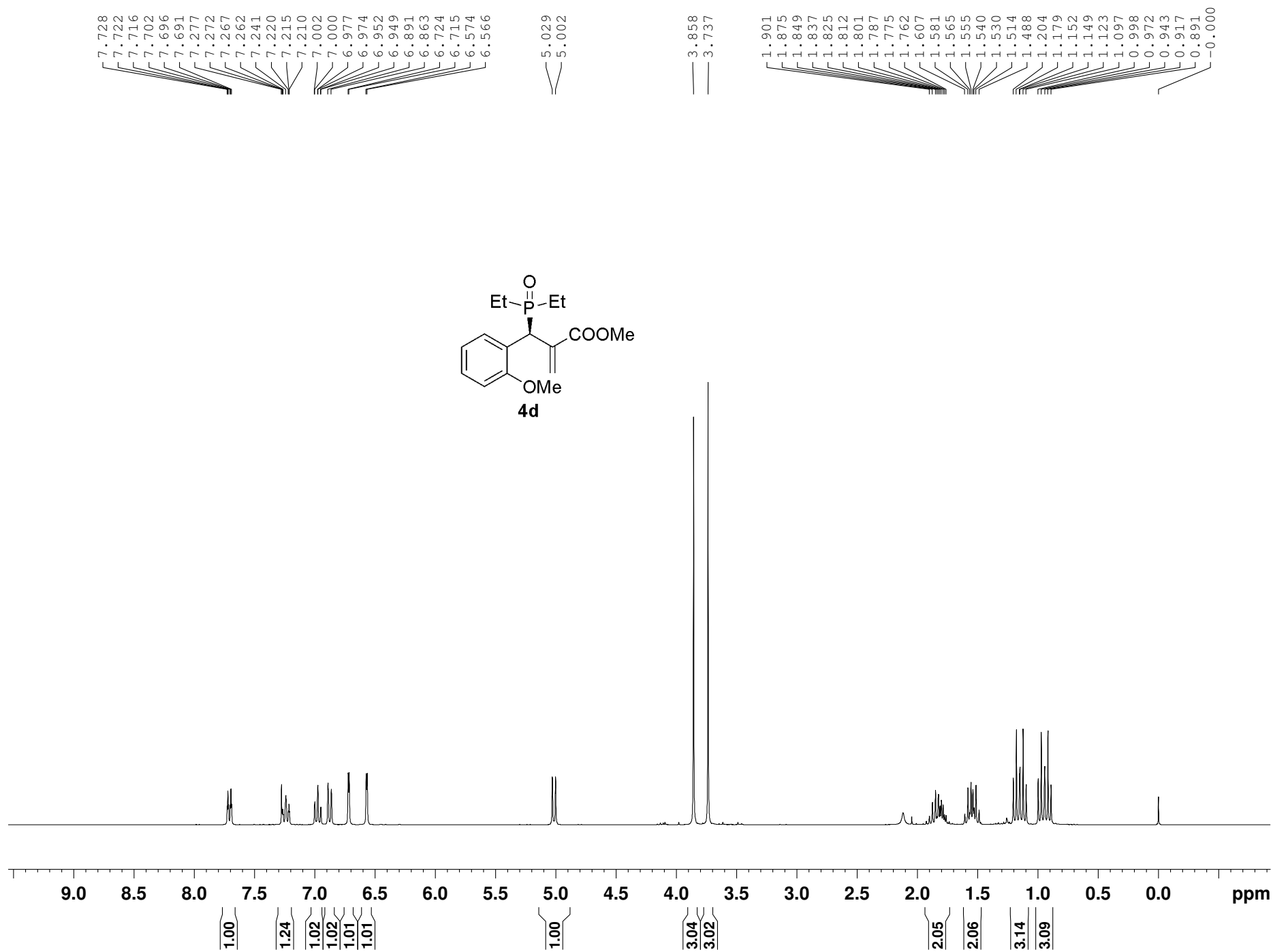


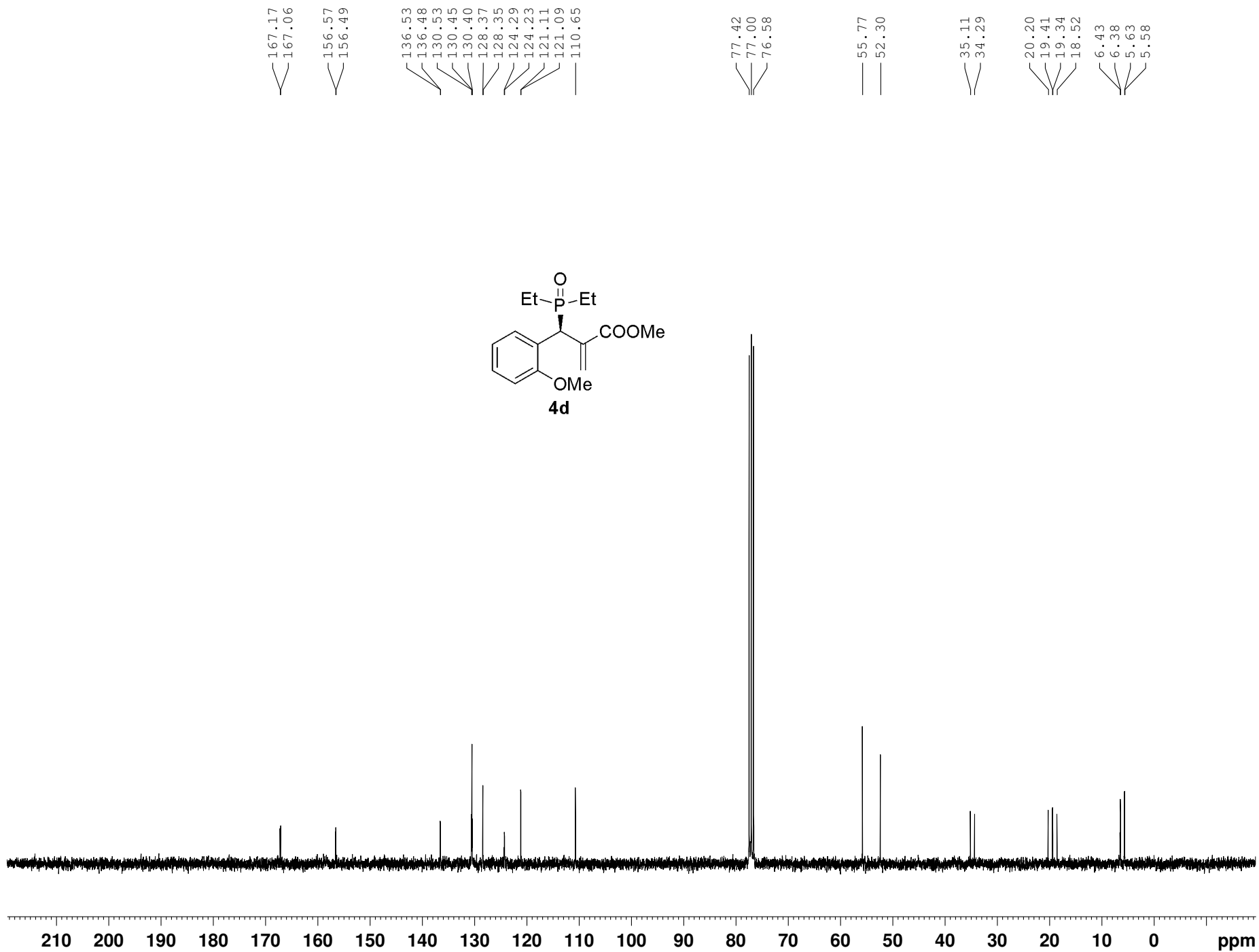




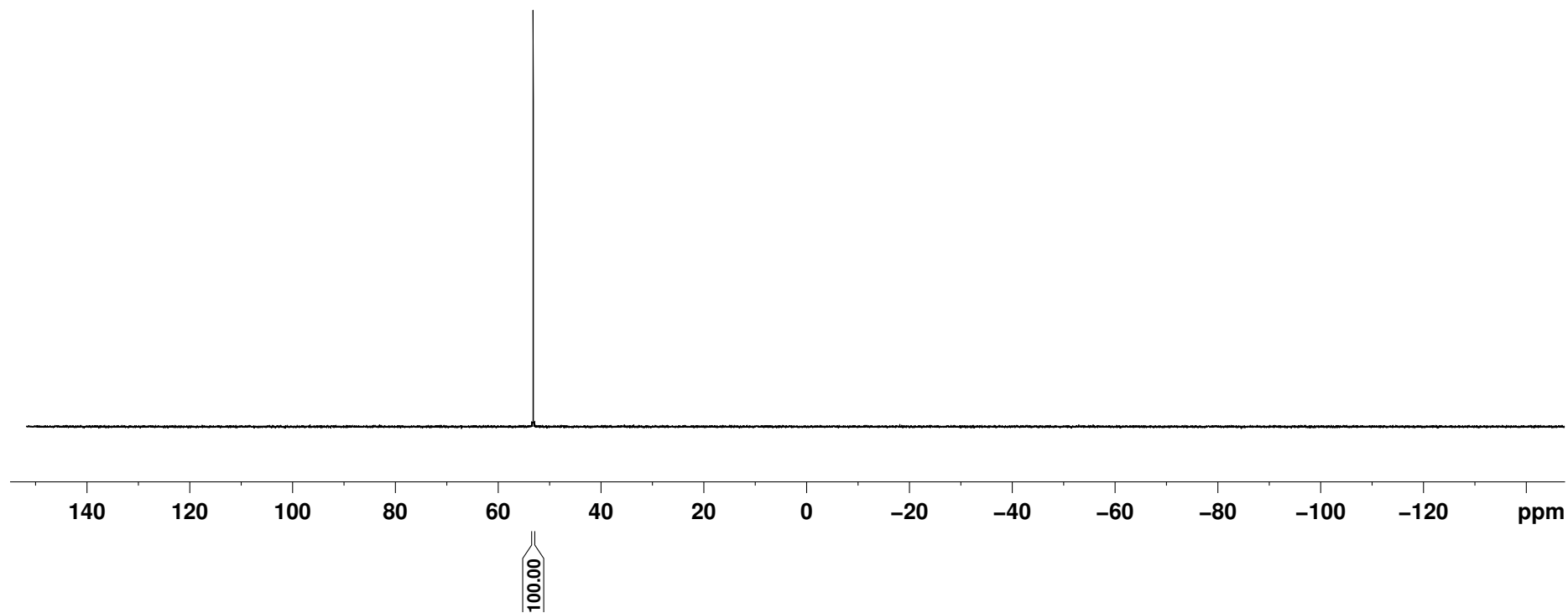
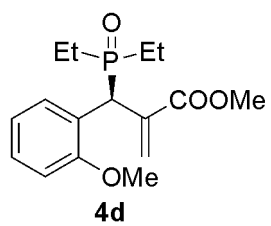
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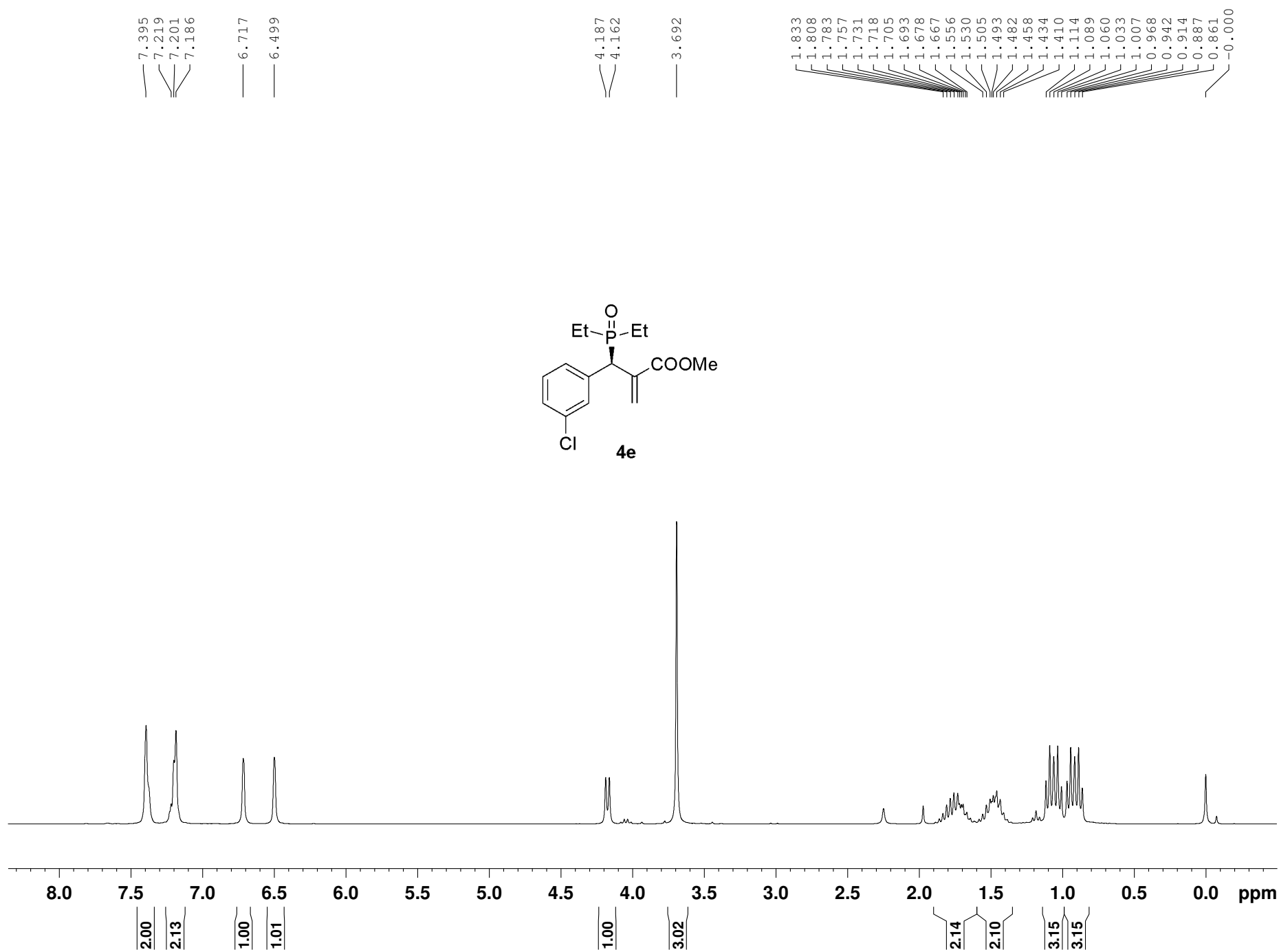


