## 1,1-Bis(dimethylamino)-2,2,2-trifluoroethane, a Readily-Available Precursor to the Novel **Fluorinated Building Block** 1,1-Bis(dimethylamino)-2,2-difluoroethene

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In 1994, Aoyama reported in a Daikin patent the facile synthesis of 1,1,1,4,4,4-hexafluoro-2-butene (HFC-356mff) from the inexpensive hydrochlorofluorocarbon 1,1,1-trifluoro-2,2-dichloroethane (HCFC-123) by heating it at 60 °C with metallic copper in diethylamine.<sup>1</sup>

$$CF_{3}CHCl_{2} \xrightarrow{Cu, Et_{2}NH} CF_{3}CH=CHCF_{3} + CF_{3}CH_{2}CI$$

We reproduced that result, but found a small but significant impurity, CF<sub>3</sub>CH<sub>2</sub>Cl, which proved very difficult to separate. In an attempt to further minimize this impurity, the reactions of CF<sub>3</sub>CHCl<sub>2</sub> with a number of different secondary amines were examined (Table 1), and to our surprise we found that, among those tried, only diethylamine gave a respectable yield of HFC-356mff. Instead, we observed another major product being formed in the case of many of the alternative secondary amines, that being the respective 1,1-bis(dialkylamino)-2,2,2trifluoroethanes **1a**-**e**.<sup>2-4</sup>

In view of considerable precedent, it seemed probable that compounds such as **1a**-**e** could be used as precursors for the potentially very useful fluorinated "enolate" building block 2.5-11 Indeed, treatment of 1a (in ether) with 1.1 equiv of *n*-BuLi (2.5 M in hexane) at -78 °C, followed by warming to room temperature where it was allowed to stir for 10 h, led to its >90% conversion to 2, which could be used readily for subsequent reactions in situ at temperatures from -78 °C to rt.<sup>12</sup>

$$CF_{3}CH(NMe_{2})_{2} \xrightarrow{r \cdot BuLi, -78 \circ C} CF_{2}=C(NMe)_{2}$$
1a 
$$Et_{2}O \qquad 2$$

(1) Aoyama, H. PCT Int. Appl. WO 94 12,454; Chem. Abstr. 1994, 121, 179088b.

(2) To our knowledge, these are the first examples of molecules of the general structure **1**. Each of the compounds **1a**-**e** was fully characterized by <sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F NMR, as well as by IR, HRMS, and CHN analysis. NMR data for **1a** are as follows: <sup>1</sup>H,  $\delta$  2.39 (q, J = 1.2 Hz, 12 H), 3.18 (q, J = 7.3 Hz, 1 H); <sup>13</sup>C,  $\delta$  41.3, 83.7 (q, J = 26.2 Hz), 126.9 (q, J = 293.6 Hz); <sup>19</sup>F,  $\delta - 67.0$  (d, J = 7.3 Hz).

(3) The Cu was a necessary ingredient for successful conversion of HCFC-123 to 1a-e.

(4) 1a underwent hydrolysis in 10% HCl to give an 89% yield of the hydrate of trifluoroacetaldehyde.

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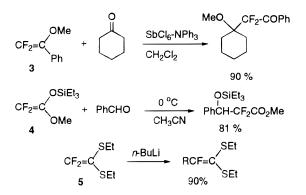
*Tetrahedron* **1995**, *51*, 12217–12228. (11) Qian, C.-P.; Nakai, T. *Tetrahedron Lett.* **1988**, *29*, 4119–4122.

(12) Compound **2** has been reported previously, although no pertinent chemistry was mentioned.<sup>13</sup> It is a voracious proton scavenger and should be used in situ, and it was characterized in ether solution by  $^{19}{\rm F}$  NMR:  $\delta$  –114.1.

