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]

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society; the Robert A. Welch Foundation; and the National Science Foundation (CHE-85-087076) for support. We thank Dr. J. A. Franz for providing kinetic data on the reactions of PhSH prior to publication and Professor A. L. J. Beckwich for exchanging information on the radical kinetics prior to submission.

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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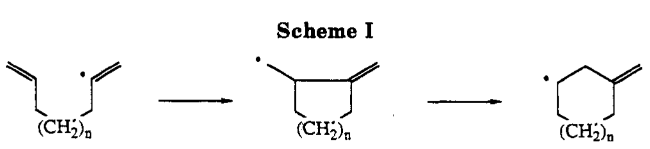
Accurate analysis of the mixture of hydroxylamines **8** formed when suitable peroxides **4** undergo homolysis in the presence of the nitroxyl radical 1,1,3,3-tetramethylisoindolin-2-yloxy (T) has afforded rate constants for ring opening of the cyclopropylmethyl radicals **2a**, **2c**, $\mathbf{2d}^{cis}$, $\mathbf{2d}^{trans}$, 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, $\mathbf{2d}^{trans}$, 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 $k_1(\mathbf{2a}) = 13.31 - 7.6/2.3RT$.

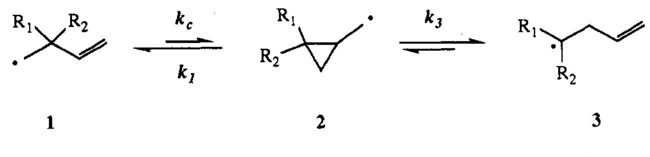
Introduction

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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[1] For reviews see: (a) Wilt, J. W. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 1, pp 333–501. (b) Davies, D. I.; Cristol, S. J. In *Advances in Free-Radical Chemistry*; Williams, G. H., Ed.; Logos Press: London, 1965; pp 156–157. (c) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; pp 178–181.

[2] Stork, G.; Mook, R. *J. Am. Chem. Soc.* **1987**, *109*, 2829–2831; *Tetrahedron Lett.* **1986**, *27*, 4529–4432.

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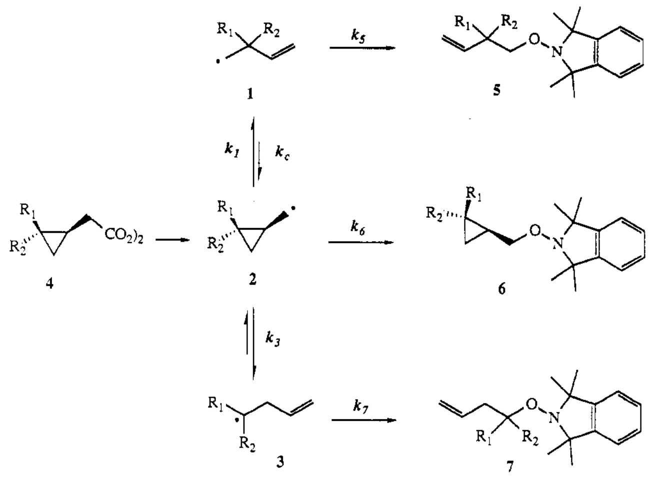
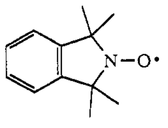
Scheme III[a]



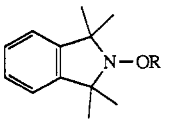
[a] **a**, $R_1 = R_2 = H$; **b**, $R_1 = R_2 = D$; **c**, $R_1 = R_2 = Me$; **d**^{cis}, $R_1 = Me$, $R_2 = H$; **d**^{trans}, $R_1 = H$, $R_2 = Me$; **e**, $R_1 = H$, $R_2 = CO_2Et$.

Product studies and labeling experiments have established that vinyl migrations occur via distinct cyclopropylmethyl (CPM) radical intermediates (Scheme II).[4] However, unless specially stabilized, the CPM radicals **2** have much shorter lifetimes than the parent homoallylic radicals **1** and they neither give rise to appreciable products nor can be detected by ESR; consequently such rearrangements can be and have been treated as one-step reactions, e.g, **1** → **3** with rate constant k_r.

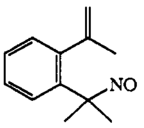
Rearrangements of 3-butenyl radicals are very sensitive to substitution. Thus, the dimethyl-substituted radical **1c**[5-7] rearranges some hundreds of times more rapidly than does 3-butenyl (**1a**)[8], while effects of similar or greater magnitude may be expected in the ring contraction–expansion reactions of cyclic homoallylic radicals. In order to define further the effects of substituents and thus facilitate the prediction of the outcome of reactions involving possible vinyl migration, rate constants for β-fission of the intermediate CPM radicals **2** are required. Unfortunately, such reactions are very fast and their kinetics difficult to measure by the usual methods; for example, hydrogen atom transfer from neat tributylstannane to the radicals **2d**^{cis} or **2d**^{trans} does not effectively compete with their ring opening; nor can any unrearranged species be detected by steady-state ESR even at −140 °C.[9]



T



8



9

The nitroxyl radical 1,1,3,3-tetramethylisoindolin-2-yloxy (T) couples with alkyl radicals with a bimolecular rate constant k_T of about 1×10^9 M^{-1} s^{-1} over a wide temperature range[10,11] to give the corresponding *O*-alkyl hydroxylamines **8**. It has been shown that the coupling of T with **2a** competes effectively with ring opening of the latter[10,12] (Scheme III) and that the hydroxylamine products **6a** and **7a** (=**5a**) can be readily separated and quantified to give the rate constant for ring opening. We now describe our investigations of ring-substituted CPM radicals **2c**, **2d**^{cis}, **2d**^{trans}, and **2e** and give complete kinetic parameters for homoallylic rearrangement of **1c**.

Results and Discussion

Generation and Trapping of Radicals 2c–e. Solutions of diacyl peroxides **4c–e** and the nitroxide T (10 molar equiv) in cyclohexane were degassed, sealed in Pyrex ampules, and then heated in thermostated baths for the required reaction times, viz., 18 h at 60 °C or 1 h at 100 °C. The product mixtures were resolved and quantified by reversed-phase HPLC with UV detection (270 nm) as previously specified.[10]

At the high concentrations, [T], of nitroxide required to trap initially formed CPM radicals before ring opening, peroxides **4c–e** probably reacted mainly through a nitroxide-induced decomposition pathway[13-15] (eq 1) although polar rearrangement[16] and direct homolysis were also important.

$$T + (RCO_2)_2 \rightarrow R^\bullet + CO_2 + RCO_2H + \mathbf{9} \qquad (1)$$

Analyses of the reaction mixtures by HPLC revealed a number of minor UV-active products, which eluted just before and after T. They were probably formed by subsequent reactions of **9** (e.g., radical addition[14] followed by nitroxide decay[15]). However, with the large excess of T employed in these experiments, byproducts arising from **9** did not interfere with HPLC detection of the products required for kinetic analysis. In preparative-scale experiments, the esters and anhydrides expected to arise by the polar route[16] were also detected. However, in the kinetic runs, neither these nor the UV-active minor products could be estimated, and a full material balance could not, therefore, be made. The total yields of trapped products based on the stoichiometry of eq 1 varied between 60% and 90%.

