Acknowledgment. We are grateful to Professor M. Newcomb for sharing the cyclopropylmethyl rearrangement data prior to publication.

Supplementary Material Available: Tabulations of kinetic data and Arrhenius plots for the entries of Table I and Fortran data acquisition and reduction programs for collection and treatment of raw transmittance data including correction for second-order termination (13 pages). Ordering information is given on any current masthead page.

A Convenient Method for Kinetic Studies of Fast Radical Rearrangements. Rate Constants and Arrhenius Function for the Cyclopropylcarbinyl Radical Ring Opening

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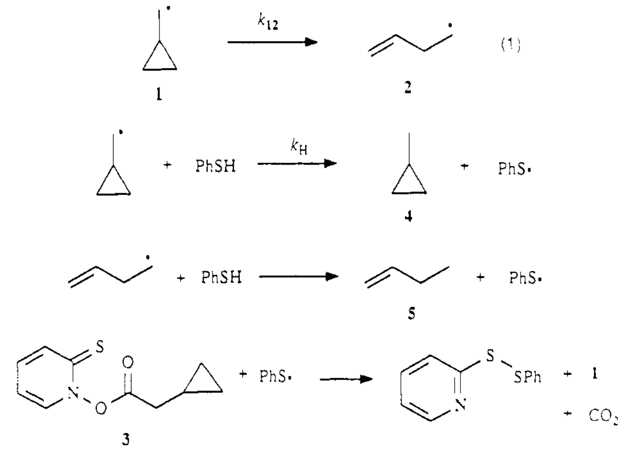
Abstract: An indirect method for studying the kinetics of radical rearrangements employing *N*-hydroxypyridine-2-thione esters as radical precursors and hydrogen atom transfer from thiophenol as the basis trapping reaction is demonstrated in a study of an archetypal fast radical reaction, the cyclopropylcarbinyl radical ring opening. Rate constants measured over the temperature range −37 to 50 °C gave a temperature-dependent function for the ring opening of $\log (k/\mathrm{s}^{-1}) = (13.0 \pm 0.14) - (6.8 \pm 0.2)/\theta$ and a rate constant for ring opening at 25 °C of $1.0 \times 10^8\ \mathrm{s}^{-1}$. The kinetic values from this work were combined with rate data from low-temperature ESR studies and higher temperature nitroxyl radical trapping studies to give an Arrhenius function of $\log (k/\mathrm{s}^{-1}) = 13.15 - 7.05/\theta$ that is recommended for calculations of rate constants for the title ring opening.

The measurement of carbon radical reaction rate constants can be accomplished by direct or indirect methods. For rearrangements of alkyl radicals that contain no chromophore and are present in low concentrations, indirect kinetic measurements, where the reaction of interest competes with a reaction with a known rate constant, are common, and the "tin hydride" method has been the most exploited indirect method. Accurate rate constants for second-order reactions of Bu_3SnH with several simple alkyl radicals are available,[1] and reactions of Bu_3SnH are relatively insensitive to carbon radical structure. These two features permit one to estimate with confidence the rate constants for radical reactions with Bu_3SnH, and some of the most widely used "radical clocks" such as 5-hexenyl have been calibrated by this approach.[2] However, the tin hydride method has been limited in the scope of radicals and in the range of rate constants that could be studied. The former limitation (usually requiring an alkyl halide precursor for the desired radical) was relieved by the development of *N*-hydroxypyridine-2-thione esters R-PTOC, where PTOC = [((1*H*)-pyridine-2-thione)oxy]carbonyl, by Barton[3] which have been shown to be excellent radical precursors in indirect kinetic studies.[4,5] The latter limitation is an inherent property of the tin hydride; very fast radical rearrangements ($k_r > 1 \times 10^8\ \mathrm{s}^{-1}$ at 25 °C) will overwhelm the trapping reaction ($k_H = 2.4 \times 10^6\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ at 25 °C).[1] Since Barton's alkyl-PTOC compounds participate in radical chain reactions with a variety of radicals including thiyl radicals, the use of these precursors permits alternative basis reactions for the indirect measurement of fast radical rearrangements. With accurate values for the rate constants for hydrogen atom transfer from PhSH now available,[6] we demonstrate this convenient method in a kinetic study of the ring opening of the cyclopropylcarbinyl radical **1** to the 3-butenyl radical **2** (Scheme I). Our results, measured over the temperature range −37 to 50 °C, give a reasonable Arrhenius function that is independently consistent with measurements of k_{12} from −145 to 122 °C.