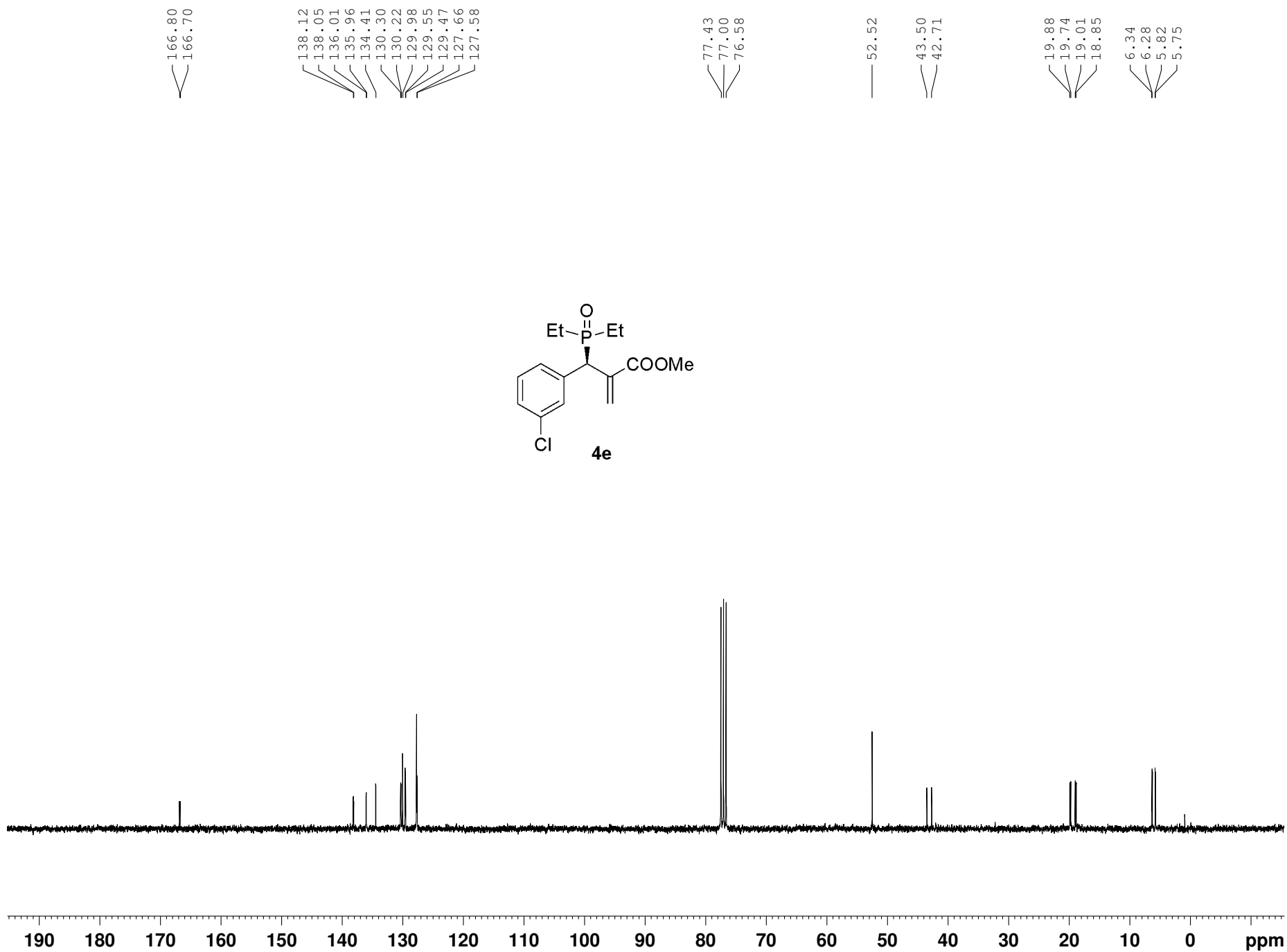
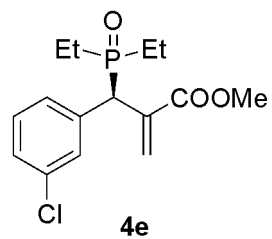


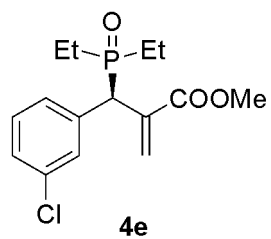


— 53.173

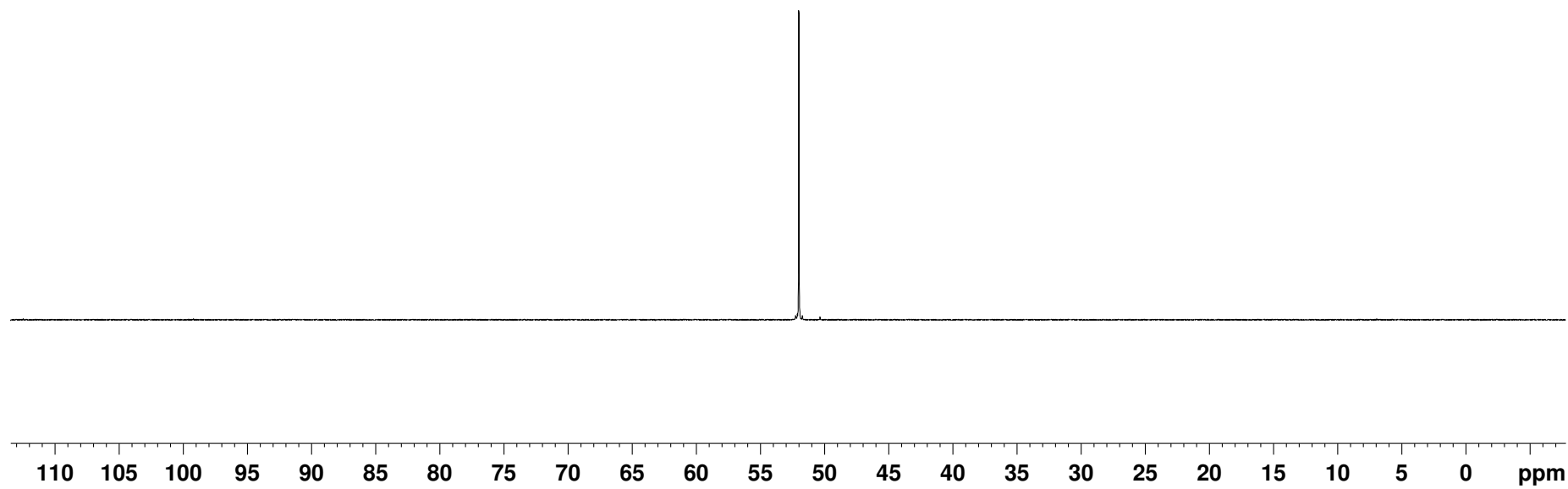


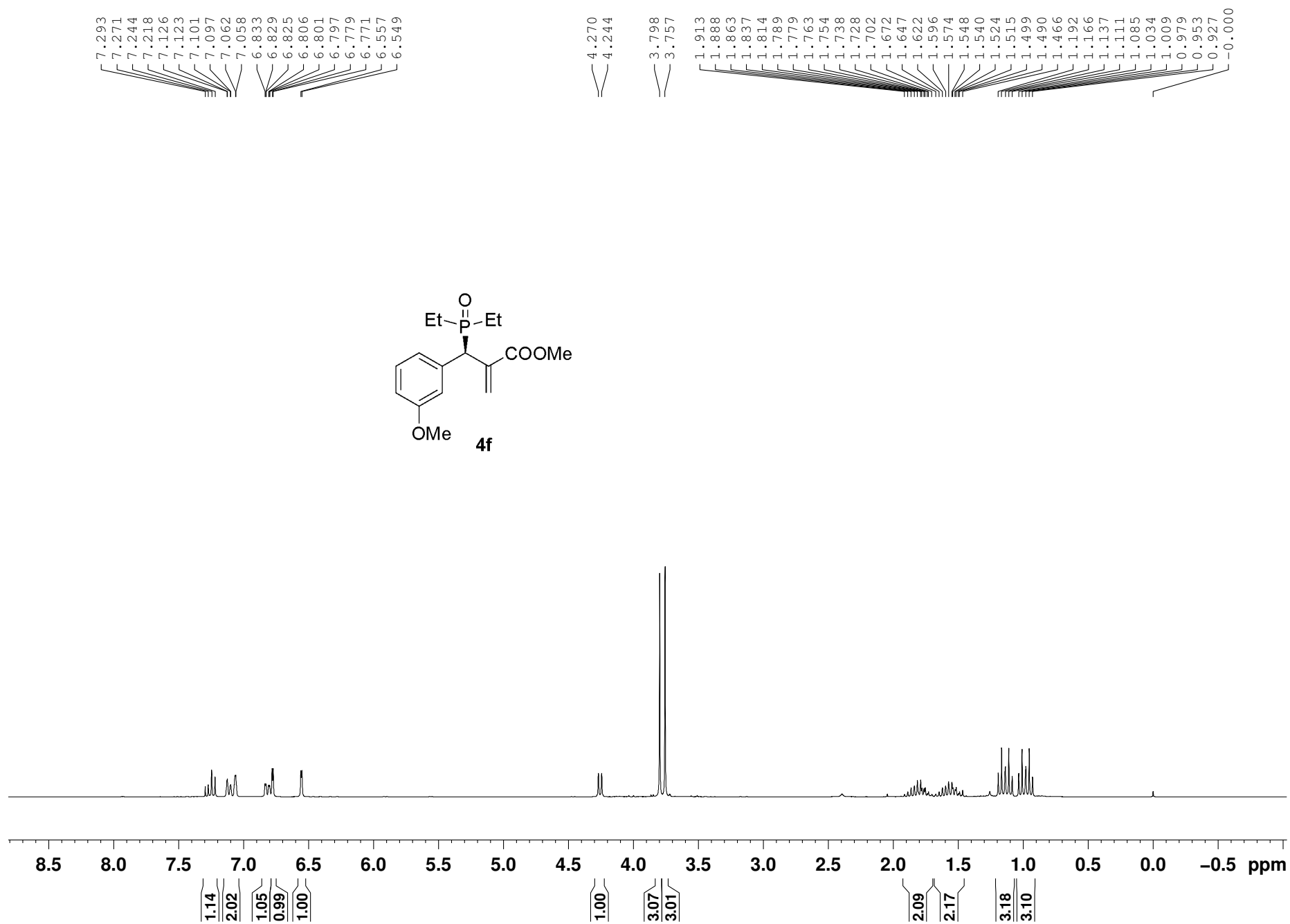


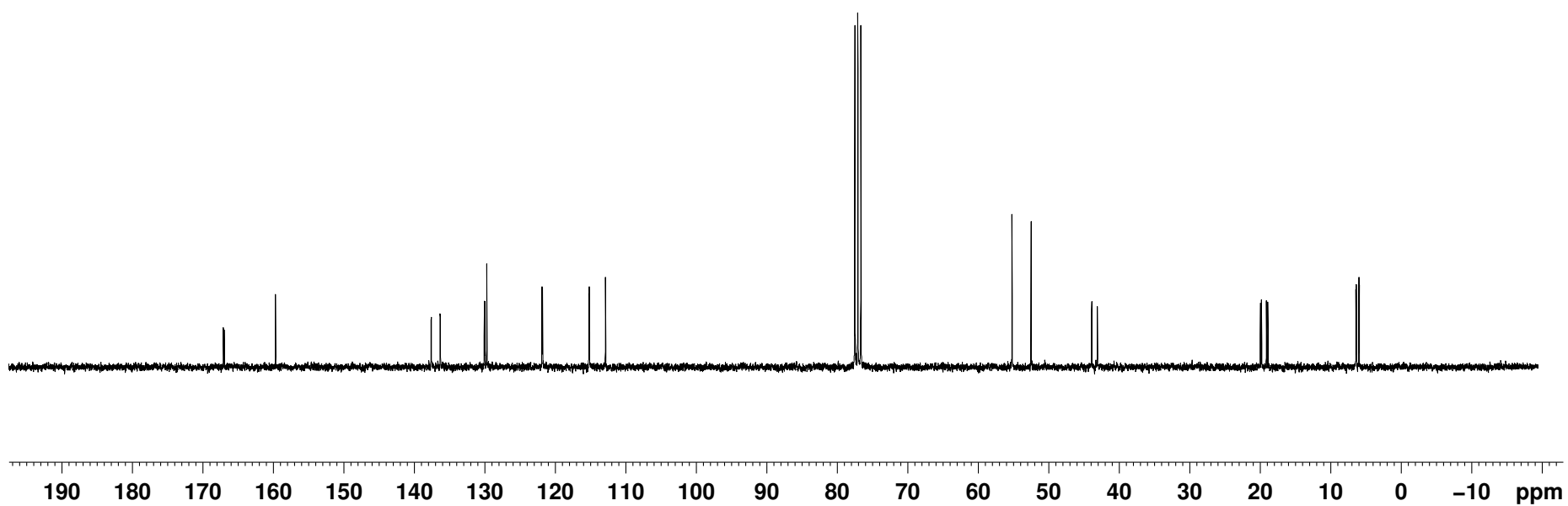
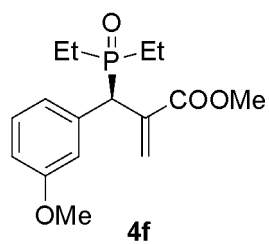


