Enantioselective Phosphonation of Isoquinolines via Chiral Phosphoric Acid-Catalyzed Dearomatization

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Supporting Information

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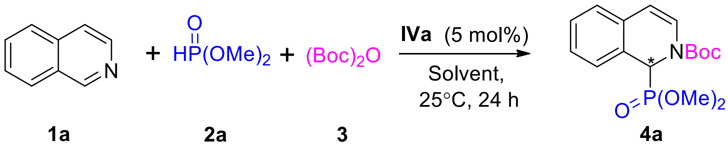
1. Experimental Section and compound characterization

1.1 General information: Reagents and solvents were purchased from common commercial suppliers and were used without further purification. Column chromatography was generally performed on silica gel (200-300 mesh). Melting points were determined with a Büchi B-545 melting-point apparatus. 600MHz ^{1}H NMR and 151MHz ^{13}C NMR spectra were recorded on Varian VMS-600 spectrometers, respectively. The chemical shifts are reported in ppm (δ scale) relative to internal tetramethylsilane, and coupling constants are reported in hertz (Hz). High-resolution mass spectra (HRMS) were obtained on Agilent 6502 Q-TOF HPLC and mass spectrometry.

1.2 Reaction conditions optimization for the enantioselective dearomatization of 1,2-dihydroisoquinoline-1-ylphosphonates 4:

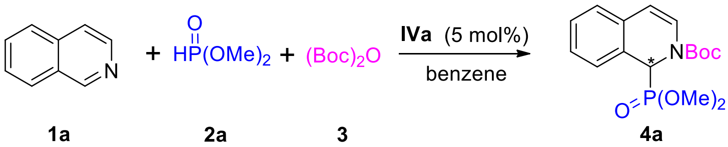
Further screening of aromatic and ether solvents[a]



Entry	Solvent	Conv. (%)[b]	ee (%)[c]
1	toluene	95	75
2	benzene	95	86
3	PhCl	75	70
4	PhOMe	60	69
5	Bn_2O	30	20
6	Et_2O	85	75
7	THF	75	72
8	MTBE	87	80
9	1,4-Dioxane	60	65

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **3** (0.4 mmol) and **IVa** (5 mol%) in solvent (4 mL).[b]Yield was determined by HPLC analysis. [c]Determined by HPLC (Chiralcel OD-RH).

Additional efforts at reaction optimization (temperature, additive, catalyst loading and concentration)[a]

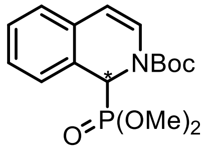


Entry	Temp. (°C)	additive	T (h)	Conv. (%)[b]	ee (%)[c]
1	0	-	24	85(92)[d]	84
2	25	-	24	>95	86
3	50	-	6	90	82
4	25	3Å MS	24	>95	86
5	25	4Å MS	24	>95	85
6	25	5Å MS	24	>95	85
7[e]	25	-	24	>95	78
8[f]	25	-	24	>95	79

9[g]	25	-	24	>95	87

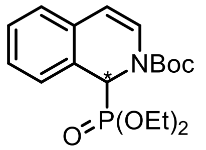
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **3** (0.4 mmol) and **IVa** (5 mol%) in benzene (4 mL).[b]Yield was determined by HPLC analysis. [c]Determined by HPLC (Chiralcel OD-RH). [d]48 h. [e] benzene (2 mL) was used. [f]**IVa** (2.5 mol%) was used. [g]**IVa** (10 mol%) was used.

1.3 Procedure for the preparation of 1,2-dihydroisoquinoline-1-ylphosphonates 4. A mixture of isoquinoline **1** (0.2 mmol), catalyst BINOL-CPAs **IVa** (5 mol%), $(Boc)_2O$ **3** (0.4mmol) and benzene (4 mL) was stirred at room temperature for 3~5 h. Then dimethyl phosphonate **2** (0.4mmol) was added and the reaction was stirred at room temperature for 20 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography with PE/EA (2/1) to obtain 1,2-dihydroisoquinoline-1-ylphosphonates **4** as a light yellow oil.



4aa

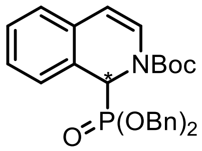
Tert-butyl 1-(dimethoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate (4aa). Light yellow oil 64 mg, yield 95%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.26-7.22 (m, 2H), 7.20 (d, J = 7.1 Hz, 1H), 7.04 (d, J = 6.9 Hz, 1H), 6.83 (d, J = 7.7 Hz, 1H), 5.90 (d, J = 8.1 Hz, 1H), 5.81 (d, J = 7.8 Hz, 1H), 3.68 (d, J = 10.6 Hz, 3H), 3.55 (d, J = 10.5 Hz, 3H), 1.53 (s, 9H); Signals corresponding to the minor rotamer: δ 7.24-7.20 (m, 2H), 7.19 (d, J = 7.4 Hz, 1H), 7.06 (d, J = 7.1 Hz, 1H), 7.01 (d, J = 7.9 Hz, 1H), 5.91 (d, J = 7.8 Hz, 1H), 5.72 (d, J = 15.6 Hz, 1H), 3.67 (d, J = 10.6 Hz, 3H), 3.46 (d, J = 10.4 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.35, 131.34 (d, J = 3.8 Hz), 128.59 (d, J = 3.4 Hz), 127.61 (d, J = 5.5 Hz), 127.25 (d, J = 2.8 Hz), 125.65, 125.35, 124.74(d, J = 3.2 Hz), 108.58, 82.23, 53.46 (d, J = 6.0 Hz), 53.34 (d, J = 7.1 Hz), 52.65 (d, J = 151.4 Hz), 28.15; Signals corresponding to the minor rotamer: δ 151.56, 131.71 (d, J = 3.6 Hz), 128.81 (d, J = 3.3 Hz), 127.45 (d, J = 5.5 Hz), 127.04 (d, J = 2.8 Hz), 125.79, 125.15, 124.87 (d, J = 2.9 Hz), 108.58, 82.36, 54.55 (d, J = 150.2 Hz), 53.65 (d, J = 7.2 Hz), 52.97 (d, J = 7.3 Hz), 28.11; ^{31}P NMR (243 MHz, $CDCl_3$): δ 22.32 (for major rotamer), 21.65 (for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{22}NO_5PNa$ $[M+Na]^+$ 362.1128, found 362.1127; $[\alpha]_D^{25}$ = +292.8 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 40/60, v/v, 1.0 mL/min, 305 nm, t_R (major) = 6.3 min, t_R (minor) = 7.1 min), 86% *ee*.



4ab

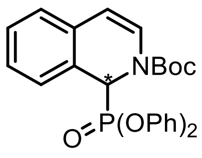
Tert-butyl 1-(diethoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate (4ab). Light yellow oil 66 mg, yield 90%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.8:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.25-7.20 (m, 2H), 7.18 (d, J = 7.3 Hz, 1H), 7.03 (d, J = 7.1 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 5.87 (d, J = 16.2 Hz, 1H), 5.79 (d, J = 7.8 Hz, 1H), 4.10-3.98 (m, 2H), 3.97-3.75 (m, 2H), 1.52 (s, 9H), 1.29-1.19 (m, 6H); Signals corresponding to the minor rotamer: δ

7.26-7.20 (m, 2H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 6.8 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 5.87 (d, *J* = 7.9 Hz, 1H), 5.68 (d, *J* = 15.7 Hz, 1H), 4.11-3.98 (m, 2H), 3.89-3.65 (m, 2H), 1.55 (s, 9H), 1.18-1.07 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) <u>Signals corresponding to the major rotamer</u>: δ 151.32 , 131.46 (d, *J* = 3.8 Hz), 128.45 (d, *J* = 3.4 Hz), 127.67 (d, *J* = 5.4 Hz), 127.12 (d, *J* = 2.8 Hz), 125.75 , 125.66 , 124.63 (d, *J* = 3.0 Hz), 108.78 , 82.00 , 62.84 (dd, *J* = 26.3, 6.8 Hz), 52.92 (d, *J* = 151.6 Hz), 28.18 , 16.35 (t, *J* = 5.5 Hz); <u>Signals corresponding to the minor rotamer</u>: δ 151.67, 131.79 (d, *J* = 3.9 Hz), 128.64 (d, *J* = 3.3 Hz), 127.44 (d, *J* = 5.4 Hz), 126.91 (d, *J* = 2.7 Hz), 125.88, 125.53, 124.77 (d, *J* = 2.9 Hz), 108.91, 82.25, 62.80 (dd, *J* = 87.9, 7.3 Hz), 54.84 (d, *J* = 150.4 Hz), 28.14, 16.46 (dd, *J* = 10.0, 5.4 Hz); ^{31}P NMR (243 MHz, $CDCl_3$): δ 19.60 (for major rotamer), 19.63 (for minor rotamer); HRMS (m/z) calcd for $C_{18}H_{26}NO_5PNa$ $[M+Na]^+$ 390.1441, found 390.1445; $[\alpha]_D^{25}$ = +228.4 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 40/60, v/v, 1.0 mL/min, 305 nm, t_R (major) = 9.6 min, t_R (minor) = 11.3 min), 79% *ee*.



4ac

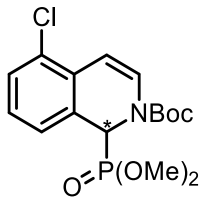
Tert-butyl 1-(bis(benzyloxy)phosphoryl)isoquinoline-2(1*H*)-carboxylate 4ac. Light yellow oil 86 mg, yield 88%; ^{1}H-NMR (600 MHz, $CDCl_3$):The compound exists as a 1.8:1 mixture of carbamate rotamers. <u>Signals corresponding to the major rotamer</u>: δ 7.31-7.14 (m, 13H), 7.04-6.99 (m, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.02 (d, *J* = 16.1 Hz, 1H), 5.76 (d, *J* = 7.8 Hz, 1H), 4.99 (dd, *J* = 11.8, 6.8 Hz, 1H), 4.94-4.85 (m, 2H), 4.72 (dd, *J* = 11.9, 8.3 Hz, 1H), 1.45 (s, 9H); <u>Signals corresponding to the minor rotamer</u>: δ 7.31-7.14 (m, 13H), 7.04-6.99 (m, 2H), 5.85 (d, *J* = 7.8 Hz, 1H), 5.79 (d, *J* = 15.5 Hz, 1H), 4.94-4.85 (m, 2H), 4.79 (dd, *J* = 11.7, 7.2 Hz, 1H), 4.54 (dd, *J* = 11.7, 8.3 Hz, 1H), 1.42 (s, 9H); ^{13}C-NMR (151 MHz, $CDCl_3$): <u>Signals corresponding to both rotamers</u>: δ 151.53, 151.35, 136.39-136.26 (m), 136.13 (d, *J* = 5.9 Hz), 136.04 (d, *J* = 6.0 Hz), 131.86 (d, *J* = 3.7 Hz), 131.51 (d, *J* = 3.8 Hz), 128.78 (d, *J* = 3.4 Hz), 128.58 (d, *J* = 3.4 Hz), 128.41 (d, *J* = 2.7 Hz), 128.31 (d, *J* = 2.9 Hz), 128.12-128.01 (m), 127.93, 127.71 (d, *J* = 10.3 Hz), 127.54 (d, *J* = 5.5 Hz), 127.20 (d, *J* = 2.7 Hz), 126.98 (d, *J* = 2.6 Hz), 125.91, 125.77, 125.32 (d, *J* = 1.2 Hz), 125.20 (d, *J* = 1.4 Hz), 124.92 (d, *J* = 2.8 Hz), 124.79 (d, *J* = 3.0 Hz), 109.00, 108.82, 82.39, 82.15, 68.30 (d, *J* = 7.4 Hz), 67.92 (d, *J* = 7.7 Hz), 67.85, 67.78 (d, *J* = 7.4 Hz), 55.01 (d, *J* = 149.6 Hz), 53.19 (d, *J* = 151.1 Hz), 28.12, 27.97;^{31}P NMR (243 MHz, $CDCl_3$): δ 20.53 (for major rotamer), 20.39 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{26}NO_5PNa$ $[M+Na]^+$ 486.1441, found 486.1444; $[\alpha]_D^{25}$ = +206.8 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 60/40, v/v, 1.0 mL/min, 305 nm, t_R (major) = 8.7 min, t_R (minor) = 12.1 min), 80% *ee*.



4ad

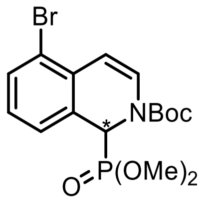
Tert-butyl 1-(diphenoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate (4ad). Light yellow oil 83 mg, yield 90%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.3:1 mixture of carbamate rotamers.

Signals corresponding to the major rotamer: δ 7.33 (d, J = 7.5 Hz, 1H), 7.27-7.18 (m, 4H), 7.16-7.08 (m, 3H), 7.07-6.99 (m, 4H), 6.93 (d, J = 8.5 Hz, 1H), 6.88 (d, J = 7.8 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 6.33 (d, J = 16.0 Hz, 1H), 5.84 (d, J = 7.8 Hz, 1H), 1.50 (s, 9H); Signals corresponding to the minor rotamer: δ 7.34 (d, J = 7.6 Hz, 1H), 7.28-7.18 (m, 4H), 7.16-7.08 (m, 3H), 7.08-6.99 (m, 5H), 6.93 (d, J = 8.5 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 6.11 (d, J = 14.2 Hz, 1H), 5.89 (d, J = 7.9 Hz, 1H), 1.51 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.47 (d, J = 29.7 Hz), 150.37 (d, J = 10.5 Hz), 131.73 (d, J = 4.0 Hz), 129.61, 129.44, 128.94 (d, J = 3.7 Hz), 127.88 (d, J = 5.7 Hz), 127.35 (d, J = 2.8 Hz), 125.70 (d, J = 3.3 Hz), 125.01 (d, J = 3.2 Hz), 124.88, 124.53, 120.45 (d, J = 4.4 Hz), 120.09 (d, J = 4.5 Hz), 109.28, 82.49, 53.87 (d, J = 154.5 Hz), 28.16; Signals corresponding to the minor rotamer: δ 150.60 (d, J = 10.5 Hz), 150.10 (d, J = 11.3 Hz), 132.09 (d, J = 4.1 Hz), 129.47, 129.12 (d, J = 3.7 Hz), 127.77 (d, J = 5.6 Hz), 127.13 (d, J = 2.9 Hz), 125.16 (d, J = 3.3 Hz), 125.11, 124.76, 124.30, 120.54 (d, J = 4.3 Hz), 120.06 (d, J = 4.4 Hz), 109.21, 82.81, 55.35 (d, J = 151.4 Hz), 28.09; ^{31}P NMR (243 MHz, $CDCl_3$): δ 11.62 (for major rotamer), 11.50 (for minor rotamer); HRMS (m/z) calcd for $C_{28}H_{30}NO_5PNa$ $[M+Na]^+$ 514.1754, found 514.1751; $[\alpha]_D^{25}$ = +233.5 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 60/40, v/v, 1.0 mL/min, 305 nm, t_R (major) = 7.4 min, t_R (minor) = 8.8 min), 72% *ee*.



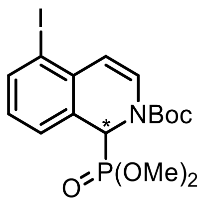
4ba

Tert-butyl 5-chloro-1-(dimethoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate (4ba). Light yellow oil 62 mg, yield 84%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.32-7.27 (m, 1H), 7.17-7.07 (m, 2H), 6.92 (d, J = 8.0 Hz, 1H), 6.19 (d, J = 8.0 Hz, 1H), 5.88 (d, J = 16.3 Hz, 1H), 3.70 (d, J = 10.6 Hz, 3H), 3.57 (d, J = 10.7 Hz, 3H), 1.53 (s, 9H); Signals corresponding to the minor rotamer: δ 7.27-7.25 (m, 1H), 7.17-7.06 (m, 3H), 6.26 (d, J = 8.1 Hz, 1H), 5.68 (d, J = 15.7 Hz, 1H), 3.68 (d, J = 10.6 Hz, 3H), 3.50 (d, J = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.13, 129.96 (d, J = 3.6 Hz), 129.57 (d, J = 3.3 Hz), 129.37 (d, J = 3.3 Hz), 127.74 (d, J = 2.9 Hz), 127.37, 127.15, 126.15 (d, J = 5.5 Hz), 104.74, 82.65, 53.54 (d, J = 6.1 Hz), 53.34 (d, J = 7.1 Hz), 52.66 (d, J = 151.5 Hz), 28.12; Signals corresponding to the minor rotamer: δ 151.28, 130.07 (d, J = 3.6 Hz), 129.72 (d, J = 3.5 Hz), 129.34 (d, J = 3.0 Hz), 127.51 (d, J = 3.0 Hz), 127.37, 127.15, 125.97 (d, J = 5.6 Hz), 104.75, 82.76, 54.58 (d, J = 150.6 Hz), 53.68 (d, J = 7.3 Hz), 53.08 (d, J = 7.3 Hz), 28.07; ^{31}P NMR (243 MHz, $CDCl_3$): δ 21.75 (for major rotamer), 21.15 (for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}ClNO_5PNa$ $[M+Na]^+$ 396.0738, found 396.0737; $[\alpha]_D^{25}$ = +275.4 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 11.6 min, t_R (minor) = 13.4 min), 81% *ee*.



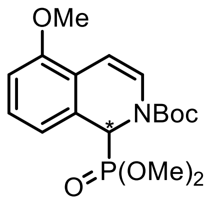
4ca

Tert-butyl 5-bromo-1-(dimethoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate (4ba). Light yellow oil 75 mg, yield 90%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.45 (d, J = 9.0 Hz, 1H), 7.18 (d, J = 9.1 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.16 (d, J = 8.0 Hz, 1H), 5.86 (d, J = 16.4 Hz, 1H), 3.70 (d, J = 10.6 Hz, 3H), 3.57 (d, J = 10.6 Hz, 3H), 1.53 (s, 9H); Signals corresponding to the minor rotamer: δ 7.46 (d, J = 8.0 Hz, 1H), 7.16 (d, J = 4.9 Hz, 1H), 7.10 (d, J = 8.1 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 6.24 (d, J = 8.1 Hz, 1H), 5.67 (d, J = 15.8 Hz, 1H), 3.68 (d, J = 10.5 Hz, 3H), 3.50 (d, J = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.08, 132.66 (d, J = 3.6 Hz), 130.98 (d, J = 3.7 Hz), 128.04 (d, J = 2.7 Hz), 127.44, 127.40, 126.86 (d, J = 5.5 Hz), 120.31 (d, J = 3.4 Hz), 107.27, 82.67, 53.54 (d, J = 6.1 Hz), 53.35 (d, J = 7.1 Hz), 52.79 (d, J = 151.4 Hz), 28.11; Signals corresponding to the minor rotamer: δ 151.24, 132.87 (d, J = 3.5 Hz), 131.36 (d, J = 3.5 Hz), 127.81 (d, J = 2.8 Hz), 127.63, 127.18, 126.67 (d, J = 5.7 Hz), 120.41 (d, J = 3.5 Hz), 107.27, 82.78, 54.71 (d, J = 150.5 Hz), 53.69 (d, J = 7.1 Hz), 53.08 (d, J = 7.2 Hz), 28.07; ^{31}P NMR (243 MHz, $CDCl_3$): δ 21.77 (for major rotamer), 21.17 (for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}BrNO_5PNa$ $[M+Na]^+$ 440.0233, found 440.0232; $[\alpha]_D^{25}$ = +248.2 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 13.6 min, t_R (minor) = 15.8 min), 82% *ee*.



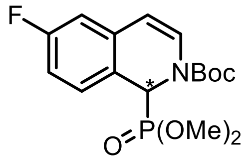
4da

Tert-butyl 1-(dimethoxyphosphoryl)-5-iodoisoquinoline-2(1*H*)-carboxylate (4da). Light yellow oil 88 mg, yield 95%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.72 (d, J = 9.0 Hz, 1H), 7.20 (d, J = 7.4 Hz, 1H), 6.91-6.84 (m, 2H), 6.04 (d, J = 8.0 Hz, 1H), 5.82 (d, J = 16.3 Hz, 1H), 3.69 (d, J = 10.5 Hz, 3H), 3.56 (d, J = 10.6 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 7.74 (d, J = 8.1 Hz, 1H), 7.19 (d, J = 6.1 Hz, 1H), 7.06 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 7.6 Hz, 1H), 6.11 (d, J = 8.1 Hz, 1H), 5.62 (d, J = 15.7 Hz, 1H), 3.67 (d, J = 10.2 Hz, 3H), 3.49 (d, J = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.02, 139.32 (d, J = 3.5 Hz), 134.07 (d, J = 3.7 Hz), 128.38 (d, J = 2.8 Hz), 127.85 (d, J = 5.5 Hz), 127.72, 126.74, 112.14, 95.99 (d, J = 3.8 Hz), 82.67, 53.53 (d, J = 6.1 Hz), 53.37 (d, J = 7.0 Hz), 53.01 (d, J = 151.1 Hz), 28.11; Signals corresponding to the minor rotamer: δ 151.20, 139.53 (d, J = 3.5 Hz), 134.46 (d, J = 3.8 Hz), 128.14 (d, J = 3.0 Hz), 127.97, 127.67 (d, J = 5.7 Hz), 126.48 , 112.17, 96.07 (d, J = 3.8 Hz), 82.78, 54.93 (d, J = 150.4 Hz), 53.71 (d, J = 7.1 Hz), 53.06 (d, J = 7.2 Hz), 28.07; ^{31}P NMR (243 MHz, $CDCl_3$): δ 21.79 (for major rotamer), 21.18 (for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}INO_5PNa$ $[M+Na]^+$ 488.0094, found 488.0090; $[\alpha]_D^{25}$ = +235.1 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 17.2 min, t_R (minor) = 20.1 min), 78% *ee*.



4ea

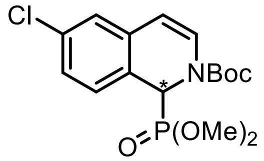
Tert-butyl 1-(dimethoxyphosphoryl)-5-methoxyisoquinoline-2(1*H*)-carboxylate (4ea). Light yellow oil 72 mg, yield 98%;^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.7:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: *δ*7.15 (d, *J* = 7.9 Hz, 1H), 6.88-6.84 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 7.9 Hz, 1H), 6.19 (d, *J* = 7.9 Hz, 1H), 5.88 (d, *J* = 16.2 Hz, 1H), 3.83 (s, 3H), 3.68 (d, *J* = 10.5 Hz, 3H), 3.56 (d, *J* = 10.6 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: *δ*7.16 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.90-6.83 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.26 (d, *J* = 8.0 Hz, 1H), 5.69 (d, *J* = 15.6 Hz, 1H), 3.83 (s, 3H), 3.67 (d, *J* = 10.2 Hz, 3H), 3.49 (d, *J* = 10.4 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: *δ*153.87 (d, *J* = 3.1 Hz), 151.46, 127.96 (d, *J* = 2.6 Hz), 126.73, 124.76, 120.53 (d, *J* = 4.1 Hz), 119.95 (d, *J* = 5.1 Hz), 110.38 (d, *J* = 3.0 Hz), 103.29, 82.07, 55.52, 53.43 (d, *J* = 6.1 Hz), 53.29 (d, *J* = 7.1 Hz), 52.53 (d, *J* = 150.5 Hz), 28.15; Signals corresponding to the minor rotamer: *δ*153.94 (d, *J* = 3.3 Hz), 151.61, 127.75 (d, *J* = 2.7 Hz), 126.47, 124.88, 120.91 (d, *J* = 4.1 Hz), 119.74 (d, *J* = 5.1 Hz), 110.58 (d, *J* = 3.2 Hz), 103.33, 82.21, 55.56, 54.46 (d, *J* = 149.5 Hz), 53.58 (d, *J* = 7.2 Hz), 52.97 (d, *J* = 7.2 Hz), 28.11; ^{31}P NMR (243 MHz, $CDCl_3$): *δ*22.43 (for major rotamer), 21.82 (for minor rotamer);HRMS (m/z) calcd for $C_{17}H_{24}NO_6PNa$ $[M+Na]^+$392.1233, found 392.1233; $[\alpha]_D^{25}$ = +296.8 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 40/60, v/v, 1.0mL/min, 305 nm, t_R (major) =7.4 min, t_R (minor) = 8.4 min), 74% *ee*.



4fa

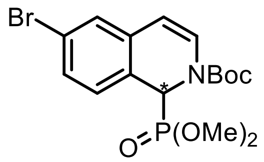
Tert-butyl 1-(dimethoxyphosphoryl)-6-fluoroisoquinoline-2(1*H*)-carboxylate (4fa). Light yellow oil 70 mg, yield 98%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.7:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: *δ* 7.24-7.16 (m, 1H), 6.91-6.83 (m, 2H), 6.75 (dd, *J* = 9.2, 2.6 Hz, 1H), 5.88 (d, *J* = 15.5 Hz, 1H), 5.75 (d, *J* = 7.9 Hz, 1H), 3.69 (d, *J* = 10.5 Hz, 3H), 3.57 (d, *J* = 10.6 Hz, 3H), 1.53 (s, 9H); Signals corresponding to the minor rotamer: *δ* 7.22-7.17 (m, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.92-6.88 (m, 1H), 6.79-6.76 (m, 1H), 5.84 (d, *J* = 7.9 Hz, 1H), 5.69 (d, *J* = 15.0 Hz, 1H), 3.68 (d, *J* = 10.4 Hz, 3H), 3.50 (d, *J* = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: *δ* 162.89 (dd, *J* = 246.6, 3.5 Hz), 151.21, 133.46 (dd, *J* = 8.7, 3.4 Hz), 129.13 (dd, *J* = 8.7, 5.4 Hz), 126.77, 120.97 (d, *J* = 2.1 Hz), 113.79 (dd, *J* = 22.1, 2.6 Hz), 111.46 (dd, *J* = 22.7, 3.1 Hz), 107.68 (d, *J* = 2.3 Hz), 82.57, 53.51 (d, *J* = 6.1 Hz), 53.35 (d, *J* = 7.1 Hz), 52.14 (d, *J* = 152.6 Hz), 28.15; Signals corresponding to the minor rotamer: *δ* 163.00 (dd, *J* = 246.9, 3.7

Hz), 151.42, 133.90 (dd, J = 8.9, 3.2 Hz), 128.97 (dd, J = 8.7, 5.4 Hz), 126.98, 120.77 , 113.57 (dd, J = 22.1, 2.4 Hz), 111.57 (dd, J = 22.6, 2.9 Hz), 107.79 (d, J = 2.0 Hz), 82.68, 54.05 (d, J = 151.7 Hz), 53.69 (d, J = 7.2 Hz), 53.02 (d, J = 7.3 Hz), 28.10; ^{31}P NMR (243 MHz, $CDCl_3$): δ 22.01(d, J = 5.9 Hz) (for major rotamer), 21.39 (d, J = 6.3 Hz)(for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}FNO_5PNa$ $[M+Na]^+$ 380.1034, found 380.1038; $[\alpha]_D^{25}$ = +275.4 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 40/60, v/v, 1.0 mL/min, 305 nm, t_R (major) = 7.3 min, t_R (minor) = 8.0 min), 83% *ee*.



4ga

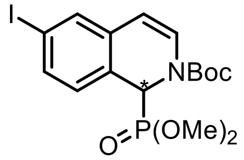
Tert-butyl 6-chloro-1-(dimethoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate (4ga). Light yellow oil 72 mg, yield 96%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.7:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.19-7.13 (m, 2H), 7.03 (d, J = 6.0 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 5.86 (d, J = 16.1 Hz, 1H), 5.73 (d, J = 7.8 Hz, 1H), 3.69 (d, J = 10.7 Hz, 3H), 3.57 (d, J = 10.6 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 7.19-7.13 (m, 2H), 7.06 (d, J = 7.8 Hz, 1H), 7.03 (d, J = 6.0 Hz, 1H), 5.82 (d, J = 7.9 Hz, 1H), 5.67 (d, J = 15.6 Hz, 1H), 3.67 (d, J = 11.6 Hz, 3H), 3.51 (d, J = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.18, 134.38 (d, J = 4.2 Hz), 133.05 (d, J = 3.5 Hz), 128.78 (d, J = 5.4 Hz), 126.98 (d, J = 2.7 Hz), 126.84, 124.53 (d, J = 2.9 Hz), 123.69, 107.36, 82.61, 53.44 (dd, J = 25.6, 6.6 Hz), 52.21 (d, J = 152.0 Hz), 28.12; Signals corresponding to the minor rotamer: δ 151.35, 134.60 (d, J = 4.3 Hz), 133.44 (d, J = 3.4 Hz), 128.60 (d, J = 5.5 Hz), 127.07, 126.77 (d, J = 2.7 Hz), 124.62 (d, J = 2.9 Hz), 123.51, 107.48, 82.72, 54.12 (d, J = 151.2 Hz), 53.37 (dd, J = 94.3, 7.3 Hz), 28.07; ^{31}P NMR (243 MHz, $CDCl_3$): δ 21.78 (for major rotamer), 21.20(for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}ClNO_5PNa$ $[M+Na]^+$ 396.0738, found 396.0737; $[\alpha]_D^{25}$ = +241.1 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 11.3 min, t_R (minor) = 13.0 min), 82% *ee*.



4ha

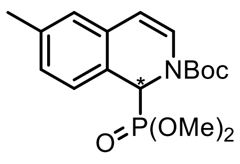
Tert-butyl 6-bromo-1-(dimethoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate (4ha). Light yellow oil 79 mg, yield 95%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.8:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.30 (dd, J = 8.1, 2.0 Hz, 1H), 7.18 (dd, J = 6.4, 1.9 Hz, 1H), 7.10 (dd, J = 8.0, 2.6 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 5.84 (d, J = 16.2 Hz, 1H), 5.72 (d, J = 7.8 Hz, 1H), 3.69 (d, J = 10.9 Hz, 3H), 3.58 (d, J = 10.6 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 7.30 (dd, J = 8.1, 2.0 Hz, 1H), 7.18 (dd, J = 6.4, 1.9 Hz, 1H), 7.08 (d, J = 2.5 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 5.81 (d, J = 7.9 Hz, 1H), 5.65 (d, J = 15.7 Hz, 1H), 3.67 (d, J = 11.5 Hz, 3H), 3.52 (d, J = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.17, 133.36 (d, J = 3.3 Hz), 129.91 (d, J = 2.8 Hz), 129.05 (d, J = 5.4 Hz), 127.42

(d, J = 3.0 Hz), 126.87, 124.21, 122.49 (d, J = 4.3 Hz), 107.22, 82.62, 53.54 (d, J = 6.1 Hz), 53.36 (d, J = 7.2 Hz), 52.27 (d, J = 152.1 Hz), 28.12; Signals corresponding to the minor rotamer: δ 151.34, 133.74 (d, J = 3.7 Hz), 129.70 (d, J = 2.8 Hz), 128.86 (d, J = 5.5 Hz), 127.51 (d, J = 3.0 Hz), 127.09, 124.03, 122.71 (d, J = 4.5 Hz), 107.35, 82.74, 54.18 (d, J = 152.5 Hz),53.69 (d, J = 6.8 Hz), 53.08 (d, J = 7.3 Hz), 28.07; ^{31}P NMR (243 MHz, $CDCl_3$): δ 21.62 (for major rotamer), 21.04(for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}BrNO_5PNa$ $[M+Na]^+$ 440.0233, found 440.0232; $[\alpha]_D^{25}$ = +215.2 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 13.2 min, t_R (minor) = 15.4 min), 81% *ee*.



4ia

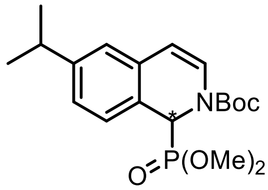
Tert-butyl 1-(dimethoxyphosphoryl)-6-iodoisoquinoline-2(1*H*)-carboxylate (4ia). Light yellow oil 91 mg, yield 98%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.50 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 4.7 Hz, 1H), 6.96 (dd, J = 8.0, 2.6 Hz, 1H), 6.84 (d, J = 7.8 Hz, 1H), 5.83 (d, J = 16.3 Hz, 1H), 5.70 (d, J = 7.8 Hz, 1H), 3.69 (d, J = 10.8 Hz, 3H), 3.57 (d, J = 10.6 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 7.50 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 4.7 Hz, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.95 (dd, J = 8.0, 2.6 Hz, 1H), 5.79 (d, J = 7.9 Hz, 1H), 5.63 (d, J = 15.7 Hz, 1H), 3.67 (d, J = 11.8 Hz, 3H), 3.52 (d, J = 10.5 Hz, 3H), 1.54 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.16, 135.90 (d, J = 2.8 Hz), 133.47 (d, J = 3.5 Hz), 133.30 (d, J = 2.9 Hz), 129.17 (d, J = 5.5 Hz), 126.74, 124.89, 107.04, 94.11 (d, J = 4.5 Hz), 82.60, 53.53 (d, J = 6.0 Hz), 53.36 (d, J = 7.1 Hz), 52.32 (d, J = 151.8 Hz), 28.11; Signals corresponding to the minor rotamer: δ 151.16, 135.90 (d, J = 2.8 Hz), 133.47 (d, J = 3.5 Hz), 133.30 (d, J = 2.9 Hz), 129.17 (d, J = 5.5 Hz), 126.74, 124.89, 107.04, 94.11 (d, J = 4.5 Hz), 82.60, 53.53 (d, J = 6.0 Hz), 53.36 (d, J = 7.1 Hz), 52.32 (d, J = 151.8 Hz), 28.11; ^{31}P NMR (243 MHz, $CDCl_3$): δ 21.62 (for major rotamer), 21.06 (for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}INO_5PNa$ $[M+Na]^+$ 488.0094, found 488.0095; $[\alpha]_D^{25}$ = +224.1 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 17.1 min, t_R (minor) = 20.5 min), 85% *ee*.



4ja

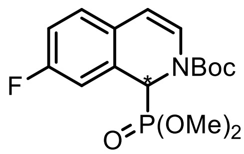
Tert-butyl 1-(dimethoxyphosphoryl)-6-methylisoquinoline-2(1*H*)-carboxylate (4ja). Light yellow oil 64 mg, yield 90%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.7:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.12 (d, J = 7.8 Hz, 1H), 7.00 (d, J = 7.3 Hz, 1H), 6.86 (d, J = 6.1 Hz, 1H), 6.81 (d, J = 7.7 Hz, 1H), 5.86 (d, J = 15.6 Hz, 1H), 5.76 (d, J = 7.8 Hz, 1H), 3.68 (d, J = 10.6 Hz, 3H), 3.55 (d, J = 10.5 Hz, 3H), 2.30 (s, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 7.13 (d, J = 7.8 Hz, 1H), 7.01 (d, J = 7.3 Hz, 1H), 6.99 (d, J = 7.3 Hz, 1H), 6.86 (d, J = 5.8 Hz, 2H), 5.85 (d, J = 7.7 Hz, 2H), 5.68 (d, J = 15.1 Hz, 1H), 3.66 (d, J = 8.8 Hz, 3H), 3.47 (d,

J = 10.4 Hz, 3H), 2.30 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.38, 138.33 (d, J = 3.3 Hz), 131.14 (d, J = 3.6 Hz), 127.97 (d, J = 2.7 Hz), 127.42 (d, J = 5.3 Hz), 125.56, 125.48 (d, J = 3.0 Hz), 122.38, 108.66, 82.13, 53.41 (d, J = 6.1 Hz), 53.32 (d, J = 7.0 Hz), 52.91, 51.90, 28.15, 21.16; Signals corresponding to the minor rotamer: δ 151.61, 138.57 (d, J = 3.5 Hz), 127.75 (d, J = 2.7 Hz), 127.25 (d, J = 5.2 Hz), 125.69, 125.60 (d, J = 3.0 Hz), 122.20, 108.80, 82.25, 54.80, 53.80, 53.62 (d, J = 7.2 Hz), 52.93 (d, J = 8.8 Hz), 28.11, 21.16; ^{31}P NMR (243 MHz, $CDCl_3$): δ 22.53 (for major rotamer), 21.89 (for minor rotamer); HRMS (m/z) calcd for $C_{17}H_{24}NO_5PNa$ $[M+Na]^+$ 376.1284, found 376.1285; $[\alpha]_D^{25}$ = +210.8 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 40/60, v/v, 1.0 mL/min, 305 nm, t_R (major) = 8.4 min, t_R (minor) = 9.7 min), 84% *ee*.



4ka

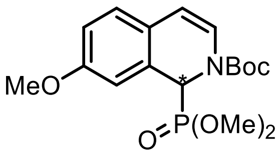
Tert-butyl 1-(dimethoxyphosphoryl)-6-isopropylisoquinoline-2(1*H*)-carboxylate (4ka). Light yellow oil 72 mg, yield 95%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.7:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.16 (d, J = 7.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.91 (d, J = 4.6 Hz, 1H), 6.81 (d, J = 7.8 Hz, 1H), 5.87 (d, J = 11.7 Hz, 1H), 5.80 (d, J = 7.8 Hz, 1H), 3.68 (d, J = 10.6 Hz, 3H), 3.55 (d, J = 10.5 Hz, 3H), 2.89-2.82 (m, 1H), 1.51 (s, 9H), 1.22 (d, J = 6.9 Hz, 6H); Signals corresponding to the minor rotamer: δ 7.16 (d, J = 7.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.99 (d, J = 7.8 Hz, 1H), 6.91 (d, J = 4.6 Hz, 1H), 5.89 (d, J = 3.8 Hz, 1H), 5.69 (d, J = 15.2 Hz, 1H), 3.66 (d, J = 10.6 Hz, 3H), 3.46 (d, J = 10.4 Hz, 3H), 2.91-2.79 (m, 1H), 1.54 (s, 9H), 1.22 (d, J = 6.9 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.37, 149.38 (d, J = 3.9 Hz), 131.15 (d, J = 3.8 Hz), 127.51 (d, J = 5.3 Hz), 125.47, 122.91 (d, J = 3.1 Hz), 122.71, 108.93, 82.08, 53.41 (d, J = 6.0 Hz), 53.31 (d, J = 6.9 Hz), 52.35 (d, J = 151.5 Hz), 33.84, 28.15, 23.84; Signals corresponding to the minor rotamer: δ 151.59, 149.68 (d, J = 3.7 Hz), 131.53 (d, J = 3.8 Hz), 127.36 (d, J = 5.4 Hz), 125.60, 125.22 (d, J = 2.8 Hz), 123.05 (d, J = 3.2 Hz), 122.51 (d, J = 1.9 Hz), 109.06, 82.21, 54.28 (d, J = 150.7 Hz), 53.63 (d, J = 7.2 Hz), 52.92 (d, J = 7.5 Hz), 33.84, 28.12, 23.84; ^{31}P NMR (243 MHz, $CDCl_3$): δ 22.47 (for major rotamer), 21.79 (for minor rotamer); HRMS (m/z) calcd for $C_{19}H_{28}NO_5PNa$ $[M+Na]^+$ 404.1597, found 404.1601; $[\alpha]_D^{25}$ = +204.2 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 15.0 min, t_R (minor) = 17.1 min), 80% *ee*.



4la

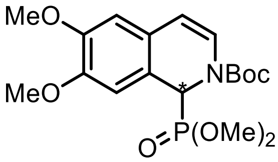
Tert-butyl 1-(dimethoxyphosphoryl)-7-fluoroisoquinoline-2(1*H*)-carboxylate (4la). Light yellow oil 40 mg, yield 56%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.8:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 7.05-6.95 (m, 2H), 6.95-6.90 (m, 1H), 6.79 (d, J = 7.7 Hz, 1H), 5.86 (d, J = 17.3 Hz, 1H), 5.78 (d, J = 7.8 Hz, 1H), 3.70 (d, J = 10.8 Hz, 3H), 3.59 (d, J

= 10.6 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 7.05-6.95 (m, 3H), 6.95-6.90 (m, 1H), 5.86 (d, J = 10.2 Hz, 1H), 5.66 (d, J = 16.2 Hz, 1H), 3.68 (d, J = 11.3 Hz, 31H), 3.54 (d, J = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 161.70 (dd, J = 247.3, 3.1 Hz), 151.34, 127.63 (t, J = 3.6 Hz), 127.52 (dd, J = 7.5, 1.5 Hz), 126.14 (dd, J = 8.3, 3.2 Hz), 124.99 (d, J = 2.5 Hz), 115.42 (dd, J = 21.6, 3.3 Hz), 114.91 (dd, J = 23.4, 5.2 Hz), 107.79, 82.42, 53.51 (d, J = 6.1 Hz), 53.37 (d, J = 7.2 Hz), 52.51 (dd, J = 151.8, 2.2 Hz), 28.13; Signals corresponding to the minor rotamer: δ 161.57 (dd, J = 247.6, 3.0 Hz), 151.45, 127.97 (t, J = 3.4 Hz), 127.30 (dd, J = 7.7, 1.5 Hz), 126.22 (dd, J = 9.0, 3.0 Hz), 125.18 (d, J = 2.1 Hz), 115.57 (dd, J = 24.0, 3.4 Hz), 114.78 (dd, J = 23.5, 5.1 Hz), 107.95, 82.56, 54.40 (dd, J = 150.8, 1.7 Hz), 53.63 (d, J = 7.2 Hz), 53.09 (d, J = 7.2 Hz), 28.09; ^{31}P NMR (243 MHz, $CDCl_3$): δ 21.70 (for major rotamer), 21.20 (for minor rotamer); HRMS (m/z) calcd for $C_{16}H_{21}FNO_5PNa$ $[M+Na]^+$ 380.1034, found 380.1033; $[\alpha]_D^{25}$ = +342.4 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-3R, CH_3CN/H_2O = 40/60, v/v, 0.6 mL/min, 305 nm, t_R (major) = 11.4 min, t_R (minor) = 12.3 min), 80% *ee*.



4ma

Tert-butyl 1-(dimethoxyphosphoryl)-7-methoxyisoquinoline-2(1*H*)-carboxylate (4ma). Light yellow oil 35 mg, yield 48%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.9:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 6.98 (d, J = 8.0 Hz, 1H), 6.83-6.79 (m, 1H), 6.79-6.76 (m, 1H), 6.72 (d, J = 7.7 Hz, 1H), 5.86 (d, J = 16.5 Hz, 1H), 5.78 (d, J = 7.8 Hz, 1H), 3.80 (s, 3H), 3.69 (d, J = 10.6 Hz, 3H), 3.55 (d, J = 10.6 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 6.99 (d, J = 7.7 Hz, 1H), 6.90 (d, J = 7.8 Hz, 1H), 6.83-6.79 (m, 1H), 6.79-6.76 (m, 1H), 5.87 (d, J = 7.9 Hz, 1H), 5.67 (d, J = 15.9 Hz, 1H), 3.81 (s, 3H), 3.67 (d, J = 10.5 Hz, 3H), 3.48 (d, J = 10.5 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 158.91 (d, J = 2.8 Hz), 151.53, 126.94, 125.94 (d, J = 3.2 Hz), 124.31 (d, J = 4.1 Hz), 123.46, 114.22 (d, J = 4.0 Hz), 113.22 (d, J = 5.1 Hz), 108.46, 82.06, 55.44, 53.45 (d, J = 6.0 Hz), 53.37 (d, J = 7.1 Hz), 52.79 (d, J = 150.4 Hz), 28.17; Signals corresponding to the minor rotamer: δ 158.78 (d, J = 2.8 Hz), 151.64 , 126.71 , 126.05 (d, J = 3.2 Hz), 124.63 (d, J = 4.0 Hz), 123.59 , 114.25 (d, J = 4.8 Hz), 113.22 (d, J = 5.1 Hz), 108.61 , 82.21 , 55.44 , 54.70 (d, J = 149.3 Hz), 53.69 (d, J = 7.2 Hz), 52.96 (d, J = 7.2 Hz), 28.14; ^{31}P NMR (243 MHz, $CDCl_3$): δ 22.36 (for major rotamer), 21.72 (for minor rotamer); HRMS (m/z) calcd for $C_{17}H_{24}NO_6PNa$ $[M+Na]^+$ 392.1233, found 392.1231; $[\alpha]_D^{25}$ = +226.2 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-3R, CH_3CN/H_2O = 40/60, v/v, 0.6 mL/min, 305 nm, t_R (major) = 10.4 min, t_R (minor) = 11.2 min), 84% *ee*.

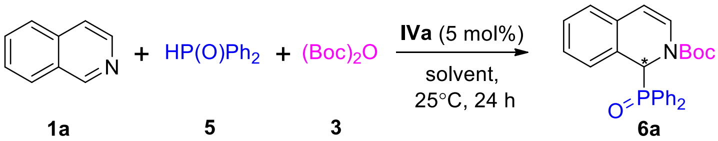


4na

Tert-butyl 1-(dimethoxyphosphoryl)-6,7-dimethoxyisoquinoline-2(1*H*)-carboxylate (4na). Light yellow oil 24 mg, yield 30%; ^{1}H NMR(600 MHz, $CDCl_3$): The compound exists as a 1.7:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 6.79 (s, 1H), 6.74 (d, J = 7.7 Hz, 1H), 6.59 (d, J = 5.8 Hz, 1H), 5.83 (d, J = 15.3 Hz, 1H), 5.74 (d, J = 7.7 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.70 (d, J = 9.8 Hz, 3H), 3.54 (d, J = 10.5 Hz, 3H), 1.52 (s, 9H); Signals corresponding to the minor rotamer: δ 6.92 (d, J = 7.8 Hz, 1H), 6.79 (s, 1H), 6.59 (d, J = 5.8 Hz, 1H), 5.82 (d, J = 5.5 Hz, 1H), 5.66 (d, J = 14.6 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.69 (d, J = 10.4 Hz, 3H), 3.47 (d, J = 10.4 Hz, 3H), 1.55 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) Signals corresponding to the major rotamer: δ 151.49, 149.04 (d, J = 3.7 Hz), 148.21 (d, J = 2.6 Hz), 124.43 (d, J = 4.5 Hz), 124.00, 117.46, 111.03 (d, J = 4.7 Hz), 108.49, 108.09 (d, J = 3.4 Hz), 82.09, 56.19, 55.93 , 53.40, 53.36 (d, J = 2.0 Hz), 52.25 (d, J = 151.6 Hz), 28.15; Signals corresponding to the minor rotamer: δ 151.64, 149.18 (d, J = 3.6 Hz), 148.03 (d, J = 2.7 Hz), 124.83 (d, J = 4.8 Hz), 124.15, 117.10, 110.92 (d, J = 4.7 Hz), 108.59, 108.13 (d, J = 3.5 Hz), 82.23, 56.19, 55.93 , 54.22 (d, J = 139.3 Hz), 53.70 (d, J = 4.3 Hz), 52.86 (d, J = 7.4 Hz), 28.13^{31}P NMR (243 MHz, $CDCl_3$): δ 22.43 (for major rotamer), 21.69 (for minor rotamer); HRMS (m/z) calcd for $C_{18}H_{26}NO_7PNa$ $[M+Na]^+$ 422.1339, found 422.1339; $[\alpha]_D^{25}$ = +165.6 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-3R, CH_3CN/H_2O = 40/60, v/v, 0.6 mL/min, 305 nm, t_R (major) = 6.9 min, t_R (minor) = 7.5 min), 55% *ee*.

1.4 Reaction conditions optimization for the enantioselective dearomatization of 1,2-dihydroisoquinoline-1-ylphenylphosphine oxides 6:

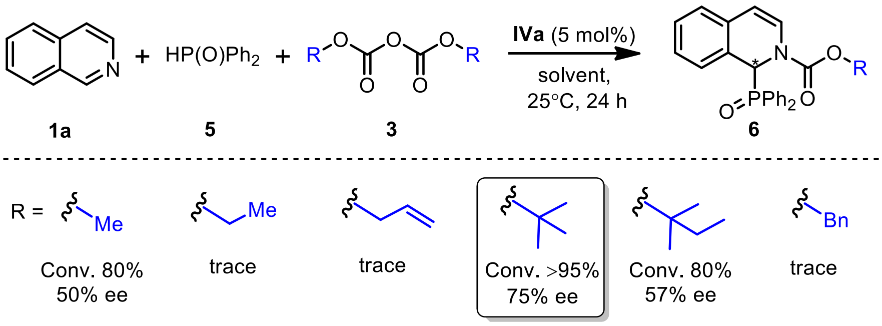
Further screening of solvents and additives[a]



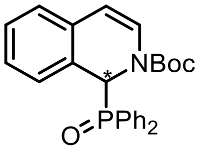
Entry	Solvent	Conv. (%)[b]	ee (%)[c]
1	toluene	>95	59
2	benzene	>95	63
3	xylene	35	21
4	PhOMe	90	53
5	MTBE	87	51
6	Et_2O	85	46
7	THF	92	14
8	1,4-Dioxane	>95	23
9[d]	benzene	>95	73
10[e]	benzene	>95	75
11[f]	benzene	>95	74

[a]Reaction conditions: **1a** (0.2 mmol), **5** (0.4 mmol), **3** (0.4 mmol), and **IVa** (5 mol%) in solvent (4 mL) for 24 h (25 °C). [b]Yield was determined by HPLC analysis. [c]Determined by HPLC (Chiralcel OD-RH). [d]3Å MS (50mg) was used. [e]4Å MS (50mg) was used. [f]5Å MS (50mg) was used.

Evaluation of Acylating Reagent

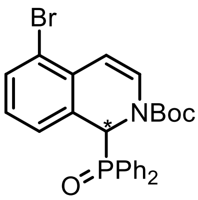


Synthesis of 1,2-dihydroisoquinoline-1-ylphenylphosphine oxides 6. A mixture of isoquinoline **1** (0.2mmol), catalyst BINOL-CPAs **IVa** (5mol%), $(Boc)_2O$ **3** (0.4mmol) and benzene (4 mL) was stirred at room temperature for 2h. Then diphenylphosphine oxide **5** (0.4mmol) and 4Å MS (50mg) was added and the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography with PE/EA (1/2) to obtain 1,2-dihydroisoquinoline-1-ylphosphonates **6** as a white soild.



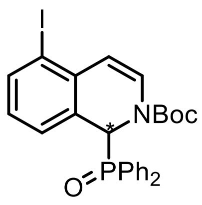
6a

Tert-butyl 1-(diphenylphosphoryl)isoquinoline-2(1*H*)-carboxylate 6a. White soild 84 mg, yield 98%; m.p. 125-130°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: *δ* 8.15-8.09 (m, 2H), 8.00-7.94 (m, 2H), 7.07-6.95 (m, 6H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.77 (dd, *J* = 15.8, 7.5 Hz, 2H), 6.71-6.67 (m, 2H), 6.52 (d, *J* = 7.5 Hz, 1H), 5.60 (d, *J* = 7.7 Hz, 1H), 1.23 (s, 9H); Signals corresponding to the minor rotamer: *δ* 7.85-7.79 (m, 2H), 7.77-7.72 (m, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.07-6.95 (m, 6H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 6.73-6.70 (m, 1H), 6.50 (d, *J* = 7.4 Hz, 1H), 6.38 (d, *J* = 10.0 Hz, 1H), 5.25 (d, *J* = 7.8 Hz, 1H), 1.36 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers:δ 151.94, 151.70, 133.34, 132.97, 132.95, 132.93, 132.86, 132.80, 132.73, 132.65, 132.59, 132.46, 132.40, 131.99, 131.93, 131.88, 131.56, 131.54, 131.52, 131.50, 131.45, 131.43, 131.29, 127.31, 127.28, 127.00, 126.98, 126.95, 126.90, 126.68, 126.62, 126.30, 125.24, 125.23, 110.84, 109.62, 81.95, 81.48,60.62 (d, *J* = 67.2 Hz), 58.59 (d, *J* = 68.8 Hz), 28.00, 27.88;^{31}P NMR (243 MHz, C_6D_6): *δ* 28.70 (for major rotamer), 25.71 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{26}NO_3PNa$ $[M+Na]^+$ 454.1543, found 454.1541; $[\alpha]_D^{25}$ = +255.9 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 6.4 min, t_R (minor) = 7.8 min), 75% *ee*.



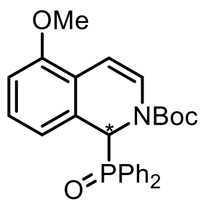
6b

Tert-butyl 5-bromo-1-(diphenylphosphoryl)isoquinoline-2(1*H*)-carboxylate 6b. White soild 75 mg, yield 74%; m.p. 140-144°C; ^{1}H-NMR (600 MHz, C_6D_6):The compound exists as a 2.4:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: *δ* 8.09-7.99 (m, 2H), 7.99-7.89 (m, 2H), 7.12 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.07-6.97 (m, 6H), 6.75 (dd, *J* = 7.9, 1.0 Hz, 1H), 6.55 (d, *J* = 4.4 Hz, 1H), 6.32 (d, *J* = 7.6 Hz, 1H), 6.30-6.26 (m, 1H), 6.14 (d, *J* = 7.9 Hz, 1H), 1.23 (s, 9H); Signals corresponding to the minor rotamer: *δ* 7.78-7.67 (m, 4H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.07-6.97 (m, 6H), 6.96-6.92 (m, 1H), 6.69 (d, *J* = 7.5 Hz, 1H), 6.32 (d, *J* = 7.6 Hz, 1H), 6.24 (d, *J* = 10.4 Hz, 1H), 5.78 (d, *J* = 8.0 Hz, 1H), 1.34 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers:*δ* 151.55, 151.41, 132.88, 132.73, 132.68, 132.62, 132.59, 132.54, 132.44, 132.42, 132.40, 132.34, 132.26, 131.89, 131.83, 131.80, 131.76, 131.74, 131.62, 131.60, 131.44, 130.84, 128.68, 128.37, 126.38, 126.35, 126.10, 126.07, 120.92, 120.90, 120.81, 120.79, 109.39, 108.05, 82.33, 81.88, 60.81 (d, *J* = 66.3 Hz), 58.80 (d, *J* = 68.0 Hz), 27.94, 27.82; ^{31}P NMR (243 MHz, C_6D_6): *δ* 28.88 (for major rotamer), 26.14 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{25}BrNO_3PNa$ $[M+Na]^+$ 532.0648, found 532.0648; $[\alpha]_D^{25}$ = +216.7 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 12.0 min, t_R (minor) = 16.0 min), 78% *ee*.



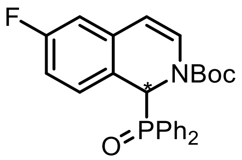
6c

Tert-butyl 1-(diphenylphosphoryl)-5-iodoisoquinoline-2(1*H*)-carboxylate 6c. White soild 106 mg, yield 95%; m.p. 165-168°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: *δ* 8.08-7.98 (m, 2H), 7.95-7.86 (m, 2H), 7.39 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 6.51 (d, *J* = 4.7 Hz, 1H), 6.34 (d, *J* = 7.4 Hz, 1H), 6.12 (t, *J* = 7.7 Hz, 1H), 6.00 (d, *J* = 7.9 Hz, 1H), 1.24 (s, 9H); Signals corresponding to the minor rotamer: *δ* 7.77-7.71 (m, 2H), 7.70-7.64 (m, 2H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 6.96-6.93 (m, 1H), 6.69 (s, 1H), 6.19 (d, *J* = 10.4 Hz, 1H), 5.64 (d, *J* = 8.0 Hz, 1H), 1.34 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: *δ* 151.53, 151.37, 139.09, 139.07, 135.57, 135.55, 132.90, 132.74, 132.68, 132.61, 132.55, 132.40, 132.33, 132.28, 131.89, 131.83, 131.79, 131.77, 131.73, 131.71, 131.61, 131.60, 131.37, 130.78, 128.99, 128.41, 127.05, 127.02, 114.22, 112.95, 96.68, 96.66, 82.33, 81.87, 61.07 (d, *J* = 66.3 Hz), 59.04 (d, *J* = 67.8 Hz), 27.95, 27.82; ^{31}P NMR (243 MHz, C_6D_6): *δ* 28.75 (for major rotamer), 26.09 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{25}INO_3PNa$ $[M+Na]^+$ 580.0509, found 580.0509; $[\alpha]_D^{25}$ = +223.6 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 60/40, v/v, 1.0 mL/min, 305 nm, t_R (major) = 6.9 min, t_R (minor) = 8.8 min), 77% *ee*.



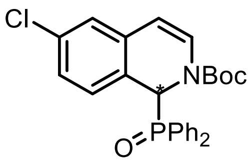
6d

Tert-butyl 1-(diphenylphosphoryl)-5-methoxyisoquinoline-2(1*H*)-carboxylate 6d. White soild 76 mg, yield 82%;m.p. 163-165°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2.3:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: *δ* 8.17-8.11 (m, 2H), 8.10-8.05 (m, 2H), 7.06-6.95 (m, 6H), 6.81 (dd, *J* = 7.8, 1.0 Hz, 1H), 6.73 (d, *J* = 3.6 Hz, 1H), 6.71-6.65 (m, 1H), 6.44 (d, *J* = 7.9 Hz, 1H), 6.28 (t, *J* = 9.2 Hz, 2H), 3.19 (s, 3H), 1.20 (s, 9H); Signals corresponding to the minor rotamer: *δ* 7.90-7.80 (m, 4H), 7.36 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.06-6.95 (m, 6H), 6.72-6.70 (m, 1H), 6.70-6.66 (m, 1H), 6.42 (s, 1H), 6.24 (d, *J* = 8.1 Hz, 1H), 6.09 (d, *J* = 8.0 Hz, 1H), 3.12 (s, 3H), 1.32 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: *δ* 154.63 (d, *J* = 2.7 Hz), 154.54 (d, *J* = 2.3 Hz), 151.91, 151.82, 133.50, 132.89, 132.83, 132.77, 132.65, 132.59, 132.46, 132.40, 132.24, 131.99, 131.93, 131.65, 131.55, 131.54, 131.46, 131.44, 131.38, 131.36, 125.97, 125.41, 122.38, 122.36, 122.20, 122.18, 119.86, 119.83, 119.45, 119.43, 110.48, 110.46, 105.80, 104.49, 81.79, 81.32, 60.71 (d, *J* = 67.0 Hz), 58.67 (d, *J* = 68.5 Hz), 55.07, 54.99, 27.99, 27.85; ^{31}P NMR (243 MHz, C_6D_6): *δ* 29.18 (for major rotamer), 26.53 (for minor rotamer); HRMS (m/z) calcd for $C_{27}H_{28}NO_4PNa$ $[M+Na]^+$ 484.1648, found 484.1652; $[\alpha]_D^{25}$ = +203.1 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 7.1 min, t_R (minor) = 9.2 min), 78% *ee*.



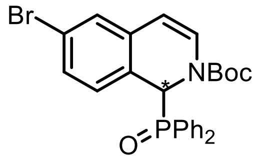
6e

Tert-butyl 1-(diphenylphosphoryl)-6-fluoroisoquinoline-2(1*H*)-carboxylate 6e. White soild 80 mg, yield 90%; m.p. 130-133°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.11-8.06 (m, 2H), 7.97-7.92 (m, 2H), 7.06-6.94 (m, 6H), 6.76 (d, J = 7.7 Hz, 1H), 6.57 (d, J = 3.2 Hz, 1H), 6.46 (dd, J = 9.2, 2.6 Hz, 1H), 6.39-6.32 (m, 1H), 6.30-6.25 (m, 1H), 5.39 (d, J = 7.7 Hz, 1H), 1.22 (s, 9H); Signals corresponding to the minor rotamer: δ 7.80-7.75 (m, 2H), 7.74-7.69 (m, 2H), 7.30-7.25 (m, 1H), 7.04-6.95 (m, 6H), 6.68-6.64 (m, 1H), 6.39-6.35 (m, 1H), 6.30-6.25 (m, 1H), 6.19 (dd, J = 9.2, 2.6 Hz, 1H), 5.03 (d, J = 7.8 Hz, 1H), 1.34 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 164.00 (d, J = 3.2 Hz), 162.38 (d, J = 3.1 Hz), 151.77, 151.54, 135.01, 133.06, 132.76, 132.70, 132.55, 132.50, 132.43, 132.37, 131.94, 131.88, 131.68, 131.67, 131.55, 131.53, 131.09, 127.55, 127.26, 122.16, 122.14, 113.40 (dd, J = 22.2, 1.9 Hz), 113.07 (dd, J = 22.2, 2.0 Hz), 111.93 (dd, J = 22.4, 2.0 Hz), 111.71 (d, J = 2.1 Hz), 109.90 (d, J = 2.2 Hz), 108.64 (d, J = 2.0 Hz), 82.22 , 81.77 , 60.02 (d, J = 67.7 Hz), 57.97 (d, J = 69.3 Hz), 27.95 , 27.83; HRMS (m/z) calcd for $C_{26}H_{25}FNO_3PNa$ $[M+Na]^+$ 472.1448, found 472.1448; $[\alpha]_D^{25}$ = +238.7 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 7.3 min, t_R (minor) = 8.4 min), 76% *ee*.



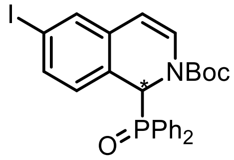
6f

Tert-butyl 6-chloro-1-(diphenylphosphoryl)isoquinoline-2(1*H*)-carboxylate 6f. White soild 91 mg, yield 98%; m.p. 95-97°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.11-8.04 (m, 2H), 7.97-7.91 (m, 2H), 7.05-6.94 (m, 6H), 6.76 (d, J = 2.1 Hz, 1H), 6.73 (dd, J = 7.7, 1.0 Hz, 1H), 6.64 (dd, J = 8.1, 2.2 Hz, 1H), 6.53 (d, J = 3.4 Hz, 1H), 6.22 (dd, J = 8.1, 1.9 Hz, 1H), 5.37 (d, J = 7.7 Hz, 1H), 1.21 (s, 9H); Signals corresponding to the minor rotamer: δ 7.80-7.73 (m, 2H), 7.73-7.67 (m, 2H), 7.25 (dd, J = 7.8, 1.1 Hz, 1H), 7.05-6.94 (m, 6H), 6.67 (dd, J = 8.1, 2.1 Hz, 1H), 6.58 (dd, J = 8.1, 2.1 Hz, 1H), 6.49 (d, J = 2.1 Hz, 1H), 6.23 (d, J = 8.6 Hz, 1H), 5.01 (d, J = 7.8 Hz, 1H), 1.34 (s, 9H);^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 151.71, 151.50, 134.64, 134.62, 134.31, 134.28, 132.90, 132.76, 132.71, 132.54, 132.48, 132.43, 132.37, 132.28, 131.94, 131.88, 131.75, 131.73, 131.71, 131.59, 131.57, 131.54, 130.95, 128.16, 128.00, 127.84, 127.32, 126.74, 126.72, 125.09, 125.07, 124.96, 124.91, 124.84, 109.66, 108.37, 82.27, 81.81, 60.07 (d, J = 67.2 Hz), 58.06 (d, J = 68.8 Hz), 27.94, 27.83; ^{31}P NMR (243 MHz, C_6D_6): δ 28.59 (for major rotamer), 25.36 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{25}ClNO_3PNa$ $[M+Na]^+$ 488.1153, found 488.1155; $[\alpha]_D^{25}$ = +219.0 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 10.5 min, t_R (minor) = 12.3 min), 76% *ee*.



