Rate Constants and Arrhenius Functions for Rearrangements of the 2,2-Dimethyl-3-butenyl and (2,2-Dimethylcyclopropyl)methyl Radicals

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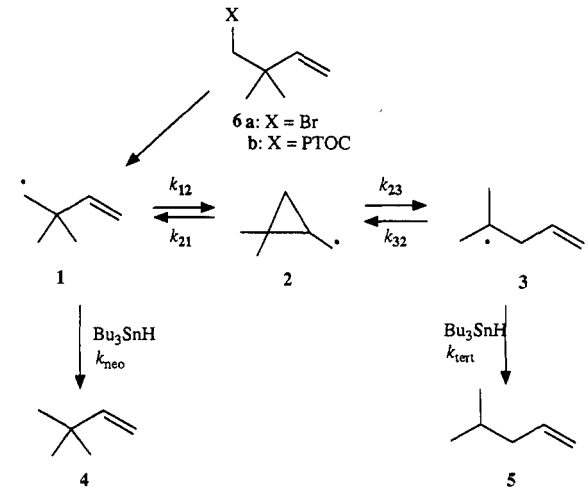
Rate constants for the rearrangement of the 2,2-dimethyl-3-butenyl radical (**1**) to the 1,1-dimethyl-3-butenyl radical (**3**) via the intermediate (2,2-dimethylcyclopropyl)methyl radical (**2**) were measured over the temperature range 74 to −78 °C by the competition method using the reaction of radical **1** with Bu_3SnH as the basis reaction. Rate constants for ring opening of radical **2** to both **1** and **3** were measured over the temperature range 50 to −78 °C by competition against reaction of **2** with PhSH. Arrhenius functions for the **1** to **3**, **1** to **2**, **2** to **1**, and **2** to **3** conversions were calculated; at 25 °C, the rate constants for these conversions are 4.8×10^6, 5.6×10^6, 1.2×10^8, and 7.7×10^8 s^{-1}, respectively. At room temperature, cyclization of *gem*-dimethyl-substituted radical **1** is accelerated by about 3 orders of magnitude over its parent, 3-butenyl radical. Ring opening of **2** is about 1 order of magnitude faster than ring opening of its parent, cyclopropylcarbinyl radical. For the **1** to **2** conversion, K_{12} varies from 0.05 at 25 °C to 0.02 at −78 °C, ΔH_{12} is 1.0 kcal/mol, ΔS_{12} is −2.7 eu, and ΔG_{12} at 25 °C is 1.8 kcal/mol.

Radicals that undergo characteristic skeletal rearrangements have been increasingly employed as "clocks" for kinetic studies of reactions that are known to proceed through free-radical intermediates.[1] In this approach, the reaction of interest competes with a first-order rearrangement, and the rate constant of interest can be determined from the product ratio and the known first-order rate constant. Carbon-centered radical clocks with rearrangement rate constants from 1×10^3 to 1×10^8 s^{-1} have been calibrated. We desired clocks that could be used to measure rate constants for electron-transfer reactions to radicals; these clocks must have structures such that they undergo a radical rearrangement that does not have an indistinguishable carbanion-rearrangement counterpart. In this paper, we report the kinetic values for rearrangement of two such radicals, the 2,2-dimethyl-3-butenyl radical (**1**) and the (2,2-dimethylcyclopropyl)methyl radical (**2**).

The 2,2-Dimethyl-3-butenyl Radical Rearrangement

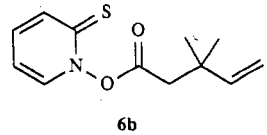
The 2,2-dimethyl-3-butenyl radical (**1**) rearranges to the 1,1-dimethyl-3-butenyl radical (**3**) via radical **2**. Rate constants for the overall rearrangement of **1** to **3** were reported by Ingold and Warkentin, who used the kinetic ESR method at low temperatures and determined one warm-temperature kinetic value by spin trapping.[2a] An attempt to measure this rate constant against trapping of **1** by CCl_4 was unsuccessful because the rearrangement was too fast.[2b] In a preliminary communication, we reported rate constants for rearrangement of **1** by competition between the rearrangement and trapping of the unrearranged radical by Bu_3SnH, the tin hydride method (Scheme I).[3] At the time of our preliminary report, the rate constants for reaction of neopentyl radical with Bu_3SnH were not available, and we used the rate constants for reactions of primary radicals with the hydride for kinetic values for the basis trapping reaction. Our warm-temperature results were combined with the low-temperature values previously reported to give an Arrhenius function.[3] In this work, we have extended the range of temperatures of the kinetic

Scheme I

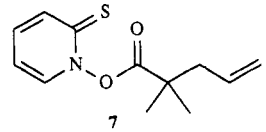


study and used a more appropriate model reaction, the reaction of neopentyl radical with Bu_3SnH, for the kinetic values of the basis trapping reaction.

In the tin hydride method, one takes advantage of the fact that the rates of reaction of Bu_3SnH with alkyl radicals are relatively insensitive to radical structure.[4] Thus, the known rate constants for reaction of Bu_3SnH with neopentyl and with tertiary radicals[4] can be taken as good approximations for the rate constants for reactions of Bu_3SnH with **1** and **3**, respectively. Accordingly, the yields of the hydrocarbon products 3,3-dimethyl-1-butene (**4**) and 4-methyl-1-pentene (**5**) found from the competition can be used to calculate the rate constant for rearrangement.



6b



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We employed two sources for radical **1**, 4-bromo-3,3-dimethyl-1-butene (**6a**) and the *N*-hydroxypyridine-2-(1*H*)-thione ester of 3,3-dimethyl-4-pentenoic acid, **6b**, where PTOC is [(2-thioxo-1(2*H*)-pyridyl)oxy]carbonyl.

