164 (8), 151 (36), 149 (8), 137 (22), 136 (9), 125 (11), 124 (100), 123 (30), 109 (41), 91 (10), 81 (11).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.22; H, 8.16.

Examination of the crude epoxidation product by VPC (SE-30, 140 °C) indicated a 49:1 mixture of **4** and **5**.

Epoxidation of 2 with *m*-Chloroperbenzoic Acid. To a solution of **2** (103 mg, 0.5 mmol) in 1 mL of CH_2Cl_2 was added at 0 °C a solution of *m*-chloroperbenzoic acid (500 mg, 2.5 mmol) in 3 mL of CH_2Cl_2, and the mixture was stirred at room temperature for 72 h. The solvent was evaporated, petroleum ether (bp 30–60 °C) was added, and the *m*-chlorobenzoic acid was removed by filtration. Evaporation of the solvent gave a quantitative yield of **4**, with properties identical with those from the alkaline peroxide oxidation.

Epoxidation of 3. To a solution of **3** (206 mg, 1 mmol) in 2 mL of CH_2Cl_2 was added at 0 °C a solution of *m*-chloroperbenzoic acid (250 mg, 1.23 mmol) in 3 mL of the same solvent. The mixture was stirred at 0 °C for 5 h and evaporated under reduced pressure, and petroleum ether (30–60 °C) was added to the residue. The *m*-chlorobenzoic acid was removed by filtration. The filtrate was washed successively with aqueous sodium bicarbonate and saturated salt solution, dried ($MgSO_4$), and evaporated to give 200 mg of a colorless oil. The crude material was a mixture of two stereoisomers, **4** and **5**, in the ratio of approximately 1:9 (NMR integration). In other preparations, VPC analysis (SE-30, 140 °C) indicated a ratio of about 1:4. The isomers were separated by preparative VPC (6 ft × 0.25 in. column, 15% SE-30 on Chromosorb W, AW-DMCS, 60/80 mesh, 165 °C, 60 mL/min of He) to give **4** (retention time 4 min), identical with that obtained from the epoxidation of **2** (vide supra), and **5** (retention time 4.5 min): IR (neat) 2975 (m), 2940 (m), 2880 (w), 1740 (s), 1470 (m), 1450 (m), 1385 (m), 1375 (m), 1310 (w), 1255 (w), 1215 (m), 1185 (w), 1105 (m), 1080 (m), 1010 (m), 890 (w), 845 (m), 720 (w) cm^{-1}; UV (MeOH) λ_{max} 308 nm (ϵ 50), 218 (830); NMR (CCl_4), see structure; mass spectrum,[19] *m/e* (relative intensity) 222 (2), 164 (10), 151 (39), 149 (10), 137 (23), 136 (10), 125 (11), 124 (100), 123 (33), 109 (42), 91 (11), 81 (12).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.21; H, 8.14.

Similar epoxidation of **3**† gave **4**†, whose spectrum was identical with that of **4** but lacked the singlet at δ 1.45, and **5**†, whose spectrum was identical with that of **5** but lacked the singlet at δ 1.34. Beautiful rhombic single crystals of **5** suitable for X-ray analysis were obtained by recrystallization from cyclohexane and pentane (1:1); mp 72.5–73.5 °C.

Acknowledgment. We are indebted to the National Institutes of Health Grant No. GM 15997 for the financial support of this research. We also thank Dr. Katsuhiko Takagi for preparing crystals of **4** and **5** suitable for X-ray structure determination and for discussions.

Registry No. **1**, 54283-35-1; **2**, 73396-38-0; **3**, 73396-39-1; **4**, 73396-40-4; **5**, 73465-13-1; **6**, 2819-86-5; **8**, 73396-41-5; **10**, 73396-42-6; **11**, 73396-43-7; **12**, 15971-76-3.

Supplementary Material Available: Table I, positional and thermal parameters for **4**; Table II, anisotropic thermal parameters for **4**; Table III, bond lengths for **4**; Table IV, bond angles for **4**; Table V, positional and thermal parameters for **5**; Tables VI, anisotropic thermal parameters for **5**; Table VII, bond lengths for **5**; Table VIII, bond angles for **5** (8 pages). Ordering information is given on any current masthead page.

