STUDIES OF THE INTERMEDIATES IN THE HYDROLYSIS OF ACETALS AND ORTHOESTERS

by

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STATEMENT

The work described in this Thesis was carried out in the Chemistry Department under the guidance of Professor Brian Capon. There is no part being submitted concurrently for another degree.

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MARIA DE NAZARÉ DE MATOS SANCHEZ

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My special thanks to the Chemistry Department, staff and colleagues for their assistance during my stay in this department.

Also I would like to thank Mrs. June Anthony for her efficiency and remarkable fastness in typing this thesis.

To Ricardo, Fernandinha and

Ricardinho

SUMMARY

This thesis consists of three parts in which the kinetics and mechanism of the breakdown of hemiorthoesters, hemiacetals and the hydrolysis of cyclic acetals are reported.

In Part I an investigation of the breakdown of hemiorthoesters generated from dialkoxy-alkyl acetates and ketene acetals is described. The following compounds were studied: 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane (I), 2-hydroxy-2-methyl-1,3-dioxolane (II), 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane (III), 2-hydroxy-1,3-dioxolane (IV), dimethyl hemiorthoformate (V) and diethyl hemiorthoformate (VI). The whole series was studied in aqueous acetonitrile ($[H_2O]$ = 8.33 $\underline{\underline{M}}$); (I), (II) and (III) were studied in aqueous acetonitrile ($[H_2O]$ = 2.22 $\underline{\underline{M}}$) and (I) and (II) in water. Complete pc_H-rate or pH-rate profiles were obtained for each reaction. The mechanisms of the hydronium-ion, hydroxide-ion and "water" catalyzed reactions are discussed and compared to those for the breakdown of hemiacetals and orthoesters.

In Part II an investigation of the breakdown of benzaldehyde t-butyl acetal (VII) and α-acetoxy-α-t-butoxy toluene (VIII) is described. At pH's below 6.2 the rate-determining step in the hydrolysis of (VII) was the breakdown of the hemiacetal and at pH's above 6.2 formation of

the hemiacetal was rate-determining. Breakdown of the hemiacetal was rate-determining in the hydrolysis of (VIII) at all pH's studied (pH 4.23 to 8.38). General acid catalysis by acetate, imidazole and cacodylate buffers was not detected in the hydrolysis of (VII) at pH's above 6.2 when formation of the hemiacetal was rate-determining nor in the hydrolysis of benzaldehyde diethyl acetal. The mechanisms for the hydronium-ion and hydroxide-ion catalyzed reactions are discussed.

In Part III an investigation of the mechanism of hydrolysis of 2-phenyl-1,3-dioxolane in aqueous acetonitrile is described. The reversibility of the initial step was studied by NMR experiments on the hydrolysis of benzaldehyde bis(2-hydroxy ethyl) acetal which should yield the same carbocation as an intermediate. Evidence for reversibility was obtained for solutions in CH_3CN-H_2O (99 - 1% v/v) and (90 - 10% v/v) but not for solutions in CH_3CN-H_2O (77 - 33% v/v). Kinetic experiments were also carried out in solutions < 1% v/v of water (0.5% and 0.25%) and the values of 1.02-1.03 were found for the α-deuterium isotope effect for the hydrolysis of 2-phenyl-1,3-dioxolane. The significance of these results is discussed.

TABLE OF CONTENTS

This thesis is divided into three parts. In Part I an investigation of the mechanism of the breakdown of a series of hemiorthoesters is described. An investigation in the mechanism of the breakdown of benzaldehyde-t-butyl hemiacetal is described in Part II and the mechanism of hydrolysis of 2-phenyl-1,3-dioxolane (and benzaldehyde bis(2-hydroxy ethyl) acetal) is reported in Part III.

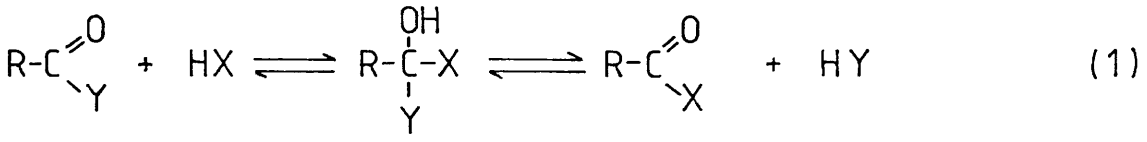
PART I

1.1 INTRODUCTION

Tetrahedral Intermediates in Acyl Transfer Reactions

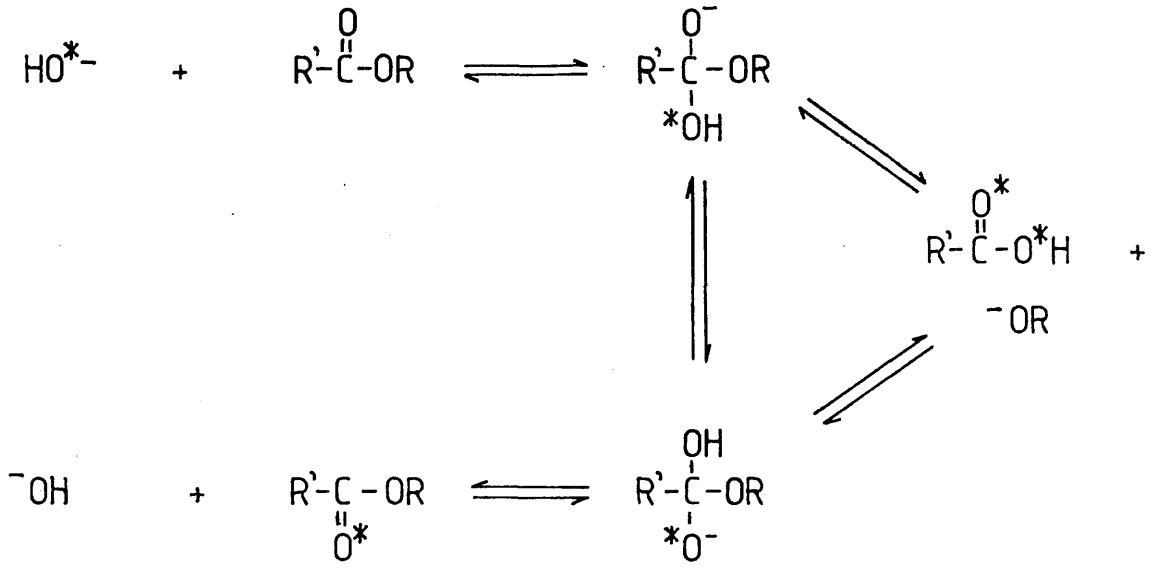
Until a few years ago the tetrahedral intermediates of most acyl transfer reactions were species whose existence had merely been postulated, but had never been detected. Now, however it is possible to generate some of these species in solution such that their nmr spectra may be measured and their reactions studied. The subject of this section of the thesis is concerned with an investigation of the reactions of the tetrahedral intermediates of some O,O acyl transfer reactions.

The possibility that the reactions of carboxylic acid derivatives might pass through tetrahedral intermediates, as shown in equation (1), has been considered for many years and Ingold[1] always assumed their "theoretical" existence when



(1)

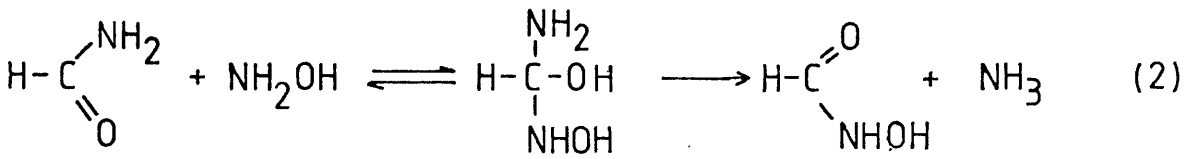
representing the possible mechanisms for such reactions, but the first definite, though indirect, evidence was provided by Bender[2] who showed that when alkyl benzoates undergo hydrolysis in aqueous dioxane with ^{18}O enriched water the label is incorporated into the starting ester. This was explained by a sequence of reactions as shown in the scheme 1:



Scheme 1

Subsequent work has demonstrated that oxygen exchange takes place in the hydrolyses of amides,[3-5] esters[6,7] and in the methanolysis of esters.[8]

Other evidence for the incursion of a tetrahedral intermediate came from the work of Jencks and Gilchrist[9] who showed that the 2nd order rate constant for the general-acid catalyzed reaction of formamide with hydroxylamine did not increase linearly with the concentration of acid ($HONH_3^+$, ImH^+). This was interpretated as resulting in a change in the rate-determining step from one at low concentration of acid which was more sensitive to acid concentration to one at high concentration of acid which was less sensitive. It was argued that if there was a change in the rate-determining step there must be an intermediate, the tetrahedral intermediate I.



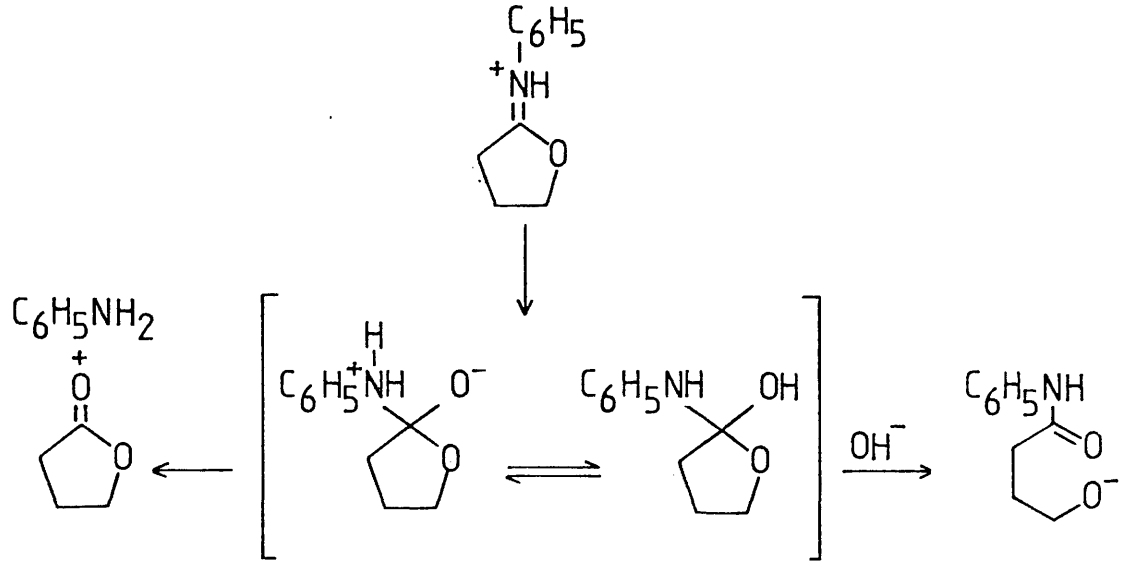
(2)

(I)

Other experiments from reactions in which the tetrahedral intermediate has been postulated on the basis of this kind of evidence include the aminolysis of benzylpenicillin.[10]

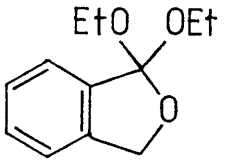
Different types of evidence for the incursion of a tetrahedral intermediate such as the partitioning of an intermediate after the rate-determining step and the change of the rate-determining step with varying the structure of the reactants have been discussed.[11]

In the former case, Schmir and Cunningham[12] have studied the hydrolysis of 2-phenyl imino tetrahydrofuran at 30° from pH's 0-14 and observed that the nature of the products of hydrolysis changed with pH giving aniline and lactone for pH's below 6 and hydroxy anilide for pH's above 8.5. This was explained as due the breakdown of the tetrahedral intermediate (in equilibrium with its zwitterionic form) in acid solutions forming mainly lactone and the breakdown of the anionic form of the tetrahedral intermediate at higher pH's giving rise to the anilide product according to the scheme:



Scheme 2

Similar behaviour was observed in the hydrolysis of 1,1-diethoxy-1,3-dihydroisobenzofuran (1) which formed the corresponding hydroxy-ester and lactone with the formation of



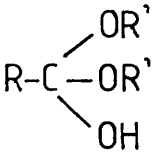
(1)

the oxocarbonium-ion being rate-limiting.[13]

The imidazole-catalyzed hydrolysis of esters[14] has provided an example of a break in the structure-reactivity correlation; however as stated by the authors,[11,14] it might indicate the formation of a tetrahedral intermediate or an asymmetric transition-state, consequently such correlations do

not provide good indirect evidence for the presence of a discrete intermediate.

In all the reactions mentioned the tetrahedral intermediate was never detected, only postulated. Examples of the structures of tetrahedral intermediates I, II and III show that they belong to the classes of compounds dialkyl



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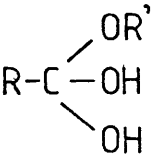

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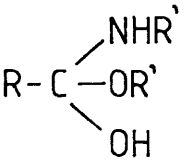
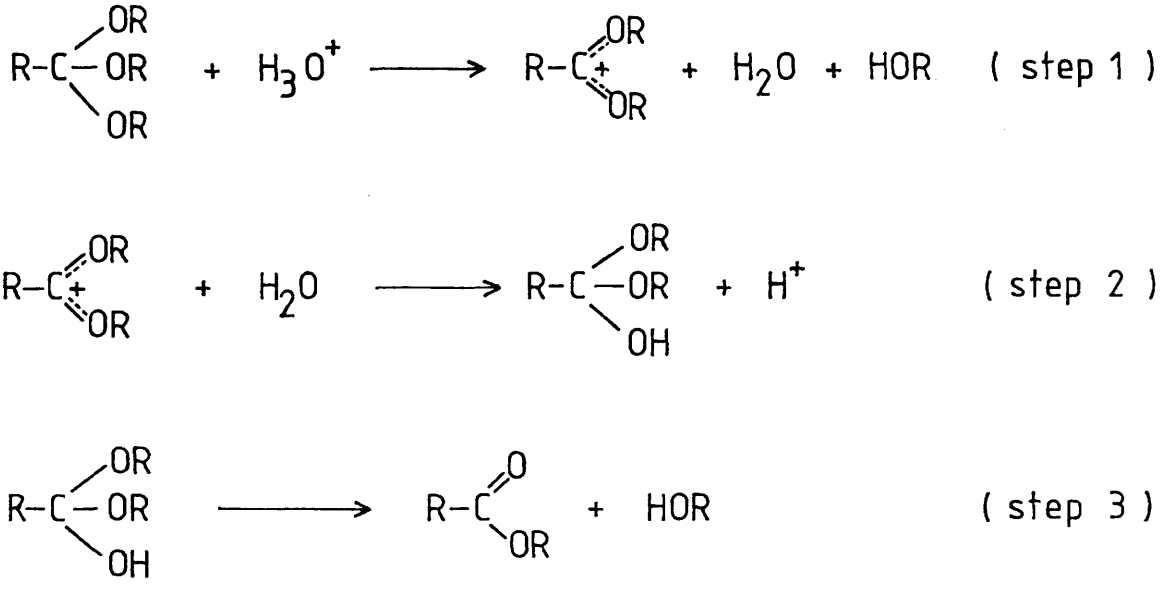


(III)

hemiorthoester (I), alkyl hemiorthoester (II) or amide hemiacetals (III). Therefore if methods could be found for generating these species in other reactions it might be possible to detect them. As will be seen later, this has in fact been done.

Tetrahedral Intermediates in the Hydrolysis of Orthoesters and Related Compounds

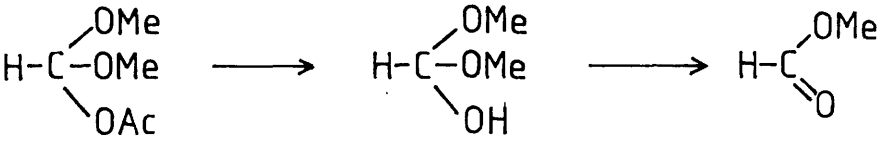
Hemiorthoesters have also been postulated as intermediates in the hydrolysis of orthoesters which are thought to hydrolyse by a similar mechanism to that for acetals and ketals:[15]



Scheme 3

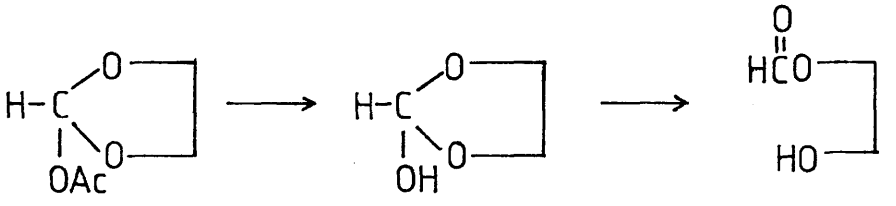
The two intermediates involved in the 2nd and 3rd steps, dialkoxy carbonium-ion and hemiorthoester are not normally detectable but if step 1 was made faster then it might be possible to detect the dialkoxy carbonium-ion or the hemiorthoester. Alternatively if step 3 was made slower, it might also be possible to detect the hemiorthoester.

The first example in which a simple tetrahedral intermediate[16,17] has been detected in solution was provided by Capon and Grieve.[18] By using a precursor with a good leaving group such as acetoxy the first step was made faster thus affording the detection of the hemiorthoester (II) in the hydrolysis of dimethoxy methyl acetate (I). Similarly by using other acetoxy compounds as precursors, such as

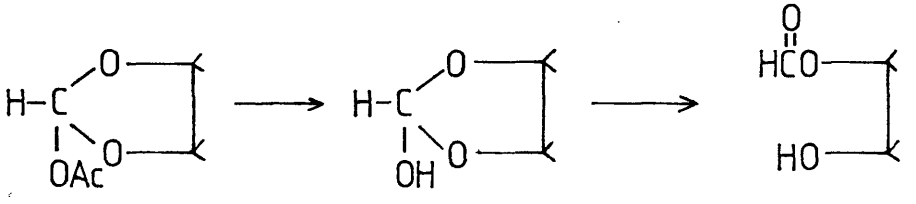


(I) (II) (3)

2-acetoxy-1,3-dioxolane (III) and 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolane (V) the corresponding hemiorthoesters (IV) and (VI) were also obtained.



(III) (IV) (4)



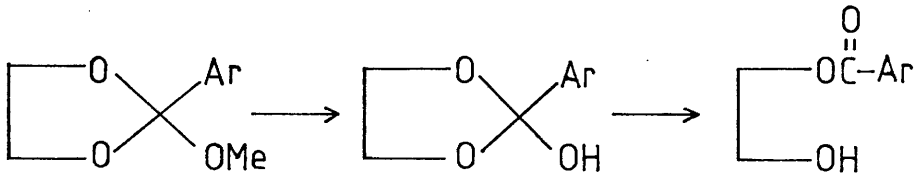
(V) (VI) (5)

The intermediates in question were characterized by ^{1}H-nmr and ^{13}C-nmr spectroscopy with the experiments being carried out at low temperature. The ^{1}H-nmr chemical shifts of the intermediates were close to those for the corresponding orthoesters with a methoxy group in the place of the hydroxy group. Some kinetic runs were carried out by following the

build up and decay of the signals in the ^{1}H-nmr spectra. The rate constants were obtained at different solvent-composition (90:10, 86:14 v/v) in CD_3COCD_3-D_2O for the decomposition of the precursors and for the acid-catalyzed breakdown of the hemiorthoesters (the acid being formed from the departure of the leaving-group) with the latter reaction being slower than the former throughout the experiments.

The tetrahedral intermediate with Me-substituents in the dioxolane ring was the most stable under these conditions, consequently its breakdown had the smallest rate-constant, whereas that of the acyclic intermediate had the largest.

Kresge amd McClelland[19] have studied another type of compound, 2-aryl-2-methoxy-1,3-dioxolane (I) for which kinetic evidence for the build up of high concentration of a tetrahedral intermediate (II) was obtained.



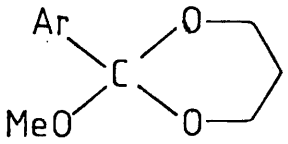
(I) (II) (6)

In this system the accumulation of the intermediate appears to arise from both a relative acceleration of step 1 compared to step 2 as a result of the aryl substituents as no intermediate could be detected in the hydrolysis of 2-methoxy-1,3-dioxolane and also to a slowing down of step 3

as a result of the ring as no intermediate was detected in the hydrolysis of trimethyl orthobenzoate.

The ratio of acceleration for the first step due to the presence of a phenyl substituent was estimated as $k_H^1(Ph)/k_H^1(H) = 31$, where $k_H^1(H)$ is the acid-catalyzed rate constant for the aliphatic orthoester. In a similar way the effect on the 3rd step was estimated as $k_H^3(Ph)/k_H^3(H) < 0.3$. It was estimated that $k_H^3(H)$ was greater than $k_H^1(H)$ by a factor of at least five and that $k_H^3(Ph)$ was smaller than $k_H^1(Ph)$ by a factor of c.a. 100.

In a further investigation McClelland and coworkers[20] observed that by using precursors with rings other than 1,3-dioxolanes, hemiorthoesters could also be detected. Such was the case of 1,3-dioxanes orthoesters derivatives represented by:



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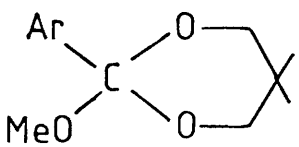

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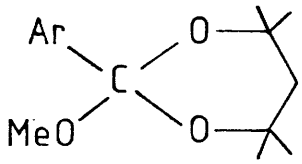
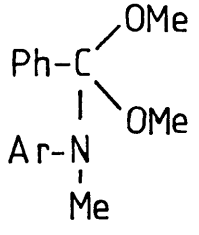


(4)

Hemiorthoesters have also been detected in acidic solutions during the hydrolysis of amide acetals[21a,b] such as N,N-methyl arylbenzamide dimethyl acetal (5) and 2,phenyl-2-(N,N-dimethyl amino)-1,3-dioxolane (6).



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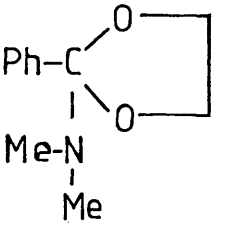
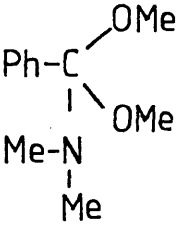


(6)

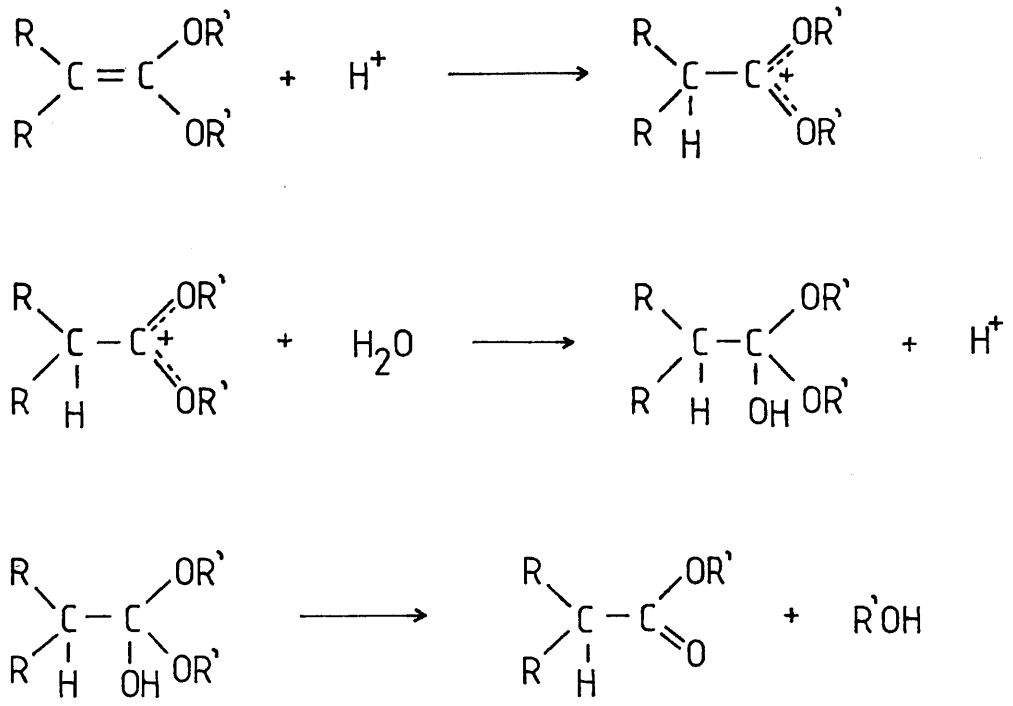


(7)

With these compounds the leaving group is the protonated amino group which is a better leaving group than methoxy and hence it is easier to detect the intermediate than with the corresponding orthoesters. With the acyclic compound (5) it is necessary to have the protonated N-methyl aniline leaving as no intermediate could be detected with (7) which has a dimethyl amino substituent.[21c]

Tetrahedral Intermediates in the hydration of Ketene Acetals

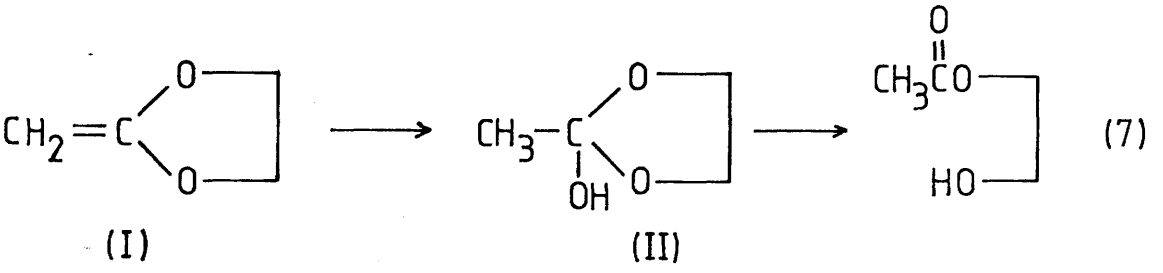
The generally accepted mechanisms for the hydrolysis of ketene acetals also involves the formation of tetrahedral intermediates:



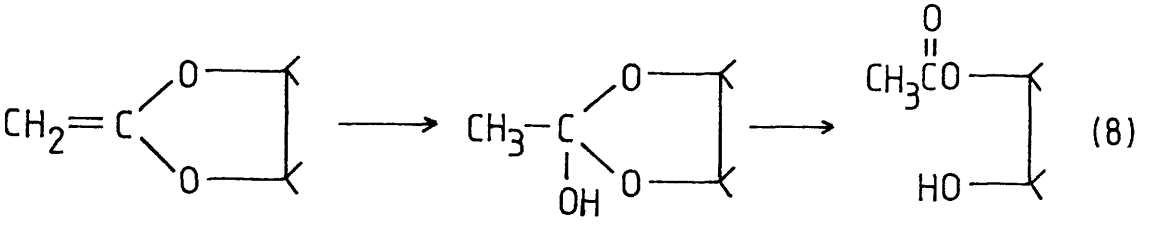
Scheme 4

There are several investigations related to the hydrolysis of ketene acetals[22-24] and Schmir[25,26] in particular has discussed the variation in products in the hydrolysis of O,O and O,S-ketene acetals with pH in terms of partitioning of the tetrahedral intermediate.

The first detection of a tetrahedral intermediate generated from the hydrolysis of ketene acetals was provided by Capon and Ghosh[27] who studied 2-methylene-1,3-dioxolane (I) and 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane (III).



(I) (II) (7)

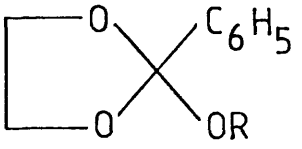


(III) (IV) (8)

The intermediates (II) and (IV) were characterized by ^{1}H-nmr in 5% D_2O-CD_3COCD_3 and 10% D_2O-CD_3CN respectively at low temperature and by ^{13}C-nmr spectroscopy in presence of CH_3CO_2H. The chemical shift in ^{13}C-nmr spectra of the carbon 2 in the intermediate (II) was found to be 7.8 ppm downfield from that in the 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane[18] and the magnitude of that shift was found to be within the expected for the presence of one methyl substituent at that position. Also the ^{1}H-nmr chemical shifts of the mono deuterated methyl groups in the carbon 2 of both intermediates at δ = 1.47 ppm and 1.45 ppm respectively were close to that, δ = 1.42 ppm, for 2-methoxy-2-methyl-1,3-dioxolane.

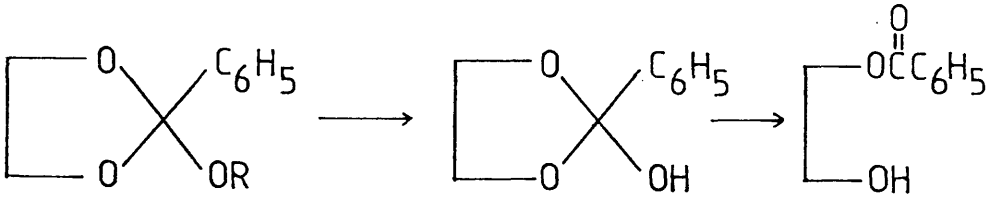
Kinetic Studies on the Breakdown of Tetrahedral Intermediates

As mentioned above, Kresge and McClelland[19] obtained evidence for the build up of hemiorthoesters in the hydrolysis of the dioxolane derivative (8). They found



(8)

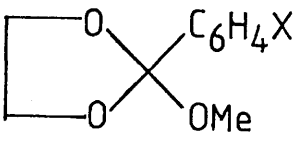
that at pH's > 3.5 the rate of formation of the ester from (8) depends on R in the expected manner (i.e. electron withdrawing substituents on R decrease the rate) but at lower pH's the rates were independent of R. This was explained as the formation of the hemiorthoester being



(9)

rate-determining at high pH where it undergoes a rapid $^-$OH-catalyzed breakdown, but its breakdown being rate-determing at low pH's where this is no longer possible.

In addition, with compound (9) they were able to detect the



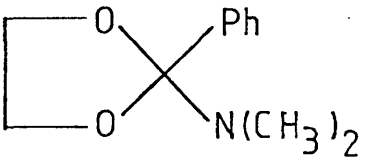
(9)

oxo-carbonium-ion intermediate when X = p-MeO by following its absorbance at 300 nm. No similar ion could be detected with the compounds with other substituents.

The breakdown of the hemiorthoesters was studied at 25°C in aqueous solutions keeping the ionic strength 0.1 M by using different electrolytes.[28] The decomposition of 2-hydroxy-2-phenyl-1,3-dioxolane in water followed the equation:

$$k(s^{-1}) = 1.5 + 300\ a_{H^+} + 6 \times 10^{10}\ a_{OH^-} \qquad (10)$$

For pH's below 2.0 the major mode of breakdown was the hydronium ion-catalyzed reaction with the uncatalyzed reaction being important from pH's 2 to 3 and the hydroxide ion-catalyzed reaction being the major reaction above pH 3.0. The last term (base catalyzed portion) in the equation (10) was obtained from the hydrolysis of the amide acetal (10) which generated the same hemiorthoester on hydrolysis in aqueous solution. The effect of the substituents on the



(10)

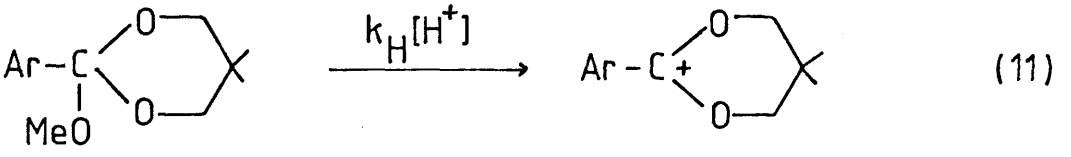
rate of breakdown of the hemiorthoesters was also studied by generating them from this type of precursor.

In 50% aqueous-acetonitrile the hydroxide ion catalyzed reaction for the breakdown of the hemiorthoesters was studied by using 2-phenyl-1,3-dioxolenium fluoroborate salt as precursor.

The importance of the aryl substituent in making detection of the tetrahedral intermediate possible was demonstrated by showing that the hydrolysis of 2-methyl-2-methoxy-1,3-dioxolane and 2-methoxy-1,3-dioxolane do not show any change in the rate-determining step, with the first step remaining rate-limiting throughout the pH range studied.

Similar behaviour to the series of compounds (9) was also observed for the hydrolysis of the orthoesters with four Me-substituents in the dioxolane ring.[29]

A change in the rate-limiting step was also observed by McClelland and coworkers[20] in the hydrolysis of a series of cyclic orthoesters containing 1,3-dioxane ring for which the rate determining breakdown of the hemiorthoesters was observed at low pH's (1 to 3). The hydrolysis of bicyclo orthoesters which proceeds similarly to the other orthoesters from the 2nd step forward (eq. 13) was also studied providing similar results.



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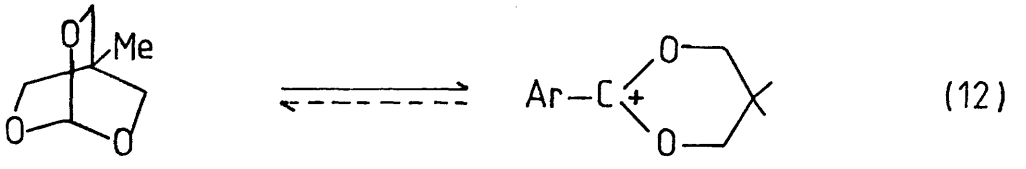

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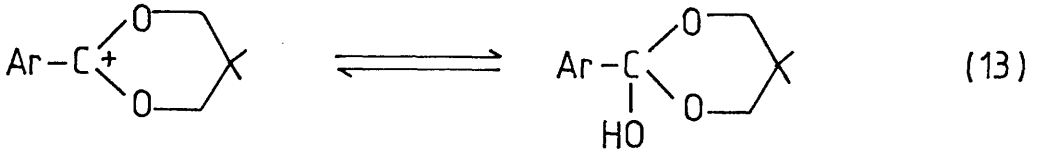

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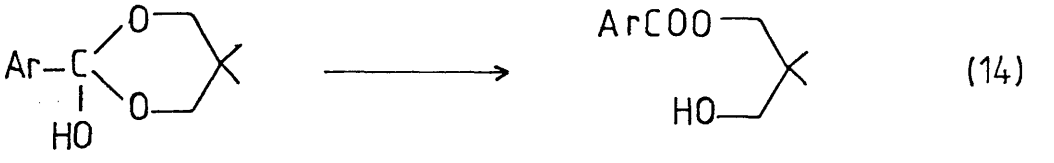


(14)

In this series the orthoesters with p-MeO substituents showed similar behaviour to the series containing 1,3-dioxolane ring and by applying the same treatment the catalytic constant for the acid-catalyzed reaction and water reaction were calculated, however k_{OH} for the break-down of the hemiorthoesters was not reported.

The hydrolysis of the ketene acetal, 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane (eq. 8) has also been studied by UV spectroscopy with the breakdown of the hemiorthoester being the rate-determing step in the low pH region.[27,30] The experiments were carried out in water at 25°C, I = 0.1 $\underline{M}$ following the appearance of the ester product at λ = 205 nm.

The pH-rate profile obtained for the breakdown of the hemiorthoester followed the equation:

$$k(s^{-1}) = 3.01 \times 10^{-2} + 77.8\ a_{H^+} + 1.6 \times 10^{7}\ a_{OH^-} \quad (15)$$

A change in the rate-determining step to the hydration of the ketene acetal was observed at pH c.a. 6.0. The proposed mechanisms for the breakdown of the hemiorthoester catalyzed by hydronium-ion, hydroxide-ion and that for water reaction were similar to those suggested by Gravitz and Jencks[31] for the hydrolysis of a phthalimidium cation.

Capon and Gosh estimated the value for the pKa of the intermediate by using Hine and Koser's[32] equation:

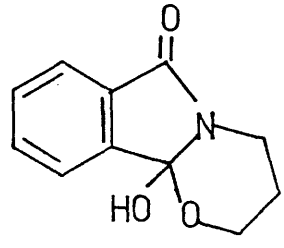
$$pKa = 14.19 - 1.315\ \Sigma\sigma^{*}_{R} \quad (16)$$

for compounds such as $RRC(OH)_2$. By making the proper compensation of the substituents and the presence of only one OH-group the expression yielded a pKa = 12.02. On the basis of this pKa value they estimated the k_2 value of $3.01 \times 10^{10}\ M^{-1}\ s^{-1}$ for the mechanism for the water reaction according to the following equation:

$$TH + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (T^- + H_3O^+) \xrightarrow{k_2} \text{Prod.} \qquad (17)$$

Also the estimate of $k_{-1} = 5 \times 10^{10}\ s^{-1}$ afforded a value of $k_1 = 5 \times 10^{-2}\ s^{-1}$ which is close to the k_{H_2O} value, $3.0 \times 10^{-2}\ s^{-1}$. That mechanism with k_1 being the rate-limiting step was supported by the k_{D_2O}/k_{H_2O} value of 0.28 which lies close to the isotope effect $Ka_{(D_2O)}/Ka_{(H_2O)} = 0.22$ using the Bell's equation to estimate $Ka_{(D_2O)}$.

In the case of Gravitz and Jencks' system the rate-limiting step for the water reaction, k_2, was explained as due to the conjugation of the nitrogen with the carbonyl group present in the molecule (11) which was responsible for



(11)

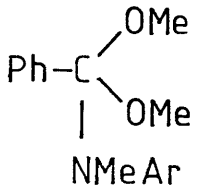
the decrease in k_2 value but it was argued that in the absence of that feature such as in a simple tetrahedral intermediate, k_2 should approach the limit of a diffusion controlled reaction and that is what was observed by Capon.

In the proposed mechanism for the hydroxide-ion catalyzed reaction, equation (18), the rate of breakdown of the anionic intermediate (k_2) was estimated to be $1.6 \times 10^5\ s^{-1}$.

$$TH + HO^- \rightleftharpoons T^- + H_2O \xrightarrow{k_2} \text{Prod.} \qquad (18)$$

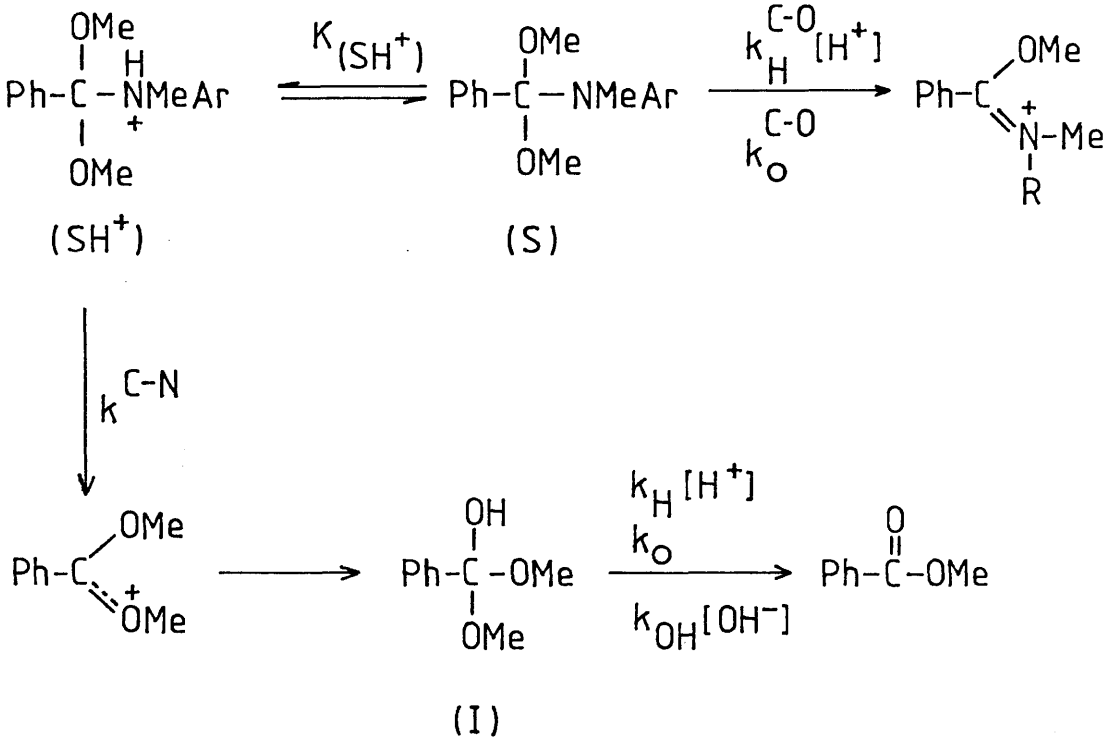
Also for the acid-catalyzed reaction the following isotope effect $k_{D_3O^+}/k_{H_3O^+} = 1.54$ was close to the value of 1.84 for the hydrolysis of triethyl orthoacetate supporting the suggestion that they were hydrolyzing by the same mechanism.

The breakdown of an acyclic hemiorthoester, diethyl hemiorthobenzoate, was studied by generating it from O,O,N-trimethyl benzanilide acetal (5) at pH's below 6.0.[21a,33]



(5)

The general proposed scheme for the hydrolysis of (5) is represented by:



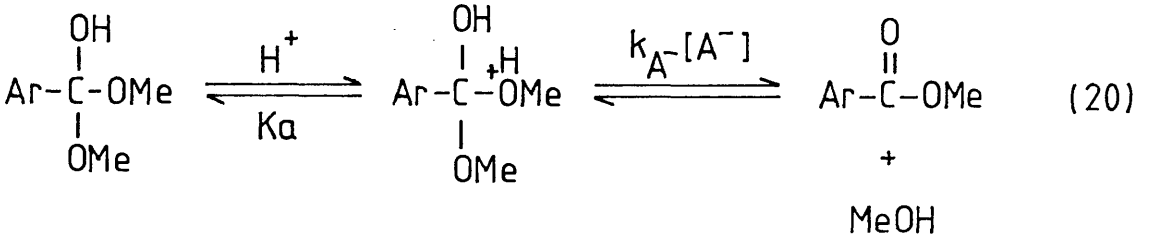
Scheme 5

For pH's below 9.0 the C-N bond was the only mode of cleavage. However the rate-limiting breakdown of (I) was only observed for pH's below 6.0 and followed the equation:

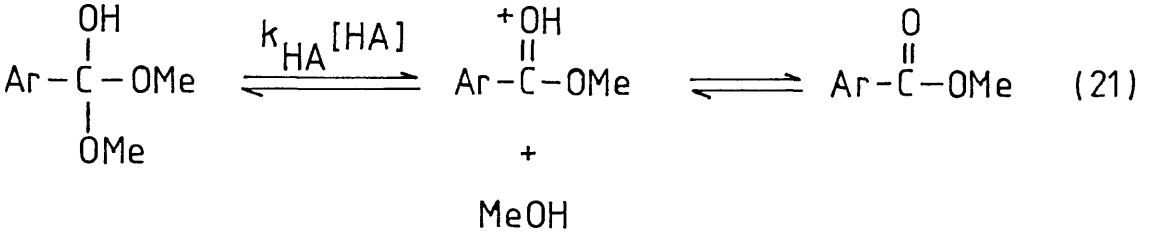
$$k(s^{-1}) = 0.6 + 1.9 \times 10^{4}\ a_{H^+} + 4 \times 10^{9}\ a_{OH^-} \qquad (19)$$

The decomposition of the tetrahedral intermediate was also general acid and base catalyzed by formate, chloroacetate, cyanoacetate and phosphate buffers. The general acid catalyzed decomposition was suggested to occur by one

of the two kinetically equivalent mechanisms proposed by Funderburk and Jencks:[34]



(20)

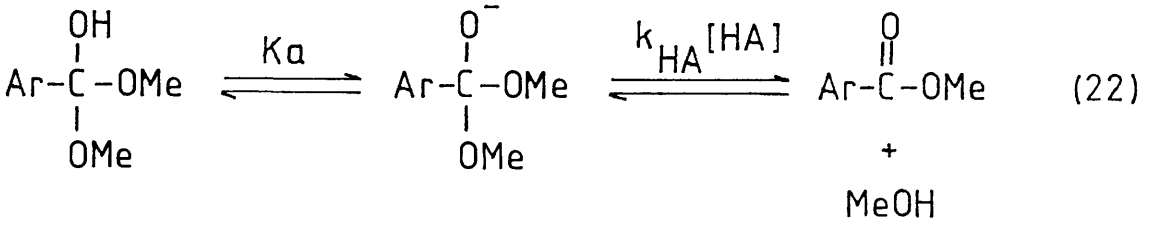


(21)

Based on the pKa of protonated formaldehyde hydrate and hemiacetals[34] the pKa of the protonated tetrahedral intermediate was estimated as -6. So, for the breakdown of $PhCH(OMe)_2OH$ catalyzed by formic acid the estimative of k_{A^-} (eq. 20) value of 10^{12} $\underline{\underline{M}}^{-1}$ s^{-1} was used to rule out the mechanism in (20). According to McClelland[35] the rate-determining step is the formation of the cation in (21) which has the presence of an $^{\delta+}$OH-group which is able to form hydrogen bond to a water solvent molecule therefore stabilizing this cation and its transition-state. Such feature could explain the low Brønsted α value (0.46) since

less proton transfer would be required to reach the transition state.

The general base catalyzed reaction was suggested to occur according to:



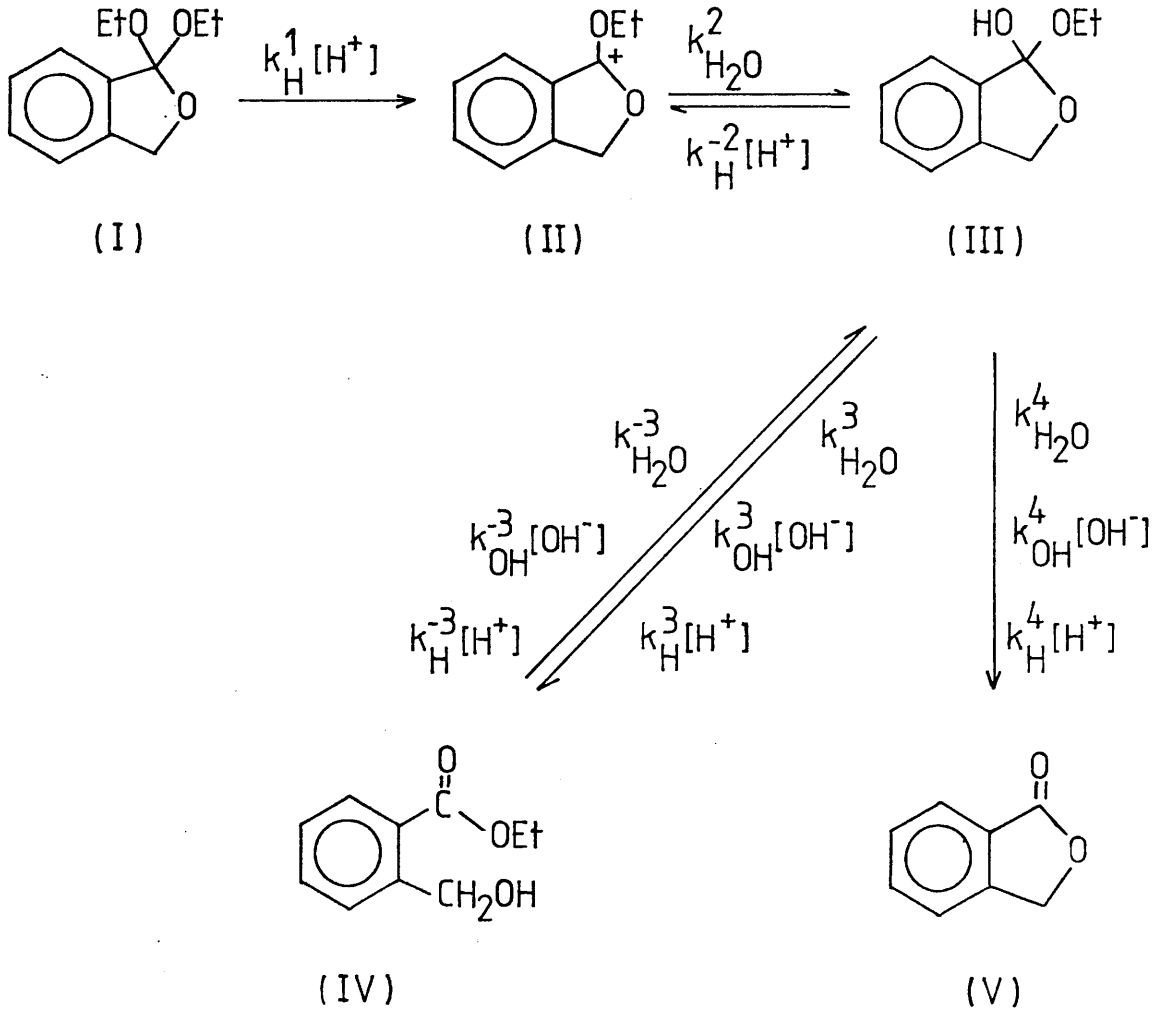
(22)

The estimated k_{HA} (less than the diffusion limit) makes the mechanism in (22) probable and the Brønsted β value (0.9) suggested a considerable degree of proton transfer in the transition-state.

The pH independent reaction was suggested to occur with a different mechanism from the acid and base catalyzed reactions in view of k_{H_2O} lying above the Brønsted lines for acid and base reactions. It was suggested that the transition state should involve a simultaneous donation and remotion of a proton by the solvent from the tetrahedral intermediate.

Rate constants for the formation and breakdown of 1-hydroxy-1-ethoxy-1,3-dihydroisobenzofuran (III), the tetrahedral intermediate in the hydrolysis of the precursor orthoester (I) and also in the lactonization reaction have

been reported by McClelland and Alibhai[13] according to the scheme 6.



Scheme 6

Although an induction period had been always observed in the hydrolysis of (I) in presence of HCℓ, the rate constants for the later linear portion of the first-order kinetic plots indicated that the rate-determining step was

the formation of (II) and this conclusion was supported by the fact that the rate constants had the same values as those obtained with phosphate buffers (pH 5-7).

The presence of an induction period afforded an estimate of the value of $k_H^3 + k_H^4$ based on the obtained value of k_H^1 (3.1×10^3 $\underline{\underline{M}}^{-1}$ s^{-1}) and on the kinetic equation for two consecutive reactions. For such estimates k_{OH} and k_{H_2O} were neglected and k_H^1 was assumed to be smaller than $k_H^3 + k_H^4$. The estimated value for $k_H^3 + k_H^4$ ($1\text{-}2 \times 10^4$ $\underline{\underline{M}}^{-1}$ s^{-1}) fitted well to the equation of the curve obtained for the ratio of the products formed in the hydrolysis of (I) with varying the pH. The partition factors which described the partitioning modes of the intermediate (III) were represented by:

$$P^+ = \frac{k_H^4}{k_H^3 + k_H^4} = 0.24 \qquad (23)$$

and

$$P^- = \frac{k_{OH}^4}{k_{OH}^3 + k_{OH}^4} = 0.075 \qquad (24)$$

The equations (23) and (24) were obtained, based on the assumption that $k_{H_2O}^3$ and $k_{H_2O}^4$ were absent or were unimportant. This assumption was supported by the fact that this treatment fitted the experimental data and by the absence of considerable k_{H_2O} for the lactonization reaction which, on the other

hand, followed the equation:

$$k_{obs}\ (lact) = k_H\ (lact)[H^+] + k_{OH}\ (lact)[OH^-] \qquad (25)$$

Similar results were obtained by Fife[36] for the lactonization of (IV) in which k_{H_2O} was absent and k_H and k_{OH} were comparable to McClelland's values.

The k_H and k_{OH} for the lactonization were represented by:

$$k_H\ (lact) = P^+ k_H^{-3} \qquad (26)$$

and

$$k_{OH}(lact) = P^- k_H^{-3} \qquad (27)$$

where P^+ and P^-, according to McClelland, have the same meaning as in (23) and (24), assuming that the partition of the intermediate (III) is independent of its source.

Based on the partitioning ratio (eqs. 23 and 24), on the other lactonization reactions,[37,38] it was suggested that the breakdown of (III) was the rate-determining step in the lactonization of (IV).

Some of the results discussed in this section will be compared later with those obtained in this investigation.

Thermodynamic Parameters for the Hydration of Esters

Although an indirect method, the thermodynamic approach used by Guthrie[39a-c] for estimating the equilibrium constant for the hydration of carboxylic acid and esters has played an important role for elucidating and studying some properties of tetrahedral intermediates and also in explaining the mechanism of some reactions involving such intermediates for which the measurement of rate constants for their formation was impracticable.

The basic feature that Guthrie[39a] utilized was the observation that the variation of the free energy change ($\Delta G°$) for a reaction such as

$$R_1R_2R_3COH + CH_3OH = R_1R_2R_3COCH_3 + H_2O \qquad (28)$$

with varying R_1, R_2 and R_3 (H, CH_3, OH or OCH_3) was small and unaffected by the structure or pKa of the hydroxyl compound. The observation that $\Delta G°$ was held constant when the degree of substitution on the central carbon was the same led to the assumption that this behaviour will also hold for orthoacid derivatives. Then, from the free energy of formation ($\Delta G_f°$) of the orthoesters and from the $\Delta G°$ for the reaction such as in (28), the $\Delta G_f°$ for the species $RC(OH)_3$ and $RC(OH)_2OCH_3$ could be evaluated. With these values available, the standard free energy changes for the

hydration of esters could be estimated as:

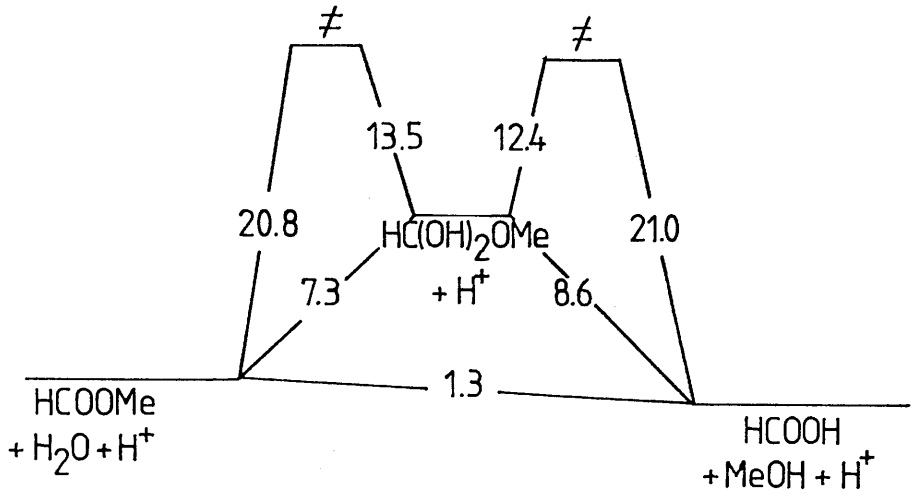
$$R - \overset{\overset{O}{\|}}{C} - OCH_3 + H_2O = R - \overset{\overset{OH}{|}}{\underset{\underset{OH}{|}}{C}} - OCH_3 \qquad (29)$$

So, the mechanisms of the hydrolysis of esters and related species could be better understood and with the values of free energy changes available from the four different types of sources the complete energetic diagram for the reactions involving tetrahedral intermediates could be drawn. For illustration, the hydrolysis of methyl formate will be taken as example.