(1) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317–323.
(2) (a) Chatgilialoglu, C.; Ingold, K. U.; Tse-Sheepy, I.; Warkentin, J. *Can. J. Chem.* **1982**, *61*, 1077–1081. (b) Lindsay, D. A.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 7087–7093.
(3) Newcomb, M.; Williams, W. G. *Tetrahedron Lett.* **1985**, *26*, 1179–1182.
(4) Johnston, L. J.; Lusztyk, J.; Wagner, D. M.; Abewickreyma, A. N.; Beckwith, A. L. J.; Scaiano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 4594–4596.

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Table I. Product Ratios and Rate Constants for Reactions of Radical 1

precursor	temp,[a] °C	$[Bu_3SnH]_m$	4/5[b]	log (k_{13}/s^{-1})[c]
6a[d]	74	0.53	0.154	7.33
	71	0.91	0.283	7.29
	61	0.53	0.185	7.19
	60	0.91	0.341	7.15
	52	0.53	0.234	7.04
	49	0.17	0.074	7.03
		0.38	0.179	6.99
		0.55	0.256	7.00
		0.90	0.398	7.02
	37	0.53	0.272	6.88
		0.91	0.524	6.83
6b[e]	3	0.35	0.455	6.25
	−20	0.35	0.787	5.81
	−77	0.35	5.88	4.26
	−78	0.26	2.68	4.47
		0.35	3.58	4.49
		0.44	4.97	4.43
		0.53	5.36	4.48

[a] Within ±1 °C. [b] Observed ratio of products 4 and 5. [c] Solved from eq 3. [d] Benzene solvent. [e] THF solvent.

N-Hydroxypyridine-2(1*H*)-thione esters (PTOC esters), developed by Barton's group,[5a] react in radical chain reactions with Bu_3SnH by the sequence (1) addition of the Bu_3Sn radical to sulfur with concomitant or rapid subsequent cleavage of the N–O bond to give a carboxy radical, (2) decarboxylation of the carboxy radical to give an alkyl radical, and (3) reduction of the alkyl radical by Bu_3SnH. The PTOC esters have been shown to be excellent sources of radicals for kinetic studies.[5b] Alkyl radicals can react with these precursors, but this self-trapping reaction is too slow to be important when a good hydride donor like Bu_3SnH is present in a large excess.[5c]

With bromide **6a** as the source of radical **1**, reactions were run in benzene over the temperature range 37–74 °C with AIBN initiation. Ester **6b** offers the advantage in kinetic studies that reactions can be initiated by visible-light photolysis of the precursor, and, thus, reactions can be conducted at low temperatures. We used **6b** as a source of **1** at temperatures down to −78 °C in THF solvent. Reactions were run to complete consumption of precursor **6**. Yields of hydrocarbon products **4** and **5** were typically 85–100% of the mass balance as determined by GC. Table I contains the results.

Scheme I shows the accepted pathway[2] for isomerization of radical **1** to radical **3**. This mechanism is believed to be operative in a broad range of 1,2-migrations of carbon radicals containing an unsaturated site bonded to atom 2 as discussed below. Nevertheless, the results in Table I only give the overall rate constant for isomerization of **1** to **3** irrespective of the pathway, and one may question whether radical **2** actually is an intermediate in this isomerization. The kinetic results for the ring openings of **2** in the next section show that Scheme I is kinetically viable, and the log *A* term we obtained for the **1** to **3** isomerization is consistent with a mechanism involving formation of intermediate **2** as opposed to one involving a fragmentation–recombination. In addition, direct confirmation of the intermediacy of **2** in the **1** to **3** isomerization was also found; when precursor **6b** was allowed to react in the presence of the trapping agent thiophenol, 1,1,2-trimethylcyclopropane from trapping of **2** was found in the predicted yield.[6]

(5) (a) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901–3924. (b) Newcomb, M.; Park, S. U. *J. Am. Chem. Soc.* **1986**, *108*, 4132–4134. (c) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1987**, *28*, 1615–1618.

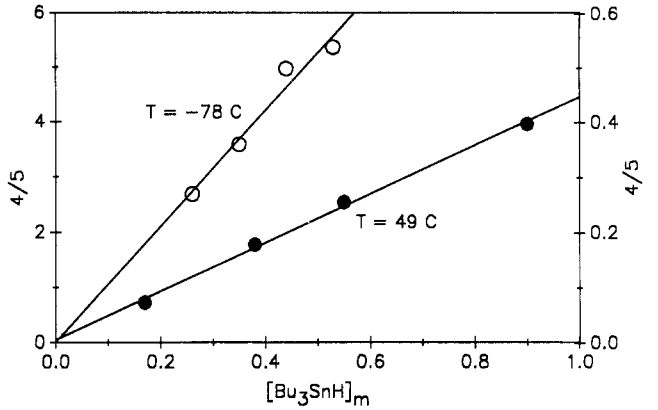


Figure 1. Data from Table I for reactions at −78 °C (left axis) and 49 °C (right axis).

All of the rate constants of interest are shown in Scheme I. The reaction of radical **2** with Bu_3SnH is also possible, but the first-order fragmentation of **2** is so fast (see below) that effectively no trapping of **2** by Bu_3SnH occurred.[6] For the sequence in Scheme I, a steady-state approximation can be made for radicals **2** and **3**. The kinetic treatment is further simplified by the fact that an excess of Bu_3SnH was employed in the studies; thus, the second-order trapping of radicals by Bu_3SnH could be treated as a pseudo-first-order process where $[Bu_3SnH]_m$ is the average concentration of the tin hydride during the course of the reaction. The ratio of products **4** to **5** can be expressed by eq 1, where the subscripts to the rate constants indicate the radical conversion in a first-order process (i.e., k_{12} is the rate constant for cyclization of **1** to **2**) or the radical trapping reaction in a second-order process.

$$4/5 = (k_{neo}k_{32}k_{21})/(k_{tert}k_{23}k_{12}) + (k_{neo}(k_{21} + k_{23})[Bu_3SnH]_m)/(k_{23}k_{12}) \quad (1)$$

