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LETTERS

Functionalization of saturated fluorocarbons[1]

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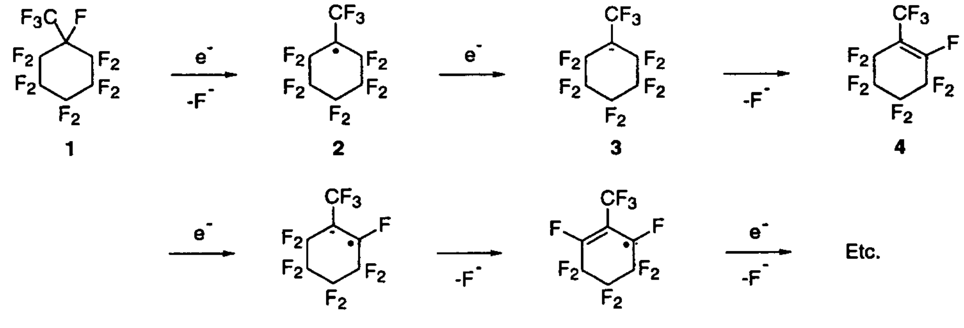
Abstract

A method is described for transforming perfluoroalkanes and perfluorocycloalkanes bearing tertiary fluorine into perfluoroenolates, which can be variously derivatized. © 1999 Elsevier Science Ltd. All rights reserved.

Much recent interest has focused on the challenge of introducing functionality into saturated fluorocarbons.[2,3] The problem is both significant and thorny: significant because introduction of functional groups could considerably broaden the range of applications of these compounds,[4] and thorny because their inertness demands reaction conditions vigorous enough to bring about wholesale destruction. In other words, intermediate species along the reaction pathways are, in general, more reactive than the starting material.[5,6]

Attack on saturated fluorocarbons requires a potent electron donor, and the most vulnerable site for attack is a tertiary C–F bond. A probable sequence of events resulting from treatment of perfluoromethylcyclohexane (**1**) with an electron donor is depicted in Scheme 1. Crabtree succeeded in producing the alkene **4** from **1** in 11.9% conversion, but further reaction led to byproduct formation. A similar reaction with perfluoro-2-methylpentane yielded the 2-methylpentene with a conversion of 1.4%.[3,7]



Scheme 1.

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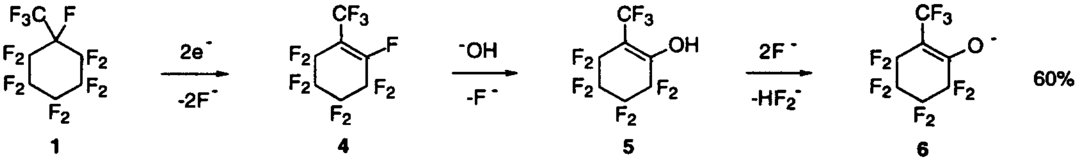
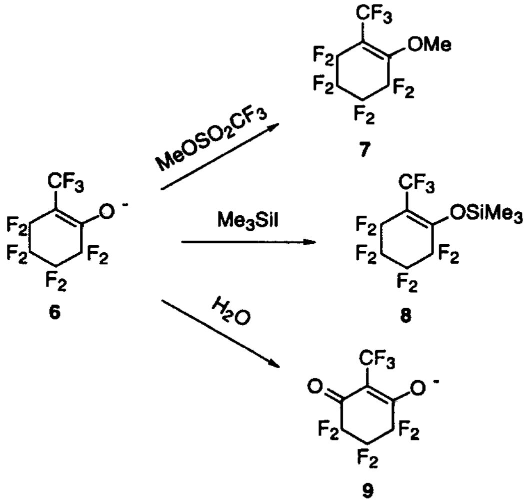
In unsuccessful attempts to trap early intermediates **2** or **3** in the reaction cascade, we discovered a way to intercept the alkene **4** that strongly inhibited further degradation. Irradiation with a Vycor-filtered medium pressure mercury arc of a solution of **1** in tetrahydrofuran (THF) containing tetrabutylammonium iodide gave enolate **6**[8,9] in 60% yield,[10] we believe via the pathway shown below. Iodide ion furnishes the required electrons by undergoing a charge-transfer-to-solvent (CTTS) transition upon irradiation.[11,12] The intermediate alkene **4** is trapped by hydroxide ion, which presumably arises from water present in the tetrabutylammonium iodide[13] via reduction or deprotonation by fluoride under the nearly anhydrous conditions. Deprotonation of the resulting enol **5** is very facile, as perfluoroenols are highly acidic.[14] The good yield of enolate **6** depends upon that fact, for its negative charge protects it from accepting an electron and undergoing further loss of fluoride (Scheme 2).



Scheme 2.

