BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

Supporting Information

for

Cathodic generation of reactive (phenylthio)difluoromethyl species and its reactions: mechanistic aspects and synthetic applications

Sadanobu Iwase, Shinsuke Inagi and Toshio Fuchigami

Beilstein J. Org. Chem. **2022,** *18,* 872–880. doi:10.3762/bjoc.18.88

Experimental section: general information, materials, and general procedure for cathodic reduction of compound 1

Experimental

General information

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a JEOL JNM EX-270 (^{1}H: 270 MHz, ^{13}C: 67.8 MHz, ^{19}F: 254.05 MHz) spectrometer in $CDCl_3$. The chemical shifts for ^{1}H NMR and ^{13}C NMR are given in δ (ppm) downfield from internal TMS and $CDCl_3$, respectively. ^{19}F NMR chemical shifts are given in δ (ppm) upfield from external trifluoroacetic acid. Oxidation potentials (E_p^{ox}) were measured in 0.1 M Bu_4NClO_4/MeCN at a scan rate of 100 mV/s by cyclic voltammetry using an ALS Instruments model 600 A. A platinum electrode (φ = 1 mm) and a platinum wire (φ = 1 mm × 30 mm) were used as working and counter electrodes, respectively. A saturated sodium chloride calomel electrode (SSCE) was used as a reference electrode. Preparative electrolysis experiments were carried out with a Hokuto Denko HABF 501 potentiostat/galvanostat. Mass spectra and high resolution mass spectra were obtained with a Shimadzu GCMS-QP-2000A or JEOL JMS-700 mass spectrometer. Deuterium incorporation to products **2** and **4** were determined by MS analyses. ^{19}F NMR yields were estimated with α,α,α-trifluorotoluene as an internal standard.

Materials

Dry MeCN was obtained by distillation in the presence of CaH_2 under nitrogen gas. THF and ether were dried over Na/benzophenone under reflux and distilled under nitrogen gas. The starting material, bromodifluoromethyl phenyl sulfide (**1**) was prepared by the modification of the known procedures [1] as follows.

Thiophenol (0.1 mol) was added dropwise to a stirred solution of 100 mL of dry THF containing NaH (0.11 mol) under a nitrogen atmosphere at room temperature. After 30 min, the solution was cooled to −10 °C, and cooled CBr_2F_2 (0.11 mol) was added dropwise to the solution of PhSNa in THF using a syringe. After 2 h, the solution was warmed to room temperature and stirred for 1 h. The solution was mixed with water, the product was extracted with ether for three times, and then the combined extracts were washed with brine followed by drying with anhydrous Na_2SO_4. The solvent was removed by evaporation, the remaining oil was distilled at 54 °C under reduced pressure (3 mmHg) to give bromodifluoromethyl sulfide (**1**) in 85% yield.

^{1}H NMR, δ = 7.38-7.68 (m, 5H, C_6H_5); ^{19}F NMR δ = 54.43 (s, 2F, SCF_2Br); ^{13}C NMR δ = 119.25, 127.17, 129.43, 131.03, 136.37; MS, 240 (M^++2), 238 (M^+), 159 (M^+-Br), 109 (M^+-CF_2Br), 77 (Ph^+).

General procedure for the cathodic reduction of 1

Constant current and constant potential electrochemical reduction of **1** (2.5 mmol) was carried out with a platinum cathode and anode (2 cm × 2 cm) in a divided glass cell with a glass frit separator containing 25 mL of 0.8 M Bu_4NClO_4/MeCN in the presence or absence of trapping olefins (10 mmol) such as α-methylstyrene and 1,1-diphenylethylene as a catholyte until **1** was completely consumed (monitored by TLC and GC–MS). After electrolysis, the NMR yield of products **2**–**5** were estimated from ^{19}F NMR spectra using $CF_3C_6H_5$ as an internal standard. After the estimation, the crude mixture was passed through a short column with silica gel to remove the supporting electrolyte, and the eluent was subjected to PTLC (eluent: hexane/AcOEt 9:1), and products **2**–**4** and **6** were isolated. 1,1-Difluoro-2-methyl-2-phenylcycopropane (**5**) [2] was detected by MS and HRMS spectra. MS: m/z 168 (M^+), 149 (M^+−F), 77 (Ph^+); HRMS: m/z calcd for $C_{10}H_{10}F_2$: 168.0751, found 168.0743.