Equation 1 suggests that kinetic solutions for the rearrangement of **1** might be complicated, but in practice they were not. Consider the terms in the intercept of the function. The ratio of the rate constants for reaction of Bu_3SnH with neopentyl radical (k_{neo}) and a tertiary radical (k_{tert}) varies from 2 to 3 over the temperature range we studied,[4] and the ratio of the rate constants for fragmentation of radical **2** (k_{21}/k_{23}) was consistently 0.14–0.15 (see below). Thus, the value of the intercept in eq 1 is controlled mainly by the ratio k_{32}/k_{12}. The rate constant for cyclization of radical **3** to **2** should be comparable to that for cyclization of 3-butenyl radical to cyclopropylcarbinyl radical (ca. 8×10^3 s^{-1} at 25 °C),[7] but that for cyclization of radical **1** is much greater since **1** experiences an appreciable accelerating Thorpe–Ingold effect. Thus, with $k_{12} \gg k_{32}$, the intercept in eq 1 was expected to be nearly equal to 0. The data for rearrangement of radical **1** at 49 °C show that this prediction is accurate at high tempera-

(6) Sealed tubes containing precursor **6b** (0.2 M) and thiophenol (1.9 M) in THF were equilibrated at 52 and 100 °C, and reactions were initiated by visible-light irradiation. Products were determined by GC. 1,1,2-Trimethylcyclopropane (**9**) was formed in 0.65% and 0.71% yields at 52 and 100 °C. From the Arrhenius functions in Table III and with the assumption that PhSH reacts with radical **1** with a rate constant equal to that for reaction with a simple primary radical, the calculated yield of **9** is 0.64% and 0.86% at the respective temperatures. These yields are close to the maximum possible yields of **9** from **6b** when PhSH is used as the trapping agent; lower yields of **9** would be obtained at lower temperatures. Lower yields of **9** from **6b** would be found at any temperature when Bu_3SnH is used as the trapping agent.

(7) The reported[8] rate constants for cyclization of 3-butenyl radical measured against trapping by Bu_3SnH must be corrected for the revised[4] rate constants for reaction of Bu_3SnH with a primary radical.

(8) Effio, A.; Griller, D.; Ingold, K. U.; Beckwith, A. L. J.; Serelis, A. K. *J. Am. Chem. Soc.* **1980**, *102*, 1734–1736.

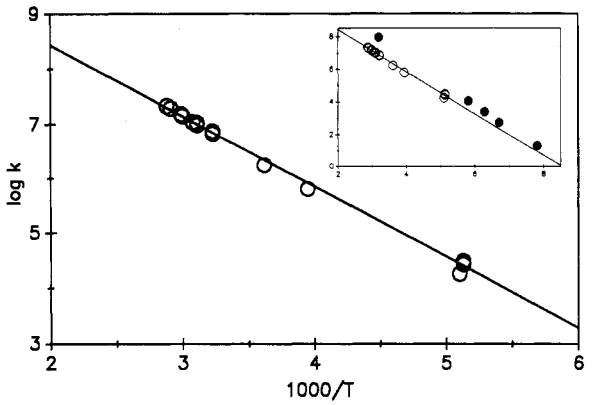


Figure 2. Arrhenius plot for isomerization of 1 to 3. The insert compares this data to that reported in ref 2.

tures (Figure 1). The graph of 4/5 vs $[Bu_3SnH]_m$ is well correlated (r = 0.9986) and has a near-zero intercept of 0.006. For the warmer temperatures we studied, the intercept in eq 1 represents only a small contribution to the 4/5 ratio and can be ignored. At low temperatures the value of the intercept in eq 1 was even less important because the ratio 4/5 was larger; for the four experiments run in one batch at −78 °C, a plot of 4/5 vs $[Bu_3SnH]_m$ had an intercept of 0.009 (Figure 1). As a further test of the expected large k_{12} to k_{32} ratio, radical 3 was formed in THF at 25 °C in radical chain reactions from its alkyl-PTOC precursor 7 in the presence of low concentrations (0.03–0.07 M) of Bu_3SnH. In these reactions, no 4 as formed to the limit of our GC detection capabilities (<0.1%).

The slope in eq 1 contains the rate constants for cyclization of 1 and 3 and for fragmentation of 2. These rate constants can be expressed in terms of the rate constant for the overall conversion of radical 1 to 3 since the velocity of the latter conversion is simply the velocity of the cyclization of radical 1 multiplied by the partition function for radical 2 as shown in eq 2. Substituting the equality in eq 2 into the slope in eq 1 and allowing that the intercept in eq 1 is approximately 0 gives eq 3. Using the experimentally measured ratio 4/5 and $[Bu_3SnH]_m$ and the appropriate value for k_{neo},[4] rate constants for isomerization of radical 1 to radical 3 were calculated. The results are included in Table I.

$$k_{13} = k_{12}k_{23}/(k_{23} + k_{21}) \quad (2)$$

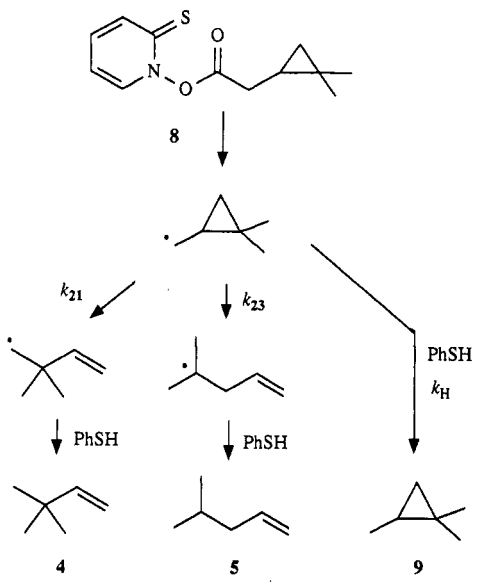
$$4/5 = (k_{neo}/k_{13})[Bu_3SnH]_m \quad (3)$$

