



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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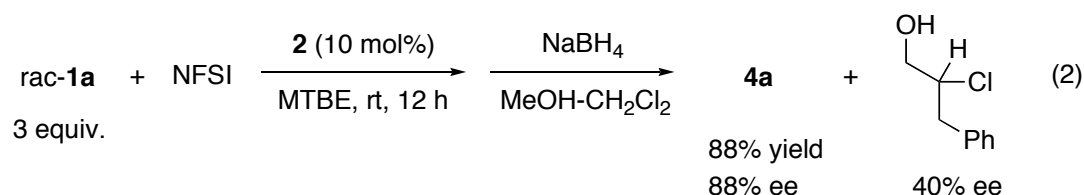
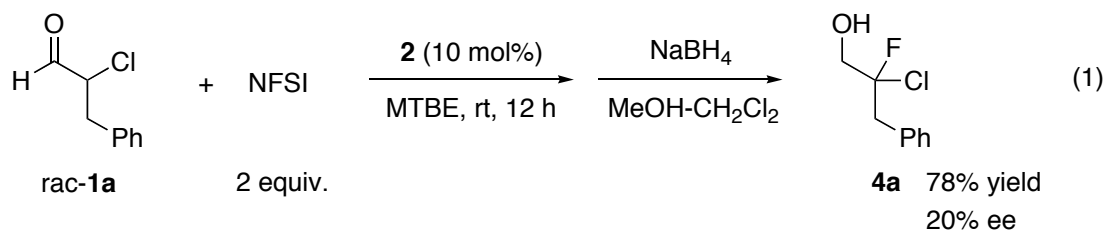
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Supporting Information

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. ¹H NMR, ¹⁹F NMR and ¹³C NMR spectra were recorded on a Bruker Avance 500 (500 MHz ¹H, 470 MHz ¹⁹F, 125 MHz ¹³C). Chemical shift values (δ) are reported in ppm (tetramethylsilane δ 0.00 ppm for ¹H; trichlorofluoromethane δ 0.00 ppm for ¹⁹F; residual chloroform δ 77.0 ppm for ¹³C).

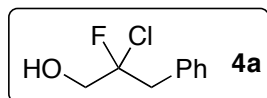
General procedure for Table 1: To a solution of α -chloroaldehyde **1** (1.5 mmol) in MTBE (2 mL), was added catalyst **2** (0.05 mmol) and *N*-fluorobenzenesulfonimide (0.5 mmol) at 0 °C. The reaction mixture was stirred at 0 °C or 25 °C for 12~30 hours. The mixture was poured into methanol-dichloromethane (1 : 4, 5 mL) at 0 °C. To this solution, NaBH₄ (5 mmol) was added, and the mixture was stirred at 0 °C for 1 hour. The reaction was quenched with saturated aqueous NH₄Cl 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.



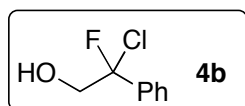
Analytical details for compounds **4a-d**:

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**.



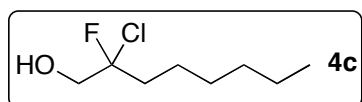
2-chloro-2-fluoro-3-phenylpropan-1-ol (4a): The crude mixture was purified by

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) $[\text{M}+\text{Cl}]^-$ 223.0, Calculated Mass 188.0; $[\alpha]_{\text{D}} = -2.79$ ($c = 1.5$, CHCl_3). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99 : 1, 1.0 mL/min) using a CHIRALPAK IC column (0.46cm ϕ 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

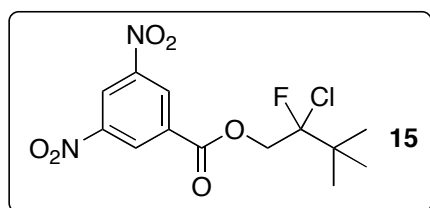
gel column chromatography (hexanes : ethyl acetate = 9:1) to give 62% yield of **4b** as colorless oil (91% ee). IR (film) 3363, 3065, 3036, 2934, 1493, 1450, 1281, 1134, 1066, 945, 856, 758, 712 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.59-7.53 (m, 2H), 7.46-7.40 (m, 3H), 4.15-4.04 (m, 2H), 2.15 (t, 1H, $J = 7.3$ 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) $[\text{M}]^+$ 174.0248, Calculated Mass 174.0248; $[\alpha]_{\text{D}} = -77.5$ ($c = 0.6$, CHCl_3). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99 : 1, 1.0 mL/min) using a CHIRALPAK IC column (0.46cm ϕ 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

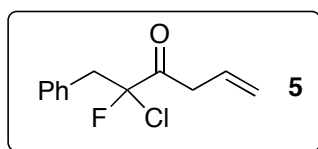
NMR (500 MHz, CDCl_3) δ 3.91–3.78 (m, 2H), 2.14–2.05 (m, 3H), 1.59–1.54 (m, 2H), 1.37–1.29 (m, 6H), 0.90 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 116.1 (d, $J = 245$ Hz), 68.3 (d, $J = 26.4$ Hz), 38.5 (d, $J = 21.3$ Hz), 31.5, 28.9, 23.3 (d, $J = 3.8$ Hz), 22.5, 14.0; ^{19}F NMR (470 MHz, CDCl_3) δ –113.9 (br); MS (APCI) $[\text{M}+\text{Cl}]^-$ 217.0, Calculated Mass 182.1; $[\alpha]_{\text{D}} = +2.3$ ($c = 0.5$, 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.



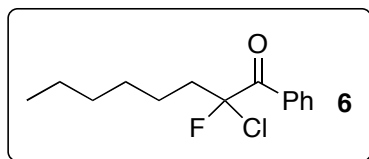
2-chloro-2-fluoro-3,3-dimethylbutyl 3,5-dinitrobenzoate (15): The

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) $[\text{M}+\text{Cl}]^-$ 383.0, Calculated Mass 348.1; $[\alpha]_{\text{D}} = -16.5$ ($c = 2.3$, CHCl_3). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 90 : 10, 1.0 mL/min) using a CHIRALPAK AD-H column (0.46cm ϕ 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 NH₄Cl 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**.

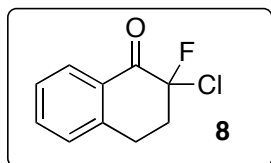


Compound 5: The reaction mixture was purified by silica gel column chromatography (hexanes : dichloromethane = 4 : 1) to give 71% yield of **5** as colorless oil (90% ee). IR (film) 3087, 3067, 3034, 1742, 1645, 1497, 1456, 1425, 1389, 1326, 1125, 1089, 994, 926, 851, 739, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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; ¹⁹F NMR (470 MHz, CDCl₃) δ -120.9 (t, *J* = 21.6 Hz); HRMS (CI) [M]⁺ 227.06387, Calculated Mass 227.06390; [α]_D = +25.2 (c = 1.0, CHCl₃). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 99.9 : 0.1, 1.0 mL/min) using a CHIRALCEL OJ-H column (0.46cm ϕ x 25cm): major isomer 15.2 min and minor isomer 33.7 min.



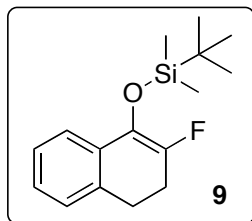
Compound 6: The reaction mixture was purified by silica gel column chromatography (hexanes : ethyl acetate = 9 : 1) to give 65% yield of **6** as colorless oil (81% ee). IR (film) 2932, 2858, 1699, 1449, 1261, 1149, 704, 686 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.15 (d, $J = 7.5$ Hz, 2H), 7.61 (t, $J = 7.5$ 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) $[\text{M}]^-$ 256.1, Calculated Mass 256.1; $[\alpha]_{\text{D}} = +5.5$ ($c = 1.4$, 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 (0.46cm ϕ 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 $^{\circ}\text{C}$. After the reaction mixture was stirred at 25 $^{\circ}\text{C}$ for 1 hour, *N*-chlorosuccinimide (1.1 mmol) was added at 0 $^{\circ}\text{C}$. The mixture was stirred at 25 $^{\circ}\text{C}$ 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) $[\text{M}]^+$ 198.0, Calculated Mass 198.0.

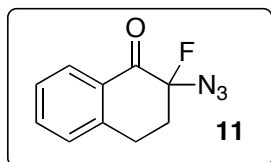


***t*-Butyldimethyl(2-fluoro-3,4-dihydronaphthalen-1-yloxy)silane (9) (Scheme 4):**

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} ; ^1H 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) $[\text{M}]^+$ 278.1502, Calculated Mass 278.1502.

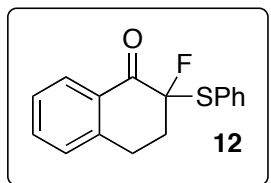
Asymmetric synthesis of 8 (Scheme 4): A Schlenk flask was charged with zirconium(IV) chloride (3.0 mmol) and di-(+)-2-(1-naphthalyl)cyclohexyl α,α -dichloromalonate² (**10**) (3.3 mmol) in a glove box. The mixture was cooled to -78 °C and dissolved in dichloromethane (60 mL). The mixture was stirred 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 liquor 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 (0.46cm ϕ 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),

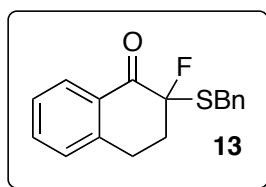
was added sodium azide (1.0 mmol) at 25 °C, and the mixture was stirred at 80°C for 10 min. The mixture was extracted with diethyl ether and water. The organic layer was dried over sodium sulfate, concentrated and chromatographed quickly on silica gel (hexanes : dichloromethane = 1 : 1) to give 77% yield 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, $[M-\text{N}_2]^+$ 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 (0.46cm ϕ 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

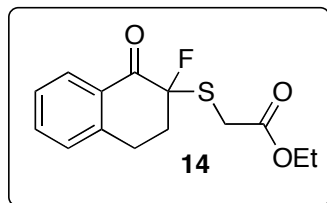
the mixture was refluxed another 30 min. The mixture was directly subjected to silica gel column chromatography (hexanes : dichloromethane = 1 : 2) to give 92 % yield of **12** as clear oil (94% ee). IR (film) 3060, 2934, 1698, 1602, 1299 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.97 (d, 1H, $J = 8.0$ Hz), 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) $[\text{M}]^+ 271.9$, $[\text{M}-\text{HF}]^+ 252.0$, Calculated Mass 272.1; $[\alpha]_{\text{D}} = -82.5$ ($c = 0.45$, CHCl_3). The enantiomeric ratio was determined by HPLC (hexanes : 2-propanol = 90 : 10, 1.0 mL/min) using a CHIRALCEL OB-H column (0.46cm \varnothing 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} ; ^1H 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) $[\text{M}-\text{HF}]^+ 266.0769$, Calculated Mass (M-HF) 266.0765; $[\alpha]_{\text{D}} = +31.0$ ($c = 0.9$, 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.

