Supporting Information for

Lewis acid-catalyzed regioselective synthesis of chiral α-fluoroalkyl amines *via* asymmetric addition of silyl dienolates to fluorinated sulfinylimines

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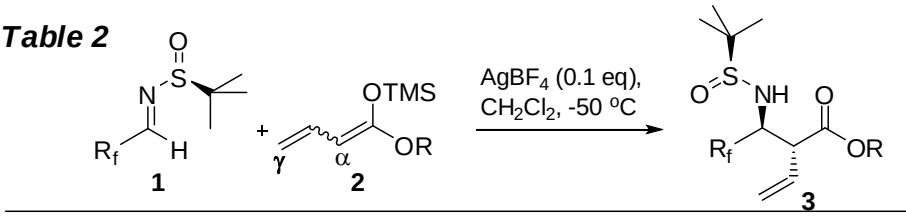
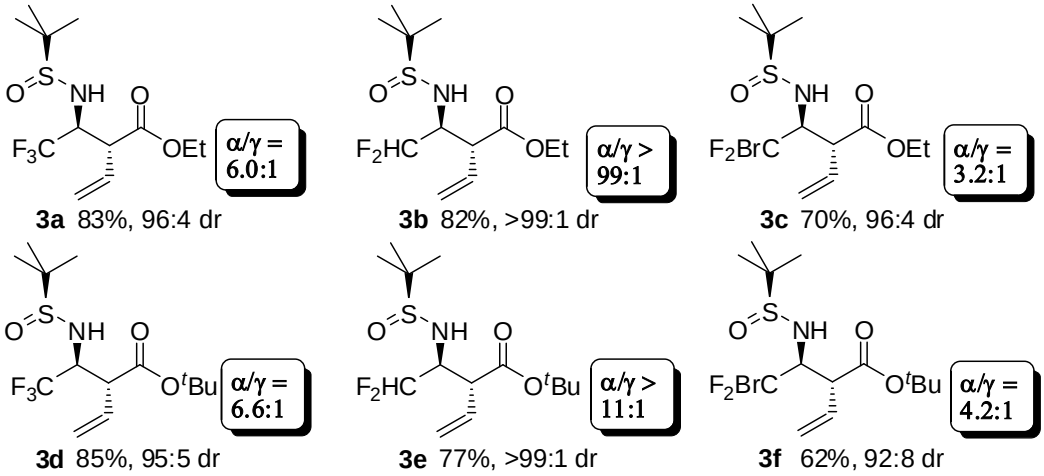
1. General Remarks

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; J-values are in Hz. Mass spectra were recorded by EI methods, and HRMS was measured on a Finnigan MA+ mass spectrometer. THF and toluene were distilled from sodium (Na) under argon (N_2) atmosphere. CH_3CN and 1,2-dichloromethane were distilled from CaH_2 under argon (Ar) atmosphere. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF 254 silica gel coated plates. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure.

2. The regioselectivities in Table 2 and 3

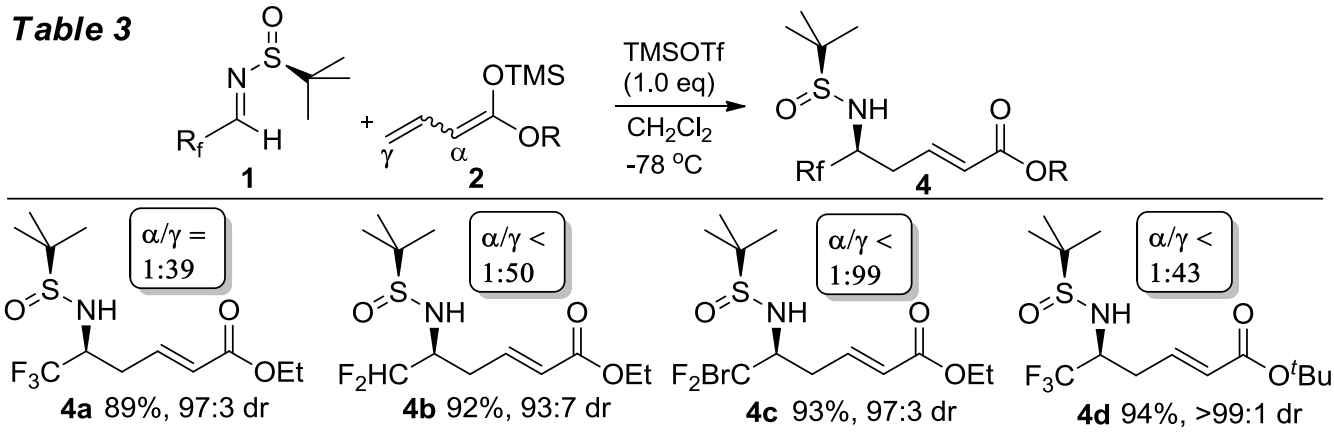
Table 2





3a 83%, 96:4 dr **3b** 82%, >99:1 dr **3c** 70%, 96:4 dr

3d 85%, 95:5 dr **3e** 77%, >99:1 dr **3f** 62%, 92:8 dr



3. Preparation of Substrates 1a, 2a, 2b.

(S,E)-2-methyl-N-(2, 2, 2-trifluoroethylidene)propane-2-sulfinamide **1a** was prepared according to the procedure of Mimura.[1] Substrates **2a** and **2b** were prepared using a literature procedure.[2]

4. General procedure for the synthesis of fluorinated aldimines 1b and 1c:

Ethyl 2, 2-difluoroacetate or ethyl 2-bromo-2,2-difluoroacetate (30 mmol) were dissolved in Et_2O (5 mL) and then this solution was added slowly to a solution of $LiAlH_4$ (342 mg, 9 mmol) in Et_2O (20 mL) at –78 °C for 10 min. After addition, the reaction mixture was stirred for 12 h at –78 °C. Then, concentrated sulfuric acid (1.4 mL) and ice water (40 mL) was added successively after the reaction mixture was warmed to 0 °C. The resulting mixture was extracted with ether (3 × 50 mL), washed with saturated NaCl solution and dried over anhydrous Na_2SO_4. After removal of the solvent, the crude product was added to a solution of (S)-*N*-*tert*-butanesulfinamide (3.8 mL, 30 mmol) in toluene, and the resulted mixture was refluxed to remove water by azeotropic distillation unitil no water was separated. After removal of toluene under reduced pressure, the residue was purified by distillation for **1b** and **1c** (the imines had only verified by ^{1}HNMR and ^{19}FNMR because of the instability).

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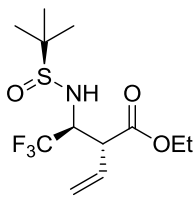
1) H. Mimura, K. Kawada, T. Yamashita, T. Sakamoto and Y. Kikugawa, *J. Fluorine Chem.*, 2010, **131**, 477; 2) B. Bazán-Tejeda, G. Bluet, G. Broustal and J-M. Campagne, *Chem. Eur. J.* 2006, **12**, 8358.

(S,Z)-N-(2,2-difluoroethylidene)-2-methylpropane-2-sulfinamide (1b). Colourless oil (40 %); bp 56-58 °C/3.8 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16–7.97 (m, 1H), 6.42–6.11 (m, 1H), 1.24 (s, 9H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -118.88 – -119.97 (m, 1F), -120.98 (ddd, *J* = 329.3, 54.5, 3.0 Hz, 1F).

(S,E)-N-(2-bromo-2,2-difluoroethylidene)-2-methylpropane-2-sulfinamide (1c). Colourless oil (21 %); bp 64-67 °C/2.9 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (t, *J* = 5.0 Hz, 1H), 1.27 (s, 9H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -56.14 (dd, *J* = 158.0, 4.7 Hz, 1F), -56.81 (dd, *J* = 158.0, 5.6 Hz, 1F).

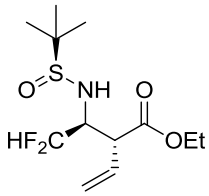
5. General Procedure for the Synthesis of α-vinyl-β-trifluoromethyl-β-amino ester 3.

$AgBF_4$ (9.7 mg, 0.05 mmol) and fluorinated aldimine **1a** (100 mg, 0.5 mmol) were charged in a dried tube under nitrogen, followed by addition of CH_2Cl_2 (1.0 mL). The solution was cooled to -50 ℃, and the dienolate **2b** (112mg, 0.6 mmol) in CH_2Cl_2 (1mL) was added. After stirring for indicated time, brine (4 mL) was added, followed by extraction with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried with Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel to afford product **3a**. The ratio of diastereomers was determined by ^{19}F or ^{1}H NMR of the crude reaction mixture.

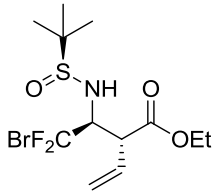


(R)-ethyl 2-((S)-1-((S)-1,1-dimethylethylsulfinamido)-2,2,2-trifluoroethyl)but-3-enoate (3a). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a pale yellow solid (83%): mp 60–61℃; [α]$_D$16.2 + 282.2 (c 0.40, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (dt, *J* = 18.0, 9.1 Hz, 1H), 5.34 (s, 1H), 5.30 (d, *J* = 7.0 Hz, 1H), 4.57 (d, *J* = 10.6 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.08–3.91 (m, 1H), 3.50 (dd, *J* = 8.3, 5.2 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 131.0, 124.4 (q, *J* =

284.4 Hz), 120.6, 61.6, 60.0 (q, J = 29.8 Hz), 57.5, 49.9, 22.5, 13.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ -72.17 (d, J = 7.3 Hz, 3F). IR $(KBr)_{max}$ 3276, 3088, 2979, 2868, 1733, 1637, 1466, 1268, 1182, 1125, 923 cm^{-1}; MS (EI) m/z 316.0 M^+; HRMS (EI) m/z M^+ calcd for $C_{12}H_{21}F_3N_1O_3S_1$, 316.1189; Found, 316.1190.

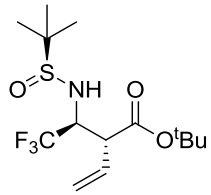


(R)-ethyl 2-((S)-1-((S)-1,1-dimethylethylsulfinamido)-2,2-difluoroethyl)but-3-enoate (3b). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a white solid (82%): mp 71–72℃; [α]$_D$13.8 +205.2 (c 0.69, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 (td, J = 55.2, 2.0 Hz, 1H), 5.95–5.81 (m, 1H), 5.35 (d, J = 11.7 Hz, 1H), 5.32 (d, J = 4.7 Hz, 1H), 4.32 (d, J = 10.7 Hz, 1H), 4.26–4.09 (m, 2H), 3.80 (dtdd, J = 17.1, 10.7, 6.5, 2.0 Hz, 1H), 3.48 (dd, J = 8.5, 6.6 Hz, 1H), 1.30 (t, J = 7.1 Hz, 3H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 131.6, 120.4, 115.2 (t, J = 247.1 Hz), 61.4, 60.4 (t, J = 22.3 Hz), 57.0, 49.6 (d, J = 3.3 Hz), 22.7, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.42 (ddd, J = 286.3, 54.8, 10.6 Hz, 1F), -129.18 (ddd, J = 286.2, 55.3, 16.8 Hz, 1F). IR $(KBr)_{max}$ 3219, 3105, 2977, 2868, 1732, 1465, 1373, 1262, 1175, 1063, 928 cm^{-1}; MS (EI) m/z 320.1 $[M + Na]^+$; HRMS (EI) m/z $[M + Na]^+$ calcd for $C_{12}H_{21}F_2N_1Na_1O_3S_1$, 320.1102; Found, 320.1103.

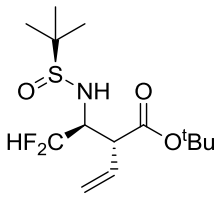


(R)-ethyl 2-((S)-2-bromo-1-((S)-1,1-dimethylethylsulfinamido)-2,2-difluoroethyl)but-3-enoate (3c). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a white solid (70%): mp 58–60℃; [α]$_D$12.5 + 208.9 (c 0.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97–5.75 (m, 1H), 5.33 (dd, J = 13.1, 9.4 Hz, 2H), 4.66 (d, J = 10.4 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 4.03–3.93 (m, 1H), 3.65 (d, J = 5.1 Hz, 1H), 1.30 (t, J = 7.1 Hz, 3H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 131.4, 123.5 (t, J = 313.5 Hz), 120.6, 66.9 (t, J = 22.8 Hz), 61.77, 57.7, 51.4, 22.7, 14.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -49.87 (d, J = 8.2 Hz, 2F). IR $(KBr)_{max}$ 3220, 2972, 1730, 1466, 1374, 1292, 1181, 1089, 1023, 928, 744 cm^{-1}; MS (EI) m/z

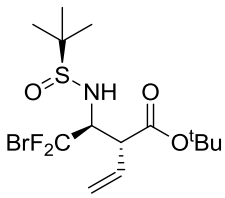
398.0 $[M+Na]^+$; HRMS (EI) m/z $[M+Na]^+$ calcd for $C_{12}H_{20}Br_1F_2N_1Na_1O_3S_1$, 398.0208; Found, 398.0218.



(R)-tert-butyl 2-((S)-1-((S)-1,1-dimethylethylsulfinamido)-2,2,2-trifluoroethyl)but-3-enoate (3d). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a yellow solid (85%): mp 64–65℃; $[\alpha]_D$16.8 + 26.6 (c 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dt, *J* = 17.7, 9.0 Hz, 1H), 5.25 (s, 1H), 5.22 (d, *J* = 7.4 Hz, 1H), 4.76 (d, *J* = 10.6 Hz, 1H), 3.95–3.77 (m, 1H), 3.33 (dt, *J* = 49.0, 24.5 Hz, 1H), 1.39 (s, 9H), 1.19 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 131.6, 124.5 (q, *J* = 284.6 Hz), 120.1, 82.5, 60.0 (q, *J* = 29.9 Hz), 57.5, 49.9, 27.7, 22.6. ^{19}F NMR (377 MHz, $CDCl_3$) δ -72.38 (d, *J* = 7.4 Hz, 3F). IR $(KBr)_{max}$ 3367, 2980, 2937, 1689, 1466, 1397, 1307, 1235, 1038, 937, 639 cm^{-1}; MS (EI) m/z 366.1 [M + Na]$^+$; HRMS (EI) m/z $[M+Na]^+$ calcd for $C_{14}H_{24}F_3N_1Na_1O_3S_1$, 366.1321; Found, 366.1330.



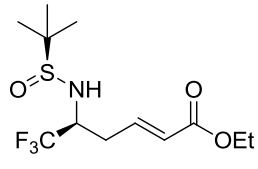
(R)-tert-butyl 2-((S)-1-((S)-1,1-dimethylethylsulfinamido)-2,2-difluoroethyl)but-3-enoate (3e). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a yellow solid (77%): mp 78–80℃; $[\alpha]_D$18.3 +348.0 (c 0.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (t, *J* = 55.2 Hz, 1H), 5.92–5.78 (m, 1H), 5.31 (d, *J* = 10.5 Hz, 1H), 5.28 (d, *J* = 6.4 Hz, 1H), 4.48 (d, *J* = 10.6 Hz, 1H), 3.72 (d, *J* = 8.3 Hz, 1H), 3.42–3.30 (m, 1H), 1.46 (d, *J* = 2.7 Hz, 9H), 1.26 (d, *J* = 2.7 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 132.2, 119.8, 115.5 (t, *J* = 247.4 Hz), 82.1, 60.5 (t, *J* = 22.6 Hz), 57.0, 49.8, 27.9, 22.8. ^{19}F NMR (377 MHz, $CDCl_3$) δ -121.40 – -123.10 (m, 1F), -128.85 (ddd, *J* = 285.9, 55.6, 17.7 Hz, 1F). IR $(KBr)_{max}$ 3368, 2980, 2933, 1690, 1466, 1398, 1308, 1235, 1039, 937, 865, 640 cm^{-1}; MS (EI) m/z 348.1 [M + Na]$^+$; HRMS (EI) m/z [M + Na]$^+$ calcd for $C_{14}H_{25}F_2N_1Na_1O_3S_1$, 348.1415; Found, 348.1420.



(R)-tert-butyl 2-((S)-2-bromo-1-((S)-1,1-dimethylethylsulfinamido)-2,2-difluoroethyl)but-3-enoate (3f). Column chromatography (petroleum ether : ethyl acetate = 3:1) on silica gel gave a white solid (62%): mp 43–44℃; [α]$_D$16.0 + 62.7 (c 0.65, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92–5.78 (m, 1H), 5.33 (d, *J* = 9.2 Hz, 1H), 5.30 (s, 1H), 4.96 (d, *J* = 10.1 Hz, 1H), 3.97 (d, *J* = 4.9 Hz, 1H), 3.60 (d, *J* = 3.9 Hz, 1H), 1.47 (s, 9H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 132.1, 122.9 (t, *J* = 313.2 Hz, 2H), 120.1, 82.7, 67.2 (t, *J* = 22.6 Hz), 57.8, 51.1, 27.9, 22.8. ^{19}F NMR (377 MHz, $CDCl_3$) δ -49.84 (dd, *J* = 162.9, 5.4 Hz, 1F), -51.51 (dd, *J* = 162.9, 12.1 Hz, 1F). IR $(KBr)_{max}$ 3194, 3084, 2973, 2868, 1723, 1465, 1364, 1260, 1153, 1090, 1018, 929, 841, 799 cm^{-1}; MS (EI) m/z 428.1 $[M+Na]^+$; HRMS (EI) m/z $[M+Na]^+$ calcd for $C_{14}H_{24}Br_1F_2N_1Na_1O_3S_1$, 426.0521; Found, 426.0534.