(19) The mass spectra of **4** and **5** are nearly identical. The base peak at *m/e* 124 corresponds to the tetramethylfuran moiety, for which plausible fragmentation routes are readily apparent. A minor peak is evident at this *m/e* value in the mass spectrum of **2** but not in that of **3**.

Acid-Catalyzed Rearrangements of the Epoxides of Hexamethylbicyclo[3.2.0]hepta-2,5-dienone

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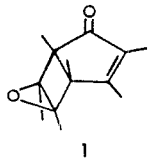
Department of Chemistry, Michigan State University, East Lansing, Michigan 48824

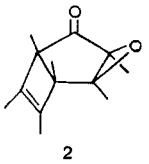
Received March 6, 1979

Epoxy enone **1** rearranges in trifluoroacetic acid (TFA) at 0 °C to hexamethyl-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (**3**). A mechanism involving initial protonation of the carbonyl oxygen of **1**, cleavage of the C–C bond of the epoxide ring, and the intermediacy of a dicyclopropylcarbinyl-type carbocation intermediate is suggested and supported by deuterium labeling. Epoxy enone **2** rearranges in TFA at 0 °C to give products containing the TFA moiety in a form not easily hydrolyzed by base. The products have a structure with a plane of symmetry and are thought to be stereoisomers containing a 7-norbornenone skeleton and an ortho ester type of moiety (**5**). A mechanism involving intramolecular trapping of a carbocation by neighboring trifluoroacetate is suggested to explain the results. Pyrolysis of **3** (500 °C) gives pentamethylphenol.

Epoxy ketones rearrange in acid in a variety of ways.[1] Our interest in these rearrangements[2] prompted us to study the title compounds **1** and **2**, whose synthesis and



1



2

novel photochemical rearrangements were described in the preceding paper.[3] Isomer **1** afforded a new synthesis of the 8-oxabicyclo[3.2.1]octane ring system, whereas isomer **2** resulted in a novel type of product which included in its structure the trifluoroacetic acid (TFA) moiety used to bring about the rearrangement.

Results and Discussion

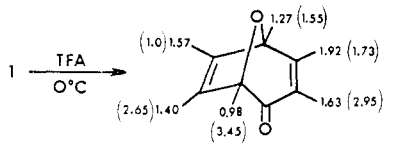
Rearrangement of 1. Treatment of **1** with TFA at 0 °C for a few minutes caused its nearly quantitative rearrangement to an isomer. Longer reaction times gave no further rearrangement. The product was a colorless liquid with a $\nu_{C=O}$ at 1700 cm^{-1} and an NMR spectrum that showed two aliphatic methyl singlets and four vinyl me-

(1) For leading references, see: House, H. "Modern Synthetic Methods", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; p 320.
(2) Hart, H.; Huang, I.; Lavrik, P., *J. Org. Chem.*, **1974**, *39*, 999. Hart, H.; Huang, I., *Ibid.* **1974**, *39*, 1005. Hart, H.; Shih, E.-M., *Ibid.* **1975**, *40*, 1128.

(3) Hart, H.; Chen, S.-M.; Lee, S.; Ward, D. L.; Kung, W.-J., *J. Org. Chem.*, preceding paper in this issue.

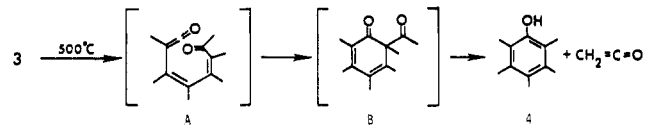
0022-3263/80/1945-2096$01.00/0

thyls, each a quartet with J = 1 Hz, typical of homoallylic coupling. We assign structure **3** to the product, with the NMR assignments (and relative Eu(fod)$_3$ shift slopes) shown on the structure.[4,5]