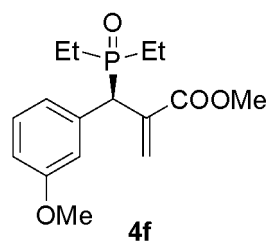


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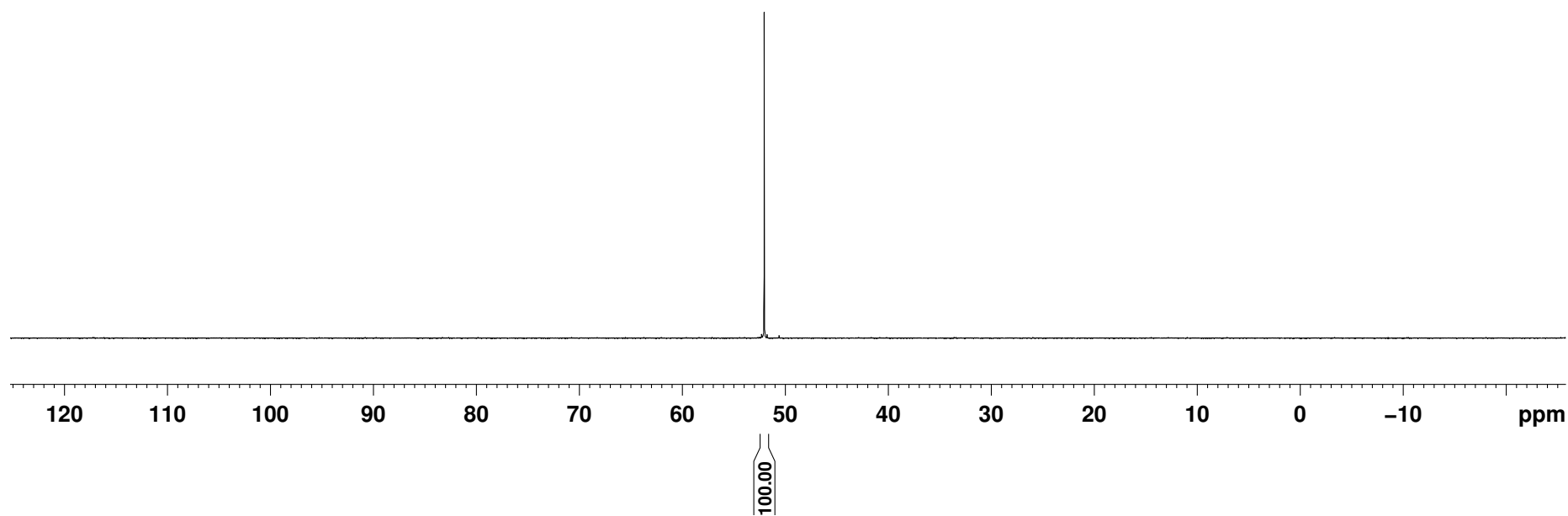