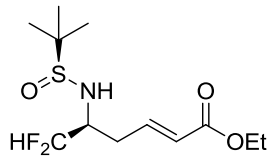
6. General Procedure for the Synthesis of δ-amino-α, β-unsaturated ester 4.

Dienolate **2a** (112mg, 0.6 mmol) was added to a solution of **1a** (100 mg, 0.5 mmol) in CH_2Cl_2 (2 mL) and the solution was cooled to - 78 °C under N_2. TMSOTf (90 μL, 0.5 mmol) was added dropwise. After being stirred for indicated time at the same temperature, the reaction was quenched by addition of a saturated aqueous $NaHCO_3$ (4mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide an oil residue. The **4a** was obtained by flash chromatography on silica gel. The ratio of diastereomers was determined by ^{19}F or ^{1}H NMR of the crude reaction mixture.

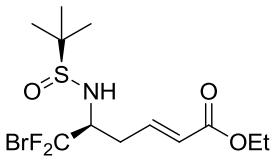


(S, E)-ethyl 5-((S)-1,1-dimethylethylsulfinamido)-6,6,6-trifluorohex-2-enoate (4a). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a yellow oil (89 %): [α]$_D$19.0 -212.0 (c 0.57, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94–6.71 (m, 1H), 5.92 (d, *J* = 15.6 Hz, 1H), 4.21 (d, *J* = 9.0 Hz, 1H), 4.14 (q, *J* =

7.1 Hz, 2H), 3.94–3.59 (m, 1H), 2.78–2.52 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H), 1.17 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 141.8, 125.3, 124.8 (q, J = 281.3 Hz), 60.4, 57.4 (q, J = 29.9 Hz), 57.3, 32.1, 22.5, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -75.00 (d, J = 7.1 Hz, 3F). IR $(KBr)_{max}$ 3266, 3178, 2975, 2872, 1716, 1655, 1474, 1370, 1270, 1175, 1127, 980 cm^{-1}; MS (EI) m/z 316.0 M^+; HRMS (EI) m/z M^+ calcd for $C_{12}H_{21}F_3N_1O_3S_1$, 316.1189; Found, 316.1190.

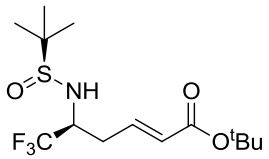


(S, E)-ethyl 5-((S)-1,1-dimethylethylsulfinamido)-6,6-difluorohex-2-enoate (4b). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a yellow solid (92%): mp 50–51℃; [α]$_D$24.3 -37.5 (c 0.51, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98–6.83 (m, 1H), 6.05 (t, J = 55.7 Hz, 1H), 5.93 (d, J = 15.4 Hz, 1H), 4.19 (q, J = 6.0 Hz, 2H), 3.65 (s, 1H), 3.56 (d, J = 9.8 Hz, 1H), 2.67 (s, 1H), 2.56–2.35 (m, 1H), 1.28 (t, J = 6.9 Hz, 3H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 142.7, 124.9, 115.3 (t, J = 245.3 Hz), 60.4, 57.9 (t, J = 23.1 Hz), 56.8, 30.5, 22.5 (d, J = 12.1 Hz), 14.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -123.24 (ddd, J = 286.1, 55.2, 4.6 Hz, 1F), -134.20 (ddd, J = 286.0, 56.2, 19.5 Hz, 1F). IR $(KBr)_{max}$ 3222, 2975, 2872, 1716, 1658, 1466, 1370, 1217, 1177, 1056, 981 cm^{-1}; MS (EI) m/z 320.1 [M + Na] $^+$; HRMS (EI) m/z [M + Na] $^+$ calcd for $C_{12}H_{21}F_2N_1Na_1O_3S_1$, 320.1102; Found, 320.1103.

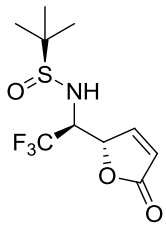


(S, E)-ethyl 6-bromo-5-((S)-1,1-dimethylethylsulfinamido)-6,6-difluorohex-2-enoate (4c). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a white oil (93%): [α]$_D$12.4 – 309.1 (c 0.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95–6.81 (m, 1H), 5.97 (d, J = 15.6 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.92–3.75 (m, 1H), 3.69 (d, J = 9.2 Hz, 1H), 2.88–2.75 (m, 1H), 2.66–2.55 (m, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.24 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 141.7, 125.7, 124.1 (t, J = 310.2 Hz), 64.1 (t, J = 23.3 Hz), 60.6, 57.5, 34.0, 22.6, 14.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -52.50 – -52.58 (m, 2F). IR $(KBr)_{max}$ 3196, 2976, 2868, 1717, 1658, 1368, 1270, 1170, 1063, 984, 915 cm^{-1}; MS (EI) m/z

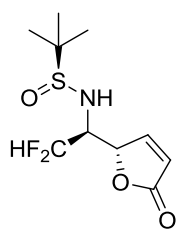
398.0 $[M+Na]^+$; HRMS (EI) m/z $[M+Na]^+$ calcd for $C_{12}H_{20}Br_1F_2N_1Na_1O_3S_1$, 398.0208; Found, 398.0218.



(S, E)-tert-butyl 5-((S)-1,1-dimethylethylsulfinamido)-6,6,6-trifluorohex-2-enoate (4d). Column chromatography (petroleum ether : ethyl acetate = 2:1) on silica gel gave a yellow solid (94%): mp 57–59℃; [α]$_D$19.5 + 77.9 (c 0.77, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80–6.65 (m, 1H), 5.83 (d, *J* = 15.6 Hz, 1H), 4.10 (dd, *J* = 21.7, 8.3 Hz, 1H), 3.78 (dt, *J* = 21.0, 9.3 Hz, 1H), 2.69–2.60 (m, 1H), 2.59–2.48 (m, 1H), 1.41 (s, 9H), 1.16 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 140.5, 127.1, 124.8 (q, *J* = 283.1 Hz), 80.6, 57.6 (q, *J* = 30.1 Hz), 57.3, 32.0, 28.0, 22.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -75.08 (d, *J* = 7.1 Hz, 3F). IR $(KBr)_{max}$ 3214, 3141, 2976, 2876, 1710, 1654, 1464, 1369, 1271, 1165, 1066, 983, 850 cm^{-1}; MS (EI) m/z 366.1 $[M + Na]^+$; HRMS (EI) m/z $[M + Na]^+$ calcd for $C_{14}H_{24}F_3N_1Na_1O_3S_1$, 366.1321; Found, 366.1306.

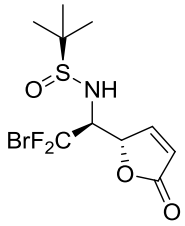


(S)-2-methyl-N-((S)-2,2,2-trifluoro-1-((S)-5-oxo-2,5-dihydrofuran-2-yl)ethyl)propane-2-sulfinamide (4e). Column chromatography (dichloromethane : methanol = 25:1) on silica gel gave a yellow solid (97%): mp 108–110℃; [α]$_D$13.0 - 172.1 (c 0.67, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 5.6 Hz, 1H), 6.35 (dd, *J* = 5.8, 1.9 Hz, 1H), 5.39 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.33 (dqd, *J* = 11.4, 7.7, 3.9 Hz, 1H), 3.85 (d, *J* = 10.3 Hz, 1H), 1.20 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 152.9, 127.3, 126.0 (q, *J* = 280.7 Hz), 82.0, 61.3(q, *J* = 28.6 Hz), 60.0, 24.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.61 (d, *J* = 7.6 Hz, 3F). IR $(KBr)_{max}$ 3207, 3113, 2962, 2872, 1764, 1467, 1363, 1261, 1175, 1134, 1063, 904, 821, 681 cm^{-1}; MS (EI) m/z 308.1 $[M + Na]^+$, HRMS (EI) m/z $[M + Na]^+$ calcd for $C_{10}H_{14}F_3N_1Na_1O_3S_1$, 308.0539; Found, 308.0533.



(S)-N-((S)-2,2-difluoro-1-((S)-5-oxo-2,5-dihydrofuran-2-yl)ethyl)-2-methylpropane-2-sulfinamide (4f). Column chromatography (dichloromethane :

methanol = 25:1) on silica gel gave a yellow solid (86%): mp 103–104 ℃; [α]$_D$13.2 -175.0 (c 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.52 (m, 1H), 6.30 (dd, *J* = 5.8, 2.0 Hz, 1H), 6.21 (dt, *J* =2.4, 53.6 Hz 1H), 5.40 (dd, *J* = 4.1, 1.9 Hz, 1H), 4.11 – 3.98 (m, 1H), 3.56 (d, *J* = 10.3 Hz, 1H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 154.3 (d, *J* = 3.9 Hz), 126.6, 116.9 (t, *J* = 246.0 Hz), 81.8, 61.7 (t, *J* = 22.1 Hz), 59.5. 24.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -123.85 (dd, *J* = 291.8, 51.5 Hz, 1F), -129.66 (dd, *J* = 289.2, 55.3 Hz, 1F). IR $(KBr)_{max}$ 3195, 3109, 2965, 2880, 1759, 1466, 1366, 1161, 1062, 896, 817 cm^{-1}; MS (EI) m/z 390.1 $[M + Na]^+$; HRMS (EI) m/z $[M + Na]^+$ calcd for $C_{10}H_{15}F_2N_1Na_1O_3S_1$, 290.0633; Found, 290.0634.

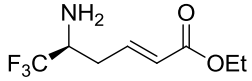


(S)-N-((S)-2-bromo-2,2-difluoro-1-((S)-5-oxo-2,5-dihydrofuran-2-yl)ethyl)-2-methylpropane-2-sulfinamide (4g). Column chromatography (dichloromethane : methanol = 40:1) on silica gel gave a pale yellow solid (91%): mp 107–108℃; [α]$_D$15.5 – 64.9 (c 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 4.8 Hz, 1H), 6.37 (d, *J* = 5.2 Hz, 1H), 5.60 (s, 1H), 4.47–4.37 (m, 1H), 3.52 (d, *J* = 10.2 Hz, 1H), 1.21 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 150.6, 125.3, 120.1 (t, *J* =308.4 Hz), 80.2, 66.0 (t, *J* = 23.0 Hz), 57.8, 22.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -51.07 (dd, *J* = 169.5, 7.7 Hz, 1F), -53.03 (dd, *J* = 169.6, 13.1 Hz, 1F). IR $(KBr)_{max}$ 3196, 3109, 2958, 2872, 1762, 1466, 1164, 1080, 939, 901, 820 cm^{-1}; MS (EI) m/z 370.0 $[M + Na]^+$; HRMS (EI) m/z $[M + Na]^+$ calcd for $C_{10}H_{14}Br_1F_2N_1Na_1O_3S_1$, 367.9738; Found, 367.9744.

7. Procedures for the Preparing of 5-7.

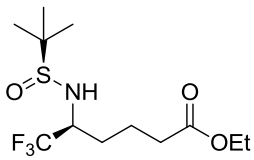
A flask equipped with a magnetic stirrer bar was charged with 4 ml of diisopropyl ether, **4a** (315 mg, 1.0 mmol) and ethanol (5.7 mL) and then cooled to 0 ^{o}C. After the addition of acetyl chloride (235 mg, 3 mmol), the mixture was aged at 0 ^{o}C for 12h. Then the mixture was condensed in vacuo. The residue was dissolved with 5 ml of water and washed with dichloromethane. Then $NaHCO_3$ (1.4 mmol) was added to the aqueous layer and extracted twice with 8 ml of dichloromethane. The organic layer was

dried over $MgSO_4$ and the solvent was removed under reduced pressure.. The residue was purified by flash chromatography on silica gel to afford product **5**.



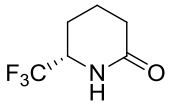
(S, E)-ethyl 5-amino-6,6,6-trifluorohex-2-enoate (5). Column chromatography (petroleum ether : ethyl acetate = 10:1) on silica gel gave a yellow oil (80%): [α]$_D$15.1 – 112.0 (c 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95–6.82 (m, 1H), 5.92 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.33–3.23 (m, 1H), 2.57 (dddd, *J* = 14.9, 6.9, 3.9, 1.6 Hz, 1H), 2.28 (dddd, *J* = 14.9, 9.3, 7.7, 1.4 Hz, 1H), 1.42 (s, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 142.8, 126.1 (q, *J* = 281.7 Hz), 124.8, 60.4, 53.0 (q, *J* = 29.3 Hz), 32.7, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -78.76 (d, *J* = 5.4 Hz, 3F). IR $(KBr)_{max}$ 3403, 3334, 2984, 2945, 1718, 1658, 1441, 1376, 1266, 1168, 1127, 1042, 981, 862, 798 cm^{-1};MS (EI) m/z 212.1 M^+; HRMS (EI) m/z M^+ calcd for $C_8H_{13}F_3N_1O_2$, 212.0893; Found, 212.0902.

In 6 ml of methanol, the **3a** (472 mg, 1.5 mmol) and Pd-black (159 mg, 10%) was hydrogenated for 72 h at room temperature. The mixture was filtered and the solvent was evaporated under reduced pressure. The residue was purified by Column chromatography on silica gel gave the **6**.



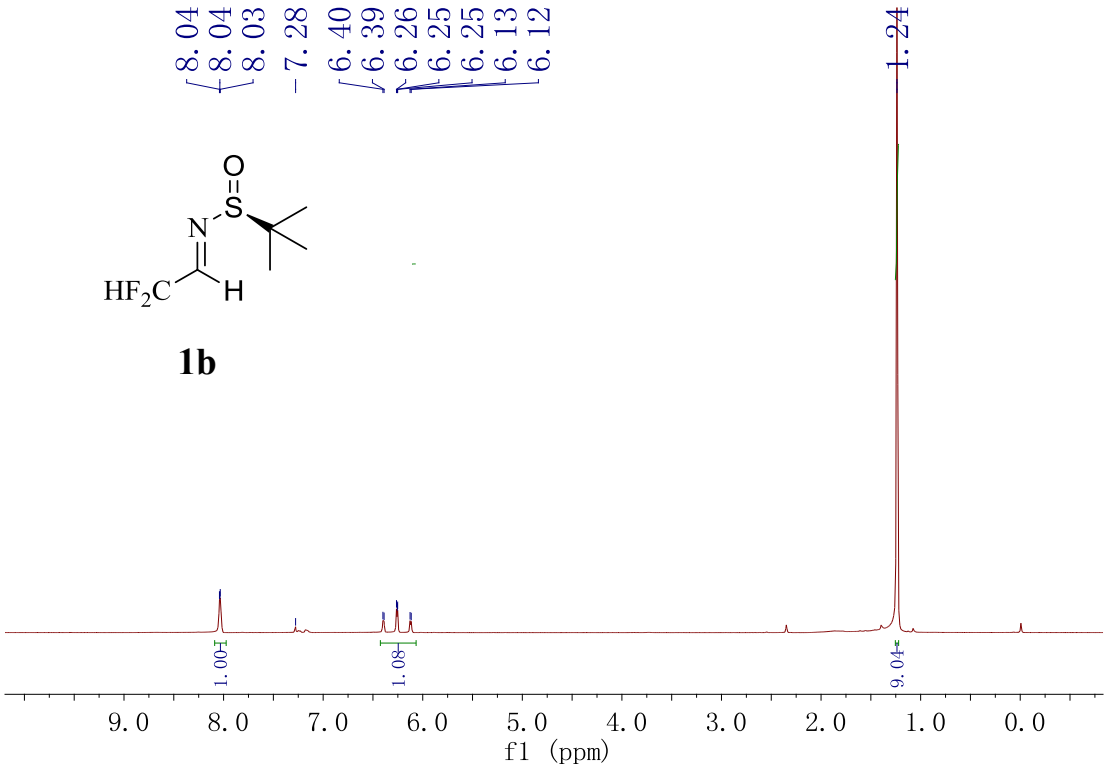
(S)-ethyl 5-((S)-1,1-dimethylethylsulfinamido)-6,6,6-trifluorohexanoate (6). Column chromatography (petroleum ether : ethyl acetate = 1.5:1) on silica gel gave a yellow oil (93%): [α]$_D$12.4 + 56.0 (c 0.55, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (q, *J* = 7.1 Hz, 2H), 3.75 (d, *J* = 9.2 Hz, 1H), 3.69–3.57 (m, 1H), 2.34 (t, *J* = 6.4 Hz, 2H), 1.98–1.77 (m, 2H), 1.71 (dd, *J* = 18.1, 9.7 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 125.2 (q, *J* = 282.7 Hz), 60.5, 58.0 (q, *J* = 29.8 Hz), 57.2, 33.4, 28.6, 22.5, 20.7, 14.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ -75.18 (d, *J* = 6.4 Hz, 3F). IR $(KBr)_{max}$ 3212, 2971, 2872, 1731, 1463, 1369, 1268, 1168, 1123, 1064, 853 cm^{-1}; MS (EI) m/z 340.1 $[M + Na]^+$; HRMS (EI) m/z $[M + Na]^+$ calcd for $C_{12}H_{22}F_3N_1Na_1O_3S_1$, 340.1165; Found, 340.1165.

