Tetrahedral Intermediates. Part 1. The Generation and Characterisation of Some Hemiorthoesters

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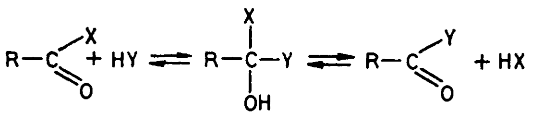
Dimethyl hemiorthoformate, the putative intermediate in the methanolysis of methyl formate, has been detected by ^{1}H n.m.r. spectroscopy as an intermediate in the hydrolysis of dimethoxymethyl acetate in solution in mixtures of [$^2H_6$]acetone (90—86 volumes) and deuterium oxide (10—14 volumes) at −35 °C. Similar experiments with 2-acetoxy-1,3-dioxolan lead to the detection of 2-hydroxy-1,3-dioxolan and with 2-acetoxy- and 2-chloroacetoxy-4,4,5,5-tetramethyl-1,3-dioxolan to 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolan. The last compound was also detected by ^{13}C n.m.r. spectroscopy. The relative rates of breakdown of dimethyl hemiorthoformate, 2-hydroxy-1,3-dioxolan, and 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolan were approximately 1, 0.3, and 0.03. The breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolan was shown to be acid catalysed with a second-order rate constant 29.4 l mol^{-1} s^{-1} in [$^2H_6$]acetone–deuterium oxide (9 : 1 v/v) at −40 °C.

Acyl transfer reactions are generally thought to proceed through tetrahedral intermediates [*e.g.* equation (1)].[1] These are not normally detectable and the evidence for their incursion is usually indirect, *e.g.* the observation of exchange of the carbonyl oxygen of the starting material in hydrolyses,[2] or of breaks in the pH–rate profile which must arise from a change in rate-determining step and therefore indicate the presence of an intermediate.[3] Some stable compounds which have the general structure (1) are known, but these usually have some stabilising feature like a group R which contains strongly electron-withdrawing groups (*e.g.* $R = CF_3$),[4] a bi- or poly-cyclic structure where formation of (I) is favoured entropically (*e.g.* tetrodotoxin),[5] or a substituent X in which the ability to conjugate with the carbonyl group of the starting material in reduced (*e.g.* the side chain of the ergot alkaloids[6] and the intermediates reported in refs. 7—12). The direct detection of an intermediate without one of these features is unusual and it is difficult to evaluate the validity of some earlier reports[13–15] which have described the detection of an intermediate by u.v. spectroscopy. In such cases it is frequently difficult to be certain that the intermediate detected is the tetrahedral intermediate since u.v. spectra are often not very characteristic of structure. However recently McLelland and his co-workers have provided good evidence for the detection of some cyclic hemiorthoesters in the hydrolysis of the corresponding orthoesters.[16] In this paper we report the generation from reactive precursors and characterisation by n.m.r. spectroscopy of the tetrahedral intermediate in *O* ⟶ *O* formyl transfers and a kinetic investigation of their breakdown. The use of n.m.r. spectroscopy enables the intermediate to be well characterised but this technique is not so good as u.v. spectroscopy for kinetic measurements. Therefore the kinetic measurements reported in this paper are preliminary and semiquantitative ones and more precise measurements will be the subject of later publications.

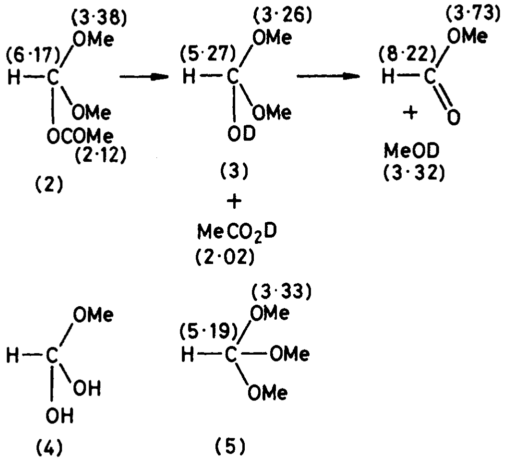


(1)

