Competitive Solvolytic Homoconjugation

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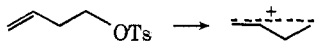
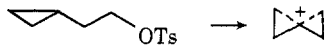
Abstract: *cis*-Bicyclo[5.1.0]oct-5-en-3-yl tosylate (*cis*-**1**-OTs) exists in two conformational forms that solvolyze by independent pathways. The less stable (saddle) conformer (**2**) solvolyzes with double bond participation to form *cis*-**1** (corresponding to retained starting material) and various hydride-shifted materials. The more stable (boat–chair) conformer **3** solvolyzes with cyclopropane participation to give the *cis*-bicyclo[5.1.0]oct-4-en-3-yl ester (*cis*-**7**). Quantitative product analysis indicates that about 80% of the reaction occurs by double bond participation and 20% by cyclopropane participation. The study thus furnishes a direct comparison of the two forms of participation under competitive circumstances.

Solvolytic participation by remote double bonds[2] or cyclopropane rings[3] has been well documented in recent years. A kinetic comparison of these two modes of forming homoconjugated transition states[4] has proved to be difficult. The simplest conceivable open-chain examples are given by eq 1 and 2. In

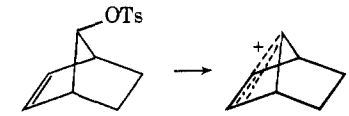


(1)



(2)

order to make a direct comparison of the allylcarbinyl system[5] in eq 1 with the β-cyclopropylethyl system[6] of eq 2, the ability of the unsaturated substituent to participate in the departure of the leaving group must be isolated from all other factors that contribute to the respective rate constants. Differences in the inductive effects of the double bond and the cyclopropane ring, for example, must be taken into account in a comparison of the rates. Differences in the extent of ion-pair formation or in the proportion of the k_Δ pathways may be substantial. Present interpretation of the data in these systems favors a very weak participation by cyclopropane in eq 2,[6] but a somewhat stronger participation by the double bond in eq 1.[5] Comparison of the relative merits of double bond and cyclopropane participation in the polycyclic systems of eq 3 and 4 likewise is not straightforward.[7,8] Differences in the inductive effects of the two types of unsaturation and in contributions from cyclopropane ring strain have not



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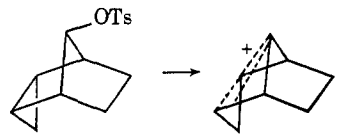
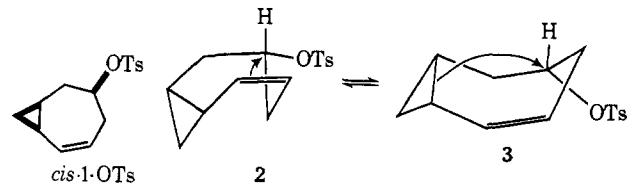


(4)

been assessed. A considerably faster rate for the system of eq 4 has led to the conclusion that cyclopropane participation is more effective in these systems. It was noted that the particular orientation of the three-membered ring in the system of eq 4, however, may be especially favorable for participation.

In order to overcome certain of the problems involved in comparing double bond and cyclopropane participation in two separate but similar molecules, we have designed and prepared a molecule that incorporates both elements capable of participation, *cis*-bicyclo[5.1.0]oct-5-en-3-yl tosylate (*cis*-**1**-OTs).[9] This molecule exists as two conformationally interconverting forms, **2** and **3**. In the less stable saddle conformation



cis-1-OTs 2 3

2, the double bond is properly situated for participation, whereas in the more stable boat–chair conformation **3**, it is the cyclopropane ring that is properly oriented. Because each conformer contains both the active and the inactive unsaturated functionalities, the inductive effect on the ionization process is identical in each case. Model systems are therefore not necessary to allow for differences in double bond and cyclopropane electron withdrawal.

Although **2** and **3** interconvert, the ions that they respectively produce should not. Interconversion at the ionic stage would require breaking up charge delocalization, in addition to overcoming the nonbonded and Pitzer interactions associated with the conformational interconversion. Therefore **2** gives only products

(1) (a) This work was supported by the Petroleum Research Fund, administered by the American Chemical Society (Grant No. 2970-AC4), and by the National Science Foundation (Grant No. GP-22942); (b) NDEA Fellow, 1967–1969; (c) NIH Predoctoral Fellow, 1968–1970; (d) NDEA Fellow, 1969.

(2) M. Hanack and H.-J. Schneider, *Angew. Chem., Int. Ed. Engl.*, **6**, 666 (1967).

(3) S. Winstein, *Quart. Rev., Chem. Soc.*, **23**, 141 (1969).

(4) By "homoconjugation" we mean delocalization of charge between two carbon atoms that are separated by at least one saturated atom. Direct conjugation, such as allylic or benzylic, requires the participating π entity to be bonded directly to the source of developing charge.

(5) K. L. Servis and J. D. Roberts, *J. Amer. Chem. Soc.*, **86**, 3773 (1964).

(6) M. J. S. Dewar and J. M. Harris, *ibid.*, **92**, 6557 (1970); Y. E. Rhodes and T. Takino, *ibid.*, **90**, 4469 (1968); M. Hanack and H.-M. Ensslin, *Justus Liebigs Ann. Chem.*, 713, 49 (1968), and references cited therein.

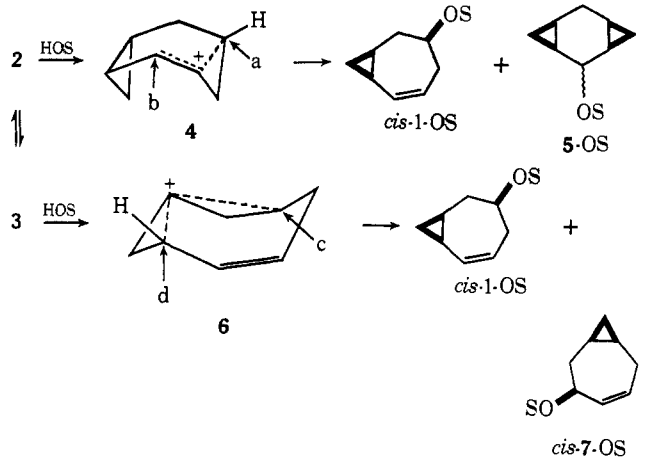
(7) S. Winstein, M. Shatavsky, C. Norton, and R. B. Woodward, *J. Amer. Chem. Soc.*, 77, 4183 (1955); S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956).

(8) H. Tanida, T. Tsuji, and T. Irie, *ibid.*, **89**, 1953 (1967); J. S. Haywood-Farmer and R. E. Pincock, *ibid.*, **91**, 3020 (1969).