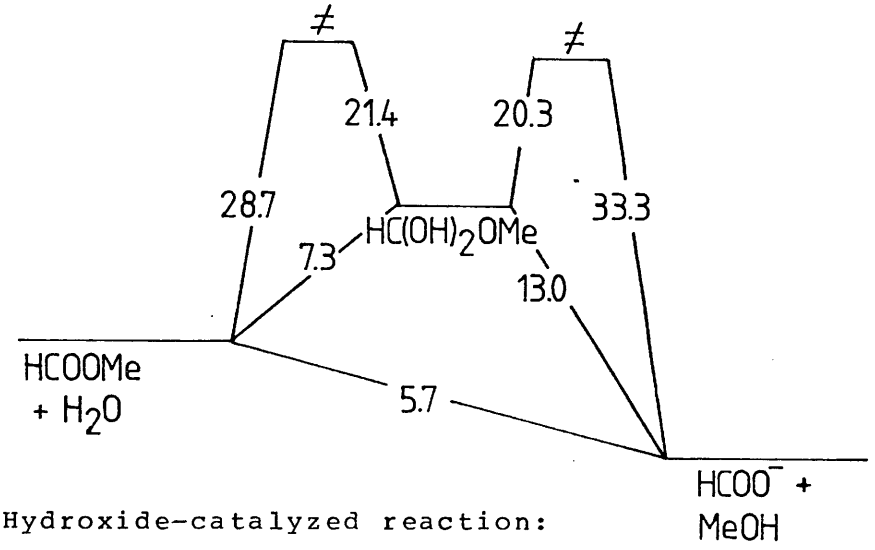
The four sources above mentioned include: $\Delta G°$ for the total reaction (reactants → products) obtained from the individuals $\Delta G°_f$; the energetic level of the tetrahedral intermediate estimated as mentioned before by using Guthrie's basic assumption on $\Delta G°$ for the hydrate species; the activation free energy for the formation of the T.I. by using some available $\Delta G^{\ddagger}$ or rate-constant for the hydrolysis (or alcoholysis) of the reactants (in this case, an ester) in the literature; and the activation free energy for the decomposition of the T.I. by using also literature values for the ^{18}O-exchange reactions, k_h/k_e, of some similar species.

The diagrams were drawn for different acidic ranges as shown below:

Acid-catalyzed reaction:



Uncatalyzed reaction: (pH7)



Hydroxide-catalyzed reaction:

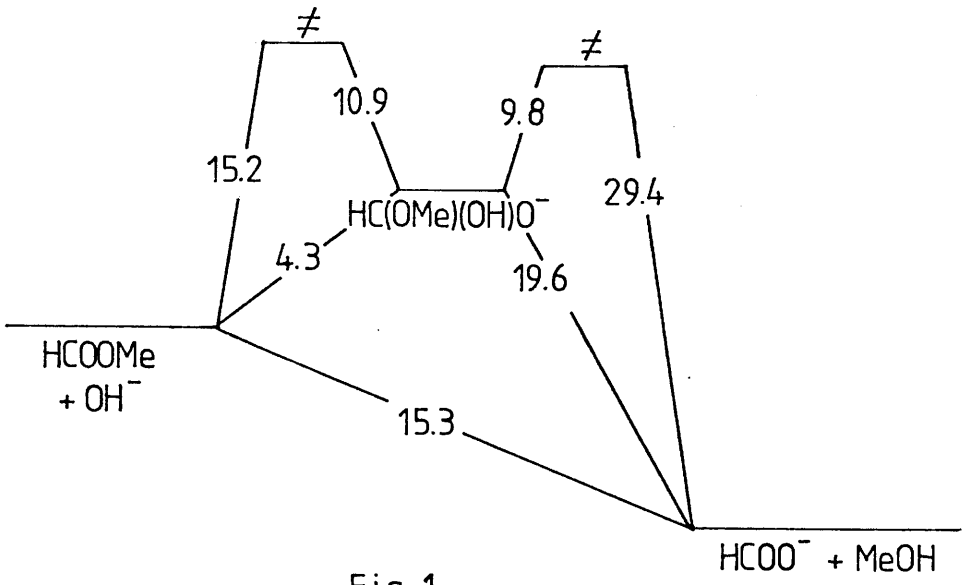
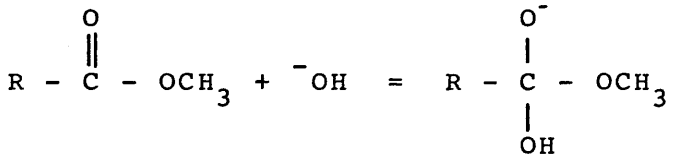
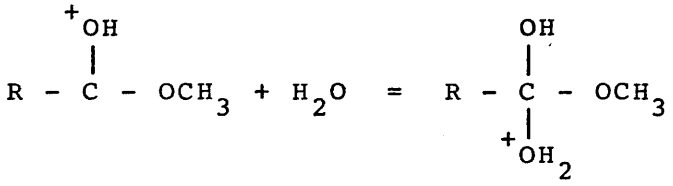


Fig. 1

In an extension of this work[39d,e] Guthrie estimated the equilibrium constants for the formation of the neutral (eq. 29) and ionic forms of the intermediates represented by the following equations where R had a large variety of substituents



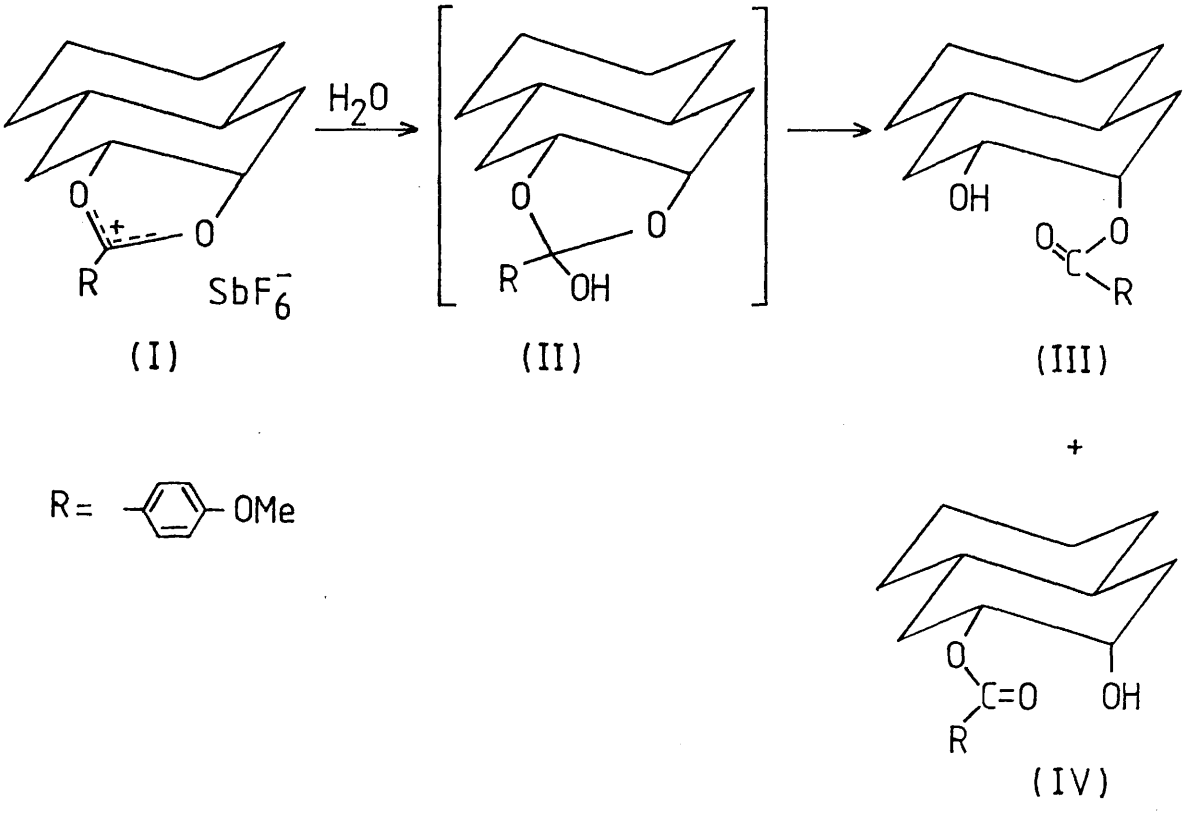
(30)



(31)

Stereoelectronic Control in the Breakdown of Tetrahedral Intermediates

Stereoselectivity was observed by King and Albutt[40] in the hydrolysis of dioxolenium ions and also in the hydrolysis of orthoesters incorporating a dioxolane ring since after some stage the further steps should be the same as those for the hydrolysis starting with dioxolenium ion. As example the hydroxy-ester (III) in the Scheme 7 constituted more than 99.5% of the products and no IV was observed.



Scheme 7

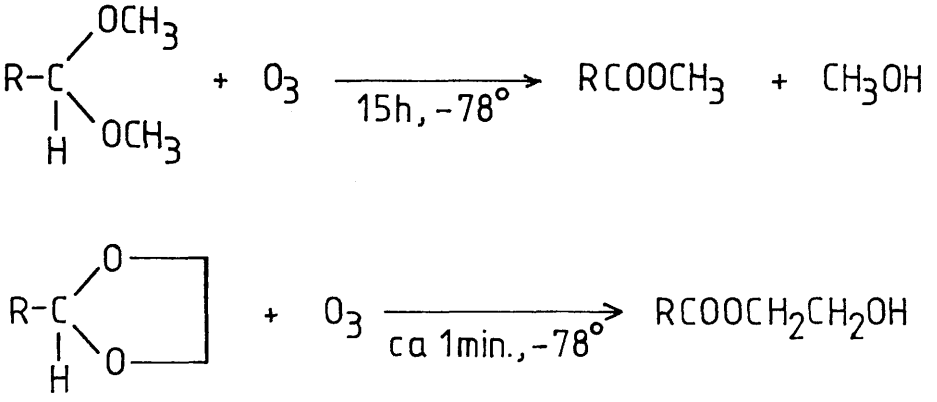
The stereoselectivity was discussed for the hydrolysis of orthoesters in terms of assistance of the lone pair orbitals antiperiplanar to the leaving group but such interpretation could also be extrapolated to the respective "orthoacids" such as the species II in the Scheme 7.

Deslongchamps[41a] has proposed a similar theory emphasizing the importance of the steric relationship of the lone pair orbitals in adjacent hetero atoms to the breaking or forming bond in the ground state conformation. The reactions investigated included the ozonolysis of acetals,[41b,c]

hydrolysis of imidate salts,[41e,f] hydrolysis of esters[41g,h] and hydrolysis of amides.[41d,e]

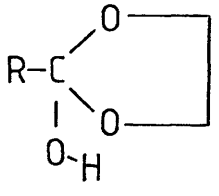
According to Deslongchamps' theory[41a] the mode of breakdown of the tetrahedral intermediate depends upon the orientation of the lone pair orbitals of the heteroatoms and the specific cleavage of a C-O or C-N bond will be allowed only if the other heteroatoms (oxygen or nitrogen) each have an orbital oriented antiperiplanar to the leaving O-alkyl or N-alkyl group. To this theory was added the assumption that the lifetime of a tetrahedral intermediate with the proper orbital orientation is smaller than the time required for a rotation of the C-N or C-O bond. However, Capon[18,27] and McClelland[13,19] have demonstrated that this assumption is not always true and recently Deslongchamps[41i] has agreed that this assumption is not always assured.

The experimental observations which led to this theory were firstly obtained with the ozonolysis of acetals[41b,c] and the results that were explained by Deslongchamps on the basis of his theory were the difference in rate of oxidation of cyclic and acyclic acetals (Scheme 8) and the selective formation of the products in the ozonolysis of 2-ethoxy-tetrahydropyran (Scheme 9)



Scheme 8

Two possible intermediates in the above reaction which could give rise to the products were (12) and (13) and sometimes Deslongchamps considered one and sometimes the other.



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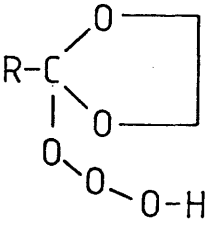
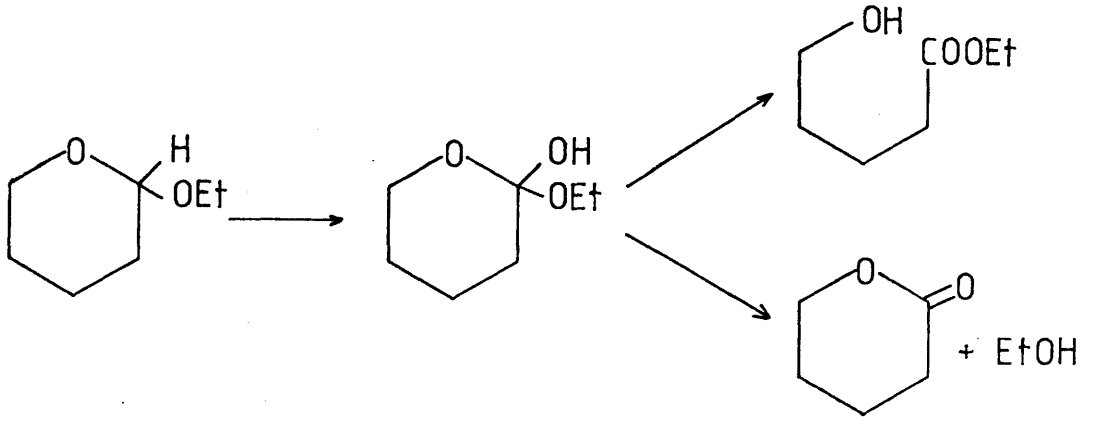


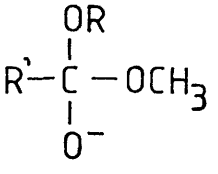
(13)



Scheme 9

The absence of detectable amount of lactone as product indicated that an intermediate (Scheme 9) was breaking down in a specific manner.

Deslongchamps[41a] discussed the results on the assumption that the intermediate was the hemiorthoester and interpreted its stereoelectronic breakdown in terms of the theoretical gauche conformation that a tetrahedral intermediate such as (14) can assume.



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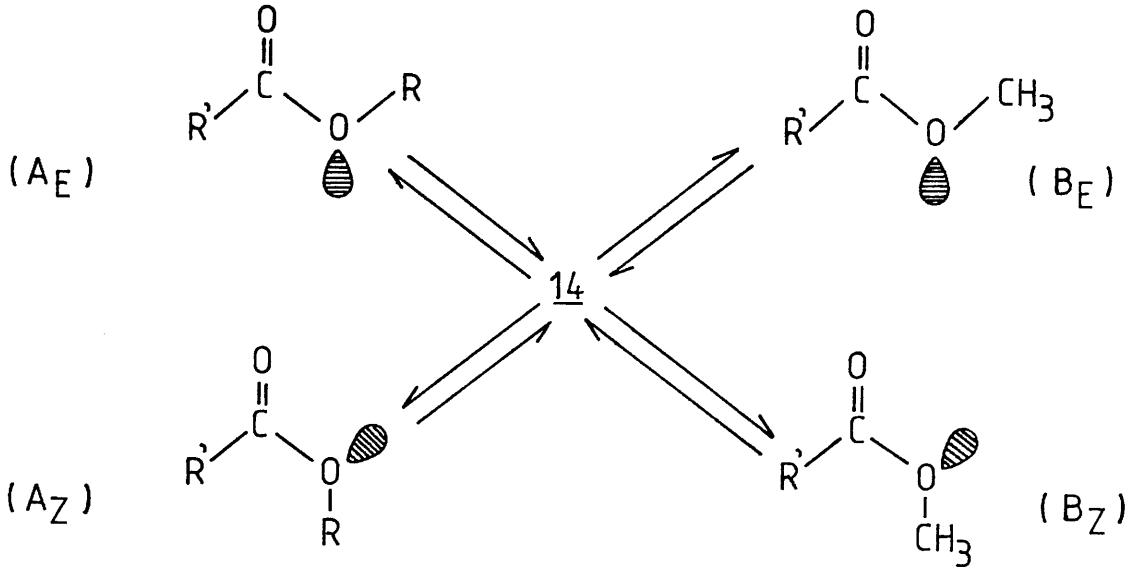
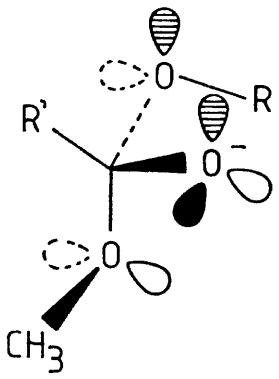


Scheme 10

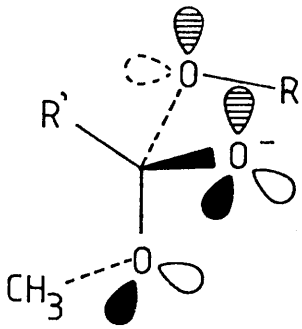
It was postulated that eight of the nine gauche conformers of (14) described in the Fig. 2 will form the esters products denominated A and B (Scheme 10) with the spacial arrangement of the conformation of the intermediate (in function of the R'-C bond and C-OR or C-OCH_3) bond which did not depart) being maintained in the ester product (E or Z).

However Plesnicar and Kovac[42] in their studies by NMR spectroscopy at low temperature related to the ozonolysis of a series of aliphatic and aromatic acetals which include those studied by Deslongchamps (Scheme 8) provided evidence for the presence of hydrotrioxides as intermediates such as (15) and c.a. 20% of the products was attributed to an



reactive: $^{-}OCH_3$

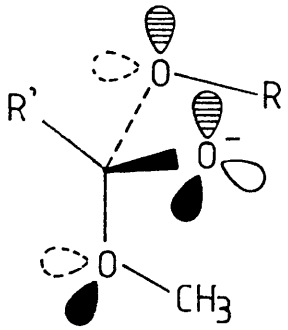
leaving → A_E



reactive: $^{-}OCH_3$ or

^{-}OR leaving →

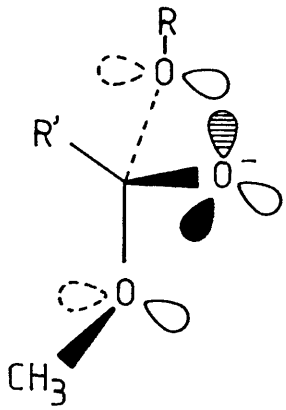
A_E or B_Z



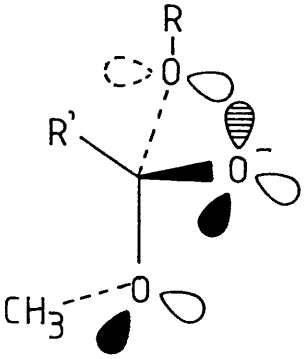
reactive: $^{-}OCH_3$ or

^{-}OR leaving →

A_E or B_E

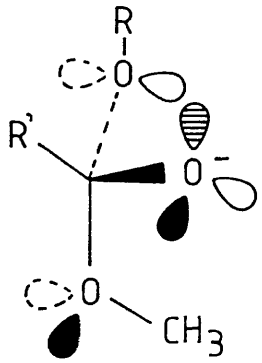


unreactive



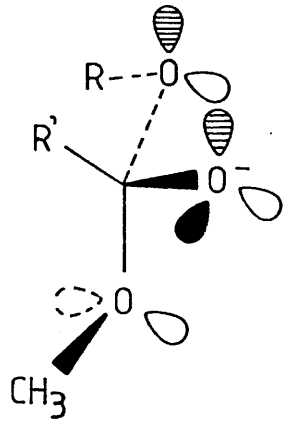
reactive: ^{-}OR

leaving → B_Z



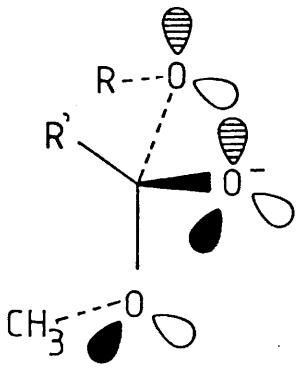
reactive: ^{-}OR

leaving → B_E



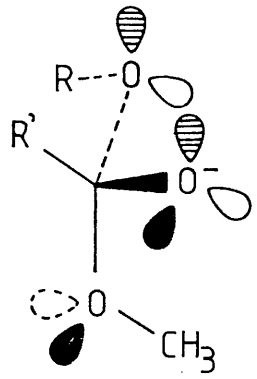
reactive: $^{-}OCH_3$

leaving → A_Z



reactive: $^{-}OCH_3$ or

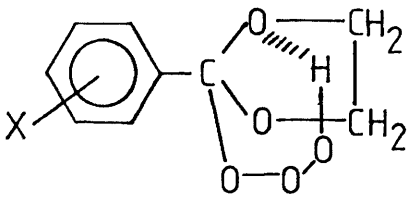
^{-}OR leaving → A_Z or B_Z



reactive: $^{-}OCH_3$ or

^{-}OR leaving → A_Z or B_E

Fig. 2



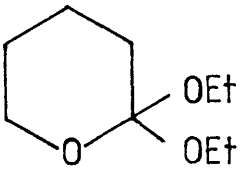
(15)

alternative mechanism involving a free-radical decomposition. Taillefer and co-workers[43] studied the kinetic of the decomposition of such intermediates in the ozonation of acyclic acetals and substituted-1,3-dioxanes in experiments carried out on a vapour phase chromatograph at low temperature (c.a. -30° to -80°C). The rate-constants for the cyclic acetals were 5.26 to 11.63 times faster (at -78°C) than the corresponding acyclic compounds.

Thus it appears that the selective product from the ozonolysis of 2-ethoxytetrahydropyran (Scheme 9) could be explained by Deslongchamps' theory if the intermediate involved was a tetrahedral intermediate. However the uncertainty about the intermediate and the difficulties to demonstrate that it was formed during the reaction resulted in the study of a series of orthoesters whose hydrolyses doubtless involve a tetrahedral intermediate.[2]

The series of cyclic orthoesters studied by Deslongchamps consisted of 2,2-diethoxy tetrahydropyran (16) and its analogues and he claimed that none of them gave the corresponding lactone as product. However this is

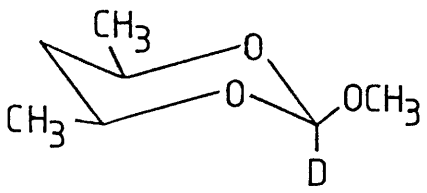
now known to be incorrect and a considerable percentage of lactone has been detected in the hydrolysis of this ortho-ester.[44,45]



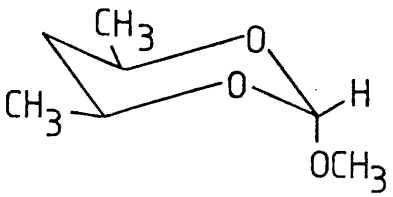
(16)

Recently Caserio and co-workers,[46] in order to obtain more conclusive data about the stereoelectronic selectivity of an axial C-O bond cleavage over the equatorial bond in cyclic orthoesters, have studied the reaction in gas phase of the ionization of orthoesters containing 1,3-dioxane ring. A similar system, the reaction of cyclic orthoesters with Grignard reagents, was studied in solution by Eliel and Nader[47] and the selective reactivity of the axial isomer over the equatorial (for the latter no reaction had taken place) was explained on the basis of stereoelectronic control several years before Deslongchamps first proposed his theory.

Caserio's results based on the reaction of a mixture of labelled equatorial orthoester (17) and unlabelled axial orthoester (18) and vice-versa with the ionic species



(17)



(18)

(obtained from electron-impact) of isopropyl ether and acetyl acetone showed a slight preferential cleavage of the axial C-O bond (10%) over the equatorial and the reaction of the unlabelled orthoesters with the cations isopropyl and (methyl thio) methyl studied by following the change of ion abundance with time showed equal selectivity for the cleavage axial versus equatorial.

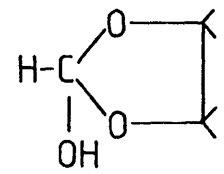
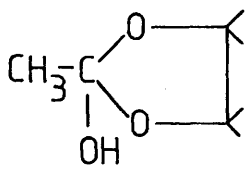
The results expected on the basis of Deslongchamps stereoelectronic theory were therefore not obtained.

1.2 DISCUSSION

This section is concerned with an investigation of the kinetics of the breakdown of hemiorthoesters generated *in situ* from dialkoxy-alkyl acetates and ketene acetals.

Only two of the hemiorthoesters: 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane and 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane could be studied in water. Consequently in order to obtain a common medium to study the whole series a change in the solvent-composition was required and, as described in the Experimental, the most suitable medium was acetonitrile-H_2O ($[H_2O]$ = 8.33 $\underline{\underline{M}}$). Some hemiorthoesters were also studied in a solution with less water ($[H_2O]$ = 2.22 $\underline{\underline{M}}$). The catalytic constants obtained in this investigation and some reported previously by McClelland and his co-workers are summarized in the following tables.

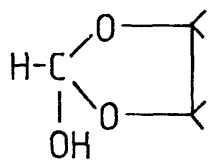
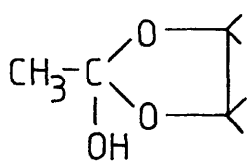
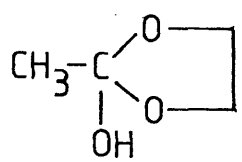
Table 1. Specific catalytic constants for the breakdown of hemiorthoesters, in water, at 15°C.[a,b]

	k_{H^+}, (s.d. %)	k_{OH^-}, (s.d. %)	k_{H_2O}
	2.85×10^{2} (6.0)	1.02×10^{9} (2.7)	1.91×10^{-1}
	2.92×10^{1} (0.8)	2.87×10^{6} (2.9)	1.80×10^{-2}

a - Units: k_{H^+}, k_{OH^-} = $\underline{\underline{M}}^{-1}\ s^{-1}$; k_{H_2O} = s^{-1}

b - This investigation.

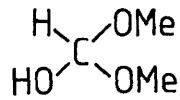
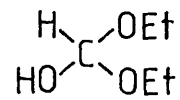
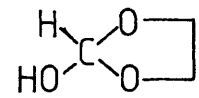
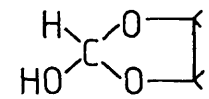
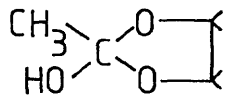
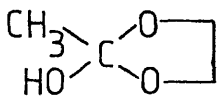
Table 2. Specific catalytic constants for the breakdown of hemiorthoesters, in CH_3CN-H_2O, $[H_2O]$ = 2.22 M, at 15°C.[a,b]

	k_{H^+}, (s.d. %)	k_{OH^-}, (s.d. %)	k_{H_2O}
	5.86×10^{4} (4.06)	1.70×10^{8} (11)	9.29×10^{-4}
	1.24×10^{4} (2.96)	3.72×10^{5} (12.4)	1.21×10^{-4}
	2.58×10^{5} (1.14)	8.99×10^{7} (4.8)	9.20×10^{-4}

a - Units: k_{H^+}, k_{OH^-} = M^{-1} s^{-1}; k_{H_2O} = s^{-1}

b - This investigation.

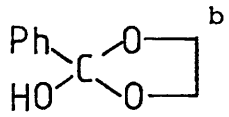
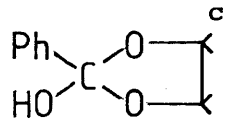
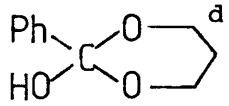
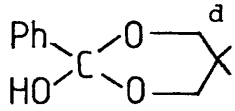
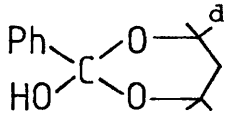
Table 3. Specific catalytic constants for the breakdown of hemiorthoesters, in CH_3CN-H_2O, $[H_2O]$ = 8.33 M, at 15°C.[a,b]

	k_{H^+}, (s.d. %)	k_{OH^-}, (s.d. %)	k_{H_2O}
	2.40×10^{5} (3.0)	3.21×10^{10} (6.5)	2.57×10^{-2}
	1.86×10^{5} (9.5)	6.53×10^{9} (7.3)	4.36×10^{-2}
	3.94×10^{3} (2.4)	6.00×10^{11} (2.0)	2.70×10^{-2}
	2.04×10^{3} (3.2)	8.39×10^{9} (5.8)	7.81×10^{-3}
	3.10×10^{2} (5.1)	3.95×10^{6} (11.4)	5.60×10^{-4}
	5.50×10^{3} (2.8)	1.97×10^{10} (9.5)	1.53×10^{-2}

a - Units: k_{H^+}, k_{OH^-} = $\underline{M}^{-1}$ s^{-1}; k_{H_2O} = s^{-1}

b - This investigation.

Table 4. Catalytic constants for the breakdown of hemiorthoesters in water, 15°C, I = 0.1 M.[a]

	k_{H^+}	k_{OH^-}	k_{H_2O}
 [b]	1.2×10^2	2.4×10^{10}	0.6
 [c]	5.2	8×10^6	0.03
 [d]	1.2×10^3	-	0.4
 [d]	4.4×10^2	-	0.52
 [d]	1.36×10^3	-	0.064

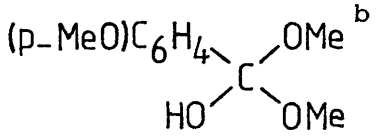
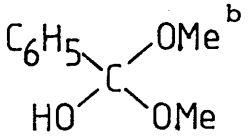
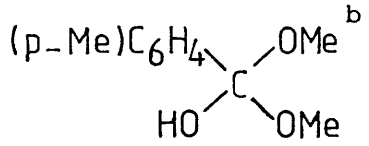
a - Units k_{H^+}, k_{OH^-} = M^{-1} s^{-1}; k_{H_2O} = s^{-1}

b - Ref: M. Ahmad, R.G. Bergstrom, M.J. Cashen, Y. Chiang, A.J. Kresge, R.A. McClelland, M.F. Powell, J. Am. Chem. Soc., 101, 2669 (1979).

c - R.A. McClelland, M. Ahmad, J. Bohonek, S. Gedge, Can. J. Chem., 57, 1531 (1979).

d - R.A. McClelland, S. Gedge, J. Bohonek, J. Org. Chem., 46, 886 (1981).

Table 5. Estimated catalytic constants for the breakdown of hemiorthoesters in water at 15°C.[a]

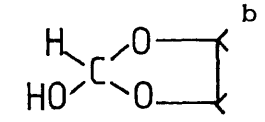
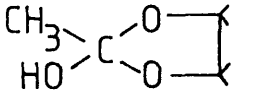
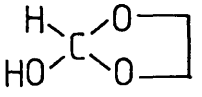
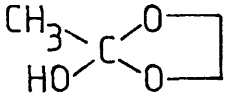
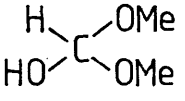
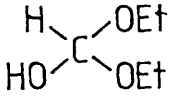
	k_{H^+}	k_{OH^-}	k_{H_2O}
 [b]	3.6×10^{4}	-	1.46
 [b]	1.52×10^{4}	9.92×10^{8}	12.48×10^{-1}
 [b]	2.4×10^{4}	-	1.46

a - Units: k_{H^+}, k_{OH^-} = $\underline{\underline{M}}^{-1}$ s^{-1}; k_{H_2O} = s^{-1}

b - R.A. McClelland, G. Patel, J. Am. Chem. Soc., 103, 6912 (1981).

In order to compare the catalytic constants already listed in the Tables 1 to 5 some extrapolations were necessary to obtain a common basis. This was done by converting all the literature values of the rate constants from 25° to 15°C (Tables 4 and 5) by dividing them by a factor of 2.5 and also by extrapolating the constants for the breakdown of the hemiorthoesters studied in this investigation to the water medium. The rate constants for the breakdown of the two hemiorthoesters, 2-hydroxy and 2-hydroxy-2-methyl-4,4,5,5-tetramethyl-1,3-dioxolanes, studied in both media, were used to estimate the factors for each catalytic constant (and water reaction) on going from acetonitrile-water ($[H_2O]$ = 8.33 $\underline{\underline{M}}$) to water. The averages (0.117 for $\underline{k}_{H^+}$, 0.42 for $\underline{k}_{OH^-}$ and 28.25 for $\underline{k}_{H_2O}$) of these factors were used to obtain the extrapolated values for the constants for the other hemiorthoesters. The extrapolated rate constants are summarized in Table 6.

Table 6. Estimated catalytic constants for the breakdown of hemiorthoesters in water at 15°C.[a]

	k_{H^+}	k_{OH^-}	k_{H_2O}
 [b]	2.85×10^{2}	1.02×10^{9}	1.92×10^{-1}
 [b]	2.92×10^{1}	2.87×10^{6}	1.80×10^{-2}
	4.61×10^{2}	2.52×10^{11}	7.63×10^{-1}
	6.44×10^{2}	8.3×10^{9}	4.32×10^{-1}
	2.81×10^{4}	1.35×10^{10}	7.26×10^{-1}
	2.18×10^{4}	2.74×10^{9}	12.3×10^{-1}

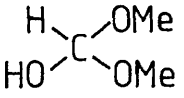
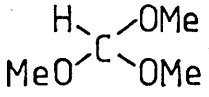
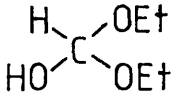
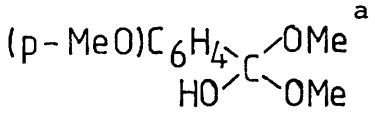
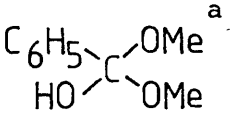
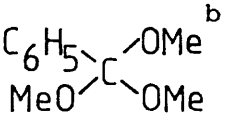
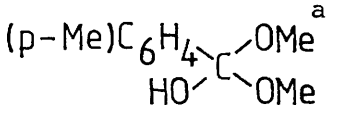
b - The respective catalytic constants were measured in water.

a - Units: k_{H^+}, $k_{OH^-} = \underline{\underline{M}}^{-1}\ s^{-1}$

$k_{H_2O} = s^{-1}$

An additional extrapolation was made in order to obtain the rate constants for the breakdown of the acyclic hemi-orthoesters containing p-X-C_6H_4 substituents[35] in water at 15°. In the absence of a better basis for comparison the rate constants were extrapolated from 25° to 15° as before by dividing the rate constants by 2.5 and from 50% aqueous dioxane to water by multiplying by 2.0, 6.2 and 5.2 which are the ratios of the rate constants for the H_3O^+, HO^- and H_2O catalyzed breakdown of the hemiacetal, m-Cℓ-benzaldehyde ethyl hemiacetal, in these media.[52] The hydronium-ion catalytic constants for the breakdown of the acyclic hemi-orthoesters are summarized in the Table 7 and the rate constants for the breakdown of some hemiacetals are also tabulated (Table 8) for comparison.

Table 7. Substituent effect for the acid-catalyzed breakdown of acyclic hemiorthoesters and orthoesters at 15°C.

	k_{H^+} ($\underline{M}^{-1}s^{-1}$)	$k_{rel.}$
	2.81×10^4	1
	1.05×10^2	-
	2.18×10^4	0.78
 [a]	3.6×10^4	1.28
 [a]	1.52×10^4	0.54
 [b]	29.6	-
 [a]	2.4×10^4	0.86

a - Ref. b in the Table 5.

b - Ref. 48 (p.149).

Table 8. Catalytic constants for the breakdown of hemiacetals and acetals in water at 15°C.

	k_{H^+} ($\underline{M}^{-1}s^{-1}$)	k_{OH^-} ($\underline{M}^{-1}s^{-1}$)	k_{H_2O} (s^{-1})
$H_2C(OMe)(OH)$ [a]	0.23	9.36×10^{2}	7.24×10^{-4}
$H_2C(OMe)_2$ [b]	8.8×10^{-5}	-	-
$H_2C(OEt)(OH)$ [a]	0.30	5.2×10^{2}	6.52×10^{-4}
$H_2C(OEt)_2$ [b]	8.8×10^{-5}	-	-
$Ph\text{-}CH(OMe)(OH)$ [c]	260	6.9×10^{5}	5.2×10^{-3}
$Ph\text{-}CH(OMe)_2$ [d]	30	-	-
$Ph\text{-}CH(OEt)(OH)$ [e]	267	7×10^{5}	3.6×10^{-4}
$Ph\text{-}CH(OEt)_2$ [e]	58	-	-

a - Ref. 34

b - Ref. 49

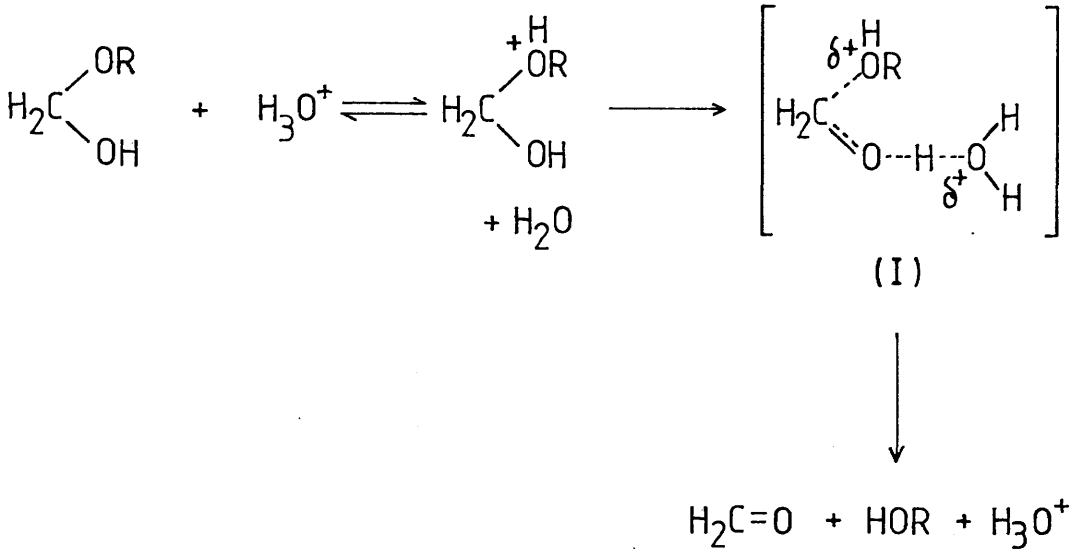
c - Ref. 50

d - Ref. 51

e - Ref. 52

The Hydronium Ion Catalyzed Breakdown of Hemiorthoesters and Hemiacetals

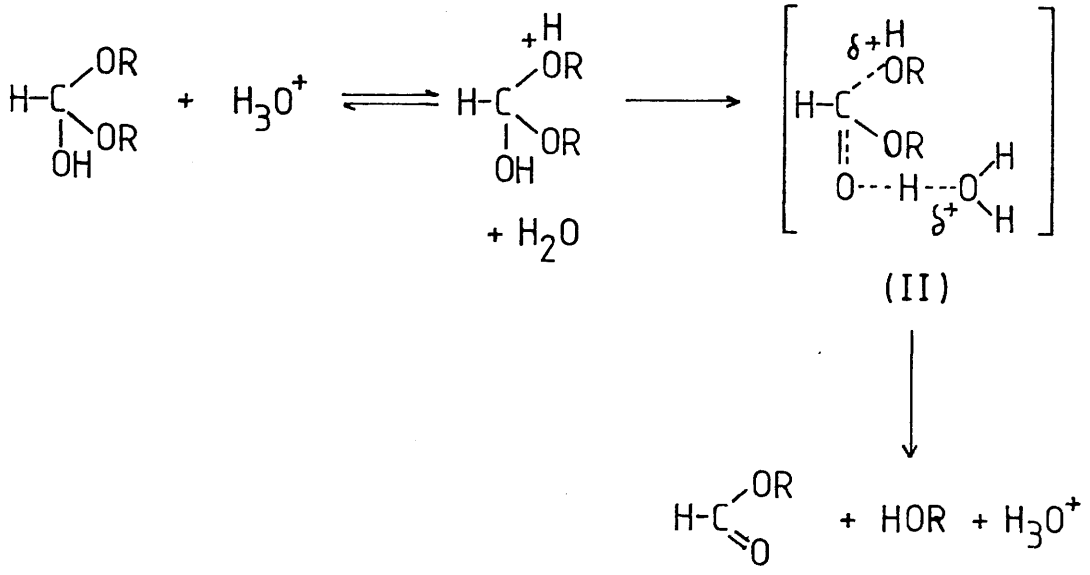
The breakdown of aliphatic hemiacetals (Table 8) has been studied by Funderburk and Jencks[34] who proposed on the basis of structure-reactivity correlations a mechanism for the acid-catalyzed breakdown represented by:



Scheme 11

The c.a. 2600 times greater rate constants for the breakdown of the aliphatic hemiacetals compared to the corresponding acetals also provides strong evidence for the above mechanism as the difference in rates could be attributed to proton transfer from the OH-group in a transition state such as (I).

A similar mechanism can be written for the breakdown of dimethyl and diethyl hemiorthoformates which occur c.a. 10^5 times faster than the corresponding hemiacetals



(II)

Scheme 12

The factor of c.a. 3 x 10^2 favouring the breakdown of dimethyl hemiorthoformate over the trimethyl orthoformate supports a mechanism involving partial proton transfer from the OH-group to the solvent in the transition-state.

The greater rate of breakdown of the hemiorthoester compared to the hemiacetal presumably arises from the conjugation of the extra methoxy group with the developing carbonyl group in the transition-state. A smaller rate enhancement (10^3) is found when a phenyl substituent is introduced as in benzaldehyde hemiacetal to the acetal the rate decrease is less than 10. This was discussed by

Fife and Przystas[52] in terms of the stabilizing effect of the phenyl group by conjugation with the developing carbonyl group resulting in a reduced requirement for proton transfer from the OH-group of the benzaldehyde hemiacetal to achieve the transition-state. However, with the hemiorthoester, where the stabilization of the methoxy group appears to be greater than that of a phenyl group, proton transfer from the OH-group appears to be larger (as measured by the hemiorthoester/orthoester rates ratio).

The presence of the phenyl on the pro-acyl carbon in hemiorthoesters has only a very small effect on $\underline{k}_{H^+}$. The effect of a phenyl group on the transition-state would be expected to be destabilizating by its electron-withdrawing inductive effect on the positively charged oxygen and stabilizating due to conjugation with the developing carbonyl group. The small decrease in the rates of breakdown of acyclic and cyclic hemiorthoesters which arises from the presence of a phenyl group may indicate that these effects almost cancel each other, with the inductive effect being slightly favoured in the transition-state.

As summarized in the Table 9, series 1 and 3, the dioxolane ring decreases the rates of breakdown by a factor of c.a. 60-100 compared to acyclic hemiorthoesters and the four methyl substituents in the ring have a major retarding effect in the series containing a phenyl and a methyl (series 2) at the carbon-2. This decrease in the rates

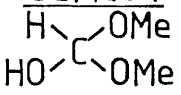
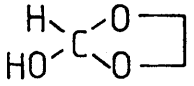
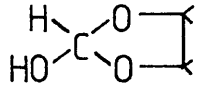
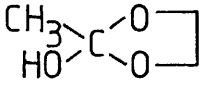
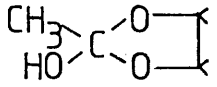
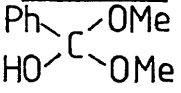
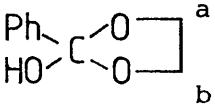
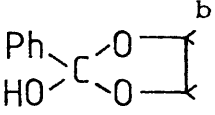
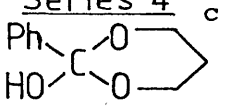
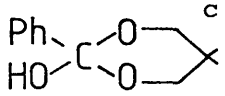
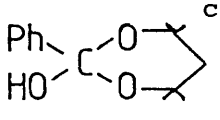
can be accounted for as due to the steric effect resulting from the methyl groups on positions 4 and 5 in the ring. Presumably as the ring begins to open the methyl groups are forced closer together and the energy of the transition-state is raised.

The reverse of this steric effect was calculated by Guthrie[39c] for the cyclization of glycol monoesters and was attributed to the relief of steric compression involving the methyl groups on cyclization.

A similar decelerating effect to that found with hemi-orthoesters when there are six substituents in the ring (positions 2,2,4,4,5,5) has also been observed in the hydrolysis of acetals. The presence of the second group at the position 2 decreased the rate of hydrolysis of 2,2,4,4,5,5-hexamethyl-1,3-dioxolane compared to 2,4,4,5,5-pentamethyl-1,3-dioxolane[53] by a factor of c.a. 10 and the same trend was also observed by Fife[54] in the hydrolysis of 2-phenyl-2,4,4,5,5-pentamethyl-1,3-dioxolane.

In the absence of the four methyl substituents at positions 4 and 5 however the reverse occurs and the presence of the second methyl group at position 2 accelerates the rate of hydrolysis of 2,2-dimethyl-1,3-dioxolane.[53]

Table 9. Substituent effect on the ring for the acid-catalyzed breakdown of hemiorthoesters at 15°C.

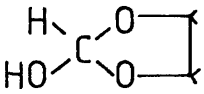
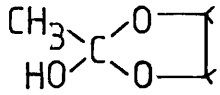
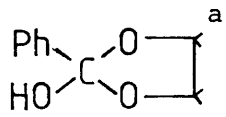
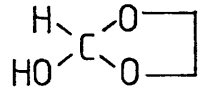
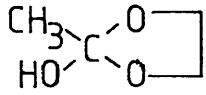
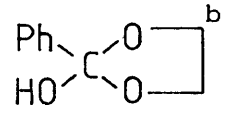
	k_{H^+} ($\underline{M}^{-1}s^{-1}$)	$k_{rel.}$
Series 1 	2.81×10^4	60.95
	4.61×10^2	1
	2.85×10^2	0.62
Series 2 	6.44×10^2	1
	2.92×10^1	0.045
Series 3 	1.52×10^4	127
 [a]	1.2×10^2	1
 [b]	5.2	0.043
Series 4  [c]	1.2×10^3	1
 [c]	4.4×10^2	0.37
 [c]	1.36×10^3	1.13

a - Obtained from ref. b (Table 4)

b - Obtained from ref. c (Table 4)

c - Obtained from ref. d (Table 4)

Table 10. Substituent effect on carbon-2 for the acid-catalyzed breakdown of cyclic hemiorthoesters at 15°C.

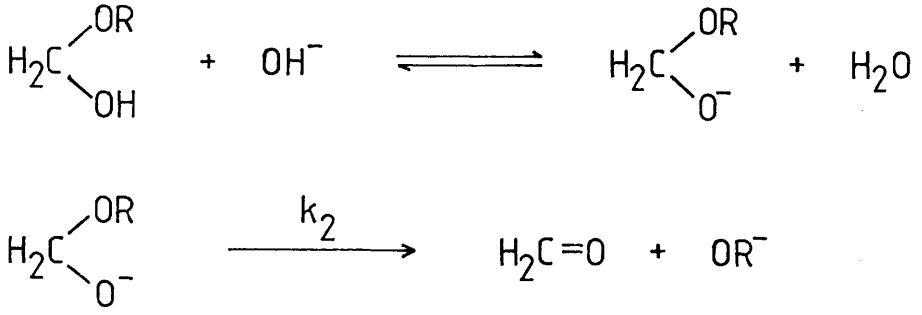
Series 1	k_{H^+} ($\underline{M}^{-1}s^{-1}$)	$k_{rel.}$
	2.85×10^2	1
	2.92×10^1	0.01
 [a]	5.2	0.018
Series 2		
	4.61×10^2	1
	6.44×10^2	1.40
 [b]	1.2×10^2	0.26

a - Obtained from ref. c (Table 4)

b - Obtained from ref. b (Table 4)

Hydroxide-Ion Catalyzed Breakdown of Hemiorthoesters and Hemiacetals

Funderburk and Jencks[34] proposed a mechanism for the breakdown of hemiacetals catalyzed by hydroxide-ion which consists of the reversible formation of the anionic species followed by its unimolecular breakdown according to:



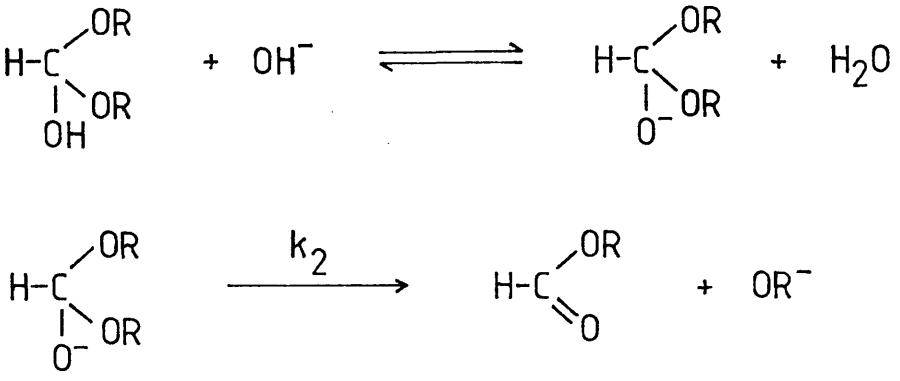
Scheme 13

Reactivity-structure correlations provided evidence for the above mechanism in which the negative charge on the oxygen of the anion has enough "driving force" to expel the leaving alkoxy group.

This mechanism has also been proposed for the hydroxide ion-catalyzed breakdown of benzaldehyde ethyl hemiacetal,[52] of the hemiorthoester, 2-hydroxy-2,4,4,5,5-pentamethyl,1,3-dioxolane[27] and for the breakdown of tetrahedral intermediate from phtalimidium cation.[31]

In a similar way we suggest that the hydroxide ion-catalyzed breakdown of the hemiorthoesters studied in this

investigation proceeds by an analogous mechanism:



Scheme 14

However, in order to compare the rate constants for the series of hemiorthoesters and hemiacetals, an estimation of the pKa's of the intermediates was necessary and this was done for the whole series by using Hine and Koser's equation for the pKa's of aldehyde hydrates, $RR'C(OH)_2$:

$$pKa = 14.19 - 1.315 \Sigma \sigma_R^*$$

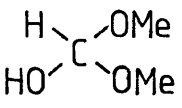
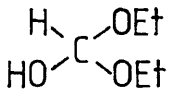
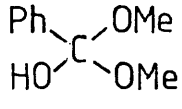
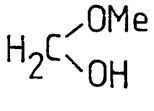
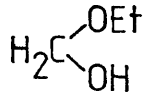
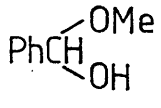
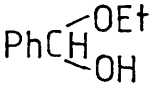
The σ^* for the substituents were obtained from the relationship

$$\sigma^* = 6.23 \sigma_I$$

where the inductive substituents constants were obtained from the list supplied by Charton.[55] (Some σ^* values were obtained from ref. 56). By making the same approximations

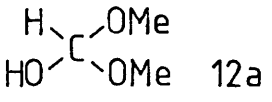
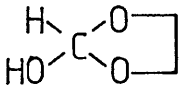
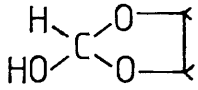
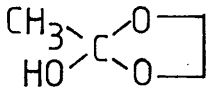
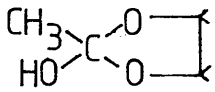
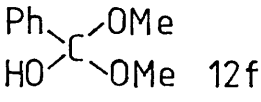
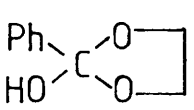
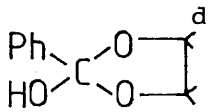
as Capon and Ghosh[27] by adding a factor of 0.27 to compensate the presence of one alkoxy group (the aldehyde hydrate has two OH-groups) and by adding a factor of 0.30 to compensate the presence of only one acidic proton, the pKa's were estimated and are summarized in the following tables. Previous estimates for two pKa's had already been made, c.a. 11 for the breakdown of dimethyl hemiorthobenzoate and 13.56 for formaldehyde ethyl hemiacetal. However, we prefer to use the same method of estimation for the pKa's of all the intermediates. The following tables also contain the estimated k_2 values for the series of hemiorthoesters and hemiacetals. These values are all considerably less than the time constant for a molecular vibration (10^{12}-10^{14} s^{-1}) and hence are reasonable values.

Table 11. Hydroxide-ion catalyzed breakdown of hemiorthoesters and hemiacetals at 15°C.

		k_{OH^-} ($M^{-1}s^{-1}$)	k_2 [a] (s^{-1})	pKa
	11a	1.35×10^{10}	2.60×10^{7}	11.28
	11b	2.74×10^{9}	5.27×10^{6}	11.28
	11c	9.92×10^{8}	2.22×10^{5}	11.14
	11d	9.36×10^{2}	6.69×10^{1}	12.85
	11e	5.2×10^{2}	3.71×10^{1}	12.85
	11f	6.9×10^{5}	3.45×10^{4}	12.70
	11g	7×10^{5}	3.5×10^{4}	12.70

a - $k_2 = k_{OH^-} \times K_w/K_a$

Table 12. Substituent effect on the ring for the hydroxide ion-catalyzed breakdown of hemiorthoesters at 15°C.

	k_{OH^-} ($\underline{M}^{-1}s^{-1}$)	k_2 [a] (s^{-1})	pKa [b]
 12a	1.35×10^{10}	2.60×10^{7}	11.28
 12b	2.52×10^{11}	4.85×10^{8}	11.28
 12c	1.02×10^{9}	2.37×10^{6}	11.37
 12d	8.3×10^{9}	6.9×10^{7}	11.92
 12e	2.87×10^{6}	3.02×10^{4}	12.02
 12f	9.92×10^{8}	1.38×10^{6}	11.14
 12g [c]	2.4×10^{10}	3.33×10^{7}	11.14
 12h [d]	8×10^{6}	1.36×10^{4}	11.23

---

a - $\underline{k}_2 = k_{HO^-} \times K_w/K_a$

b - Estimated from the eq. pKa = $14.19-1.315\ \Sigma\ \sigma_R^*$ (Ref. 32)

c - Obtained from ref. b (Table 4)

d - Obtained from ref. c (Table 4)

The comparison of the rate constants for the breakdown of the anions ($\underline{k}_2$) from the formaldehyde hemiacetals (11d, 11e) and benzaldehyde hemiacetals (11f, 11g) shows an increase by a factor of c.a. 10^3 favouring the latter. Such rate-enhancement, also reflected in the $\underline{k}_{OH^-}$ values since the hemiacetals have comparable pKa's, can be attributed to the stabilizing effect of the conjugation of the phenyl with the developing carbonyl group in the transition state. Similarly on going from an aliphatic hemiacetal (11d, 11e) to an aliphatic hemiorthoester (11a, 11b) the presence of an extra alkoxy group accelerates the rates by a factor of c.a. 10^5 which can also be attributed to the stabilizing effect by conjugation of the alkoxy group with the developing carbonyl group.

The presence of the dioxolane ring in hemiorthoesters, 12a to 12b and 12f to 12g caused an acceleration. This may arise from a difference in pKa's as the more rigid structure of the dioxolane may lead to the dipoles of C-O bonds being orientated more favourably to stabilize the anion. Our method for the estimation of the pKa does not allow for an effect of this type and so the acceleration is shown in the Table as being an effect on $\underline{k}_2$. If it is an effect on $\underline{k}_2$ a possible explanation for the greater rate of cleavage of the dioxolane compared to the acyclic hemiorthoester may arise from a stereoelectronic effect or from the leaving group being a β-alkoxy-alkoxy rather than an

alkoxy group. Unfortunately a more definite explanation can not be given at present.

