

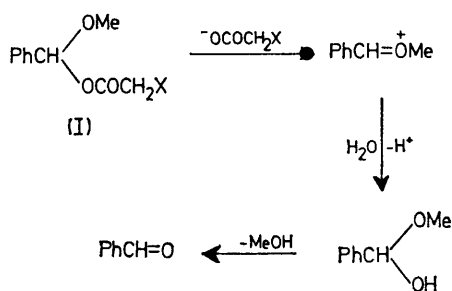
Kinetics and Mechanism of the Decomposition of α -Acetoxy- α -methoxytoluene in Aqueous Solution

By BRIAN CAPON,* KEITH NIMMO, and GORDON L. REID
(Chemistry Department, Glasgow University, Glasgow G12 8QQ)

Summary. The rate-determining step in the hydrolysis of α -acetoxy- α -methoxytoluene in the pH range 3.69–6.27 is the decomposition of the intermediate benzaldehyde methyl hemiacetal which is general-acid and general-base catalysed.

In an extension of our studies¹ on the hydrolysis of benzaldehyde methyl phenyl acetal we have investigated the hydrolysis of α -acetoxy- α -methoxytoluene (I, X = H) in which the phenoxy group of the latter has been replaced by the better leaving group, acetoxy. The rate of this reaction as determined spectrophotometrically by measuring

the rate of formation of benzaldehyde shows general-acid and general-base catalysis. The value for the catalytic constant for acetate ion, $k_{AC} = 0.180 \text{ l mol}^{-1} \text{ s}^{-1}$ at 15 °C is much larger than that for the hydrolysis of *p*-nitrophenyl acetate² ($5.64 \times 10^{-6} \text{ l mol}^{-1} \text{ s}^{-1}$ at 25 °C). This strongly suggests that the catalysis cannot be nucleophilic or general-base catalysis of a reaction at the acetoxy group of the starting material since *p*-nitrophenoxy should be a much better leaving group than α -methoxy- α -phenylmethoxy. It is also difficult to see how a catalytic constant of this magnitude could arise from attack at the pro-acyl carbon atom. It therefore seemed likely that the rate-determining



step (see Scheme) was decomposition of the hemiacetal. It seems very unlikely that the reaction of the carbonium ion with water would be rate-determining since such a reaction would not be expected to show general-acid catalysis and reactions of this type normally have rate constants of *ca.* 10^1 – 10^5 s⁻¹ at room temperature.³ Decomposition of the hemiacetal is analogous to the dehydration of aldehyde hydrates⁴ and the mutarotation of glucose⁵ both of which show general-acid and general-base catalysis. To test whether decomposition of the hemiacetal was rate-determining we studied the hydrolysis of α -chloroacetoxy- α -methoxytoluene (I, X = Cl) since if a reaction of the starting material were rate-determining different rate constants would be expected for the α -acetoxy and α -chloroacetoxy compounds, whereas if the decomposition of the hemiacetal were rate-determining, the rate constants should be identical within experimental error. The experimental results (Table) show that the latter is occurring. Further

TABLE

Comparison of the rate constants for the formation of benzaldehyde from α -acetoxy- α -methoxytoluene and α -chloroacetoxy- α -methoxytoluene at 15.0 °C.

pH	Buffer	$10^2 k_{\text{obs}}^a$ s ⁻¹	$10^2 k_{\text{obs}}^b$ s ⁻¹
4.19	Acetate	2.76	2.83
4.64	Acetate	1.62	1.64
6.12	Imidazole	3.55	3.53

^a From α -acetoxy- α -methoxytoluene. ^b From α -chloroacetoxy- α -methoxytoluene.

evidence that decomposition of the hemiacetal was slower than its formation was obtained by following the reaction in an acetate buffer (0.1M NaOAc, 0.1M DOAc) in a mixture of [2H₆] dimethyl sulphoxide and deuterium oxide (1:1 v/v) at 2 °C by n.m.r. spectroscopy (Varian HA 100). The chemical shift of the signal of the pro-acyl CH proton of the starting material was determined *ca.* 1 min after dissolution to be δ 6.48 downfield from internal sodium 2,2-dimethyl-2-silapentane-5-sulphonate. In this spectrum there was a very small signal at δ 5.44 which was ascribed to the pro-acyl CH proton of the hemiacetal since its chemical shift was close to that of the CH proton of benzaldehyde dimethyl acetyl for which the δ value is 5.35. This signal increased in intensity as the signal at δ 6.48 decreased and after *ca.* 14 min the two signals were of approximately equal intensities. In this spectrum there was also a small signal at δ 9.88 which is the chemical shift of the acyl CH proton of benzaldehyde. After 2 h the signals at δ 6.48 and 5.44 had disappeared and only the signal at δ 9.88 remained. Thus

under these conditions formation of the hemiacetal is faster than its decomposition to benzaldehyde.

