Electrophilic Cleavage of Cyclopropanes. Acetolysis of Bicyclo[2.1.0]pentane and Bicyclo[3.1.0]hexane

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Abstract: The uncatalyzed acetolysis of bicyclo[2.1.0]pentane (**1**) leads to 47% cyclopentyl acetate and 53% cyclopentene. The reaction with *p*-toluenesulfonic acid in acetic acid is much more rapid and leads to 30% cyclopentyl acetate, 24% cyclopentyl tosylate, and 46% cyclopentene. The rate of acetolysis is decreased by a factor of 2.55 on going to AcOD as the solvent, indicating that proton transfer is at least partially rate determining. The deuterium distribution in the products of the reaction was determined, and extensive hydrogen migration was found. The preparation of **1**-*endo*-5-*d* is reported, as well as the distribution of deuterium in the products of its acetolysis. Cyclopentyl acetate is formed mainly by a process involving inversion at both C_1 and C_4 whereas cyclopentyl tosylate is formed largely by a process involving inversion at the site of proton attack, migration of the endo-5 proton, and capture of the tosylate anion. A detailed mechanistic scheme is proposed. The competition between strain relief and cation stabilization was examined with use of 5,5-dimethylbicyclo[2.1.0]pentane, and the latter was found to be more important. The rate of acetolysis of **1** is 88 times faster than that of bicyclo[3.1.0]hexane whereas a much larger rate ratio would have been expected if strain relief was an important factor in determining reactivity.

Our study of the acetolysis of alkyl-substituted cyclopropanes[1] has given us a better understanding of the nature of the intermediates and activated complexes for the reaction. However, some questions concerning stereochemistry appear to be best examined via the use of bicyclic derivatives of cyclopropane. The acetolysis of bicyclo[2.1.0]pentane (**1**) has been examined along with that of other bicyclo[*n*.1.0]alkanes and related compounds.[2,3] There were two particularly interesting observations concerning the reaction of **1**. First, it was reported that it gave only cyclopentyl acetate and no cyclopentene.[2] Second, it was reported to react as the same rate as bicyclo[3.1.0]hexane.[3] These observations provided the impetus for the present study, and as we shall show, both are incorrect.

The reaction of **1** with acetic acid occurs at 86 °C and leads to 47% cyclopentyl acetate and 53% cyclopentene. The formation of cyclopentene is not surprising since the solvolysis of cyclopentyl derivatives always leads to a large amount of cyclopentene[4] and since the intermediate in the reaction must have a structure which is similar to that of the cyclopentyl cation. The reaction with *p*-toluenesulfonic acid in acetic acid proceeds at a lower temperature (17–32 °C) and gives cyclopentyl tosylate, cyclopentyl acetate, and cyclopentene.
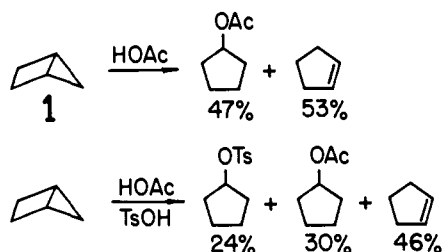
The large amount of internal return product in the reaction with TsOH provides an explanation of the previously measured low rate of reaction. When a catalytic amount of toluenesulfonic acid is used, it is quickly converted into cyclopentyl tosylate. Further reaction then involves the relatively slow solvolysis of cyclopentyl tosylate, regenerating the acid catalyst. In order to determine the rate of reaction, we have measured the rate using a stoichiometric concentration of TsOH. Here, the rate expression becomes

$$-d[A]/dt = k_1[A][B]$$

where A is **1** and B is TsOH. If *c* is defined as $(B_o - B_f)/B_o$ (i.e., the fraction of TsOH which is consumed in forming cyclopentyl tosylate), the equation becomes

$$-d[A]/dt = k_1(A_o - x)(B_0 - cx)$$

where *x* is the amount of A which has reacted. Integration gives

$$\ln \frac{(B_0/c) - x}{A_o - x} = (A_o - B_0/c)kct + d \tag{1}$$

The reaction was followed by measuring the disappearance of A via gas chromatography, and *c* was determined by titration of the remaining acid after six half-lives. The data were found to be fit by eq 1. The rate constants are given in Table I and lead to $\Delta H^{\ddagger} = 15.6 \pm 0.7$ kcal/mol and $\Delta S^{\ddagger} = -15 \pm 3$ eu.

We wished to know whether or not proton transfer was rate determining, and therefore the rate of reaction with AcOD/TsOD was determined giving the data in Table I. This leads to a solvent isotope effect $k_H/k_D = 2.87$ after correcting for the small amount of HOAc in the solvent. In one case, the reaction was carried to one half-life, and the unreacted **1** was recovered. The mass spectrum indicated no deuterium incorporation. These data indicate that proton transfer is at least partially rate determining and that if protonation is in part reversible, the proton initially added must be the one which departs. In the absence of an acid catalyst, and at a higher temperature, the solvent kinetic isotope effect was $k_H/k_D = 2.55$.

In their investigation of the acetolysis of **1** in DOAc, Lalonde and Forney[2] found considerable hydrogen migration, leading to cyclopentyl-2-*d* acetate. It was not possible at that time to examine the stereochemistry of deuterium incorporation. The availability of a ^{2}H NMR spectrometer made it attractive to reinvestigate the reaction of **1** with acetic-*d* acid. It is now possible to determine the amount of deuterium in each of the possible positions. The reaction was carried out using TsOD in acetic-*d* acid. The three products were separated and their ^{2}H NMR spectra determined. All the protons of cyclopentyl acetate were resolved with the addition of the shift reagent Eu(fod)$_2$. However, the shift reagent was not effective with cyclopentyl tosylate, and therefore it was converted to cyclopentanol via cleavage of the S–O bond with the radical anion of naphthalene in order to carry out the analysis. The compositions of the products are shown in Scheme I.

We may first note the large difference in deuterium distribution between cyclopentyl acetate and the ion pair combination product, cyclopentyl tosylate. The acetate contained mainly the *cis*-3-deuterium species, which corresponds to cleavage of the central bond with either retention or inversion of configurations at both sites. The tosylate contained mainly the *cis*-2-deuterium species

(1) Wiberg, K. B.; Kass, S. R. *J. Am. Chem. Soc.*, preceding paper in this issue.

(2) LaLonde, R.; Forney, L. *J. Am. Chem. Soc.* **1963** *85*, 3767. LaLonde, R.; Ding, J.-Y. *J. Org. Chem.* **1972**, *16*, 2555.

