J_{trans} = 13.5 Hz, J_{gem} = 1.7 Hz) , 4.35 (q, 1, J_{cis} = 5.7 Hz, J_{gem} = 1.7 Hz), 3.62 (s, 3), 3.37 (d, 1, J_{gem} = 4 Hz), 3.27 (d, 1, J_{gem} = 4 Hz).

Instrumentation. ^{1}H NMR spectra were recorded at 90 MHz in the continuous-wave mode on a Perkin-Elmer R32 spectrometer. Natural abundance ^{13}C NMR spectra were recorded with proton noise decoupling at 25.2 MHz in the pulsed Fourier transform mode on a Varian XL-100 spectrometer. Chemical shifts are reported as δ values relative to internal Me_4Si. Deuterium isotope shifts in the ^{13}C spectra were measured, following the method of Pfeffer et al.,[18] using a 5-mm NMR tube supported coaxially inside a 10-mm NMR tube. With this arrangement the volume of the outer annulus was ca. 3 times the volume of the same depth of the inner tube, but the resulting disparity in the intensity of the signals from the inner and outer solutions was not found to be a problem (results obtained with methyl α-D-glucopyranoside were essentially identical with those reported previously[18]). The two solutions had the same composition except that D_2O/DCl was added to the outer one and H_2O/HCl to the inner. The deuterium isotope effects were measured from spectra where the digital resolution was 0.6 Hz/data point and the line widths ca. 1.5 Hz.

Acknowledgment. We thank the British SRC for support and the Universidade Federal de Santa Catarina, Florianópolis, Brazil, for granting leave of absence to C.Z. and CAPES for providing a scholarship.

Tetrahedral Intermediates. 2.[1] The Detection of Hemiorthoesters in the Hydration of Ketene Acetals and the Mechanism of Their Breakdown

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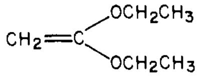
Contribution from the Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, Scotland, U.K. *Received November 2, 1980*

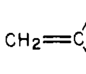
Abstract: The hemiorthoesters 2-deuterioxy-2-[$^2H_1$]methyl-4,4,5,5-tetramethyl-1,3-dioxolane (**7b**) and 2-deuterioxy-2-[$^2H_1$]methyl-1,3-dioxolane (**11**) have been detected by ^{1}H and ^{13}C NMR spectroscopy on hydration of the ketene acetals 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane (**5**) and 2-methylene-1,3-dioxolane (**9**) in mixtures of CD_3CN or CD_3COCD_3 with D_2O. **7b** was stable for several hours at −30 °C in CD_3COCD_3(90%)–D_2O (10%) (v/v) which was 1.4×10^{-2} M in CD_3CO_2D but **11** decomposed with $t_{1/2}$ = ca. 45 min at −40 °C in CD_3COCD_3 (95%)–D_2O (5%) (v/v) which was 6.8×10^{-3} M in CD_3CO_2D. The kinetics of the hydration of **5** and the decomposition of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane (**7a**) to pinacol monoacetate (**8a**) were followed by UV spectroscopy at 205 nm and 25 °C. Above pH 6.6 only the hydration step could be detected, but below pH 6.0 this was very fast and only formation of pinacol monoacetate from **7** was observed. At intermediate pHs both steps were discernible. The breakdown of **7a** followed the equation $k_0 = 3.01 \times 10^{-2} + 77.8a_{H^+} + 1.6 \times 10^7 a_{HO^-}$ s^{-1} at 25 °C. The water reaction was considered to involve a rate-determining ionization followed by breakdown of the monoanion catalyzed by the hydronium ion within the initially formed encounter complex. The hydroxide ion catalyzed reaction was thought to involve an uncatalyzed rate-limiting breakdown of the monoanion and the hydronium-ion catalyzed reaction an acid-catalyzed breakdown of the un-ionized form, similar to the hydrolysis of orthoesters.

