# Solvolysis of *cis*-Bicyclo[5.1.0]oct-4-en-3-yl Tosylate

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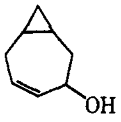
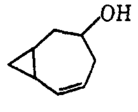
Bicyclo[5.1.0]oct-4-en-3-ol (1) has been prepared in ten steps from cycloocta-1,5-diene. Acetolysis of its tosylate gives *cis*- and *trans*-bicyclo[5.1.0]oct-2-en-4-yl acetate. As forbidden by orbital symmetry, the cyclopropane ring does not participate in the solvolysis. The cations produced from 1-OTs are not in equilibrium with those produced from the isomeric bicyclo[5.1.0]oct-5-en-3-yl (2) or tricyclo[5.1.0.0$^{3,5}$]oct-2-yl (3) esters.

The solvolyses of the esters from bicyclo[5.1.0]oct-4-en-3-ol (1), bicyclo[5.1.0]oct-5-en-3-ol (2), and tricyclo[5.1.0.0$^{3,5}$]octan-2-ol (3) produce ions that are formally valence tautomeric. Each ion represents a different mode of delocalization of charge over an eight-membered ring with unsaturation at positions 1, 2, 3, 5, and 7 relative to one another. In recent studies[2,3] we have been investigating the energy surface described by these $C_8H_{11}^+$ species. The major thrust of this study has been a description of the reactivity of 2-OTs as a function of conformation.[2] For such a study, however, it is necessary to locate the ions derived from 1 and 3 on the energy surface and to learn whether there exist allowed pathways for mutual interconversions of these ions. We have already described the solvolytic properties of 3 in relation to 2.[3] In the present paper we report the preparation of 1 and the investigations of the solvolytic properties of its tosylate. We find that the ions derived from 1-OTs are wholly insulated from the ionic manifolds generated by 2 and 3.



**1**



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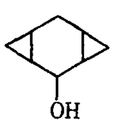
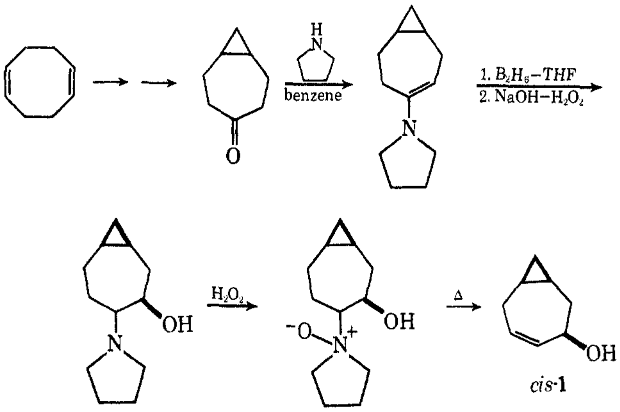


**3**

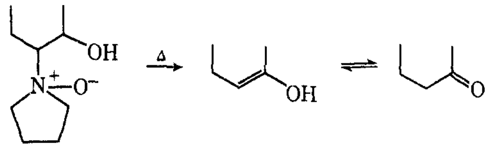
## Results

**Synthesis.**—The desired isomer of 1 has the hydroxyl and cyclopropyl groups cis to each other. A stereoselective synthesis is therefore required. The absence of symmetry in the molecule gives rise to synthetic difficulties, since use of the double bond to introduce the hydroxyl group, or vice versa, can produce undesired isomers. Several approaches of this type invariably gave the wrong isomer. The method depicted in Scheme I was finally developed to produce the desired alcohol *cis*-1. Bicyclo[5.1.0]octan-4-one may be obtained in five steps from cyclooctadiene by the method of Cope, *et al.*[4] The carbonyl group of this ketone lies on a molecular plane of symmetry. The method of Gore, Drouet, and Barieux[5] for conversion of a ketone to an allylic alcohol can therefore proceed in only one fashion. By this method the ketone is converted to its pyrrolidino derivative, and the enamine is converted to the saturated alcohol by the hydroboration procedure. Oxidation of the amino alcohol and pyrolysis of the amine oxide produce the desired alcohol.

