



# A simple procedure for nucleophilic perfluoroalkylation of organic and inorganic substrates

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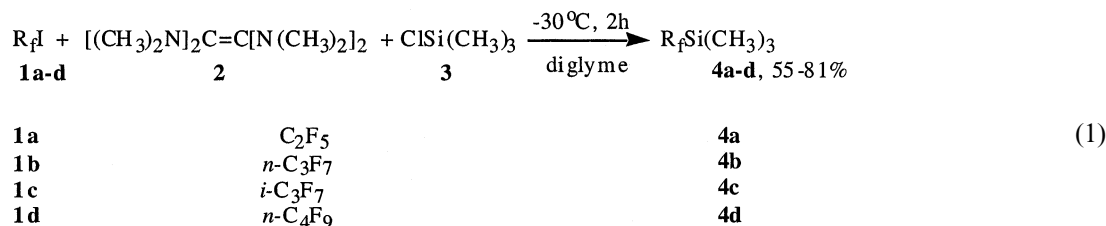
**Abstract**—The mixture  $R_fI$  and tetrakis(dimethylamino)ethylene is used for the nucleophilic perfluoroalkylation. The reaction of chlorotrimethylsilane and  $R_fI$ /tetrakis(dimethylamino)ethylene in diglyme results in the formation of  $R_fSi(CH_3)_3$  isolated in 55–81% yield. The interaction of this system with organic electrophiles such as benzoyl and benzenesulphonyl chlorides, aliphatic and aromatic aldehydes and activated ketones leads to the formation of the corresponding condensation products in 24–62% yield. © 2001 Elsevier Science Ltd. All rights reserved.

The growing interest in compounds containing polyfluoroalkyl groups has resulted in the development of a variety of methods for selective introduction of fluoroalkyl substituents into organic and inorganic molecules. Nucleophilic perfluoroalkylation is probably the most commonly used technique for preparation of this type of material. Among reagents used are perfluoroalkyl lithium, magnesium, zinc and copper<sup>1</sup> and trifluoromethyl<sup>2–4</sup> and polyfluoroalkylsilanes.<sup>2,4,5</sup> In 1984 Ruppert reported that the system based on tris(diethylamino)phosphine and  $CF_3Br$  can be used for the transfer of a trifluoromethyl group to silicon.<sup>6</sup> Later this reaction was expanded and a system based on perfluoroalkyl- (perfluoroalkenyl-) iodide (bromide) and tris(dialkylamino)phosphine was demonstrated to be effective for the synthesis of perfluoroalkyl aroyl ketones,<sup>7–9</sup> tertiary alcohols,<sup>10</sup> fluorovinyl silanes,<sup>11,12</sup> stannanes<sup>11</sup> and perfluoroalkyl germanes.<sup>13</sup> However, a few years ago it has been reported that introduction of  $CF_3$  group to silicon and boron<sup>14</sup> can be carried out using a combination of  $CF_3I$  and tetra-

kis(dimethylamino)ethylene as a reducing agent. Later tetrakis(dimethylamino)ethylene was successfully used for the introduction of *gem*-difluoroketo<sup>15</sup> or *gem*-difluoroheteroarylated moieties<sup>16,17</sup> into hydrocarbon aldehydes and ketones.

In the present work the synthetic utility of a mixture of perfluoroalkyl iodide (**1**) and tetrakis(dimethylamino)ethylene (**2**) is explored and it is demonstrated that **1** in combination with **2** can be used for the introduction of a perfluoroalkyl group into molecules of organic and inorganic electrophiles. Similar to the reaction of  $CF_3I$ ,<sup>14</sup> the reduction of longer chain perfluoroalkyl iodides (**1a–d**) by **2** in the presence of chlorotrimethylsilane (**3**) results in the formation of the corresponding silanes **4a**,<sup>18</sup> **4b**,<sup>18</sup> **4c**,<sup>19</sup> **4d** isolated in 55–81% yield (Eq. (1)).

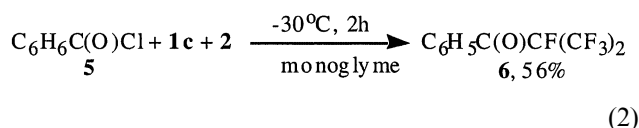
It should be pointed out that in the absence of chlorosilane, rapid reductive dimerization of  $C_4F_9I$  occurs at  $\geq -30^\circ C$  producing, according to NMR, a mixture of