To a solution of sulfinamide **6** (200 mg, 0.6 mmol) in MeOH (MeOH/HCl = 1:1, v/v) was added HCl (4 M in 1,4-dioxane, 10 equiv). The mixture was stirred at room temperature for 18 h and then concentrated under reduced pressure. The residue was dissolved in dry MeOH (0.2 M), and then K_2CO_3 (414 mg, 3 mmol) was added at room temperature. The mixture was stirred overnight. The crude was purified by flash chromatography on silica gel (dichloromethane : methanol = 25:1) to give **7**.

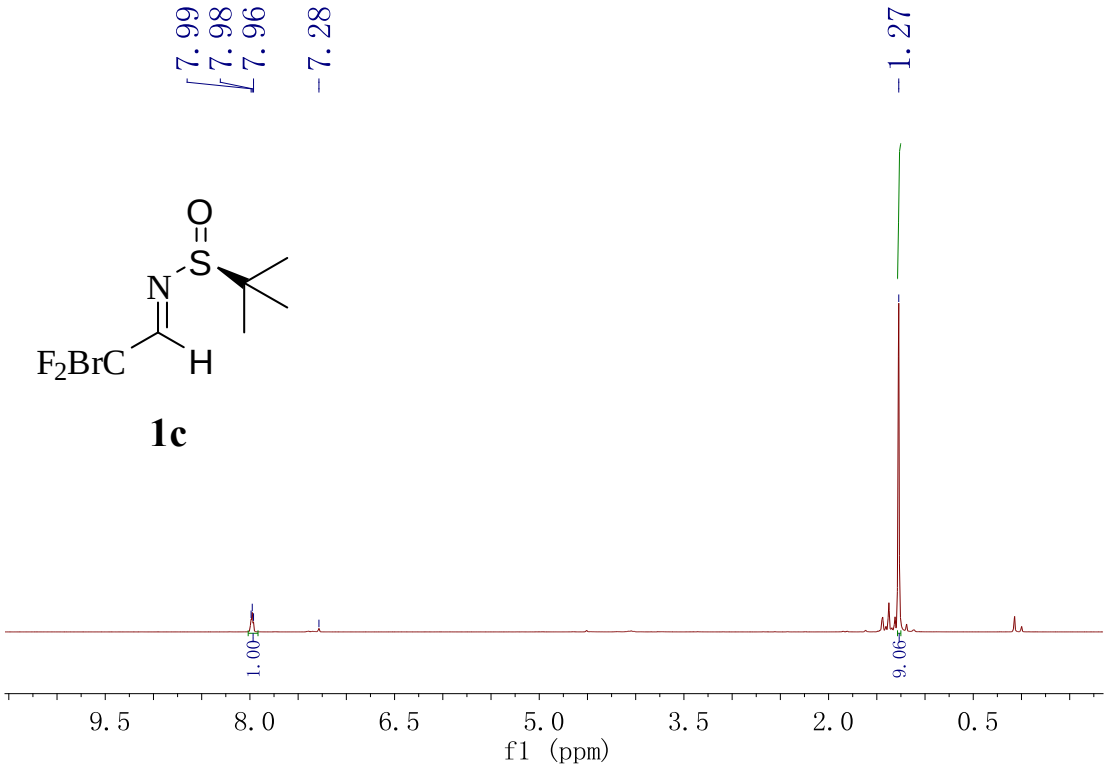


(S)-6-(trifluoromethyl)piperidin-2-one (7). Column chromatography (dichloromethane : methanol = 40:1) on silica gel gave a pale yellow solid (77%): mp 57 – 58℃; $[\alpha]_D$14.9 – 20.6 (c 0.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (s, 1H), 4.04–3.87 (m, 1H), 2.40 (s, 2H), 2.11–1.98 (m, 2H), 1.93–1.83 (m, 1H), 1.80 (dd, J = 14.2, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 124.62 (q, J = 281.1 Hz), 53.8 (q, J = 30.8 Hz), 31.2, 21.02, 18.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -77.74 (d, J = 6.8 Hz, 3F). IR $(KBr)_{max}$ 3211, 3113, 2965, 1908, 1676, 1401, 1276, 1163, 1120, 1076, 797 cm^{-1}; MS (EI) m/z 190.0 $[M + Na]^+$; HRMS (EI) m/z $[M + Na]^+$ calcd for $C_6H_8F_3N_1Na_1O_1$, 190.0450; Found, 190.0446.

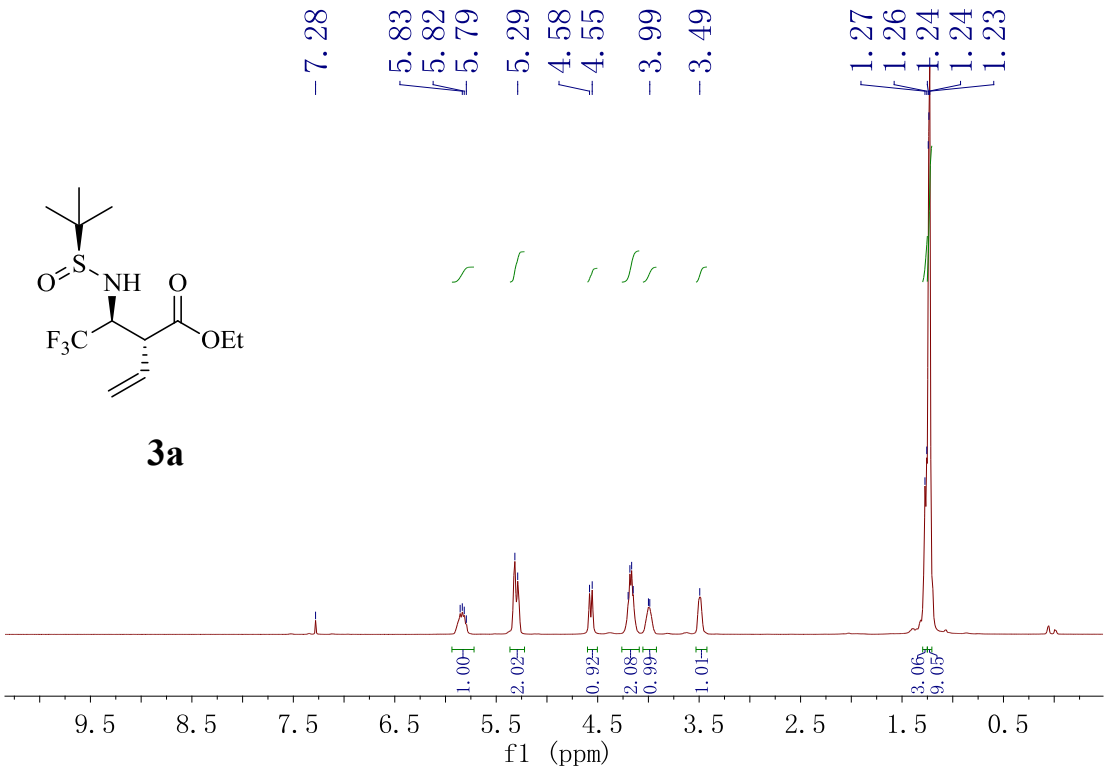
8. Copies of ^{1}H NMR and ^{13}C NMR Spectra for the new Product



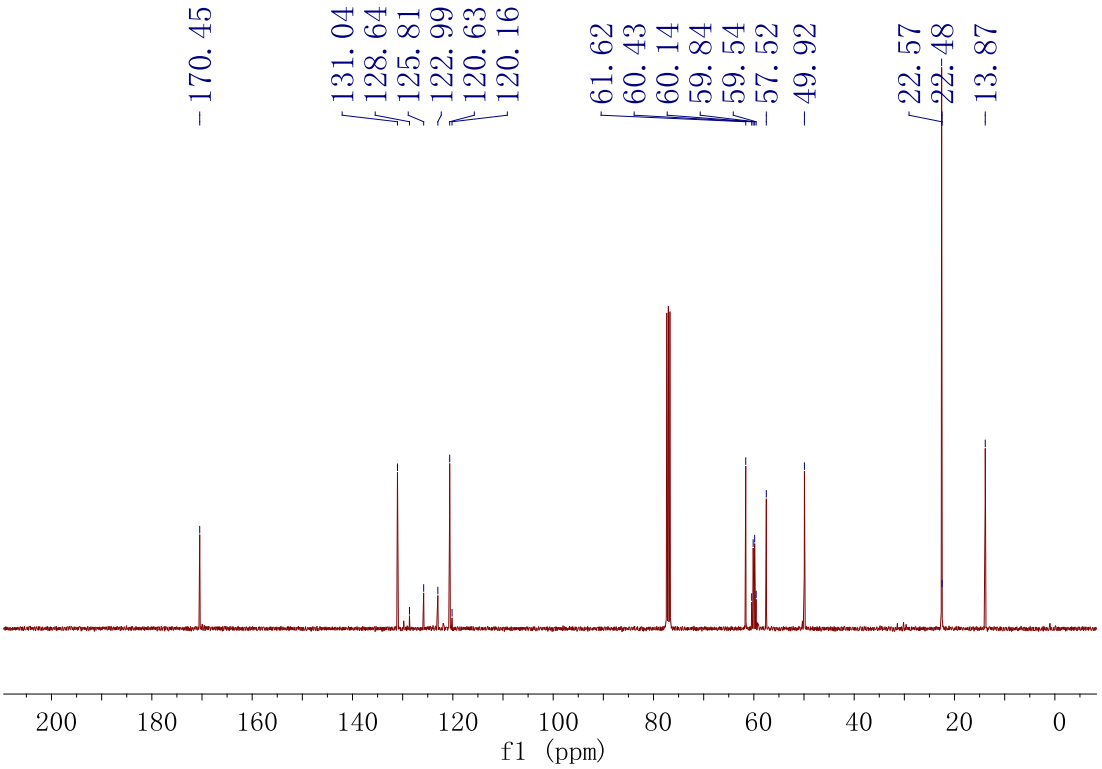
1b


7.99
7.98
7.96
7.28
1.27
O
S
N
F2BrC
H
1.00
9.06
9.5
8.0
6.5
5.0
3.5
2.0
0.5
f1 (ppm)

1c


7.28
5.83
5.82
5.79
5.29
4.58
4.55
3.99
3.49
1.27
1.26
1.24
1.24
1.23
O
S
NH
O
F3C
OEt
1.00
2.02
0.92
2.08
0.99
1.01
3.06
9.05
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

3a


170.45
131.04
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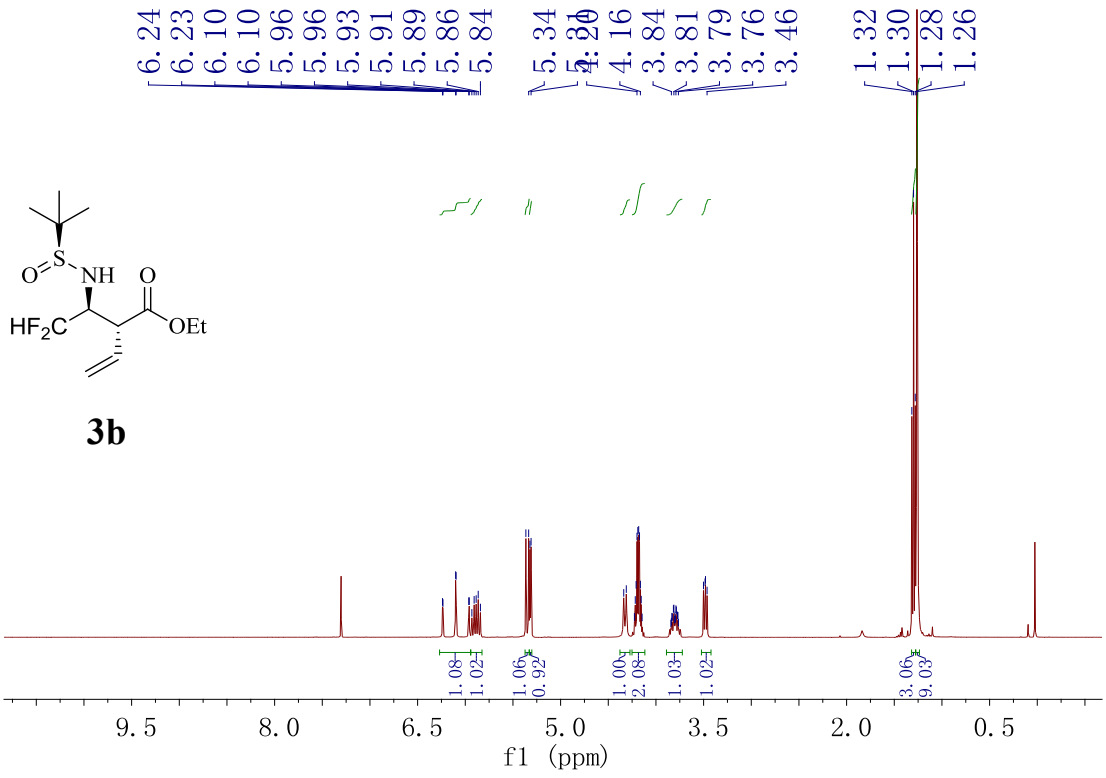
125.81
122.99
120.63
120.16
61.62
60.43
60.14
59.84
59.54
57.52
49.92
22.57
22.48
13.87
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


6.24
6.23
6.10
6.10
5.96
5.96
5.93
5.91
5.89
5.86
5.84
5.34
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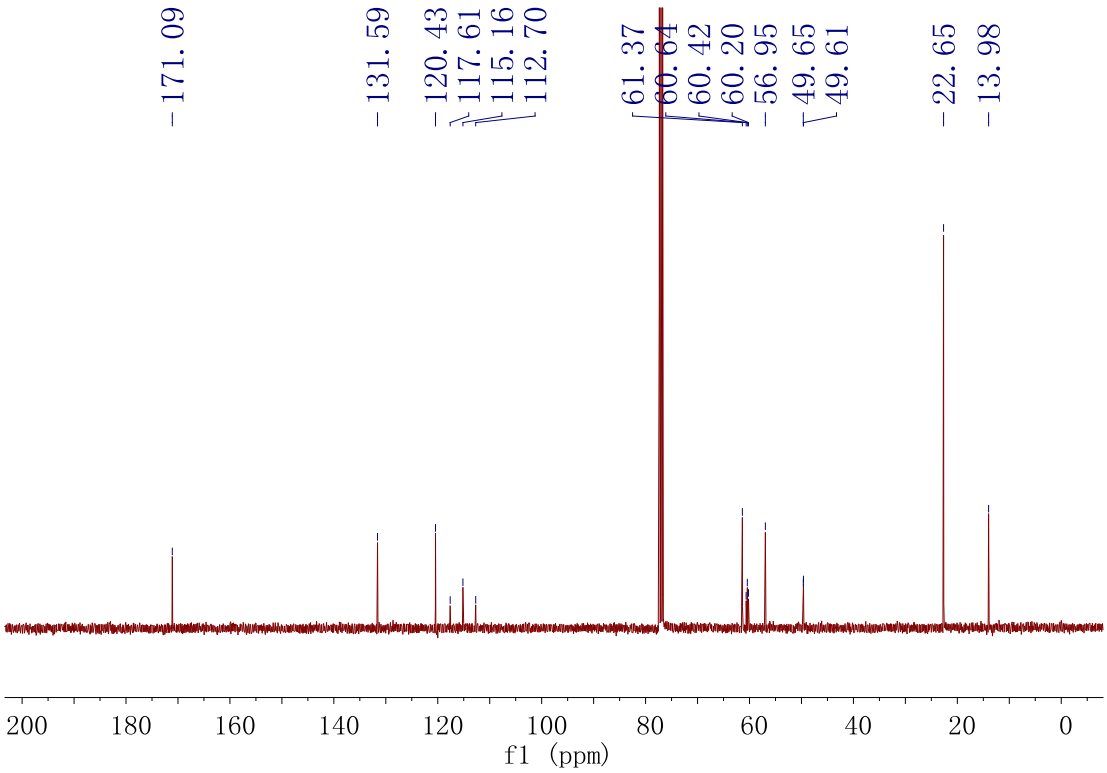
3.84
3.81
3.79
3.76
3.46
1.32
1.30
1.28
1.26
1.08
1.02
1.06
0.92
1.00
2.08
1.03
1.02
3.06
9.03
9.5
8.0
6.5
5.0
3.5
2.0
0.5
f1 (ppm)

