Kinetics for the Reaction of a Secondary Alkyl Radical with Tri-*n*-butylgermanium Hydride and Calibration of a Secondary Alkyl Radical Clock Reaction[1]

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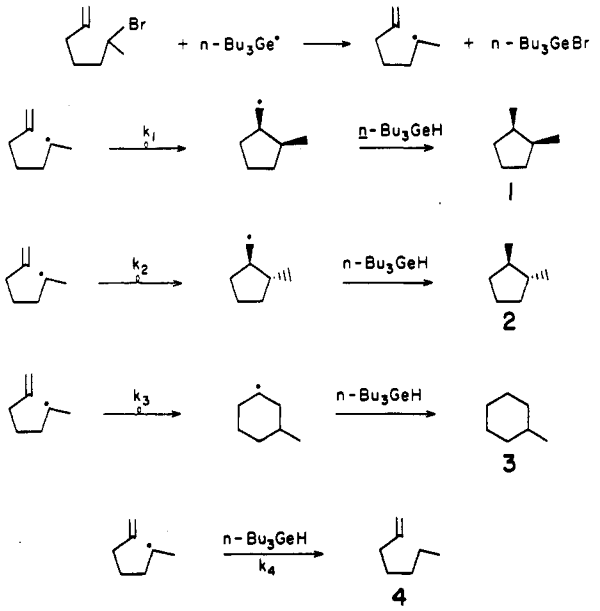
Arrhenius parameters for the reaction of a secondary alkyl radical with tri-*n*-butylgermanium hydride have been measured by using the cyclization of 1-methyl-5-hexenyl radical as a "clock" reaction. At 298 K the rate constant is 1.8×10^4 M^{-1} s^{-1}, which makes the secondary alkyl radical/*n*-Bu_3GeH reaction about 80 times slower than the corresponding reaction with tri-*n*-butyltin hydride. The secondary alkyl radical clock reaction has been rather precisely calibrated by using new data and data from the literature. An attempt to carry out similar experiments with 1,1-dimethyl-5-hexenyl yielded much less precise data for the cyclization of this tertiary alkyl radical. Reliable kinetic data for hydrogen abstraction from *n*-Bu_3GeH by tertiary alkyl radicals could not be obtained by using either the parent bromide or appropriate *N*-hydroxypyridine-2-thione esters as alkyl radical sources.

Tri-*n*-butyltin hydride has been widely employed in kinetic studies of the rearrangements of carbon-centered radicals.[4] Its popularity can be attributed to the fact that reliable absolute rate constants and Arrhenius parameters for hydrogen atom transfer from the tin hydride to primary, to secondary, and to tertiary alkyl radicals, as well as to other, more reactive radicals have been determined.[5-7] However, for radicals which undergo relatively slow rearrangements tin hydride can prove to be too reactive. In such cases, tri-*n*-butylgermanium hydride may offer a viable alternative since it is less reactive than tin hydride.[7-11]

We recently reported a detailed kinetic study of hydrogen abstraction from tri-*n*-butylgermanium hydride by primary alkyl radicals.[10] In this study we employed the cyclization of the 5-hexenyl radical to the cyclopentylmethyl radical[6] to "clock"[12] the rate of the hydrogen abstraction. We have now extended these studies to a secondary alkyl radical employing essentially the same technique with 1-methyl-5-hexenyl as the secondary alkyl "clock". Arrhenius parameters for two of the three cyclization reactions of this radical are reported as well as the Arrhenius parameters for its reaction with the germane. We have also attempted to obtain quantitative kinetic data on the cyclization of a tertiary alkyl radical, 1,1-dimethyl-5-hexenyl, and for the reaction of this radical with the germanium hydride. Unfortunately, only rough estimates of the kinetics of these reactions could be obtained with this tertiary radical.

Scheme I



Results

Reactions of 1-Methyl-5-hexenyl with *n*-Bu_3GeH. This secondary alkyl radical was formed from the corresponding alkenyl bromide (0.2 M) and the germane (ca. 1.0 or 2.0 M) by a thermal-initiated or photoinitiated, radical chain reaction in a hydrocarbon solvent. The reactions of interest are shown in Scheme I. The alkenyl radical gives rise to four hydrocarbon products: *cis*-1,2-dimethylcyclopentane (1); *trans*-1,2-dimethylcyclopentane (2); methylcyclohexane (3); hept-1-ene (4).

We were unable to achieve a complete separation of 1 and 3 in the reaction products despite considerable effort (see Experimental Section). Fortunately, 3 is only a minor reaction product. Thus, it has been reported[13] that [3]/[1] + [2] = 0.013 at 65 °C, while we find, at temperatures from 55 to 120 °C, [3]/[1] = 0.05 ± 0.03 by the technique of GC/MS using selective ion monitoring. There is no trend in this ratio with temperature within the accuracy of our measurements (see supplementary material). Because 3 is such a minor product we have included it with 1 in our kinetic calculations. To keep the reader reminded of this

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[4] For reviews, see: Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, Essay 4. Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073-3100.

[5] Carlsson, D. J.; Ingold, K. U. *J. Am. Chem. Soc.* **1968**, *90*, 7047-7055.

[6] Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739-7742.

[7] 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*, 4594-4596.

[8] Carlsson, D. J.; Ingold, K. U.; Bray, L. C. *Int. J. Chem. Kinet.* **1969**, *1*, 315-323.

[9] Kaplan, L. *Chem. Commun.* **1969**, 106-107; *React. Intermed. (Plenum)* **1981**, *2*, 251-314.

[10] Lusztyk, J.; Mallard, B.; Lindsay, D. A.; Ingold, K. U. *J. Am. Chem. Soc.* **1983**, *105*, 3578-3580.

[11] Beckwith, A. L. J.; Roberts, D. H.; Schiesser, C. H.; Wallner, A. *Tetrahedron Lett.* **1985**, *26*, 3349-3352.

[12] Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317-323.

