Stereospecific Pd(O)-Catalyzed Malonate Additions to Allylic Hydroxy Phosphonate Derivatives: A Formal Synthesis of (-) Enterolactone

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Supporting Material

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General Experimental: ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded at 300, 75 and 121 MHz, repectively in $CDCl_3$. ^{1}H NMR spectra are referenced to internal tetramethylsilane (TMS, δ= 0.00) or $CHCl_3$ (7.27 ppm), ^{13}C NMR spectra to the center-line of $CDCl_3$ (77.23 ppm) and ^{31}P NMR spectra to external 85% H_3PO_4. Coupling constants, *J*, are reported in Hz. Enantiomer ratios were measured by chiral stationary-phase HPLC on a (*S,S*)-Whelk-O column, a ChiralPak

AS or AD column, or a Chirobiotic T column. Optical rotations were determined using a polarimeter set at 589 nm.

(±) Dimethyl [1-hydroxy-2-propenyl] phosphonate 1a. To a mixture of dimethyl phosphite (27.5 mL, 300 mmol) and acrolein (24 mL, 360 mmol) was added Et_3N (21 mL, 150 mmol). The reaction mixture was stirred overnight and then the excess acrolein and Et_3N were evaporated in vacuo to give hydroxy phosphonate **1a** in quantative yield. IR (neat) 3288 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.95 (1H, m), 5.47 (1H, m), 5.27 (1H, m), 4.88 (1H, brd S), 3.77 (6H, d, J_{HP} = 11 Hz); ^{13}C NMR ($CDCl_3$) δ 132.7 (d, J_{CP} = 3.4 Hz), 117.4 (d, J_{CP} = 12 Hz), 69.3 (d, J_{CP} = 160 Hz), 53.9 (d, J_{CP} = 7 Hz), 53.7 (d, J_{CP} = 7 Hz); ^{31}P NMR ($CDCl_3$) δ 24.5; HRMS (EI, M^+) calcd. for $C_5H_{12}O_4P$: 167.0473. Found 167.0476.

(1*R*) Dimethyl [1-hydroxy-2-propenyl] phosphonate (*R*)1a. To a solution of anhydrous dimethyl (L)-tartrate (3.24g, 18.2 mmol) in freshly distilled THF (140 mL) was added distilled $Ti(O\textit{i}Pr)_4$ (5.17 g, 18.2 mmol). The mixture was stirred at –15 °C for 30 minutes to insure complete complexation. Acrolein (5.1 g, 91 mmol) was added and the mixture was stirred for an additional 15 minutes. Dimethyl phosphite (20 g, 182 mmol) was added and the reaction mixture was placed in the freezer (approx. -15°C) overnight. The reaction mixture was removed from the freezer and chelex® (approx 57g) was added. The mixture was stirred at r.t. for 2 days. The chelex® was removed by filtration and washed several times with CH_2Cl_2. The filtrate was concentrated and placed on a vacuum line until all dimethyl phosphite had evaporated (^{31}P NMR). The crude product was purified by chromatography (SiO_2, EtOAc) to give the hydroxy phosphonate **1a** (11.8 g, 78%). The enantiomeric excess was determined by ^{31}P NMR spectroscopy (Karfarski's quinine method)[1] to be 70%.

Dimethyl [1-(methoxycarbonyloxy)-2-propenyl] phosphonate 3a. Hydroxy phosphonate **1a** (4.78 g, 28.8 mmol) was dissolved in anhydrous CH_2Cl_2 (40 mL) and the solution was cooled to 0^oC. Pyridine (3.7 mL, 43.2 mmol) and DMAP (0.049 g, 0.40 mmol) were added to the reaction, followed by the slow addition of methyl chloroformate (4.9 mL, 63.3 mmol). After addition of methyl chloroformate was complete, the reaction mixture was allowed to warm to room temperature and then it was stirred until the reaction was complete (TLC, 24hr). The reaction mixture was washed with H_2O (2x) and saturated $CuSO_4$ (2x), and then the organic layer was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo and the crude product was purified by chromatography (SiO_2, EtOAc, 100%) to give **3a** as a colorless oil (5.25 g, 81%). IR (neat) 1756.5 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.79 (1H, m), 5.36 (1H, m), 5.31 (1H, m), 5.24 (1H, m), 3.66 (3H, s), 3.65 (6H, d, J_{HP} = 12 Hz); ^{13}C NMR ($CDCl_3$) δ 154.5 (d, J_{CP} = 9.3 Hz), 128.7 (d, J_{CP} = 4.1 Hz), 119.5 (d, J_{CP} = 11 Hz), 72.7 (d, J_{CP} = 169 Hz) 55.2, 53.8 (d, J_{CP} = 6.9 Hz), 53.5 (d, J_{CP} = 6.5 Hz); ^{31}P NMR ($CDCl_3$) δ 19.5; HRMS(EI, M^+) calcd. for $C_7H_{13}O_6P$: 224.0450. Found 224.0444.

(1*R*) (2*E*) Dimethyl (1-hydroxy-3-phenyl-2-propenyl) phosphonate (*R*)1b.[2] To a solution of dimethyl (L)-tartrate (2.79 g, 15.25 mmol) in freshly distilled diethyl ether (130 mL) was added distilled $Ti(O\textit{i}Pr)_4$ (4.5 mL, 15.2 mmol). The mixture was stirred at –15 °C for 30 minutes to insure complete complexation. Cinnamaldehyde (9.54 mL, 76.2 mmol) was added and the mixture was stirred for an additional 15 minutes. Dimethyl phosphite (10.5 g, 114 mmol) was added and the reaction mixture was placed in the freezer (approx. -15°C). After the reaction was complete (TLC, SiO_2, EtOAc), the reaction mixture was quenched with deionized H_2O and extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4 and evaporated in vacuo to give crude product (15.6 g, 85% y, 70% e.e.). The crude product was dissolved in hot EtOAc

and cooled to give an initial crystalline fraction (5.2g, 28%) with an e.e. of 42%. The mother liquor (e.e. 89%) was decanted, concentrated and recooled to give an additional batch of crystals (5.6 g, 30%) with an e.e. of 98%. The remaining mother liquor was evaporated to dryness and purified by chromatography (SiO_2, EtOAc) to give a third batch of phosphonate (2.2 g, 12 %) with an e.e. of 79% (total yield 13g, 71%). ^{1}H NMR ($CDCl_3$) δ 7.40 (2H, m), 7.28 (3H, m), 6.80 (1H, ddd, J_{HH} = 15, 1.5 Hz, J_{HP} = 4.9 Hz), 6.35 (1H, ddd, J_{HH} = 16, 6.2 Hz, J_{HP} = 5.6 Hz), 4.73 (1H, ddd, J_{HH} = 6.2, 1.6 Hz, J_{HP} = 13 Hz), 3.85 (3H, d, J_{HP} = 10 Hz), 3.81 (3H, d, J_{HP} = 10 Hz); ^{13}C NMR ($CDCl_3$) δ 136.1 (d, J_{CP} = 2.9 Hz), 132.2 (d, J_{CP} = 13 Hz), 128.4, 127.8, 126.5, 123.5 (d, J_{CP} = 4.3 Hz), 69.2 (d, J_{CP} = 161 Hz), 53.9 (d, J_{CP} = 7.1 Hz), 53.7 (d, J_{CP} = 7.4 Hz); ^{31}P NMR ($CDCl_3$) δ 23.8.

(2*E*) Dimethyl [1-(methoxycarbonyloxy)-3-phenyl-2-propenyl] phosphonate 3b. Hydroxy phosphonate **1b** (2.0 g, 8.26 mmol) was dissolved in anhydrous CH_2Cl_2 (30 mL) and the solution was cooled to 0^{o}C. Pyridine (1 mL, 12.4 mmol) and DMAP (0.014 g, 0.11 mmol) were added, followed by the slow addition of methyl chloroformate (1.3 mL, 16.5 mmol). After addition of methyl chloroformate was complete, the reaction mixture was allowed to warm to room temperature and then it was stirred until the reaction was complete (TLC). The reaction mixture was washed with H_2O (2x) and saturated $CuSO_4$ (2x), then the organic layer was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo and the crude product was purified by chromatography (SiO_2, EtOAc, 100%) to give phosphonate **3b** as a colorless oil (2.35 g, 95%). IR (neat) 1755.1 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.21 (2H, m), 7.09 (3H, m), 6.59 (1H, app. dd, J_{HH} = 16 Hz, J_{HP} = 4.0 Hz), 6.04 (1H, m), 5.45 (1H, ddd, J_{HH} = 1.2, 7.4 Hz, J_{HP} = 14 Hz), 3.61 (6H, d, J_{HP} = 11 Hz), 3.62 (3H, s); ^{13}C NMR ($CDCl_3$) δ 154.9 (d, J_{CP} = 9.7 Hz), 135.8 (d, J_{CP} = 12 Hz),

135.7 (d, J_{CP} = 2.2 Hz), 128.8, 127.1 (d, J_{CP} = 1.4 Hz), 119.5 (d, J_{CP} = 4.4 Hz), 73.3 (d, J_{CP} = 170 Hz), 55.6, 54.2 (d, J_{CP} = 7.0 Hz), 54.0 (d, J_{CP} = 6.4 Hz); ^{31}P NMR ($CDCl_3$) δ19.6.

3-(3-methoxyphenyl)propene 6. To 3-methoxyphenylmagnesium bromide (30 mL, 1.0M solution in THF) was added allyl bromide (5.2 mL, 60 mmol) slowly. The reaction was stirred at room temperature for 24h. The reaction mixture was partitioned between Et_2O and saturated NH_4Cl. After separation, the aqueous layer was re-extracted with Et_2O, and the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified by chromatography (SiO_2, hexane) to give 3-(3-methoxyphenyl)propene **6** as a colorless liquid (4.4 g, 97% yield); ^{1}H NMR ($CDCl_3$) δ 7.25 (1H, m), 6.80 (3H, m), 6.01 (1H, m), 5.13 (2H, m), 3.83 (3H, s), 3.41 (2H, d, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$) δ 159.9, 141.9, 137.4, 129.5, 121.2, 116.1, 114.5, 111.6, 55.3, 40.4.

(1*R*) (2*E*) Dimethyl [1-(methoxycarbonyloxy)-4-(3-methoxyphenyl)-2-butenyl]phosphonate 3d from Phosphonate 1b. 2nd generation Grubbs catalyst (0.211 g, 0.249 mmol) was dissolved in CH_2Cl_2 (23 mL). Phosphonate **1b** (2.35 g, 9.69 mmol) and 3-(3-methoxyphenyl)propene **6** (2.49 g, 16.8 mmol) were added and the reaction flask was placed in a pre-heated oil bath and heated at 40^{o}C for 12h. The reaction mixture was allowed to cool and then the solvent was evaporated in vacuo. The crude product was purified by chromatography (SiO_2, CH_2Cl_2:EtOAc, 20:80) to give a mixture of phosphonate **1b** and dimethyl [1-hydroxy-4-(3-methoxyphenyl)-2-butenyl]phosphonate **3d** as a pale yellow oil (1.96 g). The isolated mixture was cycled through the metathesis reaction three more times to give dimethyl [1-hydroxy-4-(3-methoxyphenyl)-2-butenyl]phosphonate **3d** (1.0 g, 36%). ^{31}P NMR ($CDCl_3$) δ 24.5. The hydroxy phosphonate **1d** (1.0 g, 3.49 mmol) was dissolved in anhydrous CH_2Cl_2 (15 mL) and the solution was cooled to 0^{o}C. Pyridine (0.45 mL, 5.24 mmol) and DMAP (0.006 g, 0.04 mmol)

were added to the reaction, followed by the slow addition of methyl chloroformate (0.7 mL, 8.47 mmol). After addition of methyl chloroformate was complete, the reaction mixture was allowed to warm to room temperature and then it was stirred until the reaction was complete (TLC, 24hr). The reaction mixture was washed with H_2O (2x) and saturated $CuSO_4$ (2x), and then the organic layer was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo and the crude product was purified by chromatography (SiO_2, EtOAc, 100%) to give **3d** as a colorless oil (1.14 g, 95%).