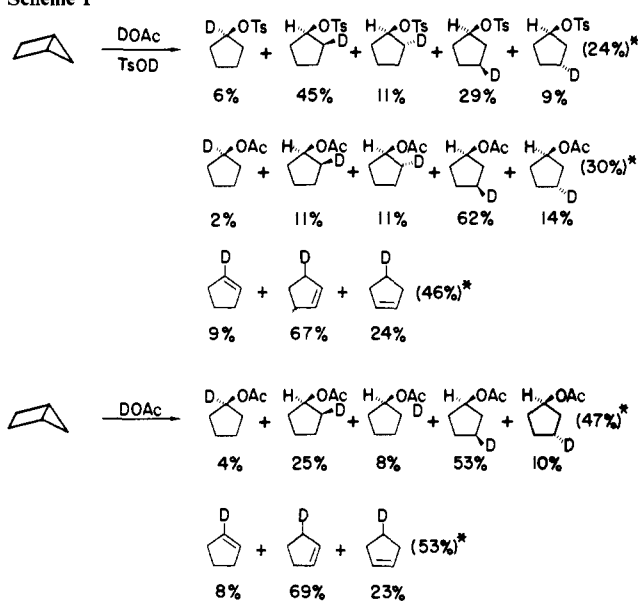(3) Wiberg, K. B.; Bishop, K. C., III; Davidson, R. B. *Tetrahedron Lett.* **1973**, 3169.

(4) Roberts, J. D.; Chambers, V. C. *J. Am. Chem. Soc.* **1951**, *73*, 5034.

Bicyclo[2.1.0]pentane and Bicyclo[3.1.0]hexane

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Table I. Rates of Acetolysis of Bicyclo[n.1.0]alkanes

compound	solvent	temp, °C	$k \times 10^5$, s^{-1}	ΔH^*, kcal/mol	ΔS^*, eu
		(a) No Acid Catalyst			
bicyclo[2.1.0]pentane	HOAc	116.27	20.6 ± 1.4	18.4 ± 1.8	−29 ± 4
		106.23	10.2 ± 0.4		
		85.89	2.52 ± 0.15		
	DOAc^a	116.21	0.93 ± 0.04		
bicyclo[3.1.0]hexane	HOAc	199.94	11.0 ± 0.4	17.2 ± 0.7	−41 ± 2
		155.94	1.53 ± 0.07		
	DOAc^b	199.94	8.30 ± 0.09		
1-methylbicyclopentane	DOAc^c	72.71	13.4 ± 0.5		
1,4-dimethylbicyclopentane	HOAc	104.70	2.93 ± 0.07	22.0 ± 1.1	−17 ± 3
		84.80	54.4 ± 1.2		
	DOAc^c	89.80	4.65 ± 0.14		
endo-5-methylbicyclopentane	DOAc^c	89.55	16.7 ± 0.4		
exo-5-methylbicyclopentane	DOAc^c	72.71	13.0 ± 0.4		
5,5-dimethylbicyclopentane	DOAc^c	70.00	22.8 ± 0.2		
		(b) Acid Catalyzed			
bicyclo[2.1.0]pentane	HOAc	32.00	24.5 ± 0.9	15.6 ± 0.7	−15 ± 3
		27.0	16.2 ± 0.8		
		17.0	6.19 ± 0.11		
	DOAc^d	32.00	9.33 ± 0.24		
bicyclo[3.1.0]hexane	HOAc	60.80	6.09 ± 0.15		

^{a}90% DOAc, 10% HOAc. ^{b}92% DOAc, 8% HOAc. ^{c}CD$_3$CO$_2$D. ^{d}95% DOAc, 5% HOAc.

Scheme I

*percent of total product

Scheme II

iodide, and a solution of the iodide in acetic acid was treated with bromine at 25 °C. A rapid reaction occurred, and cyclopentyl acetate was formed along with cyclopentyl bromide. Again, no hydrogen migration occurred. The reaction of cyclopentylamine with nitrous acid in acetic acid gave the same result. It must be concluded that hydrogen migration occurs before the formation of a cyclopentyl cation, if indeed the latter is involved in any way.
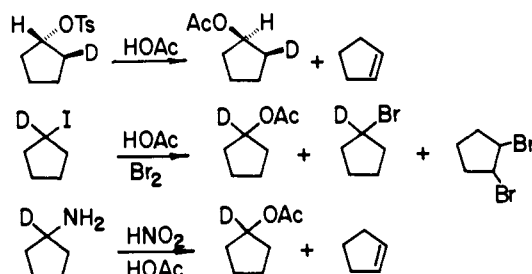
The predominent rearrangement found with the tosylate shows that it is formed in a process which is quite different than that leading to the acetate. The stereochemistry of addition of DOAc or TsOD is not sufficient to specify the nature of the reaction, and thus a deuterium-labeled bicyclopentane was prepared as shown in Scheme II. The deuterium was placed at the 5-position since one of these hydrogens must migrate to give the 2-labeled acetate or tosylate.

The reaction of the endo-5-labeled compound 3 with acetic acid in the presence of 1 equiv of toluenesulfonic acid was carried out in the same fashion as the previous case and gave the results shown in Scheme III. Migration of the exo-5 hydrogen would have led to cyclopentyl-*1-d* tosylate. Since it was not found, it is clear that the endo-5 proton is the one which undergoes migration. Similarly, an analysis of the stereochemistry of the cyclopentyl acetate formed indicates that the predominate reaction must be double inversion rather than double retention.