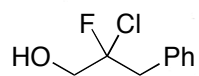
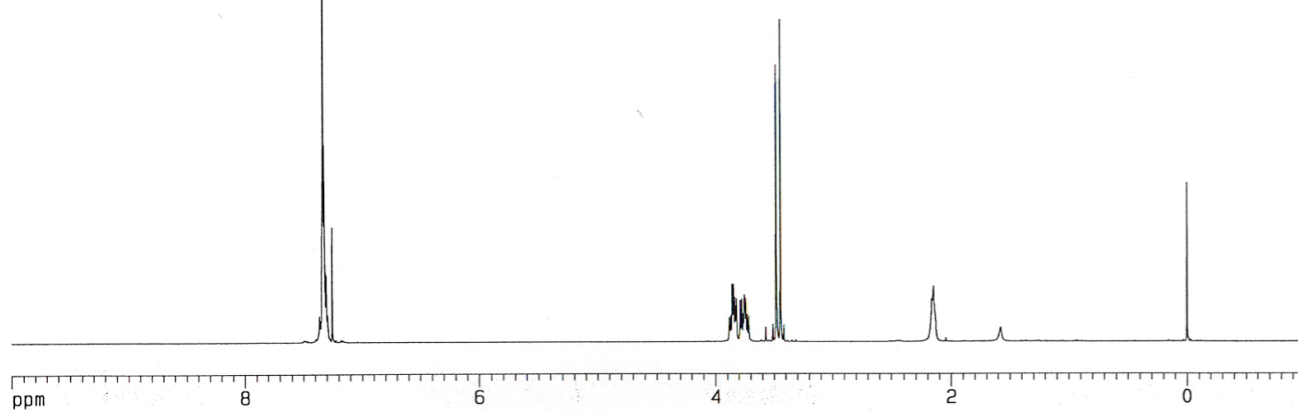
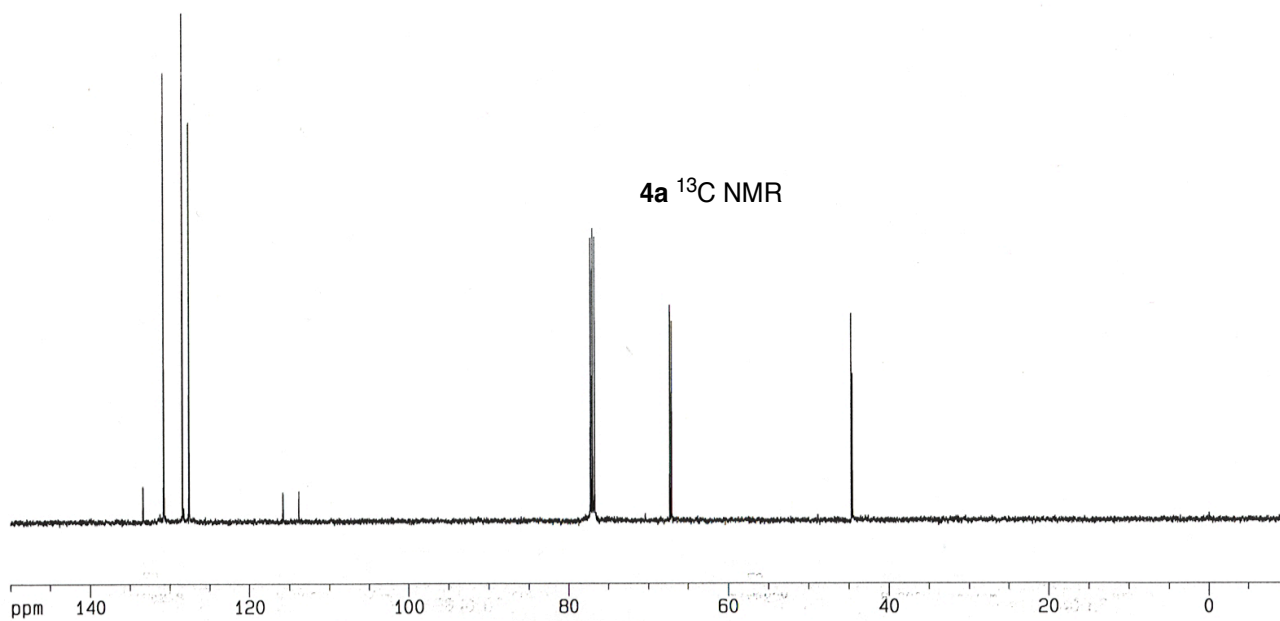
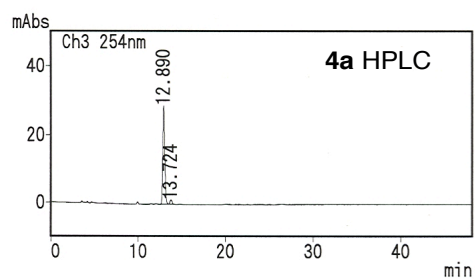
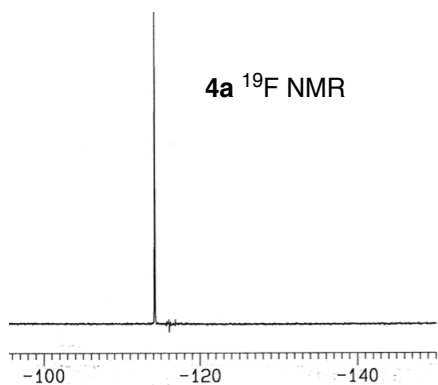


Compound 14 (Scheme 5): To a solution of (-)-**8** (0.5 mmol) in dichloromethane (2 mL), were added triethylamine (5 mmol) and ethyl 2-mercaptoacetate (2.5 mmol) at 25 °C, and the mixture was refluxed for 4 hours. Extra triethylamine (5 mmol) and ethyl 2-mercaptoacetate (2.5 mmol) were added and the 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; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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; ¹⁹F NMR (470 MHz, CDCl₃) δ -138.5 (br); HRMS (EI) [*M*]⁺ 282.07231, Calculated Mass 282.07260; [α]_D = -5.7 (c = 1.9, CHCl₃). 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.