[13] Beckwith, A. L. J.; Blair, I. A.; Phillipou, G. *Tetrahedron Lett.* **1974**, 2251-2254.

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Table I. Kinetic Data for the Reaction of 6-Bromohept-1-ene with *n*-Bu$_3$GeH at Various Temperatures[14]

T, K	[n-Bu$_3$GeH], M^a	$k_{1(+3)}/k_4$, M	k_2/k_4, M	$k_{1(+3)}/k_2$
243^b	1.01–2.03	4.12 ± 0.46	0.784 ± 0.124	5.28 ± 0.30
273^b	0.98–1.97	6.02 ± 0.40	1.44 ± 0.12	4.20 ± 0.26
328^c	0.93–1.86	7.57 ± 0.68	2.31 ± 0.26	3.28 ± 0.08
363^c	0.90–1.80	8.34 ± 0.14	3.06 ± 0.12	2.73 ± 0.08
393^c	0.88–1.75	9.27 ± 0.30	3.73 ± 0.14	2.49 ± 0.04

^{a} Range of concentrations employed. ^{b} Photoinitiation. ^{c} Thermal initiation.

fact we refer to **1(+3)** where appropriate.

The product ratio, ([**1**](+[**3**]) + [**2**])/[**4**] varied in the expected manner with a change in the germane concentration. This ratio was virtually uninfluenced by the extent of consumption of the bromide (ca. 1–90%) but, for kinetic purposes, only data obtained at ≤50% bromide consumption have been employed. Under our experimental conditions the germane concentration is essentially invariant. Provided, therefore, that the germane is the only hydrogen donor which traps the 1-methyl-5-hexenyl radicals, we can write

$$k_{1(+3)}/k_4 = [n\text{-Bu}_3\text{GeH}]([\mathbf{1}](+[\mathbf{3}]))/[\mathbf{4}]$$

$$k_2/k_4 = [n\text{-Bu}_3\text{GeH}][\mathbf{2}]/[\mathbf{4}]$$

Values of $k_{1(+3)}/k_4$ and of k_2/k_4 calculated from these equations were independent of the germane concentration at each particular temperature in the range 243–393 K. Mean values of these two rate constant ratios and of $k_{1(+3)}/k_2$ are given in Table I, while the detailed results of the individual experiments are available as supplementary material. Our results yield the Arrhenius equations below (eq 1–3), where θ = 2.303RT kcal/mol and the errors correspond to 95% confidence limits.[14]

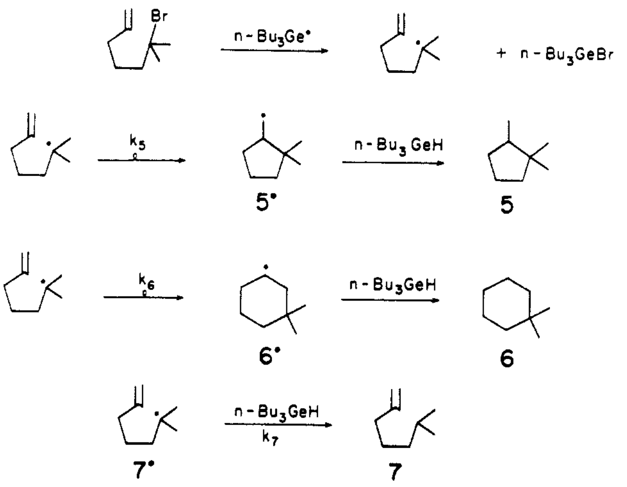
$$\log (k_{1(+3)}/k_4/\text{M}) = (1.52 \pm 0.06) - (0.98 \pm 0.08)/\theta \quad (1)$$

$$\log(k_1/k_4/\text{M}) = (1.65 \pm 0.06) - (1.93 \pm 0.08)/\theta \quad (2)$$

$$\log(k_{1(+3)}/k_2) = -(0.126 \pm 0.021) + (0.944 \pm 0.030)/\theta \quad (3)$$

Calibration of the 1-Methyl-5-hexenyl Radical Clock. The sum of the rate constants for the overall cyclization of this radical, i.e., $k_c = k_{1(+3)} + k_2$ has been measured previously by two quite independent techniques.[15,16] In this laboratory, the technique of kinetic electron paramagnetic resonance (EPR) spectroscopy was employed at temperatures in the range 183–243 K.[15] (This experiment would actually have yielded $k_1 + k_2$ rather than k_c, but once again we can neglect the minor contribution of reaction 3 to the overall process.) Burkhard, Roduner, and Fischer[16] have measured k_c by the muon spin rotation technique over the temperature range 241–373 K. It will be obvious that the Arrhenius parameters reported for k_c in these two studies do not correspond to any single reaction. Indeed, eq 3 implied that a plot of log (k_c/s^{-1}) vs. 1/T should be slightly curved. We have therefore employed eq 3 to partition each individually measured k_c value from the two studies[17] into the separate contributions from $k_{1(+3)}$ and k_2. This procedure yielded the Arrhenius parameters for $k_{1(+3)}$ and for k_2 which have been listed in Table II[18] together with the parameters for the analogous cyclizations of the 5-hexenyl[6] and 1,1-dimethyl-5-hexenyl[19] radicals.

Scheme II



Reaction of 1,1-Dimethyl-5-hexenyl with *n*-Bu$_3$GeH. We employed 6-bromo-6-methylhept-1-ene in our initial attempt to study this reaction. Unfortunately, this bromide proved to be thermally rather unstable so that its purification (preparative GC) and analysis (GC) was very difficult. In fact, we did not succeed in obtaining this bromide in better than 80% purity as judged by GC analysis. When this (possibly) impure bromide was used in a thermally initiated, radical chain reaction with n-Bu$_3$GeH (Scheme II), the ratio of the cyclized hydrocarbon products, [1,1,2-trimethylcyclopentane (**5**) plus 1,1-dimethylcyclohexane (**6**)] to the uncyclized product [6-methylheptene, (**7**)], was not reproducible at germane concentrations <1.8 M. More importantly, this ratio did not change with a change in the germane concentration in the manner that would be predicted from Scheme II. A possible origin for this problem[20] is the rather poor hydrogen-donating ability of the germane toward a tertiary alkyl radical. Indeed, we found that when the bromide was reacted with ca. 1 M n-Bu$_3$GeD at 120 °C only ca. 70% of the 6-methylheptene produced contained a deuterium atom.[21] The tertiary alkyl radical must, therefore, have abstracted some hydrogen from the nonane used as solvent or from the n-butyl groups of the germane.

