The Acid-catalysed Hydrolysis of Tetramethyloxiran: a Re-investigation

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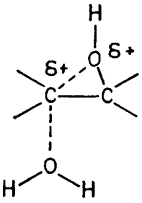
The acid-catalysed hydrolysis of tetramethyloxiran yields 2,3-dimethylbutane-2,3-diol (*ca.* 98%) and 3,3-dimethylbutan-2-one (<1%). This result differs markedly from that previously reported and widely quoted as evidence for a free carbonium ion. It must now be concluded that reaction involves bimolecular attack by water on the protonated epoxide.

THE mechanism of acid-catalysed hydrolysis of epoxides [‡] has been less intensely investigated recently, owing principally to the successful description of these reactions by Parker and Isaacs[1] as involving a pre-equilibrium protonation of the epoxide, followed by a modified S_N2 attack on the conjugate acid in which bond-breaking is much more nearly complete in the transition state (I) than is bond-making.



(I)

In such a transition state the carbon atom attacked by the water molecule bears a partial positive charge, and this rationalises a number of features of acid-catalysed hydrolyses of epoxides which appear to indicate an S_N1 (or in this case A-1[2]) type reaction. The partial bonding of a water molecule in the transition state, however, rationalises the features typical of an S_N2 (or in this case A-2[2]) type reaction.

Thus rate studies[3] and studies of the direction of attack by water[4] provide evidence favouring an A-1 mechanism, whereas the typical formation of *trans*-diols[5–7] argues for an A-2 mechanism. A further strong argument for the A-2 mechanism comes from a study of the products of reaction of the carbonium ion invoked in the A-1 mechanism. This carbonium ion typically reacts to give *different* ratios of hydrolysis to rearrangement than those for epoxide hydrolysis.[6,8]

Conflicting assignments for acid-catalysed hydrolyses of epoxides come also from a number of empirical criteria developed to distinguish between A-1 and A-2 mechanisms. An A-2 mechanism is implied by a Zucker–Hammett treatment[3] and from the value of entropies of activation,[9] whereas volumes of activation[10] and Bunnett's ω function[11] implied an A-2 mechanism. These empirical criteria seek to provide a distinction between well defined extremes of behaviour, and the confusion for an apparently intermediate reaction mechanism is understandable.

An Apparent Anomaly.—Given the very reasonable rationalisation of the bulk of experimental results which the Parker and Isaacs mechanism provides, one experimental result remains anomalous. Hydrolysis of tetramethyloxiran in aqueous perchloric acid–dioxan mixtures is reported to yield 2,3-dimethylbutane-2,3-diol (pinacol) and 3,3-dimethylbutan-2-one (pinacolone) in ratios varying from 3 : 1 to 3 : 2 depending on the water composition,[12] values which agree well with the expected products from the carbonium ion $^+CMe_2{\cdot}CMe_2OH$ which is generated in the pinacol rearrangement.[13] The epoxide hydrolysis was therefore concluded to involve a kinetically free carbonium ion. Unfortunately, full experimental details have not been published, and this result stands as an anomaly when compared with a very similar system in which a kinetically free carbonium ion is not formed.[6]

We have therefore reinvestigated the hydrolysis of tetramethyloxiran, and in so doing have found a completely different experimental result, with different mechanistic implications.

RESULTS AND DISCUSSION

Tetramethyloxiran hydrolyses rapidly in 0·045M-perchloric acid; the products of hydrolysis in water and in 10% dioxan–water are in the Table.

t/°C	Solvent	Pinacol [a] (%)	Pinacolone [b] (%)
70	H_2O	99 ± 1	0·9 ± 0·2
70	10% dioxan–H_2O	98 ± 1	0·7 ± 0·2
21·6	H_2O	99 ± 1	0·2 ± 0·2

[a] Analysis by periodate oxidation. [b] Analysis by g.l.c.

The originally published results for 0·05M-perchloric acid at 73 °C in the absence of dioxan were 75% pinacol,

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[‡] This communication deals only with alkyl-substituted epoxides; there is good reason to believe that these reactions can be described in terms of one mechanism as will be argued herein. Aryl- and acyl-substituted epoxides can react with different stereochemical results, by a different mechanism.[1]

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25% pinacolone, and in 12% dioxan–water 73% pinacol, 27% pinacolone.[12] These results are concluded to be wrong.

Our re-investigation of this acid-catalysed hydrolysis removes the anomaly in the case of tetramethyloxiran Hydrolysis does not occur with intermediacy of a kinetically free carbonium ion, so bond-making must be concluded to be occurring simultaneously with bond-breaking. A number of recent publications which state, or imply, that a kinetically free carbonium ion is formed in this hydrolysis require correction.[14]

The concerted nature of this hydrolysis throws some light on the hydrolysis of other epoxides. A tetra-alkyl-substituted oxiran would be the most likely choice amongst the alkyl-substituted oxirans of a substrate in which a kinetically free carbonium ion would be formed on hydrolysis. Such a carbonium ion would be tertiary, and steric hindrance to simultaneous attack by water would be the maximum. The clear evidence in this study for a concerted hydrolysis must indicate, *a fortiori*, that hydrolysis of other substrates is also concerted, and does not proceed through kinetically free carbonium ions (which would be less stabilised than is the ion in this study). It seems safe to conclude that the acid-catalysed hydrolysis of oxiran is markedly *A*-2 in character.

In conclusion it is worth noting that the term epoxide rearrangement should be carefully used in acid conditions. Fast hydrolysis of an epoxide to a diol followed by the much slower pinacol rearrangement should not be described by a term which implies that the epoxide is the material which rearranges, even should the conditions be such that the diol does not build up as an intermediate.