X,Y = OR, NR^1_2, SR^1, Cl *etc.*

Results and Discussion

It was reported from this laboratory that the rate-limiting step in the hydrolysis of α-acetoxy-α-methoxytoluene[17] is the decomposition of the hemiacetal and we wondered if it would be possible to extend this observation to the next highest oxidation level, that of a carboxylic acid. The hydrolysis of dimethoxymethyl acetate (2) was therefore investigated.[18] This compound was chosen since the chemical shift of the proton attached to the acyl or pro-acyl carbon should be different in the starting material, product of hydrolysis (methyl formate), and intermediate. This intermediate, dimethyl hemiorthoformate (3), is the expected intermediate in the methanolysis of methyl formate and the related intermediate in the hydrolysis of methyl formate, methyl dihemiorthoformate (4), has been the subject of some semi-empirical calculations by Guthrie.[19] On the basis of Guthrie's calculations we constructed a pH–rate profile for the breakdown of the latter (Figure 1). At the



Scheme 1 The figures in parentheses are δ values downfield from internal reference Me_4Si

minimum the rate constant for breakdown is *ca.* 10^{-1} s^{-1} at 25° which suggests that if it could be generated at high concentration it should have a sufficiently long lifetime to be detected either by fast reaction techniques at 25° or by conventional methods at low temperatures. It was thought that the rate of breakdown of dimethyl hemiorthoformate would not differ greatly from that of methyl dihemiorthoformate at acidic pH values. The presence of one hydroxy group which can form a carbonyl group by proton loss is clearly important, but the presence of a second one should not have a large effect.

After a large number of unsuccessful experiments it was found possible to detect dimethyl hemiorthoformate in the hydrolysis of dimethoxymethyl acetate in 90 : 10 v/v acetone–water mixtures at —35° and conditions close to these. A representative set of spectra is shown in Figure 2. Figure 2a shows the spectrum of dimethoxymethyl acetate with three signals corresponding to the three types of proton and Figure 2d shows the spectrum of the products of hydrolysis, methyl formate, methanol, and acetic acid. In Figures 2b and c there are, in addition to the signals of starting material and products, two new signals at δ 3.26 and 5.27. These are the expected chemical shifts of dimethyl hemiorthoformate (3) and are similar to those of trimethyl orthoformate (5) (δ 3.33 and 5.19) which is stable under these conditions. The chemical shifts are summarised in Scheme 1 and plots of the variation with time of the concentrations of starting material, intermediate, and product are given in Figure 3. In this experiment there is an initial rapid reaction which arises from the fact that the sample was initially at a higher temperature than that of the probe of the spectrophotometer.

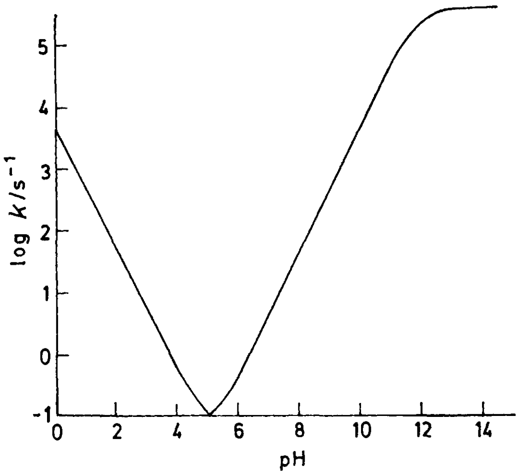


FIGURE 1 The pH–rate profile for the breakdown of methyl dihemiorthoformate based on the calculations of Guthrie.[19] The pK_a was taken to be 11.83 on the basis of the linear free energy relationship pK_a = 14.4 — 1.42σ * for the pK_a values of compounds $RCH(OH)_2$ and σ * (MeO) = 1.81 (G. B. Barlin and D. D. Perrin, *Quart. Rev.*, 1966, **20**, 75)

Similar experiments were carried out with 2-acetoxy-1,3-dioxolan (6) (Scheme 2) and 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolan (7) (Figure 4 and Scheme 3). With the latter it was possible to obtain a solution in which >90% of the starting material was present as intermediate. This reaction was also followed by ^{13}C n.m.r. spectroscopy (see Figure 5 and Scheme 4). The pro-acyl carbon atom of the starting material gave a signal at δ 109.6 p.p.m. which was replaced by a signal at δ 109.9 p.p.m. of the intermediate which subsequently changed to a signal, δ 162.9 p.p.m., for the carbon of the carbonyl group of the product, pinacol monoformate.