SCHEME I



This sequence was first tested on cycloheptanone and found to be satisfactory. Formation of the enamine in Scheme I was carried out under neutral conditions (refluxing benzene for 14 days), since the usual acid catalysis led to a considerable reduction in yield. A possible explanation of this observation may be drawn from the work of Stephen and Marcus.[6] The direction of the Cope elimination is of interest since an alternative mode of elimination would produce a ketone (eq 1). The end result of such a sequence



(1)

would have been simply the movement of the ketone function α to the original position. The lack of ketone formation has been attributed either to unfavorable eclipsing interactions in the transition state leading to the enol[7] or to unfavorable dipole–dipole interactions.[5] In all cases studied to date, formation of ketone is not an important side reaction.[5]

**Structure Proof.**—To locate the hydroxyl group both in the material prepared by the method of Scheme I and in the alcohol product of the solvolysis described in the next section, the three ketones 4–6 were prepared. It is to be noted that both 1 and 2 are related to 4. The ketones were prepared by the methods outlined in Scheme II. The structure of alcohol *cis*-2 has been

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[1] (a) This work was supported by the Petroleum Research Fund, administered by the American Chemical Society (Grant 2970-AC4,5), and by the National Science Foundation (Grants GP-9257 and GP-22942). (b) National Institutes of Health Predoctoral Fellow, 1968–1970. (c) NDEA Fellow, 1967–1969.

[2] J. B. Lambert, J. W. Hamersma, A. P. Jovanovich, F. R. Koeng, S. A. Sweet, and P. J. Kucinski, *J. Amer. Chem. Soc.*, **92**, 6372 (1970).

[3] J. B. Lambert, F. R. Koeng, and J. W. Hamersma, *J. Org. Chem.*, **36**, 2941 (1971).

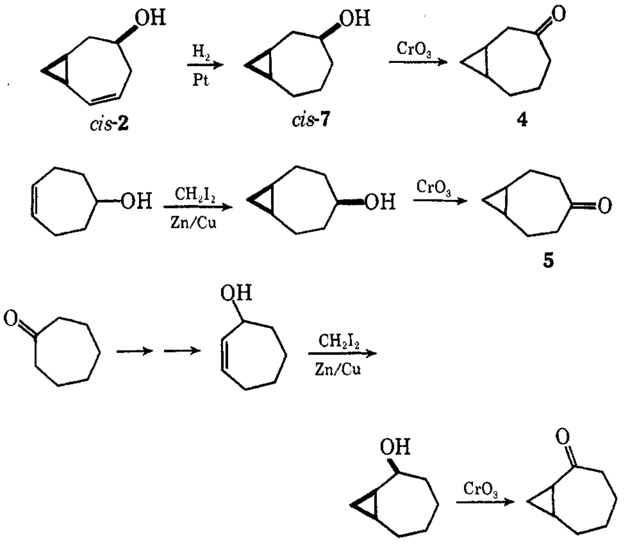
[4] A. C. Cope, S. Moon, and C. H. Park, *J. Amer. Chem. Soc.*, **84**, 4843 (1962).

[5] J. Gore, J. P. Drouet, and J. J. Barieux, *Tetrahedron Lett.*, 9 (1969).

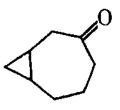
[6] J. F. Stephen and E. Marcus, *J. Org. Chem.*, **34**, 2535 (1969).

[7] A. C. Cope, E. Ciganek, and J. Lazar, *J. Amer. Chem. Soc.*, **84**, 2591 (1962).

