GENERAL ACID CATALYSIS IN ACETAL HYDROLYSIS

by

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To my wife - Isobel.

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Abstract

Recent advances in the study of acetal hydrolysis and the use of acetals in model systems for the investigation of enzymically catalysed hydrolysis are reviewed.

The kinetics of the hydrolysis of benzaldehyde substituted (X) - phenyl methyl acetals and substituted (Y) - benzaldehyde phenyl methyl acetals were measured in pivalate, acetate, d_1-deutero-acetate, ß-chloropropionate, formate and chloroacetate buffers, and in hydrochloric and deuterochloric acids. The hydrolysis rates measured in buffer solutions, of the twelve acetals studied were found to be dependent on the concentration of undissociated acid and shown to be authentic examples of general acid catalysis, with reference to current opinions that such observations might be manifestations of solvent, electrolyte or buffer effects.

The d_1-acetic acid catalysed d_4-methanolysis of benzaldehyde phenyl methyl acetal was followed in a high resolution N.M.R. spectrometer and the initial bond fission found to occur between carbon and the phenolic oxygen. It seemed not unreasonable to assume that the same process occurs also in the hydrolysis reaction.

Brønsted and Hammett linear free energy relationships were found to correlate the catalytic constants obtained from the hydrolysis of both (X) and (Y) substituted-acetal

series. The catalytic constants of the substituted (X) - phenyl acetals increased as the electron-withdrawing power of (X) increased, and the positive ρ value increased consistently as the catalytic power of the buffer decreased, viz. 0.43 in chloroacetate to 1.25 in pivalate. The ρ value for the hydronium ion catalysed reaction was -0.45.

Similarly, the negative ρ values obtained from the substituted (X) - benzaldehyde acetals increased in magnitude from -2.04 in chloroacetate to -2.34 in pivalate, with a value of -1.94 for the hydronium ion catalysed reaction.

As the electron - withdrawing power of (X) increased, the Brønsted α value decreased consistently from 0.96 for X = p-MeO to 0.49 for X = m - NO_2. Conversely as the electron - withdrawing power of (Y) increased, the α value increased from 0.68 for Y = p - MeO to 1.05 for m - NO_2.

Solvent isotope effects $k(H_3O^+)/k(D_3O^+)$, indicated not only a consistency of mechanism in the hydrolysis of all the substrates studied, but the trend in values, from 0.62 for X = p-MeO to 1.1 for X = m - NO_2, and 0.33 for Y = p-MeO to 0.66 for Y = m - F, correlated with the α and ρ values in determining the relative amount of bond making and braking in the transition states.

The results obtained were all indicative of an $A\text{-}S_E2$ mechanism in the general acid catalysed hydrolysis of aromatic aryl methyl acetals, with concerted proton transfer to

phenolic oxygen and carbon-phenolic oxygen bond fission in the rate limiting step and where incipient carbonium ion stability and leaving group ability, rather than a high relative degree of proton transfer in the transition state, were commensurate to faster hydrolysis rates. The comparison of this data with that obtained in other reaction series indicates that incipient carbonium ion stability and leaving group ability are prerequisites for the observation of general acid catalysis in acetal hydrolysis, although relief of steric strain through carbonium ion formation is also relevant.

The hydrolysis of benzaldehyde methyl acetyl acylal, the possible intermediate of acetate anion nucleophilic attack on benzaldehyde phenyl methyl acetal, was found to be general acid catalysed, and is believed to be the first reported example of buffer catalysis in acylal hydrolysis. The hydrolysis of p-methylbenzaldehyde methyl S-phenyl thioacetal was carried out in weak-acid buffers, and the results suggested, although not conclusively, that this substrate might also be catalysed by undissociated acid.

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I N T R O D U C T I O N

INTRODUCTION

"It is not generally appreciated how little is understood about the mechanism by which enzymes bring about their extraordinary and specific rate accelerations".

W.P. Jencks.[1] (1969)

The mechanism of the enzymically catalysed reaction has been studied over many years, and the recent statement by Jencks indicates the complexity of this important catalytic system. A more specific example of the problem is that the elucidation of the amino acid sequence and ultimately the three dimensional structure[2] of the glycosidase lysozyme led to an intensive chemical and biophysical investigation of that system which has not yet revealed the exact mechanistic principles involved. Workers in this field have sought model systems in an attempt to explain the mechanistic and rate differences observed between glycoside hydrolysis in the enzymic and non-enzymic systems. The significance of the "non-general" behaviour propounded in more recent work must be interpreted with caution, although it is hoped that it will lend itself to a closer insight of the enzyme problem.

The aim of this introduction will be to outline the most significant of the mechanisms suggested to account for the "extraordinary and specific rate accelerations" of the

enzymically catalysed hydrolysis of glycosides, and the model systems used to explore these hypotheses. A brief review of the generally accepted mechanism of acetal hydrolysis will be followed by a more detailed discussion of the requirements necessary for the observation of general acid catalysis and the physical parameters incorporated in such an investigation. The enzyme lysozyme will frequently be referred to because of the more detailed knowledge surrounding it, although it must be remembered that "We do not understand the mechanism of action of any glycosidase".

B. Capon.[3] (1971)

The existence of enzyme-substrate complexes as intermediates in enzymically catalysed reactions has been shown either by isolation and chemical characterisation of the complex, by accommodating observed rates with the formation and breakdown of such intermediates, or showing that a common intermediate is formed with specific substrates in the enzymatic reaction (see Ref. 1). The general enzymatically catalysed reaction is then described, on this basis, by equation (1) in which ES represents the intermediate complex.

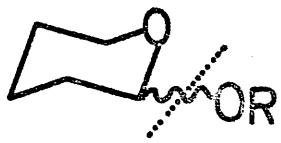
$$E+S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_3} E+P \quad \ldots\ldots\ldots\ldots (1)$$

The formation and nature of this intermediate complex is critical to the observed rate enhancements brought about

by enzymes, and the rate of formation (k_3) of products (P) will depend on the ease of the chemical breakdown of the substrate within this environment.

Glycosidase catalysed hydrolysis resemble the acid catalysed hydrolysis of alkyl and anyl glycosides in that bond fission in the substrate usually occurs between carbon 1 and the anomeric oxygen.

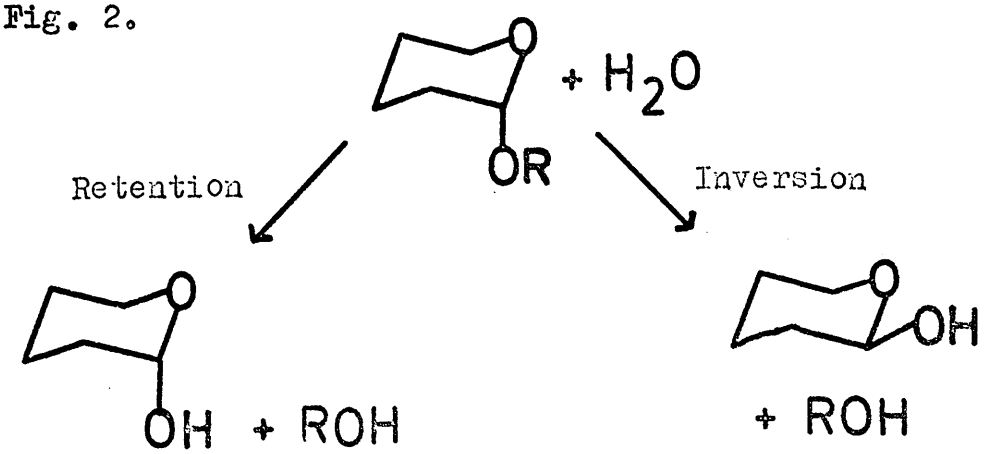
Fig. 1.



This has been demonstrated for several glycosidase catalysed hydrolysis,[5] including the lysozyme catalysed hydrolysis of tri-N-acetylchitotriose in O^{18}-enriched water, where the products, di-N-acetyl chitobiose and N-acetylglucosamine contain the label at position 1 only.[4]

Further, since these reactions are formally nucleophilic substitutions of the saturated carbon 1, the hydrolysis by the enzymes proceed either with inversion or retention of configuration (Fig. 2)

Fig. 2.



Several processes have been forwarded to explain the facilitation of glycosidic oxygen bond fission after formation of the enzyme substrate complex, and thus the enhanced rate of enzymic catalysis. Six such processes are described below, although it is unlikely that one single processes accounts for the overall catalytic power of the enzyme, or that these processes are always distinguishable from each other. Model systems have been forwarded to exemplify several of these processes, and these will also be mentioned.

i) a microscopic medium effect.

ii) electrostatic stabilization of a carbonium ion intermediate

iii) conformational distortion of the substrate

iv) nucleophilic catalysis by a functional group of the substrate

v) intra-complex nucleophilic catalysis

vi) intra-complex general acid catalysis.

i) The microscopic medium effect is somewhat of an unknown factor necessarily involving the environment within the enzyme-substrate complex, which is only realised to a limited extent at the present time. Phillips and co-workers determined not only the three-dimensional structure of lysozyme, but also the enzyme complex formed with the inhibitor tri-N-acetyl chitotriose, and identified the

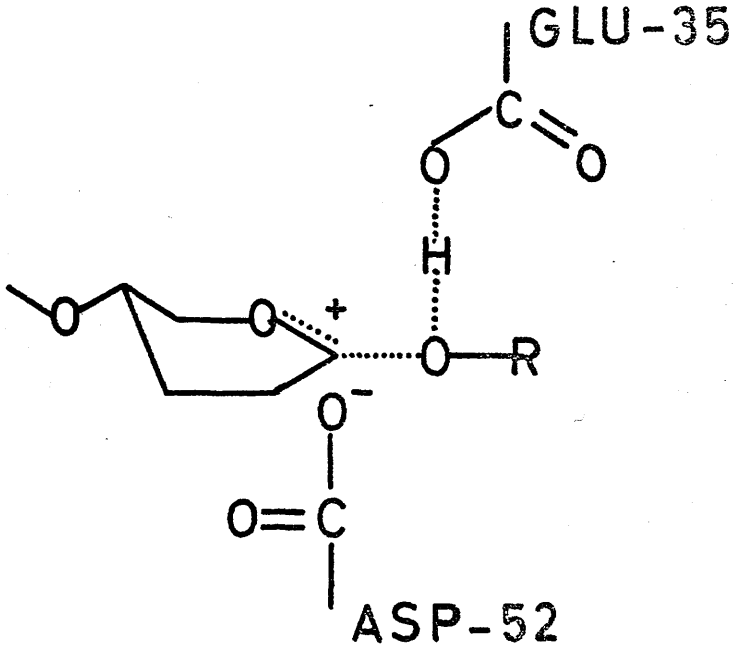
active site as a hydrophobic cleft of the enzyme made up largely of amino-acid side chains such as valine, phenylalanine, leucine and tryptophan.[6,7] Analogous hydrophobic centres have been ascertained, in several enzymes including, for example, chymotrypsin,[8] which has a "Tosyl Hole". In the case of lysozyme it has been argued by Perutz[9] that the catalytic efficiency of the enzyme may result from the reaction taking place within the low- polarity region of the hydrophobic cleft, however dispute arises over the relative importance of polarity and dielectric constant.[5] (for a discussion on hydrophobic forces see Jencks Chpt. 8[1])

Micelles have been used extensively in the study of hydrophobic forces in aqueous solution since X-ray examinations have shown them to simulate globular proteins, such as enzyme, both in structure and property.[10] Considerably more work has to be completed, however, before the rate enhancements generated by microscopic medium effects can be determined with regard to general acid catalysis, electrostatic stabilisation and nucleophilic catalysis.

ii) Electrostatic stabilisation of a carbonium ion intermediate has been forwarded as a factor in the rate enhancement of several enzymes. The concept was first suggested for the mechanism of the action of α-amylase by Koshland.[12]

More recently it has been incorporated in the mechanism of action of lysozyme proposed by Vernon[13] and Phillips[6,14] which involves the carboxylate groups of Glu-35 and Asp-52.

Fig. 3.



It is suggested that Glu-35 acts as a general acid catalytic entity, while the Asp-52 ionised residue stabilised the incipient oxocarbonium ion by formation of an ion pair (see also ref.15). This postulate, however, has recently come under scrutiny by Dunn and Bruice[16] who suggest that, on the basis of a model system employing methoxy methyl esters of substituted phenols, rate enhancement is a steric rather than electrostatic effect.

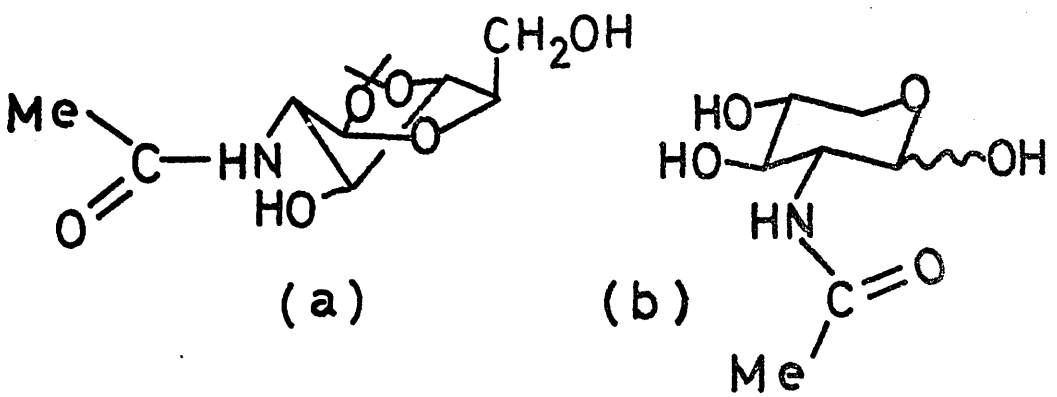
The anionic surfactant catalytic system of Cardes et al[11] which utilises reagents such as sodium dodecyl sulphate to form micelles, and consequent inclusion complexes, would appear to support the theory of electrostatic

stabilisation, although allowance is made for the possibility of geometrical distortion caused by substrate substituents. In this instance, reference is not directed at enzymic action, although the model system proceeds via an intermediate complex analogous to the enzymic process. It is difficult to estimate the relevance of this system to the enzymic reaction, as is the extrapolation made by Dunn and Bruice above.

iii) Steric requirements and conformational distortions

Strain[17,18] and orientation[19] have been studied to date with a semi-quantitative evaluation only. Conformational distortion in the N-acetyl-glucosamine-lysozyme complex was suggested by Phillips[14] and Vernon[13], where, if the reaction proceeds via a carbonium ion, it was proposed that the residue D of NAG-6 would adopt a half-chair conformation to facilitate more favourable non-bonded interactions between C(6) and O(6) and the enzyme. Fig.4(a)

Fig. 4.



The binding to lysozyme of N-acetyl-D-xylosamine Fig. 4(b) as studied by N.M.R. spectroscopy,[20] and N-acetyl-glucosamine[21] were found to be very similar.

The more recent publication by Storm and Koshland[22] has evoked some difference of opinion on the hypothesis of "Orbital Steering". This concept is postulated to account for the catalytic efficiency of an enzyme in terms of an orientation factor related to angular preferences of electron orbitals. Capon,[23] however, has argued in some considerable detail that it is not justifiable to invoke this concept to explain the variations of rates in the lactonisation of the hydroxy acids studied and Bruice et al concluded that "if orbital steering does exist, experimental and theoretical evidence to support this concept have yet to be presented".[49]

Nucleophilic Catalysis.

It was mentioned earlier that hydrolysis of glycosides proceeds with either retention or inversion of configuration. An important factor in the mechanism for those glycosidase catalysed hydrolysis which proceed with retention may be nucleophilic assistance by a group in the substrate or a group in the enzyme. The subject has come under discussion by Fisher and Stein,[29] Bender and Breslow,[30] Mayer and Larner,[31] and Van Wunendaele and De Bruyne[46] who have considered assistance by

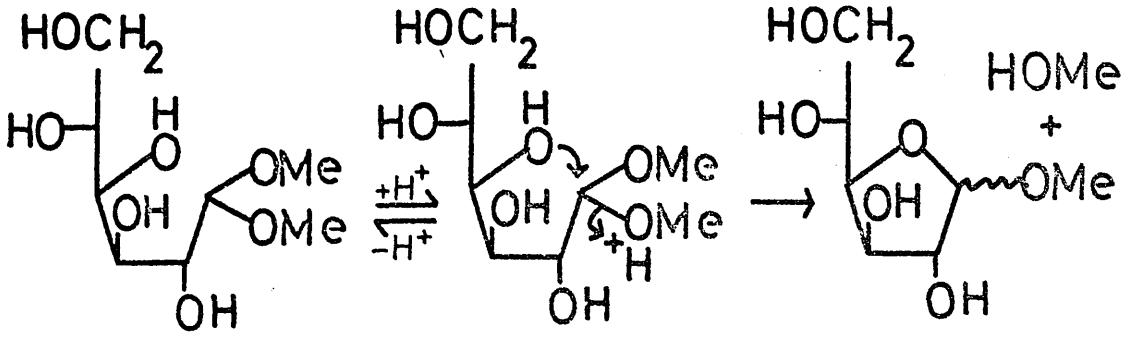
a functional group of the enzyme, and Lowe, who has considered assistance by a functional group of the substrate.

Although acetals and glycosides normally react through carbonium ions and do not require nucleophilic assistance, the situation could conceivably be different within an enzyme-substrate complex where a strong nucleophile could conceivably be held in close proximity to the glycosidic centres.

iv) Nucleophilic participation by a functional group of the substrate in the enzymic reaction has been investigated by attempting to simulate the process in a model system using acetals and glycosides.

The acid catalysed ring closure of dimethyl acetals of glucose and galactose revealed a 30-300 rate increase over that predicted from related substrates, and Capon and Thacker[33] concluded that nucleophilic attack by the C-4 hydroxyl group was synchronous with acetal bond fission.

Fig. 5.



However, the authors stated that the reaction type could not be classified as a hydrolysis. Speck et al[69] have suggested that the acid catalysed hydrolysis of methyl-thioacetaldehyde diethyl acetal occurs with neighbouring group participation of the methyl thio function to form an intermediate sulphonium ion (see page 30).

Fig. 6 shows one of the mechanisms that has been suggested for the action of hen's egg-white lysozyme on β-1-4- linked oligosaccarides of N-acetylglucosamine,[39] Lowe suggested that the neighbouring amido-group of the substrate facilitates bond fission in complement to the general-acid catalytic function of the carboxylate group of the glutamic acid residue 35 of the enzyme.

It has been demonstrated that β-glycosides of N-acetyl-glucosamine frequently react with neighbouring amido group participation[40] although Raftery and Rand-Meir[15] have indicated that the 2-acetamido group is not essential for enzyme activity. The products of lysozyme-catalysed reactions can be either inverted or non-inverted indicating that neighbouring acetamido groups of the substrate could be involved rather than nucleophilic moieties in the enzyme.

v) Intra-complex nucleophilic catalysis is shown diagrammatically in Fig.7 for hydrolysis by a β-glucosidase where the nucleophilic residue (N) acts in

Fig.6

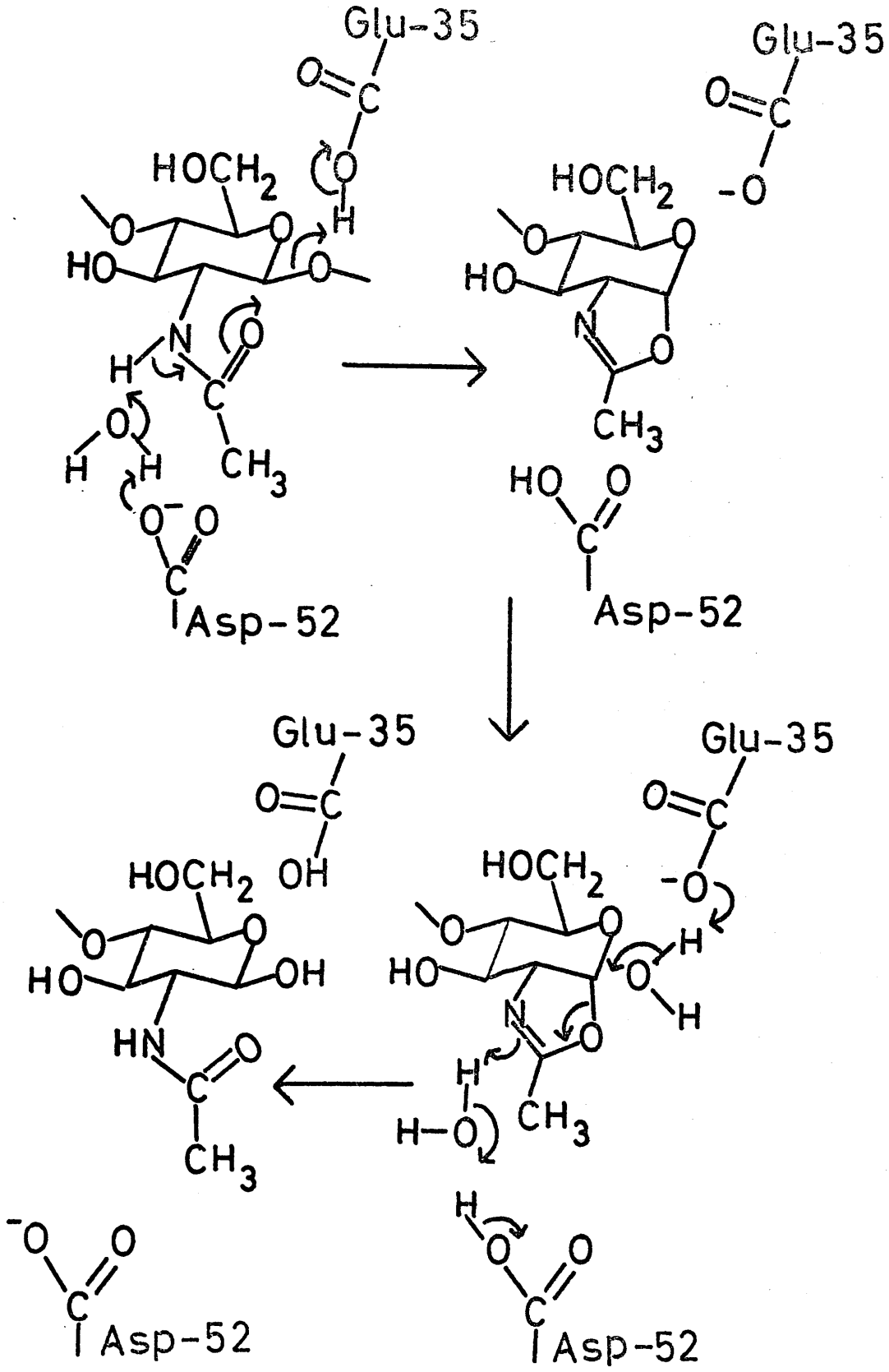
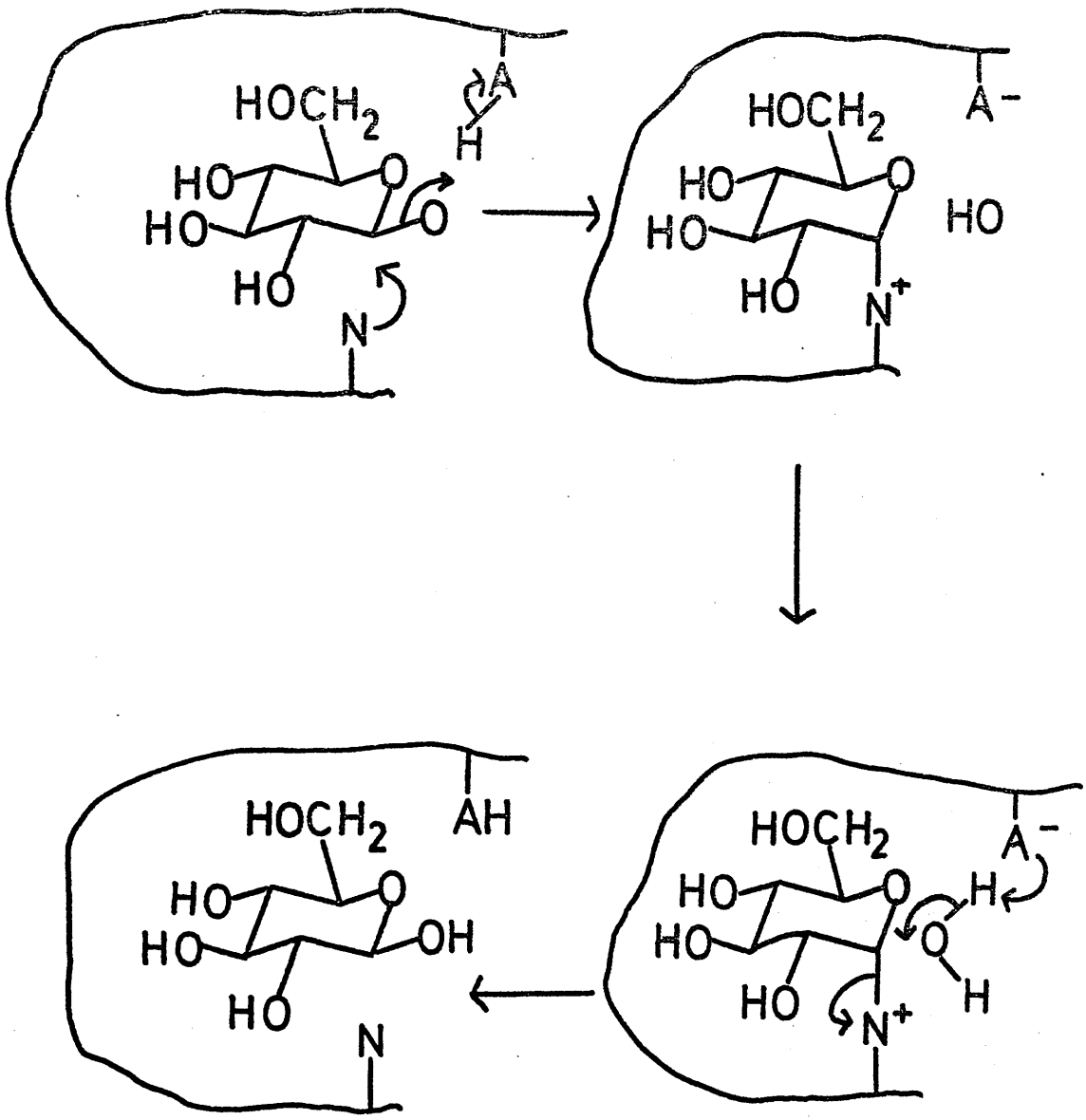

Glu-35
HOCH2
HO
O
H
N
C
CH3
Asp-52
Glu-35
HOCH2
HO
N
O
CH3
HO
C
Asp-52
Glu-35
HOCH2
OH
HO
OH
HN
CH3
Asp-52
Glu-35
HOCH2
HO
N
CH3
Asp-52

Fig.7

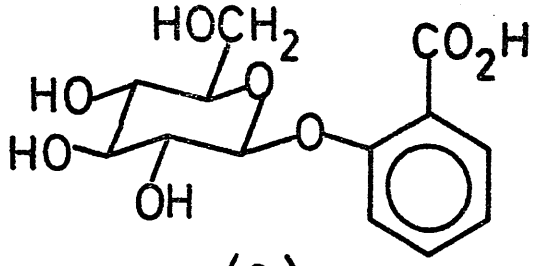


conjunction with the general acid catalytic function of the acid residue (HA) Fig.7.

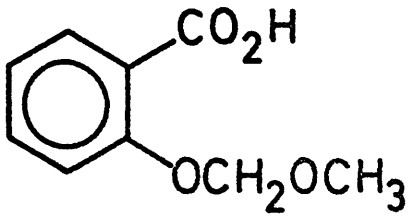
The overall retention of configuration in the substrate is then a result of two inversions in a "push-pull" mechanism. Koshland first proposed this mechanism in 1953 which was described, logically, as a double-displacement mechanism.[24,25] The intermediate in this reaction sequence would be a covalent glycosyl enzyme,[26] the intervention of which has not yet been proven in any glycosidase-catalysed reaction,[1,27] although a covalent glucosyl enzyme intermediate has recently been isolated from the reaction of sucrose with sucrose phosphorylase, where binding between the substrate and enzyme via an ester linkage was proposed.[48] A dubiety concerning this mechanistic hypothesis lies in the fact that nucleophilic participation would appear to be relevant in the reactions of both β-amylase (inverting) and α-amylase (non-inverting). The alternative suggestion is that the proposed nucleophile may, in fact, form an ion pair with the carbonium ion intermediate, and the steric cause of the catalysis then depends on the direction in which the water molecule can attack the carbonium ion of the ion pair[28] (see also Ref.5).

The possibility of carboxylate nucleophilic

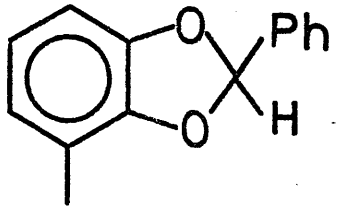
participation in the apparent intramolecular general acid catalysis of 2-carboxyphenyl-β-D-glucoside[34,35] Fig. 8(a) was excluded by investigations of Capon and Smith,[36] and Page,[37] who investigated the enhanced rates of hydrolysis of acetals (b) and (c) in Fig.8, whose behaviour resembled that of (a) Fig.8.

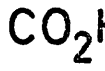


(a)



(b)





(c)

In (b) possible intermediates were synthesized and shown not to be intermediates at all, and in (c) nucleophilic catalysis was shown to be impossible because of the unfavourable stereochemical disposition of the carbonyl group.

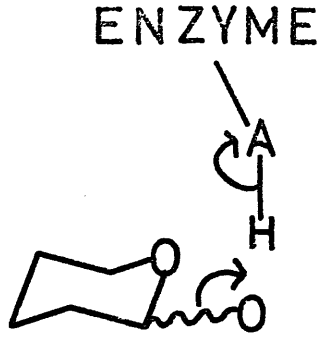
Intramolecular nucleophilic assistance by a carboxylate group was shown to function in the acid

catalysed fission of the acetal bond in the cyclization of phthalaldehydic acid acetal, however, overall nucleophilic catalysis was not prevalent.[38] Intramolecular nucleophilic catalysis has been claimed in the hydrolysis of 2-carboxybenzylidine catechol,[37] and if this claim is true, it will be the only one recorded (see Ref.33).

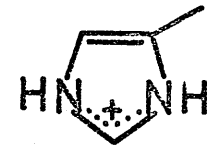
vi) Intra-complex general-acid catalysis.

Over the last two decades, intracomplex general acid catalysis has been incorporated as a relevant feature in probably every mechanism of glycosidase action (see Ref.5), and its relevance has already been suggested in the preceeding sections. After formation of the enzyme-substrate complex it is proposed that an acidic group of the active siteof the enzyme transfers a proton to the glycosidic oxygen concerted with fission of the carbon-oxygen bond of the substrate. Fig.9 shows this process diagrammatically with some of the acidic groups which have been suggested to act in this way.

Fig.9



Lysozyme —CO_2H

Amylase 

Amylase —NH_3

β-Galactosidase —SH

Some considerable amount of investigation has been carried out in the study of the glycosidase-catalysed reactions of aryl glycosides, since, in many instances, these substrates have been found to hydrolyse as well as the natural substrates (see Ref.5). It is then possible to determine such kinetic parameters as substituent effects, which, although not necessarily being a direct reflection on the natural substrates, would lend themselves to a comparative overall picture of the natural substrate catalysis mechanism. The substituent effects of a limited number of glycosidase-catalysed reactions have been reported and consequently the correlated data forms only a small part of the overall picture. Table 1 shows data extracted from several

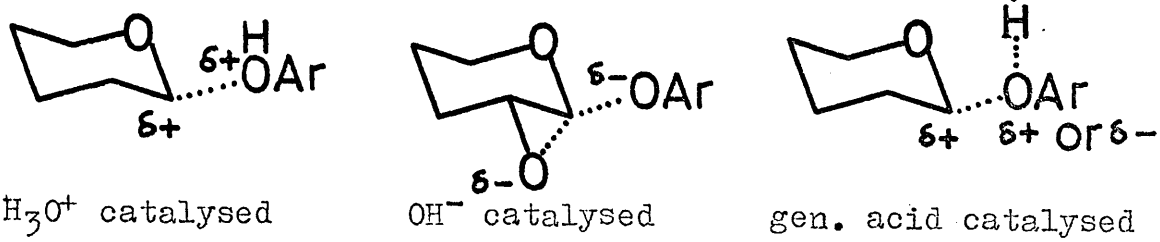
such studies. (see Ref.3).

TABLE 1

Enzyme	Substrate	rho value	ref.
β-Glucosidase	Aryl-β-D-Glucosides	1.0(meta) 1.5(para)	41
α-Amylase	Aryl-α-Maltosides	2.0	42
Lysozyme	Aryl-β-D-di-N-acetyl-chitobiose	1.32	43
α-Glucosidase	Aryl-α-D-Glucosides	0	44
β-Xylosidase	Aryl-β-D-Xylopyranosides	-0.25(meta) +0.108(para)	46
Acid Hydrolysis		-0.06 to -0.66	
Alkaline Hydrolysis		+2.5 to +2.8	

In the transition state of a general acid catalysed reaction, the proton transfer from the catalyst to substrate would be incomplete and therefore a rho value intermediate between that of a ^{-}OH catalysed reaction (involving unprotonated leaving group) and the H_3O^+ catalysed reaction (involving a completely protonated leaving group) would be expected, as is the case.

Fig. 10



H_3O^+ catalysed OH^- catalysed gen. acid catalysed

The rho values reported in Table 1 are then consistent with enzymic reactions proceeding with general acid catalysis. (see later section on Hammet $\sigma\rho$ values).

It would be extremely useful, in this light, if the enzymically catalysed reaction could be simulated under non-enzymic conditions since the ρ values obtained above could have been derived from Kcat values which were composed of several microscopic rate and equilibrium constants, rather than the microscopic rate constants (k_3 in equation 1) for the breakdown of the enzyme-(substituted) substrate complexes. Unfortunately the non-enzmyic hydrolysis of aryl glycosides almost always proceed via a specific acid catalysed mechanism,[36] and the problem must then be approached by way of the following model systems to attain a reasonable comparison.

Model Systems for General Acid Catalysis.

The following systems have been most widely used in the study of general acid catalysis in glycosides and acetals in a non-enzymic reaction.

a) The study of a system in which a catalyst, although not an enzyme, would simulate the enzymic mechanism by reacting via an intermediate complex (association-prefaced catalysis).

b) Intramolecular general acid catalysis, where the catalytic group is part of the same molecule in which

bond fission occurs. A stereochemically favourable reaction centre might then result in enhanced, and therefore observable general acid catalysis.

c) Bifunctional catalysis, where a potential nucleophile and the catalysing group are part of the same molecule in which bond fission occurs, i.e. an extension of b).

d) To study intermolecular general acid catalysis.

The use of enzyme-like catalysts has not been extensively studied although it is an attractive proposition. The use of micelles in the study of hydrophobic forces in aqueous solution (see Ref.1) and their ability to enhance the rate of hydrolysis of orthoesters and acetals[47] has already been mentioned. The rho values for the surfactant-catalysed reactions of these substrates are constantly lower than those in the aqueous phase suggesting a greater extent of carbon-oxygen bond cleavage in the transition state of the micellar phase. This behaviour was rationalised as a function of electrostatic stabilisation although the various substituents could conceivably alter the position of the substrate on the micellar surface or groups on the micellar surface could alter the polarity of the substrate substituents as was suggested by Wunendaele and De Bruyne,[46] for the enzymic hydrolysis of β-D-xylopyranosides.