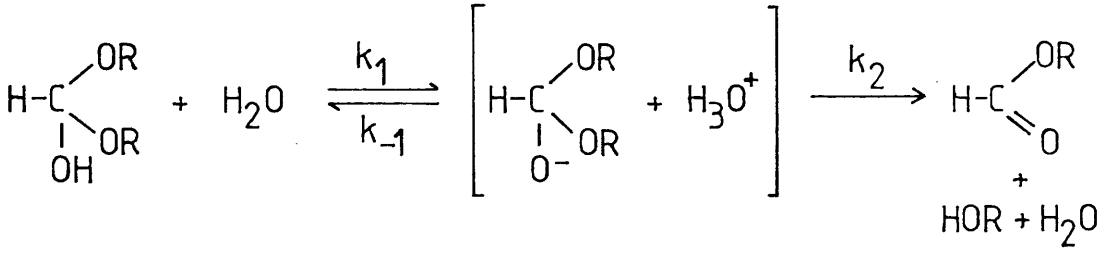
The presence of four methyl groups in the rings has a great stabilizing effect (slowing the rates by a factor of 10^2-10^3) which is reflected in the whole series. This decelerating effect is more pronounced than in the acid-catalyzed reaction (slowing the rates by a factor less than 20). It is possible that in the hydroxide-ion catalyzed reaction there is superimposed on the steric effect an electronic effect of the methyl groups which cause a decrease in the leaving group ability of the alkoxide ion due to their electron-releasing inductive effect. A similar effect is observed in the hydroxide-ion catalyzed breakdown of benzaldehyde t-butyl and methyl hemiacetals (see Part 2, Table 4A).

The presence of a phenyl group in the hemiorthoesters decreased the rate of the breakdown of the anion (k_2) in both the cyclic and acyclic series. This could be explained if we assume, on the basis of Hammond's postulate, that the transition-state closely resembles the anion. If this is so, a possible stabilization by the phenyl through conjugation with the developing carbonyl group might be unimportant since the double-bond could not be well developed. However, the electron-withdrawing inductive effect of the phenyl group would be more important in the

initial state, i.e., the anion, where the negative charge is less delocalized than in the transition-state.

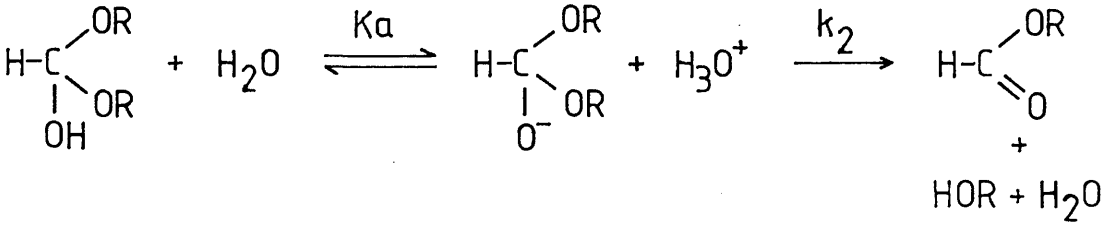
Spontaneous Reaction of the Breakdown of Hemiorthoesters and Hemiacetals

The breakdown of hemiorthoesters and hemiacetals in a "water-catalyzed" reaction has been suggested to occur by the same mechanism[27,34,52] which consists of the abstraction by water of the OH-proton from the intermediate forming an encounter complex which breaks down to products catalyzed by hydronium-ion faster than the two diffuse apart:



Scheme 15

Alternatively if the anion of the hemiorthoester and the hydronium-ion diffuse apart before the former undergoes breakdown the reaction can be formulated as:



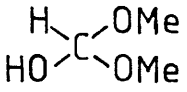
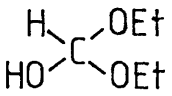
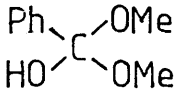
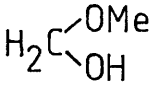
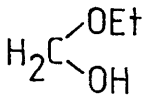
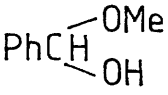
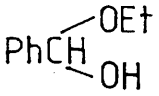
Scheme 16

On the basis of the scheme 16 it is possible to make an estimate of $\underline{k}_2$ from $\underline{k}_{H_2O}$ and K_a. If this estimation is greater than the diffusion-limit it suggests that the mechanism in the scheme 16 is incorrect and that that in scheme 15 is followed. Alternatively if the mechanism in the scheme 15 is followed $\underline{k}_{H_2O}$ should approach the value of $\underline{k}_1$ estimated from the pKa and $\underline{k}_{-1}$ which is assumed to have the diffusion-controlled limit of 5×10^{10} $\underline{M}^{-1}$ s^{-1}.

The comparison of the values listed in the Tables 13 and 14 indicates that the breakdown of hemiorthoesters are included in the first case; the estimated values of $\underline{k}_2$ are in the range of the diffusion-controlled limit and the calculated $\underline{k}_1$ values are within one order of magnitude of the values of $\underline{k}_{H_2O}$.

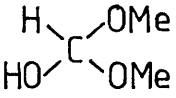
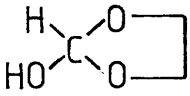
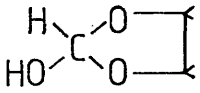
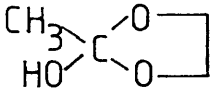
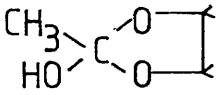
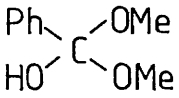
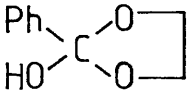
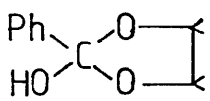
The breakdown of the tetrahedral intermediate generated from phthalimidium cation, studied by Gravitz and Jencks[31] is an example of the second case, where the second step is

Table 13. Rate constants for the water reaction for the breakdown of hemiorthoesters and hemiacetals at 15°C.

	$k_{H_2O}(s^{-1})$	pKa	$k_1^a\ (s^{-1})$	$k_2^a\ (\underline{\underline{M}}^{-1}s^{-1})$
	7.26×10^{-1}	11.28	2.62×10^{-1}	1.40×10^{11}
	12.3×10^{-1}	11.28	2.62×10^{-1}	2.36×10^{11}
	12.48×10^{-1}	11.14	3.62×10^{-1}	1.73×10^{11}
	7.24×10^{-4}	12.85	7.06×10^{-3}	5.17×10^{9}
	6.52×10^{-4}	12.85	7.06×10^{-3}	4.66×10^{9}
	5.2×10^{-3}	12.70	9.98×10^{-3}	2.6×10^{10}
	3.6×10^{-4}	12.70	9.98×10^{-3}	1.8×10^{9}

a - As described in the Scheme 15.

Table 14. Substituent effects on the ring for the "water" reaction for the breakdown of hemiorthoesters at 15°C.

	$k_{H_2O}(s^{-1})$	pKa	$k_1^a(s^{-1})$	$k_2^a(\underline{M}^{-1}s^{-1})$
	7.26×10^{-1}	11.28	2.62×10^{-1}	1.40×10^{11}
	7.63×10^{-1}	11.28	2.62×10^{-1}	1.47×10^{11}
	1.91×10^{-1}	11.37	2.15×10^{-1}	4.44×10^{10}
	4.32×10^{-1}	11.92	0.6×10^{-1}	3.6×10^{11}
	1.80×10^{-2}	12.02	4.35×10^{-2}	1.89×10^{10}
	12.48×10^{-1}	11.14	3.62×10^{-1}	1.73×10^{11}
	6×10^{-1}	11.14	3.62×10^{-1}	8.33×10^{10}
	3×10^{-2}	11.23	2.95×10^{-1}	5.08×10^{9}

a - As described in the Scheme 15.

rate-limiting (estimated $\underline{k}_2 = 5.9 \times 10^7$ $\underline{\underline{M}}^{-1}$ s^{-1}) and the estimated rate constant for ionization ($\underline{k}_1$), as estimated by Capon and Ghosh,[27] was more than 10^3 times greater than $\underline{k}_{H_2O}$.

It seems that the breakdown of hemiacetals (Table 13) is a marginal case since the estimated ionization constants are greater than $\underline{k}_{H_2O}$ (but not by the same magnitude as in the system of Gravitz and Jencks) and the $\underline{k}_2$ values are slightly less than the diffusion-controlled limit making them possible values for the rate-determining step. If the ionization were rate-determining for the breakdown of hemiacetals as it is for hemiorthoesters the ratio of the values of $\underline{k}_{H_2O}$ for both series (Table 13) should be the same as the ratio of the Ka's; however a ratio of c.a. 10^3 for $\underline{k}_{H_2O}$ is observed against a ratio of c.a. 40 estimated from the pKa's suggesting that the $\underline{k}_{H_2O}$ values for the hemiacetals are falling below the estimated values if the ionization were the rate-determining step.

Epilogue

This investigation and the complementary ones of McClelland and his co-workers show that the kinetics of the breakdown of the long-postulated but unobserved tetrahedral intermediates of O,O-acyl transfer reactions can now be investigated directly.

1.3 EXPERIMENTAL

1.3.1 Kinetic Experimental

Introduction to Kinetic Experimental

In this investigation various tetrahedral intermediates (TI) were generated from precursors (P) and the kinetics of their breakdown into esters (E) were followed by uv spectroscopy.

$$P \xrightarrow{\text{step 1}} TI \xrightarrow{\text{step 2}} E$$

It was therefore essential to be certain that step 2 had been followed. Therefore experiments were carried out by NMR spectroscopy under conditions as close as possible to those for the uv kinetics measurements in order to check that step 1 was faster than step 2. With some substrates it was found that step 1 was only faster than step 2 under some pc_H's and that in more basic solutions step 2 became faster than step 1. When this happened the pH jump method was used. For these cases the TI was generated at a pc_H where step 1 was faster than step 2 and when it was thought that all the precursor was completely converted into TI, an amount of NaOH was added in order to adjust the pc_H to that required.

Rate determinations were performed on a Pye-Unicam SP8-200 spectrophotometer with a cell compartment thermostatted at 15°C ± 0.05 using an efficient relay system.

The pH or pc_H was always measured after each run using a combined electrode GK 2401 B and a Radiometer PHM 64 pH meter and the final pH or pc_H for each solution was the average of measurement of individual runs. The variation in the pH's and pc_H measured in this way were ± 0.04 and ± 0.1 respectively.

The values of observed rate constants ($\underline{k}_{obs}$) were obtained from the weighted average of two to five runs.

For the hydrolysis of 2-acetoxy-4,4,5,5-tetramethyl and 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane in aqueous solution, the pH was measured as mentioned before, but it was not possible to follow the hydrolysis of 2-methylene-1,3-dioxolane in aqueous solution due to its speed, so we tried to find other kinetic conditions to follow it. It was thought that the conditions previously used by Capon by NMR experiments for generation of the hemiorthoester 2-hydroxy-2-methyl-1,3-dioxolane using 2-methylene-1,3-dioxolane as precursor might be better.[27] These were with CD_3CN-CD_3COOD (95-5% v/v) as solvent and with the final concentration of d_4-acetic acid 6.8×10^{-3} $\underline{\underline{M}}$.

Conditions similar to these were found to be suitable, viz: aqueous acetonitrile with $[H_2O] = 2.22$ $\underline{\underline{M}}$. Although these conditions were promising they raised the problem of how to determine the $[H^+]$ and $[HO^-]$ in that specific solvent mixture. This is discussed in the next section.

Determination of pc_H in Aqueous Acetonitrile

A long search for the usefulness of glass and calomel electrodes in mixture or non-aqueous solvent was carried out. Several investigations have been carried out using aqueous saturated calomel as reference electrode in acetonitrile since it functions satisfactorily in this medium[57-62] and it is widely utilized, mainly for potentiometric measurements.[63]

Coetzee[61] in the determination of the auto protolysis constant of acetonitrile has used a saturated calomel electrode in conjunction with a glass electrode and observed a drift in the potential which was attributed to a gradual deposition of a plug of solid potassium chloride in the interface between the salt bridge and acetonitrile solution. That problem was minimized by using tetraethylammonium perchlorate salt bridge rather than potassium chloride. He suggested that some precautions, such as a quick measurement (within 5 or 6 mins.) should be taken when using a potassium chloride salt bridge. Nevertheless he claimed that the response of the glass electrode was reversible in picric acid buffers.

Hall[59] has successfully used glass electrode for potentiometric titrations in several non-aqueous solvents and Feakins[60] has developed a procedure to get a reproducible measurement from glass electrode in nitrobenzene solutions.

The standard procedure that we have used throughout the kinetics in aqueous-acetonitrile is described as follows:

Solutions of CH_3CN-HCℓ ($[H_2O]$ = 2.22 $\underline{\underline{M}}$) at different concentrations of acid were prepared by weighing ca. 2 ml of HCℓ at a convenient concentration plus water if necessary and diluting to 50 ml with CH_3CN to the volumetric mark. The pH meter was adjusted to give a reading of pH 2.0 with a solution of CH_3CH-HCℓ ($[H_2O]$ = 2.22 $\underline{\underline{M}}$) final acid concentration of 1×10^{-2} $\underline{\underline{M}}$, with an associated reading of -289.2 mV in a 1500 mV scale. That solution became the reference buffer utilized for subsequent measurements. The combined electrode was washed three times with a solution of CH_3CN-H_2O ($[H_2O]$ = 2.22 $\underline{\underline{M}}$), dried with a soft tissue and immersed into the reference buffer for 5 minutes.

After the adjustment to -289.2 mV the washing procedure was repeated and the electrode kept in the "test solution" during 2 minutes before measuring. The electrode was kept in the solutions for a short standard interval in order to obtain as small a drift in the potential as possible, and to avoid variations in the mixture composition due to the high vapour pressure of the acetonitrile. The electrode was always stored in water between measurements.

The maximum variation obtained by the above procedure was 4 to 5 mV units which means 0.08 to 0.1 units in - log $[H^+]$ (pc_H) coordinate which represents a reproducible measurement within experimental error.

Attention has been drawn to the apparent increase of the dissociation of weak acids upon ageing of the solutions in acetonitrile.[64] However, in our case we have used aqueous-acetonitrile solutions with a considerable percentage of water. Nevertheless kinetic and mV measurements were always done with "aged" solutions prepared at least two days in advance and further mV measurements did not show any alteration in these solutions.

In spite of the attempt to keep the ionic strength constant, solubility considerations prevented a high ionic strength from being achieved. Therefore, the work has been carried out without maintaining a constant ionic strength. It was always less than 3×10^{-3} $\underline{\underline{M}}$.

The calibration of the electrode was done by using solutions of CH_3CH-HCℓ ($[H_2O] = 2.22$ $\underline{\underline{M}}$) at different final concentrations and the curve was obtained from the plot of -mV versus -log $[H^+]$ fitting to a linear least square program (Table 15, Fig. 3).

After having the system settled the determination of pKw was carried out by using a procedure similar to that used by McClelland.[33] A solution of CH_3CN-NaOH with a final concentration of 1×10^{-2} $\underline{\underline{M}}$ was prepared and five measurements of the respective mV's were done. The average (551.5 mV) was fitted to the equation (Tab. 3) and yielded the pc_H (-log $[H^+]$) value of 19.79. Then, from the equation

$$pc_{H^+} + pc_{OH^-} = pKw$$

we obtained for pKw the value 21.79 considering the pc_{OH^-} of a solution 1×10^{-2} N equals 2.0.

This value of pKw (21.79) is consistent with other values of pKw in mixed-solvents from the literature.[66,67] In dioxane-water, 20-80% w/w, 45-55% w/ww and 70-30% w/w the pKw's are 14.62, 15.74 and 17.85 respectively. The same trend of increasing the value of pKw when decreasing the amount of water was also observed in our system with acetonitrile-water.

Two assumptions were made in this work with acetonitrile solutions:

First, the liquid-junction potential is constant throughout the acidity range utilized during this work.

Second, the "potentials" of the acid solutions utilized are linear functions of the acidity in the range studied.

The first assumption is one that has frequently been made in the past for other solvent systems. Thus Bates stated:

"The liquid-junction potential between the aqueous salt bridge and a mixture - aqueous solvents has a considerable magnitude but if the solvent composition is kept constant and the glass electrode is responding to the hydrogen-ion activity in the range of acidity utilized, a practical measurement of acidity is possible".[65]

In respect to the second assumption Kolthoff[68] has obtained a calibration curve for the glass electrode in CH_3CN using tetraethylammonium salts of 2,5-dichlorobenzene-sulfonic and methanesulfonic acid as buffers. A straight line was obtained from the plot of E(mV) versus pa_H which followed the equation

$$E = 59.1\ pa_H + 13.89$$

It has been claimed that hydrochloric acid is not completely dissociated in acetonitrile,[68] however in our case the solutions had a considerable amount of water (2.22 $\underline{\underline{M}}$ and 8.33 $\underline{\underline{M}}$) and there was not a strong objection to considering the hydrogen-ion activity equal the analytical acid concentration for these solutions. Nevertheless both assumptions have provided a useful approach and we have used the maximum effort to optimize our condition. Any error from omitting any electrochemical interpretation of the acidity scale was neglected and is irrelevant if we consider the object of this work which is to obtain a suitable common medium to study the kinetics of the breakdown of a series of hemiorthoesters.

Rate Determination Procedure

The kinetics experiments were carried out at 15°C ± 0.05 by following the appearance of the ester products at 205 nm. The standard procedure for the rate determinations was as

follows: 2 ml of the "buffer" was placed in the 10 mm path length cells and kept in the four cell compartment of the spectrophotometer for 20 to 30 minutes, followed by the addition of 20 µℓ of the stock solution of the precursor. The determinations were performed always by using a reference cell and, for some cases (e.g. for the hydrolysis of trimethyl and triethyl orthoformate and for the decomposition of the most stable T.I., 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane) simultaneous multiple kinetic determinations were done. The absorbance values of each individual run were obtained from the recorded curve of the variation of absorbance against time and the rate constants obtained from a linear plot of $\ell n\ (A_\infty - A_t)$ against t according to equation (32), using the least square method[69]

$$\ell n\ (A_\infty - A_t) = - k \times t + \ell n\ (A_\infty - A_o) \qquad (32)$$

$$k = \frac{1}{t}\ \ell n\ \frac{(A_\infty - A_o)}{(A_\infty - A_t)} \qquad (33)$$

The aqueous-acetonitrile buffer solutions were prepared as mentioned before and the acid solutions were prepared in boiled and degassed water at a previously determined concentration in order to obtain after preparation of the aqueous-acetonitrile buffer solutions a final concentration not exceeding 1×10^{-3} M. The stock solutions were prepared

in small quantities (300 μℓ with 20 μℓ of the substrate) just before use and the solvent used was CD_3COCD_3 in order to avoid a fast decomposition.

The chemicals utilized for preparation of the buffers were of Analar grade.

The pH-Jump Method

Some substrates, which will be mentioned later, have shown a change in the rate determining step in the base catalyzed region. That change has been observed[27] and it is assumed to occur because the first step (assuming a three step mechanism) has become slow enough to be observed, in other words, to become the rate determining one. In order to avoid this "problem" we have used the pH jump procedure[70,71] which consisted in generating the hemiorthoester in acid solution and adding a volume of base to obtain the desired pH.

The concentration of the acid solution and the volume of base to be added were previously determined. In the first experiment using this procedure (with 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in CH_3CN-H_2O, 2.22 $\underline{M}$) the amount of base added was kept constant (100 μℓ of NaOH 1×10^{-2} $\underline{M}$) in aqueous acetonitrile of the appropriate composition) and solutions of different acid concentrations were used for generating the hemiorthoester. In later experiments the amount of base added was varied and the concentration of

the acid solution utilized depended on the precursor and the pc_H required.

In most of the runs we have added 20 µℓ of the stock solution in 2 ml of the buffer but for those runs which required a large amount of base, say for example more than 100 µℓ, the amount of stock solution was increased in order to keep the percentage of stock solution as close as 1% in spite of being negligible in view of the solvent percentage already present (with acetonitrile-H_2O, 2.22 $\underline{\underline{M}}$ and 8.33 $\underline{\underline{M}}$).

In spite of the pH jump procedure being widely used for different substrates it must be clear that for ketene acetals its use was a necessity while for the acetoxy-precursors it was a useful tool. In the first case a change in the rate determining step forced us to utilize that procedure, but in the second one we have used it in order to obtain a solution less acidic than those solutions of acetic acid. The most utilized acids throughout the kinetics were, dichloroacetic, chloroacetic, formic and acetic acid.

The experiments described up to now have dealt basically with the breakdown of three hemiorthoesters: 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane, 2-hydroxy-2-methyl-1,3-dioxolane and 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane, in aqueous solution and aqueous-acetonitrile ($[H_2O]$ = 2.22 $\underline{\underline{M}}$). The efforts to follow the breakdown of three other hemiorthoesters: di-methyl hemiorthoformate, di-ethyl hemiorthoformate and 2-hydroxy-1,3-dioxolane under these conditions

were unsuccessful. However a search by NMR experiments to find other conditions to follow the breakdown of these six hemiorthoesters has been done and the most suitable solvent was found to be CH_3-CN-acid ($[H_2O]$ = 8.33 $\underline{\underline{M}}$).

That meant that a new calibration of the electrode and preparation of stock solutions were necessary and the same procedure was repeated as for CH_3CN-Acid ($[H_2O]$ = 2.22 $\underline{\underline{M}}$).

A solution of CH_3CN-HCℓ ($[H_2O]$ = 8.33 $\underline{\underline{M}}$) final acid concentration 1 x 10^{-2} N was used as reference buffer. The pH meter was adjusted to give a reading of pH 2.5 when the corresponding mV reading was -264.3 and the further measurements were related to that value.

The new calibration curve (Fig. 3) was obtained from the plot of the values on table 16. In the very same way as before we obtained for the p$\underline{K}$w for solutions of acetonitrile ($[H_2O]$ = 8.33 $\underline{\underline{M}}$) the value 20.15. The results for each of the substrates will now be given.

Table 15. Standardization of the electrode in CH_3CN-HCℓ ($[H_2O]$ = 2.22 M)

[HCℓ], M	-log $[H^+]$	-mV [a]
1×10^{-2}	2.000	289.2
7×10^{-3}	2.155	289.2
5×10^{-3}	2.301	283.0
2.5×10^{-3}	2.602	272.1
1×10^{-3}	3.000	249.9
5×10^{-4}	3.301	238.5
3×10^{-4}	3.523	222.8

a - Average of 3 to 5 values.

The plot of -log $[H^+]$ = a(-mV) + b

yielded slope = -2.20828×10^{-2} s.d. = 4.13%

int = 8.21343 s.d. = 0.22%

Table 16. Standardization of the electrode in CH_3CN-HCℓ ($[H_2O]$ = 8.33 M)

[HCℓ], M	-log $[H^+]$	-mV [a]
1×10^{-2}	2.000	264.3
7×10^{-3}	2.155	257.8
5×10^{-3}	2.301	252.3
2.5×10^{-3}	2.602	241.9
1×10^{-3}	3.000	225.3
5×10^{-4}	3.301	208.1
3×10^{-4}	3.523	197.1

a - Average of 3 values.

The plot of -log $[H^+]$ = a(-mV) + b

yielded slope = -0.022281 s.d. = 3.57%

int = 8.0649 s.d. = 2.39%

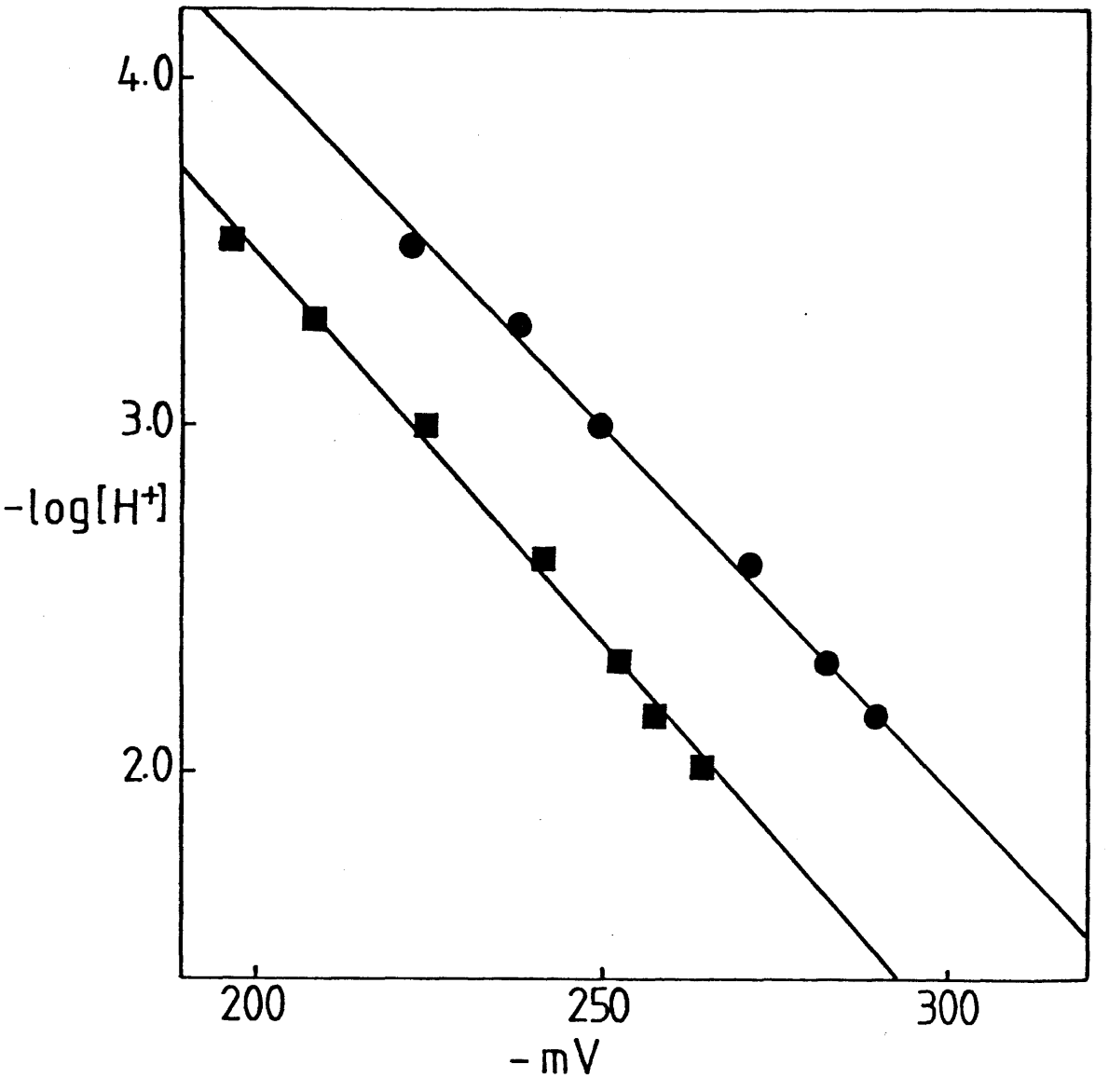


Fig. 3. Calibration curves for the electrode:

● - CH_3CN-HCℓ ($[H_2O]$ = 2.22 M)

■ - CH_3CN-HCℓ ($[H_2O]$ = 8.33 M)

Hydrolysis of 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolane.

The kinetic experiments were carried out firstly in aqueous solution, T = 15°C ± 0.05 and I = 0.1 M made up with KCℓ. The appearance of the product, monoformate of pinacol, was followed at 205 nm and the stock solution was prepared in CD_3COCD_3 with a final concentration in the cell of 5.78×10^{-3} M.

For some pH's the kinetics were done using half concentrations of substrate (2.89×10^{-3} M) and 1/4 of the concentration (1.44×10^{-3} M). The values are in the Table 17 and within experimental error they fitted to the curve of the pH profile (Fig. 4) for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane.

For the reason explained before, the hydrolysis of this precursor was followed in aqueous acetonitrile as well.

Most of the kinetics runs were done in the normal way, i.e., using solutions prepared after choosing suitable acids in order to detain the desirable pc_H. The former experiments were laborious as the pKa's of the acids were unknown in the solvent mixture, so several of the acids utilized showed quite different behaviours compared to those in aqueous solution.

Enough of these solutions were prepared for the kinetics of most of the substrates studied.

The pH jump procedure was used for both CH_3CN solutions with different $[H_2O]$. As mentioned before in solutions of CH_3CN with $[H_2O]$ = 2.22 $\underline{\underline{M}}$ the amount of base added was kept constant whereas with those having $[H_2O]$ = 8.33 $\underline{\underline{M}}$ the opposite happened. The exact amounts and concentrations are described in the tables.

Results *

The breakdown of the hemiorthoester is base and acid catalyzed and the specific catalytic constant in the computer tables were obtained from a pH-rate profile program based on equation (34) when the solvent was water and equation (35) when it was aqueous acetonitrile using a

$$\underline{k}_{obs} = \underline{k}_{o} + \underline{k}_{H^+}\, 10^{-pH} + \underline{k}_{OH^-} \times Kw/10^{-pH} \qquad (34)$$

$$\underline{k}_{obs} = \underline{k}_{o} + \underline{k}_{H^+}\, 10^{-pc_H} + \underline{k}_{OH^-} \times Kw/10^{-pc_H} \qquad (35)$$

general least square method.[69]

* Final rate constants are quoted to 3-significant figures but more significant figures are quoted for some of the intermediate values as these were used in the actual calculations in order to avoid "rounding errors".

All estimated values supplied to the pH-rate profile program were based on the values obtained from the previous plot of the equations:

$$\underline{k}_{obs} = \underline{k}_{o} + \underline{k}_{H^+} \times 10^{-pH} \quad (36)$$

$$\underline{k}_{obs} = \underline{k}_{o} + \underline{k}_{H^+} \times 10^{-pc_H} \quad (37)$$

and

$$\underline{k}_{obs} = \underline{k}_{o} + \underline{k}_{OH^-} \times Kw/10^{-pH} \quad (38)$$

or

$$\underline{k}_{obs} = \underline{k}_{o} + \underline{k}_{OH^-} \times Kw/10^{-pc_H} \quad (39)$$

respectively.

The breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane followed the equations:

$$\underline{k}(s^{-1}) = 0.191 + 2.85\times10^{2}\times10^{-pH} + 1.02\times10^{9}\times Kw/10^{-pH} \quad (40)$$

(in aqueous solution)

$$\underline{k}(s^{-1}) = 9.29\times10^{-4} + 5.86\times10^{4}\times10^{-pc_H} + 1.70\times10^{8}\times10^{-pc_{OH}} \quad (41)$$

(in CH_3CN-H_2O = 2.22 $\underline{M}$)

$$\underline{k}(s^{-1}) = 7.81\times10^{-3} + 2.04\times10^{3}\times10^{-pc_H} + 8.39\times10^{9}\times10^{-pc_{OH}} \quad (42)$$

(in CH_3CN-H_2O = 8.33 $\underline{M}$)

It is important to notice that the $\underline{k}_o$ values for several substrates show a high standard deviation. These values were recalculated, based on the kinetic equation:

$$\underline{k}_{obs} = \underline{k}_o + k_H \times C_H + \underline{k}_{OH^-} C_{OH} \qquad (43)$$

by substituting the $\underline{k}_{H^+}$ and $\underline{k}_{OH^-}$ values obtained from the computer tables and values of $\underline{k}_{obs}$, C_H and C_{OH} at the minimum of the curve. A simple comparison of the equations which follow with the respective tables will indicate which $\underline{k}_o$ values have been recalculated.

Table 17. Rate constants for the pH-profile for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in aqueous solution at 15°C, $I = 0.1$ M [a]

"Buffer"	pH	$[H^+]$ or $[A^-]$, M x 10^3	$[A^-]/[HA]$	k_{obs}, s^{-1}	(s.d.%)
HCl	2.94	1.4	-	0.5238	(3.59)
HCl	3.04	1.0	-	0.4457	(1.54)
HCl	3.26	0.5	-	0.3642	(0.72)
HCl [b]	3.38	0.5	-	0.3244	(1.25)
HCl	3.40	0.25	-	0.3122	(0.51)
HCl [c]	3.43	0.5	-	0.3171	(1.46)
-	3.52	-	-	0.2882	(2.48)
- [b]	3.73	-	-	0.2634	(3.49)
NaOAc	3.78	0.7	1:8.26	0.2690	(1.07)
"	3.89	1.0	1:5.78	0.2772	(0.23)
- [c]	3.94	-	-	0.2740	(1.02)
NaOAc	4.04	1.25	1:4.62	0.2874	(4.27)
NaOAc [b]	4.04	0.70	1:4.13	0.2554	(3.21)
NaOAc	4.39	2.50	1:2.31	0.3211	(2.28)
NaOAc [c]	4.46	0.70	1:2.06	0.3312	(1.31)
NaOAc	4.50	5.00	1:1.16	0.3336	(1.52)
NaOAc	4.62	6.00	1.04:1	0.3814	(2.65)
NaOAc [b]	4.64	2.50	1:1.16	0.3782	(1.57)
NaOAc	4.74	7.00	1.21:1	0.4665	(1.12)

Table 17 (continued)

"Buffer"	pH	$[H^+]$ or $[A^-]$, $\underline{\underline{M}} \times 10^3$	$[A^-]/[HA]$	k_{obs}, s^{-1}	(s.d.%)
NaOAc [c]	4.80	1.87	1.30:1	0.4420	(3.48)
NaOAc	4.84	9.20	1.59:1	0.5368	(1.43)
NaOAc [b]	4.86	6.0	2.08:1	0.5070	(2.58)
NaOAc	5.01	10.0	1.73:1	0.6653	(3.73)

a - Unless indicated the initial concentration of substrate and concentration of AcOH released was 5.78×10^{-3} $\underline{\underline{M}}$.

b - Initial concentration of the substrate = 2.89×10^{-3} $\underline{\underline{M}}$.

c - Initial concentration of the substrate = 1.44×10^{-3} $\underline{\underline{M}}$

Table 18. Catalytic constants for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in aqueous solution, I = 0.1M T = 15°C.

VALUE OF KW 4.49779882E-15
5 ITERATIONS USED

KO=.190771544	EST KO=.2
S.D.=8.62156637E-03	AS PERCENT 4.51931467
KH=285.445354	EST KH=280
S.D.=17.2847924	AS PERCENT 6.05537701
KOH=1.0158337E+09	EST KOH=1E+09
S.D.=27940516.5	AS PERCENT 2.75050104

PH	K	CALK	RESIDUALS
2.94	.5236	.522486111	1.31388893E-03
3.04	.4457	.45611063	-.0104106298
3.26	.3642	.355949677	8.25032313E-03
3.4	.3122	.315866236	-3.66623575E-03
3.52	.2862	.292104097	-3.90409643E-03
3.78	.269	.265674723	3.32527666E-03
3.89	.2772	.263010861	.014189119
4.04	.2874	.26690273	.0204972704
4.39	.3211	.314556057	6.54394284E-03
4.5	.3336	.344283077	-.0106830769
4.62	.3814	.388087171	-6.68717106E-03
4.74	.4665	.447051875	.0194481246
4.84	.5366	.510996131	.0258038691
5.01	.6653	.661105161	4.19481913E-03
3.38	.3244	.320725279	3.67472065E-03
3.73	.2634	.268461023	-5.06102352E-03
4.04	.2554	.26690273	-.0115027297
4.64	.3782	.396755482	-.0185554821
4.86	.507	.525707703	-.0187077029
3.43	.3171	.309122215	7.97778508E-03
3.94	.274	.263339518	.0106604818
4.8	.442	.48358094	-.04158094
4.46	.3312	.332440834	-1.24083401E-03

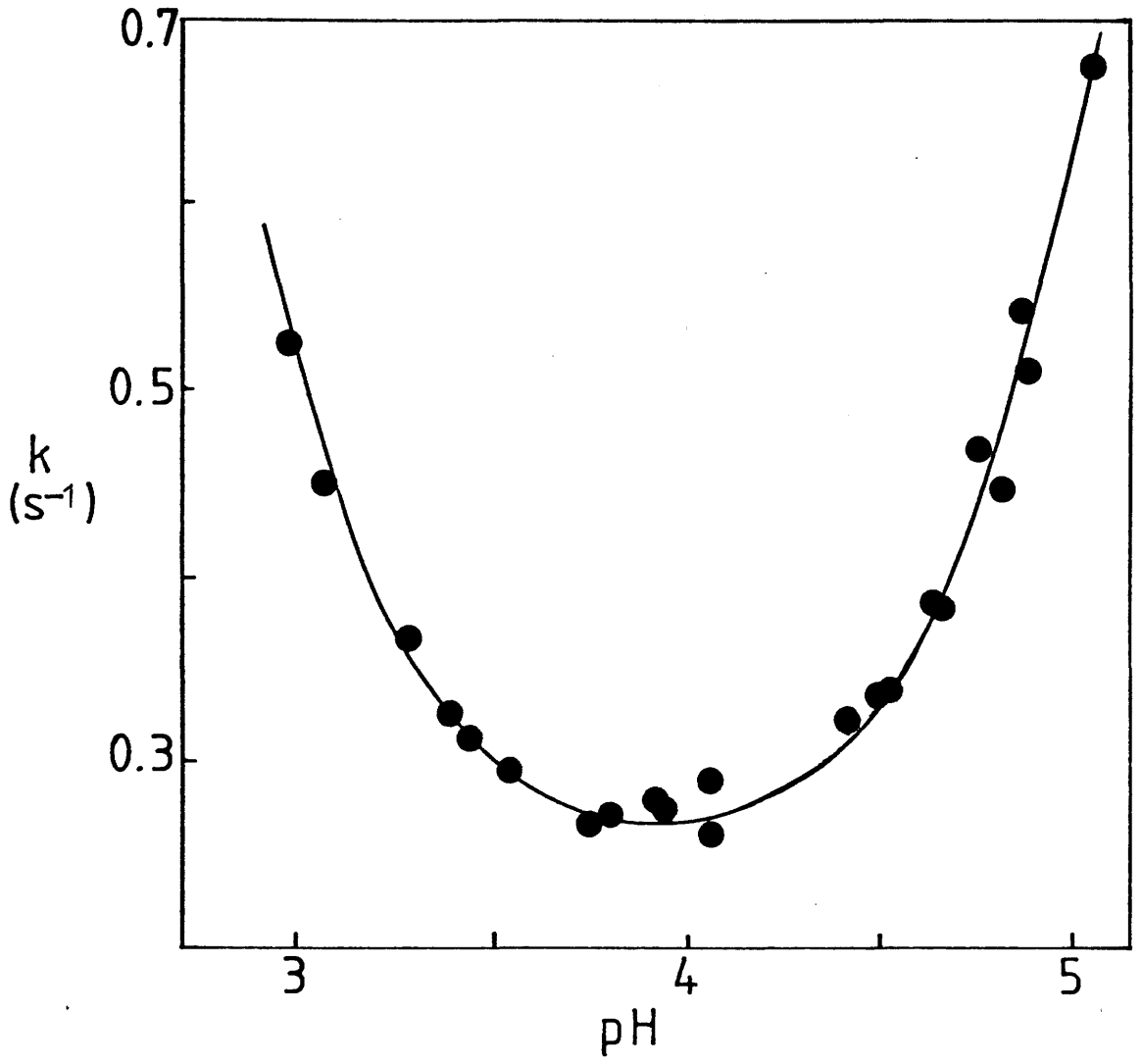


Fig. 4 . pH-rate profile for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane at 15°C, I = 0.1 M.

In Figs 4 to 14 the filled circles are the experimental values and the lines are calculated from the best values of $\underline{k}_O$, $\underline{k}_{H^+}$, and $\underline{k}_{OH^-}$ obtained by the least-squares method.

Table 19. Rate constants for the rate-profile for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in acetonitrile-acid ([H_2O] = 2.22 M) at 15°C

mV [a]	pc_H	"buffer"	[HA], M	$10^3 k_{obs}, s^{-1}$	(s.d.%)
142.5	11.23	Cl_2CHCO_2H + NaOH	3×10^{-5}+100µl (1×10^{-2})	6.116	(0.27)
130.7	10.98	"	5×10^{-5}+100µl (1×10^{-2})	3.731	(0.33)
120.2	10.78	HOAc	1×10^{-3}	2.810	(1.08)
106.4	10.47	$ClCH_2CH_2CO_2H$	5×10^{-4}	2.030	(0.58)
95.75	10.25	"	1×10^{-3}	1.548	(1.77)
87.9	10.08	HCOOH	1×10^{-3}	1.844	(0.72)
50.2	9.29	$ClCH_2CO_2H$	1×10^{-3}	1.329	(0.91)
16.8	8.59	Cl_2CHCO_2H	3×10^{-5}	1.091	(0.08)
2.55	8.29	"	5×10^{-5}	1.166	(3.42)
- 6.05	8.11	"	1×10^{-4}	1.594	(1.71)
-40.15	7.40	"	2×10^{-4}	3.514	(2.88)
-47.2	7.25	"	5×10^{-4}	4.522	(1.59)
-61.55	6.95	"	1×10^{-3}	8.806	(0.98)
-71.8	6.74	"	8×10^{-4}	11.60	(0.08)

a - Average of two to four values measured after each run.

Table 20. Catalytic constants for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 2.22 M)

VALUE OF KW 1.62181E-22
5 ITERATIONS USED

KO=1.3286515E-03	EST KO=9E-04
S.D.=2.73329452E-04	AS PERCENT 20.5719447
KH=58611.9993	EST KH=60000
S.D.=2381.53239	AS PERCENT 4.06321644
KOH=169581274	EST KOH=180000000
S.D.=18777869.8	AS PERCENT 11.0730798

PH	K	CALK	RESIDUALS
11.23	6.116E-03	5.99965231E-03	1.16347686E-04
10.98	3.731E-03	3.95576795E-03	-2.24767952E-04
10.78	2.81E-03	2.9868354E-03	-1.76835397E-04
10.47	2.029E-03	2.14230447E-03	-1.13304467E-04
10.25	1.548E-03	1.82102519E-03	-2.73025189E-04
10.08	1.844E-03	1.66418374E-03	1.7981626E-04
9.29	1.329E-03	1.41233764E-03	-8.3337638E-05
8.59	1.091E-03	1.4900074E-03	-3.99007398E-04
8.29	1.166E-03	1.63461245E-03	-4.68612454E-04
8.11	1.594E-03	1.78716853E-03	-1.93168527E-04
7.4	3.514E-03	3.66272812E-03	-1.48728122E-04
7.25	4.522E-03	4.6251356E-03	-1.03135601E-04
6.95	8.806E-03	7.90527128E-03	9.00728719E-04
6.74	.011598	.0119944334	-3.96433436E-04

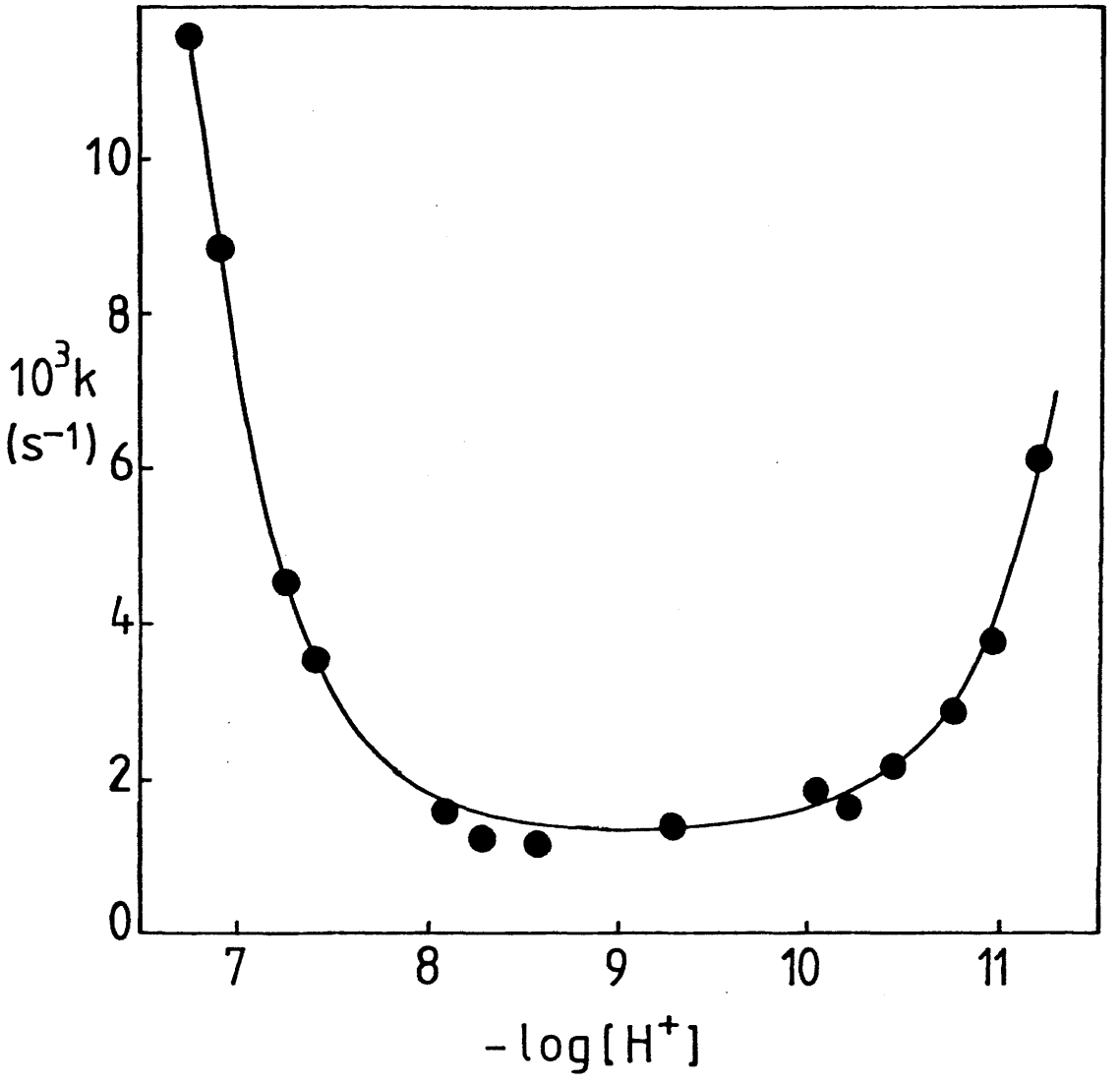


Fig. 5 . Rate-profile for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 2.22 M) at 15°C).

Table 21. Rate constants for the rate profile for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C

mV [a]	pc_H	"buffer"	[HA], M	$10^2 k_{obs}, s^{-1}$	(s.d.%)
-160.9	4.39	Cl_2CHCO_2H	1×10^{-3}	6.307	(1.48)
-150.6	4.63	"	8×10^{-4}	5.462	(1.42)
-144.2	4.77	"	6.8×10^{-4}	4.452	(0.29)
-136.3	4.96	"	6×10^{-4}	2.782	(0.99)
-123.9	5.24	"	4×10^{-4}	2.132	(1.91)
-115.6	5.43	"	3.2×10^{-4}	1.622	(0.63)
-109.2	5.57	"	2.8×10^{-4}	1.351	(4.82)
- 88.6	6.04	"	2.4×10^{-4}	0.842	(0.25)
- 60.85	6.68	"	2.0×10^{-4}	0.736	(0.03)
- 33.77	7.29	HCOOH	1×10^{-3}	0.689	(1.24)
- 26.2	7.47	HOAc	1×10^{-3}	0.604	(0.56)
- 9.6	7.84	HCOOH+NaOH	1×10^{-3} +50µl (1×10^{-2})	1.194	(1.80)
4.15	8.16	"	80µl [b]	1.562	(0.88)
11.25	8.32	"	120µl [b]	2.093	(1.46)
17.55	8.50	"	150µl [b]	2.866	(0.51)
27.9	8.70	"	200µl [b]	3.660	(0.83)
40.7	8.99	"	230µl [b]	5.150	(1.44)

a - Average of two to four values measured after each run.

b - The concentration of acid and base are the same as in the antecedent.

Table 22. Catalytic constants for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

VALUE OF KW 7.0794578E-21
5 ITERATIONS USED
KO=7.83077931E-03 EST KO=7.5E-03
S.D.=9.47750495E-04 AS PERCENT 12.1028886

KH=2034.627 EST KH=2060
S.D.=65.8668879 AS PERCENT 3.23729548

KOH=8.39311912E+09 EST KOH=8.9E+09
S.D.=491695865 AS PERCENT 5.85832106

PH	K	CALK	RESIDUALS
4.63	.05462	.0555296273	-9.09627255E-04
4.77	.04452	.0423872026	2.13279741E-03
4.96	.02782	.0301454402	-2.32544019E-03
5.24	.02132	.0195491616	1.77083838E-03
5.43	.01622	.0154061283	8.1387171E-04
5.57	.01351	.0133291249	1.80875068E-04
6.04	8.42E-03	9.75153256E-03	-1.33153256E-03
6.68	7.36E-03	8.54026908E-03	-1.18026908E-03
7.29	6.89E-03	9.09370039E-03	-2.20370039E-03
7.47	6.04E-03	9.65329253E-03	-3.61329252E-03
7.84	.01194	.0119709604	-3.09604475E-05
8.16	.01567	.0164334752	-7.63475167E-04
8.32	.02093	.0202548501	6.75149895E-04
8.5	.02866	.0266270659	2.03293413E-03
8.7	.0366	.0376147482	-1.01474821E-03

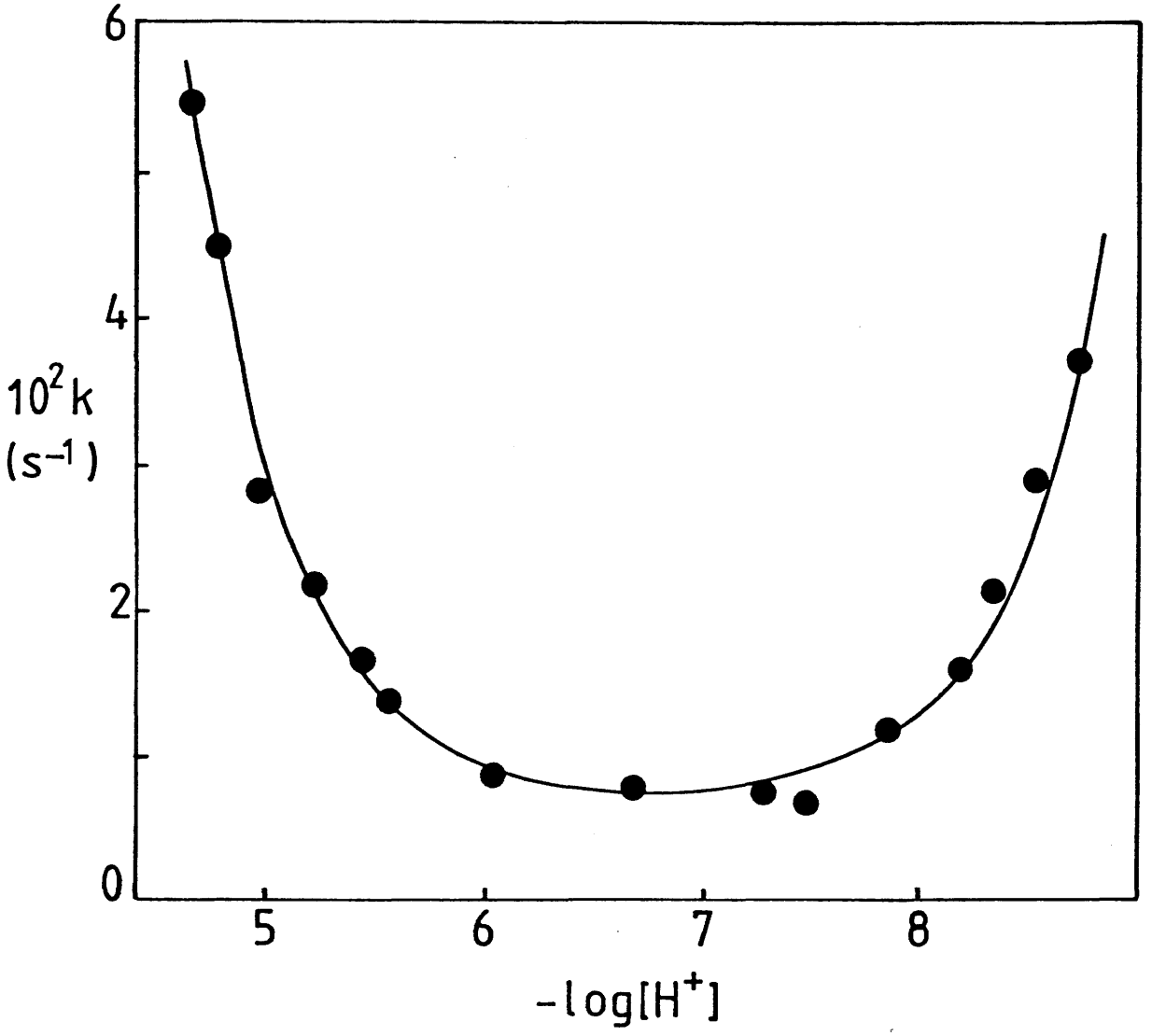


Fig. 6 . Rate profile for the breakdown of 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 $\underline{\underline{M}}$) at 15°C.

Hydrolysis of 2-methylene-1,3-dioxolane

The kinetic experiments were carried out in CH_3CN-acid ($[H_2O]$ = 2.22 M) and ($[H_2O]$ = 8.33 M) solutions. Formation of the product, monoacetate of ethylene glycol, was followed at 205 nm, T = 15°C ± 0.05°C. The mV values were measured after each run as usual and pc_H's were determined by using the equations for the respective solvent compositions.

Although we could have used the pH jump procedure for solutions with $[H_2O]$ = 2.22 M, it was not required since we had enough points in the base region to estimate the k_{-OH}-value. However that procedure was used for solutions of CH_3CN($[H_2O]$ = 8.33 M.

Some runs were done in the region where the hydration step is the rate determining in solutions of CH_3CN ($[H_2O]$ = 2.22 M), i.e., above pc_H 12.0.

These values were included in the table 23.

Results

The breakdown of the hemiorthoester 2-hydroxy-2-methyl-1,3-dioxolane followed the equations:

$$k(s^{-1}) = 9.20\times10^{-4}+2.58\times10^{5}\times10^{-pc_H}+8.99\times10^{7}\times10^{-pc_{OH}} \quad (44)$$

(in CH_3CN-H_2O, 2.22 M)

$$k(s^{-1}) = 1.53\times10^{-2}+5.50\times10^{3}\times10^{-pc_H}+1.97\times10^{10}\times10^{-pc_{OH}} \quad (45)$$

(in CH_3CN-H_2O, 8.33 M)

while the decomposition of the precursor, 2-methylene-1,3-dioxolane followed:

$$\underline{k}(s^{-1}) = 3.96 \times 10^{-3} + 9.36 \times 10^{10} \times 10^{-pc_H} \qquad (46)$$

(in CH_3CN-H_2O, 2.22 $\underline{M}$)

Table 23. Rate constants for the rate profile for the breakdown of 2-hydroxy-2-methyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 2.22 M) at 15°C

mV [a]	pc_H	"buffer"	[HA], M	$10^3 k_{obs}, s^{-1}$	(s.d.%)
171.0	11.82	HOAc	1×10^{-3}	10.43	(1.22)
169.1	11.78	$C\ell CH_2CH_2CO_2H$	6×10^{-4}	9.584	(0.04)
165.9	11.72	"	5×10^{-4}	8.361	(2.51)
134.2	11.05	HCOOH	5×10^{-4}	3.167	(2.68)
99.03	10.32	$C\ell CH_2CO_2H$	1×10^{-4}	1.109	(0.96)
90.6	10.14	HCOOH	1×10^{-3}	1.906	(1.75)
69.8	9.70	$C\ell CH_2CO_2H$	5×10^{-4}	1.783	(2.50)
54.5	9.38	$C\ell_2CHCO_2H$	3×10^{-5}	1.063	(0.34)
32.7	8.93	"	5×10^{-5}	1.306	(0.33)
- 7.06	8.09	"	1×10^{-4}	2.937	(1.27)
-34.85	7.51	"	2×10^{-4}	7.823	(2.0)
-54.35	7.10	"	5×10^{-4}	21.12	(.56)
-62.35	6.93	"	8×10^{-4}	31.54	(0.84)
-66.5	6.85	"	1×10^{-3}	37.12	(0.38)
202.2 [b]	12.48	$(CH_3)_2AsO_2H$	1×10^{-3}	33.56	(0.33)
208.3 [b]	12.60	"	7×10^{-4}	28.59	(0.87)
217.2 [b]	12.79	"	5×10^{-4}	20.21	(2.08)
226.7 [b]	12.99	HOAc	1×10^{-4}	13.75	(1.07)
258.0 [b]	13.65	$(CH_3)_2AsO_2H$	1×10^{-4}	5.01	(1.73)

a - Average of two to three runs.

b - Runs related to the hydration step of the ketene acetal (i.e. a decrease in absorbance was followed).