(9) J. B. Lambert, J. W. Hamersma, A. P. Jovanovich, F. R. Koeng, S. A. Sweet, and P. J. Kucinski, *ibid.*, **92**, 6372 (1970).

from double bond participation, and **3** gives products from cyclopropane participation. Provided that the barrier for interconversion between **2** and **3** is much smaller than their activation energies to ionization, the distribution of products will furnish a direct measure of the relative proportions of double bond and cyclopropane participation. Scheme I shows a simplified

Scheme I

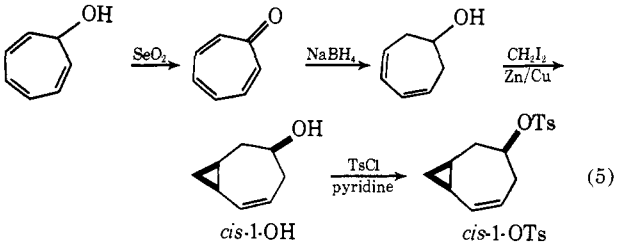


approach to this question. A more definitive diagram is given in the Discussion section. The homoallylic ion **4** produced by double bond participation in conformer **2** can react with solvent at position a to give the starting material *cis*-**1**[10] or at position b to give the tricyclic ester **5**. The bishomoallylic ion **6** produced by cyclopropane participation in conformer **3** can react with solvent at position c to give *cis*-**1**[10] or at position d to give the allylic product **7**.[10] As a first approximation, the tricyclic product is therefore taken to indicate double bond participation and the allylic product cyclopropane participation. At this point in the analysis, *cis*-**1** apparently cannot serve as an indicator of the mode of participation by which it is formed.

Determination of the relative contributions of double bond and cyclopropane participation in the solvolysis of *cis*-**1**-OTs can be reduced to six necessary steps: (1) stereoselective preparation of *cis*-**1**-OTs; (2) measurement of rates to establish that participation does in fact take place; (3) determination of activation parameters to demonstrate that the Curtin–Hammett principle is applicable and that the product distribution reflects the transition-state energies; (4) identification of products, with special attention to the presence of **5**-OS and **7**-OS; (5) demonstration that there is no crossover between ions **4** and **6**, so that product analysis can be considered to be a legitimate indicator of participation pathways; and (6) development of a method to decide how much of the product *cis*-**1** comes from double bond participation and how much from cyclopropane participation. These objectives have been fulfilled, and we have learned that double bond participation is clearly dominant in this system.

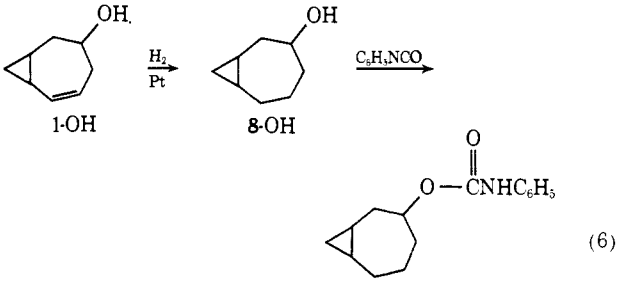
Results

For the preparation of *cis*-bicyclo[5.1.0]oct-5-en-3-yl tosylate, cycloheptatriene was oxidized to tropone with selenium dioxide, and tropone was reduced with sodium borohydride to form 3,5-cycloheptadienol.[11] This alcohol was converted to *cis*-**1**-OH by the Simmons–Smith reaction.[12] The tosylate was obtained by the standard Tipson method.[13] These transformations are outlined in eq 5. In cyclic alcohols such as the



(5)

dienol, the Simmons–Smith reaction is known to occur stereoselectively in favor of the product with the hydroxyl and cyclopropyl groups on the same side of the ring. It is important that we know with certainty that the reaction proceeds by this route, since only the cis compound is expected to show cyclopropane participation. Our reaction mixture contained >95% of a single monoadduct. A varying amount of diadduct formed, depending on the ratio of reactants. On some occasions, a second monoadduct was produced in very small amounts. On the basis of the elemental analysis, the mass, nmr, and ir spectra, and the method of preparation, the predominate monoadduct was assigned the structure *cis*-**1**-OH, and the minor monoadduct *trans*-**1**-OH. The two materials were oxidized to the same ketone. The stereochemistry was made certain by hydrogenation of the separate monoadducts to the corresponding bicyclo[5.1.0]octan-3-ol (**8**-OH), and preparation of the known phenylurethanes (eq 6).[14]



(6)

Cope, *et al.*, have related the **8**-OH compounds to methylcycloheptanols of known stereochemistry.[14] The 98°-melting phenylurethane, which had been derived from our major monoadduct, was found to have the cis stereochemistry, and the 76° isomer, derived from our minor adduct, the trans stereochemistry. These chemical results therefore confirm the usual stereochemistry of the Simmons–Smith reaction.[12]

In order to utilize a wide range of solvent nucleophilicity and ionizing power, solvolyses of *cis*-**1**-OTs were carried out in acetic acid, formic acid, and trifluoroacetic acid, each buffered with its conjugate base. Titrimetric rate constants were obtained for formic and acetic acids, but the reaction in trifluoroacetic acid was

(10) Backside attack on the delocalized ion requires that the cis isomer be formed.

(11) D. I. Schuster, J. M. Palmer, and S. C. Dickerman, *J. Org. Chem.*, 31, 4281 (1966).

(12) H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.*, 81, 4256 (1959).

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

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

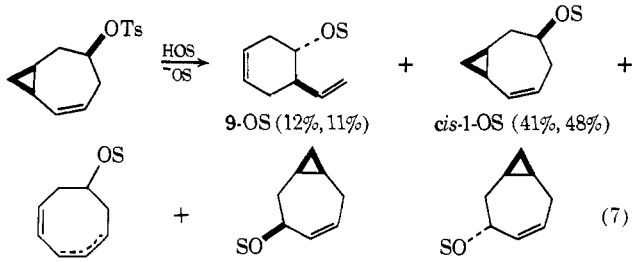
too rapid for such measurements. The rate constants at three temperatures for both solvents are given in Table I. Duplicate runs were made at each point, and

Table I. Rate Constants for the Solvolysis of *cis*-Bicyclo[5.1.0]oct-5-en-3-yl Tosylate (*cis*-**1**-OTs)

Solvent	Temp, °C	k, sec^{-1}	Corr coeff
CH_3CO_2H–CH_3CO_2Na	25.0	6.57×10^{-6}	0.998
	35.0	3.11×10^{-5}	0.998
	45.0	7.09×10^{-5}	0.999
HCO_2H–HCO_2Na	17.5	6.14×10^{-4}	0.999
	25.0	1.58×10^{-3}	0.999
	32.5	3.85×10^{-3}	0.997

the reported rates are the resulting mean. The reaction is about 600 times faster in formic acid than in acetic acid at 25°. The activation parameters (25°) obtained from these rate constants in buffered acetic acid are: $E_a = 22.5 \pm 0.5$ kcal/mol, $\Delta H^{\ddagger} = 21.9 \pm 0.5$ kcal/mol, $\Delta S^{\ddagger} = -8 \pm 4$ eu, $\Delta G^{\ddagger} = 24.5 \pm 0.5$ kcal/mol; the parameters in buffered formic acid are $E_a = 21.6$ kcal/mol, $\Delta H^{\ddagger} = 21.0$ kcal/mol, $\Delta S^{\ddagger} = -1$ eu, $\Delta G^{\ddagger} = 21.3$ kcal/mol.