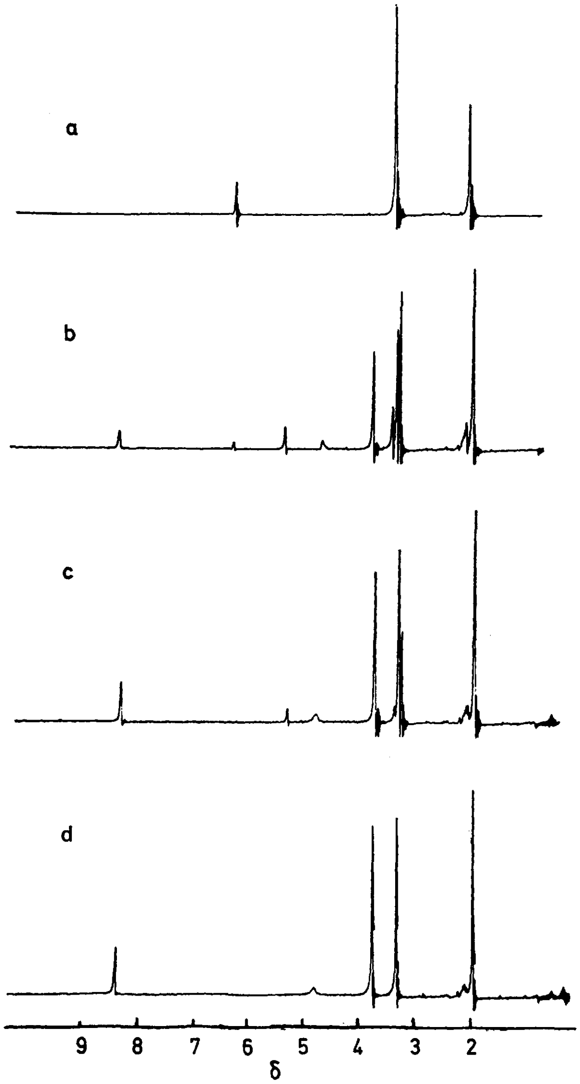


FIGURE 2 The ^1H n.m.r. spectrum of dimethoxymethyl acetate in: a, $CDCl_3$; b, [$^2H_6$]acetone–deuterium oxide (87 : 3 v/v) at — 35 °C, spectrum commenced 10 s after dissolving; c, same as b, spectrum commenced 6 min 22 s after dissolving; d, same as b, spectrum commenced 30 min after dissolving

The kinetics of these reactions were studied by following the build-up and decay of the signals in the ^1H n.m.r. spectrum. Within a rather large experimental error these followed the first-order rate expression although it is possible that more accurate measurements would show that this is incorrect. Thus, the first step in the reaction generates acetic acid at a concentration equal to that of the starting material so that if the first step were acid catalysed it should show autocatalysis. Under certain conditions, although the intermediate could be detected, it was always in the presence of starting material. When this happened no attempt was made to analyse the results using the equations for consecutive reactions (with autocatalysis?) since it was thought that this was unjustified by the accuracy of the results. First-order rate constants for the decomposition of the intermediate were only calculated for solutions in which the starting material had disappeared and of course in these solutions there is a concentration of acetic acid equal to that of the initial concentration of starting material.

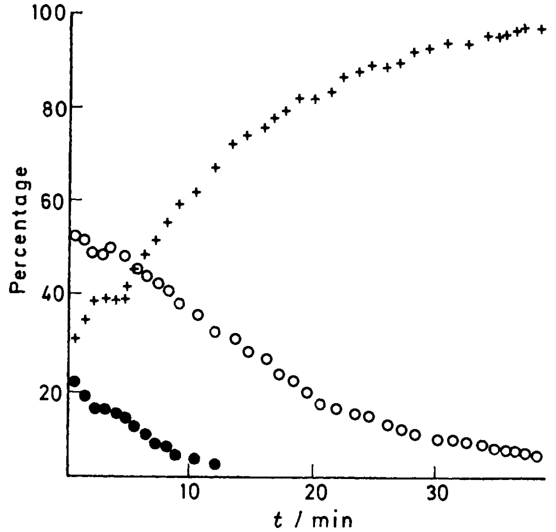
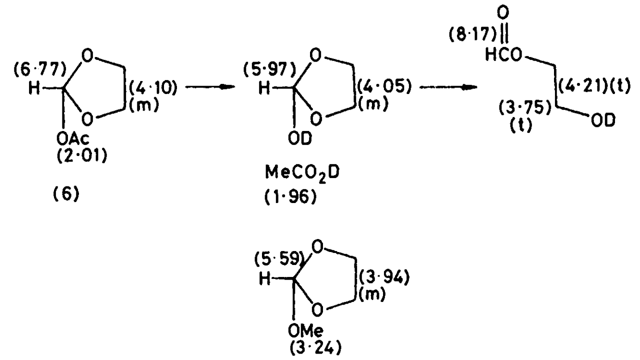
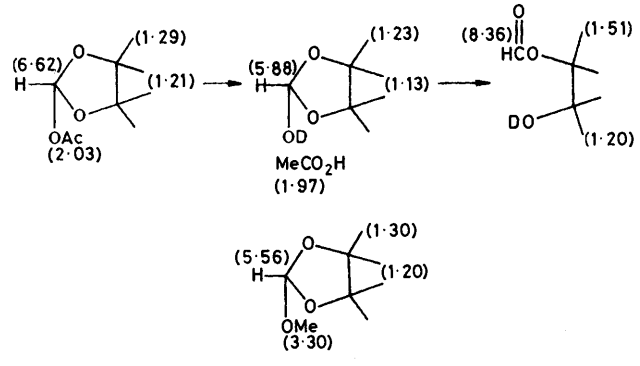