O
S
NH
O
HF2C
OEt

3b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112.70
61.37
60.84
60.42
60.20
56.95
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49.61
22.65
13.98
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180
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140
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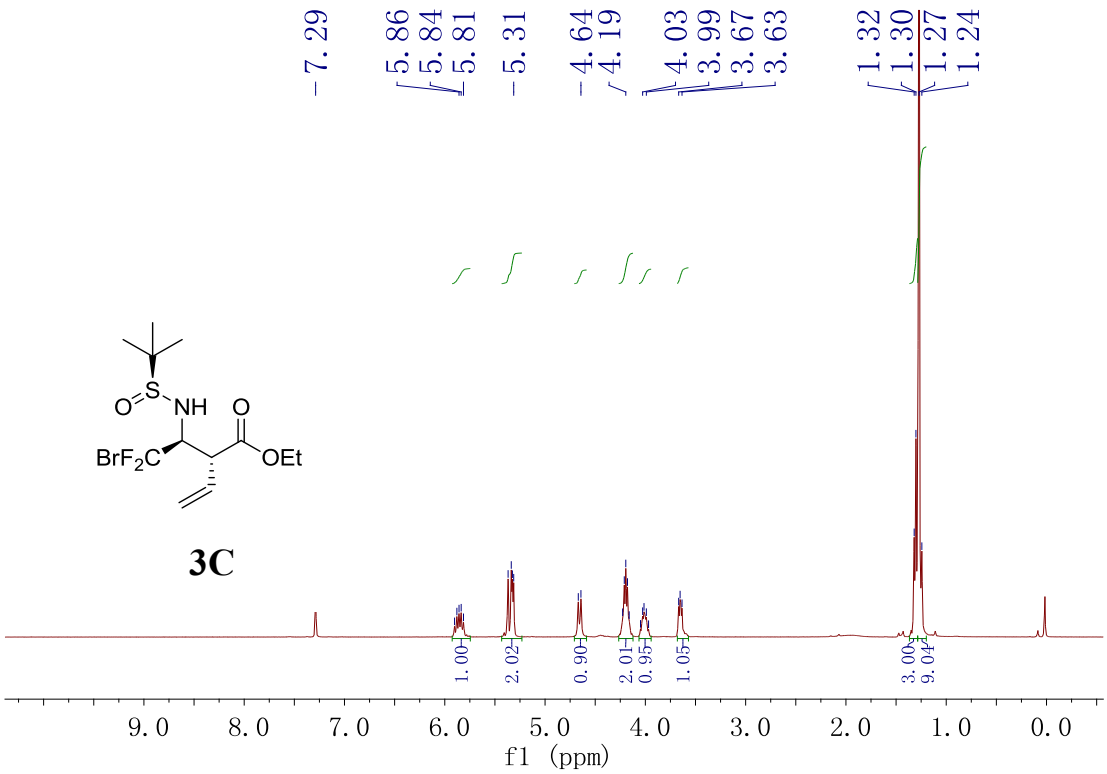
100
80
60
40
20
0
f1 (ppm)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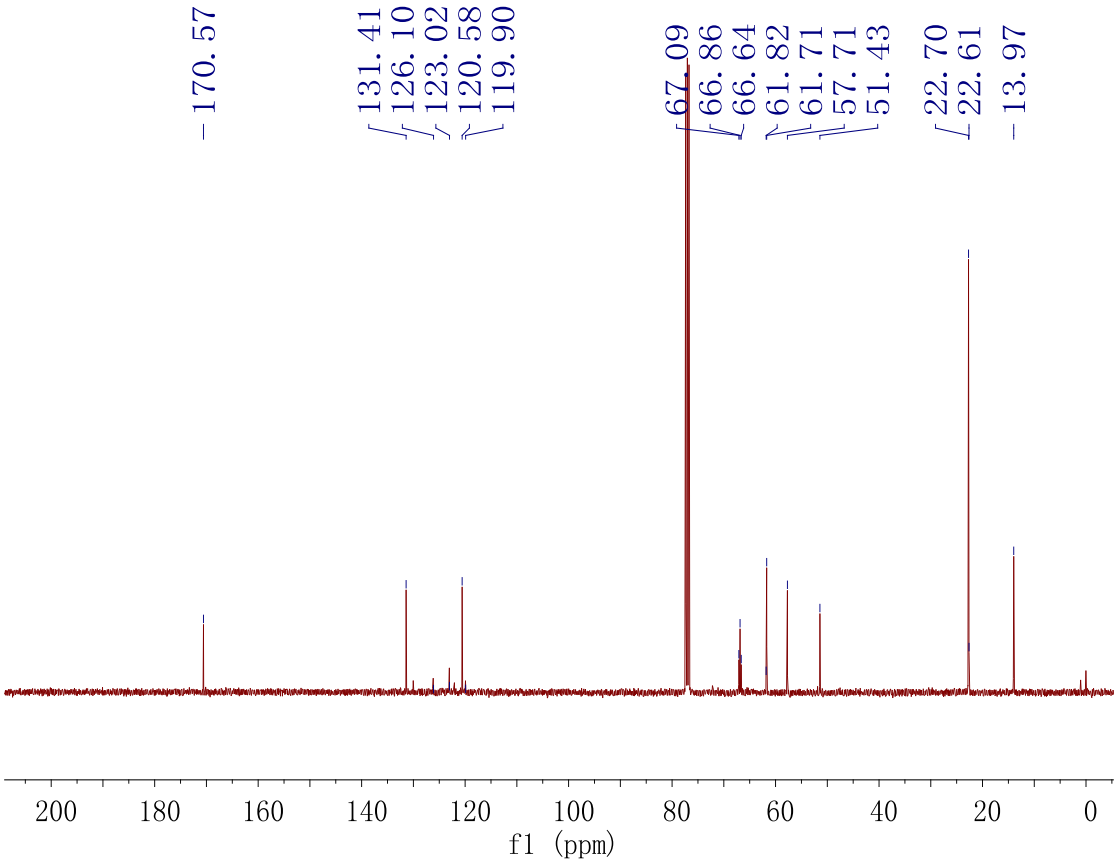
5.81
5.31
4.64
4.19
4.03
3.99
3.67
3.63
1.32
1.30
1.27
1.24
1.00
2.02
0.90
2.01
0.95
1.05
3.00
9.04
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

O
S
NH
O
BrF2C
OEt

3C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119.90
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66.86
66.64
61.82
61.71
57.71
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22.70
22.61
13.97
200
180
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140
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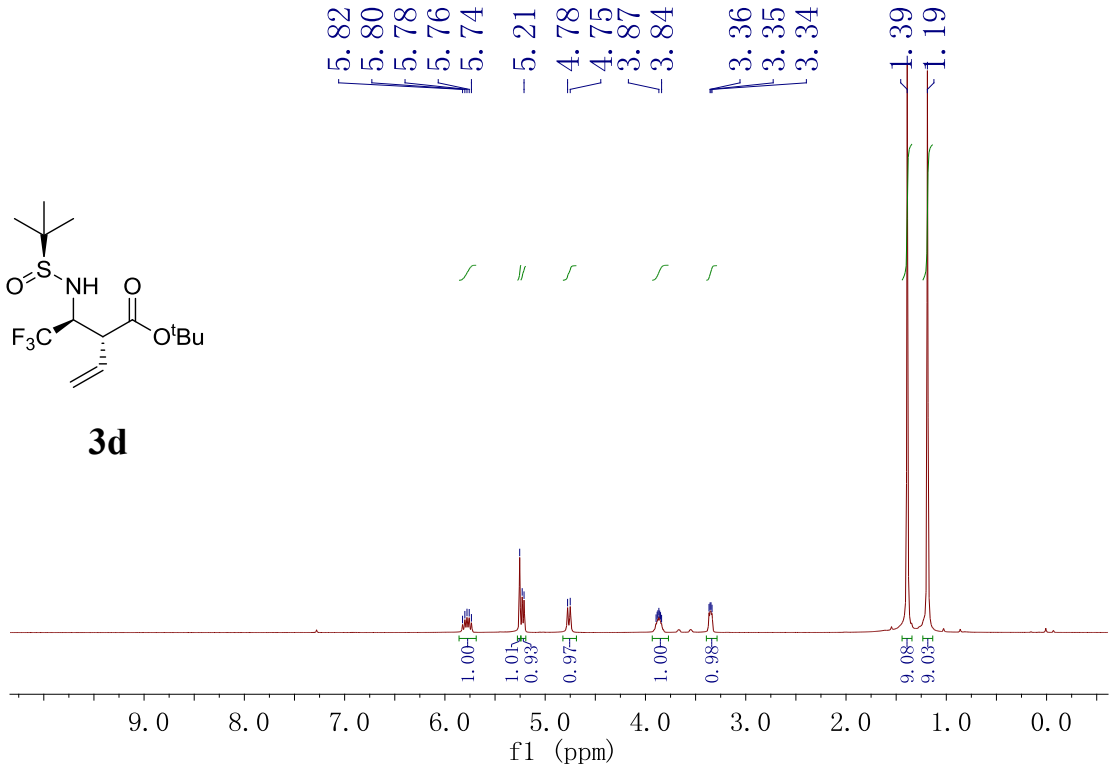
100
80
60
40
20
0
f1 (ppm)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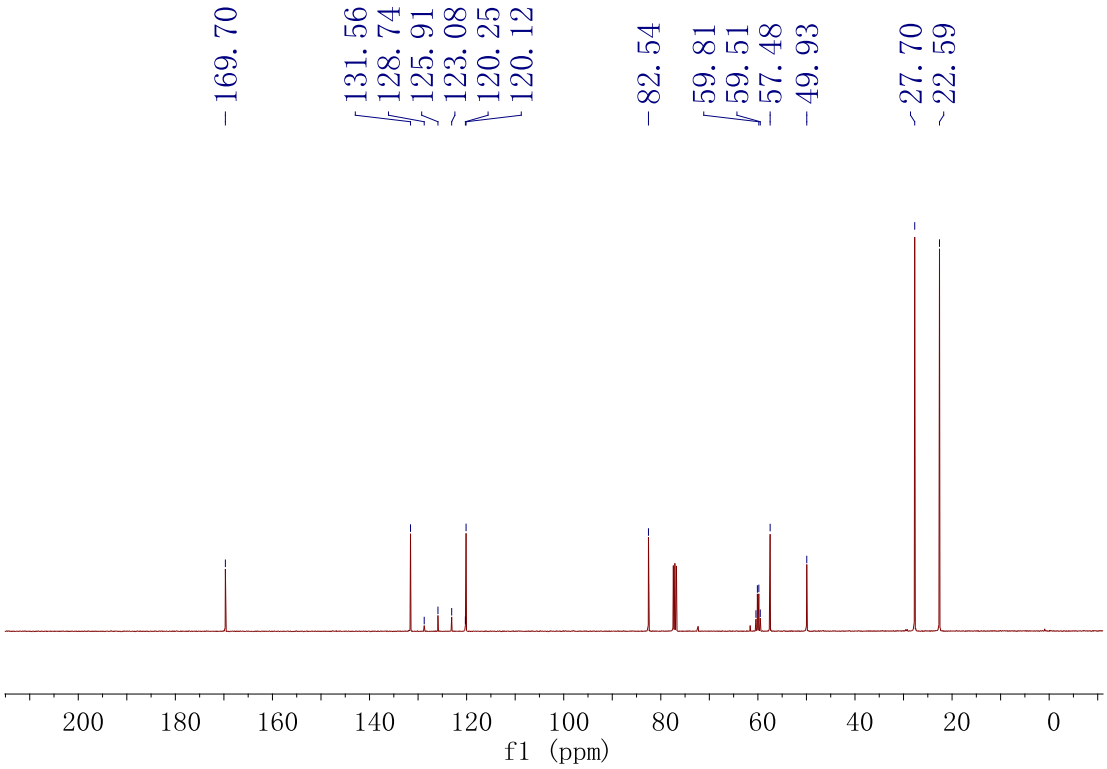
4.75
3.87
3.84
3.36
3.35
3.34
1.39
1.19
1.00
1.01
0.93
0.97
1.00
0.98
9.08
9.03
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

S
NH
O
O
F3C
OtBu

3d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120.25
120.12
82.54
59.81
59.51
57.48
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27.70
22.59
200
180
160
140
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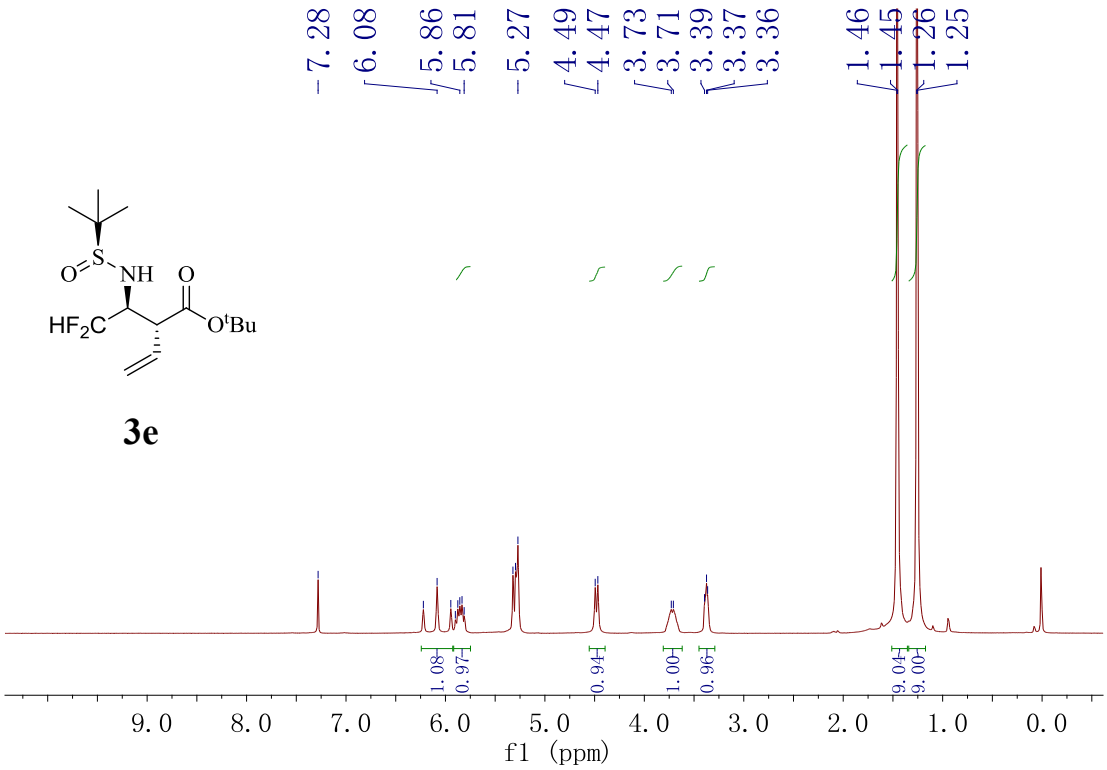
100
80
60
40
20
0
f1 (ppm)


7.28
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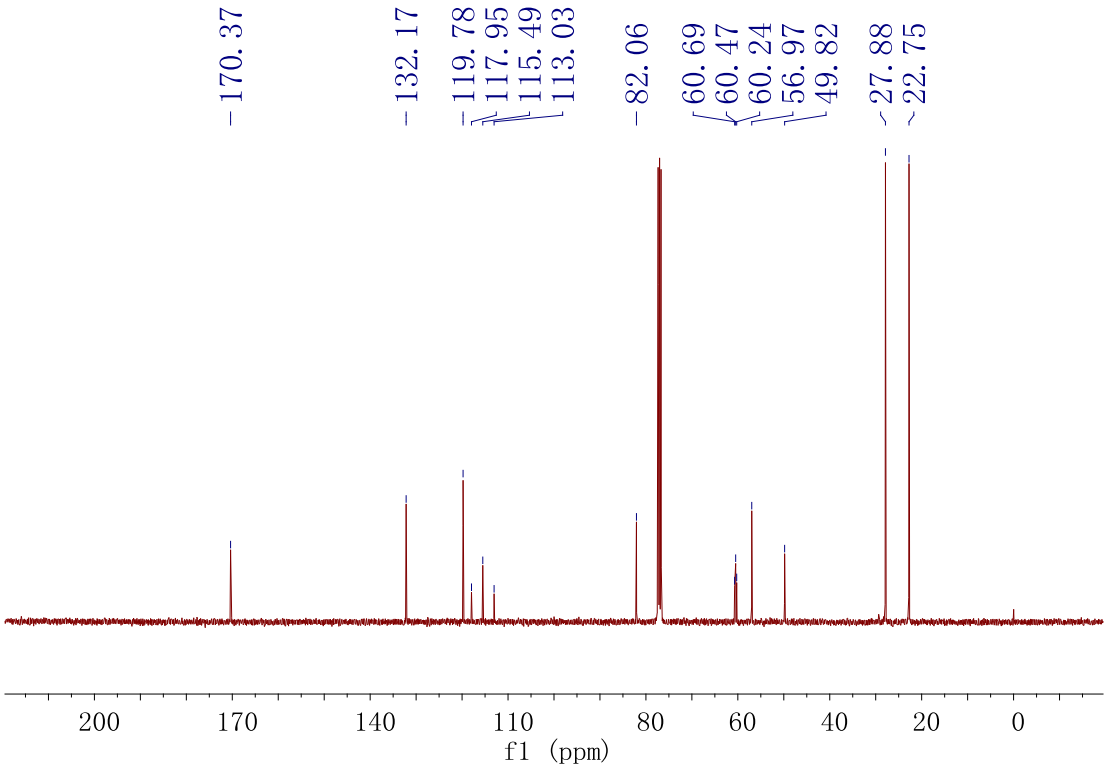
3.39
3.37
3.36
1.46
1.45
1.26
1.25
1.08
0.97
0.94
1.00
0.96
9.04
9.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

