Reactivity of Fluorinated Alkyl Radicals in Solution. Some Absolute Rates of Hydrogen-Atom Abstraction and Cyclization†

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The pure electrophilic nature and unique reactivity characteristics and perfluoro-*n*-alkyl radicals have made the quantitative determination of their reactivity a matter of fundamental significance. Initial insight into the behavior of such radicals was obtained in our recently reported study which resulted in determination of absolute rate constants for their addition to a broad spectrum of alkenes.[1,2] In these LFP experiments it was found that perfluorinated radicals were much more reactive than their hydrocarbon counterparts in additions to normal, electron-rich alkenes, such as 1-hexene (40 000 times as reactive).

In this paper we report the use of this LFP data in conjunction with a series of bimolecular competition experiments to determine approximate absolute rate constants for some hydrogen atom transfer reactions of the perfluoro-*n*-heptyl radical with substituted silanes and thiophenol, and then we demonstrate how these data can be used to determine the rates of cyclization of some fluorinated alkenyl radicals, which as such comprise the first reported fluorinated "clock" reactions.

Recently we reported that the rate of hydrogen atom transfer to *n*-$C_7F_{15}^\bullet$ by tributyltin hydride was ~75 times that to *n*-alkyl radicals at 30 °C.[2] In the present work even more greatly enhanced rates of hydrogen atom transfer to $R_f^\bullet$ (vs $R^\bullet$) by three common silane reducing agents are observed. For example, in contrast to its relatively low reactivity with hydrocarbon radicals, where it has been found to be virtually useless as an effective chain-sustaining hydrogen atom transfer agent,[3] triethylsilane was observed to reduce perfluoroalkyl bromides and iodides efficiently under photochemical initiation, transferring hydrogen atoms to the intermediate perfluoro-*n*-alkyl radicals at a rate which should make Et_3SiH a very useful competitive reducing agent for studying chain processes which involve fluorinated radicals. As seen in Table 1, Et_3SiH was >850 times more reactive with $R_f^\bullet$ than with $R^\bullet$ at 30 °C. In a similar manner, the even more reactive reducing agents $(TMS)_2SiHMe$ and $(TMS)_3SiH$ were shown to transfer hydrogen atoms ~440 and ~110 times more rapidly, respectively, to perfluoro-*n*-alkyl than to the analogous hydrocarbon radicals.[4-6]

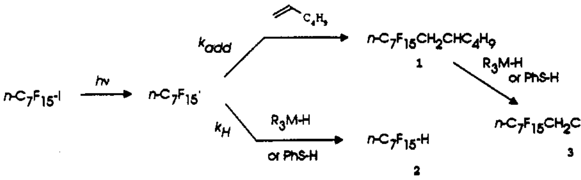

Table 1. Rate Constants for Hydrogen Atom Abstractions at 30 °C

	rate of reduction ($k_H/(10^6\ M^{-1}\ s^{-1})$)				
Radical	PhSH	Et_3SiH	$(TMS)_2$-SiMeH	$(TMS)_3$-SiH	*n*-Bu_3-SnH
n-$C_7F_{15}^\bullet$	0.28 (0.03)	0.75 (0.07)	16.3 (1.5)	51 (5)	203 (14)
R-$CH_2^\bullet$ [a]	150	0.000 85	0.037	0.46	2.7[b]

[a] Reference 7. [b] Reference 2.

The observed enhanced rates of $R_f^\bullet$ with the silanes and *n*-Bu_3-SnH are consistent with the greater exothermicity of such reductions (R_f–H BDE = 107 kcal/mol vs 98 kcal/mol for R–H).[8] However, this certainly cannot be the whole story since it was found that PhS–H, a very efficient H atom donor to hydrocarbon radicals, reduced perfluoro-*n*-alkyl radicals ~500 times *slower*! This result indicates that transition-state *polar effects* must also play a significant role in such hydrogen atom transfer reactions.[9]

Triethylsilane proved to be the most convenient reducing agent with which to study cyclizations of fluorinated alkenyl radicals. Thus quantitative product studies of the reactions of Et_3SiH with a series of four fluorinated alkenyl bromides were used to obtain rate constants for the first perfluoroalkyl radical clock reactions. These rates reveal interesting trends in the intramolecular reactivity of unsaturated fluoroalkyl radicals.

