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Concise Synthesis and Application of Enantiopure Spirobiphenoxasilin-Diol and Its Related Chiral Ligands

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Table of Contents

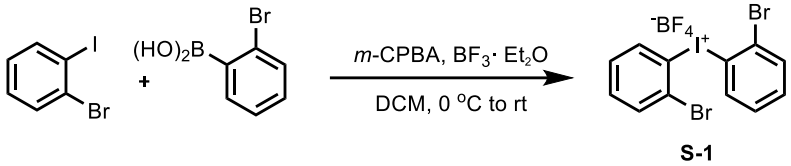
1. General Information

$Rh(COD)_2BF_4$ was purchased from Laajoo. (1*S*, 1'*S*)-bis (1-phenylethyl) amine was purchased from Accela. Chlorodiphenylphosphine was purchased from Adamas. Other reagents were purchased from TCI, Sigma-Aldrich, Aladdin, Adamas-beta, J&K, 9-Ding, and Energy Chemical of the highest purity grade and used without further purification, unless otherwise indicated. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2) and toluene were dried using the solvent purification system. Other anhydrous solvents were purchased from J&K. TMEDA was dried over NaOH. TEA was dried over CaH_2.The extent of reaction was monitored by thin–layer chromatography (TLC), performed on 0.25 mm silica gel HSGF254. The TLC plates were visualized by ultraviolet light (254 nm) or treatment with potassium permanganate stain followed by gentle heating.

NMR spectra were recorded on Varian 400, Bruker 400 and Agilent 400 (400 Hz for ^1H; 375 Hz for ^{19}F; 162 Hz for ^{31}P; 100 Hz for ^{13}C) spectrometer. The chemical shifts (δ) were quoted in parts per million (ppm) referenced to TMS (0.0 ppm for ^1H NMR), $CDCl_3$ (77.0 ppm for ^{13}C NMR), Acetone-d_6 (206.4 ppm for ^{13}C NMR) and external 85% H_3PO_4 for ^{31}P NMR respectively. The following abbreviations were used to explain multiplicities: s = singlet, d =doublet, t = triplet, q = quartet, p = pentet, h = heptet, m = multiplet, and br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were fully decoupled by broad band proton decoupling. ^{19}F NMR spectra were fully decoupled by broad band proton decoupling. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI–TOF, CI/EI or MALDI. Ultraviolet–visible spectra (UV-Vis) were recorded on a Shimadzu UV–Vis spectrophotomemter (UV-2700). HPLC analyses were performed on a SHIMADZU LC-20AT liquid chromatograph and Thermo Fisher UltiMate 3000 liquid chromatograph.

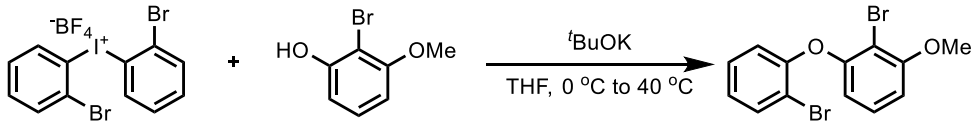
2. Experimental Section

2.1 Ligand Synthesis



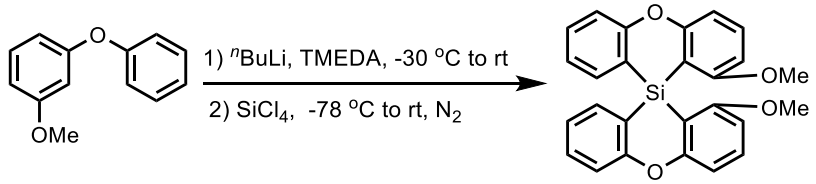
S-1

Synthesis of the bis(2-bromophenyl) iodonium tetrafluoroborate S-1[1]**:** To a suspension of *m*-chloroperbenzoic acid (*m*-CPBA, 75% active oxidant, 7.6 g, 33 mmol, 1.1 equiv.) in CH_2Cl_2 (120 mL) was added iodobromobenzene (3.9 mL, 30 mmol, 1.0 equiv.) under nitrogen, followed by slow addition of $BF_3{\cdot}Et_2O$ (9.3 mL, 75 mmol, 2.5 equiv.) at room temperature. After stirred at room temperature for 1.0 hour, the reaction was cooled to 0 °C and *o*-bromophenylboronic acid (6.6 g, 33 mmol, 1.1 equiv.) was added portionwise. The reaction was then warmed to room temperature and stirred overnight. The reaction mixture was concentrated to 2/3 of the volume and diethyl ether was added to induce precipitation of the product. The precipitate was filtered to afford the diaryliodonium salt **S-1** (12.6 g, 80% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.85 (dd, *J* =8.0, 1.6 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H).



S-1 S-2 2

Synthesis of the dibromo-3-phenoxyanisole 2[2]: ^{t}BuOK (3.4 g, 30 mmol, 1.5 equiv.) and 2-bromo-3-methoxyphenol **S-2** (4.06 g, 20 mmol, 1.0 equiv.) was suspended in THF (50 mL) under nitrogen and the reaction was left to stir at 0 °C for 10 minutes. Diaryliodonium salt **S-1** (12.6 g, 24 mmol, 1.2 equiv.) was then added in one portion at the same temperature. After warmed up to room temperature, the reaction was allowed to stir at 40 °C. The reaction was monitored by TLC until **S-2** was completely consumed. Upon completion, the reaction was quenched with H_2O at 0 °C and the aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (PE: EA = 20:1) to give product **2** (6.7 g, 94 % yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.27–7.23 (m, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.02 (td, *J* = 7.6, 1.2 Hz, 1H), 6.87 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.71 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.47 (dd, *J* = 8.4, 1.2 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.56, 154.44, 153.15, 133.76, 128.56, 128.32, 125.02, 119.64, 114.18, 111.53, 107.00, 103.88, 56.49; HRMS (EI) m/z Calcd for $C_{13}H_{10}Br_2O_2[M]^+$: 355.9048, found: 355.9042.

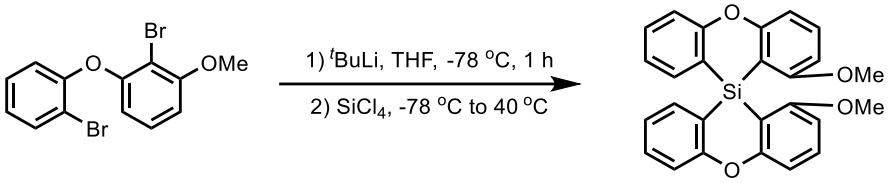


1 3

General Procedure A for the synthesis of the 1,1'-dimethoxy-10,10'-spirobi[dibenzo[*b*,*e*][1,4]oxasiline] 3[3] **:**To a solution of **1** (2.10 g, 10.5 mmol, 2.02 equiv.) in THF (10 mL) was added dropwise a premixed of ^{n}BuLi (2.5 M in Hexane, 8.8 mL, 22 mmol, 4.23 equiv.) and TMEDA (3.3 mL, 22 mmol, 4.23 equiv.) at –30 °C under N_2. The reaction

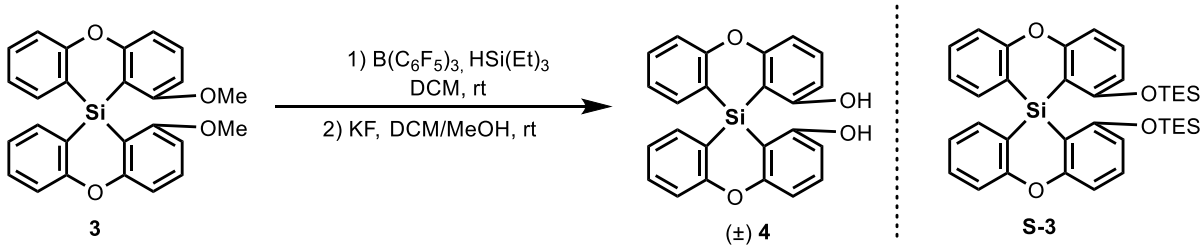
mixture was allowed to warm up to room temperature and stirred at the same temperature for 16 hours. To the reaction mixture was then added dropwise a THF (4.0 mL) solution of tetrachlorosilane (0.6 mL, 5.2 mmol, 1.0 equiv.) at –78 °C, and the reaction mixture was stirred at room temperature for another 24 hours. The reaction mixture was quenched with H_2O and the aqueous phase was extracted with DCM. The collected organic layers were dried over Na_2SO_4, and the volatiles were removed under reduced pressure. The resulted solid was washed with petroleum ether, and filtered to give part of **3** (0.44 g). Then the filtrate was evaporated and the crude material was purified by flash chromatography (PE: EA = 20:1) to give pure product **3** (75.9 mg) as a white solid.

Total weight: 0.52 g, 24 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.38 (m, 2H), 7.34 (t, *J* = 8.0 Hz, 2H), 7.28–7.22 (m, 4H), 6.99 (td, *J* = 7.2, 1.2 Hz, 2H), 6.89 (dd, *J* = 8.4, 0.8 Hz, 2H), 6.40 (d, *J* = 8.0, 2H), 3.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.53, 161.36, 160.95, 135.42, 132.30, 131.10, 122.30, 117.25, 110.74, 105.92, 103.86, 55.69; HRMS (ESI) m/z Calcd for $C_{26}H_{21}O_4Si$ $[M+H]^+$: 425.1209, found: 425.1204.



2 **3**

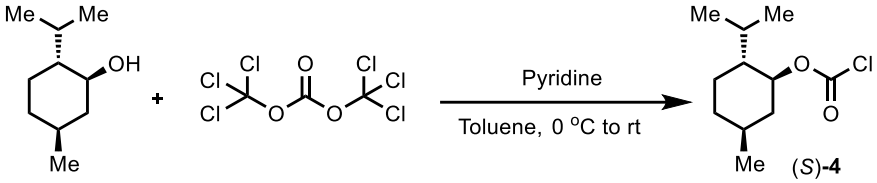
General Procedure B for the synthesis of the 1,1'-dimethoxy-10,10'-spirobi[dibenzo[*b*,*e*][1,4]oxasiline] 3[4] **:** To an anhydrous THF (32 mL) solution of 2-bromo-1-(2-bromophenoxy)-3-methoxybenzene **2** (7.3 g, 20.3 mmol, 2.03 equiv.) was added ^{t}BuLi (1.3 M in pentane, 63 mL, 81.2 mmol, 8.12 equiv.) dropwise at -78°C under N_2. After stirred at -78°C for 1.0 hour, $SiCl_4$ (1.2 mL, 10 mmol, 1.0 equiv.) was added dropwise to the above suspension at the same temperature. After warmed up to room temperature, the reaction mixture was allowed to stir at 40 °C overnight. The reaction was then quenched with H_2O, and the aqueous phase was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated to afford a yellow solid. The solid was washed with petroleum ether and filtered to get the product **3** (3.8 g, 90% yield) as a white solid.



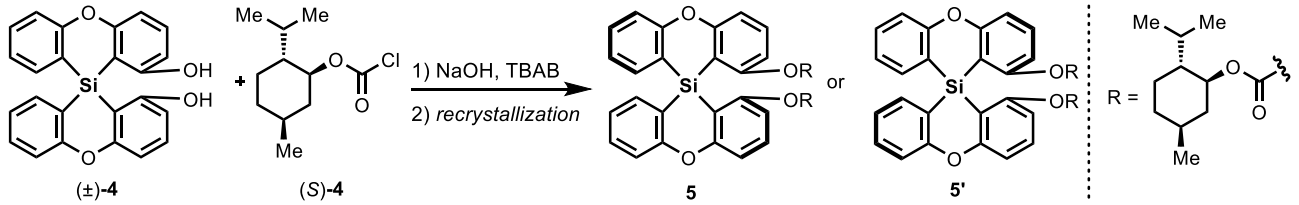
3 (±) **4** **S-3**

Synthesis of the 9'9-spirobiphenoxasilin-diol (±)-SPOSiOL (4) [4]**:** A 350 mL sealed tube with a magnetic stirring bar was charged with **3** (7.9 g, 18.6 mmol, 1.0 equiv.) and $B(C_6F_5)_3$ (1.86 g, 3.63 mmol, 20 mol%) in the glovebox. The tube was sealed and moved outside of the glovebox, followed by injection of anhydrous CH_2Cl_2 (89.0 mL). $HSiEt_3$ (8.9 mL, 55.8 mmol, 3.0 equiv.) was added dropwise to the above suspension. The reaction was monitored by TLC until **3** was completely consumed. The mixture was then filtered through a short silica gel column with a mixed solvent of PE and EA (v/v, 20/1) as the eluent. The solution was concentrated to afford the TES protected **S-3** as a yellow solid. **S-3** was dissolved in CH_2Cl_2 (50 mL) under nitrogen, followed by addition of KF (2.16 g, 37.2 mmol, 2.0 equiv.) and MeOH (50 mL). The resulting mixture was stirred at the room temperature. Upon completion, the reaction mixture was filtered to remove insoluble salts, and the filtrate was evaporated to afford a white solid. The solid was washed with petroleum ether and filtered to give (±)- **SPOSiOL** (**4**) (7.31 g, 99% yield) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) δ 7.38–7.32 (m, 2H), 7.20 (t, *J* = 8.0 Hz, 2H), 7.16–7.11 (m, 4H), 6.94 (td, *J* =

7.2, 0.8 Hz, 2H), 6.70 (d, *J* = 8.4, 2H), 6.32 (d, *J* = 8.0, 2H), 4.88 (s, 2H).

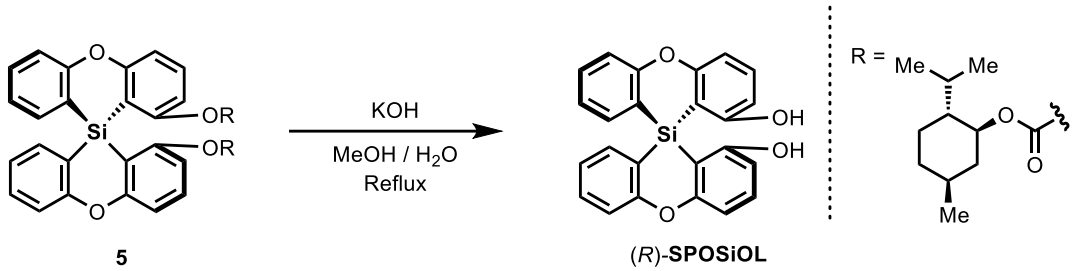


Synthesis of the (1*R*)-(-)-menthyl chloroformate (*S*)-4 [5,6]: To a toluene (260 mL) solution of triphosgene (22.0 g, 74 mmol, 0.41 equiv.) was added the toluene (150 mL) solution of pyridine (21.9 mL, 27 mmol, 0.15 equiv.) dropwise at 0 °C under N_2. The reaction mixture was then stirred at the same temperature for 15 minutes, followed by addition of the toluene (100 mL) solution of (-)-menthol (28.1g, 180 mmol, 1.0 equiv.) dropwise. After stirring for 18 h at room temperature, the reaction was quenched with H_2O and the aqueous phase was extracted with EA. The organic layers were dried over Na_2SO_4 and concentrated to afford the crude (1*R*)-(-)-menthyl chloroformate (***S*)-4** (38.1 g, 97% yield) as a yellow liquid, which could be used for the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.74 (td, *J* = 10.8, 4.4 Hz, 1H), 2.17–2.10 (m, 1H), 2.00–1.88 (m, 1H), 1.75–1.65 (m, 2H), 1.52–1.42 (m, 2H), 1.19–0.99 (m, 2H), 0.96–0.86 (m, 7H), 0.81 (d, *J* = 6.8 Hz, 3H).



Resolution of (±)-SPOSiOL (4) [5]**:** To a solution of racemic **(±)-SPOSiOL** (**4**) (7.31g, 18.4 mmol, 1.0 equiv.) and NaOH (3.24 g, 80.9 mmol, 4.4 equiv.) in water (52.0 mL) was added a chloroform (52.0 mL) solution of *tetra*-butylammonium bromide (TBAB, 3.24 g, 10.1 mmol, 0.55 equiv.). With rapid stirring, (-)-menthyl chloroformate (*S*)-**4** (12.3 g, 56.1 mmol, 3.0 equiv.) was added. Upon completion, two phases were separated, and the aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4 and concentrated to afford a crude product. The crude product was purified by flash chromatography (PE then PE: EA = 20:1) to give pure product **5 + 5'** (10.3 g, 74 % yield) as a yellow solid, which was recrystallized from PE/DCM to give **5** (3.97 g, 39% yield, >99: 1 dr) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (t, *J* = 8.2 Hz, 2H), 7.40 (td, *J* = 6.8, 1.6 Hz, 2H), 7.25–7.20 (m, 4H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.99 (td, *J* = 7.2, 1.2 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 4.18 (td, *J* = 10.8, 4.4 Hz, 2H), 1.83–1.72 (m, 2H), 1.67–1.51 (m, 6H), 1.39–1.20 (m, 4H), 1.06–0.77 (m, 16H), 0.75–0.63 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.88, 160.29, 155.76, 152.14, 135.78, 132.31, 131.91, 122.80, 117.83, 115.24, 115.13, 114.65, 108.25, 78.82, 46.74, 39.85, 34.03, 31.20, 25.70, 23.11, 21.98, 20.82, 16.16; HRMS (ESI) *m/z* Calcd for $C_{46}H_{52}O_8SiNa$ $[M+Na]^+$: 783.3329, found: 783.3324; $[\alpha]_D^{27}$ = +4.3 (c =1.0, $CHCl_3$).

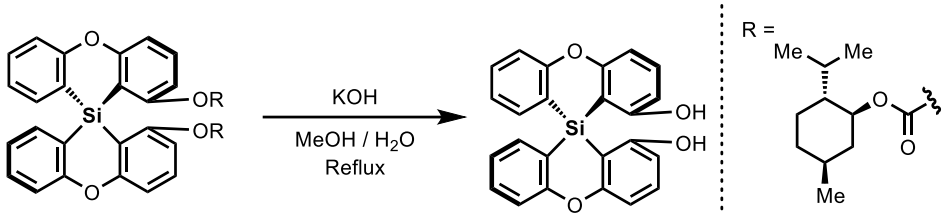
Recrystallization (PE/DCM) was performed for several times with the mother liquid to leave a yellow solution, which was then concentrated to get **5'** (4.55 g, 44% yield, 96:4 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.38 (m, 4H), 7.25–7.18 (m, 4H), 7.14 (dd, *J* = 8.4, 0.8 Hz, 2H), 6.99 (td, *J* = 7.2, 1.2 Hz, 2H), 6.95 (dd, *J* = 8.0, 0.8 Hz, 2H), 4.18 (td, *J* = 10.8, 4.4 Hz, 2H), 1.74–1.65 (m, 4H), 1.65–1.59 (m, 4H), 1.37–1.23 (m, 6H), 0.90–0.83 (m, 14H), 0.76– 0.68 (m, 2H), 0.62 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.84, 160.15, 155.90, 151.90, 135.62, 132.33, 131.76, 122.83, 117.62, 115.37, 115.26, 114.49, 108.05, 78.81, 46.66, 39.91, 34.02, 31.19, 25.48, 23.02, 21.96, 20.90, 16.07. $[\alpha]_D^{27}$ = -23.3 (c =1.0, $CHCl_3$).



5 (*R*)-**SPOSiOL**

Synthesis of the (*R*)-SPOSiOL[3,5]: To a solution of **5** (3.80 g, 5.0 mmol, 1.0 equiv.) in MeOH (83 mL)/H_2O (10 mL) was added KOH (5.37 g, 96 mmol, 19.2 equiv.) and the mixture refluxed for 8.0 hours. The mixture was then cooled to room temperature, evaporated part of solvents and extracted with *n*-hexane. The aqueous layer was separated, acidified with 6 M HCl to PH = 6 and a white precipitate appeared. Diethyl ether was then added to the above suspension. The organic phase was separated, dried over Na_2SO_4 and evaporated in vacuo to give (*R*)-**SPOSiOL** (1.82 g, 92% yield, 99.3% ee) as a white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 80/20; flow rate, 1.0 mL/min; 254 nm; t_R (major) = 6.86 min; t_R (minor) = 9.18 min.

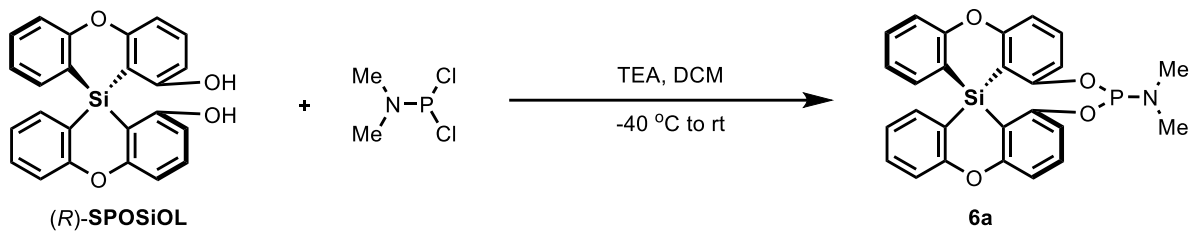
Recrystallization of (*R*)-SPOSiOL: (*R*)-**SPOSiOL** (1.42 g, 78% yield, 99.7% ee) was recrystallized from *n*-hexane/^{i}PrOH. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 80/20; flow rate, 1.0 mL/min; 254 nm; t_R (major) = 6.86 min; t_R (minor) = 9.18 min. $[\alpha]_D^{25}$ = +1.33 (c = 0.5, EtOH).



5' (*S*)-**SPOSiOL**

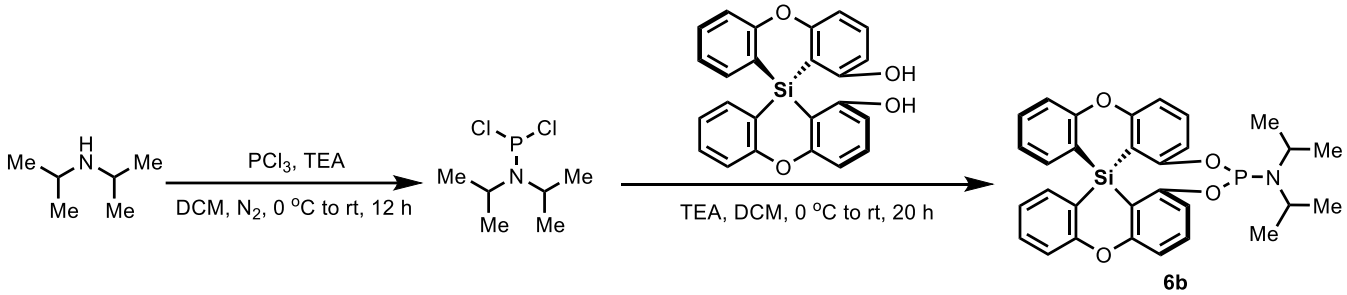
Synthesis of the (*S*)-SPOSiOL [3,5]: To a solution of **5'** (3.31 g, 4.4 mmol, 1.0 equiv., 96:4 dr) in MeOH (73.0 mL) was added KOH (17.1 g, 305 mmol, 69.3 equiv.) and H_2O (18.0 mL). The mixture was refluxed for 1.0 hour, cooled to room temperature and part of solvents was evaporated, followed by addition of *n*-Hexane. The aqueous layer was collected for further purification. In the meantime, the combined organic layers were dried over Na_2SO_4 and concentrated to recover the starting material **5'** which was further refluxed with MeOH (33.0 mL) and KOH/H_2O (5.9 g KOH in 8.0 mL H_2O) for another 1.0 hour. The mixture was then cooled to room temperature and part of solvents were evaporated. The reaction mixture was extracted with *n*-hexane again. The separated aqueous layer, combining with the above one, was acidified with 6.0 M HCl to pH = 6 and a white precipitate was appeared. Diethyl ether was then added to the above suspension. The Et_2O phase was separated, dried over Na_2SO_4 and concentrated to give (*S*)-**SPOSiOL** (1.45 g) as a white solid. Following the similar procedure, (*S*)-**SPOSiOL** (0.57 g) was obtained starting from **5'** (1.24 g, 1.6 mmol, 1.0 equiv., 96:4 dr) as a white solid.

Total weight: 2.02 g, 85 % yield, 93.6% ee. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 80/20; flow rate, 1.0 mL/min; 254 nm; t_R (major) = 9.18 min; t_R (minor) = 6.86 min. $[\alpha]_D^{25}$ = -1.35 (c =0.5, EtOH).



(*R*)-**SPOSiOL** **6a**

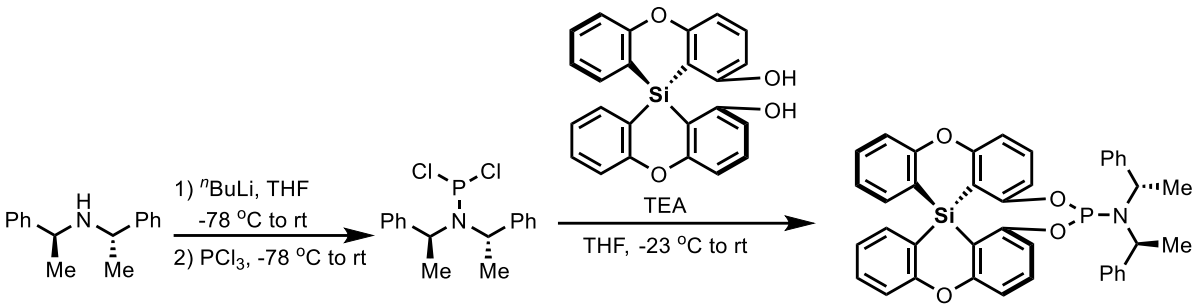
Synthesis of the *N*, *N*-dimethyl-1,5,7,11-tetraoxa-6-phospha-15*b*-silacycloocta[3,2,1-*de*:7,8,1-*d'e'*] dianthracen-6-amine 6a [4]**:** To an anhydrous and degassed DCM (2.5 mL) solution of (*R*)-**SPOSiOL** (198 mg, 0.5 mmol, 1.0 equiv.) was added triethylamine (0.35 mL, 2.5 mmol, 5.0 equiv.) under N_2, followed by addition of 1,1-dichloro-*N*,*N*-dimethylphosphanamine (0.10 mL, 0.87 mmol, 1.74 equiv.) at -40 °C. The resulting mixture was then warmed to room temperature. Upon completion, the mixture was filtered through a pad of silica gel (pretreated with hexane/Et_3N = 50/1, degassed) with PE/EA (10/1, v/v, degassed) as eluent. The filtrate was concentrated and **6a** was obtained in 80 % yield (189 mg) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.36–7.23 (m, 3H), 7.23–7.15 (m, 4H), 7.11 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.03–6.94 (m, 3H), 6.75 (d, *J* = 8.0 Hz, 1H), 2.32 (d, *J* = 9.2 Hz, 6H); $[\alpha]_D^{28}$ = +159.2 (c =0.12, $CHCl_3$).



6b

To a solution of PCl_3 (0.22 mL, 2.5 mmol, 5.0 equiv.) in DCM (4 mL) was added TEA (0.69 mL, 5 mmol, 10 qeuiv.) at room temperature, followed by the addition of distilled diisopropylamine (0.35 mL, 2.5 mmol, 5.0 equiv.) at 0 °C. The reaction mixture was then warmed to room temperature and stirred at the same temperature for 12 h to afford a DCM solution of alkylphosphine chloride.

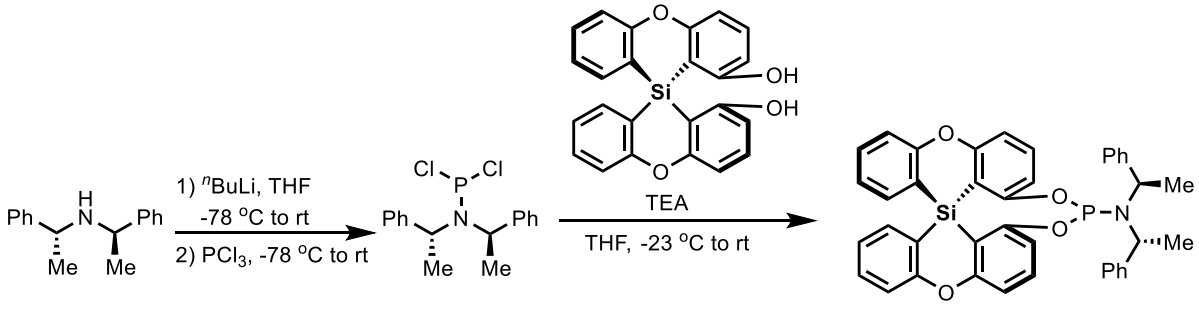
To a solution of (*R*)-**SPOSiOL** (198.2 mg, 0.5 mmol, 1.0 equiv.) and triethylamine (0.69 mL, 5 mmol, 10 equiv.) in anhydrous and degassed DCM was added the DCM solution of aforementioned alkylphosphine chloride under N_2 at 0 °C and then the reaction was stirred at room temperature. Upon completion, the reaction solution was diluted with degassed solution of PE and EA (v/v= 1:1) and filtered through a short pad of silica gel. Solvents were removed under reduced pressure and the resulting mixture was recrystallized from THF and Hexane to provide **6c** in 48% yield (126.5 mg) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (t, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.38–7.12 (m, 7H), 7.07–6.98 (m, 2H), 6.98–6.89 (m, 3H), 3.20–3.16 (m, 2H), 1.14-0.99 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.99 (d, *J* = 2.2 Hz), 162.67, 160.37, 160.15, 158.89, 158.80, 156.75, 156.63, 133.68, 133.51, 133.03 (d, *J* = 2.0 Hz), 132.43, 131.12, 113.10, 123.59, 123.47, 120.42, 120.40, 118.26, 118.25, 117.96, 117.84, 117.60 (d, *J* = 6.0 Hz), 114.69, 114.66, 114.00, 110.35 (d, *J* = 3.5 Hz), 109.14, 46.56, 45.29, 24.46, 19.29; ^{31}P NMR (162 MHz, $CDCl_3$) δ 139.11; HRMS (ESI) m/z calcd for $C_{30}H_{29}NO_4SiP$ $[M+H]^+$: 526.1598, found: 526.1605. $[\alpha]_D^{25}$= 119.20 (*c* = 1.0, THF).



6c

Synthesis of 6c[4]: A flame-dried 10 mL Schlenk tube were charged with (*1S, 1'S*)-bis(1-phenylethyl)amine (0.20 mL, 0.89 mmol, 1.8 equiv.) and anhydrous THF (2.0 mL) under nitrogen, the solution was then cooled to -78 °C and ^{n}BuLi (2.5 M in Hexane, 0.38 mL, 0.95 mmol, 1.9 equiv.) was added dropwise. After stirred at the same temperature for 2 hours, the THF (1.0 mL) solution of phosphorus trichloride (74 μL, 0.85 mmol, 1.7 equiv.) was added dropwise to the above THF solution of lithium amide at -78 °C under N_2. The reaction mixture was warmed to room temperature and stirred for 12 hours to afford a THF solution of alkylphosphine chloride.

To a solution of (*R*)**-SPOSiOL** (198.8 mg, 0.5 mmol, 1.0 equiv.) in anhydrous and degassed THF (2.5 mL) was added triethylamine (0.35 mL, 2.5 mmol, 5.0 equiv.) under N_2, followed by the slow addition of the THF solution of aforementioned alkylphosphine chloride at -23 °C. The reaction mixture was then stirred at room temperature. Upon completion, the mixture was filtered through a pad of silica gel (pretreated with hexane/Et_3N = 50/1, degassed) with PE/EA (5/1, v/v, degassed) as eluent. The resulting mixture was concentrated and the crude product was purified by flash chromatography (PE:EA = 50:1, degassed) to give pure product **6c** (147 mg, 45 % yield) as a white solid.^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.76 (t, J = 8.0 Hz, 1H), 7.42–7.35 (m, 3H), 7.38–7.27 (m, 2H), 7.27–7.13 (m, 10H), 7.11–7.00 (m, 2H), 6.98–6.93 (m, 1H), 6.80–6.73 (m, 4H), 5.61 (d, J = 6.8 Hz, 1H), 4.58–4.48 (m, 2H), 1.65 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 164.04 (d, J = 2.1 Hz), 163.93, 161.41, 161.37, 159.70, 159.61, 157.07, 156.94, 144.11, 135.01 (d, J = 2.1 Hz), 134.32, 134.24, 134.16, 132.83, 132.77, 129.4 (d, J = 2.2 Hz), 128.97, 128.04, 125.0 (d, J = 2.4 Hz), 121.56, 121.14, 119.71, 119.69, 119.09 (d, J = 6.6 Hz), 118.86 (d, J = 6.2 Hz), 116.06, 116.04, 115.14, 110.90, 110.86, 110.20, 110.18, 55.67, 55.55; ^{31}P NMR (162 MHz, CD_3COCD_3) δ 139.49; HRMS (ESI) m/z Calcd for $C_{40}H_{32}NO_4PSi$ $[M+Na]^+$: 672.1736, found: 672.1730; $[\alpha]_D^{28}$ = -89.6 (c = 0.1, EtOH).

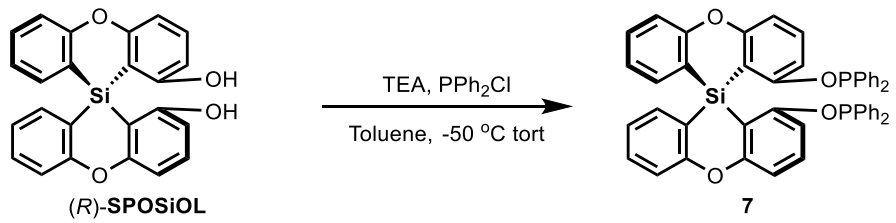


6d

Synthesis of 6d[4]: A flame-dried 10 mL Schlenk tube were charged with (*1R, 1'R*)-bis(1-phenylethyl)amine (157.8 mg, 0.7 mmol, 1.7 equiv.) and anhydrous THF (1.0 mL) under nitrogen, the solution was then cooled to -78 °C and ^{n}BuLi (2.5 M in Hexane, 0.31 mL, 0.772 mmol, 1.88 equiv.) was added dropwise. After stirred at the same temperature for 2 hours, the THF (1.0 mL) solution of phosphorus trichloride (61 μL, 0.7 mmol, 1.7 equiv.) was

added dropwise to the above THF solution of lithium amide at -78 °C under N_2. The reaction mixture was warmed to room temperature and stirred for 12 hours to afford a THF solution of alkylphosphine chloride.

To a solution of (*R*)-**SPOSiOL** (163.1 mg, 0.411 mmol, 1.0 equiv.) in anhydrous and degassed THF (2.1 mL) was added triethylamine (285 μL, 2.055 mmol, 5.0 equiv.) under N_2, followed by the slow addition of the THF solution of aforementioned alkylphosphine chloride at -23 °C. The reaction mixture was then stirred at room temperature. Upon completion, the mixture was filtered through a pad of silica gel (pretreated Et_3N, degassed) with PE/EA (5/1, v/v, degassed) as eluent. The resulting mixture was concentrated and the crude product was purified by recrystallization (Hexane/Et_2O) to give pure product **6d** (157.1 mg, 59 % yield) as a white solid.^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.79 (t, J = 8.2 Hz, 1H), 7.64 (t, J = 8.2 Hz, 1H), 7.45–7.36 (m, 3H), 7.32–7.23 (m, 5H), 7.22–7.17 (m, 1H),7.15–6.96 (m, 13H), 6.76 (d, J = 8.0 Hz, 1H), 4.49 (brs, 2H), 1.47 (brs, 6H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ ^{13}C NMR (125 MHz, CD_3COCD_3) δ 164.30, 163.88, 161.63, 161.25, 159.39, 159.31, 158.04, 157.95, 135.07, 134.51, 134.04, 132.92, 132.85, 128.77, 127.65, 125.16, 124.95, 122.37, 120.34, 119.94, 119.18, 119.15, 118.35, 118.30, 115.83, 115.62, 110.97, 110.15, 110.13, 53.65; ^{31}P NMR (162 MHz, CD_3COCD_3) δ 135.23; HRMS (ESI) m/z Calcd for $C_{40}H_{32}NO_4PSi$ $[M+Na]^+$: 672.1730, found: 672.1735; $[\alpha]_D^{28}$ = 151.9 (c = 0.1, EtOH).

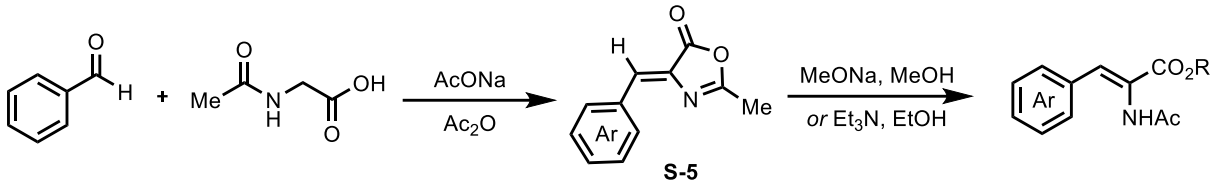


(*R*)-**SPOSiOL** **7**

Synthesis of the 1,1'-bis((diphenylphosphaneyl)oxy)-10, 10'-spirobi[dibenzo[*b,e*][1,4]oxasiline] 7: To a toluene (5.0 mL) suspension of (*R*)-**SPOSiOL** (199.3 mg, 0.5 mmol, 1.0 equiv.) was added triethylamine (0.51 mL, 3.67 mmol, 7.34 equiv.) under N_2. The resulting mixture was stirred at -50 °C for 20 minutes. Then the toluene (2.0 mL) solution of chlorodiphenylphosphane (0.3 mL, 1.67 mmol, 3.34 equiv.) was added into the above mixture. The resulting mixture was allowed to stir at room temperature. Upon completion, the mixture was filtered through a pad of silica gel (pretreated with Petroleum ether/Et_3N = 50/1, degassed) with petroleum ether/EtOAc (5/1, v/v, degassed) as eluent. The filtrate was concentrated and **7** was obtained in 73 % yield (281 mg) as a white solid. ^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.44–7.38 (m, 2H), 7.36 (t, J = 8.0 Hz, 2H), 7.33–7.24 (m, 4H), 7.21–7.11 (m, 10H), 7.08 –6.94 (m, 10H), 6.94–6.86 (m, 4H), 6.76 (dd, J = 8.4, 0.8 Hz, 2H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 206.40, 162.83, 162.73, 162.54, 160.78, 140.36, 140.19, 136.46, 133.76, 133.74, 132.64, 131.72, 131.57, 131.48, 131.33, 130.77, 130.68, 130.06, 129.60, 129.56, 129.53, 129.48, 129.34, 126.42, 123.83, 118.83, 118.43, 113.58, 109.56, 109.28, 107.21, 107.18, 30.73, 30.53, 30.34, 30.15, 29.96, 29.76, 29.57; ^{31}P NMR (162 MHz, CD_3COCD_3) δ 105.24; MS (MALDI-TOF) *m/z* Calcd for $C_{48}H_{34}O_4P_2Si$ $[M]^+$: 765.1780, found: 765.1774; $[\alpha]_D^{28}$ = -19.5 (c = 0.1, EtOH).

2.2 Rh-Catalyzed Asymmetric Hydrogenation of α-Dehydroamino Acid Derivatives

2.2.1 Preparation of α-Dehydroamino Acid Derivatives

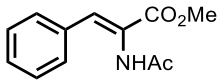


S-5

Method A: A suspension of *N*-acetylglycine (10 mmol, 1.0 equiv.), sodium acetate (10 mmol, 1.0 equiv.), acetic anhydride (9.2 mL) and the corresponding aldehyde (10 mmol, 1.0 equiv.) was stirred at 100 °C for 4 hours. Then the mixture was left stirring overnight at room temperature. After that, this suspension was mixed with water and stirred at room temperature for half an hour. The insoluble material was separated by filtration, washed with water or purified by flash chromatography on silica gel to get **S-5**. To **S-5** was added MeOH (10 mL) and sodium methoxide in methanol (2.0 mL of 25% CH_3ONa in CH_3OH). The reaction mixture was stirred at room temperature for 15 min. The reaction was quenched with H_2O and the aqueous phase was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated to afford a crude product. Then the crude material was purified by flash chromatography to give pure product.

Method B: A suspension of *N*-acetylglycine (5.0 mmol, 1.2 equiv.), sodium acetate (5.0 mmol, 1.2 equiv.), acetic anhydride (5.0 mL) and the corresponding aldehyde (1.0 equiv.) was stirred at 100 °C for 4 hours. After that, this suspension was poured into ice water. The insoluble material was separated by filtration and washed with cold ethanol to get **S-5**. To **S-5** was added MeOH (11.2 mL) and sodium methoxide (5 mmol, 1.2 equiv.) and stirred at room temperature for 30 min. The reaction was quenched with H_2O and the aqueous phase was extracted with CH_2Cl_2 until TLC detected the shadowless point of view. The combined organic layers were dried over Na_2SO_4 and concentrated to afford a crude product. Then the crude material was purified by flash chromatography to give pure product.

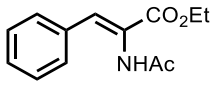
Method C: A suspension of *N*-acetylglycine (20 mmol, 1.0 equiv.), sodium acetate (20 mmol, 1.0 equiv.), acetic anhydride (12.0 mL) and the corresponding aldehyde (20 mmol, 1.0 equiv.) was stirred at 80 °C overnight. After this time, this suspension was mixed with water and stirred at room temperature for half an hour. The insoluble material was separated by filtration to get **S-5**. To **S-5** was added EtOH (100 mL) and trimethylamine (2 ml). The reaction mixture was then stirred at 80 °C for 2 hours. The reaction was quenched with H_2O and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to afford a crude product. Then the crude material was purified by flash chromatography to give pure product.