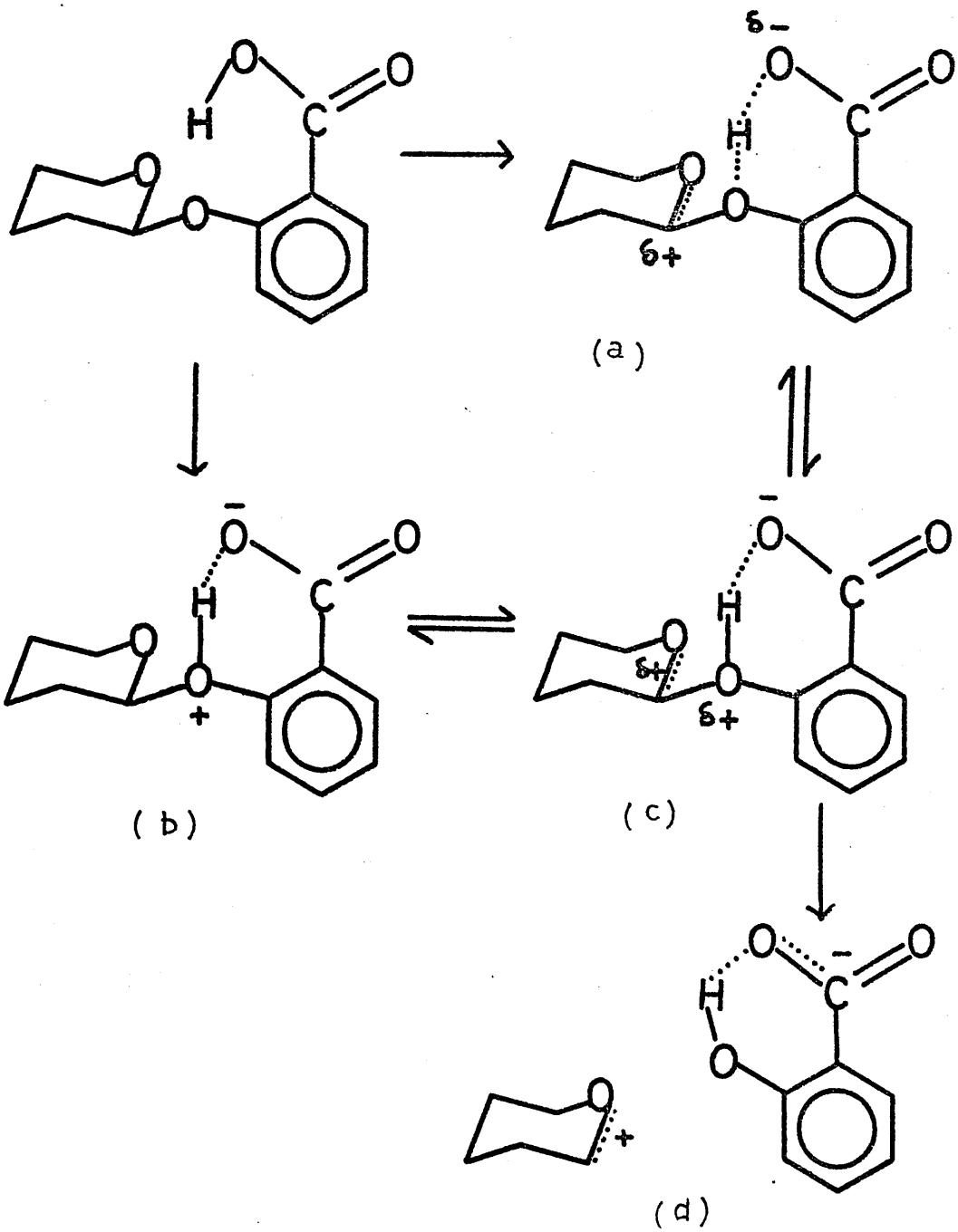
Other enzyme models have been used, usually

implementing the binding of small molecules to polymers of known structure in aqueous solution, and of these clathrates have been most widely used. (see Ref.1).

b) Intramolecular General Acid Catalysis has already been mentioned with reference to 2-carboxyphenyl-β-D-Glucoside.[34,35] The pH-Rate profile of this compound was found to be sigmoidal with a pseudo - first order rate constant dependent only on the concentration of glycoside with ionised carboxyl group. At pH 4 the hydrolysis rate is 10^3 times that for 4-carboxyphenyl-β-D-glucoside.[34] This type of behaviour would appear to be general for phenolic glycosides and acetals with ortho carboxyl groups. Intramolecular nucleophilic participation has already been eliminated[36,37] and the two possible mechanisms left are; intramolecular general acid catalysis with simultaneous proton transfer and aglycon carbon - oxygen bond fission (Fig.11(a), or specific acid catalysis involving a special electrostatic or field effect being exerted by the carboxylate anion on the protonated intermediate Fig. 11(b). It has been pointed out that it is extremely difficult to differentiate between these two types of mechanisms,[1] since transition state 11(a) could be regarded as being stabilised by intramolecular hydrogen bonding, of which much of the

energy is electrostatic, the transition states 11(a) and 11(b) are very similar and could pass through the same intermediate 11(c).

Fig. 11.

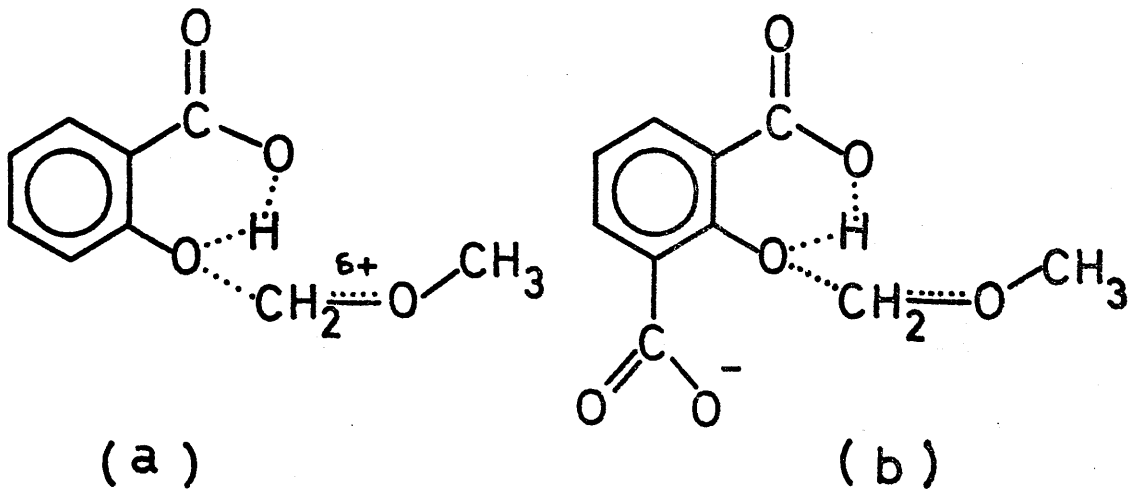


The hydrolysis of similar glycosides and acetals all lead to the formation of the highly stabilised salicyclic anion 11(d), and this factor, rather than carboxylate group proximity, may be of greatest importance. Attempts to study possible intramolecular general acid catalysis without this stabilising feature have proved abortive.[52,53]

The hydrolysis of many acetals and glycosides has been shown to involve specific rather than general acid catalysis with rate enhanced by a neighbouring carboxyl group.[51] Several workers have investigated the possibility of intramolecular general acid catalysis with suitable stereochemical and structural requirements. (see Ref.34). Larsen et al[54] have shown substantial rate enhancement in the hydrolysis of glucopyranosides containing carboxylic residues in the aglycon group, whereas other substituents in the aglycon moiety of alkyl glycosides affect the rate only slightly (see Ref.5). Bruice and Piszkiewicz[53] have interpreted several such reactions involving carboxylate groups as A-1 mechanisms with rate enhancement due to inductive effects and although the kinetic equivalence of such mechanisms has been shown to be similar, orientation of carboxylate group, and basicity of the acetal or glycoside oxygen atom are also factors of considerable importance.[34] It is therefore rather

dangerous to classify all such reactions in the same mechanism.

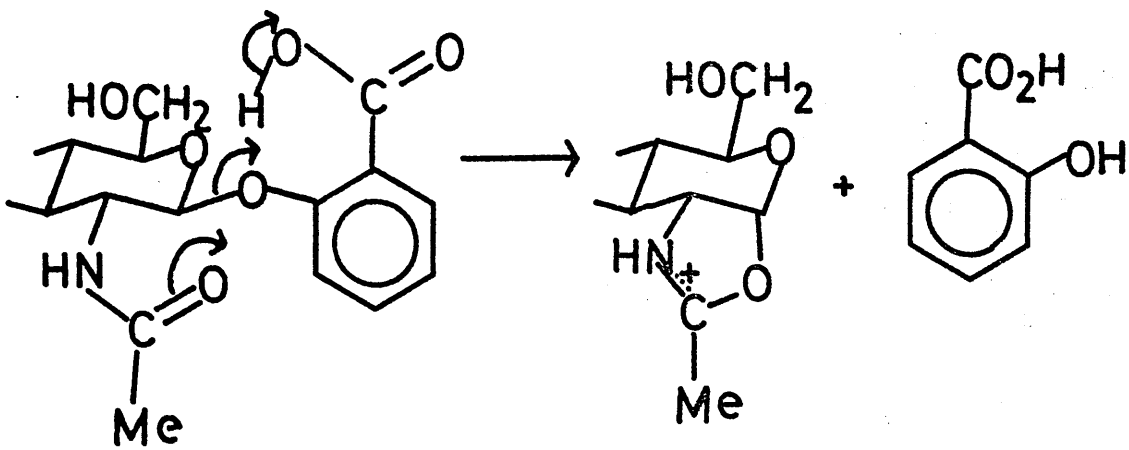
The recent work of Dunn and Bruice[16] has shown intramolecular general-acid catalysis in the hydrolysis of ortho-carboxyphenyl methyl acetals of formaldehyde, where the positive rate enhancements were too large to compare with the calculated specific acid catalysed rate constant for the undissociated form of the same acetal 12(a)



The concept of general acid catalysis is most pertinent to the mechanism of action of lysozyme since it is argued that the glycoside is general acid catalysed by proton donation from an acidic group of the enzyme (Glu-35). However, the electrostatic role of Asp-52 has been questioned by Dunn and Bruice who found the di-ortho-

carboxylate substrate 12(b) insensitive to the ionisation of the second carboxyl group and concluded that steric, rather than nucleophilic or electrostatic participation was involved.

c) Bifunctional Catalysis Bruice and Piszkiewicz[35,40] found that the rate constant for the spontaneous hydrolysis of o-carboxyphenyl-2-acetamido-2-deoxy-β-D-glucopyranoside was 7.1 times greater at 78.2°C than that for the o-carboxyphenyl-β-D-glucopyranoside mentioned previously. Because of the similarity of the σ* constants for acetamido and hydroxyl groups, the authors suggested a concerted nucleophilic general acid mechanism. Fig.13.



It has been pointed out however, that since specific acid catalysed reactions of the acetamido glucosides are generally 2-3 times faster than the unsubstituted glucosides at 78.2°C, this would give a rate difference of

only 2-3 times for the di-substituted compound, assuming the enhancement in general acid catalysis followed that of specific acid catalysis.[37]

d) Intermolecular General Acid Catalysis. The mechanism of the hydrolysis of acetals and glycosides has been reviewed by Vernon,[57] Long,[58] Cordes,[59] Be Miller[60] and Ingold,[61] and general acid catalysis by Bell,[62] Jencks,[1] Bunnett[63] and Eigen,[104] consequently, only a brief discussion of the salient factors involved will be given here.

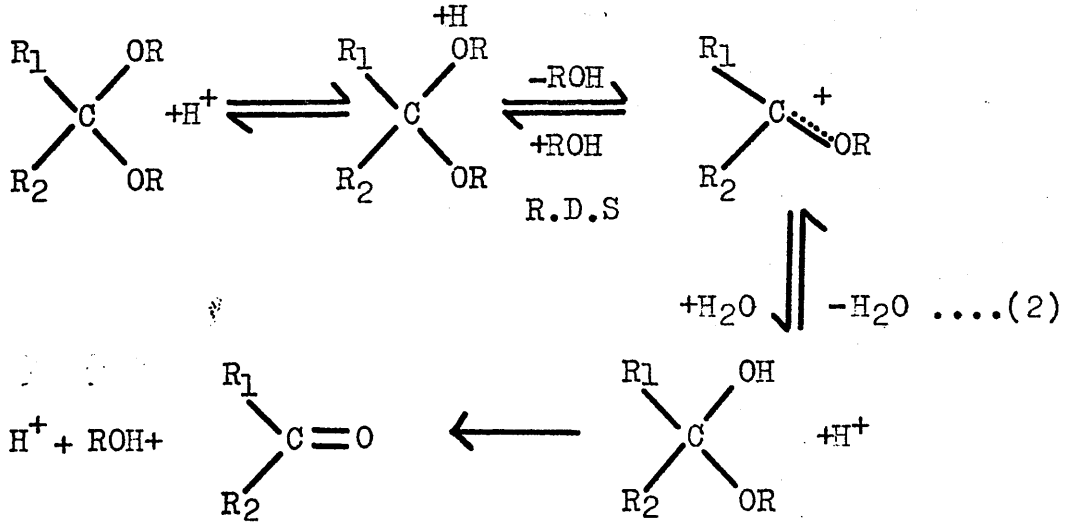
Whereas acetals appear to be exclusively acid catalysed, certain glycosides do undergo hydrolysis in basic conditions, however, the main concern here is with acetals since they have been used more extensively in the search for general acid catalysis. The hydrolysis of glycosides and other acetals until very recently have provided a classical example of specific acid catalysis (A-1) in acidic aqueous solution, and the detection of general acid catalysis has been the detection of "non-general" behaviour.

The concept of general acid catalysis has already been mentioned in systems where the catalytic group is held in close proximity to the site of bond fission. It is relevant, therefore, to outline the factors involved in

the classical A-1 mechanism, and the structural and other changes which must be made to observe intermolecular catalysis by the undissociated acid in aqueous solution.

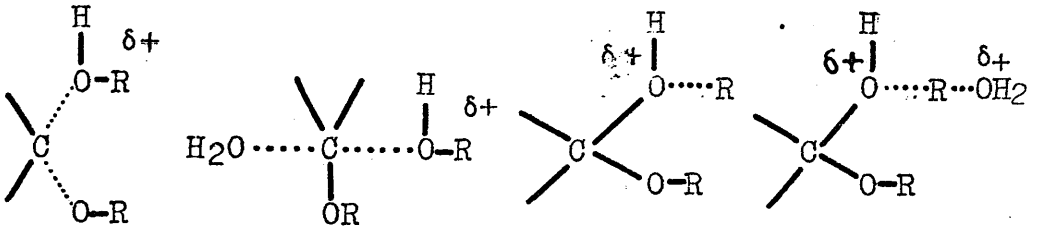
A-1 mechanism

The following discussion is adapted mainly from the comprehensive review of Cordes.[59] The first step in classical acetal hydrolysis in acidic aqueous solution is a fast pre-equilibrium protonation of the substrate followed by a rate-determining loss of alcohol to give an oxonium-carbonium ion, which is attacked in a fast step by water, equation 2.



Cordes originally proposed four possible transition states for the acid catalysed hydrolysis of acetals and ketals, each of which were derived from the conjugate acid of the substrate since a proton, or its kinetic equivalent was shown to be involved in the transition

state from the rate law of these hydrolysis (Fig.14)



(1) (2) (3) (4)

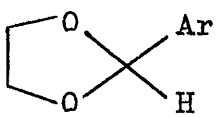
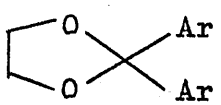
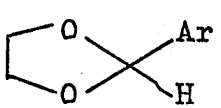
Transition states (3) and (4) above, were ruled out after it was established that, for most cases, the hydrolysis of acetals proceeded with carbonyl carbon-oxygen bond cleavage. Lucas and O'Gorman[65] found that hydrolysis of acetals derived from optically active alcohols yielded the alcohol with the same optical rotation as the starting material. The possibility that the alkyl carbonium ion (3) above might be formed during the hydrolysis of acetals prepared from alcohols capable of forming stable carbonium ions was studied, however even here no racemisation or rearrangement was observed.[66] Transition state (4) was excluded by the observation that methanolysis of phenethyl alcohol - derived acetal yielded phenethyl alcohol and not the corresponding methyl ether.[59] Isotope tracer studies by Bourns et al[67] corroborated these findings, since the hydrolysis of benzaldehyde di-n-butyl acetal and n-butyraldehyde di-n-butyl acetal in O^{18} enriched water yielded alcohols of normal isotopic content.

Lines of evidence derived from several sources indicated that solvent was not involved as a nucleophilic reagent, and therefore (1) in Fig.14 described the transition state for the initial reaction in which covalent bonds to carbon are broken.

Second order rate constants for acetal and ketal hydrolysis are extremely sensitive to structural alterations in both the aldehyde and alcohol moieties. The acid catalysed hydrolysis of a series of m-substituted diethyl acetals of benzaldehyde in 80% aqueous dioxan are correlated by the Hammett σ values and yield a rho value of -3.35,[68] which is thought consistent with a rate determining carbonium ion formation, where electron donation from a polar substituent favours both pre-equilibrium protonation and carbonium ion stabilisation. The electronic requirements of these two processes are reflected in the reduced ρ value of -0.66 obtained by Nath and Rydon[41] for the acid catalysed hydrolysis of a series of substituted aryl-β-D-glucopyranosides. Table 2 shows the ρ values obtained in the hydrolysis of various acetals. (see chapter on Hammett Equation).

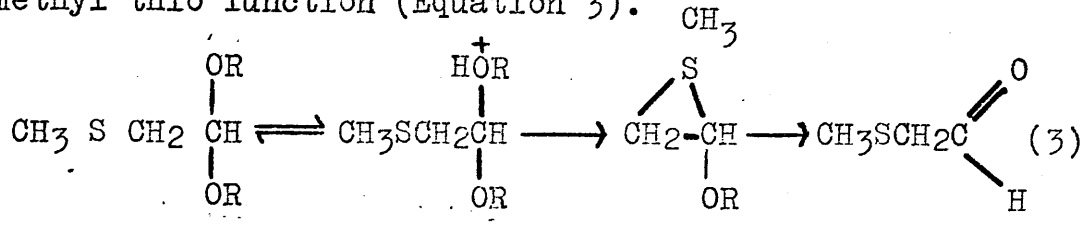
TABLE 2

Rho values for the acid catalysed hydrolysis of various acetals

Substrate and substituent position		Solvent	Temp °C	Correlation	Rho	Ref.
$ArCH(OEt)_2$	m	50% aqueous dioxan.	30	$\log k/k_o = \rho\sigma$	$\rho = -3.35$	68
ditto	m & p	ditto	30	$\log k/k_o = \rho[\sigma+r(\sigma^{+}-\sigma)]$	$\rho = -3.35$ $r = 0.5$	68,127
ditto	p	H_2O	25	$\log k/k_o = \rho\sigma$	$\rho = -3.35$ $\rho = -4.1$[a]	11
	p	50% aqueous dioxan	30	$\log k/k_o = \rho[\sigma+r(\sigma^{+}-\sigma)]$	$\rho = -3.25$ $r = 0.5$	68,127
	p	20% dioxan water	30	$\log k/k_o = \rho\sigma$	$\rho = -4.7$	100
	p	H_2O	30	$\log k/k_o = \rho\sigma$	$\rho = -2.0$	84

a) In the presence of sodium dodecyl sulphate.

Speck et al[69] suggest that the acid-catalysed hydrolysis of methyl-thioacetaldehyde diethyl acetal occurs with neighbouring group participation of the methyl thio function (Equation 3).



(3)

Although the polar substituent constants for methyl thio and methoxy functions are similar, the former compound hydrolysis about 100 times faster than the latter, indicating rate determining formation of the cyclic sulphonium ion since both molecules of ethanol liberated appear simultaneously. Such nucleophilic participation has not been observed intermolecularly. Schalegar and Long[70] have reviewed the use of entropies of activation as a criterion for acid catalysed reactions in aqueous solution. Compiled data[57] indicates that ΔS is usually near zero or slightly positive in acetal hydrolysis indicating an A-1 mechanism proceeding with unimolecular decomposition of the protonated substrate.

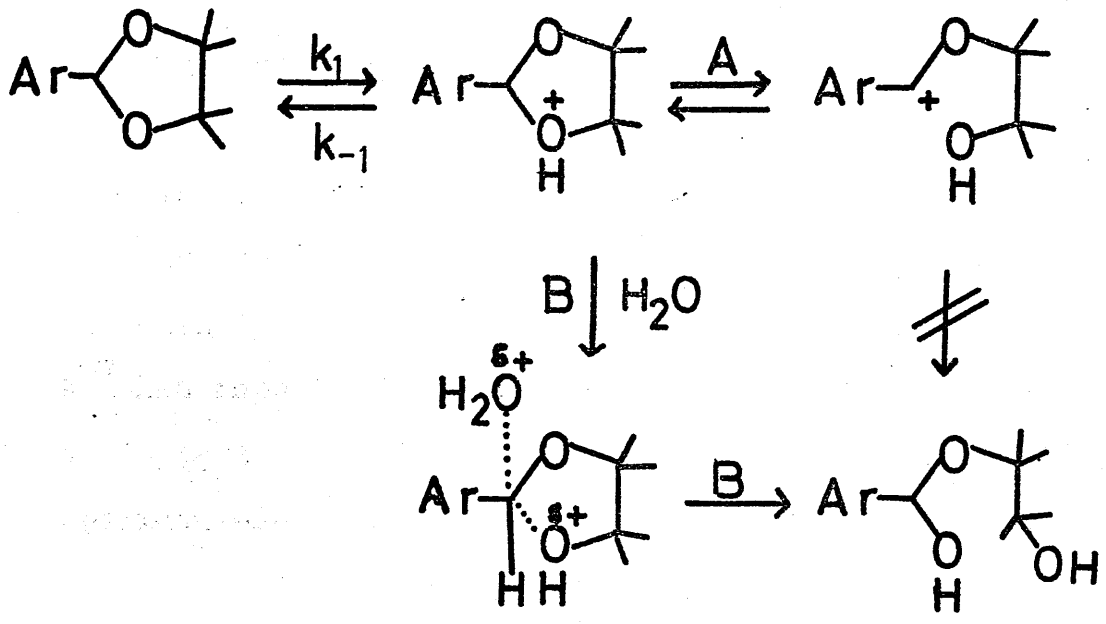
The values obtained for the volumes of activation of these reactions fall into the range $\Delta V = -2$ to $+6 cm^3$/mole which is also indicative of a unimolecular reaction. When solvent participation is encountered $V = -6$ to $-10 cm^3$/mole.[71]

Correlated data has shown that deuterium solvent isotope effects on the rates of hydrolysis of acetals, ketals and glucosides fall into the range kD_3O^+/kH_3O^+ 2 to 3 which is in agreement with the theoretically predicted values for a unimolecular (A-1) specific acid catalysed mechanism.[72,73]

A-2 Mechanism.

Cyclic acetals, derived from diols, are of interest because of the possibility that ring opening, i.e. carbon-oxygen bond cleavage, other than carbonium ion formation, might be the slow step in the hydrolysis mechanism. Reversibility of the unimolecular opening of a dioxolan ring, for example, could result in an A-2 mechanism, since internal recapture of the carbonium ion by the bound hydroxy leaving group will be faster than capture by solvent water, and hydrolysis can then proceed only with solvent attack on the forming carbonium ion (see ref[159]) Fife and Brod[74] have substantiated such a mechanism with their findings on the hydrolysis of 2-aryl-4,4,5,5 tetra-methyl dioxolanes, where this compound is hydrolysed approx. 5×10^5 more slowly than acetophenone diethyl acetal (Fig. 15)

Fig. 15.



Only when attack by water on C(2) is concerted with fission of the ring (pathway B) can hydrolysis occur, a process which is slowed down about 540 fold on the introduction of a 2-methyl group.

There have been several studies of cyclic acetals[77-84] however the mechanisms of their hydrolysis are not as unanimously accepted as is that of their acyclic counterparts. Although the general census of opinion favours the A-1 mechanism for cyclic acetal and ortho ester[88] hydrolysis. Fife[74,84] and Orvik[83] favour the A-2

mechanism for tetramethyl dioxolan hydrolysis.

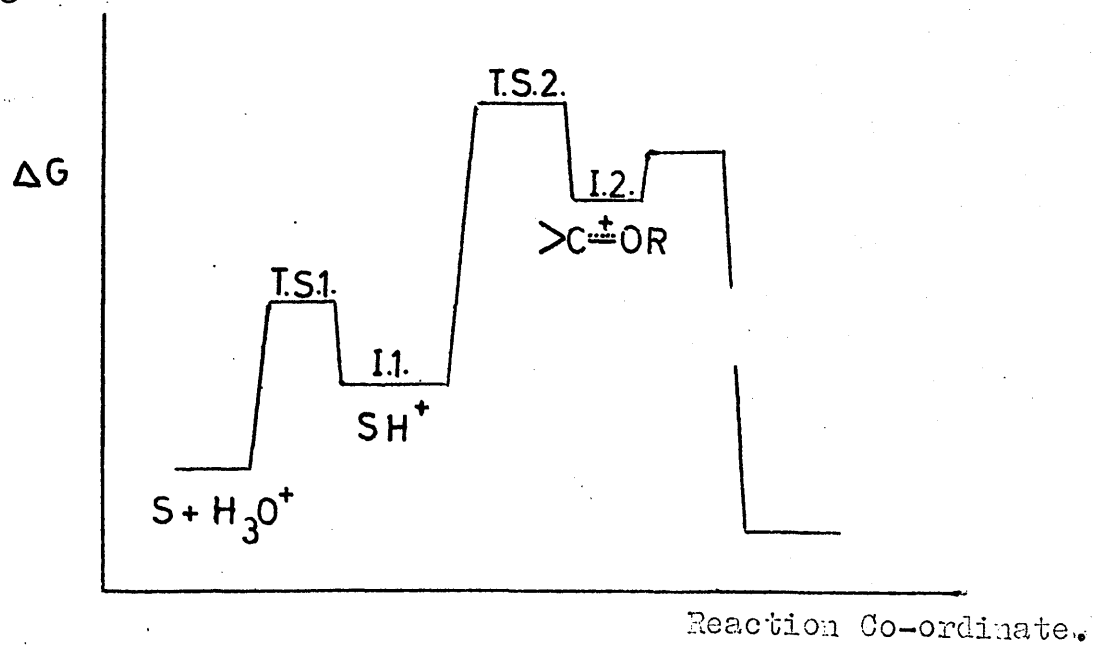
Credibility for a mechanistic pathway other than A-1 would be lent by showing that reversibility of the ring opening step occured during the acid catalysed hydrolysis. If ring closure of the intermediate resulted in an isomer or different compound, this might be detected, however studies by Watts[85] and Cedar[86] were not sufficiently accurate to be conclusive, although Hughes[87] has reported an authentic acetal migration which occurs, in part, in the hydrolysis of 1,6-anhydro-2,3-o-isopropylidene-β-D-talopyranose. Capon and Page[56] have recently reported ring opening reversibility and consequent isomerisation during the acid catalysed hydrolysis of benzaldehyde acetals of 2,3-exo-norbornanediol, and an A-2 mechanism suggested.

In an attempt to understand the comparable rates of the lysozyme-catalysed hydrolysis of thioglycosides and corresponding glycosides,[75] an acetal oxygen was replaced by sulphur in order to study mechanistic differences which might arise due to lower basicity in the latter in the acid hydrolysis of 2-aryl-1,3-oxathiolanes.[76] The rate limiting step was indicated by low isotope effect and $\rho = -2.81$ to be unimolecule-decomposition via limiting fission of the carbon-sulphur bond.

A-S_E2 Mechanism.

Intermolecular general acid catalysis has been well established in the hydrolysis of ortho esters,[59,92] however the search for such catalysis in the hydrolysis of alkyl acetals has been unsuccessful.[89] If general acid catalysis does occur in the enzymatically catalysed hydrolysis of glycosides, it should be observable also in acetals with favourable structural features.

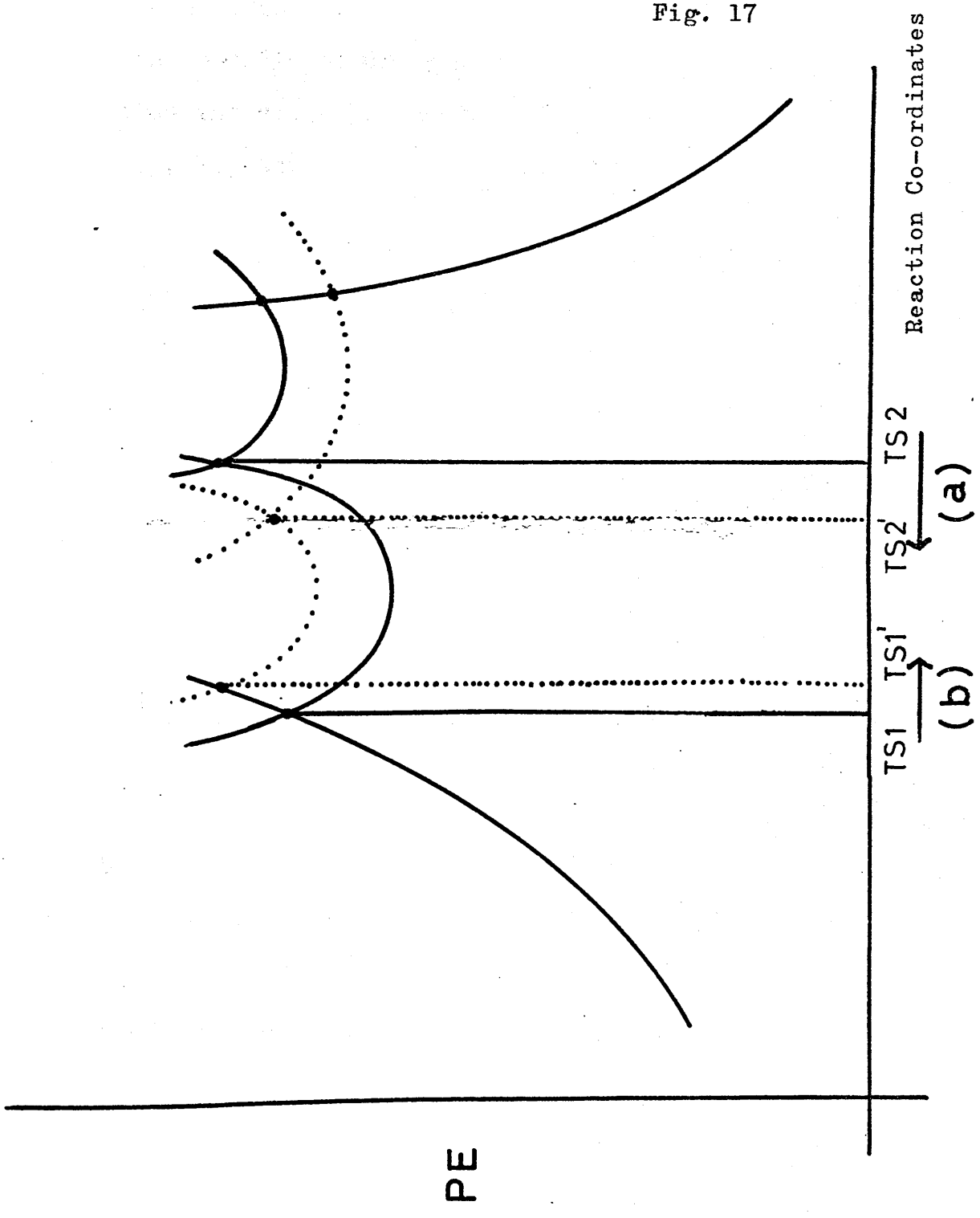
Mechanistically, specific acid catalysis implies a reversible initial proton transfer, whereas general acid catalysis implies rate-determining, or partial rate-determining proton transfer, which may or may not be reversible. The free energy versus reaction co-ordinate diagram for a specific acid catalysed reaction is shown in Fig. 16.



To obtain rate limiting proton transfer it is necessary to change the acetal structure such that T.S.1 has a greater free energy than T.S.2, which may be achieved, assuming the free energies of T.S.1 and T.S.2 follow those of I1 and I2,[90] by lowering T.S.2 or raising T.S.1, or both.

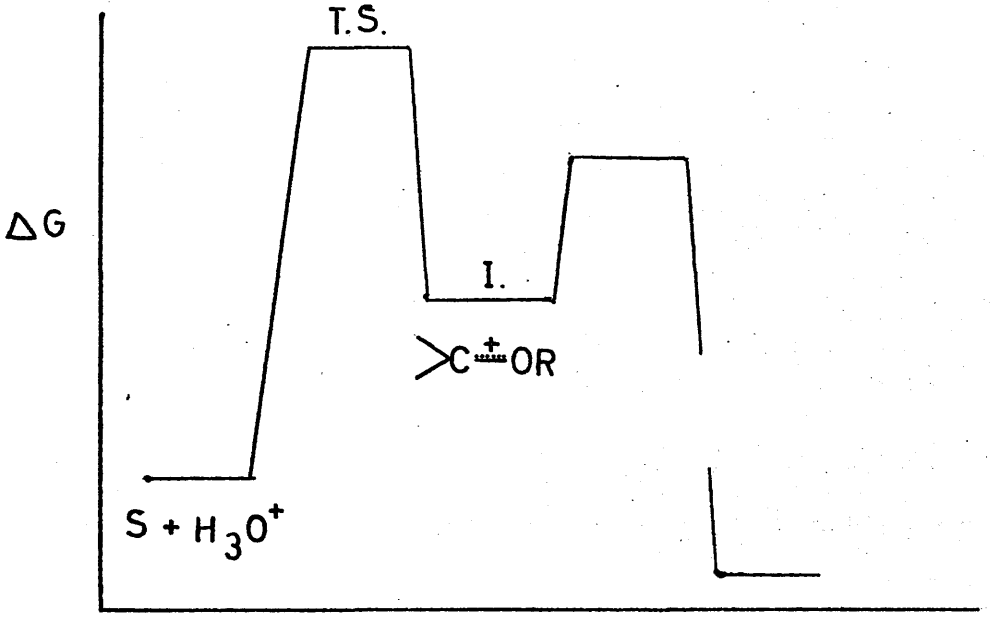
If the reaction co-ordinate can be used as a guide to the amount of bond fission when plotted against the potential energy curves of the reaction,[92] then, if T.S.2 is lowered by having either a more stable carbonium ion or a better leaving group, there should be less carbon-oxygen bond fission in the new transition state Fig.17(a). Similarly, if the basicity of the acetal oxygen is reduced T.S.1 will occur later along the reaction co-ordinate, indicating a greater degree of proton transfer to the acetal oxygen.

Fig. 17



If the two transition states do not merge (Fig.17) then the slow step would be proton transfer between the two oxygen atoms (T.S.1' T.S.2'). The free energy versus reaction co-ordinate diagram Fig.18, similar to Fig.16, indicates the situation where T.S.1' and T.S.2' merge (see Fig.17), and describes a concerted A-S_E2 mechanism.

Fig.18.



Decreased basicity and increased carbonium ion stability as a result of replacing the acetal proton by an alkoxy group is manifested in the general acid catalysis of ortho esters.

Bunton and De Wolfe[93] have formulated a quantitative estimate of specific - acid catalysed hydrolysis of an

of an ortho-ester or acetal.

$$S + H_3O^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SH^+ + H_2O$$

$$SH^+ \xrightarrow[k_2]{} \text{Products}$$

A steady-state treatment of the conjugate acid SH^+ results in a second order rate constant

$$k_H = k_1 k_2 / (k_{-1}[H_2O] + k_2)$$

In an A-1 mechanism $k_{-1}[H_2O] \gg k_2$, so that

$$k_H = k_1 k_2 / k_{-1}[H_2O] = k_2 / Ka$$

or, $k_2 = k_H K_a$ .....(4)

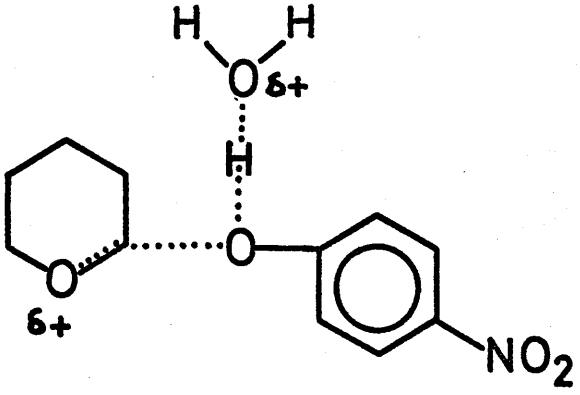
In order that the inequality $k_{-1}[H_2O] \gg k_2$ should not hold, but $k_{-1}[H_2O] \approx k_2$, the authors suggest that k_2 could be increased by increases either in k_H or K_A. By estimating the pKa of the conjugate acid of the substrate and knowing the second order rate constant, it is possible to evaluate whether or not $k_2 \ll k_{-1}[H_2O]$ and therefore the mechanistic type. Anderson and Capon[94] have calculated, on this basis, that on going from dimethyl formal (specific acid catalysed) to benzaldehyde phenyl methyl acetal, general acid catalysis should be observed in hydronium ion catalysis, and therefore possibly by other acids in

this latter compound which exhibits all the structural requirements for general acid catalysis. These authors did, in fact, observe such catalysis in mixed aryl methyl acetals of benzaldehyde in several aqueous acid solutions. The rho value of +0.86 obtained for the acetic acid catalysed reaction of m-substituted phenoxy-group derivatives was interpreted as indicating an A-S_E2 mechanism and the importance of carbonium ion stability was stressed although a phenolic leaving group with low pKa would increase k_2 (equation 4) and thus the observed catalysis. A closer look at this mechanism will be presented in the discussion section.

A continuous change in mechanism has been reported by Fife and Jao[76] in the hydrolysis of a series of tetrahydropyrans, by changing the moiety on the acetal carbon. The solvent isotope effect for the hydronium-ion catalysed hydrolysis of 2-ethoxytetrahydropyran is $k(D_3O^+)/k(H_3O^+)=2.82$ whereas for the 2-substituted aryloxytetrahydropyrans they are less than this, decreasing with increasing electron-withdrawing power of the substituent to a minimum of 1.33 with the p-nitro substituent. The entropies of activation also became more negative traversing the same series; 2-ethoxy-(+7.9e.u); 2-phenoxy-(-3.0e.u); to the 2-(p-Nitrophenoxy)-tetrahydropyran (-7.6e.u). General acid

catalysis was observed in these two latter compounds with formate buffers in 50% aqueous dioxan. A rho value of -0.92 was obtained for the H_3O^+ - catalysed hydrolysis of the series of 2-substituted phenoxy compounds. There would appear, then, to be a continuous change of mechanism, with complete proton transfer in the transition state of the 2-ethoxy compound (A-1), to a concerted proton transfer and C-O bond breaking with the p-nitrophenoxy derivative ($A\text{-}S_E2$).

Fig.19.



The authors emphasise the importance of oxygen basicity in facilitating general acid catalysis, they did not, however, report the Brønsted α-coefficient nor the solvent isotope effect and rho value for the formic acid catalysed reaction. A rho value of +0.9 was later

reported by Fife and Brod[64] for the formic acid catalysed hydrolysis of the p-chloro and p-nitro compounds which indicates a greater degree of C-O bond fission in the p-nitro intermediate than in the p-chloro. Since the basicity of the p-nitro compound is less than that of the p-chloro, and the resulting alkoxy carbonium ions are identical, the greater degree of C-O bond fission and consequent rate enhancement might then be attributed to increased leaving group stability in the p-nitroxyphenyl compound. Again, this aspect will be discussed later.