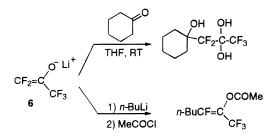
Table 1.	Conversion of HCFC-123 to
1,1-Bis(dialky	lamino)-2,2,2-trifluoroethanes 1

	CF <sub>3</sub> CHCl <sub>2</sub>	Cu, R <sub>1</sub> R <sub>2</sub> NH 60 °C, 12 h	CF₃CH(NR₁R 1a- <del>o</del>	2)2
product	R <sub>1</sub>	$R_2$	conditions	yield (%)
1a	$CH_3$	$CH_3$	60 °C, 12 h	60.2
1b	$C_2H_5$	$C_2H_5$	60 °C, 12 h	14.7
1c	$-(CH_2)_5-$		50 °C, 12 h	56.8
1d	$-(CH_2)_6-$		50 °C, 12 h	51.5
1e	$-(CH_2)_4-$		60 °C, 12 h	54.5
	$C_4H_9$	$C_4H_9$	60 °C, 12 h	—

Reagents such as 2 have attracted much interest because of their ambiphilic character, which allows them to exhibit either nucleophilic or electrophilic character in their reactions. 5,8,10,11,14-22 For example, enol ethers **3** and **4** condense readily with aldehydes or ketones,<sup>10,21</sup> and it has been observed that the related difluoroketene thioacetal, 5, undergoes nucleophilic attack by either alkyllithiums or Grignard reagents.<sup>5</sup> Nakai and his co-



workers have, moreover, observed that perfluoroenolates, such as 6, undergo both electrophilic and nucleophilic attack.11,16



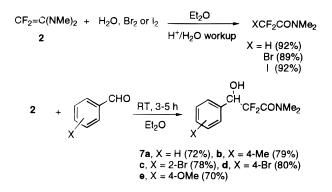
Our preliminary studies of the reactivity of 2 have confirmed that it can also exhibit both nucleophilic

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and electrophilic behavior. It undergoes virtually quantitative reaction with water, bromine, or iodine to give the respective N,N-dimethyldifluoroacetamide, -bromodifluoroacetamide, and -iododifluoroacetamides in isolated yields of 92, 89, and 92%, respectively,23 and it was found to condense with various substituted benzaldehydes to give good yields of the respective N,Ndimethyl-2,2-difluoro-3-hydroxy-3-arylpropionamides 7a-e.<sup>24</sup> However, in reactions with a number of ketones or aldehydes bearing an  $\alpha$ -hydrogen, such as acetophe-



none, acetone, or butyraldehyde, no condensation products analogous to 7 were observed. In each case, N,Ndimethyldifluoroacetamide was obtained as the only

product, a result which indicated that 2 must prefer to act as a base instead of a nucleophile in such reactions.

2 was also found to undergo a facile addition-elimination process upon addition of 1 equiv of alkyllithium at room temperature, with the net result that, upon hydrolytic workup one could obtain reasonable yields of the respective  $\alpha$ -fluoroacetamides 8.<sup>24</sup>

2 
$$\frac{\text{RLi}}{\text{RT, 8-10 h}}$$
 RCF=C(NMe)<sub>2</sub>  $\frac{\text{H}^{+}/\text{H}_2\text{O}}{\text{Et}_2\text{O}}$  RCHFCONMe<sub>2</sub>  
Et<sub>2</sub>O **8a**, R = n-Bu (85%)  
b, R = C<sub>6</sub>H<sub>5</sub> (77%)

In view of the ease of preparation of both 1 and 2, it is likely that 2 will find considerable synthetic utility in the future.<sup>25</sup> We are presently investigating its reactivity with respect to various other nucleophilic and electrophilic reagents, and it indeed has a rich and diverse chemistry the full extent of which will be reported in due course.

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Supporting Information Available: Experimental procedures and characterization data for all new compounds (8 pages).

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<sup>(23)</sup> All given yields are based on **1a**. (24) Products **7a**–**e** and **8a–b** were fully characterized by NMR, IR, HRMS, and CHN analysis.

<sup>(25)</sup> The syntheses of 1a-e require an autoclave. Compound 1a is commercially available from SynQuest Laboratories, Inc., Alachua, FL.