Introduction

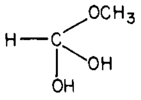
The kinetics of the hydration of ketene acetals has been studied by several groups,[2-5] but the initially formed hemiorthoesters had never been detected. Nevertheless when strongly electron-withdrawing groups are absent from the β-carbon atom, the reported rate constants for hydration are sufficiently high to suggest that in favorable cases the intermediates might be detectable. Thus Kankaanpera and Tuominen[2] estimated that the second-order constants (k_{H^+}) for the hydronium ion catalyzed hydration of ketene diethyl acetal (**1**) and 2-methylene-1,3-dioxolane (**2**) to be of the order of 10^6–10^7 M^{-1} s^{-1} at 25 °C. In contrast, we have estimated[1] on the basis of Guthrie's calculations,[6] that k_{H^+} for the breakdown of methyl dihemiorthoformate (**3**) is only 10^3–10^4 M^{-1} s^{-1} at 25 °C, and McClelland and Kresge and their co-workers have determined k_{H^+} for the breakdown of 2-hydroxy-2-phenyl-1,3-dioxolane (**4**) to be 300 M^{-1} s^{-1} at 25 °C.[7] These values suggest that under conditions where the rate depends mainly on k_H^+ it should be possible to detect the initially formed hemiorthoesters in the hydration of suitable ketene acetals.



1



2



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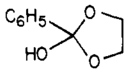

4

NMR Results

The first compound that we investigated was 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane (**5**). This would be expected to yield pinacol monoacetate (**8**) via two intermediates, the dioxolenium ion **6** and the hemiorthoester **7**. The proton NMR spectrum of (**5**) (Figure 1a) in CD_3CN at −30 °C showed two singlets at δ 1.25 (12 protons) and 3.04 (2 protons). When 10%

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[1] Part 1: Capon, B.; Grieve, D. McL. A. *J. Chem. Soc., Perkin Trans. 2* **1980**, 300-305.

[2] Kankaanperä, A.; Tuominen, H. *Suom. Kemistil. B* **1967**, *40*, 271-276. Kankaanperä, A.; Aaltonen, R. *Acta Chem. Scand.* **1972**, *26*, 1698-1706.

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[7] Ahmad, M.; Bergstrom, R. G.; Cashen, M. J.; Chiang, Y.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *J. Am. Chem. Soc.* **1979**, *101*, 2669-2677.

0002-7863/81/1503-1765$01.25/0

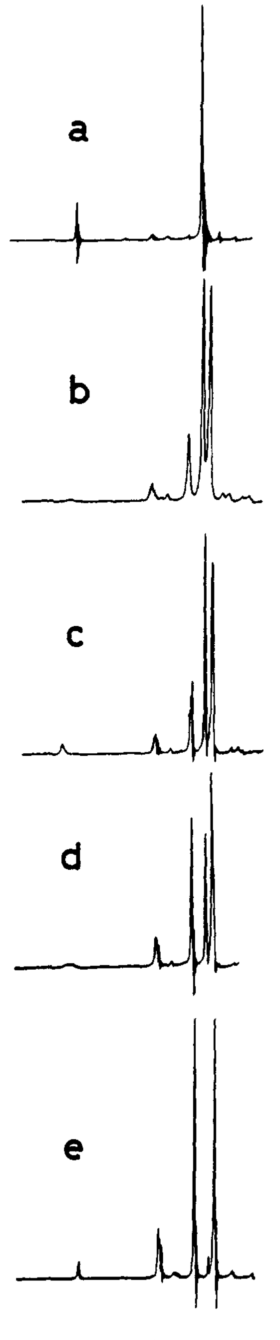
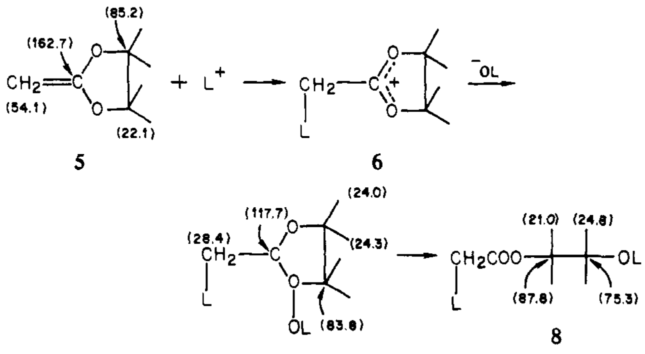