Table 24. Catalytic constants for the breakdown of 2-hydroxy-2-methyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 2.22 M) at 15°C)

VALUE OF KW 1.62181E-22
5 ITERATIONS USED
K0=7.88646516E-04 EST K0=9E-04
S.D.=3.23201115E-04 AS PERCENT 40.9817464

KH=258410.203 EST KH=260000
S.D.=2952.52727 AS PERCENT 1.1425738

KOH=89932501.9 EST KOH=86000000
S.D.=4335383 AS PERCENT 4.82070765

PH	K	CALK	RESIDUALS
11.82	.01043	.0104254779	4.52213863E-06
11.78	9.584E-03	9.57761333E-03	6.38667188E-06
11.72	8.361E-03	8.44363544E-03	-8.26354444E-05
11.05	3.167E-03	2.42745195E-03	7.3954805E-04
10.32	1.109E-03	1.1057458E-03	3.25419614E-06
10.14	1.906E-03	1.00870045E-03	8.97299546E-04
9.7	1.783E-03	9.13306006E-04	8.69693993E-04
9.38	1.063E-03	9.31357621E-04	1.31642379E-04
8.93	1.306E-03	1.10466618E-03	2.01333819E-04
8.09	2.937E-03	2.89087795E-03	4.61220488E-05
7.51	7.823E-03	8.7747574E-03	-9.517574E-04
7.1	.02112	.0213150827	-1.95082685E-04
6.93	.03154	.0311493228	3.9067716E-04
6.85	.03712	.037290162	-1.7016202E-04

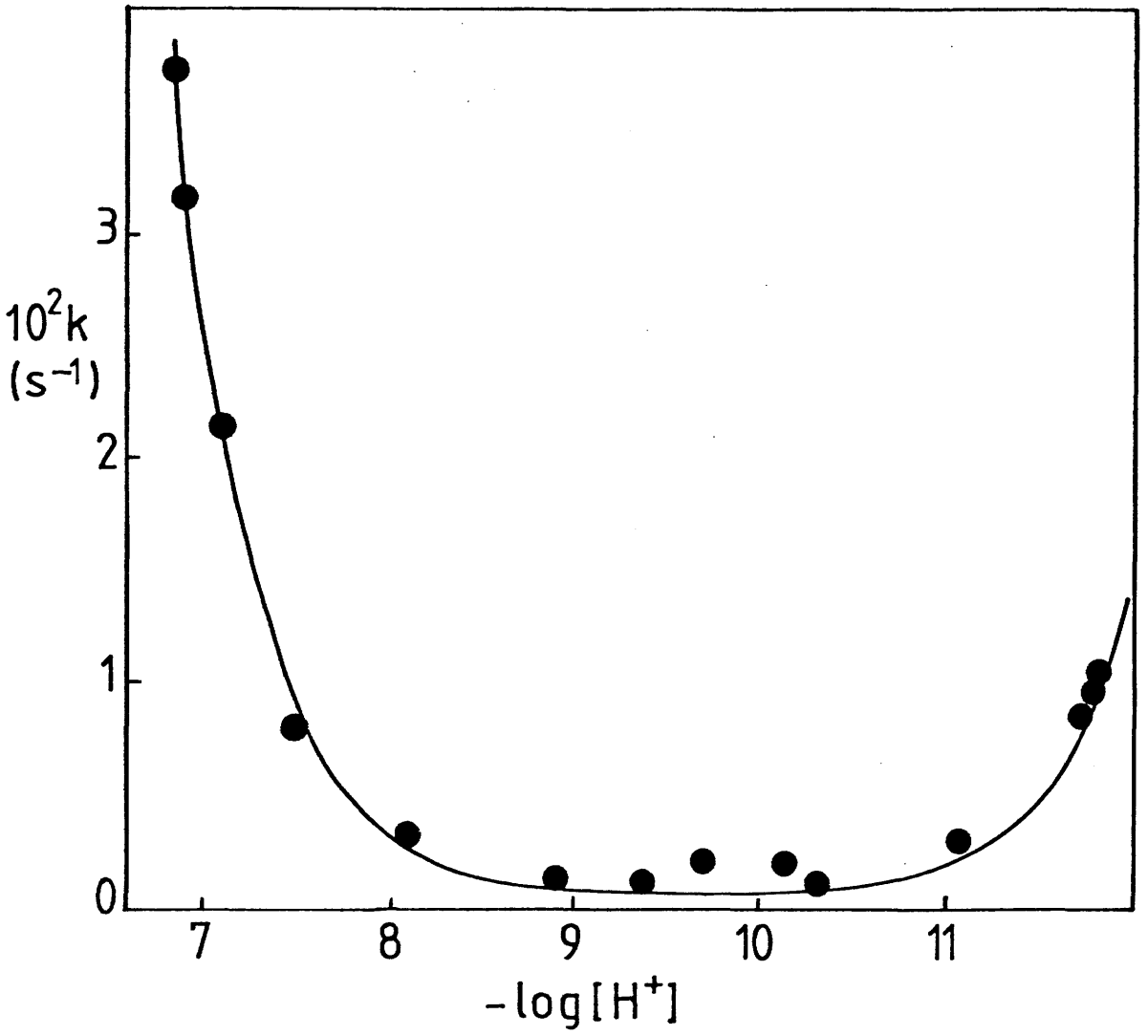


Fig. 7 . Rate-profile for the breakdown of 2-hydroxy-2-methyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 2.22 M) at 15°C.

Table 25. Rate constants for the breakdown of 2-hydroxy-2-methyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

mV [a]	pc_H	"buffer"	[HA], M	$10^2 k_{obs}, s^{-1}$	(s.d.%)
-151.2	4.61	Cl_2CHCO_2H	8×10^{-4}	14.926	(1.55)
-143.6	4.79	"	6.8×10^{-4}	10.335	(1.04)
-135.2	4.98	"	6×10^{-4}	7.735	(0.09)
-122.1	5.28	"	4×10^{-4}	5.150	(1.60)
-110.7	5.54	"	3.2×10^{-4}	3.483	(1.73)
- 99.3	5.80	"	2.8×10^{-4}	2.658	(5.39)
- 76.85	6.31	"	2.4×10^{-4}	1.500	(1.63)
- 69.1	6.49	HCOOH	1×10^{-3}	1.029	(3.39)
- 55.3	6.80	"	8×10^{-4}	0.841	(0.95)
- 51.6	6.89	"	7×10^{-4}	0.771	(0.89)
- 48.0	6.97	"	6×10^{-4}	0.712	(2.08)
- 38.75	7.18	"	4×10^{-4}	0.776	(0.81)
- 30.5	7.37	"	2×10^{-4}	0.943	(1.14)
- 4.8	7.96	HCOOH+NaOH	1×10^{-3} + 50 µl (1×10^{-2})	2.333	(1.29)
13.4	8.37	"	70 µl [b]	4.428	(1.12)
14.9	8.52	"	80 µl [b]	6.418	(2.45)

a - Average of two to three values.

b - Acid and base concentrations are the same as in the antecedent.

Table 26. Rate constants for the breakdown of 2-hydroxy-2-methyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

VALUE OF KW 7.0794578E-21
5 ITERATIONS USED

K0=.0153080769	EST K0=.02
S.D.=2.38362564E-03	AS PERCENT 15.5710326
KH=5502.17658	EST KH=4900
S.D.=153.393768	AS PERCENT 2.78787433
KOH=1.97432965E+10	EST KOH=2.6E+10
S.D.=1.87095568E+09	AS PERCENT 9.47640978

PH	K	CALK	RESIDUALS
4.61	.14926	.150376192	-1.11619232E-03
4.79	.10335	.104551552	-1.20155173E-03
4.98	.07735	.0729362876	4.41371242E-03
5.28	.0515	.0442105436	7.28945643E-03
5.54	.03483	.0312249918	3.60500823E-03
5.8	.02658	.0241166293	2.46337071E-03
6.31	.015	.0182883039	-3.28830393E-03
6.49	.01029	.0175204826	-7.23048259E-03
6.8	8.42E-03	.0170620137	-8.64201375E-03
6.89	7.71E-03	.0171018693	-9.39186934E-03
6.97	7.11E-03	.0172020723	-.0100920723
7.18	7.76E-03	.0177871344	-.0100271344
7.37	9.43E-03	.01881936	-9.38935999E-03
7.96	.02333	.0281157494	-4.78574945E-03
8.37	.04428	.048097263	-3.81726303E-03
8.52	.06418	.061607496	2.57250402E-03

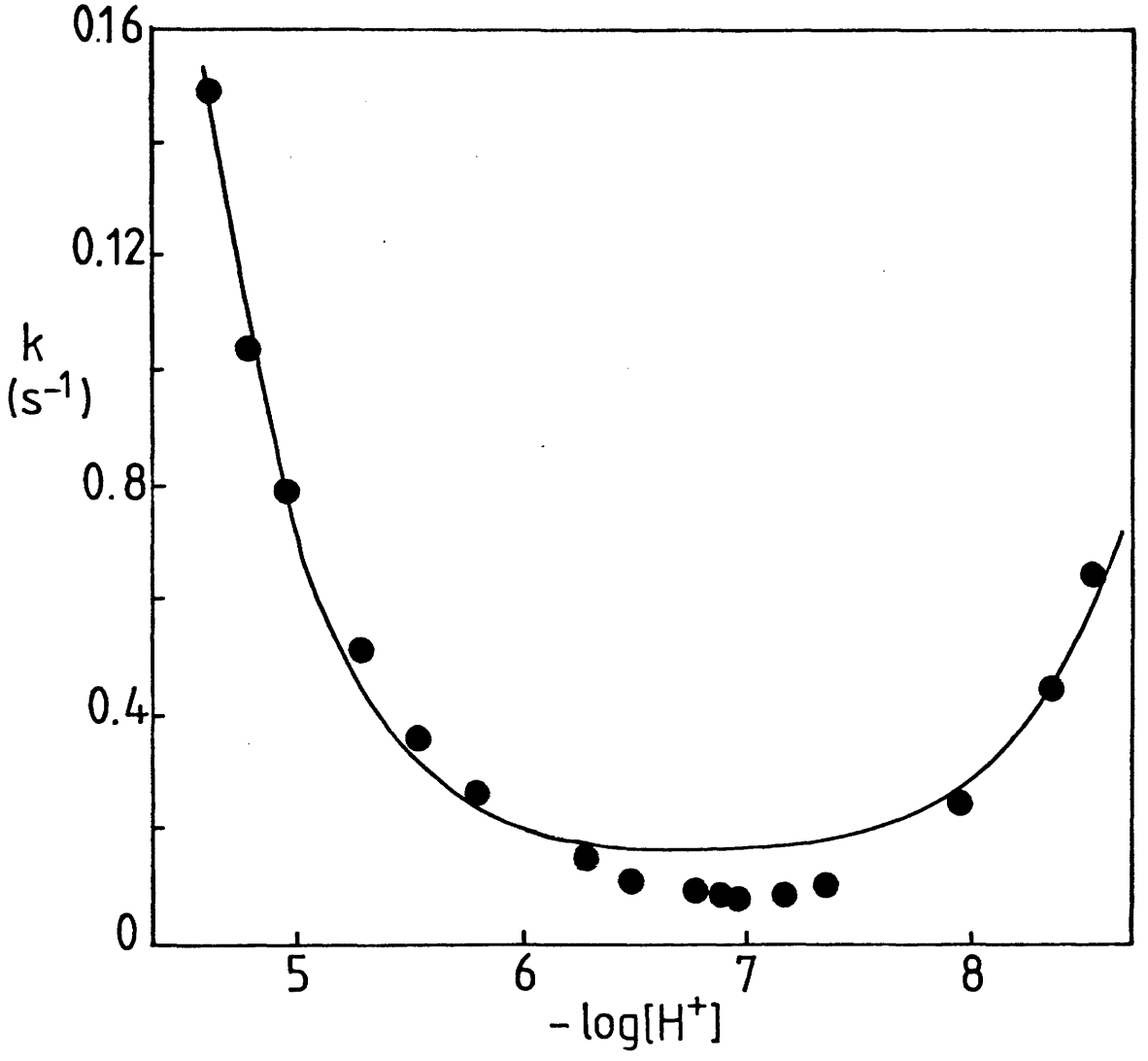


Fig. 8 . Rate profile for the breakdown of 2-hydroxy-2-methyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

Hydrolysis of 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane

The hemiorthoester generated from this precursor was studied in total aqueous solution keeping the ionic strength 0.1 M made up with KCℓ and in aqueous-acetonitrile solutions ($[H_2O]$ = 2.22 M) and ($[H_2O]$ = 8.33 M) respectively. For these three conditions the procedure used was that described when using 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolane as precursor.

In aqueous and acetonitrile solutions ($[H_2O]$ = 2.22 M) some runs were done in the region where the hydration of the ketene acetal was the rate determining step. These values were fitted to the equations 36 and 37 by a linear least square program and the k_{H^+} and k_O values are in the Result Section.

Results

The breakdown of the hemiorthoester 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane followed the equations:

$$\underline{k}(s^{-1}) = 1.80\times10^{-2}+2.92\times10^{+1}\times10^{-pH}+2.87\times10^{6}\times10^{-pOH} \quad (47)$$

(in aqueous solution)

$$\underline{k}(s^{-1}) = 1.21\times10^{-4}+1.24\times10^{4}\times10^{-pc_H}+3.72\times10^{5}\times10^{-pc_{OH}} \quad (48)$$

(in CH_3CN-H_2O, 2.22 M)

$$\underline{k}(s^{-1}) = 5.604\times10^{-4}+3.10\times10^{2}\times10^{-pc_H}+3.95\times10^{6}\times10^{-pc_{OH}} \quad (49)$$

(in CH_3CN-H_2O, 8.33 M)

The decomposition of the precursor 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane followed the equations:

$$\underline{k}(s^{-1}) = 9.11 \times 10^{-2} + 1.58 \times 10^{7} \times 10^{-pH} \quad (50)$$

(in aqueous solution)

$$\underline{k}(s^{-1}) = 4.3 \times 10^{-3} + 1.71 \times 10^{11} \times 10^{-pc_H} \quad (51)$$

(in CH_3CN-H_2O, 2.22 $\underline{M}$)

Table 27. Rate constants for the pH-rate profile for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in aqueous solution at 15°C, I = 0.1 M

"Buffer"	pH	10^3[HA], M	$[A^-]/[HA]$	$10^2 k_{obs}$, s^{-1}	(s.d.%)
HCℓ	2.19	10.0	-	20.43	(6.57)
"	2.23	8.0	-	19.11	(1.44)
"	2.47	5.0	-	11.92	(0.66)
"	2.60	3.0	-	8.980	(0.79)
"	3.02	1.4	-	4.961	(0.03)
"	3.15	1.0	-	4.020	(0.40)
"	3.87	0.25	-	2.177	(0.31)
Acetate	4.31	4.0	1:2	1.839	(1.96)
"	4.60	2.0	1:1	1.860	(1.01)
"	4.85	2.0	2:1	1.885	(0.96)
"	5.18	2.0	4:1	1.960	(0.96)
Cacodylate	5.49	4.0	1:4	2.180	(0.48)
"	5.78	2.0	1:2	2.350	(2.44)
"	6.06	1.0	1:1	3.040	(0.62)
"	6.36	1.0	2:1	4.450	(0.33)
"	6.59	1.0	4:1	6.660	(2.60)
"	6.74	1.0	6:1	9.060	(2.49)
Tris-HCℓ [a]	7.69	4.0	1:4	41.02	(1.22)
" [a]	8.33	1.0	1:1	18.28	(2.18)
" [a]	9.11	1.0	6:1	11.21	(3.22)
NaOH [a]	11.68	5.0 [b]	-	6.92	(0.81)

a - The hydration was the rate determining step.

b - Concentration of NaOH.

Table 28. Catalytic constants for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in aqueous solution, I = 0.1 M, T = 15°C.

VALUE OF KW 4.49779882E-15
5 ITERATIONS USED

K0=.0180210439	EST K0=.02
S.D.=1.08773813E-03	AS PERCENT 6.03593296
KH=29.1496364	EST KH=30
S.D.=.247282617	AS PERCENT .848321444
KOH=2867464.04	EST KOH=3000000
S.D.=83712.7225	AS PERCENT 2.91939921

PH	K	CALK	RESIDUALS
2.19	.2043	.206228903	-1.9289034E-03
2.23	.1911	.18966902	1.4309797E-03
2.47	.1192	.11679669	2.40330963E-03
2.6	.0898	.0912467553	-1.44675528E-03
3.02	.0496	.0458722359	3.72776407E-03
3.15	.0402	.0386756242	1.5243758E-03
3.87	.0218	.0220488305	-2.48830525E-04
4.31	.0184	.0197120599	-1.31205995E-03
4.6	.0186	.0192666995	-6.66699467E-04
4.85	.0188	.0193458507	-5.45850679E-04
5.18	.0196	.0201657154	-5.65715367E-04
5.49	.0218	.0221010096	-3.01009612E-04
5.78	.0235	.0258407976	-2.34079759E-03
6.06	.0304	.0328544864	-2.45448637E-03
6.36	.0445	.0475797207	-3.07972071E-03
6.59	.0666	.0682047629	-1.60476289E-03
6.74	.0906	.0889021519	1.69784811E-03

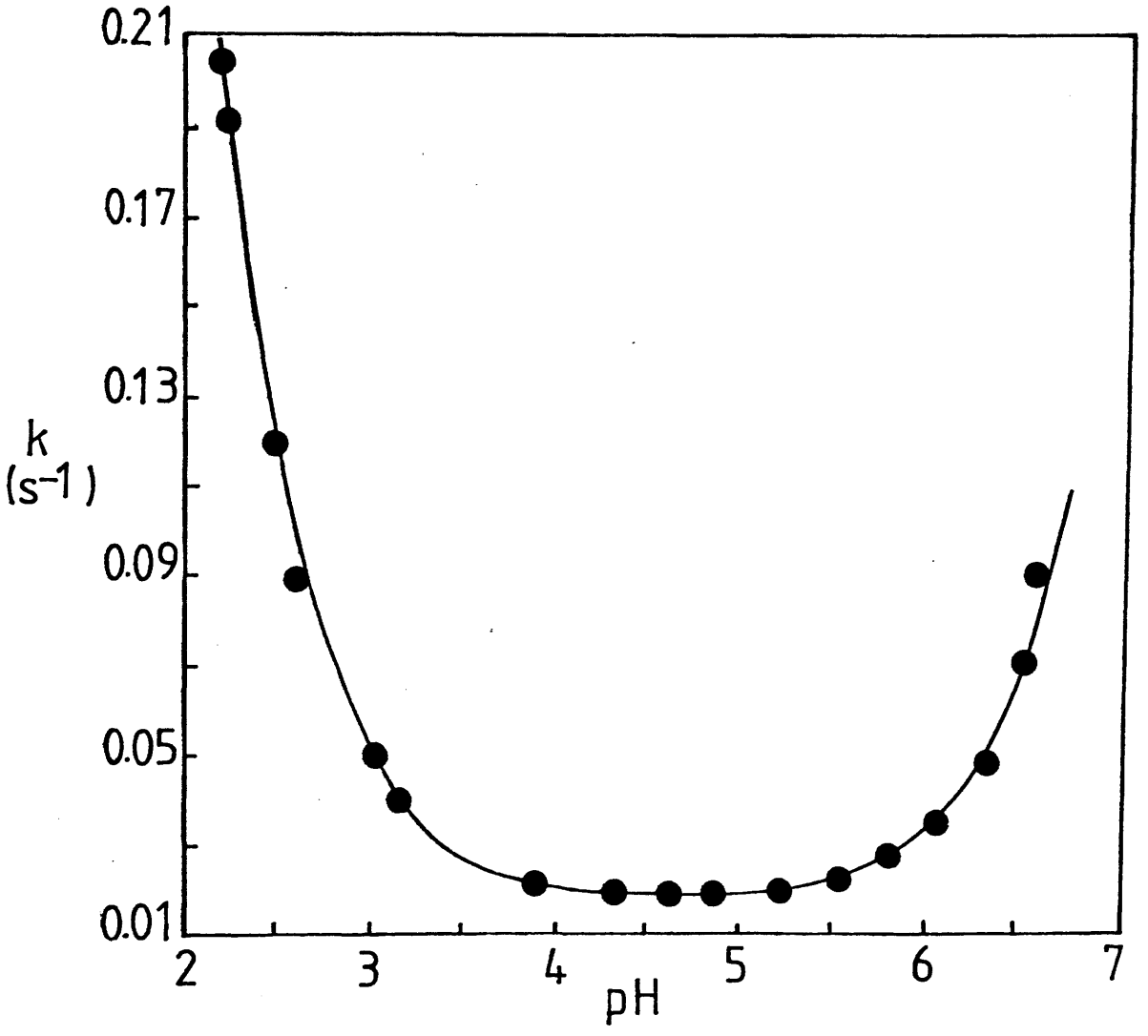


Fig. 9 . pH-rate profile for the breakdown of 2-hydroxy-2,4,4, 5,5-pentamethyl-1,3-dioxolane at 15°C, I = 0.1 M.

Table 29. Rate constants for the rate-profile for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 2.22 M) at 15°C.

mV [a]	pc_H	"Buffer"	[HA], M	$10^4 k_{obs}, s^{-1}$	(s.d.%)
- 73.3	6.71	Cl_2CHCO_2H	8×10^{-4}	25.232	(1.04)
- 66.5	6.85	"	1×10^{-3}	18.551	(0.44)
- 64.1	6.90	"	3×10^{-4}	15.298	(1.50)
- 54.35	7.10	"	5×10^{-4}	9.556	(1.63)
- 38.4	7.44	"	2×10^{-4}	5.804	(6.95)
15.5	8.57	"	5×10^{-5}	1.232	(0.19)
29.3	8.86	"	1×10^{-4}	1.252	(1.63)
76.2	9.84	Cl_2CHCO_2H + NaOH	1×10^{-4} +20µl (1×10^{-2})	1.233	(1.84)
124.1	10.84	"	30µl [b]	1.457	(1.42)
180.7	12.03	"	50µl [b]	2.289	(1.08)
205.9	12.55	"	80µl [b]	3.246	(0.35)
215	12.74	"	100µl [b]	4.418	(0.04)
232.2	13.10	"	150µl [b]	8.117	(0.58)
204.2 [c]	12.52	$(CH_3)_2AsO_2H$	1×10^{-3}	5.571×10^{-2}	(0.82)
211.8 [c]	12.68	"	7×10^{-4}	4.101×10^{-2}	(0.02)
217.1 [c]	12.79	"	5×10^{-4}	3.124×10^{-2}	(0.30)
260.1 [c]	13.69	"	1×10^{-4}	0.693×10^{-2}	(0.80)
330.1 [c]	15.16	NaOH	2.5×10^{-3}	0.533×10^{-2}	(3.82)

Table 29 (continued)

a - Average of two to three values.

b - Acid and base concentrations are the same as the antecedent.

c - Runs when hydration step was the rate-determining. The magnitudes of the rate constants are different from the antecedent.

Table 30. Rate constants for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 2.22 M) at 15°C.

VALUE OF KW 1.62181E-22
5 ITERATIONS USED

KO=6.83410279E-05	EST KO=1.5E-04
S.D.=5.13163659E-05	AS PERCENT 75.0886656
KH=12413.2531	EST KH=12000
S.D.=367.68504	AS PERCENT 2.96203612
KOH=372397.527	EST KOH=330000
S.D.=46204.4427	AS PERCENT 12.4072904

PH	K	CALK	RESIDUALS
6.71	2.5232E-03	2.48873285E-03	3.44671489E-05
6.85	1.8551E-03	1.8217601E-03	3.33398971E-05
6.9	1.5298E-03	1.63107752E-03	-1.01277519E-04
7.1	9.556E-04	1.05436155E-03	-9.87615545E-05
7.44	5.804E-04	5.1904068E-04	6.13593199E-05
8.57	1.232E-04	1.01774171E-04	2.14258292E-05
8.86	1.252E-04	8.55198406E-05	3.96801594E-05
9.84	1.233E-04	7.05531258E-05	5.27468742E-05
10.84	1.457E-04	7.26988226E-05	7.30011774E-05
12.03	2.289E-04	1.33067879E-04	9.58321206E-05
12.55	3.246E-04	2.82636914E-04	4.19630861E-05
12.74	4.418E-04	4.00242899E-04	4.15571012E-05
13.1	8.117E-04	8.28680097E-04	-1.69800967E-05

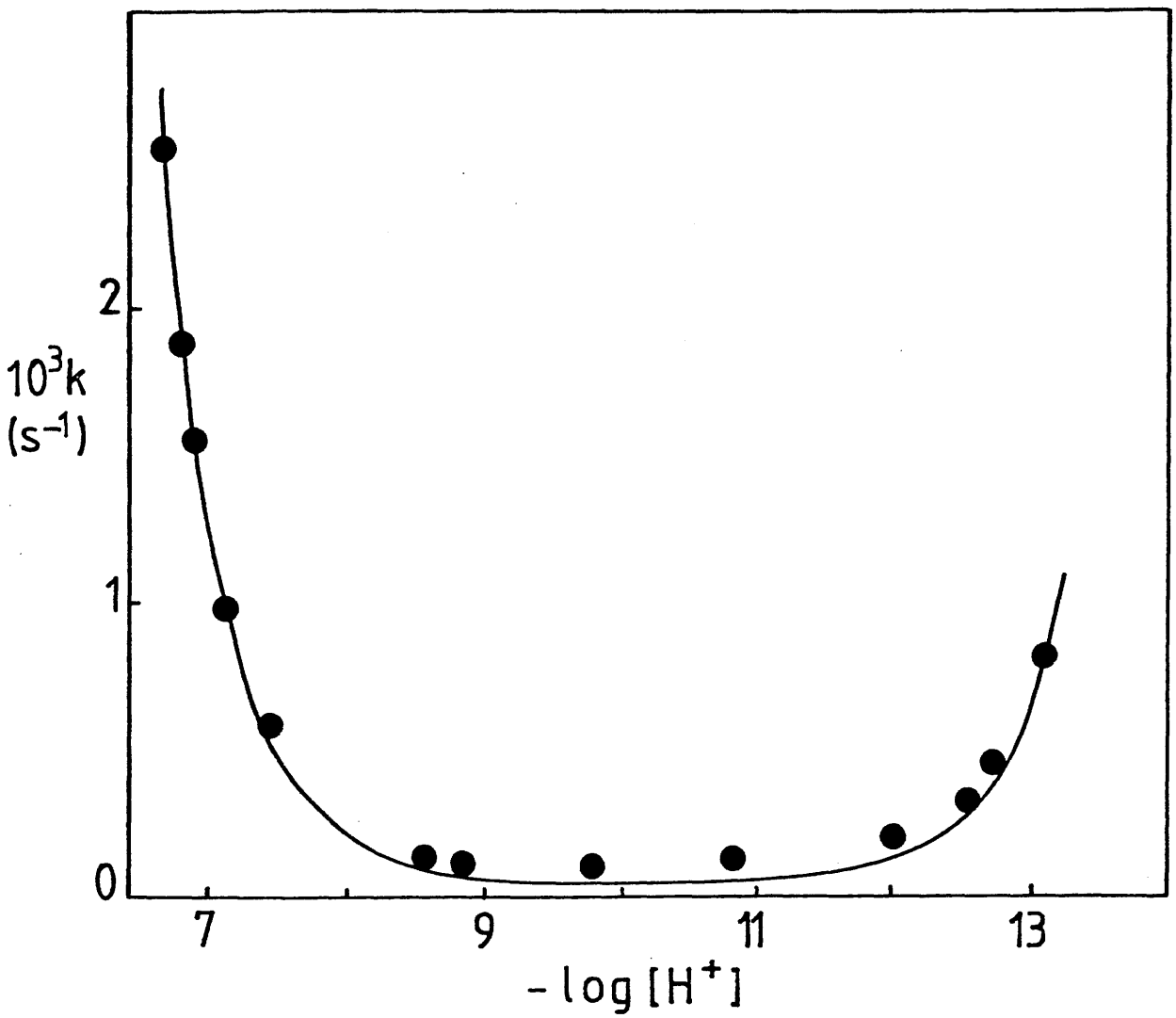


Fig. 10. Rate-profile for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in CH_3CH-acid ($[H_2O]$ = 2.22 M) at 15°C.

Table 31. Rate constants for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C

mV [a]	pc_H	"Buffer"	[HA], M	$10^3 k_{obs}, s^{-1}$	(s.d.%)
-169.7	4.19	Cl_2CHCO_2H	1×10^{-3}	20.40	(1.18)
-162.9	4.35	"	9×10^{-4}	17.72	(1.70)
-151.3	4.61	"	8×10^{-4}	8.025	(0.15)
-142.7	4.81	"	7×10^{-4}	4.931	(2.02)
-140.7	4.85	"	6.8×10^{-4}	4.910	(0.74)
-134.8	4.99	"	6×10^{-4}	4.605	(4.21)
-132.1	5.05	"	2×10^{-4}	3.317	(0.98)
-113.5	5.47	"	4×10^{-4}	2.586	(0.18)
-111.9	5.51	"	1×10^{-4}	3.054	(1.11)
- 63.7	6.61	HCOOH	1×10^{-3}	0.947	(0.33)
- 41.5	7.12	HCOOH+NaOH	1×10^{-3}+20µℓ (1×10^{-2})	0.374	(0.31
15.4	8.42	"	200µℓ [b]	0.569	(0.03)
64.8	9.54	"	1×10^{-3}+250µℓ (1×10^{-2})	0.746	(0.92
81.9	9.93	"	300µℓ [b]	1.809	(0.25)
93.5	10.20	"	320µℓ [b]	2.344	(1.82)
112.6	10.63	"	340µℓ [b]	3.241	(1.60)
134.9	11.14	"	360µℓ [b]	5.858	(0.35)
154.0	11.58	"	400µℓ [b]	12.02	(1.04)

a - Average of two to three values.

b - Acid and base concentrations are the same as the antecedent.

Table 32. Catalytic constants for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

VALUE OF KW 7.0794578E-21
5 ITERATIONS USED

K0=1.49489934E-03	EST K0=1.9E-03
S.D.=6.33653187E-04	AS PERCENT 42.3876825
KH=310.090672	EST KH=316
S.D.=15.9036978	AS PERCENT 5.12872501
KOH=3950799.45	EST KOH=3800000
S.D.=449787.78	AS PERCENT 11.3847282

PH	K	CALK	RESIDUALS
4.19	.0204	.0215160354	-1.11603539E-03
4.35	.01772	.0153461417	2.37385828E-03
4.61	8.025E-03	9.10672399E-03	-1.08172399E-03
4.81	4.931E-03	6.29763711E-03	-1.36663711E-03
4.85	4.91E-03	5.87504856E-03	-9.65048563E-04
4.99	4.605E-03	4.66803824E-03	-6.30382438E-05
5.05	3.317E-03	4.25858855E-03	-9.41588546E-04
5.47	2.586E-03	2.54563174E-03	4.03682652E-05
5.51	3.054E-03	2.4531802E-03	6.00819802E-04
6.61	9.47E-04	1.57113152E-03	-6.2413152E-04
7.12	3.74E-04	1.51879084E-03	-1.14479084E-03
8.42	5.69E-04	1.50343501E-03	-9.34435007E-04
9.54	7.46E-04	1.5919694E-03	-8.45969396E-04
9.93	1.809E-03	1.73299497E-03	7.60050257E-05
10.2	2.344E-03	1.93820588E-03	4.05794122E-04
10.63	3.241E-03	2.68802893E-03	5.52971072E-04
11.14	5.858E-03	5.3557697E-03	5.02230301E-04
11.58	.01202	.0121286139	-1.08613942E-04

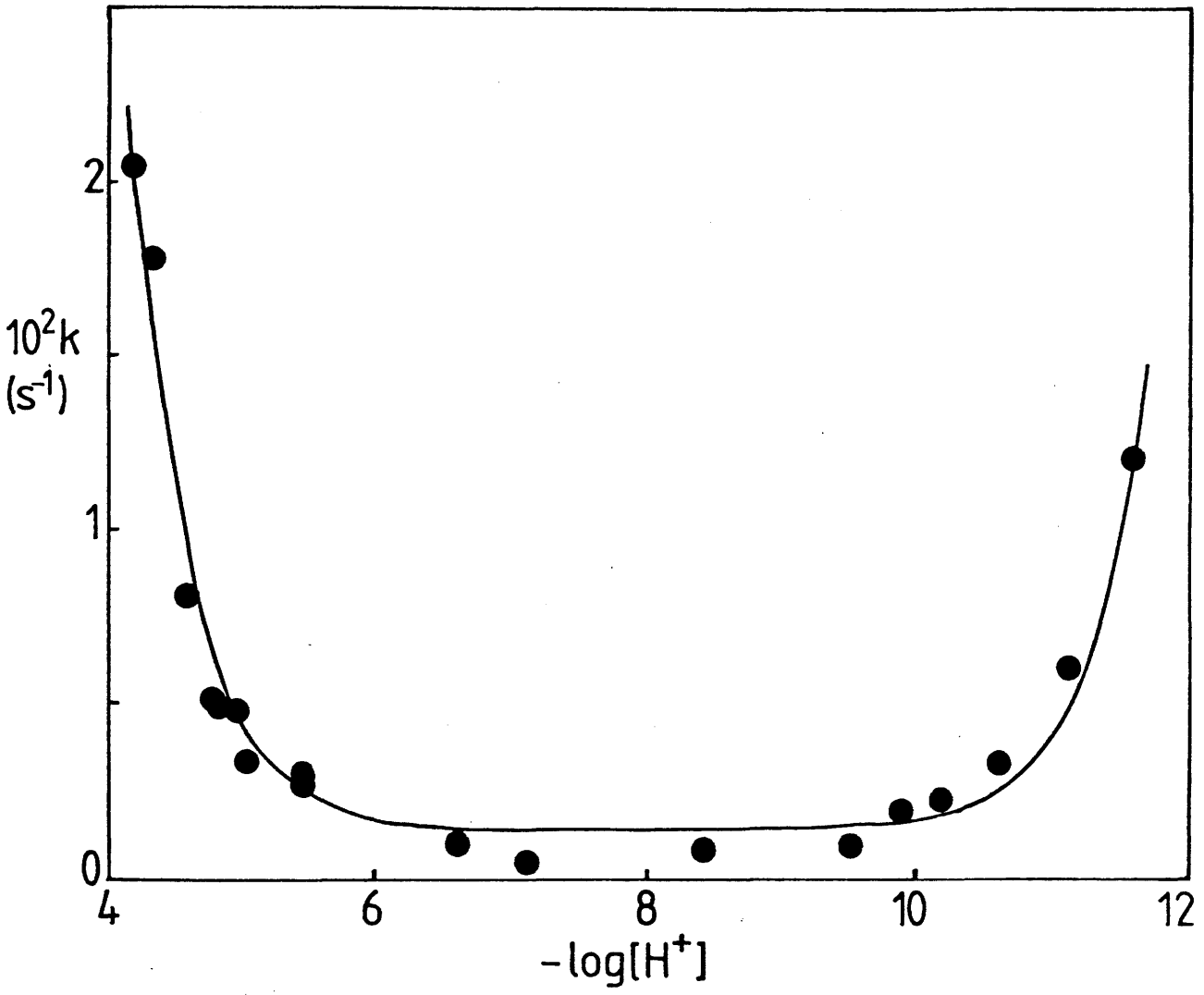


Fig. 11. Rate-profile for the breakdown of 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

Hydrolysis of acetoxy-dimethoxy-methane

The breakdown of dimethyl hemiortoformate was studied only in solutions of acetonitrile ($[H_2O]$ = 8.33 M). The appearance of the product, methyl formate, was followed at 205 nm, T = 15°C ± 0.05.

Part of the rate constants in the base catalyzed region were obtained by the pH jump procedure and the values are summarized on the next tables.

Results

The rate profile for breakdown of dimethyl hemiorthoformate which is acid and base catalyzed, follows the equation:

$$k(s^{-1}) = 2.57\times10^{-2} + 2.40\times10^{5}\times10^{-pc_H} + 3.21\times10^{10}\times10^{-pc_{OH}} \quad (52)$$

(in CH_3CN-H_2O, 8.33 M)

The rate constants are summarized on the next tables.

Table 33. Rate constants for the breakdown of dimethyl hemiortho-formate in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

mV [a]	pc_H	"Buffer"	[HA], M	$10^2 k_{obs}, s^{-1}$	(s.d.%)
-85.8	6.11	$Cl CHCO_2H$	1×10^{-4}	21.521	(3.30)
-77.1	6.30	"	9×10^{-5}	14.366	(0.50)
-72.0	6.42	HCOOH	1×10^{-3}	10.94	(0.26)
-63.2	6.62	Cl_2CHCO_2H	7×10^{-5}	9.142	(1.30)
-53.6	6.84	HCOOH	9×10^{-4}	5.408	(0.30)
-49.4	6.94	"	8×10^{-4}	4.929	(1.56)
-40.2	7.15	"	6×10^{-4}	4.173	(0.12)
-33.35	7.30	"	4×10^{-4}	3.815	(2.43)
-25.8	7.48	"	2×10^{-4}	4.211	(2.11)
- 8.6	7.87	HCOOH+NaOH	4×10^{-4} 50µl (1×10^{-2})	5.182	(1.21)
- 3.45	7.99	"	70µl [b]	6.242	(3.48)
9.35	8.28	"	100µl [b]	7.124	(0.84)
14.0	8.38	"	4×10^{-4} +120µl (1×10^{-2})	8.469	(2.30)
19.55	8.51	"	150µl [b]	9.845	(4.42)
23.5	8.60	"	170µl [b]	11.43	(4.08)

a - Average of two to three values.

b - Acid and base concentrations are the same as in the antecedent.

Table 34. Rate constants for the breakdown of dimethyl hemiorthoformate in CH_3CN-acid [(H_2O] = 8.33 M) at 15°C.

VALUE OF KW 7.0794578E-21
5 ITERATIONS USED

KO=.0256639358	EST KO=.03
S.D.=3.417284E-03	AS PERCENT 13.3155102
KH=239941.554	EST KH=250000
S.D.=7332.35389	AS PERCENT 3.05589164
KOH=3.21405627E+10	EST KOH=2.7E+10
S.D.=2.10290221E+09	AS PERCENT 6.54282948

PH	K	CALK	RESIDUALS
6.11	.2152	.212211005	2.98899488E-03
6.3	.1437	.14637358	-2.67357967E-03
6.42	.1094	.117485658	-8.08565819E-03
6.62	.0914	.0841704424	7.22955764E-03
6.84	.0541	.0619202198	-7.82021983E-03
6.94	.0493	.0551946838	-5.89468383E-03
7.15	.0417	.0458645536	-4.16455358E-03
7.3	.0381	.0422294755	-4.12947551E-03
7.48	.0421	.0404806779	1.61932214E-03
7.87	.0518	.0457682649	6.03173512E-03
7.99	.0624	.0503550769	.0120449231
8.28	.0712	.0702795917	9.20408289E-04
8.38	.0847	.0812466837	3.45331631E-03
8.51	.0984	.100035198	-1.63519851E-03
8.6	.1143	.116851052	-2.55105205E-03

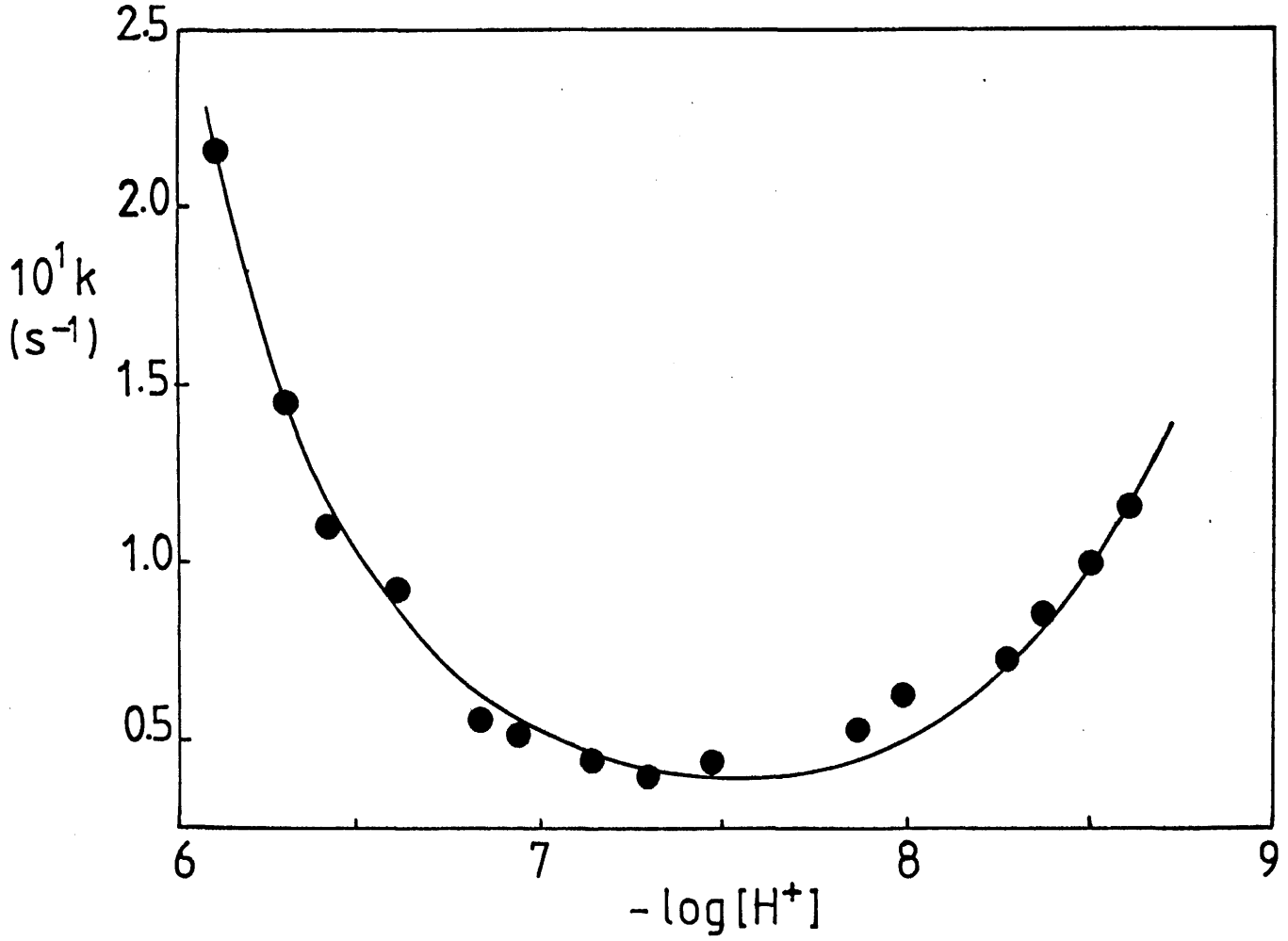


Fig. 12. Rate profile for the breakdown of dimethyl hemiorthoformate in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

Hydrolysis of acetoxy-diethoxy-methane

The breakdown of diethyl hemiorthoformate was studied in solutions of acetonitrile ($[H_2O]$ = 8.33 M with the product, ethyl formate, being followed at 205 nm, T = 15°C ± 0.05.

Results

The rate profile for this intermediate followed the equation:

$$k(s^{-1}) = 4.36\times10^{-2}+1.86\times10^{5}\times10^{-pc_H}+6.53\times10^{9}\times10^{-pc_{OH}} \quad (53)$$

The rate constants are on the next tables.

Table 35. Rate constants for the breakdown of diethyl hemiorthoformate in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

mV [a]	pc_H	"Buffer"	[HA], M	$10^2 k_{obs}$, s^{-1}	(s.d.%)
-59.45	6.71	Cl_2CHCO_2H	7×10^{-5}	8.350	(0.15)
-49.7	6.93	"	6×10^{-5}	6.267	(1.08)
-45.4	7.03	HCOOH	8×10^{-4}	6.019	(1.89)
-43.0	7.08	Cl_2CHCO_2H	5×10^{-5}	5.839	(1.69)
-36.9	7.22	HCOOH	6×10^{-4}	5.291	(2.33)
-35.3	7.26	"	4×10^{-4}	5.059	(1.56)
-21.5	7.57	"	1×10^{-4}	5.093	(0.69)
- 6.0	7.93	HCOOH+NaOH	4×10^{-4} +100µl (1×10^{-2})	5.324	(2.38)
5.8	8.20	"	150µl [b]	5.264	(0.66)
14.4	8.39	"	200µl [b]	5.723	(1.09)
17.5	8.46	"	250µl [b]	5.926	(0.67)
26.25	8.66	"	300µl [b]	6.831	(1.25)
36.5	8.90	"	400µl [b]	7.685	(0.31)
38.85	8.95	"	450µl [b]	8.585	(0.12)

a - Average of two to three values.

b - Acid and base concentration are the same as in the antecedent.

Table 36. Rate constants for the breakdown of diethyl hemiorthoformate in CH_3CN-acid ($[H_2O]$ = 8.33 M at 15°C.

VALUE OF KW 7.0794578E-21
5 ITERATIONS USED

KO=.0436163105	EST KO=.04
S.D.=1.76518711E-03	AS PERCENT 4.0470803
KH=186402.804	EST KH=250000
S.D.=17646.093	AS PERCENT 9.46664569
KOH=6.52645031E+09	EST KOH=5.6E+09
S.D.=479912552	AS PERCENT 7.35334722

PH	K	CALK	RESIDUALS
6.71	.0835	.0801989226	3.30107738E-03
6.93	.06267	.0659099883	-3.23998829E-03
7.03	.06019	.0615075146	-1.31751457E-03
7.08	.05839	.0596761117	-1.2861117E-03
7.22	.05291	.0556149815	-2.70498145E-03
7.26	.05059	.0547006764	-4.11067637E-03
7.57	.05093	.0503500382	5.7996175E-04
7.93	.05324	.0497389276	3.50107244E-03
8.2	.05264	.0521152301	5.2476993E-04
8.39	.05723	.0557173491	1.51265088E-03
8.46	.05926	.0575879385	1.67206152E-03
8.66	.06831	.0651432938	3.16670616E-03
8.9	.07685	.0805519034	-3.70190339E-03
8.95	.08585	.0850045738	8.45426199E-04

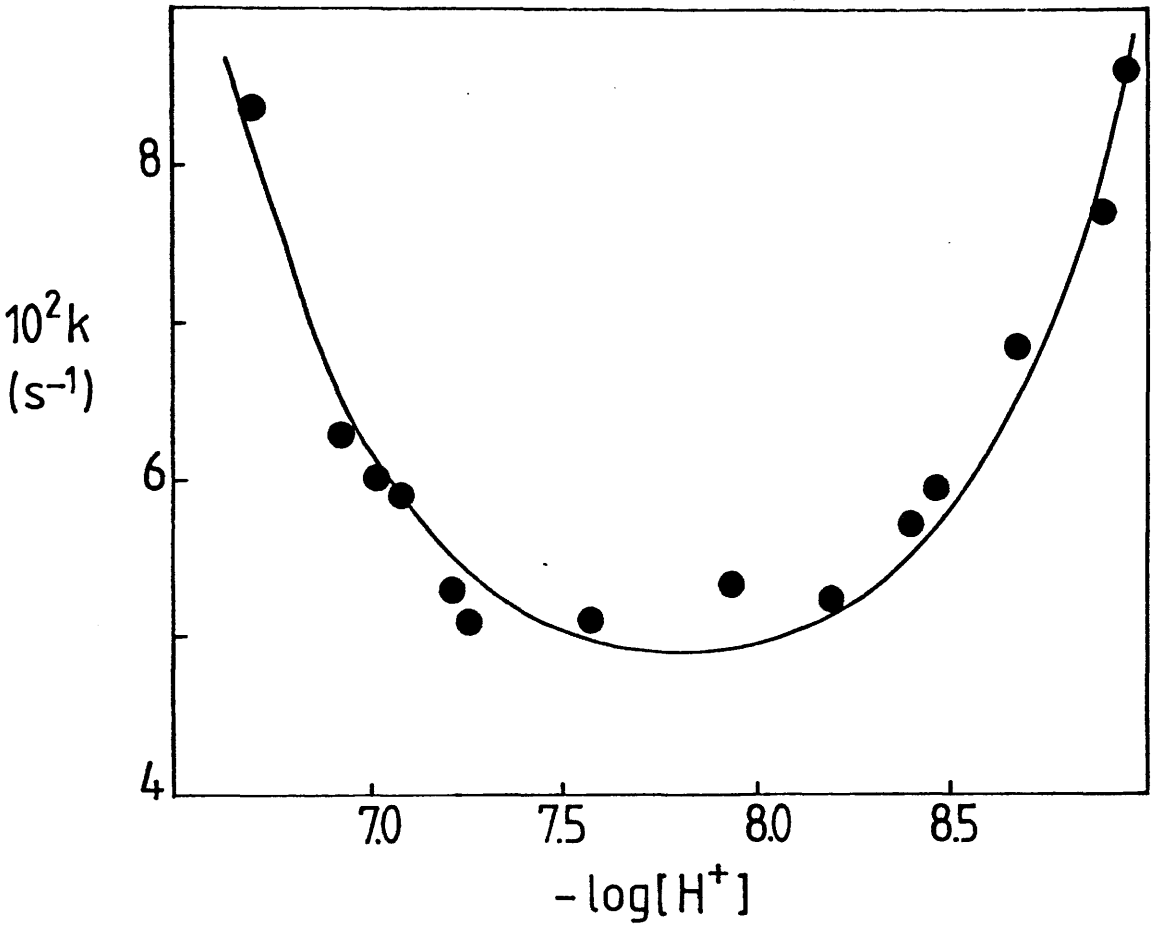


Fig. 13. Rate-profile for the breakdown of diethyl hemiorthoformate in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

Hydrolysis of 2-acetoxy-1,3-dioxolane

The attempt to follow the breakdown of the hemiorthoester, 2-hydroxy-1,3-dioxolane, in solutions of acetonitrile ($[H_2O]$ = 2.22 M) was unsuccessful. In fact some runs were done at different pc_H's but the results indicated that we were following the decomposition of the precursor.

This conclusion was supported by the NMR experiments carried out in the same conditions as the uv experiments which showed the slow decomposition of the acetoxy-compound. Nevertheless these values were utilized to calculate the k_{H^+} for that species. The complete rate profile for breakdown of the hemiorthoester was obtained in solutions of acetonitrile ($[H_2O]$ = 8.33 M), following the appearance of the product, monoformate of ethylene glycol, at 205 nm, T = 15°C ± 0.05.

Results

The breakdown of 2-hydroxy-1,3-dioxolane followed the equation:

$$k(s^{-1}) = 2.70\times10^{-2}+3.94\times10^{3}\times10^{-pc_H}+6.00\times10^{11}\times10^{-pc_{OH}} \quad (54)$$

(in CH_3CN-H_2O, 8.33 M)

and the decomposition of the 2-acetoxy-1,3-dioxolane followed:

$$k(s^{-1}) = 3.69\times10^{-3}+1.28\times10^{5}\times10^{-pc_H} \quad (55)$$

(in CH_3CN-H_2O, 2.22 M)

Table 37. Rate constants for decomposition of 2-acetoxy-1,3-dioxolane in CH_3-CN-acid ($[H_2O]$ = 2.22 M) at 15°C.

mV[a]	pc_H	"Buffer"	[HA], M	$10^2 k_{obs}, s^{-1}$	(s.d.%)
- 69.6	6.78	$C\ell_2CHCO_2H$	8×10^{-4}	2.355	(1.05)
- 63.3	6.91	"	1×10^{-3}	1.842	(0.74)
- 61.65	6.95	"	3×10^{-4}	2.087	(0.37)
- 40.4	7.39	"	2×10^{-4}	1.029	(1.87)
129.2	10.95	HOAc	1×10^{-3}	0.202	(4.96)

The plot of k_{obs} versus $[H^+]$ yielded a straight line with:

Slope = k_{H^+} = 1.283×10^5 M^{-1} s^{-1} s.d. = 13.30%

Int = k_{H_2O} = 3.685×10^{-3} s^{-1} s.d. = 49.00%

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a - Average of two values measured after each run.

Table 38. Rate constants for the rate profile for the breakdown of 2-hydroxy-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

mV [a]	pc_H	"Buffer"	10^4[HA], M	$10^2 k_{obs}, s^{-1}$	(s.d.%)
-151.3	4.61	$C\ell_2CHCO_2H$	9.0	12.338	(1.93)
-144.9	4.76	"	8.0	9.489	(1.27)
-139.3	4.89	"	6.8	7.929	(0.31)
-128.4	5.13	"	6.0	5.923	(1.02)
-199.6	5.34	"	4.0	4.912	(0.45)
-112.1	5.51	"	3.5	4.072	(1.64)
-107.3	5.62	"	3.2	4.256	(1.16)
-101.5	5.75	"	2.8	3.528	(0.24)
- 81.1	6.21	"	2.2	3.676	(3.65)
- 66.3	6.55	HCOOH	10.0	3.948	(0.57)
- 59.8	6.70	$C\ell_2CHCO_2H$	1.0	4.292	(2.18)
- 48.1	6.97	HCOOH	9.0	6.528	(0.10)
- 42.2	7.11	"	8.5	8.060	(1.20)
- 37.0	7.25	"	8.0	10.449	(1.37)
- 31.7	7.34	"	4.0	12.068	(1.13)
- 31.5	7.36	"	6.0	12.416	(2.41)

a - Average of two to three values measured after each run.

