The Regio and Stereoselective Cleavages of P-S/C-S bonds by Lithium and the Formation of P-Stereogenic Functional Phosphine Derivatives

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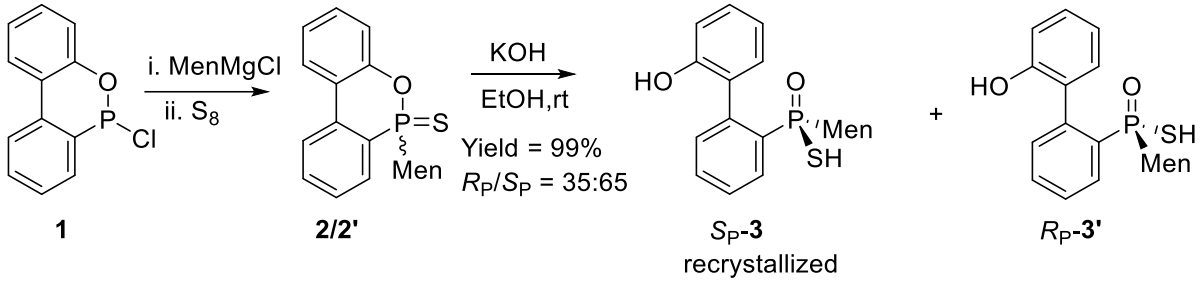
General Chemistry:

^{1}H NMR spectrum were recorded on a 400-MHz spectrometer. Chemical shift for ^{1}H NMR spectrum (in parts per million) relative to internal tetramethylsilane (Me_4Si, δ = 0.00 ppm) with $CDCl_3$. ^{13}C NMR spectrum were recorded at 101 MHz. Chemical shifts for ^{13}C NMR spectrum are reported (in parts per million) relative to $CDCl_3$ (δ = 77.0 ppm). ^{31}P NMR spectrum were recorded at 162 MHz, and chemical shifts reported (in parts per million) relative to external 85% phosphoric acid (δ = 0.0 ppm). TLC plates were visualized by UV. All products were further characterized by HRMS (high resolution mass spectrum) or Elemental Analysis. Copies of their ^{1}H, ^{31}P and ^{13}C NMR spectrum were provided. Melting points were determined on a Reichert Thermovar melting point apparatus and are uncorrected. The diasteroselective ratio were assign as the ratio of *R*-stereoisomer/*S*-stereoisomer.

Reagent and solvents:

All the solvents used were dried and freshly distilled prior to use. Toluene, chloroform and dichloromethane distilled under calcium hydride. THF, ether and hexane were distilled under sodium and benzophenone. Unless otherwise stated, the commercially available reagents were used without further purification. Some of the Grignard reagent was prepared according standard procedure in ca. 0.8 M solution in ether or THF. All reactions were carried out under N_2 atmosphere in dry glassware using Schlenk-line techniques. Air and moisture sensitive liquids and solutions were transferred via syringe.

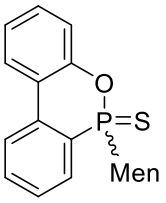
Part 1. Preparations of optically pure starting material S_P-3 and R_P-3'.



The preparation of 6-(-)-menthyl-6H-dibenz[*c,e*][1,2]-oxaphosphinine 6-sulfide 2/2'.

To the solution of CDOP (5.00 g, 21.31 mmol) in THF (5 mL), the solution of (-)-menthyl magnesium chloride (prepared according standard procedure, 0.8 M solution in THF, 40 mL, 32 mmol) was added dropwise. The mixture was stirred at room temperature for 8 hours, and S_8 (0.75 g, 23.44 mmol) was added. After stirring for 5 hours at room temperature, the reaction was quenched with diluted hydrochloric acid (7%) and the solvent was removed. The mixture was extracted with dichloromethane (3×10 mL), washed with water (3×10 mL), dried over magnesium sulfate. After removing solvent, the residue was purified with column chromatography on silica gel (petroleum ether/ ethyl acetate = 3/1) to afford **2/2'** (7.0 g, 90%, 50:50 dr_P).

***R*P/*S*P-6-(-)-Menthyl-6H-dibenzo[*c,e*][1,2]-oxaphosphinine 6-sulfide (2/2')**

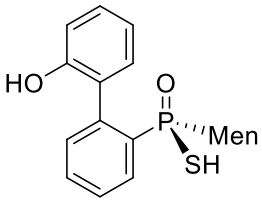


The pure 2/2' was obtained as a white solid, m.p. 79.0 – 81.2 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 96.85 (s), 93.51 (s); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.16 – 8.07 (m, 1H), 7.99 (ddd, *J*=13.7, 7.6, 0.9, 1H), 7.90 (ddd, *J*=7.4, 5.0, 1.3, 1H), 7.83 (dd, *J*=7.9, 4.7, 1H), 7.78 (dd, *J*=7.8, 4.7, 1H), 7.64 (q, *J*=7.5, 1H), 7.54 – 7.47 (m, 1H), 7.43 – 7.33 (m, 1H), 7.28 (d, *J*=7.9, 1H), 7.25 (s, 1H), 7.24 – 7.12 (m, 1H), 2.80 – 2.67 (m, 1H), 2.21 – 2.06 (m, 1H), 2.06 – 1.93 (m, 2H), 1.93 – 1.82 (m, 1H), 1.77 – 1.58 (m, 3H), 1.44 (ddd, *J*=25.1, 12.4, 8.0, 1H), 1.04 (t, *J*=6.7, 3H), 0.90 (dd, *J*=11.1, 6.1, 3H), 0.83 (d, *J*=11.9, 1H), 0.79 (d, *J*=6.8, 2H), 0.72 (d, *J*=5.9, 2H), 0.67 (d, *J*=6.9, 1H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 149.8 (dd, *J*=21.7), 134.5 (dd, *J*=87.2), 133.5 (d, *J*=11.3), 133.0 – 131.9 (m), 130.6 (d, *J*=48.1), 129.1 (d, *J*=89.2), 128.4 (dd, *J*=29.3), 126.3 (d, *J*=92.0), 125.1 (d, *J*=19.3), 124.6 (d, *J*=13.0), 123.8 (t, *J*=8.8), 121.1 (d, *J*=5.6), 120.5 (d, *J*=5.6), 44.0 (s), 42.7 (d, *J*=2.7), 41.0 (dd, *J* = 188.8), 35.4 (s), 34.3 (dd, *J*=42.1), 32.7 (dd, *J*=19.9), 28.5 (dd, *J*=25.8), 24.0 (dd, *J*=15.1), 22.5 (d, *J*=20.4), 21.5 (d, *J*=47.8), 16.9 (s), 14.1 (s). **HRMS (ESI$^+$)** Calcd. for $C_{22}H_{27}OPS$ [M+Na^+]: 393.1418, Found: 393.1448.

The preparation of S_P-(2'-hydroxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioic *S*-acid (S_P-3).

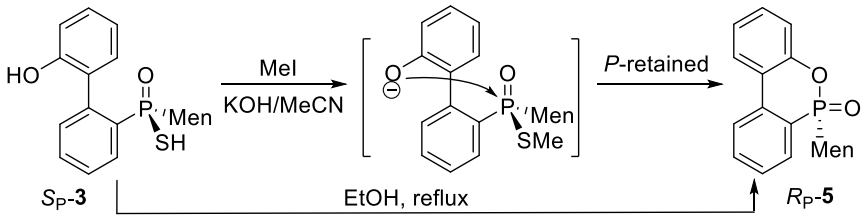
To the solution of **2/2'** (5.00 g, 13.50 mmol, 50:50 dr_P) in ethanol (10 mL) and water (1 mL), potassium hydroxide (1.78 g, 27.01 mmol) was added, and the solution was stirred at 50 °C for 5 hours. After the reaction is completed, the ethanol was removed and the solution was twice washed with petroleum ether (2×10 mL), diluted hydrochloric acid (7%) was added to adjust PH to 8-9. The mixture was extracted with dichloromethane (3×10 mL), washed with water (3×10 mL), dried over magnesium sulfate. After removing solvent **3/3'** (5.18 g, 99%, 65:35 dr_P) was afforded. The crude product was recrystallized from dichloromethane: petroleum ether = 2:1 at -40 °C to afford S_P-**3** (1.45 g, 28%, <1:99 dr_P).

S_P-(2'-Hydroxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioic *S*-acid (S_P-3)



The optically pure S_P-**3** was obtained as a white solid, m.p. 166.9 – 169.8 °C; **^{31}P NMR (202 MHz, MeOD)** δ = 82.74 (s); **^{1}H NMR (500 MHz, MeOD)** δ = 8.60 – 8.50 (m, 1H), 7.31 (p, *J*=7.3, 2H), 7.23 – 7.14 (m, 1H), 7.00 – 6.95 (m, 1H), 6.94 – 6.89 (m, 2H), 6.86 (d, *J*=8.0, 1H), 2.61 – 2.49 (m, 1H), 1.58 (td, *J*=11.0, 5.5, 1H), 1.47 – 1.34 (m, 2H), 1.19 (s, 1H), 0.90 (ddd, *J*= 20.6, 11.1, 3.1, 1H), 0.72 (d, *J*=6.9, 4H), 0.66 – 0.48 (m, 6H), 0.36 (d, *J*=6.7, 3H); **^{13}C {^{1}H} NMR (126 MHz, MeOD)** δ = 153.7 (s), 140.3 (d, *J*=7.5), 138.7 (d, *J*=88.3), 135.6 (d, *J*=1.6), 132.8 (d, *J*=11.7), 131.1 (d, *J*=9.4), 130.8 (s), 129.3 (d, *J*=1.6), 128.7 (s), 126.2 (d, *J*=11.6), 121.3 (s), 121.0 (s), 43.5 (d, *J*=2.7), 42.8 (d, *J*=73.7), 36.9 (s), 34.6 (s), 32.6 (d, *J*=16.1), 27.4 (d, *J*=2.6), 24.06 (d, *J*=13.9), 21.7 (s), 20.7 (s), 14.5 (s). **HRMS (ESI$^+$)** Calcd. for $C_{22}H_{29}O_2PS$ [M+H$^+$]: 388.1626, Found: 388.1590.

The cyclization of S_P-3 to form R_P-5.



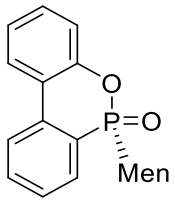
Cyclization of S_P-3 with methyl iodide in the presence of base.

To the suspension of ***S*P-3** (80.0 mg, 0.205 mmol) and potassium hydroxide (14.9 mg, 0.225 mmol) in acetonitrile (1 mL), was added methyl iodide (51.2 μL, 0.822 mmol) and the mixture was stirred at room temperature for 5 hours. After the reaction was completed, as monitored with TLC, saturated solution of ammonium chloride (10 mL) was added. The mixture was extracted with dichloromethane (3×10 mL), washed with water (3×10 mL), dried over magnesium sulfate. After removing the solvents, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent) to afford ***R*P-5** (48.1 mg, 80%, >99:1 dr_P).

Thermal cyclization of S_P-3.

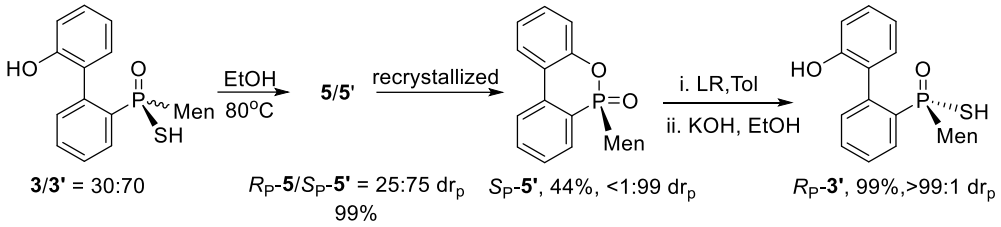
The solution of ***S*P-3** (200.0 mg, 0.513 mmol) in ethanol (10 mL) was heated with reflux at 80 °C for 8 hours. After the reaction was completed, the solvent was removed, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent) to afford ***R*P-5** (175.8 mg, 99%, >99:1 dr_P).

***R*P-6-((-)-Menthyl)dibenzo[c,e][1,2]-oxaphosphinine 6-oxide (*R*P-5)**



The pure ***R*P-5** was obtained as white solid, m.p. 126.8 – 129.0 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 43.21 (s); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.88 (dd, *J*=15.6, 5.7, 3H), 7.67 (s, 1H), 7.50 (s, 1H), 7.36 (s, 1H), 7.24 (d, *J*=7.5, 1H), 7.17 (d, *J*=8.1, 1H), 2.72 – 2.50 (m, 1H), 1.95 – 1.77 (m, 2H), 1.79 – 1.69 (m, 1H), 1.65 (d, *J*=12.0, 1H), 1.43 (d, *J*=6.3, 1H), 1.08 (dd, *J*=14.6, 8.3, 2H), 1.01 (t, *J*=8.9, 3H), 0.97 – 0.83 (m, 2H), 0.75 (t, *J*=6.9, 6H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 149.4 (d, *J*=8.1), 135.7 (d, *J*=7.1), 133.0 (d, *J*=2.2), 131.8 (d, *J*=8.4), 130.5 (s), 128.1 (d, *J*=12.2), 124.9 (s), 124.8 (s), 124.3 (s), 123.8 (d, *J*=9.6), 122.6 (d, *J*=10.7), 120.7 (d, *J*=6.0), 42.6 (d, *J*=4.1), 38.9 (d, *J*=91.2), 35.3 (s), 34.2 (d, *J*=1.3), 32.8 (d, *J*=16.2), 29.0 (d, *J*=2.3), 24.3 (d, *J*=14.5), 22.4 (s), 21.8 (s), 16.4 (s). **HRMS (ESI$^+$)** Calcd. for $C_{22}H_{27}O_2P$ [M+Na^+]: 377.1646, Found: 377.1655.

Preparation of optically pure R_P-3'.

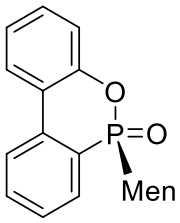


3/3' = 30:70 dr_p | R_P-**5**/S_P-**5'** = 25:75 dr_p 99% | S_P-**5'**, 44%, <1:99 dr_p | R_P-**3'**, 99%,>99:1 dr_p

The preparation of S_P-6-((-)-menthyl)dibenzo[c,e][1,2]-oxaphosphinine 6-oxide S_P-5'.

The solution of **3/3'** (300.0 mg, 0.771 mmol, 30:70 dr_P) in ethanol (15 mL) was heated with reflux at 80 °C for 8 hours. After removing solvent, **5/5'** was afforded (267.4 mg, 99%, 25:75 dr_P). The crude product was recrystallized from dichloromethane: petroleum ether = 1:1 at room temperature to afford S_P-**5'** (117.6 mg, 44%, <1:99 dr_P).

S_P-6-((-)-Menthyl)dibenzo[c,e][1,2]-oxaphosphinine 6-oxide (S_P-5').



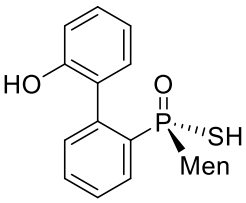
The pure S_P-**5'** was obtained as white solid, m.p. 126.2 – 128.3 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 40.34 (s); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.98 – 7.85 (m, 3H), 7.67 (t, *J*=7.6 Hz, 1H), 7.50 (tt, *J*= 8.9, 4.3 Hz, 1H), 7.38 (t, *J*= 7.6 Hz, 1H), 7.22 (dd, *J*=11.5, 8.1 Hz, 2H), 2.43 – 2.33 (m, 1H), 2.11 (td, *J*= 13.8, 2.9 Hz, 1H), 1.83 (d, *J*=3.1 Hz, 1H), 1.77 – 1.67 (m, 3H), 1.63 (s, 3H), 1.24 (dd, *J*=10.9, 4.2 Hz, 1H), 1.12 – 0.93 (m, 3H), 0.86 (d, *J*=6.8 Hz, 3H), 0.62 (d, *J*=6.8 Hz, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 149.4 (s), 135.6 (d, *J*=1.9), 132.7 (s), 130.5 (s), 130.4 (s), 128.3 (d, *J*=13.0), 126.1 – 125.8 (m), 124.9 (s), 124.3 (s), 123.7 (d, *J*=9.3), 122.5 (s), 120.4 (d, *J*=6.0), 43.4 (d, *J*=3.5), 40.8 (d, *J*=94.2), 35.7 (s), 34.4 (s), 33.1 (d, *J*=14.9), 28.8 (s), 24.7 (d, *J*=14.9), 22.4 (s), 21.5 (s), 15.2 (s). **HRMS (ESI$^+$)** Calcd. for $C_{22}H_{27}O_2P$ [M+Na^+]: 377.1646, Found: 377.1653.

The preparation of R_P-(2'-Hydroxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioic *S*-acid (R_P-3').

Under nitrogen atmosphere, S_P-**5'** (80 mg, 0.226 mmol) was dissolved in toluene (1 mL). Lawson's reagent (100.5 mg, 0.248 mmol) was added dropwise and the solution was heated at 100 °C with stirring for 3 hours. After removing toluene in vacuo, potassium hydroxide (29.8 mg, 0.452 mmol) and ethanol (5 mL) were added, and the solution was stirred at 50 °C for 5 hours. After the reaction was completed, the ethanol was removed. Diluted hydrochloric acid (7%) were added to adjust PH to 6-7. The mixture was extracted with dichloromethane (3×10 mL), washed with water (3×10 mL), dried over magnesium sulfate. After removing solvent, the residue was

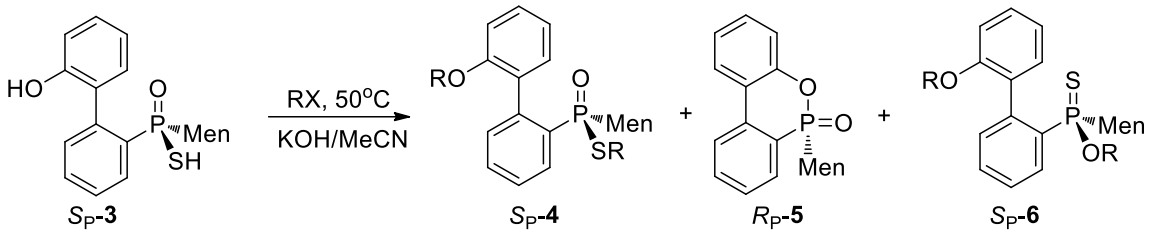
purified with preparative TLC (silica gel, ethyl acetate as eluent) to afford ***R*P-3'** (78.4 mg, 99%, >99:1 dr_P).

R_P-(2'-Hydroxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioic *S*-acid (R_P-3')



The optically pure ***R*P-3'** was obtained as a white solid; **^{31}P NMR (202 MHz, DMSO)** δ = 78.81 (s); **^{1}H NMR (500 MHz, DMSO)** δ = 12.27 (d, *J*=23.8 Hz, 1H), 8.65 – 8.52 (m, 1H), 7.42 – 7.28 (m, 2H), 7.25 – 7.13 (m, 1H), 6.94 (d, *J*=3.0 Hz, 1H), 6.87 (d, *J*=3.9 Hz, 2H), 6.78 (d, *J*=7.9 Hz, 1H), 5.75 (s, 1H), 2.73 – 2.59 (m, 1H), 1.56 (s, 1H), 1.41 (s, 2H), 1.06 (dd, *J*=22.5, 11.3 Hz, 1H), 0.82 (d, *J*=9.7 Hz, 1H), 0.72 (d, *J*=6.9 Hz, 4H), 0.61 – 0.52 (m, 5H), 0.36 (d, *J*=6.6 Hz, 3H); **^{13}C {^{1}H} NMR (126 MHz, DMSO)** δ = 156.2 (s), 141.1 (d, *J*=7.6), 140.7 – 140.0 (m), 136.0 (s), 133.2 (d, *J*=11.8), 131.3 (d, *J*=8.5), 130.9 (s), 129.2 (s), 128.9 (s), 126.3 (d, *J*=11.7), 121.7 (s), 119.9 (s), 43.36 (s), 42.9 (d, *J*=74.5), 37.3 (s), 34.9 (s), 32.6 (d, *J*=15.7), 27.1 (s), 24.4 (d, *J*=13.5), 23.3 (s), 22.3 (s), 15.7 (s).

Part 2. The alkylation of S_P-3 with alkyl halides.



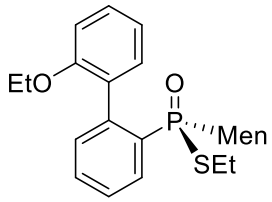
S_P-3 S_P-4 R_P-5 S_P-6

The preparation of optically pure S_P-4.

Typical procedure:

To the suspension of ***S_P*-3** (80.0 mg, 0.205 mmol) and potassium hydroxide (14.9 mg, 0.225 mmol) in acetonitrile (1 mL), was added bromoethane (61.3 μL, 0.822 mmol) and the mixture was stirred at 50 °C for 10 hours. After the reaction was completed, as monitored with TLC, saturated solution of ammonium chloride (10 mL) was added. The mixture was extracted with dichloromethane (3×10 mL), washed with water (3×10 mL), dried over magnesium sulfate. After removing the solvents, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent) to afford ***S_P*-4b** (76.3 mg, 83%, <1:99 dr_P and 80:20 dr_A).

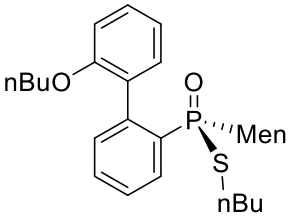
***S_P*-*S*-Ethyl-(2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphinothioate (*S_P*-4b)**



The crude ***S_P*-4b** was obtained from bromoethane, and the pure compound was obtained as a colorless oil (76.3 mg, 83%, <1:99 dr_P and 80:20 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 65.84 (s, 80%), 60.42 (s, 20%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.21 (ddd, *J*=14.4, 7.6, 1.0, 0.8H), 8.15 – 8.03 (m, 0.2H), 7.62 (dd, *J*=7.5, 1.6, 0.8H), 7.50 – 7.37 (m, 2H), 7.31 (dt, *J*=12.8, 3.4, 2H), 7.14 (dd, *J*=7.3, 1.5, 0.2H), 7.01 (t, *J*=7.4, 1H), 6.91 (d, *J*=8.2, 1H), 4.07 – 3.86 (m, 2H), 3.03 – 2.90 (m,1.6H), 2.88 – 2.73 (m, 0.4H), 2.65 – 2.53 (m, 0.8H), 2.52 – 2.41 (m, 0.2H), 1.94 (d, *J*=10.6, 0.2H), 1.58 (ddt, *J*=22.9, 20.3, 6.9, 4H), 1.39 (t, *J*=7.4, 2H), 1.28 (t, *J*=7.4, 1H), 1.25 – 1.12 (m, 4H), 1.09 – 0.87 (m, 1H), 0.76 (ddd, *J*=28.4, 16.2, 5.7, 8H), 0.51 (dd, *J*=11.8, 7.3, 0.8H), 0.33 (d, *J*=6.8, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.5 (d, *J*=108.1), 142.6 – 141.2 (m), 134.0 (d, *J*=18.8), 133.0 – 132.8 (m), 132.8 (d, *J*=10.3), 131.1 (s), 130.2 (d, *J*=2.6), 129.3 (d, *J*=5.0), 129.1 (d, *J*=3.3), 126.5 (d, *J*=12.0), 119.4 (d, *J*=85.0), 111.4 (d, *J*=126.7), 63.7 (d, *J*=43.6), 44.2 (dd, *J*=11.9, 3.7), 42.9 (d, *J*=66.8), 35.3 (s), 34.4 (d, *J*=1.1), 33.0 (d, *J*=16.6), 27.8 (d, *J*=2.0), 24.5 (d, *J*=14.7), 22.9 (d, *J*=2.0), 22.5 (s), 21.5 (d, *J*=8.2), 17.1 (d, *J*=3.7), 14.9 (d, *J*=3.2), 14.7 (d,

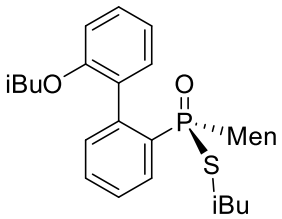
J=12.7). **HRMS (ESI$^+$)** Calcd. for $C_{26}H_{37}O_2PS$ [M+Na^+]: 467.2150, Found: 467.2169.

S_P-*S*-Butyl-(2'-butoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphinothioate (S_P-4c)



The crude ***S*$_P$-4c** was obtained from 1-bromobutane, and the pure compound was obtained as a colorless oil (37.7 mg, 58%, <1:99 dr_P and 80:20 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 66.10 (s, 80%), 60.54 (s, 20%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.26 – 8.13 (m, 0.8H), 8.09 (dd, *J*=13.1, 7.6, 0.2H), 7.63 (dd, *J*=7.5, 1.5, 0.8H), 7.51 – 7.38 (m, 2H), 7.33 (d, *J*=1.6, 2H), 7.15 (dd, *J*=7.3, 1.4, 0.2H), 7.01 (d, *J*=7.4, 1H), 6.91 (d, *J*=8.2, 1H), 3.89 (ddd, *J*=14.3, 7.2, 5.3, 2H), 3.03 – 2.89 (m, 1.6H), 2.76 (ddt, *J*=19.3, 14.8, 5.9, 0.4H), 2.63 – 2.53 (m, 0.8H), 2.53 – 2.45 (m, 0.2H), 1.98 (d, *J*=10.6, 0.2H), 1.70 (dt, *J*=15.1, 7.4, 2H), 1.66 – 1.50 (m, 6H), 1.50 – 1.41 (m, 2H), 1.40 – 1.19 (m, 3H), 1.16 (s, 1H), 0.92 (t, *J*=7.4, 3H), 0.88 – 0.83 (m, 3H), 0.83 – 0.77 (m, 4H), 0.77 – 0.72 (m, 2H), 0.69 (t, *J*=6.2, 3H), 0.53 (d, *J*=7.3,0.8H), 0.34 (t, *J*=6.3, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.6 (d, *J*=93.6), 141.5 (d, *J*=9.6), 134.0 (d, *J*=11.6), 133.3 (s), 133.0 (d, *J*=11.0), 132.7 (d, *J*=10.3), 131.1 – 130.4 (m), 130.1 (d, *J*=2.5), 129.5 – 128.9 (m), 126.5 (t, *J* =11.1), 119.4 (d, *J*=94.4), 111.4 (d, *J*=122.3), 67.8 (d, *J*=26.3), 44.3 (d, *J*=3.7), 43.0 (d, *J*=66.6), 35.4 (s), 34.4 (d, *J*=1.4), 33.6 (d, *J*=3.5), 33.0 (d, *J*=16.6), 31.2 (s), 28.1 (d, *J*=2.3), 27.8 (d, *J*=2.3), 24.6 (d, *J*=14.7), 22.5 (s), 21.9 (d, *J*=3.4), 21.5 (d, *J*=9.3), 19.1 (d, *J*=3.5), 15.0 (d, *J*=6.4), 13.8 (d, *J*=7.8), 13.6 (d, *J*=6.7). **HRMS (ESI$^+$)** Calcd. for $C_{30}H_{45}O_2PS$ [M+Na^+]: 523.2776, Found: 523.2792.

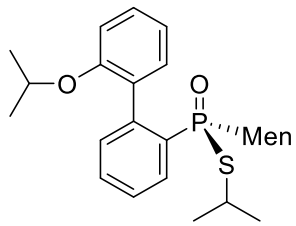
S_P-*S*-Isobutyl-(2'-isobutoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphinothioate (S_P-4d)



The crude ***S*$_P$-4d** was obtained from bromoisobutane, and the pure compound was obtained as white solid (39.8 mg, 62%, <1:99 dr_P and 80:20 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); m.p. 93.6 – 95.0 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 66.38 (s, 80%), 61.29 (s, 20%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.21 (dd, *J*=14.4, 7.6, 0.8H), 8.08 (dd, *J*=13.3, 7.8, 0.2H), 7.67 (dd, *J*=7.5, 1.4, 0.8H), 7.44 (dt, *J*=25.3, 7.5, 2H), 7.36 – 7.28 (m, 2H), 7.14 (d, *J*=7.3, 0.2H), 7.01 (t, *J*=7.5, 1H), 6.91 (t, *J*=8.3, 1H), 3.74 (dd, *J*=8.6, 5.3, 1H), 3.68 – 3.61 (m, 0.2H), 3.55 (t, *J*=8.5,0.8H), 2.86 (dtd, *J*=14.3, 12.3, 7.2, 1.6H), 2.70 (ddd, *J*=12.1, 9.1, 6.9, 0.4H), 2.64 – 2.50 (m, 1H), 1.95 (dd, *J*=13.4, 6.7, 1H), 1.87 – 1.71 (m, 2H), 1.67 – 1.43 (m, 4H), 1.16 (dd, *J*=12.7, 6.1, 1H), 1.04 (dd, *J*=6.6, 2.7, 5H), 0.95 (d, *J*=6.6, 1H), 0.85 (d,

J=6.8, 3H), 0.80 (dd, *J*=13.3, 6.8, 6H), 0.77 – 0.70 (m, 3H), 0.67 (d, *J*=6.4, 2H), 0.53 (dd, *J*=11.9, 7.3, 1H), 0.35 (dd, *J*=15.8, 6.8, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.6 (d, *J*=100.6), 141.5 (dd, *J*=16.2), 134.1 (d, *J*=7.3), 133.2 (d, *J*=10.9), 132.6 (d, *J*=10.5), 130.5 (s), 130.0 (d, *J*=2.5), 129.3 (d, *J*=6.1), 129.1 (d, *J*=3.3), 126.6 (d, *J*=12.0), 119.8 (s), 111.4 (d, *J*=124.9), 74.4 (d, *J*=45.0), 44.3 (d, *J*=3.7), 43.2 (s), 42.7 (s), 36.7 (d, *J*=2.2), 35.4 (s), 34.5 (s), 32.9 (d, *J*=16.7), 30.0 (d, *J*=3.5), 28.3 (d, *J*=23.8), 27.7 (d, *J*=2.1), 24.6 (d, *J*=14.7 Hz), 22.4 (s), 22.1 – 21.7 (m), 21.4 (s), 19.5 (s), 19.1 (d, *J*=11.2), 14.9 (s). **HRMS (ESI$^+$)** Calcd. for $C_{30}H_{45}O_2PS$ [M+Na$^+$]: 523.2776, Found: 523.2784.

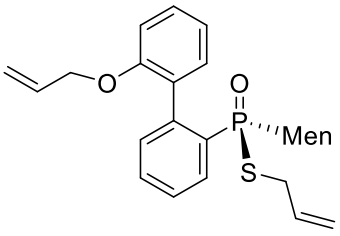
***S*$_P$-*S*-Isopropyl-(2'-isopropoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphinothioate (*S*$_P$-4e)**



The crude ***S*$_P$-4e** was obtained from bromoisopropane, and the pure compound was obtained as white solid (53.6 mg, 85%, <1:99 dr_P and 81:19 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); m.p. 65.6 – 66.9 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 65.88 (s, 81%), 59.13 (s, 19%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.23 (dd, *J*=14.4, 7.6, 0.8H), 8.12 (dd, *J*=13.1, 7.6, 0.2H), 7.63 (dd, *J*=7.5, 1.5, 0.81H), 7.50 – 7.36 (m, 2H), 7.33 – 7.27 (m, 1H), 7.25 (s, 1H), 7.17 (d, *J*=7.3, 0.19H), 6.96 (ddd, *J*=19.6, 13.2, 6.4, 2H), 4.49 (dd, *J*=12.0, 6.0, 0.19H), 3.64 (dd, *J*=6.9, 1.8, 0.81H), 3.53 – 3.39 (m, 0.19H), 2.65 (dd, *J*=13.4, 6.7, 1H), 2.04 (d, *J*=11.0, 0.19H), 1.64 (dddd, *J*=23.5, 20.0, 15.2, 6.4, 4H), 1.45 (dd, *J*=11.0, 6.9, 5H), 1.38 (d, *J*=6.9, 1H), 1.30 – 1.19 (m, 3H), 1.14 (dd, *J*=13.6, 3.8, 5H), 0.81 (dd, *J*=11.6, 7.0, 4H), 0.78 – 0.70 (m, 2H), 0.68 (d, *J*=6.4, 2H), 0.47 (dd, *J*=11.6, 7.7, 0.81H), 0.40 (d, *J*=6.8, 1H), 0.34 (d, *J*=6.7, 2H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 155.6 (d, *J*=96.5), 142.2 (d, *J*=9.3), 134.3 (d, *J*=17.2), 133.5 (s), 133.1 (s), 133.0 (d, *J*=3.4), 130.5 (d, *J*=2.7), 129.9 (d, *J*=2.4), 129.1 (s), 126.6 – 124.9 (m), 119.5 (d, *J*=88.1), 113.7 (d, *J*=64.3), 70.9 (d, *J*=51.1), 44.1 (d, *J*=3.6), 43.2 (s), 42.7 (s), 35.6 (d, *J*=2.0), 35.3 (s), 34.4 (d, *J*=1.0), 32.6 (d, *J*=16.5), 27.7 (d, *J*=1.6), 26.3 (d, *J*=9.7), 24.5 (d, *J*=14.7), 22.7 (s), 22.5 (d, *J*=7.5), 21.9 (d, *J*=23.0), 21.4 (d, *J*=10.7), 15.1 (d, *J*=45.1).

HRMS (ESI$^+$) Calcd. for $C_{28}H_{41}O_2PS$ [M+Na$^+$]: 495.2463, Found: 495.2466.

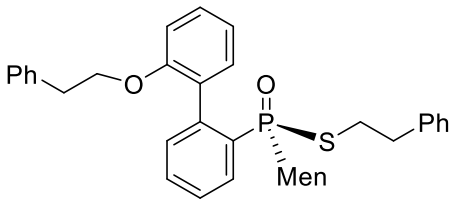
***S*$_P$-*S*-Allyl-(2'-(allyloxy)-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphinothioate (*S*$_P$-4f)**



The crude ***S*$_P$-4f** was obtained from allyl chloride, and the pure compound was obtained as a colorless oil (37.7 mg, 62%, <1:99

dr_P and 82:18 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 65.83 (s, 82%), 60.97 (s, 18%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.22 (dd, *J*=14.4, 7.7, 0.82H), 8.08 (dd, *J*=13.6, 7.8, 0.18H), 7.63 (d, *J*=7.4, 0.82H), 7.49 (s, 1H), 7.43 (s, 1H), 7.34 (t, *J*=7.8, 2H), 7.14 (d, *J*=7.3, 0.18H), 7.05 (d, *J*=7.5, 1H), 6.91 (d, *J*=8.2, 1H), 6.01 – 5.89 (m, 1H), 5.85 (dd, *J*=17.0, 10.8, 1H), 5.27 (d, *J*=16.9, 0.81H), 5.14 (s,0.19H), 5.12 – 5.05 (m, 2.4H), 5.03 (d, *J*=6.0, 0.6H), 4.56 – 4.38 (m, 2H), 3.64 – 3.54 (m, 2.4H), 3.48 – 3.38 (m, 0.6H), 2.63 – 2.51 (m, 0.82H), 2.49 – 2.39 (m, 0.18H), 2.00 – 1.81 (m, 0.18H), 1.69 – 1.46 (m, 4H), 1.16 (t, *J*=9.8, 1H), 0.87 (dd, *J*=14.9, 7.7, 1H), 0.83 – 0.70 (m, 6H), 0.64 (d, *J*=6.4, 2H), 0.52 (dd, *J*=11.7, 7.4, 0.82H), 0.33 (t, *J*=5.5, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.0 (d, *J*=142.9), 141.4 (d, *J*=9.7), 134.9 (d, *J*=3.7), 134.1 (s), 132.9 (d, *J*=7.4), 132.7 (s), 130.4 (d, *J*=2.5), 129.2 (d, *J*=26.8), 126.7 (d, *J*=12.0), 120.1 (s), 117.6 (d, *J*=10.2), 116.1 (d, *J*=5.6), 110.9 (s), 68.5 (d, *J*=119.7), 44.3 (t, *J*=5.4), 43.3 (s), 42.8 (s), 35.4 (s), 34.3 (d, *J*=1.4), 33.4 (d, *J*=15.7), 33.1 (s), 32.9 (s), 30.9 (d, *J*=2.1), 27.8 (d, *J*=2.3), 24.6 (s), 24.5 (s), 22.4 (s), 21.4 (d, *J*=4.4), 14.9 (d, *J*=3.5). **HRMS (ESI$^+$)** Calcd. for $C_{28}H_{37}O_2PS$ [M+Na^+]: 491.2150, Found: 491.2166.

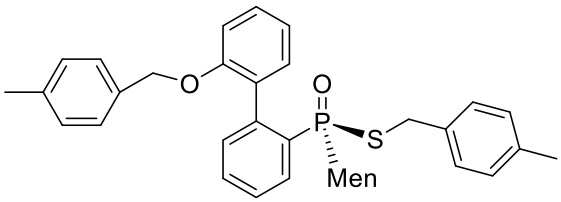
S_P-*S*-Phenethyl-((-)-menthyl) (2'-phenethoxy-[1,1'-biphenyl]-2-yl) phosphinothioate (S_P-4g)



The crude ***S_P*-4g** was obtained from (2-Bromoethyl) benzene, and the pure compound was obtained as a colorless oil (41.8mg, 54%, <1:99 dr_P and 80:20 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 66.57 (s, 80%), 61.34 (s, 20%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.18 – 8.11 (m, 0.8H), 8.08 (dd, *J*=13.5, 7.5, 0.2H), 7.65 – 7.60 (m, 0.8H), 7.41 (dd, *J*=6.1, 2.6, 2H), 7.37 – 7.27 (m, 3H), 7.23 (d, *J*=7.5, 4H), 7.14 (d, *J*=7.2, 2H), 7.08 (d, *J*=7.4, 0.2H), 7.02 (t, *J*=7.2, 2H), 6.96 – 6.86 (m, 2H), 4.09 (dd, *J*=9.6, 4.9, 2H), 3.29 – 3.14 (m, 2H), 3.06 (d, *J*=6.9, 1H), 2.98 (dd, *J*=29.3, 21.5, 1H), 2.89 – 2.77 (m, 2H), 2.62 (dd, *J*=13.3, 6.7, 0.8H), 2.57 – 2.50 (m, 0.2H), 1.97 (dd, *J*=20.5, 10.0, 0.2H), 1.70 – 1.51 (m, 5H), 1.21 (d, *J*=10.2, 1H), 0.81 (d, *J*=7.0, 3H), 0.74 (d, *J*=6.7, 2H), 0.70 (d, *J*=6.5, 3H), 0.54 (dd, *J*=11.9, 7.2, 0.8H), 0.38 (d, *J*=6.8, 1H), 0.35 (d, *J*=6.7, 2H); **^{13}C {^{1}H} NMR (126 MHz, CDCl3)** δ = 155.8 (s), 141.3 (d, *J*=9.3), 140.1 (d, *J*=3.4), 138.4 (d, *J*=68.9), 134.1 (d, *J*=5.4), 133.1 (s), 133.1 (d, *J*=3.0), 132.8 (s), 132.7 (s), 130.9 – 130.7 (m), 130.3 (d, *J*=2.5), 129.3 (s), 129.2 (s), 129.1 (s), 128.8 (s), 128.7 (s), 128.4 (s), 128.4 (s), 128.1 (s), 126.6 (s), 126.5 (s), 126.4 (d, *J*=6.2), 126.1 (s), 119.6 (d,

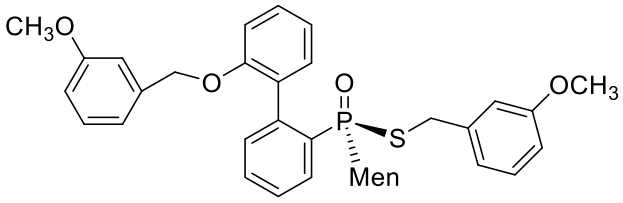
J=97.4), 111.1 (d, *J*=128.3), 68.7 (d, *J*=5.4), 44.3 (t, *J*=4.5), 43.3 (s), 42.8 (s), 37.8 (d, *J*=3.3), 35.7 (s), 35.4 (s), 34.6 – 34.2 (m), 33.1 (d, *J*=16.5), 29.5 (t, *J*=17.0), 27.8 (t, *J*=17.9), 24.6 (d, *J*=14.6), 22.5 (d, *J*=12.2), 21.5 (s), 15.0 (d, *J*=12.3). **HRMS (ESI$^+$)** Calcd. for $C_{38}H_{45}O_2PS$ [M+Na$^+$]: 619.2776, Found: 619.2789.

S_P-*S*-(4-Methylbenzyl)-((-)-menthyl)(2'-((4-methylbenzyl)oxy)-[1,1'-biphenyl]-2-yl) phosphinothioate (S_P-4j)



The crude ***S*$_P$-4j** was obtained from 4-methyl benzyl chloride, and the pure compound was obtained as a colorless oil (49.6 mg, 64%, <1:99 dr_P and 81:19 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 65.66 (s, 81%), 61.25 (s, 19%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.08 (dd, *J*=14.5, 7.7, 0.81H), 7.95 (dd, *J*=13.7, 7.7, 0.19H), 7.68 (d, *J*=7.5, 0.81H), 7.50 (t, *J*=7.5, 1H), 7.37 (dd, *J*=15.9, 7.8, 3H), 7.33 – 7.28 (m, 1H), 7.13 – 7.06 (m, 3H), 7.04 (d, *J*=8.0, 2H), 7.00 (dd, *J*=12.1, 8.1, 3H), 6.97 – 6.94 (m, 0.19H), 6.92 (d, *J*=7.7, 1H), 5.08 (d, *J*=12.0, 0.19H), 5.01 (d, *J*=11.9, 1H), 4.95 (d, *J*=11.9, 0.81H), 4.11 (dd, *J*=10.5, 8.4,1.6H), 3.90 (ddd, *J*=19.9, 12.5, 8.1, 0.4H), 2.71 – 2.60 (m, 0.81H), 2.56 – 2.48 (m,0.19H), 2.27 (dd, *J*=21.8, 9.8, 6H), 2.01 (d, *J*=10.8, 0.19H), 1.69 – 1.52 (m, 3H), 1.46 (d, *J*=10.3, 1H), 1.10 (t, *J*=9.7, 1H), 1.10 (t, *J*=9.7, 1H), 0.92 – 0.85 (m, 1H), 0.79 (t, *J*=9.0, 3H), 0.73 (d, *J*=6.6, 1H), 0.66 (dd, *J*=26.2, 12.0, 2H), 0.47 – 0.39 (m, 0.81H), 0.37 (d, *J*=6.7, 2H), 0.31 (d, *J*=5.7, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.2 (d, *J*=154.1), 141.6 (dd, *J*=10.9, 6.0), 137.1 (s), 136.9 (s), 135.4 (d, *J*=4.5), 133.9 (d, *J*=6.5), 133.7 (s), 133.0 (d, *J*=10.3), 132.8 (d, *J*=11.0), 130.6 (d, *J*=5.0), 130.3 (d, *J*=2.4), 129.6 (d, *J*=2.9), 129.4 (s), 129.2 (s), 129.2 (s), 129.1 (s), 128.9 (s), 128.8 (s), 126.9 (s), 126.7 (s), 126.6 (s), 126.2 (s), 120.4 (s), 111.4 (s), 69.8 (d, *J*=83.6), 44.3 (d, *J*=3.9), 43.3 (s), 42.8 (s), 35.4 (s), 34.3 (s), 32.9 (d, *J*=16.6), 31.8 (s), 27.9 (dd, *J*=24.8, 2.2), 24.7 (d, *J*=9.5), 22.0 (s), 21.4 (s), 21.1 (d, *J*=5.5), 14.9 (s). **HRMS (ESI$^+$)** Calcd. for $C_{38}H_{45}O_2PS$ [M+Na$^+$]: 619.2776, Found: 619.2784.

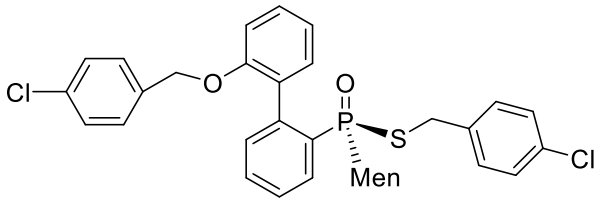
S_P-*S*-(3-Methoxybenzyl)-((-)-menthyl)(2'-((3-methoxybenzyl)oxy)-[1,1'-biphenyl]-2-yl) phosphinothioate (S_P-4k)



The crude ***S*P-4k** was obtained from 3-methoxybenzyl chloride, and the pure compound was obtained as a colorless oil (27.7 mg, 34%, <1:99 dr_P and 83:17 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 65.66 (s, 83%), 61.34 (s, 17%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.14 – 7.93 (m, 1H), 7.67 (dd, *J*=7.5, 1.6, 0.83H), 7.53 – 7.45 (m, 1H), 7.36 (dddd, *J*=18.8, 11.0, 5.5, 3.5, 3H), 7.21 – 7.06 (m, 3H), 7.02 (d, *J*=8.1, 1H), 6.99 – 6.97 (m, 0.17H), 6.95 (d, *J*=7.7, 1H), 6.91 (d, *J*=2.1, 1H), 6.79 – 6.68 (m, 3H), 6.60 (s, 1H), 5.04 (ddd, *J*=44.7, 27.6, 12.4, 2H), 4.11 (dd, *J*=20.1, 10.0,1.6H), 3.99 – 3.81 (m, 0.4H), 3.70 (d, *J*=16.8, 3H), 3.63 (d, *J*=7.4, 3H), 2.69 – 2.59 (m, 0.83H), 2.53 – 2.43 (m, 0.17H), 2.03 – 1.98 (m, 0.17H), 1.71 – 1.54 (m, 6H), 1.45 (d, *J*=5.7, 1H), 1.11 (s, 1H), 0.79 (dd, *J*=10.6, 7.0, 3H), 0.74 (d, *J*=6.5, 1H), 0.62 (s, 1H), 0.49 – 0.38 (m, 0.83H), 0.35 (d, *J*=6.7, 2H), 0.30 (d, *J*=6.8, 1H), 0.26 (d, *J*=5.6, 2H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 159.7 (d, *J*=2.4), 155.5 (s), 141.7 (d, *J*=9.1), 140.0 (s), 138.5 (s), 134.0 (s), 133.2 (s), 133.1 (s), 132.8 (s), 132.7 (s), 130.4 (d, *J*=2.4), 129.6 (s), 129.5 (d, *J*=2.1), 129.5 (s), 129.3 (s), 126.6 (d, *J*=12.1), 121.6 (s), 120.5 (s), 118.2 (s), 114.4 (s), 113.6 (s), 113.4 (s), 111.2 (s), 110.8 (s), 69.5 (d, *J*=106.7), 56.7 – 53.1 (m), 44.3 (d, *J*=4.0), 43.4 (s), 42.8 (s), 35.5 (s), 34.3 (s), 33.1 (d, *J*=16.6), 32.08 (d, *J*=1.6), 29.73 (s), 27.8 (d, *J*=2.0), 24.6 (d, *J*=14.8), 21.9 (s), 21.4 (s), 14.9 (d, *J*=6.1).