A General Procedure for the Addition of Malonates to Allylic Carbonates 3b-d. NaH (3.47 mmol) was suspended in anhydrous THF (16 mL) and then the malonate (3.47 mmol) in THF (1 mL) was added. The mixture was stirred at room temperature for 3-4 minutes. The phosphonate (2.9 mmol) was added, followed by $Pd(PPh_3)_4$ (0.09 mmol, 3 mol%). The reaction flask was placed in a pre-heated oil bath and heated at 70^{o}C for 1h. The reaction mixture was allowed to cool, and then it was partitioned between brine and Et_2O. After separation, the aqueous layer was re-extracted with Et_2O and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo to give the crude product.

Addition of Dimethyl Malonate 10a to (1*R*) (2*E*) Dimethyl [1-(methoxycarbonyloxy)-3-phenyl-2-propenyl] phosphonate 3b. NaH (0.056 g, 1.4 mmol), THF (10mL), phosphonate **3b** (0.28 g, 0.93 mmol), malonate **10a** (0.16 mL, 1.4 mmol) and $Pd(PPh_3)_4$ (0.032 g, 0.028 mmol). The crude compound was purified by chromatography (SiO_2, EtOAc:hexanes, 2:1) to give the *E*-isomer **11a(*E*)** as a pale yellow oil (0.249 g, 75%). IR (neat) 1737.5 cm^{-1}; ^{1}HNMR ($CDCl_3$) δ 7.20 (5H, m), 6.83 (1H, ddd, J_{HH} = 7.7, 17 Hz, J_{HP} = 25 Hz), 5.59 (1H, ddd, J_{HH} = 1.2, 17 Hz, J_{HP} = 19 Hz), 4.17 (1H, m), 3.82 (1H, d, J_{HH} = 11 Hz), 3.68 (3H, s), 3.62 (3H, d, J_{HP} = 11 Hz), 3.58 (3H, d, J_{HP} = 11 Hz), 3.42 (3H, s); ^{13}C NMR ($CDCl_3$) δ 167.9, 167.4, 152.2 (d, J_{CP} = 5.4 Hz),

137.9, 129.1, 128.4, 128.0, 118.1 (d, J_{CP} = 186 Hz), 56.8, 53.0, 52.81, 52.6 (d, J_{CP} = 5.7 Hz), 49.9 (d, J_{CP} = 22 Hz); ^{31}P NMR ($CDCl_3$) δ 20.7; HRMS (EI, M^+) calcd. for $C_{16}H_{21}O_7P$: 356.1025. Found 356.1021, and a small amount of the *Z*-isomer contaminated with Ph_3PO (0.0453g, 13%) ^{1}H NMR 7.25 (5H, m), 6.69 (1H, ddd, J_{HH} = 10, 13 Hz, J_{HP} = 49 Hz), 5.55 (1H, dd, J_{HH} = 13 Hz, J_{HP} = 17 Hz), 5.11 (1H, app. t, J_{HH} = 10 Hz), 3.81 (1H, d, J_{HH} = 10 Hz), 3.65 (3H, s), 3.64 (3H, d, J_{HP} = 11 Hz), 3.54 (3H, d, J_{HP} = 11 Hz), 3.47 (3H, s); ^{31}P NMR 18.9.

Addition of Dimethyl 2-(3-methoxyphenyl) Malonate 10b to (1*R*) (2*E*) Dimethyl [1-(methoxycarbonyloxy)-3-phenyl-2-propenyl] phosphonate 3b. NaH (0.038 g, 1.59 mmol) in THF (8 mL), malonate **10b** (0.0.4 g, 1.59 mmol) in THF (1 mL), phosphonate **3b** (0.24 g, 0.79 mmol), and $Pd(PPh_3)_4$ (0.018 g, 0.016 mmol) gave the malonate adduct **11b** as a colorless oil (0.17 g, 45%). ^{1}H NMR δ 7.30 (3H, m), 7.22 (1H, m), 7.08 (3H, m), 6.71 (1H, m), 6.60 (2H, m), 5.37 (1H, ddd, *J* = 1.2, 17, 20 Hz), 4.21 (1H, m), 3.72 (3H, s), 3.70 (3H, s), 6.63 (3H, d, *J* = 11 Hz), 3.62 (3H, d, *J* = 11 Hz), 3.52 (3H, s), 314, (1H, d, *J* = 14 Hz), 2.89 (1H, d *J* = 14 Hz); ^{13}C NMR δ 170.1, 159.3, 153.7 (d, J_{CP} = 6.6 Hz), 137.3, 136.6, 129.6, 128.5, 128.7, 127.9, 122.5, 117.1 (d, J_{CP} = 186 Hz), 115.9, 112.6, 63.5, 55.0, 54.9, 54.7, 52.1, 40.4.

Attempted Addition of tert-Butyl Methyl 2-(3-methoxyphenyl) Malonate 10c to Dimethyl [1-(methoxycarbonyloxy)-4-(3-methoxyphenyl)-2-butenyl]phosphonate 3d. NaH (0.0275 g, 0.696 mmol) in THF (9 mL), malonate **10c** (0.256 mL, 0.87 mmol), phosphonate **3d** (0.2 g, 0.58 mmol), and $Pd(PPh_3)_4$ (0.047 g, 0.041 mmol). The crude product was purified by chromatography (SiO_2, hexane:acetone, 50:50) to give the diene **12** contaminated with Ph_3PO as a yellow oil (38%) ^{1}HNMR ($CDCl_3$) δ 7.26 (1H, t, J_{HH} = 8 Hz), 7.17 (1H, m), 7.06 (2H, m), 6.89 (2H, m), 6.82 (1H, m) 5.90 (1H, dd, J_{HH} = 16 Hz, J_{HP} = 19 Hz,), 3.82 (3H, s), 3.67 (6H, d, J_{HP} = 11 Hz); ^{13}C NMR ($CDCl_3$) δ 161.2, 149.6 (d, J_{CP} = 6.0 Hz), 140.4, 138.6, 130.8, 128.7 (d, J_{CP} =

27 Hz), 120.8, 117.8 (d, J_{CP} = 188 Hz), 115.8, 113.0, 55.7, 52.5 (d, J_{CP} = 5.4 Hz); ^{31}P NMR ($CDCl_3$) δ 21.3; HRMS (EI, M^+) calcd. for $C_{13}H_{17}O_4P$: 268.0865. Found 268.0867.

Addition of tert-Butyl Methyl 2-(3-methoxyphenyl) Malonate 10c to (2*E*) Dimethyl [1-(methoxycarbonyloxy)-2-butenyl] phosphonate 3c. NaH (0.0389 g, 0.973 mmol) in THF (10 mL), malonate **10c** (0.38 g, 1.3 mmol), phosphonate **3c** (0.144 g, 0.65 mmol),[3] and $Pd(PPh_3)_4$ (0.022 g, 0.019 mmol). The crude product was purified by chromatography (SiO_2, hexane:acetone, 50:50) to give a diastereoisomeric mixture (50:50) of malonate adducts **11c** contanimated with Ph_3PO (0.07 g, 24 %) IR (neat) 1719 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.16 (1H, t, J_{HH} = 7.5 Hz), 6.90 (1H, m), 6.75(3H, m), 5.64 (1H, m), 3.77 (3H, s), 3.69 (9H, m), 3.20 (2H, m), 2.99 (1H, m), 1.42 (4.5H, s), 1.41 (4.5H, s), 1.17 (3H, m); ^{13}C NMR ($CDCl_3$) δ 170.8, 170.7, 168.7, 168.6, 159.6, 155.3 (d, J_{CP} = 5.5 Hz), 154.7 (d, J_{CP} = 5.2 Hz), 137.8, 129.3, 129.2, 122.8, 122.7, 117.1 (d, J_{CP} = 187 Hz), 116.5 (d, J_{CP} = 187 Hz), 116.2, 116.15, 112.6, 112.5, 82.8, 82.7, 62.9, 62.9, 55.3, 52.5 (m), 52.1, 52.0, 41.8 (d, J_{CP} = 22 Hz), 41.2 (d, J_{CP} = 22 Hz), 39.8, 39.5, 28.1, 16.1 (d, J_{CP} = 1.3 Hz), 15.4 (d, J_{CP} = 0.9 Hz); ^{31}P NMR ($CDCl_3$) δ 21.8, 21.5; HRMS (EI, M^+) calcd. for $C_{22}H_{33}O_8P$: 456.1913. Found 456.1907.

