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Supporting Information

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Stereoselective Synthesis of α,α-Chlorofluoro Carbonyl Compounds Leading to the Construction of Fluorinated Chiral Quaternary Carbon Centers

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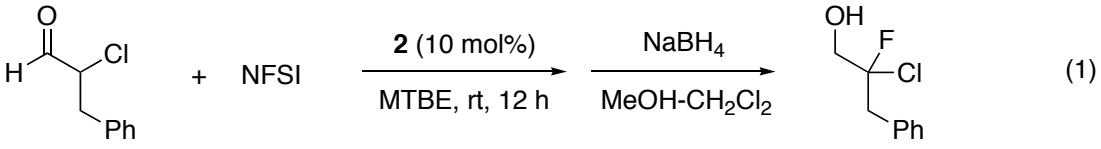
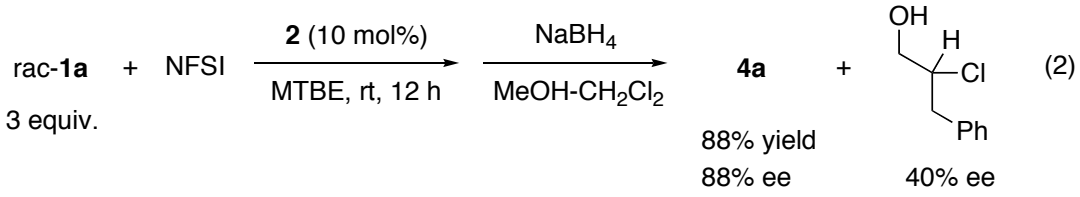
Supporting Information

General: All non-aqueous reactions were carried out in flame-dried glassware under argon atmosphere and stirred via magnetic stir-plates. Thin-layer chromatography analyses were performed using Merck pre-coated silica gel plates with F254 indicator. Visualization was accomplished by UV light (256 nm), potassium permanganate, phosphomolybdic acid, iodine, or vanillin. Flash column chromatography was performed according to the method of Still using silica gel 60 (mesh 230-400) supplied by E. Merck. All reactions were carried out with anhydrous solvents unless otherwise noted. Anhydrous dichloromethane, THF and diethyl ether were dried with a M BRAUN solvent purification system (A2 Alumina). Anhydrous *t*-butylmethyl ether (MTBE) and dimethylsulfoxide (DMSO) were purchased from Aldrich and used without further purification. Infrared spectra were recorded as thin films on sodium chloride plates using a Nicolet 20 SXB FTIR. ^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 500 (500 MHz ^{1}H, 470 MHz ^{19}F, 125 MHz ^{13}C). Chemical shift values (δ) are reported in ppm (tetramethylsilane δ 0.00 ppm for ^{1}H; trichlorofluoromethane δ 0.00 ppm for ^{19}F; residual chloroform δ 77.0 ppm for ^{13}C).

General procedure for Table 1: To a solution of α-chloroaldehyde **1** (1.5 mmol) in MTBE (2 mL), was added catalyst **2** (0.05 mmol) and *N*-fluorobenzenesulfonimide (0.5 mmol) at 0 °C. The reaction mixture was stirred at 0 °C or 25 °C for 12~30 hours. The mixture was poured into methanol-dichloromethane (1 : 4, 5 mL) at 0 °C. To this solution, $NaBH_4$ (5 mmol) was added, and the mixture was stirred at 0 °C for 1 hour. The reaction was quenched with saturated aqueous NH_4Cl solution, and the mixture was extracted by diethyl ether. The organic layer was dried over sodium sulfate, concentrated and chromatographed on silica gel to give **4**.

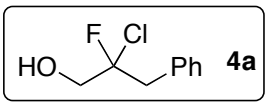
Effect of the proportion of reagents: When 1:2 ratio of **1a** and NFSI were subjected to this reaction at room temperature, 20% ee of product **4a** was obtained (Equation 1). The use of 3 equivalent of **1a** against to NFSI increased the selectivity dramatically to 88% ee, and the optical purity of recovered monochloro alcohol was determined to be 40% ee (Equation 2). These result suggest that this organocatalysis involves a sort of kinetic resolution mechanism. Detail studies on reaction mechanism are undergoing.



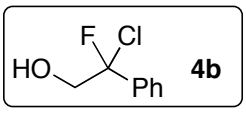


Analytical details for compounds 4a-d:

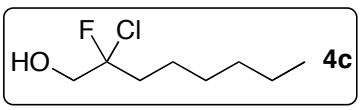
Racemic compounds **4a-d** were prepared for chiral HPLC or GC analyses using racemic α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether as a catalyst instead of **2**.



2-chloro-2-fluoro-3-phenylpropan-1-ol (4a): The crude mixture was purified by silica gel column chromatography (hexanes : ethyl acetate = 9:1) to give 85% yield of **4a** as colorless oil (91% ee). IR (film) 3387, 3065, 3033, 2933, 1496, 1455, 1075, 966, 850, 756, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.30 (m, 5H), 3.88-3.71 (m, 2H), 3.46 (dd, 2H, *J* = 32.3, 15.0 Hz), 2.15 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.3 (d, *J* = 3.8 Hz), 130.7, 128.4, 127.6, 114.8 (d, *J* = 247 Hz), 67.2 (d, *J* = 26.4 Hz), 44.6 (d, *J* = 21.4 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –114.2 (m); MS (APCI) $[M+Cl]^-$ 223.0, Calculated Mass 188.0; $[\alpha]_D$ = –2.79 (c = 1.5, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99 : 1, 1.0 mL/min) using a CHIRALPAK IC column (0.46cmø x 25cm): major isomer 12.9 min and minor isomer 13.7 min.

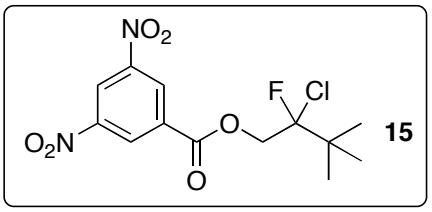


2-chloro-2-fluoro-2-phenylethanol (4b): The crude mixture was purified by silica gel column chromatography (hexanes : ethyl acetate = 9:1) to give 62% yield of **4b** as colorless oil (91% ee). IR (film) 3363, 3065, 3036, 2934, 1493, 1450, 1281, 1134, 1066, 945, 856, 758, 712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59-7.53 (m, 2H), 7.46-7.40 (m, 3H), 4.15-4.04 (m, 2H), 2.15 (t, 1H, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.7 (d, *J* = 22.6 Hz), 129.8, 128.6, 125.3 (d, *J* = 7.5 Hz), 112.9 (d, *J* = 247 Hz), 70.2 (d, *J* = 26.4 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –118.2 (t, *J* = 18.8 Hz); HRMS (EI) $[M]^+$ 174.0248, Calculated Mass 174.0248; $[\alpha]_D$ = –77.5 (c = 0.6, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99 : 1, 1.0 mL/min) using a CHIRALPAK IC column (0.46cmø x 25cm): major isomer 19.1 min and minor isomer 21.1 min.



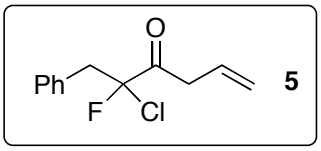
2-chloro-2-fluorooctan-1-ol (4c): The crude mixture was purified by silica gel column chromatography (hexanes : ethyl acetate = 9:1) to give 81% yield of **4c** as colorless oil (81% ee). IR (film) 3361, 2957, 2933, 2859, 1458, 1379, 1279, 1132, 1056, 903, 848, 726, 701 cm^{-1}; ^1H

NMR (500 MHz, $CDCl_3$) δ 3.91-3.78 (m, 2H), 2.14-2.05 (m, 3H), 1.59-1.54 (m, 2H), 1.37-1.29 (m, 6H), 0.90 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 116.1 (d, *J* = 245 Hz), 68.3 (d, *J* = 26.4 Hz), 38.5 (d, *J* = 21.3 Hz), 31.5, 28.9, 23.3 (d, *J* = 3.8 Hz), 22.5, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ –113.9 (br); MS (APCI) $[M+Cl]^-$ 217.0, Calculated Mass 182.1; $[\alpha]_D$ = +2.3 (c = 0.5, $CHCl_3$). The enantiomeric ratio was determined by GC (100~150 °C, 3 °C/min) using a Chiral DEX B-DM column: major isomer 12.4 min and minor isomer 13.3 min.

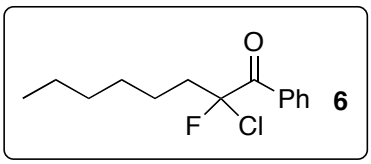


2-chloro-2-fluoro-3,3-dimethylbutyl 3,5-dinitrobenzoate (15): The reaction was performed according to general procedure. After quenching the reaction by aqueous NH_4Cl solution, the mixture was extracted by pentane. The organic layer was dried over sodium sulfate and concentrated. This crude mixture was dissolved into dichloromethane (10 mL). To this solution, triethylamine (7.5 mmol) and 3,5-dinitrobenzoyl chloride (4.5 mmol) were added at 0 °C, and the mixture was stirred at 25 °C for 5 hours. The mixture was poured into aqueous $NaHCO_3$ solution and extracted by dichloromethane. The organic layer was dried over sodium sulfate, concentrated and chromatographed on silica gel (pentane : diethyl ether = 5:1) to give 86% yield of **15** as a white powder (99% ee). IR (film) 3101, 2977, 1740, 1629, 1545, 1457, 1345, 1273, 1168, 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.27 (br, 1H), 9.22 (br, 2H), 4.93-4.80 (m, 2H), 1.26 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0, 148.8, 133.1, 129.7, 122.8, 118.5 (d, *J* = 253 Hz), 67.1 (d, *J* = 23.9 Hz), 40.8 (d, *J* = 3.8 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –120.5 (dd, *J* = 25.6, 7.9 Hz); MS (APCI) $[M+Cl]^-$ 383.0, Calculated Mass 348.1; $[\alpha]_D$ = –16.5 (c = 2.3, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 90 : 10, 1.0 mL/min) using a CHIRALPAK AD-H column (0.46cmø x 25cm): major isomer 9.7 min and minor isomer 11.4 min.

