

parts of the spectrum of durosemiquinone and **2** decay at similar rates, indicating that they belong to the same species. Like **2**, durosemiquinone undergoes pH-dependent disproportionation in 50% ethanol-water, giving durohydroquinone and duroquinone as the stable products.¹⁹

The pK_a calculated for $(2-H)^+ \rightleftharpoons 2 + H^+$ implies that $(2-H)^+$ is not as acidic as other protonated phenoxyl radicals²⁰ including protonated durosemiquinone,¹⁹ which has a pK_a of -1.1. Methoxy groups, which can be used as a model for the oxymethylene moiety in **2**, are suggested to have approximately the same ability to stabilize phenolic cation radicals as the hydroxyl moiety.^{21,22} X-ray studies²³ of α -tocopherol and several analogues, including both **1** and **5**, have shown that the angle between the 2p-type orbital of the para oxygen and the adjacent p-orbital in the aromatic ring is approximately 17°. Motion of the six-membered ring attached to the aromatic ring is constrained and the 2p-type orbital of the oxygen remains in a conformation that facilitates orbital overlap. Therefore, the calculated pK_a of 2.3 is most likely

explained by postulating that extended conjugation stabilizes the positive charge, making $(2-H)^+$ a weaker acid relative to other phenol radical cations.

Conclusion

Phenoxyl radicals from Trolox c and its analogues disproportionate in aqueous solution, giving starting phenol and a product from intramolecular cyclization. This latter product could not be formed from α -tocopherol radicals and therefore Trolox and its derivatives that have a hydroxymethyl or carboxy moieties at the 2-position are not good models for the behavior of α -tocopherol radicals in the absence of oxygen.

Acknowledgment. The work of M.J.T. was supported in part by Grants RO1 GM 29611-04 and RO1 HL 33532 from the National Institutes of Health. The NMR was purchased in part with funds from NSF Grant PCM-8313203. The research of B.H.J.B. was supported by National Institutes of Health Grant RO1 GM23656-10, and it was carried out at Brookhaven National Laboratory, which is operated under contract DE-ACO2-76CH00016 to the U.S. Department of Energy.

Registry No. (\pm)-**1**, 56305-04-5; (\pm)-**1** (ethyl ester), 53174-07-5; (\pm)-**2**, 119681-33-3; (\pm)-**3**, 119681-34-4; (\pm)-**4**, 119719-96-9; (\pm)-**5**, 53101-54-5; (\pm)-**6**, 119719-97-0; Br_2^- , 12595-70-9.

(20) Land, E. J.; Porter, G.; Strachan, E. *Trans. Faraday Soc.* **1961**, 57, 1885.

(21) Dixon, W. T.; Murphy, D. *Trans. Faraday Soc.* **1976**, 72, 1221.

(22) Steenken, S.; Neta, P. *J. Phys. Chem.* **1979**, 83, 1134.

(23) Burton, G. W.; Doba, T.; Gabe, E. J.; Hughes, L.; Lee, F. L.; Prasad, L.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, 107, 7053.

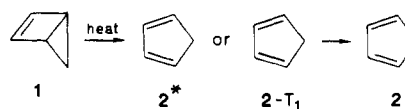
Deuterium and Carbon-13 Kinetic Isotope Effects for the Isomerization of 5,5-Dimethylbicyclo[2.1.0]pent-2-ene to 5,5-Dimethylcyclopentadiene

John E. Baldwin* and Naresh D. Ghatlia

Contribution from the Department of Chemistry, Syracuse University, Syracuse, New York 13244. Received August 12, 1988

Abstract: The relative rates of electrocyclic isomerization of 5,5-dimethylbicyclo[2.1.0]pent-2-ene and the 2-²H, 1,2,4-²H₃, 1,2,3,4-²H₄, and 1,4-¹³C₂ isotopic variants of this system have been determined at 43.6–44.0 °C. There is no detectable carbon-13 effect; deuterium substitution at C(2) is associated with a small k_H/k_D effect, 1.02, and a deuterium at C(1) results in a very large effect, 1.26. The $k_H/k_D(d_3)$ effect between 24.6 and 54.7 °C shows some sensitivity to temperature, ranging from 1.83 to 1.64. The data exclude an important magnetic isotope effect on the isomerization and provide no support for a singlet → triplet intersystem crossing along the reaction coordinate.

The thermal isomerization of bicyclo[2.1.0]pent-2-ene (**1**) with cleavage of the C(1)–C(4) bond to give cyclopentadiene (**2**)^{1,2} is geometrically constrained to occur in a disrotatory and thus orbital symmetry forbidden process.³ Kinetic,¹ thermochemical,⁴ and spectroscopic^{5,6} studies have delineated the energetic parameters characterizing reactant, transition structure, and S_0 and T_1 states of the product. The overall reaction is exothermic by 47.8 kcal/mol;⁴ the ΔH^\ddagger value for the isomerization is 26.3 kcal/mol,¹ and the S_0 – T_1 energy gap for cyclopentadiene is 58.0 kcal/mol.^{5,6} It follows that the transition structure lies 74.1 kcal/mol above the ground state singlet **2** and 16.1 kcal/mol above $2-T_1$; the



thermochemical facts delineate a relatively rare situation for a thermal isomerization of a hydrocarbon, one where the singlet ground state of the reactant might lead to the triplet state of the final product.

Recent studies have shown that rates of intersystem crossings between singlet and triplet organic radical pairs or diradicals may be influenced by magnetic isotope effects.^{7,8} The thermal decomposition of 9,10-diphenylanthracene endoperoxide, for example, gives different proportions of ³Σ or ¹Δ dioxygen depending upon whether ¹⁷O ($\mu = -1.893$ nuclear magneton, nuclear spin

(1) Brauman, J. I.; Golden, D. M. *J. Am. Chem. Soc.* **1968**, 90, 1920–1921.

(2) Andrews, G. D.; Baldwin, J. E. *J. Am. Chem. Soc.* **1977**, 99, 4853–4854.

(3) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie-Academic Press: Weinheim, 1971.

(4) Roth, W. R.; Klärner, F.-G.; Lennartz, H.-W. *Chem. Ber.* **1980**, 113, 1818–1829.

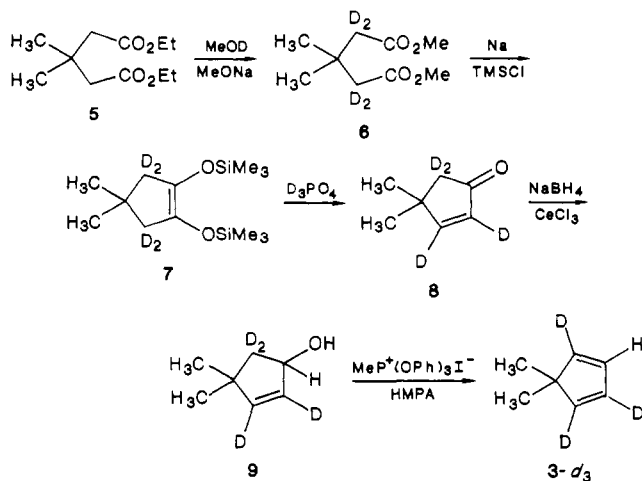
(5) Evans, D. F. *J. Chem. Soc.* **1960**, 1735–1745.

(6) Gorman, A. A.; Gould, I. R.; Hamblett, I. J. *J. Am. Chem. Soc.* **1981**, 103, 4553–4558.

(7) Turro, N. J. *Pure Appl. Chem.* **1981**, 53, 259–286. Turro, N. J.; Kraeutler, B. In *Isotopes in Organic Chemistry, Vol. 6: Isotope Effects: Recent Developments in Theory and Experiment*; Buncl, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1984; p 107–160 and references therein.

(8) Salikhov, K. M.; Molin, Yu. N.; Sagdeev, R. Z.; Buchachenko, A. L. *Spin Polarization and Magnetic Effects in Radical Reactions*; Molin, Yu. N., Ed.; Elsevier: Amsterdam, 1984; Chapter 6.