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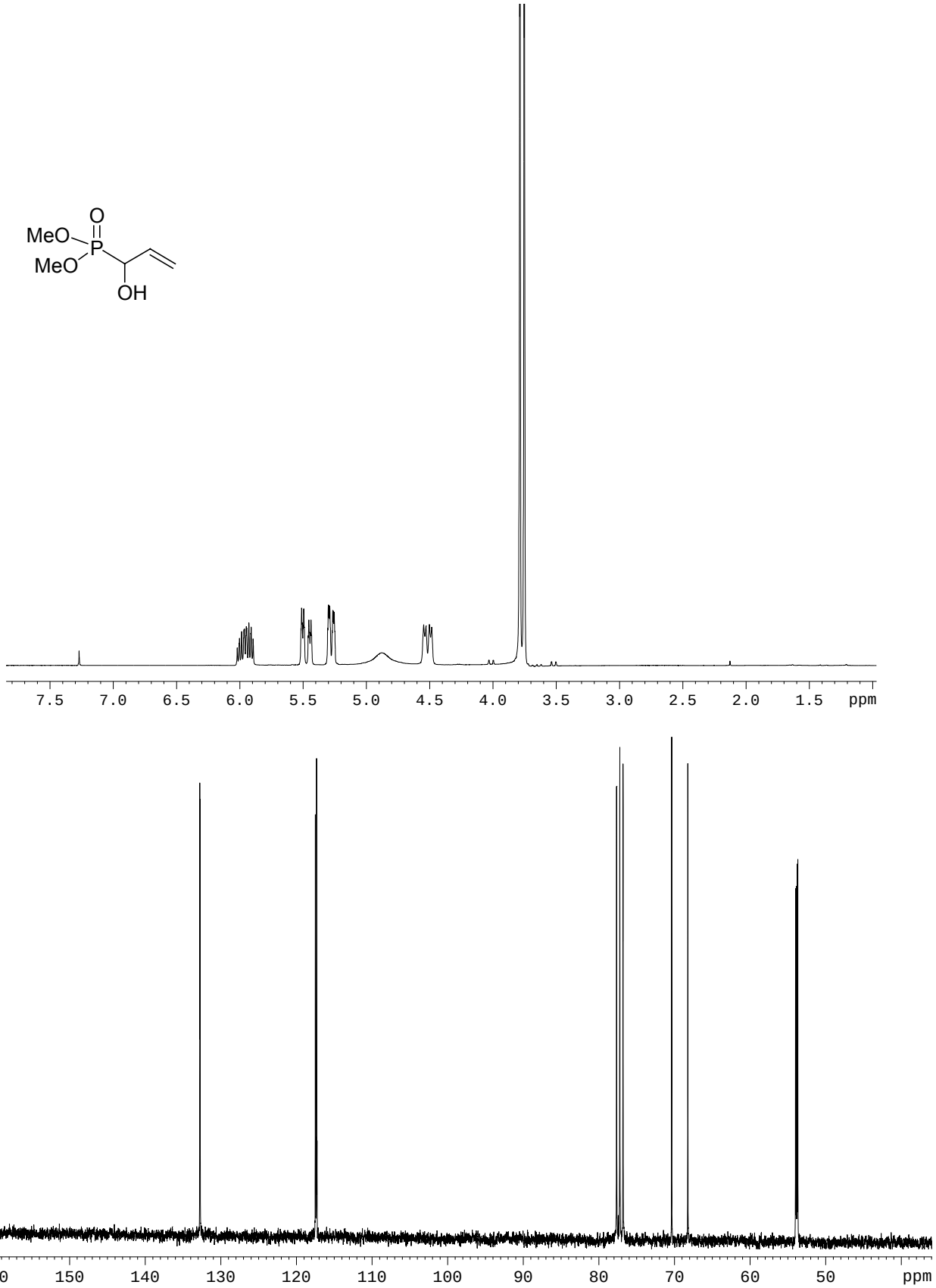
2. Rowe, B. J.; Spilling, C. D. *Tetrahedron: Asymmetry* **2001**, *12*, 1701; Blazis, V. J.; Koeller, K. J.; Spilling, C. D. *J. Org. Chem.* **1995**, *60*, 931.
3. Rowe, B. J.; Spilling, C. D. *J. Org. Chem.* **2003**, *68*, 9502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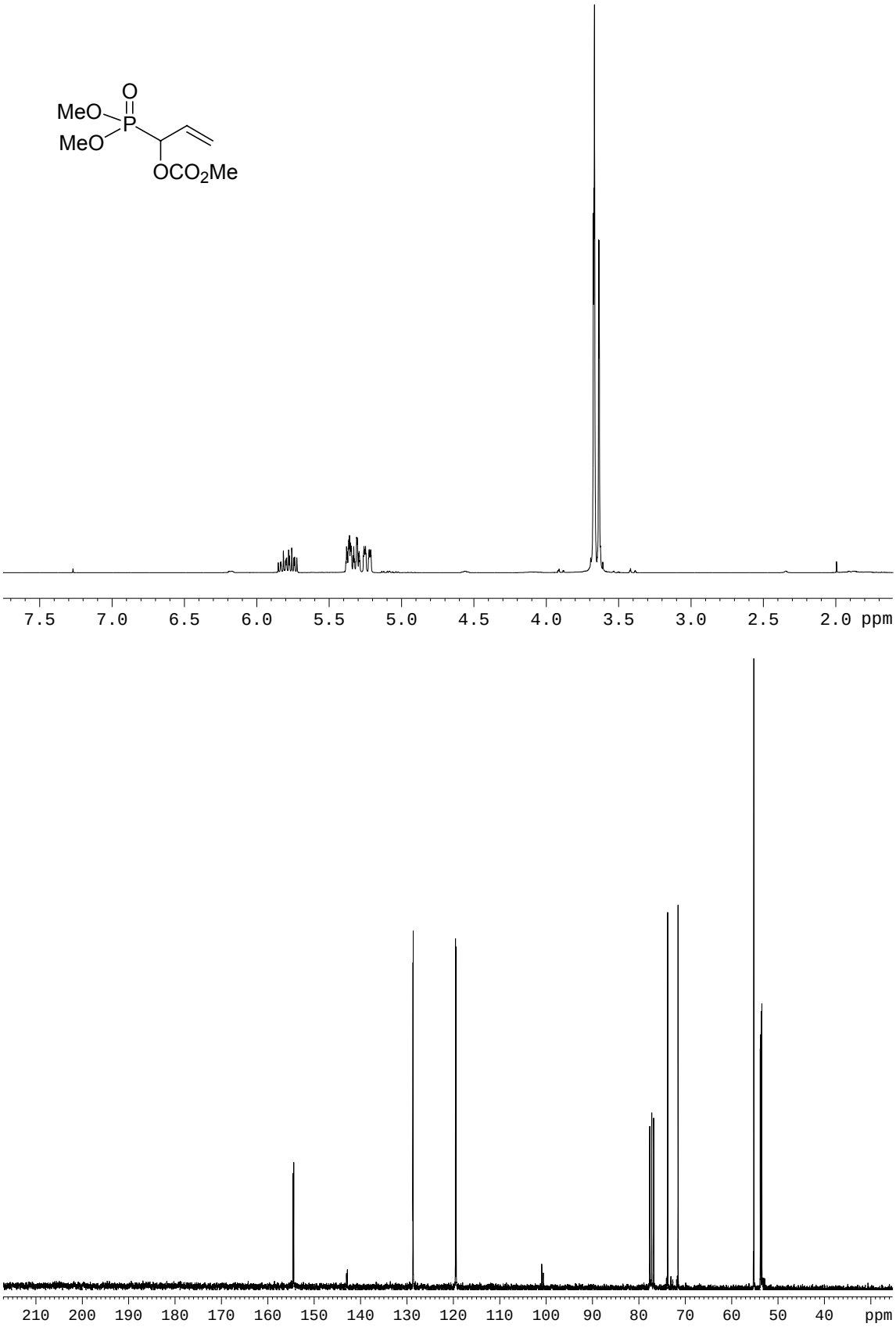