HRMS (ESI$^+$) Calcd. for $C_{38}H_{45}O_4PS$ [M+Na^+]: 651.2674, Found: 651.2684.

***S*P-*S*-(4-Chlorobenzyl)-(2'-((4-chlorobenzyl)oxy)-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate (*S*P-4l)**



The crude ***S*P-4l** was obtained from 4-chlorobenzyl chloride, and the pure compound was obtained as a colorless oil (40.5 mg, 49%, <1:99 dr_P and 76:24 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 65.66 (s, 76%), 62.05 (s, 24%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.99 (ddd, *J*=14.4, 8.2, 1.2, 0.76H), 7.87 – 7.81 (m, 0.24H), 7.65 (dd, *J*=7.5, 1.7, 0.76H), 7.50 (dd, *J*=7.5, 1.4, 1H), 7.36 (ddd, *J*=7.7, 4.8, 1.2, 2H), 7.29 (d, *J*=8.5, 2H), 7.24 – 7.18 (m, 3H), 7.16 (d, *J*=8.5, 0.24H), 7.10 (d, *J*=7.5, 2H), 7.06 (d, *J*=8.5, 1H), 7.00 (dt, *J*=8.2, 2.8, 3H), 4.97 (d, *J*=18.2, 2H),

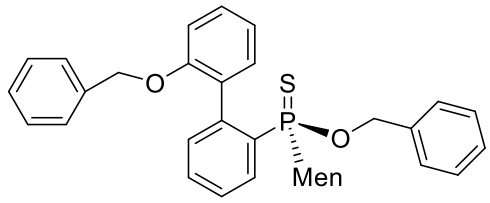
4.13 – 4.06 (m, 1.48H), 3.86 (dd, *J*=9.0, 7.7, 0.52H), 2.64 – 2.55 (m, 0.76H), 2.53 – 2.44 (m, 0.24H), 2.04 – 1.97 (m, 0.24H), 1.69 – 1.52 (m, 6H), 1.47 (d, *J*=6.1, 1H), 1.15 – 1.01 (m, 1H), 0.80 (d, *J*=6.9, 1H), 0.76 (t, *J*=7.4, 3H), 0.63 (t, *J*=9.9, 1H), 0.48 – 0.39 (m,0.76H), 0.35 (d, *J*=6.7, 2H), 0.30 (d, *J*=5.7, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 155.4 (s), 141.5 (d, *J*=9.2), 137.3 (d, *J*=3.6), 135.4 (s), 133.9 (s), 133.5 (s), 133.3 (s), 133.1 (s), 133.0 (s), 132.9 (s), 132.7 (d, *J*=11.0), 130.7 (s), 130.5 (s), 130.5 (d, *J*=2.8), 129.7 (d, *J*=3.3), 129.5 (d, *J*=6.4), 128.6 (s), 128.5 (s), 128.4 (d, *J*=13.2), 128.3 (s), 127.5 (s), 126.7 (d, *J*=12.3), 120.9 (s), 111.7 (s), 69.3 (s), 44.3 (d, *J*=3.9), 43.1 (d, *J*=65.9), 35.4 (s), 34.4 (s), 33.0 (d, *J*=16.6), 31.3 (d, *J*=2.1), 27.9 (d, *J*=2.3), 24.6 (d, *J*=14.7), 22.0 (s), 21.5 (s), 14.9 (d, *J*=5.4). **HRMS (ESI$^+$)** Calcd. for $C_{36}H_{39}Cl_2O_2PS$ [M+Na$^+$]: 659.1683, Found: 659.1693.

The reaction of *S*$_P$-3 with benzyl bromide.

Typical procedure:

To the solution of ***S*$_P$-3** (80.0 mg, 0.205 mmol) and potassium hydroxide (14.9 mg, 0.225 mmol) in acetonitrile (1 mL), was added benzyl bromide (100.4 μL, 0.822 mmol) and the mixture was stirred at 50 °C for 8 hours. After the reaction was completed, as monitored with TLC, saturated solution of ammonium chloride (10 mL) was added. The mixture was extracted with dichloromethane (3×10 mL), washed with water (3×10 mL), dried over magnesium sulfate. After removing the solvents, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent) to afford ***S*$_P$-6h** (63.7 mg, 70%, <1:99 dr$_P$ and 68:32 dr$_A$).

***S*$_P$-*O*-Benzyl-(2'-(Benzyloxy)-[1,1'-biphenyl]-2-yl)((-)-Menthyl)phosphinothioate (*S*$_P$-6h)**

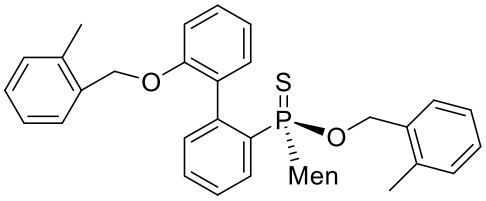


The crude ***S*$_P$-6h** was obtained from benzyl bromide, and the pure compound was obtained as a colorless oil (63.7 mg, 70%, <1:99 dr$_P$ and 68:32 dr$_A$) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 50.07 (s, 68%), 46.43 (s, 32%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.95 – 7.85 (m, 0.32H), 7.80 – 7.71 (m, 0.68H), 7.65 (d, *J*=7.4,0.68H), 7.52 (d, *J*=7.6, 1H), 7.38 (td, *J*=16.2, 8.3, 6H), 7.33 – 7.27 (m, 2H), 7.25 – 7.17 (m, 4H), 7.08 (t, *J*=7.7, 2H), 6.96 (d, *J*=8.0, 1H), 6.86 (t, *J*=7.4, 0.32H), 5.23 (dd, *J*=12.0, 7.8, 0.68H), 5.08 (s, 0.68H), 5.06 – 5.03 (m, 0.64H), 4.93 (dd, *J*=59.8, 12.2, 1.36H), 4.76 – 4.71 (m, 0.32H), 4.70 (s, 0.32H), 2.53 (s, 0.68H), 2.32 (s, 0.32H), 1.68 (d, *J*=6.6, 1H), 1.62 – 1.42 (m, 2H), 1.41 –

1.23 (m, 3H), 0.71 (dd, *J*=36.7, 6.7, 7H), 0.37 (dd, *J*=15.3, 5.9, 4H), 0.21 (d, *J*=6.8, 1H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 155.9 (d, *J*=75.2), 141.6 (d, *J*=11.9), 137.5 (d, *J*=6.1), 137.4 (s), 136.9 (s), 133.4 (s), 132.7 (d, *J*=7.0), 132.4 (d, *J*=11.7), 131.7 (d, *J*=6.6), 131.1 (s), 130.5 (d, *J*=2.0), 129.7 (d, *J*=3.1), 129.2 (d, *J*=4.5), 128.4 (s), 128.3 (s), 128.2 (s), 127.9 (d, *J*=5.4), 127.6 (s), 127.4 (s), 126.8 (s), 126.7 (d, *J*=6.5), 126.1 (s), 120.1 (d, *J*=58.8), 111.9 (d, *J*=114.1), 69.7 (d, *J*=84.1), 65.8 (d, *J*=6.0), 42.9 (d, *J*=4.4), 40.3 (d, *J*=94.4), 35.7 (d, *J*=1.5), 34.4 (d, *J*=4.1), 32.9 (d, *J*=15.5), 28.2 (d, *J*=1.6), 24.6 (d, *J*=14.5), 22.3 (d, *J*=50.6), 21.4 (d, *J*=24.8), 14.9 (d, *J*=31.1).

HRMS (ESI$^+$) Calcd. for $C_{36}H_{41}O_2PS$ [M+Na$^+$]: 591.2463, Found: 591.2447.

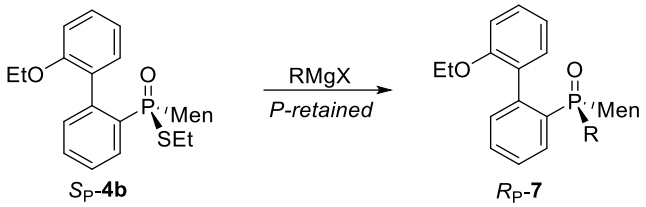
***S*$_P$-*O*-(2-Methylbenzyl)-((-)-menthyl)(2'-((2-methylbenzyl)oxy)-[1,1'-biphenyl]-2-yl)phosphin othioate (*S*$_P$-6i)**



The crude ***S*$_P$-6i** was obtained from 2-methylbenzyl bromide, and the pure compound was obtained as a colorless oil (19.3 mg, 25%, <1:99 dr_P and 71:29 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 49.38 (s, 71%), 46.26 (s, 29%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.89 (dd, *J*=11.4, 7.8, 0.29H), 7.79 (dd, *J*=10.8, 7.8, 0.71H), 7.61 (dd, *J*=7.5, 1.6, 0.71H), 7.54 – 7.47 (m, 1H), 7.44 – 7.38 (m, 1H), 7.35 (ddd, *J*=17.1, 8.2, 1.2, 3H), 7.23 – 7.17 (m, 2H), 7.17 – 7.12 (m, 2H), 7.11 – 7.05 (m, 2H), 7.00 (dd, *J*=11.6, 5.1, 2H), 6.89 (d, *J*=7.6, 1H), 6.85 (t, *J*=7.4, 0.29H), 5.18 (dd, *J*=12.4, 6.4, 0.58H), 5.01 (ddd, *J*=20.8, 13.0, 5.9, 1.42H), 4.86 (d, *J*=12.4, 0.58H), 4.70 (dd, *J*=12.2, 3.5, 1.42H), 2.49 (dt, *J*=6.6, 4.2, 0.71H), 2.30 (s, 0.29H), 2.23 (d, *J*=8.1, 3H), 2.19 (s, 1H), 2.13 (s, 2H), 1.76 (dd, *J*=6.3, 4.4, 1H), 1.55 (dddd, *J*=25.4, 22.2, 12.6, 7.4, 2H), 1.44 – 1.22 (m, 3H), 0.86 – 0.58 (m, 7H), 0.46 – 0.33 (m, 4H), 0.18 (d, *J*=6.8, 1H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.0 (d, *J*=51.1), 142.1 (dd, *J*=85.3, 10.7), 136.5 (d, *J*=32.6), 135.6 (d, *J*=6.9), 134.9 (s), 134.9 (s), 133.1 (s), 132.4 (d, *J*=11.6), 132.0 (d, *J*=7.0), 131.2 (s), 130.6 (d, *J*=2.0), 130.1 (s), 129.9 (s), 129.9 (d, *J*=9.2), 129.2 (d, *J*=6.1), 128.6 (s), 128.0 (d, *J*=2.6), 127.9 (s), 127.4 (s), 126.8 (d, *J*=10.8), 126.5 (s), 125.9 (s), 125.8 (s), 120.1 (d, *J*=55.2), 111.9 (d, *J*=75.0), 68.2 (d, *J*=111.5), 63.7 (dd, *J*=52.8, 6.5), 43.1 (d, *J*=4.0), 41.0 (s), 40.2 (s), 35.7 (d, *J*=2.1), 34.5 (s), 32.9 (d, *J*=15.3), 28.3 (d, *J*=1.7), 24.7 (d, *J*=14.7), 22.2 (s), 21.4 (d, *J*=18.4), 18.8 (dd, *J*=15.0, 5.2), 14.9 (d, *J*= 40.1).

HRMS (ESI$^+$) Calcd. for $C_{38}H_{45}O_2PS$ [M+Na$^+$]: 619.2776, Found: 619.2782.

Part 3. Cleavage of P-S bond of S_P-4b bond with Grignard reagents.

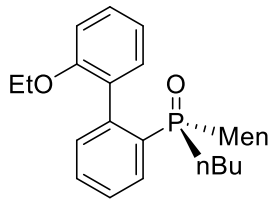


S_P-**4b** R_P-**7**

Typical procedure:

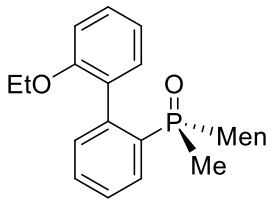
The solution of $\boldsymbol{S_P}$**-4b** (50 mg, 0.112 mmol) was dissolved in THF (1 mL) under N_2, and the *n*-butyl magnesium bromide (0.8 M solution in THF, 0.29 mL, 0.23 mmol) was added dropwise at 0 °C. The solution was stirred at 50 °C for 8 hours, and monitored with NMR spectrum, which indicated the reaction didn't occur. Toluene (1 mL) was added and the solution was stirred at 90 °C for 12 hours. Saturated solution of ammonium chloride (5 mL) was added. The mixture was extracted with dichloromethane (3×5 mL), washed with water (3×5 mL), dried over magnesium sulfate. After removing solvents, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent) to afford $\boldsymbol{R_P}$**-7c** (13.8 mg, 28.9%, >99:1 dr_P and 51:49 dr_A).

R_P-Butyl (2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphine oxide (R_P-7c)



The crude $\boldsymbol{R_P}$**-7c** was obtained from n-butyl magnesium bromide, and the pure compound was obtained as white solid (13.8 mg, 29%, >99:1 dr_P and 51:49 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent), The compound had the same spectrum to that obtained as below.

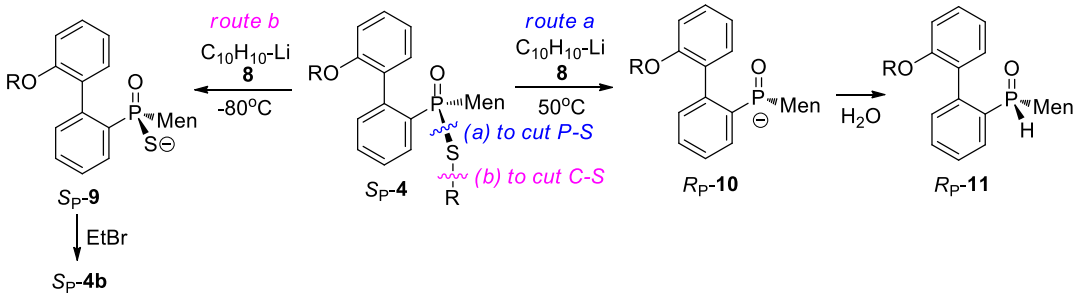
R_P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl) (methyl) ((-)-menthyl) phosphine oxide (R_P-7a)



The crude $\boldsymbol{R_P}$**-7a** was obtained from methyl magnesium iodide, and the pure compound was obtained as white solid (13.2 mg, 29.7%, >99:1 dr_P and 69:31 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent), The compound had the same spectrum to that obtained as below.

Part 4. Exploring the mechanism of cleavage of P-S/C-S bonds

A. The regio-selective cleavage of P-S or C-S bond of biphenylphosphinothioate.



Preparations of naphthalene-lithium solution 8.

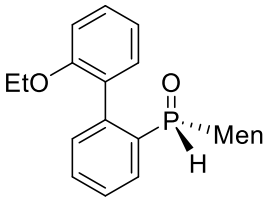
Naphthalene:Li = 1.5:1, The naphthalene-lithium solution **8** was prepared from stirring of naphthalene (961.4 mg, 7.5 mmol) and lithium (34.7 mg, 5 mmol) in THF (5 mL) at room temperature for 3 hours, as a 1 M solution based on lithium.

Naphthalene:Li = 0.9:1, The naphthalene-lithium solution **8** was prepared from stirring of naphthalene (691.2 mg, 5.4 mmol) and lithium (41.6 mg, 6 mmol) in THF (5 mL) at room temperature for 3 hours, as a 1M solution based on naphthalene.

Typical procedure (for entry 6 of Table 2):

S*P-4b** (50 mg, 0.11 mmol) was dissolved in THF (1 ml), and excess naphthalene of lithium-naphthalene **8** (naphthalene:Li = 1.5:1, 0.23 ml, 1 M, 0.23 mmol) was added at 50 °C for 0.5 h. After cooling, the sample was analyzed with NMR spectrum. Two peaks at 36.63 (50%) and 33.87 ppm (49%) were observed, which were assigned as ***R*P-11**. The conversion of ***S*P-4b** was 99% and the ratio of ***S*P-9**/R*P-10** was 1:99.

(*R*P)-(-)-Menthyl (2'-ethoxy-[1,1'-biphenyl]-2-yl)phosphine oxide (*R*P-11)



***R*P-11** was obtained as white solid (41.9 mg, 99%, >99:1 dr_P and 52:48 dr_A) from preparative TLC (silica gel, hexane/ethyl acetate = 1/3 as eluent), m.p. 100.3 – 102.0 °C; **^{31}P NMR (162 MHz, $CDCl_3$)** δ = 36.63 (s, 52%), 33.87 (s, 48%); **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.14 – 7.96 (m, 1H), 7.82 (s, 0.24H), 7.64 (s, 0.26H), 7.52 (dd, *J*=18.0, 6.8, 2H), 7.36 (t, *J*=7.7, 1H), 7.30 – 7.11 (m, 2H), 6.99 (dt, *J*=17.7, 8.0, 2H), 6.63 (s, 0.24H), 6.44 (s, 0.26H), 4.09 – 3.87 (m, 2H), 2.17 – 1.96 (m, 1H), 1.58 (d, *J*=7.7, 3H), 1.45 (s, 1H), 1.25 (t, *J*=7.0, 3H), 1.09 – 0.90 (m, 2H), 0.84 (d, *J*=6.3, 2H), 0.80 (d, *J*=6.7, 3H), 0.73 (d, *J*=4.5, 4H), 0.30 (t, *J*=6.3, 3H); **^{13}C {^{1}H} NMR**

(101 MHz, $CDCl_3$) δ = 155.6 (d, *J*=63.3), 141.5 – 140.1 (m), 131.5 (s), 131.5 (s), 131.2 (d, *J*=11.8), 130.7 (s), 130.5 (d, *J*=9.5), 129.8 (s), 128.6 (s), 127.3 (t, *J*=9.9), 120.5 (d, *J*=36.9), 111.9 (d, *J*=26.0), 63.7 (d, *J*=43.8), 42.5 (d, *J*=3.4), 39.9 (d, *J*=19.9), 37.7 (s), 36.9 (s), 33.9 (s), 33.4 (dd, *J* = 51.9, 16.2), 28.7 (d, *J*=28.3), 24.3 (dd, *J*=24.8, 12.7), 22.2 (d, *J*=10.3), 21.5 (d, *J*=12.0), 14.8 (d, *J*=41.5). **HRMS (ESI^+)** Calcd for $C_{24}H_{34}O_2P$ $[M+H^+]$: 385.2296, Found: 385.2318.

Entry 1 of Table 2: The mixture of ***S*P-4b** (50 mg, 0.11 mmol) and lithium (1.52 mg, 0.23 mmol) was stirred in THF (1 mL) at 0 °C to room temperature for 6 hours. Five peaks located at 98.57 (***S*P-9**, 27%), 66.33 (36%)/60.98 (7%) (***S*P-4b**), and 38.87 (16%)/34.82 (14%) ppm (***R*P-11**). The conversion of ***S*P-4b** was 57% and the ratio of ***S*P-9**/ ***R*P-10** was 46:54.

Entry 2 of Table 2: The mixture of ***S*P-4b** (50 mg, 0.11 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.23 ml, 1 M, 0.23 mmol) was stirred at room temperature for 5 hours. Three peaks were observed to located at 98.60 (58%), 36.46 (22%)/34.10 (20%) ppm. The conversion of ***S*P-4b** was 99% and the ratio of ***S*P-9**/ ***R*P-10** was 58:42.

Entry 3 of Table 2: The mixture of ***S*P-4b** (50 mg, 0.11 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.23 ml, 1 M, 0.23 mmol) was stirred at 50 °C for 1 hours. Five peaks were observed to located at 97.89 (50%), 65.66 (9%) /60.17 (2%), 36.27 (19%)/33.80 (20%) ppm. The conversion of ***S*P-4b** was 89% and ratio of ***S*P-9**/ ***R*P-10** was 44:56.

Entry 4 of Table 2: The mixture of ***S*P-4b** (50 mg, 0.11 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.23 ml, 1 M, 0.23 mmol) was stirred at -80 °C for 8 hours. The peaks were observed to located at 98.64 (31%), 67.63 (27%) /60.47 (6%), 52.37 (unknown product, 26%), 48.96 ppm (unknown product, 11%). The conversion of ***S*P-4b** was 69% and the ratio ***S*P-9**/ ***R*P-10** was 99:1.

Entry 5 of Table 2: The mixture of ***S*P-4b** (50 mg, 0.11 mmol) and lithium-naphthalene **8** (naphthalene:Li = 1.5:1, 0.23 ml, 1 M, 0.23 mmol) was stirred at room temperature for 3 hours. Three peaks were observed, 97.81 (6%), 36.70 (48%)/33.62 (46%) ppm. The conversion of ***S*P-4b** was 99% and the ratio of ***S*P-9**/ ***R*P-10** was 6:94.

Entry 7 of Table 2: The mixture of ***S*P-4b** (50 mg, 0.11 mmol) and lithium-naphthalene **8** (naphthalene:Li = 1.5:1, 0.23 ml, 1 M, 0.23 mmol) was stirred at -80 °C for 5 hours. Five peaks were observed, 97.97 (38%), 65.56 (12%)/60.06 (4%), 52.49 (31%)/49.29 (16%) ppm (the peaks of 52.49/49.29 was speculated to be phosphoric acid, but was not confirmed). The conversion of

S*P-4b** was 84% and the ratio of ***S*P-9**/R*P-10** was 99:1.

Entry 8 of Table 2:. The mixture of ***S*P-4e** (50 mg, 0.11 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.22 ml, 1 M, 0.22 mmol) was stirred at -80 °C for 8 hours. Four peaks were observed, 97.97 (52%), 67.89 (unknown product, 9%), 66.08 (33%)/59.54 (6%) ppm (***S*P-4e**). The conversion of ***S*P-4e** was 60% and the ratio of ***S*P-9**/***R*P-10** was 99:1.

Entry 9 of Table 2: The mixture of ***S*P-4j** (50 mg, 0.08 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.16 ml, 1 M, 0.16 mmol) was stirred at -80 °C for 8 hours. Four peaks were observed, 98.69 (57%), 53.39 (unknown product, 21%), 49.78 (unknown product, 10%), 44.83 ppm (unknown product, 12%). The conversion of ***S*P-4j** was 99% and the ratio of ***S*P-9**/***R*P-10** was 99:1.

Entry 10 of Table 2: The mixture of ***S*P-4g** (50 mg, 0.08 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.16 ml, 1 M, 0.16 mmol) was stirred at -80 °C for 8 hours. Four peaks were observed, 98.89 (51%), 51.74 (unknown product, 15%), 50.71 (unknown product, 17%), 43.46 ppm (16%). The conversion of ***S*P-4g** was 99% and the ratio of ***S*P-9**/***R*P-10** was 99:1.

Entry 11 of Table 2: The mixture of ***S*P-4m** (50 mg, 0.10 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.21 ml, 1 M, 0.21 mmol) was stirred at room temperature for 3 hours. Three peaks were observed, 39.21 (unknown, 2%), 35.75 (52%)/32.48 (46%) ppm. The conversion of ***S*P-4m** was 98% and the ratio of ***S*P-9**/***R*P-10** was 1:99.

Entry 12 of Table 2: The mixture of ***S*P-4m** (50 mg, 0.10 mmol) and lithium-naphthalene **8** (naphthalene:Li = 1.5:1, 0.21 ml, 1 M, 0.21 mmol) was stirred at room temperature for 3 hours. Four peaks were observed, 62.70 (5%)/58.55 (2%) (***S*P-4m**), 37.04 (48%)/33.99 (45%) ppm. The conversion of ***S*P-4m** was 93% and the ratio of ***S*P-9**/***R*P-10** was 1:99.

Entry 13 of Table 2: The mixture of ***S*P-4m** (50 mg, 0.10 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.21 ml, 1 M, 0.21 mmol) was stirred at -80 °C for 8 hours. Six peaks were observed, 62.12 (3%)/57.94 (1%), 52.17 (67%)/49.34 (28%), 36.39 (1%)/33.21 (1%) ppm. The conversion of ***S*P-4m** was 96% and two unidentified peaks at 52.17 and 49.34 ppm were observed.

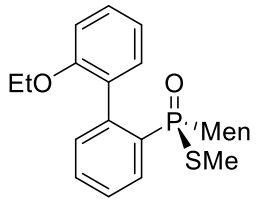
B. To capture *S*P-9 with the formation of

***S*P-*S*-methyl-(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate.**

***S*P-4b** (50 mg, 0.11 mmol) was dissolved in THF (1 ml) and the solution was cooed to -80 °C.

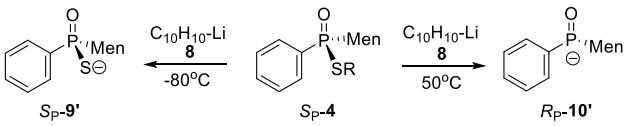
Lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.23 ml, 1 M, 0.23 mmol) was added and the mixture was stirred for 5 h. After the solution was warmed to room temperature, methyl iodide (14.3 μL, 0.23 mmol) was added with stirring for 3 h. Saturated solution of ammonium chloride (5 mL) was added. The mixture was extracted with dichloromethane (3×5 mL), washed with water (3×5 mL), dried over magnesium sulfate. After removing the solvents, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent) to afford S_P-*S*-methyl-(2'-mthoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate (21.3 mg, 45%, <1:99 dr_P and 77:23 dr_A).

S_P-*S*-Methyl-(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate S_P-4a



The pure **S_P-4a** was obtained as a colorless oil (21.3 mg, 45%, <1:99 dr_P and 77:23 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 3/1 as eluent); **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 65.79 (s, 77%), 61.18 (s, 23%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.15 (dd, *J*=14.2, 7.6 Hz, 0.77H), 8.05 (dd, *J*=13.3, 7.7 Hz, 0.23H), 7.60 (dd, *J*=7.5, 1.6 Hz, 0.77H), 7.52 – 7.44 (m, 1H), 7.41 (dd, *J*=10.6, 4.6 Hz, 1H), 7.32 (dt, *J*=12.5, 3.2 Hz, 2H), 7.13 (dd, *J*=7.3, 1.4 Hz, 0.23H), 7.01 (t, *J*=7.4 Hz, 1H), 6.92 (dd, *J*=8.2, 3.8 Hz, 1H), 4.08 – 3.88 (m, 2H), 2.55 (dt, *J*=13.4, 6.7 Hz, 0.77H), 2.49 – 2.39 (m, 0.23H), 2.33 (d, *J*=10.2 Hz, 2.31H), 2.19 (d, *J*=10.5 Hz, 0.69H), 1.60 (dd, *J*=11.2, 5.3 Hz, 4H), 1.20 (dd, *J*=8.9, 5.0 Hz, 5H), 0.88 – 0.78 (m, 4H), 0.71 (d, *J*=6.5 Hz, 4H), 0.55 (s, 1H), 0.33 (dd, *J*= 9.6, 6.9 Hz, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.5 (d, *J*=97.8), 141.9 (t, *J*=32.1), 133.9 (s), 133.0 (s), 132.9 (s), 132.6 (d, *J*=4.7), 132.5 (s), 130.3 (d, *J*=2.6), 129.3 (d, *J*=9.2), 126.7 (d, *J*=11.9), 119.5 (d, *J*=81.2), 111.4 (d, *J*=119.3), 63.7 (d, *J*=46.3), 44.3 (d, *J*=3.6), 43.3 (s), 42.7 (s), 35.4 (s), 34.4 (d, *J*=9.6), 33.0 (d, *J*=16.6), 27.9 (d, *J*=2.4), 24.6 (d, *J*=14.7), 22.4 (s), 21.5 (d, *J*=5.7), 14.9 (s), 14.7 (s), 10.0 (d, *J*=2.7). **HRMS (ESI$^+$)** Calcd. for $C_{25}H_{35}O_2PS[M+Na^+]$: 453.1993, Found: 453.2007.

C. The regio-selective cleavage of P-S or C-S bond of phenyl phosphinothioates.



S_P-**9'** S_P-**4** R_P-**10'**

entry	R of S_P-**4**	Naph. (equiv)	Temp.	Conversion of S_P-**4** % (S_P-**9'** /R_P-**10'**)
1	**4n**, Me	0.9	-80 °C	94 (99:1) [a]
2	**4o**, Et	0.9	-80 °C	94 (99:1) [a,b]
3	**4p**, Ph	0.9	-80 °C	86 [a]
4	**4n**, Me	1.5	50 °C	99 (42:58)
5	**4o**, Et	1.5	50 °C	99 (47:53)
6	**4p**, Ph	1.5	50 °C	98 (9:91) [a]

[a] Major byproduct was observed at 49 ppm on ^{31}P NMR spectrum whose structure was not confirmed. [b] **4o** was used in 67:33 dr, and **9'** was detected as two stereoisomers in the corresponding ratio.

Entry 1 of Scheme 6: The mixture of ***S*P-4n** (50 mg, 0.16 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.33 ml, 1 M, 0.33 mmol) was stirred -80 °C for 8 hours. Four peaks were observed to located at 90.97 (39%) (***S*P-9'**), 62.12 (6%) (***S*P-4n**), 49.91 (62%, unconfirmed), 47.68 (3%) ppm. The conversion of ***S*P-4n** was 94% and the ratio of ***S*P-9'**/ ***R*P-10'** was 99:1.

Entry 2 of Scheme 6: The mixture of **4o**/**4o'** (***S*P**/***R*P** = 67:33, 50 mg, 0.15 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.31 ml, 1 M, 0.31 mmol) was stirred -80 °C for 8 hours. Six peaks were observed to located at 90.99 (32%)/87.78 (9%) (***S*P-9'**/***R*P-9'**=78:22), 62.08 (4%)/60.93(2%) (**4o**/**4o'**), 52.10 (4%), 49.81 (48%) ppm. The conversion of **4o**/**4o'** was 94% and the ratio of ***S*P-9'**/ ***R*P-10'** was 99:1.

Entry 3 of Scheme 6: The mixture of ***S*P-4p** (50 mg, 0.13 mmol) and lithium-naphthalene **8** (naphthalene:Li = 0.9:1, 0.27 ml, 1 M, 0.27 mmol) was stirred -80 °C for 8 hours. Two peaks were observed to located at 58.01 (14%) (***S*P-4p**), 49.38 (86%) ppm. The conversion of ***S*P-4p** was 86% and major byproduct was observed at 49 ppm on ^{31}P NMR spectrum whose structure was not confirmed.

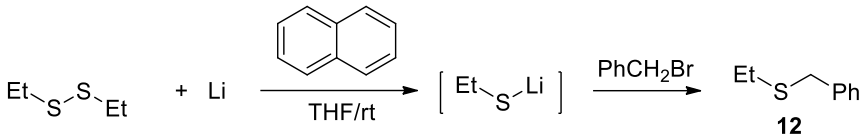
Entry 4 of Scheme 6: The mixture of ***S*P-4n** (50 mg, 0.16 mmol) and lithium-naphthalene **8** (naphthalene:Li = 1.5:1, 0.33 ml, 1 M, 0.33 mmol) was stirred 50 °C for 8 hours. Four peaks were observed to located at 89.82 (32%) (***S*P-9'**), 43.43 (22%, unknown), 33.49 (43%) (***R*P-10'**), 30.08 (2%) ppm. The conversion of ***S*P-4n** was 99% and the ratio of ***S*P-9'**/ ***R*P-10'** was 42:58.

Entry 5 of Scheme 6: The mixture of **4o**/**4o'** (***S*P**/***R*P**=67:33, 50 mg, 0.15 mmol) and lithium-naphthalene **8** (naphthalene:Li = 1.5:1, 0.31 ml, 1 M, 0.31 mmol) was stirred 50 °C for 5 hours. Four peaks were observed to located at 90.63 (33%)/87.32 (14%) (***S*P-9'**/***R*P-9'**=71:29),

33.66 (33%)/31.08 (20%) (**10'**/**10**, $\boldsymbol{R_P/S_P}$ = 63:37) ppm. The conversion of **4o/4o'** was 99% and the ratio of $\boldsymbol{S_P}$**-9'**/ $\boldsymbol{R_P}$**-10'** was 47:53.

Entry 6 of Scheme 6: The mixture of $\boldsymbol{S_P}$**-4p** (50 mg, 0.13 mmol) and lithium-naphthalene **8** (naphthalene:Li = 1.5:1, 0.27 ml, 1 M, 0.27 mmol) was stirred 50 °C for 8 hours. Five peaks were observed to located at 90.46 (6%) ($\boldsymbol{S_P}$**-9'**), 58.33 (2%), 49.59 (35%), 33.73 (36%)/28.79 (22%) (**10'/10**, $\boldsymbol{R_P/S_P}$ = 62:38) ppm. The conversion of $\boldsymbol{S_P}$**-4p** was 98% and the ratio of $\boldsymbol{S_P}$**-9'**/ $\boldsymbol{R_P}$**-10'** was 9:91.

D. Cleavage of S-S bond of 1,2-diethyldisulfane.



To the solution of 1,2-diethyldisulfane (0.1 ml, 0.818 mmol) in THF (1 mL), naphthalene-lithium **8** (naphthalene/Li = 0.9:1, 1.64 mL, 1 M, 1.64 mmol) was added dropwise at room temperature. After the solution was stirred for 0.5 hours, benzyl bromide (0.21 mL, 1.80 mmol) was added and the mixture was stirred at room temperature for 5 hours. Saturated solution of ammonium chloride (5 mL) was added. The mixture was extracted with dichloromethane (3×5 mL), washed with water (3×5 mL), dried over magnesium sulfate. After removing the solvents，the crude **12** was obtained in 99% yield, as seen its NMR spectrum (Figure S1) .

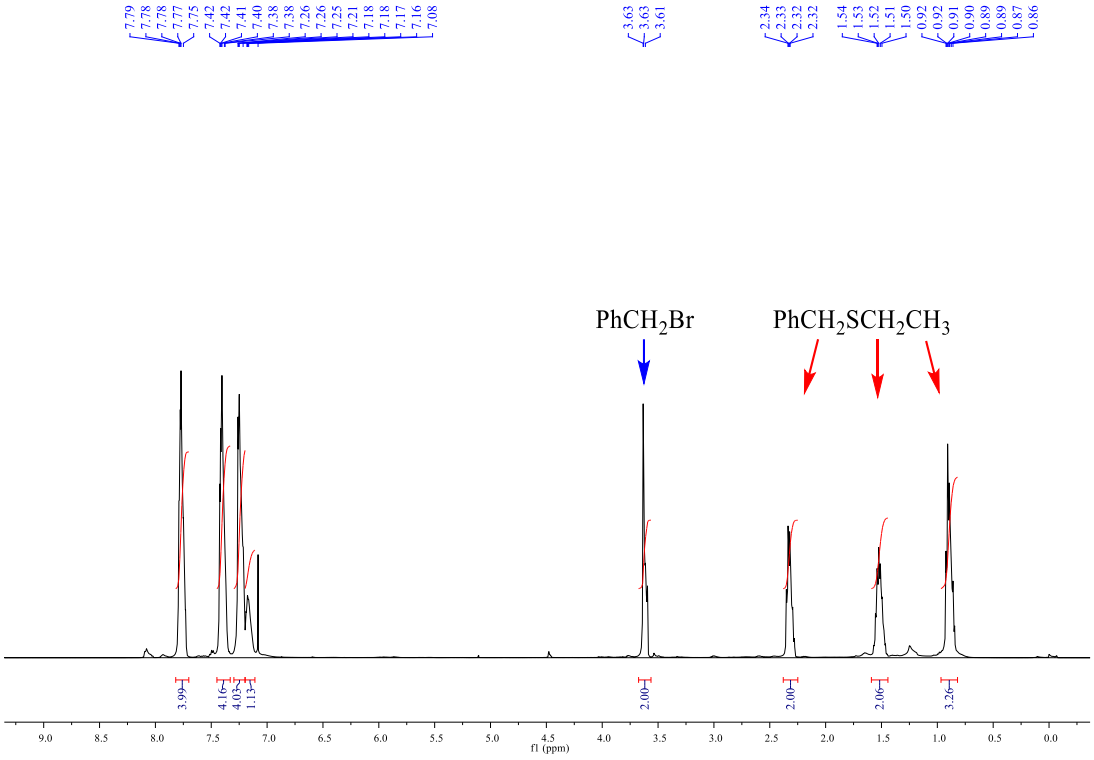
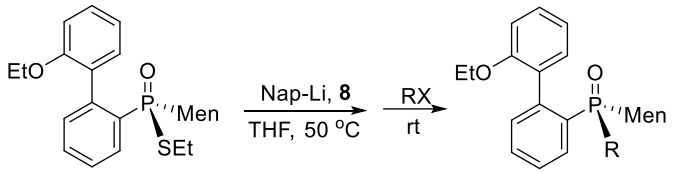


Figure S1. Cleavage of S-S bond of 1,2-diethyldisulfane and treatment with benzyl bromide.

Part 5. The *P*-alkylation of S_P-4b with alkyl halides and formaldehyde.



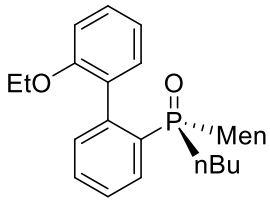
S_P-**4b** R_P-**7**, dr_P > 99:1

R = Me,	**7a**, 82%,69:31 dr_A	R = *o*$MeC_6H_4CH_2$,	**7g**, 56%,72:28 dr_A
Et,	**7b**, 85, 53:47	*p*$MeC_6H_4CH_2$,	**7h**, 96, 64:36
*n*Bu,	**7c**, 94, 51:49	*p*-*t*$BuC_6H_4CH_2$,	**7i**, 88, 70:30
*i*Bu,	**7d**, 95, 43:57	*m*$MeOC_6H_4CH_2$,	**7j**, 86, 63:37
allyl,	**7e**, 50, 84:16	*o*$ClC_6H_4CH_2$,	**7k**, 72, 74:26
$PhCH_2$,	**7f**, 85, 65:35	*p*$ClC_6H_4CH_2$,	**7l**, 90, 64:36

Typical procedure:

The solution of S_P-**4b** (50 mg, 0.112 mmol) in THF (1 mL) was warmed to 50 °C, then the lithium naphthalene **8** (naphthalene/Li = 1.5:1, 0.23 mL,1 M, 0.23 mmol) was added dropwise. After stirred for 0.5 hours, the mixture was cooled to room temperature. 1-Bromobutane (36.3 μL, 0.336 mmol) was added and the mixture was stirred at room temperature for 5 hours. Saturated solution of ammonium chloride (5 mL) was added. The mixture was extracted with dichloromethane (3×5 mL), washed with water (3×5 mL), dried over magnesium sulfate. After removing solvents, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent) to afford R_P-**7c**.

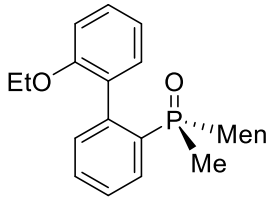
R_P-Butyl (2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphine oxide (R_P-7c)



The crude R_P-**7c** was obtained from n-butyl bromide, and the pure compound was obtained as white solid (41.7 mg, 84%, > 99:1 dr_P and 51:49 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent); m.p. 117.5 – 122.6 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 45.00 (s, 51%), 44.74 (s, 49%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.13 – 8.09 (m, 0.49H), 8.01 – 7.94 (m,0.51H), 7.48 – 7.41 (m, 2H), 7.39 (dd, *J*=6.6, 5.5, 1H), 7.36 – 7.33 (m, 0.51H), 7.22 – 7.16 (m, 1H), 7.02 (dd, *J*=7.5, 1.4, 0.49H), 6.95 (ddd, *J*=20.2, 15.9, 7.8, 2H), 4.07 – 3.98 (m, 1.02H), 3.93 (d, *J*=7.0, 0.98H), 2.40 (dd, *J*=8.7, 4.1, 1H), 2.35 – 2.17 (m, 1H), 2.05 – 1.99 (m, 1H), 1.86 (tt, *J*=9.0, 4.5, 1H), 1.70 – 1.55 (m, 5H), 1.35 – 1.29 (m, 2H), 1.26 (t, *J*=7.0, 2H), 1.18 (t, *J*=6.9, 2H), 0.88 (ddd, *J*=10.6, 9.2, 3.2, 6H), 0.83 (dd, *J*=6.8, 1.5, 4H), 0.75 (dd, *J*=7.8, 6.2, 4H), 0.30 (d, *J*=6.8, 1.53H), 0.21 (d, *J*=6.9, 1.47H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.2 (d, *J*=62.7), 140.7 (dd, *J*=28.5, 9.2), 133.3 (d, *J*=6.6), 132.2 (t, *J*=4.8), 131.5 (d, *J*=10.3),

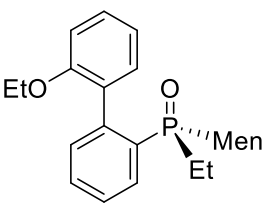
130.1 (d, *J*=2.2), 130.1 – 129.9 (m), 129.7 (s), 129.4 (s), 126.9 (d, *J*=9.9), 119.5 (s), 111.7 (d, *J*=37.6), 63.7 (d, *J*=24.8), 43.6 (dd, *J*=12.7, 3.7), 41.5 (d, *J*=65.5), 40.0 (d, *J*=65.5), 36.3 – 35.4 (m), 34.3 (d, *J*=8.2), 33.6 (dd, *J*=38.4, 13.7), 29.1 (d, *J*=66.7), 28.2 (dd, *J*=18.4, 1.7), 24.9 (dd, *J*=12.3, 5.1), 24.4 (dd, *J*=48.8, 14.8), 23.7 (dd, *J*=15.7, 4.0), 22.6 (d, *J*=3.9), 21.7 (d, *J*=21.5), 15.2 (d, *J*=6.4), 14.7 (d, *J*=8.1), 13.8 (d, *J*=1.1). **HRMS (ESI$^+$)** Calcd. for $C_{28}H_{40}O_2P$ [M+Na$^+$]: 463.2742, Found: 463.2750.

***R*$_P$-(2'-ethoxy-[1,1'-biphenyl]-2-yl) (methyl) ((-)-menthyl) phosphine oxide (*R*$_P$-7a)**



The crude ***R*$_P$-7a** was obtained from methyl iodide, and the pure compound was obtained as white solid (51.5 mg, 73.6%, >99:1 dr$_P$ and 69:31 dr$_A$) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent), m.p. 149.3 – 150.6°C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 45.64 (s, 70%), 43.30 (s, 30%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.97 – 7.89 (m, 0.3H), 7.83 (dd, *J*=12.1, 7.5, 0.7H), 7.44 (dd, *J*=7.5, 1.4, 0.7H), 7.36 (dq, *J*=15.0, 7.4, 2H), 7.30 – 7.23 (m, 1H), 7.20 – 7.16 (m,0.7H), 7.15 – 7.11 (m, 0.3H), 6.98 (dd, *J*=7.3, 1.2, 0.3H), 6.93 (t, *J*=7.5, 1H), 6.90 – 6.82 (m, 1H), 4.01 – 3.81 (m, 2H), 2.43 – 2.37 (m, 0.7H), 2.32 (d, *J*=1.7, 0.3H), 1.88 (dd, *J*=15.3, 3.3, 0.3H), 1.65 – 1.49 (m, 3H), 1.40 (dd, *J*=11.7, 6.9, 3H), 1.29 (d, *J*=12.6, 1H), 1.16 (dt, *J*=21.3, 6.9, 4H), 0.83 (s, 1H), 0.77 (t, *J*=9.6, 4H), 0.73 – 0.68 (m, 2H), 0.67 (t, *J*=7.6, 3H), 0.60 – 0.49 (m, 0.7H), 0.35 (d, *J*=6.7, 2H), 0.24 (d, *J*=6.8, 1H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.2 (d, *J*=7.7), 140.9 (d, *J*=8.4), 134.2 (d, *J*=90.1), 132.7 (s), 132.3 – 132.1 (m), 131.7 (t, *J*=9.5), 131.3 (d, *J*=8.3), 130.2 – 130.0 (m), 129.5 (d, *J*=16.6), 126.9 (dd, *J*=10.6, 4.1), 119.6 (d, *J*=35.3), 111.6 (d, *J*=72.7), 63.6 (d, *J*=48.5), 43.8 (dd, *J*=29.3, 3.2), 40.5 (d, *J*=67.7), 36.1 (d, *J*=13.8), 34.4 (d, *J*=10.1), 33.1 (d, *J*=14.5), 28.1 (d, *J*=2.3), 24.8 (d, *J*=12.6), 22.5 (d, *J*=9.9), 21.6 (d, *J*=9.9), 15.2 (d, *J*=15.4), 14.7 (d, *J*=10.4), 12.6 (d, *J*=67.2). **HRMS (ESI$^+$)** Calcd. for $C_{25}H_{35}O_2P$ [M+Na$^+$]: 421.2272, Found: 421.2281.