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[14] All errors in this work correspond to 95% confidence limits but include only random and not systematic errors.

[15] Maeda, Y.; Ingold, K. U. *J. Am. Chem. Soc.* **1979**, *101*, 4975–4981.

[16] Burkhard, P.; Roduner, E.; Fischer, H. *Int. J. Chem. Kinet.* **1985**, *17*, 83–93.

[17] We thank Professor Fischer for providing us with the individual values for k_c at nine different temperatures. This information is given as supplementary material together with the individual k_c values calculated from the data in ref 15.

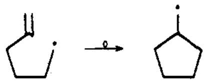
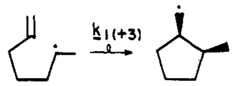
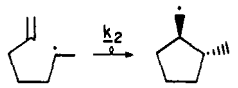
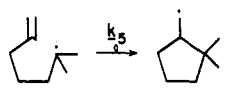
[18] These parameters can be compared with the Arrhenius equations reported for the overall cyclization, viz.,[15] log (k_c/s^{-1}) = (9.8 ± 0.3) – (6.4 ± 0.3)/θ and[16] log (k_c/s^{-1}) = (9.1 ± 0.3) – (5.31 ± 0.60)/θ.

[19] This work.

[20] The possibility that the cyclization **7**• → **5**• was reversible was considered unlikely. Nevertheless, we synthesized 2,2,3,3-tetramethylchlorobutane by photochlorination of hexamethylethane using Cl_2. The monochloride was purified by preparative GC and identified by GC/MS. A free radical chain reaction of 0.2 M $(CH_3)_3CC(CH_3)_2CH_2Cl$ with 2.0 M n-Bu$_3$GeH in n-octane was initiated by the thermal decomposition of di-*tert*-butyl peroxide and of benzoyl peroxide at 120 °C. In both reactions the only products that could be identified by GC were hexamethylethane and n-Bu$_3$GeCl. Neither isobutylene nor isobutane were detected. It is clear that the β-scission reaction $Me_3CCMe_2CH_2^\bullet \rightarrow Me_3C^\bullet + Me_2C{=}CH_2$ does not occur. We therefore presume the less entropically favored ring-opening **5**• → **7**• will not occur either.

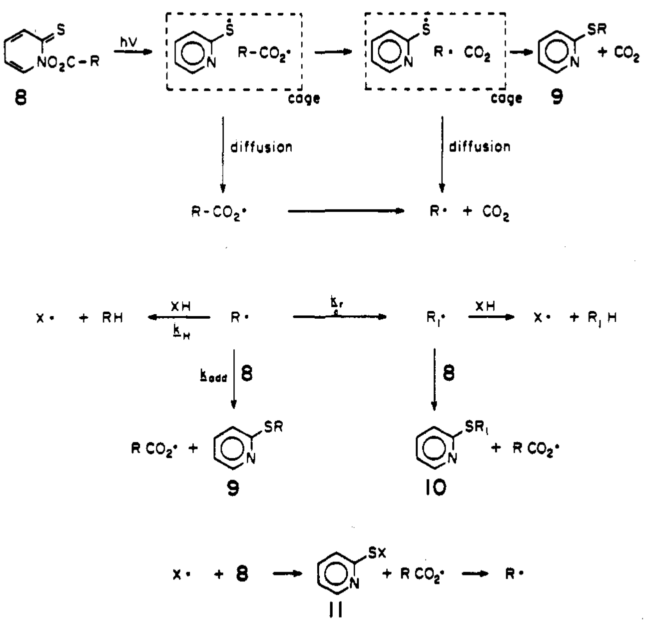
[21] Comparable experiments in which n-Bu$_3$GeD (99+ atom % D) was reacted with 2-bromohept-6-ene showed that the hydrocarbon products **1**–**4** were essentially 100% labeled with a single deuterium. The ratio of the products formed in these experiments compared with the ratio of the products formed under comparable conditions with n-Bu$_3$GeH yielded a kinetic isotope effect, $k_4^{\text{H}}/k_4^{\text{D}} \approx 2$ at 120 °C. For comparison, with tin hydride/tin deuteride the deuterium kinetic isotope effects for a variety of alkyl radicals lie in the range 2–3 at room temperature.[5,6]

Table II. "Best" Arrhenius Parameters for Some Alkyl Radical "Clocks"[14]

reaction	log (A/s^{-1})	E, kcal/mol	k^{298K}, s^{-1}	ref
	10.42 ± 0.32	6.85 ± 0.42	2.5×10^5	6
	9.79 ± 0.24	6.50 ± 0.26	1.0×10^5	19
	9.92 ± 0.26	7.44 ± 0.29	2.9×10^4	19
	(10.0 ± 0.6)^a	(6.1 ± 0.5)^a	(3.3×10^5)^a	19

^{a}These numbers are less reliable than the other data in this table (see text).

Scheme III



a, -R = -CMe$_2$(CH$_2$)$_3$CH=CH$_2$; b, -R = -CH$_2$CMe$_2$CH=CH$_2$;
c, -R = -(CH$_2$)$_4$CH = CH$_2$ d, -R = -CMe$_2$(CH$_2$)$_2$CH$_3$

If we assume that the expected kinetic rate law is obeyed with germane concentrations of ca. 1.8 M then our analytical data obtained in the range 338–393 K (see supplementary material) yield $k_5/k_6 \approx 12$–20 with no measureable temperature variation[22] and $k_5/k_7 \approx 22$–30 M with a small temperature dependence that can be described by eq 4.

$$\log (k_5/k_7/\mathrm{M}) = (2.3 \pm 0.5) - (1.5 \pm 0.8)/\theta \quad (4)$$

However, the true errors are probably much greater than those implied by this Arrhenius equation,[14] since we have implicitly assumed that none of the (probable) impurities in the starting bromide yield **5**, **6**, or **7** nor products that are anayzed as any of these hydrocarbons.