Scheme I



The ring opening of the cyclopropylcarbinyl radical to the 3-butenyl radical (eq 1 in the scheme) is a fast radical rearrangement that holds a position of distinction in mechanistic studies involving "radical clocks" and "mechanistic probes". Numerous studies have employed potential precursors of this radical or its analogues in attempts to implicate radical intermediates in a reaction pathway by detection of the products from the radical ring opening, and the rate constant for the conversion in eq 1 is probably the most often quoted fast radical rearrangement velocity. Rate constants for this ring opening were

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(1) Johnston, L. J.; Lusztyk, J.; Wayner, D. D. M.; Abeywickreyma, A. N.; Beckwith, A. L. J.; Scaiano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 4595.

(2) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317.

(3) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901.

(4) Newcomb, M.; Park, S.-U. *J. Am. Chem. Soc.* **1986**, *108*, 4132.

(5) *N*-hydroxypyridine-2-thione esters are also useful radical precursors for ESR studies: Ingold, K. U.; Lusztyk, J.; Maillard, B.; Walton, J. C. *Tetrahedron Lett.* **1988**, *29*, 917.

(6) Franz, J. A.; Bushaw, B. A.; Alnajjar, M. S. *J. Am. Chem. Soc.*, preceding paper in this issue.

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Table I. Products and Rate Constants for Reactions of Cyclopropylcarbinyl Radical[a]

temp,[b] °C	$[\mathrm{PhSH}]_m$,[c] M	[5]/[4]	$\log (k_{12}/\mathrm{s}^{-1})$[d]
−37	0.49	0.17	6.72
−19	0.49	0.35	7.16
3	0.49	0.78	7.62
20	0.49	1.43	7.94
20	0.98	0.68	7.94
38	0.49	2.38	8.23
50	0.49	2.86	8.41

[a] Reactions were run in THF. [b] ±1 °C. [c] Average concentration of PhSH. [d] Calculated from eq 2 by using a value of $\log (k_H/\mathrm{M}^{-1}\,\mathrm{s}^{-1}) = 9.41 - 1.74/\theta$ (ref 6).

studied by Ingold at low temperature by the kinetic ESR method.[7] At higher temperatures, a crude rate constant for the ring opening could be estimated from the product distribution observed by Bergman in reactions of cyclopropylcarbinyl bromide with $\mathrm{Bu_3SnH}$[8a] and by Beckwith in the reaction of cyclopropylcarbinyl chloride with $\mathrm{Ph_3SnH}$.[8b] Mathew and Warkentin measured rate constants for the **1** to **2** conversion in the temperature range 30–89 °C by allowing the rearrangement of **1** to compete with trapping by a nitroxyl radical (1,1,3,3-tetramethylisoindolin-2-yloxy) and with assumptions concerning the rate of radical coupling in this system.[9] Quite recently, Beckwith's group has used the same nitroxyl trapping method for measuring rate constants for opening of **1** in the temperature range 40–125 °C employing an experimentally determined rate constant for the basis trapping reaction.[10]

The necessary PTOC precursor for our study (**3**) was prepared by the standard method[3] from cyclopropylacetic acid. Precursor **3** was allowed to react (with photochemical initiation) in the presence of thiophenol. The cyclopropylcarbinyl radical **1** formed from **3** was trapped by thiophenol to give methylcyclopropane (**4**) in competition with ring opening to radical **2**, and radical **2** was also trapped by thiophenol. Although alkylthiyl radicals are known to react with alkyl-PTOC precursors in radical chain propagation steps, it was not clear that the more stable thiophenoxy radical would successfully propagate a chain reaction by addition to precursor **3**. This propagation step apparently did occur as evidenced by our detection of phenyl 2-pyridyl disulfide in the product mixture; however, the reaction was complex, and diphenyl disulfide was also detected. Irrespective of the details of the propagation reactions, under our conditions products **4** and **5** were the only products from the carbon radicals, no alkyl pyridyl sulfides or alkyl phenyl sulfides were formed in detectable amounts. Thus, the method is useful for the kinetic information we sought even if the details of the chain propagation steps are unclear. A simplified reaction scheme is presented in Scheme I.

Alkyl radicals can add to esters like **3**, but this self-trapping reaction is too slow[11] to compete with the reaction with PhSH. In the presence of a large excess of PhSH, the rate constant k_{12} can be calculated by eq 2 where k_H is the rate constant for reaction

$$k_{12} = k_H[\mathrm{PhSH}]_m[\mathbf{5}]/[\mathbf{4}] \qquad (2)$$

of **1** with PhSH, $[\mathrm{PhSH}]_m$ is the average concentration of PhSH over the course of the reaction, and [**5**]/[**4**] is the observed product ratio.

