Stereochemistry, Kinetics, and Mechanism of the Hydrolysis of 3-Azetidinyl Tosylates

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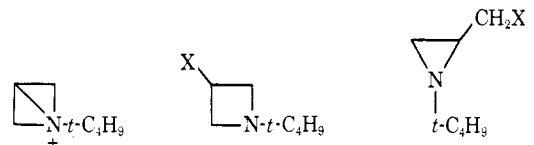
Abstract: The hydrolyses of *cis*- and *trans*-1-*tert*-butyl-2-methyl-3-azetidinyl tosylates (**5** and **6**, respectively) proceed with stereospecific retention of configuration in 60% aqueous acetone. The order of the rates of hydrolysis of **5**, **6**, and 1-*tert*-butyl-3-azetidinyl tosylate (**2c**) is **5** > **2c** > **6**. These facts along with the nonlinearity of the Arrhenius plot for the hydrolysis of **6** are rationalized in terms of anchimeric assistance leading to intermediate 1-azabicyclo[1.1.0]butonium ions as the exclusive mechanism by which **5** undergoes hydrolysis and at least an important mechanism by which **6** undergoes hydrolysis.

Recently several proposals of an intermediate 1-*tert*-butyl-1-azabicyclo[1.1.0]butonium ion (**1**) in the solvolysis reactions of 1-*tert*-butyl-3-azetidinyl tosylate[1,2] and chloride[3,4] have appeared. Deyrup and Moyer[2] explained the formation of **2a** and **2b** from the reaction of **3a** with aqueous ethanol by invoking the intermediate bridged ion **1**. Gaertner, likewise, proposed intermediate **1** for the ring expansion of **3b** to **2a**.[4]

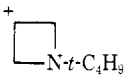


1

2a; X = OH
b; X = OEt
c; X = OTs

3a; X = OTs
b; X = Cl

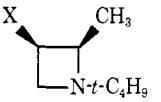
In a previous report[1] from this laboratory it was reported that the rate of the reaction of **2c** with methanolic potassium cyanide is independent of the concentration of cyanide and is equal, within experimental error, to the rate of methanolysis of **2c**, both reactions apparently proceeding through the same cationic intermediate (**1** or **4**). The rate and activation parameters ($\Delta H^{\pm}$ and $\Delta S^{\pm}$) for the hydrolysis of **2c** in 60% aqueous acetone[1] were also compared with those of cyclobutyl tosylates in this solvent;[5] the results of this comparison were interpreted as evidence for the existence of an intermediate bridged ion (**1**) in the solvolysis of the azetidinyl tosylates.



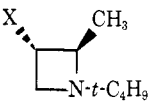
4

Gaertner[4] indicated that ion **4** is incapable of explaining the rearrangement–substitution reaction of **3b** to **2a**, but apparently left unanswered the question of whether or not **4** may be important in the solvolysis of 3-azetidinyl tosylates and halides. In order to gather additional evidence concerning the nature of the intermediate (or intermediates) involved in the solvolysis reactions of 3-azetidinyl tosylates, and in order to investigate the possible synthetic utility of the hydrolysis reactions for the preparation of diastereomeric 2-substituted azetidin-3-ols which are not available by direct synthesis,[6a] the present study was initiated.

The stereochemistry[6b] of the products resulting from the hydrolysis of **5** and **6** in 60% aqueous acetone should



5; X = OTs
7; X = OH



6; X = OTs
8; X = OH

provide valuable information concerning the nature of the mechanism (or mechanisms) involved in these reactions. In the most simple terms, three types of mechanisms merit consideration.