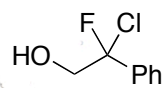
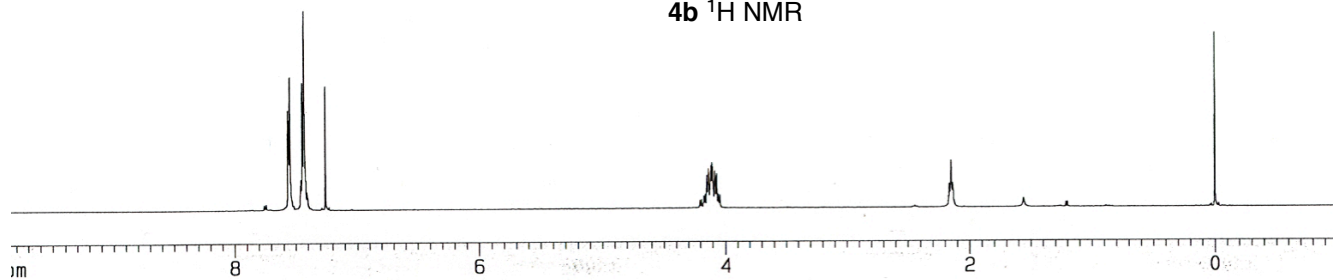
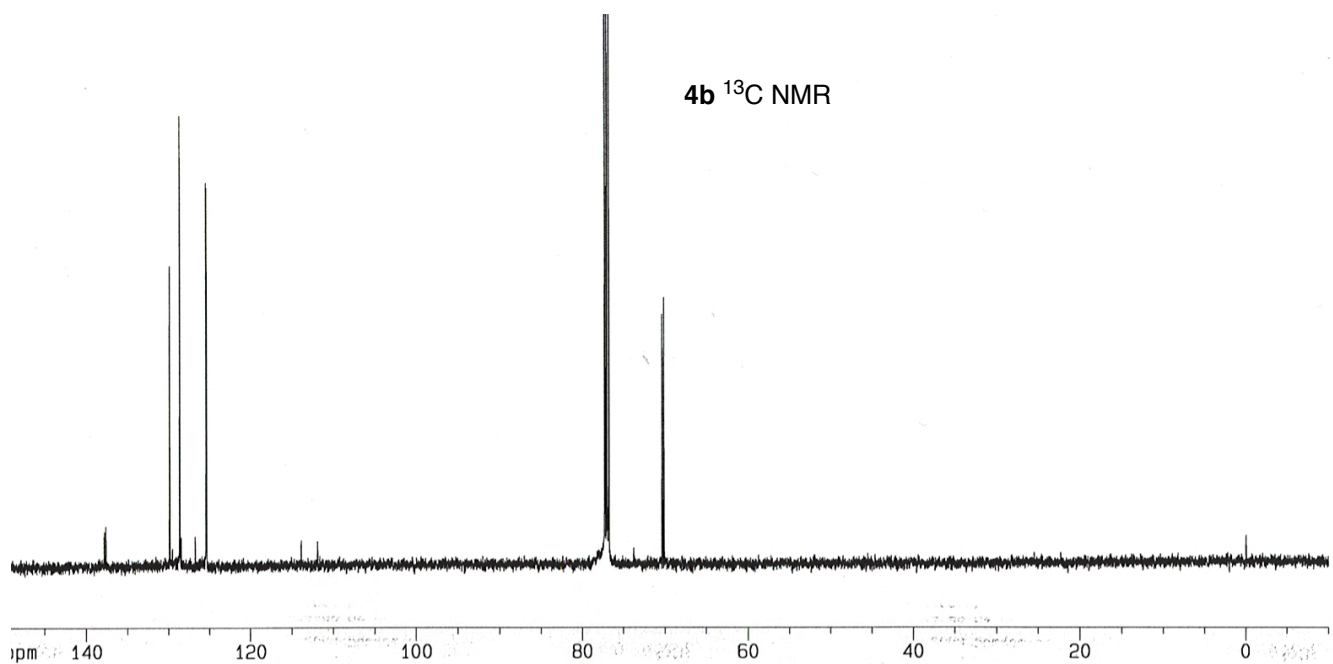
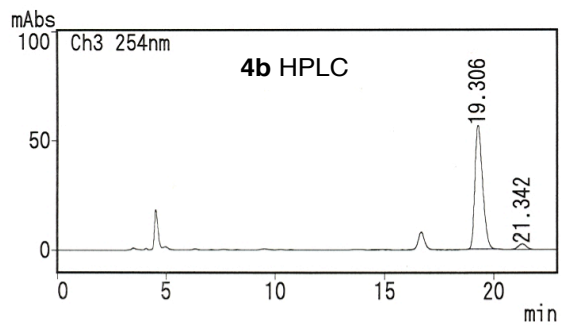
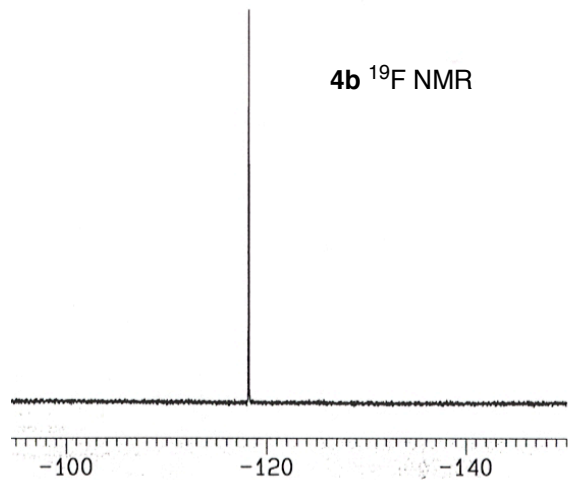
^1H , ^{13}C , ^{19}F -NMR spectra
and
chiral HPLC, GC analyses

**4a** ^1H NMR**4a** ^{13}C NMR**4a** ^{19}F NMR

*** ピークレポート ***

PKNO	ChNO	TIME	CONC	NAME
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3	1	12.890	95.6447	A
2	1	13.728		
3	1	13.724	4.3553	B

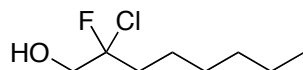
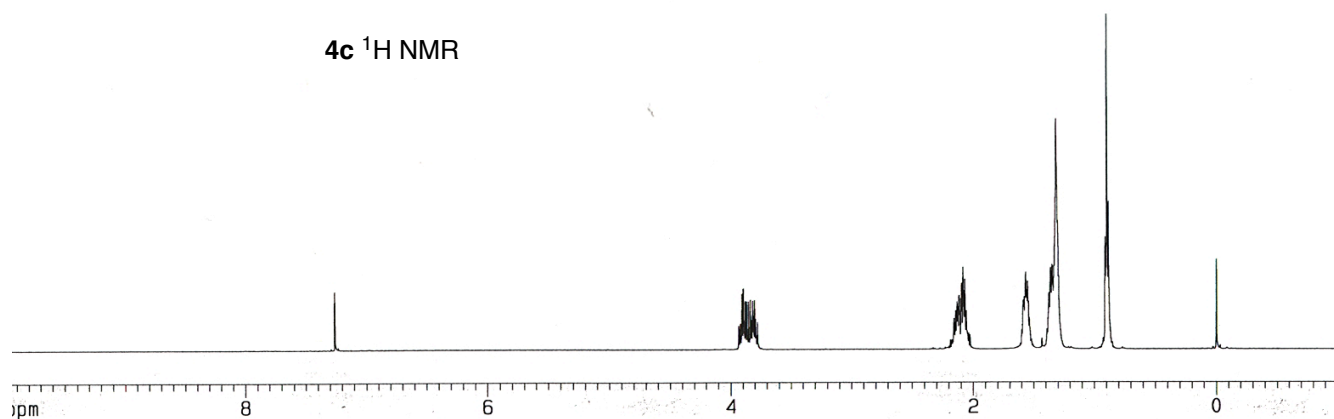
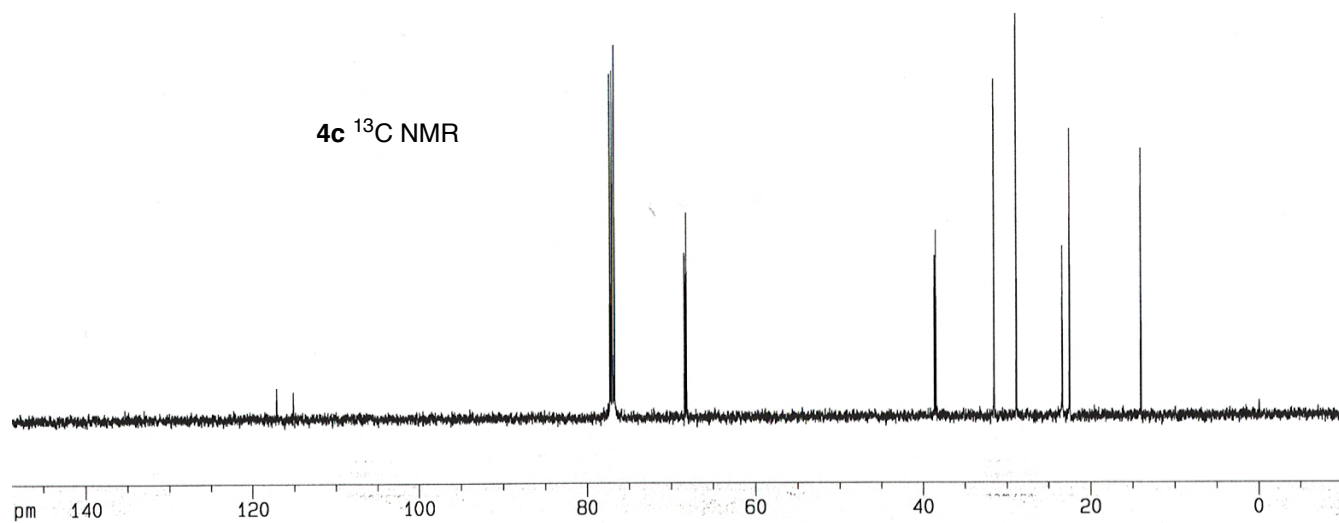
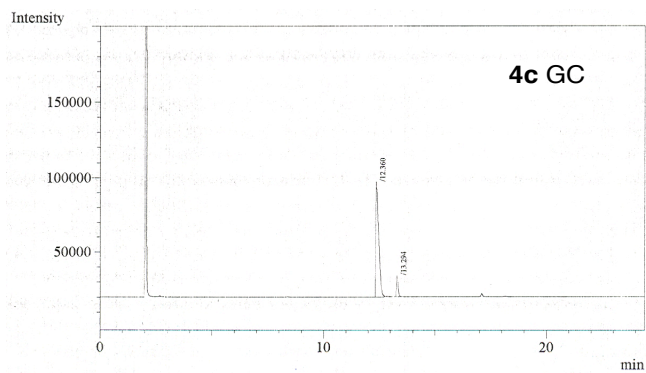
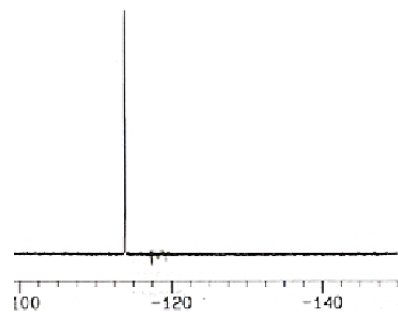
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**4b** ^1H NMR**4b** ^{13}C NMR**4b** ^{19}F NMR