General procedure for Scheme 2: To a solution of α-chloroaldehyde **1** (1.5 mmol) in MTBE (2 mL), was added catalyst **2** (0.05 mmol) and *N*-fluorobenzenesulfonimide (0.5 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 24 hours. The reaction mixture was poured into a solution of PhMgBr (6.0 mmol) in THF (12 mL) or a solution of AllylMgBr (6.0 mmol) in diethyl ether–THF (1 : 1, 12 mL) at 0 °C. After the mixture was stirred for 2 hours at 0 °C, the mixture was poured into ice-cold aqueous NH_4Cl solution and extracted by diethyl ether. The organic layer was dried over sodium sulfate, concentrated and subjected to short silica gel column chromatography (hexanes : ethyl acetate = 5 : 1) to give a crude mixture of secondary alcohol. To a solution of this crude mixture in dichloromethane (10 mL), was added Dess-Martin periodinate (1.5 mmol) at room temperature, and the mixture was stirred for 2 hours at room temperature. The mixture was directly subjected to silica gel column chromatography to give desired α,α-chlorofluoroketone **5** or **6**.

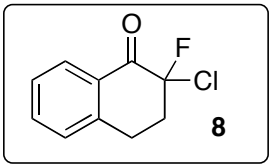


Compound 5: The reaction mixture was purified by silica gel column chromatography (hexanes : dichloromethane = 4 : 1) to give 71% yield of **5** as colorless oil (90% ee). IR (film) 3087, 3067, 3034, 1742, 1645, 1497, 1456, 1425, 1389, 1326, 1125, 1089, 994, 926, 851, 739, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34-7.23 (m, 5H), 5.85-5.77 (m, 1H), 5.18 (dd, *J* = 7.5, 1.5 Hz 1H), 5.08 (dd, *J* = 17.0, 1.5 Hz 1H), 3.69-3.46 (m, 3H), 3.20-3.14 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.1 (d, *J* = 31.4 Hz), 132.2, 130.9, 128.5, 127.8, 119.8, 108.5 (d, *J* = 259 Hz), 44.5 (d, *J* = 20.1 Hz), 41.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ –120.9 (t, *J* = 21.6 Hz); HRMS (CI) $[M]^+$ 227.06387, Calculated Mass 227.06390; $[\alpha]_D$ = +25.2 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99.9 : 0.1, 1.0 mL/min) using a CHIRALCEL OJ-H column (0.46cmø x 25cm): major isomer 15.2 min and minor isomer 33.7 min.



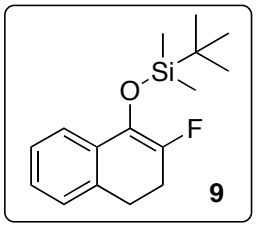
Compound 6: The reaction mixture was purified by silica gel column chromatography (hexanes : ethyl acetate = 9 : 1) to give 65% yield of **6** as colorless oil (81% ee). IR (film) 2932, 2858, 1699, 1449, 1261, 1149, 704, 686 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.5 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz 2H), 2.51-2.35 (m, 2H), 1.69-1.62 (m, 1H), 1.55-1.50 (m, 1H), 1.41-1.22 (m, 6H), 0.89 (t, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.0 (d, *J* = 28.9 Hz), 133.8, 132.0, 130.42, 130.38, 128.4, 39.5 (d, *J* = 21.6 Hz), 31.4, 28.8, 22.9 (d, *J* = 2.3 Hz), 22.4, 13.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ –115.3 (t, *J* = 21.4 Hz); MS (APCI) $[M]^-$ 256.1, Calculated Mass 256.1; $[\alpha]_D$ = +5.5 (c = 1.4, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99.9 : 0.1, 1.0 mL/min) using a CHIRALCEL OJ-H column (0.46cmø x 25cm): major isomer 6.4 min and minor isomer 7.2 min.

α-Fluorotetralone (**7**) was synthesized by reported procedure (**Scheme 3**).[1] The compound was identical in all respects to the known literature compound.



Racemic synthesis of α,α-chlorofluoro-1-tetralone (8) (Scheme 3): To a solution of **7** (1.0 mmol) in dichloromethane (2 mL), were added triethylamine (1.1 mmol) and trimethylsilyl trifluoromethanesulfonate (1.0 mmol) at 0 °C. After the reaction mixture was stirred at 25 °C for 1 hour, *N*-chlorosuccinimide (1.1 mmol) was added at 0 °C. The mixture was stirred at 25 °C for 3 hours. The mixture was quenched with water and extracted with diethyl ether. The organic layer was dried over sodium sulfate, concentrated and chromatographed on silica gel (hexanes : ethyl acetate = 5 : 1) to give 99% yield of **8** as a white powder. IR (film) 2922, 1706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, 1H, *J* = 8.0 Hz), 7.58 (t, 1H, *J* = 7.5 Hz), 7.41 (t, 1H, *J* = 7.5 Hz), 7.29 (d, 1H, *J* = 8.0

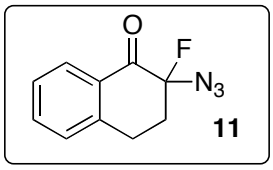
Hz), 3.39-3.32 (m, 1 H), 3.14-3.09 (m, 1H), 2.83-2.67 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.3 (d, *J* = 21.4 Hz), 141.9, 134.8, 129.2, 128.9, 128.8, 127.5, 105.2 (d, *J* = 257 Hz), 37.3 (d, *J* = 20.1 Hz), 27.0 (d, *J* = 8.8 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –116.8 (br); MS (EI) $[M]^+$ 198.0, Calculated Mass 198.0.



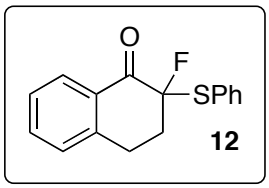
***t*-Butyldimethyl(2-fluoro-3,4-dihydronaphthalen-1-yloxy)silane (9) (Scheme 4)**: To a solution of **7** (10 mmol) in dichloromethane (20 mL), were added triethylamine (10.1 mmol) and trifluoromethanesulfonyl chloride (10 mmol) at 0 °C. The reaction mixture was stirred at 25 °C for 5 hours. The mixture was poured into aqueous $NaHCO_3$ solution and extracted by dichloromethane. The organic layer was dried over sodium sulfate, concentrated and chromatographed on silica gel (hexanes : diethyl ether = 10 : 1) to give 99% yield of **9** as a clear oil. IR (film) 2931, 2893, 2858, 1690, 1472, 1324, 1254, 1192, 1090, 952, 901, 835, 784, 760 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, 1H, *J* = 7.5 Hz), 7.20 (t, 1H, *J* = 7.5 Hz), 7.12-7.05 (m, 2H), 2.94 (t, 2H, *J* = 8.5 Hz), 2.61 (td, *J* = 8.0, 4.5 Hz, 2H), 1.02 (s, 9H), 0.19 (d, *J* = 2.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2 (d, *J* = 258 Hz), 133.5, 133.1, 129.4 (d, *J* = 11.3 Hz), 126.8, 126.39, 126.37 (d, *J* = 1.3 Hz), 121.7, 28.4 (d, *J* = 7.9 Hz), 25.9, 24.5 (d, *J* = 22.3 Hz), 18.5, –4.6 (d, J = 3.1 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –127.4 (s); HRMS (EI) $[M]^+$ 278.1502, Calculated Mass 278.1502.

Asymmetric synthesis of 8 (Scheme 4): A Schlenk flask was charged with zirconium(IV) chloride (3.0 mmol) and di-(+)-2-(1-naphthalyl)cyclohexyl α,α-dichloromalonate[2] (**10**) (3.3 mmol) in a glove box. The mixture was cooled to –78 °C and dissolved in dichloromethane (60 mL). The mixture was stirred at 25 °C for 10 min to give light blue solution. The solution was cooled to –78 °C and a solution of **9** (3.0 mmol) in dichloromethane (2 mL) was dropwised. After the mixture was stirred at –78 °C for 72 hours, the mixture was poured into aqueous $NaHCO_3$ solution and extracted by dichloromethane. The organic layer was dried over sodium sulfate, concentrated and chromatographed on silica gel

(hexanes : benzene = 1 : 1) to give 82% yield of **8** as a white powder (87% ee). A single recrystallization from hexane/2-propanol (9/1) gave 35% yield of crystal with 74% ee and then 65% yield of **8** was recovered from mother liquar with 94% ee. $[\alpha]_D$ = –77.6 (c = 1.3, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 90 : 10, 1.0 mL/min) using a CHIRALCEL OB-H column (0.46cmø x 25cm): minor isomer 11.0 min and major isomer 12.9 min.

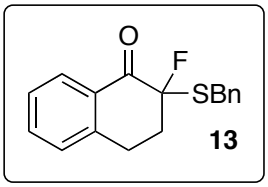


Compound 11 (Scheme 5): To a solution of (-)-**8** (0.5 mmol) in DMSO (2 mL), was added sodium azide (1.0 mmol) at 25 °C, and the mixture was stirred at 80°C for 10 min. The mixture was extracted with diethyl ether and water. The organic layer was dried over sodium sulfate, concentrated and chromatographed quickly on silica gel (hexanes : dichloromethane = 1 : 1) to give 77% yield of **11** as a clear oil (94% ee). IR (film) 3069, 2942, 2129, 1700, 1604, 1457, 1313, 1229, 1060, 932, 906, 744 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, 1H, *J* = 7.9 Hz), 7.58 (t, 1H, *J* = 7.5 Hz), 7.40 (t, 1H, *J* = 7.5 Hz), 7.29 (d, 1H, *J* = 7.7 Hz), 3.14-3.02 (m, 2 H), 2.47-2.41 (m, 1H), 2.38-2.30 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.9 (d, *J* = 28.7 Hz), 143.2, 134.9, 129.5, 128.9, 128.8, 127.5, 100.6 (d, *J* = 227 Hz), 33.1 (d, *J* = 21.4 Hz), 25.6 (d, *J* = 6.3 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –128.4 (dd, *J* = 17.4, 8.6 Hz); MS (EI) $[M]^+$ 205.2, $[M–N_2]^+$ 177.1, Calculated Mass 205.1; $[\alpha]_D$ = –217 (c = 0.5, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 98 : 2, 1.0 mL/min) using a CHIRALCEL OB-H column (0.46cmø x 25cm): major isomer 8.9 min and minor isomer 11.1 min.