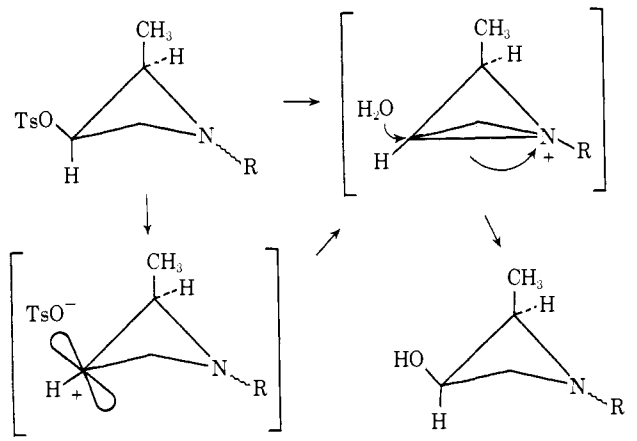
Attack at the 3 position by solvent water may be more or less synchronous with the cleavage of the C–OTs bond, *i.e.*, an SN2 reaction showing pseudo-first-order kinetics. One would anticipate a stereospecific inversion of configuration by this mechanism.

If a simple carbonium ion, *e.g.*, **4**, were involved, one would expect loss of stereospecificity in that isomer or those isomers which undergo hydrolysis by this mechanism. Furthermore, if both tosylates (**5** and **6**) undergo hydrolysis entirely by this mechanism, the ratio of **7** to **8** should be independent of the configuration of the starting tosylates. Molecular models suggest that attack by solvent should be from the least hindered side yielding primarily the trans alcohol **8**.

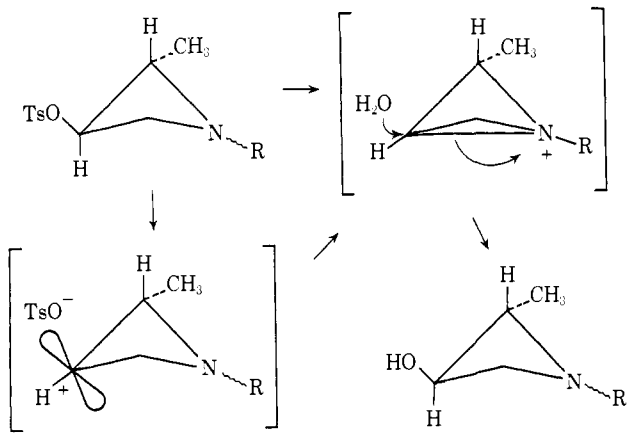
Finally, formation of a bridged cation either by anchimeric assistance[7,8] or by ionization to a tight carbonium ion–tosylate ion pair followed by a very rapid formation of the bridged ion should give a stereospecific retention of configuration (see Schemes I and II).

(1) R. H. Higgins, F. M. Behlen, D. F. Eggli, J. H. Kreymborg, and N. H. Cromwell, *J. Org. Chem.*, **37**, 524 (1972).
(2) J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1968).
(3) V. R. Gaertner, *ibid.*, 5919 (1968); however, see ref 4.
(4) V. R. Gaertner, *J. Org. Chem.*, **35**, 3952 (1970).
(5) P. v. R. Schleyer, P. LePerches, and D. J. Raber, *Tetrahedron Lett.*, 4389 (1969).
(6) (a) R. H. Higgins and N. H. Cromwell, *J. Heterocycl. Chem.*, **8**, 1059 (1971). (b) The stereochemical assignments reported[6a] for **5** and **6** have been supported by use of (2,2,6,6-tetramethylheptanedioate)europium(III).
(7) For a discussion of anchimeric assistance by heteroatoms see W. R. Dolbier, Jr., *J. Chem. Educ.*, **47**, 42 (1970); A. Streitweiser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962, pp 103–126; and ref 8.
(8) J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure," McGraw-Hill, New York, N. Y., 1968, pp 263–268, and references cited therein.

Scheme I[9]



Scheme II[9]



R = t-C_4H_9

Results

The products obtained from the hydrolysis of **5** and **6** result from *stereospecific retention* of configuration. Thus, **5** on hydrolysis yielded exclusively **7**, and **6** yielded exclusively **8** (determined by pmr analysis of the crude reaction products after neutralization by excess potassium hydroxide). This result is consistent with the interpretation of previously reported[1] kinetic data for the solvolysis of **2c**, and with the observation that tosylates **5** and **6** appear to react stereospecifically with methanolic potassium cyanide to yield 3-cyanoazetidines with retention of configuration.[10]

Discussion

The observation of retention of configuration in the hydrolysis of **5** and **6** along with the fact that the rate of the reaction of **2c** with methanolic postassium cyanide is independent of cyanide concentration[1] unequivocally establish that the mechanism does not involve direct displacement by cyanide or by solvent. Furthermore, the free carbonium ion is ruled out as an important intermediate in at least one (presumably the cis; *vide supra*) and possibly in both the cis and the trans tosylates.

