Conversion of MT-Sulfone to a Trifluoromethyl group by IF_5; the Application of an MT-Sulfone Anion as a Trifluoromethyl Anion Equivalent

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SUPPORTING INFORMATION

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General

The IR spectra were recorded using a JASCO FT/IR-410. The ^{1}H NMR (400 MHz) spectra, ^{19}F NMR (376 MHz) spectra, and ^{13}C NMR (100 MHz) were recorded in $CDCl_3$ on a JEOL JNM-A400II FT NMR and the chemical shift, δ, is referred to TMS (^{1}H, ^{13}C) and $CFCl_3$ (^{19}F), respectively. The EI-high-resolution mass spectra were measured on a JEOL JMS-700TZ. A TeflonFEP centrifuge tube (27 mL) with a screw cap was used as a reaction vessel. IF_5 in a stainless-steel cylinder was supplied by Asahi Glass Co., Ltd, and was transferred through a Teflon tube into a TeflonFEP bottle from the cylinder under an N_2 atmosphere. IF_5/Et_3N-5HF was prepared by the addition of an equimolar amount of Et_3N-5HF to IF_5 in TeflonFEP bottle. IF_5 decomposes in air emitting HF fume, and therefore, it should be carefully handled in a bench hood with rubber-gloved hands. (*S*)-2-[Diphenyl{(trimethylsilyl)oxy}methyl]pyrrolidine was prepared from (*S*)-methyl pyrrolidine-2-carboxylate according to the literature.[1] MT-sulfone, Et_3N-5HF, and $MeSSO_2Me$ were purchased from Tokyo Kasei Co. Ltd. TBAF in THF (1M) and SmI_2 in THF (0.1 M) were purchased from Aldrich. Compounds **1a** and **1d** were prepared from MT-sulfone and corresponding alkyl halides using phase transfer method.[2] Compounds **1b**, **1c**, and **1e** were prepared from MT-sulfone and corresponding alkyl halides using NaH in DMF[3] or by the reduction of ketene dithioacetal S,S-dioxides[4] prepared from MT-sulfone and corresponding aldehydes[5].

Conversion of methyl(1-tosyltridecyl)sulfane 1a to 1,1,1-trifluorotridecane 2a

Methyl(1-tosyltridecyl)sulfane **1a** (192 mg, 0.5 mmol) and IF_5/Et_3N-5HF (1.27 g, 3 mmol) were placed in a TeflonFEP bottle under an N_2 atmosphere. The bottle was tightly screw-caped and the mixture was stirred at 60 °C for 48 h. Then the mixture was poured into water and neutralized with aq $NaHCO_3$. The product was extracted with ether (30 mL X 3), and the organic phase was washed with aq $Na_2S_2O_3$ and dried over $MgSO_4$. After concentration under reduced pressure, **2a** was isolated by column chromatography (silica gel / hexane) in 87% yield.

Characterization Data of Compound 2

1,1,1-Trifluorotridecane (2a)

IR (neat) 2926, 2856, 1255, 1143 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.1 Hz), 1.21-1.40 (18H, m), 1.51-1.58 (2H, m), 1.99-1.12 (2H, m). ^{13}C NMR (100MHz, $CDCl_3$) δ 14.1, 22.0 (q, $^{3}J_{C\text{-}F}$ = 3.1 Hz), 22.8, 28.8, 29.3, 29.5, 29.6, 29.7, 29.8 (2C),

32.1, 33.8 (q, $^{2}J_{C\text{-}F}$ = 28.4 Hz), 127.4 (q, $^{1}J_{C\text{-}F}$ = 276.3 Hz). ^{19}F NMR (373MHz, $CDCl_3$) δ -67.40 (3F, t, *J* = 11.0 Hz), (lit.[6] -66.9 (t, *J* = 10.8 Hz)).

Ethyl 7,7,7-trifluoroheptanoate (2b)

IR (neat) 2947, 1737, 1256, 1037 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) δ 1.26 (3H, t, *J* = 7.1 Hz), 1.37-1.44 (2H, m), 1.54-1.69 (4H, m), 2.02-2.11 (2H, m), 2.32 (2H, q, *J* = 7.6 Hz), 4.13 (2H, q, *J* = 7.2 Hz). ^{13}C NMR (100MHz, $CDCl_3$) δ 14.2, 21.6 (q, $^{3}J_{C\text{-}F}$ = 2.9 Hz), 24.4, 28.1, 33.5 (q, $^{2}J_{C\text{-}F}$=28.4 Hz), 33.9, 60.3, 127.1 (q, $^{1}J_{C\text{-}F}$=276.4 Hz), 173.4. ^{19}F NMR (373MHz, $CDCl_3$) δ -67.0 (3F, t, *J* = 11.0 Hz). HRMS (EI) calcd for $C_9H_{15}F_3O_2$ 212.1024, found 212.1034.

13-Chloro-1,1,1-trifluorotridecane (2c)

IR (neat) 2927, 2856, 1255, 1136 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) δ 1.27-1.58 (16H, m), 1.75-1.80 (2H, m), 2.00-2.12 (2H, m), 3.53 (2H, t, *J* = 6.8 Hz). ^{13}C NMR (100MHz, $CDCl_3$) δ 21.8 (q, $^{3}J_{C\text{-}F}$ = 2.9 Hz) 26.9, 28.7, 28.9, 29.2, 29.3, 29.4, 29.5 (2C), 32.7, 33.7 (q, $^{2}J_{C\text{-}F}$ = 28.6 Hz), 45.0, 127.3 (q, $^{1}J_{C\text{-}F}$ = 275.6 Hz). ^{19}F NMR (373MHz, $CDCl_3$) δ -67.03, (3F, t, *J* = 11.1 Hz). HRMS (EI) calcd for $C_{13}H_{24}F_3Cl$ 272.15186, found 272.14910

1,1,1,12,12,12-Hexafluorododecane (2d)

IR (neat) 2930, 2859, 1255, 1145 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) δ 1.26-1.35 (12H, m), 1.50-1.59 (4H, m), 2.00-2.12 (4H, m). ^{13}C NMR (100MHz, $CDCl_3$) δ 21.8 (2C, q, $^{3}J_{C\text{-}F}$ = 2.9 Hz), 28.6 (2C), 29.1 (2C), 29.2 (2C), 33.7 (2C, q, $^{2}J_{C\text{-}F}$ = 28.4 Hz), 127.3 (2C, q, $^{1}J_{C\text{-}F}$ = 276.3 Hz). ^{19}F NMR (373MHz, $CDCl_3$) δ -67.04 (6F, t, *J* = 11.0 Hz), (lit.[7] -66.9 (t, *J* = 11 Hz).

7,7,7-Trifluoroheptyl benzoate (2e)

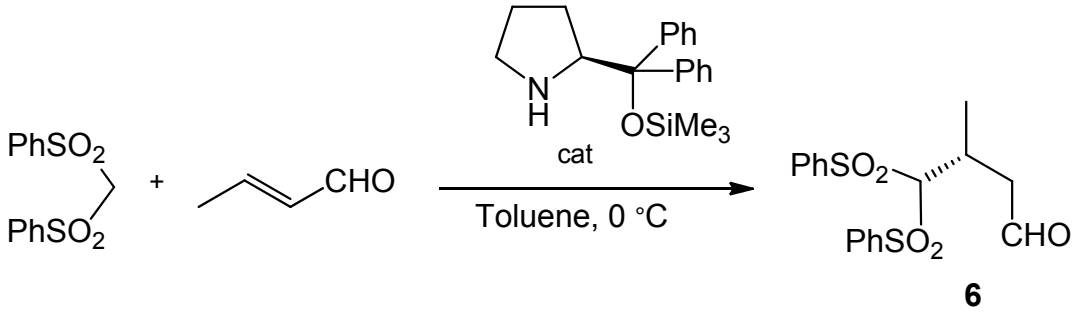
IR (neat) 2945, 1718, 1275, 712 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) δ 1.44-1.52 (4H, m), 1.56-1.63 (2H, m), 1.76-1.82 (2H, m), 2.02-2.14 (2H, m), 4.33 (2H, t, *J* = 6.3 Hz), 7.45 (2H, t, *J* = 7.9 Hz), 7.56 (1H, t, *J* = 7.5 Hz), 8.04 (2H, d, *J* = 7.5 Hz). ^{13}C NMR (100MHz, $CDCl_3$) δ 21.8 (q, $^{3}J_{C\text{-}F}$ = 2.9 Hz), 25.7, 28.3, 28.4, 33.6 (q, $^{2}J_{C\text{-}F}$ = 28.4 Hz), 64.7, 127.2 (q, $^{1}J_{C\text{-}F}$ = 276.3 Hz), 128.3 (2C), 129.5 (2C), 130.3, 132.8, 166.6. ^{19}F NMR (373MHz, $CDCl_3$) δ -67.01 (3F, t, *J* = 11.2 Hz). HRMS (EI) calcd for $C_{14}H_{17}F_3O_2$ 274.1181, found 274.1180.