The kinetic data in Table I was used to determine the temperature-dependent function for the rearrangement of 1 to 3 of

$$\log (k_{13}/s^{-1}) = (11.00 \pm 0.14) - (5.88 \pm 0.16)/\theta$$

where the errors are 2σ and $\theta = 2.3RT$. This Arrhenius function for the 1 → 3 conversion is displayed graphically in Figure 2. In the insert in Figure 2 we compare our results with the kinetic values determined by Ingold, Warkentin, et al.[2a] for the 1 to 3 rearrangement. The high-temperature (40 °C) measurement in that work was determined by spin-trapping results with the assumption that the neopentyl-like radical 1 reacted with the trap with a rate constant equal to that for reaction of undecyl with the trap, and that kinetic value might be expected to be too large. Extrapolation of our function into the low-temperature region shows that our values are slower than those measured by ESR[2] by about a factor of 3. In the ESR study, the rate of rearrangement in CF_2Cl_2 was measured relative to the rate of radical coupling, and rate constants for rearrangement of 1 to 3 were determined by multiplying that ratio by the calculated rate constants for diffusion using the temperature-dependent function for coupling in methylcyclopropane solvent. Solvent CF_2Cl_2 apparently is more viscous than methylcyclopropane,[9] and we would speculate that the diffusion constants used as the basis reaction in the ESR study were accordingly somewhat too large.

Scheme II



The (2,2-Dimethylcyclopropyl)methyl Radical Rearrangement

Since the cyclopropylcarbinyl radical is known to open with a rate constant of 1×10^8 s^{-1} at 25 °C[10] and the opening of radical 2 was expected to be even faster, it was clear that the tin hydride method, with a Bu_3SnH trapping rate constant of 2.4×10^6 M^{-1} s^{-1} at 25 °C,[4] could not be used readily to determine rate constants for reactions of 2. Further, since cyclization of 1 competes with reaction of 1 with Bu_3SnH, the kinetic solution would be complex. Mercaptans reduce carbon radicals faster than does Bu_3SnH, and thiophenol is an especially fast trapping agent; rate constants for reactions of simple alkyl radicals with thiophenol have been studied recently by Franz by the UV-laser flash method.[11] Since the thiyl radicals including (apparently) thiophenoxy will add to *N*-hydroxypyridine-2(1*H*)-thione esters in radical chain propagating steps, it is possible to use Barton's PTOC esters as precursors for cyclopropylcarbinyl radicals with thiophenol as the trapping agent. Recently, we demonstrated this approach in measurements of the rate constants for ring opening of cyclopropylcarbinyl radical;[10] we have labeled the technique the "PTOC/thiol method".

The (2,2-dimethylcyclopropyl)methyl radical (2) was produced from precursor 8 (Scheme II). For radical 2, the *N*-hydroxypyridine-2(1*H*)-thione ester route was especially attractive. Previously our group was not able to prepare a pure sample of the corresponding bromide precursor, but 8 was synthesized and purified with no special precautions. Radical 2 was produced in the presence of PhSH over the temperature range −78 to 50 °C. The reactions were quite

(9) Riddick, J. A.; Bunger, W. B.; Sakano, T. K. *Techniques of Chemistry Organic Solvents Physical Properties and Methods of Purification*, 4th ed.; Weissberger, A., Ed.; Wiley and Sons: New York, 1986; Vol. II.

(10) Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275–277.

(11) Franz, J. A.; Bushaw, B. A.; Alnajjar, M. S. *J. Am. Chem. Soc.* **1989**, *111*, 268–275.

Table II. Products from Reactions of Radical 2 in the Presence of PhSH

temp,[a] °C	$[PhSH]_m$	rel % yield 4	5	9	log (k_{21}/s^{-1})[b,c]	log (k_{23}/s^{-1})[c,d]
50	0.98	12	78	11	8.26	9.07
	1.96	12	70	17	8.37	9.14
26	0.98	12	78	12	8.17	8.98
1	0.48	11	77	12	7.66	8.51
0	0.47	12	76	12	7.69	8.49
	0.95	12	72	16	7.87	8.65
	1.44	11	67	21	7.89	8.68
−19	0.48	11	74	15	7.46	8.29
	0.96	10	66	24	7.51	8.33
	1.45	9	58	34	7.50	8.30
	1.94	8	57	35	7.56	8.41
−20	0.48	10	74	16	7.38	8.25
−37	0.98	8	59	32	7.19	8.05
−78	0.48	5	47	48	6.16	7.13

[a] Within ±1 °C. [b] From eq 5. [c] The value for k_H was taken to be equal to that for reaction of butyl radical: log $(k/(M^{-1} s^{-1})) = 9.41-1.74/\theta$ (ref 11). [d] From eq 6.

clean; precursor 8 was completely consumed, and the hydrocarbon products 3,3-dimethyl-1-butene (4), 4-methyl-1-pentene (5), and 1,1,2-trimethylcyclopropane (9) accounted for all of the mass balance. The yields of these products are collected in Table II.