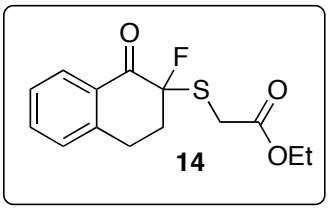
Compound 12 (Scheme 5): To a solution of (-)-**8** (0.5 mmol) in dichloromethane (2 mL), were added triethylamine (2.5 mmol) and phenylthiol (1.25 mmol) at 25 °C, and the mixture was refluxed for 30 min. Extra triethylamine (2.5 mmol) and phenylthiol (1.25 mmol) were added and

the mixture was refluxed another 30 min. The mixture was directly subjected to silica gel column chromatography (hexanes : dichloromethane = 1 : 2) to give 92 % yield of **12** as clear oil (94% ee). IR (film) 3060, 2934, 1698, 1602, 1299 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, 1H, *J* = 8.0 Hz), 7.55 (t, 1H, *J* = 7.5 Hz), 7.49-7.22 (m, 7H), 3.38-3.30 (m, 1 H), 3.02 (br d, 1H, *J* = 17.5 Hz), 2.64-2.50 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.6 (d, *J* = 21.3 Hz), 141.7, 136.1, 134.0, 130.6, 130.0, 129.1, 128.6, 128.4, 127.7, 127.2, 103.4 (d, *J* = 238 Hz), 33.9 (d, *J* = 22.6 Hz), 27.6 (d, *J* = 7.5 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –130.5 (br); MS (EI) $[M]^+$ 271.9, $[M–HF]^+$ 252.0, Calculated Mass 272.1; $[\alpha]_D$ = –82.5 (c = 0.45, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 90 : 10, 1.0 mL/min) using a CHIRALCEL OB-H column (0.46cmø x 25cm): major isomer 16.1 min and minor isomer 22.5 min.



Compound 13 (Scheme 5): To a solution of (-)-**8** (0.5 mmol) in dichloromethane (2 mL), were added triethylamine (5 mmol) and benzylthiol (2.5 mmol) at 25 °C, and the mixture was refluxed for 2 hours. Extra triethylamine (5 mmol) and benzylthiol (2.5 mmol) were added and the mixture was refluxed another 2 hours. The mixture was directly subjected to silica gel column chromatography (hexanes : ethyl acetate = 9 : 1) to give 98 % yield of **13** as white solid (94% ee). IR (film) 3062, 3029, 2935, 1695, 1602, 1455, 1299, 1223, 924 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, 1H, *J* = 7.5 Hz), 7.53 (t, 1H, *J* = 7.0 Hz), 7.37 (t, 1H, *J* = 7.5 Hz), 7.29-7.18 (m, 6 H), 4.06 (d, 1H, *J* = 12.5 Hz), 3.77 (d, 1H, *J* = 12.5 Hz), 3.26-3.19 (m, 1H), 3.05-3.00 (m, 1H), 2.72-2.59 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.6 (d, *J* = 23.9 Hz), 141.6, 136.2, 134.0, 130.2, 129.2, 128.62, 128.56, 128.53, 127.3, 127.2, 100.8 (d, *J* = 236 Hz), 34.8 (d, *J* = 18.9 Hz), 32.3, 27.7 (d, *J* = 6.3 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ –137.5 (br); HRMS (EI) $[M–HF]^+$ 266.0769, Calculated Mass (M–HF) 266.0765; $[\alpha]_D$ = +31.0 (c = 0.9, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99 :

1, 1.0 mL/min) using a CHIRALPAK IC column (0.46cmø x 25cm): major isomer 17.9 min and minor isomer 22.8 min.



14

Compound 14 (Scheme 5): To a solution of (-)-**8** (0.5 mmol) in dichloromethane (2 mL), were added triethylamine (5 mmol) and ethyl 2-mercaptoacetate (2.5 mmol) at 25 °C, and the mixture was refluxed for 4 hours. Extra triethylamine (5 mmol) and ethyl 2-mercaptoacetate (2.5 mmol) were added and the mixture was refluxed another 4 hours. The mixture was directly subjected to silica gel column chromatography (hexanes : ethyl acetate = 5 : 1) to give 90 % yield of **14** as white solid (94% ee). IR (film) 2982, 2937, 1735, 1694, 1603, 1456, 1331, 1243, 1156, 1028, 926, 735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, 1H, *J* = 8.0 Hz), 7.53 (t, 1H, *J* = 7.5 Hz), 7.37 (t, 1H, *J* = 7.5 Hz), 7.24 (d, 1 H, *J* = 8.0 Hz), 4.19-4.09 (m, 2H), 3.58 (s, 2H), 3.30-3.23 (m, 1H), 3.05 (br d, 1H, *J* = 17.0 Hz), 2.72-2.62 (m, 2H), 1.22 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.4 (d, *J* = 22.6 Hz), 168.8, 141.6, 134.2, 130.0, 128.72, 128.71, 128.6, 127.3, 99.6 (d, *J* = 236 Hz), 61.7, 34.6 (d, *J* = 20.1 Hz), 27.5 (d, *J* = 6.3 Hz), 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ –138.5 (br); HRMS (EI) $[M]^+$ 282.07231, Calculated Mass 282.07260; $[\alpha]_D$ = –5.7 (c = 1.9, $CHCl_3$). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 90 : 10, 1.0 mL/min) using a CHIRALCEL OB-H column (0.46cmø x 25cm): major isomer 25.9 min and minor isomer 29.7 min.

References:

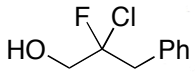
1. Stavber, S.; Jereb, M.; Zupan, M. *Synthesis* **2002**, 2609.

2. Zhang, Y.; Shibatomi, K.; Yamamoto, H. *J. Am. Chem. Soc.* **2004**, *126*, 15038.

^{1}H, ^{13}C, ^{19}F-NMR spectra

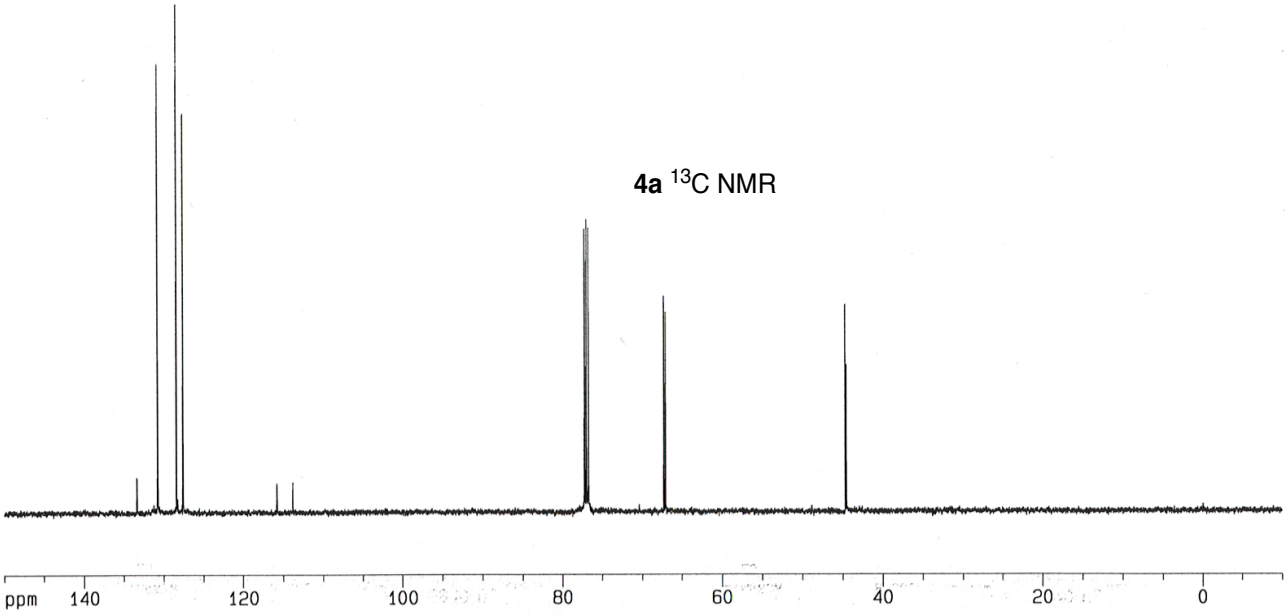
and

chiral HPLC, GC analyses

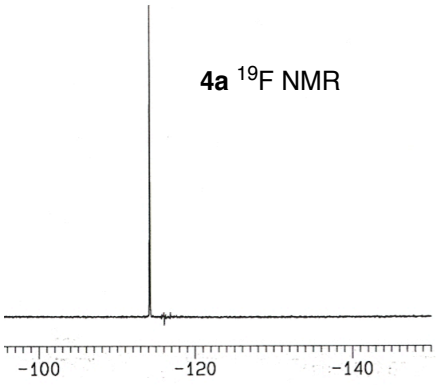


4a ^{1}H NMR

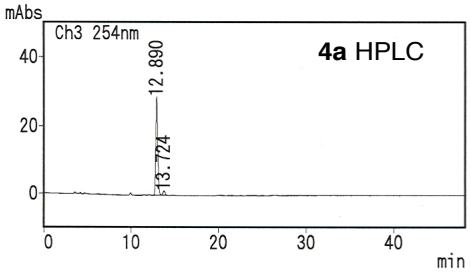
4a ^{13}C NMR



4a ^{19}F NMR



4a HPLC



*** ﾋﾟｰｸﾚﾎﾟｰﾄ ***

PKNO	ChNO	TIME	CONC	NAME
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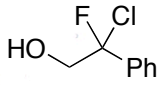
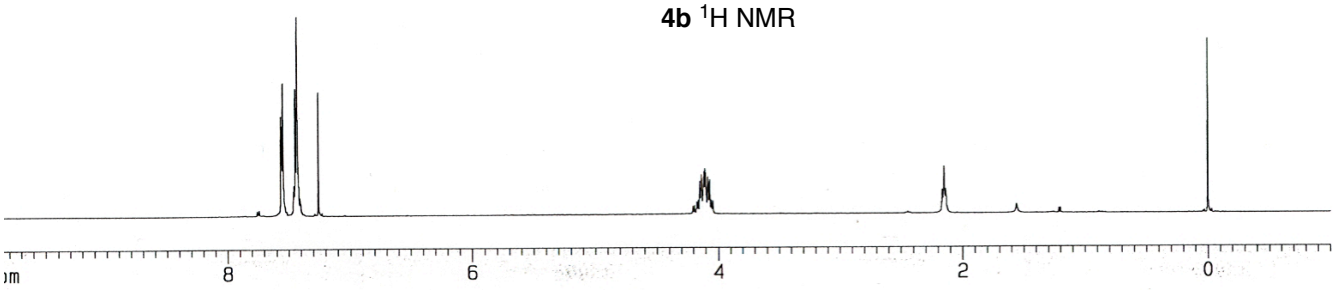
	3	13.724	4.3553	B