Figure 1. (a) ^1H NMR spectrum of **5** in CD_3CN at −30 °C. (b) The spectrum after addition of 10% D_2O–CD_3CO_2D so that final concentration of acid is 1.4×10^{-2} M at −30 °C. (c) The spectrum after the termperature was allowed to rise to +20 °C. (d) The spectrum after 9 min at +20 °C. (e) The spectrum after the temperature was allowed to rise to that of the probe +32 °C. The signal at δ 3–4 is that of HDO, and there is a small signal at δ 1.98 of HCD_2CN in the solvent.

Scheme I[a]



a, L = H; b, L = D

[a] The figures in parentheses are $\delta_{C^{13}}$ values.

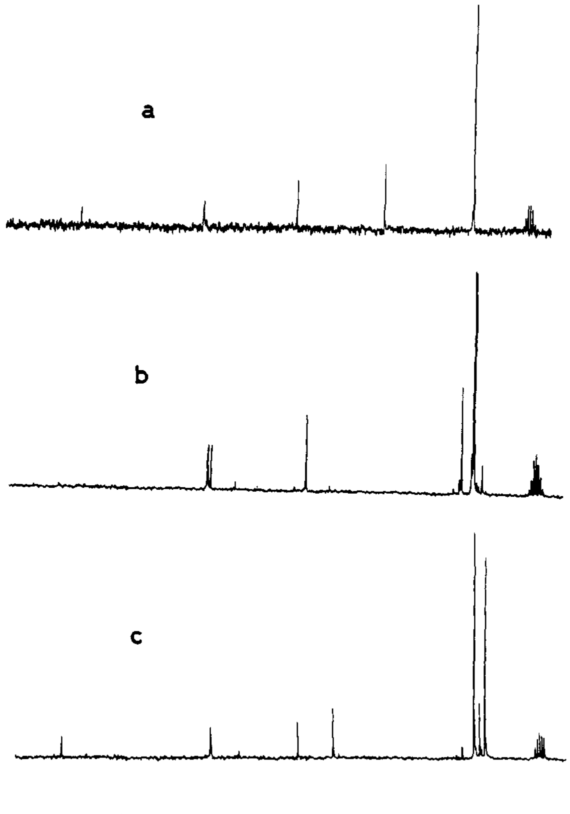


Figure 2. (a) ^{13}C NMR spectrum of **5** in CD_3CN at −30 °C. (b) The spectrum after addition of 10% D_2O–CD_3CO_2D so that final concentration of acid is 1.4×10^{-2} M at −30 °C. (c) The spectrum after 1 h at +20 °C. The signals at δ 1.66 (m) and 118.9 (s) are those of the solvent.