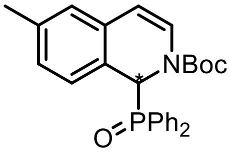
6g

Tert-butyl 6-bromo-1-(diphenylphosphoryl)isoquinoline-2(1*H*)-carboxylate 6g. White soild 97 mg, yield 95%; m.p. 150-153°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2.5:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.10-8.05 (m, 2H), 7.96-7.91 (m, 2H), 7.05-6.94 (m, 6H), 6.92 (d, *J* = 2.0 Hz, 1H), 6.78 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.74-6.71 (m, 1H), 6.51 (d, *J* = 3.6 Hz, 1H), 6.15 (dd, *J* = 8.1, 2.1 Hz, 1H), 5.35 (d, *J* = 7.7 Hz, 1H), 1.21 (s, 9H); Signals corresponding to the minor rotamer: δ 7.78-7.72 (m, 2H), 7.71-7.66 (m, 2H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.05-6.94 (m, 6H), 6.82-6.80 (m, 1H), 6.65 (d, *J* = 2.0 Hz, 1H), 6.51 (d, *J* = 3.6 Hz, 1H), 6.21 (d, *J* = 9.6 Hz, 1H), 4.99 (d, *J* = 7.8 Hz, 1H), 1.34 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 151.70, 151.49, 134.94, 134.92, 132.87, 132.76, 132.70, 132.54, 132.48, 132.43, 132.40, 132.36, 132.25, 131.94, 131.88, 131.75, 131.73, 131.72, 131.60, 131.58, 131.49, 130.90, 129.67, 129.66, 129.33, 128.64, 128.62, 127.33, 125.36, 125.30, 122.48, 122.45, 122.42, 109.54, 108.24, 82.27, 81.82, 60.11 (d, *J* = 67.2 Hz), 58.11 (d, *J* = 68.6 Hz), 27.94, 27.82; ^{31}P NMR (243 MHz, C_6D_6): δ 28.49 (for major rotamer), 25.21 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{25}BrNO_3PNa$ $[M+Na]^+$ 532.0648, found 532.0647; $[\alpha]_D^{25}$ = +204.6 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 11.9 min, t_R (minor) = 14.1 min), 70% *ee*.



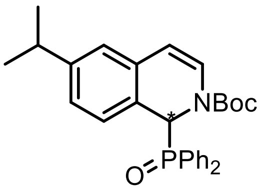
6h

Tert-butyl 1-(diphenylphosphoryl)-6-iodoisoquinoline-2(1*H*)-carboxylate 6h. White soild 95 mg, yield 85%; m.p. 155-159°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2.2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.11-8.03 (m, 2H), 7.96-7.89 (m, 2H), 7.12 (d, *J* = 1.5 Hz, 1H), 7.05-6.94 (m, 7H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 3.5 Hz, 1H), 6.02 (dd, *J* = 8.0, 1.9 Hz, 1H), 5.33 (d, *J* = 7.7 Hz, 1H), 1.21 (s, 9H); Signals corresponding to the minor rotamer: δ 7.79-7.72 (m, 2H), 7.71-7.65 (m, 2H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.05-6.94 (m, 7H), 6.86 (d, *J* = 1.4 Hz, 1H), 6.38 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.20 (d, *J* = 9.6 Hz, 1H), 4.98 (d, *J* = 7.8 Hz, 1H), 1.34 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 151.71, 151.50, 135.71, 135.70, 135.38, 135.05, 135.04, 133.85, 133.83, 133.77, 132.91, 132.78, 132.72, 132.54, 132.49, 132.43, 132.36, 132.29, 131.95, 131.89, 131.74, 131.72, 131.69, 131.58, 131.57, 131.50, 130.91, 127.20, 125.99, 109.41, 108.11, 93.99, 93.96, 93.93, 93.90, 82.24, 81.79, 60.15 (d, *J* = 66.9 Hz), 58.17 (d, *J* = 68.6 Hz), 27.94, 27.84;^{31}P NMR (243 MHz, C_6D_6): δ 28.43 (for major rotamer), 25.16 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{25}INO_3PNa$ $[M+Na]^+$ 580.0509, found 580.0511; $[\alpha]_D^{25}$ = +170.8 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 60/40, v/v, 1.0 mL/min, 305 nm, t_R (major) = 15.0 min, t_R (minor) = 17.1 min), 76% *ee*.



6i

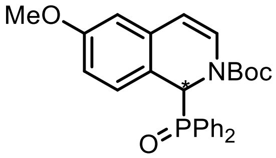
Tert-butyl 1-(diphenylphosphoryl)-6-methylisoquinoline-2(1*H*)-carboxylate 6i. White soild 71 mg, yield 80%; m.p. 155-157°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.19-8.10 (m, 2H), 8.06-7.98 (m, 2H), 7.09-6.97 (m, 6H), 6.85-6.79 (m, 1H), 6.70 (d, J = 2.9 Hz, 1H), 6.61 (s, 1H), 6.53 (d, J = 7.6 Hz, 1H), 6.46 (dd, J = 7.7, 1.7 Hz, 1H), 5.65 (d, J = 7.7 Hz, 1H), 1.96 (s, 3H), 1.22 (s, 9H); Signals corresponding to the minor rotamer: δ 7.90-7.82 (m, 2H), 7.82-7.74 (m, 2H), 7.34 (d, J = 7.8 Hz, 1H), 7.09-6.97 (m, 6H), 6.85-6.79 (m, 1H), 6.56 (d, J = 7.7 Hz, 1H), 6.39 (d, J = 9.4 Hz, 1H), 6.35 (s, 1H), 5.29 (d, J = 7.8 Hz, 1H), 1.93 (s, 3H), 1.36 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 151.99, 151.73, 138.07, 137.95, 137.94, 133.64, 133.45, 132.91, 132.86, 132.83, 132.65, 132.60, 132.48, 132.42, 132.10, 132.04, 131.98, 131.54, 131.52, 131.48, 131.40, 131.38, 127.17, 127.14, 126.83, 126.80, 126.78, 126.19, 126.12, 126.10, 126.06, 123.79, 123.68, 111.09, 109.81, 81.87, 81.40, 60.42 (d, J = 67.7 Hz), 58.37 (d, J = 69.6 Hz), 28.00, 27.88, 21.04, 20.96; ^{31}P NMR (243 MHz, C_6D_6): δ 28.65 (for major rotamer), 25.56 (for minor rotamer); HRMS (m/z) calcd for $C_{27}H_{28}NO_3PNa$ $[M+Na]^+$ 468.1699, found 468.1698; $[\alpha]_D^{25}$ = +225.8 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 8.3 min, t_R (minor) = 9.9 min), 75% *ee*.



6j

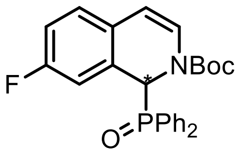
Tert-butyl 1-(diphenylphosphoryl)-6-isopropylisoquinoline-2(1*H*)-carboxylate 6j. White soild 86 mg, yield 91%; m.p. 162-165°C; ^{1}H-NMR (600 MHz, C_6D_6):The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.17-8.09 (m, 2H), 7.99-7.92 (m, 2H), 7.07-6.96 (m, 6H), 6.85 (d, J = 8.3 Hz, 1H), 6.72 (s, 1H), 6.61 (dd, J = 7.8, 1.6 Hz, 1H), 6.53 (dd, J = 7.8, 1.8 Hz, 1H), 5.63 (d, J = 7.7 Hz, 1H), 2.60-2.54 (m, 1H), 1.26 (s, 9H), 1.04 (dd, J = 6.9, 5.8 Hz, 6H); Signals corresponding to the minor rotamer: δ 7.86-7.79 (m, 2H), 7.77-7.71 (m, 2H), 7.35 (d, J = 8.3 Hz, 1H), 7.07-6.96 (m, 6H), 6.90-6.87 (m, 1H), 6.72 (d, J = 4.1 Hz, 1H), 6.63 (dd, J = 7.8, 1.5 Hz, 1H), 6.46-6.43 (m, 1H), 6.41 (d, J = 9.5 Hz, 1H), 5.29 (d, J = 7.8 Hz, 1H), 2.54-2.49 (m, 1H), 1.37 (s, 9H), 1.02 (dd, J = 6.9, 2.9 Hz, 6H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 151.71, 151.49, 149.09 (d, J = 3.1 Hz), 148.74 (d, J = 2.9 Hz), 133.46, 133.26, 132.65, 132.62, 132.57, 132.41, 132.36, 132.15, 132.09, 131.72, 131.66, 131.64, 131.14, 131.12, 131.10, 131.07, 131.05, 130.47, 129.88, 126.61, 126.59, 126.46, 125.93, 124.83, 124.81, 124.49, 124.47, 123.94, 123.92, 123.19, 123.17, 123.16, 110.74, 109.50, 81.56, 81.10, 60.06 (d, J = 67.5 Hz), 58.05 (d, J = 69.2 Hz), 33.76, 27.72, 27.58, 23.68 (d, J = 24.9 Hz), 23.61 (d, J = 17.5 Hz); ^{31}P NMR (243 MHz, C_6D_6): δ 28.46 (for major rotamer), 25.84 (for minor rotamer); HRMS (m/z) calcd for $C_{29}H_{32}NO_3PNa$ $[M+Na]^+$ 496.2012, found 496.2013; $[\alpha]_D^{25}$ = +181.8 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O

= 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) =12.2 min, t_R (minor) = 14.2 min), 72% *ee*.



6k

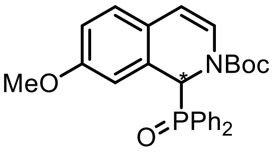
Tert-butyl 1-(diphenylphosphoryl)-6-methoxyisoquinoline-2(1*H*)-carboxylate 6k. White soild 89 mg, yield 96%; m.p. 140-144°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.18-8.11 (m, 2H), 8.05-7.98 (m, 2H), 7.10-6.96 (m, 6H), 6.86-6.79 (m, 1H), 6.68 (d, J = 2.6 Hz, 1H), 6.50 (d, J = 2.5 Hz, 1H), 6.46 (dd, J = 8.3, 2.0 Hz, 1H), 6.33 (dd, J = 8.3, 2.6 Hz, 1H), 5.60 (d, J = 7.7 Hz, 1H), 3.19 (s, 3H), 1.23 (s, 9H); Signals corresponding to the minor rotamer: δ 7.89-7.83 (m, 2H), 7.82-7.76 (m, 2H), 7.34 (d, J = 7.8 Hz, 1H), 7.10-6.96 (m, 6H), 6.86-6.79 (m, 1H), 6.38 (d, J = 8.4 Hz, 2H), 6.24 (d, J = 2.6 Hz, 1H), 5.24 (d, J = 7.8 Hz, 1H), 3.17 (s, 3H), 1.36 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 160.35 (d, J = 2.6 Hz), 160.25 (d, J = 2.4 Hz), 151.99, 151.70, 134.30, 134.21, 134.19, 133.70, 133.51, 132.92, 132.90, 132.86, 132.66, 132.60, 132.48, 132.42, 132.15, 132.04, 131.98, 131.56, 131.53, 131.51, 131.49, 131.39, 131.37, 127.24, 126.60, 118.75, 118.64, 112.56, 112.25, 110.93, 110.91, 110.75, 110.73, 109.63, 81.92, 81.45, 60.11 (d, J = 68.6 Hz), 58.08 (d, J = 70.2 Hz), 54.73, 54.67, 28.00, 27.89; ^{31}P NMR (243 MHz, C_6D_6): δ 28.43 (for major rotamer), 25.39 (for minor rotamer); HRMS (m/z) calcd for $C_{27}H_{28}NO_4PNa$ $[M+Na]^+$ 484.1648, found 484.1647; $[\alpha]_D^{25}$ = +180.0 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 6.7 min, t_R (minor) = 7.5 min), 62% *ee*.



6l

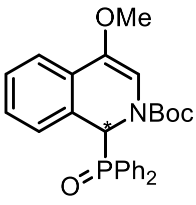
Tert-butyl 1-(diphenylphosphoryl)-7-fluoroisoquinoline-2(1*H*)-carboxylate 6l. White soild 86 mg, yield 96%; m.p. 162-165°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2.3:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.14-8.06 (m, 2H), 8.01-7.94 (m, 2H), 7.05-6.95 (m, 6H), 6.71 (d, J = 7.7 Hz, 1H), 6.60-6.55 (m, 1H), 6.55-6.51 (m, 2H), 6.23-6.19 (m, 1H), 5.55 (d, J = 7.7 Hz, 1H), 1.21 (s, 9H); Signals corresponding to the minor rotamer: δ 7.82-7.72 (m, 4H), 7.24 (d, J = 7.8 Hz, 1H), 7.05-6.95 (m, 6H), 6.95-6.91 (m, 1H), 6.60-6.55 (m, 1H), 6.51-6.47 (m, 1H), 6.28-6.24 (m, 1H), 5.19 (d, J = 7.8 Hz, 1H), 1.33 (s, 9H);^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 162.76 (d, J = 2.8 Hz), 161.13 (d, J = 2.5 Hz), 151.78, 151.63, 132.86, 132.70, 132.65, 132.43, 132.38, 132.37, 132.24, 131.88, 131.82, 131.80, 131.78, 131.69, 131.68, 131.66, 131.59, 131.57, 131.55, 131.00, 129.20, 129.18, 129.16, 128.76, 128.73, 128.71, 128.68, 128.50, 128.43, 126.59, 126.57, 126.54, 126.52, 126.48, 126.46, 126.24, 126.23, 125.56, 125.55, 115.11, 115.10, 114.97, 114.95, 114.61, 114.59, 114.46, 114.43, 114.26, 114.23, 114.10, 114.08, 82.08, 81.60, 60.45 (dd, J = 66.2, 2.2 Hz), 58.40 (dd, J = 67.9, 2.5 Hz), 27.95, 27.83; ^{31}P NMR (243 MHz, C_6D_6): δ 28.92 (for major rotamer), 25.84 (for minor rotamer); HRMS (m/z) calcd for $C_{26}H_{25}FNO_3PNa$ $[M+Na]^+$ 472.1448, found 472.1451; $[\alpha]_D^{25}$ = +203.6 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-

3R, CH_3CN/H_2O = 50/50, v/v, 0.6 mL/min, 305 nm, t_R (major) = 10.9 min, t_R (minor) = 11.9 min), 62% *ee*.



6m

Tert-butyl 1-(diphenylphosphoryl)-7-methoxyisoquinoline-2(1*H*)-carboxylate 6m. White soild 76 mg, yield 82%; m.p. 175-178°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 2.4:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.18-8.10 (m, 2H), 8.05-7.97 (m, 2H), 7.07-6.95 (m, 6H), 6.73 (dd, J = 7.6, 4.0 Hz, 1H), 6.67 (d, J = 4.2 Hz, 1H), 6.62-6.59 (m, 1H), 6.60-6.54 (m, 1H), 6.18 (s, 1H), 5.65 (d, J = 7.6 Hz, 1H), 3.06 (s, 3H), 1.23 (s, 9H); Signals corresponding to the minor rotamer: δ 7.87-7.80 (m, 4H), 7.23 (d, J = 7.8 Hz, 1H), 7.07-6.95 (m, 6H), 6.94-6.91 (m, 1H), 6.73 (dd, J = 7.6, 4.0 Hz, 1H), 6.48 (d, J = 8.3 Hz, 1H), 6.38 (d, J = 10.9 Hz, 1H), 5.31 (d, J = 7.7 Hz, 1H), 3.15 (s, 3H), 1.34 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 159.11 (d, J = 2.6 Hz), 159.01 (d, J = 2.4 Hz), 151.97, 151.90, 133.24, 132.88, 132.83, 132.66, 132.62, 132.60, 132.48, 132.42, 132.09, 131.98, 131.92, 131.60, 131.58, 131.51, 131.50, 131.45, 131.42, 131.40, 126.51, 126.49, 125.96, 125.93, 124.51, 124.06, 114.70, 114.68, 114.46, 114.44, 112.70, 112.68, 112.49, 112.46, 110.85, 109.62, 81.76, 81.30, 61.18 (d, J = 67.1 Hz), 58.90 (d, J = 68.9 Hz), 54.75, 54.58, 28.01, 27.88; ^{31}P NMR (243 MHz, C_6D_6): δ 28.51 (for major rotamer), 25.88 (for minor rotamer); HRMS (m/z) calcd for $C_{27}H_{28}NO_4PNa$ $[M+Na]^+$ 484.1648, found 484.1650; $[\alpha]_D^{25}$ = +131.2 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-3R, CH_3CN/H_2O = 50/50, v/v, 0.6 mL/min, 305 nm, t_R (major) = 9.8 min, t_R (minor) = 10.8 min), 74% *ee*.

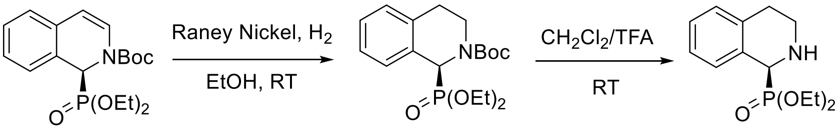


6n

Tert-butyl 1-(diphenylphosphoryl)-4-methoxyisoquinoline-2(1*H*)-carboxylate 6n. White soild 89 mg, yield 96%; m.p. 168-170°C; ^{1}H-NMR (600 MHz, C_6D_6): The compound exists as a 1.5:1 mixture of carbamate rotamers. Signals corresponding to the major rotamer: δ 8.21-8.15 (m, 2H), 7.97-7.91 (m, 2H), 7.58 (d, J = 7.6 Hz, 1H), 7.09-6.93 (m, 7H), 6.72 (d, J = 8.2 Hz, 2H), 6.55 (d, J = 7.6 Hz, 1H), 6.25 (s, 1H), 3.29 (s, 3H), 1.32 (s, 9H); Signals corresponding to the minor rotamer: δ 7.85-7.78 (m, 4H), 7.37 (d, J = 7.6 Hz, 1H), 7.09-6.93 (m, 8H), 6.79 (t, J = 7.5 Hz, 1H), 6.73 (d, J = 5.4 Hz, 1H), 6.36 (d, J = 10.8 Hz, 1H), 3.04 (s, 3H), 1.41 (s, 9H); ^{13}C-NMR (151 MHz, C_6D_6): Signals corresponding to both rotamers: δ 152.40, 152.15, 145.05, 144.32, 133.42, 133.37, 132.80, 132.76, 132.74, 132.68, 132.42, 132.37, 132.31, 132.12, 131.98, 131.92, 131.53, 131.51, 131.02, 131.00, 130.94, 130.84, 126.99, 126.96, 126.71, 126.68, 121.71, 121.69, 121.60, 121.58, 104.61, 104.36, 81.39, 80.99, 60.56 (d, J = 65.8 Hz), 58.10 (d, J = 68.6 Hz), 55.46, 54.91, 28.15, 28.05; ^{31}P NMR (243 MHz, C_6D_6): δ 28.04 (for major rotamer), 24.79 (for minor rotamer); HRMS (m/z) calcd for $C_{27}H_{28}NO_4PNa$ $[M+Na]^+$ 484.1648, found 484.1652; $[\alpha]_D^{25}$ = +352.1 (c = 0.20, $CHCl_3$); The *ee* was determined by HPLC analysis (Chiralpak OD-

RH, CH_3CN/H_2O = 50/50, v/v, 1.0 mL/min, 305 nm, t_R (major) = 6.4 min, t_R (minor) = 8.0 min), 76% *ee*.

1.5 Procedure for the preparation of diethyl (*S*)-(1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate 8:

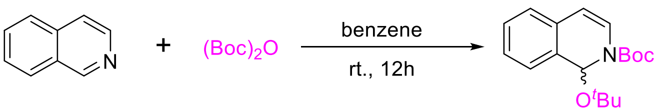


4ab **7** **8**

To a solution of tert-butyl 1-(diethoxyphosphoryl)isoquinoline-2(1*H*)-carboxylate **4ab** (0.1 mmol) in 5 ml EtOH was added Raney Nickel, the mixture was stirred under hydrogen atmosphere (1 atm) at room temperature for 10 h. The mixture was filtered through Celite, the solution was concentrated under reduced pressure to obtain **7**.

To a solution of **7** in 2 ml CH_2Cl_2 was added TFA 0.1 ml, the mixture was stirred at room temperature for 3 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography to obtain (*S*)-(1,2,3,4-tetrahydroisoquinolin-1-yl) phosphonate **8** as a colorless oil (24 mg, 0.089 mmol; 2steps 89% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 – 7.43 (m, 1H), 7.14 (dt, *J* = 7.1, 4.9 Hz, 3H), 4.47 (d, *J* = 16.3 Hz, 1H), 4.20 – 3.96 (m, 3H), 3.89 (dd, *J* = 8.2, 7.1 Hz, 1H), 3.40 (ddd, *J* = 12.2, 6.1, 2.1 Hz, 1H), 3.09 – 2.93 (m, 1H), 2.83 (dt, *J* = 5.8, 2.8 Hz, 2H), 2.19 (s, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$): δ 135.69 (d, J = 6.8 Hz), 129.93 (d, J = 3.9 Hz), 129.42 (d, J = 2.5 Hz), 128.00 (d, J = 4.1 Hz), 126.85 (d, J = 3.4 Hz), 125.62 (d, J = 3.3 Hz), 62.94 (d, J = 7.2 Hz), 62.18 (d, J = 7.3 Hz), 54.42 (d, J = 145.2 Hz), 40.86 (d, J = 5.9 Hz), 29.38 , 16.43 (d, J = 6.3 Hz), 16.31 (d, J = 6.3 Hz); **^{31}P NMR** (121 MHz, $CDCl_3$): *δ* 24.62; The *ee* was determined by HPLC analysis (Phenomenex C-1 column, Hexane/IPA = 90/10, v/v, 1.0 mL/min, 210 nm, t_R (major) = 8.6 min, t_R (minor) = 15.0 min), 79% *ee*. $[\alpha]_D^{22}$ = +23.1 (c = 1.00, $CHCl_3$) for an enantiomerically. (The *ee* was determined by HPLC analysis (Phenomenex C-1 column, Hexane/IPA = 90/10, v/v, 1.0 mL/min, 210 nm, t_R (major) = 9.2 min, t_R (minor) = 13.9 min), 75% *ee*. $[\alpha]_D^{22}$ = +19.3 (c = 1.00, $CHCl_3$) for an enantiomerically. *Chem. Sci*. 2016, **7**, 6940-6945)

1.6 Procedure for the preparation of tert-butyl 1-(tert-butoxy)isoquinoline-2(1H)-carboxylate A:



1a **3** **A**
96% yield by recrystallization

A mixture of isoquinoline (3.87 g, 30 mmol) and Boc2O (7.86g, 36 mmol) in benzene (30 mL) was stirred at room temperature for 12 h. After concentration in vacuo, the residue was purified by recrystallization frome Et_2O-hexane to give A(8.79g, 96%). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.37 – 7.15 (m, 4H), 6.88 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.66 (d, *J* = 1.5 Hz, 1H), 6.10 (d, *J* = 7.6 Hz, 1H), 1.52 (s, 9H), 1.30 (s, 9H). HRMS (m/z) calcd for $C_{18}H_{25}NO_3Na$ $[M+Na]^+$ 326.1732, found 326.1728.