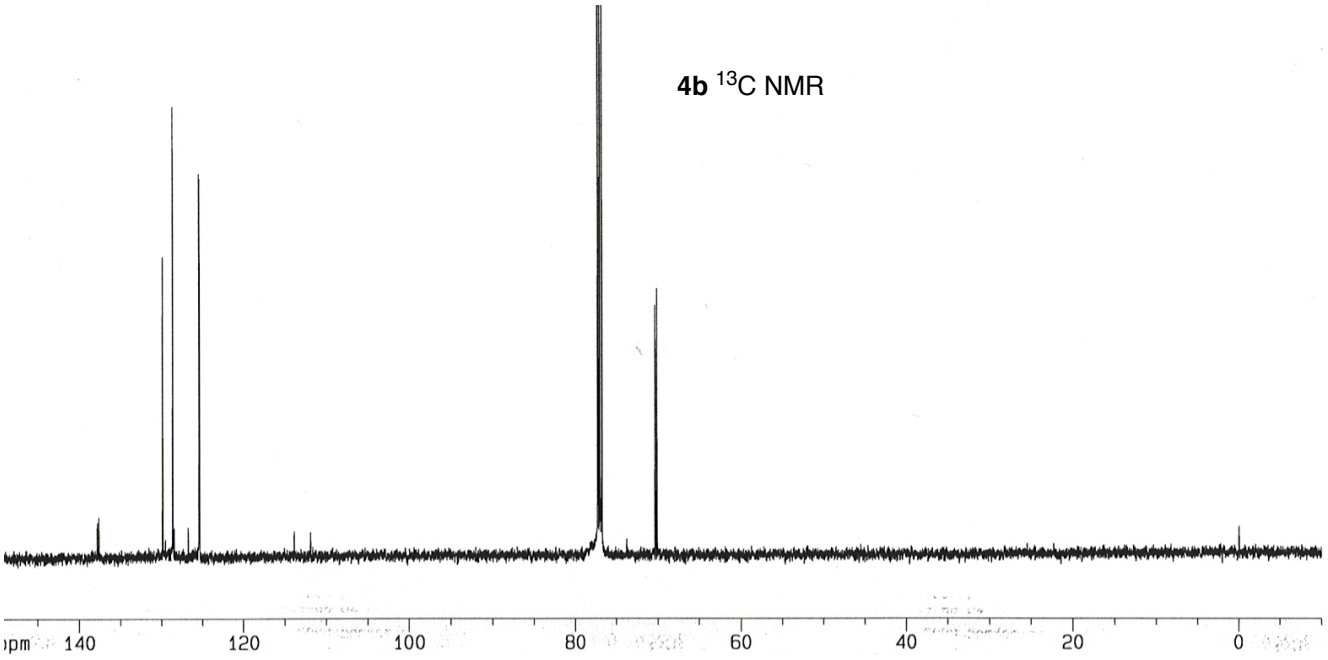
100.0000



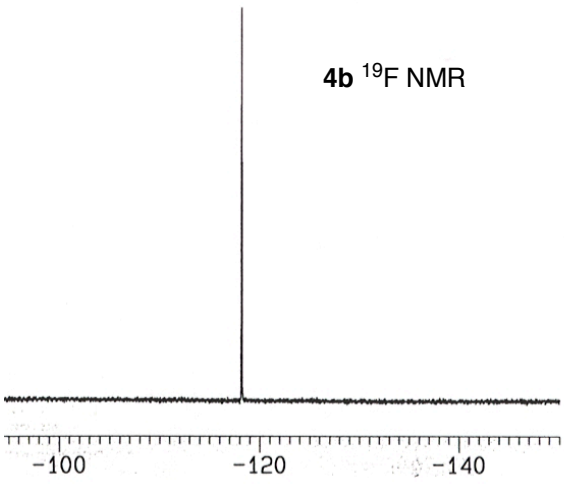
4b ^{1}H NMR



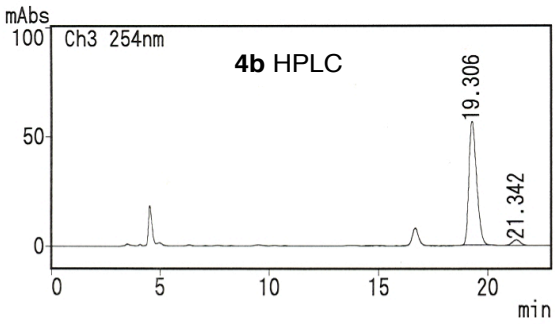
4b ^{13}C NMR



4b ^{19}F NMR



4b HPLC



*** ﾋﾟｰｸﾚﾎﾟｰﾄ ***

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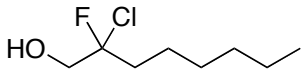
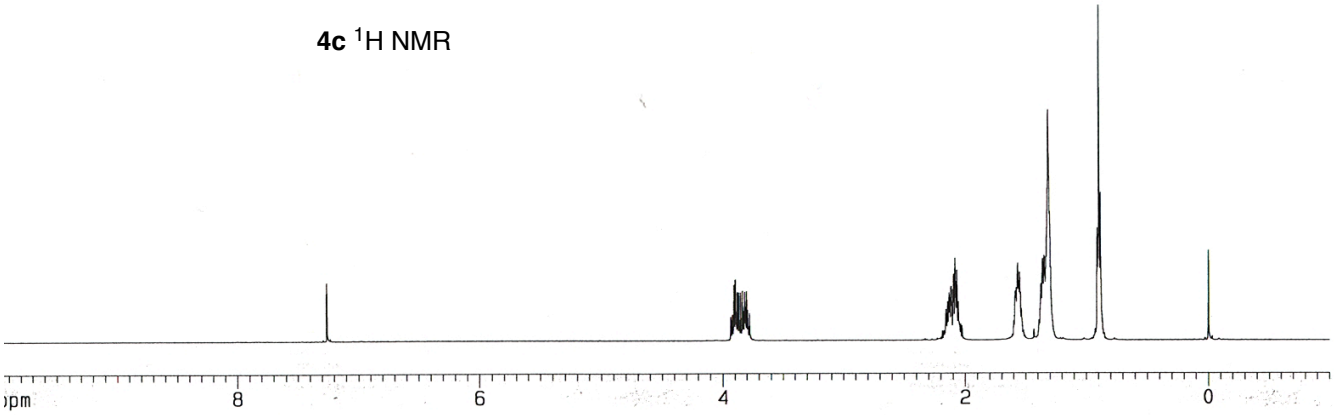
	3	21.342	4.3698	B

