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## **Synthesis of S-difluoromethyl dithiocarbamates**

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### **Contents**

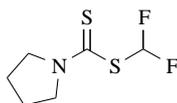
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**General Methods.** All reactions were performed under an argon atmosphere. Column chromatography was carried out employing silica gel (230-400 mesh). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography visualizing with UV and aq. KMnO<sub>4</sub> solution. High resolution mass spectra (HRMS) were measured using electrospray ionization (ESI) and time-of-flight (TOF) mass analyzer. The measurements were done in a positive ion mode (interface capillary voltage – 4500 V) or in a negative ion mode (3200 V); mass range from m/z 50 to m/z 3000. Me<sub>3</sub>SiCF<sub>2</sub>Br was obtained according to a literature procedure.<sup>1</sup>

**General procedure for reactions of amines 1a-g.** Amine **1a-g** (2.0 mmol) was added to a stirred suspension of K<sub>2</sub>CO<sub>3</sub> (304 mg, 2.20 mmol, 1.10 equiv.) in dry methanol (2.0 ml), and the reaction flask was immersed into ice/water bath. Carbon disulfide (175 mg, 2.30 mmol, 1.15 equiv.) was added dropwise at 0 °C, and stirring was continued for 5 min, the ice/water bath was removed and the mixture was stirred for additional 5 min at room temperature. Then, the reaction mixture was cooled to 0 °C, TMSCF<sub>2</sub>Br (609 mg, 3.00 mmol, 1.50 equiv.) was added dropwise, the mixture was stirred for 5 min at 0 °C, and then at room temperature (for **1a-e,g**, 5 min; for **1f**, 60 min). For the workup, the mixture was diluted with ethyl acetate (4.0 ml) and water (6.0 ml), the aqueous layer was extracted with ethyl acetate (3×4 ml), the combined organic extracts were concentrated under vacuum, and the residue was passed through short pad of silica gel (approx. 5 g), (for **2a-c,e-g**, eluting with CH<sub>2</sub>Cl<sub>2</sub>; for **2d**, eluting with CCl<sub>4</sub>).

**Reaction of sarcosine 1h.** Sarcosine **1h** (178 mg, 2.0 mmol) was added to a stirred suspension of K<sub>2</sub>CO<sub>3</sub> (580 mg, 4.20 mmol) in dry methanol (2.0 ml), the mixture was stirred at room temperature for 30 min, and the reaction flask was immersed into ice/water bath. Carbon disulfide (175 mg, 2.30 mmol, 1.15 equiv.) was added dropwise at 0 °C, and stirring was continued for 5 min, the ice/water bath was removed and the mixture was stirred for additional 5 min at room temperature. Then, the reaction mixture was cooled to 0 °C, TMSCF<sub>2</sub>Br (609 mg, 3.00 mmol, 1.50 equiv.) was added dropwise, the mixture was stirred for 5 min at 0 °C, and then for 5 min at room temperature. For the workup, the mixture was diluted ethyl acetate (4.0 ml) and water (6.0 ml) followed by portionwise addition of citric acid (1.05 g, 5.0 mmol) with stirring (*Caution! Gas evolution!*). The aqueous layer was extracted with ethyl acetate (3×4 ml), the combined organic extracts were concentrated under vacuum. The residue was filtered through short pad of silica gel (approx. 5 g) eluting with CH<sub>2</sub>Cl<sub>2</sub>. The solvent was evaporated, the residue was dissolved in a minimum amount of 1,2-dichloroethane (ca. 1 ml) at room temperature, and the solution was placed in a freezer (ca. –25 °C) to effect crystallization. The crystals were filtered and dried under vacuum.

<sup>1</sup> M. D. Kosobokov, A. D. Dilman, V. V. Levin and M. I. Struchkova, *J. Org. Chem.*, 2012, **77**, 5850–5855.

**Difluoromethyl pyrrolidine-1-carbodithioate (2a).**

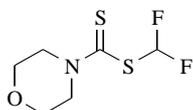
Yield 351 mg (89%). Colorless crystals. Mp 75–78 °C.  $R_f = 0.73$  ( $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.72 (t,  $J = 55.2$  Hz, 1H), 3.88 (t,  $J = 6.9$  Hz, 2H), 3.62 (t,  $J = 6.9$  Hz, 2H), 2.10 (qn,  $J = 6.8$  Hz, 2H), 2.00 (qn,  $J = 6.5$  Hz, 2H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 184.3 (t,  $J = 5.2$  Hz), 125.2 (t,  $J = 271.3$  Hz), 54.5, 51.2, 25.9, 24.1.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : -100.2 (d,  $J = 55.2$  Hz).