Scheme I



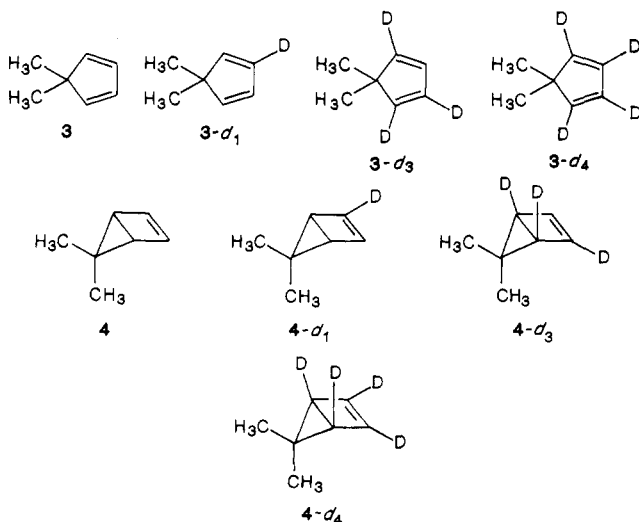
$I = 5/2$) is incorporated in the reactant.⁹ The heavier but non-magnetic isotope ^{18}O shows no similar effect.⁹

Whether this phenomenon would be detected in the thermal isomerization of a bicyclo[2.1.0]pent-2-ene was addressed in the present work. For various technical reasons,⁴ 5,5-dimethylbicyclo[2.1.0]pent-2-ene (4) was selected as model substrate; whether deuterium substitution at C(1) to C(4) would result in surprisingly large normal secondary deuterium isotope effects, a possible manifestation of magnetic isotope effects on an intersystem crossing, was set as an initial objective.

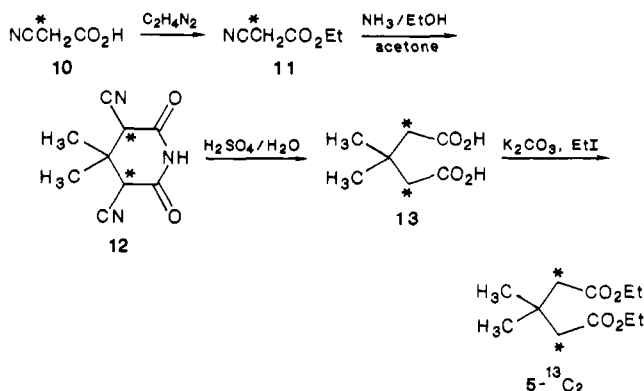
The thermochemical parameters for the isomerization of 5,5-dimethylbicyclo[2.1.0]pent-2-ene differ in detail from those of the parent system,⁴ but again one estimates that the transition state lies above triplet 5,5-dimethylcyclopentadiene, by 8.3 kcal/mol. The thermochemical possibility of reaction by way of an intersystem crossing and a triplet 5,5-dimethylcyclopentadiene intermediate remains.

Results

Syntheses. The synthetic routes to 5,5-dimethylcyclopentadiene reported by Holder and co-workers¹⁰ and by Jefford's group¹¹ were adapted to secure 5,5-dimethylcyclopentadiene (3) and the three deuterium-labeled analogues 3- d_1 , 3- d_3 , 3- d_4 . These dienes in turn were photolyzed in methylcyclohexane with a low pressure mercury lamp to form the corresponding bicyclic isomers 4 and 4- d_i ($i = 1, 3$, or 4).



Scheme II



Scheme I outlines the reaction sequence used to obtain 3- d_3 . Dimethyl 3,3-dimethylpentanedioate-2,2,4,4- d_2 (6) was obtained from diethyl 3,3-dimethylpentanedioate through repeated exchanges (and concomitant transesterification) with *O*-deuterio-methanol and sodium methoxide.¹² An acyloin condensation in the presence of trimethylsilyl chloride¹⁰ gave the bis(trimethylsilyl)cyclopentene intermediate 7, which was hydrolyzed and dehydrated with D_3PO_4 to form 4,4-dimethylcyclopent-2-en-1-one-2,3,5,5- d_2 (8).¹⁰ Reduction of this enone with sodium borohydride in the presence of cerous chloride gave the allylic alcohol 9, which was dehydrated with methyltriphenoxyposphonium iodide¹¹ in dry HMPA to yield the desired 5,5-dimethylcyclopentadiene-2,3,4- d_3 (3- d_3).

The 3- d_1 analogue was made from 4,4-dimethylcyclopent-2-en-1-one by reduction using sodium borodeuteride-cerous chloride, followed by dehydration. Synthesis of the 3- d_4 diene was achieved by a borodeuteride reduction of the cyclopentenone- d_4 8, shown in Scheme I, and a subsequent dehydration.

5,5-Dimethylcyclopentadiene-1,4- $^{13}\text{C}_2$ (3- $^{13}\text{C}_2$) was made from diethyl 3,3-dimethylpentanedioate-2,4- $^{13}\text{C}_2$ (5- $^{13}\text{C}_2$), which was derived from commercial cyanoacetic-2- ^{13}C acid (Scheme II) following in large part the precedent provided by Vogel.¹³

Ethyl cyanoacetate-2- ^{13}C (11) was obtained by the esterification of the commercial labeled cyanoacetic acid (99% 2- ^{13}C) with diazoethane.¹⁴ The cyano ester was then condensed with acetone and ammonia to the corresponding Guereschi imide 12. Acid hydrolysis and decarboxylation of 12 was accomplished with concentrated sulfuric acid to yield 13, which was esterified with ethyl iodide with potassium carbonate in dimethylformamide to give the diester 5- $^{13}\text{C}_2$.

The ^1H NMR spectrum of 5- $^{13}\text{C}_2$ confirmed the site specificity and the high extent of incorporation of the two ^{13}C nuclei. The protons directly bonded to the ^{13}C atoms appeared as a doublet of doublets with a one bond coupling constant of $^1J_{\text{C-H}} = 128.4$ Hz and a three bond coupling constant $^3J_{\text{C-H}} = 3.7$ Hz. The six protons comprising the geminal dimethyl group appeared as a triplet due to a three-bond coupling with the two equivalent ^{13}C nuclei with $^3J_{\text{C-H}} = 4.4$ Hz. However no four-bond coupling to the methylene protons of the ethoxyl group was evident.

At this point only 65 mg of the $^{13}\text{C}_2$ -labeled diester 5 was available for the conversion to 3- $^{13}\text{C}_2$ and 4- $^{13}\text{C}_2$, and it was diluted with 260 mg of unlabeled 5. The resultant mixture was converted to 3- $^{13}\text{C}_2$ by adaptations of the Holder¹⁰ and Jefford¹¹ routes (cf. Scheme I) with the final dehydration to 5,5-dimethylcyclopentadiene-1,4- $^{13}\text{C}_2$ effected with the Burgess reagent¹⁵ instead of methyltriphenoxyposphonium iodide. The mass spectra of the intermediates and the final diene showed $\text{M}:\text{M} + 2$ ratios of approximately 4:1 as expected. Photolysis of the mixture of 3 and

(9) Turro, N. J.; Chow, M.-F. *J. Am. Chem. Soc.* **1980**, *102*, 1190-1192.

(10) Holder, R. W.; Daub, J. P.; Baker, W. E.; Gilbert, R. H., III; Graf, N. A. *J. Org. Chem.* **1982**, *47*, 1445-1451.

(11) Jefford, C. W.; Wallace, T. W.; Can, N.-T. H.; Rimbault, C. J. *J. Org. Chem.* **1979**, *44*, 689-691.

(12) Lambert, J. B.; Keske, R. G. *J. Org. Chem.* **1966**, *31*, 3429-3431.

(13) Vogel, A. I. *J. Chem. Soc.* **1934**, 1758-1765.

(14) Marshall, J. A.; Partridge, J. J. *J. Org. Chem.* **1968**, *33*, 4090-4097.

(15) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26-31.