O
S
NH
O
HF2C
OtBu

3e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115.49
113.03
82.06
60.69
60.47
60.24
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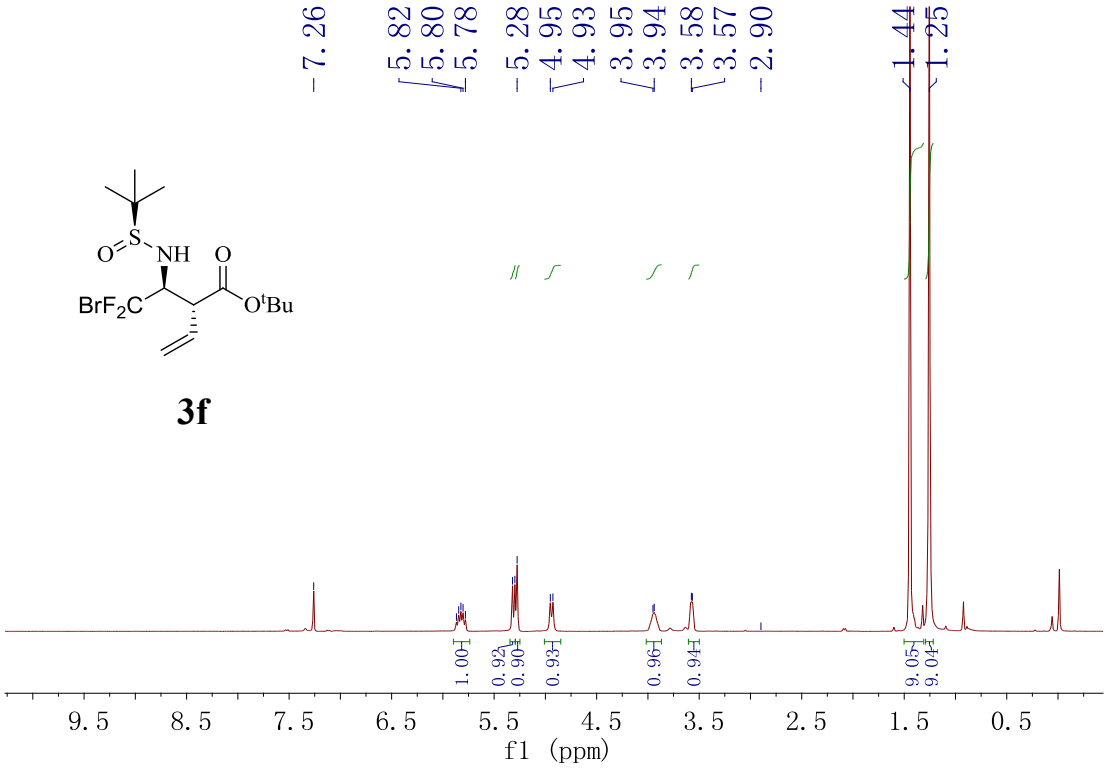
49.82
27.88
22.75
200
170
140
110
80
60
40
20
0
f1 (ppm)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3.57
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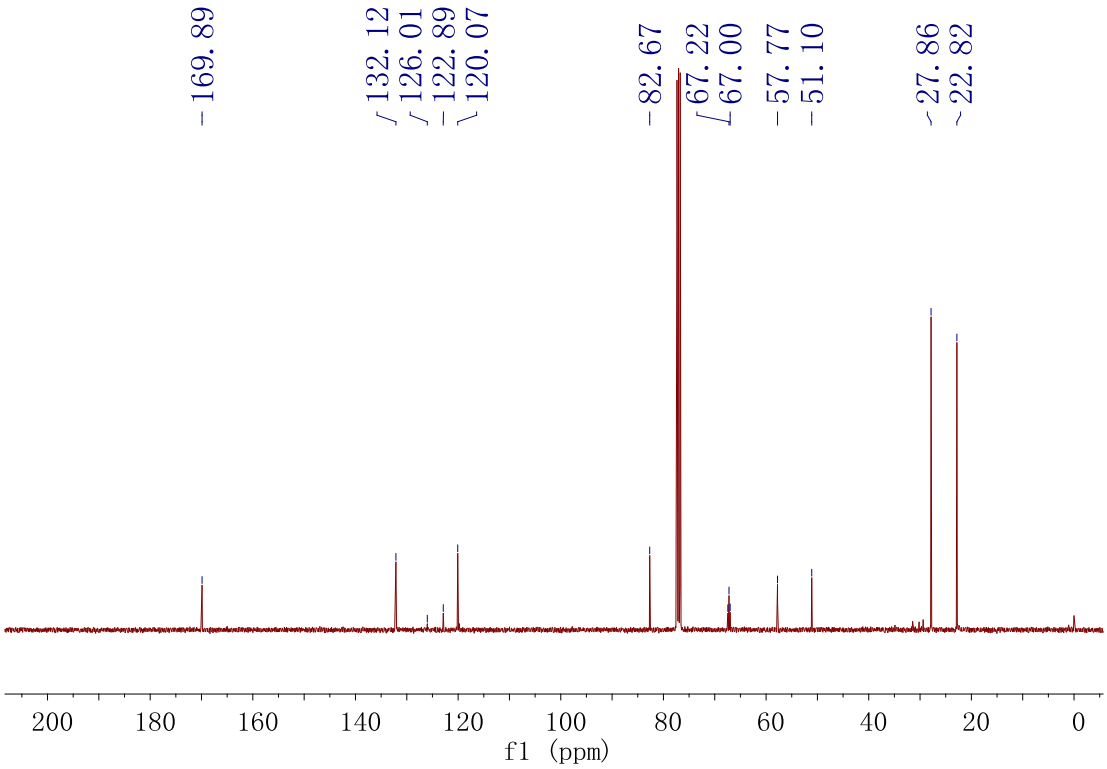
1.44
1.25
1.00
0.92
0.90
0.93
0.96
0.94
9.05
9.04
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

O
S
NH
O
BrF2C
OtBu

3f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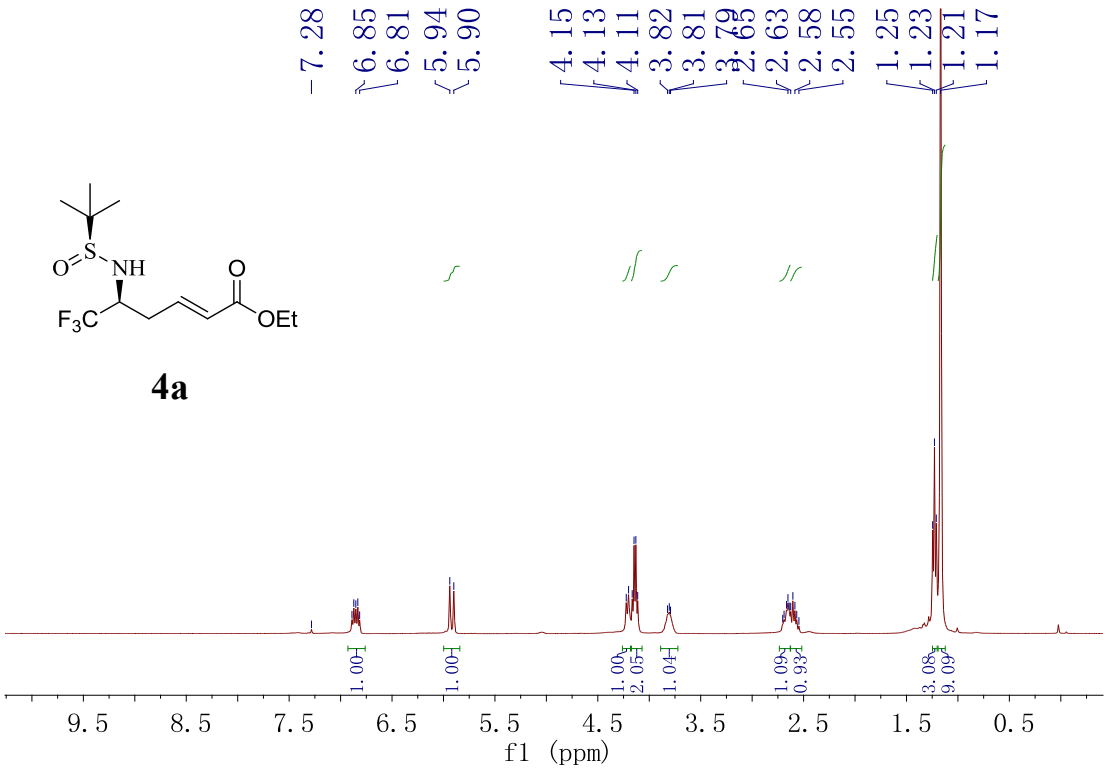
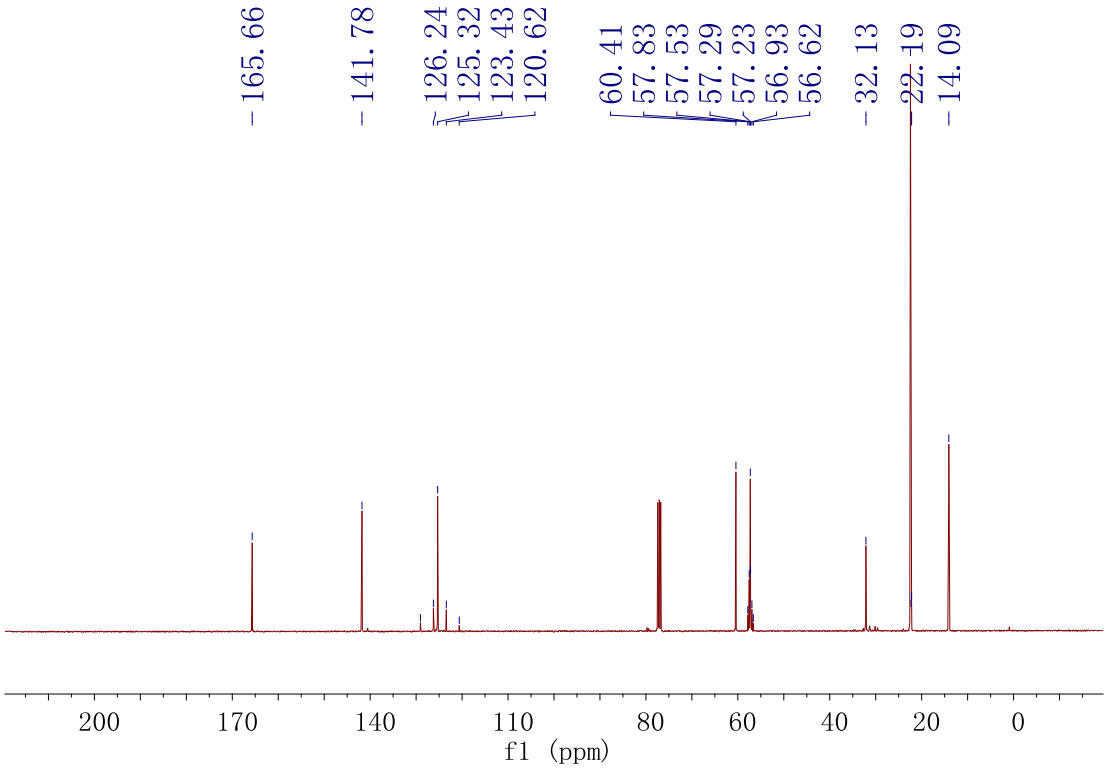
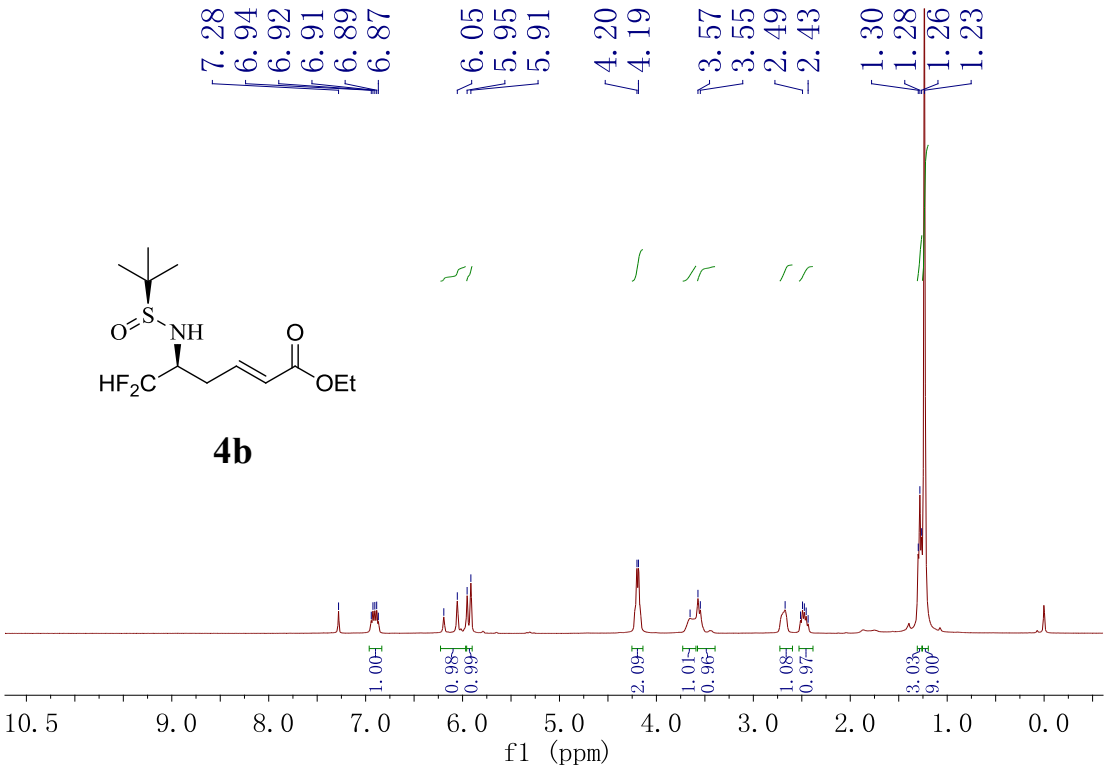
132.12
126.01
122.89
120.07
82.67
67.22
67.00
57.77
51.10
27.86
22.82
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.28
6.85
6.81
5.94
5.90
4.15
4.13
4.11
3.82
3.81
3.79
3.65
2.63
2.58
2.55
1.25
1.23
1.21
1.17
1.00
1.00
1.00
2.05
1.04
1.09
0.93
3.08
9.09
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