It is not possible on the basis of present data to unequivocally distinguish between anchimeric assistance and a 3-azetidinyl cation of a tight ion pair which is rapidly converted to the azabicyclobutonium ion. In view of the high energy of a carbonium ion, such as **4**, and its low energy barrier to solvent capture, it seems unlikely that this ion should be converted entirely to the azabicyclobutonium ion as would be required in the solvolysis of **5**. The apparent stereospecificity observed in the hydrolysis of **6** seems difficult to rationalize entirely in terms of a free carbonium ion (or a tight ion pair). It is suggested that hydrolysis of **6** occurs to a large extent, if not exclusively, *via* an intermediate bicyclobutonium ion. This intermediate could be achieved *via* anchimeric assistance and/or collapse of a precursor tight ion pair (see Scheme II).

Rate enhancement, which is necessary for anchimeric assistance, is present in the hydrolysis of **2c**,[1] relative to cyclobutyl tosylate,[5] but it is of much smaller magnitude than is ordinarily observed for anchimeric assistance.[8] However, in view of the uncertainty[11] surrounding the nature of the intermediate resulting from solvolysis of cyclobutyl tosylate, it is possible, perhaps likely, that any rate enhancement of **2c** relative to that of cyclobutyl tosylate is indicative of anchimeric assistance. Perhaps a sizeable increase in $\Delta S^{\ddagger}$ represents a sufficient criterion for determining the significance of anchimeric assistance[7,8] (an increase in $\Delta S^{\ddagger}$ for the hydrolysis of **2c**, relative to that of cyclobutyl tosylate, has been reported).[1]

The rates of hydrolysis of **5** and **6** (Tables I and II) may be compared with the rate of hydrolysis of **2c**[1] in 60% aqueous acetone at 30°. The order of the hydrolysis rates of **2c**, **5**, and **6** is somewhat reminiscent of the order of the solvolysis rates (Table III) of analogous cyclopentyl tosylates **9**–**11**.[12,13]

Table I. Mean Conductometric Hydrolysis Rates[a] of **5**

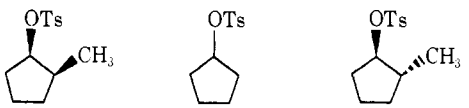
T, °C	Rate, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
0.0	(9.22×10^{-5})[b]		
14.9	$(8.48 \pm 0.18) \times 10^{-4}$	23.7 ± 1.0	10.1 ± 3.5
30.0	$(7.67 \pm 0.11) \times 10^{-3}$[c]		

[a] In 60% aqueous acetone. Unless otherwise indicated, rates are the average of two determinations. [b] Single determination. [c] From three determinations.

Table II. Mean Conductometric Hydrolysis Rates[a] of **6**

T, °C	Rate, sec^{-1}	T, °C	Rate, sec^{-1}
19.8	$(4.43 \pm 0.13) \times 10^{-6}$	30.1	$(2.23 \pm 0.02) \times 10^{-5}$
25.0	(1.21×10^{-5})[b]	39.9	$(5.11 \pm 0.13) \times 10^{-5}$

[a] In 60% aqueous acetone. Unless otherwise indicated, rates are the result of two determinations. [b] Single determination.



9 **10** **11**

(9) The rationale for showing the tosylates to have these conformations will become apparent below.

(10) R. H. H., Ph.D. Dissertation, University of Nebraska, Lincoln, Neb., 1971.

(11) See, for example, R. H. Mazur, W. N. White, D. A. Semenov, C. C. Lee, M. S. Silver, and J. D. Roberts, *J. Amer. Chem. Soc.*, **81**, 4390 (1959); R. E. Davis and A. Ohno, *Tetrahedron*, 24, 2063 (1968).