Table I. Concentration versus Time Data for the Simultaneous Isomerization of **4** and **4-d₃** at 43.6 °C

time, min	(94)/(97) ^a	[4]/[4-d₃] ^b
0	1.682	1.444
14	1.596	1.282
26	1.503	1.189
38	1.448	1.134
50	1.359	1.046
62	1.304	0.990
74	1.184	0.871
86	1.132	0.818
98	1.076	0.762
110	1.020	0.706
122	0.964	0.650

^a Ratio of observed intensities of ions at *m/e* 94 and 97. ^b Ratio of concentrations of **4** and **4-d₃** obtained from the ratio of observed ion intensities.

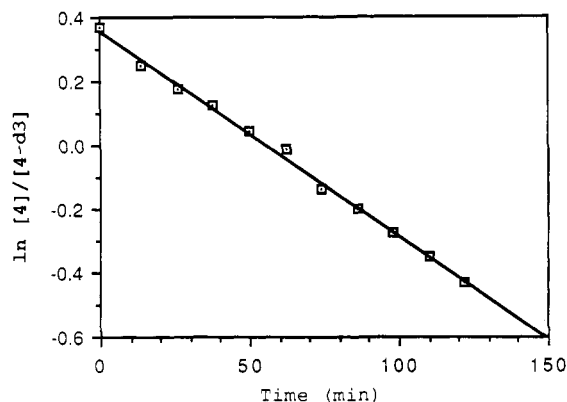
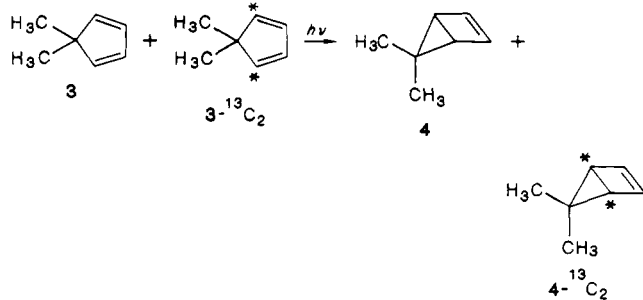


Figure 1. Plot of natural logarithm of the ratio of concentrations of bicyclopentenes **4** and **4-d₃** as a function of time at 43.6 °C; slope = $-1.071 \times 10^{-4} \text{ s}^{-1}$ ($r = 0.998$).

¹³C₂ gave unlabeled 5,5-dimethylbicyclo[2.1.0]pent-2-ene, **4**, and the **¹³C₂**-labeled system **4-¹³C₂**.



Deuterium Isotope Effects. Secondary deuterium kinetic isotope effects on the thermal isomerization of 5,5-dimethylbicyclo[2.1.0]pent-2-ene were determined by following simultaneously pairs of reactants, **4** and **4-d_i**, rearranging to **3** and **3-d_i**. Dilute solutions of approximately equal amounts of **4** and **4-d_i** in methylcyclohexane were kept in a constant-temperature bath; samples were withdrawn periodically and analyzed by GC/MS. The molecular ions of **4** and **4-d_i** (*m/e* 94 and 95, 97, or 98) were detected in the single ion monitoring (SIM) mode. From the ratios of molecular ion intensities as functions of time were calculated concentration ratios as functions of time, by utilizing the correction factors obtained by having measured *m/e* 94 and (94 + *i*) ion-intensity ratios for individual samples of **4** and each **4-d_i**.

For these simultaneous first-order isomerizations a plot of $\ln \{[\mathbf{4}]/[\mathbf{4-d}_i]\}$ against time should give a straight line corresponding to the terms in eq 1. The value for $k_D(d_i)$ can then be calculated

$$\ln \{[\mathbf{4}]/[\mathbf{4-d}_i]\} = (k_D(d_i) - k_H)t + \ln \{[\mathbf{4}]_{t=0}/[\mathbf{4-d}_i]_{t=0}\} \quad (1)$$

with the slope of this line and the value for k_H at the reaction

Table II. Rate Constant Differences and Ratios for Isomerizations of **4** and **4-d_i** at 43.4–44.0 °C

<i>T</i> , °C	4-d_i	$k_H \times 10^4 \text{ s}^{-1}$	$(k_D(d_i) - k_H) \times 10^4 \text{ s}^{-1}$	r^c	$k_H/k_D(d_i)$
43.9	4-d₄	2.828	-1.156	0.997	1.69
44.0	4-d₄	2.863	-1.106	0.999	1.63
43.6	4-d₃	2.727	-1.071	0.998	1.65
43.6	4-d₃	2.727	-1.025	0.998	1.60
43.8	4-d₁	2.794	-0.056	0.925	1.02
43.4	4-d₁	2.662	-0.042	0.953	1.02

^a Calculated from data in ref 4. ^b From least-squares plot based on eq 1. ^c Correlation coefficient.

Table III. Rate Constants, Differences, and Ratios for Isomerizations of **4** and **4-d₃** as a Function of Temperature

<i>T</i> , °C	$k_H^{a,b}$	$(k_D(d_3) - k_H)^{a,c}$	$k_D(d_3)^a$	$k_H/k_D(d_3)$
24.6	0.236	-0.113	0.123	1.91
24.6	0.236	-0.108	0.128	1.84
34.6	0.894	-0.393	0.501	1.78
34.6	0.894	-0.371	0.524	1.71
43.6	2.73	-1.071	1.66	1.65
43.6	2.73	-1.025	1.70	1.60
54.7	9.98	-4.182	5.80	1.72
54.7	9.98	-4.033	5.95	1.68

^a All rate constants have been multiplied by a factor of 10^4 s^{-1} . ^b Calculated from data in ref 4. ^c From least-squares plots based on eq 1; correlation coefficients ranged from 0.987 to 0.999.

temperature, determined from the data published by Roth and co-workers⁴ for the temperature dependence of the rate constant for the isomerization of **4** to **3**.

Preliminary experiments with **4** and **4-d_i** showed that reproducible results could be obtained when the glass vials in which thermolyses were conducted had been thoroughly base washed and dried and when the methylcyclohexane solutions of **3** and **3-d_i** were dried just before photoisomerizations to **4** and **4-d_i** by filtration through a plug of activated 3A molecular sieves.

A typical data set is summarized in Table I and presented graphically in Figure 1. All of the simultaneous isomerizations of **4** and **4-d_i** gave excellent agreement with the behavior predicted by eq 1, with correlation coefficients sensitive to the magnitude of the slope (Table II).

Carbon-13 Isotope Effects. A methylcyclohexane solution containing **3** and **3-¹³C₂** was photoisomerized to a mixture of the bicyclic isomers **4** and **4-¹³C₂**, which were allowed to react thermally at 44 °C. Ratios of ion intensities at *m/e* 94 and 96 for the mixture of **4** and **4-¹³C₂** were determined as a function of time. To calculate concentration ratios, the *m/e* 94:92 ratio observed with authentic **4** was taken to be the 96:94 ratio to be expected for **4-¹³C₂**.

In three independent kinetic runs, each with seven or eight data points extending to 77–96 min (from 1.9 to 2.4 half-lives) at 43.9–44.2 °C, the concentration ratio $[\mathbf{4}]/[\mathbf{4-^{13}C_2}]$ did not vary: the mole fraction of **4** remained constant ($79.1 \pm 0.7\%$, $78.9 \pm 1.1\%$, $78.4 \pm 1.1\%$). To within the sensitivity limits of the analytical methods employed, there was no discernible $k_H/k(\mathbf{4-^{13}C_2})$ isotope effect.

Temperature-Dependent Deuterium Isotope Effects. A possible temperature dependence in secondary deuterium isotope effects on the isomerization **4** to **3** was probed with **4-d₃**. The simultaneous isomerizations of **4** and **4-d₃** were followed by GC/MS as described above, at three additional temperatures; the rate constants and rate constant ratios found are summarized in Table III.