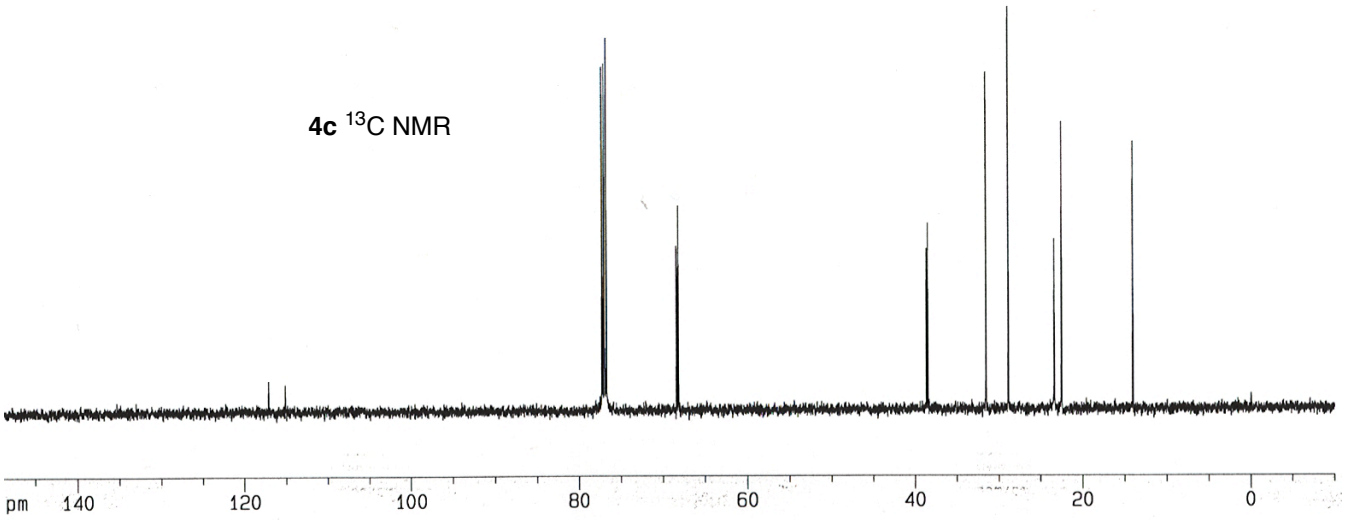
100.0000



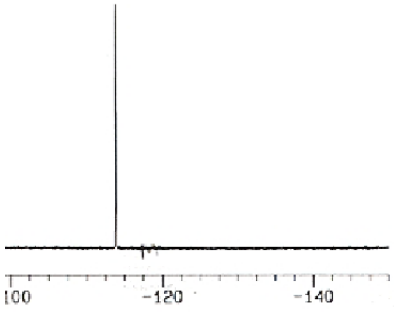
4c ^{1}H NMR



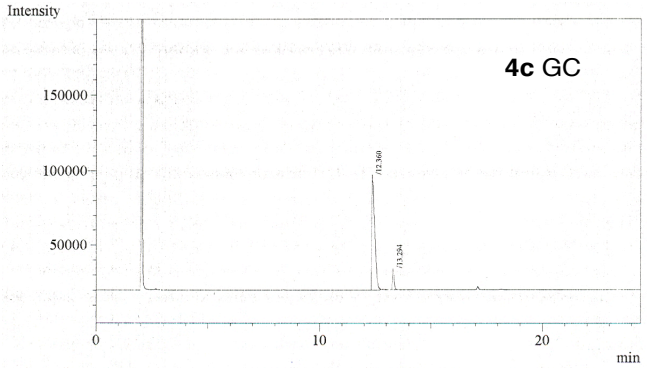
4c ^{13}C NMR



4c ^{19}F NMR

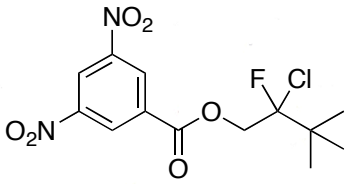


4c GC



Peak Table Channel1 - Channel 1

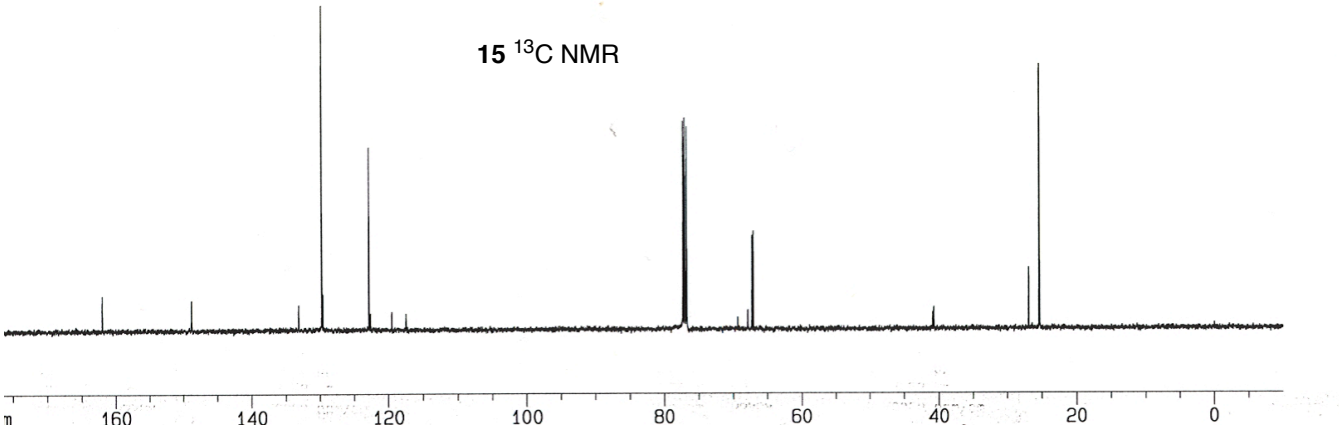
Peak#	Ret.Time	Area	Area%	Height	Mark	ID#	Cmpd Name
1	12.360	678202	90.700	76531			
2	13.294	69541	9.300	14127			
Total		747743	100.000	90658			



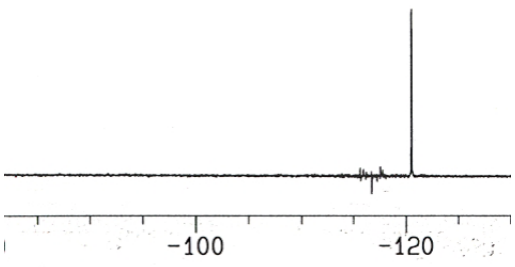
15 ^{1}H NMR

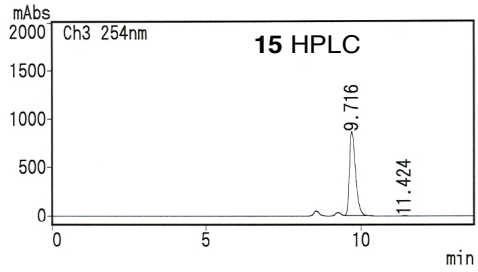

```
AQ              2.9999924 sec
RG                    128
DW                 62.400 usec
DE                  4.50 usec
TE                 300.0 K
D1              3.00000000 sec

============ CHANNEL f1 ========
NUC1                  1H
P1                 9.50 usec
PL1                0.00 dB
SFO1          500.1325006 MHz

F2 - Processing parameters
SI                 65536
SF            500.1300112 MHz
WDW                   EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                20.00 cm
F1P               10.000 ppm
F1                5001.30 Hz
F2P               -1.000 ppm
F2                -500.13 Hz
PPMCM              0.55000 ppm/cm
HZCM             275.07150 Hz/cm
```

15 ^{13}C NMR



15 ^{19}F NMR





*** ﾋﾟｰｸﾚﾎﾟｰﾄ ***

PKNO	ChNO	TIME	CONC	NAME
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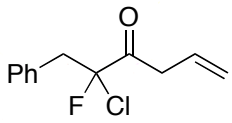
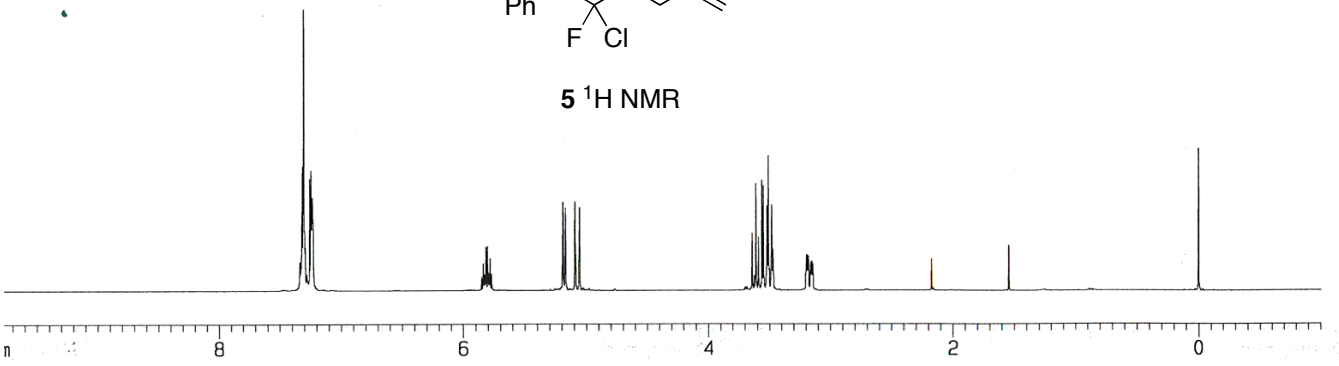
	3	9.716	99.8489	A
4	1	11.422		
	3	11.424	0.1511	B

