



Rate Constants for Reaction of a Fluorous Tin Hydride Reagent with Primary Alkyl Radicals

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Abstract: Rate constants for 6-*exo* cyclization of the 7,7-diphenyl-6-heptenyl radical (**3**) in benzotrifluoride (BTF, PhCF₃) were determined by laser flash photolysis, and radical clock **3** was used in competition kinetic studies for determination of rate constants of reactions of the fluorous tin hydride reagent *tris*(2-(perfluorohexyl)ethyl)tin hydride with primary alkyl radicals. © 1997 Elsevier Science Ltd.

Fluorinated solvents provide a third liquid phase that is effectively immiscible with the conventional organic and aqueous liquid phases and can be employed for convenient separations of organic products from highly fluorinated reagents.² Recently, Curran and Hadida introduced a fluorous tin hydride reagent, *tris*(2-(perfluorohexyl)ethyl)tin hydride ((C₆F₁₃CH₂CH₂)₃SnH, **1**), for applications with fluorous phase extractions.³ Tin hydride **1** can be used for radical reductions in the partially fluorinated solvent benzotrifluoride (BTF, trifluoromethylbenzene, PhCF₃) which dissolves both **1** and organic substrates. The reactions are similar to those with the conventional tin hydride reagent Bu₃SnH, but separations of desired products from both **1** and tin halide by-products of this reagent can be achieved conveniently by distribution between an organic solvent and a fluorous solvent.³

The rate constants of radical reactions are fundamentally interesting and are crucial for planning synthetic applications, so it is important ask whether the fluorinated tin hydride reagent **1** reacts with rate constants similar to those of Bu₃SnH and whether a kinetic solvent effect is associated with the use of BTF. We report in this Letter direct laser flash photolysis (LFP) measurements of rate constants for cyclization of a primary alkyl radical clock in BTF and the use of this clock reaction for calibration of reagent **1**. The partially fluorinated solvent appears to have little effect on the rate constants of the radical reactions, but reagent **1** was found to react approximately twice as fast as Bu₃SnH with a primary alkyl radical.

The LFP method employed for calibration of the radical clock was similar to that described previously (Scheme 1).⁴ The PTOC⁵ ester **2**^{4a,c} served as the radical precursor. Irradiation of **2** with a 355 nm laser

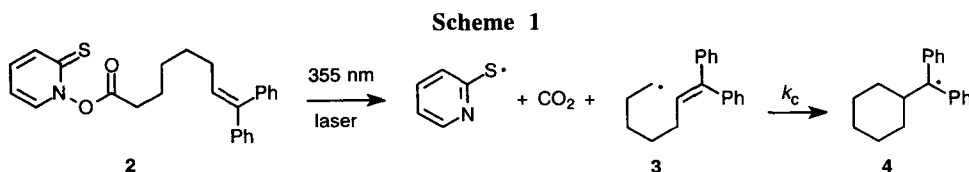


Table 1. Observed Rate Constants for Cyclization of Radical 3.

$T (^{\circ}\text{C})^{\text{a}}$	$10^{-5} \times k_{\text{c}} (\text{s}^{-1})^{\text{b}}$	$T (^{\circ}\text{C})^{\text{a}}$	$10^{-5} \times k_{\text{c}} (\text{s}^{-1})^{\text{b}}$	$T (^{\circ}\text{C})^{\text{a}}$	$10^{-5} \times k_{\text{c}} (\text{s}^{-1})^{\text{b}}$
4.8	2.46	13.0	3.24	24.5	4.49
8.5	2.80	16.9	3.77	31.8	5.55
8.7	2.89	19.2	3.94	41.4	7.18

