Addition of Optically Pure *H*-Phosphinate to Ketones: the Selectivity, Stereochemistry and Mechanism

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General

All solvents if needed were freshly distilled prior to use. The purity of the products was checked by TLC on precoated plates of Silica gel GF254 using as mobile phase a 3:1 mixture of Petrol ether and ethyl acetate. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. The ^{1}H, ^{13}C, and ^{31}P NMR spectra were obtained with a Varian Mercury Plus 400 MHz spectrometer at 400.13, 100.63 and 161.99 MHz, respectively. Chemical shifts were downfield relative to 85% H_3PO_4 or TMS. Chemical shifts δ were reported in ppm, and coupling constants J were reported in Hz. All X-ray crystallographic data were collected on a Bruker SMART CCD 1000. Elemental analyses were performed with a PE-2400II apparatus.

S1. Hydrophosphorylation of ketones with 1a to afford α-hydroxyphosphinates

S1-1. Optimization of condition for hydrophosphorylation of ketones

To the solution of R_P-(*L*)-(–)menthyl phenylphosphinate **1a** (0.100 g, 0.357 mmol) in solvent, *p*-bromoacephenone **2b** (0.073 g, 0.357 mmol) and base were added in turn. The mixture was stirred at room temperature and the reaction was monitored with ^{31}P-NMR spectroscopy (ca. 0.1 ml suspension of reaction mixture dissolved in 0.5 ml chloroform).

S1-2. Preparation of α-hydroxyphosphinates 3 via hydrophosphorylation of ketones

General procedure: To the solution of R_P-(*L*)-(–)menthyl phenylphosphinate **1a** (0.103 g, 0.368 mmol) in DMSO (1 ml), ketone **2** (0.368 mmol) and potassium carbonate (0.013 g, 0.092 mmol) were added in turn. The mixture was stirred at room temperature for 24 to 100 hours, and the reaction was monitored with ^{31}P-NMR spectroscopy (ca. 0.1 ml suspension of reaction mixture dissolved in 0.5 ml chloroform). After the reaction finished, water (2 ml) was added to the mixture and the solid was filtered, dried in the air. The crude product was recrystallized with DCM/PE (dichloromethane/petroleum ether, 30-60^{o}C) to afford pure **3**.

The spectral data of compounds **3a**, **3b**, **3c**, **3d/3d'**, **3e/3e'**, **3f**, **3g'**, **3h**, **3i**, **3j**, **3l or 3l'**, **3m**/**3m'**, **3p**, **3q**, **3r**, **3s**, **3t or 3t'**, **3u**, **3v/3v'** and **3w-3w'''** were shown in Supporting Information of our previous publication (H. Zhang, Y.-M. Sun, L. Yao, S.-Y. Ji, C.-Q. Zhao and L.-B. Han, *Chem. Asian J.* **2014**. *9*, 1329-1333.).

S1-3. Improvement of dr_C for formation of 3/3' with reaction time

Isolation of 3b/3b'

To the solution of R_P-(*L*)-(–)menthyl phenylphosphinate **1a** (1.090 g, 3.89 mmol) in DMSO (6 ml), *p*-bromoacetophenone **2b** (0.778 g, 3.89 mmol) and potassium carbonate (0.025 g, 0.184 mmol) were added in turn. The mixture was stirred at room temperature for 0.5 hours, then water (10 ml) was added to the mixture. The white solid was filtered, weighted 1.080 g after drying in the air.

^{31}P NMR (162 MHz, $CDCl_3$) δ 38.3 (**3b**, 59 %) 37.6 (**3b'**, 41 %)

Improvement of dr_C for formation of 3b/3b'

The same reaction as above was monitored with ^{31}P-NMR spectroscopy (ca. 0.1 ml suspension of reaction mixture dissolved in 0.5 ml chloroform). The peaks located at 38.4 (**3b**, s, 60 %), 37.8 ppm (**3b'**, s, 40 %) in 79 % yield after the mixture was stirred for 0.25 h; 38.4 (**3b**, s, 62 %), 38.4 ppm (**3b'**, s, 38 %) in 91 % yield for 1 h; 38.4 (**3b**, s, 77 %), 37.8 ppm (**3b'**, s, 23 %) for 5 h in 97 % yield; 38.4 (**3b**, s, 97 %),

37.8 ppm (**3b'**, s, 3 %) for 10 h in 97 % yield; 38.4 (**3b**, s, 97 %), 37.8 ppm (**3b'**, s, 3 %) for 24 h in 98 % yield; 38.4 (**3b**, s, 98 %), 37.8 ppm (**3b'**, s, 2 %) for 72 h in 98 % yield.

Improvement of dr_C for isolated 3b/3b'

To the solution of pure **3b/3b'** (0.114 g, 0.238 mmol, 59:41 dr_C) in DMSO (1 ml), potassium carbonate (0.096 g, 0.060 mmol) were added. The mixture was stirred at room temperature, and the reaction was monitored with ^{31}P-NMR spectroscopy (ca. 0.1 ml suspension of reaction mixture dissolved in 0.5 ml chloroform). The peaks located at 38.4 (**3b**, s, 94 %), 37.8 ppm (**3b'**, s, 6 %) after the mixture was stirred for 1.5 h; 38.4 (**3b**, s, 97 %), 37.8 ppm (**3b'**, s, 3 %) for 3 h, respectively.

Solubilities of two diastereomers 3b/3b' in DMSO

The suspension of **3b/3b'** (0.601 g, 1.25 mmol, 59:41 dr_C) in DMSO (3.6 ml) was stirred for 30min at room temperature. The white solid was filtered, that and the filtrate were analyzed with ^{31}P-NMR spectroscopy respectively. The peaks located at δ 38.4 (**3b**, s, 61.7 %), 37.8 ppm (**3b'**, s, 38.3 %) for solid; and δ 38.4 (**3b**, s, 22.5 %), 37.8 ppm (**3b'**, s, 77.5 %) for filtrate.

S1-4. Preparation of various *H*-phosphinates 1b to 1e

To the solution of dichlorophenylphosphine (8 ml, 58.95 mmol) in 40 ml dry ether, triethylamine (8.21 ml, 58.95 mmol) and alcohol (58.95 mmol) was added dropwise at 0 ^{o}C in turn. The mixture was stirred at room temperature for 8 hours, then another 20 ml ether was added to the mixture. The mixture was washed with water (3 x 20 ml), dried over anhydrous magnesium sulfate, and concentrated in vacuo. The resulted colorless oil was purified with column chromatography (silica gel, PE/EtOAc=4:1 as eluent).

Ethyl phenylphosphinate (**1b**) was obtained as colorless oil, weighted 8.5 g, yielding 72 %.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J_{P-H} = 564 Hz, 1H), 7.89 – 7.70 (m, 2H), 7.66 – 7.57 (m, 1H), 7.52 (d, J = 1.6 Hz, 2H), 4.33 – 4.03 (m, 2H), 1.39 (dd, J = 12.8, 6.9 Hz, 3H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.26 (s).

Isopropyl phenylphosphinate (**1c**) was obtained as colorless oil, weighted 9.1 g, yielding 77 %.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J_{P-H} = 560 Hz, 1H), 7.83 – 7.59 (m, 2H), 7.59 – 7.32 (m, 3H), 4.66 (dt, J = 15.1, 6.0 Hz, 1H), 1.37 (t, J = 5.6 Hz, 3H), 1.29 (t, J = 5.5 Hz, 3H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.85 (s).

Cyclohexyl phenylphosphinate (**1d**) was obtained as colorless oil, weighted 9.8 g, yielding 80 %.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J_{P-H} = 564 Hz, 1H), 7.99 – 7.70 (m, 2H), 7.67 – 7.38 (m, 3H) 4.54 – 4.33 (m, 1H), 2.14 – 1.10 (m, 10H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.71 (s).

***tert*-Butyl phenylphosphinate** (**1e**)

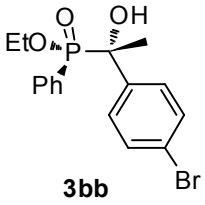
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J_{P-H} = 552 Hz, 1H), 7.77 (dd, J = 13.9, 7.7 Hz, 2H), 7.56 (d, J = 7.6 Hz, 1H), 7.50 (dd, J = 9.2, 5.3 Hz, 2H), 1.58 (d, J = 1.8 Hz, 9H).^{31}P NMR (162 MHz, $CDCl_3$) δ 15.63 (s).

S1-5. Hydrophosphorylation of *p*-bromoacetophenone 2b with *H*-Phosphinates 1a/1a' to 1e

Typical procedure: **Addition to 2b with R_P/S_P-1a/1a'**

To the solution of R_P/S_P-(*L*)-(–)menthyl phenylphosphinate **1a/1a'** (0.106 g, 0.378 mmol, dr_P ca. 50:50) in DMSO (1 ml), *p*-bromoacephenone **2b** (0.079 g, 0.378 mmol) and potassium carbonate (0.025 g, 0.198 mmol) were added in turn. The mixture was stirred at room temperature, and the reaction was monitored with ^{31}P-NMR spectroscopy (0.1 ml the suspension was dissolved in 0.5 ml chloroform). The results were presented in Table S1-1. After reaction completed, water was added dropwise to the mixture and the solid was filtered. After drying, the solid was recrystallized with DCM/PE.

Ethyl [1-hydroxy-1-(4-bromophenyl)ethyl]phenylphosphinate (**3bb**). The mixture of two diastereomers was obtained 0.750 g, in 81 % yield after 3 h, having the peaks at 40.7 and 40.9 ppm on ^{31}P-NMR spectroscopy. Major isomer (*l*)-**3bb** was obtained as white solid, weighted 0.383 g (41 % yield), m. p. 164.4-165.0 ^{o}C.