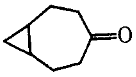
SCHEME II



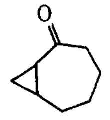
rigorously proved in a previous study.[2] Hydrogenation and Jones oxidation[8] therefore give the 3-ketone (**4**). The 4-ketone (**5**) was available from the synthesis of **1** (Scheme I). An alternative synthesis is given in Scheme II. Cyclohept-4-enol is available by a six-step synthesis due to Stork and Cope.[9] The Simmons–Smith reaction[10] on this alcohol, followed by Jones oxidation,[8] gives **5**. Cycloheptanone may be converted by the Gore procedure[5] to cyclohept-2-enol, which gives the 2-ketone (**6**) by the Simmons–Smith reaction[10] and the Jones oxidation.[8] All three ketones were easily differentiable by analytical vapor phase chromatography.



**4**



**5**

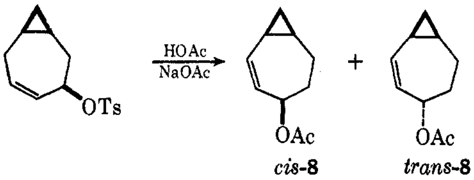


**6**

The alcohol produced by the procedure of Scheme I possessed the expected nmr and ir spectra. Hydrogenation with the Adams catalyst ($PtO_2$) and Jones oxidation[8] gave a ketone that proved to be **4**. The intermediate saturated alcohol was found to be identical with *cis*-**7** (Scheme II), for which an authentic sample of proved structure was available for comparison.[2] The alcohol *trans*-**1** has been produced by another procedure[11] and found to give the known[2] *trans*-**7** on hydrogenation and the same ketone **4** on subsequent oxidation. The hydroxyl group of the synthesized alcohol is therefore in the 3 position and the stereochemistry is unequivocally cis. Finally, manganese dioxide oxidation, a reaction specific for allylic alcohols,[12] gave an $\alpha,\beta$-unsaturated ($\nu_{CO}$ = 1660 $cm^{-1}$) ketone. The double bond must therefore be in the assigned position.

The nonallylic isomer *cis*-**2** was inert to treatment with manganese dioxide.

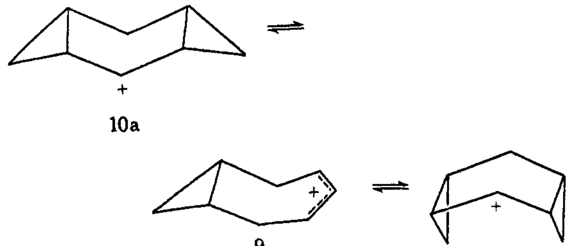
**Solvolysis.**—*cis*-Bicyclo[5.1.0]oct-4-en-3-ol was converted to the tosylate by Tipson's method.[13] The tosylate was solvolyzed in acetic acid buffered with sodium acetate for 14 hr at 45°. The products were isolated and reduced with lithium aluminum hydride to give two alcohols in about a 60:40 ratio. The mixture was hydrogenated and then oxidized with Jones reagent. Two different saturated alcohols in the same ratio remained after hydrogenation, but only one ketone was produced after subsequent oxidation. This material was identical with the authentic sample (Scheme II) of bicyclo[5.1.0]octan-4-one (**5**). The double bond may be introduced into the 4-alcohol in only one fashion; so the two products must be the *cis*- and *trans*-bicyclo[5.1.0]oct-2-en-4-yl acetates (**8**) (eq 2). The stereochemistry of the individual isomers in the 60:40 mixture could not be determined.



(2)

## Discussion

The primary question we desired to answer was whether the allylic ion formed from *cis*-**1**-OTs is in equilibrium with the ions formed from *cis*-**2**-OTs and *cis,cis*-**3**-OPNB.[14] The allylic ion **9** may be obtained from the tricyclic ions **10** by the process depicted in eq 3[15] (note that **9** is rotated by 90° with respect to **10a** and **10b**). The ion(s) from 2-OTs (**11**, drawn without the delocalization of charge demonstrated elsewhere[2]) can give **9** by the process in eq 4 (again note the 90° rotation). Both processes have the appearance of simple valence tautomerizations to form the presumably more stable planar allylic ion, although there are also small attendant conformational



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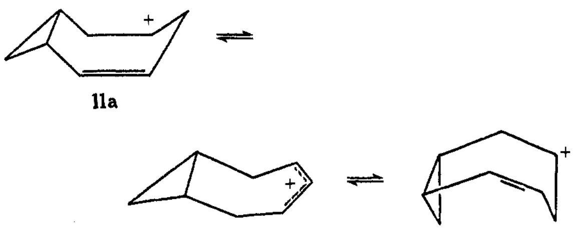

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[8] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1968, p 142.