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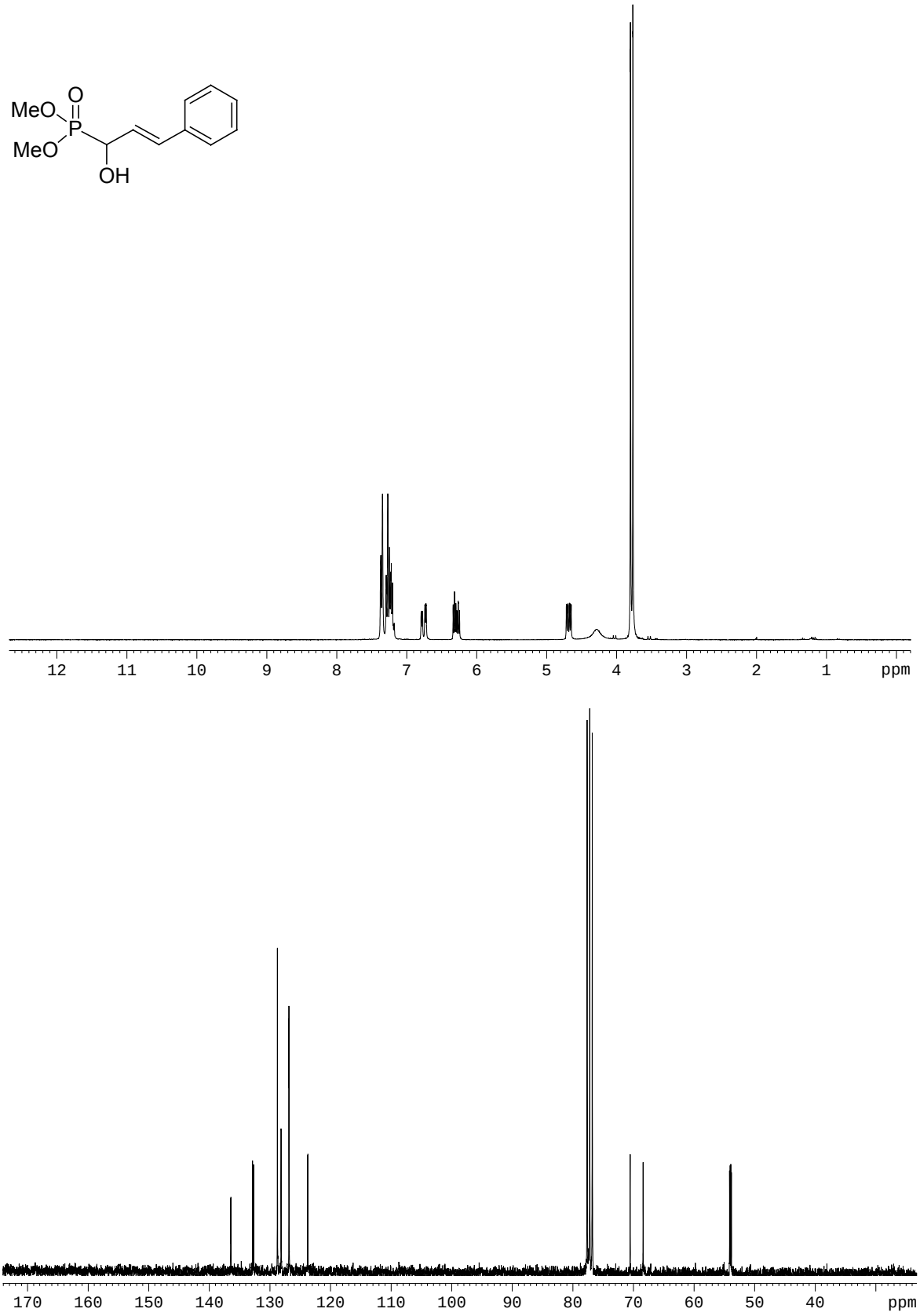
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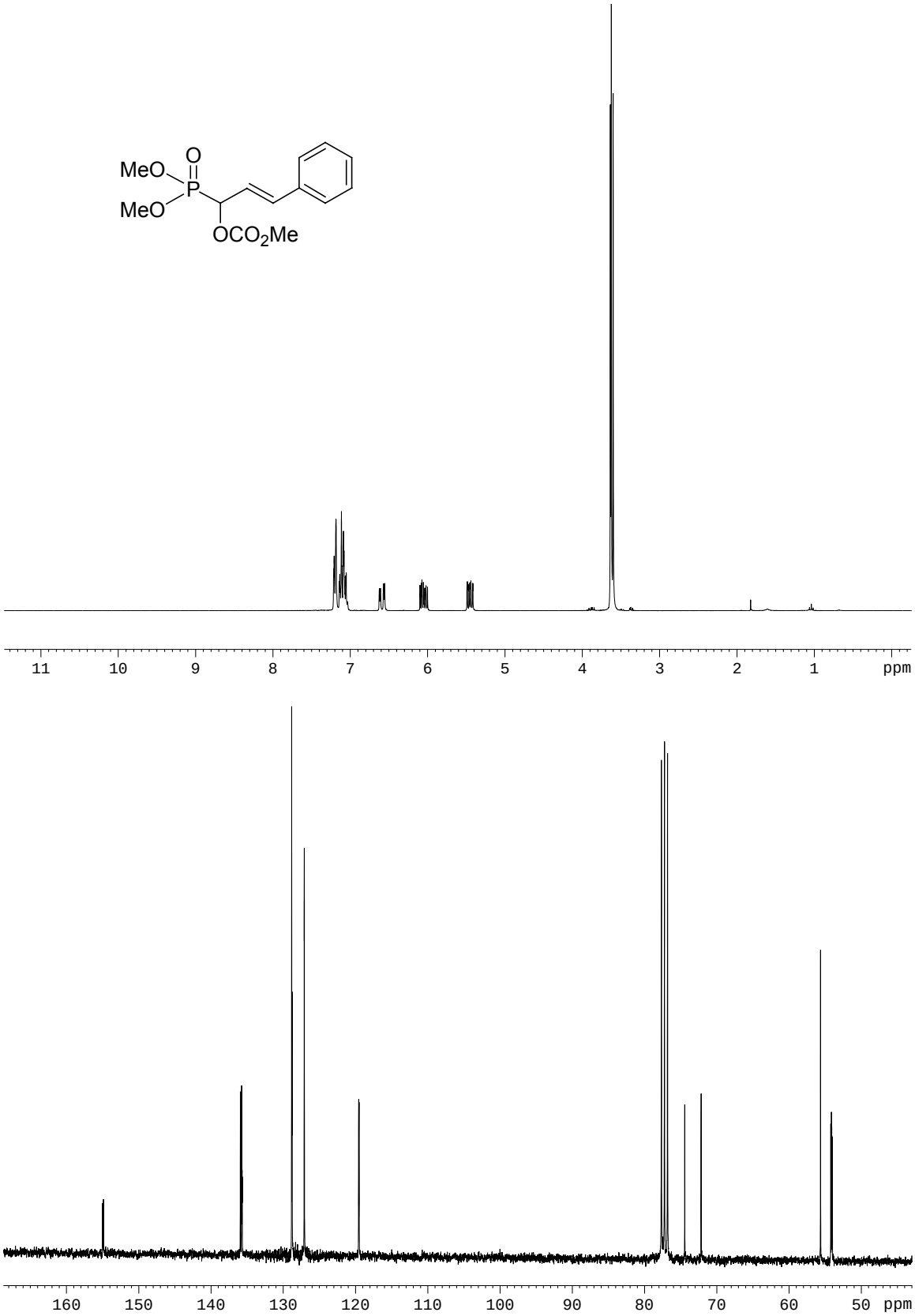
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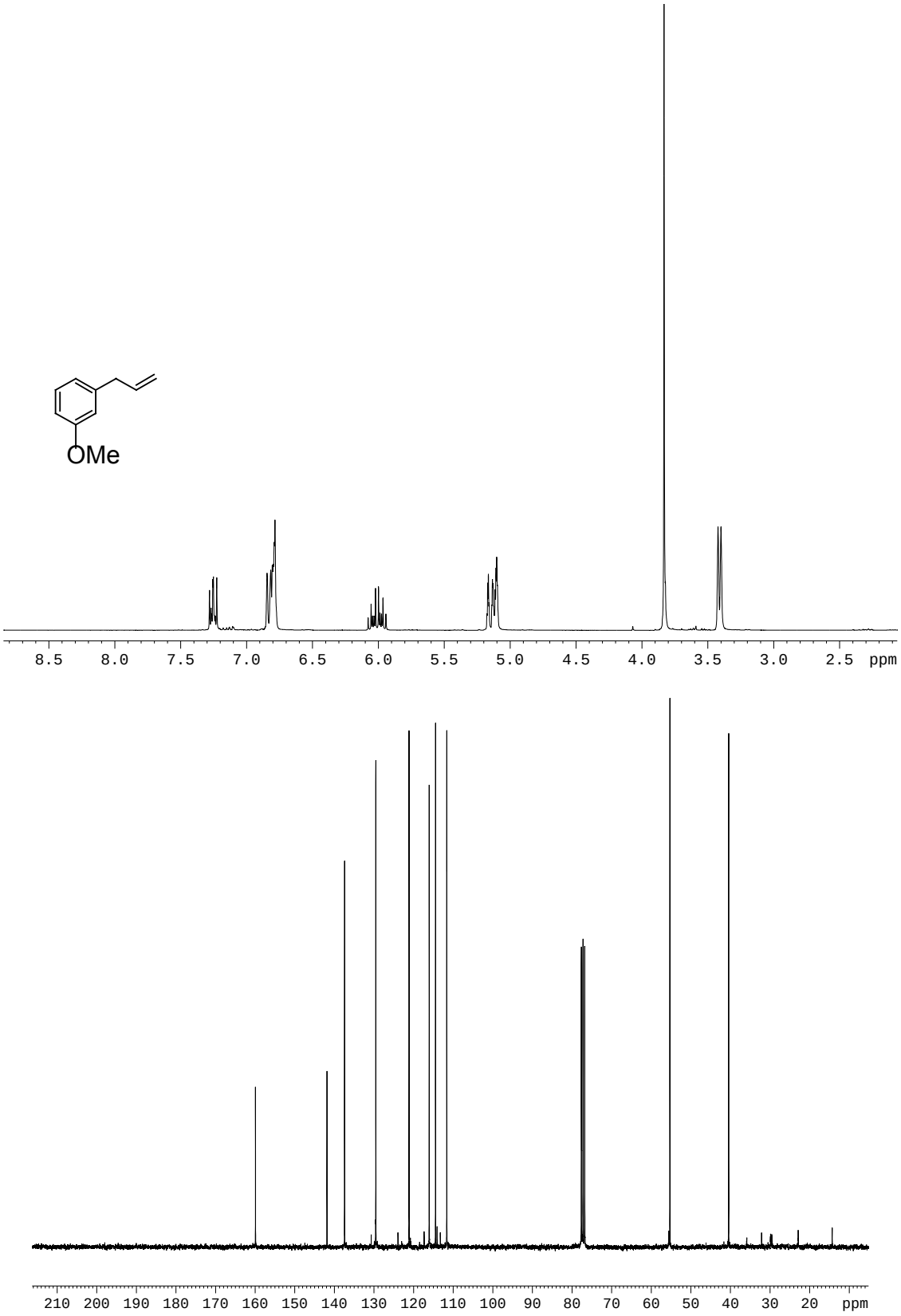
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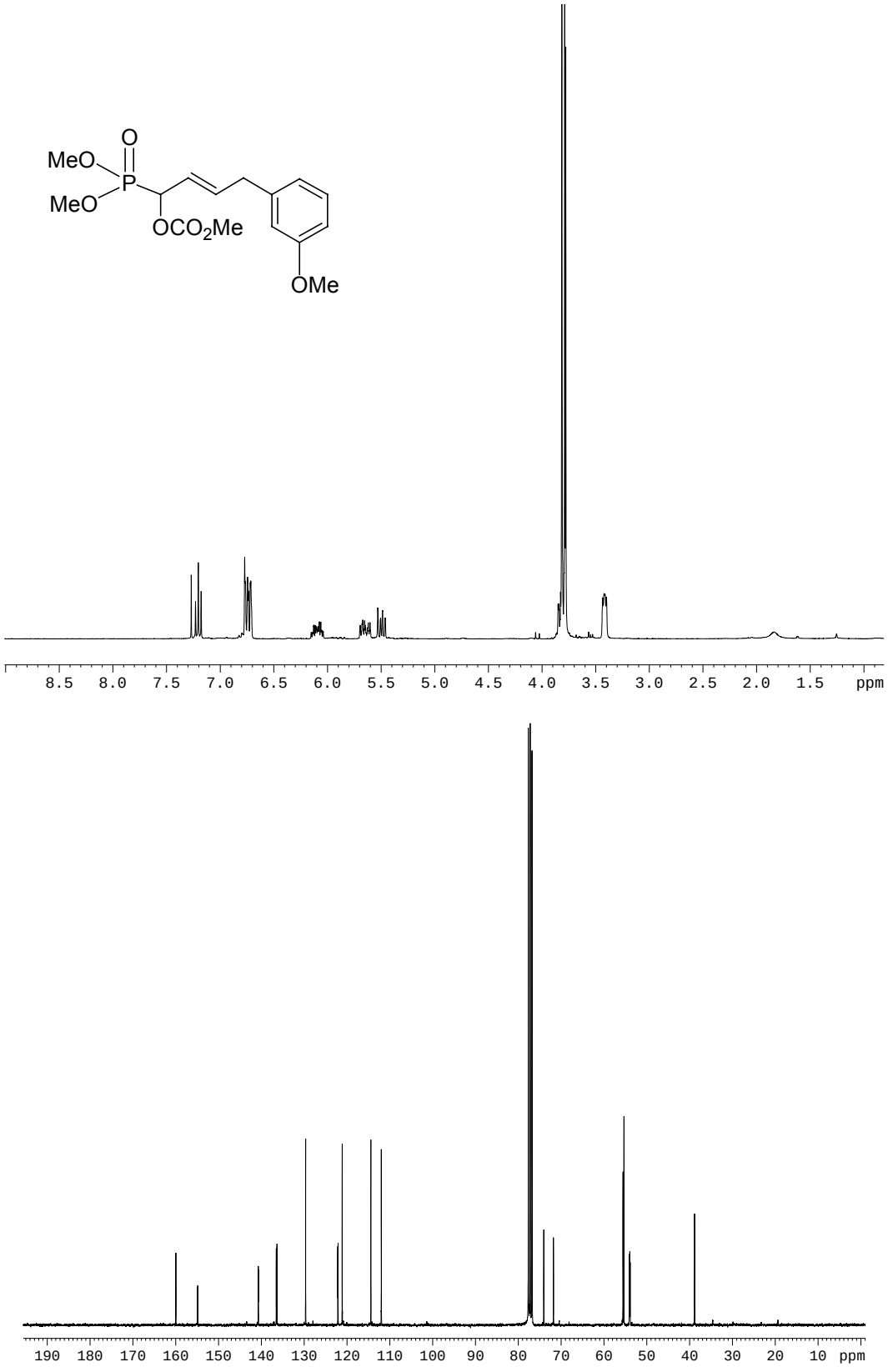
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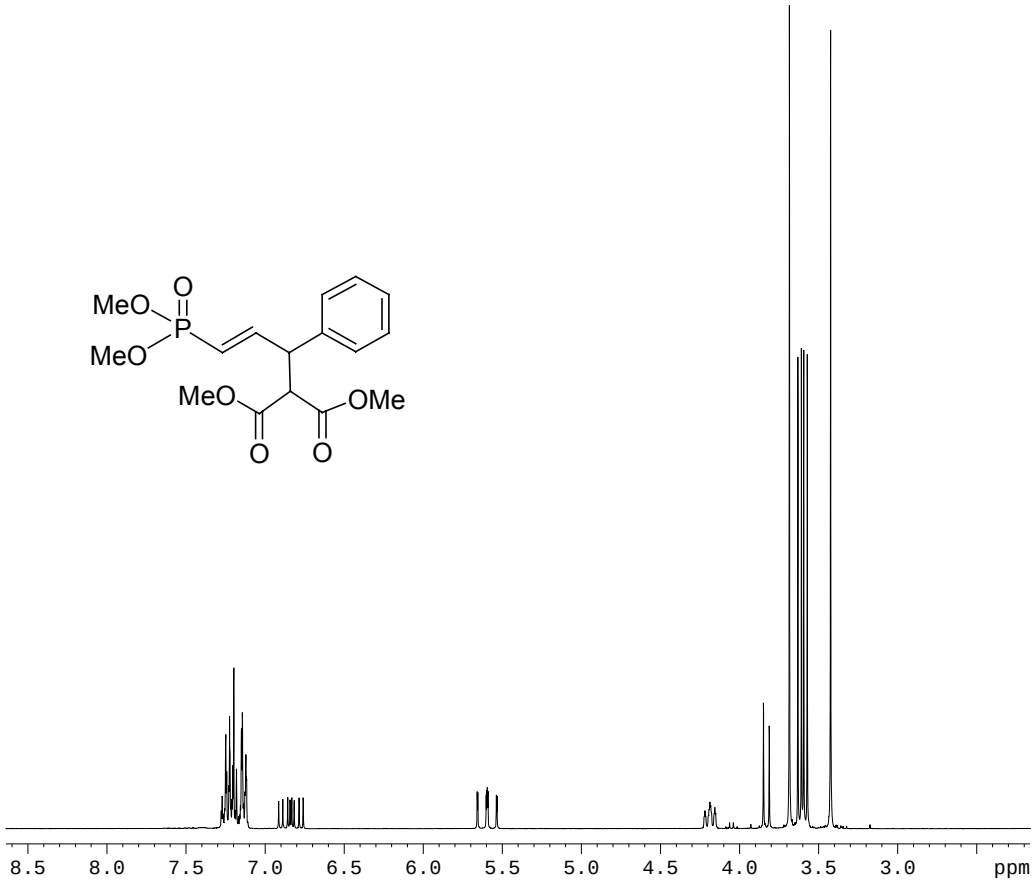