2. NMR spectrum of 1,2-dihydroisoquinoline-1-ylphosphonates 4

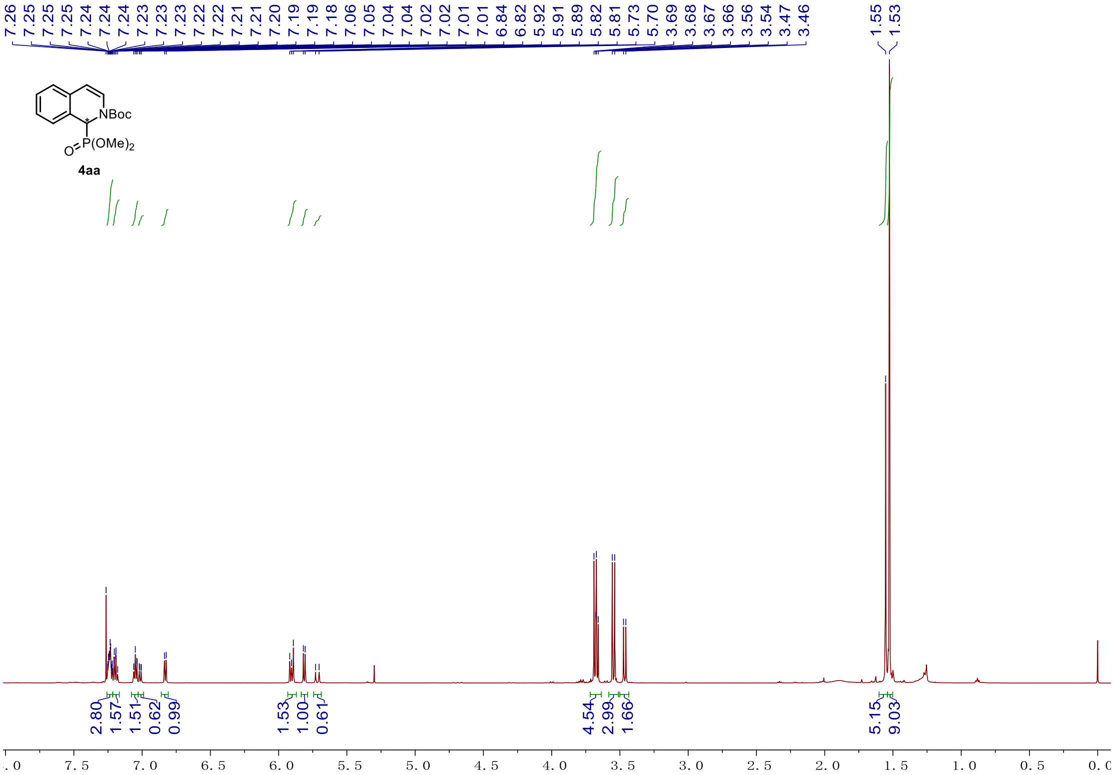


Fig.S 1 ^{1}H NMR of compound **4aa**

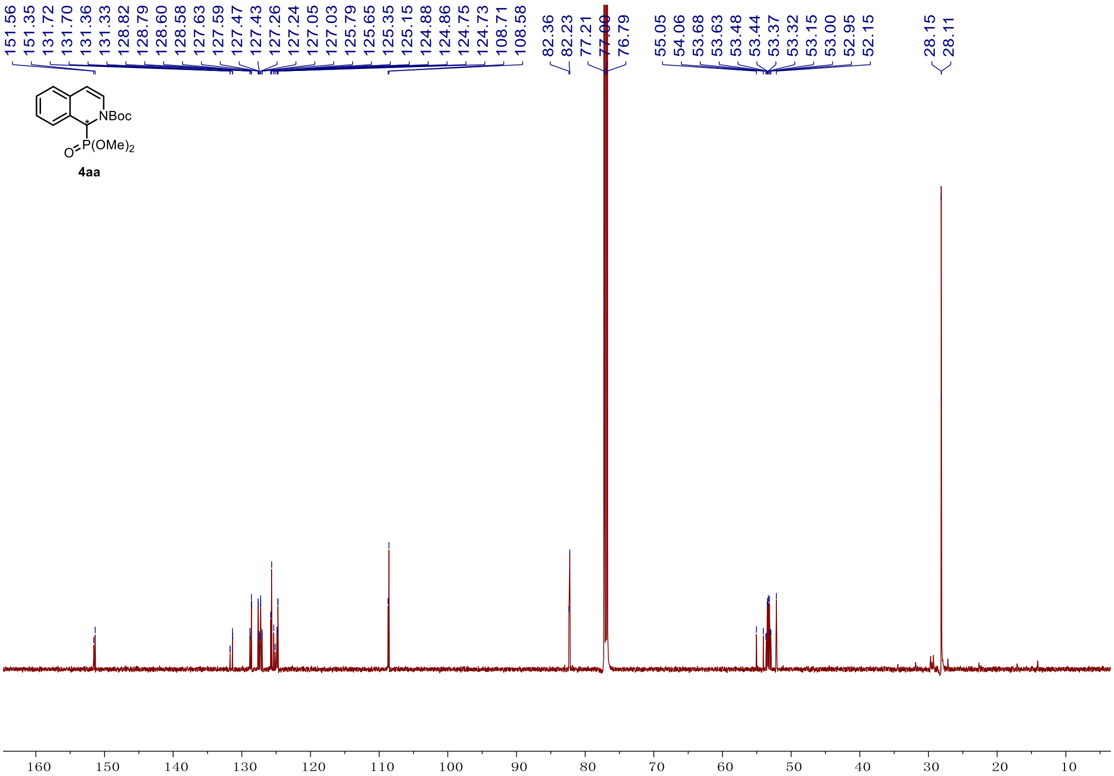


Fig.S 2 ^{13}C NMR of compound **4aa**

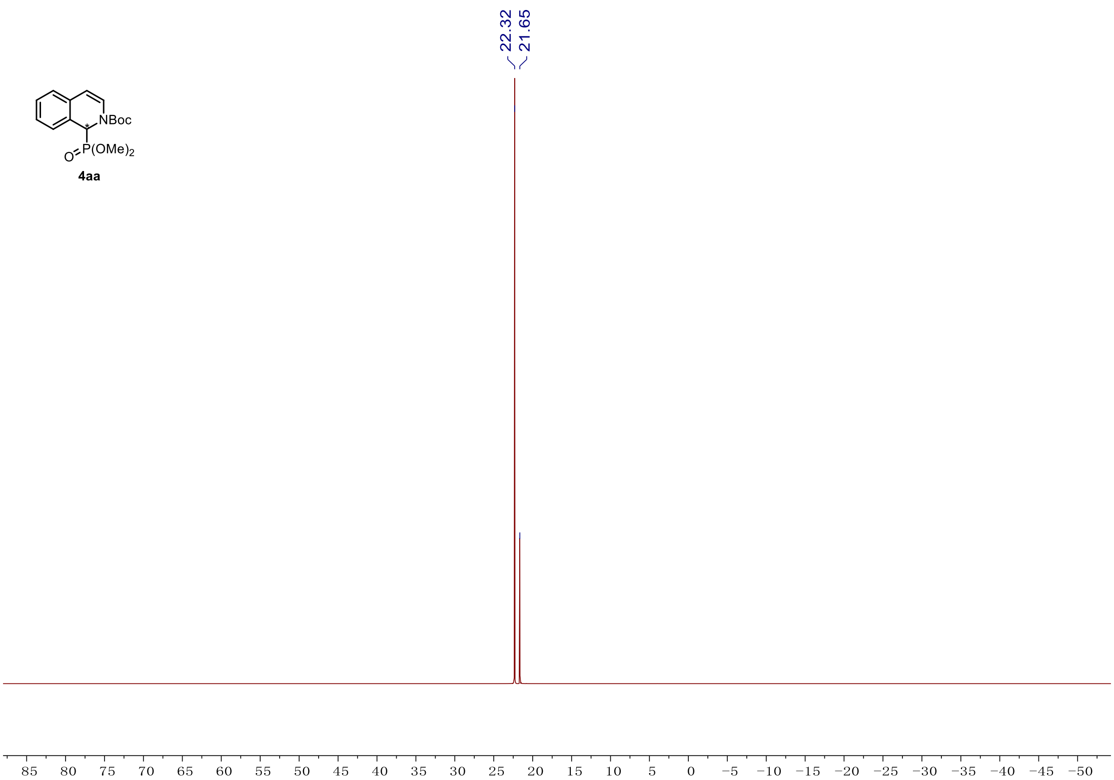


Fig.S 3 ^{31}P NMR of compound **4aa**

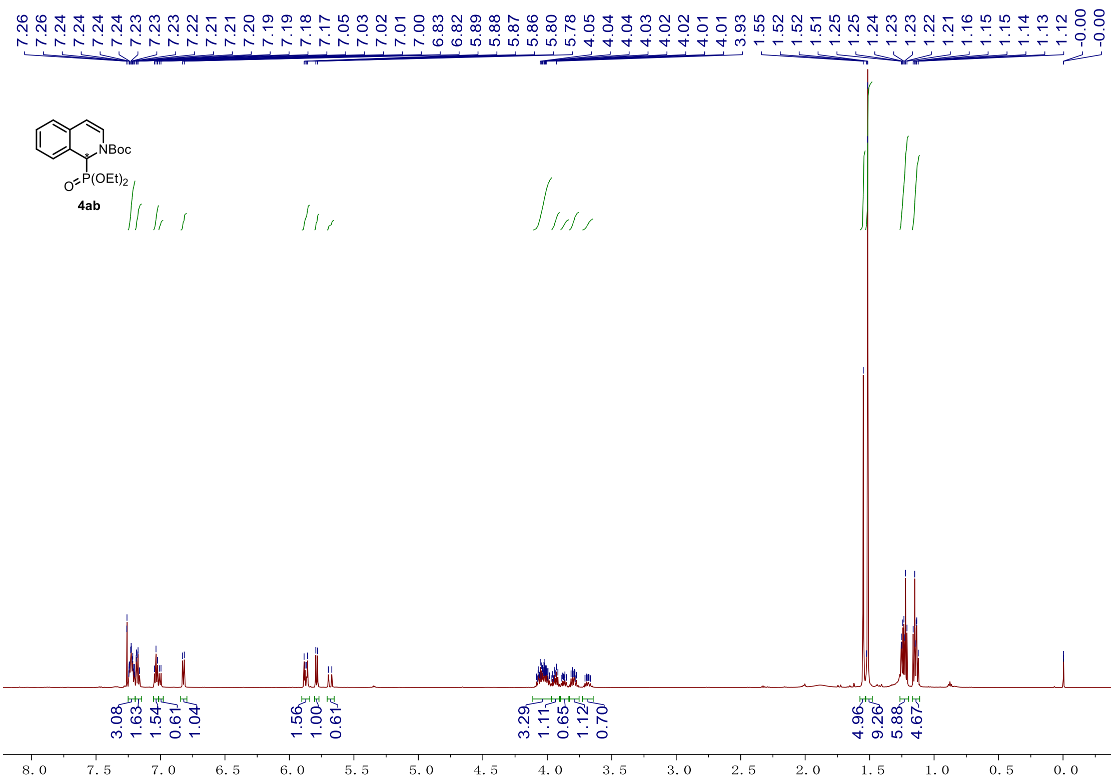


Fig.S 4 ^{1}H NMR of compound **4ab**

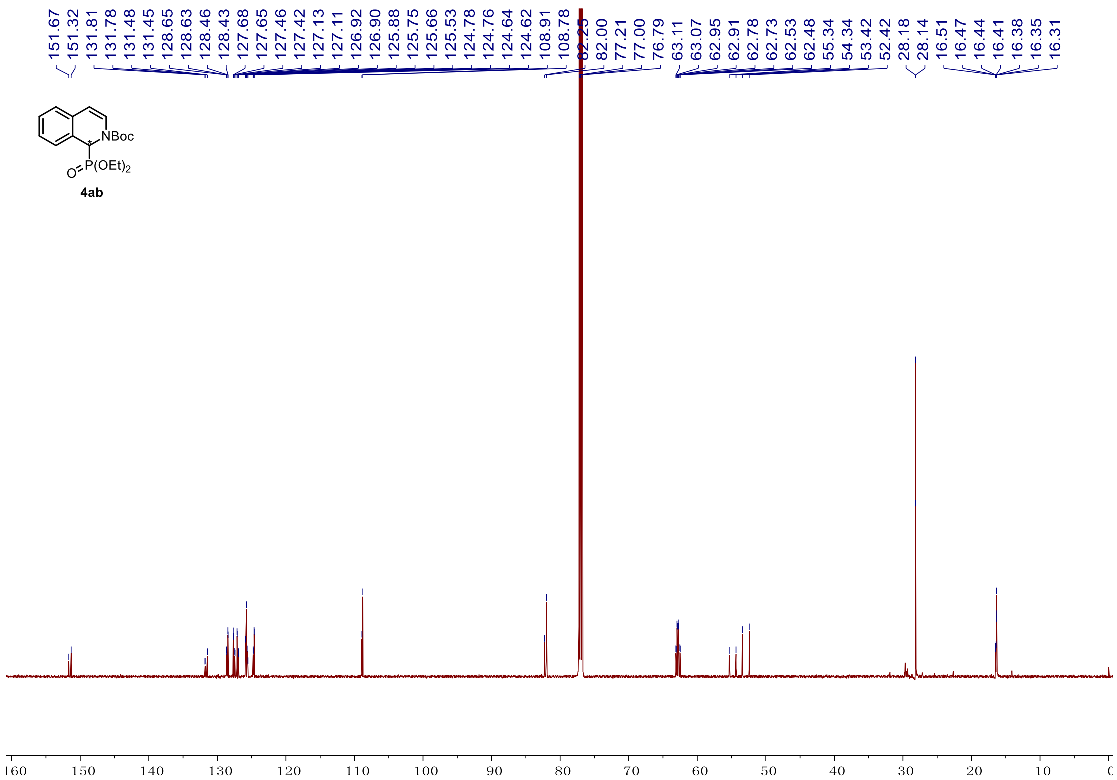


Fig.S 5 ^{13}C NMR of compound **4ab**

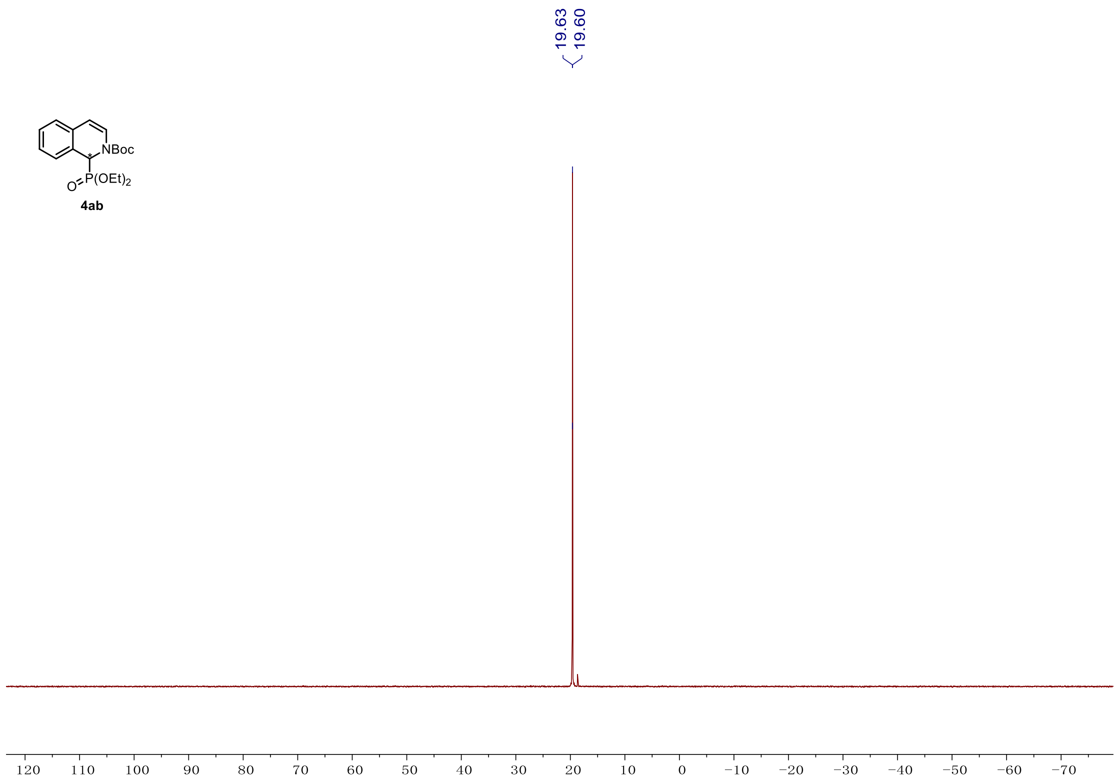


Fig.S 6 ^{31}P NMR of compound **4ab**

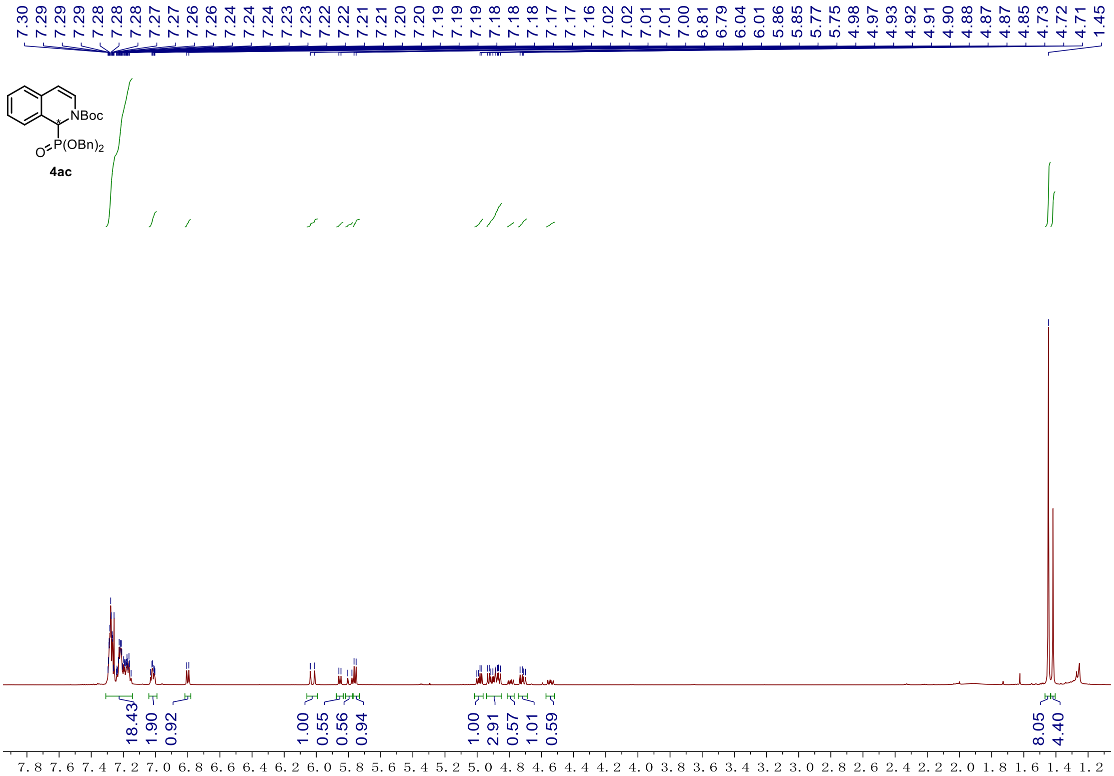


Fig.S 7 ^{1}H NMR of compound **4ac**

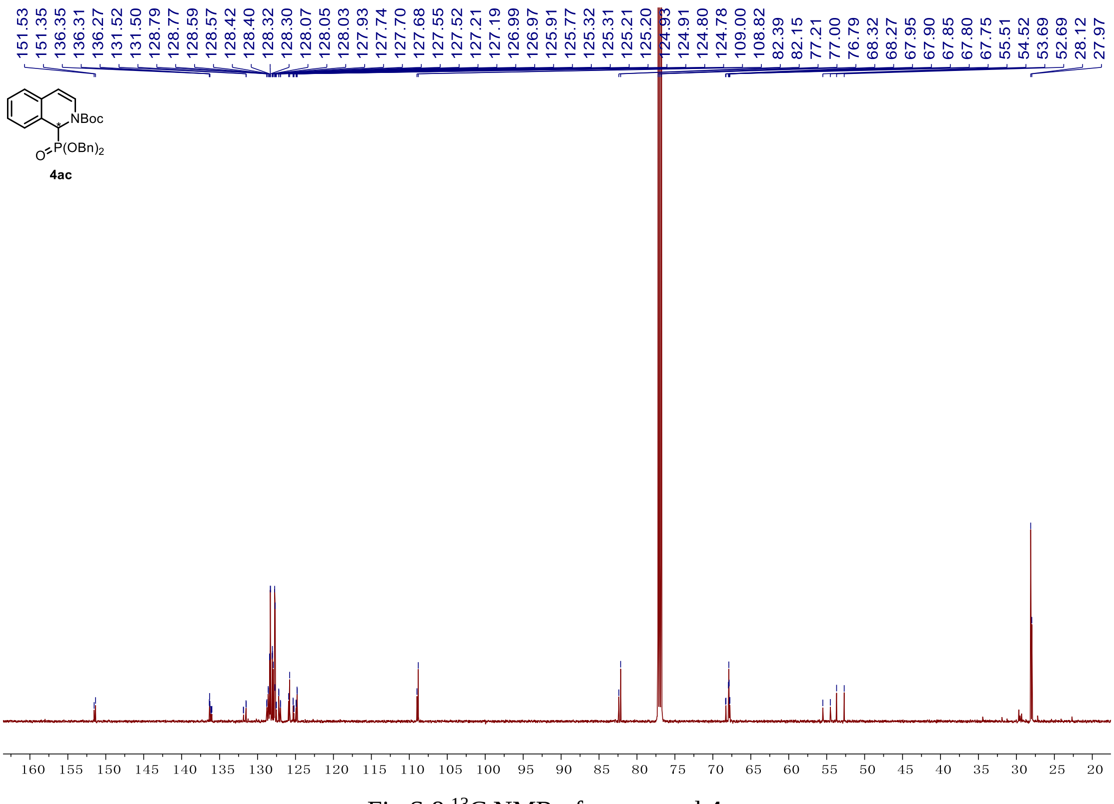


Fig.S 8 ^{13}C NMR of compound **4ac**

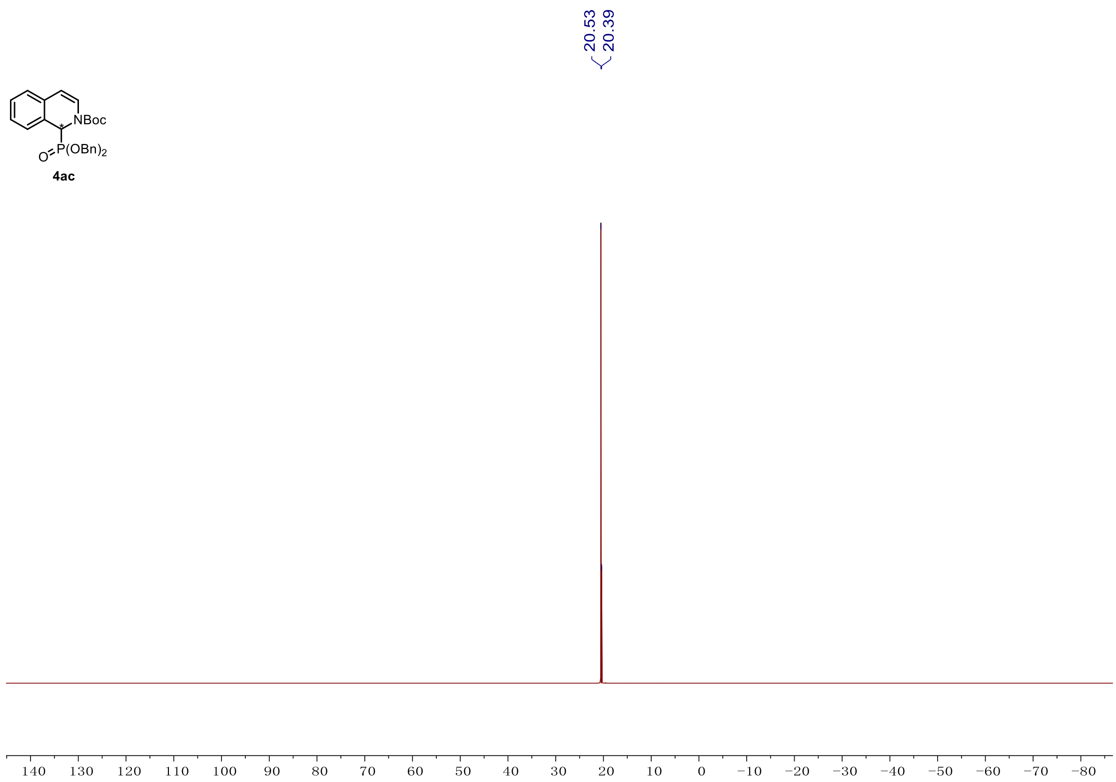


Fig.S 9 ^{31}P NMR of compound **4ac**

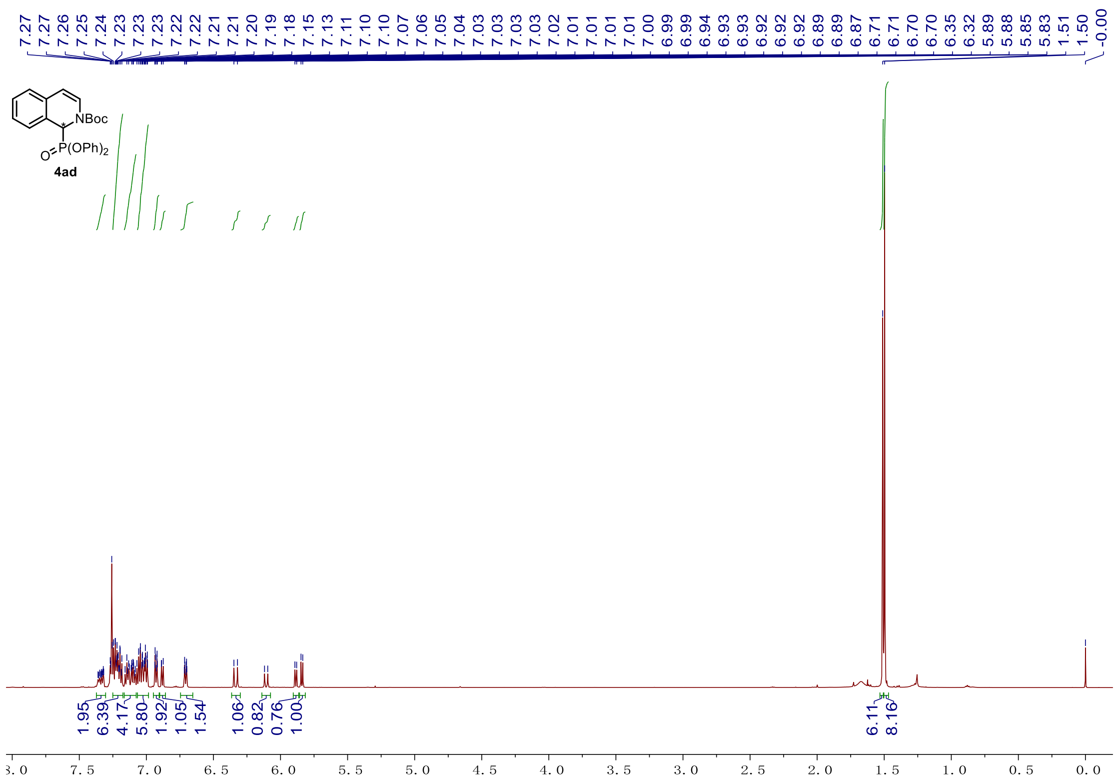


Fig.S 10 ^{1}H NMR of compound **4ad**

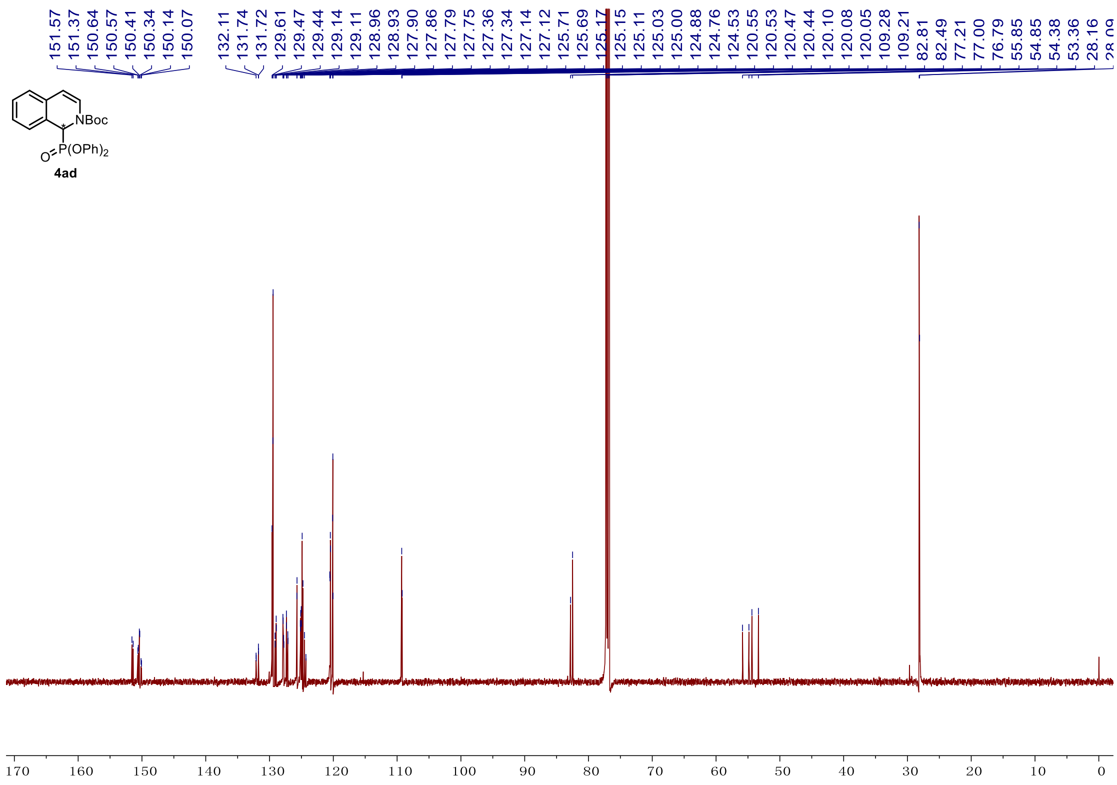


Fig.S 11 ^{13}C NMR of compound **4ad**

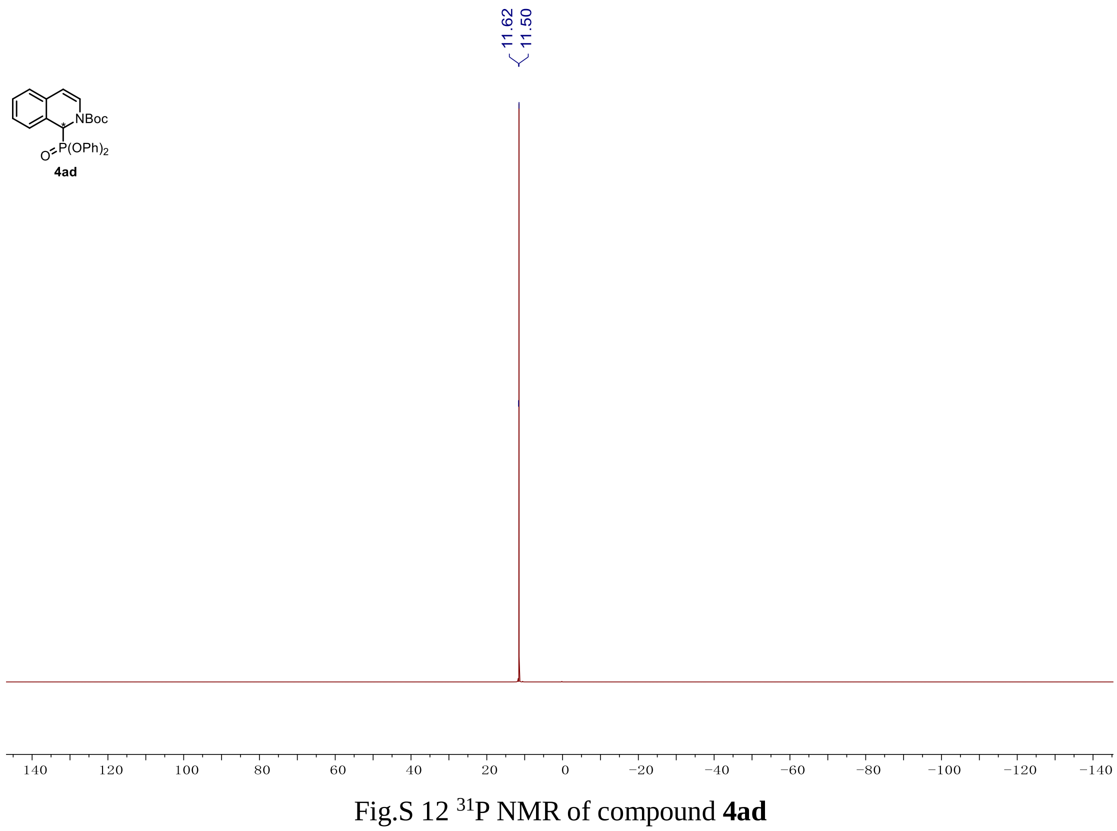


Fig.S 12 ^{31}P NMR of compound **4ad**

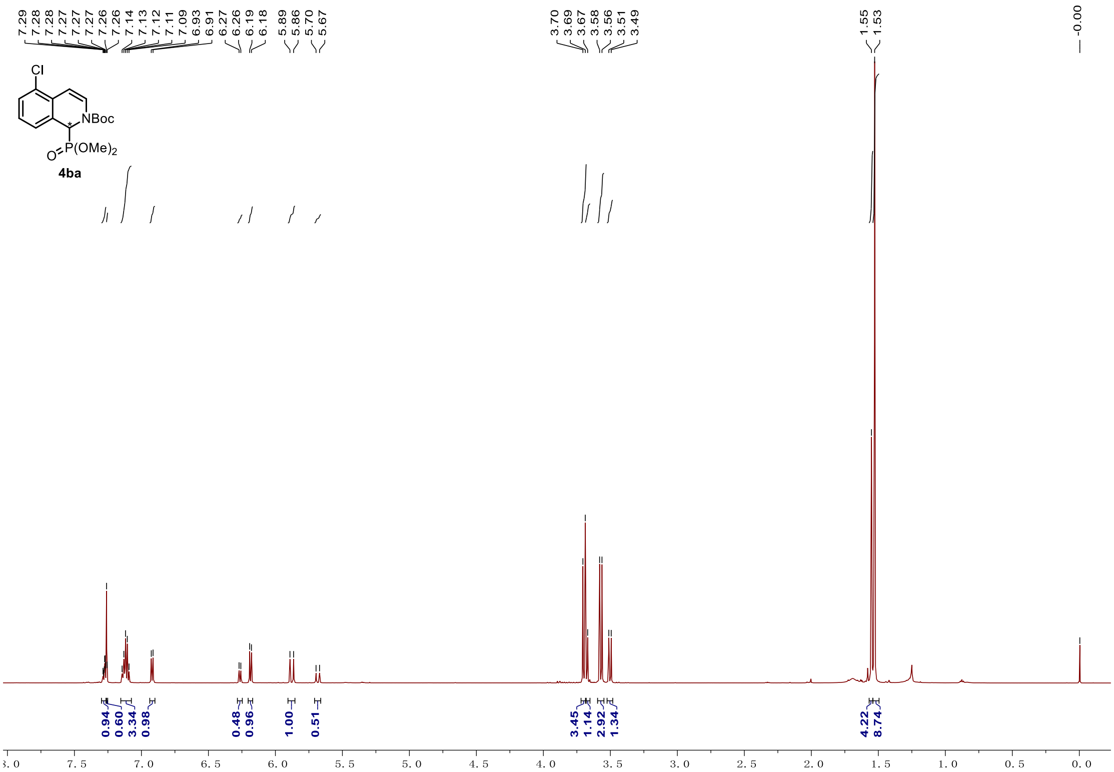


Fig.S 13 ^{1}H NMR of compound **4ba**

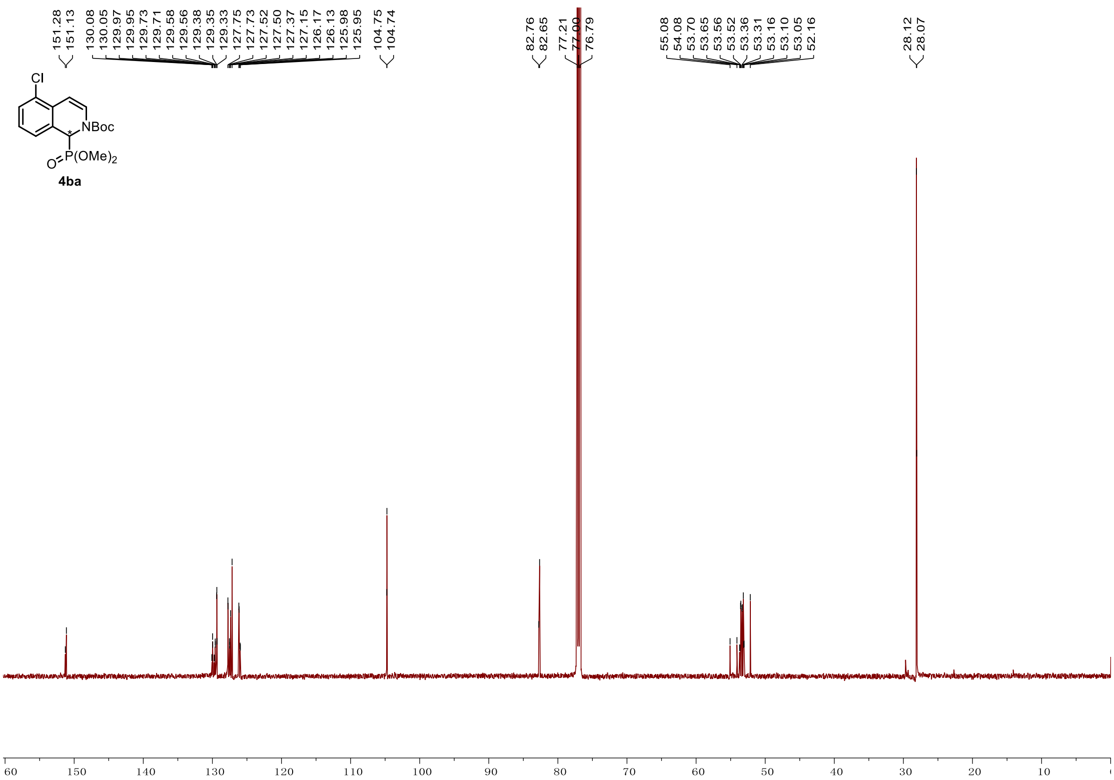


Fig.S 14 ^{13}C NMR of compound **4ba**

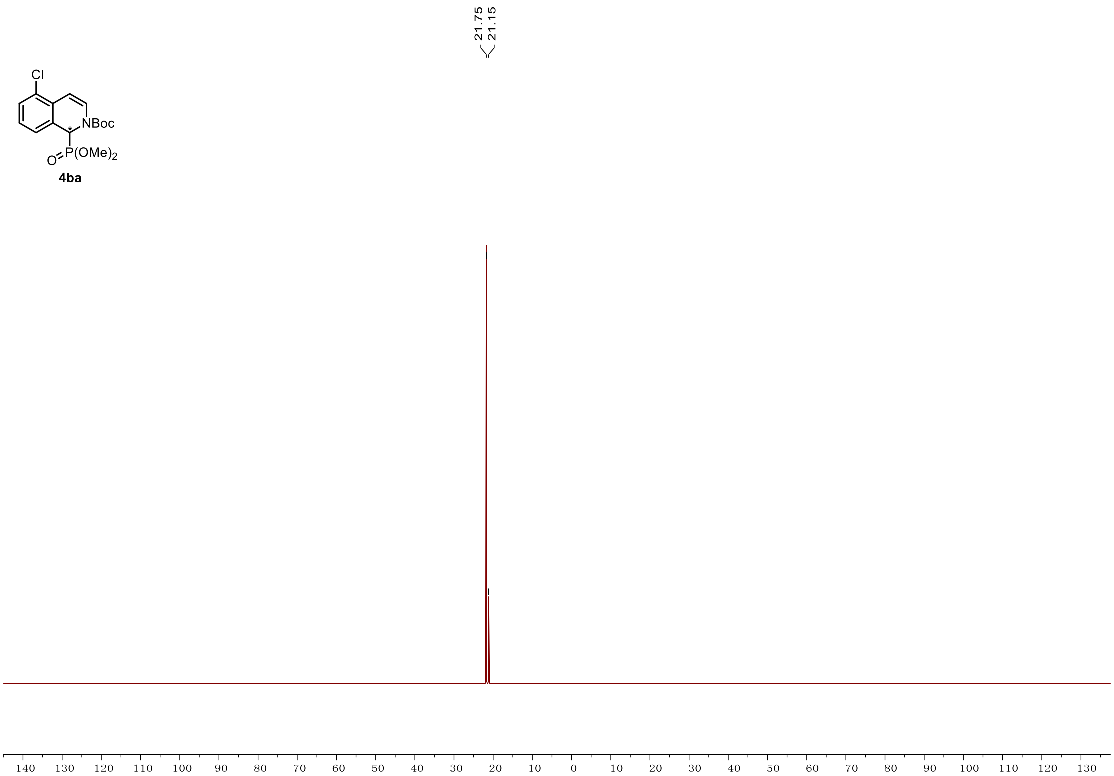


Fig.S 15 ^{31}P NMR of compound **4ba**

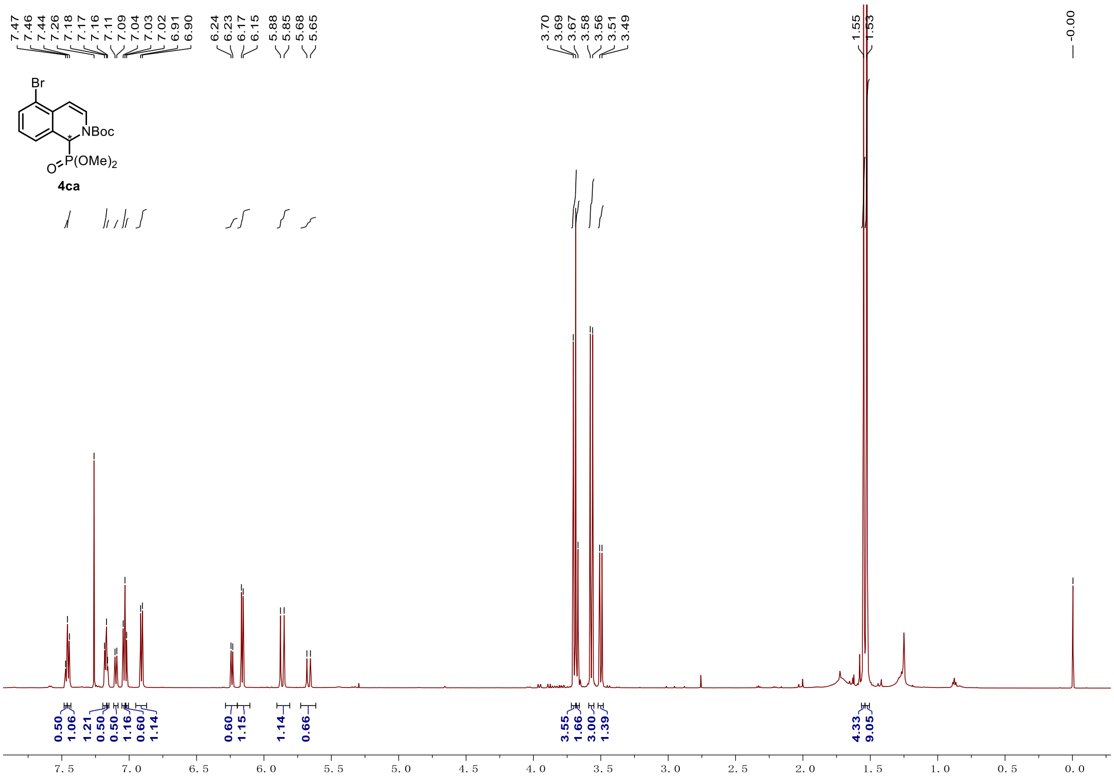


Fig.S 16 ^{1}H NMR of compound **4ca**

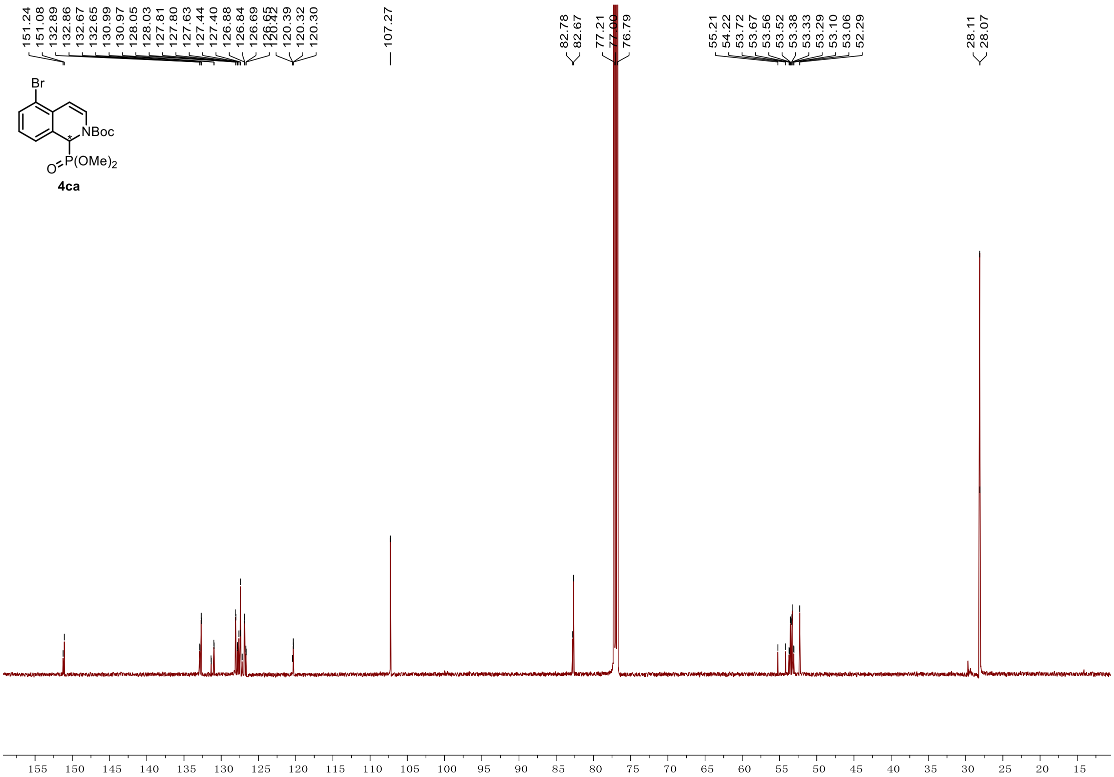


Fig.S 17 ^{13}C NMR of compound **4ca**

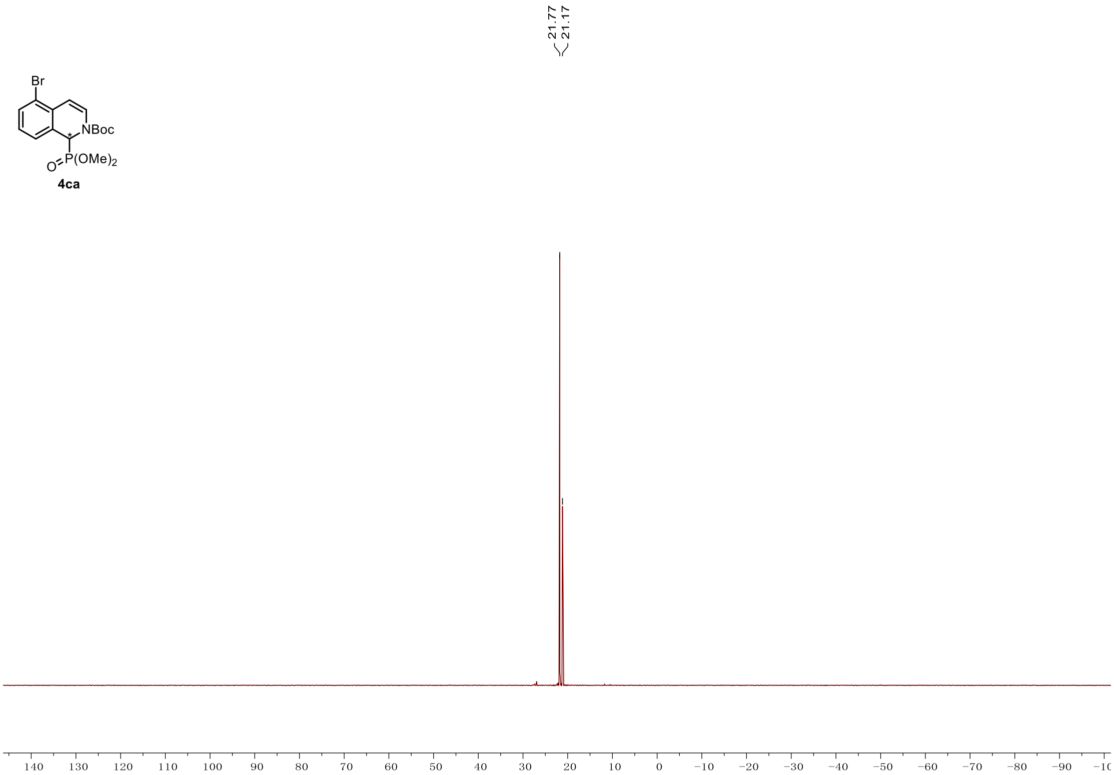


Fig.S 18 ^{31}P NMR of compound **4ca**

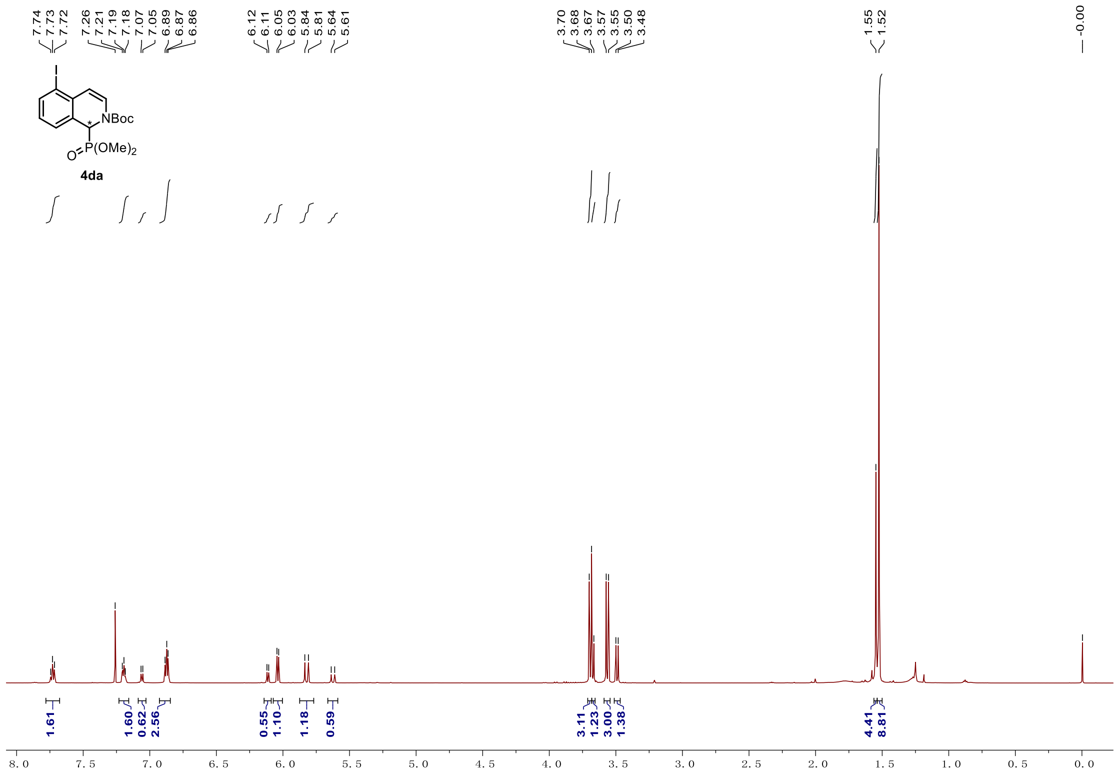


Fig.S 19 ^{1}H NMR of compound **4da**

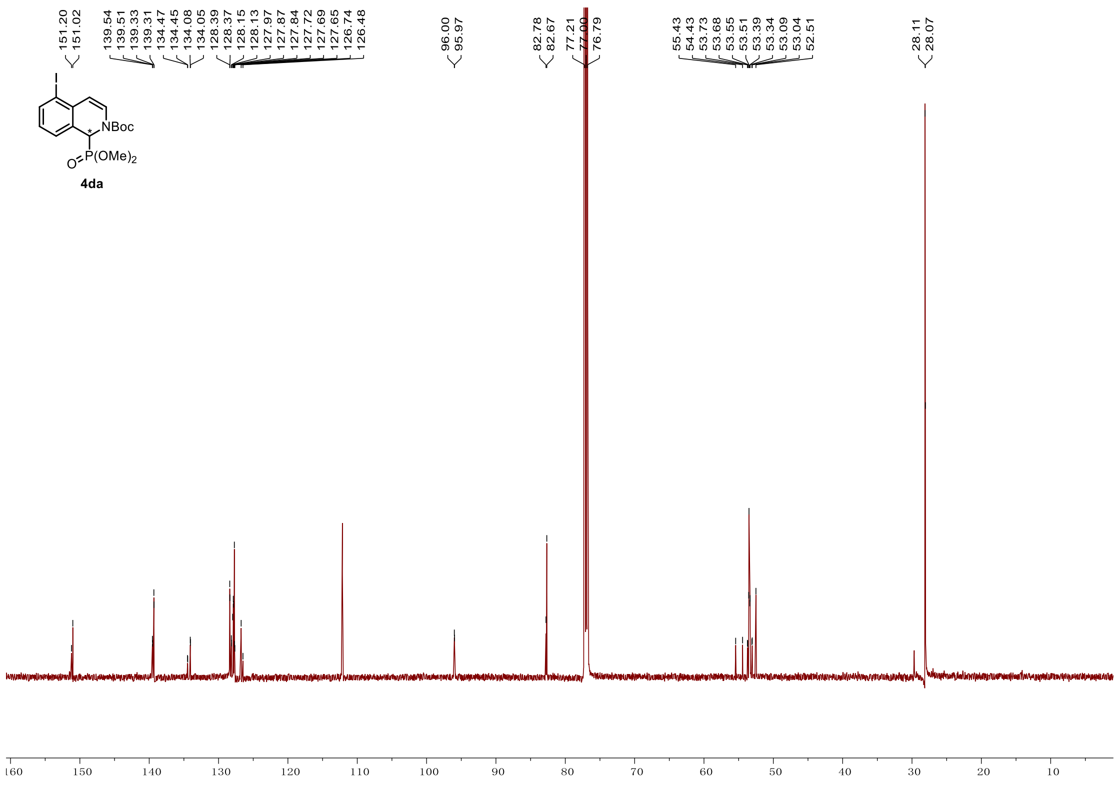


Fig.S 20 ^{13}C NMR of compound **4da**

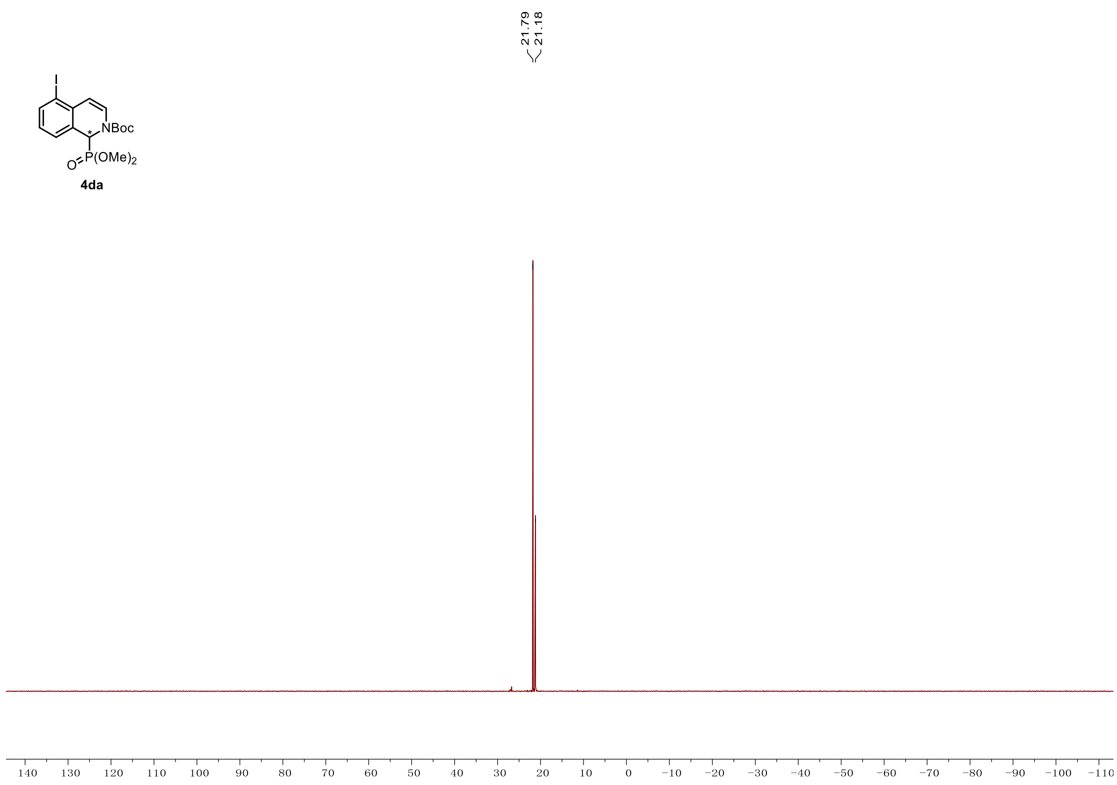


Fig.S 21 ^{31}P NMR of compound **4da**

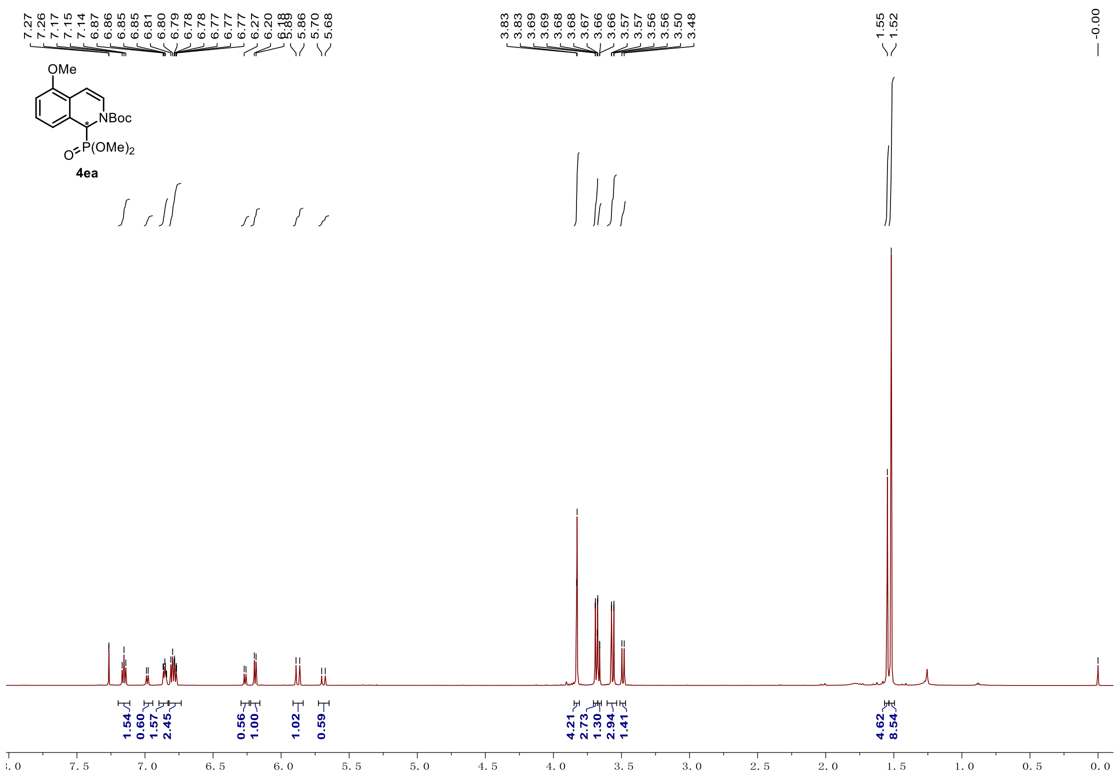


Fig.S 22 ^{1}H NMR of compound **4ea**

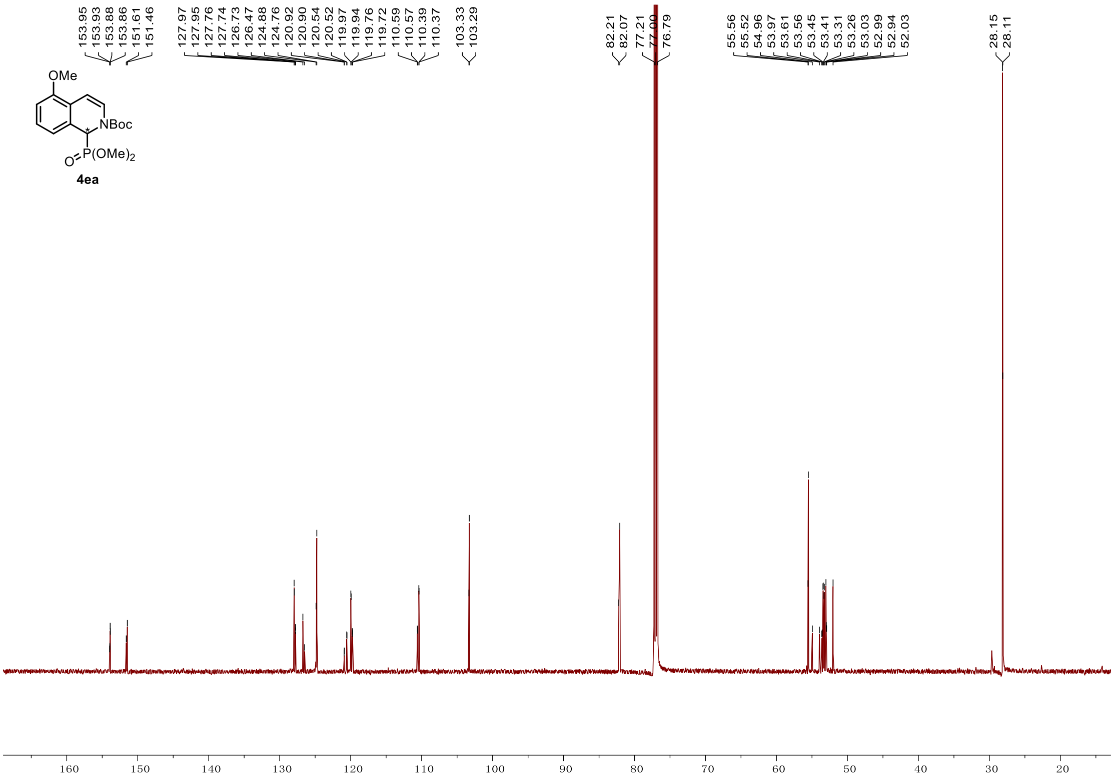


Fig.S 23 ^{13}C NMR of compound **4ea**

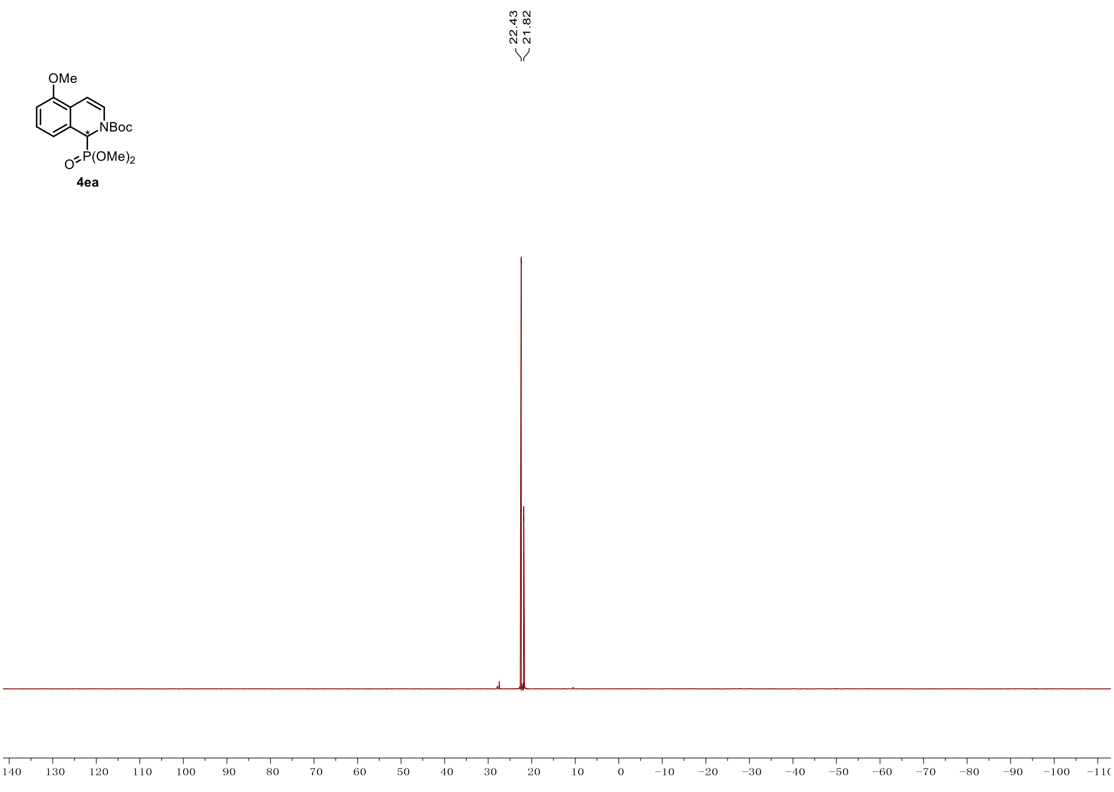


Fig.S 24 ^{31}P NMR of compound **4ea**

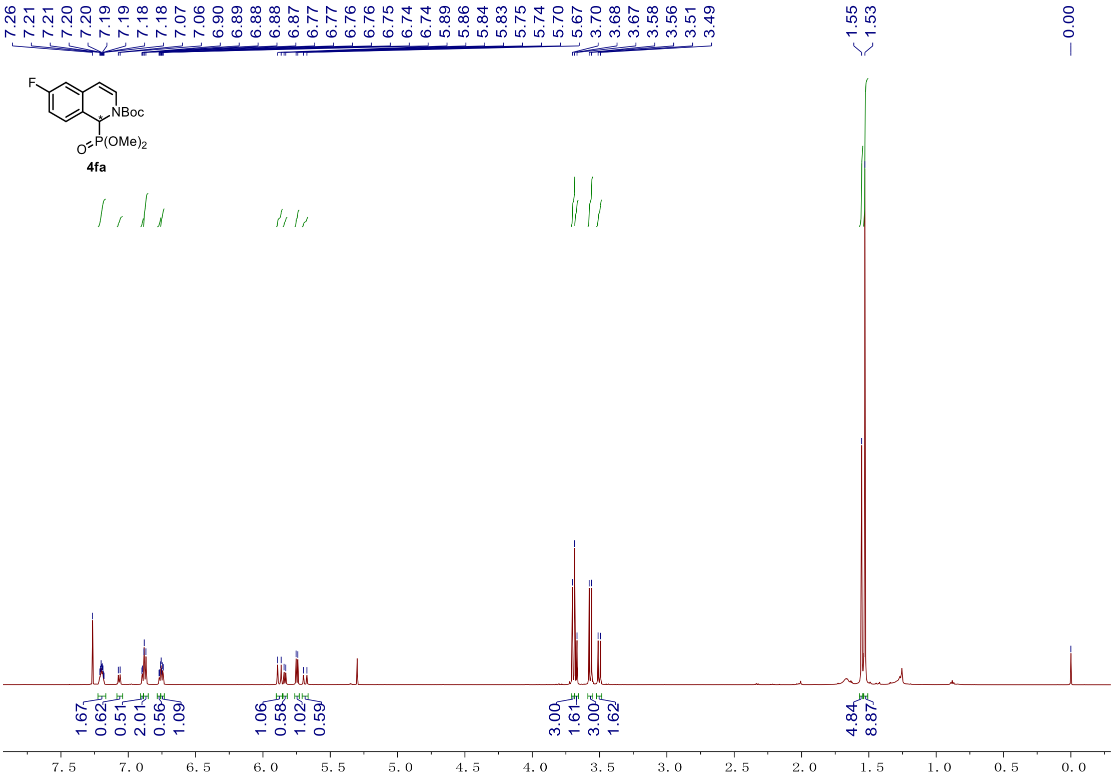


Fig.S 25 ^{1}H NMR of compound **4fa**

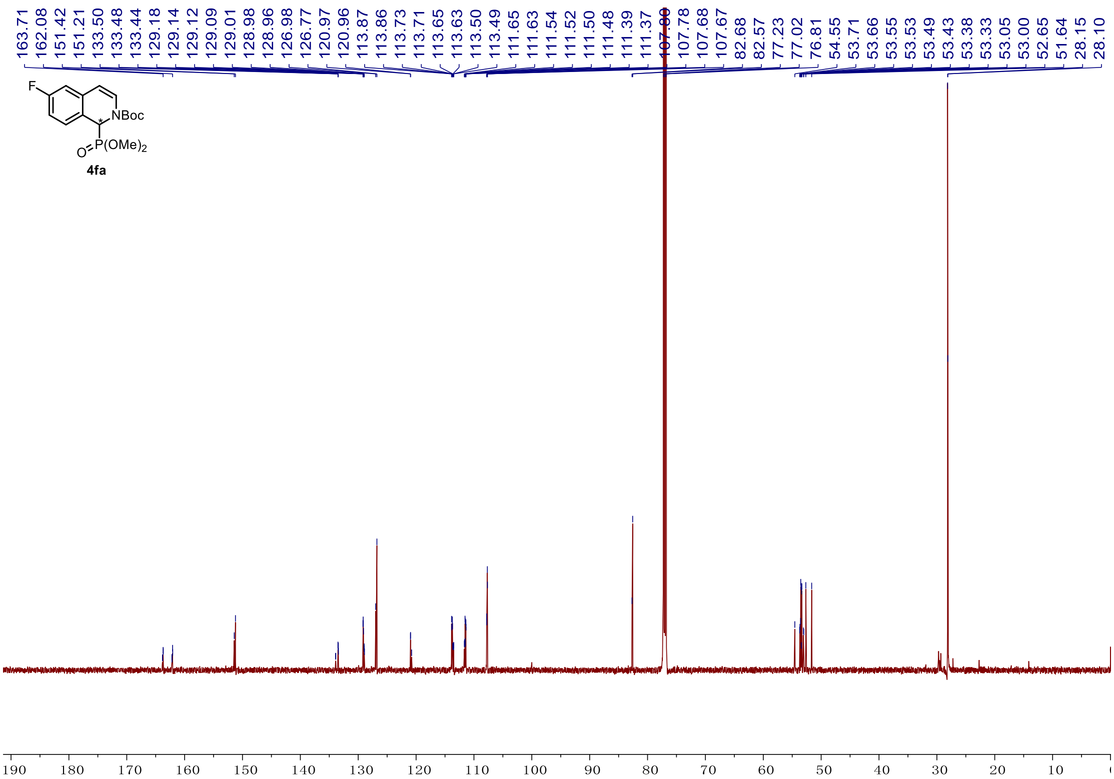


Fig.S 26 ^{13}C NMR of compound **4fa**

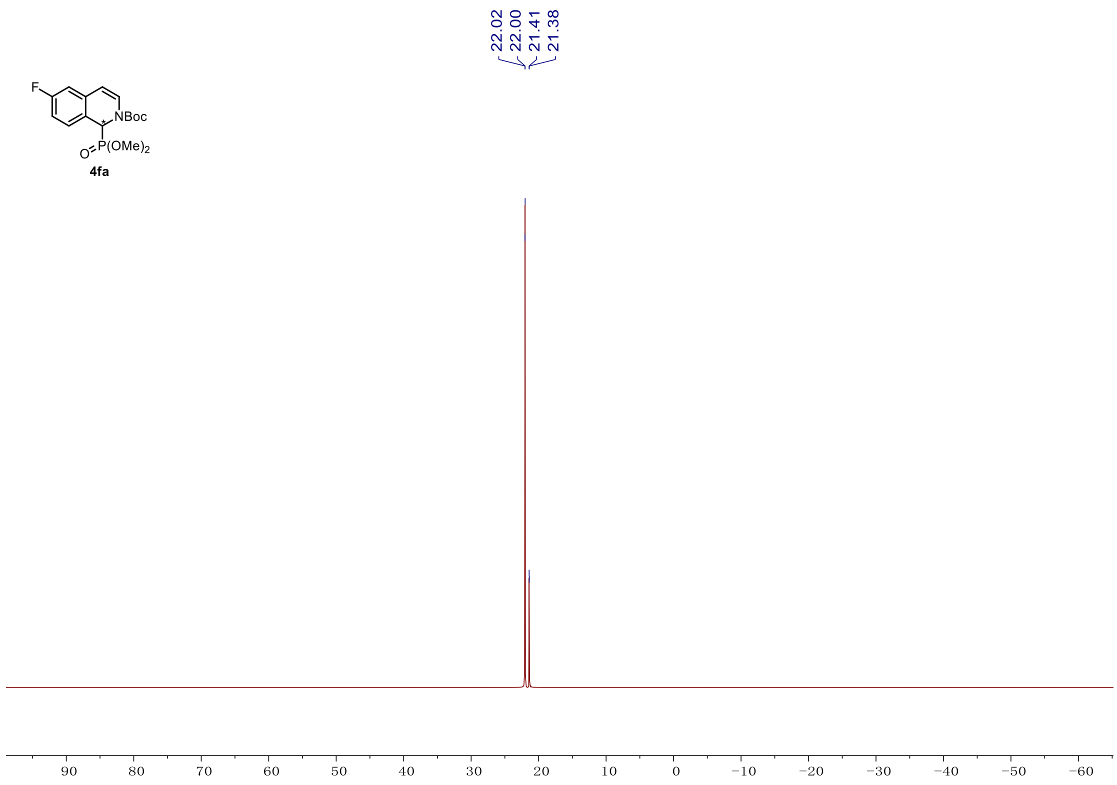


Fig.S 27 ^{31}P NMR of compound **4fa**

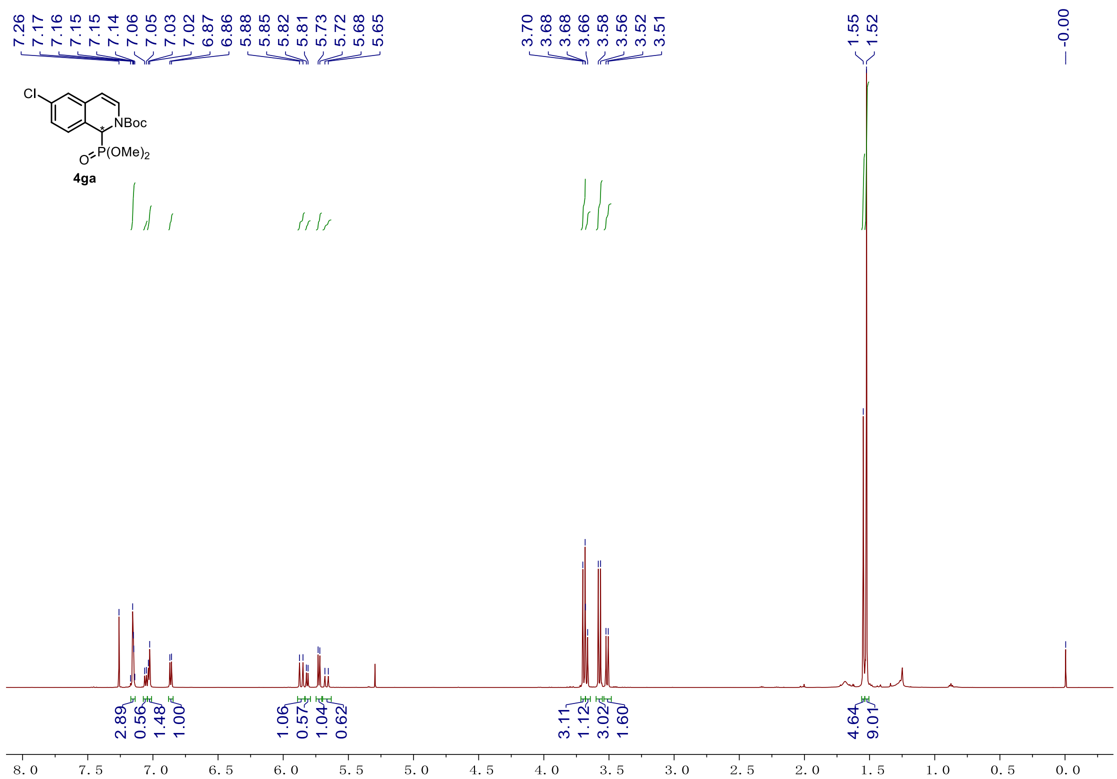


Fig.S 28 ^{1}H NMR of compound **4ga**

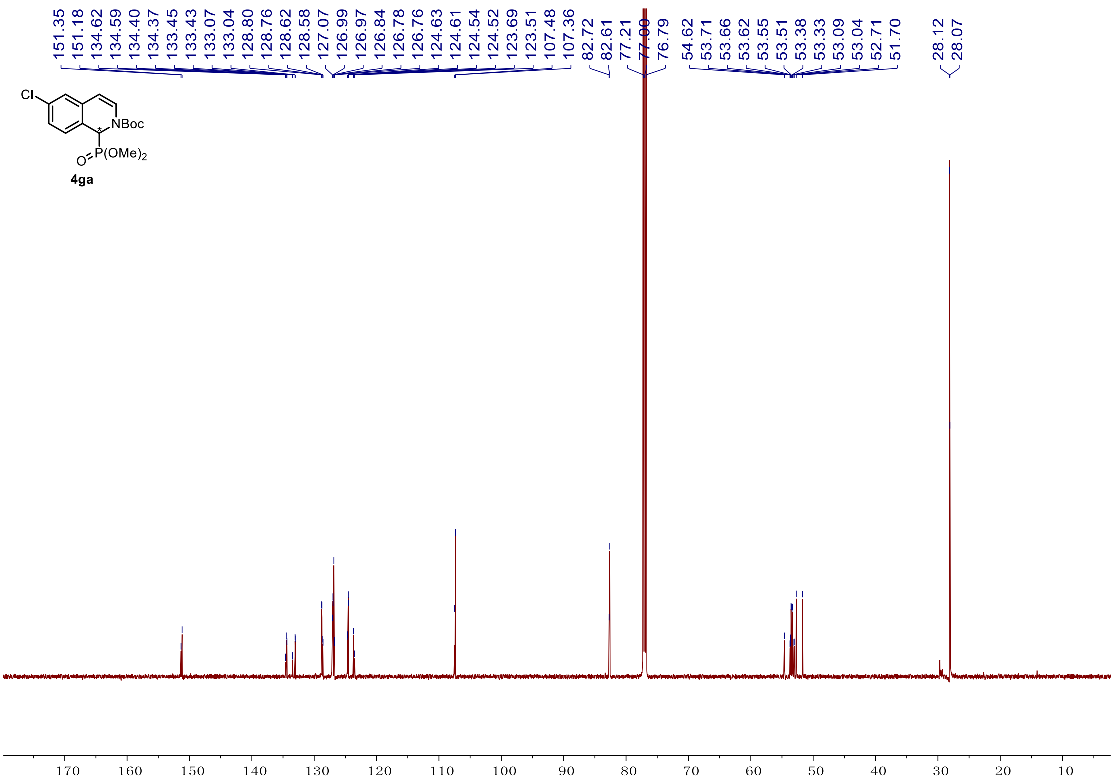


Fig.S 29 ^{13}C NMR of compound **4ga**

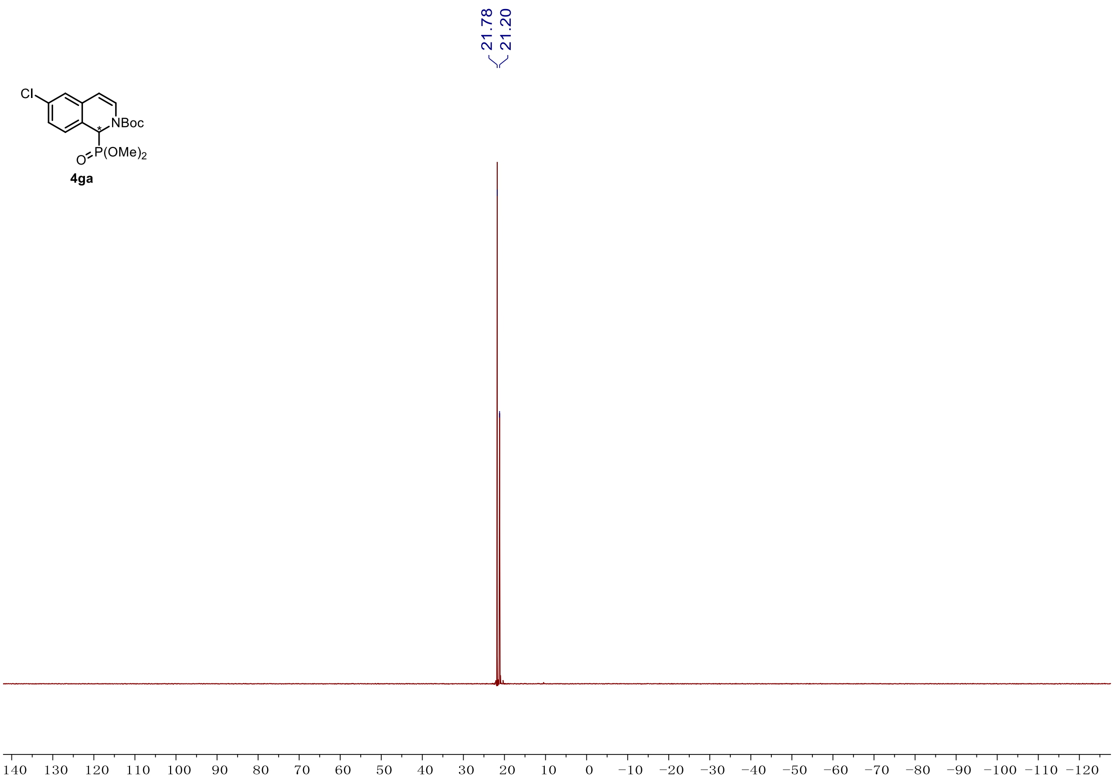


Fig.S 30 ^{31}P NMR of compound **4ga**