Cyclopentene is produced in the reaction of 3, but it contains only half of the original deuterium label. Loss of the endo-deuteron at C$_5$ would lead to cyclopentene-d_0 whereas loss of the exo-proton
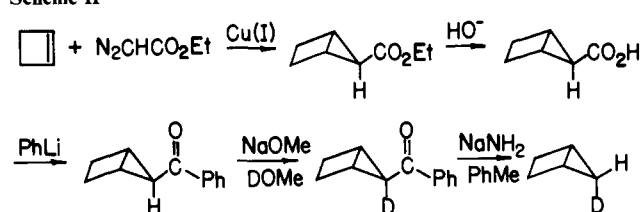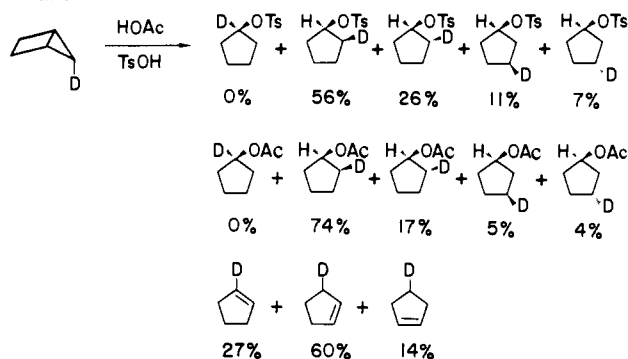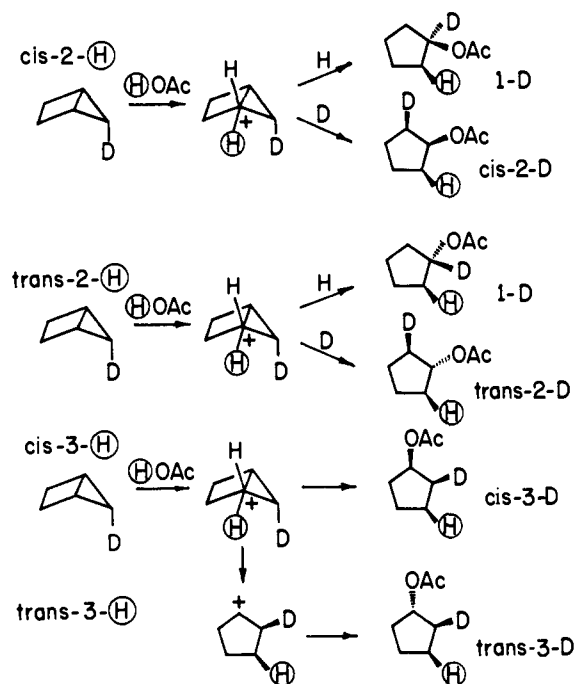
which must be derived via a hydrogen migration from the initially formed species. The deuterium distributions in the acetates and olefins formed in the presence and absence of TsOD are quite similar, although there is somewhat more hydrogen migration in the latter reaction in the case of the acetate products.

It is possible that the normal product is formed via a nucleophilic displacement on a protonated cyclopropane species and that the rearranged products are formed via an "open" cyclopentyl cation. In order to determine whether or not a cyclopentyl cation would give significant hydrogen migration before capture in acetic acid, the following experiments were performed. Cyclopentan-*trans*-2-*d*-ol was prepared by the reduction of cyclopentene oxide with lithium aluminum deuteride. Conversion to the tosylate and solvolysis in acetic acid led to cyclopentyl-*cis*-2-*d* acetate along with cyclopentene. Essentially complete inversion and no hydrogen migration was observed. It seemed likely that the process was an S$_N$2 displacement, and thus a better leaving group was examined. We have shown that the IBr$_2$ group is one of the best of the leaving groups.[5] Cyclopentan-*1-d*-ol was converted to the

(5) Wiberg, K. B.; Pratt, W. E.; Matturro, M. G. *J. Org. Chem.* **1982**, *47*, 2720.

Scheme III

Scheme IV

Table II. Correlation between Deuterium-Labeled Products Formed by Reaction of 1 with DOAc and of 3 with HOAc

1 + DOAc	3 + HOAc
1	cis-2, trans-2, cis-3, trans-3
cis-2	1, cis-2
cis-3	cis-2
trans-2	1, trans-2
trans-3	trans-2

would give cyclopentene-1-d_1. The observed ratio of these compounds (3.6:1) should be corrected for the kinetic isotope effect for the loss of the endo-deuteron, leading to a preference for endo-proton loss of 10:1 if k_H/k_D = 3 and of 20:1 if k_H/k_D = 6. The ionic species produced in the protonation of 3 is also capable of distinguishing between protons at C_3 and C_5. The ratio of the loss of a hydrogen from C_5 vs. C_3 is 5:1 or 10:1 depending on the choice of k_H/k_D. The selectivity in deuterium loss shows that the species forming cyclopentene cannot be a cyclopentyl cation. It would appear that the bridged species involved in the major tosylate product can react via a competing pathway which involves the loss of the endo-5 proton (deuteron) to produce cyclopentene.

The deuterium distribution in the products derived from the reaction of 1 with DOAc/TsOD can be related to the isomers arising from the reaction of 3 with HOAc/TsOH. Scheme IV illustrates the relationship for the acetates. Since 1-deuterio-cyclopentyl acetate and tosylate were not formed from the reaction of 3, the pathways leading to these products in Scheme IV may be ignored. As a result, the products of the reaction of 3 may

Table III. Deuterium Distribution in Cyclopentyl Acetate Produced from Reaction of 1 and 3

	1 + TsOD/DOAc	3 + TsOH/HOAc		
isomer	obsd	predicted[a]	predicted[b]	obsd
1	2%			
cis-2	11%	74%	79%	83%
cis-3	62%			
trans-2	11%	26%	21%	17%
trans-3	14%			

[a] Assuming that the 1 isomer from 1 would lead to equal amounts of cis-2 and trans-2 isomers from 3. [b] Calculated as before but assuming k_H/k_D = 3.

Table IV. Deuterium Distribution in Cyclopentyl Tosylate Produced from Reaction of 1 and 3

	1 + TsOD/DOAc	3 + TsOH/HOAc		
isomer	obsd	predicted[a]	predicted[b]	obsd
1	6%			
cis-2	45%	77%	75%	56%
cis-3	29%			11%
trans-2	11%	23%	25%	26%
trans-3	9%			7%

[a] Assuming that the 1 isomer from 1 would lead to equal amounts of cis-2 and trans-2 isomers from 3. [b] Calculated as before but assuming k_H/k_D = 3.

Table V. Energies of Protonated Bicyclo[2.1.0]pentanes

compound	energy (3-21G)	E_{rel}, kcal/mol
	−192.839 81	
	−192.901 80	
	−193.203 16	5.5
	−193.151 76	32.2
	−193.211 88	0.0

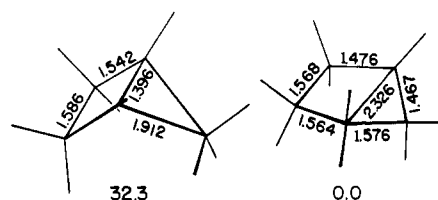**Figure 1.** 3-21G optimized structures for protonated bicyclopentanes. The relative energies are given in kilocalories/mole.

be quantitatively related to those of 1 (Table II). The result for the acetates is shown in Table III, and it can be seen that there is a quantitative agreement. The data for the tosylates is shown in Table IV and can be seen to be qualitatively correct. A protonated bicyclo[2.1.0]pentane ion intermediate in the acetolysis of 1 is consistent with the solvolytic and stereochemical data presented above. The cyclopentyl cation, on the other hand, appears to play a limited role in these reactions. In order to further investigate the nature of the intermediate, ab initio calculations were carried out for bicyclo[2.1.0]pentane protonated at C_1 or at C_5 and for the cyclopentyl cation. The 3-21G basis set was used, and complete geometry optimizations were performed. The energies are given in Table V, and the geometries are summarized in Figure 1. In agreement with the observation on the direction of ring cleavage, the C_1-protonated species has a lower energy than that protonated at C_5 and accounts for cleavage of the central bond.