(12) W. Huckel and H. D. Sauerland, *Justus Leibigs Ann. Chem.*, **593**, 190 (1955).

(13) There apparently have been no reports in the literature of the solvolysis rates of the corresponding 2-methylcyclobutyl tosylates.

Table III. Relative Solvolysis Rates of Cyclic Tosylates at 30°

Azetidinyl[a]			Cyclopentyl[b]		
Compd	Rel rate	E_{act}	Compd	Rel rate	E_{act}
5	28.6	24.3	**10**	2.6	21.6
2c	1.0[c]	22.65	**9**	1.0	22.4
6	0.083	*d*	**11**	0.25	24.7

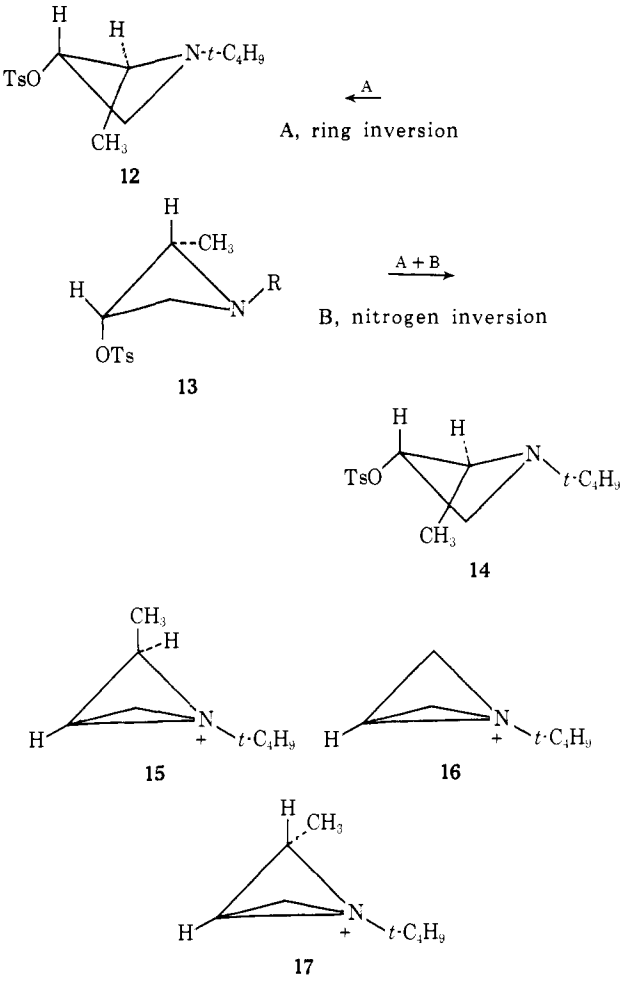
[a] In 60% aqueous acetone. [b] In ethanol, abstracted from the data reported in ref 12. [c] Rate data are reported from ref 1. [d] The Arrhenius plot for **6** is nonlinear; see Figure 1.

By examination of the data reported in Table III some similarities and some significant differences in the relative rates of the heterocyclic and carbocyclic tosylates become apparent. In both series the order of rates is *cis*-2-methyl > parent > *trans*-2-methyl; however, the relative rate differences in the heterocyclic tosylates are considerably magnified relative to those of the carbocyclic series. Furthermore, the rate enhancement observed in **5**, relative to **2c**, is due only to an increase in $\Delta S^{\pm}$. The rate enhancement of **10** (relative to **9**) is probably best described in terms of a greater lowering of E_{act} (and consequently $\Delta H^{\pm}$) by increased relief of nonbonded interactions in the transition state of **10**, relative to that of **9**. One might also anticipate a lowering of E_{act} (and $\Delta H^{\pm}$) in the hydrolysis of **5**, relative to that of **2c**, for the same reasons. It is apparent, however, that if any lowering of E_{act} by greater relief of nonbonded interactions in **5** is present, other factors more than compensate for this effect.