Because of the problems encountered with the tertiary bromide we turned to some of Barton's[23] recently developed radical chemistry. The N-hydroxypyridine-2-thione ester **8a** (see Scheme III), promised to provide a convenient source of the desired tertiary alkyl radical, **7**$^•$. Newcomb and Park[24] have successfully employed similar esters, **8b** and **8c**, as sources of primary alkyl radical "clocks" in kinetic studies of hydrogen atom abstraction. For relatively poor hydrogen donors, XH, many of the alkyl radicals were trapped by the thione ester to form the alkyl pyridyl sulfides **9** and **10**. However, the rate constant for hydrogen abstraction by the primary alkyl radical, k_H, could be roughly estimated from the relative yields of hydrocarbon products and alkyl pyridyl sulfides, i.e., from the ratio, ([RH] + [R$_1$H])/[**9** + **10**]. This was possible because the rate constant for addition to **8** of primary alkyl radicals, k_{add}, had been measured by using the radical clocks in the absence of hydrogen donors. It was assumed that the value of k_{add} found for primary alkyl radicals, viz.,[24] $\sim 2 \times 10^6$ M^{-1} s^{-1} at 50 °C would be a reasonable approximation for other radicals.

Table III. Kinetic Data for the Photodecomposition of 8a in a Radical Chain Reaction at 30 °C in *n*-Nonane

[**8a**], M	k_{add}/k_r, M$^{-1\,a}$ GC	k_{add}/k_r, M$^{-1\,a}$ HPLC	k_{add}/k_r, M$^{-1\,b}$ GC	k_{add}/k_r, M$^{-1\,b}$ HPLC
0.1	2.2	2.5	1.1	1.4
0.2	1.9	2.1	1.0	1.5
0.4	1.4	1.8	1.1	1.4

^{a}Uncorrected, based on measured [**9a**]/[**10a**] ratio. ^{b}Corrected assuming a 4.5% in-cage conversion of **8a** to **9a**.

We employed **8a** and the general procedure of Newcomb and Park[24] in an attempt to measure k_{add}/k_r for the tertiary alkyl radical **7**$^•$ prior to measuring k_7 (i.e., k_H, R$^•$ = **7**$^•$, XH = n-Bu$_3$GeH in Scheme III). The product ratio [**9a**]/[**10a**] was measured by both GC and HPLC following 5-min irradiation of **8a** in degassed nonane at 30 °C using light from a 100-W tungsten lamp. Compound **8a** was completely decomposed under these conditions, and so values of k_{add}/k_r were calculatd from the usual integrated rate expression.[25] To our surprise k_{add}/k_r decreased significantly as the initial concentration of **8a** was increased from 0.1 to 0.4 M (see Table III). We believe this is due to some in-cage decarboxylation of the radical pair formed in the initial photolytic step of the chain reaction, followed by cage collapse to form **9a** (see Scheme III).[20] The variation in the calculated values of k_{add}/k_r can be reduced to a minimum by assuming an in-cage contribution to the yield of **9a** of only 4.5%, corresponding to an average chain length of ca. 20 for the overall reaction. Although the validity of this assumption has not been checked by varying the rate (light intensity) or method (thermal) of chain initiation, we believe it to be reasonable. At all events, with this correction, i.e., [**9a**]$_{corr}$ = [**9a**]$_{meas}$ − 0.045[**8a**], we

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[22] At 338 K, $k_5/k_6 = 68$ has been previously reported.[13]

[23] Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901–3924 and references therein.

[24] Newcomb, M.; Park, S. U. *J. Am. Chem. Soc.* **1986**, *108*, 4132–4134.

[25] Beckwith, A. L. J. Moad, G. *J. Chem. Soc., Chem. Commun.* **1974**, *472*–473.

Table IV. EPR Results for the Cyclization of the 1,1-Dimethyl-5-hexenyl Radical in Cyclopropane

T, K	$10^8[\mathbf{5}^\bullet]$, M	$10^8[\mathbf{7}^\bullet]$, M	$10^8 k_5/2k_t$, M	$10^{-8} 2k_t$,[a] $M^{-1}\ s^{-1}$	k_5, s^{-1}
170	12.7	20.8	20.5	8.0	163
173	14.9	14.0	30.8	8.8	271
176	18.0	23.5	31.8	9.8	311
179	20.4	17.1	44.7	10.8	483
182	18.9	24.1	33.7	11.9	401
183	20.8	17.3	45.8	12.3	564
187	18.4	15.8	39.8	13.9	554
192	19.6	10.8	55.2	16.2	894
193	16.5	10.0	43.7	16.6	726
338					1.37×10^6[b]

[a] Calculated from Arrhenius parameters given in ref 27 for the *n*-hexyl radical bimolecular self-reaction in cyclopropane. [b] This rate constant was calculated from $k_5/k_{SnH} = 0.41$ M (ref 13) and $k_{SnH} = 3.33 \times 10^6\ M^{-1}\ s^{-1}$. The latter rate constant was calculated from the Arrhenius parameters for the $Me_3C^\bullet$ + *n*-Bu_3SnH reaction given in ref 6.

calculate that $k_{add}/k_r = 1.09 \pm 0.06$ and $1.45 \pm 0.06\ M^{-1}$ from the GC and HPLC data, respectively, that are given in Table III. The mean value for k_{add}/k_r of 1.27 M^{-1} at 30 °C can be combined with the "best" value for k_5 ($=k_r$) at this temperature ($3.6 \times 10^5\ s^{-1}$, vide infra) to obtain $k_{add} = 4.6 \times 10^5\ M^{-1}\ s^{-1}$ for $\mathbf{7}^\bullet + \mathbf{8a}$.