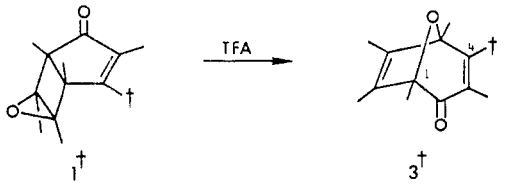
3

Further evidence for the structure of **3** was obtained from its thermal rearrangement. When a benzene solution of **3** was passed through a hot tube at 500 °C the product



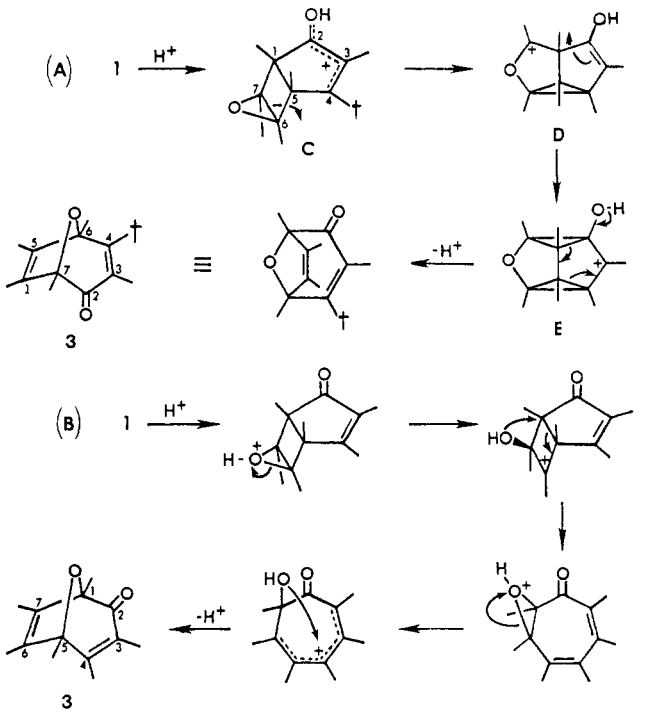
was pentamethylphenol[6] (38% conversion, 100% yield). Presumably the intermediates are the ketene A and dienone B which, at these temperatures, is further pyrolyzed to **4** and ketene. Attempts to isolate B by lowering the pyrolysis temperature failed, and below 350 °C **3** was recovered unchanged. Similar pyrolyses of phenyl-substituted analogues of **3** have been described by Potts.[8]

A labeling experiment helped limit the mechanistic possibilities for the conversion of **1** to **3**. When **1**† labeled with a CD_3 group at C_4[3] was treated with TFA, the resulting **3**† was labeled exclusively at C_4.



Two possible mechanisms which accommodate the labeling result are shown in Scheme I. In mechanism A rearrangement is initiated by protonation of the carbonyl oxygen, whereas in mechanism B the epoxide oxygen is protonated. We believe mechanism A to be the more likely one. It involves extremely favorable intermediates throughout (C is allylic and is stabilized by a terminal

Scheme I



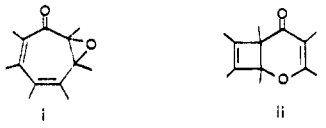
hydroxyl, D has the positive charge α to oxygen and is homoallylic, and E is a dicyclopropylcarbinyl cation). Indeed, mechanism A is reminiscent of those encountered in our earlier work on circumambulation in related systems.[9] The initial protonation on the carbonyl group of **1** required by this mechanism is precedented.[2] Mechanism B, on the other hand, requires in its initial steps generation of a positive charge adjacent to the carbonyl group and a rather novel epoxide "walk" prior to final product formation.

