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ACETOLYSIS OF OXIRYLCARBINYL CHLORIDE (EPICHLOROHYDRIN) AND OXIRYLCARBINYL p-BROMOBENZENESULFONATE

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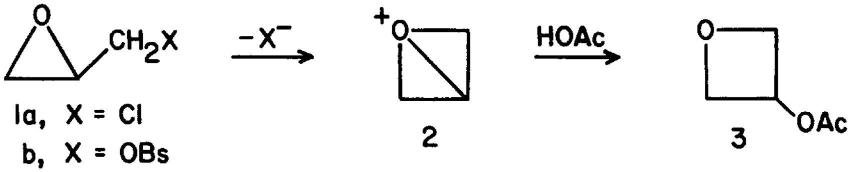
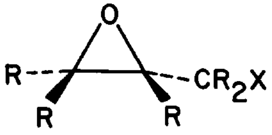
Epichlorohydrin (1a) is *ca.* 3 times more reactive than cyclopropylcarbinyl chloride and 100 times more reactive than allyl chloride toward solvolysis in acetic acid.[1] This greater reactivity of 1a has been attributed to anchimeric assistance of the oxiryl group in the ionization reaction at the carbinyl position, with formation of an intermediate oxabicyclobutonium ion 2. Additional evidence for oxygen participation was based on the identification of 3-acetoxyoxetane (3) as one of the acetolysis products (11 % yield).



The hydrolyses of the other oxirylcarbinyl systems 4 and 5, in which the carbinyl position is secondary,[2,3] tertiary,[2] or located in a medium ring,[4] have led to formation of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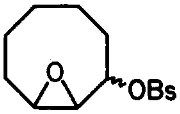
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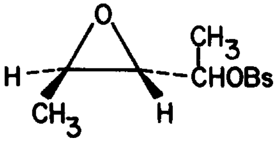
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products that arise from rupture of the oxirane ring. Neighboring group participation by the oxiryl group has been invoked to explain the formation of rearranged products, although the extent of rate acceleration induced by the oxiryl group over that of a model system is minor at best, and is somewhat uncertain for lack of a suitable model. The diastereomeric secondary oxirylcarbinyl brosylates of structure 6 solvolyzed *ca.* 10^6 times slower than their cyclopropylcarbinyl analogs, and yielded mostly inverted product.[5] These results were taken to indicate the lack of significant participation by the oxirane ring.

The published rate data for the solvolysis of compounds 4-6 are all consistent in that the relative reactivities of 4-6 toward solvolysis can be estimated to be *ca.* 10^5-10^7 times less that the reactivities of their related cyclopropylcarbinyl systems. The solvolysis of epichlorohydrin therefore appears as an exception in that this oxirylcarbinyl system is *more* reactive in acetic acid than cyclopropylcarbinyl chloride. Since the acetolysis of epichlorohydrin is often quoted as being an example of oxiryl oxygen participation in a solvolytic reaction,[6] and since it appeared to us to be rather unusual for 1a to be 3 times more reactive than cyclopropylcarbinyl chloride toward solvolysis while compounds 4-6 are ca. 10^5-10^7 times less reactive toward solvolysis than their cyclopropylcarbinyl analogs, we have reinvestigated the acetolysis of 1a and also studied the acetolysis of the related p-bromobenzenesulfonate ester 1b. Our results indicate that the acetolysis of 1a does not involve initial ionization at the carbinyl position, but rather occurs by initial opening of the oxirane ring by the solvent.

If the acetolysis of 1a were proceeding by the initial ionization at the carbinyl position to yield either the oxabicyclobutonium ion 2 or a highly stabilized oxirylcarbinyl cation, then it can be estimated that the rate of acetolysis of the corresponding p-bromobenzenesulfonate ester 1b should be ca. 10^2-10^5 times greater than that of 1a due to the better leaving group ability of the p-bromobenzenesulfonate ion compared to that of chloride ion. For example, the solvolysis rate of isopropyl p-bromobenzenesulfonate is ca. 1.5 x 10^4 times greater than that for isopropyl chloride.[7] For the adamantyl system, the leaving group ability of $^-$OBs is calculated to be ca. 5 x 10^5 greater than that for Cl$^-$.[8] Even in displacement reactions of the S_N2 type, p-bromobenzenesulfonate esters are estimated to be ca. 10^3 more reactive than chlorides.[9] Therefore we have prepared oxirylcarbinyl p-bromobenzenesulfonate 1b,[10] and determined the rates of acetolysis of 1a and 1b by following the loss of starting material at 100°C. The half-life for 1a was found to be 3.5 hr ($k = 5.6 \times 10^{-5} s^{-1}$),[11] and the half-life for 1b was ca. 2.5 hr ($k = 7.7 \times 10^{-4} s^{-1}$).[12] The fact that 1a solvolyzes only slightly slower than 1b provides strong evidence that 1a is not reacting by initial ionization (with or without anchimeric assistance by the oxiryl group) at the carbinyl position.