It will be clear from Scheme III that the measurement of k_H from a relatively poor H donor via k_{add} and the [hydrocarbon]/[alkyl pyridyl sulfide] product ratio does not require the use of an ester, **8**, which yields an $R^\bullet$ radical that can undergo a rearrangement. Indeed, such a rearrangement simply complicates the measurement of k_H since it increases the number of products. We therefore employed **8d** under the same conditions as those used to measure k_{add}/k_r with **8a** except for the addition of tri-*n*-butylgermanium hydride. Somewhat to our surprise, the yield of **9d** was found to pass through a maximum and then to decrease substantially. We presume that as the concentration of **8d** falls, although **8d** can still initiate a chain reaction. propagation increasingly involves the initial product **9d**; that is, the two principal propagation steps become

$$n\text{-}Bu_3Ge^\bullet + \mathbf{9d} \rightarrow \mathbf{11}\ (X = n\text{-}Bu_3Ge) + CH_3(CH_2)_2CMe_2^\bullet$$

$$CH_3(CH_2)_2\dot{C}Me_2 + n\text{-}Bu_3GeH \rightarrow CH_3(CH_2)_2CHMe_2 + n\text{-}Bu_3Ge^\bullet$$

This approach to the measurement of k_7 ($=k_H$, XH = *n*-Bu_3GeH) was therefore abandoned.

Approximate Calibration of the 1,1-Dimethyl-5-hexenyl Radical Clock by Kinetic EPR Spectroscopy. We used the same techniques that we have previously employed to calibrate the 5-hexenyl[26,27] and 1-methyl-5-hexenyl[15] clocks. The desired radical $\mathbf{7}^\bullet$ was generated photochemically in cyclopropane solvent from the bromide **12** by the reaction sequence

$$Me_3COOCMe_3 \xrightarrow{h\nu} 2\ Me_3CO^\bullet$$

$$Me_3CO^\bullet + Me_3SiH \rightarrow Me_3COH + Me_3Si^\bullet$$

$$Me_3Si^\bullet + (CH_3)_2CBr(CH_2)_3CH{=}CH_2 \rightarrow Me_3SiBr + \mathbf{7}^\bullet$$

Absolute concentrations of $\mathbf{7}^\bullet$ and the exo-cyclized (2,2-dimethylcyclopentyl)methyl radical, $\mathbf{5}^\bullet$, under steady photolysis were measured in the usual way. Neither the endo-cyclized radical $\mathbf{6}^\bullet$ nor any other radicals arising from the impurities in **12** could be observed, presumably because their concentrations are insignificant relative to $\mathbf{5}^\bullet$ and $\mathbf{7}^\bullet$. Concentration of $\mathbf{5}^\bullet$ and $\mathbf{7}^\bullet$ at various temperatures are given in Table IV. These concentrations have been used to calculate values for $k_5/2k_t$ at each temperature in the usual way,[15,26,27] where $2k_t$ is the (diffusion-controlled) bimolecular rate constant for the alkyl radical/alkyl radical reaction. The values of $2k_t$ that are given in Table IV have been assumed to be equal to those previously measured for the *n*-hexyl radical in cyclopropane.[27] The derived values for k_5 yield eq 5. The preexponential factor is

$$\log (k_5/s^{-1}) = (7.6 \pm 1.2) - (4.1 \pm 1.0)/\theta \qquad (5)$$

unacceptably low,[28] but the rate constants themselves, particularly those measured in the middle of the temperature range, are probably fairly reliable. If we include the single value for k_5 at 338 K (see Table IV), which was calculated by combining the results of a product study of the reaction of **12** with *n*-Bu_3SnH[13] with the absolute rate constant for the reaction of *tert*-butyl radicals with the tin hydride at this temperature,[6] we obtain eq 6. This

$$\log (k_5/s^{-1}) = (10.0 \pm 0.6) - (6.1 \pm 0.5)/\theta \qquad (6)$$

equation is probably more reliable than eq 5, but additional high-temperature measurements are required. We did not attempt such measurements because of our problems with the purity of the bromide **12** and because of our inability to attain our primary objective—reliable kinetic data on the tertiary alkyl radical/*n*-Bu_3GeH reaction using the **12**/*n*-Bu_3GeH system.

Table V. Kinetic Parameters for the Reactions of Alkyl Radicals with *n*-Bu_3GeH and *n*-Bu_3SnH[14]

alkyl radical	hydride	log ($A/M^{-1}\ s^{-1}$)	E, kmol/mol	$10^{-5}k^{298K}$, $M^{-1}\ s^{-1}$
primary[a]	*n*-Bu_3GeH	8.44 ± 0.47	4.70 ± 0.62	0.98
primary[b]	*n*-Bu_3SnH	9.07 ± 0.24	3.69 ± 0.32	23
secondary[c]	*n*-Bu_3GeH	8.30 ± 0.30	5.52 ± 0.35	0.18
secondary[d]	*n*-Bu_3SnH	8.71 ± 0.37	3.47 ± 0.49	15

[a] 5-Hexenyl; ref 10. [b] Combined data for ethyl and *n*-butyl radical; ref 6. [c] 1-Methyl-5-hexenyl; this work. [d] Isopropyl; ref 6.

Discussion

Relative rate constants and Arrhenius parameters calculated from the product yield data can be converted to absolute rate constants and Arrhenius parameters for hydrogen abstraction from the germane via the absolute kinetic data for the clock reactions. "Best values" for the latter are summarized in Table II for the two radicals studied in this work and for the 5-hexenyl cyclization. The preexponential factors for these four exo cyclizations are of similar magnitude, as would be expected for such similar reactions. Furthermore, the magnitudes of the A factors are consistent with the freezing-out of four hindered rotations in the transition state. An additional check on the kinetic data for reactions 1 and 2 is available from studies of the products of the reaction between 6-bromoheptene and tri-*n*-butyltin hydride.[13,29,30] Combination of this data with the absolute Arrhenius parameters for the reaction of secondary alkyl radicals with tin hydride[6] yields[30] eq 7 and 8, with $k_1^{298K} = 4.0 \times 10^5\ s^{-1}$ and $k_2^{298K} = 1.1 \times 10^5$

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(26) Lal, D.; Griller, D.; Husband, S.; Ingold, K. U. *J. Am. Chem. Soc.* **1974**, *96*, 6355–6357.