Scheme V

Scheme VI
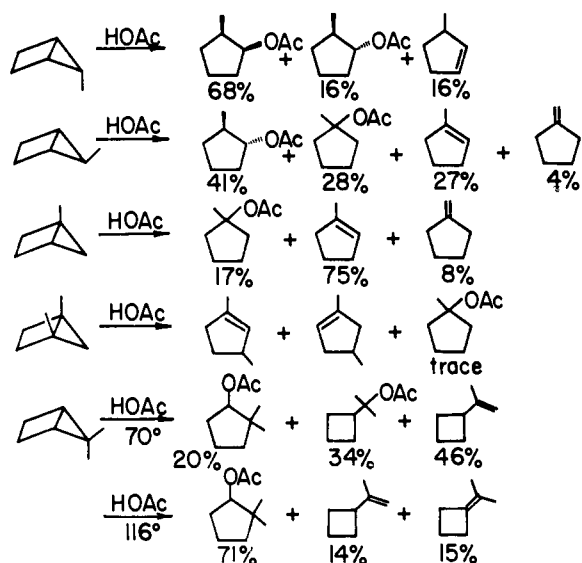
The difference in energy may be due either to destabilization for protonation at C_5 or stabilization for reaction at C_1. The energies of the hypothetical proton transfers from cyclopentyl cation to cyclopropane and to **1** are shown below.[6] It can be seen

$$\Delta E = 3.7 \text{ kcal/mol}$$

$$\Delta E = -1.2 \text{ kcal/mol}$$

$$\Delta E = -33.4 \text{ kcal/mol}$$
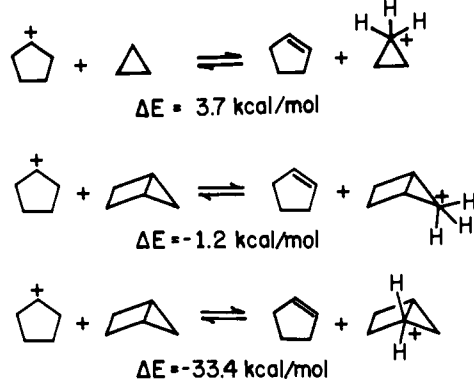
that the energy for reaction at C_5 is almost thermoneutral, whereas reaction at C_1 is unusually exothermic. This arises from strain energy relief in stretching the central bond. The calculated structure of the ion formed is close to that of the cyclopentyl cation and probably would have gone to that ion if the very slowly converging geometry optimization had been continued further. However, in the reaction in acetic acid, the ion must be intercepted by solvent before it reaches the cyclopentyl cation in order to account for the stereochemistry of deuterium introduction and the specificity of deuterium migration and loss.

Substituent effects were helpful in studying the acetolysis of monocyclic cyclopropanes, and they have been examined in this case also (Table I, Scheme V). A 1-methyl substituent leads to only a 15-fold increase in rate, but a second methyl substituent at the bridgehead almost cancels the effect of the first. A 5-methyl substituent also gives a small rate acceleration. In these cases, central bond cleavage is still the only reaction observed. These observations are in accord with the formation of a bridged ion and an early transition state since the stability of the ion does not greatly affect the rate. The rate retardation by the second methyl group in the 1,4-dimethyl compound is probably a steric effect

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(6) It is recognized that the inclusion of polarization functions and electron correlation often leads to significant changes in energy. When the 3-21G basis set was used, the energy change in the reaction of the isopropyl cation with cyclopropane to give propene and corner-protonated cyclopropane was calculated[1] to be −1.2 kcal/mol, whereas using MP3/631G* it was calculated to be +1.9 kcal/mol, as compared to the observed value of 1.0 kcal/mol. Thus, at least in this case, the energies calculated by using the two basis sets are close and agree with the observed value. The present reaction is similar to the above.
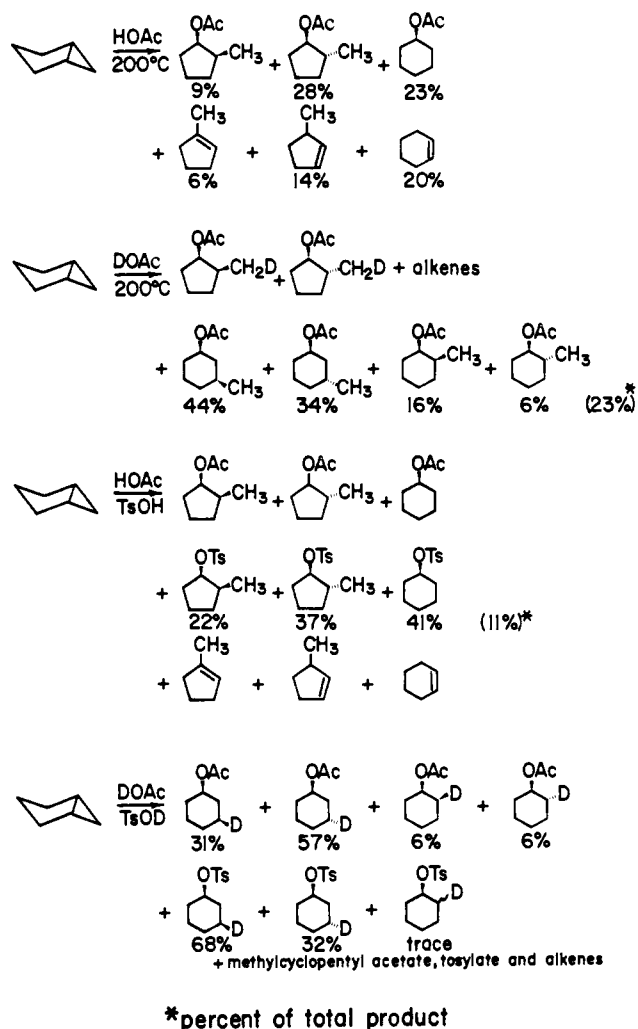
retarding the transfer of a proton from a bulky donor to this crowded center.