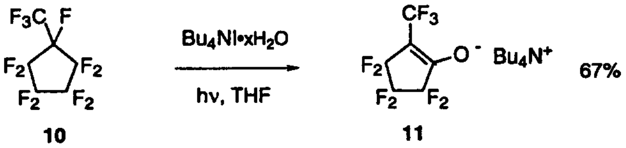
Enolate **6** reacts rapidly to form the methyl ether **7**[15] and trimethylsilyl ether **8**.[16] Moist air suffices to hydrolyze **6** to β-diketone enolate **9** (Scheme 3).[17,18]



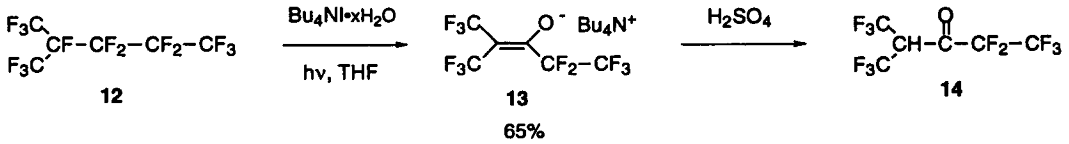
Scheme 3.

Fluorocarbon **10** reacted analogously to **1**, giving tetrabutylammonium enolate **11**[19] in 67% yield (Scheme 4). Like **6**, this enolate was derivatized as the methyl ether, trimethylsilyl ether and β-diketone enolate.[20] Perfluoro-2-methylpentane (**12**) gave a 65% yield of enolate **13** under the same reaction conditions. Addition of concentrated sulfuric acid to the reaction mixture produced **14** quantitatively (Scheme 5).[21] Perfluoro-1,3-dimethylcyclohexane (**15**) yielded tetrabutylammonium enolate **16**[22] which, like **6** and **11**, hydrolyzes readily on addition of water to the corresponding β-diketone enolate (Scheme 6). The fact that **15** reacts at only one of its two tertiary sites attests to the effectiveness with which a negative charge protects against further reduction, and the clean regioselectivity of the reaction is striking.[23]

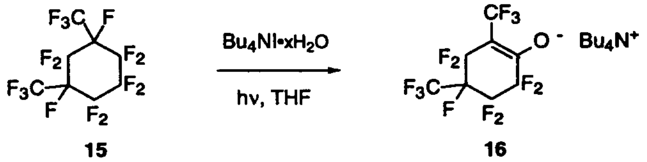
The behavior of perfluorodecalin (**17**) is exceptional, but as such it provides evidence in support of the mechanism proposed above. The reaction products are Δ^9-decalin **18** (minor) and hydroxy-β-diketonate



Scheme 4.

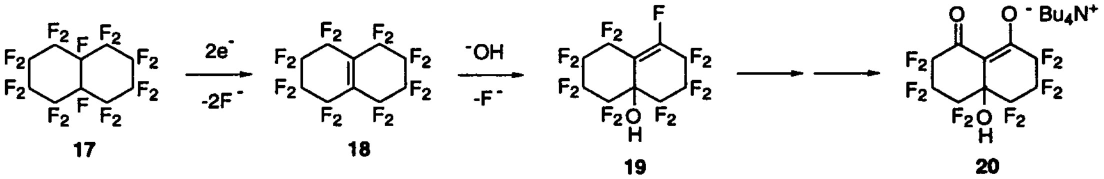


Scheme 5.



Scheme 6.

20 (major) (Scheme 7).[24] Since **17** has *adjacent* tertiary fluorines, the initially formed alkene **18** is tetrasubstituted. Attack of hydroxide cannot result in addition–elimination as in the above cases, so S_N2' reaction takes place instead to give **19**. This trisubstituted alkene reacts analogously to **4**, proceeding all the way to β-diketonate **20**.[25] Thus, the inability of the molecule to acquire a negative charge early in the reaction cascade results in the loss of many fluorines.



Scheme 7.

In summary, we have found a novel method for functionalization of saturated fluorocarbons that possess tertiary fluorine. It is the first such method to give good yields of product with complete conversion of starting material and without extensive fluoride loss. The products are tetrabutylammonium perfluoroenolates, useful synthetic intermediates for the preparation of a variety of other derivatives.