A choice between mechanisms A and B is possible in principle by additional labeling at either C_1, C_5, C_6, or C_7 of the starting epoxy enone, as shown by the small numbers on structures C and **3** in Scheme I. Unfortunately, a simple way of introducing a label in one of these positions is not available.[10]

Rearrangement of 2. Treatment of **2** with TFA at 0 °C for 1 h gave a mixture of two stereoisomeric products as a solid with a broad melting range. Efforts to separate the isomers were unsuccessful. From the mass spectrum and elemental analysis, the products corresponded to an adduct of **2** with trifluoroacetic acid. The IR spectrum showed a strong ν_{OH} at 3400 cm^{-1} and a $\nu_{C=O}$ at 1755 cm^{-1}. The UV spectrum indicated that the carbonyl group was not conjugated. The ^{19}F NMR spectrum of the mixture showed two singlets, one for the CF_3 group in each isomer, and integration of these singlets gave the isomer ratio of 10:9.

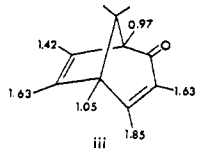
The proton NMR spectrum of the product mixture showed that each component was highly symmetric, with three pairs of equivalent methyl groups. Indeed, the chemical shifts in the two isomers were virtually identical in CCl_4, where the spectrum consisted of two singlets at δ 1.20 and 1.67, in a ratio of 2:1. Shift reagent resolved the spectrum into three equal singlets. In acetone-d_6, however, the separate spectra of two of the three sets of methyls could be observed. One isomer had peaks at δ 1.12, 1.33, and 1.70 and the other at δ 1.15, 1.20, and 1.70.

(4) Alternative structures i and ii which meet the requirements of the NMR data can be ruled out from the $\nu_{C=O}$ which should be below 1660 cm^{-1} for i and at least below 1680 cm^{-1} for ii.



i ii

(5) The NMR spectrum of **3** is very similar to that previously described (Hart, H.; Love, G. M., *J. Am. Chem. Soc.*, **1971**, *93*, 6266) for iii.



iii

(6) Kolka, A. J.; Vogt, R. R., *J. Am. Chem. Soc.*, **1939**, *61*, 1463.

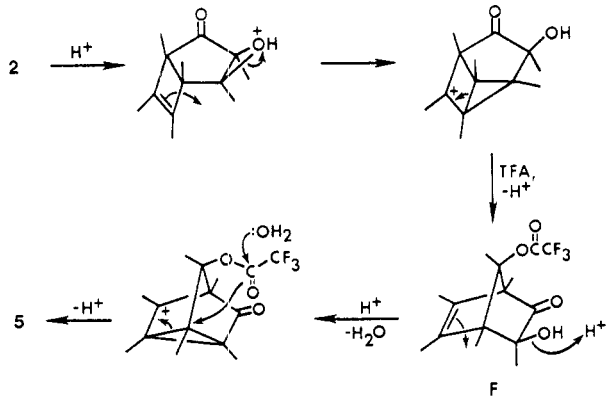
(7) There is ample precedent for such cyclizations: Hobson, J.; Holly, M.; Malpass, J., *Chem. Commun.*, **1968**, 765; Griffiths, J.; Hart, H., *J. Am. Chem. Soc.*, **1968**, *90*, 3297; Quinkert, G., *Angew. Chem., Int. Ed. Engl.*, **1972**, *11*, 1072.

(8) Potts, K. T.; Elliott, A. J.; Sorm, M., *J. Org. Chem.*, **1972**, *37*, 3838.

(9) Hart, H.; Kuzuya, M., *J. Am. Chem. Soc.*, **1976**, *98*, 1551.

(10) We also note that a particular enantiomer of **1** would give different enantiomers of **3**, depending on the mechanism.

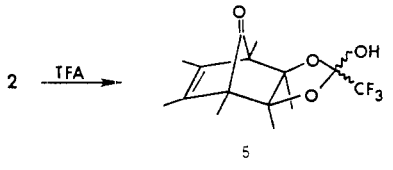
Scheme II



Integration of the two higher field peaks confirmed the 10:9 ratio of isomers.

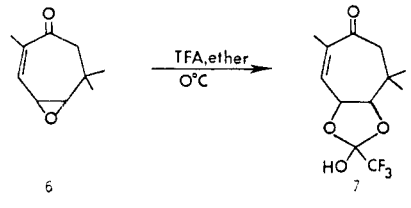
The products were stable toward treatment with aqueous methanolic potassium carbonate, showing that they were not simple esters of trifluoroacetic acid.