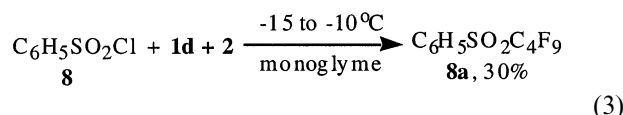
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branched perfluorooctenes  $C_8F_{16}$  along with some  $C_4F_9H$ . The system of  $R_fI/2$  as perfluoroalkylating agent is less efficient than the widely employed combination of perfluoroalkyltrimethylsilane/metal fluoride.<sup>2,5,18</sup> For instance, no product of the transfer  $C_4F_9$ -group is found in reactions of either cyclopentanone, adamantanone-2 or acetophenone (in THF or ether as a solvent) and  $C_4F_9I/2$ . However, moderate yield formation of  $R_fH$  and  $C_8F_{16}$  olefins is observed in all reactions. On the other hand, with more active carbonyl substrates the perfluoroalkylation proceeds rapidly and practically without formation of products of the reductive dimerization. For example, the interaction of benzoyl chloride (**5**) with the mixture of **1c/2** results in the formation of ketone **6**<sup>7</sup> (Eq. (2)).

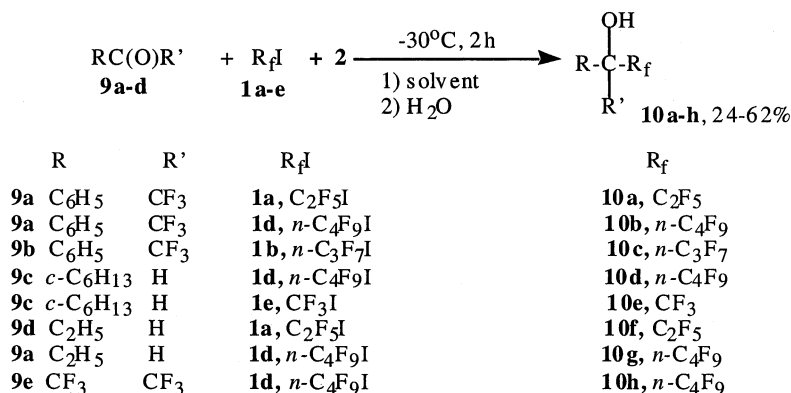


The reaction of **5** with 2 mol of **1a** leads to the formation of mixture of  $C_6H_5C(O)C_2F_5$  (**7**)<sup>7</sup> and  $C_6H_5C(C_2F_5)_2OH$  (**7a**)<sup>10</sup> in 33 and 17% yields, respectively (see Table 1). Compound **8** reacts with **1d/2** under similar conditions giving sulfone **8a**<sup>20</sup> (Eq. (3)).



Electrophiles, such as 1,1,1-trifluoroacetophenone (**9a**), benzaldehyde (**9b**), cyclohexanecarboxyaldehyde (**9c**), propionaldehyde (**9d**) or hexafluoroacetone (**9e**) react with perfluoroalkyl iodides (**1a–d**) and  $CF_3I$  (**1e**) in the presence of equimolar amount of **2** producing alcohols **10a**,<sup>10</sup> **10b**,<sup>19</sup> **10d**, **10e**,<sup>21</sup> **10f**,<sup>22</sup> **10g**, **10h**<sup>23</sup> and **10c**,<sup>18</sup> respectively, in low to moderate yield (see Table 1 and Eq. (4)). Formation of the corresponding monohydroperfluoroalkane (10–40% based on alkyl iodide depending on the temperature, solubility of the reagents and polarity of solvent) is probably responsible for decreased yields of the products and this is observed in all reactions. In most cases unreacted carbonyl compound can be recovered. Despite the fact that higher homologs of  $R_fI$  ( $>C_4$ ) were not tried in this reaction at this moment there is no reason to believe that they will behave differently in this reaction.

In conclusion, a simple method for nucleophilic perfluoroalkylation is described. Using readily available starting materials [tetrakis(dimethylamino)ethylene and perfluoroalkyl iodides], a variety of organic and inor-