3bb

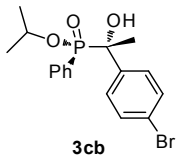
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 19.7, 9.9 Hz, 3H), 7.34 (d, *J* = 8.1 Hz, 4H), 7.21 (d, *J* = 7.5 Hz, 2H), 4.26 – 4.11 (m, 1H), 4.11 – 3.93 (m, 1H), 3.30 (d, *J* = 5.2 Hz, 1H), 1.80 (d, *J* = 13.8 Hz, 4H), 1.33 (t, *J* = 7.0 Hz, 3H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 40.28 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.52 (s), 133.33 (d, *J* = 8.9 Hz), 132.73 (d, *J* = 2.5 Hz), 131.01 (d, *J* = 2.5 Hz), 128.61 – 127.79 (m), 126.75 (s), 121.71 (d, *J* = 3.9 Hz), 77.54 (s), 77.32 (d, *J* = 20.5 Hz), 76.90 (s), 75.71 (s), 74.61 (s), 62.27 (d, *J* = 7.2 Hz), 25.13 (d, *J* = 4.7 Hz), 16.77 (d, *J* = 5.6 Hz). Anal. Calcd. for $C_{16}H_{18}O_3PBr$: C, 52.05; H, 4.91. Found: C, 51.92; H, 4.83.

Table S1-1. Time-dependences of yield (%) and dr for the reactions of various *H*-phosphinates to 2b

Time /h	**1a** (R=Men)[a]	**1a/1a'** (R=Men)[b]	**1b** (R=Et)	**1c** (R= *i*Pr)	**1d** (R= *c*-Hex)	**1e** (R= *t*Bu)
0.25	79 (60:40)	NR				
0.5			80 (62:38)	82.7(57:43)		
1	91 (62:38)	82(31:14:30:26)				
5	97 (77:23)	73 (49:5:28:18)		80 (51:49)	84 (38:62)	
10	97 (90:10)	83 (42:4:28:26)				
17			53 (19:81)	80 (20:80)		54 (44:56)
24	98 (97:3)	67 (47:3:26:24)			87 (33:67)	
41			38 (21:79)	69 (20:80)		81 (38:62)
54					80 (29:71)	
66			20 (46:54)	70.0(22:78)		77 (35:65)
72	98 (98:2)	66 (54:1:25:20)			73 (28:72)	
88					71 (28:72)	73 (31:69)

[a] Yields and dr were estimated by ^{31}P-NMP spectroscopy. The dr were presented in parentheses, and assigned as ratio of S_PR_C/S_PS_C stereomers for reaction of **1a**, or ratio of (*u/l*)-stereomers for reactions of **1b-1e**. [b] R_P/S_P-**1a/1a'** (ca. 50:50) was used. The ratio was assignen as S_PR_C:S_PS_C :(R_PR_C/R_PS_C), and the later two stereomers weren't confirmed.

Isopropyl [1-hydroxy-1-(4-bromophenyl)ethyl]phenylphosphinate (**3cb**). The mixture of two diastereomers was obtained 0.534 g, in 54 % yield after 66 h, having the peaks at 39.2 and 39.4 ppm on ^{31}P-NMR spectroscopy. Major isomer was obtained as white solid, weighted 0.352 g (41 % yield), m. p. 171.5-172.9 ^{o}C.

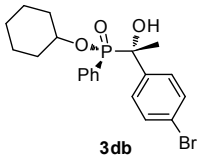


3cb

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.43 (m, 3H), 7.34 (dd, *J* = 12.1, 5.9 Hz, 3H), 7.21 (dd, *J* = 8.6, 2.1 Hz, 2H), 4.82 – 4.52 (m, 1H), 3.49 (s, 1H), 3.19 (br, 1H), 1.79 (d, *J* = 13.7 Hz, 3H), 1.39 (d, *J* = 6.1 Hz, 3H), 1.23 (d, *J* = 6.1 Hz, 3H). ^{31}P NMR (162 MHz,

$CDCl_3$) δ 38.96 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.46 (d, J = 2.8 Hz), 133.34 (d, J = 8.9 Hz), 132.60 (d, J = 2.8 Hz), 130.92 (d, J = 2.6 Hz), 128.78 (s), 128.16 (t, J = 7.7 Hz), 127.58 (s), 121.62 (d, J = 3.8 Hz), 77.54 (s), 77.32 (d, J = 20.3 Hz), 76.90 (s), 75.64 (s), 74.54 (s), 71.42 (d, J = 7.5 Hz), 51.00 (s), 25.06 (d, J = 4.7 Hz), 24.58 (d, J = 3.5 Hz), 24.29 (d, J = 4.2 Hz). Anal. Calcd. for $C_{17}H_{20}O_3PBr$: C, 53.28; H, 5.26. Found: C, 53.11; H, 5.15.

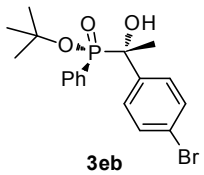
Cyclohexyl [1-hydroxy-1-(4-bromophenyl)ethyl]phenylphosphinate (**3db**). The mixture of two diastereomers was obtained 0.380 g, in 57 % yield after 88 h, having the peaks at 39.4 and 39.7 ppm on ^{31}P-NMR spectroscopy. Major isomer was obtained as white solid, weighted 0.250 g (yield 37 %), m. p. 179.1-182.3 ^oC.



3db

^1H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.47 (m, 3H), 7.36 (d, J = 8.3 Hz, 3H), 7.30 (s, 1H), 7.23 (d, J = 8.3 Hz, 2H), 4.42 (s, 1H), 2.01 (s, 1H), 1.81 (d, J = 13.8 Hz, 3H), 1.67 (s, 3H), 1.48 (d, J = 22.0 Hz, 2H), 1.43 – 1.16 (m, 4H), 0.91 (s, 1H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 39.17 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.16 (s), 133.06 (d, J = 8.9 Hz), 132.33 (d, J = 2.6 Hz), 130.65 (d, J = 2.4 Hz), 128.60 (s), 128.14 – 127.64 (m), 127.40 (s), 121.34 (d, J = 3.7 Hz), 75.81 (d, J = 7.6 Hz), 75.37 (s), 74.28 (s), 33.97 (d, J = 3.0 Hz), 33.72 (d, J = 3.7 Hz), 25.08 (s), 24.82 (d, J = 4.8 Hz), 23.55 (s). Anal. Calcd. for $C_{20}H_{24}O_3PBr$: C, 56.75; H, 5.72. Found: C, 56.52; H, 5.60.

***tert*-Butyl [1-hydroxy-1-(4-bromophenyl)ethyl]phenylphosphinate** (**3eb**). The mixture of two diastereomers was obtained 0.650 g, in 53 % yield after 88 h, having the peaks at 35.8 and 36.1 ppm on ^{31}P-NMR spectroscopy. Major isomer was obtained as white solid, weighted 0.436 g (yield 35 %). m. p. 177.6-179.2 ^oC.



3eb

^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.50 (m, 2H), 7.46 (d, J = 7.5 Hz, 1H), 7.32 (d, J = 8.2 Hz, 4H), 7.21 (d, J = 7.3 Hz, 2H), 3.12 (s, 1H), 1.74 (d, J = 13.8 Hz, 3H), 1.44 (s, 9H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 35.47 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.59 (s), 133.16 (d, J = 8.9 Hz), 132.26 (d, J = 2.8 Hz), 130.76 (d, J = 2.6 Hz), 129.53 (s), 128.35 (d, J = 4.0 Hz), 128.00 (d, J = 12.3 Hz), 121.47 (s), 84.52 (d, J = 10.0 Hz), 75.69 (s), 74.57 (s), 30.91 (d, J = 3.6 Hz), 24.83 (d, J = 4.7 Hz). Anal. Calcd. for $C_{18}H_{22}O_3PBr$: C, 54.42; H, 5.58. Found: C, 54.16; H, 5.43.

S2. Ketone and/or aldehyde exchanging reaction for 3 or 6

Typical procedure: Reaction of 3b to 2i

To the solution of optically pure **3b** (0.102 g, 0.21 mmol) in DMSO (0.8 ml), *p*-methoxyacephenone **2i** (0.065 g, 0.42 mmol) and potassium carbonate (8 mg, 0.053 mmol) were added in turn, and the mixture was stirred at room temperature. After 48h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 39.0 (**3i**, 13 %), 38.4/37.8 (**3b/3b'**, in the ratio of 97:3, 60 %), 25.1 (R_P-**1a**, 9 %).

Reaction of 3b to 2p

After 24 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 40.5 (**3p**, 70 %), 38.4 (**3b**, 24 %)

Reaction of 3b/3b' to 2p

After 24 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 40.5 (**3p**, 31 %), 38.4/37.8 (**3b/3b'** in the ratio of 90:10, 66 %)

Reaction of R_PR_C-6a to 2p catalyzed by K_2CO_3

After 48 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 41.4 (R_P-**3p**, 15 %), 35.7/36.9 (R_PR_C-**6a**/R_PS_C-**6a** in the ratio of 87:13, 82 %).

Reaction of (R_PR_C)-6a to 5b at 80°C in neat state

(R_PR_C)-**6a** (0.050 g, 0.129 mmol) and *o*-anisaldehyde **5b** (0.046 g, 0.306 mmol) were heated at 80°C in neat state for 24 h. The tardy substance (ca. 10 mg) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 35.7 (R_PR_C-**6a**, 99 %).

Reaction of R_PR_C-6a to 5b catalyzed by K_2CO_3

After 24 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 35.7/36.7 (R_PR_C-**6b**/R_PS_C-**6b**, in the ratio of 24:76, 29 %), 36.0/36.2 (R_PR_C-**6a**/R_PS_C-**6a**, in the ratio of 59:41, 57 %), 18.7 (*O*-phosphorylated product, 14 %).

Reaction of 3p to 2r catalyzed by K_2CO_3

After 24 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 41.2 (**3r**, 10 %), 40.5 (**3p**, 90 %)

Reaction of 3p to 2r catalyzed by KOH

After 24 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 41.2 (**3r**, 13 %), 40.5 (**3p**, 74 %)

Reaction of 3p to 5b catalyzed by K_2CO_3

After 24 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 18.3 ($\mathbf{4_{ald}}$, 1 %), 40.5 (**3p**, 99 %).