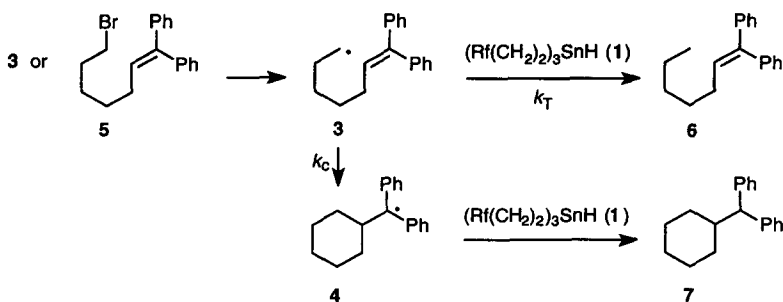
^a ± 0.2 $^{\circ}\text{C}$. ^b Observed rate constants had errors of $\leq 2\%$ at 2σ .

pulse cleaved the weak N–O bond to give the (2-pyridyl)thiyl radical and an acyloxy radical that rapidly decarboxylated to provide the target, radical clock 3. A 6-*exo* cyclization of 3 gave the diphenylalkyl radical 4, the formation of which was followed readily by time-resolved UV-spectroscopy.⁶

Rate constants for cyclization of radical 3 in PhCF_3 were determined between 5 and 41 $^{\circ}\text{C}$. The observed rate constants were in the range of $2\text{--}7 \times 10^5 \text{ s}^{-1}$ (Table 1) which is optimal for LFP studies because bimolecular reactions of 3 with another radical or with oxygen are too slow to contribute significantly to the total kinetics.⁷ From the values in Table 1, the temperature-dependent function for cyclization of 3 is given in eq 1 where θ is $2.3RT$ kcal/mol and errors limits are 2σ . The rate constant for cyclization of 3 at 20 $^{\circ}\text{C}$ is $4.0 \times 10^5 \text{ s}^{-1}$. The function in eq 1 differs slightly from that determined for cyclization of 3 in THF, and the rate constants for cyclization of 3 in BTF are slightly smaller than those measured in THF.^{4a,c} For example, the cyclization rate constant for 3 in THF at 20 $^{\circ}\text{C}$ is $4.8 \times 10^5 \text{ s}^{-1}$. Small solvent effects on the rate constants for cyclization of radical 3 were observed previously.^{4c}

$$\log (k_{\text{c}} \times \text{s}) = (9.32 \pm 0.13) - (4.98 \pm 0.17)/\theta \quad (1)$$

The rate constants for bimolecular trapping of primary radical 3 by the fluoros tin hydride reagent 1 were determined by competition kinetics (Scheme 2). Reactions of PTOC ester 2 were conducted in the presence of 0.1–0.5 M tin hydride 1 in BTF at -25 , 3, 34, and 54 $^{\circ}\text{C}$, and the bromide precursor to radical 3, 7-bromo-1,1-diphenyl-1-heptene (5), was allowed to react in BTF in the presence of 1 at 60 and 80 $^{\circ}\text{C}$ with catalytic amounts of AIBN for initiation. After evaporation of the BTF, the products 6 and 7 were isolated by distribution between the fluoros solvent perfluorohexanes (FC-72) and CH_2Cl_2 as previously described³ and analyzed by GC. Due to the low total yields of 6 plus 7 from reactions of 2 at 54 $^{\circ}\text{C}$ (as little as 13% yield),

Scheme 2

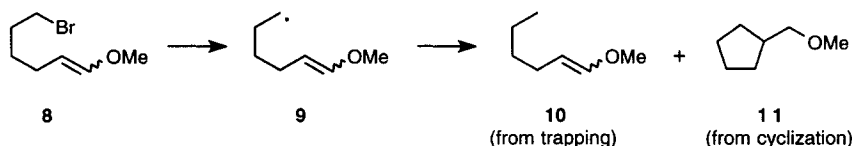
the results obtained at this temperature were discarded; PTOC esters are activated acyl derivatives, and we assume that hydrolysis by adventitious water occurred at 54 °C.⁸ With the exception of the results at 54 °C, the total GC yields of **6** plus **7** from reactions of **2** were 46–94%, and the total GC yields from reactions of bromide **5** were 74–111%.