For product analyses, samples were allowed to react in the buffered solvent for 5 half-lives. Samples run for 20 to 40 half-lives showed no alteration in the product distribution, so internal return to a more slowly reacting tosylate need not be considered. The reaction products were analyzed directly as the esters. To aid in identification of the products, the reaction mixture was reduced with lithium aluminum hydride, and these unsaturated alcohols were hydrogenated with Adams catalyst, which does not open the three-membered ring. Finally, the saturated alcohols were oxidized with the Jones reagent to the saturated ketones. Complete spectral and chromatographic analysis of the products was carried out at each step of this sequence. The observed products and their respective percentages in acetolysis (first figure under the structure) and formolysis (second figure) are given in eq 7,



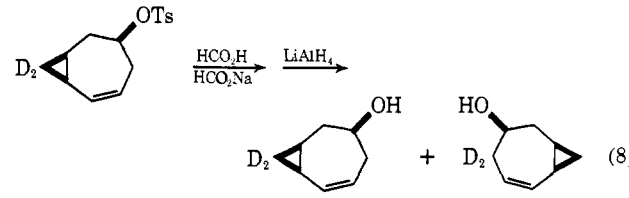
9-OS (12%, 11%) *cis*-**1**-OS (41%, 48%)

10-OS (15%, 11%) *cis*-**7**-OS (22%, 16%) *trans*-**7**-OS (10%, 14%) (7)

arranged in order from the shortest to the longest vpc retention time. There were no products from internal return (rearranged tosylates) or from elimination (dienes). The structure proofs for all the products except *cis*-**7** have been given elsewhere.[15] The structure of *cis*-**7**-OH, formed by reduction of the product ester, was proved by hydrogenation to the known *cis*-**8**-OH, and by manganese dioxide oxidation (specific for allylic alcohols) to the corresponding α,β-unsaturated ketone. Only structure *cis*-**7** can accommodate these observations. All the products were subjected to the conditions of the reaction and found to be stable. The three isomeric tricyclo[5.1.0.0^{3,5}]octan-2-ols (**5**-OH) were prepared[15] and found to be absent in the reaction mixture of *cis*-**1**-OTs. Trifluoroacetolysis produces almost entirely the hydride-shifted product **9**-OTFA.

Four brief observations should be made at this point, before continuing with a description of other experimental results. (1) The major product is *cis*-**1**-OS, corresponding to the starting alcohol with retained stereochemistry. (2) If any *trans*-**1**-OS is formed, it is a very minor product. (3) A portion of the products must come from hydride-shift pathways (**9** and **10**). (4) No tricyclic ester **5**-OS is formed, but a significant amount of the allylic ester *cis*-**7**-OS is observed (Scheme I).

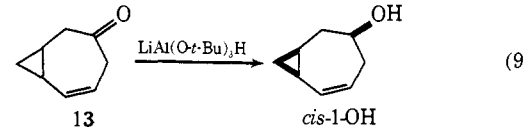
To learn more about the mechanism by which *cis*-**1**-OS is formed, we prepared and solvolyzed (buffered formolysis) the 8,8-dideuterio derivative of *cis*-**1**-OTs (eq 8). The fraction corresponding to *cis*-**1** was col-



(8)

lected and examined for deuterium content. The appearance of the expected proportion of cyclopropyl proton in the spectrum of *cis*-**1**-OH showed that scrambling had in fact occurred. A more detailed analysis of the deuterium content was obtained from ^{2}H resonance spectra.[16] The ^{2}H spectrum of the product *cis*-**1**-OH-d_2 showed there to be experimentally equal amounts of deuterium on the two carbon atoms indicated in eq 8. Since the deuterium atoms on both these carbons are nonequivalent, four deuterium resonances of equal area (two cyclopropyl and two allylic) were actually observed.

Finally, some information about the steric environment at the 3-position in *cis*-**1** was obtained from reduction of bicyclo[5.1.0]oct-5-en-3-one (**13**, eq 9).



13 *cis*-**1**-OH (9)

This ketone was prepared by the Barton oxidation of *cis*-**1**-OH. Reduction with the bulky lithium aluminum tri-*tert*-butoxyhydride yielded only *cis*-**1**-OH, without a trace of *trans*-**1**-OH, which was available for purposes of comparison. Similar results were obtained with lithium aluminum hydride and sodium borohydride. To produce the cis isomer, hydride must enter from the side of the molecule opposite to the cyclopropane ring, and this face is therefore indicated to be less sterically hindered than the cis face. Consequently, in the solvolysis reaction, the solvent must enter from the more hindered side to form the retained product *cis*-**1**-OS.

Discussion

Kinetic Studies. Since the objective of this research was to determine which mode of participation

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

(16) We are indebted to Professor John Grutzner, Purdue University, for these deuterium spectra, taken on a Varian XL-100.

(double bond or cyclopropane) is preferred in the solvolysis of *cis*-**1**-OTs, the first order of business is to establish that there is indeed some form of participation. One approach is to compare the observed rate with that calculated from the carbonyl stretching frequency in the corresponding ketone (ν_{CO} 1713 cm^{-1}) according to the method of Schleyer and Foote.[17] The observed rate at 25° in acetic acid–sodium acetate (6.57×10^{-6} sec^{-1}) is more than two orders of magnitude larger than the calculated rate. Such a factor is indicative of a modest anchimeric assistance. A second approach is to compare the solvolysis rate of *cis*-**1**-OTs with that of an entirely saturated model compound. Cycloheptyl tosylate should solvolyze without anchimeric assistance since it lacks unsaturated functionalities. Comparison of the rates shows that *cis*-**1**-OTs solvolyzes twice as fast as cycloheptyl tosylate,[18] despite the presence in *cis*-**1** of the electron-withdrawing double bond and cyclopropane ring, which are rate retarding.

The presence of participation can also be inferred from examination of the stereochemistry of the products. The major component in the reaction is *cis*-**1**-OS, for both acetolysis and formolysis. Retained stereochemistry is not consistent with a nucleophilic displacement by solvent (k_s). Common rings without unsaturated functionalities, such as cyclohexyl tosylate, acetolyze by a k_s mechanism with complete inversion.[19] The observation of retention in the solvolysis of *cis*-**1**-OTs is therefore strong evidence for a k_Δ (participation) pathway.

Similar conclusions come from consideration of the reduction of the ketone that corresponds to **1** (eq 9). The ketone can be used as a model for the classical carbonium ion that would be obtained from *cis*-**1**-OTs by a "k_C" process, since the ketone is sp^2 hybridized at the 3-position. The fact that hydride reduction produces only the cis alcohol establishes that, as expected, the face of the ketone that is trans to the cyclopropane ring is sterically less hindered. Nucleophilic solvent attack on a localized carbonium ion intermediate should therefore also occur on the trans face to form *trans*-**1**-OS. The observed formation of the sterically less favored *cis*-**1**-OS is therefore best explained in terms of backside solvent attack on the partial bond in the delocalized intermediates **4** or **6** (positions a and c, respectively, in Scheme I).