Table 39. Rate constants for the breakdown of 2-hydroxy-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

VALUE OF KW 7.0794578E-21
5 ITERATIONS USED
KO=.0269666292 EST KO=.03
S.D.=1.29286953E-03 AS PERCENT 4.79433125

KH=3945.7794 EST KH=4000
S.D.=93.7472778 AS PERCENT 2.37588745

KOH=5.99927783E+11 EST KOH=6.5E+11
S.D.=1.19529522E+10 AS PERCENT 1.9923985

PH	K	CALK	RESIDUALS
4.61	.12338	.123997051	-6.1705074E-04
4.76	.09489	.0957808163	-8.908163E-04
4.89	.07929	.0781278003	1.16219971E-03
5.13	.05923	.0567900232	2.4399768E-03
5.34	.04912	.0459314993	3.18850072E-03
5.51	.04072	.0405346086	1.85391371E-04
5.62	.04256	.0382024073	4.35759276E-03
5.75	.03528	.0363716831	-1.09168308E-03
6.21	.03676	.0362876695	4.72330517E-04
6.55	.03948	.0431482051	-3.66820514E-03
6.7	.04292	.0490401561	-6.12015608E-03
6.97	.06528	.0670262613	-1.74626132E-03
7.11	.0806	.0819869815	-1.38698154E-03
7.25	.10449	.102714947	1.77505257E-03
7.34	.12068	.120064795	6.1520483E-04
7.36	.12416	.124435759	-2.75759085E-04

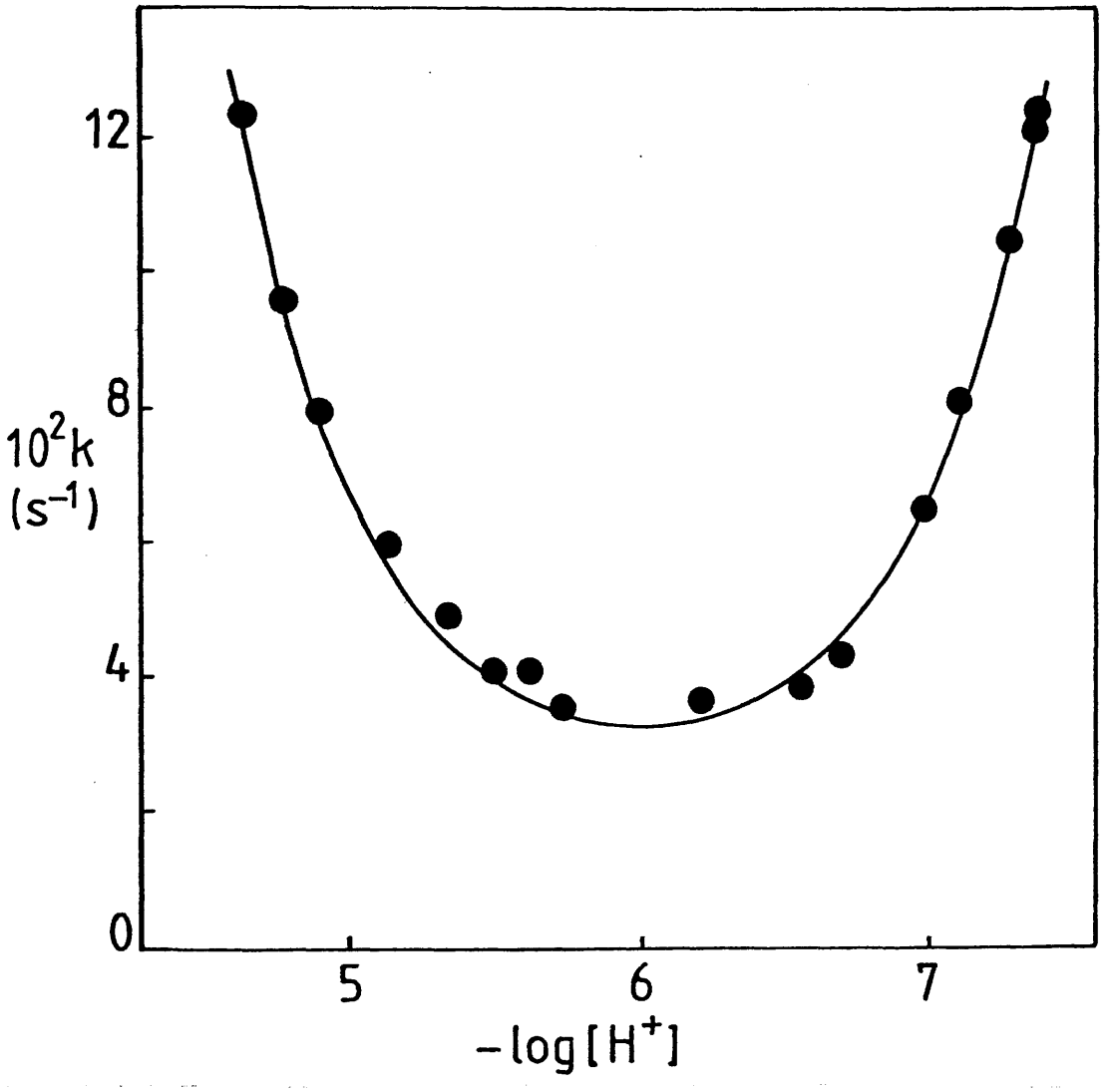


Fig. 14. Rate profile for the breakdown of 2-hydroxy-1,3-dioxolane in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

Hydrolysis of trimethyl orthoformate

The hydrolysis of this orthoester was studied in solutions of acetonitrile ($[H_2O]$ = 8.33 M) in order to compare its reactivity and way of breakdown with the respective acyclic hemiorthoester. Five different acid concentrations were utilized and two of them were in the same acidity range as that used for studying the hemiorthoformate.

Results

The decomposition of the trimethyl orthoformate followed the equation:

$$k(s^{-1}) = 4.03 \times 10^{-4} + 1.21 \times 10^{2} \times 10^{-pc_H} \quad (56)$$

(in CH_3CN-H_2O, 8.33 M)

The large standard deviation of the intercept (Table 40) indicates that it is zero within experimental error.

Table 40. Hydrolysis of trimethyl orthoformate in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

mV [a]	pc_H	"Buffer"	[HA], M	$10^4 k_{obs}, s^{-1}$	(s.d.%)
-177.7	4.01	Cl_2CHCO_2H	1×10^{-3}	122.5	(2.18)
-165.5	4.29	"	6×10^{-4}	65.71	(1.31)
-121.0	5.30	"	2×10^{-4}	15.44	(2.35)
- 62.7	6.63	HCOOH	1×10^{-3}	2.850	(2.22)
- 50.0	6.92	"	8×10^{-4}	0.880	(2.00)

The plot of k_{obs} versus $[H^+]$ yielded a straight line with:

Slope = k_{H^+} = 121.2 M^{-1} s^{-1} s.d. = 3.54%

Int = k_{H_2O} = 4.030×10^{-4} s^{-1} s.d. = 52.6%

---

a - Average of two to three values.

Hydrolysis of triethyl orthoformate

The same observations for the hydrolysis of trimethyl orthoformate is extended to this case, where for the same purpose it was studied in solutions of acetonitrile ($[H_2O]$ = 8.33 M).

Results

The decomposition of this orthoformate followed the equation:

$$\underline{k}(s^{-1}) = 2.94 \times 10^{-3} + 8.00 \times 10^{2} \times 10^{-pc_H} \quad (57)$$

(in CH_3CN-H_2O, 8.33 M)

Again the standard deviation of the intercept was large indicating that it was zero within experimental error.

Table 41. Hydrolysis of triethyl orthoformate in CH_3CN-acid ($[H_2O]$ = 8.33 M) at 15°C.

mV [a]	pc_H	"Buffer"	[HA], M	$10^3 k_{obs}, s^{-1}$	(s.d.%)
-179.5	3.97	$C\ell_2CHCO_2H$	1×10^{-3}	88.58	(1.27)
-167.0	4.25	"	6×10^{-4}	47.62	(1.89)
-122.9	5.26	"	2×10^{-4}	10.74	(1.86)
- 67.6	6.52	HCOOH	1×10^{-3}	2.795	(3.74)
- 43.9	7.06	"	8×10^{-3}	0.306	(0.36)

The plot of k_{obs} versus $[H^+]$ yielded a straight line with:

Slope = k_{H^+} = 800.09 M^{-1} s^{-1} s.d. = 3.33%

Int = k_{H_2O} = 2.938×10^{-3} s^{-1} s.d. = 49.2%

a - Average of two to three values.

1.3.2 NMR Experimental

The NMR experiments were carried out on a Perkin-Elmer R32 (90 MHz) spectrophotometer. The chemical shifts were measured downfield from internal tetramethyl silane (TMS) and are quoted in δ values. The abbreviations are represented by: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.

As mentioned before, the kinetic experiments carried out by UV spectroscopy for a series of hemiorthoesters were preceded by NMR experiments in order to be certain about the species being observed during the rate-determining step. The hemiorthoesters in question have been previously detected[18,27] and characterized by ^{1}H-nmr and ^{13}C-nmr spectroscopy. Therefore the main concern was to find a suitable common medium in order to follow the breakdown of the hemiorthoesters. In the series studied the three more stable intermediates, 2-hydroxy-2,4,4,5,5-pentamethyl-1,3-dioxolane, 2-hydroxy-4,4,5,5-tetramethyl-1,3-dioxolane and 2-hydroxy-1,3-dioxolane were studied in solutions of d_3-acetonitrile - D_2O 96%-4% v/v. The normal procedure utilized during the experiments consisted in adding the solvent (acetonitrile) and the precursor to the NMR tube, placing the latter in the probe at -35° to -40°C and running the first spectrum before adding the required amount of D_2O which contained CD_3CO_2D. After addition of D_2O the

temperature was regularly increased up to 15°C (the temperature utilized in the UV experiments).

The conditions in which the complete series was studied was d_3-acetonitrile - D_2O (85-15% v/v). The spectra for the faster-reacting orthoesters were recorded only in the range covering the chemical shifts of the CH proton from the starting material, intermediate and product. The exact conditions are summarized in Tables 42 and 43.

A set of spectra for the experiments in CD_3CN-D_2O (96-4% v/v) is represented in the figures 15, 16 and 17.

Table 42. Conditions utilized for the NMR experiments for the breakdown of hemiorthoesters in CD_3CN-D_2O (96-4% v/v).[a]

Precursor[b]	$[CD_3COOD]_f$, M	C-H proton (ppm)[c] Precursor	Intermed.
I	1.6×10^{-1}	6.60	5.81
II	9.2×10^{-3}	3.11	1.43
III	1.6×10^{-1}	3.03	1.45

a - CD_3CN(288µℓ) + D_2O(µℓ)

b - Amount added (4µℓ)

c - For ketene acetals the precursor is represented by the methylene protons; intermediate by CH_3 at position 2.

I - 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolane

II - 2-methylene-1,3-dioxolane

III - 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane.

Table 43. Conditions utilized for the nmr experiments for the breakdown of hemiorthoesters in CD_3CN-D_2O (85-15% v/v).[a]

Precursor[b]	$[CD_3CO_2D]_f$, M	C-H proton (ppm)[c] Precursor	Intermed.
I (4µℓ)	2.3×10^{-1}	6.60	5.82
II (4µℓ)	2.3×10^{-1}	3.13	1.47
III (4µℓ)	2.3×10^{-2}	3.02	1.46
IV (2µℓ)	2.3×10^{-2}	6.70	5.83
V (1µℓ)	-	6.14	5.16
VI (1µℓ)	-	6.25	5.01

a - CD_3CN(425µℓ) + CD_3CO_2D(75µℓ)

b - For ketene acetals the precursor is represented by the methylene protons; intermediate by CH_3 at position 2.

I - 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolane

II - 2-methylene-1,3-dioxolane

III - 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane

IV - 2-acetoxy-1,3-dioxolane

V - dimethoxy methyl acetate

VI - diethoxy methyl acetate.

Fig. 15. ^{1}H-nmr spectra of 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolane.

a - in CD_3CN at -30°C

b - in CD_3CN-D_2O (96:4 v/v) at -30°C, $[CD_3COOD] = 1.6 \times 10^{-1}$ M, spectrum commenced c.a. 20 sec after dissolving

c - same as b, at -10°C, spectrum commenced 8 min after dissolving

d - same as b, at 15°C, spectrum commenced 21 min after dissolving.

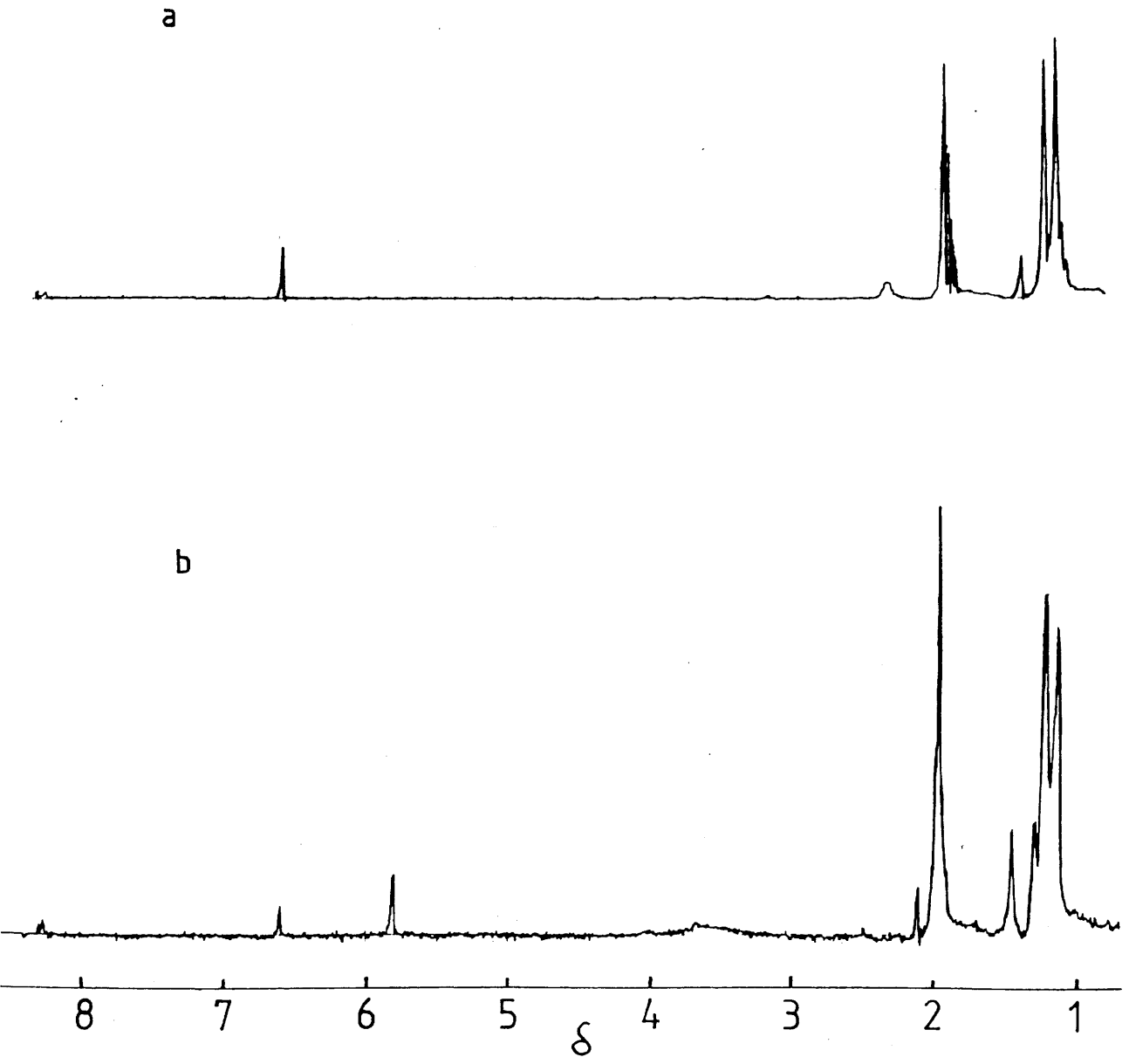


Fig.15

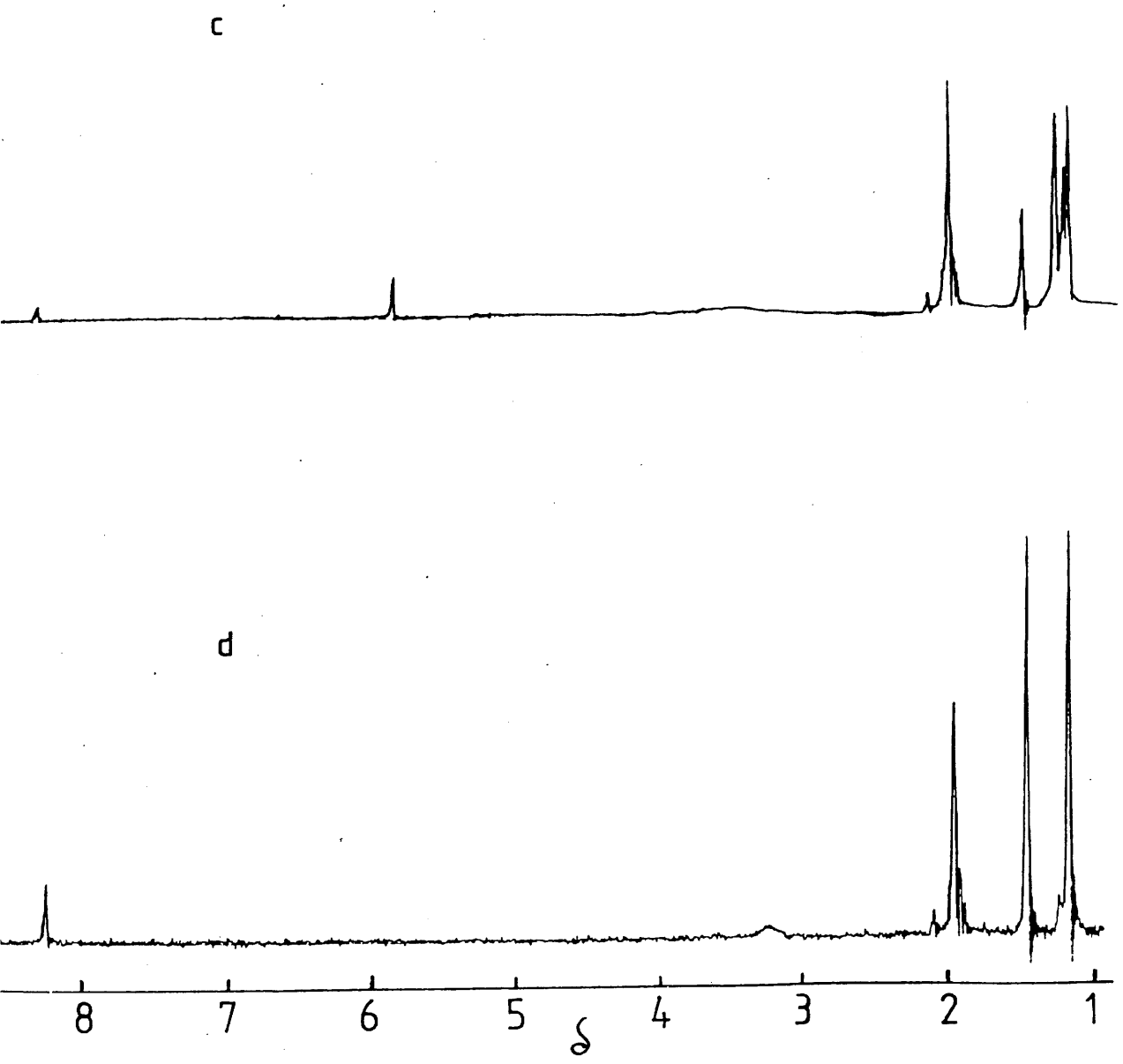


Fig. 15

Fig. 16. ^{1}H-nmr spectra of 2-methylene-1,3-dioxolane.

a - in CD_3CN at -40°C

b - in CD_3CN-D_2O (96:4 v/v) at -40°C, $[CD_3COOD] = 9.2 \times 10^{-3}$ M, spectrum commenced c.a. 20 sec after dissolving

c - same as b, at -20°C, spectrum commenced 12 min after dissolving

d - same as b, at 15°C, spectrum commenced 42 min after dissolving.

The position of Figures 16 and 17 have been interchanged

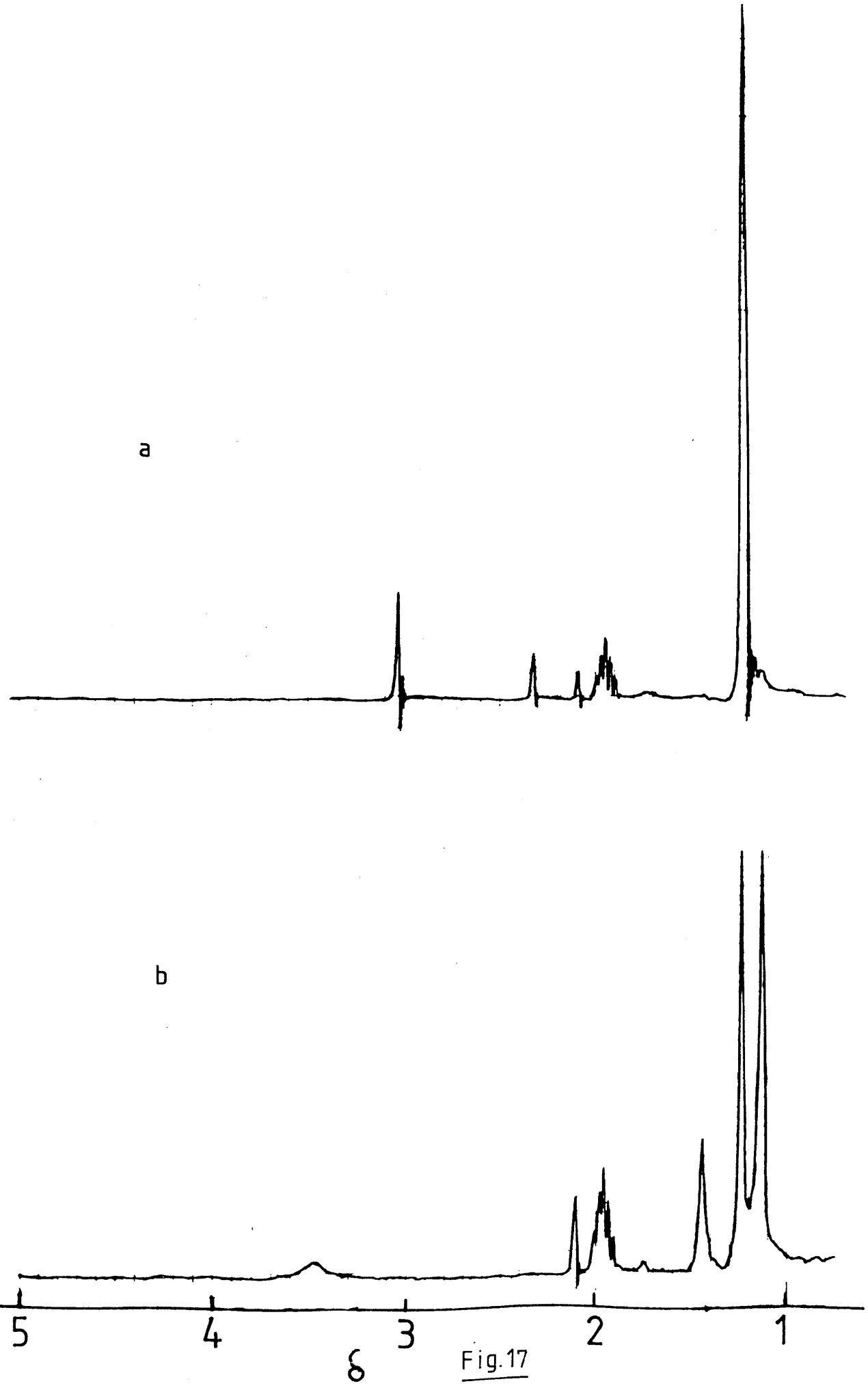


Fig.17

Fig. 17. ^{1}H-nmr spectra of 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane.

a - in CD_3CN at -40°C.

b - in CD_3CN-D_2O (96:4 v/v) at -30°C, $[CD_3CO_2D]_f = 1.6 \times 10^{-1}$ $\underline{\underline{M}}$, spectrum commenced c.a. 20 sec after dissolving

c - same as b, at 15°C, spectrum commenced 12 min after dissolving

d - same as b, at 15°C, spectrum commenced 49 min after dissolving.

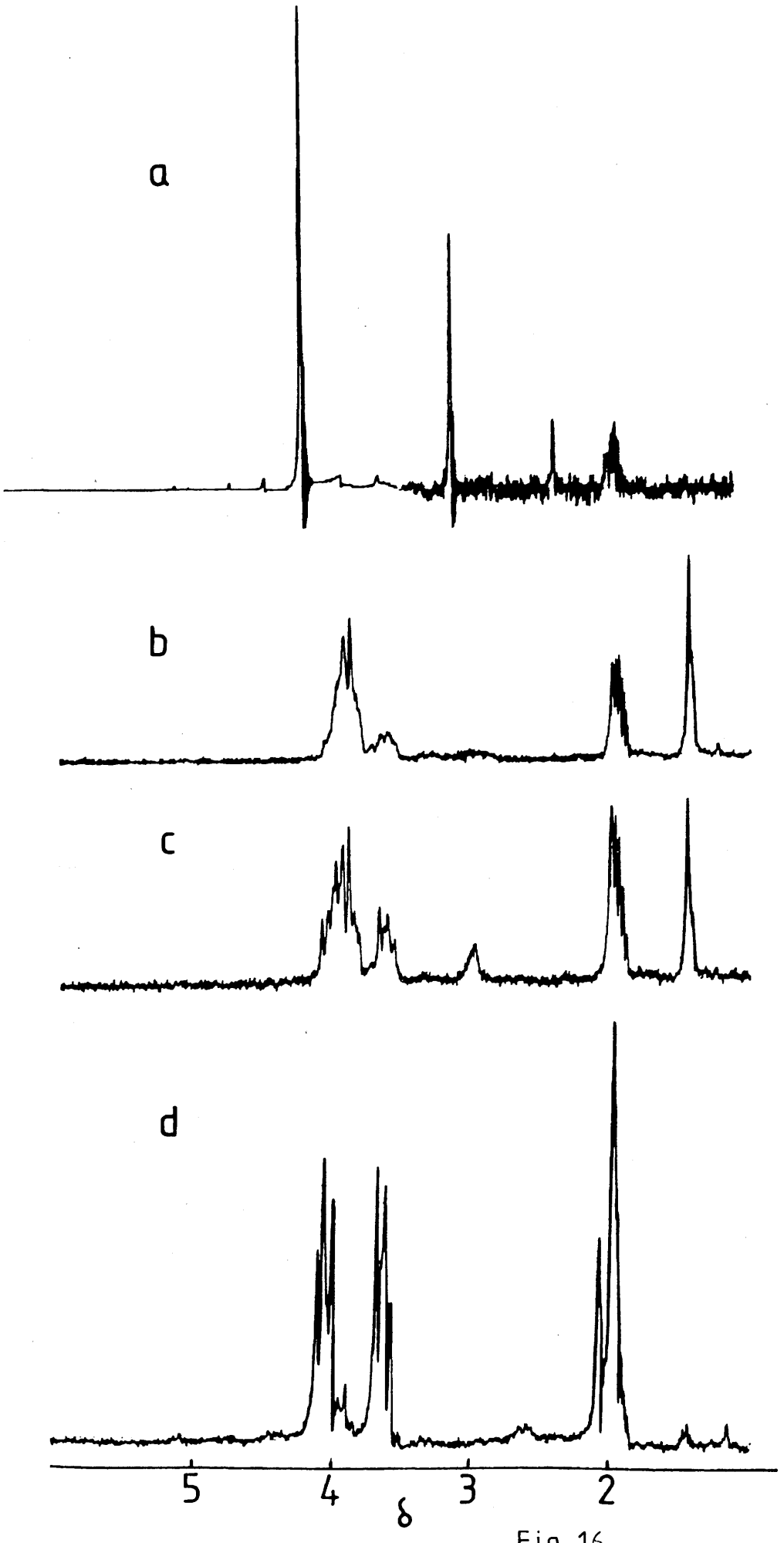


Fig. 16

1.3.3 Preparative Experimental

Preparation of dimethoxy methyl acetate

The method of Scheeren and Stevens was followed.[72]

Formic acid (94 ml, 2.21 moles) was mixed with acetic anhydride (200 µℓ, 2 moles) and allowed to stand during 1 hour. Trimethyl orthoformate (202 ml, 1.85 moles) was added and the solution allowed to react c.a. 5 days at room temperature (R.T.) with the reaction being monitored by NMR. The mixture was fractionated and the product distilled.

b.p. = 47°C/c.a. 13 mm Hg

NMR ($CDC\ell_3$)	90 MHz	δ = 2.08 ppm (s, 3H)
		δ = 3.40 ppm (s, 6H)
		δ = 6.18 ppm (s, 1H)
NMR ($CDC\ell_3$)[44]	90 MHz	δ = 2.07 ppm (s, 3H)
		δ = 3.45 ppm (s, 6H)
		δ = 6.15 ppm (s, 1H)

Preparation of 2-methoxy-4,4,5,5-tetramethyl-1,3-dioxolane

Pinacol (30g, 0.25 moles) was mixed with trimethyl orthoformate (27g, 0.25 moles) and benzene (30 ml), toluene-p-sulphonic acid was added as catalyst and the azeotrope benzene-MeOH was collected at 58°C. After

neutralizing the acid the mixture was fractionated and the product collected.

NMR ($CDC\ell_3$) 90 MHz δ = 1.17 ppm (s, 6H)
δ = 1.27 ppm (s, 6H)
δ = 3.35 ppm (s, 3H)
δ = 5.09 ppm (s, 1H)

Preparation of 2-acetoxy-4,4,5,5-tetramethyl-1,3-dioxolane

The method of Scheeren and Steven[73] was followed.

Dimethoxymethyl acetate (9.7g, 0.082 moles) was mixed with 2-methoxy-4,4,5,5-tetramethyl-1,3-dioxolane (13.1g, 0.082 moles) and dried
The mixture was allowed to react under vacuum (c.a. 13 mm Hg) during c.a. 10 hours with $HC(OMe)_3$ being distilled off during the reaction. The mixture was fractionated and the product collected.

b.p. = 32-33°C/0.06 mm Hg

NMR ($CDC\ell_3$) 90 MHz δ = 1.20 ppm (s, 6H)
δ = 1.30 ppm (s, 6H)
δ = 2.01 ppm (s, 3H)
δ = 6.68 ppm (s, 1H)

NMR ($CDC\ell_3$)[44] 90 MHz δ = 1.23 ppm (s, 6H)

δ = 1.33 ppm (s, 6H)

δ = 2.05 ppm (s, 3H)

δ = 6.73 ppm (s, 1H)

Preparation of 2-methoxy-1,3-dioxolane

This was prepared in a similar way to 2-methoxy-4,4,5, 5-tetramethyl-1,3-dioxolane. The product was distilled.

b.p. = 30-32°C/c.a. 13 mm Hg

NMR ($CDC\ell_3$) 60 MHz δ = 3.25 ppm (s, 3H)

δ = 3.80-4.07 ppm (m, 4H)

δ = 5.61 ppm (s, 1H)

Preparation of 2-acetoxy-1,3-dioxolane

This was prepared in a similar way to 2-acetoxy-4,4,5, 5-tetramethyl-1,3-dioxolane.

b.p. = 34-35°C/0.09 mm Hg

NMR ($CDC\ell_3$) 90 MHz δ = 2.03 ppm (s, 3H)

δ = 4.02-4.30 ppm (m, 4H)

δ = 6.87 ppm (s, 1H)

NMR ($CDC\ell_3$)[44] 90 MHz δ = 2.02 ppm (s, 3H)

δ = 4.10 ppm (m, 4H)

δ = 6.84 ppm (s, 1H)

2-methylene-1,3-dioxolane and 2-methylene-4,4,5,5-tetramethyl-1,3-dioxolane

These were supplied by Dr. A.K. Ghosh.

NMR (CD_3CN)	90 MHz	δ = 3.11 ppm (s, 2H)
		δ = 4.19 ppm (s, 4H)
NMR (CD_3COCD_3)	90 MHz	δ = 1.22 ppm (s, 16H)
		δ = 2.97 ppm (s, 2H)

Diethoxymethyl acetate, trimethyl orthoformate and triethyl orthoformate

These were commercially available from Aldrich and BDH.

NMR ($CDC\ell_3$)	90 MHz	δ = 1.19 ppm (t, 6H)
		δ = 2.04 ppm (s, 3H)
		δ = 3.69 ppm (g, 4H)
		δ = 6.30 ppm (s, 1H)
NMR ($CDC\ell_3$)	90 MHz	δ = 3.32 ppm (s, 9H)
		δ = 4.96 ppm (s, 1H)
NMR ($CDC\ell_3$)	90 MHz	δ = 1.21 ppm (t, 9H)
		δ = 3.63 ppm (g, 6H)
		δ = 5.18 ppm (s, 1H)

REFERENCES

1. J.N.E. Day, C.K. Ingold, Trans. Faraday Soc., 37, 686 (1941).
C.K. Ingold, "Structure and Mechanism in Organic Chemistry". Cornell University Press, Ithaca, N.Y. (1953) p.751-796.

2. M.L. Bender, J. Am. Chem. Soc., 73, 1626 (1951). Chem. Rev., 60, 53 (1960).

3. C.A. Bunton, T.A. Lewis, D.H. Llewellyn, Chem. & Ind., 1154 (1954).

4. M.L. Bender, R.D. Giner, J. Am. Chem. Soc., 77, 348 (1955).

5. P. Deslongchamps, U.O. Cheriyan, A. Guida, R.J. Taillefer, Nouv. J. Chim., 2, 631 (1978).

6. S.A. Shain, J.F. Kirsch, J. Am. Chem. Soc., 90, 5848 (1968).

7. M.L. Bender, H. d'A. Heck, J. Am. Chem. Soc., 89, 1211 (1967).

8. L.B. Jones, T.M. Sloane, Tetr. Lett., 831 (1966).

9. W.P. Jencks, M. Gilchrist, J. Am. Chem. Soc., 86, 5616 (1964).

10. N.P. Gensmatel, M.I. Page, J. Chem. Soc. Chem. Comm., 374 (1978). J. Chem. Soc. Perkin II, 137 (1979).

11. W.P. Jencks, "Catalysis in Chemistry and Enzymology", McGraw-Hill. 1969. p.463.

12. G.L. Schmir, B.A. Cunningham, J. Am. Chem. Soc., 87, 5692 (1965).
B.A. Cunningham, G.L. Schmir, J. Am. Chem. Soc., 88, 551 (1966).

13. R.A. McClelland, M. Alibhai, Can. J. Chem., 59, 1169 (1981).

14. J.F. Kirsch, W.P. Jencks, J. Am. Chem. Soc., 86, 837 (1964).

15. E.H. Cordes, Progr. Phys. Org. Chem., 4, 1 (1967).
E.H. Cordes, H.G. Bull, Chem. Rev., 74, 581 (1974).

16. A simple tetrahedral intermediate has been defined by Capon in analogy of Hart's definition[17] of a simple enol.

17. H. Hart, Chem. Rev., 79, 515 (1979).

18. B. Capon, J.H. Gall, D. McL. A. Grieve, J. Chem. Soc. Chem. Comm., 1034 (1976).
B. Capon, D. McL. A. Grieve, J. Chem. Soc. Perkin II, 300 (1980).

19. M. Ahmad, R.G. Bergstrom, M.J. Cashen, Y. Chiang, A.J. Kresge, R.A. McClelland, M.F. Powell, J. Am. Chem. Soc., 101, 2669 (1979).
M. Ahmad, R.G. Bergstrom, M.J. Cashen, A.J. Kresge, R.A. McClelland, M.F. Powell, J. Am. Chem. Soc., 99, 4827 (1977).

20. R.A. McClelland, S. Gedge, J. Bohonek, J. Org. Chem., 46, 886 (1981).

21a R.A. McClelland, R. Somani, J. Chem. Soc. Chem. Comm., 407 (1979).

21b R.A. McClelland, M. Ahmad, J. Org. Chem., 44, 1855 (1979).

21c R.A. McClelland, J. Am. Chem. Soc., 100, 1844 (1978).

22. A. Kankaanperä, R. Aaltoneu, Acta Chem. Scand., 26, 1698-1706 (1972).

23. V. Gold, D.C.A. Waterman, J. Chem. Soc. B, 839 (1968).

24. P.G.J. Huurdeman, J.B.F.N. Engberts, J. Org. Chem., 44, 297 (1979).

25. R. Hershfield, G.L. Schmir, J. Am. Chem. Soc., 94, 1263 (1972).

26. R. Hershfield, M.J. Yeager, G.L. Schmir, J. Org. Chem., 40, 2940 (1975).

27. B. Capon, A.K. Ghosh, J. Am. Chem. Soc., 103, 1765 (1981).

28. P. Salomaa, A. Kankaanperä, M. Lahti, J. Am. Chem. Soc., 93, 2084 (1971).

29. R.A. McClelland, M. Ahmad, J. Bohonek, S. Gedge, Can. J. Chem., 57, 1531 (1979).

30. B. Capon, A.K. Ghosh, D. McL. A. Grieve, Acc. Chem. Res., 14, 306 (1981).

31. N. Gravitz, W.P. Jencks, J. Am. Chem. Soc., 96, 489 (1974).

32. J. Hine, G.F. Koser, J. Org. Chem., 36, 1348 (1971).

33. R.A. McClelland, G. Patel, J. Am. Chem. Soc., 103, 6908 (1981).

34. L.H. Funderburk, L. Aldwin, W.P. Jencks, J. Am. Chem. Soc., 100, 5444 (1978).

35. R.A. McClelland, G. Patel, J. Am. Chem. Soc., 103, 6912 (1981).

36. T.H. Fife, B.M. Benjamin, J. Am. Chem. Soc., 95, 2059 (1973).

37. D.R. Storm, D.E. Koshland, J. Am. Chem. Soc., 94, 5805 (1972).

38. S. Milstein, L. Cohen, J. Am. Chem. Soc., 94, 9158 (1972).

39a J.P. Guthrie, J. Am. Chem. Soc., 95, 6993 (1973).

39b J.P. Guthrie, Can. J. Chem., 54, 202 (1976).

39c J.P. Guthrie, Can. J. Chem., 55, 3562 (1977).

39d J.P. Guthrie, J. Am. Chem. Soc., 100, 5892 (1978).

39e J.P. Guthrie, P.A. Cullimore, Can. J. Chem., 58, 1281 (1980).

40. J.F. King, A.D. Allbutt, Can. J. Chem., 48, 1754 (1970)

41a P. Deslongchamps, Tetrahedron, 31, 2463 (1975).

41b P. Deslongchamps, C. Moreau, Can. J. Chem., 49, 2465 (1971).

41c P. Deslongchamps, C. Moreau, D. Fréhel, P. Atlanti, Can. J. Chem., 50, 3402 (1972).

41d P. Deslongchamps, Pure & Appl. Chem., 43, 351 (1975).

41e P. Deslongchamps, C. Lebreux, R.J. Taillefer, Can. J. Chem., 48, 1665 (1973).

41f P. Deslongchamps, S. Dubé, C. Lebreux, D.R. Patterson, R.J. Taillefer, Can. J. Chem., 53, 2791 (1975).

41g P. Deslongchamps, P. Atlanti, D. Fréhel, A. Malaval, Can. J. Chem., 50, 3405 (1972).

41h P. Deslongchamps, R. Chênevert, R.J. Taillefer, C. Moreau, J.K. Saunders, Can. J. Chem., 53, 1601 (1975).

41i P. Deslongchamps, Heterocycles, 7, 1271 (1977).

42. F. Kovač, B. Plesničar, J. Am. Chem. Soc., 101, 2677 (1979).
F. Kovač, B. Plesničar, J. Chem. Soc. Chem. Comm., 122 (1978).

43. R.J. Taillefer, S.E. Thomas, Y. Nadeau, H. Beierbeck, Can. J. Chem., 57, 3041 (1979).
R.J. Taillefer, S. Fliszar, Y. Nadeau, S.E. Thomas, H. Henry, Can. J. Chem., 58, 1138 (1980).

44. D. McL. A. Grieve, Ph.D. Thesis, Glasgow University, 1978.

45. P. Deslongchamps. Personal Communication.

46. M.G. Caserio, Y. Souma, J.K. Kim, J. Am. Chem. Soc., 103, 6712 (1981).

47. E.L. Eliel, F.W. Nader, J. Am. Chem. Soc., 92, 584 (1970).

48. H.G. Bull, K. Koehler, T.C. Pletcher, J.J. Ortiz, E.H. Cordes, J. Am. Chem. Soc., 93, 3002 (1971).

49. A. Skrabal, H.H. Eger, Z. Phys. Chem., 122, 349 (1926).

50. B. Capon, K. Nimmo, G.L. Reid, J. Chem. Soc. Chem. Comm., 871 (1976).

51. B. Capon, K. Nimmo, J. Chem. Soc. Perkin Trans. 2, 1113 (1975).

52. T.J. Przystas, T.H. Fife, J. Am. Chem. Soc., 103, 4884 (1981).

53. P. Salomaa, A. Kankaanperä, Acta Chem. Scand., 15, 871 (1961).

54. T.H. Fife, I.H. Brod, J. Org. Chem., 33, 4137 (1968).

55. M. Charton, J. Org. Chem., 29, 1222 (1964).

56. J. Shorter, "Correlation Analysis in Organic Chemistry: an introduction to linear free-energy relationships". Oxford Chemistry Series. 1973. p.35.

57. D.H. Geske, J. Phys. Chem., 63, 1062 (1959).

58. I.M. Kolthoff, J.F. Coetzee, J. Am. Chem. Soc., 79, 870, 1062 (1959).

59. H.K. Hall Jr., J. Phys. Chem., 60, 63 (1956).

60. D. Feakins, W.A. Last, R.A. Shaw, J. Chem. Soc., 2387 (1964).

61. J.F. Coetzee, G.R. Padmanabhan, J. Am. Chem. Soc., 66, 1708 (1962).

62. A.L. Bacarella, E. Grunwald, H.P. Marshall, E.L. Purlee, J. Phys. Chem., 62, 856 (1958).

63. R.C. Larson, R.T. Iwamoto, R.N. Adams, Anal. Chim. Acta, 25, 371 (1961).

64. I.M. Kolthoff, S. Bruckenstein, M.K. Chantooni, Jr., J. Am. Chem. Soc., 83, 3927 (1961).

65. R.G. Bates, "Solute-Solvent Interactions". Ed. J.F. Coetze and C.D. Ritchie, 1969. Marcel Dekker. N.Y. p.48.

66. R.A. Robinson, R.H. Stokes, "Electrolyte Solutions". Butterworths p.363.

67. H.S. Harned, B.B. Owen, "The Physical Chemistry of Electrolytic Solutions". Reinhold Publ. Corp. p.756.

68. J.M. Kolthoff, M.K. Chantooni, Jr., J. Am. Chem.Soc., 87, 4428 (1965).

69. W.E. Wentworth, J. Chem. Ed., 42, 162 (1965).

70. J.L. Jensen, P.A. Lenz, J. Am. Chem. Soc., 100, 1291 (1978).

71. R.A. McClelland, R.L. Finley, D.G. Kubler, J. Org. Chem., 45, 644 (1980).

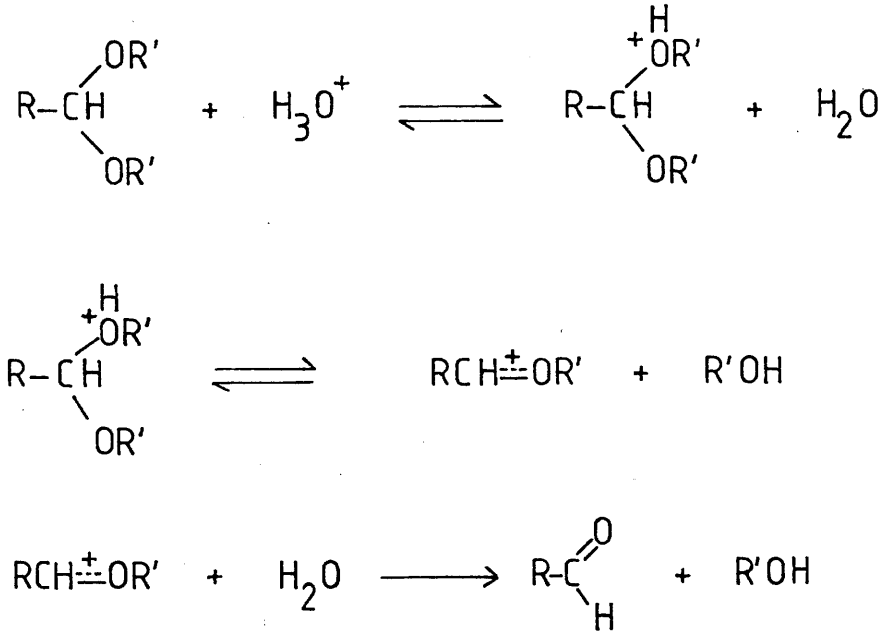
72. J.W. Scheeren, W. Stevens, Rec. Trav. Chim., 85, 793 (1966).

73. J.W. Scheeren, A.P.M. Van der Veek, W. Stevens, Rec. Trav. Chim., 88, 195 (1969).

2.1 INTRODUCTION

Hydrolysis of acetals

The mechanism of hydrolysis of acetals has been a subject of extensive study. By the 1960's on the basis of a large amount of data collected over the years, a general mechanism had been proposed[1] and largely accepted. It involves a pre-equilibrium protonation of the acetal by hydronium ion followed by a unimolecular rate determining decomposition to an alcohol and a resonance-stabilized carbonium ion, represented by the general scheme below:



Scheme 1

This was based on studies with alkyl acetals of aliphatic and aromatic aldehydes like $PhCH(OEt)_2$ and $CH_3CH(OEt)_2$. The evidence for this mechanism was based on criteria such as:[1] determination of the position of C-O bond cleavage, entropies of activation, isotope effects and structure-reactivity correlations.

The oxygen-18 labelling experiments[2] for hydrolysis and formation of benzaldehyde di-butyl acetal show that cleavage of the carbonyl C-O bond is taking place:

$$RCH(OR')_2 + H_2{}^{18}O \rightleftharpoons RCH^{18}O + 2R'OH \qquad (1)$$

This finding was confirmed by results from the hydrolysis of acetals derived from optically active alcohols such as the D(+)-2-octanol acetal of acetaldehyde which yielded 2-octanol as the product with the same optical configuration.[3]

The values of the entropy of activation (ΔS^*) near zero or slightly positive are associated with A1 reactions whereas large and negative values are associated with the A2 mechanism[4] and these obtained for the hydrolysis of alkyl acetals were included in the former category. Also the values of the solvent deuterium isotope effect fell in the range $k_{D_3O^+} / k_{H_3O^+} = 2.5$ to 3.3.

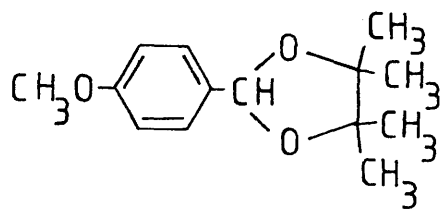
The effect of electron-donating substituents in the carbonyl moiety of the substrate tends to increase the rate

constants and that is in agreement with A1 reactions since the protonation will be made easier and the developing carbonium ion will be stabilized and the Hammett plot of log $\underline{k}_H$ versus σ for a series of substituted diethyl acetals of benzaldehyde yielded $\rho = -3.35$.[5] In the aliphatic series Kreevoy and Taft[6,7] found that the second order rate constants for the hydrolysis of a series of diethyl acetals and ketals of non-conjugated aldehydes and ketones were well correlated by the Taft equation and a value of $\rho^* = -3.60$ was found.

Since the 1960's there has been a long search for other mechanisms such as those which involve general catalysis, rate determining attack of water on the protonated substrate (A2 mechanism) and even general catalysis of the breakdown of the hemiacetal, a step which was not included in the above scheme. In order for such mechanisms to occur an alteration in the system is obviously necessary such as changing the solvents, buffers, leaving groups, substituents or structures of the acetals. The number of exceptions and special cases[8] has now grown so large that in the 1980's generalization of the mechanism for the hydrolysis of an acetal is difficult because any conclusion depends on the conditions and especially the structure of the acetal. Some of these special cases will now be described.

General acid catalysis

Fife[9] claimed the first observation of general-acid catalysis in the hydrolysis of an acetal with 2-(p-methoxyphenyl)-4,4,5,5-tetramethyl-1,3-dioxolan (1)



(1)

which was catalyzed by formic acid in aqueous solution at 40°C, I = 0.5 M with the catalytic constant k_{HA} = 0.0026 M^{-1} s^{-1}. This claim was not supported by any further evidence and a mechanistic suggestion was not offered. On the other hand mechanistic discussion was drawn to an A2 reaction.

The first authentic example of general-acid catalysis was observed in the hydrolysis of 2-(p-nitrophenoxy) and 2-(p-chlorophenoxy) tetrahydropyrans[10] with formate buffer in 50% dioxan-H_2O at 50°C. The catalytic constants obtained were k_{HA} = 0.013 M^{-1} s^{-1} and k_{HA} = 0.0041 M^{-1} s^{-1} respectively. Although 2-(p-methoxyphenoxy)tetrahydropyran has been studied no general acid catalysis was detected in formate buffer.

Some reported values of ΔS^* and k_D/k_H are put together in a single table to facilitate comparison.

Table 1. Activation entropy and solvent isotope effects for hydrolysis of tetra hydropyrans in 50% dioxan-H_2O

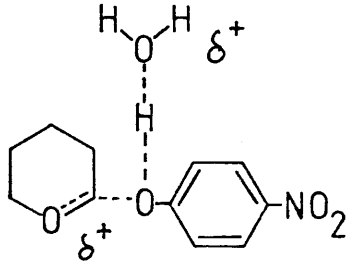
Substrate	ΔS^*, eu [a]	k_D/k_H
2-Ethoxytetrahydropyran	+ 7.9 ± 2.0	2.82
2-(p-Methoxyphenoxy) tetrahydropyran	-	2.48
2-Phenoxy tetrahydropyran	- 3.0 ± 1.2	2.29
2-(p-Nitrophenoxy) tetrahydropyran	- 7.6 ± 0.6	1.33

a - Calculated at 30° (rate constant units = $\underline{\underline{M}}^{-1}$ s^{-1}).

The solvent isotope effect of 2.82 obtained for the hydrolysis of 2-ethoxytetrahydropyran was thought to fall in the range associated with the A1 reaction (2.3 to 3.3)[11] and that of 1.33 for hydrolysis of 2-(p-nitrophenoxy-tetra hydropyran would indicate some degree of solvent participation in the transition state. That also could be concluded from the decreasing values of ΔS^* with the increasing of electron-donation from the substituents.

The ΔS^* values and solvent isotope effects were also consistent with an A2 reaction but Fife preferred a mechanism involving a "partial rate-determining protonation" of the oxygen in view of the solvent attack is a less favourable process and with the p-nitro substituted compound it should need the least nucleophilic catalysis because it has the best leaving group in that series. On the other hand a linear $\sigma\rho$ plot was obtained for the series (of which only three substrates were included in table 1) indicating no abrupt change in the mechanism.

The suggested structure in the transition state was:

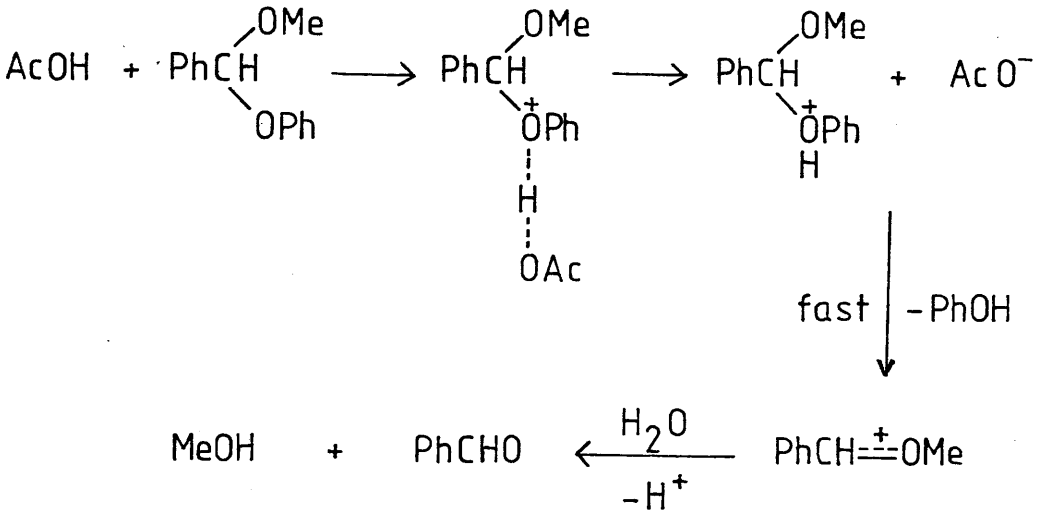


(2)

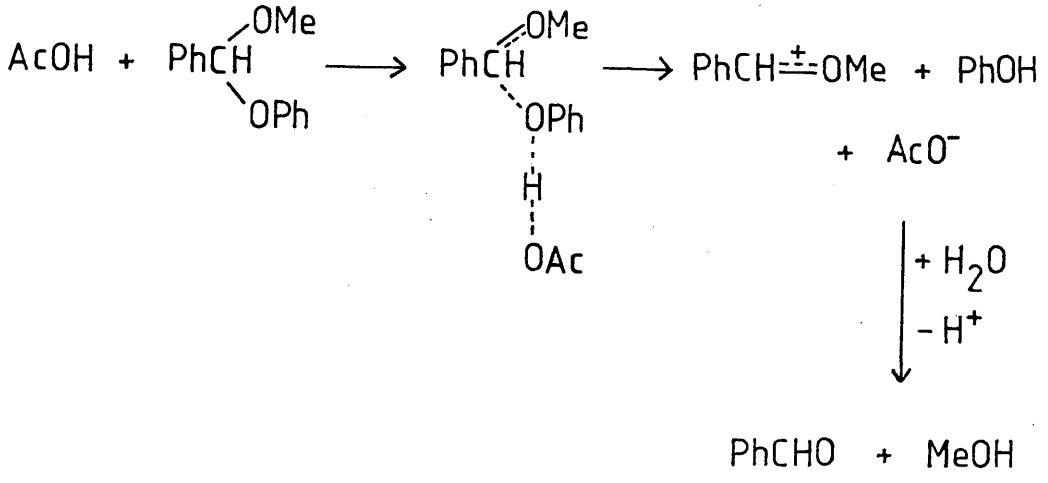
The structural requirements to observe general acid catalysis in the hydrolysis of acetals were discussed by Capon.[12] Two basic modifications related to the intermediates (protonated substrate and carbonium ion) present in the A1 reaction were proposed in order to obtain the desirable increase (and decrease) of the free energy content of their respective transition states. It was considered that a

change to a mechanism which involved general-acid catalysis could be achieved by making the acetal oxygen less basic and the carbonium ion more stable. A mixed acetal, benzaldehyde methyl phenyl acetal, was chosen due to its suitability in obtaining a less basic oxygen acetal without decreasing the stability of the carbonium ion compared to that from benzaldehyde dimethyl acetal.

General acid catalysis by chloroacetate, formate, acetate and phosphate buffers was observed. Two possible mechanisms were postulated:



Mechanism 1



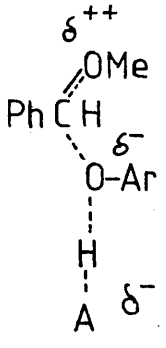
Mechanism 2

The second one was supported by the fact that electron withdrawing substituents in the leaving group (phenoxy) increased the rate whereas if there was a slow proton transfer to that phenoxy group (as in mechanism 1) the rate should decrease. The Brønsted coefficient $\alpha = 0.60$ and isotope effect $k(CH_3CO_2H)/k(CH_3CO_2D) = 2.14$ and $k(H_3O^+)/k(D_3O^+) = 1.01$ were compared to those of orthoesters[1] (α is c.a. 0.7 and $k_{H_3O^+}/k_{D_3O^+} < 1$) indicating a smaller degree of proton transfer than in the latter case and consequently a substantial C-O bond breaking in the transition state which is in agreement with mechanism 2.

