Solvolysis of Bicyclo[2.1.1]hexyl-5 and Bicyclo[1.1.1]pentyl-2 Derivatives[1]

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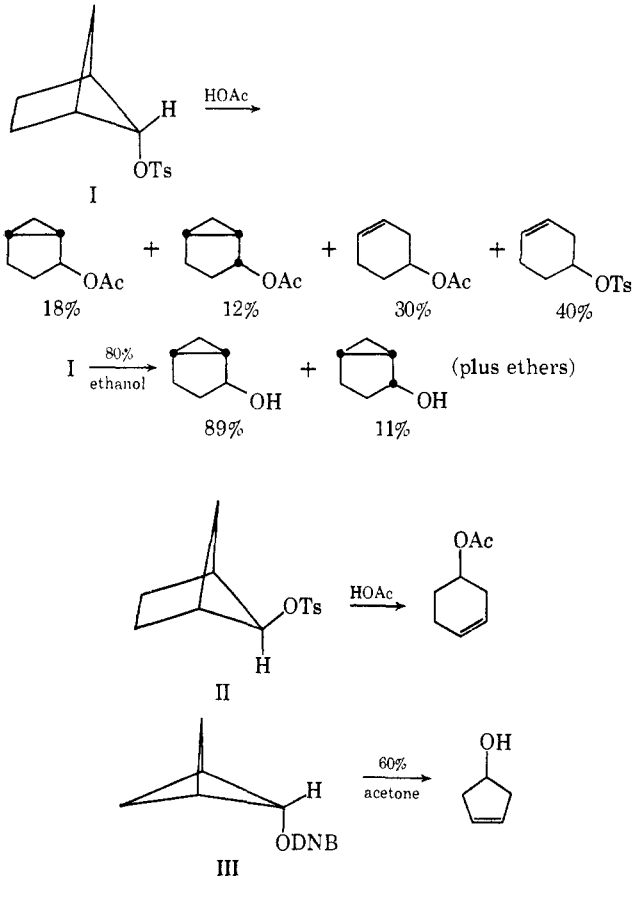
Abstract: The solvolyses of the bicyclo[1.1.1]pentyl-2 and bicyclo[2.1.1]hexyl-5 derivatives are compared with those of the bicyclo[3.1.1]heptyl-6 derivatives. The *endo* compounds are 10^3 more reactive than cyclobutyl itself. No evidence was found for an intermediate cyclobutyl cation, and it is concluded that the reactions involve concerted rearrangements to more stable cations. The *exo* compounds are 10^3–10^5 less reactive than cyclobutyl. This probably results from the axial location of the substituent which makes impractical participation by a cyclobutyl C–C bond.

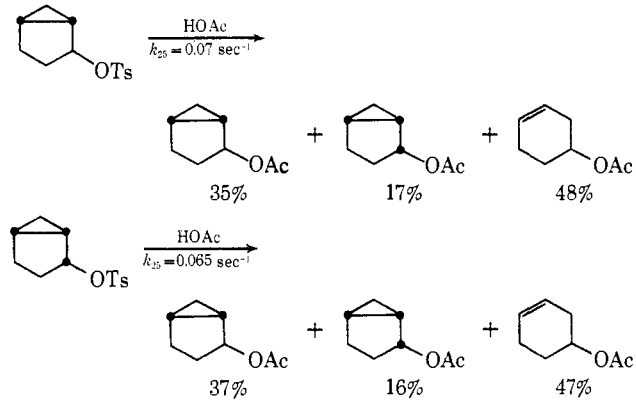
The bicyclo[*n*.1.1]alkyl derivatives provide a convenient way in which to fix the geometry of a cyclobutyl ring so that substituents will occupy either an *axial* or an *equatorial* position. We have previously indicated that a marked difference in reactivity is found in comparing the two epimeric tosylates.[3,4] We now wish to present the data in more detail and to include a bicyclo[1.1.1]pentyl-2 derivative in the series. The preparation of the reactants has been described.[4–6]

