

## The Quantitative Effect of Terminal Fluorine Substituents on the Rate of 5-Hexenyl Radical Cyclization

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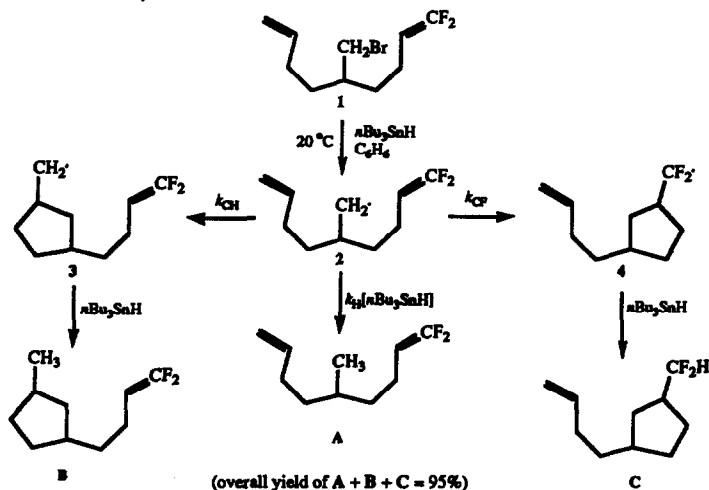
**Summary:** Direct intramolecular competition experiments demonstrate that terminal fluorine-substitution has negligible effect on the rate of cyclization of 5-hexenyl radical.

Quantitative aspects of addition reactions of radicals to alkenes are both of intrinsic interest to physical organic chemists and of practical importance to chemists using such reactions commercially. In contrast to the large and useful database available for hydrocarbon systems,<sup>1</sup> there has thus far been little effort devoted towards obtaining absolute rate data for radical processes involving *fluorinated* substrates. Recently we reported the first absolute rate constants for the addition of perfluoroalkyl radicals to a series of alkenes in solution, the data being obtained via laser flash photolysis experiments,<sup>2</sup> with the result that *n*-perfluoroalkyl radicals were found to be ~1340 times more reactive than *n*-alkyl radicals in their addition to  $\alpha$ -methylstyrene.

In the quest for absolute rate data for fluorinated systems, one can utilize competitive studies as well as direct rate measurements in order to obtain the desired rate constants. A method which has proved particularly useful for obtaining quantitative information about the effect of substituents on rates of radical addition has been the 5-hexenyl radical cyclization process.<sup>3</sup>

In this paper, we report unexpected results for the first quantitative determination of the effect of *olefinic* fluorine substitution on the 5-hexenyl cyclization. For this study we chose a bifurcated system, **1**,<sup>4</sup> which would permit direct comparison of the rates of

cyclization to a hydrocarbon and a fluorine-substituted olefinic component via intramolecular competition.



Substrate 1, in the presence of  $n\text{-Bu}_3\text{SnH}$ , underwent homolytic cleavage at 20 °C in benzene solution to initiate competitive chain processes which led to three isomeric reduced products, A, B and C,<sup>5</sup> the ratio of which led to unambiguous and accurate determination of the two cyclization rate constants,  $k_{\text{CH}}$  and  $k_{\text{CF}}$ , as shown below:

**Table.** Data for Cyclization Reactions of 1

No. of reaction	[R-Br]	[ $\text{Bu}_3\text{SnH}$ ]	[A]/[B] <sup>a</sup>	[A]/[C] <sup>a</sup>	(A/B) <sup>b</sup>	(A/C) <sup>b</sup>
1	0.132	0.302	0.429	0.513	0.504	0.577
2	0.150	0.470	0.708	0.833	0.831	0.937
3	0.152	0.565	0.923	0.904	1.084	1.017
4	0.156	0.658	1.063	1.084	1.248	1.220
5	0.010	1.050	1.595	1.703	1.873	1.916
6	0.012	0.893	1.350	1.470	1.585	1.654

<sup>a</sup>: GC ratios, <sup>b</sup>: Calibrated ratios by relative sensitivities:  $S_{\text{A/B}} = 1.174$ ;  $S_{\text{A/C}} = 1.125$ .

$S_{\text{A/B}} = S_{\text{A}}/S_{\text{B}}$ ;  $S_{\text{A/C}} = S_{\text{A}}/S_{\text{C}}$   $S_{\text{A}} = 1.35$ ;  $S_{\text{B}} = 1.15$ ;  $S_{\text{C}} = 1.20$ .

$$\frac{[\text{A}]}{[\text{B}]} = \frac{k_{\text{H}}}{k_{\text{CH}}} [n\text{Bu}_3\text{SnH}] \quad \frac{[\text{A}]}{[\text{C}]} = \frac{k_{\text{H}}}{k_{\text{CF}}} [n\text{Bu}_3\text{SnH}]$$

By varying  $[n\text{-Bu}_3\text{SnH}]$  and plotting separately the corrected product ratios  $[\text{A}]/[\text{B}]$  and  $[\text{A}]/[\text{C}]$  versus  $[n\text{-Bu}_3\text{SnH}]$ , one can obtain the ratios  $k_{\text{H}}/k_{\text{CH}}$  and  $k_{\text{H}}/k_{\text{CF}}$  from the respective slopes:  $k_{\text{H}}/k_{\text{CH}} = 1.80 \pm 0.09$  and  $k_{\text{H}}/k_{\text{CF}} = 1.78 \pm 0.05$ . Since the rate parameters for