It is conceivable that induced decomposition might produce hydroxylamines, e.g., **6**, without the intermediacy of dissociated radicals. However, this possibility was precluded by the fact that the relative yields of products varied with trap concentration as expected from the rate equations. Thus, the ratio of product concentrations [**6**]/[**7**] was directly proportional to trap concentration, [T], over a wide range. It was also established for **2a**[10] that the product ratios did not depend on whether the appropriate diacyl peroxide (**4a**), *tert*-butyl perester, or hydroxydiazene[12] precursor was used. Unfortunately, *tert*-butyl peresters were not practical radical sources for **2c** and **2d** in cyclohexane alone because the hydroxylamine (**8**, R =

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cyclohexyl) formed by trapping of cyclohexyl radicals generated by hydrogen abstraction from the solvent by *tert*-butoxy radicals could not be separated from some of the products (e.g., **7c**).

This problem could be overcome, at least in part, by addition of 1,4-cyclohexadiene as a hydrogen donor cosolvent. It readily undergoes hydrogen atom abstraction by *tert*-butoxy radicals, but not by alkyl radicals, to generate cyclohexadienyl radicals which react with the trap not by coupling but by disproportionation to give benzene and the hydroxylamine **8** (R = H). Thus, when reaction mixtures containing **4c** or the corresponding perester, the nitroxide (T), and 1,4-cyclohexadiene (10% v/v) in benzene were degassed, heated, and analyzed in the usual way, product mixtures consistent with the reactions in eq 2–5 were found for the peresters. Moreover, the choice of precursor had no apparent effect on the observed molar product ratios [**5**]/[**6**] or [**7**]/[**6**].

$$RCO_2Bu^t \rightarrow R^\bullet + Bu^tO^\bullet + CO_2 \qquad (2)$$

$$R^\bullet + T \rightarrow \mathbf{8} \qquad (3)$$

$$Bu^tO^\bullet + \text{1,4-cyclohexadiene} \rightarrow Bu^tOH + C_6H_7^\bullet \qquad (4)$$

$$C_6H_7^\bullet + T \rightarrow C_6H_6 + \mathbf{8}\ (R = H) \qquad (5)$$

The reduced trap, **8** (R = H), was rapidly oxidized to T on exposure to air;[17] it was identified by HPLC by coinjection with authentic 2-hydroxy-1,1,3,3-tetramethylisoindoline, freshly prepared by admixture of ascorbic acid and T in aqueous methanol.[17]

Kinetic Equations for Scheme III. Steady-state treatment of the reactions of Scheme III under pseudo-first-order conditions (i.e., a large excess of T) and with the assumption of the irreversibility of **2** → **3** affords the following relationships between the hydroxylamine product ratios and rate constants (eq 6–8).

$$[\mathbf{6}]/[\mathbf{5}] = ([T] + k_c/k_5)k_6/k_1 \qquad (6)$$

$$[\mathbf{6}]/[\mathbf{7}] = (k_6/k_3)[T] \qquad (7)$$

$$[\mathbf{7}]/[\mathbf{5}] = (1 + [T]k_c/k_5)k_3/k_1 \qquad (8)$$

When the concentration of T is sufficiently low, trapping of **2** becomes too slow to compete effectively with ring opening, and product **6** cannot be detected. Under these conditions, the rate constant, k_r, for the vinyl migration **1** → **3** is given by eq 9, while stationary-state treatment of the reactions of Scheme II gives eq 10, defining the relationship between cyclization and migration rate constants.

$$[\mathbf{7}]/[\mathbf{5}] = (k_r/k_6)[T]^{-1} \qquad (9)$$

$$k_c = k_r(1 + k_1/k_3) \qquad (10)$$

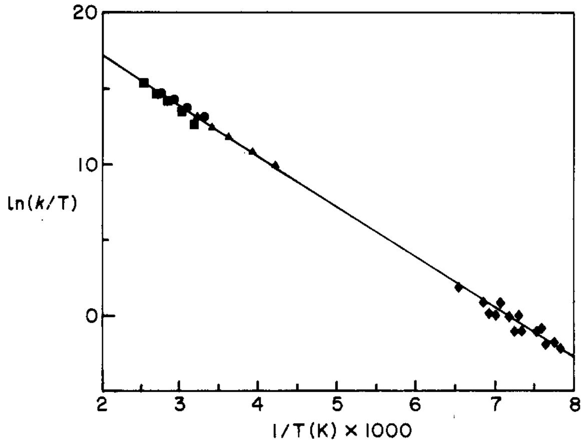

Figure 1. Plot of ln (k/T) against $1/T$ for the ring opening of cyclopropylmethyl radical (**2a**); data from ref 10 (■), ref 12 (●), ref 18 (◆), and ref 19 (▲).

Table I. Relative Yields[a] of Products for Coupling of 2c with the Nitroxyl Radical T at 60 °C[b] in Cyclohexane

	relative yields[a]			
[T],[c] mM	**6c/5c**	**7c/5c**	**6c/7c**	k_3/k_T,[d] M
271	1.0	7.2	0.14	1.9
270	1.08	7.1	0.15	1.8
144	0.50	7.2	0.069	2.1
72	0.32	8.2	0.041	1.8
18		13.1		
4.5		35.9		

[a] Total combined yield ca. 40%; see text. [b] Within ±0.3 °C. [c] Average concentration during the reaction, corrected for thermal expansion. [d] Calculated by means of eq 7 from experimental values of **6c/7c**.

Cyclopropylmethyl Radical (2a). Kinetic data for the ring opening of **2a**, obtained by the nitroxide trapping method, were presented in our previous paper.[10] Two similar studies involving nitroxide trapping[12] and kinetic ESR spectroscopy, respectively,[18] had been published earlier, while very recently Newcomb has presented data obtained by the use of hydrogen atom transfer from benzenethiol as a kinetic standard.[19] Since the combined data (see Experimental Section) cover a very wide temperature range (≃280 °C), it is appropriate to use the Eyring equation. Figure 1 shows the graph of ln (k_1/T) against $1/T$. There is excellent correlation $\langle r \rangle = 0.9987$) with the linear plot of eq 11 (RT in kilocalories per mole).

$$\ln (k_1/T) = (23.9 \pm 0.35) - (6.68 \pm 0.15)/RT \qquad (11)$$

As it combines the results of four different sets of workers using three different experimental techniques, eq 11 should provide a reliable basis for the calculation of values of the rate constant, $k_1(\mathbf{2a})$, for the ring opening of cyclopropylmethyl radical over a wide temperature range. Such values can then be used to derive the Arrhenius equation for more limited ranges. For ordinary temperatures (0–80 °C), we recommend eq 12 ($\theta = 2.3RT$).

$$\log k_1(\mathbf{2a}) = 13.31 - 7.26/\theta \qquad (12)$$

2′,2′-Dimethylcyclopropylmethyl Radical (2c). Analysis by HPLC of reactions of the peroxide **4c** with T (10 molar equiv) in cyclohexane at 60 °C revealed hydroxylamine products **5c**, **6c**, and **7c** in the ratios listed in Table I. Yields based on the usual stoichiometry for peroxide decay were low (30–45%), reflecting the extensive nitroxide-induced decay and (at low [T]) the polar decomposition that bis(cyclopropylacetyl) peroxides readily undergo[16] (see above).