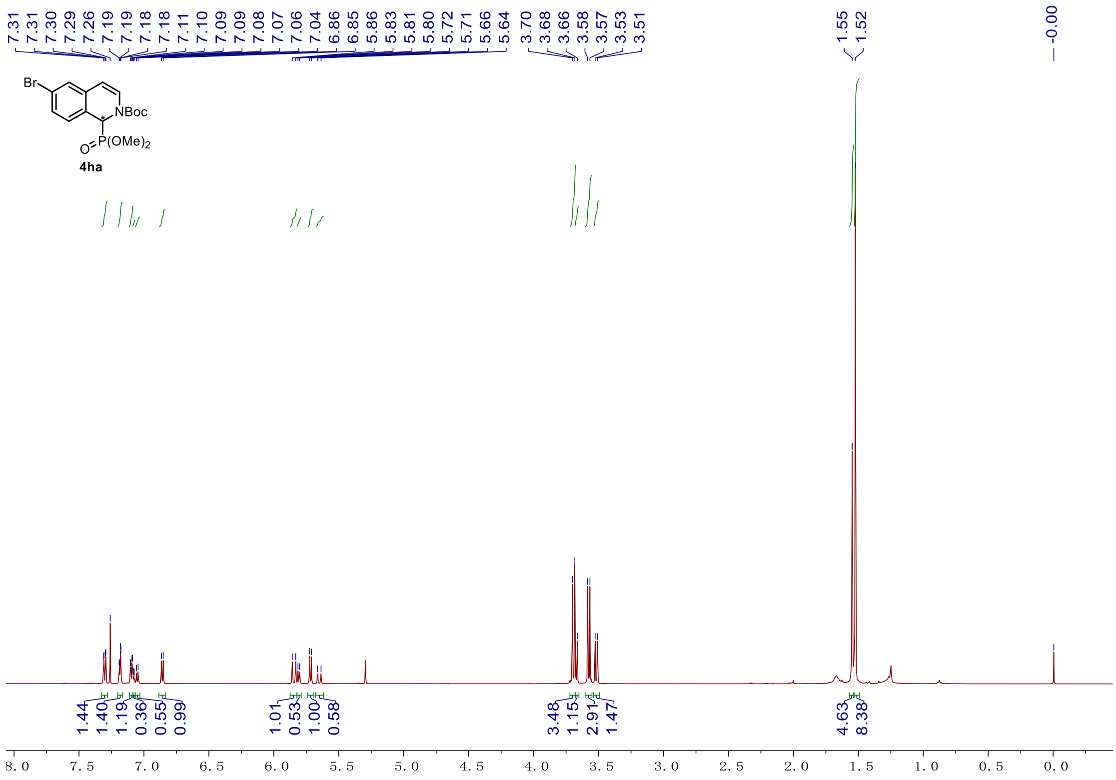


Fig.S 31 ^{1}H NMR of compound **4ha**

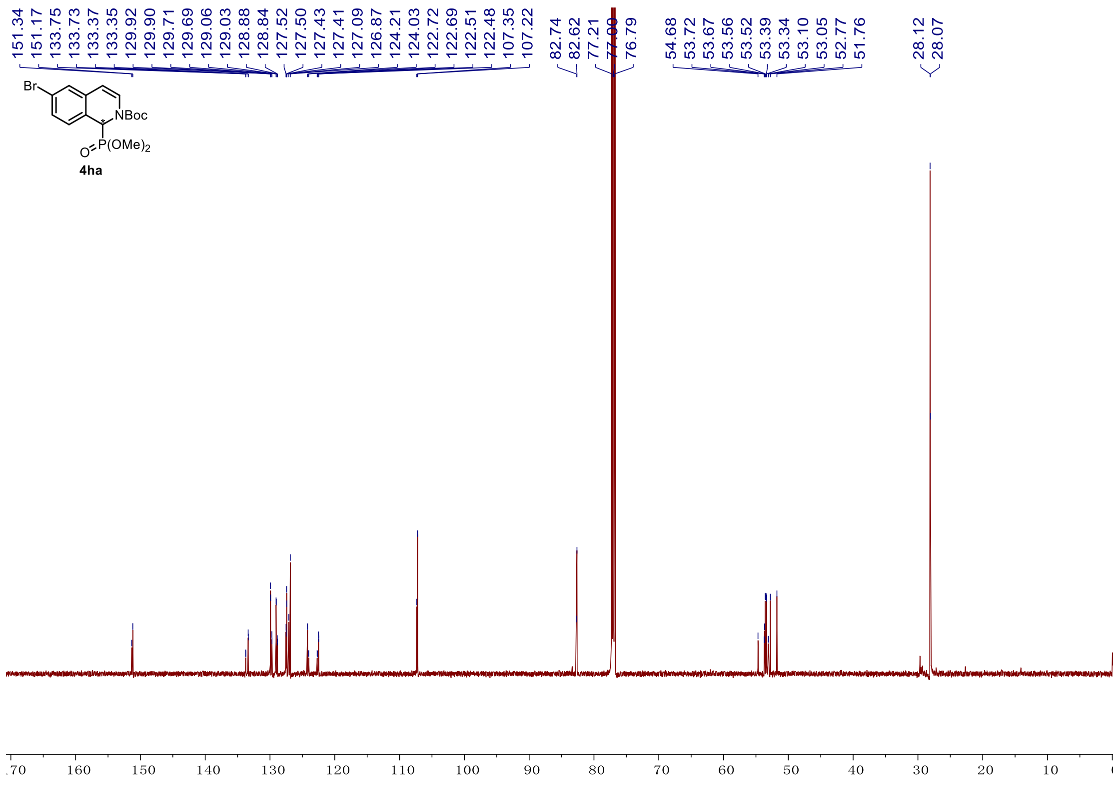


Fig.S 32 ^{13}C NMR of compound **4ha**

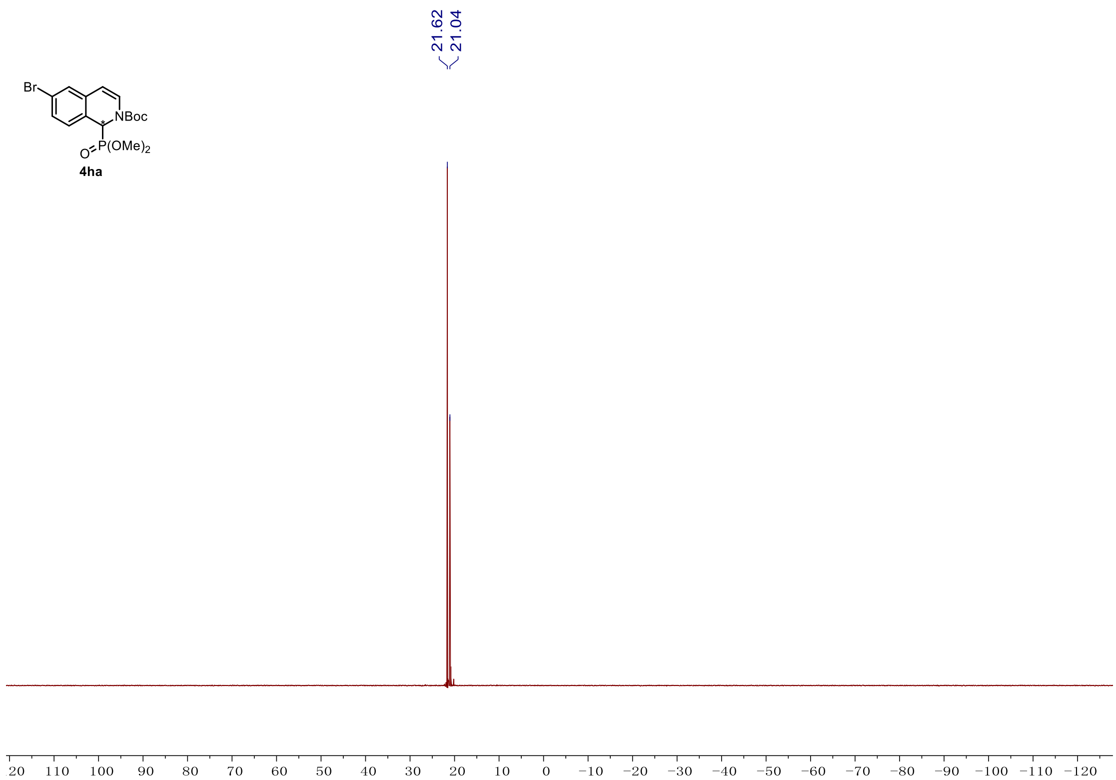


Fig.S 33 ^{31}P NMR of compound **4ha**

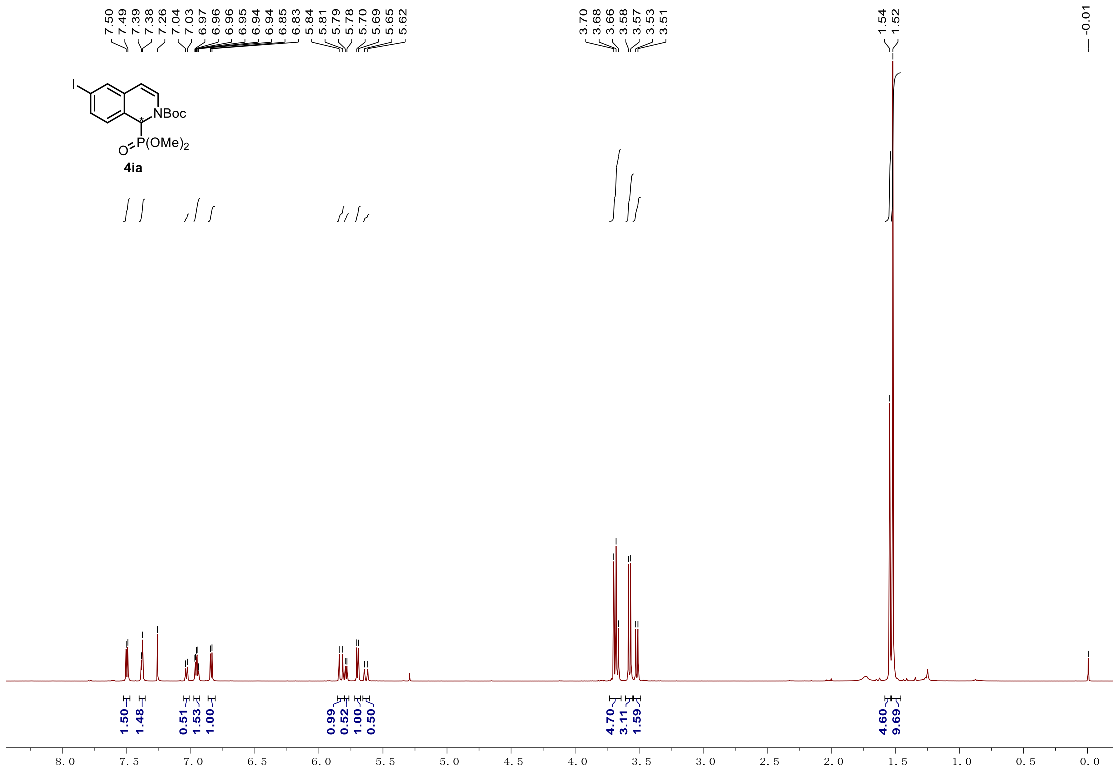


Fig.S 34 ^{1}H NMR of compound **4ia**

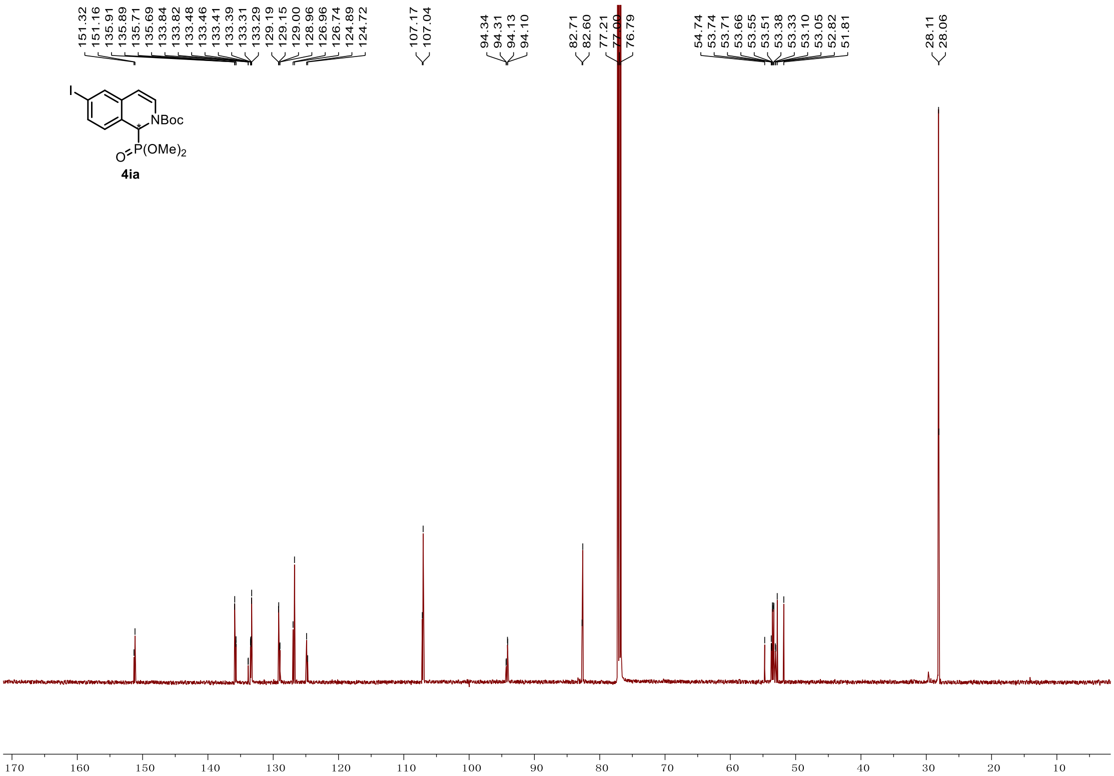


Fig.S 35 ^{13}C NMR of compound **4ia**

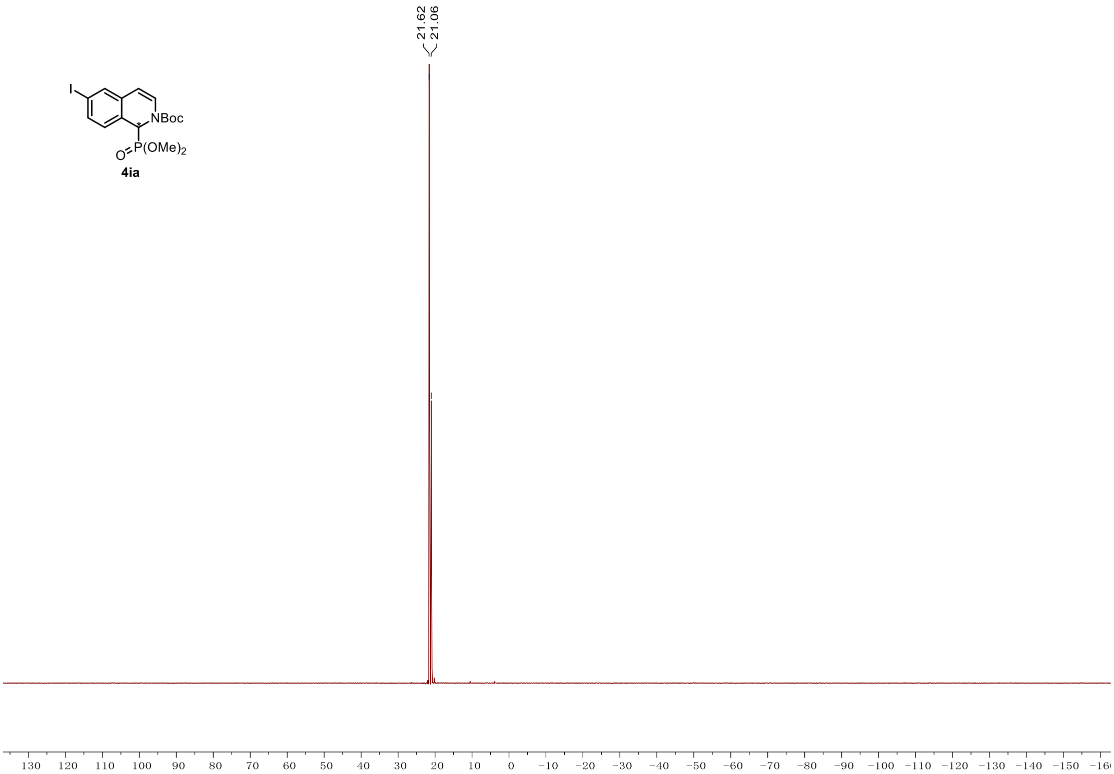


Fig.S 36 ^{31}P NMR of compound **4ia**

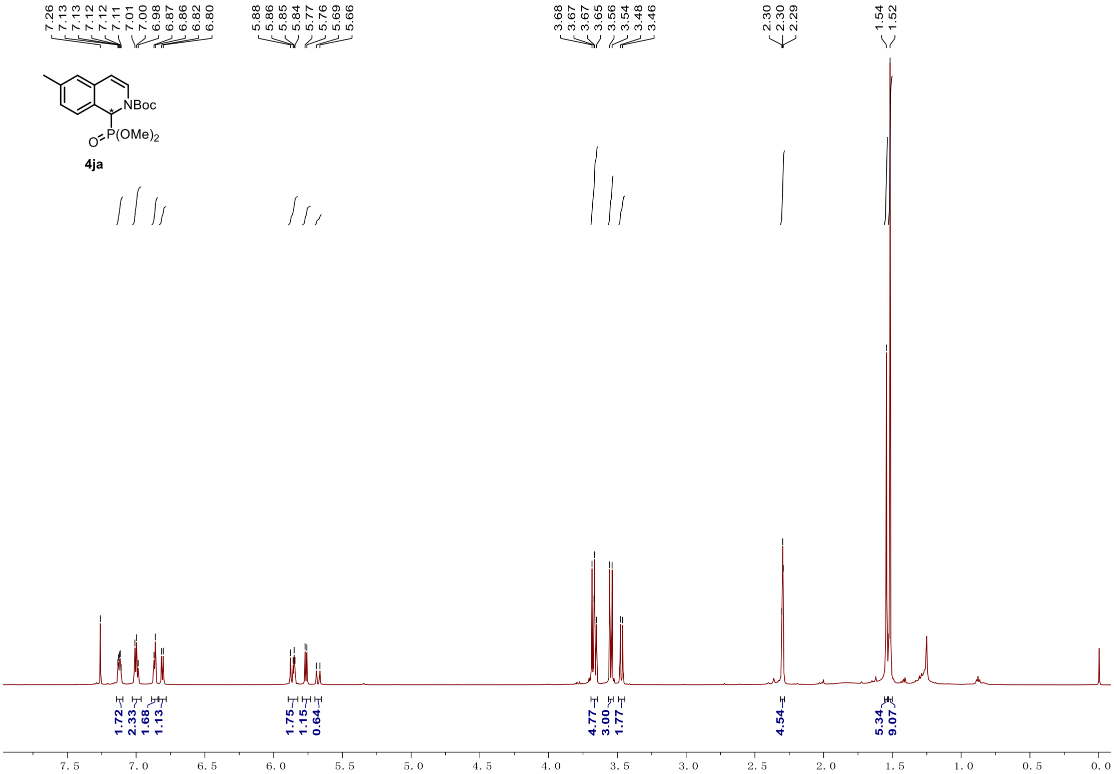


Fig.S 37 ^{1}H NMR of compound **4ja**

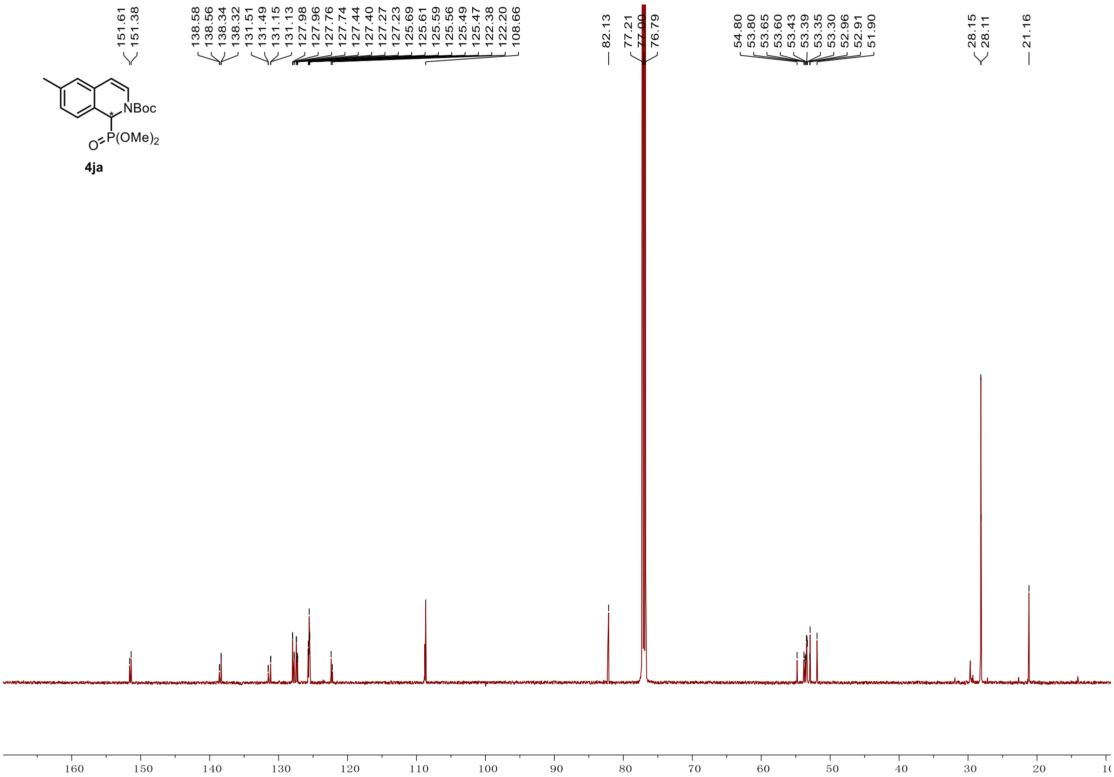


Fig.S 38 ^{13}C NMR of compound **4ja**

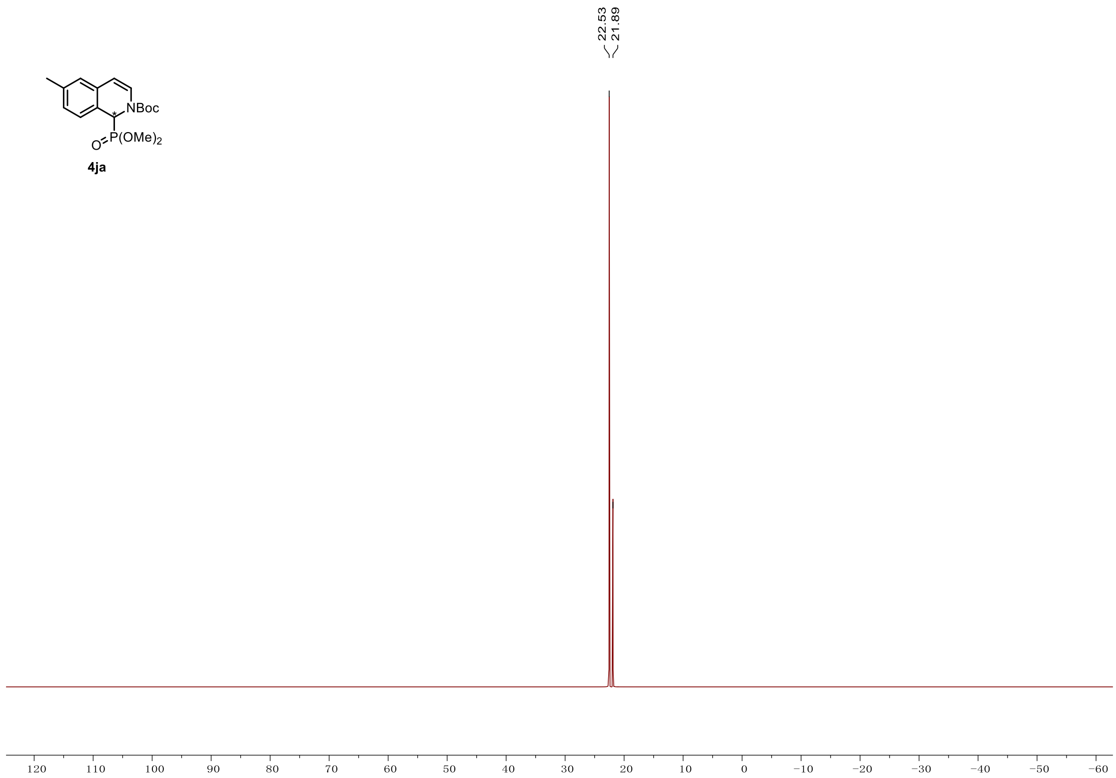


Fig.S 39 ^{31}P NMR of compound **4ja**

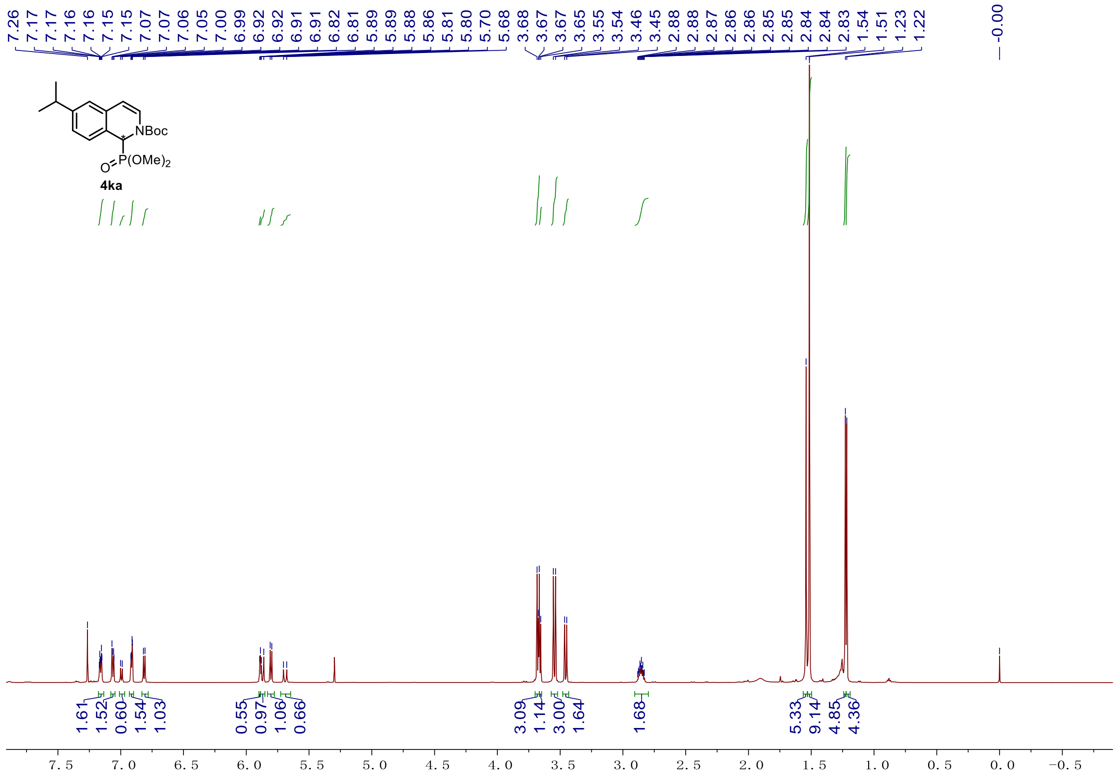


Fig.S 40 ^{1}H NMR of compound **4ka**

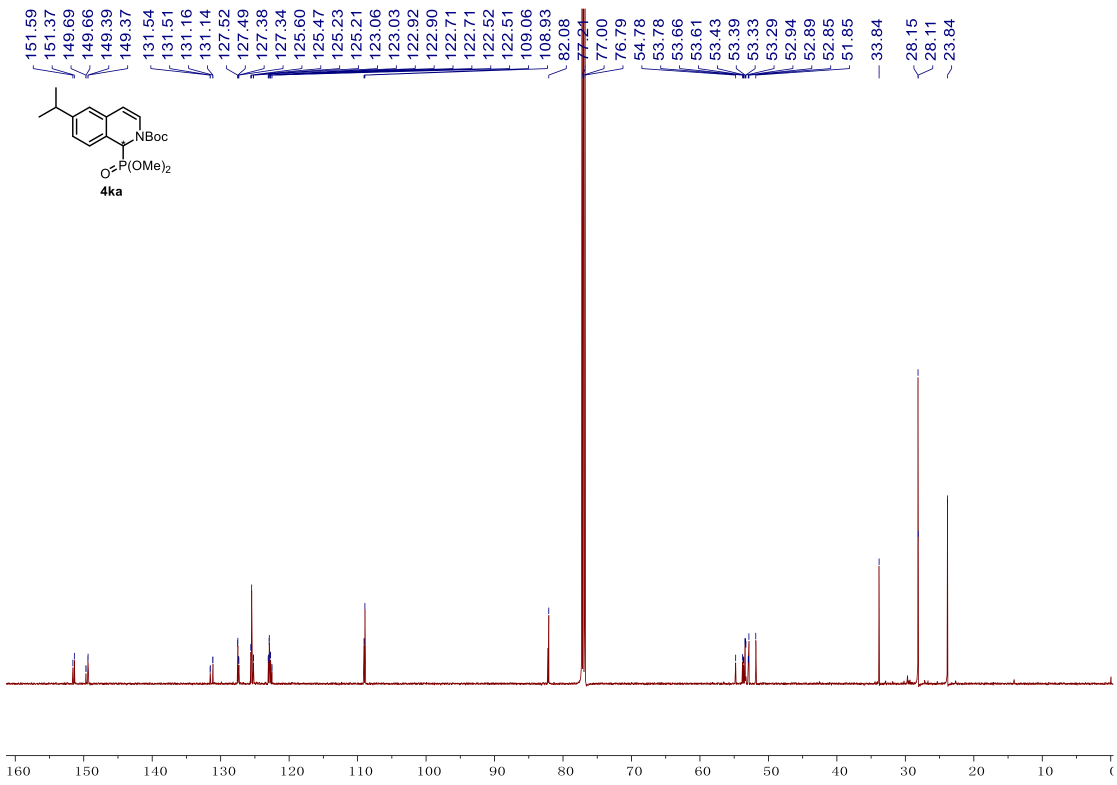


Fig.S 41 ^{13}C NMR of compound **4ka**

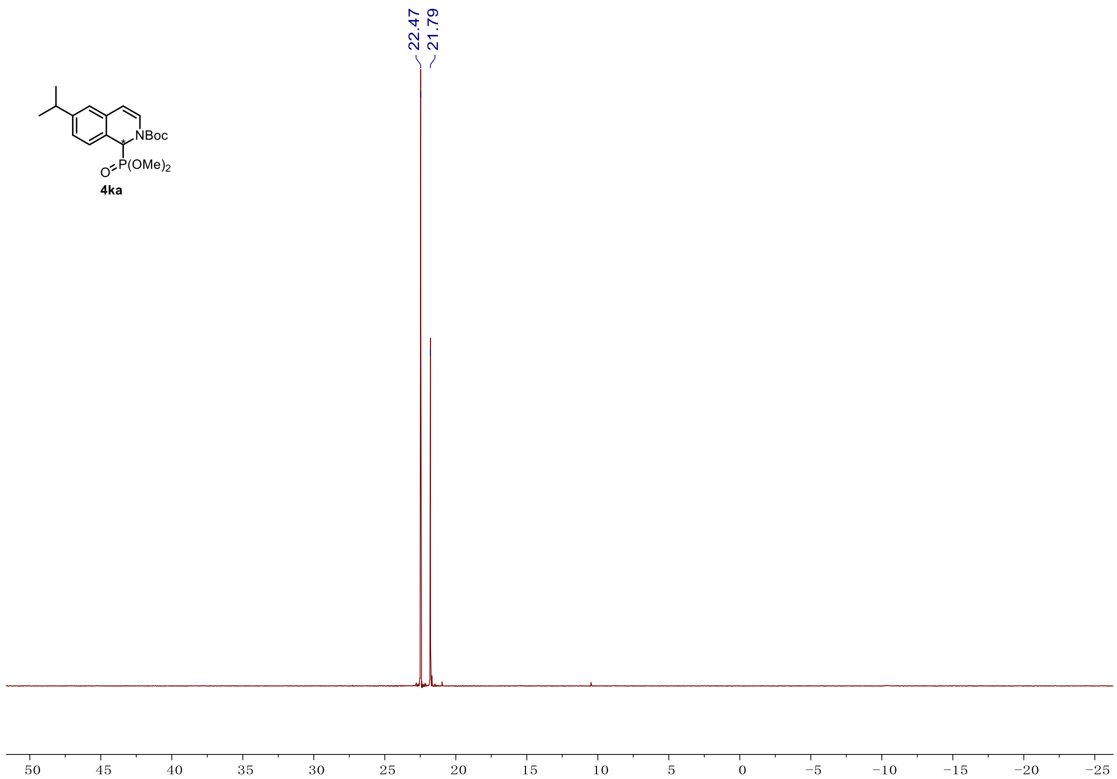


Fig.S 42 ^{31}P NMR of compound **4ka**

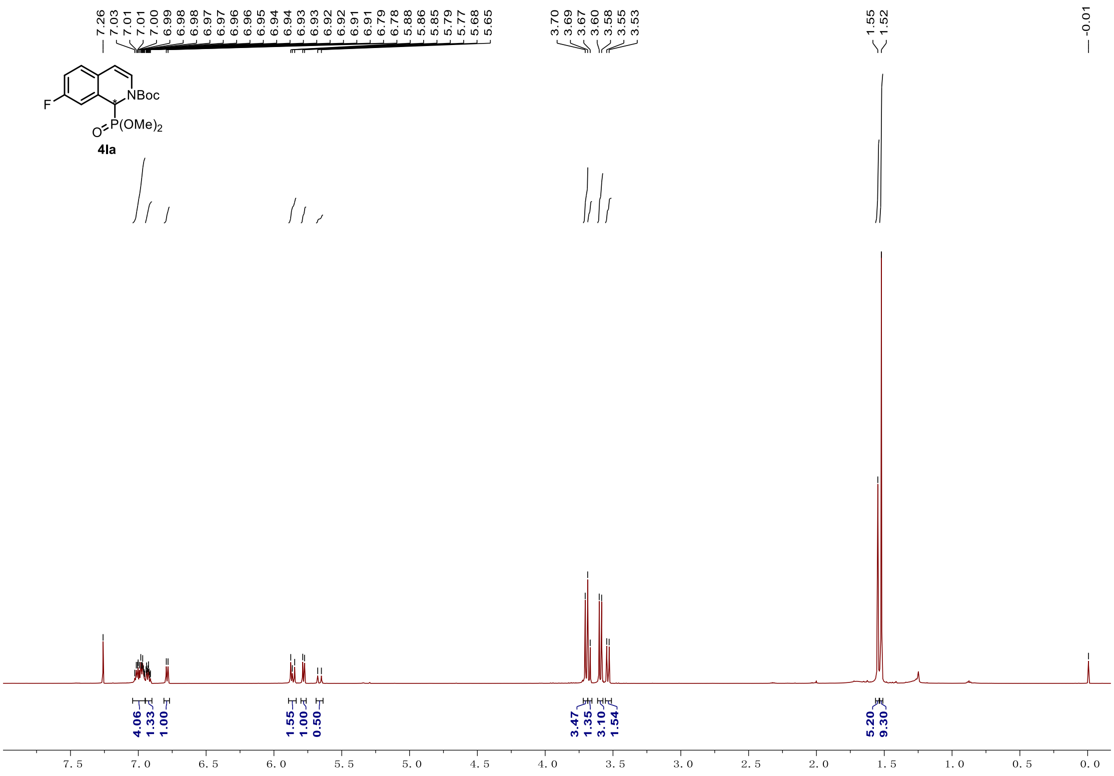


Fig.S 43 ^{1}H NMR of compound **4la**

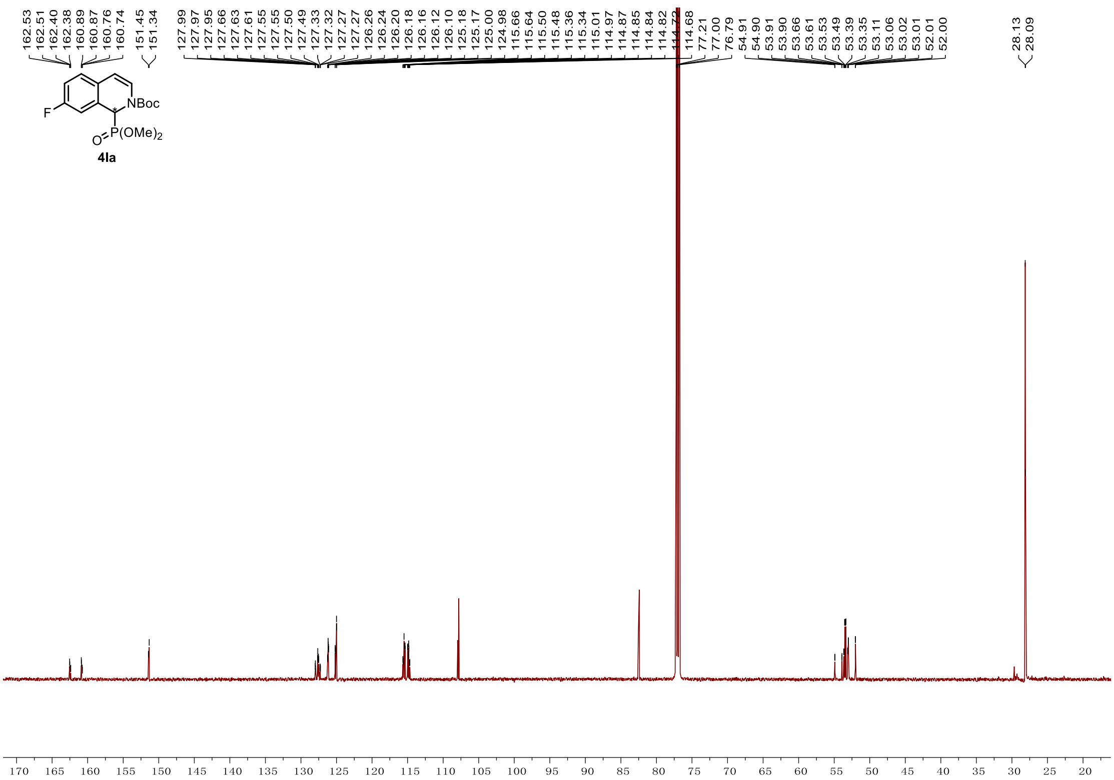


Fig.S 44 ^{13}C NMR of compound **4la**

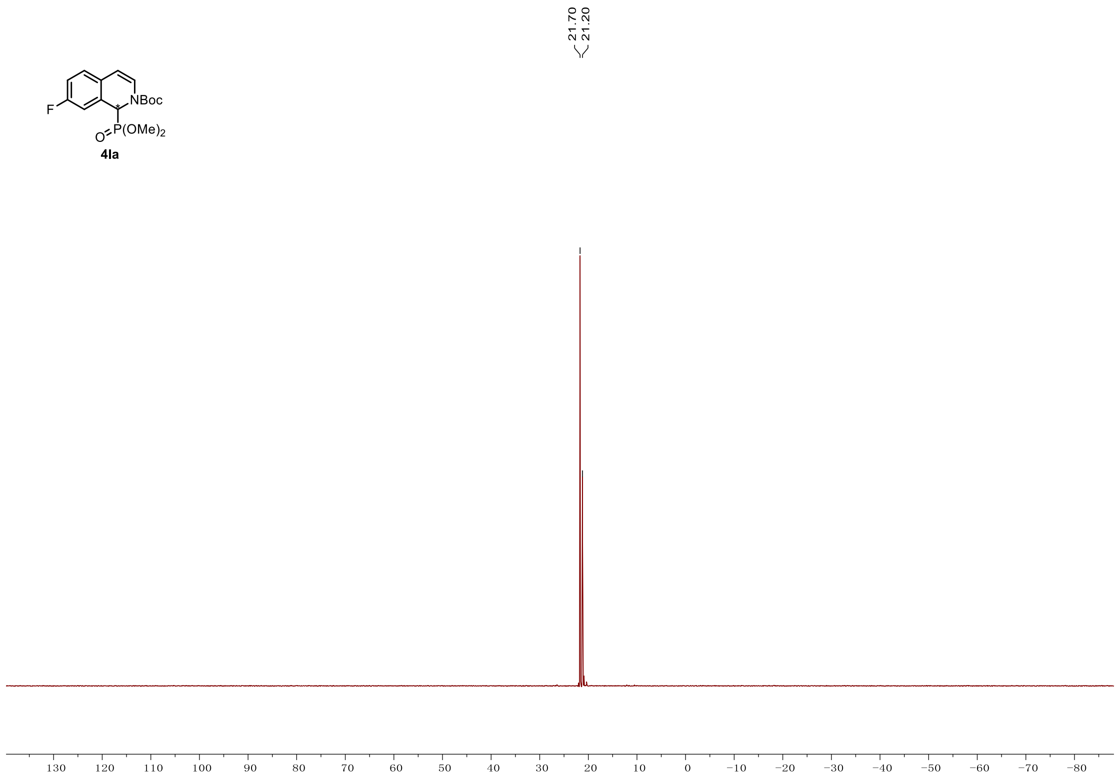


Fig.S 45 ^{31}P NMR of compound **4la**

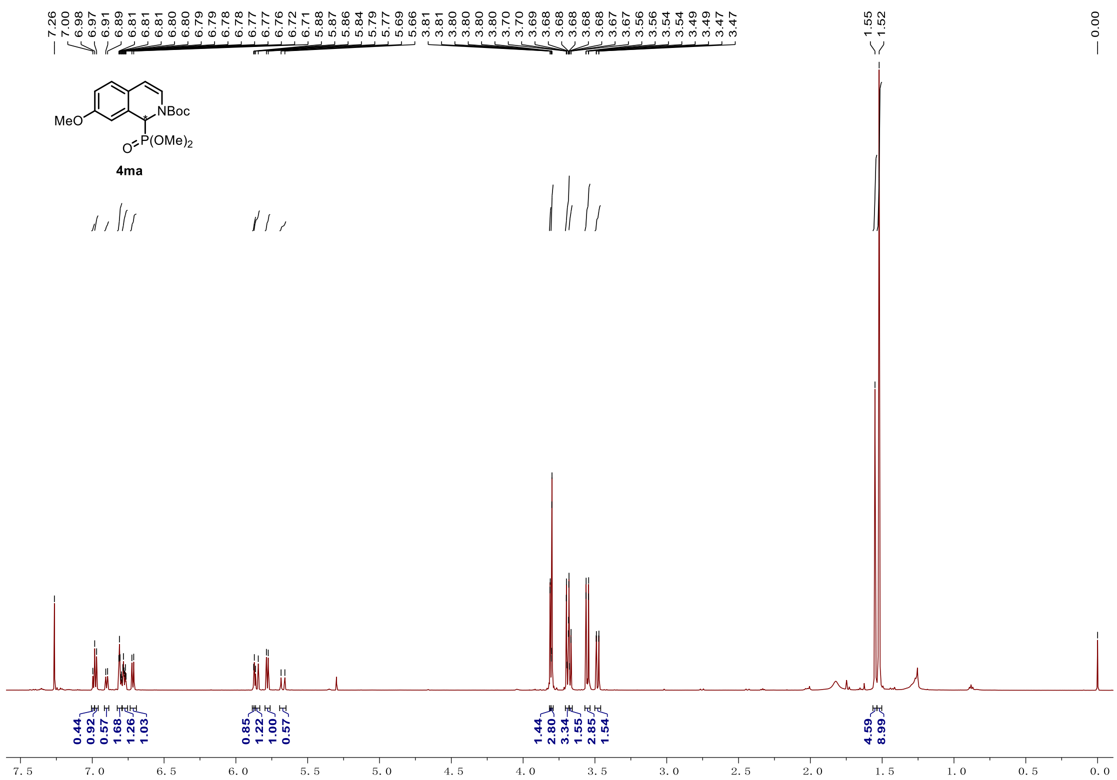


Fig.S 46 ^{1}H NMR of compound **4ma**

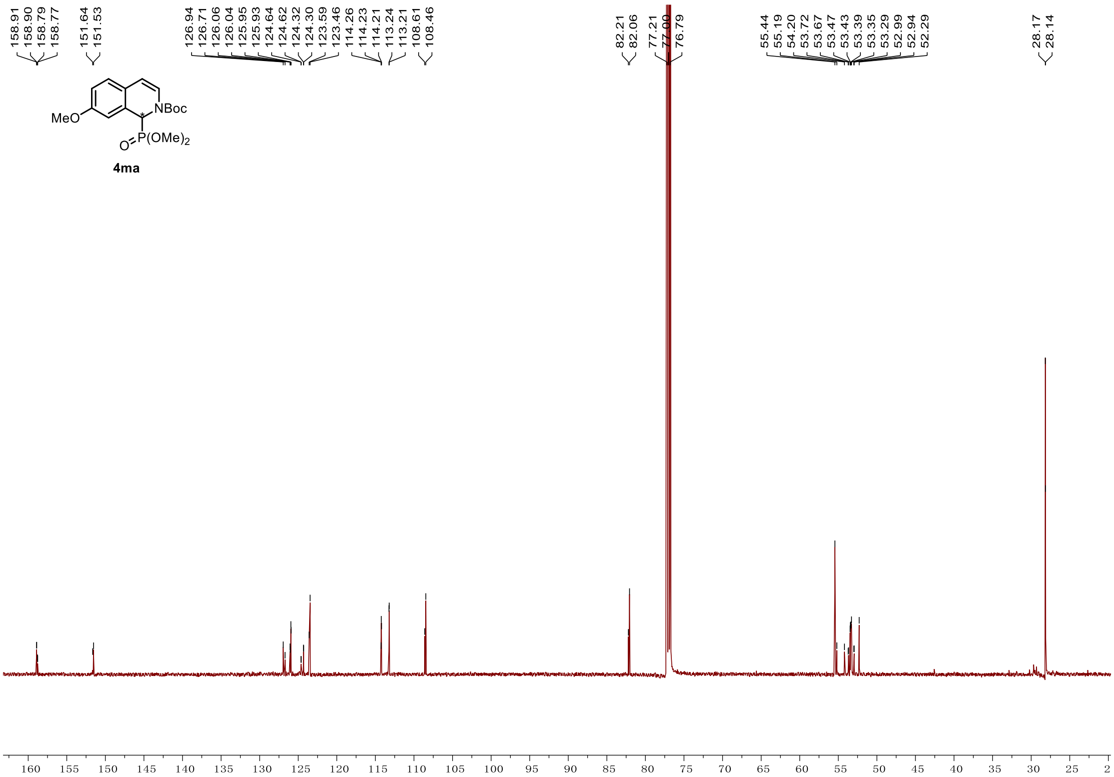


Fig.S 47 ^{13}C NMR of compound **4ma**

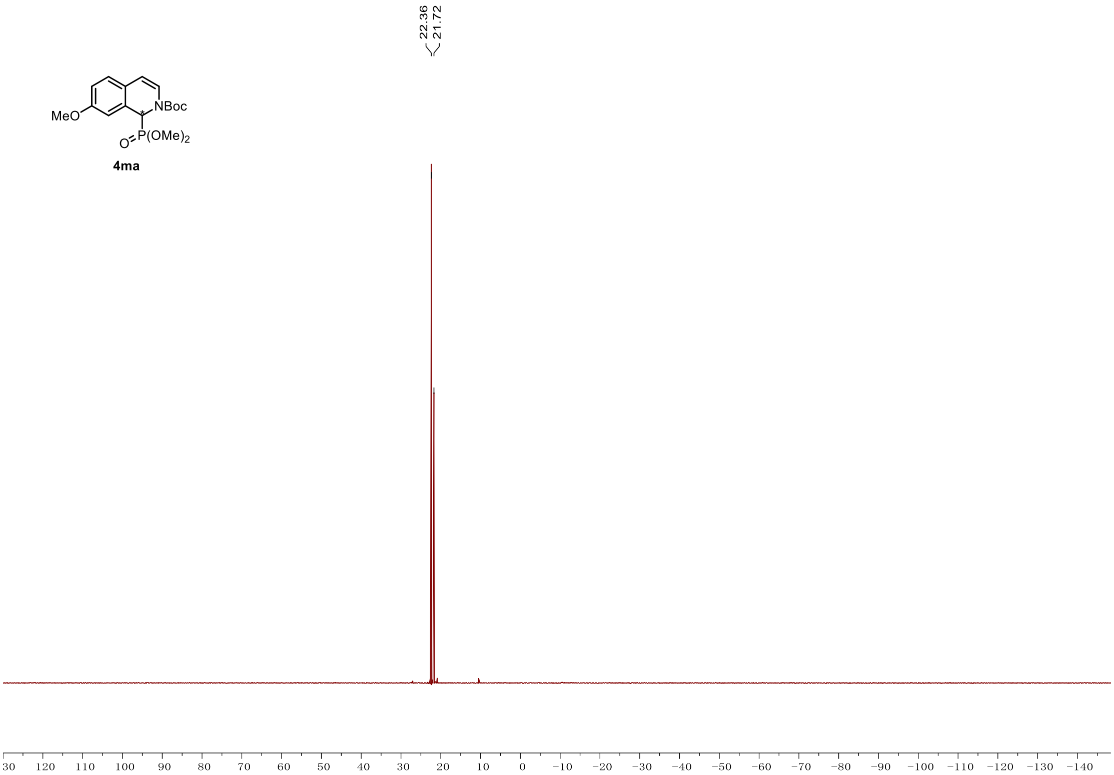


Fig.S 48 ^{31}P NMR of compound **4ma**

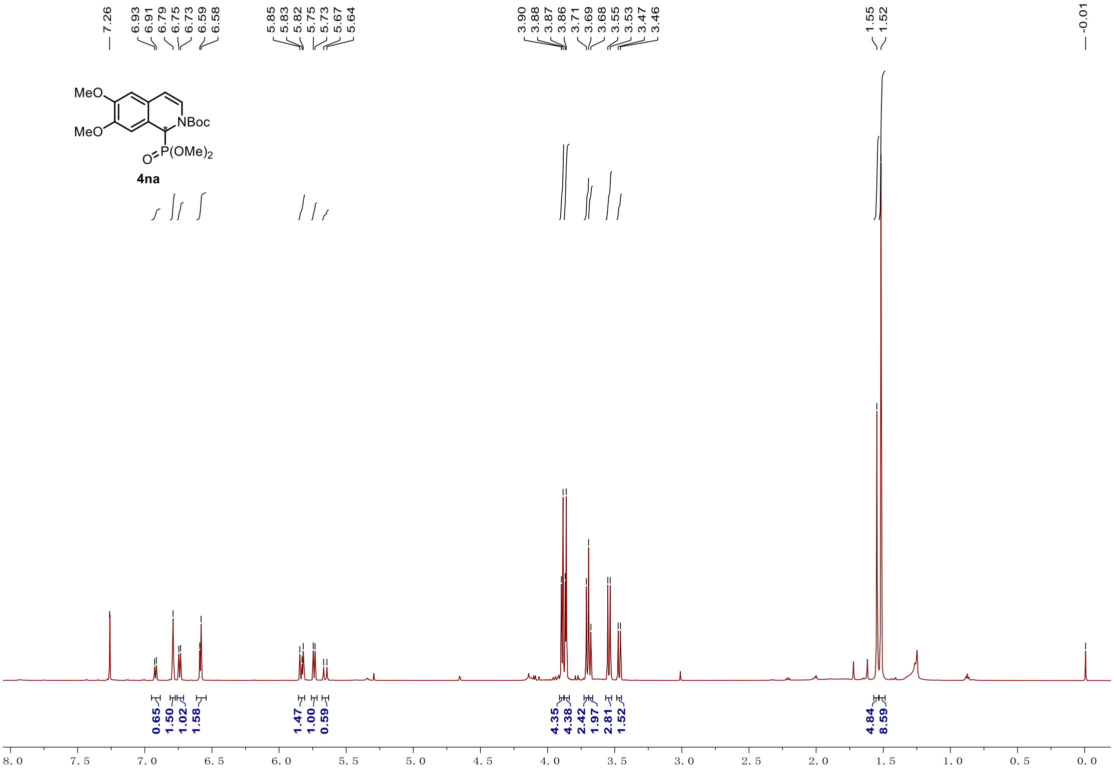


Fig.S 49 ^{1}H NMR of compound **4na**

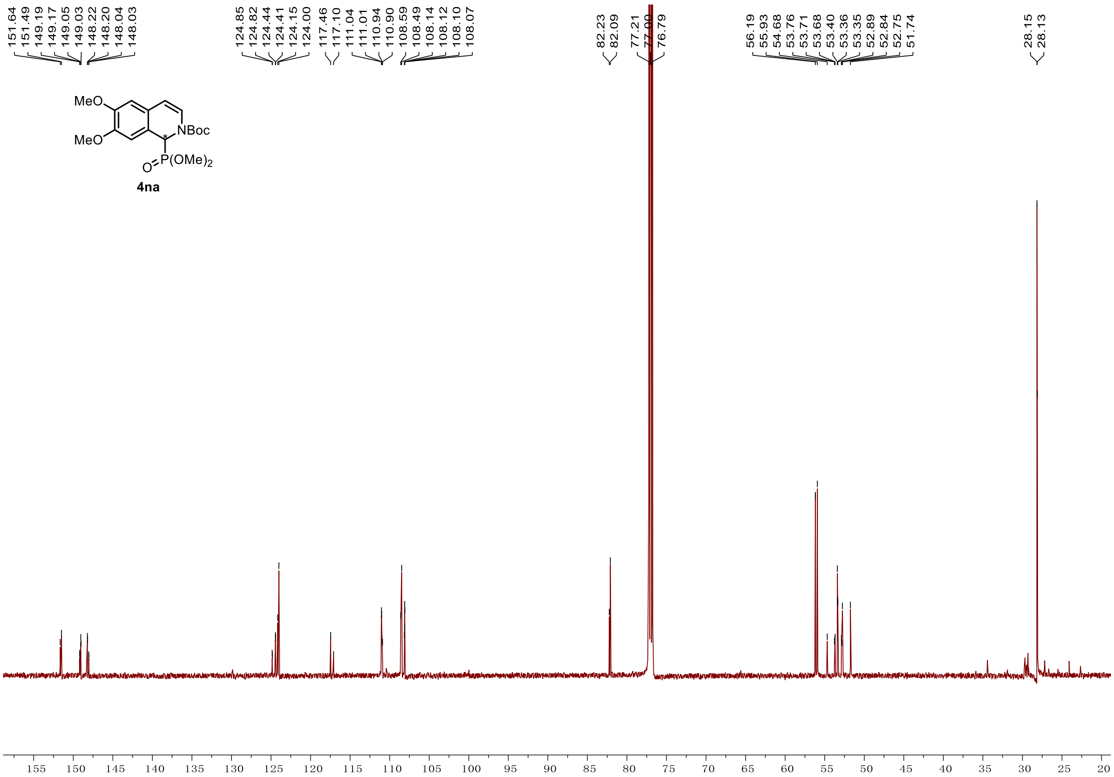


Fig.S 50 ^{13}C NMR of compound **4na**

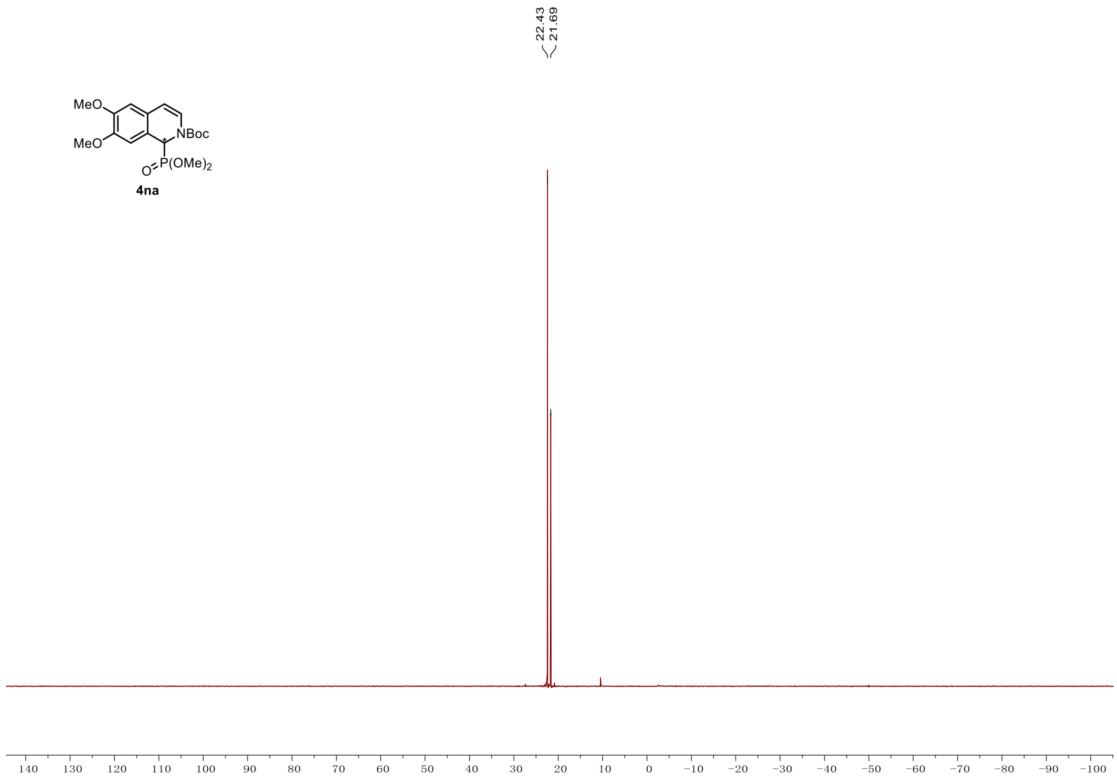


Fig.S 51 ^{31}P NMR of compound **4na**

3. NMR spectrum of 1,2-dihydroisoquinoline-1-ylphenylphosphine oxides 6

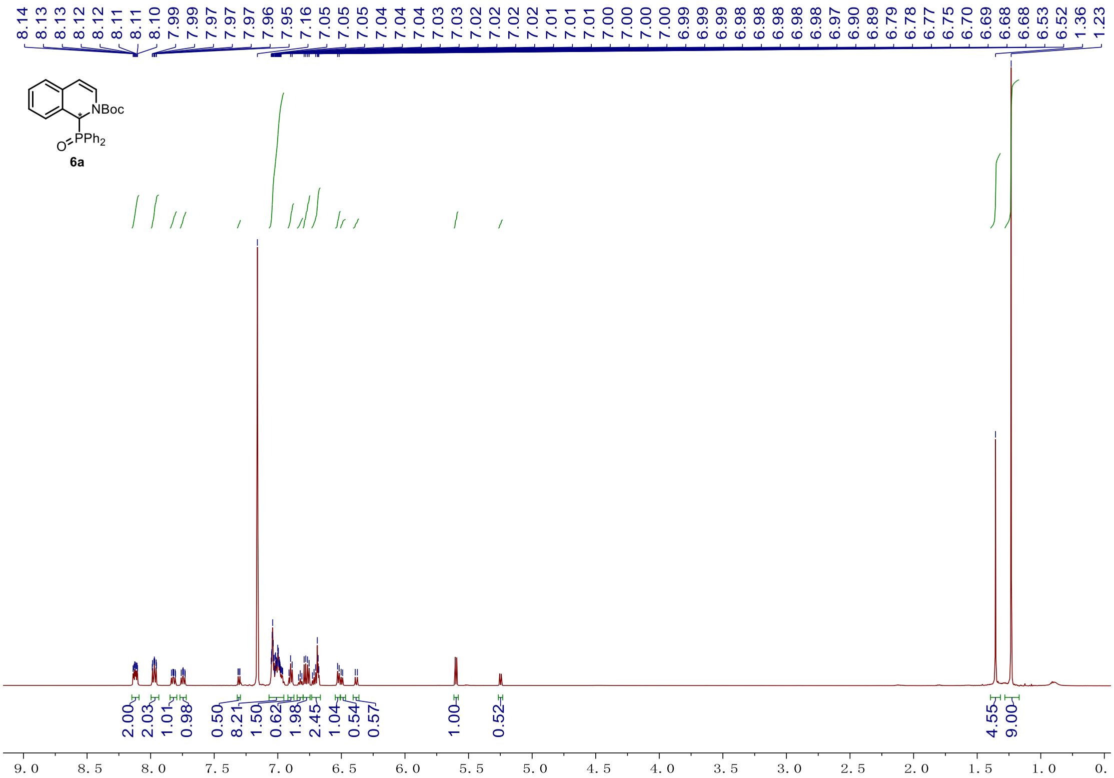


Fig.S 52 ^{1}H NMR of compound **6a**

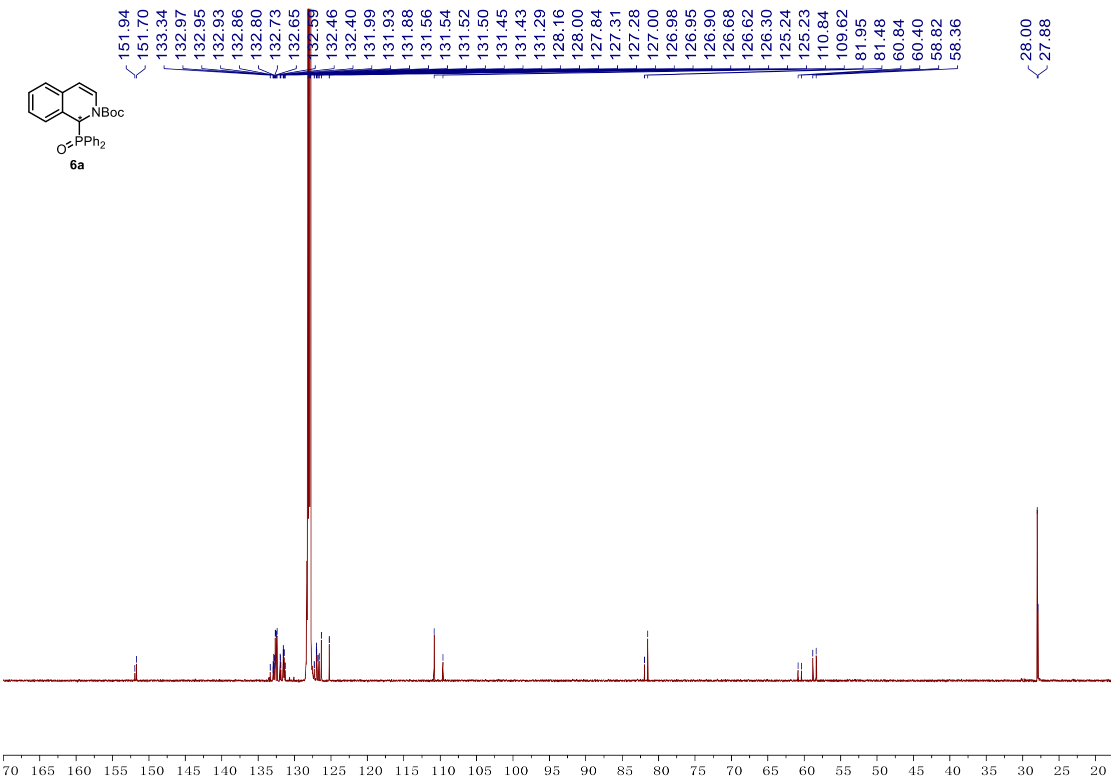


Fig.S 53 ^{13}C NMR of compound **6a**

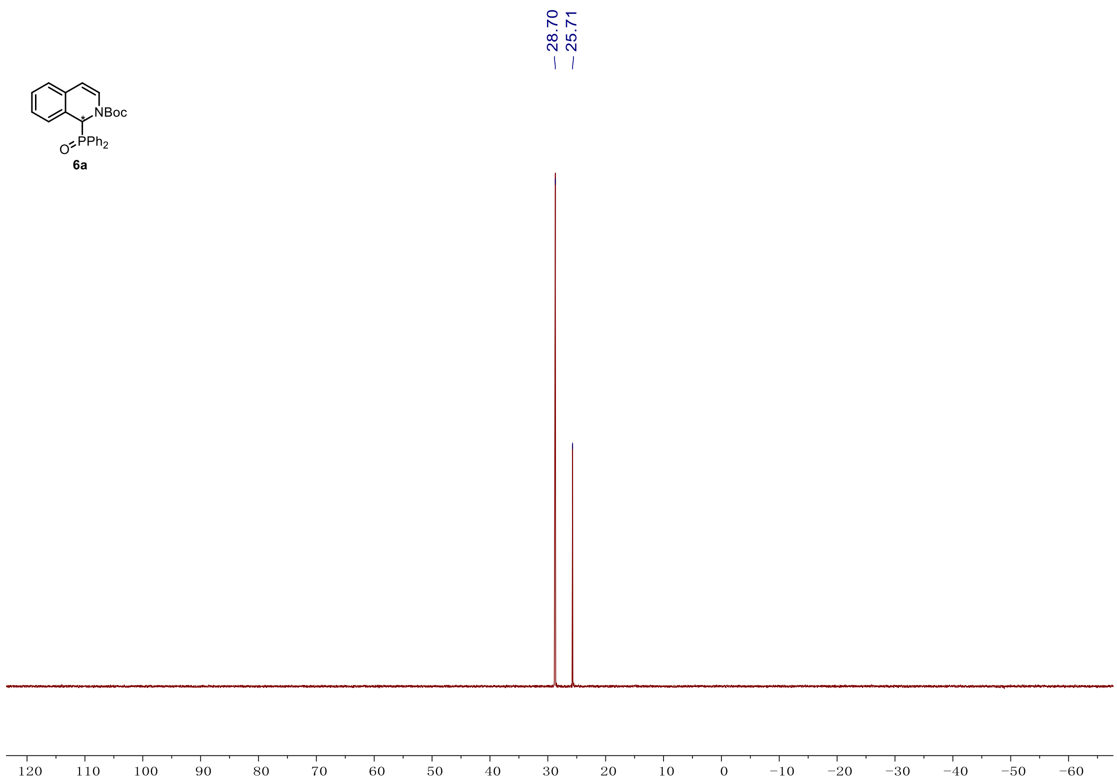


Fig.S 54 ^{31}P NMR of compound **6a**

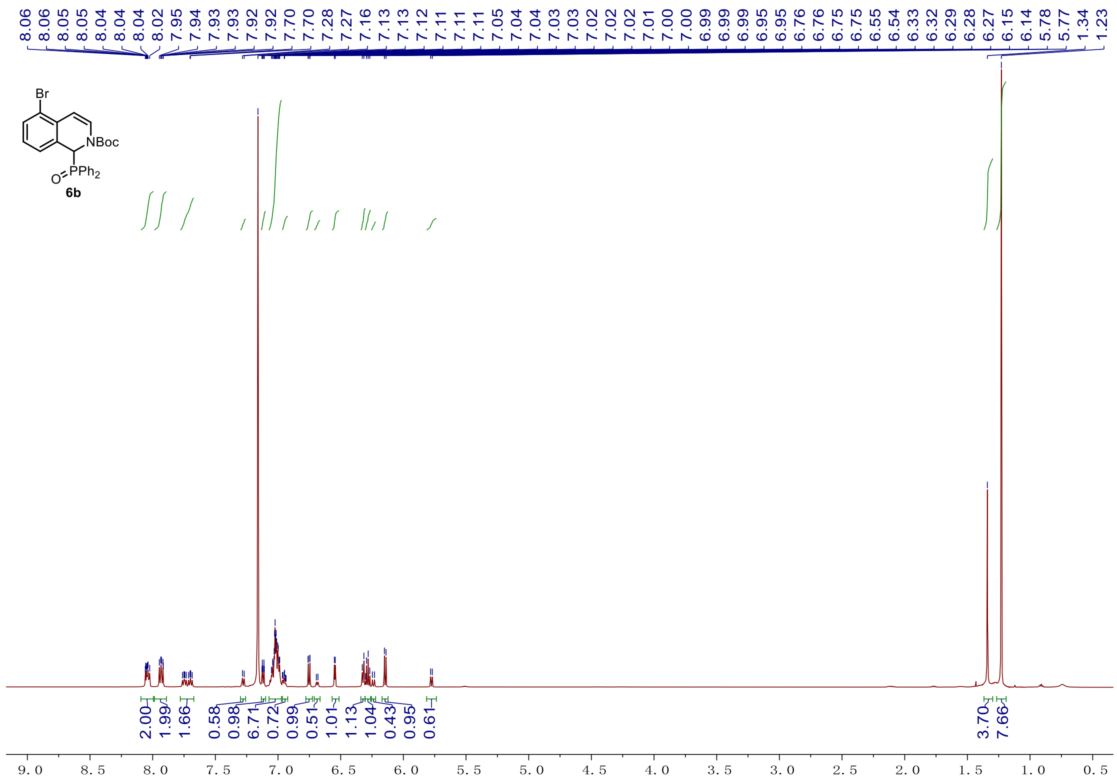


Fig.S 55 ^{1}H NMR of compound **6b**

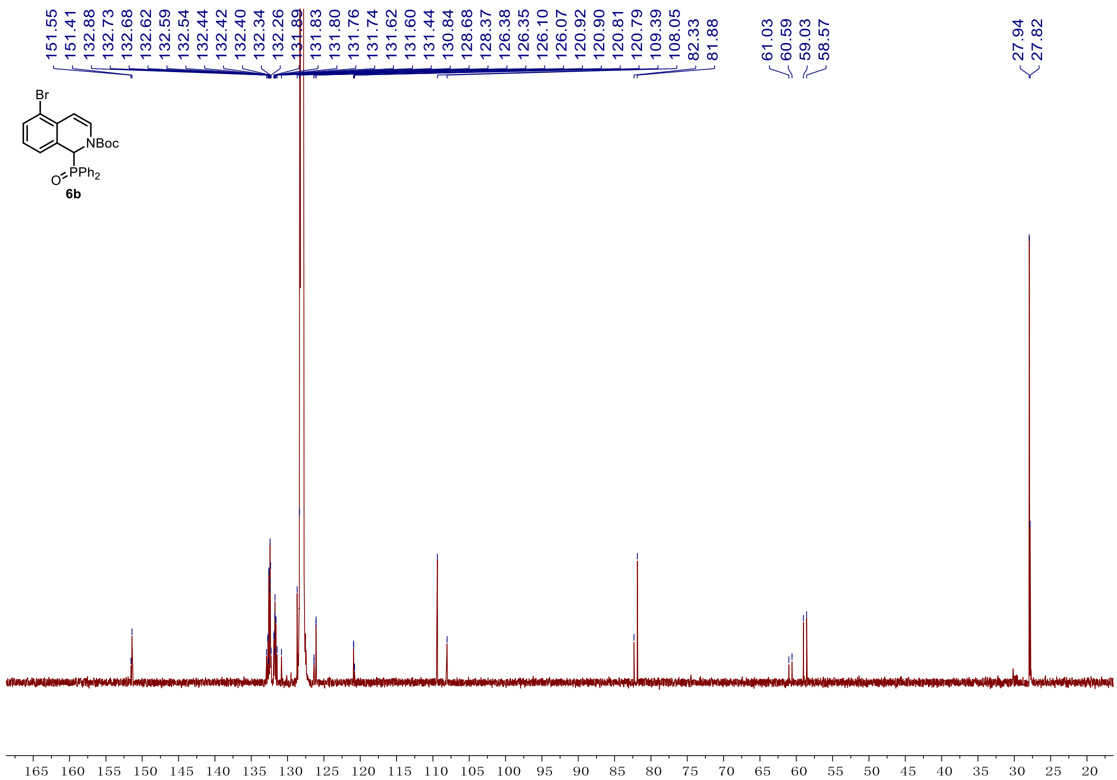


Fig.S 56 ^{13}C NMR of compound **6b**

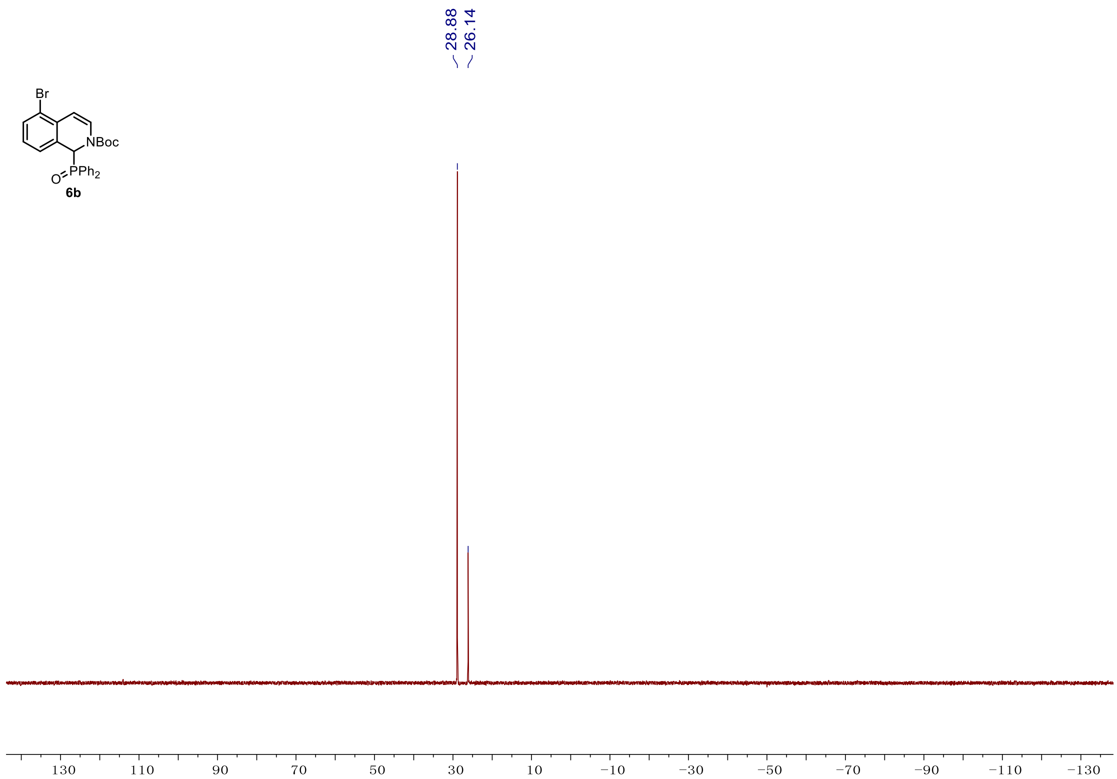


Fig.S 57 ^{31}P NMR of compound **6b**

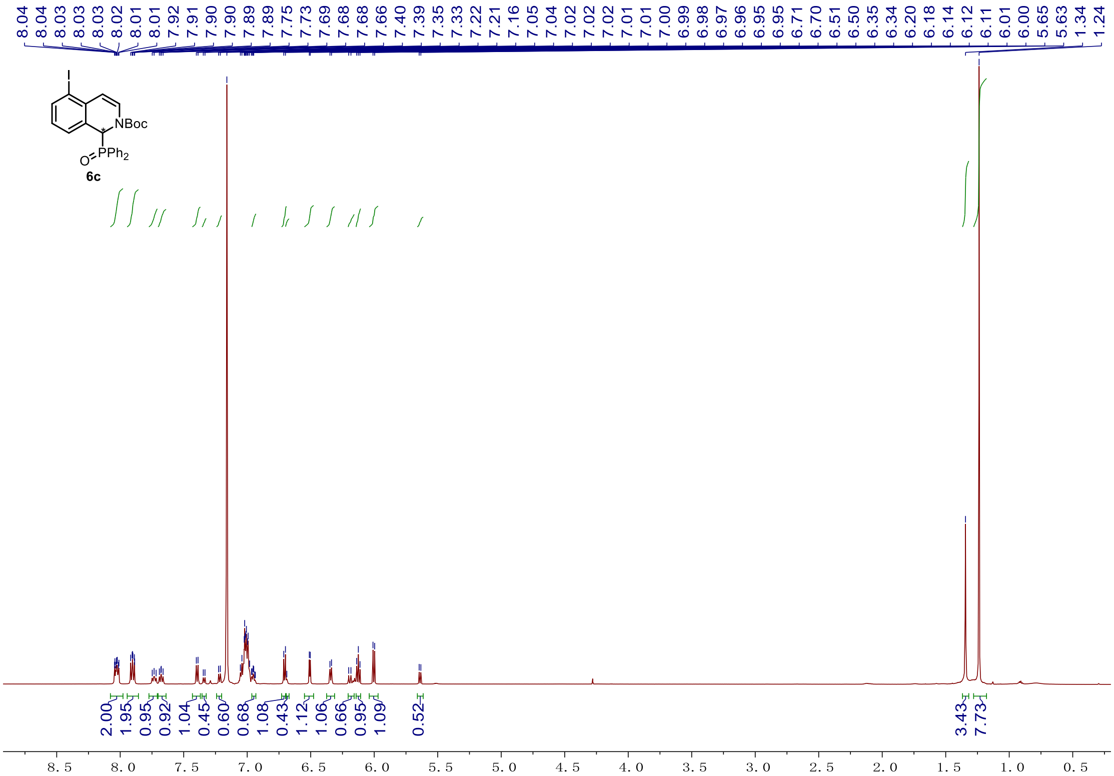


Fig.S 58 ^{1}H NMR of compound **6c**

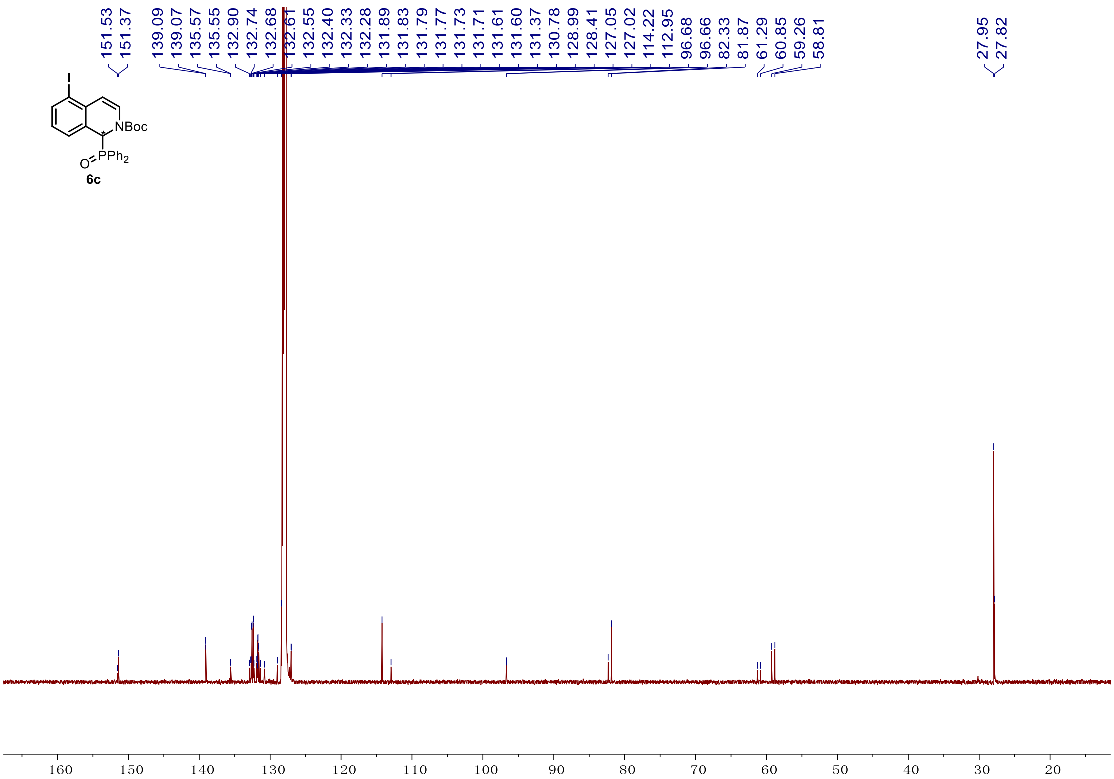


Fig.S 59 ^{13}C NMR of compound **6c**

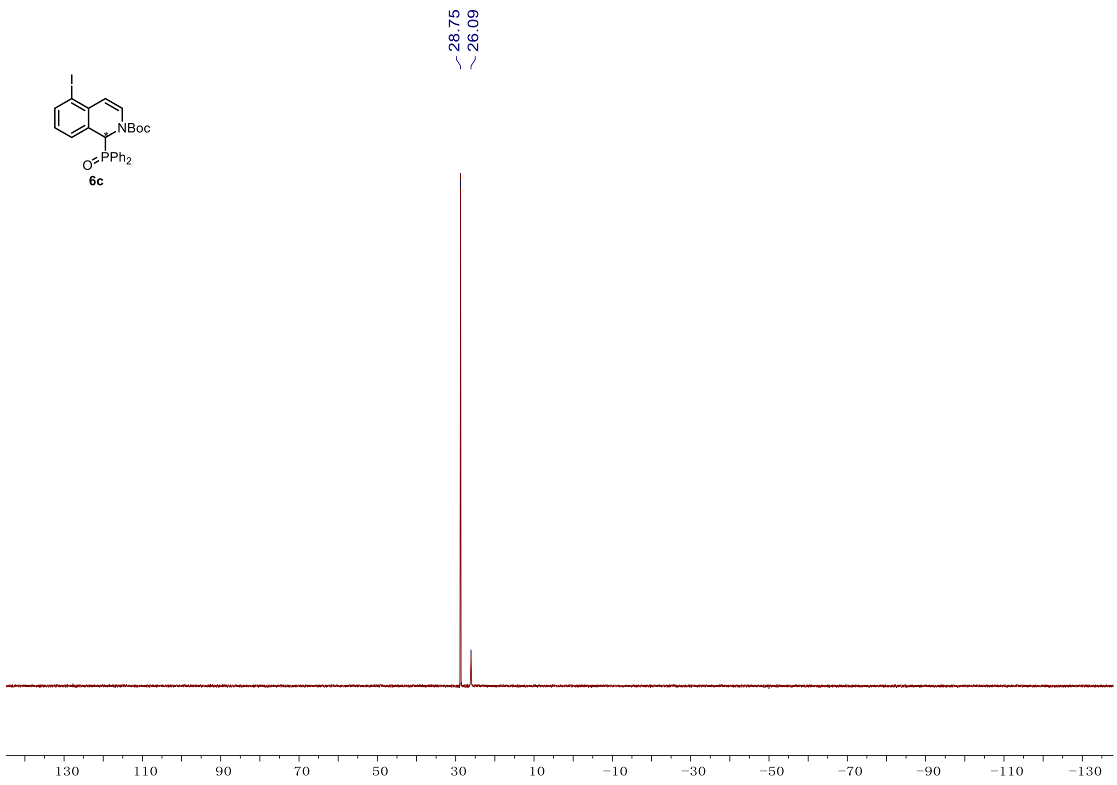


Fig.S 60 ^{31}P NMR of compound **6c**

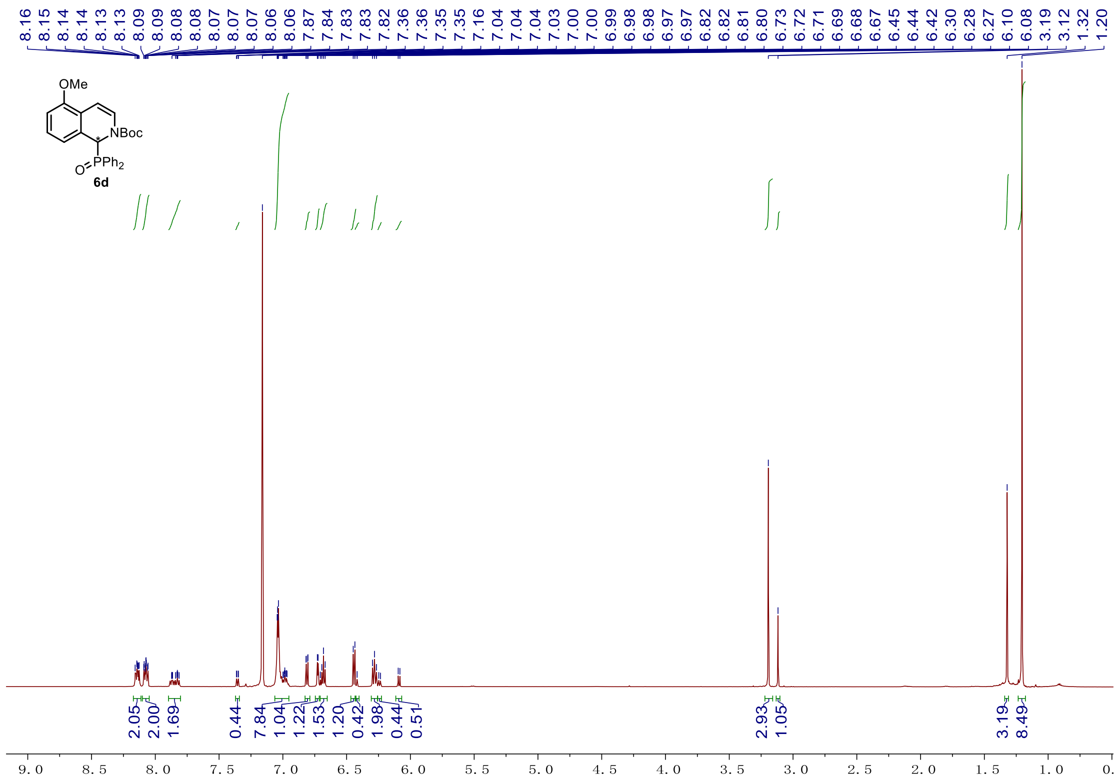