Acknowledgements

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8. All ^{19}F NMR spectra were measured on the Φ scale (i.e. ppm relative to internal $CFCl_3$, upfield negative) in $CDCl_3$ containing a minor amount of the reaction solvent THF (CH_2Cl_2 in the case of **14**).
9. ^{19}F NMR of **6**: –54.9 (3F, CF_3), –94.0 (2F, C3), –120.9 (2F, C6), –131.7 (2F, C4 or 5), –134.8 ppm (2F, C4 or 5).
10. The yields reported here are based on NMR integration relative to hexafluorobenzene as area standard.
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13. Since too much water in the reaction mixture results in very low yields, the tetrabutylammonium iodide is dried in vacuum at 55°C for 5 h.
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15. ^{19}F NMR of **7**: –59.0 (3F, CF_3), –107.9 (2F, C3), –114.7 (2F, C6), –134.6 (2F, C4 or 5), –134.8 ppm (2F, C4 or 5). These values agree well with those reported by Carter, P. A.; Patrick, C. R.; Tatlow, J. C. *J. Fluorine Chem.* **1982**, *21*, 407. MS of **7**: m/e 324 (M^+–F), 305, 271, 243, 224, 159.
16. ^{19}F NMR of **8**: –58.9 (3F, CF_3), –106.2 (2F, C3), –118.7 (2F, C6), –134.6 (2F, C4 or 5), –135.0 ppm (2F, C4 or 5).
17. For analogous reactions of enolates, see: Bekker, R. A.; Popkova, V. Ya.; Knunyants, I. L. *Izvest. Akad. Nauk SSSR, Ser. Khim. No. 2* **1978**, 493 (Engl. Transl. **1978**, 430); *No. 5* **1978**, 1193 (Engl. Transl. **1978**, 1038), and references cited therein; Smith, J. R.; Lemal, D. M. *J. Fluorine Chem.* **1999**, *97*, 145. Loss of a fluoride ion, the initial step of the hydrolysis, is assisted by hydrogen bonding to water.
18. ^{19}F NMR of **9**: –57.3 (3F, CF_3), –123.7 (4F, C4,6), –135.8 ppm (2F, C5).
19. ^{19}F NMR of **11**: –56.2 (3F, CF_3), –97.1 (2F, C3), –124.6 (2F, C5), –131.2 ppm (2F, C4).
20. ^{19}F NMR of the methyl ether: –59.0 (3F, CF_3), –106.8 (2F, C3), –114.1 (2F, C5), –130.2 ppm (2F, C4); of the trimethylsilyl ether: –60.1 (3F, CF_3), –106.3 (2F, C3), –120.3 (2F, C5), –131.1 ppm (2F, C4); of the β-diketonate: –59.8 (3F, CF_3), –128.9 ppm (4F, C4,5).
21. ^{19}F NMR of **13**: –48.8 (3F, *gem* CF_3), –54.1 (3F, *gem* CF_3), –80.3 (3F, C5), –115.9 ppm (2F, C4); of **14**: –62.7 (6F, *gem* CF_3's), –81.1 (3F, C5), –121.8 ppm (2F, C4). The values for both compounds agree well with literature data: Martini, T.; Schumann, C. *J. Fluorine Chem.* **1976**, *8*, 535.
22. The labels '*cis*' and '*trans*' in the NMR assignments for **16** locate fluorine atoms relative to the CF_3 group at C4. The assignments were made with the help of NOE measurements. ^{19}F NMR of **16**: –54.8 (3F, CF_3C2), –70.0 (3F, CF_3C4), –80.9 (d, J=292 Hz, 1F, *cis*, C3), –93.3 (d, J=292 Hz, 1F, *trans*, C3), –111.9 (d, J=292 Hz, 1F, *trans*, C6), –119.2 (d, J=277 Hz, 1F, *cis*, C5), –129.7 (d, J=292 Hz, 1F, *cis*, C6), –134.6 (d, J=277 Hz, 1F, *trans*, C5), –180.0 ppm (1F, C4). ^{19}F NMR of the β-diketone enolate from **16**: –57.6 (3F, CF_3C2); –72.4 (3F, CF_3C4); –120.5, –126.2 (ABq, J=288 Hz, 2F); –126.7, –129.4 (ABq, J=273 Hz, 2F); –183.0 ppm (1F, C4).
23. The regioselectivity may be primarily steric in origin. Since elimination of fluoride ion is greatly assisted by solvation or ion pairing, and since the bulky tetrabutylammonium ion is the only species abundantly available to assist in this process, loss of fluorine vicinal to the CF_3 group may be sterically hindered.
24. ^{19}F NMR of **18**: –111.7 (8F, C1,4,5,8), –135.2 ppm (8F, C2,3,6,7); of **20**: –110.7 (d, J=288 Hz, 2F), –119.4 (d, J=269 Hz, 2F), –119.9 (d, J=266 Hz, 2F), –126.5 (d, J=288 Hz, 2F), –134.0 (d, J=269 Hz, 2F), –137.8 ppm (d, J=266 Hz, 2F).
25. A nitrogen analog of **20** was formed when a mixture of perfluorodecalin, mercury and ammonia was photolyzed in the gas phase (Ref. 4).