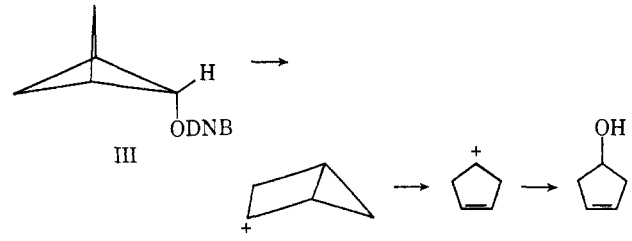
The rates of solvolysis are summarized in Table I, and the products are given below. The products of the solvolysis of the bicyclo[3.1.1]heptyl-6 derivatives have previously been reported in detail.[4]

It is interesting to compare the product distribution obtained with I in acetic acid with that found by Winstein and Friedrich[7] for the *cis*- and *trans*-bicyclo[3.1.0]-hexyl 2-tosylates. Here, no internal return product (cyclohexenyl tosylate) was found. Thus, the bicyclo-[3.1.0]hexyl 2-tosylates are not intermediates in the formation of cyclohexenyl tosylate, and it is unlikely that this internal return product is formed from the bicyclo-[3.1.0]hexyl-2 cation.

The product derived from bicyclo[1.1.1]pentyl 2-dinitrobenzoate is that which has been observed starting with bicyclo[2.1.0]pentyl-2 derivatives. Thus, the cation derived from the latter may be an intermediate in the reaction.







(1) This investigation was supported by the U. S. Army Research Office, Durham.

(2) (a) Taken in part from the Ph.D. Thesis of R. A. F., 1967. (b) Proctor and Gamble Fellow, 1966–1967; Heyl Fellow, 1967–1968. (c) National Science Foundation Predoctoral Fellow, 1965–1968.

(3) K. B. Wiberg and R. A. Fenoglio, *Tetrahedron Lett.*, 1273 (1963).

(4) K. B. Wiberg and B. A. Hess, Jr., *J. Am. Chem. Soc.*, **89**, 3015 (1967).

(5) K. B. Wiberg, B. R. Lowry, and T. H. Colby, *ibid.*, **83**, 3998 (1961).

(6) K. B. Wiberg and V. Z. Williams, Jr., *J. Org. Chem.*, **35**, 369 (1970).

(7) S. Winstein and E. Friedrich, private communication.

Table I. Rates of Solvolysis of Bicyclo[2.1.1]hexyl and Bicyclo[1.1.1]pentyl Derivatives

Compound	Solvent	T, °C	k, sec^{-1}	$\Delta H^{\ddagger}$ kcal/mole	$\Delta S^{\ddagger}$ eu
endo-Bicyclo[2.1.1]hexyl 5-tosylate (I)	HOAc	16.9	$1.10 \pm 0.01 \times 10^{-3}$	18.4	−8.5
		32.0	$5.60 \pm 0.05 \times 10^{-3}$		
		25.0	2.64×10^{-3} [a]		
	80% EtOH	25.0	$3.48 \pm 0.14 \times 10^{-2}$		
	95% EtOH	25.0	$1.29 \pm 0.02 \times 10^{-2}$		
	97.7% EtOH	25.0	9.96×10^{-3} [a]		
exo-Bicyclo[2.1.1]hexyl 5-tosylate (II)	HOAc	164.4	$5.88 \pm 0.14 \times 10^{-4}$	30.8	−2.7
		190.0	$4.52 \pm 0.09 \times 10^{-3}$		
		25.0	2.24×10^{-11} [a]		
endo-Bicyclo[2.1.1]hexyl 5-(3,5-dinitrobenzoate) (Ia)	60% acetone	110.0	1.72×10^{-5}	29.8	−3.0
		130.0	1.26×10^{-4}		
		100.0	5.75×10^{-6} [a]		
Bicyclo[1.1.1]pentyl 2-(3,5-dinitrobenzoate) (III)	60% acetone	110.0	3.22×10^{-6}	32.1	−0.3
		120.0	9.70×10^{-6}		
		130.0	2.75×10^{-5}		
		100.0	1.00×10^{-6} [a]		

[a] Extrapolated rates.