There have been relatively few previous investigations of the decomposition of hemiacetals⁶ and to our knowledge none of those derived from aromatic aldehydes. In the hydrolysis of acetals the decomposition of the hemiacetal is normally a fast step⁷ and for aromatic aldehydes the equilibrium constant for the formation of hemiacetals is normally unfavourable unless electron-withdrawing substituents are present.⁸ The generation of hemiacetals of aromatic aldehydes as intermediates in the hydrolysis of their *O*-acetates therefore provides for the first time a general method for studying their decomposition. The pH-rate profile for the decomposition of benzaldehyde methyl hemiacetal generated in this way in the pH range 3.69–6.27 is shown in the Figure. There are spontaneous, hydronium-ion, and hydroxide-ion catalysed reactions.

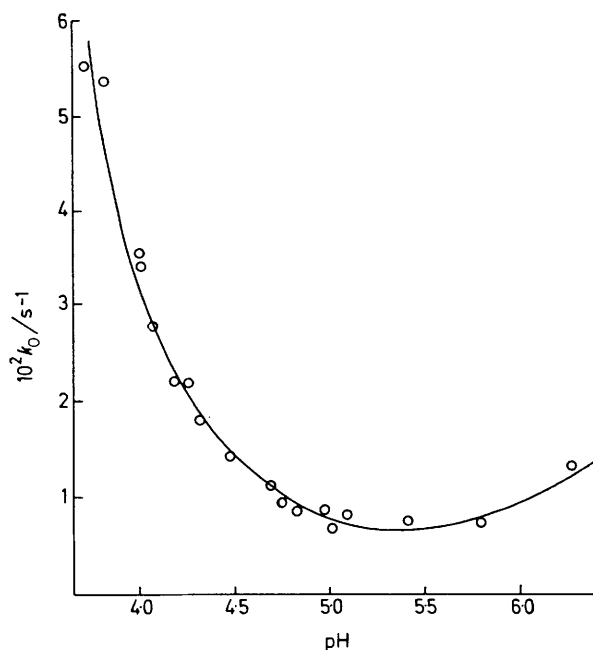


FIGURE. Plot of k_0 (rate constant extrapolated to zero buffer concentration) against pH for the decomposition of benzaldehyde methyl hemiacetal in water at 15.0 °C, $I = 0.05\text{M}$. The circles are the experimental points and the line follows the equation $k_0 = k(\text{H}_2\text{O}) + k(\text{H}_3\text{O}^+) \times 10^{-\text{pH}} + k(\text{HO}^-) \times K_w / 10^{-\text{pH}}$, with $k(\text{H}_2\text{O}) = 5.18 \times 10^{-3} \text{ s}^{-1}$, $k(\text{H}_3\text{O}^+) = 261 \text{ l mol}^{-1} \text{ s}^{-1}$, $k(\text{HO}^-) = 6.87 \times 10^3 \text{ l mol}^{-1} \text{ s}^{-1}$, and $K_w = 5.670 \times 10^{-15} \text{ mol}^2 \text{ l}^{-2}$.

In this pH range there is no indication of a change in the rate-determining step to formation of the hemiacetal but this may occur at higher pH values.

Previous work^{9–14} on the hydrolysis of acylals has been interpreted in terms of a rate-limiting fission of the bond between the pro-acyl carbon and the acyloxy or alkoxy group or in terms of a reaction at the acyl carbon atom. This is understandable since all the compounds previously studied have structural features which would make formation of the intermediate carbonium ion relatively less favourable compared to α -acetoxy- α -methoxytoluene.