A study of the acid catalysed hydrolysis of benzaldehyde methyl S-(substituted phenyl)thioacetals has been made by Fife and Anderson[95] in 20% dioxane-water. The reduced basicity of the acetal was expected to give rise to observable general acid catalysis with partial rate determining protonation since the rate of proton transfer parallels the series OH.....O⟩OH .....N⟫OH.....S and the pKa of thiophenol is 6.5 compared to 9.98 of phenol. (ref. 97). That this system reportedly gave no such catalysis is rather surprising, considering the observations of Anderson and Capon[94] above. In both cases the carbonium ion stability is identical and in the thioacetal reduced basicity should enhance general acid catalysis since the carbon-sulphur bond was found to break in the rate determining step. However an A-1 mechanism was suggested with pre-equilibrium protonation, i.e. similar to that postolulated

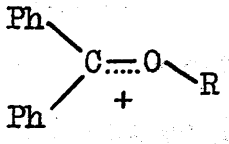
for the hydrolysis of 2-aryl,-1,3-oxathiolanes.[76]

Buffer catalysis has recently been observed in acetals with low basicity due to highly electronegative substituents in the alcohol moiety,[98] and in tropane diethyl ketal which has a poor leaving group but very great stability in the incipient carbonium ion.[99] Although general acid catalysis has been reported in the hydrolysis of benzophenone ketals,[100] other workers have been unable to observe any buffer catalysis.[89,99]

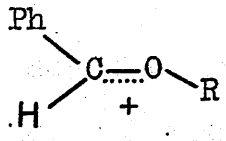
Steric Effects.

It has been suggested that steric effects may be of some importance in helping the developing carbonium ion alkoxy at the reaction centre to go from a tetrahedral towards a trigonal configurative during acid hydrolysis.[101] This effect could be less important in ortho ester hydrolysis because of decreased carbonium ion character caused by electron delocalisation of the neighbouring alkoxy groups. In the hydrolysis of benzophenone ketals where 20(a) is a possible intermediate, both phenyl groups cannot be in the plane of the carbon-oxygen bond, and the inductive effect of the forming trigonal transition state may be destroyed, resulting in reduced stability and consequent slower hydrolysis than that observed with benzaldehyde acetals. Fig. 20(b).

Fig. 20.



(a)



(b)

TRANSITION-STATE THEORIES AND SOLVENT EFFECTS.

Several empirical parameters are frequently used in the study of the mechanisms of hydrolysis. It seems pertinent, therefore, to discuss them in view of the work undertaken in this thesis. Jencks[1] has pointed out that rate accelerations brought about by general acid or base catalysis cannot be attributed only to hydrogen bond formation in the transition state, but also the amount of carbon-oxygen bond formation and breakdown that is stabilised by the presence of a proton, the amount of proton transfer in the transition state, and the strength of the acid catalyst. These quantitative relationships may be approached empirically by the use of structure-reactivity correlations.

There is also an increasing awareness of the role of solvent and electrolyte effects on the mechanism of a reaction, and their relevance in acid catalysis will also be discussed.

ELECTROLYTE AND SOLVENT EFFECTS.

It is generally accepted that salt effects can be compensated for in general acid catalysis by maintaining constant ionic strength with added electrolyte, and thus obtain a range of buffers with constant ionic strength and pH. This assumption implies that all the activity coefficients involved, i.e. of buffer components,

reactants, and intermediates, are influenced equally by ions derived from the buffer components and added electrolytes.

Long and McIntyre[102] found that the salt effects upon the acid hydrolysis of dimethoxy methane could be explained, in part, in terms of the effects of salts on the activity coefficient of the substrate. Bunton and Reinheimer[103] have extended this investigation to more reactive substrates in the hope of finding a relationship between salt effects and mechanism. These authors compared the kinetic salt effects upon acetal and ortho-ester hydrolysis with those upon the protonation of primary amines and triaryl carbinols, since added salts affected the protonation of those substrates differently. It was observed that salt effects on the transition states, relative to those of the anilonium ion, decreased in the sequence orthoacetate orthoformate>ketal>acetal, and it was suggested that the transition state structures are close to those of the conjugate acids and consistent with a mechanistic change from A-1 to A-S_E2 along the series from acetal to ortho-ester, i.e. with increasing carbonium ion stability. Therefore as an acetal attains a more stabilised carbonium ion, i.e. tends towards an A-S_E2 mechanism, salt effects could conceivably be increased, with systemation variations in solvation effects

around the forming carbonium ion as the extent of delocalisation of charge varies.

The rate of proton transfer is decisively determined by the distance between the donor and accepter groups at the moment of transfer, and, in the classical picture, this distance will have a great influence on the activation energy since it will determine how well the potential curves along the reactive co-ordinate overlap. Experimental data has shown that proton transfer can become quite slow when there is interference between accepter and donor. (for references to this discussion see ref. 104)

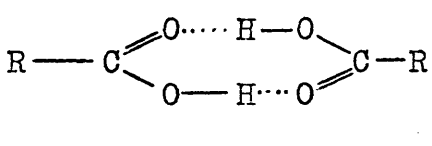
In the transfer of a proton through an aqueous medium it is known that the species does not exist as an isolated elementary particle but rather as the hydronium ion H_3O^+, in which the positive charge is delocalised through the protons, which are therefore able to form relatively strong hydrogen bonds, building up secondary hydration $H_9O_4^+$. Tertiary hydration at the peripheral protons of this complex also exists, simulating the hydrogen binding in water structure. It is therefore plausible that a salt or aprotic solvent could disrupt the transfer of a proton through such an "ice-like" cluster, resulting in reduced rate of proton transfer, the rate limiting step of which is solvent sphere rearrangement,

although this need not necessarily inhibit pre-equilibrium proton transfer. When the pKa of the acid formed in a reaction is less than that of H_3O^+, the reaction is no longer diffusion controlled, but proton transfer becomes the rate limiting step. It is apparent then that these two mechanistic types, i.e.pre-equilibrium, and rate determining proton transfer, could be confused when the ionic strength of the buffer and electrolyte increase, and when aprotic solvents are used.

In view of the claimed general acid catalysis in the hydrolysis of trimethyl orthobenzoate,[107] Salomaa et al[108] have measured the catalysis of triethyl orthobenzoate in 67.4/32.6 w/w dioxan-water chloroacetate buffers using three different electrolytes to maintain constant ionic strength, in an attempt to show that apparent buffer catalysis may in fact be a manifestation of electrolyte and solvent effects. These authors did, in fact, obtain three slopes of differing magnitudes and even different sign when they plotted [HA] versus k_{obs} for the three sets of buffers, and the importance of this finding and its direct implication on the work reported in this thesis will be discussed later.

An interesting example of a non-linear relationship between k_{obs} and acid concentration in the general acid

catalysis of keten acetals has been demonstrated by Gold and Waterman.[105] These authors found that at high concentrations [0.02M] of buffer solutions, especially for weaker acids, the rate of the buffer catalysed reaction to the rate, increases less rapidly than expected from the results at low buffer concentrations, and they explained the apparent discrepancy by postulating dimerisation of the undissociated acid, and association between the carboxylic acid and its anion. Fig. 21



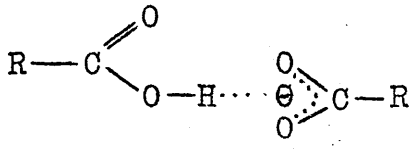


Fig.21

These associations were assumed to be catalytically inactive, although catalytically active association has been suggested by Rossotti[106] to account for the anomalous rate enhancement in buffer catalysis of a mechanistically different reaction.

These apparent electrolyte, buffer and solvent effects, and the conclusion of Bunton and Reinheimer[103] that "....adventitious salt effects could be a source of apparent buffer catalysis in these reactions in which general acids or bases are only weakly catalytic, especially when large amounts of an added salt were used to maintain ionic strength" will be compared

to the corresponding effects observed in the hydrolysis of mixed aryl alkyl acetals in the discussion section, where it will be shown that, in aqueous solution containing about 1% dioxan and low ionic strength, pronounced buffer catalysis is observable, although at higher concentrations there is a "falling off" effect.

α BRONSTED CORRELATION.

Proton transfer from catalyst to substrate is a prerequisite for all acid-catalysed reactions. The reaction rates of H_3O^+ in aqueous solutions have been studied for a great variety of organic bases, and in most cases the rate constants of recombination approach the limiting values for a diffusion controlled reaction, i.e. $10^{10} - 10^{11}$ M^{-1} $sec.^{-1}$ For the reaction

$$H_3O^+ + S \rightleftharpoons SH^+ + H_2O$$

an appreciable gain in free energy is connected with proton transfer since H_3O^+ is a very strong acid, and $pK_{H_3O^+} \ll pK_{SH}$. However, if the pK of the acid formed is less than that of H_3O^+ the reaction is no longer diffusion controlled and the proton transfer can become the rate limiting step in the reaction and thereby accessible to direct kinetic investigation, especially if this step is the first one (see ref.104) Such a reaction type has been studied by Kresge et al[109] with the hydrolysis of vinyl esters, and their findings are discussed shortly.

Although transition states cannot be observed directly there has been reason to believe that the Brønsted relation[110] may be capable of lending some insight to the problem, although the extent of its usefulness is subject to question. The constant in the relation (equation 5) has been considered to equal the degree of proton transfer

at the transition state[111(a)] to equate the bond order of the forming bond,[112] to be inexact in any quantitative capacity.[105]

The general process for proton transfer may be represented in equation 5 as

$$S + HA \rightleftharpoons (S^{\delta+} \cdots H \cdots A^{\delta-})^{\ddagger} \rightleftharpoons SH^{+} + A^{-} \quad \ldots\ldots(5)$$

and the Brønsted relation for the forward reaction can be represented as in equation 6, where K_{HA} is the acidity constant

$$\log k_{HA} = \log G + \alpha \log K_{HA} \quad \ldots\ldots(6)$$

of the catalysing acid and k_{HA} represents the catalytic activity of the acid. It is an empirical fact that plots of log k_{HA} against log K_{HA} are linear with slope α, the Brønsted ~~experiment~~ exponent, when a homogeneous set of catalysing acids is employed. G is ignored in most discussions although it might include an individual statistical correction for multifunctional groups, whereas α indicates the dependence of the reaction on the catalysing acid and has a value between zero and unity, as Brønsted anticipated, although the linear relationship, which results from a mechanism expansion, should hold only for a limited pK range. (see refs. 62 and 104). Examples of α greater than unity and less than zero have been reported recently in deprotonation reactions.[122]

The equilibrium constant of the overall reaction shown in equation (5) is K, and is equalto the acidity constant of the catalysing acid, K_{HA} , divided by the acidity constant of the protonated substrate K_{SH} , thus giving rise to equation 7

$$\log K_{HA} = \log G + \alpha(\log K + \log K_{SH}) \quad \ldots\ldots(7)$$

This expression indicates that the Brønsted relation not only correlates the rate and acidity constants described earlier, but also the rate and equilibrium constants of the proton transfer process itself. Kresge et al[109] further reduced this equation to that shown in (8), where δR is the substituted

$$\alpha = \frac{\delta R \, \Delta F^{\ddagger}}{\delta R \, \Delta F^{\circ}} \quad \ldots\ldots\ldots(8)$$

stabilisation operator[111(b)] for the catalysing acid, and ΔF is a free energy change. The Brønsted exponent is now reduced to a ratio of the substituent effects on the free energy of activation of a proton transfer process, to a substituent effect on its overall free energy change. If Z represents the order of bond being formed between substrate and transferring proton, i.e. the extent of proton transfer at the transition state, then for $\alpha = Z$, $\delta R \Delta F^{\ddagger}$ must equal $Z \, \delta R \Delta F^{\circ}$. Although the authors concluded from their studies that they did not consider this equality to hold for any real and complex system

since intermolecular effects could produce a difference of 0.1 or more between α and Z, these effects might be closely similar for a series of similar substrates undergoing the same reaction with a set of homogeneous catalysts. Therefore, although α would not numerically equal Z, it might provide a good relative measure of transition state structure.

On this basis, for the hydrolysis, by a set of homogeneous catalysts, of a reaction series in which the substrate structure change is very small, the variation in α may be interpreted as indicating the extent of separation of the proton from its base in the slow step of the reaction. A high α value (near 1.00) would indicate a large degree of separation and attachment to the substrate, while an α value near zero indicates a relatively low degree of bond fission. That general acid catalysis is difficult to observe if the value of α falls near to these two extremes is discussed by Bunnett.[63] When α is high, a high buffer concentration is required to counteract the high hydronium ion catalysis and consequently salt effects could be involved. High α values usually accompany specific acid catalysis. Spontaneous water catalysis competes with buffer catalysis when low α values are encountered, and general catalysis may no longer be recognisable.

The rate constants for general acid-base catalysis are subject to statistical corrections to take account of the number of sites in the acid or base that can donate or accept a proton.[136] The modified Brønsted expression then for general acid catalysis then becomes:

$$\log(k_{HA}/p) = \log G_A - \alpha(pK_a + \log P/q) \quad ....(9)$$

where p is the number of equivalent protons which can be transferred from the acid and q is the number of sites which can accept a proton in the base. Such corrections are not usually large, but they will be discussed later when implementing the Brønsted equation.

The small consistent deviations, or "non-conformity" of some carboxylic acid buffers in Brønsted plots has recently been investigated by Kresge et al,[109] and will be discussed with the Brønsted plots obtained in this work.

ISOTOPE EFFECTS.

(for references to this discussion see Jencks[1] and Bell[62,113])

Empirical data has indicated that for acid catalysis reactions involving slow proton transfers, the deuterium solvent isotope effect $kH_2O/kD_2O > 1$, and for pre-equilibirum proton transfer $kH_2O/kD_2O < 1$.[1,116,117]

Isotope effects are frequently used as evidence for or against the occurrence of rate determining proton transfer, and in the diagnosis of reaction mechanism in general, however it has become increasingly evident that the detailed interpretation of such effects is more complex than has been supposed.[1] The existence of solvent isotope effects smaller than "normal" means that there is a difference in the zero-point energy and position of hydrogen in the starting material and the transition state. Reactions which are subject to specific acid catalysis exhibit inverse deuterium isotope effects although such effects have also been observed in general acid catalysed reactions.[1,92,94,103]

It should be mentioned, however, that isotope effects carried out in mixed solvents may lead to erroneous conclusions because of the differences in rate of proton exchange between the transferring proton and solvent.

The nature of the atom which is being transferred is then dependent on the solvent composition e.g. the primary solvent isotope effect for triphenyl ortho-formate is different for reactions in aqueous dioxane and in water with added solubilising agent.[118]

Primary kinetic isotope effects are useful, for an investigation or reaction mechanisms,[113,115] however quantitative estimates must necessarily involve simplifications[114] and it has been suggested that secondary isotope effects might lend themselves better to an investigation of reaction mechanism.[1]

Cordes et al[118] have studied the kinetic secondary deuterium isotope effects for hydrolysis of acetals and ortho-formates. The variation in isotope effect for the hydrolysis of substituted benzaldehyde diethyl acetals indicated that the extent of carbon-oxygen bond cleavage in the transition states of these acetals increased as the stability of the derived carbonium ion decreased, i.e. C-O bond cleavage increased along the series, p-methoxy < p-hydrogen < p-nitro substituted compound. If the Bronsted α values could be compared with these findings then it would be expected that α would also increase along the same series since this would also reflect the tendency of the transition state to resemble more the intermediate carbonium ion, with protonated leaving group. This aspect

will be discussed in the next chapter, although the authors do point out the dangers of correlating these parameters since the Brønsted α values for ortho-ester hydrolysis[92,107] do not reflect the extent of C-O bond cleavage in the transition states as indicated from the corresponding α-deuterium isotope effects. It should be mentioned however, that the parameters obtained from the hydrolysis of trimethyl ortho-benzoate in 70% methanol-water solvent[107] must be considered suspect after the findings of Salomaa et al on the mixed solvent studies of the closely related triethyl ortho-benzoate hydrolysis.[108]

It was predicted theoretically that when

$$\Delta pK = pK_{HA} - pK_{HB} = 0$$

i.e. when there is a "symmetrical stretch"

$$\overleftarrow{A}\cdots\cdots H\cdots\cdots\overrightarrow{B}$$

in the transition state of the reaction

$$AH + B \longrightarrow A + HB \text{ (charges omitted)}$$

then the primary isotope effect should reach a maximum since the focus acting on the hydrogen atom are in balance and consequently there is no motion of the hydrogen atom and isotopic substitution leads to a lack of zero-point energy change to offset that in the stretching vibration of the reactant.[119,120,113,1] Several workers have reported an apparent maximum near $\Delta pK = 0$,

and it has been frequently used as a guide to the transition state structure in the rate-limiting proton transfer reaction having a sensitivity greater than that of the Brønsted α component.[122,124,125] (see also ref. 121)

Whereas the results of Dixon and Bruice[124] supported the findings of Goodall and Bell[125] who presented a 20-point graph covering a ΔpK range of about 20 units with k_H/k_D maximum near ΔpK 0, Bordwell and Boyle[121] suggested that corrections for secondary isotope effects would have the effect of "flattening" the curve, although a slight maximum did still exist in the curve around $\Delta pK = -1$ to -2. These authors concluded that "the hope, which at one time seemed bright, for a simple general correlation of Brønsted coefficients, kinetic isotope effects and solvent isotope effects with the extent of proton transfer in the transition state has proved vain".

Although it is appreciated that a direct comparison of these parameters cannot, as yet, be made, their relative values will be discussed later with reference to the hydrolysis of mixed aryl alkyl acetals.

HAMMETT SIGMA RHO CORRELATION[126]

The linear free energy relationship (L.F.E.R.) between the logarithms of rate or equilibrium constants can be expressed by a formulation similar to that of the Brønsted relation as shown in equation (10);

$$\log K_A - \log K_{AO} = \rho\sigma \qquad (10)$$

where K_A and K_{AO} represent the rate or equilibrium constants of the substituted and unsubstituted substrates respectively. The interpretation and implications of the Hammett Relationship have been excellently reviewed,[63,130,131] and only the observed deviations from the empirically expected linearity will be discussed here.

The proportionality factor ρ is usually obtained from the plot of the rate constant for the reaction versus the substituent constant (σ) for meta- and para-substituted compounds. In these latter compounds, however, difficulties arise when the substituent is capable of electron donation by resonance, and here σ^+ values are used.

Although deviations from Hammett plots can be removed by accounting for varying polar and resonance effects in a modified substituent constant[132,133,134] curvature can also be a manifestation of a mechanistic change caused by the presence of certain substituents,

or when the measured rate constant is a composite quantity dependent on the rate and equilibrium constants of several steps.[135] It is apparent then, that, as with the Brønsted plot, deviations from linearity may not be a result of experimental error, as often hitherto assumed, but indicative of a mechanistic, or otherwise significant change. A. L.F.E.R.must therefore be calculated with caution to fit the electronic requirements of the reaction, and conversely, these requirements must be estimated cautiously from the best fitting relationship.

In contrast to acid or base catalysis, the spatial requirements within an enzyme-substrate complex would appear to introduce a supplementary factor which necessitates separate Hammett plots for meta- and para- substituted phenoxy substrates (see Table 1 page 17). Several authors have observed this phenomenon in enzymically catalysed hydrolysis, and it has been suggested that the meta- and para- substituents are no longer held rigidly from the reaction centre such that steric interactions are negated, but rather the proximity of a residue on the enzyme surface may affect, for example, the normal polar effect (σ) of the substituent, and although these substituent derivatives do not fit an isokinetic line, it is thought that the substrates are all hydrolysed by the same basic mechanism (see ref. 46 and references therein)

These above considerations, with the observation that

the ρ values obtained from enzymically catalysed hydrolysis may be derived from K_{cat} values containing more than one rate or equilibrium constant then demand caution when comparing ρ values of enzymically and non-enzymically catalysed hydrolysis.

D I S C U S S I O N

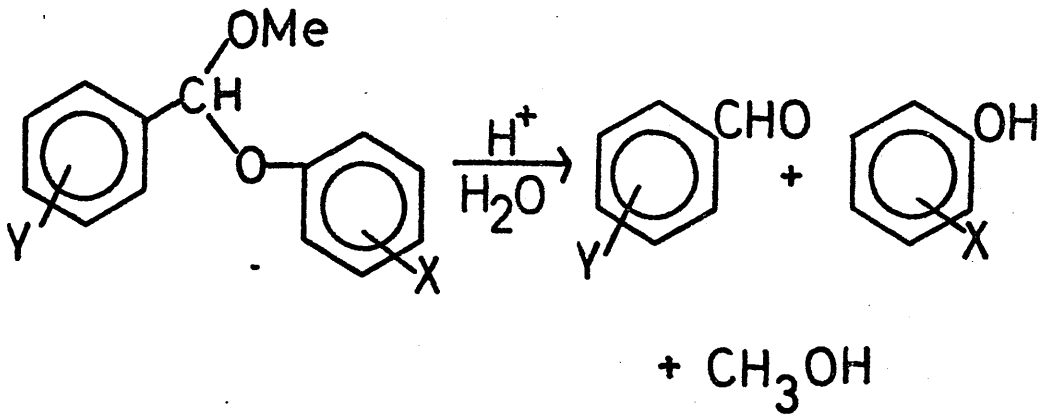
All Tables and Graphs referred to numerically, but not alphabetically, in this discussion are to be found in the experimental section.

Discussion

Until 1968 there were no reported observations of general acid catalysis in acetal hydrolysis, since when, however, there have been several and these will be reported in this discussion. Varying opinions have been expressed concerning the authenticity of these reports, and it would seem pertinent, therefore, to discuss this topic before all else and to allay any suspicion which might be directed at the authenticity of the observed general acid catalysis reported in this thesis.

1. Buffer Catalysis: Solvent and Electrolyte Effects.

Throughout the experimental work the technique of Bell[116] was used, and the pseudo first order rate constant for the hydrolysis of mixed aryl alkyl acetals (1) were determined at various buffer concentrations, but with buffer ratio, ionic strength, and pH held constant.



.....(1)

For all the buffer solutions used, the concentration of the undissociated acid was taken as the stoichiometric concentration and the results of the variation of the rate constants with buffer concentration at 25°C and at ionic strength 0.05M are given in Tables 1 to 106 of the experimental section. From these tables it is readily apparent that the observed rate constants (k_{obs}) increase with increasing buffer concentration at constant pH (see Table 107). The catalytic coefficients (k_{HA}) of the carboxylic acids were obtained from a least squares plot of k_{obs} versus concentration of the undissociated acid [HA]. These plots were linear when determined at low buffer concentrations, <0.03M and ionic strength 0.05M, however curvature concave to the horizontal axis [HA] became apparent at higher buffer concentrations, 0.030 to 0.100M

Tables 32 and 35, and Graph 1 indicate clearly this phenomenon, and Tables 34 and 35 indicate the small but significant difference in catalytic coefficient obtained when ionic strength changes from I = 0.050 to I = 0.100M.

The dependence of the acetic acid catalysed hydrolysis of benzaldehyde phenyl methyl acetal on acetic acid concentration, and not acetate ion, has been shown by the pH - independence of the reaction in three acetate buffers of differing pH but constant ionic strength,[94] and the theoretical considerations that this compound should exhibit catalysis by general acids has been mentioned in the introduction. A detailed investigation of the rate law, however, will be left until section 3 of this discussion.

The phenomenon of curvature in plots of k_{obs} vs. [HA] in a general acid catalysed reaction has been reported infrequently,[37,105,106] however, in the author's opinion, in many instances failure to observe such curvature could be an oversight resulting either from the assumption that deviation from linearity was a result of experimental error (it is extremely simple to draw a straight line through an obtuse curve) or from the range of buffer concentration employed being such that there were too few points, especially at lower concentrations, to detect any "abnormality" or deviation from linearity. Gold and Waterman[105] observed that, in the general acid catalysed hydrolysis of keten

acetals, a slight curvature concave to the concentration axis was perceptible at higher concentrations in the graphs of k_{obs} vs. [HA]. This observation was explained by the authors as involving a diminution in the concentration of the free acid caused by dimerisation of acid and association of acid and anion:

$$2\,HA \rightleftharpoons (HA)_2 \qquad \ldots\ldots\ldots K_d$$

$$HA + A^- \rightleftharpoons HA_2^- \qquad \ldots\ldots\ldots K_{ass}$$

which is described by equation (2):

$$\Delta[HA] = [HA]_{stoich} - [HA]_{eff}$$

$$= 2K_d [HA]^2_{eff} + K_{ass} [HA]_{eff}[A^-]_{eff} \qquad \ldots\ldots\ldots (2)$$

where stoich = stoichiometric, and eff = effective.

Experimental curves were satisfactorily computed using reasonable values for K_d and K_{ass}, and since then this interpretation has been applied to similar results obtained in methanol.[137] Whereas Gold and Waterman found this non-linearity with weaker acids only and not, for example, with dichloro-, cyano-, and chloro-acetic acids, the slopes of k_{obs} vs [HA] obtained in the hydrolysis of mixed aryl methyl acetals would appear to be concave for all of the acids used including formic (Table 32 and Graph 1) and apparently so for chloroacetic when the catalytic coefficient reported in this work (3.77×10^{-1} M^{-1} sec^{-1} over the buffer range 0.005 to 0.025 M, I = 0.05) is compared with that

obtained by Capon and Anderson[94] (6.58×10^{-2} $\underline{M}^{-1}$ sec^{-1} over the buffer range 0.030 to 0.444, I = 0.10$\underline{M}$) where the intercepts and pH values were respectively 3.49×10^{-2} sec^{-1} (pH = 3.10) and 5.15×10^{-2} sec^{-1} (pH = 2.99). This discrepancy is unlikely to be caused by the change in ionic strength considering the analogous results shown in Tables 34 and 35 for the acetic acid catalysed hydrolysis when I = 0.05 and 0.10.

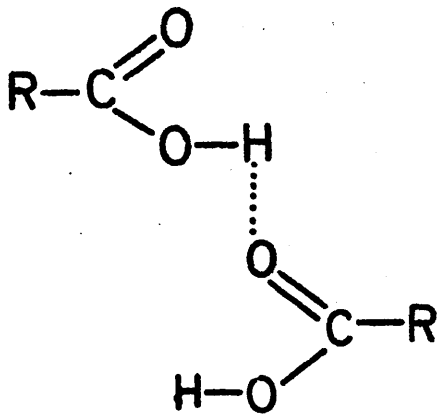
When using stronger acids, Gold and Waterman corrected for the contribution to the catalytic coefficient from hydronium ion catalysis, although they found that the corrected values of k_{HA} and k_{int} from equation (3) were then dependent on the value of $k_{H_3O^+}$ used.

$$k_{obs} = k_o + k_{H_3O}+[H_3O] + k_{OH^-}[OH^-] + k_{AH}\,[AH] + k_{A^-}\,[A^-]$$
$$= k_{int} + k_{HA}\,[HA]$$

Most acids, however, were found to require very little, if any, correction as can be seen from their results,[105] whereas some considerable correction would be necessary to "straighten out" the concave curve shown in Graph 1 and that described above for the chloroacetic acid catalysed hydrolysis. The catalytic inactivity brought about by dimerisation and association might then be applicable throughout the range of buffers used in this work, including the stronger acids, although Gold and Waterman thought it to exist only in weaker acids where they

concluded hydrogen bonding to be more important.

The observations of Rosotti[106] are in complete contrast to those mentioned above, where, in a mechanistically different reaction to that of keten acetal hydrolysis, Rossotti considered an association which led to a catalytically active species to explain an anomalous rate enhancement. This explanation is also feasible considering the suggestion that carboxylic acid dimers exist as the mono-hydrogen bonded species.[138]



Although these explanations conveniently account for the observed phenomena, the possibility of a mechanistic complication rather than a property of the buffer cannot readily be omitted. In such cases curvature has been accounted for by correcting the k_{obs} values in view of the

established mechanism for the reaction, e.g. see ref 139.

Bell[116] has shown that for the general reaction sequence:

$$S + HA \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} S H^+ + A^-$$

$$S H^+ \xrightarrow{k_2} \text{Products}$$

if $k_{-1} \gg k_1$, i.e. basicity of S<<A^-, and $k_2 \approx k_{-1}$ then experimental results would indicate catalysis by acids other than hydrogen ion, although a complex quantitative behaviour would result since velocity (k) is partially dependent on the actual proton transfer and partially on an equilibrium controlled by hydrogen-ion concentration:

$$k = (k_2[H^+]\pi_{HA,S}[AH]) / (K_{SH^+}\pi_{AH,S}[AH] + k_2[H^+])$$

where $\pi_{AH,S}$ is the catalytic coefficient characteristic of acid and substrate.

Considering the reaction under discussion (1) for which the reaction pathway is shown in (4) - see section 2 and ref 94.

$$PhCH(OMe)OPh + HA \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} PhCH\overset{+}{\text{---}}OMe + HOPh + A^- \qquad \text{.....(4)}$$

$$PhCH\overset{+}{\text{---}}OMe + H_2O \xrightarrow{k_2} \text{Products}$$

Since the basicity of PhCH(OMe)OPh < HOPh and A^-, then

$$k_{-1}[HOPh][A^-] \gg k_1[HA]$$

assuming a first order reaction dependent on [HA], and steady-state concentration of SH^+. However, for the approximation $k_2 \approx k_{-1}$ to be applicable to (4) would require

$k_2 [H_2O] \approx k_{-1} [HOPh][A^-]$ which is highly unlikely considering the relative basicities of H_2O and HOPh. It then seems much more probable that $k_2[H_2O] \gg k_{-1} [HOPh][A^-]$ so that

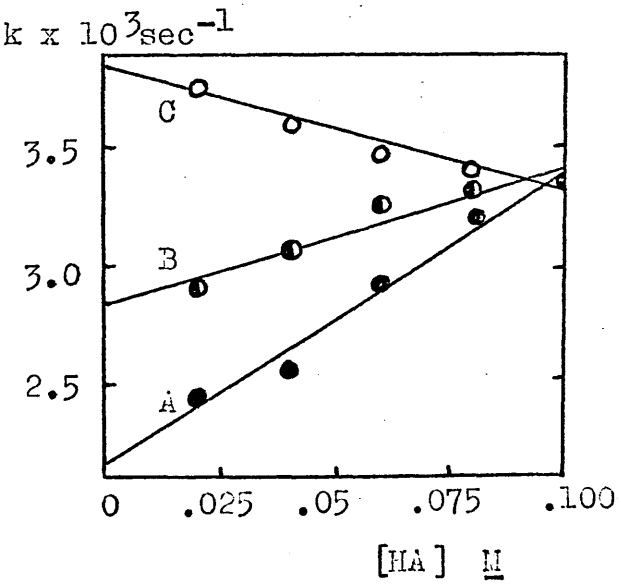
$$k = k_1 = \pi_{AH,S} [AH].$$

The possibility that observed general acid catalysis might be a manifestation of specific salt and electrolyte effects has also been proposed recently (see introduction and ref. 103).

It was mentioned earlier that Salomaa et al[107] had investigated the hydrolysis of triethyl orthobenzoate, a similar reaction to that previously investigated by Kwart and Price[108] who concluded that trimethyl orthobenzoate was subject to hydrolysis by general acids in 70% methanol-water solvent. This latter reaction was recently investigated by Cordes et al[140] who sought general buffer catalysis for the hydrolysis of methyl orthobenzoates in both aqueous and 70% dioxan-water media. The hydrolysis of trimethyl orthobenzoate and the ortho-p-methoxy-, p-methyl-, p-chloro-, and p-nitro-benzoate anologues in a wide range of buffers and buffer concentrations showed no consistent evidence for general acid catalysis in either aqueous or 30% dioxan-water solvents. The observations of Salomaa et al are even more surprising. Whereas Cordes et al employed lithium chloride to maintain ionic strength, I = 0.50, Kwart and Price used potassium chloride, I = 0.01,

and Salomaa *et al* used three different electrolytes, viz. sodium chloride, sodium nitrate and sodium perchlorate, I = 0.10. These latter authors using sodium chloride found what appeared to be a general acid catalysed hydrolysis of triethyl orthobenzoate in 67.4: 32.6 w/w dioxane-water chloroacetate buffers with slope (k_{HA}) of 1.23×10^{-2} M^{-1} sec^{-1}, which alone is inconsistent with the above observations of Cordes *et al* considering the similarity of substrates and the very small deviation caused by substituting lithium for sodium salts of chlorine.[108] It would be expected therefore that the trimethyl and triethyl orthobenzoates would be expected to hydrolyse by very similar mechanisms in aqueous dixoane, and if this were the case (compare, for example, the similar hydrolysis mechanisms of methyl and ethyl orthoformates,[141] benzaldehyde dimethyl and diethyl acetals[68,89] and the reduced steric effects prevalent in ortho-ester hydrolysis[103]) then presumably the apparent mechanistic change is a result of the 37.4% alteration in the dioxane content of the aqueous-dioxane buffers. However, even more inconsistent are the rate constants observed by Salomaa *et al* for the hydrolysis of triethyl orthobenzoate employing sodium nitrate and sodium perchlorate buffers (0.580×10^{-2} M^{-1} sec^{-1} and -0.515×10^{-2} M^{-1} sec^{-1}, Fig 1

which demonstrates clearly the complications involved not only when the media is a mixed aqueous-aprotic solvent where the type or even content of the aprotic species is altered, but also when different electrolytes (anionic change) are used to maintainionic strength in such a medium.



A: Sodium chloride
B: Sodium nitrate
C: Sodium perchlorate

Fig. 1. The hydrolysis of triethyl orthoformate in aqueous dioxane chloroacetic acid buffers with varying electrolyte, I = 0.10M, and at 45°C.[10]

An important omission in the data of Salomaa *et al* is the individual pH values of the various chloroacetic acid buffer solutions used. It has been reported earlier[109] and was also experienced by the author, that unless freshly prepared buffer solutions are used, erroneous kinetic results can be obtained, arising from a pH variation in chloroacetic acid buffers caused by hydrolysis of chloroacetate ion to glycolate ion and hydrochloric acid, especially at high ionic strengths. Also Salomaa *et al* indicate no corrections to pH values obtained in solutions containing about 70% dioxane and since pH meter readings pH(app.) in mixed solvents may not give the correct pH values of the buffers (see ref 68) then it would be difficult to justify a plot of k_{obs} vs. [HA] even if pH(app.) were constant, which they do not state it is.

Kankaanpera and Lahti have found general acid catalysis in the hydrolysis of 2-methoxyethyl orthoformate in aqueous media, and an A-S_E2 mechanism suggested whereas the same reaction is proposed to proceed via an A-1 mechanism in 65%: 35% dioxane-water solvent.[141,154] Also the hydrolysis of ethyl orthoformate was thought by these authors to be A-1 in aqueous dioxane contrary to the earlier findings of De Wolfe and Roberts[145] that in this solvent system there was strong catalysis by general acids although in aqueous buffers specific hydronium ion catalysis only was apparent.

It has been calculated that proton transfer is faster in ice than in water[142] and that any salt or aprotic solvent which disrupts the proton transfer from a hydronium ion to an orthoester by changing the "ice-like" clusters of water should hinder this process although an equilibrium proton transfer may not necessarily be inhibited (see introduction and refs 103, 143). If equilibrium proton transfer were inhibited it might reasonably be expected that general acid catalysis involving concerted or rate determining proton transfer should become more apparent in aprotic-aqueous solvents. De Wolfe and Roberts accounted for observed buffer catalysis in aqueous dioxane and not in water by suggesting that in the latter the high oxonium ion concentration renders it unobservable whereas the addition of dioxane reduces this concentration without affecting the buffer acid concentration i.e. in the equation

$$k_{obs} = k_{H_3O^+} [H_3O^+] + k_{AH} [AH]$$

the term $k_{H_3O^+} [H_3O]$ is reduced thereby allowing $k_{HA} [HA]$ to become more apparent. Although the catalytic coefficient of the acetic acid catalysed hydrolysis was observed by De Wolfe and Roberts to increase with decreasing dioxane content of the buffer, the swamping effect of the oxonium ion renders it unoberservable in totally aqueous buffers. These authors then lend weight to the suggestion by Swain[169]

that general acid catalysis is much more common than formerly supposed and that its observation is made difficult by the magnitude of the hydronium ion catalysed reaction which necessitates the use of inordinately high concentrations of weak acids and electrolytes, but which in turn considerably complicates the task of interpreting the experimental results.

It seems anomalous that there is no apparent consistency of mechanistic change in going from aqueous to aprotic-aqueous solvents and vice-versa, and in view of the complexity of the mixed media, especially with regard to the results of Salomaa et al, the hydrolysis reactions reported in this thesis pertain to 99% aqueous solutions as described in the Kinetic Experimental chapter, except in the hydrolysis of benzaldehyde diphenyl acetal and p-methylbenzaldehyde S-phenyl methyl acetal (Tables 41 and 106) where solubility problems were encountered, although these results were interpreted only on a comparative basis.

Bunton and Reinheimer,[103] and Cordes et al[140] have carried the investigations of Long and McIntyre,[102] concerning salt effects on substrate and transition state, to more reactive orthoformates and acetals. The observation was made that the addition of salts with small high-charge/density cations such as lithium increased both the Hammett H_o acidity function by reducing the affinity of

water molecules to protons, and also effectively catalysed an acid hydrolysis, and the hypothesis presented that large specific cation effects, in the sequence $Li^+ < Na^+ < K^+$, are characteristic of slow proton transfer to electronegative atoms. Also that anionic effects, although large upon the measured reaction rate constants (cf Salomaa et al[107]), are reduced when effects upon initial state activity are accounted for.[103] It is also of interest to note that the semilogarithmic plots of k/k_o (k and k_o represent the first order rate constants in the presence and absence of added salt) versus the alkali halide concentration for the hydrolysis of p-nitrobenzaldehyde diethyl acetal in 0.005M HCl with varying salt concentration (alkali chlorides) were plotted as "sensible straight lines"[140] although it would appear that they would in fact be fitted better by curves concave to the salt concentration (horizontal) axis (see also ref 116). This observation would support the theory that specific salt effects rather than buffer effects, would explain the "falling off" effect described earlier in plots of k_{obs} vs. [HA], since buffer effects were proposed to be effective only in weaker acids whereas salt effects would be consistent throughout the range of buffers used in the hydrolysis of mixed aryl methyl acetals. Also Bunton and Reinheimer[103] observed a decrease in the relative salt effects on the transition state of orthoacetate>

orthoformate > ketal > acetal, and suggested that the structures of the transition states were close to those of the conjugate acids and were consistent with a mechanistic change from A-1 to $A\text{-}S_E2$ in going from acetal to orthoester. Therefore if the mechanism of an acetal hydrolysis were described by an $A\text{-}S_E2$ rather than A-1 mechanism, as is the hydrolysis of mixed aryl methyl acetals, it seems reasonable to presume that specific salt effects should be increased and might be manifested as the "falling-off"effect described earlier.