Table II. Rates of Solvolysis of Cyclobutane Derivatives

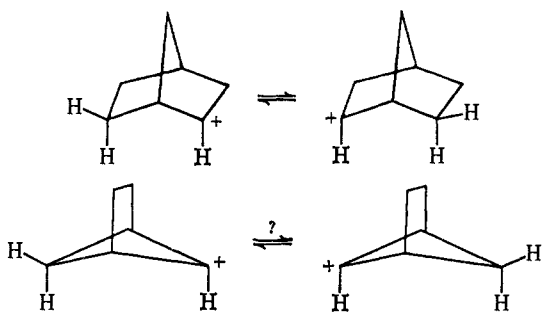
Compound	T, °C	k, sec^{-1}	k_{rel}	Ref
endo-Bicyclo[3.1.1]heptyl 6-tosylate	25	4.40×10^{-3}	1.00	4
endo-Bicyclo[2.1.1]hexyl 5-tosylate (I)	25	2.64×10^{-3}	0.60	
endo-Bicyclo[2.1.1]hexyl 5-(3,5-dinitrobenzoate)	100	5.75×10^{-6}	(0.6)	
Bicyclo[1.1.1]pentyl 2-(3,5-dinitrobenzoate) (III)	100	1.00×10^{-6}	0.1	
Cyclobutyl tosylate	25	3.00×10^{-6}	7×10^{-4}	*a*
exo-Bicyclo[3.1.1]heptyl 6-tosylate	25	1.01×10^{-9}	2×10^{-7}	4
exo-Bicyclo[2.1.1]hexyl 5-tosylate (II)	25	2.24×10^{-11}	5×10^{-9}	
7-Norbornyl	25	6.40×10^{-15}	1×10^{-12}	*b*

[a] J. D. Roberts and V. C. Chambers, *J. Am. Chem. Soc.*, **73**, 5034 (1951); H. C. Brown and G. Ham, *ibid.*, **78**, 2735 (1956). [b] S. Winstein, M. Shatavsky, C. Norton, and R. B. Woodward, *ibid.*, **77**, 4183 (1955).

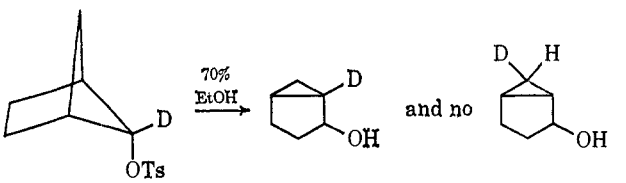
The relative rates of solvolysis of a series of cyclobutyl derivatives are given in Table II. The *endo*-bicyclo[*m*.1.1]alkyl derivatives are 10^3 more reactive than cyclobutyl itself, and the *exo* derivatives are 10^3–10^5 less reactive than cyclobutyl. Thus there is a marked conformational preference for the *endo* (equatorial) position.

The high reactivity of the *endo* isomers could be interpreted in either of two ways. First, the puckered cyclobutyl cation might be a relatively stable species, and this stabilization might be felt in the activated complex only if the leaving group were in the equatorial position. CNDO calculations[8] suggest that only an equatorial leaving group could lead to a stabilized activated complex and that the stabilization might be a function of the degree of puckering. Second, rearrangement to a secondary cyclopropylcarbinyl cation might be the driving force in each case. Despite the difference in strain in the reactants, the net effect in each case is to lose one cyclobutane ring. Thus, the strain relief might be relatively constant throughout the series.

In order to try to distinguish between these possibilities, two types of experiments were tried. In view of the facile 2,6-hydride shift in the norbornyl cation,[9] and the rather similar geometry in the bicyclo[2.1.1]hexyl-5 cation, the cation might be expected to undergo this type of hydride shift. This possibility was examined



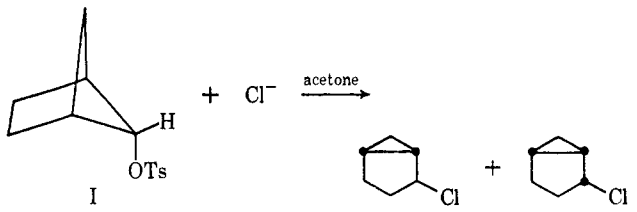
using a deuterium-labeled tosylate. The deuterium distribution in the northujyl product was determined by nmr. All of the deuterium was found in the 1 position, indicating absence of a hydride shift. If the hydride shift occurred, deuterium should be found in the 6 position.