8a

Methyl (*Z*)-2-acetamido-3-phenylacrylate (8a) [7,10]:

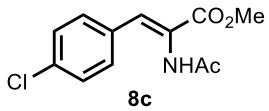
8a was synthesized following the method A. 0.39 g, 18% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.30 (m, 6H), 6.98 (s, 1H), 3.85 (s, 3H), 2.14 (s, 3H).



8b

Ethyl (*Z*)-2-acetamido-3-phenylacrylate (8b) [8]:

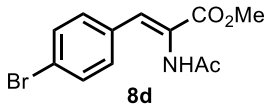
8b was synthesized following the method C. 1.82 g, 39% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.29 (m, 6H), 7.02 (s,1H), 4.31 (q, J = 6.8 Hz, 2H), 2.13 (s, 3H), 1.36 (t, J = 6.8 Hz, 3H).



8c

Methyl (*Z*)-2-acetamido-3-(4-chlorophenyl) acrylate (8c) [9]:

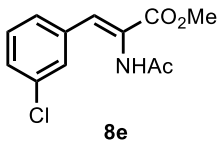
8c was synthesized following the method A. 1.19 g, 47% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.29 (m, 5H), 7.06 (s, 1H), 3.86 (s, 3H), 2.14 (s, 3H).



8d

Methyl (*Z*)-2-acetamido-3-(4-bromophenyl) acrylate (8d) [7]:

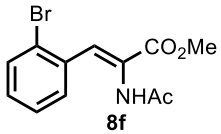
8d was synthesized following the method B. 0.60 g, 40% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 6.8 Hz, 2H), 7.30 (s, 1H), 7.08 (s, 1H), 3.86 (s, 3H), 2.14 (s, 3H).



8e

Methyl (*Z*)-2-acetamido-3-(3-chlorophenyl) acrylate (8e) [10]:

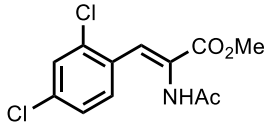
8e was synthesized following the method A. 1.56 g, 61% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.36–7.28 (m, 4H), 7.10 (s, 1H), 3.86 (s, 3H), 2.14 (s, 3H).



8f

Methyl (*Z*)-2-acetamido-3-(2- bromophenyl) acrylate (8f) [10]:

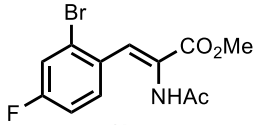
8f was synthesized following the method A. 1.15 g, 39% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.46–7.38 (m, 2H), 7.31–7.25 (m, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.01 (s, 1H), 3.88 (s, 3H), 2.05 (s, 3H).



8g

Methyl (*Z*)-2-acetamido-3-(2,4-dichlorophenyl) acrylate (8g):

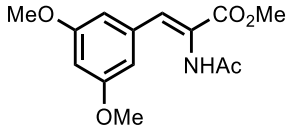
8g was synthesized following the method A. 1.36 g, 47% yield, yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.40 (m, 2H), 7.36 (d, *J* = 8.4Hz, 1H), 7.30 (s, 3H), 7.20 (d, *J* = 7.6 Hz, 1H), 3.87 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.33, 165.13, 134.89, 134.65, 131.42, 129.94, 129.36, 126.85, 125.94, 52.84, 23.18; HRMS (ESI) *m/z* Calcd for $C_{12}H_{12}Cl_2NO_3$ $[M+H]^+$: 288.0194, found: 288.0189.



8h

Methyl (*Z*)-2-acetamido-3-(2-bromo-4-fluorophenyl) acrylate (8h):

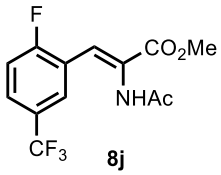
8h was synthesized following the method A. 1.10 g, 35% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.29 (m, 4H), 7.04–6.95 (m, 1H), 3.87 (s, 3H), 2.02 (s, 3H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -109.63 (d, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.79, 165.12, 161.87 (d, *J* = 253.6 Hz), 130.65, 130.50 (d, *J* = 8.6 Hz), 128.8, 125.87, 124.61 (d, *J* = 9.4 Hz), 119.92 (d, *J* = 24.3 Hz), 114.50 (d, *J* = 21.3 Hz), 52.68, 22.92.; HRMS (ESI) *m/z* Calcd for $C_{12}H_{12}BrFNO_3$ $[M+H]^+$: 315.9985, found: 315.9979.



8i

Methyl (*Z*)-2-acetamido-3-(3,5-dimethoxyphenyl) acrylate (8i):

8i was synthesized following the method A. 1.03 g, 37% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.12 (s, 1H), 6.62 (s, 2H), 6.44 (s, 1H), 3.84 (s, 3H), 3.77 (s, 6H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.98, 165.56, 160.56, 135.20, 132.00, 124.96, 107.45, 101.56, 55.22, 52.57, 23.08; HRMS (ESI) *m/z* Calcd for $C_{14}H_{18}NO_5$ $[M+H]^+$: 280.1185, found: 280.1180.

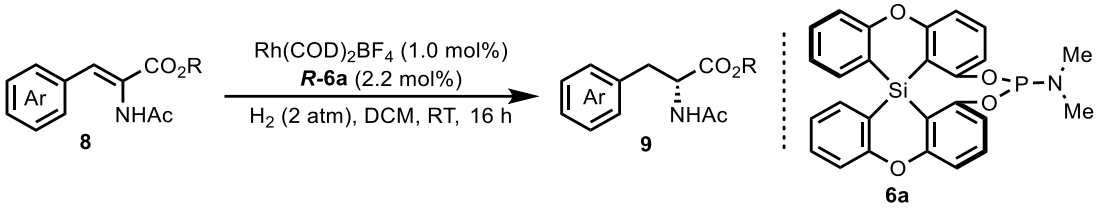


8j

Methyl (*Z*)-2-acetamido-3- (2-fluoro-5-(trifluoromethyl) phenyl)) acrylate (8j):

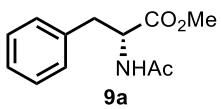
8j was synthesized following the method A. 0.87 g, 29% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 5.6 Hz, 1H), 7.58–7.53(m, 1H), 7.43 (s, 1H), 7.38 (s, 1H), 7.18 (t, *J* = 9.2 Hz, 1H), 3.90 (s, 3H), 2.10 (s, 3H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -62.24, -106.78; ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.49, 164.31, 161.10 (d, *J* = 254.0 Hz), 129.51 (d, *J* = 2.0 Hz), 127.61, 126.69, 124.88 (q, *J* = 35.3 Hz), 123.23 (q, *J* = 270.4 Hz), 122.11 (d, *J* = 14.3 Hz), 119.62 (d, *J* = 3.4 Hz), 116.56 (d, *J* = 23.6 Hz), 52.00, 21.75; HRMS (ESI) *m/z* Calcd for $C_{13}H_{12}F_4NO_3$ $[M+H]^+$: 306.0753, found: 306.0748.

2.2.2 General Procedure for Asymmetric Hydrogenation



8 **9** **6a**

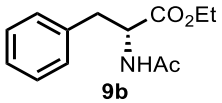
An 8.0 mL reaction tube was charged with $[Rh(cod)_2]BF_4$ (0.41 mg, 0.001 mmol,) and ligand ***R*-6a** (1.0 mg, 0.0022 mmol) in CH_2Cl_2 (0.5 mL), and stirred at room temperature for 15 min. The above solution was then injected into another 8.0 mL reaction tube containing substrate **8** (0.1 mmol, 1.0 equiv.), followed by the injection of CH_2Cl_2 (2.5 mL). The reaction tube was placed in an autoclave and pressed with 2.0 atm of H_2. The reaction was stirred at room temperature for 16 hours. After releasing H_2, the solution was concentrated, and the residue was then purified by preparative thin-layer chromatography to afford **9**.



9a

Methyl (*R*)-acetylphenylalaninate (9a) [10]

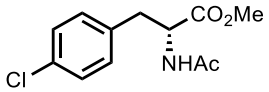
9a was synthesized following the general procedure**.** 99% yield, 93% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 9.61 min; t_R (minor) = 11.29 min. $[\alpha]_D^{27}$ = -83.2 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.23 (m, 3H), 7.12–7.06 (m, 2H), 5.92 (s, 1H), 4.89 (dt, *J* = 7.8, 5.8 Hz, 1H), 3.73 (s, 3H), 3.16 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.10 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.99 (s, 3H).



9b

Ethyl (*R*)-acetylphenylalaninate (9b) [12]

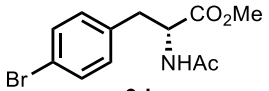
9b was synthesized following the general procedure. 99% yield, 95% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 8.20 min; t_R (minor) = 10.31 min; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.21 (m, 3H), 7.13–7.08 (m, 2H), 5.99 (d, *J* = 7.8 Hz, 1H), 4.87 (dt, *J* = 7.8, 5.8 Hz, 1H), 4.20–4.14 (m, 2H), 3.14 (dd, *J* = 13.6, 5.6 Hz, 1H), 3.10 (dd, *J* = 14.0, 5.6 Hz, 1H)., 1.99 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H).



9c

Methyl (*R*)-2-acetamido-3-(4-chlorophenyl) propanoate (9c) [13]

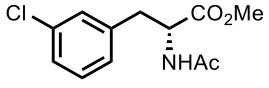
9c was synthesized following the general procedure. 99% yield, 95% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 10.89 min; t_R (minor) = 12.71 min; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.09 (s, 1H), 4.90–4.83 (m, 1H), 3.73 (s, 3H), 3.13 (dd, *J* = 13.6, 5.6 Hz, 1H), 3.05 (dd, *J* = 13.6, 5.6 Hz, 1H), 1.99 (s, 3H).



9d

Methyl (*R*)-2-acetamido-3-(4-bromophenyl) propanoate (9d) [13]

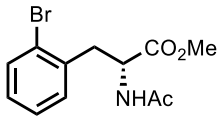
9d was synthesized following the general procedure. 99% yield, 95% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 220 nm; t_R (major) = 11.51 min; t_R (minor) = 13.48 min; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.05 (s, 1H), 4.90–4.83 (m, 1H), 3.73 (s, 3H), 3.12 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.03 (dd, *J* = 14.0, 5.6 Hz, 1H), 1.99 (s, 3H).



9e

Methyl (*R*)-2-acetamido-3-(3-chlorophenyl) propanoate (9e) [14]

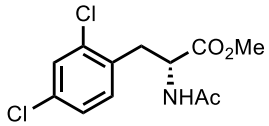
9e was synthesized following the general procedure. 99% yield, 94% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 9.78 min; t_R (minor) = 11.12 min; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26–7.19 (m, 2H), 7.09 (s, 1H), 7.03– 6.94 (m, 1H), 6.01 (s, 1H), 4.90–4.83 (m, 1H), 3.74 (s, 3H), 3.14 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.06 (dd, *J* = 13.6, 5.6 Hz, 1H), 2.01 (s, 3H).



9f

Methyl (*R*)-2-acetamido-3-(2-bromophenyl) propanoate (9f) [13]

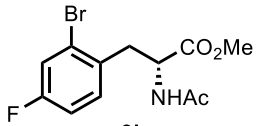
9f was synthesized following the general procedure. 99% yield, 91% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 10.91 min; t_R (minor) = 13.54 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6, 1H), 7.28–7.22 (m, 1H), 7.20 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.11 (td, *J* = 7.6, 2.0 Hz, 1H), 6.07 (d, *J* = 8.0 Hz, 1H), 4.96–4.88 (m, 1H), 3.73 (s, 3H), 3.32 (dd, *J* = 13.6, 6.0 Hz, 1H), 3.19 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.96 (s, 3H).



9g

Methyl (*R*)-2-acetamido-3-(2,4-dichlorophenyl) propanoate (9g)

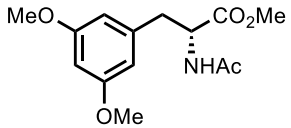
9g was synthesized following the general procedure. 99% yield, 93% ee, colorless liquid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 10.09 min; t_R (minor) = 12.69 min; $[\alpha]_D^{28}$ = -44.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 2.0 Hz, 1H), 7.19 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.10 (d, *J* = 8.0 Hz, 1H), 4.92–4.85 (m, 1H), 3.73 (s, 3H), 3.28 (dd, *J* = 14.0, 6.4 Hz, 1H), 3.14 (dd, *J* = 14.0, 6.8 Hz, 1H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.89, 169.65, 135.09, 133.59, 132.74, 131.99, 129.40, 127.21, 52.55, 52.19, 34.96, 23.04; HRMS (ESI) *m/z* Calcd for $C_{12}H_{13}BrFNO_3Na$ $[M+Na]^+$:312.0170, found:312.0165.



9h

Methyl (*R*)-2-acetamido-3-(2-bromo-4-fluorophenyl) propanoate (9h)

9h was synthesized following the general procedure. 99% yield, 93% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 10.50 min; t_R (minor) = 13.42 min. $[\alpha]_D^{27}$ = -25.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 8.2, 2.8 Hz, 1H), 7.18 (dd, *J* = 8.4, 6.0 Hz, 1H), 6.98 (td, *J* = 8.0, 2.4 Hz, 1H), 6.08 (d, *J* = 8.4 Hz, 1H), 4.93–4.86 (m, 1H), 3.73 (s, 3H), 3.29 (dd, *J* = 14.0, 6.4 Hz, 1H), 3.15 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.97 (s, 3H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -112.99 (td, *J* = 8.0, 5.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.97, 169.65, 161.33 (d, *J* = 250.5 Hz), 131.87, 131.87 (d, *J* = 8.2 Hz), 124.81 (d, *J* = 9.4 Hz), 120.10 (d, *J* = 24.3 Hz), 114.77 (d, *J* = 21.0 Hz), 52.55, 52.41, 37.17, 23.07; HRMS (ESI) *m/z* Calcd for $C_{12}H_{13}BrFNO_3Na$ $[M+Na]^+$: 339.9961, found:339.9955.

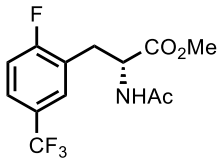


9i

Methyl (*R*)-2-acetamido-3-(3,5-dimethoxyphenyl) propanoate (9i)

9i was synthesized following the general procedure. 99% yield, 96% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 96/4; flow rate, 1.0 mL/min; 220 nm; t_R (major) = 33.88 min; t_R

(minor) = 37.42 min; $[\alpha]_D^{26}$ = -65.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (t, *J* = 2.4 Hz, 1H), 6.24 (d, *J* = 2.4 Hz, 2H), 5.94 (d, *J* = 7.2 Hz, 1H), 4.90–4.83 (m, 1H), 3.76 (s, 6H), 3.75 (s, 3H), 3.13–2.99 (m, 2H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.01, 169.61, 160.81, 137.98, 107.22, 98.89, 55.21, 52.93, 52.32, 37.93, 23.11; HRMS (ESI) *m/z* Calcd for $C_{14}H_{19}NO_5Na$ $[M+Na]^+$: 304.1161, found: 304.1155.

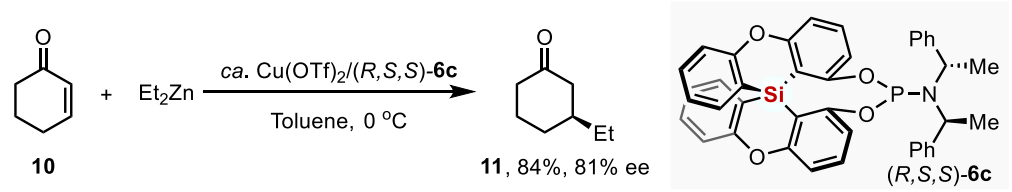


9j

Methyl (*R*)-2-acetamido-3- (2-fluoro-5-(trifluoromethyl) phenyl) propanoate (9j)

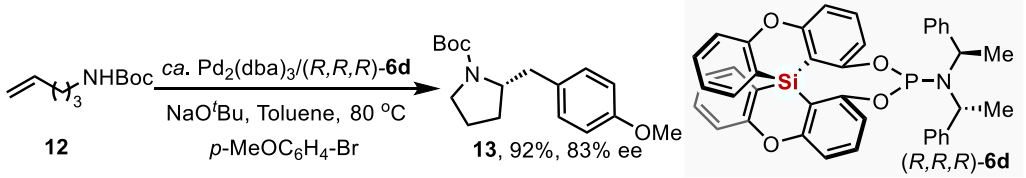
9j was synthesized following the general procedure. 94% yield, 96% ee, white solid. Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 92/8; flow rate, 1.0 mL/min; 40 °C, 254 nm; t_R (major) = 7.48 min; t_R (minor) = 8.37 min. $[\alpha]_D^{26}$ = -65.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.50 (m, 1H), 7.40 (dd, *J* = 6.8, 2.4 Hz, 1H) , 7.14 (t, *J* = 8.8 Hz, 1H), 6.04 (d, *J* = 6.0 Hz, 1H), 4.92–4.85 (m, 1H), 3.76 (s, 3H), 3.31 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.16 (dd, *J* = 14.0, 5.6 Hz, 1H), 1.99 (s, 3H); ^{19}F NMR (375 MHz, $CDCl_3$) δ -62.05, -112.30 (t, *J* = 3.7 Hz).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.66, 169.79, 163.05 (d, *J* = 251.5 Hz), 129.18 (dd, *J* = 5.8, 3.6 Hz), 126.83 (d, *J* = 3.5 Hz), 126.54–126.40 (m), 124.26 (d, *J* = 17.4 Hz), 123.58 (q, *J* = 270 Hz), 115.92 (d, *J* = 23.9 Hz), 52.51, 52.17, 31.35, 22.80; HRMS (ESI) *m/z* Calcd for $C_{13}H_{13}F_4NO_3Na$ $[M+Na]^+$: 330.0729, found: 330.0724.

2.3 Other Applications with SPOSiOL-Derived Ligands



10 **11**, 84%, 81% ee (*R,S,S*)-**6c**

A 12 mL tube was charged with $Cu(OTf)_2$ (1.1 mg, 0.003 mmol, 1.0 mol%), (*R,S,S*)-**6c** (3.9 mg, 0.006 mmol, 2.0 mol%) and toluene (0.9 mL) in the glovebox. The reaction mixture was then stirred at room temperature for 30 min. After that, Et_2Zn (1.0 M in hexane, 0.45 mmol, 1.5 equiv.) and **10** (29 μL, 0.3 mmol, 1.0 equiv.) were injected at 0 °C under N_2 outside of the glovebox and the reaction was kept at the same temperature for another 3 hours. The reaction was quenched with saturated NH_4Cl and the mixture was extracted with Et_2O for 3 times. The combined organic layers were dried with Na_2SO_4 and carefully concentrated. The residue was purified by chromatography (PE/Et_2O = 6/1 as eluent) to give **11**[15] (31.9 mg, 84% yield, 81% ee). Determined by chiral GLC using SUPELCO GAMMA DEX 225 column (2 min at 60 °C, 3 °C/min until 120 °C, 10 min at 120 °C), t_R (major) = 23.97 min; t_R (minor) = 24.18 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52–2.21 (m, 3H), 2.12–1.89 (m, 3H), 1.78–1.61 (m, 2H), 1.48–1.25 (m, 3H), 0.93 (t, *J* = 7.6 Hz, 3H).



12 **13**, 92%, 83% ee (*R,R,R*)-**6d**

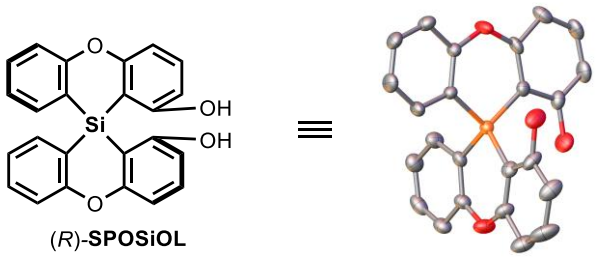
A 12 mL tube was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 5.0 mol%), (*R,R,R*)-**6c** (6.5 mg, 0.01 mmol, 10

mol%), NaO^{t}Bu (19.2 mg, 0.2 mmol, 2.0 equiv.) and toluene (0.5 mL) in the glovebox, followed by the injection of **12** (18.5 mg, 0.1 mmol, 1.0 equiv.) and *p*-bromoanisole (25 μL, 0.2 mmol, 2.0 equiv.) under N_2 outside of the glovebox. The reaction mixture was then heated to 80 °C for 6 hours. After cooled to room temperature, the mixture was filtered through a short pad of silica gel with EtOAc as eluent. The resulting solution was evaporated, and the residue was purified by preparative thin-layer chromatography to afford **13**[16] (26.9 mg, 92%, 83% ee). Determined by HPLC analysis: Chiralcel IA column (25 cm); hexane/2-propanol = 99/1; flow rate, 1.0 mL/min; 30 °C, 229 nm; t_R (major) = 8.37 min; t_R (minor) = 10.44 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19–7.03 (m, 2H), 6.83 (d, J = 7.9 Hz, 2H), 4.04–3.85 (m, 1H), 3.79 (s, 3H), 3.43–3.21 (m, 2H), 3.13–2.92 (m, 1H), 2.61–2.42 (m, 1H), 1.83–1.64 (m, 4H), 1.51 (s, 6H).

3. X-Ray Structures

3.1 X-Ray Structure of (*R*)-SPOSiOL (CCDC 2112131)

Single crystals of (*R*)-**SPOSiOL** were obtained by recrystallization from PE/Et_2O. The molecular structure and X-ray diffractional data/refinement of *R*-SPOSiOL were shown below.



(*R*)-**SPOSiOL**

Bond precision: C-C = 0.0150 Å Wavelength=0.71073

Cell: a=9.1800(5) b=27.5745(18) c=9.1884(6)

alpha=90 beta=111.569(2) gamma=90

Temperature: 293 K

	Calculated	Reported
Volume	2163.0(2)	2163.0(2)
Space group	P 21	P 21
Hall group	P 2yb	P 2yb
Moiety formula	C24 H16 O4 Si, 2(H_2O)	?
Sum formula	C24 H20 O6 Si	C24 H20 O6 Si
Mr	432.49	432.49
Dx,g cm^{-3}	1.328	1.328
Z	4	4
Mu (mm-1)	0.147	0.147
F000	904.0	904.0
F000'	904.79	
h,k,lmax	11,33,11	11,33,11
Nref	8051[4116]	8019
Tmin,Tmax	0.981,0.988	0.645,0.746
Tmin'	0.980	

Correction method= # Reported T Limits: Tmin=0.645 Tmax=0.746 AbsCorr = MULTI-SCAN

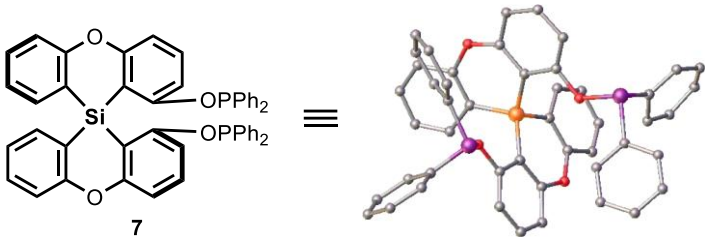
Data completeness= 1.95/1.00 Theta(max)= 25.497

R(reflections)= 0.0502(6455) wR2(reflections)= 0.1259(8019)

S = 1.086 Npar= 559

3.2 X-Ray Structure of **7** (CCDC 2112132)

Single crystals of **7** were obtained by recrystallization from PE/THF. The molecular structure and X-ray diffractional data/refinement of **7** were shown below.



7

Bond precision: C-C = 0.0141 Å Wavelength=0.71073

Cell: a=9.4128(3) b=9.5763(4) c=26.1896(10)

alpha=92.004(1) beta=96.554(1) gamma=115.774(1)

Temperature: 293 K

	Calculated	Reported
Volume	2102.51(14)	2102.51(14)
Space group	P 1	P 1
Hall group	P 1	P 1
Moiety formula	C48 H34 O4 P2 Si [+ solvent]	?
Sum formula	C48 H34 O4 P2 Si [+ solvent]	C48 H34 O4 P2 Si
Mr	764.78	764.78
Dx,g cm-3	1.208	1.208
Z	2	2
Mu (mm-1)	0.174	0.174
F000	796.0	796.0
F000'	796.88	
h,k,lmax	11,11,32	11,11,32
Nref	16532[8266]	16270
Tmin,Tmax	0.973,0.986	0.578,0.746
Tmin'	0.967	

Correction method= # Reported T Limits: Tmin=0.578 Tmax=0.746 AbsCorr = MULTI-SCAN

Data completeness= 1.97/0.98 Theta(max)= 25.999

R(reflections)= 0.0672(11254) wR2(reflections)= 0.1965(16270)

S = 1.031 Npar= 980

4. References

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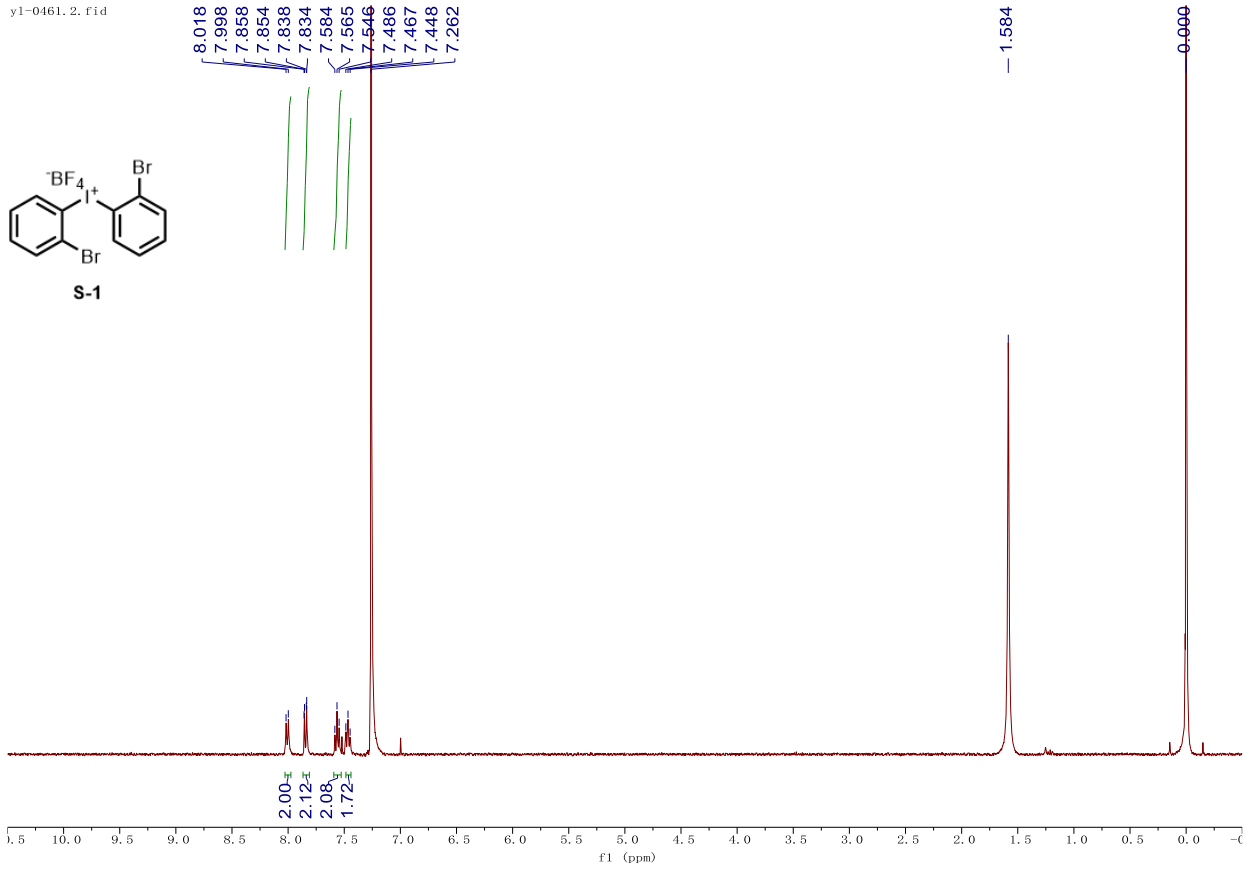
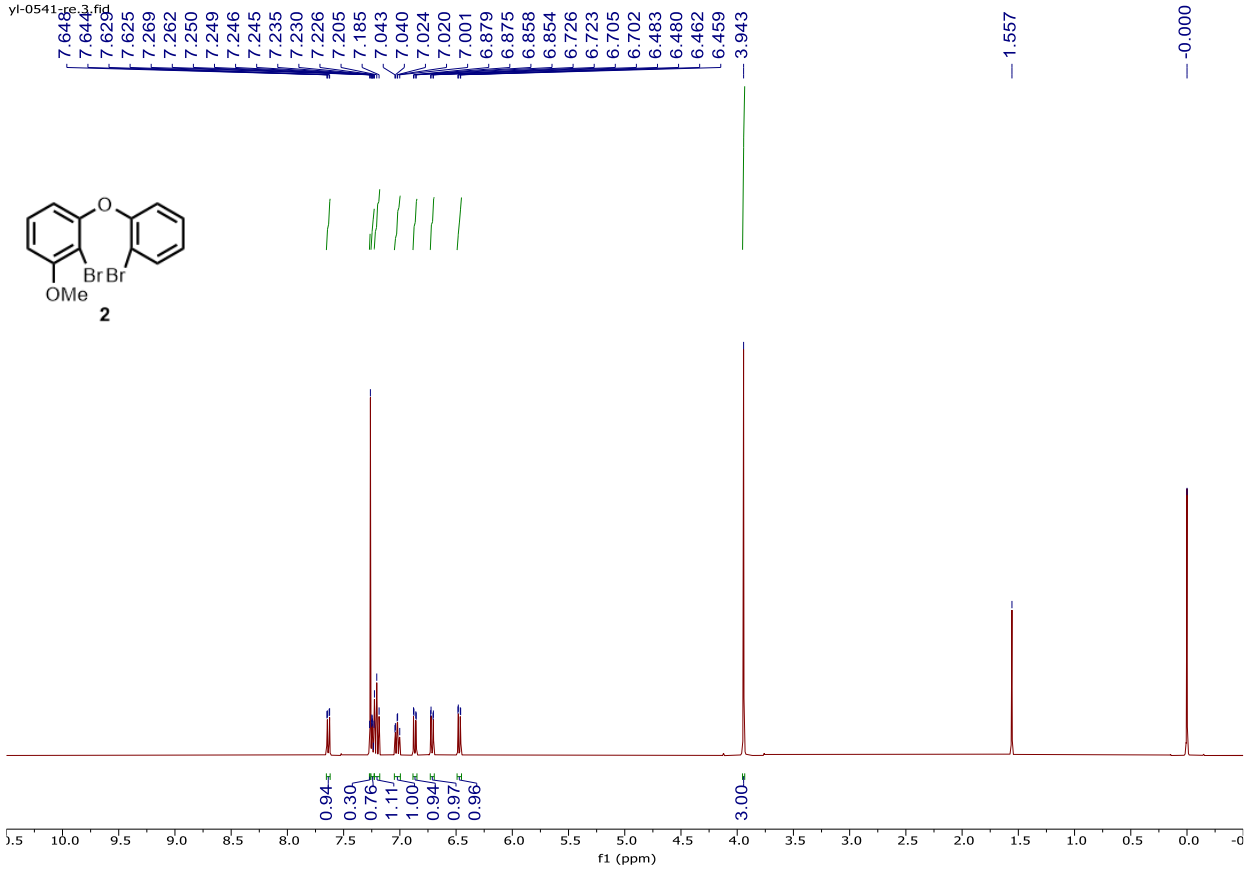
5. NMR Spectra

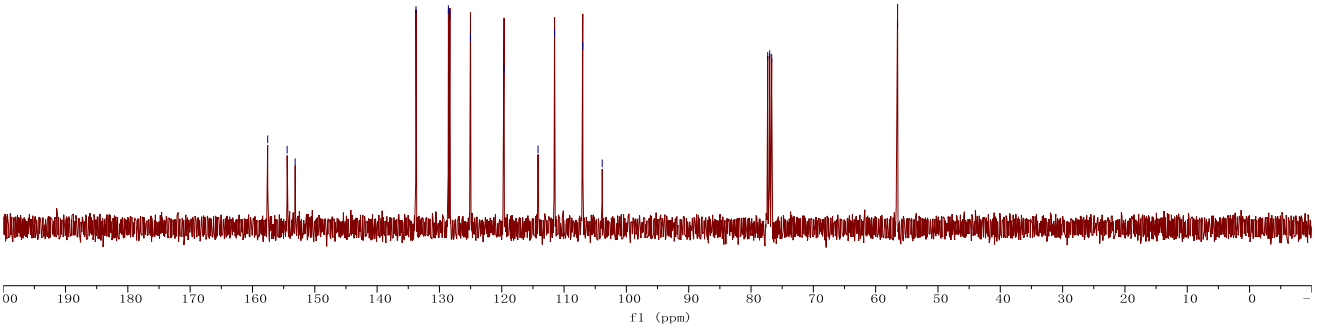




yl-OMe-Br.4.fid

157.56
154.44
153.15
133.76
128.56
128.32
125.02
119.64
114.18
111.53
107.00
103.88
77.32
77.00
76.69
56.49

2



yl20201012_2.fid

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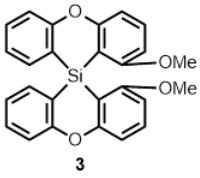
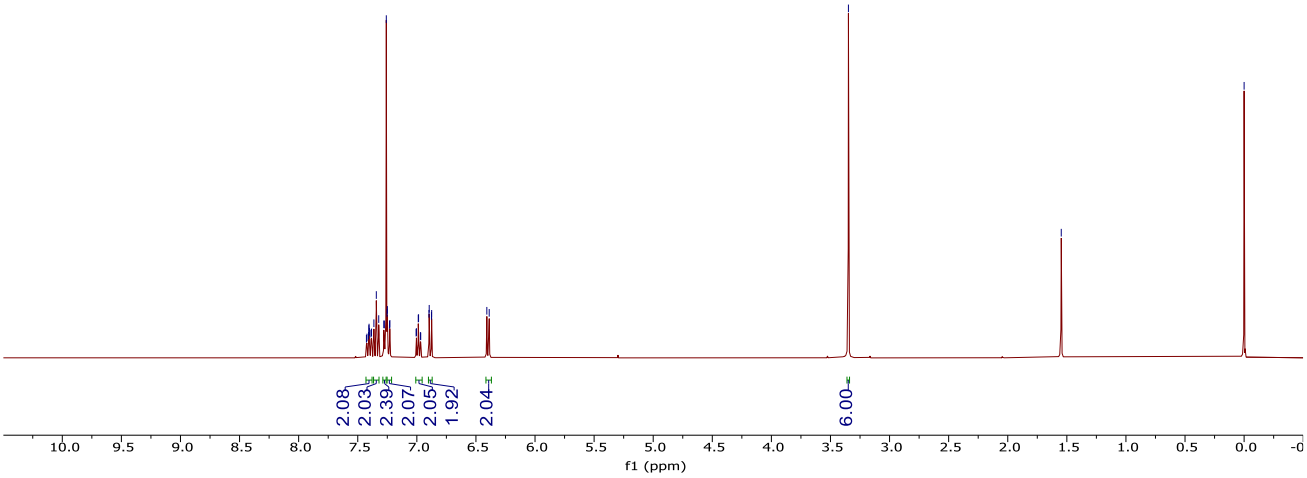
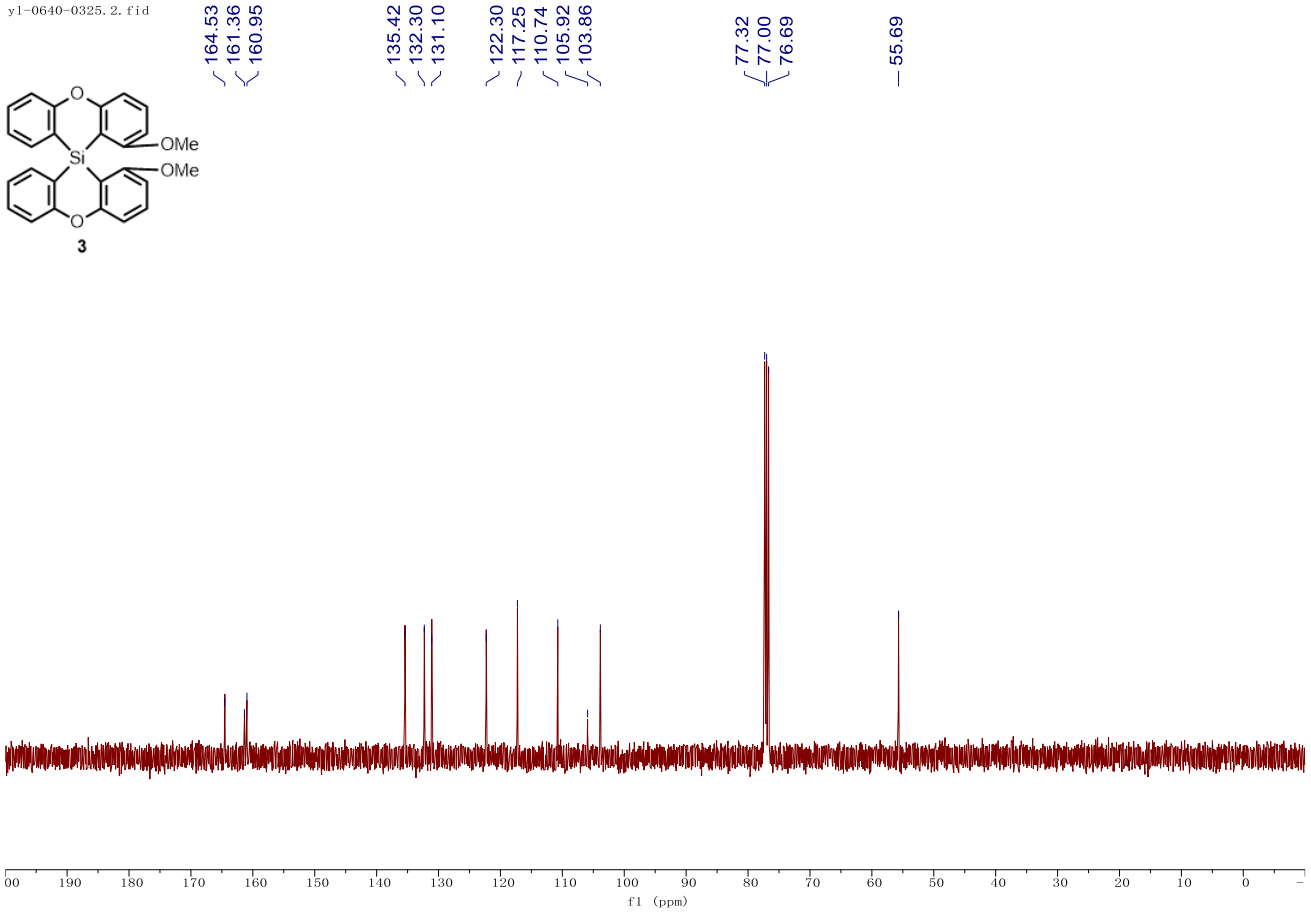
7.404
7.401
7.363
7.343
7.322
7.280
7.275
7.258
7.252
7.249
7.231
7.228
7.003
6.988
6.985
6.897
6.895
6.876
6.874
6.408
6.388
3.348
1.547
-0.000