FIGURE 3 Plots of the percentages of dimethoxymethyl acetate, ●; dimethylhemiorthoformate, ○; and methyl formate, +, against time in [$^2H_6$]acetone–deuterium oxide (86 : 14 v/v) at −35°



SCHEME 2 The figures in parentheses are δ values downfield from internal reference Me_4Si



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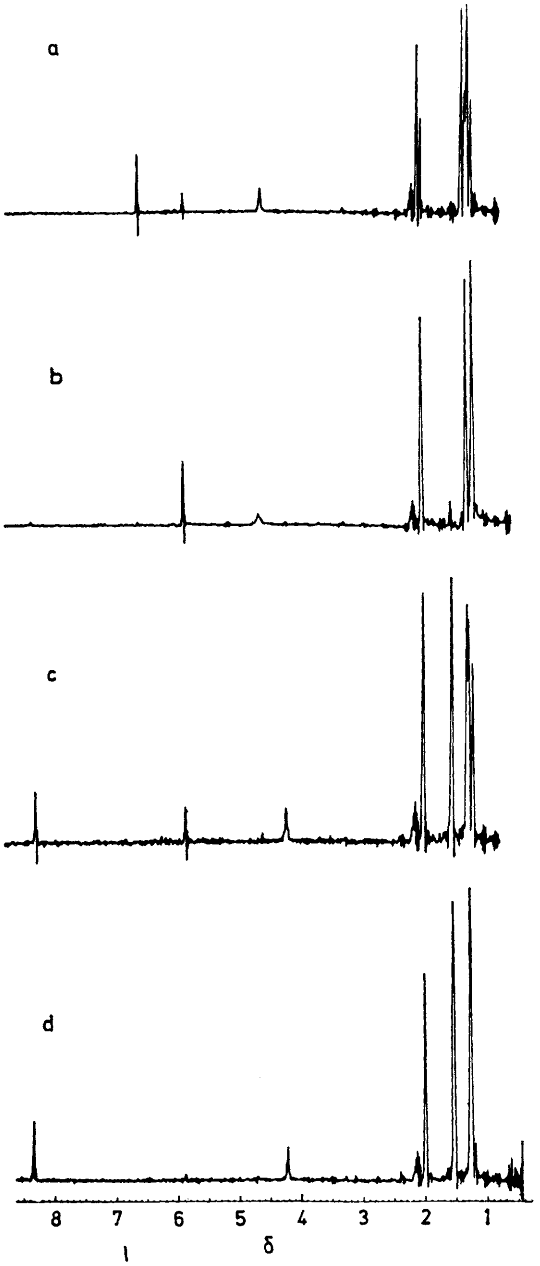


FIGURE 4 The ^1H n.m.r. spectrum of 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolan in [$^2H_6$]acetone–deuterium oxide (9 : 1 v/v) at: a, −40°, spectrum commenced 2 m in after dissolving; b, −40°, spectrum commenced 108 min after dissolving; c, 0°, same solution as b but temperature raised to 0° and left 23 min; d, 0°, same solution as b but temperature raised to 0° and left 64 min

The results in Table 1 show the effect on k_1 of changing the concentration of deuterium oxide. This increases 5.8 times on going from 90 : 10 to 86 : 14 v/v [$^2H_6$]acetone–deuterium oxide. The value of k_2 increases much less and although the dimethyl hemiorthoformate can be