(v/v) D_2O which contained CD_3CO_2D to give a final concentration of 0.014 M was added, this spectrum changed immediately to a new spectrum (Figure 1b) with two singlets at δ 1.14 and 1.24 (each 6 protons) and a broad singlet at δ 1.45 (2 protons). This is thought to be the spectrum of 2-deuterioxy-2-[$^2H_1$]methyl-4,4,5,5-tetramethyl-1,3-dioxolane (**7b**) since there are now two magnetically nonequivalent methyl groups at carbons 4 and 5, and the monodeuterated methyl group at C_2 (δ 1.45) has a chemical shift almost identical with that reported for 2-methoxy-2-methyl-1,3-dioxolane (δ 1.42 (m, CCl_4)).[8] This spectrum was stable for several hours at −30 °C, but at +20 °C it changed into the spectrum of pinacol [$^2H_1$]monoacetate (**8b**) (δ 1.17 (s, 6 H), 1.46 (s, 6 H), 1.97 (br s, 2 H)) (Figure 1c–e) with a half-life of ca. 5 min. Confirmation that the final spectrum was that of **8b** was obtained by comparison with the spectrum of an authentic sample of **8a** in CD_3CN. Similar results were obtained when the solvent was [$^2H_1$]acetone–D_2O (9:1, v/v). The formation of **7** as an intermediate was confirmed by following the changes in the ^{13}C NMR spectrum in CD_3CN–H_2O (9:1, v/v) which contained CH_3CO_2H (1.4×10^{-2} M) (cf. Figure 2 and Scheme I). The presence of the hemiorthoester group in the intermediate (now **7a**) was confirmed by the presence of a signal at δ 117.7 for carbon 2. This is 7.8 ppm downfield from the signal of the corresponding carbon of 2-hydroxy-4,4,5,5-tetramethyldioxolane[1] and a shift of this magnitude is that expected on the introduction of one α-methyl substituent.[9] No signals which could be attributed to the ion **6**

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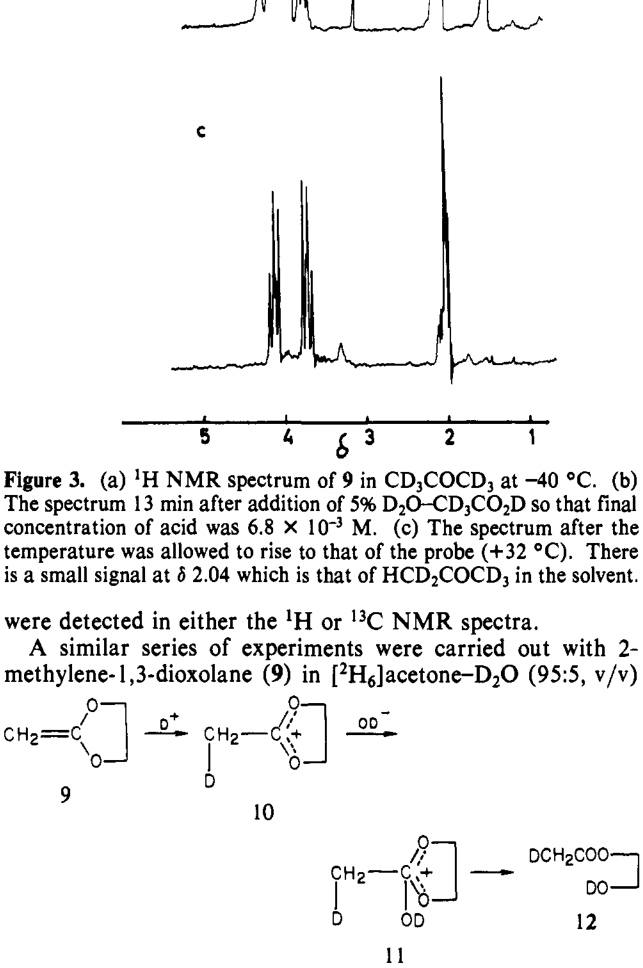
[8] Story, P. R.; Saunders, M. *J. Am. Chem. Soc.* **1962**, *84*, 4876–4882.

Figure 3. (a) ^1H NMR spectrum of **9** in CD_3COCD_3 at −40 °C. (b) The spectrum 13 min after addition of 5% D_2O–CD_3CO_2D so that final concentration of acid was 6.8×10^{-3} M. (c) The spectrum after the temperature was allowed to rise to that of the probe (+32 °C). There is a small signal at δ 2.04 which is that of HCD_2COCD_3 in the solvent.

were detected in either the ^1H or ^{13}C NMR spectra.