The rate constants for hydrogen-atom transfer from thiophenol to alkyl radicals are quite insensitive to radical structure,[11] and it is reasonable to assume that PhSH will trap radical 2 with rate constants equal to those for trapping butyl radical. We also assume that there is no solvent effect on the rate constants for trapping in changing from nonane[11] to THF. The back-cyclization of radical 3 to radical 2 will be much too slow[8] to compete with trapping of 3 by PhSH, and the opening of 2 to 3 can be treated as an irreversible process for this work. Back-cyclization of radical 1 to radical 2 in competition with trapping of 1 by PhSH could become important at high temperatures if the concentration of PhSH was low; for example, assuming that 1 reacts with PhSH with a rate constant equal to that for butyl radical and using the kinetic value determined in this work for the cyclization of 1, the back-cyclization of 1 to 2 at 50 °C will be about 7% of the rate of trapping when the concentration of PhSH is 1.0 M and 40% when [PhSH] is 0.1 M. Because of the small activation energy for PhSH trapping,[11] the back-cyclization of 1 becomes less important at lower temperatures. Our kinetic studies of radical 2 employed PhSH at 1 M or greater concentrations at high temperatures, and the total amount of product 4 was only about 10%; thus, it was reasonable for us to treat the 2 to 1 conversion as an irreversible process. Accordingly, the rate constant for loss of 2 (k_r) is given by eq 4, where k_H is the rate constant for reaction of 2 with PhSH and $[PhSH]_m$ is the average concentration of PhSH over the course of the reaction. The rate constant for loss of 2 can be divided into its constituent rate constants by simple multiplication by the mole fraction of the appropriate product as shown in eq 5 and 6.

$$k_r = k_H[PhSH]_m(4 + 5)/9 \quad (4)$$

$$k_{21} = k_r 4/(4 + 5) = k_H[PhSH]_m 4/9 \quad (5)$$

$$k_{23} = k_r 5/(4 + 5) = k_H[PhSH]_m 5/9 \quad (6)$$

Rate constants for the 2 → 1 and 2 → 3 conversions were used to determine Arrhenius functions for each ring opening, and the temperature-dependent functions for the rate constants k_r, k_{21}, and k_{23} are listed in Table III. Figure 3 shows the graphical presentation of the latter two functions. The experimentally measured ratio of products 4 and 5 formed from the ring openings of radical 2 permit one to evaluate the partition function contained in eq 2,

Table III. Kinetic Parameters for Radical Rearrangements[a]

reactn	log (A/s^{-1})	E_a[b]	$k_{25°C}$, s^{-1}	$\Delta G^{\ddagger}_{(25°C)}$[b]
1 → 3	11.00 ± 0.14	5.88 ± 0.16	4.8×10^6	
2 → 1 + 3	12.27 ± 0.28	4.52 ± 0.34	8.9×10^8	
2 → 1	11.67 ± 0.34	4.87 ± 0.41	1.2×10^8	6.4
2 → 3	12.17 ± 0.28	4.47 ± 0.34	7.7×10^8	5.3
1 → 2	11.1 ± 0.4	5.9 ± 0.4	5.6×10^6	8.2
3 → 2			$<3 \times 10^4$	>11.3
c-$C_3H_5CH_2$· ring opening[c]	12.7 ± 0.14	6.8 ± 0.2	5×10^7	6.9
3-butenyl cyclization[d]	10.3 (12.1)	9.0 (11.1)	5000 (8000)	12.4

[a] Errors are 2σ for the fit of the Arrhenius function; they do not include estimates of the accuracy or precision of the corresponding basis reactions. [b] In kilocalories per mole. [c] From ref 10; the log A term for the reaction (13.0) and the rate constant for the reaction at 25 °C (1.0×10^8 s^{-1}) have been corrected for cleavage of one of the cyclopropyl bonds. [d] From ref 8; the values in parentheses are those calculated by using corrected[7] high-temperature rate constants.

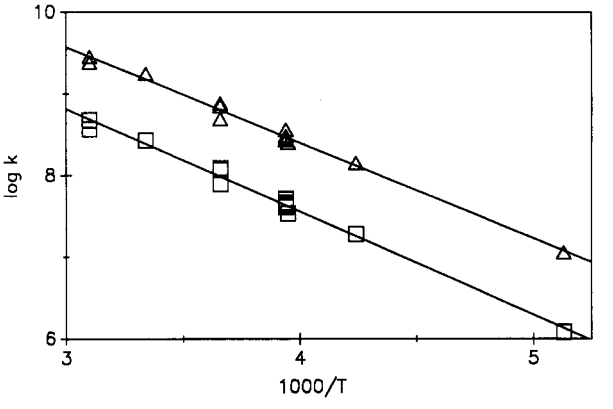


Figure 3. Arrhenius plots for the 2 to 3 (△) and 2 to 1 (□) isomerizations.

and the rate constants for cyclization of radical 1 to radical 2 were calculated from this partition function and the overall rate constant for conversion of 1 to 3 via eq 7. The calculated k_{12} values were then used to give an Arrhenius function for the 1 → 2 cyclization that is included in Table III.

$$k_{12} = k_{13}(k_{23} + k_{21})/k_{23} \quad (7)$$

Discussion

With the rate constants for both the rearrangement of 1 and the fragmentation of 2, we can consider the ener-

getics of the 1, 2, 3 reaction manifold. For the 1 to 2 conversion, the equilibrium constant (K_{12}) varies from about 0.05 at room temperature to about 0.02 at −78 °C. By combining the Arrhenius functions for the 1 → 2 and 2 → 1 reactions, one can express the equilibrium constant by eq 8, which can be evaluated to give ΔH_{12} and ΔS_{12}. At

$$\ln K_{12} = 2.3(\log A_{12} - \log A_{21}) - (E_{12} - E_{21})/RT \quad (8)$$

$$\ln K_{12} = -1.38 - 1000/RT$$

$$\Delta H_{12} = 1.0 \text{ kcal/mol}$$

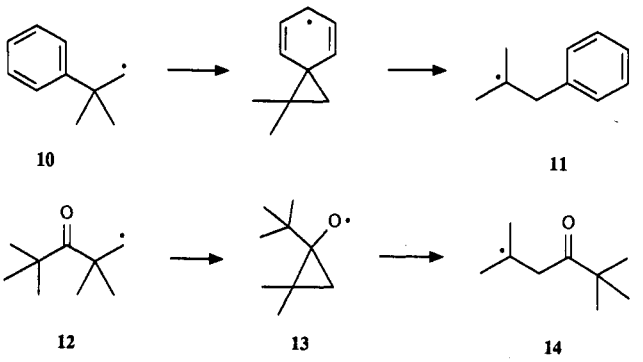
$$\Delta S_{12} = -2.6 \text{ eu}$$

25 °C, ΔG_{12} is 1.8 kcal/mol. The cyclic radical 2 is seen to be only slightly unfavored entropically and enthalpically in comparison to the primary radical 1. The activation free energies for the 1 → 2, 2 → 1, and 2 → 3 conversions can be evaluated from the kinetics. A limit for the rate of cyclization of radical 3 is available from the studies with precursor 7 ($k < 3 \times 10^4$ s^{-1} at 25 °C). Table III contains the activation energies at 25 °C for the 1, 2, 3 manifold.