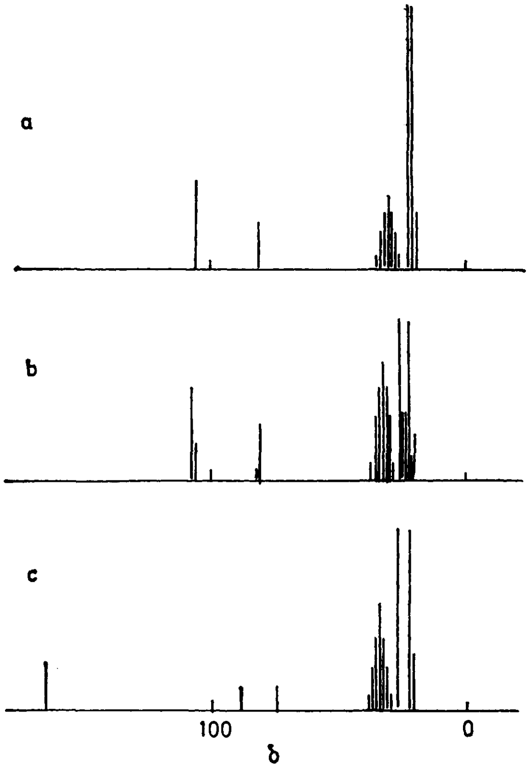
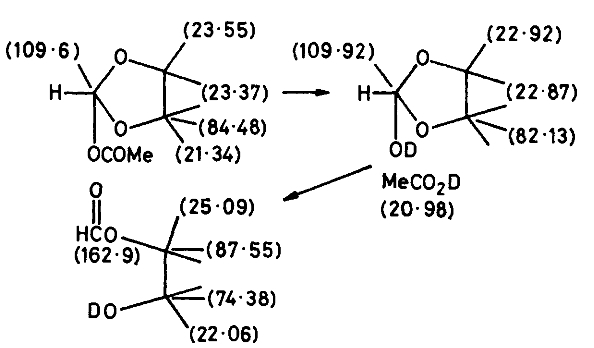


FIGURE 5 a, The ^{13}C n.m.r. spectrum of 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolan in [$^2H_6$]acetone at −35°; b, same as a after addition of deuterium oxide (10% v/v), spectrum commenced 20 min after addition; c, same as b, 3 h at −35° and warming to 0°

detected in 90 : 10 v/v [$^2H_6$]acetone–deuterium oxide the acetoxy compound appears to be present. A similar effect is found with 2-acetoxy-1,3-dioxolan (Table 2). The cyclic hemiorthoester 2-hydroxy-1,3-dioxolan breaks down *ca.* 3 times more slowly than the acyclic dimethyl hemiorthoformate.

The hemiorthoester is much easier to detect in the hydrolysis of 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolan than in that of 2-acetoxy-1,3-dioxolan since the acetoxy compound is hydrolysed *ca.* 5 times more rapidly and the hemiorthoester breaks down *ca.* 10 times more slowly (*cf.* Tables 2 and 3). When the chloroacetoxy compound is used as the precursor it was not detected in [$^2H_6$]acetone–deuterium oxide (90 : 10 v/v) at −20 and 0° and the first spectrum obtained showed the presence of only 2-hydroxy-3,3,4,4-tetramethyl-1,3-dioxolan and the final product pinacol monoformate. The rate constant for the breakdown of the hemiorthoester generated in this way is *ca.* 2.7 times greater than when it was generated from the acetoxy-compound (*cf.* Tables 3 and 4). This presumably arises from the presence of the stronger acid, chloroacetic acid, at a slightly higher concentration, 0.20M compared to 0.16M. Acid-catalysed breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolan was studied at −40° in the presence of deuterium chloride (Figure 6). The value of k_2 increased linearly with acid concentration to yield a second-order constant 29.4 l mol^{-1} s^{-1} (s.d. 1.6). The intercept was -1.44×10^{-4} s^{-1} (s.d. 0.62×10^{-4}) which is, within experimental error, zero. Clearly the major mode of breakdown under these conditions is an acid-catalysed one and the spontaneous hydrolysis is not very important. This agrees with the calculations of Guthrie[19] for the breakdown of methyl dihemiorthoformate for which the maximum



SCHEME 4 The figures in parentheses are δ values downfield from internal reference Me_4Si

TABLE 1

The rate constants for hydrolysis of dimethoxymethyl acetate[a] (k_1) and for the breakdown of dimethyl hemiorthoformate (k_2) in mixtures of [$^2H_6$]acetone and deuterium oxide at −35° [b,c]

Solvent composition (v/v)	10^4k_1/s^{-1}	10^4k_2/s^{-1}
90 : 10 CD_3COCD_3–D_2O	3.49 (0.04) [d]	
86 : 14 CD_3COCD_3–D_2O	20.4 (1.6) [d]	11.3 (0.3) [d]

[a] Initial concentration 0.26M. [b] Based on C–H peaks. [c] These values are considered to be more accurate than those given in our preliminary publication[18] when the solvent composition was determined less accurately. [d] Standard deviation.

