ORGANIC LETTERS

2001
Vol. 3, No. 15
2365−2366

A Novel Strategy for the Synthesis of ω-Functionalized Perfluoroalkyl Iodides

Zoltán Szlávik, Gábor Tárkányi,[†] Zsolt Skribanek,[†] Elemér Vass, and József Rábai*

*Department of Organic Chemistry, Eötvös Loránd University, P.O. Box 32,
H-1518 Budapest 112, Hungary*

rabai@szerves.chem.elte.hu

Received May 24, 2001

ABSTRACT

$$H\text{-}(CF_2)_{10}\text{-}CH_2OH \xrightarrow{\text{5 steps}} I\text{-}(CF_2)_8\text{-}CH_2OAc$$

The applicability of telomeric alcohols, $H(CF_2CF_2)_nCH_2OH$, for the synthesis of ω-functionalized *F*-alkylating reagents, $I(CF_2CF_2)_{n-1}CH_2OAc$ (6, $n = 5$), is demonstrated. The key steps of this optimized method are the “activation” of the HCF_2- terminus in a lithiation process yielding olefin 2 [(Z+E)-$BuCF{=}CF(CF_2CF_2)_4CH_2OH$, 86%] and a successive ozonation reaction in trifluoroethanol media affording ester 3b [$CF_3CH_2O_2C(CF_2CF_2)_4CH_2OH$, 93%]. Highly stereospecific ozone cleavage of the (E)-2 isomer was observed in methanol due to the competitive oxidation of the solvent.

The concept of fluorous biphase systems (FBS), drafted in 1994, served as a basis of several novel applications in homogeneous catalysis and synthetic chemistry utilizing the unique properties of perfluorocarbon solvents (nontoxicity, inertness, hydrophobicity, lipophobicity).[1] The techniques of fluorous synthesis (FS)[2] and fluorous mixture synthesis (FMS)[2e] developed by Curran and co-workers capitalize on the application of fluorous solvents and/or fluorous solid surfaces (perfluoroalkylated reverse phase silica gel, F-SiO_2)[2d] for facile product separation, where the phase behavior of target molecules is purposefully modified by the attachment of adequate fluorous phase labels.[1−3] Either fluorous liquid−liquid extraction[1] or solid-phase extraction and chromatography using F-SiO_2 (“light FS” [2d] and FMS[2e]) can be the method of choice for isolation, depending on the “fluorousness” [3] of molecules involved in these systems.

Fluorous methods have opened wide perspectives also in combinatorial synthesis[2c] and produced a firm market for designed[3] fluorous reagents and labels. Since the commonly used perfluoroalkyl iodides are monofunctional reagents, they allow the introduction of perfluorinated units only into terminal positions.[3,4] Consequently, the development of effective synthesis of $X(CF_2)_nY$ type reagents could provide larger structural versatility for the synthesis of fluorophilic[3] and multiblock compounds, including liquid crystalline structures,[5] biomaterials,[6] and self-assembled polymeric systems.[7]

In this Letter we describe a convenient method for the synthesis of ω-functionalized perfluoroalkyl iodides, useful building blocks of compounds containing the $-(CF_2)_n-$ segments in an inner position. A molecule of this kind, $I(CF_2)_8CO_2Me$, was synthesized recently from perfluorose-

---

[†] Present address: Chemical Works of Gedeon Richter, Spectroscopic Research Division, Budapest, Hungary.

(1) (a) Horváth, I. T.; Rábai, J. *Science* **1994**, *266*, 72. (b) Horváth, I. T. *Acc. Chem. Res.* **1998**, *31*, 641. (c) Cavazzini, M.; Montanari, F.; Pozzi, G.; Quici, S. *J. Fluorine Chem.* **1999**, *94*, 183. (d) de Wolf, E.; van Koten, G.; Deelman, B.-J. *Chem. Soc. Rev.* **1999**, *28*, 37. (e) Fish, R. D. *Chem. Eur. J.* **1999**, *5*, 1677. (f) Yeung, L. K.; Crooks, R. M. *Nano Lett.* **2001**, *1*, 14.

