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ACETIC ACID CATALYSIS IN THE HYDROHALOGENATION OF GLYCOLS

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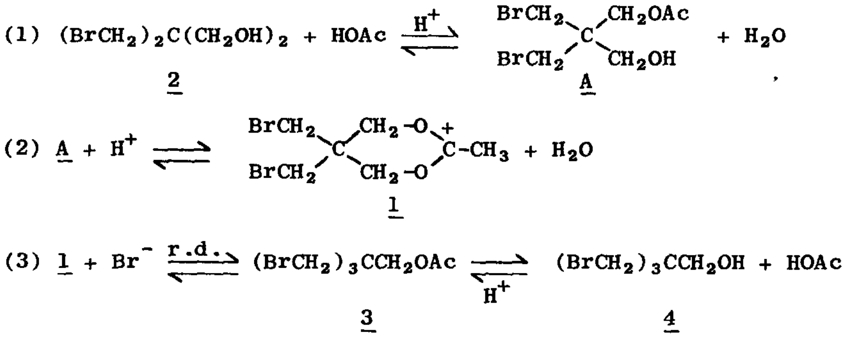
The synthetic benefits of acetic acid as a co-solvent in the preparation of organic haloacetates from triols and diols[1,2,3] are well-known. Mechanistic proposals for the role of acetic acid in hydrohalogenation have swung from medium effects[4] to the intermediacy of 1,3-dioxan-2-ylium cationic intermediates (1)[2,3,5] which react readily with nucleophiles. As part of our studies of concentrated acid solutions, we have examined the kinetics of hydrobromination of pentaerythritol and its derivatives in concentrated hydrobromic acid (≥48% w/w) containing small amounts of acetic acid. Kinetic data for the reaction of 2,2-bis(bromomethyl)-1-3-propanediol (2), a neopentyl glycol that reacts very slowly *via* normal S_N2 reactions, show that acetic acid acts catalytically in hydrohalogenation of polyols and that the reaction proceeds *via* the pathway shown in eqns. (1)-(3).



$$(1)\quad \underset{2}{(BrCH_2)_2C(CH_2OH)_2} + HOAc \overset{H^+}{\rightleftharpoons} \underset{A}{(BrCH_2)_2C(CH_2OAc)(CH_2OH)} + H_2O$$

$$(3)\quad 1 + Br^- \overset{r.d.}{\rightleftharpoons} \underset{3}{(BrCH_2)_3CCH_2OAc} \underset{H^+}{\rightleftharpoons} \underset{4}{(BrCH_2)_3CCH_2OH} + HOAc$$

Inspection of the Table shows that the ratio of the hydrobromination rate of alcohol 2 with and without acetic acid, k/k_o, increases greatly upon addition of very small amounts of acetic acid. It is unlikely that the bulk

Table

Effect of Acetic Acid on the Rate of Reaction of Alcohol 2 in 64% Hydrobromic Acid at 122°

[HOAc] , M	0	0.01	0.02	0.05	0.10	0.50	1.0
k/k_0	1	2.51	4.46	10.0	20.0	100	200

solvent properties of hydrobromic acid are altered significantly by addition of ca. 0.28% v/v (0.05M) of acetic acid. Consequently, medium effects are not a reasonable source of the 10-fold rate increase. In addition, the rate of hydrobromination of alcohol 4, which contains only one hydroxyl group, is unaffected by addition of acetic acid. With 0.25% acetic acid, the enthalpy of activation, $\Delta H^{\ddagger}$, for the reaction of 2 ⟶ 4 is lowered by over 13 kcal/° mol, from over 33 kcal/° mol to 20.0 kcal/° mol. The entropy of activation, $\Delta S^{\ddagger}$, is -25 e.u. in the presence of acetic acid. These activation parameters are consistent with a reaction path involving a cyclic intermediate. In 62% hydrobromic acid containing 5% (ca. 0.83M) acetic acid, equilibrium (1) is established within 25 min. at 37°, as determined by nmr. Therefore, these esterifications are about 100 times faster than the hydrohalogenation.

In summary, large rate increases upon addition of small amounts of acetic acid, the insensitivity of the reaction of alcohol 4, which cannot form a cyclic intermediate, to acetic acid, the activation parameters, and the rapid equilibration (eqn. 1) all support the intermediacy of cation 1 in the acetic acid catalyzed hydrobromination of glycols. In the presence of small amounts of acetic acid, acetate 3 exists predominantly as alcohol 4. Consequently, haloalcohols can be prepared directly from glycols in concentrated hydrohalic acids containing low concentrations of acetic acid and water.

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