TABLE 2

The rate constants for the hydrolysis of 2-acetoxy-1,3-dioxolan[a] (k_1) and for the breakdown of 2-hydroxy-1,3-dioxolan (k_2) at −35° [b]

Solvent composition (v/v)	10^4k_1/s^{-1}	10^4k_2/s^{-1}
90 : 10 CD_3COCD_3–D_2O	1.24 (0.01) [c]	
88 : 12 CD_3COCD_3–D_2O	1.35 (0.01) [c]	
86 : 14 CD_3COCD_3–D_2O	9.87 (0.25) [c]	3.60 (0.04) [c]

[a] Initial concentration 0.20M. [b] Based on C–H peaks. [c] Standard deviation.

TABLE 3

The rate constants for hydrolyses of 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolan[a] (k_1) and for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolan (k_2) in [$^2H_6$]acetone–deuterium oxide (90 : 10 v/v)

Temperature (°C)	10^4k_1/s^{-1}	10^4k_2/s^{-1}
−40	4.16 (0.08) [b,c]	
−40	4.55 (0.19) [b,c]	
−10		3.91 (0.08) [b,e]
−10		4.11 (0.08) [b,d]
0		5.48 (0.09) [b,e]
0		6.31 (0.20) [b,d]

[a] Initial concentration in all experiments 0.16M. [b] Standard deviation. [c] Based on acetate signals. [d] Based on C–H signals. [e] Based on CH_3 signals.

contribution to the overall rate of breakdown from the spontaneous reaction is never >0.1%.

Attempts were made to generate hemiorthoesters using dialkoxycarbonium salts as precursors. Experiments with dimethoxycarbonium fluoroborate, dimethoxyphenylcarbonium fluoroborate, 2-phenyl-1,3-dioxolenium fluoroborate, and methyl-δ-valerolactonium fluoroborate were carried out but no hemiorthoester could be detected. It was thought that this was because of inefficient mixing and dispersal of the heat of reaction. The reaction generates considerable heat and also strong acid equivalent to the starting concentration of the salt (0.1—0.2M) which would catalyse the breakdown of the hemiorthoester. To check the stability of the dimethyl hemiorthoacetate under the conditions used the reaction of dimethylcarbonium tetrafluoroborate was investigated in the presence of the normal precursor dimethoxymethyl acetate in the same solution. No dimethyl hemiorthoformate could be detected.

TABLE 4

The rate constant for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolan (k_2) generated from 2-chloroacetoxy-4,4,5,5-tetramethyl-1,3-dioxolan [a] in [$^2H_6$]-acetone–deuterium oxide [b] (90 : 10 v/v)

Temperature (°C)	$10^4k_2/s^{-1}$
−20	6.41 (0.16) [c]
0	16.4 (0.5) [c]

[a] Initial concentration 0.20M. [b] Based on C–H peaks. [c] Standard deviation.

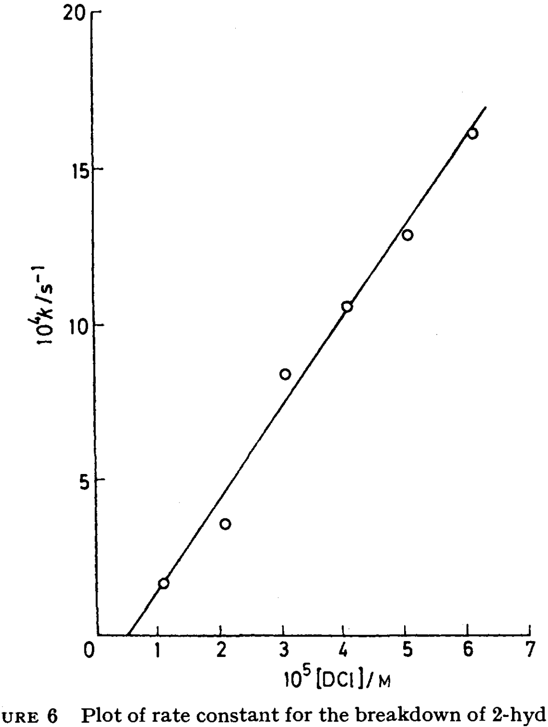


FIGURE 6 Plot of rate constant for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolan against [DCl] in [$^2H_6$]acetone–deuterium oxide (9 : 1 v/v) at −40°. The circles are the experimental points and the line is that determined by the method of least square and has slope 29.4 l mol^{-1} s^{-1} (s.d. 1.6) and intercept -1.44×10^{-4} s^{-1} (s.d. 0.62×10^{-4})

