Pergamon

Tetrahedron Letters 42 (2001) 3267–3269

TETRAHEDRON LETTERS

A simple procedure for nucleophilic perfluoroalkylation of organic and inorganic substrates

Viacheslav A. Petrov*

DuPont Central Research and Development, Experimental Station, PO Box 80328, Wilmington, DE 19880-0328, USA†

Received 15 March 2001; accepted 16 March 2001

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 benzensulphonyl chlorides, aliphatic and aromatic aldehydes and activated ketones leads to the formation of the corresponding condensation products in 24–62% yield.

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[1] and trifluoromethyl-[2–4] and polyfluoroalkylsilanes.[2,4,5] 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.[6] Later this reaction was expanded and a system based on perfluoroalkyl- (pefluoroalkenyl-) iodide (bromide) and tris(dialkylamino)phosphine was demonstrated to be effective for the synthesis of perfluoroalkyl aroyl ketones,[7–9] tertiary alcohols,[10] fluorovinyl silanes,[11,12] stannanes[11] and perfluoroalkyl germanes.[13] However, a few years ago it has been reported that introduction of CF_3 group to silicon and boron[14] can be carried out using a combination of CF_3I and tetrakis(dimethylamino)ethylene as a reducing agent. Later tetrakis(dimethylamino)ethylene was successfully used for the introduction of *gem*-difluoroketo-[15] or *gem*-difluoroheteroarylated moieties[16,17] 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,[14] 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**,[18] **4b**,[18] **4c**,**d**[19] 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 $\geq -30°C$ producing, according to NMR, a mixture of

$$\underset{\textbf{1a-d}}{R_fI} + \underset{\textbf{2}}{[(CH_3)_2N]_2C{=}C[N(CH_3)_2]_2} + \underset{\textbf{3}}{ClSi(CH_3)_3} \xrightarrow[\text{diglyme}]{-30\,^{\circ}C,\ 2h} \underset{\textbf{4a-d},\ 55\text{-}81\%}{R_fSi(CH_3)_3} \quad (1)$$

1a	C_2F_5	**4a**
1b	*n*-C_3F_7	**4b**
1c	*i*-C_3F_7	**4c**
1d	*n*-C_4F_9	**4d**

* Corresponding author.
† Publication No 8157.

0040-4039/01/$ - see front matter
PII: S0040-4039(01)00447-6

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.[2,5,18] 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**[7] (Eq. (2)).

$$\underset{\mathbf{5}}{C_6H_6C(O)Cl} + \mathbf{1c} + \mathbf{2} \xrightarrow[\text{monoglyme}]{-30^\circ C,\ 2h} \underset{\mathbf{6},\ 56\%}{C_6H_5C(O)CF(CF_3)_2} \quad (2)$$

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

$$\underset{\mathbf{8}}{C_6H_5SO_2Cl} + \mathbf{1d} + \mathbf{2} \xrightarrow[\text{monoglyme}]{-15 \text{ to } -10^\circ C} \underset{\mathbf{8a},\ 30\%}{C_6H_5SO_2C_4F_9} \quad (3)$$

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**,[10] **10b**,[19] **10d**, **10e**,[21] **10f**,[22] **10g**, **10h**[23] and **10c**,[18] 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-

$$\underset{\mathbf{9a\text{-}d}}{RC(O)R'} + \underset{\mathbf{1a\text{-}e}}{R_fI} + \mathbf{2} \xrightarrow[\text{2) } H_2O]{-30^\circ C,\ 2h;\ \text{1) solvent}} \underset{\mathbf{10a\text{-}h},\ 24\text{-}62\%}{R\text{-}\overset{\overset{OH}{|}}{\underset{\underset{R'}{|}}{C}}\text{-}R_f}$$

R	R'	R_fI	R_f
9a C_6H_5	CF_3	**1a**, C_2F_5I	**10a**, C_2F_5
9a C_6H_5	CF_3	**1d**, n-C_4F_9I	**10b**, n-C_4F_9
9b C_6H_5	CF_3	**1b**, n-C_3F_7I	**10c**, n-C_3F_7
9c c-C_6H_{13}	H	**1d**, n-C_4F_9I	**10d**, n-C_4F_9
9c c-C_6H_{13}	H	**1e**, CF_3I	**10e**, CF_3
9d C_2H_5	H	**1a**, C_2F_5I	**10f**, C_2F_5
9a C_2H_5	H	**1d**, n-C_4F_9I	**10g**, n-C_4F_9
9e CF_3	CF_3	**1d**, n-C_4F_9I	**10h**, n-C_4F_9

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

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

[a] Isolated yield unless indicated otherwise.
[b] Determined by NMR.

ganic substrates are easily alkylated in good to moderate yield.