It is apparent that although the most suspect reports of observed general acid catalysis are those carried out in mixed aqueous-aprotic solvents the effects of electrolyte and buffer concentrations, and change in both cationic and anionic moieties in the electrolyte should be examined in any solvent system employed. With reference to the work reported in this thesis, the effect of buffer and electrolyte concentrations has already been discussed, and Tables, 24, 25, 26; 53, 54, 55; 75, 76, 77 describe the effects of the electrolytes potassium chloride, sodium nitrate, and sodium perchlorate on the formic acid catalysed hydrolysis of benzaldehyde m-methoxyphenyl methyl and m-methoxybenzaldehyde phenyl methyl acetals, and the acetic acid catalysed hydrolysis of benzaldehyde p-methoxyphenyl methyl acetal Maximum deviations between the catalytic coefficients

reported in Tables 24 to 26 is 8.1%; between Tables 53 to 55 is 2.8%; and between Tables 75 to 77 is 7.1%. General buffer catalysis is also apparent in the chloroacetic acid catalysed of benzaldehyde phenyl methyl acetal in 20:80 - dioxane-water (v/v) solvent at 40°C (Table 40) where the catalytic coefficient calculated at 25°C (approx. 2.346×10^{-1} $\underline{M}^{-1}$ sec^{-1} when assuming that a temperature decrease of 10C° approximately halves the observed rate) is only slightly less than that observed in aqueous medium (3.771×10^{-1} $\underline{M}^{-1}$ sec^{-1}, Table 31)

On the strength of the above observations it is assumed that specific salt effects (anionic or cationic), if not totally absent in the acid catalysed hydrolysis of mixed aryl methyl acetals are small enough to be ignored when working in the buffer range 0.005 to 0.030 $\underline{M}$ and with ionic strength, $I = 0.05$, i.e. that the influence of the ions, derived from the buffer components and added electrolyte, on the activity coefficients involved, if not identical, differ by a negligibly small margin. Although salt effects may be extremely useful in the kinetic investigations of hydrolysis reactions it is not the author's intention to investigate them here, but rather chose the above conditions where they are ineffectual, however a suggestion for further research might be to investigate specific salt effects especially in mixed solvent systems where the reaction mechanism would not seem to be drastically

changed.

2. Site of Bond Fission

The hydrolysis of aromatic aryl methyl acetals, (1) could follow two pathways, Fig. 2, involving phenoxyl- or methoxyl- carbon bond fission. The relative rates of these two modes will depend on the relative abilities of methoxy- and phenoxy-groups to stabilise the developing carbonium ion in the transition state, also on their relative leaving group abilities in the acid catalysed hydrolysis reaction. Although proton transfer to oxygen would favour the methoxy rather than the phenoxy group, bond fission between carbon and the phenoxy oxygen, which is the more favourable leaving group, would result in the more stable methoxy carbonium ion. The possibility of phenoxy-carbon bond fission process is supported by the greater hydrolysis rate of benzaldehyde phenyl methyl acetal than that of benzaldehyde dimethyl acetal, Graph 1. Therefore, if methoxyl-carbon bond fission were occurring in the slow step of hydrolysis of the phenyl methyl acetal, the rate should be increased and not decreased on replacing the phenoxy by a methoxy group.

The following kinetic N.M.R. experiment describes the acetic acid catalysed methanolysis of benzaldehyde phenyl methyl acetal, and shows that bond fission occurs

between carbon and the phenoxy oxygen, and it would seem reasonable to suppose that the same process applies to the acetic acid catalysed hydrolysis also.[34]

The acetic acid catalysed methanolysis of benzaldehyde phenyl methyl acetal.

The site of initial bond fission in the d_1-acetic acid catalysed d_4-methanolysis of benzaldehyde phenyl methyl acetal was investigated by following the reaction in a Varian HA-100 N.M.R. Spectrometer. The two possible modes of bond fission are shown in Fig.2.

If the reaction proceeded via pathway A, an initial shift of the mixed acetal methoxy protons (c) to the dimethyl acetal methoxy protons (d) would be observed, along with an upfield shift of the methine acetal proton (a) to that of (b). Subsequently a free-methanol signal (e) would be observed.

Fission via pathway B would show a loss of the methoxy protons (c) with immediate production of free methanol (e) and no initial change in the methine proton (a).

If pathway A were followed, the equality (5) would be applicable:

since $[H_c] = 3[H_a]$ and $[H_d] + [H_e] = 3[H_b]$

then $[H_a]/[H_b] = [H_a]/([H_d] + [H_e])$ .....(5)

whereas if pathway B were followed, the inequality (6) would

be applicable:

since $[H_c] < 3[H_a]$, $[H_e] > 3[H_b]$, and $[H_d] = 0$

then $[H_a]/[H_b] > [H_c]/([H_d]+[H_e])$ .....(6)

Although the methine signals were clearly distinguishable on the 1000 Hz - sweep spectrum:

phenyl methyl acetal methine (a).....611 Hz.

dimethyl acetal methine (b) .....534 Hz.

a 50Hz - sweep - spectrum was required for the necessary resolution in the methoxy region of the spectrum, 328 to 335 Hz:

phenyl methyl acetal methoxy (c).....334 Hz.

dimethyl acetal methoxy (d) .....328 Hz.

free methanol methoxy (e) .....335 Hz.

These signals were identified by the addition of 12 µls of absolute methanol to standard 10% solutions of the appropriate acetal in tetradeuterated methanol. Experimental: 0.050 gms of analytically pure benzaldehyde phenyl methyl acetal in 0.50 mls. tetradeuterated methanol (0.47 M solution) were injected into an N.M.R. tube with 2 µls (2M) mono-deuterated acetic acid, and the tube sealed. The d_4 -methanol was supplied by CIBA and found to be 99.98% pure by N.M.R. Spectroscopy against Merck "Spectrograde" dioxane standard. Internal T.M.S. standard was used.

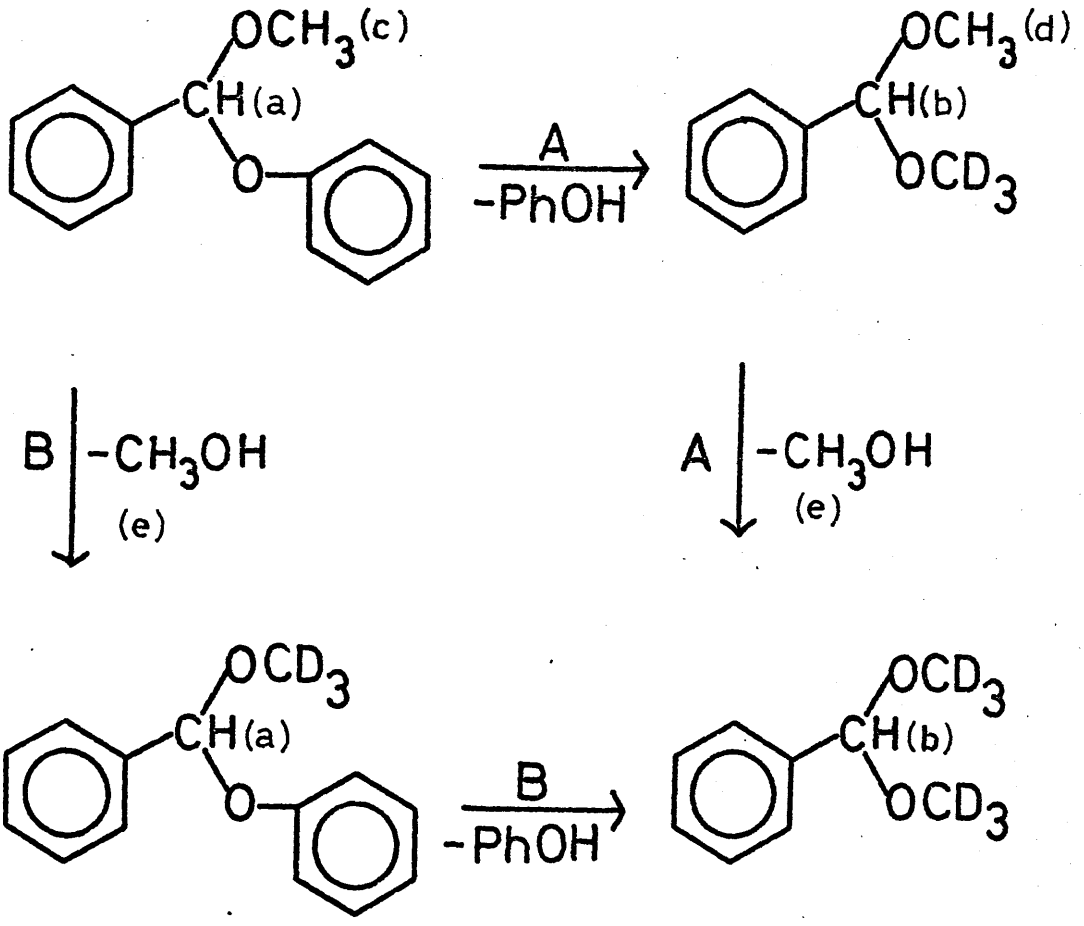
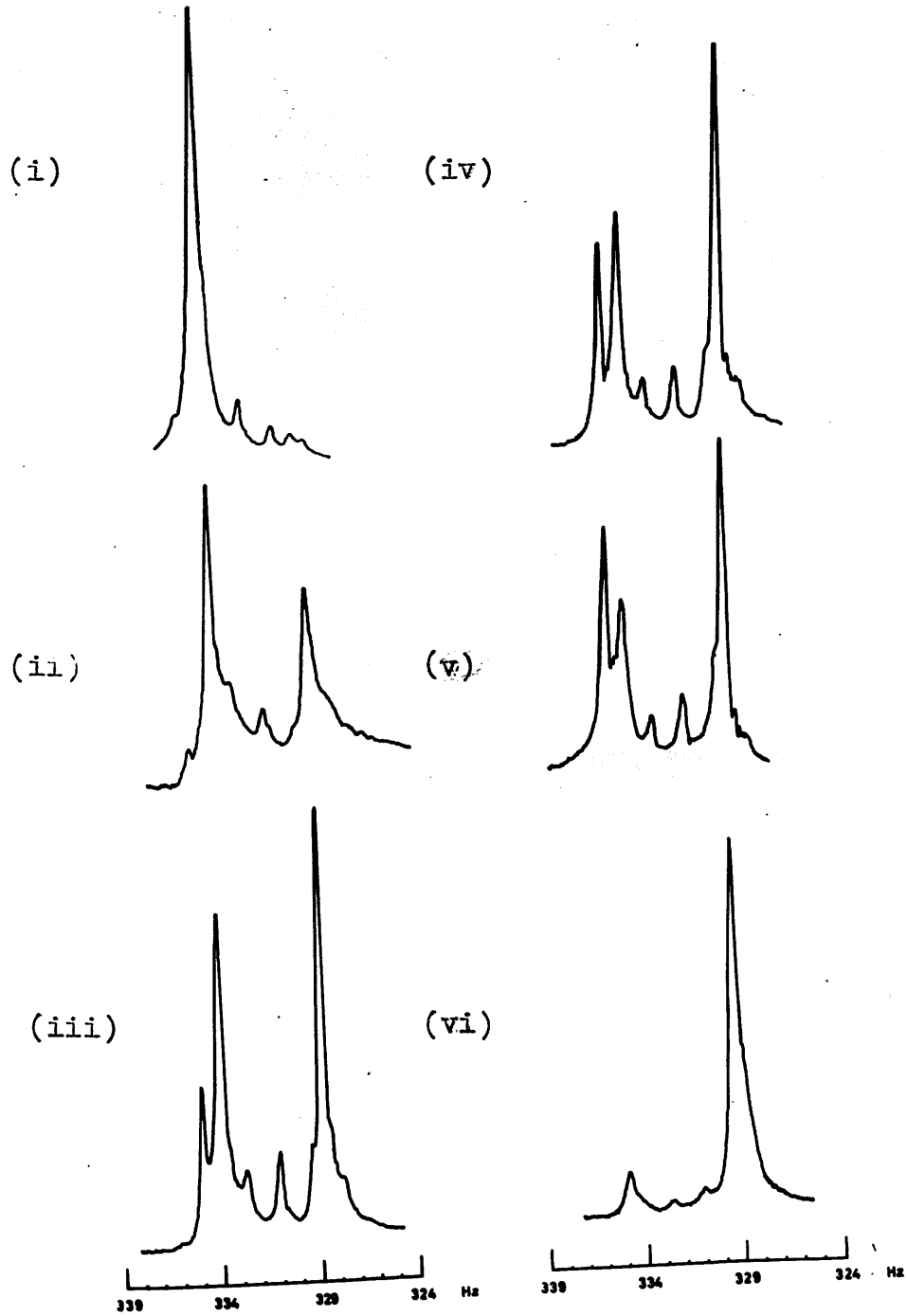


Fig. 2. d_4- methanolysis of benzaldehyde phenyl methyl acetal (d_1 acetic acid catalyst)

Fig 3



Integration of the methoxy peaks was perfomed by repeatedly cutting out and weighing the signals, and using the average values so obtained. Although this procedure is somewhat crude, it was found to be more satisfactory than measurement or using integrals, and the deviations were small enough to make the results meaningful. A program to calculate peak areas is at present being written in this department, and will be applied to the data as soon as possible.

Between each spectrum the sealed tube was incubated in a thermostat bath retained at 65°C by an efficient electronic relay system. Fig. 3 (i) to (v) shows the expanded methoxy signals obtained after (i) zero time, (ii) 60 mins., (iii) 100 mins., (iv) 140 mins., (v) 180 mins. Fig. 3 (vi) shows the spectrum obtained from the d_1- acetic acid catalysed d_4-methanolysis of benzaldehyde dimethyl acetal after 60 mins at 65°C.

Although the complete spectra are not shown here, a signal of increasing strength at 534 Hz (dimethyl acetal methine) was observed in the spectra (ii) to (v) indicating an immediate loss of phenol as described in pathway A. Fig. 3 (ii) also shows a substantial signal corresponding to the methoxy of dimethyl acetal (328 Hz) with a small signal at 335 Hz corresponding to free methanol. It is

difficult to decide, even with the use of Fig 3 (vi) whether this latter signal is produced entirely by the breakdown of the dialkoxy intermediate of pathway A, or if a small proportion is a direct product of the first step of pathway B. Throughout the series, the mixed acetal methoxy decreases steadily, the dialkoxy acetal methoxy reaches a maximum near that shown in Fig. 3(iv) before decreasing again, and the product, methanol, increases steadily.

The peak areas of the methoxy groups were measured, and the ratios $[H_a]/[H_b]$ and $[H_c]/([H_d]+[H_e])$ calculated, Table A. An equality of these ratios (5) would appear to hold within the limits of experimental error, and certainly the inequality (6) would not seem to be applicable.

Table A.

Fig. 3	$[H_a]/[H_b]$	$[H_c]/([H_e]+[H_d])$	% error from equality (5)
(i)	1/0	1/0	-
(ii)	1.60	1.52	5%
(iii)	0.93	1.00	-7%
not shown	0.50	0.52	-4%
(iv)	0.31	0.29	6%
(v)	0.26	0.28	-7%

It is therefore concluded that the site of initial bond

fission in the methanolysis of benzaldehyde phenyl methyl acetal is between the acetal carbon and the phenoxy oxygen as described in Fig. 2 pathway A.

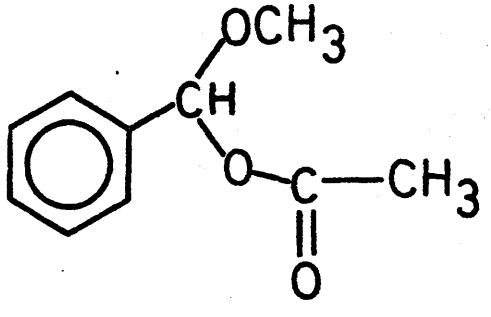
3. Kinetic Rate Law.

The general equation for a general acid-base catalysed hydrolysis is:

$$k_{obs.} = k_o + k_{H_3O^+}[H_3O^+] + k_{OH^-}[OH^-] + k_A[A^-] + k_{AH}[AH] \quad \ldots\ldots(7)$$

Mixed aryl alkyl acetals, in common with the majority of acetals studied, are not subject to base catalysed hydrolysis[59] and therefore the term $k_{OH^-}[OH^-]$ in (7) may be omitted. The possibility of involvement of the term $k_A[A^-]$ has been eliminated by the investigations of Capon and Anderson[94] who, as described earlier, found the general acid catalysedhydrolysis of benzaldehyde phenyl methyl acetal dependent only on the concentration of undissociated acid and not on conjugate base, although the possibility of nucleophilic participation by A^- cannot be ruled out since specific hydronium ion catalysis with nucleophilic participation is kinetically equivalent to catalysis by HA (see introduction). Presumably, if nucleophilic catalysis was prevalent in the hydrolysis of mixed aryl alkyl acetals it should also be apparent in the hydrolysis of benzaldehyde dimethyl acetal, although Table 102 and Graph 1 would indicate the independence of hydrolysis rate

of this latter compound on undissociated acid, and therefore acid anion [A^-] concentration. The hydrolysis of the potential intermediate in the acetic acid catalysed hydrolysis of benzaldehyde phenyl methyl acetal, benzaldehyde methyl acetyl acylal (I), was investigated in sev ral buffer solutions, Tables 97 to 101.



(I)

Conclusive general acid catalysis was observed in the hydrolysis of (I) and is believed to be the first reported case of general buffer catalysis in acylal hydrolysis, however, the reaction rates of this substrate were too fast to compare directly with those of the substituted-phenyl methyl acetals, which is not surprising considering the vast difference of pKa in the leaving group of (I), 4.76, and those of the substituted-phenyl acetals, 8.4 to 10, and the presence of (I) was never observed in the reactions studied. It may be significant, however, that the presence

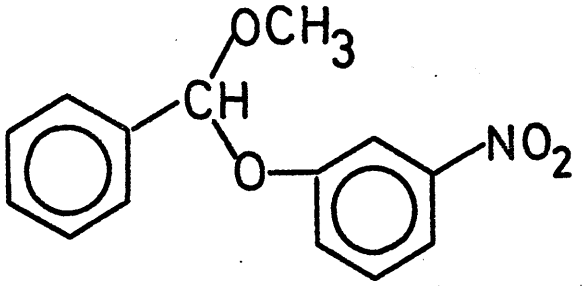
of an acylal intermediate was not observed in the N.M.R. experiment described in the preceeding section.

Equation (7) is reduced to:

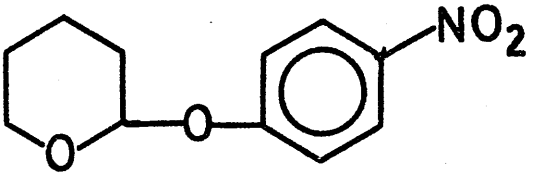
$$k_{obs} = k_{int} + k_{HA}[HA] \quad \ldots\ldots\ldots\ldots(8)$$

$$\text{where } k_{int} = k_o + k_{H_3O^+}[H_3O^+] \quad \ldots\ldots\ldots\ldots(9)$$

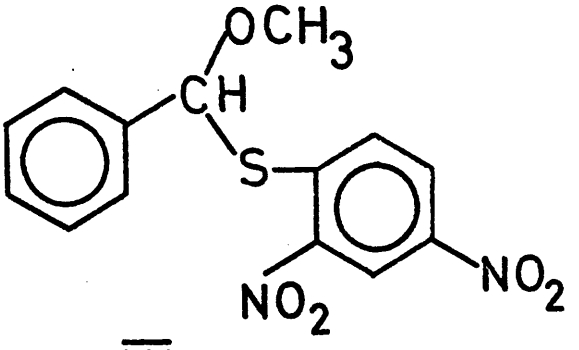
Where an evaluation of k_{int} can be made from the intercept of the plot of k_{obs} vs. [HA] which has a slope of k_{HA}, and the k_{int} values obtained from the hydrolysis of mixed aryl methyl acetals are shown in Tables 136 and 137. The values for $k_{H_3O^+}[H_3O^+]$ in (9) were calculated from the plots of k_{obs} vs. $[H_3O^+]$ in the hydrochloric acid catalysed hydrolysis reactions with [HCl] = 0.001 to 0.0002 M and I = 0.050 again maintained with KCl. The intercepts of these plots were, with one exception, observed to be slightly negative, which, although indicating a negligible spontaneous factor k_o, would suggest a degree of experimental error caused by the lower acid concentrations which were made necessary by the reaction velocities encountered. With acid concentrations 4 and 2 x 10^{-4} M HCl, there is apparently a more complex behaviour with the substrate of comparative concentration (approx. 2.5 x 10^{-4}), and therefore k_{obs} [0.001] M HCl values were used in determinations such as solvent isotope effects, rather than values of $k_{H_3O^+}$.



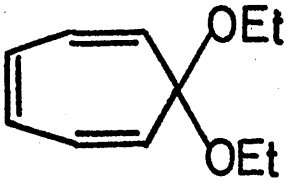
II



III



IV



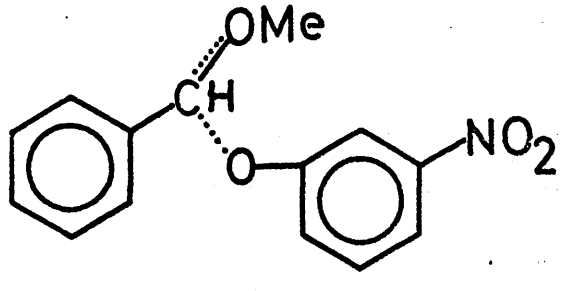
V

The substantially positive intercept (5.18×10^{-4} sec^{-1}) in the plot of k_{obs} vs. [HCl] in the hydrochloric acid catalysed hydrolysis of benzaldehyde m-nitrophenyl methyl acetal (II) would suggest a significant spontaneous factor k_o to be applicable to the kinetic rate law of this compound. This is reflected in Table 136 where the relative constancy of the intercept values k_{int} obtained in the acetic and pivalic acid catalysed hydrolysis would suggest a spontaneous pH-independent reaction at pH values greater than about 4.5 ($k_{int} \approx 1.3 \times 10^{-3}$ sec^{-1}) and Table 140 where the pH-corrected values of k_{int} (logarithmic)indicate the increasing importance of spontaneous catalysis as pKa of the catalysing acid decreases, whereas the other acetals studied show approximately constant values. Similar observations have been made in the hydrolysis of substrates in which there is both a good leaving group and a relatively stable incipient carbonium ion. The hydrolysis of 2-(p-nitrophenoxy)-tetrahydropyran (III)[64] is characterised by a pH-independent reaction at pH values greater than 4.0 and benzaldehyde methyl S-(2,4-dintrophenyl)thioacetal(IV)[95] at pH values greater than 1.5.

Increasing the ease of bond breaking by strong electron withdrawal in the leaving group would be expected to greatly increase the rate of spontaneous reaction but decrease the rate of hydronium ion catalysis by decreasing basicity,

thereby making the pH-independent reaction easy to detect with these compounds. Accordingly (II) is pH-independent at pH 4.5 (leaving group pKa 8.40); (III) is pH-independent at pH 4 (pKa of leaving group 7.15); and (IV) is pH-independent at pH 1.5 (pKa of leaving group 4.1) Pronounced general acid catalysis and a fast pH independent reaction at pH greater than 10 is also observed in the hydrolysis of tropone diethyl ketal (V)[99] where C-O bond breaking is facilitated by the great incipient carbonium ion stability, although the hydronium ion catalysed reaction is also facilitated by the comparatively high basicity (poor leaving group ability) so that the pH-independent reaction is observable only at higher pH values.

An alternative formulation to the proposed spontaneous unimolecular breakdown of the unprotonated acetal which is shown below,



would involve water catalysis with proton transfer not having progressed to a significant extent in the transition state. The functioning of water as a general acid is unlikely, however, considering that the point for spontaneous catalysis would lie far above the extrapolation of the plot of log k_{HA} versus pKa in Graph 2, where the Brønsted coefficient is 0.49. It might also be reasonably expected that the reaction would be much slower in D_2O than in H_2O solvent whereas the solvent isotope effects $k(H_2O)/K(D_2O)$ of compounds II, III and IV are all less than or near unity and increase with increased ease of spontaneous catalysis; k_H/k_D = 0.46, 0.9, and 1.1 respectively, while that for V is k_H/k_D = 1.2.

Fife and Brod also observed the point for spontaneous catalysis to lie far above the line obtained in the Brønsted plot for 2-(p-nitrophenoxy)-tetrahydropyran(III) where the Brønsted coefficient, α = 0.5, is almost identical to that obtained for benzaldehyde m-nitrophenyl methyl acetal (II). These authors also suggested a unimolecular decomposition to occur, rather than general catalysis by water, as did Fife and Anderson for the spontaneous catalysis of tropone diethyl ketal (V) and benzaldehyde methyl S-(2,4-dinitrophenyl) thioacetal (IV) although with (V) a water-catalysed reaction could not be conclusively eliminated.

The low relative abundance of the molecular ion in the

mass spectral analysis of m-nitrobenzaldehyde phenyl methyl acetal (II) and the observation that the parent peak is the incipient methoxycarbonium ion (see Preparative Experimental), would also reflect the comparative stabilities of these moieties. Whereas the parent peaks in the m.s. analysis of the corresponding H and p-methylbenzaldehyde homologues of (II) and the p-methylbenzaldehyde methyl thiophenyl homologue of (IV) are also the incipient methoxycarbonium ions, the lack of observable molecular ion signals in the two latter p-methylbenzaldehyde compounds would indicate extremely facile C-O and C-S bond cleavage because of the very stable incipient carbonium ions formed, similar to that obtained in tropone diethyl ketal (V). Therefore, as was the case with (V), it might be reasonable to expect that these two compounds would also show a pH-independent reaction, although again at higher pH values than those studied, because of the increased ease of the hydronium ion catalysed hydrolysis.

The dependence on buffer catalysis of p-methylbenzaldehyde methyl thiophenyl hydrolysis is shown in Table 106, and although a rate increase is observable, it cannot be considered conclusive evidence for general acid catalysis because of the small change in both k_{obs} and O.D. Therefore both the p-methylbenzaldehyde thiophenyl and

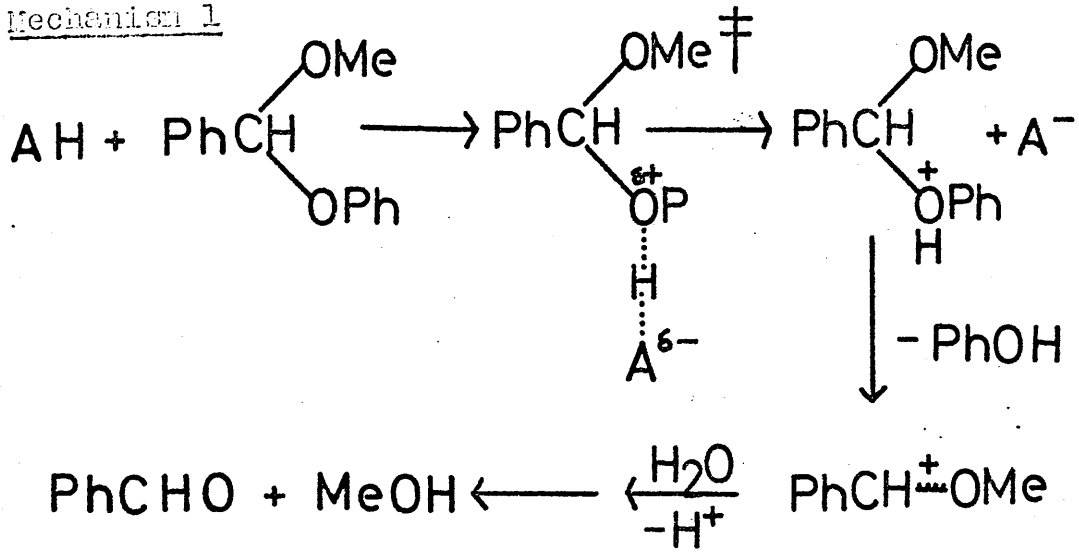
2,4-dinitrothiophenyl mixed acetals may be considered borderline between A-1 and A-S_E2 mechanisms where the increased carbonium ion stability and leaving ability facilitates C-S bond cleavage, which is considered more difficult than in the oxygen acetal analogues, and where ease of proton transfer to sulphur is less than that to oxygen.[95]

4. Mechanism

It was concluded that the site of initial bond fission in the general acid catalysed hydrolysis of benzaldehyde phenyl methyl acetal occurs between carbon and the phenoxy oxygen, and the ineffectuality of anionic change with reference to Cl^-, NO_3^- and ClO_4^-, and the lack of observation of an acylal intermediate has been described. There are then two possible mechanisms to describe the observed buffer catalysis viz. a rate determining proton transfer from molecular acid to phenoxy oxygen followed by a rapid breakdown of the resulting conjugate acid (Mechanism 1); or a concerted displacement of the $Ph.CH\overset{+}{\cdots}OMe$ group by the catalysing acid (Mechanism 2).

The reverse of the rate determining step (R.D.S.) of Mechanism 1 can be considered as a diffusion controlled proton transfer from the very strong conjugate acid of the substrate to the conjugate base A^-, and should therefore be independent of the base strength of A^-, and consequently

Mechanism 1



Mechanism 2

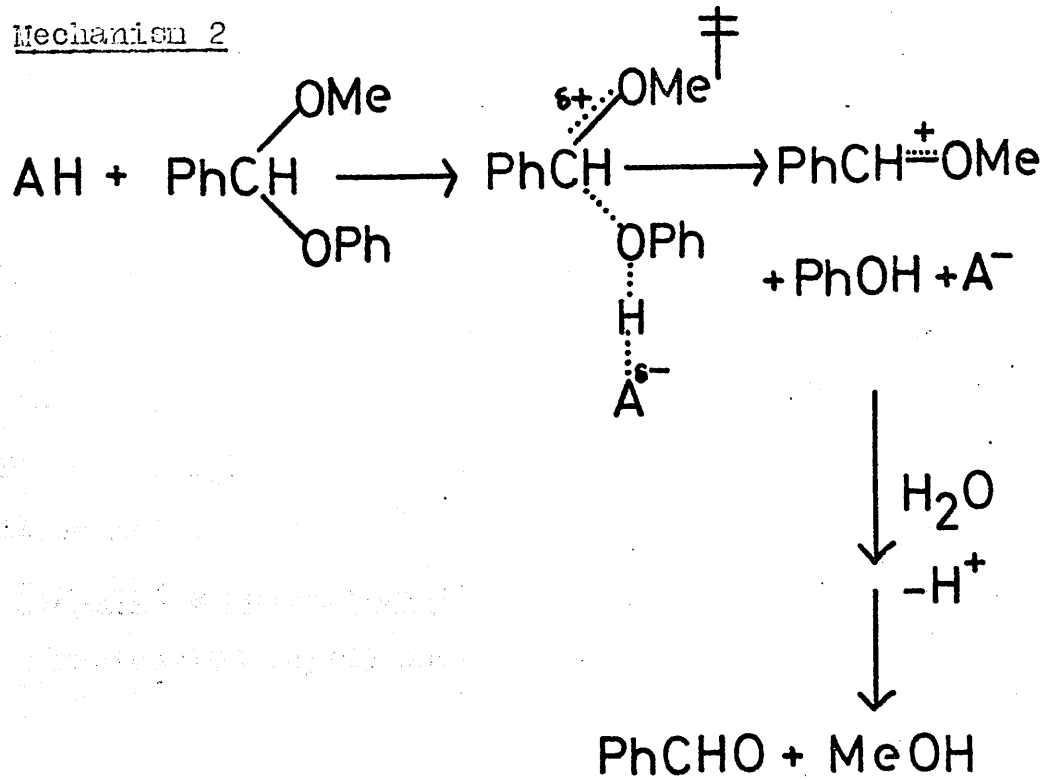


exhibit a Brønsted coefficient of $\beta = 0$, within the range of acid catalysts used. Then, assuming $\alpha = 1-\beta$, the α value for the forward reaction would be expected to equal 1, which is not the case, except when m-nitrobenzaldehyde phenyl methyl acetal is employed as substrate.[63,168] Also, if the reaction proceeded with proton transfer as the R.D.S. it might be expected that the reaction velocity should increase with increasing basicity of the acetal, the reverse of which was found in practice. The catalytic constants were found to increase as the basicity of the acetal oxygen was decreased by substituting more electronegative groups in the phenoxy moiety; p-Me<H<...m-F<... m-NO_2. Evidence supporting the applicability of Mechanism 2 will be presented in the following sections with reference to Brønsted and Hammett coefficients, and to solvent isotope effects. A comparative correlation of these results, their significance regarding the current opinions described in the introduction, and a comparison of them with other reported examples of buffer catalysis in acetal hydrolysis will be made.

5. Brønsted α coefficient

Tables 108 to 119 and Graphs 2 to 6 describe the α values obtained in the acid catalysed hydrolysis of aromatic aryl methyl acetals. Kresge et al[109] observed that when

the number of points in a Brønsted plot was greater than three, standard deviations became reasonably small, and this was the case in the above plots where the five points taken in each case gave relatively low standard deviations and high correlation coefficients. Whereas Kwart and Price[107] concluded that small structural changes in the carboxylic acid catalysts did not cause any significant alteration in the Brønsted slopes for the acid catalysed hydrolysis of methyl orthobenzoates, and that "the strengths of the acids chosen is their most significant, distinguishing characteristic", Kresge et al observed small but real deviations from such a relationship when employing substituted - carboxylic acids in vinyl ether hydrolysis (Kwart and Price included in their investigation the catalysts, tri-, di-, and mono- chloroacetic acids, and 2-chloropropionic acid). Kresge et al attributed the observed positive deviations to intermolecular interactions between catalyst and substrate, and the negative deviations of pivalic acid catalysed reactions to hydrophobic forces. The positive deviations were suggested to result from an additional energy-lowering interaction between electronegatively - substituted catalysts and the substrates to which a proton (positive charge) was being transferred, and conversely that positively charged catalysts e.g. H_3O^+ and anilinium ion, should experience an energy-raising interaction. In the reaction series studied in this

thesis, equation 1, the catalytic coefficient for the anilinium perchlorate catalysed hydrolysis of benzaldehyde phenyl methyl acetal (k_{AH} = 3.75 x 10^{-3} M^{-1} sec^{-1} Table 105) is approximately 3.5 times slower than the corresponding acetic acid catalysed reaction (k_{AH} = 1.29 x 10^{-2} M^{-1} sec^{-1}, Table 34) although the catalyst pKa values, 4.60 and 4.76 respectively, are very similar, and the hydronium ion catalytic coefficients invariably fell below that expected from the Brønsted slope, Graphs 2 to 6. The negative deviations of the points for hydronium ion catalysis have frequently been observed in the extrapolation of Brønsted plots even where statistical corrections have been applied, and it has been suggested that either the concentration of non-hydrogen-bonded water might be better applied, therefore lowering the conventional magnitude of the acidity constant, pK_{H_3O} = -1.74, and consequently moving a negatively deviating catalytic coefficient toward the correlation line, or that the true acidity constant might be best evaluated by fitting the hydronium ion catalytic coefficients to Brønsted correlation lines. The literature values of pK_{H_3O} obtained by fitting the observed catalytic coefficients to the correlation lines show a rather wide variation from reaction to reaction. Whereas Kresge et al observed a range of values from -0.2 (ethyl cyclohexenyl ether), to +0.7 (ethyl isopropenyl ether) in the hydrolysis of several vinyl ethers, Gold and Waterman[105,158] obtained

values of 1.52 and 1.96 in the hydrolysis of cyanoketen dimethyl acetal and 2-dichloromethylene-1,3-dioxolane. With reference to mixed aryl methyl acetals a similar evaluation of the negatively deviating $k_{H_3O^+}$ catalytic coefficients from Graphs 2 to 6 gave rise to the following $pK_{H_3O^+}$ values, which, although being varied, were so in a systematic manner viz. in the hydrolysis of benzaldehyde substituted (X) - phenyl methyl acetals: X= m-NO_2(0.1); X=m-F (0.25); X=H(0.25); X=p-Me(0.65); X=p-MeO(1.1); and in the corresponding substituted (Y) - benzaldehyde acetals: Y=m-F(0.35); Y=H(0.25); Y=p-MeO(0.25).

These results would indicate that the apparent acid strength of the hydronium ion decreases as substrate leaving group ability and incipient carbonium ion stability decrease i.e. as the α values increase (see Tables 134 and 135).

The difference in k_{H_3O} values is then less than that for the k_{HA} values amongst the substrates used indicating that electronic requirements are of reduced importance in the hydronium ion catalysed reaction than in the undissociated weak acid catalysed reaction, where increasing leaving group ability and carbonium ion stability are much more influential. This point will be taken up again in section 6 (Hammett relation), although it is interesting to note here that the point for hydronium ion catalysis of

benzaldehyde-di-^{t}bu-acetal is considered to fit the Brønsted correlation line, extrapolated from three points, and that electronegative effects were found to be of more importance in hydronium ion, than in undissociated weak acid, hydrolysis ($\alpha = 0.6$).[165]

The spread of values for pK_{H_3O} obtained in the hydrolysis of vinyl ethers was interpreted by Kresge et al[109] as being suggestive of such factors as intermolecular effects and that the value of pK_{H_3O} might best be deduced from the fit of the hydronium ion catalytic coefficients based not on carboxylic acids but rather on positively charged catalysts. Gold and Waterman[158] suggested that the negative deviations of the hydronium ion catalysed reaction cannot be read into too deeply because of the long extrapolation required of the logarithmic catalysis-law relation and the consequent sensitivity to the homogeneity of the catalysts used. With regard to these two points, it seems apparent that no definite conclusions can be drawn from the negative deviations from the Brønsted plots in Graphs 2 to 6 which were obtained from carboxylic acid catalysts whose absolute homogeneity must be considered suspect with regard to the following observations, although the constancy of catalysts employed in each case should render the deviations available for comparative examination as described above.