3

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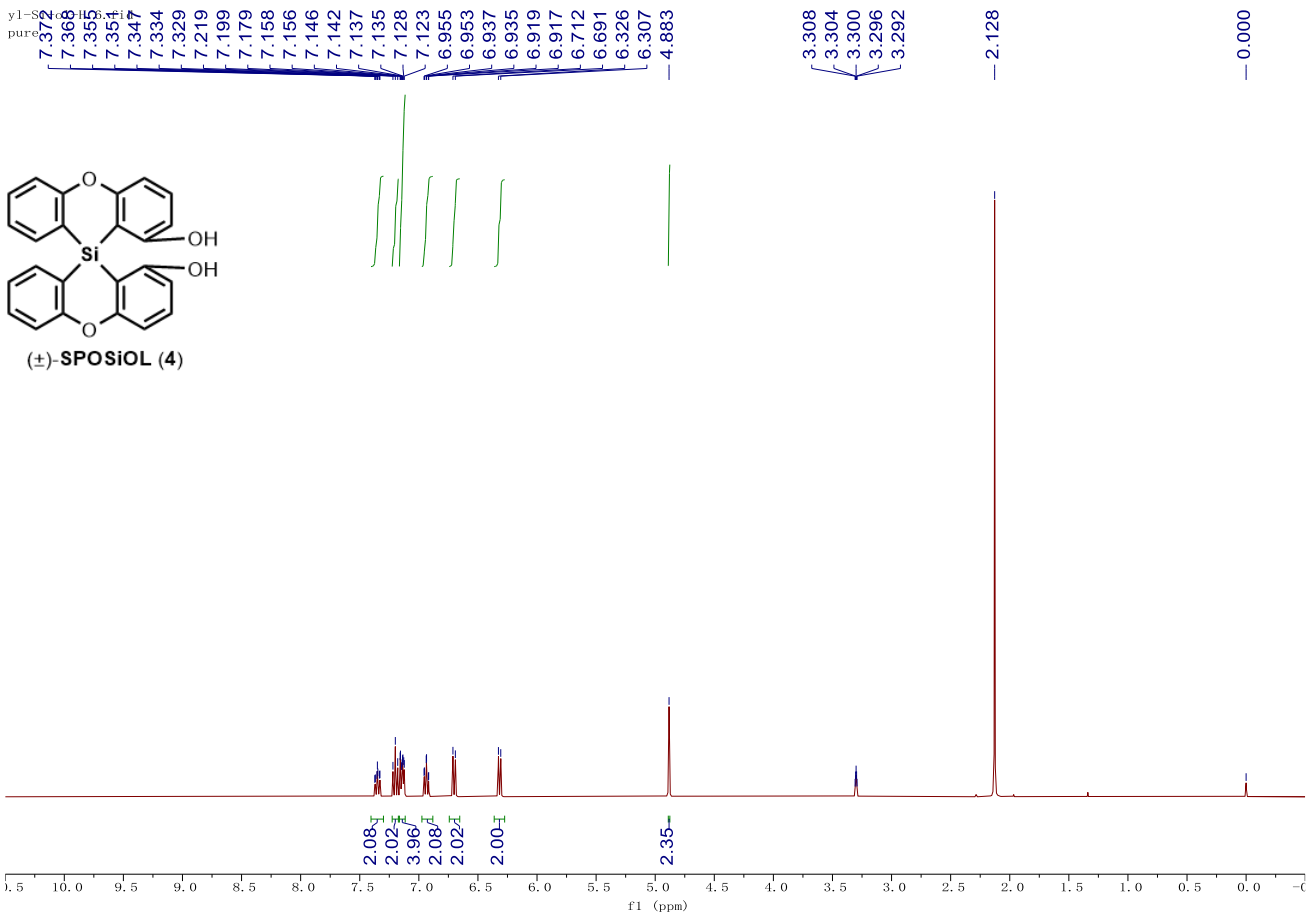
161.36
160.95
135.42
132.30
131.10
122.30
117.25
110.74
105.92
103.86
77.32
77.00
76.69
55.69
OMe
OMe
Si
O
O
3
f1 (ppm)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7.355
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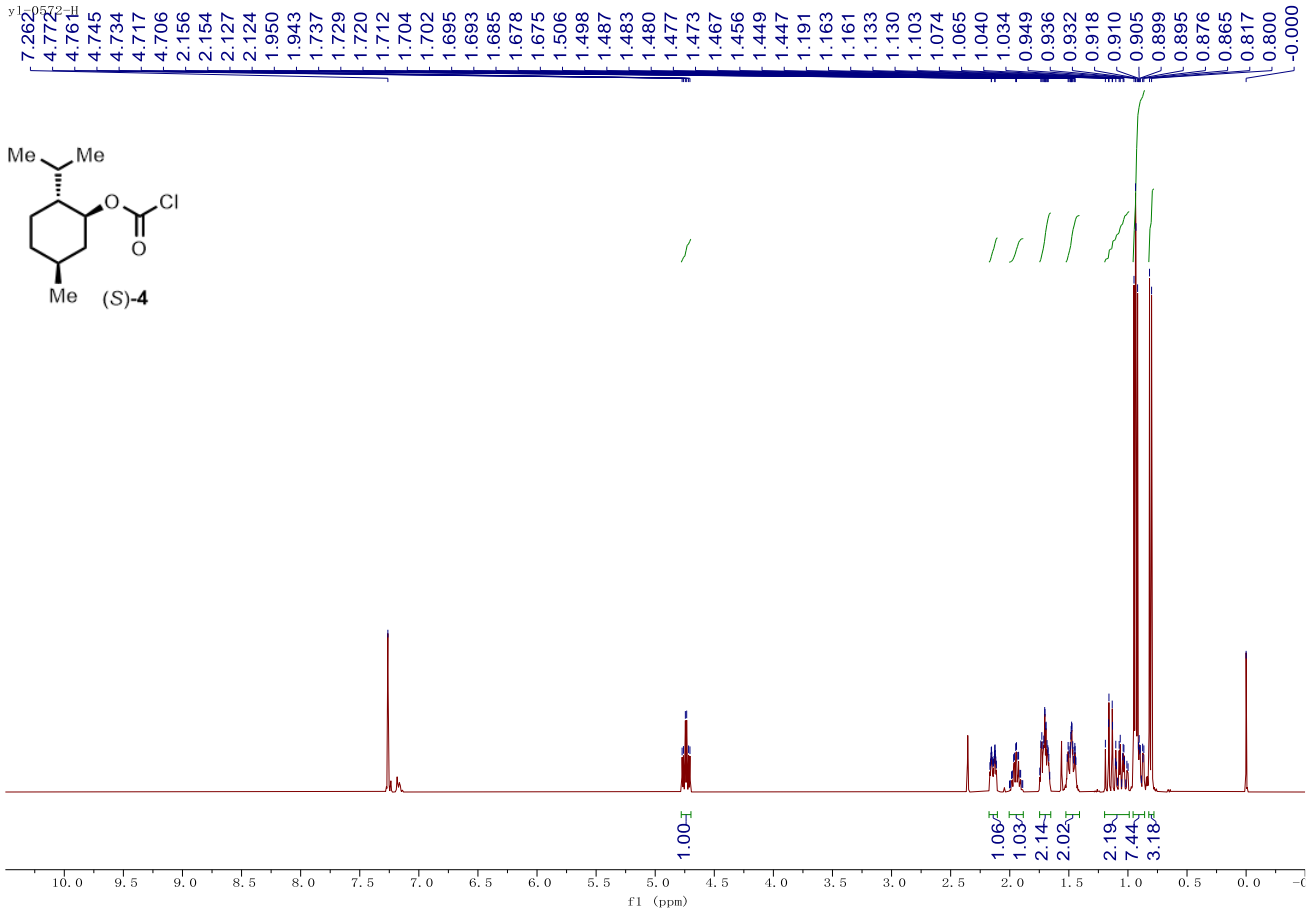
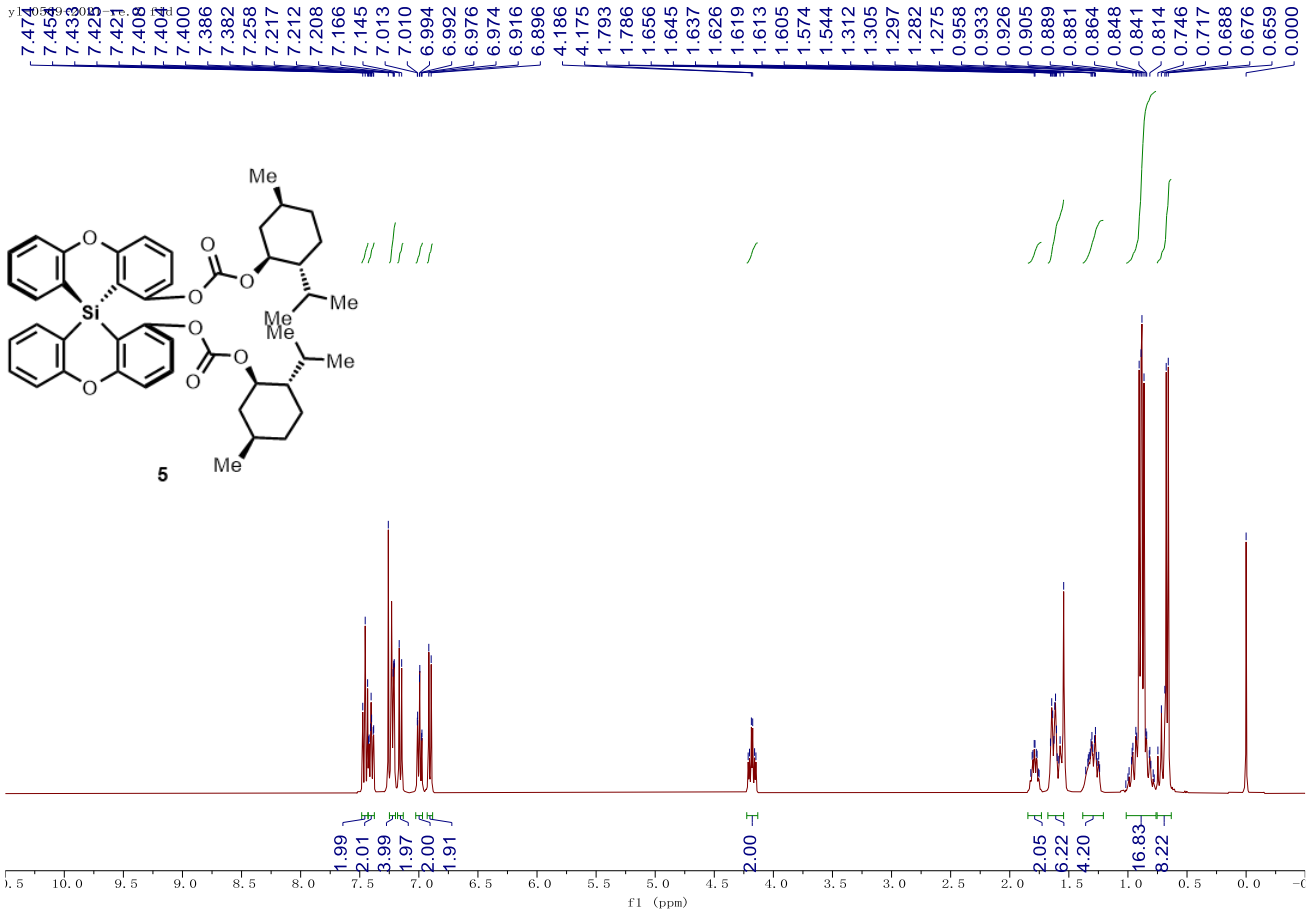
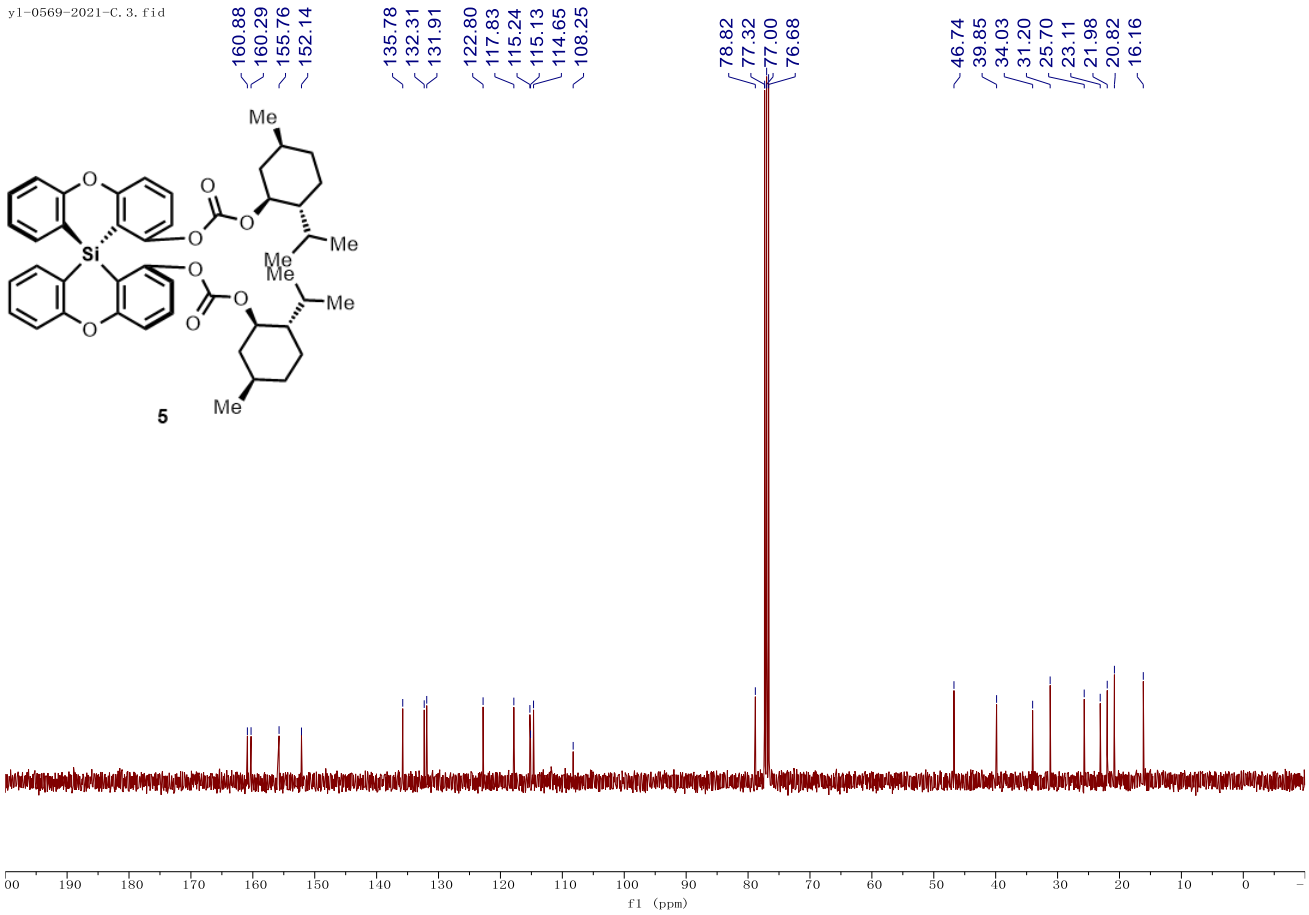
7.347
7.334
7.329
7.219
7.199
7.179
7.158
7.156
7.146
7.142
7.137
7.135
7.128
7.123
6.955
6.953
6.937
6.935
6.919
6.917
6.712
6.691
6.326
6.307
4.883
3.308
3.304
3.300
3.296
3.292
2.128
0.000
OH
OH
Si
O
O
(±)-SPOSiOL (4)
2.08
2.02
3.96
2.08
2.02
2.00
2.35
f1 (ppm)


Me
Me
O
Cl
O
Me
(S)-4
f1 (ppm)


Si
Me
Me
Me
Me
Me
Me
5
f1 (ppm)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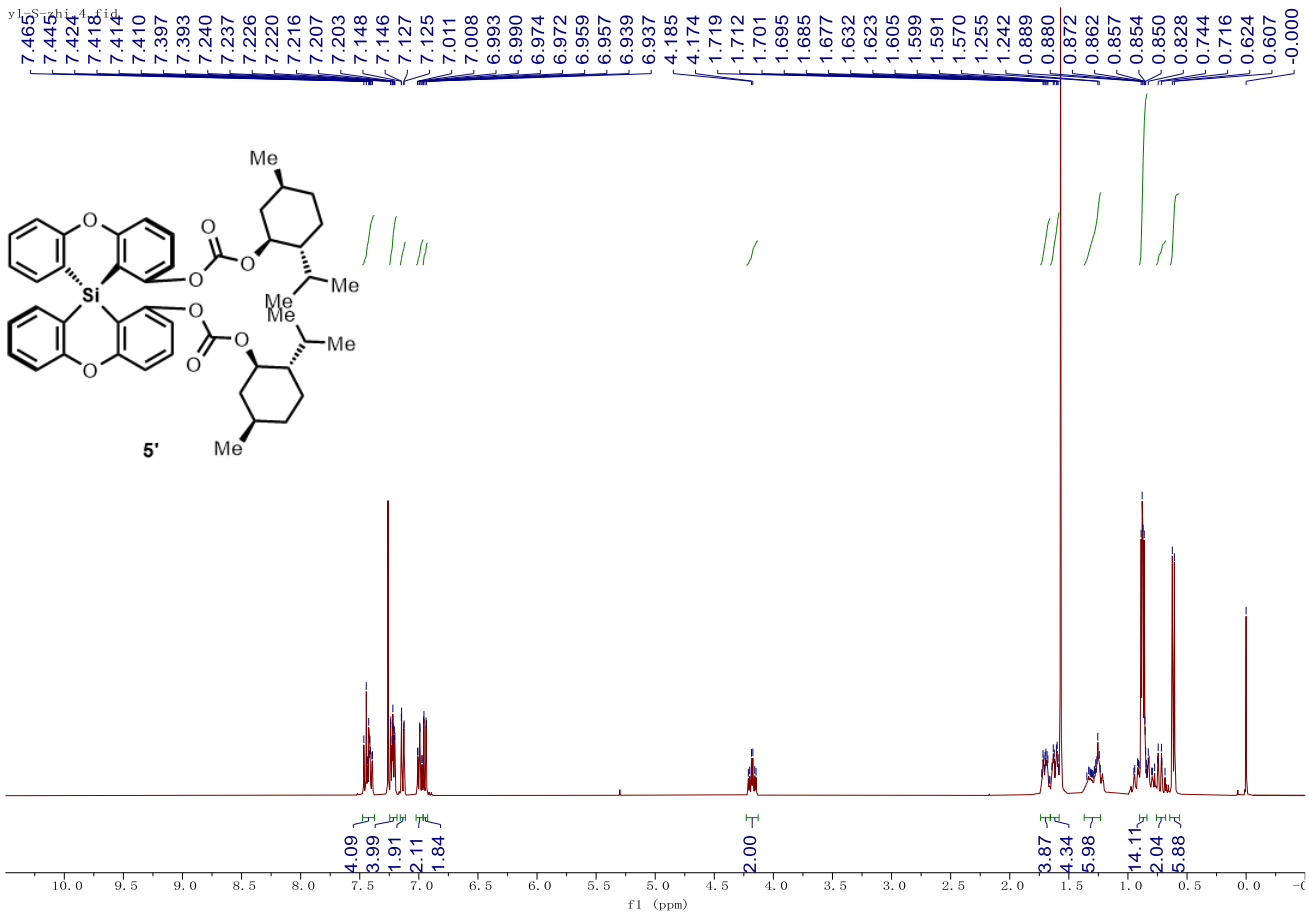
160.29
155.76
152.14
135.78
132.31
131.91
122.80
117.83
115.24
115.13
114.65
108.25
78.82
77.32
77.00
76.68
46.74
39.85
34.03
31.20
25.70
23.11
21.98
20.82
16.16
Me
O
Si
Me
Me
Me
Me
5
f1 (ppm)


yls-zhi-4.fid
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7.445
7.424
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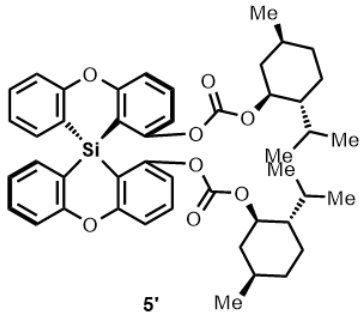
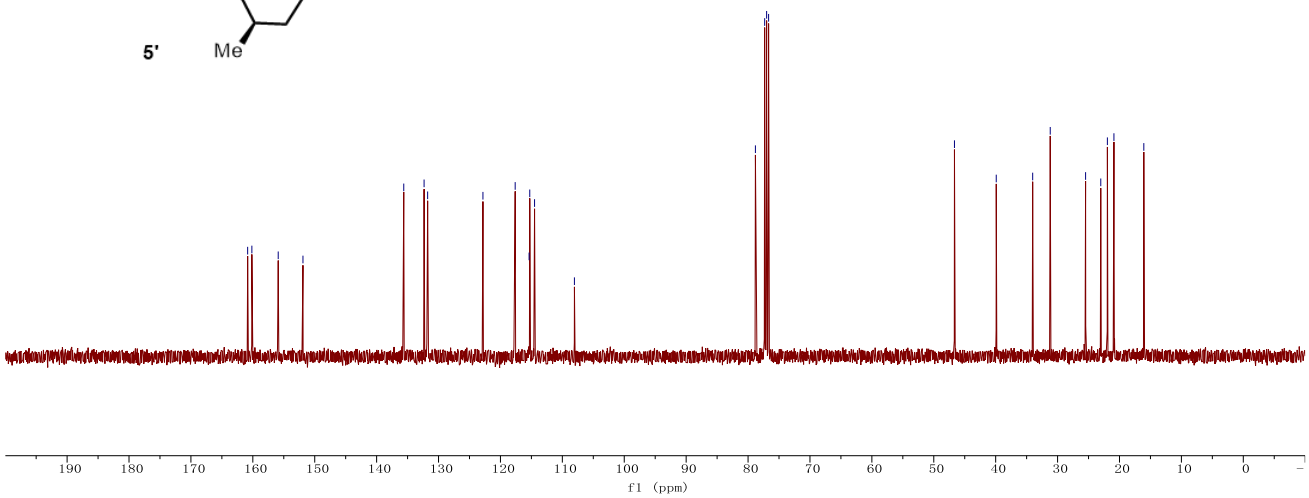
7.414
7.410
7.397
7.393
7.240
7.237
7.226
7.220
7.216
7.207
7.203
7.148
7.146
7.127
7.125
7.011
7.008
6.993
6.990
6.974
6.972
6.959
6.957
6.939
6.937
4.185
4.174
1.719
1.712
1.701
1.695
1.685
1.677
1.632
1.623
1.605
1.599
1.591
1.570
1.255
1.242
0.889
0.880
0.872
0.862
0.857
0.854
0.850
0.828
0.744
0.716
0.624
0.607
-0.000
Me
O
Si
Me
Me
Me
Me
5'
4.09
3.99
1.91
2.11
1.84
2.00
3.87
4.34
5.98
14.11
2.04
5.88
f1 (ppm)

wdm-20210916-L-S-H.3.fid

160.84
160.15
155.90
151.90
135.62
132.33
131.76
122.83
117.62
115.37
115.26
114.49
108.05
78.81
77.32
77.00
76.68
46.66
39.91
34.02
31.19
25.48
23.02
21.96
20.90
16.07



5'



y1-0994H.4.fid

7.574
7.553
7.534
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7.495
7.475
7.348
7.327
7.305
7.282
7.261
7.251
7.240
7.218
7.214
7.204
7.195
7.190
7.183
7.170
7.165
7.118
7.113
7.099
7.095
7.023
7.009
7.002
6.991
6.973
6.955
6.759
6.739
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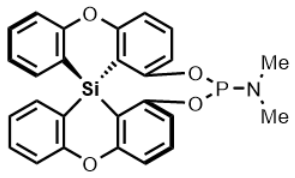
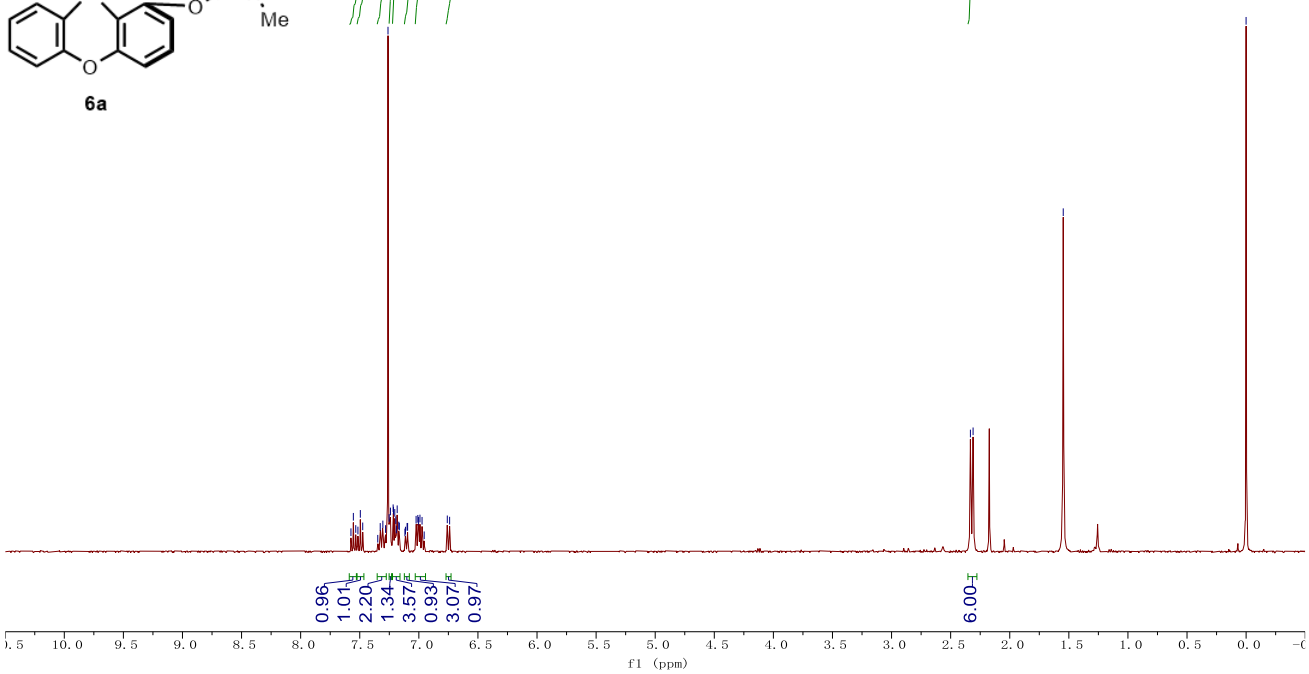
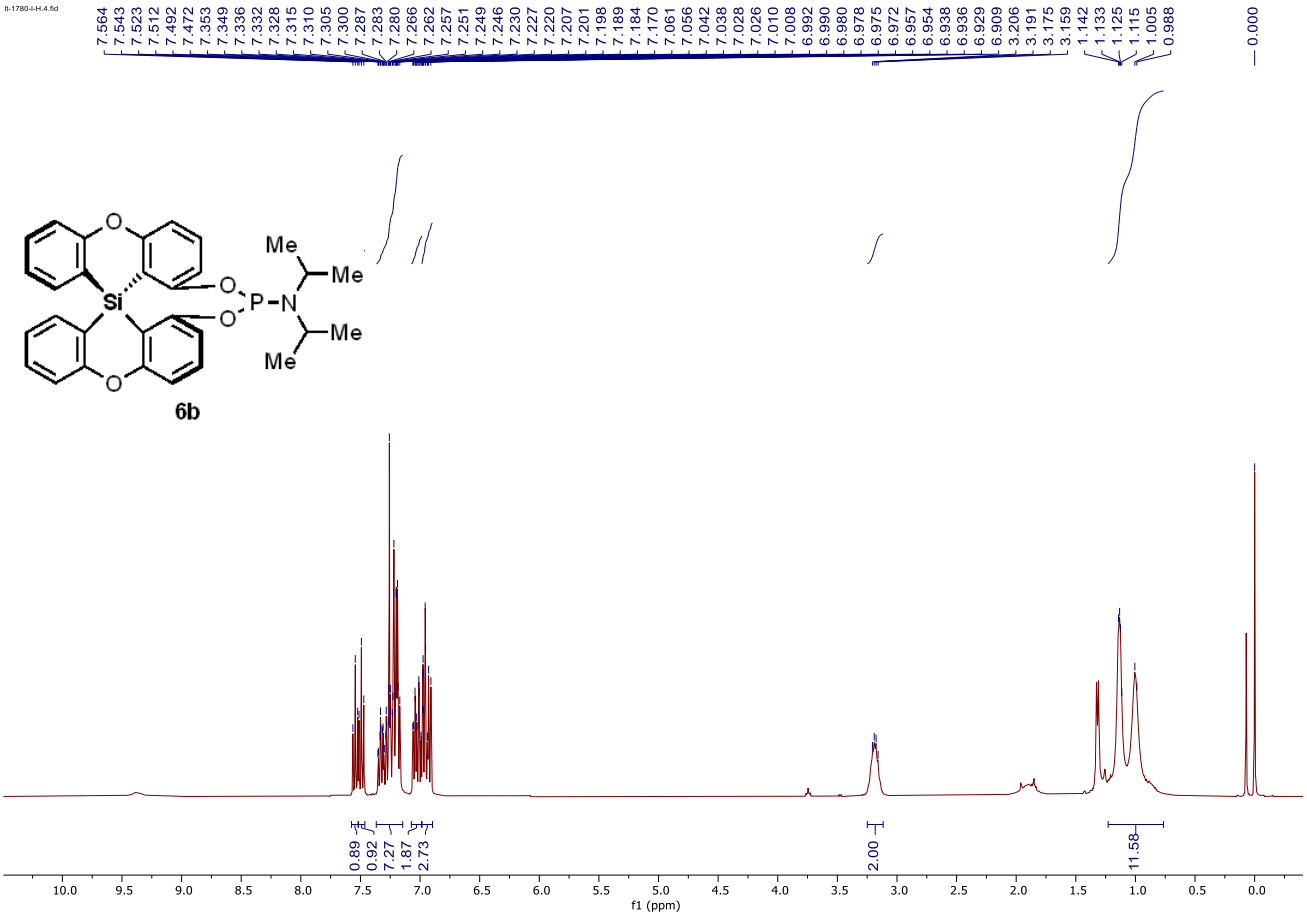
2.310
1.547
0.000



6a

0.96
1.01
2.20
1.34
3.57
0.93
3.07
0.97
6.00

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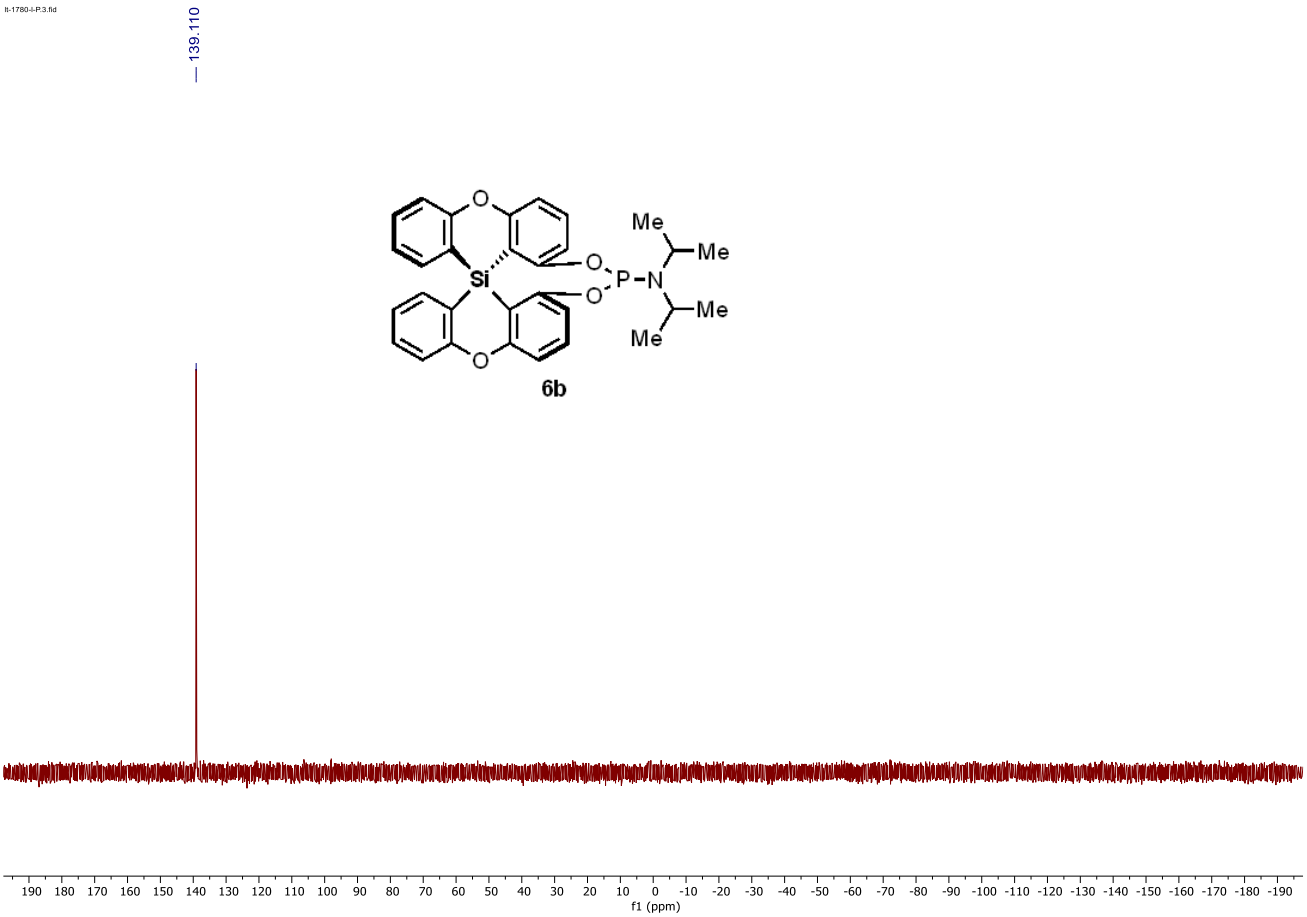
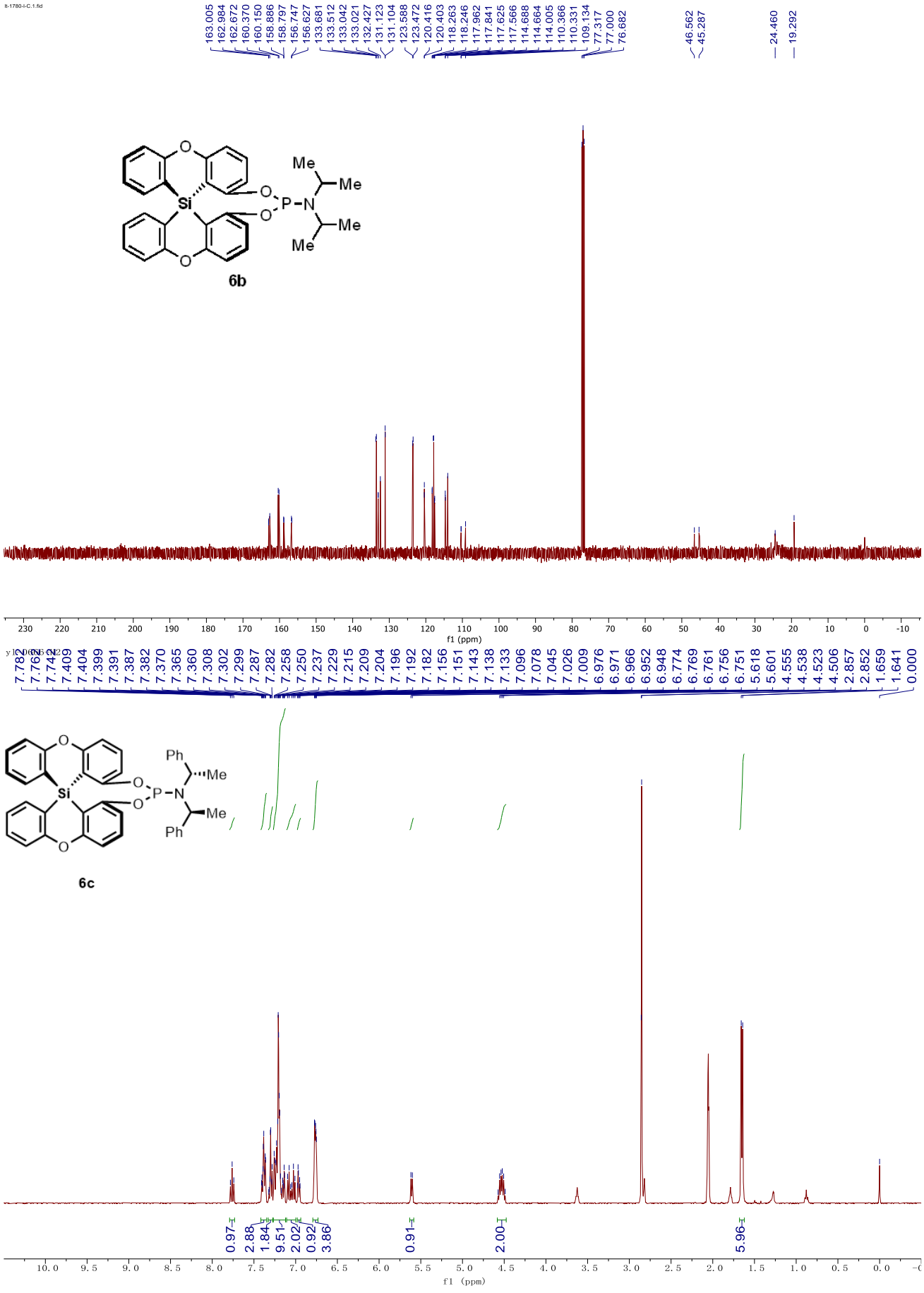
7.523
7.512
7.492
7.472
7.353
7.349
7.336
7.332
7.328
7.315
7.310
7.305
7.300
7.287
7.283
7.280
7.266
7.262
7.257
7.251
7.249
7.246
7.230
7.227
7.220
7.207
7.201
7.198
7.189
7.184
7.170
7.061
7.056
7.042
7.038
7.028
7.026
7.010
7.008
6.992
6.990
6.980
6.978
6.975
6.972
6.957
6.954
6.938
6.936
6.929
6.909
3.206
3.191
3.175
3.159
1.142
1.133
1.125
1.115
1.005
0.988
0.000
Me
Me
Me
Me
O
Si
O
P
N
O
O
6b
0.89
0.92
7.27
1.87
2.73
2.00
11.58
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