In a second experiment, the tosylate I was treated with tetrabutylammonium chloride in acetone. Reaction occurred and led to chlorides which were identified as the isomeric northujyl chlorides. Thus, it was not

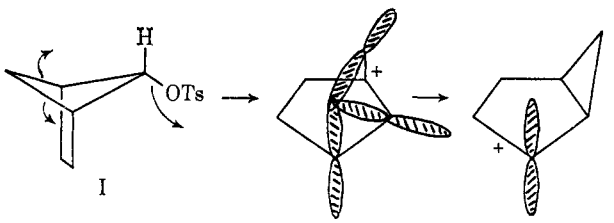
(8) K. B. Wiberg, *Tetrahedron*, **24**, 1083 (1968).
(9) M. Saunders, P. von R. Schleyer, and G. A. Olah, *J. Am. Chem. Soc.*, **86**, 5680 (1964).

possible to capture an intermediate cyclobutyl cation.[10] Similar results also were obtained with *endo*-bicyclo[3.1.1]heptyl 6-tosylate.[4]



In the absence of evidence for a cyclobutyl cation intermediate, and in view of the other results we have obtained with cyclobutyl derivatives, we are led to the conclusion that the reaction involves a concerted rearrangement, and that cyclobutyl solvolyses which lead to significant rate acceleration over that of cyclobutyl itself generally involve such a rearrangement.

As DePuy has suggested,[11] and as we have shown for other cases,[12,13] the *endo* isomer has the correct geometry to permit a concerted rearrangement. Further, a disrotatory process leads to bond movement which



will contribute to a relief of strain. The question remains, how is the cyclohexenyl tosylate formed. The formation of this product requires the cleavage of two C–C bonds. It is possible that the two bonds could be involved in a single concerted process. However, this will require further investigation.

The low reactivity of the *exo* isomers probably results from geometrical constraints. No cyclobutane C–C bond is located so that it can interact with the developing p orbital. The difference in reactivity between bicyclo[3.1.1]heptyl-6 and bicyclo[2.1.1]hexyl-5 derivatives probably results from the difference in the C–C–C bond angle at the reaction site.[14]

Experimental Section

***endo*-Bicyclo[2.1.1]hexyl 5-(3,5-Dinitrobenzoate).** A solution of 0.175 g (1.8 mmoles) of *endo*-bicyclo[2.1.1]hexan-5-ol[5] in 5 ml of dry pyridine was treated with 0.440 g (1.9 mmoles) of 3,5-dinitrobenzoyl chloride with ice bath cooling. The solution was stirred for 1 hr and placed in a refrigerator overnight. The solution was poured over 20 g of ice and extracted with several portions of ether. The ether solution was washed with 10% hydrochloric acid, saturated sodium bicarbonate solution, and water. After drying over sodium sulfate, removal of ether gave the solid nitrobenzoate. After two recrystallizations from hexane there was obtained 0.42 g (80%) of *endo*-bicyclo[2.1.1]hexyl 5-dinitrobenzoate, mp 139–140°.

Bicyclo[1.1.1]pentyl 2-(3,5-Dinitrobenzoate). The procedure given above was followed using 0.124 g (1.47 mmoles) of bicyclo[1.1.1]pentan-2-ol.[6] There was obtained 0.345 g (85%) of the ester, mp 126.4–127.4° after two recrystallizations from hexane.