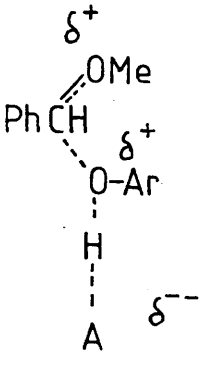
The conclusion for the position of C-O bond breaking being the phenoxyl-carbon bond was supported by a slower rate observed for hydrolysis of benzaldehyde dimethyl acetal (8.5×10^{-4} s^{-1}) than the rate of 8×10^{-3} s^{-1} for the

hydrolysis of the phenyl acetal under the same condition. If a methoxy bond breaking was taking place for the latter the opposite magnitude of rates should be observed. Other evidence was the effect of electron withdrawing substituents in the phenoxy moiety which increased the rate constants.

In an extension study of hydrolysis of benzaldehyde methyl phenyl acetal Capon and Nimmo[13] obtained interesting supplementary results in which electron-donating and withdrawing substituents in the phenoxy group increased the rate of hydrolysis. That afforded the suggestion of two structures for the transition state:



(3)



(4)

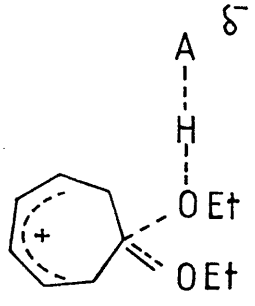
The structure (3) was that suggested when the substituents are electron-withdrawing. The C-O bond breaking is taking place ahead of H-O bond making and there will be a net negative charge in the oxygen (where the substitution is occurring). On the other hand the structure (4) is correlated with electron-donating substituents where the O-H bond making is occurring ahead of C-O bond breaking and

there will be a net positive charge in the oxygen.

Buffer catalysis was also detected in the hydrolysis of benzaldehyde ethyl 2-methoxy carboxy phenyl acetals by Buffet and Lamaty.[14]

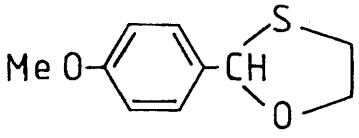
In the light of these examples Fife[15] studied the hydrolysis of tropone diethyl ketal culminating with the observation of general acid catalysis. The most important factor for such observation was the great stability of the carbonium ion in spite of the poor leaving group. The reaction was carried out in water at 15°C with Tris-HCℓ and phosphate buffer with the former having the $\underline{k}_{HA}$ catalytic constant (3–5 x 10^{-3} $\underline{\underline{M}}^{-1}$ s^{-1} at 15°C) much less than that for the latter (8.2 x 10^{-3} $\underline{\underline{M}}^{-1}$ s^{-1}). A spontaneous reaction has also been reported being pH independent above pH 10.

The suggested mechanism for hydrolysis of tropone diethyl ketal was a partially rate determining protonation by the general acid with the following structure in the transition state.

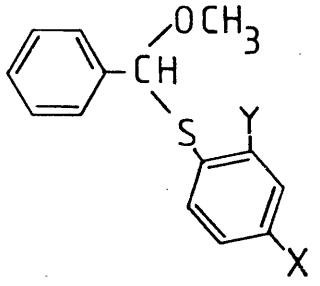


(5)

The efforts to observe general acid catalysis in the hydrolysis of 2-(p-methoxy phenyl) oxathiolane[16] (6) and a series of benzaldehyde S-(substituted phenyl thio acetals)[17] (7) were unsuccessful.



(6)

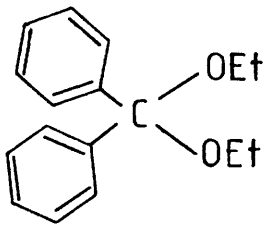


(7)

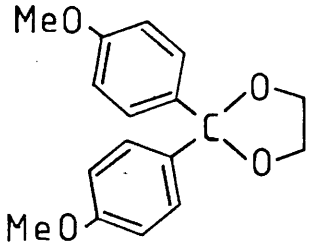
It led to the conclusion that the simple reduction of the basicity is not enough to observe general acid catalysis and the ease of C-O bond breaking has a more important deal for such observation.[17] Both are suggested to hydrolyze with C-S bond breaking (although for the former the C-O bond breaking was not completely excluded) and more convincing evidence was offered for (7) in which a reaction in presence of isopropyl alcohol showed the formation of benzaldehyde isopropyl methyl acetal which subsequently formed the di-isopropyl acetal with release of MeOH.

Jensen and Jencks[18] also found that in the hydrolysis of benzaldehyde O-ethyl S-phenyl acetal in 90% MeOH-water, T = 25°C only C-S cleavage was taking place with the observed rate constant 2.5 fold faster than the corresponding O-methyl compound.

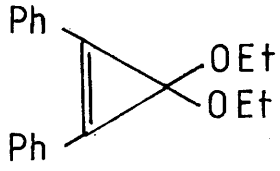
The search for general acid catalysis in the hydrolysis of the following acetals and ketals,[19] benzophenone diethyl ketal (8), 2,2-(p-methoxy phenyl)-1,3-dioxolane (9), 2,3-diphenyl cyclopropenone diethyl ketal (10) and ferrocene carboxaldehyde dimethyl acetal (11)



(8)



(9)



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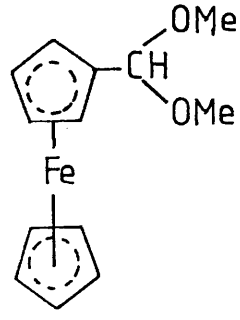


(11)

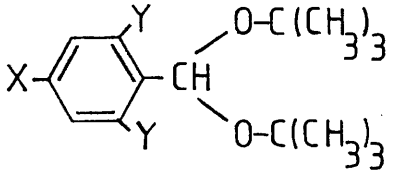
was also unsuccessful. The relative stability of the carbonium ions from the series above was compared with a series of related ions which have an equilibrium constant

according to the equation:

$$-\overset{|}{\underset{|}{C}}^{+} \; + \; 2\,H_2O \rightleftharpoons -\overset{|}{\underset{|}{C}}\text{-}OH \; + \; H_3O^{+} \qquad (2)$$

The pK_r^+ for tropylium ion[20] is 4.7 and for 2.3-diphenyl cyclopropenyl[21] -0.67. According to Fife, the observation of general acid catalysis for tropone ketal was due to the extreme stability of the carbonium ion and such further observations with acetals or ketals with these characteristics (poor leaving group and a reasonably stable carbonium ion) was most probable with those which pK_r^+ lies in this range (-0.67 to 4.7).

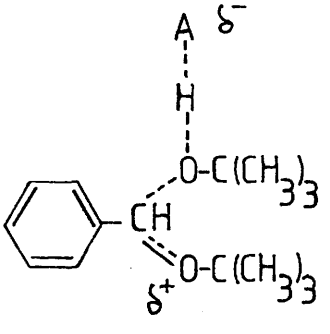
The hydrolysis of benzaldehyde di-t-butyl acetal has been claimed to be general acid catalyzed[22] in phosphate, succinate and acetate buffers in H_2O at 25°, I = 1.0 M. The series of acetals studied is represented by the structure:



(12)

	X	Y
I	OCH_3	H
II	CH_3	H
III	H	H
IV	Cℓ	H
V	H	Cℓ

The D_2O solvent isotope effect, k_{HA}/k_{DA} = 2.52 and k_{H^+}/k_{D^+} = 0.9 were obtained for hydrolysis of III and the Brønsted plot (log k_{HA} versus pKa) yielded a straight line with a slope -0.6. The plot of log k_{HA} versus σ (Hammett substituents constants)[23] yielded a straight line with ρ = -2.0. In that series only V did not show general acid catalysis and the hydrolysis of I, II and IV were studied only in phosphate buffer. The mechanism suggested for hydrolysis of benzaldehyde di-t-butyl acetal was a concerted protonation with C-O bond breaking with the following structure in the transition-state



(13)

The observation of general acid catalysis was attributed basically to the release of steric strain in the transition state.

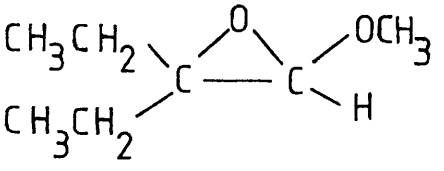
Jensen[8] has also claimed to observe general acid catalysis in the hydrolysis of benzaldehyde diethyl acetal in acetate, cacodylate, formate and mes(2-(N-morpholino) ethane sulfonic acid) buffers in water at 25°C, I = 0.5 M. Also a series of p-substituted benzaldehydes were studied. m-Chlorobenzaldehyde diethyl acetal was used as a "calibration" acetal to make sure that the specific salt effect was not responsible for such rate increasing since it did not show general acid catalysis under the same condition and has a related structure to the substrates studied. The system was analyzed in terms of Jencks, More - O'Ferral diagram and the rate determining step was proposed to be the diffusional separation of the aggregate (carboxonium ion). (conjugate base of the catalyzing acid). (alcohol).

Fife's[22] and Jensen's[8] papers are strictly related to the work in this Section and they will be subject to a more detailed discussion.

Change in the Rate Determining Step to Breakdown of the Hemiacetal

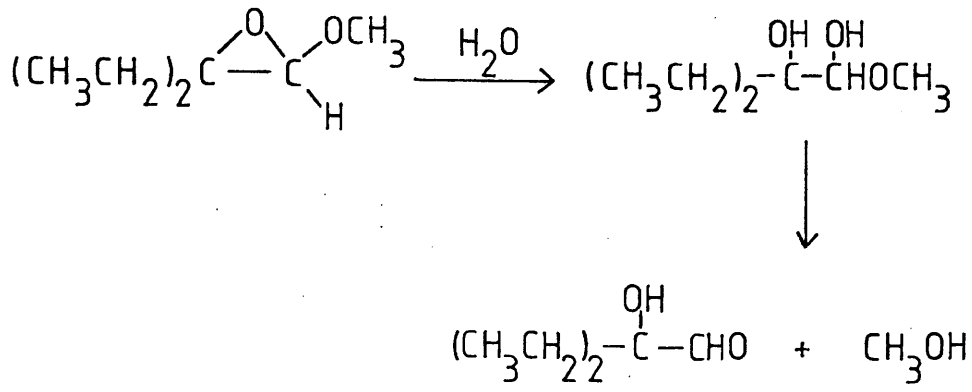
In the overall scheme for hydrolysis of an acetal (Scheme 1) the step representing the breakdown of the intermediate hemiacetal was not included. Usually this step has been taken to be much faster than that which involves the breaking of the C-O bond of the acetal.[24,25]

The first observation of rate determining breakdown of the hemiacetal was made by Schaleger[26] and co-workers in an investigation of the hydrolysis of 1-methoxy-2-ethyl-1,2-epoxy butane (14)



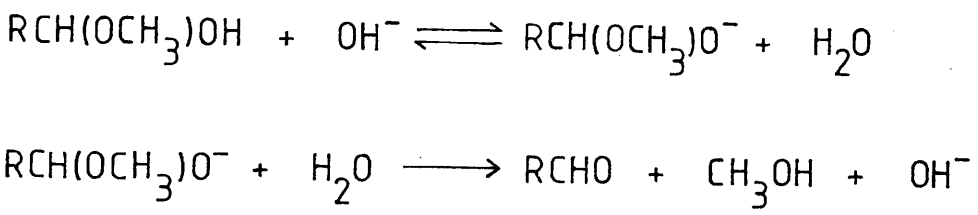
(14)

in 10% dioxone-water at 25°C. At pH's below 7.91 and above 8.0 the reaction was first order but in the intermediary pH's an induction period was observed. It was suggested that the rate determining step was the breakdown of the acetal at pH's above 8.0 and the breakdown of the hemiacetal at pH's below 7.91 and for pH's between those both steps were kinetically observable and no first order kinetics were obtained.



Scheme 2

The breakdown of the hemiacetal was general acid and base catalyzed but the mechanistic attention was focussed to the hydroxyde ion reaction which would proceed according to the scheme



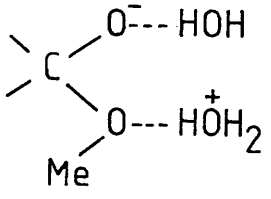
Scheme 3

with the rate limiting step being the departure of the leaving group (methoxide) assisted by a general acid.

That possibility (two step ionization) was extended to the water reaction and k_2 was evaluated to be 5×10^9 M^{-1} s^{-1} from the equation

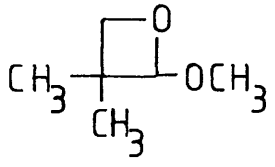
$$k_{H_2O} = K_a \cdot k_2 \qquad (3)$$

utilising the estimated[27] pKa of 13 for α-hydroxy hemiacetal and $k_{H_2O} = 4.8 \times 10^{-4}\ s^{-1}$. This led to the conclusion that the pH independent reaction could proceed by the two-step ionization mechanism with a possible structure in the transition state:



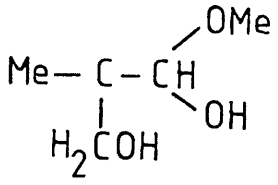
(15)

A similar proposal was made by Bruice and Atkinson[28] for the hydrolysis of 2-methoxy-3,3-dimethyloxetane (16).



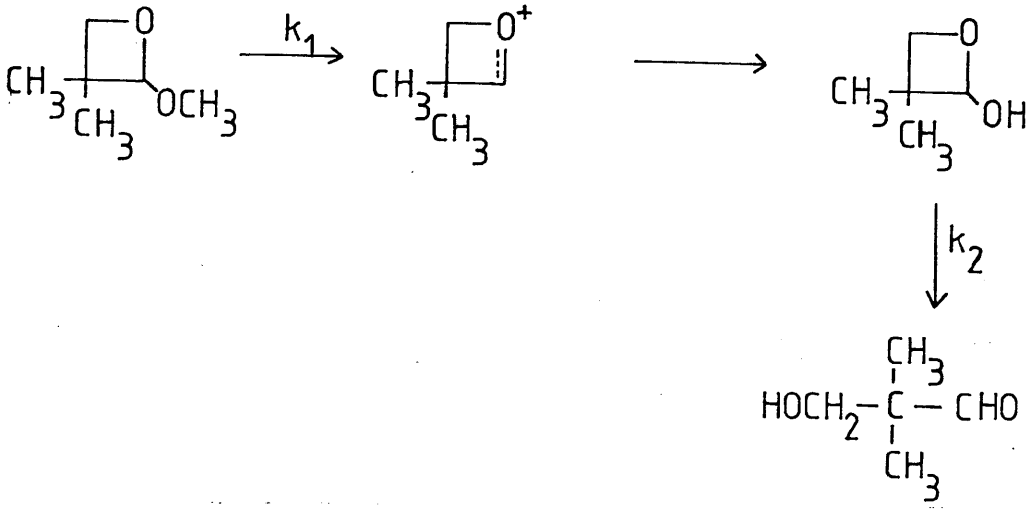
(16)

It was found that the breakdown of the corresponding hemiacetal (17) was rate determining at low pH and an induction period was observed between pH's 6.1 and 7.0.

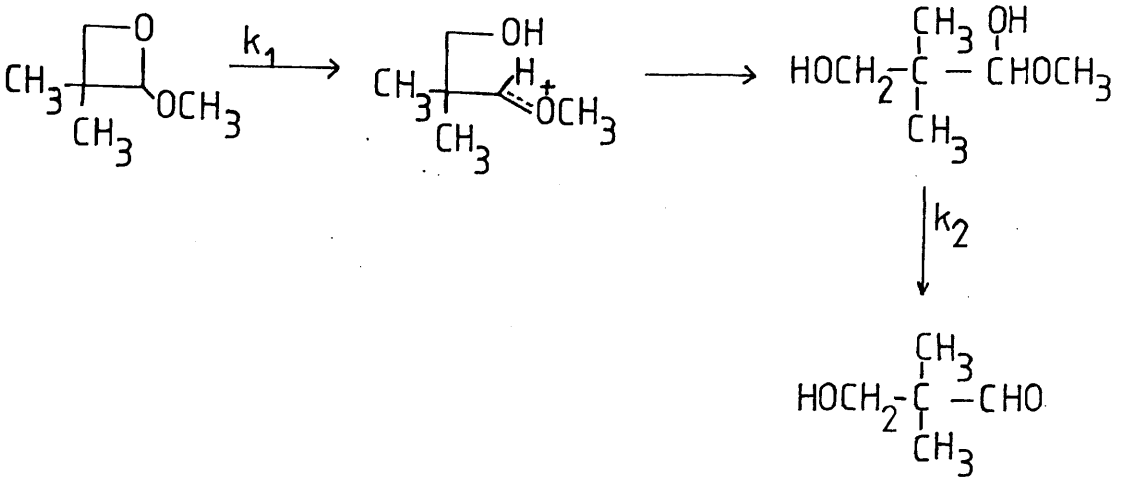


(17)

Two possible pathways were considered for the hydrolysis of (16).



Pathway 1



Pathway 2

According to the pathway 1 a rate enhancement should be expected in k_2 since the cyclic hemiacetal is highly strained. On the other hand in the pathway 2 the expected rate enhancement is in the C-O bond breaking step and this pathway was favoured by comparing the rates with those for acyclic acetals (see table below).

Table 2. Rates of acid-catalyzed acetal hydrolyses

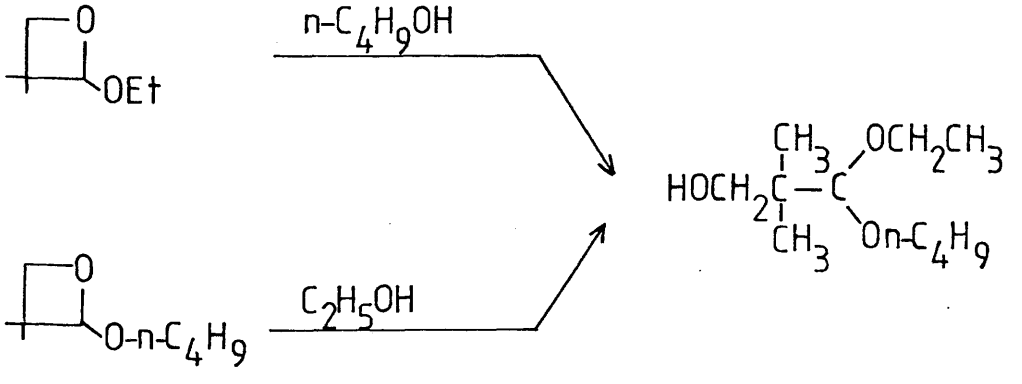
Cpd	Solvent	T, °C	k, $\underline{M}^{-1}$ s^{-1}
$CH_3CH(OEt)_2$	50% dioxane	25	0.248[a]
$(CH_3)_2CHCH(OEt)_2$	50% dioxane	25	0.164[a]
$CH_3CH(OEt)_2$	H_2O	30	0.490[b]
16	10% dioxane	30	2.24×10^5
14	10% dioxane	30	1.90×10^6 [c]

a - M. Kreevoy; Taft, R.W.Jr. J. Am. Chem. Soc., 77, 5590 (1955).

b - Koskikallio, J; Whalley, E., Trans Faraday Soc. 55, 809 (1959).

c - Reference 26

Other evidence was obtained from the products of reaction of analogous acetals with n-butyl and ethyl alcohols.



Scheme 4

The hydrolysis of the precursor (16) at 30°C followed the expression below

$$k'_1 = k_H a_H + k_{HA} [HA] \quad (4)$$

with

$$k_{H_3O^+} = 2.24 \times 10^5 \underline{\underline{M}}^{-1} s^{-1}$$

$$k_{H_2PO_4^-} = 0.418 \underline{\underline{M}}^{-1} s^{-1}$$

$$k_{ImH^+} + 0.207 \underline{\underline{M}}^{-1} s^{-1}$$

and the decomposition of the hemiacetal (17) followed:

$$k'_2 = k_{H^+} a_{H^+} + k_{OH^-} [OH^-] + k_{HA} [HA] + k_{A^-} [A^-] \quad (5)$$

with

$$k_{H_3O^+} = 80 \underline{\underline{M}}^{-1} s^{-1}$$

$$k_{OH^-} = 3.24 \times 10^5 \underline{\underline{M}}^{-1} s^{-1}$$

$$k_{H_2PO_4^-} = 6.20 \times 10^{-2} \underline{\underline{M}}^{-1} s^{-1}$$

$$k_{HPO_4^{-2}} = 2.38 \times 10^{-1} \underline{\underline{M}}^{-1} s^{-1}$$

$$k_{HOAc} = 3.07 \times 10^{-2} \underline{\underline{M}}^{-1} s^{-1}$$

$$k_{AcO^-} = 7.71 \times 10^{-3} \underline{\underline{M}}^{-1} s^{-1}$$

Capon[29,30] has found that α-acetoxy-α-methoxy-toluene hydrolyses with the rate determining step being the breakdown of hemiacetal. The pH rate profile was obtained in

water, T = 15°C, I = 0.05M showing that the decomposition of the hemiacetal is acid and base catalyzed. The hydrolysis of the analogous α-chloroacetoxy-α-methoxy toluene confirmed that finding since both substrates hydrolyse with the same rate constants indicating a common rate determining step which is the breakdown of the hemi-acetal.

Since both have different leaving groups the hydrolysis of the acetals should have different observed rate constants and that is not the case.

Other evidence was the observation of the reaction by NMR spectroscopy in (0.1M NaOAc, 0.1M DOAc) buffer in DMSO-D_2O (1:1 v/v) at 2°C. The experiments showed the fast formation of the hemiacetal (signal at δ = 5.44) attributed to the CH proton and its slow decomposition with formation of the final product, benzaldehyde (signal at 9.88).

The pH rate profile in question was obtained in the range 3.5 to 6.5 pH units and followed the equation:

$$k_o(s^{-1}) = 5.18 \times 10^{-3} s^{-1} + 261\ M^{-1}s^{-1}\ a_{H^+} + 6.87 \times 10^{5}\ M^{-1}s^{-1}\ a_{OH^-} \qquad (6)$$

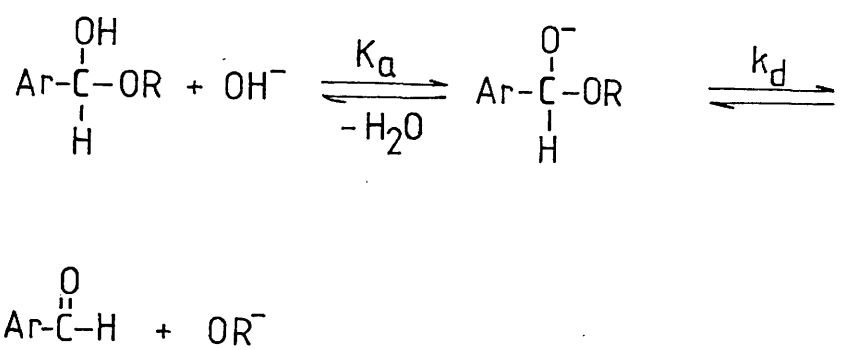
Jensen and Lenz[31] showed that the hemiacetal accumulates in the hydrolysis of substituted benzaldehyde diethyl acetals. Thus on quenching after c.a. 10% of

reaction by injection of base a rapid increase in absorbance was observed which was attributed to the base-catalyzed decomposition of the hemiacetal which had accumulated during reaction. It was concluded that the hemiacetal builds up a maximum of 40% of the total substrate concentration.

McClelland[32] has used a similar technique to study the hydrolysis of a series of substituted benzaldehyde alkyl hemiacetals.

The decomposition of benzaldehyde ethyl hemiacetal from the hydrolysis of benzaldehyde diethyl acetal as precursor is general-base catalyzed in phosphate buffer. The results reported are valid only for pH's above 7.0 because below that the reactions were not first order.

The proposed hydroxyde reaction mechanism is represented by the scheme:

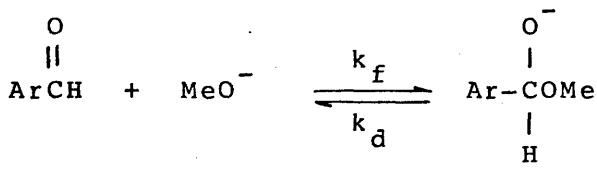


Scheme 5

with

$$k^3_{OH^-} = k_d K_a \qquad (7)$$

McLelland utilised a similar relationship to that used by Sorensen[33] for the reversible reaction of methoxide to substituted benzaldehydes in methanol.

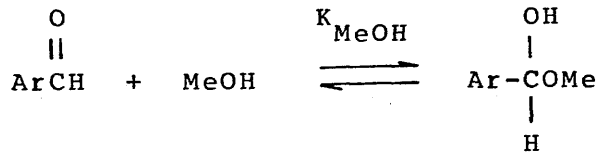


(8)

with an equilibrium constant

$$K_{MeO^-} = k_f/k_d \qquad (9)$$

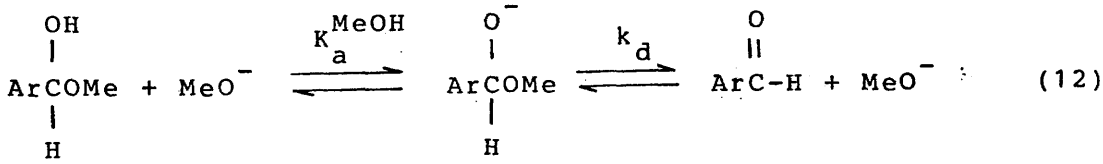
and the addition of neutral methanol according to the equation:



(10)

where $K_a^{MeOH} = K_{MeO^-} / K_{MeOH}$ (11)

is defined by the equation



(12)

The relationship obtained

$$k^{3}_{MeO^-} = k_d K_a^{MeOH} \qquad (13)$$

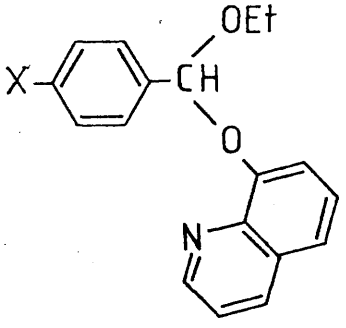
was utilised to calculate $\rho(k^{3}_{MeO^-})$

where

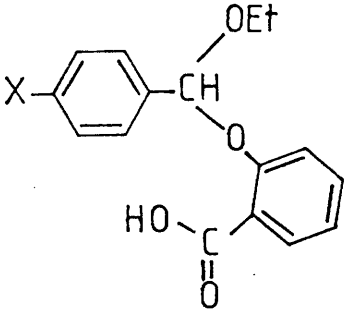
$$\rho(k^{3}_{MeO^-}) = \rho(k_d) + \rho(K_{MeO^-}) - \rho(K_{MeOH}) \qquad (14)$$

The $\rho(k^{3}_{MeO^-})$ value zero supported the small substituent effect for $k^{3}_{MeO^-}$ that was found.

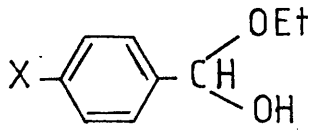
The breakdown of substituted benzaldehyde ethyl hemiacetals has received further attention lately. Fife[34] has studied the hydrolysis of substituted benzaldehyde ethyl salicyl and substituted benzaldehyde ethyl 8-quinolyl acetals, (18) and (19) and detected the hemiacetal (20)under



(19)



(18)



(20)

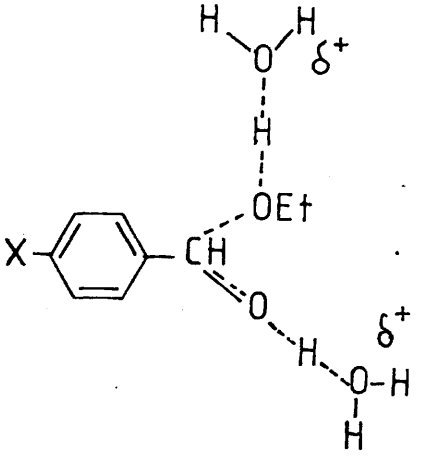
conditions where it could not be observed in the hydrolysis of the corresponding benzaldehyde diethyl acetals. Using (18) and (19) as precursors the pH-rate profiles for breakdown of the hemiacetals and for decomposition of the acetals were obtained by following the appearance of the aldehyde product at 260 nm and the release of salicylic acid at 303 nm respectively. Both were obtained in H_2O, T = 30°C, I = 0.1 M and in 50% dioxane-H_2O (v/v), T = 30°C, I = 0.1 M.

The breakdown of the hemiacetals was catalyzed by hydronium and hydroxide ions and a pH independent reaction was also observed from pH's 4 to 6.

Mechanistic possibilities were discussed for these three individual reactions in function of ρ values, solvent effects and D_2O solvent isotope effects.

The value of ρ = -1.90 was found for breakdown of the hemiacetal catalyzed by hydronium ion contrasting with ρ = -3.25 for hydronium catalyzed reaction of substituted

benzaldehyde diethyl acetals. That indicated that bond breaking has not proceeded to a great extent in the transition state. That value for ρ and solvent effect (k_D/k_H = 1.7 for m-chlorobenzaldehyde ethyl hemiacetal) indicated some degree of proton transfer in the transition state and the suggested structure is

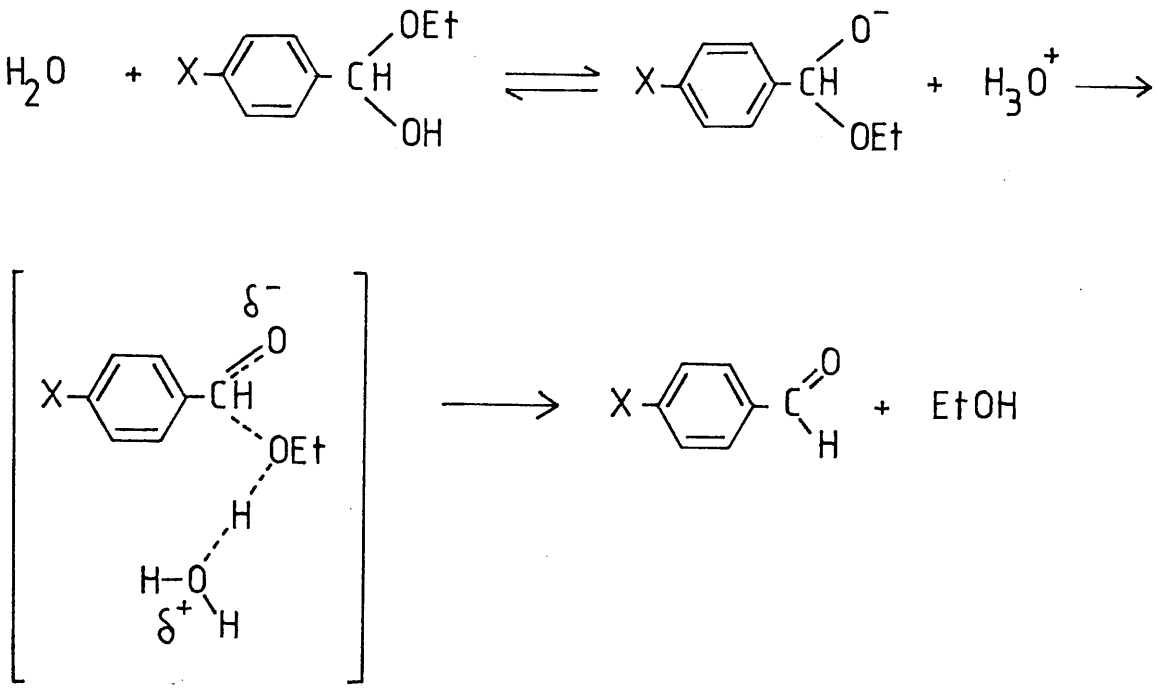


(21)

with less proton transfer from H_3O^+ to the leaving group than in the case of the transition state for hydrolysis of benzaldehyde diethyl acetals.

The latter value was compared with that for H_3O^+ catalyzed hydrolysis of acetals which are general acid catalyzed and shows proton transfer in the transition state (k_D/k_H = 1.0-1.5) and with k_D/k_H > 2.7 found for benzaldehyde diethyl acetals.

For the pH independent reaction (ρ = +0.35) the suggested mechanism involves concerted proton transfer with C-O bond breaking according to the scheme:

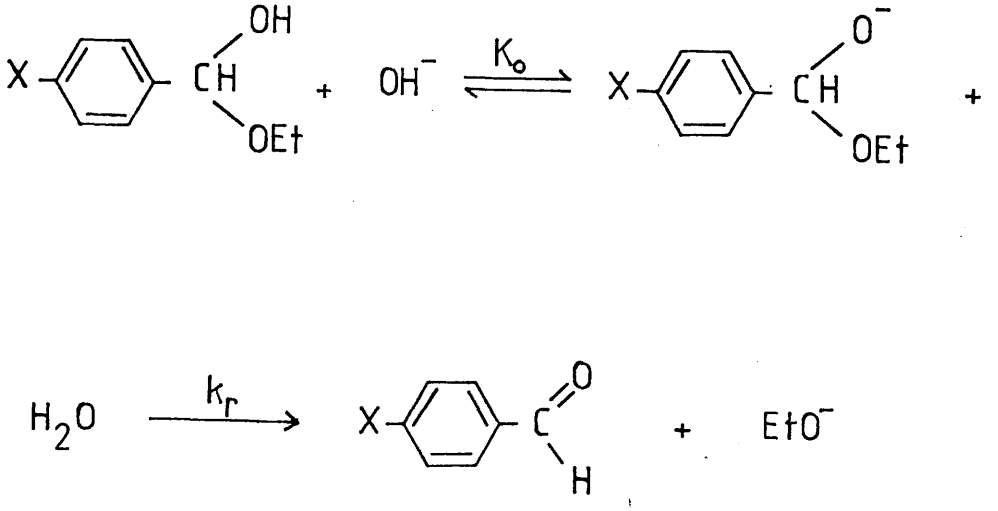


Scheme 6

That was the preferred mechanism in view of the electron withdrawing substituent in the benzaldehyde which should facilitate the removal of a proton from -OH group and hinder the protonation of -OEt and C-O bond breaking resulting in a small value of ρ. Similar mechanism was suggested for the general base-catalyzed breakdown of hemiacetals.[32,35]

In the case of hydroxide ion catalyzed breakdown of hemiacetal (ρ = -0.3) the suggested mechanism was the

two-step route represented by the scheme



Scheme 7

Other Mechanisms

Other variations in the mechanisms of acetal hydrolysis such as nucleophilically assisted breakage of the C-O bond and a change in the rate determining step to attack of water on the reversibly formed carbonium ion will be discussed in the Chapter III.

2.2 DISCUSSION

Breakdown of the hemiacetal

The hydrolysis of α-acetoxy-α-t-butoxy toluene has been studied in water, T = 15°C, I = 1.0 M by following the formation of benzaldehyde at λ = 250 nm. Also some kinetic runs were done with α-chloroacetoxy-α-t-butoxy toluene. The variation in the rate constants with pH is shown in Fig. 1 (p.218).

It was concluded that the rate determining step in the formation of benzaldehyde was the breakdown of the hemiacetal since rate constants obtained from the two precursors under identical conditions were, within experimental error, the same. The departure of two different leaving groups (acetoxy and chloroacetoxy) should have different effects on the observed rate if the decomposition of the precursors were the rate limiting step. This behaviour is similar to that observed by Capon[29] in a related work for the hydrolysis of the acylal with a methyl group instead of t-butyl.

From the pH rate profile it can be noted that there are hydronium-ion and hydroxide-ion catalyzed reactions which is the expected behaviour for decomposition of hemiacetals but not for acetals.[24,25] Other evidence came from NMR experiments in which rapid formation and slow breakdown of the hemiacetal was observed (Fig. 4, p246).

Hydrolysis of benzaldehyde di-t-butyl acetal

Benzaldehyde-di-t-butyl acetal was studied under the same conditions as those for α-acetoxy-α-t-butoxy toluene. For pH's below 6.42 identical rate constants were observed (within experimental error) suggesting that we were following the same rate determing step (Fig. 3, p223). An induction period was observed[36,37] at pH 6.42 (Fig. 2, p220) indicating that consecutive reactions with similar rate constants were taking place. However for pH's above 6.42 the reaction became again first-order but the rate constants were much smaller than those for the other precursors (in the highest pH studied with this acetal, 7.82, the reaction was 140-fold slower than that of the acetoxy compound). These observations indicated that in some way the hydrolysis of the acetal was occurring differently from the others for pH's above 6.42, in other words, a change in the mechanism of hydrolysis or in the rate determining step was taking place.

The most reasonable explanation is that at these high pH's the rate determining step is the decomposition of the acetal, because decomposition of the hemiacetal has become very fast due to OH^- catalysis.

NMR experiments were also carried out with this acetal in a similar way to that with α-acetoxy-α-t-butoxy toluene (Fig. 5, p247) and the hemiacetal was detected.

Buffer catalysis

Buffer catalysis by acetate, imidazole and phosphate was observed in the hydrolysis of α-acetoxy-α-t-butoxy toluene and in view of the already accepted rate determining step it was clear that the breakdown of the hemiacetal was being catalyzed by these buffers. With borate buffer an anomalous behaviour was observed with the rate constants decreasing with increasing the acid concentration (Table 14, p208). Nevertheless the main concern with this buffer was to obtain and keep a constant desirable pH. Although the [HA] has been varied the intercepts were the only values utilized for further calculations (pH rate profile). However for the hydrolysis of benzaldehyde di-t-butyl acetal for pH's at and above 6.42 no buffer catalysis was observed (Tables 27 to 30, p229 to 232). There is a trend for the rates to be constant on increasing the weak acid concentration but even so the values plotted in the pH profile were the intercepts from plots of k_{obs} against [HA] and no meaning can be attributed to the negative slopes (with standard deviations in the range of 15-50%). However these plots were utilized to provide the intercepts which were represented in the pH profile for formation of benzaldehyde (Fig. 3, p223).

Analysis of results

The results shown on the tables 27 to 30 in which the rate determining step was, as stated before, the breakdown of the acetal indicated that general-acid catalysis was absent. The decrease of the $\underline{k}_o$ with increasing pH (6.42 to 7.81) suggested on the other hand that the hydrolysis of the acetal was hydronium-ion catalyzed and the usual plot of $\underline{k}_o$ versus $[H^+]$ yielded $\underline{k}_{H^+} = 7.02 \times 10^3$ $\underline{\underline{M}}^{-1}$ s^{-1} (s.d. 3.63%), (T = 15°C). The rate constant for the water reaction $\underline{k}_{H_2O} = 1.28 \times 10^{-4}$ s^{-1} showed a high standard deviation (38%) and so can be taken to be zero within experimental error.

Jensen and co-workers[8] claimed the observation of general acid catalysis for the hydrolysis of benzaldehyde diethyl acetal in cacodylate buffer and we have chosen that buffer and applied the same equation (23) (p222) in an attempt to observe general acid catalysis in the hydrolysis of benzaldehyde di-t-butyl acetal at pH's 7.26 to 7.16.

The $\underline{k}_{HA}$ value obtained in that way was 6.93×10^{-3} $\underline{\underline{M}}^{-1}$ s^{-1} (s.d. 32%), (T = 25°C) and $\underline{k}_{H^+} = 2.70 \times 10^4$ $\underline{\underline{M}}^{-1}$ s^{-1}. Although the positive value for $\underline{k}_{HA}$ would indicate a general-acid catalysis the high standard deviation prevented a further conclusion. In addition we applied Jensen's equation (23) to our results with imidazole and phosphate (pH 6.42-7.81) but the plots all had negative slopes which indicate that there is no detectable general acid catalysis.

Anderson and Fife[22] claimed the observation of an "extremely large general acid catalysis" in the hydrolysis of benzaldehyde di-t-butyl acetal with its decomposition being the rate determining step. They studied the reaction in acetate, succinate and phosphate buffers but only reported the pH's for acetate buffers; these were 5.42 and 5.67. More recently Fife and Przystas[34] reaffirmed that "conclusions regarding general-acid catalysis in reactions of benzaldehyde acetals have not been influenced by hemi-acetal build up" but only mentioned that benzaldehyde di-t-butyl acetal was studied in phosphate buffers at pH's 6.5-7.0.

Table 3 affords a better comparison of the rate constants.

Table 3. Rate constants for decomposition of $PhCH(OBu^t)(OH)$ and $PhCH(OBu^t)_2$, I = 1.0 M (KCℓ)

	k_{H^+}(15°C) M^{-1} s^{-1}	k_{H^+}(25°C) M^{-1} s^{-1}
$PhCH(OBu^t)(OH)$	1.26×10^3 [a]	3.62×10^3 [b]
$PhCH(OBu^t)_2$	7.02×10^3 [c]	2.70×10^4 [d]
"$PhCH(OBu^t)_2$"		3.31×10^3 [e]

a - Value obtained from the pH profile eq. (21) using $PHCH(OBu^t)(OAc)$ and $PhCH(OBu^t)_2$ as precursors.

b - Value obtained at pH 4.48 (with HCℓ, table 32) using $PhCH(OBu^t)_2$ as precursor.

c - Value reported in the table (33) for pH's in the range 6.42 to 7.81.

d - Value obtained with cacodylate buffer (table 31) $[HA]/[A^-] = 1/10$ applying Jensen's equation.

e - Value reported by Fife[22] using acetate buffer.

The conditions utilized in this work were very similar to those of Anderson & Fife. The basic difference was the temperature (15°C in this work) and the lack of observation of an induction period by Anderson & Fife could be attributed to that factor. However we have carried out some runs in acetate and cacodylate buffer at 25°C (cf table 21, p221) in which an induction period was observed. Then it can be concluded that either Anderson & Fife had carried out the experiments in a pH range "outside" that where there were consecutive reactions with similar rates or that they have failed to observe the induction period.

From the above considerations and comparing the $\underline{k}_{H^+}$ value reported by Anderson & Fife with those for breakdown of the hemiacetal and acetal it is clear that their values lie closest to that for breakdown of the hemiacetal. In order to be certain of this we carried out an experiment under the exact conditions as those reported by Anderson & Fife (Ref. 22, Table 3) and obtained a value of 3.31×10^3 $\underline{\underline{M}}^{-1}$ s^{-1} for $\underline{k}_{H^+}$ at 25°C compared to their value of 3.62×10^3 $\underline{\underline{M}}^{-1}$ s^{-1}. Since we had already observed that the rate determining step was the breakdown of the hemiacetal it is assumed that Anderson & Fife were observing the same in acetate and probably succinate buffers.

We have also searched for general-acid catalysis in the hydrolysis of benzaldehyde diethyl acetal using similar conditions to those of Jensen and co-workers.[8] For acetate and cacodylate buffers most of the slopes from the plots of equation (23) yielded considerable negative values. In the case of acetate buffer ($[HA]/[A^-] = 1/10$) the experimental was carried out in presence of two different electrolytes, KCℓ and $NaNO_3$. This was the procedure recommended by Salomaa and Kankaanpera[41] to test whether a marginal case of general-acid catalysis really arises from salt effects. The only condition which yielded a positive slope (table 36) was when $NaNO_3$ was used but the standard deviation was so high that the observed value was zero within experimental error. This is in agreement with Fife and Jao[5] who did not find general-acid catalysis for the hydrolysis of benzaldehyde diethyl acetal in 50% dioxane-water (see also ref. 34 footnote 27).

Comparing the hydronium ion catalytic constants for benzaldehyde acetals with those of the hemiacetals (Table 4) it can be noted that methyl and ethyl substituents show the same trend with the decomposition of the acetal being slower (c.a. 19-fold for methyl and 2.4-5.0-fold for ethyl) than the hemiacetal. However for t-butyl substituents the

Table 4

	$PhCH(OR)_2$		$PhCH(OR)(OH)$	
R	$k_{H_3O^+}$, M^{-1} s^{-1}		$k_{H_3O^+}$, M^{-1} s^{-1}	
CH_3	29.7[a]	(25°C, I=0.05M)	557[b]	(25°C)
CH_2CH_3	203[c]	(30°C, I=0.1M)	936[c]	(30°C, I=0.1M)
	145[d]	(25°C, I=0.5M)	350[d]	(25°C, I=0.5M)
$C(CH_3)_3$	7020	(15°C, I=1.0M)	1260	(15°C, I=1.0M)

a. E. Anderson, B. Capon, J. Chem Soc. Chem. Comm., 1969, 390-91.

b. B. Capon, K. Nimmo, G.L. Reid, J. Chem. Soc. Chem. Comm., 871 (1976).

c. T.H. Fife, T.J. Przystas, J. Am. Chem. Soc., 103, 4884 (1981).

d. J.L. Jensen, P.A. Lenz, J. Am. Chem. Soc., 100, 1291 (1978).

acetal decomposes ca. 5.6-fold faster than the hemiacetal indicating that in this case the accumulation of the hemiacetal is going to be higher than in the others (Me and Et substituents) in view of its faster formation compared to its breakdown.

The failure to observe general-acid catalysis enables a limit to be placed of the α-value by use of an expression derived by Jensen and Jencks.[18] This was $\alpha > 0.91$ for benzaldehyde di-t-butyl acetal in cacodylate buffer, $[HA]/[A^-] = 1/10$ (cf table 31, p233) and $\alpha > 0.82$, $\alpha > 0.85$ for benzaldehyde diethyl acetal in acetate and cacodylate buffers respectively (cf table 35, p239; table 38, p242).

The same treatment for Jensen's result yielded $\alpha_{min} = 0.88$ while the reported α-value by Jensen and co-workers[8] was $\alpha = 0.87$.

The results from the hydrolysis of benzaldehyde di-t-butyl acetal and α-acetoxy-α-t-butoxy toluene indicated that the former was hydrolysing with two different rate determining steps depending on the pH range whereas for the latter the limiting step was always the breakdown of the hemiacetal under the condition studied.

For comparison purposes the pH-rate profile for decomposition of benzaldehyde methyl hemiacetal[29] was included in the Fig. 1. Both profiles have the same shape and followed the kinetic equations (21) and (22) which were

written based on the results on the tables 15 and 16. From the negative value (with a high standard deviation) for $\underline{k}_o$ term for breakdown of the t-butyl hemiacetal we can assume that experimentally this term is absent. The catalytic constants for both hemiacetals are summarised in the following table.

Table 4-A. Catalytic constants for breakdown of hemiacetals [a]

	PhCH(OR)(OH)			$CH_2(OR)(OH)$	
R	CH_3 [b]	CH_2CH_3 [c]	$C(CH_3)_3$	CH_3 [d]	CH_2CH_3 [d]
k_{H^+}	261	936	1260	0.58	0.74
k_{OH^-}	1.82×10^{6}	2.47×10^{6}	4.86×10^{4}	2.34×10^{3}	1.3×10^{3}
k_{H_2O}	6.17×10^{-3}	1.26×10^{-2}	-	1.81×10^{-3}	1.63×10^{-3}
k_{AcOH}	7.79×10^{-2}	-	9.40×10^{-2}	5.1×10^{-3}	6.7×10^{-3}
k_{AcO^-}	18.5×10^{-2}	-	4.12×10^{-2}	9.6×10^{-3}	6.9×10^{-3}

a - The units are $\underline{\underline{M}}^{-1}$ s^{-1} except for k_{H_2O} which is s^{-1}.

b - At 15°C. B. Capon, K. Nimmo, G.L. Reid, Chem. Comm., 871 (1976)

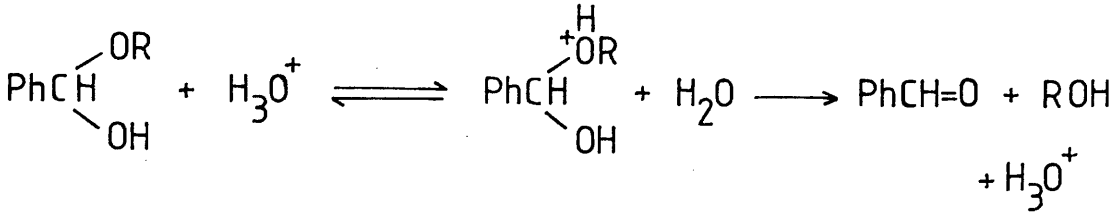
c - At 30°C. T.H. Fife, T.J. Przystas, J. Am. Chem. Soc., 103, 4844 (1981).

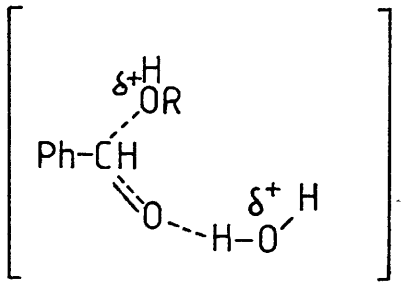
d - L.H. Funderburk, L. Aldwin, W.P. Jencks, J. Am. Chem. Soc., 100, 5444 (1978).

The replacement of a methyl group by a more electron-releasing substituent such as t-butyl enhanced the rate for the H_3O^+-catalyzed reaction in the hydrolysis of benzaldehyde hemiacetal by a factor of ca. 5-fold. That is the expected behaviour once that this substituent should facilitate the protonation of the oxygen in the alkyl group whereas the opposite effect was observed in the OH^--catalyzed reaction with the removal of the proton from the OH-group being accelerated by methyl (ca. 37-fold faster) rather than by t-butyl substituents. The same trend is observed for the general acid and base catalyzed reactions although the magnitude of enhancement is much less than for the specific reactions. The value of k_{AcOH} is 1.2-fold smaller for methyl while k_{AcO^-} is ca. 5-fold faster than t-butyl substituents. Similar behaviour was observed by Funderburk and Jencks[35] for breakdown of formaldehyde methyl and ethyl hemiacetals. The trend was the same with the acid-catalyzed reactions being ca. 1.3 faster for ethyl substituents and the base-catalyzed reactions ca. 1.4-1.8 faster for methyl substituents.

The most likely mechanism for the hydrolysis of benzaldehyde t-butyl hemiacetal catalyzed by hydronium-ion and hydroxide-ion should involve transition states similar to those suggested by Funderburk and Jencks and according to the following scheme:

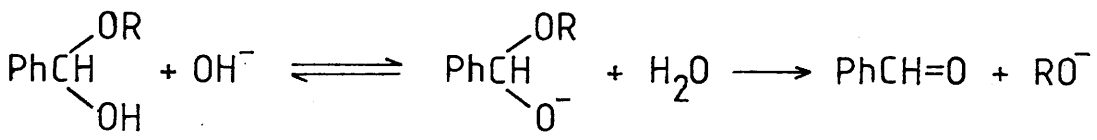
Acid-catalyzed reaction.

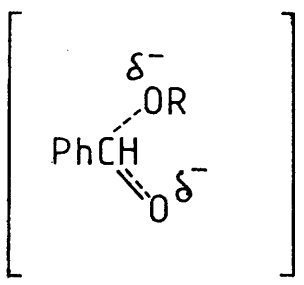




transition state

Base-catalyzed reaction.





transition state

2.3 EXPERIMENTAL

2.3.1 Kinetic experimental

Spectrophotometric determination

The spectrophotometric rate determinations were performed on a Cary 16 spectrophotometer working on-line to a Digico Micro 16P Computer and on a Pye-Unicam SP8-200 spectrophotometer, both with a thermostatted cell compartment. The temperature was usually kept constant at 15° ± 0.05 and measured in the cell after each run. In some cases, which will be indicated, the temperature was kept at 25° ± 0.05. The experimental data were fitted to the equation:

$$\ell n\ (A_\infty - A_t) = -kt + \ell n\ (A_\infty - A_o)$$

by the linear least squares method using a computer program. A check was kept on whether the reactions were really first-order by looking for the incursion of an induction period and testing whether the 1st, 2nd and 3rd half-lives were all equal to one another. When the reaction was not first-order the rate constant for the breakdown of the acetal, k_1, was evaluated from the equation for the variation of the extinction coefficient with time for two consecutive first-order reactions.[42]

$$A \xrightarrow{k_1} B \xrightarrow{k_2} C$$

$$\varepsilon_{calc} = \varepsilon_A e^{-k_1 t} + \varepsilon_B k_1 (e^{-k_1 t} - e^{-k_2 t})/(k_2 - k_1) + \varepsilon_C [1 - (k_1 e^{-k_2 t} - k_2 e^{-k_1 t})/(k_1 - k_2)]$$

The values of ε_A and ε_B were taken to be equal and calculated from the initial absorbance and the value of ε_C was calculated from the ∞- absorbance. The value of $\underline{k}_2$, rate constants for breakdown of the hemiacetal, was that obtained from experimental with α-acetoxy-α-t-butoxy toluene. The value of $\underline{k}_1$ was varied to minimize the sum of the square of the relative residuals, i.e.,

$$\Sigma (A_{obs} - A_{calc})^2 / A_{obs}^2$$

A_{obs} were the experimental values of absorbance at various times and the values of A_{calc} were obtained from the value of ε_{calc} as calculated from the above equation. The rate constant obtained in this way was not as accurate as that obtained when the reaction was first-order.

The values of observed rate constants ($\underline{k}_{obs}$) were obtained from the weighted average of two to six runs using a suitable program for that purpose.

2 ml of the buffer solution was put in a quartz cell of 10 mm pathlength, allowed to equilibrate at least for 20 minutes and 20 µℓ of the stock solution, prepared in dioxan.

For the pH measurements a combined electrode 6K2401B and a Radiometer PHM64 pH meter were used.

Solutions

All the chemicals used were ANALAR grade and no further purification was required.

The ionic strength of the buffer solutions, prepared with distilled and degassed water, was kept constant by adding an electrolyte.

Diluted buffer solutions were made by using a stock solution of the same electrolyte at the same ionic strength.

Hydrolysis of α-acetoxy-α-t-butoxy-toluene

The kinetics of α-acetoxy-α-t-butoxy-toluene was carried out at pH's from 4.23 to 8.38 using acetate, phosphate, borate and imidazole buffers.

The ionic strength was made up to 1.0M with KCℓ and formation of the aldehyde product followed at λ = 250 nm, T = 15°C ± 0.05.

α-Chloroacetoxy-α-t-butoxy-toluene was studied under the same conditions. In this case, due to the very fast decomposition of the substrate, the stock solution was prepared in a different way: 1 μℓ of the substrate was added to 150 μℓ of dioxan and 5 μℓ of this stock solution was put into the cell containing 2 ml of buffer and 15 μℓ of dioxan.

The observed rate constants for both substrates were the same within the experimental error, suggesting that we were following the breakdown of the benzaldehyde t-butyl hemiacetal as the rate determining step.

Small variations in pH (0.05-0.08) were observed with buffers of different dilutions and the values quoted in the following tables were those obtained by extrapolation to zero-buffer concentration.

Table 5 . Acetate catalyzed hydrolysis of α-t-butoxy-α-acetoxy-toluene at 15°C

[AcOH] = 2 [AcO^-] I = 1.0 M pH = 4.23

[HA], M	10^1 k_{obs} (s^{-1})	s.d. (%)
0.05	0.7842, (0.7813)[a]	2.67 (2.70)
0.04	0.7756	3.19
0.03	0.7600	2.31
0.02	0.7568	2.51
0.01	0.7350	3.16

The plot of k_{obs} versus [HA] yielded

Slope = 0.117 M^{-1} s^{-1} s.d. = 12.44%

Int = 0.727 x 10^{-1} s^{-1} s.d. = 0.66%

a - The values in brackets were obtained from hydrolysis of α-chloroacetoxy-α-t-butoxy-toluene.