5,5-Dimethylbicyclo[2.1.0]pentane reacted 80 times faster than **1**, and here there was a dramatic change in products. Both cyclopentyl and cyclobutyl products were formed. It was possible that all of the products were formed by cleavage of the C_1-C_5 bond, and the cyclopentyl derivatives were formed via a subsequent rearrangement. This was examined by carrying out the reaction in DOAc and determining the deuterium distribution. Direct cleavage would place the deuterium at the 3-position in the cyclopentyl acetate, whereas formation via the cyclobutyl ion would place deuterium equally at C_3 and C_5:
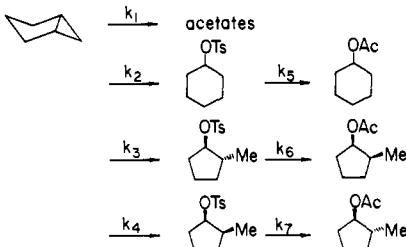
percent of total product
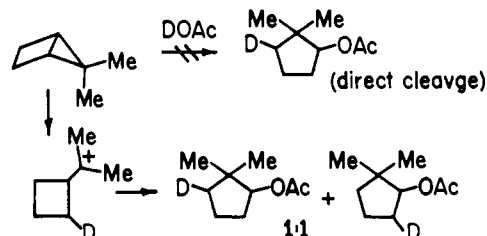
The latter distribution was found. Further evidence for this mode of reaction was obtained by carrying out the solvolysis at a lower temperature, which led to isolation of cyclobutyldimethylcarbinyl acetate. Thus, the formation of a particularly good carbocation takes precedence over ring cleavage, despite the potential strain energy relief, again showing that the process has not proceeded far toward open cations at the activated complex.

In order to be able to compare the rate of acetolysis of **1** with that of other bridged cyclopropanes, the rate of acetolysis of

Table VI. Rate Constants in Acid-Promoted Acetolysis of Bicyclo[3.1.0]hexane

$k_1 = 5.00 \times 10^{-3}$ L mol^{-1} s^{-1}
$k_2 = (4.12 \pm 0.42) \times 10^{-4}$ L mol^{-1} s^{-1}
$k_3 = (4.20 \pm 0.40) \times 10^{-4}$ L mol^{-1} s^{-1}
$k_4 = (2.49 \pm 0.24) \times 10^{-4}$ L mol^{-1} s^{-1}
$k_5 = 7.20 \times 10^{-6}$ s^{-1}
$k_6 = 1.10 \times 10^{-4}$ s^{-1}
$k_7 = 1.00 \times 10^{-4}$ s^{-1}
$k_{obsd} = (6.09 \pm 0.15) \times 10^{-3}$ L mol^{-1} s^{-1}
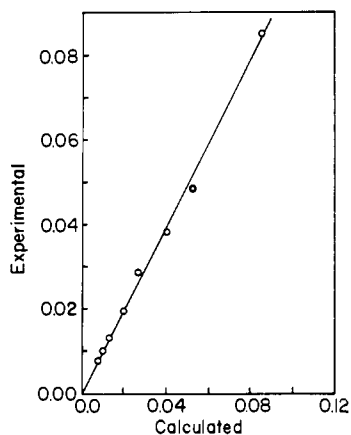
Figure 2. Experimental vs. calculated concentrations of bicyclo[3.1.0]-hexane for the reaction with 1 equiv of *p*-toluenesulfonic acid in acetic acid. Each point corresponds to a different time of reaction.

bicyclo[3.1.0]hexane (**2**) was determined at 60.8 °C using a stoichiometric concentration of TsOH. The products of the reaction are shown in Scheme VI, and unfortunately the two methylcyclopentyl tosylates were found to be reactive under the experimental conditions. The disappearance of **2** was followed by gas chromatography. The amount of TsOH after 1 and after 7.5 half-lives was determined by titration, and the amounts of the three tosylates were determined at these times by isolation and analysis by ^{13}C NMR spectroscopy. The course of the reaction was simulated via Runge–Kutta[7] integration of the kinetic expressions, making use of the known rate of solvolysis of cyclohexyl tosylate and adjusting the other rate constants to fit all the data. The rate constants are given in Table VI and are shown to be satisfactory by a plot of the experimental concentrations of 2 against the calculated concentrations (Figure 2). The rate constant thus obtained is in very good agreement with that found using a catalytic amount of TsOH.[8] The rate of reaction also was determined in the absence of toluenesulfonic acid (Table I). Here, the ratio of rates of reaction for **1:2** is 88, whereas for the reaction in the presence of TsOH it was 41.

The rate ratios correspond to a 3 kcal/mol difference in enthalpy of activation, whereas the difference in strain energy relief on going to the open cations (cyclopentyl and 2-methylcyclopentyl) is 22 kcal/mol.[9] Again, it is seen that only a very small fraction of

the potential strain relief is found in the relative reactivities.

The deuterium distribution in the products of reaction of **2** with acetic-*d* acid was determined and is shown in Scheme VI. It can be seen that cleavage of one of the external bonds is somewhat preferred over cleavage of the central bond, although the latter is favored energetically. An open 2-methylcyclopentyl cation cannot be involved since it would quickly rearrange to the 1-methylcyclopentyl cation, and none of the corresponding acetate was formed.

In the absence of TsOH, *cis*-3-deuteriocyclohexyl acetate is slightly favored over the trans isomer, and 20% of the acetate is rearranged (deuterium in the 2-position). In the presence of TsOH, essentially no deuterium shift is found in the cyclohexyl tosylate product. The cyclohexyl acetate formed under these conditions is predominently the cis-3 isomer, and the amount of deuterium shift is decreased to 12%. These distributions are rather different than those found in the reaction of **1**, but the details of the process cannot be specified at this time.

The solvent isotope effect for **2** in acetic-*d* acid was measured in order to ascertain whether or not protonation was involved in the rate-determining step for this compound. The data are given in Table I and lead to $k_H/k_D = 1.36$ after correcting for the HOAc present in the solvent. Therefore, protonation is partially rate determining. As was found for cyclopropane,[10] when the reaction was carried out for one half-life and **2** was recovered, a small amount of deuterium incorporation (2–3%) was detected by mass spectrometry. The location of the deuterium was determined by ^{2}H NMR spectroscopy, and equal amounts were found in the exo- and endo-6 positions.
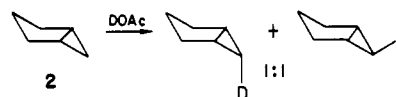
Protonated bicyclo[3.1.0]hexane has previously been postulated as an intermediate by Cacace et al.[11] and by Saunders et al.[12] It must be involved in the acetolysis of **2** since some deuterium incorporation is found. The location of the deuterium is consistent with the observed preference for Markovnikov addition. The equal distribution between the exo and endo positions at C_6 is necessary but not sufficient to demonstrate that the intermediate is a rapidly rotating protonated cyclopropane. However, Hariharan et al.[13] have suggested on the basis of calculations that protonated cyclopropane should have a low barrier to rotation, and present results are consistent with this conclusion.