Fig.S 61 ^{1}H NMR of compound **6d**

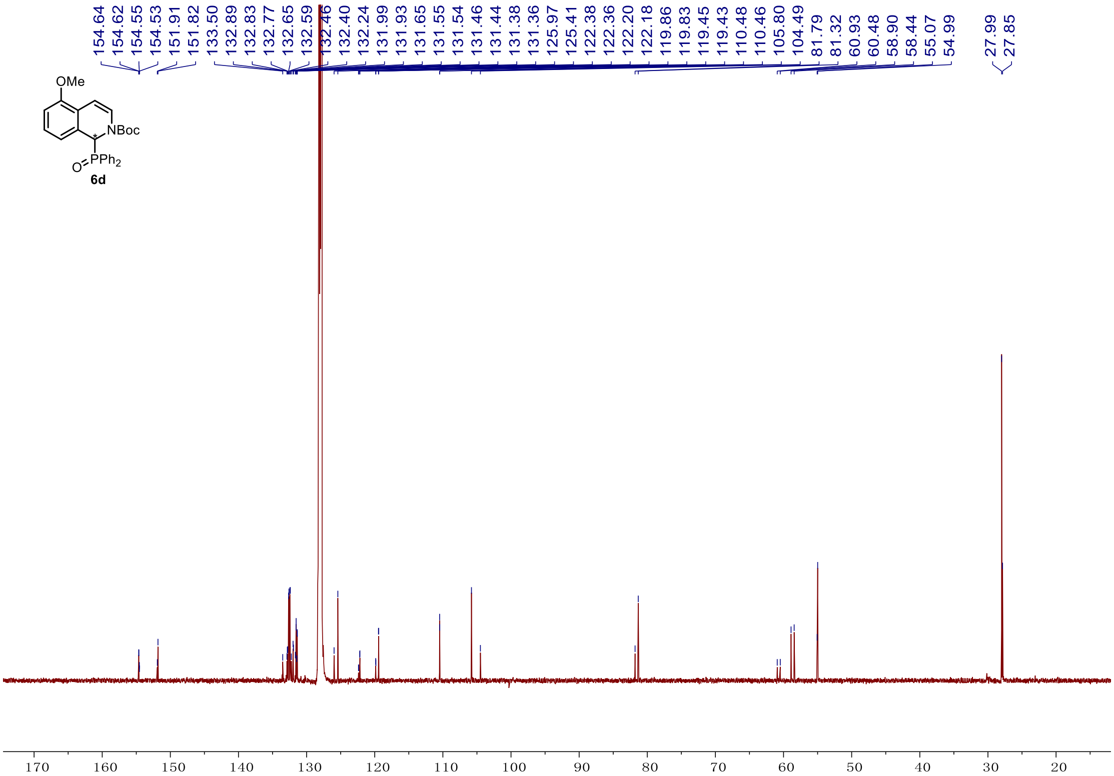


Fig.S 62 ^{13}C NMR of compound **6d**

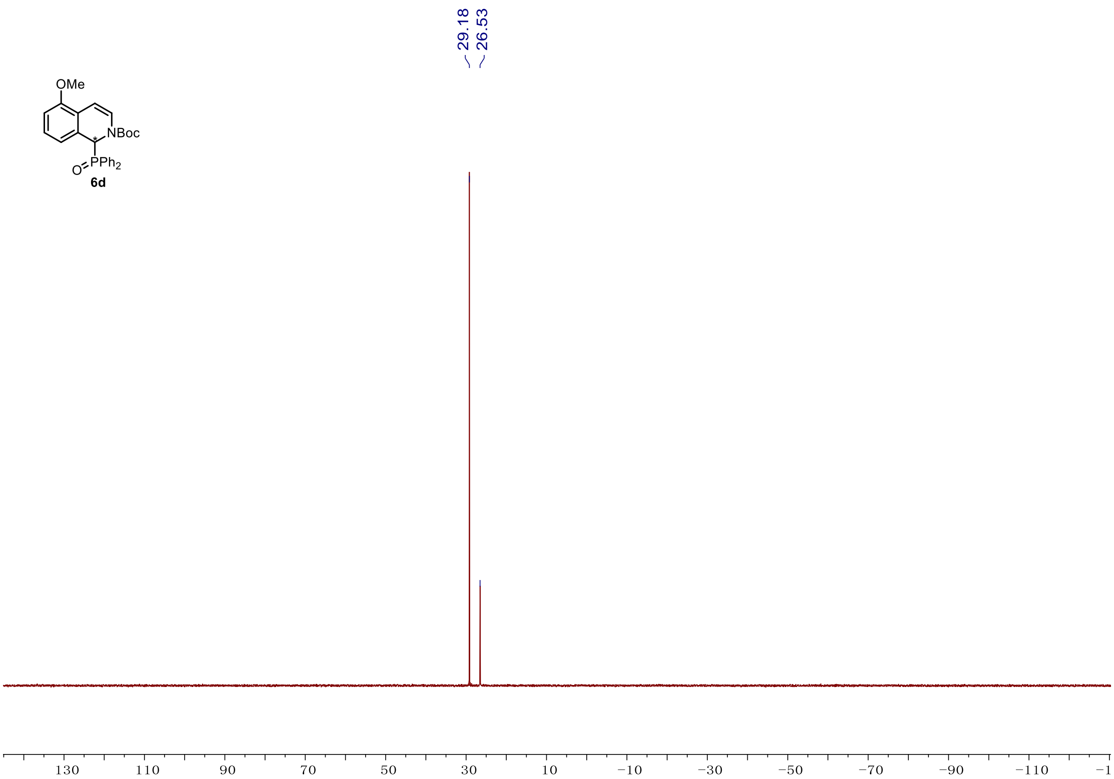


Fig.S 63 ^{31}P NMR of compound **6d**

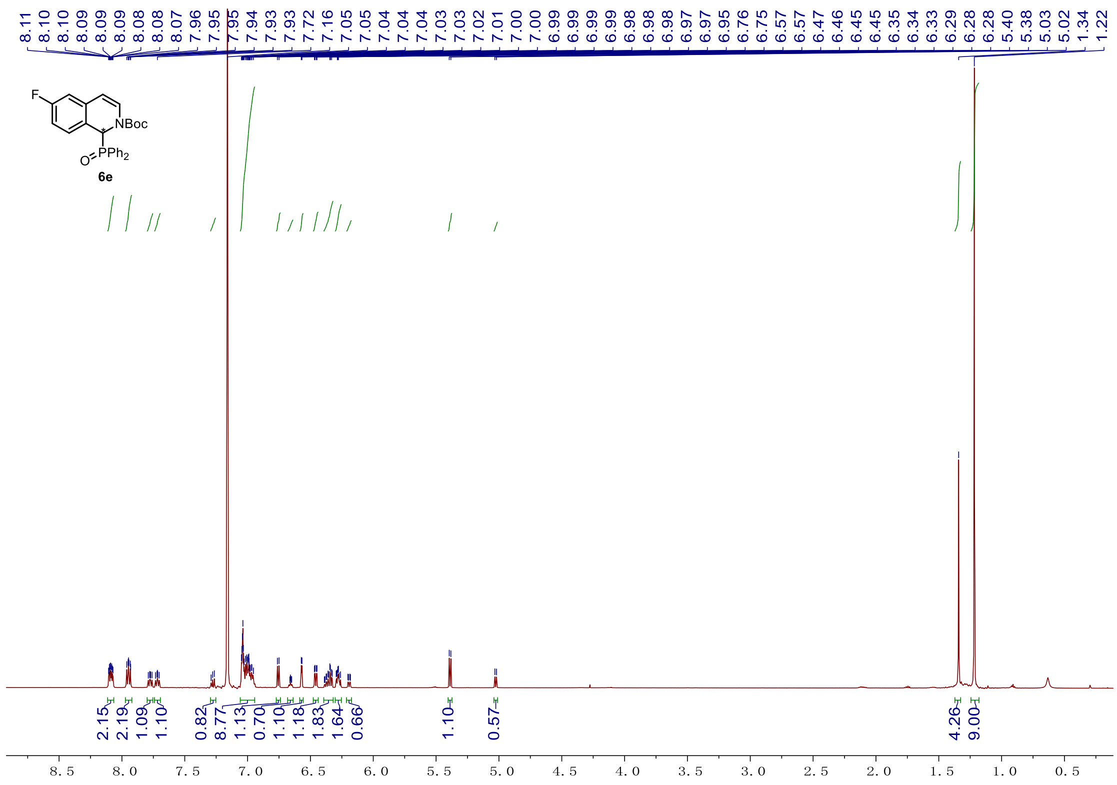


Fig.S 64 ^{1}H NMR of compound **6e**

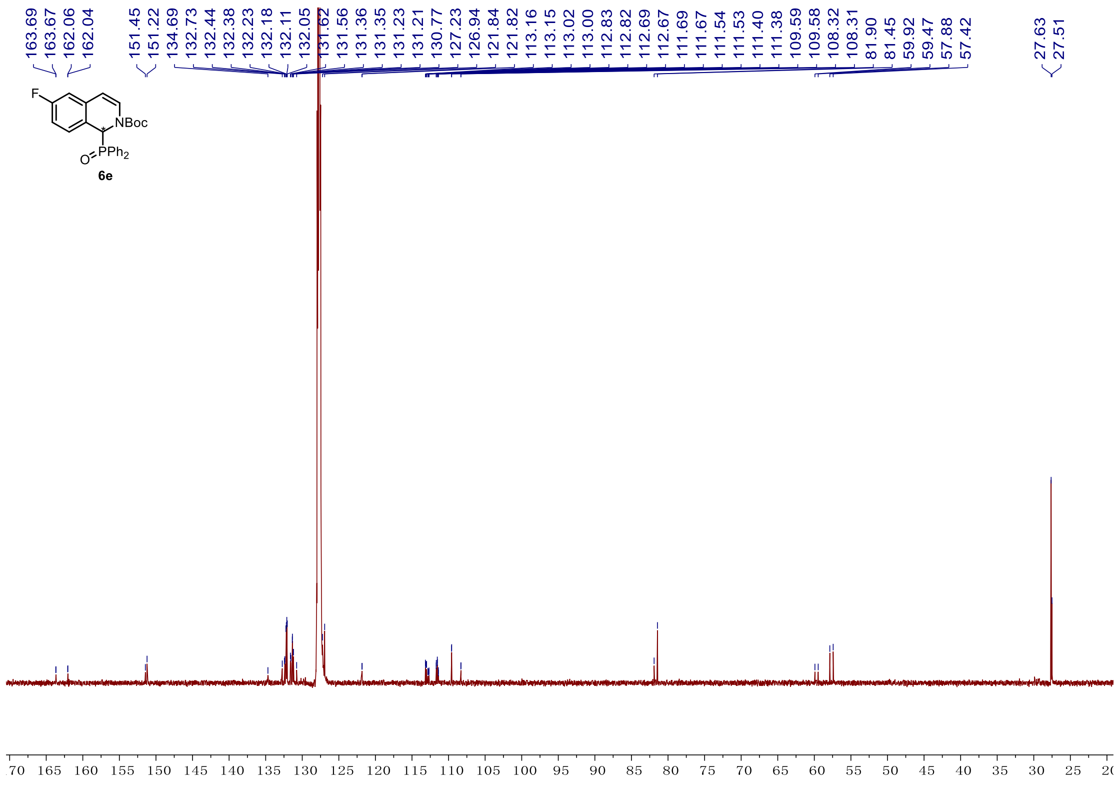


Fig.S 65 ^{13}C NMR of compound **6e**

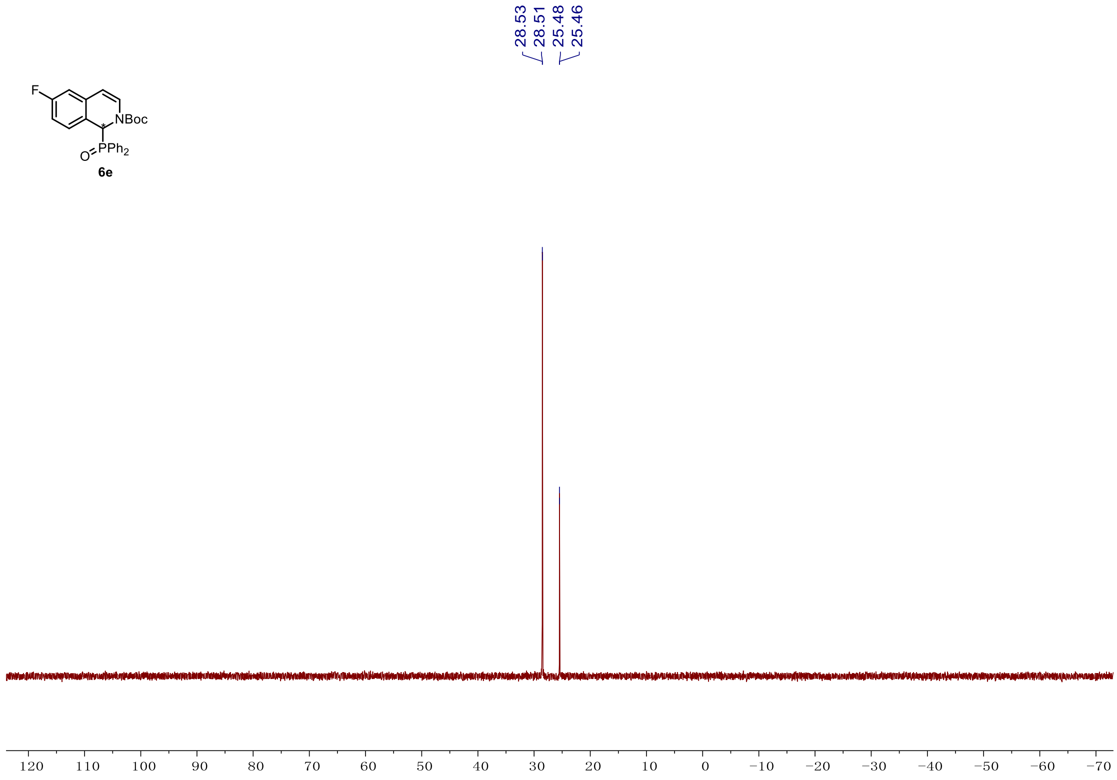


Fig.S 66 ^{31}P NMR of compound **6e**

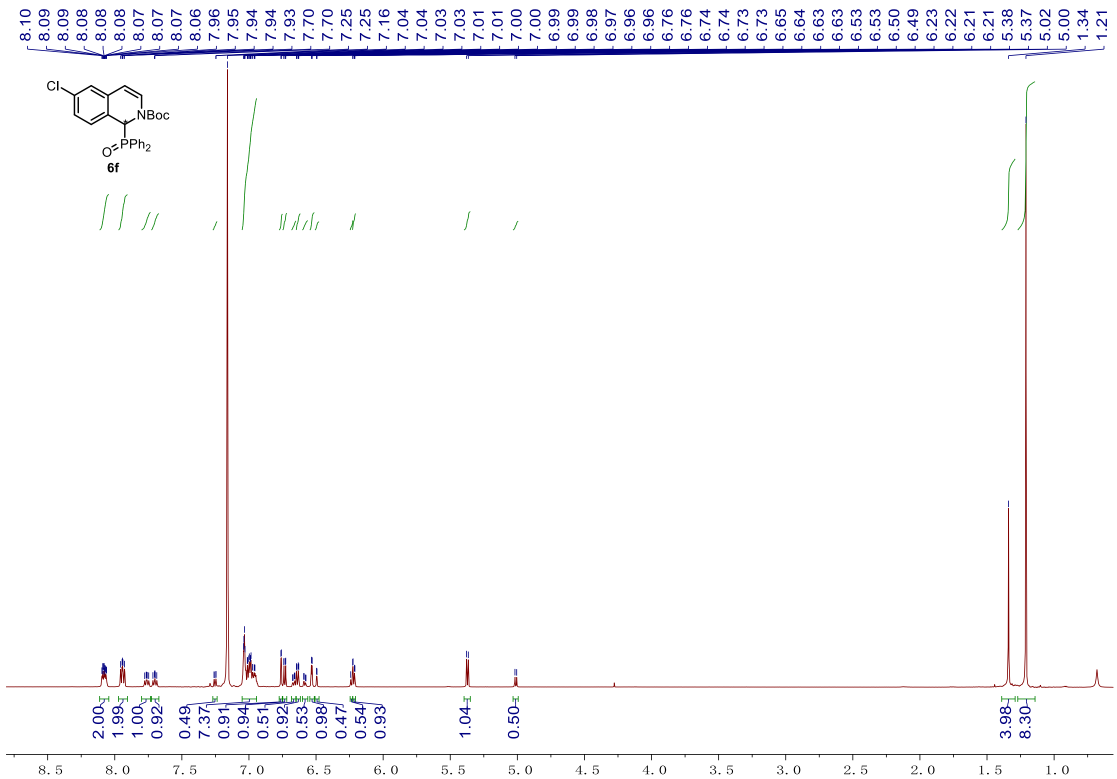


Fig.S 67 ^{1}H NMR of compound **6f**

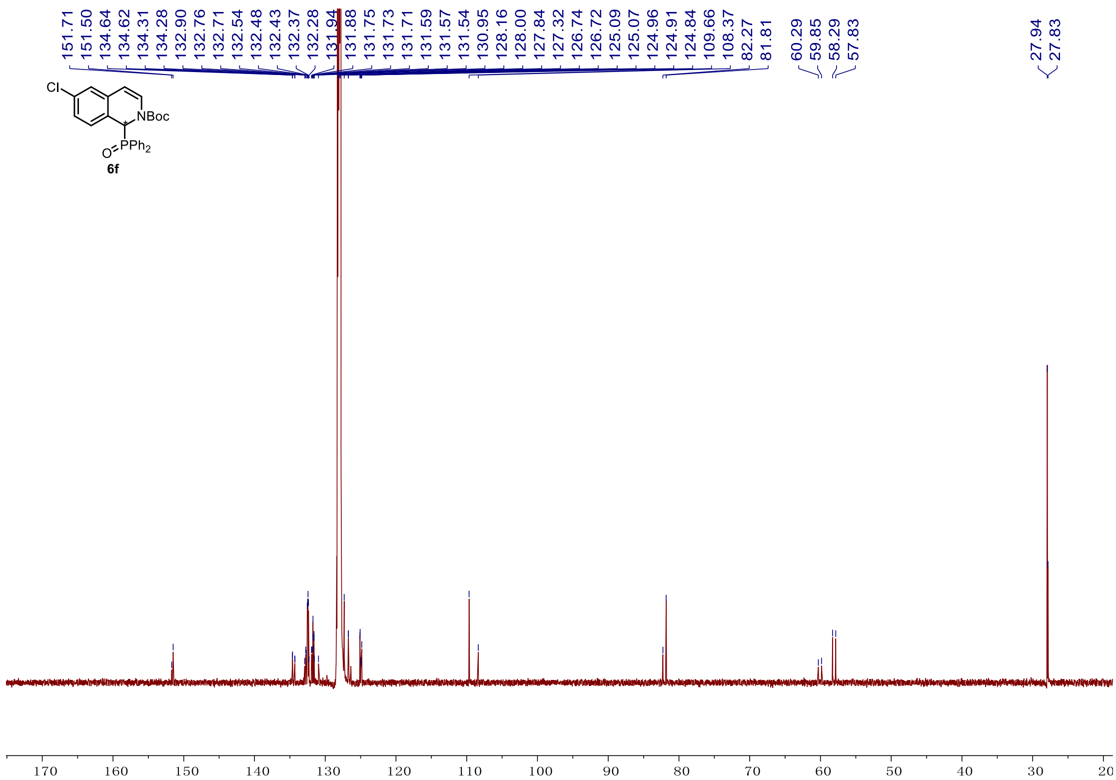


Fig.S 68 ^{13}C NMR of compound **6f**

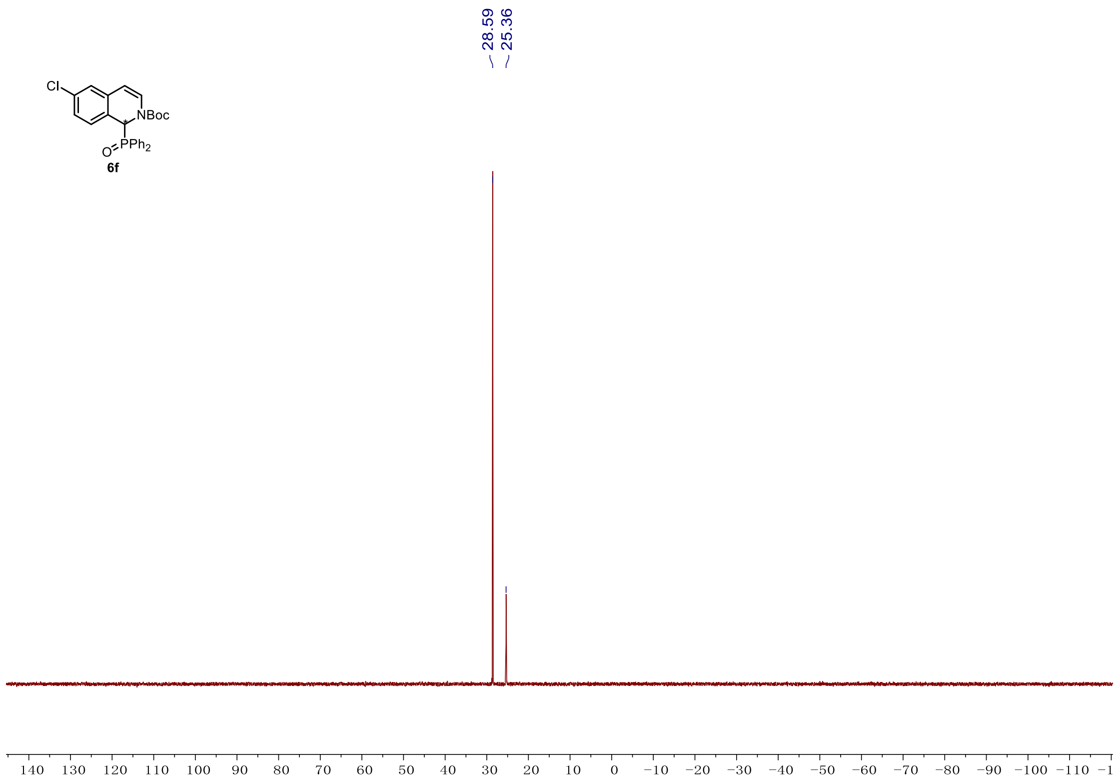


Fig.S 69 ^{31}P NMR of compound **6f**

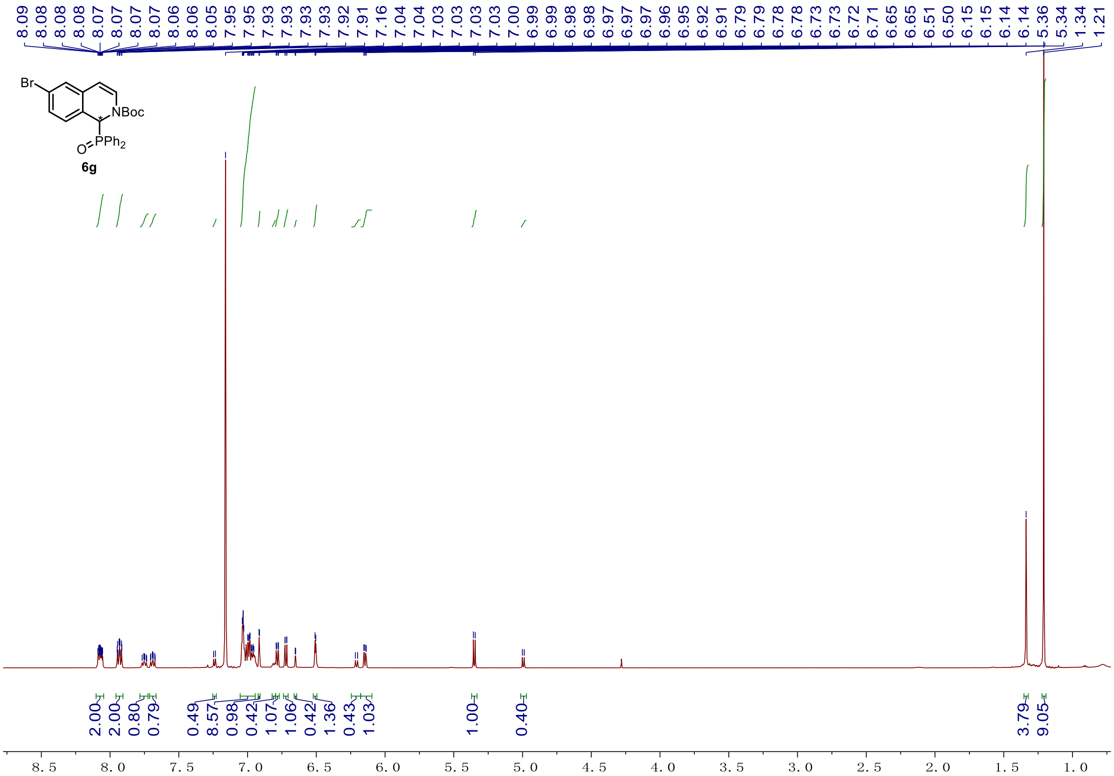


Fig.S 70 ^{1}H NMR of compound **6g**

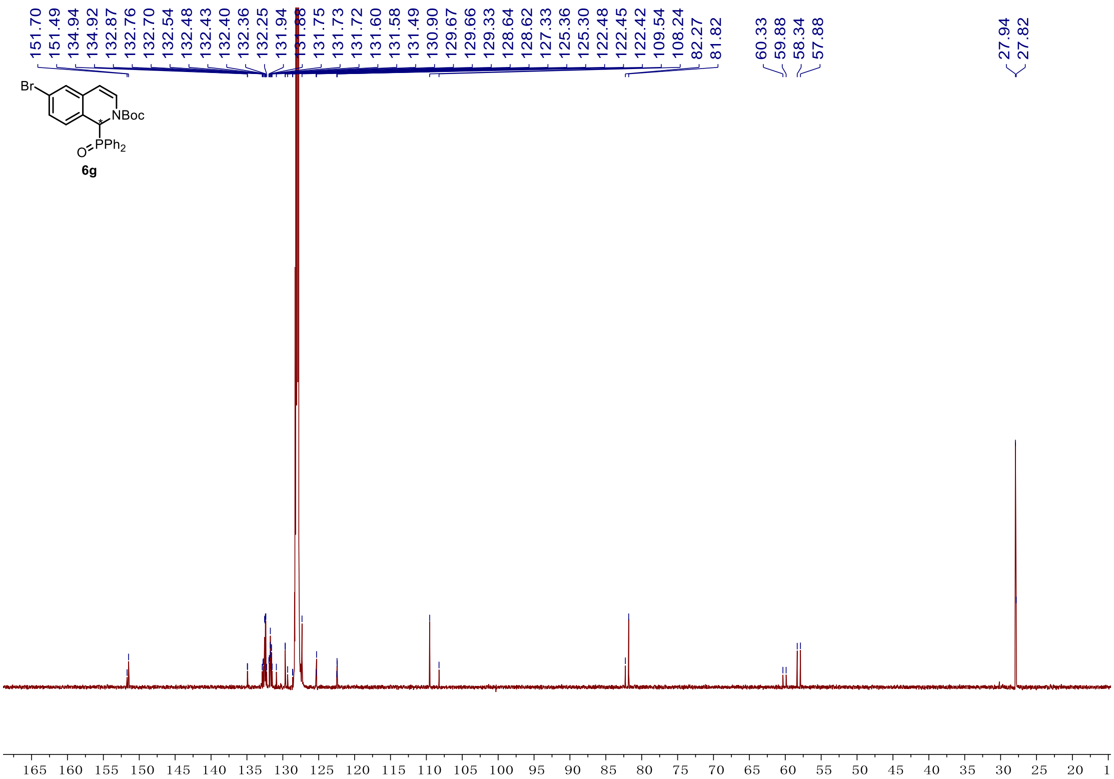


Fig.S 71 ^{13}C NMR of compound **6g**

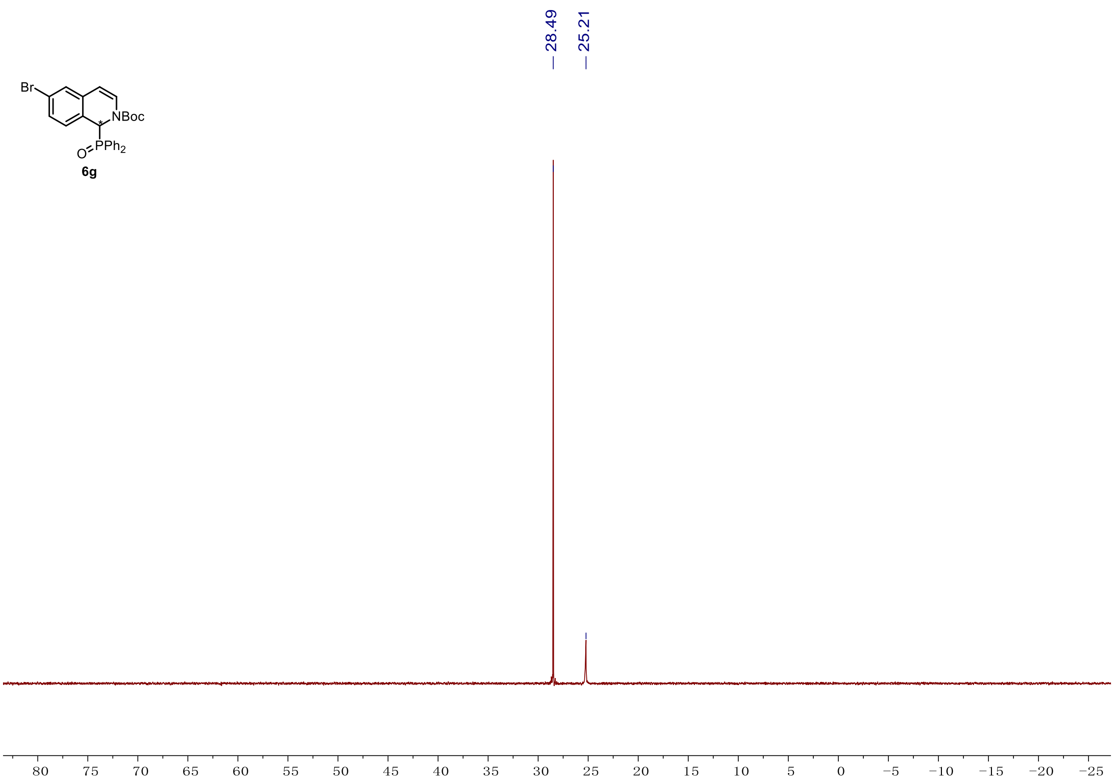


Fig.S 72 ^{31}P NMR of compound **6g**

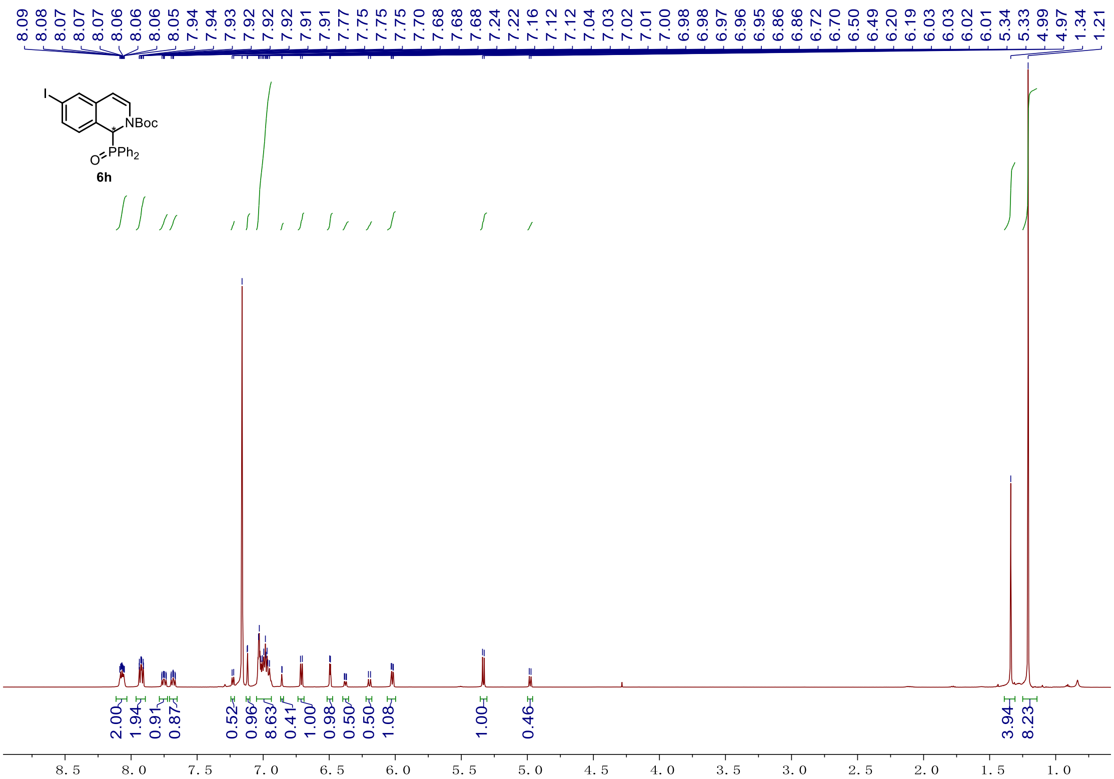


Fig.S 73 ^{1}H NMR of compound **6h**

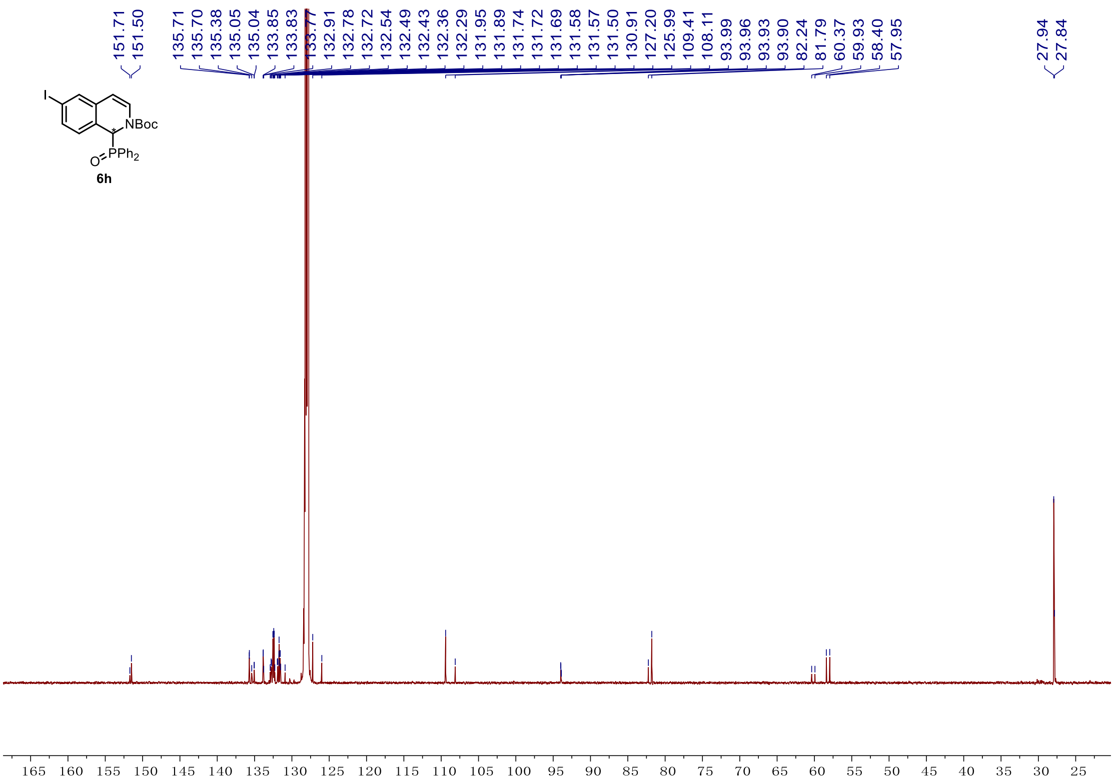


Fig.S 74 ^{13}C NMR of compound **6h**

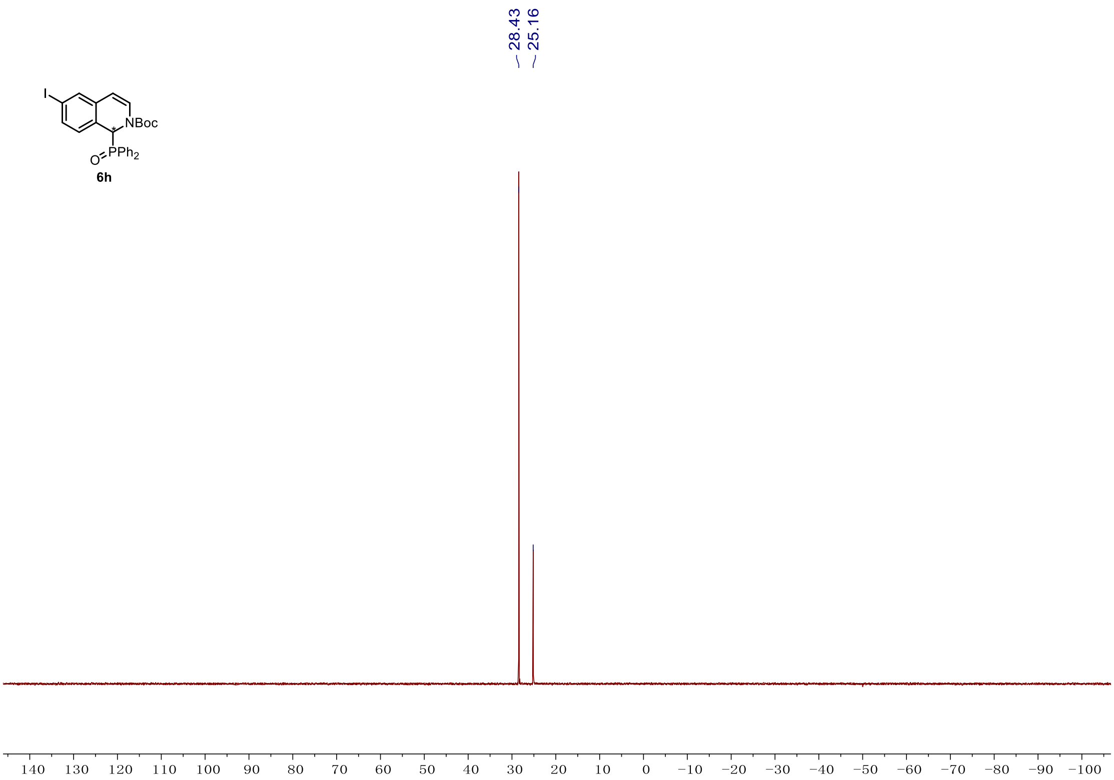


Fig.S 75 ^{31}P NMR of compound **6h**

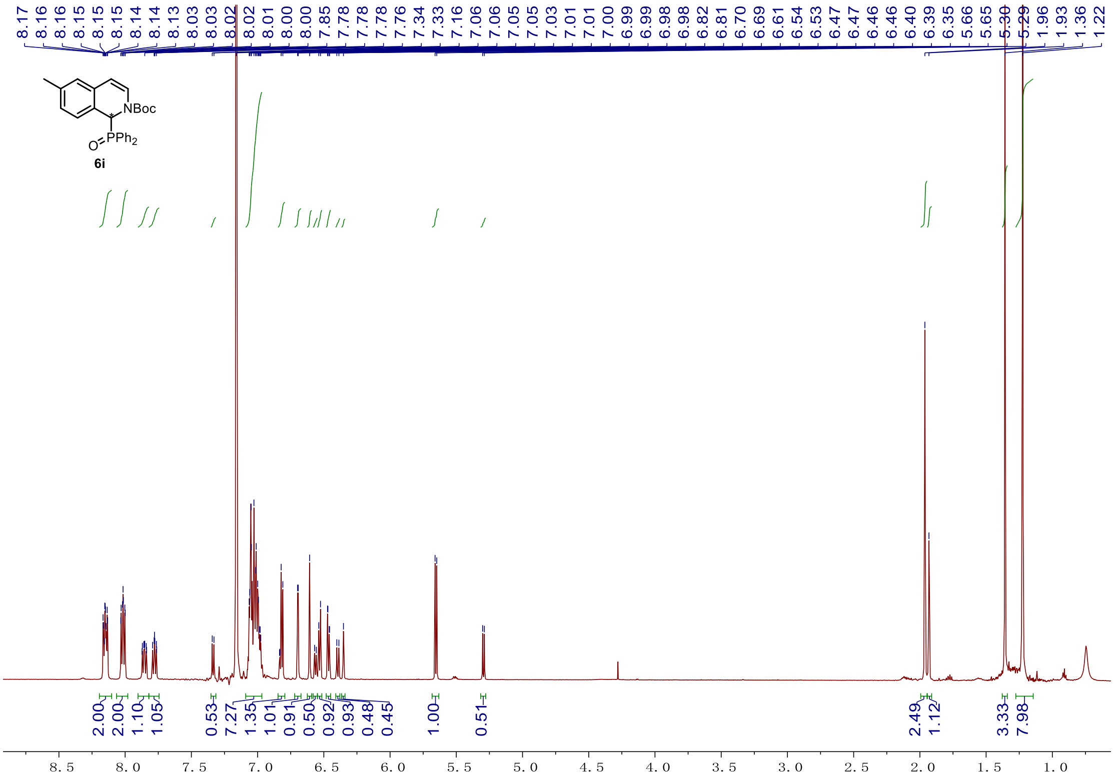


Fig.S 76 ^{1}H NMR of compound **6i**

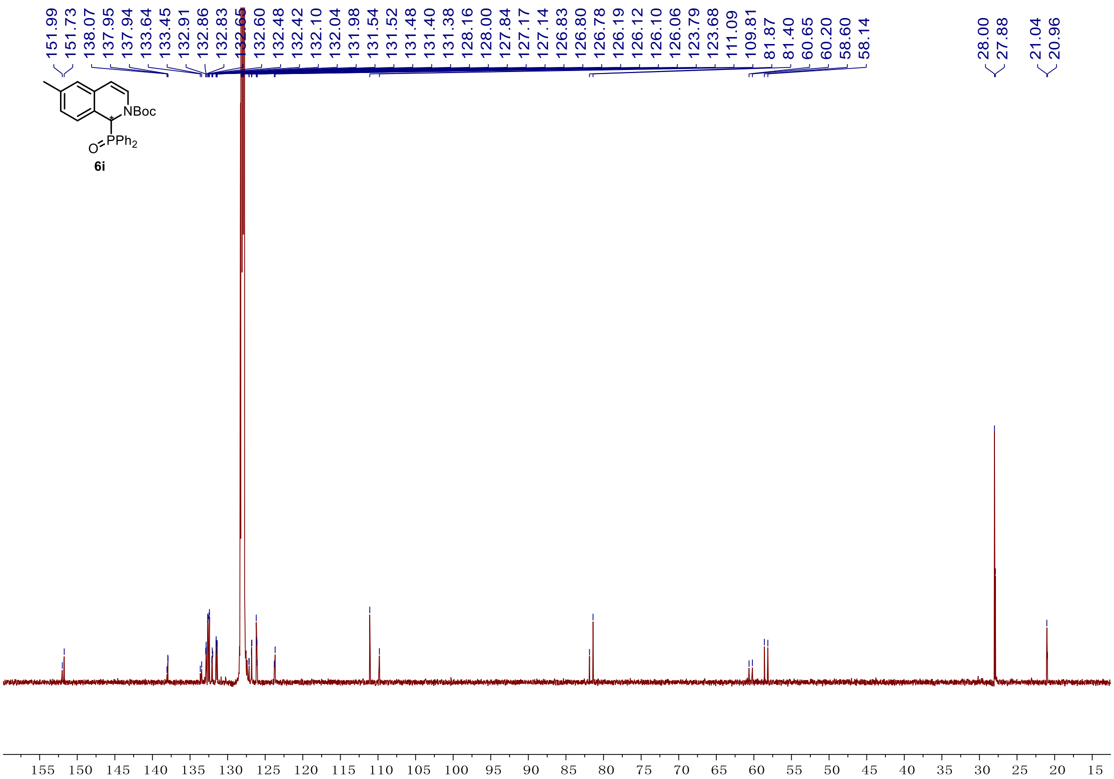


Fig.S 77 ^{13}C NMR of compound **6i**

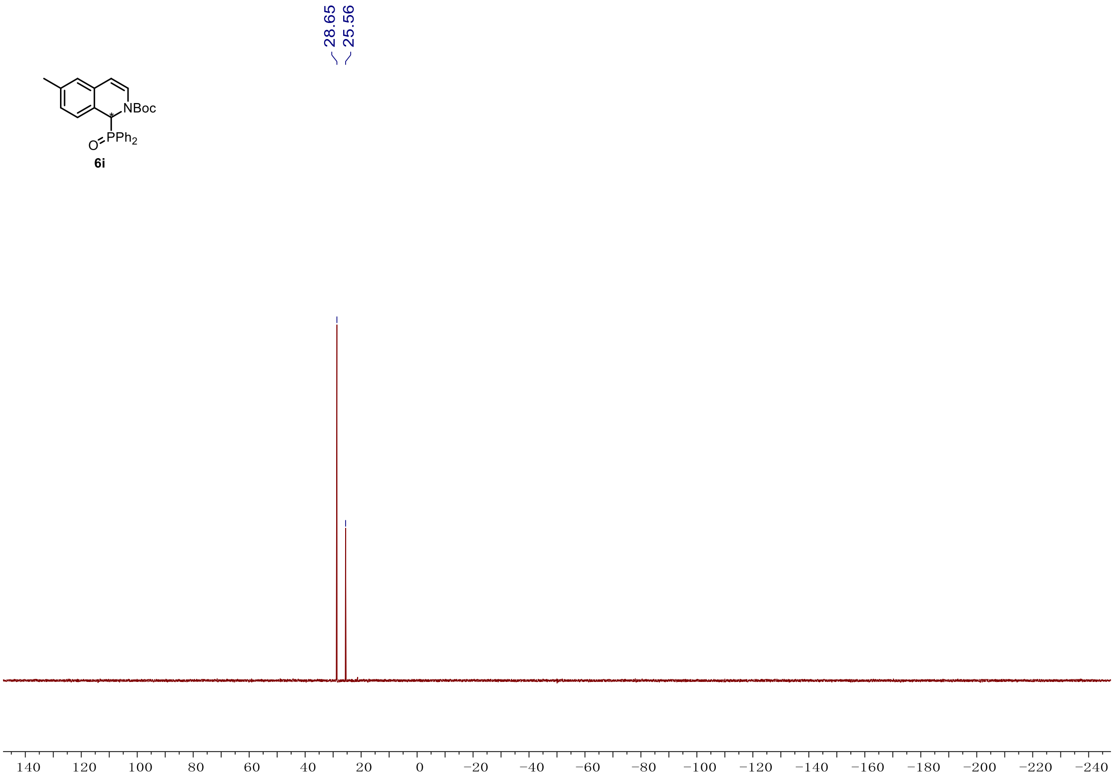


Fig.S 78 ^{31}P NMR of compound **6i**

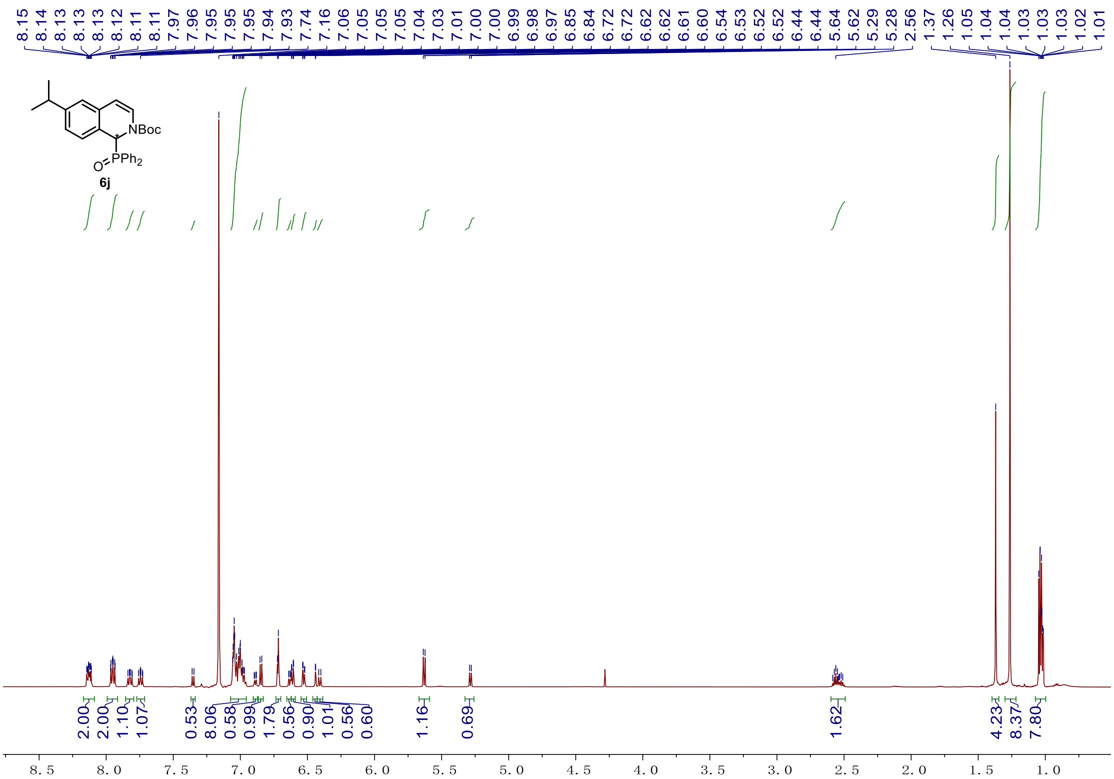


Fig.S 79 ^{1}H NMR of compound **6j**

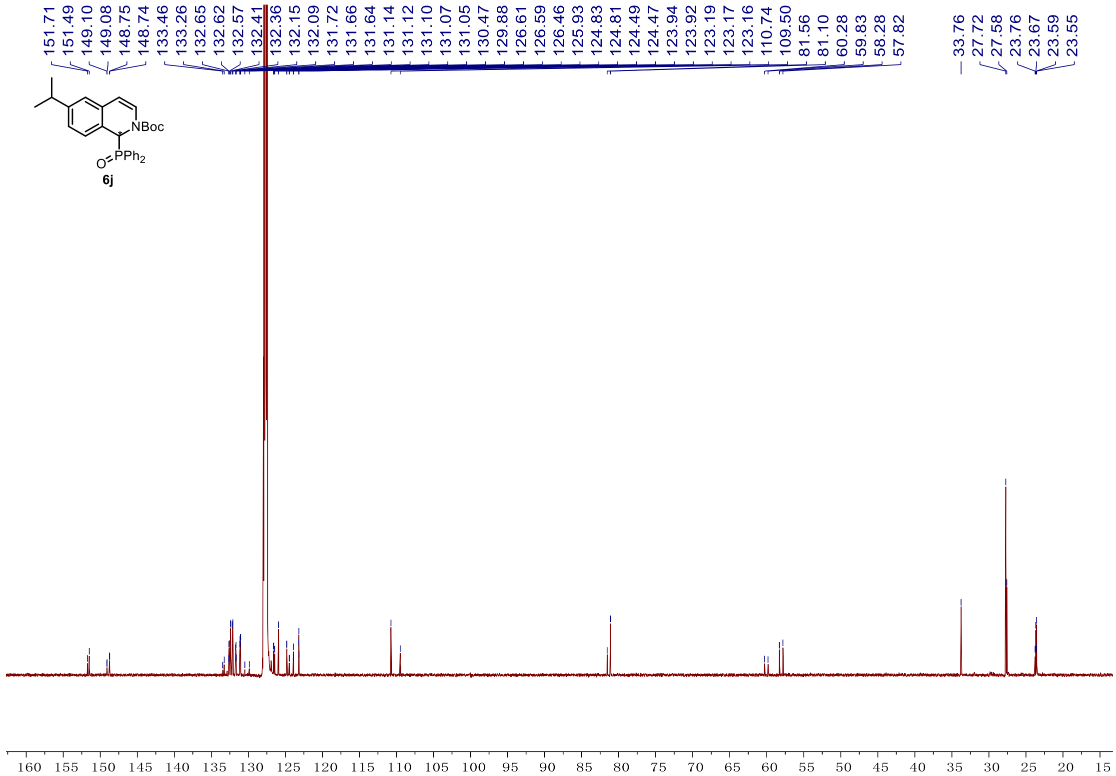


Fig.S 80 ^{13}C NMR of compound **6j**

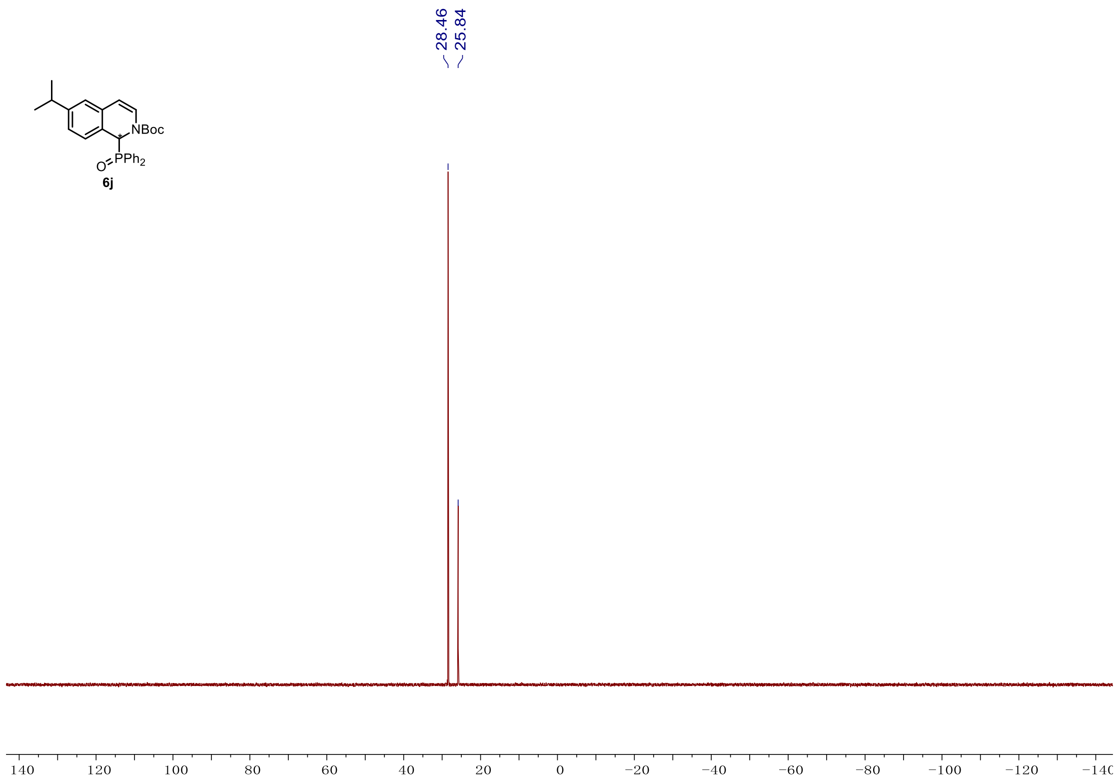


Fig.S 81 ^{31}P NMR of compound **6j**

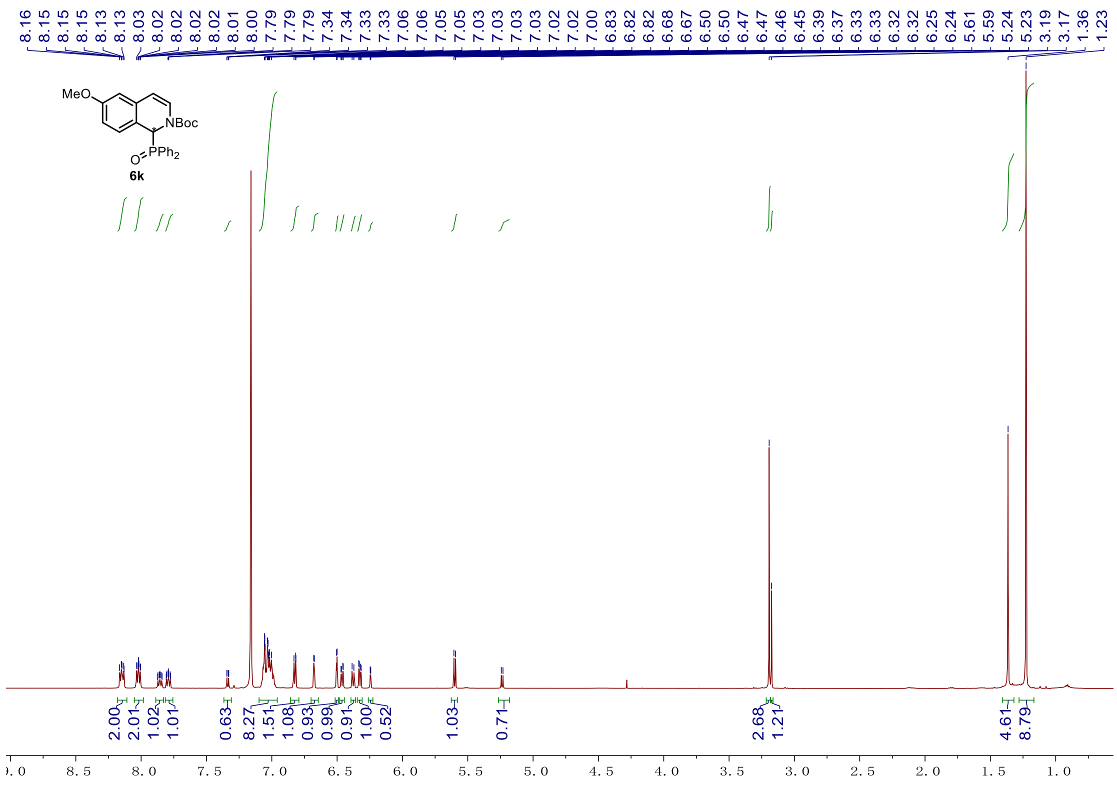


Fig.S 82 ^{1}H NMR of compound **6k**

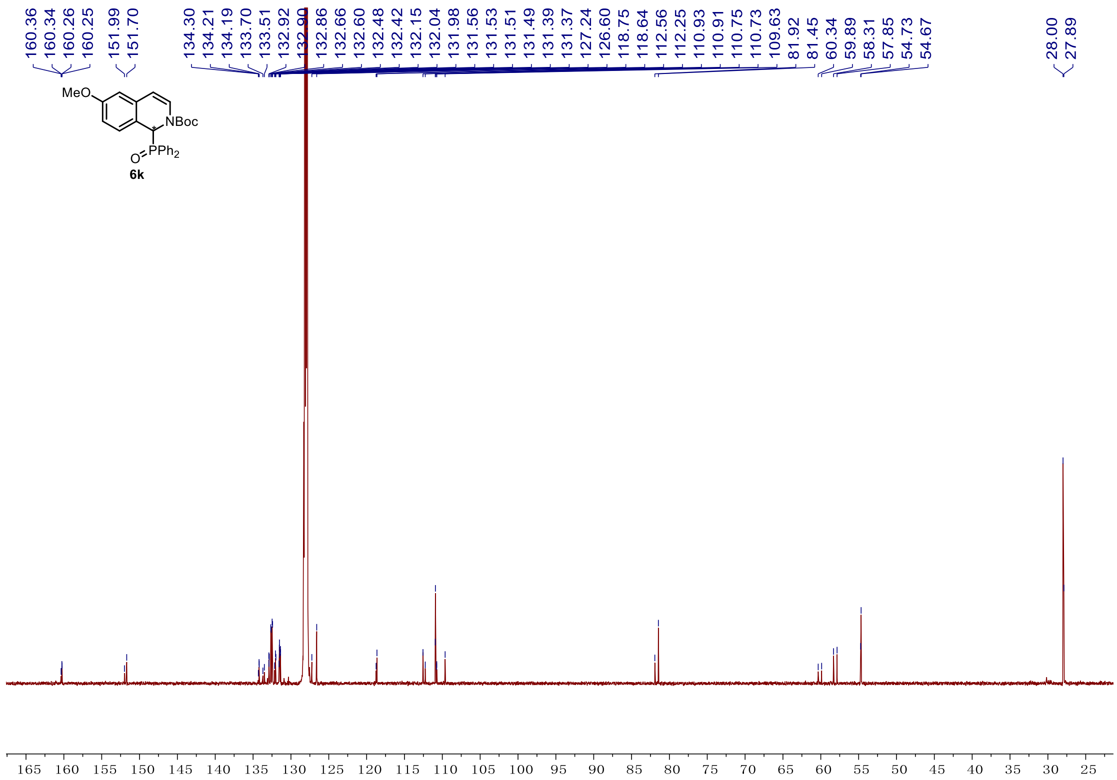


Fig.S 83 ^{13}C NMR of compound **6k**

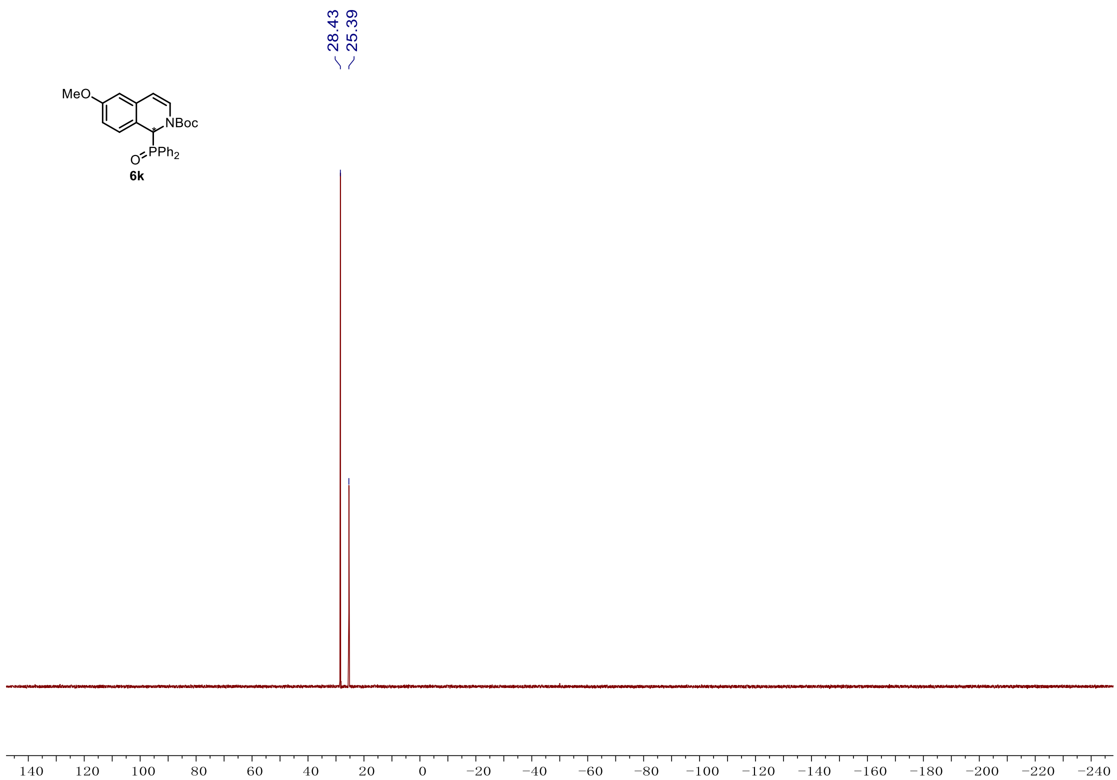


Fig.S 84 ^{31}P NMR of compound **6k**

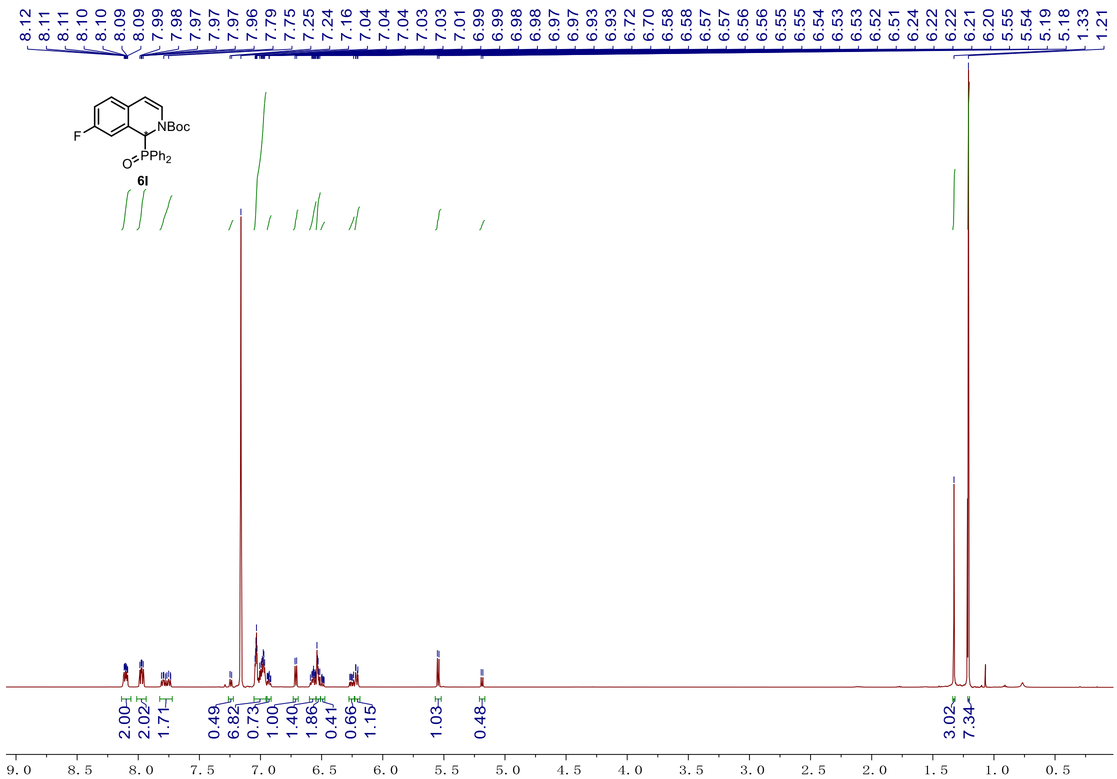


Fig.S 85 ^{1}H NMR of compound **6l**

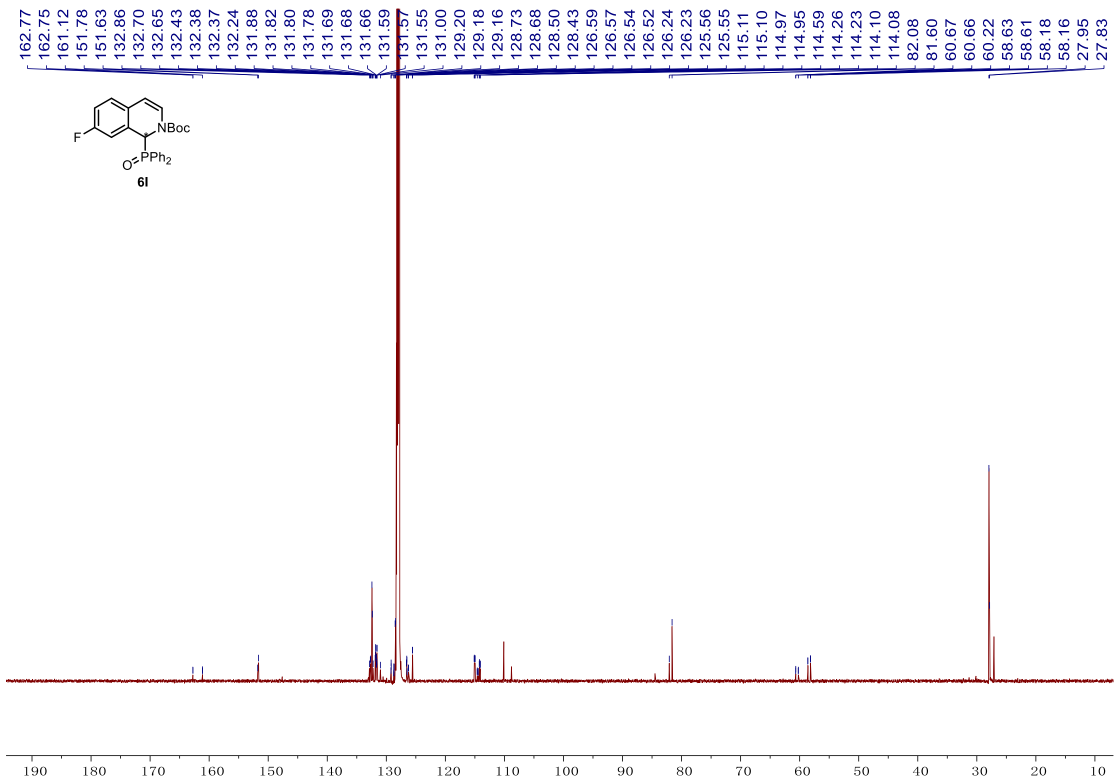


Fig.S 86 ^{13}C NMR of compound **6l**

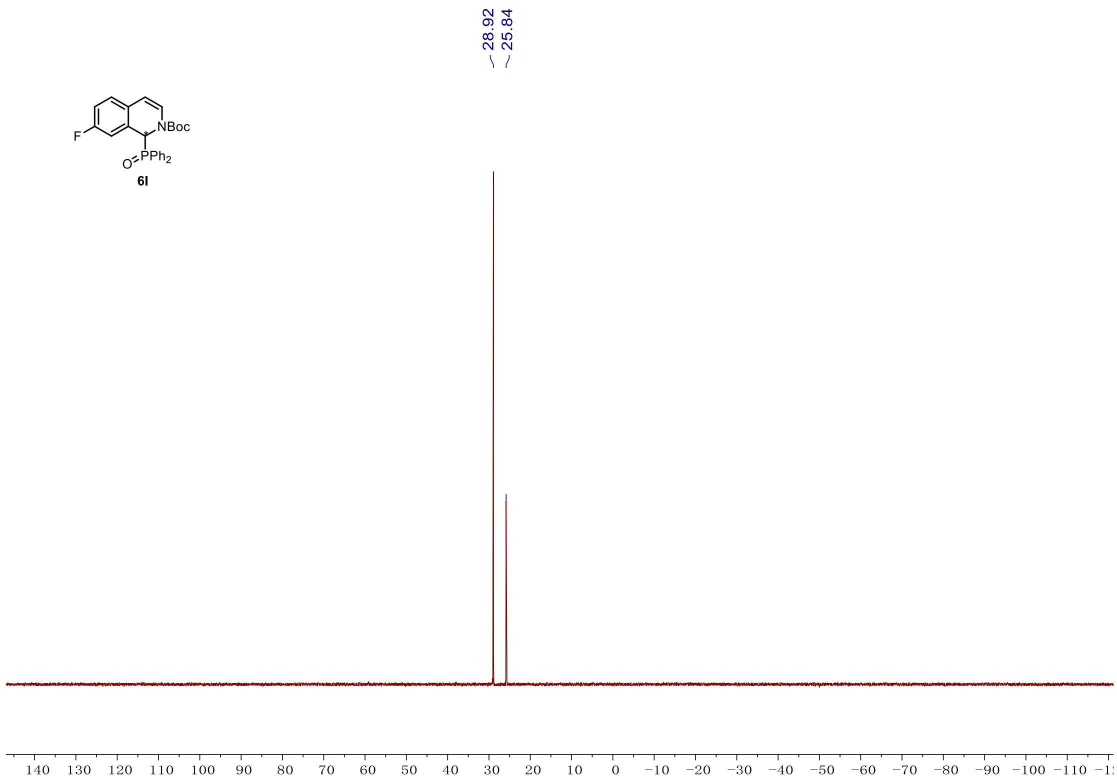


Fig.S 87 ^{31}P NMR of compound **6l**

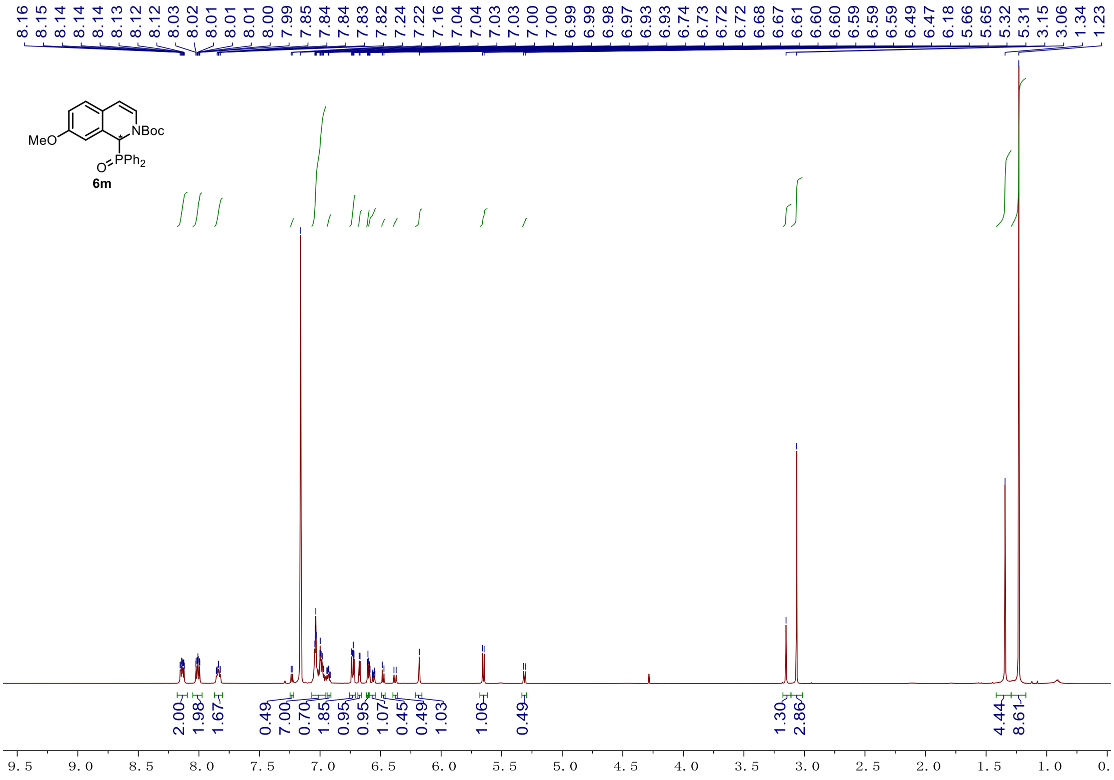


Fig.S 88 ^{1}H NMR of compound **6m**

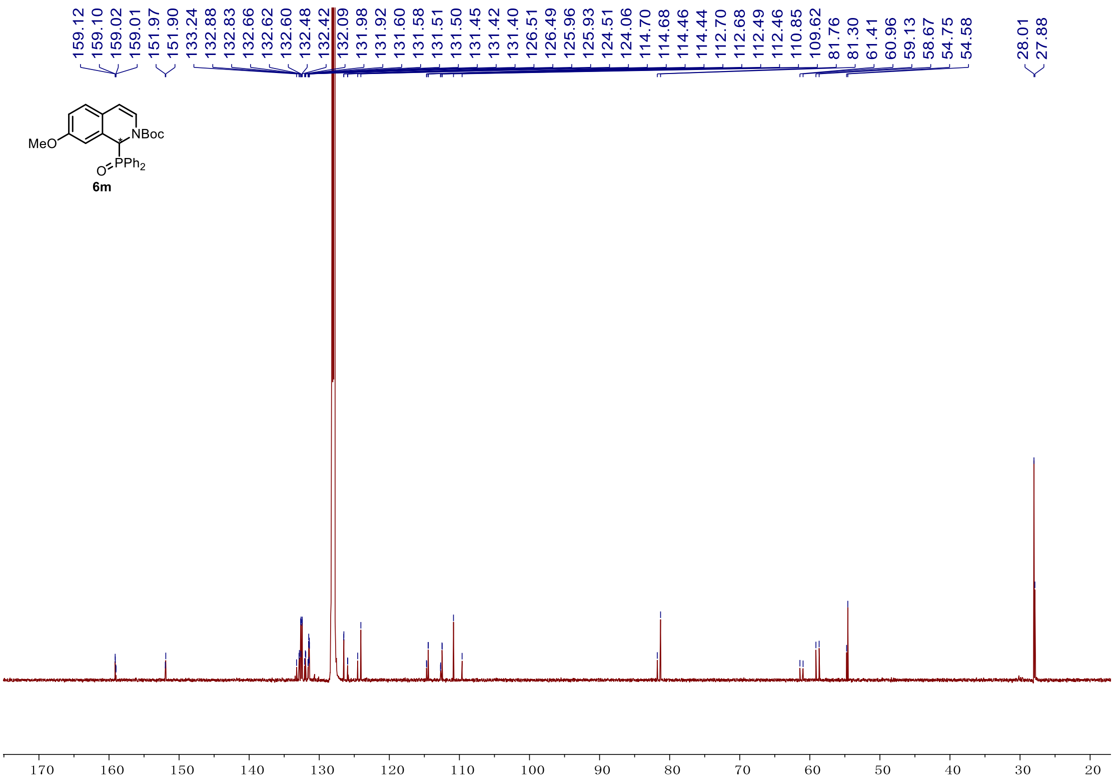


Fig.S 89 ^{13}C NMR of compound **6m**

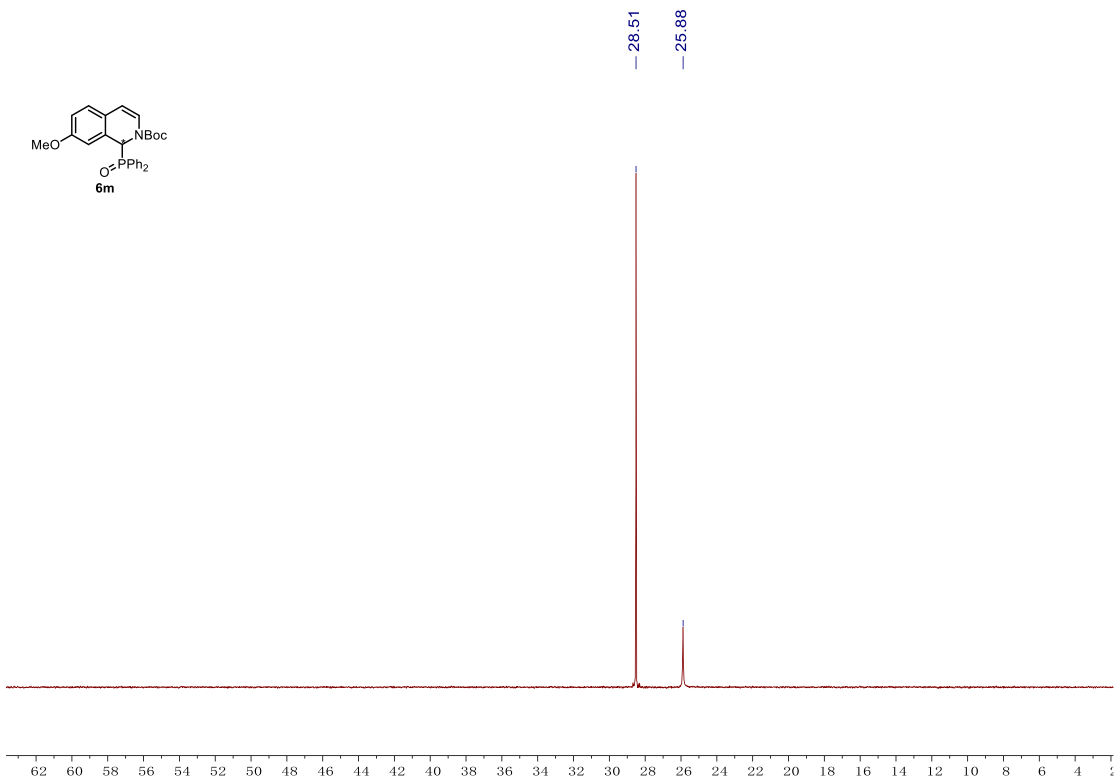


Fig.S 90 ^{31}P NMR of compound **6m**

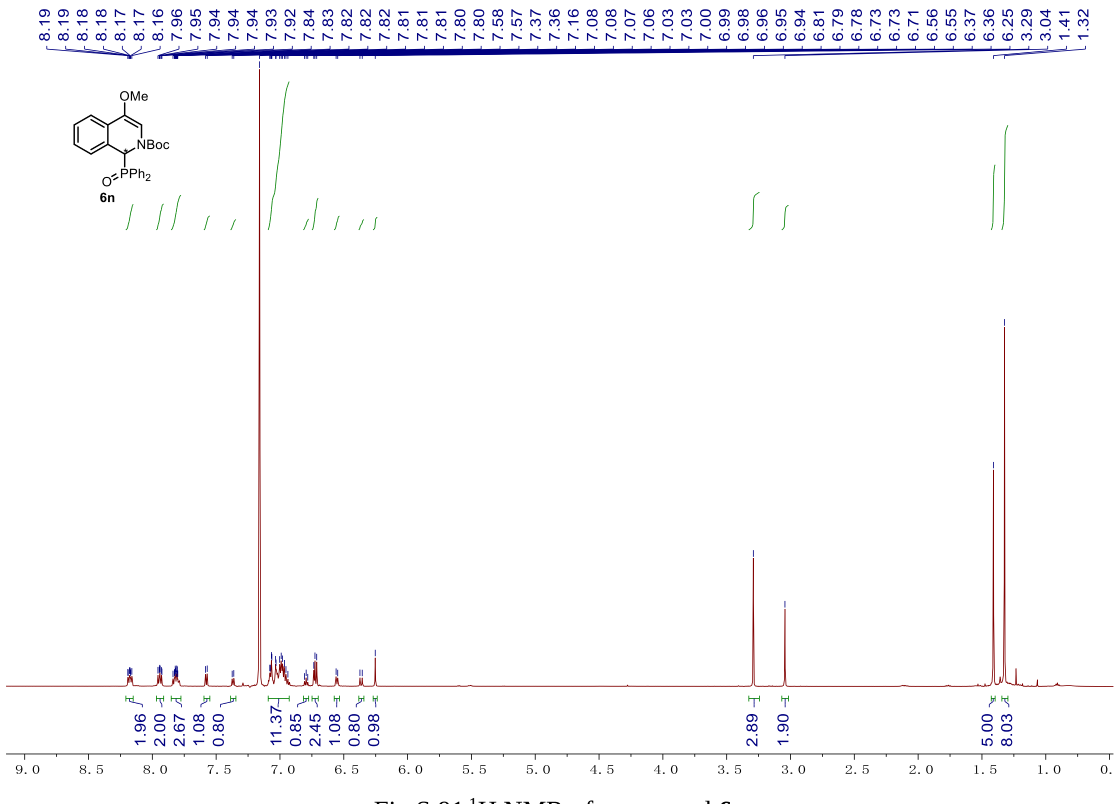


Fig.S 91 ^{1}H NMR of compound **6n**

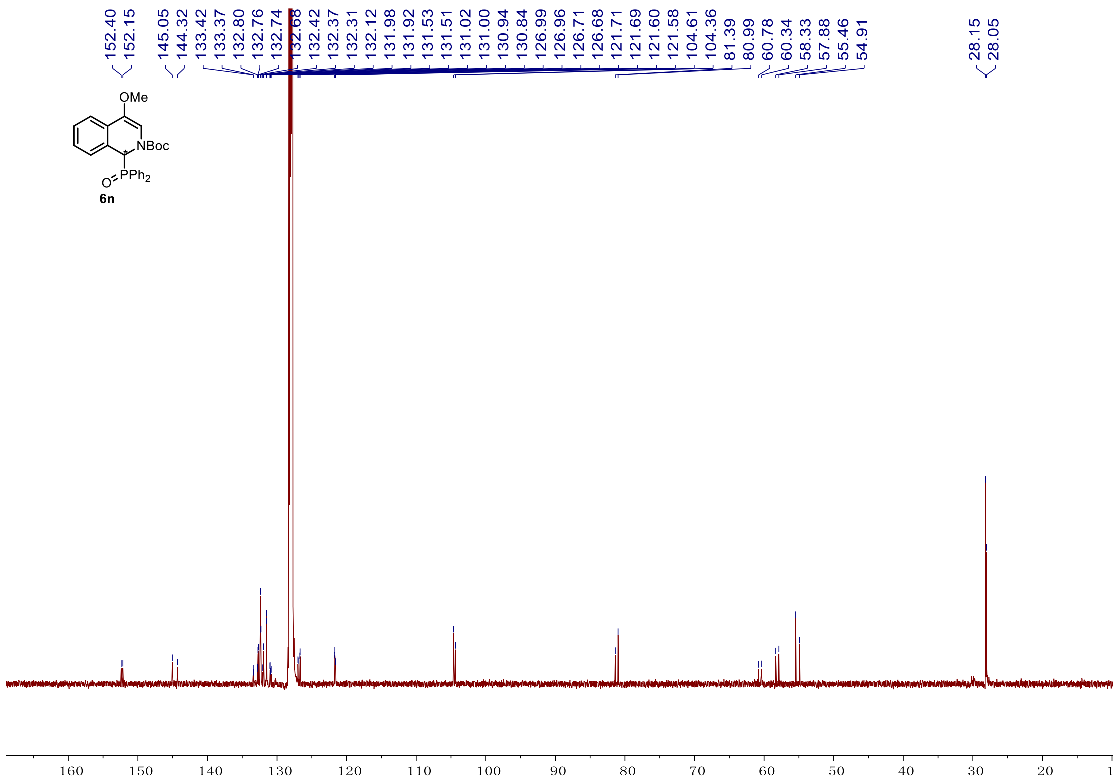