***N,N*-Diethyl-7,7,7-trifluoroheptanamide (2f)**

IR (neat) 2939, 1643, 1255, 1133 cm^{-1}. ^{1}H NMR (400MHz, $CDCl_3$) δ 1.11 (3H, t, J = 7.1 Hz), 1.20 (3H, t, J = 7.1 Hz), 1.38-1.46 (2H, m), 1.55-1.72 (4H, m), 2.02-2.15 (2H, m), 2.31 (2H, t, J = 7.3 Hz), 3.30 (2H, q, J = 7.1 Hz), 3.37 (2H, q, J = 7.1 Hz). ^{13}C NMR (100MHz, $CDCl_3$) δ 12.9, 14.2, 21.6 (q, $^{3}J_{C-F}$ = 2.4 Hz), 24.7, 28.3, 32.5, 33.4 (q, $^{2}J_{C-F}$ = 28.4 Hz), 39.9, 41.8, 127.1 (q, $^{1}J_{C-F}$ = 276.1 Hz), 171.6. ^{19}F NMR (373 MHz, $CDCl_3$) δ -67.0 (3F, t, J = 11.2 Hz). HRMS (EI) calcd for $C_{11}H_{20}F_3NO$ 239.1497, found 239.1503.

Formal asymmetric Michael-addition of trifluoromethyl anion to crotonaldehyde

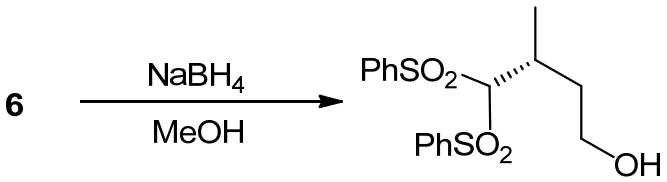
(*R*)-3-Methyl-4,4-bis(phenylsulfonyl)butanal (6)



6

The reaction was carried out according to the literature.[8] A mixture of bis(phenylsulfonyl)methane (2.07 g, 7 mmol), (*S*)-2-[diphenyl{(trimethylsilyl)oxy}methyl]pyrrolidine (0.46 g, 1.4 mmol), and crotonaldehyde (0.735 g, 10.5 mmol) in toluene (56 mL) was stirred at 0 °C for 24h. Then a volatile part was removed under reduced pressure and the residue was purified by column chromatography (silica gel / hexane:acetone = 3:2) to give **6** (2.192 g, 6 mmol) in 86% yield.

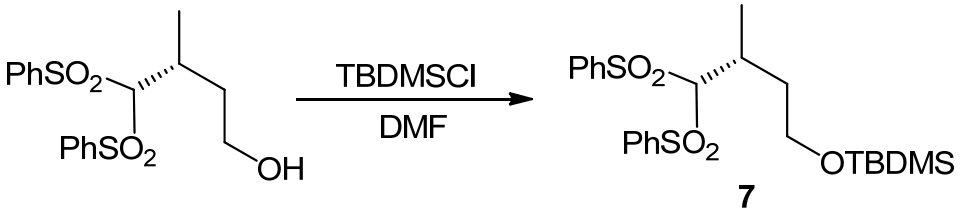
(*R*)-3-Methyl-4,4-bis(phenylsulfonyl)butan-1-ol



To a MeOH solution (14 mL) of **6** (2.192 g, 6 mmol) was added $NaBH_4$ (0.53 g, 14 mmol) at 0 °C and the mixture was stirred for 2 h. Then the mixture was poured into water (20 mL) and extracted with EtOAc (30 mL X 3). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (silica gel / hexane:acetone = 3:2) gave

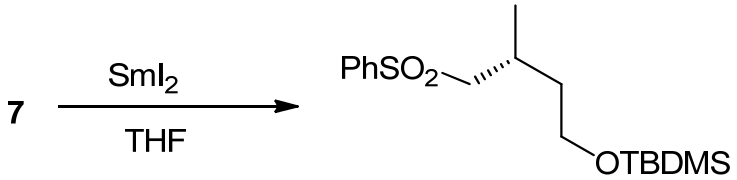
3-methyl-4,4-bis(phenylsulfonyl)butan-1-ol (2.0 g, 5.4 mmol) in 91% yield. Optical purity of 3-methyl-4,4-bis(phenylsulfonyl)butan-1-ol (85 %ee) was determined by HPLC analysis using CHIRAPAK IC column (DAICEL CHEMICAL INDUSTRIES Ltd.) (4.6 mm I.D. x 250 mm) (5 μm) (hexane:i-PrOH = 80:20), 1.0 mL/min; 20 °C (major enantiomer appeared at 42.3 min, and minor enantiomer appeared at 55.8 min, respectively).

(*R*)-3-Methyl-4,4-bis(phenylsulfonyl)butan-1-ol *tert*-butyldimethylsilyl ether (7)



To a DMF solution (20 mL) of (*R*)-3-methyl-4,4-bis(phenylsulfonyl)butan-1-ol (2.0 g, 5.4 mmol) were added imidazole (1.53 g, 22.5 mmol) and TBDMSCl (3.3 g 22.0 mmol) at 0 °C, successively, and the mixture was stirred at room temperature overnight. The mixture was poured into water (20 mL) and extracted with EtOAc (20 mL X 3). The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (silica gel / hexane:acetone = 3:1) gave **7** (2.57 g, 5.3 mmol) in 97% yield.

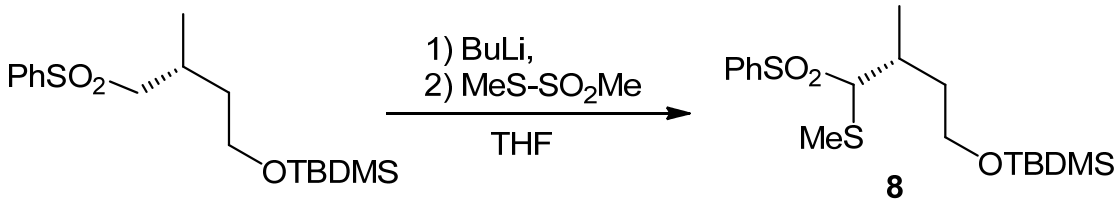
(*R*)-3-Methyl-4-(phenylsulfonyl)butan-1-ol *tert*-butyldimethylsilyl ether



To a THF solution (7 mL) of **7** (1.7 g, 3.5 mmol) was added 0.1M THF solution of SmI_2 (100 mL, 10 mmol) at room temperature under nitrogen atmosphere and the resulting yellow solution was stirred at room temperature for 30 min. The reaction was quenched by the addition of aq NH_4Cl (10 mL) and the product was extracted with ether (30 mL X 3). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (silica gel / hexane:acetone = 6:1) gave (*R*)-3-methyl-4-(phenylsulfonyl)butan-1-ol *tert*-butyldimethylsilyl ether (1,12 g, 3.3 mmol) in 93% yield.

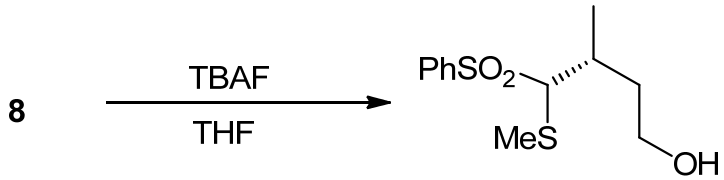
(3*R*)-3-Methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butan-1-ol

***tert*-butyldimethylsilyl ether (8)**



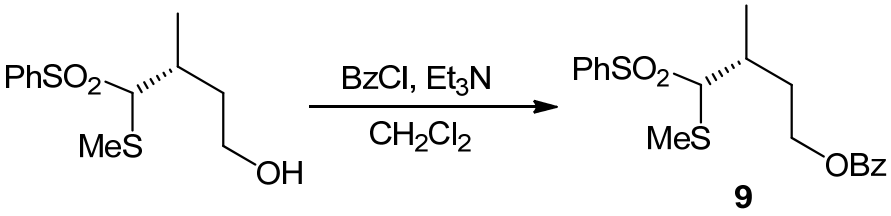
To a THF solution (7 mL) of (*R*)-3-methyl-4-(phenylsulfonyl)butan-1-ol *tert*-butyldimethylsilyl ether (1.1 g, 3.3 mmol) was added a 1.65 M hexane solution of BuLi (2 mL, 3.3 mmol) at -78 °C under nitrogen atmosphere and the mixture was stirred for 30 min. After the addition of $MeSSO_2Me$ (1.5 ml, 16 mmol), the mixture was stirred at –78 °C for 24h. The mixture was poured into water (20 mL) and extracted with ether (20 mL X 3). The combined organic layer was washed with aq NH_4Cl, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (silica gel / hexane:acetone = 6:1) gave **8** (1.0 g, 2.6 mmol) in 79 % yield.