(2) (a) Curran, D. P.; Hadida, S. *J. Am. Chem. Soc.* **1996**, *118*, 2531. (b) Studer, A.; Hadida, S.; Ferritto, R.; Kim, S.-Y.; Jeger, P.; Wipf, P.; Curran, D. P. *Science* **1997**, *275*, 823. (c) Curran, D. P. *Angew. Chem., Int. Ed.* **1998**, *37*, 1175. (d) Curran, D. P.; Luo, Z. *J. Am. Chem. Soc.* **1999**, *121*, 9069. (e) Luo, Z.; Zhang, Q.; Oderaotoshi, Y.; Curran, D. P. *Science* **2001**, *291*, 1766.

(3) (a) Herrera, V.; de Rege, P. J. F.; Horváth, I. T.; Husebo, T. L.; Hughes, R. P. *Inorg. Chem. Commun.* **1998**, *1*, 197. (b) Barthel-Rosa, L. P.; Gladysz, J. A. *Coord. Chem. Rev.* **1999**, *190−192*, 587. (c) Rocaboy, C.; Rutherford, D.; Bennett, B. L.; Gladysz, J. A. *J. Phys. Org. Chem.* **2000**, *13*, 596. For calculation of “fluorousness” from partition data, see: (d) Kiss, L. E.; Kövesdi, I.; Rábai, J. *J. Fluorine Chem.* **2001**, *108*, 95.

(4) Deev, L. E.; Nazarenko, T. I.; Pashkevich, K. I.; Ponomarev, V. G. *Russ. Chem. Rev.* **1992**, *61*, 40.

(5) Pensec, S.; Tournilhac, F. G.; Bassoul, P.; Durliat, C. *J. Phys. Chem. B* **1998**, *102*, 52.

(6) Mougenot, P.; Mertens, P.; Nguyen, M.; Touillaux, R.; Marchand-Brynaert, J. *J. Org. Chem.* **1996**, *61*, 408.

(7) Sun, F.; Castner, D. G.; Mao, G.; Wang, W.; McKeown, P.; Grainger, D. W. *J. Am. Chem. Soc.* **1996**, *118*, 1856.

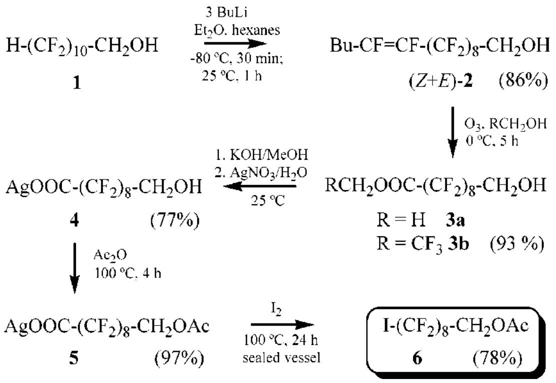
10.1021/ol0161662 CCC: $20.00

bacic acid[8] and used for the construction of a reverse *F*-amphiphile.[8,9] Some other types of longer ω-functionalized perfluoroalkyl iodides [$I(CF_2)_nR$, $n \geq 4$] are also known,[10] which could allow selective transformations at both their terminuses.[4]

The present study was inspired by the early work of Wakselman and co-workers.[11] Accordingly, in the first step of our optimized procedure alcohol **1** was converted to olefin **2** using an organolithium reagent.[12] Then, in the next step we used ozone, a hazardous but clean oxidant, to cleave **2** at the double bond, since previous studies have demonstrated its effectiveness in different solvents.[13,14]

As a media for ozonation, we tested several alcohols and found that trifluoroethanol was the most effective one.[15] Surprisingly, ozonation in methanol showed highly stereoselective transformation of the (*E*)-**2** isomer to methyl ester **3a**, leaving (*Z*)-**2** unchanged (Scheme 1, R = H). This can be explained by the participation of methanol in the ozone reaction as proved by the presence of methyl formate in the crude reaction mixture (GC), indicating that the solvent could inhibit the transformation of the (*Z*)-**2** form in a competitive oxidation process.

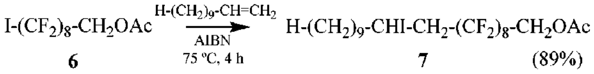
Scheme 1



Trifluoroethanol, a highly resistant solvent to ozone oxidation, consequently, allowed both (*Z*)-**2** and (*E*)-**2** isomers to be converted to trifluoroethyl ester **3b** in high yield (Scheme 1, R = CF_3). Afterward, **3b** was transformed to silver salt **4,** which on acylation with acetic anhydride yielded the hydroxyl-protected salt **5**, a suitable precursor for a Hunsdiecker-type reaction with iodine to afford the expected ω-functionalized *F*-alkyl iodide **6**.