Reaction of 3p to 5b catalyzed by KOH

After 13 h, the suspension (0.1 ml) was dissolved in chloroform (0.5 ml), and was analyzed by NMR spectroscopy.

^{31}P NMR (162 MHz) δ (ppm) 18.3 ($\mathbf{4_{ald}}$, 91 %), 40.5 (**3p**, 5 %).

Cross aldehyde exchanging reaction for 6 catalyzed by potassium carbonate

To the solution of optically pure S_PS_C-**6a** (0.051 g, 0.133 mmol) and R_PS_C-**6c** (0.049 g, 0.122 mmol) in DMSO (1 ml), potassium carbonate (0.012 g, 0.087 mmol) were added. The mixture was stirred at room temperature, and the reaction was monitored with ^{31}P-NMR spectroscopy (ca. 0.1 ml suspension of reaction mixture dissolved in 0.5 ml chloroform). Two groups of adducts **6a** to and **6c** were observed to have eight peaks at δ 34.86, 34.95, 35.06, 35.11, 35.41, 35.54, 36.31 and 36.38 ppm.

S3. Crystallographic Information

General

Crystals were mounted in lindemann capillaries under nitrogen. All X-ray crystallographic data were collected on a Bruker SMART CCD 1000 diffractometer with graphite monochromated Mo-Kα radiation (λ=0.71073 Å) at 298(2) K. A semi-empirical absorption correction was applied to the data. The structure was solved by direct methods using SHELXS-97 and refined against F2 by full-matrix least squares using SHELXL-97.[S1] Hydrogen atoms were placed in calculated positions. The absolute configurations were confirmed by evaluation of the Flack parameter.[S2]

[S1] G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *64*, 112-122.

[S2] H. D. Flack, *Acta Crystallogr., Sect. A: Found. Crystallogr.* **1983**, *39*, 876-881.

S3-1.
(*S*)-(*L*)-menthyl [(*R*)-1-(4-bromophenyl)-1-hydroxyethyl]phenylphosphinate (3b)

The crystal suitable for X-ray diffraction was obtained from recrystallization with DCM and methanol.

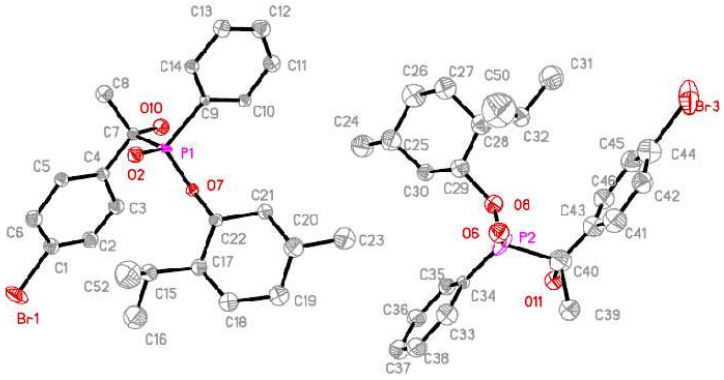


Table S3-1. Crystallographic Data of **3b**

Empirical formula	$C_{24}H_{32}O_3PBr$
Formula weight	479.37
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P2(1)
a (Å)	19.80(2)
b (Å)	5.863(6)
c (Å)	20.83(2)
α(°)	90
β(°)	101.188(12)
γ(°)	90
V (Å3)	2372(4)
Z	4
Dcalc (Mg/m^3)	1.342
μ (mm^{-1})	1.822
F(000)	1000
Crystal size (mm)	0.48 x 0.30 x 0.27
Reflections collected	11609
Unique reflections [R_{int}]	7063 [R(int) = 0.0445]
Data/restraints/parameters	7063 / 325 / 558
Goodness-of-fit on F^2	1.083
Final R indices [I>2σ (I)]	R1 = 0.1350, wR2 = 0.2983
R indices (all data)	R1 = 0.1719, wR2 = 0.3188
Flack parameter	0.08(3)
CCDC number	CCDC 950075

S3-2.
(*S*)-(*L*)-menthyl [(*S*)-1-(3-nitrophenyl)-1-hydroxyethyl] phenylphosphinate (3g')

The crystal suitable for X-ray diffraction was obtained from recrystallization with DCM and methanol.

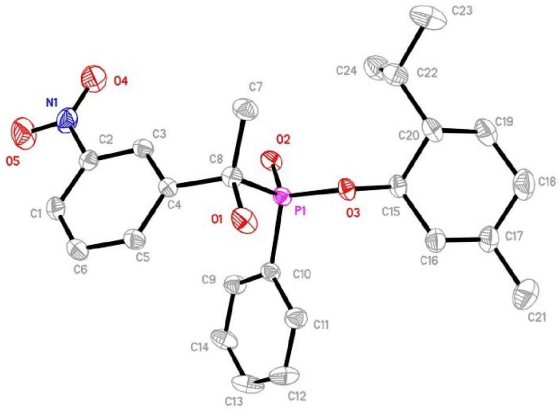


Table S3-2. Crystallographic Data of **3g'**

Empirical formula	$C_{24}H_{32}NO_5P$
Formula weight	446.48
Wavelength (Å)	0.71073
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
a (Å)	5.8926(18)
b (Å)	18.289(2)
c (Å)	22.043
α(°)	90
β(°)	90
γ(°)	90
V (Å3)	2375.7(8)
Z	4
Dcalc (Mg/m^3)	1.248
μ (mm^{-1})	0.150
F(000)	956
Crystal size (mm)	0.45 x 0.40 x 0.31
Reflections collected	17624
Unique reflections [R_{int}]	5517 [R(int) = 0.0755]
Data/restraints/parameters	5517 / 0 / 300
Goodness-of-fit on F^2	1.035
Final R indices [I>2σ (I)]	R1 = 0.0614, wR2 = 0.1032
R indices (all data)	R1 = 0.1158, wR2 = 0.1242
Flack parameter	0.07(13)
CCDC number	CCDC 950078

S3-3.

(*S*)-(*L*)-menthyl [(*R*)-1-(4-methoxylphenyl)-1-hydroxyethyl] phenylphosphinate (3i)

The crystal suitable for X-ray diffraction was obtained from recrystallization with DCM and methanol.

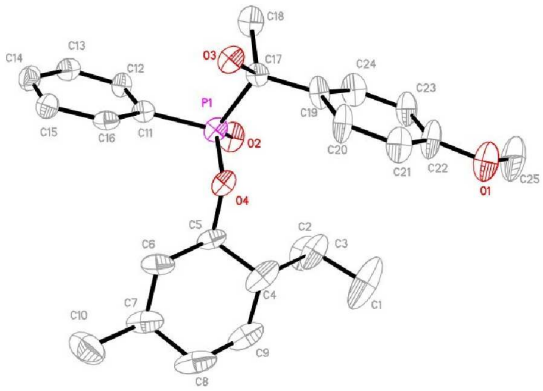


Table S3-3. Crystallographic Data of **3i**

Empirical formula	$C_{25}H_{35}O_4P$
Formula weight	425.46
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P2(1)
a (Å)	12.436(13)
b (Å)	5.7781(7)
c (Å)	15.9687(16)
α(°)	90
β(°)	92.5340(10)
γ(°)	90
V (Å3)	1146.3(12)
Z	2
Dcalc (Mg/m^3)	1.233
μ (mm^{-1})	0.148
F(000)	454
Crystal size (mm)	0.43 x 0.19 x 0.12
Reflections collected	5868
Unique reflections [R_{int}]	3683 [R(int) = 0.1238]
Data/restraints/parameters	3683 / 37 / 288
Goodness-of-fit on F^2	1.092
Final R indices [I>2σ (I)]	R1 = 0.1367, wR2 = 0.3229
R indices (all data)	R1 = 0.1811, wR2 = 0.3557
Flack parameter	0.3(4)
CCDC number	CCDC 950076

S3-4.
(*S*)-(*L*)-menthyl [(*R*)-1-biphenyl-1-hydroxyethyl] phenylphosphinate (3j)

The crystal suitable for X-ray diffraction was obtained from recrystallization with DCM and methanol.

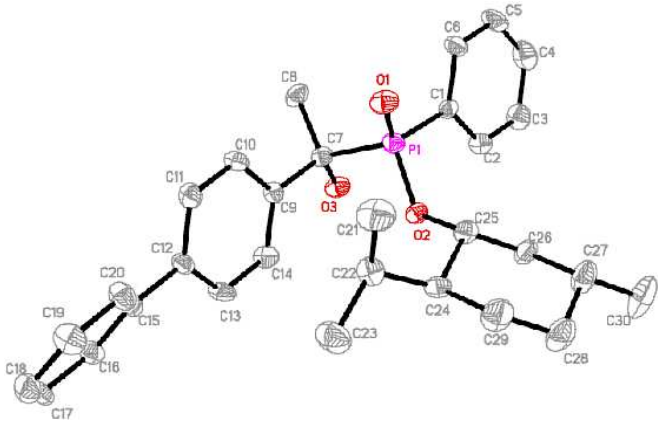


Table S3-4. Crystallographic Data of **3j**

Empirical formula	$C_{30}H_{37}O_3P$
Formula weight	475.56
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	C2
a (Å)	24.450(4)
b (Å)	5.8577(7)
c (Å)	20.328(3)
α(°)	90
β(°)	114.063(17)
γ(°)	90
V (Å3)	2658.4(7)
Z	4
Dcalc (Mg/m^3)	1.188
μ (mm^{-1})	0.132
F(000)	1020
Reflections collected	8280
Unique reflections [R_{int}]	4237 [R(int) = 0.0790]
Data/restraints/parameters	4237 / 1 / 312
Goodness-of-fit on F^2	1.027
Final R indices [I>2σ (I)]	R1 = 0.0707, wR2 = 0.1028
R indices (all data)	R1 = 0.1435, wR2 = 0.1390
Flack parameter	0.4(2)
CCDC number	CCDC 950080

S3-5.
(*S*)-(*L*)-menthyl [(*R*)-(2-hydroxy-4-methyl pentan-2-yl)] phenylphosphinate (3u)

The crystal suitable for X-ray diffraction was obtained from recrystallization with DCM and methanol.