(27) Schmid, P.; Griller, D.; Ingold, K. U. *Int. J. Chem. Kinet.* **1979**, *11*, 333–338.

(28) Low *A* factors are not uncommon in this type of kinetic EPR experiment, see, e.g., ref 27.

(29) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron Lett.* **1985**, *26*, 373–376.

(30) Beckwith, A. L. J., private communication.

$$\log (k_1/\mathrm{s}^{-1}) = (10.3 \pm 0.4) - (6.4 \pm 0.6)/\theta \qquad (7)$$

$$\log (k_2/\mathrm{s}^{-1}) = (10.4 \pm 0.4) - (7.3 \pm 0.5)/\theta \qquad (8)$$

s^{-1}. The agreement with the data in Table II is reasonably satisfactory considering the different procedures employed to obtain the two sets of kinetic parameters.

Kinetic parameters for the reactions of primary[10] and secondary alkyl radicals with tri-*n*-butylgermane[31] are compared in Table V with the analogous parameters for their reactions with tri-*n*-butylstannane. The germanium hydride is a notably less reactive hydrogen donor than the tin hydride, presumably because Ge–H bonds are ca. 8–10 kcal/mol stronger than comparable Sn–H bonds.[8,32] This difference in bond strengths manifests itself in both the entropies and enthalpies of activation. Thus, the *A* factors for abstraction from the germane are ca. $10^{0.5}$ M^{-1} s^{-1} smaller than that for abstraction from the stannane. Presumably there is either a "tighter" transition state for removal of the more strongly bound hydrogen or steric hindrance for reaction with the germane is greater than for reaction with the stannane.[33] The larger activation energies for attack upon the germane must be due to the fact that reaction with germane is less exothermic. The actual rate constants at ambient temperatures for reaction of primary and secondary (and tertiary) alkyl radicals with tin hydride are remarkably similar,[6] as are the rate constants for reactions of the primary and secondary alkyl radicals[31] with germanium hydride. However, the germane is much less reactive than the stannane, which suggests that it could be a useful replacement for stannane in helping to solve those synthetic and mechanistic problems in which a relatively slow radical rearrangement or scission must occur before the radical is trapped by the metal hydride.[34]

Our measurement of the rate constant for the addition of a tertiary alkyl radical to the *N*-hydroxypyridine ester **8a**, viz., $k_{add} = 4.6 \times 10^5$ M^{-1} s^{-1} at 30 °C, supports Newcomb and Park's assumption[24] that the rate constants they measured for addition of a primary alkyl radical, viz., $\sim 2 \times 10^6$ M^{-1} s^{-1} at 50 °C, will be "a reasonable approximation for the rate constant for reaction of any (alkyl) radical". However, we should add that although **8** and related compounds have enormous synthetic utility[23] they are not ideally suited to certain types of kinetic study as evidenced by the destruction of **8d** by $n\text{-Bu}_3\text{Ge}^\bullet$ radicals.

Experimental Section

Materials. Tri-*n*-butylgermane and its deuteriated analogue were prepared by reduction of $n\text{-Bu}_3\text{GeCl}$ (Alfa) with lithium aluminum hydride[36] or deuteride. 6-Bromohept-1-ene was prepared following a previously described procedure[15] and purified by preparative GC.

6-Bromo-6-methylhept-1-ene (**12**) was synthesized from 2-methylhept-6-en-2-ol by a slight modification to the literature procedure for *tert*-butyl bromide.[37] The alcohol was obtained by condensing 4-pentenylmagnesium bromide [from 1-bromopent-4-ene (5 g, 0.033 mol) and magnesium turnings (0.8 g)] with acetone (2 g, 0.033 mol): yield, 3.1 g (73%); bp 69–70 °C (25 mmHg); ^{1}H NMR (CCl_4, Me_4Si internal) δ 1.18 (s, 6 H, $(CH_3)_2$), 1.3–2.3 (m, 6 H, $(CH_2)_3$), 4.8–6.2 (m, 3 H, $CH_2{=}CH$). To a mixture of this alcohol (2.6 g, 0.02 mol) and LiBr (2.6 g, 0.03 mol) at 0 °C was added concentrated hydrobromic acid 4.6 mL, 47% HBr, 0.04 mol). After 2 h the mixture was extracted with pentane (2 × 40 mL), washed with ethylene glycol (2 × 2 mL) and water (3 × 10 mL), and dried over $MgSO_4$. Removal of pentane and distillation under reduced pressure gave **12**: yield, 3.5 g (90%); NMR (CCl_4, Me_4Si internal) δ 0.8–2.4 (m, 6 H, $(CH_2)_3$), 1.73 (s, 6 H, $(CH_3)_2$), 4.8–6.2 (m, 3 H, $CH{=}CH_2$). This bromide was "purified" by preparative GC, but we could not obtain material that by analytical GC was better than 80% pure.

The *N*-hydroxypyridine-2-thione ester precursor of the 1,1-dimethyl-5-hexenyl radical and the 2-methylpent-2-yl radical were obtained from the appropriate acids and *N*-hydroxypyridine-2-thione sodium salt (Fluka) following the previously described procedure.[23]

The compounds used for GC identification of the products in the tri-*n*-butylgermane reactions with 1-methyl-5-hexenyl and 1,1-dimethyl-5-hexenyl radicals were available (National Bureau of Standards, Washington, DC).