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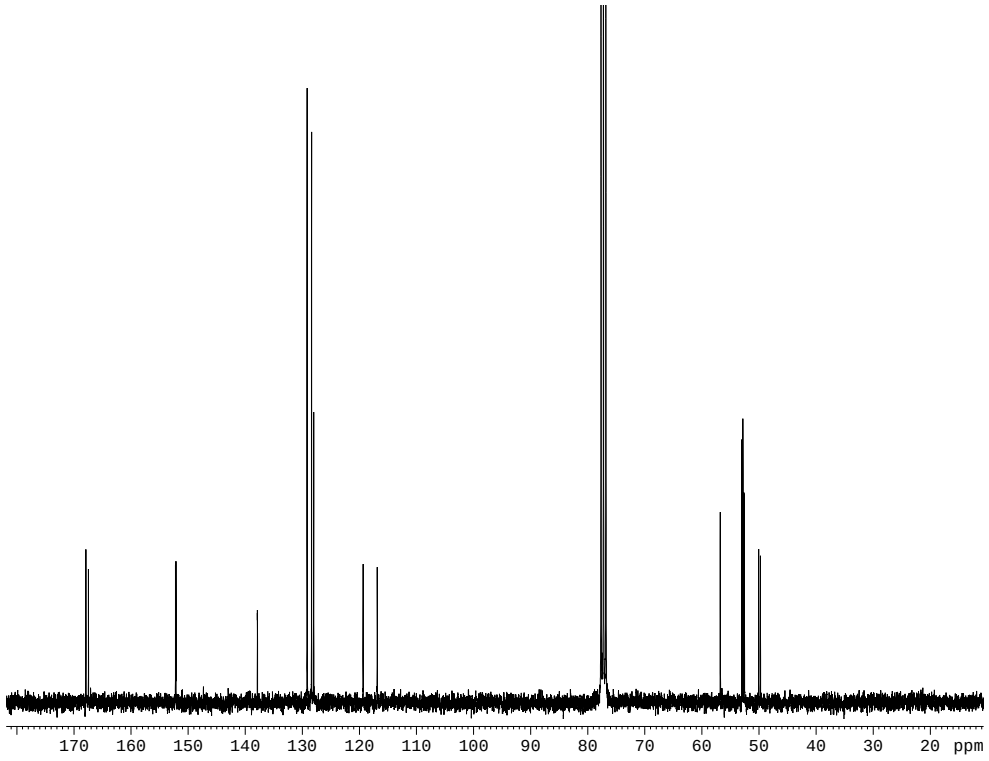
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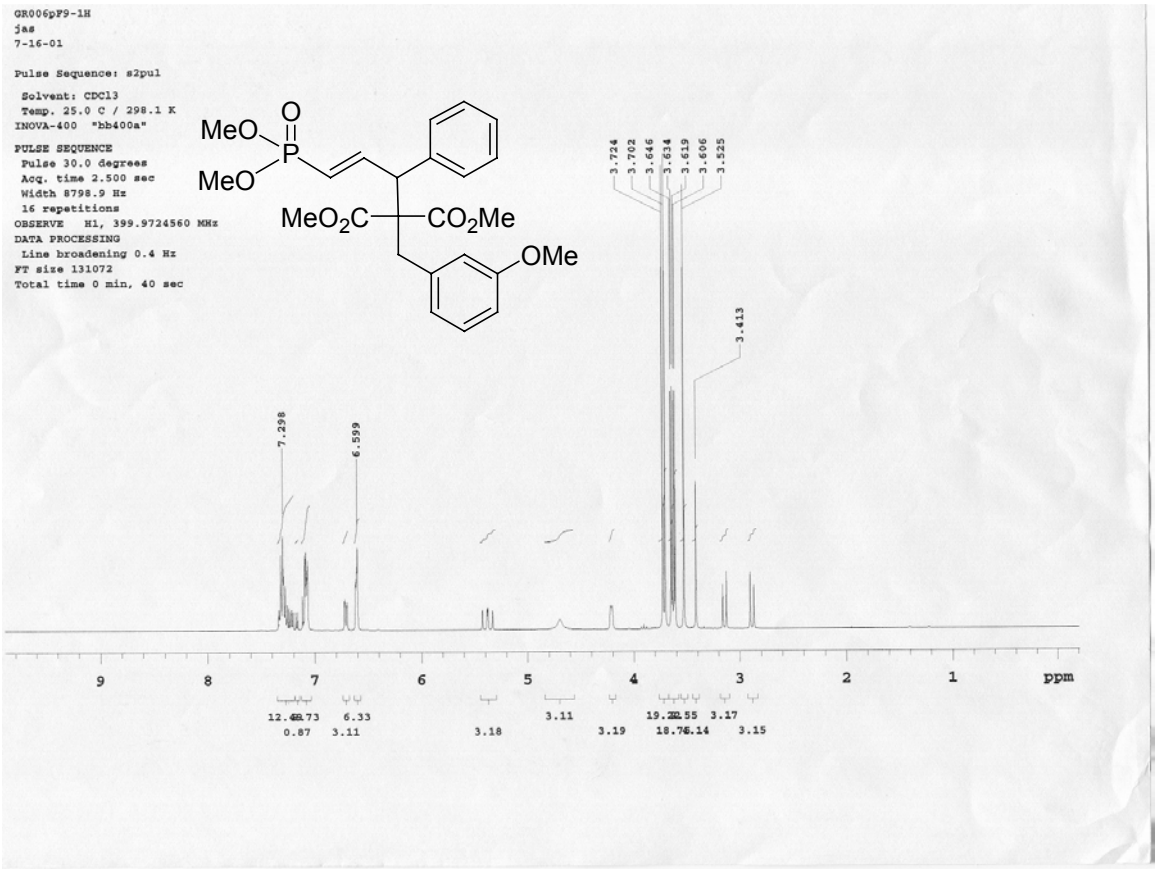
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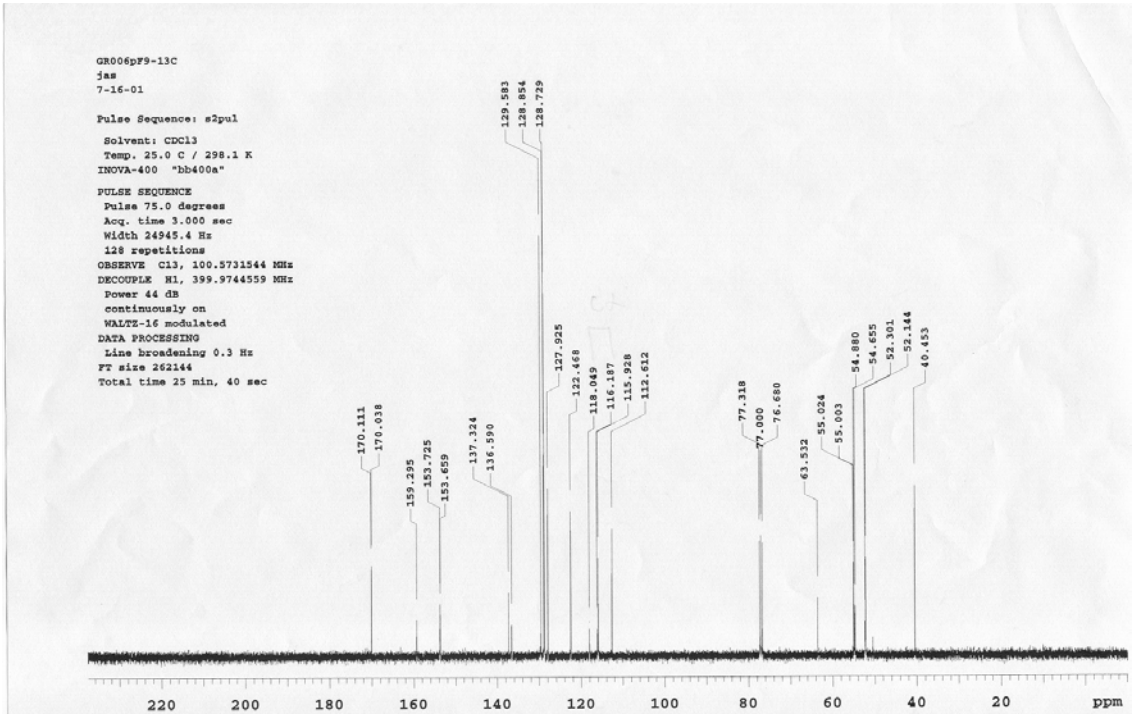
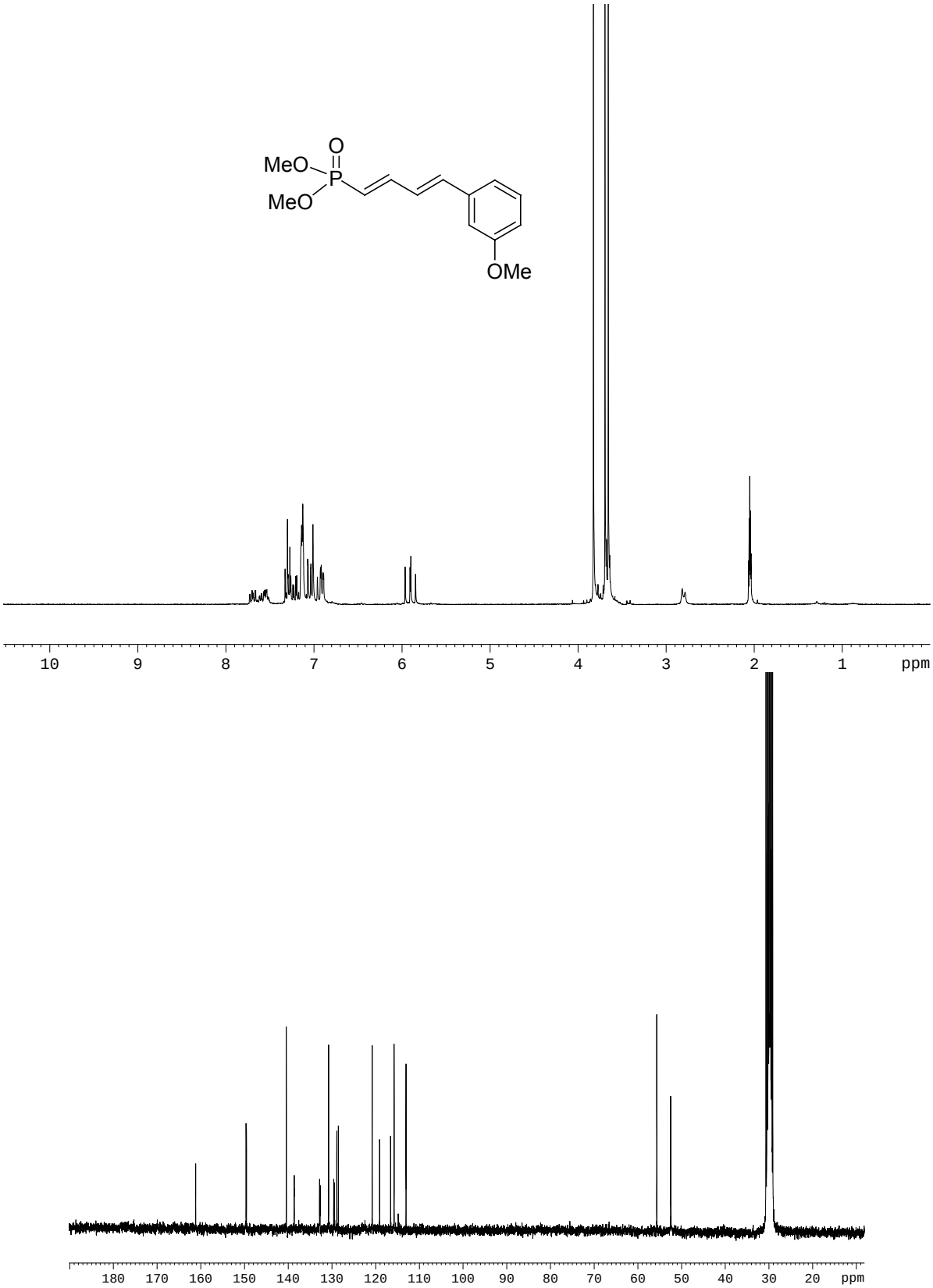
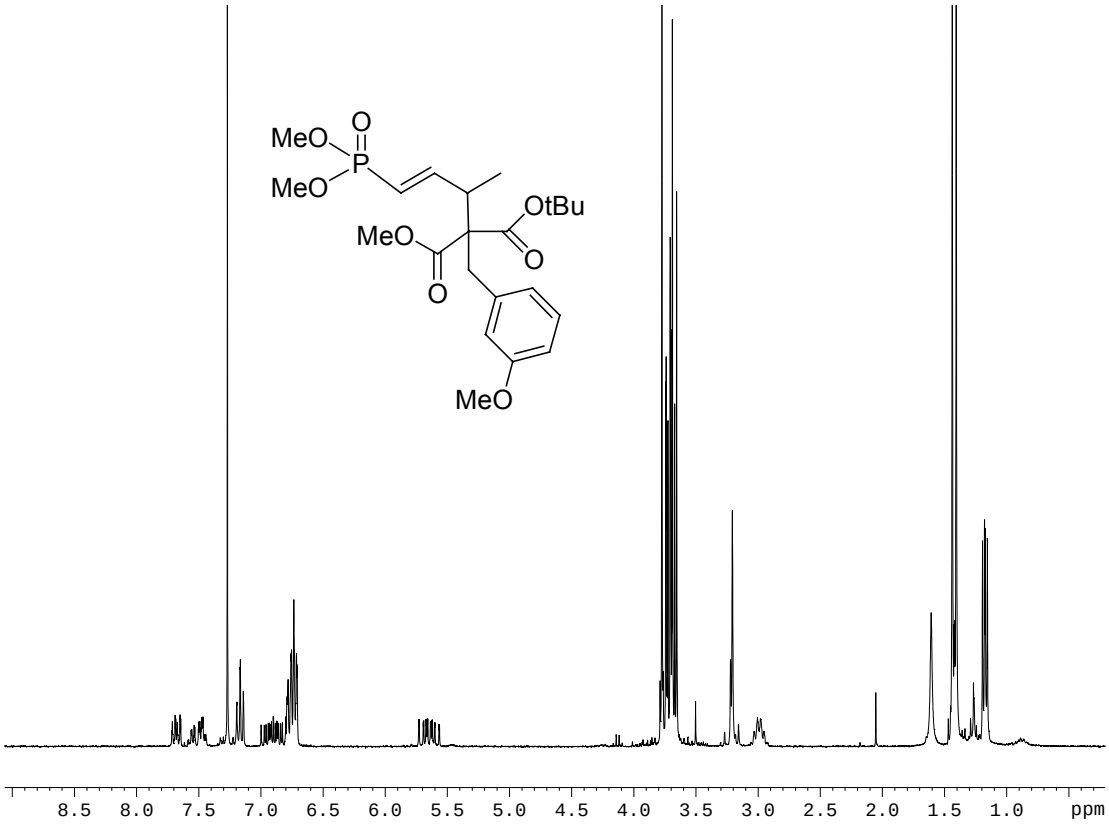
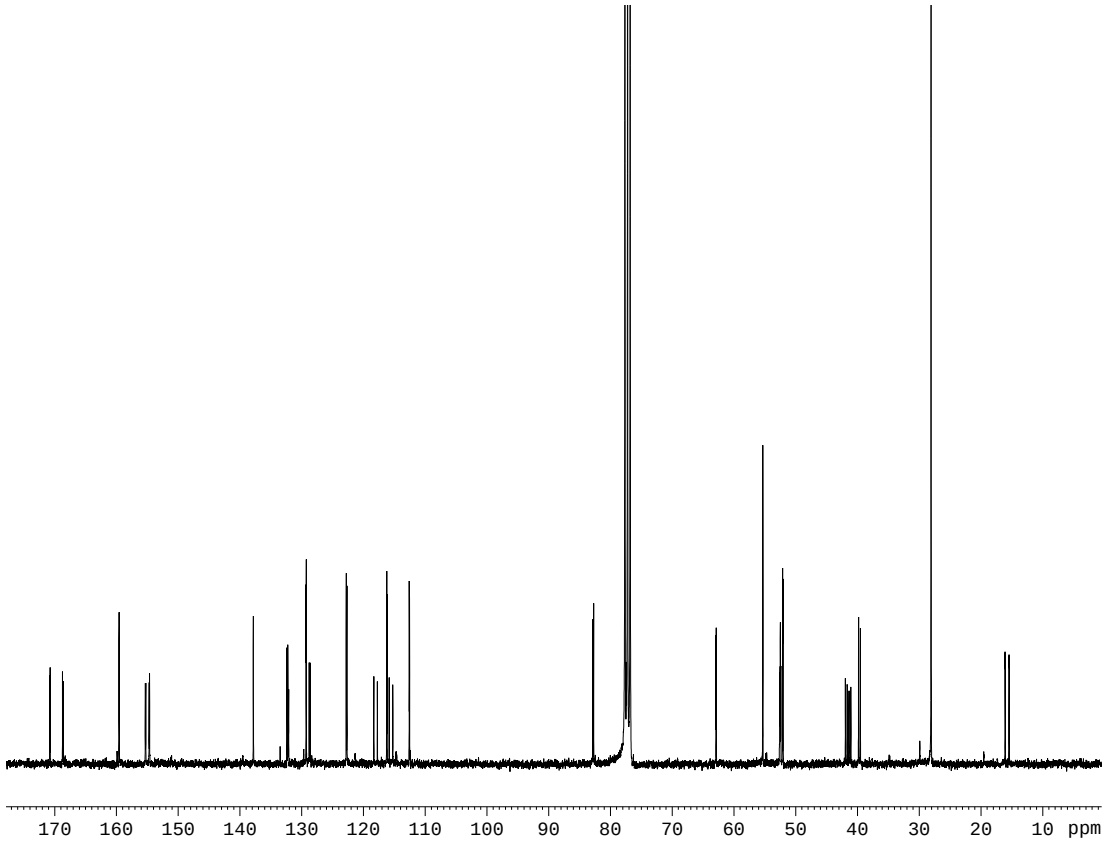
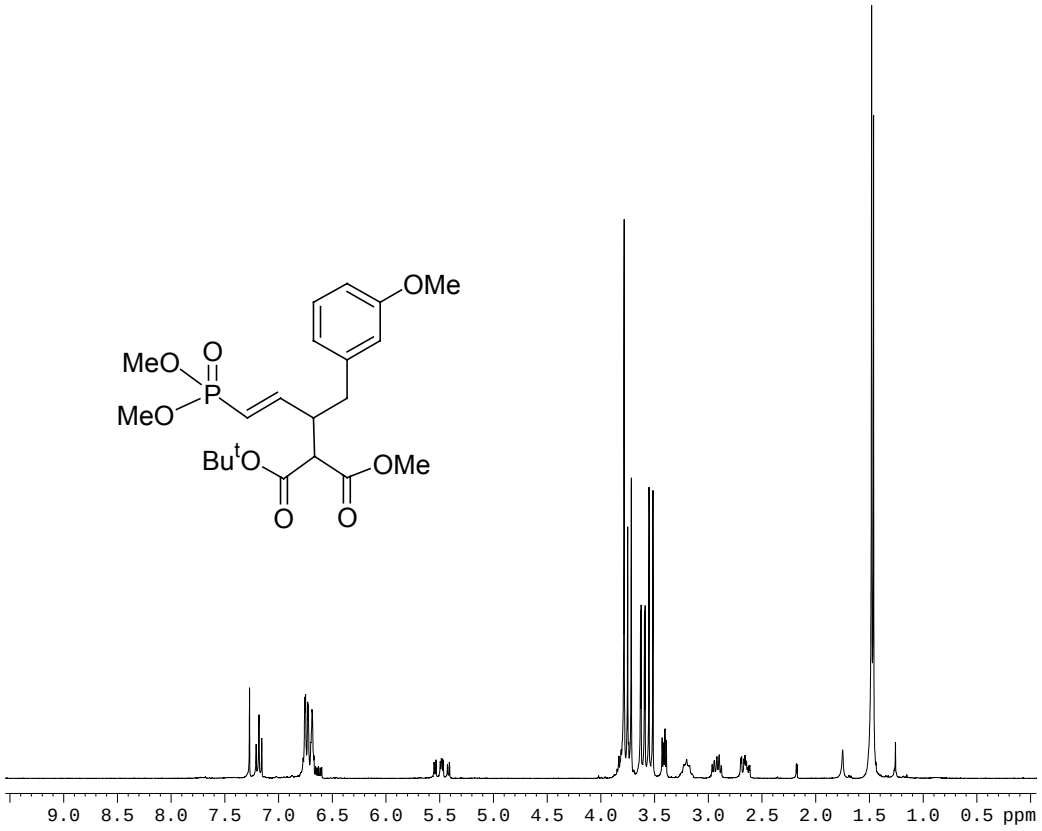
ppm