The known compounds, **2** [3] and **3** [4] were identified by comparison of the spectral data with those reported in the literature.

1,1-Difluoro-1-phenylthio-3-phenylbutane (**4**).

^{1}H NMR, δ = 7.19–7.58 (m, 10H, $C_6\mathit{H}_5$), 3.21 (m, 1H, C*H*Ph), 2.43 (m, 2H, $CF_2C\mathit{H}_2$), 1.35 (d, *J* = 7.3 Hz, 3H, $C\mathit{H}_3$); ^{19}F NMR δ = 7.2 (dd, *J* = 204, 16 Hz, 1F, SCF*F* CH_2), 4.8 (ddd, *J* = 206, 15, 12 Hz, 1F, C*F*FCH_2); MS: m/z 278 (M^+), 159 ($PhSCF_2^+$), 153 (M^+−$PhCHCH_3$), 109 (PhS^+), 105 (M^+−$PhSCF_2$ CH_2), 77 (Ph^+); HRMS: m/z calcd for $C_{16}H_{16}F_2S$: 278.0941, found 278.0940.

1,1-Difluoro-1-phenylthio-3,3-diphenylpropane (**6**)

^{1}H NMR, δ = 7.18–7.54 (m, 15H, $C_6\mathit{H}_5$), 4.41 (t, *J* = 6.9 Hz,1H, $Ph_2C\mathit{H}$ CH_2), 2.96 (dt, *J* = 15.0 Hz, 2H, $CF_2C\mathit{H}_2CH$); ^{19}F NMR δ = 5.96 (t, *J* = 14.7, 2F, $SC\mathit{F}_2$ CH_2); MS: m/z 340 (M^+), 230 (M^+−PhSH), 152 (M^+−PhSH-PhH), 109 (PhS^+), 77 (Ph^+); HRMS: m/z calcd for $C_{21}H_{18}F_2S$: 340.1097, found 340.1094.

Deuterated products **7** and **8** were identified by ^{19}F NMR and MS spectra as follows.

α-Deuterio-α,α-difluoromethyl phenyl sulfide (**2D**)

^{19}F NMR δ = −15.83 (t, *J* = 8.7 Hz, 1F, SCF_2D); MS: m/z 161 (M^+), 111 (M^+−CF_2), 109 (PhS^+), 77(Ph^+).

3-Deuterio-1,1-difluoro-1-phenylthio -3-phenylbutane (**4D**)

^{19}F NMR δ = 7.1 (m, 1F, SCF*F* CH_2), 4.8 (dt, *J* = 203, 14 Hz, 1F, SC*F*F CH_2); MS: m/z 279 (M^+), 259 (M^+−HF), 109 (PhS^+), 106 (M^+−$PhSCF_2CH_2$), 77 (Ph^+).

References

1. Toulgoat, F.; Langlois, B. R.; Médebielle, M.; Sanchez, J.-Y. *J. Org. Chem*. **2007**, *72*, 9046-9052. doi: 10.1021/jo701318n
2. Dolbier W. R., Jr.; Wojtowicz, H.; Burkholder, C. R. *J. Org. Chem*., **1990**, *5*5, 5420–5422. doi: 10.1021/jo00306a027
3. Burton, D. J.; Wiemers, D. M. *J. Fluorine Chem*., **1981**, *18*, 573–582. doi: 10.1016/S0022-1139(00)82673-1
4. Rico, I.; Wakselman, C. *Tetrahedron Lett.* **1981**, *22*, 323–326. doi: 10.1016/0040-4039(81)80087-1