Fig.S 92 ^{13}C NMR of compound **6n**

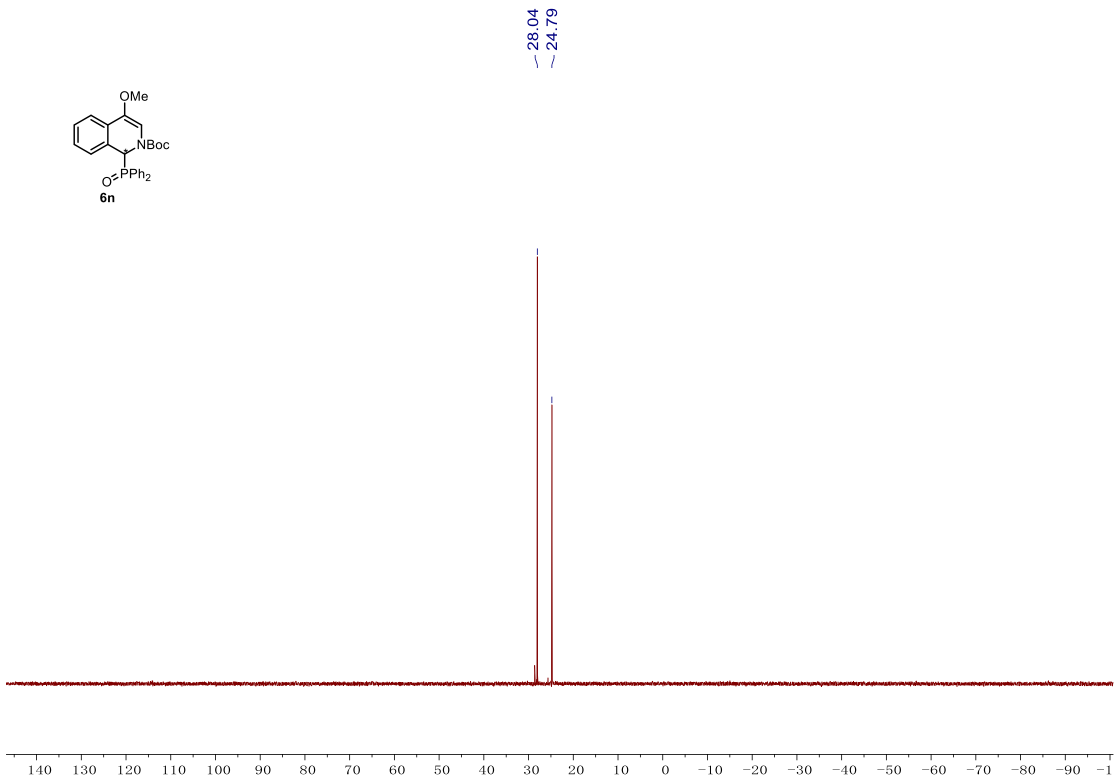
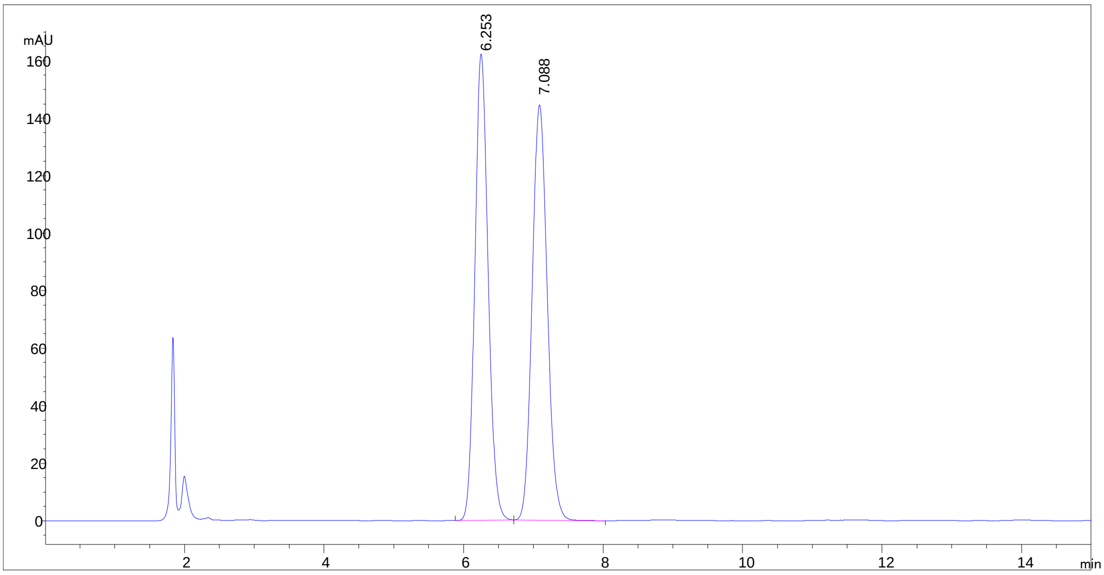


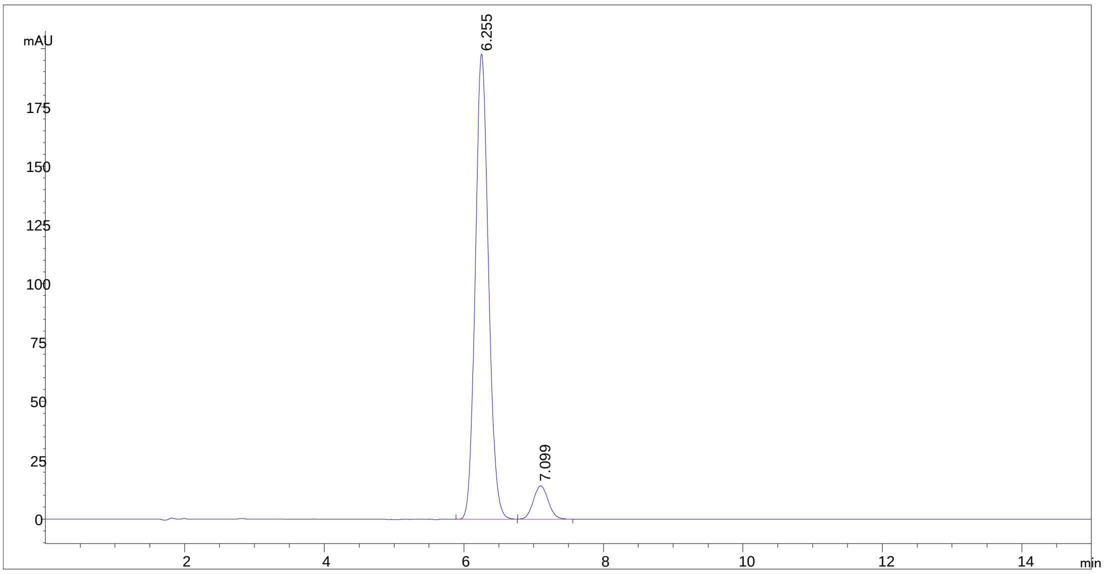
Fig.S 93 ^{31}P NMR of compound **6n**

4. HPLC of 1,2-dihydroisoquinoline-1-ylphosphonates 4



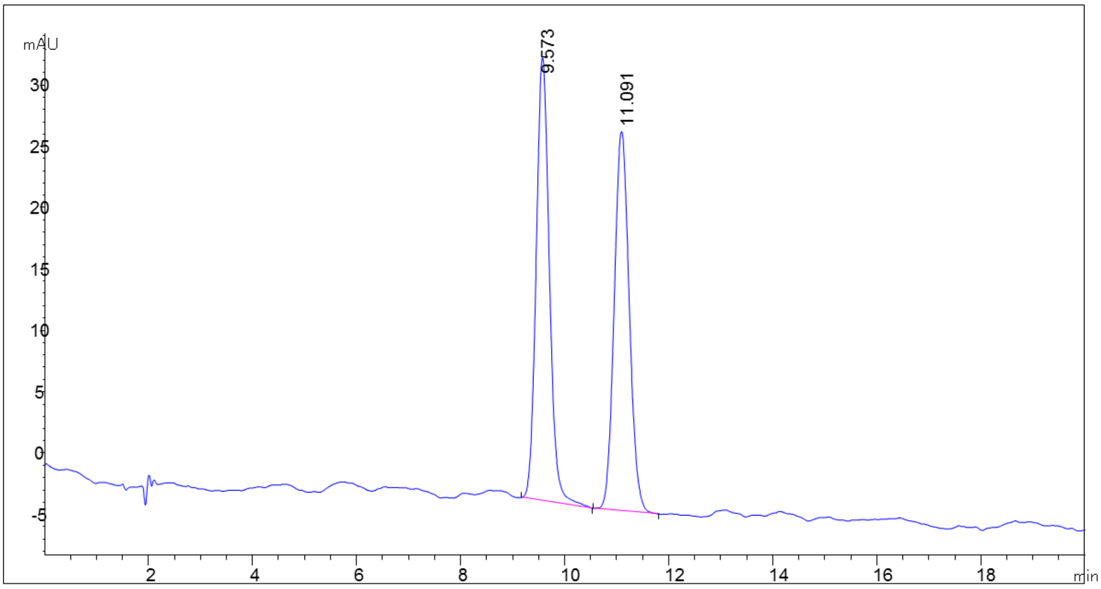
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.253	2163.2	162.2	49.986
2	7.088	2164.4	144.5	50.014

Fig.S 94 HPLC for racemic compound **4aa**



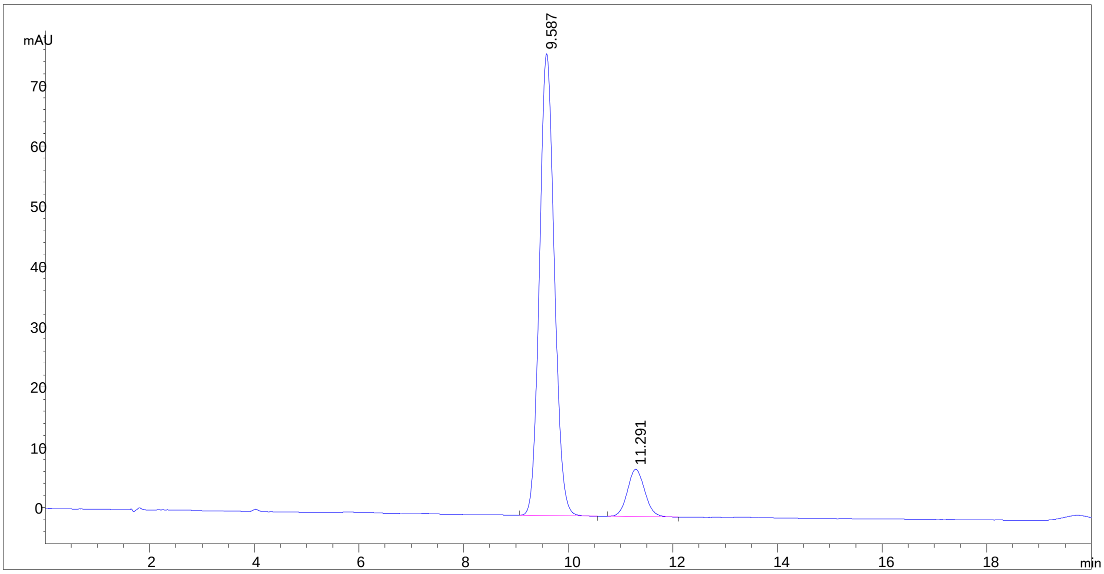
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.255	2624.1	197.6	92.693
2	7.099	206.9	14.1	7.307

Fig.S 95 HPLC for pure enantioenriched compound **4aa**



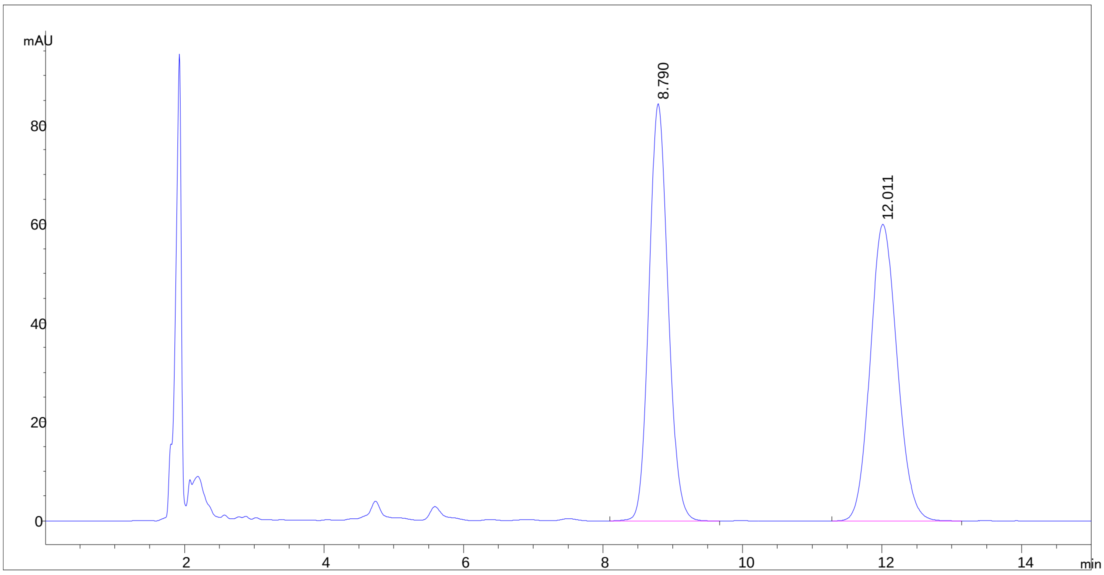
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	9.573	635.7	36.1	50.583
2	11.091	621	30.9	49.417

Fig.S 96 HPLC for racemic compound **4ab**



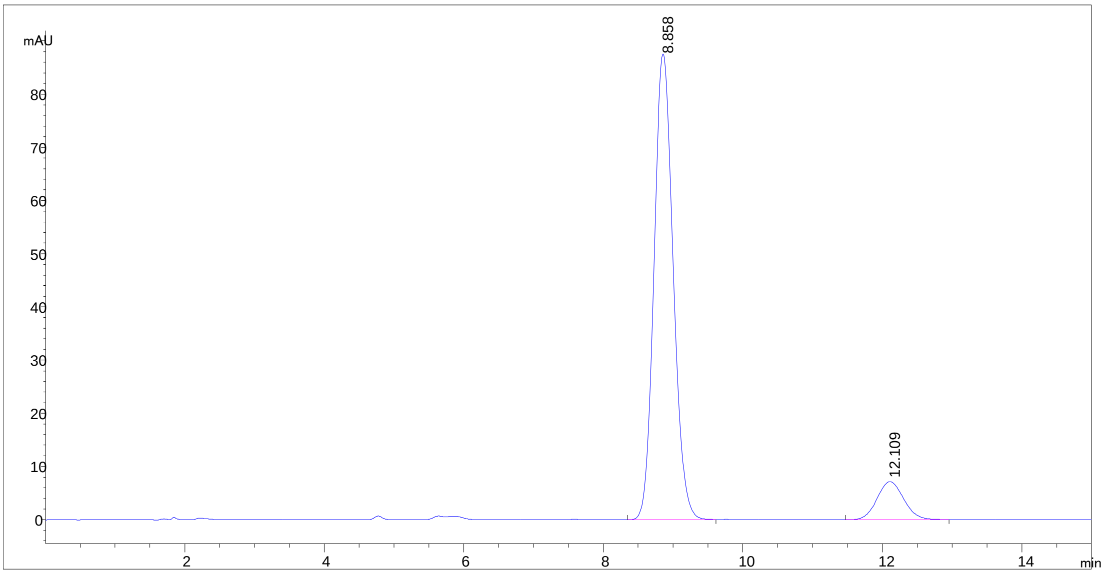
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	9.587	1516.1	76.6	89.436
2	11.291	179.1	7.8	10.564

Fig.S 97 HPLC for pure enantioenriched compound **4ab**



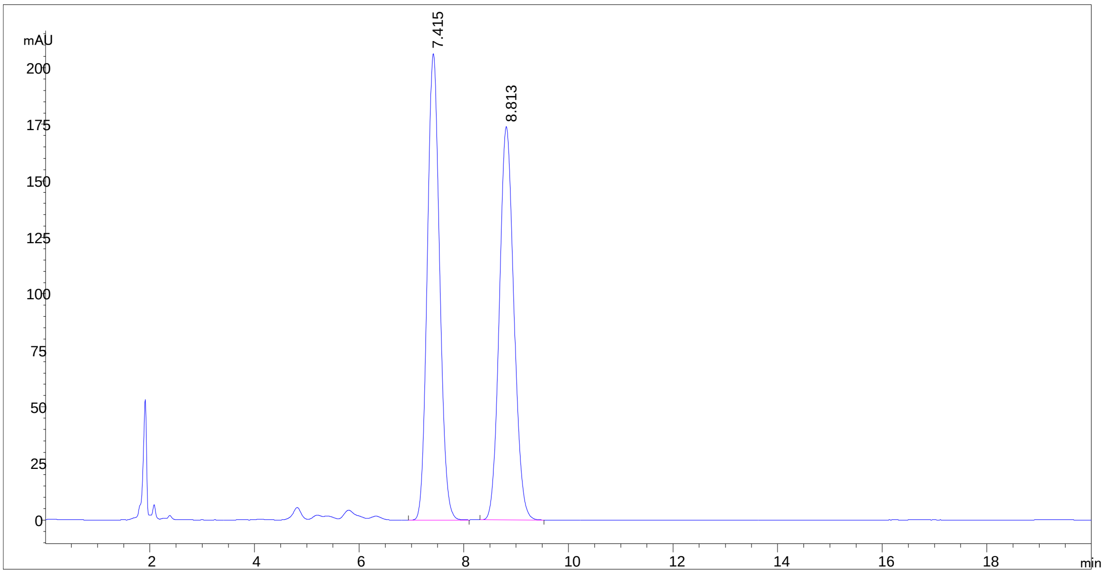
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.79	1614.9	84.4	50.082
2	12.011	1609.7	60	49.918

Fig.S 98 HPLC for racemic compound **4ac**



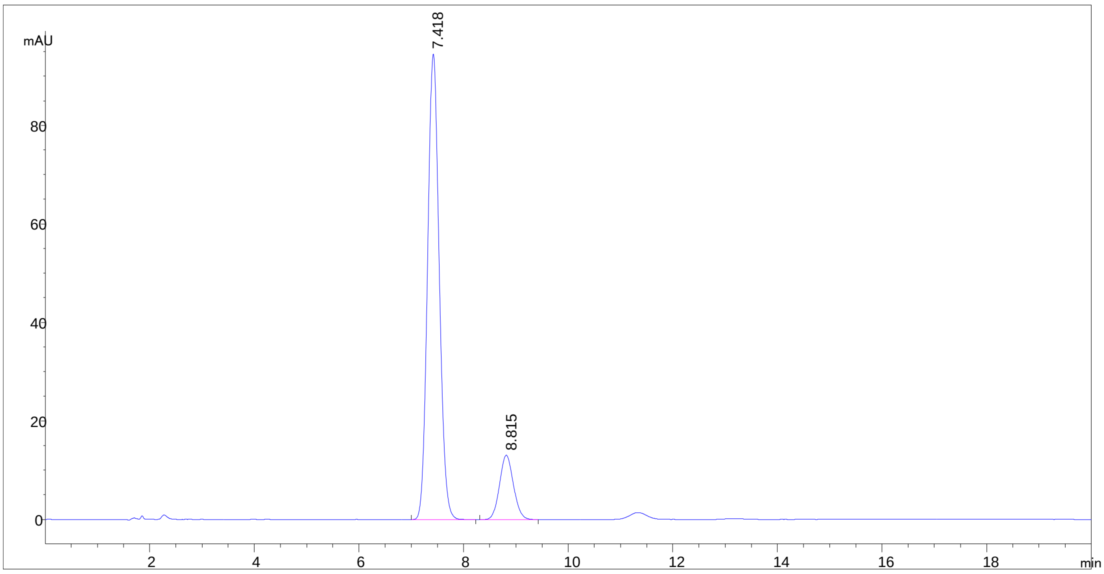
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.858	1670.6	87.5	89.882
2	12.109	188.1	7.1	10.118

Fig.S 99 HPLC for pure enantioenriched compound **4ac**



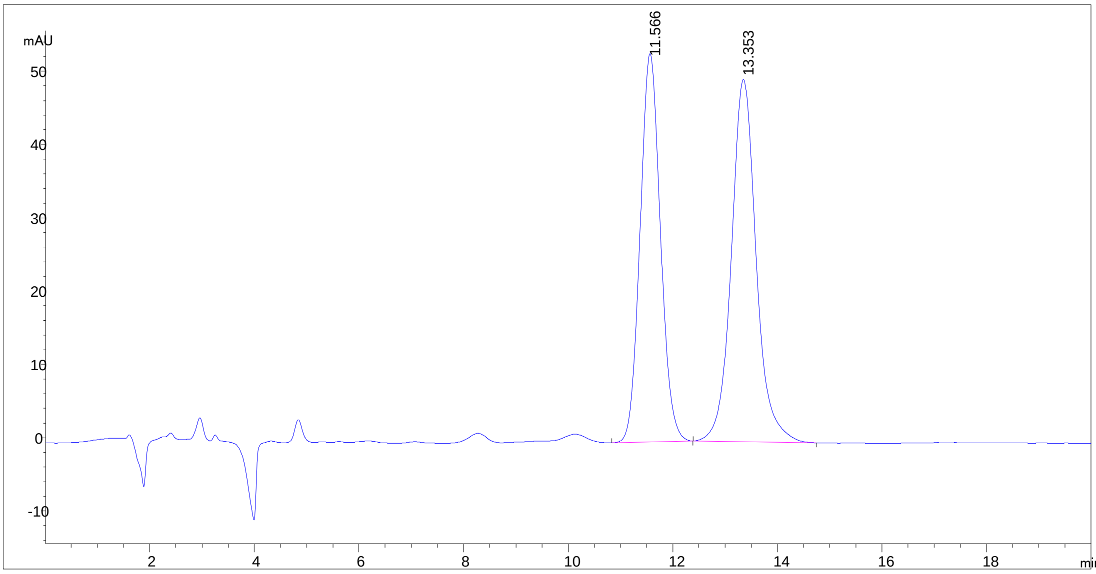
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.415	3378.8	206.3	50.064
2	8.813	3370.2	174	49.936

Fig.S 100 HPLC for racemic compound **4ad**



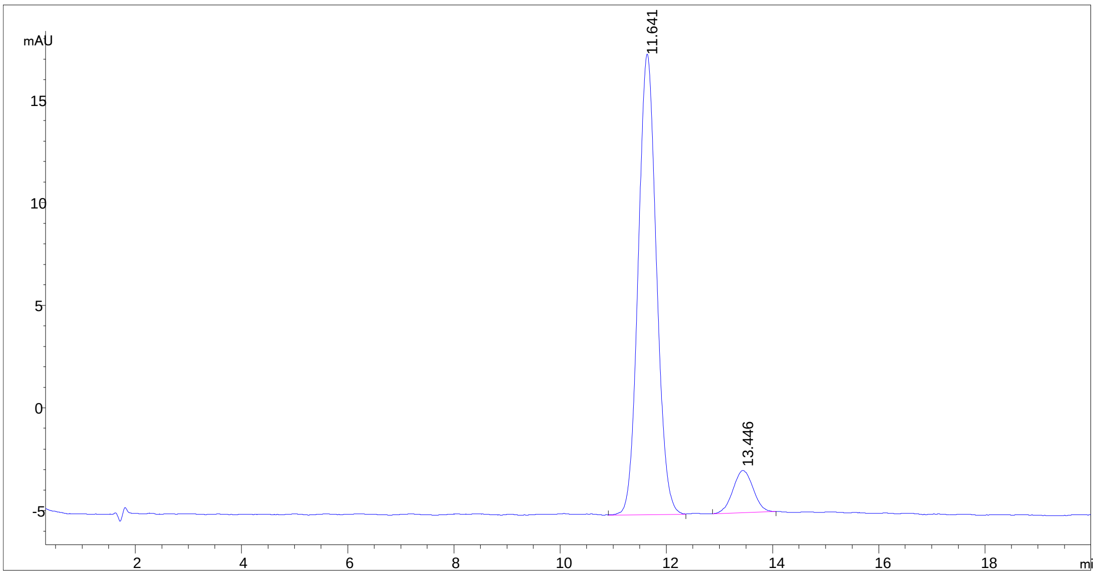
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.418	1456.6	94.5	85.771
2	8.815	241.7	13.1	14.229

Fig.S 101 HPLC for pure enantioenriched compound **4ad**



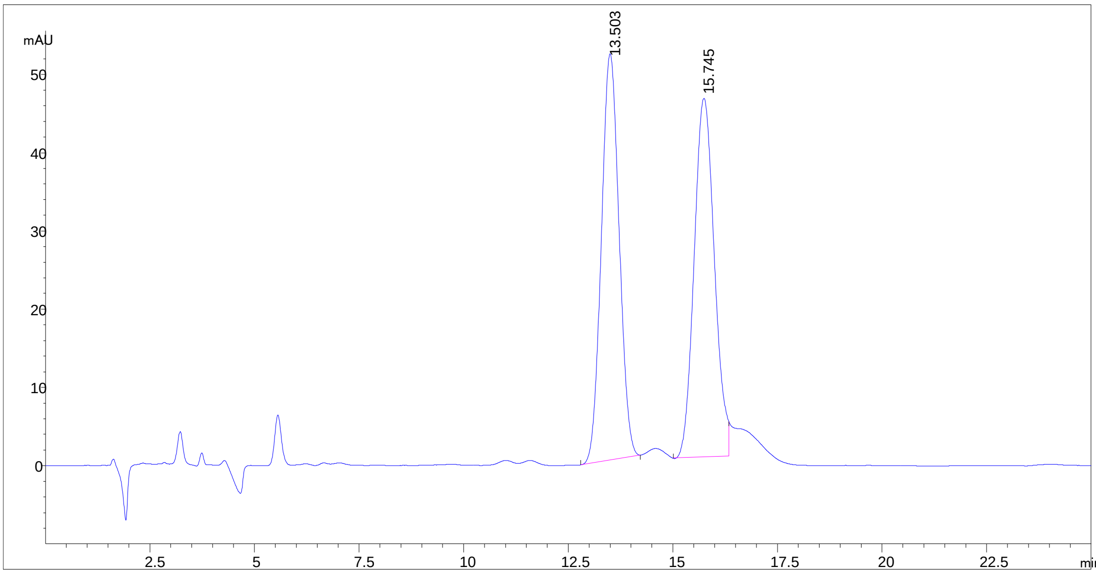
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.566	1430.9	53	46.717
2	13.353	1632	49.4	53.283

Fig.S 102 HPLC for racemic compound **4ba**



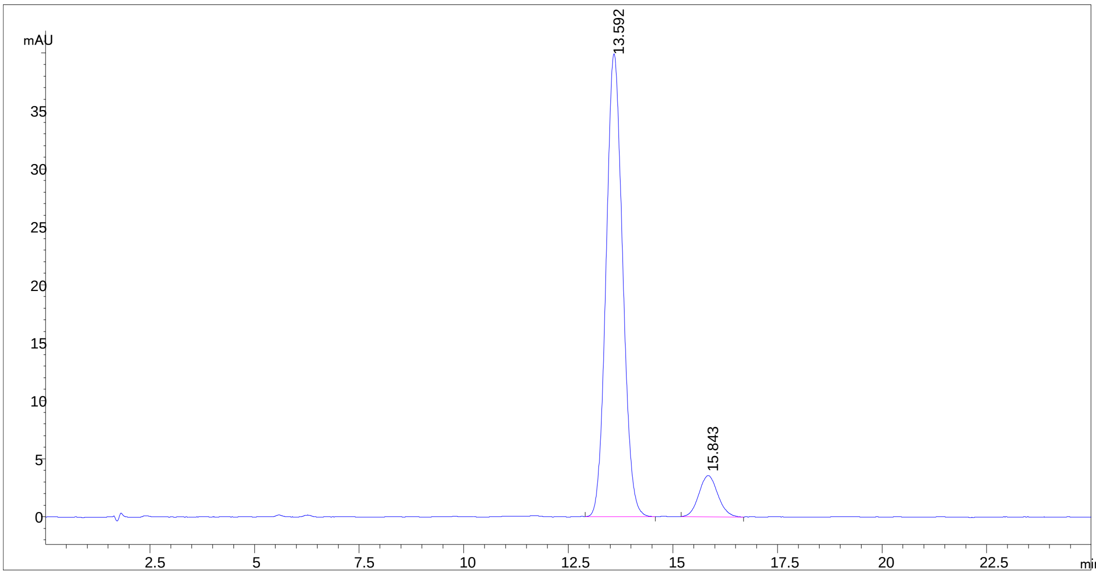
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.641	534.8	22.4	90.716
2	13.446	54.7	2.1	9.284

Fig.S 103 HPLC for pure enantioenriched compound **4ba**



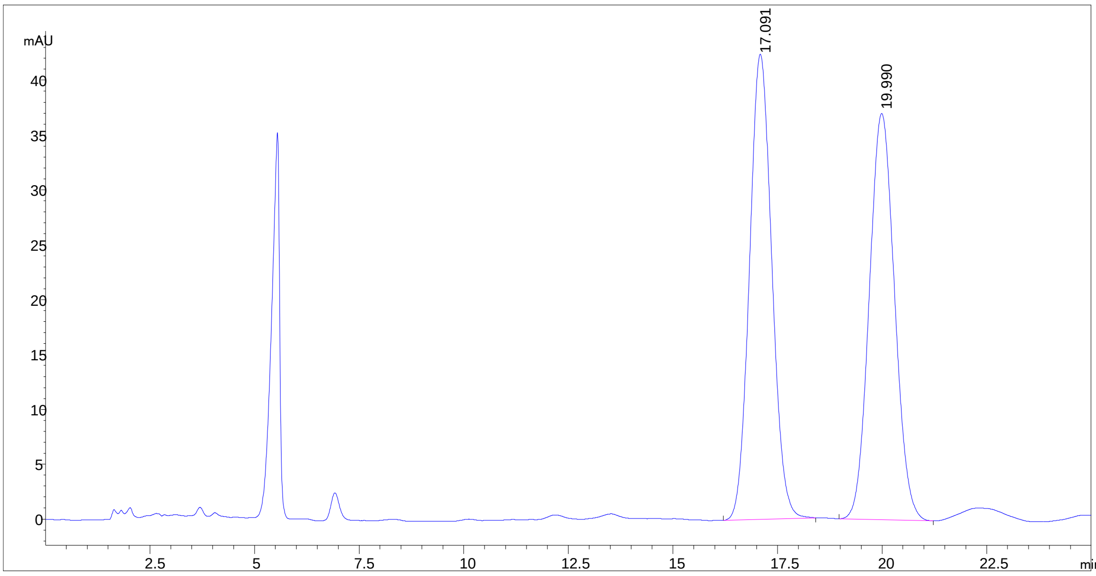
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	13.503	1535.9	51.9	49.921
2	15.745	1540.8	45.8	50.079

Fig.S 104 HPLC for racemic compound **4ca**



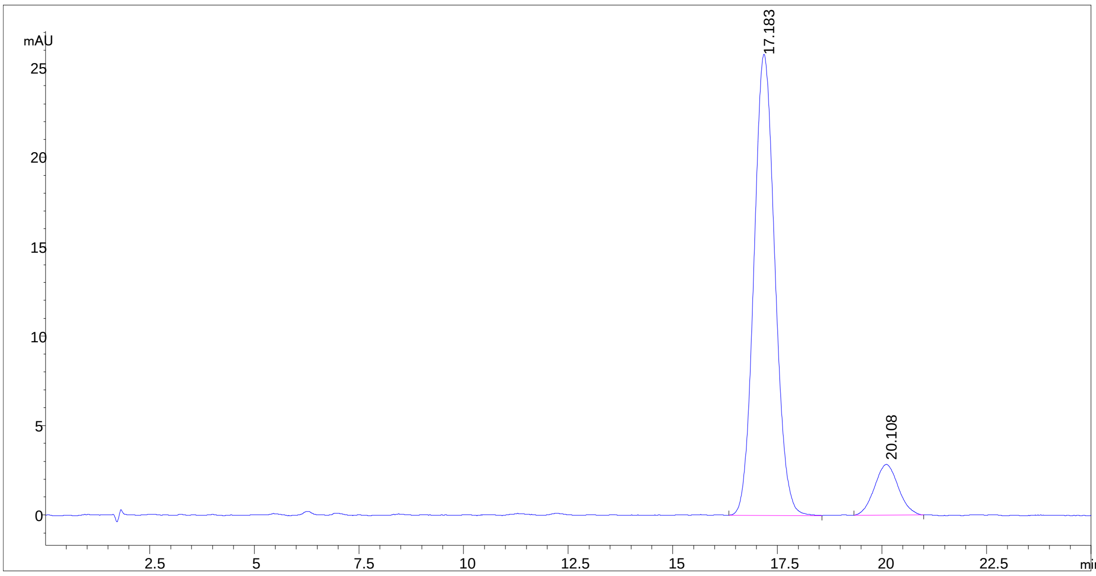
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	13.592	1099	39.9	90.769
2	15.843	111.8	3.6	9.231