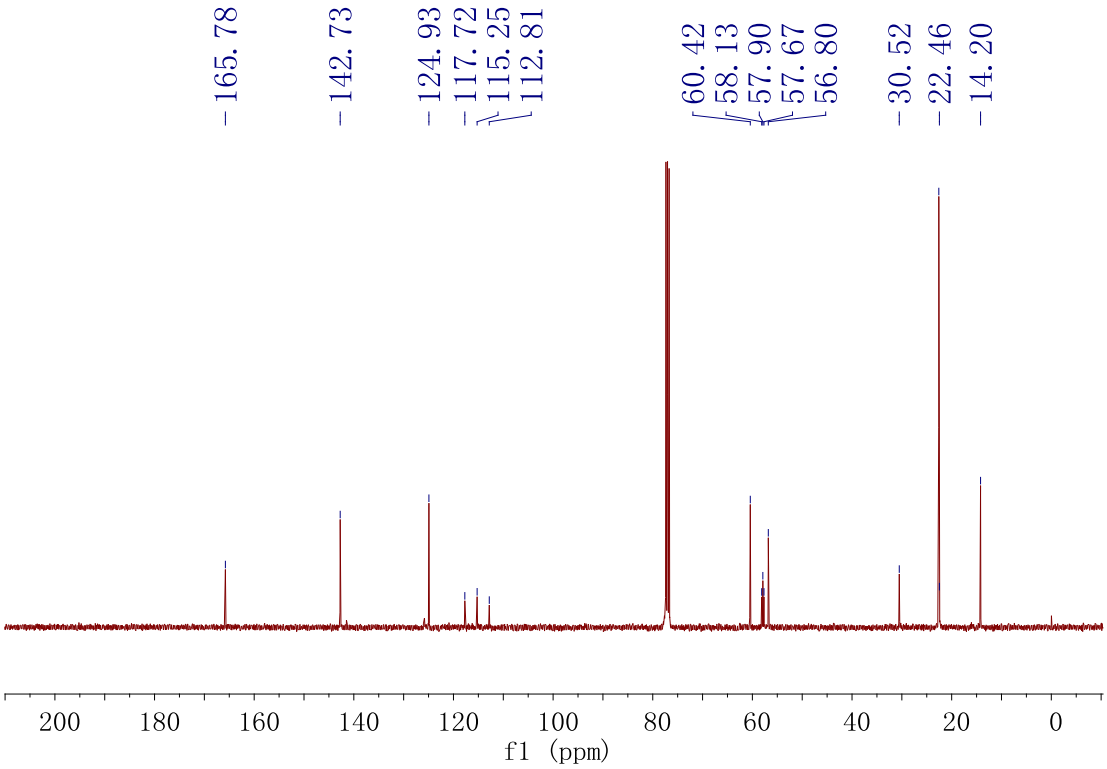
O
S
NH
O
F3C
OEt

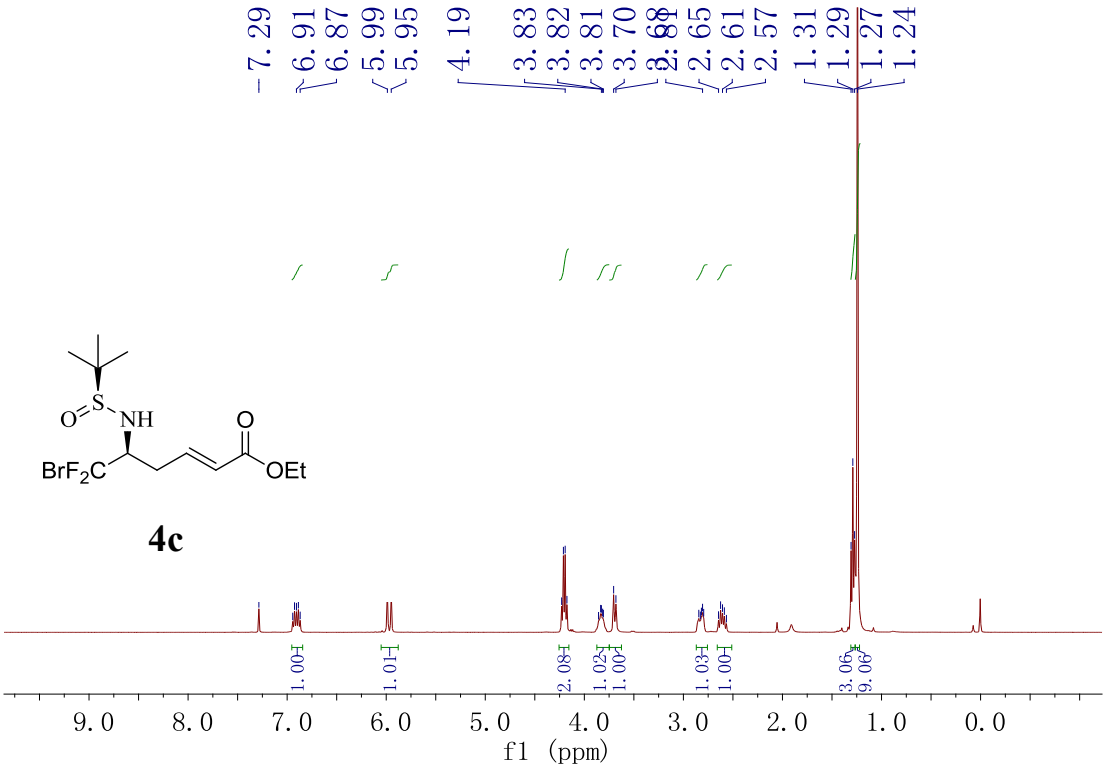
4a

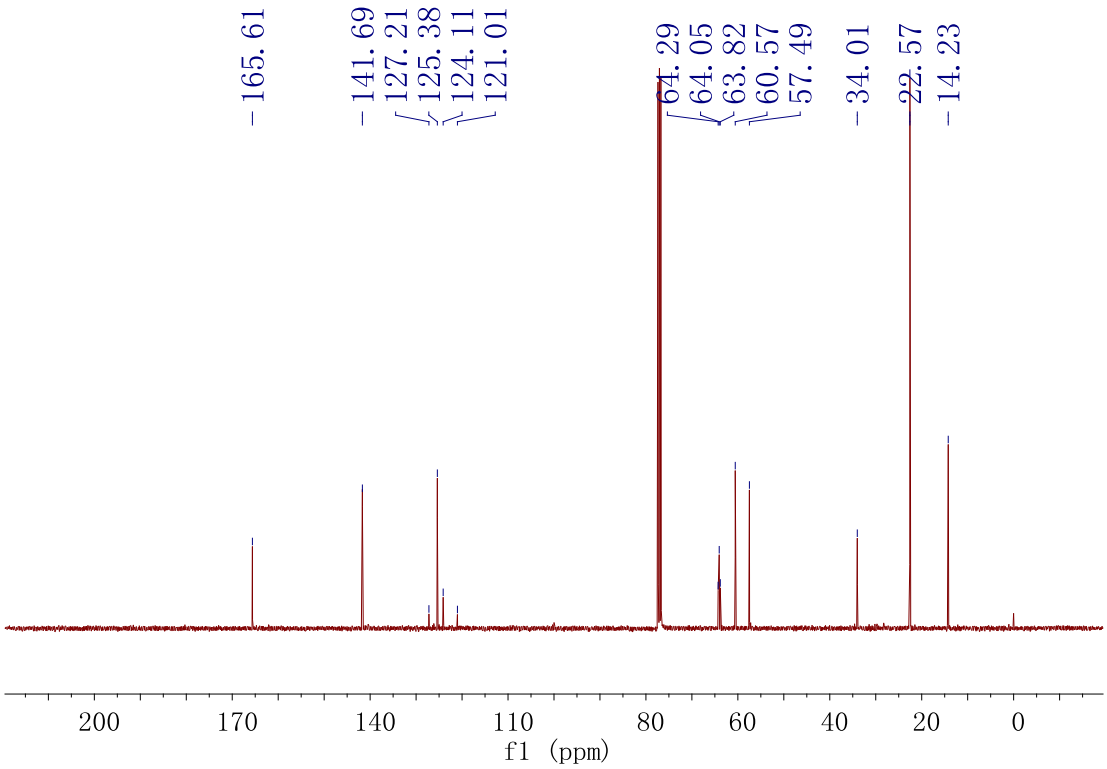

165.66
141.78
126.24
125.32
123.43
120.62
60.41
57.83
57.53
57.29
57.23
56.93
56.62
32.13
22.19
14.09
200
170
140
110
80
60
40
20
0
f1 (ppm)


7.28
6.94
6.92
6.91
6.89
6.87
6.05
5.95
5.91
4.20
4.19
3.57
3.55
2.49
2.43
1.30
1.28
1.26
1.23
O
S
NH
O
HF2C
OEt
1.00
0.98
0.99
2.09
1.01
0.96
1.08
0.97
3.03
9.00
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

4b


165.78
142.73
124.93
117.72
115.25
112.81
60.42
58.13
57.90
57.67
56.80
30.52
22.46
14.20
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.29
6.91
6.87
5.99
5.95
4.19
3.83
3.82
3.81
3.70
2.65
2.61
2.57
1.31
1.29
1.27
1.24
O
S
NH
O
BrF2C
OEt
4c
1.00
1.01
2.08
1.02
1.00
1.03
1.00
3.06
9.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)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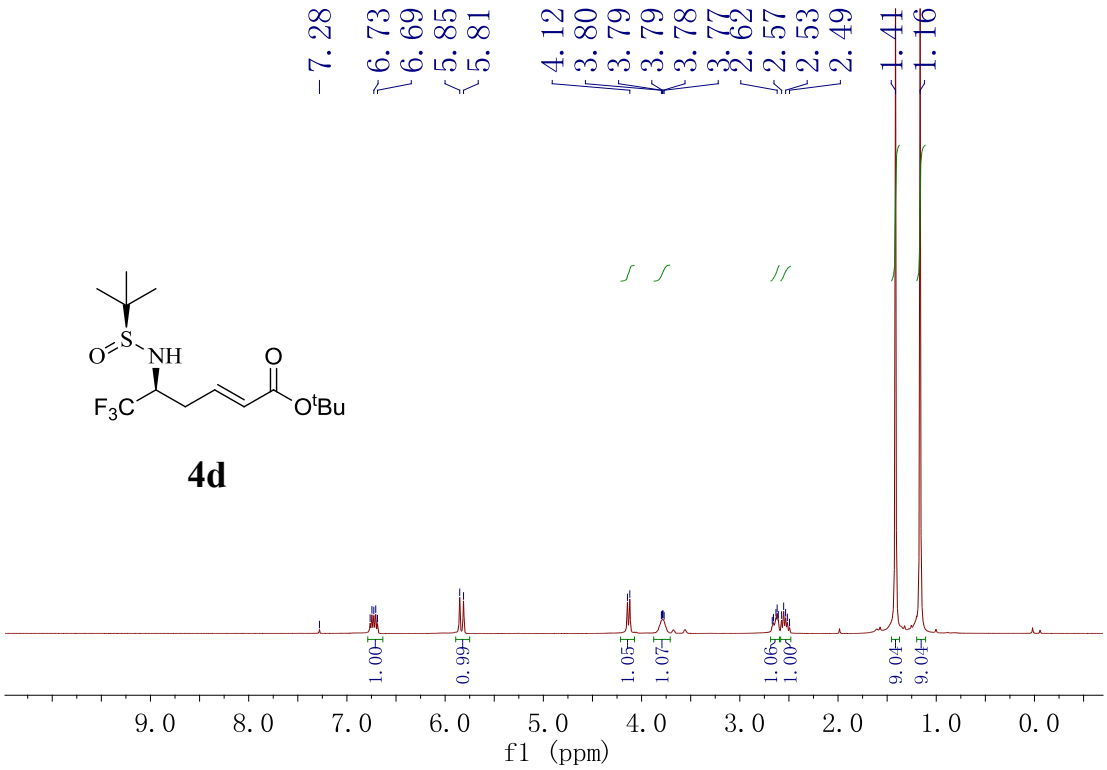
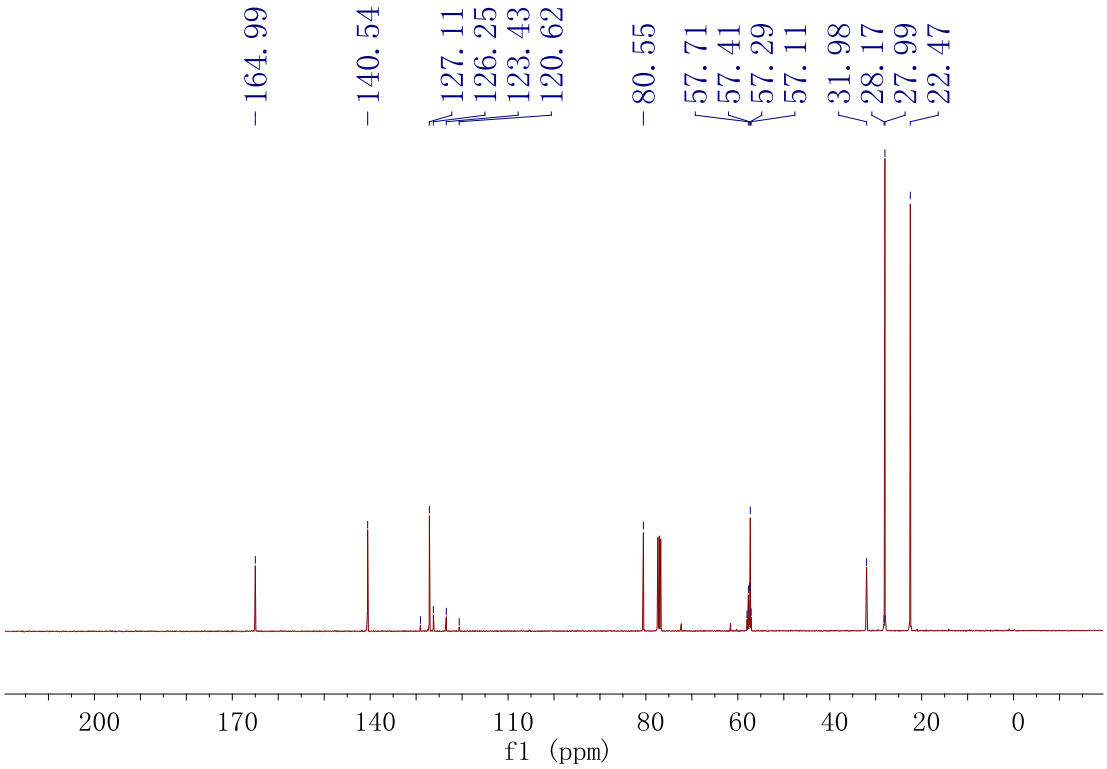
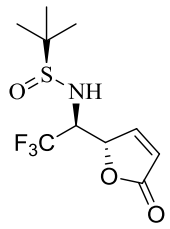
141.69
127.21
125.38
124.11
121.01
64.29
64.05
63.82
60.57
57.49
34.01
22.57
14.23
200
170
140
110
80
60
40
20
0
f1 (ppm)


7.28
6.73
6.69
5.85
5.81
4.12
3.80
3.79
3.79
3.78
3.77
2.62
2.57
2.53
2.49
1.41
1.16
1.00
0.99
1.05
1.07
1.06
1.00
9.04
9.04
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

O
S
NH
O
F3C
OtBu

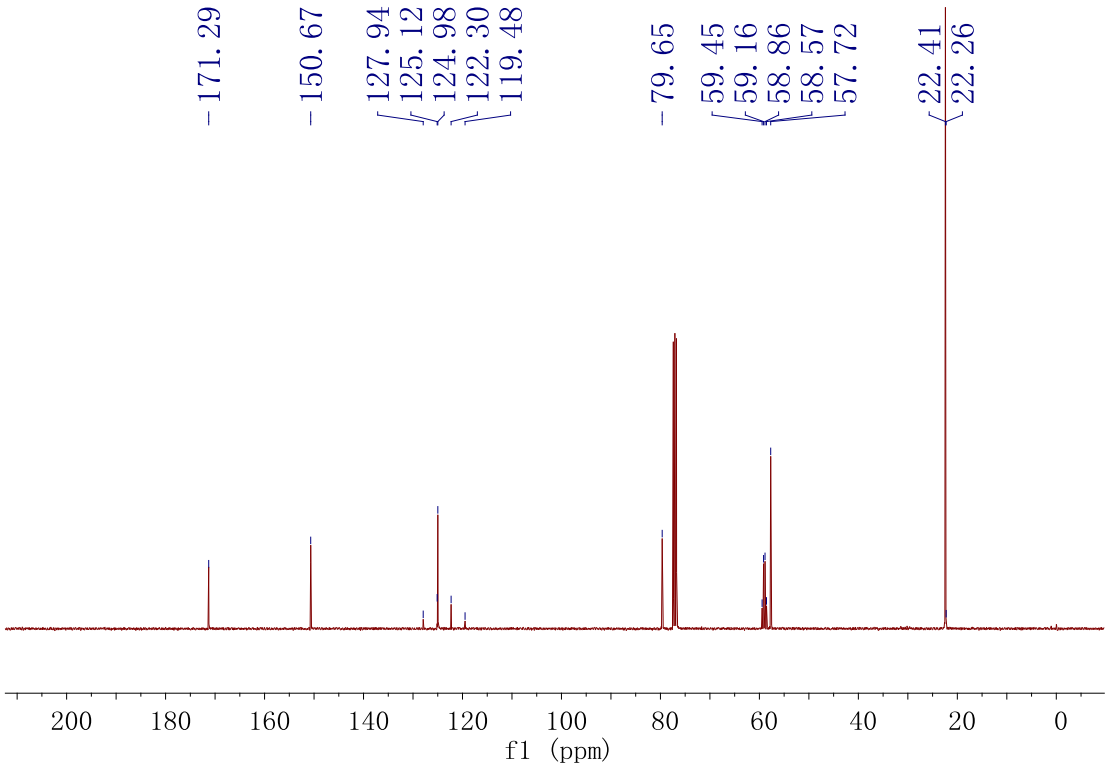
4d

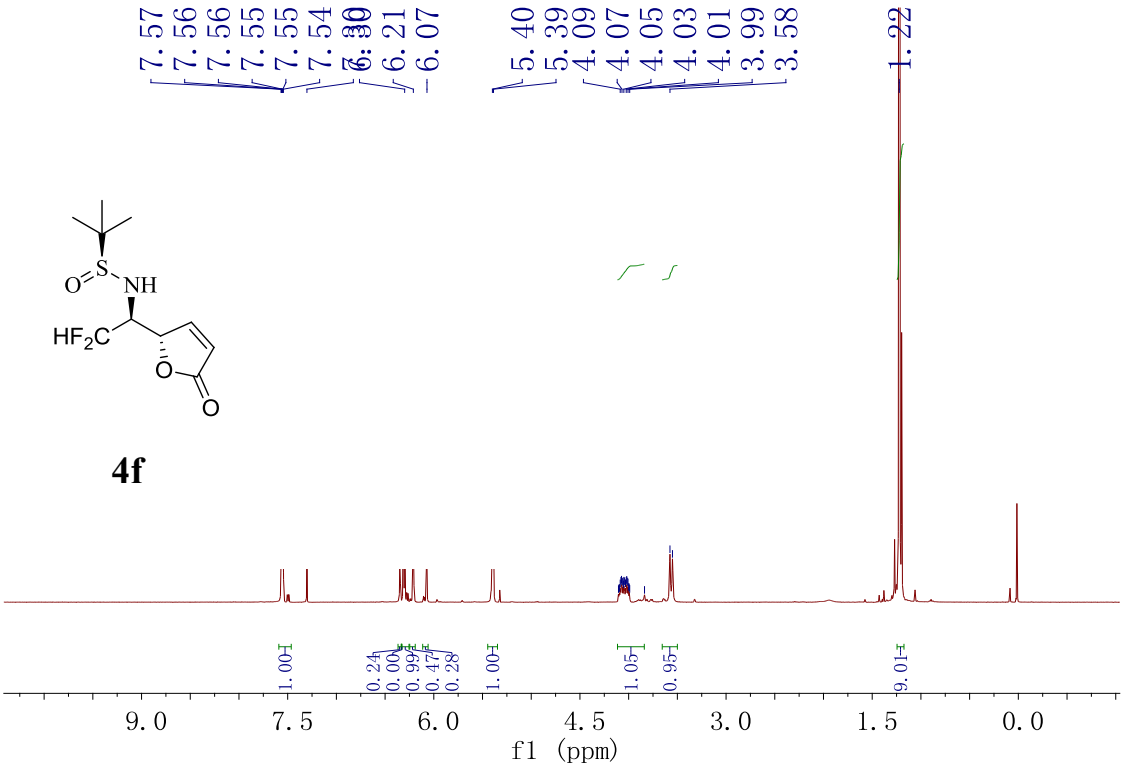

164.99
140.54
127.11
126.25
123.43
120.62
80.55
57.71
57.41
57.29
57.11
31.98
28.17
27.99
22.47
200
170
140
110
80
60
40
20
0
f1 (ppm)