lt-1780-i-P.3.fid
139.110
Me
Me
Me
Me
O
Si
O
P
N
O
O
6b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)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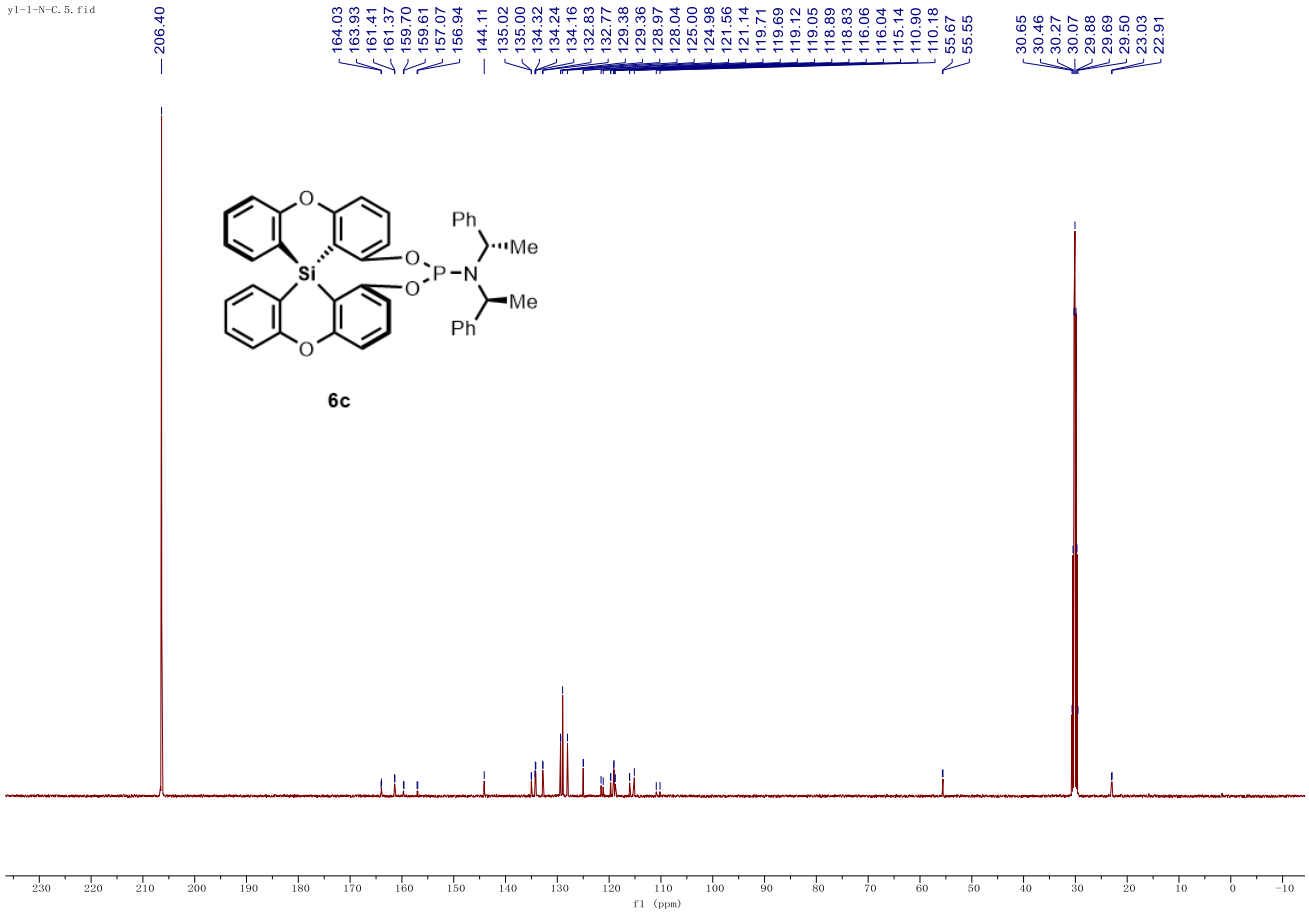
158.797
156.747
156.627
133.681
133.512
133.042
133.021
132.427
131.123
131.104
123.588
123.472
120.416
120.403
118.263
118.246
117.962
117.841
117.625
117.566
114.688
114.664
114.005
110.366
110.331
109.134
77.317
77.000
76.682
46.562
45.287
24.460
19.292
Me
Me
Me
Me
O
Si
O
P
N
6b
f1 (ppm)
7.782
7.767
7.744
7.409
7.404
7.399
7.391
7.387
7.382
7.370
7.365
7.360
7.308
7.302
7.299
7.287
7.282
7.258
7.250
7.237
7.229
7.215
7.209
7.204
7.196
7.192
7.182
7.156
7.151
7.143
7.138
7.133
7.096
7.078
7.045
7.026
7.009
6.976
6.971
6.966
6.952
6.948
6.774
6.769
6.761
6.756
6.751
5.618
5.601
4.555
4.538
4.523
4.506
2.857
2.852
1.659
1.641
0.000
Ph
Me
Me
Ph
6c
0.97
2.88
1.84
9.51
2.02
0.92
3.86
0.91
2.00
5.96
f1 (ppm)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164.03
163.93
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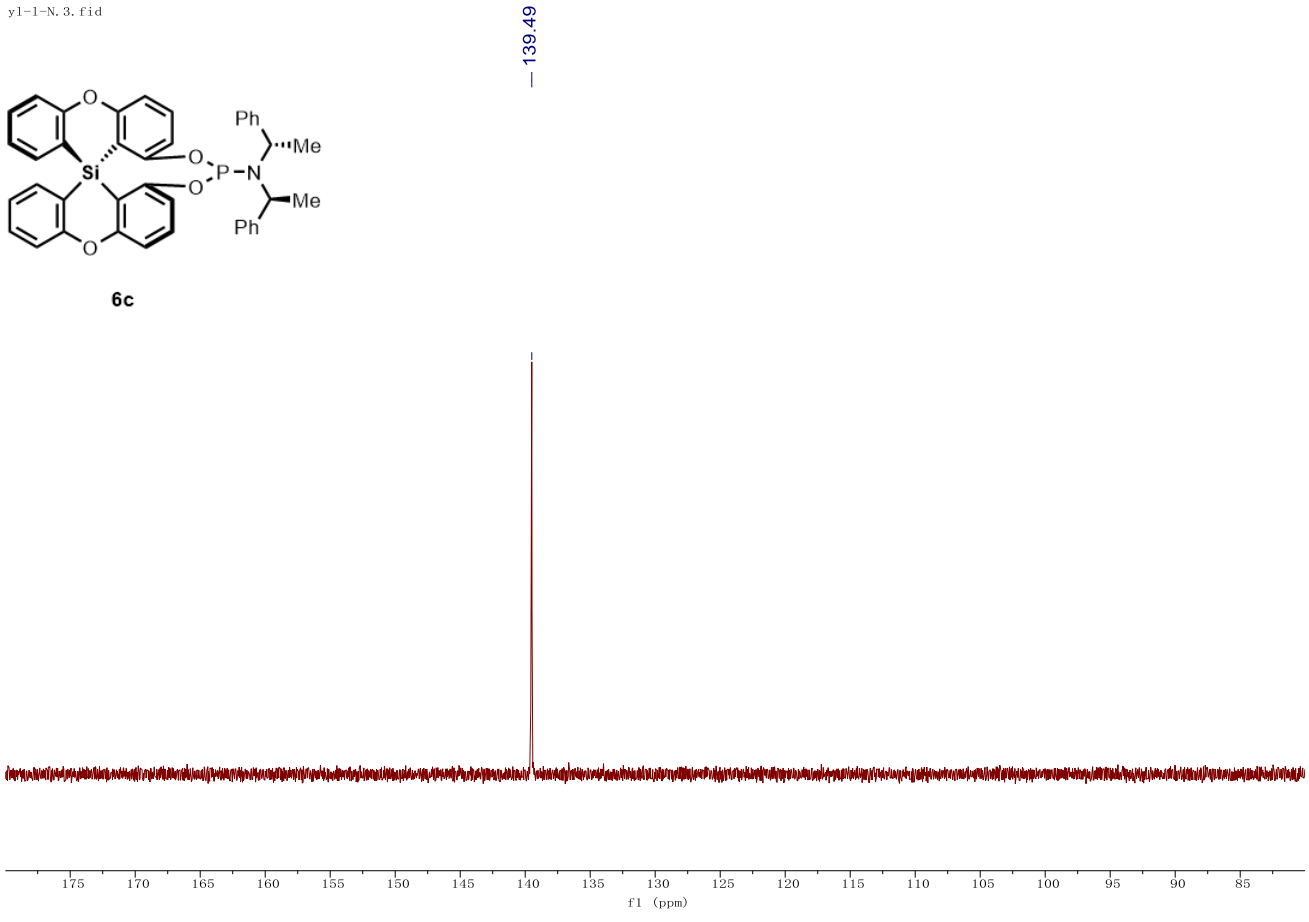
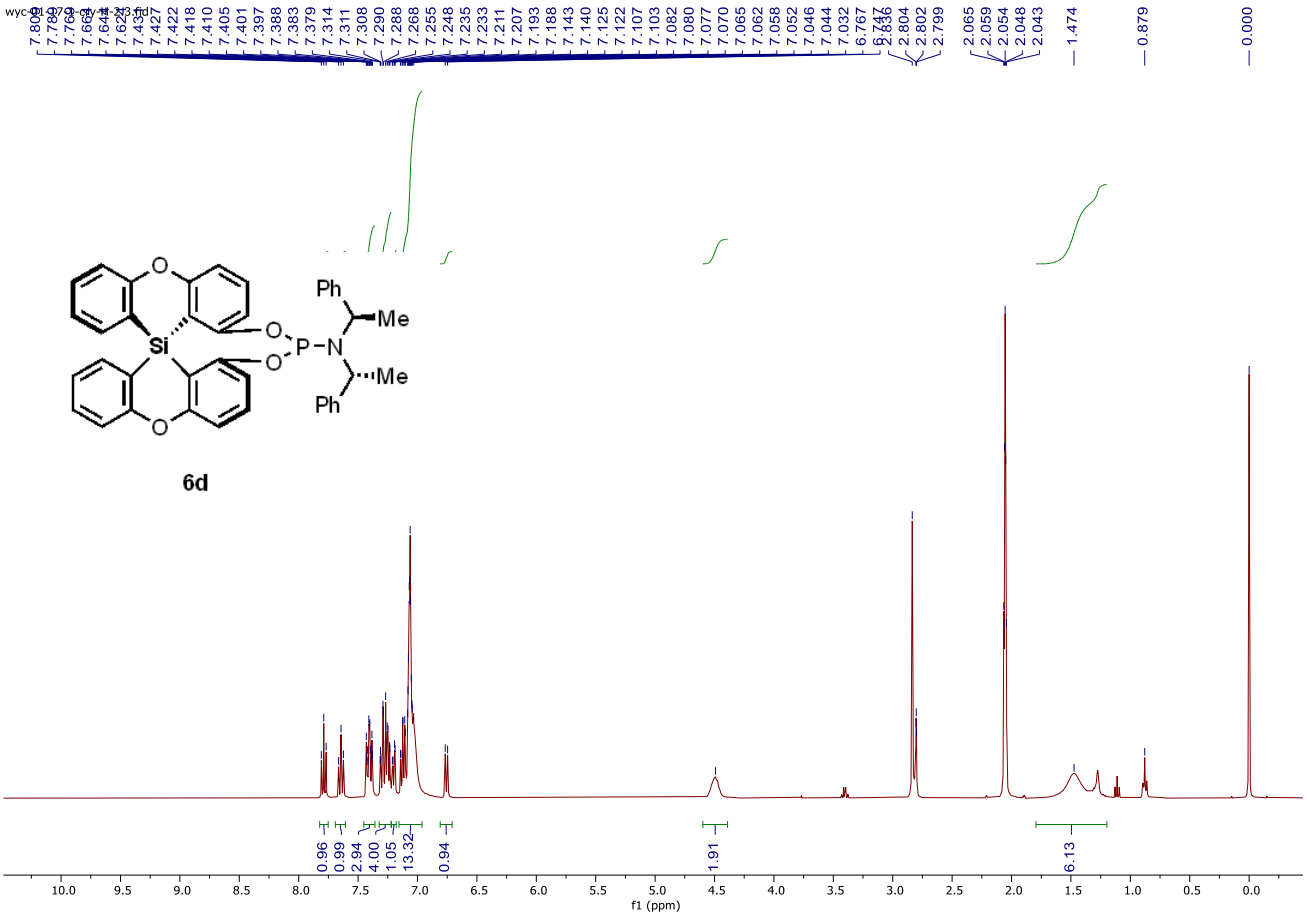
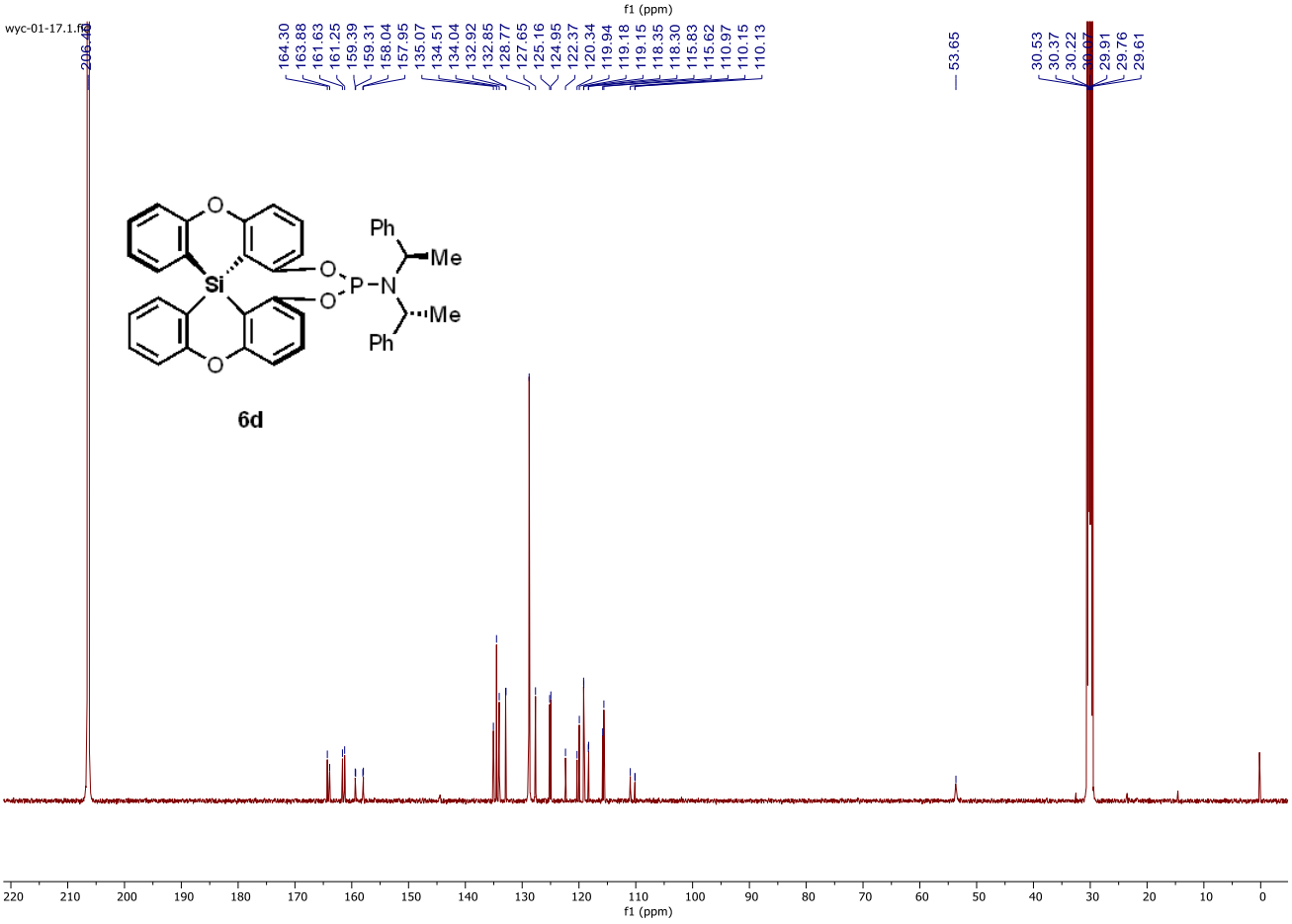
161.37
159.70
159.61
157.07
156.94
144.11
135.02
135.00
134.32
134.24
134.16
132.83
132.77
129.38
129.36
128.97
128.04
125.00
124.98
121.56
121.14
119.71
119.69
119.12
119.05
118.89
118.83
116.06
116.04
115.14
110.90
110.18
55.67
55.55
30.65
30.46
30.27
30.07
29.88
29.69
29.50
23.03
22.91
Ph
Me
Me
Ph
O
Si
O
P
N
O
O
f1 (ppm)

6c


y1-1-N.3.fid
139.49
Ph
Me
Me
Ph
O
Si
O
P
N
O
O
f1 (ppm)

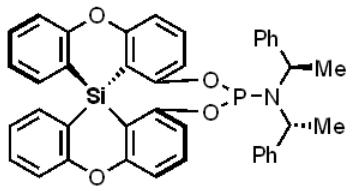
6c


6d
0.96
0.99
2.94
4.00
1.05
13.32
0.94
1.91
6.13
f1 (ppm)

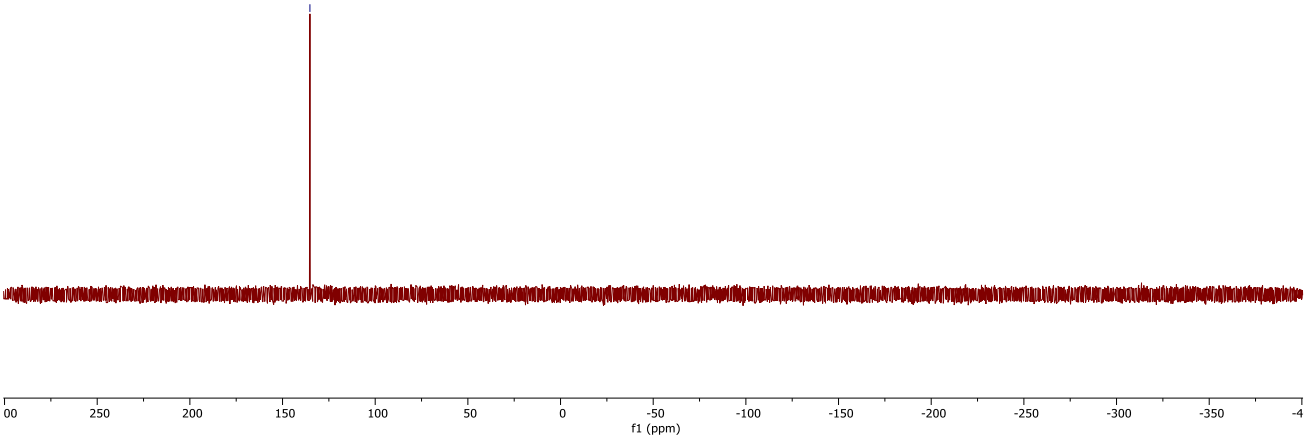

6d
f1 (ppm)

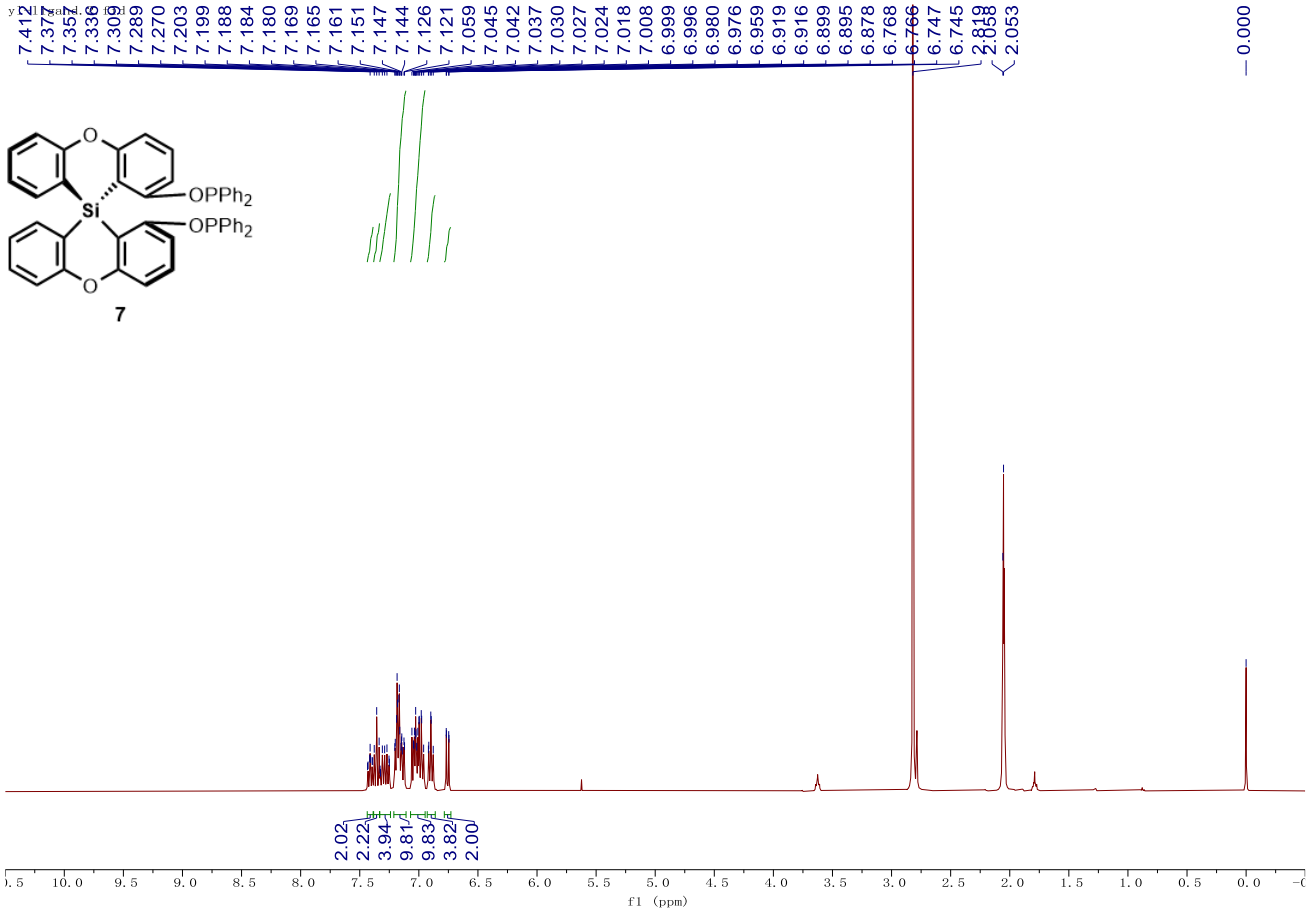
wyc-01-17-1-cry.1.fid

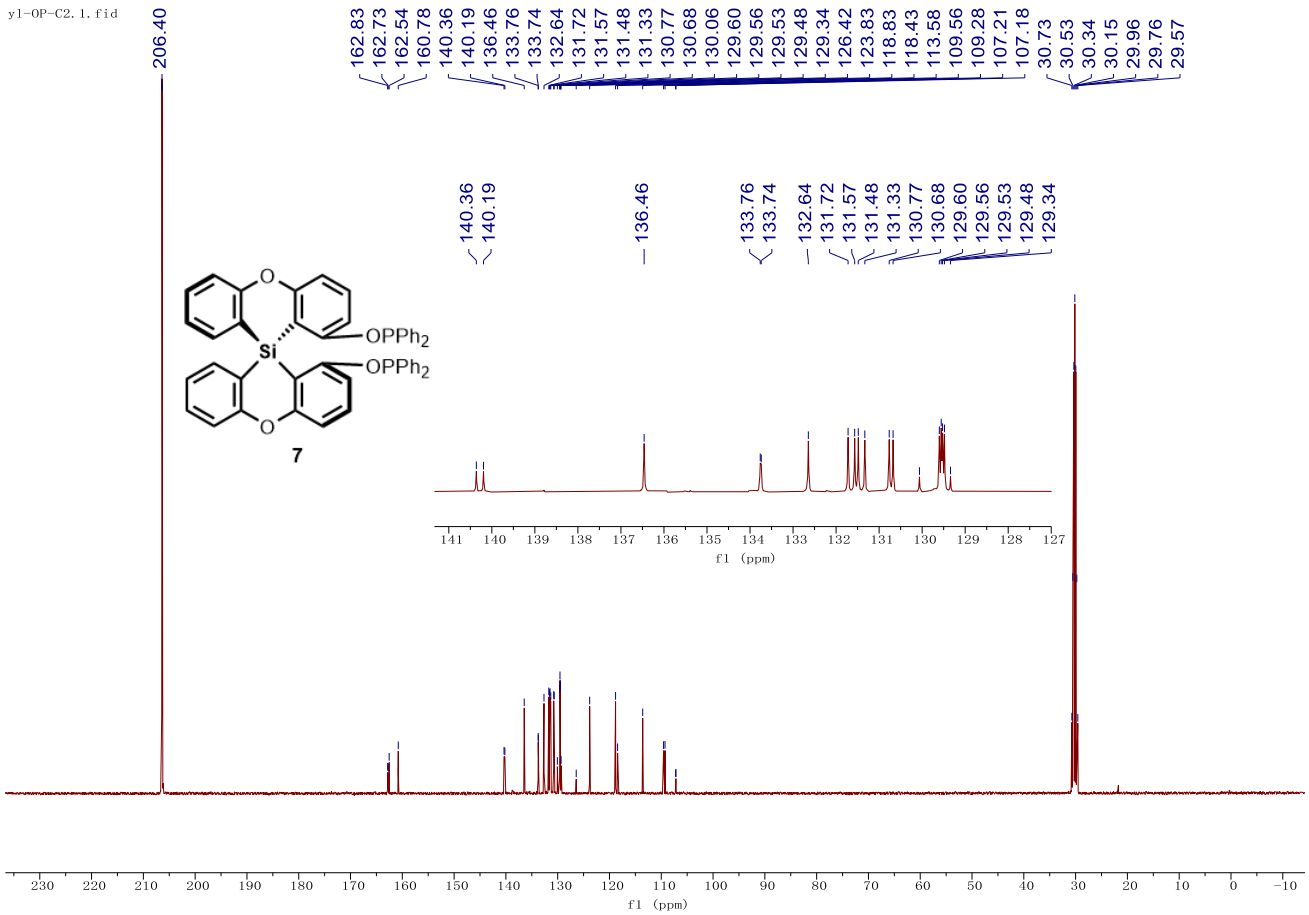
135.231



6d

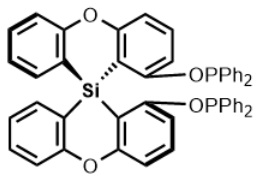



7.412
7.377
7.357
7.336
7.309
7.289
7.270
7.203
7.199
7.188
7.184
7.180
7.169
7.165
7.161
7.151
7.147
7.144
7.126
7.121
7.059
7.045
7.042
7.037
7.030
7.027
7.024
7.018
7.008
6.999
6.996
6.980
6.976
6.959
6.919
6.916
6.899
6.895
6.878
6.768
6.766
6.747
6.745
2.819
2.053
0.000
OPPh2
OPPh2
Si
O
7
2.02
2.22
3.94
9.81
9.83
3.82
2.00
f1 (ppm)

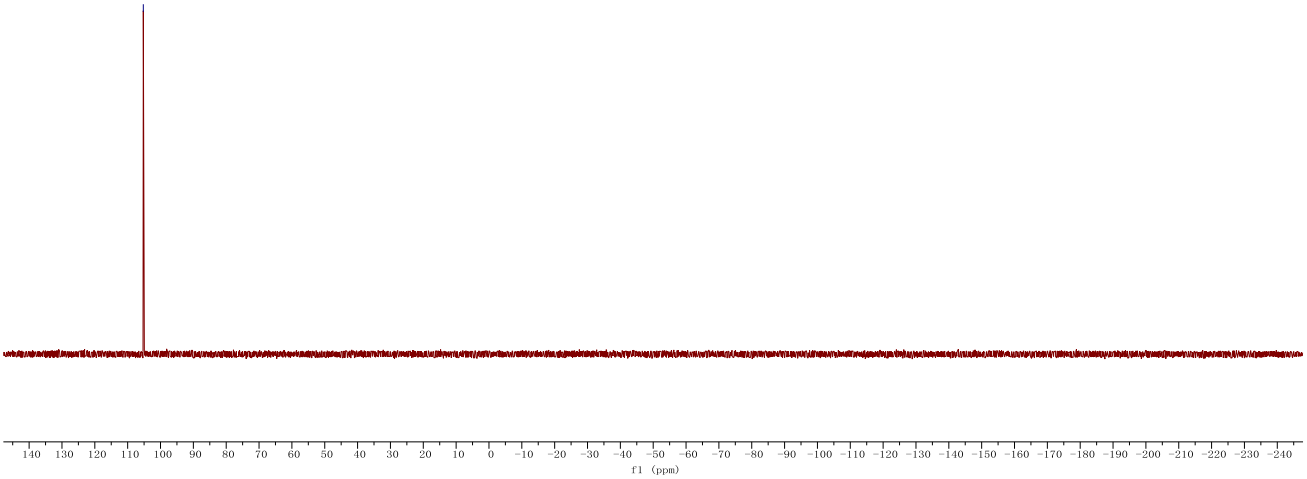

y1-OP-C2.1.fid
206.40
162.83
162.73
162.54
160.78
140.36
140.19
136.46
133.76
133.74
132.64
131.72
131.57
131.48
131.33
130.77
130.68
130.06
129.60
129.56
129.53
129.48
129.34
126.42
123.83
118.83
118.43
113.58
109.56
109.28
107.21
107.18
30.73
30.53
30.34
30.15
29.96
29.76
29.57
OPPh2
OPPh2
Si
O
7
f1 (ppm)
f1 (ppm)

YL-Ligand-2.1.fid

105.24

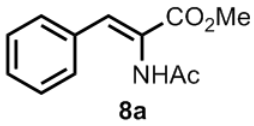


7

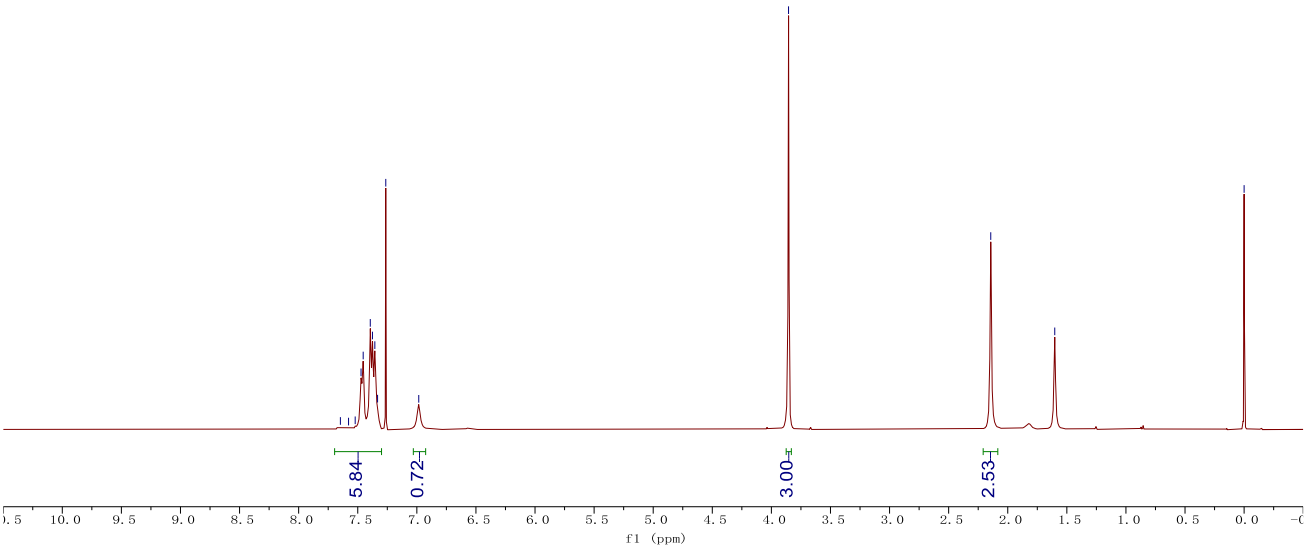


yl-s-1.4.fid

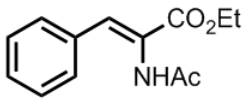
7.647
7.578
7.522
7.472
7.454
7.394
7.375
7.355
7.332
7.263
6.984
3.855
2.144
1.602
0.000