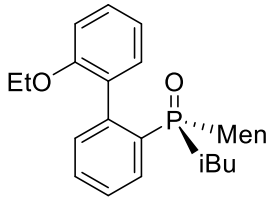
***R*$_P$-(2'-ethoxy-[1,1'-biphenyl]-2-yl) (ethyl) ((-)-menthyl) phosphine oxide (*R*$_P$-7b)**



The crude ***R*$_P$-7b** was obtained from bromoethane, and the pure compound was obtained as white solid (53.3 mg, 72.2%, >99:1 dr$_P$ and 53:47 dr$_A$)from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent), m.p. 109.5 – 112.6 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 46.16 (s, 53%), 45.99 (s, 47%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.08 – 7.99 (m,

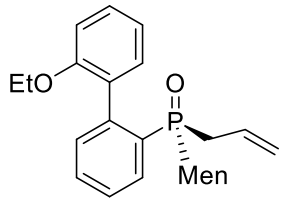
0.47H), 7.93 (dd, *J*=10.4, 8.0, 0.53H), 7.37 (t, *J*=7.0, 2H), 7.32 – 7.28 (m, 1H), 7.27 (s, 0.53H), 7.16 – 7.08 (m, 1H), 6.97 (d, *J*=7.2,0.47H), 6.93 – 6.81 (m, 2H), 4.00 – 3.92 (m, 1H), 3.87 (dd, *J*=9.0, 7.2, 1H), 2.34 (qd, *J*=13.3, 6.4, 1H), 2.01 – 1.90 (m, 1H), 1.82 (td, *J*=12.6, 3.3, 1H), 1.75 – 1.62 (m, 1H), 1.56 (ddd, *J*=9.3, 7.2, 3.6, 3H), 1.47 – 1.34 (m, 1H), 1.18 (t, *J*=7.0, 2H), 1.11 (t, *J*=7.0, 2H), 1.04 – 0.91 (m, 4H), 0.85 (dd, *J*=12.3, 6.9, 2H), 0.80 – 0.73 (m, 4H), 0.67 (d, *J*=6.3, 3H), 0.24 (d, *J*=6.8, 2H), 0.16 (d, *J*=6.9, 1H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.2 (d, *J*=55.6), 140.8 (dd, *J*=17.1, 9.1), 133.3 (d, *J*=7.0), 132.6 (d, *J*=7.2), 132.2 – 131.9 (m), 131.6 (d, *J*=9.5), 131.4 (s), 130.1 (dd, *J*=7.4, 2.3), 129.7 (s), 129.4 (s), 126.8 (dd, *J*=10.0, 5.2), 119.5 (d, *J*=4.1), 111.6 (d, *J*=58.0), 63.6 (d, *J*=48.8), 43.6 (dd, *J*=18.8, 3.9), 41.2 (d, *J*=65.5), 40.1 (d, *J*=65.8), 36.1 – 35.4 (m), 34.3 (d, *J*=3.5), 33.5 (dd, *J*=37.9, 13.7), 28.2 (dd, *J*=13.8, 1.7), 24.9 (dd, *J*=12.3, 6.3), 22.5 (d, *J*=3.3), 21.6 (d, *J*=17.8), 19.4 (d, *J*=67.1), 15.2 (d, *J*=9.2), 14.6 (d, *J*=12.3), 5.9 (dd, *J*=30.1, 5.2). **HRMS (ESI+)** Calcd. for $C_{26}H_{38}O_2P$ [M+H$^+$]: 413.2609, Found: 413.2668.

***R*$_P$-(2'-Ethoxy-[1,1'-biphenyl]-2-yl)(isobutyl)((-)-menthyl) phosphine oxide (*R*$_P$-7d)**



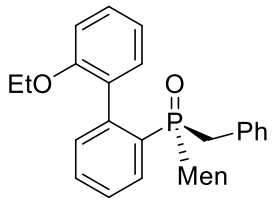
The crude ***R*$_P$-7d** was obtained from isobutane, and the pure compound was obtained as white solid (63.2 mg, 80%, >99:1 dr_P and 43:57 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent), m.p. 118.6 – 123.1 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 44.89 (s, 43%), 43.68 (s, 57%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.24 – 8.03 (m, 0.57H), 7.99 – 7.84 (m, 0.43H), 7.51 – 7.39 (m, 2H), 7.39 – 7.30 (m, 1H), 7.26 – 7.18 (m, 1H), 7.05 (d, *J*=7.2, 1H), 7.00 – 6.87 (m, 2H), 4.10 – 3.99 (m, 1.14H), 3.95 (d, *J*=6.7, 0.86H), 2.53 – 2.38 (m, 1H), 2.10 (dt, *J*=14.3, 7.0, 0.43H), 2.05 – 1.92 (m, 0.57H), 1.87 (d, *J*=3.2, 0.43H), 1.76 (s,0.57H), 1.57 (tdd, *J*=19.2, 14.8, 9.8, 5H), 1.33 – 1.15 (m, 4H), 1.08 (dd, *J*=16.8, 6.5, 3H), 0.97 (d, *J*=6.5, 1H), 0.91 (dd, *J*=20.4, 9.8, 4H), 0.83 (t, *J*=8.6, 4H), 0.78 – 0.70 (m, 4H), 0.32 (d, *J*=6.7, 1.3H), 0.23 (d, *J*=6.9, 1.7H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.1 (d, *J*=31.2), 140.9 (dd, *J*=70.3, 8.9), 133.2 (d, *J*=6.7), 132.6 (d, *J*=10.0), 131.8 (dt, *J*=9.5, 7.2), 130.0 (d, *J* = 1.9), 129.8 – 129.7 (m), 129.7 (s), 129.3 (s), 127.7 – 125.9 (m), 119.9 – 118.9 (m), 111.5 (t, *J*=24.7), 63.7 (d, *J*=20.6), 43.7 (dd, *J*=14.8, 3.4), 40.9 (dd, *J*=157.8, 65.5), 37.2 (d, *J*=65.5), 36.3 – 35.5 (m), 34.4 (d, *J*=23.7), 33.7 (d, *J*=13.6), 33.5 – 33.2 (m), 28.1 (dd, *J*=29.9, 1.8), 25.5 (dd, *J*=12.7, 6.8), 24.9 (d, *J*=12.5), 24.2 (dd, *J*=27.6, 4.5), 23.8 (dd, *J*= 5.1, 3.8), 22.6 (d, *J*=7.6), 21.6 (d, *J*=24.6), 15.2 (d, *J*=9.5), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{28}H_{40}O_2P$ [M+Na$^+$]: 463.2742, Found: 463.2744.

***R*P-Allyl (2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphine oxide (*R*P-7e)**



The crude ***R*P-7e** was obtained from allyl chloride, and the pure compound was obtained as white solid (79.5 mg, 81%, >99:1 dr_P and 84:16 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/1 as eluent), m.p.132.8 – 134.8 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 38.66 (s, 84%), 33.50 (s, 16%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.96 – 7.91 (m, 0.16H), 7.77 (dd, *J*=7.5, 1.6, 0.84H), 7.73 – 7.65 (m, 1H), 7.43 (t, *J*=7.5, 1H), 7.35 (ddd, *J*=9.3, 4.0, 1.6, 3H), 7.04 (dd, *J*=12.7, 5.5, 1H), 6.92 (d, *J*=8.4, 1H), 5.96 – 5.83 (m, 1H), 4.07 – 3.89 (m, 2H), 2.54 – 2.43 (m, 1H), 2.02 (d, *J*=6.5, 2H), 1.79 (d, *J*=6.3, 1H), 1.57 – 1.51 (m, 2H), 1.17 – 1.07 (m, 2H), 0.91 – 0.79 (m, 5H), 0.73 (d, *J*=7.0, 4H), 0.69 (d, *J*=6.4, 4H), 0.47 (t, *J*=14.4, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 155.9 (s), 148.1 (s), 141.4 (d, *J*=8.0), 133.9 (s), 132.5 (d, *J*=34.2), 132.3 (s), 129.7 (d, *J*=1.8), 129.3 (s), 126.7 (d, *J*=18.8), 121.5 – 120.2 (m), 119.9 (s), 110.9 (s), 63.3 (s), 44.2 (s), 39.5 (d, *J*=68.0), 36.0 (s), 34.6 (s), 33.1 (d, *J*=14.7), 29.7 (s), 27.7 (s), 24.7 (d, *J*=22.6), 22.5 (s), 21.5 (s), 20.6 (s), 20.5 (s), 15.2 (s), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{27}H_{37}O_2P$ [M+Na^+]: 447.2429, Found: 447.2438.

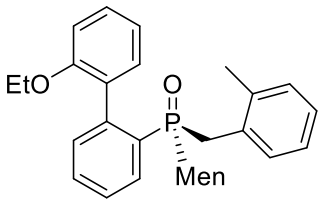
***R*P-Benzyl (2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphine oxide (*R*P-7f)**



The crude ***R*P-7f** was obtained from benzyl chloride, and the pure compound was obtained as white solid (61.3 mg, 72%, >99:1 dr_P and 65:35 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 2/1 as eluent), m.p. 67.3 – 71.4 °C; **^{31}P NMR (202 MHz, CDCl3)** δ = 41.74 (s, 65%), 40.86 (s, 35%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.81 (ddd, *J*=11.3, 5.5, 2.2,0.35H), 7.77 – 7.68 (m, 0.65H), 7.48 – 7.37 (m, 2H), 7.38 – 7.28 (m, 4H), 7.17 (ddd, *J*=19.2, 13.7, 7.0, 4H), 7.05 – 6.89 (m, 2H), 4.08 – 4.00 (m, 0.7H), 3.97 (dd, *J*=13.9, 7.0, 1.3H), 3.43 – 3.12 (m, 2H), 2.44 – 2.34 (m,0.35H), 2.32 – 2.22 (m, 0.65H), 2.13 – 2.03 (m, 0.35H), 1.86 – 1.79 (m, 0.65H), 1.77 (d, *J*=2.4, 1H), 1.63 – 1.50 (m, 2H), 1.35 – 1.15 (m, 5H), 0.83 – 0.63 (m, 7H), 0.53 (d, *J*=6.9, 2H), 0.27 (dd, *J*=9.1, 7.0, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.1 (d, *J*=45.6), 141.9 (d, *J*=7.5), 133.5 (s), 133.2 (d, *J*=7.3), 132.9 (d, *J*=9.2), 131.4 (d, *J*=8.2), 130.7 (d, *J*=5.2), 130.3 (dd, *J*=20.7, 4.0), 129.9 (d, *J*=2.0), 129.3 (s), 128.1 (dd, *J*=6.4, 1.2), 126.6 (s), 126.5 (d, *J*=3.6), 126.4 (s), 126.4 (d, *J*=2.3), 126.3 (d, *J*=1.8),

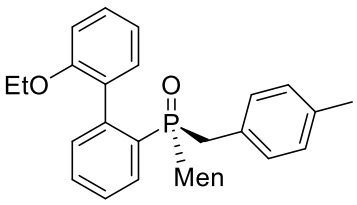
119.6 (d, *J*=27.6), 111.7 (d, *J*=98.9), 63.8 (d, *J*=30.4), 43.7 (dd, *J*=9.2, 3.6), 41.6 (s), 40.8 (d, *J*=54.0), 36.6 – 36.1 (m), 34.4 (d, *J*=33.6), 33.9 – 33.5 (m), 33.4 – 33.1 (m), 27.9 (d, *J*=1.4), 25.1 (d, *J*=12.5), 22.5 (d, *J*=13.5), 21.4 (d, *J*=44.3), 15.2 (d, *J*=4.8), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{31}H_{39}O_2P$ [M+Na$^+$]: 497.2585, Found: 497.2592.

***R*$_P$-(2'-Ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl)(2-methylbenzyl)phosphine oxide (*R*$_P$-7g)**



The crude ***R*$_P$-7g** was obtained from 2-methylbenzyl bromide, and the pure compound was obtained as white solid (41.3 mg, 47%, >99:1 dr$_P$ and 72:28 dr$_A$) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 2/1 as eluent), m.p. 50.0 – 53.6 °C; **^{31}P NMR (202 MHz, CDCl$_3$)** δ = 42.49 (s, 72%), 41.21 (s, 28%); **^{1}H NMR (500 MHz, CDCl$_3$)** δ = 7.88 – 7.81 (m, 0.28H), 7.78 – 7.69 (m, 0.72H), 7.43 (t, *J*=7.5, 1H), 7.37 (t, *J*=7.2, 1H), 7.33 – 7.26 (m, 1H), 7.23 (dd, *J*=6.8, 3.0, 1H), 7.12 (dd, *J*=11.8, 4.4, 1H), 7.08 (d, *J*=7.3, 1H), 7.06 (s, 0.56H), 6.99 – 6.92 (m, 2H), 6.88 (t, *J*=7.6, 1.42H), 4.03 (qd, *J*=6.9, 1.8, 0.56H), 3.95 (q, *J*=7.0, 1.42H), 3.38 (dd, *J*=14.5, 12.9,0.56H), 3.33 – 3.01 (m, 1.42H), 2.34 (s, 2H), 2.24 – 2.20 (m, 1H), 1.89 (dt, *J*=13.3, 6.7, 1H), 1.67 – 1.53 (m, 2H), 1.21 (dt, *J*=22.7, 7.0, 4H), 0.98 – 0.90 (m, 1H), 0.81 (t, *J*=6.3, 3H), 0.76 – 0.73 (m, 2H), 0.56 (d, *J*=6.9, 2H), 0.27 (t, *J*=7.9, 3H); **^{13}C {^{1}H} NMR (126 MHz, CDCl$_3$)** δ = 156.1 (d, *J*=68.0), 141.1 (d, *J*=151.2), 137.1 (s), 133.9 (d, *J*=85.5), 132.9 (d, *J*=5.0), 132.8 (s), 131.9 (dd, *J*=12.7, 7.5), 131.5 (s), 131.4 (d, *J*=8.8), 131.0 (d, *J*=4.2), 130.2 (t, *J*=4.4), 129.8 (d, *J*=2.0), 129.6 – 129.4 (m), 129.1 (s), 126.3 (d, *J*=26.1), 125.5 (s), 119.5 (s), 111.7 (d, *J*=116.4), 63.7 (d, *J*=35.8), 43.6 (dd, *J*=37.9, 3.4), 41.7 (d, *J*=65.1), 36.5 – 35.4 (m), 34.3 (d, *J*=18.8), 33.6 – 33.0 (m), 30.8 (d, *J*=60.7), 27.9 (dd, *J*=26.7, 1.5), 24.9 – 24.3 (m), 22.5 (d, *J*=18.1), 21.4 (d, *J*=43.3), 20.6 (d, *J*=3.9), 15.2 (d, *J*=9.0), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{32}H_{41}O_2P$ [M+K$^+$]: 527.2481, Found: 497.2511.

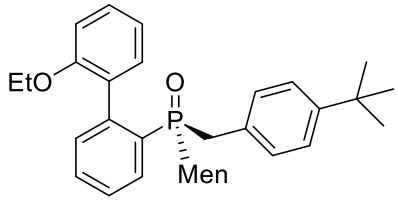
***R*$_P$-(2'-Ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl)(4-methylbenzyl) phosphine oxide (*R*$_P$-7h)**



The crude ***R*$_P$-7h** was obtained from 4-methylbenzyl chloride, and the pure compound was obtained as white solid (71.9 mg, 82%, >99:1 dr$_P$ and 64:36 dr$_A$) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 2/1 as eluent), m.p. 150.3 – 153.8 °C; **^{31}P NMR (202 MHz, CDCl$_3$)** δ = 41.81 (s, 64%), 40.96 (s, 36%); **^{1}H NMR (500 MHz, CDCl$_3$)** δ = 7.82 (ddd, *J*=11.4, 7.8, 0.8, 0.36H), 7.73 (ddd, *J*=11.3, 7.7, 0.8, 0.64H), 7.41 (ddd,

J=8.9, 7.5, 0.9, 1H), 7.36 – 7.28 (m, 2H), 7.25 – 7.23 (m, 0.36H), 7.22 – 7.18 (m, 2H), 7.13 (dd, *J*=12.8, 3.7, 0.64H), 7.10 – 7.06 (m, 0.36H), 7.05 – 7.00 (m, 2H), 7.00 – 6.93 (m, 2H), 6.92 – 6.89 (m, 0.64H), 4.03 (dd, *J*=7.0, 4.9, 0.72H), 3.97 (q, *J*=7.0, 1.28H), 3.24 (ddt, *J*=40.6, 14.9, 9.6, 2H), 2.42 – 2.35 (m, 0.36H), 2.27 (d, *J*=13.2, 3H), 2.08 (dd, *J*=8.2, 3.6, 0.64H), 1.79 (dd, *J*=11.8, 2.6, 1H), 1.56 (dd, *J*=22.6, 19.8, 2H), 1.37 – 1.30 (m, 1H), 1.21 (dt, *J*=17.0, 7.0, 3H), 0.94 (d, *J*=6.8, 2H), 0.83 – 0.67 (m, 7H), 0.54 (d, *J*=6.9, 2H), 0.27 (dd, *J*=6.7, 4.9, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.1 (d, *J*=42.5), 141.4 (dd, *J*=132.0, 8.2), 135.8 (dd, *J*=17.1, 2.2), 134.0 (d, *J*=9.8), 133.4 (d, *J*=13.3), 133.0 (d, *J*=7.3), 132.9 (d, *J*=9.6), 131.9 – 131.7 (m), 131.4 (d, *J*=8.4), 130.5 (d, *J*=5.1), 130.2 (d, *J*=5.8), 129.9 (t, *J*=6.7), 129.7 – 129.5 (m), 129.2 (s), 128.8 (d, *J*=1.5), 126.5 (dd, *J*=15.6, 10.3), 119.6 (d, *J*=22.9), 111.7 (d, *J*=103.0), 63.8 (d, *J*=36.5), 43.6 (dt, *J*=10.4, 5.4), 41.8 – 40.9 (m), 36.7 – 35.8 (m), 34.4 (d, *J*=33.9), 33.6 (d, *J*=13.6), 33.4 – 33.2 (m), 32.8 (s), 28.6 – 27.3 (m), 25.5 – 24.5 (m), 22.5 (d, *J*=12.2), 21.1 (d, *J*=21.1), 15.2 (d, *J*=4.9), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{31}H_{39}O_2P$ [M+Na^+]: 511.2742, Found: 511.2744.

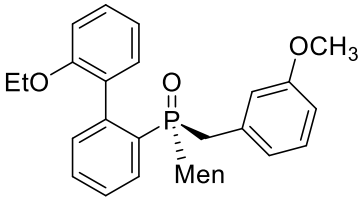
***R*$_P$-(4-(tert-Butyl)benzyl)(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphine oxide (*R*$_P$-7i)**



The crude ***R*$_P$-7i** was obtained from 4-tert-buthylbenzyl bromide, and the pure compound was obtained as white solid (71.5 mg, 75%, >99:1 dr_P and 70:30 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 2/1 as eluent), m.p. 71.4 – 75.6 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 41.89 (s, 70%), 40.93 (s, 30%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.83 – 7.78 (m, 0.3H), 7.76 – 7.68 (m, 0.7H), 7.43 (t, *J*=7.2, 1H), 7.38 – 7.33 (m, 1H), 7.30 (d, *J*=7.3, 1H), 7.19 (d, *J*=8.1, 1.4H), 7.15 (d, *J*=7.8, 0.6H), 6.96 (dt, *J*=15.0, 7.1, 1.4H), 6.89 (d, *J*=8.2, 0.6H), 4.04 (s, 0.6H), 3.96 (q, *J*=6.8, 1.4H), 3.35 (dt, *J*=25.7, 14.1, 1.4H), 3.18 (t, *J*=12.0, 0.6H), 2.43 – 2.35 (m, 0.3H), 2.29 – 2.18 (m, 0.7H), 2.07 (ddd, *J*=14.2, 8.5, 5.7, 0.3H), 1.95 (s, 0.7H), 1.75 (d, *J*=12.2, 1H), 1.68 – 1.53 (m, 2H), 1.49 (s, 1H), 1.27 (t, *J*=9.9, 9H), 1.20 (t, *J*=6.7, 2H), 1.08 – 0.87 (m, 2H), 0.84 – 0.66 (m, 7H), 0.46 (d, *J*=6.7, 2H), 0.25 (dd, *J*=21.8, 6.7, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.1 (d, *J*=48.0), 149.1 (dd, *J*=23.6, 2.2), 142.9 – 141.0 (m), 133.6 (s), 133.0 (d, *J*=9.8), 131.8 (s), 131.1 (d, *J*=8.4), 130.4 (d, *J*=5.2), 130.1 (s), 129.9 (d, *J*=4.9), 129.9 – 129.8 (m), 129.6 (s), 129.5 (s), 129.2 (s), 126.5 (dd, *J*=15.0, 10.3), 125.0 (d, *J*=6.9), 119.6 (d, *J*=24.3), 111.6 (d, *J*=118.0), 63.7 (d, *J*=38.6),

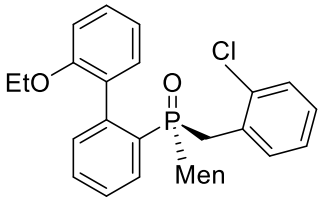
43.7 (d, *J*=3.4), 41.6 (s), 41.1 (s), 36.5 (s), 36.4 – 35.9 (m), 34.5 (d, *J*=27.8), 33.4 – 32.9 (m), 31.3 (d, *J*=3.4), 27.8 (d, *J*=1.3), 25.1 (d, *J*=12.5), 22.5 (d, *J*=12.5), 21.3 (d, *J*=44.4), 15.1 (s), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{35}H_{47}O_2P$ [M+Na$^+$]: 553.3211, Found: 553.3220.

R_P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl)(3-methoxybenzyl) phosphine oxide (R_P-7j)



The crude ***R*$_P$-7j** was obtained from 3-methoxybenzyl chloride, and the pure compound was obtained as white solid (66.1 mg, 73%, >99:1 dr$_P$ and 63:37 dr$_A$) from preparative TLC (silica gel, petroleum ether/ethyl acetate =2/1 as eluent), m.p. 53.5 – 58.6 °C; **^{31}P NMR (202 MHz, CDCl$_3$)** δ = 41.87 (s, 63%), 41.10 (s, 37%); **^{1}H NMR (500 MHz, CDCl$_3$)** δ = 7.84 (dd, *J*=11.2, 7.7, 1H), 7.73 (dd, *J*=11.1, 8.0, 1H), 7.41 (dd, *J*=14.6, 7.3, 1H), 7.38 – 7.29 (m, 2H), 7.24 (dd, *J*=6.9, 3.2, 1H), 7.21 – 7.18 (m, 1H), 7.15 – 7.06 (m, 1H), 7.04 – 6.90 (m, 2H), 6.87 (t, *J*=6.2, 2H), 6.81 (d, *J*=7.5, 1H), 6.74 (s, 1H), 4.04 (dd, *J*=6.8, 5.8, 1H), 3.97 (q, *J*=7.0, 1H), 3.69 (d, *J*=8.9, 3H), 3.39 – 3.06 (m, 2H), 2.41 – 2.38 (m, 1H), 2.34 – 2.28 (m, 1H), 2.13 – 2.07 (m, 1H), 1.83 (dd, *J*=12.1, 2.5, 1H), 1.62 – 1.50 (m, 2H), 1.38 – 1.32 (m, 1H), 1.24 (t, *J*=7.0, 1H), 1.20 (t, *J*=7.0, 2H), 1.02 – 0.95 (m, 1H), 0.86 – 0.69 (m, 8H), 0.58 (d, *J*=6.9, 2H), 0.27 (d, *J*=6.7, 3H); **^{13}C {^{1}H} NMR (126 MHz, CDCl$_3$)** δ = 159.3 (dd, *J*=10.1, 1.4), 156.0 (d, *J*=42.2), 141.9 (d, *J*=7.6), 134.6 (dd, *J*=7.1, 3.5), 133.9 (s), 133.3 (d, *J* =11.0), 132.9 (d, *J*=9.6), 132.0 – 131.6 (m), 131.5 (d, *J*=8.3), 130.2 (d, *J*=2.0), 129.9 (d, *J*=2.3), 129.7 (s), 129.3 (s), 129.1 – 128.9 (m), 126.5 (dd, *J*=14.9, 10.4), 122.9 (dd, *J*=51.7, 5.7), 119.6 (d, *J*=16.9), 115.4 (dd, *J*=59.7, 5.3), 113.0 – 111.8 (m), 111.3 (s), 63.7 (d, *J*=32.4), 55.1 (d, *J*=10.5), 43.6 (dd, *J*=13.1, 3.6), 41.7 – 40.8 (m), 36.6 – 35.7 (m), 34.5 (s), 34.2 (d, *J*=7.9), 33.6 (d, *J*=12.0), 33.3 (d, *J*=14.0), 28.0 (dd, *J*=38.6, 1.5), 24.9 (dd, *J*=12.5, 8.2), 22.5 (d, *J*=12.5), 21.4 (d, *J*=46.3), 15.2 (s), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{32}H_{41}O_3P$ [M+Na$^+$]: 527.2691, Found: 527.2700.

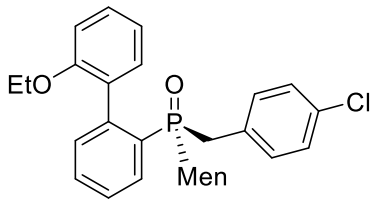
R_P-(2-Chlorobenzyl)(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl)phosphine oxide (R_P-7k)



The crude ***R*$_P$-7k** was obtained from 2-chlorobenzyl chloride, and the pure compound was obtained as white solid (56.6 mg, 62%, >99:1 dr$_P$ and 74:26 dr$_A$) from preparative TLC (silica gel, petroleum ether/ethyl acetate =2/1 as eluent), m.p. 58.2 – 61.8 °C; **^{31}P NMR (202 MHz, CDCl$_3$)** δ = 43.88 (s, 74%), 42.12 (s, 26%); **^{1}H NMR (500 MHz, CDCl$_3$)** δ = 7.91 – 7.74 (m, 2H), 7.45 (t, *J*=7.1, 2H), 7.38 (dd, *J*=13.4, 6.4, 1H), 7.32 (t, *J*=7.8, 2H), 7.23 (d,

J=4.0, 1H), 7.17 – 7.08 (m, 2H), 6.98 (dd, *J*=16.8, 8.7, 1H), 6.92 (d, *J*=8.3, 1H), 4.07 – 4.01 (m, 0.52H), 3.96 (q, *J*=6.8, 1.48H), 3.70 (dd, *J*=14.8, 10.4, 0.74H), 3.57 – 3.50 (m, 0.26H), 3.44 (t, *J*=15.2, 0.74H), 3.30 (d, *J*=14.1, 0.26H), 2.40 – 2.30 (m, 0.26H), 2.29 – 2.17 (m, 0.74H), 2.05 (d, *J*=10.8, 0.26H), 1.76 (q, *J*=12.5, 0.74H), 1.67 – 1.44 (m, 3H), 1.38 – 1.15 (m, 5H), 1.07 – 0.93 (m, 1H), 0.90 – 0.82 (m, 1H), 0.72 (dd, *J*=15.5, 7.7, 5H), 0.44 (d, *J*=6.8, 2H), 0.26 (dd, *J*=21.4, 6.7, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.2 (d, *J*=38.5), 141.7 (dd, *J*=47.2, 8.1), 134.1 – 133.9 (m), 133.3 (s), 132.9 (d, *J*=9.8), 132.8 (d, *J*=3.5), 132.1 (dd, *J*=8.5, 4.6), 131.9 (t, *J*=5.5), 131.2 (s), 130.9 (d, *J*=8.2), 130.4 – 130.0 (m), 130.1 (d, *J*=2.0), 129.5 (d, *J*=3.8), 129.3 (d, *J*=4.0), 127.9 – 127.6 (m), 126.7 (t, *J*=7.8), 119.8 (d, *J*=9.0), 111.6 (d, *J*=88.4), 63.7 (d, *J*=33.3), 43.5 (dd, *J*=45.5, 3.4), 41.5 (dd, *J*=65.3, 37.0), 36.4 – 35.1 (m), 34.6 – 33.4 (m), 33.8 – 32.7 (m), 29.1 (d, *J*=60.3), 28.0 (dd, *J*=28.5, 1.3), 24.9 (t, *J*= 11.9), 22.4 (d, *J*=15.7), 21.3 (d, *J*=42.9), 15.1 (d, *J*=14.6), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{31}H_{38}ClO_2P$ [M+Na$^+$]: 531.2196, Found: 531.2203.

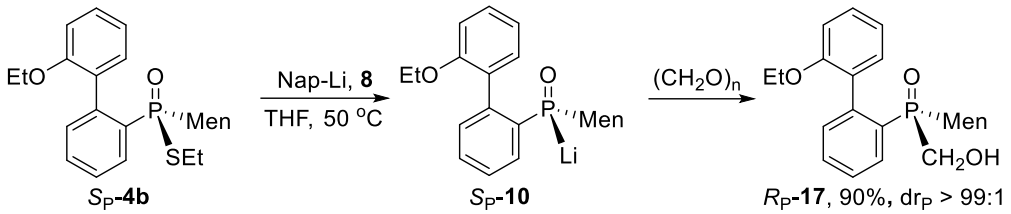
R_P-(4-Chlorobenzyl) (2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphine oxide (R_P-7l)



The crude ***R*$_P$-7l** was obtained from 4-chlorobenzyl chloride, and the pure compound was obtained as white solid (69.4 mg, 76%, >99:1 dr_P and 64:36 dr_A) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 2/1 as eluent), m.p. 80.9 – 84.6 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 41.51 (s, 64%), 40.84 (s, 36%); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.81 (dd, *J*=11.1, 8.2, 0.36H), 7.70 (dd, *J*=11.0, 8.1, 0.64H), 7.42 (dd, *J*=17.6, 8.3, 2H), 7.37 – 7.27 (m, 3H), 7.21 (t, *J*=6.2, 2H), 7.16 (dd, *J*=11.6, 8.2, 2H), 7.09 (d, *J*=4.3, 0.36H), 6.99 (dt, *J*=14.1, 7.2, 1H), 6.93 (d, *J*=8.3, 0.64H), 4.10 – 3.87 (m, 2H), 3.25 (tt, *J*=17.3, 8.8, 1.28H), 3.10 (dd, *J*=14.8, 10.2,0.64H), 2.42 – 2.36 (m, 0.36H), 2.34 – 2.21 (m, 1H), 2.19 – 2.01 (m, 0.64H), 1.87 (d, *J*=11.1, 1H), 1.59 (dd, *J*=25.3, 13.4, 2H), 1.36 (s, 1H), 1.21 (dt, *J*=14.1, 6.9, 3H), 1.04 – 0.91 (m, 2H), 0.78 (dt, *J*=15.3, 7.0, 6H), 0.60 (d, *J*=6.8, 2H), 0.28 (t, *J*=5.9, 3H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 156.1 (d, *J*=44.4), 141.3 (dd, *J*=110.6, 8.6), 133.2 (s), 132.9 (d, *J*=5.7), 132.8 (s), 132.3 (dd, *J*=13.3, 2.5), 131.9 (d, *J*=4.8), 131.6 (d, *J*=3.2), 131.6 (s), 130.2 (d, *J*=2.2), 129.8 (s), 129.5 – 129.3 (m), 128.5 – 127.4 (m), 126.8 (s), 126.7 (d, *J*=4.8), 126.6 (s), 119.6 (d, *J*=33.3), 111.8 (d, *J*=79.8), 63.8 (d, *J*=22.8), 43.7 (dd, *J*=7.7, 3.7), 42.3 – 40.9 (m), 36.3 (dd, *J*=17.0, 15.6), 34.3 (d, *J*=28.2), 33.8 – 33.1 (m), 32.8 (s), 28.1 (dd, *J*=31.4, 1.3), 24.9 (dd,

J=12.5, 8.0), 22.5 (d, *J*=12.7), 21.7 – 20.4 (m), 15.2 (d, *J*=6.7), 14.7 (s). **HRMS (ESI$^+$)** Calcd. for $C_{31}H_{38}ClO_2P$ [M+Na$^+$]: 531.2196, Found: 531.2204.

The reaction of 10 with formaldehyde.

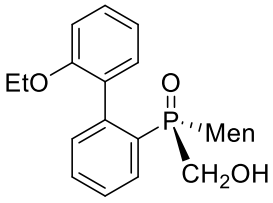


S_P-**4b** S_P-**10** R_P-**17**, 90%, dr_P > 99:1

To the solution of ***S*P-4b** (50 mg, 0.112 mmol) in THF (1 mL), lithium naphthalene **8** (naphthalene /Li = 1.5:1, 0.23 mL,1 M, 0.23mmol) was added dropwise at 50 °C. After stirred for 0.5 hours, the mixture was cooled to room temperature. Paraformaldehyde (10.1 mg, 0.336 mmol) was added and the mixture was stirred at room temperature for 5 hours. Saturated solution of ammonium chloride (5 mL) was added. The mixture was extracted with dichloromethane (3×5 mL), washed with water (3×5 mL), dried over magnesium sulfate. After removing the solvents, the residue was purified with preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/2 as eluent) to afford ***R*P-17**.

***R*P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl)(hydroxymethyl)((-)-menthyl) phosphine oxide (*R*P-17)**

The crude ***R*P-17** was obtained from paraformaldehyde, and the pure compound was obtained as

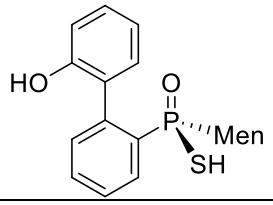


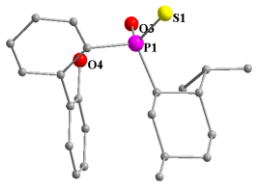
white solid (33.4 mg, 72%, >99:1 dr_P) from preparative TLC (silica gel, petroleum ether/ethyl acetate = 1/2 as eluent), m.p. 157.5 – 161.3 °C; **^{31}P NMR (202 MHz, $CDCl_3$)** δ = 43.32 (s); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.00 (d, *J*=8.1 Hz, 1H), 7.49 – 7.25 (m, 4H), 7.19 – 7.13 (m, 1H), 7.03 – 6.86 (m, 2H), 4.01 – 3.87 (m, 2H), 3.71 (dd, *J*=77.5, 15.2 Hz, 2H), 2.32 – 2.16 (m, 1H), 1.95 (t, *J*=11.3 Hz, 1H), 1.67 (dd, *J*=21.0, 10.1 Hz, 1H), 1.62 – 1.49 (m, 3H), 1.15 (dt, *J*=33.2, 6.9 Hz, 4H), 0.75 (dt, *J*=13.2, 6.6 Hz, 5H), 0.71 – 0.62 (m, 4H), 0.27 (d, *J*=6.7 Hz, 2H), 0.16 (d, *J*=6.8 Hz, 1H); **^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$)** δ = 155.1 (d, *J*=46.2), 139.9 (dd, *J*=31.5, 9.6), 131.4 (d, *J*=7.1), 131.2 (s), 130.9 (d, *J*=8.4), 129.6 (s), 128.9 (s), 128.8 (s), 126.2 (d, *J*=10.1), 126.1 (d, *J*=10.3), 118.9 (d, *J*=23.2), 110.6 (d, *J*=16.9), 62.7 (d, *J*=7.2), 60.3 (d, *J*=69.9), 57.7 (d, *J*=70.3), 42.4 (d, *J*=3.7), 39.4 (dd, *J*=62.2, 52.2), 33.9 (s), 33.1 (d, *J*=14.6), 32.5 (dd, *J*=38.1, 13.9), 27.4 (d, *J*=25.7), 23.7 (dd, *J*=12.2, 6.3), 21.4 (s), 20.6 (d, *J*=15.7), 14.1 (d, *J*=21.0), 13.6 (d, *J*=6.1). **HRMS (ESI$^+$)** Calcd. for $C_{25}H_{35}O_3P$ [M+Na^+]: 437.2221, Found: 437.2221.

Part 6. Crystallographic information 3/3', 4e and 5.

Table S1. Crystallography data of S_P-3

The single crystal suited for the X-ray diffraction was obtained from the evaporation of the solution of ***S*P-3** in dichloromethane : petroleum ether = 2:1 at -40 °C.

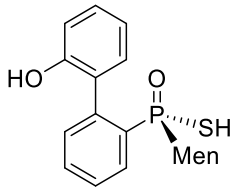


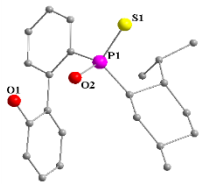


Empirical formula	C22 H29 O2 PS
Crystal system	Monoclinic
space group	P21 (No. 4)
Formula weight	742.90
a, Å	8.7606(8)
b, Å	16.4868(14)
c, Å	14.1957(12)
α, deg	90
β, deg	97.089(3)
γ, deg	90
V, Å3	2034.7(3)
Z	2
T, K	298
λ, Å	0.71073
ρ, Mg m-3	1.213
Rint	0.028
R1 [I N 2σ(I)]	0.0444
R1 (all data)	0.0742
wR2 [I N 2σ(I)]	0.0958
wR2 (all data)	0.1104
Flack	0.03(5)
CCDC	1975584

Table S2. Crystallography data of R_P-3'.

The single crystal suited for the X-ray diffraction was obtained from the evaporation of the solution of ***R*P-3'** in dichloromethane : petroleum ether = 2:1 at -40 °C.

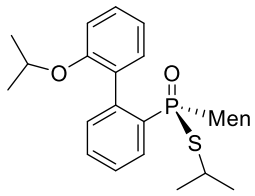


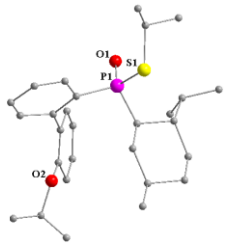


Empirical formula	C22 H29 O2 PS
Crystal system	Monoclinic
space group	P21(No.4)
Formula weight	507.86
a, Å	9.8758(8)
b, Å	10.6484(9)
c, Å	12.6525(11)
α, deg	90
β, deg	100.229(2)
γ, deg	90
V, Å3	1309.41(19)
Z	2
T, K	298
λ, Å	0.71073
ρ, Mg m-3	1.288
Rint	0.026
R1 [I N 2σ(I)]	0.0486
R1 (all data)	0.0775
wR2 [I N 2σ(I)]	0.1065
wR2 (all data)	0.1227
Flack	0.07(4)
CCDC	1975582

Table S3. Crystallograph data of S_P-4e

The single crystal suited for the X-ray diffraction was obtained from the evaporation of the solution of ***S*P-4e** in dichloromethane and petroleum ether.

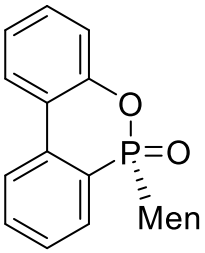


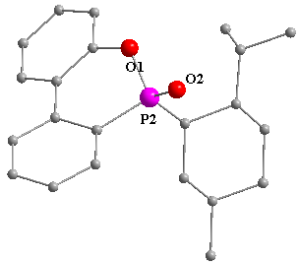


Empirical formula	$C_{28}H_{41}O_2PS$
Crystal system	Monoclinic
space group	P21 (No.4)
Formula weight	472.65
a, Å	9.9896(9)
b, Å	29.437(3)
c, Å	10.1391(12)
α, deg	90
β, deg	115.543(4)
γ, deg	90
V, Å3	2690.1(5)
Z	4
T, K	298
λ, Å	0.71073
ρ, Mg m-3	1.167
Rint	0.113
R1 [I N 2σ(I)]	0.1207
R1 (all data)	0.2120
wR2 [I N 2σ(I)]	0.3072
wR2 (all data)	0.3554
Flack	0.31(17)
CCDC	1975583

Table S4. Crystallograph data of R_P-5

The single crystal suited for the X-ray diffraction was obtained from the evaporation of the solution of ***R*P-5** in dichloromethane and petroleum ether.

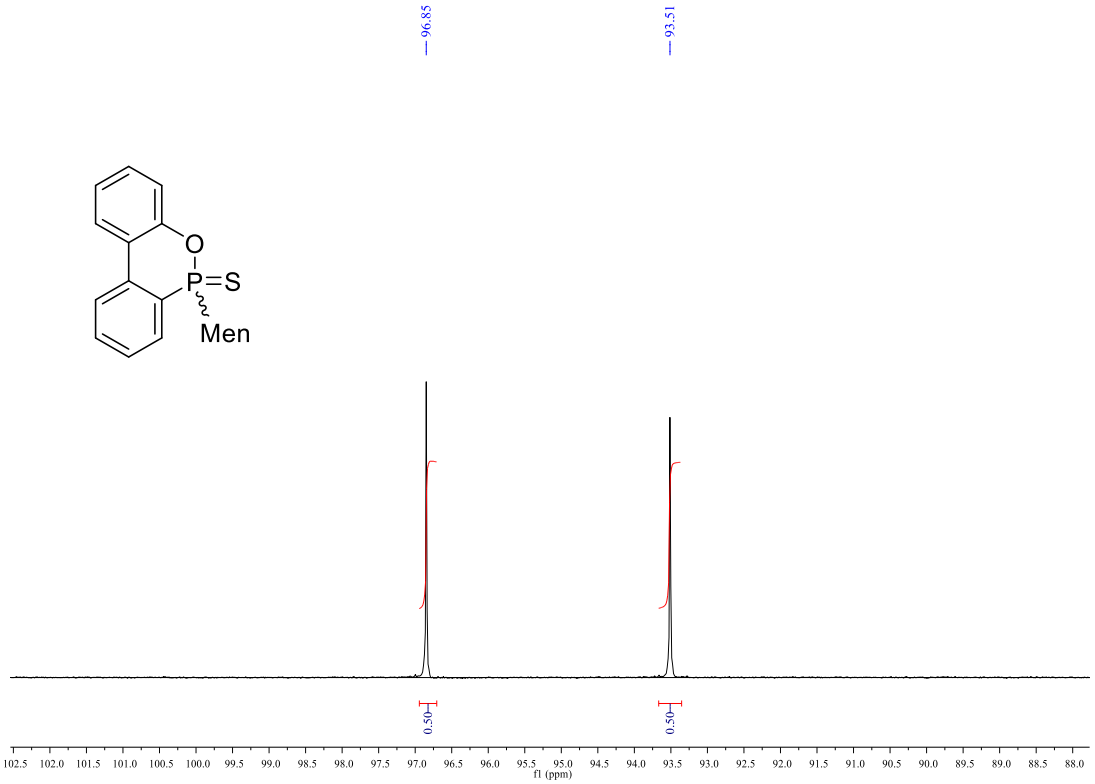


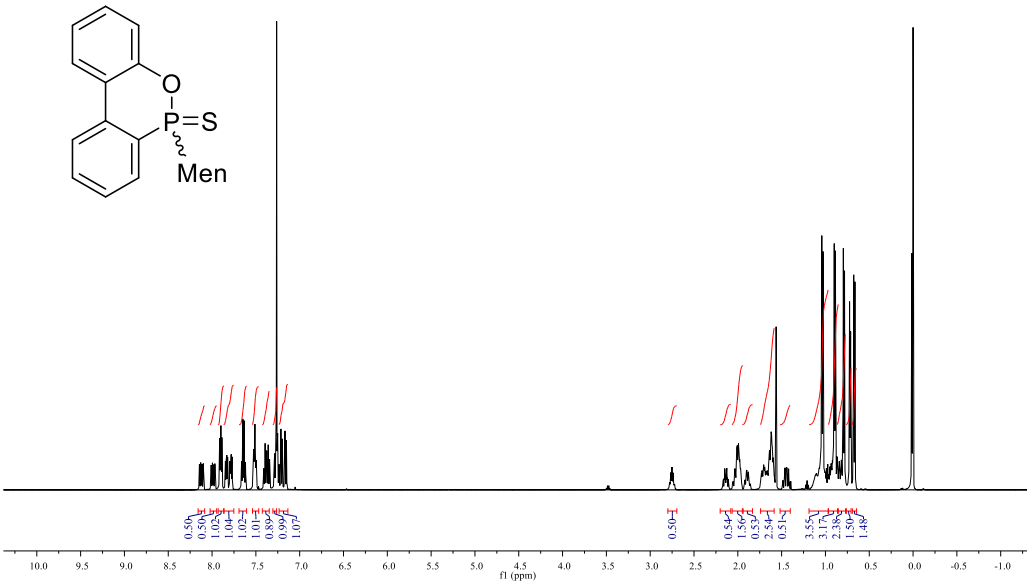


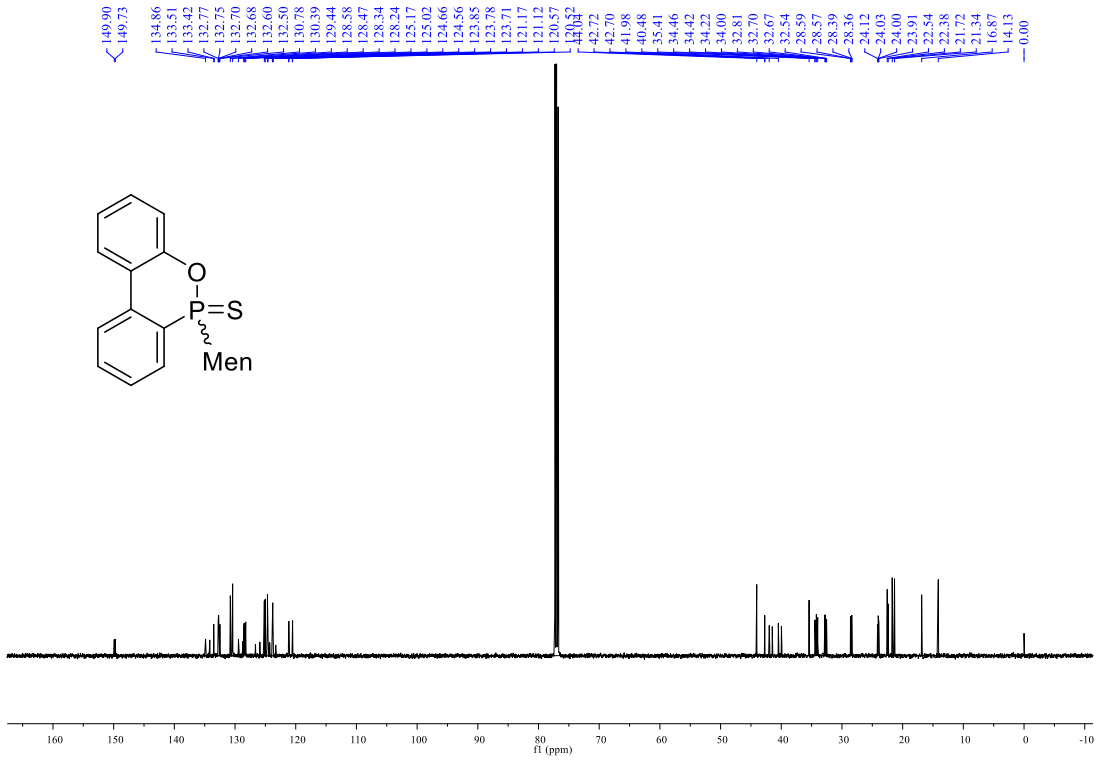
Empirical formula	C22H27O2P
Crystal system	Monoclinic
space group	P21 (No.4)
Formula weight	354.41
a, Å	8.6104(9)
b, Å	5.6083(6)
c, Å	19.2726(19)
α, deg	90
β, deg	92.639(3)
γ, deg	90
V, Å3	929.68(17)
Z	2
T, K	298
λ, Å	0.71073
ρ, Mg m-3	1.266
Rint	0.064
R1 [I N 2σ(I)]	0.0789
R1 (all data)	0.1090
wR2 [I N 2σ(I)]	0.1500
wR2 (all data)	0.1669
Flack	-0.03(19)
CCDC	2010827