The synthetic applicability of this novel *F*-alkylating reagent **6** was demonstrated via its successful radical addition reaction to the C═C double bond of 1-undecene in the presence of AIBN to produce the long hydrocarbon and fluorocarbon mixed chain coupled product **7** (Scheme 2).

Scheme 2



Further reactions of this diblock compound **7** toward reverse fluorinated amphiphiles along with transformation of shorter chain alcohols [$H(CF_2CF_2)_nCH_2OH$; $n = 2-4$] to bifunctional derivatives will soon be published in detail.

Acknowledgment. We thank the Hungarian Scientific Research Foundation (OTKA, T 034871) and the COST Action D12 "Fluorous medium: a tool for environmentally compatible oxidation processes" for their support.

Supporting Information Available: ^1H, ^{13}C, and ^{19}F NMR, MS, and FT-IR data and detailed descriptions of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0161662

---

(8) Szlávik, Z.; Csámpai, A.; Krafft, M. P.; Riess, J. G.; Rábai, J. *Tetrahedron Lett.* **1997**, *38*, 8757.

(9) Szlávik, Z.; Tárkányi, G.; Gömöry, Á.; Rábai, J. *Org. Lett.* **2000**, *2*, 2347.

(10) Selected examples: (a) **R = Cl**. Chen, Q.-Y.; Su, D.-B.; Yang, Z. Y.; Zhu, R.-X. *J. Fluorine Chem.* **1987**, *36*, 483. (b) **R = Br**. Brace, N. O. U.S. Pat. 3145222, 1961; *Chem. Abstr.* **1964**, *61*, 10589g. (c) **R = COCl**. McLaughlin, V. C. R. *Tetrahedron Lett.* **1968**, 4761. (d) **R = CO_2H**. Huang, W.-Y.; Huang, B.-N.; Hu, C.-M. *J. Fluorine Chem.* **1983**, *23*, 229. (e) **R = SO_2F or SO_2Cl**. Qiu, W.; Burton, D. J. *J. Fluorine Chem.* **1993**, *62*, 273.

(11) Nguyen, T.; Rubinstein, M.; Wakselman, C. *Synth. Commun.* **1983**, *13*, 81.

(12) Experimental conditions for **2**: In a predried and nitrogen-purged reaction flask, **1** (3.54 g, 6.65 mmol) was dissolved in absolute diethyl ether (70 mL) and cooled to −78 °C. Continuous stirring and bypass nitrogen flow was applied during reaction. A solution of *n*-buthyllithium in hexanes (9 mL, 2.5 M, 22.5 mmol) was added dropwise over 30 min. The mixture was stirred for 1 h at room temperature and then the reaction was quenched by the addition of a dilute solution of HCl. The organic phase was separated, washed twice with distilled water, and dried over Na_2SO_4 and the solvent was removed by rotary evaporation. The residue was distilled under reduced pressure (170−180 °C bath temperature, approximately 20 mmHg) to yield **2** (3.13 g, 86%); (*Z*):(*E*) = 3.3:1 (determined by GC and NMR).

(13) Moiseeva, N. I.; Gekhman, A. E.; Rumyantsev, E. S.; Klimanov, V. I.; Moiseev, I. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 1706; *Chem. Abstr.* **1990**, *112*, 76130.

(14) Odinokov, V. N.; Akhmetova, V. R.; Savchenko, R. G.; Bazunova, M. V.; Fatykhov, A. A.; Zapevalov, A. Y. *Izv. Akad. Nauk., Ser. Khim.* **1997**, 1239; *Chem. Abstr.* **1998**, *128*, 22618.

(15) Experimental conditions for **3b**: In a glass reactor with the appropriate gas inlet and outlet (*Z*+*E*)-**2** (8.94 g, 16.2 mmol) was dissolved in trifluoroethanol (80 mL) and cooled to 0 °C. Dry O_2 gas was bubbled through the system for 30 min; then the ozone generator, operating at a yield of ~1 g/h ozone (CAUTION!), was switched on for 5 h. The reactor was then purged successively with O_2 and N_2 to remove ozone residues. Complete reaction was observed by GC. The solvent was regenerated using atmospheric distillation (70 mL, 99.4% GC purity). The residue was distilled at reduced pressure in a short path apparatus (85−100 °C bath temperature/ 0.1 mmHg) to afford **3b** (8.47 g, 93%, 92% purity by GC).