Discussion and Conclusions

The synthetic and kinetic work summarized above establishes four points relevant to the thermal isomerization of 5,5-dimethylbicyclo[2.1.0]pent-2-ene, **4**, to its monocyclic isomer **3**. The secondary k_H/k_D effect for deuterium labels at C(1,4) is very large. This isotope effect is temperature dependent. The secondary deuterium kinetic isotope effect for deuterium substitution at

Table IV. Calculated and Experimental Rate Constants and Isotope Effects on 4- d_3 as a Function of Temperature

$T, ^\circ\text{C}$	$k_D(d_3)(\text{expt})^{a,b}$	$k_D(d_3)(\text{calcd})^{a,c}$	$k_H/k_D(d_3)^d$	$k_H/k_D(d_3)^e$
24.6	0.123	0.128	1.84	1.83
24.6	0.128			
34.6	0.501	0.507	1.76	1.76
34.6	0.524			
43.6	1.66	1.60	1.71	1.70
43.6	1.70			
54.7	5.80	6.09	1.64	1.64
54.7	5.95			

^a All rate constants have been multiplied by a factor of 10^4 s.
^b Values reproduced from Table III. ^c Calculated from the least-squares fit of the Arrhenius plot of the eight experimental $k_D(d_3)$ values versus T^{-1} (K). ^d Evaluated by using the $k_D(d_3)$ values from the Arrhenius plot (column 3). ^e Calculated with the nonlinear multivariate analysis derived parameters ($E_a^D - E_a^H$) = 0.72 kcal/mol and (A^D/A^H) = 1.85.

C(2,3) is almost negligible. Substitution of carbon-13 at C(1) and C(4) of 5,5-dimethylbicyclo[2.1.0]pent-2-ene does not discernibly perturb its rate constant for the thermal disallowed electrocyclic isomerization under scrutiny.

The isotope effects recorded in Table II for three different deuterated variants of bicyclopentene **4** demonstrate the first and third of these points. According to the geometric-mean rule,¹⁶ the $k_H/k_D(d_i)$ ratios for 4- d_1 , 4- d_3 , and 4- d_4 should be given by products of effects for single deuterium substitutions. If $\alpha = k_H/k_D$ for 5,5-dimethylbicyclo[2.1.0]pent-2-ene-1- ^2H and $\beta = k_H/k_D$ for 4- d_1 , then the observed isotope effects $k_H/k_D(d_i)$ should be given by β when $i = 1$, $\alpha^2\beta$ when $i = 3$, and $\alpha^2\beta^2$ when $i = 4$. The β term is directly measured as 1.02 (entries 5 and 6, Table II) and the four $k_H/k_D(d_i)$ entries when $i = 3$ or 4 in Table II provide estimates of α^2 : 1.62, 1.57, 1.62, and 1.57. The average value, 1.60 ± 0.03 , corresponds to $\alpha = 1.26$, the k_H/k_D value for a single deuterium substitution at C(1).

The possibility that $\alpha = 1.26$ at 44 $^\circ\text{C}$ might be signaling a magnetic isotope effect on reaction rate, with ^1H (magnetic moment $\mu = 2.79$ nuclear magneton, $I = 1/2$) at C(1) and C(4) facilitating an intersystem crossing from singlet to triplet more efficiently than ^2H ($\mu = 0.86$, $I = 1$) substituents on the bridgehead carbons, was diminished, in our view, by the very small k_H/k_D effect at C(2,3). One might have supposed that magnetic isotope contributions to intersystem crossing would have been comparably important at C(1,4) and at C(2,3), extrapolating from an expectation of comparable hyperfine couplings for H-C(1,4) and H-C(2,3) in the 5,5-dimethylcyclopentadiene triplet.

The preparation and competitive isomerization of 4- $^{13}\text{C}_2$ provided grounds for a clear dismissal of the magnetic isotope effect/facilitated intersystem crossing rationale for the large k_H/k_D effect shown by 4- d_3 and 4- d_4 . The substitution of ^{13}C ($\mu = 0.70$, $I = 1/2$) at both bridgehead positions should have given, according to the magnetic isotope effect speculation, an enhanced rate of thermal isomerization. A substantial inverse [$k_H(4)/k(4-^{13}\text{C}_2)$ < 1] ^{13}C isotope effect would have conclusively implicated a magnetic origin for the unusually large secondary deuterium isotope effect observed. However no $k_H(4)/k(4-^{13}\text{C}_2)$ effect was detected, effectively ruling out any mechanism for the isomerization of **4** to **3** dependent on magnetic interactions as a possible rationale for $\alpha = 1.26$ at 44 $^\circ\text{C}$.

Determinations of $k_H/k_D(d_3)$ values from 24.6 to 54.7 $^\circ\text{C}$ were secured in an effort to assess the importance of quantum mechanical tunneling for the large secondary deuterium isotope effects in evidence. Table IV presents the variations in the isomerization rate constants and in the isotope effects on the isomerization of 4- d_3 to 3- d_3 as a function of temperature. An Arrhenius plot of the eight experimentally determined $k_D(d_3)$ values (cf. Table III) at four different temperatures gives a straight line with a correlation coefficient = 0.9997.

Using the slope and the y intercept of the Arrhenius plot for the $k_D(d_3)$ values,¹⁷ one calculates the energy of activation for 4- d_3 as $E_a^D = 24.8$ kcal/mol and the corresponding preexponential factor as $A^D = 2.1 \times 10^{13}$. These values and those obtained by Roth and co-workers⁴ for the parent undeuterated hydrocarbon **4** ($E_a^H = 24.1$ kcal/mol, $A^H = 1.2 \times 10^{13}$) give ($E_a^D - E_a^H$) = 0.7 kcal/mol and $A^D/A^H = 1.75$. A nonlinear multivariate statistical treatment¹⁸ of the eight experimental $k_H/k_D(d_3)$ values in terms of the expression $k_H/k_D(d_3) = \exp \{(E_a^D - E_a^H)/RT\} / (A^D/A^H)$ gave the parameters ($E_a^D - E_a^H$) = 0.72 kcal/mol and (A^D/A^H) = 1.85. These parameters were highly correlated: at the extremes given by the calculated asymptotic standard errors, these parameters were (0.47, 1.08) and (0.97, 2.60), respectively. While this alternative treatment of data gives nearly the same best values for ($E_a^D - E_a^H$) and (A^D/A^H) parameters, it serves usefully as a reminder that they are not defined individually with great precision. The average deviation between the eight experimentally determined $k_H/k_D(d_3)$ values (Table III) and the values obtained using the parameters derived by the multivariate nonlinear least-squares fit (Table IV) was 3.1%, a value well within the range of experimental uncertainty to be expected for such kinetic investigations.

The differences in activation energies and preexponential factors observed for 4- d_3 and **4** are very similar to those observed by Caldwell and co-workers¹⁹ [$(E_a^D - E_a^H) = 0.77$ kcal/mol, $A^D/A^H = 1.64$] for the isomerization of *trans*-1-phenylcyclohexene to the corresponding *cis* isomer.

The $k_H/k_D(d_3)$ ratio at 24.6 $^\circ\text{C}$, 1.83, is equivalent to $\alpha^2\beta$ at this temperature; if β is assumed to be temperature independent and thus still 1.02, the per deuterium k_H/k_D effect at C(1), α , is 1.34, a value well beyond the usual range of observed secondary deuterium kinetic isotope effects.²⁰ This effect may be associated with a substantial tunneling²¹ or vibrationally assisted tunneling²² component, or an unusually large change in hybridization and force constant for the C(1)-H bond may be involved.²³

Calculations of geometry at the HF/3-21G level for **1** and for the transition structure for **1** \rightarrow **2** have been reported.²⁴ Interestingly, the C(1)-C(4) bond is considerably longer by the transition state, 1.818 versus 1.531 Å, but the angles between the planes of the three- and four-membered rings increases only slightly from 112.5 $^\circ$ to 121.1 $^\circ$.²⁴ The location of the hydrogens in the transition structure was, unfortunately, not included. Yet the carbon skeletal geometry of this structure provides a telling clue to why the reaction **4** \rightarrow **3** does not proceed by way of an intersystem crossing and an energetically accessible triplet intermediate. The transition state energy may well be higher than that of triplet state 5,5-dimethylcyclopentadiene, but unless the two potential energy surfaces intersect—unless the singlet and triplet states have simultaneously similar energies and geometries—intersystem crossing will be prohibitively improbable. The highly nonplanar transition structure and the presumably planar monocyclic triplet diene lack geometrical commonality, and the

(17) Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980; p 118, 148.