(3*R*)-3-Methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butan-1-ol



To a THF solution (5 mL) of **8** (1.0 g, 2.6 mmol) was added 1.0 M THF solution of TBAF (7.8 mL, 7.8 mmol) at room temperature and the mixture was stirred overnight. The mixture was poured into water (30 mL), extracted with ether (30 mL X 3), and washed with aq $NaHCO_3$ (20 mL). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (silica gel / hexane:acetone 2:1) gave (3*R*)-3-methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butan-1-ol (0.52 g, 1.9 mmol) in 74 % yield.

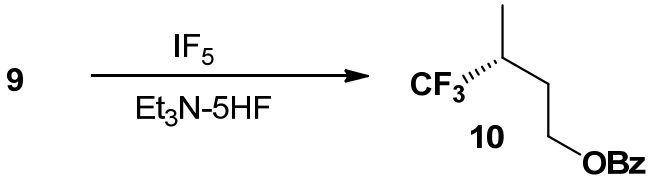
(3*R*)-3-Methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butyl benzoate (9)



9

To a CH_2Cl_2 solution (4 mL) of (3*R*)-3-methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butan-1-ol (0.52 g, 1.9 mmol) and Et_3N (0.58 g, 5.7 mmol) was added benzoyl chloride (0.8 g, 5.7 mmol) at 0 °C and the mixture was stirred at room temperature overnight. The mixture was poured into water (30 mL) and extracted with ether (30 mL X 3). The combined organic layer was washed with brine (20 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography (silica gel / hexane:acetone = 4:1) gave **9** (0.70 g, 1.85 mmol) in 97% yield as a mixture of diastereomers (ca. 5:1). IR (neat) 2925, 1716, 1306, 1275, 1146 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$) δ 1.09 (2.5H, d, *J* = 6.7 Hz), 1.21 (0.5H, d, *J* = 6.7 Hz), 1.89-1.97 (2H, m), 2.07 (2.5H, s), 2.08 (0.5H, s), 2.59-2.64 (1H, m), 3.64 (0.15H, s), 3.83 (0.85H, d, *J* = 1.8 Hz), 4.25-4.36 (2H, m), 7.43-7.61 (6H, m), 7.93-8.06 (4H, m). ^{13}C NMR (100MHz, $CDCl_3$) δ 14.8, 18.1, 18.5, 30.0, 34.3, 62.1, 128.4 (2C), 129.0 (2C), 129.2 (2C), 129.5 (2C), 129.9, 133.1, 133.8, 137.8, 166.4. HRMS (EI) calcd for $C_{19}H_{22}S_2O_4Na$ (M^++Na) 401.08517, found 401.08471.

(*R*)-4,4,4-Trifluoro-3-methylbutyl benzoate (10)



9 (189 mg, 0.5 mmol) and IF_5/Et_3N-5HF (0.3 g, 1.5 mmol) were placed in a TeflonFEP bottle under an N_2 atmosphere. The bottle was tightly screw-caped and the mixture was stirred at 60 °C for 48 h. Then the mixture was poured into water and neutralized with aq $NaHCO_3$. The product was extracted with ether (30 mL X 3), and combined organic phase was washed with aq $Na_2S_2O_3$ and dried over $MgSO_4$. After concentration under reduced pressure, **10** was isolated by column chromatography (silica gel / hexane:CH_2Cl_2 = 3:1) in 52% yield. Optical purity of **10** (84 %ee) was determined by HPLC analysis using CHIRAPAK IC column (DAICEL CHEMICAL INDUSTRIES Ltd.) (4.6 mm I.D. x 250 mm)(5 μm)(hexane:i-PrOH = 99.2:0.8), 1.0 mL/min; 20 °C

(major enantiomer appeared at 20.2 min, and minor enantiomer appeared at 19.4 min, respectively). Absolute stereochemistry of **10** was determeind to be *R* by the comparison of its optical rotation with the reported data.[9] $[\alpha]^{19}_{D}$ = 12.5 (c = 1.04, $CHCl_3$) lit.[9] $[\alpha]^{17}_{D}$ = +21.2 (c = 1.02, $CHCl_3$) for 98%ee). IR (neat) 2987, 1722, 1270 cm^{-1}. ^1H NMR (400MHz, $CDCl_3$) δ 1.21 (3H, d, *J* = 7.0 Hz), 1.72-1.81 (1H, m), 2.18-2.26 (1H, m), 2.39-2.46 (1H, m), 4.34-4.47 (2H, m), 7.44-7.60 (3H, m), 8.02-8.05 (2H, m). ^{13}C NMR (100MHz, $CDCl_3$) δ 12.5 (q, $^3J_{C\text{-}F}$ = 2.8 Hz), 28.7 (q, $^3J_{C\text{-}F}$ = 2.9 Hz), 35.2 (q, $^2J_{C\text{-}F}$ = 26.7 Hz), 61.7, 128.1 (q, $^1J_{C\text{-}F}$ = 279.5 Hz), 128.4 (2C), 129.5 (2C), 132.3, 133.1, 166.3. ^{19}F NMR (373MHz, $CDCl_3$) δ -74.04 (3F, d, *J* = 9.0 Hz). HRMS (EI) calcd for $C_{12}H_{13}F_3O_2$ 246.08676, found 246.08629.