For the purpose of comparisons, the kinetic parameters for reactions of the parent system, the cyclopropylcarbinyl radical ring opening and the 3-butenyl radical cyclization, are included in Table III. The ring opening of cyclopropylcarbinyl radical has been predicted to have $\Delta S^{\ddagger}$ equal to 0 eu,[12] which gives log A_{298} = 13.1.[13] Experimentally, the PTOC/thiol method gave log A = 13.0 for cyclopropylcarbinyl in the same temperature range as we have studied here,[10] and the log A terms for various cyclobutylcarbinyl ring openings are 12.4–13.2.[14] For comparison to the 2 → 1 and 2 → 3 rearrangements, the log A term for cyclopropylcarbinyl must be reduced by log 2 in order to correct for the equivalent ring-opening paths; this gives log A = 12.7. Our experimental value for log A of the 2 → 3 ring opening of 12.2 ± 0.3 falls slightly below the value for the parent system. Our value for log A of the 2 → 1 ring opening is less than that of the parent system but just within experimental error of that for the 2 → 3 rearrangement. Since the same competition reaction (PhSH trapping) was used for the cyclopropylcarbinyl[10] and radical 2 studies, any error in the basis trapping rate constants will cancel, and a comparison of these two systems should be reasonable provided that the assumption that both react with PhSH with the same rate constants holds. The transition states for openings of radical 2 apparently experience a slightly increased entropy demand (ca. 3 eu) relative to the parent system. However, a substantially reduced activation energy (2 kcal/mol) for opening of 2 relative to that of the parent system more than offsets the entropy effect. The result is that at 25 °C ring opening of 2 to the more stable radical 3 is 15 times faster than the parent radical reaction, and even ring opening to the less stable radical 1 is over twice as fast as the statistically corrected parent reaction. The ring opening of radical 2 is thus one of the fastest radical rearrangements yet calibrated.

The cyclization of 1 to 2 also can be compared to the parent system, but the kinetic parameters for the cyclization of the 3-butenyl radical must be viewed with some caution. In the study of this reaction, kinetics at and below 0 °C were determined by the kinetic ESR method and rate constants at 40, 60, and 80 °C were determined by the tin hydride method.[8] The use of the presently accepted values for the rate constants for reaction of Bu_3SnH with a primary radical[7] gives new rate constants for the high-temperature reactions. We have combined these new values with the low-temperature rate constants to give a new Arrhenius function that is included in Table II. Unfortunately, while this new function may predict rate constants in the region of room temperature, conclusions based on the value for log A and E_a may not be warranted. However, *gem*-dimethyl substitution in 1 clearly leads to a significant acceleration in the rate of radical cyclization. The reaction is nearly 3 orders of magnitude faster than cyclization of the parent at 25 °C, and all of the acceleration results from a dramatic reduction in the activation energy. Hence, the equilibrium constant at 25 °C for the cyclization reaction is increased from about 1×10^{-4} for the parent system to about 0.05 for the dimethyl analogues 1 and 2.

It is perhaps more interesting to compare the overall isomerization of 1 to 3 with other related 1,2-migrations of carbon radicals. As noted above, the mechanism in Scheme I is the accepted pathway for isomerization of $RCX_2CH_2^{\bullet}$ to $RCH_2C(\cdot)X_2$ where R contains a site of unsaturation bonded to the CX_2 group. For the direct analogues of 1 (i.e., $RCMe_2CH_2^{\bullet}$), Arrhenius functions for isomerization are available for two species that contain sp^2-hybridized carbon atoms in the migrating R group, the neophyl radical (10) and the pivaloyl-substituted radical 12. The rate constant for isomerization of 10 to 11 is



described by log (k/s^{-1}) = 11.6 − 11.8/θ,[15] and that for isomerization of 12 to 14 is described by log (k/s^{-1}) = 10.9 − 7.8/θ.[2b] The log A values for these two rearrangements are quite similar to our log A for the 1 to 3 isomerization of 11.0, which is consistent with the common pathway, and, in fact, Ingold et al. predicted a log A of 11.25 for the 1 to 3 rearrangement based on the results for 10 and 12.[2b] The carbonyl migration of 12 is remarkably similar to the vinyl migration of 1. If one assumes that the partitioning function for intermediate 13 will be similar to that of 2, then the difference in rates of isomerization (1 rearranges ca. 30 times faster than 12 at 25 °C) results almost entirely from the differences in the E_a terms and reflects the instability of the incipient oxygen-centered radical 13. One should expect to find similar effects in comparisons of radical additions to other vinyl–carbonyl analogue pairs.