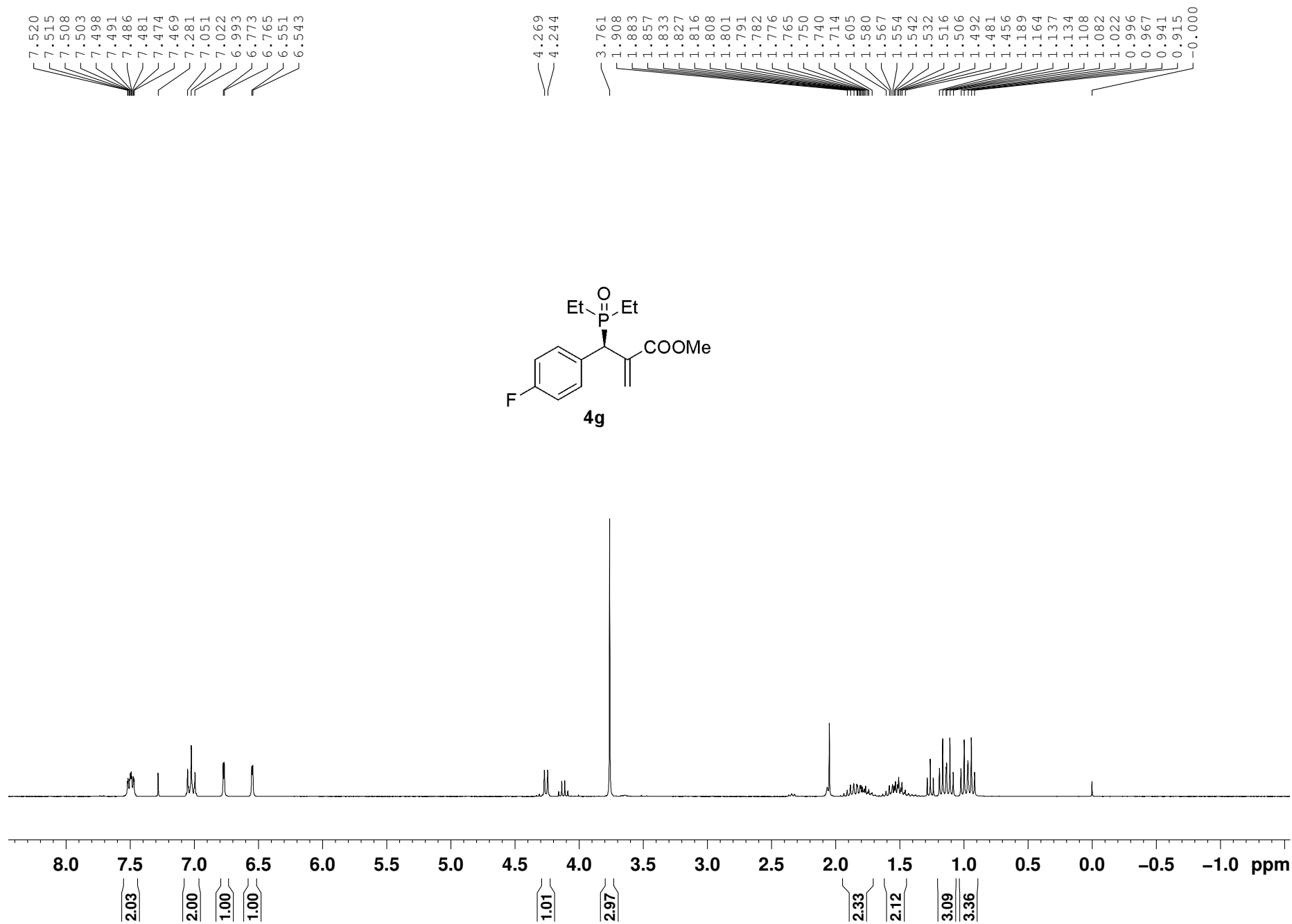


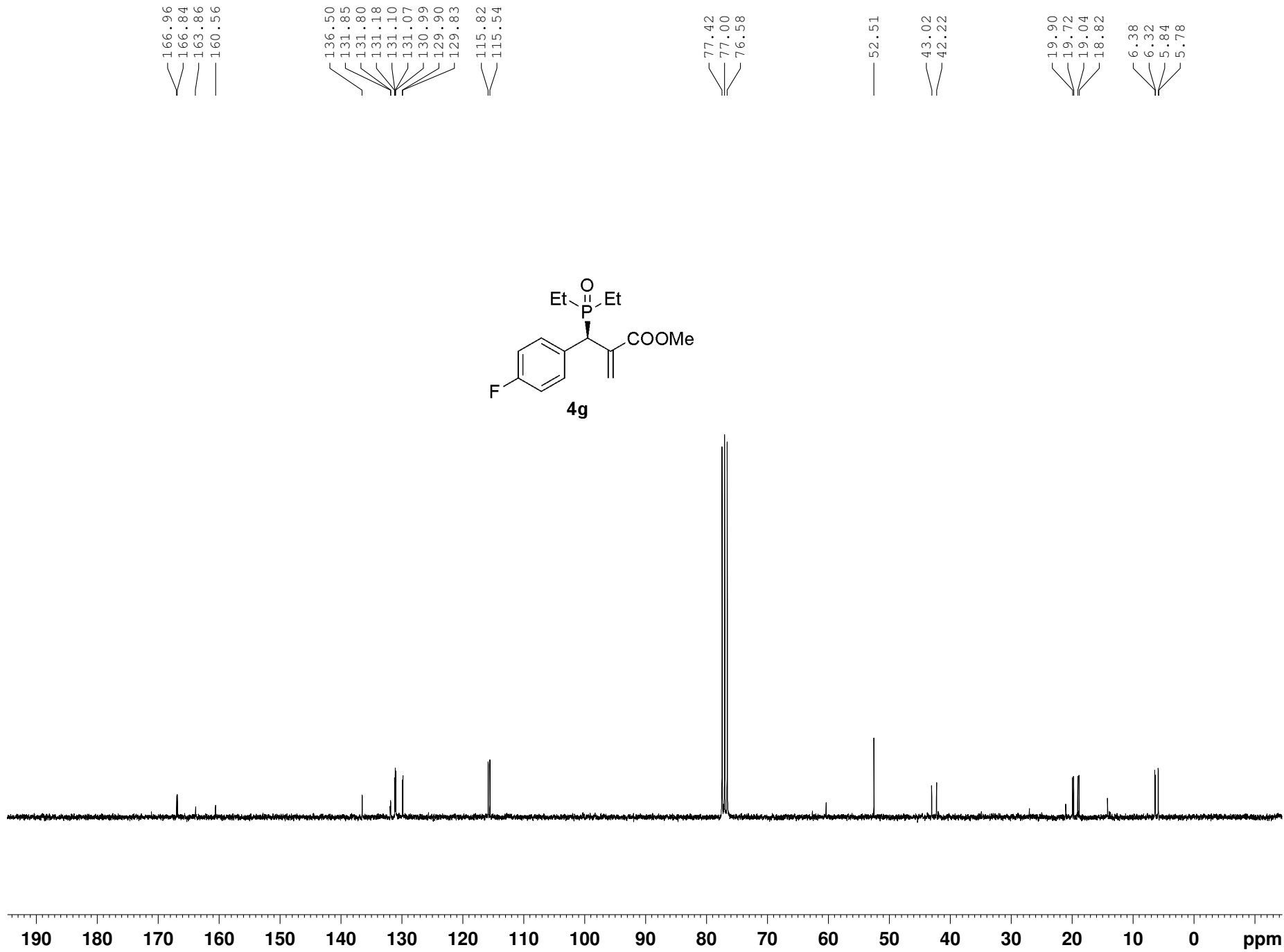


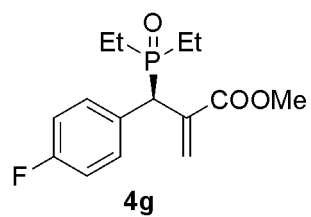


— 52.021

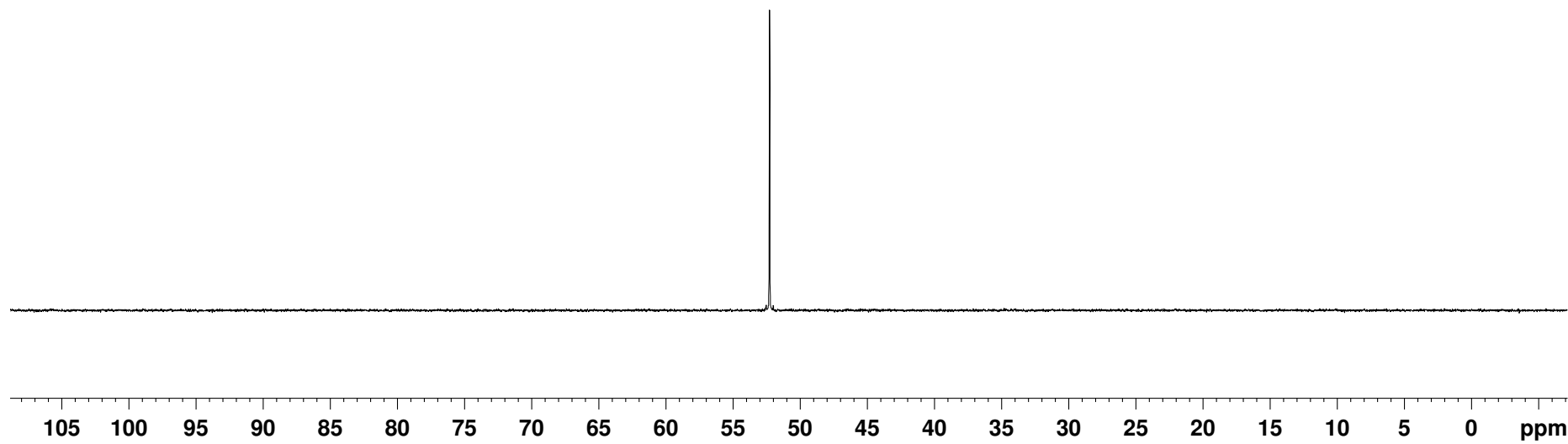


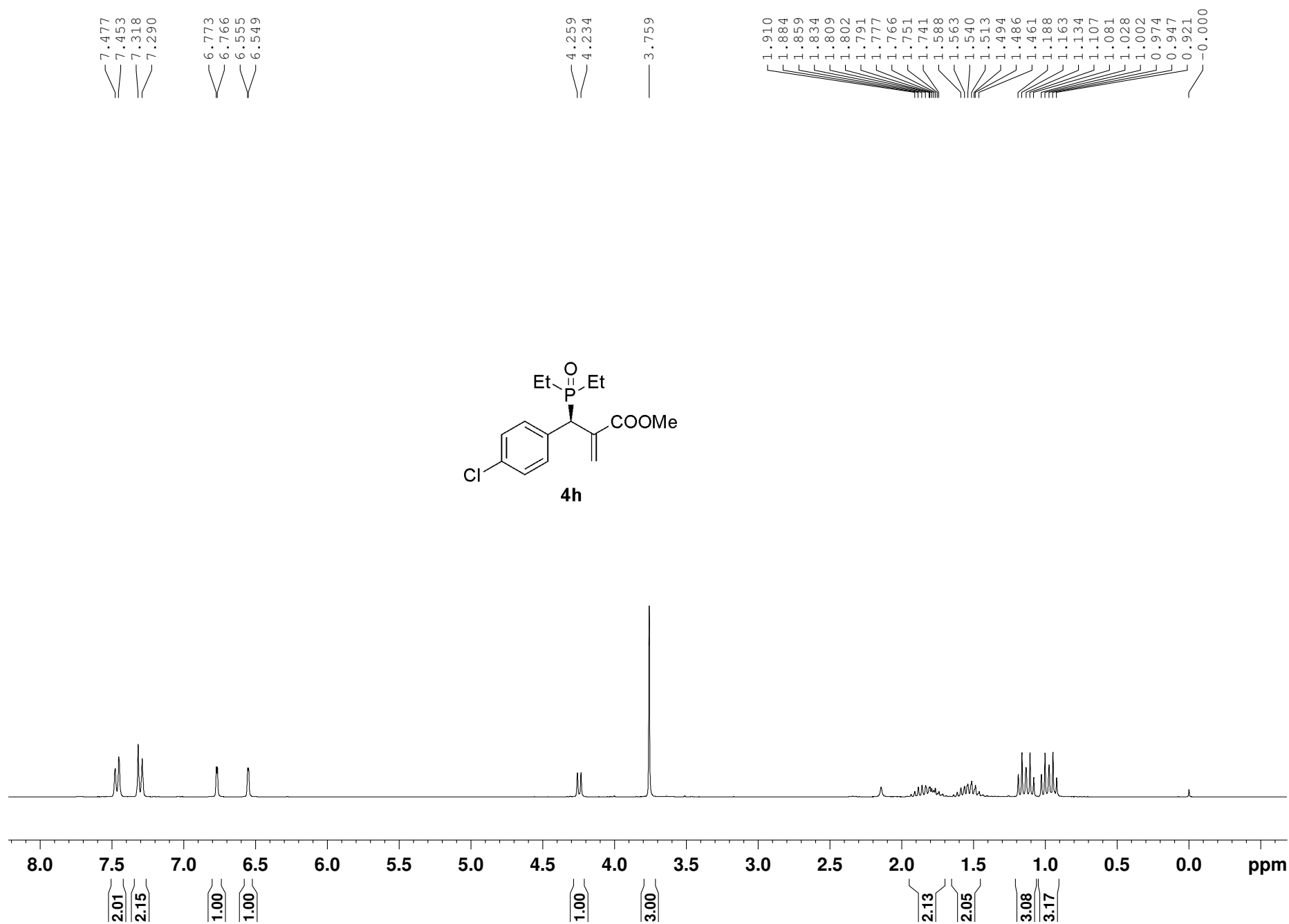


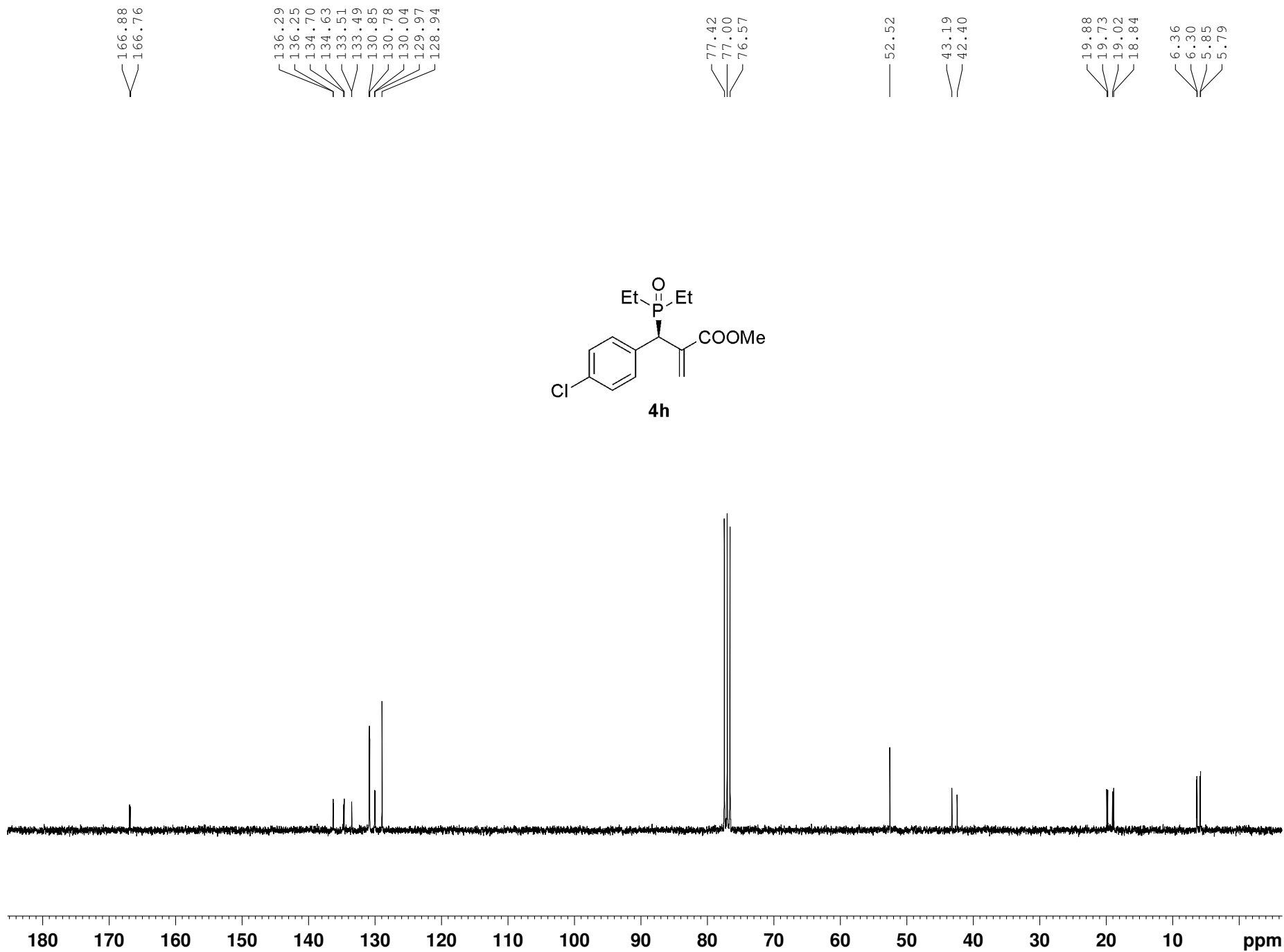
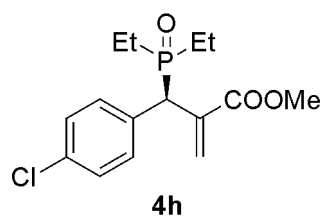


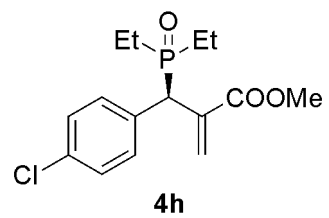


52.282

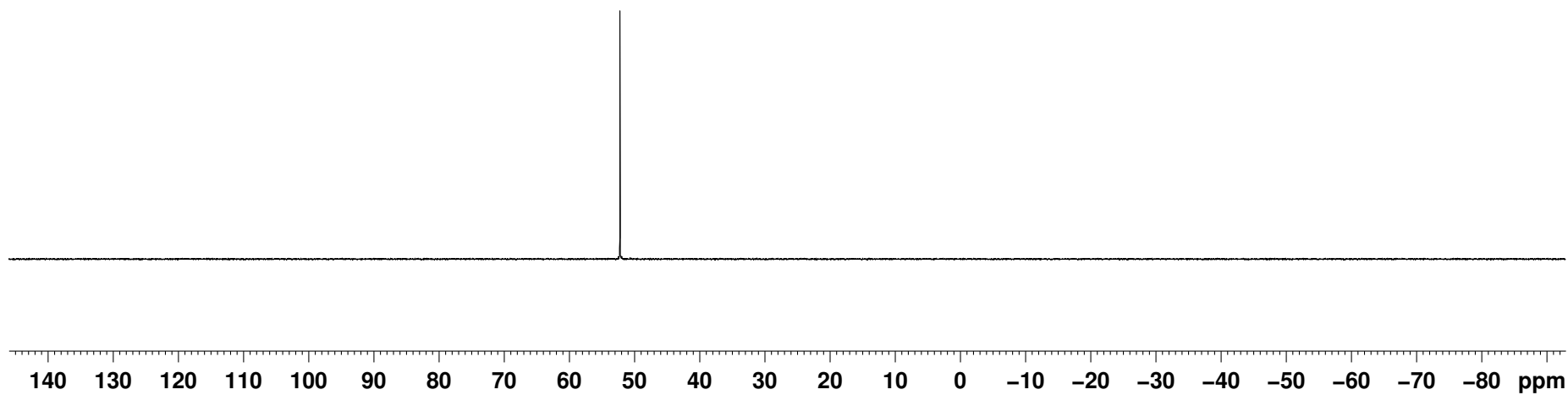


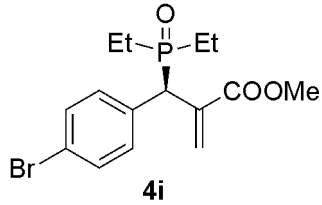
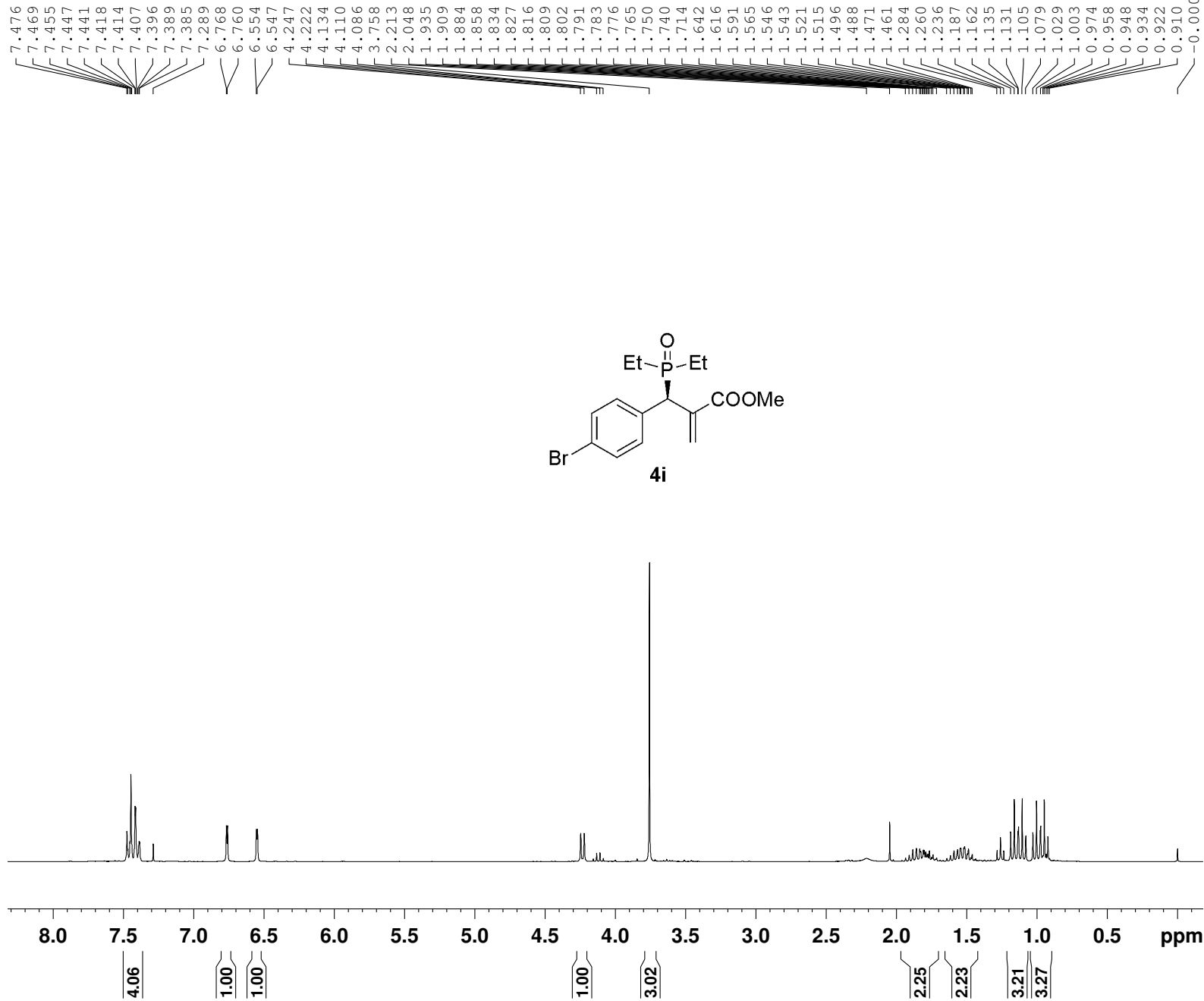