Acknowledgements

The author thanks Dr. V. Grushin for discussion and the review for a number of valuable comments. Technical support by R. Smith, Jr., is also acknowledged.

References

1. Burton, D. J.; Yang, Z.-Y. *Tetrahedron* **1992**, *48*, 189–275.
2. Prakash, S. G. K.; Yudin, A. *Chem. Rev.* **1997**, *97*, 757–786.
3. Singh, R. P.; Shreeve, J. M. *Tetrahedron* **2000**, *56*, 7613–7632.
4. Furin, G. G. In *Methods of Organic Chemistry (Houben-Weyl)*, additional and suppl. Vol. to the 4th ed.; Baasner, B.; Hagelmann, H.; Tatlow, J. C., Eds.; Georg Thieme Verlag: New York, 1999; Vol. E10b/Part 1, pp. 402–447.
5. Farnham, W. B. In *Synthetic Fluorine Chemistry*; Olah, G. A.; Chambers, R. D.; Prakash, G. K. S., Eds.; Wiley: New York, 1992; pp. 243–257.
6. Ruppert, I.; Schlich, K.; Volbach, W. *Tetrahedron Lett.* **1984**, *25*, 2195–2198.
7. Kruse, A.; Ruppert, I.; Schlich, K. European Patent EP 0 301 4444 B1; *Chem. Abstr.* **1989**, *111*, 57289.
8. Huang, W.-Y.; Hu, C.-M.; He, Y.-B.; Zho, H.-F. *J. Fluorine Chem.* **1990**, *48*, 145–147.
9. Chen, J.; Kirchmeier, R. L.; Shreeve, J. M. *J. Fluorine Chem.* **1998**, *89*, 5–8.
10. Kruse, A.; Ruppert, I. US Patent 5 017 719; *Chem. Abstr.* **1989**, *111*, 77646.
11. Petrov, V. A.; Mlsna, T. E.; DesMarteau, D. D. *Mendeleev Commun.* **1993**, 240.
12. Bardin, V. V.; Presman, L. S.; Cherstkov, V. F. *Synth. Commun.* **1995**, *25*, 2425–2433.
13. Bardin, V. V. *Synth. Commun.* **1993**, *23*, 1409–1413.
14. Pawelke, G. *J. Fluorine Chem.* **1989**, *42*, 429–433.
15. Burkholder, C.; Dolbier, R.; Medebielle, M.; Ndedi, A. *Tetrahedron Lett.* **1998**, *39*, 8853–8856.
16. Burkholder, C.; Dolbier, R.; Medebielle, M. *J. Org. Chem.* **1998**, *63*, 5385–5394.
17. Dolbier, R.; Burkholder, C.; Medebielle, M. *J. Fluorine Chem.* **1999**, *95*, 127–130.
18. Krishnamurti, R.; Bellew, D. R.; Prakash, G. K. S. *J. Org. Chem.* **1991**, *56*, 984–989.
19. 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_fH and a small amount of chlorosilane. The product is treated with a solution of sodium thiosulfate, dried over $MgSO_4$ and distilled. All isolated silanes are 97–99% purity (NMR), contaminated with hexamethyldisiloxane. Selected data for compound **4c**: bp 90–90.5°C; ^{1}H NMR ($CDCl_3$): 0.34 ppm; ^{19}F NMR: −70.85 (6F, d; 11 Hz), −208.11 (1F, m; 11 Hz); selected data compound **4d**: bp 99–100°C; ^{1}H NMR ($CDCl_3$): 0.31 ppm; ^{19}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_2Cl_2 (3×50–100 mL), washed with 10% HCl (2×100 mL), solution of sodium thiosulfate (2×100 mL), and dried over $MgSO_4$. 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; ^{1}H NMR ($CDCl_3$): 3.52 (1H, OH), 7.51 (3H, m), 7.80 (2H, m) ppm; ^{19}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 $C_{12}H_6F_{12}O$: C, 36.57; H, 1.53; found: C, 36.41; H, 1.30.
20. Joglekar, B.; Miyake, T.; Kawase, R.; Shibata, K.; Muramatsu, H.; Matsui, M. *J. Fluorine Chem.* **1995**, *74*, 123–126.
21. Folleas, B.; Marek, I.; Normant, J.-F.; Sant-Jalmes, L. *Tetrahedron* **2000**, *56*, 275–283.
22. McBee, E. T.; Higgins, J. F.; Pierce, O. R. *J. Am. Chem. Soc.* **1952**, *74*, 1387–1389.
23. Zeifman, Yu. V. *Izv. Akad. Nauk. Ser. Khim.* **1992**, 464–467.