*** ヒート ***

PKNO	ChNO	TIME	CONC	NAME
7	1	19.307		
	3	19.306	95.6302	A
8	1	21.336		
	3	21.342	4.3698	B

100.0000

**4c** ^1H NMR**4c** ^{13}C NMR**4c** ^{19}F NMR

Peak Table Channel1 - Channel 1

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

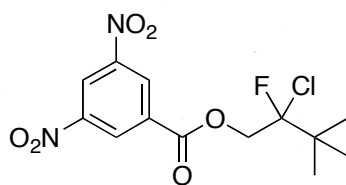
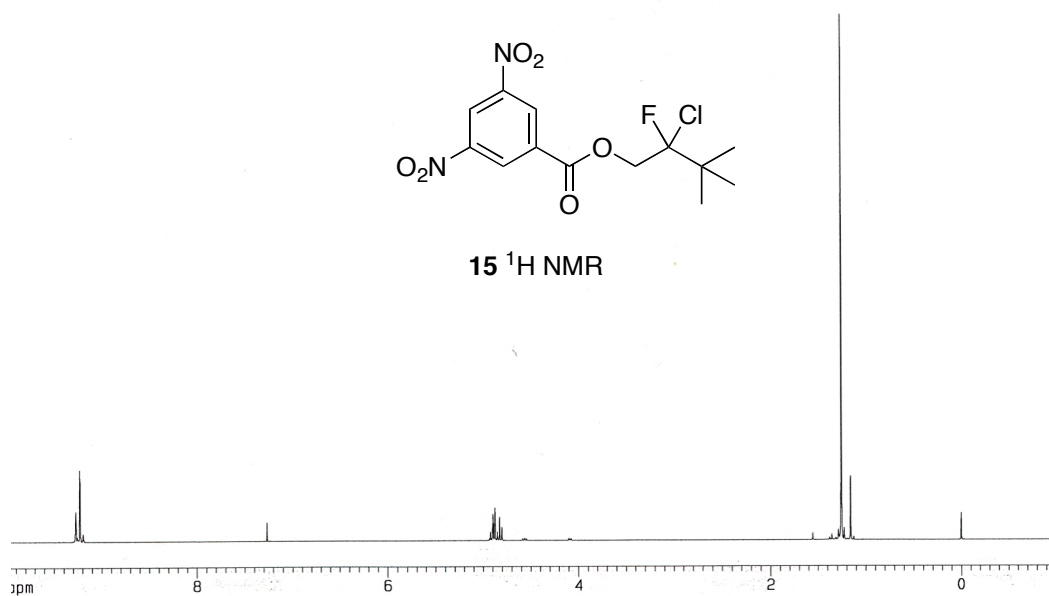
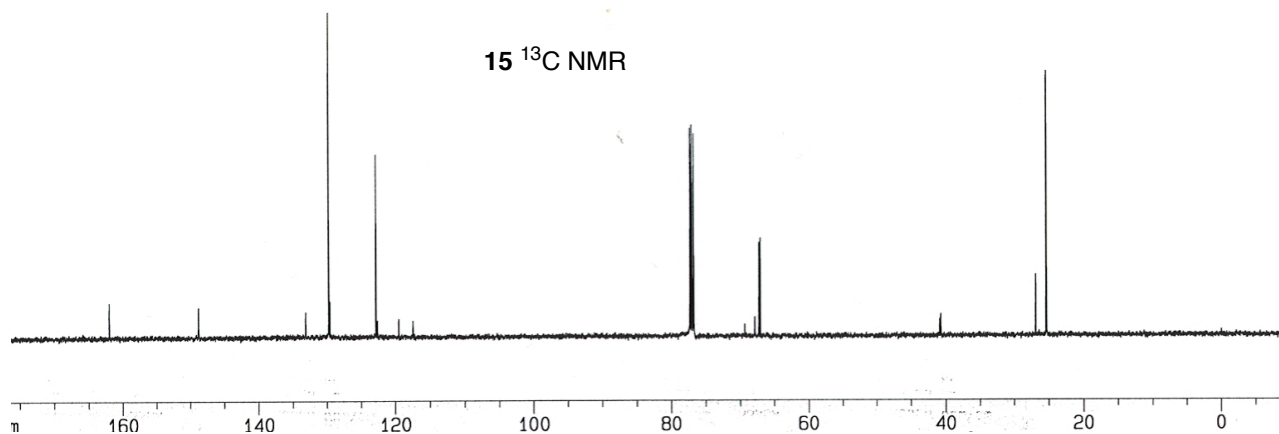
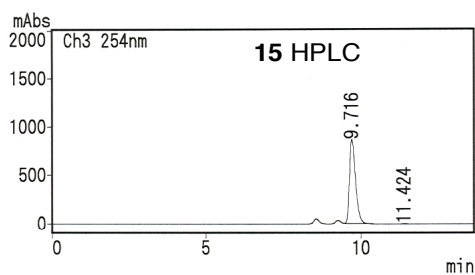
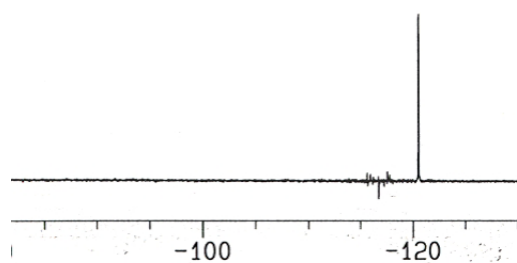
**15 ¹H NMR**

FIGURE 1
AQ 2.9999924 sec
RG 128
DW 62.400 usec
DE 4.50 usec
TE 300.0 K
D1 3.0000000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.50 usec
PL1 0.00 dB
SF01 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

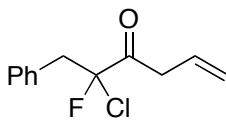
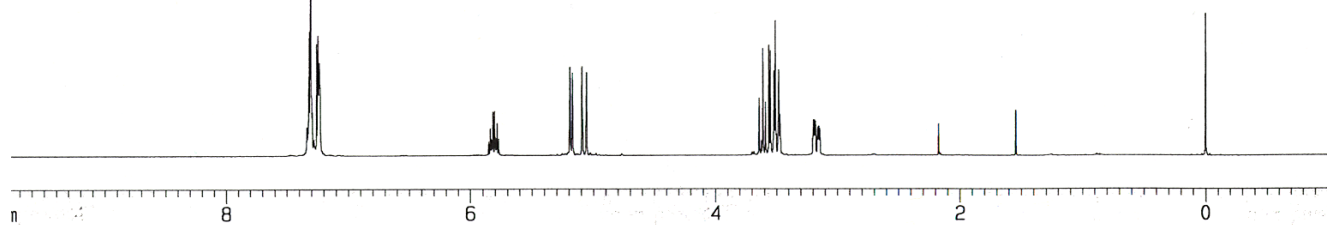
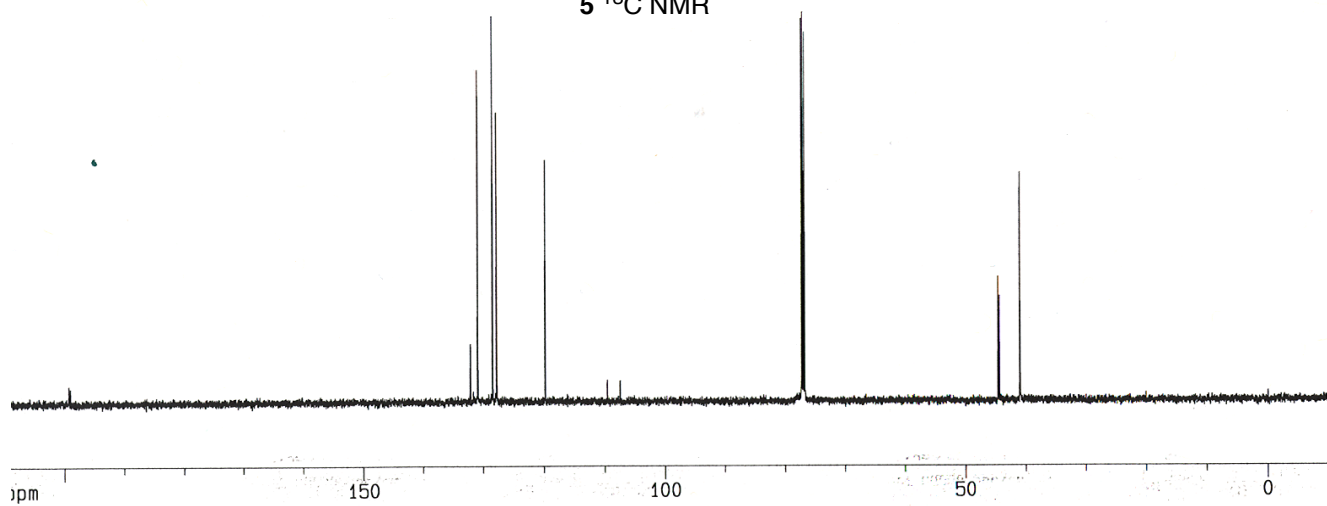
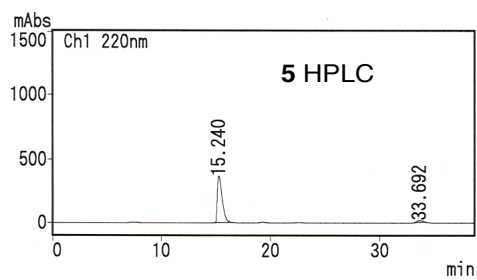
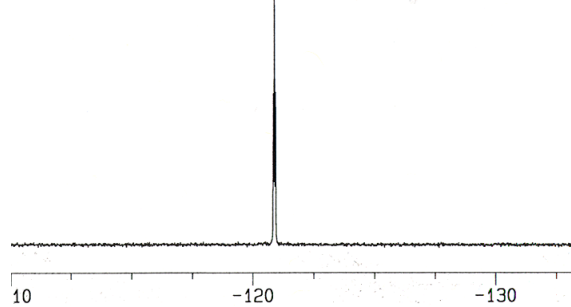
1D NMR plot parameters
CX 20.00 cm
F1P 10.000 ppm
F1 5001.30 Hz
F2P -1.000 ppm
F2 -500.13 Hz
PPMCM 0.55000 ppm/cm
HZCM 275.07150 Hz/cm

