Conversion of MT-Sulfone to a Trifluoromethyl group by IFS; 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, \( \delta \), is referred to TMS \( (^{1}H, \ ^{13}C) \) and CFCl\(_3\) \( (^{19}F) \), respectively. The ESI-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\(_3\) 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\(_3\)N-5HF was prepared by the addition of an equimolar amount of Et\(_3\)N-5HF to IF\(_3\) in TeflonFEP bottle. IF\(_3\) 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\(_3\)N-5HF, and MeSSO\(_2\)Me 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\(_3\)N-5HF (1.27 g, 3 mmol) were placed in a TeflonFEP bottle under an \( N_2 \) atmosphere. The bottle was tightly screw-cap was used as a reaction vessel. IF\(_3\) 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\(_3\)N-5HF was prepared by the addition of an equimolar amount of Et\(_3\)N-5HF to IF\(_3\) in TeflonFEP bottle. IF\(_3\) 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\(_3\)N-5HF, and MeSSO\(_2\)Me 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\(^5\).

Characterization Data of Compound 2

1,1,1-Trifluorotridecane (2a)
IR (neat) 2926, 2856, 1255, 1143 cm\(^{-1}\). \( ^{1}H \) NMR (400MHz, CDCl\(_3\)) \( \delta \) 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\(_3\)) \( \delta \) 14.1, 22.0 (q, \( ^3J_{C,F} = 3.1 \) Hz), 22.8, 28.8, 29.3, 29.5, 29.6, 29.7, 29.8 (2C),
32.1, 33.8 (q, \(J_{C,F} = 28.4\) Hz), 127.4 (q, \(J_{C,F} = 276.3\) Hz). \(^{19}\)F NMR (373MHz, CDCl\(_3\)) \(\delta\) -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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 14.2, 21.6 (q, \(J_{C,F} = 2.9\) Hz), 24.4, 28.1, 33.5 (q, \(J_{C,F} = 28.4\) Hz), 33.9, 60.3, 127.1 (q, \(J_{C,F} = 276.4\) Hz), 173.4. \(^{19}\)F NMR (373MHz, CDCl\(_3\)) \(\delta\) -67.0 (3F, t, \(J = 11.0\) Hz). HRMS (EI) calcd for C\(_9\)H\(_{15}\)F\(_3\)O\(_2\) 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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 21.8 (q, \(J_{C,F} = 2.9\) Hz) 26.9, 28.7, 28.9, 29.2, 29.3, 29.4, 29.5 (2C), 32.7, 33.7 (q, \(J_{C,F} = 28.6\) Hz), 45.0, 127.3 (q, \(J_{C,F} = 275.6\) Hz). \(^{19}\)F NMR (373MHz, CDCl\(_3\)) \(\delta\) -67.03, (3F, t, \(J = 11.0\) Hz). HRMS (ESI) calcd for C\(_{13}\)H\(_{24}\)F\(_3\)Cl 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\(_3\)) \(\delta\) 1.26-1.35 (12H, m), 1.50-1.59 (4H, m), 2.00-2.12 (4H, m). \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \(\delta\) 21.8 (q, \(J_{C,F} = 2.9\) Hz), 28.6 (2C), 29.1 (2C), 29.2 (2C), 33.7 (2C, q, \(J_{C,F} = 28.4\) Hz), 127.3 (2C, q, \(J_{C,F} = 276.3\) Hz). \(^{19}\)F NMR (373MHz, CDCl\(_3\)) \(\delta\) -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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 21.8 (q, \(J_{C,F} = 2.9\) Hz), 25.7, 28.3, 28.4, 33.6 (q, \(J_{C,F} = 28.4\) Hz), 64.7, 127.2 (q, \(J_{C,F} = 276.3\) Hz), 128.3 (2C), 129.5 (2C), 130.3, 132.8, 166.6. \(^{19}\)F NMR (373MHz, CDCl\(_3\)) \(\delta\) -67.01 (3F, t, \(J = 11.2\) Hz). HRMS (EI) calcd for C\(_{14}\)H\(_{17}\)F\(_3\)O\(_2\) 274.1181, found 274.1180.