— 52.22



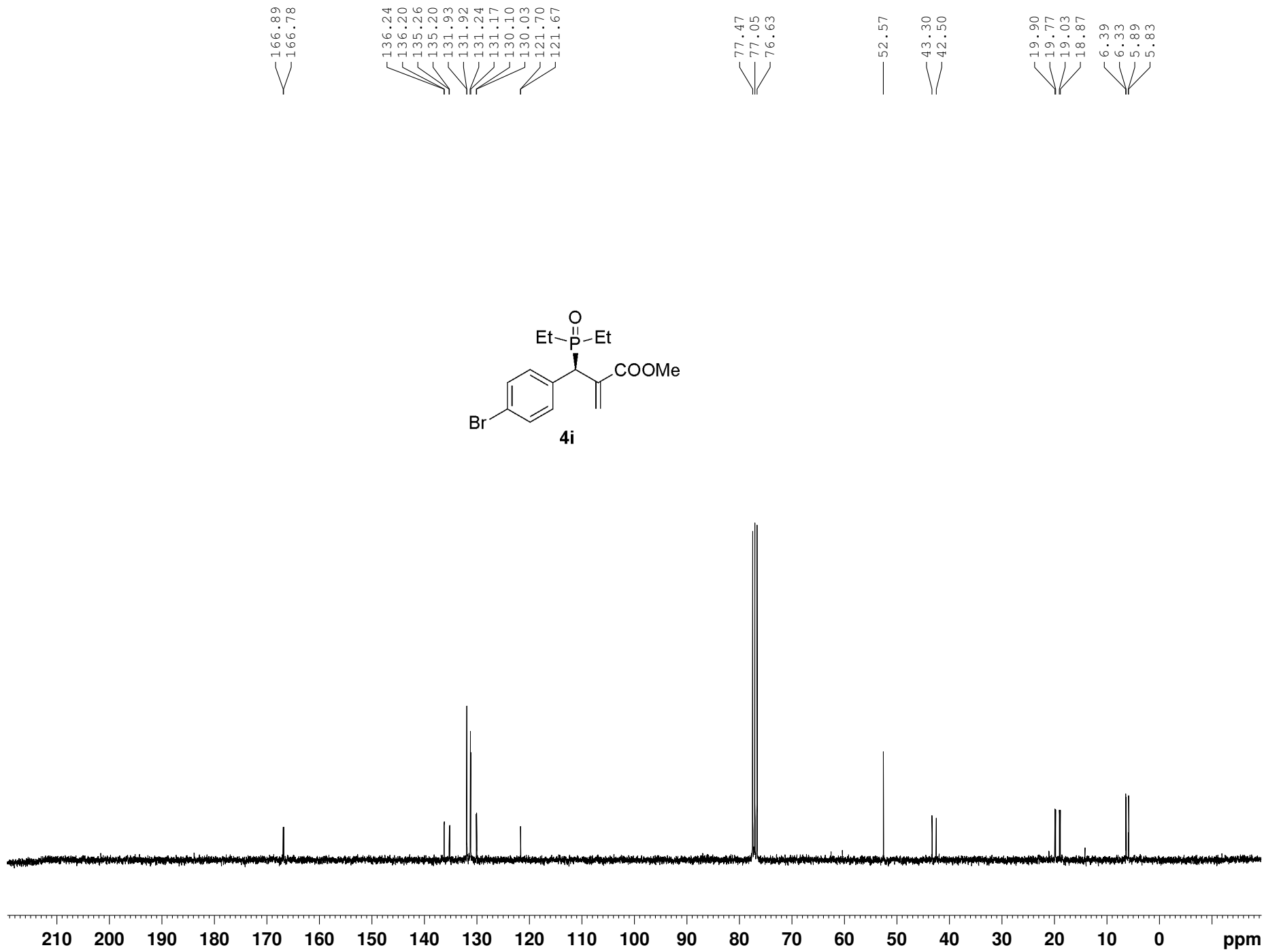
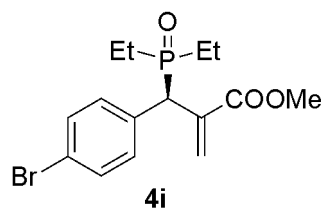


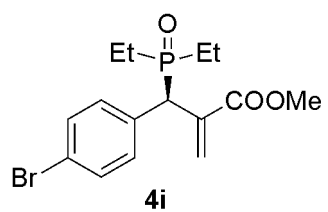
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EXPNO     41
PROCNO    1
Date_     20100313
Time      11.34
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zg30
TD         65536
SOLVENT   CDCl3
NS         8
DS         2
SWH        6188.119 Hz
FIDRES     0.094423 Hz
AQ         5.2953587 sec
RG         50.8
DW         80.800 usec
DE         6.50 usec
TE         290.1 K
D1         1.00000000 sec
TD0        1

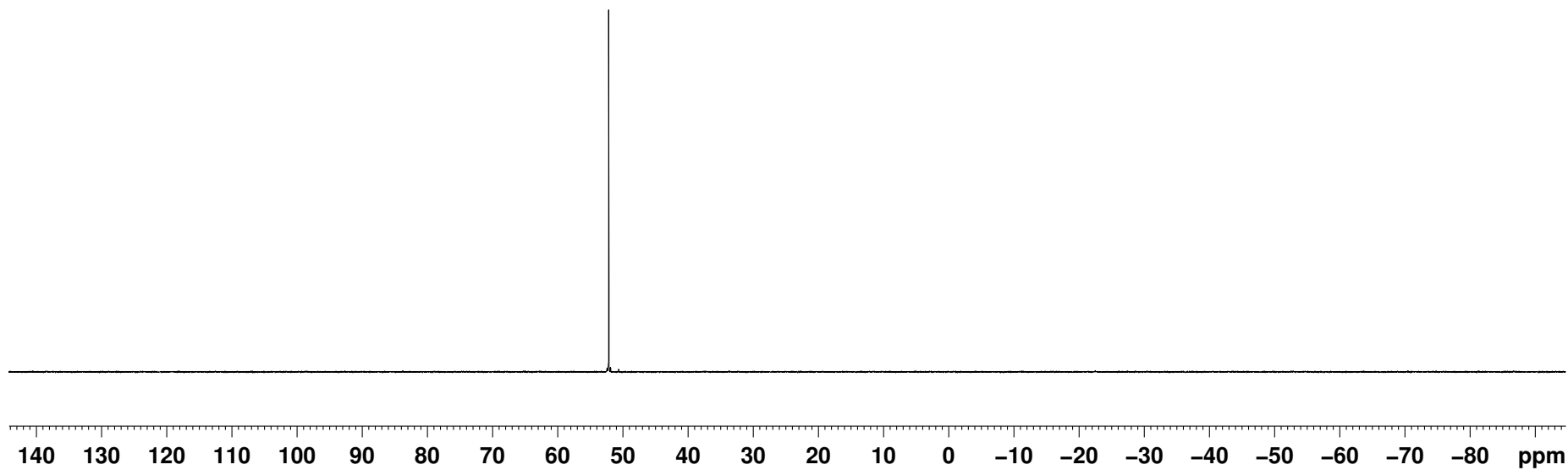
===== CHANNEL f1 =====
NUC1       1H
P1         11.80 usec
PL1        0.00 dB
PL1W       11.55467796 W
SFO1       300.1318534 MHz
SI         32768
SF         300.1299936 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

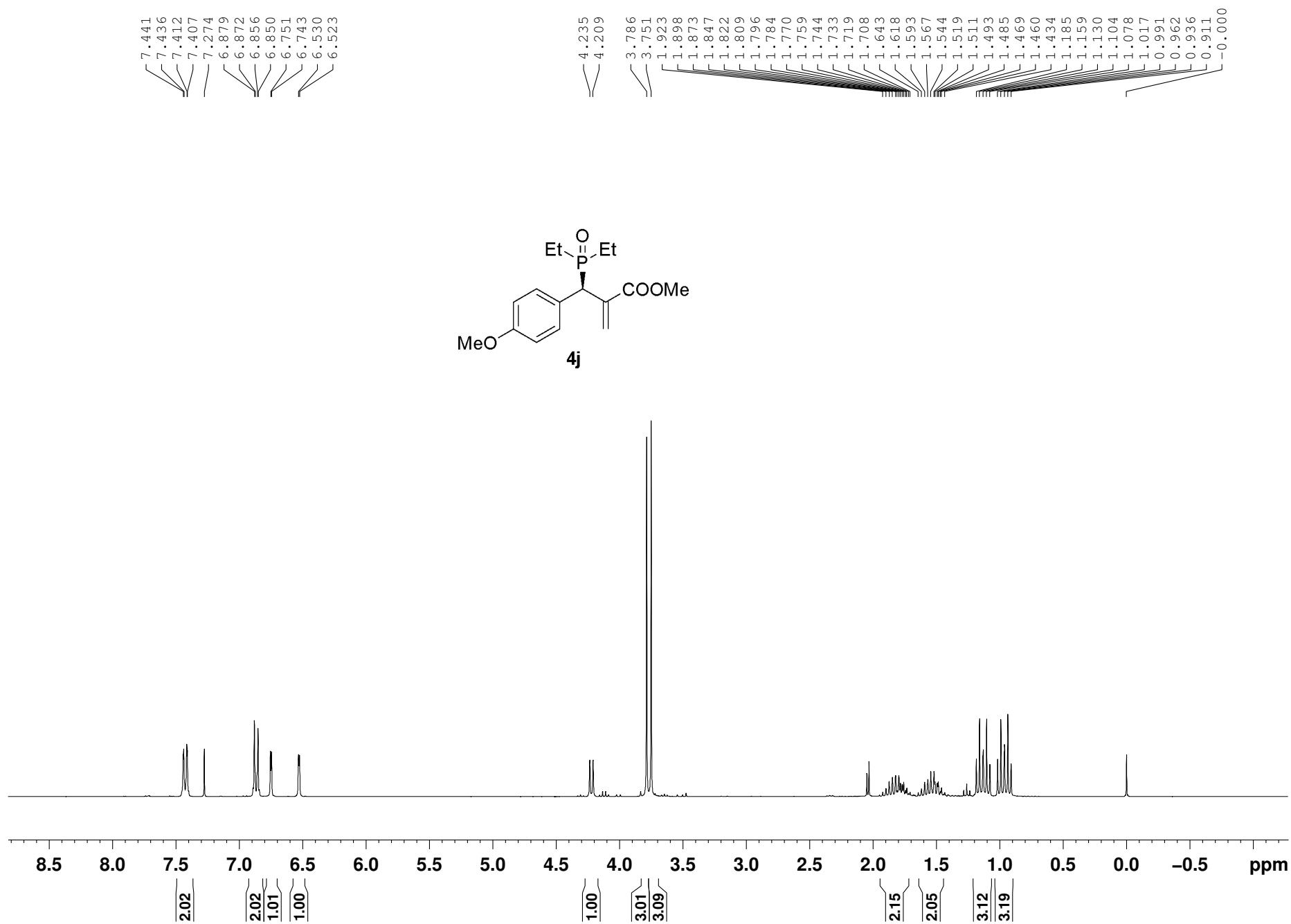
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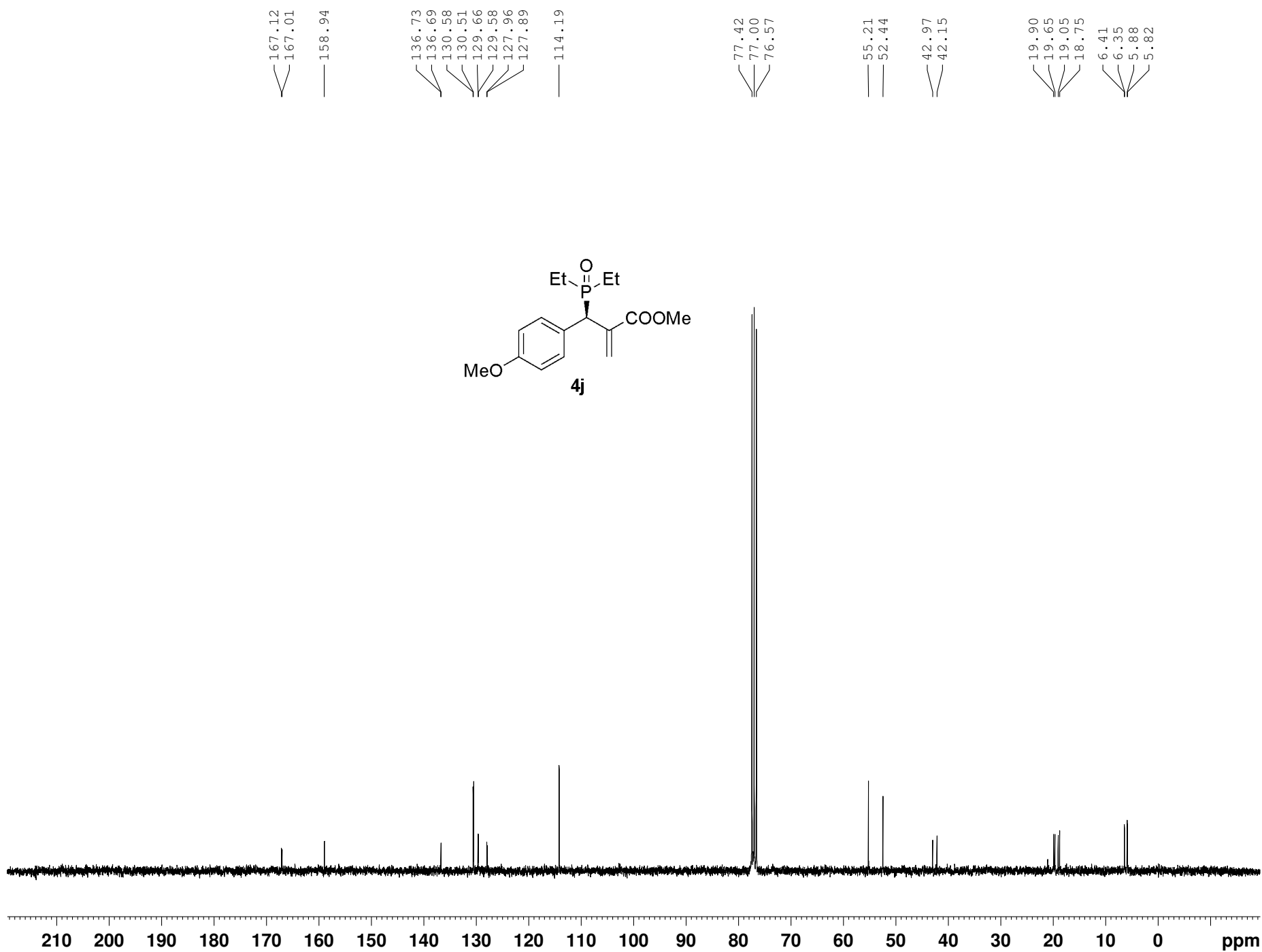
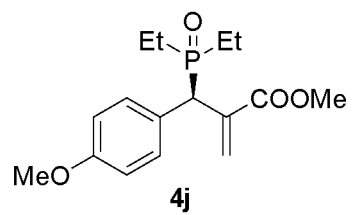