The prototypical perfluoro-5-hexenyl radical **5**, which could be generated photochemically at 30 °C from bromide **4**, was thus observed to undergo dominant *exo-trig* cyclization to form cyclopentylmethyl product **8** (3–4% cyclohexane product observed). Its rate of cyclization turned out, probably fortuitously, to be not much larger than that for cyclization of the hydrocarbon species ($k_{rel} = 2.04$),[10] with the similarity in rates probably deriving from the contrasting reactivity characteristics of fluorinated vs

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(4) Typically, a solution of perfluoro-*n*-heptyl iodide in benzene-d_6 (for $(TMS)_2SiMeH$ and $(TMS)_3SiH$) or in neat reductant (for Et_3SiH and PhSH) was photolyzed at 30 °C in the presence of appropriate amounts of 1-hexene and a reductant. The thus-generated *n*-$C_7F_{15}^\bullet$ radicals underwent competitive, kinetically controlled formation of products **2** and **3**. The ratio of **3**:**2** was determined directly by ^{19}F NMR analysis of the CF_2H peak (δ −136.35 ppm) of **2** versus the CF_2CH_2 peak (δ − 114.05 ppm) of **3**. This ratio, obtained for varied concentrations of 1-hexene, combined with the respective ratios of 1-hexene to reductant, allowed the determination of the ratio k_H/k_{add} according to the equation

$$\frac{[3]}{[2]} = \frac{k_{add}}{k_H}\frac{[\text{1-hexene}]}{[Et_3SiH]}$$

The LFP-determined value for k_{add} for *n*-$C_7F_{15}^\bullet$ ($7.9 \times 10^6\ M^{-1}\ s^{-1}$ at ~298 K)[1,2] can then be used to convert the various ratios of k_H/k_{add} to the values of k_H which are reported in Table 1.[5] Overall yields for **2** + **3** were always in the 94–100% range. The accuracy of the values of k_H can, of course, be no better than those reported for k_{add}, which was ±8.9%. Thus the error estimates reported in Table 1 reflect both the least squares fit of the line and the error in k_{add} and largely derive from the latter.

(5) Activation parameters for the addition of *n*-$C_7F_{15}^\bullet$ are not yet available. However, using the analogy of nucleophilic *n*-alkyl radicals adding to electrophilic olefins, one would expect activation energies of *only 1.5–2.1 kcal/mol* and thus little temperature dependence in the addition of *n*-$C_7F_{15}^\bullet$ to 1-hexene.[6]

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(10) In a typical competition experiment, a solution of perfluoro-5-hexenyl bromide (**4**) in hexane or benzene-d_6 was photolyzed in the presence of variable amounts of triethylsilane. The thus-generated perfluoro-5-hexenyl radical (**5**) underwent competitive, kinetically controlled formation of products **7** and **8**. The ratio of **8**:**7** was determined directly by ^{19}F NMR analysis of the two respective CF_2H peaks, δ −138.29 ppm for **7** and δ −136.41 ppm for **8**. Combined yields for **7** + **8** were in the range of 92–97%. For reaction of **9**, the ratios of products were determined from the integral ratios of the CF_2H peak of **13** (δ −137.1 ppm) versus $^1/_2$ the sum of the AB system due to the $C_2(C_5)$ CF_2 peak of **14** (δ −130.8 and −134.0 ppm) and $^1/_2$ of the broad singlet due to the $C_1(C_4)$ CF_2 groups of **15** (δ −118.2 ppm). Overall yields ranged from 96 to 100%.

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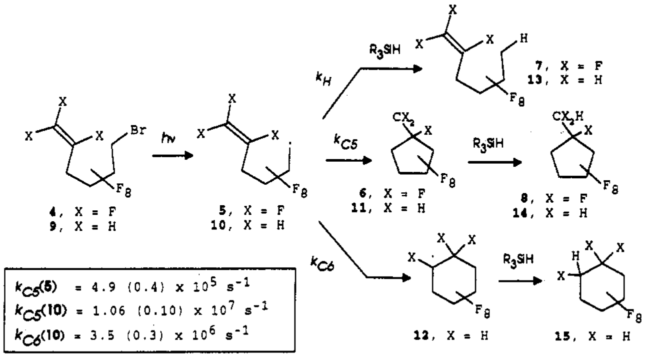
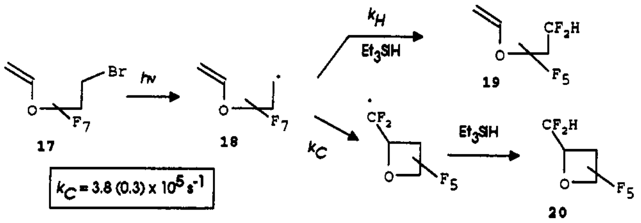
hydrocarbon radicals.[1,2,11-13] The hydrocarbon cyclization, after all, involves a nucleophilic radical adding to an electron-rich double bond,[13] whereas cyclization of **5** involves an electrophilic radical adding to an electron-poor double bond.[11] Neither polarity matchup is ideal.