Table 6. Acetate catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C

[AcOH] = 1.43 [AcO^-] I = 1.0 M pH = 4.53

[HA], M	10^1 k_{obs} (s^{-1})	s.d. (%)
0.025	0.4662	0.11
0.020	0.4505	0.44
0.015	0.4348	0.21
0.010	0.4090	0.51
0.005	0.3548	0.24

The plot of k_{obs} versus [HA] yielded

Slope = 0.529 M^{-1} s^{-1} s.d. = 17.25%

Int = 0.344 x 10^{-1} s^{-1} s.d. = 4.40%

Table 7. Acetate catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C

[AcOH] = 1/2 [AcO^-] I = 1.0 M pH = 4.72

[HA], M	10^1 k_{obs} (s^{-1})	s.d. (%)
0.025	0.2579	2.00
0.020	0.2461	0.79
0.015	0.2471	3.50
0.010	0.2362	1.08
0.005	0.2285	0.34

The plot of k_{obs} versus [HA] yielded

Slope = 0.137 M^{-1} s^{-1} s.d. = 15.22%

Int = 0.222 x 10^{-1} s^{-1} s.d. = 1.56%

Table 8. Acetate catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C

[AcOH] = 1/4 [AcO^-] I = 1.0M pH = 5.10

[HA], M	10^1 k_{obs} (s^{-1})	s.d. (%)
0.025	0.1344, (0.1294)[a]	1.39 (0.70)
0.020	0.1239	0.35
0.015	0.1161	1.08
0.010	0.1108	0.38
0.005	0.1029	0.49

The plot of k_{obs} versus [HA] yielded

Slope = 0.152 M^{-1} s^{-1} s.d. = 6.52%

Int = 0.948 x 10^{-2} s^{-1} s.d. = 1.74%

a - The values in brackets were obtained from hydrolysis of α-chloroacetoxy-α-t-butoxy-toluene.

Table 9. Acetate catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C

[AcOH] = 1/10 [AcO^-] I = 1.0M pH = 5.36

[HA], M	10^1 k_{obs} (s^{-1})	s.d. (%)
0.025	0.1224	1.20
0.020	0.1098	1.36
0.015	0.0948	0.23
0.010	0.0883	0.52
0.005	0.0676	0.26

The plot of k_{obs} versus [HA] yielded

Slope = 0.274 M^{-1} s^{-1} s.d. = 1.85%

Int = 0.541 x 10^{-2} s^{-1} s.d. = 1.55%

Table 10. Imidazole catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C

$[ImH^+]$ = 10 [Im] I = 1.0M pH = 6.42

$[Im]_T$, M	10^2 k_{obs} (s^{-1})	s.d. (%)
0.110	0.8865 (0.8763)[a]	0.59 (3.39)
0.088	0.7241	0.71
0.066	0.5867	0.31
0.044	0.4442	2.15
0.022	0.3016	0.94

The plot of k_{obs} versus [HA] yielded

Slope = 0.725×10^{-1} M^{-1} s^{-1} s.d. = 1.62%

Int = 0.154×10^{-2} s^{-1} s.d. = 0.51%

a - The values in brackets were obtained from hydrolysis of α-chloroacetoxy-α-t-butoxy-toluene.

Table 11. Imidazole catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C

$[ImH^+] = [Im]$ $I = 1.0\underline{M}$ pH = 7.36

$[Im]_T$, $\underline{M}$	$10^1\ \underline{k}_{obs}(s^{-1})$	s.d. (%)
0.20	0.6375, (0.6022)[a]	1.00 (2.33)
0.16	0.5149	0.87
0.12	0.4054	2.19
0.08	0.2880	1.57
0.04	0.1709	0.75

The plot of $\underline{k}_{obs}$ versus [HA] yielded

Slope = 0.494 $\underline{M}^{-1}\ s^{-1}$ s.d. = 0.85%

Int = $0.553 \times 10^{-2}\ s^{-1}$ s.d. = 5.92%

a - The values in brackets were obtained from hydrolysis of α-chloroacetoxy-α-t-butoxy-toluene.

Table 12. Imidazole catalyzed hydrolysis of α-acetoxy-α-acetoxy-α-t-butoxy-toluene at 15°C

$[ImH^+] = 1/3\ [Im]$ $I = 1.0\underline{M}$ pH = 7.81

$[Im]_T$, $\underline{M}$	$10^1\ \underline{k}_{obs}(s^{-1})$	s.d. (%)
0.40	0.1793	2.86
0.32	0.1577	1.44
0.24	0.1250	3.48
0.16	0.0837	0.44
0.08	0.0507	2.21

The plot of $\underline{k}_{obs}$ versus [HA] yielded

Slope = $1.66\ \underline{M}^{-1}\ s^{-1}$ s.d. = 5.80%

Int = $0.199 \times 10^{-1}\ s^{-1}$ s.d. = 32.00%

Table 13. Phosphate catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene

$[KH_2PO_4] = 1/10\ [K_2HPO_4]$ I = 1.0M pH = 7.48

[HA], M	$10^1\ k_{obs}\ (s^{-1})$	s.d. (%)
0.010	0.1445	0.65
0.008	0.1283	0.72
0.006	0.1108	0.96
0.004	0.0915	0.09
0.002	0.0744	0.12

The plot of k_{obs} versus [HA] yielded

Slope = 0.845 $M^{-1}\ s^{-1}$ s.d. = 1.61%

Int = $0.568 \times 10^{-2}\ s^{-1}$ s.d. = 1.66%

Table 14. Borate catalyzed hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C

$[H_3BO_3] = 4\ [H_4BO_4^-]$ $\quad I = 1.0\underline{M}$ $\quad pH = 8.38$

$[H_3BO_3]$, $\underline{M}$	$10^1\ \underline{k}_{obs}(s^{-1})$	s.d. (%)
0.10	0.3706	0.36
0.08	0.3977	0.39
0.06	0.4262	0.57
0.04	0.4531	0.08
0.02	0.4825	0.39

The plot of $\underline{k}_{obs}$ versus [HA] yielded

Slope = $-0.139\ \underline{M}^{-1}\ s^{-1}$ $\quad$ s.d. = 0.80%

Int = $5.10 \times 10^{-2}\ s^{-1}$ $\quad$ s.d. = 0.14%

RESULTS

The pH rate profile for breakdown of benzaldehyde t-butyl hemiacetal (Fig. 1) was based on the general kinetic equation

$$k_{obs} = k_O + k_{H^+}[H^+] + k_{OH^-}[OH^-] + k_{HA}[HA] + k_{A^-}[A^-] \quad (15)$$

Considering the dissociation of the acid species:

$$HA \rightleftharpoons H^+ + A^-$$

the dissociation constant will be

$$Ka = \frac{[H^+][A^-]}{[HA]} \quad (16)$$

where

$$[A^-] = \frac{Ka}{[H^+]}[HA] \quad (17)$$

Putting eq.(17) into eq.(15) we have:

$$\underline{k}_{obs} = k_O + k_{H^+}[H^+] + k_{OH^-}[OH^-] + \left(k_{HA} + \frac{Ka}{[H^+]}\right)[HA] \quad (18)$$

Therefore if $\underline{k}_{obs}$ is plotted against [HA] a straight line should be obtained with

$$\text{Int} = k = k_O + k_{H^+}[H^+] + k_{OH^-}[OH^-] \quad (19)$$

and

$$\text{Slope} = k_{HA} + k_{A^-}\frac{Ka}{[H^+]} \quad (20)$$

The intercept values were used for the pH profile (Table 15) which follows the equation

$$k(s^{-1}) = 1.26 \times 10^3\, a_{H^+} + 4.86 \times 10^4\, a_{OH^-} \quad (21)$$

No k_O term could be detected within experimental error.

The breakdown of the benzaldehyde methyl hemiacetal follows the equation:

$$k(s^{-1}) = 6.17 \times 10^{-3} + 2.32 \times 10^{2}\, a_{H^+} + 1.82 \times 10^{6}\, a_{OH^-} \qquad (22)$$

These values were obtained from Ref. 29 and were introduced in this Section in order to compare the reactivity of both hemiacetals.

General catalysis for breakdown of benzaldehyde t-butyl hemiacetal was found with acetate and imidazole buffers using equation (20) and the constants (Tables 19 and 20) obtained are:

$$\underline{k}_{AcOH} = 9.40 \times 10^{-2}\ \underline{\underline{M}}^{-1}\ s^{-1} \qquad s.d. = 3 \times 10^{2}$$

$$\underline{k}_{AcO^-} = 4.12 \times 10^{-2}\ \underline{\underline{M}}^{-1}\ s^{-1} \qquad s.d. = 1.5 \times 10^{-2}$$

$$\underline{k}_{ImH^+} = 5.73 \times 10^{-4}\ \underline{\underline{M}}^{-1}\ s^{-1} \qquad s.d. = 7.6 \times 10^{-3}$$

$$\underline{k}_{Im} = 5.23 \times 10^{-1}\ \underline{\underline{M}}^{-1}\ s^{-1} \qquad s.d. = 3.90 \times 10^{-3}$$

Table 15. Rate constants for the pH rate profile for breakdown of benzaldehyde t-butyl hemiacetal[a].

pH	10^2 k(s^{-1})	s.d. (%)
4.23	7.272 (7.493)[b]	0.60 (0.50)
4.53	3.438 (3.355)	4.50 (5.60)
4.72	2.225 (2.176)	1.60 (1.80)
5.10	0.948 (0.910)	1.70 (1.80)
5.36	0.541 (0.541)	1.50 (3.30)
6.42	0.154	5.10
7.36	0.553	5.9
7.48	0.568	1.6
7.81	1.994	32
8.38	5.09	0.14

a - T = 15°C. I = 1.0 M (KCℓ)

b - When using benzaldehyde di-t-butyl acetal as precursor.

Table 16. Rate constants for the pH rate profile for breakdown of benzaldehyde methyl hemiacetal at 15°, I = 0.1M.[a]

pH	10^2 k_{obs} (s^{-1})
4.65	1.119
4.41	1.566
4.96	0.883
4.82	0.950
4.20	2.230
3.70	5.474
3.95	3.520
4.76	0.959
5.05	0.845
3.64	5.650
4.63	1.170
5.37	0.790
6.12	1.460
6.26	1.384
6.42	3.080

a - Ref. 29; using α-acetoxy-α-methoxy toluene as precursor.

Table 17. Catalytic constants for breakdown of benzaldehyde t-butyl hemiacetal at 15°C, I = 1.0M.

VALUE OF KW 4.49779882E-15 TEMPERATURE 15DEGS
5 ITERATIONS USED
KO=-8.05007515E-04 EST KO=4E-04
S.D.=1.45308307E-03 AS PERCENT -180.505529

KH=1256.64742 EST KH=1000
S.D.=33.3937265 AS PERCENT 2.65736642

KOH=48570.5791 EST KOH=50000
S.D.=2183.76146 AS PERCENT 4.49605811

PH	K	CALK	RESIDUALS
4.23	.07493	.0731955893	1.73441067E-03
4.23	.07272	.0731955893	-4.75589331E-04
4.53	.03438	.0362886901	-1.90869006E-03
4.53	.03355	.0362886901	-2.73869006E-03
4.72	.02225	.0231513807	-9.01380721E-04
4.72	.02176	.0231513807	-1.39138071E-03
5.1	9.48E-03	9.20440048E-03	2.75599523E-04
5.1	9.1E-03	9.20440048E-03	-1.04400475E-04
5.36	5.41E-03	4.73050397E-03	6.79496026E-04
5.36	5.41E-03	4.73050397E-03	6.79496026E-04
6.42	1.54E-03	2.47366674E-04	1.29263333E-03
7.36	5.53E-03	4.25449236E-03	1.27550764E-03
7.48	5.68E-03	5.8340113E-03	-1.54011295E-04
7.81	.01994	.0133194623	6.62053773E-03
8.38	.0509	.0516053001	-7.05300103E-04

Table 18. Catalytic constants for breakdown of benzaldehyde methyl hemiacetal at 15°C, I = 0.1M.

VALUE OF KW 4.49779882E-15 TEMPERATURE 15DEGS
5 ITERATIONS USED
KO=6.16624198E-03 EST KO=5.7E-03
S.D.=1.6363084E-03 AS PERCENT 26.5365584

KH=232.113223 EST KH=243
S.D.=10.810271 AS PERCENT 4.65732665

KOH=1825598.74 EST KOH=980000
S.D.=258271.341 AS PERCENT 14.147213

PH	K	CALK	RESIDUALS
3.64	.0565	.059376153	-2.87615298E-03
3.7	.05474	.0525200725	2.21992751E-03
3.95	.0352	.0322829564	2.91704359E-03
4.2	.0223	.0209417348	1.35826516E-03
4.41	.01566	.0154075541	2.52445941E-04
4.63	.0117	.0119577791	-2.57779066E-04
4.65	.01119	.0117293896	-5.39389585E-04
4.76	9.59E-03	.0106724114	-1.0824114E-03
4.82	9.5E-03	.0102219248	-7.21924825E-04
4.96	8.83E-03	9.46018103E-03	-6.30181024E-04
5.05	8.45E-03	9.15626235E-03	-7.06262352E-04
5.37	7.9E-03	9.08127693E-03	-1.18127693E-03
6.12	.0146	.0171667556	-2.56675556E-03
6.26	.01384	.0212356811	-7.3956811E-03
6.42	.0308	.0278520814	2.94791861E-03

Table 19. Slopes from the plot of $\underline{k}_{obs}$ versus [Acetic acid] for the hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C.

I = 1 $\underline{\underline{M}}$

[HA]/[A^-]	pH	Slope ($\underline{\underline{M}}^{-1}$ s^{-1})
2.0	4.23	0.1172
0.5	4.72	0.1374
0.25	5.10	0.1522
0.10	5.36	0.2744

The plot of Slope versus [H^+] (cf eq.20) yielded:

Slope = $\underline{k}_{A^-}$ x Ka* = 7.19×10^{-7} s^{-1}

Then: $\underline{k}_{A^-} = 4.12 \times 10^{-2}$ $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 29%

Int = $\underline{k}_{HA} = 9.40 \times 10^{-2}$ $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 32%

* $K^{15°}_{Acet} = 1.745 \times 10^{-5}$ $\underline{\underline{M}}$. Ref: Handbook of Chemistry and Physics. 59th Ed. 1978-79.

Table 20. Slopes of the plot of $\underline{k}_{obs}$ versus $[ImH^+]$ for the hydrolysis of α-acetoxy-α-t-butoxy-toluene at 15°C, I = 1.0M

$[HA]/[A^-]$	pH	10^2 x Slope ($\underline{\underline{M}}^{-1}s^{-1}$)
10	6.42	7.248
1	7.36	58.00
0.33	7.81	165.6

The plot of Slope versus $1/[H^+]$ (cf eq. 20) yielded:

Slope = $\underline{k}_{A^-}$. Ka^* = 2.56×10^{-8} s^{-1}

Then, $\underline{k}_{A^-} = 5.23 \times 10^{-1}$ $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 0.75%

Int = $\underline{k}_{HA} = 5.74 \times 10^{-4}$ $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 13%

* $Ka^{15°}_{Im.} = 4.898 \times 10^{-8}$ $\underline{\underline{M}}$. Ref: Dissociation Constants of Organic Bases in Aqueous Solution. Perrin p.190.

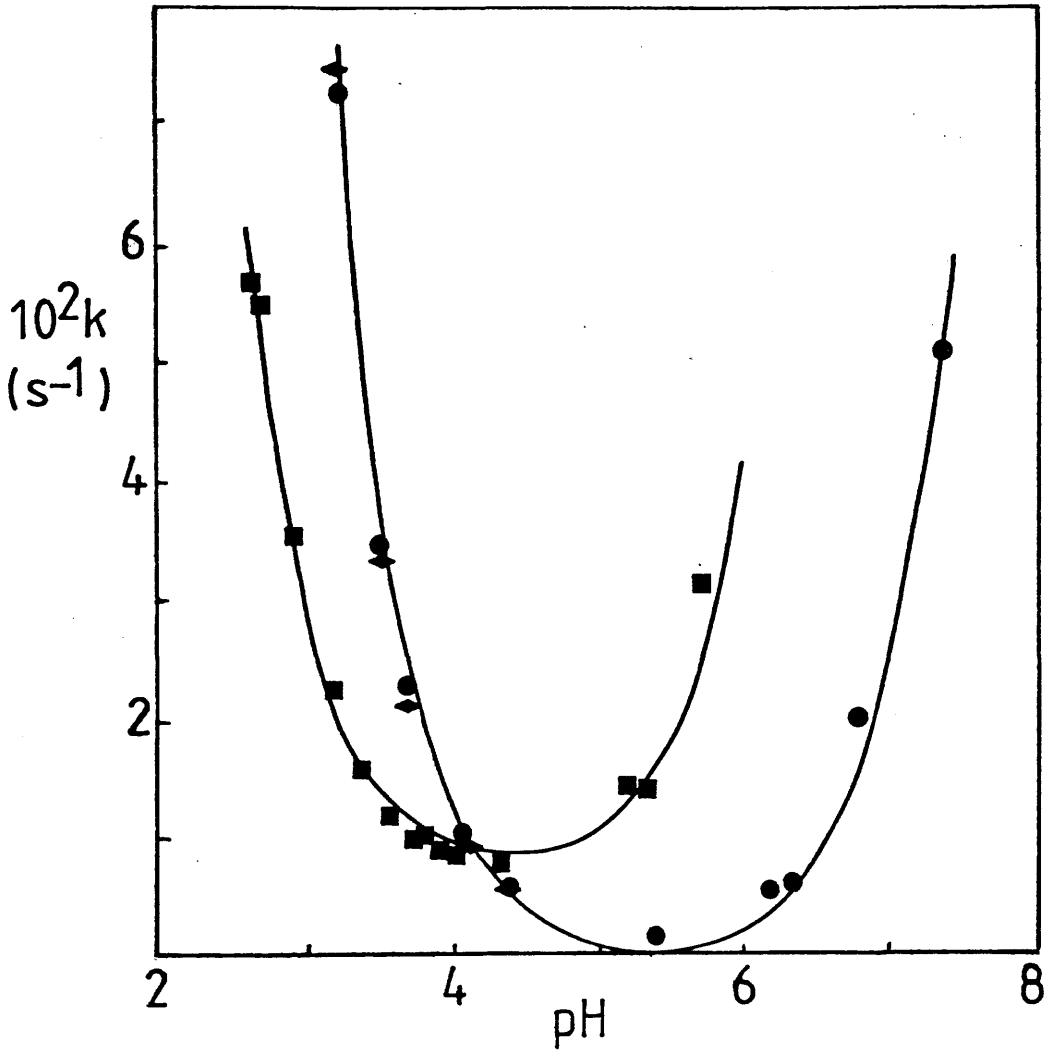


Fig. 1. pH-rate profile at 15°C for breakdown of:

a - benzaldehyde t-butyl hemiacetal

● - when using $PhCH(OBu^t)(OAc)$ as precursor,

◆ - when using $PHCH(OBu^t)_2$ as precursor,

b - benzaldehyde methyl hemiacetal

■ - when using $PhCH(OMe)(OAc)$ as precursor.

The lines were drawn according to the equations (21) and (22).

Hydrolysis of benzaldehyde di-t-butyl acetal

The hydrolysis of benzaldehyde di-t-butyl acetal was carried out under the same condition as those for α-acetoxy-α-t-butoxy-toluene, i.e. T = 15°C, I = 1.0M (KCℓ). From pH's 4.23 to 5.36 the observed rate constants were very close to those for α-acetoxy-α-t-butoxy-toluene suggesting that both substrates had the same rate limiting step. However at pH 6.42 an induction period was observed [39] (Fig. 2) and the rate constants at that pH were calculated by fitting the data to a consecutive reaction program using the k_2 value already obtained from hydrolysis of α-acetoxy-α-t-butoxy-toluene.

For pH's above 6.42 the kinetics again became pseudo first order and the rate values became smaller with increasing pH. Also it can be noted that there is a trend for the values to become constant with the variation of [HA] (Tables 27 to 30). For these cases only the intercept was considered as indicated on the respective tables.

Attempts were made to observe general catalysis in acetate and cacodylate buffers using different conditions as specified in the table below.

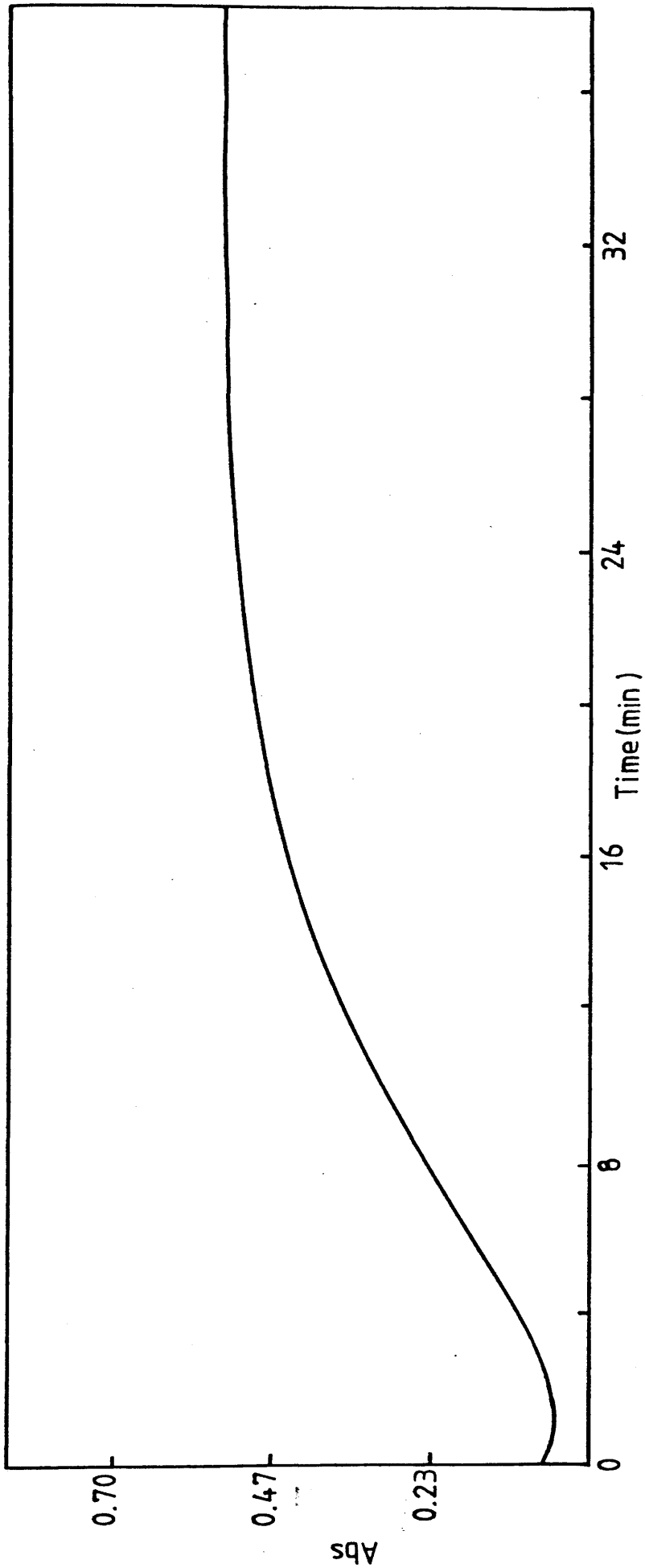


Fig. 2. Plot of Absorbance at 250 nm versus time for the hydrolysis of benzaldehyde di-t-butyl acetal at pH = 6.43 in imidazole buffer, $[HA]/[A^-] = 10:1$, T = 15°C, I = 1.0 M.

Table 21

Buffer	$[HA]/[A^-]$	I (M)	pH
Acetate	1:1	4.0	4.78
Acetate	1:10	0.5	5.60
Cacodylate	2:1	0.5	5.80
Cacodylate	1:1	0.5	6.11

In none of them were the kinetics first order and another attempt was made in Cacodylate, buffer ratio 1:10 at 25°C, I = 1.0M. The rate constants are in the Table 31 Some runs were done in HCℓ pH 4.48, T = 25°C and I = 1.0M, condition where the rate determining step is expected to be the breakdown of the hemiacetal, in order to obtain the k_{H^+} value (Table 32) and compare it with that from Anderson and Fife[22].

As will be seen in the Results Section the tables are related to different rate determining steps but each case will be clearly mentioned.

RESULTS

From the pH rate profile for formation of benzaldehyde (Fig. 3) it can be observed that the points represented by circles are related to breakdown of benzaldehyde t-butyl hemiacetal while those above pH 6.42 (triangles) are related to decomposition of $PhCH(OBu^t)_2$. These rate constants were plotted against $[H^+]$ (Table 33) yielding the specific acid catalytic constant for the hydrolysis of $PhCH(OBu^t)_2$ the value below

$$k_{H^+} = 7.01 \times 10^3 \ \underline{\underline{M}}^{-1} \ s^{-1} \qquad \text{s.d.} = 3.63\%$$

To determine if there was general catalysis by cacodylate buffer the equation described by Jensen[8] was used:

$$\frac{k_{obs}}{[H^+]} = k_{H^+} + k_{HA} \frac{[HA]}{[H^+]} \qquad (23)$$

Jensen claimed that the utilisation of eq. (23) could avoid any effect due to the small pH variation that usually arises from dilutions (Table 31).

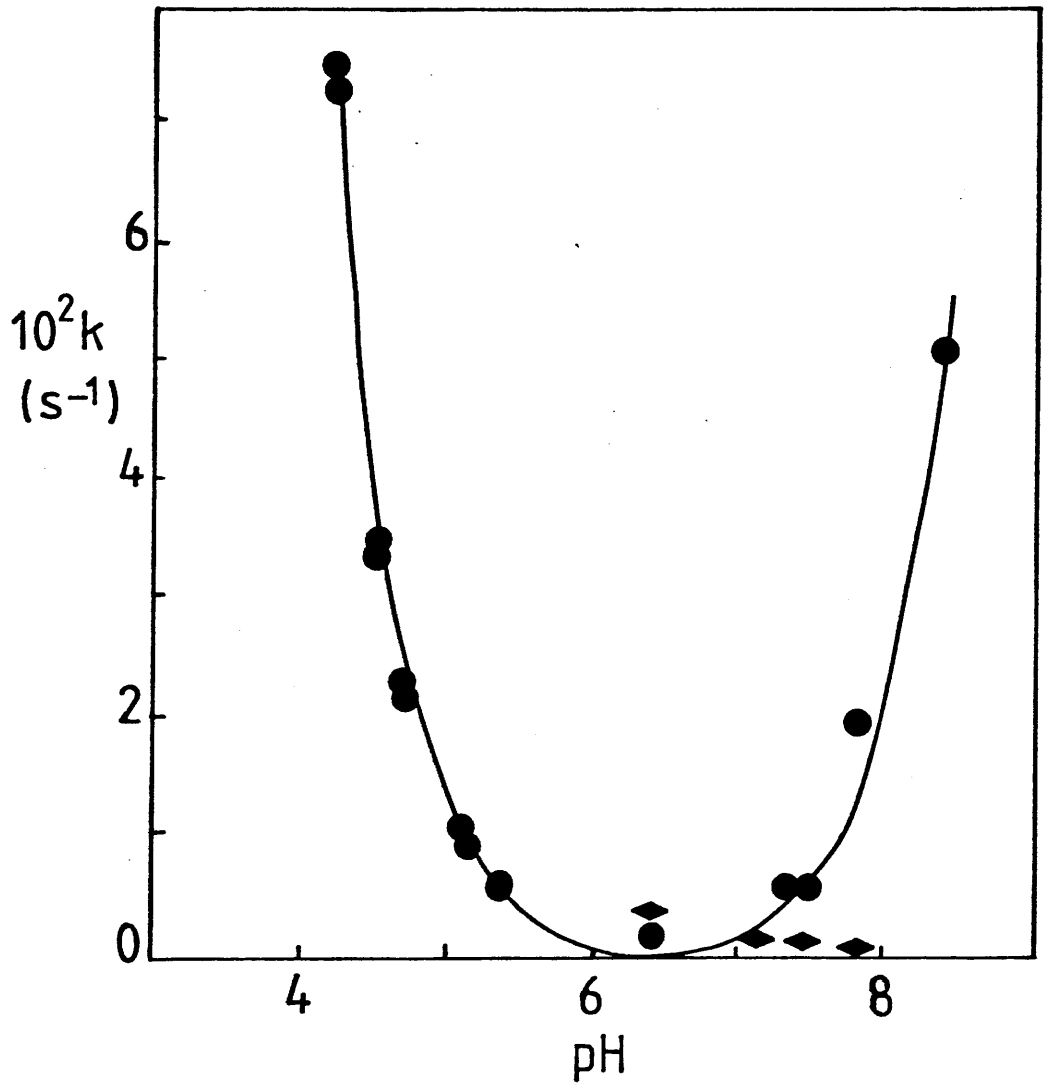


Fig. 3. pH-rate profile for formation of benzaldehyde at 15°C, I = 1.0 M.

● - from decomposition of benzaldehyde t-butyl hemiacetal

◆ - from decomposition of benzaldehyde di-t-butyl acetal.

Table 22. Acetate catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

[AcOH] = 2[AcO^-] I = 1.0M pH = 4.23

[HA], M	10 k_{obs} (s^{-1})	s.d. (%)
0.05	0.7669	2.57
0.04	0.7596	2.49
0.03	0.7612	5.24
0.02	0.7602	4.65
0.01	0.7497	4.79

The plot of k_{obs} versus [HA] yielded

Slope = 0.338×10^{-1} M^{-1} s^{-1} s.d. = 34.14%

Int = 0.749×10^{-1} s^{-1} s.d. = 0.51%

a - Rate limiting step is the breakdown of hemiacetal.

Table 23. Acetate catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

[AcOH] = 1.43 [AcO^-] I = 1.0 M pH = 4.23

[HA], M	10 k_{obs} (s^{-1})	s.d. (%)
0.025	0.4625	0.11
0.020	0.4481	0.44
0.015	0.4354	0.21
0.010	0.4052	0.51
0.005	0.3445	0.24

The plot of k_{obs} versus [HA] yielded

Slope = 0.558 M^{-1} s^{-1} s.d. = 20.39%

Int = 0.335 x 10^{-1} s^{-1} s.d. = 5.62%

a - Rate limiting step is the breakdown of hemiacetal.

Table 24. Acetate catalyzed hydrolysis of benzaldehyde di-t-butyl acetal [a]

[AcOH] = 1/2 [AcO^-] I = 1.0 M pH = 4.72

[HA], M	10 k_{obs} (s^{-1})	s.d. (%)
0.025	0.2534	3.37
0.020	0.2429	0.17
0.015	0.2417	0.98
0.010	0.2294	0.37
0.005	0.2253	1.8×10^{-2}

The plot of k_{obs} versus [HA] yielded

Slope = 0.139 M^{-1} s^{-1} s.d. = 12.52%

Int = 0.218×10^{-1} s^{-1} s.d. = 1.33%

a - Rate limiting step is the breakdown of the hemiacetal.

Table 25. Acetate catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

[AcOH] = 1/4 [AcO^-] I = 1.0 M pH = 5.10

[HA], M	10 k_{obs} (s^{-1})	s.d. (%)
0.025	0.1267	1.68
0.020	0.1214	2.76
0.015	0.1118	1.78
0.010	0.1073	0.80
0.005	0.0972	0.90

The plot of k_{obs} versus [HA] yielded

Slope = 0.146 M^{-1} s^{-1} s.d. = 6.79%

Int = 0.909 x 10^{-2} s^{-1} s.d. = 1.81%

a - Rate limiting step is the breakdown of the hemiacetal.

Table 26. Acetate catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

[AcOH] = 1/10 [AcO^-] I = 1.0 M pH = 5.36

[HA], M	10 k_{obs} (s^{-1})	s.d. (%)
0.025	0.1143	0.25
0.020	0.1038	0.07
0.015	0.0932	0.51
0.010	0.0790	0.71
0.005	0.0651	0.19

The plot of k_{obs} versus [HA] yielded

Slope = 0.247 M^{-1} s^{-1} s.d. = 4.34%

Int = 0.541 x 10^{-2} s^{-1} s.d. = 3.28%

a - Rate limiting step is the breakdown of the hemiacetal.

Table 27. Imidazole catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

$[ImH^+] = 10\ [Im]$ $\quad I = 1.0\underline{M}$ $\quad pH = 6.42$

$[Im]_T$, $\underline{M}$	$10^2\ k_{obs}\ (s^{-1})$	s.d. (%)
0.110	0.3237	6.4
0.088	0.3335	1.0
0.066	0.3175	5.0
0.044	0.2796	2.1
0.022	0.2982	17.8

The plot of k_{obs} versus [HA] yielded

Slope = $5.245 \times 10^{-3}\ \underline{M}^{-1}\ s^{-1}$ $\quad$ s.d. = 47.9%

Int = $0.279 \times 10^{-2}\ s^{-1}$ $\quad$ s.d. = 5.97%

a - Rate constants for breakdown of acetal evaluated from the equation for consecutive first-order reactions.

Table 28. Imidazole catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

$[ImH^+] = [Im]$ I = 1.0 M pH = 7.36

$[Im]_T$, M	10^3 k_{obs} (s^{-1})	s.d. (%)
0.20	0.4488	2.45
0.16	0.4523	0.48
0.12	0.4439	1.19
0.08	0.4657	1.93
0.04	0.4722	1.50

The plot of k_{obs} versus [HA] yielded

Slope = -3.01×10^{-4} M^{-1} s^{-1} s.d. = 43.3%

Int = 0.475×10^{-3} s^{-1} s.d. = 1.82%

a - Rate constants for breakdown of acetal evaluated from the first-order rate equation.

Table 29. Phosphate catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

$[KH_2PO_4]$ = 1/10 $[K_2HPO_4]$ I = 1.0M pH = 7.48

[HA], M	10^3 k_{obs} (s^{-1})	s.d. (%)
0.010	0.3407	0.17
0.008	0.3555	2.41
0.006	0.3817	2.94
0.004	0.3832	1.13
0.002	0.3963	1.47

The plot of k_{obs} versus [HA] yielded

Slope = -6.95×10^{-3} M^{-1} s^{-1} s.d. = 15.1%

Int = 4.13×10^{-4} s^{-1} s.d. = 1.68%

a - Rate constants for breakdown of acetal evaluated from the first-order rate equation.

Table 30. Imidazole catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 15°C [a]

$[ImH^+]$ = 1/3 [Im] I = 1.0M pH = 7.81

$[Im]_T$, M	10^3 k_{obs} (s^{-1})	s.d. (%)
0.40	0.1870	1.92
0.32	0.1436	2.12
0.24	0.1457	0.34
0.16	0.1460	0.12
0.08	0.1490	1.35

The plot of k_{obs} versus [HA] yielded

Slope = -8.25×10^{-5} M^{-1} s^{-1} s.d. = 21%

Int = 0.150×10^{-3} s^{-1} s.d. = 0.63%

a - Rate constants for breakdown of acetal evaluated from the first-order rate equation.

Table 31. Cacodylate catalyzed hydrolysis of benzaldehyde di-t-butyl acetal at 25°C [a]

$[(CH_3)_2AsO_2H]$ = 1/10 $[(CH_3)_2AsO_2^-]$ I = 1.0 M (KCl)

$10^3 k_{obs}$	[HA], M	pH	$10^{-4} k_{obs}/[H^+]$	10^{-7} [HA]/$[H^+]$
2.0529	0.090	7.263	3.7615	0.1649
2.1734	0.085	7.236	3.7424	0.1464
2.2041	0.080	7.223	3.6833	0.1337
2.2508	0.075	7.212	3.6672	0.1222
2.2957	0.070	7.156	3.2879	0.1002

The plot of $k_{obs}/[H^+]$ versus $[HA]/[H^+]$ yielded

Slope = k_{HA} = 6.93×10^{-3} M^{-1} s^{-1} s.d. = 32%

Int = k_{H^+} = 2.70×10^{4} M^{-1} s^{-1} s.d. = 11%

a - Rate determining step is the breakdown of the acetal.

Table 32. Hydrolysis of benzaldehyde di-t-butyl acetal in HCℓ, T = 25°C, I = 1.0M (KCℓ)[a]

pH	[HCℓ], M	k_{obs}[b] (s^{-1})	a_{H^+}
4.480	1×10^{-4}	0.1200	3.311×10^{-5}

$k_{H^+} = 3.62 \times 10^{3}\ M^{-1}\ s^{-1}$

The k_{H^+} value was obtained by dividing k_{obs} by a_{H^+}. The k_o value was not considered since the contribution of water reaction at this pH is minimum. That was supported by the results from this pH range already stated.

a - The rate determining step is the breakdown of hemiacetal.

b - Weighted average of 11 values.

Table 33. Acid catalyzed decomposition of benzaldehyde di-t-butyl acetal at 15°C, I = 1.0 M [a]

pH	10^3 k (s^{-1})	10^8 $[H^+]$
6.42	2.79 (5.97)[b]	38.019
7.36	0.475 (1.82)	4.365
7.48	0.413 (1.68)	3.311
7.81	0.150 (0.63)	1.549

The plot of k versus $[H^+]$ yielded

Slope = k_{H^+} = 7.02×10^3 M^{-1} s^{-1} s.d. = 3.63%

Int = k_{H_2O} = 1.28×10^{-4} s^{-1} s.d. = 38%

a - The rate determining step is the breakdown of the acetal.

b - Values in brackets are standard deviations.

Hydrolysis of benzaldehyde di-ethyl acetal

The kinetics of the hydrolysis of benzaldehyde di-ethyl acetal were carried out at 25°C following the appearance of the product at λ = 250 nm.

The efforts to reproduce Jensen's results[8] in order to observe general acid catalysis in acetate and cacodylate buffers were unsuccessful.

In addition we have tried to use a high ionic strength made up with KCℓ but the concentration of 4.0 M was the limit.

Also we have used the ionic strength 0.5 M made up with KCℓ and $NaNO_3$. The pH's of these solutions were measured twice at 25°C and the values are summarised in the next tables.

RESULTS

The specific and general catalytic constants for acetate and cacodylate buffers for the hydrolysis of $PhCH(OEt)_2$ were calculated using equation (23).

The values are listed in each corresponding table.

Table 34. Acetate catalyzed hydrolysis of benzaldehyde di-ethyl acetal at 25°C, I = 4.0$\underline{\underline{M}}$ (KCℓ)

[AcOH] = [AcO^-]

$10^2\ \underline{k}_{obs}$	[HA], $\underline{\underline{M}}$	pH	$10^{-2}\underline{k}_{obs}/[H^+]$	10^{-4}[HA]/$[H^+]$
0.5536	1.0	4.781	3.343	6.040
0.5971	0.8	4.778	3.581	4.798
0.6164	0.6	4.754	3.498	3.405
0.6464	0.4	4.748	3.618	2.239
0.6657	0.2	4.741	3.666	1.102

The plot of $\underline{k}_{obs}/[H^+]$ versus [HA]/$[H^+]$ yielded

Slope = $\underline{k}_{HA}$ = $-5.45 \times 10^{-4}\ \underline{\underline{M}}^{-1}\ s^{-1}$ s.d. = 36%

Int = $\underline{k}_{H^+}$ = $3.73 \times 10^{2}\ \underline{\underline{M}}^{-1}\ s^{-1}$ s.d. = 2.1%

Table 35. Acetate catalyzed hydrolysis of benzaldehyde di-ethyl acetal at 25°C, I = 0.5$\underline{\underline{M}}$ (KCℓ)

[AcOH] = 1/10 [AcO^-]

10^3 $\underline{k}_{obs}$	[HA], $\underline{\underline{M}}$	pH	$10^{-2}\underline{k}_{obs}/[H^+]$	10^{-5}[HA]/$[H^+]$
0.383	0.05	5.630	1.635	0.213
0.398	0.04	5.603	1.594	0.160
0.402	0.03	5.585	1.546	0.115
0.423	0.02	5.595	1.666	0.079
0.428	0.01	5.575	1.608	0.037

The plot of $\underline{k}_{obs}/[H^+]$ versus [HA]/$[H^+]$ yielded

Slope = $\underline{k}_{HA}$ = -1.08×10^{-5} $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 35%

Int = $\underline{k}_{H^+}$ = 161 $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 3.1%

Table 36. Acetate catalyzed hydrolysis of benzaldehyde di-ethyl acetal at 25°C, I = 0.5$\underline{\underline{M}}$ ($NaNO_3$)

[AcOH] = 1/10 [AcO^-]

10^3 $\underline{k}_{obs}$	(sd%)	[HA], $\underline{\underline{M}}$	pH	$10^{-2}\underline{k}_{obs}/[H^+]$	10^{-5}[HA]/$[H^+]$
0.383	(0.22)	0.05	5.630	1.635	0.213
0.407	(0.75)	0.04	5.592	1.593	0.156
0.437	(0.99)	0.03	5.575	1.642	0.113
0.448	(2.80)	0.02	5.550	1.591	0.071
0.479	(0.03)	0.01	5.503	1.524	0.032

The plot of $\underline{k}_{obs}/[H^+]$ versus [HA]/$[H^+]$ yielded

Slope = $\underline{k}_{HA}$ = 4.83×10^{-4} $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 54%

Int = $\underline{k}_{H^+}$ = 154 $\underline{\underline{M}}^{-1}$ s^{-1} s.d. = 2.3%

Table 37. Cacodylate catalyzed hydrolysis of benzaldehyde di-ethyl acetal at 25°C, I = 0.5$\underline{\underline{M}}$ (KCℓ)

$[(CH_3)_2AsO_2H] = [(CH_3)_2AsO_2^-]$

$10^4\ \underline{k}_{obs}$	(sd%)	[HA], $\underline{\underline{M}}$	pH	$10^{-2}\underline{k}_{obs}/[H^+]$	$10^{-6}[HA]/[H^+]$
1.191	(1.54)	0.40	6.113	1.545	0.519
1.291	(0.77)	0.30	6.105	1.644	0.382
1.369	(1.33)	0.20	6.100	1.723	0.252
1.450	(0.55)	0.10	6.086	1.768	0.122
1.581	(0.19)	0.04	6.080	1.901	0.048

The plot of $\underline{k}_{obs}/[H^+]$ versus $[HA]/[H^+]$ yielded

Slope = $\underline{k}_{HA} = -6.82 \times 10^{-5}\ \underline{\underline{M}}^{-1}\ s^{-1}$ s.d. = 13.2%

Int = $\underline{k}_{H^+} = 190\ \underline{\underline{M}}^{-1}\ s^{-1}$ s.d. = 1.50%

Table 38. Cacodylate catalyzed hydrolysis of benzaldehyde di-ethyl acetal at 25°C, I = 0.5$\underline{\underline{M}}$ (KCℓ)

$[(CH_3)_2AsO_2H] = 2\,[(CH_3)_2AsO_2^-]$

$10^3\,\underline{k}_{obs}$	(sd%)	[HA], $\underline{\underline{M}}$	pH	$10^{-2}\underline{k}_{obs}/[H^+]$	$10^{-4}[HA]/[H^+]$
0.243	(0.40)	0.80	5.805	1.549	5.106
0.280	(0.44)	0.40	5.760	1.612	2.302
0.290	(1.72)	0.20	5.737	1.583	1.091
0.305	(0.39)	0.16	5.730	1.639	0.873
0.317	(0.82)	0.08	5.714	1.640	0.414

The plot of $\underline{k}_{obs}/[H^+]$ versus $[HA]/[H^+]$ yielded

Slope = $\underline{k}_{HA} = -1.72 \times 10^{-4}\ \underline{\underline{M}}^{-1}\ s^{-1}$ s.d. = 38%

Int = $\underline{k}_{H^+} = 164\ \underline{\underline{M}}^{-1}\ s^{-1}$ s.d. = 1%

2.3.2 NMR experimental

NMR spectra were determined on a Varian T60 (60 MHz) or a Perkin Elmer R32 (90 MHz) NMR spectrometer. Chemical shifts were measured downfield from internal tetramethyl silane (TMS) and are quoted in δ values.

The integration and signal species are in brackets. The latter are represented by abbreviations: s = singlet, d = doublet, t = triplet and m = multiplet.

Purification of the reagents were carried out when required, after checking the purity by NMR.

Hydrolysis of α-acetoxy, α-t-butoxy toluene

According to the results from UV spectroscopy the breakdown of the benzaldehyde t-butyl hemiacetal was the rate determining step in the hydrolysis of α-acetoxy-α-t-butoxy toluene at 15°C.

We have found conditions where we could observe this behaviour by NMR spectroscopy:

Acetone (300 µℓ) was put into the NMR tube and mixed with 210 µℓ of (0.1M NaOAc, 0.1M DOAc). The NMR tube was put into the probe maintained at 8°C. After being kept a sufficient time for equilibration, α-acetoxy-α-t-butoxy toluene (15 µℓ) was added, the tube vigorously shaken and replaced into the probe. The spectra were recorded at a convenient time.

One minute after addition of the substrate, the spectrum showed the disappearance of the signal of the CH proton of the acylal at δ = 7.03 ppm and the appearance of a new signal at 5.91 ppm attributed to the CH proton from the hemiacetal (Fig. 4). The spectrum recorded 3 min. later showed a new signal at 9.99 ppm from the CH proton of the product benzaldehyde.

The hemiacetal under these conditions had a half life of 6 minutes. Although the spectra have been recorded using acetone as lock, the chemical shifts were corrected by adding 2.17 ppm which is the chemical shift for acetone[39].

Hydrolysis of benzaldehyde-di-t-butyl acetal

Although we have tried to observe the hemiacetal in the same condition as that when using the acylal as precursor, the starting material (acetal) did not appear to hydrolyse as quickly as expected. Nevertheless we managed to observe it in another condition, described as follows:

Acetone (300 µℓ) and DCℓ 5.74 x 10^{-4}M (25 µℓ) were mixed in the NMR tube and put into the probe maintained at 10°C. Benzaldehyde di-t-butyl acetal (10 µℓ) was added and the spectra recorded at regular intervals. Benzaldehyde t-butyl hemiacetal was observed at 5.90 ppm downfield from TMS, used as reference. The small signal at 5.85 ppm corresponded to the starting material not completely hydrolysed. The slow decomposition of the hemiacetal was followed with

the parallel appearance of the product benzaldehyde and the hemiacetal had a half life of c.a. 6 minutes.

A representative set of spectra is showed in the Fig. 5.

Fig. 4. The ^{1}H nmr spectrum of α-acetoxy-α-t-butoxy toluene.

a - in acetone,

b - acetone (300 μℓ) - 0.1 M NaOAc, 0.1 M DOAc) (210 μℓ) at 8°C, spectrum commenced 1 min. after dissolving,

c - same as b, spectrum commenced 4 min. after dissolving,

d - same as b, spectrum commenced 15 min. after dissolving.

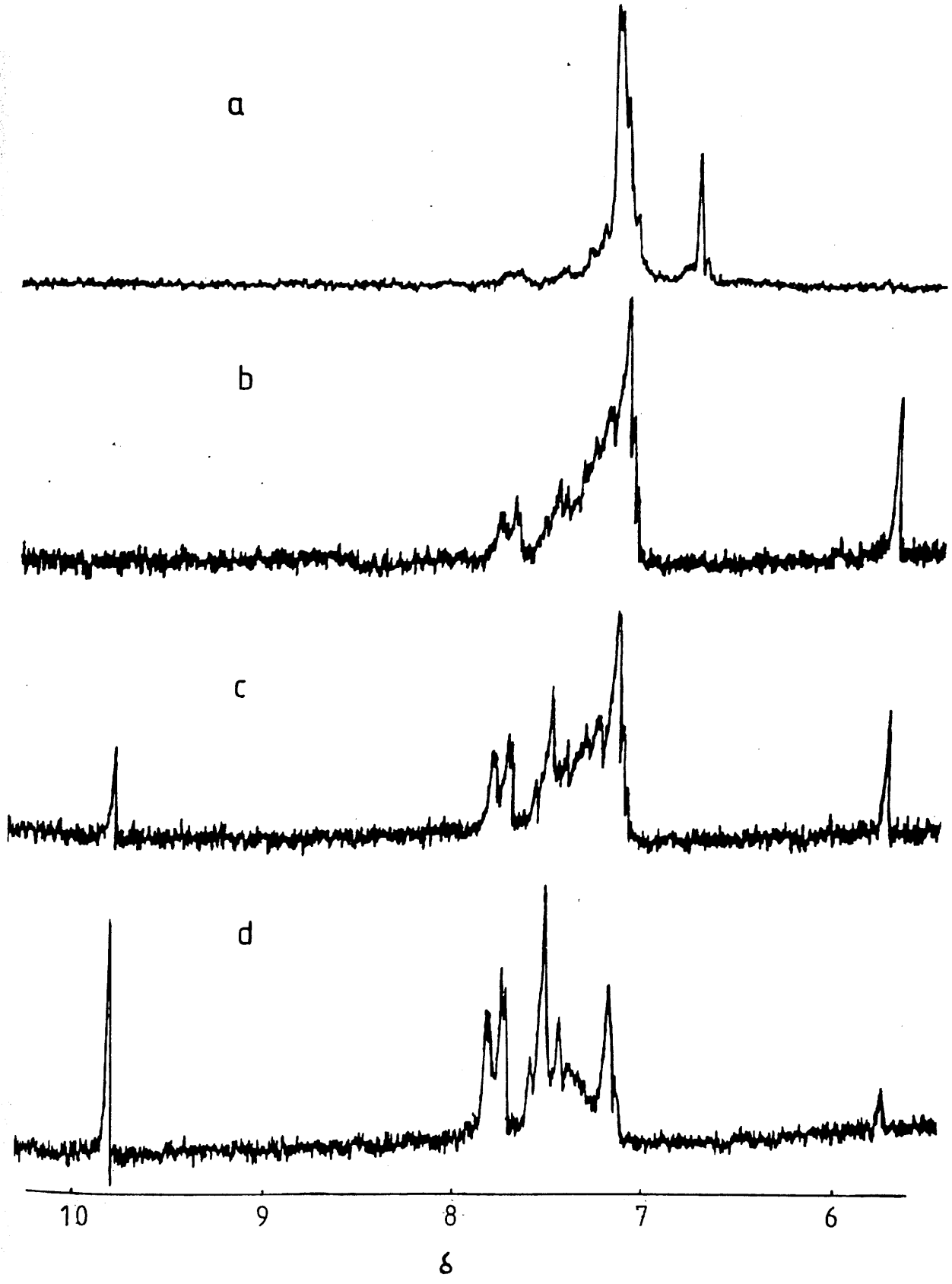


Fig. 4

Fig. 5. The ^{1}H nmr spectrum of benzaldehyde di-t-butyl acetal.

a - in acetone,

b - acetone (300 μℓ) - DCℓ 5.74×10^{-4} M (25 μℓ at 10°C, spectrum commenced 40 s. after dissolving,

c - same as b, spectrum commenced 5 min. 40 s. after dissolving,

d - same as b, spectrum commenced 13 min. 40 s. after dissolving.

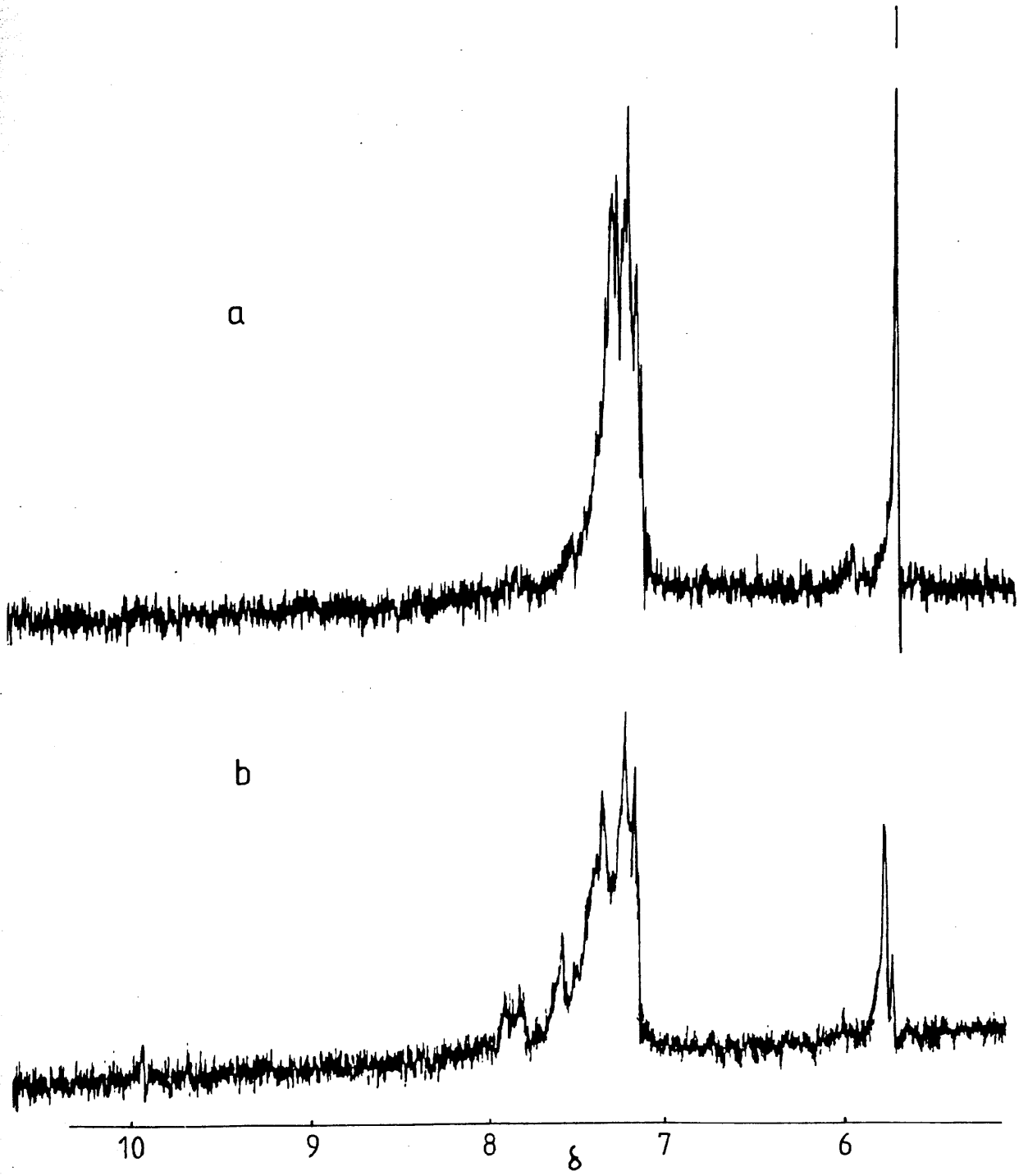


Fig. 5

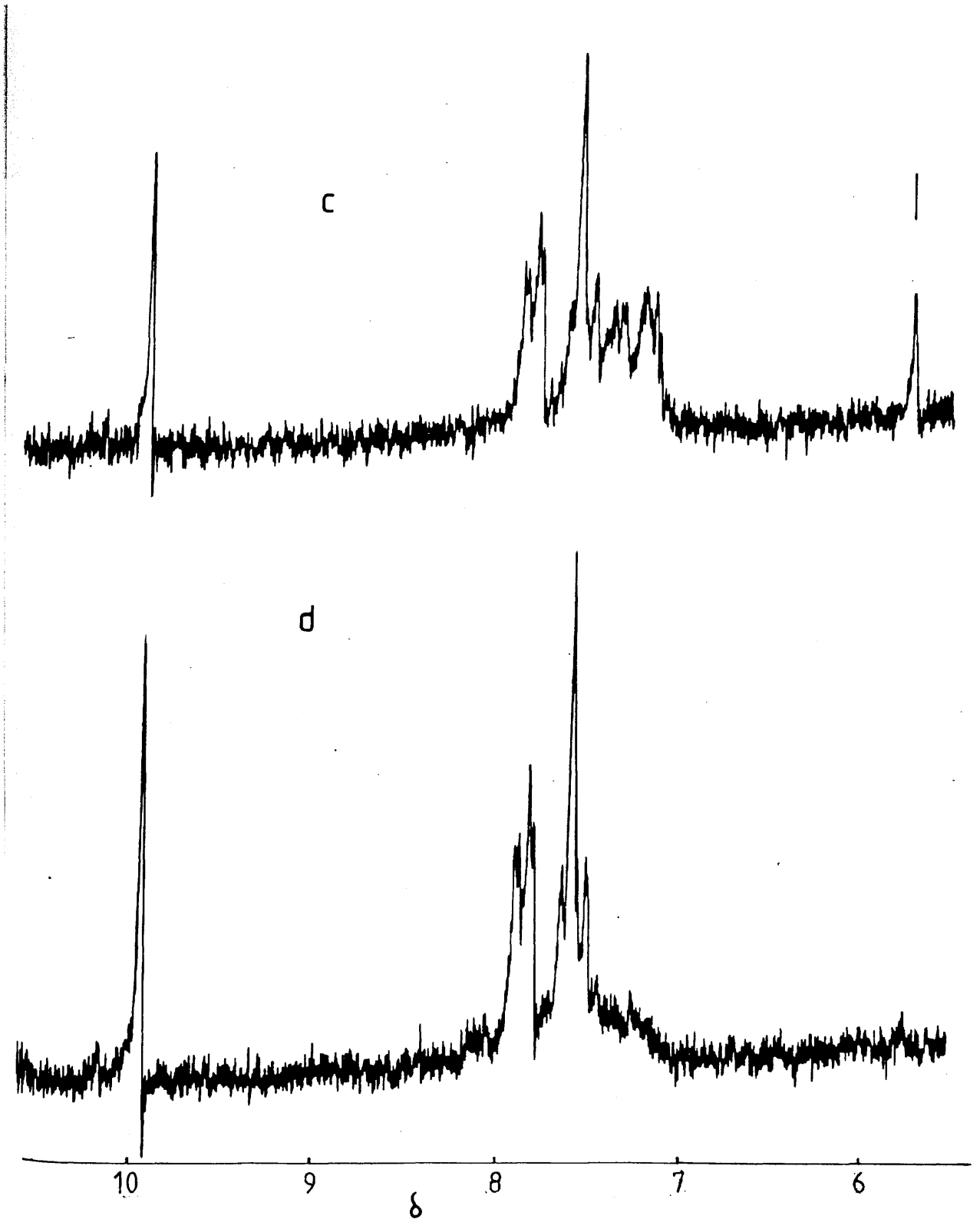


Fig. 5

2.3.3 Preparative experimental

Preparation of benzaldehyde di-t-butyl acetal

The method of Cawley and Westheimer[40] was followed.