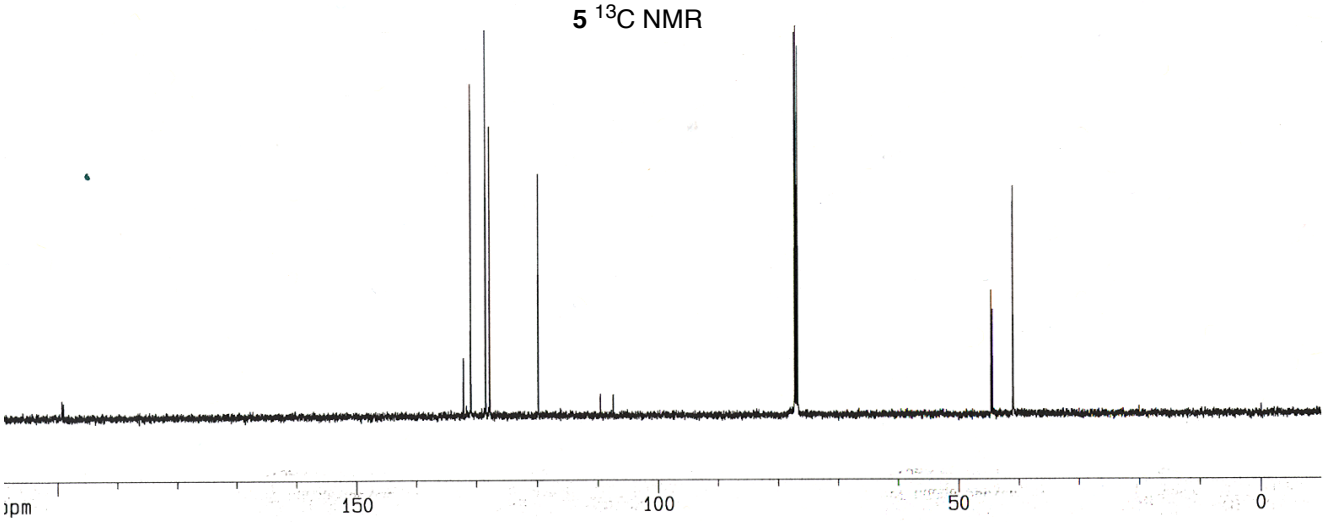
100.0000



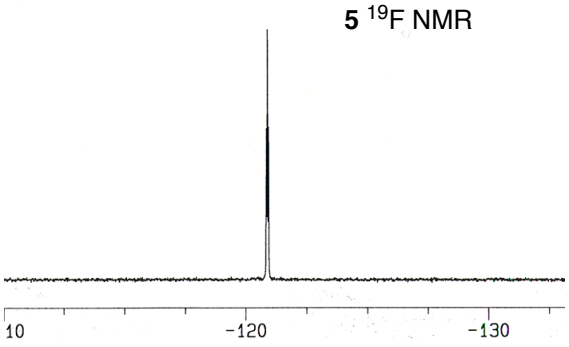
5 ^{1}H NMR



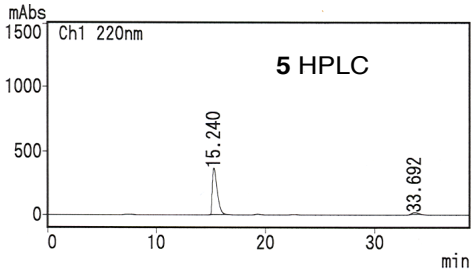
5 ^{13}C NMR



5 ^{19}F NMR



5 HPLC



*** ピーク レポート ***

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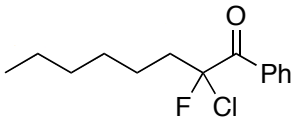
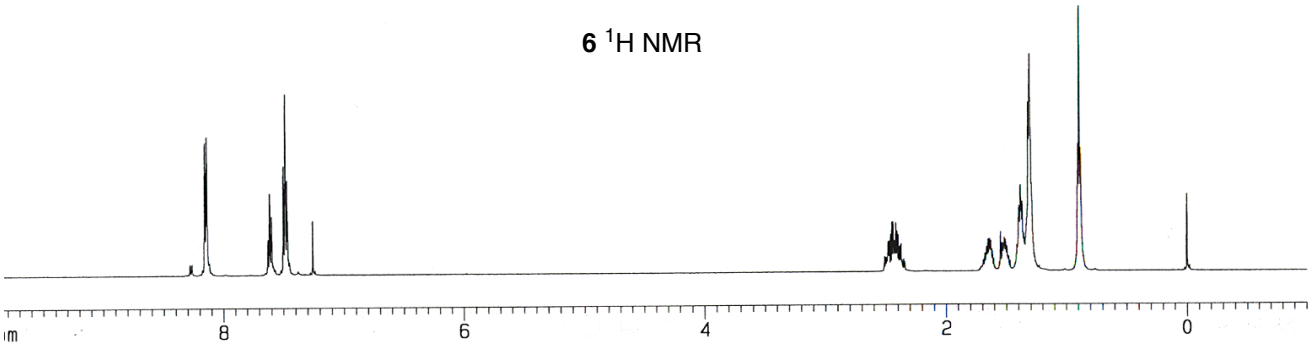
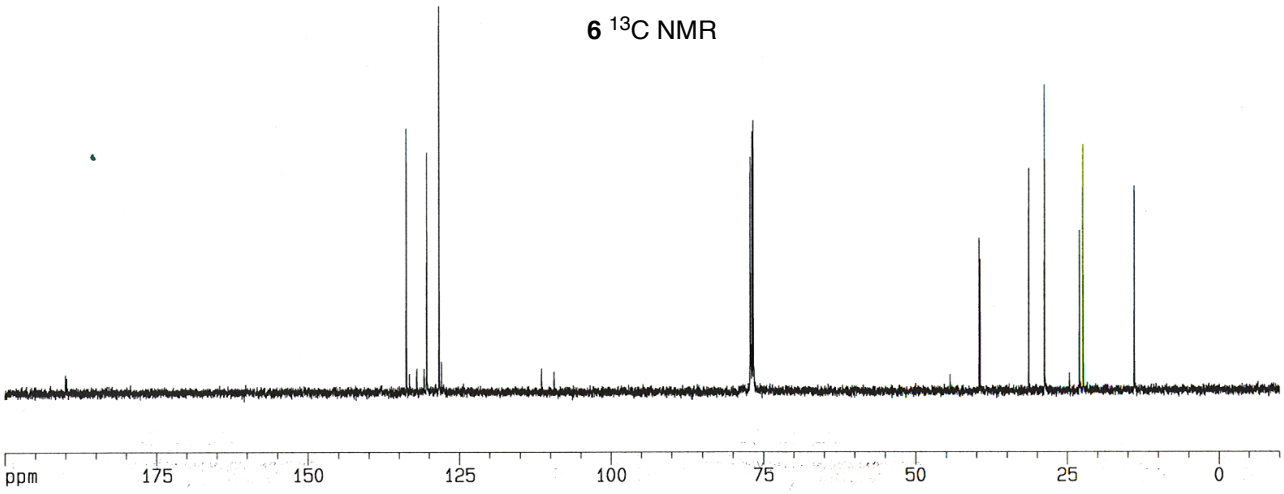
	3	15.240		
2	1	33.692	5.1106	B
			100.0000	



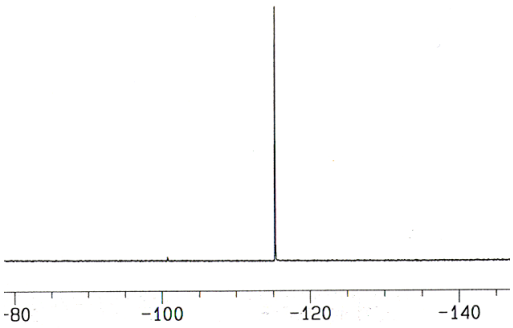
6 ^{1}H NMR



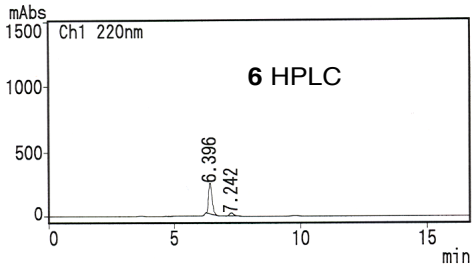
6 ^{13}C NMR



6 ^{19}F NMR



6 HPLC



*** ﾋﾟｰｸﾚﾎﾟｰﾄ ***

PKNO	ChNO	TIME	CONC	NAME
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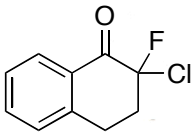
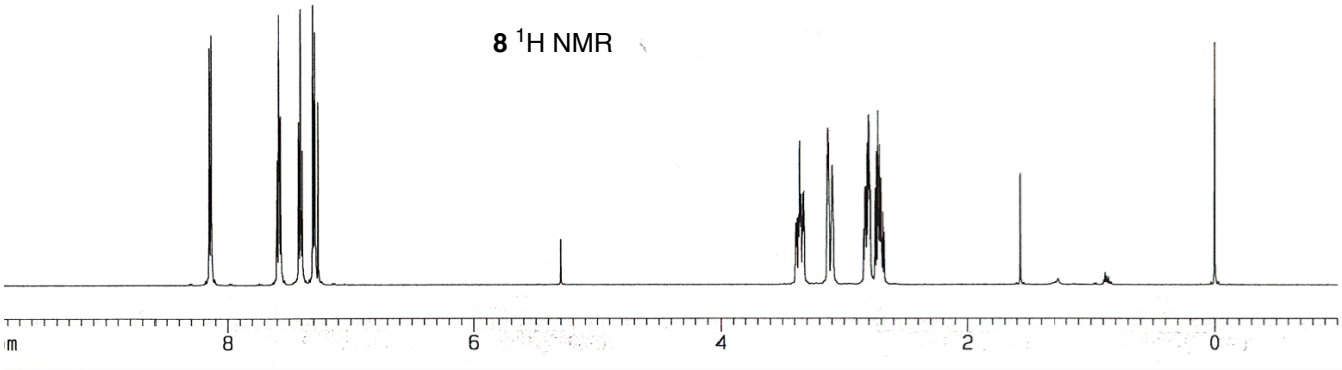
	3	7.242		