[9] G. Stork and H. Landesman, *J. Amer. Chem. Soc.*, **78**, 5129 (1956); A. C. Cope and G. L. Woo, *ibid.*, **85**, 3601 (1963); A. C. Cope, C. H. Park, and P. Scheiner, *ibid.*, **84**, 4862 (1962).

[10] H. E. Simmons and R. D. Smith, *ibid.*, **84**, 4843 (1962).

[11] A. P. Jovanovich, Ph.D. Dissertation, Northwestern University, 1969.

[12] H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, p 86 ff.

[13] R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

[14] The tosylate of **3** was not prepared.[3]

[15] Although there are two conformational forms of **10** and **11** (and even of **9**, not shown), the arguments presented herein are applicable to either.

changes. It has previously been demonstrated that the ions from 2-OTs and 3-OPNB are in equilibrium.[2,3]

We look to the solvolysis products to give information concerning possible ion equilibration. Under appropriate conditions,[2,3] both ions **10** and **11** give a product mixture containing *cis*-**2**, *trans*-**1**, cycloocta-3,5-dienol, and *trans*-2-vinylcyclohex-4-enol in similar proportions. Under no conditions does either **2**-OTs or **3**-OPNB produce the materials **8** obtained from the acetolysis of **1**-OTs. Conversely, it is seen that **1**-OTs produces none of the solvolytic products of **2** or **3**. Thus, although the ions **10** and **11** are in equilibrium, the allylic ion **9** appears to reside in an isolated region of the energy surface without communication with the other ions under consideration.

The absence of cyclopropyl participation (**9** $\rightleftarrows$ **10**) can be understood if the process is considered to be a 2 + 2 cycloaddition of one cyclopropane bond to the allylic cation (eq 5). A concerted addition of the $2_s$ + $2_s$ type is thermally forbidden by orbital symmetry. The orbitals of interest are given in Chart I for one of the conformations.[15] Although the lower energy bonding orbitals correlate with each other and the higher energy antibonding orbitals correlate, the reaction is forbidden because the higher bonding orbitals correlate with the lower antibonding orbitals. Other modes of cycloaddition are forbidden because they would give rise to trans-fused cyclopropane rings.[16]

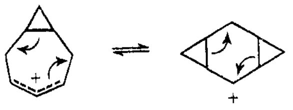
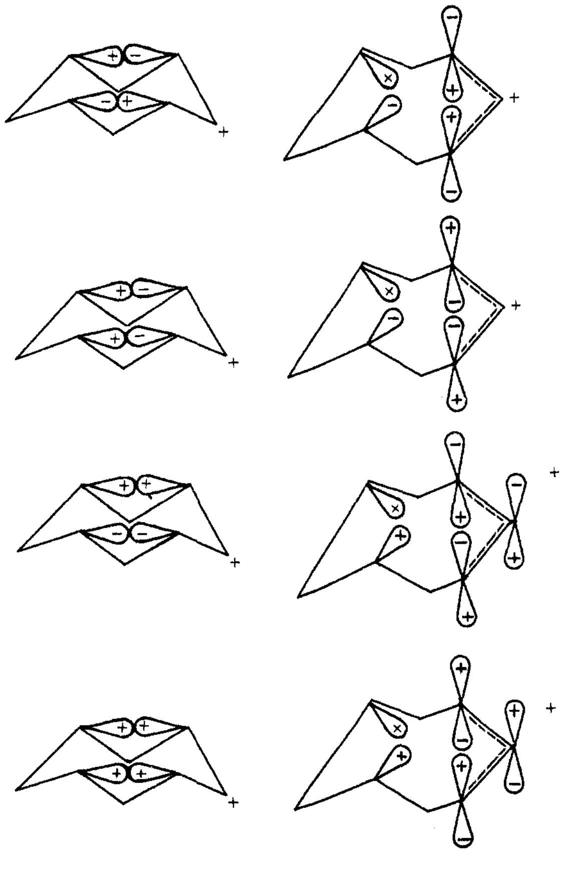
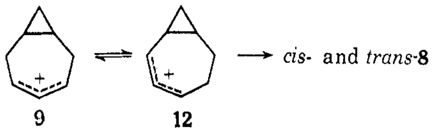