Molar ratios of cyclic to ring-opened products given in Table I, e.g., [**6c**]/[**5c**], show linear relationships against [T], whereas the ratio of ring-opened products, [**7c**]/[**5c**], is constant at high [T] but rises rapidly when the trap concentration is reduced below about 20 mM. This behavior is consistent with Scheme III and the known rapid rearrangement of **1c** to **3c**.[5,7] At high quenching rates (high [T]), the product ratios reflect the kinetics of ring fission and, as expected, indicate that ring fission to give the tertiary alkyl radical **3c**, is substantially favored over fission

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Table II. Relative Yields of Hydroxylamines and Rate Constants for Reactions of 1c

temp, °C	[T], mM	relative yield (5c/7c)	k_c/k_r
59.9	11.9	0.52	43.6
80.6	18.2	0.504	27.7
80.6	11.6	0.31	26.6
80.6	4.46	0.115	25.8
99.5	10.8	0.174	16.1
122.2	10.3	0.123	11.9
122.0	16.3	0.190	11.6
124.5	16.8	0.190	11.25

to give the primary alkyl radical **1c**. At very low concentrations of T, radicals are trapped much less effectively, the equilibrium between **1c** and **2c** comes into play, and the relative rate of formation of **3c** is increased, giving an increase in the ratio [**7c**]/[**5c**].

Fitting of the data into the kinetic equations 6–10 by linear regression or graphical analysis gives relative rearrangement rate constants. For example, a plot of [**7c**]/[**5c**] against the reciprocal trap concentration $[T]^{-1}$ at 60 °C is linear ([**7c**]/[**5c**] = $6.38 + 0.13[T]^{-1}$; $\langle r \rangle = 0.999$), as expected from eq 8, and gives $k_c/k_5 = 0.020$ M and $k_3/k_1 = 6.38$. Similar treatment of other data in Table I gives $k_1/k_6 = 0.26$ M (by eq 6) and $k_3/k_6 = 1.9$ M (eq 7).

Laser flash photolysis[11] and radical-clock[10] calibrations have shown that k_T is not very sensitive to radical stability or geometry at least to the benzyl or tertiary alkyl radical level. The assumption that $k_6(\mathbf{2c}) = k_T(5\text{-hexenyl})^{10} = 1.3 \times 10^9\ M^{-1}\ s^{-1}$ at 60 °C is unlikely therefore to incur serious error.[20] However, a small correction to $k_5(\mathbf{1c})$ for steric factors does seem to be justified by the laser flash photolysis results, i.e, $k_T(\text{nonyl}) = 1.28\ (\pm 0.16) \times k_T(\text{neopentyl})$ for trapping with Tempo at 20 °C in isooctane. On these grounds we have chosen $k_6(\mathbf{2c}) = 1.3k_5(\mathbf{1c})$ with a temperature variation represented by $\log k_5(\mathbf{2c}) = 9.7 - 0.9/\theta$,[10] to derive the absolute rate constants for rearrangements of **2c**, viz, $k_1 = 3.3 \times 10^8\ s^{-1}$, $k_3 = 2.2 \times 10^9\ s^{-1}$, $k_c = 2.2 \times 10^7\ s^{-1}$, and $k_r = 1.9 \times 10^7\ s^{-1}$ at 60 °C. Values of these rate constants at 106 °C were similarly calculated from the results of experiments conducted at this temperature (see Experimental Section and Table III).

In the above treatment, the value of k_r was deduced indirectly and thus is liable to compounded random and systematic errors. A much more precise value for k_r was established by direct nitroxide calibration of the vinyl migration reaction **1c** → **3c**. Product ratios and kinetic data obtained by thermolysis of bis(3,3-dimethyl-4-pentenoyl) peroxide with an excess of T over a range of temperatures[10] are given in Table II. At 60 °C this data gives $k_r = 2.4 \times 10^7\ s^{-1}$. The good agreement with the indirect value given above engenders confidence in values obtained for the ring fission rate constants, k_1 and k_3. The usual treatment of the data in Table II gave the temperature dependence of k_6/k_r from which the Arrhenius parameters given in Table III were derived by substitution of the values for k_r. Table III also contains the best experimental values for $k_1(\mathbf{2c})$, $k_3(\mathbf{2c})$, $k_r(\mathbf{1c})$, and $k_c(\mathbf{1c})$ at 60 and 106 °C and associated Arrhenius parameters.

Kinetic data for reactions of **1c** and **2c** have recently been determined by Newcomb,[7] who used their reactions with benzenethiol as kinetic standards after making the reasonable assumption that the rate constants for hydrogen atom transfer to alkyl radicals would be relatively insensitive to radical structure. His data is also presented in Table III for comparison with the present results. In view of the assumptions in both of the experimental methods employed, the agreement between the two sets of data, although not close, is acceptable. Generally our values of the log A term are about 0.8 units higher than Newcomb's, and the values of E are also correspondingly greater. Although Newcomb's figures should be the more reliable (because they are obtained from a greater number of data points), ours appear to be more consistent with those for ring fission of the unsubstituted and monomethyl CPM radicals **1a**, $\mathbf{2d}^{cis}$, and $\mathbf{2d}^{trans}$ (see below).

A rather surprising feature of the data in Table III is the smallness of the ratio k_3/k_1 for **2c**, which varies from 6.7 at 60 °C to 5.3 at 106 °C. Not only should the formation of the tertiary radical **3c** be the thermodynamically preferred reaction but it should also be favored by the relief of steric repulsion between the radical center and the syn methyl group. The selectivity of fission should also be enhanced by stereoelectronic features: if the transition structures require good overlap between the SOMO and the bond undergoing fission, nonbonded interactions between the radical C–H group and the syn methyl will be less in that transition structure leading to **3c**. The sum of these factors might be expected to give rise to highly selective ring fission. The fact that it does not may reflect the more obvious anomoly exhibited by the ring fission of $\mathbf{2d}^{trans}$ and discussed below.

The equilibrium constant between **1c** and **2c** can be calculated from the reaction rates in forward and reverse directions, e.g., $K_{12} = k_c/k_1 = 0.08$ at 60 °C. The temperature dependence of K_{12}, i.e., $\log K_{12} = -1.6 + 0.7/\theta$, indicates that the ring-closure reaction (**1c** → **2c**) is slightly exothermic ($\Delta H^\circ = -0.7$ kcal/mol) but is unfavorable because of the relatively low entropy of the ring-closed form ($\Delta G^\circ = +1.6$ kcal/mol, $\Delta S^\circ = -7.3$ eu). This contrasts with the estimated thermodynamics of the ring closure of the 3-butenyl radical (**1a**) (Table III), which is endothermic by ca. 1.6 kcal/mol, with $\Delta G^\circ = +6.2$ kcal/mol, $\Delta S^\circ = -11.8$ eu.[22] Features of this reaction are examined further below.

