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## A Facile Synthesis of Trifluoromethylamines by Oxidative Desulfurization-Fluorination of Dithiocarbamates

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Abstract: Reaction of methyl dithiocarbamates  $R^1R^2N$ -C(S)SMe with *n*-Bu<sub>4</sub>N<sup>+</sup>H<sub>2</sub>F<sub>3</sub><sup>-</sup> and N-bromosuccinimide provides trifluoromethylamines  $R^1R^2N$ -CF<sub>3</sub> in good yields.

The basicity and nucleophilicity of trifluoromethylamines are expected to be much less than the corresponding methylamines and thus biological and/or physical properties of parent compounds may be modified drastically. Preparative methods of trifluoromethylamines reported so far involve fluorination of formamides<sup>1</sup> or thiuram sulfides with SF<sub>4</sub>.<sup>2</sup> Use of the highly toxic gaseous reagent and low yields of products, however, have hampered wide applications of these reactions. Oxidative desulfurization-fluorination of organosulfur compounds allows us to replace C-S bonds with C-F bonds under extremely mild conditions.<sup>3</sup> We have applied the reaction to methyl dithiocarbamates (R<sup>1</sup>R<sup>2</sup>N-C(S)SMe) and found trifluoromethylamines (R<sup>1</sup>R<sup>2</sup>N-CF<sub>3</sub>) are readily prepared in good yields.

$$R^{1} \bigvee_{\substack{N \\ R^{2}}}^{S} SMe \xrightarrow{TBA^{+}H_{2}F_{3}^{-}, (HF)_{9}/Py \text{ or } (HF)_{3}/NEt_{3}}_{NBS, NIS \text{ or } DBH} R^{1} \bigvee_{\substack{N \\ R^{2}}}^{CF_{3}} CF_{3}$$

To a dichloromethane (1.5 mL) solution of methyl dithiocarbamate (0.5 mmol) and tetrabutylammonium dihydrogentrifluoride (TBA<sup>+</sup>H<sub>2</sub>F<sub>3</sub><sup>-</sup>, 1.5 mmol) was added *N*-bromosuccinimide (NBS, 2 mmol) at 0 °C, and the resulting mixture was stirred for 1 h at room temperature. Work-up<sup>3c,4</sup> and purification by chromatography or distillation afforded trifluoromethylamines in good yields as shown in Table 1. Employing less than 1.5 mmol of NBS resulted in a mixture of trifluoromethylamine and the starting material, and none of mono- and difluorination products could be detected.

Entry	Product	Yield/% <sup>a</sup>	Entry	Product	Yield/%"
1	4-MeOC <sub>6</sub> H <sub>4</sub> N(CH <sub>2</sub> Ph)CF <sub>3</sub>	97	8 <sup>b</sup>	4-O <sub>2</sub> NC <sub>6</sub> H₄N(Me)CF <sub>3</sub>	94
2	4-ClC <sub>6</sub> H <sub>4</sub> N(CH <sub>2</sub> Ph)CF <sub>3</sub>	88	9 <sup>e</sup>	$(3-\text{MeC}_6\text{H}_4)_2\text{NCF}_3$	74
3	4-FC <sub>6</sub> H <sub>4</sub> N(CH <sub>2</sub> Ph)CF <sub>3</sub>	84			
4	4-NCC <sub>6</sub> H <sub>4</sub> N(CH <sub>2</sub> Ph)CF <sub>3</sub>	78	10	$\langle - \rangle - N - CF_3$	76
$5^{b}$	4-NCC <sub>6</sub> H <sub>4</sub> N(CH <sub>2</sub> Ph)CF <sub>3</sub>	93			
6 <sup>c</sup>	4-NCC <sub>6</sub> H <sub>4</sub> N(CH <sub>2</sub> Ph)CF <sub>3</sub>	97	11	(PhCH <sub>2</sub> ) <sub>2</sub> NCF <sub>3</sub>	62
7 <sup>d</sup>	4-NCC <sub>6</sub> H <sub>4</sub> N(CH <sub>2</sub> Ph)CF <sub>3</sub>	99	12	PhCH <sub>2</sub> N( <i>n</i> -Pr)CF <sub>3</sub>	67

Table 1. Synthesis of Trifluoromethylamines

<sup>*d*</sup>Isolated yields. TBAH<sub>2</sub>F<sub>3</sub> (3 eq. 9 eq of F) and NBS (4 eq) were used unless otherwise noted. <sup>*b*</sup>DBH (4 eq) was used. <sup>*c*</sup>(HF)<sub>9</sub>/Py (80 eq of F) was used. <sup>*d*</sup>(HF)<sub>3</sub>/NEt<sub>3</sub> (30 eq of F) was used. <sup>*e*</sup>NIS (4 eq) was used.

Kinds of *N*-halo-imide reagent were critical for selective transformation. A substrate containing an aromatic ring substituted by an electron-donating group underwent ringbromination with NBS. Hereby, *N*-iodosuccinimide (NIS) is a reagent of choice which allows us to effect the reaction without ring halogenation (entry 9). For substrates bearing an electronwithdrawing group, 1,3-dibromo-5,5-dimethylhydantoin (DBH) or HF-amine complex as either part of the reagent system was applicable and the desired trifluoromethylamines could be isolated almost quantitatively (entries 5, 6, and 7).

The present method allows us to prepare trifluoromethylamines under extremely mild conditions, starting from readily accessible materials, dithiocarbamates and, accordingly, should find wide applications particularly in the synthesis of new drugs, agrochemicals, and photoelectrical materials. Studies along this line are in progress in our laboratories.

## REFERENCES AND NOTES

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- 4. Since dialkyltrifluoromethylamines are moisture-sensitive, the reaction mixtures of entries 11 and 12 were diluted with hexane-diethyl ether (4 : 1). Precipitated materials were removed and the filtrates were passed through a short column packed with Wakogel-C 100 and Na<sub>2</sub>SO<sub>4</sub>. Concentration *in vacuo* and distillation gave the desired products.

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