The competition kinetic values were obtained from plots of the product ratio **6/7** versus the concentration of **1** for three to eight independent measurements at each temperature. These plots had slopes (equal to k_T/k_C) of (17.3 ± 2.1) , (11.8 ± 1.7) , (10.5 ± 1.8) , (5.7 ± 0.4) , and $(5.5 \pm 0.5) \text{ M}^{-1}$ at -25 , 3 , 34 , 60 , and 80 °C, respectively (errors at 2σ). The relative temperature-dependent function for k_T/k_C , determined with equal weighting of each of 24 independent measurements, is given in eq 2. Addition of eqs 1 and 2 gives eq 3, the temperature dependent function for reaction of the fluororous tin hydride reagent **1** with primary alkyl radical **3**. The rate constant for reaction of **1** with the primary radical at 20 °C is $3.8 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$.

$$\log ((k_T/k_C) \times M) = -(0.38 \pm 0.18) + (1.83 \pm 0.24)/\theta \quad (2)$$

$$\log (k_T \times Ms) = (8.9 \pm 0.2) - (3.1 \pm 0.3)/\theta \quad (3)$$

The rate constant for reaction of **1** at 80 °C was checked against another primary alkyl radical clock. Reactions of bromide **8**⁹ in BTF in the presence of **1** gave acyclic (**10**) and cyclic (**11**) products from trapping and cyclization, respectively, of radical **9**. From the product distributions and concentrations of tin hydride from six experiments, the ratio of rate constants k_T/k_C was $(13 \pm 7) \text{ M}^{-1}$. Combining this ratio with the rate constant for cyclization of radical **9** at 80 °C (ca. $2 \times 10^6 \text{ s}^{-1}$)⁹ and assuming a negligible solvent effect on the rate constant for cyclization gives an approximate value for k_T at 80 °C of $2\text{--}3 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$, a reasonable agreement with the value of $1.0 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ calculated from eq 3.



The rate constants for radical trapping by the fluororous tin hydride reagent **1** are about 2 times as great as those for reaction of Bu_3SnH with a primary alkyl radical; for example, the rate constants for reactions of **1** with radical **3** and Bu_3SnH with a primary alkyl radical at 20 °C are $3.8 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ and $2.2 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$, respectively.^{10,11} Rate constants for reactions of hydrogen atom donors with alkyl radicals should be relatively insensitive to solvent effects, and it was possible to demonstrate the absence of a significant solvent effect for the reaction of Bu_3SnH with radical **3** in BTF.¹¹ The increased rate constants for reaction of **1** apparently reflect an inherently slightly greater reactivity of the fluororous tin hydride with the primary alkyl radical. We speculate that this is due to electron withdrawal by the fluorinated groups that imparts a slightly more “electrophilic” character to this tin hydride in comparison to Bu_3SnH resulting in an acceleration in the reaction with the “nucleophilic” primary alkyl radical.

While the kinetic differences between fluororous tin hydride **1** and tributyltin hydride are interesting from the standpoint of radical rate constants, from the preparative standpoint they are not significant. In other words, the fluororous tin hydride **1** should closely mimic tributyltin hydride in preparative chemistry applica-

tions. The small kinetic difference further suggests that modifications incorporating perfluoroalkyl chains with "ethylene spacers" should be generally applicable for converting standard radical reagents into fluororous analogs.

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References and Notes

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- A series of reactions of bromide **5** with Bu₃SnH in BTF at 80 °C was conducted. The value of k_T/k_C from this study was $(2.9 \pm 0.2) M^{-1}$. Using the rate constant for cyclization of **3**, this gives a value for k_T for Bu₃SnH at 80 °C of $5 \times 10^6 M^{-1} s^{-1}$ which is essentially the same value as one calculates ($6 \times 10^6 M^{-1} s^{-1}$) from the Arrhenius function for reaction of Bu₃SnH with a primary alkyl radical at 80 °C in hydrocarbon solvent.¹⁰ Note that **1** reacted with radical **3** at 80 °C with a rate constant of $1.0 \times 10^7 M^{-1} s^{-1}$.

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