Solvolysis of Bicyclo[1.1.1]pentyl 2-(3,5-Dinitrobenzoate). A solution of 0.156 g of the dinitrobenzoate in 10 ml of 80% acetone was sealed in a thick-walled ampoule. After heating for 108 hr at 120°, the cooled solution was made slightly basic with sodium bicarbonate, and acetone was distilled through a short Vigreux column. The residue was diluted with saturated salt solution and extracted with ether. After drying, the ether solution was concentrated and the residue was analyzed by vpc. Only one peak was found using a 10 ft × 3/8 in. Carbowax column. This was collected and identified as Δ^3-cyclopentenol by comparison of its nmr spectrum with that of an authentic sample.[15]

Acetolysis of *exo*-Bicyclo[2.1.1]hexyl 5-Tosylate. A solution of 0.5 g of *exo*-bicyclo[2.1.1]hexyl 5-tosylate[5] in 150 ml of 0.02 *M* potassium acetate in acetic acid was heated to 165° for 2 hr. The solution was diluted with 50 ml of cold water and then extracted with four 200-ml portions of 1:1 ether–pentane. The organic extracted was washed with 100 ml of 10% sodium bicarbonate solution and 150 ml of cold water. The solution was dried over potassium carbonate and the solvent was removed by distillation. The product was bulb-to-bulb distilled giving an acetate and a residue of unreacted tosylate. The nmr spectrum of the acetate indicated it to be 4-acetoxycyclohexene.

Acetolysis of *endo*-Bicyclo[2.1.1]hexyl 5-Tosylate. A solution of 0.5 g of *endo*-bicyclo[2.1.1]hexyl 5-tosylate in 100 ml of 0.02 *M* sodium acetate in acetic acid was allowed to stand at room temperature for 24 hr. The solution was diluted with 125 ml of cold water and extracted with four 50-ml portions of pentane and 50 ml of ether. The organic extract was washed with 25 ml of water, three 10-ml portions of 10% sodium carbonate, and four 20-ml portions of cold water. After drying over potassium carbonate, the solvent was removed by distillation. After bulb-to-bulb distillation of the product there was found 40% of cyclohexenyl tosylate. The volatile portion was analyzed by vpc on a Carbowax column at 150° and contained 30% 4-acetoxycyclohexene, 18% *trans*-bicyclo[3.1.0]-hexyl 2-acetate, and 12% *cis*-bicyclo[3.1.0]hexyl 2-acetate.

Bicyclo[2.1.1]hexane-*exo*-5-*d*-*endo*-5-carboxylic Acid. A solution of 48.0 g (0.35 mole) of diazonorcamphor[5] in 1000 ml of dioxane which contained 300 ml of deuterium oxide was irradiated for 72 hr with a 450-W quartz immersion lamp using a Corex filter. During that time, 7700 ml (98%) of nitrogen was evolved. Anhydrous sodium carbonate was added to the solution and the solvent was removed by distillation *in vacuo* until 300 ml of solution remained. The resulting solution was diluted with 500 ml of water and again the solution was concentrated to 300 ml. The basic solution was extracted twice with 50 ml of methylene chloride. The solution was made acidic with concentrated hydrochloric acid and extracted five times with 150 ml of pentane. The pentane solution was washed with 50 ml of saturated sodium chloride solution. After drying over sodium sulfate, the pentane was removed on a rotary evaporator leaving 17.0 g (38%) of an orange oil. The crude acid (17.0 g) was converted to the acid chloride by treatment with 32 g of thionyl chloride. Distillation gave 14.3 g (73%) of the acid chloride, bp 65–67° (15–16 mm).

Ethyl Bicyclo[2.1.1]hexyl-*exo*-5-*d* *endo*-5-Ketone. A solution of 11.0 g (76 mmoles) of the acid chloride in 25 ml of ether was added to a solution of 7.0 g (56 mmoles, 1.5 equiv) of diethylzinc in 200 ml of ether at a rate to maintain rapid reflux. The mixture was then stirred at reflux for 1 hr. The cloudy solution was cooled in an ice bath and 100 ml of saturated ammonium chloride solution was cautiously added. The heterogeneous mixture was filtered and the solid was washed with 50 ml of ether. The ether solution was washed with 20 ml of saturated sodium carbonate solution and twice with 20 ml of saturated sodium chloride solution. After drying the solution over magnesium sulfate, the ether was removed by distillation through a 12-in. Vigreux column leaving 10.5 g (100%) of a colorless oil. The ethyl ketone was used in the Baeyer–Villiger reaction without further purification.