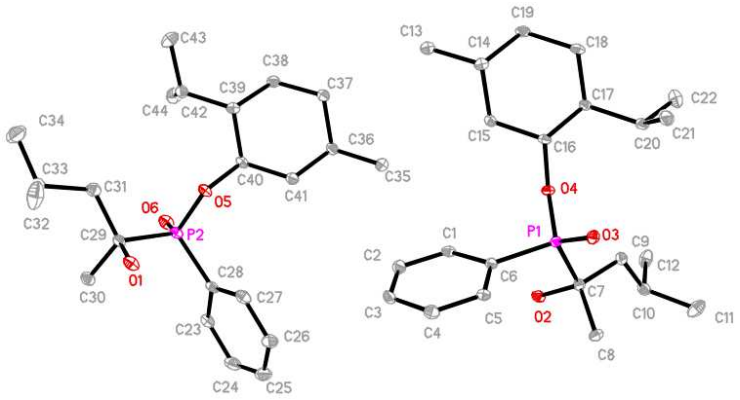


Table S3-5. Crystallographic Data of **3u**

Empirical formula	$C_{22}H_{37}O_3P$
Formula weight	380.49
Wavelength (Å)	0.71073
Crystal system	Triclinic
Space group	P1
a (Å)	5.7766(4)
b (Å)	12.2080(12)
c (Å)	16.2225(15)
α(°)	83.552(2)
β(°)	82.7850(10)
γ(°)	78.7770(10)
V (Å3)	1108.71(17)
Z	2
Dcalc (Mg/m^3)	1.140
μ (mm^{-1})	0.141
F(000)	416
Crystal size (mm)	0.32 x 0.20 x 0.16
Reflections collected	6610
Unique reflections [R_{int}]	5141 [R(int) = 0.0346]
Data/restraints/parameters	5141 / 3 / 483
Goodness-of-fit on F^2	1.032
Final R indices [I>2σ (I)]	R1 = 0.0435, wR2 = 0.0898
R indices (all data)	R1 = 0.0534, wR2 = 0.0973
Flack parameter	-0.12(9)
CCDC number	CCDC 950077

S3-6.
Cyclohexyl [1-hydroxy-1-(4-bromophenyl)ethyl] phenylphosphinate (3db)

The crystal suitable for X-ray diffraction was obtained from recrystallization with DCM and methanol.

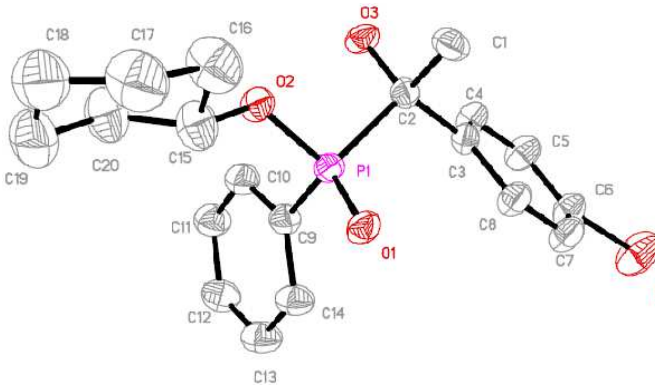


Table S3-6. Crystallographic Data of **3db**

Empirical formula	$C_{20}H_{24}O_3PBr$
Formula weight	423.26
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P2(1)/n
a (Å)	10.4511(12)
b (Å)	19.5742(6)
c (Å)	11.0005(11)
α(°)	90
β(°)	117.362(2)
γ(°)	90
V (Å3)	1998.6(3)
Z	4
Dcalc (Mg/m^3)	1.400
μ (mm^{-1})	2.152
F(000)	864
Crystal size (mm)	0.50 x 0.20 x 0.20
Reflections collected	7242
Unique reflections [R_{int}]	3373 [R(int) = 0.0630]
Data/restraints/parameters	3373 / 162 / 228
Goodness-of-fit on F^2	1.039
Final R indices [I>2σ (I)]	R1 = 0.0889, wR2 = 0.2117
R indices (all data)	R1 = 0.1627, wR2 = 0.2647
CCDC number	CCDC 950079

S3-7.

***tert*-Butyl [1-hydroxy-1-(4-bromophenyl) ethyl]phenylphosphinate (3eb)**

The crystal suitable for X-ray diffraction was obtained from recrystallization with DCM and methanol.

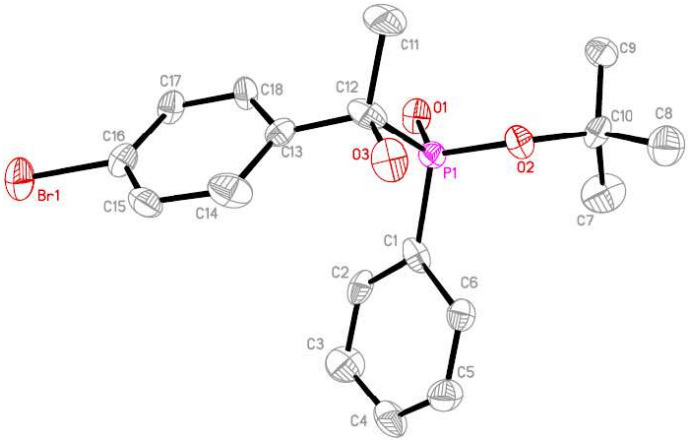


Table S3-7. Crystallographic Data of **3eb**

Empirical formula	$C_{18}H_{22}O_3PBr$
Formula weight	397.24
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P2(1)/c
a (Å)	15.6312(13)
b (Å)	5.9562(4)
c (Å)	19.6323(17)
α(°)	90
β(°)	92.0060(10)
γ(°)	90
V (Å3)	1826.7(3)
Z	4
Dcalc (Mg/m^3)	1.444
μ (mm^{-1})	2.349
F(000)	816
Crystal size (mm)	0.50 x 0.18 x 0.17
Reflections collected	8535
Unique reflections [R_{int}]	3197 [R(int) = 0.1362]
Data/restraints/parameters	3197 / 0 / 213
Goodness-of-fit on F^2	1.110
Final R indices [I>2σ (I)]	R1 = 0.1842, wR2 = 0.4463
R indices (all data)	R1 = 0.2615, wR2 = 0.4999
CCDC number	CCDC 950081

S4. Density Functional Computations for 3b/3b' and 3g/3g'

S4-1. Computational Details

The whole calculations were performed in Gaussian 09[S3] using the B3LYP density functional. This basis has previously been shown to perform well for silicon and phosphorus compounds.[S4] The diastereomeric structures derived from chiral carbon of **3g/3g'** were optimized using the 6-31G (d,p) full-electron double-zeta polarized basis set for H, C, O, and P, and the groups were optimized using tight convergence criteria, fixing irrelevant atoms and increasing calculated steps' length. The diastereomeric structures derived from chiral carbon of **3b/3b'** were optimized using the 6-311G (2d) triple-zeta doubly polarized basis set for Br. An ultrafine integration grid was applied in combination with tight convergence criteria for SCF and geometry. Structures of **3g'** and **3b** were referred from X-ray structures. Subsequent single-point energies were calculated with each polarized basis which had been used to optimization.

S4-2. Optimized Energies

Table S4-1. Density functional calculations of **3b/3b'** and **3g/3g'**

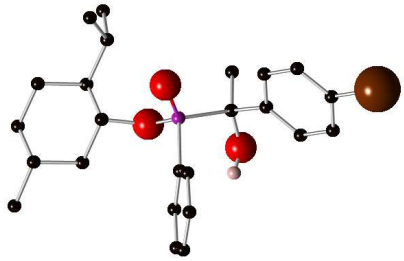
Compounds	$E_{SpRc\text{-}opt}$	$E_{SpSc\text{-}opt}$	$E_{SpRc\text{-}opt} - E_{SpSc\text{-}opt}$ (kcal/mol)
3b/**3b'**	-4075.37267009 a.u.	-4075.34996024 a..u.	-14.25
3g/**3g'**	-1706.07392557 a.u.	-1706.07415733 a.u.	0.15

[S3] Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

[S4] a) E. P. A. Couzijn, J. C. Slootweg, A. W. Ehlers, K. Lammertsma, *J. Am. Chem. Soc.* **2010**, *132*, 18127–18140. b) E. P. A. Couzijn, D. W. F. van den Engel, J. C. Slootweg, F. J. J. de Kanter, A. W. Ehlers, M. Schakel, K. Lammertsma, *J. Am. Chem. Soc.* **2009**, *131*, 3741–3751.

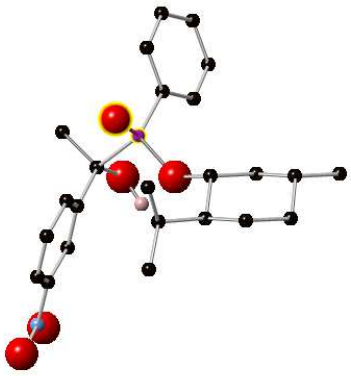
S4-3. Optimized Structures:

(*S*)-(–)-menthyl [(*S*)-1-(4-bromophenyl)-1-hydroxyethyl]phenylphosphinate (3b')