Part 7. Selected photocopies of ^{1}H, ^{31}P and ^{13}C NMR spectrum

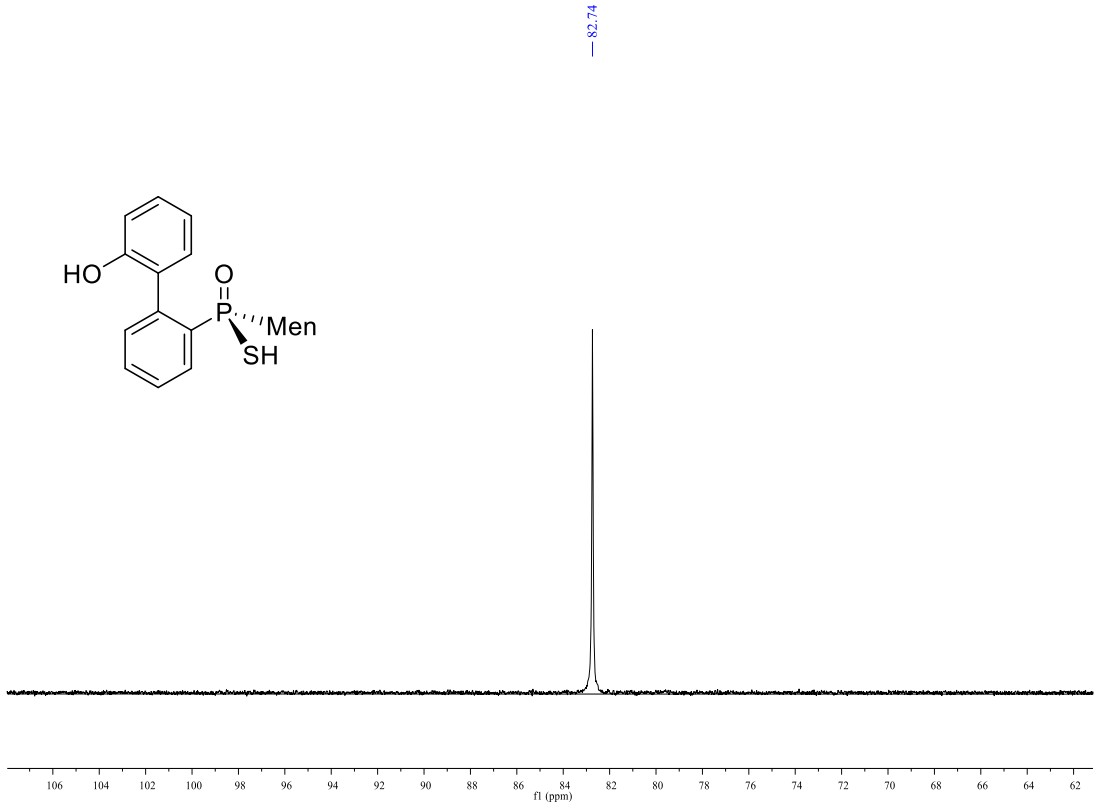
***R*P/*S*P-6-(-)-Menthyl-6H-dibenzo[c,e][1,2]-oxaphosphinine 6-sulfide (2/2')**

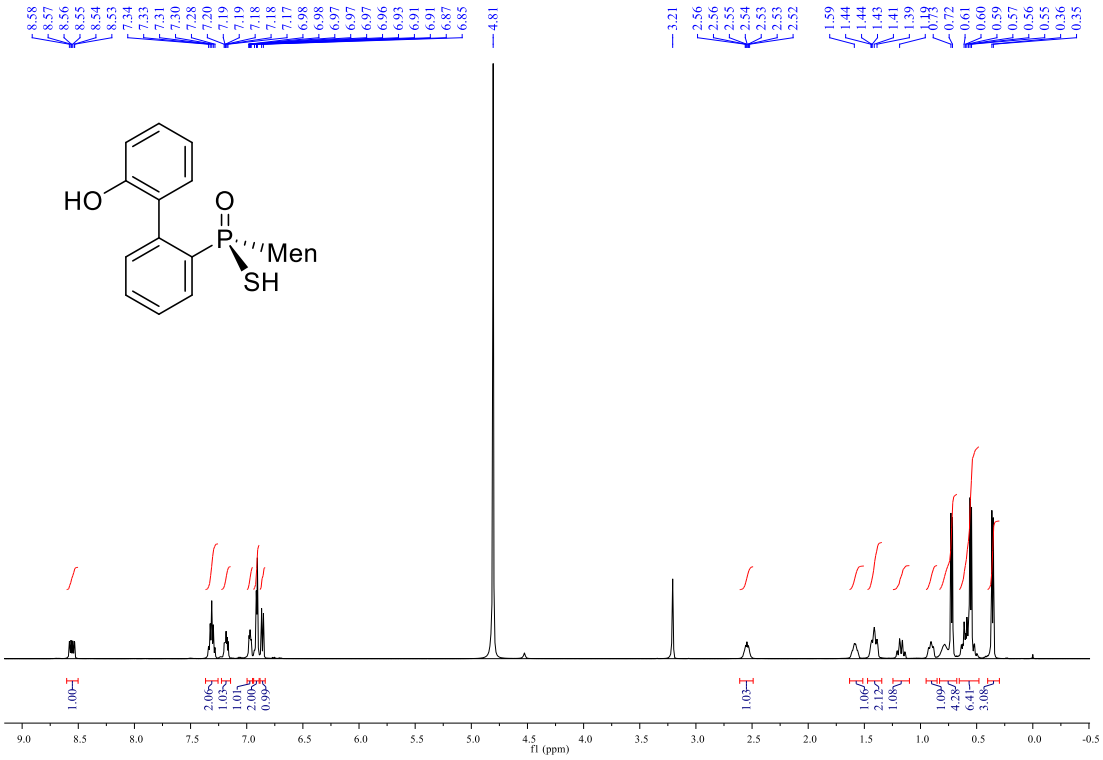


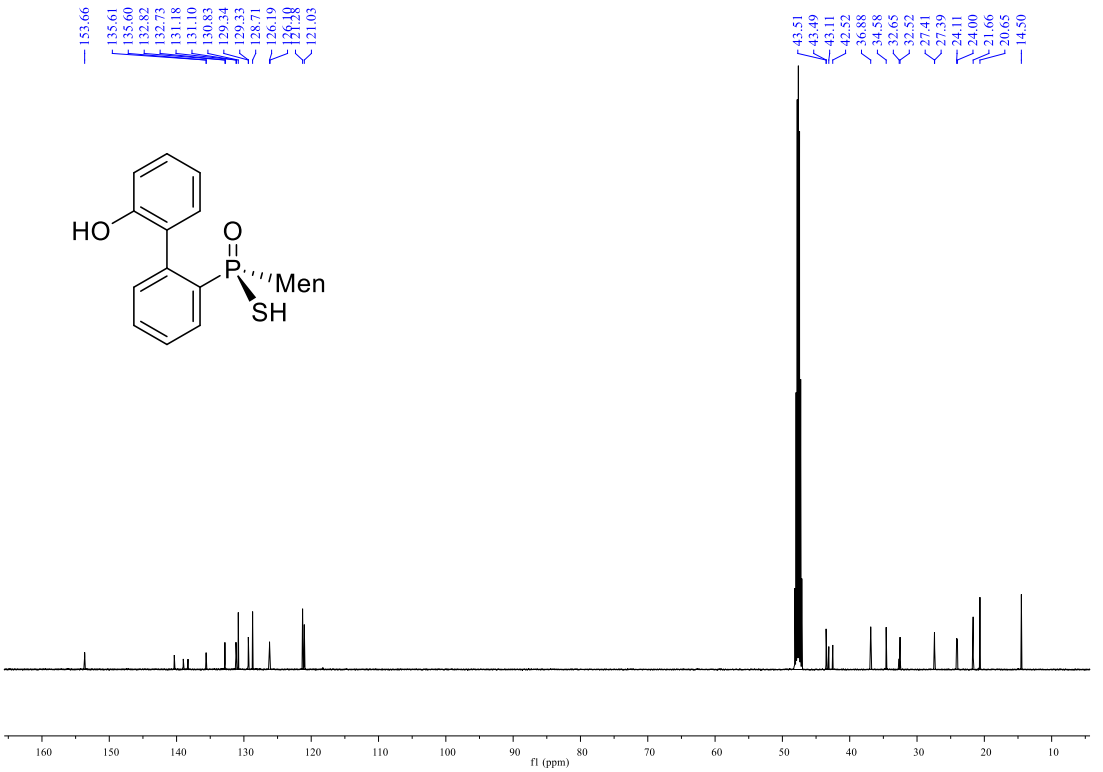




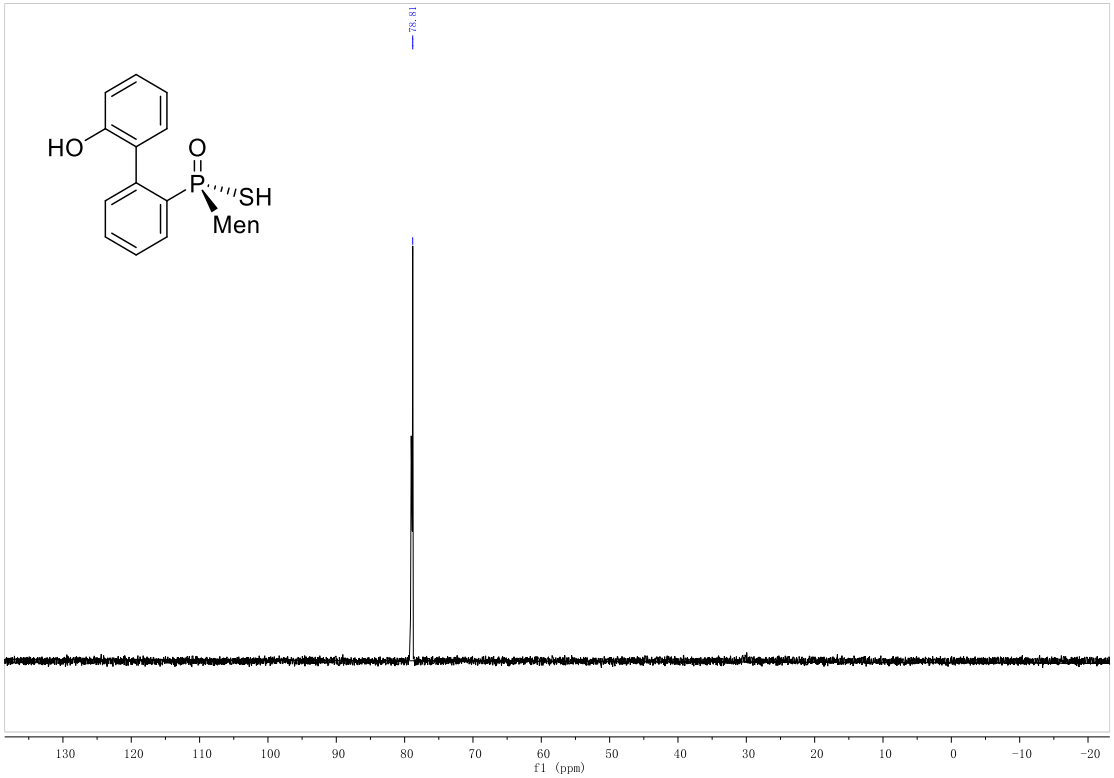
S_P-(2'-Hydroxy-[1,1'-biphenyl]-2-yl)((-)-Menthyl)phosphinothioic *S*-acid (S_P-3)

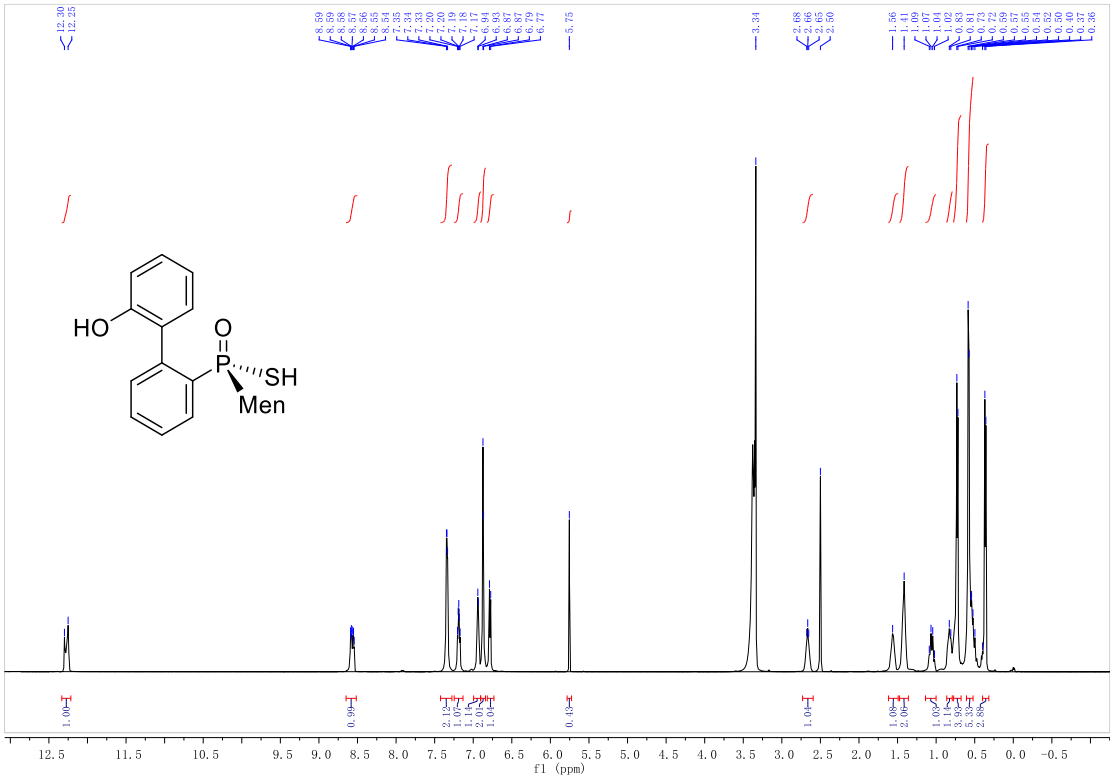


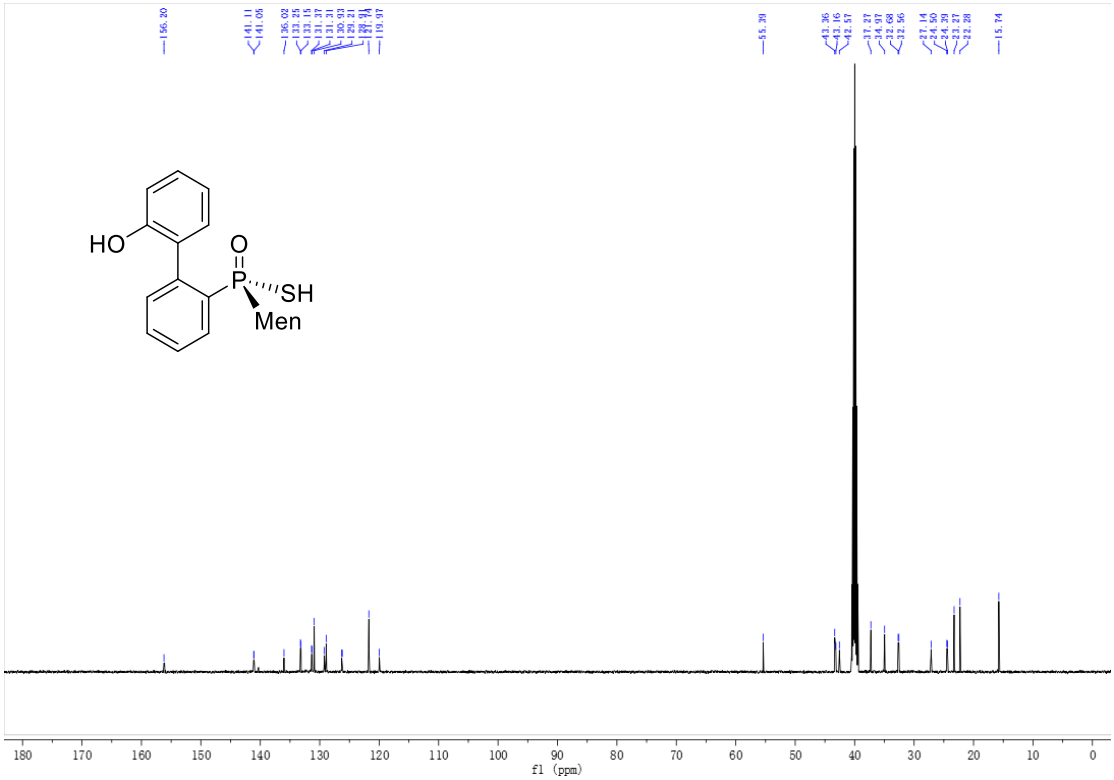

HO
O
P
Men
SH
fl (ppm)


HO
O
P
Men
SH
fl (ppm)

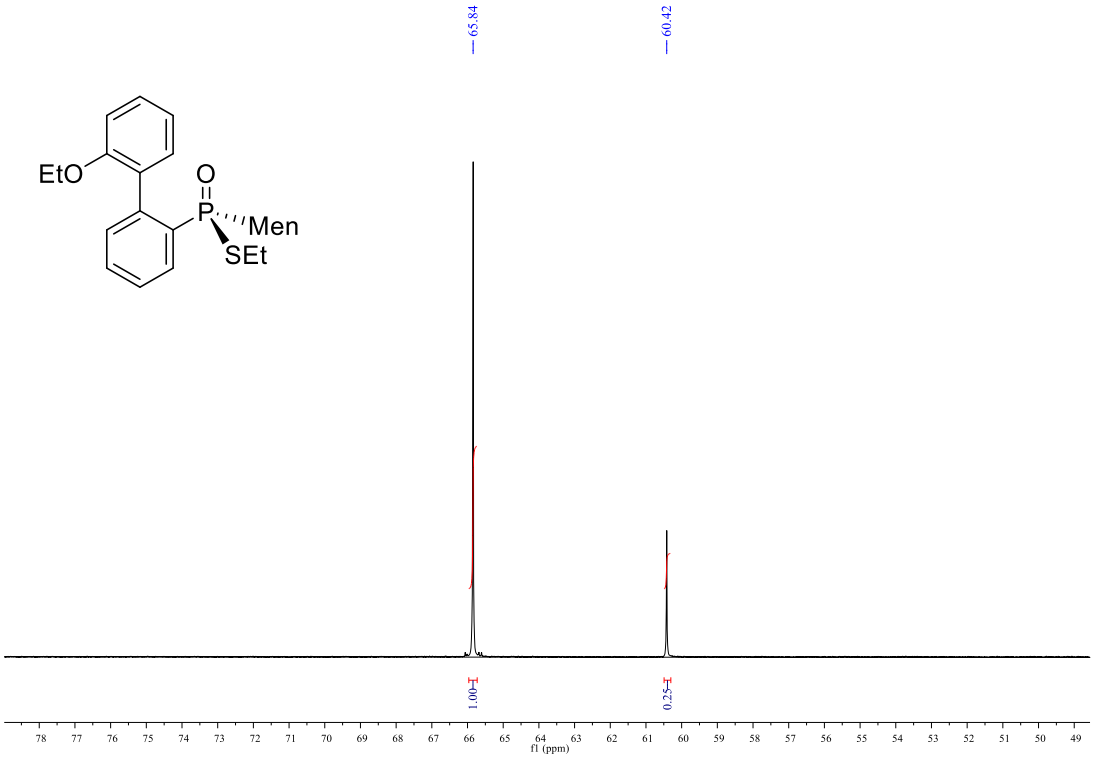
R_P-(2'-Hydroxy-[1,1'-biphenyl]-2-yl)((-)-menthyl)phosphinothioic *S*-acid (R_P-3')

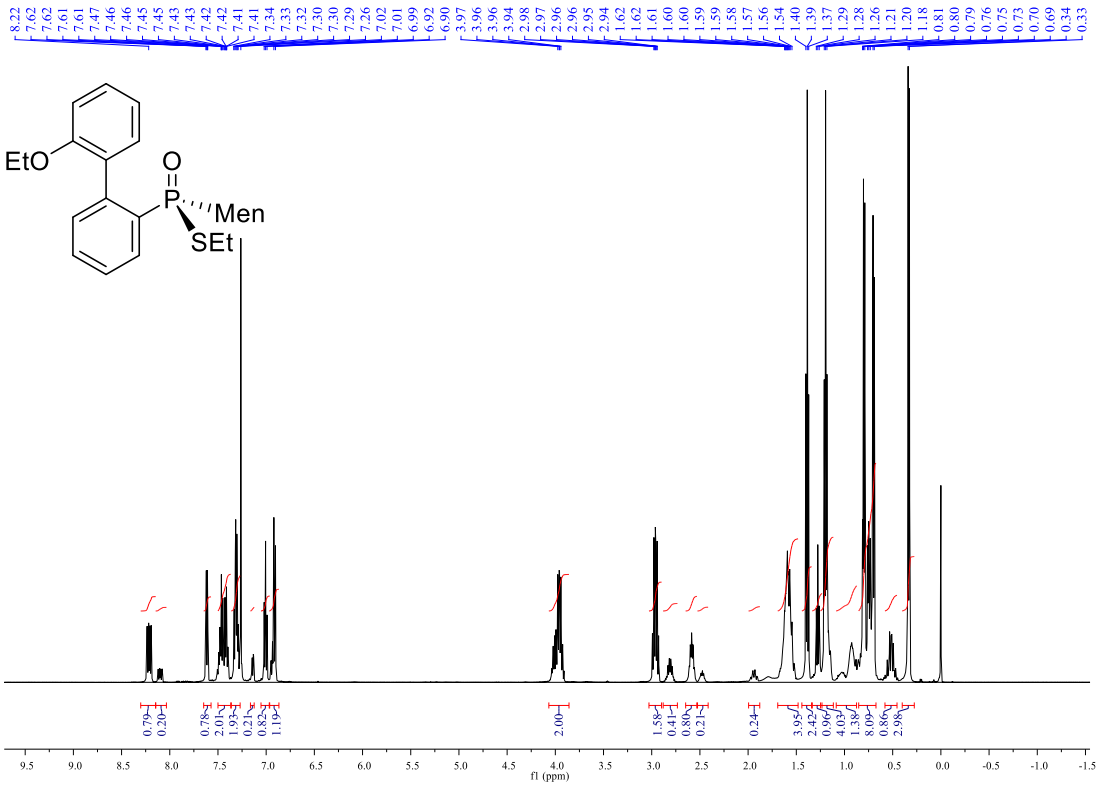


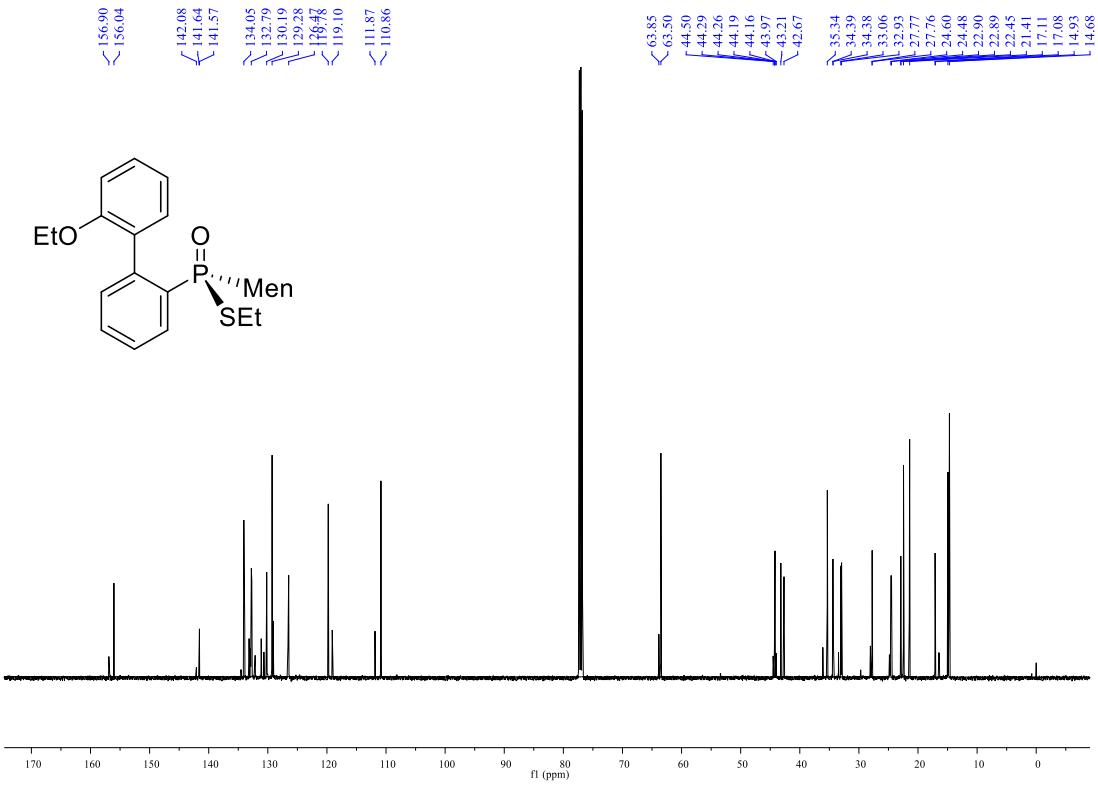




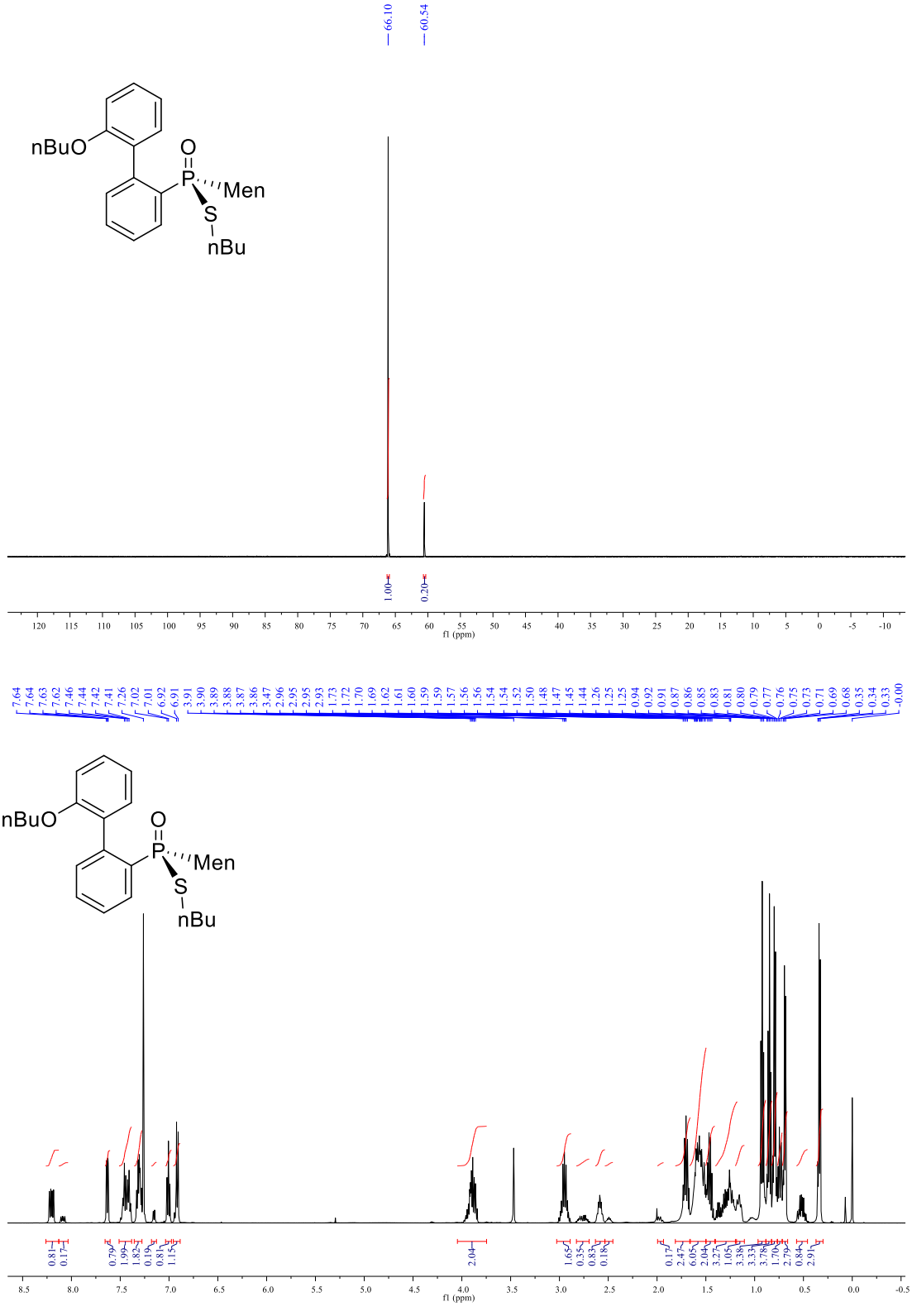
S_P-*S*-Ethyl-(2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl)phosphinothioate (S_P-4b)

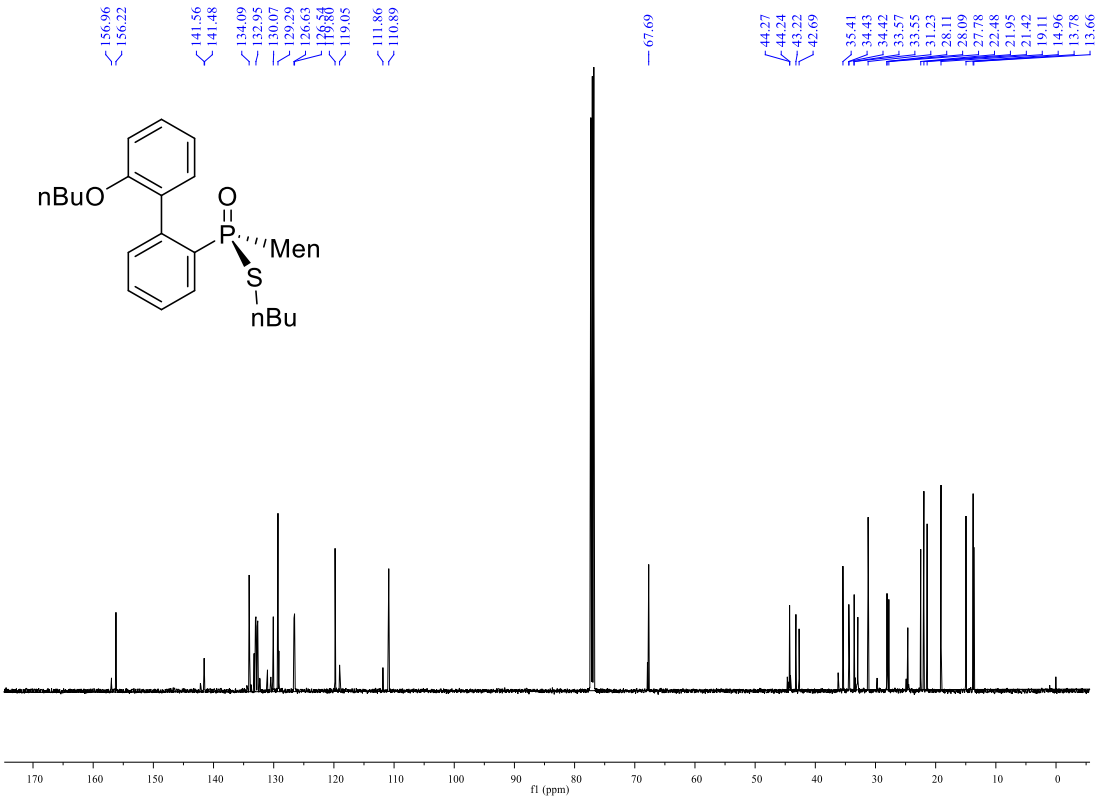



EtO
O
P
Men
SEt
f1 (ppm)

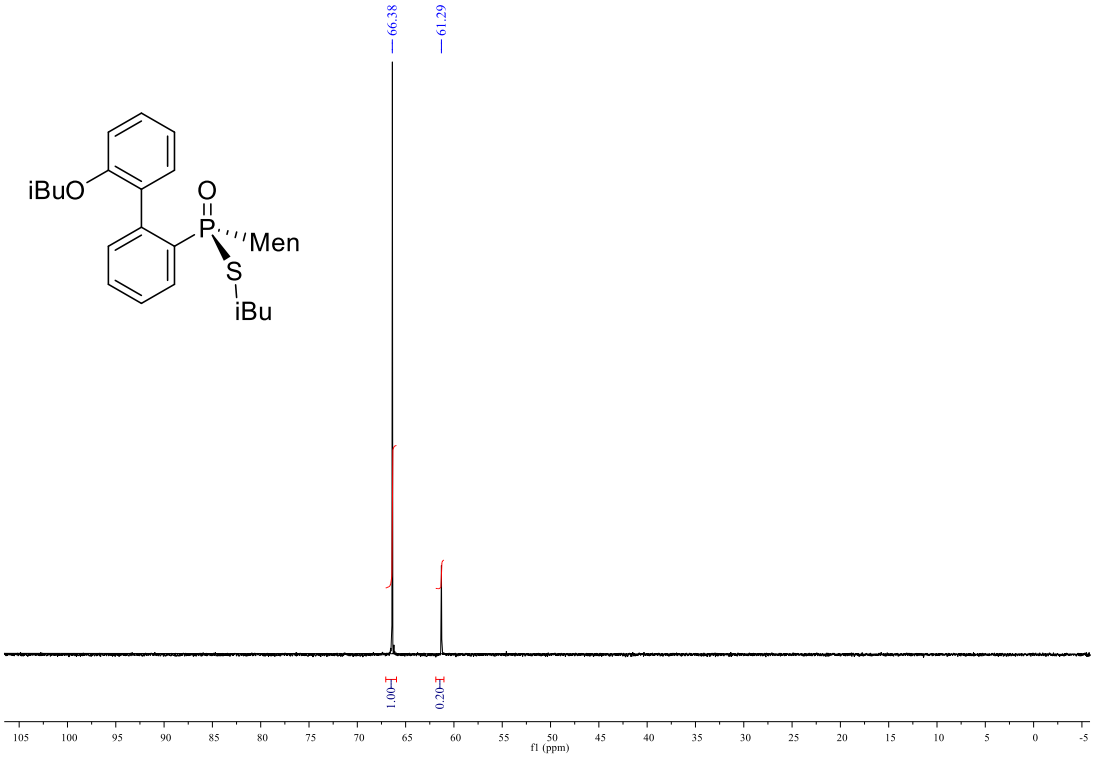

EtO
O
P
Men
SEt
f1 (ppm)

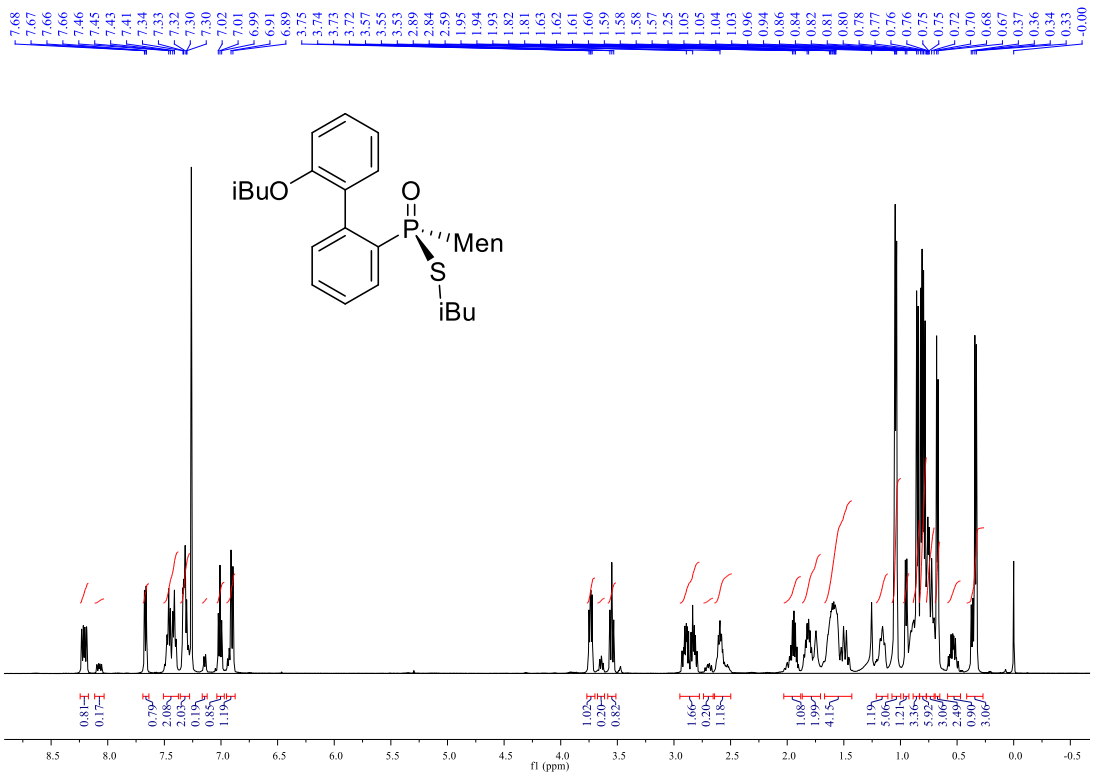
***S*P-*S*-Butyl-(2'- butoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl)phosphinothioate (*S*P-4c)**

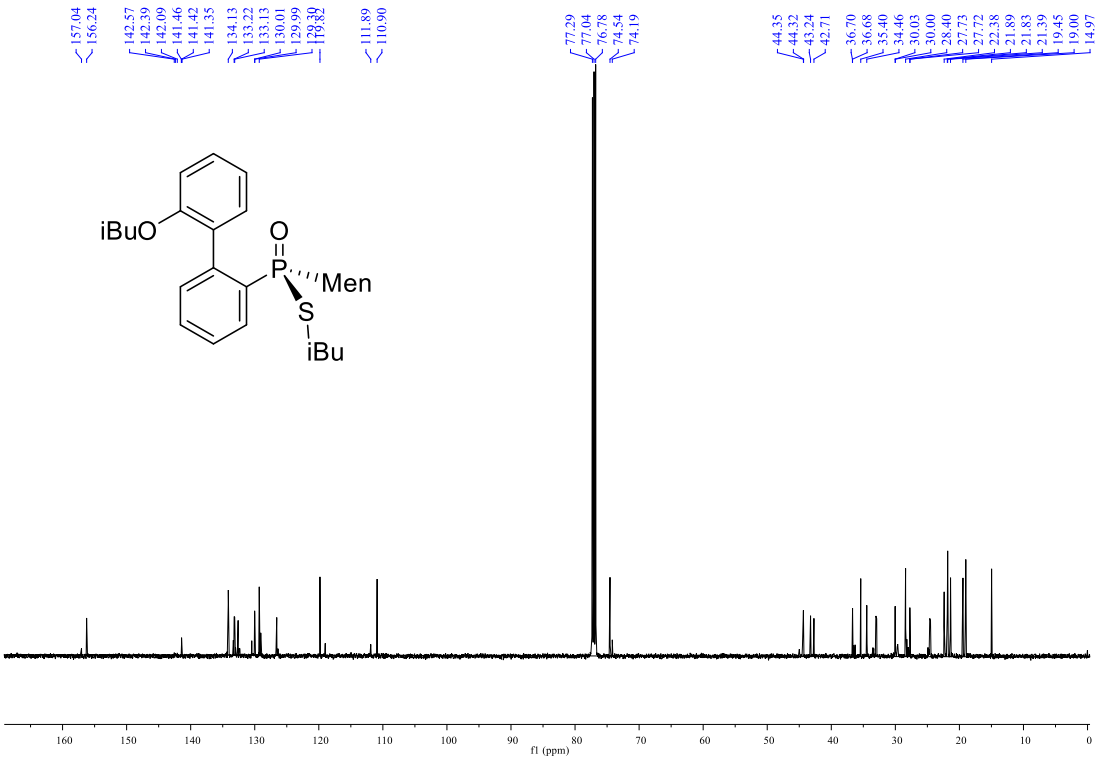




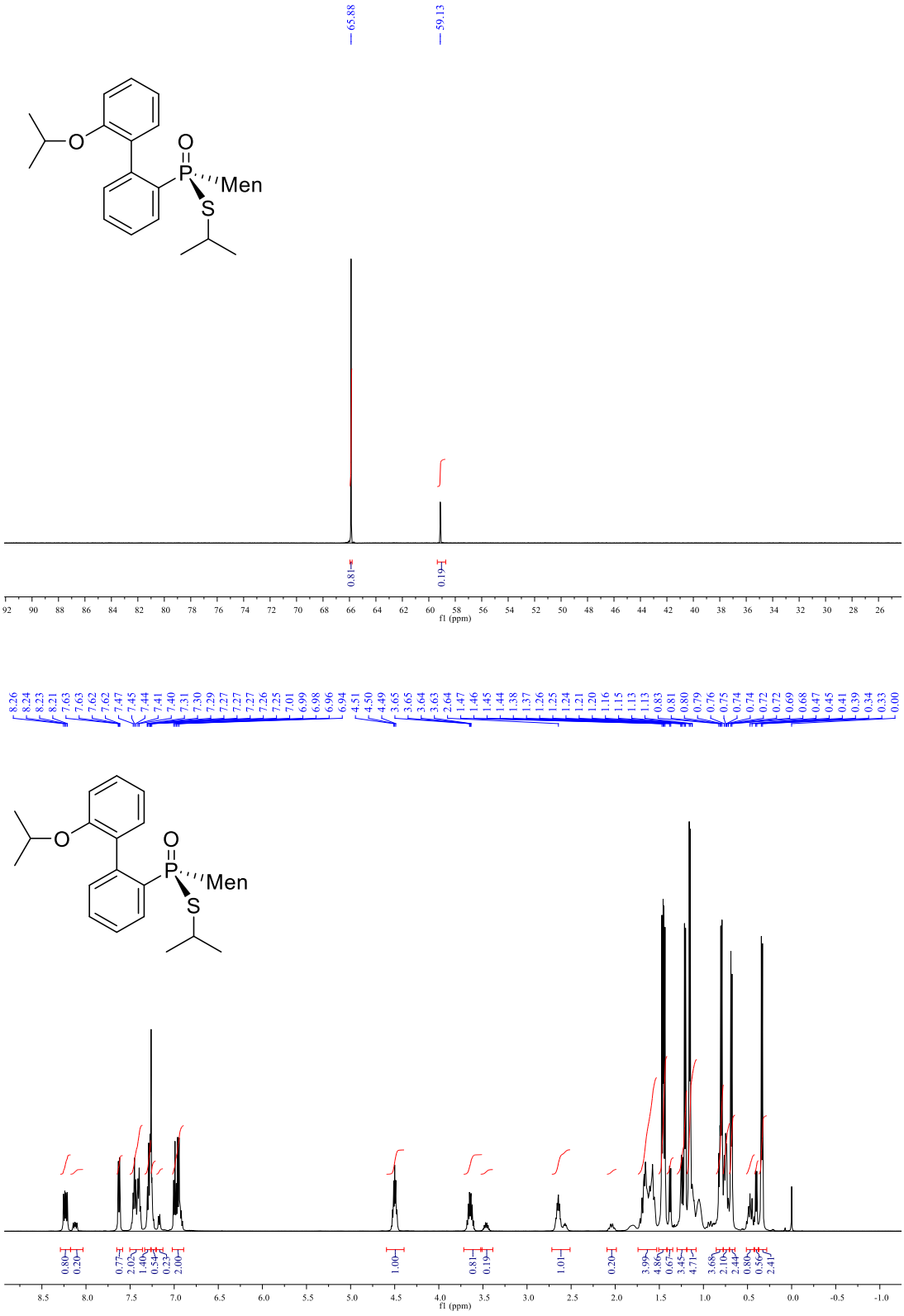
S_P-*S*-Isobutyl-(2'-isobutoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate (S_P-4d)

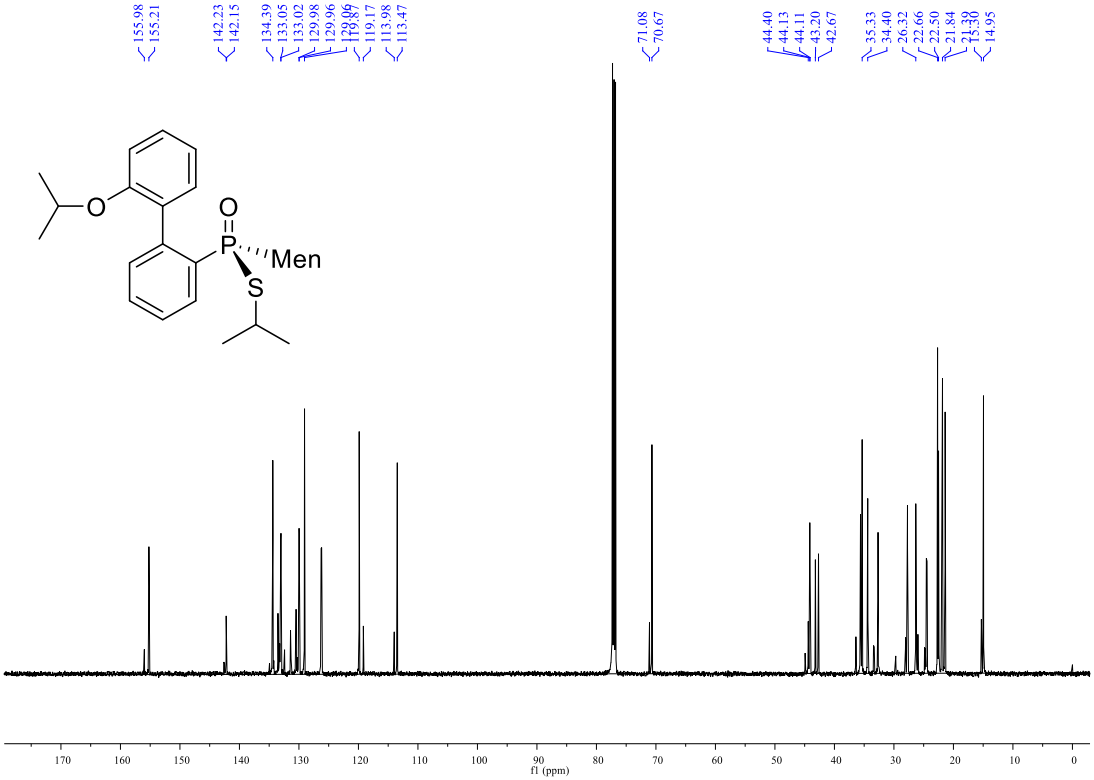



iBuO
O
P
Men
S
iBu
f1 (ppm)