The results reported in this paper show that quite simple tetrahedral intermediates in $O \longrightarrow O$ acyl transfer reactions are sufficiently stable to be detected. Deslongchamps has suggested that some tetrahedral intermediates in certain conformations have a lifetime short compared with the time for rotation about a single bond.[20,21] Our results show that this cannot always be true.[22]

EXPERIMENTAL

Materials.—Dimethoxymethyl acetate was prepared by the method of Scheeren and Stevens [23] from trimethyl orthoformate and mixed formic acetic anhydride, yield 55%, b.p. 40° at 20 mmHg (lit.,[20] 69° at 35 mmHg), δ ($CDCl_3$) 3.45 (6 H, s), 2.07 (3 H, s), and 6.17 (1 H, s).

2-Acetoxy-1,3-dioxolan was prepared from 2-methoxy-1,3-dioxolan and dimethoxymethyl acetate by the method of Scheeren *et al.*,[24] b.p. 41—43° at 0.4 mmHg (lit.,[21] 42—43° at 0.4 mmHg), δ ($CDCl_3$), 2.02 (3 H, s), 4.10 (4 H, m), and 6.84 (1 H, s). 2-Acetoxy-4,4,5,5-tetramethyl-1,3-dioxolan was prepared by a similar method from the corresponding 2-methoxy compound, b.p. 58—59° at 0.8 mmHg (lit.,[23] 50—51° at 0.4 mmHg), δ ($CDCl_3$) 2.02 (3 H, s), 1.21 (6 H, s), 1.31 (6 H, s), and 6.69 (1 H, s).

2-Chloroacetoxy-4,4,5,5-tetramethyl-1,3-dioxolan was prepared by reacting equimolar quantities of the corresponding acetoxy compound and chloroacetic acid with heating under reduced pressure in a flask attached to a spinning band column. The temperature of the flask was kept below 50° and the acetic acid was distilled off slowly. Remaining liquid was then distilled under high vacuum, b p. 108—110° at 0.03 mmHg, yield 80%, δ ($CDCl_3$) 1.26 (12 H, apparent s), 4.06 (3 H, s), and 6.76 (1 H, s). This compound was very unstable and a satisfactory analysis could not be obtained.

Dimethoxycarbonium fluoroborate,[25] dimethoxyphenylcarbonium fluoroborate,[26] 2-phenyl-1,3-dioxolenium fluoroborate,[26] and methyl δ-valerolactonium fluoroborate [20] were prepared by literature methods.

N.m.r. Measurements.—An n.m.r. tube to which the solvent (0.5 ml) containing tetramethylsilane had been added, was placed in the probe of the spectrometer (Perkin-Elmer R32; 90 MHz) and allowed to equilibrate thermally. The tube was then removed from the probe, the required amount of substrate (10—20 mg) added, and the tube was shaken and replaced. After the lock signal (Me_4Si) had been reset, spectra were run at convenient time intervals.

The percentage of each material present was calculated from the height of one of its signals. This required calibration factors since all the signals did not have the same width. These were obtained by weighing 25 μl of the formate ester and the corresponding orthoester, running the n.m.r. spectrum, and measuring the heights of the signals for the protons attached to the acyl and pro-acyl carbon atoms. From these and the concentrations calibration factors for the protons attached to the acyl carbon atoms of the formate esters were obtained as follows: methyl formate, 1.54; ethyl formate, 1.33; pinacol monoformate, 1.0. The calibration factor for glycolmonoformate was taken to be the same as that for ethyl formate. The percentage of each species present could then be obtained by assuming that the signal heights multiplied by the calibration factors added up to 100%. First-order rate constants were calculated by a generalised least squares method,[27] using a Digico Micro 16P computer.

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REFERENCES

[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] M. L. Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626.

[3] W. P. Jencks and M. L. Gilchrist, *J. Amer. Chem. Soc.*, 1964, **86**, 5616.