15 ¹³C NMR**15 ¹⁹F NMR**

*** ヒートマップ ***

PKNO	ChNO	TIME	CONC	NAME
3	1	9.718		
3	3	9.716	99.8489	A
4	1	11.422		
3	3	11.424	0.1511	B

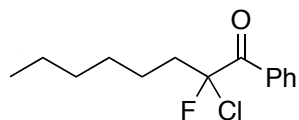
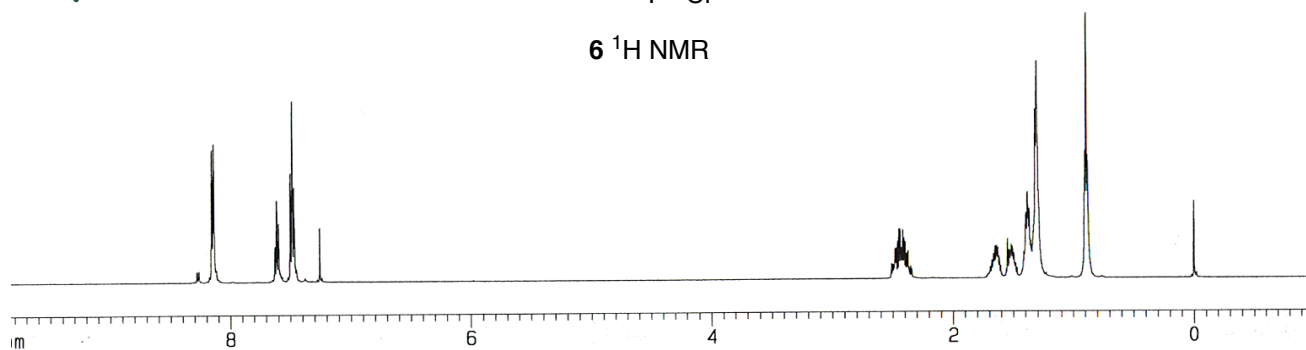
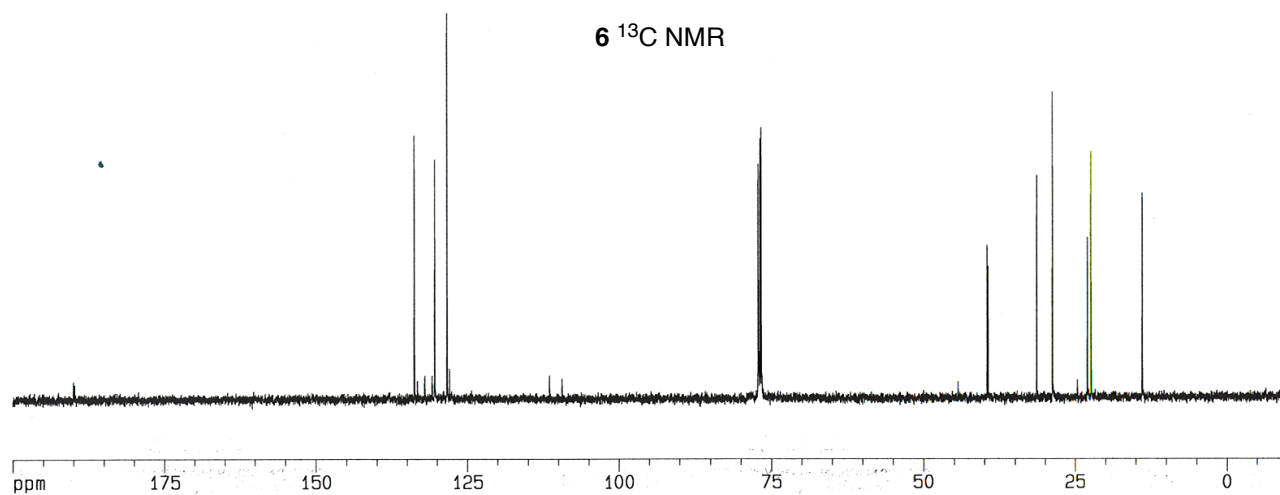
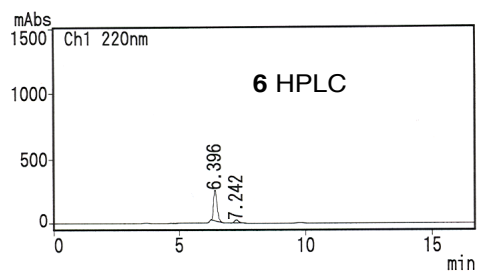
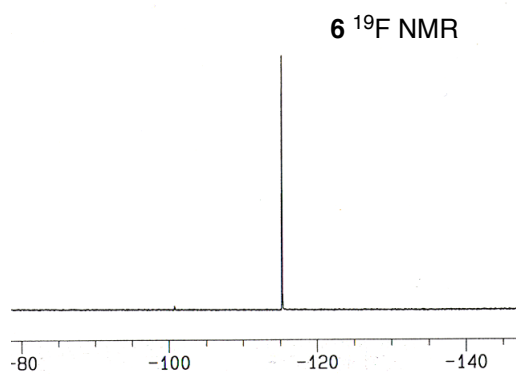
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**5 ^1H NMR****5 ^{13}C NMR****5 ^{19}F NMR**

*** ピークレポート ***

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3	1	15.240		
2	1	33.692	5.1106	B

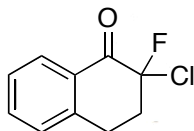
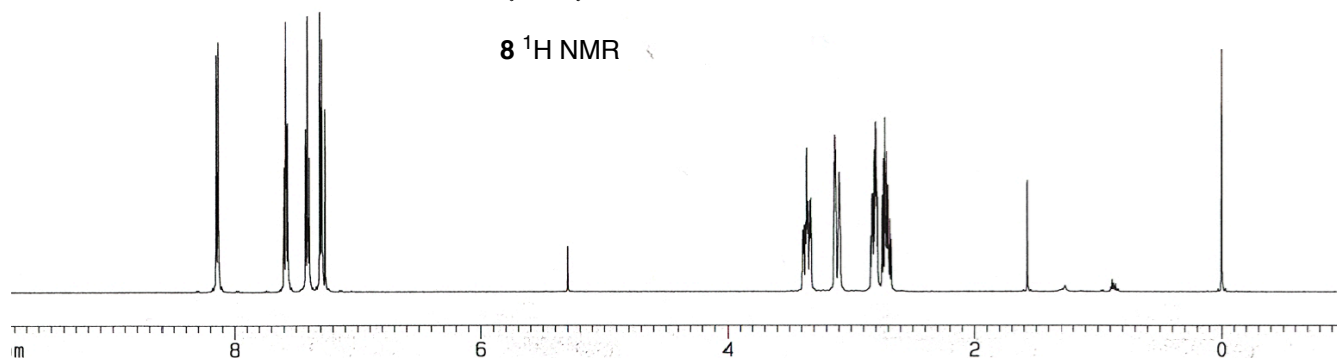
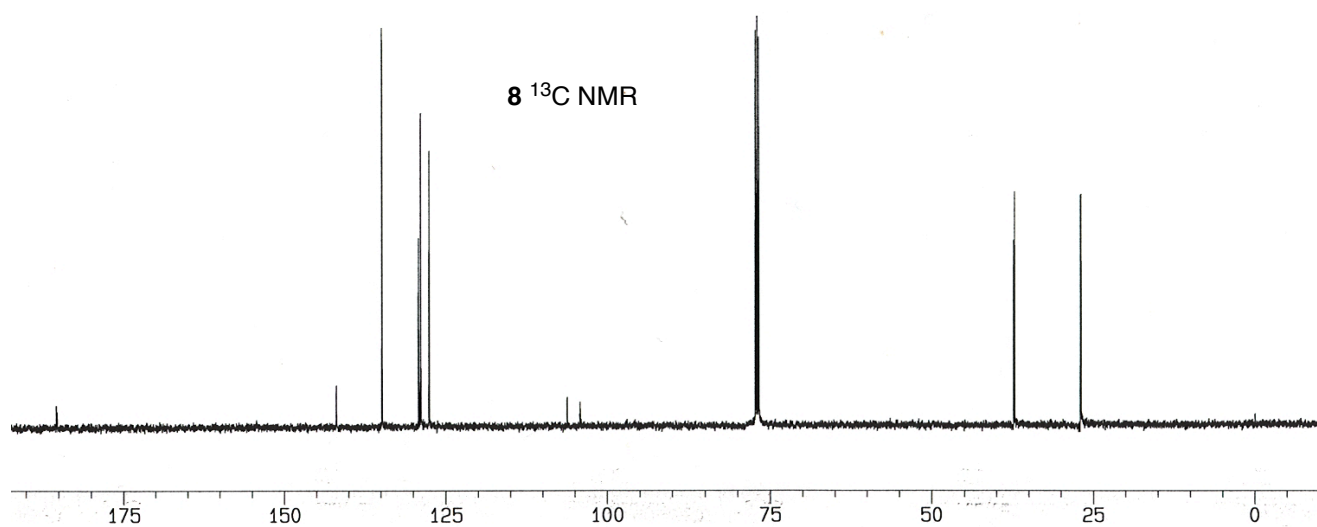
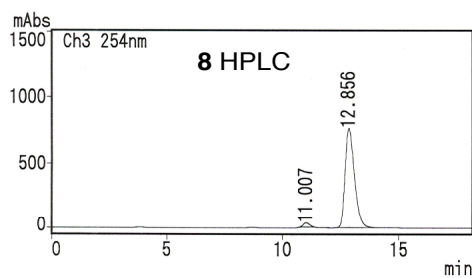
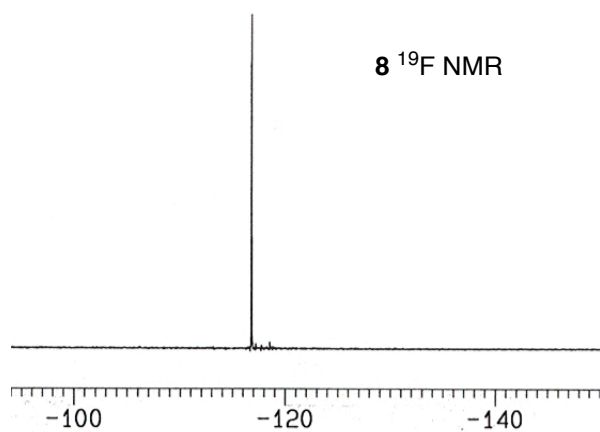
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**6** ^1H NMR**6** ^{13}C NMR**6** ^{19}F NMR