A similar series of experiments were carried out with 2-methylene-1,3-dioxolane (**9**) in [$^2H_6$]acetone–D_2O (95:5, v/v)



which contained CD_3CO_2D (6.8×10^{-3} M) at −40 °C (Figure 3). The spectrum of **9** (Figure 3a) in [$^2H_6$]acetone at −40 °C had two singlets at δ 3.08 (2 H) and 4.25 (4 H). On addition of D_2O–CD_3CO_2D this changed to yield two new signals, a broad singlet at δ 1.47 and a multiplet at δ ca. 3.9, plus the signals of glycol monoacetate (**12**) (δ 2.04 (s), 3.69 (m), 4.10 (m)). The new signals were attributed to 2-deuterioxy-2-[$^2H_1$]methyl-1,3-dioxolane (**11**), and after 13 min at −40 °C the solution contained ca 70% of this, 10% of **9**, and 20% of **12** (Figure 3b). After 40 min at −40 °C **9** had disappeared and the mixture contained ca. 60% **11** and 40% of **12**, and after 75 min, it contained ca. 40% of **11** and 60% of **12**. On being warmed to +30 °C **11** was converted completely into **12** (Figure 3c). Again the ion, now **11**, could not be detected.

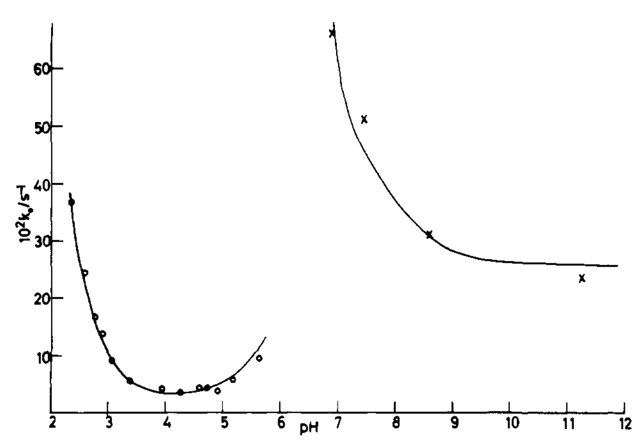


Figure 4. PH–rate profile for the hydration of **5** (crosses) and the breakdown of **7** (circles) at 25 °C (I = 0.1 M). The crosses and circles are experimental points, and the lines were drawn by using the rate constants given in the text.

These results show that the ketene acetals **5** and **9** are suitable precursors under slightly acidic conditions for the generation of the hemiorthoesters **7** and **11** which would be the tetrahedral intermediates in the intramolecular *O,O*-acyl transfer reactions of pinacol monoacetate and ethylene glycol monoacetate.

Kinetic Studies

The kinetics of hydration of 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane (**5**) and of the breakdown of the resulting hemiorthoester **7** were investigated by UV spectroscopy at 205 nm at 25 °C. Since **5** has a strong absorbance at this wavelength, **7** has no absorbance, and the product pinacol monoacetate (**8**) has a weak absorbance, the reaction sequence **5** → **7** → **8** should show a large decrease in absorbance followed by a small increase. Above pH 6.7 only the hydration step could be detected (large decrease in absorbance) and below pH 6 only formation of **8** (small increase in absorbance), but in the intermediate range both the decrease and increase in absorbance were discernible. It was therefore concluded that hydration of the double bond was rate determining at high pHs and decomposition of the hemiorthoester **7** at low pHs with a change in the rate-determining step in the pH range 6–6.7 (cf. Figure 4). The rate constants for the hydration step were found to be $k_{H^+} = 3.44 \times 10^6\ M^{-1}\ s^{-1}$ and $k_{H_2O} = 2.7 \times 10^{-1}\ s^{-1}$ at 25 °C. These are very similar to those reported for the hydration of 2-methylene-1,3-dioxolane:[2] $k_{H^+} = 10^6$–10^7 at 25 °C and $k_{H_2O} = 8.42 \times 10^{-2}\ s^{-1}$ at 10 °C.