Kinetics of the 1, 2, 3 radical system are now also available from a nitroxyl radical trapping competition study conducted by Beckwith's group.[16] For cyclization of radical 1 to radical 2, Beckwith and Bowry (BB) ob-

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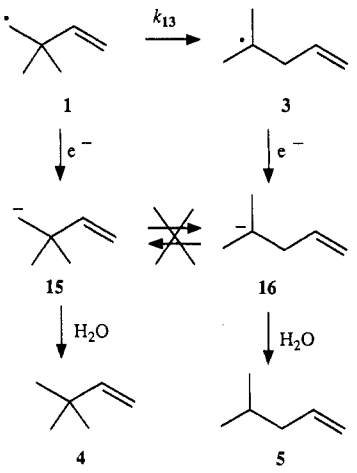
Scheme III



tained rate constants at 60 and 106 °C that are 1.6 and 1.9 times greater, respectively, than the values for those temperatures calculated from our Arrhenius function. Similar differences exist in the 1 to 3 conversion. The differences almost certainly originate in the values of the basis competition reactions employed by the two groups. Our basis reaction was trapping by Bu_3SnH, which reacts with a neopentyl radical about 1.3 times faster than with a primary radical at 30 °C.[4] The BB basis reaction was a nitroxyl radical coupling, which is about 1.3 times faster for a primary radical than for a neopentyl radical at 20 °C.[16] Ironically, if both groups had chosen to ignore the neopentyl corrections and instead had used the rate constants for reactions with primary radicals, then the results from the two groups would have been virtually indistinguishable.

For ring openings of radical **2**, the relative rate constants for formation of **1** and **3** at 60 °C (i.e., k_{23}/k_{21}) found by BB and in this work are in excellent agreement. Indeed, the kinetic values at 60 °C for reactions of **2** found by the two groups vary by only 10–15%. Given the significant differences in the experimental approaches, such agreement suggests that both approaches are reasonably accurate at this temperature. However, the situation at 106 °C is confusing. The BB values for reactions of **2** are 1.6–1.7 times greater than those calculated from our Arrhenius functions. Accordingly, with large kinetic differences at 106 °C and similar values at 60 °C, the log A and E_a values for reactions of **2** calculated by BB[16] differ significantly from those we report in Table III. Because of the high product yields we obtained and the variety of temperatures we studied, our results should be more reliable, but the BB[16] values for log A for reactions of **2** are more consistent with those found for other, related ring openings. The results of the cyclopropylcarbinyl ring opening studies by the two groups using the same methods[10,17] show similar trends, with the Beckwith[17] approach giving greater log A (by 0.6) and E_a (by 1.1 kcal/mol) than those found by our approach.[10] We can only conclude that one or both of the methods contain(s) systematic errors in the Arrhenius functions of the basis reactions that are about equal to 0 (or at least equal to one another) in the temperature range near 60–80 °C.

Both the rearrangement of radical **1** to radical **3** and the ring opening of radical **2** meet our criteria for providing radical clocks that might be used in electron-transfer reactions (Scheme III). In the former case, the primary radical **1** rearranges to the tertiary radical **3**, but if radical **1** is reduced to anion **15**, the analogous anionic rearrangement (**15** → **16**) will be energetically unfavorable. Further, reduction of radical **3** to anion **16** subsequent to the radical rearrnagement is possible, but one would not expect the rearrangement of this tertiary anionic species to the primary anion (**16** → **15** in Scheme III) to be facile.[18] Indeed, in preliminary studies, we have generated **16** as its sodium salt in THF and found no evidence for its rearrangement to **15** before reaction of **16** with the solvent occurred.[19] Given the apparent skeletal stability of anions **15** and **16**, radical **2** may prove to be an especially useful probe for electron-transfer studies although it may be somewhat more difficult to interpret the results since radical **2** partitions to both **1** and **3** and, once formed, radical **1** can subsequently rearrange to **3**. Before radical **2** can be used for such studies, one must determine the product distribution for ring opening of the cyclic anion formed upon reduction of **2**. The rearrangements of **1** and **2** might prove useful in studies of other fast radical reactions, and it is even conceivable that radical **2** can be employed in studies of reactions occurring at diffusion-control rates in relatively nonviscous solvents.

Conclusion

The **1** → **3** and **2** → (**1** + **3**) rearrangements are reasonably well calibrated. The ring opening of (2,2-dimethylcyclopropyl)methyl radical (**2**) is one of the fastest radical skeletal rearrangements for which an Arrhenius function is now available. Geminal dimethyl substitution in **1** accelerates the cyclization by reducing the barrier for obtaining a reactive conformation (Thorpe–Ingold effect), and it accelerates ring opening of **2** presumably by destabilizing the cyclic radical. The PTOC/thiol method for studying the kinetics of fast radical rearrangements which capitalizes on Barton's versatile radical precursors and the recently reported values for reactions of simple alkyl radicals with PhSH should be applicable in studies of radical rearrangements exceeding 1×10^9 s^{-1} at 25 °C.

Experimental Section

Materials. Reagents were purchased from Aldrich Chemical Co. and were used as received unless otherwise noted. *N*-Hydroxy-2(1*H*)-pyridinethione was purchased from Olin Chemicals Co. as a 40% aqueous solution of the sodium salt; the neutral compound was prepared by precipitation from the aqueous solution by addition of concentrated HCl. Thiophenol was distilled from $CaSO_4$ prior to use.

3,3-Dimethyl-4-bromo-1-butene (6a). The preparation from the corresponding alcohol using CBr_4 or CCl_3Br as the bromide source has been reported.[20]

1-[[(2,2-Dimethyl-3-butenyl)carbonyl]oxy]-2(1*H*)-pyridinethione (6b). The preparation from the corresponding acid chloride and *N*-hydroxy-2(1*H*)-pyridinethione sodium salt has been reported.[5b]

1-[[[(2,2-Dimethylcyclopropyl)methyl]carbonyl]oxy]-2-(1*H*)-pyridinethione (8). (2,2-Dimethylcyclopropyl)acetic acid was prepared by basic hydrolysis of the corresponding ethyl ester,[21] which had been prepared via a Simmons–Smith reaction on ethyl 4-methyl-3-pentenoate.[22] The acid (0.50 g, 3.9 mmol), *N*-hydroxy-2(1*H*)-pyridinethione (0.58 g, 3.9 mmol), and 4-(dimethylamino)pyridine (0.05 g, 0.39 mmol) were dissolved in 50

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mL of CH_2Cl_2. 1,3-Dicyclohexylcarbodiimide (0.89 g, 4.3 mmol) was dissolved in 10 mL of CH_2Cl_2, and the resulting solution was added dropwise to the reaction mixture. The reaction vessel was covered with Al foil to shield the mixture from light, and the reaction mixture was stirred overnight. The solvent was evaporated, the residue was dissolved in ethyl acetate, and the resulting solution was washed with 1 M $KHSO_4$, H_2O, and 5% $NaHCO_3$. The solvent was evaporated, and the residual yellow-green oil was crystallized from benzene/hexanes to yield 0.55 g (61%) of **8**: mp 68–69.5 °C; ^1H NMR (200 MHz) δ 0.2 (t, 1 H), 0.65 (dd, 1 H), 1.0 (m, 1 H), 2.7 (d, 2 H), 6.6 (t, 1 H), 7.2 (t, 1 H), 7.6 (d, 1 H), 7.7 (d, 1 H).