Conclusions. The acetolysis of bicyclo[2.1.0]pentane proceeds mainly via inversion of configuration at both ends of the central bond which is cleaved. In the reaction of **1** with TsOD in DOAc, stereospecific endo-5 hydrogen migration occurs leading to 2-deuteriocyclopentyl tosylate. In addition, cyclopentene is formed with stereoselective loss of the *endo*-5 proton. These observations clearly show that the products are not formed from an open cyclopentyl cation.

5,5-Dimethylbicyclo[2.1.0]pentane reacts via cleavage of one of the outside C–C bonds, leading to cyclobutyldimethylcarbinyl products, rather than via cleavage of the central bond. This shows that potential carbocation stabilization is more important than ring strain relief in determining the products of the reaction. Bicyclo[3.1.0]hexane is only 40–80 times less reactive than bi-

(7) Southworth, R. W.; Deleeuw, S. L. "Digital Computation and Numerical Values"; McGraw-Hill: New York, 1965; p 455.

(8) The rate constant obtained using 0.005 M TsOH was 9.8×10^{-6} s^{-1} at 60.0 °C. Wiberg, K. B.; Kass, S. R.; de Meijere, A.; Bishop, K. C., III. *J. Am. Chem. Soc.*, following paper in this issue. This corresponds to a second-order rate constant of 4.9×10^{-3} L mol^{-1} s^{-1}.

(9) The strain energies of the product cyclopentyl cations are essentially the same. Therefore the difference in strain relief is the difference in strain energy between bicyclo[2.1.0]pentane (55 kcal/mol) and bicyclo[3.1.0]hexane (32 kcal/mol). Cf.: Wiberg, K. B. In "Determination of Organic Structure by Physical Methods"; Nachod, F. C., Zuckerman, J. J., Eds.; Academic Press: New York, 1971; Vol. 3, p 238.

(10) Cf. ref 1 for the reaction in acetic acid, and for the reaction with aqueous sulfuric acid, see: Baird, R. L.; Aboderin, A. A. *J. Am. Chem. Soc.* **1964**, *86*, 252, 2300.

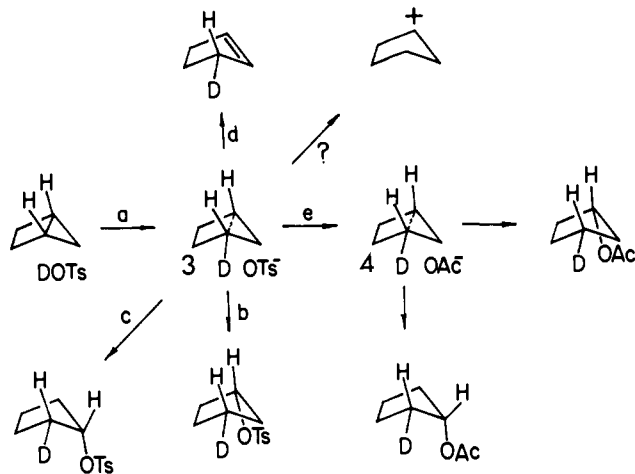(11) Cacace, F.; Guarino, A.; Speranza, M. *J. Chem. Soc., Perkin Trans. 2* **1973**, 66.

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Bicyclo[2.1.0]pentane and Bicyclo[3.1.0]hexane

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Scheme VII

cyclo[2.1.0]pentane despite the large difference in potential strain relief, again showing that the activated complex has a structure resembling the reactant. Further, the product is 2-methylcyclopentyl acetate, whereas an open cation would lead to 1-methylcyclopentyl acetate.

The data indicate that proton transfer is rate determining and that the developing cation is captured by the solvent well before it relaxes to an energetically more favorable open cation. A reasonable interpretation of these data for bicyclo[2.1.0]pentane is shown in Scheme VII. The initial reaction with TsOD (a) probably leads to the ion pair **3**, which can collapse (b) to form the *cis*-3-deuterio tosylate, undergo an endo-5 hydrogen shift followed by collapse (c) to give the *cis*-2-deuterio tosylate, lose the endo-5 proton (d) to give cyclopentene, or undergo ion-pair exchange (e) to give the acetate ion pair **4**. This, in turn, may undergo a similar set of reactions. The trans-2 and 3-deuterio acetates and tosylates may be formed in any of several ways. It is possible that the initial intimate ion pair may dissociate to a solvent separated cyclopentyl ion pair which could react with the nucleophile in a nonstereospecific fashion. However, there appears to be no evidence for open carbocations as intermediates in any of these reactions. In view of the lack of stereospecificity for the attacking proton found in other cases,[1] it seems more likely that a part of the reaction proceeds via attack of the proton with retention of configuration, followed by attack of the nucleophile with inversion.

Experimental Section

Materials. Bicyclo[2.1.0]pentane was prepared by the published procedure.[14] *endo*-5-Bicyclo[2.1.0]pentane-5-*d* was prepared in the following fashion. Bis[copper(I)trifluoromethanesulfonate]benzene complex (3 g) was added to 12.4 g (0.23 mol) of cyclobutene in 80 mL of cyclohexane under nitrogen in a flask with a dry ice/acetone condenser. The solution was cooled to 0 °C, and 11 g (0.11 mol) of ethyl diazoacetate was added dropwise to the stirred solution over 2 h. It was allowed to warm to room temperature where it was kept for 6 h. The solution was extracted with a pH 9 aqueous ammonium chloride/ammonium hydroxide solution. The organic layer was dried and concentrated to give 9.9 g (64%) of a 4:1 ratio of *exo-* to *endo*-5-carboethoxybicyclo[2.1.0]pentane. The ester was hydrolyzed with 4.2 g of sodium hydroxide in 85% aqueous ethanol by heating to reflux overnight. Extraction with pentane was followed by acidification with hydrochloric acid to pH 2. Filtration gave 2.6 g of *exo*-bicyclo[2.1.0]pentane-5-carboxylic acid, mp 43–45 °C: ^{1}H NMR spectrum (CDCl$_3$, 270 MHz) δ 2.26 (d, 7.9 H$_2$, 2 H); ^{13}C NMR (CDCl$_3$, 22.6 MHz) 180.0, 30.3, 26.6, and 23.2 ppm.