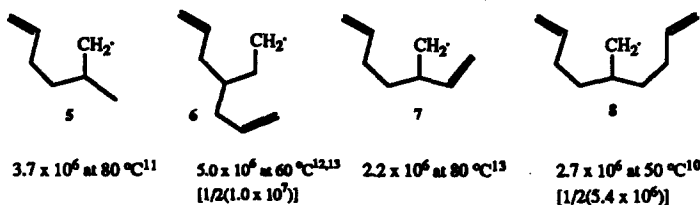
reduction of primary radicals by  $n\text{Bu}_3\text{SnH}$  have been determined [ $\text{Log } A = 9.07 \mp 0.24$ ,  $E_a = 3.69 \mp 0.32$  kcal/mol, thus  $k_H = 2.066 \times 10^6$  at  $20^\circ\text{C}$ ]<sup>6</sup>, and have been found to be relatively insensitive to the specific identity of the primary radical, one can readily calculate the values for the two cyclization rate constants:

$$k_{\text{CH}} = 1.15 \mp 0.06 \times 10^6 \text{ sec}^{-1} \quad \text{and} \quad k_{\text{CF}} = 1.16 \mp 0.03 \times 10^6 \text{ sec}^{-1}.$$

Indeed, quite unexpectedly, it was found that the rates of cyclization of the alkyl radical to the fluorine-substituted and non-fluorine-substituted olefins were *virtually identical*.<sup>7</sup> This was surprising in view of the earlier-reported competitive rate data, mostly of Tedder and Walton,<sup>9</sup> which indicated a greater reactivity of alkyl radicals with fluorine-substituted ethylenes than with ethylene.

A comparison, below, of our value for  $k_{\text{CH}}$  with expectations based upon earlier hydrocarbon studies, including our own study of hydrocarbon analog, 8,<sup>10</sup> indicates that there is nothing unusual kinetically about the bifurcated system.

#### Rates of Cyclization:



It is too early for us to reach any definitive conclusions as to *why* terminal fluorine substitution does not affect the rate of cyclization. Certainly, these cyclizations are exothermic (ca. -15 kcal/mol), have low activation energies (i.e., 6.8 kcal/mol for the 1-hexenyl radical),<sup>6</sup> and therefore have early transition states. Of potential significance is the fact that the large negative entropies of activation which are observed for such cyclizations [i.e., -17 cal/deg for the 5-hexenyl cyclization],<sup>6</sup> combined with the low activation enthalpies, give the reactions considerable entropy control. Future studies on variously-fluorine-substituted non-bifurcated 5-hexenyl systems, along with temperature-

dependence studies, should provide us with a more complete understanding of the present results.<sup>14</sup>

**Acknowledgement.** Support of this work, in part, by the National Science Foundation is gratefully acknowledged.

#### References and Footnotes

1. Landolt-Bornstein, New Series, *Radical Reaction Rates in Liquids*. Fischer, H., Ed., Springer-Verlag: Berlin, 1984, Vol. 13, Part a, Part b.
2. Avila, D. V.; Ingold, K. U.; Luszyk, J., Dolbier, W. R. Jr., Pan, H. Q. *J. Am. Chem. Soc.* **1993**, *115*, 1577.
3. (a) Beckwith, A. L. J., Ingold, K. U. in P. de Mayo: *Rearrangements in Ground and Excited States, Vol. 1*, Academic Press, New York, 1980, p161; (b) Beckwith, A.L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925; (c) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959, (d) Park, S.-U.; Chung, S.-K.; Newcomb, M. *J. Am. Chem. Soc.* **1986**, *108*, 240.
4. The substrate **1** was synthesized in six steps from 5-hexenoic acid: (a) 2 equiv. LDA, then 2-(3-bromopropyl)-1,3-dioxolane (75%); (b) LAH (95%); (c) TosCl/pyr, followed by LiBr (76%); (d) H<sub>2</sub>O, wet silica gel (70%); (e) CF<sub>2</sub>Br<sub>2</sub>/(Me<sub>2</sub>N)<sub>3</sub>P (75%) to form **1**. It was satisfactorily characterized by <sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F NMR and by HRMS.
5. Products **A**, **B** and **C** were fully characterized after isolation either from the product mixture or via independent synthesis. Quantitative analyses of **A**, **B** and **C** were carried out by glpc using a 20' SE-30 column which did not separate cis/trans isomers of **B** or **C**. No indication of the ratio of such cis/trans isomers could be gleaned from either their <sup>1</sup>H or <sup>19</sup>F NMR spectra.
6. Chatgililoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739.
7. The nature of the results was foreshadowed by some earlier-reported results of Kobayashi and coworkers.<sup>8</sup>
8. Morikawa, T.; Nishiwaki, T.; Iitaka, Y.; Kobayashi, Y. *Tetrahedron Lett.* **1987**, *28*, 671.
9. Tedder, J. M.; Walton, J. C. *Tetrahedron* **1980**, *36*, 701; (b) Tedder, J. M.; Walton, J. C. *Acc. Chem. Res.* **1976**, *9*, 183.
10. Dolbier, W. R., Jr.; He, Y.-H. unpublished results.
11. Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. *Aust. J. Chem.* **1983**, *36*, 545.
12. Note that substitution at the 3-position generally enhances rate by ca. 28% over that due to 2-substitution.
13. Beckwith, A. L. J.; Lawrence, T.; Serelis, A. K. *J. Chem. Soc., Chem. Comm.* **1980**, 484.
14. A preliminary study of the cyclization of 6,6-difluoro-5-hexenyl radical has corroborated the lack of kinetic effect of the terminal fluorine substituents.