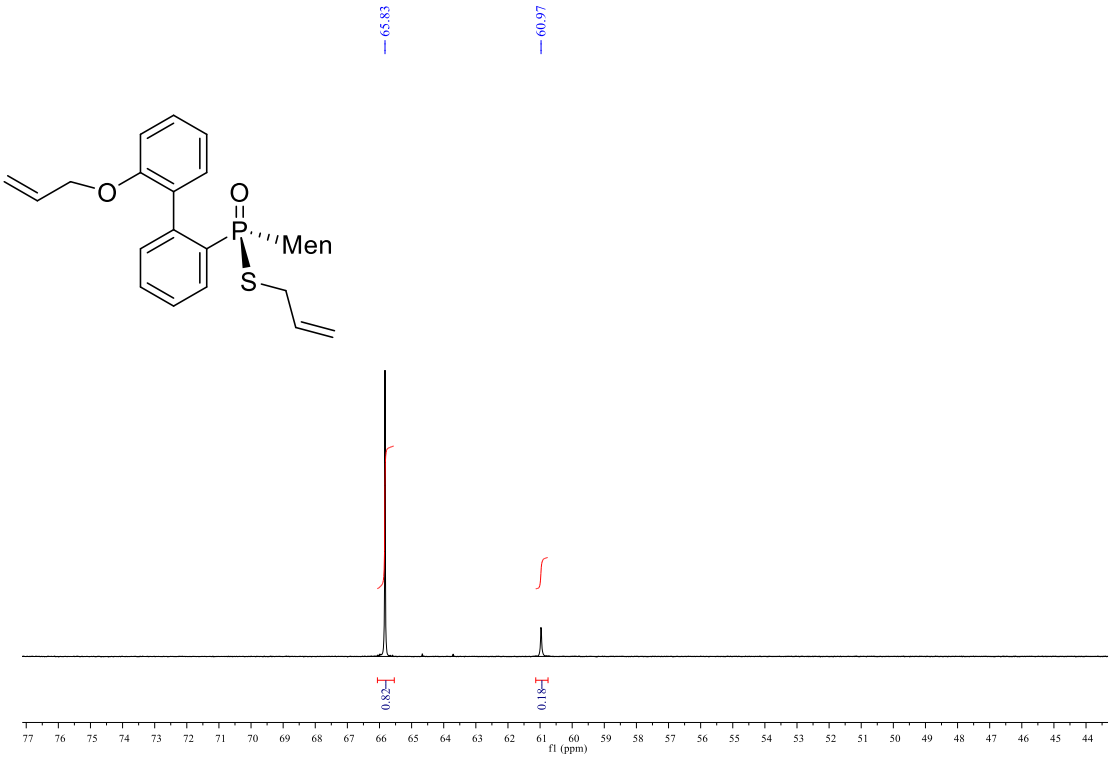

iBuO
O
P
Men
S
iBu
f1 (ppm)

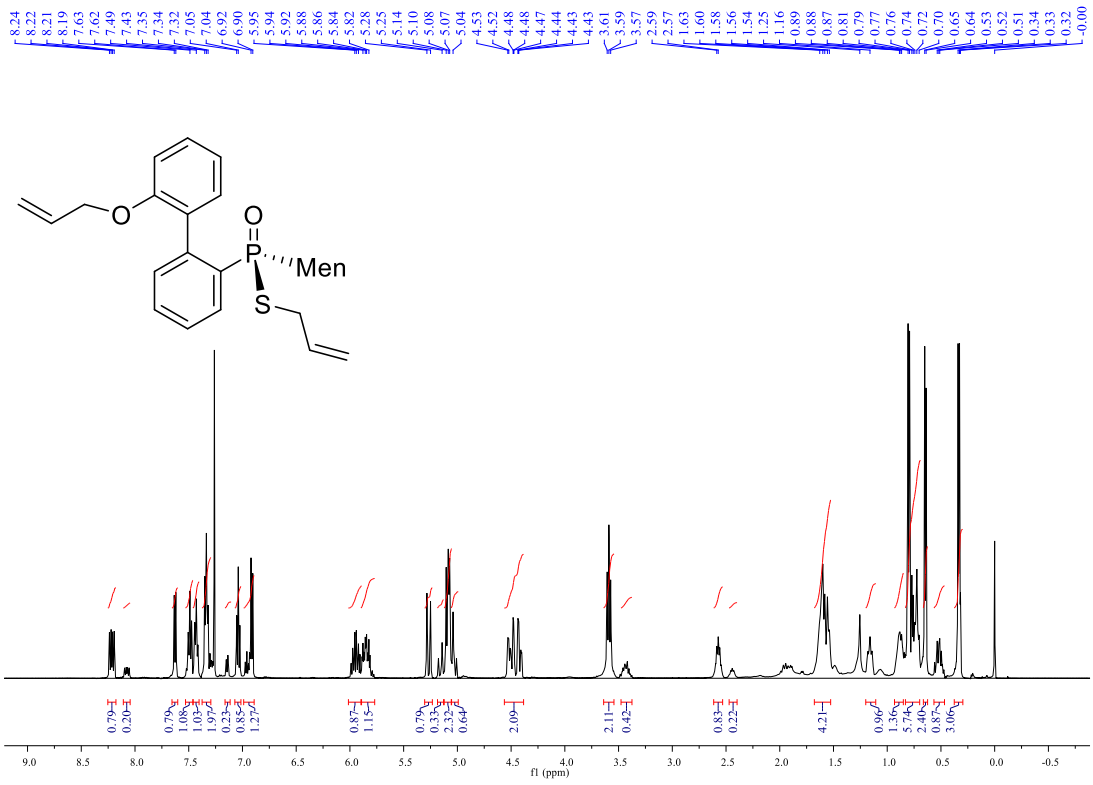
S_P-*S*-Isopropyl-(2'-isopropoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate (S_P-4e)

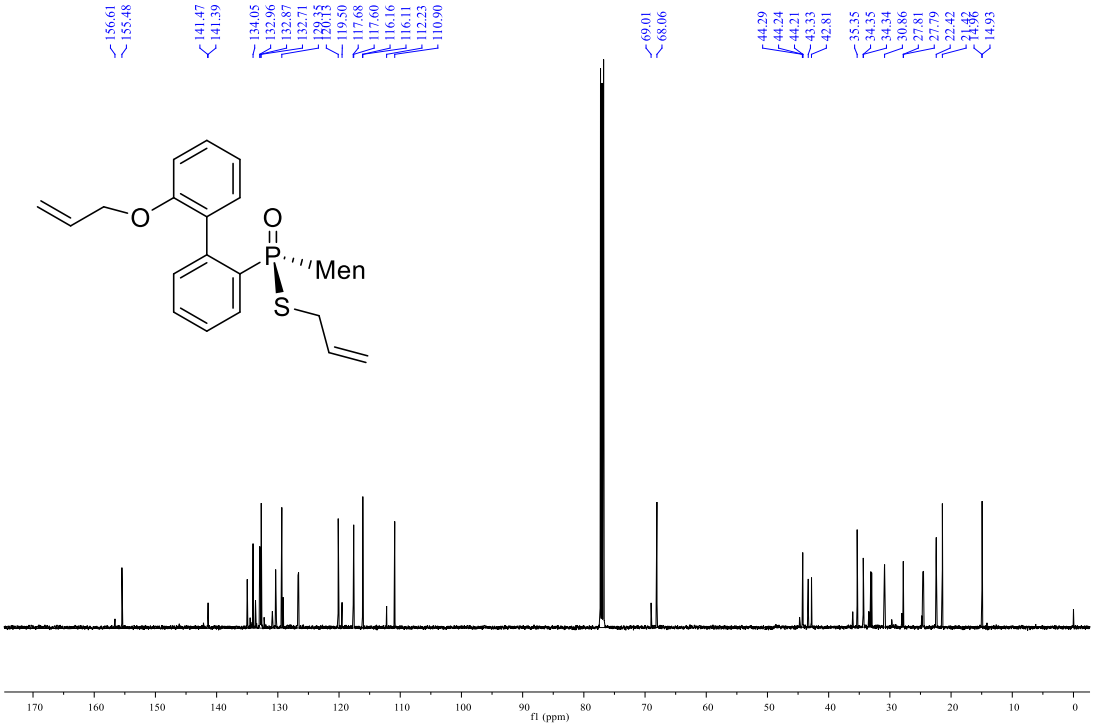




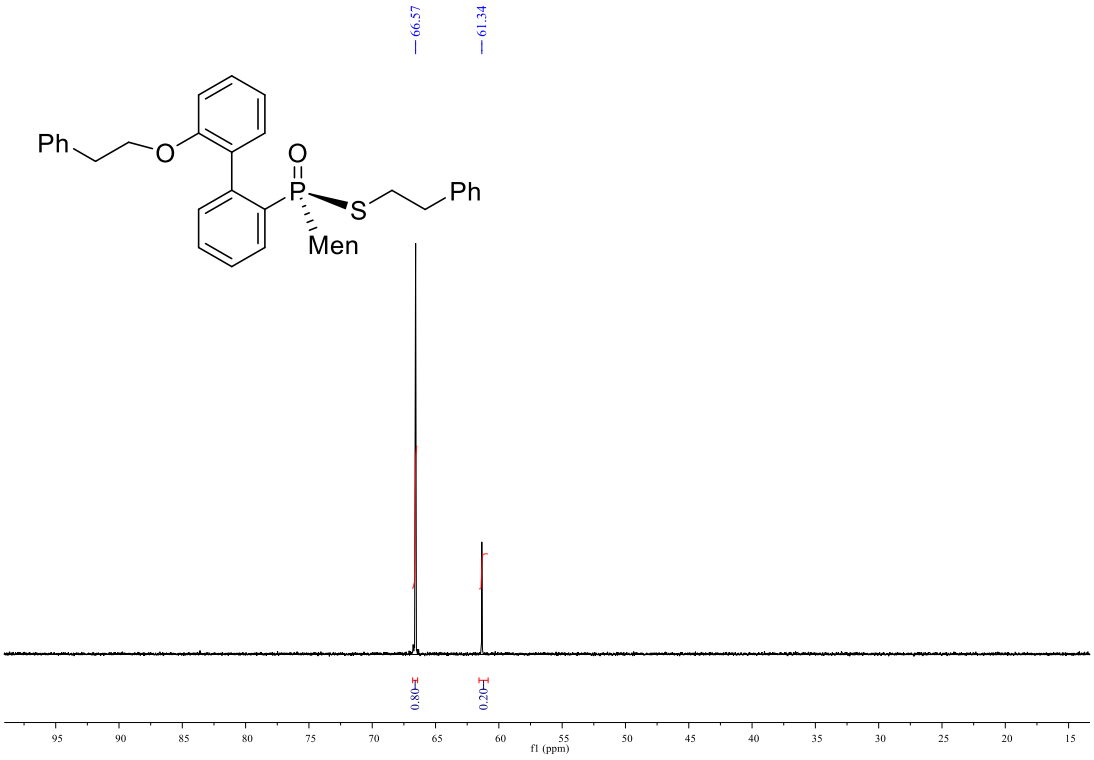
S_P-*S*-Allyl-(2'-(allyloxy)-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate (S_P-4f)

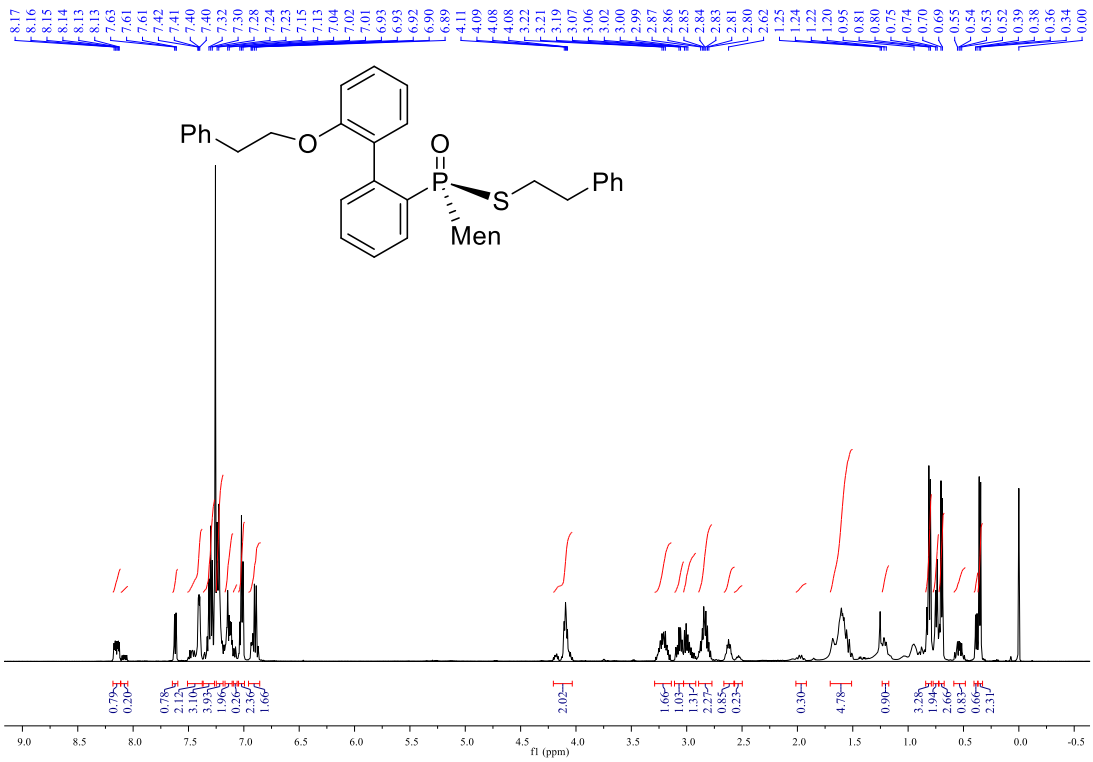


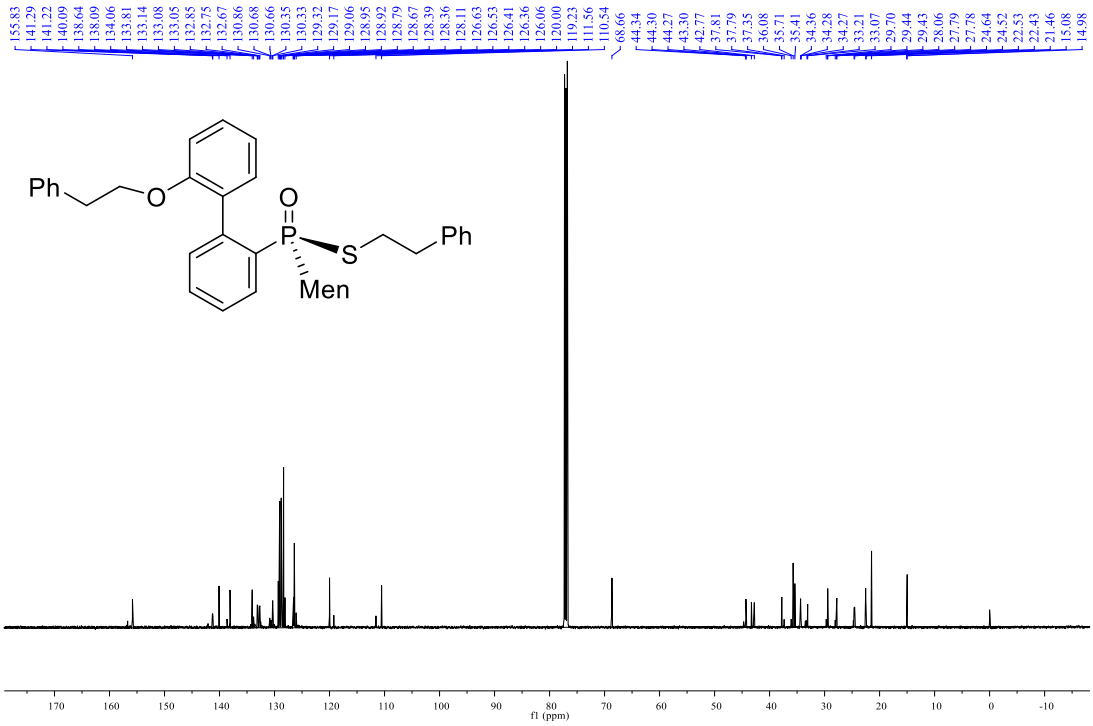

O
O
P
Men
S
f1 (ppm)


O
O
P
Men
S
f1 (ppm)

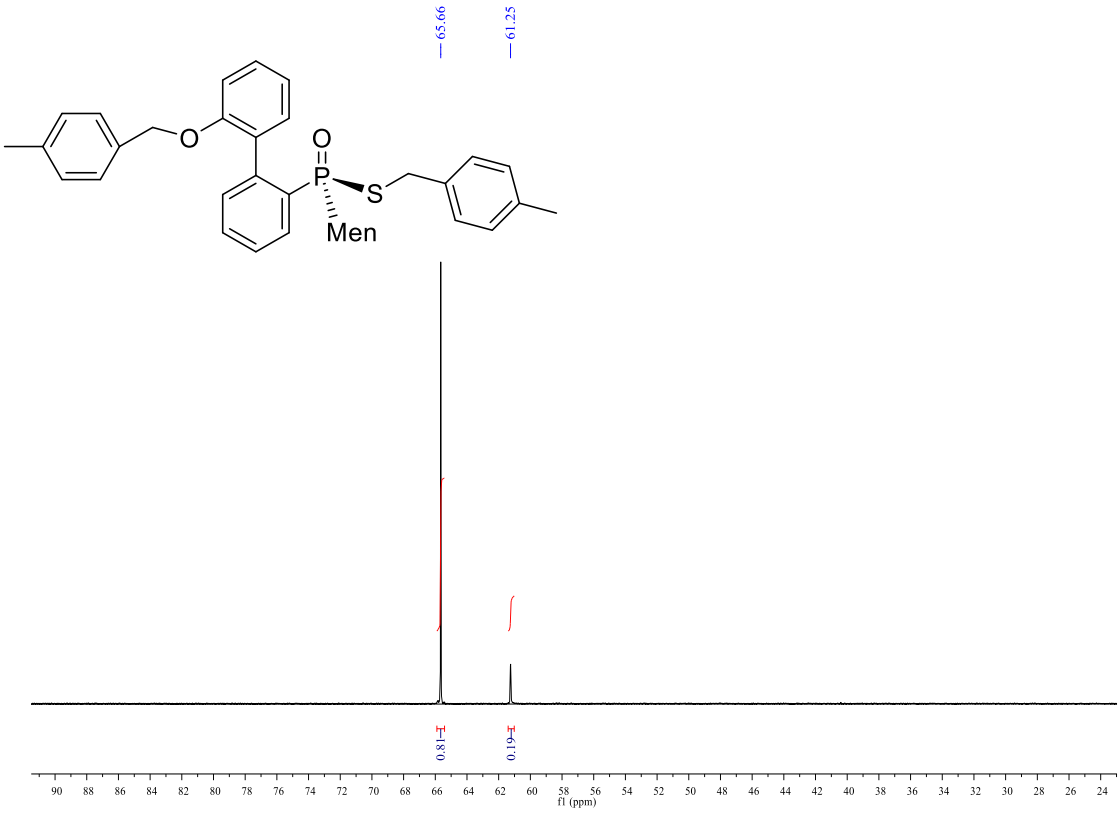
S_P-*S*-Phenethyl-((-)-menthyl)(2'-phenethoxy-[1,1'-biphenyl]-2-yl) phosphinothioate (S_P-4g)

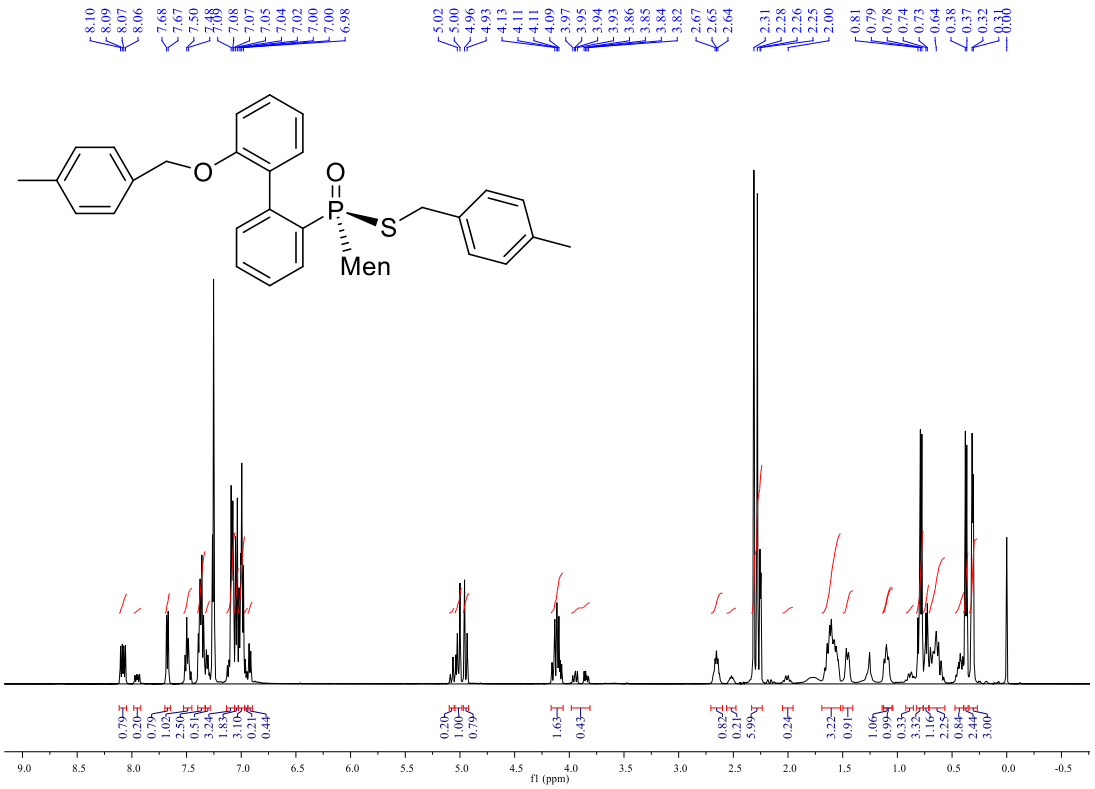


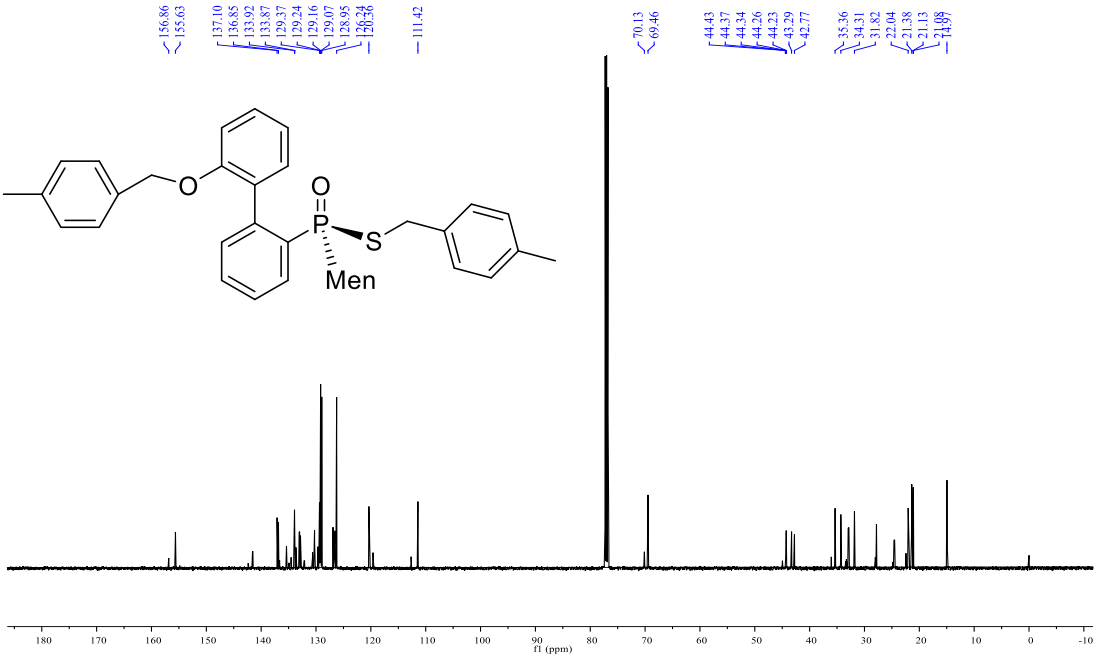




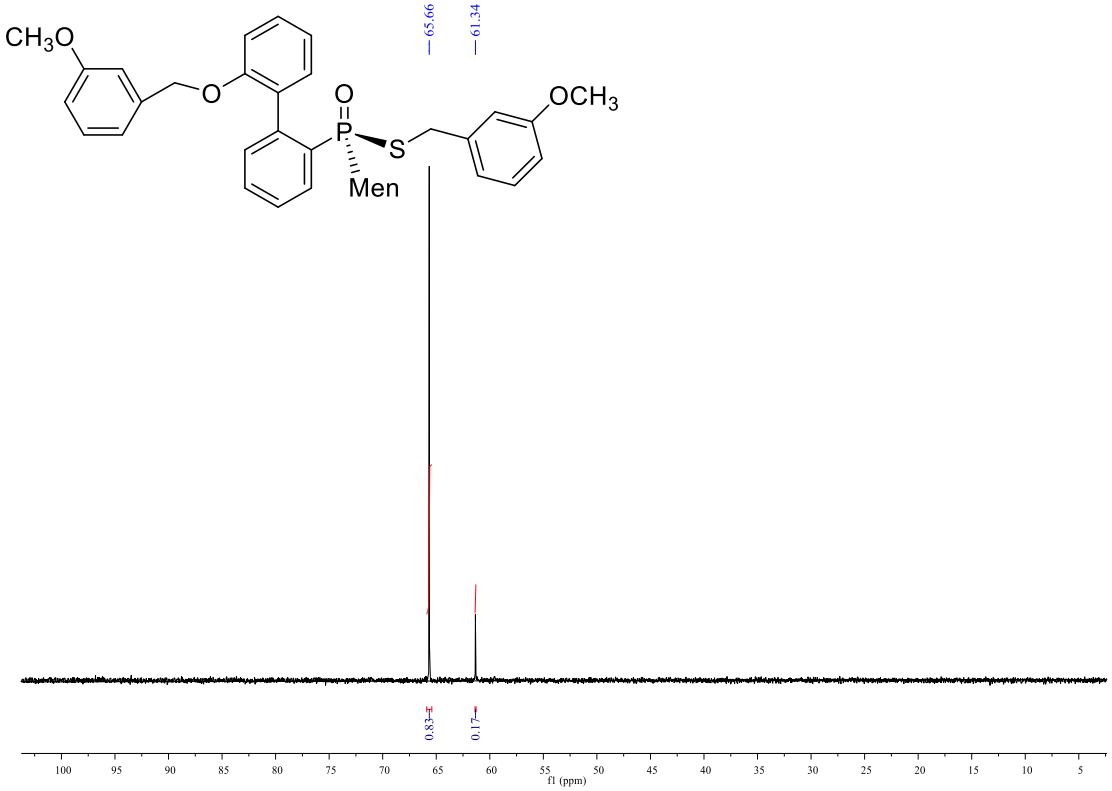
S_P-*S*-(4-Methylbenzyl)-((-)-Menthyl)(2'-((4-Methylbenzyl)oxy)-[1,1'-biphenyl]-2-yl)phosphin othioate (S_P-4j)

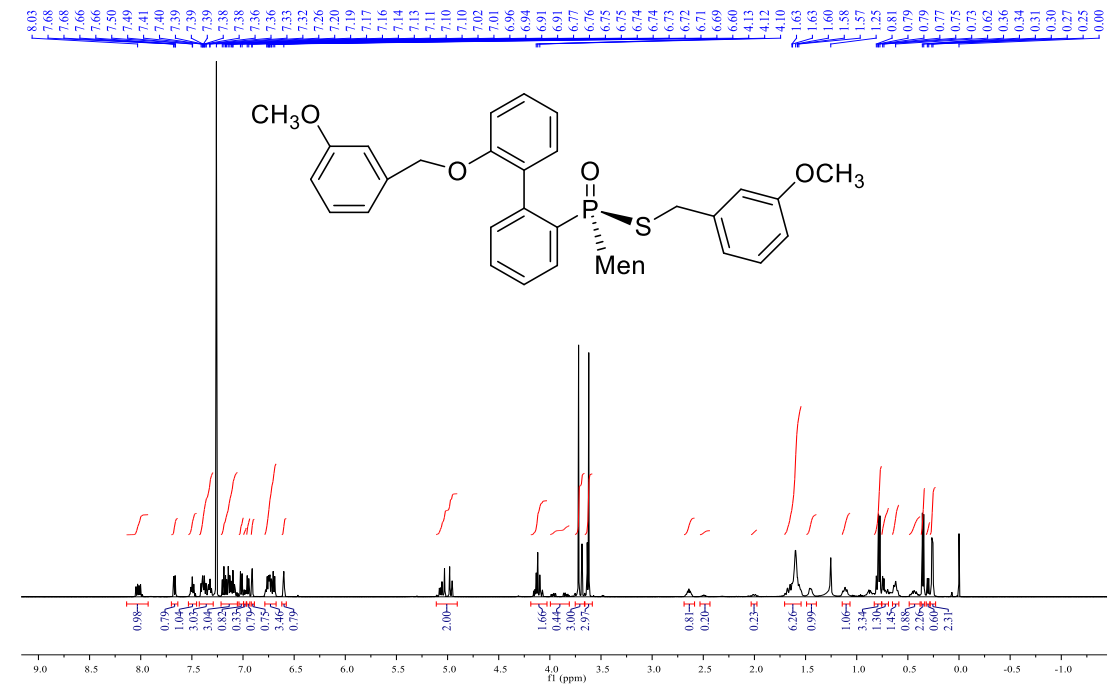


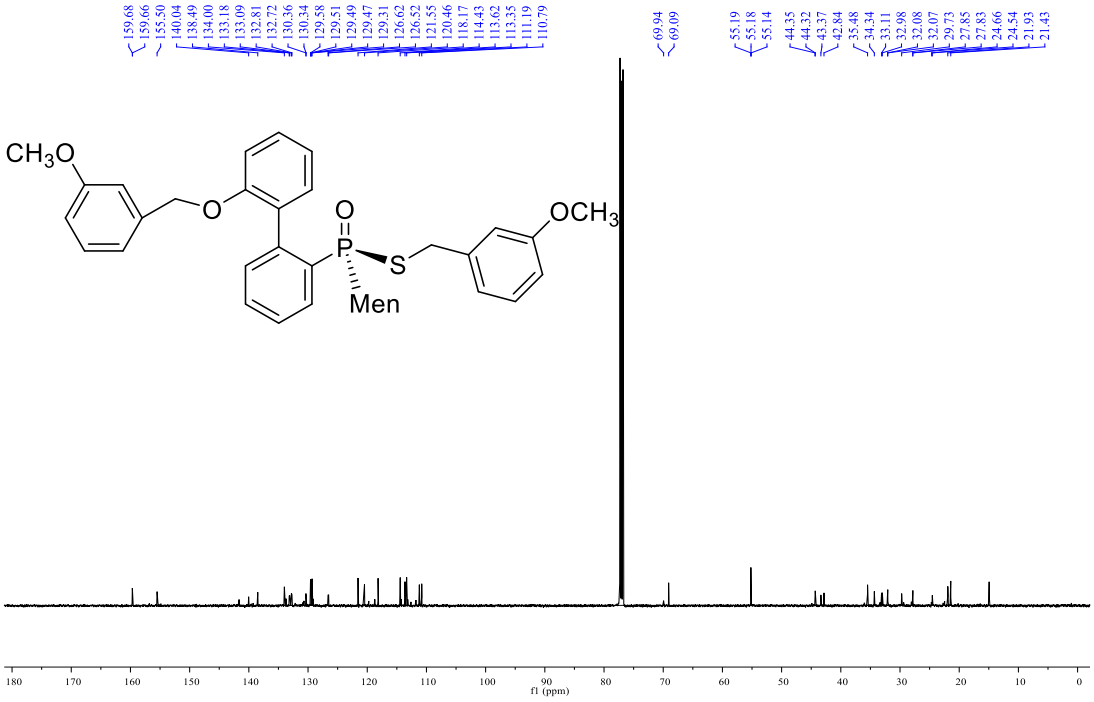

8.10
8.09
8.07
8.06
7.68
7.67
7.50
7.48
7.08
7.07
7.05
7.04
7.02
7.00
7.00
6.98
5.02
5.00
4.96
4.93
4.13
4.11
4.11
4.09
3.97
3.95
3.94
3.93
3.86
3.85
3.84
3.82
2.67
2.65
2.64
2.31
2.28
2.26
2.25
2.00
0.81
0.79
0.78
0.74
0.73
0.64
0.38
0.37
0.32
0.00
O
O
P
S
Men
f1 (ppm)


156.86
155.63
137.10
136.85
133.92
133.87
129.37
129.24
129.16
129.07
128.95
126.34
126.26
111.42
70.13
69.46
44.43
44.37
44.34
44.26
44.23
43.29
42.77
35.36
34.31
31.82
22.04
21.38
21.13
21.08
14.97
O
O
P
S
Men
f1 (ppm)

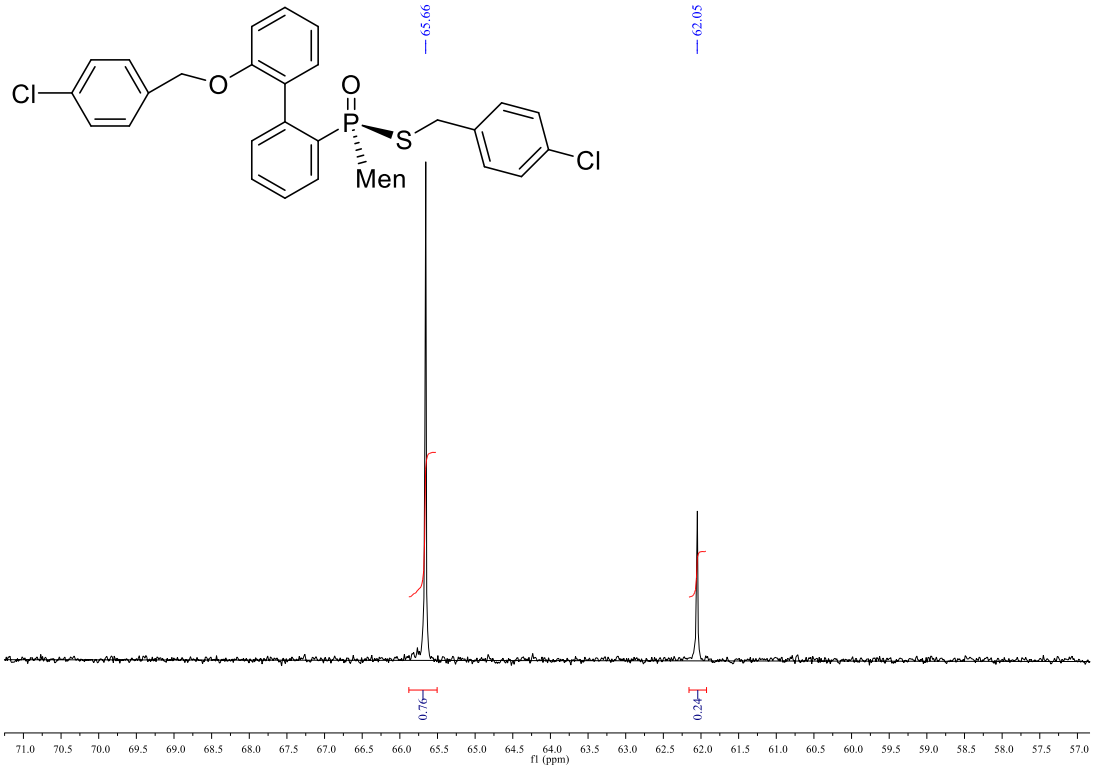
S_P-*S*-(3-Methoxybenzyl)-((-)-menthyl)(2'-((3-methoxybenzyl)oxy)-[1,1'-biphenyl]-2-yl)phosphinothioate (S_P-4k)

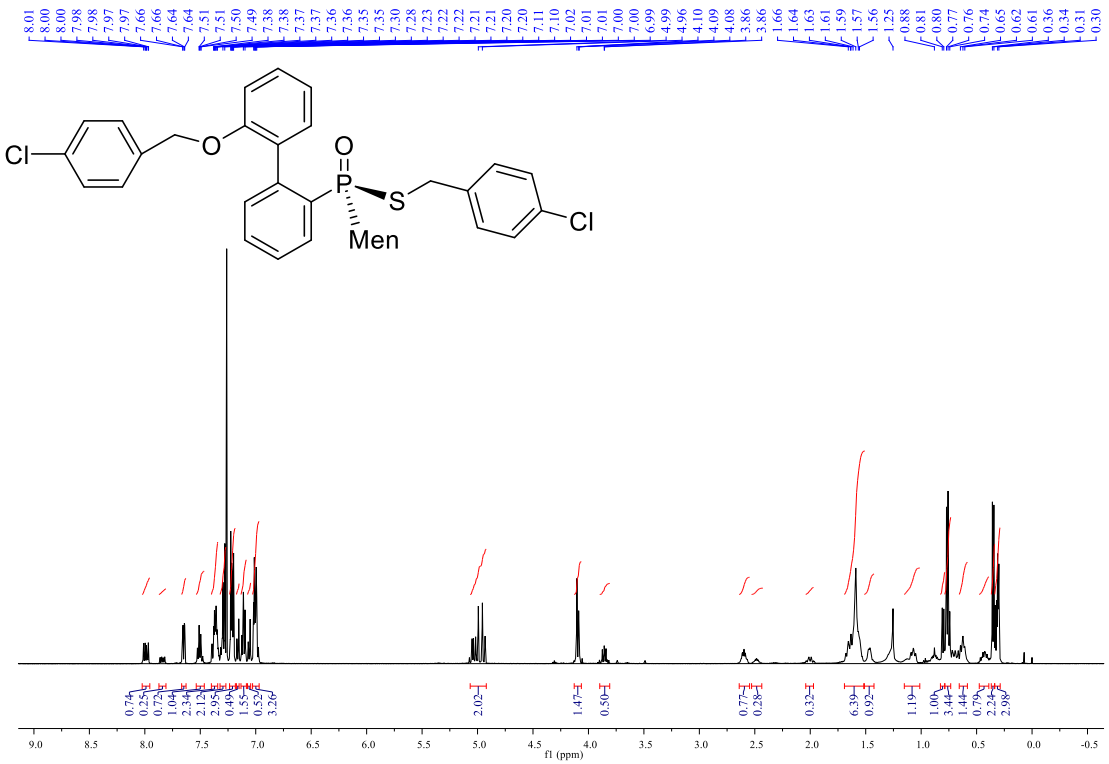


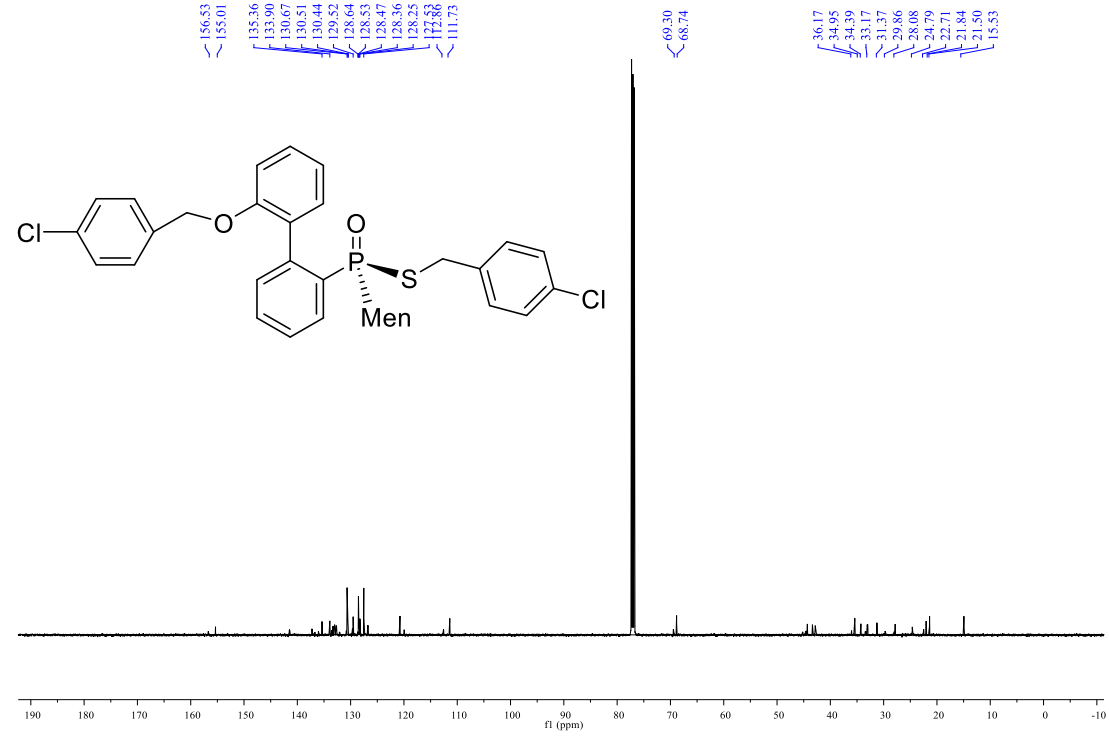




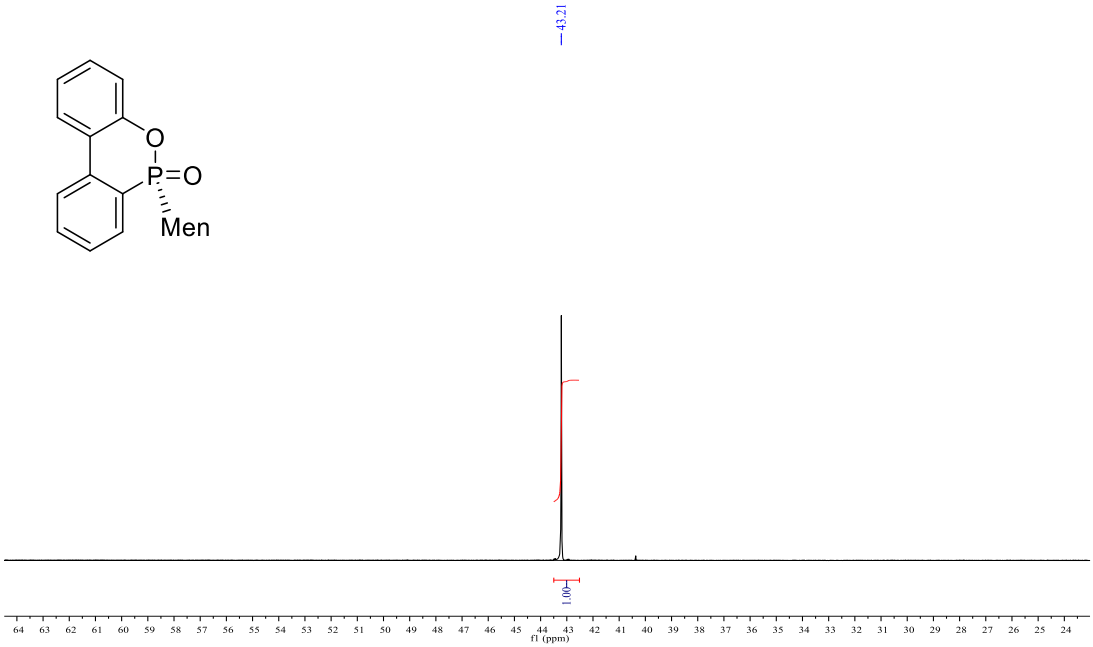
S_P-*S*-(4-Chlorobenzyl)-(2'-((4-chlorobenzyl)oxy)-[1,1'-biphenyl]-2-yl)((-)-menthyl)phosphinothioate (S_P-4l)