O
S
NH
F3C
O
O

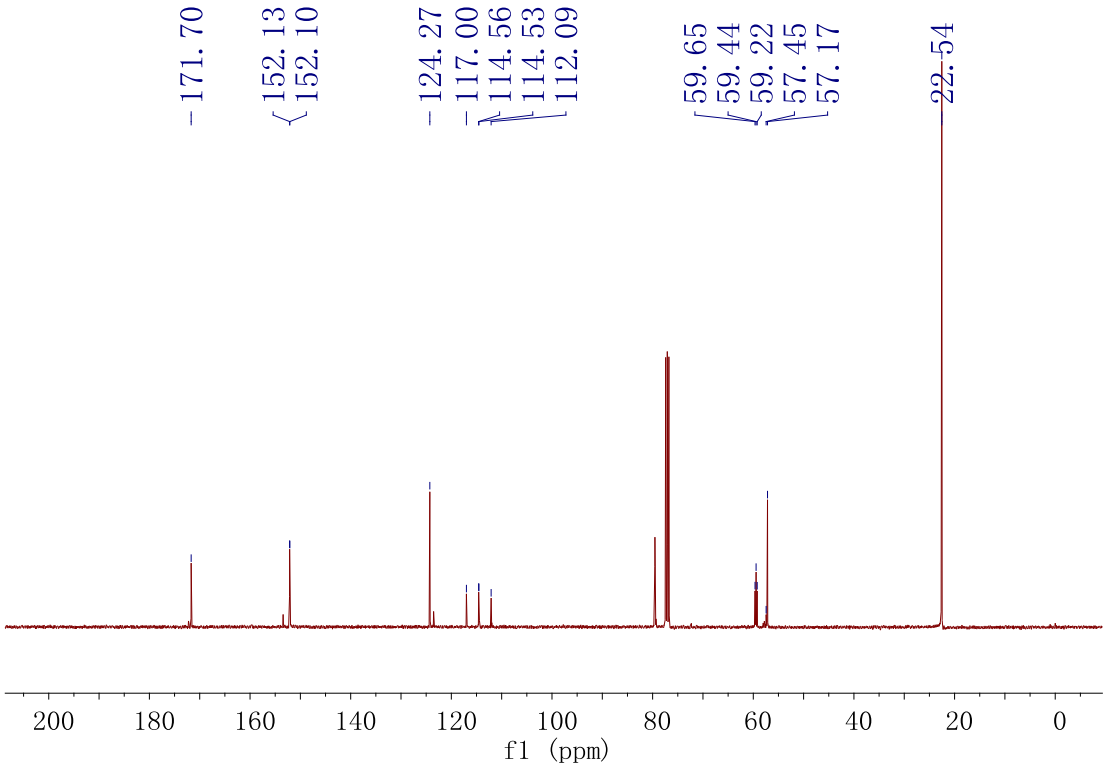
4e

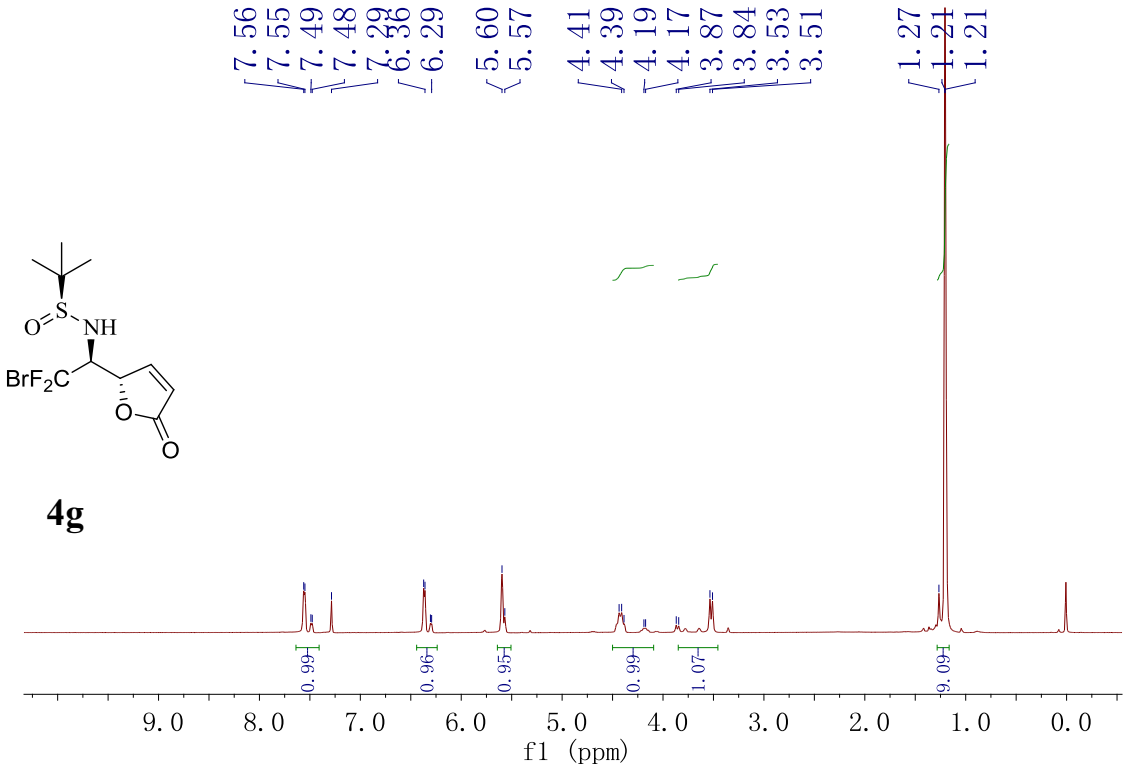
7.50
7.48
7.28
6.37
6.35
5.40
5.40
5.39
4.34
4.31
3.67
3.65
1.20
1.04
1.00
1.04
1.00
1.02
9.00
9.5
8.0
6.5
5.0
3.5
2.0
0.5
f1 (ppm)

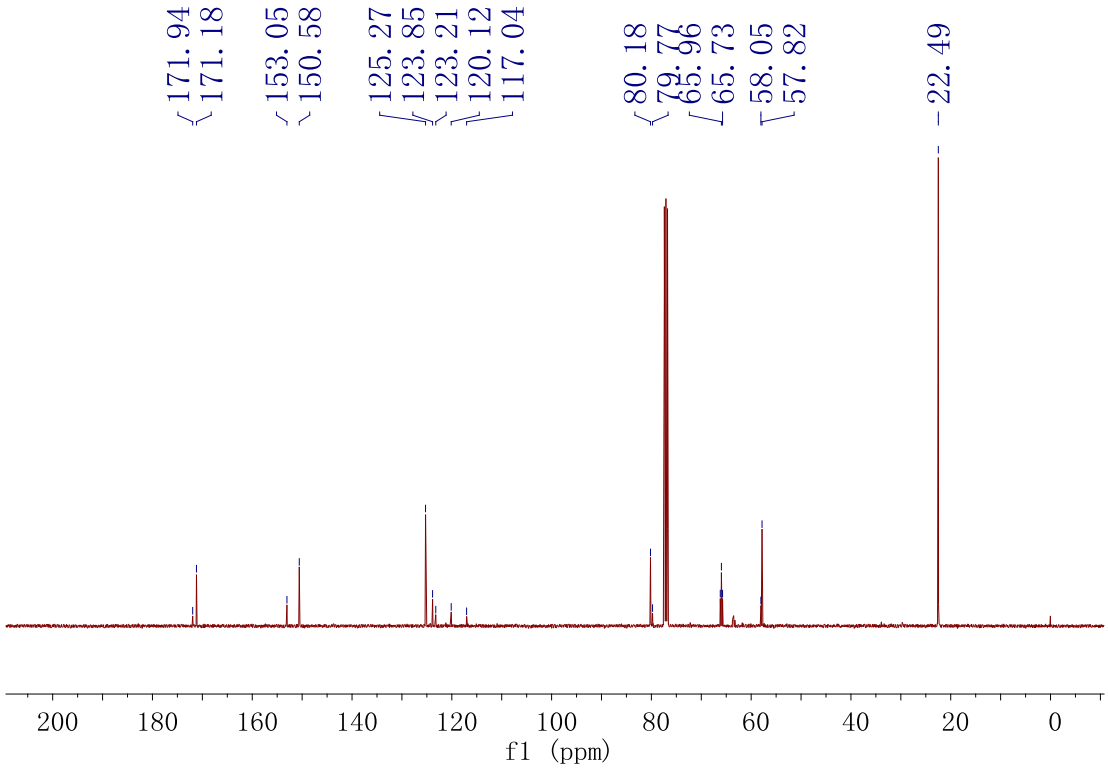

171.29
150.67
127.94
125.12
124.98
122.30
119.48
79.65
59.45
59.16
58.86
58.57
57.72
22.41
22.26
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

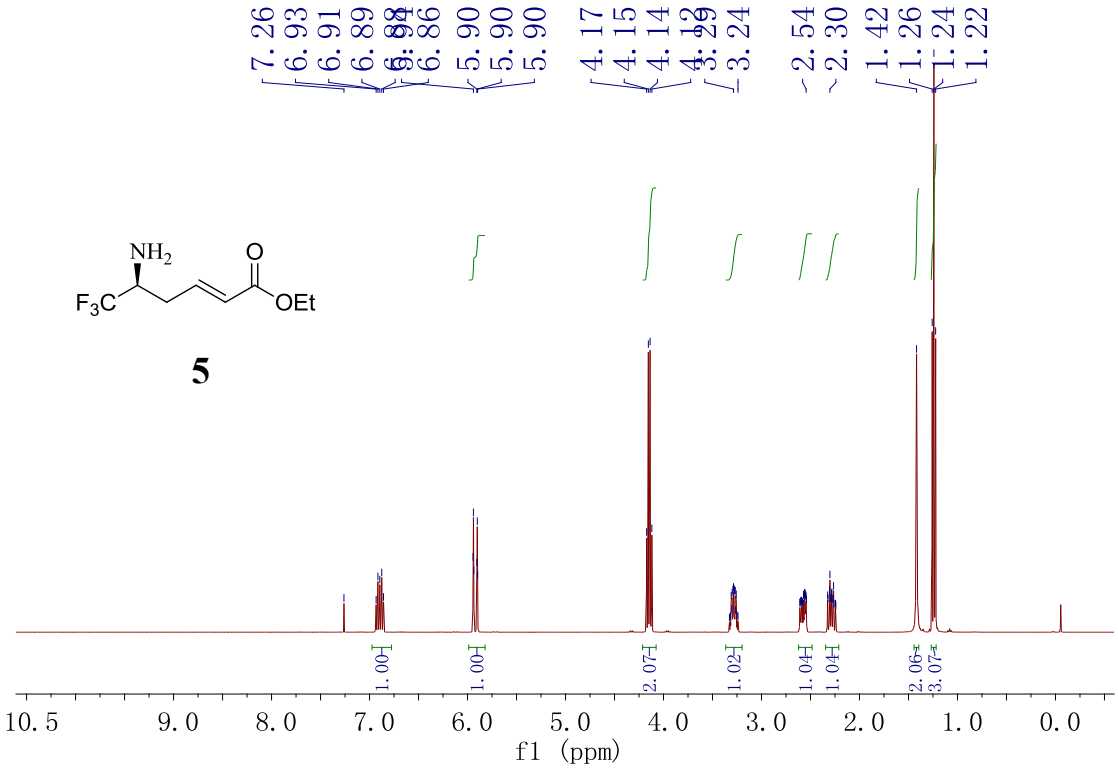

7.57
7.56
7.56
7.55
7.55
7.54
6.21
6.07
5.40
5.39
4.09
4.07
4.05
4.03
4.01
3.99
3.58
1.22
O
S
NH
HF2C
O
O
1.00
0.24
0.00
0.99
0.47
0.28
1.00
1.05
0.95
9.01
9.0
7.5
6.0
4.5
3.0
1.5
0.0
f1 (ppm)