It has been suggested[6a,14,15] that 1,2 interactions in 1-alkylazetidines are generally of greater significance than are 1,3 interactions, and that the preferred conformation of **7** is that conformer with a pseudoaxial hydroxyl group.[6a] In view of the rather similar effective sizes of hydroxyl and *p*-toluenesulfonate substituents[16,17] it seems likely that 1,2 nonbonded interactions are of greater significance in **5** than are 1,3 nonbonded interactions, and that the preferred conformation of **5** resembles that of **7** (see structure **13** in Scheme III). Anchimeric assistance directly from **13** is not possible; however ring inversion to **12** or ring plus nitrogen inversion orients the tosylate substituent into the position necessary for anchimeric assistance to proceed. The energy of intermediates **15** and **16** is undoubtedly well above that of the ground-state molecules (or in the case of **5**, above that of **12** or **14**), thus what is said concerning the intermediates should be directly applicable to that of the transition state, achieved by anchimeric assistance, leading to the intermediate.[18]

It is apparent that there are considerably larger 1,3-pseudodiaxial interactions present in **15** than in **16** and that the effect that is produced in going from **12** (or **14**) to **15** is larger than in going from **18** (presumably the preferred conformation of **2c**)[6a] to **16**. Furthermore, the nonbonded interactions of the *tert*-butyl substituent

Scheme III

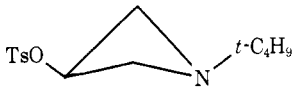


with substituents at C-2 are higher in **15** than in **16**, and probably undergo a greater increase relative to the ground state of **5** than do those in **16** with respect to **18**. Both of these effects should tend to increase E_{act} for the hydrolysis of **5** relative to that for **2c**. In addition the pseudoaxial methyl group of **5** probably limits the stabilizing effect of solvation on cation **15**; consequently an increase in E_{act} might be expected from this effect as well (however, see the discussion below for the effect on $\Delta S^{\pm}$).

The Arrhenius activation plot for the hydrolysis of **6** is nonlinear (Figure 1), a result which may be explained by competitive mechanisms with differing E_{act}'s. It is apparent from the data in Table III that solvolysis at the temperatures studied occurs much more rapidly for **2c** than for **6**. Since meaningful activation parameters cannot be determined for the hydrolysis of **6** and since there would be no decrease in $\Delta S^{\pm}$ expected for the hydrolysis of **6**, relative to **2c** (*vide infra*), we feel that the sluggishness of this reaction (relative to that of **2c**) is primarily due to the high E_{act} (and consequently $\Delta H^{\pm}$) for the hydrolysis of **6**. Examination of structure **17** indicates the only significant difference (relative to structure **16**) is the increased nonbonded interactions between the *tert*-butyl and 2-methyl substituents. This difference, however, is important as models of **17** suggest near eclipsing of these substituents in structure **17**. Apparently the E_{act} for conversion of the ground state directly to intermediate **17** is sufficiently high that formation of a tight ion pair, with subsequent

(14) R. H. Higgins, N. H. Cromwell, and W. W, Paudler, *J. Heterocycl. Chem.*, **8**, 961 (1971).
(15) R. H. Higgins, E. Doomes, and N. H. Cromwell, *ibid.*, **8**, 1063 (1971).
(16) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 236.
(17) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley-Interscience, New York, N. Y., 1966, p 44.
(18) G. S. Hammond, *J. Amer. Chem. Soc.*, 77, 334 (1955).

stereospecific (or nearly so) reaction with solvent, collapse to **17**, and/or collapse to **6** becomes an important competing rate-limiting step.



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Anchimeric assistance tends to increase $\Delta S^{\pm}$,[1,7,8] presumably by demanding less perturbation of the solvent in the transition state than does the free carbonium ion. Thus any factor which would tend to hinder solvation at the transition state might be expected to result in an increased $\Delta S^{\pm}$. The pseudoaxial methyl substituent of **15** presumably helps insulate the intermediate, and consequently the species in the transition state[18] achieved *via* anchimeric assistance, from solvation on that side of the species. This insulating effect by the methyl group in the transition state of **5** presumably produces the increase in $\Delta S^{\pm}$ observed in the hydrolysis. The pseudoequatorial methyl of intermediate **17** could conceivably raise $\Delta S^{\pm}$ for the hydrolysis of **6** relative to that of **2c**; however, models suggest that this increase should be less than that observed in the hydrolysis of **5**.