*** ヒートマップ ***

PKNO	ChNO	TIME	CONC	NAME
2	1	6.396	91.2600	A
	3	6.396		
3	1	7.242	8.7400	B
	3	7.242		

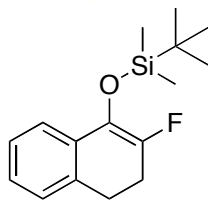
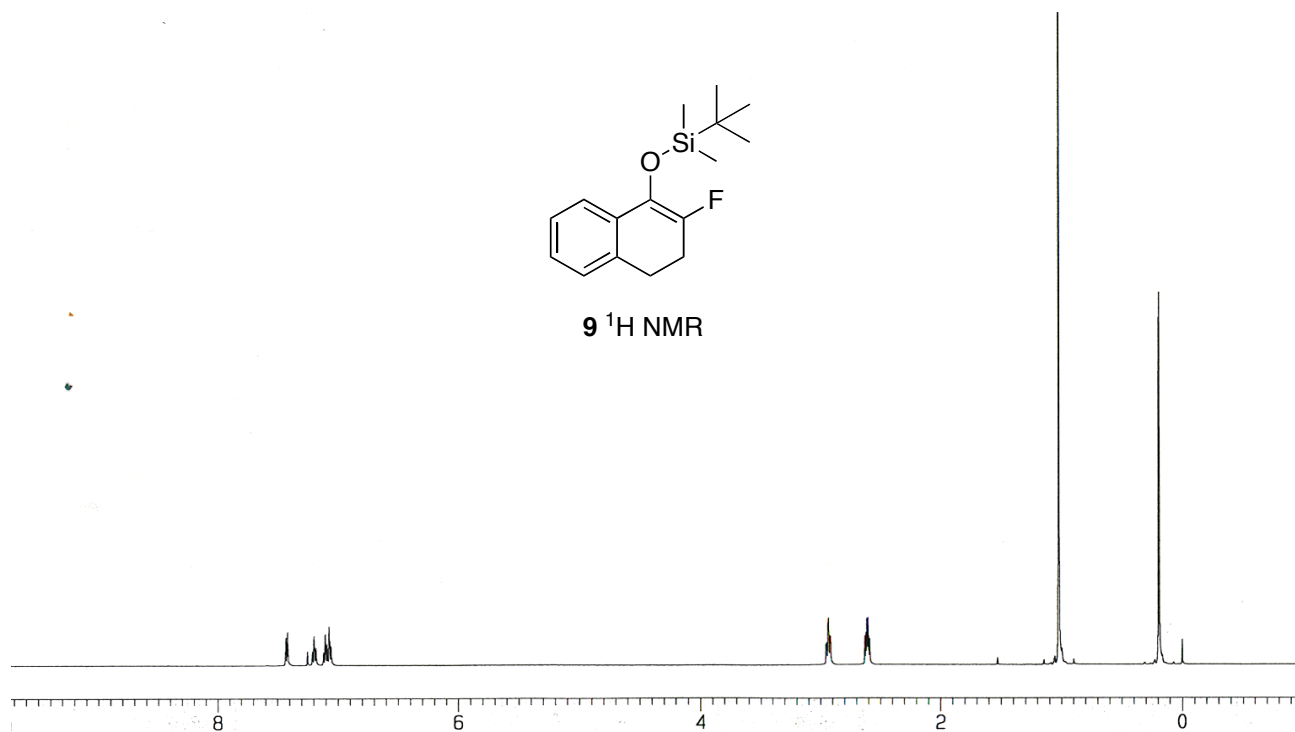
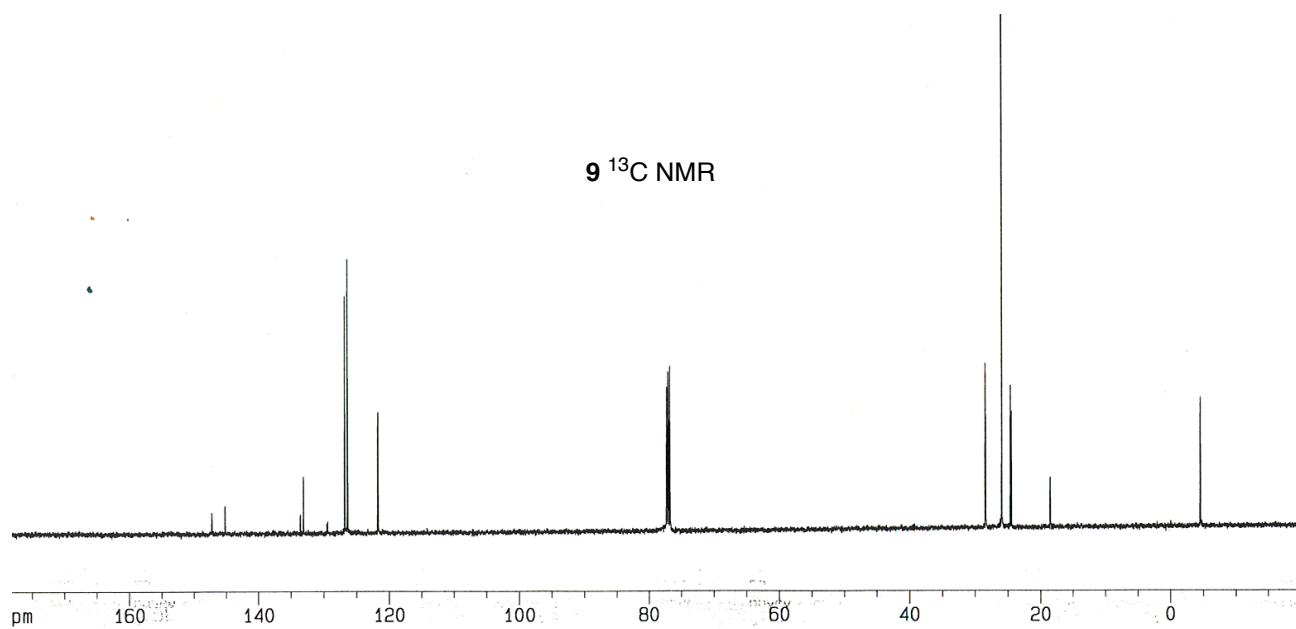
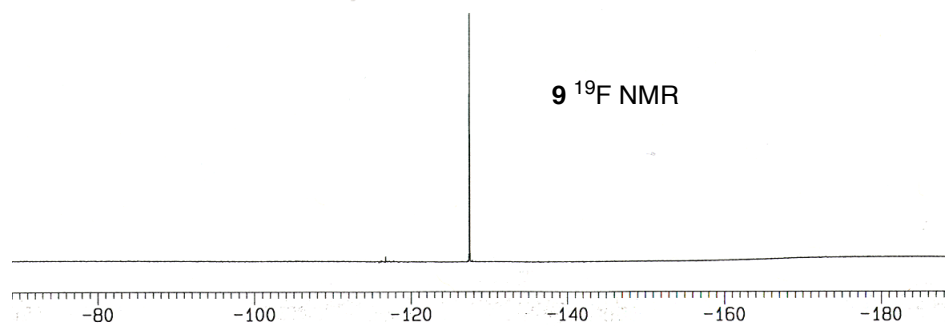
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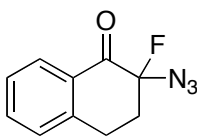
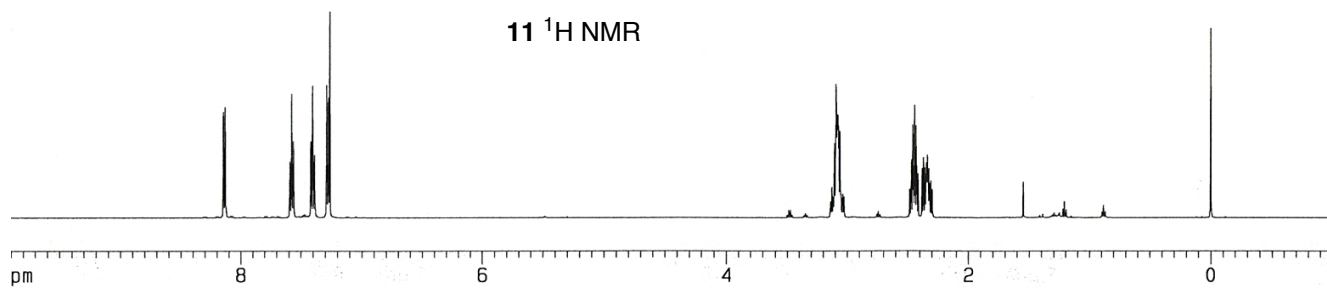
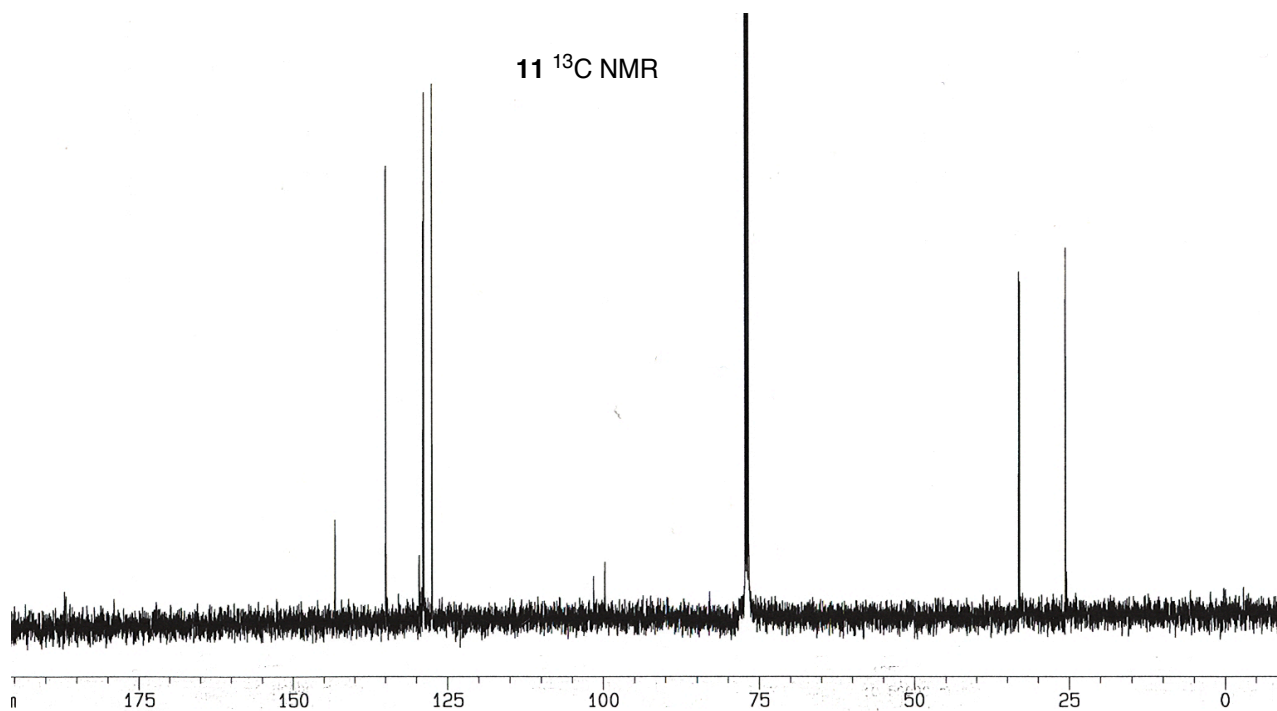
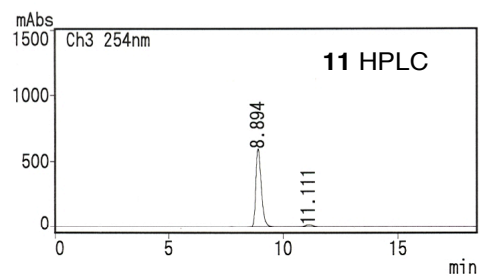
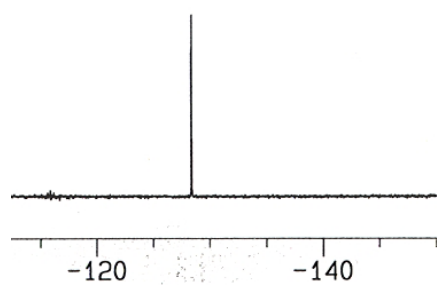
**8** ^1H NMR**8** ^{13}C NMR**8** ^{19}F NMR