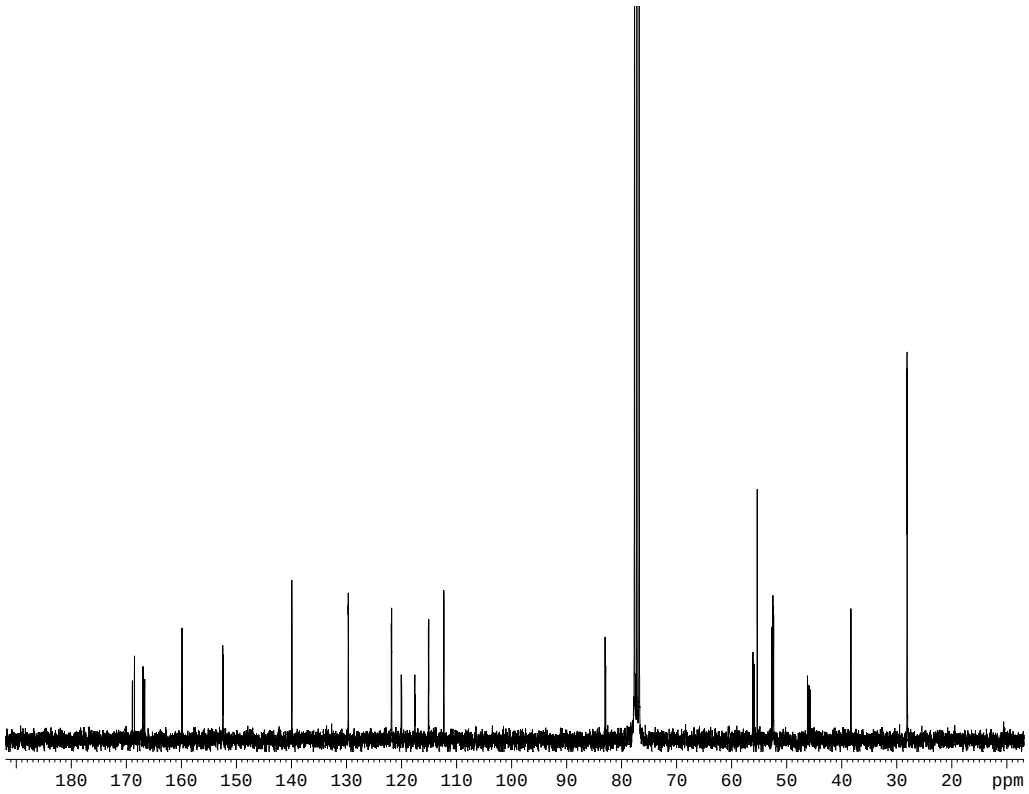

GR006pF9-13C
jas
7-16-01
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
INOVA-400 "bb400a"
PULSE SEQUENCE
Pulse 75.0 degrees
Acq. time 3.000 sec
Width 24945.4 Hz
128 repetitions
OBSERVE C13, 100.5731544 MHz
DECOUPLE H1, 399.9744559 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.3 Hz
FT size 262144
Total time 25 min, 40 sec
170.111
170.038
159.295
153.725
153.659
137.324
136.590
129.583
128.854
128.729
127.925
122.468
118.049
116.187
115.928
112.612
77.318
77.000
76.680
63.532
55.024
55.003
54.880
54.655
52.301
52.144
40.453
ppm

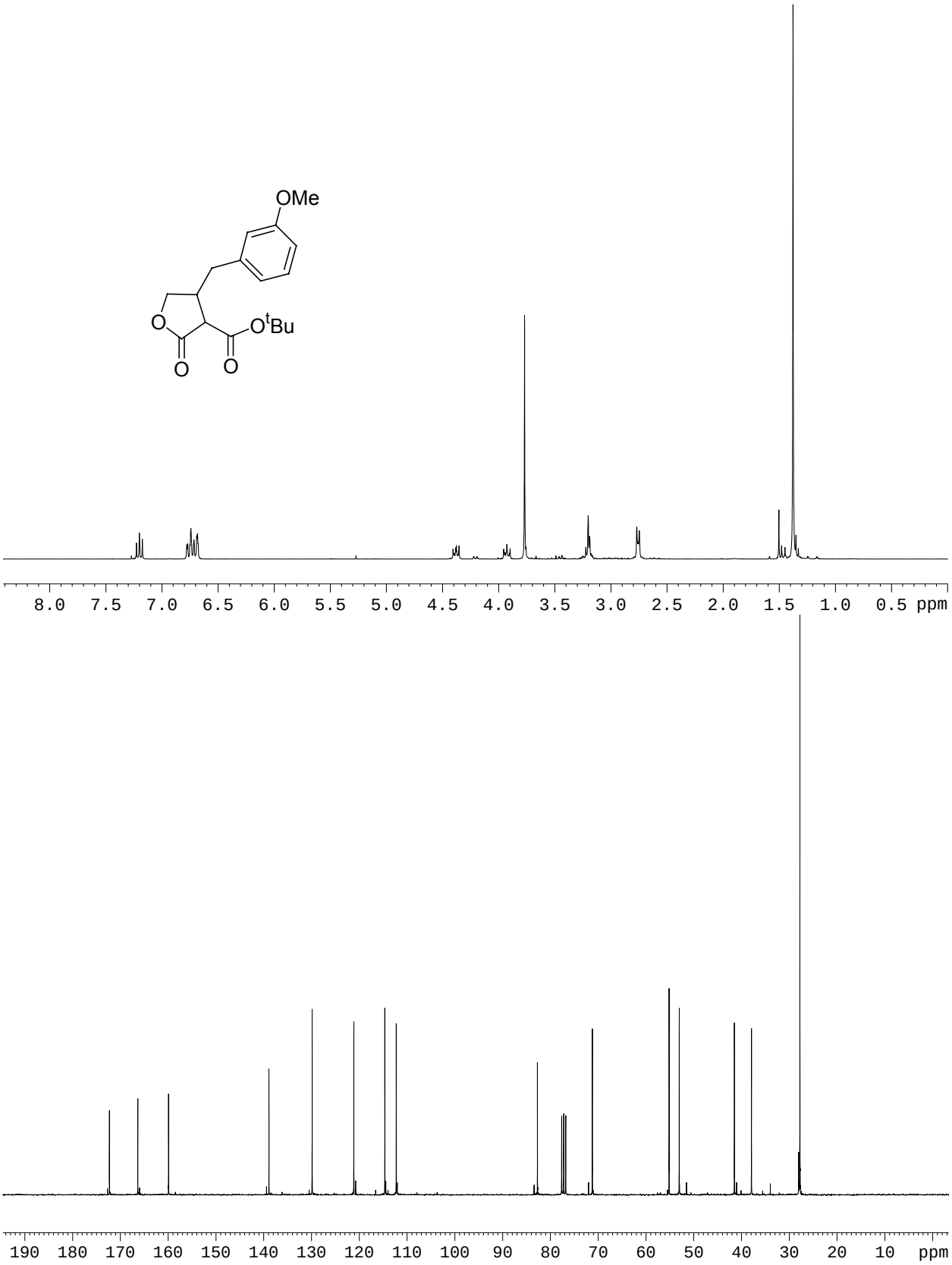

MeO
O
P
MeO
OMe
10
9
8
7
6
5
4
3
2
1
ppm
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