***cis*- and *trans*-(2-Methylcyclopropyl)methyl Radicals ($\mathbf{2d}^{cis}$ and $\mathbf{2d}^{trans}$).** Earlier work[9] on these radicals afforded the interesting observation that $\mathbf{2d}^{cis}$ gives mostly the thermodynamically favored secondary alkyl radical **3d** at −125 and −70 °C (**1d**:**3d** = 0.20 and 0.25, respectively, by ESR signal integration), whereas the trans radical ($\mathbf{2d}^{trans}$) rearranges mainly to the primary alkyl radical at −115 °C (**1d**:**3d** = 4.0 by ESR). Further investigation of $\mathbf{2d}^{trans}$ by tributylstannane reduction[9] revealed that from 25 to 45 °C the β-fission rates were about equal ($k_1 = k_2$). In similar experiments, the use of low stannane concentrations (0.01 M) gave products arising almost entirely from **3d**, thus confirming that **3d** is the thermodynamically favored species and that ring opening to this radical is essentially irreversible (an assumption made in the derivation of kinetic equations). However, rate constants for ring fission of $\mathbf{2d}^{cis}$ and $\mathbf{2d}^{trans}$ were too high to be studied accurately by stannane or ESR methods, and consequently it was not possible to prove the basis of the unusual selective ring fission of $\mathbf{2d}^{trans}$.

Rearrangements of $\mathbf{2d}^{cis}$ and $\mathbf{2d}^{trans}$ were studied by the experimental and kinetic analysis methods described for **2c**. The kinetic data summarized in the Experimental Section and Table III are consistent with the earlier observations.[9] Combination of nitroxide trapping data with the low temperature ESR data gives $\log (k_1/k_3) = -0.4 -$

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[20] Stabilization energies in CPM and benzyl are ca. 0.7 and 10 kcal/mol, respectively.[21]

[21] McMillan, D. F.; Golden, D. M.; Benson, S. W. *Int. J. Chem. Kinet.* **1971**, *3*, 359–374.

[22] Calculated from combined ESR/nitroxide data[10] for **2a** and the previous calibration[8] of $k_c(\mathbf{1b})$.

Table III. Kinetic Data for Rearrangements of Cyclopropylmethyl Radicals

reactn	rate constants, s^{-1} (temp, °C)	log $(A/s^{-1})^b$	E,[b] kcal/mol	rate constant at 60 °C, s^{-1}	log A	E
2a → **1a**[c]	1.75×10^8 (60); 6.7×10^9 (106)	13.0	7.26	1.7×10^8	12.7	6.8
1b → **2b**[d]				2.7×10^4	10.2	8.8
2c → **1c**	3.3×10^8 (60); 1.2×10^9 (106)	13.2	7.2	3.0×10^8	11.67	4.87
2c → **3c**	2.2×10^9 (60); 6.3×10^9 (106)	13.3	6.1	1.7×10^9	12.17	4.47
1c → **2c**	2.7×10^7 (60); 9.3×10^7 (106)	11.8	6.7	1.7×10^7	11.1	5.9
1c → **3c**	2.4×10^7 (60); 7.7×10^7 (106)	11.6	6.5	1.4×10^7	11.0	5.88
$\mathbf{2c}^{cis}$ → **1d**	2.8×10^8 (59); 7.7×10^8 (100)	12.7	6.5			
$\mathbf{2d}^{cis}$ → **3d**	1.0×10^9 (59); 2.7×10^9 (100)	13.0	6.1			
$\mathbf{2d}^{trans}$ → **1d**	3.8×10^8 (59); 1.4×10^9 (100)	13.5	7.5			
$\mathbf{2d}^{trans}$ → **3d**	4.6×10^8 (59); 1.9×10^9 (100)	14.2	8.4			
1d → **3d**	1.9×10^5 (59); 7.8×10^6 (100)	10.6	8.0			
1d → **2d**	3.4×10^5 (59); 1.2×10^6 (100)	10.6	7.7			
2e → **3e**	$>5 \times 10^{10}$ (60)					

[a] Except where otherwise noted, data are from ref 7; rate constants are calculated from the Arrhenius data. [b] Except for the reaction **1c** → **3c**, Arrhenius coefficients for reactions of **1c**, **2c**, **1d**, and **2d** are approximate. [c] Literature values are from ref 19; statistically corrected to give rate constant per bond. [d] Literature values are from ref 8.

$0.2/\theta$ for $\mathbf{2d}^{cis}$ and $\log (k_1/k_3) = -0.6 + 0.9/\theta$ for $\mathbf{2d}^{trans}$. The latter expression predicts an isokinetic temperature for fission of the trans radical $\mathbf{2d}^{trans}$; above about 60 °C, ring fission preferentially affords **3d**, but at lower temperatures, it preferentially affords **1d**. Hence, if the rearrangement had been studied only at normal temperatures, the unusual selectivity manifested at low temperatures would not have been suspected.

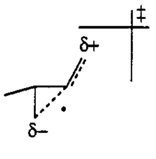
The above Arrhenius equations were derived from data obtained over a wide temperature range. They indicate a slight entropic preference for fission to the secondary radical (**3d**) in both cases; i.e., $\Delta S^{\ddagger}(\mathbf{2d}\rightarrow\mathbf{3d}) - \Delta S^{\ddagger}(\mathbf{2d}\rightarrow\mathbf{1d}) = 2$–$3$ eu. This is surprising in view of the calculated relative product radical entropies (viz., $\Delta S^\circ(\mathbf{3d}) - \Delta S^\circ(\mathbf{1d}) \simeq -1$ eu)[23] and the expectation of an earlier (tighter) transition state for fission to **3d**, because it is the more exothermic.

The different selectivities for ring fission of the cis and the trans species probably reflect the nonbonded interactions between the eclipsed exocyclic groups in $\mathbf{2d}^{cis}$. The difference in strain energy arising from this interaction is estimated from molecular mechanics calculations (MM2) to be ca. 1.0 kcal/mol. The reason that $\mathbf{2d}^{trans}$ opens preferentially to the primary radical **1d** under kinetic control at lower temperatures is not immediately obvious. There are several documented cases of β-fission to give primary rather than secondary radicals in bicyclic systems,[24,25] but in those cases, clear-cut explanations could usually be based on orbital-overlap grounds.[25] Clearly, such arguments are not applicable to $\mathbf{2d}^{trans}$, where the substituent is very unlikely to engender the stereoelectronic biases found in bicyclic systems or in $\mathbf{2d}^{cis}$.