(18) Calculated with SAS release 5.16; SAS Institute, Inc., Cary, NC 27511.

(19) Caldwell, R. A.; Misawa, H.; Healy, E. F.; Dewar, M. J. S. *J. Am. Chem. Soc.* **1987**, *109*, 6869–6871.

(20) For another example of a comparably large secondary deuterium kinetic isotope effect for a thermal isomerization, see: Newman-Evans, R. H.; Carpenter, B. K. *J. Am. Chem. Soc.* **1984**, *106*, 7994–7995.

(21) That secondary deuterium kinetic isotope effects may involve tunneling is supported in recent work: Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 164–169. Saunders, W. H., Jr.; Price, R. C.; Subramanian, Rm. *Phys. Org. Chem. 1986; Stud. Org. Chem.* **1987**, *31*, 197–202.

(22) Dewar, M. J. S.; Merz, K. M., Jr.; Stewart, J. J. P. *J. Chem. Soc., Chem. Commun.* **1985**, 166–168.

(23) See also: McLennan, D. J. *Aust. J. Chem.* **1979**, *32*, 1883–1896. Carpenter, B. K. *J. Am. Chem. Soc.* **1983**, *105*, 1700–1701. Baldwin, J. E.; Reddy, V. P.; Hess, B. A., Jr.; Schaad, L. J. *J. Am. Chem. Soc.* **1988**, *110*, 8554–8555. Baldwin, J. E.; Reddy, V. P.; Schaad, L. J.; Hess, B. A., Jr. *Ibid.* **1988**, *110*, 8555–8556.

(24) Skancke, P. N.; Yamashita, K.; Morokuma, K. *J. Am. Chem. Soc.* **1987**, *109*, 4157–4162.

(16) Bigeleisen, J. *J. Chem. Phys.* **1955**, *23*, 2264–2267.

reaction occurs start to finish on the singlet potential energy surface.

Experimental Section

Proton NMR spectra were recorded for CDCl_3 solutions on a "Mohawk 250", an in-house designed 5.87 T FT spectrometer based on Cryomagnet Systems rf equipment and a Nicolet 1280 computer or on a GE QE-300 NMR spectrometer; chemical shifts are reported in δ (ppm) downfield from Me_4Si as an internal standard. Analytical gas-liquid chromatographic analyses (capillary GC) were done with 0.2-mm id 25-m cross-linked dimethyl silicone and phenyl methyl silicone fused silica capillary columns on a Hewlett-Packard 5790 gas chromatograph with both columns connected to a single injection port and the two FID detectors connected to HP 3390A and 3392A reporting integrators. Preparative gas chromatographic separations were accomplished with a Varian Aerograph A-90P3 with He as a carrier gas on a 300-cm 20% β,β' -ODPN on Chromosorb D 60–80-mesh column. Mass spectra and GC/MS data were obtained with a Hewlett-Packard 5970B mass selective detector interfaced to a 5890 series gas chromatograph and a 9336 computer. Methylcyclohexane, toluene, HMPA, and TMSCl were dried by distillation from CaH_2 . Dimethylformamide was dried by distillation from MgSO_4 . The kinetic runs were carried out in a well-insulated oil bath which was heated with a Bayley precision temperature controller (Model 253). The temperature in the bath was monitored with a HP 2802A thermometer equipped with a platinum resistance probe. An overhead mechanical stirrer was used to provide agitation in the oil bath. The oil bath was equilibrated at a given temperature for at least 6 h prior to kinetic runs.

The specific procedures given below for the synthesis of 5,5-dimethylcyclopentadiene-1,2,4- $^2\text{H}_3$ are representative of the general procedures used to prepare the unlabeled and all deuterated variants of the system. All labeled synthetic intermediates exhibited analytical gas chromatographic retention times identical with those characteristic of the corresponding known unlabeled materials on both the GC columns. Satisfactory ^1H NMR spectra were recorded for the various deuterated intermediates.

Dimethyl 3,3-Dimethylpentanedioate-2,2,4,4- $^2\text{H}_4$ (6).¹² Diethyl 3,3-dimethylglutarate¹⁰ (23.43 g, 0.106 mmol), MeOD (58 g, 1.76 mmol), and MeONa (2.08 g) were combined in a dry 200-mL flask which contained a magnetic stirring bar. A reflux condenser was attached to the flask; the reaction mixture was stirred under an atmosphere of N_2 and was heated to 55–60 °C for 23 h. At the end of this period the flask was cooled and most of the MeOD/MeOH was removed by rotary evaporation. A fresh batch of 30 mL of MeOD was added and heating was continued for another 24 h. This procedure was repeated twice more with 15 mL of fresh MeOD added each time. The reaction mixture was cooled to 0 °C and slowly quenched with 30 mL of cold water. The contents of the flask were then immediately extracted with three 30-mL portions of ether and then with two 20-mL portions of pentane. The organic extracts were combined, dried over MgSO_4 , filtered, and concentrated by rotary evaporation to give 17.27 g (81%) of **6**, which had 96% D incorporation as determined by ^1H NMR. Mass spectrum: m/e 161 (M^+ – CH_3O , 37.2), 131 (23.1), 117 (44.4), 84 (30.8), 73 (100), 59 (39.6), 57 (22.9).

1,2-Bis(trimethylsiloxy)-4,4-dimethylcyclopentene-3,3,5,5- $^2\text{H}_4$ (7).¹⁰ A 500-mL three-necked flask was equipped with a high-speed stirrer (SKIL Model 146), a reflux condenser, and an addition funnel. The entire setup was flame dried after assembly and cooled under N_2 . The flask was then charged with dry toluene (165 mL) and small pieces of sodium (6.14 g, 267 mmol). The toluene was heated to reflux until all the sodium had melted, and then the stirrer was switched on at a high speed until all the sodium had been dispersed as a fine sand. Stirring and heating were stopped and the contents of the flask were allowed to cool. The addition funnel was then charged with diester **6** (10.12 g, 52.7 mmol), toluene (25 mL), and dry TMSCl (40 mL). The contents of the flask were heated with stirring to just below reflux and the solution from the addition funnel was added at a rate fast enough to maintain reflux. The addition funnel was then rinsed with toluene (20 mL) and TMSCl (11 mL). Toluene (20 mL) and TMSCl (11 mL) were added again, 3 h after the end of the first addition. At the end of 6 h, heating and stirring were stopped. The contents of flask were allowed to settle and cool. The reaction mixture was filtered under N_2 on a sintered-glass funnel and the purple residue was washed with anhydrous ether. The filtrate was concentrated to a yellow oil by rotary evaporation to give crude product estimated by GC to contain 12.25 g (84%) of **7**. Mass spectrum: m/e 276 (M^+ , 45.6), 275 (17.5), 147 (28.5), 73 (100), 45 (37.4).

4,4-Dimethylcyclopent-2-en-1-one-2,3,5,5- $^2\text{H}_4$ (8).¹¹ In a dry 50-mL flask with a magnetic stirring bar was placed crude **7** (5.9 g, 21.4 mmol) and 85% D_3PO_4 (10 mL). A short-path condenser, cooled with ice water,

was attached to the flask. The receiving flask was cooled in an ice-water bath. The reaction flask was then immersed in an oil bath preheated to 100 °C and the pressure in the system was gradually reduced, with the aid of a vacuum controller attached to a water aspirator, until the distillation became vigorous. The pressure was reduced to 40 mm over a period of 30 min; the temperature in the bath was raised to 170 °C, and the distillation was continued for 50 min. At the end of this period the pressure was reduced to 20 mm and heating was continued at 170 °C for another 45 min. Heating was then stopped and the vacuum was released. The two phases in the distillate were separated and the aqueous phase was extracted with ether (2 \times 5 mL). The combined organic phases were dried over MgSO_4 , filtered, and concentrated by simple distillation. The sharp-smelling, oily concentrate was then distilled (bp 75–79 °C, 55 mm) to yield **8** (1.395 g, 57% yield). Mass spectrum: m/e 114 (M^+ , 35.0), 99 (100), 71 (91.7), 70 (20.7), 69 (15.7), 43 (32.7), 41 (31.5).