In summary, the stereospecificity observed in the hydrolysis of **5** suggests that a 1-azabicyclo[1.1.0]-butonium ion, reached *via* anchimeric assistance, is the predominant, if not exclusive, mechanism by which hydrolysis occurs. The apparent stereospecificity observed in the hydrolysis of **6** suggests that a different bridged ion is an important intermediate in this reaction as well; however, the nonlinearity of the Arrhenius plot for the hydrolysis of **6** coupled with the much lower hydrolysis rate of **6**, relative to that of **2c** or **5**, suggest that this intermediate may be reached *via* a tight carbonium ion pair as well as *via* anchimeric assistance.[19]

Experimental Section[20]

***cis*-1-*tert*-Butyl-2-methyl-3-azetidinyl Tosylate (5).** To a stirred suspension of 0.645 g (0.0268 mol) of sodium hydride in 100 ml of ether was added 3.83 g (0.0268 mol) of **7**.[6a] The suspension was stirred at room temperature for 2.5 hr and then treated with a dropwise addition of freshly recrystallized *p*-toluenesulfonyl chloride (5.10 g, 0.0268 mol) in 50 ml of ether. After stirring for an additional 15 hr, the suspension was filtered. The oil which resulted from evaporation of the ether was dissolved in 20 ml of petroleum ether (bp 60–69°) and cooled to −78° to induce crystallization. Two recrystallizations from petroleum ether (bp 60–69°) afforded 0.75 g (9.3%) of **5**, mp 55.5–56°. The pmr spectrum of **5** gave peaks at δ 7.79 (d (J = 8 Hz), 2 H aromatic), 7.32 (d, 2 H, aromatic), 4.75–5.10 (m, 1 H, C-3 proton), 3.02–3.95 (m, 3 H, C-2 and C-4 protons), 2.43 (s, 3 H, tosyl methyl), 1.20 (d = 6.5 Hz), 3 H, C-2 methyl), and 0.92 (s, 9 H, *tert*-butyl protons).

Anal. Calcd for $C_{15}H_{23}NO_3S$: C, 60.61; H, 7.80; N, 4.72. Found: C, 60.41; H, 7.68; N, 4.57.

***trans*-1-*tert*-Butyl-2-methyl-3-azetidinyl Tosylate (6).** To a stirred suspension of 0.785 g (0.0327 mol) of sodium hydride in 100 ml of ether was added a solution of 4.68 g (0.0327 mol) of **8**.[6a] After stirring for 2 hr at room temperature 6.23 g (0.0327 mol) of freshly recrystallized *p*-toluenesulfonyl chloride in 100 ml of ether was added. The suspension was stirred for 15 hr and filtered. The ether was removed *in vacuo* using no heat. The residue was dissolved in petroleum ether and allowed to stand for several hours in the freezer. A rather large quantity of the hydrochloride of **8**, mp 167.5–168°, was deposited and was removed by filtration. The petroleum ether filtrate was placed on a column of Florisil and eluted with petroleum ether until the eluent seemed to contain no *p*-toluenesulfonyl chloride. The column was then eluted with 500 ml of 50:50 ether–petroleum ether. The ethereal eluent was concentrated to a pale yellow oil which could not be induced to crystallize. The pmr spectrum of this oil gave peaks at δ 7.78 (d (J = 8 Hz), 2 H, aromatic), 7.33 (d, 2 H, aromatic), 4.32 (apparently a quartet (J = 6 Hz), 1 H, C-3 proton), 2.8–3.7 (m, 3 H, C-2 and C-4 protons), 2.45 (s, 3.5 H, tosyl methyl), 1.14 (d (J = 6 Hz), 3 H, C-2 methyl), and 0.92 (s, 9–10 H, *tert*-butyl protons).