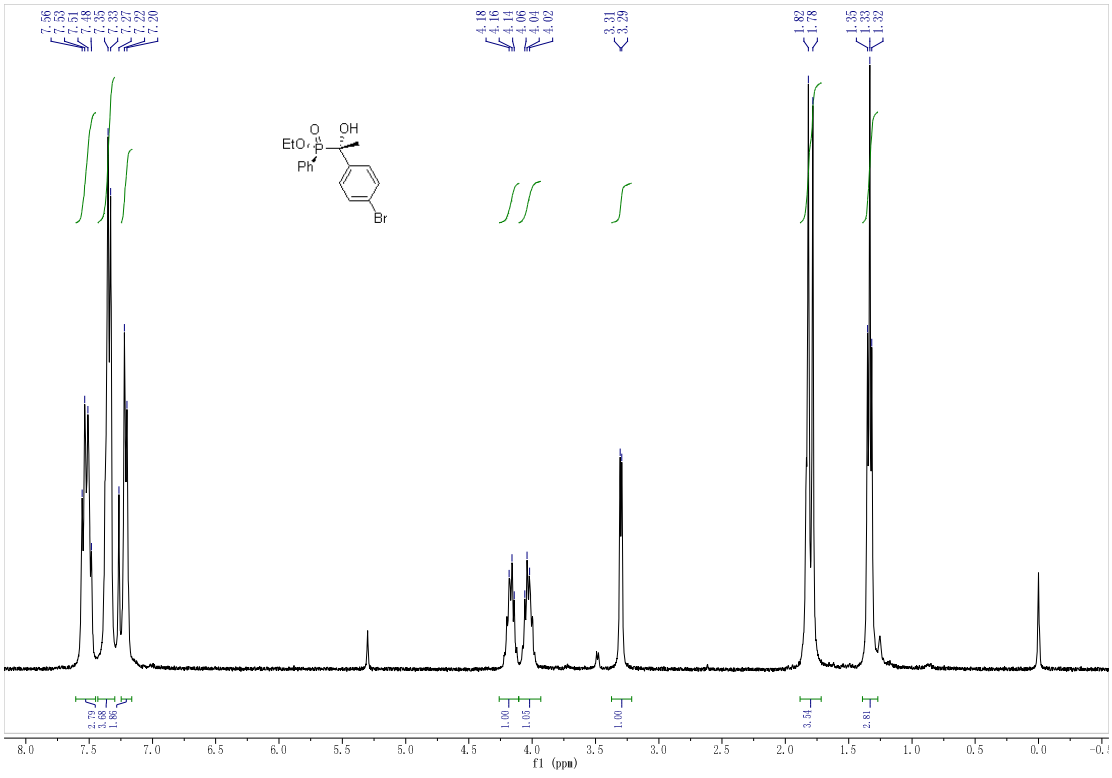
P	-0.54324	-0.01694	-0.08907	C	-5.38	-1.29919	-0.59006	C	0.605754	2.194815	-1.25695	C	2.513325	-1.24496	-0.37239
C	-3.11397	-2.94836	-1.7911	H	-5.22736	-1.25105	-1.66986	H	1.009713	1.482351	-1.96921	C	3.001457	0.189696	1.484178
H	-2.20571	-3.50497	-2.01644	H	-5.97082	-2.1936	-0.39274	C	-0.22801	1.742423	-0.22889	H	1.800961	-1.78246	-0.98901
H	-3.05818	-2.00963	-2.33695	C	-4.01393	-1.42082	0.117852	C	-0.74775	2.685812	0.671674	C	3.848992	-1.22554	-0.74798
H	-3.96442	-3.51517	-2.17231	H	-4.19758	-1.47305	1.196063	H	-1.39269	2.353998	1.481965	H	2.686526	0.75175	2.353843
O	-0.41328	-0.70459	-1.39972	C	-3.22164	-0.14224	-0.13407	C	-0.46955	4.034793	0.534615	C	4.341813	0.227351	1.111251
O	-1.97088	-0.16158	0.630314	H	-2.97784	-0.05679	-1.19313	H	-0.88475	4.74829	1.240976	C	4.758719	-0.51334	0.017404
C	-6.11692	2.475265	0.084706	C	-3.99943	1.100635	0.31118	C	0.34293	4.473544	-0.50808	H	4.180104	-1.7605	-1.63371
H	-6.07555	2.576172	1.171028	H	-4.14994	1.041122	1.392412	H	0.525597	5.535295	-0.64566	H	5.044538	0.832631	1.673516
H	-7.16679	2.421196	-0.20581	H	-3.38658	1.984878	0.125215	C	0.896588	3.546423	-1.37884	Br	6.61676	-0.49303	-0.47339
H	-5.6963	3.382729	-0.35124	C	-3.87284	-3.94844	0.419644	H	1.579375	3.874993	-2.16102	H	0.930742	-2.42336	2.434996
C	-5.35603	1.23036	-0.38404	H	-4.92515	-4.05528	0.155533	C	0.594259	-0.68288	1.249732	H	-0.76592	-2.15438	2.009059
H	-5.18122	1.320947	-1.46157	H	-3.80338	-3.86488	1.505305	C	0.258139	-2.08838	1.644714	H	0.369314	-2.75386	0.790871
C	-6.1618	-0.0603	-0.14799	H	-3.36353	-4.86531	0.119048	O	0.417487	0.152942	2.430186				
H	-6.39973	-0.13326	0.917033	C	-3.24011	-2.72804	-0.26542	H	0.443357	1.086893	2.123148				
H	-7.11247	-0.00745	-0.68379	H	-2.23695	-2.61346	0.136836	C	2.071335	-0.55848	0.771215				

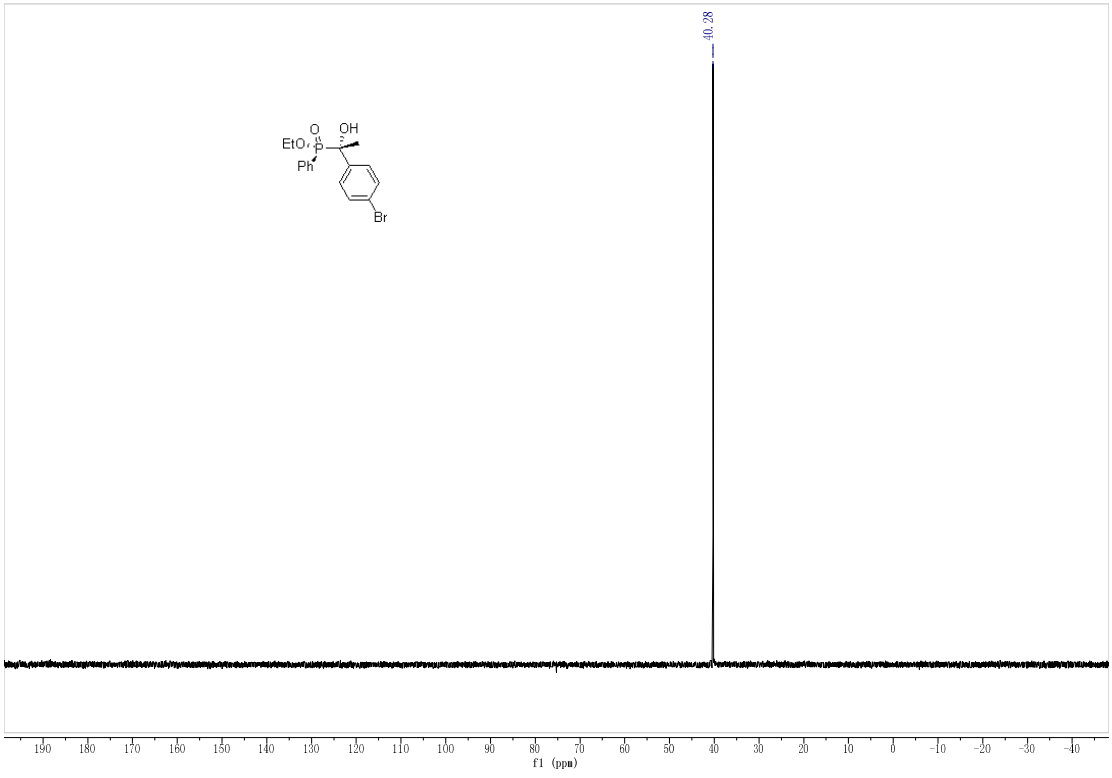
(*S*)-(–)-menthyl [(*R*)-1-(3-nitrophenyl)-1-hydroxyethyl] phenylphosphinate (3g)