We have also examined the rates of production of Cl$^-$ from 1a and OBs$^-$ from 1b by titration,[13] and these results are graphically presented in Figures 1 and 2. The rate of formation of Cl$^-$ from 1a does not conform to first-order kinetics, and at one half-life for disappearance of starting material, it is significant that only ca. 1% of the theoretical amount of chloride ion has been generated. Epichlorohydrin must therefore undergo reaction without appreciable ionization at the carbinyl position, since such ionization would liberate chloride ion.

Table 1. Product distributions from acetolysis of epichlorohyrin (1a) at 100°C.[a]

Experiment	Reaction Time (hr)	Product (%)				
		$\overset{\text{Cl}}{\text{CH}_2}\text{-}\overset{\text{OH}}{\text{CH}}\text{-}\overset{\text{Cl}}{\text{CH}_2}$	$\overset{\text{Cl}}{\text{CH}_2}\text{-}\overset{\text{OAc}}{\text{CH}}\text{-}\overset{\text{Cl}}{\text{CH}_2}$	$\overset{\text{OAc}}{\text{CH}_2}\text{-}\overset{\text{OH}}{\text{CH}}\text{-}\overset{\text{Cl}}{\text{CH}_2}$	$\overset{\text{OAc}}{\text{CH}_2}\text{-}\overset{\text{OAc}}{\text{CH}}\text{-}\overset{\text{Cl}}{\text{CH}_2}$	$\overset{\text{AcO}}{\text{CH}_2}\text{-}\overset{\text{AcO}}{\text{CH}}\text{-}\overset{\text{OAc}}{\text{CH}_2}$
1[b]	67	-	18	-	52	30
2[c,d]	4	5	-	77	5	-
3[b,e]	14	8	8	11	57	14
4[f]	4	55	ca. 2	29	8	-

[a] Products were analyzed by gas chromatography, and collected from a 20% silicone UCC-W-982 column. [b] 0.14 M 1a initial concentration, 0.016 M NaOAc, 0.01 M Ac$_2$O. [c] 0.13 M 1a initial concentration, glacial HOAc. [d] ca. 13% of unidentified materials with retention time close to that of major product. NMR and IR indicate this material to be mainly 3-chloro-2-acetoxy-1-propanol. [e] ca. 2% unidentified material. [f] 0.31 M 1a initial concentration, 0.2 M tetrabutylammonium chloride. ca. 4-5% of unidentified material with same retention time in footnote d above.

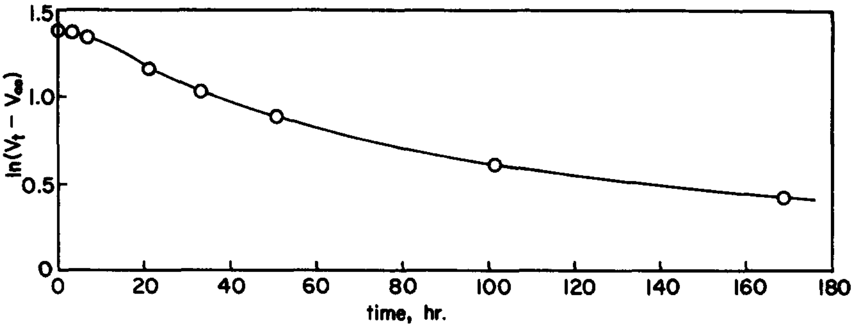

Figure 1. Plot of $\ln(V_t-V_\infty)$ vs time for acetolysis of 1a at 100° in HOAc containing 0.016 M NaOAc, where V_t refers to the volume of perchloric acid solution required to backtitrate a given aliquot to a bromphenol blue end point, and V_∞ is the theoretical volume of backtitrant at infinite time.

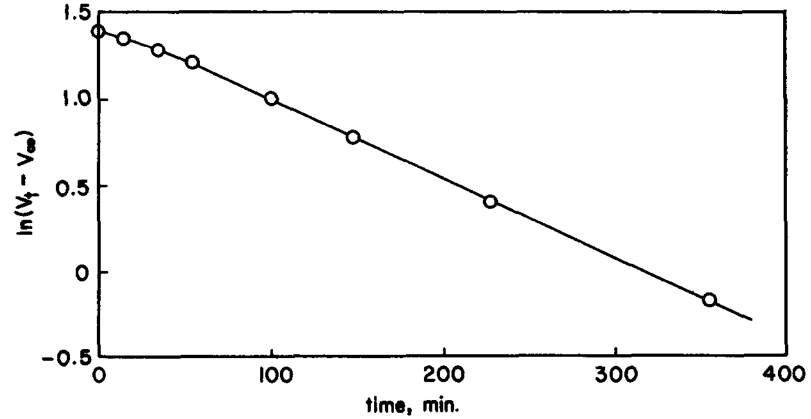

Figure 2. Plot of $\ln(V_t-V_\infty)$ vs time for acetolysis of 1b at 100° in HOAc containing 0.016 M NaOAc. V_t is defined above for Figure 1, and V_∞ is the volume of backtitrant required at 10 half-lives for reaction.