**N,N-Diethyl-7,7,7-trifluoroheptanamide (2f)**
IR (neat) 2939, 1643, 1255, 1133 cm⁻¹. ¹H NMR (400MHz, CDCl₃) 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). ¹³C NMR (100MHz, CDCl₃) δ 12.9, 14.2, 21.6 (q, J₃C-F = 2.4 Hz), 24.7, 28.3, 32.5, 33.4 (q, J₂C-F = 28.4 Hz), 39.9, 41.8, 127.1 (q, J₁C-F = 276.1 Hz), 171.6. ¹⁹F NMR (373 MHz, CDCl₃) δ -67.0 (3F, t, J = 11.2 Hz). HRMS (EI) calcd for C₁₁H₂₀F₃NO 239.1497, found 239.1503.

Formal asymmetric Michael-addition of trifluoromethyl anion to crotonaldehyde

(R)-3-Methyl-4,4-bis(phenylsulfonyl)butanal (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 24 h. 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 NaBH₄ (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 MgSO₄ 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)

![Diagram](image)

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 MgSO₄, 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

![Diagram](image)

To a THF solution (7 mL) of 7 (1.7 g, 3.5 mmol) was added 0.1M THF solution of SmI₂ (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 NH₄Cl (10 mL) and the product was extracted with ether (30 mL X 3). The combined organic layer was dried over MgSO₄ 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.

(3R)-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 MeSSO₂Me (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 NH₄Cl, dried over MgSO₄, 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.

(3R)-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 NaHCO₃ (20 mL). The combined organic layer was dried over MgSO₄ and concentrated under reduced pressure. Purification by column chromatography (silica gel / hexane:acetone 2:1) gave (3R)-3-methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butan-1-ol (0.52 g, 1.9 mmol) in 74 % yield.

(3R)-3-Methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butyl benzoate (9)
To a CH₂Cl₂ solution (4 mL) of (3R)-3-methyl-4-(methylsulfanyl)-4-(phenylsulfonyl)butan-1-ol (0.52 g, 1.9 mmol) and Et₃N (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 MgSO₄, 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, CDCl₃) 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). ¹³C NMR (100MHz, CDCl₃) 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 C₁₉H₂₂S₂O₄Na (M⁺+Na) 401.08517, found 401.08471.

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

9 (189 mg, 0.5 mmol) and IF₅/Et₃N-5HF (0.3 g, 1.5 mmol) were placed in a TeflonFEP bottle under an N₂ atmosphere. The bottle was tightly screw-capped and the mixture was stirred at 60 °C for 48 h. Then the mixture was poured into water and neutralized with aq NaHCO₃. The product was extracted with ether (30 mL X 3), and combined organic phase was washed with aq Na₂S₂O₃ and dried over MgSO₄. After concentration under reduced pressure, 10 was isolated by column chromatography (silica gel / hexane:CH₂Cl₂ = 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 determined 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\(^{-1}\). \(^1\)H NMR (400MHz, CDCl\(_3\)) \( \delta \) 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\(_3\)) \( \delta \) 12.5 (q, \( J_{C-F} = 2.8 \) Hz), 28.7 (q, \( J_{C-F} = 2.9 \) Hz), 35.2 (q, \( J_{C-F} = 26.7 \) Hz), 61.7, 128.1 (q, \( J_{C-F} = 279.5 \) Hz), 128.4 (2C), 129.5 (2C), 132.3, 133.1, 166.3. \(^{19}\)F NMR (373MHz, CDCl\(_3\)) \( \delta \) -74.04 (3F, d, \( J = 9.0 \) Hz). HRMS (EI) calcd for C\(_{12}\)H\(_{13}\)F\(_3\)O\(_2\) 246.08676, found 246.08629.

References

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