The remaining point to be gleaned from the kinetic studies concerns the activation parameters. The enthalpy of activation for the solvolysis of *cis*-**1**-OTs is about 22 kcal/mol. The barrier to interconversion of the two conformers, **2** and **3**, is probably much less than 10 kcal/mol, by comparison with other rings of this general size (cycloheptatriene, cyclooctane, and cyclooctadiene).[20] It is our aim to use product distribution to indicate the proportion of double bond and cyclopropane participation, *i.e.*, the proportion of molecules reacting by conformations **2** and **3**. Provided that the activation energy for the reaction is much larger than the barrier to interconversion between the conformers, the ratio of products from the two pathways depends

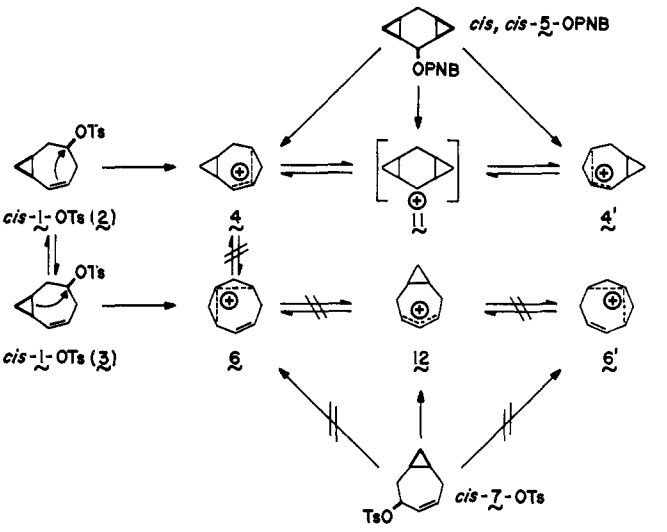
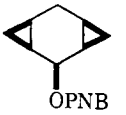


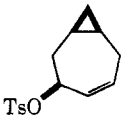
Figure 1. The relationships among the ions produced by the solvolyses of *cis*-**1**-OTs, *cis,cis*-**5**-OPNB, and *cis*-**7**-OTs. Vertical equilibration of the ions (not found) would involve the transformation of **4**, **11**, or **4'** into **6**, **12**, or **6'**. Horizontal equilibration would involve the interconversion of the mirror-image pairs: **4** ⇌ **4'** or **6** ⇌ **6'**.

only on the difference between the transition-state energies (the "Curtin–Hammett principle").[21] The observed activation energy to solvolysis is 2–3 times as large as the barrier to ring interconversion, so the Curtin–Hammett principle holds. The fact that the stable conformation **3** must first interconvert to **2** before double bond participation can occur is therefore not relevant. Observation of products that can be designated as having arisen specifically from **2** or **3** can serve as a direct measure of the difference in transition-state energies for the two modes of participation.

Product Studies. Preliminary analysis of the products, according to the method outlined in the discussion of Scheme I, does not yield clear-cut results. The expected product from cyclopropane participation, the allylic *cis*-**7**-OS, is present to the extent of about 20%. The expected product from double bond participation, the tricyclic **5**-OS, is completely absent. The remainder of the mixture consists of *cis*-**1**-OS (~45%) and various hydride-shift products (~35%),[22] none of which can be assigned to a particular participation pathway without additional experimentation. In order to determine the source of these ambiguous products, we prepared materials that enter the ionic manifold at different, but well-defined points. Figure 1 presents a complete illustration of the ionic manifold pertinent to this study. *cis,cis*-Tricyclo[5.1.0.0^{3,5}]oct-2-yl *p*-nitrobenzoate[15] (*cis,cis*-**5**-OPNB) solvolyzes directly to the tricyclic ion **11** (Figure 1) or possibly to the homoallylic species **4** and **4'**, all of which reside in the upper ionic



cis,cis-**5**-OPNB

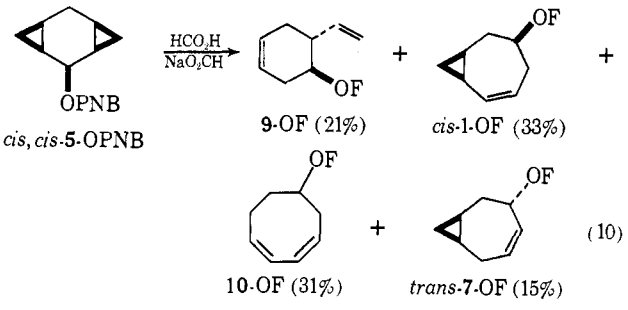


cis-**7**-OTs

(17) C. S. Foote, *J. Amer. Chem. Soc.*, **86**, 1853 (1964); P. v. R. Schleyer, *ibid.*, **86**, 1854, 1856 (1964).
(18) H. C. Brown and G. Ham, *ibid.*, **78**, 2735 (1956).
(19) J. B. Lambert, G. J. Putz, and C. E. Mixan, *ibid.*, **94**, 5132 (1972).
(20) G. Binsch, *Top. Stereochem.*, **3**, 97 (1968).
(21) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, pp 151, 152, 238.
(22) Suggested mechanisms of formation of **9**, **10**, and *trans*-**7** by hydride-shift processes have been given in ref 15.

manifold associated with double bond participation. On the other hand, solvolysis of *cis*-bicyclo[5.1.0]oct-4-en-3-yl tosylate,[23] *cis*-7-OTs, leads directly to the allylic ion **12** in the lower, cyclopropane-participation manifold of Figure 1. The purpose of studying the solvolysis reactions of these two compounds is twofold. (1) The identification of products from these solvolyses may lead to an orderly determination of which products in the solvolysis of *cis*-**1**-OTs come from double bond participation and which come from cyclopropane participation. (2) Observation that *cis,cis*-**5**-OPNB and *cis*-7-OTs give entirely different product mixtures would demonstrate that there is no vertical equilibration (**4**⇌**6**) among the ions in the upper and lower manifolds. Such a demonstration is necessary in order for any sort of product analysis to serve as a measure of double bond *vs.* cyclopropane participation in the solvolysis of *cis*-**1**-OTs.