The products from acetolysis of 1a varied substantially with reaction conditions, and are summarized in Table 1. With our reaction conditions and isolation techniques, we were unable to detect the presence of 3-acetoxyoxetane in any of the product mixtures from 1a. We did note, however, that the yield of 1,3,dichloro-2-propanol or its acetate ester appeared to be a function of the initial concentration of 1a. Indeed, when the acetolysis of 1a is carried out in 0.2 M tetrabutylammonium chloride, the yield of the dichloride increased to 55%. Therefore, this product must arise from nucleophilic addition of chloride ion to the less hindered carbon of the oxirane ring, a reaction presumably catalyzed by the acetic acid solvent. The high yields of 3-acetoxy-1-chloro-2-propanol formed at ca. one half-life for reaction of 1a in unbuffered glacial acetic acid also appears to be the result of addition of solvent to the less hindered carbon of the oxirane ring. Chloride ion is thus generated almost exclusively from a number of intermediate chloride derivatives of glycerol, and not directly from 1a. The complexity of the mixture readily accounts for the deviation of Figure 1 from a first-order kinetic plot.

From Figure 2 it can be seen that the apparent first-order rate constant for production of $^-$OBs from 1b increases with time throughout ca. 20% reaction, and then remains constant with a value of $7.7 \times 10^{-4}\,s^{-1}$. At one half-life for reaction, the NMR spectrum of the product mixture indicated that the remaining p-bromobenzenesulfonate ester was still predominantly 1b. These data indicate that at least part of the $^{-}$OBs is generated from an intermediate ester, present at rather low concentrations. The product mixture from acetolysis of 1b for 10 half-lives contained 98% of glyceryl triacetate. The reactive intermediate p-bromobenzenesulfonate ester is therefore most likely derived from initial addition of acetic acid to the oxirane ring, and part or all of the product can be derived from this intermediate. The product distributions and similarity in rates for acetolysis of 1a and 1b, measured by the loss of starting material, suggests that perhaps both 1a and 1b undergo initial opening of the oxirane ring by the acetic acid solvent. However, one cannot rule out some ionization of 1b at the carbinyl position. Oxirylcarbinyl acetate, if formed from 1b, is unstable to the reaction conditions[1] and would also be expected to ultimately yield glyceryl triacetate. The actual rate for acetolysis of 1b at 100° by ionization at the carbinyl position must therefore be some fraction (perhaps very small) of $7.7 \times 10^{-4} s^{-1}$. From the published rate of solvolysis of cyclopropylcarbinyl methanesulfonate in 96% ethanol-water,[14] with corrections for temperature, leaving group ability, and solvent, it can be estimated the the cyclopropylcarbinyl system is a minimum of 20 times more reactive toward solvolysis by ionization at the carbinyl position than the oxirylcarbinyl analog. The actual reactivity ratio may be much larger because of the uncertainty about the fraction of 1b that undergoes initial ionization at the carbinyl carbon.

References and Notes

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6. For example see: (a) H.G. Richey, Jr., "Carbonium Ions", Vol 3, G.A. Olah and P.v.R. Schleyer, Ed., Wiley, New York, N.Y. 1972, pp. 1285-6; (b) B. Capon and S.P. McManus, "Neighboring Group Participation," Vol. 1, Plenum Press, New York, N.Y., 1976, pp. 145-6.
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10. Ester 1b was prepared by stirring a solution of glycidol and p-bromobenzenesulfonyl chloride in ether with powdered KOH; NMR (CCl_4) δ 2.51 (doublet of doublets, 1 H, J = 2.6,5.0), 2.71 (doublet of doublets, 1 H, J = 4.0,5.0), 3.10 (m, 1 H), 3.88 (doublet of doublets, 1 H, J = 5.9,11.5), 4.27 (doublet of doublets, 1 H, J = 3.5,11.5), 7.70 (s, 4 H).
11. The rate of reaction of 1a at 100° in a solution originally 10% wt/vol of 1a in glacial acetic acid was measured by NMR. This rate was increased by a factor of ca. 3 if the acetic acid contained 0.1 M sodium acetate.
12. Determined titrimetrically at 100° in acetic acid containing 0.016 M sodium acetate and 0.01 M acetic anhydride. The reaction of 1b was also monitored by NMR.
13. Titrimetric rates were determined by the sealed tube technique in acetic acid containing 0.016 M sodium acetate and 0.01 M acetic anhydride, S. Winstein, E. Grunwald, and L.L. Ingraham, J. Am. Chem. Soc., 70, 821 (1948).
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