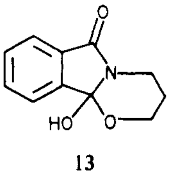
The pH–rate profile for the decomposition of the hemiorthoester **7a** follows eq 1. It is interesting to compare these results with

$$k_0\ (s^{-1}) = 3.01 \times 10^{-2} + 77.8a_{H^+} + 1.6 \times 10^7 a_{HO^-} \quad (1)$$

$$k_0\ (s^{-1}) = 1.5 + 300a_{H^+} + 6 \times 10^{10} a_{HO^-} \quad (2)$$

$$k_0\ (s^{-1}) = 1.84 + 10.6a_{H^+} + 6.2 \times 10^9 a_{HO^-} \quad (3)$$

those for the breakdown of two other tetrahedral intermediates:[7] **4**, eq 2; **13**, eq 3.[10] The pK_a of **13** is probably considerably lower



13

than those of **7a** and **4** owing to the strong electron-withdrawing effect of the phthalimide nucleus and was estimated to be ca. 7.5.[10] Application of Hine and Koser's equation for the ionization of

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(9) Cf. Wehri, F. W.; Wirthlin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden: London, 1976; pp 22–48.

(10) Gravitz, N.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 489–499.

aldehyde hydrates yields values of ca. 12 and 11.2 for **7a** and **4**, respectively.[11,12] It was proposed that the "water" reaction of **13** was in fact a hydronium ion catalyzed breakdown of its monoanion, and, on the basis of a pK_a of 7.5, the rate constant for this process was estimated to be 5.9 × 10^7 M^{-1} s^{-1}.[10] If it is assumed that the "water" reactions of **7a** and **4** follow a similar mechanism, the rate constants for the hydronium ion catalyzed breakdown of their monoanions are estimated to be 3.01 × 10^{10} and 2.3 × 10^{11} M^{-1} s^{-1}, respectively, on the basis of the pK_as given above. These much greater values were predicted by Gravitz and Jencks for "a more ordinary tetrahedral intermediate" than **13**, and they appear to be of such a magnitude as to preclude a mechanism in which the ionization equilibrium is established. It seems more likely that ionization is followed by hydronium ion catalyzed breakdown within the initially formed encounter complex (eq 4).[13] Calculation of k_1 on the assumption that the rate

$$TH + H_2O \underset{k_1}{\overset{k_1}{\rightleftharpoons}} [T^- + H_3O^+] \xrightarrow{k_2} \text{product} \qquad (4)$$

constant for protonation of the monoanion, a proton transfer between electronegative and oppositely charged elements,[14] has a value of 5 × 10^{10} M^{-1} s^{-1} leads to value of k_1 for **7a** and **4** of 5 × 10^{-2} s^{-1} and 0.32 which are within 1 order of magnitude of the values of k_{H_2O} (see eq 1 and 2). It therefore appears that when **7a** and **4** undergo ionization, they immediately undergo a rapid breakdown catalyzed by the hydronium ion formed at the same time rather than reprotonation on oxygen. Calculation of the rate constant for ionization of **13** however gives a value 1.55 × 10^3 s^{-1} which is almost 3 powers of 10 greater than k_{H_2O}. With this substrate then it appears that the ionization equilibrium is established before breakdown in agreement with Gravitz and Jencks's conclusions.

If the mechanism of eq 4 is correct for the water reaction of **7** and the rate is controlled by k_1, the deuterium isotope effect should be almost the same for the K_a since the recombination step $RO^- + L_3O^+$ should have similar rates in D_2O and H_2O, i.e., at the diffusion-controlled limit. An estimate of the isotope effect on the K_a can be obtained from Bell's equation[15]

$$\Delta pK = 0.41 + 0.020pK_a = 0.65$$

Therefore $K_a(D_2O)/K_a(H_2O) = 0.22$.[16] This lies close to our value of $k_{D_2O}/k_{H_2O} = 0.28$ which is therefore consistent with this mechanism.