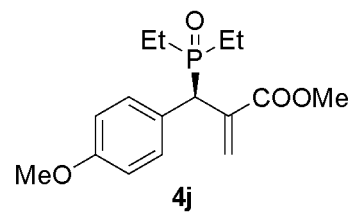


— 52.15

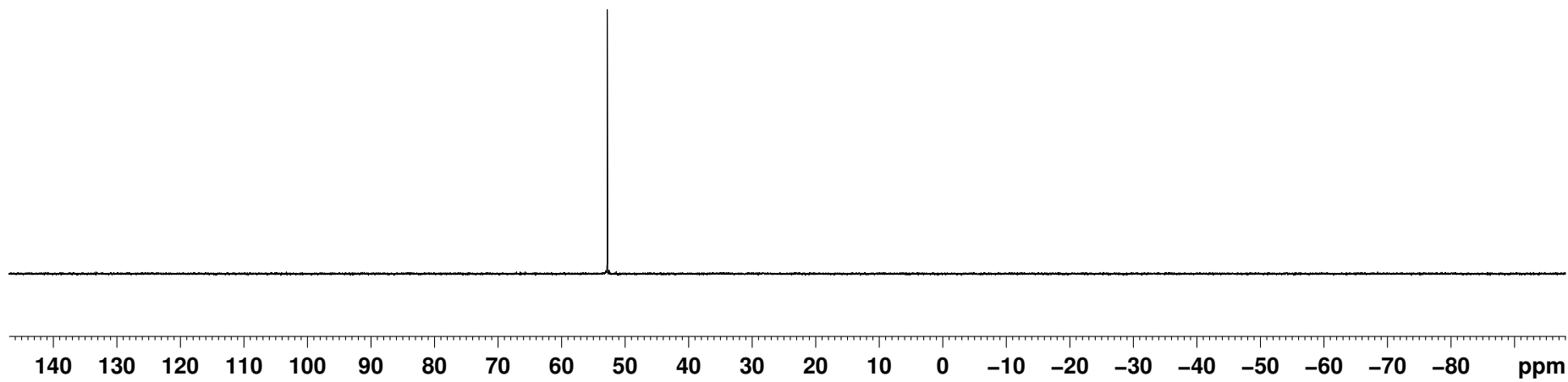


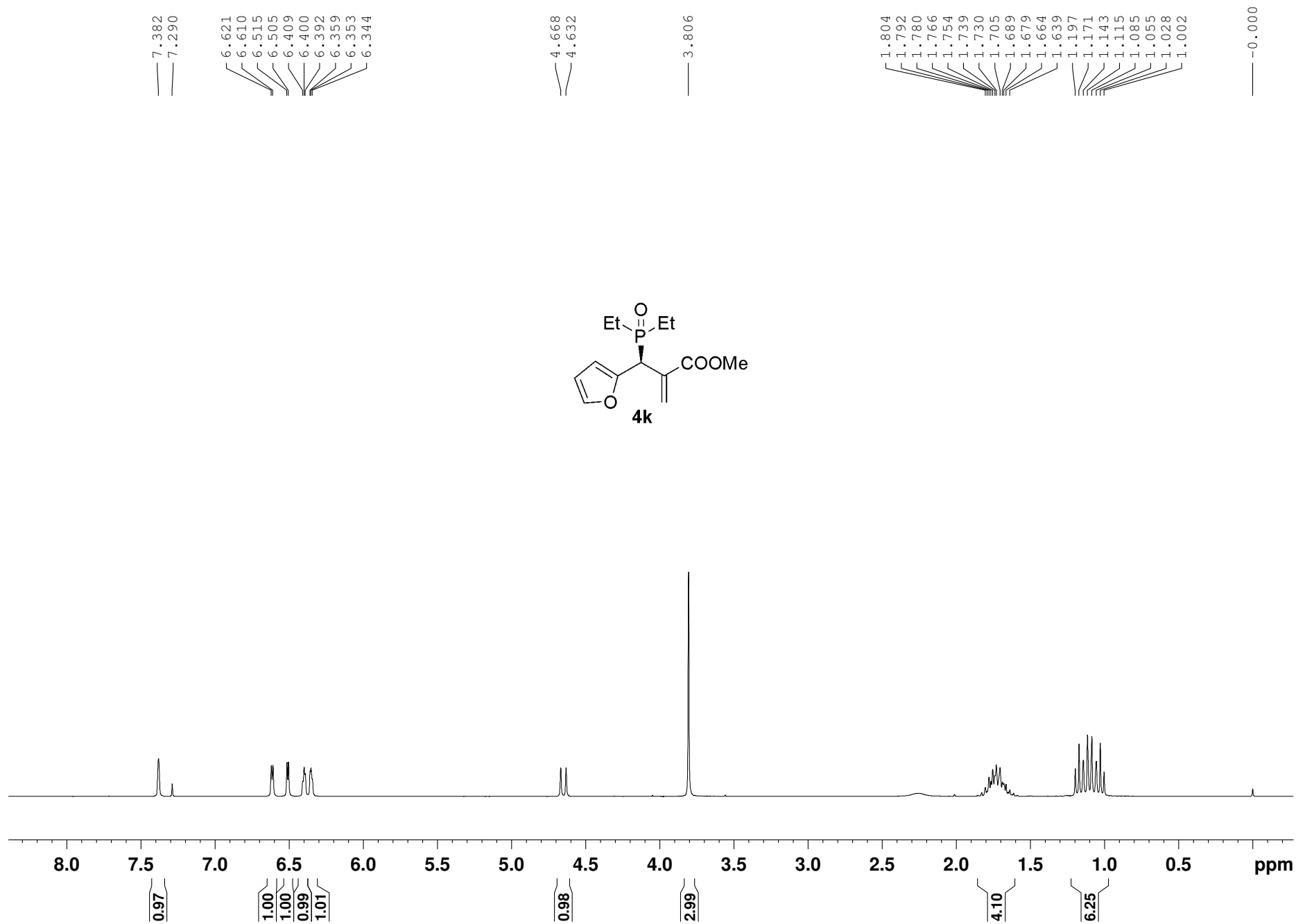


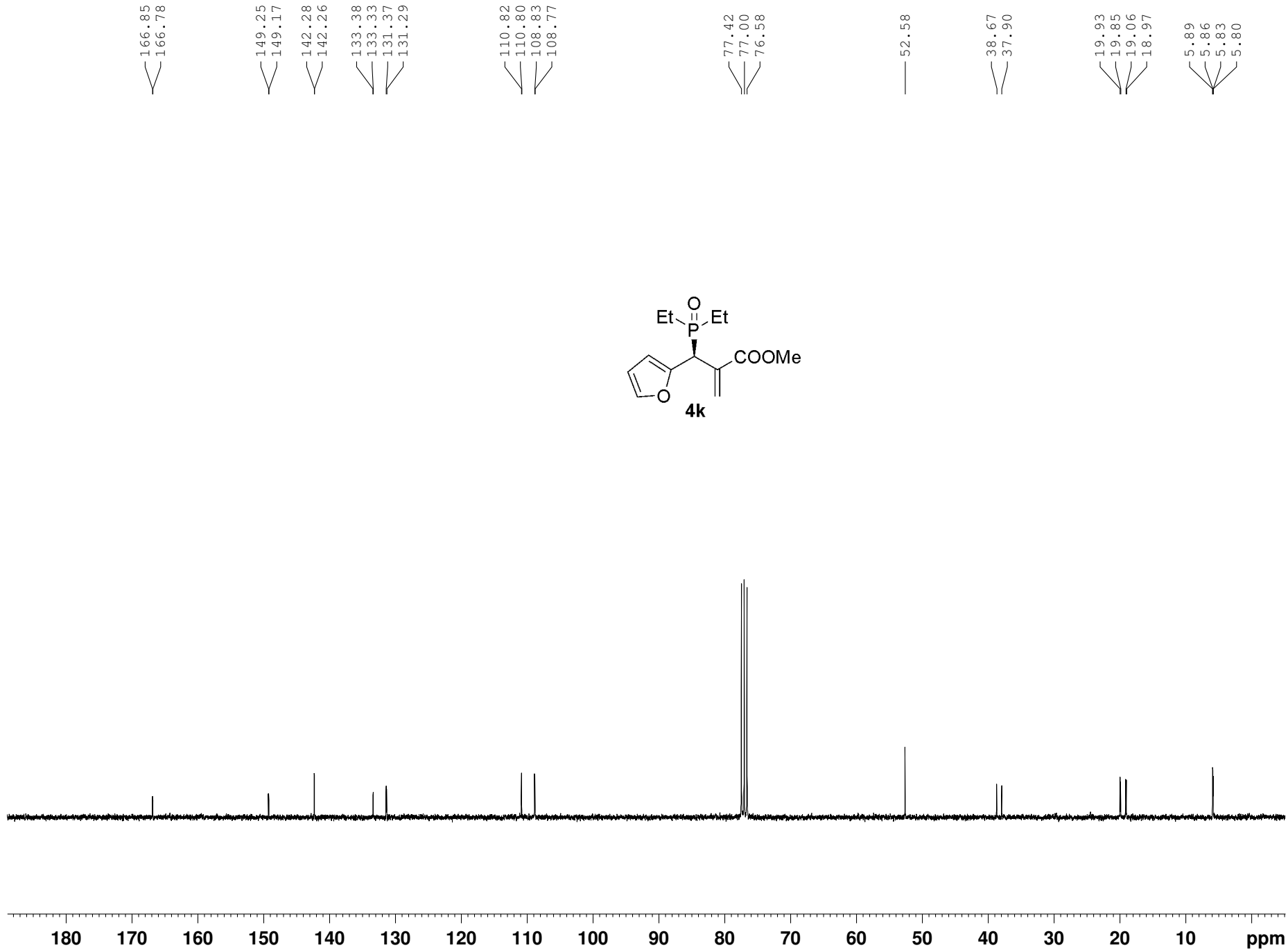


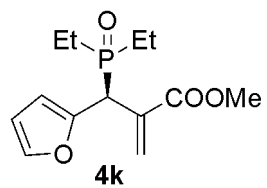


— 52.77

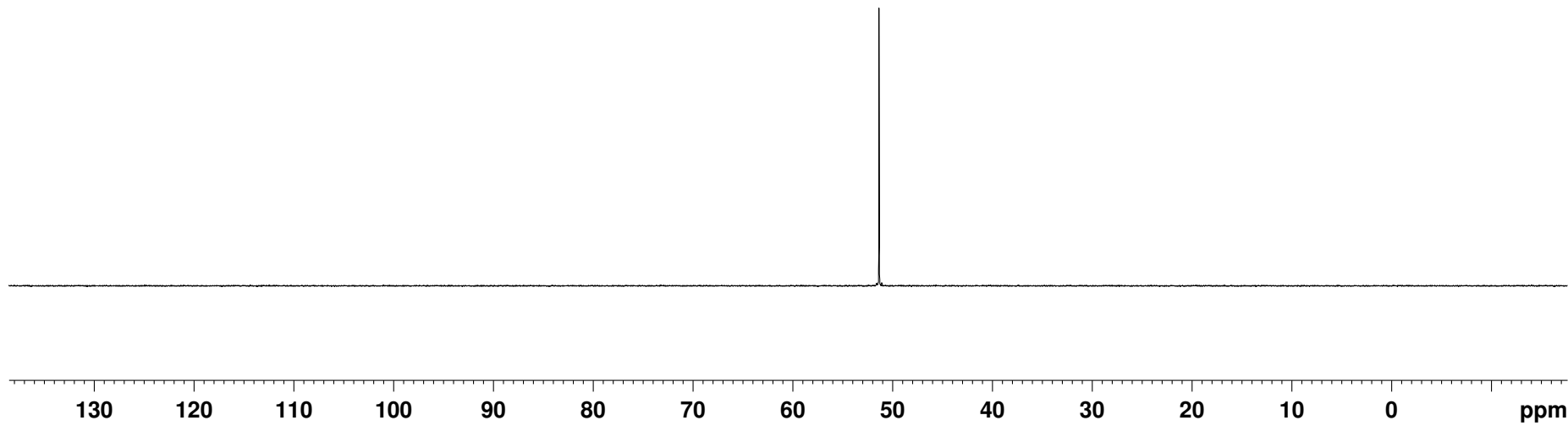


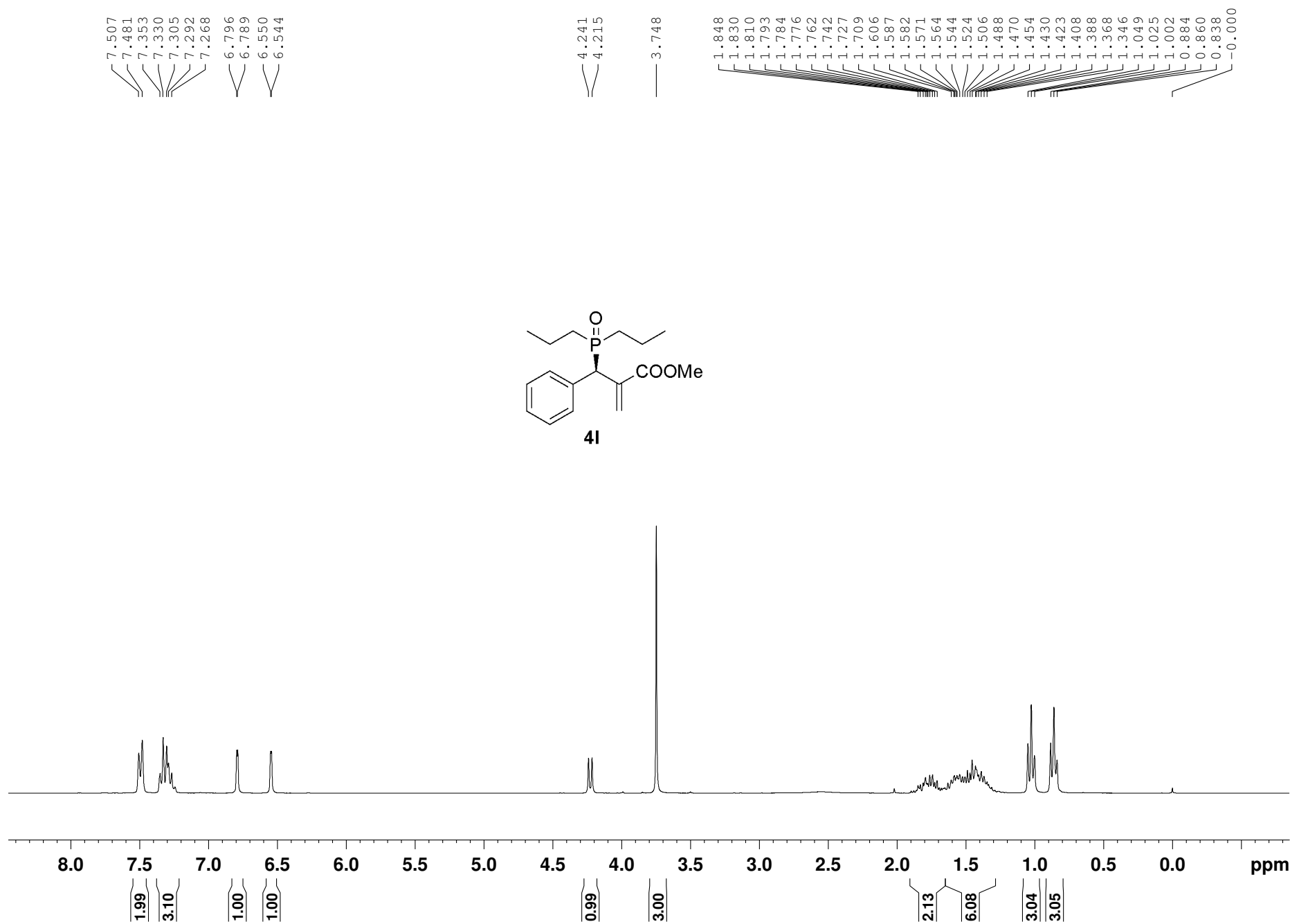


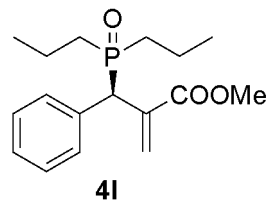
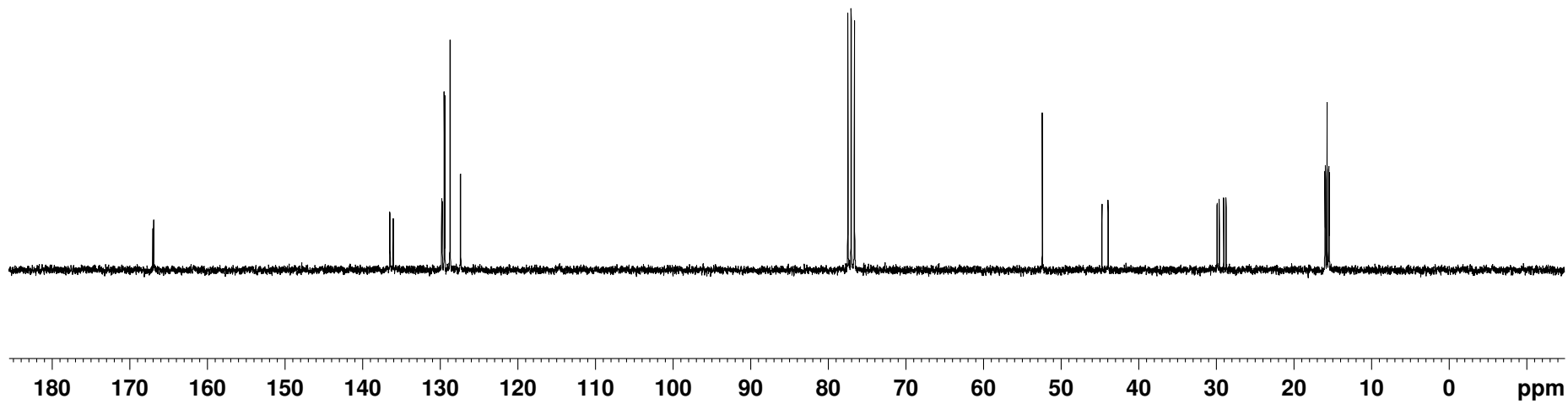




51.35