On the basis of these data and mechanistic considerations, we suggest that the products are stereoisomers of structure **5**. The carbonyl frequency is consistent with



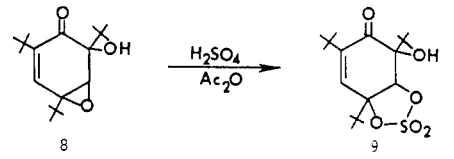
a strained five-membered ring ketone. The presence of only two isomers instead of four and the near equivalence of the methyl chemical shifts suggest that the dioxolane ring has the same configuration in both products, and mechanistic considerations suggest that it should be exo. The structure has the required symmetry and should show two sets of aliphatic methyl signals and one set of allylic methyls with the expected chemical shifts, as observed.

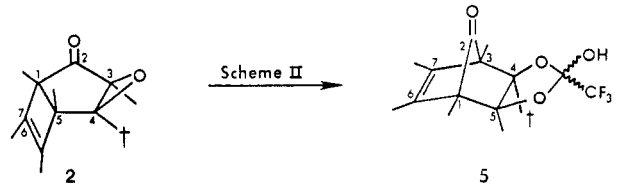
A plausible mechanism for the formation of **5** is shown in Scheme II. A 1,2 vinyl shift, presumably via a cyclopropylcarbinyl intermediate, gives a 7-norbornenyl-type carbocation which is captured stereospecifically by trifluoroacetate to give the intermediate F. Although simple ionization of F would place a positive charge α to the carbonyl group, the ion is also tertiary and norbornenyl.[11] Capture of carbocations by weak nucleophiles such as trifluoroacetic acid is less documented, though we recently isolated a similar product, **7**, from eucarvone epoxide.[12]



Other weak nucleophiles, such as sulfuric acid, can capture carbocations, particularly when the product is cyclic. An example of an epoxide which reacts in this manner is **8** → **9**.[13]

If the mechanism in Scheme II is correct, then a CD_3 group at C_4 in **2** should end up as one of the aliphatic methyls in the product. This requirement was fulfilled experimentally. One can write other mechanisms to explain our results, but we believe the one shown in Scheme II is plausible.





In conclusion, we have described two novel acid-catalyzed rearrangements of epoxy ketones.

Experimental Section[14]

Rearrangement of 1. A solution of **1**[3] (206 mg, 1 mmol) in 3 mL of ice-cold trifluoroacetic acid was stirred at 0 °C for 5 min and then quenched by adding it dropwise to saturated sodium carbonate solution precooled to −5 °C. When monitored by VPC, the reaction was complete within 5 min, and no further changes were observed in several hours. The mixture was extracted with ether, and the combined ether layers were extracted successively with saturated $NaHCO_3$, water, and saturated salt solution and dried ($MgSO_4$). Evaporation of the solvent left 192 mg of a light yellow oil which was purified by preparative VPC (5 ft × 0.25 in. column, 10% SE-30 on Chromosorb W, AW-DMCS 60/80 mesh, 135 °C, 100 mL/min of He, retention time 2 min) to give 185 mg (90%) of **3**: IR (neat) 3000 (m), 2910 (m), 1700 (s), 1660 (m), 1450 (m), 1390 (m), 1330 (m), 1285 (w), 1255 (w), 1225 (m), 1175 (w), 1075 (w), 1025 (w), 995 (w), 925 (w), 900 (w), 850 (w) cm^{-1}; UV (EtOH) λ_{max} 340 nm (ϵ 500), 270 (820), 230 (6500); NMR ($CDCl_3$), see structure; mass spectrum (70 eV), *m/e* (relative intensity) 206 (29), 165 (10), 164 (100), 163 (12), 149 (86), 124 (10), 43 (30).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C 75.53; H, 8.86.

Repetition of this reaction with **1** labeled with a CD_3 group at C_4[3] gave **3**, whose NMR spectrum lacked the quartet at δ 1.92 and had the peak at δ 1.63 sharpened to a singlet.