Statistical evidence from Tables 103 to 119 indicates that the α coefficients from the Brønsted plots may be

consistently high because of the use of electronegatively-substituted catalysts. From the twelve tables shown, although only 55% of the points corresponding to catalysis by chloroacetic acid lie above the correlation line, 80% of those corresponding to 2-chloropropionic acid do, while 75% of those corresponding to formic acid catalysis, of pKa between the two electronegatively-substituted acids, lie below the line (omitting those values where the residual $<10^{-2}$).

The effect of intermolecular forces has been described in the introduction as producing a difference of 0.1 units or more between α and the order of bond being formed (Z) although the values of α within a closely similar series of substrates undergoing the same reaction with a set of homogeneous catalysts might provide a good relative measure of transition state structure. Gold and Waterman[158] have also stated that although they did not consider α to be a quantitative measure of the degree of proton transfer, they thought it should still be correct to interpret the increase in the value of α along a series of related reactions as reflecting the increasing resemblance of the transition state to the reaction product.

It seems reasonable to conclude that the consistent increase in α (0.49 to 0.96) along the series of benzaldehyde substituted-phenyl methyl acetals m-NO_2 < m-Br

m-F<m-MeO<H<p-Me<p-MeO shown in Table 134 is indicative of the transition states going from "reactant-like" to "product-like" i.e. PhCH^{+}...OMe, although these values are representative of a relative rather than absolute order of proton transfer. Although the hydrolysis rates of those acetals with higher α values are more dependent on the strength of the catalysing acid, and the transferring proton considered to be nearer the substrate, those acetals with lower α values have greater catalytic coefficients indicating that the increased leaving group ability, and therefore increased ease of C-O bond fission, must be dominant, which is consistent with an A-S_E2 mechanism, described by Mechanism 2 (the anomalous rate increases of the p-Me and p-MeO homologues will be discussed shortly).

A similar argument can be applied to the substituted-benzaldehyde phenyl methyl acetal series, Table 135, where the α values decrease consistently from 1.05 (standard deviation = 0.036) for the m-nitro homologue to 0.63 for the p-methoxy homologue. Therefore the transition states may be considered to have a relatively greater degree of proton transfer, or be more "product-like" along the series: p-MeO<p-Me<H≈m-MeO<m-F<m-NO_2. Again the greater catalytic coefficients were observed when α was low, indicating that although proton transfer is more advanced and that there may be a greater degree of C-O bond fission caused by

electronegative substituents in the benzaldehyde moiety, the overall hydrolysis rate is increased when the incipient carbonium ion is made more stable.

The study of the secondary kinetic isotope effects on the hydrolysis of substituted-benzaldehyde diethyl acetals by Cordes *et al*[118] indicated that the extent of C-O bond cleavage in the transition state increased, as the stability of the incipient carbonium ion decreased, along the series p-MeO<H<p-NO_2 although hydrolysis rates increase with increasing stability of the incipient carbonium ion, i.e. p-MeO>H>p-NO_2. Considering that the intermediate methoxy-carbonium ions in this series is comparable with that of the mixed aryl methyl acetals, and the leaving group, although different, is also constant, there would appear to be a favourable correlation of secondary isotope effects and Brønsted parameters with regard to the amount of bond breaking and making in the transition states.

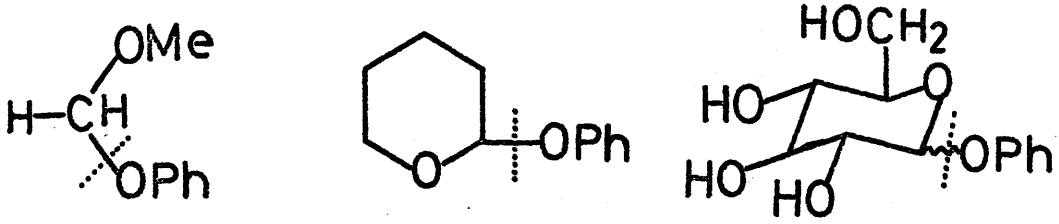
It is also pertinent to note that although the extremely high α values obtained for benzaldehyde p-methoxyphenyl methyl acetal (0.96) and m-nitrobenzaldehyde phenyl methyl acetal (1.05) might be considered indicative of a specific acid catalysed mechanism, general acid catalysed reactions have been observed when α is equal to or near 1.0, and is considered detectable because of the negative deviation of the hydronium ion catalysed reaction from the Brønsted correlation line as described earlier (see ref. 163).

Whereas Jencks and Sander [163] required relatively high concentrations of weaker acid buffers to determine catalytic coefficients in the Brønsted plot with $\alpha = 1.0$, this was not necessary with the m-nitrobenzaldehyde and p-methoxyphenyl mixed acetals.

It is concluded that the general acid catalysed hydrolysis of aromatic aryl methyl acetals proceeds by an A-S_E2 mechanism described by Mechanism 2 where leaving group ability (with consequent reduced acetal basicity) and incipient carbonium ion stability are both of considerable importance in facilitating carbon-phenoxy oxygen bond fission in the R.D.S.

Table B has been constructed in order to determine the influence of leaving group ability and carbonium ion stability in the reported general acid catalysed hydrolysis of other acetals which are also thought to proceed via an A-S_E2 mechanism. Whereas Table 135 shows the importance of carbonium ion stability in the methoxy-carbonium ion moiety, Table B(i) shows the dramatic rate decrease, about 300 fold, when this stability is further decreased (Tables 40, 41 and ref.37). When the incipient carbonium ion stability is further reduced, again with the same phenoxy leaving group, general acid catalysis is no longer observable as has been shown for the compounds in Fig.4.

Fig. 4.



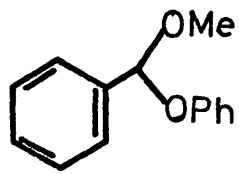
Ref: 16,34 76 36

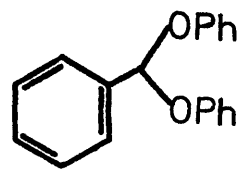
Table B(ii) shows the catalytic coefficients obtained for 2-(p-nitrophenyl)-tetrahydropyran (III),[64] tropone diethyl ketal (V)[99] and benzaldehyde phenyl methyl acetal (VI), Table 34. Although the leaving group ability of III > VI, the increased carbonium ion stability of VI makes the hydrolysis rates comparable. When the leaving group ability is further decreased general acid catalysis is usually no longer observable, e.g. in the substrates shown in Fig. 5.

TABLE B

Second Order Rate Constants for Reported Buffer Catalysis in Acetal Hydrolysis

(i) dependence on incipient carbonium ion stability (constant leaving group)





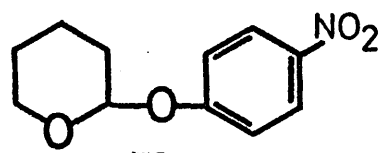
chloroacetic acid

20% dioxane-water

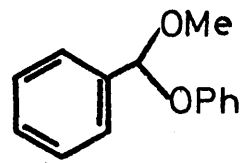
40°C

$k_{HA}(\underline{M}^{-1}sec^{-1})$	6.26×10^{-1}	2.44×10^{-3}

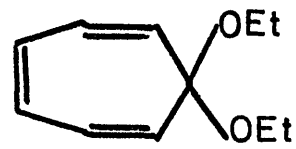
)(ii) dependence on incipient carbonium ion stability and leaving group ability



III



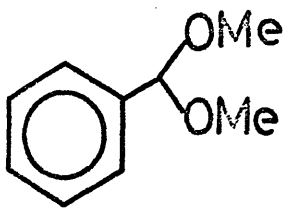
VI

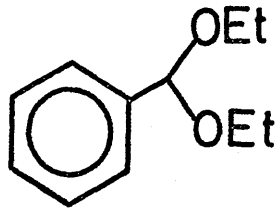


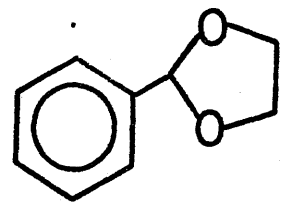
V

$k_{HA}(\underline{M}^{-1}sec^{-1})$	1.3×10^{-2}[a]	1.3×10^{-2}	1.6×10^{-1}[a]
buffer (aqueous)	Acetate	Acetate	Phosphate

a: estimated values, assuming that a 10°C temperature decrease halves the observed rate[64,59]







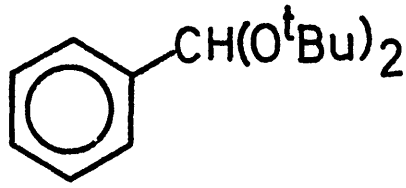
Ref: - 63, 89 68

Table 10

Graph 1

although when the incipient carbonium ion is made extremely stable, as in tropone diethyl ketal (V), buffer catalysis is observable.

The acetic acid catalysed hydrolysis of benzaldehyde di-^{t}bu-acetal(VII) also has a pronounced general acid catalysis,



VII

(3.25×10^{-1} $M^{-1}sec^{-1}$ in aqueous acetate buffer at 25°C) and its hydrolysis thought to proceed by an $A\text{-}S_E2$ mechanism[165] although its leaving group ability must be considerably less than that of a phenoxy group. Therefore, although carbonium ion stability and leaving group ability are of extreme importance in the observation of general acid catalysis in acetal hydrolysis, it appears that release of steric strain in forming the alkoxy carbonium ion of VII can also give rise to such a mechanism. It seems feasible to extrapolate this argument to the lysozyme-substrate complex where the formation of a carbonium ion might relieve steric strain in the ground state of the distorted hexose unit which is undergoing cleavage from the stable chair conformation to a half-chair conformation resembling that of the carbonium ion intermediate. Hereby enhancing the ease of formation of the transition state and making possible catalysis by a weak acid in the enzyme-substrate complex (see introduction and refs. 165, 13-15, 20, 21 and 43).

6. Hammett ρ correlation

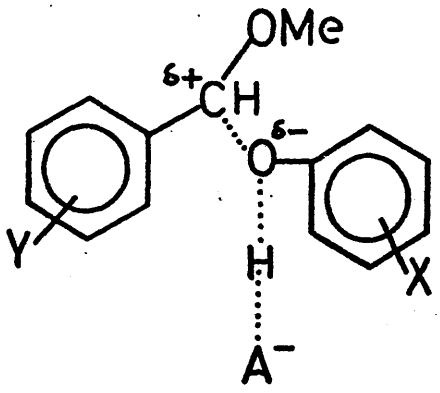
The ρ values obtained from the general acid catalysed hydrolysis of benzaldehyde substituted (X)-phenyl methyl acetals, implementing the Hammett linear free energy relationship (L.F.E.R).

$$\log k/k_o = \rho\sigma \qquad \text{.....(10)}$$

are shown in Tables 121 to 125, and Graph 7. The values obtained were all positive, and increased in magnitude with decreasing strength of the catalysing acid, therefore indicating that the amount of C-O bond fission in the transition state varies with the catalysing acid.

In Fig. 6 where a general acid HA is transferring a proton, H , to the acetal oxygen, as A^- becomes a stronger base (HA a weaker acid) the amount of negative charge

Fig. 6



on the phenolic oxygen, and therefore the amount of C-O bond cleavage, will increase. If this were not the case, and all the acids were transferring a proton to a base of the same strength, it would be expected on the basis of Hammond's postulate[1,90] that the degree of proton transfer

in the transition state would increase as the strength of the acid increased. This would lead to the ρ value becoming progressively more negative as the strength of the catalysing acid increased, the reverse of what is found. Conversely, the increasing negativety of the ρ values for the general acid catalysed hydrolysis of substituted (Y) - benzaldehyde phenyl methyl acetals with decreasing strength of the catalysing acid would indicate that the amount of positive charge on the acetal carbon must increase, C-O bond fission increases, as A^- becomes a stronger base,[3] Tables 126 to 130, Graph 8.

It is rather difficult to compare these results with other reported examples of general acid catalysis in acetal hydrolysis since such an extensive study has not been published, although a small positive ρ value (0.9) has recently been found for the formic acid catalysed hydrolysis of a series of 2-(para-substituted-phenoxy)-tetrahydropyrans[64] which is comparable with the corresponding value (0.67) for benzaldehyde substituted-phenyl methyl acetals, and the value (-2.0) obtained from the acetic acid catalysed hydrolysis of sbustituted-benzaldehyde di-^{t}bu-acetals[165] which is comparable to the corresponding value obtained from the substituted-benzaldehyde phenyl methyl acetals (-2.3), with the small differences in magnitude presumably being incurred by the culminative effects

of experimental errors and slightly differing electronic requirements brought about by the differing relative stabilities of incipient carbonium ion and leaving group.

The "non-conformity" to a Hammett L.F.E.R. of meta-substituted compounds by homologous para-(electron releasing) substituents has been observed frequently,[63,135,167] and although an overall linear fit can often be obtained when σ^+ rather than σ substituent constants, or a Yukowa-Tsuno L.F.E.R. is implemented (see e.g. Table 2, introduction), as will be demonstrated shortly for substituted-benzaldehyde mixed acetals, such relationships cannot be applied when positive deviations from a positively sloped Hammett relationship are incurred, such as that shown in Graph 7 for the benzaldehyde substituted-phenyl methyl acetal series. The positive deviations of the para-methyl-, and para-methoxy, phenyl acetals can only be accounted for by assuming a resonance interaction of these substituents with the phenoxy oxygen, whereby, although leaving group ability is comparatively poor, the much increased basicity facilitates greatly the proton transfer process, and the deviation becomes more pronounced as the strength of the catalysing acid increases. I_n the hydronium ion catalysed hydrolysis, the small negative slope shown in Graph 9 would indicate that electronic requirements are of different importance here than in the weak-acid catalysed reaction, and that

proton transfer is dependent on the acetal basicity rather than ease of C-O bond fission, which conclusion is substantiated by the better L.F.E.R. obtained when σ^+ substituent constants are implemented (compare Tables 131, 148, 149 and Graph 12). Although the use of σ^+ constants are usually indicative of substituent-carbonium ion resonance stability, this is not always the case.[67] If the upward curvature in the Brønsted plot of log k_{HA} vs. σ Graph 7, were to denote a mechanistic change in the hydrolysis of the para-substituted phenyl acetals, the pronounced buffer catalysis observed might indicate that a rate limiting proton transfer were occurring, Mechanism 1, or even a specific hydronium ion catalysis with nucleo-philic participation, although, again the intermediary of an acylal intermediate was unobservable. Further discussion of these two possibilities will be deferred to the following section (7) where the solvent isotope effects obtained are indicative of a constancy of mechanism.

The small positive ρ values obtained with weak general acids in the hydrolysis of benzaldehyde substituted-phenyl methyl acetals (ρ = 0.43 to 1.25), and the smallnegative value obtained with hydronium ion catalysis (-0.45 with σ^+ Table 149), are comparable not only to the corresponding values obtained from the formic and hydronium ion catalysed hydrolysis of 2-(para-substituted phenoxy) -

tetrahydropyrans, ρ = +0.9 and -0.9 respectively, but also to the lysozyme-catalysed hydrolysis of phenolic glycosides where ρ = +1.23, and the hydronium ion catalysed reaction where ρ = -0.66 and -0.43,[41,170] and, in fact, to the ρ values of enzymically and hydronium ion catalysed hydrolysis shown in Table 1 of the introduction.

There is evidence that some of the carboxylic acid groups of lysozyme have abnormally high pKa values, one of these being the glutamic acid -35 residue, which, as was described in the introduction would be mainly ionised in the pH region 5 to 6 and able to provide general acid catalysis for the rupture of the glycosidic bond. This suggestion was described earlier as being supported by the observations of intramolecular catalysis, analagous to the proposed "intra-complex" general acid catalysis, where an internal carboxylic acid group is suitably orientated[5,16,36,37]. The recent observations of intermolecular general acid catalysed hydrolysis in acetals, where the site of hydrolysis is structurally identical to that of glycosides, would substantiate the theory, and it is interesting to note that the ρ factor obtained from the pivalic acid catalysed hydrolysis (pKa = pH =5.05) of benzaldehyde substituted-phenyl acetals, 1.25, is almost identical to that obtained from the lysozyme-catalysed hydrolysis of substituted-phenolic glycosides, ρ =1.23, although this latter value might have been derived from k_{cat} values

which are composites of several rate and equilibrium constants (see introduction).

Graph 8 indicates substantially positive deviations, from the Hammett L.F.E.R. of substituted (meta)-benzaldehyde phenyl methyl acetals, of the para-substituted (electron donating) homologues although the residuals of k_{HA} obs. and k_{HA} calc. for the p-methyl compound are comparable with the residuals for the other four compounds. Excellent correlations are obtained for both meta- and para- substituted compounds when the data is fitted to a Yukawa-Tsuno L.F.E.R.[127] when $r = 0.5$:

$$\log k/k_o = \rho[\sigma + r(\sigma^+ - \sigma)] \qquad \ldots\ldots\ldots(11)$$

where $r = 0.5$

although increasingly negative ρ values with decreasing acid basicity are still observed, Tables 142 to 146, Graph 10. The magnitude of the ρ value obtained from the hydronium ion catalysed hydrolysis, $\rho = -1.9$ implementing equation (11) Graph 11, would indicate that electronic effects are more important in the weak-acid catalysed hydrolysis, where $\rho = -0.04$ to $-.34$, suggesting again a more facile proton transfer reaction and reduced importance of C-O bond fission in the R.D.S. of the hydronium ion catalysed reaction. Were the benzaldehyde-moiety substituents affecting more the acetal basicity than incipient carbonium ion stability in the hydrolysis of mixed acetals, it would be expected that the hydronium ion catalysed reaction would exhibit a greater

negative ρ value, as those observed in the specific acid catalysed hydrolysis of benzaldehyde diethyl acetals where ρ = -3.35 (see Table 2 introduction).

Although the ρ value for the acetic acid catalysed hydrolysis of substituted-benzaldehyde di -^{t}butyl acetals(VII) was found to be -2.0, and is comparable to the corresponding value of -2.8 for the substituted-benzaldehyde phenyl methyl acetals, the hydronium ion catalysed hydrolysis of series (VII) was found to be more dependent on electronic requirements ($\rho_{H_3O^+}$ = -4.0), also the $k_{H_3O^+}$ catalytic coefficient was observed to lie on, or very near, the Brønsted correlation line obtained from weak general acids. If the observations mentioned in section 5 could be applied here, i.e. the less negative deviations of the $k_{H_3O^+}$ point from the Brønsted slope was indicative of a greater carbonium ion stability and/or better leaving group ability, it would indicate that ^{t}butanol was a better leaving group than phenol, which is extremely unlikely, and the hydronium ion catalysed hydrolysis, whose ρ value is similar to that of benzaldehyde diethyl acetal,[68] might then be regarded as undergoing an A-1 mechanism withC-O bond fission only in the R.D.S.

The intermediacy of the substituent constants σ and σ^+ observed by Fife and Jao[68] for the acid catalysed hydrolysis of substituted-benzaldehyde diethyl acetals was interpreted by these authors as indicating a transition state resembling more the conjugate acid than the substrate, and by

Cordes as being fully consistent with rate determining carbonium ion formation.[59] Although the R.D.S. in an $A\text{-}S_E2$ mechanism does involve carbonium ion formation, it also involves proton transfer, and the α values reported in Tables 134 and 135 indicate a varying range of "product-like" transition states. It seems, therefore, that the interpretation of the intermediacy of σ and σ^+ is best given by Capon, Perkins and Rees[129] who suggested that the observed rate constants were composite values of the equilibrium constant for protonation, represented by σ, and the rate constant for heterolysis, represented by σ^+.

Hammett plots which product "concave-upward" curves, and are thought to be indicative of mechanistic or transition state change, have been reported although invariably for nucleophilic substitution reactions.[135] The dependence of the degree of "non-linearity" in such a reaction has been shown by Fuchs and Hisbet[162] to be strongly influenced by the solvent polarity, and the measurement of enthalpies of transfer of transition state from one solvent to another has been suggested to be an experimental measure of transition state structure.[163] Therefore an application of these observations might be of interest regarding the substituent effects in mixed aryl alkyl acetals.

Schreck[135] concluded from his review of non-linear Hammett plots that deviations from a straight line appear

TABLE C.

Deviations from 'Linear' Hammett Plots.

The following observations are from 'Linear' Hammett Plots; $\log k/k_o = \rho\sigma$, in which the substituents referred to (X) are in the para position, and the catalyst in each case was HCl.

Substrate	obs.<theor.[a]	obs≈theor.[a]	obs. >theor.[a]	ref.
(x) benzaldehyde di-^{t}bu acetals	$-OCH_3$	$-CH_3$	H	165
		$-NO_2$		
$\rho = -4.0$				
benzaldehyde methyl (x) thiophenyl acetals	$-OCH_3$	$-CH_3$	H	95
		$-Cl$		
$\rho = -0.9$		$-NO_2$		
2-(x)phenoxy tetrahydropyrans	$-OCH_3$	$-CH_3$	H	76
		$-Cl$		
$\rho = -0.9$		$-NO_2$		

a: obs = $k_{H_3O^+}$ observed: theor. = theoretical $k_{H_3O^+}$ from Hammett correlation line

more striking when the line is flat (ρ is small) than when the line is steep (ρ is large) and that small deviations from the latter may not be taken too seriously whereas those observed from flat curves might be interpreted as evidence for a maximum, minimum, or curvature in the plot. Although there is undoubtedly some truth in this statement, Table C would indicate that whether ρ is large or small, constancy in deviations might be equally significant.

7. Solvent Isotope Effects.

The k_{H_3O}/k_{D_3O} solvent isotope effects referred to in this discussion are those obtained from k_{obs} values at 0.001 M HCl and DCl, and not those obtained from the slopes of k_{obs} versus [HCl] or [DCl] for reasons mentioned in section 3.

Solvent isotope effects (S.I.E) for acetal hydrolysis reactions involving pre-equilibrium proton transfer have been found to fall into the range k_H/k_D = 0.3 to 0.5,[59] where the two to three fold rate increases in D_2O compared to H_2O are taken to be representative of a unimolecular A-1 reaction in accord with the theoretical prediction. The difference in overall rate is postulated to occur because the equilibrium constant of the conjugate acid is some two to three times higher in D_2O than in H_2O at a given acidity since the deuterated substrate in D_2O is

TABLE D

Solvent Isotope Effects of the hydrolysis reactions believed to involve proton transfer to oxygen in the rate limiting step.

Substrate	Solvent	Temperature	k_H/k_D	Ref.
2-(p-nitrophenyl)-tetrahydropyran	50% dioxan water	30°C	$H_3O^+/D_3O^+ = 0.75$	76
tropone diethyl ketal	water	15°C	tris H^+/ tris D^+=1.49	99
			$H_2O/D_2O = 1.16$	
Benzaldehyde di-^{t}bu-acetals	ditto	25°C	$H_3O^+/D_3O^+ = 1.11$	165
Catechol Benzaldehyde acetals	ditto	65°C	$H_3O^+/D_3O^+ = 0.92$	37
Benzaldehyde diphenyl acetals	20% dioxan water		$H_3O^+/D_3O^+ = 0.67$	37

generally a weaker acid than the protonated substrate in H_2O.[1,59,72]

Although pre-equilibrium proton transfer reactions (A-1 and A-2) have faster rates in D_2O than H_2O it does not follow that reactions with proton transfer occurring in the rate limiting step should show S.I.E. in the normal direction. The most commonly and accepted reason for the occurrence of small or inverse isotope effects has been reckoned to be the maintenance of zero-point energy because of the transferring proton being bonded to either product or reactant and not undergoing translation at the highest energy point, i.e. transition state.[1] The classification of general acid catalysed hydrolysis of acetals in this category is exemplified in Table D which shows both small and inverse S.I.Es. observed from reactions believed to involve proton transfer in the rate limiting step. The values for ortho ester hydrolysis also show inverse values; $H_3O^+/D_3O^+ = 0.4$ to 0.5.[59] Whereas all the hydrolysis reactions in Table D are postulated to proceed via an $A\text{-}S_E2$ mechanism, when proton transfer only becomes the rate limiting step the S.I.E.is usually much higher.[105,158]

Fife and Jao[76] observed an increase in $k(H_3O^+)/k(D_3O^+)$ with increasing electron-withdrawing power of the substituent in the series 2-(para-substituted phenoxy)-tetrahydropyran,

viz: p-MeO(0.35); p-Me(0.40); H(0.42); p-Cl(0.50); p-NO_2 (0.75), and concluded that the increasing S.I.E. reflected the extent of proton transfer in the transition state being almost complete with the p-MeO compound, and steadily decreasing until, with the p-NO_2 compound, reduced acetal basicity brought about by increased leaving group ability made protonation more difficult and facilitated C-O bond cleavage, such that proton transfer and bond breaking were concerted (Fig 19 introduction). The S.I.Es. observed in the hydronium ion catalysed hydrolysis of benzaldehyde substituted-phenyl methyl acetals, Table 138, are similar in trend with those found above, increasing from 0.62 for the p-MeO compound to 1.10 for the m-NO_2 compound, but whereas the values obtained by Fife and Jao, with the exception of the p-nitrophenyl homologue, were all in the accepted region for an A-1 mechanism, and were indeed found to be described by such a mechanism, the values for the substituted-phenyl mixed acetals and p-nitrophenyl tetrahydropyran are all greater than 0.6 and are described by a concerted A-S_E2 mechanism. Also the S.I.Es. reported in Table 138 corroborate with the α values reported in Table 134 in indicating a reduced relative degree of proton transfer, or "product-like" transition state, along the series: p-MeO(k_H/k_D = 0.62); p-Me(0.65); H(0.69); m-F(0.37); and m-NO_2(1.10), and would

also indicate that there was no mechanistic change involved within the series, as might have been suggested from the non-linearity of the Hammett Plots, section 6.

In agreement with the above results, the $k(H_3O^+)/k(D_3O^+)$ S.I.Es. for the hydrolysis of substituted-benzaldehyde phenyl methyl acetals, Table 139, are all greater than 0.6 and increase as the relative amount of proton transfer in the transition state decreases along the series: m-F(0.66); H(0.69); p-Me(approx. 0.97); p-MeO(0.83), in accord not only with the observed values reported in Table 135 but also with the secondary kinetic isotope effects observed by Cordes et al for the acid catalysed hydrolysis of substituted-benzaldehyde diethyl acetals (ref. 113, 140 and section 5).

The values of k_o (AcOH)/k_o(AcOD) shown in Tables 138 and 139 do not agree well with the corresponding k(HCl)/k(DCl) values, with their numerical significance open to speculation and only their overall magnitude indicating the possibility of them belonging to a mechanism involving proton transfer in the rate limiting step. Similarly the values of k(AcOH)/k(AcOD) would appear to be somewhat inconsistent, although it might be tentatively suggested that the values reach a maximum with p-methylbenzaldehyde and m-methoxy-phenyl acetals if the irregularities of the other values were construed as arising from experimental error. This maximum should only be reached when:

$\Delta pK = pK(HA) - pK(BH)$

$= 0$ (approximately)

in the reaction:

$HA + B \longrightarrow HB + A$ (charges omitted)

where the transferring proton is equidistant from A and B.

$\overleftarrow{A} \ldots\ldots\ldots H \ldots\ldots\ldots \overrightarrow{B}$ (see introduction)

Although this would not be the case in the ground states, it might be considered applicable to the transition states, where the relative amount of proton transfer to the substrates in question, p-methylbenzaldehyde and m-methoxyphenyl acetals, may be considered similar with respect to their observed α values which are 0.692 and 0.708 respectively, with a combined standard deviation of 0.134. If the degree of C-O bond fission were that much more advanced in the transition state of p-methyl-benzaldehyde than in m-methoxyphenyl, which is conceivable considering the high degree of stabilisation of the incipient carbonium ion brought about by the p-methyl substituent, then the basicities of the developing phenolic leaving groups might be equal at some point along their reaction co-ordinates where they approximate the basicity of the developing conjugate base of the catalysing acid (see section 6 and mechanism 2)

It is appreciated that this is rather far reaching speculation based on somewhat irregular values but is possibly supported by the following observations: (i) that the

observed α values were thought to be about 0.1 unit too high, i.e. greater than the order of bond being formed (Z) between proton and acetal, therefore bringing the values nearer the theoretical values of 0.5 which is considered indicative of a symmetrical transition state. (ii) that maximum isotope effects have been observed from $\Delta pK \neq 0$, although near it (see introduction and ref 121), and (iii) that it has been forwarded that the concept of a symmetrical transition state involving the rupture and formation of two <u>different</u> bonds becomes somewhat elusive and therefore $\alpha = 0.5$ may not, in fact, characterise the transition state for proton transfer between two bases of equal strength. This latter was postulated by Gold and Waterman[158,105] who found the S.I.E. corresponding to $\alpha=0.62$ much greater than that found when $\alpha = 0.5$ in the general acid catalysed hydrolysis of keten acetals.

Dixon and Bruice,[124] amongst others, concluded that, if their results were not fortuitous, then transition state symmetry is dependent on ground state basicities, although criticism has been levelled at their experimental evidence to support their claimed maximum S.I.E. and at the insensitivity of k_H/k_D to the symmetry of the transition state in general (see introduction and ref.121)

It would be extremely interesting, therefore, to study the general acid catalysed hydrolysis of benzaldehyde methyl acetyl acylal (I). The relatively small deviation of (I) from the slope in Graph 13 might indicate that the reaction mechanism is differente from that observed with the mixed aryl alkyl acetals. If this were the case the high S.I.Es. k(AcOH)/k(AcOD) = 3.04 and k (AcOH)/k(AcOD) = 2.59 would indicate a rate determining proton transfer mechanism, however if the mechanism is constant, these S.I.Es. might be indicative of a maximum where ground state basicities are equal.

RESULTS

RESULTS

The following parameters may be assumed constant throughout the following results section unless otherwise stated.

Temperature = 25°C Ionic Strength = 0.050

Absorbance change during hydrolysis measured between O.D. = 0.1 to O.D. = 0.9

pH values of the buffer series were strictly monitored and the maximum allowed deviation was 0.02pH units.

The hydrolysis of the compounds was followed by measuring the release of the aldehydic product at the appropriate wavelength:

Benzaldehyde Substituted-Phenyl Methyl Acetals .. 250mμ

Substituted - Benzaldehyde Phenyl Methyl Acetals....

m -NO_2;	245 mμ	p -Me ;	261.5 mμ
m -F ;	248 mμ	p -Meo;	278 mμ
m -Meo;	255 mμ		

The values quoted in the following tables were obtained from the generalised least squares programmes described in the Kinetic Experimental Section. Although these values are given to four figures this does not reflect the reproducibility of the technique, which was usually ± 2%, and the last of these figures is therefore not significant.

Individual pH measurements are shown in Table 107.

TABLE 1

The Chloroacetic Acid Catalysed Hydrolysis of Benzaldehyde M-Nitrophenyl Methyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; $pH_{25} = 3.10$

[AH] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	3.650; 3.622; 3.870	3.789
0.020	3.358; 3.362; 3.365	3.366
0.015	3.132; 2.873	2.842
0.010	2.608; 2.582; 2.559	2.518
0.005	2.068; 2.030; 2.085	2.094

$k_{HA} = 8.474 \times 10^{-1}\ M^{-1}\ sec^{-1}$ 0.85% error

$k_{int} = 1.671 \times 10^{-2}\ sec^{-1}$ 0.49% error

TABLE 2

The Formic Acid Catalysed Hydrolysis of Benzaldehyde m-Nitrophenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.0225	10.11; 10.19; 10.77	10.39
0.018	9.293; 9.107; 9.640	9.322
0.0135	8.543	8.253
0.008	7.208; 7.580; 7.669	7.185
0.0045	6.125; 5.941 6.312	6.116

$k_{HA} = 2.374 \times 10^{-1}\ M^{-1}\ sec^{-1}$ 1.07% error

$k_{int} = 5.047 \times 10^{-3}\ sec^{-1}$ 0.61% error

TABLE 3

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde m-Nitrophenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	10.36; 9.596; 9.333	9.882
0.020	9.088; 8.954; 8.715	8.727
0.015	7.073	7.572
0.010	6.165; 6.588; 6.546	6.417
0.005	5.417; 5.202; 5.303	5.262

$k_{HA} = 2.309 \times 10^{-1}\ M^{-1}\ sec^{-1}$ 0.93% error

$k_{int} = 4.1075 \times 10^{-3}\ sec^{-1}$ 0.74% error

TABLE 4

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde m-Nitrophenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc} 10^3\ sec^{-1}$
0.025	3.374; 3.412; 3.473	3.482
0.020	3.028; 3.123; 2.945	3.039
0.015	2.757	2.597
0.010	2.214; 2.254; 2.138	2.155
0.005	1.864; 1.695; 1.555	1.712

$k_{HA} = 8.849 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 0.79% error

$k_{int} = 1.269 \times 10^{-3}\ sec^{-1}$ 0.67% error

TABLE 5

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde m-Nitrophenyl Methyl Acetal

$[(CH_3)_3CCOOH] = [(CH_3)_3CCOO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	2.997; 3.171	3.061
0.020	2.721; 2.735; 2.667	2.711
0.015	2.311; 2.280; 2.402	2.361
0.010	1.978; 2.007; 2.087	2.011
0.005	1.747; 1.689; 1.576	1.661

$k_{HA} = 6.998 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 0.86% error

$k_{int} = 1.311 \times 10^{-3}\ sec^{-1}$ 0.56% error

TABLE 6

The Deuteroacetic Acid Catalysed Hydrolysis of Benzaldehyde m-Nitrophenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[DA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	4.130; 4.263; 4.091	4.119
0.020	3.513; 3.319	3.484
0.015	2.837; 2.755; 2.890; 2.892	2.849
0.010	2.362; 2.212; 2.129; 2.153	2.215
0.005	1.601; 1.572	1.580

$k_{DA} = 1.269 \times 10^{-1}\ M^{-1}\ sec^{-1}$ 0.77% error

$k_{int} = 9.455 \times 10^{-4}\ sec^{-1}$ 1.24% error

TABLE 7

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde m-Nitrophenyl Methyl Acetal

$pH_{25} = 3.10$

$[H^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	2.181; 2.156	2.084
0.0008	1.643; 1.674	1.678
0.0006	1.255; 1.170	1.271
0.0004	0.9128; 0.8535	0.8646
0.0002	0.4512; 0.4729	0.4582

$k_{H^+} = 2.032 \times 10^1\ M^{-1}\ sec^{-1}$ 0.69% error

$k_{int} = 5.18 \times 10^{-4}$

TABLE 8

The Deuterochloric Acid Catalysed Hydrolysis of Benzaldehyde m-Nitrophenyl Methyl Acetal

$pD_{25} = 3.13$

$[D^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	2.006; 1.953	1.985
0.0008	1.593; 1.509	1.555
0.0006	1.176; 1.093	1.126
0.0004	0.6894; 0.7007	0.6973

$k_{D^+} = 2.145 \times 10^1\ M^{-1}\ sec^{-1}$ 1.24% error

$k_{int} = -2.601 \times 10^{-3}$

TABLE 9

The Chloroacetic Acid Catalysed Hydrolysis of Benzaldehyde m-Bromophenyl Methyl Acetal

$[CH_2ClCOOH] = [ClCH_2COO^-]/2$; $pH_{25} = 3.10$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	3.955; 3.973	3.938
0.020	3.660; 3.634	3.553
0.015	3.071	3.168
0.010	2.858; 2.588	2.784
0.005	2.444; 2.481	2.399
$k_{HA} = 7.695 \times 10^{-1}\ M^{-1}\ sec^{-1}$		1.29% error
$k_{int} = 2.014 \times 10^{-2}\ sec^{-1}$		0.64% error

TABLE 10.

The Formic Acid Catalysed Hydrolysis of Benzaldehyde m-Bromophenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.027	9.901; 9.932; 9.754	10.149
0.018	8.392; 8.923	8.198
0.009	6.866; 6.058; 5.941	6.247
$k_{HA} = 2.168 \times 10^{-1}\ M^{-1}\ sec^{-1}$		1.28% error
$k_{int} = 4.296 \times 10^{-3}\ sec^{-1}$		1.01% error

TABLE 11

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde m-Bromophenyl Methyl Acetal.