Procedures. Reaction of n-$\mathbf{Bu_3GeH}$ with Bromides. *n*-Decane or *n*-nonane (or, in some cases, *tert*-butylbenzene) containing a small amount of *n*-heptane or *n*-octane as an internal GC standard was used as solvent. The $n\text{-Bu}_3\text{GeH}$ was added at a concentration of ca. 1 or 2 M and the 6-bromohept-1-ene or 6-bromo-6-methylhept-1-ene at a concentration of ca. 0.2 M. A small quantity of di-*tert*-butyl peroxide (2×10^{-3} M in the photolysis experiments and from 4×10^{-4} to 1×10^{-3} M for the thermal experiments) was added to act as the free radical chain initiator. Samples of these reaction mixtures were degassed and sealed under vacuum in Pyrex tubes and were then thermalized or photolyzed. Each tube provided just one sample for product analysis. Reactions were initiated by thermal decomposition of the di-*tert*-butyl peroxide at temperatures above 328 K and by photolysis at 273 and 243 K. The consumption of the bromides was varied from a low of 1% to a high of 90%. Results were generally calculated from runs in which the consumption was in the range 1–30%. Reaction times varied from a few minutes to several hours.

The products of reaction of 6-bromohept-1-ene were analyzed by GC using a 30 ft × $^1/_8$ in. 20% Carbowax 20 M column with temperature programming from 75 to 200 °C using a Varian 6000 chromatograph. The hydrocarbon products of interest were identified by comparison of their mass spectra and retention times with authentic materials. We were unable to separate **1** and **3** on this column and they were therefore measured as a single fraction, i.e., the product ratios measured were [(**1** + **3**)]/[**2**]/[**4**]. The [**1**]/[**3**] ratio was estimated by selective ion monitoring utilizing an HP 5995 GC/MS instrument with a 10 m, 0.2 mm i.d. Ultra I (cross-linked methyl silicone) column with temperature programming from −20 to +200 °C. The ratio of the ions, (m/e = 69)/(m/e = 70), was monitored and was converted into a [**1**]/[**3**] ratio by using a calibration curve. The calibration curve had been constructed by running standard mixtures containing known [**1**]/[**3**] ratios in which the quantity of **3** varied from 0% to 10% of the quantity of **1**.[38]

The products of reaction of 6-bromo-6-methylhept-1-ene were analyzed by GC using a 40 m, 0.2 mm i.d. Ultra I column with temperature programming from 50 to 260 °C using the HP GC/MS instrument. Products were identified by comparison of their retention times and mass spectra with those of authentic materials. Compounds with retention times equal to those of the hydrocarbon products **5**, **6**, and **7** were not present in the reactants.

Decomposition of *N*-Hydroxypyridine-2-thione Esters 8. The 2-methylhept-6-ene-2-yl radical, $\mathbf{7}^\bullet$, was generated by photodecomposition of **8a** (0.1, 0.2 and 0.4 M) in *n*-nonane at 30 °C. The solutions were placed in Pyrex tubes, degassed, and sealed under vacuum. Irradiation was provided by a 100-W tungsten filament lamp at a distance of 20 cm. The reaction was complete

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(31) We consider the parameters that can be derived for the tertiary alkyl radical (viz., $\log (A/M^{-1}\,s^{-1}) \sim 7.7$, $E \sim 4.6$ kcal/mol, $k^{298K} \sim 2 \times 10^4$ M^{-1} s^{-1}) to be too unreliable to require further comment.

(32) Jackson, R. A. *J. Organomet. Chem.* **1979**, *166*, 17–19.

(33) We have previously attributed the decrease in *A* factors along the series primary, secondary, and tertiary alkyl radical for their reaction with the stannane to the increase in steric hindrance of the attacking radical.[6]

(34) Pentamethyldisilane is an alternative.[35]

(35) Lusztyk, J.; Maillard, B.; Ingold, K. U. *J. Org. Chem.* **1986**, *51*, 2457–2460.

(36) Stang, P. J.; White, M. R. *J. Am. Chem. Soc.* **1981**, *103*, 5429–5433. Kuivila, H. G.; Beumel, O. F., Jr. *Ibid.* **1961**, *83*, 1246–1250.

(37) Masada, H.; Murotani, Y. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1181–1182.

(38) A variety of methylsilicone capillary columns of different length (up to 100 m) and film thickness (down to 0.5 μm) failed to resolve authentic mixtures of **1** and **3**.

in 5 min or less. Products were analyzed both by GC (50 m, 0.2 mm i.d. HP Pona column, cross-linked methylsilicone with a 0.5 μm film thickness) and by HPLC (25 cm, 4 mm, Lichrosorb Si 60 (10 μm) column eluted over 30 min with a graded hexane/chloroform mixture (100% hexane → 100% $CHCl_3$) and detection by UV absorption at 290 nm).

The same system was used with **8d**.

EPR Kinetic Measurements. These were carried out following previously described procedures.[15,26,27]

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Registry No. **1**, 1192-18-3; **2**, 822-50-4; **3**, 108-87-2; **4**, 592-76-7; **7**·, 38295-12-4; **8a**, 108743-45-9; **12**, 15424-05-2; *n*-Bu_3SnH, 688-73-3; *n*-Bu_3GeH, 998-39-0; 1-methyl-5-hexenyl radical, 38295-10-2; cyclopropane, 75-19-4; 4-pentenylmagnesium bromide, 34164-50-6; acetone, 67-64-1; 2-methylhept-6-en-2-ol, 77437-98-0; 6-bromohept-1-ene, 38334-98-4.

Supplementary Material Available: Tables VI–IX giving detailed product ratios for the 6-bromohept-1-ene/*n*-Bu_3GeH reaction, kinetic data for calibration of the 1-methyl-5-hexenyl radical clock, and some product ratios for the 2-bromo-2-methylhept-6-ene/*n*-Bu_3GeH reaction (4 pages). Ordering information is given on any current masthead page.