It was argued[10] that k_{HO^-} for **13** corresponds to a mechanism which involves a unimolecular breakdown of the reversibly formed anion, and the rate constant for this process was calculated to be 1.6 × 10^3 s^{-1}. The same mechanism appears to be followed by **7a** and **4** as the rate constants calculated on this basis for the breakdown of their anions are 1.6 × 10^5 and 9.52 × 10^7 s^{-1}, respectively. Again the fact that the nitrogen of **13** is already conjugated to one carbonyl group reduces the rate of reaction to form a second one. The slower reaction of the anion of **7a** compared to that of **4** is presumably partly the result of the ring-stabilizing effect[17] of the four methyl substituents at C_4 and C_5 of **7a** and partly as a result of a rate-enhancing effect which may arise from conjugation of the phenyl substituent of **4** with the developing carbonyl group in the transition state.

The mechanism of the hydronium catalyzed breakdown of all three species is probably the same and involves protonation of the leaving oxygen, possibly concerted with C–O bond breaking such that the O-protonated form is bypassed, i.e., similar to the mechanism of hydrolysis of orthoesters.[10] The effect on the rate of the H_3O^+-catalyzed breakdown of having an OH group in the hemiorthoester instead of an OR group in the orthoester appears to be small, as far as can be determined from the scanty data at present available. Thus, $k_{H_3O^+}$ for the hydrolysis of triethyl orthoacetate is 2.66 × 10^4 M^{-1} s^{-1} at 25 °C,[18] i.e., 340 times greater than for **7a**. Thus the rate-enhancing effect of having a hydroxyl instead of an ethoxyl attached to the proacyl carbon, if any, is insufficient by a large margin to compensate for the rate-determining effect of the tetramethyl-substituted dioxolane ring. The similarity of deuterium isotope effects $k_{D_3O^+}/k_{H_3O^+} = 1.84$ for the hydrolysis of triethyl orthoacetate and 1.54 and **7a**, again suggest that they react by the same mechanism.

Experimental Section

2-Methylene-1,3-dioxolane (**9**) and 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane (**5**) were made by dehydrochlorination of the corresponding chloroacetaldehyde acetals with potassium *tert*-butoxide in *tert*-butyl alcohol.[2,19,20] They were distilled from the reaction mixture and collected in flasks that were lightly dusted with potassium *tert*-butoxide in order to prevent polymerization. **9**: bp 44 °C (15 mm) (lit.[2] 50–55 °C (50 mm)); NMR ($CDCl_3$) δ 4.19 (s, 4 H), 3.24 (s, 2 H). **5**: bp 40 °C (10 mm); NMR (CD_3CN) δ 3.04 (s, 2 H), 1.25 (s, 12 H). ^1H NMR spectra were measured on a Perkin-Elmer R32 spectrophotometer at 90 MHz and ^{13}C NMR spectra on a Varian XL-100 spectrophotometer. Kinetic measurements were made on a Pye-Unicam SP8-200 spectrophotometer using the 0–0.1 absorbance scale for following the formation of pinacol monoacetate and the 0–2 scale for following the disappearance of the ketene acetal. The stock solution of substrate was made up in CD_3CN in order that any decomposition could be checked by ^1H NMR spectroscopy; 20 μL was added to the reaction solution (2 mL) in a 10-mm quartz cuvette which was vigorously shaken and replaced in the thermostated cell holder (25.0 ± 0.05 °C). The recorder was started (2 cm/s), and rate constants were calculated from the resulting trace of absorbance vs. time from the integrated first-order rate equation by using a linear least-square method. The concentration of substrate in the cuvette was 1.4 × 10^{-3} M. The reaction solutions were dilute solutions of HCl or NaOH in boiled-out distilled water with the ionic strength made up to 0.1 M with KCl. A constant check was maintained to detect any drifts in the pH of solutions (Radiometer PHM 64 pH meter). Similar solutions were made up in D_2O with DCl, and the pDs were evaluated by using the equation pD = pH (meter reading) + 0.4.[21]