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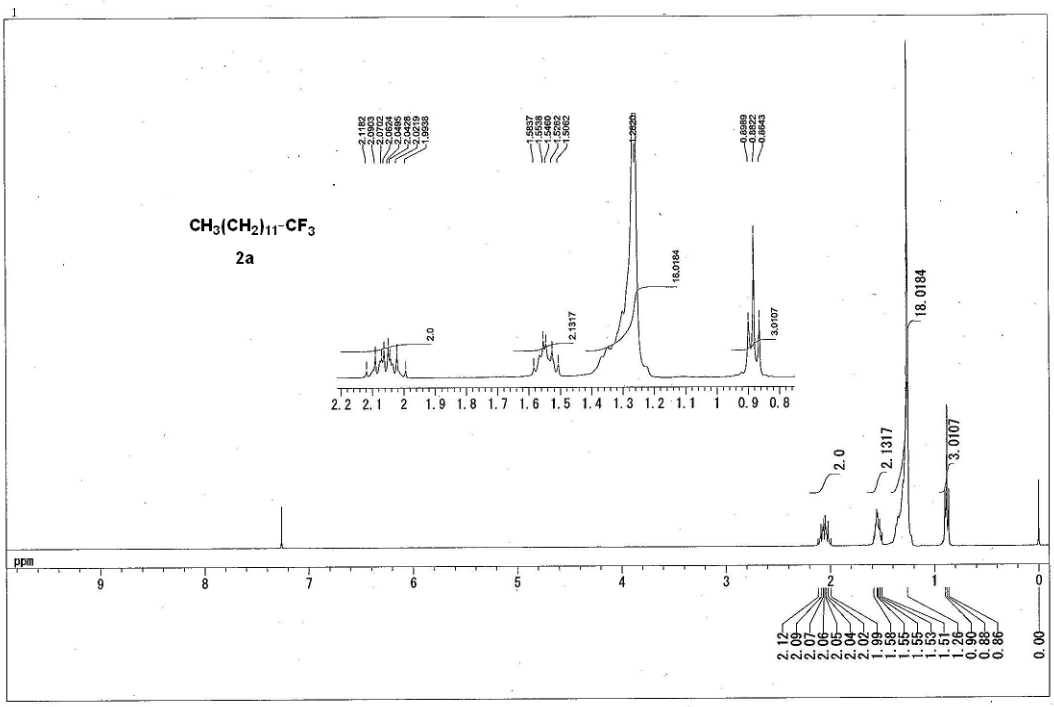
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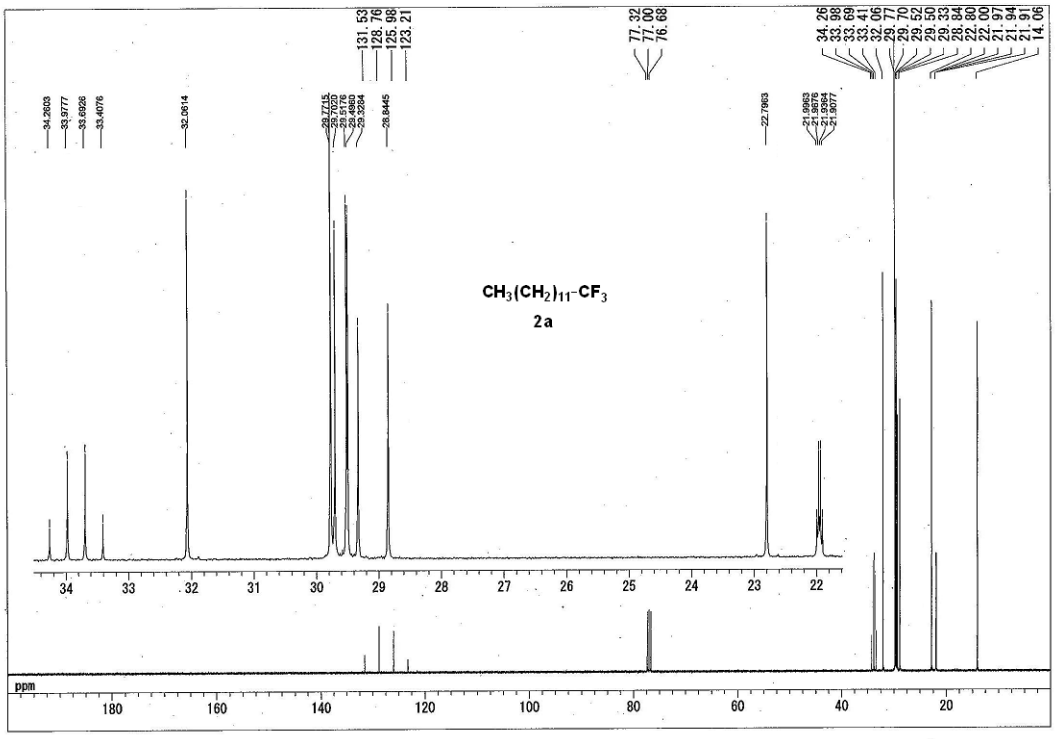
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2a
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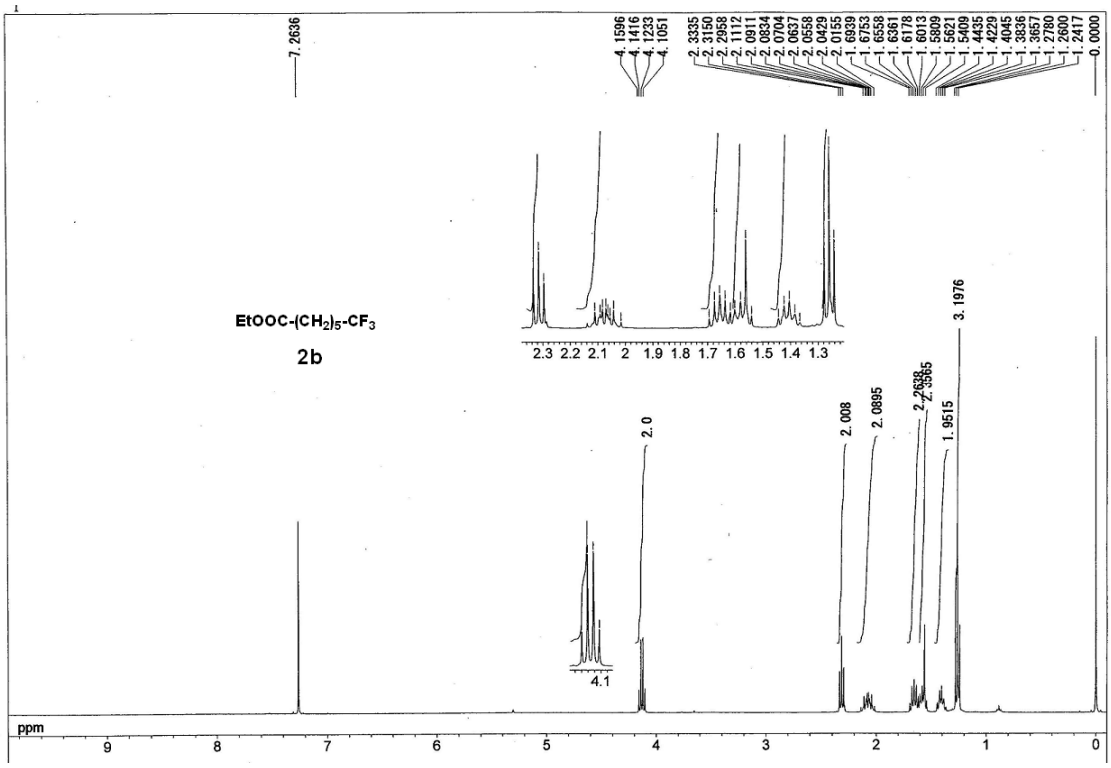