A solution of 2.9 g (20 mmol) of *exo*-bicyclo[2.1.0]pentane-5-carboxylic acid in 20 mL of dry ether was treated with 65 mL of 1.2 N phenyllithium in ether at room temperature. After 20 min, the reaction mixture was poured with rapid stirring into 125 mL of 3 N aqueous ammonium chloride. The organic layer was dried and concentrated. The residual oil was heated in a Kugelrohr at 70 °C (1 torr) to remove most

of the bromobenzene and biphenyl. The ketone was purified by using a flash-grade silica gel column and was eluted with 99.5% hexane/0.5% tetrahydrofuran, giving 2.6 g (58%) of *exo*-5-benzoylbicyclo[2.1.0]pentane: ^{1}H NMR (CDCl$_3$, 270 MHz) δ 1.67 (d, J = 7.3 Hz, 2 H), 2.29 (s, 2 H), 2.34 (d, J = 7.3 Hz, 2 H), 2.83 (s, 1 H), 7.48 (t, J = 7.7 Hz, 2 H), 7.57 (t, J = 7.2 Hz, 1 H), 8.04 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (CDCl$_3$, 22.5 MHz) 199.0, 137.9, 132.4, 128.3, 127.8, 35.7, 30.0, 23.9 ppm. Anal. C, H.

Sodium (0.35 g) was dissolved in 15 mL of methanol-*d* under nitrogen, and 2.0 g of the above ketone was then added, and the solution was heated to reflux for 30 min. After the solution was cooled to room temperature, 15 mL of 3 N hydrochloric acid was added. The solution was extracted with three 25-mL portions of ether. The ether solution was dried and concentrated, giving 1.4 g of deuterium-labeled ketone containing 56% D.

An oven-dried 250-mL flask was equipped with a stirrer, nitrogen inlet, and a spiral condenser attached to a trap cooled to −78 °C. To the flask were added 2.3 g of the deuterium-labeled ketone, 100 mL of dry toluene, and 4 g of sodium amide (Fisher). The solution was vigorously stirred and heated to reflux for 3 h. The trap contained ammonia and a solution of bicyclo[2.1.0]pentane in toluene. The ammonia evaporated on warming to room temperature, and bicyclo[2.1.0]pentane-*endo*-5-*d*, was isolated by gas chromatography using a $^1/_4$-in. 20% SE-30 column at 25 °C: ^{1}H NMR (CDCl$_3$, 270 MHz) δ 0.52 (d, 0.44 H), 0.69 (m, 1 H), 1.36 (d, 2 H), 1.49 (m, 2 H), 2.11 (d, 2 H); ^{1}H NMR 0.53.

Methyl-substituted bicyclopentanes were obtained as follows. A mixture of methylcyclopentadienes was prepared by methylation of cyclopentadiene.[15] To an ethereal solution of the dienes was added dimethyl azodicarboxylate dropwise until the orange color of the azo compound persisted. The product was converted to a mixture of methylbicyclopentanes by using the procedure of Baldwin.[16] They were separated by gas chromatography using a 10 ft × $^1/_4$ in 25% β,β'-oxydipropionitrile column at 30 °C and a flow rate of 30 mL/min. The retention times were 4.2 min for the 1-methyl isomer, 5.5 and 7.3 min for the 2-methyl isomers, and 6.5 min for *exo*-5-methyl- and 9.3 min for *endo*-5-methylbicyclopentane.

1,4-Dimethylbicyclo[2.1.0]pentane was prepared by the addition of methylene to 1,2-dimethylcyclobutene.[17] To a 50% solution of the cyclobutene in ether was added 0.3 g of bis[copper(I)trifluoromethanesulfonate]benzene, giving a homogeneous solution. A stream of diazomethane in argon formed from *N,N*-nitrosomethylurea and potassium hydroxide solution was passed through the solution. After 15 g of NMU had been used, 300 mg of fresh catalyst was added. This was repeated until a total of 45 g of NMU and 900 mg of catalyst had been added. The reaction mixture was shown by ^{1}H NMR to consist of 37% product and 63% starting alkene. The product was separated by GC using a 12-ft × $^1/_4$-in. silver nitrate in ethylene glycol on 60–80 Chrom P AW column at 30 °C: ^{1}H NMR (270 MHz, CDCl$_3$) δ 1.79 (d, J = 6.2 Hz, 2 H), 1.44 (d, J = 2 Hz, 2 H), 1.15 (s, 6 H), 0.64 (d, J = 3.6 Hz, 2 H), 0.17 (m, 1 H).

5,5-Dimethylbicyclo[2.1.0]pentane was prepared from 5,5-dimethylcyclopentadiene.[18] To a solution of 5.4 g (0.037 M) of dimethylazodicarboxylate in 30 mL of dry ether was added 3.4 g (0.036 M) of the diene. After heating to reflux for 48 h, ether was removed under reduced pressure to give 6.4 g (74%) of an orange oil. The product was converted to 5,5-dimethylbicyclo[2.1.0]pentane in the same fashion as has been used for the preparation of bicyclo[2.1.0]pentane:[8] ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.01 (d, J = 8.1 Hz, 2 H), 1.37 (d, J = 7.7 Hz, 2 H), 1.28 (bns, 2 H), 1.17 (s, 3 H), 0.90 (s, 3 H); ^{13}C NMR (CDCl$_3$) 26.0 (d, J = 174 Hz), 24.2 (g, J = 188 Hz), 19.6 (s) 19.1 (t, J = 135 Hz), 12.6 (g, J = 186 Hz); Mass spectrum calcd for C$_7$H$_{12}$ 96.0939; found 96.0935.

Bicyclo[3.1.0]hexane was prepared by using the published procedure.[19]

Kinetic Studies (a) Bicyclo[2.1.0]pentane. In the reaction with TsOH/HOAc, 30–40 mg of **1** was placed in a 5-mL volumetric flask which was filled to the mark with dry acetic acid. In another 5-mL flask was placed an equivalent of *p*-toluenesulfonic acid monohydrate (80–100 mg) and 10–30 mg of octane (internal standard), and it was filled to the mark with acetic acid. The two solutions were allowed to equilibrate in a thermostat and then mixed at zero time in a 10-mL volumetric flask. Ten 0.5-mL aliquots were withdrawn at appropriate time intervals and placed in capped vials containing 0.2 mL of NaOAc in HOAc to quench the acid. The samples were analyzed as quickly as possible via GC using a 10-ft silver nitrate in ethylene glycol on firebrick column at 40 °C. The

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retention times were 2.3 min for **1**, 4.7 min for octane, and 24 min for cyclopentene. The response ratio for **1** and octane was determined independently. After six to eight half-lives, some of the remaining solution was titrated with standard NaOAc in HOAc to determine the amount of TsOH which remained.

For the uncatalyzed reaction, 0.1249 g of **1** and 0.1354 g of octane were placed in a 25-mL volumetric flask which was filled with acetic acid. Eighty test tubes were filled with 0.3-mL portions of the solution and, while protected from moisture, were frozen in dry ice/acetone and sealed. Eight to ten of the tubes were used for each rate measurement. The samples were placed in a thermostat and allowed to equilibrate for a few minutes. The first tube was removed and the timer was started. The remaining tubes were removed at regular intervals. Analysis was performed by GC as described above.