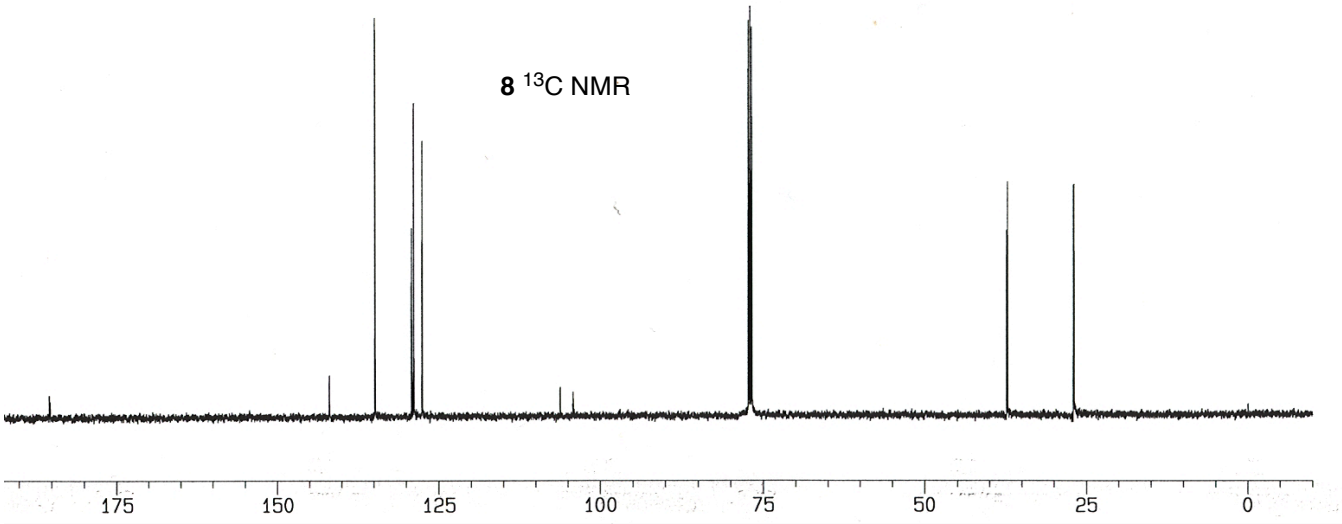
100.0000



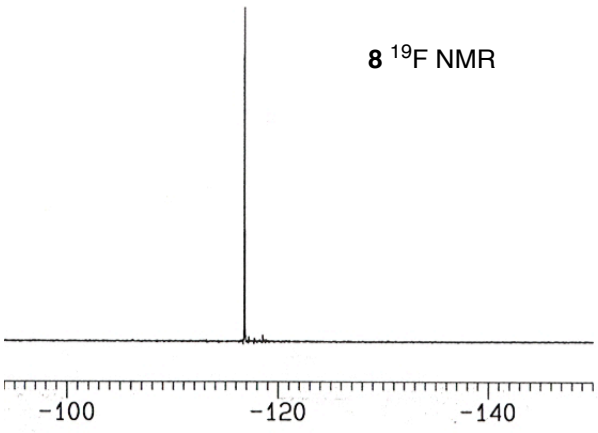
8 ^{1}H NMR



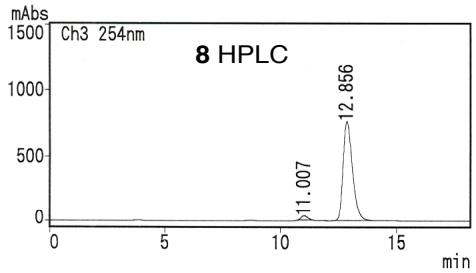
8 ^{13}C NMR



8 ^{19}F NMR



8 HPLC



*** ﾋﾟｰｸﾚﾎﾟｰﾄ ***

PKNO	ChNO	TIME	CONC	NAME
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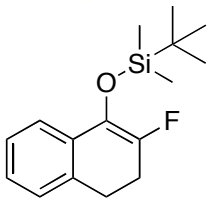
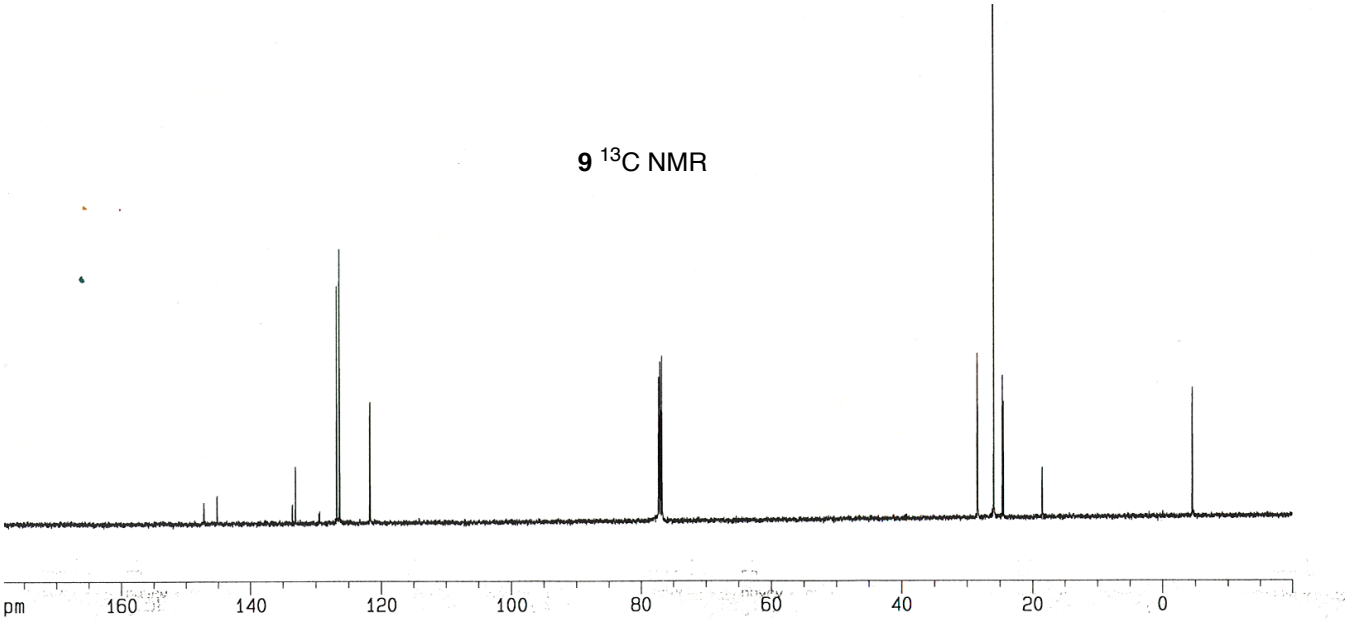
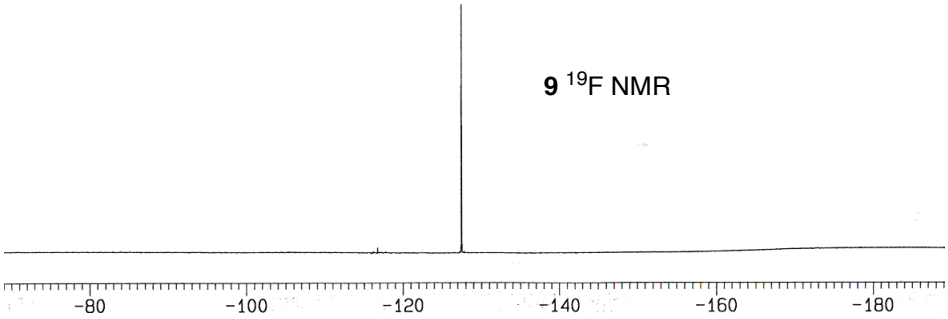