We have prepared and solvolyzed *cis,cis*-**5**-OPNB and *cis*-7-OTs.[15,23] The products in the formolysis of the tricyclic ester are given in eq 10. Despite the less re-

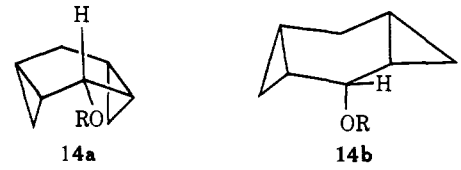


(10)

active leaving group used in the formolysis of *cis,cis*-**5**, the products bear a remarkable resemblance to those from *cis*-**1**-OTs. The major product is *cis*-**1**-OF; all forms of **5**-OF are entirely absent; the remainder of the products can be attributed to hydride-shift processes. The most significant difference between the reaction mixtures from the **1**-OTs and the **5**-OPNB is the complete absence of the allylic isomer *cis*-7-OS in the latter case. This compound is the one we have posited as the indicator of cyclopropane participation. Its absence in the formolysis of *cis,cis*-**5**-OPNB gives strong evidence that the ions formed do not cross over to the lower manifold.[24] The great similarity between the two reaction mixtures, aside from the concentration of *cis*-**7**, indicates that *cis,cis*-**5**-OPNB and conformer **2** of *cis*-**1**-OTs (double bond participation) probably lead to the same ionic intermediates (some combination of **4**, **11**, and **4′** in Figure 1). The reactive conformer of *cis,cis*-**5** is **14a**, in which two cyclopropane bonds are backside to the leaving-group bond.[15] The alternative, and in fact more stable, conformer **14b** does not possess this necessary requirement for cyclopropylcarbinyl participation, and is therefore unreactive. Conformers **2** and **14a**, as can be seen, are very closely related in structure, so it is to be expected that they proceed to a common set of ions. Our previous analysis of the reactivity of *cis,cis*-**5** led us to conclude that solvolysis most likely

(23) J. B. Lambert, F. R. Koeng, and A. P. Jovanovich, *J. Org. Chem.*, 37, 374 (1972).

(24) This argument is not vitiated by the presence of *trans*-7-OS in both reaction mixtures. Only *cis*-7-OS can be formed by solvent attack on the delocalized ion **6** (Scheme I), so its concentration is the significant factor. The trans isomer may result from a hydride-shift process.[22]

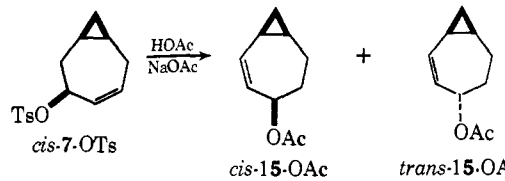


14a **14b**

gives the homoallylic ion (**4**, **4′**) directly.[15] Furthermore, this ion (or set of ions) does not equilibrate with those ions from cyclopropane participation that produce the *cis*-7-OS product (**4**, **11**, **4′**⇌**6**, **12**, **6′**). This condition is recognized explicitly by the lines drawn through the reversible arrows connecting **4** and **6** in Figure 1.

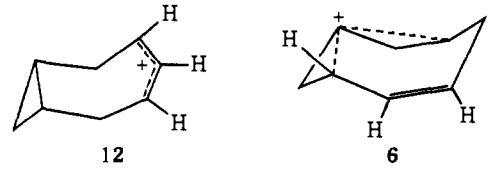
It is interesting that formolysis of *cis,cis*-**5**-OPNB produces no material corresponding to the starting tricyclic structure **5**. This structure, it will be recalled, was the original suggestion for an indicator of double bond participation. Its absence in the reaction mixture from *cis*-**1**-OTs is thus not relevant to the question, since formolysis of even the less reactive *p*-nitrobenzoate of *cis,cis*-**5** gives no **5**-OF. The experiments with **5** have therefore given us two very important pieces of information. (1) There is no crossover between the upper (double bond participation) and lower (cyclopropane participation) manifolds of Figure 1, since entrance directly into the upper manifold *via* *cis,cis*-**5**-OPNB does not give *cis*-**7**-OS. (2) The portion of the *cis*-**1**-OTs solvolysis products composed of retained starting material and the hydride-shift products can be derived entirely from the upper (double bond participation) ionic manifold, since they are obtained in similar proportions from the solvolysis of *cis,cis*-**5**-OPNB. If these products are attributed entirely to double bond participation in *cis*-**1**-OTs, then at this stage in the analysis, one can assign about 20% of the products to cyclopropane participation and 80% to double bond participation.

It remains to examine the solvolytic properties of *cis*-7-OTs, which should enter the lower (cyclopropane participation) ionic manifold directly at ion **12**. We have prepared and solvolyzed this compound,[23] and found to our initial surprise that the only products from acetolysis are similar amounts of *cis*- and *trans*-bicyclo[5.1.0]oct-2-en-4-yl acetate (**15**, eq 11). Neither



(11)

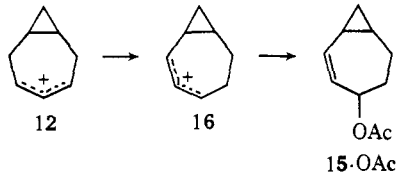
the expected allylic isomer corresponding to this starting material, **7**, nor the various products attributed to double bond participation (*cis*-**1**, **9**, **10**) were observed. The reasons for these observations become clear when the conformation of ion **12** is examined. The ion that is produced from conformer **3** of *cis*-**1**-OTs (**6**) has one



12 **6**

hydrogen atom orthogonal to the plane of the adjacent

double bond, whereas in the allylic ion **12**, produced from *cis*-**7**-OTs, these three hydrogen atoms must necessarily be in a plane. The favored pathway for decomposition of **12** leads to the more stable allylic ion **16** (eq 12),[23] rather than to the less stable bishomoallylic



(12)

ion **6**, a process that would require destruction of the allylic system. The observed *cis*-**7** in the solvolysis of *cis*-**1**-OTs cannot then derive from ion **12**, but must come directly from the homoconjugated species **6** (Scheme I, Figure 1). The absence of **15** in the reaction mixture of *cis*-**1**-OTs furthermore demonstrates that ion **6** does not isomerize to the more stable allylic ion **12**, as indicated by the lines through the reversible arrows in Figure 1. Ion **12** appears to reside in an entirely isolated portion of the $C_8H_{11}^+$ energy surface. Isomerization of **12** to **6** is energetically unfavorable because of disruption of the allylic system; vertical isomerization of **12** to the tricyclic ion **11** is an orbital-symmetry forbidden ${}_{\sigma}2_s + {}_{\pi}2_s$ process.[23] A corollary of these considerations is that complete horizontal equilibration in the lower manifold (**6**⇌**6′**) is not possible, since the process would have to pass through **12** and hence be shunted to **16** and finally to the unobserved **15**-OS (eq 12). The experiments with *cis*-**7**-OTs have thus accomplished two goals. (1) They have shown that ion **12** is not involved in the solvolysis of *cis*-**1**-OTs, so that the mirror images **6** and **6′** cannot equilibrate. (2) The product *cis*-**7**-OS must then derive directly from ion **6**.

Horizontal equilibration in the upper ionic manifold between the mirror-image forms **4** and **4′**, on the other hand, is expected to occur rapidly. This difference between the upper and lower ionic manifolds provides a handle to determine the source of the major product in the solvolysis of *cis*-**1**-OTs, which corresponds to starting material with retained stereochemistry. For material that passes through the upper manifold (double bond participation), deuterium placed at the 8 position should equilibrate between the 8 and 4 positions. For material that enters the lower manifold (cyclopropane participation), however, it should remain exclusively in the 8 position. Tosylate that was so labeled produced formate ester with the label scrambled between the 4 and 8 positions, according to analysis by both proton and deuterium spectra. This observation confirms our previous conclusion that the major product *cis*-**1**-OS comes entirely from the pathway involving double bond participation.