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	8.433	8.417
0.020	7.472	7,543
0.015	6.701; 6.738	6.670
0.010	5.775	5.797

$k_{HA} = 1.746 \times 10^{-1}\ M^{-1}\ sec^{-1}$ 2.46% error

$k_{int} = 4.051 \times 10^{-3}\ sec^{-1}$ 1.70% error

TABLE 12

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde m-Bromophenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.713	1.731
0.020	1.537; 1.464	1.495
0.015	1.220	1.259
0.010	1.093; 3.003	1.023
0.005	0.7530	0.7867

$k_{HA} = 4.722 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 1.31% error

$k_{int} = 5.507 \times 10^{-4}\ sec^{-1}$ 1.53% error

TABLE 13

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde m-Bromophenyl Methyl Acetal

$[(CH_3)C\ COOH] = [(CH_3)CCOO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.090; 1.140; 1.132	1.132
0.020	1.043; 0.9629; 0.9645	0.9878
0.015	0.9160; 0.8823	0.8433
0.010	0.7262; 0.6622	0.6989
0.005	0.6008; 0.5338; 0.5064	0.5544

$k_{HA} = 2.839 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 0.78% error

$k_{int} = 4.099 \times 10^{-4}\ sec^{-1}$ 0.63% error

TABLE 14

The Deuteroacetic Acid Catalysed Hydrolysis of Benzaldehyde m-Bromophenyl Methyl Acetal

$[CH_3COOD] = [CH_3CO\bar{O}]$; $pD_{25} = 5.14$

[DA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.687; 1.556	1.589
0.020	1.261; 1.347	1.348
0.015	1.126; 1.027	1.105
0.010	1.064; 0.7749	0.8629
0.005	0.5788; 0.6496	0.6207

$k_{DA} = 4.846 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 0.98% error

$k_{int} = 3,784 \times 10^{-4}\ sec^{-1}$ 1.57% error

TABLE 15

The Chloroacetic Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; $pH_{25} = 3.10$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	2.981	2.990
0.020	2.615; 2.648	2.702
0.015	2.497	2.415
0.010	2.147; 2.207	2.127
0.005	1.816; 1.785	1.839

$k_{HA} = 5.752 \times 10^{-1}\ M^{-1}\ sec^{-1}$ 1.25% error

$k_{int} = 1.552 \times 10^{-2}\ sec^{-1}$ 0.57% error

TABLE 16

The Formic Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.0225	7.844	7.856
0.0180	7.456	7.432
0.0135	6.817; 7.189	7.007
0.0090	6.626; 6.392	6.582
0.0045	5.943; 6.368	6.157

$k_{HA} = 9.439 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 2.97% error

$k_{int} = 5.732 \times 10^{-3}\ sec^{-1}$ 0.62% error

TABLE 17

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [CLCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.030	5.925; 5.768; 5.544	5.835
0.020	5.234; 4.929	5.038
0.010	4.352; 4.258; 4.092	4.241

$k_{HA} = 7.969 \times 10^{-2} M^{-1}\ sec^{-1}$ 0.47% error

$k_{int} = 3.444 \times 10^{-3}\ sec^{-1}$ 0.34% error

TABLE 18

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.040	1.562; 1.629; 1.651	1.553
0.030	1.207; 1.355; 1.291	1.307
0.015	0.9353; 0.8656	0.9391
0.005	0.7118: 0.6918; 0.6890	0.6936

$k_{HA} = 2.455 \times 10^{-2} M^{-1}\ sec^{-1}$ 0.47% error

$k_{int} = 5.708 \times 10^{-4}\ sec$ 0.34% error

TABLE 19

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal

$[(CH_3)_3\ CCOOH] = [(CH_3)_3C.COO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	8.562; 8.583	8.584
0.020	7.554	7.573
0.015	6.563; 6.777	6.563
0.010	5.577; 5.388	5.552

$k_{HA} = 2.022 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 1.89% error

$k_{int} = 3.530 \times 10^{-4}\ sec^{-1}$ 1.98% error

TABLE 20

The Deuteroacetic Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.411; 1.430; 1.398	1.409
0.020	1.164; 1.256	1.219
0.015	1.061; 1.013; 0.9628	1.031
0.010	0.9242; 0.8761; 0.9000	0.8416
0.005	0.6063; 0.6642; 0.6452	0.6525

$k_{HA} = 3.783 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 0.89% error

$k_{int} = 4.633 \times 10^{-4}\ sec^{-1}$ 0,95% error

TABLE 21

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal.

$pH_{25} = 3.10$

$[H^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	2.486; 2.472	2.377
0.0008	1.778; 1.889	1.884
0.0006	1.394; 1.346	1.391
0.0004	0.9083; 0.8720	0.8978
0.0002	0.4175; 0.3983	0.4047

$k_H = 2.466 \times 10^1\ \underline{M}^{-1}\ sec^{-1}$ 0.85% error

$k_{int} = -8.89 \times 10^{-4}\ sec^{-1}$

TABLE 22

The Deuterochloric Acid Catalysed Hydrolysis of Benzaldehyde m-Fluorophenyl Methyl Acetal

$pD_{25} = 3.13$

$[D^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	2.805; 2.903	2.873
0.0008	2.133; 2.229	2.191
0.0006	1.495; 1.499	1.509
0.0004	0.8323; 0.8485	0.8271
0.0002	0.1432; 0.1438	0.1453

$k_D = 3.409 \times 10^1\ M^{-1}\ sec^{-1}$ 0.66% error

$k_{int} = -5.365 \times 10^{-3}\ sec^{-1}$

TABLE 23

The Chloroacetic AcidCatalysed Hydrolysis of Benzaldehyde m-Methoxy-phenyl Methyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; $pH_{25} = 3.10$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	4.671; 4.509	4.579
0.020	4.167; 4.293	4.276
0.015	3.937; 3.987	3.973
0.010	3.752; 3.647	3.669
$k_{HA} = 6.062 \times 10^{-1}\ M^{-1}\ sec^{-1}$		3.09% error
$k_{int} = 3.064 \times 10^{-2}\ sec^{-1}$		1.05% error

TABLE 24

The Formic Acid Catalysed Hydrolysis of Benzaldehyde m-Methoxyphenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$; Electrolyte KCl

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	1.329; 1.332	1.350
0.015	1.252; 1.261	1.236
0.010	1.173; 1.189	1.179
0.005	1.109; 1.113	1.122
$k_{HA} = 1.142 \times 10^{-1}\ M^{-1} sec^{-1}$		3.19% error
$k_{int} = 1.065 \times 10^{-2}\ sec^{-1}$		0.47% error

TABLE 25

The Formic Acid Catalysed Hydrolysis of Benzaldehyde m-Methoxyphenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$; Electrolyte $NaNO_3$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	1.359; 1.392	1.376
0.015	1.244; 1.265	1.251
0.010	1.215; 1.178	1.188
0.005	1.124; 1.121	1.126
$k_{HA} = 1.249 \times 10^{-1}\ M^{-1}\ sec^{-1}$		3.29% error
$k_{int} = 1.063 \times 10^{-2}\ sec^{-2}$		0.53% error

TABLE 26

TheFormic Acid Catalysed Hydrolysis of Benzaldehyde m-Methoxyphenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$; Electrolyte $NaClO_4$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	1.388; 1.392	1.399
0.020	1.358; 1.319	1.338
0.015	1.283; 1.254	1.277
0.010	1.242; 1.219	1.216
0.005	1.105; 1.171	1.155
$k_{HA} = 1.220 \times 10^{-1}\ M^{-1}\ sec^{-1}$		2.48% error
$k_{int} = 1.094 \times 10^{-2}\ sec^{-1}$		0.42% error

TABLE 27

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde m-Methoxy-phenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	6.110; 6.015	6.097
0.020	5.546; 5.766	5.806
0.015	5.494; 5.619	5.515
0.020	5.407; 5.360	5.224
0.005	4.733; 4.864	4.932

$k_{HA} = 5.822 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 3.15% error

$k_{int} = 4.641 \times 10^{-3}\ sec^{-1}$ 0.535% error

TABLE 28

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde m-MethoxyphenylMethyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.596; 1.574	1.591
0.020	1.431; 1.479	1.463
0.015	1.336; 1.350	1.335
0.010	1.217; 1.214	1.208
0.005	1.052; 1.137	1.079

$k_{HA} = 2.554 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 1.19% error

$k_{int} = 9.522 \times 10^{-4}\ sec^{-1}$ 0.41% error

TABLE 29

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde m-Methoxyphenyl Methyl Acetal.

$[(CH_3)_3C\ COOH] = [(CH_3)CCOO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	9.645; 9.728	9.712
0.020	9.074; 8.692	8.865
0.015	7.838; 7.884	8.018
0.010	7.393; 7.136	7.170
0.005	6.249; 6.315	6.323

$k_{HA} = 1.695 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 1.45% error

$k_{int} = 5.476 \times 10^{-4}\ sec^{-1}$ 0.64% error

TABLE 30

The Deuteroacetic Acid Catalysed Hydrolysis of Benzaldehyde m-Methoxyphenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[DA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	8.035; 8.221	8.145
0.020	7.362	7.493
0.015	6.925; 6.922	6.842
0.010	6.387; 5.988	6.190
0.005	5.625; 5.203	5.538

$k_{DA} = 1.303 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 1.98% error

$k_{int} = 4.837 \times 10^{-4}\ sec^{-1}$ 0.76% error

TABLE 31

The Chloroacetic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; $pH_{25} = 3.10$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	4.328; 4.469	4.437
0.020	4.346; 4.244	4.248
0.015	4.044; 4.052	4.059
0.010	3.865; 3.864	3.871

$k_{HA} = 3.771 \times 10^{-1}\ M^{-1}\ sec^{-1}$ 2.65% error

$k_{int} = 3.494 \times 10^{-2}\ sec^{-1}$ 0.67% error

TABLE 32

The Formic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.045	1.318; 1.317	1.317
0.036	1.273; 1.261	1.267
0.027	1.223; 1.214; 1.218	1.218
$k_{HA} = 5.535 \times 10^{-2}\ M^{-1}\ sec^{-1}$		3.99% error
$k_{int} = 1.069 \times 10^{-2}\ sec^{-1}$		0.71% error

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.027	1.223; 1.214; 1.218	1.219
0.018	1.161; 1.163; 1.146	1.153
0.009	1.086; 1.082; 1.085	1.086
$k_{HA} = 7.453 \times 10^{-2}\ M^{-1}\ sec^{-1}$		2.30% error
$k_{int} = 1.019 \times 10^{-2}\ sec^{-1}$		0.31% error

for [HA] = 0.045 to 0.009;

$k_{HA} = 6.610 \times 10^{-2}\ M^{-1}\ sec^{-1}$	1.42% error
$k_{int} = 1.031 \times 10^{-2}\ sec^{-1}$	0.22% error

TABLE 33

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.030	8.027; 7.791	7.843
0.020	7.341; 7.220; 7.303	7.357
0.010	6.959; 6.872; 6.872	6.870

$k_{HA} = 4.865 \times 10^{-2}\ M^{-1} sec^{-1}$ 3.18% error

$k_{int} = 6.384 \times 10^{-3}\ sec^{-1}$ 0.49% error

TABLE 34

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.342; 1.339	1.348
0.020	1.284; 1.309	1.284
0.015	1.209; 1.220	1.219
0.010	1.143	1.155
0.005	1.092; 1.099	1.090

$k_{HA} = 1.290 \times 10^{-2}\ M^{-1} sec^{-1}$ 1.85% error

$k_{int} = 1.026 \times 10^{-3}\ sec^{-1}$ 0.36% error

TABLE 35

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.46$; Ionic Strength 0.100

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.010	1.331; 1.352	1.342
0.020	1.455; 1.482	1.478
0.030	1.630; 1.638	1.613
0.040	1.752; 1.718	1.748
0.050	1.875; 1.878	1.883
$k_{HA} = 1.352 \times 10^{-2}\ M^{-1}\ sec^{-1}$		1.227% error
$k_{int} = 1.207 \times 10^{-3}\ sec^{-1}$		0.37% error

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.070	2.147; 2.149	2.138
0.080	2.259; 2.243	2.233
0.090	2.282; 2.326; 2.338	2.328
0.100	2.426; 2.473; 2.407	2.422
$k_{HA} = 9.485 \times 10^{-3}\ M^{-1}\ sec^{-1}$		3.51% error
$k_{int} = 1.474 \times 10^{-3}\ sec^{-1}$		1.91% error
for [HA] = 0.010 to 0.100		
$k_{HA} = 1.242 \times 10^{-2}\ M^{-1}\ sec^{-1}$		0.54% error
$k_{int} = 1.231 \times 10^{-3}\ sec^{-1}$		0.27% error

TABLE 36

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[(CH_3)_3C.COOH] = [(CH_3)_3COO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.030	8.335; 8.073; 8.589	8.334
0.020	7.439; 7.834; 7.531	7.577
0.010	6.676; 6.785; 6.949	6.819

$k_{HA} = 7.573 \times 10^{-3}\ M^{-1}\ sec^{-1}$ 2.12% error.

$k_{int} = 6.063 \times 10^{-4}\ sec^{-1}$ 0.46% error

TABLE 37

The Deuteroacetic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[DA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	7.008; 6.864	7.028
0.020	6.544; 6.529	6.525
0.015	6.223; 6.104	6.023
0.010	5.626; 5.491; 5.608; 5.267	5.519
0.005	5.069; 4.955; 4.995	5.017

$k_{DA} = 1.005 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 1.61

$k_{int} = 4.514 \times 10^{-4}\ sec^{-1}$ 0.55

TABLE 38.

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$pH_{25} = 3.10$

$[H^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	4.111; 4.084	3.919
0.0008	2.891; 3.154	3.092
0.0006	2.234	2.267
0.0004	1.402; 1.403	1.441
0.0002	0.6015; 0.6422	0.6155
$k_{H^+} = 4.129 \times 10^1\ M^{-1}\ sec^{-1}$		0.69%
$k_{int} = -2.100 \times 10^{-3}\ sec^{-1}$		

TABLE 39

The Deuterochloric Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$pD_{25} = 3.13$

$[D^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	5.816; 6.060	6.102
0.0008	4.694; 4.798	4.639
0.0006	3.210; 3.232	3.178
0.0004	1.672	1.715
0.0002	0.2519; 0.2546	0.2532
$k_{D^+} = 7.311 \times 10^1\ M^{-1}\ sec^{-1}$		0.65% error
$k_{int} = -1.2086 \times 10^{-2}\ sec^{-1}$		

TABLE 40

The Chloroacetic Acid (20%-Dioxan; 80%-Water; v/v) Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; $T = 40^oC$; $pH_{40} = 3.21$

$[HA]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.020	4.409	4.376
0.015	4.007; 4.009	4.063
0.010	3.845; 3.751	3.750
0.005	3.414	3.437
$k_{HA} = 6.255 \times 10^{-1}\ M^{-1}\ sec^{-1}$		2.92% error
$k_{int} = 3.124 \times 10^{-2}\ sec^{-1}$		0.69% error

TABLE 41

The Chloroacetic Acid (20% - Dioxan; 80% - Water; v/v) Catalysed Hydrolysis of Benzaldehyde Diphenyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; $T = 40^oC$; $pH_{40} = 3.21$

$[HA]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	3.161;	3.198
0.020	3.069; 3.086	3.076
0.015	3.012	2.954
0.010	2.831; 2.863	2.833
0.005	2.667	2.711
$k_{HA} = 2.435 \times 10^{-3}\ M^{-1}\ sec^{-1}$		3.97% error
$k_{int} = 2.589 \times 10^{-4}\ sec^{-1}$		0.63% error

TABLE 42

The Chloroacetic Acid Catalysed Hydrolysis of Benzaldehyde p-Methyl-phenyl Methylacetal

$[Cl\ CH_2COOH] = [ClCH_2COO^-]/2$; $pH_{25} = 3.21$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	6.403; 6.435; 6.389	6.389
0.020	6.232; 6.081; 6.085	6.152
0.015	5.934; 5.842; 6.024	5.914
0.010	5.704; 5.670; 5.653	5.676
k_{HA} =	$4.755 \times 10^{-1}\ M^{-1}\ sec^{-1}$	4.31% error
k_{int} =	$5.200 \times 10^{-2}\ sec^{-1}$	0.68% error

TABLE 43

The Formic Acid Catalysed Hydrolysis of Benzaldehyde p-Methylphenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	1.562; 1.559	1.565
0.020	1.502; 1.514; 1.469; 1.477	1.504
0.015	1.447; 1.462; 1.427	1.444
0.010	1.417	1.384
0.005	1.339; 1.306; 1.317; 1.317	1.323
k_{HA} =	$1.208 \times 10^{-1}\ M^{-1}\ sec^{-1}$	1.99% error
k_{int} =	$1.263 \times 10^{-2}\ sec^{-1}$	0.28% error

TABLE 44

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde p-Methylphenyl Methyl Acetal

$[ClCH_2.CH_2COOH]=[ClCH_2CH_2COO^-]$; pH_{25}= 4.00

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	9.325; 9.472; 9.523; 9.394	9.429
0.020	9.203; 9.064; 8.862	9.054
0.015	8.591; 8.724; 8.859	8.678
0.010	8.263; 8.289; 8.351	8.302
0.005	7.951; 7.965; 7.844; 7.897	7.926

k_{HA} = 7.521 x 10^{-2} M^{-1} sec^{-1} 2.16% error

k_{int} = 7.549 x 10^{-3} sec^{-1} 0.34% error

TABLE 45

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde p-Methylphenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; pH_{25} = 4.675

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.520; 1.540; 1.563	1.532
0.020	1.460; 1.424; 1.466	1.465
0.015	1.438; 1.367; 1.392	1.399
0.010	1.309; 1.287	1.333
0.005	1.304; 1.258; 1.243	1.267

k_{HA} = 1.322 x 10^{-2} M^{-1} sec^{-1} 2.12% error

k_{int} = 1.201 x 10^{-3} sec^{-1} 0.38% error

TABLE 46

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde p-Methylphenyl Methyl Acetal

$[(CH_3)_3CCOOH] = [(CH_3)_3CCOO^-]$; $pH_{25} = 4.91$

[HA] M	K_{obs} 10^4 sec^{-1}	K_{calc} 10^4 sec^{-1}
0.025	9.135	9.178
0.020	8.864	8.903
0.015	8.797	8.629
0.010	8.580; 8.174	8.354
0.005	8.182; 7.907	8.079

$k_{HA} = 5.493 \times 10^{-3}$ M^{-1} sec^{-1} 4.05% error

$k_{int} = 7.805 \times 10^{-4}$ sec^{-1} 0.42% error

TABLE 47

The Deuteroacetic Acid Catalysed of Benzaldehyde p-Methylphenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[DA] M	K_{obs} 10^3 sec^{-1}	K_{calc} 10^3 sec^{-1}
0.025	1.693; 1.703; 1.718	1.735
0.020	1.658; 1.649; 1.622	1.633
0.015	1.555; 1.538; 1.519	1.532
0.010	1.417; 1.459; 1.479	1.430
0.005	1.309; 1.282; 1.327	1.328

$k_{DA} = 2.033 \times 10^{-2}$ M^{-1} sec^{-1} 1.75% error

$k_{int} = 1.227 \times 10^{-3}$ sec^{-1} 0.41% error

TABLE 48

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde p-Methylphenyl Methyl Acetal

pH_{25} = 3.10

$[H^+]$ M	K_{obs} 10^2 sec^{-1}	K_{calc} 10^2 sec^{-1}
0.001	5.650; 5.589	5.580
0.0008	4.467; 4.350	4.427
0.0006	3.272; 3.237	3.274
0.0004	2.119; 2.134	2.121
0.0002	0.9681; 0.9689	0.9682
k_{H^+} = 5.765 x 10^1 M^{-1} sec^{-1}		0.64% error
k_{int} = 1.846 x 10^{-3} sec^{-1}		

TABLE 49

The Deuterochloric Acid Catalysed Hydrolysis of Benzaldehyde p-Methylphenyl Methyl Acetal

pD_{25} = 3.13

$[D^+]$ M	K_{obs} 10^2 sec^{-1}	K_{calc} 10^2 sec^{-1}
0.001	8.322; 9.005	8.650
0.0008	6.720; 6.734	6.595
0.0006	4.414; 4.512	4.539
0.0004	2.480; 2.378	2.484
0.0002	0.4498; 0.4286	0.4280
k_{D^+} = 1.028 x 10^2 M^{-1} sec^{-1}		0.63% error
k_{int} = 1.628 x 10^{-3} sec^{-1}		

TABLE 50

The Chloroacetic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxy Phenyl Methyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; pH = 3.10

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	8.903; 9.118	8.979
0.020	8.313	8.334
0.015	7.589; 7.684	7.688
0.010	7.103; 7.010	7.043
0.005	6.391; 6.413	6.398
k_{HA} = 1.291 x 10^0 M sec		1.48% error
k_{int} = 5.752 x 10^{-2} sec^{-1}		0.39% error

TABLE 51

The Formic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; pH_{25} = 3.565

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.0180	2.326; 2.296	2.329
0.0135	2.253; 2.252	2.239
0.0090	2.167; 2.197	2.149
0.0045	2.031; 2.043	2.060
k_{HA} = 1.989 x 10^{-1} $M^{-1}sec^{-1}$		3.35% error
k_{int} = 1.971 x 10^{-2} sec^{-1}		0.41% error

TABLE 52

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	2.205; 2.148	2.178
0.020	2.094; 2.144	2.108
0.015	2.088	2.036
0.010	1.972; 1.939	1.965
0.005	1.933; 1.843	1.894
$k_{HA} = 1.422 \times 10^{-1}\ M^{-1}\ sec^{-1}$		2.33% error
$k_{int} = 1.823 \times 10^{-2}\ sec^{-1}$		0.27% error

TABLE 53

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$; Electrolyte KCl

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	2.231; 2.192	2.219
0.020	2.154; 2.149	2.137
0.015	2.042; 2.055	2.055
0.010	2.006; 1.931	1.973
0.005	1.911; 1.897	1.890
$k_{HA} = 1.648 \times 10^{-2}\ M^{-1}\ sec^{-1}$		3.11% error
$k_{int} = 1.808 \times 10^{-3}\ sec^{-1}$		0.46% error

TABLE 54

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.685$; Electrolyte $NaNO_3$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	2.346; 2.243	2.306
0.020	2.207; 2.209	2.224
0.015	2.161; 2.152	2.143
0.010	2.034; 2.094	2.061
0.005	1.969; 1.968	1.979
k_{HA} =	$1.630 \times 10^{-2}\ M^{-1} sec^{-1}$	3.33% error
k_{int} =	$1.898 \times 10^{-3}\ sec^{-1}$	0.42% error

TABLE 55

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.695$; Electrolyte $NaClO_4$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	2.307; 2.290	2.310
0.020	2.223	2.226
0.015	2.135; 2.165	2.142
0.010	2.081; 2.076	2.059
0.005	1.902; 2.008	1.975
k_{HA} =	$1.677 \times 10^{-2} M^{-1}\ sec^{-1}$	3.08% error
k_{int} =	$1.891 \times 10^{-3} sec^{-1}$	0.38% error

TABLE 56

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$[(CH_3)_3C.COOH] = [(CH_3)_3C.COO^-]$; pH = 4.91

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.263; 1.254	1.277
0.020	1.219; 1.228	1.215
0.015	1.144; 1.185	1.154
0.010	1.121; 1.092	1.092
0.005	1.046; 1.003	1.031

$k_{HA} = 1.229 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 1.54% error

$k_{int} = 9.693 \times 10^{-4}\ sec$ 0.26% error

TABLE 57

The Deuteroacetic Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.209; 1.224	1.229
0.015	1.147; 1.118	1.121
0.010	1.074; 1.089	1.067
0.005	1.009; 0.9963	1.013

$k_{HA} = 1.078 \times 10^{-2}\ M^{-1}\ sec^{-1}$ 2.23% error

$k_{int} = 9.594 \times 10^{-4}\ sec^{-1}$ 0.38% error

TABLE 58

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$pH_{25} = 3.10$

$[H^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	9.090; 7.783	8.511
0.0008	7.292; 5.952	6.728
0.0006	4.833; 4.906	4.945
0.0004	3.089; 3.223; 3.619	3.162
0.0002	1.417; 1.468; 1.198	1.379
		0.61% error

$k_{H^+} = 8.914 \times 10^1\ M^{-1}\ sec^{-1}$

$k_{int} = -4.04 \times 10^{-3}\ sec^{-1}$

TABLE 59

The Deuterochloric Acid Catalysed Hydrolysis of Benzaldehyde p-Methoxyphenyl Methyl Acetal

$pD_{25} = 3.13$

$[D^+]$ M	$K_{obs}\ 10^1\ sec^{-1}$	$K_{calc}\ 10^1\ sec^{-1}$
0.001	1.356; 1.354	1.344
0.0008	1.034; 1.043	1.038
0.0006	0.7407; 0.7256	0.7313
0.0004	0.3874; 0.4478	0.4249
0.0002	0.1210	0.1185
		0.72% error

$k_{D^+} = 1.532 \times 10^2\ M^{-1}\ sec^{-1}$

$k_{int} = -1.879 \times 10^{-2}\ sec$

TABLE 60

The Chloroacetic Acid Catalysed Hydrolysis of m-Nitrobenzaldehyde Phenyl Methyl Acetal

$[ClCH_2COOH]=[ClCH_2COO^-]/2$; $pH_{25} = 3.10$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.919; 1.932; 1.885	1.919
0.020	1.810; 1.819	1.821
0.015	1.726; 1.747	1.723
0.010	1.621; 1.639	1.624
0.005	1.492; 1.513; 1.542; 1.473	1.526
	$k_{HA} = 1.968 \times 10^{-2}\ M^{-1}\ sec^{-1}$	2.57% error
	$k_{int} = 1.428 \times 10^{-3}\ sec^{-1}$	0.59% error

TABLE 61

The Formic Acid Catalysed Hydrolysis of m-Nitrobenzaldehyde Phenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.027	4.504; 4.464; 4.464	4.467
0.018	4.356; 4.375	4.334
0.009	4.222; 4.210	4.201
	$k_{HA} = 1.476 \times 10^{-3}\ M^{-1}\ sec^{-1}$	4.76% error
	$k_{int} = 4.068 \times 10^{-4}\ sec^{-1}$	0.77% error

TABLE 62

The β-Chloropropionic Acid Catalysed Hydrolysis of m-Nitrobenzaldehyde Phenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	2.007; 1.850	1.927
0.020	1.907; 1.879	1.872
0.015	1.732	1.817
0.010	1.791	1.762

$k_{HA} = 1.105 \times 10^{-3}\ M^{-1}\ sec^{-1}$ 7.47% error

$k_{int} = 1.651 \times 10^{-4}\ sec^{-1}$ 0.95% error

TABLE 63

The Acetic Acid Catalysed Hydrolysis of m-Nitrobenzaldehyde Phenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^5\ sec^{-1}$	$K_{calc}\ 10^5\ sec^{-1}$
0.025	4.536; 4.274	4.396
0.020	4.298; 4.269	4.263
0.015	4.087; 4.112	4.130
0.010	3.942; 3.989	3.997
0.005	3.930	3.865

$k_{HA} = 2.656 \times 10^{-4}\ M^{-1}\ sec^{-1}$ 4.09% error

$k_{int} = 3.732 \times 10^{-5}\ sec^{-1}$ 0.49% error

TABLE 64

The Pivalic Acid Catalysed Hydrolysis of m-Nitrobenzaldehyde Phenyl Methyl Acetal

$[(CH_3)_3C.COOH] = [(CH_3)_3C.COO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^5\ sec^{-1}$	$K_{calc}\ 10^5\ sec^{-1}$
0.025	2.281; 2.254	2.261
0.020	2.237; 2.215	2.225
0.015	2.179; 2.173	2.188
0.010	2.144	2.151
0.005	2.127	2.114
	$k_{HA} = 7.387 \times 10^{-5}\ M^{-1} sec^{-1}$	5.00% error
	$k_{int} = 2.077 \times 10^{-5}\ sec^{-1}$	0.88% error

TABLE 65

The Deuteroacetic Acid Catalysed Hydrolysis of m-Nitrophenyl Methyl Acetal.

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[DA] M	$K_{obs}\ 10^5\ sec^{-1}$	$K_{calc}\ 10^5\ sec^{-1}$
0.025	4.304; 4.359	4.299
0.020	4.115; 4.131	4.174
0.015	4.085	4.049
0.010	3.866; 3.926	3.923
0.005	3.856; 3.799	3.798
	$k_{DA} = 2.504 \times 10^{-4}\ M^{-1}\ sec^{-1}$	5.57% error
	$k_{int} = 3.673 \times 10^{-5}\ sec^{-1}$	0.72% error

TABLE 66

The Hydrochloric Acid Catalysed Hydrolysis of m-Nitrobenzaldehyde Phenyl Methyl Acetal

$[H^+]$ M	$K_{obs}\ 10^3\ sec^{-1}$
0.001	1.418; 1.483

TABLE 67

The Chloroacetic Acid Catalysed Hydrolysis of m-Fluorobenzaldehyde Phenyl Methyl Acetal

$$[ClCH_2COOH] = [ClCH_2COO^-]/2; \quad pH_{25} = 3.10$$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.024	10.65; 11.14; 10.76	10.87
0.020	10.00; 9.351	10.14
0.015	9.482; 10.07	9.413
0.010	8.827; 8.912	8.685
0.005	7.784; 7.882	7.957
$k_{HA} = 1.456 \times 10^{-1}\ M^{-1}\ sec^{-1}$		1.31% error
$k_{int} = 7.229 \times 10^{-3}\ sec$		0.39% error

TABLE 68

The Formic Acid Catalysed Hydrolysis of m-Fluorobenzaldehyde Phenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.0225	2.605; 2.662; 2.633; 2.669	2.641
0.0180	2.491; 2.576	2.552
0.0135	2.540; 2.472; 2.469	2.462
0.0090	2.361; 2.311; 2.373	2.372
0.0045	2.254; 2.349	2.282

$k_{HA} = 1.994 \times 10^{-2}\ M^{-1}\ sec$

$k_{int} = 2.193 \times 10^{-3}\ sec^{-1}$

TABLE 69

The β-Chloropropionic Acid Catalysed Hydrolysis of m-Fluorobenzaldehyde Phenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.020	1.241; 1.203	1.212
0.015	1.145; 1.173	1.163
0.010	1.129; 1.116	1.114
0.005	1.057; 1.061	1.065

$k_{HA} = 9.816 \times 10^{-3}\ M^{-1}\ sec^{-1}$ 4.49% error

$k_{int} = 1.016 \times 10^{-3}\ sec^{-1}$ 0.54% error

TABLE 70

The Acetic Acid Catalysed Hydrolysis of m-Fluorobenzaldehyde Phenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	2.617; 2.589	2.614
0.020	2.546	2.504
0.015	2.238	2.395
0.010	2.343; 2.167	2.286
0.005	2.185; 2.196	2.177
	$k_{HA} = 2.185 \times 10^{-3}\ M^{-1}\ sec^{-1}$	4.24% error
	$k_{int} = 2.067 \times 10^{-4}\ sec^{-1}$	0.79% error

TABLE 71

The Pivalic Acid Catalysed Hydrolysis of m-Fluorobenzaldehyde Phenyl Methyl Acetal

$[(CH_3)_3C.COOH] = [(CH_3)_3C.COO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	1.609; 1.479	1.537
0.020	1.445	1.459
0.015	1.369	1.381
0.010	1.286; 1.409; 1.283	1.303
0.005	1.235	1.224
	$k_{HA} = 1.563 \times 10^{-3}\ M^{-1}\ sec^{-1}$	2.45% error
	$k_{int} = 1.146 \times 10^{-4}\ sec^{-1}$	0.66% error

TABLE 72

The Hydrochloric Acid Catalysed Hydrolysis of m-Fluorobenzaldehyde Phenyl Methyl Acetal

$pH_{25} = 3.10$

$[H^+]$ M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
.001	8.676; 9.159	9.182
.0008	7.649; 6,853	7.219
.0006	6.067; 5.341	5.256
.0004	3.209; 3.225	3.293
.0002	1.522; 1.199; 1.272	1.330

$k_{H^+} = 9.815 \times 10^0\ M^{-1}\ sec^{-1}$ 0.63% error

$k_{int} = -6.33 \times 10^{-4}\ sec^{-1}$

TABLE 73

The Deuterochloric Acid Catalysed Hydrolysis of m-Fluorobenzaldehyde Phenyl Methyl Acetal

$pH_{25} = 3.13$

$[D^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	1.329; 1.370	1.397
0.0008	1.080; 1.115	1.083
0.0006	0.7826; 0.8395	0.7698
0.0004	0.4280; 0.4485	0.4564
0.0002	0.1499; 0.1376	0.1429

$k_{D^+} = 1.567 \times 10^1\ M\ sec$ 0.63% error

$k_{int} = -1.706 \times 10^{-3}\ sec^{-1}$

TABLE 74

The Chloroacetic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]/2$; $pH_{25} = 3.10$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	3.629; 3.587	3.584
0.020	3.398; 3.405	3.434
0.015	3.358; 3.342	3.284
0.010	3.106; 3.130	3.134
k_{HA} =	$2.999 \times 10^{-1}\ M^{-1}\ sec^{-1}$	3.63% error
k_{int} =	$2.834 \times 10^{-2}\ sec^{-1}$	0.64% error

TABLE 75

The Formic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$; Electrolyte KCl

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	10.01; 10.02	10.06
0.020	9.468; 9.882	9.629
0.015	9.302; 9.101	9.195
0.010	8.917; 8.715	8.760
0.005	8.271; 8.400	8.326
k_{HA} =	$8.685 \times 10^{-2}\ M^{-1}\ sec^{-1}$	1.95% error
k_{int} =	$7.892 \times 10^{-3}\ sec^{-1}$	0.33% error

TABLE 76

The Formic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$; Electrolyte $NaNO_3$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	10.02; 10.08	10.26
0.020	10.01; 9.951	9.847
0.015	9.576; 9.309	9.433
0.010	9.206	9.018
0.005	8.166	8.603
k_{HA} =	$8.295 \times 10^{-2}\ M^{-1}\ sec^{-1}$	2.97% error
k_{int} =	$8.189 \times 10^{-3}\ sec^{-1}$	0.52% error

TABLE 77

The Formic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$; Electrolyte $NaClO_4$.