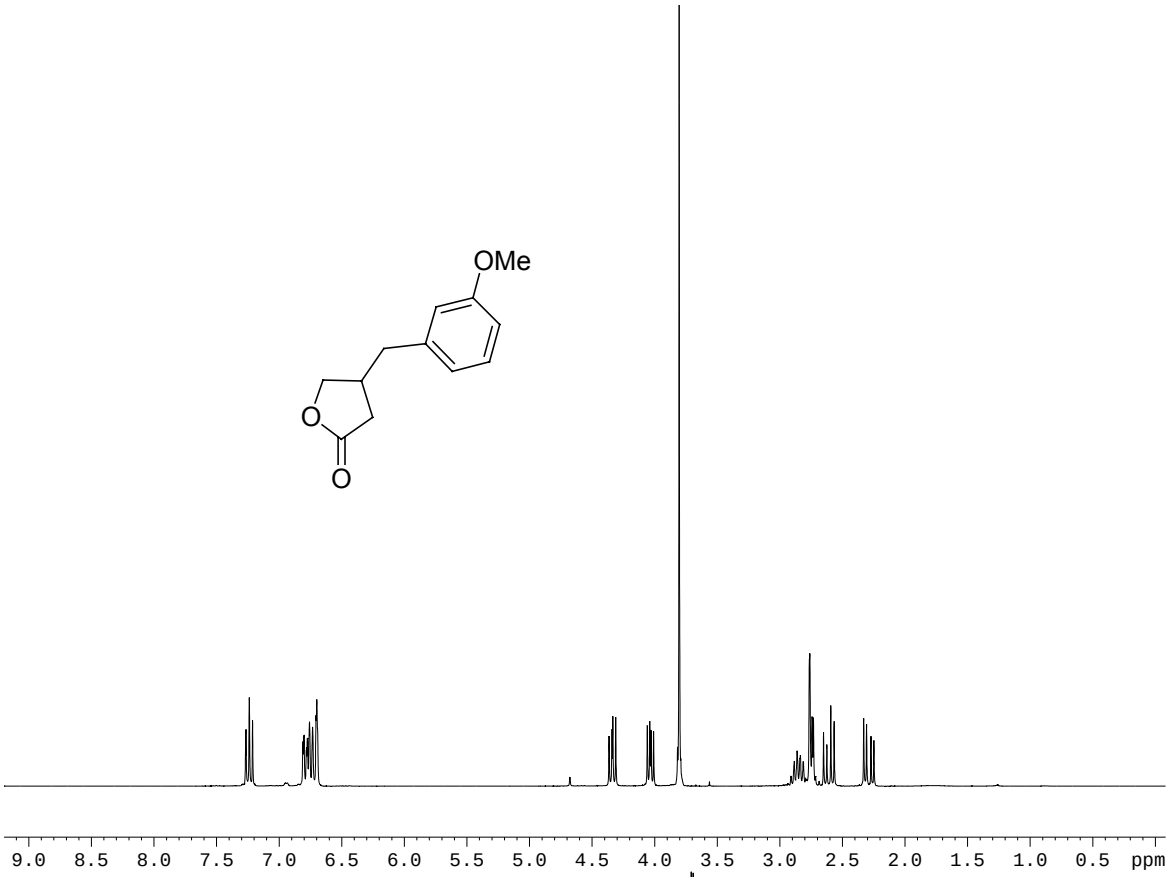

MeO
O
P
MeO
OtBu
MeO
O
O
MeO
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm

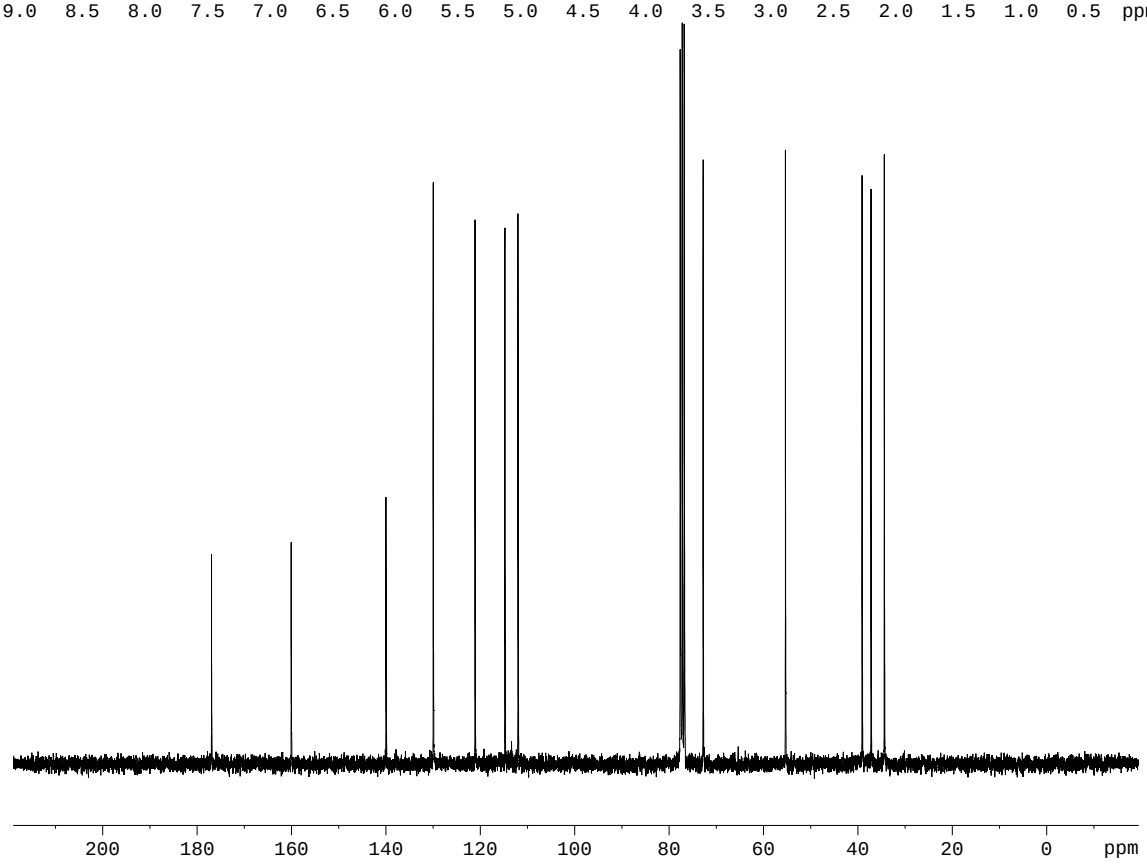

170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OMe
MeO
O
P
MeO
Bu^tO
OMe
O
O
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 ppm

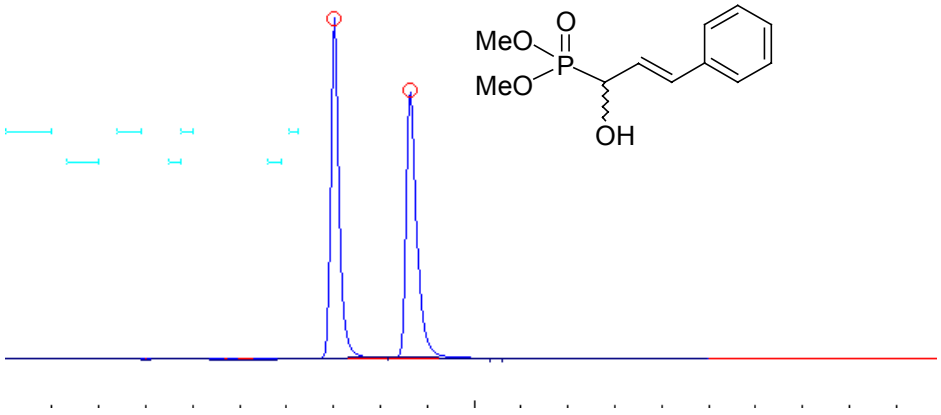

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


OMe
O
O
O
O
tBu
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 ppm
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OMe
O
O
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 ppm

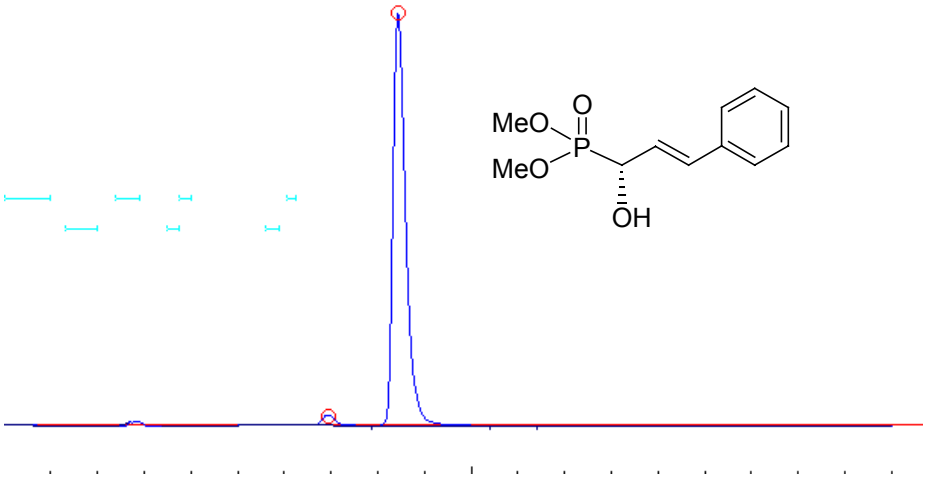

200 180 160 140 120 100 80 60 40 20 0 ppm

Column-S,S Whelk-O, EtOH:hexane (20:80), 1 mL/min, det 254 nm



Racemic

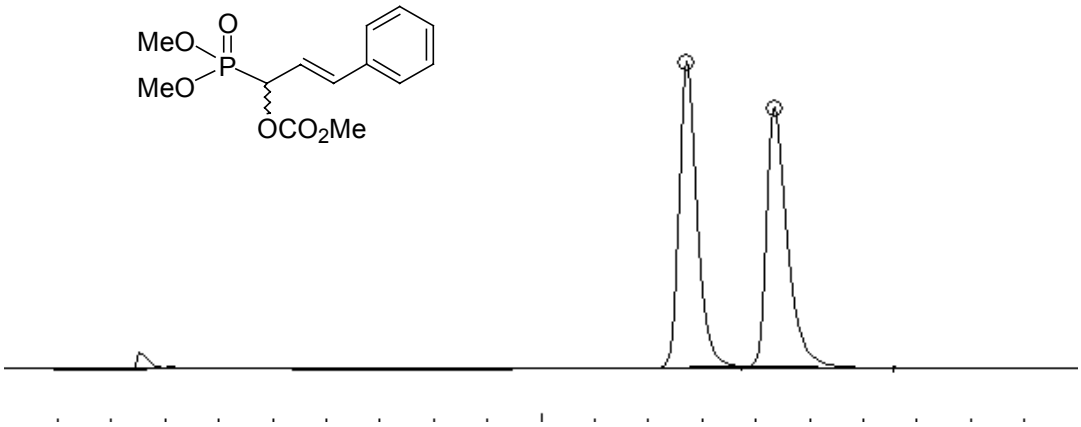
Retention time (min)	Area	% Area
6.97	5211	49.7
8.58	5281	50.3



R Isomer (95% e.e.)