Fig.S 105 HPLC for pure enantioenriched compound **4ca**



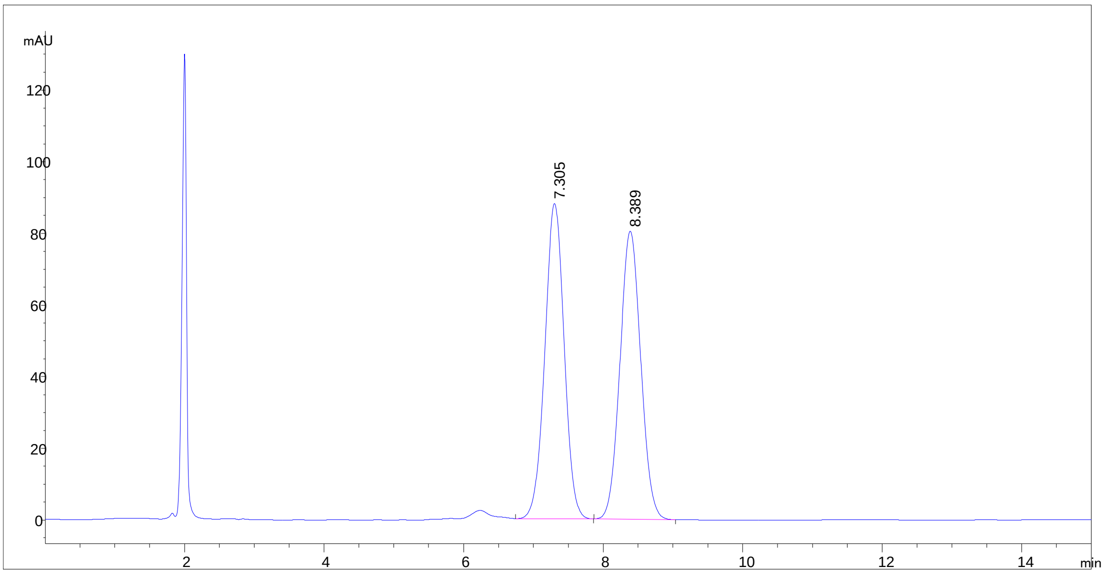
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	17.091	1574.2	42.4	50.281
2	19.99	1556.6	37	49.719

Fig.S 106 HPLC for racemic compound **4da**



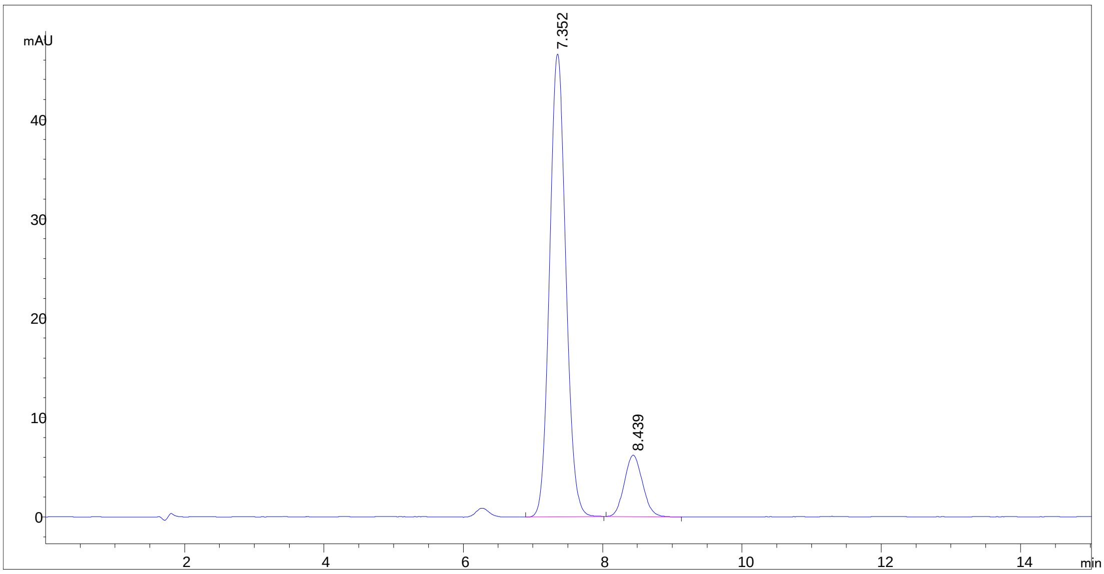
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	17.183	896.5	25.8	88.907
2	20.108	111.9	2.8	11.093

Fig.S 107 HPLC for pure enantioenriched compound **4da**



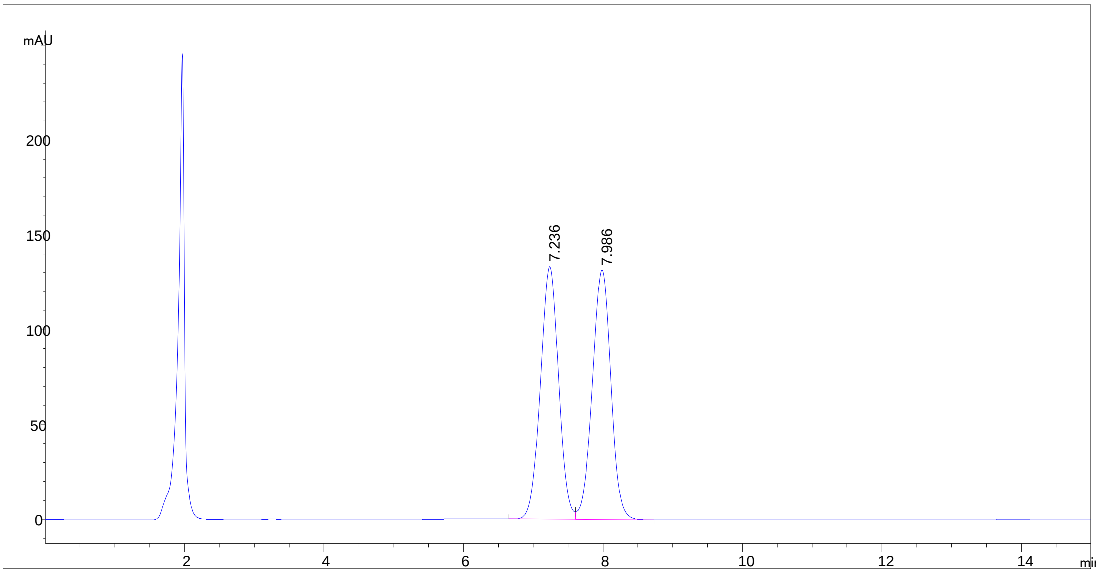
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.305	1695.2	88	50.444
2	8.389	1665.4	80.4	49.556

Fig.S 108 HPLC for racemic compound **4ea**



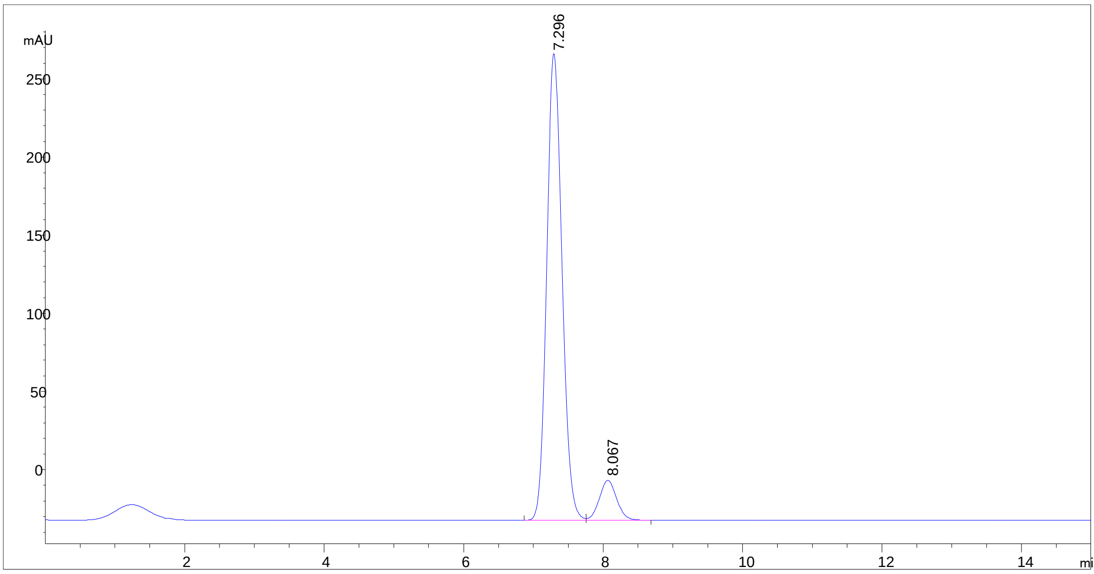
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.352	756.1	46.6	87.089
2	8.439	112.1	6.2	12.911

Fig.S 109 HPLC for pure enantioenriched compound **4ea**



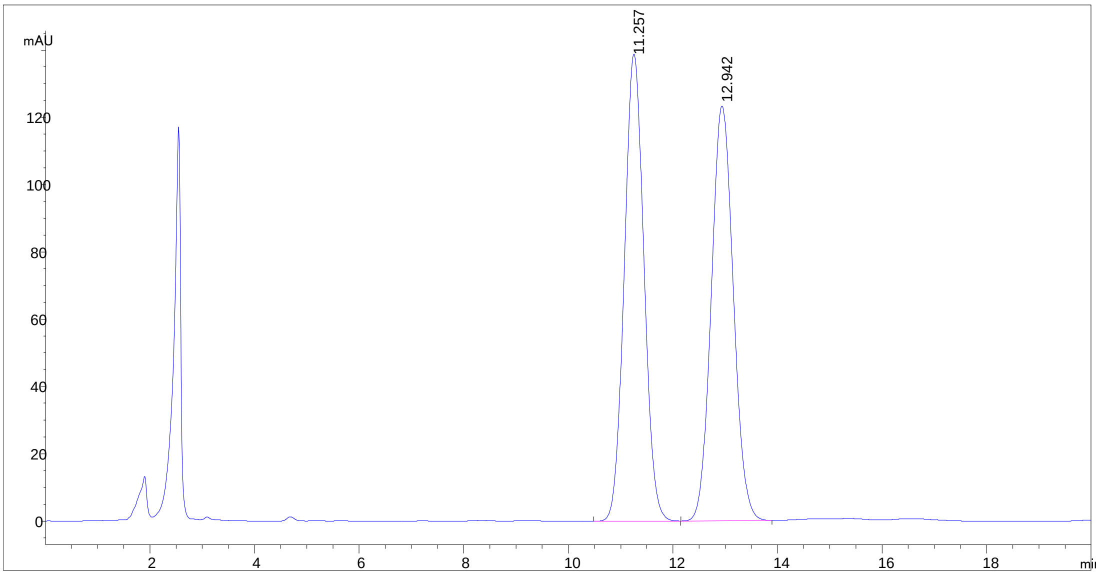
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.236	2432.4	133.3	49.994
2	7.986	2433	131.6	50.006

Fig.S 110 HPLC for racemic compound **4fa**



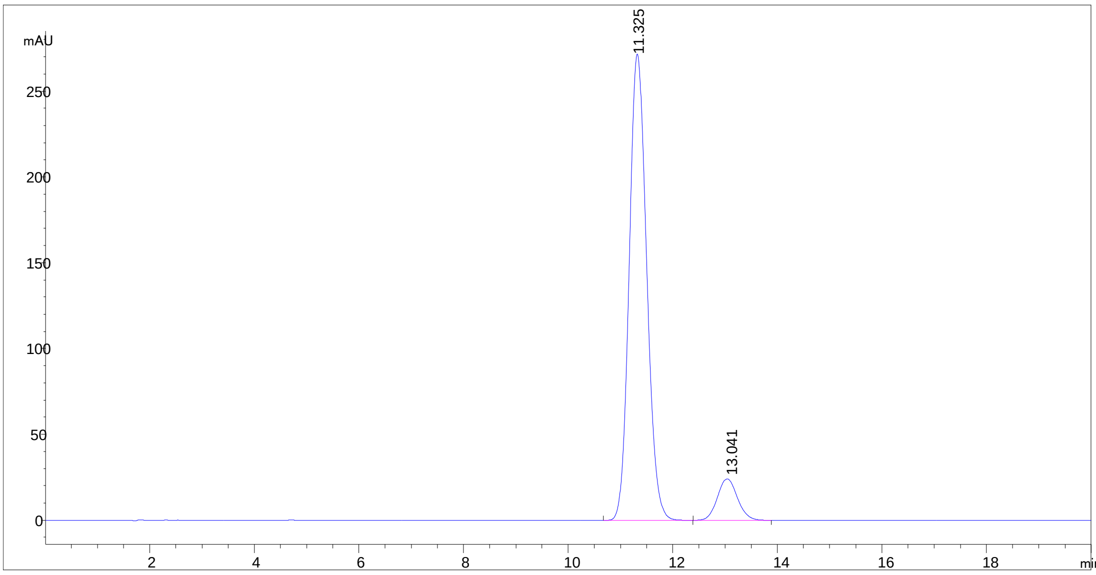
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.296	4561.7	298.4	91.267
2	8.067	436.5	25.4	8.733

Fig.S 111 HPLC for pure enantioenriched compound **4fa**



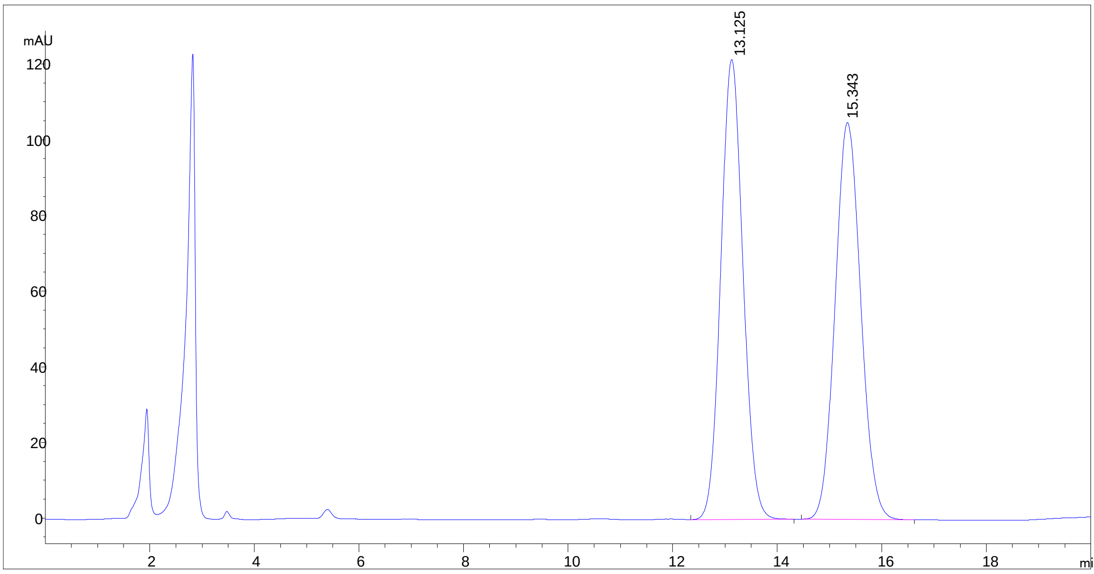
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.257	3622.5	138.9	50.066
2	12.942	3613.1	123.4	49.934

Fig.S 112 HPLC for racemic compound **4ga**



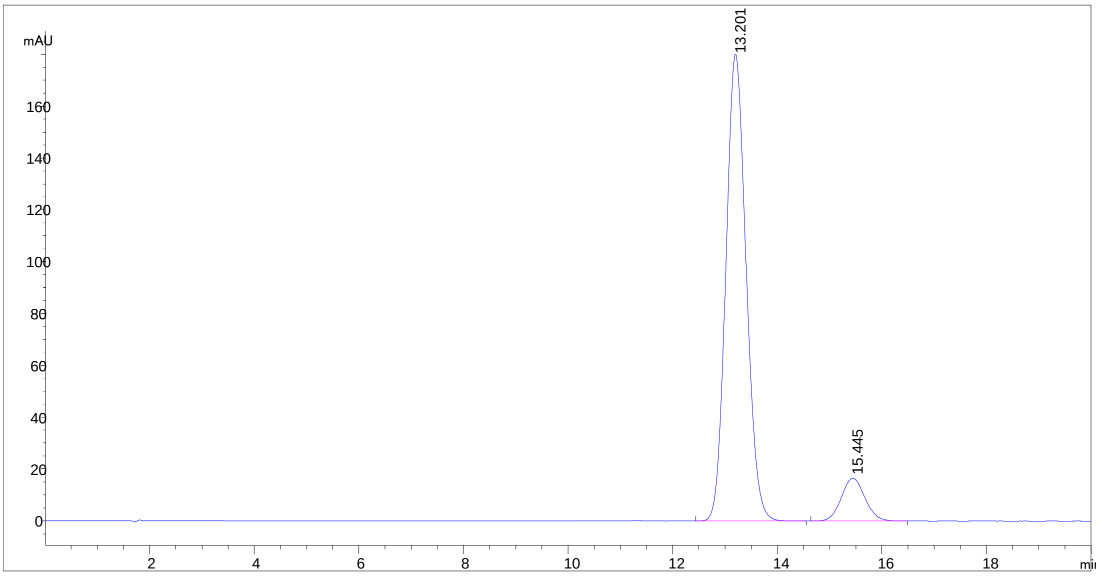
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.325	6299.5	271.7	90.754
2	13.041	641.8	24.1	9.246

Fig.S 113 HPLC for pure enantioenriched compound **4ga**



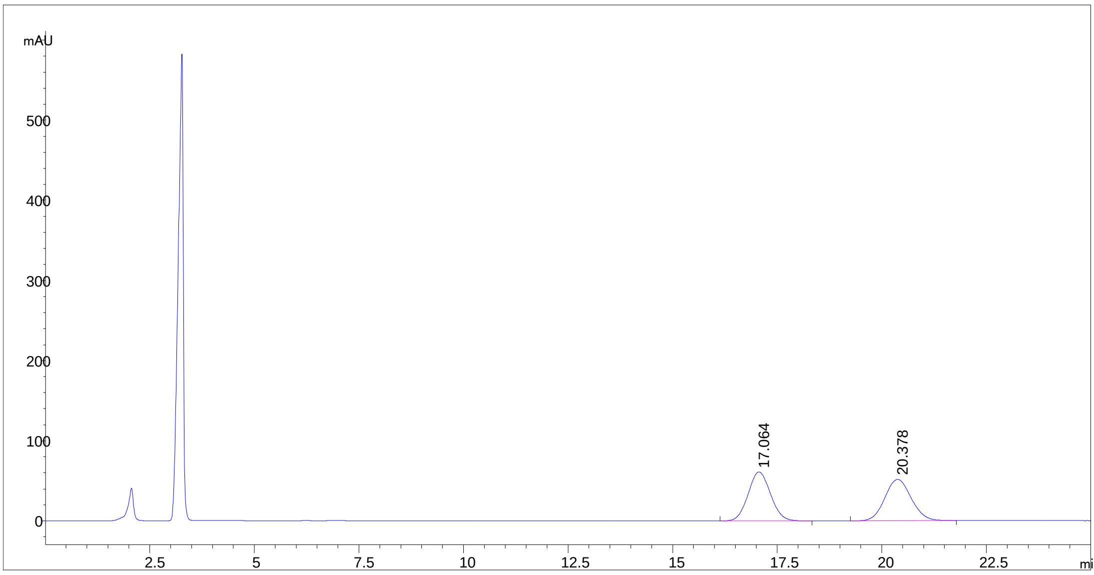
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	13.125	3583	121.5	50.030
2	15.343	3578.7	104.8	49.970

Fig.S 114 HPLC for racemic compound **4ha**



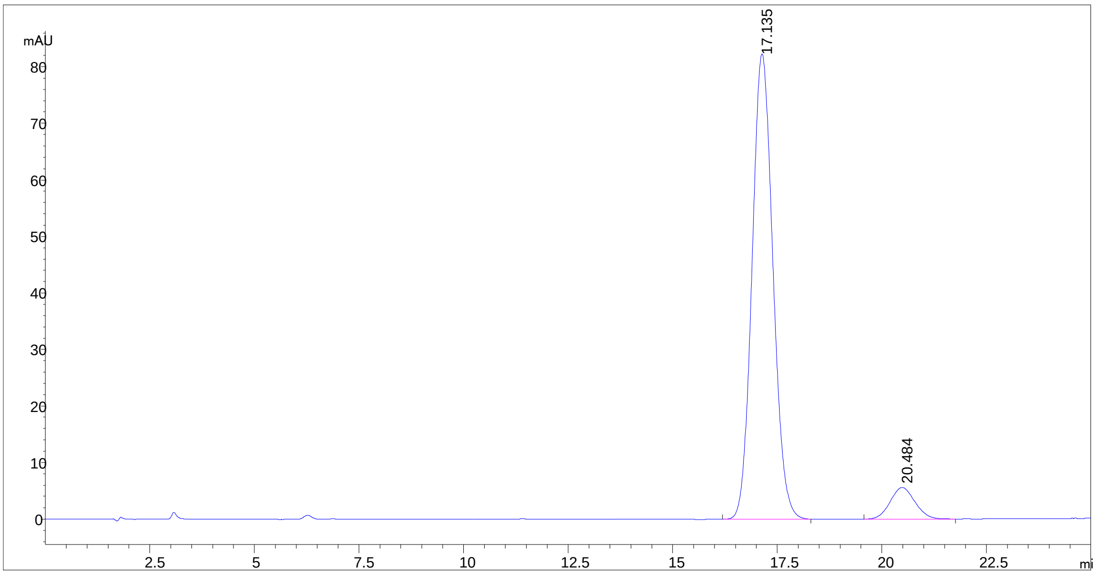
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	13.201	4840.6	180.1	90.347
2	15.445	517.2	16.4	9.653

Fig.S 115 HPLC for pure enantioenriched compound **4ha**



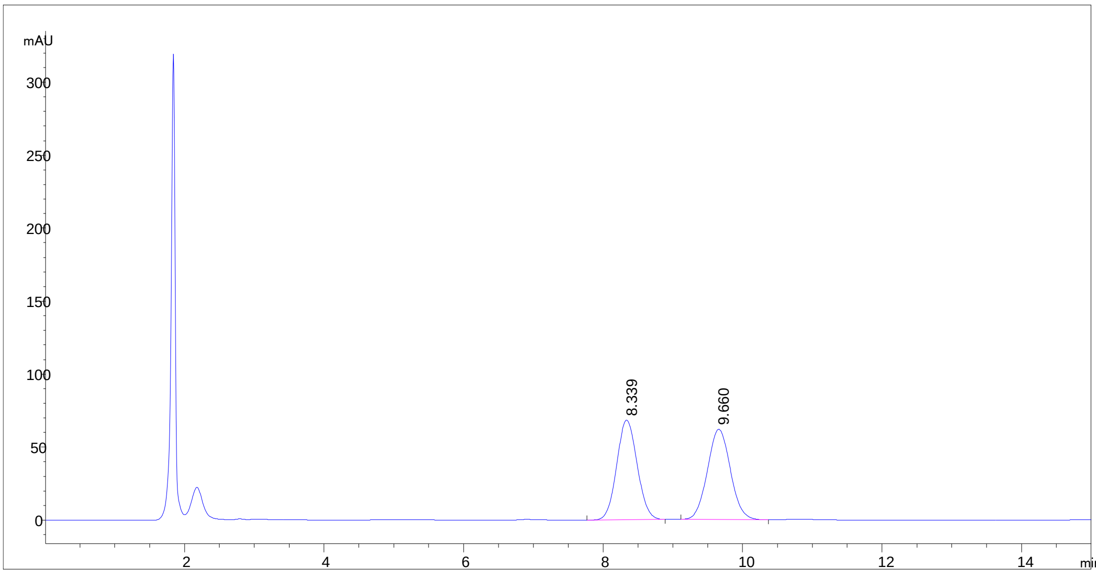
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	17.064	2264.4	60.9	50.079
2	20.378	2257.3	51.5	49.921

Fig.S 116 HPLC for racemic compound **4ia**



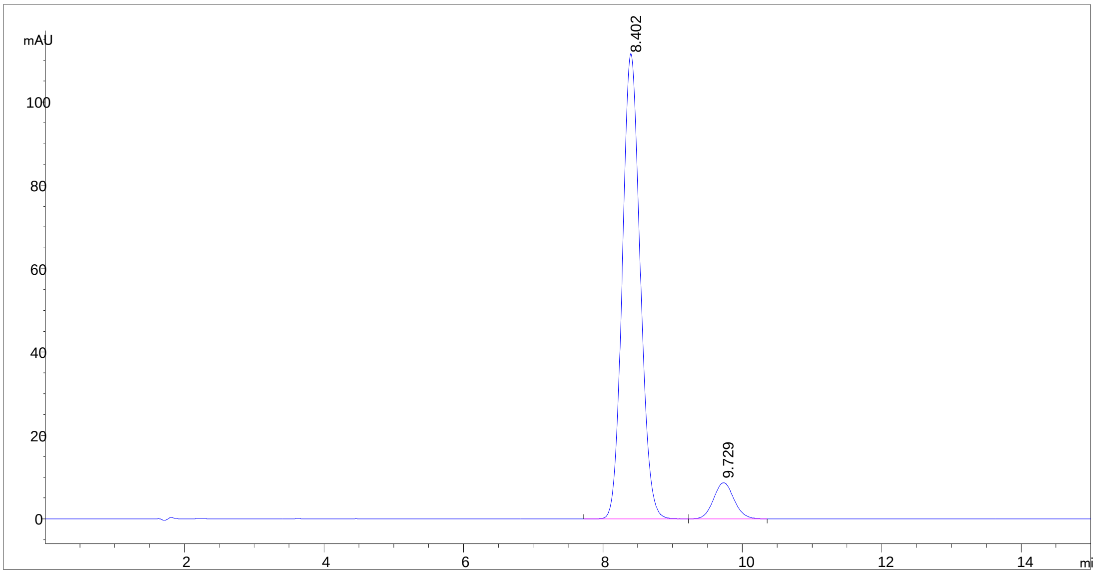
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	17.135	2854.6	82.3	92.523
2	20.484	230.7	5.6	7.477

Fig.S 117 HPLC for pure enantioenriched compound **4ia**



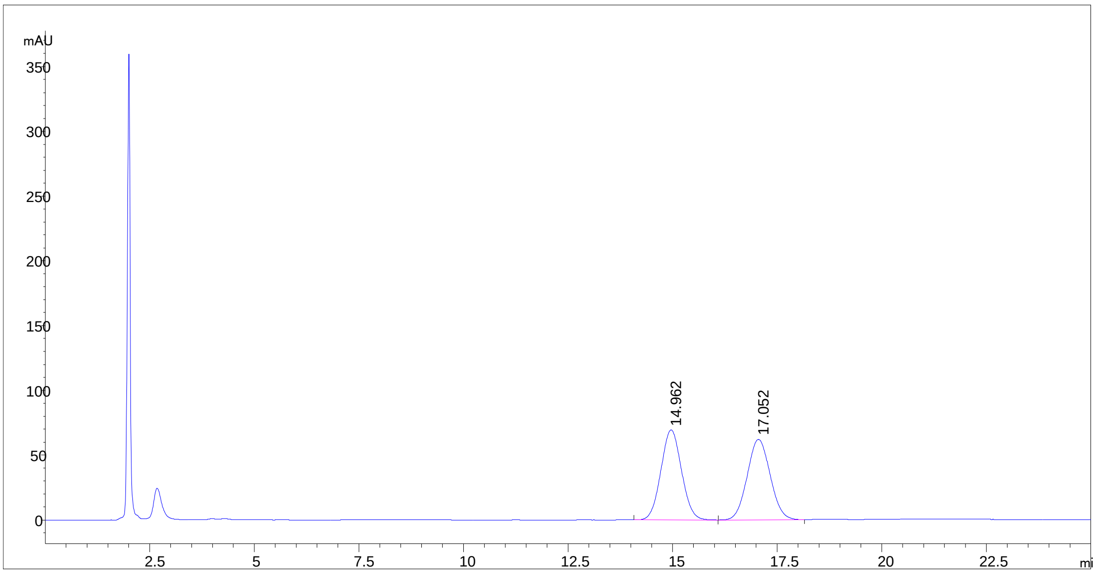
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.339	1390.9	68.2	49.724
2	9.66	1406.4	61.7	50.276

Fig.S 118 HPLC for racemic compound **4ja**



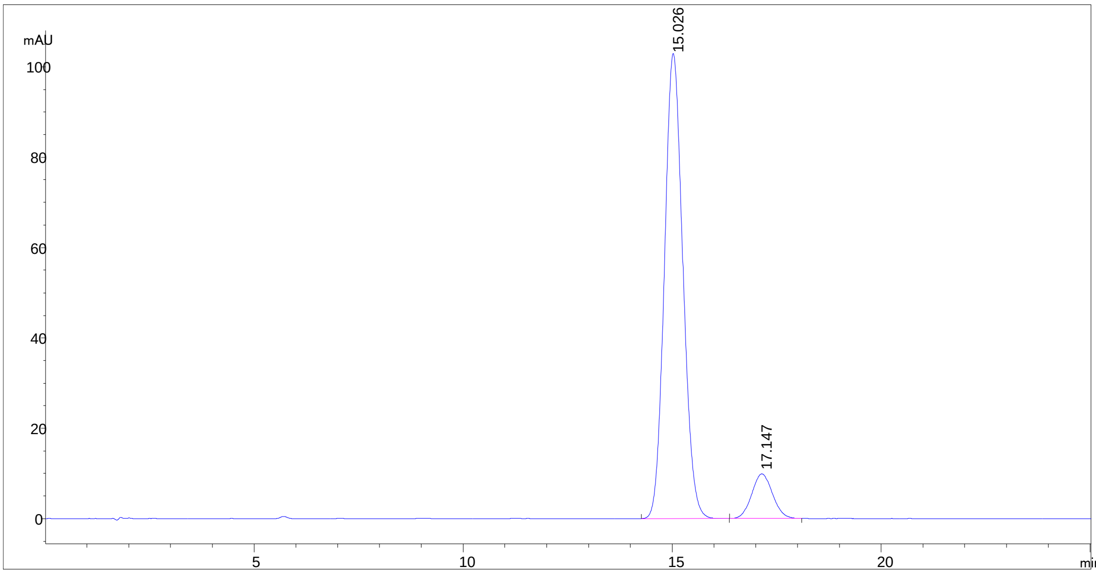
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.402	1982.1	111.6	91.858
2	9.729	175.7	8.6	8.142

Fig.S 119 HPLC for pure enantioenriched compound **4ja**



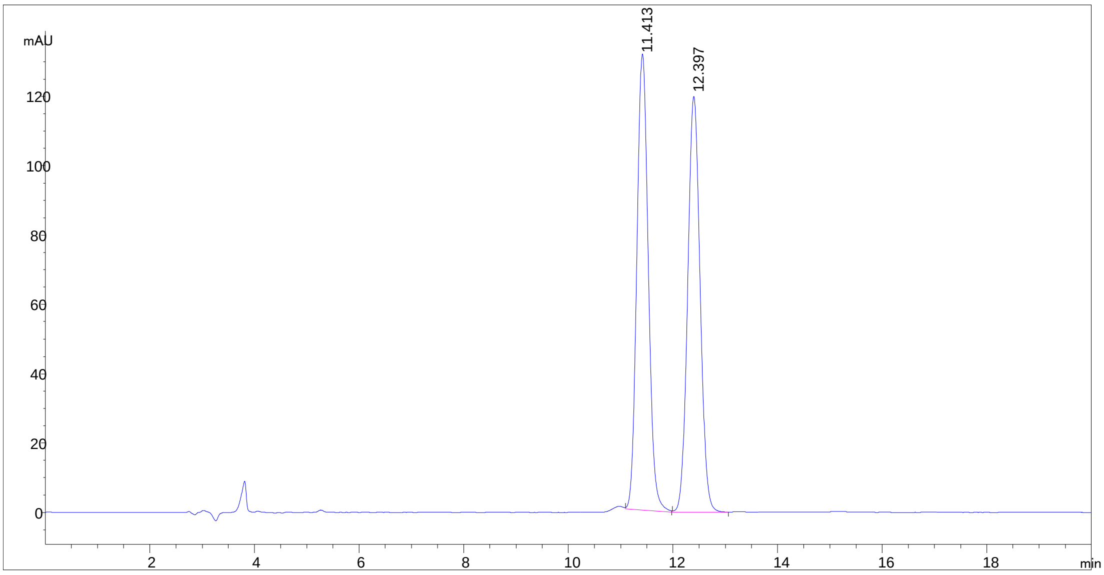
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	14.962	2372.4	69.3	50.106
2	17.052	2362.4	62	49.894

Fig.S 120 HPLC for racemic compound **4ka**



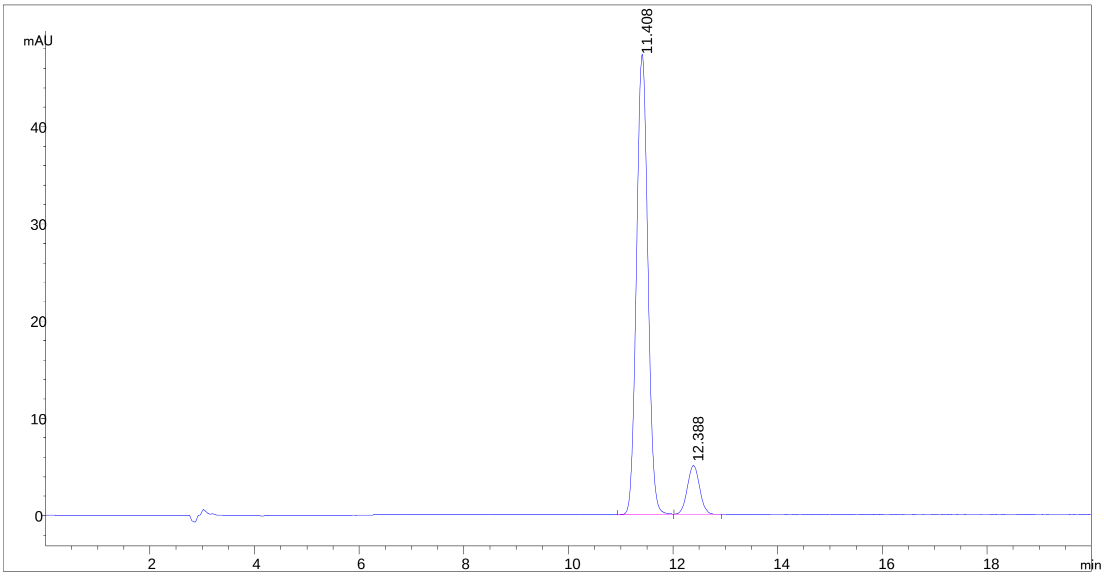
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	15.026	3153.1	102.9	90.235
2	17.147	341.2	9.9	9.765

Fig.S 121 HPLC for pure enantioenriched compound **4ka**



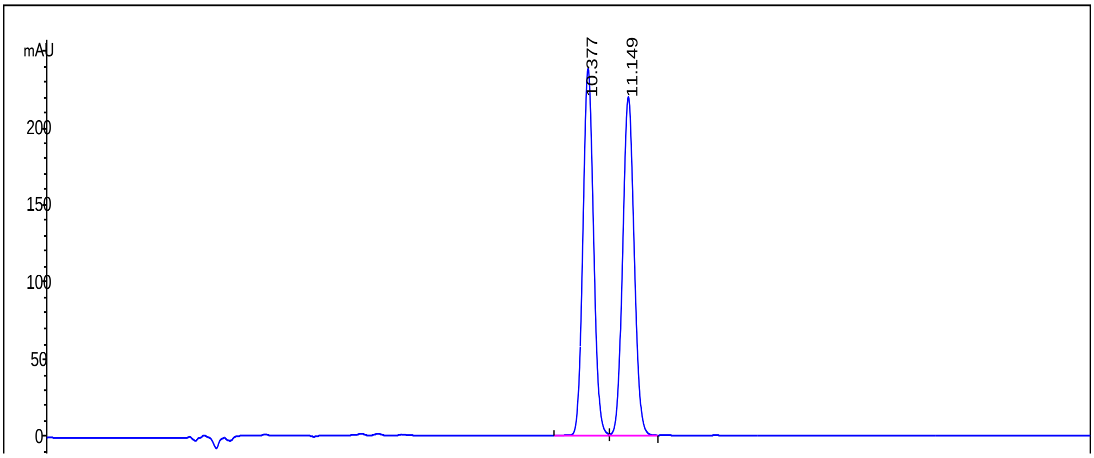
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.413	1990	131.6	50.107
2	12.397	1981.5	120	49.893

Fig.S 122 HPLC for racemic compound **4la**



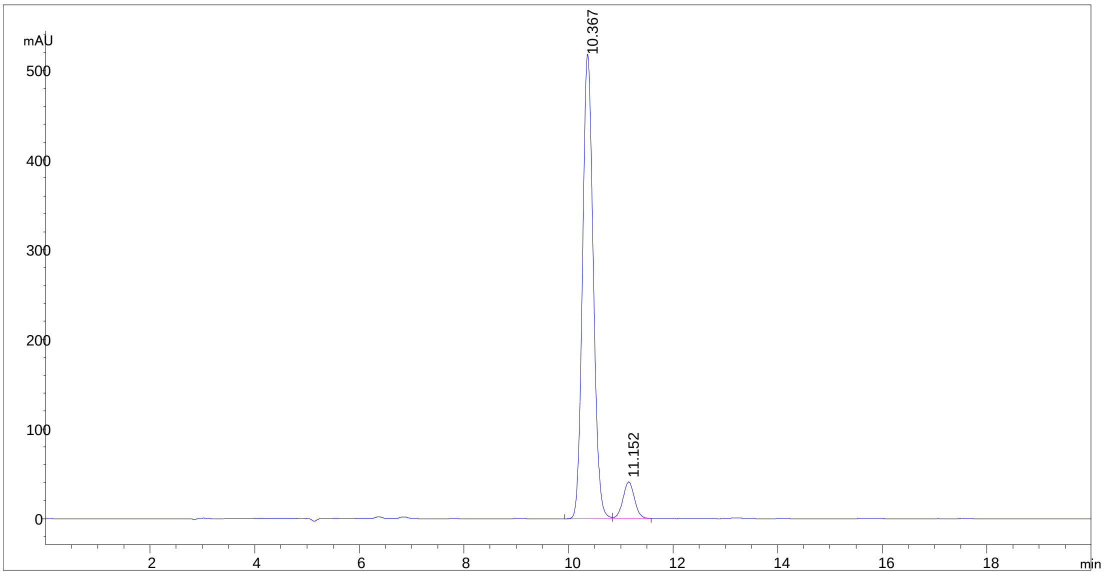
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.408	708.8	47.3	89.665
2	12.388	81.7	5	10.335

Fig.S 123 HPLC for pure enantioenriched compound **4la**



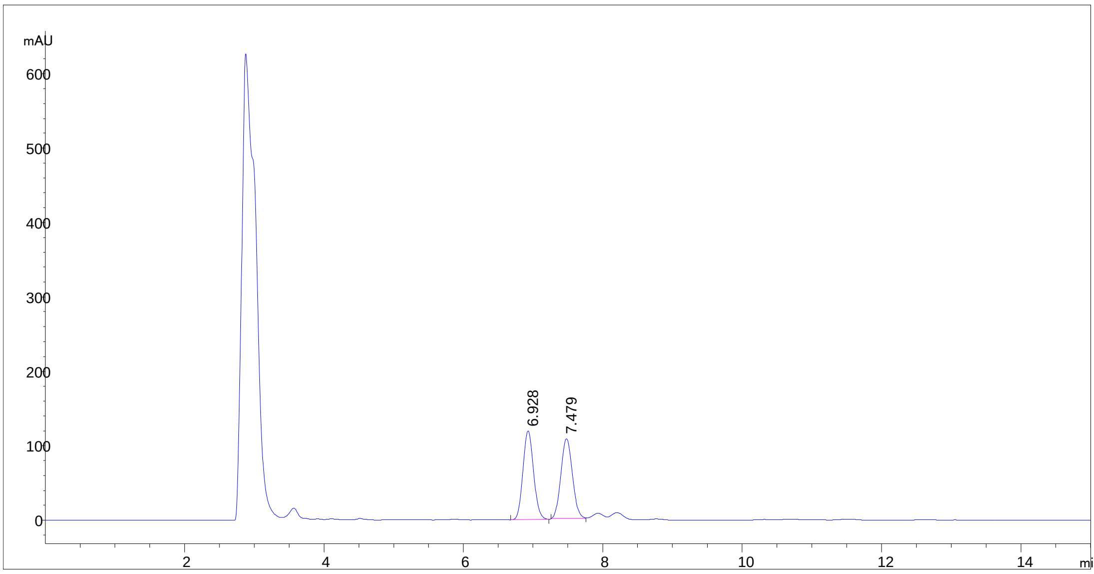
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	10.377	3389.7	237.6	50.001
2	11.149	3389.6	219.3	49.999

Fig.S 124 HPLC for racemic compound **4ma**



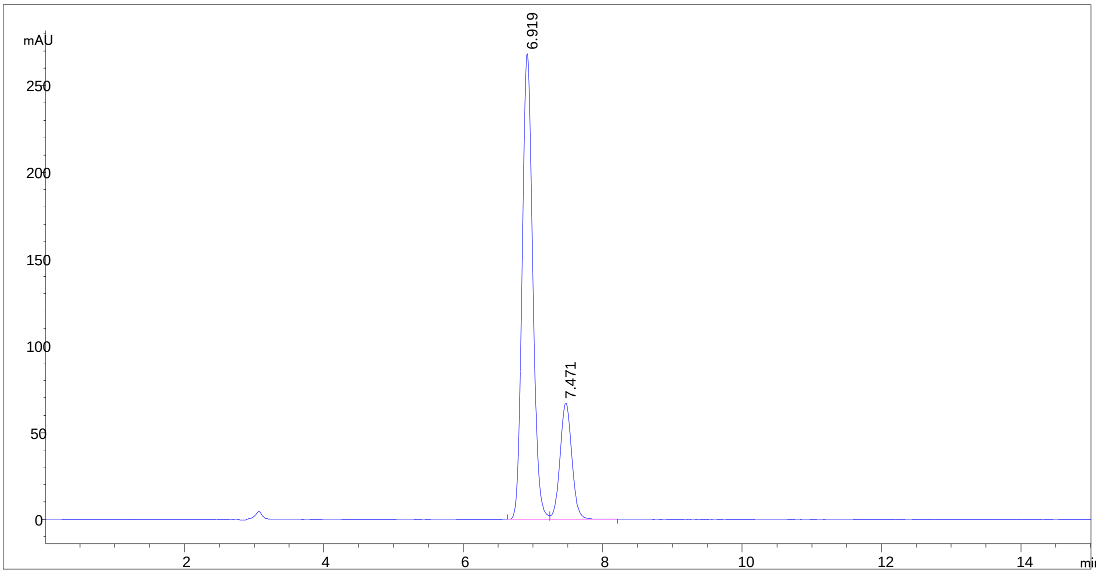
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	10.367	7422.1	518.4	92.253
2	11.152	623.3	40.6	7.747

Fig.S 125 HPLC for pure enantioenriched compound **4ma**



#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.928	1255.6	119.1	50.628
2	7.479	1224.4	107.2	49.372

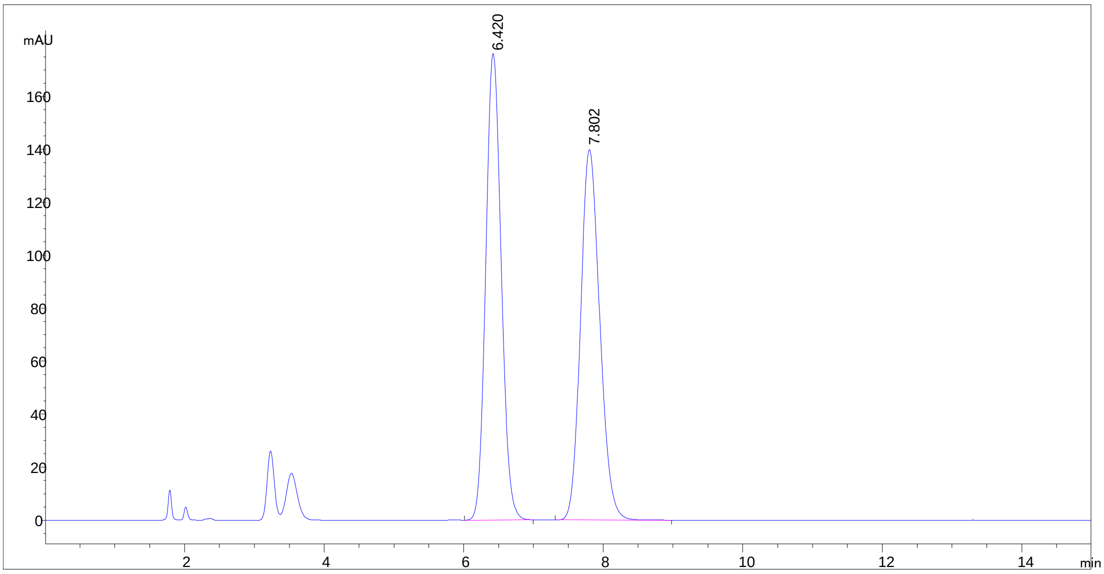
Fig.S 126 HPLC for racemic compound **4na**



#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.919	2826.7	268.4	78.154
2	7.471	790.1	67	21.846

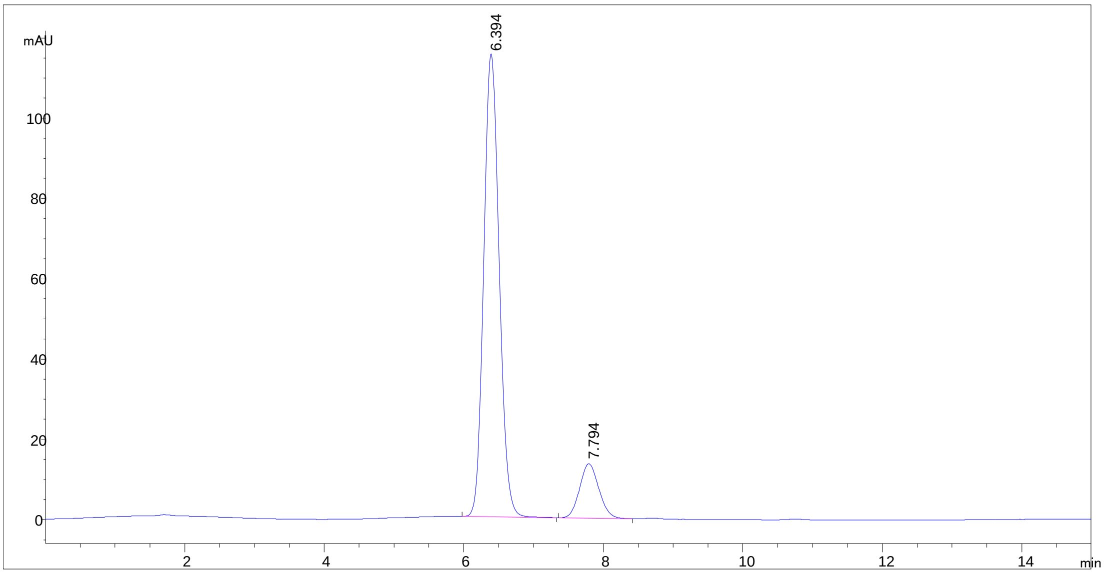
Fig.S 127 HPLC for pure enantioenriched compound **4na**

5. HPLC of 1,2-dihydroisoquinoline-1-ylphenylphosphine oxides 6



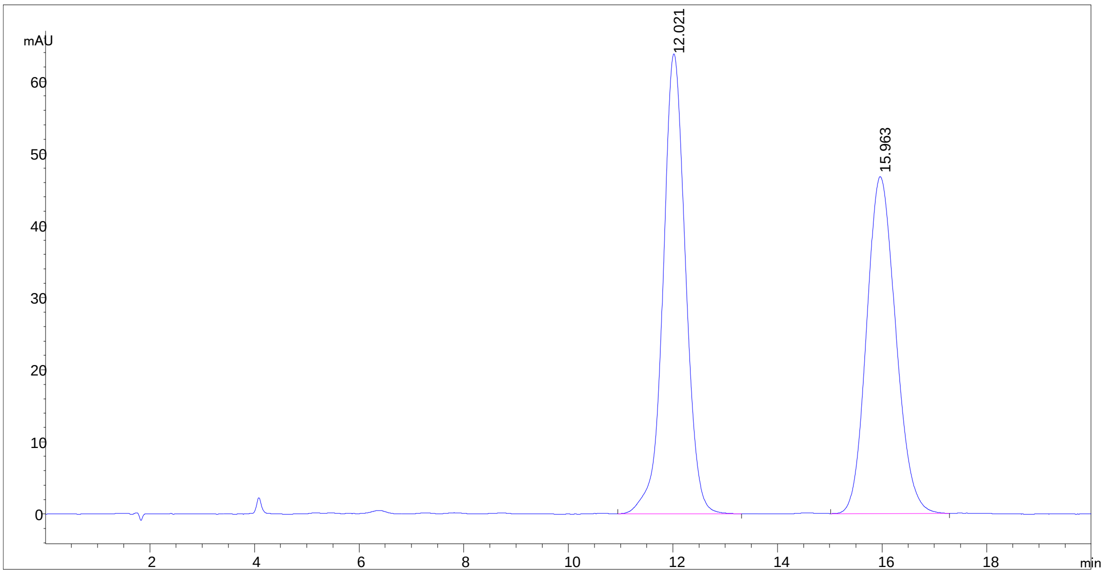
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.42	2689.7	176.1	49.981
2	7.802	2691.7	139.9	50.019

Fig.S 128 HPLC for racemic compound **6a**



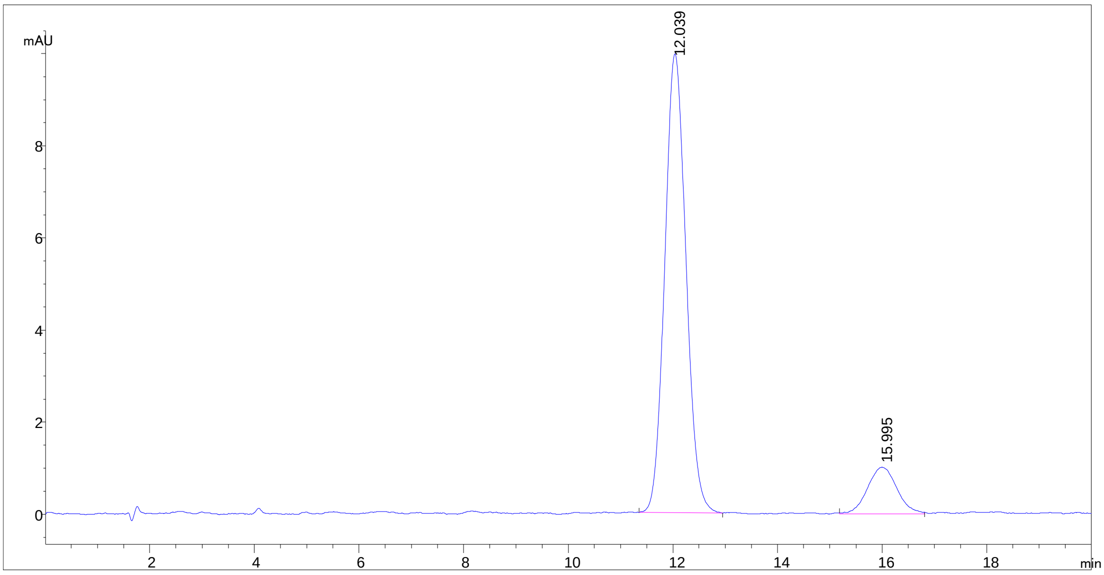
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.394	1765.5	115.3	87.176
2	7.794	259.7	13.5	12.824

Fig.S 129 HPLC for pure enantioenriched compound **6a**



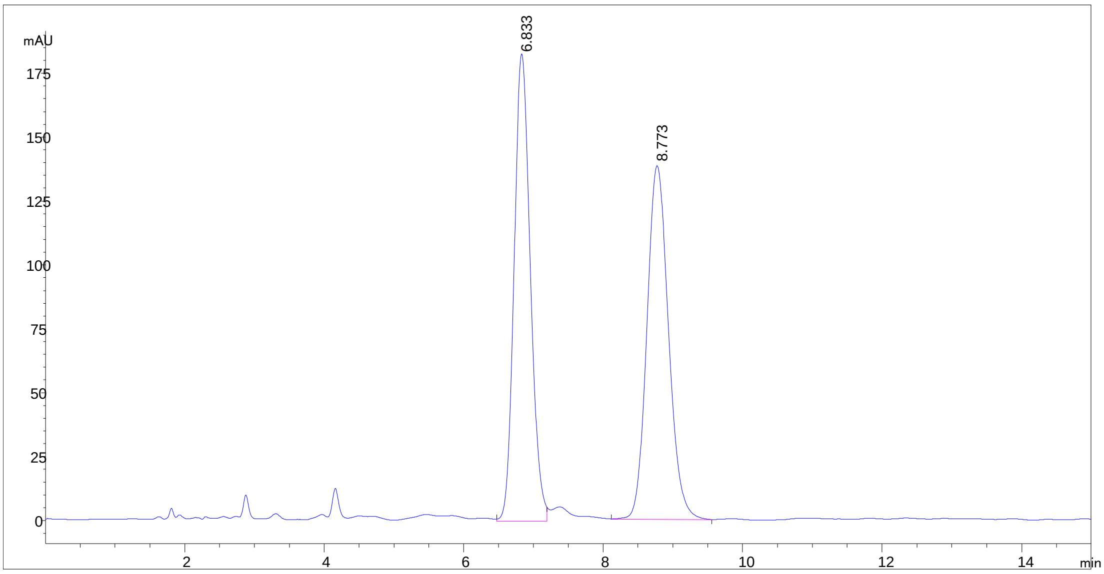
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	12.021	1908.3	63.8	51.378
2	15.963	1805.9	46.7	48.622

Fig.S 130 HPLC for racemic compound **6b**



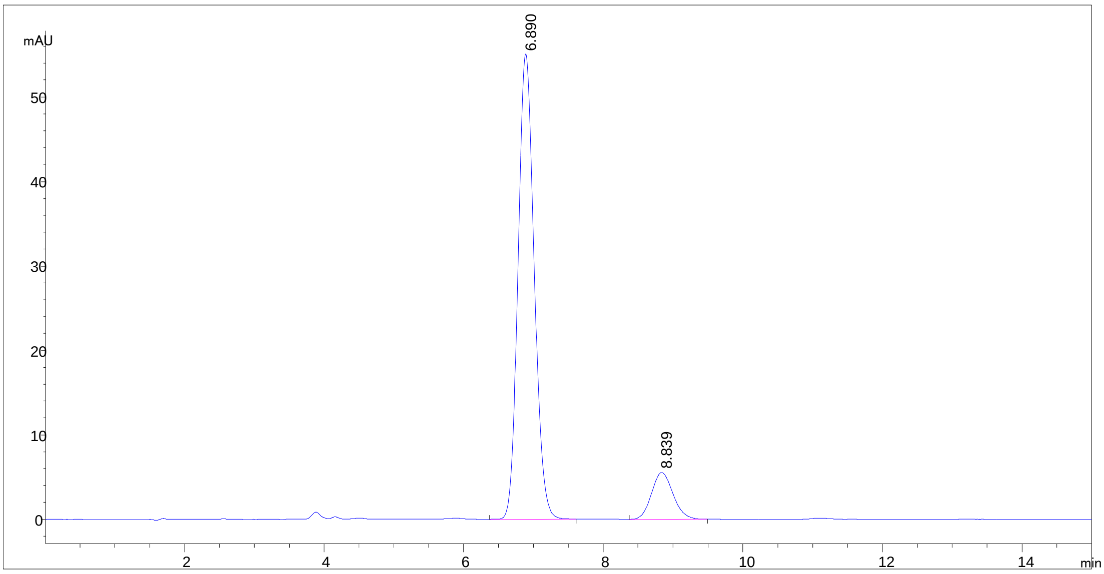
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	12.039	281	10	87.711
2	15.995	39.4	1	12.289

Fig.S 131 HPLC for pure enantioenriched compound **6b**



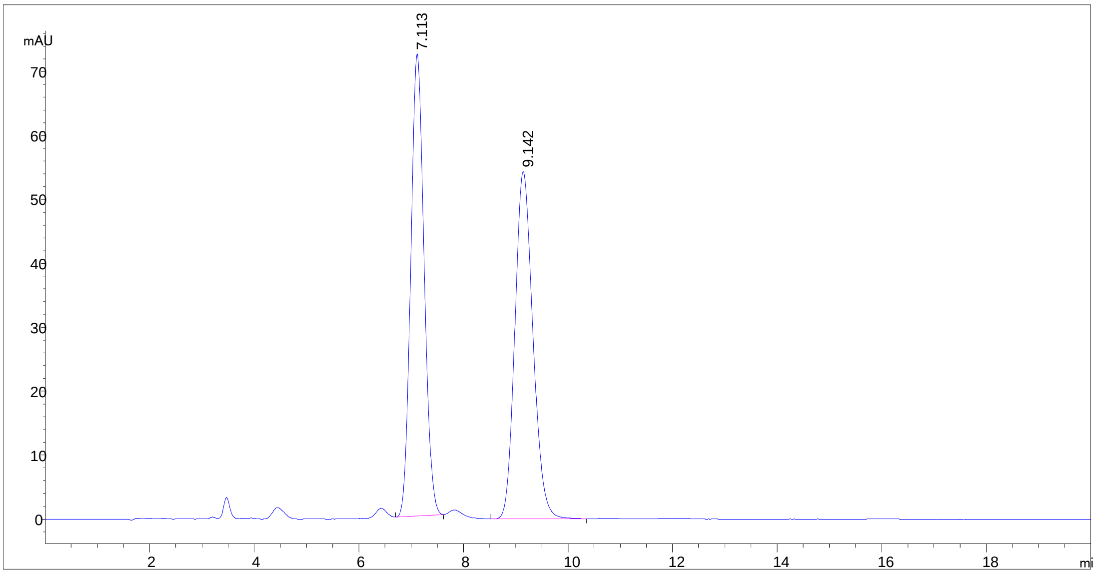
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.833	2978.1	183.1	50.030
2	8.773	2974.6	138.3	49.970

Fig.S 132 HPLC for racemic compound **6c**



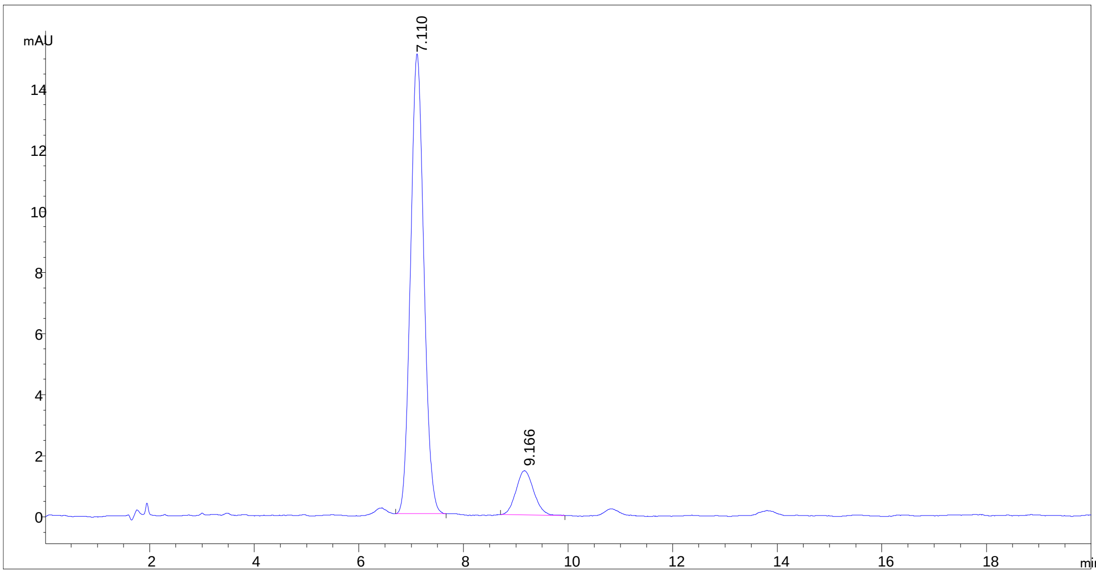
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.89	884	55.1	88.143
2	8.839	118.9	5.5	11.857

Fig.S 133 HPLC for pure enantioenriched compound **6c**



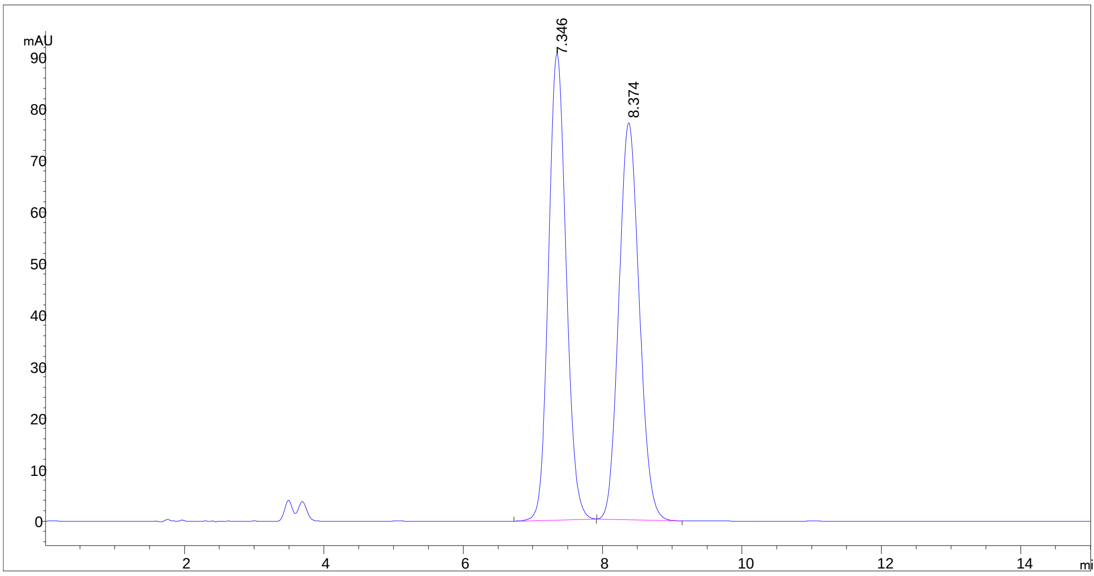
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.113	1288.1	72.3	49.696
2	9.142	1303.8	54.3	50.304