(b) Methylbicyclo[2.1.0]pentanes. *endo*-5-Methylbicyclo[2.1.0]pentane, *exo*-5-methylbicyclo[2.1.0]pentane, and 1-methylbicyclo[2.1.0]-pentane were separately sealed under reduced pressure in NMR tubes containing acetic-d_4 acid and a small amount of benzene as an internal standard. The NMR spectra were obtained, and the tubes were then heated at the appropriate temperature for a measured time. After removal from the thermostat, the tubes were cooled and again analyzed by NMR. The analysis for the 5-endo isomer made use of the methylene doublet, that for the 5-exo isomer made use of the bridgehead or upfield ethanyl bridge protons, and that for the 1-methyl isomer made use of the cyclopropyl methylene protons.

(c) 1,4-Dimethylbicyclo[2.1.0]pentane. A mixture of 30 mg of 1,4-dimethylbicyclopentane and 15 mg of 2-methylpentane was diluted to 10 mL with acetic acid. The rate of reaction was determined as described above for bicyclopentane. The tosylate ratios were determined at two different times by ^{13}C NMR.

(d) 5,5-Dimethylbicyclo[2.1.0]pentane. A mixture of 5,5-dimethylbicyclohexane and bicyclopentane was dissolved in acetic-d_4 acid and sealed into a set of NMR tubes. The rate of reaction was determined as described above for the methylbicyclopentanes using bicyclopentane as the internal standard.

(e) Bicyclo[3.1.0]hexane. A mixture of 349.8 mg (4.258 mmol) of bicyclohexane and 125.01 mg of octane was diluted to 25 mL with acetic acid. A solution of 810.4 mg (4.259 mmol) of *p*-toluenesulfonic acid monohydrate in 25 mL also was prepared. Equal volumes of the two solutions were mixed and sealed into test tubes. A set of 10 tubes was placed in a thermostat and allowed to come to thermal equilibrium. The rate constant was determined as described above for bicyclopentane.

For the uncatalyzed reaction, 136.1 mg of bicyclohexane and 83.9 mg of octane were placed in a 25-mL flask and made up to volume with acetic acid. Small portions (0.3 mL) of the solution were sealed into test tubes. The rate of reaction was determined as described for bicyclopentane.

Product Studies. (a) Bicyclo[2.1.0]pentane. The products of the acetolysis reaction were determine by diluting the solution with water and extracting with carbon tetrachloride. The more volatile products were isolated by passing nitrogen through the solution for 15 min and collecting the material in a dry ice/acetone trap. The ^{1}H NMR spectrum showed that the only volatile product was cyclopentene. The remaining cyclopentene and carbon tetrachloride were removed under reduced pressure, and the residue was transferred by bulb-to-bulb distillation at 0.2 torr. The material was found to be cyclopentyl acetate. In the reaction with TsOH, a residue was found which was shown to be cyclopentyl tosylate.

The reaction with acetic-*d* acid was carried out by mixing 1 g of bicyclopentane with 2.84 g of TsOD·D$_2$O in 280 mL of acetic-*d* acid

(95%). After 20 min in 32 °C, the solution was quenched with 70 mL of 0.21 M sodium acetate in acetic acid. The unreacted bicyclopentane along with cyclopentene was isolated by bubbling nitrogen through the solution and collecting the material in a dry ice/acetone trap. Cyclopentyl acetate and cyclopentyl tosylate were isolated as described above. The deuterium distribution in cyclopentyl acetate was determined by ^{2}H NMR spectroscopy using Eu(fod)$_3$ as a shift reagent. The order of protons from most downfield to farthest upfield was found to be 1, acetate methyl, 2-cis, 2-trans, 3-cis, and 3-trans by examination of specifically labeled cyclopentyl acetates. Cyclopentyl tosylate was cleaved with the naphthalene radical anion[10] to give cyclopentanol. The relative positions of the cyclopentanol protons in the presence of Eu(fod)$_3$ have been reported[21] and were verified.

The uncatalyzed reaction was studied in essentially the same fashion. The 5-*endo*-deuteriobicyclopentane was studied in the same way.

(b) Methylbicyclo[2.1.0]pentanes. One of the NMR tubes described above for the endo-5 isomer was heated for 120 min at 90 °C and then analyzed by NMR. The structures of the compounds were determined by comparison with authentic samples. The products were 68% *cis*-2-methylcyclopentyl acetate, 16% 3-methylcyclopentene, and 16% *trans*-2-methylcyclopentyl acetate. In the case of *exo*-5-methylbicyclopentane, one of the NMR tubes was heated for 160 min at 73 °C and analyzed by NMR. The products were 27% 1-methylcyclopentene, 41% *trans*-2-methylcyclopentyl acetate, 28% 1-methylcyclopentyl acetate, and 4% methylenecyclopentane. An NMR tube containing 1-methylbicyclo-pentane was heated for 140 min at 73 °C and analyzed by NMR. The products were 68% 1-methylcyclopentene, 15% 1-methylcyclopentyl acetate, and 17% methylenecyclopentane.

(c) 1,4-Dimethylbicyclo[2.1.0]pentane. A sample of the dimethylbi-cyclopentane in acetic-d_4 acid was heated for 258 min at 90 °C. Analysis by NMR showed that the major products were 1,3- and 1,4-dimethyl-cyclopentene, along with a trace of 1,3-dimethylcyclopentyl acetate.

(d) 5,5-Dimethylbicyclo[2.1.0]pentane. Approximately 50 mg of the dimethylbicyclopentane was dissolved in 3 mL of acetic acid and sealed in a test tube. It was heated for 397 min at 116 °C, cooled, diluted with water, and extracted with chloroform-*d*. Both ^{1}H and ^{13}C NMR showed that the products were 71% 2,2-dimethylcyclopentyl acetate, 14% 2-cyclobutylpropene, and 15% isopropylidenecyclobutane. When a similar solution was heated at 70 °C for 90 min, the products were 20% 2,2-dimethylcyclopentyl acetate, 46% 2-cyclobutylpropene, and 34% 2-cyclobutyl-2-propyl acetate. The products were assigned on the basis of authentic independently prepared materials.

(e) Bicyclo[3.1.0]hexane. The products of the reaction both in the presence and absence of TsOH were determined essentially as described for bicyclo[2.1.0]pentane.

Calculations. Ab initio calculations and geometry optimizations were carried out by using the program GAMESS.[22]

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