*** ピークレポート ***

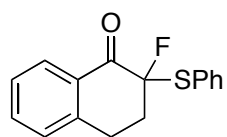
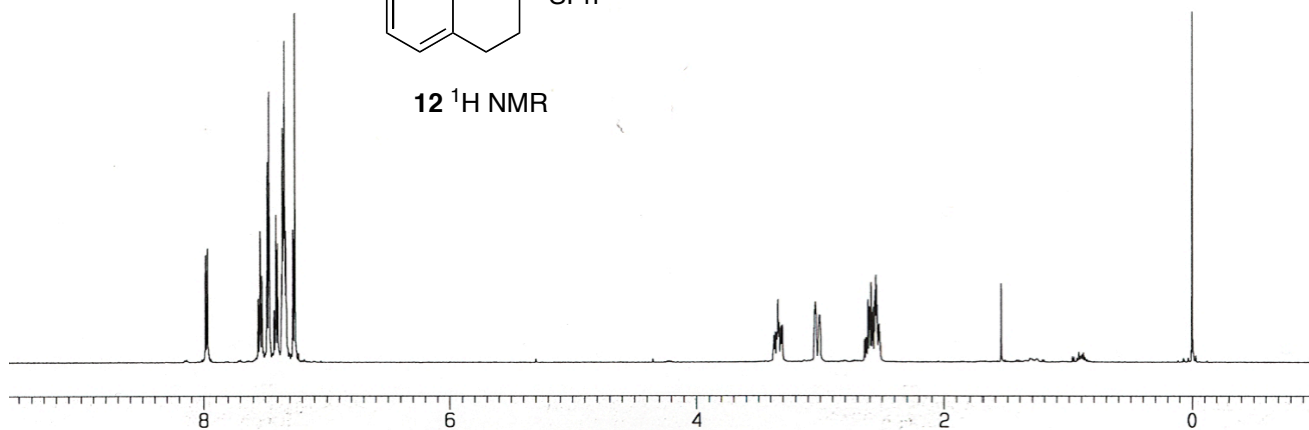
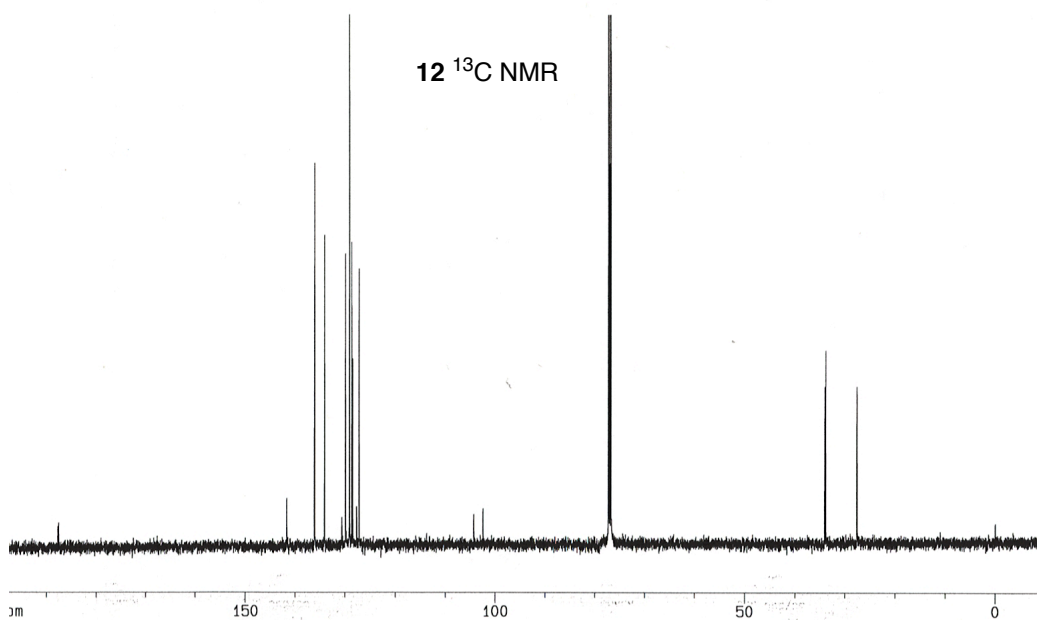
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1	1	11.006		
	3	11.007	3.0881	A
2	1	12.855		
	3	12.856	96.9119	B

100.0000

**9** ^1H NMR**9** ^{13}C NMR**9** ^{19}F NMR

**11** ^1H NMR**11** ^{13}C NMR**11** ^{19}F NMR

*** ピークレポート ***				
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** ^1H NMR**12** ^{13}C NMR

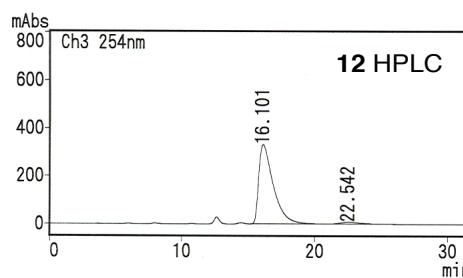
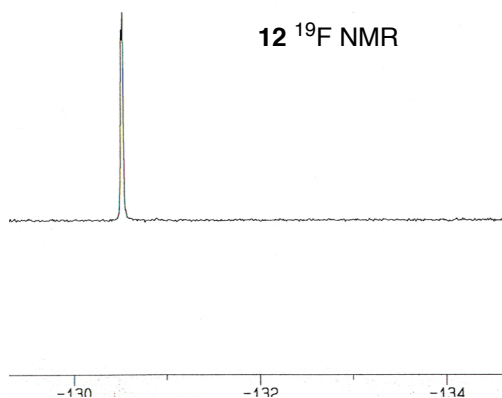
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 FIDRES 0.500026 Hz
 AQ 0.9999972 sec
 RG 8192
 DW 13.300 usec
 DE 7.50 usec
 TE 300.0 K
 D1 0.10000000 sec
 d11 0.03000000 sec

===== CHANNEL f1 =====
 NUC1 ^{13}C
 P1 4.60 usec
 PL1 0.00 dB
 SF01 125.7690572 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 ^1H
 PCPD2 90.00 usec
 PL2 120.00 dB
 PL12 19.00 dB
 SF02 500.1320005 MHz