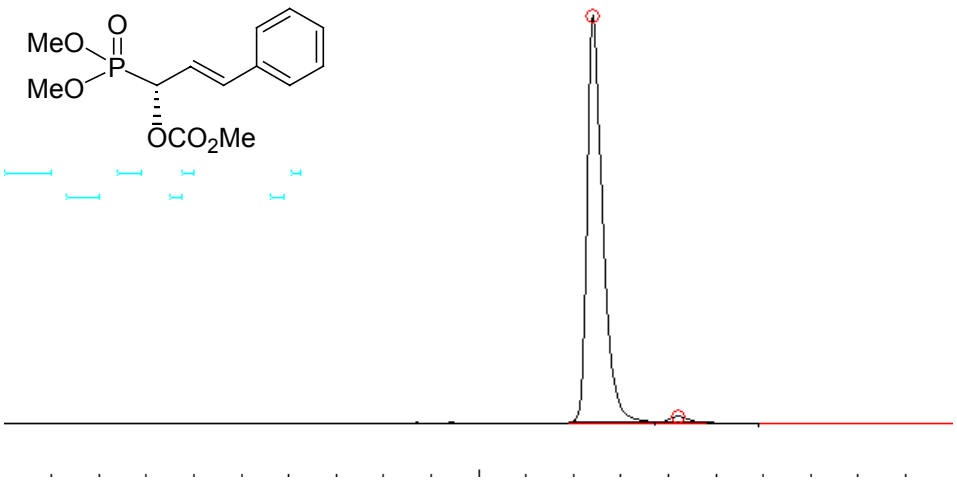
Retention time (min)	Area	% Area	Ratio
6.88	503	2.5	39
8.38	19854	97.5	1

Column-S,S Whelk-O, EtOH:hexane (20:80), 1 mL/min, det 210 nm



Racemic

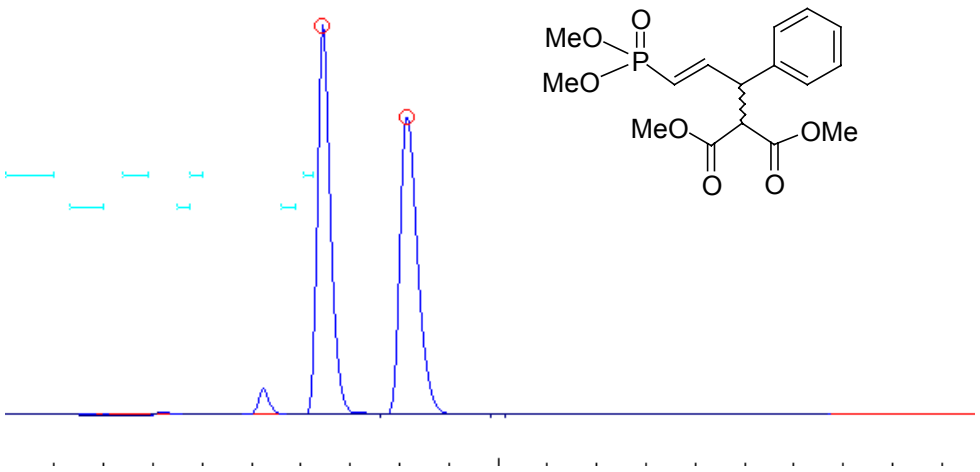
Retention time (min)	Area	% Area
12.65	5152	50.2
14.28	5115	49.8



R Isomer (95% e.e.)

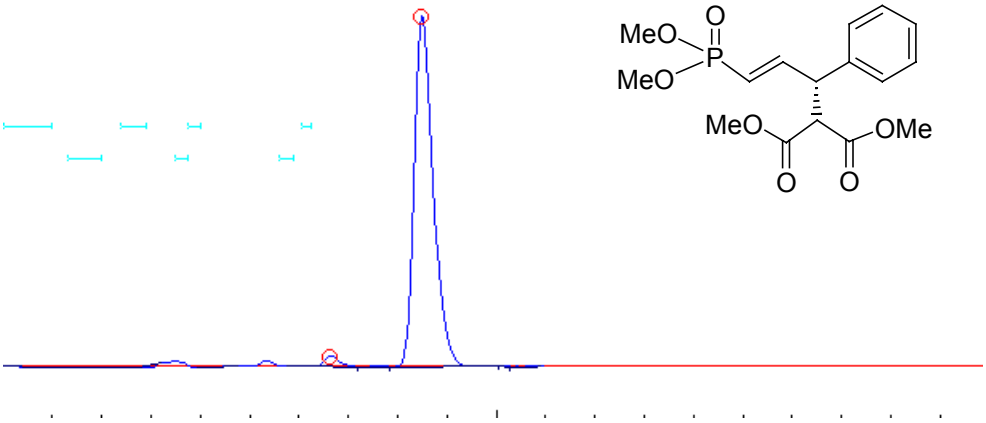
Retention time (min)	Area	% Area	Ratio
12.35	27003	97.5	39
14.15	681	2.5	1

Column-ChiralPak AS, EtOH:hexane (20:80), 1 mL/min, det 210 nm



Racemic

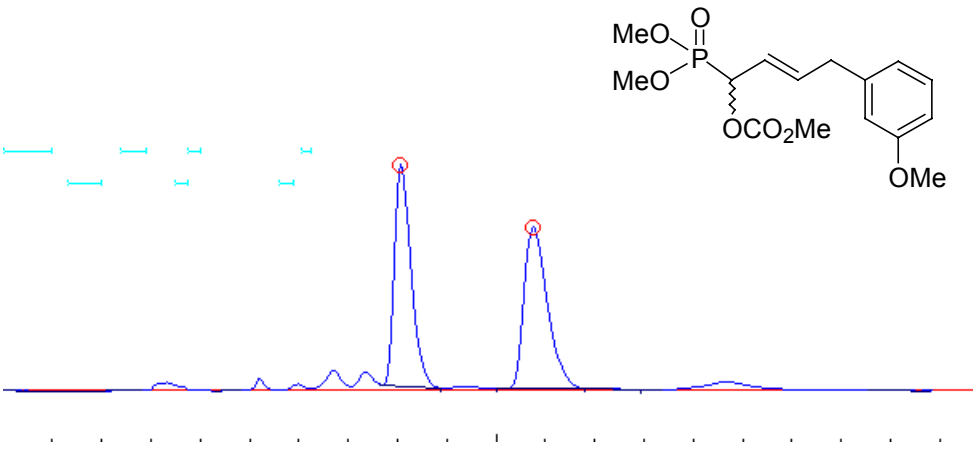
Retention time (min)	Area	% Area
6.38	34130	49.9
8.10	34349	50.1



R Isomer (95% e.e.)

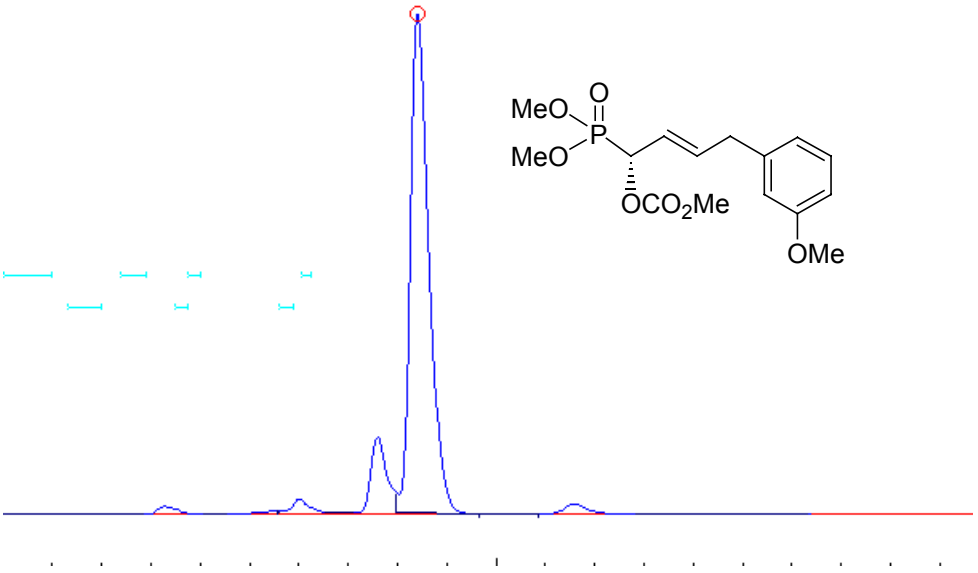
Retention time (min)	Area	% Area	Ratio
6.58	333	2.3	42
8.43	14210	97.7	1

Column-ChiralPak AS, EtOH:hexane (20:80), 1 mL/min, det 210 nm



Racemic

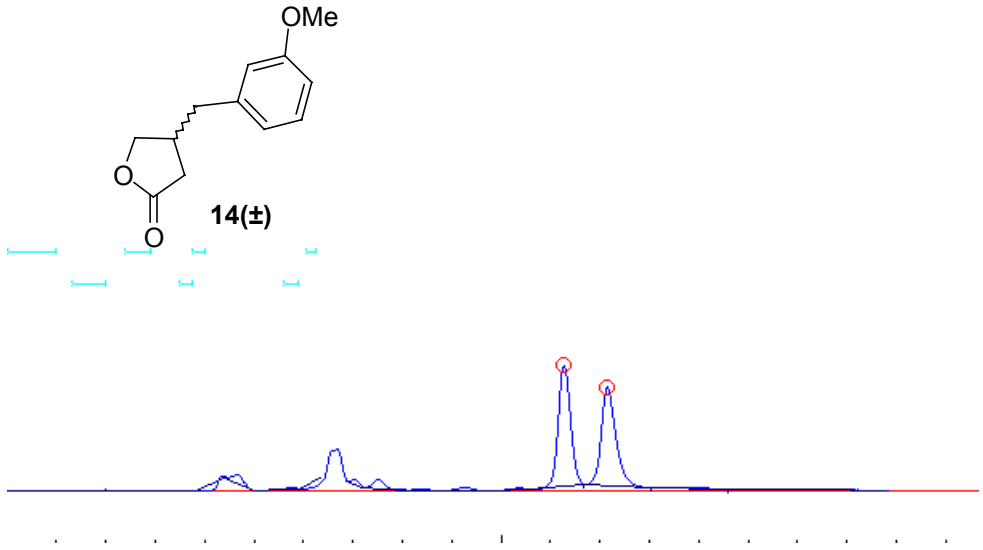
Retention time (min)	Area	% Area
8.02	12114	49.14
10.7	12536	50.86



R Isomer (95% e.e.)

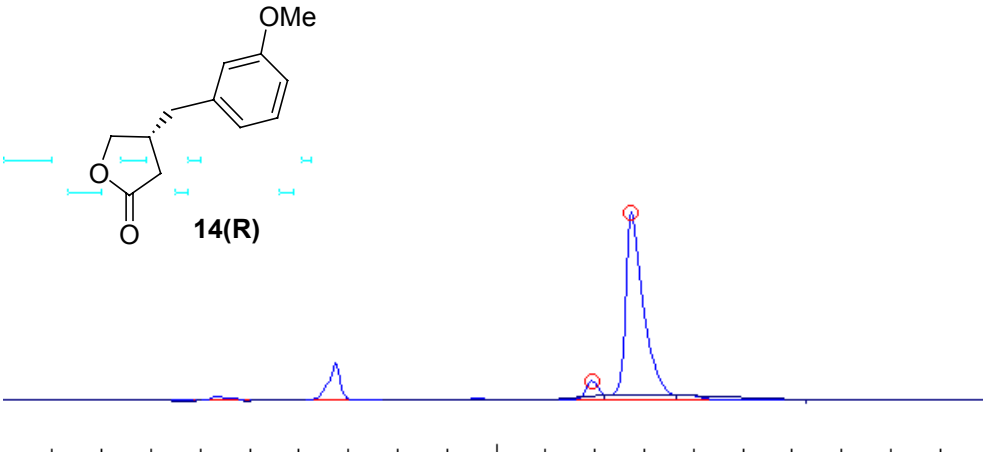
Retention time (min)	Area	% Area	Ratio
8.35	30870	97.69	41
11.5	753	2.31	1

Column-Chirobiotic-T, EtOH:hexane (50:50), 0.6 mL/min, det 210 nm



Racemic

Retention time (min)	Area	% Area
11.2	599	49.9
12.1	603	50.1



R Isomer (92% e.e.)

Retention time (min)	Area	% Area	Ratio
11.4	223	3.7	26
12.2	5802	96.3	1