# Generation and Detection by Nuclear Magnetic Resonance Spectroscopy of a Simple Tetrahedral Intermediate, Dimethyl Hemiorthoformate†

By BRIAN CAPON*, JAMES H. GALL, and DUNCAN MCL. A. GRIEVE
(*Chemistry Department, Glasgow University, Glasgow* G12 8QQ)

*Summary* Dimethyl hemiorthoformate has been shown to be an intermediate in the hydrolysis of acetoxydimethoxymethane in a mixture of [$^2H_6$]acetone (9 vols.) and deuterium oxide (1 vol.) at −35 °C and its formation and decomposition have been studied by following the changes in the n.m.r. spectrum.

MOST reactions which involve nucleophilic attack at the carbonyl group of derivatives of carboxylic acids are considered to pass through tetrahedral intermediates.[1] Although a number of stable tetrahedral intermediates are known these have either complex, usually polycyclic, structures[2] or have electron withdrawing groups attached to the proacyl carbon atom.[3] Until now there has been no method for studying directly the reactions of simple tetrahedral intermediates and indeed it has been suggested that sometimes, in certain conformations, their lifetime is short compared with the time for molecular rotation.[4]

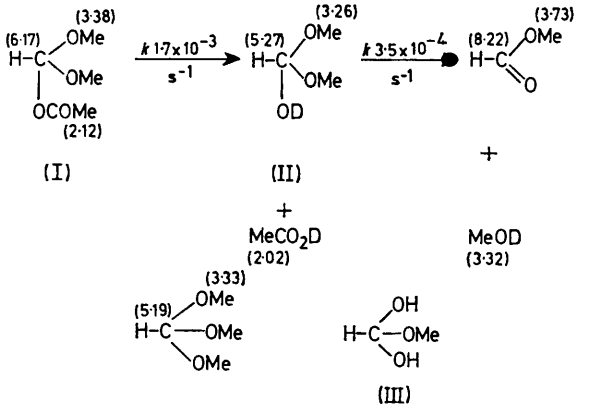
It has recently been shown[5] that the hemiacetal of benzaldehyde can be generated from its *O*-acetate in aqueous solution and that use can be made of this to study the kinetics of its decomposition. We have now extended this work to the next highest oxidation level, that of a carboxylic acid, by studying the hydrolysis of acetoxydimethoxymethane[6] (I) to see if it would decompose to the tetrahedral intermediate, dimethyl hemiorthoformate (II), in an analogous process.

The $^1H$ n.m.r. spectrum of acetoxydimethoxymethane

† This work was described at the 3rd IUPAC Conference on Physical Organic Chemistry, La Grande Motte, France, 7th September, 1976.

(I) in $CDCl_3$ consists of three signals with δ 6·17 (s, 1H), 3·42 (s, 6H), and 2·08 (s, 3H). In a mixture of [$^2H_6$]acetone (9 vols.) and deuterium oxide (1 vol.) at −60 °C the spectrum (Varian XL100) is almost identical with δ 6·17 (s, 1H), 3·38 (s, 6H), and 2·12 (s, 3H). When the solution [concentration of (I), 0·15 M] was warmed to −35 °C this spectrum decreased in intensity ($k = 1·7 \times 10^{-3}$ s$^{-1}$) with formation of acetic acid (δ 2·02) but not of methyl formate [δ 8·22 (s) and 3·73 (s)]. Instead the spectrum of a new species appeared with δ 5·27 (s) and 3·26 (s). The signal at δ 3·26 was close to that for methanol but careful examination showed it to be at slightly higher field as δ for methanol was 3·32. This new spectrum increased in intensity as the spectrum of the acetoxydimethoxymethane decreased and reached a maximum after *ca.* 20 min when it accounted for *ca.* 75% of the starting material. At the same time there was much slower formation of methyl formate as shown by the appearance of signals at δ 8·22 and 3·73 and also of methanol (δ 3·32). The chemical shifts of the signals of the new species are very similar to those of trimethyl orthoformate (δ 5·19 and 3·33). The difference in chemical shift between the signals at δ 5·27 of the new species and δ 5·19 of trimethyl orthoformate, 0·08 p.p.m., is almost the same as that between the signals of the proton attached to the proacyl carbon of benzaldehyde methylhemiacetal (δ 5·44) and benzaldehyde dimethylacetal (δ 5·35), 0·09 p.p.m.[5] The new spectrum is therefore that to be expected for the species which would result from replacement of one methoxy group of trimethyl orthoformate by hydroxy, *i.e.* dimethyl hemiorthoformate (II). Additional evidence that this was the species present was made by measuring the rate constant for disappearance of the signal at δ 5·27 ($3·5 \times 10^{-4}$ s$^{-1}$) after all the acetoxydimethoxymethane (I) had disappeared. This value was identical within experimental error with the rate constant for formation of the signal at δ 8·22 of methyl formate ($3·3 \times 10^{-4}$ s$^{-1}$). Thus, the species present has an n.m.r. spectrum very similar but not identical to that of trimethyl orthoformate and decomposes to form methyl formate on a 1:1 basis. There is little doubt that it must be the tetrahedral intermediate methyl hemiorthoformate (II), and that the reaction proceeds as shown in the Scheme.