[4] F. Swarts, *Bull. Soc. chim. belges*, 1929, **35**, 414; M. L. Bender, *J. Amer. Chem. Soc.*, 1953, **75**, 5986; A. Moffat and H. Hunt, *ibid.*, 1959, **81**, 2082; P. Bladon and G. C. Forrest, *Chem. Comm.*, 1966, 481; J. Hine, D. Ricard, and R. Perz, *J. Org. Chem.*, 1973, **38**, 110; G. Fraenkel and D. Watson, *J. Amer. Chem. Soc.*, 1975, **97**, 231.

[5] R. B. Woodward, *Pure Appl. Chem.*, 1964, **9**, 49; R. B. Woodward and J. Z. Gougoutas, *J. Amer. Chem. Soc.*, 1964, **86**, 5030; T. Goto, Y. Kishi, S. Takahashi, and Y. Hirata, *Tetrahedron*, 1965, **21**, 2059.

[6] A. Stoll, A. Hofman, and T. Petrzilka, *Helv. Chim. Acta*, 1951, **34**, 1544.

[7] M. M. Shemyakin, V. K. Antonov, A. M. Shkrob, Y. N. Sheinker, and L. B. Senyavina, *Tetrahedron Letters*. 1962, 701; V. K. Antonov, A. M. Shkrob, and M. M. Shemyakin, *ibid.*, 1963, 439; M. M. Shemyakin, V. K. Antonov, A. M. Shkrob, V. I. Shchelokov, and Z. E. Agadzhanyan, *Tetrahedron*, 1965, **21**, 3537; V. K. Antonov, A. M. Shkrob, and M. M. Shemyakin, *Zhur. Obschei Khim.*, 1965, **35**, 1380; *J. Gen. Chem. U.S.S.R.* 1965, **35**, 1385.

[8] R. G. Griot and A. J. Frey, *Tetrahedron*, 1963, **19**, 1661.

[9] M. Rothe and R. Steinberger, *Angew. Chem. Internat. Edn.*, 1968, **7**, 884; *Tetrahedron Letters*, 1970, 649, 2467.

[10] G. A. Rogers and T. C. Bruice, *J. Amer. Chem. Soc.*, 1973, **95**, 4452; 1974, **96**, 2481.

[11] N. Gravitz and W. P. Jencks, *J. Amer. Chem. Soc.*, 1974, **96**, 489.

[12] A. Cipiciani, P. Linda, and G. Savelli, *J.C.S. Chem. Comm.*, 1977, 857.

[13] R. Kuhn and D. Wieser, *Angew. Chem.*, 1957, **69**, 371.

[14] C. E. Stauffer, *J. Amer. Chem. Soc.*, 1972, **94**, 7887; 1974, **96**, 2489; *cf.* J. P. Guthrie, *ibid.*, 1974, **96**, 588.

[15] D. R. Robinson, *Tetrahedron Letters*, 1968, 5007; *J. Amer. Chem. Soc.*, 1970, 92, 3138.

[16] M. Ahmad, R. G. Bergstrom, M. J. Cashen, A. J. Kresge, R. A. McClelland, and M. F. Powell, *J. Amer. Chem. Soc.*, 1977, **99**, 4827.

[17] B. Capon, K. Nimmo, and G. P. Reid, *J.C.S. Chem. Comm.*, 1976, 871.

[18] B. Capon, J. H. Gall, and D. McL. A. Grieve, *J.C.S. Chem. Comm.*, 1976, 1034.

[19] J. P. Guthrie, *J. Amer. Chem. Soc.*, 1973, **95**, 6999.

[20] P. Deslongchamps, R. Chênevert, R. Taillefer, C. Moreau, and J. K. Saunders, *Canad. J. Chem.*, 1975, **53**, 1601.

[21] P. Deslongchamps, *Tetrahedron*, 1975, **31**, 2463.

[22] P. Deslongchamps, *Heterocycles*, 1977, **7**, 1271.

[23] J. W. Scheeren and W. Stevens, *Rec. Trav. chim.*, 1966, **85**, 793.

[24] J. W. Scheeren, A. P. M. Van Der Veek, and W. Stevens, *Rec. Trav. chim.*, 1969, **88**, 195.

[25] R. F. Borch, *J. Org. Chem.*, 1969, **34**, 627.

[26] H. Meerwein, K. Bodenberner, P. Borner, F. Kunert, and K. Wunderlich, *Annalen*, 1960, **632**, 38.

[27] W. E. Deming, 'Statistical Adjustment of Data,' Dover, New York, 1964; W. E. Wentworth, *J. Chem. Educ.*, 1965, **42**, 96, 162.