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	10.11; 10.23	10.38
0.020	10.02; 9.907	9.930
0.015	9.374; 9.594	9.484
0.010	9.289; 9.409	9.037
0.005	8.274; 8.294	8.591
k_{HA} =	$8.928 \times 10^{-2}\ M^{-1}\ sec^{-1}$	1.903% error
k_{int} =	$8.144 \times 10^{-3}\ sec^{-1}$	0.36% error

TABLE 78

The β-Chloropropionic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[ClCH_2.CH_2.COOH] = [ClCH_2.CH_2.COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	4.452; 4.482	4.477
0.020	4.268; 4.295	4.294
0.015	4.005; 4.171	4.111
0.010	3.999; 3.921	3.927
0.005	3.703; 3.713	3.744
$k_{HA} = 3.667 \times 10^{-2}\ M^{-1}\ sec^{-1}$		2.73% error
$k_{int} = 3.561 \times 10^{-3}\ sec^{-1}$		0.46% error

TABLE 79

The Acetic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	10.21; 10.04	10.01
0.020	9.496; 9.560	9.528
0.015	8.747; 9.156	9.046
0.010	8.330;	8.564
0.005	8.153; 8.045	8.082
$k_{HA} = 9.638 \times 10^{-3}\ M^{-1}\ sec^{-1}$		2.16% error
$k_{int} = 7.600 \times 10^{-4}\ sec^{-1}$		0.38% error

TABLE 79(a)

The Deuteroacetic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pH_{25} = 5.14$

[DA] M	K_{obs} 10^4 sec^{-1}	K_{calc} 10^4 sec^{-1}
0.025	5.469; 5.291	5.363
0.020	5.011; 4.923	4.934
0.015	4.383; 4.494	4.501

$k_{DA} = 8.667 \times 10^{-3}$ M^{-1} sec^{-1} 5.29% error

$k_{int} = 3.201 \times 10^{-4}$ sec^{-1} 2.98% error

TABLE 80

The Pivalic Acid Catalysed Hydrolysis of m-Methoxybenzaldehyde Phenyl Methyl Acetal

$[(CH_3)_3C.COOH] = [(CH_3)_3C.COO^-]$; pH = 4.91

[HA] M	$K_{obs}\ 10^4\ sec^{-1}$	$K_{calc}\ 10^4\ sec^{-1}$
0.025	5.734; 5.492	5.501
0.020	5.359; 5.009	5.138
0.015	4.461; 4.710	4.775
0.010	4.188; 4.508	4.412
0.005	4.263	4.049

$k_{HA} = 7.259 \times 10^{-3}\ M^{-1}\ sec^{-1}$ 1.98% error

$k_{int} = 3.686 \times 10^{-4}\ sec^{-1}$ 0.62% error

TABLE 81

The Chloroacetic Acid Catalysed Hydrolysis of p-Methylbenzaldehyde Phenyl Methyl Acetal

$[ClCH_2COOH] = [ClCH_2COO^-]/2$; $pH_{25} = 3.10$

[HA] M	$K_{obs}\ 10^1\ sec^{-1}$	$K_{calc}\ 10^1\ sec^{-1}$
0.025	1.346	1.324
0.020	1.178; 1.204; 1.220	1.218
0.015	1.172; 1.162; 1.051	1.111
0.010	1.009; 1.009	1.004
0.005	0.9121; 0.9696; 0.7559; 0.8947	0.8979

$k_{HA} = 2.131 \times 10^{0}\ M^{-1}\ sec^{-1}$ 1.79% error

$k_{int} = 7.914 \times 10^{-2}\ sec^{-1}$ 0.64% error

TABLE 82

The Formic Acid Catalysed Hydrolysis of p-Methylbenzaldehyde Phenyl Methyl Acetal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	K_{obs} 10^2 sec^{-1}	K_{calc} 10^2 sec^{-1}
0.025	4.902; 3.826	4.278
0.020	3.798; 4.506; 4.149	4.096
0.015	4.171; 3.496	3.914
0.010	3.779; 3.595	3.732
0.005	3.832; 3.442	3.549
k_{HA} =	3.644×10^{-1} M^{-1} sec^{-1}	3.98% error
k_{int} =	3.367×10^{-2} sec	0.60% error

TABLE 83

The β-Chloropropionic Acid Catalysed Hydrolysis of p-Methylbenzaldehyde Phenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	K_{obs} $10^2 sec^{-1}$	K_{calc} 10^2 sec^{-1}
0.025	3.200; 3.141	3.137
0.020	2.912; 2.963; 3.005; 3.147	3.019
0.015	2.851	2.902
0.010	2.819	2.784
0.005	2.729; 2.644; 2.641	2.666
k_{HA} =	2.351×10^{-1} M^{-1} sec^{-1}	3.69% error
k_{int} =	2.549×10^{-2} sec^{-1}	0.54% error

TABLE 84

The Acetic Acid Catalysed Hydrolysis of p-Methylbenzaldehyde PhenylMethyl Acetal

$[CH_3COOH]=[CH_3COO^-]$; pH_{25} = 4.675

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	3.420; 3.951	3.839
0.020	3.216; 3.345	3.293
0.015	2.535; 3.051	2.747
0.010	2.166; 2.178	2.201
k_{HA} = 1.092 x 10^{-1} M^{-1} sec^{-1}		1.82% error
k_{int} = 1.109 x 10^{-3} sec^{-1}		2.59% error

TABLE 85

The Pivalic Acid Catalysed Hydrolysis of p-Methylbenzaldehyde Phenyl Methyl Acetal

$[(CH_3)_3C.COOH]=[(CH_3)_3C.COO^-]$; pH_{25} = 4.91

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	2.557; 2.533	2.546
0.020	2.321; 2.333	2.322
0.015	2.063; 2.135	2.099
0.010	1.817; 1.815	1.875
0.005	1.661	1.652
k_{HA} = 4.469 x 10^{-2} M^{-1} sec^{-1}		1.34% error
k_{int} = 1.428 x 10^{-3} sec^{-1}		0.60% error

TABLE 86

The Deuteroacetic Acid Catalysed Hydrolysis of p-Methylbenzaldehyde Phenyl Methyl Acetal

$[CH_3COOD]=[CH_3COO^-]$; $pD_{25}=$ 5.14

[DA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.835	1.795
0.020	1.529; 1.697	1.639
0.015	1.423	1.484
0.010	1.404	1.329
0.005	1.178; 1.165	1.173
$k_{DA} = 3.110 \times 10^{-2}\ M^{-1}\ sec^{-1}$		1.66% error
$k_{int} = 1.018 \times 10^{-3}\ sec^{-1}$		0.66% error

TABLE 87

The Hydrochloric Acid Catalysed Hydrolysis of p-Methylbenzaldehyde Phenyl Methyl Acetal

$pH_{25} = 3.10$

$[H^+]$	$K_{obs}\ 10^{-1}\ sec^{-1}$
0.001	1.083; 1.082

TABLE 88

The Deuterochloric Acid Catalysed Hydrolysis of p-Methylbenzaldehyde Phenyl Methyl Acetal

$pD_{25} = 3.13$

$[D^+]$	$K_{obs}\ 10^{-1}\ sec^{-1}$
0.001	1.178; 1.109

TABLE 89

The Chloroacetic Acid Catalysed Hydrolysis of p-Methoxybenzaldehyde Phenyl Methyl Acetal

$[CH_3COOH]=[CH_3COO^-]/2$; pH_{25} = 3.10

[HA] M	K_{obs} 10^1 sec^{-1}	K_{calc} 10^1 sec^{-1}
0.025	3.473; 3.496	3.486
0.020	3.182	3.193
0.015	2.912	2.901
0.005	2.219; 2.468	2.316
k_{HA} = 5.849 x 10^0 M^{-1} sec^{-1}		3.85% error
k_{int} = 2.023 x 10^{-1} sec^{-1}		1.73% error

TABLE 90

The Formic Acid Catalysed Hydrolysis of p-Methoxybenzaldehyde Phenyl Methyl Acetal

$[HCOOH]=[HCOO^-]$; pH_{25} = 3.565

[HA] M	K_{obs} 10^2 sec^{-1}	K_{calc} 10^2 sec^{-1}
0.025	11.74	11.138
0.020	9.821	10.326
0.015	9.016	9.270
0.010	8.460; 8.495	8.214
0.005	7.082; 7.047	7.157
k_{HA} = 2.112 x 10^0 M^{-1} sec^{-1}		1.77% error
k_{int} = 6.102 x 10^{-2} sec^{-1}		0.69% error

TABLE 91

The β-Chloropropionic Acid Catalysed Hydrolysis of p-Methoxy-benzaldehyde Phenyl Methyl Acetal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	8.303; 7.847	8.217
0.020	7.495; 7.766; 7.463	7.601
0.015	6.797; 7.000	6.984
0.010	6.653; 6.716; 6.414	6.368
0.005	5.981; 5.248	5.751
$k_{HA} = 1.232 \times 10^{0}\ M^{-1}\ sec^{-1}$		1.56% error
$k_{int} = 5.135 \times 10^{-2}\ sec$		0.51% error

TABLE 92

The Acetic Acid Catalysed Hydrolysis of p-Methoxy-benzaldehyde Phenyl Methyl Acetal

$[CH_3COOH] = [CH_3COO^-]$; $pH_{25} = 4.675$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	1.554; 1.583	1.587
0.020	1.420; 1.368; 1.639	1.446
0.015	1.349; 1.350; 1.300	1.305
0.010	1.165; 1.195	1.164
0.005	1.075; 1.050; 0.9403	1.024
$k_{HA} = 2.814 \times 10^{-1}\ M^{-1}\ sec^{-1}$		1.07% error
$k_{int} = 8.830 \times 10^{-3}\ sec^{-1}$		0.46% error

TABLE 93

The Pivalic Acid Catalysed Hydrolysis of p-Methoxybenzaldehyde Phenyl Methyl Acetal

$[(CH_3)_3C.COOH] = [(CH_3)_3C.COO^-]$; $pH_{25} = 4.91$

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	1.185; 1.226	1.204
0.020	1.080; 1.081	1.087
0.015	0.9831; 0.9554	0.9699
0.010	0.8392; 0.8693	0.8528
0.005	0.7196; 0.7430	0.7357
$k_{HA} = 2.342 \times 10^{-1}\ M^{-1}\ sec^{-1}$		1.05% error
$k_{int} = 6.186 \times 10^{-3}\ sec^{-1}$		0.48% error

TABLE 94

The Deuteroacetic Acid Catalysed Hydrolysis of p-Methoxybenzaldehyde Phenyl Methyl Acetal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[DA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	7.767; 7.738	7.736
0.020	7.007; 7.205	7.096
0.015	6.337; 6.423	6.456
0.010	5.827; 5.818	5.816
0.005	5.209; 5.159	5.175
$k_{DA} = 1.279 \times 10^{-1}\ M^{-1}\ sec^{-1}$		1.29% error
$k_{int} = 4.536 \times 10^{-3}\ sec^{-1}$		0.50% error

TABLE 95

The Hydrochloric Acid Catalysed Hydrolysis of p-Methoxybenzaldehyde Phenyl Methyl Acetal

$pH_{25} = 3.10$

$[H^+]$ M	$K_{obs}\ 10^1\ sec^{-1}$	$K_{calc}\ 10^1\ sec^{-1}$
0.001	3.042; 3.062	3.263
0.0008	2.469; 2.589	2.584
0.0006	1.875; 1.803	1.904
0.0004	1.442; 1.266	1.225
0.0002	0.5118; 0.5461	0.5449

$k_H = 3.398 \times 10^2\ M^{-1}\ sec^{-1}$ 0.88% error

$k_{int} = -1.352 \times 10^{-2}\ sec^{-1}$

TABLE 96

The Deuterochloric Acid Catalysed Hydrolysis of p-Methoxybenzaldehyde Phenyl Methyl Acetal

$pD_{25} = 3.13$

$[D^+]$ M	$K_{obs}\ 10^1\ sec^{-1}$	$K_{calc}\ 10^1\ sec^{-1}$
0.001	3.650; 3.750	3.797
0.0008	3.061; 3.059	2.950
0.0006	2.180; 2.126	2.103
0.0004	1.213; 1.218	1.256
0.0002	0.4148; 0.4125	0.4095

$k_{D+} = 4.235 \times 10^2\ M^{-1}\ sec^{-1}$ 1.01% error

$k_{int} = -4.370 \times 10^{-2} sec^{-1}$

TABLE 97

The Formic Acid Catalysed Hydrolysis of Benzaldehyde Methyl Acetyl Acylal

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^{1}\ sec^{-1}$	$K_{calc}\ 10^{1}\ sec^{-1}$
0.025	2.109; 2.074; 2.092	2.099
0.020	1.944	1.993
0.015	1.903; 1.898	1.886
0.010	1.844; 1.793	1.780
0.005	1.636; 1.685	1.674
$k_{HA} = 2.122 \times 10^{0}\ M^{-1}\ sec^{-1}$		5.96% error
$k_{int} = 1.568 \times 10^{-1}\ sec^{-1}$		1.18% error

TABLE 98

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde Methyl Acetyl Acylal

$[ClCH_2CH_2COOH] = [ClCH_2CH_2COO^-]$; $pH_{25} = 4.00$

[HA] M	$K_{obs}\ 10^{2}\ sec^{-1}$	$K_{calc}\ 10^{2}\ sec^{-1}$
0.025	7.255; 7.284	7.320
0.020	7.133; 7.060	7.071
0.015	6.946; 6.838	6.822
0.010	6.616; 6.590	6.573
0.005	6.274; 6.281	6.324
$k_{HA} = 4.980 \times 10^{-1}\ M^{-1}\ sec^{-1}$		4.40% error
$k_{int} = 6.075 \times 10^{-2}\ sec^{-1}$		0.58% error

TABLE 99

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde Methyl Acetyl Acylal

$[CH_3COOH]=[CH_3COO^-]$; pH_{25} = 4.675

[HA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	3.341	3.343
0.020	3.069; 3.091	3.084
0.015	2.746; 2.838	2.825
0.010	2.689; 2.465	2.566
0.005	2.286; 2.317	2.307

k_{HA} = 5.179 x 10^{-1} M^{-1} sec^{-1} 1.56% error

k_{int} = 2.048 x 10^{-2} sec^{-1} 0.49% error

TABLE 100

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde Methyl Acetyl Acylal

$[(CH_3)_3CCOOH] = [(CH_3)_3CCOO^-]$; pH_{25} = 4.91

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.025	1.609; 1.601	1.599
0.020	1.444; 1.454	1.450
0.015	1.293; 1.309	1.302
0.010	1.146; 1.147	1.153
0.005	1.010; 1.010	1.005

k_{HA} = 2.972 x 10^{-1} M^{-1} sec^{-1} 1.36% error

k_{int} = 8.559 x 10^{-3} sec 0.79% error

TABLE 101

The Deuteroacetic Acid Catalysed Hydrolysis of Benzaldehyde Methyl Acetyl Acylal

$[CH_3COOD] = [CH_3COO^-]$; $pD_{25} = 5.14$

[DA] M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.025	1.353; 1.353	1.354
0.020	1.264; 1.269	1.269
0.015	1.174; 1.175	1.184
0.010	1.122	1.099
0.005	1.002	1.013
$k_{DA} = 1.705 \times 10^{-1}\ M^{-1}\ sec^{-1}$		2.33% error
$k_{int} = 9.281 \times 10^{-3}\ sec^{-1}$		0.62% error

TABLE 102

The Formic Acid Catalysed Hydrolysis of Benzaldehyde Dimethyl Acetal.

$[HCOOH] = [HCOO^-]$; $pH_{25} = 3.565$

[HA] M	$K_{obs}\ 10^3\ sec^{-1}$	$K_{calc}\ 10^3\ sec^{-1}$
0.045	7.381; 7.428	7.433
0.036	7.346; 7.444	7.387
0.027	7.448; 7.364	7.341
0.018	7.237; 7.281	7.295
0.009	7.361; 7.124	7.249
$k_{HA} = 4.599 \times 10^{-3}\ M^{-1}\ sec^{-1}$		38.95% error
$k_{int} = 7.203 \times 10^{-3}\ sec^{-1}$		0.83% error

TABLE 103

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde Dimethyl Acetal

$pH_{25} = 3.10$

$[H^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	2.964; 2.968	2.958
0.0008	2.449; 2.377; 2.406	2.347
0.0006	1.719; 1.628	1.736
0.0004	1.097; 1.113	1.125
0.0002	0.5305; 0.5159; 0.5042	0.5135
$k_H = 3.055 \times 10^{1}\ M^{-1}\ sec^{-1}$		0.58% error
$k_{int} = -9.80 \times 10^{-4}\ sec^{-1}$		

TABLE 104

The Deuterochloric Acid Catalysed Hydrolysis of Benzaldehyde Dimethyl Acetal

$pD_{25} = 3.13$

$[D^+]$ M	$K_{obs}\ 10^2\ sec^{-1}$	$K_{calc}\ 10^2\ sec^{-1}$
0.001	9.032	9.204
0.0008	7.531	7.108
0.0006	5.327; 4.832	5.013
0.0004	2.561	2.918
0.0002	0.8803; 0.8133	0.8224

$k_{D^+} = 1.048 \times 10^2\ M^{-1}\ sec^{-1}$ 0.78% error

$k_{int} = -1.2732 \times 10^{-2}\ sec^{-1}$

TABLE 105

The Aniline/Anilinium Perchlorate Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal

[Aniline] = [Anilinium$^+$] pH_{25} = 4.685; Ionic Strength = 0.10

[BH] M	K_{obs} 10^4 sec^{-1}	K_{calc} 10^4 sec^{-1}
0.050	7.633; 7.497	7.597
0.040	7.115; 7.293	7.222
0.030	6.706; 6.940	6.848
0.020	6.607; 6.578; 6.425	6.473
0.015	6.493	6.285
0.010	5.902; 6.053	6.098
k_{BH} = 3.749 x 10^{-3} M^{-1} sec^{-1}		3.60% error
k_{int} = 5.723 x 10^{-4} sec^{-1}		0.82% error

TABLE 106

The Formic Acid (20% Dioxan/80% water; v/v) Catalysed Hydrolysis of p-Methylbenzaldehyde Thiophenyl Methyl Acetal. (Maximum O.D. Change during hydrolysis 0.20 units)

[HCOOH] = [$HCOO^-$]; pH_{25} = 4.00

[HA] M	K_{obs} 10^3 sec^{-1}	K_{calc} 10^3 sec^{-1}
0.025	7.537; 7.537; 7.520	7.530
0.020	7.349	7.365
0.015	7.221; 7.179; 7.217	7.199
0.010	7.034	7.034
0.005	6.969; 6.716	6.869
k_{HA} = 3.309 x 10^{-2} M^{-1} sec^{-1}		5.00% error
k_{int} = 6.703 x 10^{-3} sec^{-1}		2.13% error

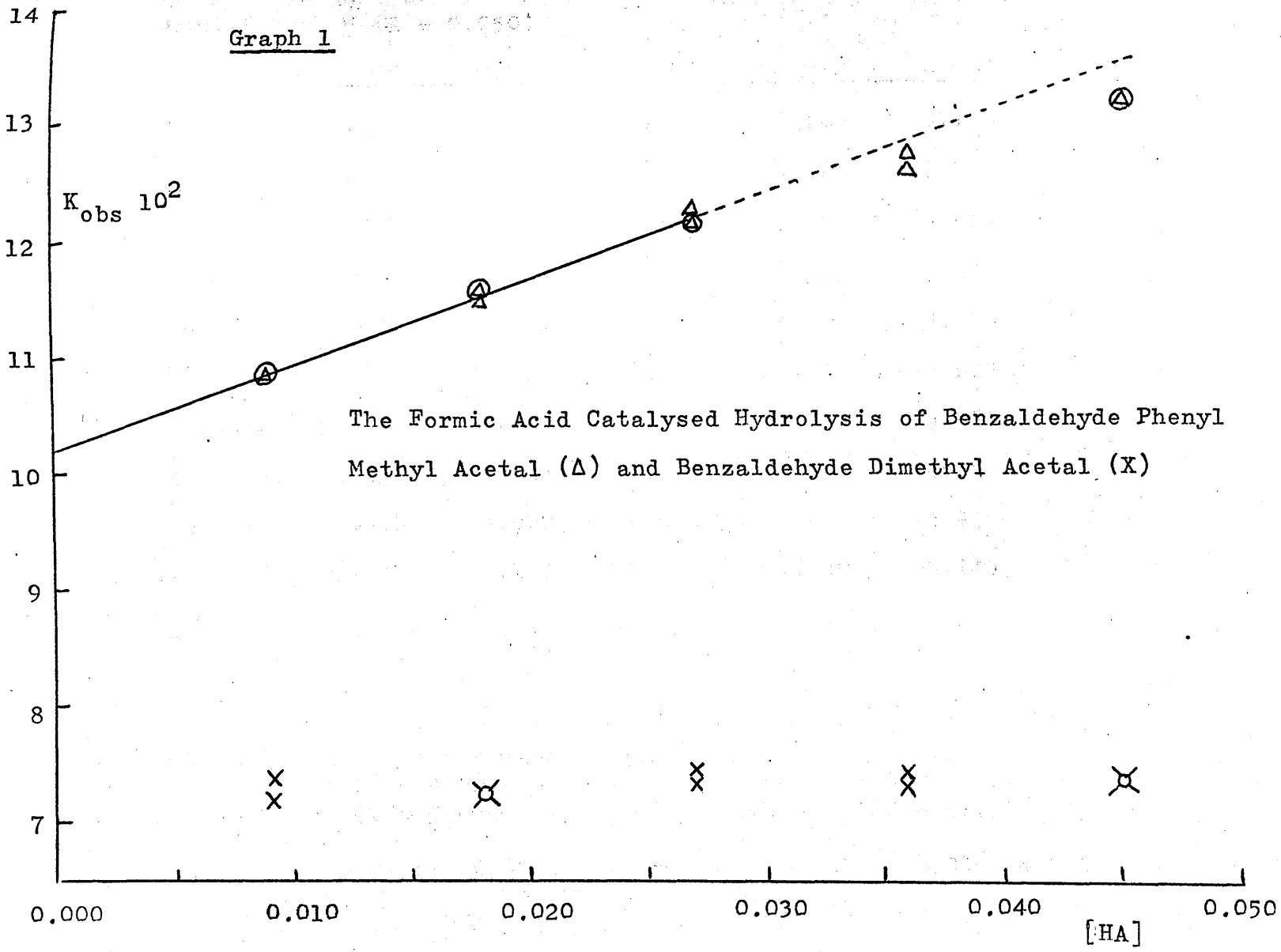

Graph 1
14
13
12
11
10
9
8
7
$K_{obs}\ 10^2$
0.000
0.010
0.020
0.030
0.040
0.050
[HA]
The Formic Acid Catalysed Hydrolysis of Benzaldehyde Phenyl Methyl Acetal (Δ) and Benzaldehyde Dimethyl Acetal (X)

TABLE 107

The individual pH_{25} values of the buffer solutions used in the preceeding experimental work [a] (I = 0.050)

Buffer	0.025	0.020	0.015	0.010	0.005 [HA]
Chloroacetate	3.090	3.100	3.090	3.120	3.120
Formate(KCl)	3.560	3.565	3.565	3.570	3.570
Formate($NaClO_4$)	3.560	3.565	3.565	3.565	3.565
Formate($NaNO_3$)	3.560	3.565	3.565	3.565	3.565
β-Chloropropionate	4.000	4.000	4.000	4.005	4.000
Acetate(KCl)	4.670	4.675	4.675	4.675	4.675
Acetate($NaClO_4$)	4.690	4.690	4.695	4.695	4.695
Acetate($NaNO_3$)	4.685	4.685	4.685	4.685	4.685
Pivalate	4.900	4.900	4.900	4.900	4.910
Deuteroacetate[b]	5.140	5.135	5.140	5.140	5.145
Formate[c]	4.000	4.015	4.020	4.015	4.025
Aniline-Aniliniumd					

a: The fourth figure is estimated to the nearest 0.005 unit
b: The values quoted are $pD_{25} = pH_{25}$ reading +0.4 units
c: Solvent system (20% dioxane - 80% water; v/v); no correction made to observed pH reading.
d: The pH_{25} values were: [0.050]-4.680; [0.040]-4.670; [0.030]-4.675; [0.020]-4.675; [0.010]-4.680.

Brønsted Plots

The following tables indicate the dependence of the catalytic coefficients (k_{HA} for the general acid catalysed hydrolysis of mixed aryl alkyl acetals) on the dissociation constant of the catalysing acids (K_{HA}) by plotting log k_{HA} versus pKa according to the Brønsted equation:[110]

$$\log k_{HA} = \log G_A - \alpha pKa$$

Statistical corrections have not been applied because of the uniformity of the catalysing carboxylic acids where, in each case, p = 1 and q = 2 in the equation:

$$\log (k_{HA}/P) = \log G_A - \alpha(pKa - \log P/q)$$

The following values of pKa are used:[157]

Chloroacetic acid	2.870
Formic acid	3.752
β-Chloropropionic acid	4.100
Acetic acid	4.756
Pivalic acid	5.050
H_3O^+	-1.74

abbreviations:

C.C. = correlation coefficient

S.d. = standard deviation.

TABLE 103

Benzaldehyde m-Nitrophenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc.	residual
2.870	$\bar{1}$.9281	$\bar{1}$.9009	-2.7239×10^{-2}
3.752	$\bar{1}$.3754	$\bar{1}$.4661	$+9.0671 \times 10^{-2}$
4.100	$\bar{1}$.3634	$\bar{1}$.2945	-6.8879×10^{-2}
4.756	$\bar{2}$.9469	$\bar{2}$.9711	$+2.4239 \times 10^{-2}$
5.050	$\bar{2}$.8450	$\bar{2}$.8262	-1.8791×10^{-2}

α = 0.493 C.C. = 9.90×10^{-1}

S.d. = 0.041 (8.23%)

TABLE 109

Benzaldehyde m-Bromophenyl Methyl Acetal.

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	$\bar{1}$.8862	$\bar{1}$.9104	$+2.4185 \times 10^{-2}$
3.752	$\bar{1}$.2902	$\bar{1}$.3395	$+4.9323 \times 10^{-2}$
4.100	$\bar{1}$.2420	$\bar{1}$.1143	-1.2772×10^{-1}
4.756	$\bar{2}$.6741	$\bar{2}$.6897	$+1.5598 \times 10^{-2}$
5.050	$\bar{2}$.4608	$\bar{2}$.4994	$+3.8610 \times 10^{-2}$

α = 0.647 C.C. = 9.926×10^{-1}

S.d. = 0.065 (7.52%)

TABLE 110

Benzaldehyde m-Fluorophenyl Methyl Acetal.

pKa	log k_{HA} obs	log k_{HA} calc.	residual
2.870	$\bar{1}$.7599	$\bar{1}$.6917	-6.8161×10^{-2}
3.752	$\bar{2}$.9749	$\bar{1}$.1027	$+1.2775 \times 10^{-1}$
4.100	$\bar{2}$.9014	$\bar{2}$.8702	-3.1173×10^{-2}
4.756	$\bar{2}$.3901	$\bar{2}$.4321	$+4.1987 \times 10^{-2}$
5.050	$\bar{2}$.3058	$\bar{2}$.2354	-7.0408×10^{-2}

α = 0.668

C.C. = 9.89×10^{-1}

S.d. = 0.057 (8.49%).

TABLE 111

Benzaldehyde m-Methoxyphenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	$\bar{1}$.7826	$\bar{1}$.7228	-5.9807×10^{-2}
3.752	$\bar{1}$.0577	$\bar{1}$.0986	$+4.0888 \times 10^{-2}$
4.100	$\bar{2}$.7650	$\bar{2}$.8523	$+8.7303 \times 10^{-2}$
4.756	$\bar{2}$.4072	$\bar{2}$.3880	-1.9158×10^{-2}
5.050	$\bar{2}$.2292	$\bar{2}$.1800	-4.9227×10^{-2}

α = 0.708

C.C. = 9.948×10^{-1}

S.d. = 0.042 (5.93%)

TABLE 112

Benzaldehyde Phenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	$\bar{1}$.5764	$\bar{1}$.5840	$+7.5807 \times 10^{-3}$
3.752	$\bar{2}$.8724	$\bar{2}$.8995	$+2.7138 \times 10^{-2}$
4.100	$\bar{2}$.6870	$\bar{2}$.6295	-5.7514×10^{-2}
4.756	$\bar{2}$.1106	$\bar{2}$.1204	$+9.8216 \times 10^{-3}$
5.050	$\bar{3}$.8793	$\bar{3}$.8923	$+1.2974 \times 10^{-2}$

α = 0.776

C.C. = 9.99×10^{-1}

S.d. = 0.022 (2.85%)

TABLE 113

Benzaldehyde p-Methylphenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	$\bar{1}$.6772	$\bar{1}$.7933	$+1.1612 \times 10^{-1}$
3.752	$\bar{1}$.0820	$\bar{1}$.0124	-6.9616×10^{-2}
4.100	$\bar{2}$.8763	$\bar{2}$.7043	-1.7204×10^{-1}
4.756	$\bar{2}$.1212	$\bar{2}$.1234	$+2.224 \times 10^{-3}$
5.050	$\bar{3}$.7398	$\bar{3}$.8631	$+1.2331 \times 10^{-1}$

α = 0.885

C.C. = 9.87×10^{-1}

S.d. = 0.034 (9.51%)

TABLE 114

Benzaldehyde p-Methoxyphenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	0.1109	0.1600	$+4.9117 \times 10^{-2}$
3.752	$\bar{1}$.2986	$\bar{1}$.3133	$+1.4668 \times 10^{-2}$
4.100	$\bar{1}$.1529	$\bar{2}$.9792	-1.7372×10^{-1}
4.756	$\bar{2}$.2170	$\bar{2}$.3494	$+1.3239 \times 10^{-1}$
5.050	$\bar{2}$.0896	$\bar{2}$.0671	-2.2455×10^{-2}

α = 0.960

C.C. = 9.91×10^{-1}

S.d. = 0.076 (7.87%)

TABLE 115

m-Nitrobenzaldehyde Phenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	$\bar{2}$.2940	$\bar{2}$.2518	-4.2240×10^{-2}
3.752	$\bar{3}$.1690	$\bar{3}$.3295	$+1.6054 \times 10^{-1}$
4.100	$\bar{3}$.0434	$\bar{3}$.9657	-7.7725×10^{-2}
4.756	$\bar{4}$.4242	$\bar{4}$.2798	-1.4444×10^{-1}
5.050	$\bar{5}$.8685	$\bar{5}$.7236	$+1.0386 \times 10^{-1}$

α = 1.046

C.C. = 9.90×10^{-1}

S.d. = 0.086 (8.19%)

TABLE 116

m-Fluorobenzaldehyde Phenyl Methyl Acetal.

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	$\bar{1}$.1631	$\bar{1}$.1205	-4.2637×10^{-2}
3.752	$\bar{2}$.2541	$\bar{2}$.3125	$+5.8356 \times 10^{-2}$
4.100	$\bar{3}$.9920	$\bar{3}$.9937	$+1.6502 \times 10^{-3}$
4.756	$\bar{3}$.3395	$\bar{3}$.3927	$+5.3184 \times 10^{-2}$
5.050	$\bar{3}$.1939	$\bar{3}$.1233	-7.0552×10^{-2}

α = 0.916

C.C. = 9.97×10^{-1}

S.d. = 0.038 (4.18%)

TABLE 117

m-Methoxybenzaldehyde Phenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.87	$\bar{1}$.4770	$\bar{1}$.5237	$+4.6650 \times 10^{-2}$
3.752	$\bar{2}$.9383	$\bar{2}$.8394	-9.9415×10^{-2}
4.100	$\bar{2}$.5643	$\bar{2}$.5694	$+5.1021 \times 10^{-3}$
4.756	$\bar{3}$.9340	$\bar{2}$.0605	$+7.6470 \times 10^{-2}$
5.050	$\bar{3}$.3608	$\bar{3}$.8320	-2.8807×10^{-2}

α = 0.776 C.C. = 9.945×10^{-1}

S.d. = 0.046 (5.92%)

TABLE 118

p-Methylbenzaldehyde Phenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	0.3286	0.2743	-5.4285×10^{-2}
3.752	$\bar{1}$.5616	$\bar{1}$.6636	$+1.0200 \times 10^{-1}$
4.100	$\bar{1}$.3713	$\bar{1}$.4226	$+5.1338 \times 10^{-2}$
4.756	$\bar{1}$.1821	$\bar{2}$.9684	-2.1369×10^{-1}
5.050	$\bar{2}$.6502	$\bar{2}$.7648	$+1.1464 \times 10^{-1}$

α = 0.692 C.C. = 9.75×10^{-1}

S.d. = 0.092 (13.24%)

TABLE 119

p-Methoxybenzaldehyde Phenyl Methyl Acetal

pKa	log k_{HA} obs	log k_{HA} calc	residual
2.870	0.7671	0.8402	$+7.3089 \times 10^{-2}$
3.752	0.3247	0.2406	-8.4072×10^{-2}
4.100	0.0906	0.0041	-8.6533×10^{-2}
4.756	$\bar{1}$.4493	$\bar{1}$.5581	$+1.0883 \times 10^{-1}$
5.050	$\bar{1}$.3696	$\bar{1}$.3583	-1.1319×10^{-2}

α = 0.679

C.C. = 9.89×10^{-1}

S.d. = 0.059 (8.80%)

TABLE 120

Benzaldehyde Methyl Acetyl Acylal

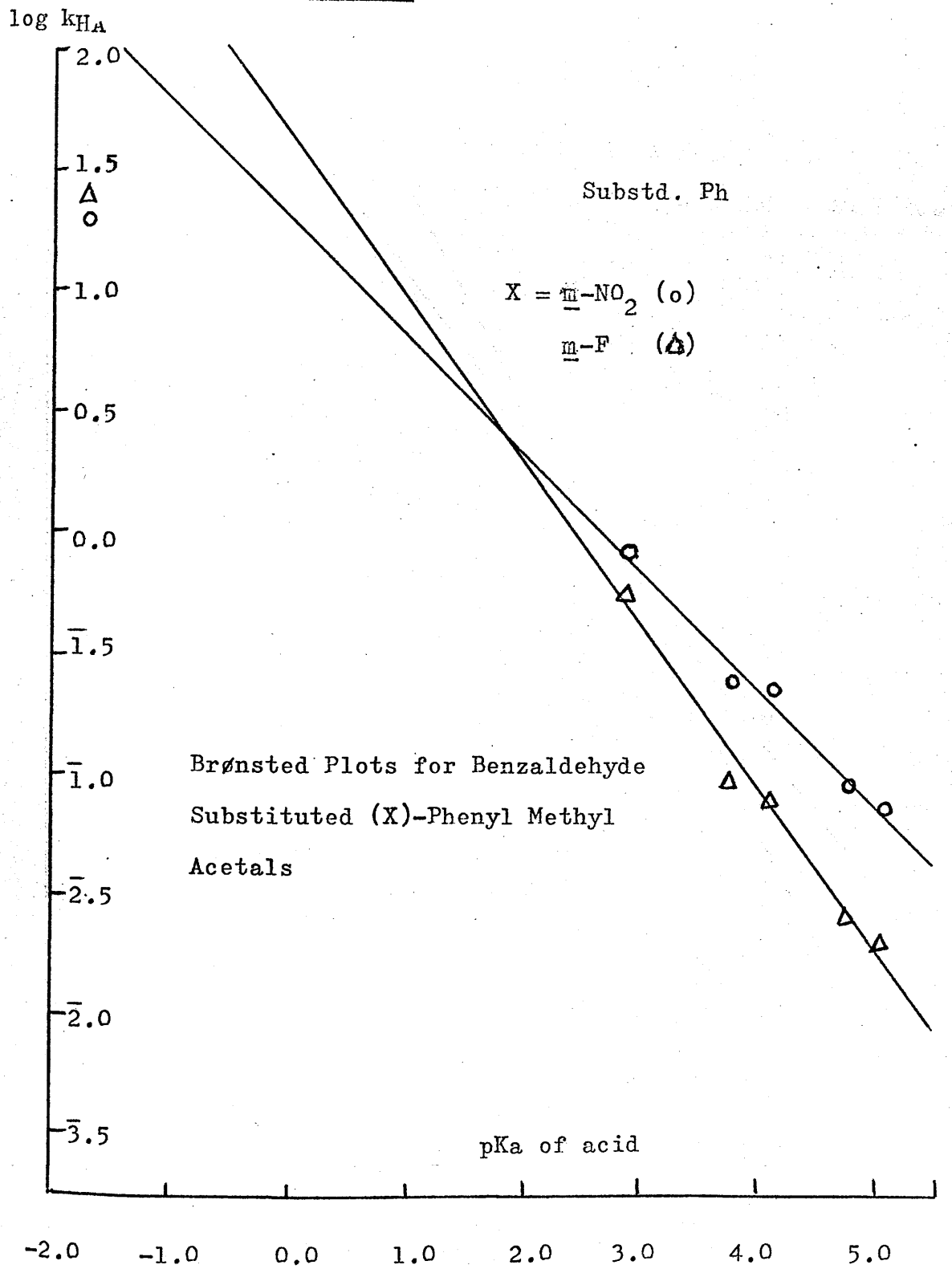
pKa	log k_{HA} obs	log k_{HA} calc	residual
3.752	0.3267	0.3333	$+6.5880 \times 10^{-3}$
4.756	$\bar{1}$.7145	$\bar{1}$.6854	-2.9086×10^{-2}
5.050	$\bar{1}$.4732	$\bar{1}$.4957	$+2.2498 \times 10^{-2}$

α = 0.645

C.C. = 9.98×10^{-1}

S.d. = 0.039 (6.01%)