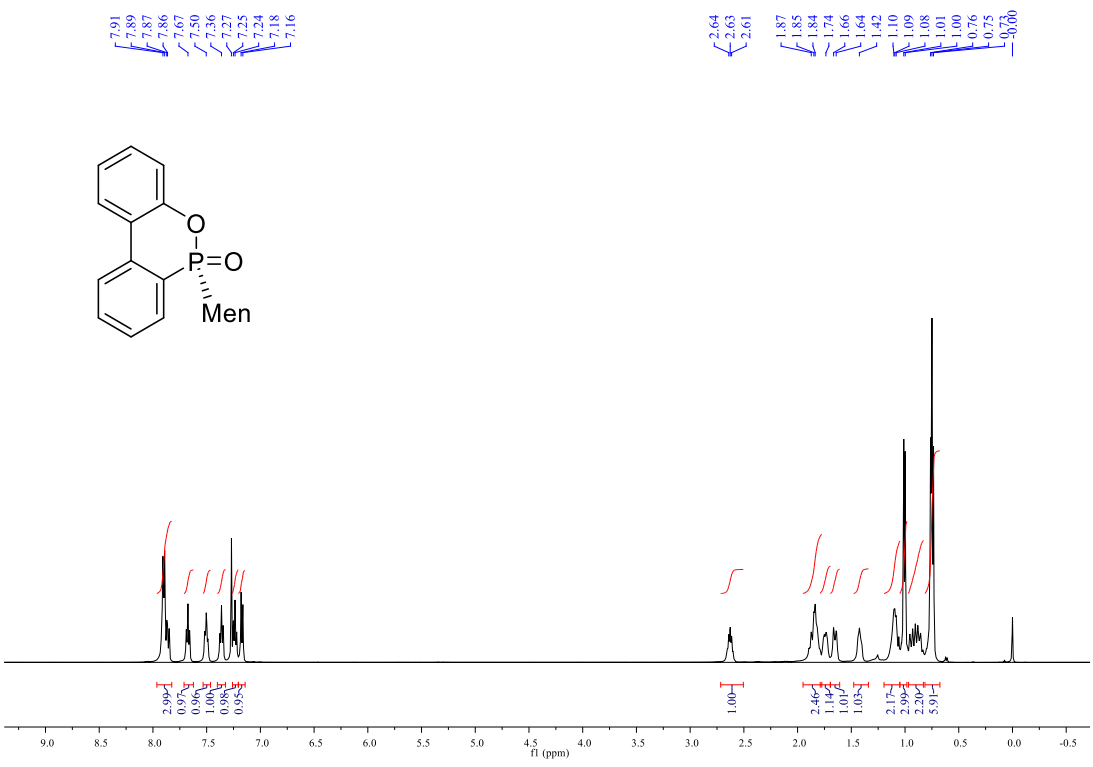


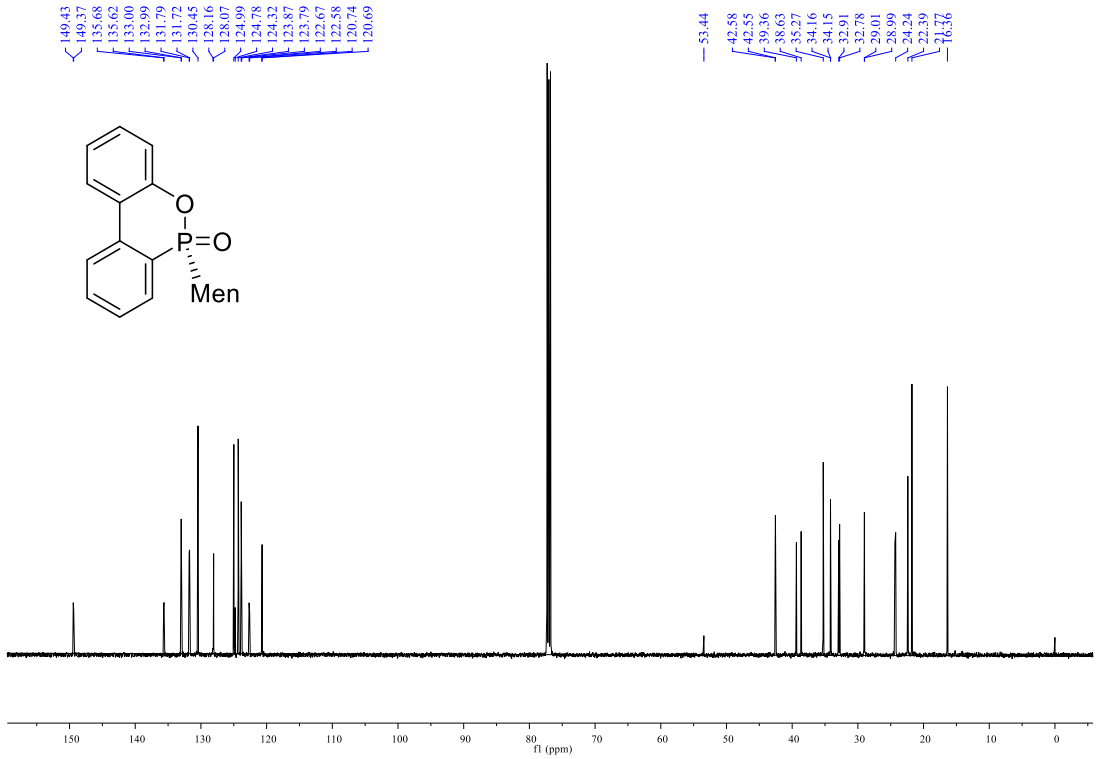

Cl
O
O
P
S
Men
Cl
f1 (ppm)


Cl
O
O
P
S
Men
Cl
f1 (ppm)

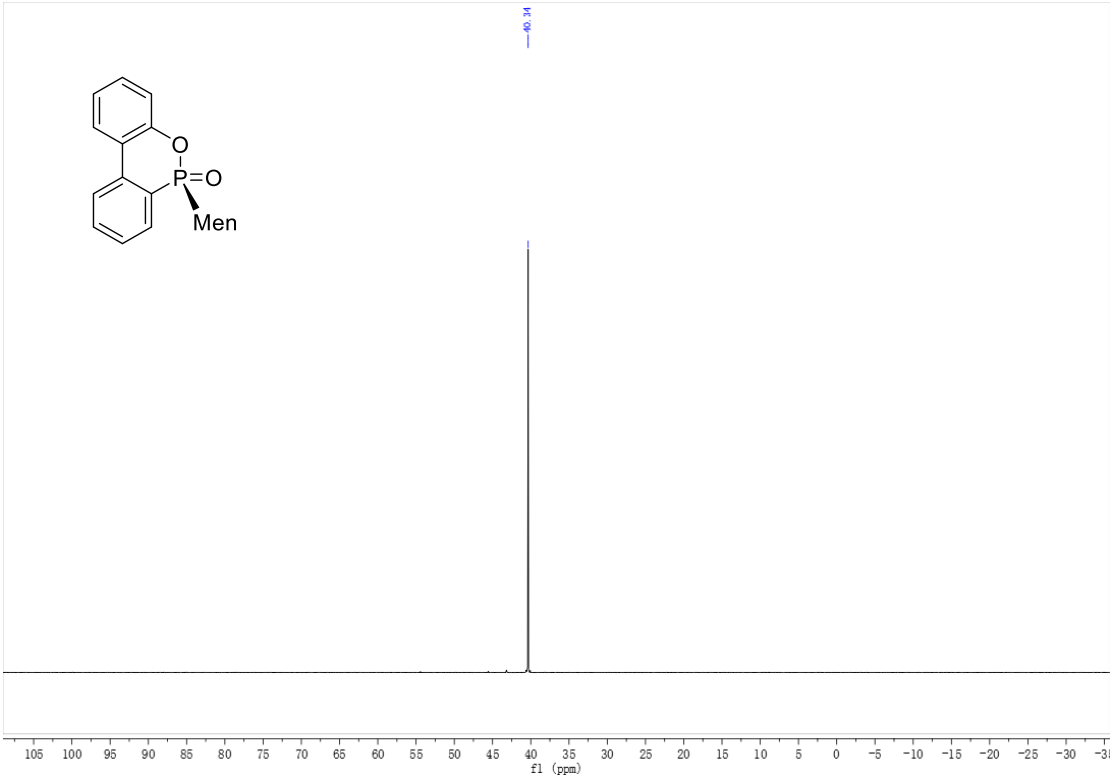
R_P-6-((-)-Menthyl)dibenzo[c,e][1,2]-oxaphosphinine 6-oxide (R_P-5)

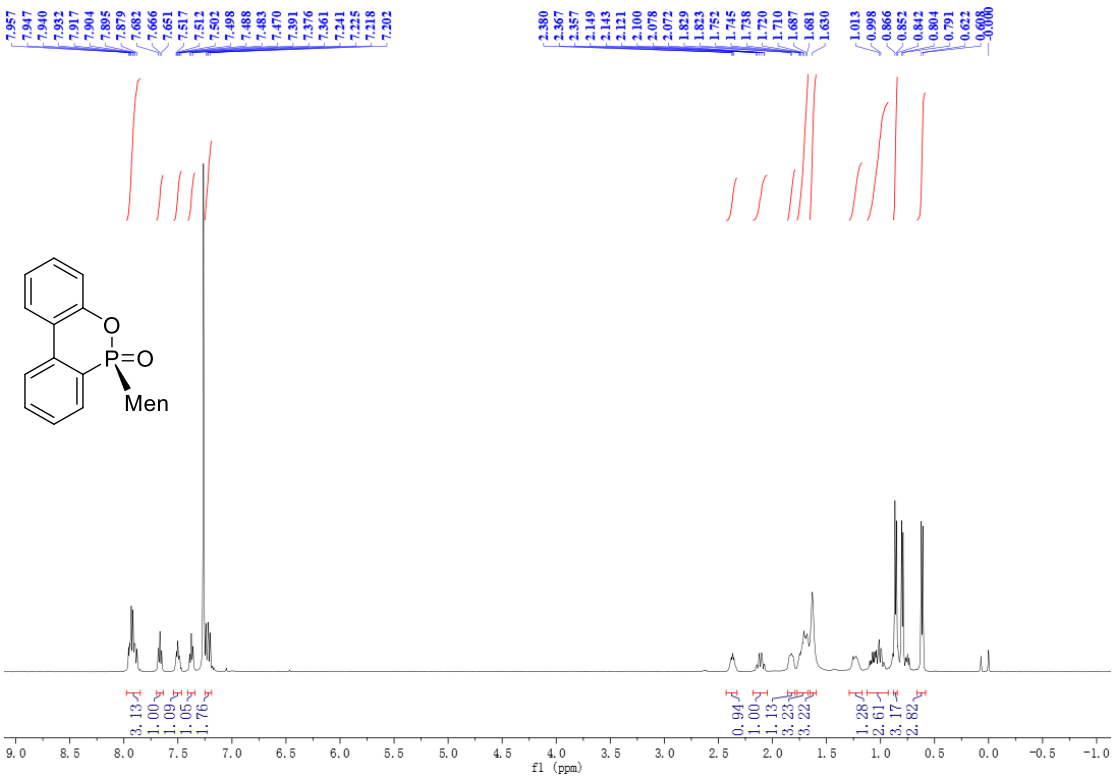


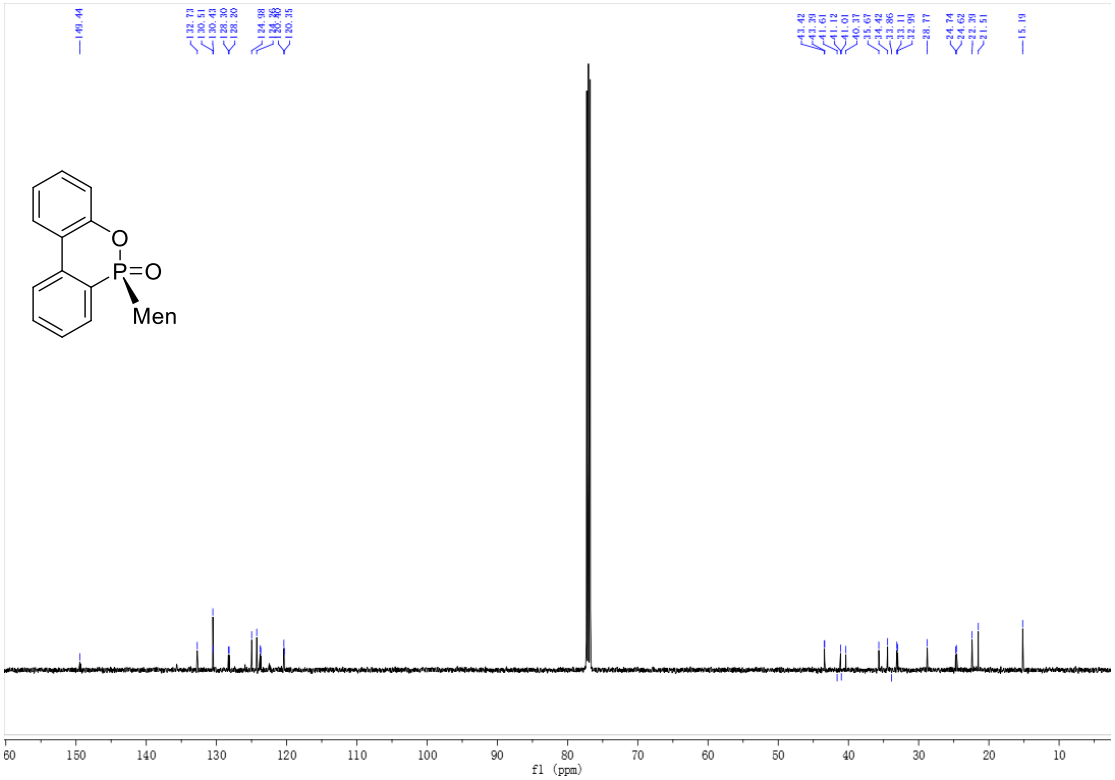




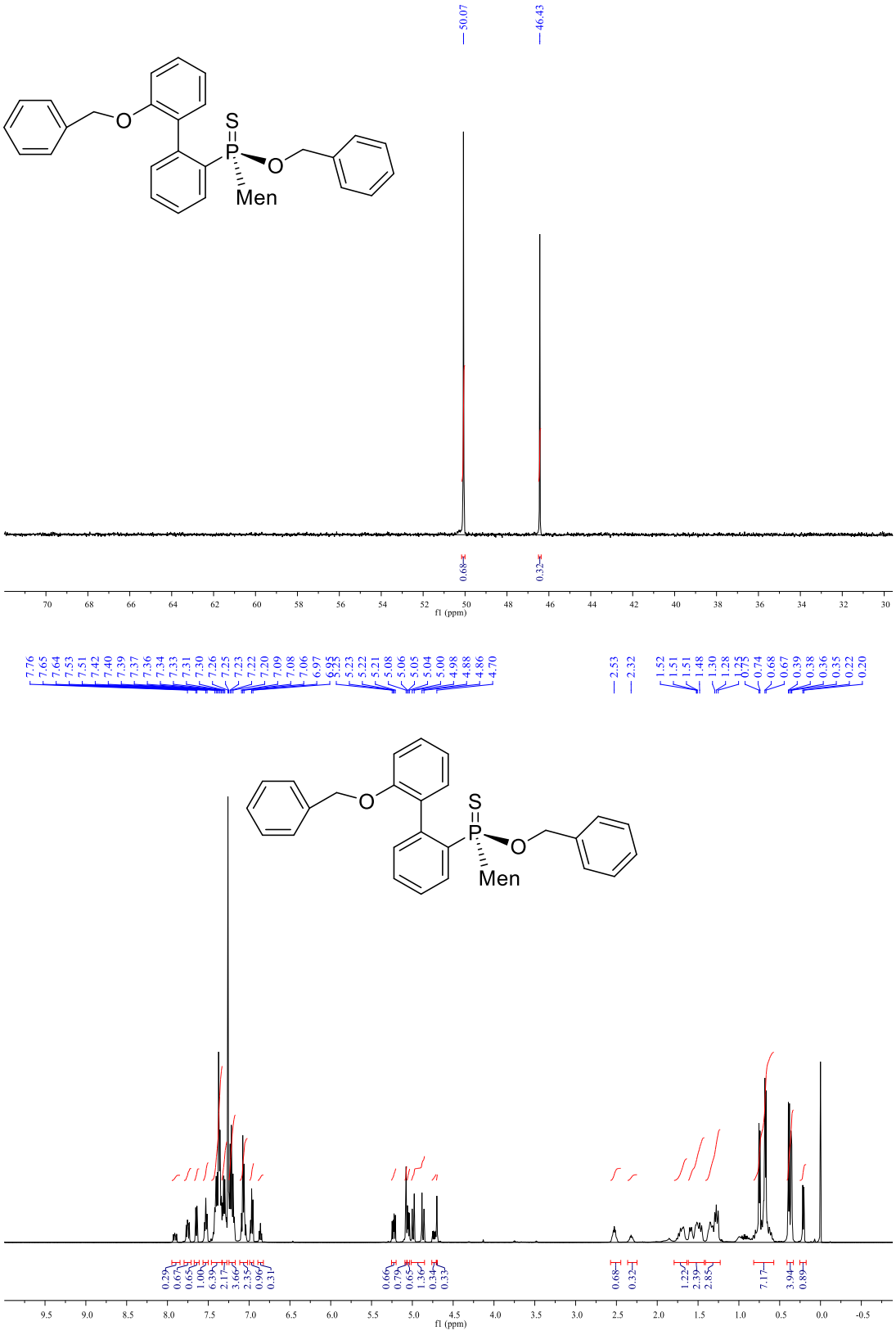
S_P-6-((-)-Menthyl)dibenzo[c,e][1,2]-oxaphosphinine 6-oxide (S_P-5')

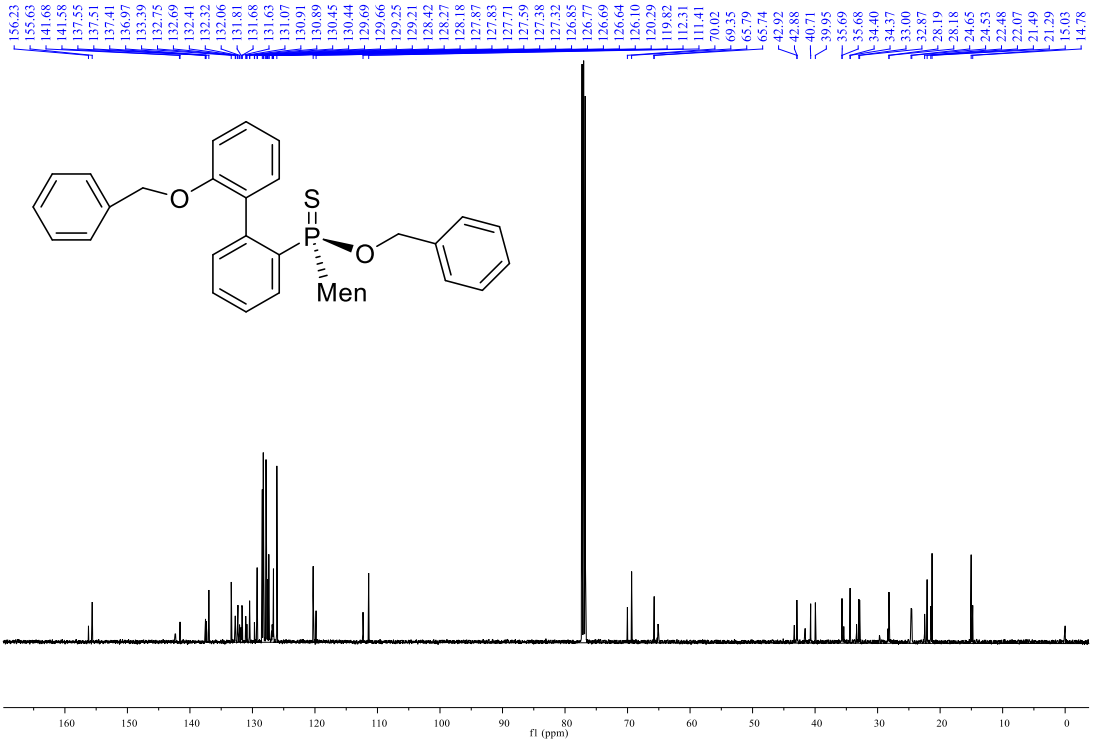



O
P=O
Men
f1 (ppm)

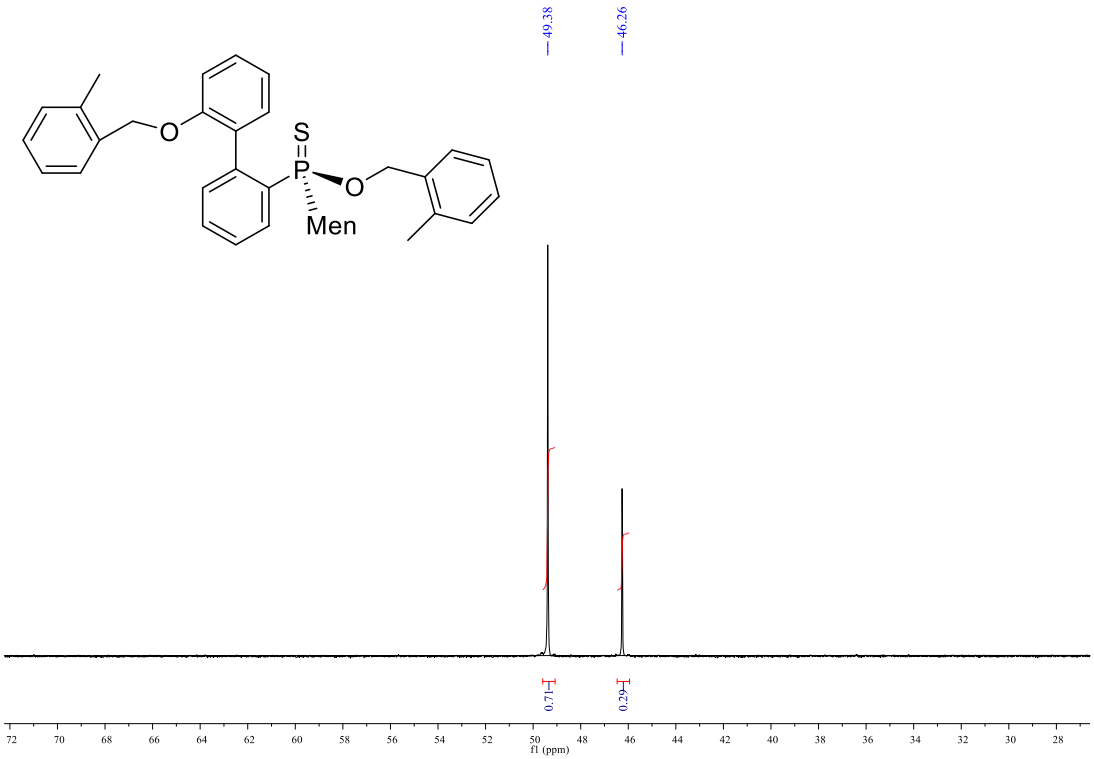

O
P=O
Men
f1 (ppm)

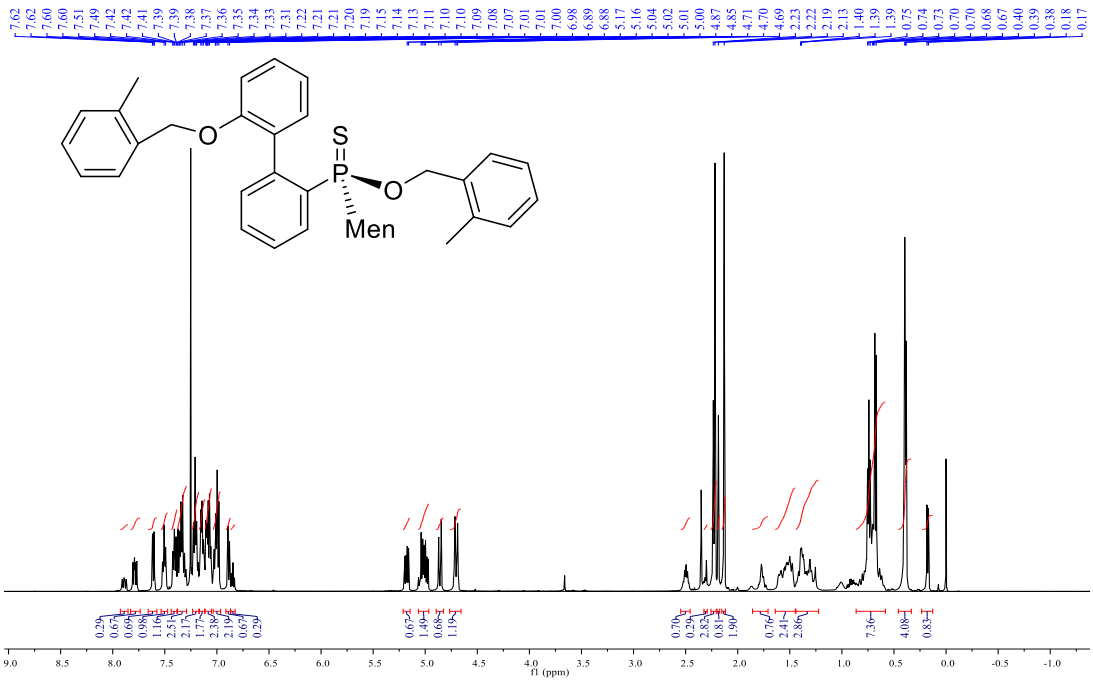
S_P-*O*-Benzyl-(2'-(benzyloxy)-[1,1'-biphenyl]-2-yl)((-)-menthyl)phosphinothioate (S_P-6h)

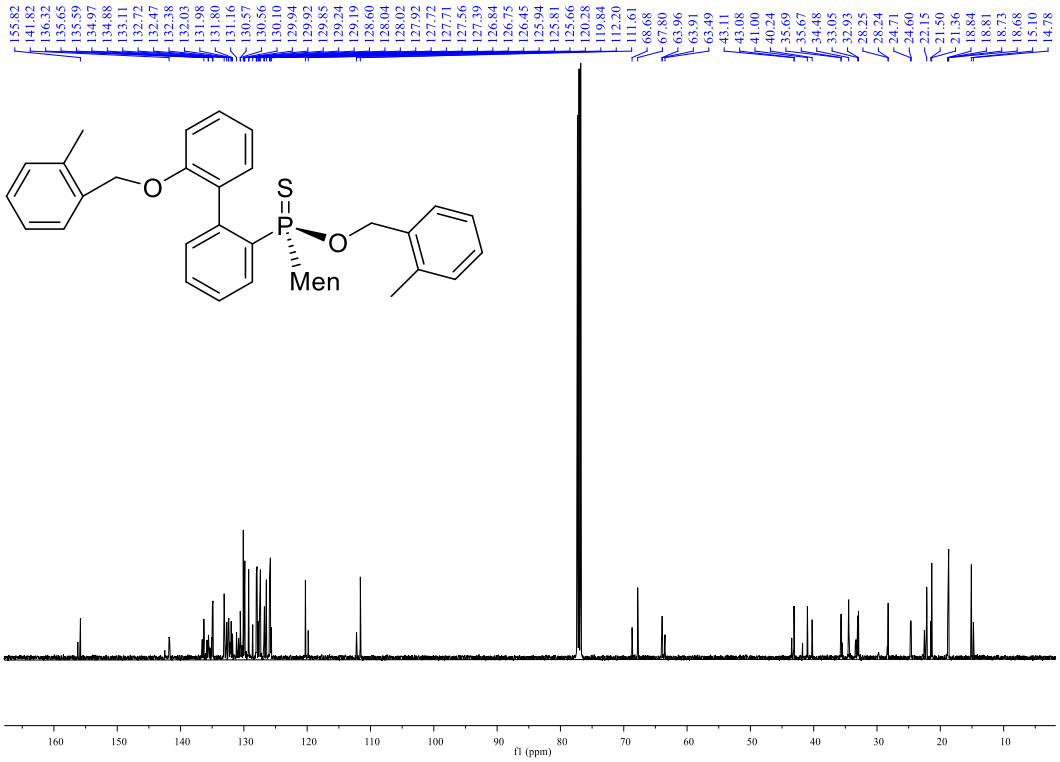




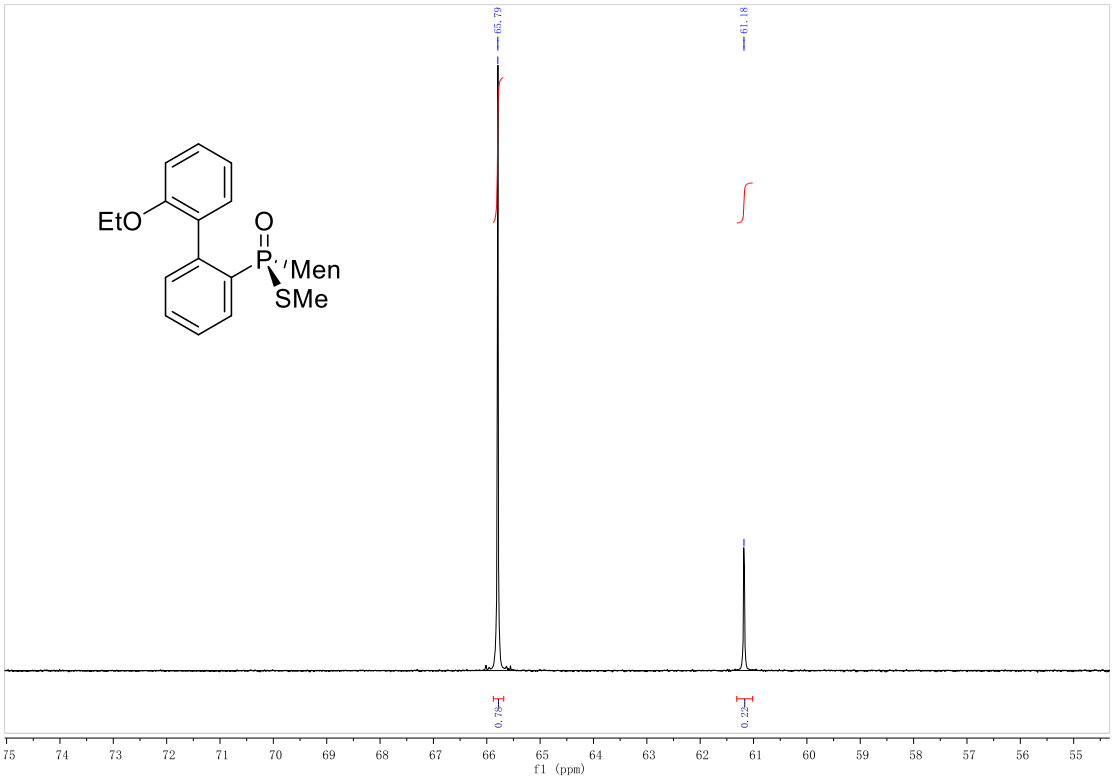
S_P-*O*-(2-Methylbenzyl)-((-)-menthyl)(2'-((2-methylbenzyl)oxy)-[1,1'-biphenyl]-2-yl)phosphin othioate (S_P-6i)

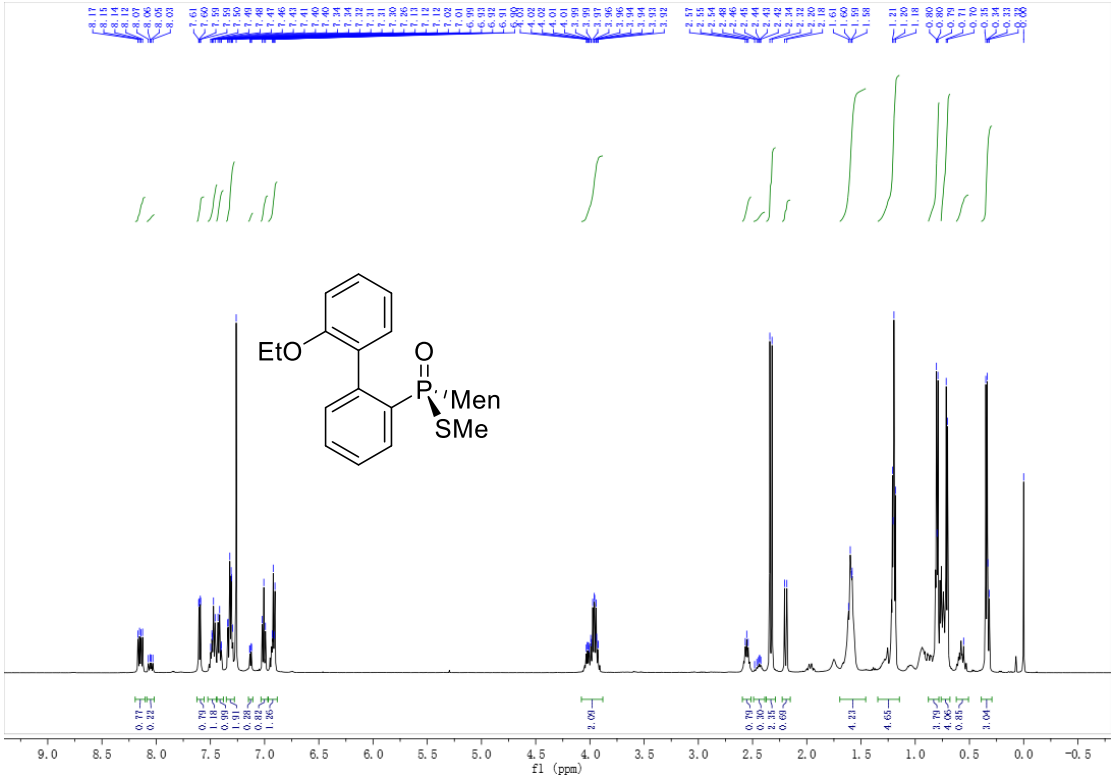


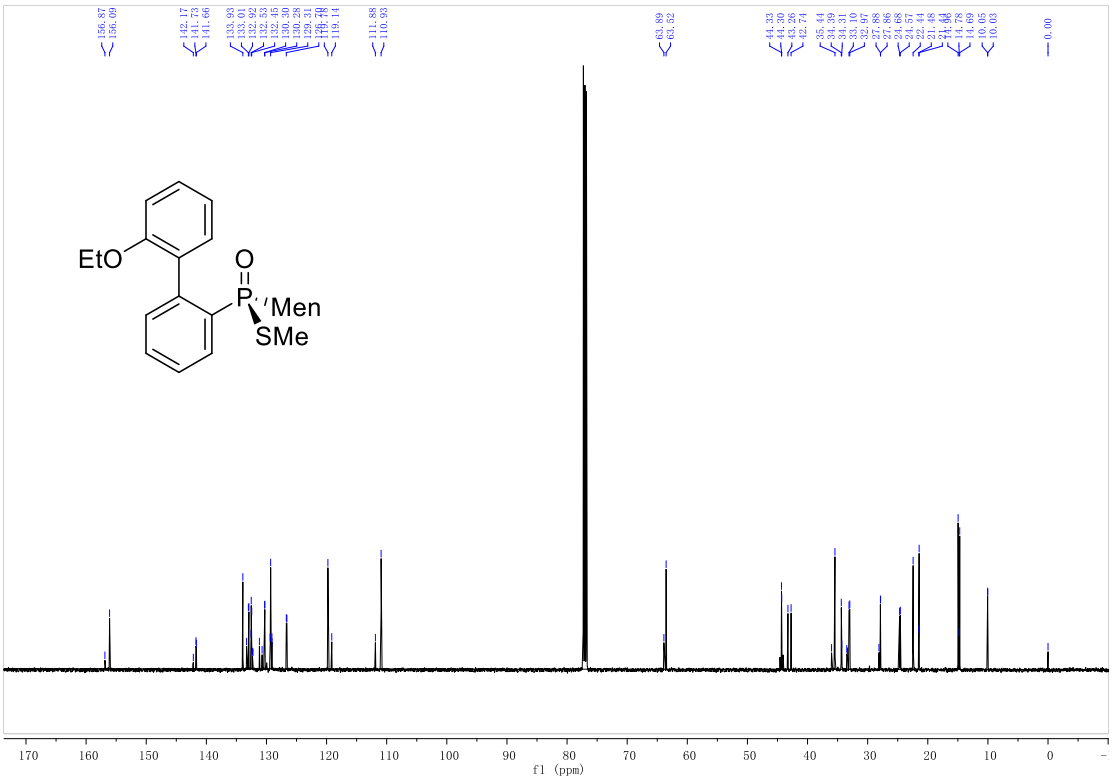

S
P
O
O
Men
f1 (ppm)


S
P
O
O
Men
f1 (ppm)

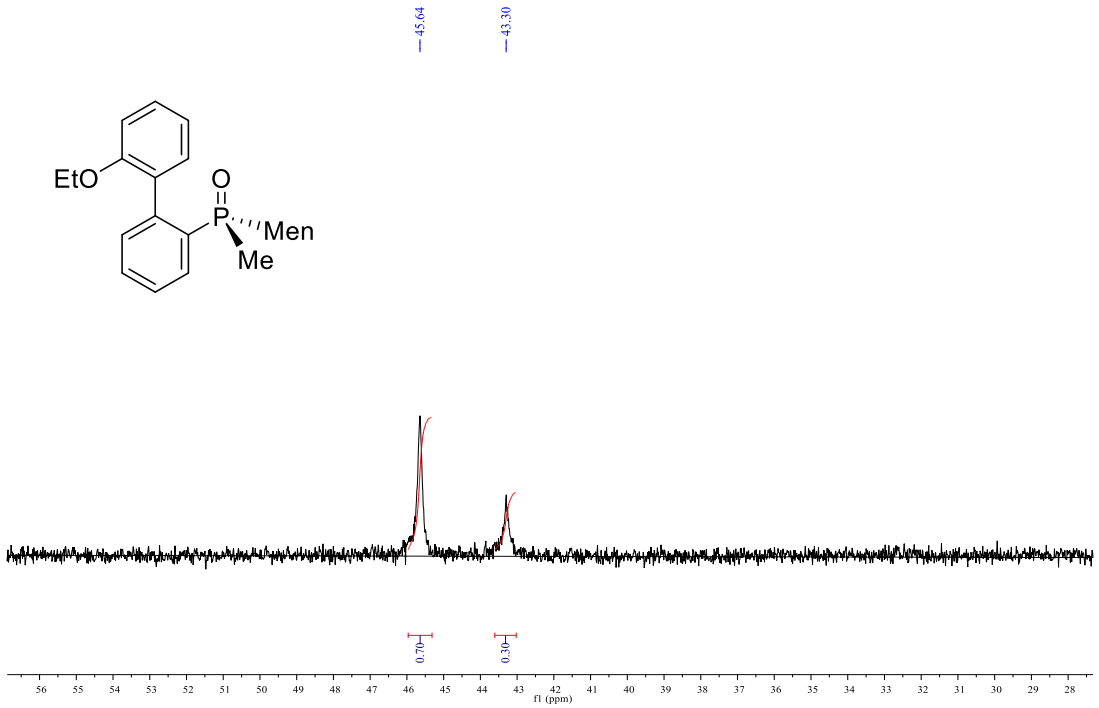
***S*P-*S*-Methyl-(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphinothioate(*S*P-4a).**

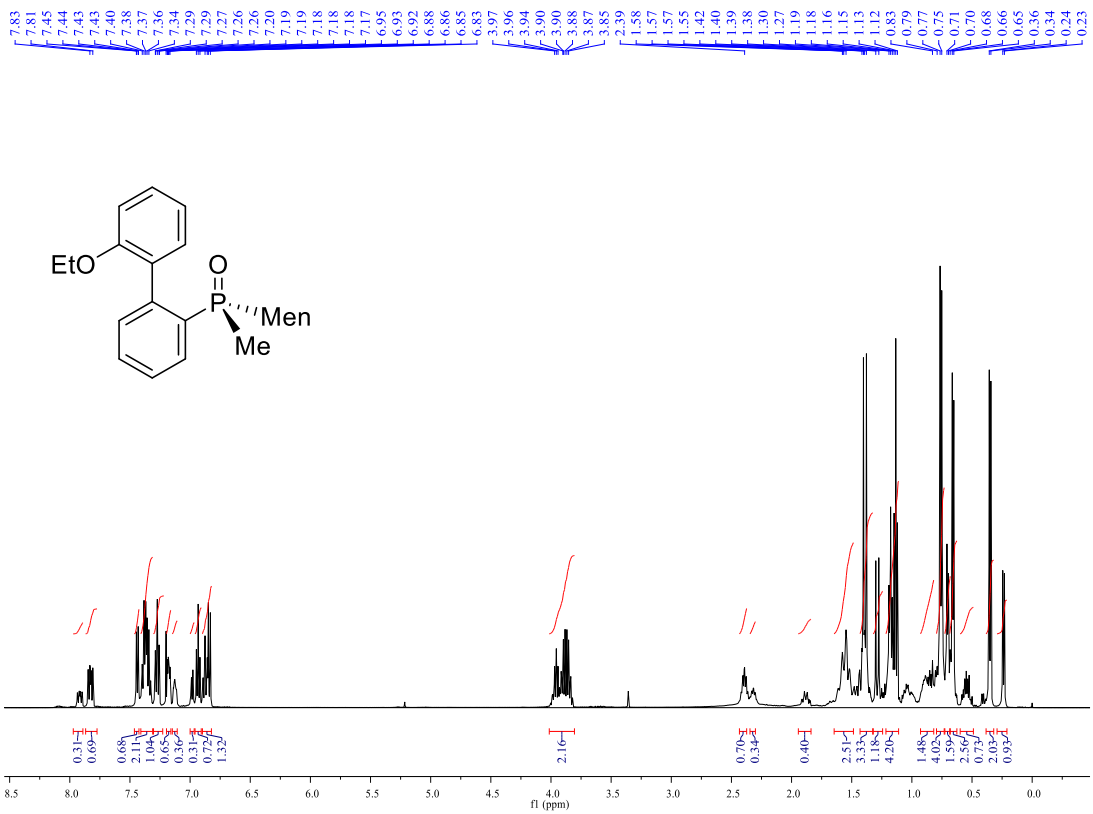


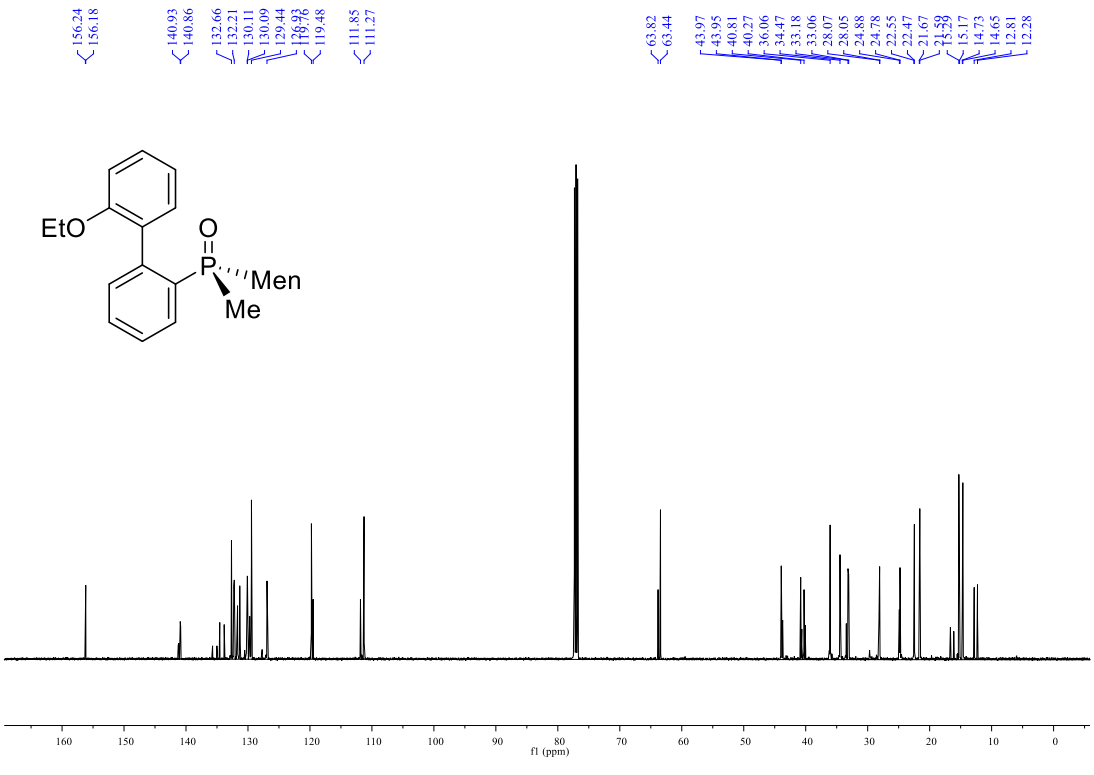




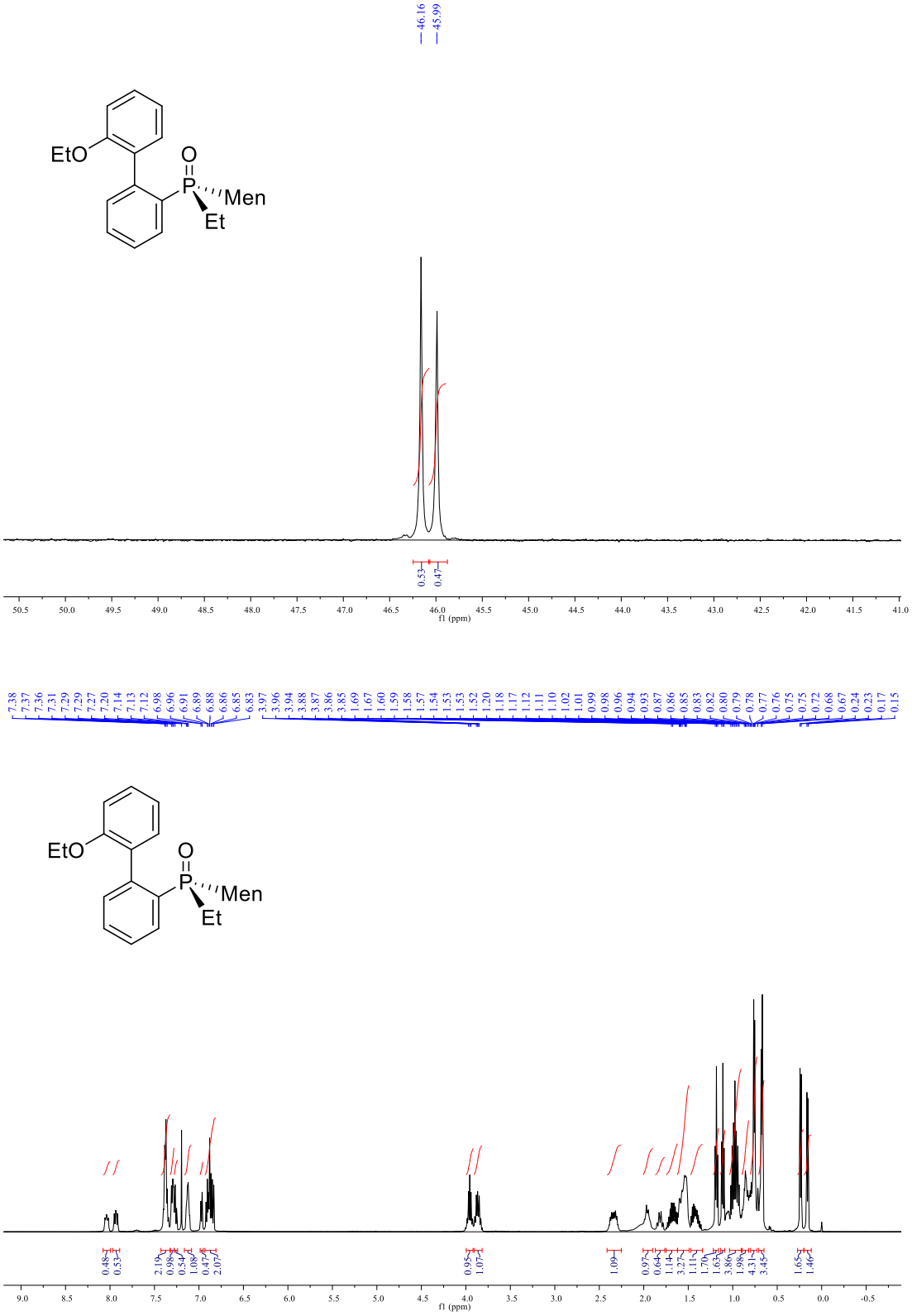
***R*P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl)(methyl)((-)-menthyl) phosphine oxide (*R*P-7a)**