4,4-Dimethylcyclopent-2-en-1-ol-2,3,5,5- $^2\text{H}_4$ (9).¹¹ In a dry 100-mL three-necked flask equipped with a magnetic stir bar was placed 30 mL of CH_3OH . Cerous chloride ($\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, 4.48 g) and then **8** (1.395 g, 12.2 mmol) were dissolved in the methanol under N_2 . Sodium borohydride (470 mg, 12.3 mmol) was added in small portions over a period of 30 min. The reaction mixture was stirred for another 10 min after the addition was complete, treated with H_2O (24 mL), and extracted with ether (3 \times 60 mL). The combined ether extracts were washed with brine (6 \times 40 mL), dried over MgSO_4 , filtered, and concentrated by simple distillation to afford **9** (1.206 g, 85% yield). Mass spectrum: m/e 116 (M^+ , 11.7), 101 (100), 100 (25.5), 82 (15.7), 73 (20.6), 71 (20.0), 70 (17.7), 57 (26.8), 56 (19.6), 43 (65.5).

Mass spectral data for the allylic alcohols corresponding to **9** that were obtained en route to the syntheses of the dienes **3-d₁** (**9-d₁**) and **3-d₄** (**9-d₅**) are listed below. **9-d₅**: m/e 117 (M^+ , 11.5), 102 (100), 101 (27.5), 83 (15.8), 74 (20.9), 72 (16.6), 71 (16.6), 58 (23.2), 57 (26.0), 45 (64.7). **9-d₁**: m/e 113 (M^+ , 10.6), 98 (100), 80 (21.8), 78 (13.0), 70 (28.5), 56 (20.2), 55 (20.5), 43 (51.8).

5,5-Dimethylcyclopentadiene-1,2,4- $^2\text{H}_3$ (3-d₃).¹¹ A dry 100-mL three-necked flask was fitted with a magnetic stirring bar, a reflux condenser, and an addition funnel. This entire assembly was flame dried and cooled under a stream of N_2 . The alcohol **9** (1.206 g, 10.4 mmol) dissolved in 1 mL of dry HMPA was transferred under N_2 to the addition funnel. Methyltriphenoxyposphonium iodide (8.62 g) was added to the flask followed by dry HMPA (20 mL). Stirring was then begun and the alcohol was added dropwise into the flask. The flask was then heated for 2 h at 50 °C under a positive pressure of N_2 . The contents of the flask were then Kugelrohr distilled at aspirator pressure and 50 °C, with the receiving flask cooled to –78 °C. The material which distilled (733 mg) was estimated to contain 671 mg (crude yield = 68%) of **3-d₃** by capillary GC. Final purification was achieved by preparative gas chromatography. Mass spectrum: m/e 97 (M^+ , 34.6), 96 (15.8), 94 (10.8), 93 (12.5), 82 (100), 81 (54.1), 80 (47.5), 79 (52.8), 78 (23.6), 53 (14.5), 52 (17.0).

Mass spectral data for the two other deuterated variants of **3** are listed below. **3-d₁**: m/e 95 (M^+ , 44), 94 (23.6), 92 (23.7), 80 (100), 79 (62.1), 78 (77.7), 77 (43.0), 52 (21.2), 51 (25.8). **3-d₄**: m/e 98 (M^+ , 38.7), 97 (17.8), 94 (14.1), 83 (100), 82 (55.9), 81 (51.2), 80 (58.5), 79 (38.0), 53 (18.1), 52 (20.7).

Ethyl Cyanoacetate-2- ^{13}C (11). Cyanoacetic-2- ^{13}C acid (**10**; 99% ^{13}C , 1 g, 11.6 mmol) obtained from ICON Services, Inc.) was dissolved in 25 mL of ether. This solution was cooled in an ice bath and to it was slowly added a cold ethereal solution of diazoethane¹⁴ in small portions with swirling of the reaction solution after every addition until a pale yellow color persisted. The excess diazoethane was quenched by adding a 10% ethereal solution of acetic acid, dropwise, until no more evolution of gas occurred. The reaction solution was then dried over MgSO_4 , filtered, and concentrated by rotary evaporation to give **11** (917 mg, 8.04 mmol) in 69% yield.

2,4-Dicyano-3,3-dimethylpentanamide-2,4- $^{13}\text{C}_2$ (12).¹³ A saturated ethanolic solution of NH_3 was prepared by bubbling anhydrous NH_3 through absolute ethanol at –5 to 0 °C for at least 5.5 h. The labeled cyanoacetate **11** (917 mg, 8.04 mmol) and dry acetone (250 mg, 4.3 mmol) were combined in a dry vial, and to it was added 6 mL of the ethanolic NH_3 solution. The vial was capped and placed in a freezer at –20 °C for 7 h. The vial was then transferred to a warmer freezer at –10 °C for 3.5 days. A precipitate which had formed in the vial was collected by filtration. The precipitate was dried in air and then dissolved in a minimum quantity of boiling water; the aqueous solution was acidified with concentrated HCl. The acidic solution was concentrated by distillation until a white solid separated; it was filtered from the remaining liquid and dried under vacuum to give **12** (290 mg, 1.5 mmol) in 37.4% yield.

3,3-Dimethylpentanedioic-2,4- $^{13}\text{C}_2$ Acid (13).¹⁰ Intermediate **12** (380 mg, 1.97 mmol) was dissolved in 1.06 mL of concentrated H_2SO_4 in a 10-mL round-bottomed flask. This was warmed to 55 °C and to it was

added 310 μL of H_2O over a period of 46 min with a syringe pump. A reflux condenser was attached and the temperature of the flask was raised to 165 $^\circ\text{C}$. At 140 $^\circ\text{C}$ vigorous frothing commenced and heating was continued for about 1 h after it had subsided. The oil bath was removed and the flask was allowed to cool for 8 min. Then 385 μL of H_2O was added over a period of 40 min with a syringe pump. Heating at 165 $^\circ\text{C}$ was resumed for 20 h. At the end of this period the reaction mixture was cooled in the freezer and the dark supernatant solid was separated from the black liquid by filtration through a sintered-glass funnel. The solid was vigorously stirred with three 7-mL portions of ether. The combined ether washes were then dried over MgSO_4 along with some Norit A. The ethereal solution was filtered and concentrated by rotary evaporation to yield a white solid which was thoroughly dried under vacuum (100 mg, 31% yield).

Diethyl 3,3-Dimethylpentanedioate-2,4- $^{13}\text{C}_2$ (5- $^{13}\text{C}_2$). The labeled diacid **13** (100 mg, 0.671 mmol) was dissolved in 9 mL of dry DMF under N_2 . To this solution was added anhydrous K_2CO_3 (341 mg); the reaction mixture was stirred for 2 h, then ethyl iodide (390 mg, 2.5 mmol) was injected into the mixture. The reaction flask was covered with foil and stirring at room temperature was continued for 24 h. At the end of this period the reaction mixture was poured into a separatory funnel and diluted with H_2O (8 mL). Extraction with ether (3×8 mL) gave a combined ethereal solution which was washed once with 8 mL of H_2O . The ethereal solution was dried over MgSO_4 and filtered to give a solution which contained DMF and 5- $^{13}\text{C}_2$ (65 mg, 45% yield as estimated by NMR integrations). NMR: 4.12 (q, $J = 7.2$ Hz, 4 H), 2.40 (dd, $J = 128.8$ Hz, $J = 3.7$ Hz, 4 H), 1.25 (t, $J = 7.2$ Hz, 6 H), 1.11 (t, $J = 4.4$ Hz, 6 H). Mass spectrum: m/e 173 ($\text{M}^+ - \text{C}_2\text{H}_5\text{O}$, 100), 145 (48.1), 144 (59.0), 130 (72.1), 129 (38.5), 102 (34.5), 87 (74.6), 84 (69.6), 59 (43.5), 57 (43.2), 56 (38.9).