167.07
166.95

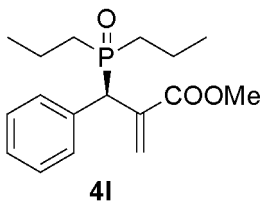
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76.66

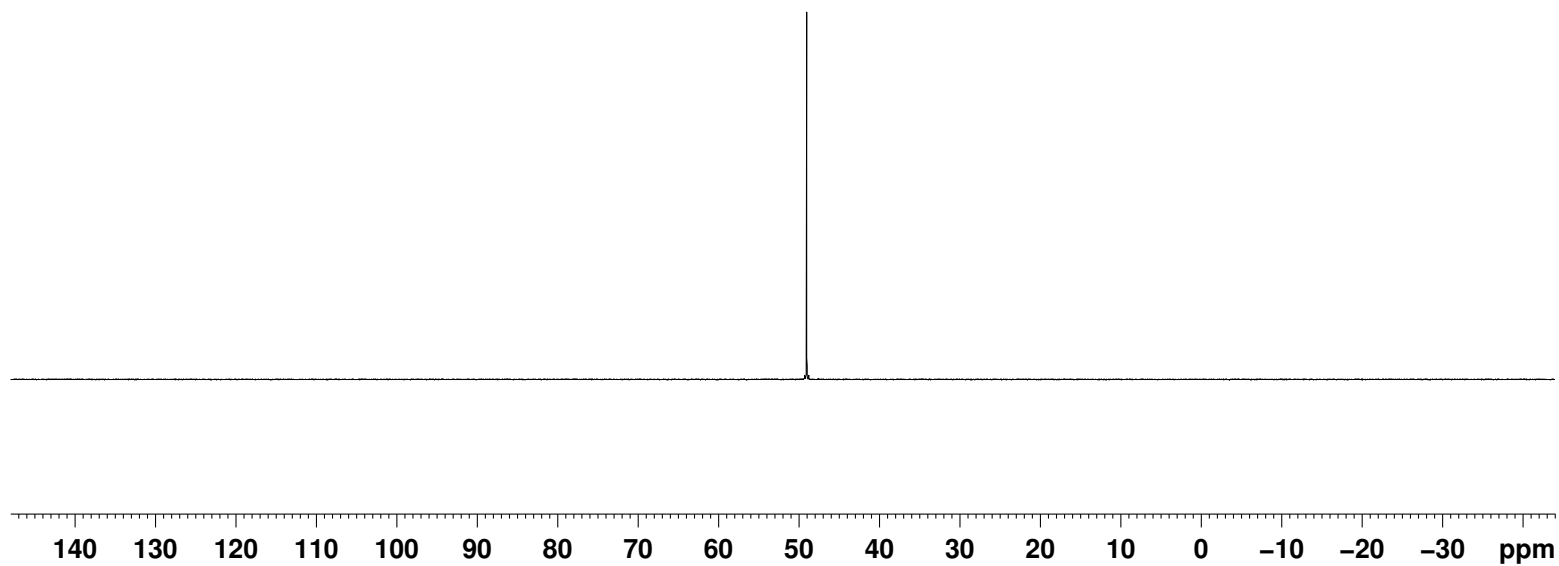
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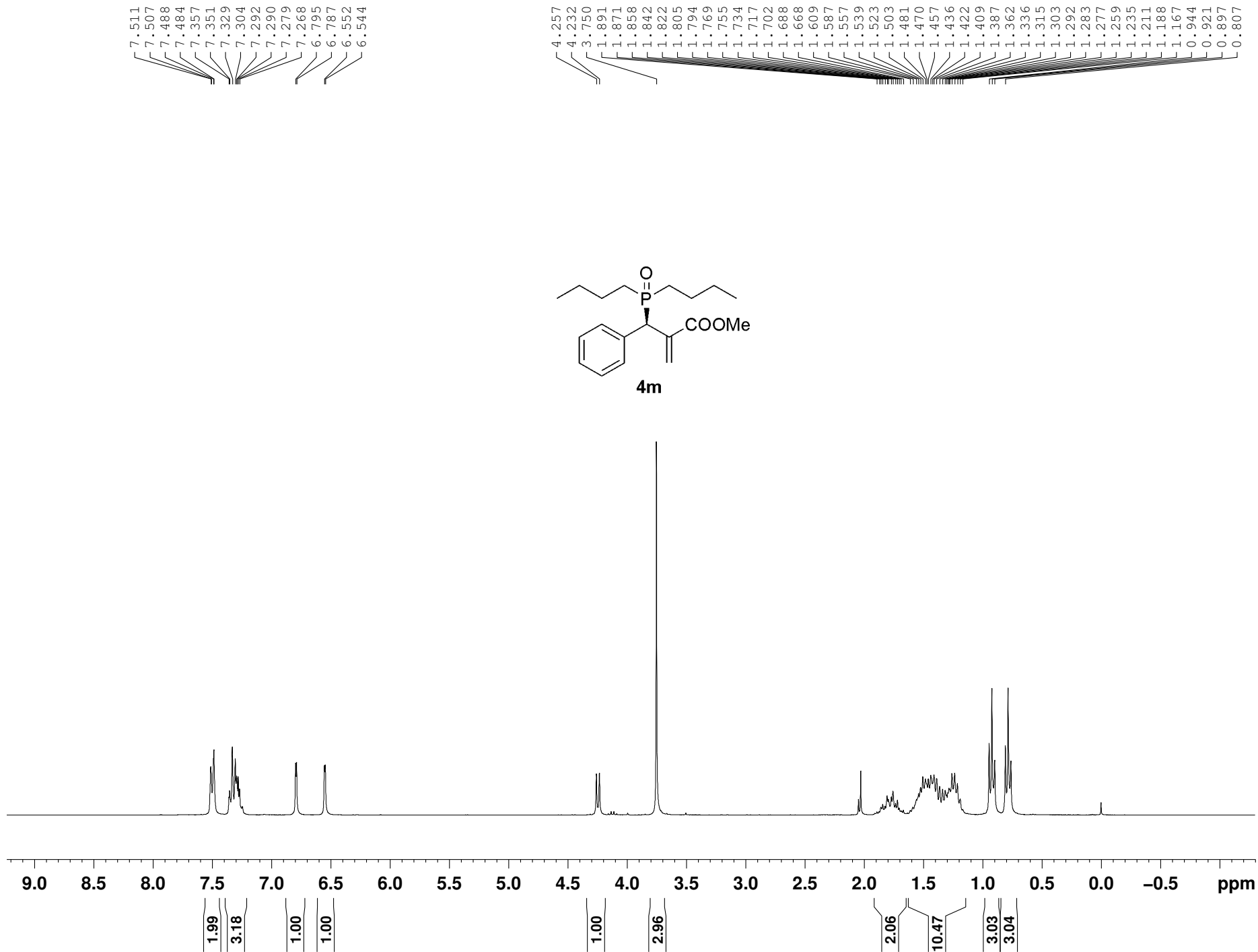
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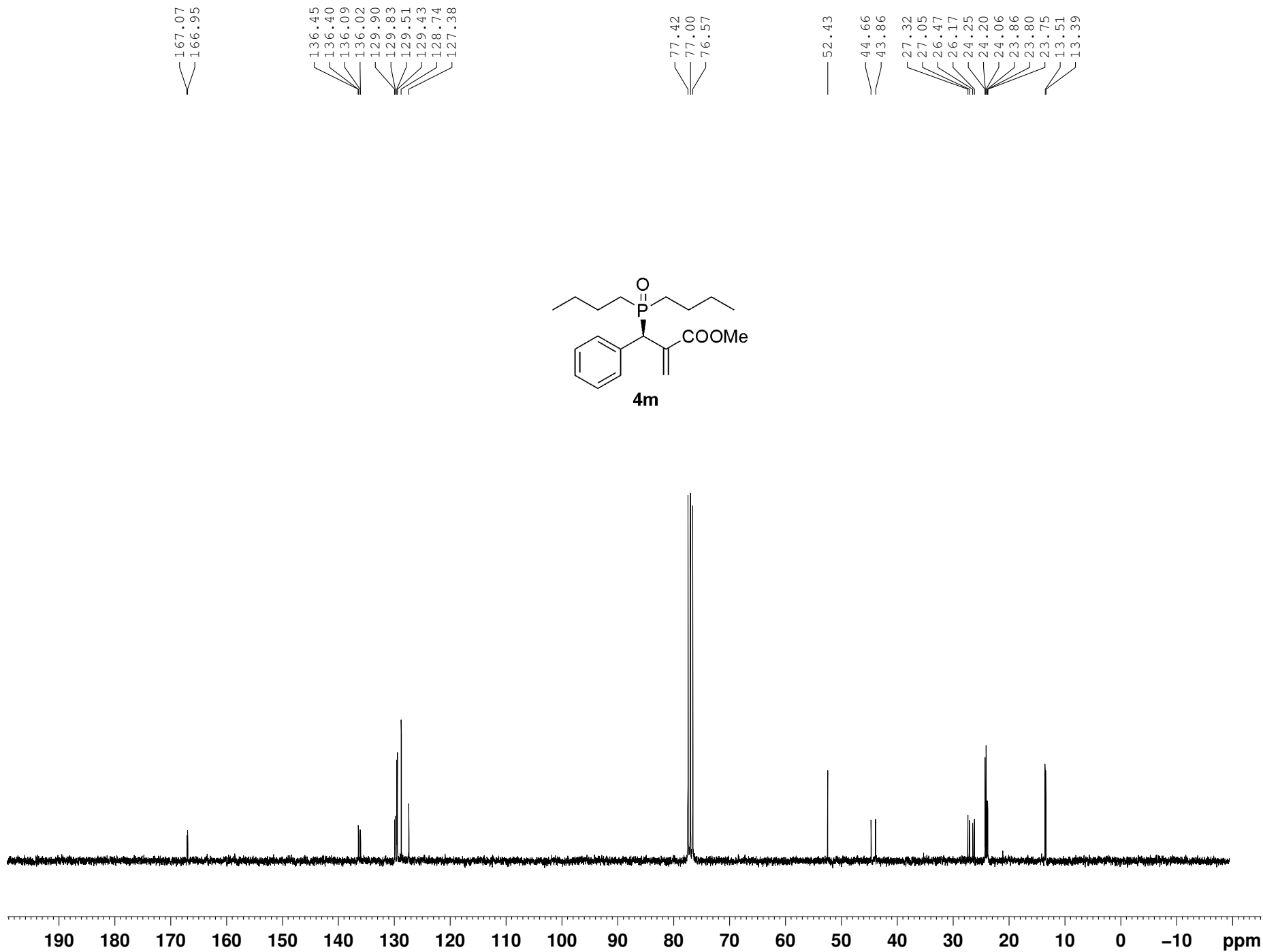
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15.53
15.48