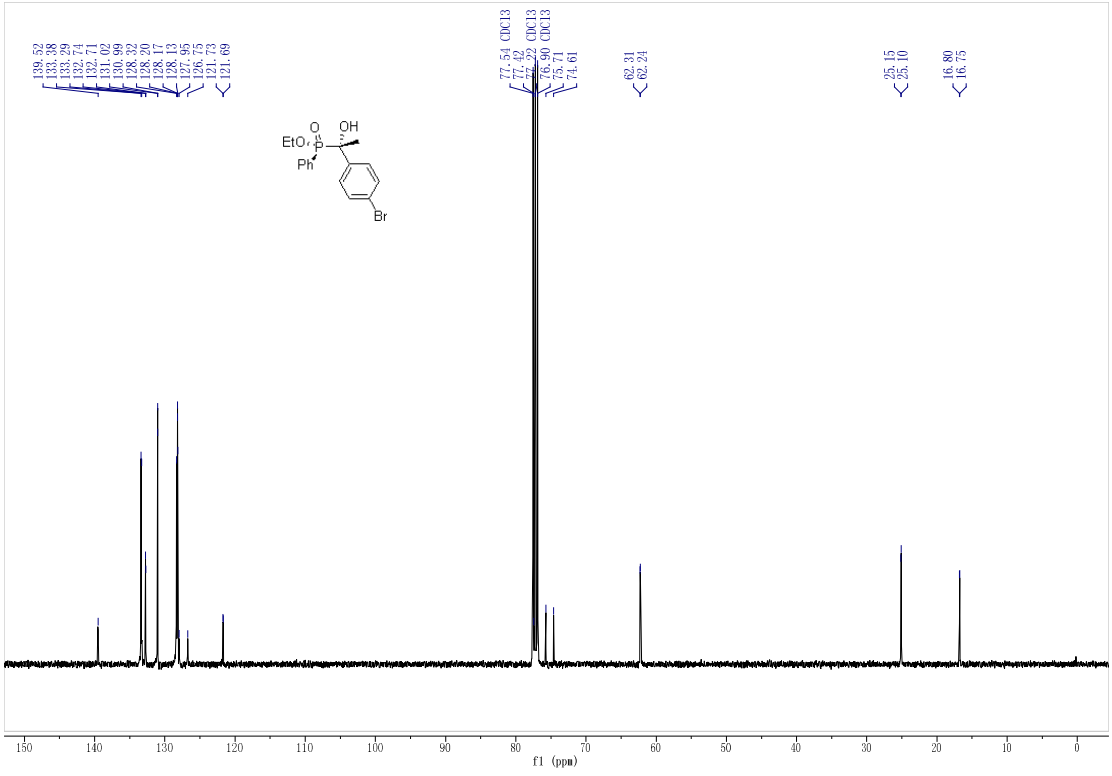


P	-0.78855	-1.096	0.603228	C	-3.85867	-2.94688	-1.44985	C	-1.21417	3.981934	0.226159	C	2.961856	-1.02354	-0.69051
O	-0.69994	-0.88465	2.083783	H	-4.12632	-3.1751	-2.47726	H	-1.40696	4.002445	1.306937	C	2.316927	-1.2683	1.622365
O	-0.73674	0.259175	-0.31076	C	-3.47221	2.92453	-0.2766	H	-0.57476	4.843763	0.010826	C	4.197091	-0.54454	-0.26043
C	-2.31454	-1.98327	0.14969	H	-3.709	2.899384	0.798543	C	1.898373	3.62598	0.039858	H	2.766869	-1.12291	-1.74939
O	0.496947	-1.82632	-1.6251	C	-4.35975	-3.03645	0.91573	H	1.928981	3.677526	-1.05445	H	1.572509	-1.52616	2.366877
H	0.390894	-0.8774	-1.80079	H	-5.01693	-3.33092	1.728561	H	2.914106	3.41547	0.390013	C	3.562956	-0.78692	2.026854
C	0.666036	-1.97383	-0.21426	C	0.926929	2.539037	0.528616	H	1.626741	4.619213	0.413986	N	5.196625	-0.16077	-1.27211
C	-1.40565	1.491345	0.124705	H	1.32773	1.578818	0.184821	C	-4.79101	3.042859	-1.04812	C	4.52217	-0.41702	1.086897
H	-1.58915	1.401972	1.201185	C	-4.70597	-3.32482	-0.40496	H	-5.32792	3.957665	-0.77531	H	3.785156	-0.69736	3.085383
C	0.620519	-3.47944	0.074079	H	-5.63432	-3.8454	-0.62174	H	-5.4511	2.193127	-0.84352	O	6.286716	0.248395	-0.87206
C	-3.16599	-2.37053	1.195095	C	-2.73402	1.619811	-0.62426	H	-4.61152	3.072602	-2.12949	O	4.884594	-0.26899	-2.45793
H	-2.88241	-2.1388	2.216565	H	-3.36669	0.754466	-0.39911	C	0.88993	2.491954	2.065411	H	5.496146	-0.04018	1.371258
C	-2.66752	-2.27566	-1.17856	H	-2.52793	1.591107	-1.70332	H	0.496895	3.421248	2.493014	H	1.450558	-3.96125	-0.45002
H	-2.00348	-1.99795	-1.98905	C	-2.54694	4.126622	-0.52053	H	1.904376	2.360629	2.456607	H	0.722325	-3.67538	1.144145
C	-0.46773	2.680421	-0.14097	H	-2.35533	4.216583	-1.5999	H	0.290906	1.656485	2.439543	H	-0.31636	-3.91374	-0.28083
H	-0.2937	2.697626	-1.22867	H	-3.04878	5.053244	-0.21567	C	2.002662	-1.38772	0.257434				

S5. Selected ^{1}H, ^{31}P and ^{13}C NMR spectroscopy of compounds 3.



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75.71
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OH
EtO
P
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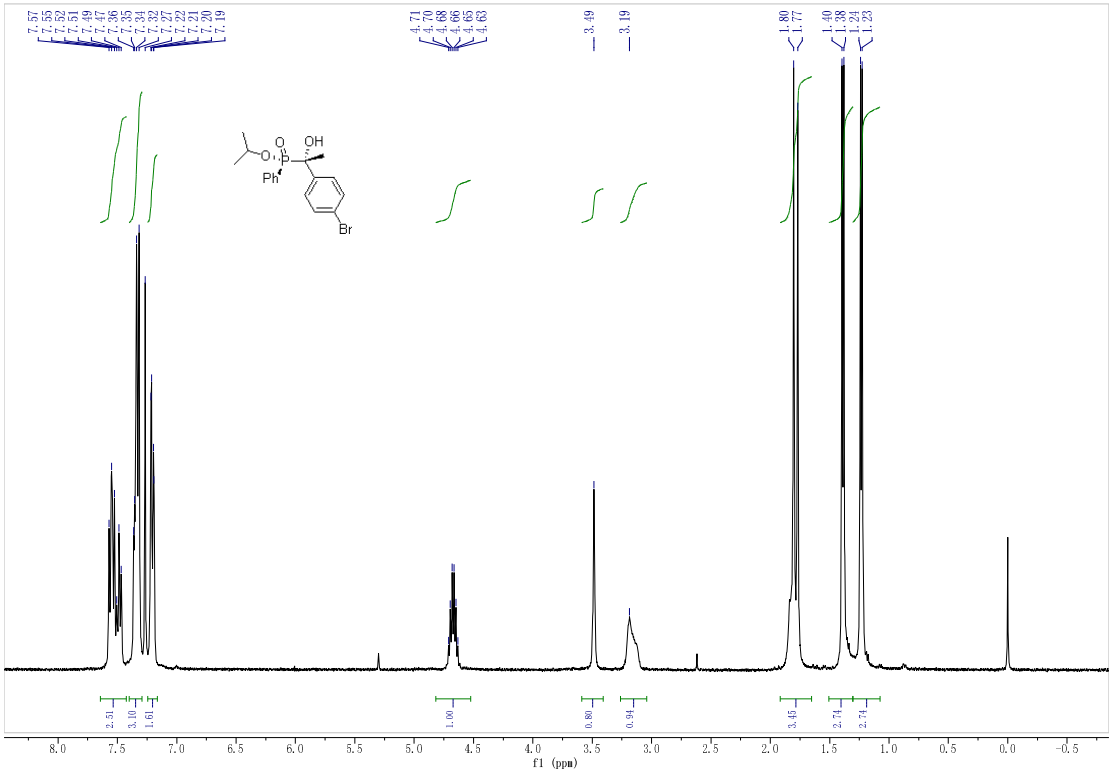
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OH
Ph
Br
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7.0
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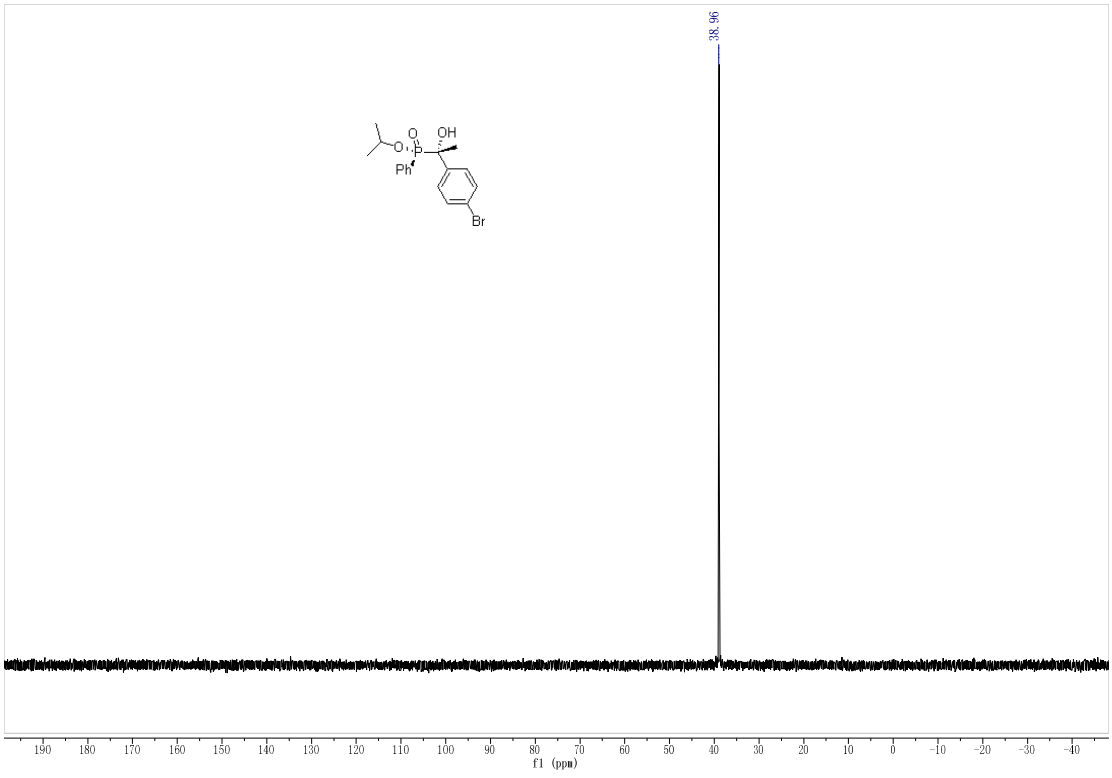
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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OH
O
P
Ph
Br
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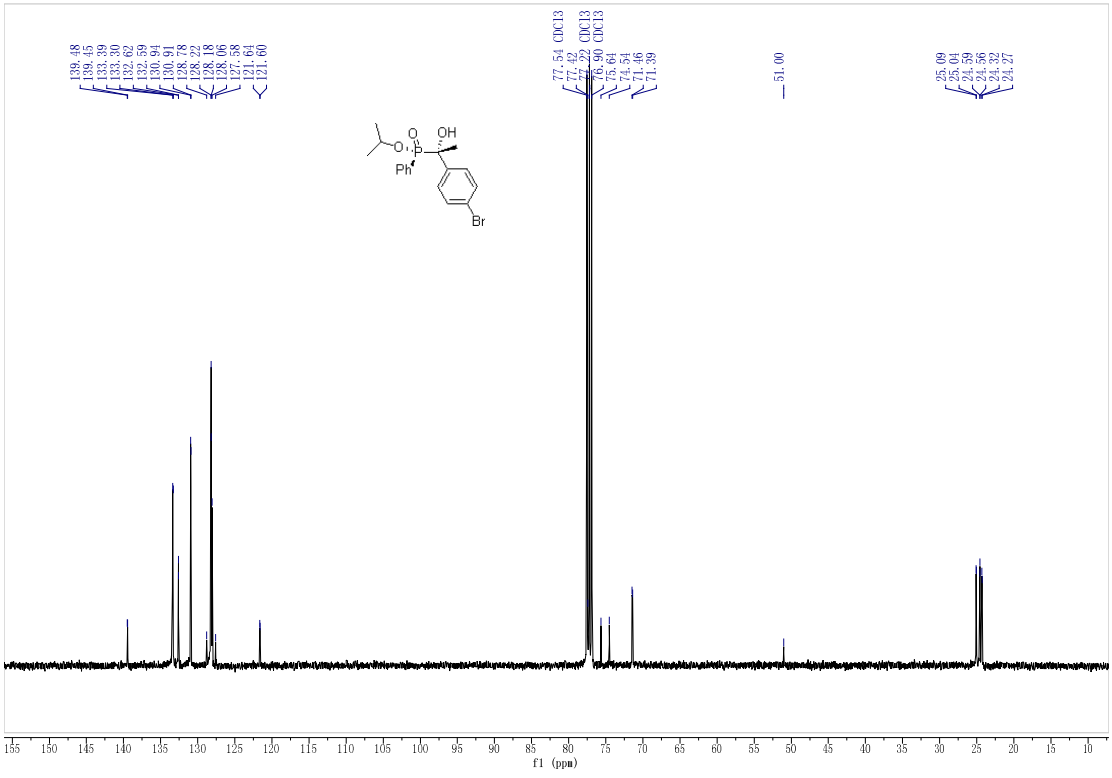
f1 (ppm)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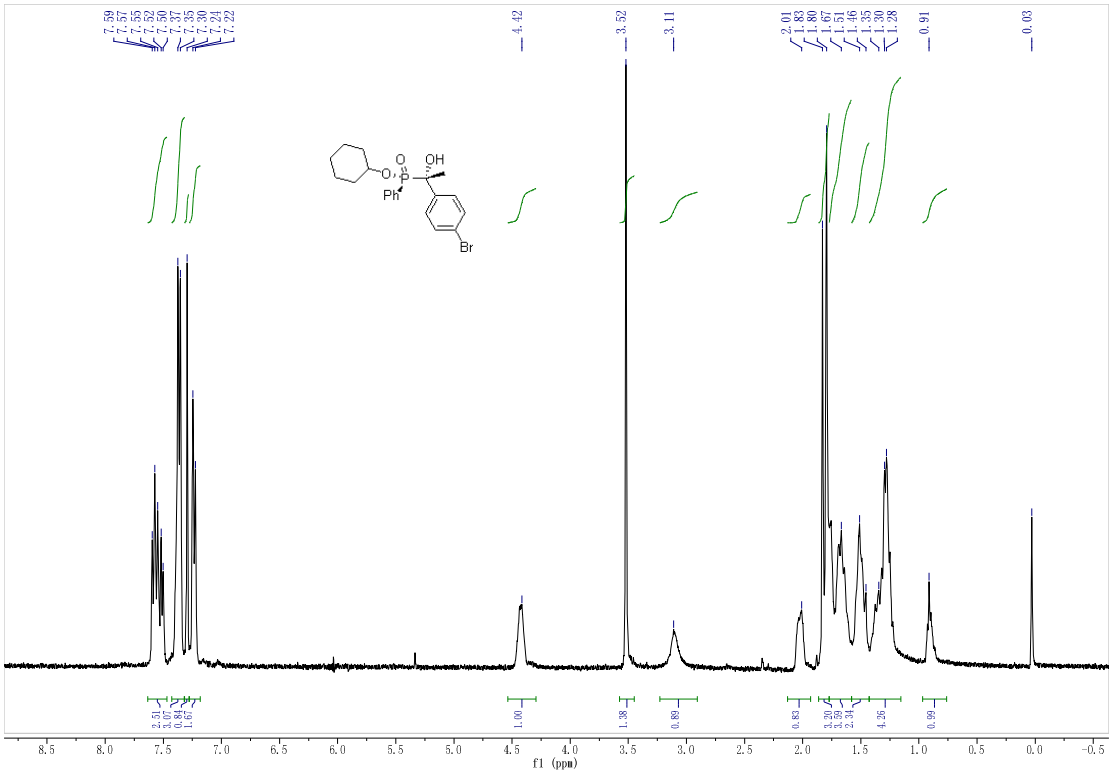
139.45
133.39
133.30
132.62
132.59
130.94
130.91
128.78
128.22
128.18
128.06
127.58
121.64
121.60
77.54 CDCl3
77.42
77.22 CDCl3
76.90 CDCl3
75.64
74.54
71.46
71.39
51.00
25.09
25.04
24.99
24.95
24.32
24.27
O
OH
O
P
Ph
Br
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)