Bicyclo[2.1.1]hexyl-*exo*-5-*d* *endo*-5-Propionate. A solution of 10.0 g (72 mmoles) of the ethyl ketone, 38 g of *m*-chloroperbenzoic

(10) We had previously reported that the reaction of I with chloride ion under these conditions led to *endo*-bicyclo[2.1.1]hexyl-5-chloride.[5] This appears to be incorrect and resulted from an erroneous interpretation of 40-mc nmr spectra.

(11) C. H. DePuy, *Accounts Chem. Res.*, 1, 33 (1968).

(12) K. B. Wiberg and J. G. Pfeiffer, *J. Am. Chem. Soc.*, 90, 5324 (1968).

(13) K. B. Wiberg, V. Z. Williams, Jr., and L. E. Friedrichs, *ibid.*, 90, 5338 (1968).

(14) G. Dallinga and L. H. Toneman [*Rec. Trav. Chim.*, 86, 171 (1967)] have reported that the corresponding bond angle in bicyclo[2.1.1]hexane is 84.5°, whereas bicyclo[3.1.1]heptane would be expected to have an angle similar to that in cyclobutane (88°).

(15) S. Winstein, E. L. Allred, and J. Sonnenberg, *J. Am. Chem. Soc.*, 81, 5833 (1959).

acid, and 300 ml of methylene chloride was stirred at room temperature for 10 days. The excess peracid was destroyed by the cautious addition of saturated sodium sulfite solution. The mixture was filtered and the layers were separated. The organic layer was washed with 100 ml of saturated sodium carbonate solution and 100 ml of saturated sodium chloride solution. After drying over sodium sulfate, the solvent was removed by distillation through a 12-in. Vigreux column leaving 10.5 g of a slightly yellow oil. Vpc and ir analysis indicated the presence of less than 5% of recovered ethyl ketone.

Bicyclo[2.1.1]hexan-*exo*-5-*d*-*endo*-5-ol. A solution of 10.5 g (68 mmoles) of the bicyclo[2.1.1]hexyl 5-propionate in 25 ml of ether was slowly added to a suspension of 5.0 g of lithium aluminum hydride in 150 ml of ether. The mixture was then stirred at reflux for 45 min. The excess lithium aluminum hydride was destroyed by the careful addition of 15 ml of water. The mixture was filtered and the solids were washed with 50 ml of ether. After drying the solution over magnesium sulfate, the solution was concentrated to a volume of 15 ml by distillation through a 12-in. Vigreux column. The mixture was separated by vpc ($^3/_8$ in. × 10 ft 20% Carbowax 20M at 135°) and the alcohol was collected as 4.6 g (69%) of a volatile solid. Except for the hydrogen which had been replaced by deuterium, the nmr spectrum corresponded to that of an authentic sample of the alcohol.[5] The alcohol was converted to the tosylate as previously described.[5]

Solvolysis of Bicyclo[2.1.1]hexyl-*exo*-5-*d* *endo*-5-Tosylate in 70% Aqueous Ethanol. An ether solution of the tosylate derived from 1.68 g of the alcohol was added over 5 min to a solution of 2.0 g (51 mmoles) of sodium hydroxide in 500 ml of 70% aqueous ethanol. The mixture was stirred at room temperature for 2 hr and then was poured into 500 ml of ice water. The resulting solution was extracted eight times with 50 ml of pentane. The pentane solution was washed with 50 ml of saturated sodium chloride solution. After drying over potassium carbonate, the pentane was removed by distillation through a 12-in. Vigreux column. The residue was bulb-to-bulb distilled *in vacuo* at 0.05 mm (bath at 40°). The distillate was analyzed by vpc ($^3/_8$ in. × 15 ft 20% Carbowax 20M at 80°) showing four components with retention times of 30, 35, 60, and 70 min. The first and major component (55%) was identified as *exo*-2-ethoxybicyclo[3.1.0]hexane-1-d_1. The second component (35%) was a mixture of two ethyl ethers which could not be separated by vpc. Inspection of the nmr spectrum indicated that the collected peak was a 3:1 mixture of *endo*-2-ethoxybicyclo[3.1.0]-hexane-1-d_1 and probably 4-ethoxycyclohexene-2-d_1. The remaining peaks corresponded to the epimeric northujyl alcohols.