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

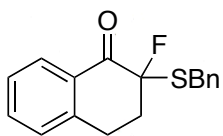
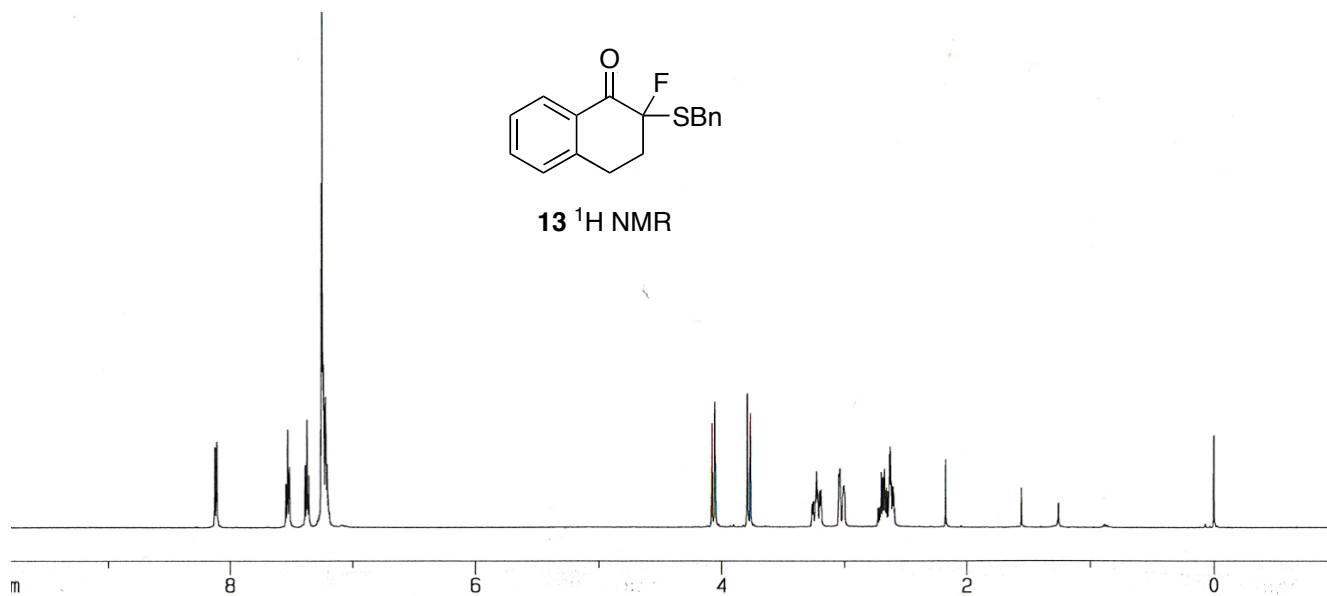
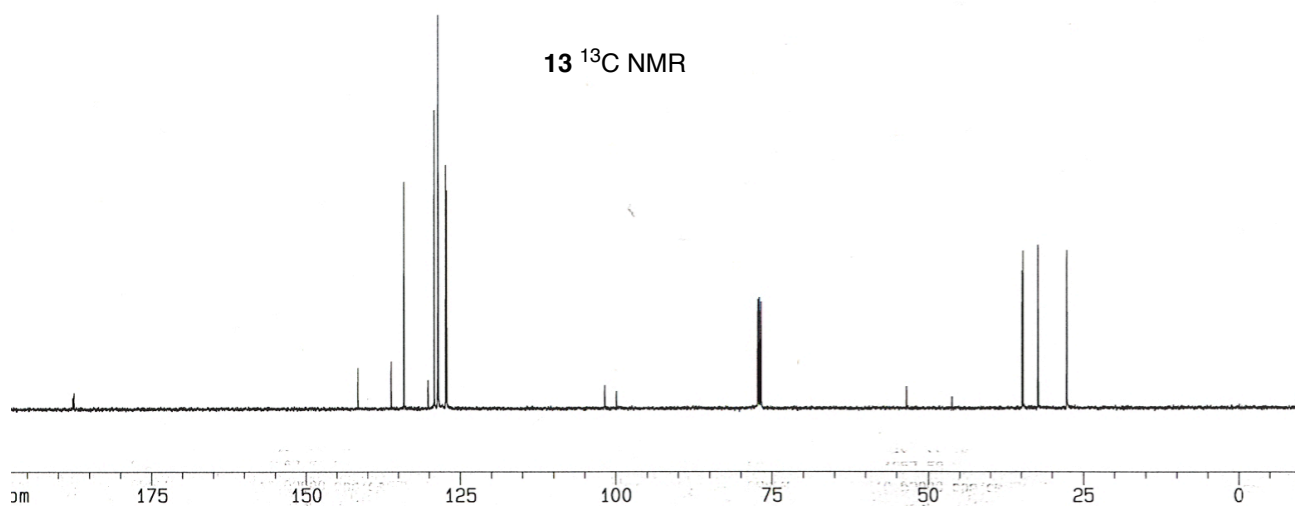
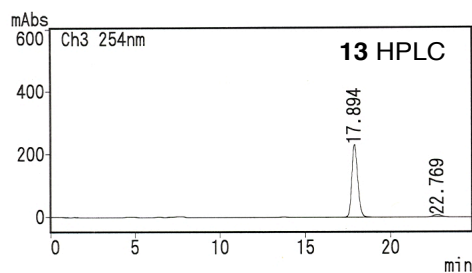
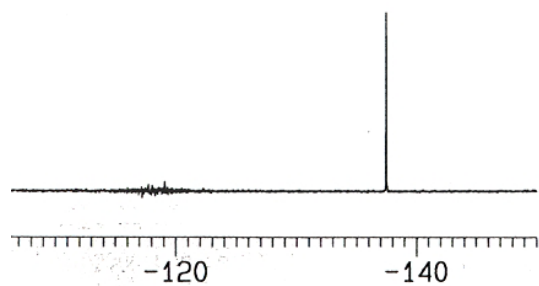
1D NMR plot parameters
 CX 20.00 cm
 F1P 200.000 ppm
 F1 25151.56 Hz
 F2P -10.000 ppm
 F2 -1257.58 Hz
 PPMCM 10.50000 ppm/cm
 HZCM 1320.45679 Hz/cm

12 ^{19}F NMR

*** ヒートマップ ***

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

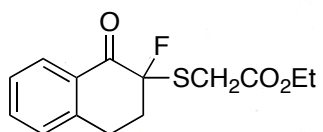
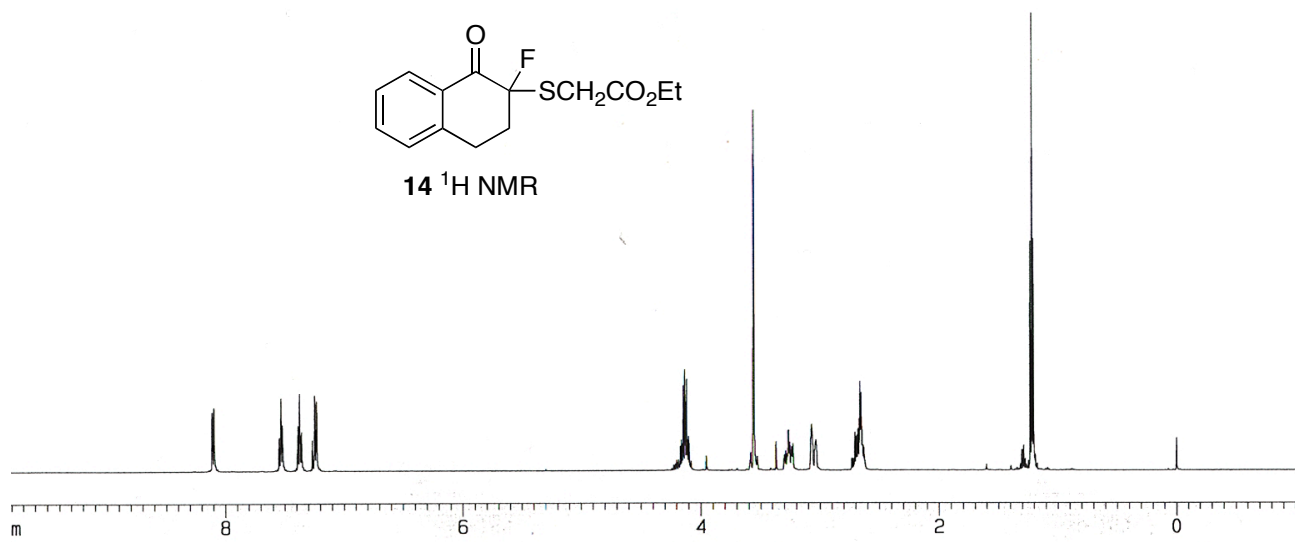
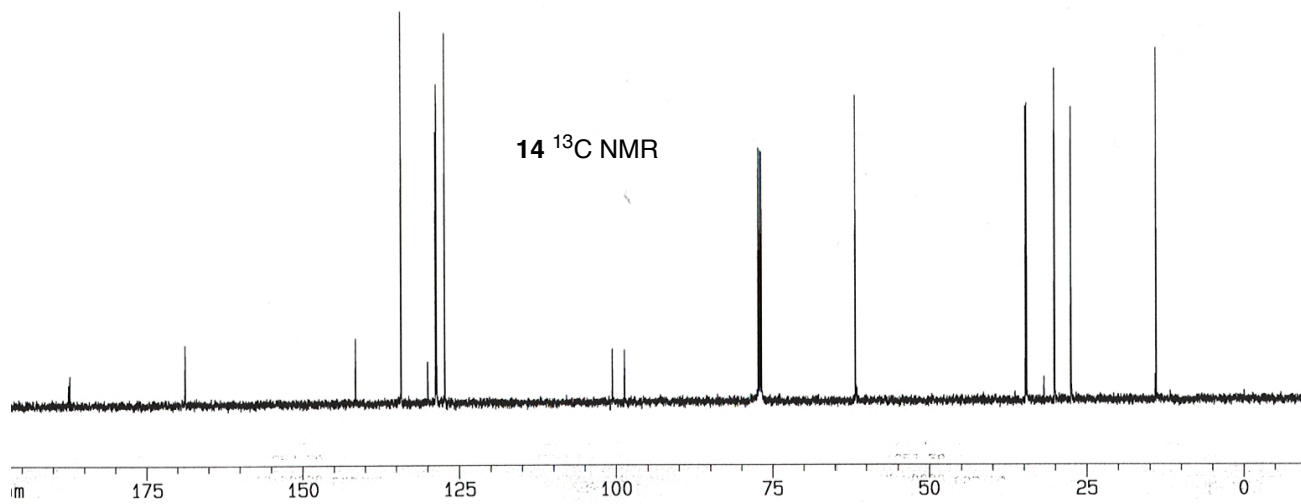
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**13** ^1H NMR**13** ^{13}C NMR**13** ^{19}F NMR

*** ヒートレポート ***

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

100.0000

**14** ^1H NMR**14** ^{13}C NMR**14** ^{19}F NMR