8a

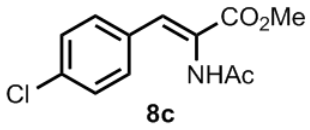


yl-Et-s.1.fid

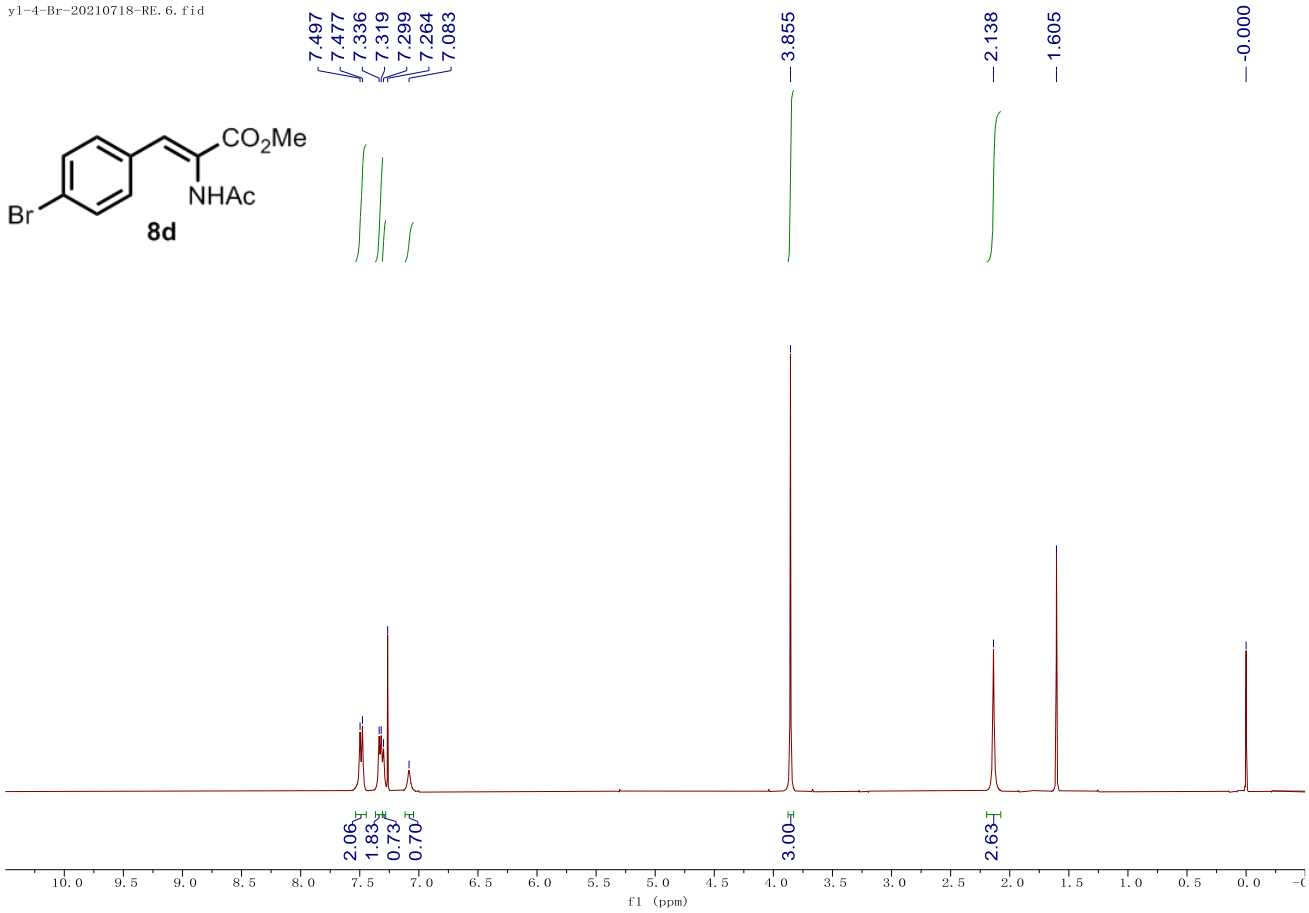


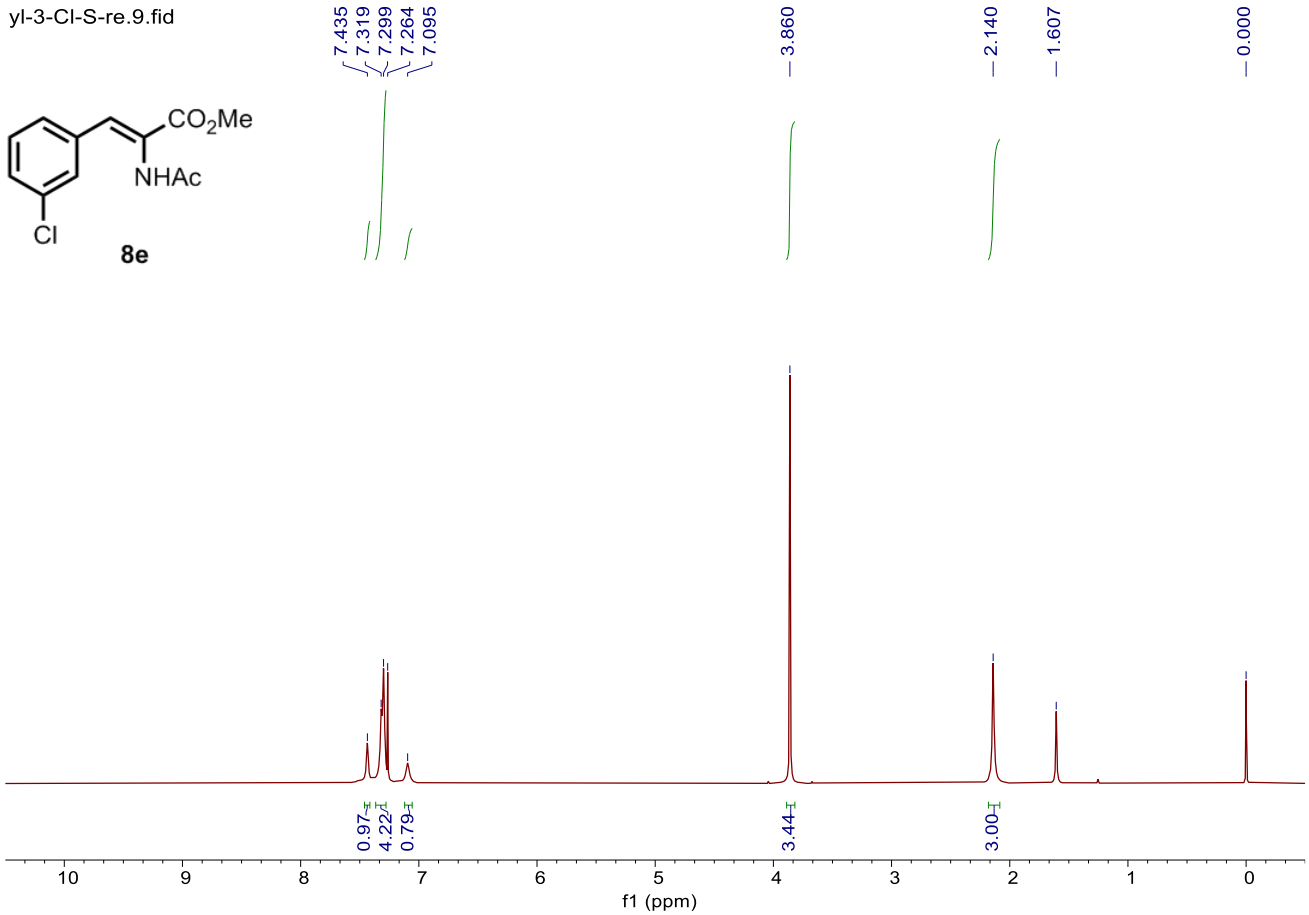
8b

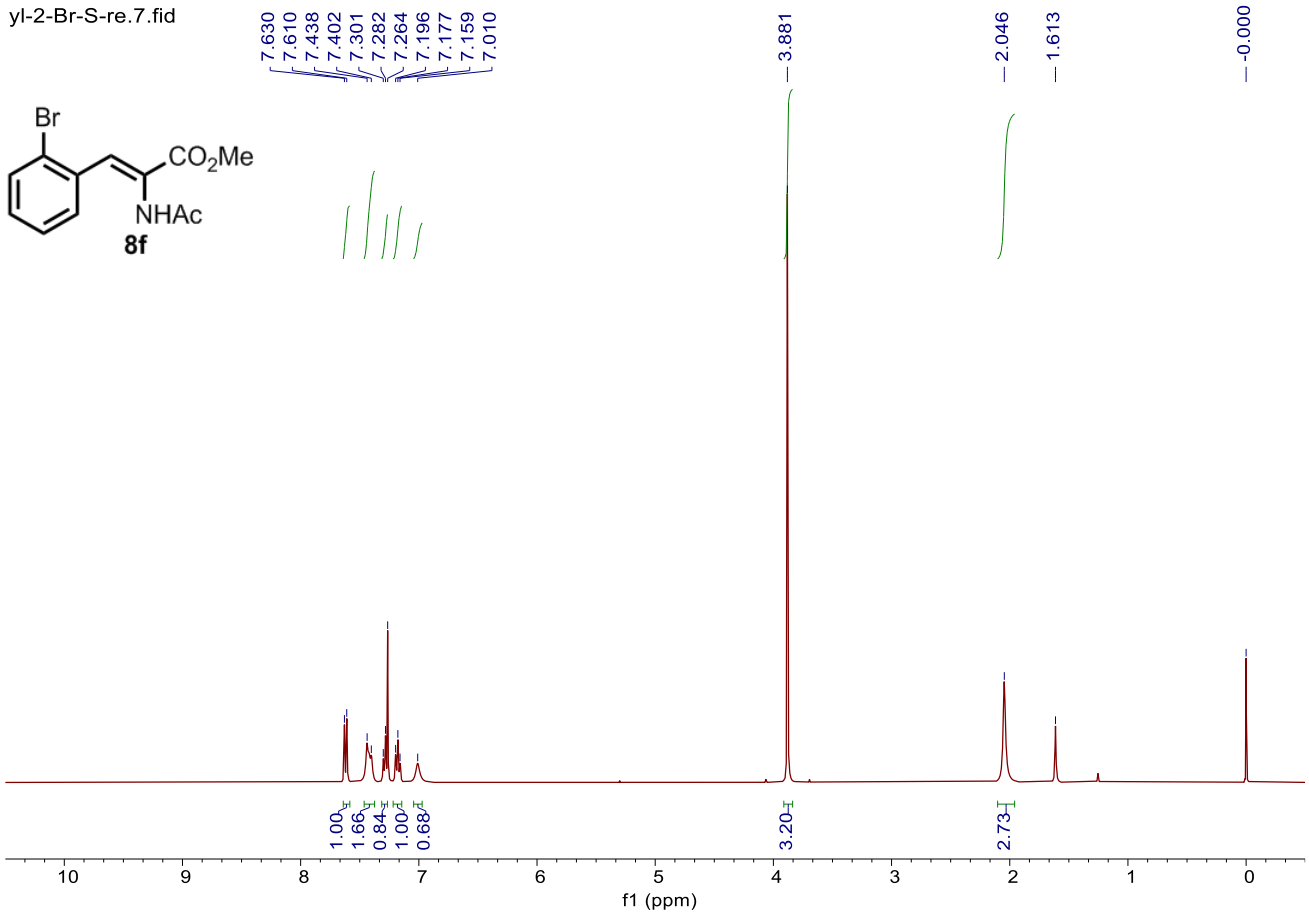
yl-4-Cl-S-re.8.fid

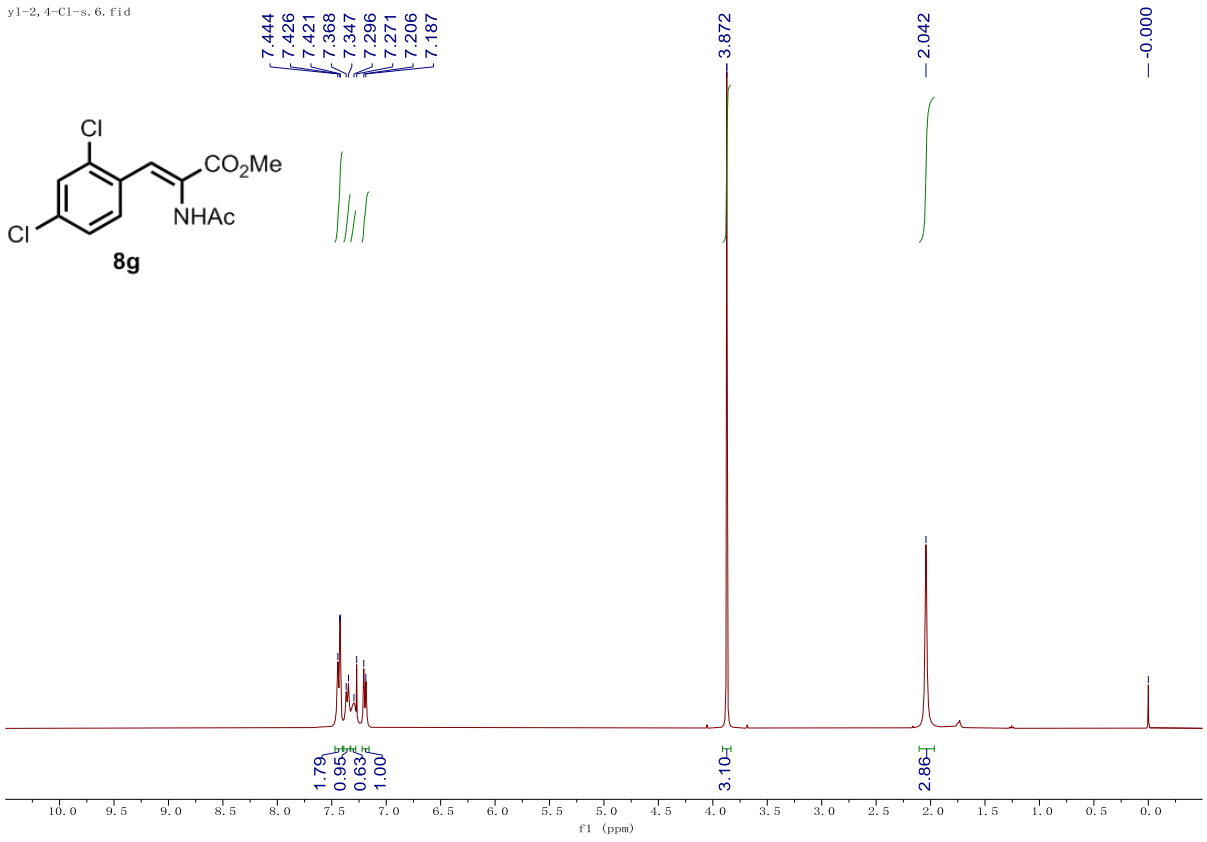


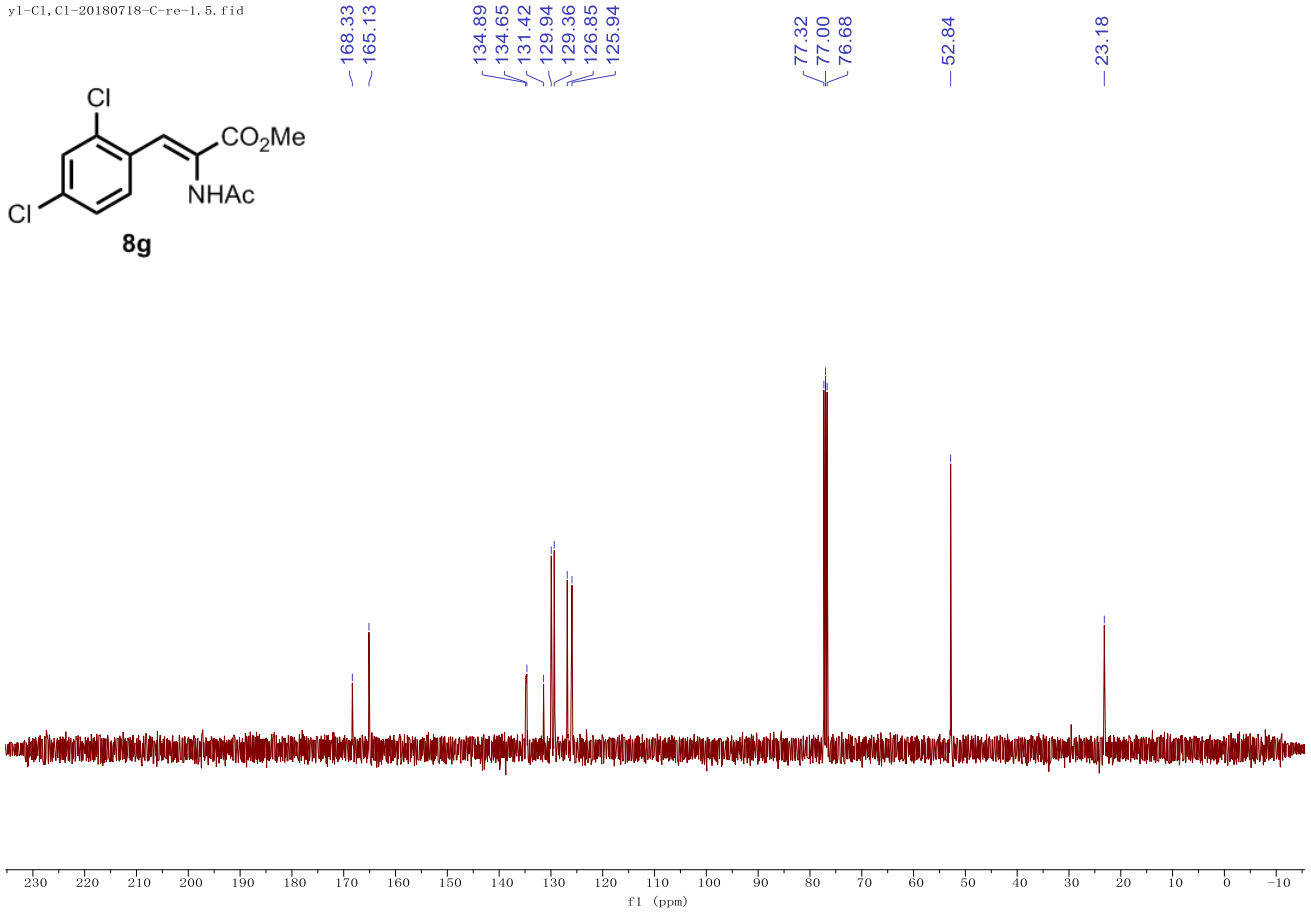
8c

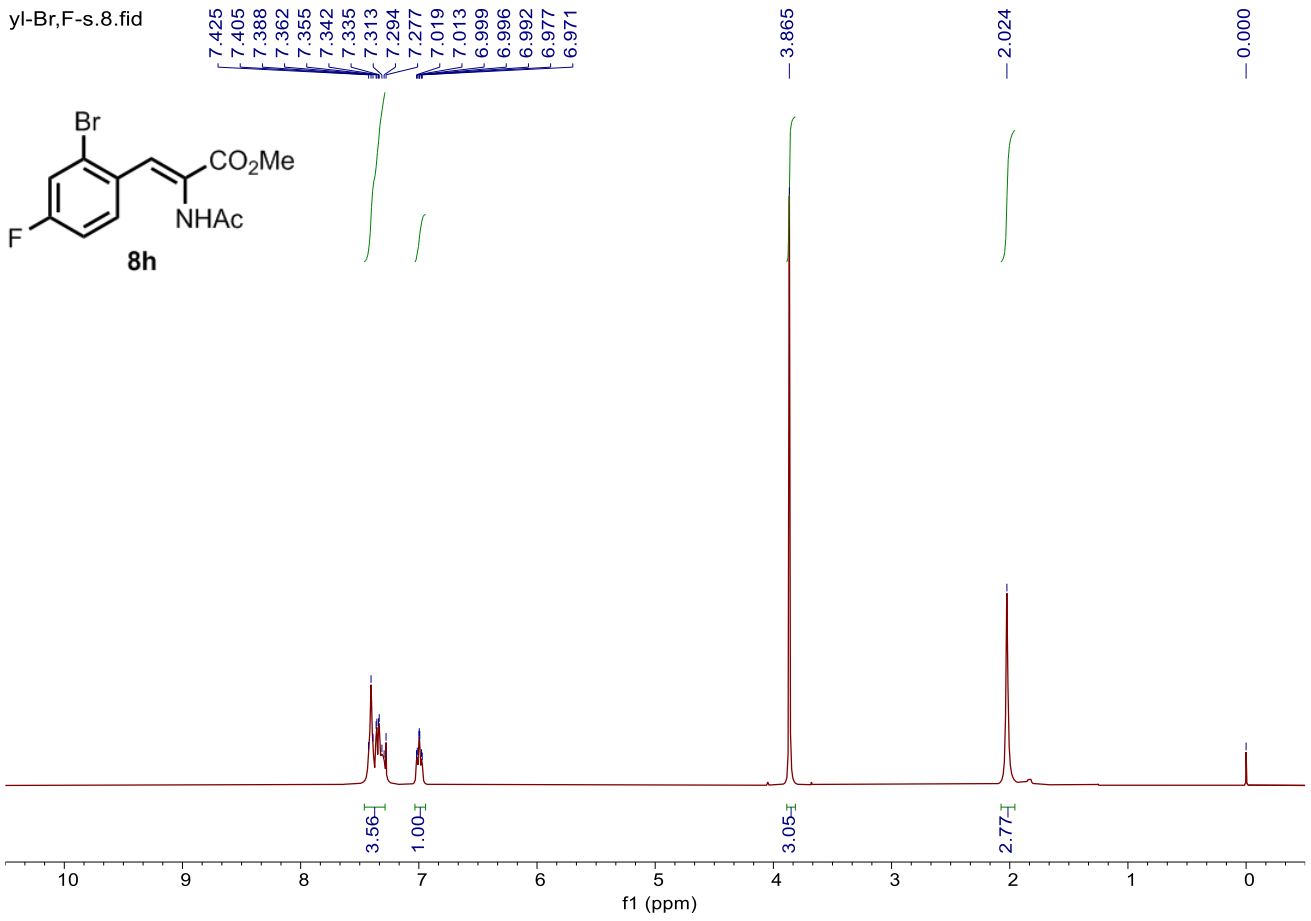

yl-4-Br-20210718-RE.6.fid
7.497
7.477
7.336
7.319
7.299
7.264
7.083
3.855
2.138
1.605
-0.000
CO2Me
NHAc
Br
8d
2.06
1.83
0.73
0.70
3.00
2.63
f1 (ppm)


yl-3-Cl-S-re.9.fid
7.435
7.319
7.299
7.264
7.095
3.860
2.140
1.607
0.000
CO2Me
NHAc
Cl
8e
0.97
4.22
0.79
3.44
3.00
f1 (ppm)

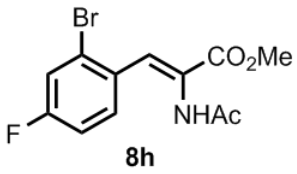

yl-2-Br-S-re.7.fid
7.630
7.610
7.438
7.402
7.301
7.282
7.264
7.196
7.177
7.159
7.010
3.881
2.046
1.613
-0.000
Br
CO2Me
NHAc
8f
1.00
1.66
0.84
1.00
0.68
3.20
2.73
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


yl-2,4-Cl-s.6.fid
7.444
7.426
7.421
7.368
7.347
7.296
7.271
7.206
7.187
3.872
2.042
-0.000
Cl
Cl
CO2Me
NHAc
8g
1.79
0.95
0.63
1.00
3.10
2.86
f1 (ppm)


yl-Cl,Cl-20180718-C-re-1.5.fid
168.33
165.13
134.89
134.65
131.42
129.94
129.36
126.85
125.94
77.32
77.00
76.68
52.84
23.18
Cl
CO2Me
NHAc
Cl
8g
f1 (ppm)

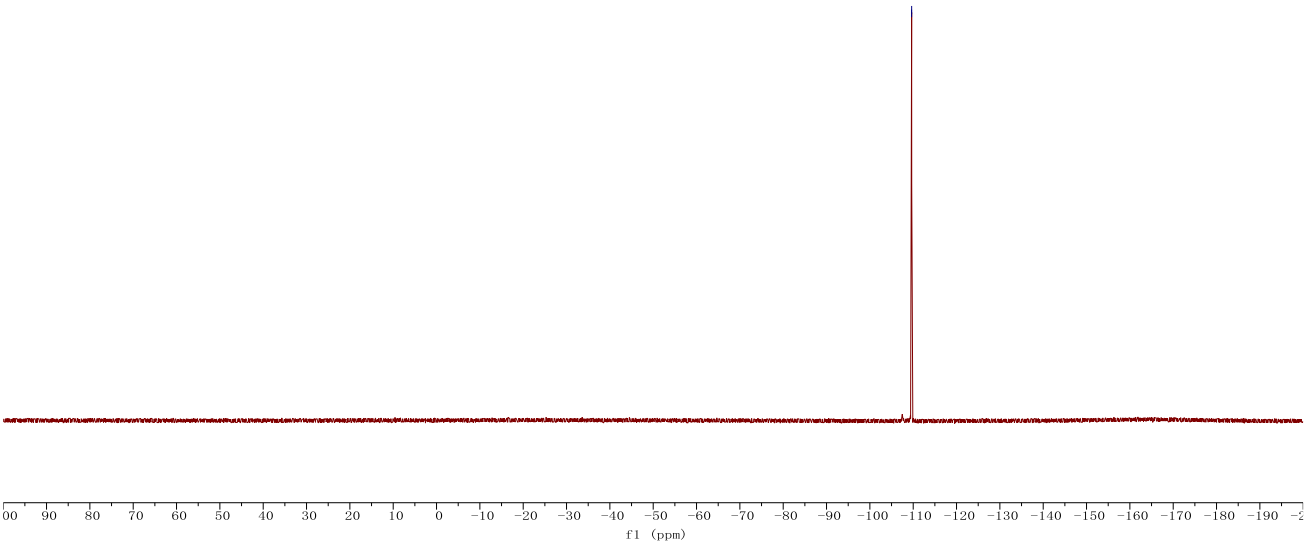

yl-Br,F-s.8.fid
7.425
7.405
7.388
7.362
7.355
7.342
7.335
7.313
7.294
7.277
7.019
7.013
6.999
6.996
6.992
6.977
6.971
3.865
2.024
0.000
Br
CO2Me
NHAc
F
8h
3.56
1.00
3.05
2.77
f1 (ppm)

yl-Br, F-s-F. 9. fid



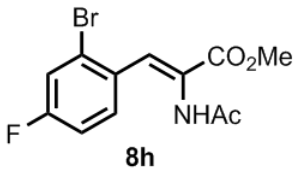
8h

-109.63
-109.64

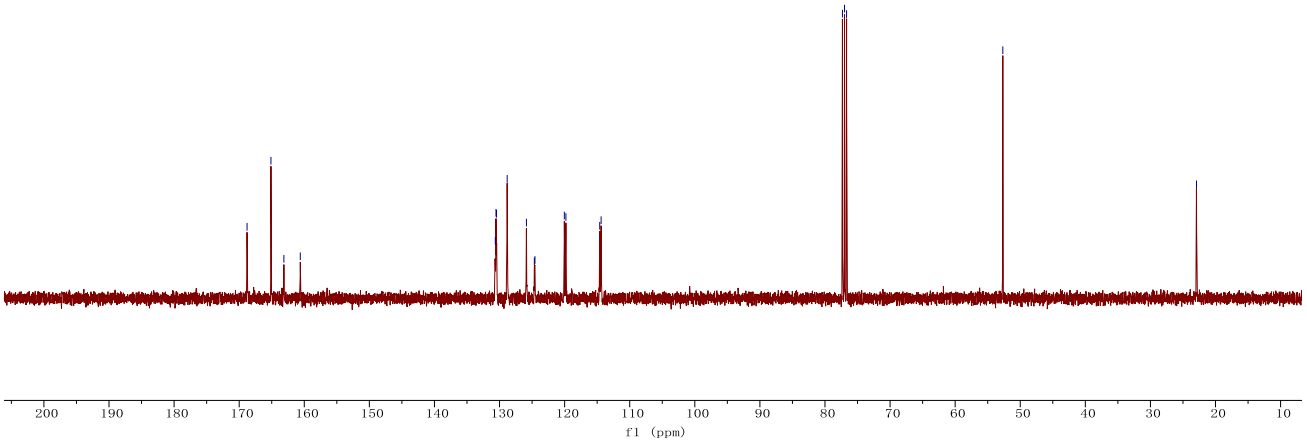


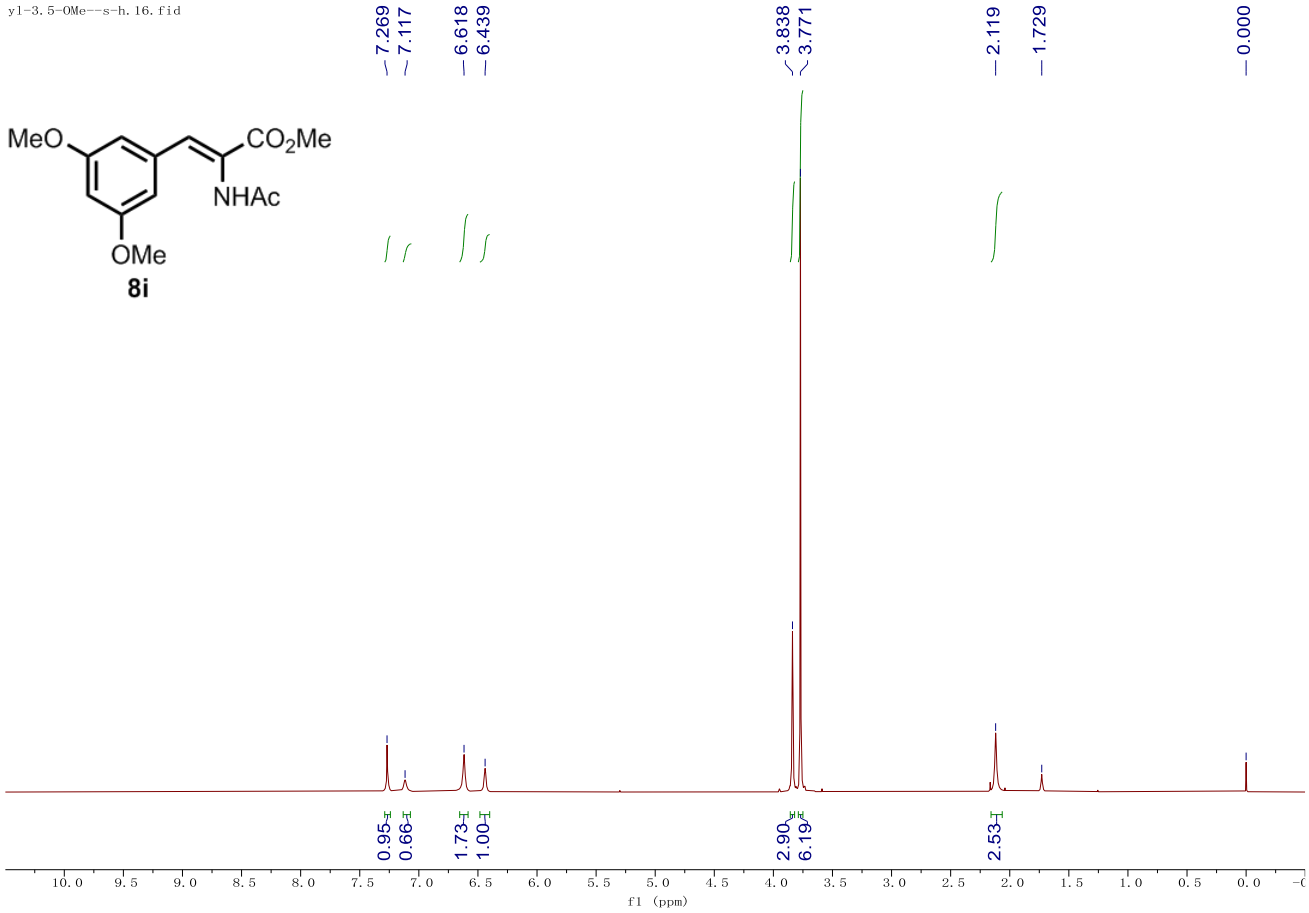
yl-Br-f-c. 4. fid

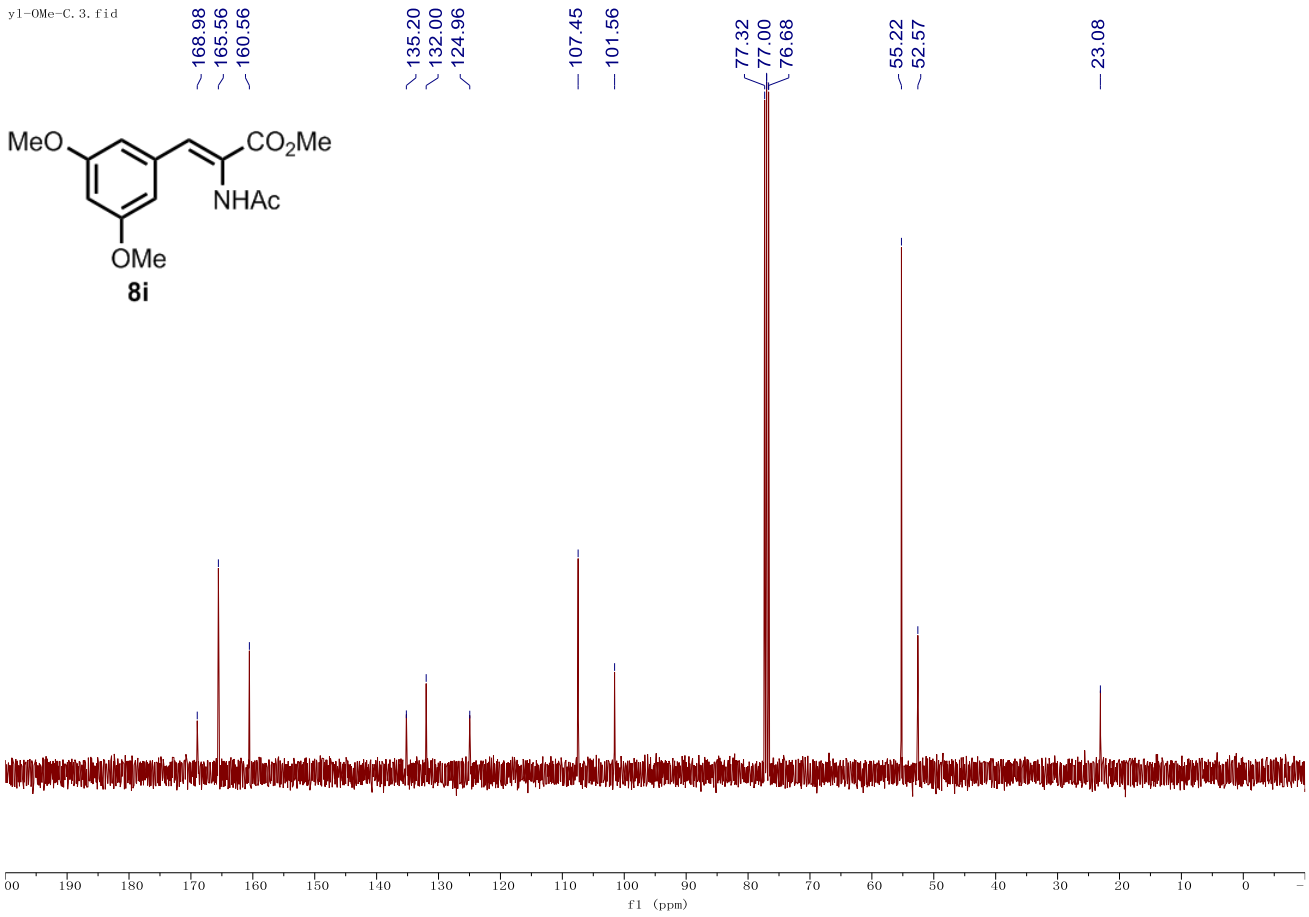
168.79
165.12
163.13
160.61
130.65
130.55
130.46
128.83
125.87
124.65
124.56
120.05
119.80
114.61
114.39
77.32
77.00
76.68
52.68
22.92

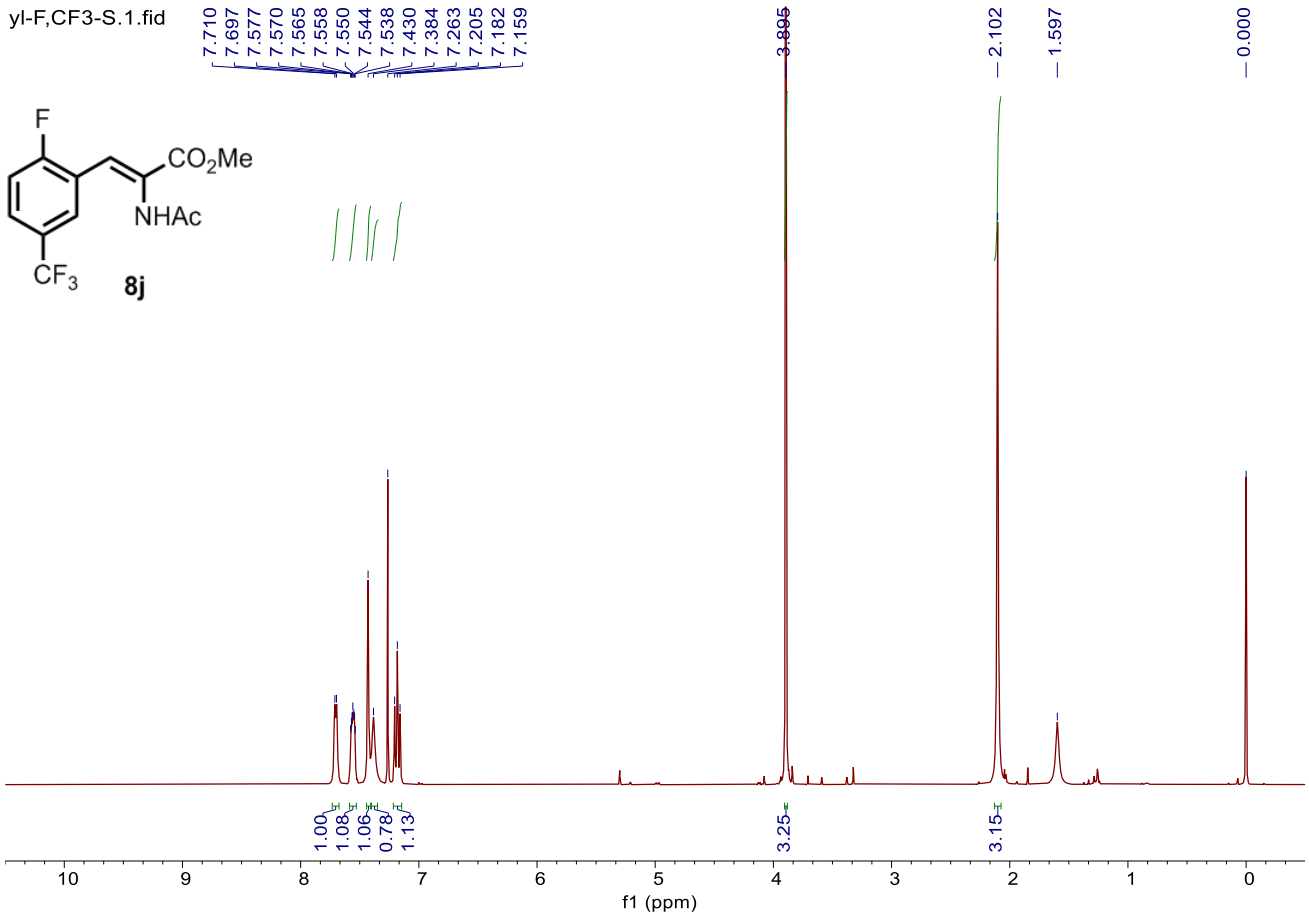


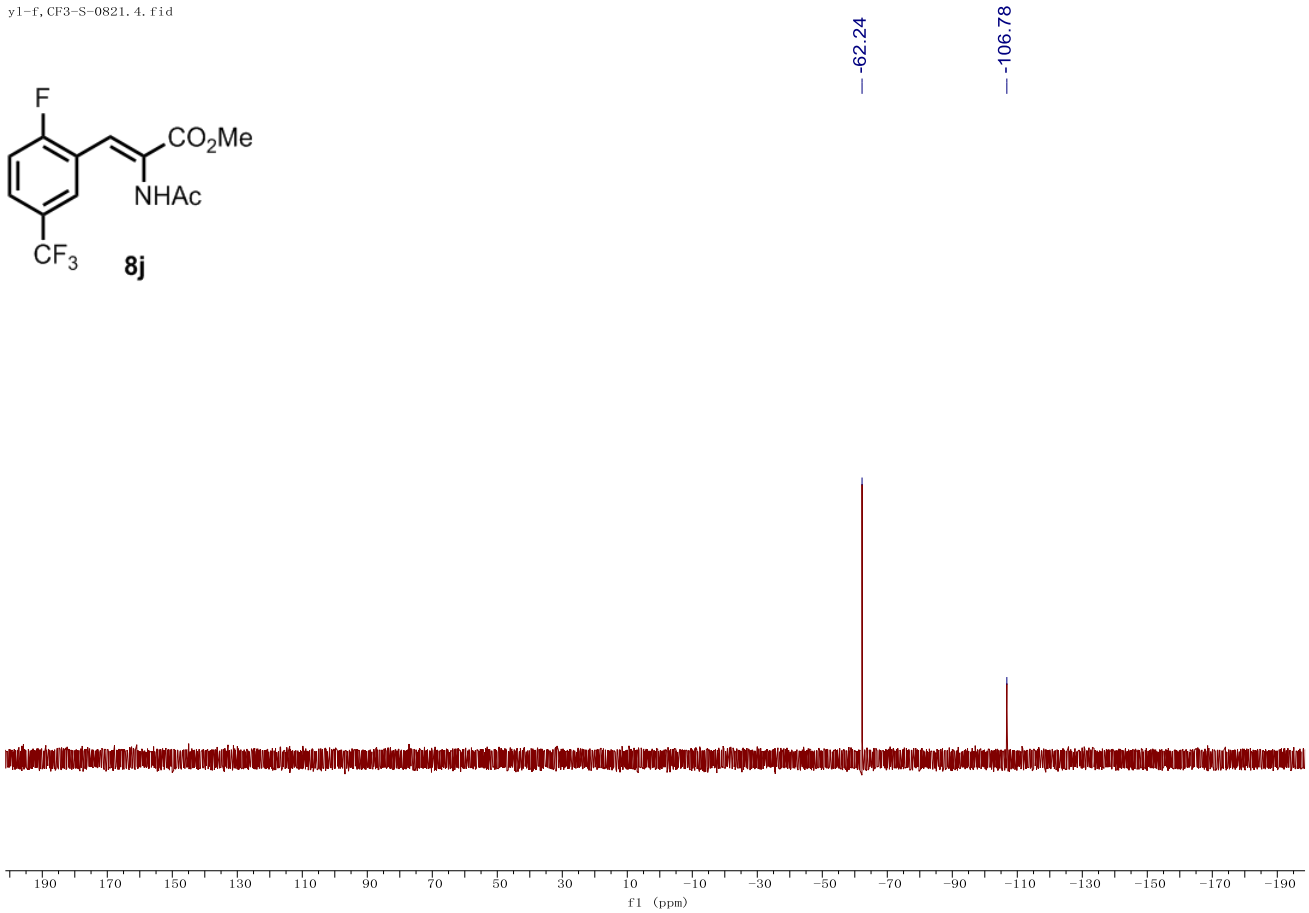
8h

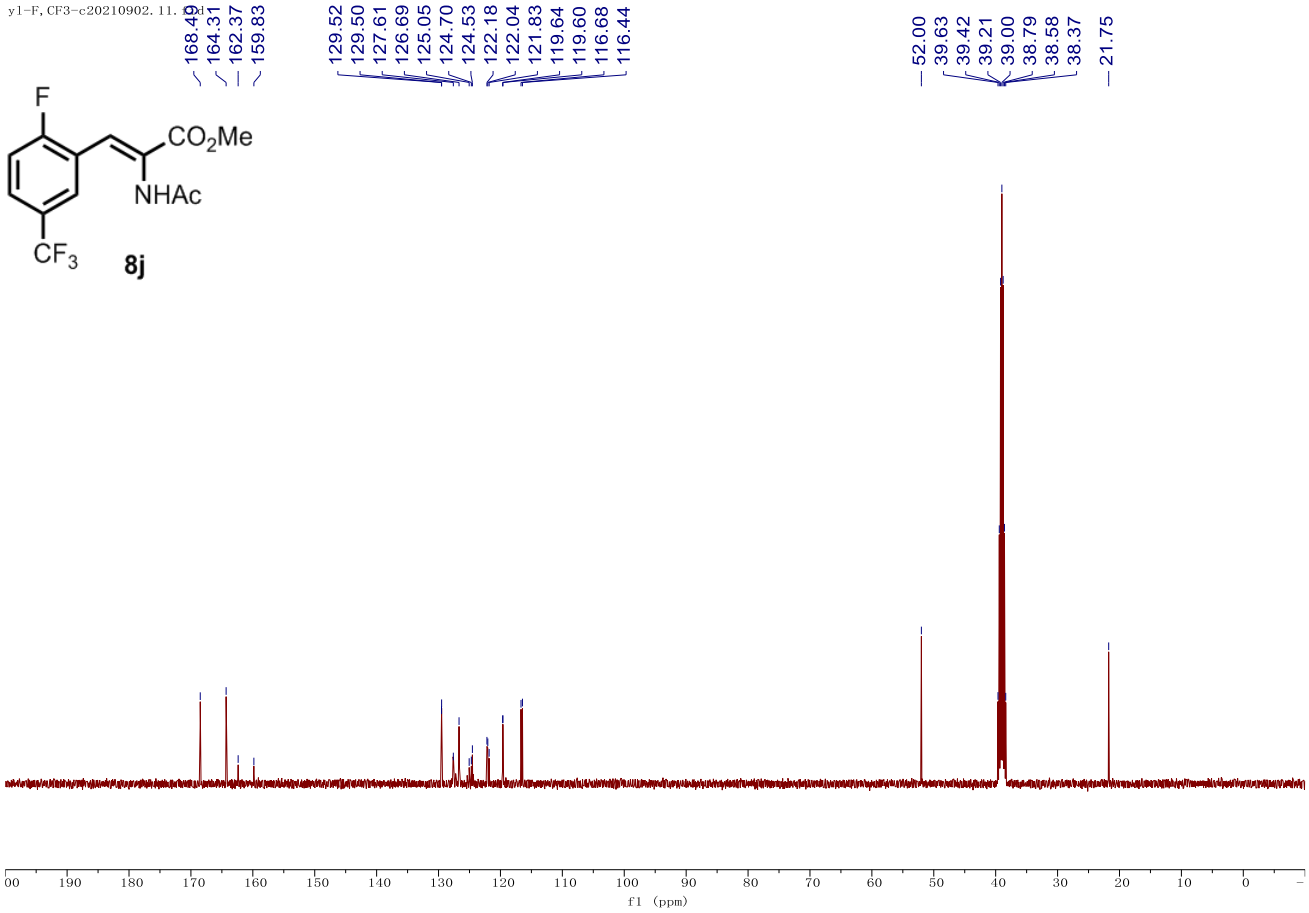


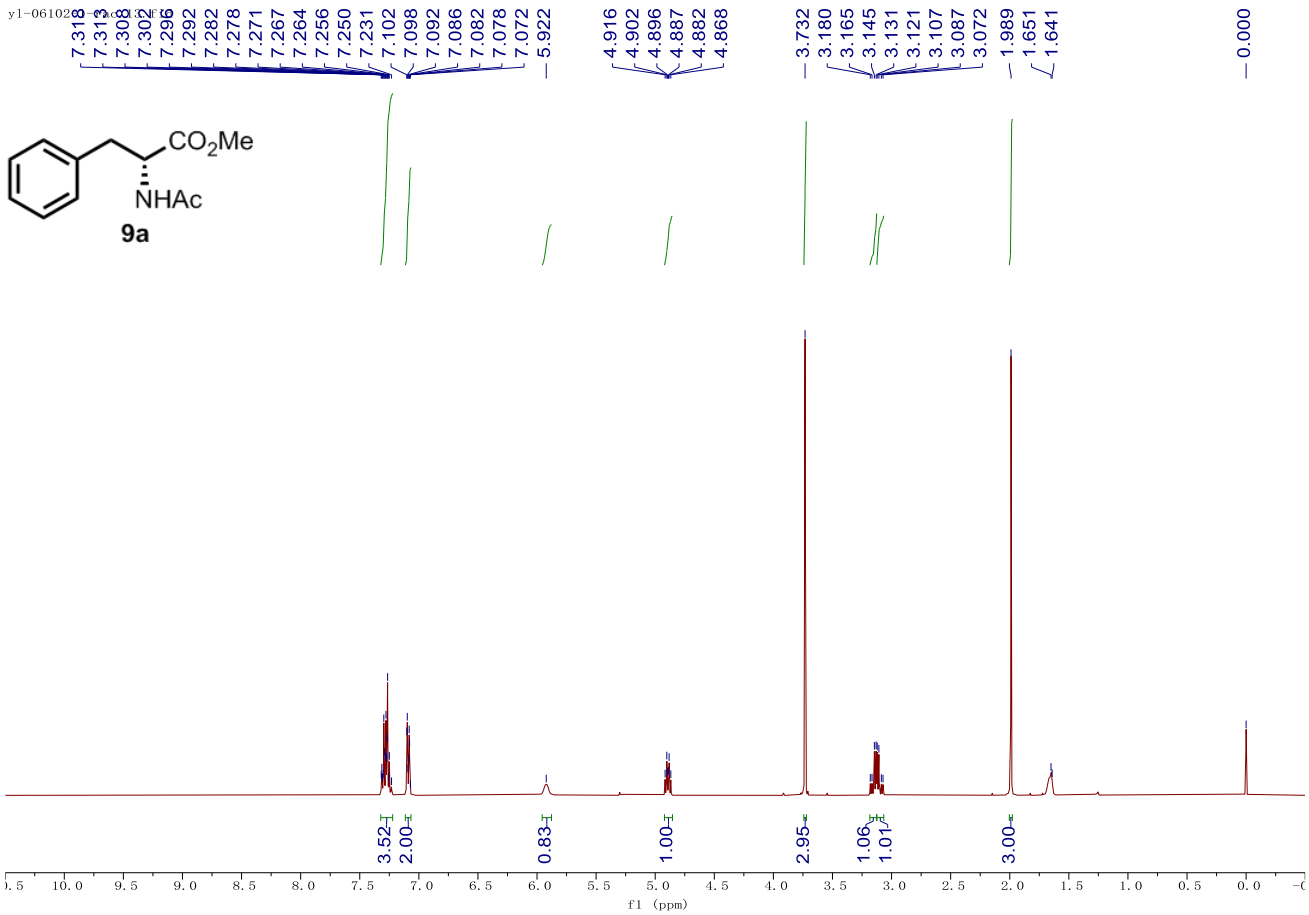

yl-3.5-OMe--s-h.16.fid
7.269
7.117
6.618
6.439
3.838
3.771
2.119
1.729
0.000
MeO
CO2Me
NHAc
OMe
8i
0.95
0.66
1.73
1.00
2.90
6.19
2.53
f1 (ppm)

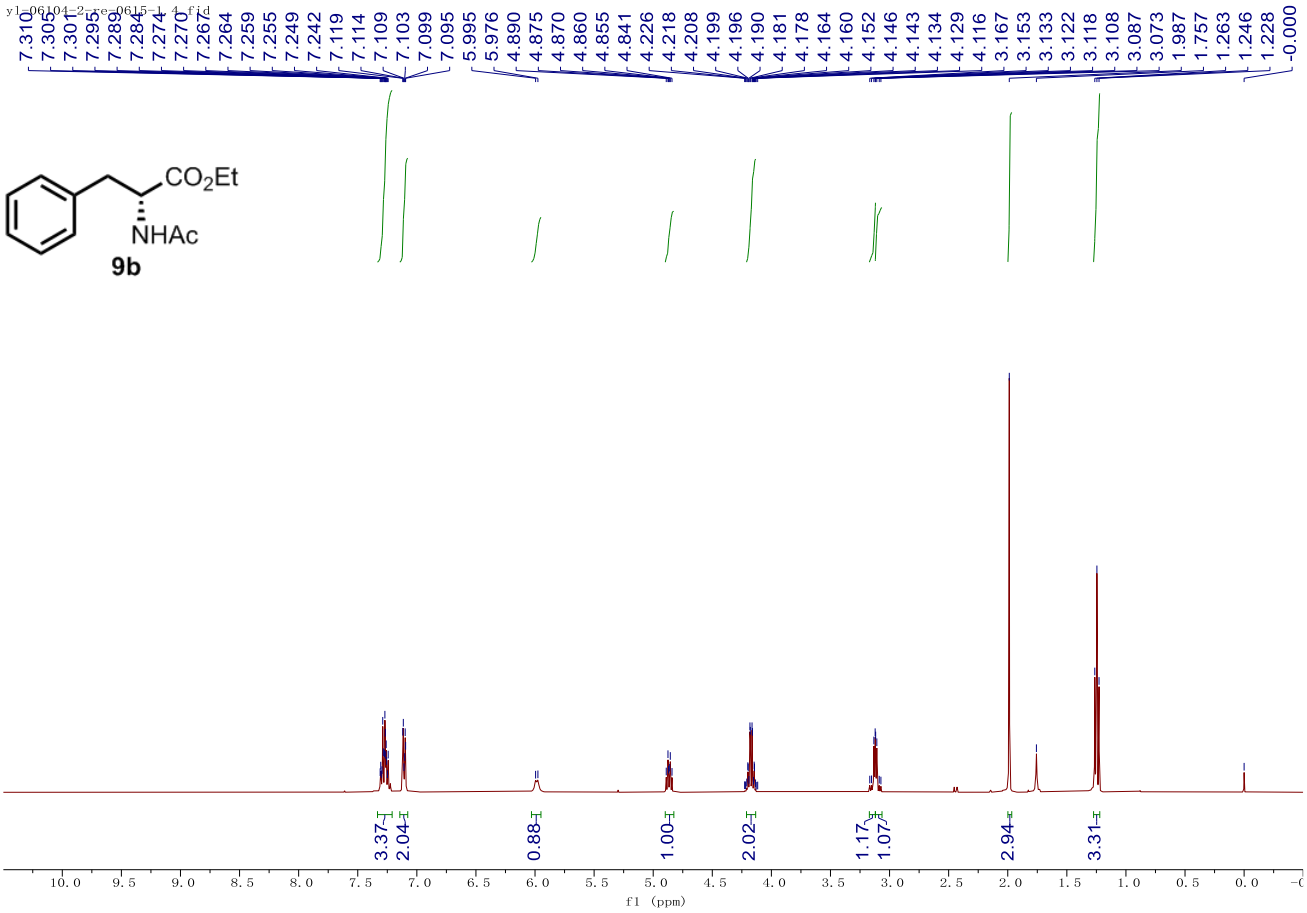

yl-OMe-C.3.fid
168.98
165.56
160.56
135.20
132.00
124.96
107.45
101.56
77.32
77.00
76.68
55.22
52.57
23.08
MeO
CO2Me
NHAc
OMe
8i
f1 (ppm)