The nmr spectrum of *exo*-2-ethoxybicyclo[3.1.0]hexane-d_1 showed absorption at τ 6.19 (one-proton doublet, J = 5 cps), 6.53 (two-proton quartet, J = 7 cps), 7.90–9.25 (eight-proton complex multiplet), 9.42–9.74 (one-proton multiplet), and 9.90–10.16 (one-proton multiplet).

The nmr spectra of the other components were not clearly definable, either because of an impure sample or because of a scarcity of sample.

From the nmr spectrum of the labeled *exo*-2-ethoxybicyclo-[3.1.0]hexane, it can be concluded that no hydride shift occurs during the solvolysis process.

Reaction of *endo*-Bicyclo[2.1.1]hexyl 5-Tosylate with Tetra-*n*-butylammonium Chloride. An ethereal solution (50 ml) of 1.43 g (5.7 mmoles) of *endo*-bicyclo[2.1.1]hexyl 5-tosylate was added to an ice-cooled solution of 29.0 g (100 mmoles) of tetra-*n*-butylammonium chloride in 110 ml of acetone. The solution was allowed to stand in a refrigerator for 48 hr. The mixture was poured into 200 ml of ice water and the layers were separated. The aqueous layer was extracted five times with 50 ml of pentane. The combined organic extracts were washed with 50 ml of saturated sodium chloride solution. After drying over sodium sulfate, the solvent was removed by distillation through an 18-in. column packed with glass beads. The residue was bulb-to-bulb distilled *in vacuo* (1 mm, bath at 50–60°) into a Dry Ice–acetone cooled trap.

The nmr spectrum of the distillate indicated that the product was mainly a mixture of the *exo*- and *endo*-northujyl chlorides (~4:1). Attempted separation by vpc was unsuccessful, probably due to the decomposition of the chlorides on the column. No evidence for *endo*-5-chlorobicyclo[2.1.1]hexane was found in the nmr spectrum.

Kinetic Method. The kinetic method was the same as that described earlier.[4]

Acid-Catalyzed Solvolyses of Bicyclobutane Derivatives. Stereochemistry of the Cyclopropylcarbinyl–Cyclopropylcarbinyl and Related Rearrangements[1]

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Abstract: The stereochemistry of the acid-catalyzed addition of acetic acid, methanol, and water to bicyclobutane and tricyclo[4.1.0.0^{2,7}]octane has been determined. The proton addition proceeds with retention of configuration. Similar results have been obtained in the addition of chlorine to bicyclobutane. The cyclopropylcarbinyl–cyclopropylcarbinyl rearrangement has been found to proceed in a stereoselective fashion. Similar results were obtained for the conversion of the allylcarbinyl ion to the cyclopropylcarbinyl ion. CNDO calculations, with parameters optimized for hydrocarbons, give results which are in accord with the observations, and suggest that the lower energy form of the cyclobutyl cation is puckered.

We have previously observed that bicyclobutane and its derivatives react rapidly with electrophiles.[3] It was of interest to us to determine whether or not the reactions were stereospecific, and to determine the direction from which the proton was transferred. In two previously reported cases, the stereochemistry was determined. Blanchard and Cairncross[4] reported that the reaction of 3-methylbicyclobutane-1-nitrile with water gave *cis* addition to the central C–C bond. Dauben and coworkers[5] found that the reaction with

(1) This investigation was supported by the U. S. Army Research Office and the National Science Foundation. We also wish to acknowledge NSF Grant GP-6938 which enabled the purchase of a 100-MHz nmr spectrometer.

(2) Institute for Organic Chemistry, University of Munich.

(3) K. B. Wiberg, G. M. Lampmann, D. S. Connor, P. Schertler, and J. Lavanish, *Tetrahedron*, 21, 2749 (1965).

(4) E. P. Blanchard, Jr., and A. Cairncross, *J. Am. Chem. Soc.*, 88, 487 (1966).

(5) W. G. Dauben and F. G. Willey, *Tetrahedron Lett.*, 893 (1962); W. G. Dauben and W. T. Wipke, *Pure Appl. Chem.*, 9, 539 (1964).