Isotopic Dilution. The $^{13}\text{C}_2$ -labeled diester 5- $^{13}\text{C}_2$ (65 mg, 0.3 mmol) was diluted with unlabeled ester **5** (260 mg, 1.2 mmol). All subsequent synthetic steps and spectral data refer to this approximately 1:4 combination of labeled and unlabeled compounds, even though this fact is not always reflected in the nomenclature employed.

1,2-Bis(trimethylsiloxy)-4,4-dimethylcyclopentene-2,4- $^{13}\text{C}_2$.¹⁰ As described for the synthesis of **7**, a fine suspension of Na (1.9 g) in toluene (40 mL) was made. This suspension was agitated and about 6 mL was withdrawn using a wide-bore needle and syringe. It was injected into a flame-dried 25-mL three-necked flask, under N_2 , equipped with a magnetic stirring bar, addition funnel, and reflux condenser. This suspension was brought to reflux and the addition funnel was charged with the mixture of diesters **5** and 5- $^{13}\text{C}_2$ (1.5 mmol), toluene (1 mL), and dry TMSCl (2 mL). This solution was dripped into the flask over a period of 2.5 h. The addition funnel was then rinsed with toluene (0.6 mL). Some 2.5 h after the end of the first addition, another batch of TMSCl (1 mL) was added, and 2.5 h later yet another batch of TMSCl (1 mL) was added. After another 3 h the heating and stirring were stopped and the reaction was allowed to cool under N_2 . The reaction mixture was filtered on a sintered-glass funnel under an inert atmosphere and the purple solid collected was washed thoroughly with anhydrous ether. The filtrate was concentrated by rotary evaporation to yield 254 mg (0.93 mmol, 62% yield) of the bis(siloxy) product as estimated by capillary GC analysis.

4,4-Dimethylcyclopent-2-en-1-one-2,4- $^{13}\text{C}_2$. The bis(siloxy) material prepared immediately above (0.93 mmol) was placed in a 50-mL flask. To it was added a solution of P_2O_5 in 85% H_3PO_4 (3.5 mL). This was attached to a Kugelrohr distillation apparatus with the air bath already warmed to 50 $^\circ\text{C}$. The receiving flask was cooled to -78 $^\circ\text{C}$. Over a period of 45 min the temperature of the air bath was raised to 195 $^\circ\text{C}$. Concomitant with this heating, the pressure in the system was reduced to 80 Torr. At the end of 45 min from the initiation of the reaction, the pressure was reduced to full aspirator vacuum and the heating at 195 $^\circ\text{C}$ was continued for another 17 min. The vacuum was then released and the heating was discontinued. The two-phase distillate was separated and the aqueous layer was extracted with three 1-mL portions of ether. The combined ethereal extracts were dried over MgSO_4 , filtered, and concentrated by micro spinning band distillation. The concentrate was purified by flash column chromatography using 15:1 pentane-ether as the eluting solvent. The combined flash fractions were again concentrated by micro spinning band distillation to give 48.6 mg (0.44 mmol, 47% yield) of the mixture of enones. Mass spectrum: m/e 112 ($\text{M}^+ [8-^{13}\text{C}_2]$, 9.9), 110 ($\text{M}^+ [8-d_0]$, 35.5), 97 (27.9), 95 (100), 69 (24.9), 67 (82.3), 41 (47.6).

4,4-Dimethylcyclopent-2-en-1-ol-2,4- $^{13}\text{C}_2$. A standard solution was prepared by dissolving cerous chloride ($\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, 745 mg) in MeOH (5 mL). The mixture of enones (0.43 mmol) from above was dissolved in 1.2 mL of the methanolic CeCl_3 solution in a 5-mL flask. To this was added NaBH_4 (39 mg, 1.03 mmol) over a period of 20 min. The reaction mixture was allowed to stir for 30 min at ambient temperature before

Table V. Ion-Intensity Ratios of **4** and Isotopically Labeled Analogues

compd	94/95 ^a	94/97 ^a	94/98 ^a
4	13.027	0.0	0.0
4-d₁	0.484	0.0	0.0
4-d₃		0.314	
4-d₄			0.432

^a Ratio of observed m/e intensities in pure samples of **4** or **4-d_i**.

it was quenched with water (1.3 mL). The quenched solution was stirred for 3 h and then poured into a separatory funnel; it was extracted with three 1-mL portions of ether. The combined ether extracts were washed with water (4×0.8 mL) and then dried over MgSO_4 and filtered. The filtrate was concentrated by subjecting it to a vacuum of 140 Torr at 0 $^\circ\text{C}$ to give 44.9 mg (39.9 mmol, 93% yield) of the mixture of alcohols. Mass spectrum: m/e 114 ($\text{M}^+ [9-^{13}\text{C}_2]$, 3.2%), 112 ($\text{M}^+ [9-d_0]$, 11.9), 99 (26.8), 97 (100), 79 (28.2), 70 (22.0), 69 (33.8), 55 (35.1), 43 (90.1), 41 (70.1).

5,5-Dimethylcyclopentadiene-1,4- $^{13}\text{C}_2$ (3- $^{13}\text{C}_2$). The mixture of allylic alcohols prepared immediately above (39.9 mmol) was dissolved in dry methylcyclohexane (1.1 mL) in a 10-mL flask containing a magnetic stirring bar. To this solution was added the Burgess salt¹⁵ (196 mg, 0.82 mmol) in one portion. The flask was stoppered with an adapter attached to a positive pressure of N_2 . The contents of the flask were heated for 2 h at 67 $^\circ\text{C}$. The flask was then cooled to 0 $^\circ\text{C}$ and attached to a Kugelrohr distillation apparatus. The receiving flask was cooled to -78 $^\circ\text{C}$ and the pot temperature was not raised above 85 $^\circ\text{C}$. The distillate was filtered through a plug of silica gel to remove any traces of moisture or polar impurities that might have been present in the sample. The material was pure according to capillary GC analysis. This solution was used for the photolysis and kinetic experiments without any further treatment. Mass spectrum: m/e 96 ($\text{M}^+ [3-^{13}\text{C}_2]$, 7.1), 94 ($\text{M}^+ [3]$, 24.5), 93 (16.1), 91 (17.4), 81 (21.6), 79 (100), 77 (49.7).

Photoisomerizations of 5,5-Dimethylcyclopentadienes to 5,5-Dimethylbicyclo[2.1.0]pent-2-enes. Photoisomerizations were done in a quartz test tube (12-cm long, ~ 20 mL) which was attached to a standard taper 14/20 glass joint via a graded seal. This tube was soaked in concentrated NH_4OH for at least 30 min followed by rinsing with distilled water and drying in an oven. Solutions for photolyses were prepared, just prior to use, by dissolving an approximately 1:1 ratio of $d_i d_0$ dienes ($i = 1, 3$, or 4), or the approximately 1:4 combination of 3- $^{13}\text{C}_2$:3 in dry methylcyclohexane. A typical solution would contain about 15 mg of the labeled and unlabeled dienes in 5 mL of the solvent. This solution was then filtered through either activated 3A sieves or through silica gel to eliminate traces of moisture that might have been associated with the preparative gas chromatographically purified dienes; it was placed in the dry quartz test tube which was then capped with a glass stopper. The quartz tube was strapped to the side of a quartz immersion well and this entire assembly was wrapped with aluminum foil. This apparatus was then supported in a Dewar flask containing a salt-ice-water mixture at a temperature of -5 $^\circ\text{C}$ or lower. A low pressure Hg lamp (Ace Glass) was placed in the immersion well and the solution of the dienes was photolysed for 8–9 h. At the end of this period, capillary GC analysis usually indicated a 40–50% conversion to the bicyclic isomer. This solution was then directly used for the kinetic rate determinations without further treatment.

Determination of Ion Intensity Ratios 94/(94 + i) for **4 and Isotopically Labeled Analogues.** Methyl cyclohexane solutions of pure **3** or pure **3-d_i** were photoisomerized to **4** or **4-d_i** in a manner similar to that described above. Mass spectra for these pure compounds were recorded and the necessary ion-intensity ratios were determined. These ratios (Table V) allowed for the determination of ratios of concentrations of **4**/[**4-d_i**] from the observed parent-ion intensities²⁵ when mixtures of **4** and **4-d_i** were thermolyzed for the kinetic runs.