Pyrolysis of 3. A solution of **3** (100 mg, 0.48 mmol) in 10 mL of benzene was added dropwise over 20 min to a hot tube (1 × 15 cm) packed with glass beads and preheated under N_2 to 500 °C. The flow rate of the carrier gas was 12 mL/min. The pyrolyzate (86 mg after solvent removal) was collected in a dry ice/acetone bath. The NMR spectrum of the crude pyrolyzate integrated for 38% pentamethylphenol (**4**) and 62% recovered **3**. Preparative TLC on silica gel (CH_2Cl_2 eluent) gave 20 mg of pure **4**, identified by melting point, IR, and NMR.[3]

Rearrangement of 2. A solution of **2**[3] (200 mg, 0.97 mmol) in 3 mL of ice-cold trifluoroacetic acid was stirred at 0 °C for 1 h. The reaction was quenched by adding the mixture dropwise to a saturated sodium carbonate solution precooled to 0 °C. The mixture was extracted with methylene chloride, and the combined organic layers were washed successively with aqueous sodium bicarbonate and saturated sodium chloride and dried ($MgSO_4$). Evaporation of the solvent left 220 mg of light brown crystals. An NMR spectrum of the crude product showed it to be 95% **5**. The crude product was recrystallized from methylene chloride to give 198 mg (64%) of white crystals, mp 140–150 °C, considered to be a 10:9 mixture of the two stereoisomers of **5**: NMR (CCl_4) δ 1.20 (s, 12 H), 1.67 (s, 6 H); NMR (acetone-d_6) δ 1.12 (s, 3 H), 1.15 (s, 2.7 H), 1.20 (s, 2.7 H), 1.33 (s, 3 H), 1.70 (s, 5.7 H); ^{19}F NMR (acetone-d_6) δ 84.4, 85.9 (s, upfield from CCl_3F, ratio 10:9); IR (KBr) 3400 (s), 3000 (m), 1755 (s), 1470 (m), 1450 (m), 1430 (m), 1400 (m), 1255 (m), 1220 (s), 1190 (s), 1115 (s), 1080 (s), 1060 (s), 980 (w), 930 (m), 750 (m) cm^{-1}; UV (MeOH) λ_{max} 232 nm (ϵ 590), 214 (1030); mass spectrum (70 eV), *m/e* (relative intensity) 320 (3), 206 (13), 165 (14), 164 (100), 163 (18), 149 (49), 147 (10),

(11) For a recent study of α-keto carbocations in similar systems, see: Creary, X., *J. Org. Chem.*, **1979**, *44*, 3938.
(12) Hart, H.; Gupta, R., unpublished results.
(13) Nishinaga, A.; Wakabayashi, S., *Chem. Lett.*, **1978**, 913.
(14) For general procedures, see the preceding paper.[3]

137 (23), 136 (26), 135 (15), 121 (12), 119 (11), 105 (14), 91 (15), 77 (13), 69 (11).

Anal. Calcd for $C_{15}H_{19}O_4F_3$: C, 56.24; H, 5.97. Found: C, 56.28; H, 5.55.

Repetition of this reaction with **2** labeled with a CD_3 group at C_4[3] gave **5** in which the peak at δ 1.20 (CCl_4) was reduced in area by 25%.

Attempted Hydrolysis of 5. A solution of **5** (46 mg) in 2 mL of 7% potassium carbonate in aqueous methanol (2:5 v/v) was stirred at room temperature for 4 h. Workup gave a quantitative recovery of **5**.

Acknowledgment. We are indebted to the National Institutes of Health (Grant No. GM 15997) for financial support of this research.

Registry No. 1, 73396-38-0; 2, 73396-39-1; 3, 73396-44-8; 4, 2819-86-5; 5, isomer 1, 73396-45-9; 5, isomer 2, 73465-14-2.