1-[[(1,1-Dimethyl-3-butenyl)carbonyl]oxy]-2(1*H*)-pyridinethione (7) was prepared by the procedure given above from 2,2-dimethyl-4-pentenoic acid (0.5 g, 3.9 mmol). The crude product (0.65 g, 70%) was isolated as a yellow-green oil that was 85% pure by ^1H NMR spectroscopy and was not further purified: ^1H NMR (200 MHz) δ 1.45 (s, 6 H), 2.55 (d, 2 H), 5.2 (m, 2 H), 5.95 (m, 1 H), 6.65 (dt, 1 H), 7.2 (dt, 1 H), 7.45 (dd, 1 H), 7.7 (dd, 1 H).

Kinetic Studies. The following procedure is representative for studies with **6b** and **8**. A stock solution of the radical precursor and a hydrocarbon standard was prepared in degassed THF. Aliquots were added to oven-dried, 20-cm, 10-mm-o.d. tubes that had been equipped with stirbars, sealed with septa, and flushed with dry N_2. The volume of each reaction was adjusted to 2.0 mL with solvent, and the reactions were allowed to equilibrate at the desired temperature (ca. 2 min) while protected from light. The H-atom source was added via syringe (>10-fold excess), and the reaction mixtures were irradiated with a 150-W tungsten filament lamp until no starting material was detectable by TLC (usually <5 min). The initial concentration of precursor **6b** or **8** was 0.02 M, the concentrations of PhSH for studies of **8** ranged from 0.48 to 1.98 M, and the concentrations of Bu_3SnH for studies of **6b** ranged from 0.26 to 0.53 M. The reaction mixtures were analyzed by GC using both a J & W Scientific DB-1 Megabore column (0.5 mm i.d., 15 m) and a packed glass column with an $AgNO_3$ active phase[23] consisting of 10% $AgNO_3$ in ethylene glycol, 30% by weight on Chromosorb P (3.2 mm i.d., 2.2 m). The packed column was used to separate cyclopropane **9** from alkenes **4** and **5**, while the Megabore column was used to separate alkene **5** from compounds **4** and **9**.

For studies using precursor **7** (initial concentration 0.02 M), the procedure was the same as that given above except that lower concentrations of Bu_3SnH were used (0.03–0.07 M).

Kinetic studies with bromide **6a** have been reported.[3]

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Registry No. 1, 87110-24-5; 2, 90429-69-9; 3, 87110-25-6; 4, 558-37-2; 5, 691-37-2; 6a, 97797-99-4; 6b, 102735-95-5; 7, 120172-69-2; 8, 120172-70-5; 9, 4127-45-1; (2,2-dimethylcyclopropyl)acetic acid, 68258-20-8; *N*-hydroxy-2(1*H*)-pyridinethione, 1121-30-8; 2,2-dimethyl-4-pentenoic acid, 16386-93-9.

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Kinetics and Regioselectivity of Ring Opening of Substituted Cyclopropylmethyl Radicals

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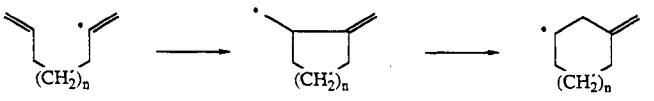
Accurate analysis of the mixture of hydroxylamines **8** formed when suitable peroxides **4** undergo homolysis in the presence of the nitroxyl radical 1,1,3,3-tetramethylisoindolin-2-yloxy (T) has afforded rate constants for ring opening of the cyclopropylmethyl radicals **2a**, **2c**, **2d**^{cis}, **2d**^{trans}, and **2e** and cyclization of the but-3-enyl radicals **1a**, **1c**, and **1d**. The presence of methyl substituents enhances the rates both of cyclization and of ring opening to give primary radicals. In the case of the *trans*-2-methylcyclopropyl radical, **2d**^{trans}, this effect leads to preferential formation of the less thermodynamically stable possible product, **1d**, below about 60 °C. In general, the effects of substituents support the view that the transition structure for the cyclopropylmethyl–butenyl radical interconversion is dipolar. Combination of data from four sets of workers using three different kinetic techniques affords the following recommended Arrhenius equation for the cyclopropylmethyl radical clock reaction: $\log k_1(\mathbf{2a}) = 13.31 - 7.6/2.3RT$.

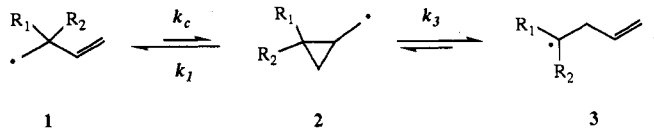
Introduction

1,3-Vinyl migrations, both planned and adventitious, are common in free-radical chemistry and have been the subject of numerous studies over the last 30 years.[1] Interest in such rearrangements has recently been stimulated by synthetic[2] and mechanistic[3] studies of ring closures of suitably constituted vinyl radicals: exo intramolecular addition of vinyl radicals to double bonds produces homoallylic radicals which may rearrange further under suitable reaction conditions (Scheme I) to give the endo cyclization product.

Scheme I



Scheme II



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