Enhancement of k_1 in $\mathbf{2d}^{trans}$ relative to k_3 might be attributed either to a weakening of the 2,4-bond caused by the methyl substituent (i.e., a ring-strain effect) or to electronic stabilization of the transition state, or both. The former is corroborated to some extent by electron-density calculations on substituted cyclopropanes.[26] They indicate some lengthening of the bond opposite electron-donor substituents and an increase in the overall ring strain upon substitution, and this is supported by experimental evidence. However, enhancement of *both* formation and cyclization of **1d** relative to **1a** implies a reduction of the intrinsic energy barrier to reaction which is independent of the stability of one or the other ground state.

The basis of this effect, which is not found in the cyclobutylmethyl system,[27] probably involves the exceptional features of cyclopropane ring bonding, namely, its considerable π character, and a large degree of configuration interaction (involvement of vacant carbon orbitals). These make CPM radicals very polarizable and greatly improve the homolytic overlap between the radical and ring-bonding orbitals, as manifested by the 10^4 difference between the rates of fission of **2a** and cyclobutylmethyl radical, a species estimated to have a similar ring strain.[28] Polar transition states **1c**[29,30] have been proposed to rationalize this and similar ring-fission anomalies.

In terms of the configuration mixing model[31] of reactivity, the proposed polarity[1c,29] of the transition state might be caused by a combination of the low ionization energies of CPM radicals and low-lying acceptor orbitals on the ring.[32] In this model, the barrier to β-fission is reduced by substituents which stabilize the "natural" polarity of the reaction and vice versa; enhancement of the fission rate may result either from electron-donor stabilization of the cationic element of the transition structure (the original radical center) or by electron withdrawal at the incipient radical center. Similarly, an electron-donating substituent at the incipient radical center will destabilize the transition structure. In these terms the transition structure (**10**) for the ring opening $\mathbf{2d}^{trans}$ → **1d** would be expected to be of lower energy than that (**11**) on the alternative reactions pathway.



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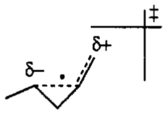

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(25) Beckwith, A. L. J.; Phillipou, G. *J. Chem. Soc., Chem. Commun.* 1971, 658–657.

(26) Creamer, D.; Kraka, E. *J. Am. Chem. Soc.* **1985**, *107*, 3811–3819.

(27) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1083–1090.

(28) Strain energies of cyclopropane and cyclobutane are 27.6 and 26.2 kcal/mol, respectively, by Benson's definition.[23]

(29) Blum, P.; Davies, A. G.; Peyeyre, M.; Ratier, M. *J. Chem. Soc., Chem. Commun.* **1976**, 814–816.

(30) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1473–1482.

(31) Shaik, S. S. *Prog. Phys. Org. Chem.* **1985**, *15*, 197–337. Pross, A.; Shaik, S. S. *Acc. Chem. Res.* **1983**, *16*, 363–370.

(32) These are manifested by the ready reduction of cyclopropanes by one-electron reagents.[33]

(33) Staley, S. W. In *Selective Organic Transformations*; Thyagarajan, B. S., Ed.; Wiley: New York, 1972; Vol. 2, pp 309–348.

The anomolous ring fission of $\mathbf{2d}^{trans}$ shows that the proposed polar effect can outweigh small thermodynamic countertendencies and it may play a significant role, in addition to thermodynamic and stereoelectronic factors, in determining the outcome of homoallylic rearrangements of more complex species.

Although the cyclization of **1d** is clearly faster than that of **1a**, the kinetics of the overall vinyl migration, **1d** → **3d**, are complicated by the fact that there are two possible pathways, viz., via $\mathbf{2d}^{cis}$ or via $\mathbf{2d}^{trans}$. The relative importance of these two pathways cannot be directly assessed from these experiments because the intermediate radicals are not trapped in sufficient amounts to be quantified under conditions in which the vinyl migration takes place (i.e., very low [T]). Although the rate constants for cyclization through the cis and trans forms of **2d** cannot be independently determined, it seems reasonable to assume that most migration occurs via the low-energy trans species. The values of k_c at 60 and 100 °C for **1d** can thus be calculated from the product ratio data for $\mathbf{2d}^{trans}$ by use of eq 9, and from them values of k_c are available through eq 10. The results are included in Table III.

The expression for k_r and the assumptions made to derive it are in good agreement with data from tributylstannane reduction of 4-bromo-3-methyl-1-butene,[9] which give[34] $k_r = 0.8\text{–}1.3 \times 10^5\ \mathrm{s}^{-1}$ at 45 °C; the radical-trapping data give a value of ca. $0.9 \times 10^5\ \mathrm{s}^{-1}$ at this temperature.

[2-(Ethoxycarbonyl)cyclopropyl]methyl Radical (2e). Thermolysis of diacyl peroxide **4e** in concentrated benzene solutions of T (0.5–1.0 M) gave just one identifiable hydroxylamine product (**7e**) at both 60 and 100 °C. Thus, with a trapping rate constant of $1 \times 10^9\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$ and a 2% limit of detection (relative to **7e**), this implies a β-fission rate constant greater than $5 \times 10^{10}\ \mathrm{s}^{-1}$ and selectivity for 2,3-bond fission greater than 50.

The large stabilization afforded to the product radical **3e** by the ethoxycarbonyl substituent (ca. 6–7 kcal/mol)[36] could explain the increased selectivity, which is equivalent to a kinetic free energy preference of >2.7 kcal/mol. However, the reaction is predicted to have an early transition state, and the magnitude of the effect does, therefore, lend some credence to the hypothesis, discussed above, that the transition state for ring opening of CPM radicals is dipolar and may be stabilized by appropriate electron-donating or -attracting substituents.

Effects of Ring Substitution on the Thermodynamics and Kinetics of CPM Ring Fission. Kinetic data for ring opening of various CPM radicals and for cyclization and/or rearrangement of related butenyl radicals are summarized in Table III. Values of log *A* and activation energy (*E*) are also included in the table, but the limited data bases and the assumptions made about k_T suggest that detailed comparisons of these parameters are not justified except to consider large effects or unless supported by low-temperature data (e.g., k_1/k_3 for $\mathbf{2d}^{trans}$)[9] or by data from other sources (e.g., k_1 for **2a**[18] or k_r for **1c**[7]). Nevertheless, it is noteworthy that all but one ($\mathbf{2d}^{trans}$ → **3d**) of the ring-opening reactions studied in the present work have values of log *A* in the range 13.0–13.5. The activation energy is more variable and is the factor mainly responsible for the observed variation of rate constants.