The results of studies over the temperature range −37 to 50 °C are given in Table I. The value for k_H was determined from the Arrhenius function for reaction of PhSH with butyl radical recently measured by Franz.[6] Rate constants for reactions of PhSH with simple alkyl radicals are relatively insensitive to radical structure, even less sensitive than those for reactions of $\mathrm{Bu_3SnH}$, and it would appear to be reasonable to assume that **1** and butyl radical react with PhSH with equal rate constants.[12] We also must assume that there is no solvent effect on k_H in changing from nonane[6] to THF. Rate constants for trapping of **1** calculated by eq 2 are included in Table I. These rate constants give the Arrhenius function for the **1** to **2** conversion in eq 3 where θ is

$$\log (k_{12}/\mathrm{s}^{-1}) = (13.0 \pm 0.14) - (6.8 \pm 0.2)/\theta \qquad (3)$$

$2.3RT$ kcal/mol and the errors in the fit of the function are 2σ; the error limits do not contain the uncertainty of the values for k_H. The calculated rate constant for ring opening at 25 °C is $1.0 \times 10^8\ \mathrm{s}^{-1}$, about half of the value reported by Mathew and Warkentin,[9] and slightly higher than the value found by Beckwith.[10]

The well-correlated Arrhenius function ($r^2 = 0.999$) of eq 3 is shown graphically in Figure 1. Also included in the figure are the low-temperature kinetic ESR results,[7] the nitroxyl trapping results,[9,10] and the rate constants calculated for tin hydride trapping[8] of **1**. The pioneering kinetic ESR studies of the **1** to **2** rearrangement reported by Ingold[7] gave kinetic values at too low a temperature range to permit an accurate extrapolation to 25 °C. Thus, kinetic values for this reaction at warmer temperatures have relied upon competition methods. The nitroxyl trapping study reported by Mathew and Warkentin[9] was elegant, but unfortunately, it was apparent that radical couplings were not occurring at the diffusion rate constant. The authors[9] were thus required to modify their kinetic values determined against diffusion by a correction factor, and they chose a factor of 0.2 which gave a rate constant at 25 °C of $2.1 \times 10^8\ \mathrm{s}^{-1}$. This value at 25 °C was close to the rate constant calculated from the product distribution reported by Bergman[8a] for the reaction of **1** with 0.74 M $\mathrm{Bu_3SnH}$ (a 90:1 mixture of **5** to **4**) and the known[1] rate constant for the tin hydride reaction with primary radicals. However, Bergman reported another product distribution (11:1 in neat, 3.8 M, $\mathrm{Bu_3SnH}$) that gives a rate constant for k_{12} of $1 \times 10^8\ \mathrm{s}^{-1}$ at 25 °C and that would lead to a correction factor for the nitroxyl results of 0.1. Indeed, Beckwith's kinetic results[10] for trapping by the same nitroxyl radical give a correction factor of 0.08.

The Beckwith, Bowry, and Moad (BBM)[10] kinetic values for ring opening of **1** are based on the assumption that trapping of **1** by the nitroxyl radical will have the same rate constant as trapping of 5-hexenyl by the nitroxyl radical. Ultimately then, these values are derived from the well-trusted rate constants for reactions of $\mathrm{Bu_3SnH}$ with simple primary radicals[1] that were used to calibrate the 5-hexenyl system. The trapping rate constants are further supported by absolute rate constants for reactions of nitroxyl with radicals recently measured by the laser flash method.[13] Accepting the caveat concerning the kinetic assumption,[12] these results should be highly reliable. The function in eq 3 agrees remarkably well with the BBM kinetic results in the temperature range 80–122 °C; the differences are only 6–8%. However, the differences at 40 and 59 °C, while well within the experimental errors, are ~25%. The result is that the BBM data give a greater log A and E_A than our data, and the extrapolated BBM value at −37 °C is smaller than our experimental value by a factor of 2.5.

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(7) Maillard, B.; Forrest, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 7024.

(8) (a) Kinney, R. J.; Jones, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 7902. (b) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1473.

(9) Mathew, L.; Warkentin, J. *J. Am. Chem. Soc.* **1986**, *108*, 7981.

(10) Beckwith, A. L. J.; Bowry, V. W.; Moad, G. *J. Org. Chem.* **1988**, *53*, 1632.

(11) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1987**, *28*, 1615.