**Table 1.** Reaction conditions, ratio of reactants and yields of products

| Entry | Solvent    | Reactants (ratio)                          | Temperature (°C) | Time (h) | Product (yield%) <sup>a</sup>               |
|-------|------------|--------------------------------------------|------------------|----------|---------------------------------------------|
| 1     | Diglyme    | <b>1a</b> , <b>2</b> , <b>3</b> (1.2:1:1)  | –30              | 2        | <b>4a</b> (81)                              |
| 2     | Diglyme    | <b>1b</b> , <b>2</b> , <b>3</b> (1.2:1:1)  | –30              | 2        | <b>4b</b> (75)                              |
| 3     | Diglyme    | <b>1c</b> , <b>2</b> , <b>3</b> (1.2:1:1)  | –30              | 2.5      | <b>4c</b> (55)                              |
| 4     | Diglyme    | <b>1d</b> , <b>2</b> , <b>3</b> (1.2:1:1)  | –30              | 1.5      | <b>4d</b> (68)                              |
| 5     | THF        | <b>1c</b> , <b>2</b> , <b>5</b> (1.1:1:1)  | –40 to –20       | 2        | <b>6</b> (56)                               |
| 6     | THF        | <b>1a</b> , <b>2</b> , <b>5</b> (2:1.5:1)  | –40 to –20       | 2        | <b>7a</b> (33), <b>7b</b> (17) <sup>b</sup> |
| 7     | Monoglyme  | <b>1d</b> , <b>2</b> , <b>8</b> (1.2:1:1)  | –15 to –10       | 2        | <b>8a</b> (30)                              |
| 8     | THF        | <b>1a</b> , <b>2</b> , <b>9a</b> (1.2:1:1) | –40 to –20       | 2        | <b>10a</b> (45)                             |
| 9     | Monoglyme  | <b>1d</b> , <b>2</b> , <b>9a</b> (1.2:1:1) | –40 to –30       | 2        | <b>10b</b> (59)                             |
| 10    | Monoglyme  | <b>1b</b> , <b>2</b> , <b>9b</b> (1.2:1:1) | –40 to –30       | 1.5      | <b>10c</b> (30)                             |
| 11    | THF        | <b>1d</b> , <b>2</b> , <b>9c</b> (1.2:1:1) | –40 to –30       | 2        | <b>10d</b> (30)                             |
| 12    | DMF        | <b>1e</b> , <b>2</b> , <b>9c</b> (1.3:1:1) | –20 to –10       | 2        | <b>10e</b> (62)                             |
| 13    | $CH_2Cl_2$ | <b>1a</b> , <b>2</b> , <b>9d</b> (1.2:1:1) | –40 to –20       | 2        | <b>10f</b> (24)                             |
| 14    | DMF        | <b>1d</b> , <b>2</b> , <b>9d</b> (1.2:1:1) | –20 to –10       | 8        | <b>10g</b> (35)                             |
| 15    | DMF        | <b>1d</b> , <b>2</b> , <b>9e</b> (1.1:1:1) | –30 to –20       | 2        | <b>10h</b> (42)                             |

<sup>a</sup> Isolated yield unless indicated otherwise.

<sup>b</sup> Determined by NMR.

ganic substrates are easily alkylated in good to moderate yield.

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- The synthesis of silanes is typically carried out on a 0.1 mol scale by addition of the mixture of **1** and chlorotrimethylsilane to a solution of **2** in 200 mL of diglyme at –30°C. The crude product removed from the reaction mixture under vacuum contains silane **4a–d** along with 10–15% of R<sub>3</sub>H and a small amount of chlorosilane. The product is treated with a solution of sodium thiosulfate, dried over MgSO<sub>4</sub> and distilled. All isolated silanes are 97–99% purity (NMR), contaminated with hexamethyldisiloxane. Selected data for compound **4c**: bp 90–90.5°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): 0.34 ppm; <sup>19</sup>F NMR: –70.85 (6F, d; 11 Hz), –208.11 (1F, m; 11 Hz); selected data compound **4d**: bp 99–100°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>): 0.31 ppm; <sup>19</sup>F NMR: –81.69 (3F, t), –120.43 (2F, m), –126.60 (2F, m), –129.07 (2F, m). Substrates other than chlorotrimethylsilane (typical experiment): mixture of **2** (0.05–0.1 mol) and an equal volume of the corresponding solvent is slowly added to a solution of **1a–e** (0.06–0.12 mol) and **9b–d** (0.05–0.1 mol) in 200 mL of the corresponding solvent at low temperature (the synthesis of compounds **10a** and **10e** is carried out by reversed addition of the mixture of **9a** (or **9e**) and the corresponding iodide to a solution of **2**). The reaction mixture is kept at the indicated temperature for 1.5–3 h (Table 1), warmed up to ambient temperature, diluted with an equal volume of 10% HCl, extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×50–100 mL), washed with 10% HCl (2×100 mL), solution of sodium thiosulfate (2×100 mL), and dried over MgSO<sub>4</sub>. The solvent is removed under vacuum and the crude product distilled. The ratio of reactants and yields of products are given in Table 1. Compound **10b**: bp 33–34/0.35 mmHg; <sup>1</sup>H NMR (CDCl<sub>3</sub>): 3.52 (1H, OH), 7.51 (3H, m), 7.80 (2H, m) ppm; <sup>19</sup>F NMR: –73.37 (3F, t; 11 Hz), –81.20 (3F, tt; 10, 2.5 Hz), –116.52 (2F, dm, AB pattern; 285 Hz), –119.80 (2F, dm, AB pattern; 296 Hz), –126.31 (2F, dm, AB pattern; 292 Hz). Anal. calcd for C<sub>12</sub>H<sub>6</sub>F<sub>12</sub>O: C, 36.57; H, 1.53; found: C, 36.41; H, 1.30.
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