(5)

CHART I



Without the option of simple cyclopropane participation, the modes of reactivity available to the allylic ion are severely limited. Stepwise isomerization of **9** to the more stable allylic ion **12** (eq 6) occurs under the reaction conditions, and the products are derived from this cation.



(6)

## Experimental Section

Infrared spectra were measured on Beckman IR-5 and IR-10 infrared spectrometers. Nmr spectra were taken on Varian Associates A-60 and T-60 nuclear magnetic resonance spectrometers. A Consolidated Electrodynamics Corp. 21-104 mass spectrometer was used for the mass spectral work. Analytical vapor phase chromatography was carried out on either a Hewlett-Packard Model 700 laboratory chromatograph or a Varian Associates Aerograph Series 1520B. Preparative vpc work was performed on the Hewlett-Packard chromatograph. Elemental analyses were performed by Miss H. Beck, Analytical Services Laboratory, Northwestern University.

**Bicyclo[5.1.0]octan-4-one (5)** was made by the method of Cope, *et al.*[4] According to this procedure, cycloocta-1,5-diene is converted to bicyclo[6.1.0]non-4-ene by the Simmons-Smith reaction,[10] and this material is oxidized to *cis*-1,2-cyclopropanedipropionic acid by $KMnO_4$. The diacid is converted to the methyl diester with diazomethane, and the diester is cyclized (NaH) to 3-carbomethoxybicyclo[5.1.0]octan-4-one, which is hydrolyzed and decarboxylated (NaOH, HCl, 100°) to the desired product. The alternative procedure[9] (Scheme II) is more laborious and lower in yield.

**4-Pyrrolidinobicyclo[5.1.0]oct-4-ene.**[5]—A mixture of 7.6 g (0.061 mol) of bicyclo[5.1.0]octan-4-one (**5**), 13 g (0.18 mol) of pyrrolidine, and 60 ml of benzene was refluxed for 6 days in a flask equipped with a Dean-Stark trap and a magnetic stirrer. The calculated amount of water was removed from the trap (1.1 ml). The mixture was distilled under vacuum to give 10.3 g of crude product (95%).

**4-Pyrrolidinobicyclo[5.1.0]octan-3-ol.**[5]—Boron trifluoride etherate (20 g, 0.14 mol) was added dropwise to a solution of lithium aluminum hydride (3.2 g, 0.084 mol) in 200 ml of ether contained in a three-necked flask equipped with a stirrer and a nitrogen-inlet tube. The solution was stirred and cooled in an ice bath, as a slow stream of dry nitrogen swept the diborane through a sintered-glass stick into a second flask containing 10.3 g (0.058 mol) of 4-pyrrolidinobicyclo[5.1.0]oct-4-ene in 70 ml of dry tetrahydrofuran. The addition of boron trifluoride took 60 min, and the nitrogen sweep was continued for another 2 hr. The tetrahydrofuran solution of the organoboron compound was kept at room temperature for an additional 12 hr. The solution was then evaporated under vacuum to give a solid product.

The solid was dissolved in 150 ml of 95% ethanol. Sodium hydroxide (8 g, 0.2 mol) was added, followed by the dropwise addition of 24 ml of 30% $H_2O_2$ to give an exothermic reaction. Additional ethanol (30 ml) was added, and the mixture was heated at reflux for 2 hr. It was then continuously extracted with ether for 36 hr. The organic phase was dried over $MgSO_4$ and after distillation gave 9 g (80%) of crude product, bp 81° (0.2 mm).