Anal. Calcd for $C_{13}H_{23}NO_3S$: C, 60.61; H, 7.80; N, 4.72; S, 10.78. Found: C, 60.52; H, 7.72; N, 4.71; S, 10.94; Cl, 0.00.

Product Studies. A small quantity (*ca.* 0.2 g) of **5** was dissolved in 50 ml of 60% aqueous acetone. After 2 hr the acetone was removed *in vacuo*. The residual aqueous solution was made strongly alkaline with potassium hydroxide and extracted repeatedly with ether. The combined ethereal extracts were dried (sodium car-

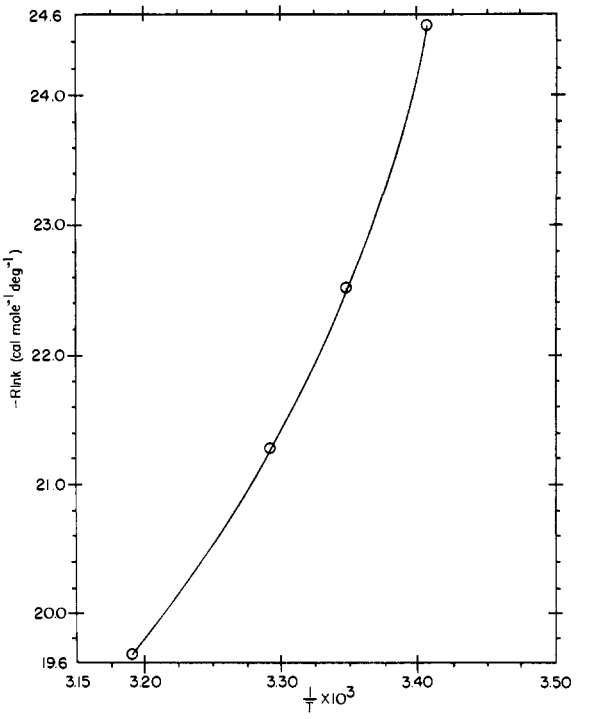
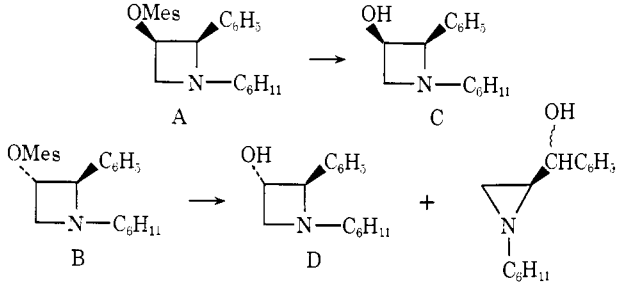


Figure 1. Arrhenius plot for the hydrolysis of **6** in 60% aqueous acetone.

(19) It has recently come to our attention that *cis*- and *trans*-1-cyclohexyl-2-phenyl-3-azetidinyl mesylates (A and B, respectively) undergo hydrolysis with sodium hydroxide in 50% aqueous dioxane to give products which were rationalized in terms of intermediate 1-azabicyclobutonium ions. Thus A was reported to yield *cis*-azetidinol (C), and B was reported to yield *trans*-azetidinol (D) along with



erythro + *threo*

erythro- and *threo*-1-cyclohexyl-2-(α-hydroxybenzyl)aziridine. The observation of ring contracted products in the hydrolysis of B along with the retention of configuration observed in the azetidinol products C and D further substantiate bridged-ion intermediates. The authors suggested that the steric hindrance in the "carbonium ions" accounts for the difference in the products of these reactions. See T. Okutani, A. Morimoto, and K. Masuda, Third International Congress of Heterocyclic Chemistry, Sendia, Japan, Aug 1971, Abstract No. D-23-6.

(20) Microanalyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, Hohweg, West Germany. Pmr spectra were determined on a Varian A-60 or Varian A-60-D spectrometer in deuteriochloroform solutions, with tetramethylsilane as the internal standard. Melting points are uncorrected. Yields are probably not optimum.

bonate) and evaporated *in vacuo*. The last traces of ether and acetone were removed by dissolution in carbon tetrachloride and evaporation *in vacuo*. The pmr spectrum of the resulting white solid was superimposable in all respects on that of **7**.[6a]

When **6** was treated by exactly the same procedure (except the solvolysis was allowed to proceed for 4 days), the pmr spectrum of the oily solid indicated *ca.* 70% of **8** and 30% of unreacted **6**. No peaks were observed which could be attributed to **7**.

