The Oxidation of Secondary and Tertiary Alcohols by Nitrous Acid

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The oxidation of 2-phenylpropan-2-ol to acetophenone by nitrous acid in aqueous sulphuric acid takes place following rate-determining dehydration to α-methylstyrene, and the nitrous acid oxidation of 1-arylethanols consists of two competing reactions which are α-hydride abstraction by nitrosonium ion to give the acetophenone and dehydration followed by oxidation of the styrene to give the benzaldehyde.

We have recently reported that the oxidation of benzyl alcohols proceeds by hydride abstraction by nitrosonium ion;[1] a similar conclusion has been drawn independently by Ross and his co-workers.[2] We now report a study of the oxidation by nitrous acid of 2-phenylpropan-2-ol to acetophenone[3] and of some ring-substituted 1-phenylethanols to a mixture of the correspondingly substituted acetophenone and benzaldehyde.

Several pieces of evidence show that the oxidation of 2-phenylpropan-2-ol proceeds by way of rate-determining dehydration to α-methylstyrene (Scheme 1), which is then rapidly oxidised by nitrous acid to acetophenone. Firstly, the kinetics of the reaction are first order in 2-phenylpropan-2-ol but zeroth order in nitrous acid (Table 1). Secondly, the observed first-order rate coefficients are similar, but not identical, to those reported in the literature[4] for dehydration of 2-phenylpropan-2-ol over a range of acidity. We have re-examined the kinetics and equilibrium for dehydration of 2-phenylpropan-2-ol in 25.5% H_2SO_4 at 25 °C. We obtained an equilibrium constant (k_f/k_r) of 0.024, which is rather different from that previously reported,[4] and a rate coefficient for the approach to equilibrium of $6.9 \times 10^{-3}\,s^{-1}$. From these results, k_f is $1.6 \times 10^{-4}\,s^{-1}$ which agrees well with the rate coefficient for nitrous acid oxidation at this acidity (first entry in Table 1). Thirdly, we have shown that α-methylstyrene reacts very rapidly with nitrous acid in aqueous sulphuric acid to give acetophenone; the yield by g.c. analysis following reaction in 25.0% H_2SO_4 was 90%. The rate coefficient for this reaction (*ca.* 500 $mol^{-1}\,dm^3\,s^{-1}$ in 25.5% H_2SO_4 at 25 °C) multiplied by the lowest concentration of nitrous acid used is about 50 times greater than the first-order rate constant for hydration (k_r, Scheme 1) which accords with the dehydration step being rate-determining in the oxidation of the alcohol.

$$\mathrm{ArCMe_2OH} \underset{k_r}{\overset{k_f}{\rightleftarrows}} \mathrm{ArCMe{=}CH_2} \xrightarrow{\mathrm{HNO_2}} \mathrm{ArCOMe}$$

Scheme 1

Table 1. Observed first-order rate coefficients, k_1, for oxidation of 2-phenylpropan-2-ol[a] by nitrous acid in aqueous H_2SO_4 at 25 °C.

H_2SO_4 (%)	$10^4[HNO_2]/mol\,dm^{-3}$	$10^4k_1/s^{-1}$
25.5	8, 16	1.32, 1.31
35.0	4, 16	10.2, 10.1
39.6	16, 32, 64	28.5, 27.8, 29.3

[a] Substrate concentration 8×10^{-5} mol dm^{-3}.

The contrasting behaviour of benzyl alcohol (which undergoes hydride abstraction by nitrosonium ion to give benzaldehyde) and 2-phenylpropan-2-ol (which must first undergo dehydration in a step which is independent of nitrous acid before oxidation of the alkene to acetophenone) led us to investigate the fate of 1-arylethanols where both types of mechanism might be expected (Scheme 2).

The first-order rate coefficients, k, show a linear dependence on the concentration of nitrous acid, with a non-zero intercept (equation 1). Values of A and B (equation 1) are in Table 2.

$$k = \mathrm{A}[\mathrm{HNO_2}] + \mathrm{B} \qquad (1)$$

$$\mathrm{XPhCOMe} \xleftarrow[\mathrm{a}]{\mathrm{HNO_2}} \mathrm{XPhCHMeOH} \underset{k_r}{\overset{k_f}{\rightleftarrows}} \mathrm{XPhCH{=}CH_2} \xrightarrow[\mathrm{b}]{\mathrm{HNO_2}} \mathrm{XPhCHO}$$

Scheme 2

Table 2. Kinetics of oxidation of 1-(4-X-phenyl)ethanols[a] at 25 °C.

X	H_2SO_4 (%)	n[b]	$10^4[HNO_2]$[c] /mol dm^{-3}	A[d] /mol^{-1} dm^3 s^{-1}	10^4B[d] /s^{-1}
H	46.0	5	2—32	1.80 (0.01)	0.40 (0.05)
Me	46.0	4	2—15	4.40 (0.01)	3.32 (0.05)
Me	35.2	3	4—16	0.15 (0.001)	0.37 (0.01)
MeO	35.2	7	4—99	0.400 (0.004)	5.01 (0.08)

[a] Substrate concentration less than 0.1 [HNO_2]. [b] Number of runs. [c] Range of concentrations studied. [d] Parameters in equation (1) (standard deviations) by weighted least-squares analysis.

Table 3. Yields of 4-X-benzaldehyde and 4-X-acetophenone from the oxidation of 1-(4-X-phenyl)ethanol[a] at 25 °C

X	H_2SO_4 (%)	$10^4[HNO_2]$ /mol dm^{-3}	Yields (%)[b] 4-X-PhCHO	4-X-PhCOMe
H	40.1	8.0	Trace	90
Me	46.0	4.0	7	84
MeO	35.2	8.0	59	38
MeO	35.2	16.0	38	59
MeO	35.2	99.0	7	74

[a] Substrate concentration 4—8 × 10^{-5} mol dm^{-3}. [b] Mean of 2—3 determinations in each case.

This accords with Scheme 2. The intercepts B represent rate coefficients k_f for dehydration (measured in this work by nitrous acid scavenging of the alkene, and we believe more accurately than by direct determination[5] because the hydration–dehydration equilibrium favours the alcohol). The slopes, A, are second-order rate coefficients for nitrous acid oxidation (step a of Scheme 2).

These conclusions are supported by the yields of the two products (the benzaldehyde and the acetophenone) measured independently by g.c. (Table 3). The yields are not exactly as predicted from the kinetics; they suggest that a relatively minor side-reaction accompanies step b of Scheme 2.

Rate coefficients A (equation 1 and Table 2), and the way in which they vary with acidity[6] are in each case closely similar to those for the reaction of the correspondingly substituted benzyl alcohol with nitrous acid.[1] This reinforces the view that the same mechanism of hydride abstraction by nitrosonium ion is operative.

Electron-releasing substituents and low nitrous acid concentrations and acidities favour the dehydration–alkene oxidation pathway giving benzaldehydes, and the opposite conditions favour hydride abstraction giving acetophenones.

The mechanism of the nitrous acid oxidation of styrenes is currently under investigation.

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