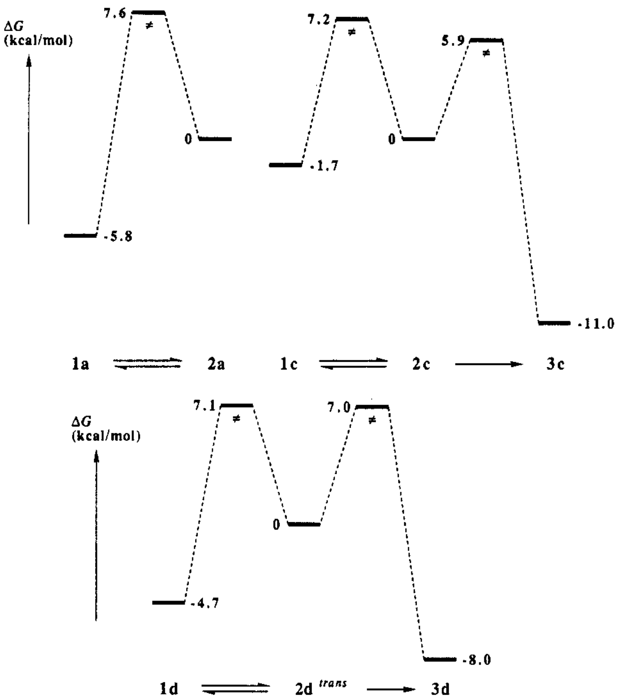

Figure 2. Free energy levels for ring opening and cyclizations at 60 °C. The approximate free energies of **3c** and **3d** were obtained relative to that of **1a** from thermochemical data (ref 23).

However, comparisons between the various systems are best made through the free energy diagrams of Figure 2. Relative free energy levels have been calculated for $\mathbf{2d}^{trans}$ on the basis of the assumptions about $k_c(\mathbf{1d})$ made above.

The data show that the introduction of one or two methyl substituents at position 2 of the but-3-enyl radical enhances the cyclization rate constant by factors of 13 and 1000, respectively, at 60 °C (i.e., $\Delta\Delta G^{\ddagger} = 1.6$ and 4.5 kcal/mol). This is a much more dramatic effect that found in the 5-hexenyl system, where $\Delta\Delta G^{\ddagger} \simeq 1.4$ kcal/mol upon introduction of *gem*-dimethyl substituents at the 2- or 3-position.[37]

A major driving force for cyclization of **1c** is the relief of steric compression (Thorpe–Ingold effect). In addition, nonbonded interactions in **1c** restrict rotations about bonds emanating from the quaternary carbon. The reduction of nonbonded interactions during cyclization might therefore contribute both to the low energy barrier and the high frequency factor for cyclization and vinyl migration for **1c**.

It can be seen from the energy diagrams for the reactions **1a** → **2a** and **1c** → **2c** that the *gem*-dimethyl group in **1c** both increases the thermodynamic driving force for cyclization and reduces the energy barrier. However, contrary to the conventional picture[40] of reactivity, the kinetic effect is slightly larger than the thermodynamic effect, i.e., the reduction of the energy barrier appears to be greater than the improvement in the thermodynamic driving force. Similarly, the state of ring fission to the primary radical (**2c** → **1c**) is greater than the rate of **2a** → **1a** despite the decreased thermodynamic driving force of the former reaction.

Comparison of the free energy diagrams for **1d** ⇌ $\mathbf{2d}^{trans}$ and **1a** ⇌ **2a** leads to similar conclusions. The presence

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[34] Estimated from data in ref 8 (Table II) with the most recent k_H for isopropyl.[35]

[35] Johnston, L. J.; Lusztyk, J.; Wayner, D. D. M.; Abeywickrema, A. N.; Beckwith, A. L. J.; Scaiano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 4594–4596.

[36] Based on C–H bond dissociation energy which can be estimated by Nonhebel and Walton's ESR relationshjip[37] with Lung-Min and Fischer's data.[38]

[37] Nonhebel, D. C.; Walton, J. C. *J. Chem. Soc., Chem. Commun.* **1984**, 731–732.

[38] Lung-Min, W.; Fischer, H. *Helv. Chim. Acta* **1983**, *66*, 138–144.

[39] Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. *Aust. J. Chem.* **1982**, *36*, 545–560.

[40] Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963; pp 156–161.

of the methyl group lowers the driving force *and* the energy barrier. On the other hand, the reactions **2c** → **3c** and **2d** → **3d** are normal by comparison with **2a** → **1a**. Since kinetic data for the ring closure of **3c** and **3d** are not available, accurate values for their free energies cannot be given. However, the free energy barriers *decrease* in the same order (although not as much as might have been expected) as the *increase* in the expected thermodynamic stabilities of the products, **1a** < **3b** < **3c**. We conclude that for each of **2d**^{trans} and **2c**, the ring opening leading to the primary radical product has a lower intrinsic energy barrier[41,42] than the alternative pathway. In both cases this can be reasonably assigned to the electronic effects of the substituents on the stability of the dipolar transition structures.

Conclusions

Kinetic analysis of the products obtained when suitable peroxy compounds are thermolyzed in the presence of the nitroxide T has afforded kinetic data for the ring opening of substituted cyclopropylmethyl radicals and, in some cases, the reverse reaction. The data show that the introduction of methyl substituents at the 2-position of the but-3-enyl radical strongly accelerates the rates of cyclization and vinyl migration (by factors of 13 and 1000 at 60 °C for mono- and dimethyl substituents, respectively).

Ring opening of the monomethyl-substituted radical **2a**^{trans} to give the primary radical **1d** is favored over formation of the secondary radical in the enthalpy term of the Arrhenius equation but not in the entropy term; log $(k_1/k_3) = -0.6 + 0.9/\theta$, giving an isokinetic temperature near 60 °C. The preferential formation of the less thermodynamically stable primary radical **1d** at lower temperatures is a manifestation of the lower intrinsic energy barrier of this reaction as compared with that of the alternative pathway. Similarly, the rates of formation of **1c** from **2c** and of **1e** from **2e** are faster than expected while the rate of formation of **3c** from **2c** is slower. All of these observations conform to the hypothesis that the transition structure for β-fission is dipolar; it is stabilized by electron-accepting substituents at the radical center and destabilized by electron-donating substituents.

Experimental Section

Spectra were recorded on the following instruments: JEOL PMR-60 (60-MHz ^{1}H NMR), JEOL FX-200 (200-MHz ^{1}H NMR), Perkin-Elmer 683 (IR), and Varian DMS-90 (UV-vis). Gas chromatography was performed on a Varian Vista 600 chromatograph with a vitreous silica capillary column (25 m) (25QC2/BP5 1.0). Elemental analyses were performed by the ANU Analytical Service unit. Thermostated baths accurate to ±0.3 °C were used for temperature control. Reversed-phase high-pressure liquid chromatography (HPLC) was performed with a Spectra-Physics SP-8000B proportionating pump, UV detector, and integrator; for analysis, Alltech ODS (5 μm) 4.6 × 250 mm and, for preparation, Altex ODS (5 μm) 10 × 250 mm columns were used with optimized $MeOH/H_2O$ mobile phases at 1.3 and 4.5 mL/min, respectively. Spectroscopic grade methanol and cyclohexane were used; all other solvents and reagents were analytical grade used without purification. The preparation of the nitroxyl radical T has been described.[43]

Bis[(2,2-dimethylcyclopropyl)acetyl] Peroxide (4c). 2,2-Dimethylcyclopropaneacetic acid[44] was converted to its acid chloride with oxalyl chloride. Pyridine (400 μL, 5 mmol) was added dropwise to a stirred mixture of 20 M H_2O_2 (150 μL, 3 mmol) and the acid chloride (380 mg, 2.5 mmol) at −10 °C. After 30 min at 0 °C, the reaction mixture was diluted with pentane and washed successively with ice-cold water, 10% H_2SO_4, aqueous $NaHCO_3$, and brine, then dried ($MgSO_4$), and evaporated to afford **4c** (280 mg, 82%), no impurities by NMR or IR, and 90% pure by iodometric titration:[45] ^{1}H NMR (60 MHz, CCl_4) δ −0.1–1.1 (m, 3 H), 0.95 (s, 3 H), 1.02 (s, 3 H), 2.04 (d, 2 H); IR ν_{max} (CCl_4) 1740, 1785 cm^{-1} (C=O).