The results for the disappearance of **7a** (Figure 4) were fitted to the equation $k_O = k_{H_2O} + k_{H^+}$ by a least-squares method to yield values of $k_{H_2O} = 2.7 \times 10^{-1}$ s^{-1} (esd = 0.1 × 10^{-1}) and $k_{H^+} = 3.44 \times 10^6$ M^{-1} s^{-1} (esd = 0.4 × 10^6). The results for the formation of **8a** (Figure 4, Table S1) were fitted to the equation $k_0 = k_{H_2O} + k_{H^+}a_{H^+} + k_{HO^-}a_{HO^-}$ by using a least-squares method to yield values $k_{H_2O} = 3.01 \times 10^{-2}$ s^{-1} (esd 0.1 × 10^{-2}), $k_{H^+} = 77.8$ M^{-1} s^{-1} (esd 3), and $k_{HO^-} = 1.6 \times 10^7$ M^{-1} s^{-1} (esd 0.3 × 10^7). The results for D_2O (Table S2) which were only obtained for the acid limb of the pD–rate profile were fitted to the equation $k_O = k_{D_2O} + k_{D^+}a_{D^+}$ to yield $k_{D_2O} = 8.4 \times 10^{-3}$ s^{-1} (esd = 1.2 × 10^{-3}) and $k_{D^+} = 1.20 \times 10^2$ M^{-1} s^{-1} (esd 0.4 × 10^2). The slope was obtained from all eight points but the intercept from the three points at lowest acid concentrations.

Acknowledgment. We thank the British SRC for support.

Supplementary Material Available: Tables S1 and S2 of observed rate constants (1 page). Ordering information is given on any current masthead page.

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(11) Hine, J.; Koser, G. F. *J. Org. Chem.* **1971**, *36*, 1348–1351.

(12) The equation of ref 11 is pK_a = 14.19 − 1.315$\sum\sigma^*_R$. For **7a** one of the σ^*_R values was taken to be that for O-*i*-Pr, 1.61, and a factor +0.27 was used to take account of the fact that **7a** has an *O*-alkyl group not an OH group. In addition a factor 0.30 was added to take account of the fact that an aldehyde hydrate has two acid protons and **7a** has only one. This gives pK_a = 14.19 − 1.315(1.61 + 0.27) + 0.30 = 12.02. For **13** it is necessary to include σ^* for the phenyl group also so that pK_a = 14.19 − 1.315(0.60 + 1.61 + 0.27) + 0.30 = 11.23.

(13) Cf. Eigen, M. *Discuss. Faraday Soc.* **1965**, *35*, 7–15.

(14) Eigen, M. Angew. *Chem.* **1963**, *75*, 489–508.

(15) Bell, R. P. "The Proton in Chemistry"; Cornell University Press: Ithaca, N.Y., 1959; Chapter XI. Cf. Laughton, P. M.; Robertson, R. E. In "Solute-Solvent Interaction"; Coetzee, J. F.; Ritchie C. D. Eds.; Marcel Dekker: New York, 1969; p 406.

(16) A value of 0.24 is obtained if the slope is taken to be 0.017. Cf. Bell, R. P.; Kuhn, A. K. *Trans. Faraday Soc.* **1963**, *59*, 1789–1793.

(17) Cf. Guthrie, J. P. *Can. J. Chem.* **1977**, *55*, 3562–3574.

(18) Bunton, C. A.; Reinheimer, J. D. *J. Phys. Chem.* **1970**, *74*, 4457–4463.

(19) McElvain, S. M.; Curry, M. J. *J. Am. Chem. Soc.* **1948**, *70*, 3781–3786.

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(21) Glasoe, P. K.; Long, F. A. *J. Phys. Chem.* **1960**, *64*, 188–190.