HRMS (ESI): Calcd for  $\text{C}_6\text{H}_{10}\text{F}_2\text{NS}_2$  ( $\text{M} + \text{H}$ ): 198.0217. Found: 198.0217.

**Difluoromethyl morpholine-4-carbodithioate (2b).**

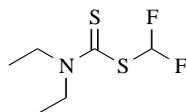
Yield 205 mg (48%). Colorless crystals. Mp 42–44 °C.  $R_f = 0.53$  ( $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.70 (t,  $J = 55.4$  Hz, 1H), 4.28 (br s, 2H), 3.83 (br s, 2H), 3.77 (br s, 4H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 188.5 (t,  $J = 5.2$  Hz), 125.1 (t,  $J = 272.8$  Hz), 66.1 (br s), 51.1 (br s), 50.4 (br s).

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : -99.7 (d,  $J = 55.4$  Hz).

HRMS (ESI): Calcd for  $\text{C}_6\text{H}_{10}\text{F}_2\text{NOS}_2$  ( $\text{M} + \text{H}$ ): 214.0166. Found: 214.0173.

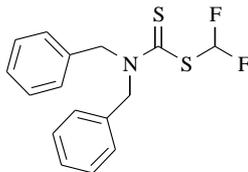
**Difluoromethyl *N,N*-diethyl(dithiocarbamate) (2c).<sup>2</sup>**

Yield 327 mg (82%). Colorless oil.  $R_f = 0.59$  ( $\text{CH}_2\text{Cl}_2/\text{CCl}_4$ , 1/1).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.69 (t,  $J = 55.4$  Hz, 1H), 3.99 (q,  $J = 7.0$  Hz, 2H), 3.67 (q,  $J = 7.2$  Hz, 2H), 1.31 (t,  $J = 7.6$  Hz, 3H), 1.28 (t,  $J = 7.6$  Hz, 3H).

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : -100.2 (d,  $J = 55.4$  Hz).

<sup>2</sup> Q. Chen and S. Wu, *J. Org. Chem.*, 1989, **54**, 3023.

**Difluoromethyl *N,N*-dibenzyl(dithiocarbamate) (2d).**

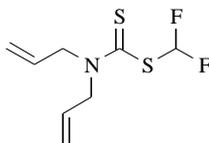
Yield 344 mg (53%). Colorless oil.  $R_f = 0.38$  ( $\text{CCl}_4$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.80 (t,  $J = 55.4$  Hz, 1H), 7.55–7.08 (m, 10H), 5.31 (s, 2H), 4.85 (s, 2H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 190.8 (t,  $J = 5.2$  Hz), 134.8, 133.7, 129.3, 129.0, 128.5, 128.3, 128.2, 127.2, 125.8 (t,  $J = 272.8$  Hz), 55.3, 54.8.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : -99.7 (d,  $J = 55.4$  Hz).

HRMS (ESI): Calcd for  $\text{C}_{16}\text{H}_{16}\text{F}_2\text{NS}_2$  ( $\text{M} + \text{H}$ ): 324.0687. Found: 324.0681.

**Difluoromethyl *N,N*-diallyl(dithiocarbamate) (2e).**

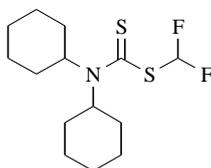
Yield 338 mg (76%). Colorless oil.  $R_f$  0.60 ( $\text{CH}_2\text{Cl}_2/\text{CCl}_4 = 1/1$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.67 (t,  $J = 55.4$  Hz, 1H), 5.96–5.70 (m, 2H), 5.38–5.17 (m, 4H), 4.61 (d,  $J = 5.5$  Hz, 2H) 4.25 (d,  $J = 5.0$  Hz, 2H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 189.4 (t,  $J = 5.2$  Hz), 130.2, 129.6, 125.6 (t,  $J = 272.2$  Hz), 119.4, 55.8, 54.3.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : -100.0 (d,  $J = 55.4$  Hz).