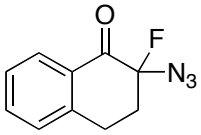
9 ^{1}H NMR

9 ^{13}C NMR

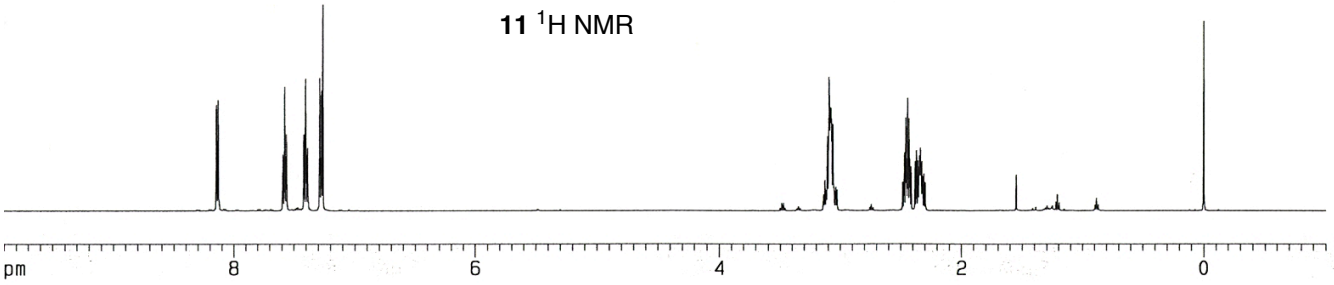


9 ^{19}F NMR

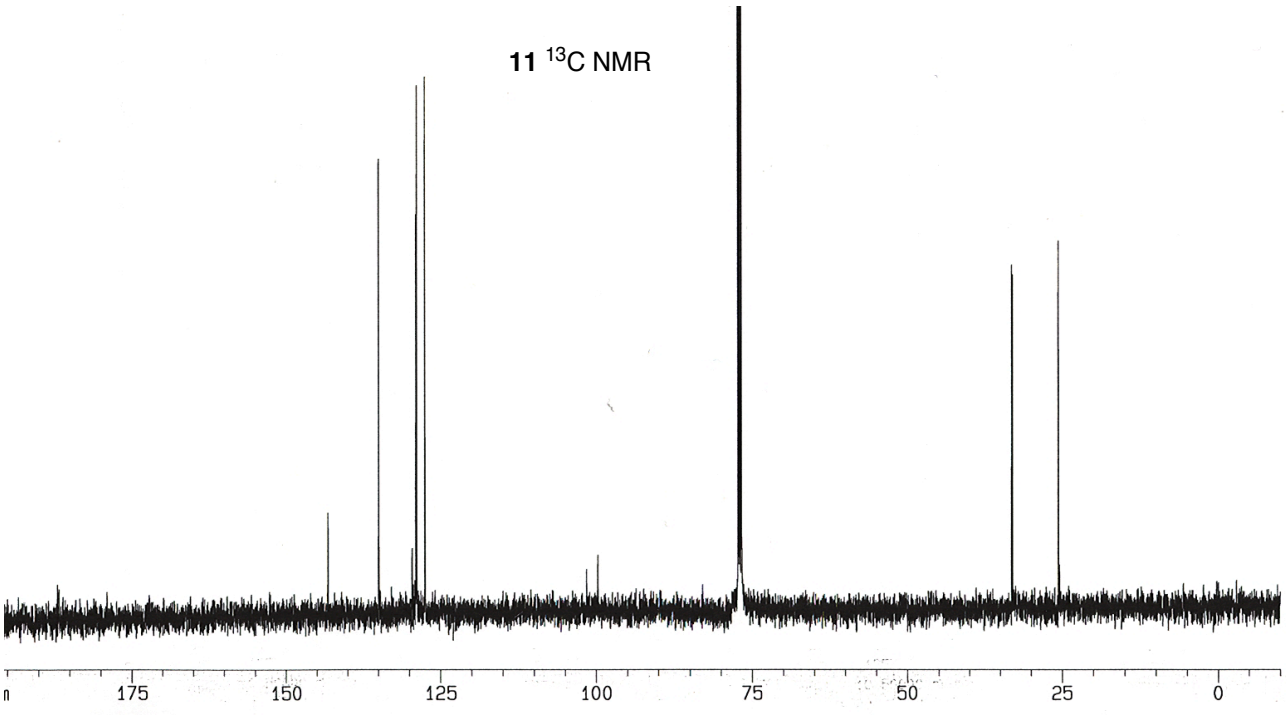




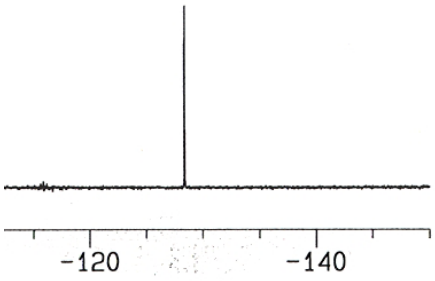
11 ^{1}H NMR



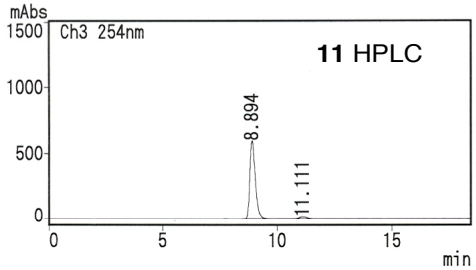
11 ^{13}C NMR



11 ^{19}F NMR



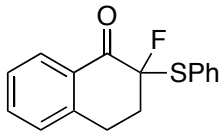
11 HPLC



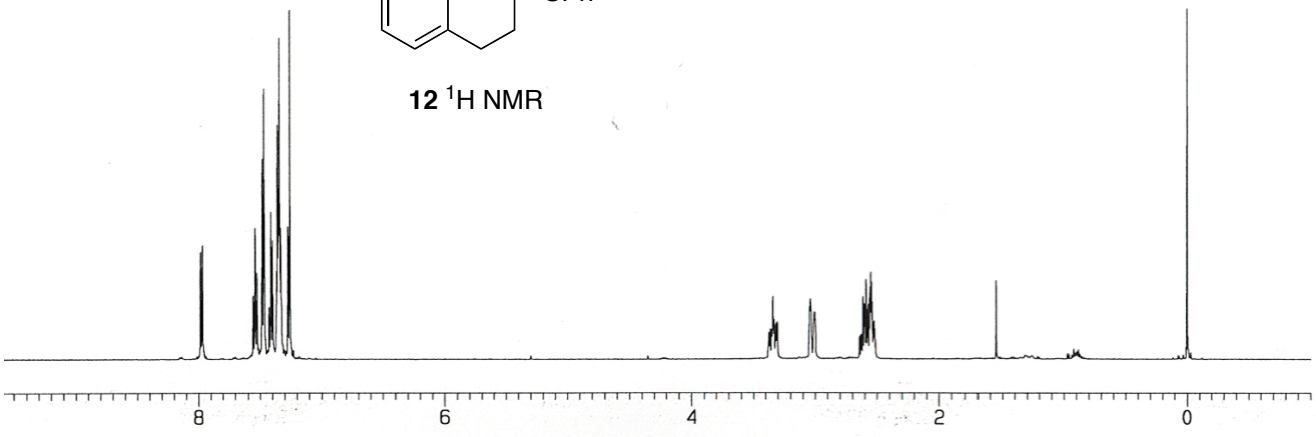
*** ﾋﾟｰｸﾚﾎﾟｰﾄ ***

PKNO	ChNO	TIME	CONC	NAME
1	1	8.894		
	3	8.894	96.6070	A
2	1	11.113		
	3	11.111	3.3930	B

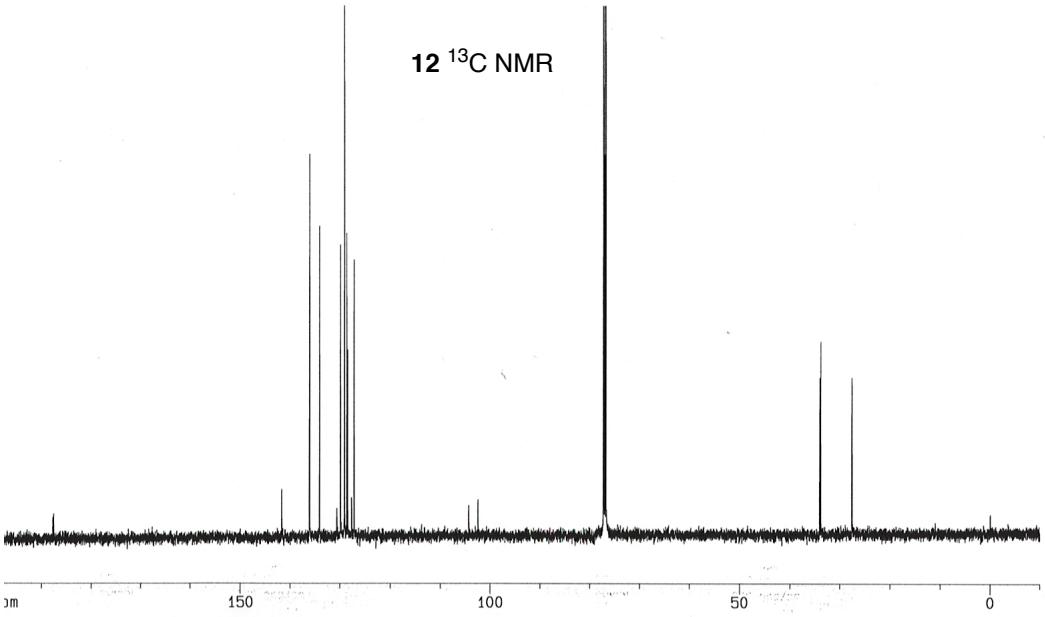
100.0000



12 ^{1}H NMR

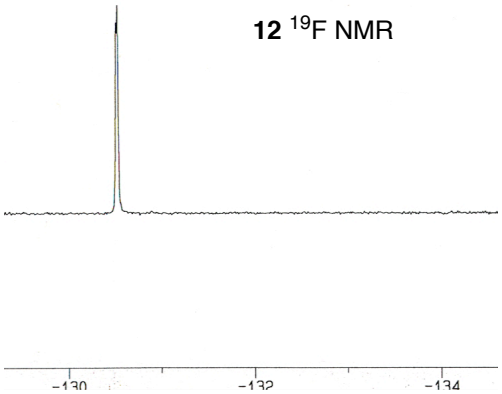


12 ^{13}C NMR

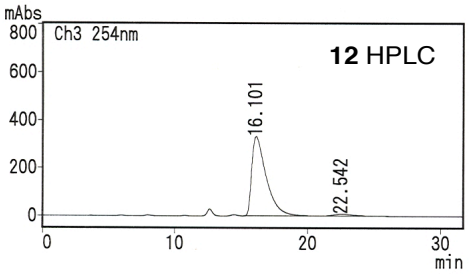



```
SWH          37593.984 Hz
FIDRES           0.500026 Hz
AQ               0.9999972 sec
RG                  8192
DW                 13.300 usec
DE                  7.50 usec
TE                300.0 K
D1           0.10000000 sec
d11          0.03000000 sec

============ CHANNEL f1 ==========
NUC1                13C
P1                 4.60 usec
PL1                0.00 dB
SFO1         125.7690572 MHz

============ CHANNEL f2 ==========
CPDPRG2          waltz16
NUC2                1H
PCPD2             90.00 usec
PL2              120.00 dB
PL12              19.00 dB
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                 32768
SF           125.7577929 MHz
WDW                EM
SSB                0
LB                 1.00 Hz
GB                 0
PC                 1.40

1D NMR plot parameters
CX                20.00 cm
F1P              200.000 ppm
F1             25151.56 Hz
F2P              -10.000 ppm
F2             -1257.58 Hz
PPMCM             10.50000 ppm/cm
HZCM           1320.45679 Hz/cm
```

12 ^{19}F NMR



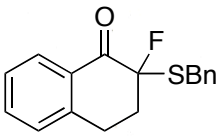
12 HPLC



*** ピーク レポート ***

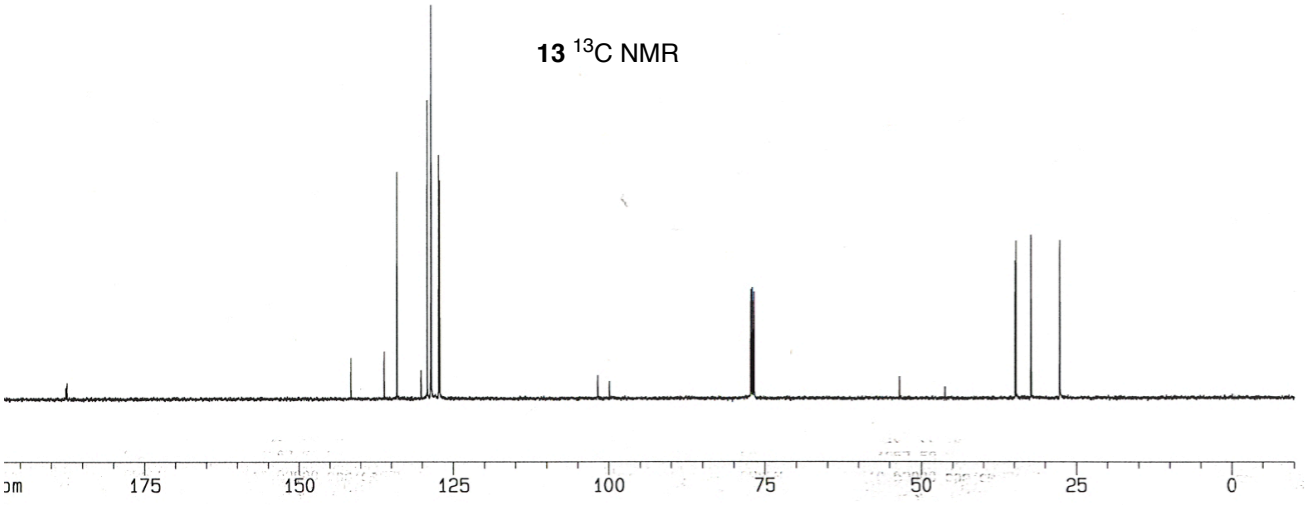
PKNO	ChNO	TIME	CONC	NAME
7	1	16.098		
	3	16.101	96.7507	A
8	3	22.542	3.2493	B

100.0000

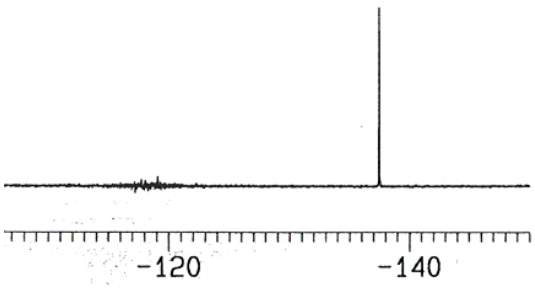


13 ^{1}H NMR

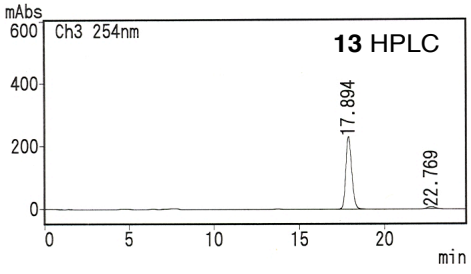
13 ^{13}C NMR



13 ^{19}F NMR



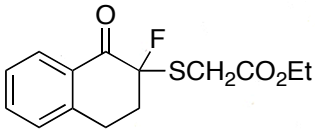
13 HPLC



*** ピーク レポート ***

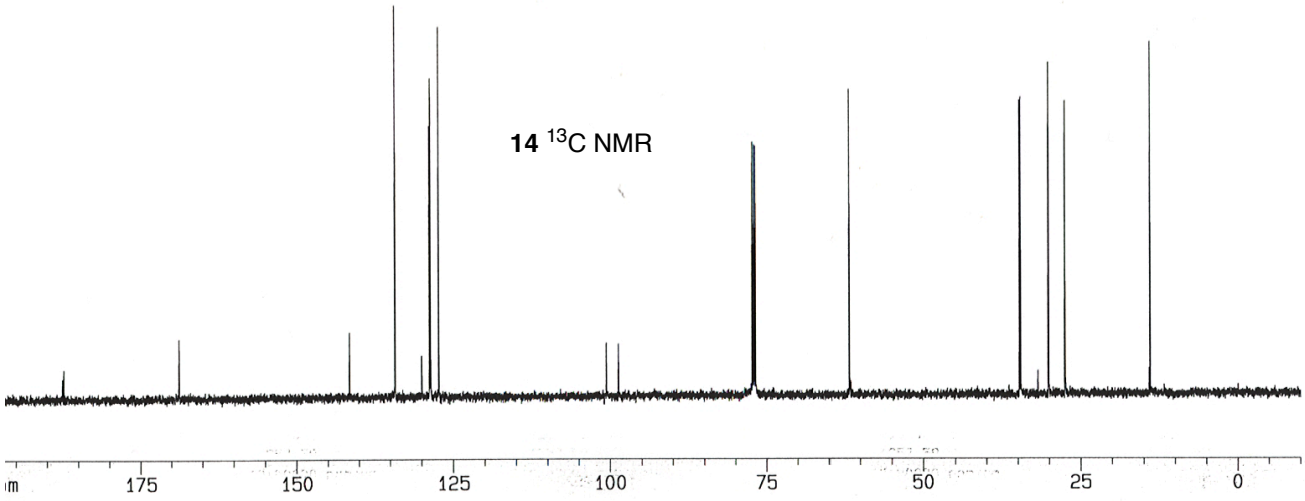
PKNO	ChNO	TIME	CONC	NAME
2	1	17.894		
	3	17.894	96.6925	A
3	1	22.754		
	3	22.769	3.3075	B

100.0000



14 ^{1}H NMR

14 ^{13}C NMR



14 ^{19}F NMR