Kinetics of Thermal Isomerizations of 5,5-Dimethylbicyclo[2.1.0]pent-2-enes to 5,5-Dimethylcyclopentadienes. From 1 to 2 mL of a photolysis solution containing two isotopically different 5,5-dimethylbicyclo[2.1.0]pent-2-enes was placed in a vial which had been base washed with NH_4OH , rinsed with distilled water, and dried in an oven. The vial was closed with a cap containing a septum to allow for easy removal of aliquots of the solution at different time intervals.

The vial was then placed in a thermostated oil bath, with care taken to ensure that the level of the solution in the vial was below the surface of the bath fluid. The vial was allowed to equilibrate for 45–60 s before

(25) Engel, P. S.; Chae, W. K.; Baughman, S. A.; Marschke, G. E.; Lewis, E. S.; Timberlake, J. W.; Luedtke, A. E. *J. Am. Chem. Soc.* **1983**, *105*, 5030–5034. Kwart, H.; Wilk, K. A. *J. Org. Chem.* **1985**, *50*, 817–820.

any sampling was begun. For the kinetic analyses carried out in the range of 43.4–44.0 °C, 1- μ L aliquots were withdrawn every 12–15 min and analyzed directly by GC/MS. For the analyses carried out at other temperatures, 150- μ L aliquots were withdrawn at various time intervals and placed in cooled (0–4 °C) sample vials, which had been rinsed with distilled water and oven dried. These vials were then capped, wrapped with parafilm, and stored in a freezer at –20 °C. Once all the samples had been accumulated, they were immediately subjected to GC/MS analysis. The GC/MS analyses for a given kinetic run were carried out in one sitting over the shortest possible period of time to prevent inherent instabilities in the performance of the MS system from biasing the data. The mass spectra for the kinetic runs were acquired in the single ion monitoring (SIM) mode.

Acknowledgment. We thank the National Science Foundation

for supporting our studies on hydrocarbon isomerizations and Syracuse University for Graduate Fellowship awards to N.D.G. in 1985–1987.

Registry No. 3, 4125-18-2; 3-¹³C₂, 119787-48-3; 3-*d*₁, 104309-53-7; 3-*d*₃, 119770-93-3; 3-*d*₄, 119770-96-6; 4, 74503-34-7; 4-*d*₁, 104309-51-5; 4-*d*₃, 119771-03-8; 4-*d*₄, 119771-04-9; 4-¹³C₂, 119771-05-0; 5, 17804-59-0; 5-¹³C₂, 119770-99-9; 6, 119770-89-7; 7, 119770-90-0; 8, 119770-91-1; 9, 119770-92-2; 9-*d*₀, 68757-99-3; 9-*d*₁, 119770-94-4; 9-*d*₅, 119770-95-5; 9-¹³C₂, 119771-02-7; 10, 119770-97-7; 11, 56267-17-5; 12, 119787-47-2; 13, 119770-98-8; D₂, 7782-39-0; 4,4-dimethylcyclopent-2-en-1-one, 22748-16-9; 1,2-bis(trimethylsiloxy)-4,4-dimethylcyclopentene-2,4-¹³C₂, 119771-00-5; 1,2-bis(trimethylsiloxy)-4,4-dimethylcyclopentene, 54851-48-8; 4,4-dimethylcyclopent-2-en-1-one-2,4-¹³C₂, 119771-01-6.

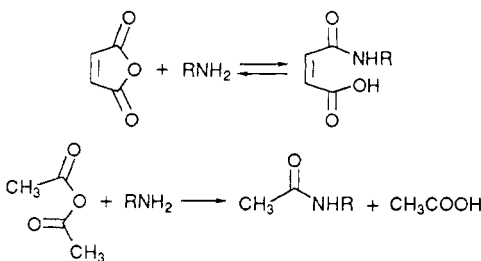
Circumventive Catalysis: Contrasting Reaction Patterns of Tertiary and Primary Amines with Cyclic Anhydrides and the Avoidance of Intermediates

Ronald Kluger* and John C. Hunt

Contribution from the Lash Miller Laboratories, Department of Chemistry, University of Toronto, Toronto, Ontario, Canada M5S 1A1. Received September 9, 1988

Abstract: The aminolysis of cyclic anhydrides proceeds via initial formation of a zwitterionic tetrahedral intermediate which tautomerizes to an uncharged intermediate. The aminolysis of acyclic anhydrides does not involve formation of the uncharged tautomer. The dichotomy of the reaction patterns was investigated by examining the reaction of tertiary amines with cyclic anhydrides. These amines catalyze the hydrolysis of acyclic anhydrides through the formation of reactive acylammonium ions. Pyridine, which reacts with acyclic anhydrides, does not promote the hydrolysis of maleic anhydride and does not form detectable intermediates (pH 7.3, 25 °C). 4-(Dimethylamino)pyridine does not promote the hydrolysis of succinic anhydride (the reaction with pyridine was not observed due to spectral overlap) but does produce the succinyl 4-(dimethylamino)pyridinium ion (pH 7.3, 7.8, 8.3, 9.0). The divergence in reactivity patterns between the cyclic and acyclic species is consistent with the function of the tautomerization step being the circumvention of an O-protonated amide carboxylate species. Presumably, these are generated from the cyclic anhydrides but are reconverted too fast for hydrolysis to compete. Tautomerization permits the less reactive N-protonated amide to form and this reacts with water. Catalysis by added acids permits the reaction to circumvent the O-protonated amide with a neighboring carboxylate group. Such circumventive catalysis permits release of products where their departure would normally be hindered by their affinity.

A primary or secondary amine reacts readily with an anhydride in water to produce an amide and a carboxylic acid.^{1–3} The



reverse of this exergonic process, acylolysis of an amide, is observed only for intramolecular reactions^{4–6} where the cyclic anhydride

which is produced is in favorable equilibrium with the corresponding diacid.⁷ Such diacids also must have carboxyl groups in a *synperiplanar* conformation, as in derivatives of maleic acid.⁸

Intramolecular acylolysis reactions (and aminolysis of the related cyclic anhydrides) are subject to specific-acid catalysis and/or general-acid catalysis.^{5–9} In contrast, the reactions of acyclic anhydrides with amines are not subject to acid catalysis. These observations require that a catalytic mechanism be available uniquely to the cyclic compounds and also implies that proton-transfer steps are kinetically significant. Kinetic studies in the cyclic series support a mechanism in which acid catalysis promotes proton transfer between nitrogen and oxygen centers of a tetrahedral intermediate (see Scheme 1).^{1–10} The initially formed tetrahedral intermediate is zwitterionic and the transfer of the proton converts it to the uncharged tautomer. The reaction may also be subject to general-acid catalysis (as specific-acid–general-base catalysis) and this catalysis is associated with a similar proton-transfer process.^{9,10}

- (1) Kluger, R.; Hunt, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 5667.
- (2) Pitman, I. H.; Uekama, K.; Higuchi, T.; Hall, W. E. *J. Am. Chem. Soc.* **1972**, *94*, 8147.
- (3) Hall, W. E.; Higuchi, T.; Pitman, I. H.; Uekama, K. *J. Am. Chem. Soc.* **1972**, *94*, 8153.
- (4) Bender, M. L. *J. Am. Chem. Soc.* **1951**, *73*, 1626.
- (5) Kirby, A. J.; Lancaster, P. W. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1206.

- (6) Kluger, R.; Chin, J.; Choy, W.-W. *J. Am. Chem. Soc.* **1979**, *101*, 6976.
- (7) Ebersson, L.; Welinder, H. *J. Am. Chem. Soc.* **1971**, *93*, 5821.
- (8) Kluger, R.; Brandl, M. *Can. J. Chem.* **1984**, *62*, 2515.
- (9) Aldersley, M. F.; Kirby, A. J.; Lancaster, P. W.; McDonald, R. S.; Smith, C. R. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1487.
- (10) Kluger, R.; Lam, C.-H. *J. Am. Chem. Soc.* **1978**, *100*, 2191.