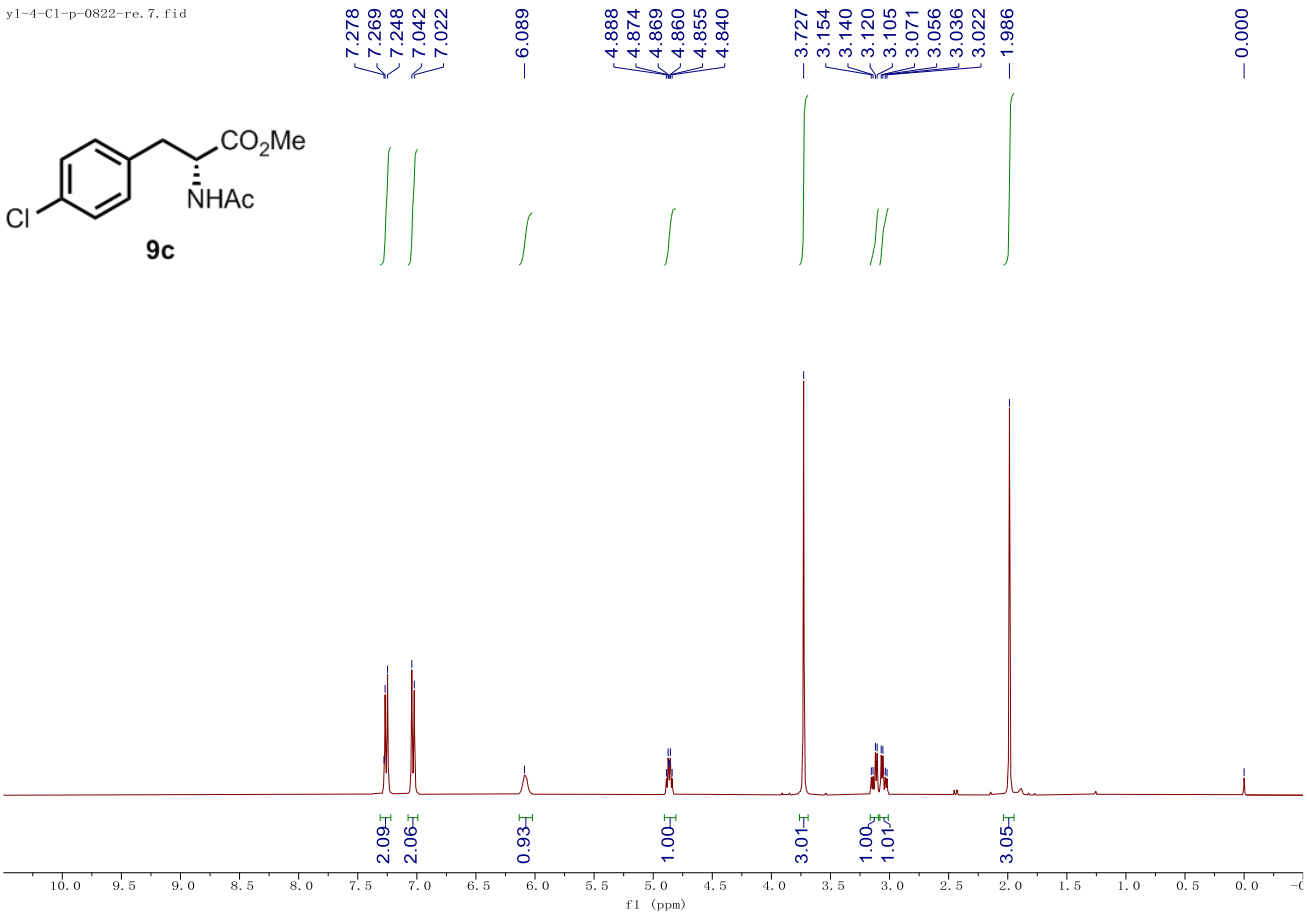

yl-F,CF3-S.1.fid
7.710
7.697
7.577
7.570
7.565
7.558
7.550
7.544
7.538
7.430
7.384
7.263
7.205
7.182
7.159
3.895
2.102
1.597
0.000
F
CO2Me
NHAc
CF3
8j
1.00
1.08
1.06
0.78
1.13
3.25
3.15
f1 (ppm)

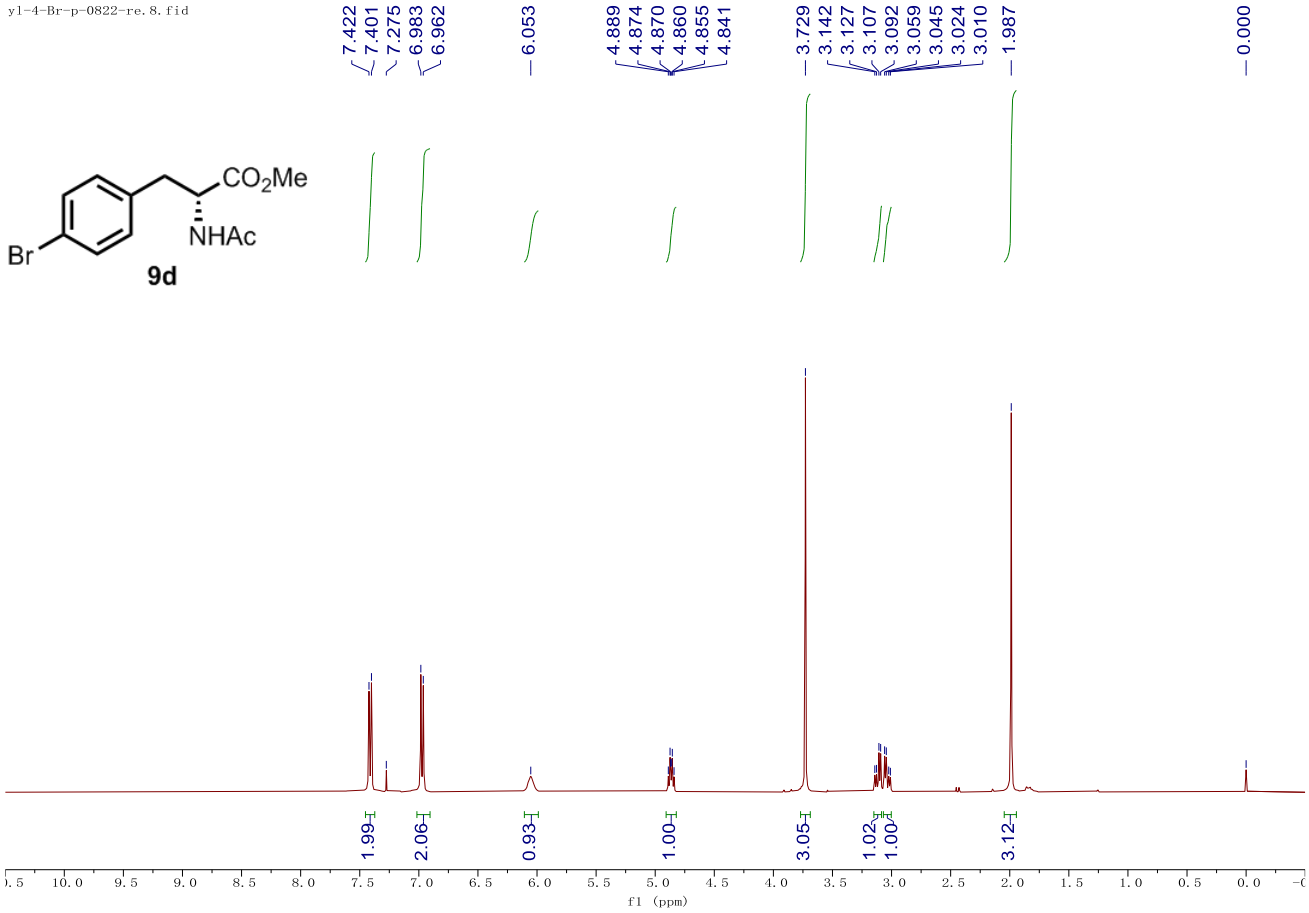

yl-f,CF3-S-0821.4.fid
-62.24
-106.78
F
CO2Me
NHAc
CF3
8j
f1 (ppm)

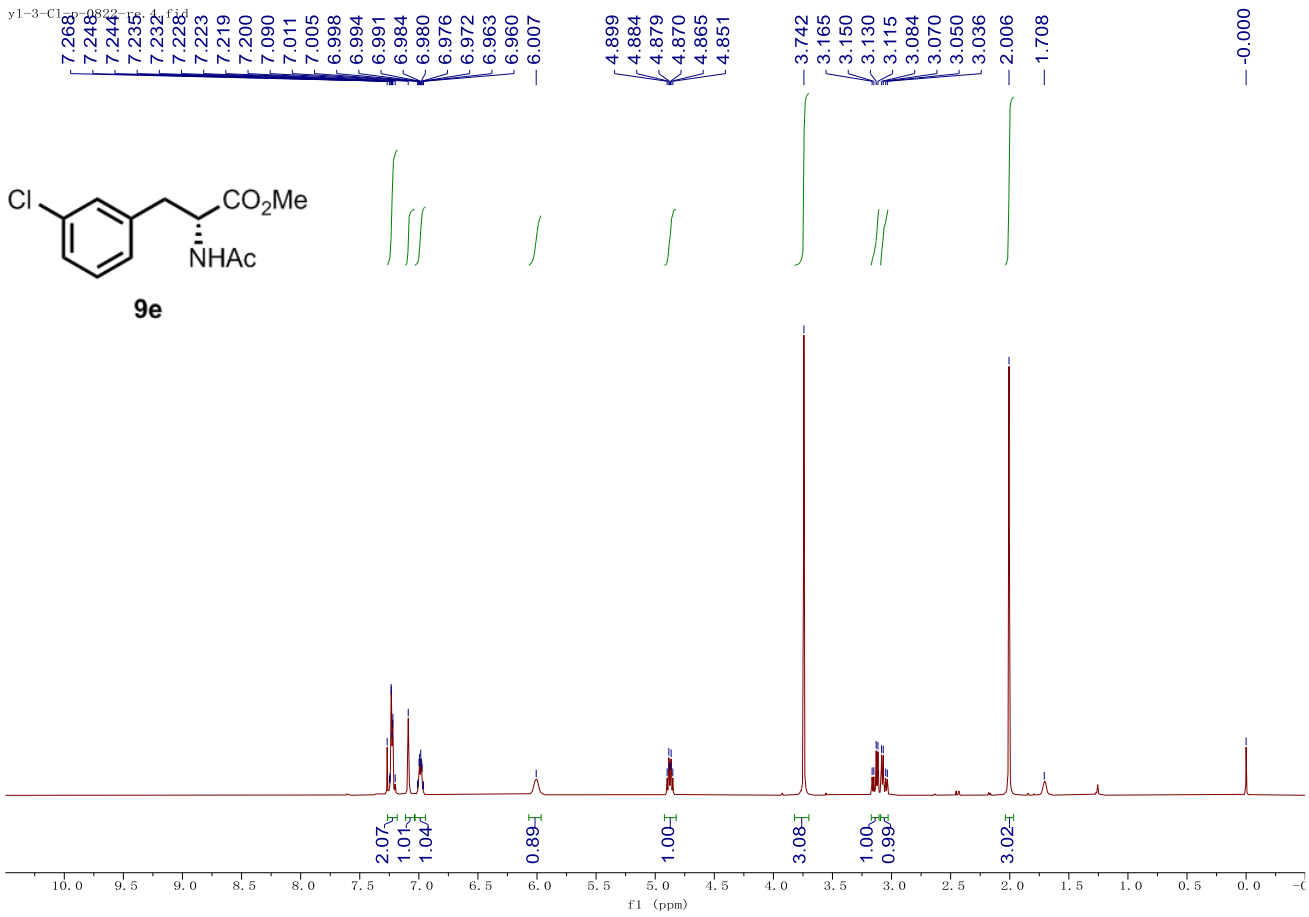

168.49
164.31
162.37
159.83
129.52
129.50
127.61
126.69
125.05
124.70
124.53
122.18
122.04
121.83
119.64
119.60
116.68
116.44
52.00
39.63
39.42
39.21
39.00
38.79
38.58
38.37
21.75
F
CO2Me
NHAc
CF3
8j
f1 (ppm)

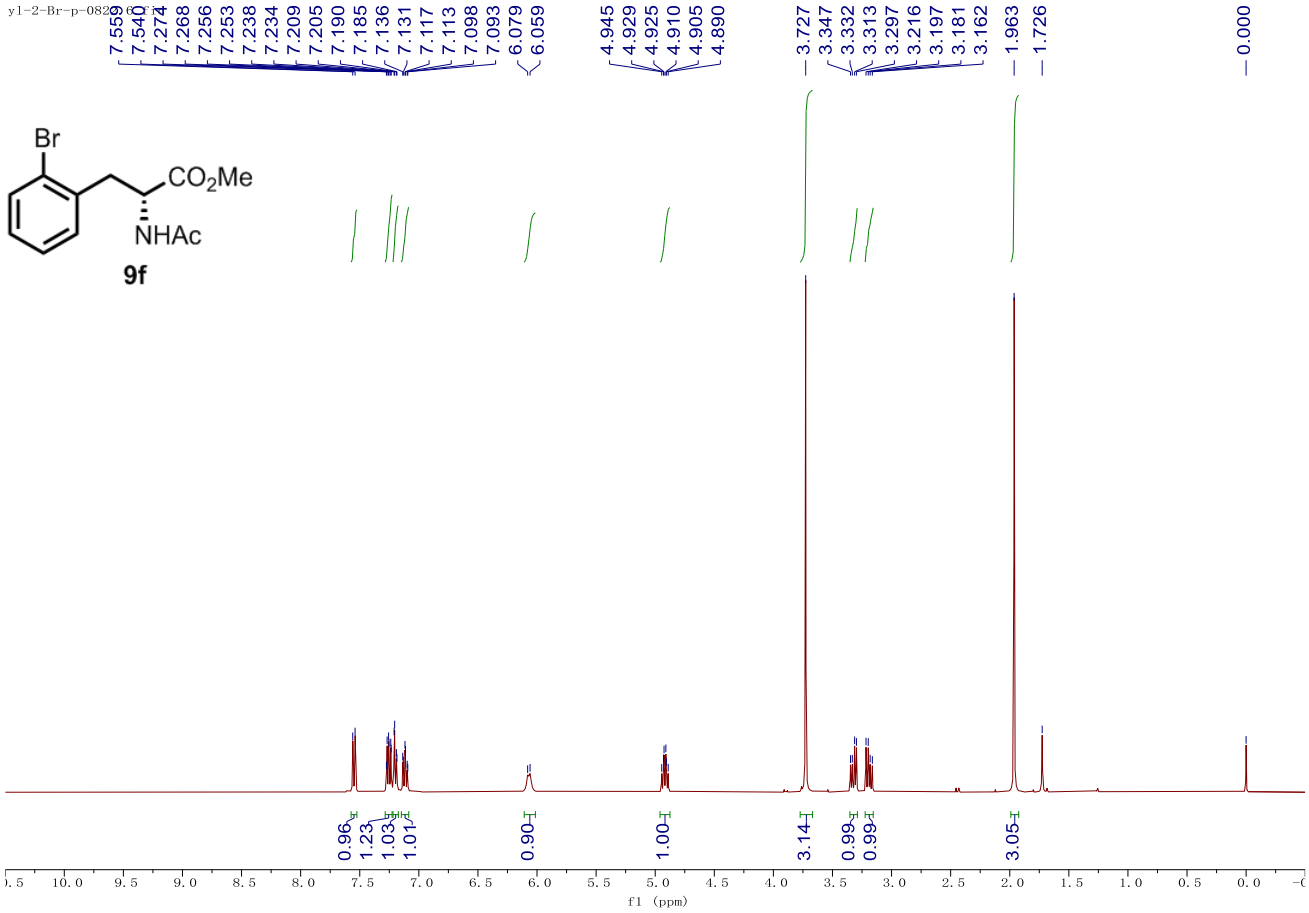

7.318
7.313
7.308
7.302
7.296
7.292
7.282
7.278
7.271
7.267
7.264
7.256
7.250
7.231
7.102
7.098
7.092
7.086
7.082
7.078
7.072
5.922
4.916
4.902
4.896
4.887
4.882
4.868
3.732
3.180
3.165
3.145
3.131
3.121
3.107
3.087
3.072
1.989
1.651
1.641
0.000
CO2Me
NHAc
9a
3.52
2.00
0.83
1.00
2.95
1.06
1.01
3.00
f1 (ppm)

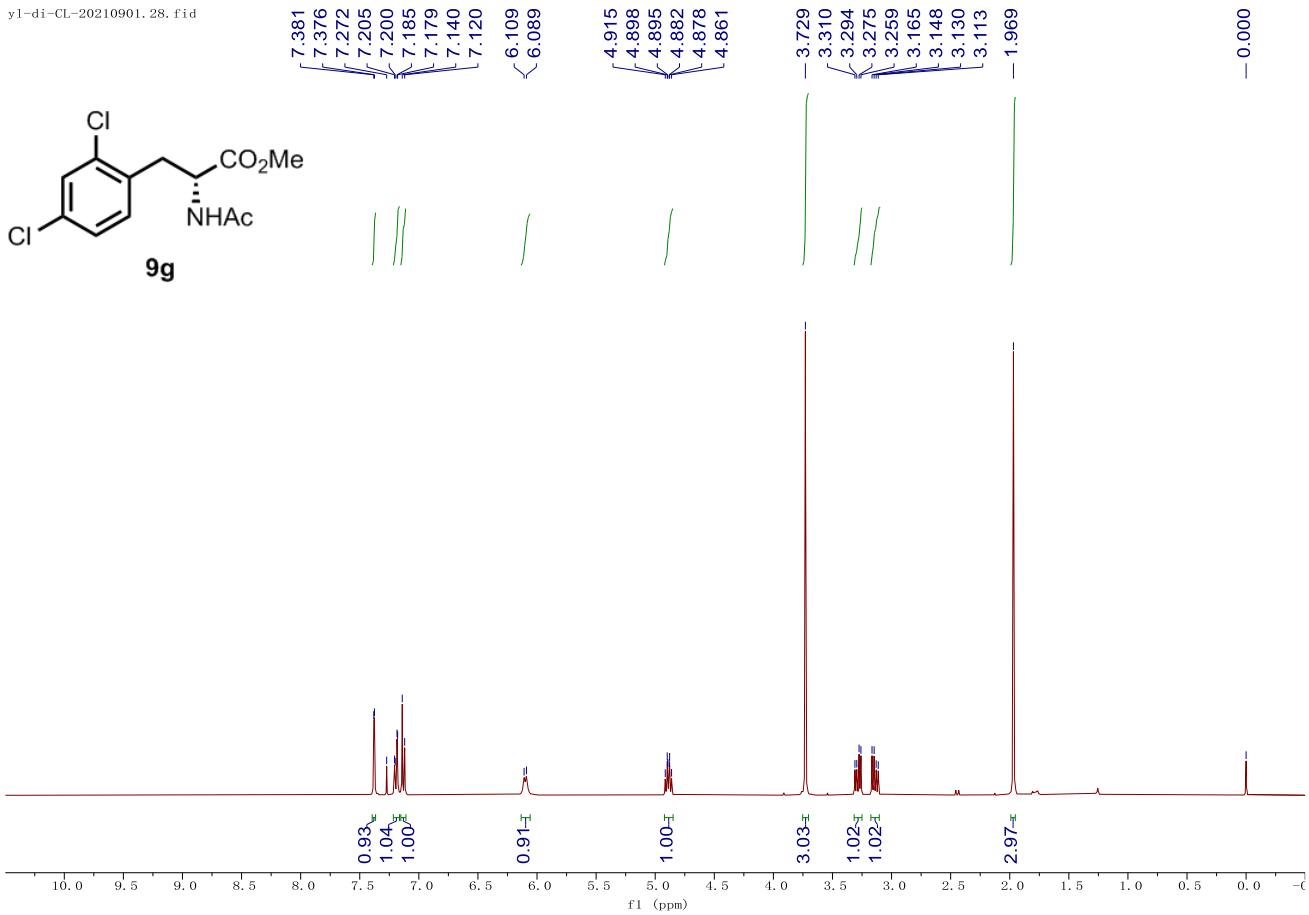

yl-06104-2-re-0615-1-4.fid
7.310 7.305 7.301 7.295 7.289 7.284 7.274 7.270 7.267 7.264 7.259 7.255 7.249 7.242 7.119 7.114 7.109 7.103 7.099 7.095 5.995 5.976 4.890 4.875 4.870 4.860 4.855 4.841 4.226 4.218 4.208 4.199 4.196 4.190 4.181 4.178 4.164 4.160 4.152 4.146 4.143 4.134 4.129 4.116 3.167 3.153 3.133 3.122 3.118 3.108 3.087 3.073 1.987 1.757 1.263 1.246 1.228 -0.000
CO2Et
NHAc
9b
3.37 2.04 0.88 1.00 2.02 1.17 1.07 2.94 3.31
f1 (ppm)

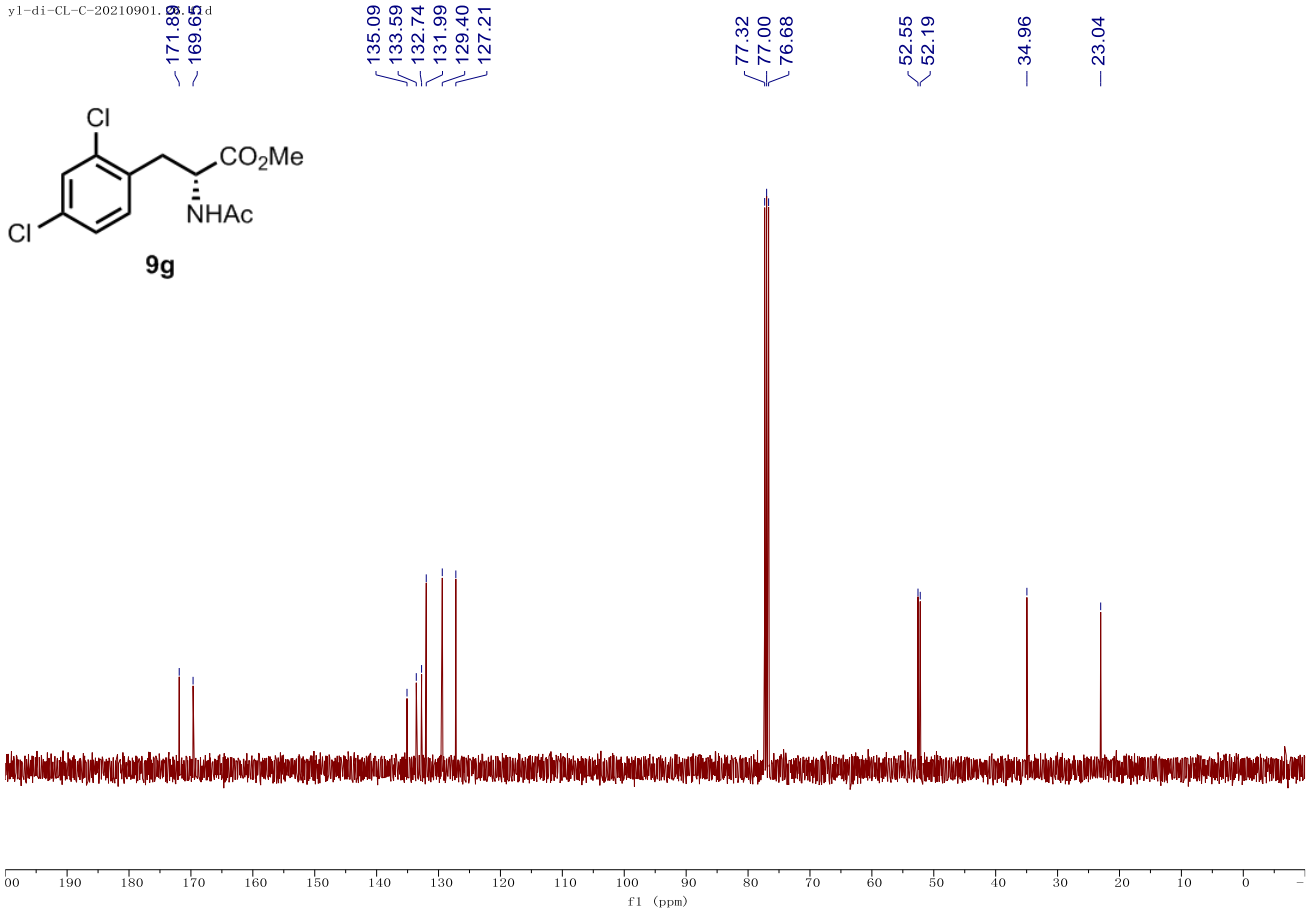

yl-4-Cl-p-0822-re.7.fid
7.278 7.269 7.248 7.042 7.022 6.089 4.888 4.874 4.869 4.860 4.855 4.840 3.727 3.154 3.140 3.120 3.105 3.071 3.056 3.036 3.022 1.986 0.000
CO2Me
NHAc
Cl
9c
2.09 2.06 0.93 1.00 3.01 1.00 1.01 3.05
f1 (ppm)

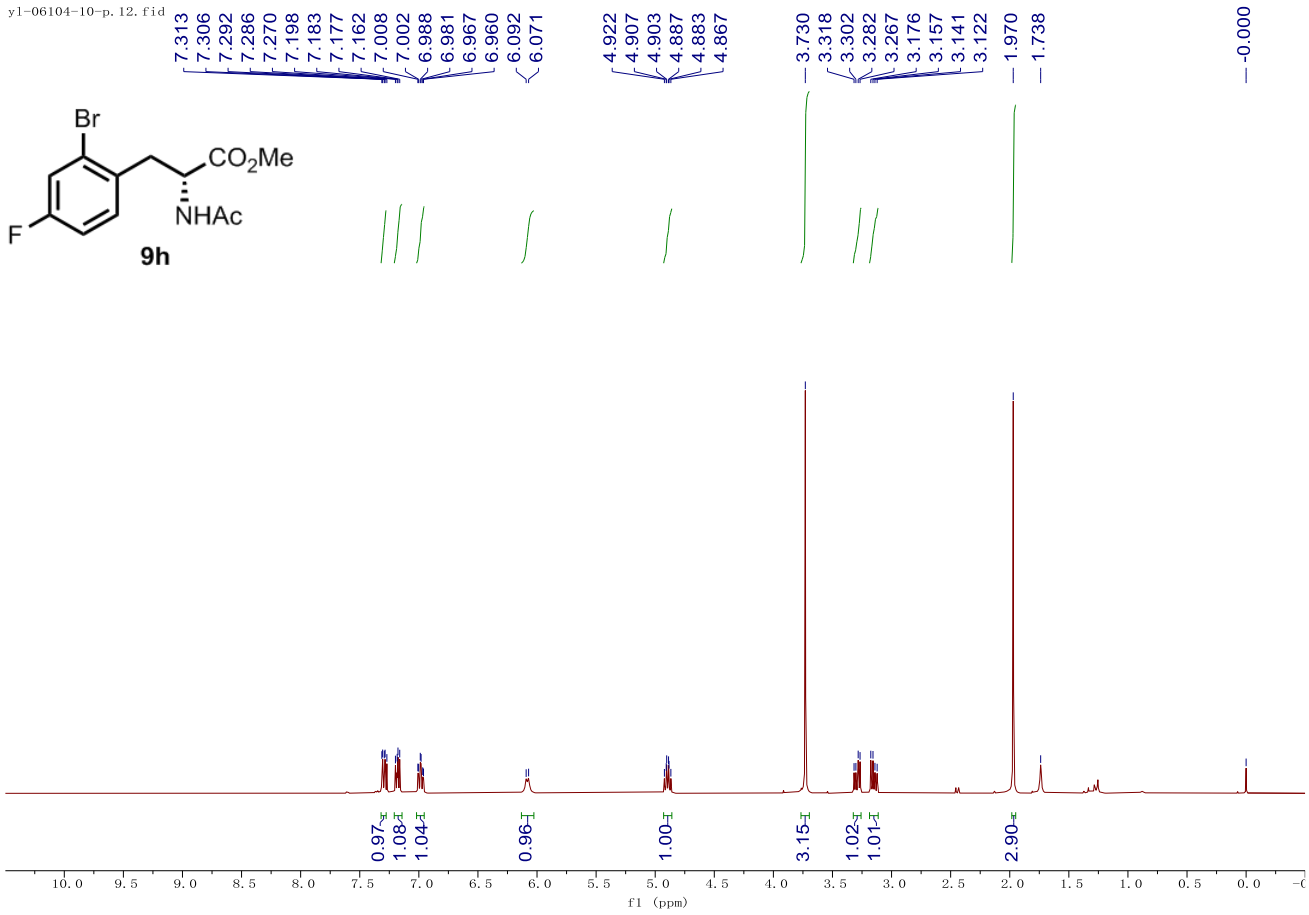

yl-4-Br-p-0822-re.8.fid
7.422
7.401
7.275
6.983
6.962
6.053
4.889
4.874
4.870
4.860
4.855
4.841
3.729
3.142
3.127
3.107
3.092
3.059
3.045
3.024
3.010
1.987
0.000
CO2Me
NHAc
Br
9d
1.99
2.06
0.93
1.00
3.05
1.02
1.00
3.12
f1 (ppm)


yl-3-Cl-p-0822-re.4.fid
7.268
7.248
7.244
7.235
7.232
7.228
7.223
7.219
7.200
7.090
7.011
7.005
6.998
6.994
6.991
6.984
6.980
6.976
6.972
6.963
6.960
6.007
4.899
4.884
4.879
4.870
4.865
4.851
3.742
3.165
3.150
3.130
3.115
3.084
3.070
3.050
3.036
2.006
1.708
-0.000
CO2Me
NHAc
Cl
9e
2.07
1.01
1.04
0.89
1.00
3.08
1.00
0.99
3.02
f1 (ppm)

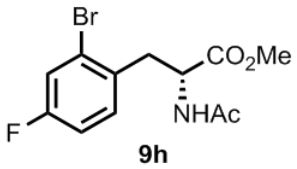

yl-2-Br-p-08
7.559
7.541
7.274
7.268
7.256
7.253
7.238
7.234
7.209
7.205
7.190
7.185
7.136
7.131
7.117
7.113
7.098
7.093
6.079
6.059
4.945
4.929
4.925
4.910
4.905
4.890
3.727
3.347
3.332
3.313
3.297
3.216
3.197
3.181
3.162
1.963
1.726
0.000
Br
CO2Me
NHAc
9f
0.96
1.23
1.03
1.01
0.90
1.00
3.14
0.99
0.99
3.05
f1 (ppm)


yl-di-CL-20210901.28.fid
7.381
7.376
7.272
7.205
7.200
7.185
7.179
7.140
7.120
6.109
6.089
4.915
4.898
4.895
4.882
4.878
4.861
3.729
3.310
3.294
3.275
3.259
3.165
3.148
3.130
3.113
1.969
0.000
Cl
CO2Me
NHAc
Cl
9g
0.93
1.04
1.00
0.91
1.00
3.03
1.02
1.02
2.97
f1 (ppm)


yl-di-CL-C-20210901.fid
171.89
169.65
135.09
133.59
132.74
131.99
129.40
127.21
77.32
77.00
76.68
52.55
52.19
34.96
23.04
Cl
CO2Me
NHAc
Cl
9g
f1 (ppm)


yl-06104-10-p.12.fid
7.313
7.306
7.292
7.286
7.270
7.198
7.183
7.177
7.162
7.008
7.002
6.988
6.981
6.967
6.960
6.092
6.071
4.922
4.907
4.903
4.887
4.883
4.867
3.730
3.318
3.302
3.282
3.267
3.176
3.157
3.141
3.122
1.970
1.738
-0.000
Br
CO2Me
NHAc
F
9h
0.97
1.08
1.04
0.96
1.00
3.15
1.02
1.01
2.90
f1 (ppm)

yl-06104-10-p-f.14.fid



9h

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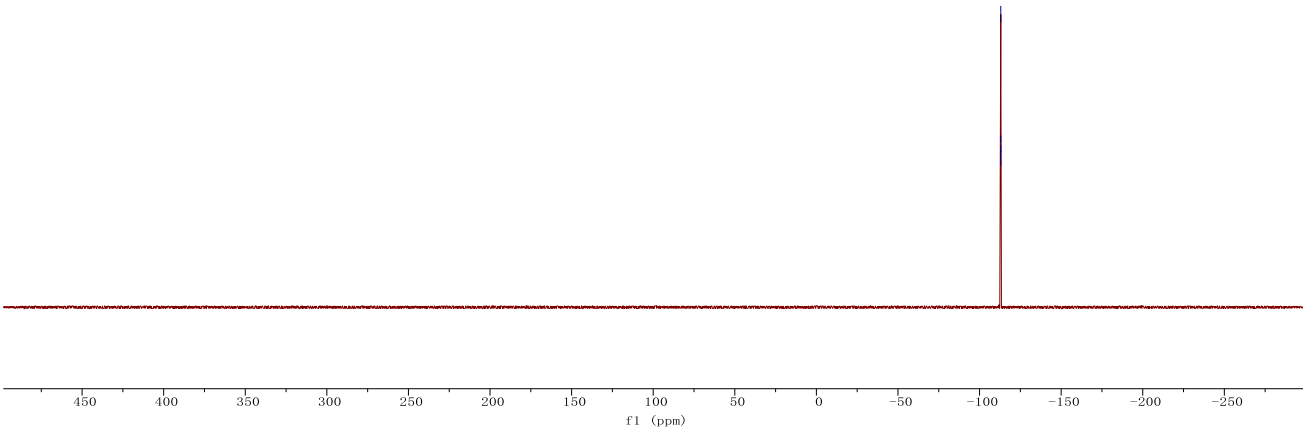
-112.983
-113.000
-113.005
-113.021



yl-06104-10-p-C.13.fid

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162.58
160.09
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131.87
131.83
124.86
124.76
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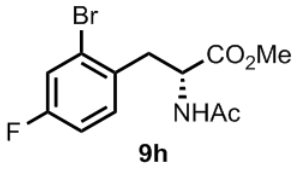
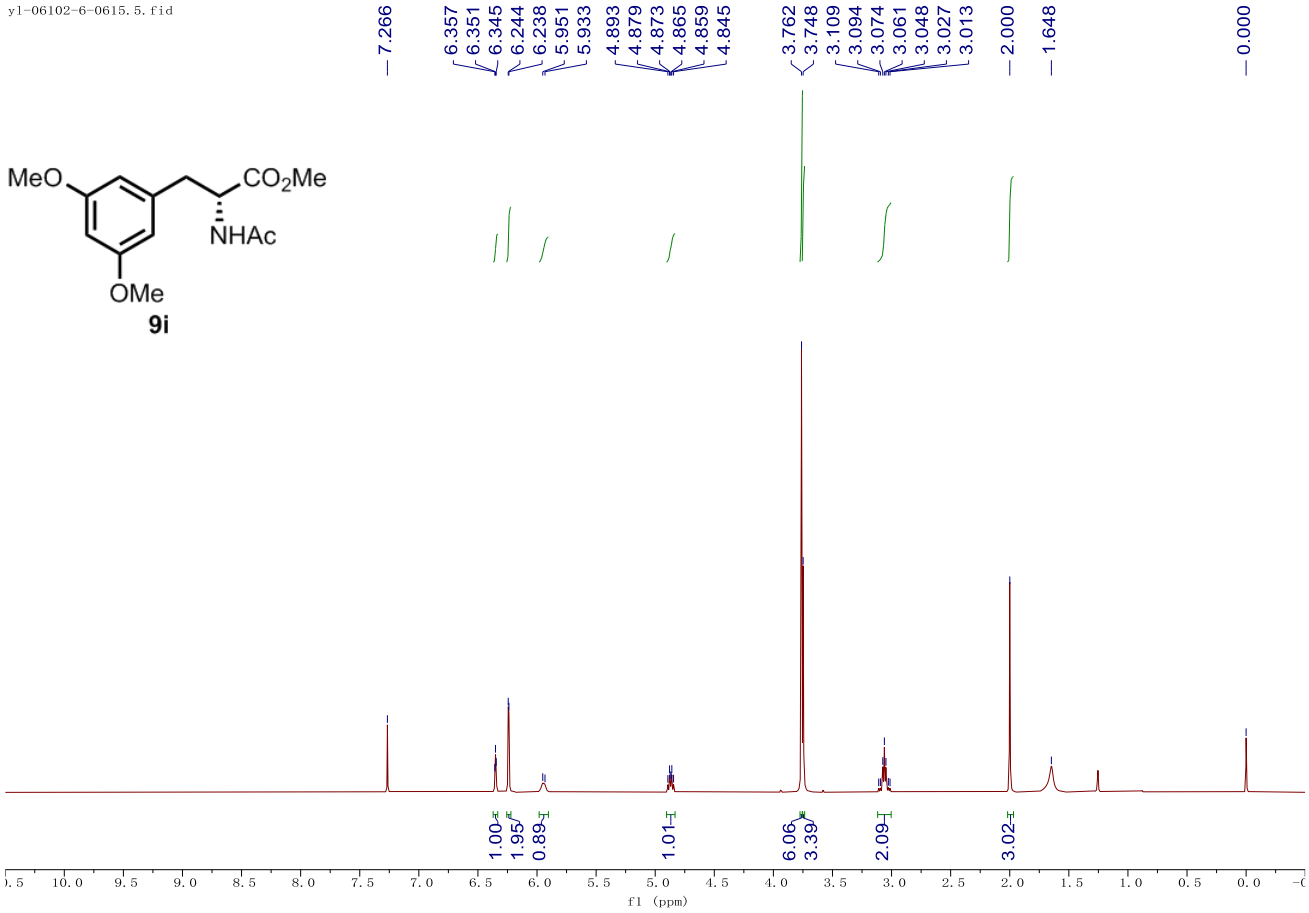
119.98
114.87
114.67
77.32
77.00
76.68
52.55
52.41
37.17
23.07