*cis*-**Bicyclo[5.1.0]oct-4-en-3-ol** (*cis*-**1**).—To a solution of 5 g (26 mmol) of the amino alcohol in 3.5 ml of methanol was added 2.9 g (26 mmol) of 30% $H_2O_2$. A considerable amount of heat was generated after the peroxide addition. After 2 hr at room temperature, another portion (2.9 g) of $H_2O_2$ was added. A third portion (2.9 g) of peroxide was added after an additional 4 hr. The reaction mixture was allowed to stand for 45 hr, and

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[16] Since the preparation of this manuscript, the failure of a cyclopropane ring to cycloadd to an allylic cation has also been demonstrated in a different system by A. F. Diaz, D. L. Harris, M. Sakai, and S. Winstein, *Tetrahedron Lett.*, 303 (1971).

excess $H_2O_2$ was destroyed with platinum black. Most of the methanol and water in the reaction mixture was removed on a rotary evaporator. The residue was then dried under vacuum to give a white solid (the amine oxide).

The flask containing the dry white solid was connected to a Dry Ice–acetone trap by means of a stopcock adapter. The system was evacuated to <0.3 mm. The flask containing the solid was then heated slowly to 150° and kept at this temperature until no further material distilled from the flask. The distillate in the trap was transferred to a separatory funnel with 120 ml of ether. The ether solution was extracted three times with 30-ml portions of 1 *N* HCl. The aqueous acid extracts were combined and extracted once with 50 ml of ether. The ether solutions were combined, extracted twice with 20-ml portions of saturated aqueous $NaHCO_3$ solution, and dried over $MgSO_4$. The solution was filtered and stripped of solvent. The reaction mixture was purified by column chromatography with silica gel as the solid phase and 15% ether–85% hexane (by volume) as the eluent. A mass spectrum of the purified product had the correct parent at *m/e* 124. *Anal.* Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.19; H, 9.52.

That the product possessed the correct structure was shown by the following chemical tests. Approximately 75 mg of the product was stirred with 0.5 g of $MnO_2$ in 5 ml of $CHCl_3$ for 48 hr at room temperature. The mixture was filtered and the solvent removed under aspirator vacuum distillation. The infrared spectrum of this product had a strong absorption at 1660 $cm^{-1}$, indicating than an $\alpha,\beta$-unsaturated ketone was present and consequently that the starting material was an allylic alcohol. The position and stereochemistry of the hydroxyl group was proved by hydrogenation over platinum and subsequent Jones oxidation[8] of the purified pyrolysis product. The hydrogenation product was *cis*-**7** and not *trans*-**7**, as indicated by comparison with an authentic sample (ir spectrum and vpc retention time with 20 ft × 1/8 in. 12% Carbowax on Chromosorb G column). The ketone obtained after Jones oxidation was **4** (verified by vpc retention time and ir analysis). Prominent infrared absorptions ($cm^{-1}$) of *cis*-**1** are as follows: 3350 (s), 3010 (m), 2870 (m), 2720 (w), 1650 (w), 1465 (m), 1040 (s), and 990 (s). The nmr spectrum ($CDCl_3$) consisted of $\delta$ 0.1 (m, 2, cyclopropane ring), 1.5 (m, 6, cyclopropane and cycloheptane ring), 3.2 (s, 1, OH), 4.2 (m, 1, CHO), and 5.7 (m, 2, alkenic protons).

*cis*-**Bicyclo[5.1.0]oct-4-en-3-yl tosylate** (*cis*-**1-OTs**) was prepared by Tipson's method.[13] Though not crystalline, the material was pure by nmr spectroscopy. The tosylate was subjected to buffered acetolysis for 14 hr at 45°[3] and analyzed by the procedures previously described (acetates → unsaturated alcohols → saturated alcohols → ketone). The products from this solvolysis were identified as the *cis*- and *trans*-bicyclo[5.1.0]-oct-2-en-4-yl acetates.