(12) This assumption may be questioned. The cyclopropylcarbinyl radical might be stabilized by a resonance interaction not available in the simple primary radical, and the rate constants for trapping of **1** might not be equal to those for trapping of butyl. Unfortunately, this potential problem plagues all of the indirect measurements of the ring opening of **1** since each is dependent on basis rate constants for the trapping reactions determined for reactions of simple primary radicals. However, the consistency of the kinetic values determined for ring opening of **1** at 25 °C by the tin hydride method,[8a] the nitroxyl trapping method,[10] and the PTOC/thiol method of this work suggests either that the assumption is valid for each trapping reagent or that the rate constants for reaction of **1** with each trapping reagent studied thus far are slower than those for reaction of the trapping agents with primary radicals by about the same percentage. Further, AM1 calculations[6] indicate that the methylene rotation barrier in **1** is only 1 kcal/mol, and thus no appreciable resonance interaction is evident. Given the kinetic constraint, the results from the MO calculations, and the fact that our data can be extrapolated successfully to the low-temperature region in which direct ESR measurements of the opening of **1** were made, we believe the assumption is reasonable.

(13) Chateauneuf, J.; Lusztyk, J.; Ingold, K. U. *J. Org. Chem.* **1988**, *53*, 1629.

Undoubtedly, the divergence in the results from the two studies represents accumulated systematic errors in the basis rate constants.[14]

Extrapolation of the Arrhenius function of eq 3 to low temperatures gives values that are only slightly greater than the low-temperature ESR kinetic results as shown in the figure, and extrapolation to higher temperatures gives values that are virtually coincident with the BBM results. Thus, the kinetic results in this work may represent the most accurate single set of kinetic results. More importantly, however, our results provide kinetic values at temperatures intermediate to those studied by the Beckwith and Ingold groups. An equally weighted combination of our data with the kinetic data from these two groups[7,10] gives the Arrhenius function in eq 4, which is also shown graphically in the figure.

$$\log (k_{12}/\mathrm{s}^{-1}) = 13.15 - 7.05/\theta \qquad (4)$$

Given the variations in the methods and the wide temperature range of the measurements, the function in eq 4 should prove to be quite reliable, and we recommend its use for calculation of the rate constants for opening of cyclopropylcarbinyl radical; the calculated rate constant at 25 °C using eq 4 is $k_{12} = 9.4 \times 10^7$ s^{-1}. The kinetic values calculated by eq 3 and 4 differ by less than 5% in the range 45–150 °C.[15]

In summary, the recently determined values for reactions of alkyl radicals with PhSH[6] combined with the use of Barton's PTOC radical precursors (the PTOC/thiol method) provides a powerful and convenient method for measuring the rate constants of very fast carbon radical rearrangements at intermediate and warm temperatures.[17] Simple GC analyses are possible, and rate constants exceeding 1×10^9 s^{-1} at 25 °C can be determined by using PhSH trapping as the basis reaction. Since the immediate precursors to the PTOC compounds are carboxylic acids and since the PTOC compounds are easily managed and stable when shielded from light, the kinetics of a wide variety of alkyl radicals containing highly strained skeletons can now be studied.

Experimental Section

1-[[(Cyclopropylmethyl)carbonyl]oxy]-2(1*H*)-pyridinethione (3) was prepared by the standard method.[3] Cyclopropylacetic acid[18] (0.5 g, 5.0 mmol), *N*-hydroxypyridine-2-thione (0.63 g, 5.0 mmol), and *p*-(dimethylamino)pyridine (65 mg, 0.55 mmol) were dissolved in 50 mL of CH_2Cl_2 at room temperature in a vessel shielded from light. To the reaction mixture was added dropwise a solution of dicyclohexylcarbodiimide (1.13 g, 5.5 mmol) in 10 mL of CH_2Cl_2 over 15 min. The mixture was stirred for 12 h. Solvent was distilled at reduced pressure, and the residue was dissolved in ethyl acetate and washed with aqueous 1 M $KHSO_4$, water, and aqueous 5% $NaHCO_3$. The solution was dried over $MgSO_4$, and the solvent was distilled at reduced pressure to give a residue that was purified by radial chromatography on silica gel with 3:1 (v/v) ethyl acetate/hexanes elution. Compound **3** was isolated in 45% yield: mp 45–47 °C; ^{1}H NMR (200 MHz) δ 0.3 (q, 2 H), 0.65 (dd, 2 H), 1.2 (m, 1 H), 2.6 (d, 2 H), 6.6 (m, 1 H), 7.2 (m, 1 H), 7.6 (d, 1 H), 7.7 (d, 1 H).