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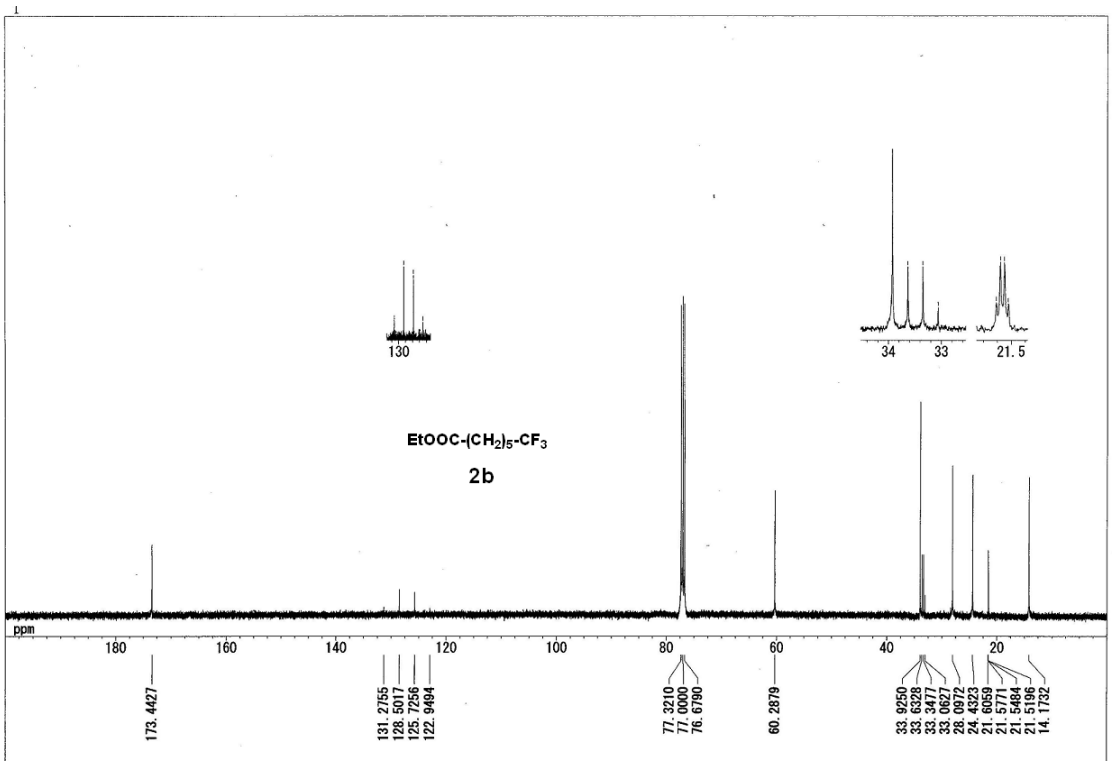
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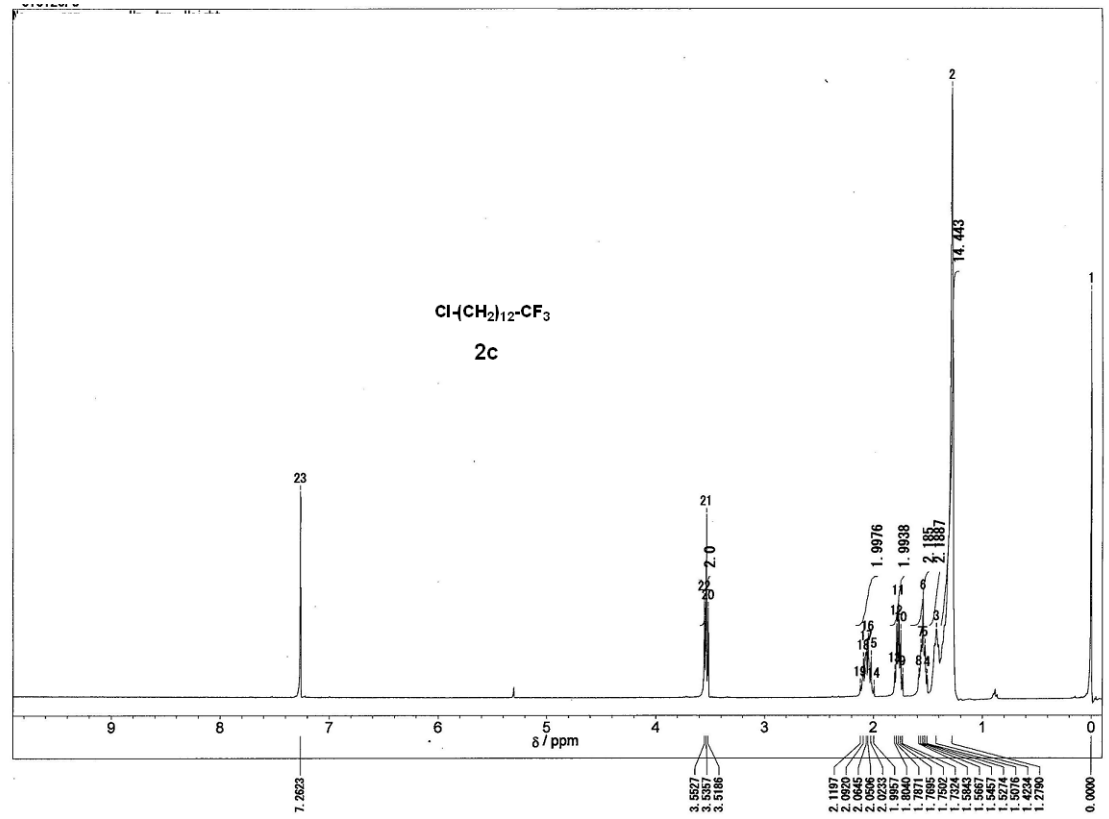
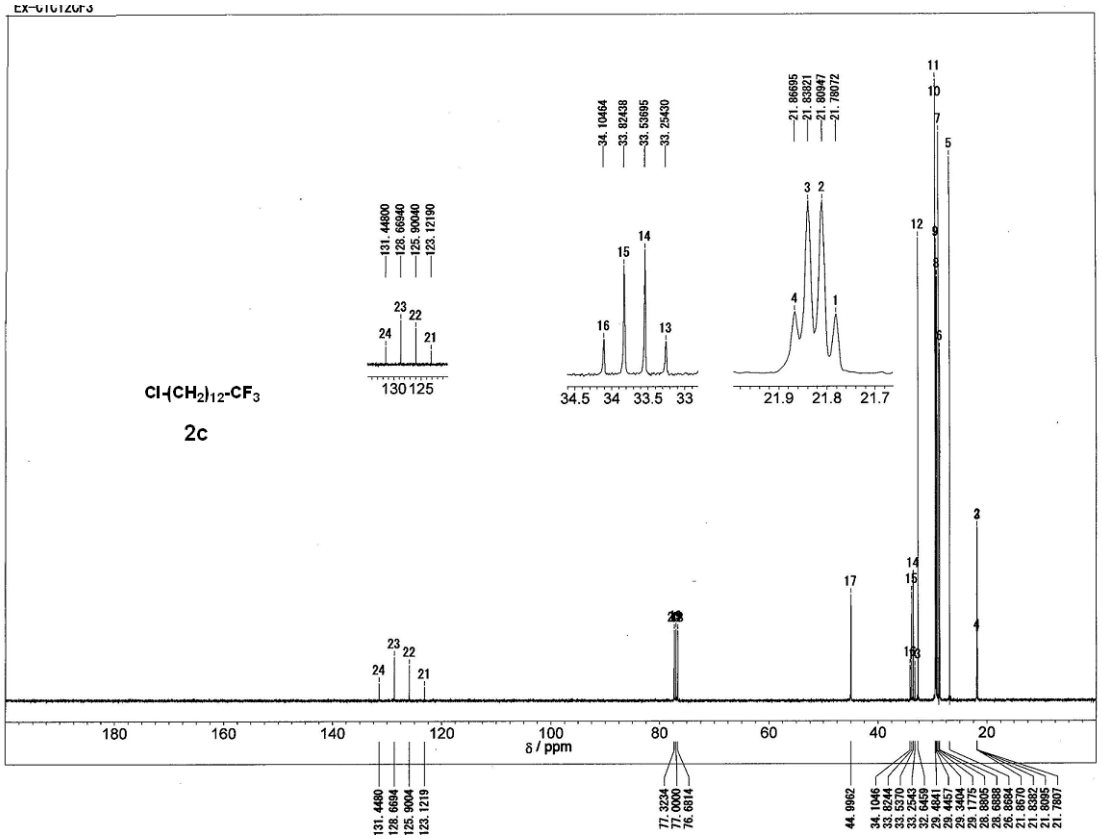
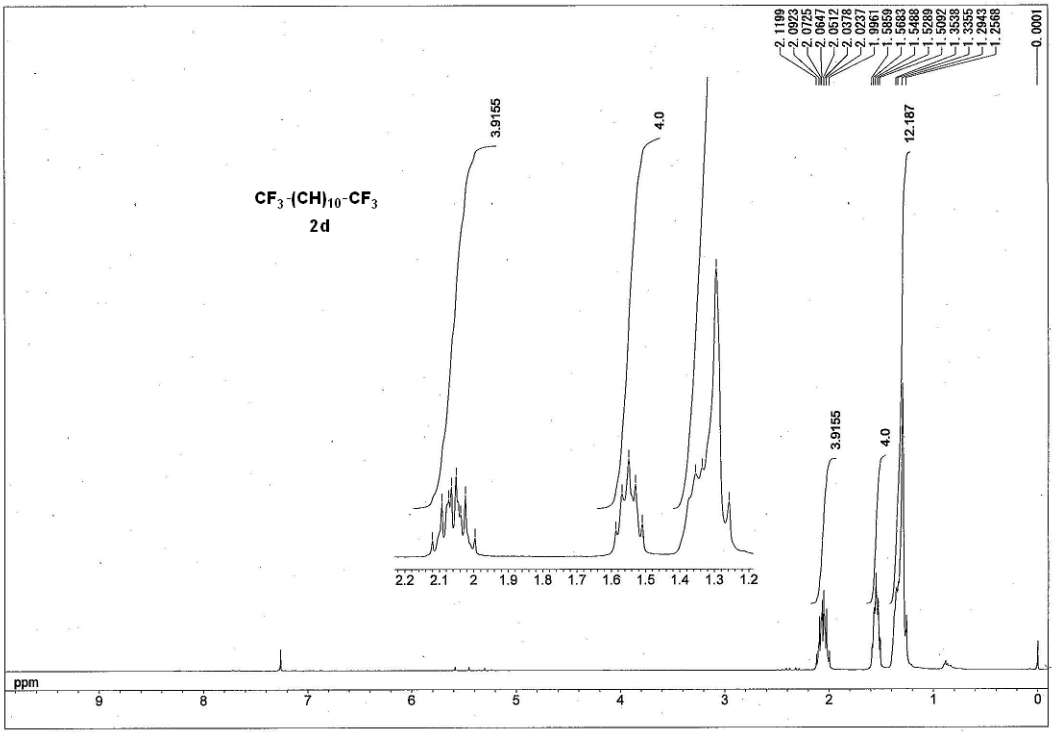
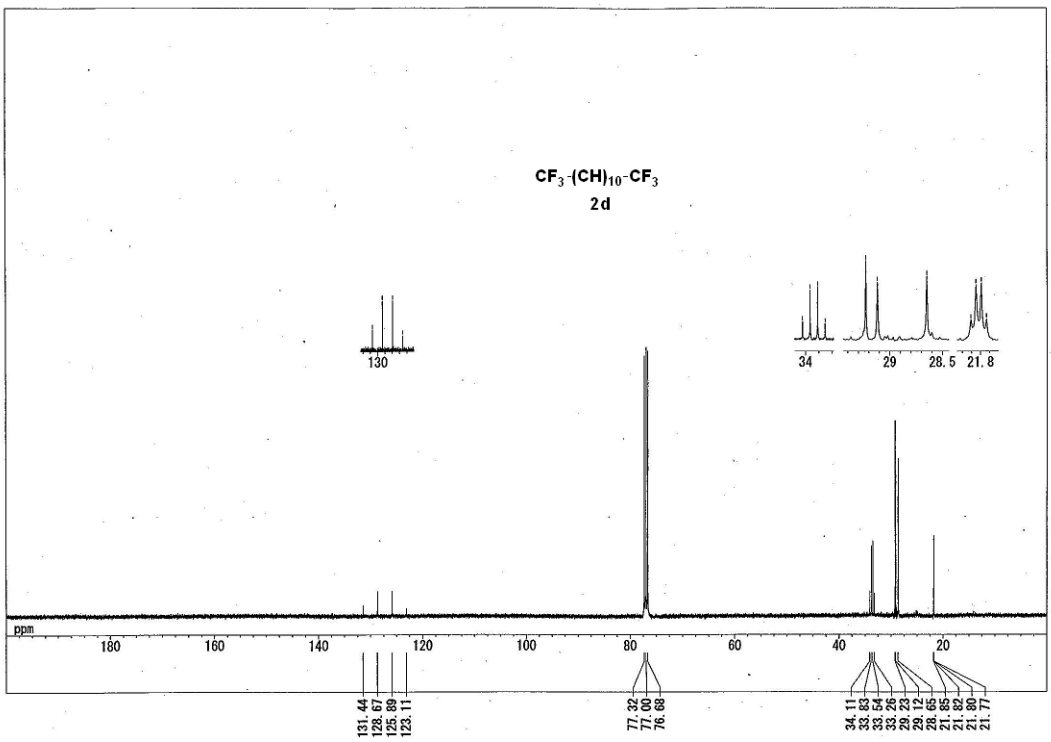
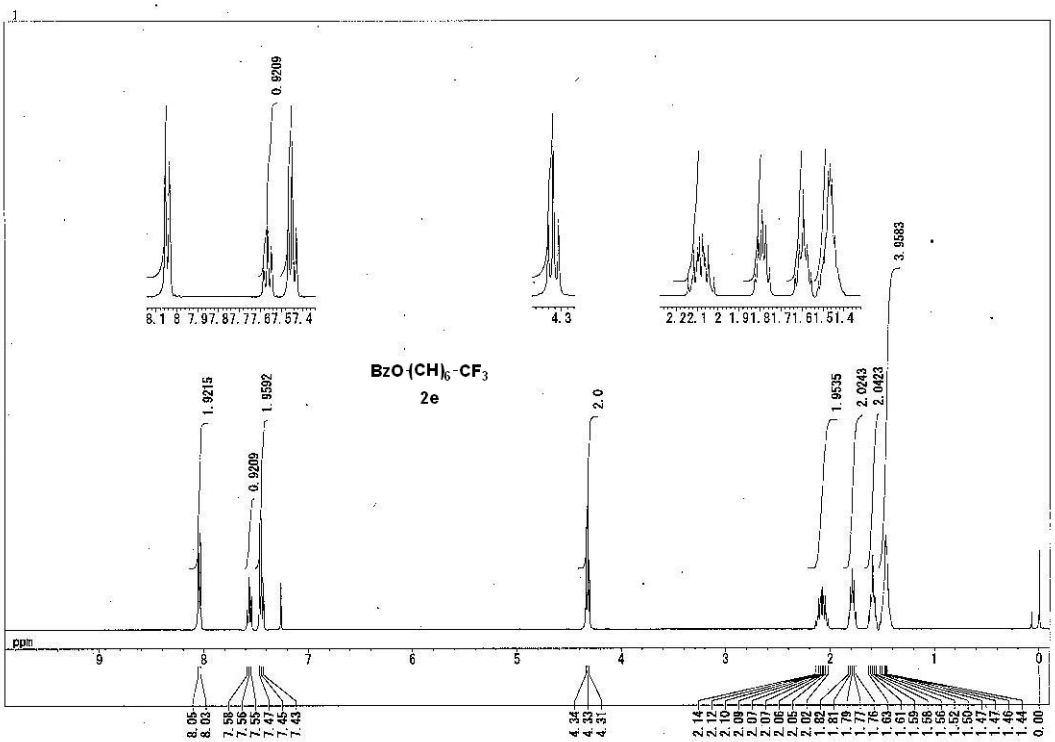
21.5196
14.1732