The radical species **10** with hydrogen in place of fluorine on the double bond should provide a better match of polarities in its cyclization, and indeed it cyclized 22 times faster than perfluoro species **5**. Unexpectedly, in the kinetically-controlled cyclization of **10**, a significant amount of *endo-trig*, six-membered-ring formation (to form product **15**) occurred in competition with the expected five-membered-ring formation (to form product **14**). Rate constants for these cyclizations at 30 °C were determined to be $k_{C5} = 1.06\ (\pm 0.10) \times 10^7\ \mathrm{s}^{-1}$ (a value almost 40 times faster than the *exo-trig* cyclization of **5**) and $k_{C6} = 3.5\ (\pm 0.3) \times 10^6\ \mathrm{s}^{-1}$. The unexpected, highly competitive *endo–trig* cyclization of **10** is thus occurring *>700 times faster* than that reported for the parent hydrocarbon system.[14]

An interesting aspect of fluorinated 4-pentenyl radical cyclizations that distinguishes them from their hydrocarbon counterparts[7] is their ability to cyclize to form four-membered rings. Piccardi and his co-workers, for example, reported considerable cyclization to a four-membered-ring product in the free-radical chain addition of C_2F_5I to 3,3,4,4-tetrafluoro-1,5-hexadiene.[15] Nevertheless, the perfluoro-4-pentenyl radical, **16**, derived from the photolysis of perfluoro-5-bromopentene, failed to cyclize even when Et_3SiH was employed as the hydrogen atom transfer reagent. Thus the rate constant for **16**'s cyclization must be $< 1 \times 10^4\ \mathrm{s}^{-1}$ at 30 °C (assuming that >3% of the cyclized product could be detected).

At this point, it is uncertain whether this failure of **16** to cyclize derives from kinetic or thermodynamic factors. However, ether analog **18** was expected to be both kinetically and thermodynamically more reactive toward cyclization than **16**.[7,16] Indeed, cyclization of intermediate radical **18** competed quite efficiently with its reduction by Et_3SiH in benzene-d_6, and a rate constant for cyclization of $3.8\ (\pm 0.3) \times 10^5\ \mathrm{s}^{-1}$ was derived from the competition data.[17] In marked contrast to Piccardi's results, no products deriving from competitive five-membered-ring formation could be observed.



Partially fluorinated and heteroatom-substituted alkenyl radicals can undoubtedly be designed which will define optimal polar, steric, and conformational factors and thus give rise to maximal rates of cyclization in 4-pentenyl and 5-hexenyl radical systems. Such studies are currently in progress. In addition, studies to determine C–H reactivities of perfluoro-*n*-alkyl radicals are in progress which should determine whether perfluoroalkyl radicals might be good kinetic and regioselective mimics of •OH in biological systems.

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Supplementary Material Available: Experimental details included data from competition experiments (22 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS. See any current masthead page for ordering information.

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(16) From reactivity ratios of hexafluoropropylene and perfluoropropyl perfluoro vinyl ether ($C_3F_7OCH{=}CF_2$) in copolymerizations with tetrafluoroethylene at 60 °C, the vinyl ether is about 8 times more reactive toward (bimolecular) $-CF_2CF_2^{\bullet}$ radical addition (D. P. Carlson, DuPont, private communication).

(17) Cyclization of **18** was carried out under conditions similar to those of **5** and **10**, with the ratio of cyclized to uncyclized reduction products, **19** and **20**, being obtained by ^{19}F NMR integration of the respective OCF_2 peaks, an AB doublet at δ −80.6 and −85.6 ppm for **20** and a singlet at δ −90.8 ppm for **19**. Overall yields for **19** and **20** ranged between 87 and 91%.