Summary and Conclusions

Both conformers of *cis*-**1**-OTs give rise to demonstrable portions of the solvolytic products. Conformer **2** leads by double bond participation to the homoallylic ion **4** (**4′**), which reacts with solvent to give the product *cis*-**1**-OS with retained stereochemistry and to various products arising from hydride-shift pathways. These products comprise about 80% of the total. The solvolysis of *cis,cis*-**5**-OPNB leads to a nearly identical

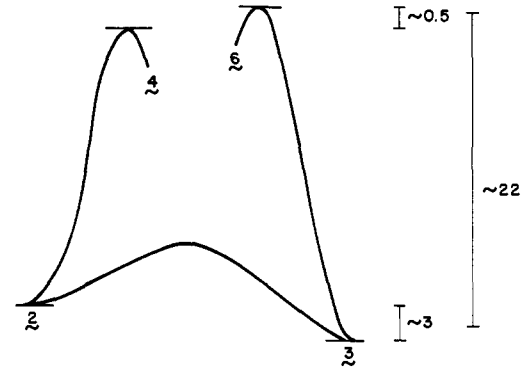


Figure 2. The relative ground-state and transition-state energies determined in this study (not drawn to scale but labeled at the right in kcal/mol).

set of products, so that similar ionic intermediates are implicated.[15] Conformer **3** leads by cyclopropane participation to the bishomoallylic ion **6**, which reacts with solvent to give *cis*-**7**-OS (about 20% of the total). Since none of this material was obtained in the solvolysis of *cis,cis*-**5**-OPNB, the ionic manifolds that are produced by double bond and cyclopropane participation do not equilibrate. Solvolysis of *cis*-**7**-OTs leads directly to ion **12** in the lower manifold (Figure 1). This ion, however, rearranges to the more stable ion **16** and thence to **15**-OS (eq 12). Ions **6** and **12** thus are not in equilibrium. Deuterium exchange between the 8 and 4 positions of the product *cis*-**1**-OS therefore can only arise by interconversion of the mirror-image ions **4** and **4′**, rather than **6** and **6′**. The observed scrambling of deuterium between the two positions requires that the product *cis*-**1**-OS come entirely from the upper ionic manifold (double bond participation).

The fact that 80% of the product arises from conformer **2** and 20% from conformer **3** implies that the transition state for double bond participation is about 0.5 kcal/mol lower in energy than the transition state for cyclopropane participation.[21] The difference in activation energies reflects not only the transition-state difference but also the ground-state difference. Conformer **2** is destabilized by 2–4 kcal/mol with respect to **3** because of the strong prow–prow nonbonded interaction. The higher energy conformer has the lower energy transition state. This state of affairs is illustrated in Figure 2. The net difference in activation energies is thus the sum of the ground-state and transition-state differences, or about 3–5 kcal/mol. For this system, in which the two modes of participation are in competition, participation by the double bond is strongly favored.

The conclusions drawn from these experiments are only appropriate to the particular geometry that relates the participating functionalities and the leaving group in **2** and **3**. The relative orientation between the double bond or cyclopropane ring and the tosylate group in **2** and **3** is quite different from those in eq 3 and 4. The dominance of double bond participation in *cis*-**1**-OTs contrasts to the results for the polycyclic systems of eq 3 and 4, to other similar situations,[25]

(25) M. A. Battiste, J. Haywood-Farmer, H. Milkus, P. Seidl, and S. Winstein, *J. Amer. Chem. Soc.*, **92**, 2144 (1970); G. D. Sargent and M. A. Herkenham, *ibid.*, **94**, 2892 (1972).

and to some HMO calculations.[26] In yet other cases, however, cyclopropane participation is weaker.[6,27] The conclusions relevant to a given system are therefore critically dependent on the orientation between the participating functionality and the leaving group, and on the amount of angle strain in the cyclopropane ring that can be relieved in the transition state. Conclusions cannot be transferred from system to system without appropriate geometric considerations.

Experimental Section

Infrared spectra were taken on a Beckman IR-5 spectrophotometer. Nmr spectra were measured on Varian Associates A-60 and T-60 spectrometers. A Consolidated Electrodynamics Corp. 21-104 mass spectrometer was used for the mass spectral work. Analytical vapor phase chromatograms were obtained from Hewlett-Packard F & M Scientific Model 700 and Varian Associates Aerograph Series 1520B instruments. Preparative vpc work was performed on the Hewlett-Packard instrument. Elemental analyses were performed by Miss Hildegard Beck of the Northwestern University Chemistry Department Analytical Services Laboratory.

3,5-Cycloheptadien-1-ol was prepared from cycloheptatriene *via* tropone according to the method of Schuster, *et al.*[11]

Zinc-Copper Couple. Zinc (50 g) was placed in a 150-ml sintered-glass funnel and washed with the following solutions, 1 min each, taking great care during each washing to break up all chunks with a glass rod: 4 × 50 ml of 3% aqueous HCl; 5 × 100 ml of distilled H_2O; 2 × 70 ml of 2.5% aqueous copper sulfate; 5 × 100 ml of distilled H_2O; 4 × 100 ml of absolute ethanol; 5 × 100 ml of anhydrous ether. The zinc–copper couple was dried in a vacuum desiccator over P_2O_5.

***cis*-Bicyclo[5.1.0]oct-5-en-3-ol (*cis*-1-OH).** In a 500-ml three-necked flask equipped with a magnetic stirrer, pressure-equalized addition funnel, reflux condenser capped with a drying tube, and a heating mantle were placed 200 ml of anhydrous ether, 26.2 g (0.403 mol) of Zn–Cu couple, and 86.2 g (0.322 mol) of CH_2I_2. The mixture was refluxed with stirring for 2 hr and cooled. 3,5-Cycloheptadien-1-ol (20 g, 0.161 mol) in 50 ml of ether was added dropwise at such a rate that the ether refluxed gently. After the addition, the mixture was refluxed with stirring for 6 hr, cooled, and filtered. The ether solution was washed with 5 × 50 ml of saturated aqueous NH_4Cl, 5 × 50 ml of saturated aqueous $NaHCO_3$, and 3 × 50 ml of saturated aqueous NaCl, and then dried over anhydrous $MgSO_4$. The ether was removed under vacuum. The crude product was analyzed by vpc on a $^1/_8$ in. × 20 ft 11% Carbowax 20M on Chromosorb G acid-washed DMCS column at 180°, 30 ml/min flow rate. A shoulder on the longer retention time side of this peak indicated the presence of any *trans*-1-OH. If present, the trans isomer was removed by silica gel column chromatography (40 g of silica gel per 1.0 g of crude product) using a 25% ether–hexane solvent mixture. Appearance of the products, first cis then trans alcohol, was followed by vpc. This purification step was seldom necessary, since the trans isomer was normally absent. Pure cis product was recovered by removal of the solvent and careful distillation through a 9-in. vacuum-jacketed, silvered, helix-filled microcolumn with a cold-finger take-off head to yield 13.5 g (60%) of a clear viscous oil: bp 65° (3 mm); nmr (CCl_4) δ 0.0 (m, secondary cyclopropyl protons), 0.52–1.4 (m, tertiary cyclopropyl and methylene protons), 1.7–3.0 (m, allylic methylene protons), 3.9 (m, proton α to the hydroxyl), 4.35 (s, OH), and 5.5–5.9 (m, alkenic protons); ir 3275 (s), 3050 (m), 2985 (s), 2900 (s), 1660 (m), 1448 (s), 989 (s), 846 (s), and 694 (s) cm^{-1}; molecular weight (mass spectral) *m/e* 124 (parent peak). *Anal.* Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 76.57; H, 9.62.