EXPERIMENTAL

Preparation of Tetramethyloxiran.—Tetramethyloxiran was prepared by standard methods. 2,3-Dimethylbutan-2-ol was prepared by addition of methylmagnesium iodide to 3-methylbutan-2-one, and subsequent hydrolysis.[15] Dehydration of this alcohol was affected by heating at 100 °C with anhydrous oxalic acid.[16] The mixture of 2,3-dimethylbut-2-ene and 2,3-dimethylbut-1-ene (*ca.* 2 : 1) was fractionated on a Nester–Faust spinning-band column and 2,3-dimethylbut-2-ene (>99·5% pure by g.l.c.), b.p. 73 °C (lit.,[17] 73·24 °C), n_D^{25} 1·4094 (lit.,[17] 1·4092) was obtained. The olefin was epoxidised with peroxy-n-octanoic acid by the method of Swern *et al.*,[18] the only modification of their procedure being that the peroxy-acid was isolated by diluting the reaction mixture with ice–water and filtration, rather than by ether extraction. The epoxide was purified by distillation through a Nester–Faust spinning band column (>98% by g.l.c.), b.p. 90—91 °C (lit.,[18] 90·4—91·5 °C), n_D^{25} 1·3935 (lit.,[18] 1·3938). (Some thermal rearrangement to pinacolone was observed so distillation at reduced pressure is advisable. The sample used in the hydrolyses was not contaminated by pinacolone; <0·05% by g.l.c.)

Hydrolysis and Analysis for Pinacol.—Perchloric acid solution (0·045M, 50 ml) in either water or 10% dioxan–water (v/v) was pipetted into a thick-walled stoppered flask, which was then equilibrated in a thermostat. A weighed amount of tetramethyloxiran (*ca.* 0·2 g) sealed in a thin-walled glass vial was added, and after a few minutes the flask was shaken to break the vial. After 5 min the flask was cooled to room temperature and the contents analysed for pinacol. That hydrolysis was complete in these conditions was shown by the absence of epoxide in an ether extract from the hydrolysate (<0·02%) whereas at least 90% of the epoxide could be extracted from deionised water in a separate experiment.

Pinacol was oxidised with an excess of sodium periodate[19] in an NH_3–NH_4^+ buffer. Residual periodate was analysed by titration of the iodine liberated on addition of excess of potassium iodide solution against standard sodium arsenite solution. This procedure gave accurate analyses of pinacol solutions of known concentration both in the presence and absence of pinacolone, indicating that periodate does not rapidly oxidise pinacolone, the other possible product.

Aliquot portions (10 ml) of the reaction mixture were added to flasks containing ammonia solution (0·165M, 4 ml) and water (6 ml). Sodium periodate solution (*ca.* 0·1M, 5 ml) was added and the flasks left overnight in the dark. At timed intervals periodate remaining in the flasks was estimated by the following procedure. Perchloric acid solution (0·045M, 4·2 ml), sodium hydrogen carbonate (*ca.* 0·25 g), and excess of potassium iodide solution (10% w/v) was added. After 10 min the iodine liberated was titrated against standard sodium arsenite solution (*ca.* 0·025M) with starch as indicator. Titres were constant after 16—24 h indicating that the oxidation product (acetone) was stable to further oxidation. Blanks with perchloric acid in place of the aliquot portions were also examined.

In one determination the following results were recorded: weight of epoxide = 0·1733 g; titres with sodium arsenite solution (0·02445M), after 17 h, 6·86 ml; after 20 h, 6·78 ml; after 24 h, 6·83 ml; blank titre 20·78 ml. Hence weight of epoxide forming pinacol = (20·78 − 6·82) × 5 × 0·02445 × 100/1000 = 0·171 g, *i.e.*, 98·5%. Other results are tabulated in the Table.

In a separate experiment a sample (*ca.* 0·1 g) of tetramethyloxiran was hydrolysed in perchloric acid solution (0·045M) and the solution cooled in ice. Crystals, m.p. 42—43 °C, were deposited (an authentic sample of pinacol recrystallised from water melted at 43—44 °C. Adams[20] reports that pinacol melts at 46—47 °C but that this m.p. varies, depending on the degree of hydration). The hydrolysis product also had identical retention time relative to that of toluene (7·07) as an authentic sample of pinacol (6 ft column packed with polypropylene glycol on 80—100

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[20] R. Adams and E. W. Adams, *Org. Synth., Coll. Vol. I*, 459.

mesh Chromosorb W, operating at 80 °C, flow rate 15 ml hydrogen/min). These experiments establish that pinacol is the hydrolysis product.

Analysis for Pinacolone.—Analysis was by g.l.c., toluene being used as a non-reacting marker for quantitative determinations.

A test-tube containing perchloric acid (0·045M, 2 ml) and sealed with a serum cap was equilibrated in a thermostat. A mixture of epoxide and toluene (*ca.* 0·05 g) of known composition was injected into the test-tube, the tube shaken, and after 5 min the tube was removed from the thermostat and cooled. Pure ether (2 ml) was added through the serum cap and the tube thoroughly shaken. The ether extract was analysed by g.l.c. (6 ft × $\frac{1}{8}$ in polypropylene glycol on 80—100 Chromosorb W, 80 °C, flow rate 15 ml/min). This procedure was repeated with a mixture of toluene and pinacolone, of known composition close to that found in the ether extract, in place of the mixture of epoxide and toluene. By this means errors due to differential partitioning between ether and water are avoided; the small values for the percentage of pinacolone in the Table can be regarded as accurate within the range shown.

The pinacolone formed in the hydrolysis was shown not to be formed by rearrangement of the major product, pinacol. Pinacol and perchloric acid (0·045M) when left at 70 °C for six times the above reaction time gave on ether extraction less than 0·03% of pinacolone.

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