Potassium (12.22 g) was added to t-butyl alcohol (23.19 g). After fully dissolved, benzal chloride (25.23 g) was added and the solution allowed to reflux for 4 hrs. in N_2 atmosphere.

A second preparation, which showed to be a better and faster reaction, was made by dissolving potassium t-butoxide (27.8 g) in t-butyl alcohol (60 ml) and adding benzal chloride (20 g). The reaction was monitored by NMR.

b.p. = 60-63°C/0.25 mm Hg.

NMR (CD_3CN) 60 MHz δ = 1.2 (s, 18H)

δ = 5.83 (s, 1H) , δ = 7.3-7.6 (m, 5H)

NMR ($CDC\ell_3$)[37] 60 MHz δ = 1.2 (s, 18H)

δ = 5.7 (s, 1H) , δ = 6.73-7.6 (m, 5H).

Preparation of α-acetoxy-α-t-butoxy-toluene

Benzaldehyde di-t-butyl acetal and acetic anhydride were mixed in equimolecular amounts and allowed to react under N_2 atmosphere. The product was distilled.

b.p. = 76°C/0.1 mm Hg

NMR ($CDC\ell_3$) 60 MHz δ = 1.35 (s, 9H)

δ = 2.05 (s, 3H) , δ = 7.03 (s, 1H)

δ = 7.26-7.65 (m, 5H)

NMR ($CDC\ell_3$)^{37} 60 MHz δ = 1.33 (s, 9H)

δ = 2.06 (s, 3H) , δ = 7.0 (s, 1H)

δ = 7.22-7.67 (m, 5H).

α-t-butoxy-α-chloroacetoxy-toluene

This was supplied by Dr. D. Grieve

NMR (CD_3CN) 60 MHz δ = 1.27 (s, 9H)

δ = 4.08 (s, 2H) , δ = 6.98 (s, 1H)

δ = 7.3-7.5 (m, 5H)

Preparation of benzaldehyde diethyl acetal

Benzaldehyde (50g, 0.5 moles) was mixed with $HC(OEt)_3$ (74g, 0.5 moles) and EtOH (40 ml). One drop of $MeSO_3H$ was added as catalyst and the mixture was allowed to react during 48 hours at R.T. being monitored by NMR. The acid was neutralized with anhydrous K_2CO_3 and the mixture fractionated.

The final product was collected:

b.p. = 96°C/13 mm Hg

NMR ($CDC\ell_3$) 60 MHz δ = 1.24 ppm (t, 6H)

δ = 3.65 ppm (q, 4H)

δ = 5.60 ppm (s, 1H)

δ = 7.35-7.79 ppm (m, 6H)

REFERENCES

1. E.H. Cordes, Progr. Phys. Org. Chem., 4, 1 (1967).
2. F. Stasiuk, W.A. Sheppard, A.N. Bourns, Can. J. Chem., 34, 123 (1956).
3. J.M. O'Gorman, H.J. Lucas, J. Am. Chem. Soc., 72, 5489 (1950).
4. L.L. Schaleger, F.A. Long, Adv. Phys. Org. Chem., 1, 1 (1963).
5. T.H. Fife, L.K. Jao, J. Org. Chem., 30, 1492 (1965).
6. M.M. Kreevoy, R.W. Jr. Taft, J. Am. Chem. Soc., 77, 5590 (1955).
7. R.W. Jr. Taft. J. Am. Chem. Soc., 75, 4231 (1953).
8. J.L. Jensen, L.R. Herold, P.A. Lenz, S. Trusty, V. Sergi, K. Bell, P. Rogers, J. Am. Chem. Soc., 101, 4672 (1979).
9. T.H. Fife, J. Am. Chem. Soc., 89, 3228 (1967).
10. T.H. Fife, L.K. Jao, J. Am. Chem. Soc., 90, 4081 (1968).
11. T.H. Fife, L.J. Hagopian, J. Org. Chem., 31, 1772 (1966).
12. B. Capon, E.A. Anderson, J. Chem. Soc. B., 1033 (1969). B. Capon, E.A. Anderson, Chem. Comm., 390 (1969).
13. B. Capon, K. Nimmo, J. Chem. Soc. Perkin II, 1113 (1975).
14. C. Buffet, G. Lamaty, Rec. Trav. Chim., 95, 1 (1976).
15. E. Anderson, T.H. Fife, J. Am. Chem. Soc., 91, 7163 (1969).
16. T.H. Fife, L.K. Jao, J. Am. Chem. Soc., 91, 4217 (1969).

17. T.H. Fife, E. Anderson, J. Am. Chem. Soc., 92, 5464 (1970).

18. J.L. Jensen, W.P. Jencks, J. Am. Chem. Soc., 101, 1476 (1979).

19. T.H. Fife, E.A. Anderson, J. Org. Chem., 36, 2357 (1971).

20. W. Von E. Doering, L.H. Knox, J. Am. Chem. Soc., 76, 3203 (1954).

21. R. Breslow, H. Hover, H.W. Chang, J. Am. Chem. Soc., 84, 3168 (1962).

22. T.H. Fife, E.A. Anderson, J. Am. Chem. Soc., 93, 1701 (1971).

23. L.P. Hammett, "Physical Organic Chemistry". McGraw-Hill, N.Y., 1940. Chap. VII.

24. A.W. Willi, Comprehensive Chemical Kinetics. Ed. Bamford and Tipper. Vol. 8.

25. E.H. Cordes, H.G. Bull, Chem. Rev., 74, 581 (1974).

26. L.L. Schaleger, M.A. Porzio, A.L. Mori, J. Am. Chem. Soc., 94, 5034 (1972).

27. R.P. Bell, Adv. Phys. Org. Chem., 4, 1 (1966).

28. T.C. Bruice, R.F. Atkinson, J. Am. Chem. Soc., 96, 819 (1974).

29. B. Capon, K. Nimmo, G.L. Reid, Chem. Comm., 871 (1976).

30. B. Capon, Pure & Appl. Chem., 49, 1001 (1977).

31. J.L. Jensen, P.A. Lenz, J. Am. Chem. Soc., 100, 1291 (1978).

32. R.A. McClelland, R.L. Finley, D.G. Kubler, J. Org. Chem., 45, 644 (1980).

33. P.E. Sorensen, M. Arora, B.G. Cox, J. Chem. Soc. Perkin II, 103 (1979).

34. T.H. Fife, T.J. Przystas, J. Am. Chem. Soc., 103, 4884 (1981).

35. L.H. Funderburk, L. Aldwin, W.P. Jencks, J. Am. Chem. Soc., 100, 5444 (1978).

36. A similar induction period was observed by D. McL. A. Grieve[37] in a previous work.

37. D. McL. A. Grieve, Ph.D. Thesis, Glasgow University, 1978.

38. M. Lahti, A. Kankaanpera, Acta Chem. Scand., 24, 706 (1970).

39. High Resolution NMR. Spectra Catalog. VARIAN. 1963. Vol. 2, p.1.

40. J.J. Cawley, F.H. Westheimer, Chem. Ind., 656 (1960).

41. P. Salomaa, A. Kanpaanpera, M. Lahti, J. Am. Chem. Soc., 93, 2084 (1971).

42. K.B. Wiberg, "Physical Organic Chemistry". John Wiley & Sons, New York, 1963. Appendix 9.

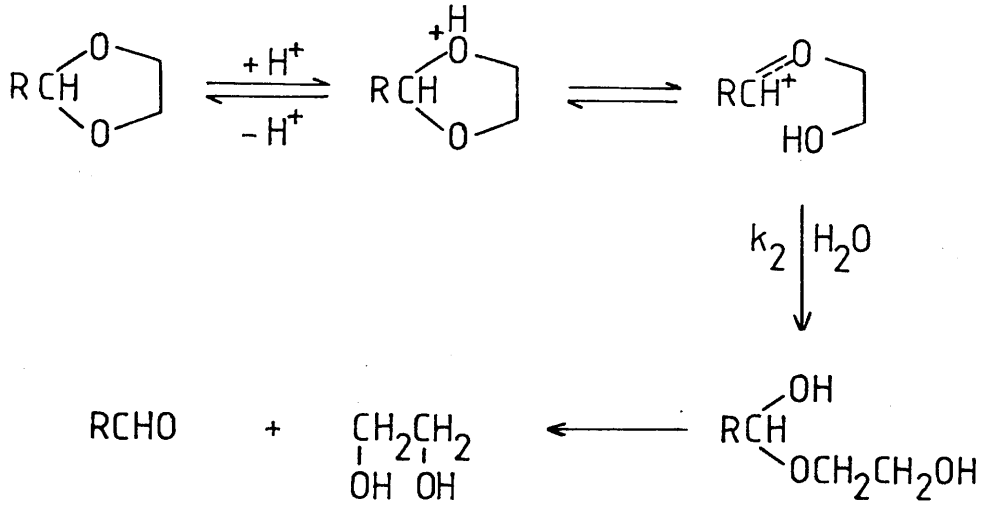
PART III

3.1 INTRODUCTION

A2 and $A2^+$ Mechanisms

There are several examples of acetals which have been suggested to hydrolyze by the A2 mechanism.

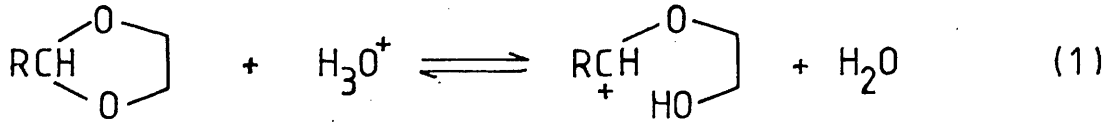
Capon and Thacker[1] in a study of the hydrolysis of glycofuranosides found negative values for ΔS^* contrasting with positive ΔS^* for hydrolysis of pyranosides. The incursion of an A2 mechanism for the hydrolysis of furanosides was thought to be reasonable in view of a nucleophilic attack being favoured (faster) for five-membered rings compared to six-membered rings.[2] However an alternative mechanism for the hydrolysis of these furanosides and for the hydrolysis of 1,3-dioxolanes (for which negative values of ΔS^* had also been found[3]) was proposed[1] which could also explain the negative values of ΔS^*. This involved a reversible ring-opening and rate limiting attack of water on the cation as shown in Scheme 1:



Scheme 1

where $\underline{k}_{obs} = k_2 \cdot K$

with K being the equilibrium constant for the system:



(1)

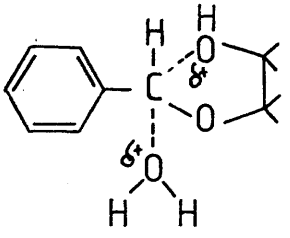
So, the observed entropy of activation could be:

$$\Delta S^* = \Delta S^o + \Delta S_2^* \qquad (2)$$

The value of ΔS^o is expected to be positive and ΔS_2^* strongly negative resulting in a negative value for ΔS^*. This mechanism (Scheme 1) was also considered by Watts[4] at about the same time and was subsequently designated A2$^+$ by Willi.[5] Another possibility that was also considered[1] was that the ring-opening was concerted with the attack of water.

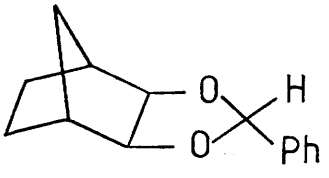
Fife[6] also suggested an A2 mechanism for the hydrolysis of 2-(p-substituted phenyl)-4,4,5,5-tetramethyl-1,3-dioxolanes in water at 30°C. The classic methods to distinguish A1 from A2 mechanism were applied. The plot of log $\underline{k}_{obs}$ against log $c_{H_3O^+}$ yielded a straight line with slope 2.0 and the plot of log $\underline{k}_{obs} + H_o$ versus log a_{H_2O} yielded a line with slope, w = 1.9. Also ΔS^* was -14.2 e.u. and the solvent isotope effect k_D/k_H = 2.4 for the hydrolysis of 2-phenyl-4,4,5,5-tetramethyl-1,3-dioxolane, but the most important evidence was the fact that substitution of a methyl group in the reaction centre decreased the rate constant by

a factor of 540.[7] The suggested structure in the transition was:

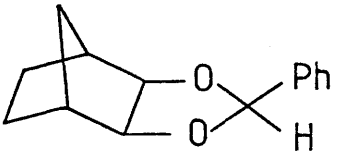


(1)

The hydrolysis of 2,3-OO-benzylidene-norbornane-exo-2,-exo-3-diols (2) and (3) have been studied by Capon and Page[8] in aqueous hydrochloric acid, T = 22-25°C.



(2)



(3)

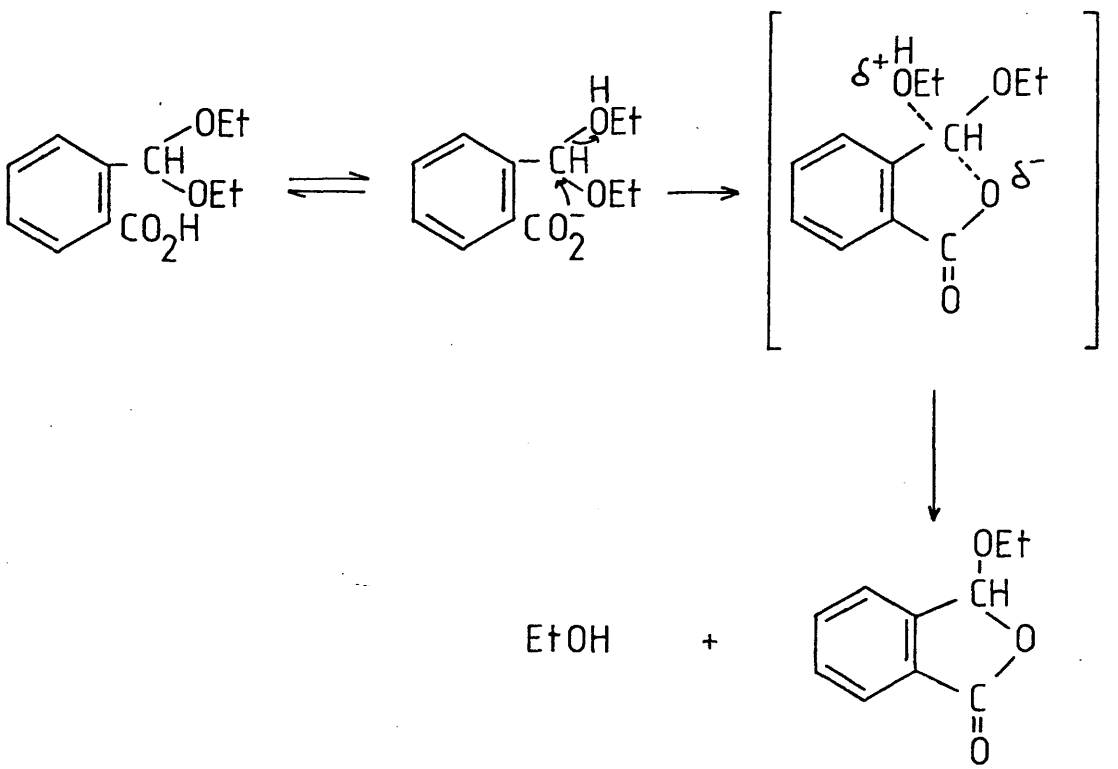
For the unsubstituted compounds the interconversion of the two isomers occurred concurrently with the hydrolysis. It was faster for p-OMe and slower for p-NO_2 substituted compounds. This result excludes an A1 mechanism for the hydrolysis and it was concluded on the basis of the relative effects of substituents on the hydrolysis and rearrangement that the hydrolysis probably involved a bimolecular attack of water on the conjugate acid.

Also a related study has been carried out by McClelland and co-workers[9] for the hydrolysis of tropone ethylene and trimethylene ketals for which a reclosure was mainly observed in a hydroxide-catalyzed reaction whereas only a small amount of recyclization occurred in the acid-catalyzed reaction. Lamaty and co-workers[10] also reported the attack of water on the cation to be the rate-determining step in the hydrolysis of cyclic orthoesters (2,4,10-trioxaadamantanes) in dioxane-water (60:40 v/v). This conclusion was supported by McClelland[11] who showed that the cation which will be formed in the hydrolysis of 2,4,10-trioxaadamantane cyclised in aqueous sulphuric acid farther than it reacted with water.

Intramolecular Nucleophilic Attack

Intramolecular nucleophilic assistance was proposed by Capon and Thacker[12] in the acid-catalyzed reaction of glucose and galactose acetals in water. The former yielded a greater proportion of furanosides compared to the free sugar than the galactose acetal and the observed rate constant was ca. 10 times greater. The suggested mechanism involved a nucleophilic attack synchronous with the rupture of the acetal bond. The rate of ring closure of the acetals were compared with the estimated unassisted rate of ionization of pentahydroxyhexanal acetal and enhancements of 340-fold for the glucose and 29-fold for galactose acetals were found.

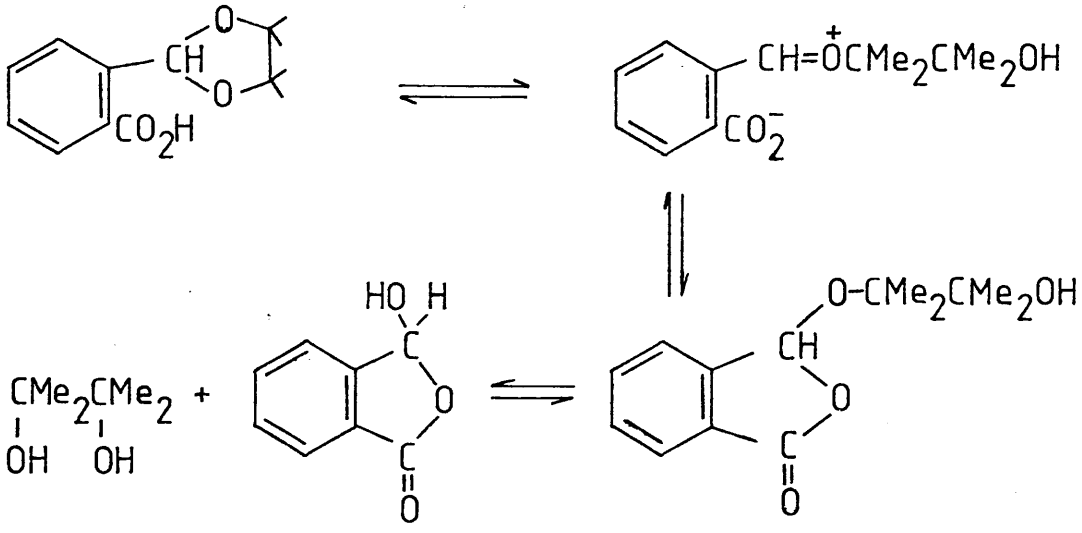
Anderson and Capon[13] studied a series of acetals with potential neighbouring groups in order to try to find further examples of intramolecular nucleophilic assistance in their reactions. The best example was the reaction of phthalaldehydic acid diethyl acetal in 82% aqueous-dioxan at 60°C (Scheme 2).



Scheme 2

A rate enhancement of ca. 3000 times compared to the hydrolysis of terephthalaldehydic acid diethyl acetal was observed at pH* = 9.46. The same reaction in water provided little evidence for nucleophilic assistance being 2-3.5 times faster than the reference compound.

In both cases, water and aqueous-dioxan, 3-ethoxy-phthalide was formed and Capon suggested that its formation in water resulted from the intramolecular capture of the carbonium ion. Also intramolecular nucleophilic catalysis was observed in the hydrolysis of 2(o-carboxy phenyl)-4,4,5,5-tetramethyl-1,3-dioxolan in 50% w/w dioxan-water at 95°C (Scheme 3)

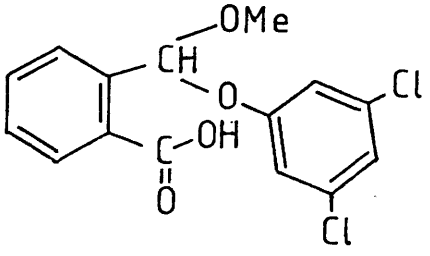


Scheme 3

A comparison with the p-carboxy phenyl dioxolane was made and the hydrolysis of the ortho compound was 44 times faster at pH* 5.03 and the estimated rate enhancement at pH* 5.83 (= pK_a) was 150.

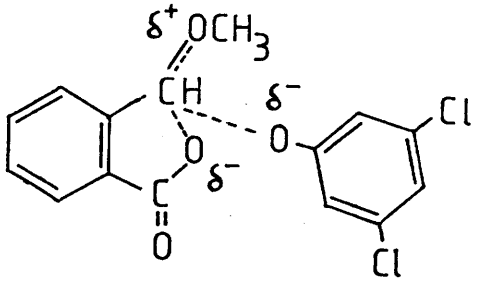
The study of substituted acetals has been carried out by Fife and Przystas.[14] They selected phthalaldehydic acid methyl substituted phenyl acetals and an intramolecular nucleophilic attack was suggested for the pH-independent

reaction of the phthalaldehydic acid methyl-3,5-dichlophenyl acetal (4) for pH's above 7.0 in 50% v/v dioxane-water at 30°C.



(4)

The pH-independent reaction of (4) was 100 times faster than the p-carboxylate acetal and the solvent isotope effect k_D/k_H = 1.0 indicated that a unimolecular reaction had taken place with the structure in the transition state as:



(5)

Similar behaviour was observed[15] in the hydrolysis of phthalaldehydic acid methyl S-phenyl thioacetal in water at 50°C with the pH-independent reaction being accelerated by a factor of 22 compared to p-carboxylate thioacetal.

3.2 DISCUSSION

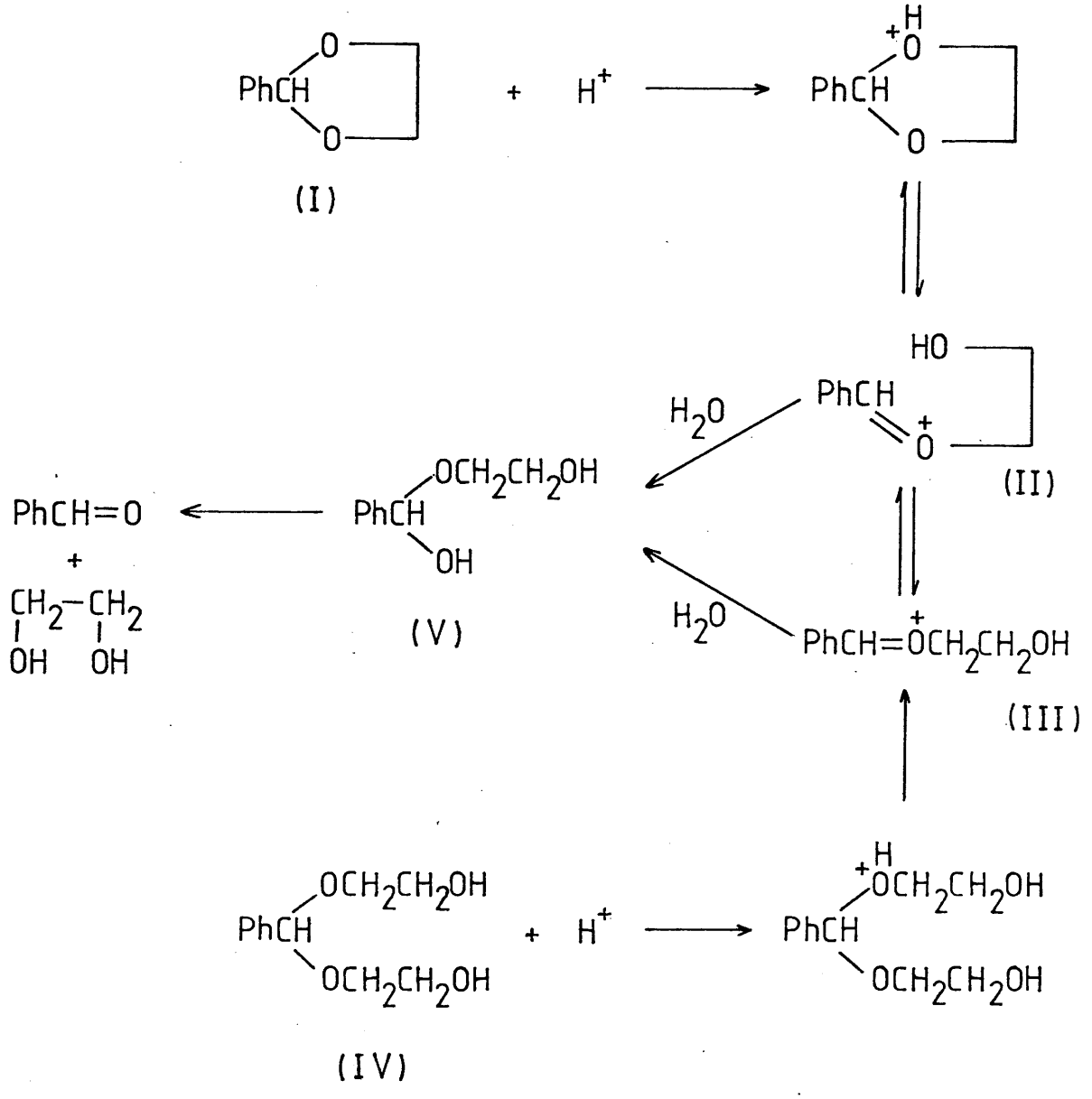
Reversibility of the Ring-Opening Step

The reversibility of the second step (which is represented in the Scheme 1, p.254) in the hydrolysis of acetals or ketals should be easier for cyclic acetals because the reverse process is the intramolecular attack of the OH-group on the cationic centre. So, there is the possibility that the water attack cannot compete with the reclosure due to the proximity of a OH-group, resulting in a change in the rate-determining step or mechanism.

As described in the Introduction such reversibility has been demonstrated in the hydrolysis of 2,3-O-O-benzylidene norbonane-exo-2-exo-3-diols.[8] The purpose of this investigation was to find if there were conditions under which recyclization of the initial cation (II) in the hydrolysis of 2-phenyl-1,3-dioxolane (I) could occur. This was done by studying the hydrolysis of benzaldehyde bis(2-hydroxy ethyl)acetal (IV) which should yield the same carbocation as 2-phenyl-1,3-dioxolane but possibly with a different conformation. Therefore, if interconversion between the conformers were rapid benzaldehyde bis(2-hydroxy ethyl)acetal should yield the dioxolane if cation (II) recyclizes faster than it reacts with water to yield hemiacetal (V).

Therefore one can say that if (IV) yields (I), (II) must undergo recyclization faster than reaction to (V), but

if the recyclization does not occur it may mean that (II) reacts with water more rapidly than it recyclises or that the conversion of the cation (III) into (II) is slower than its reaction with water.*



* It is assumed in this argument that no dioxolane is formed by a concerted cyclization of the protonated starting material. This is thought to be unlikely but has not been rigorously excluded.

Analysis of the Results

It has been suggested that 2-phenyl-1,3-dioxolane hydrolyses by an A1 mechanism in 50% v/v dioxane-water at 30°C. The observed small negative values for ΔS^* were explained as being due to the high solvation of the conjugated acids (or transition states) or restriction of rotation about the breaking bond in the transition state. In this work we have studied the hydrolysis of benzaldehyde bis(2-hydroxy ethyl)acetal in order to observe the degree of cyclization under different solvent compositions and to obtain the initial product of hydrolysis.

By NMR experiments with a mixture of ca. 33% D_2O - 77% CH_3CN v/v the hydrolysis of benzaldehyde bis(2-hydroxy ethyl)acetal yielded no 2-phenyl-1,3-dioxolane (see p.273) which is in agreement with Fife's results[3] and with the mechanism of hydrolysis being A1. Under these conditions water competes effectively with the internal hydroxy to capture the cation. The reaction was also studied by NMR spectroscopy in less aqueous media. In ca. 10% D_2O - 90% CH_3CN about 33% dioxolane was detected and in 1% D_2O - 99% CD_3CN v/v about 73% of dioxolane was detected. Therefore as the amount of water in the medium is decreased it competes less successfully with the internal hydroxyl group for capture of the cationic centre. The reaction was also studied by uv spectroscopy and it was thought that the

benzaldehyde which was formed directly from the acetal would be formed in a fast reaction while that which was formed via dioxolane would be formed in a slow reaction with the same rate as when it was formed from the dioxolane as starting material. In fact in 0.5% H_2O - 99.5% CH_3CN and 0.25% H_2O - 99.75% CH_3CN no detectable benzaldehyde was formed in a fast reaction and all benzaldehyde that was formed was formed at the same rate as when the dioxolane was the starting material (Tables 1 to 4, p268 to 271).

These results suggest that under these conditions the ions (III and II) cyclise to give dioxolane faster than they react with water and that the mechanism of the hydrolysis of the dioxolane cannot therefore be A1. If this is correct there are two possible mechanisms for the hydrolysis of the dioxolane, A2 and $A2^+$. The α-deuterium isotope effect for the hydrolysis of the dioxolane supports the former. In highly aqueous media when the mechanism appears to be A1 the α-deuterium isotope effect for the hydrolysis of the dioxolane is k_H/k_D = 1.08[16] but in 99.5% and 99.75% of CH_3CN it is 1.02 and 1.03 respectively.

This suggests that the transition state has a bimolecular character and that the mechanism is A2. If it was $A2^+$ the transition state would still have four groups coordinated to the reaction centre. This is similar to the transition state for the A1 mechanism and a similar isotope effect would be expected.

3.3 EXPERIMENTAL

3.3.1 Kinetic Experimental

The hydrolyses of 2-phenyl-1,3-dioxolane, 2-deuterio-2-phenyl-1,3-dioxolane and benzaldehyde bis(2-hydroxy ethyl)-acetal were carried out in CH_3CN-H_2O solutions (< 1% v/v H_2O) by following the appearance of the product, benzaldehyde, at λ = 250 nm. The rate determinations were performed in a Cary 16 spectrophotometer with a cell compartment thermostatted at 30°C $\pm$ 0.05 with the rate constants being calculated from the weighted average of four to nine runs. A Digico Micro-16P computer was always used to collect the data and calculate the rate constants.

Solutions

The solutions were prepared by placing a volume of HCℓ (0.1$\underline{\underline{M}}$ or 0.2$\underline{\underline{M}}$) in a volumetric flask and adding CH_3CN to the volumetric mark in order to obtain a final concentration of HCℓ of 5×10^{-3} $\underline{\underline{M}}$ in solutions of 0.5% and 0.25% H_2O. The stock solutions were prepared in dioxane with a final concentration in the cell of ca. 7.8×10^{-5} $\underline{\underline{M}}$.

Results

Although NMR experiments have been carried out under conditions where the solvent-composition changed from ca. 1% to 40% v/v H_2O, which will be discussed later, kinetics

experiments were carried out in solutions > 99% of CH_3CN.

For solutions of CH_3CN-H_2O (99.5 - 0.5% v/v) the rate constants for the hydrolysis of the acetal and dioxolane were the same, 8.85×10^{-3} s^{-1}. Similar behaviour was observed in solutions of CH_3CN-H_2O (99.75 - 0.25% v/v) with the rate constant 3.32×10^{-3} s^{-1} for the dioxolane and 3.14×10^{-3} s^{-1} for the acetal which are, within experimental error, the same. Under these conditions the acetal re-cyclized 100% to dioxolane (by NMR experiments the acetal recyclized ca. 73% to dioxolane using double the amount of water (D_2O).

The α-deuterium isotope effect was calculated for the hydrolysis of 2-phenyl-1,3-dioxolane in both solutions (0.5 and 0.25%) and the values found are: $k_H/k_{\alpha D} = 1.02$ (s.d. = 0.67%) and $k_H/k_{\alpha D} = 1.03$ (s.d. = 3.1%) respectively. The rate constants and weighted averages are summarized in the following tables.

Table 1. Acid hydrolysis of 2-phenyl-1,3-dioxolane and 2-deuterio-2-phenyl-1,3-dioxolane in solution of CH_3CN-HCℓ (99.5 - 0.5% v/v)

T = 30°C $\quad [HC\ell]_f = 5 \times 10^{-3}$ M

$10^3 k_H$, s^{-1} (s.d. %)	$10^3 k_D$, s^{-1} (s.d. %)
8.430 (0.60)	8.840 (0.18)
8.775 (0.50)	8.580 (0.19)
8.792 (0.45)	8.714 (0.22)
8.940 (0.44)	8.756 (0.15)
8.888 (0.28)	8.487 (0.14)
8.995 (0.39)	8.629 (0.15)
8.914 (0.34)	8.573 (0.23)
8.881 (0.42)	8.610 (0.20)
8.772 (0.38)	8.622 (0.19)

Weighted average = $\underline{k}_H = 8.852 \times 10^{-3}$ s^{-1}

s.d. = 1.91%

$\underline{k}_D = 8.639 \times 10^{-3}$ s^{-1}

s.d. = 1.24%

Table 2. Acid hydrolysis of benzaldehyde bis(2-hydroxy ethyl)acetal in solution of CH_3CN-HCℓ (99.5 - 0.5% v/v)

T = 30°C	$[HC\ell]_f = 5 \times 10^{-3}$ M
10^3 k, s^{-1}	s.d. (%)
8.845	0.23
8.911	0.28
8.753	0.21
8.883	0.16
8.845	0.19

Weighted average $\underline{k} = 8.846 \times 10^{-3}$ s^{-1}

s.d. = 0.67%

Table 3. Acid hydrolysis of 2-phenyl-1,3-dioxolane and 2-deuterio-2-phenyl-1,3-dioxolane in solution of CH_3CN-HCℓ (99.75 - 0.25% v/v)

T = 30°C $\quad\quad$ $[HC\ell]_f = 5 \times 10^{-3}$ M

$10^3 k_H$, s^{-1} (s.d. %)	$10^3 k_D$, s^{-1} (s.d. %)
3.710 (0.20)	3.316 (0.24)
3.348 (0.19)	3.430 (0.26)
3.376 (0.24)	3.187 (0.35)
3.309 (0.20)	3.184 (0.18)
3.304 (0.21)	3.289 (0.25)
3.100 (0.20)	3.148 (0.21)
3.232 (0.22)	3.177 (0.17)
3.307 (0.43)	3.193 (0.25)

Weighted average $\underline{k}_H = 3.323 \times 10^{-3}$ s^{-1}

s.d. = 5.24%

$\underline{k}_D = 3.222 \times 10^{-3}$ s^{-1}

s.d. = 3.05%

Table 4. Acid hydrolysis of benzaldehyde bis(2-hydroxy ethyl)acetal in solution of CH_3CN-HCℓ (99.75 - 0.25% v/v)

T = 30°C $\quad\quad$ $[HC\ell]_f = 5 \times 10^{-3}$ M

10^3 k, s^{-1}	s.d. (%)
3.148	0.27
3.152	0.27
3.169	0.32
3.082	0.28

Weighted average = $\underline{k} = 3.136 \times 10^{-3}$ s^{-1}

s.d. = 1.23%

3.3.2 NMR Experimental

NMR experiments were carried out in a Perkin-Elmer R32 90 MHz NMR spectrophotometer.

The most suitable conditions would be those under which the acetal hydrolyses slowly giving rise to the dioxolane and/or the aldehyde but further hydrolysis of the dioxolane is much slower than that of the acetal, thus allowing an estimate to be made of the percentage of dioxolane formed from the acetal.

The first solvent-composition utilized was CD_3CN-D_2O (99-1% v/v) and after several attempts the best conditions found consisted in putting 7 µℓ of the acetal $PhCH(OCH_2CH_2OH)_2$ (in NaOMe) into the NMR tube with 500 µℓ of CD_3CN (with TMS) allowing to equilibrate thermally (at the temperature of the probe) and adding 5 µℓ of DCℓ 0.43 M.

Under these conditions the acetal hydrolyzed ca. 27% to aldehyde and ca. 73% recyclising to dioxolane. The final acid concentration in the NMR tube could not be accurately determined because some was used in neutralizing the NaOMe present which remained from the previous stage. In fact some NMR experiments were carried out by using the acetal free of NaOMe but due to its unstability in forming dioxolane the further experiments were always carried out with the acetal in presence of the base.

Another solvent-composition with a larger amount of D_2O was utilized (ca. 10% D_2O - 90% CH_3CN v/v) for the same purpose. In this case the NMR tube with 300µℓ of CH_3CN and 7µℓ of the substrate was maintained at 0°C before adding 30µℓ of DCℓ 2.6×10^{-3} $\underline{\underline{M}}$; then the temperature was increased up to 8°C and the spectra recorded in a suitable δ range to observe the CH protons from the acetal, dioxolane and behzaldehyde. The signal of the CH_3CN was used as the 'lock' and the chemical shifts were corrected by adding 2.00 ppm which is the chemical shift of the acetonitrile.[17] After addition of the acid the signal corresponding to the CH proton from the acetal (δ = 5.59 ppm) decreased with the appearance of two signals attributed to the CH proton from the dioxolane (5.74 ppm) and benzaldehyde (9.98 ppm).

A set of spectra for this experiment is shown in the Fig. 1 with the spectrum like c remaining unaltered for at least 6 min. after recording the last one (c). Under these conditions the acetal hydrolyzed ca. 66.9% to aldehyde and 33.1% cyclized to dioxolane.

The last experiment with different solvent-composition consisted of adding 300µℓ of CH_3CN and 20µℓ of the substrate into the NMR tube maintained at T = 8°C before adding 150µℓ of DCℓ 5.74×10^{-3} $\underline{\underline{M}}$. In this case the acetal was hydrolyzed slowly to benzaldehyde without cyclizing to dioxolane. A further addition of a drop of dioxolane in the tube showed that it was stable under these conditions

suggesting that with this concentration of water and above the reaction was giving rise to 100% of benzaldehyde.

The intention was to carry out similar experiments with acetophenone and benzophenone bis(2-hydroxy ethyl)acetal but they were prevented by difficulties in purifying the precursor acetals. Also attempts to prepare a similar benzaldehyde acetal from pinacol were unsuccessful.

Fig. 1. ^{1}H nmr spectra of $PhCH(OCH_2CH_2OH)_2$ in 300µℓ CH_3CN.

a - Spectrum started 1 min. after addition of 30µℓ of DCℓ 2.3×10^{-3} M at 0°C.

b - Spectrum started 51 mins. after a, T = 8°C.

c - Spectrum started 43 mins. after b, T = 8°C.

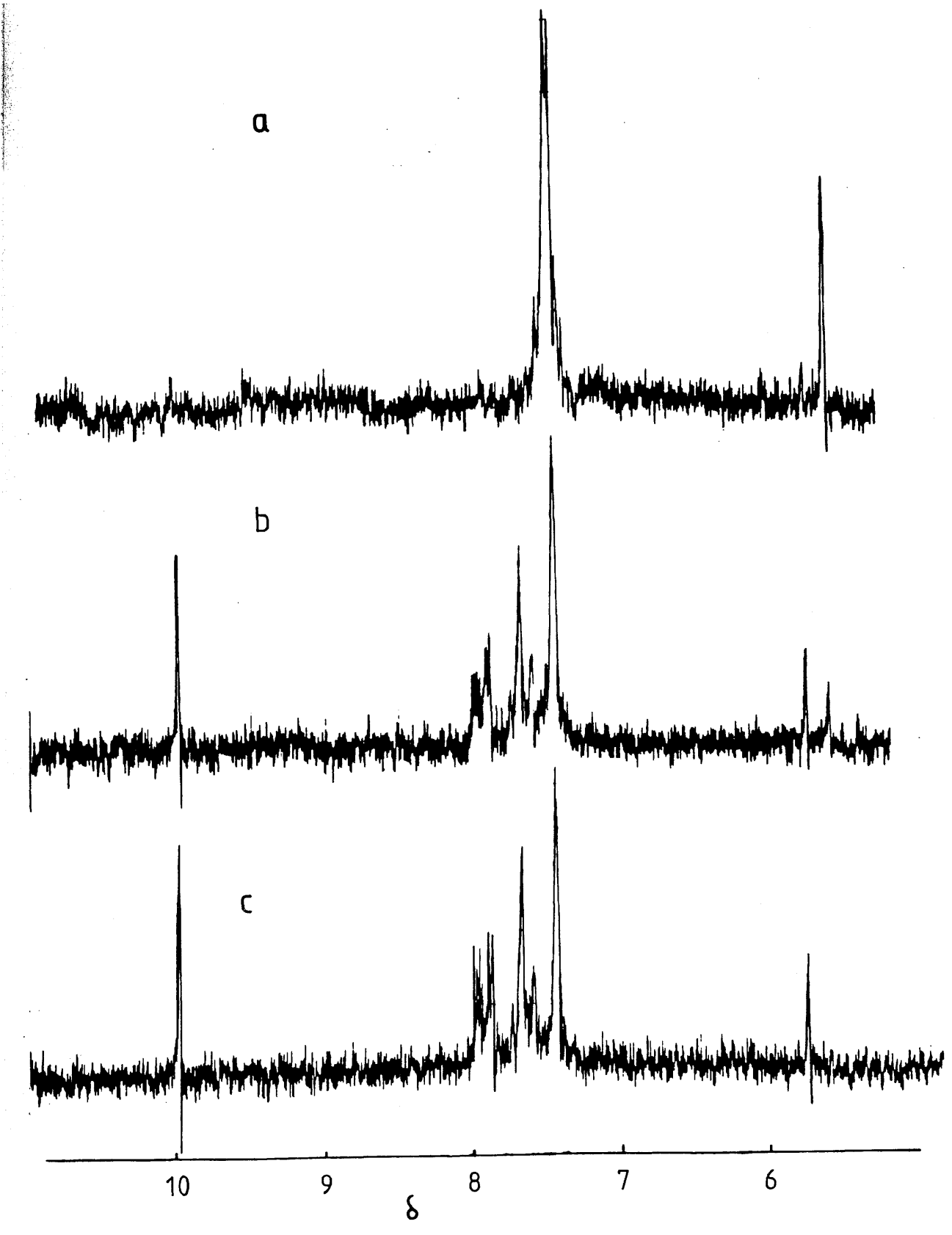


Fig.1

3.3.3 Preparative Experimental

NMR spectra were recorded on a Varian T60 (60 MHz) and/or a Perkin Elmer R32 (90 MHz) spectrophotometer. Chemical shifts were measured downfield from internal tetramethyl silane and are quoted in delta values with the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.

IR spectra were determined on a Perkin-Elmer 580 spectrophotometer and the abbreviations were as follows: sh = sharp, b = broad, m = medium.

Elemental analyses were carried out in the Glasgow University and are represented in percentages.

The purity of the chemicals utilized was checked by NMR and previous purification was done when required.

Preparation of benzaldehyde dimethyl acetal

The procedure used was that described by Fife and Jao.[3] Benzaldehyde (100g, 96.1 ml) was mixed with trimethyl orthoformate (100g, 103 ml) and MeOH (75 ml). One drop of $MeSO_3H$ was added as catalyst. After 24 hrs. at room temperature (R.T.) anhydrous K_2CO_3 was added to neutralize the acid. MeOH was distilled off at atmospheric pressure and the final product distilled at reduced pressure.

b.p. = 61-62°C/13 mm Hg		Clear oil (lit[16] b.p. = 102-104°C/40 mm)
NMR($CDC\ell_3$)	90 MHz	δ = 3.31 ppm (s, 6H)
		δ = 5.36 ppm (s, 1H)
		δ = 7.22-7.50 ppm (m, 6H)

Preparation of benzaldehyde bis(2-acetoxy ethyl)acetate

$PhCH(OMe)_2$ (50 ml, 0.3 moles) was mixed with a ca. 50:50 mixture of the mono and diacetate of ethylene glycol (56.7 ml, 0.6 moles in monoacetate). One drop of $MeSO_3H$ was added and the reaction mixture was heated under a fractioning column system with MeOH being collected. The desired product was distilled under high vacuum.

b.p. = 140-142°C/0.15 mm		Clear liquid
NMR($CDC\ell_3$)	60 MHz	δ = 2.10 ppm (s, 6H)
		δ = 3.69-3.85 ppm (m, 4H)
		δ = 4.22-4.41 ppm (m, 4H)
		δ = 5.75 ppm (s, 1H)
		δ = 7.35-7.69 ppm (m, 6H)
NMR(CD_3CN)	90 MHz	δ = 1.98 ppm (s, 6H)
		δ = 3.63-3.82 ppm (m, 4H)
		δ = 4.15-4.33 ppm (m, 4H)
		δ = 5.59 ppm (s, 1H)
		δ = 7.30-7.60 ppm (m, 6H)

Microanalysis: $C_{15}H_{20}O_6$ Found C = 60.50% H = 6.62%

Calc. C = 60.81% H = 6.78%

IR (thin layer) υ cm^{-1} 3035, 3070, 3090 (CH aromatic)

2930, 2955 (CH aliphatic stretch)

2880 (CH acetal)

1740 b (carbonyl C=O)

1453 sh (CH_3 asym. bend)

1378 sh (CH_3 sym. bend)

1240 b (C-O-C stretch).

Preparation of benzaldehyde bis(2-hydroxy ethyl)acetal

Sodium (small amount) was dissolved in MeOH (25 ml), the precursor benzaldehyde bis(2-acetoxy ethyl)acetal (ca. 1g) was added and allowed to stand overnight. Methanol was removed, the mixture dissolved in $CH_2C\ell_2$ (2 ml), washed 3 times with water (2 ml) and dried with $MgSO_4$. After filtration $CH_2C\ell_2$ was removed under vacuum.

Further preparations were made without the washing procedure, consequently the acetal was usually stored in the presence of NaOMe.

NMR($CDC\ell_3$) 90 MHz δ = 3.59 ppm (s, 8H)

δ = 5.55 ppm (s, 1H)

δ = 7.28-7.55 ppm (m, 6H)

δ = 3.25 (Methoxy from NaOMe)

Preparation of monoacetate of pinacol

The acylation of pinacol was done following the method of Höfle.[18]

Pinacol (23.6g, 0.2 moles), Ac_2O (20 ml, 0.2 moles), triethylamine (27 ml, 0.20 moles) and 4-dimethylamino-pyridine (0.5g) (catalyst) were dissolved in pyridine (50 ml) and allowed to react at R.T. for about 3 days monitoring the reaction by NMR.

Pyridine was distilled off at 110-115°C (atomospheric pressure) and the mixture was fractionated at high vacuum. Further preparations were done using a large excess of pinacol which was removed after the reaction had been completed by dissolving the mixture in $CH_2C\ell_2$ and extracting with water. The solution in $CH_2C\ell_2$ was dried with $MgSO_4$ and the final product distilled.

b.p. = 48°C/0.12 mm		Clear liquid
NMR ($CDC\ell_3$)	60 MHz	δ = 1.18 ppm (s, 6H)
		δ = 1.48 ppm (s, 6H)
		δ = 2.02 ppm (s, 3H)
NMR $CDC\ell_3$)	90 MHz	δ = 1.17 ppm (s, 6H)
		δ = 1.46 ppm (s, 6H)
		δ = 2.01 ppm (s, 3H)

Attempted preparation of benzaldehyde bis(2-acetoxy of pinacol)acetal

Monoacetate of pinacol (40g, 0.25 moles) was mixed with $MeOCH_2CH_2OMe$ (30 ml), NaH (80% in oil) was wasted 3 times with petroleum ether then dried under vacuum and added to the solution. After a strong reaction controlled by cooling the flask, $PhCHCl_2$ (20g, 0.12 moles) was added and the solution allowed to reflux (oil bath at 110°C). The reaction was monitored by NMR but the signals of the product were not observed.

Variations of that method by adding potassium, change of the solvent such as DMSO, addition of $PhCHBr_2$ (instead of $PhCHCl_2$), excess of the alcohol or strong temperature condition (180°C overnight) were tried but still no product was observed. A new preparation was tried by mixing PhCHO (2g), $HC(OMe)_3$ (2g), monoacetate of pinacol (3g) and $MeSO_3H$ (1 drop). The reaction was allowed to reflux but no product was observed.

Preparation of benzophenone dimethyl ketal

Benzophenone (31g, 0.17 moles) and $HC(OMe)_3$ (18.5 ml, 0.17 moles) were mixed with MeOH (13 ml). One drop of $MeSO_3H$ was added as catalyst and the mixture allowed to react during 48 hrs. at R.T. The acid was neutralized with anhydrous K_2CO_3 and the solution filtered. The white

precipitate formed was filtered, washed with MeOH and recrystalized with ether.

m.p. = 47.48°C

NMR($CDC\ell_3$) 60 MHz δ = 3.11 ppm (s, 6H)

δ = 7.18-7.61 ppm (m, 12H)

Preparation of benzophenone bis(2-acetoxy ethyl)ketal

Benzophenone dimethyl ketal (8.4g, 0.037 moles) was mixed with monoacetate of ethylene glycol (7.7g, 0.074 moles) and $MeSO_3H$ (1 drop) added as catalyst. The solution was allowed to react and the formed MeOH distilled off. After neutralizing the acid with anhydrous K_2CO_3 the mixture was fractionated. The best fraction distilled at 106-112°C/ 0.10 mm but some dioxolane and monoacetate of ethylene glycol were present. That fraction was dissolved in $CH_2C\ell_2$, washed 3 times with water and dried.

NMR($CDC\ell_3$) 90 MHz δ = 2.05 ppm (s, 6H)

δ = 3.60-3.87 ppm (m, 4H)

δ = 4.15-4.40 ppm (m, 4H)

δ = 7.40-7.90 ppm (m, 12H)

Microanalysis: $C_{21}H_{24}O_6$ Found C = 67.5% H = 6.7%

Calc. C = 67.73% H = 6.50%

Preparation of acetophenone dimethyl ketal

Acetophenone (45 ml, 0.38 moles), $HC(OMe)_3$ (42 ml, 0.38 moles), MeOH (30 ml) and $MeSO_3H$ (1 drop) were mixed and the reaction (at R.T.) was monitored by NMR. The mixture was fractionated and the product collected.

b.p. = 84°C/13 mm Hg

NMR($CDC\ell_3$) 60 MHz δ = 1.53 ppm (s, 3H)

δ = 3.20 ppm (s, 6H)

δ = 7.30-7.62 ppm (m, 6H)

Attempted preparation of acetophenone bis(2-acetoxy ethyl)ketal

Acetophenone dimethyl ketal (3g) was mixed with mono-acetate of ethylene glycol (6g) and $MeSO_3H$ (1 drop). The NMR spectrum showed the presence of the product but a further attempt of purification was unsuccessful.

REFERENCES

1. B. Capon, D. Thacker, J. Chem. Soc. (B), 185 (1967).
2. E.L. Eliel, "Stereochemistry of Carbon Compounds", McGraw Hill, N.Y., 1962, p.265.
3. T.H. Fife, L.K. Jao, J. Org. Chem., 30, 1492 (1965; T.H. Fife, L. Hagopian, Ibid, 31, 1772 (1966).
4. P. Watts, J. Chem. Soc. (B), 543 (1968).
5. A.W. Willi, "Comprehensive Chemical Kinetics". Brandford and Tipper, Vol. 8, p.51.
6. T.H. Fife, J. Am. Chem. Soc., 89, 3228 (1967).
7. T.H. Fife, L.H. Brod, J. Org. Chem., 33, 4136 (1968).
8. B. Capon, M.I. Page, J. Chem. Soc. Chem. Comm., 1443 (1970).
9. R.A. McClelland, R.A. Ahmad, G. Mandrapilias, J. Am. Chem. Soc., 101, 970 (1975).
10. O. Bouab, G. Lamaty, C. Moreau, O. Pomares, Nouv. J. Chim., 5, 175 (1981).
11. R.A. McClelland, P.W.K. Lam, J. Chem. Soc. Chem. Comm., 883 (1980).
12. B. Capon, D. Thacker, J. Am. Chem. Soc., 87, 4119 (1965).
13. E. Anderson, B. Capon, J. Chem. Soc. Perkin II, 515 (1972).
14. T.H. Fife, T.J. Przystas, J. Am. Chem. Soc., 99, 6693 (1977).
15. T.H. Fife, T.J. Przystas, J. Am. Chem. Soc., 102, 292 (1980).

16. R.V. Patterson, Ph.D. Thesis, Glasgow University, 1978.

17. High Resolution NMR, Spectra Catalog. VARIAN 1963, Vol. 2, p.1.

18. Höfle, Angew. Chem. Int. Edit., 8, 981 (1969).