Kinetic Methods. Commercial platinum plate electrodes were used in the hydrolysis experiments. The bridge was carefully calibrated. Solvolysis rates were determined on *ca.* 10^{-3} *M* solutions of **5** or **6** in 60% aqueous acetone, and were followed for 1–2 half-lives. The computer program used for computation of the rates was that mentioned previously.[1]

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Mechanism of the Wolff Rearrangement. IV. The Role of Oxirene in the Photolysis of α-Diazo Ketones and Ketenes

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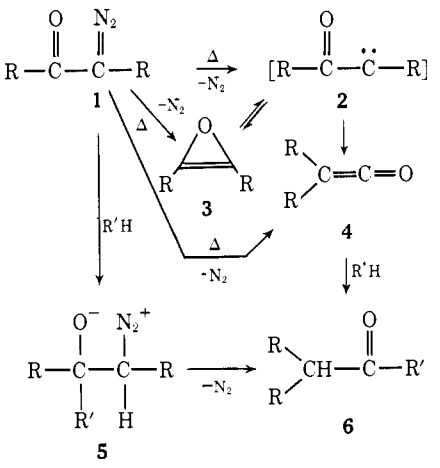
Abstract: Oxirenes, the family of unsaturated epoxides, have been detected as reactive transients in the photochemical Wolff rearrangement sequence of α-diazo ketones and in the photolysis of ketenes.[1-3] Photolyses of 3-diazo-2-propanone, 3-diazo-2-butanone, azibenzil, and α-diazoacetophenone, carbon-13 labeled in the carbonyl group, yield the corresponding ketene in which the carbon-13 atom is scrambled. The extent of scrambling was determined by mass spectrometric analysis of the CO and the carbene insertion products from the secondary *in situ* photolysis of the ketene or from its solvolysis product. The yield of scrambling, indicative of oxirene participation, is dependent on the substituents in the diazo ketone, phase, solvent, and to some extent wavelength of excitation. The highest yield of oxirenes obtains from the gas-phase photolysis of symmetrically substituted diazo ketones. Oxirene is shown to be a characteristic photoproduct; the thermolysis of azibenzil does not give oxirene. From a consideration of the kinetic behavior of the $O(^3P) + CH_3C{\equiv}CCH_3$ and other triplet systems, it is also concluded that oxirene formation occurs *via* a singlet reaction surface. The photolysis of dimethylketene and diphenylketene, carbon-13 labeled in the carbonyl group, yields labeled carbene and unlabeled CO as products. The extent of isotopic scrambling in these cases is decidedly lower than from the corresponding diazo ketones. It is proposed that the reaction path to oxirene is *via* the vibrationally excited ground-state ketene formed through internal conversion of the electronically excited molecule.

The conversion of α-diazo ketones into acids and their derivatives was discovered by Wolff[4,5] and independently by Schroeter.[6,7] The decomposition–rearrangement sequence has proved to be of great synthetic value.[8,9] A notable feature of the Wolff rearrangement (WR) is that it can be brought about catalytically, thermally, or photochemically;[10-13] however, in spite of its facility and widespread application, still, after some sixty years of intensive research, no unified mechanistic picture of this reaction has emerged.

Scheme I shows the different mechanistic pathways which have been proposed for the thermal WR. All mechanisms consider the migration of the R group to be an intramolecular process which does not involve ionic or free radical intermediates. This postulate is based on the well-documented experimental observation that during migration, the stereochemical information content of the R group is retained.[10]

Scheme I



R' = OH, OAc, NH_2, etc.

The path **1** → **2** → **4** → **6** was first proposed by Wolff[4,5] and is still favored, although there are few direct proofs for the intermediacy of **2**. Huisgen and coworkers[14-16] succeeded in isolating oxazole deriva-

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