Bis[(*cis*-2-methylcyclopropyl)acetyl] Peroxide (4d^{cis}). 3-Pentyn-1-ol was oxidized to 3-pentynoic acid (36%) with Jones' reagent at room temperature. The acid was methylated with BF_3 in methanl,[46] and the methyl ester was hydrogenated in pyridine over Pd on a $BaSO_4$ catalyst at 10 psi for 2 h, to give pure methyl *cis*-3-pentenoate (GC 98% cis) in 30% overall yield. The ester was heated to reflux with 2 molar equiv of Simmons–Smith reagent[47] in ether for 22 h to afford methyl *cis*-2-methylcyclopropaneacetate (71%), bp 85–87 °C at 100 mm, 98% cis by GC. Hydrolysis of the ester and conversion into the peroxide as described above gave **4d**^{cis} (52% from the ester), no impurities by NMR or IR, and 93% pure by iodometric titration: ^{1}H NMR (60 MHz, CCl_4) δ −0.2 (m, 2 H), 0.2–1.5 (m, 12 H), 2.15 (d, 4 H); IR ν_{max} (CCl_4) 1750, 1788 cm^{-1} (C=O).

Bis[(*trans*-2-methylcyclopropyl)acetyl] Peroxide (4d^{trans}). Crotyl bromide was heated with cuprous cyanide at 100 °C to give *trans*-pent-3-enenitrile, which was hydrolyzed to *trans*-pent-3-enoic acid with concentrated hydrochloric acid. Treatment of the methyl ester with Simmons–Smith reagent[47] and hydrolysis of the resultant ester[48] gave *trans*-2-methylcyclopropaneacetic acid,[44] which was converted by the general method described above into **4d**^{trans} (72% from the ester), no impurities by NMR or IR, and 91% pure by iodometric titration: ^{1}H NMR (60 MHz, CCl_4) δ 0.0 (m, 2 H), 0.3–1.5 (m, 12 H), 2.35 (d, 4 H); IR ν_{max} (CCl_4) 1755, 1794 cm^{-1} (C=O).

Bis[[2-(ethoxycarbonyl)cyclopropyl]acetyl] Peroxide (4e). Ethyl diazoacetate (ca. 2 molar equiv) was added dropwise to a suspension of anhydrous $CuSO_4$ (4% molar) in *tert*-butyl but-3-enoate at 50 °C (monitored by GC). After completion of the reaction, the mixture was washed successively with water, dilute NH_3, and brine, and the resulting brown oil was selectively hydrolyzed by treatment with 90% aqueous formic acid (2 volumes) for 4 h at ca. 50 °C. The usual isolation of the acidic component followed by distillation gave 2-(ethoxycarbonyl)cyclopropaneacetic acid (21% from the ester), bp 140–145 °C at 0.4 mm, cis:trans = 35:65 by ^{1}H NMR (cis methylene at δ 2.68, trans at δ 2.36). Treatment of the acid with oxalyl chloride and then Na_2O_2 with wet ether[10] at <10 °C gave **4e** (70%), no impurities by NMR or IR, and 89% pure by iodometric titration: ^{1}H NMR (200 MHz $CDCl_3$) δ 0.6–1.3 (m, 2 H), 1.28 (t, 3 H, 7.1 Hz), 1.4 (m, 1 H), 1.55 (m, 1 H), 2.43 + 2.76 (m + m, 1:1.8, 2 H), 4.18 (q, 2 H, 7.1 Hz, cis downfield 0.8 Hz); IR ν_{max} (CCl_4) 1743, 1755, 1785 cm^{-1} (C=O).

Hydroxylamine Products. Product mixtures were prepared by adding peroxides to concentrated refluxing solutions of T in benzene. The mixtures were resolved by flash chromatography on silica (ether in pentane) followed by preparative RP-HPLC of the hydroxylamine fractions (this procedure achieved some separations not practical by HPLC alone and allowed the identification of non UV active byproducts). General UV and NMR spectral features of 2-alkoxy-1,1,3,3-tetramethylisoindolines have been described,[10,49] as have the spectra of **5c** and **7c**.[10]

In a typical experiment, a mixture of T (100 mg) and **4d**^{cis} (60 mg) in cyclohexane (3.0 mL) was heated under reflux for 1 h under N_2, by which time all of the peroxide had been consumed [TLC, $Fe(SCN)_2$ spray]. The solution was then subjected to flash chromatography on silica with gradient elution (ether/pentane, 2–10%) to give a mixture (35 mg) of **7d** and **6d**^{cis} (3:1) and three further major fractions, which were tentatively identified on the basis of their IR, UV, and ^{1}H NMR spectra as (i) a mixture (11 mg) of pent-4-en-2-yl *cis*-2-methylcyclopropaneacetate and (*cis*-2-methylcyclopropyl)methyl *cis*-2-methylcyclopropaneacetate; (ii)

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2-[(*cis*-2-methylcyclopropyl)acetoxy]-1,1,3,3-tetramethylisoindoline (5 mg); and (iii) a nonaromatic polar carbonyl compound (4 mg), possibly a carbonic anhydride.

2-[(2,2-Dimethylcyclopropyl)methoxy]-1,1,3,3-tetramethylisoindoline (6c): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.2 (m, 1 H), 0.6–1.1 (m, 2 H), 1.04 (s, 3 H), 1.09 (s, 3 H), 1.42 (br s, 12 H), 3.72 (m, 2 H), 7.01 (m, 2 H), 7.15 (m, 2 H). Anal. Calcd for $C_{18}H_{27}NO$: C, 79.07; H, 9.95. Found: C, 79.01; H, 9.64.

2-[(*cis*-2-Methylcyclopropyl)methoxy]-1,1,3,3-tetramethylisoindoline (6d^{cis}): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.3–1.0 (m, 4 H), 1.02 (m, 3 H), 1.44 (br s, 12 H), 3.74 (m, 2 H), 7.01 (m, 2 H), 7.14 (m, 2 H). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71. Found: C, 78.46; H, 9.44.

2-[(*trans*-2-Methylcyclopropyl)methoxy]-1,1,3,3-tetramethylisoindoline (6d^{trans}): ^{1}H NMR (200 MHz, $CDCl_3$) –0.33 (m, 1 H), 0.10 (m, 1 H), 0.64 (m, 1 H), 0.86 (m, 1 H), 0.97 (d, 3 H, 6 Hz), 1.4 (br s, 12 H), 3.70 (d, 2 H, 6.8 Hz), 7.02 (m, 2 H), 7.16 (m, 2 H). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71. Found: C, 78.61; H, 9.79.