On the basis of the calculations of Guthrie[7] it is possible to construct a pH-rate profile for decomposition of the closely related tetrahedral intermediate, methyl hemiorthoformate (III). In the pH range 5 to 2 the calculated rate constant at 25 °C for the reaction in $H_2O$ is the range $10^{-1}$—$10^2$ s$^{-1}$. It was thought that the tetrahedral intermediates (II) and (III) would probably decompose at similar rates and although it is difficult to make a precise comparison our value of $3·5 \times 10^{-4}$ s$^{-1}$ for the rate constant for the decomposition of (II) in a mixture of [$^6H_2$]acetone (9 vols.) and $D_2O$ (1 vol.) which contains 0·15 M in acetic acid [formed in the decomposition of (I)] at −35 °C does not seem to be inconsistent with Guthrie's calculations.




The figures in parentheses are δ-values in p.p.m. downfield from internal reference $Me_4Si$.

This work shows that one simple tetrahedral intermediate at least can be generated by the hydrolysis of its *O*-acetate and suggests that it may be possible to generate related species similarly from their *O*-acyl derivatives or from other high energy species (*e.g.* dialkoxymethyl carbocations).

(*Received*, 14*th October* 1976; *Com.* 1167.)

[1] *Cf.* M. L. Bender, *Chem. Rev.*, 1960, **60**, 53; 'Mechanisms of Homogeneous Catalysis from Protons to Proteins,' Wiley–Interscience, New York, 1971, p. 108; W. P. Jencks, 'Catalysis in Chemistry and Enzymology,' McGraw–Hill, New York, 1968, pp. 465, 526; T. C. Bruice and S. J. Benkovic, 'Bio-organic Mechanisms,' Benjamin, New York, 1966, Vol. 1; S. L. Johnson, *Adv. Phys. Org. Chem.*, 1967, **5**, 237; A. J. Kirby in 'Comprehensive Chemical Kinetics,' eds. C. H. Bamford and C. F. H. Tipper, Elsevier, Amsterdam, 1972, p. 104.
[2] T. Goto, Y. Kishi, S. Takahashi, and Y. Hirata, *Tetrahedron*, 1965, **21**, 2059; G. Fodor, F. Letourneau, and N. N. Mandava, *Canad. J. Chem.*, 1970, **48**, 1465; H. Wevers and W. Drenth, *Rec. Trav. chim.*, 1974, **93**, 99; B. Bobranski and M. Sladowska, *Roczniki Chem.*, 1972, **46**, 451; G. Lucente and A. Romeo, *Chem. Comm.*, 1971, 1605; S. Cerrini, W. Fedeli, and F. Mazza, *ibid.*, 1971, 1607; G. A. Rogers and T. C. Bruice, *J. Amer. Chem. Soc.*, 1973, **95**, 4452; 1974, **96**, 2481; N. Gravitz and W. P. Jencks, *ibid.*, 1974, **96**, 489.
[3] F. Swarts, *Bull. Soc. chim. belges*, 1926, **35**, 414; M. L. Bender, *J. Amer. Chem. Soc.*, 1953, **75**, 5986; J. P. Guthrie, *Canad. J. Chem.*, 1976, **54**, 202; J. Hine, D. Ricard, and R. Perz, *J. Org. Chem.*, 1973, **38**, 110.
[4] *Cf.* P. Deslongchamps, *Tetrahedron*, 1975, **31**, 2463.
[5] B. Capon, K. Nimmo, and G. L. Reid, *J.C.S. Chem. Comm.*, 1976, 871.
[6] *Cf.* H. W. Post and E. R. Erickson, *J. Org. Chem.*, 1937, **2**, 260; J. W. Scheeren and W. Stevens, *Rec. Trav. chim.*, 1966, **85**, 793.
[7] J. P. Guthrie, *J. Amer. Chem. Soc.*, 1973, **95**, 6999.