9h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6.345
6.244
6.238
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4.879
4.873
4.865
4.859
4.845
3.762
3.748
3.109
3.094
3.074
3.061
3.048
3.027
3.013
2.000
1.648
0.000
MeO
CO2Me
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9i
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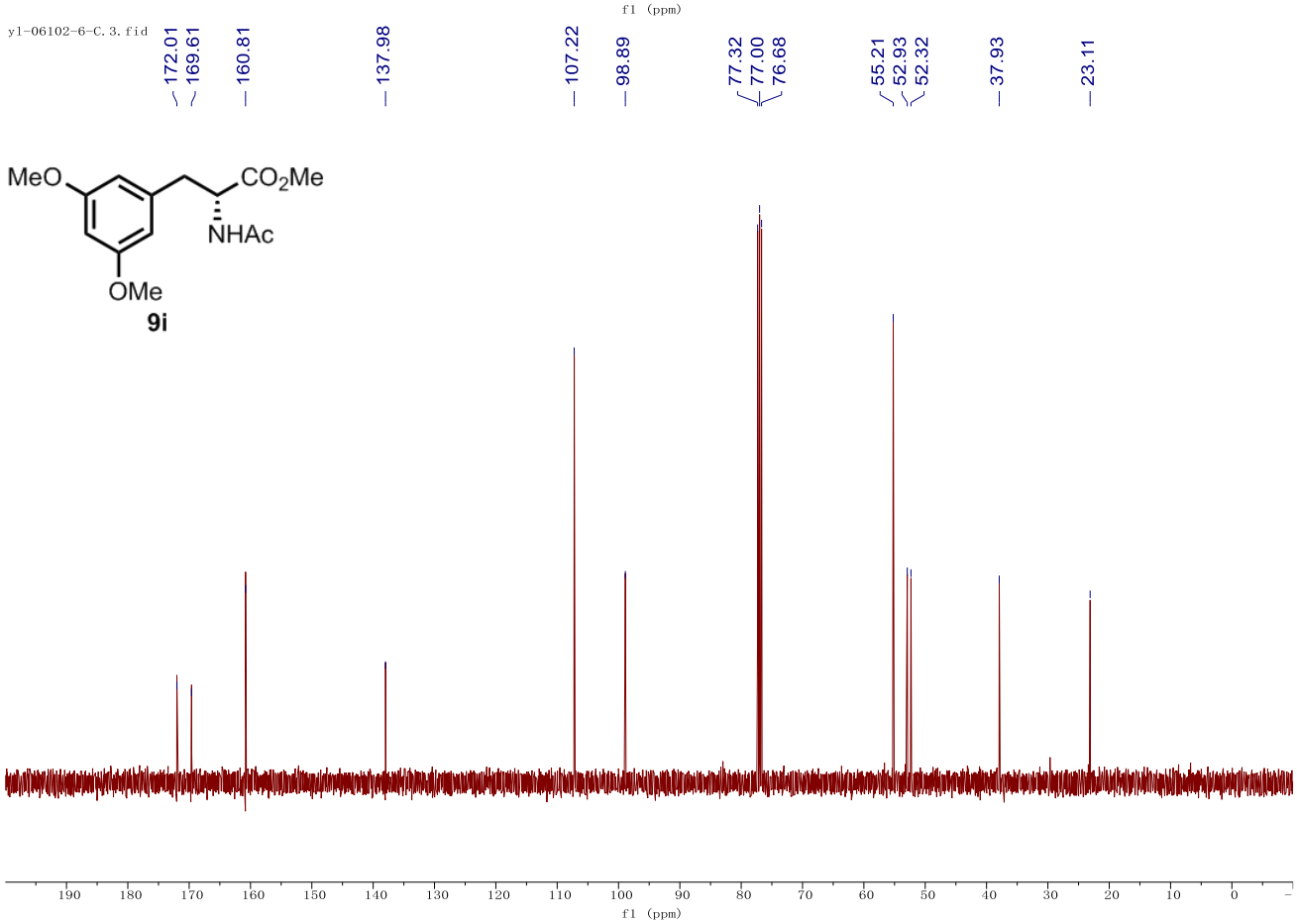
f1 (ppm)


y1-06102-6-C.3.fid
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160.81
137.98
107.22
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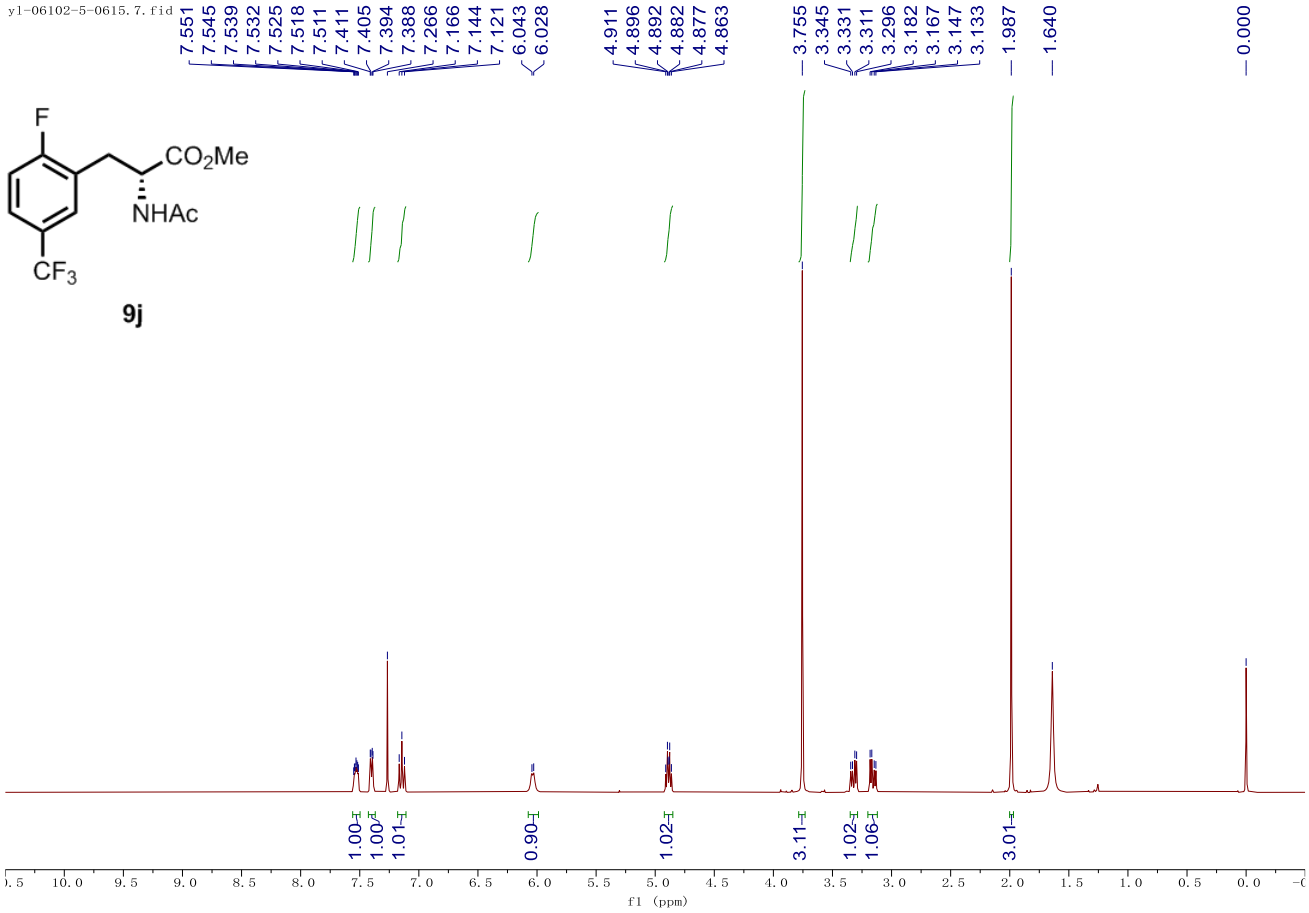
CO2Me
NHAc
OMe
9i
f1 (ppm)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7.388
7.266
7.166
7.144
7.121
6.043
6.028
4.911
4.896
4.892
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4.877
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3.755
3.345
3.331
3.311
3.296
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3.147
3.133
1.987
1.640
0.000
F
CO2Me
NHAc
CF3
9j
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1.00
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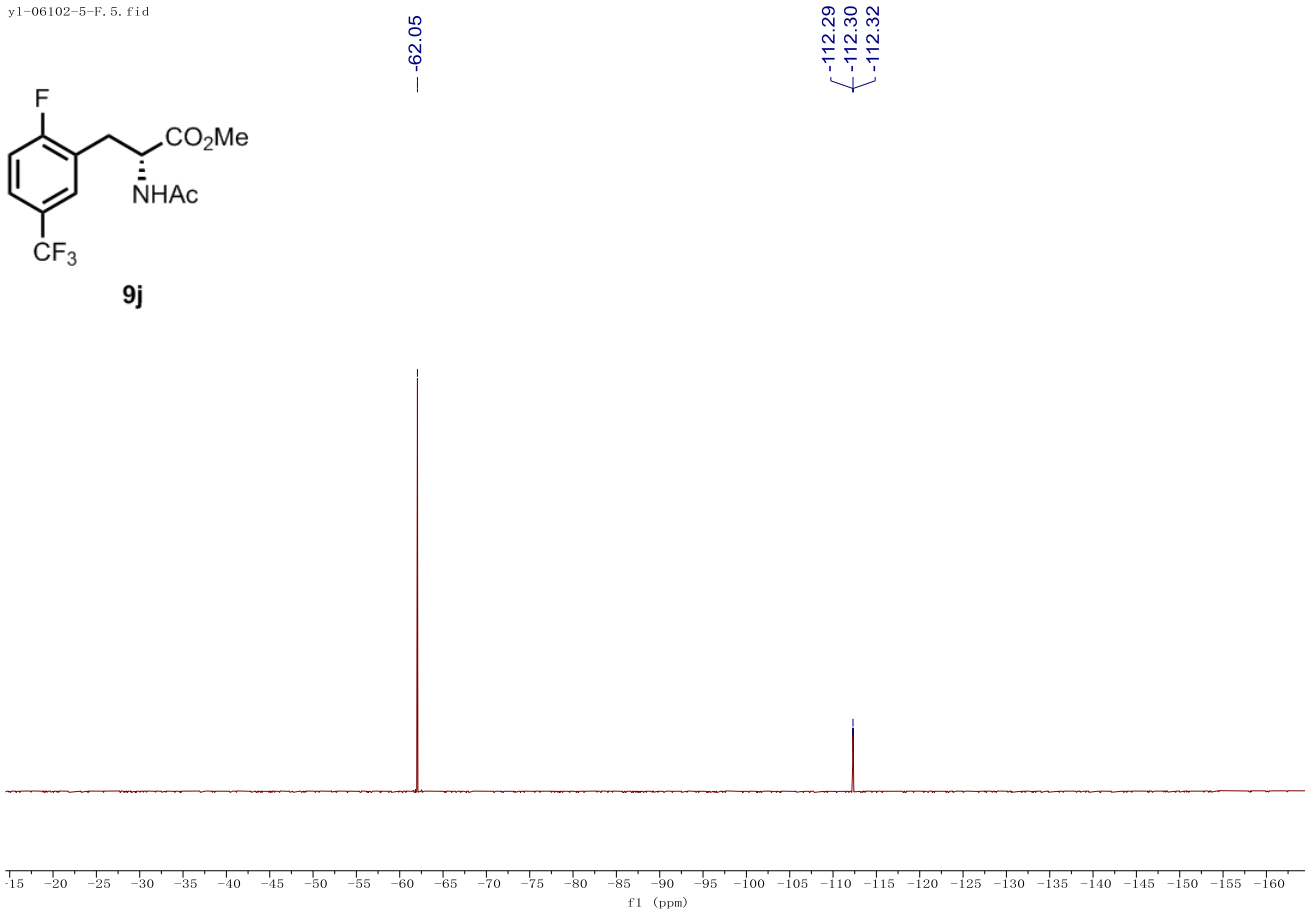
3.11
1.02
1.06
3.01
f1 (ppm)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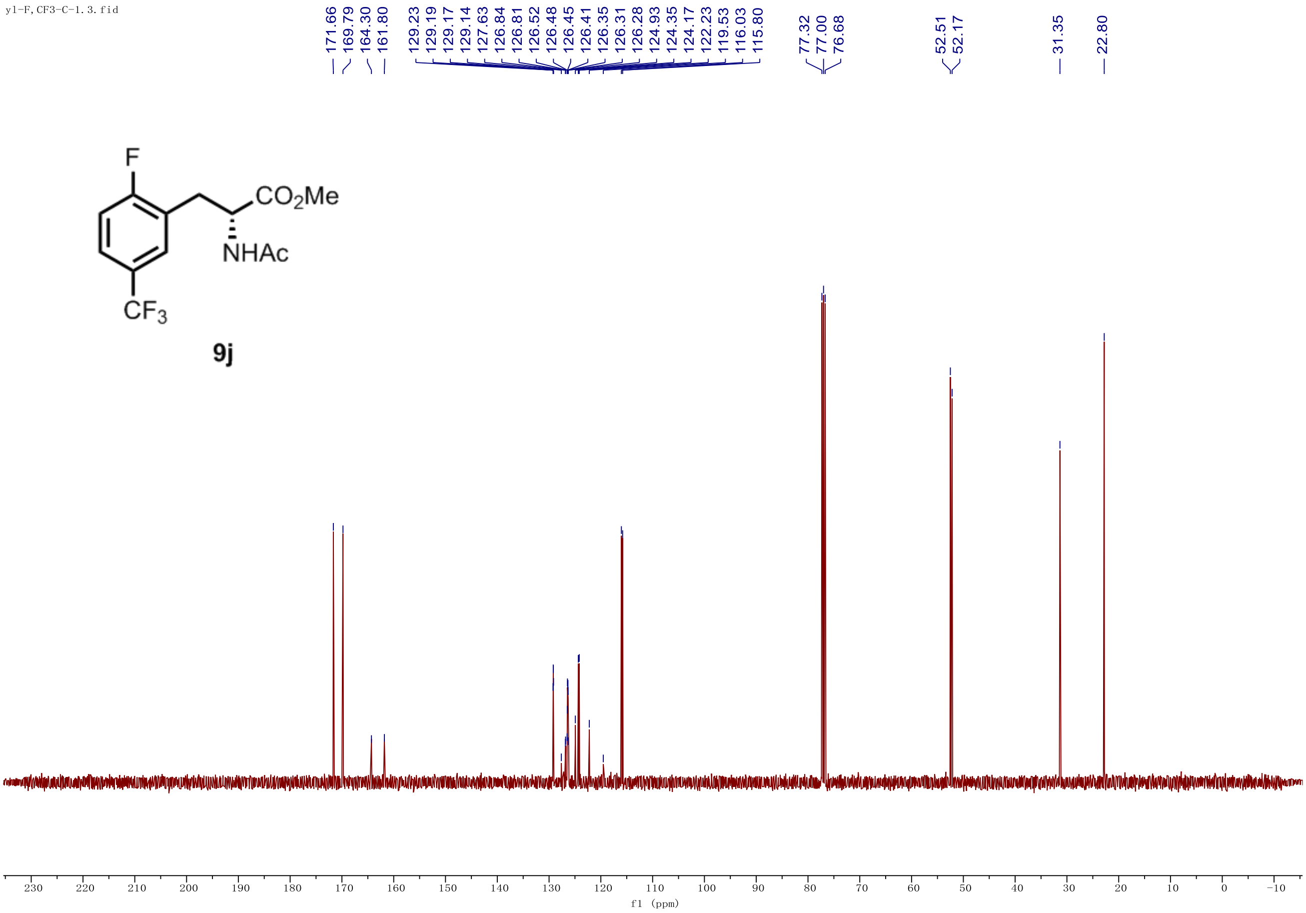
9j
f1 (ppm)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126.45
126.41
126.35
126.31
126.28
124.93
124.35
124.17
122.23
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77.00
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52.17
31.35
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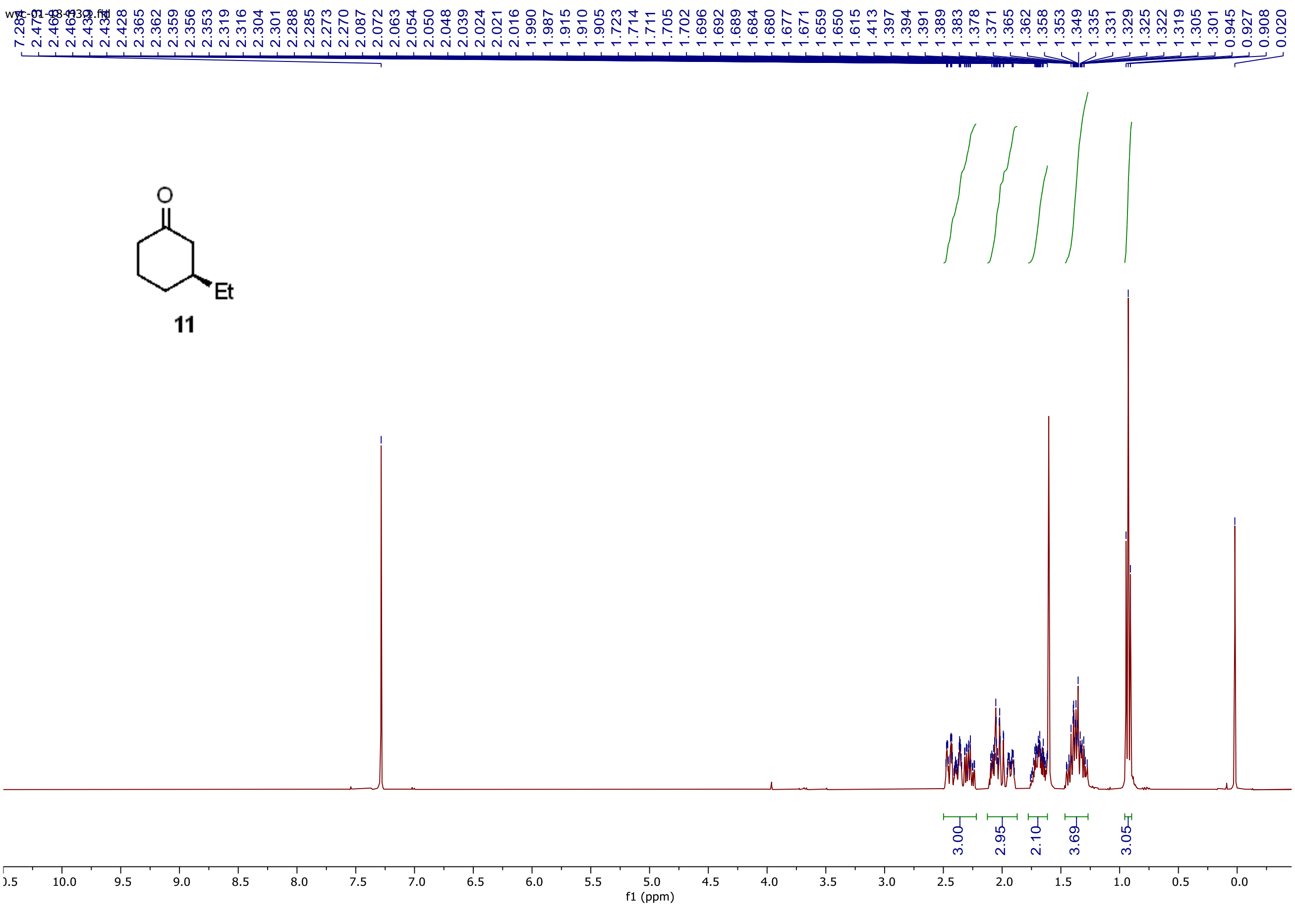
CO2Me
NHAc
CF3
9j
f1 (ppm)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2.087
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2.050
2.048
2.039
2.024
2.021
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1.910
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1.692
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1.671
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1.650
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1.349
1.335
1.331
1.329
1.325
1.322
1.319
1.305
1.301
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0.927
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0.020
O
Et
11
3.00
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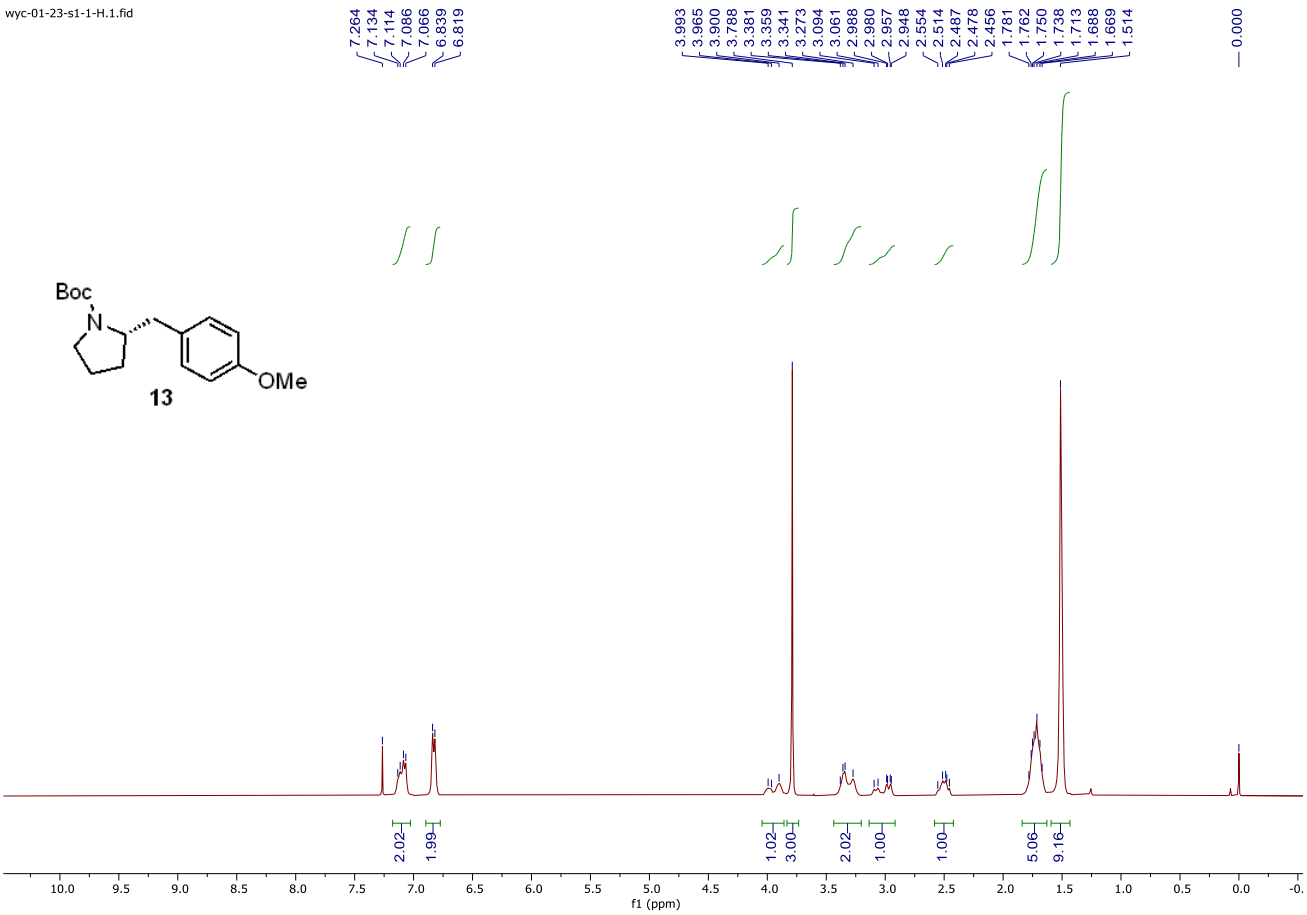
2.10
3.69
3.05
f1 (ppm)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3.273
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3.061
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2.980
2.957
2.948
2.554
2.514
2.487
2.478
2.456
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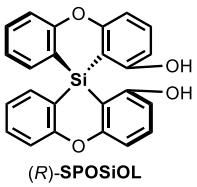
1.762
1.750
1.738
1.713
1.688
1.669
1.514
0.000
Boc
N
OMe
13
2.02
1.99
1.02
3.00
2.02
1.00
1.00
5.06
9.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

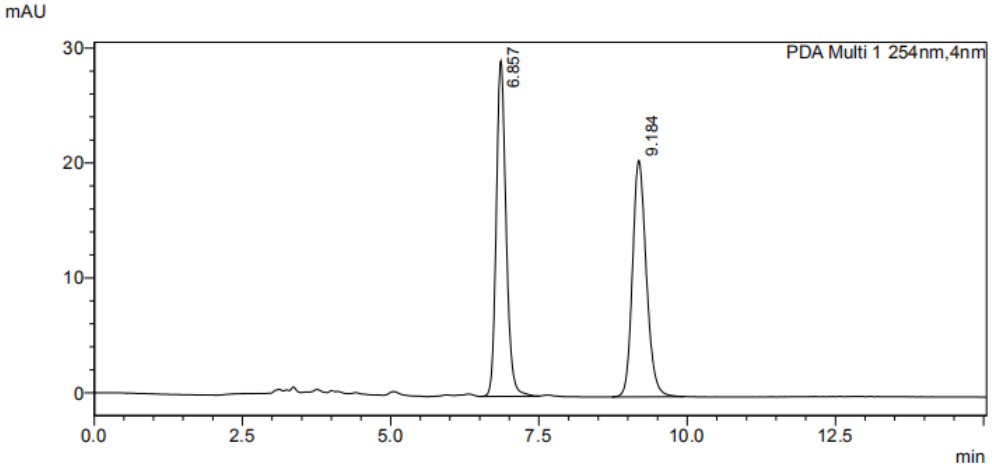
6. HPLC Charts:

(*R*)-9'9-Spirobiphenoxasilin-diol:



(*R*)-**SPOSiOL**

<Chromatogram>

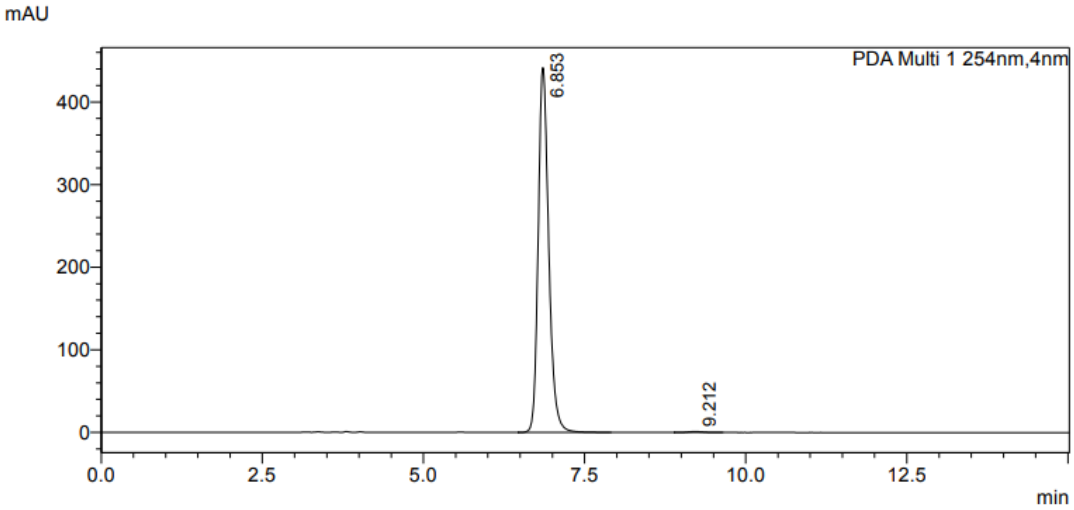


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.857	335950	29178	50.113			
2	9.184	334435	20570	49.887			
Total		670385	49747				

<Chromatogram>

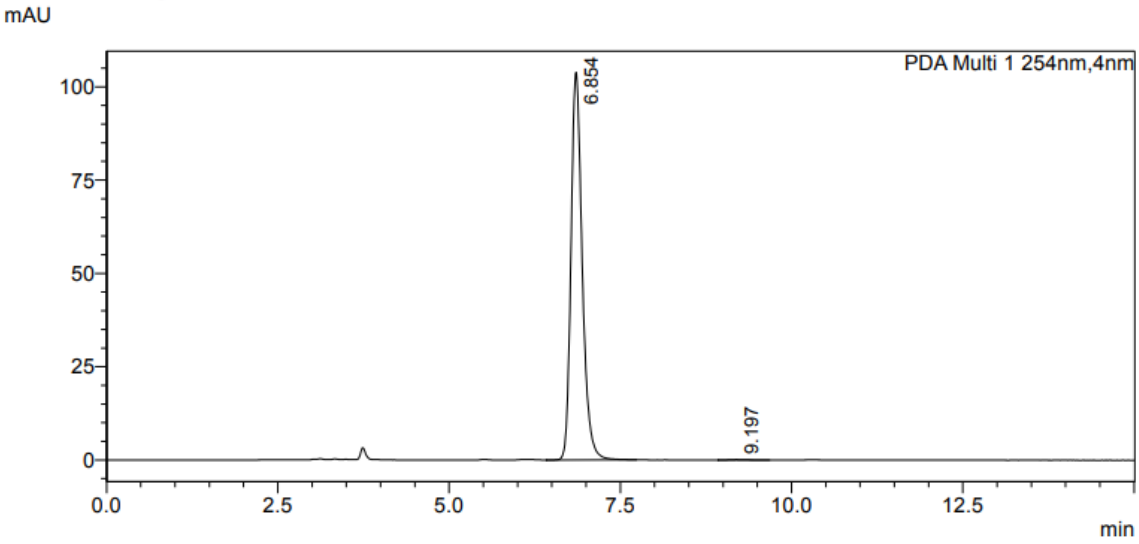


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.853	5022857	441188	99.645			
2	9.212	17902	1113	0.355			
Total		5040759	442301				

<Chromatogram>

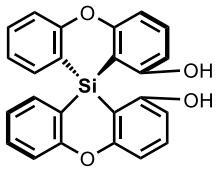


<Peak Table>

PDA Ch1 254nm

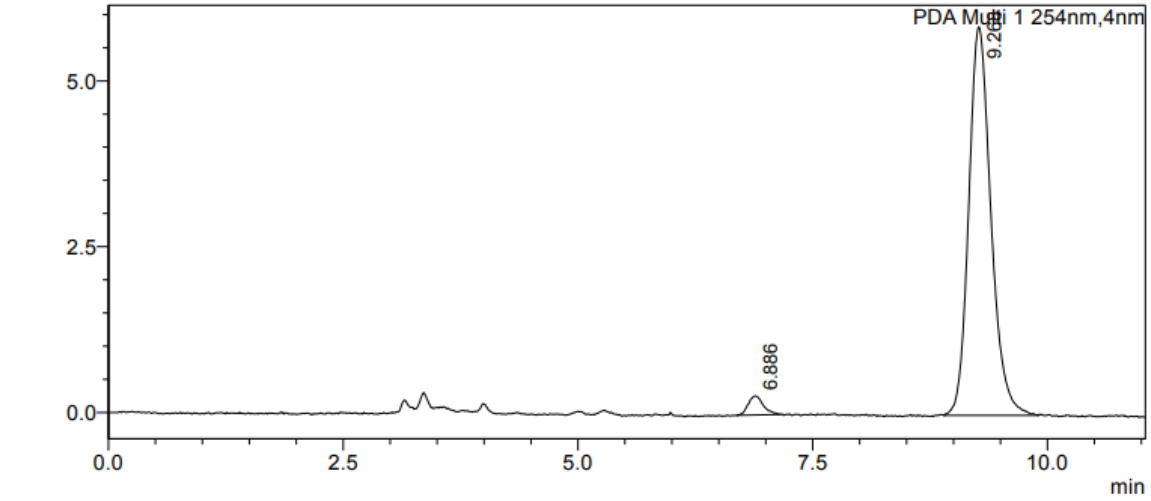
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.854	1187059	103743	99.853			
2	9.197	1743	114	0.147		M	
Total		1188802	103857				

(*S*)-9’9-Spirobiphenoxasilin-diol:



(*S*)-**SPOSiOL**

<Chromatogram>

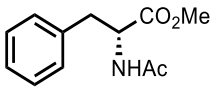


<Peak Table>

PDA Ch1 254nm

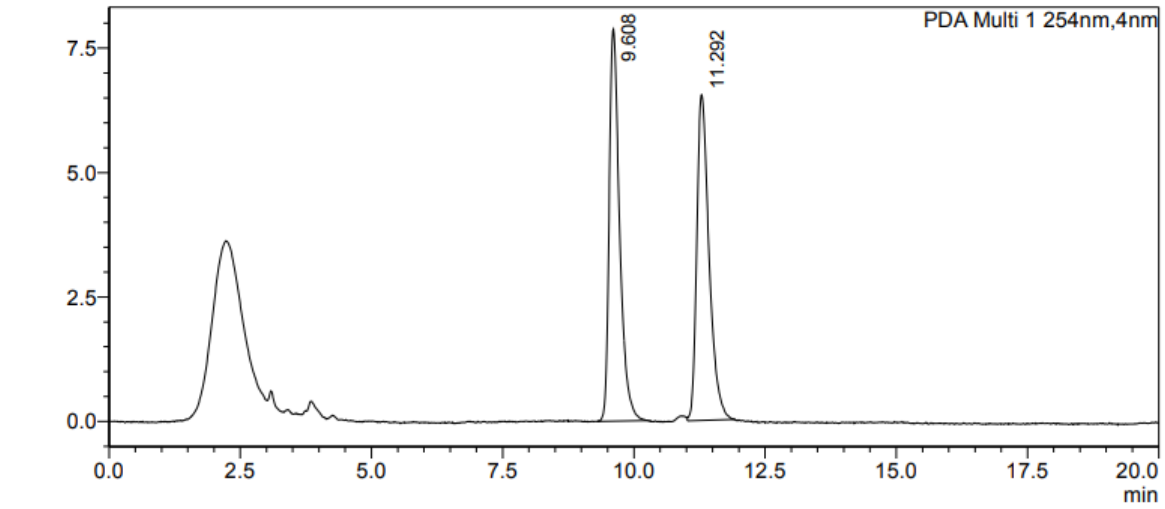
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.886	3172	284	3.188			
2	9.268	96337	5856	96.812			
Total		99509	6140				

Methyl (*R*)-acetylphenylalaninate (9a):



9a

<Chromatogram>

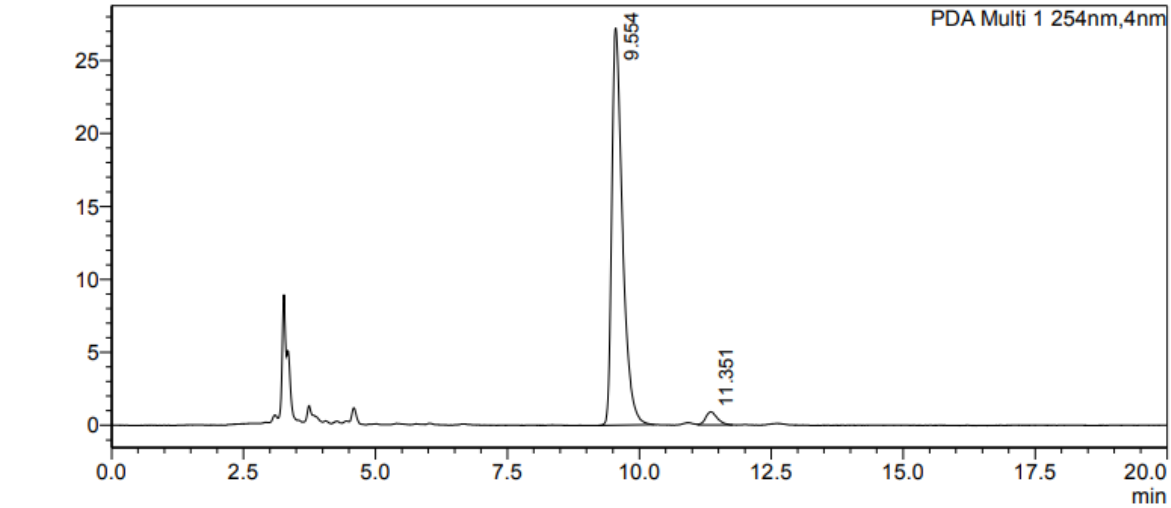


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.608	108715	7874	50.465			
2	11.292	106710	6546	49.535			
Total		215424	14419				

<Chromatogram>

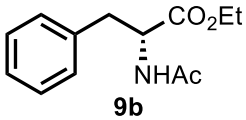


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.554	383670	27219	96.573			
2	11.351	13615	893	3.427			
Total		397285	28112				

Ethyl (*R*)-acetylphenylalaninate (9b):



9b

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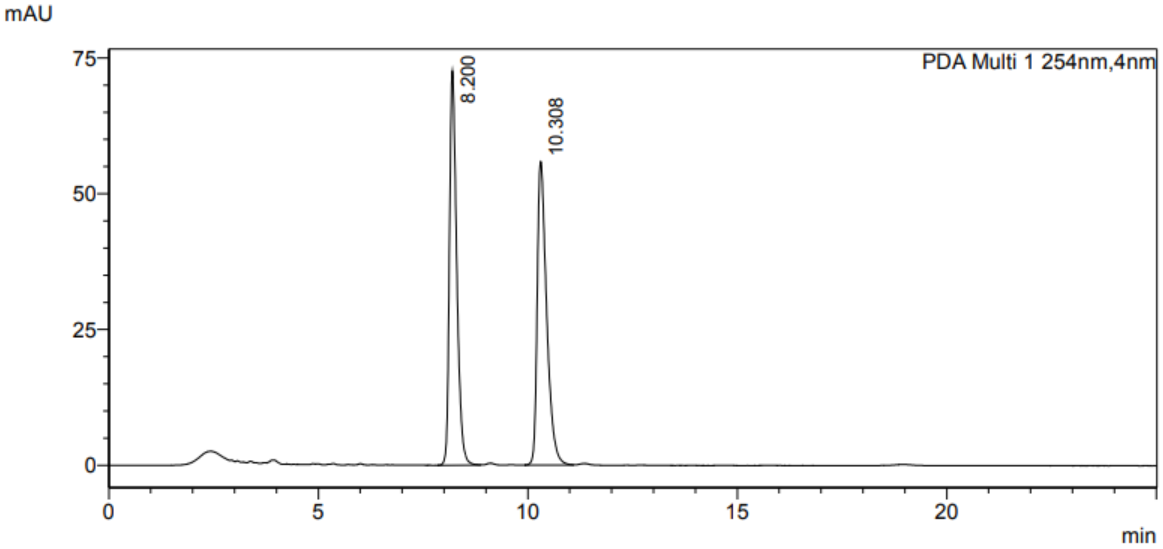
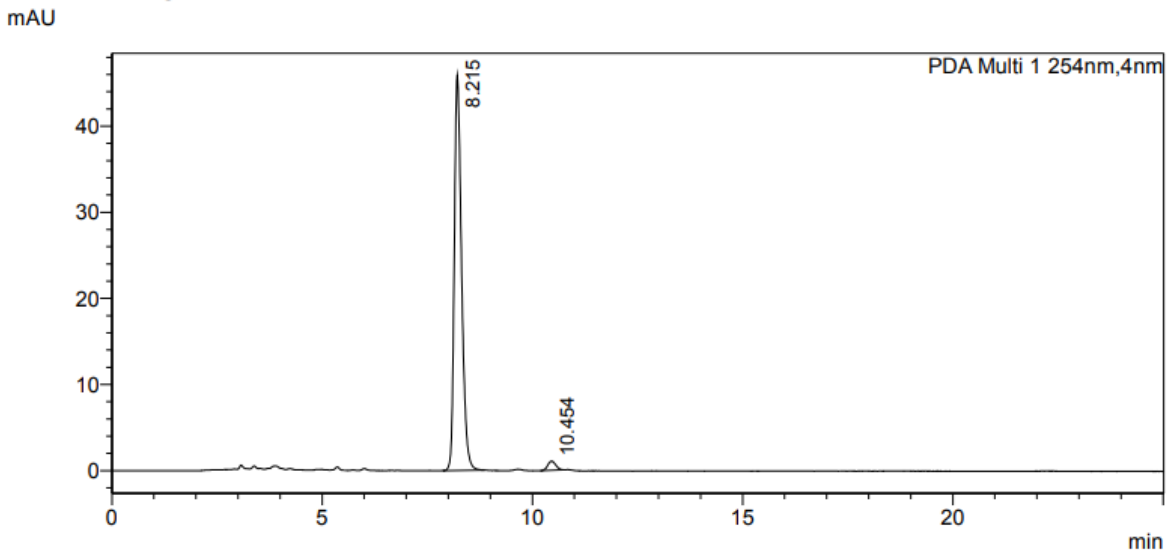


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.200	877916	72584	50.020			
2	10.308	877228	55907	49.980			
Total		1755144	128492				

<Chromatogram>

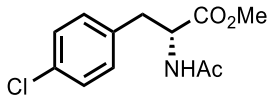


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.215	551635	45854	97.493			
2	10.454	14187	1075	2.507			
Total		565822	46929				

Methyl (*R*)-2-acetamido-3-(4-chlorophenyl)propanoate (9c):



9c

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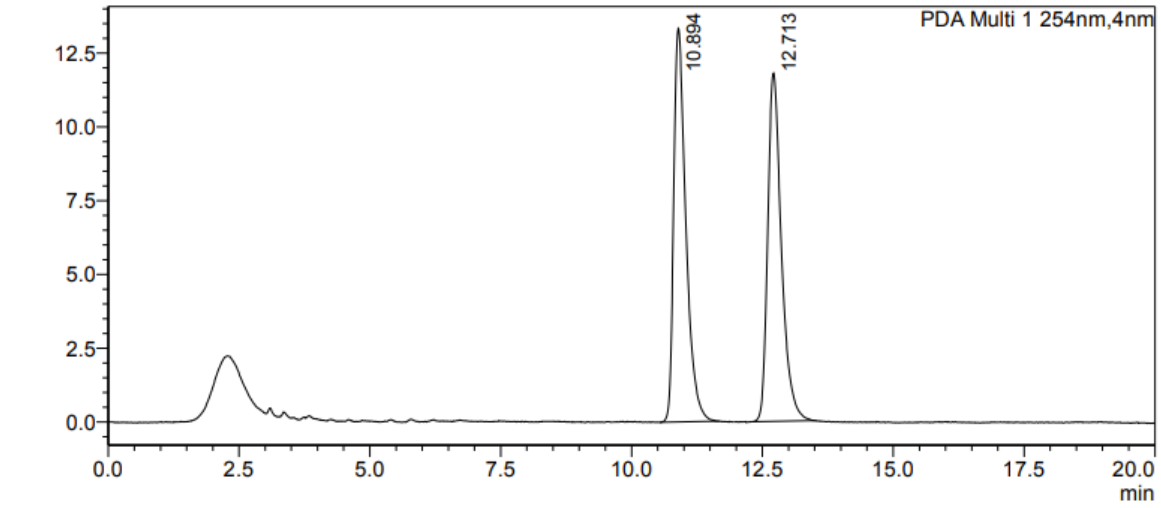

<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.894	216289	13329	50.244			
2	12.713	214188	11790	49.756			
Total		430477	25118				