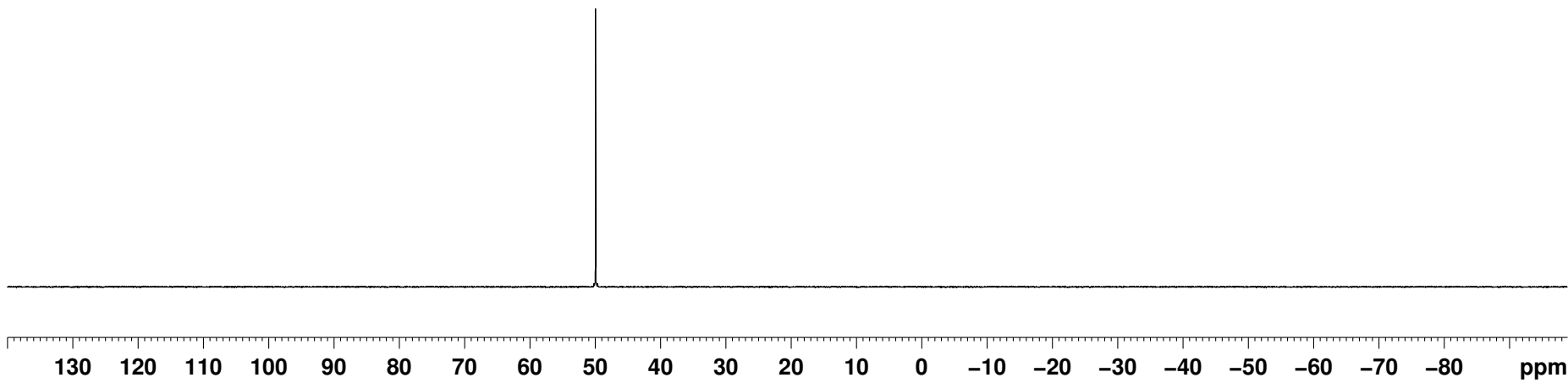
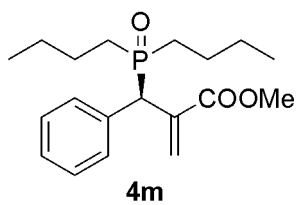
— 49.04

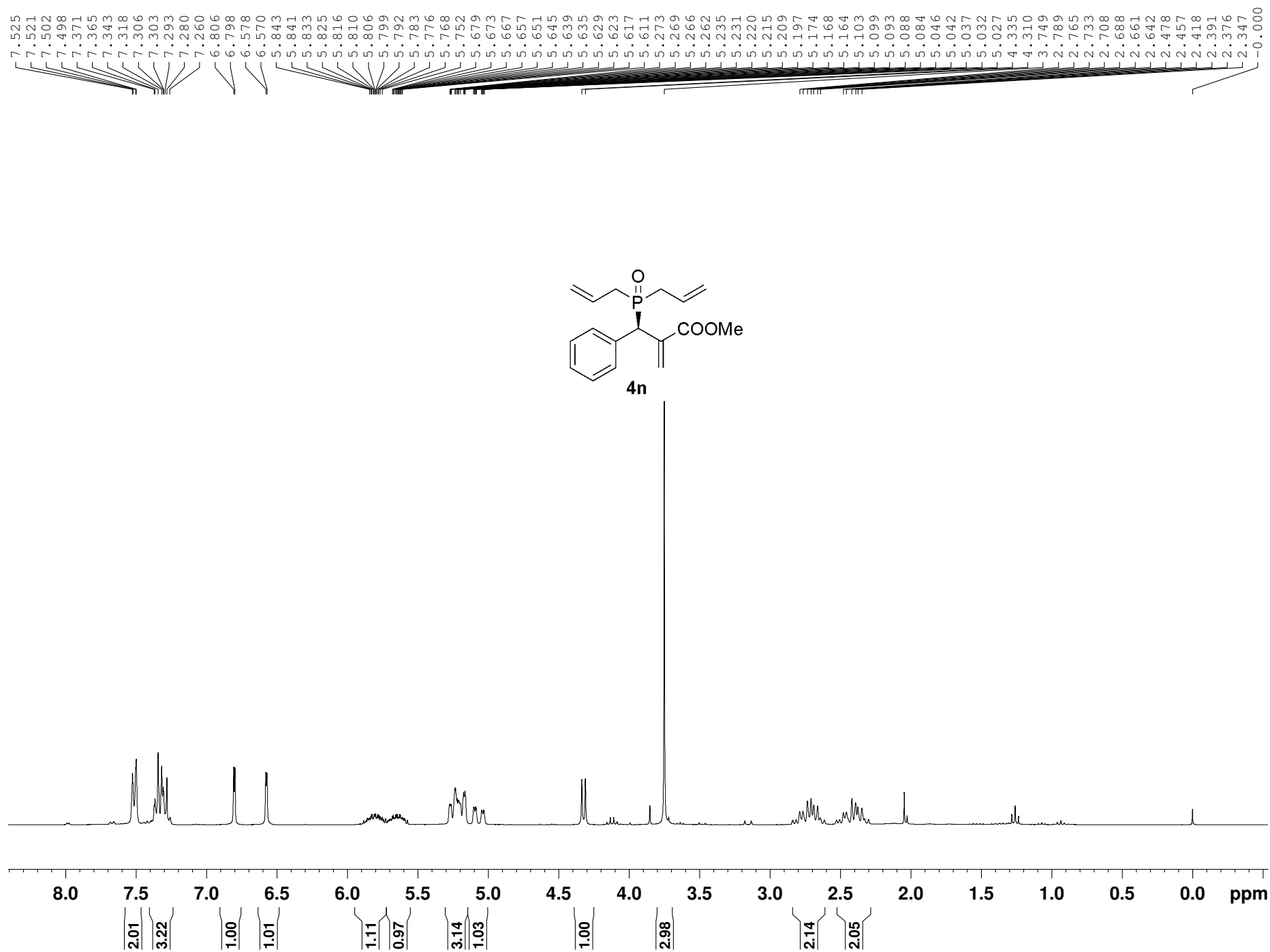


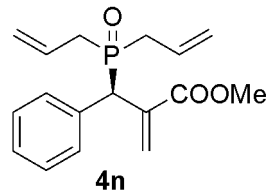
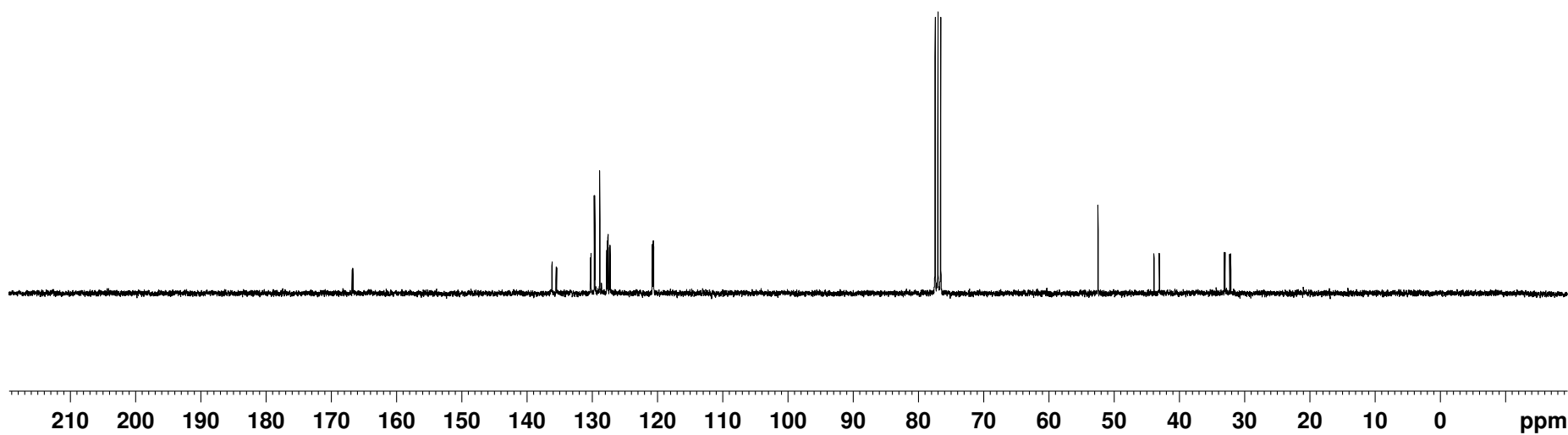




— 49.92







— 45.28