7.59
7.57
7.55
7.52
7.50
7.37
7.35
7.30
7.24
7.22
4.42
3.52
3.11
2.01
1.83
1.80
1.67
1.51
1.46
1.35
1.30
1.28
0.91
0.03
O
P
OH
Ph
Br
3.51
3.07
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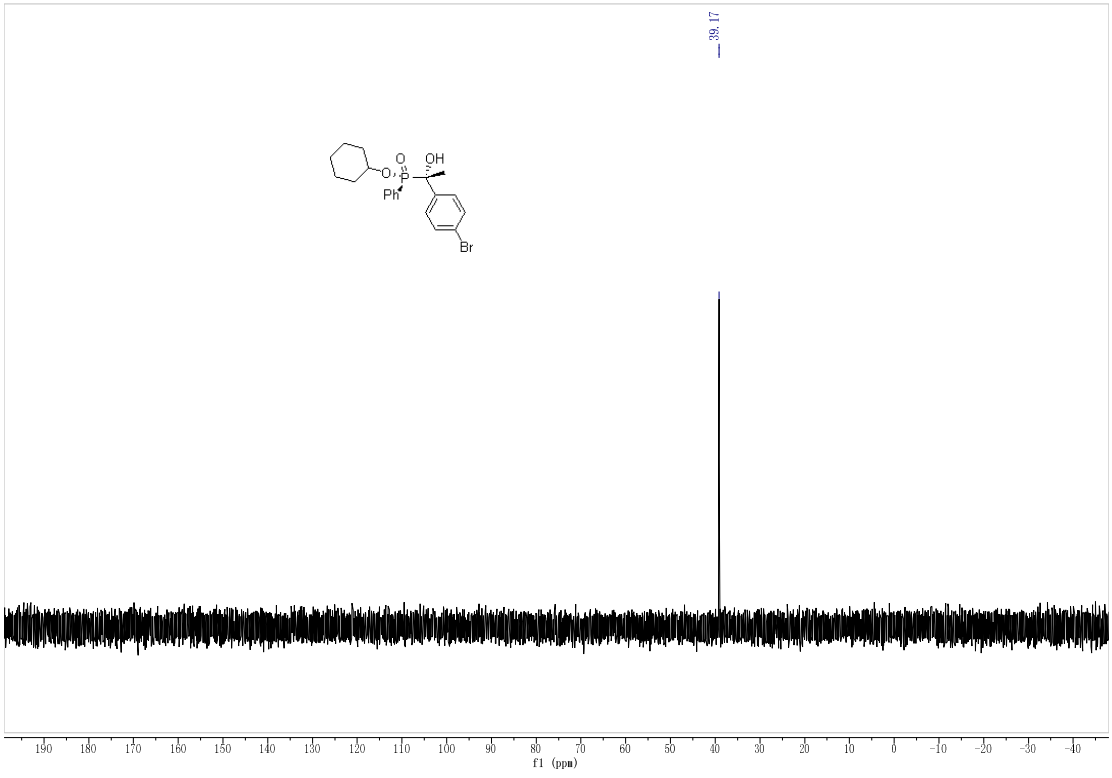
0.89
0.83
3.30
3.09
2.34
4.36
0.99
f1 (ppm)