**Bicyclo[5.1.0]octan-2-one** (**6**) was obtained by the method of Scheme II. Since the material is not related to any described in this study, the details have been recorded elsewhere.[11]

*cis*-**Bicyclo[5.1.0]octan-3-ol** (*cis*-**7**) was obtained by hydrogenation of *cis*-bicyclo[5.1.0]oct-5-en-3-ol[2] over the Adams catalyst (hydrogenated $PtO_2$). This catalyst was found not to open the three-membered ring, whereas palladium on charcoal gave considerable ring opening. Cope, *et al.*,[4] prepared the identical material by a different route.

**Bicyclo[5.1.0]octan-3-one** (**4**) was prepared by the Jones oxidation[8] of *cis*-**7**. This material was identical with that prepared by Cope, *et al.*[4]

**Registry No.**—*cis*-**1**, 32675-19-7; *cis*-**1** tosylate, 31026-60-5; **4**, 32675-20-0; 4-pyrrolidinobicyclo[5.1.0]octan-3-ol, 32675-21-1.

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# The Persistence of the 1-Axial Preference in Thianes

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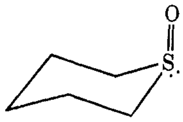
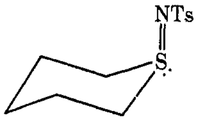
The axial preference of the oxide in thiane 1-oxide and of the imide in thiane 1-(*N*-tosyl)imide is reversed in the presence of a 3,3-dimethyl group, because of the syn-axial interaction. In protonated 3,3-dimethylthiane, however, the 1 proton persists in the axial position, despite the syn-axial interaction. The 4,4-dimethyl derivatives of the 1-oxide, the 1-(*N*-tosyl)imide, and the protonated form all have the normal 1-axial preference. 4,4-Dimethylthiane 1-oxide 1-imide and its *N*-tosyl derivative have also been examined and found to exist as two conformers.

A curious property of the thiane system is the preference of certain 1 substituents for the axial position. Thus in thiane 1-oxide (**1**),[2] thiane 1-(*N*-tosyl)imide (**2**),[3] and protonated thiane (**3**),[4] the 1-axial conformation is favored, respectively, by 175 cal/mol (−90°), 145 cal/mol (−89°), and >1500 cal/mol (−30°). An attractive interaction between the 1 substituent and the 3,5-axial protons has been invoked to explain this unusual preference for the case of the 1-oxide.[5] The preference must be unrelated to similar observations recently reviewed in terms of the "gauche effect,"[6] of which the anomeric effect is one example, since interactions between two polar bonds are the determining factor in these systems.



**1**



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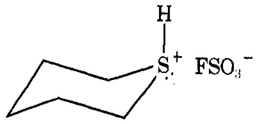

**3**

If the 1-axial preference is caused by an attractive 1,3 interaction, replacement of a 3-axial proton by a methyl group should make the interaction repulsive (or less attractive) and decrease the proportion of the 1-axial isomer. We have previously used this technique to explore the NH axial preference in piperidine[7] and the methyl–halogen syn-axial interaction in the 1-halo-

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[1] (a) This work was supported by the National Science Foundation (Grants GP-9257 and GP-22942) and the Petroleum Research Fund, administered by the American Chemical Society (Grant 2970-AC4,5). (b) National Science Foundation Trainee, 1968–1969.

[2] J. B. Lambert and R. G. Keske, *J. Org. Chem.*, **31**, 3429 (1966).

[3] J. B. Lambert, C. E. Mixan, and D. S. Bailey, *Chem. Commun.*, 316 (1971).

[4] J. B. Lambert, R. G. Keske, and D. K. Weary, *J. Amer. Chem. Soc.*, **89**, 5921 (1967).

[5] N. L. Allinger, J. A. Hirsch, M. A. Miller, and I. J. Tyminski, *ibid.*, **91**, 337 (1969).

[6] S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc. B*, 136 (1971).

[7] J. B. Lambert, D. S. Bailey, and B. F. Michel, *Tetrahedron Lett.*, 691 (1970).