Hence the hydrolysis follows a completely different pathway or if it follows the same pathway, the formation of the carbonium ion (and hemiacetal) becomes rate limiting. Thus α -acetoxy- α -*p*-nitrophenoxystoluene studied by Fife and De¹³ would form an α -*p*-nitrophenoxy carbonium ion in place of an α -methoxy carbonium ion and it is significant that the rate constants for its hydrolysis are 10^{-3} to 10^{-5} times those for the hydrolysis of α -acetoxy- α -methoxy toluene. Some of the other compounds are derived from aliphatic aldehydes^{9-11,14} and replacement of the phenyl

group of (I) by an alkyl group or hydrogen would cause a greater decrease in the rate of formation of the carbonium ion than in that of the decomposition of the hemiacetal and hence a change in the rate limiting step (or in the overall pathway). In yet other compounds^{10,12} the acyl group forms part of a ring and would be a poorer leaving group for this reason.

We thank the S.R.C. for support.

(Received, 6th July 1976; Com. 765.)

¹ E. Anderson and B. Capon, *Chem. Comm.*, 1969, 390; *J. Chem. Soc. (B)*, 1969, 1033; B. Capon and K. Nimmo, *J.C.S. Perkin II*, 1975, 1113.

² V. Gold, D. G. Oakenfull, and T. Riley, *J. Chem. Soc. (B)*, 1968, 515.

³ Cf. R. A. Diffenback, K. Sano, and R. W. Taft, *J. Amer. Chem. Soc.*, 1966, **88**, 4747; J. J. Brauman and W. C. Archie, *ibid.*, 1970, **92**, 5981; E. A. Hill and W. J. Mueller, *Tetrahedron Letters*, 1968, 2565; H. Nicholson and P. A. H. Wyatt, *J. Chem. Soc. (B)*, 1968, 198; J. N. Ride, P. A. H. Wyatt, and Z. M. Zochowski, *J.C.S. Perkin II*, 1974, 1188.

⁴ R. P. Bell, *Adv. Phys. Org. Chem.*, 1966, **4**, 1.

⁵ J. N. Brønsted and E. A. Guggenheim, *J. Amer. Chem. Soc.*, 1927, **49**, 2554; cf. B. Capon, *Chem. Rev.*, 1969, **69**, 454.

⁶ R. P. Bell and E. C. Baughan, *J. Chem. Soc.*, 1937, 1947; R. P. Bell and J. P. H. Hirst, *ibid.*, 1939, 1777; P. Le Henaff, *Compt. rend. (C)*, 1967, **262**, 1677; A. L. Mori, M. A. Porzio, L. L. Schaleger, *J. Amer. Chem. Soc.*, 1972, **94**, 5034; R. F. Atkinson and T. C. Bruice, *J. Amer. Chem. Soc.*, 1974, **96**, 819.

⁷ Cf. E. H. Cordes, *Progr. Phys. Org. Chem.*, 1967, **4**, 24; E. H. Cordes and H. G. Bull, *Chem. Rev.*, 1974, **74**, 581.

⁸ Cf. R. Fuchs, T. M. Young, and R. E. Rodewald, *Canad. J. Chem.*, 1973, **51**, 4122; M. R. Crampton, *J.C.S. Perkin II*, 1975, 185.

⁹ P. Salomaa, *Acta Chem. Scand.*, 1957, **11**, 132, 141, 235, 239; P. Salomaa and S. Laiho, *ibid.*, 1963, **17**, 103; P. Salomaa, *Suomen Kem. B.* 1964, **37**, 86.

¹⁰ T. H. Fife, *J. Amer. Chem. Soc.*, 1965, **87**, 271.

¹¹ A. Brown and T. C. Bruice, *J. Amer. Chem. Soc.*, 1973, **95**, 1593.

¹² D. P. Weeks, A. Grodski, and R. Fanucci, *J. Amer. Chem. Soc.*, 1968, **90**, 4958; D. P. Weeks and G. W. Zuorick, *ibid.*, 1969, **91**, 477; D. P. Weeks and J. P. Crane, *J. Org. Chem.*, 1973, **38**, 3375.

¹³ T. H. Fife and N. C. De, *J. Amer. Chem. Soc.*, 1974, **96**, 6158.

¹⁴ R. A. McClelland, *Canad. J. Chem.*, 1975, **53**, 2763.