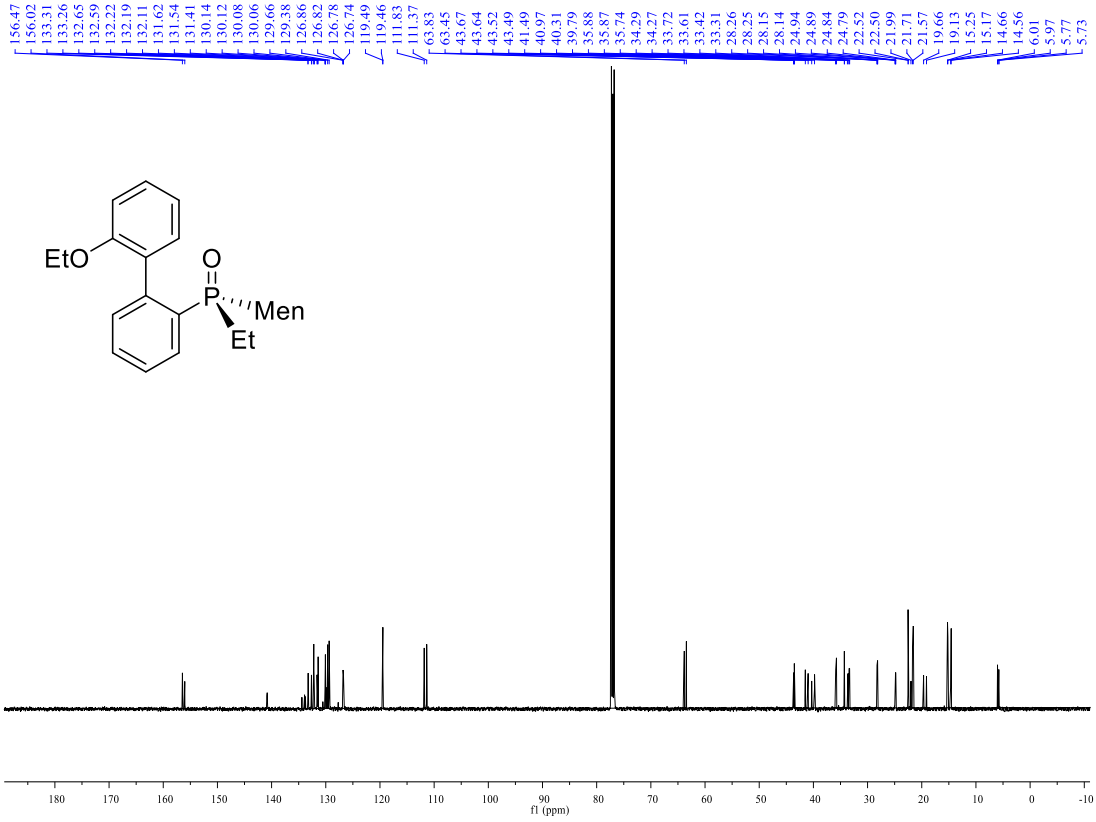



EtO
O
P
Men
Me
fl (ppm)

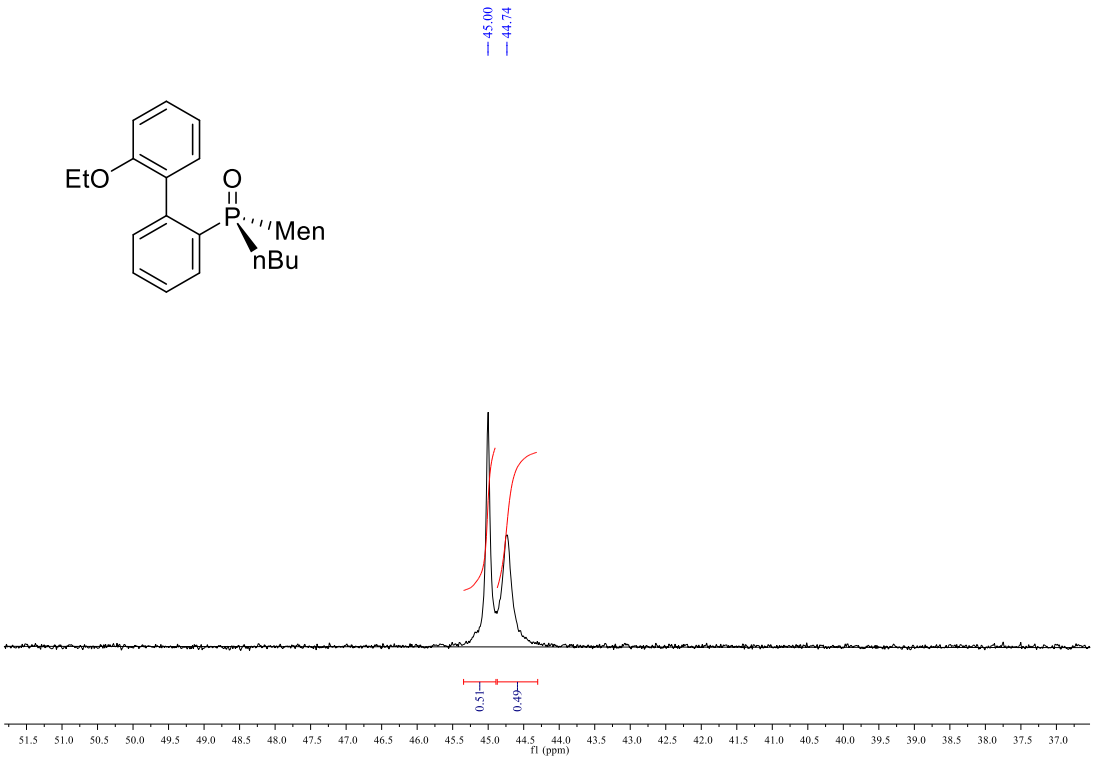

EtO
O
P
Men
Me
fl (ppm)

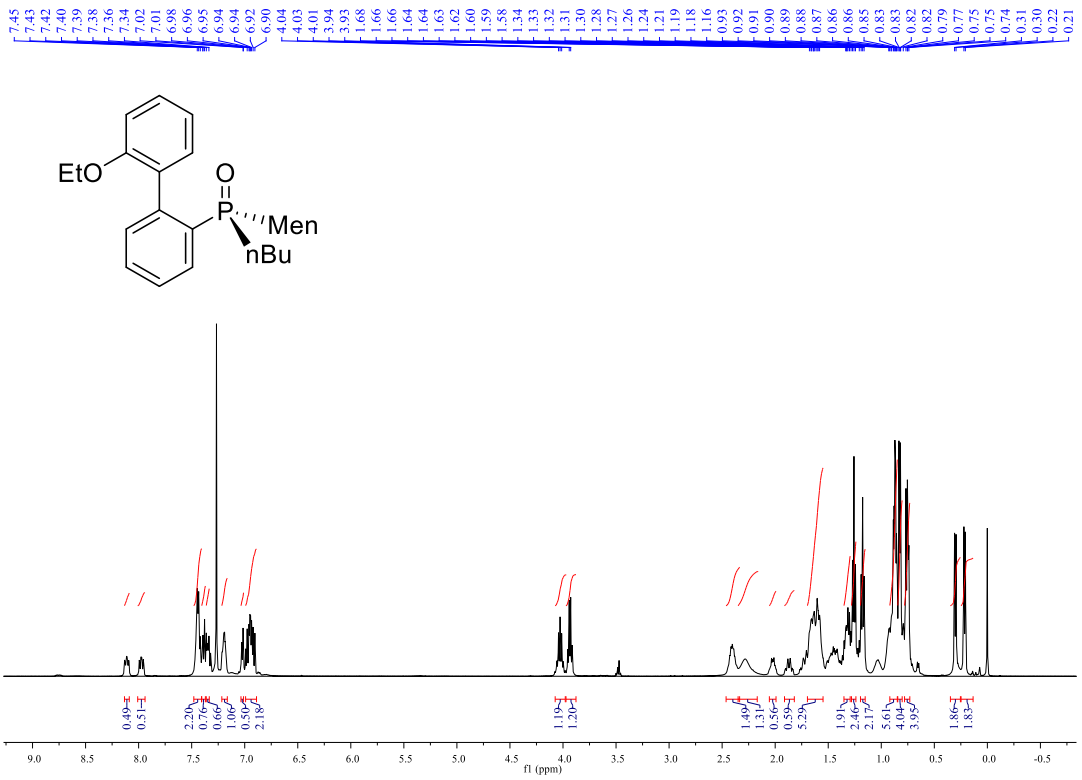
R_P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl)(ethyl)((-)-menthyl) phosphine oxide (R_P-7b)

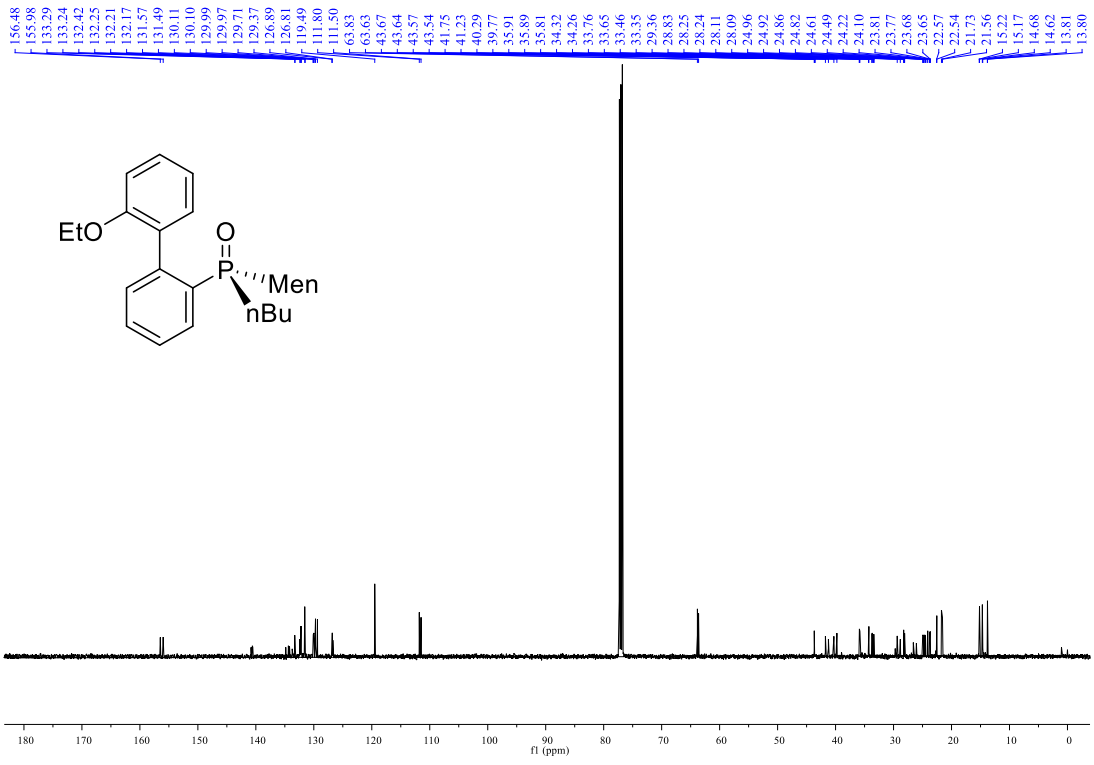




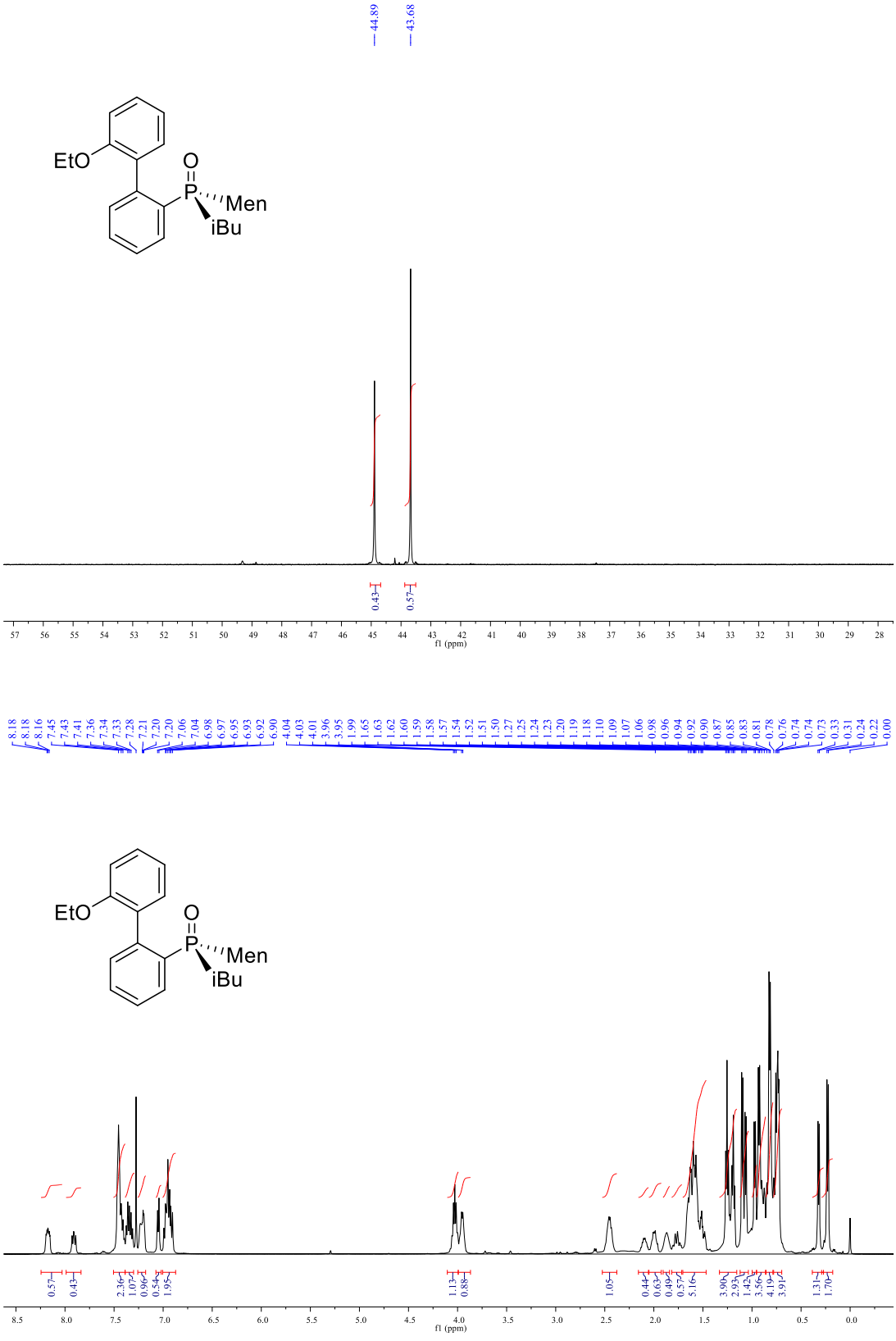
R_P-Butyl (2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphine oxide (R_P-7c)

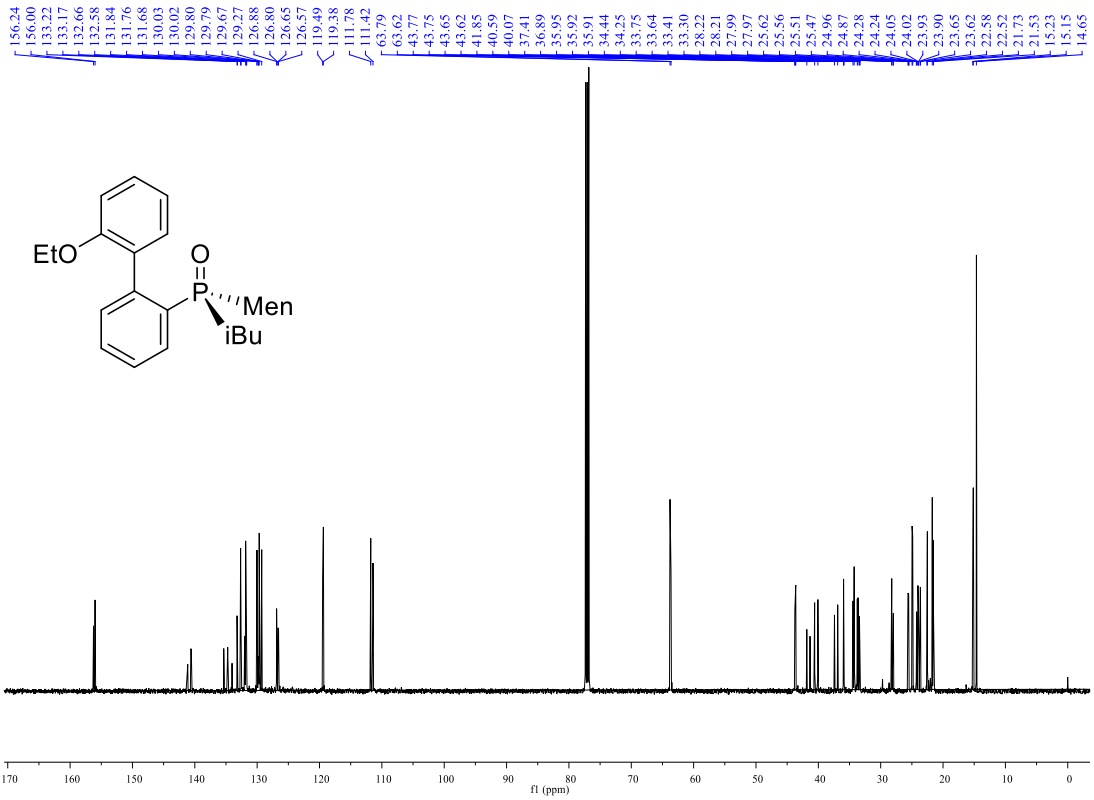



EtO
O
P
Men
nBu
f1 (ppm)

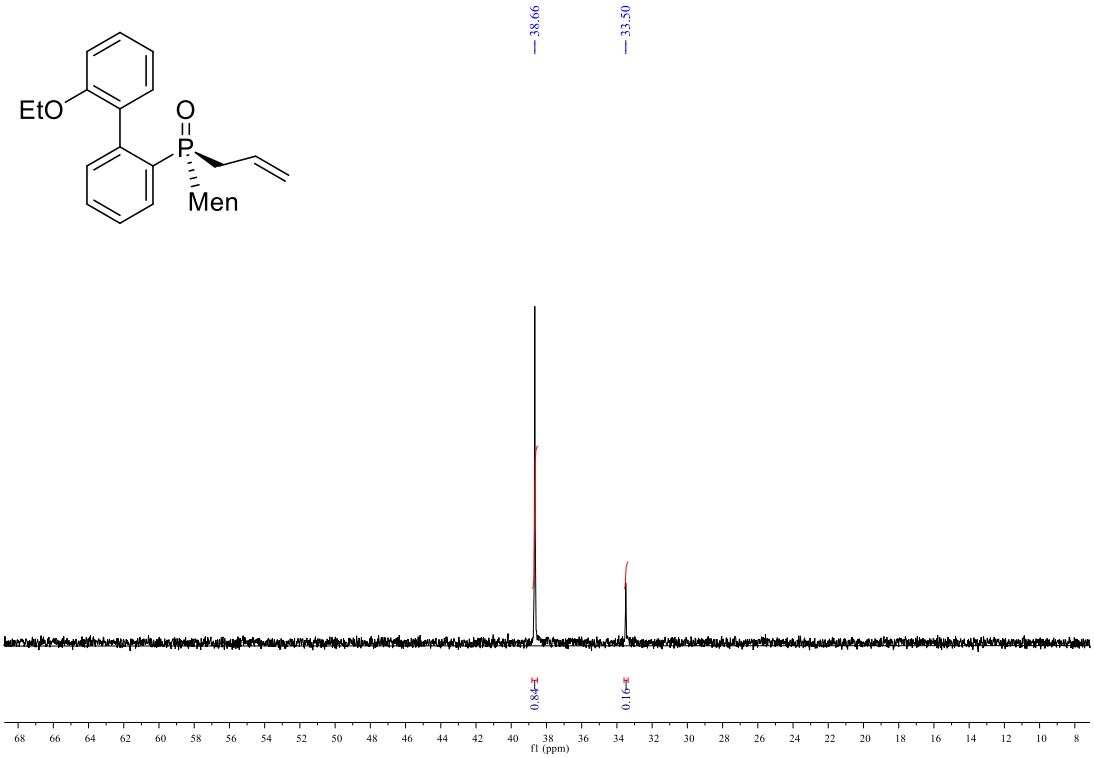

EtO
O
P
Men
nBu
f1 (ppm)

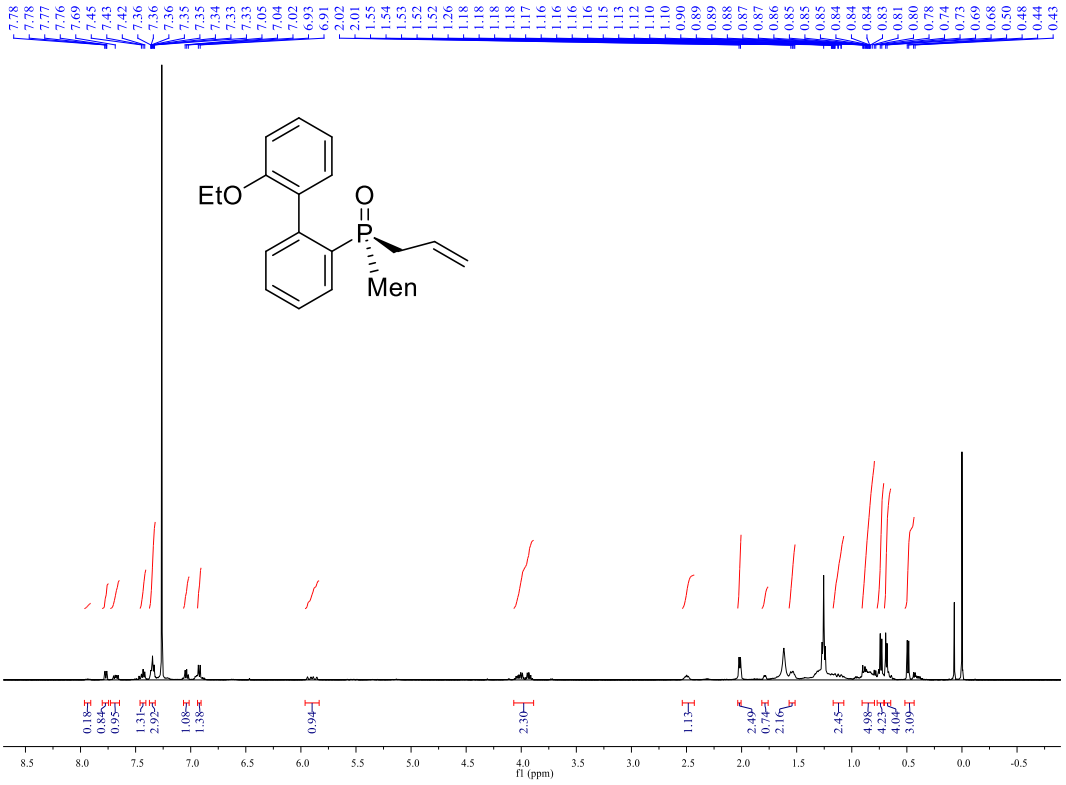
R_P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl)(isobutyl)((-)-menthyl) phosphine oxide (R_P-7d)

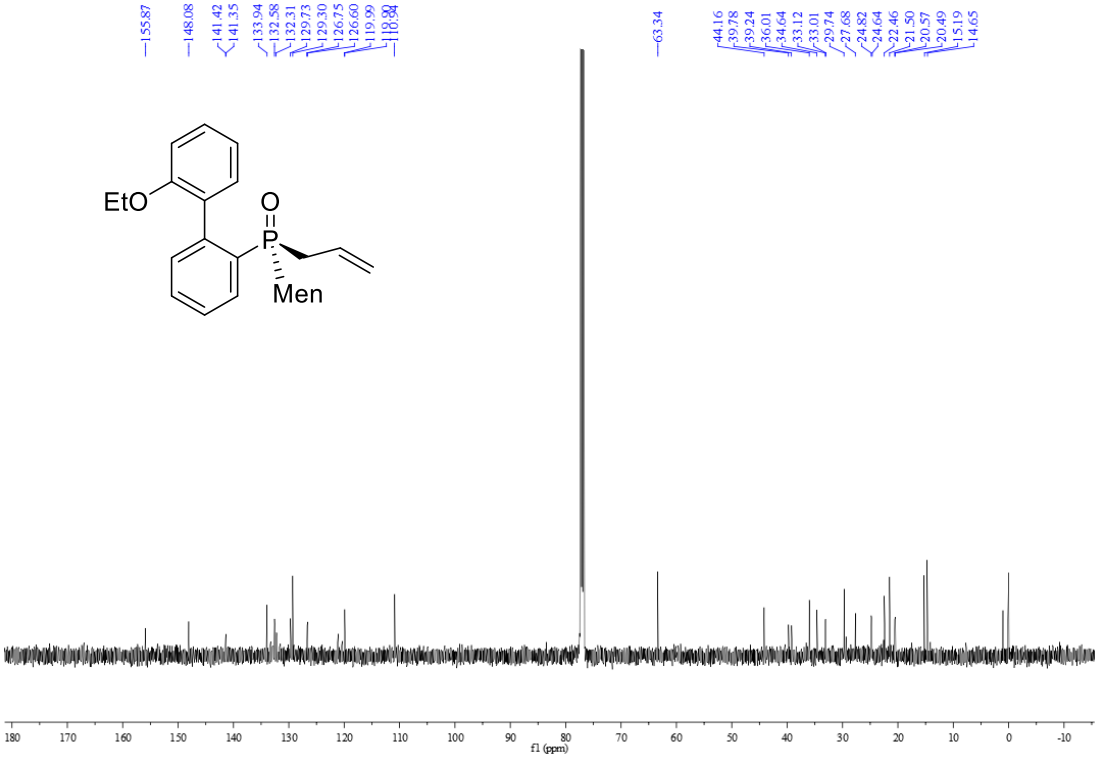




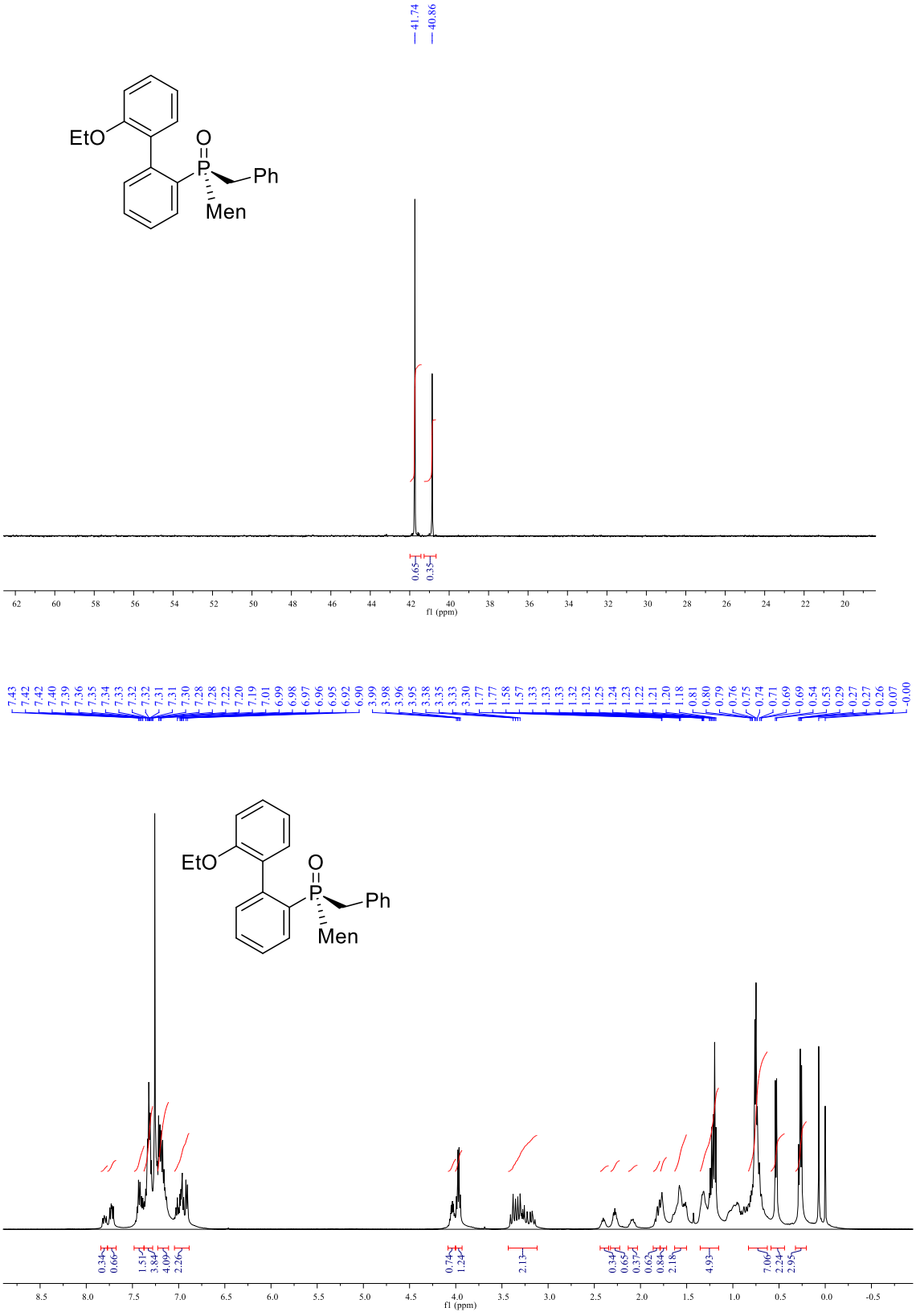
R_P-Allyl (2'-ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl) phosphine oxide (R_P-7e)

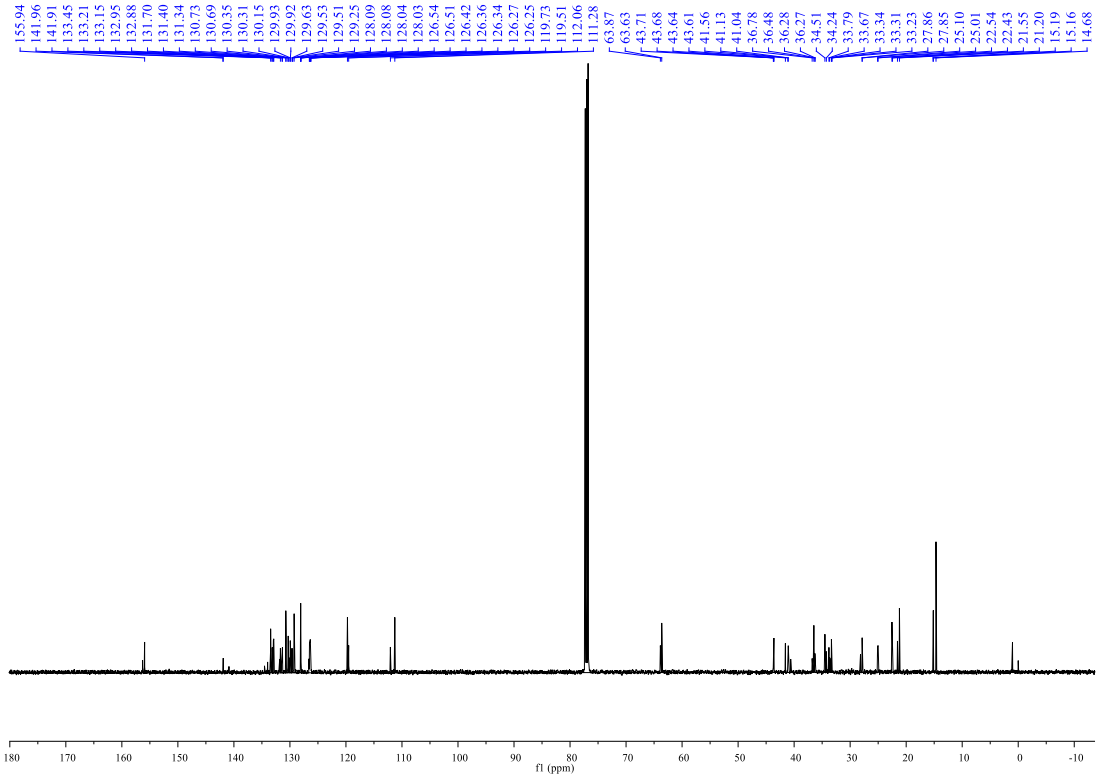



EtO
O
P
Men
f1 (ppm)

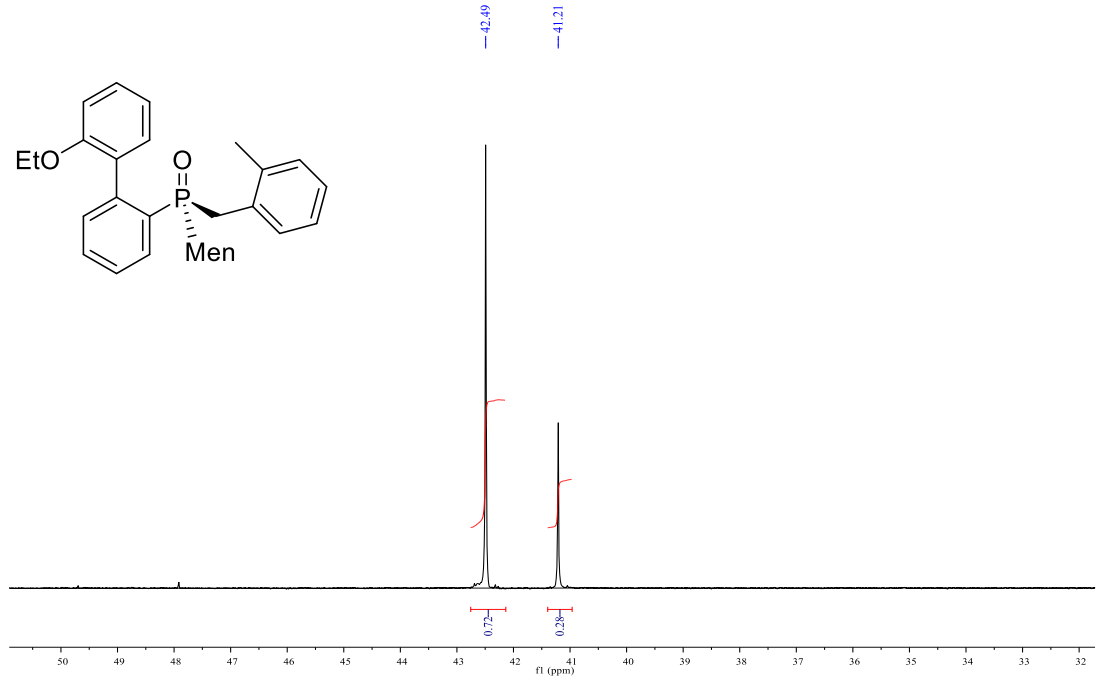

EtO
O
P
Men
f1 (ppm)

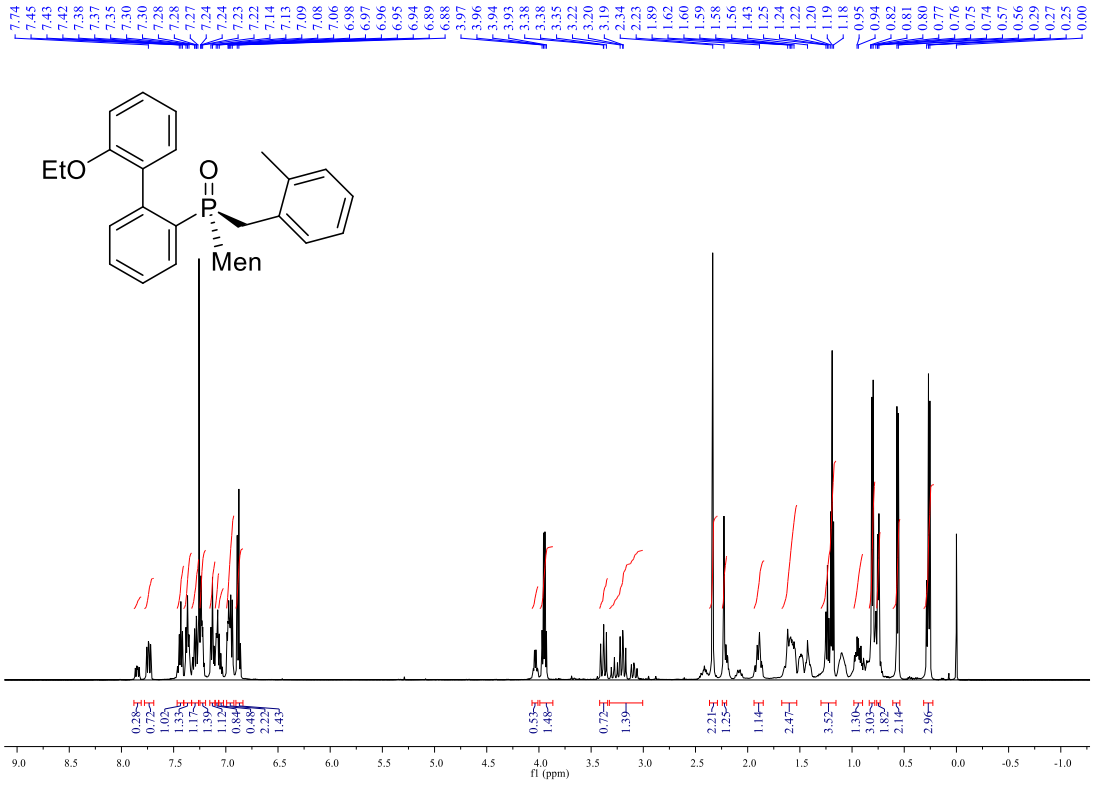
R_P-Benzyl (2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphine oxide (R_P-7f)

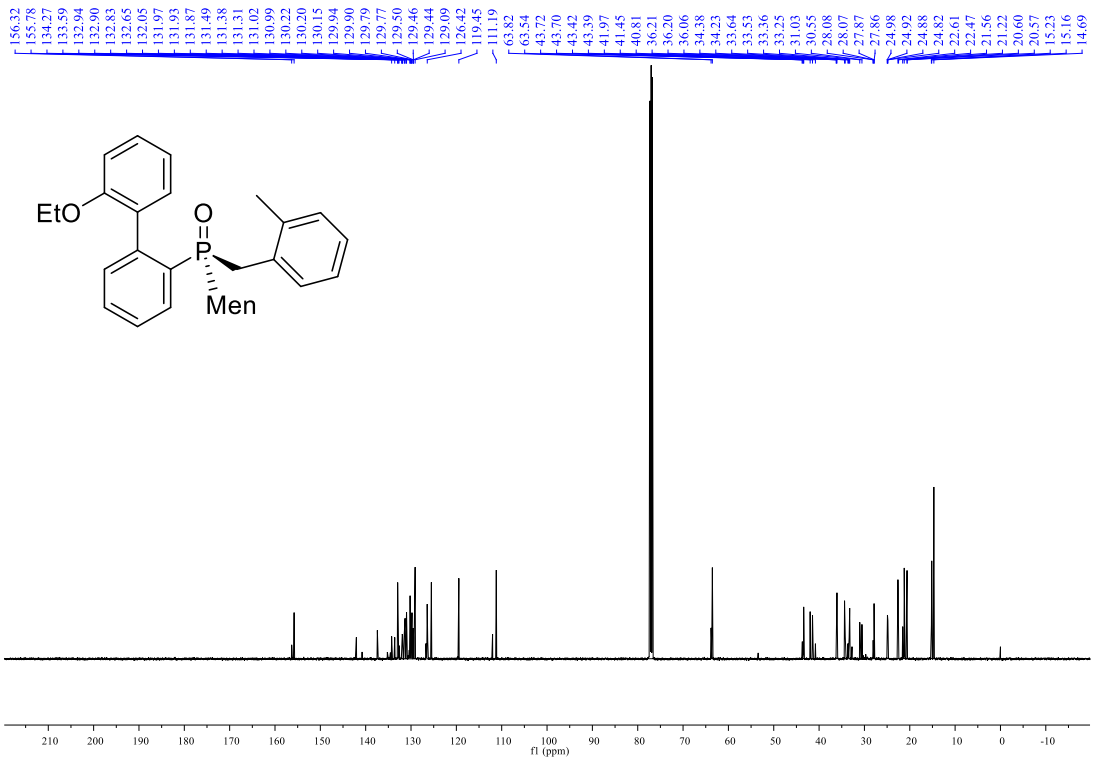




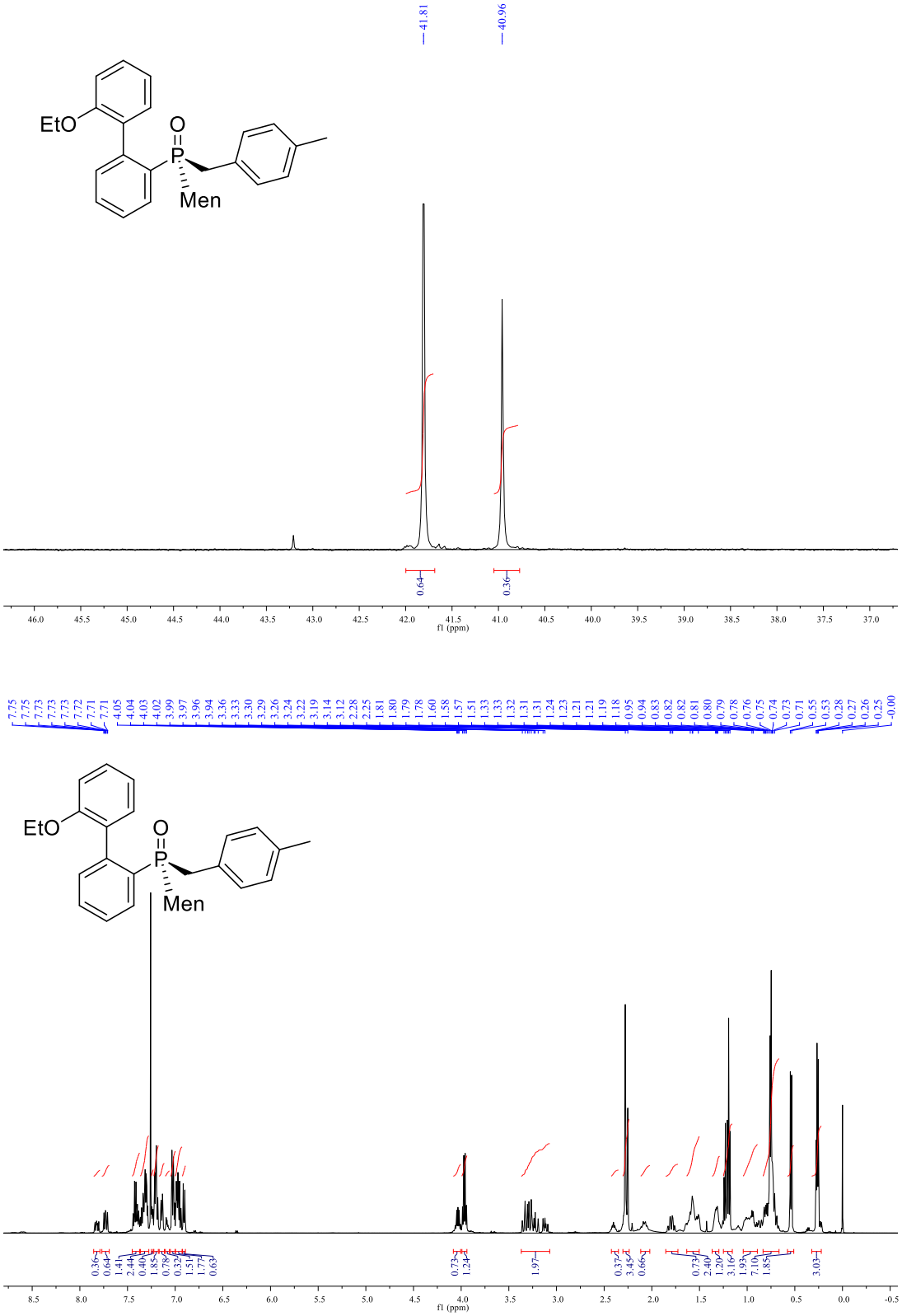
***R*P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl)(2-methylbenzyl) phosphine oxide (*R*P-7g)**

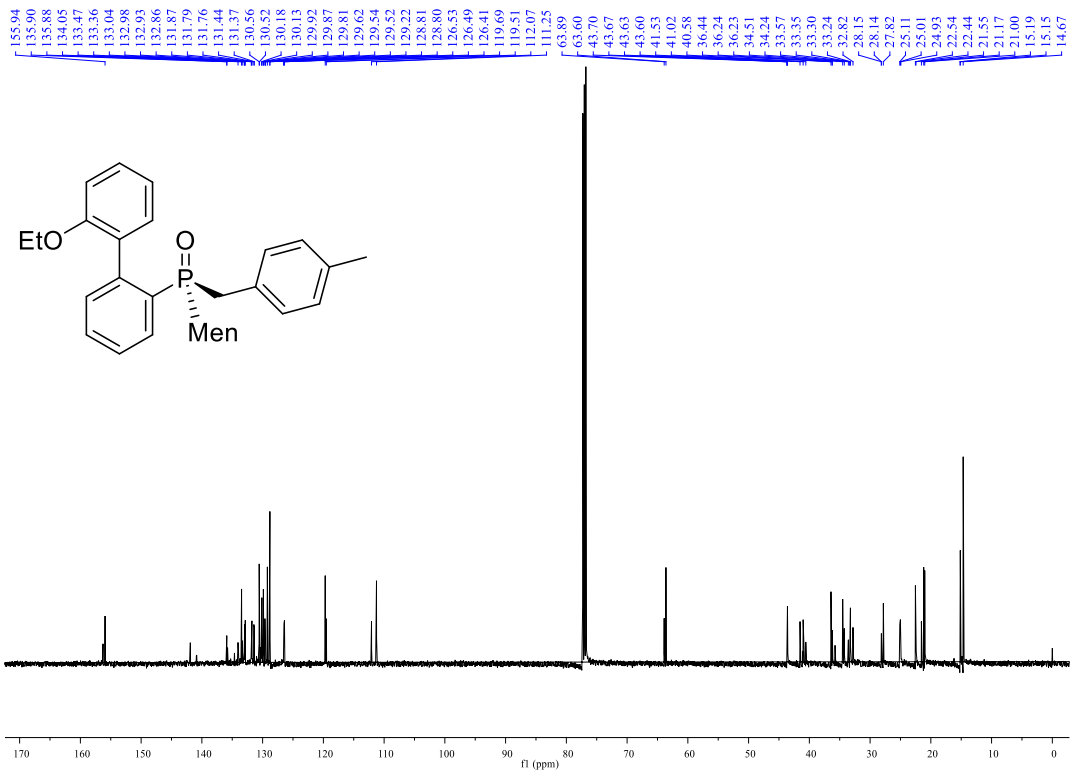



EtO
O
P
Men
f1 (ppm)