***cis*-Bicyclo[5.1.0]oct-5-en-3-yl Tosylate (*cis*-1-OTs).** Pyridine was refluxed over tosyl chloride, distilled, refluxed over CaH_2, and again distilled. In 158 ml of dried pyridine was dissolved 9.4 g (0.076 mol) of *cis*-1-OH. The solution was cooled to 0° and 14.4 g (0.076 mol) of *p*-toluenesulfonyl chloride (recrystallized twice from ether) was added. The resulting solution was allowed to react at 0° for 24 hr until a large amount of pyridinium hydrochloride had crystallized out. The solution was then poured into 600 ml of pentane. The pentane solution was washed with 3 × 100 ml of 1.0 *M* HCl and with 1 × 100 ml of saturated aqueous NaCl and dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum. The resulting clear oil was crystallized out of pentane at Dry-Ice temperature five times and then dried under high vacuum for 1 hr, yielding 12.1 g (60%) of pure tosylate, mp ~16°. Thin layer silica gel chromatography showed one component: nmr ($CDCl_3$) δ 0.0 (m, secondary cyclopropyl protons), 0.46–1.60 (m, tertiary cyclopropyl and methylene protons), 1.76–2.82 (m, allylic protons), 2.54 (s, CH_3), 4.53–5.92 (m, alkenic protons), and 7.63 (AB q, aromatic protons); ir 3060 (w), 2995 (m), 2940 (m), 2875 (w), 1654 (w), 1360 (s), 1178 (s), 906 (s), 817 (s), and 665 (s) cm^{-1}.

Product Studies. In 15 ml of solvent, buffered (0.1 *M*) or unbuffered, was dissolved 0.4 g of *cis*-bicyclo[5.1.0]oct-5-en-3-yl tosylate (a solution 0.1 *M* in tosylate), and the reaction was allowed to run for 5 half-lives. The reaction mixture was then poured into 100 ml of saturated aqueous NaCl and the products were removed by extraction with five 40-ml portions of ether. The combined ether extracts were washed with 50-ml portions of saturated aqueous $NaHCO_3$ until neutral and once with saturated aqueous NaCl and dried over anhydrous $MgSO_4$; the solvent was removed under vacuum. The products were analyzed at this stage by vapor phase chromatography. The recovered products were dissolved in 25 ml of anhydrous ether and refluxed with 0.5 g of $LiAlH_4$ for 2 hr. The reaction was neutralized by dropwise addition of 0.5–2.0 ml of water. The solution was filtered, and the ether was removed under vacuum. These alcohol products were collected by preparative vpc. Structure proofs have been given elsewhere.[15]

Columns Used for Gas Chromatographic Experiments. Analyses utilized a $^1/_8$ in. × 20 ft column, 11% Carbowax 20M on 70–80 Chromosorb G acid-washed DMCS, at 165–185° with a flow rate of 30 ml/min, and a $^1/_8$ in. × 6 ft column, 5% silicone gum rubber SE-30 on 60–80 Chromosorb G acid-washed DMCS, at 120–150° with a flow rate of 30 ml/min. Preparative vpc work utilized a 0.5 in. × 12 ft column, 10% silicone gum rubber SE-30 on 70–80 Chromosorb G acid-washed DMCS, at 130–160° with a flow rate of 175–240 ml/min, and a 0.5 in. × 12 ft column, 9% FFAP on 60–80 Chromosorb B, at 185° and a flow rate of 175–240 ml/min.

Manganese Dioxide Oxidation.[28] In 25 ml of reagent $CHCl_3$ were dissolved 0.5 g of dried *cis*-7-OH and 1.0 g of MnO_2. The mixture was stirred and refluxed for 3 days and cooled; the MnO_2 was filtered off and the solvent air-evaporated to leave the oxidized product. Although this procedure was successful in the oxidation of *cis*-7-OH, the nonallylic *cis*-1-OH was found to be inert.

***cis*- and *trans*-3-Bicyclo[5.1.0]octanol (8-OH).** To 25 ml of ethyl acetate were added 2.0 g of *cis*-bicyclo[5.1.0]oct-5-en-3-ol (*cis*-1-OH) and 80 mg of platinum oxide catalyst. The stirred mixture was hydrogenated at atmospheric pressure for 5 hr. The solution was then filtered and the solvent air-evaporated to yield a clear oil, which contained only one component by vpc analysis (*cis*-8-OH). A sample purified by preparative vpc was allowed to react with phenyl isocyanate to give a phenylurethane, mp 98.0–98.4° (lit.[14] 98.0–98.5°). A sample of *trans*-1-OH, obtained by the column chromatographic method described above, was hydrogenated in a similar fashion to give *trans*-8-OH, phenylurethane mp 75–76° (lit.[14] 76–77°).

Bicyclo[5.1.0]oct-5-en-3-one (13). Phosgene gas was bubbled slowly through 30 ml of ether, chilled to 0° and contained in a 100-ml graduated cylinder, until about 2.5 ml had collected. Meanwhile, 0.65 g of quinoline was dissolved in 30 ml of anhydrous ether in a 200-ml three-necked flask equipped with a magnetic stirrer and a condenser. This solution was cooled to 0°, and the phosgene–ether mixture was added. Quinoline hydrochloride precipitated immediately. A solution of 2.0 g of *cis*-bicyclo[5.1.0]oct-5-en-3-ol (*cis*-1-OH) in 35 ml of anhydrous ether was added dropwise to this mixture, which was stirred at 0° for 3 hr. The solution was allowed to return to room temperature and to sit overnight. The mixture was filtered to remove the hydrochloride and then stirred in the hood for 2 days for the last vestiges of phosgene to evaporate. The solvent was then removed by rotary evaporation to give the crude chloroformate. Anhydrous dimethyl sulfoxide (16 ml, previously heated over CaH_2 at 65–70° for 2 hr and distilled under vacuum), cooled to 15°, was added, and the mixture was stirred for 20 min, until CO_2 evolution ceased. Triethylamine (14.2 ml, previously refluxed overnight with CaH_2 and distilled) was added, and the solution was stirred for 15 min. Ether (150 ml) was added, and the organic solution was poured over 150 ml of

(26) R. Hoffman, *Tetrahedron Lett.*, 3819 (1965).