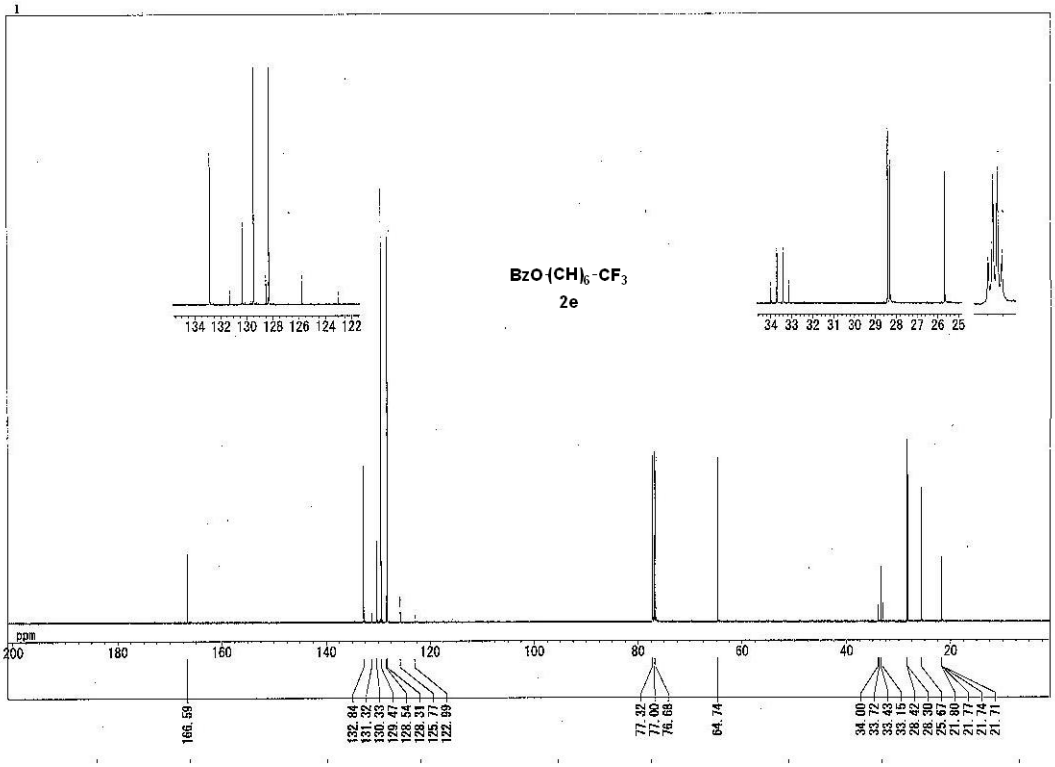

Cl-(CH2)12-CF3
2c
δ / ppm

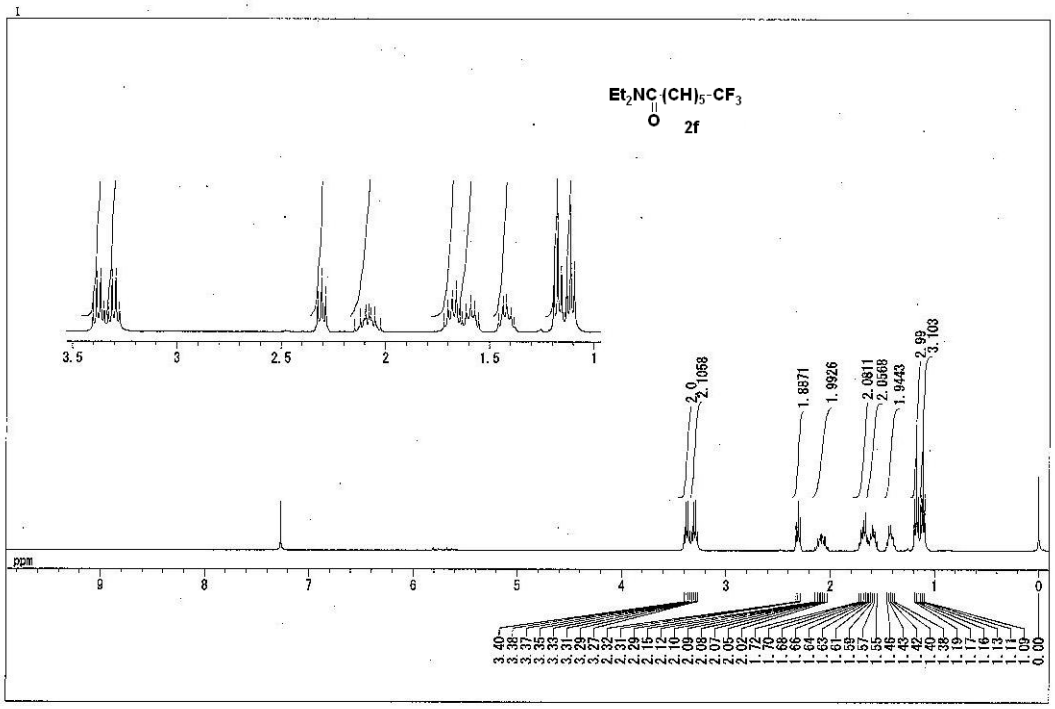

Cl-(CH2)12-CF3
2c
δ / ppm

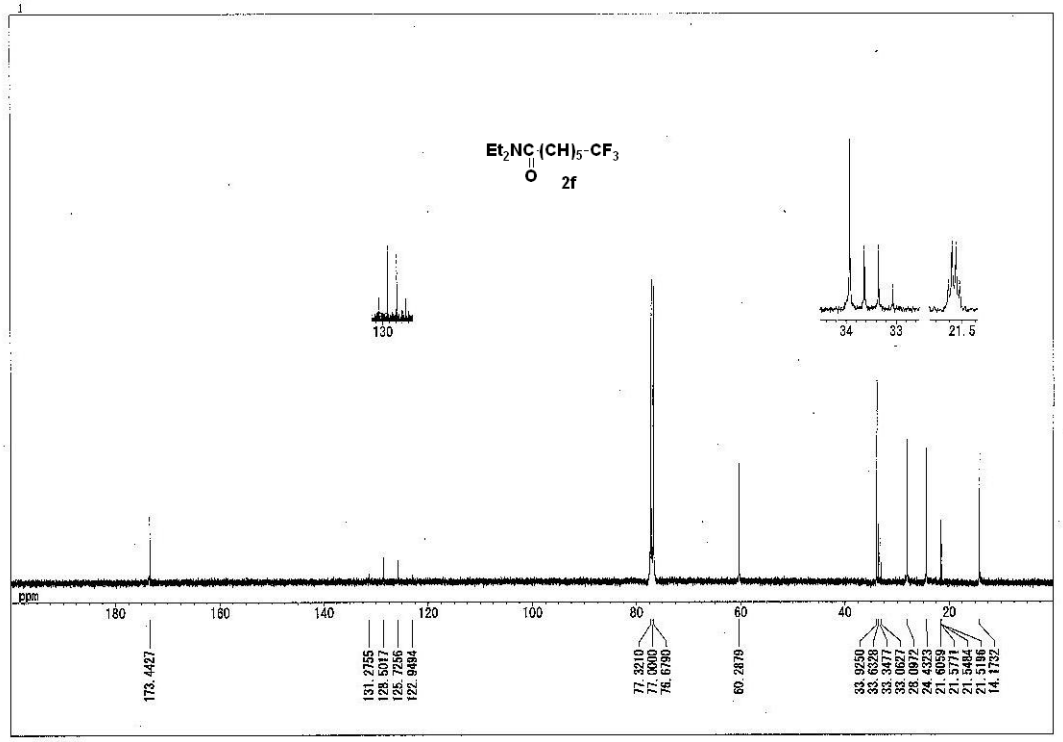

CF3-(CH)10-CF3
2d
3.9155
4.0
12.187
ppm

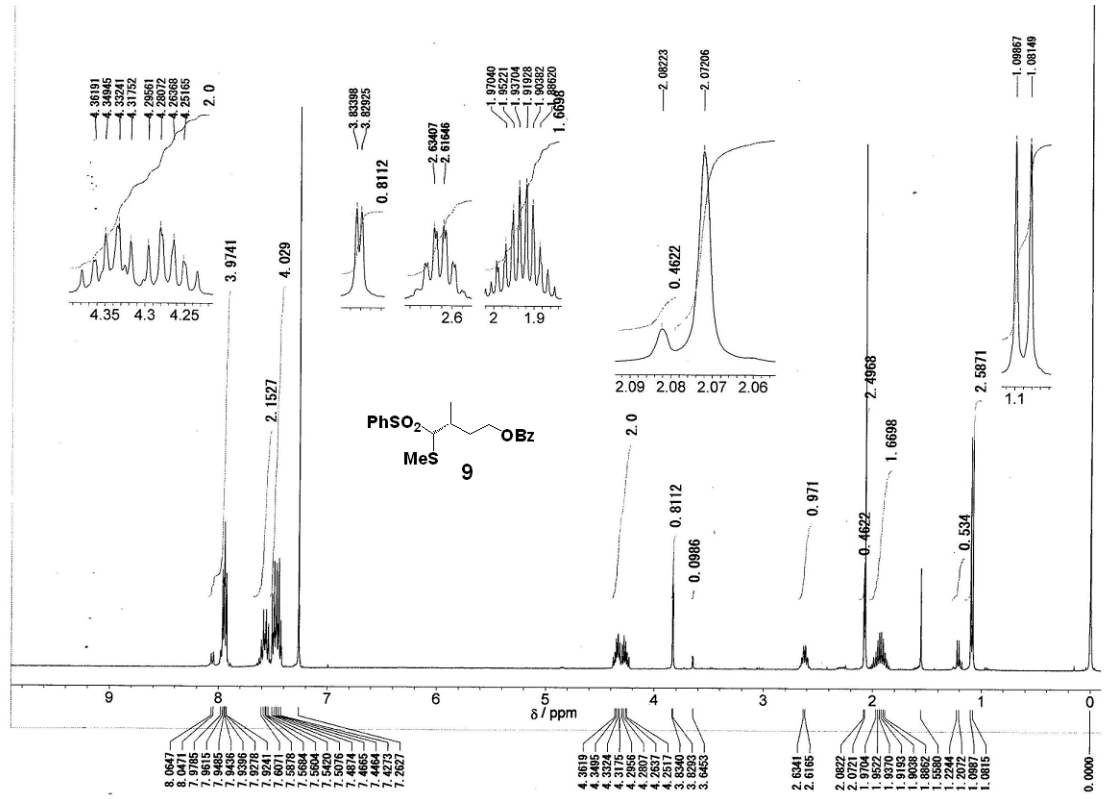

CF3-(CH)10-CF3
2d
ppm

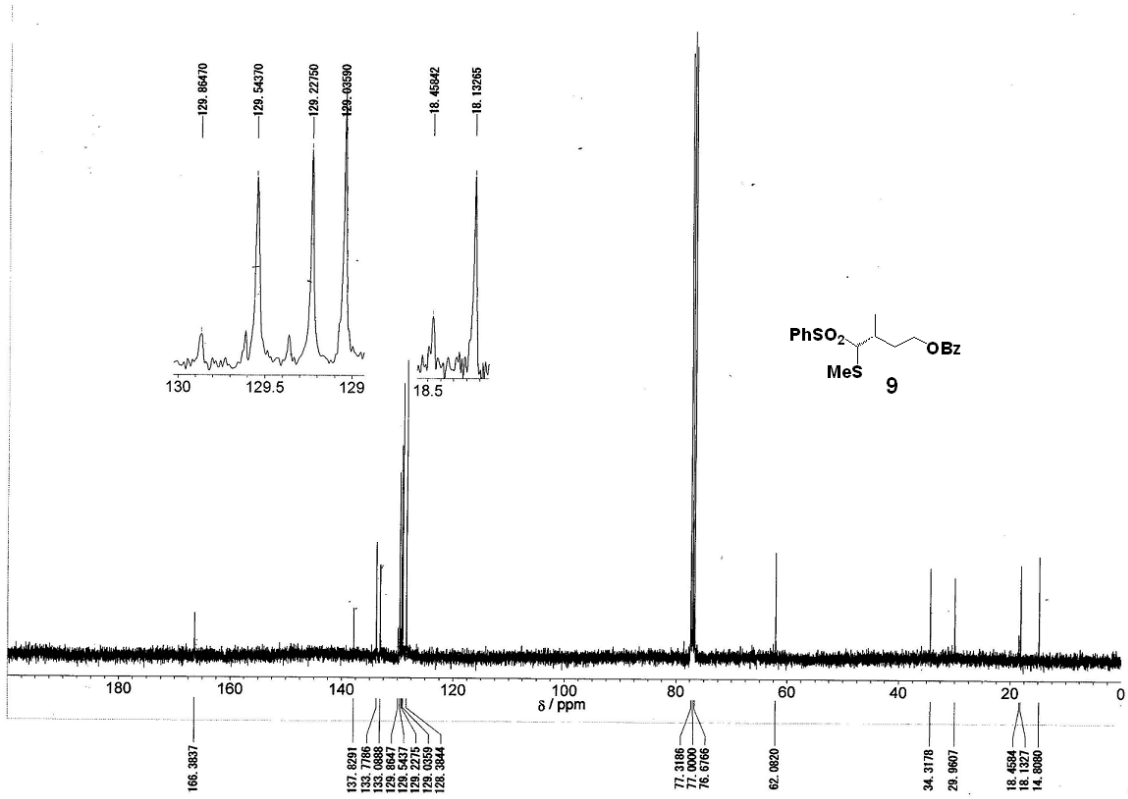

BzO-(CH)6-CF3
2e
ppm

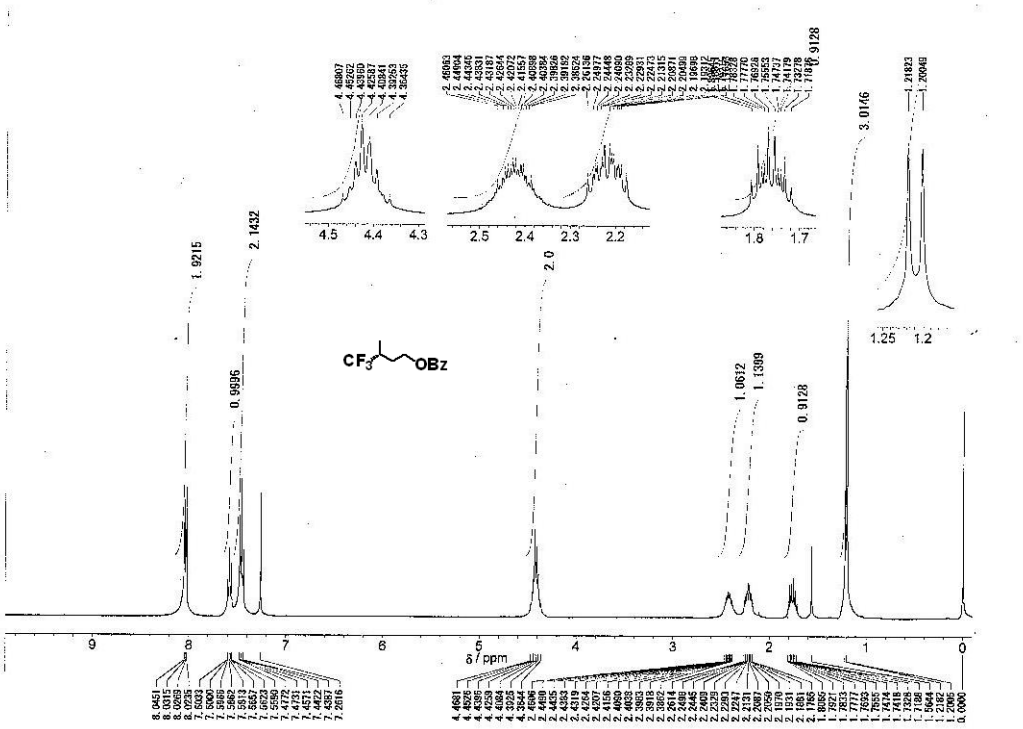

BzO-(CH)6-CF3
2e
ppm

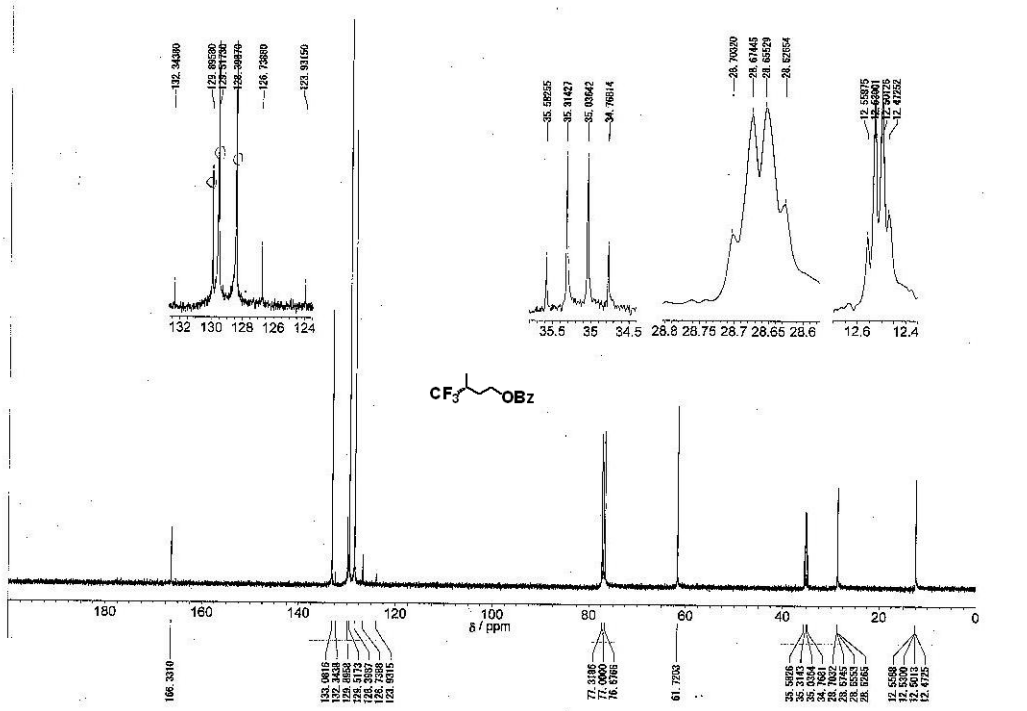

Et2NC(=O)-(CH)5-CF3