Fig.S 134 HPLC for racemic compound **6d**



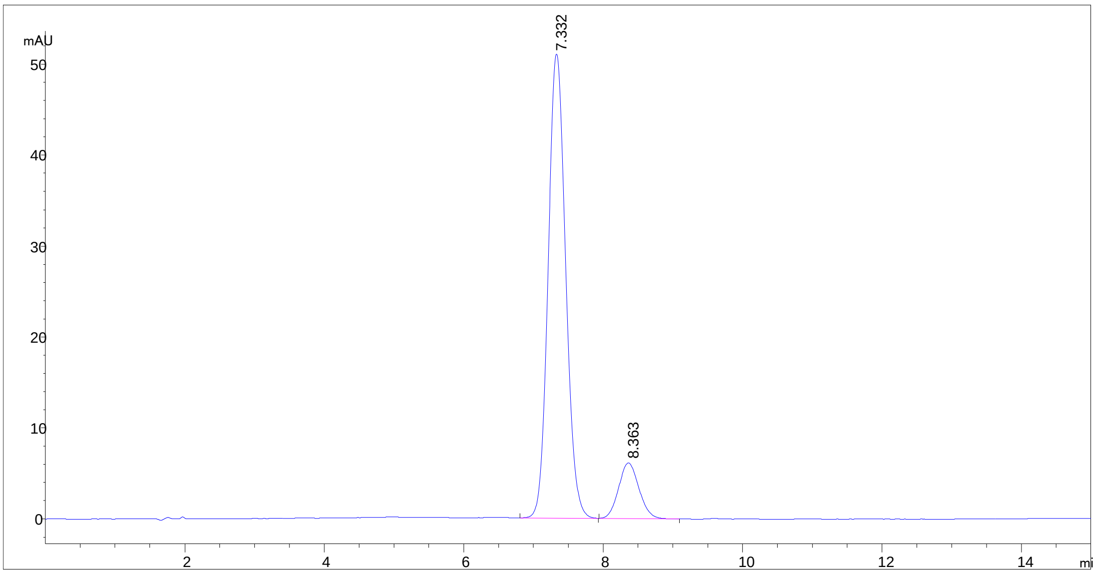
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.11	268.1	15.1	88.724
2	9.166	34.1	1.4	11.276

Fig.S 135 HPLC for pure enantioenriched compound **6d**



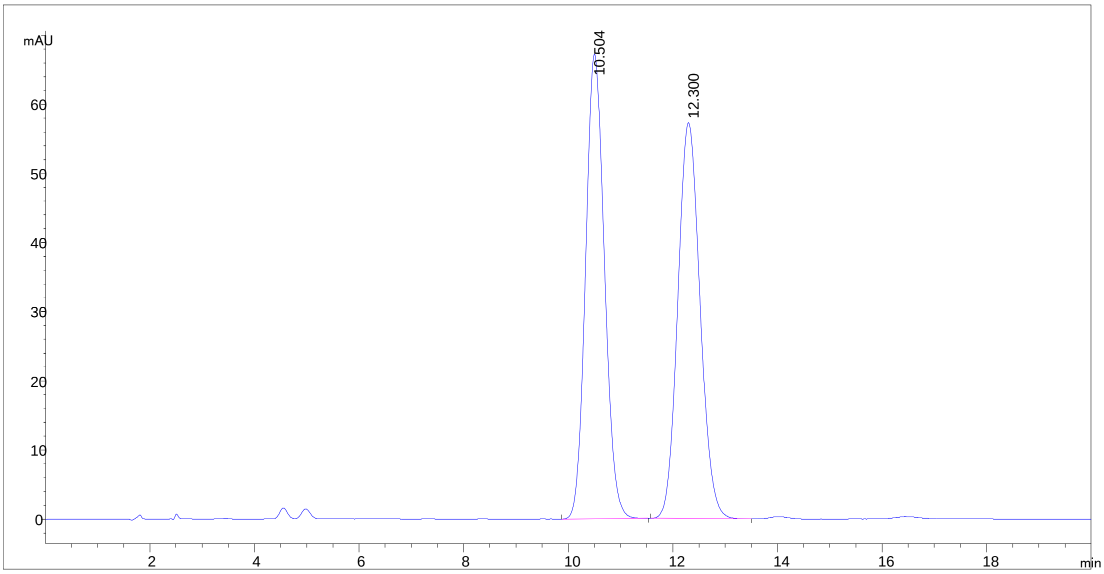
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.346	1587.1	90.4	50.311
2	8.374	1567.4	77	49.689

Fig.S 136 HPLC for racemic compound **6e**



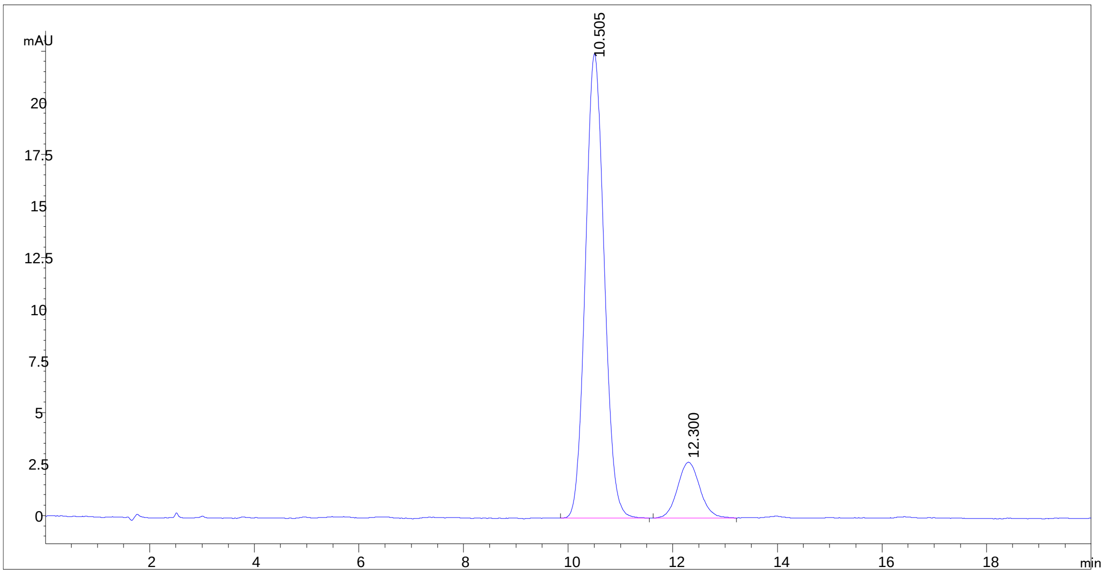
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	7.332	888.3	51	87.752
2	8.363	124	6.1	12.248

Fig.S 137 HPLC for pure enantioenriched compound **6e**



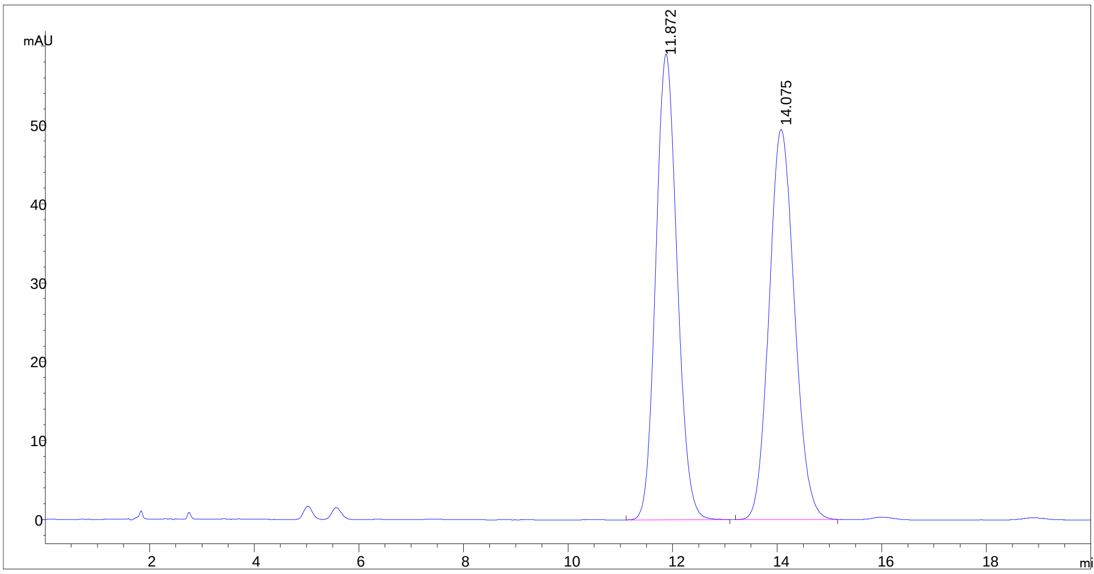
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	10.504	1684.3	67.2	49.921
2	12.3	1689.7	57.2	50.079

Fig.S 138 HPLC for racemic compound **6f**



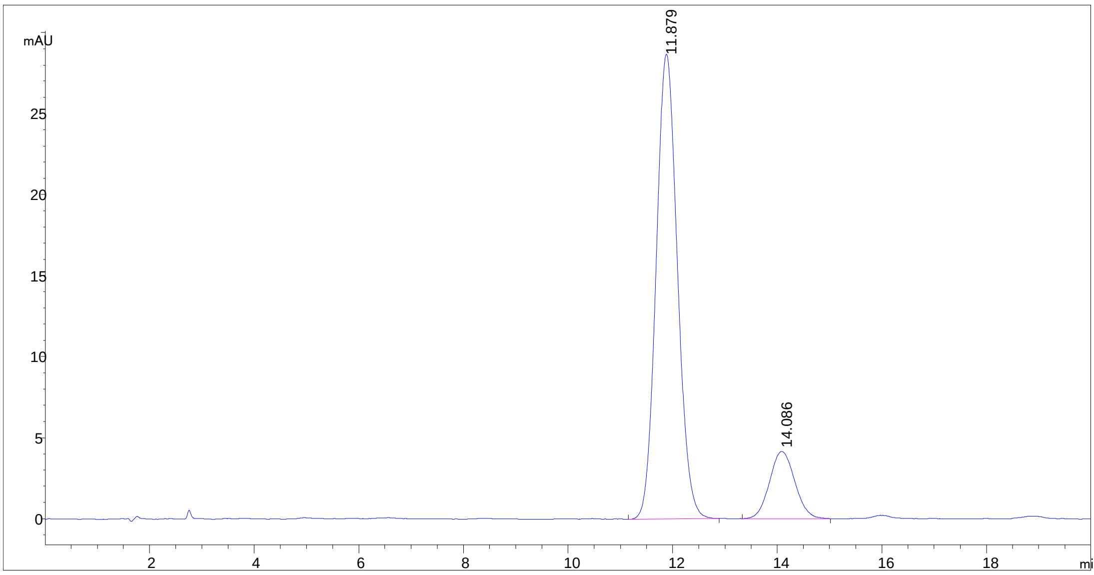
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	10.505	561.9	22.5	87.559
2	12.3	79.8	2.7	12.441

Fig.S 139 HPLC for pure enantioenriched compound **6f**



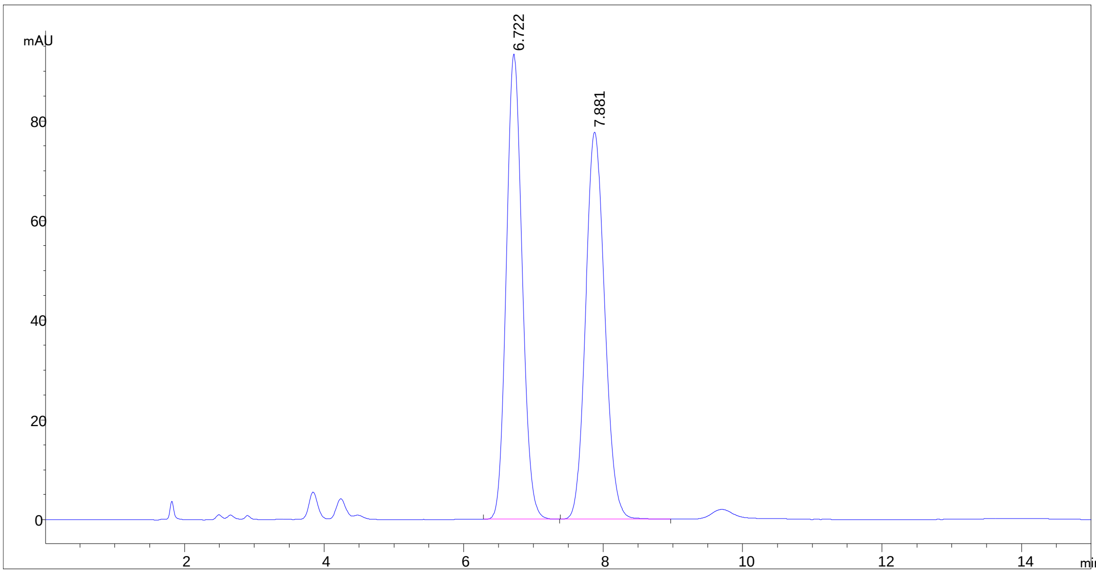
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.872	1676.8	59	50.050
2	14.075	1673.4	49.5	49.950

Fig.S 140 HPLC for racemic compound **6g**



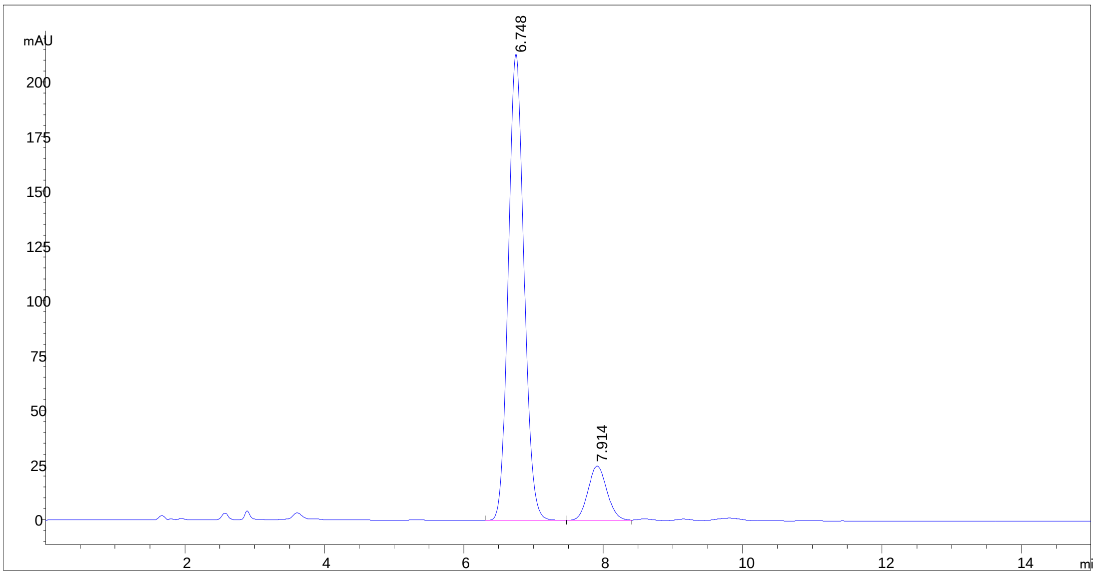
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	11.879	809.2	28.7	85.288
2	14.086	139.6	4.2	14.712

Fig.S 141 HPLC for pure enantioenriched compound **6g**



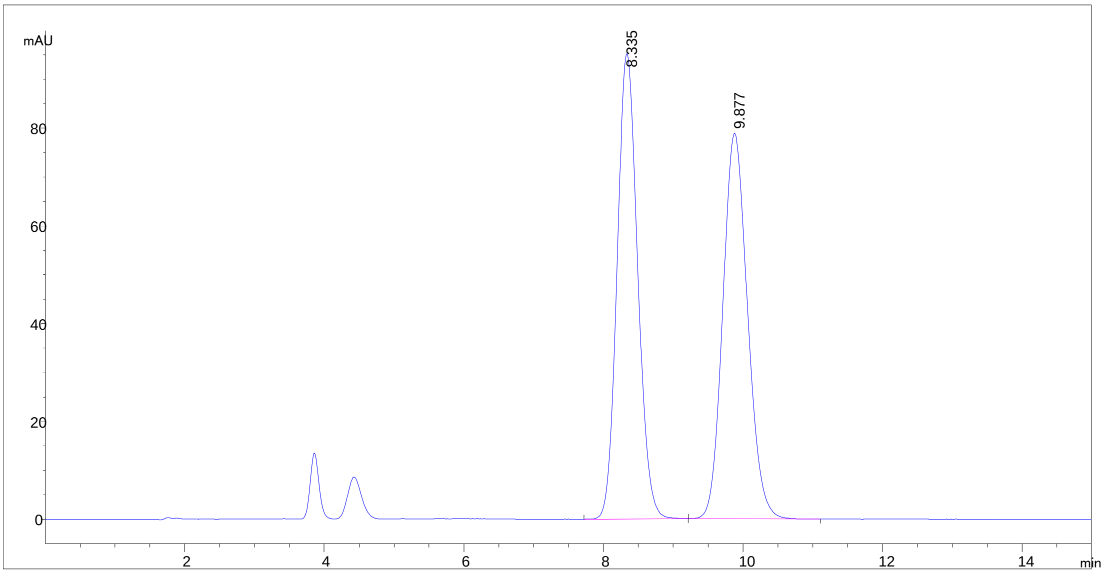
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.722	1479.5	93.4	49.997
2	7.881	1479.7	77.7	50.003

Fig.S 142 HPLC for racemic compound **6h**



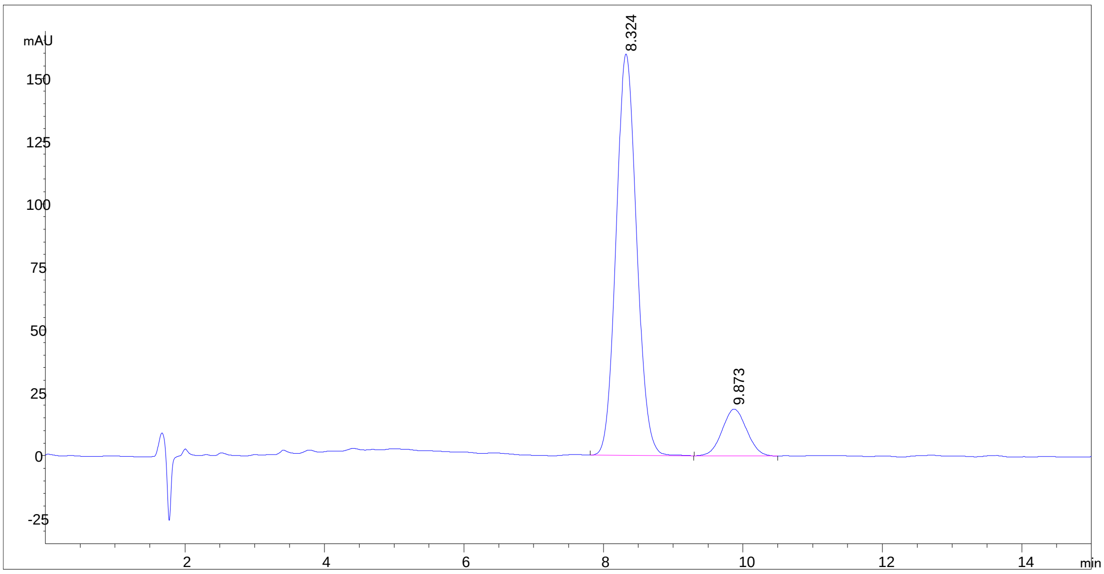
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.748	3365	212.9	87.894
2	7.914	463.5	24.7	12.106

Fig.S 143 HPLC for pure enantioenriched compound **6h**



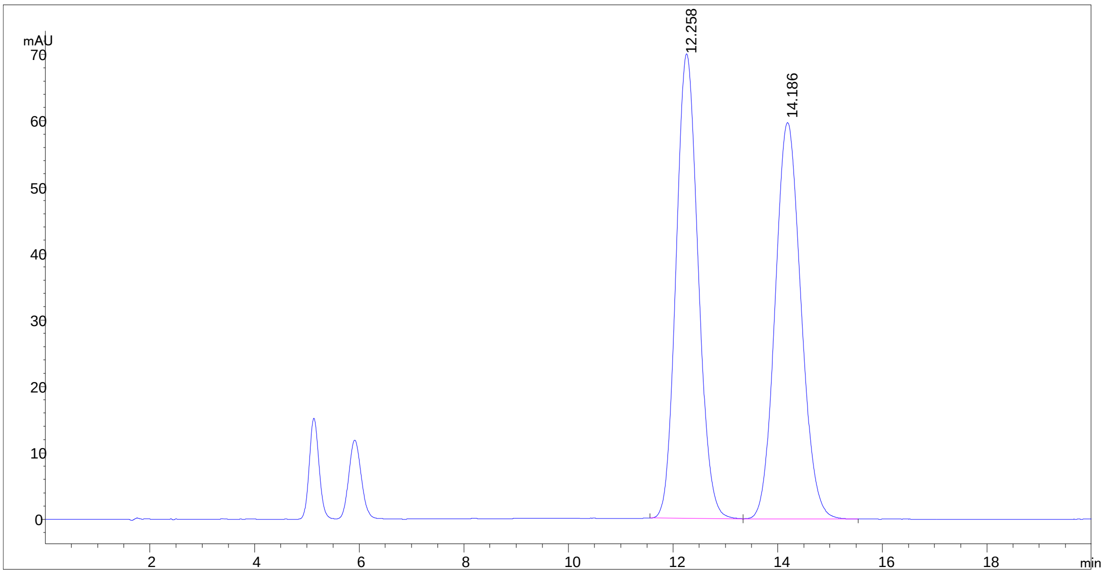
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.335	1946.3	95.1	50.041
2	9.877	1943.2	78.8	49.959

Fig.S 144 HPLC for racemic compound **6i**



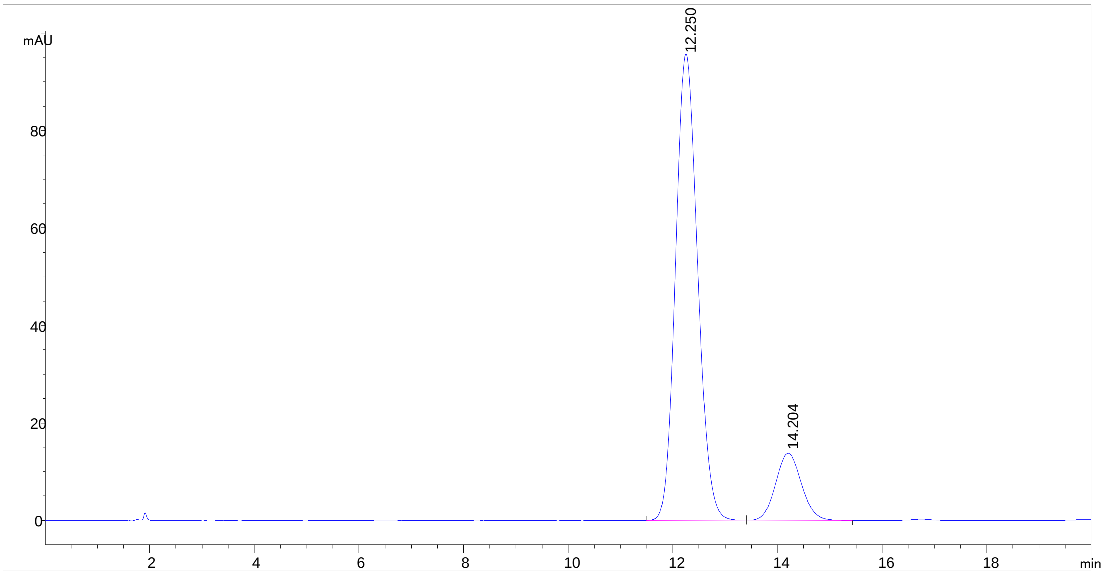
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.324	3277.4	159.6	87.729
2	9.873	458.4	18.7	12.271

Fig.S 145 HPLC for pure enantioenriched compound **6i**



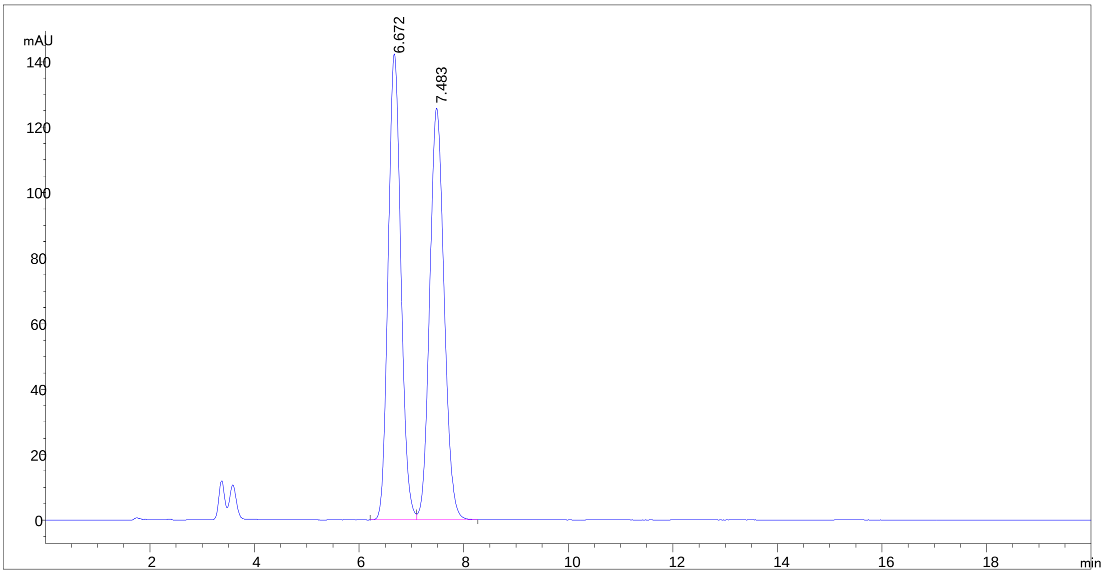
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	12.258	2047.1	70	49.992
2	14.186	2047.7	59.7	50.008

Fig.S 146 HPLC for racemic compound **6j**



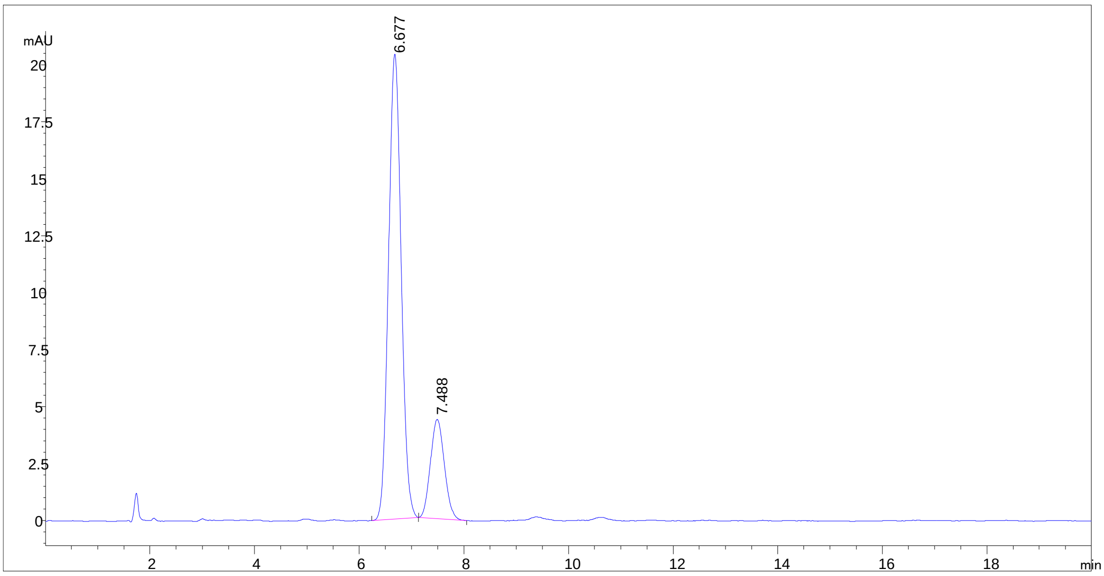
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	12.25	2803.7	95.7	85.620
2	14.204	470.9	13.8	14.380

Fig.S 147 HPLC for pure enantioenriched compound **6j**



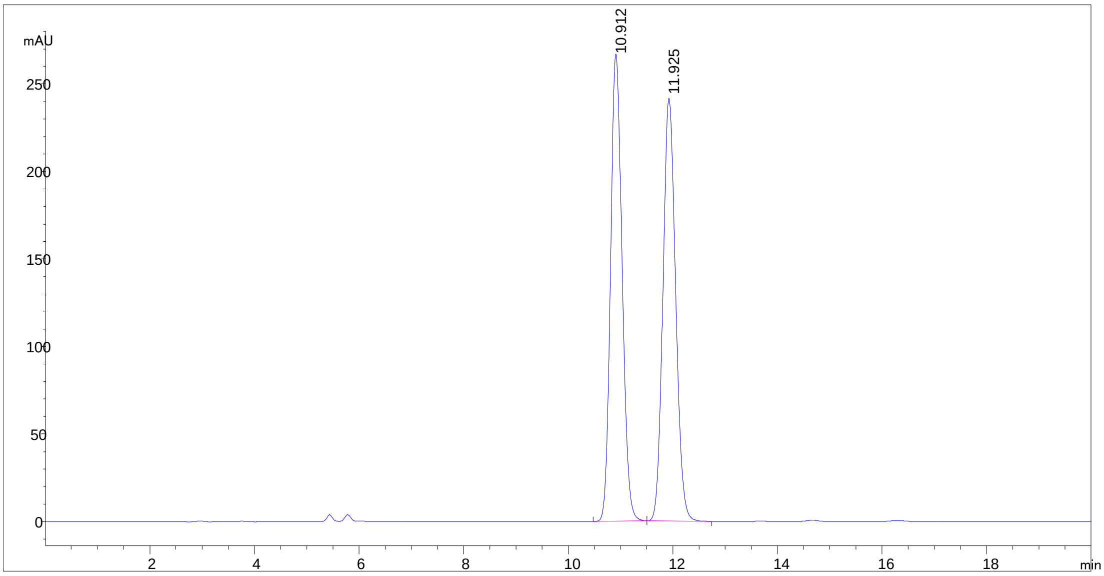
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.672	2408.6	142.4	49.893
2	7.483	2419	125.8	50.107

Fig.S 148 HPLC for racemic compound **6k**



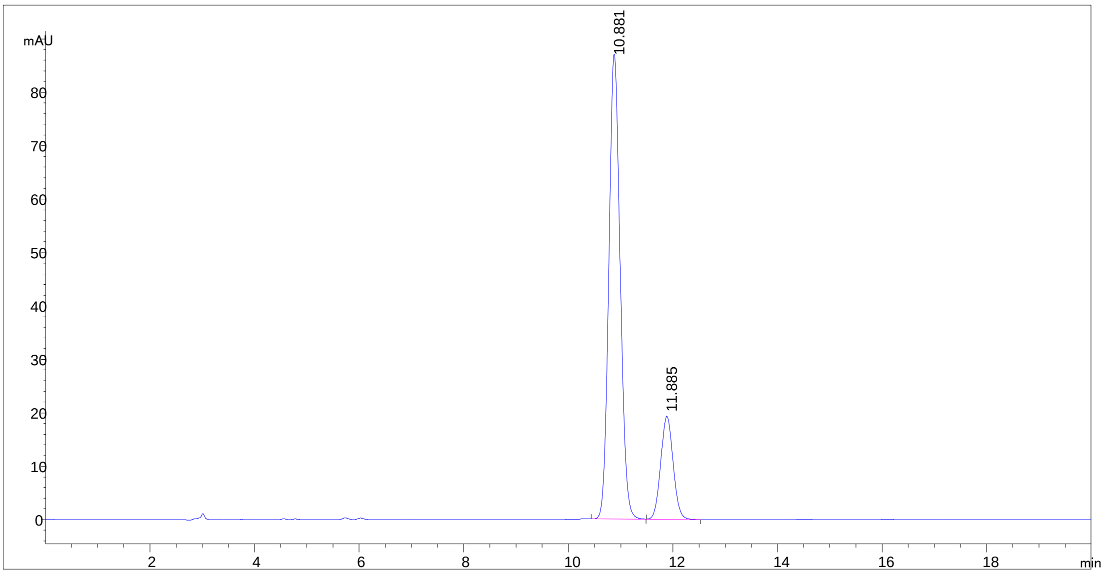
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.677	342.9	20.4	80.949
2	7.488	80.7	4.3	19.051

Fig.S 149 HPLC for pure enantioenriched compound **6k**



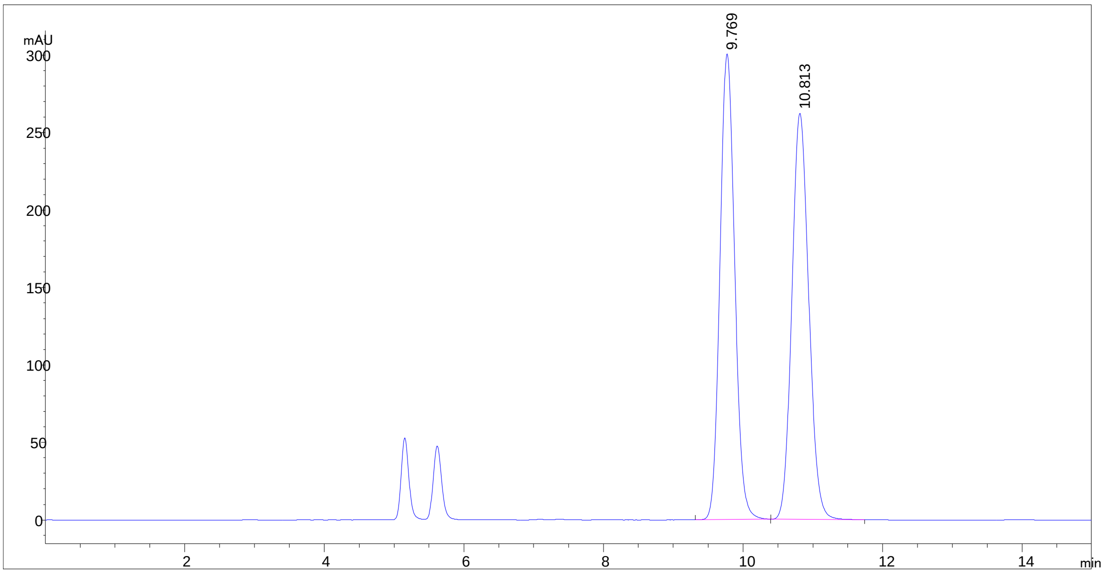
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	10.912	4087.5	266.9	50.002
2	11.925	4087.1	241.3	49.998

Fig.S 150 HPLC for racemic compound **6l**



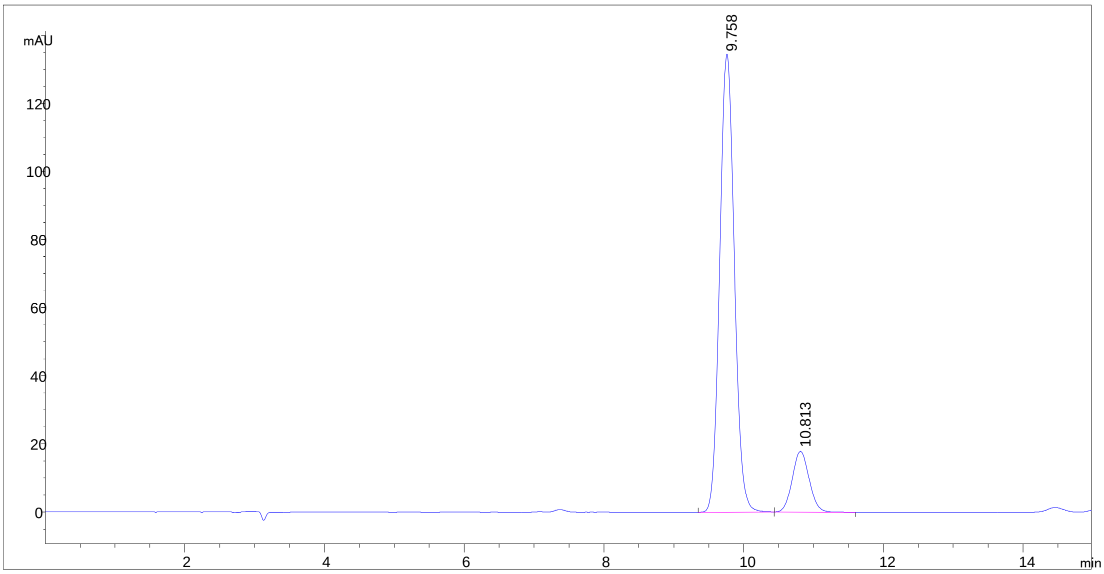
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	10.881	1310	87.1	80.456
2	11.885	318.2	19.3	19.544

Fig.S 151 HPLC for pure enantioenriched compound **6l**



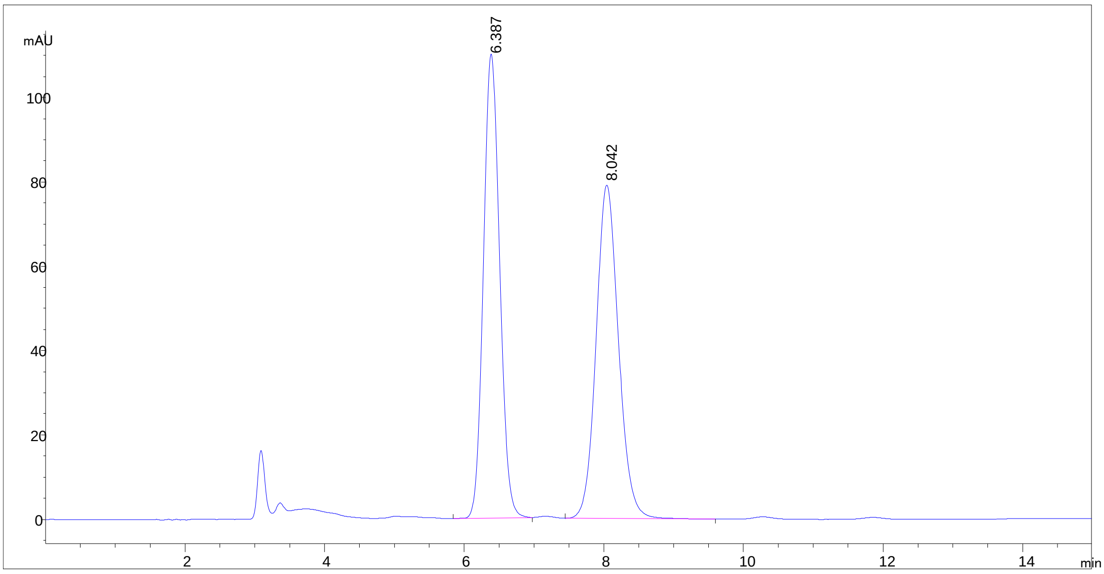
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	9.769	4410.6	300.7	50.026
2	10.813	4406	262	49.974

Fig.S 152 HPLC for racemic compound **6m**



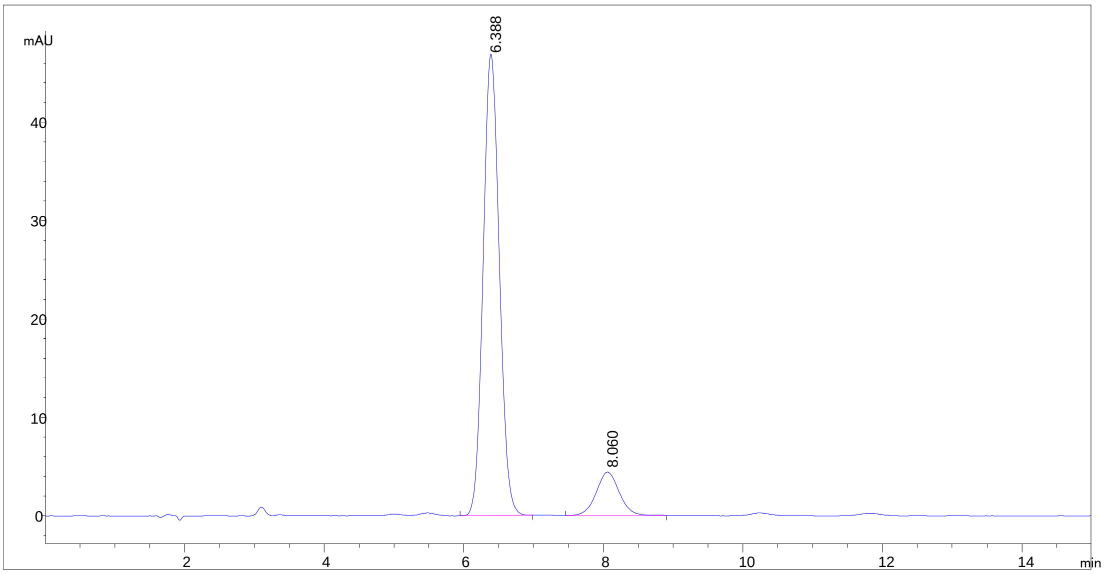
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	9.758	1957.8	134.5	86.798
2	10.813	297.8	17.9	13.202

Fig.S 153 HPLC for pure enantioenriched compound **6m**



#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.387	1771.5	110.1	50.157
2	8.042	1760.4	79.1	49.843

Fig.S 154 HPLC for racemic compound **6n**



#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	6.388	751.5	46.9	88.115
2	8.06	101.4	4.4	11.885

Fig.S 155 HPLC for pure enantioenriched compound **6n**

6. NMR spectrum and HPLC of diethyl (*S*)-(1,2,3,4-tetrahydroisoquinolin-1-yl) phosphonate 8

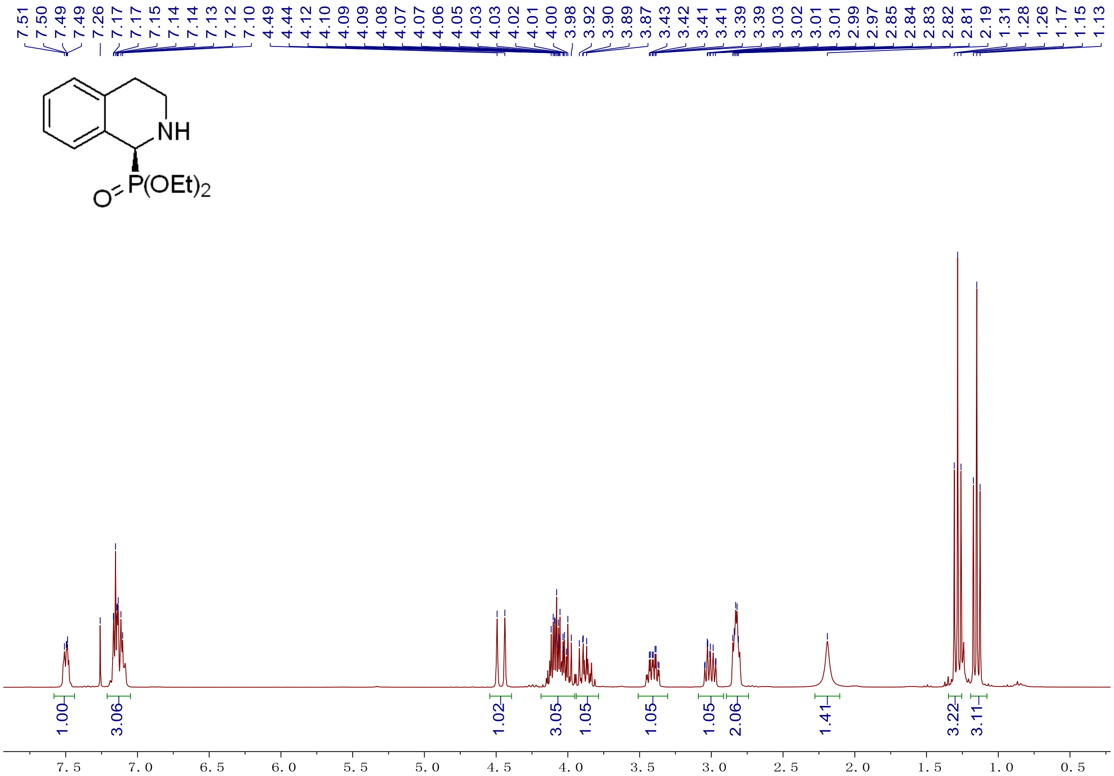


Fig.S 156 ^{1}H NMR of compound **8**

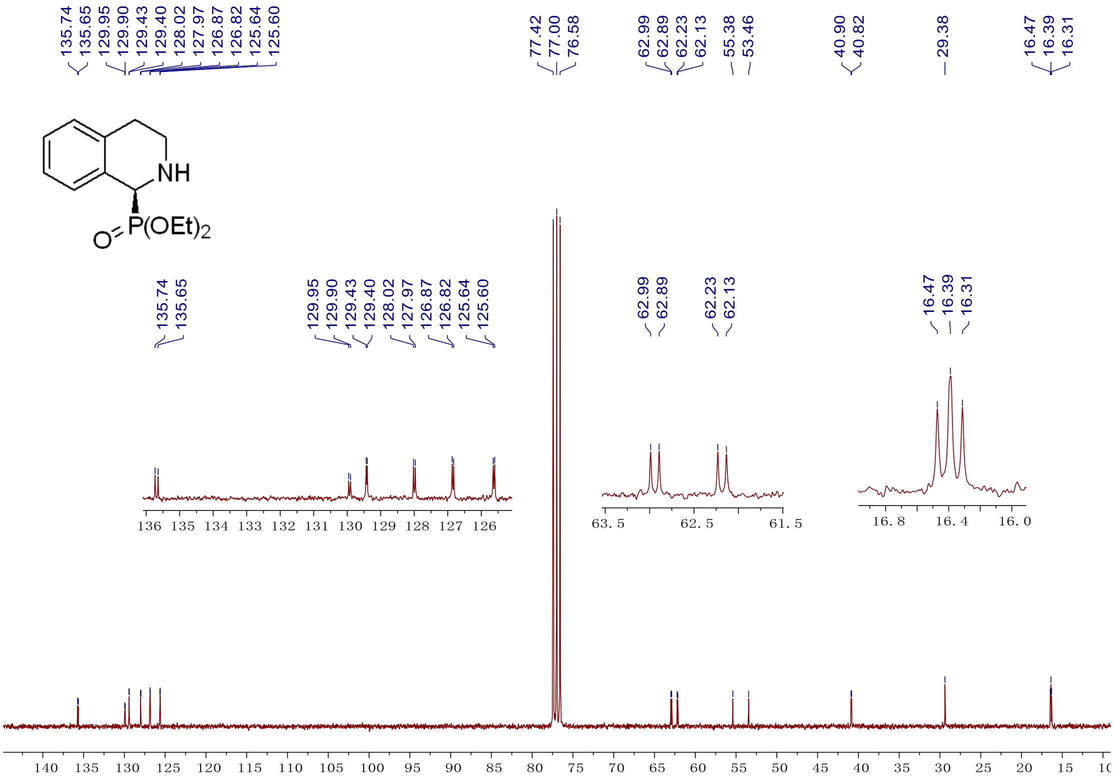


Fig.S 157 ^{13}C NMR of compound **8**

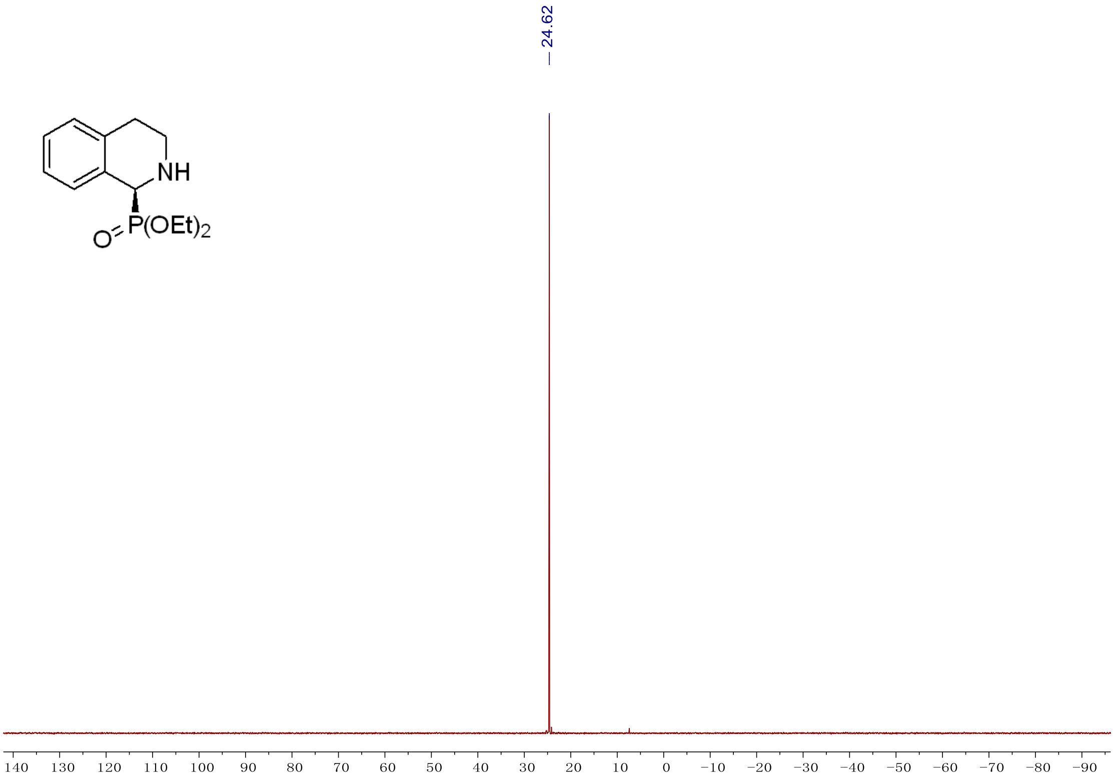
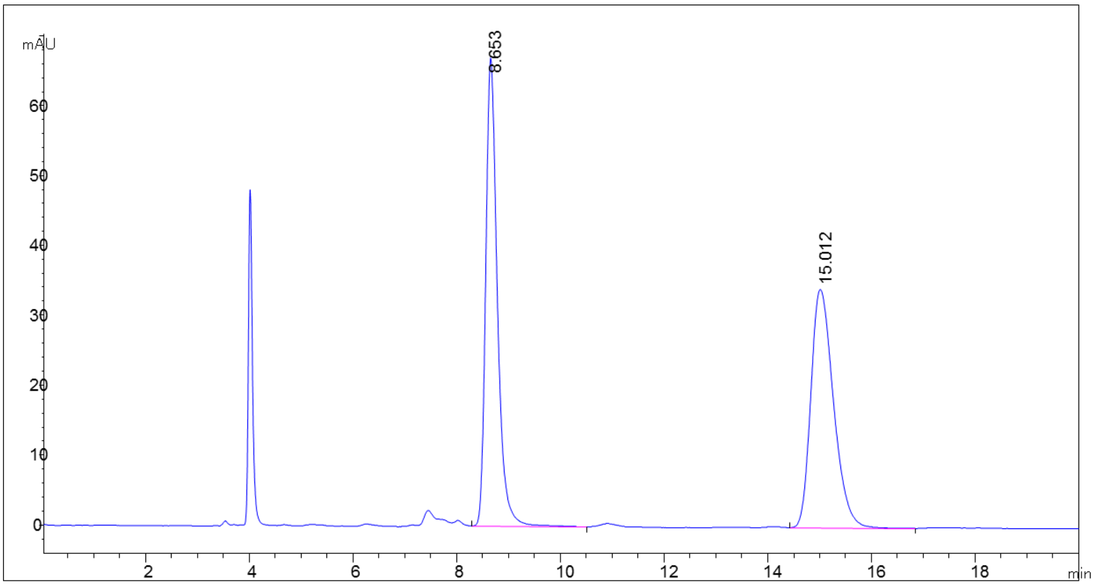
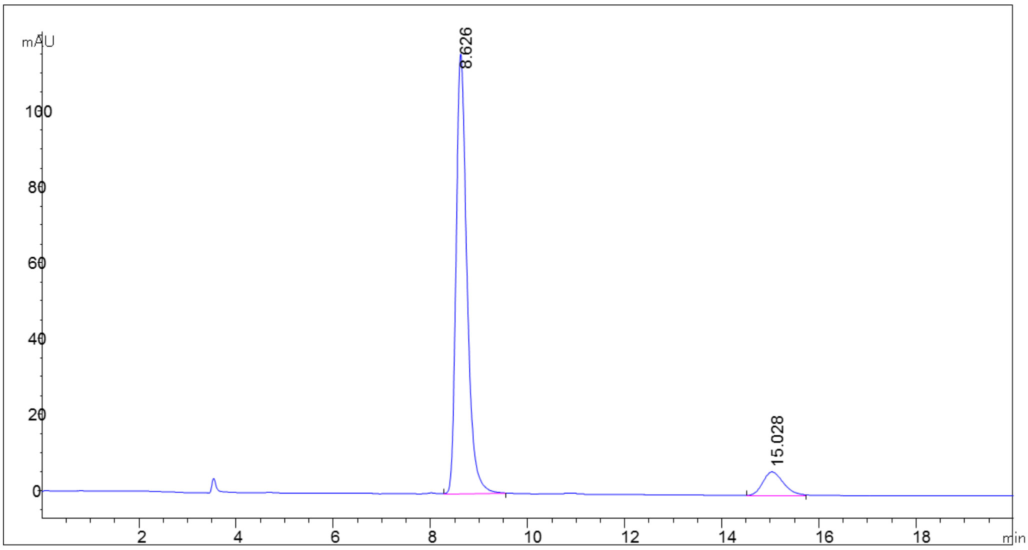


Fig.S 158 ^{31}P NMR of compound **8**



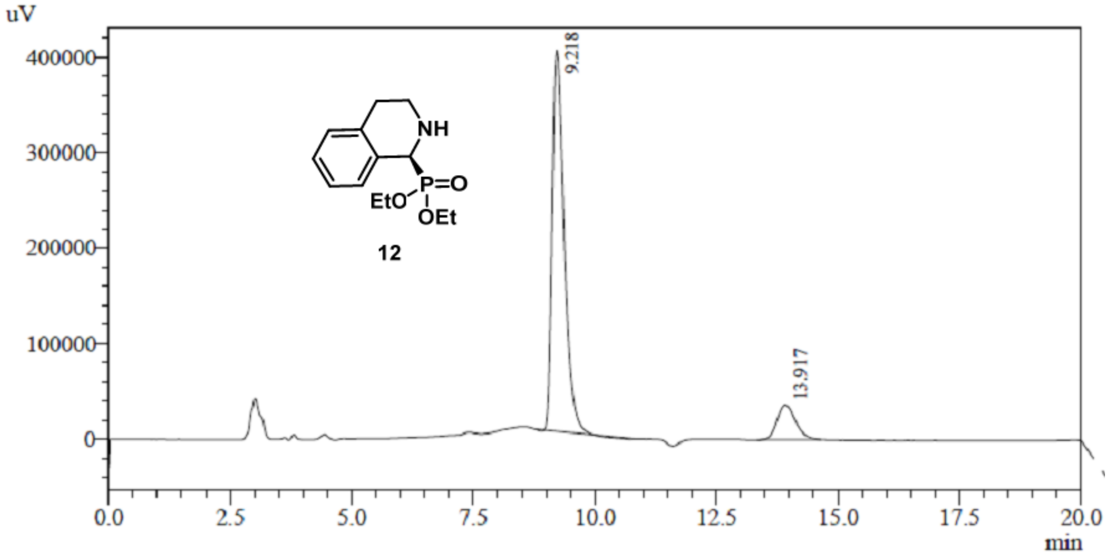
#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.653	1448.5	67.1	50.303
2	15.012	1035.9	34	49.697

Fig.S 159 HPLC for racemic compound **8**



#	Time (min)	Area (mAU*s)	Height(mAU)	Area %
1	8.626	1798.1	116	90.48
2	15.028	189.2	6.3	9.52

Fig.S 160 HPLC for pure enantioenriched compound **8**



PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Area %
1	9.218	6779973	87.473
2	13.917	970988	12.527
Total		7750961	100.000

Fig.S 161 HPLC for diethyl (*S*)-(1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate **8** (from *Chem. Sci*. 2016, 7, 6940-6945)

7. NMR spectrum of tert-butyl 1-(tert-butoxy)isoquinoline-2(1H)-carboxylate A.

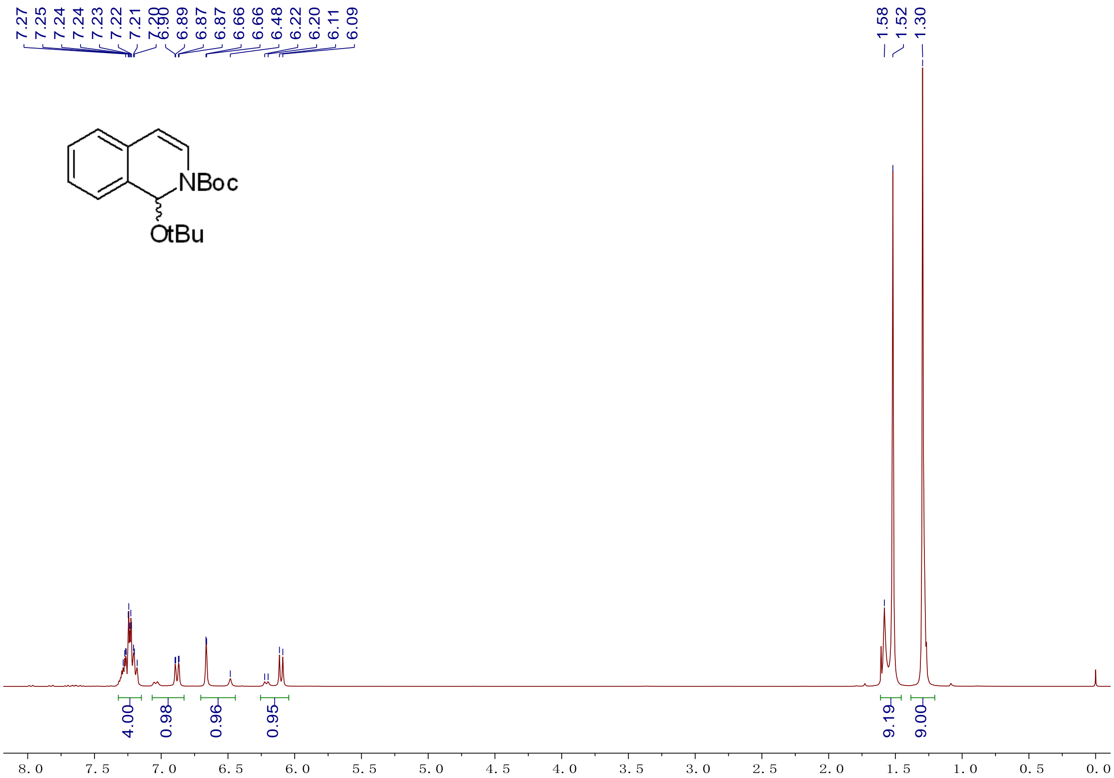


Fig.S 162 ^{1}H NMR of compound **A**

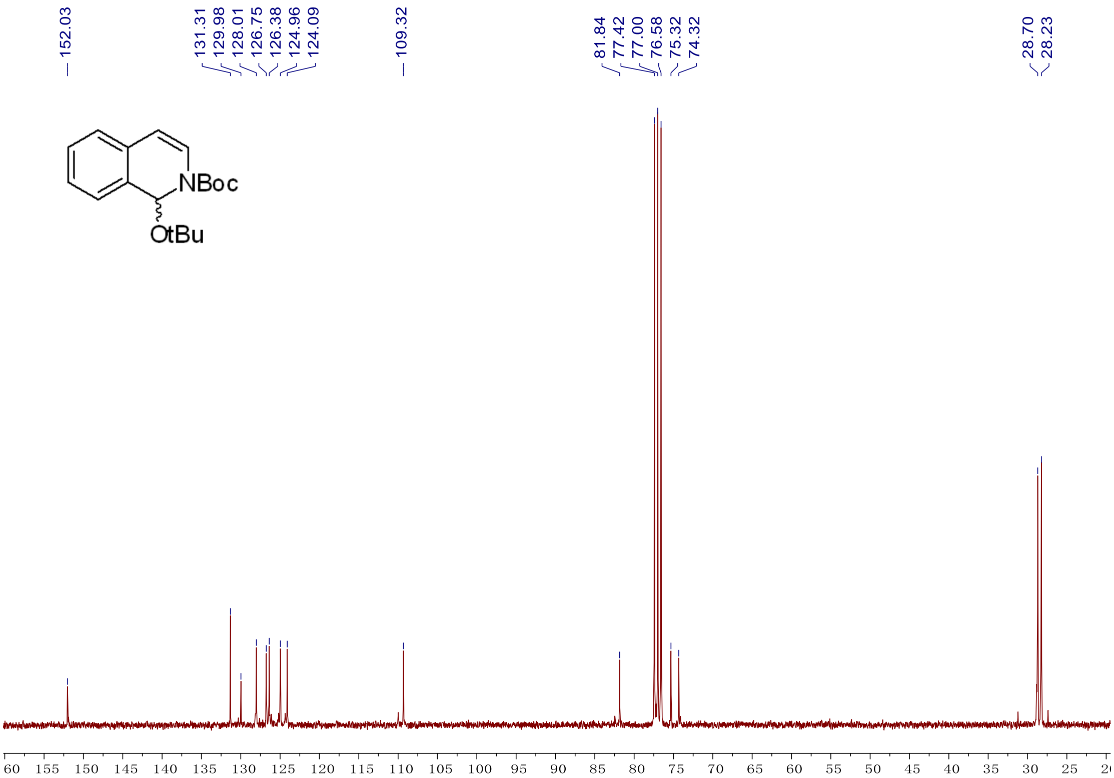


Fig.S 163 ^{13}C NMR of compound **A**