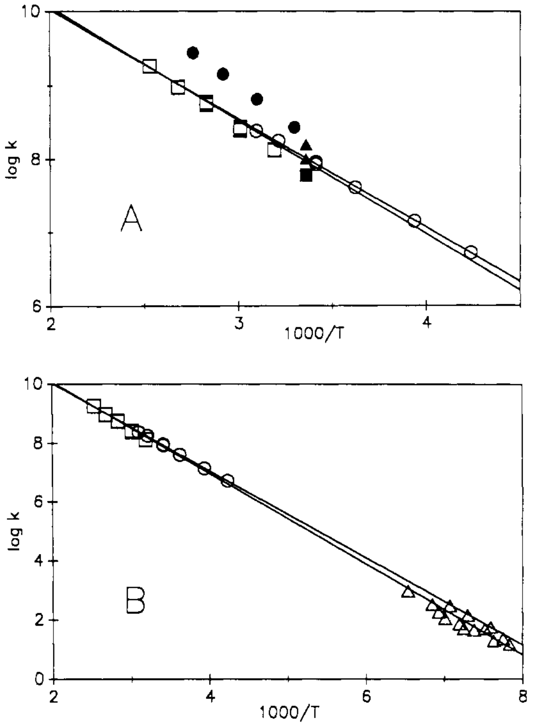

Figure 1. Rate constants and calculated Arrhenius functions (eq 3 and 4) for ring opening of cyclopropylcarbinyl radical: (○) this work; (△) ref 7; (●) ref 9; (□) ref 10; (▲) calculated from data in ref 8a; (■) ref 8b. In both graphs, eq 3 is the upper line.

Kinetic Study. Pyrex tubes (20 cm, 10-mm o.d.) were equipped with a stir bar, sealed with a septum, and flushed with N_2. The tubes were then shielded with Al foil and cooled to −78 °C. A stock solution of **3** in degassed THF was prepared, and an aliquot containing 0.02 mmol of **3** was added to each of the tubes. The desired amount of PhSH (distilled from $CaSO_4$) was then added, and the volume was adjusted to 1.0 mL with additional degassed THF. The tubes were sealed under vacuum and allowed to equilibrate at the desired temperature for ca. 2 min. The shields were removed, and the reactions were irradiated with a 300-W tungsten filament lamp for 15 min. (In control reactions with other PTOC precursors, reactions were complete within 5 min in our apparatus.) The tubes were then cooled to −78 °C and opened. The mixtures were analyzed by GC using a 2.2-m, 3-mm i.d. glass column containing an active phase[19] of $AgNO_3$ in ethylene glycol supported on Chromasorb P (1:10:25, w/w/w, respectively) at 25 °C. Hydrocarbons **4** and **5** were identified by their retention times. The GC was equipped with a flame-ionizing detector; weight response factors were assumed to be equal.

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(14) Extrapolation of each data set to the low-temperature region of the kinetic ESR measurements suggests that our log A and E_A terms are slightly low and the BBM terms are somewhat high. The same trend has recently been observed in as yet unreported measurements of the rate constants for ring opening of the 2,2-dimethylcyclopropylcarbinyl radical made in the two laboratories.

(15) The log A terms in eq 3 and eq 4 are in the range expected for a first-order reaction in which ΔS^* would be negligible as discussed previously by Ingold;[7] specifically, log A_{298} = 13.1 for $\Delta S^* = 0$ eu.[16a] Similar log A values (12.4–13.2) have been reported for various cyclobutylcarbinyl radical ring openings.[16b] The small entropy change in the **1** to **2** conversion is confirmed in the calculations by Franz.[6] The combination of the high-temperature results from our work and the BBM study with the low-temperature measurements to give the expected log A term suggests that the kinetic values at the higher temperatures are reasonably accurate and provides support for the assumptions in our work and the BBM study concerning the rate constants of the trapping reaction.

(16) (a) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley-Interscience: New York, 1976. (b) Beckwith, A. L. J. In *Landolt-Börnstein Numerical Data and Functional Relationships in Science and Technology*, New Series; Fischer, H., Ed.; Springer-Verlag: Berlin, 1984; Group II, Vol. 13, Subvol. a.

(17) We have used the technique between −78 and 60 °C; at temperatures above 60 °C, radical chain initiation by thermal decomposition of the precursors during the temperature equilibration stage could introduce errors, and the precursor should be added to a preequilibrated reaction mixture.

(18) (a) Rawson, R. J.; Harrison, I. T. *J. Org. Chem.* **1970**, *35*, 2057. (b) Bigley, D. B.; Fetter, C. L. *J. Chem. Soc., Perkin Trans. 2* **1979**, 122.

(19) Shabtai, J.; Herling, J.; Gil-Av, E. *J. Chromatogr.* **1963**, *11*, 32.