(27) G. D. Sargent, R. L. Taylor, and W. Demisch, *ibid.*, 2275 (1968); A. K. Colter and R. C. Mussor, *J. Org. Chem.*, **30**, 2462 (1965); K. B. Wiberg and G. R. Wenzinger, *ibid.*, **30**, 2278 (1965).

(28) L. F. Fieser and M. Fieser, "Reagents in Organic Synthesis," Vol. 1, Wiley, New York, N. Y., 1967, pp 637–643.

aqueous NaCl. The ether layer was washed consecutively with saturated NaCl solution, 2 *N* HCl, and saturated NaCl solution and dried over $MgSO_4$. After filtration, the solution was stripped of solvent to give 1.75 g of the ketone. Reduction of this ketone with $LiAlH_4$, $NaBH_4$, or $LiAl(O\text{-}t\text{-}C_4H_9)_3H$ produced exclusively *cis*-**1**-OH. The ketone is very sensitive to both acid and base. This procedure[29] was used because contact with base is kept to a minimum. The Jones, Sarett, Oppenauer, and Moffatt procedures failed.

Kinetic Runs. Buffered formolyses and acetolyses were run in solutions 0.10 *M* in sodium formate and sodium acetate, respectively. A 10-ml solution, 0.10 *M* in tosylate (*cis*-**1**-OTs), was prepared by dissolving 0.278 g (1 mmol) in 10 ml of buffered solvent already equilibrated in a bath at the desired temperature. At specific times, 1-ml portions of this solvolysis solution were pipetted into 10 ml of dioxane and the resulting solution was titrated with 0.01 *N* perchloric acid in acetic acid to a bromphenol blue end point (yellow to clear).

The acetic acid solvent mixture was prepared by refluxing acetic acid with 5% acetic anhydride for 24 hr, distilling the dried acid, and adding acetic anhydride to make the solution 1% in anhydride. Formic acid was dried by refluxing over boric anhydride for 24 hr, followed by distillation. The 0.01 *N* perchloric acid in acetic acid was prepared by mixing 70% perchloric acid, acetic acid–1% anhydride, and enough acetic anhydride to neutralize the water. This solution was then allowed to stand for 2 days before use. The indicator was a saturated solution of bromphenol blue in acetic acid–1% anhydride.

(29) D. H. R. Barton, B. J. Garner, and R. H. Wightman, *J. Chem. Soc.*, 1855 (1964).

Catalysis of the Dedeuteration of Isobutyraldehyde-*2-d* by Linear Diamines Including 1-Dimethylamino-8-amino-2-octyne, a Bifunctional Catalyst[1a]

Jack Hine,* Jesse L. Lynn, Jr.,[1c] James H. Jensen, and Frank C. Schmalstieg

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Abstract: The catalytic activity of monoprotonated diamines of the type $Me_2N(CH_2)_nNH_2$ (n = 2–5) in the dedeuteration of isobutyraldehyde-*2-d* in water increases monotonically with n, *i.e.*, with the basicity of the catalysts. In 50% aqueous methanol monoprotonated hexane-1,6-diamine, undecane-1,11-diamine, and dodecane-1,12-diamine are of about equal catalytic activity. None of the preceding diamines is believed to act as a bifunctional catalyst to a major extent. The catalytic activity of 1-dimethylamino-8-amino-2-octyne (**2**) was studied in water under conditions where it existed in the monoprotonated and the diprotonated forms to comparable extents. The term in the kinetic equation that was first order in monoprotonated diamine and first order in isobutyraldehyde-*2-d* was about 7.7 times as large as would be expected, from the catalytic activities of 3-dimethylaminopropyne and 1-dimethylamino-2-butyne and other observations, in the absence of bifunctional catalysis. Therefore, the monoprotonated diamine is believed to act largely as a bifunctional catalyst by using its primary amino group to transform the aldehyde to an iminium ion and then removing the deuterium atom of the iminium ion internally by attack of the dimethylamino group. Compound **2** has an advantage over the four ω-dimethylaminoalkylamines that were studied in that it is long enough for its dimethylamino group to reach the deuterium atom in the trans isomer of the intermediate iminium ion.

Earlier papers in this series showed that, in the presence of a primary amine salt and a base, isobutyraldehyde-*2-d* may be dedeuterated by rate-controlling attack of base on the reversibly formed intermediate iminium ion.[2] It therefore seemed plausible

$$Me_2CDCHO + RNH_3^+ \rightleftharpoons Me_2CDCH{=}NHR^+ + H_2O$$
$$Me_2CDCH{=}NHR^+ + B \longrightarrow Me_2C{=}CHNHR + BD^+ \quad (1)$$

that a compound of the type B–R–NH_2 would act as a bifunctional catalyst if the divalent radical R permitted the groups B and NH_2 to have the proper relative geometric orientation. Investigation of the amino acids containing one through five methylene groups between the amino and carboxy groups gave no evidence for bifunctional catalysis.[3] It seemed possible that the failure of these catalysts to act bifunctionally was partly due to the use of the carboxylate anion group, which is known to be relatively ineffective at removing deuterons from isobutyraldehyde-*2-d*,[4] as the basic group. Hence we have studied a similar set of catalysts in which the basic group is an unhindered saturated tertiary amino group, the most effective type for isobutyraldehyde-*2-d*.[4,5] It seemed more likely, however, that the failure of the amino acid catalysts was due to the tendency of the intermediate iminium ion to have a trans configuration **1**. Models show that the R groups used would not be long enough to permit the basic group B to reach the deuterium atom in a trans iminium ion like **1**. Therefore, we have also studied

(1) (a) This work was supported in part by Public Health Service Grants AM 06829 MCB and AM 10378 from the National Institute of Arthritis and Metabolic Diseases. Address correspondence to The Ohio State University. The material related to catalysis by acetylenic amines was abstracted largely from the Ph.D. Dissertation of J. L. Lynn, Jr., 1971. This paper is part XII of the series "Catalysis of α-Hydrogen Exchange." For part XI, see (b) J. Hine, J. C. Kaufmann, and M. S. Cholod, *J. Amer. Chem. Soc.*, **94**, 4590 (1972). (c) National Institutes of Health Predoctoral Fellow (No. FO1 GM38177), 1967–1970.

(2) J. Hine, B. C. Menon, J. Mulders, and J. P. Idoux, *J. Org. Chem.*, **32**, 3850 (1967), and references cited therein.

(3) J. Hine, B. C. Menon, J. Mulders, and R. L. Flachskam, Jr., *ibid.*, **34**, 4083 (1969).

(4) J. Hine, J. G. Houston, J. H. Jensen, and J. Mulders, *J. Amer. Chem. Soc.*, **87**, 5050 (1965).

(5) J. Hine and J. Mulders, *J. Org. Chem.*, **32**, 2200 (1967).