HRMS (ESI): Calcd for  $\text{C}_8\text{H}_{12}\text{F}_2\text{NS}_2$  ( $\text{M} + \text{H}$ ): 224.0374. Found: 224.0375.

**Difluoromethyl *N,N*-dicyclohexyl(dithiocarbamate) (2f).**

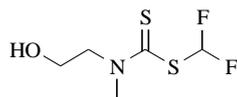
Yield 214 mg (35%). Colorless crystals. Mp 107–111 °C.  $R_f$  0.73 ( $\text{CH}_2\text{Cl}_2/\text{CCl}_4 = 1/1$ ).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 0.93–2.18 (br m, 18H), 2.49 (br), 2.86–3.88 (br), 4.20 (br), 5.72 (br), 7.73 (br t, 1H,  $J = 54.8$  Hz).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 25.3, 26.3 (br), 29.5 (br), 30.6 (br), 61.8 (br), 63.6 (br), 65.6 (br), 125.0 (t,  $J = 271.3$  Hz), 186.9 (br), 188.8 (br).

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : -101.8 (br), -99.5 (br m).

HRMS (ESI): Calcd for  $\text{C}_{14}\text{H}_{24}\text{F}_2\text{NS}_2$  ( $\text{M} + \text{H}$ ): 308.1313. Found: 308.1315.

**Difluoromethyl *N*-(2-hydroxyethyl)-*N*-methyl(dithiocarbamate) (2g).**

Yield 267 mg (66%). Colorless oil.  $R_f$  0.10 ( $\text{CH}_2\text{Cl}_2$ ).

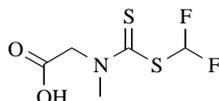
In NMR spectra appears as a mixture of two rotamers in ~2:1 ratio.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : (major) 7.61 (t,  $J = 55.2$  Hz, 1H), 4.19 (t,  $J = 5.3$  Hz, 2H), 3.96 (t,  $J = 5.3$  Hz, 2H), 3.40 (s, 3H), 2.38 (br s, 1H); (minor) 7.65 (t,  $J = 55.4$  Hz, 1H), 3.87 (br s, 4H), 3.52 (s, 3H), 2.38 (br s, 1H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : (major) 190.3 (t,  $J = 5.2$  Hz), 125.3 (t,  $J = 272.2$  Hz), 60.2, 57.9, 41.9; (minor) 188.8 (t,  $J = 5.2$  Hz), 125.5 (t,  $J = 272.2$  Hz), 59.8, 57.0, 43.9.

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : (major)  $-100.3$  (d,  $J = 55.2$  Hz); (minor)  $-99.8$  (d,  $J = 55.4$  Hz).

HRMS (ESI): Calcd for  $\text{C}_5\text{H}_{10}\text{F}_2\text{NOS}_2$  ( $\text{M} + \text{H}$ ): 202.0166. Found: 202.0171.

***N*-[(Difluoromethylthio)carbonothioyl]-*N*-methylglycine (2h).**

Yield 238 mg (55%). Colorless crystals. Mp 95–99 °C.  $R_f$  0.02 ( $\text{CH}_2\text{Cl}_2$ ).

In NMR spectra appears as a mixture of two rotamers in ~6:1 ratio.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : (major) 11.38 (br s, 1H) 7.56 (t,  $J = 54.9$  Hz, 1H), 4.79 (s, 2H), 3.41 (s, 3H); (minor) 11.38 (br s, 1H) 7.58 (t,  $J = 54.9$  Hz, 1H), 4.51 (s, 2H), 3.52 (s, 3H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : (major) 192.0 (t,  $J = 5.2$  Hz), 173.3 125.3 (t,  $J = 272.8$  Hz), 56.4, 41.3; (minor) 55.0, 44.0 [for minor isomer, the observed peaks are listed].

$^{19}\text{F}$  NMR (282 MHz,  $\text{CDCl}_3$ )  $\delta$ : (major)  $-100.0$  (d,  $J = 54.9$  Hz); (minor)  $-99.5$  (d,  $J = 54.9$  Hz).

HRMS (ESI): Calcd for  $\text{C}_5\text{H}_8\text{F}_2\text{NO}_2\text{S}_2$  ( $\text{M} + \text{H}$ ): 215.9959. Found: 215.9969.