Oxygenations of Vitamin E (α-Tocopherol) and Its Model Compound 2,2,5,7,8-Pentamethylchroman-6-ol in the Presence of the Superoxide Radical Solubilized in Aprotic Solvents: Unique Epoxidations and Recyclizations[1]

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Vitamin E (**1a**, α-tocopherol) and its model compound 2,2,5,7,8-pentamethylchroman-6-ol (**1b**) were oxygenated in aprotic solvents in the presence of the solubilized superoxide radical under an oxygen atmosphere to give diepoxides **2a** and **2b** as main products, respectively. The reactions proceeded only slightly under anaerobic conditions. Extensive product analysis was carried out on the oxygenation of **1b**, revealing that it gave rise to the products **2b**, **3b**, **4b**, **5b**, **6b**, and **7b**. The novel compounds were determined to be 4a,5;7,8-diepoxy-4a,7,8,8a-tetrahydro-8a-hydroxy-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5*H*)-one (**2a**), 4a,5;-7,8-diepoxy-4a,7,8,8a-tetrahydro-8a-hydroxy-2,2,5,7,8-pentamethylchroman-6(5*H*)-one (**2b**), 1,1-dimethyl-3-(2,3-epoxy-2,3,5-trimethylbenzoquinon-6-yl)propanol (**5b**), 6-acetyl-7,8-epoxy-6-hydroxy-2,2,7,8-tetramethyl-1-oxaspiro[4.5]nonan-9-one (**6b**), and 6-acetyl-6-hydroxy-2,2,7,8-tetramethyl-1-oxaspiro[4.5]non-7-en-9-one (**7b**); the previously suggested structures of **6b** and **7b** should be revised. Compounds **6b** and **7b** are unique spiro compounds containing two five-membered rings. The structures of **2b**, **5b**, and **6b** were confirmed by X-ray crystallography. The reactions are suggested to be superoxide-catalyzed oxygenations, being characteristic of epoxidations and recyclizations, in which hydroperoxides **9a** and **9b** may be key intermediates. Possible reaction pathways for the formation of the products are discussed.

Currently, vitamin E (mainly α-tocopherol) attracts increasing attention as an efficient biological antioxidant playing an important role in the protection of organisms against oxidative damage.[2,3] From a chemical point of view, it is of great interest that α-tocopherol is very reactive not only toward the peroxyl radical,[4,5] i.e., exhibiting a high chain-breaking antioxidant activity, but also toward a variety of radicals and related reaction species. For example, α-tocopherol traps some radicals generated from radical reaction initiators, such as benzoyl peroxide[6,7] and 2,2′-azobis(isobutyronitrile),[8,9] and reacts with the alkyl and alkoxyl radicals to give the alkylated derivatives.[10,11] With α-tocopherol, singlet oxygen is quenched into triplet oxygen[12] and also reacts chemically to yield a hydroperoxide.[13,14] Further, it has been found that the reactions of α-tocopherol and its model compounds occur in the presence of the superoxide radical,[1,15–19] a causative agent

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(1) Issued as TMIG-I No. 96. For a preliminary account of part of this work, see: Matsuo, M.; Matsumoto, S.; Iitaka, Y.; Hanaki, A.; Ozawa, T. *J. Chem. Soc., Chem. Commun.* **1979**, 105–106.

(2) McCay, P. B.; King, M. M. In *Vitamin E, A Comprehensive Treatise*; Machlin, L. J., Ed.; Marcel Dekker: New York, 1980; pp 289–317.

(3) Witting, L. A. In *Free Radicals in Biology*; Pryor, W. A., Ed.; Academic: New York, 1980; Vol. IV, pp 295–319.

(4) Burton, G. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 6472–6477.

(5) Matsumoto, S.; Matsuo, M.; Iitaka, Y.; Niki, E. *J. Chem. Soc., Chem. Commun.* **1986**, 1076–1077.

(6) Goodhue, C. T.; Risley, H. A. *Biochem. Biophys. Res. Commun.* **1964**, *17*, 549–553.

(7) Skinner, W. A.; Parkhurst, R. M. *J. Org. Chem.* **1966**, *31*, 1248–1251.

(8) Skinner, W. A. *Biochem. Biophys. Res. Commun.* **1964**, *15*, 469–472.

(9) Winterle, J.; Dublin, D.; Mill, T. *J. Org. Chem.* **1984**, *49*, 491–495.

(10) (a) Urano, S.; Matsuo, M. *Lipids* **1976**, *11*, 380–383. (b) Urano, S.; Yamanoi, S.; Hattori, Y.; Matsuo, M. *Lipids*, **1977**, *12*, 105–108. (c) Urano, S.; Yamanoi, S.; Matsuo, M. *Chem. Pharm. Bull.* **1981**, *29*, 1162–1165.

(11) Kaneko, T.; Matsuo, M. *Chem. Pharm. Bull.* **1985**, *33*, 1899–1905.

(12) (a) Fahrenholtz, S. R.; Doleiden, F. H.; Trozzolo, A. M.; Lamola, A. A. *Photochem. Photobiol.* **1974**, *20*, 505–509. (b) Foote, C. S.; Ching, T.-Y.; Geller, G. G. *Photochem. Photobiol.* **1974**, *20*, 511–513. (c) Stevens, B.; Small, R.; Perez, S. *Photochem. Photobiol.* **1974**, *20*, 515–517.

(13) Clough, R. L.; Yee, B. G.; Foote, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 683–686.

(14) Yamauchi, R.; Kato, K.; Ueno, Y. *Agric. Biol. Chem.* **1981**, *45*, 2855–2861.

(15) Nishikimi, M.; Machlin, L. J. *Arch. Biochem. Biophys.* **1975**, *170*, 684–689.

(16) (a) Matsumoto, S.; Matsuo, M.; Iitaka, Y. *Tetrahedron Lett.* **1981**, *22*, 3649–3652. (b) Matsumoto, S.; Matsuo, M. *Tetrahedron Lett.* **1977**, 1999–2000.

0022-3263/87/1952-3514$01.50/0