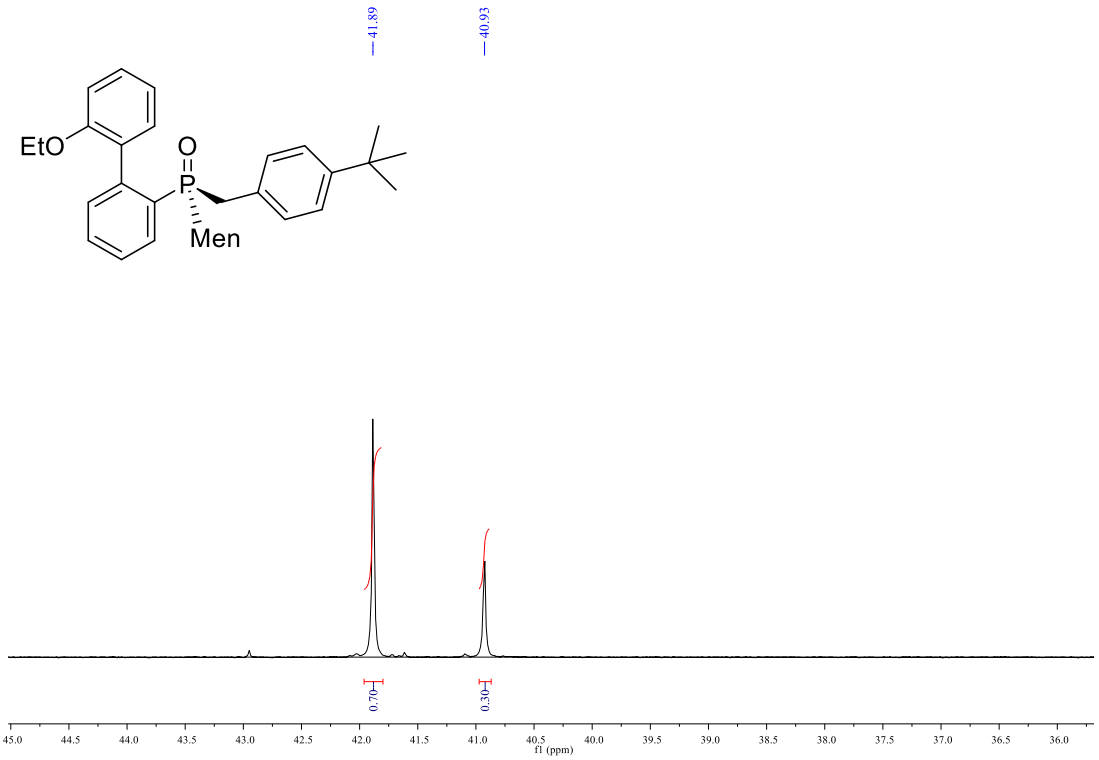

EtO
O
P
Men
f1 (ppm)

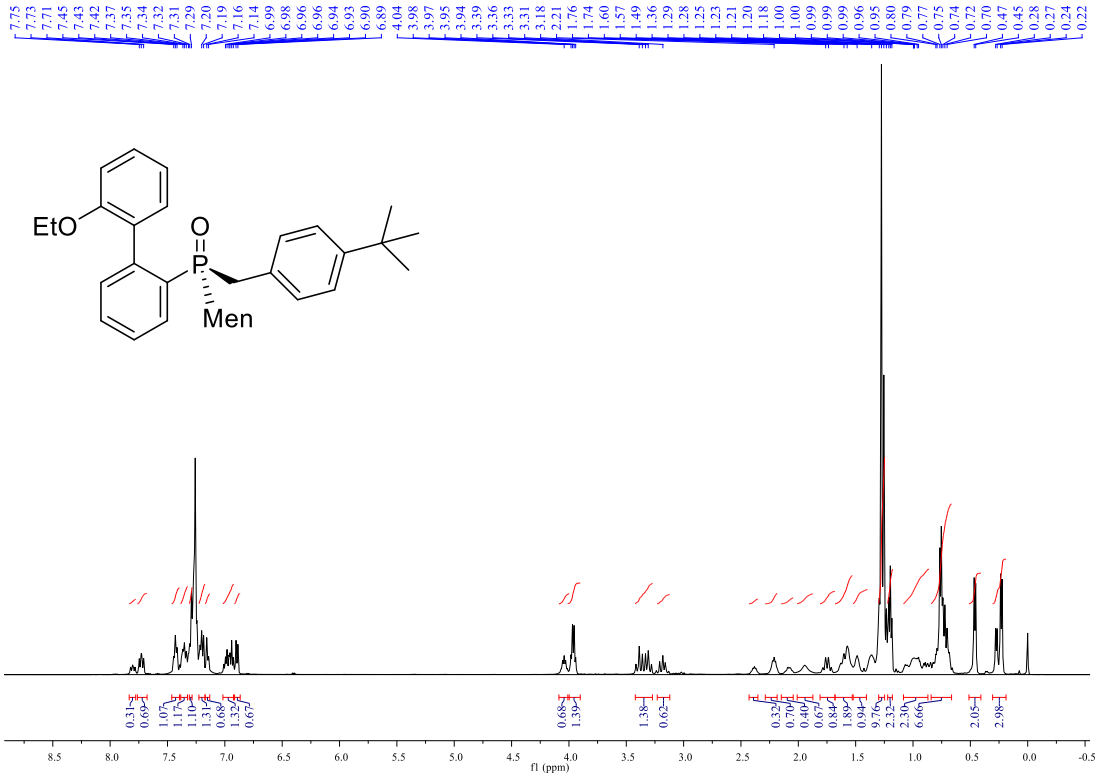
R_P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl) ((-)-menthyl)(4-methylbenzyl) phosphine oxide (R_P-7h)

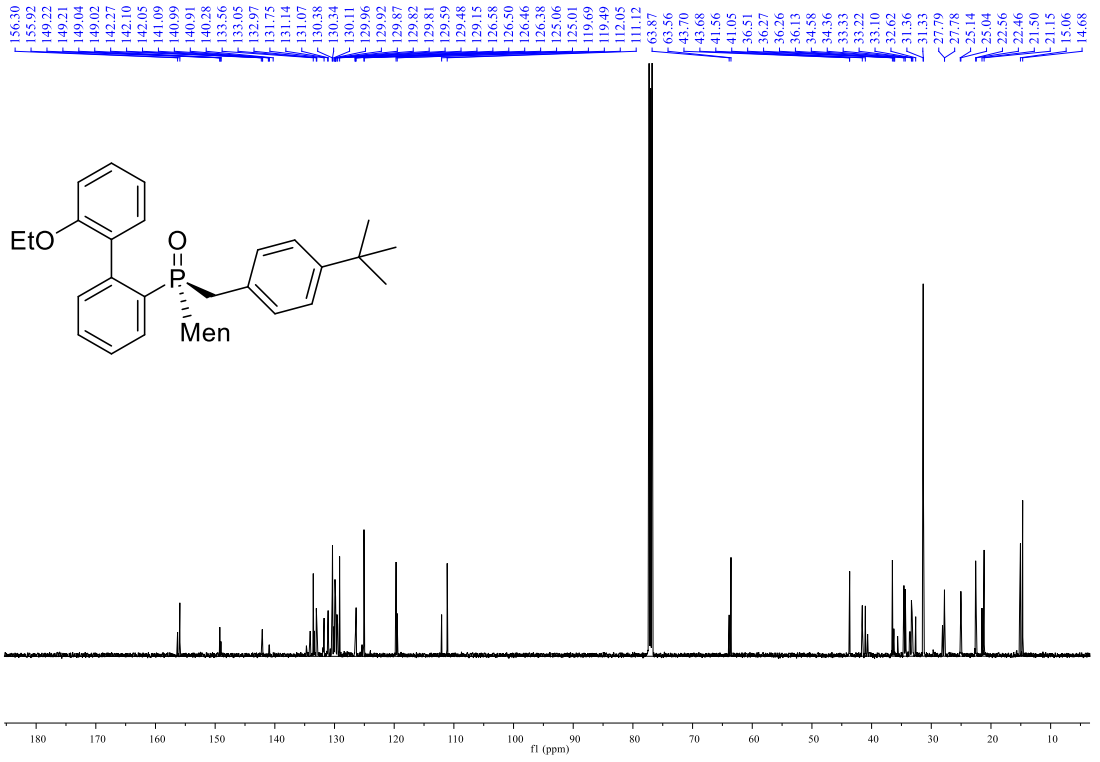




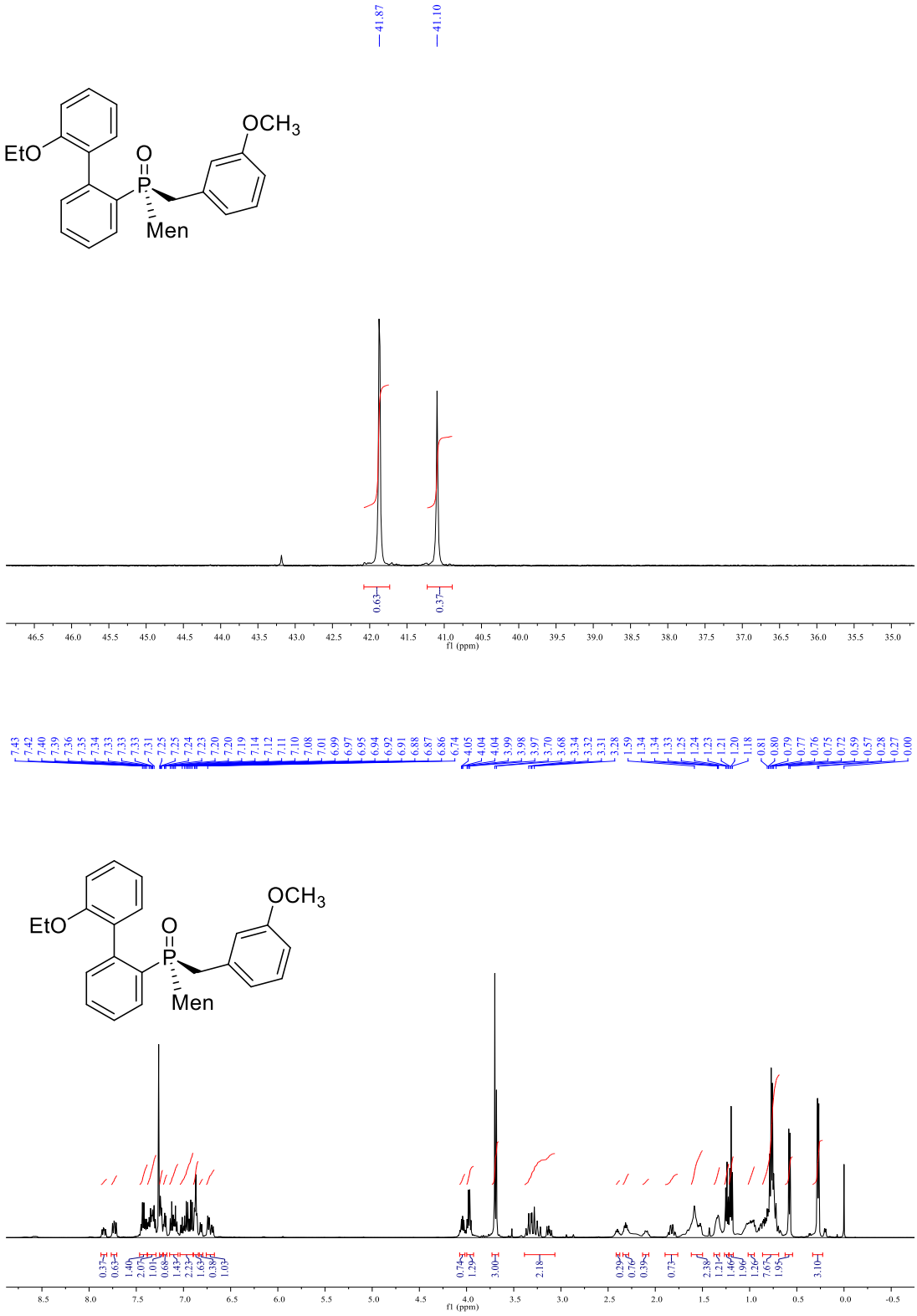
R_P-(4-(tert-Butyl)benzyl)(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphine oxide (R_P-7i)

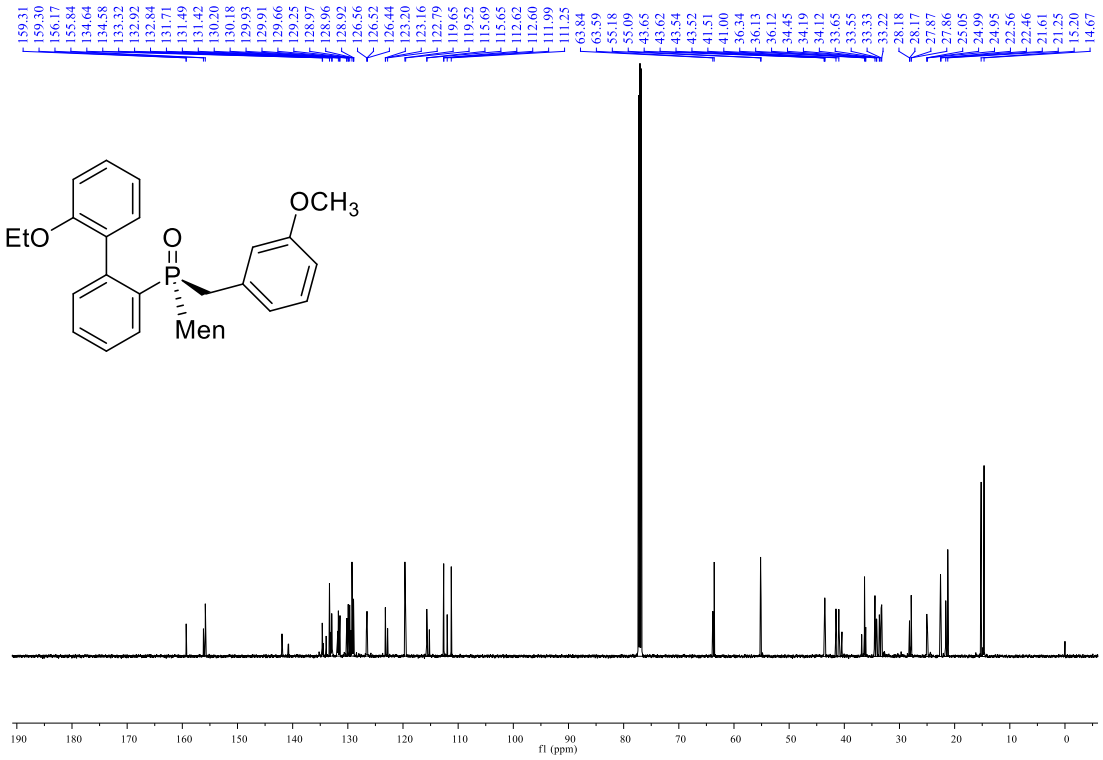



EtO
O
P
Men
f1 (ppm)

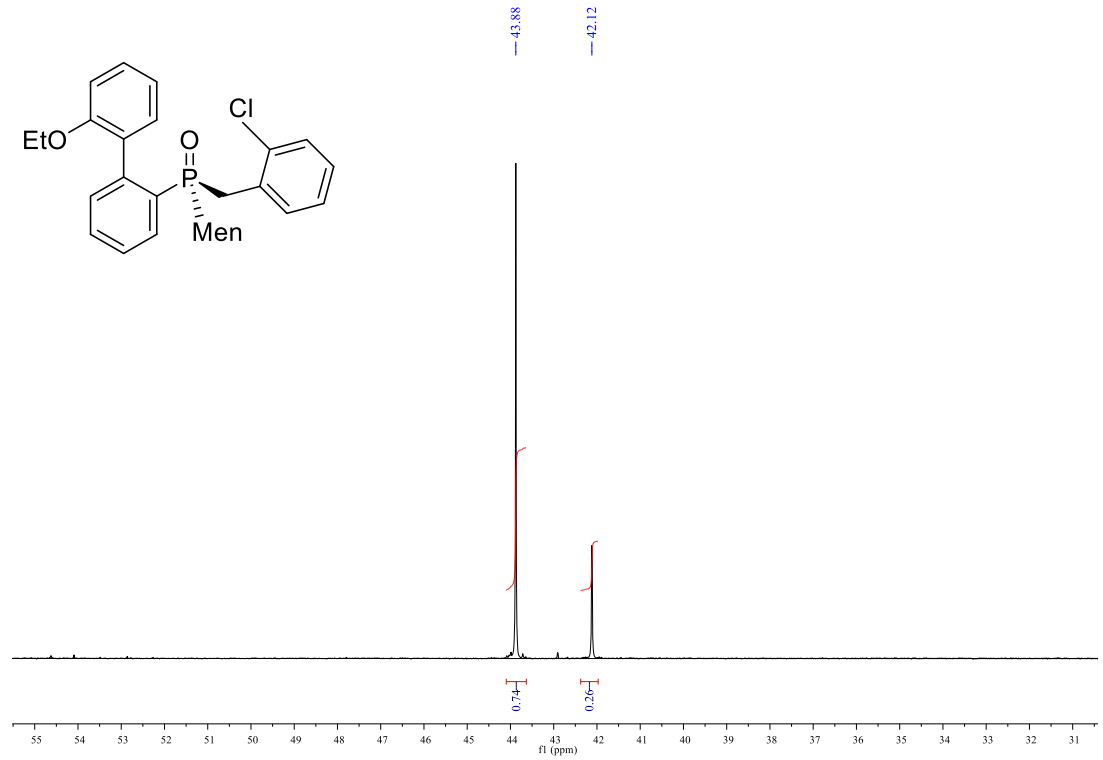

EtO
O
P
Men
f1 (ppm)

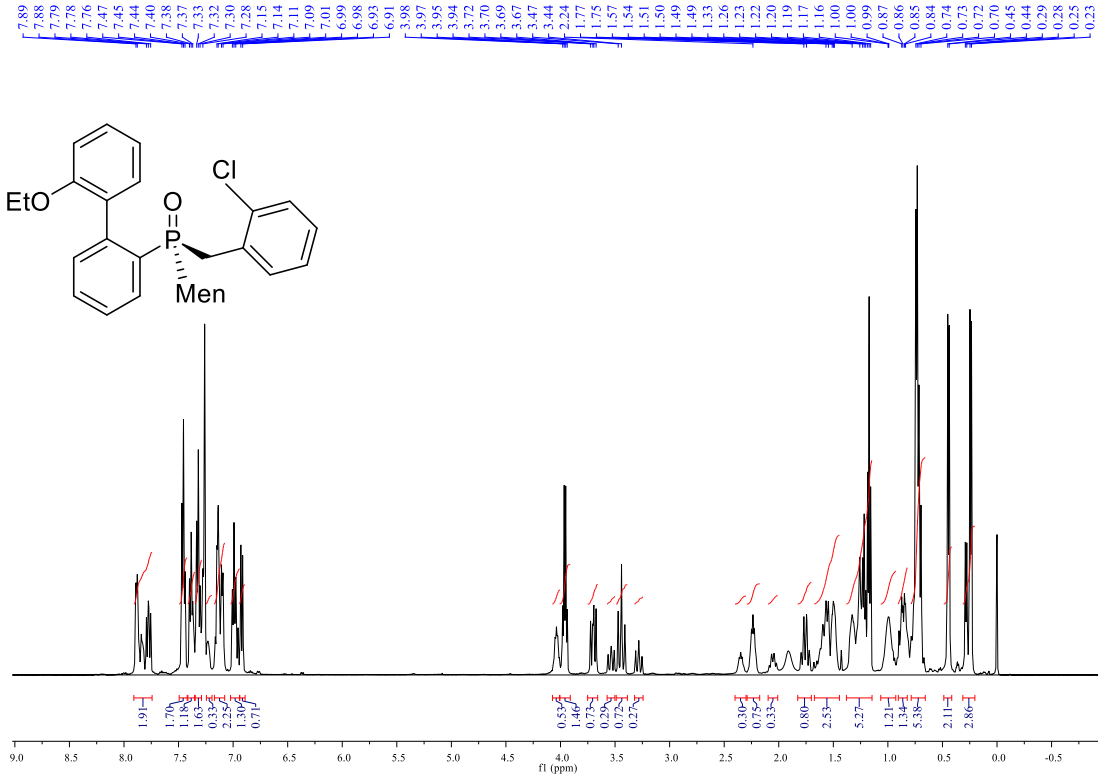
R_P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl)(3-methoxybenzyl) phosphine oxide (R_P-7j)

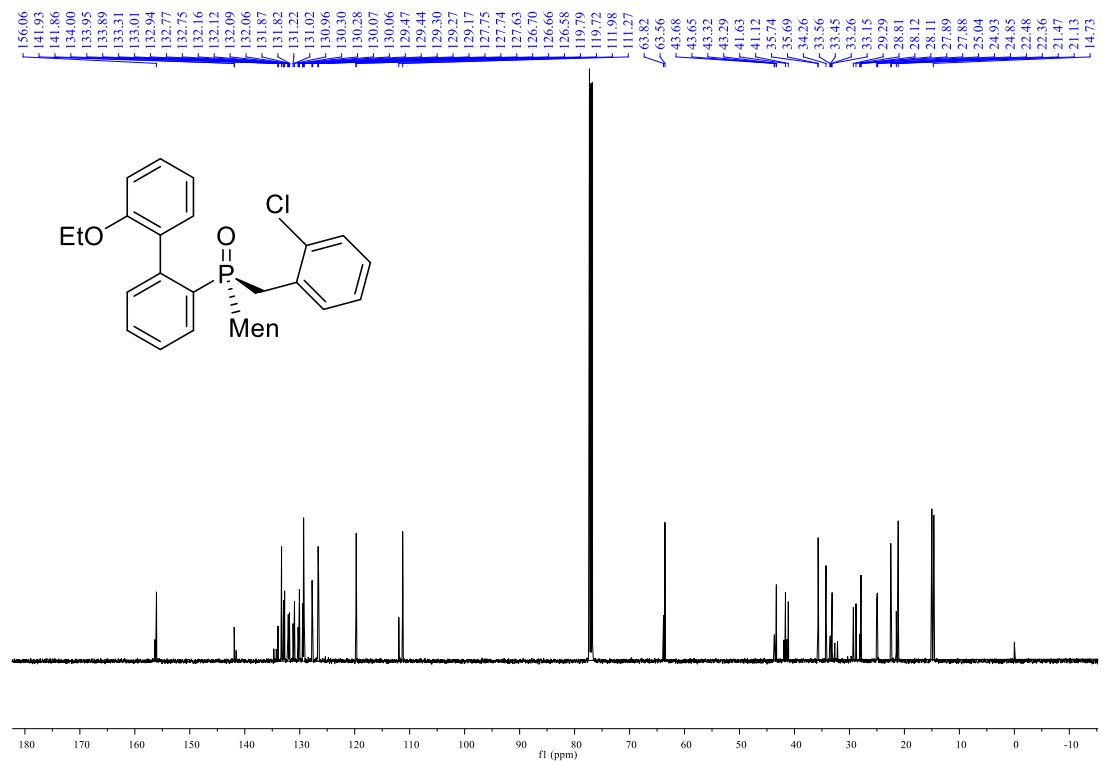




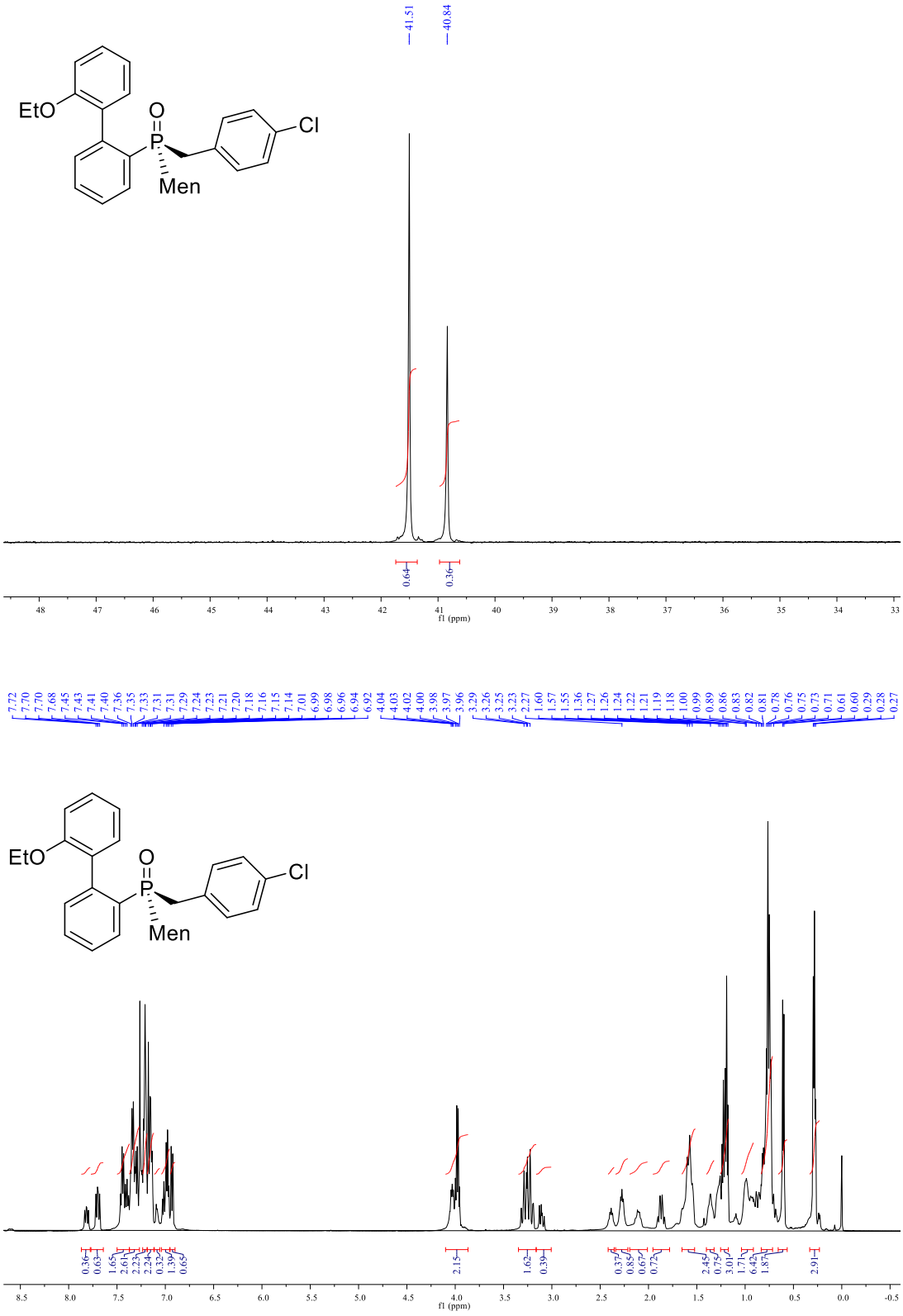
R_P-(2-Chlorobenzyl)(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphine oxide (R_P-7k)

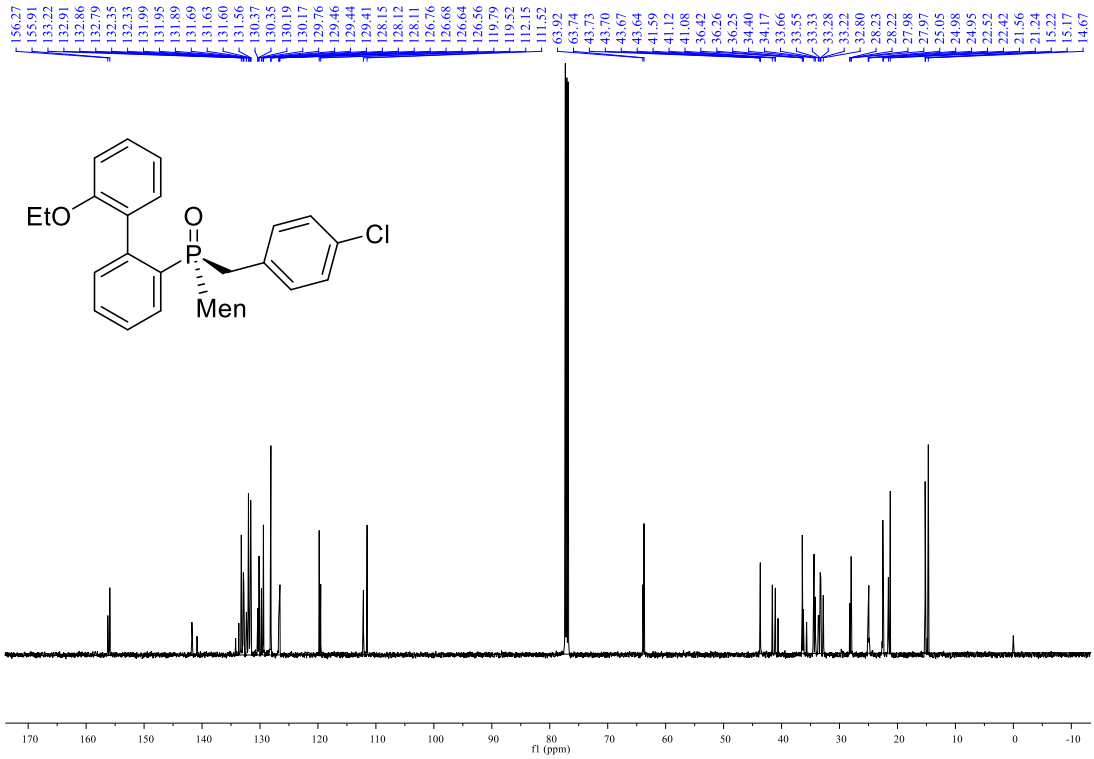



EtO
O
P
Cl
Men
f1 (ppm)

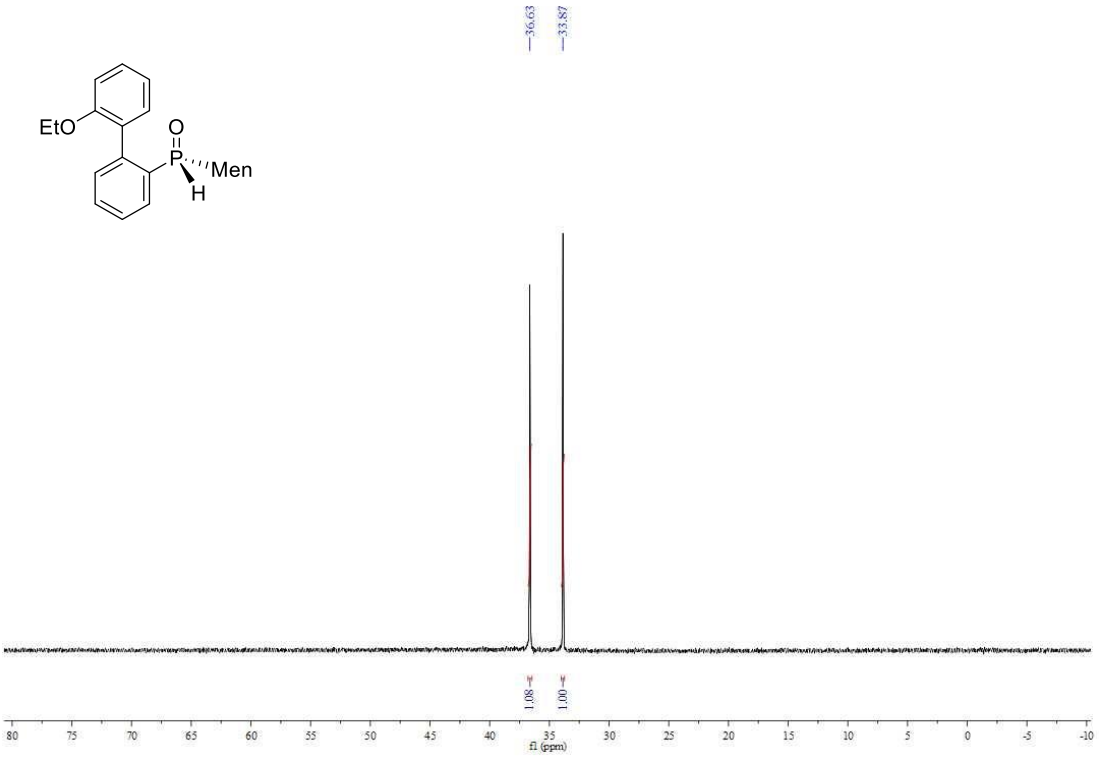

EtO
O
P
Cl
Men
f1 (ppm)

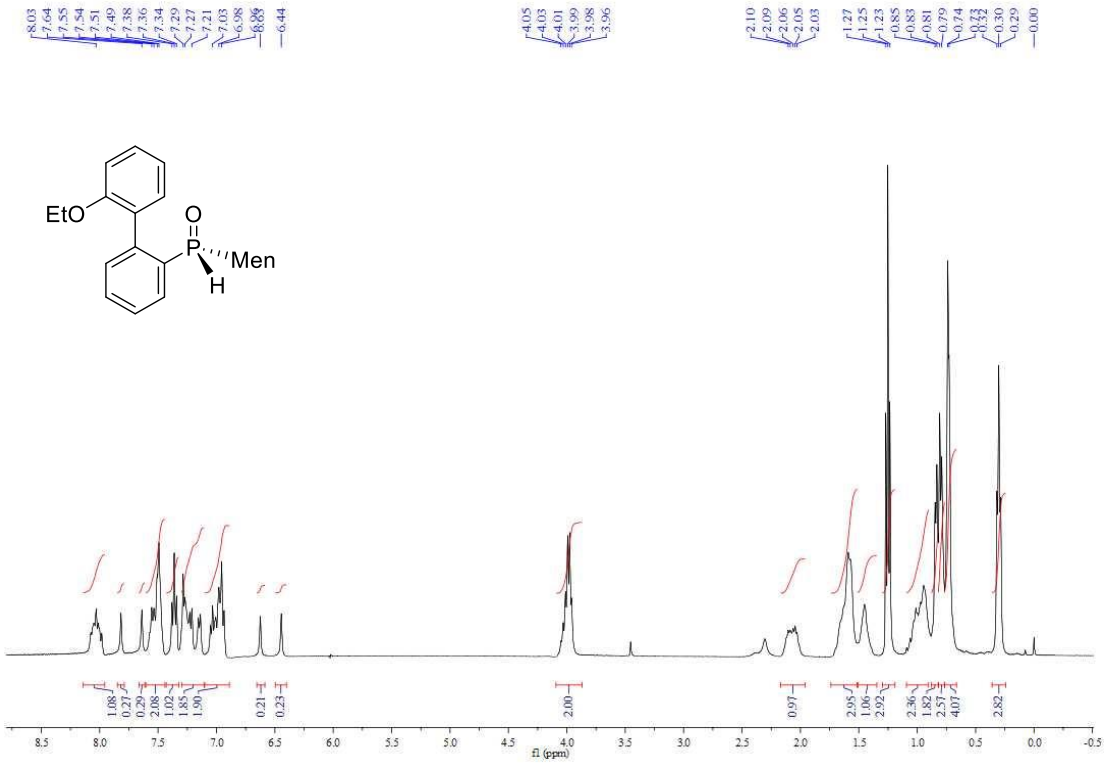
R_P-(4-Chlorobenzyl)(2'-ethoxy-[1,1'-biphenyl]-2-yl)((-)-menthyl) phosphine oxide (R_P-7l)

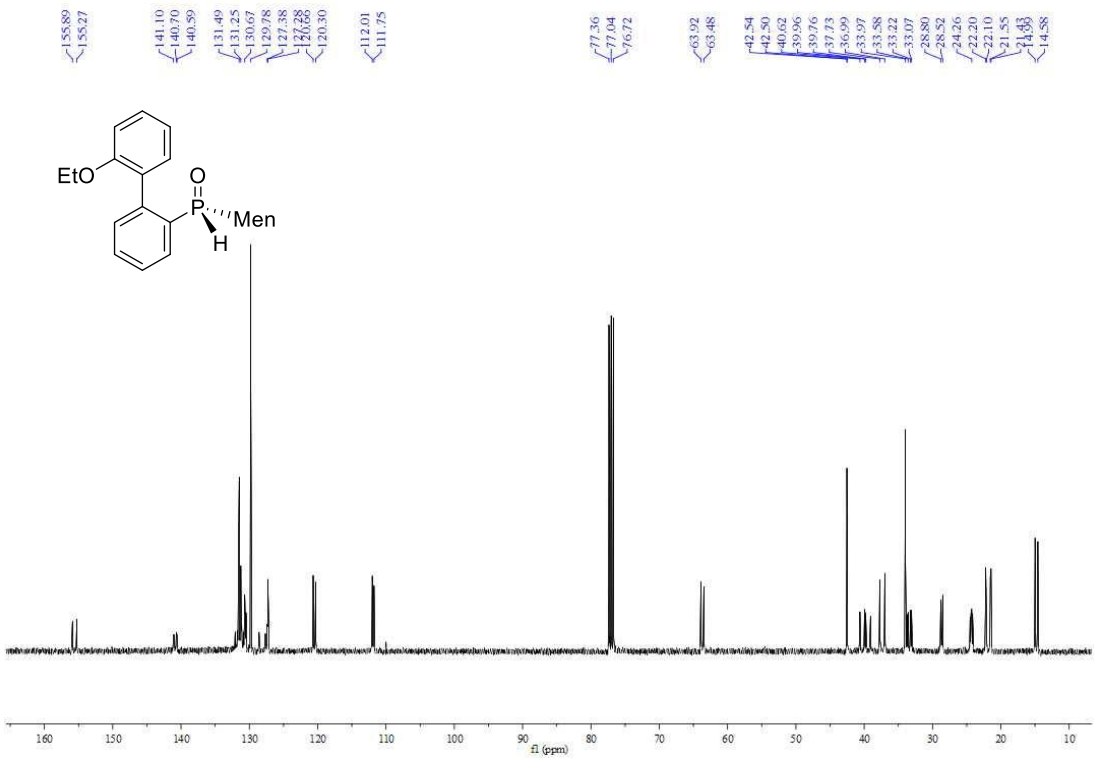




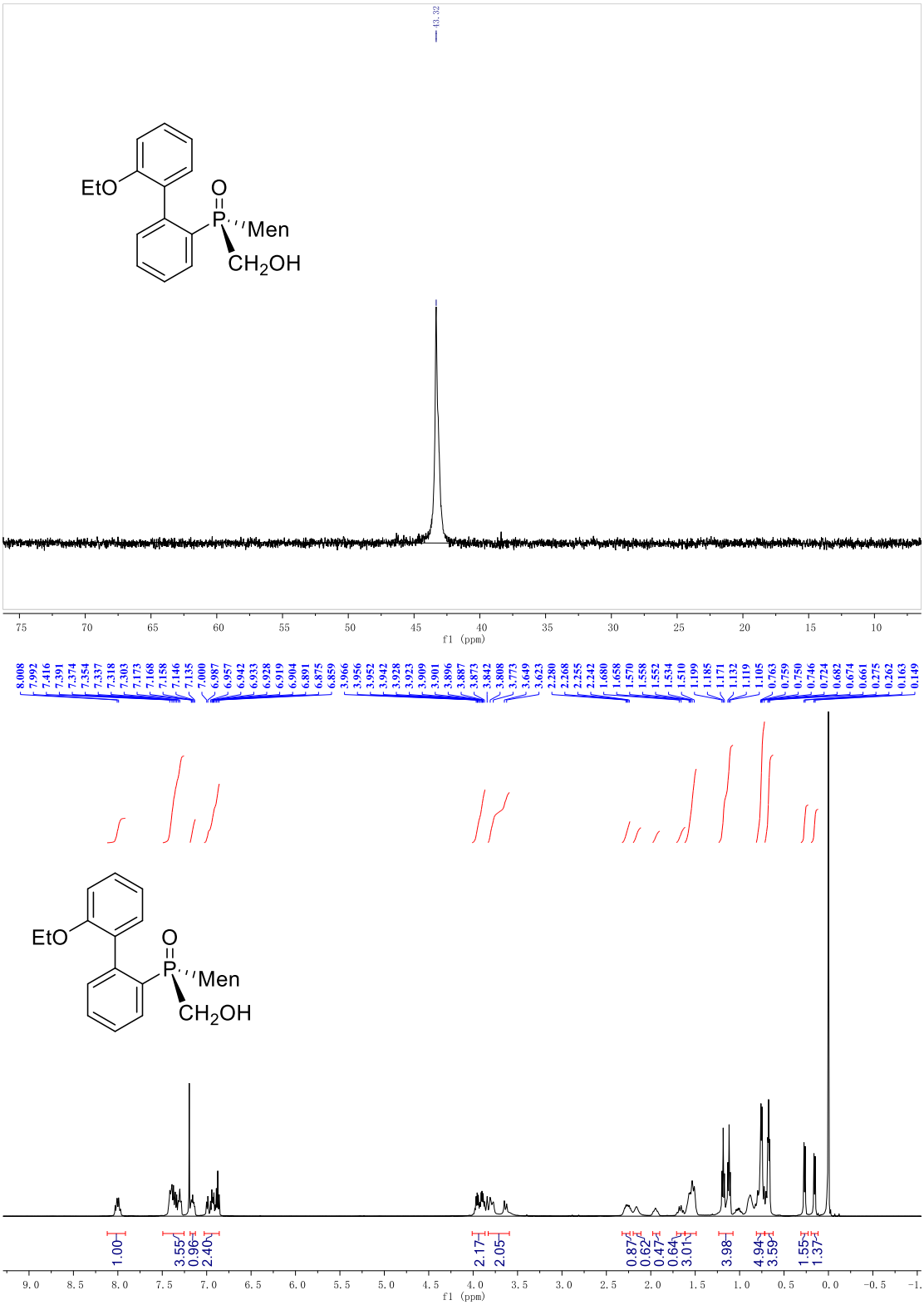
(R_P)-(-)-Menthyl (2'-ethoxy-[1,1'-biphenyl]-2-yl) phosphine oxide (R_P-11)

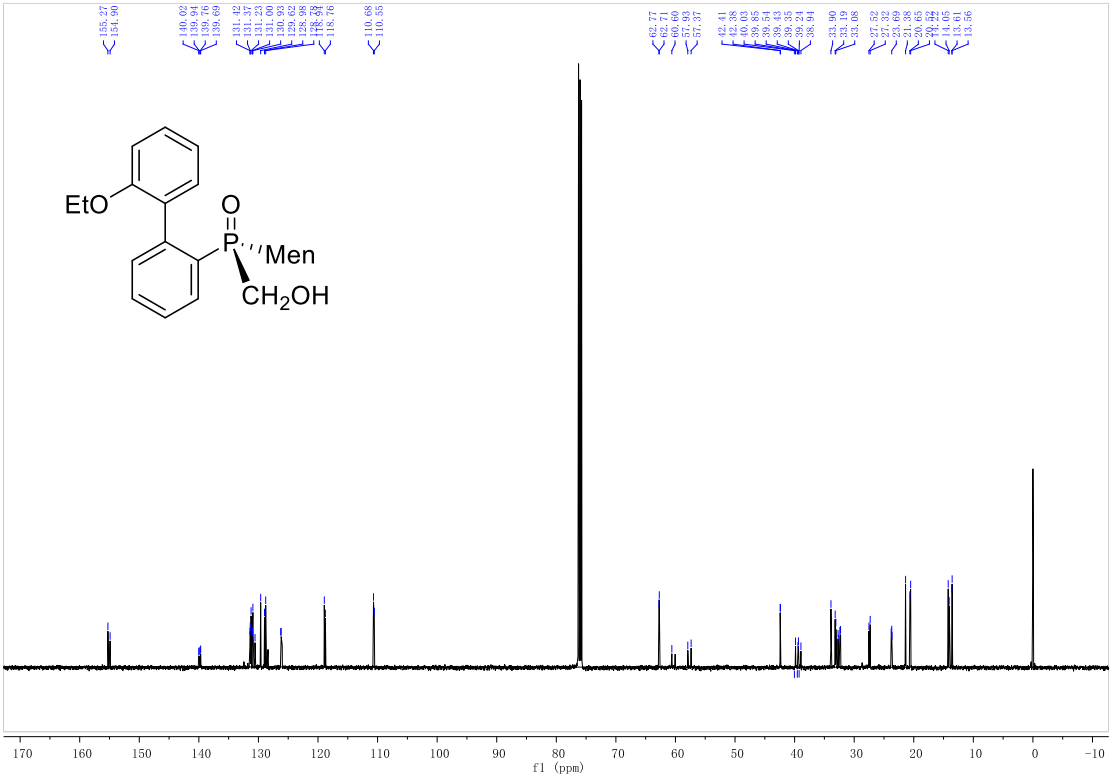



EtO
O
P
Men
H
fl (ppm)


EtO
O
P
Men
H
fl (ppm)

R_P-(2'-Ethoxy-[1,1'-biphenyl]-2-yl)(hydroxymethyl)((-)-menthyl) phosphine oxide (R_P-17)




155.27
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140.02
139.94
139.76
139.69
131.42
131.37
131.23
131.00
129.93
129.62
128.98
118.76
110.68
110.55
62.77
62.71
60.60
57.93
57.37
42.41
42.38
40.03
39.85
39.54
39.43
39.35
39.24
38.94
33.90
33.19
33.08
27.52
27.32
23.69
21.38
20.65
14.05
13.61
13.56
EtO
O
P
Men
CH2OH
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)