4f

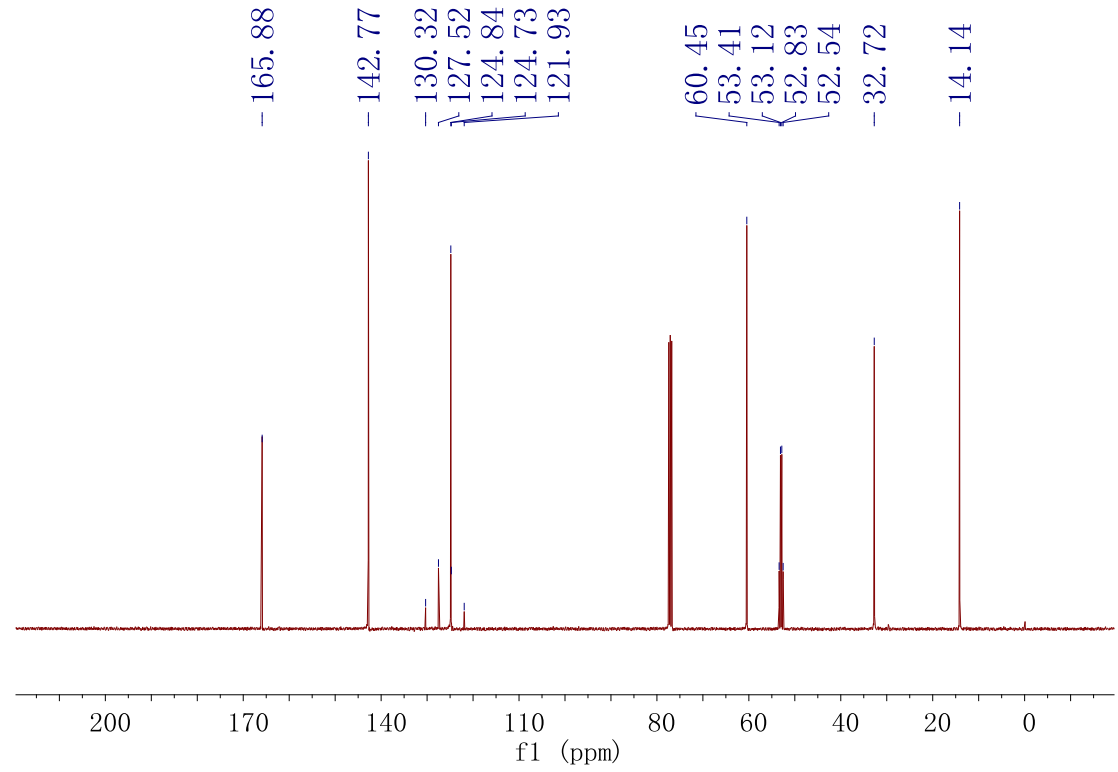


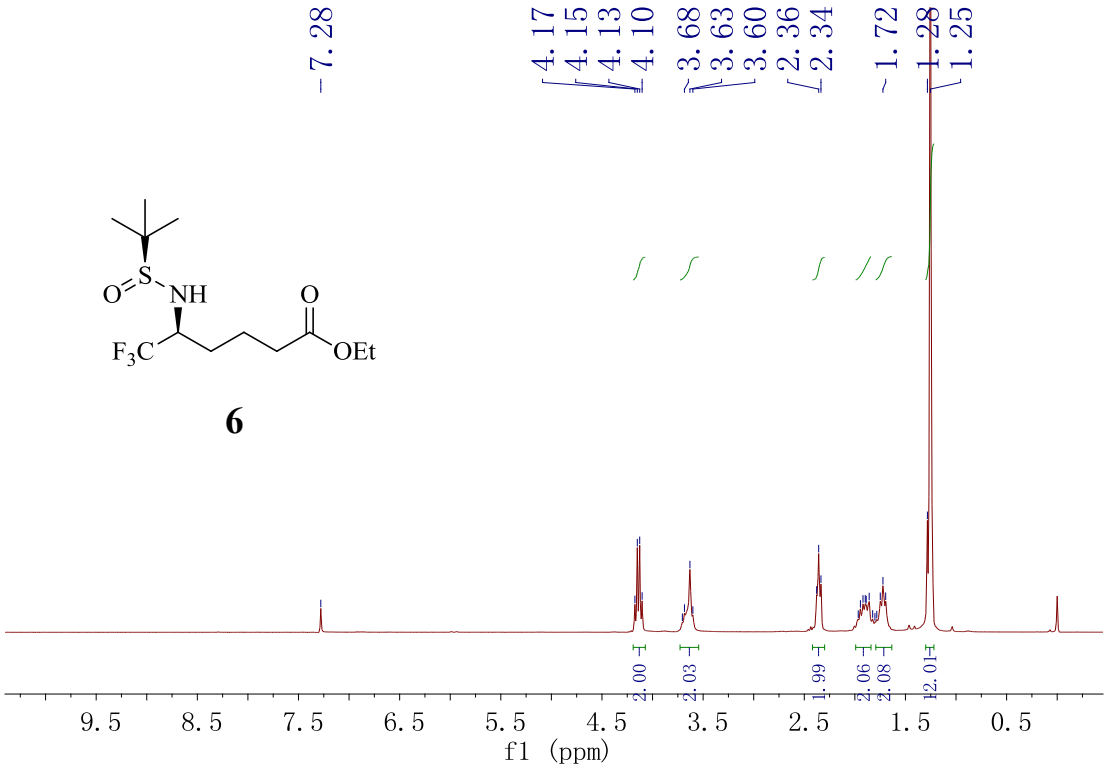



171.94
171.18
153.05
150.58
125.27
123.85
123.21
120.12
117.04
80.18
79.77
65.96
65.73
58.05
57.82
22.49
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.26
6.93
6.91
6.89
6.86
5.90
5.90
5.90
4.17
4.15
4.14
3.24
2.54
2.30
1.42
1.26
1.24
1.22
NH2
O
F3C
OEt
1.00
1.00
2.07
1.02
1.04
1.04
2.06
3.07
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

5


165.88
142.77
130.32
127.52
124.84
124.73
121.93
60.45
53.41
53.12
52.83
52.54
32.72
14.14
200
170
140
110
80
60
40
20
0
f1 (ppm)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4.17
4.15
4.13
4.10
3.68
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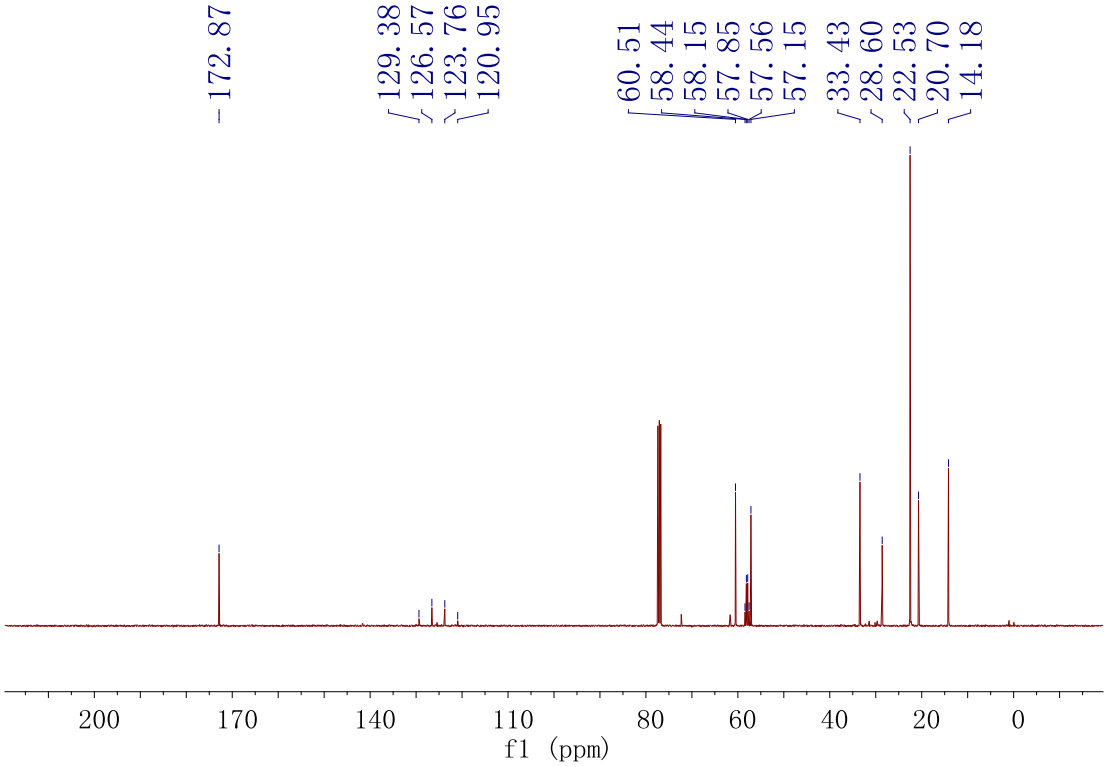
3.60
2.36
2.34
1.72
1.28
1.25
2.00
2.03
1.99
2.06
2.08
12.01
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

O
S
NH
O
F3C
OEt

6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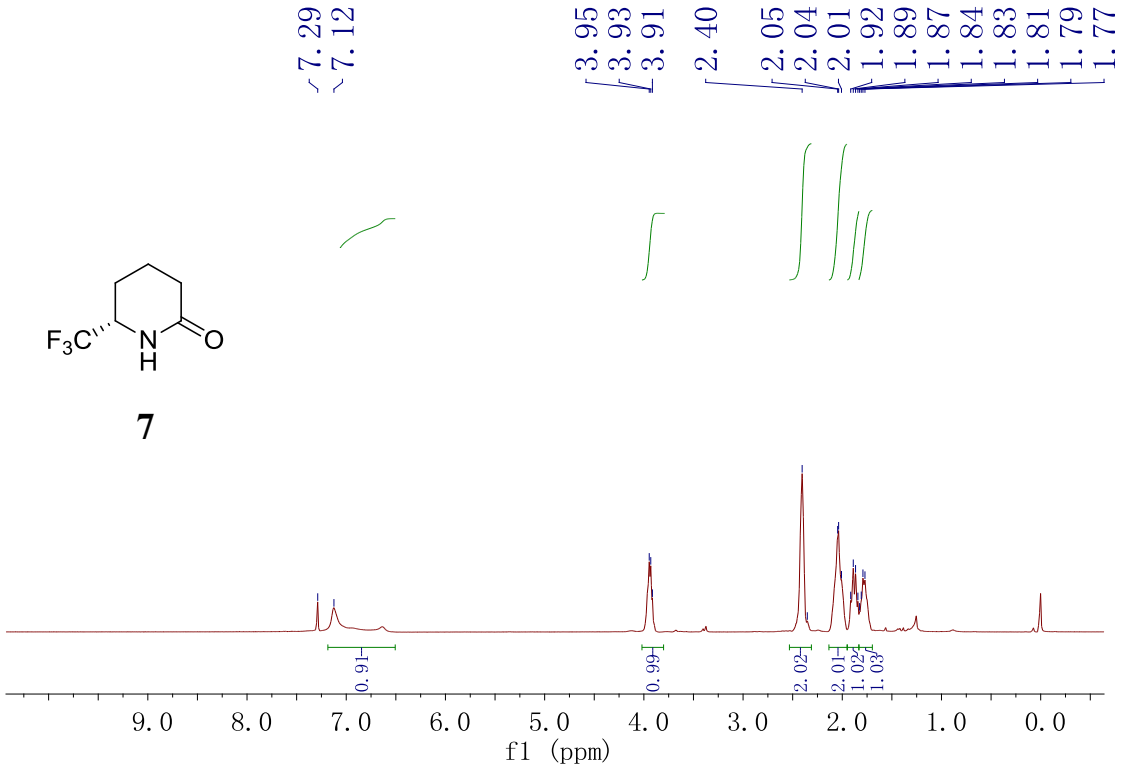
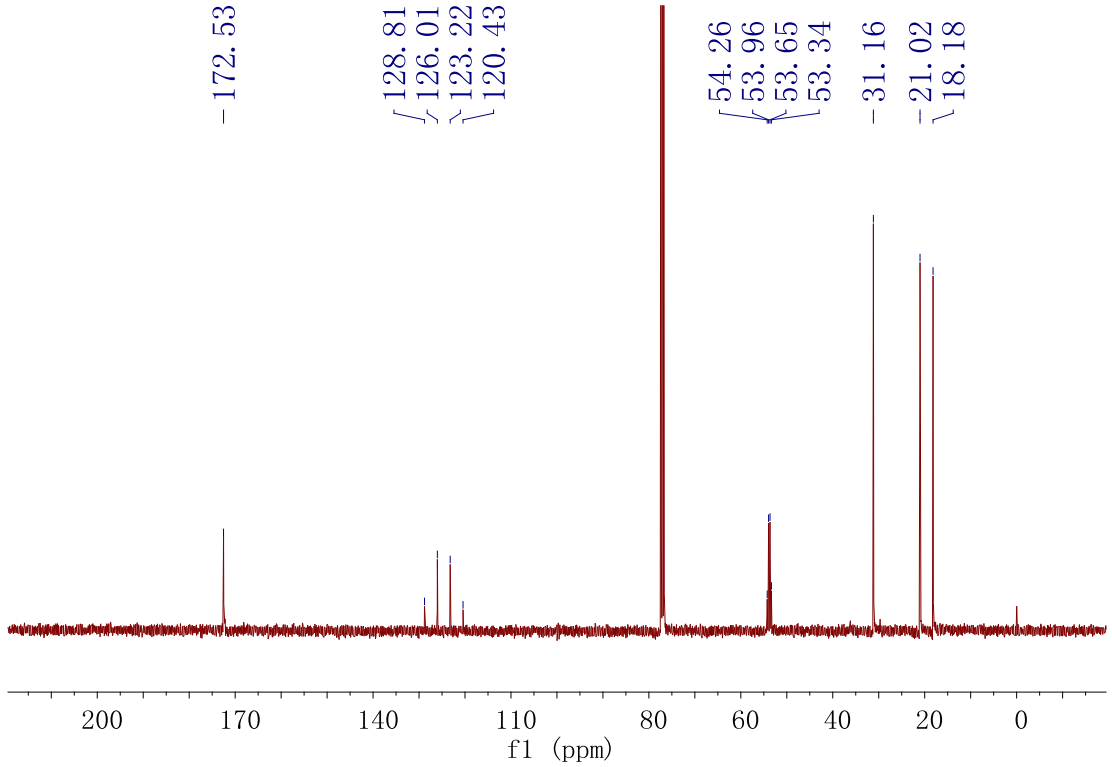
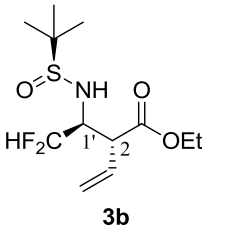
129.38
126.57
123.76
120.95
60.51
58.44
58.15
57.85
57.56
57.15
33.43
28.60
22.53
20.70
14.18
200
170
140
110
80
60
40
20
0
f1 (ppm)


7.29
7.12
3.95
3.93
3.91
2.40
2.05
2.04
2.01
1.92
1.89
1.87
1.84
1.83
1.81
1.79
1.77
F3C
N
H
O
0.91
0.99
2.02
2.01
1.02
1.03
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

7

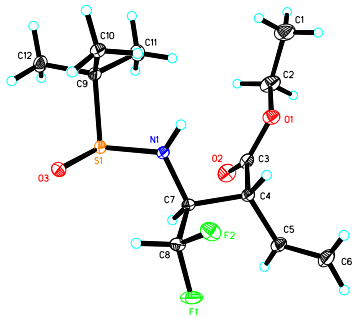

172.53
128.81
126.01
123.22
120.43
54.26
53.96
53.65
53.34
31.16
21.02
18.18
200
170
140
110
80
60
40
20
0
f1 (ppm)

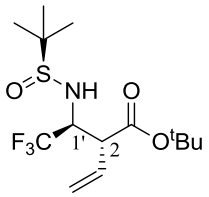
9. ORTEP drawing of the X-ray crystallographic structure of 3b, 3d, 4e.



3b

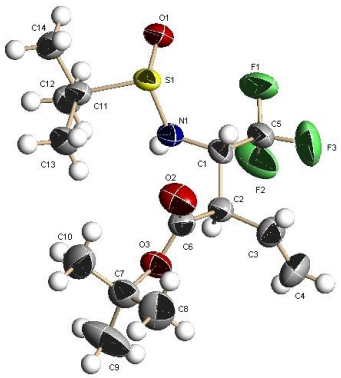
A

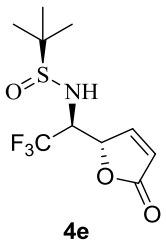




3d

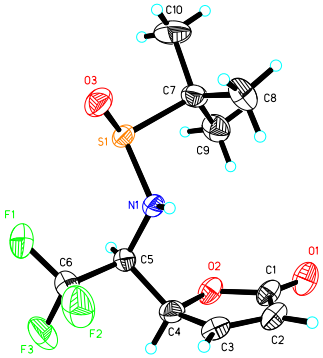
B





4e

C



CCDC 932085 contains the supplementary crystallographic data for the target compound **3b**.

CCDC 932084 contains the supplementary crystallographic data for the target compound **3d**.

CCDC 938431 contains the supplementary crystallographic data for the target compound **4e**.

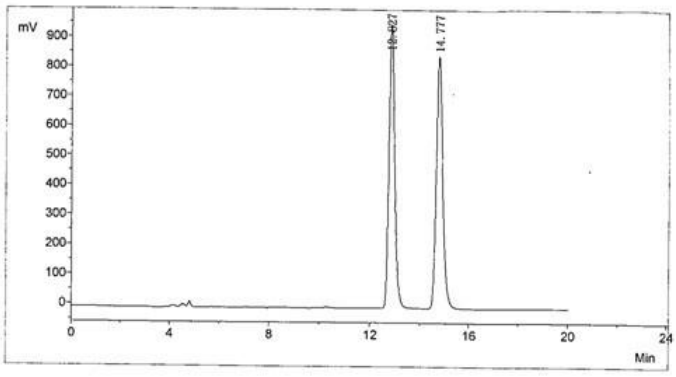
This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

10. Chiral HPLC spectra of compound 5.

HPLC Report

Sample Name:
Operator:
Time:08:43

Data File:CC2009157-5a+-AD-H910.7214.che
Date:2013-05-08

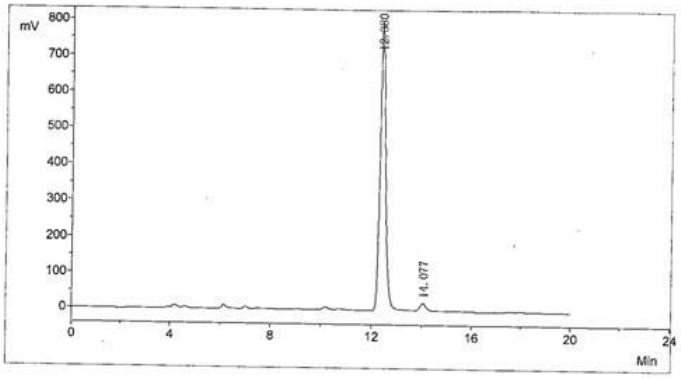


No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1		12.827	946446.9	15085373.2	49.3812
2	2		14.777	848215.2	15463440.4	50.6188
Total				1794662.1	30548813.6	100.0000

HPLC Report

Sample Name:
Operator:
Time:13:53

Data File:cc5a.che
Date:2013-05-02



No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1		12.380	787648.2	12202587.0	97.8035
2	2		14.077	20187.1	274047.6	2.1965
Total				807835.3	12476634.7	100.0000