39.17
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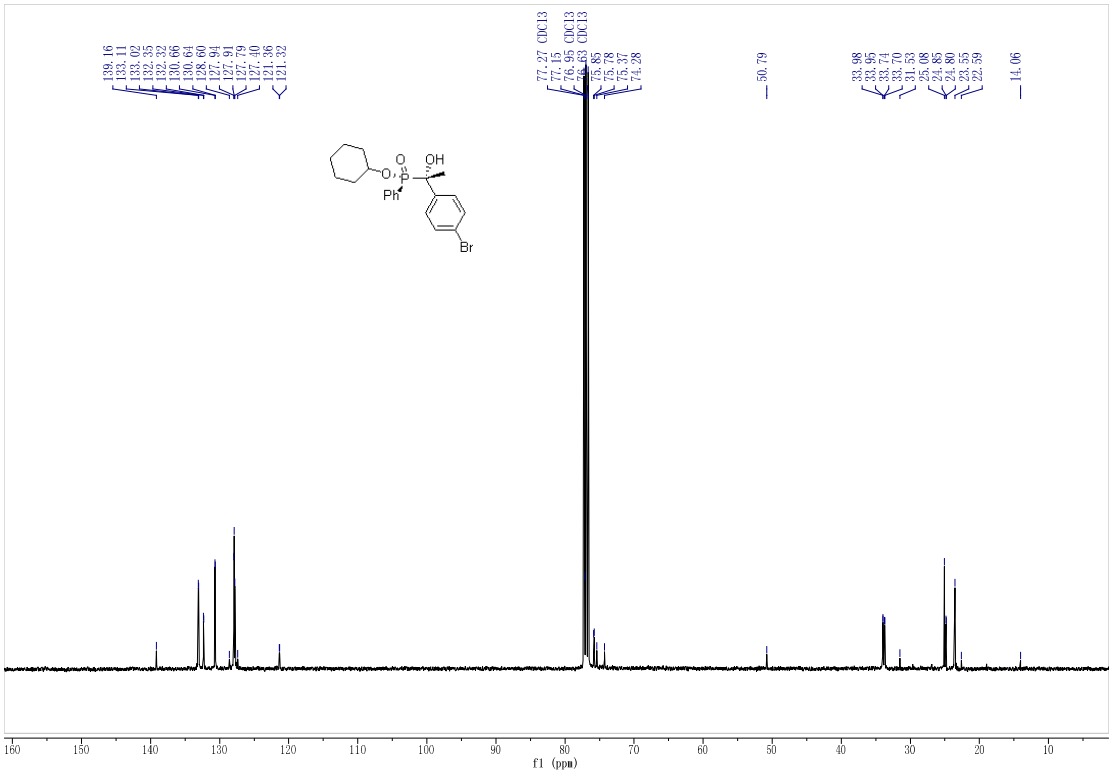
P
OH
Ph
Br
f1 (ppm)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132.32
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128.60
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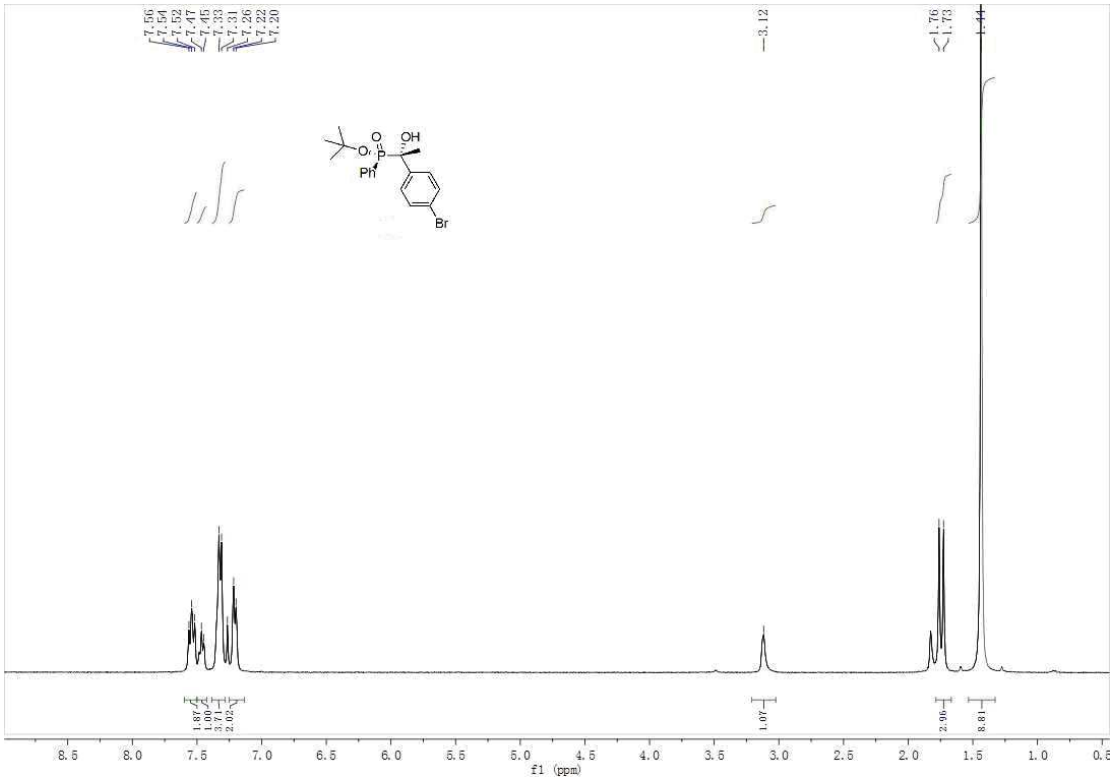
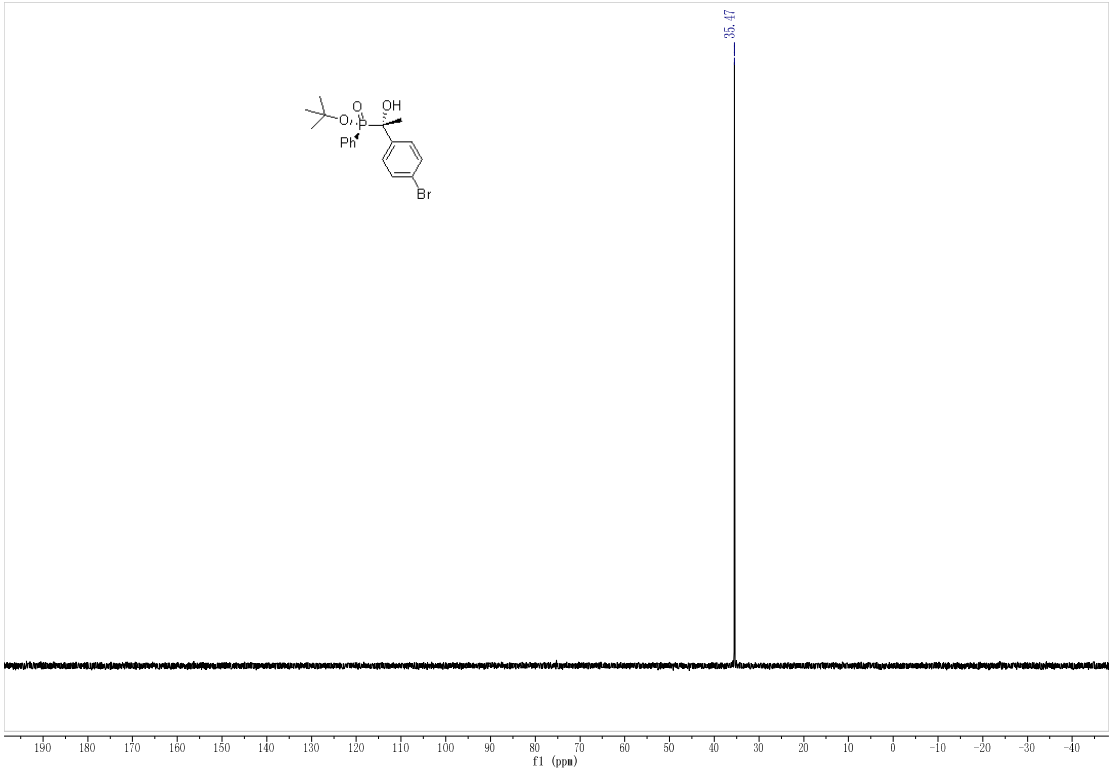
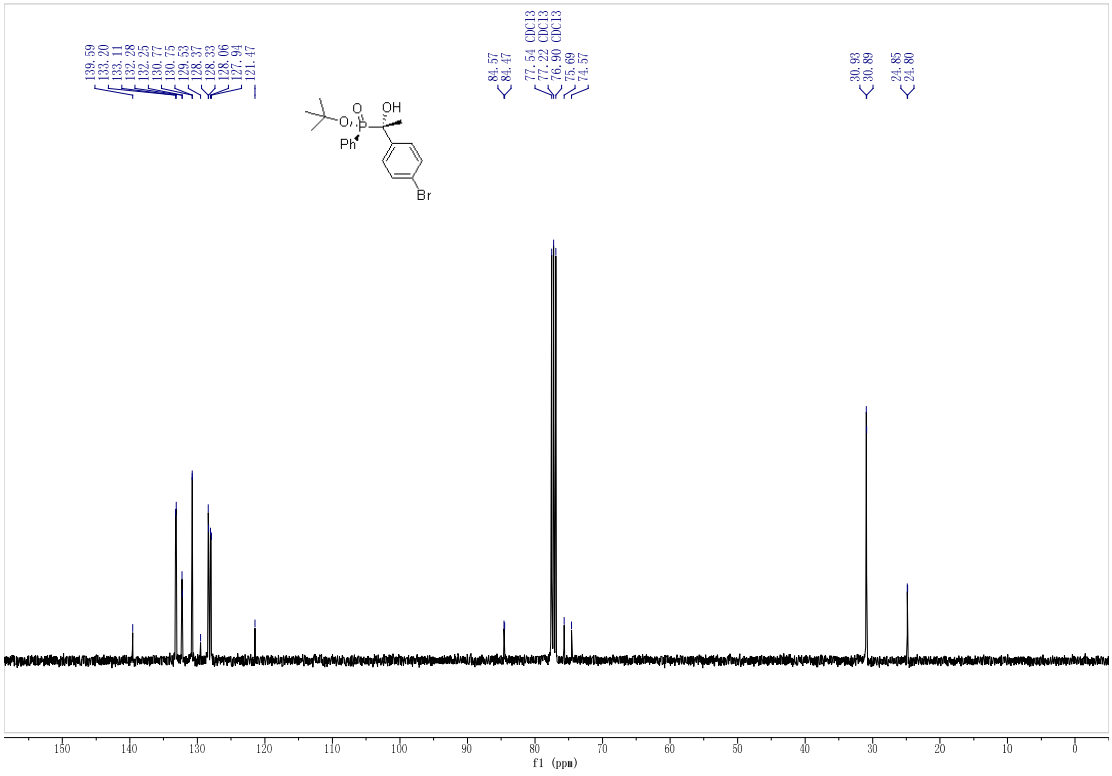
127.91
127.79
127.40
121.36
121.32
77.27 CDCl3
77.15
76.95 CDCl3
76.63 CDCl3
75.85
75.78
75.37
74.28
50.79
33.98
33.95
33.74
33.70
31.53
25.08
24.85
24.80
23.55
22.59
14.06
O
P
OH
Ph
Br
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.56
7.54
7.52
7.47
7.45
7.33
7.31
7.26
7.22
7.20
3.12
1.76
1.73
1.44
O
P
OH
Ph
Br
1.87
1.00
3.71
2.02
1.07
2.96
8.81
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


35.47
OH
O
O
P
Ph
Br
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)


139.59
133.20
133.11
132.28
132.25
130.77
130.75
129.52
128.33
128.06
127.94
121.47
84.57
84.47
77.54 CDCl3
77.22 CDCl3
76.90 CDCl3
75.69
74.57
30.93
30.89
24.85
24.80
OH
O
O
P
Ph
Br
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)