General-Acid-Catalyzed Ring Opening of Oxazolidines. Hydrolysis of 2-[4-(Dimethylamino)styryl]-*N*-phenyl-1,3-oxazolidine

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Received December 26, 1979

A cationic Schiff-base intermediate is detectable at pH <10 in the hydrolysis of 2-[4-(dimethylamino)-styryl]-*N*-phenyl-1,3-oxazolidine. Thus, ring opening proceeds with C–O bond breaking, i.e., in the direction which gives the most stable carbonium ion intermediate. Ring opening is hydronium ion catalyzed at low pH and only slightly affected by the protonation state of the *p*-dimethylamino group. From pH 5 to 7.5 ring opening occurs in a pH-independent reaction which probably involves unimolecular C–O bond breaking. At higher pH apparent hydroxide ion catalysis is observed in the reversible ring opening, which reflects reclosure of the ring by attack of the neighboring alkoxide ion on the iminium ion. The value of pK_{eq} for ring opening determined both spectroscopically and from the kinetic data is 8.05. General-acid catalysis occurs in ring opening. Proton transfer and C–O bond breaking are concerted, as shown by the Brønsted coefficient α of 0.53. Concerted general-acid catalysis in these reactions is due to the ease of C–O bond breaking brought about by stabilization of the developing carbonium ion in the transition state. The hydrolysis of the intermediate cationic Schiff base is pH independent in the pH range 8–13 and hydronium ion catalyzed at low pH due to protonation of the *p*-dimethylamino group.

The mechanism of hydrolysis of acetal analogues in which one oxygen is replaced by nitrogen is of considerable importance not only because of the theoretical significance of the general catalysis found in these reactions[1] but also because compounds of this general type are of great biochemical importance. The hydrolysis of glycosylamines[2-4] and nucleosides[2,5-8] has been extensively studied. Glycosylamine hydrolysis appears to proceed via a Schiff-base intermediate,[2,3] but there has been considerable difference of opinion in regard to the mechanism of hydrolysis of nucleosides.[2,5-8]

Oxazolidines (cyclic *N,O*-acetal analogues) hydrolyze rapidly.[1] Ring opening of 2-(substituted phenyl)-*N*-ethyl-1,3-oxazolidines occurs to give a cationic Schiff-base intermediate.[1] Thus, the reaction proceeds with C–O bond breaking even though the nitrogen is quite basic and is protonated at low pH. The ring opening of 2-(*p*-methoxyphenyl)-*N*-ethyl-1,3-oxazolidine was found to be buffer catalyzed,[1] but kinetically equivalent possibilities in those reactions complicated mechanistic interpretation. General-acid catalysis in oxazolidine ring opening would be in accord with the great stabilization of the developing carbonium ion that is possible by the adjoining nitrogen. In the hydrolysis of acetals, ease of bond breaking is a critical feature in giving rise to general-acid catalysis.[9,10] An easily broken C–O bond can be due to a good leaving group[11] or to a highly stabilized carbonium ion,[12] and in both cases general-acid catalysis is found. However, the Schiff-base intermediate in the hydrolysis of 2-(*p*-methoxyphenyl)-*N*-ethyl-1,3-oxazolidine could only be directly observed at pH values less than 4, presumably because at higher pH it is present only at steady-state concentrations. This prevented study of the neutral species reactions. A number of extremely important mechanistic questions remain to be answered. Among these questions are the following. (1) What is the mechanistic significance of the observed general catalysis? (2) Does a neutral-species pH-independent reaction occur at high pH as in the hydrolysis of acetals which are subject to general-acid catalysis?[11,12] Would such a reaction also give a Schiff-base intermediate? (3) How significant is the substituent on nitrogen in directing ring opening? Will a Schiff base also arise from an *N*-phenyl derivative or if there is the possibility of substantial carbonium ion stabilization by the 2-substituent? In order to approach these questions, one must be able to observe oxazolidine ring opening at high pH. The Schiff-base intermediate must therefore be reasonably stable and have a large extinction coefficient, with λ_{max} preferably in the visible portion of the spectrum, so that

(1) Fife, T. H.; Hagopian, L. *J. Am. Chem. Soc.* **1968**, *90*, 1007.
(2) Capon, B. *Chem. Rev.* **1969**, *69*, 407.
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