2f
2.0
2.1068
1.8871
1.9926
2.0811
2.0568
1.9443
2.99
3.103
ppm

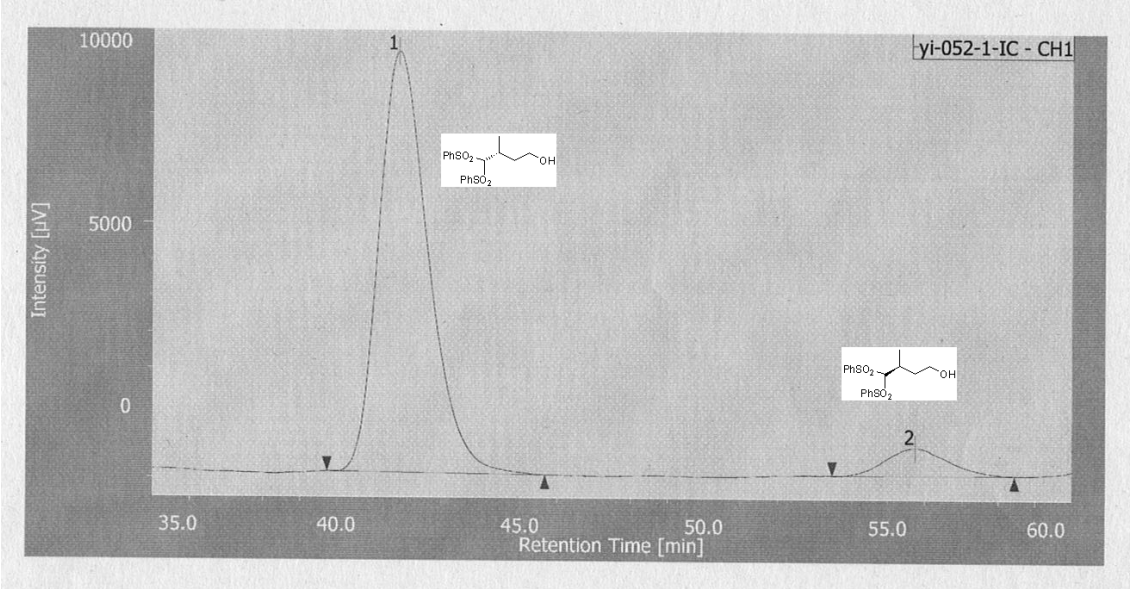

Et2NC(=O)-(CH)5-CF3
2f
130
34
33
21.5
ppm
173.4427
131.2755
128.5017
125.7256
122.9484
77.3210
77.0000
76.6790
60.2879
33.9250
33.6328
33.3477
33.0627
28.0972
24.4323
21.6059
21.5771
21.5484
21.5196
14.1732

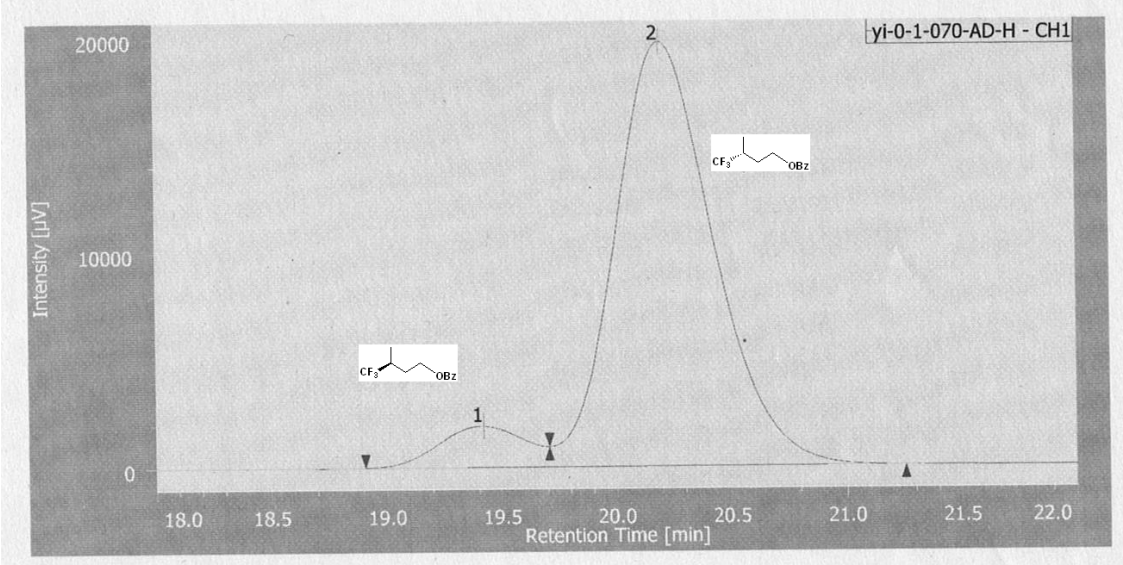

PhSO2
OBz
MeS
9
δ / ppm


PhSO2
OBz
MeS
9
δ / ppm


1.9215
2.1432
0.9696
2.0
1.0612
1.1399
0.9128
3.0146
CF3
OBz
δ / ppm


132.34390
129.89580
129.51700
128.39870
126.73800
123.93150
35.58595
35.31427
35.03642
34.76814
29.70320
29.61445
29.65529
29.82604
12.55875
12.49261
12.39735
12.47252
CF3
OBz
δ / ppm
166.3310
77.3196
77.0000
76.6805
61.7293


yi-052-1-IC - CH1
10000
5000
0
Intensity [µV]
1
2
35.0
40.0
45.0
50.0
55.0
60.0
Retention Time [min]


yi-0-1-070-AD-H - CH1
20000
10000
0
Intensity [µV]
1
2
18.0
18.5
19.0
19.5
20.0
20.5
21.0
21.5
22.0
Retention Time [min]