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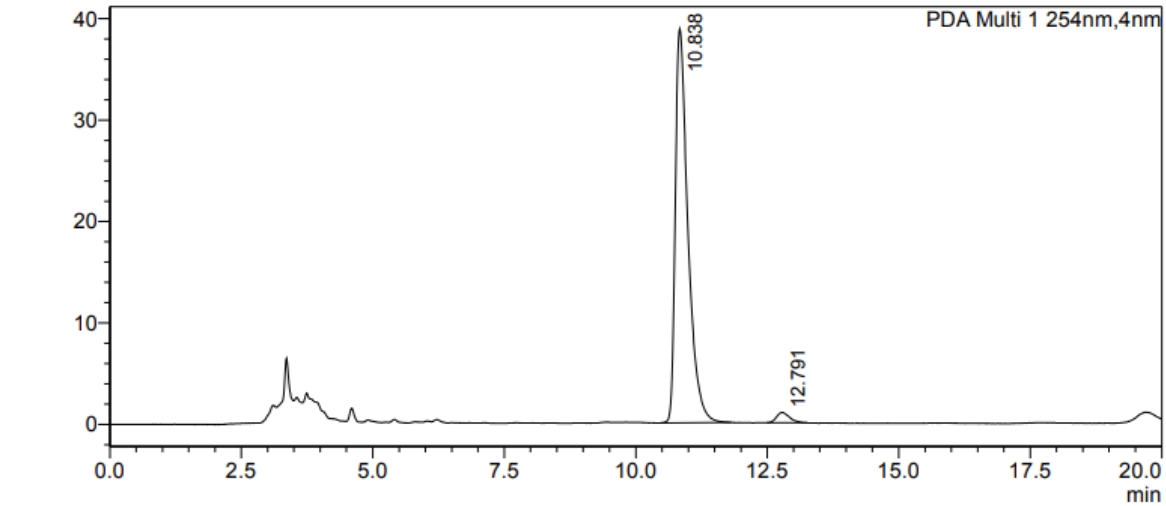
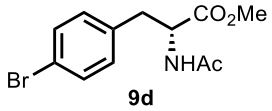


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.838	646966	38822	97.384			
2	12.791	17380	1007	2.616			
Total		664347	39829				

Methyl (*R*)-2-acetamido-3-(4-bromophenyl)propanoate (9d):



9d

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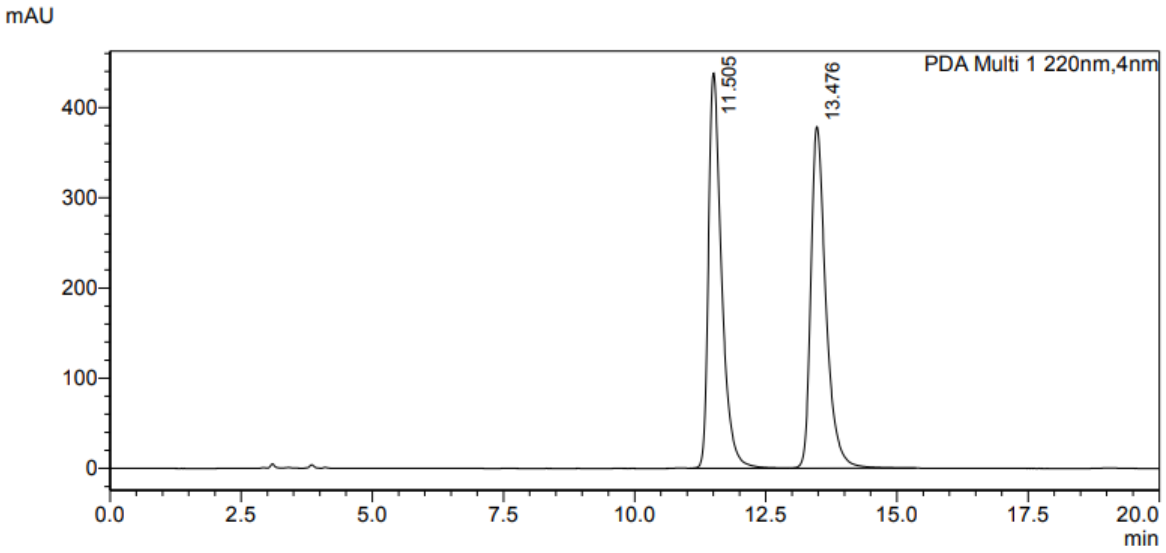
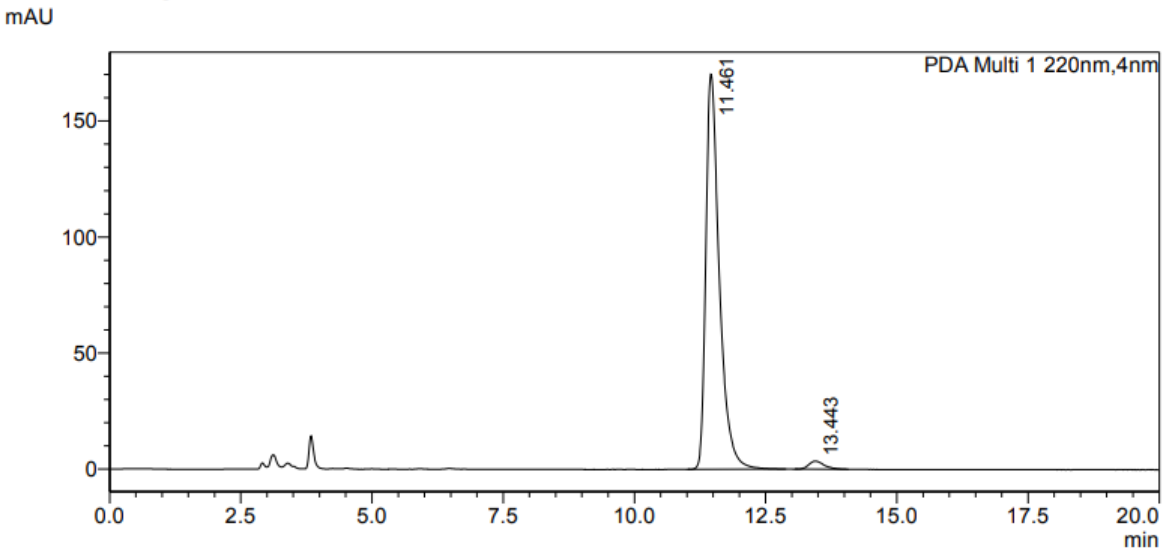


<Peak Table>

PDA Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.505	7609948	438031	50.121		S	
2	13.476	7573254	378620	49.879		V	
Total		15183202	816651				

<Chromatogram>

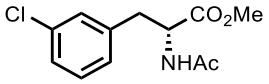


<Peak Table>

PDA Ch1 220nm

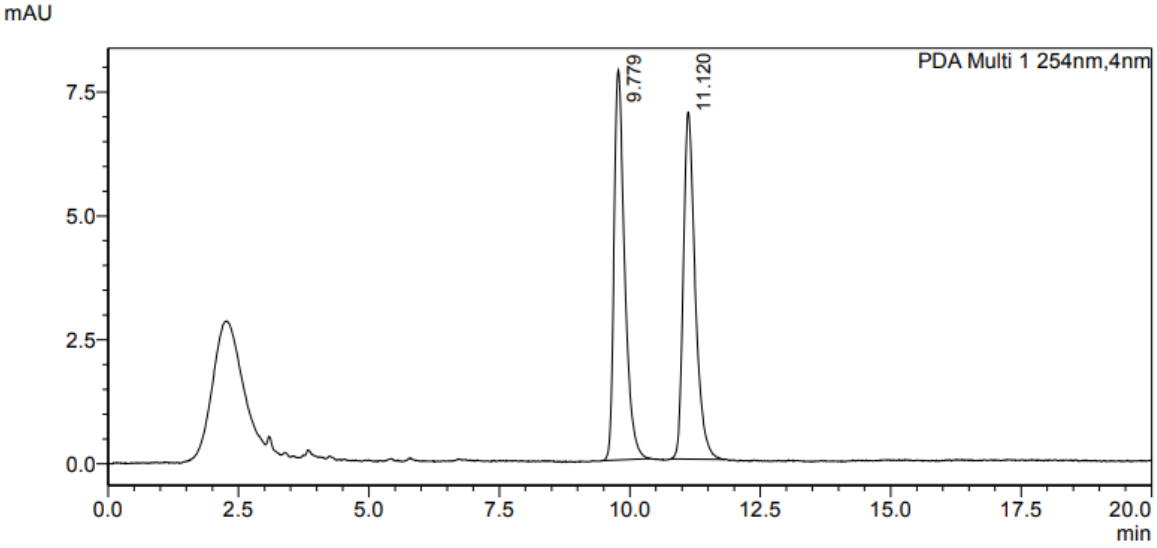
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.461	3051005	170236	97.708			
2	13.443	71571	3490	2.292			
Total		3122577	173726				

Methyl (*R*)-2-acetamido-3-(3-chlorophenyl)propanoate (9e):



9e

<Chromatogram>

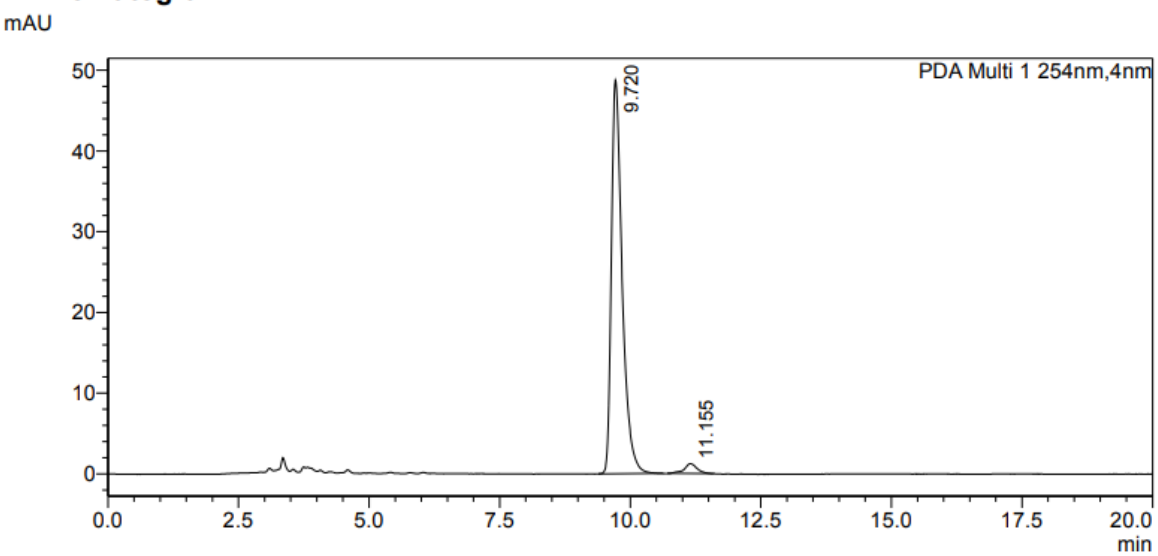


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.779	111367	7865	50.137			
2	11.120	110757	6995	49.863			
Total		222123	14860				

<Chromatogram>

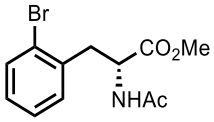


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.720	702681	48737	97.048			
2	11.155	21372	1229	2.952			
Total		724053	49965				

Methyl (*R*)-2-acetamido-3-(2-bromophenyl)propanoate (9f):



9f

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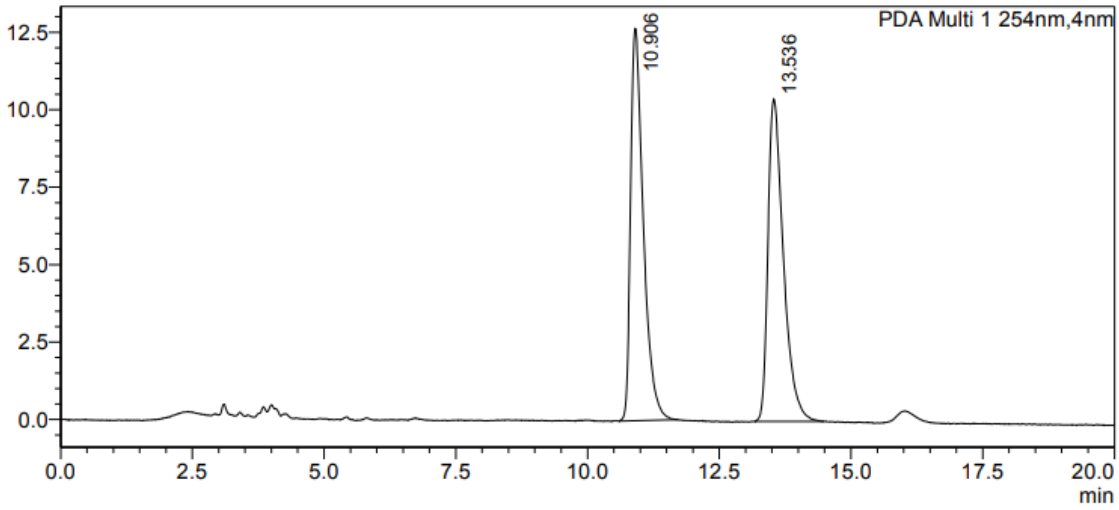

<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.906	213077	12657	50.101			
2	13.536	212220	10396	49.899			
Total		425297	23053				

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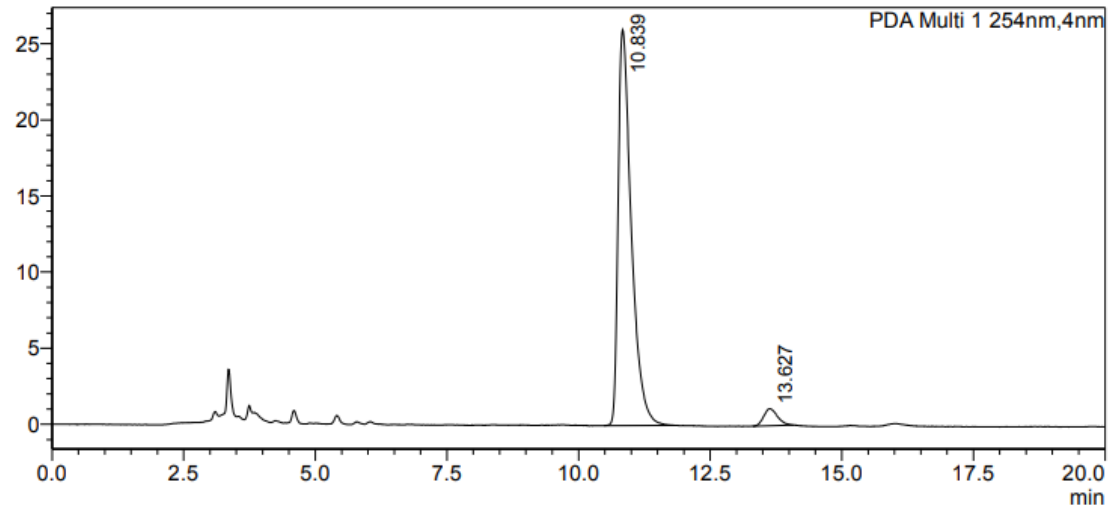
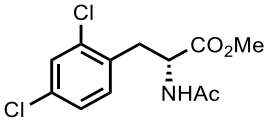


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.839	452502	25994	95.664			
2	13.627	20511	1113	4.336			
Total		473013	27107				

Methyl (*R*)-2-acetamido-3-(2,4-dichlorophenyl)propanoate (9g):



9g

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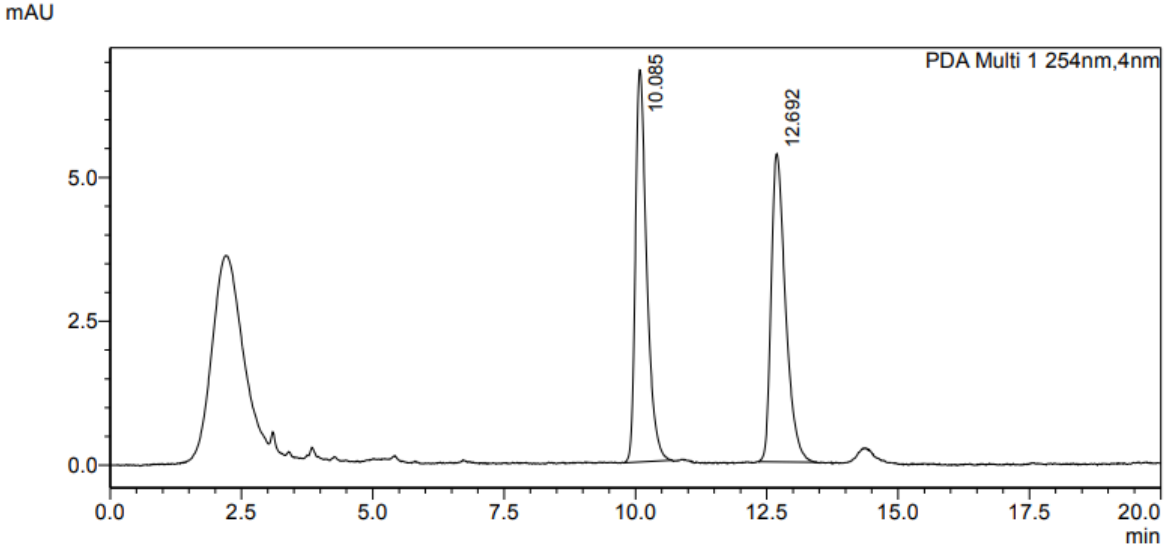

<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.085	102042	6813	50.017			
2	12.692	101972	5358	49.983			
Total		204014	12171				

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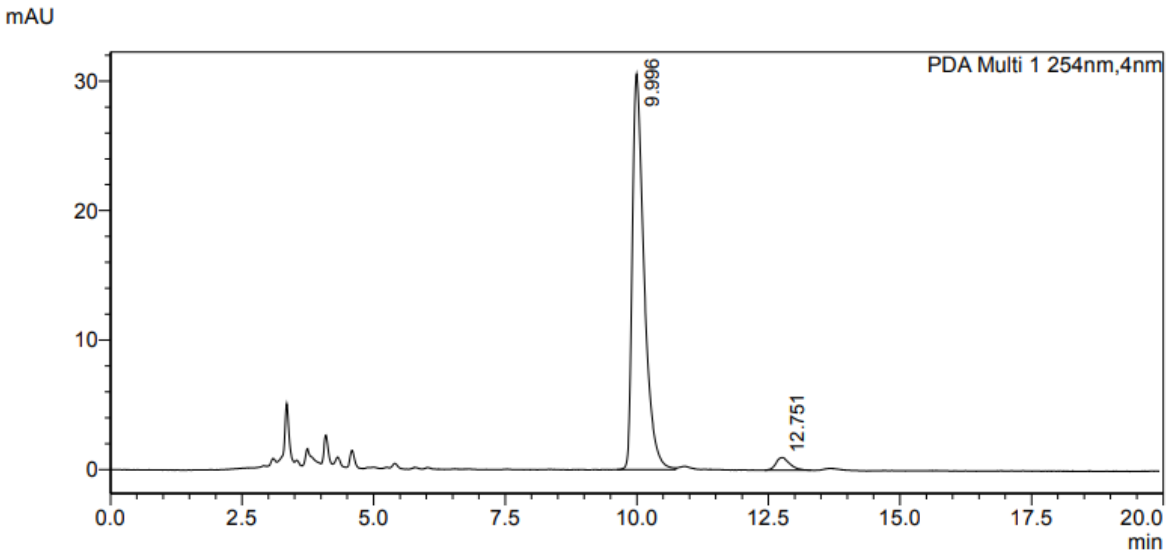
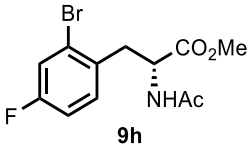


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.996	474860	30526	96.422			
2	12.751	17622	962	3.578			
Total		492482	31488				

Methyl (*R*)-2-acetamido-3-(2-bromo-4-fluorophenyl)propanoate (9h):



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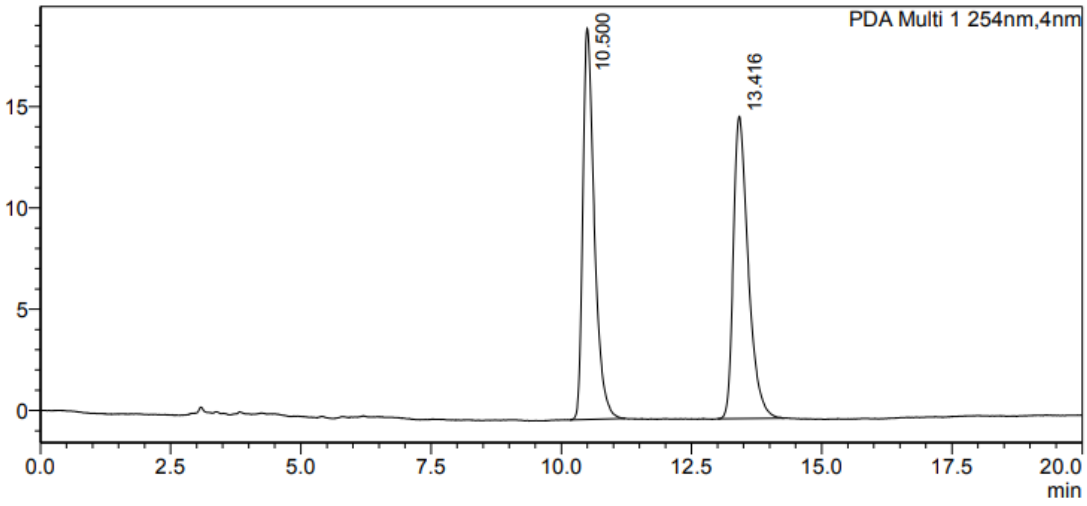

<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.500	297037	19298	50.033			
2	13.416	296650	14918	49.967			
Total		593687	34216				

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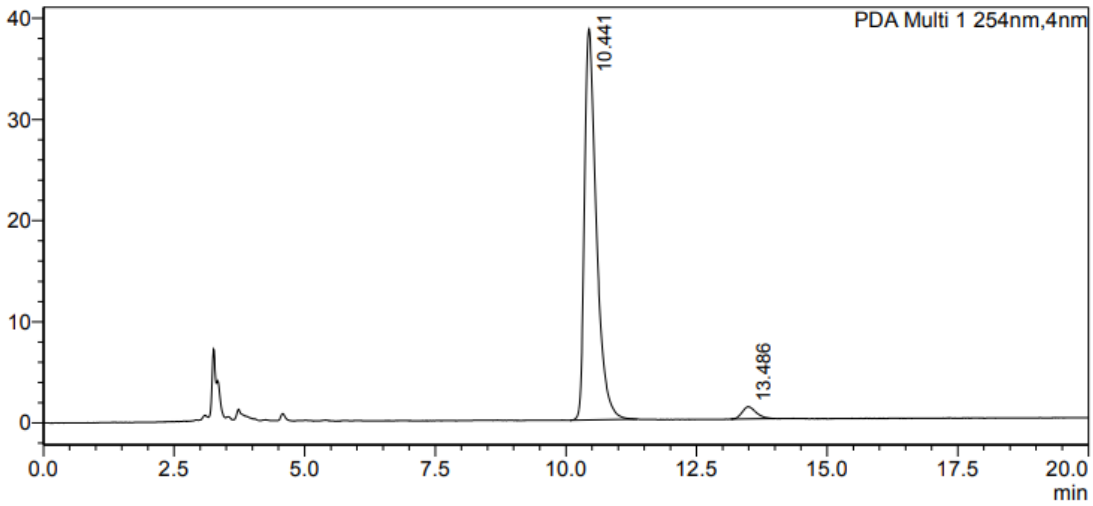
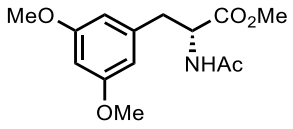


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.441	611751	38612	96.501			
2	13.486	22183	1193	3.499			
Total		633934	39805				

Methyl (*R*)-2-acetamido-3-(3,5-dimethoxyphenyl)propanoate (9i):



9i

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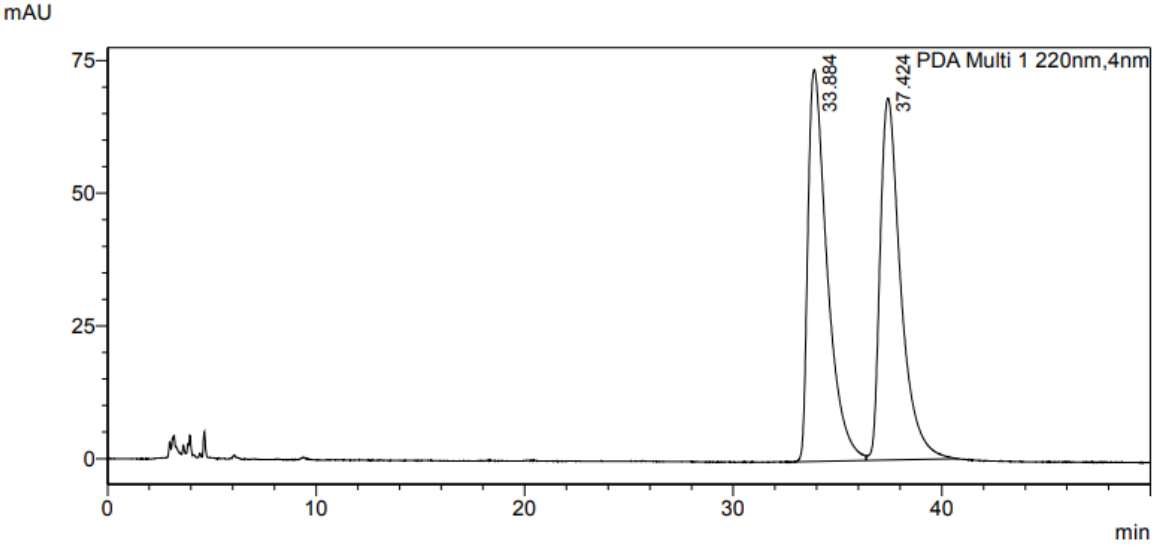
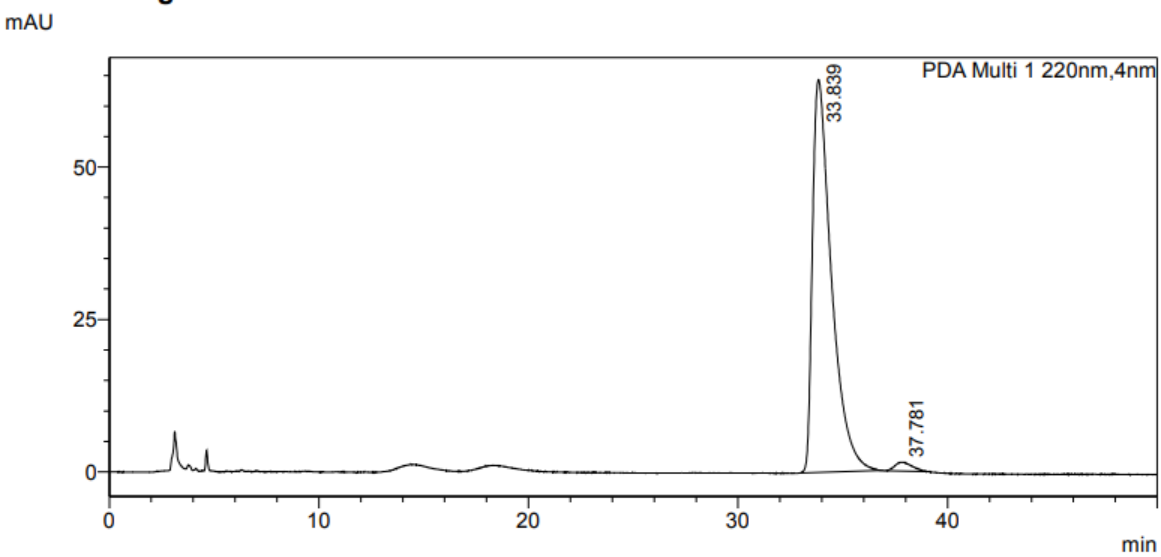


<Peak Table>

PDA Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	33.884	4738955	73832	50.252			
2	37.424	4691346	68218	49.748		SV	
Total		9430301	142051				

<Chromatogram>

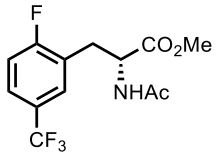


<Peak Table>

PDA Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	33.839	4063897	64416	98.004		S	
2	37.781	82764	1451	1.996			
Total		4146661	65867				

Methyl (*R*)-2-acetamido-3- (2-fluoro-5-(trifluoromethyl)phenyl)propanoate (9i):



9j

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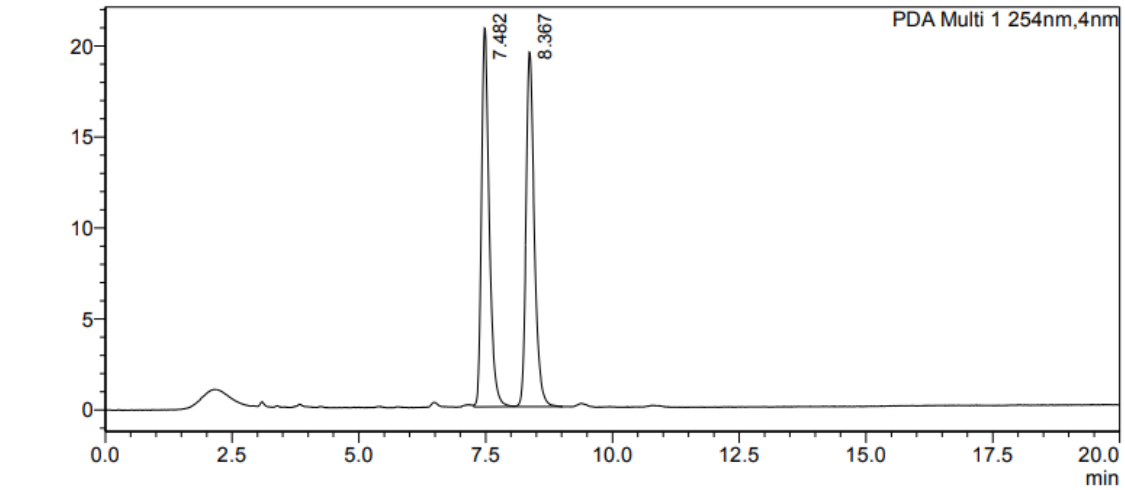
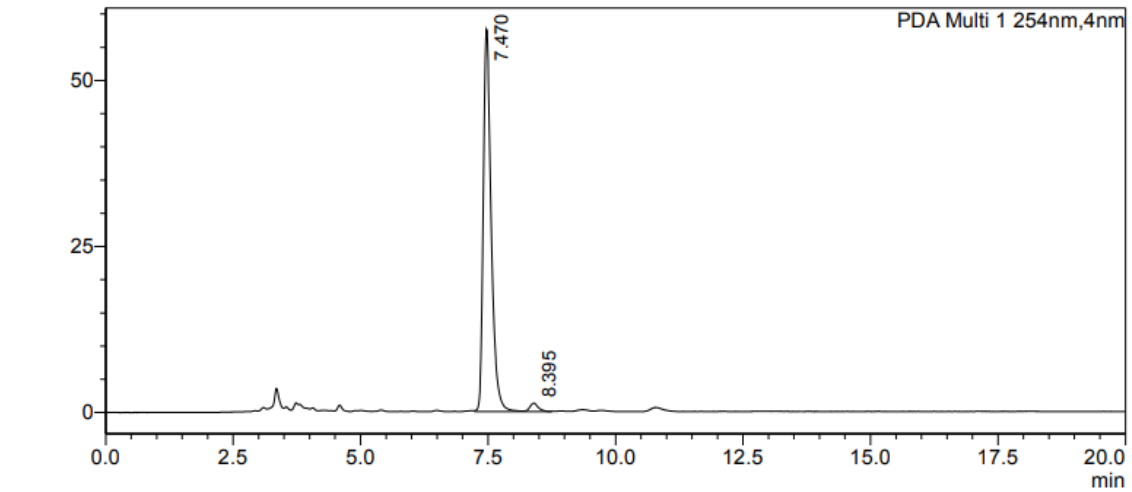


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.482	221433	20795	49.977			
2	8.367	221635	19479	50.023		V	
Total		443068	40273				

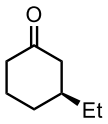
<Chromatogram>



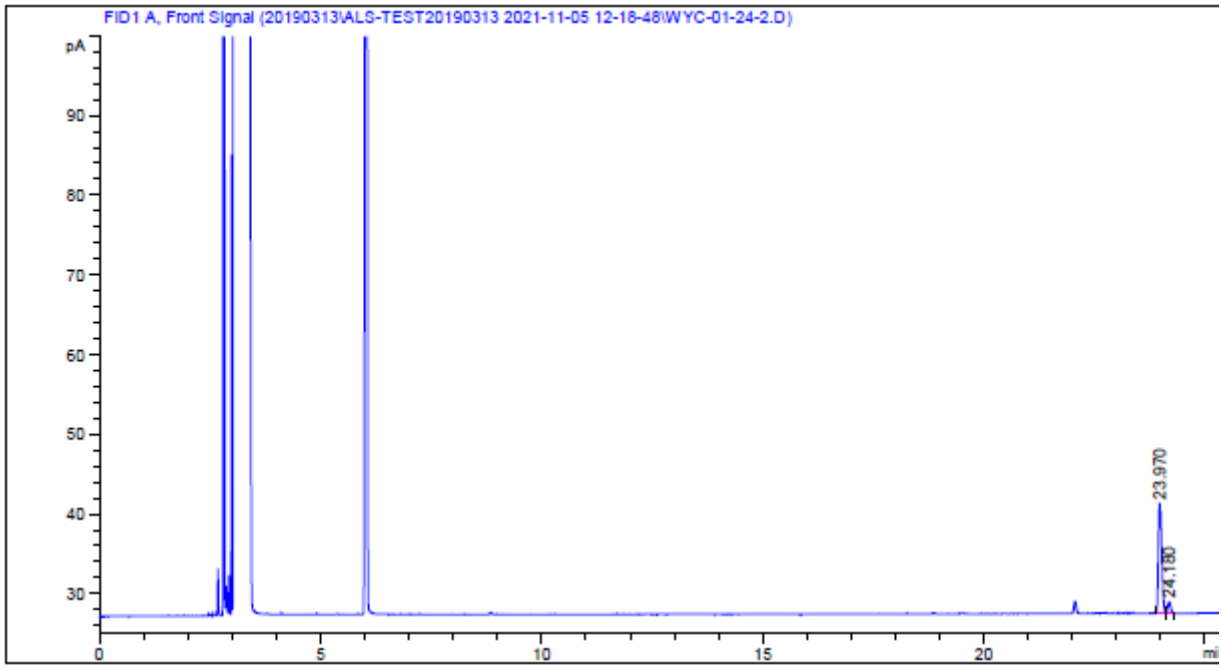
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.470	618492	57514	97.756			
2	8.395	14197	1251	2.244		V	
Total		632688	58765				



11

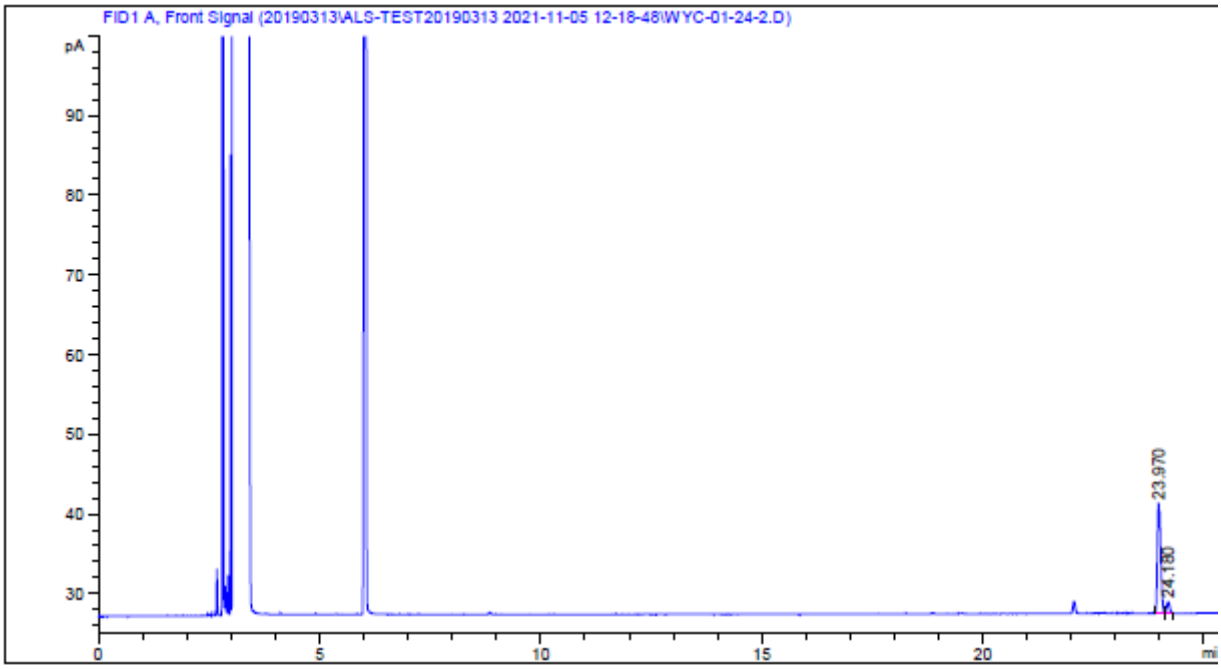



```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  23.970 BV    0.0726   67.38173   13.75987 90.41273
   2  24.180 VB    0.0736    7.14509    1.47174  9.58727
```




```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  23.970 BV    0.0726   67.38173   13.75987 90.41273
   2  24.180 VB    0.0736    7.14509    1.47174  9.58727
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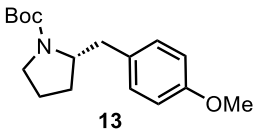

13

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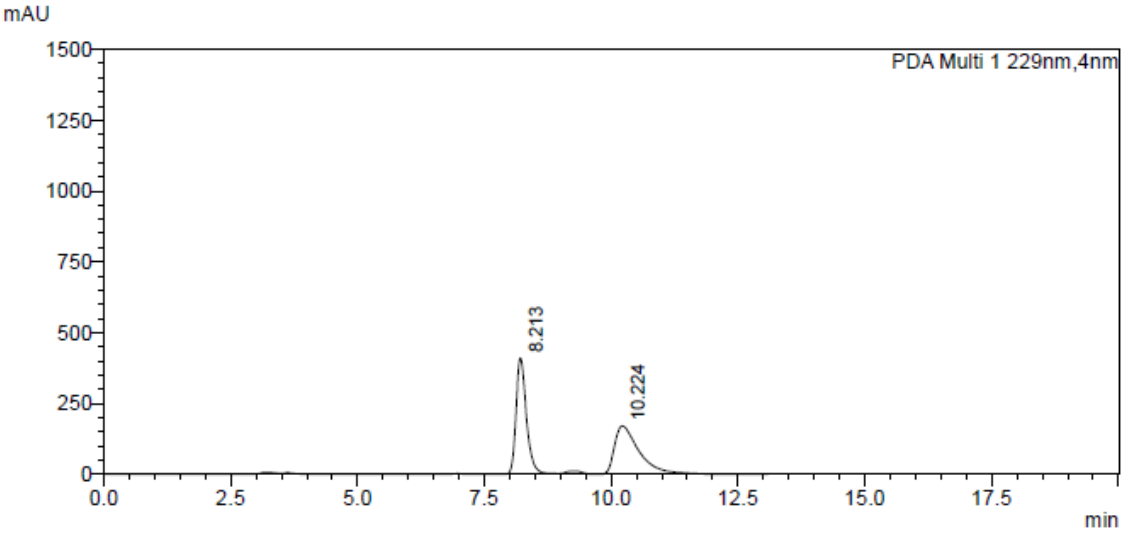
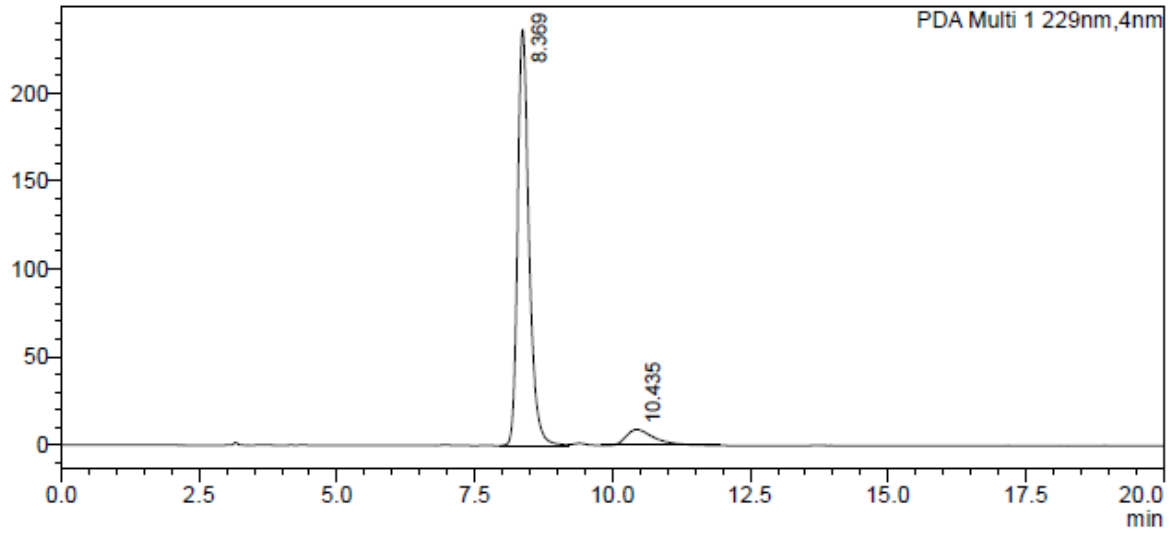


<Peak Table>

PDA Ch1 229nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.213	5894532	411065	50.115			
2	10.224	5867520	170671	49.885		M	
Total		11762052	581736				

<Chromatogram>



<Peak Table>

PDA Ch1 229nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.369	3400611	236194	91.341		M	
2	10.435	322362	8991	8.659			
Total		3722973	245185				