2-(2-Methyl-3-buten-1-oxy)-1,1,3,3-tetramethylisoindoline (5d): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (d, 3 H, 7.2 Hz), 1.4 (v br d, 12 H), 2.22 (m, 1 H), 3.76 (d, 2 H, 7 Hz), 5.02 (m, 2 H), 5.82 (m, 1 H), 7.00 (m, 2 H), 7.11 (m, 2 H). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71. Found: C, 78.76; H, 9.53.

2-(4-Penten-2-oxy)-1,1,3,3-tetramethylisoindoline (7d): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.22 (d, 3 H, 7 Hz), 1.3–1.5 (m, 12 H), 2.19 (m, 2 H), 3.92 (sec, 1 H), 5.01 (m, 2 H), 5.81 (m, 1 H), 7.00 (m, 2 H), 7.11 (m, 2 H). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71. Found: C, 79.01; H, 9.97.

2-[1-(Ethoxycarbonyl)-3-buten-1-oxy]-1,1,3,3-tetramethylisoindoline (7e): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.28 (t, 3 H, 7 Hz), 1.2–1.5 (m, 12 H), 2.55 (m, 2 H), 4.17 (q, 2 H, 7 Hz), 4.40 (t, 1 H), 5.05 (m, 2 H), 5.75 (m, 1 H), 7.04 (m, 2 H), 7.19 (m, 2 H). Anal. Calcd for $C_{19}H_{27}NO_3$: C, 71.89; H, 8.57. Found: C, 71.80; H, 8.45.

Kinetic Experiments. For kinetic studies, reaction mixtures were made up volumetrically from common stock solutions, then degassed by the freeze/thaw method, and sealed in 1-mL Pyrex ampules.

Whenever possible, a series of reaction mixtures were heated simultaneously and analyzed under identical conditions. After completion of the reaction, the mixture was carefully evaporated, and the residue was dissolved in MeOH and analyzed by HPLC with isocratic elution (H_2O/MeOH; 1.3 mL/min). Trapped products were detected by their UV absorption at 270 nm, identified by comparison of retention times with those of the authentic compounds, and quantified by integration of the chromatographic trace using the known extinction coefficients. Tests with mixtures of authentic samples showed the analytical precision to be better than 5% for yields and 3% for product ratios. The relative yields of substituted hydroxylamines obtained from the peroxide **4d** at 60 °C are given in Table I. The ratios of yields from experiments conducted at 106 °C were as follows (data are given in the order [T] mM, **7c**/**5c**, **6c**/**7c**; nd = not determined): 256, 5.81, 0.052; 137, 6.39, 0.024; 106, 9.09, nd; 9.0, 29.4, nd.

From the peroxide **4d**^{cis} at 59 °C, the relative yields of products **7d**/**5d** and **6d**^{cis}/**7d** were as follows: 273, 4.22, 0.33; 145, 4.23, 0.19; 71, 450, 0.075; 9.0, 4.51, nd; 4.5, 4.63, nd; 0.90, 5.60, nd. At 100 °C: 256, 3.65, 0.14; 138, 3.64, 0.073; 67, 3.94, 0.032; 9.0, 3.31, nd; 4.5, 4.51, nd; 0.85, 8.02, nd.

From the peroxide **4d**^{trans} at 59 °C, the relative yields of products **7d**/**5d** and **6d**^{trans}/**7d** were as follows: 271, 1.15, 0.73; 143, 1.04, 0.39; 72, 1.10, 0.20; 9.0, 1.14, nd; 4.6, 1.22, nd; 0.84, 6.02, nd. At 100 °C: 255, 1.38, 0.18; 139, 1.42, 0.097; 67, 1.39, 0.050; 8.4, 1.53, nd; 4.2, 1.75, nd; 0.84, 3.03, nd.

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Registry No. **1b**, 120034-57-3; **1c**, 87110-24-5; **1d**, 52898-42-7; **2a**, 2154-76-9; **2c**, 90429-69-9; **2d**^{cis}, 62131-98-0; **2d**^{trans}, 62131-99-1; **2e**, 118089-50-2; **4c**, 120034-58-4; **4d**^{cis}, 120034-61-9; **4d**^{trans}, 120142-70-3; **4e**, 120034-59-5; **5d**, 120034-66-4; **6c**, 120034-63-1; **6d**^{cis}, 120034-64-2; **6d**^{trans}, 120034-65-3; **7d**, 120034-67-5; **7e**, 120034-68-6; T, 80037-90-7; 2,2-dimethylcyclopropaneacetic acid, 68258-20-8; 2,2-dimethylcyclopropaneacetyl chloride, 120034-60-8; 3-pentyn-1-ol, 10229-10-4; 3-pentynoic acid, 36781-65-4; methyl 3-pentynoate, 22377-43-1; methyl *cis*-3-pentenoate, 36781-66-5; crotyl bromide, 4784-77-4; *trans*-pent-3-enenitrile, 16529-66-1; *trans*-pent-3-enoic acid, 1617-32-9; methyl *trans*-pent-3-enoate, 20515-19-9; *trans*-2-methylcyclopropaneacetic acid, 54353-00-3; methyl *cis*-2-methylcyclopropaneacetate, 120142-68-9; methyl *trans*-2-methylcyclopropaneacetate, 120142-69-0; *tert*-butyl but-3-enoate, 14036-55-6; *cis*-2-(ethoxycarbonyl)cyclopropaneacetic acid, 120034-62-0; *trans*-2-(ethoxycarbonyl)cyclopropaneacetic acid, 120034-69-7.

Calculation of the Unusual NMR Chemical Shifts in Bicyclic Molecules Containing Strained Frameworks. A Simple Empirical Model for Predicting the Magnitude of the Anomalous Shift Increments

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Many strained bicyclic and tricyclic alkenes and dienes show unusually large ^{13}C NMR shifts of the homoallylic carbons relative to the saturated reference compound, whereas the allylic carbons show only small shift increments. The direction of the homoallylic shift increment depends on whether the unsaturated bridge is a monoene or diene. Theoretical calculations with the Garber–Ellis INDO model for chemical shifts correctly reproduce the pattern of shift increments and identify them with variations in the local paramagnetic anisotropy. An empirical correlation between the shift increments and the change in carbon 2s population is demonstrated. A simple Hückel model for estimating the dependence of the shift increment on the structure of the bridge is presented.

Introduction

Christl et al.[1] reported that hydrocarbons containing a rigid cyclopentene ring give an unusually large downfield ^{13}C NMR shift of the homoallylic carbon atoms. For example, the ^{13}C NMR absorption of C-7 in norbornene (**1**) is shifted downfield by 9.8 ppm relative to C-7 in norbornane (**2**). With bicyclo[2.1.1]hexene (**3**) and bicyclo[2.1.1]hexane (**4**) the downfield shift increment of C-1, C-4

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[1] Christl, M.; Herbert, R. *Org. Magn. Reson.* 1979, *12*, 150.