Graph 2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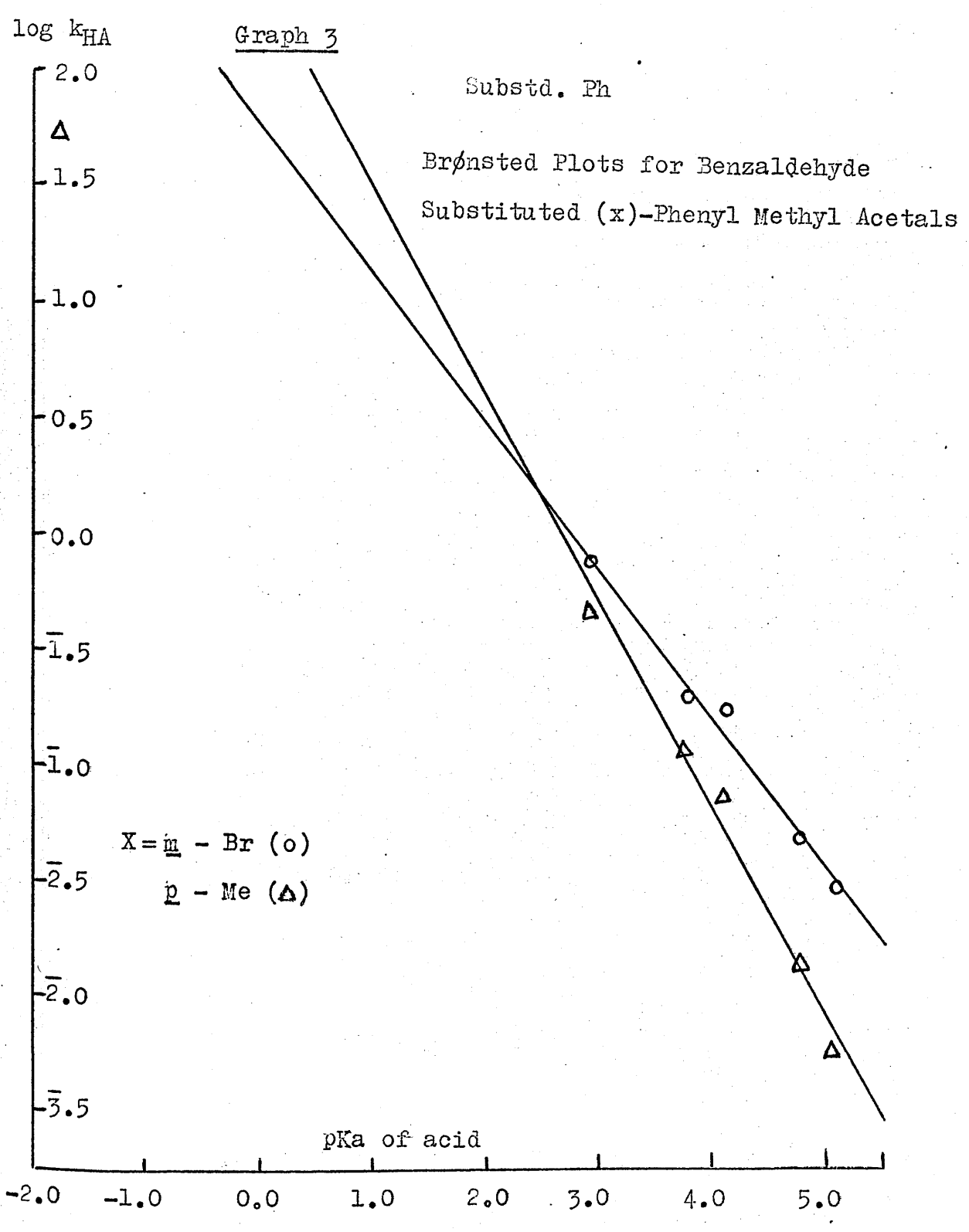
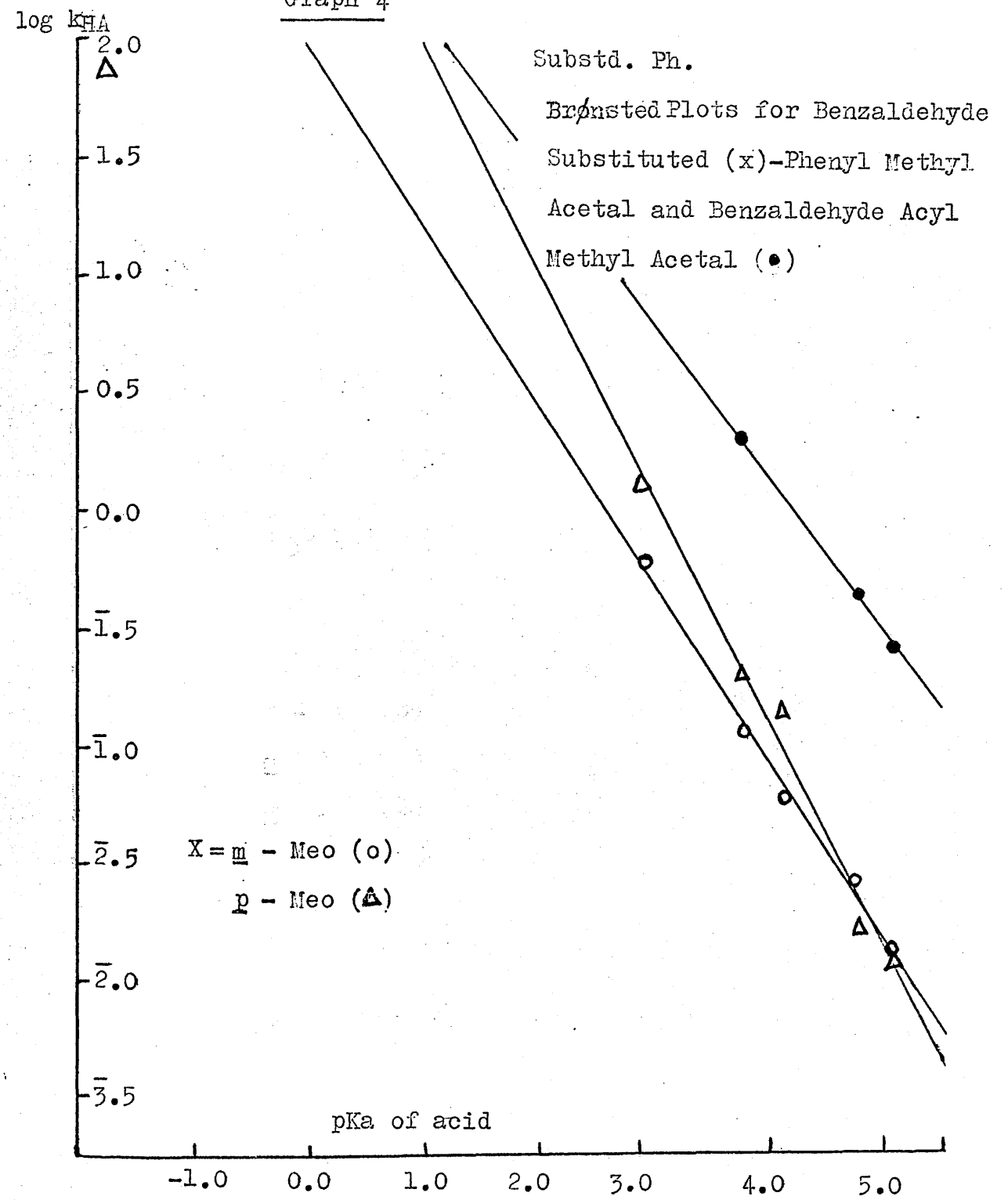
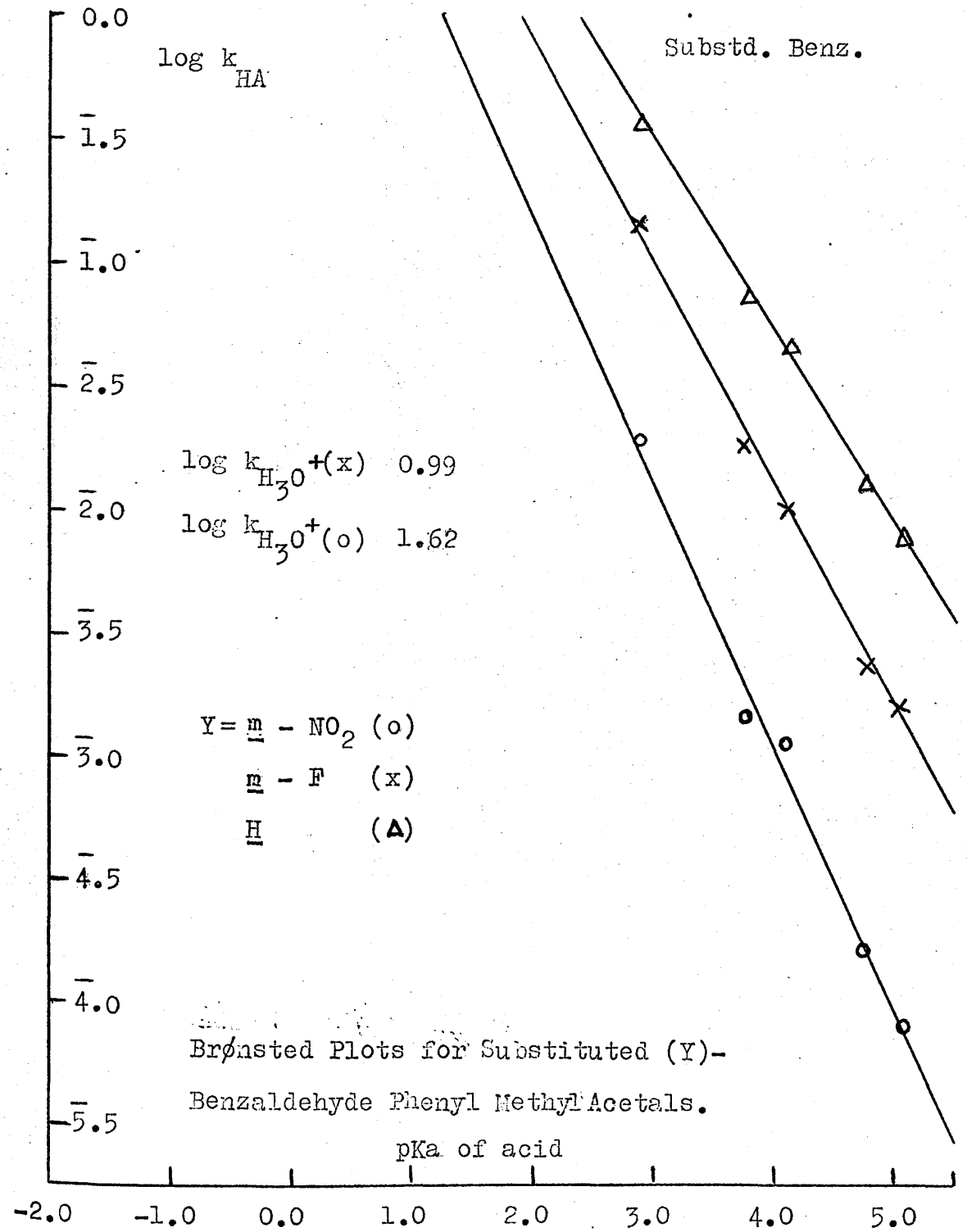
1.5
1.0
0.5
0.0
$\bar{1}.5$
$\bar{1}.0$
$\bar{2}.5$
$\bar{2}.0$
$\bar{3}.5$
Substd. Ph
X = m-NO_2 (o)
m-F (Δ)
Brønsted Plots for Benzaldehyde Substituted (X)-Phenyl Methyl Acetals
pKa of acid
-2.0
-1.0
0.0
1.0
2.0
3.0
4.0
5.0


log k_{HA}
Graph 3
Substd. Ph
Brønsted Plots for Benzaldehyde
Substituted (x)-Phenyl Methyl Acetals
2.0
1.5
1.0
0.5
0.0
$\bar{1}.5$
$\bar{1}.0$
$\bar{2}.5$
$\bar{2}.0$
$\bar{3}.5$
X = m - Br (o)
p - Me (Δ)
pKa of acid
-2.0
-1.0
0.0
1.0
2.0
3.0
4.0
5.0

Graph 4

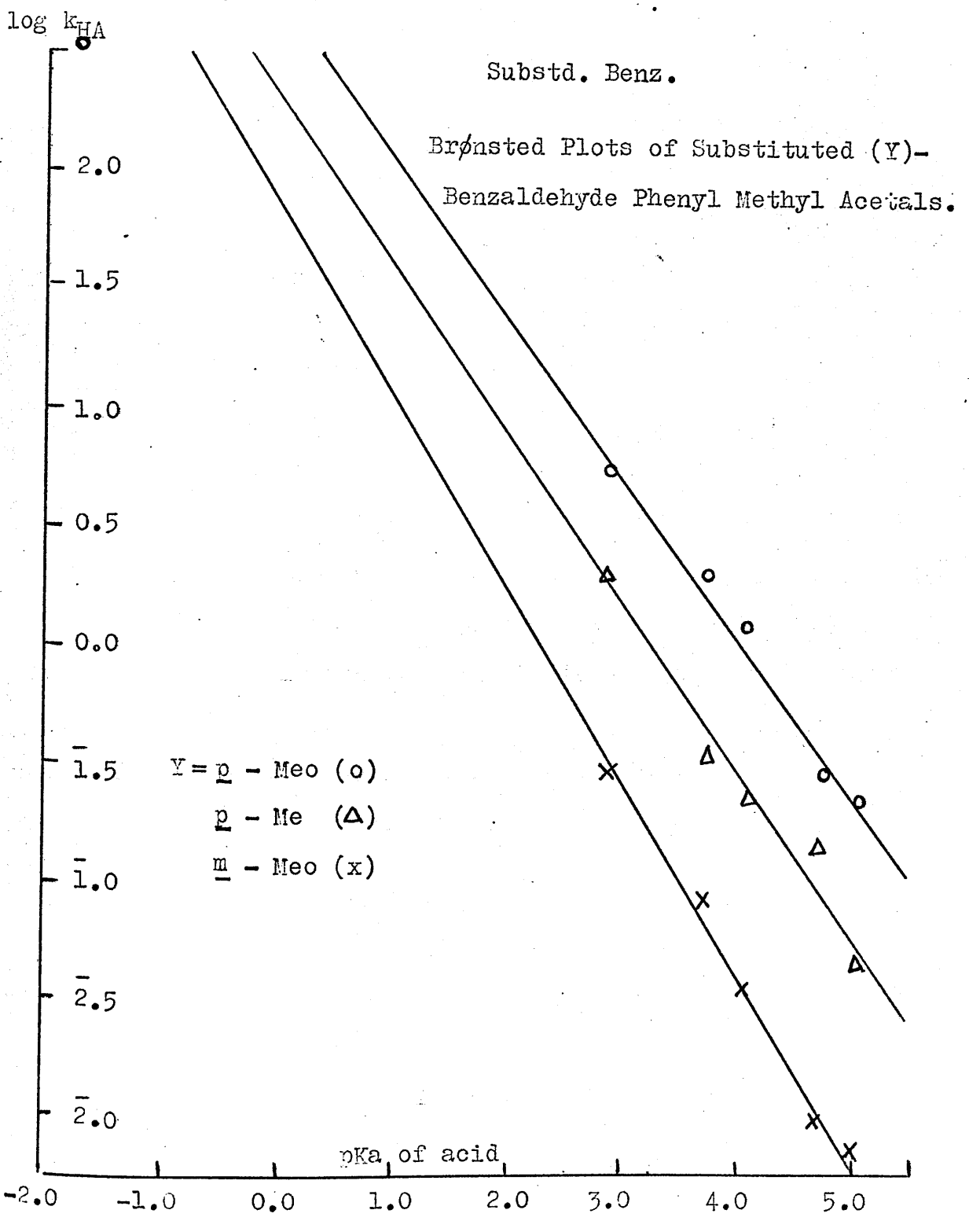

log k_{HA}
2.0
1.5
1.0
0.5
0.0
$\bar{1}.5$
$\bar{1}.0$
$\bar{2}.5$
$\bar{2}.0$
$\bar{3}.5$
Substd. Ph.
Brønsted Plots for Benzaldehyde Substituted (x)-Phenyl Methyl Acetal and Benzaldehyde Acyl Methyl Acetal (●)
X = m - Meo (o)
p - Meo (Δ)
pKa of acid
-1.0
0.0
1.0
2.0
3.0
4.0
5.0

Graph 5



Brønsted Plots for Substituted (Y)-Benzaldehyde Phenyl Methyl Acetals.

Graph 6


log k_{HA}
Substd. Benz.
Brønsted Plots of Substituted (Y)-
Benzaldehyde Phenyl Methyl Acetals.
2.0
1.5
1.0
0.5
0.0
$\bar{1}$.5
$\bar{1}$.0
$\bar{2}$.5
$\bar{2}$.0
Y = p - Meo (o)
p - Me (Δ)
m - Meo (x)
pKa of acid
-2.0
-1.0
0.0
1.0
2.0
3.0
4.0
5.0

Hammett Plots

The following tables indicate the dependence of the observed catalytic coefficients (k_{HA} for the general acid catalysed hydrolysis of mixed aryl alkyl acetals) on the substituent constant (σ) of the substrate, according to the Hammett Equation.[126]

$$\log k_{HA} = \rho\sigma + \log k_{HA}\,(o)$$

The following values ofσ are used.[155]

m - NO_2	0.710	H	0.000
m - Br	0.391	p - Me	-0.170
m - F	0.337	p - MeO	-0.268
m - MeO	0.115		

The values of k_{HA} corresponding to the hydrolysis of p-Me-, and p-MeO- substituted-phenyl, and p-MeO- substituted-benzaldehyde acetals are omitted from the calculations because of their consistently large positive deviations from the slopes (ρ)

abbreviations: C.C. = correlation coefficient

S.d. = standard deviation

TABLE 121

The Chloroacetic Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{1}$.9281	$\bar{1}$.9588	$+3.0654 \times 10^{-2}$
0.391	$\bar{1}$.8862	$\bar{1}$.8213	-6.4913×10^{-2}
0.337	$\bar{1}$.7599	$\bar{1}$.7980	$+3.8117 \times 10^{-2}$
0.115	$\bar{1}$.7826	$\bar{1}$.7023	-8.0250×10^{-2}
0.000	$\bar{1}$.5764	$\bar{1}$.6528	$+7.6393 \times 10^{-2}$

ρ = 0.431 C.C. = 8.65×10^{-1}

S.d. = 0.145 (33.5%)

TABLE 122

The Formic Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{1}$.3754	$\bar{1}$.3804	$+4.9979 \times 10^{-3}$
0.391	$\bar{1}$.2902	$\bar{1}$.1677	-1.2248×10^{-1}
0.337	$\bar{2}$.9749	$\bar{1}$.1317	$+1.5632 \times 10^{-1}$
0.115	$\bar{1}$.0577	$\bar{2}$.9337	-7.3986×10^{-2}
0.000	$\bar{2}$.8724	$\bar{2}$.9070	$+3.4645 \times 10^{-2}$

ρ = 0.667 C.C. = 8.62×10^{-1}

S.d. = 0.226 (33.9%)

TABLE 123

The β-Chloropropionic Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals.

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{1}$.3634	$\bar{1}$.3962	$+3.2751 \times 10^{-2}$
0.391	$\bar{1}$.2420	$\bar{1}$.0732	-1.6884×10^{-1}
0.337	$\bar{2}$.9014	$\bar{1}$.0185	$+1.1709 \times 10^{-1}$
0.115	$\bar{2}$.7650	$\bar{2}$.7937	$+2.8716 \times 10^{-2}$
0.000	$\bar{2}$.6870	$\bar{2}$.6773	-9.7211×10^{-3}

ρ = 1.012 C.C. = 9.34×10^{-1}

S.d. = 0.221 (21.84%)

TABLE 124

The Acetic Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	2.9469	2.9413	-5.5791×10^{-3}
0.391	2.6741	2.5935	-8.0645×10^{-2}
0.337	2.3901	2.5346	$+1.4447 \times 10^{-1}$
0.115	2.4072	2.2925	-1.1472×10^{-1}
0.000	2.1106	2.1671	$+5.6474 \times 10^{-2}$

ρ = 1.090 C.C. = 9.44×10^{-1}

S.d. = 0.219 (20.17%)

TABLE 125

The Pivalic Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{2}$.8450	$\bar{2}$.8413	-3.7099×10^{-3}
0.391	$\bar{2}$.4608	$\bar{2}$.4441	-1.6679×10^{-2}
0.337	$\bar{2}$.3058	$\bar{2}$.3769	$+7.1089 \times 10^{-2}$
0.115	$\bar{2}$.2292	$\bar{2}$.1005	-1.2871×10^{-1}
0.000	$\bar{3}$.8793	$\bar{3}$.9573	$+7.8010 \times 10^{-2}$

$\rho = 1.245$ C.C. = 9.71×10^{-1}

S.d. = 0.176 (14.13%)

TABLE 126

The Chloroacetic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{2}.2940$	$\bar{2}.2825$	-1.1501×10^{-2}
0.337	$\bar{1}.1631$	$\bar{1}.0738$	-8.9309×10^{-2}
0.115	$\bar{1}.4770$	$\bar{1}.5447$	$+6.7747 \times 10^{-2}$
0.000	$\bar{1}.5764$	$\bar{1}.7887$	$+2.1231 \times 10^{-1}$
-0.170	0.3286	0.1494	-1.7925×10^{-1}

$\rho = -2.121$

C.C. = 9.79×10^{-1}

S.d. = 0.254 (11.99%)

TABLE 127

The Formic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{3}.1690$	$\bar{3}.2148$	$+4.5328 \times 10^{-2}$
0.337	$\bar{2}.2541$	$\bar{2}.1950$	-5.9125×10^{-2}
0.115	$\bar{2}.9388$	$\bar{2}.7783$	-1.6047×10^{-1}
0.000	$\bar{2}.8724$	$\bar{1}.0805$	$+2.0812 \times 10^{-1}$
-0.170	$\bar{1}.5616$	$\bar{1}.5272$	-3.4360×10^{-2}

$\rho = -2.628$

C.C. = 9.88×10^{-1}

S.d. = 0.234 (8.89%)

TABLE 128

The β-Chloropropionic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals.

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{3}.0434$	$\bar{3}.0287$	-1.4671×10^{-2}
0.337	$\bar{3}.9920$	$\bar{3}.9786$	-1.3367×10^{-2}
0.115	$\bar{2}.5643$	$\bar{2}.5440$	-2.0309×10^{-2}
0.000	$\bar{2}.6870$	$\bar{2}.8369$	$+1.4986 \times 10^{-1}$
-0.170	$\bar{1}.3713$	$\bar{1}.2698$	-1.0151×10^{-1}

$\rho = -2.547$ C.C. = 9.94×10^{-1}

S.d. = 0.155 (6.10%)

TABLE 129

The Acetic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

σ	log k_{HA} obs	log k_{HA} calc	residual
0.710	$\bar{4}.4242$	$\bar{4}.3419$	-8.2307×10^{-2}
0.337	$\bar{3}.3395$	$\bar{3}.3899$	$+5.0385 \times 10^{-2}$
0.115	$\bar{3}.9840$	$\bar{2}.0136$	$+2.9623 \times 10^{-2}$
0.000	$\bar{2}.1106$	$\bar{2}.3367$	$+2.2613 \times 10^{-1}$
-0.170	$\bar{1}.0382$	$\bar{2}.8144$	-2.2383×10^{-1}

$\rho = -2.809$ C.C. = 9.85×10^{-1}

S.d. = 0.083 (10.08%)

TABLE 130

The Pivalic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

σ	log k obs HA	log k calc HA	residual
0.710	$\bar{5}$.8685	$\bar{5}$.9367	$+6.8195 \times 10^{-2}$
0.337	$\bar{3}$.1939	$\bar{3}$.0696	-1.2432×10^{-1}
0.115	$\bar{3}$.8608	$\bar{3}$.7438	-1.1696×10^{-1}
0.000	$\bar{3}$.8793	$\bar{2}$.0931	$+2.1383 \times 10^{-1}$
-0.170	$\bar{2}$.6502	$\bar{2}$.6095	-4.0746×10^{-2}

ρ = -3.037

C.C. = 9.91×10^{-1}

S.d. = 0.242 (7.96%)

Legend for Graphs 7, 8 and 10.

Hydrolysis by:

Chloroacetic Acid .....O

Formic Acid X

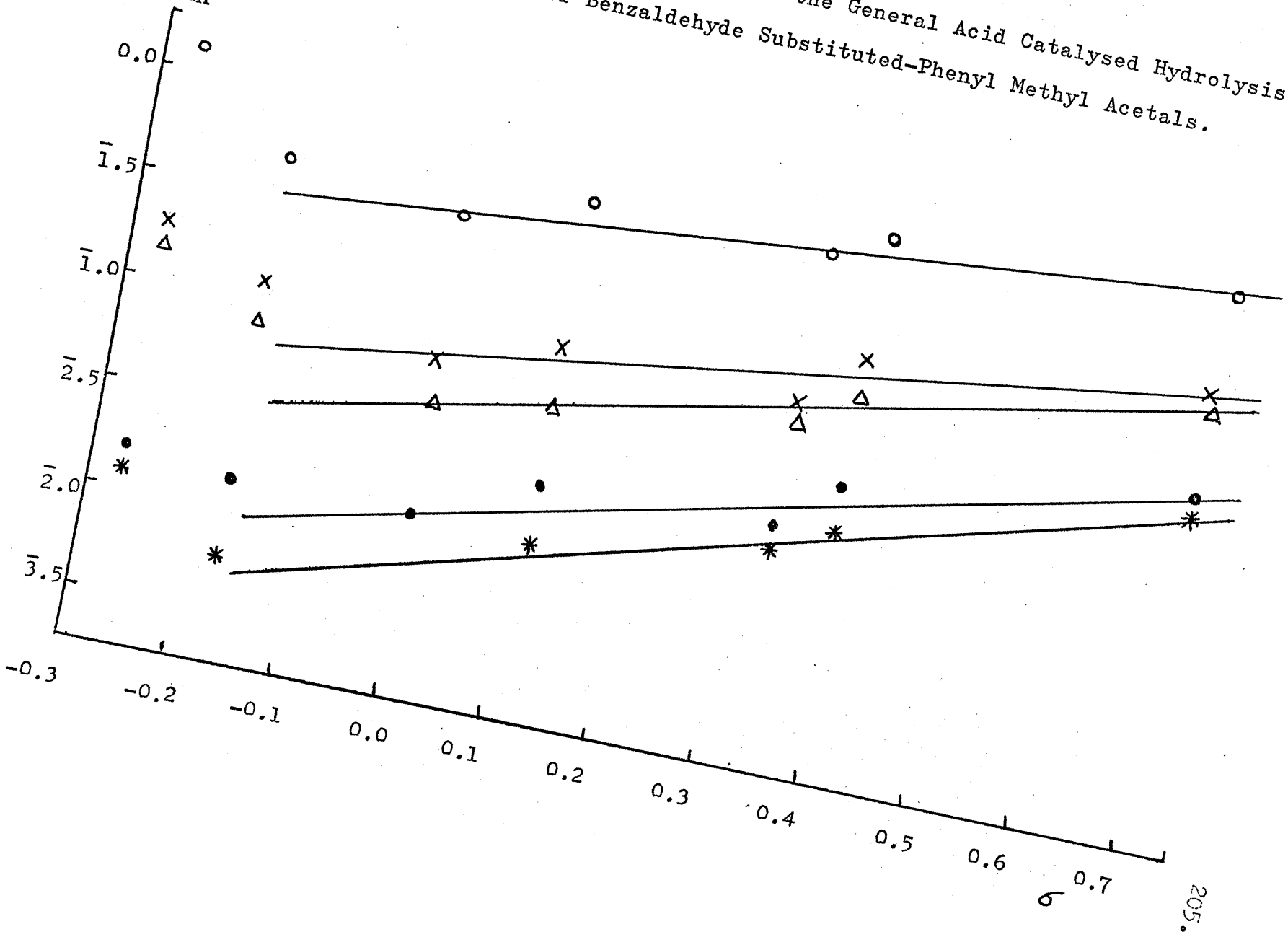
β-Chloropropionic Acid .....Δ

Acetic Acid .....●

Pivalic Acid .....✳

Graph 7

Hammett Plots for the General Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals.



Graph 8 Hammett Plots for the General Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals.

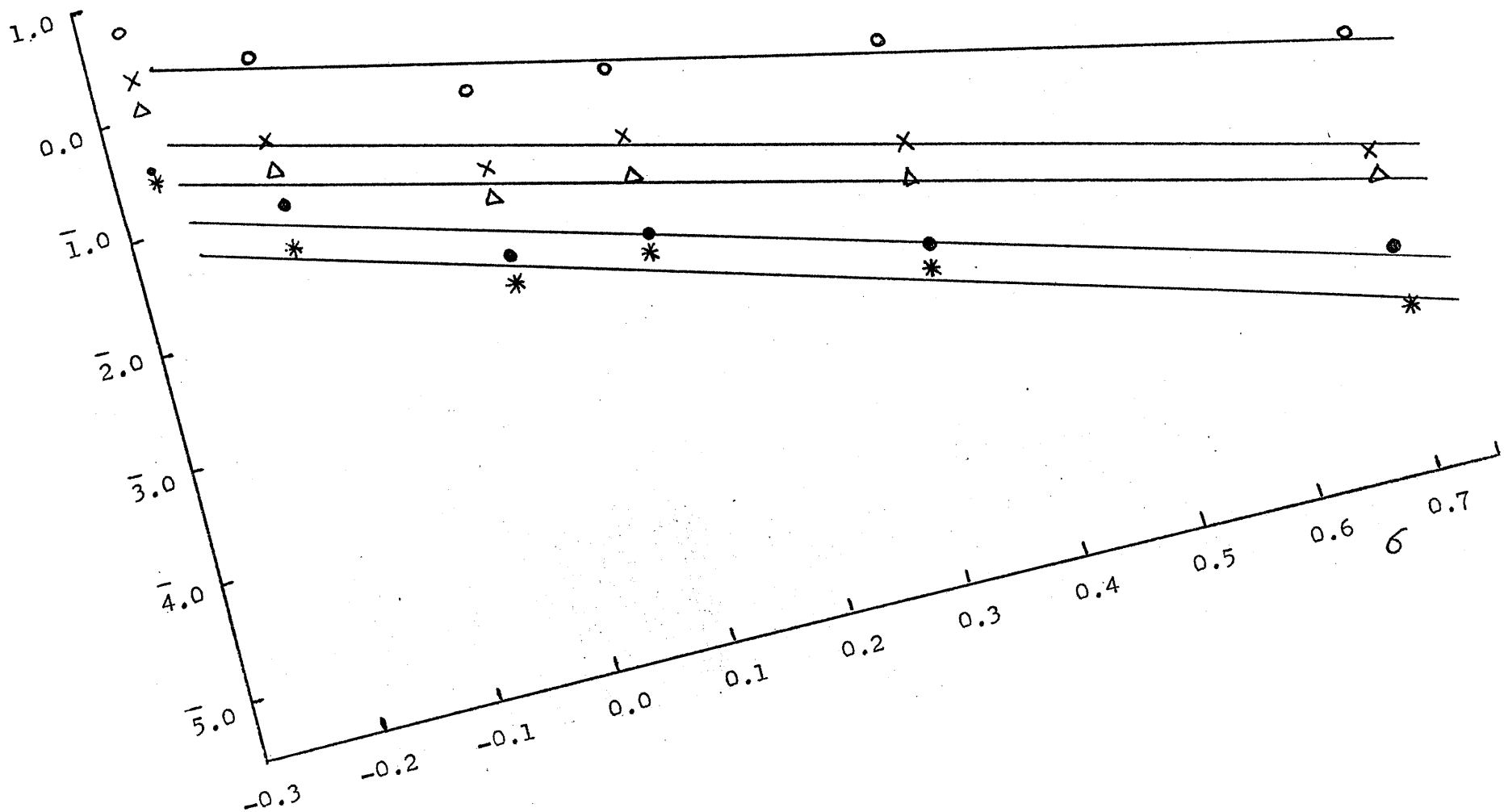


TABLE 131

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetal (0.001 M HCl)

σ	log k obs	log k_{HA} calc	residual
0.710	$\bar{2}$.3094	$\bar{2}$.2858	-2.3581×10^{-2}
0.337	$\bar{2}$.3941	$\bar{2}$.4438	$+4.9682 \times 10^{-2}$
0.000	$\bar{2}$.6126	$\bar{2}$.5865	-2.6101×10^{-2}

ρ = -0.423 C.C. = 9.61×10^{-1}

S.d. = 0.12 (28.62%)

When Hammett plot is inclusive of p- Me and p-MeO substituted compounds (see graph 9)

ρ = -0.602 C.C. = 9.55×10^{-1}

S.d. = 0.108 (17.97%)

TABLE 132

The Hydrochloric Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetal (0.001 M HCl)

σ	log k obs	log k calc	residual
0.710	$\bar{3}$.1617	$\bar{3}$.1162	-4.5503×10^{-2}
0.337	$\bar{3}$.9503	$\bar{3}$.9620	$+1.1743 \times 10^{-2}$
0.000	$\bar{2}$.6126	$\bar{2}$.7263	$+1.1367 \times 10^{-1}$
-0.170	$\bar{1}$.0410	$\bar{1}$.1118	$+7.0773 \times 10^{-2}$
-0.263	$\bar{1}$.4347	$\bar{1}$.3340	-1.5069×10^{-1}

ρ = -2.263 C.C. = 9.94×10^{-1}

S.d. = 0.149 (6.57%)

Graph 9

Hammett Plots for the Hydronium Ion Catalysed Hydrolysis (0.001M HCl) of Aromatic Aryl Methyl Acetals.

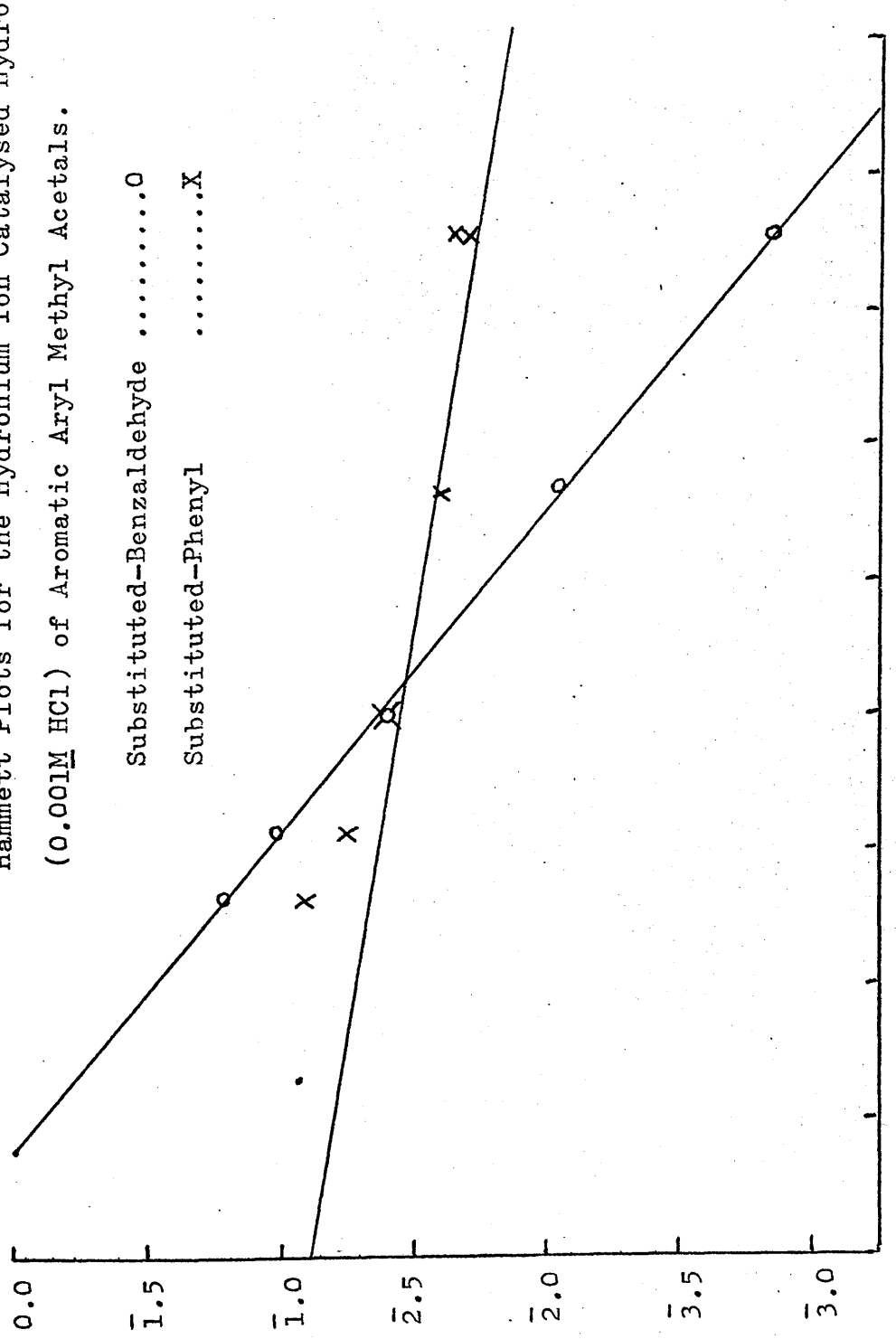


TABLE 134

Catalytic Coefficients, Bronsted α, and Hammett ρ^a, values for Substituted(X)-Phenyl Methyl Acetals.

	Chloro-acetic A	Formic A	β-Chloro-propionic A	Acetic A	Pivalic A	α
X=m-NO_2	8.474×10^{-1}	2.374×10^{-1}	2.309×10^{-1}	8.849×10^{-2}	6.998×10^{-2}	0.493
m-Br	7.695×10^{-1}	2.168×10^{-1}	1.746×10^{-1}	4.722×10^{-2}	2.889×10^{-2}	0.647
m-F	5.752×10^{-1}	9.439×10^{-2}	7.969×10^{-2}	2.455×10^{-2}	2.022×10^{-2}	0.668
m-Meo	6.062×10^{-1}	1.142×10^{-1}	5.822×10^{-2}	2.554×10^{-2}	1.695×10^{-2}	0.708
H	3.771×10^{-1}	7.453×10^{-2}	4.865×10^{-2}	1.290×10^{-2}	7.573×10^{-3}	0.776
p-Me	4.755×10^{-1}	1.208×10^{-1}	7.521×10^{-2}	1.322×10^{-2}	5.493×10^{-3}	0.885
p-Meo	1.291×10^{0}	1.989×10^{-1}	1.422×10^{-1}	1.648×10^{-2}	1.229×10^{-2}	0.960
ρ	+0.431	+0.667	+1.012	+1.090	+1.245	

a: calculated from m-NO_2, m-Br, m-F, m-Meo, and H only

TABLE 135

Catalytic Coefficients, Brønsted α, and Hammett ρ^a values for Substituted (Y) - Benzaldehyde Phenyl Methyl Acetals

	Chloro-acetic A	Formic A	β-Chloro-propionic A	Acetic A	Pivalic A	α
Y=m-NO_2	1.968×10^{-2}	1.476×10^{-3}	1.105×10^{-3}	2.656×10^{-4}	7.387×10^{-5}	1.046
m-F	1.456×10^{-1}	1.994×10^{-2}	9.816×10^{-3}	2.185×10^{-3}	1.563×10^{-3}	0.916
m-Meo	2.999×10^{-1}	8.685×10^{-2}	3.667×10^{-2}	9.638×10^{-3}	7.259×10^{-3}	0.776
H	3.771×10^{-1}	7.453×10^{-2}	4.865×10^{-2}	1.290×10^{-2}	7.573×10^{-3}	0.776
p-Me	2.131×10^{0}	3.644×10^{-1}	2.351×10^{-1}	1.092×10^{-1}	4.469×10^{-2}	0.692
p-Meo	5.849×10^{0}	2.112×10^{0}	1.232×10^{0}	2.814×10^{-1}	2.342×10^{-1}	0.679
ρ	-2.121	-2.628	-2.547	-2.809	-3.037	

a: calculated from m-NO_2, m-F, m-Meo, H, and p-Me only

TABLE 136

k_{int} values for Benzaldehyde Substituted (X)-Phenyl Methyl Acetals

	Chloro-acetic A	Formic A	β-Chloro-Propionic A	Acetic A	Pivalic A
X=m-NO_2	1.671×10^{-2}	5.047×10^{-3}	4.1075×10^{-3}	1.269×10^{-3}	1.311×10^{-3}
m-Br	2.014×10^{-2}	4.296×10^{-3}	4.051×10^{-3}	5.507×10^{-4}	4.099×10^{-4}
m-F	1.552×10^{-2}	5.732×10^{-3}	3.444×10^{-3}	5.708×10^{-4}	3.530×10^{-4}
m-Meo	3.064×10^{-2}	1.065×10^{-2}	4.641×10^{-3}	9.522×10^{-4}	5.476×10^{-4}
H	3.494×10^{-2}	1.019×10^{-2}	6.384×10^{-3}	1.026×10^{-3}	6.063×10^{-4}
p-Me	5.200×10^{-2}	1.263×10^{-2}	7.549×10^{-3}	1.201×10^{-3}	7.805×10^{-4}
p-Meo	5.752×10^{-2}	1.971×10^{-2}	1.823×10^{-2}	1.808×10^{-3}	9.693×10^{-4}

TABLE 137

k_{int} values for Substituted (Y)-Benzaldehyde Phenyl Methyl Acetals

	Chloro-acetic A	Formic A	β-Chloro-propionic A	Acetic A	Pivalic A
Y=m-NO_2	1.428×10^{-3}	4.068×10^{-4}	1.651×10^{-4}	3.732×10^{-5}	2.077×10^{-5}
m-F	7.229×10^{-3}	2.193×10^{-3}	1.016×10^{-3}	2.067×10^{-4}	1.146×10^{-4}
m-Meo	2.834×10^{-2}	7.892×10^{-3}	3.561×10^{-3}	7.600×10^{-4}	3.686×10^{-4}
H	3.494×10^{-2}	1.019×10^{-2}	6.384×10^{-3}	1.026×10^{-3}	6.063×10^{-4}
p-Me	7.914×10^{-2}	3.367×10^{-2}	2.549×10^{-2}	1.109×10^{-3}	1.428×10^{-3}
p-Meo	2.023×10^{-1}	6.102×10^{-2}	5.135×10^{-2}	8.830×10^{-3}	6.186×10^{-3}

TABLE 138

Primary Detuerium Isotope Effects for Benzaldehyde Substituted (X)-Phenyl Methyl Acetals, Benzaldehyde Acylal Methyl Acetal, and Benzaldehyde Dimethyl Acetal.

	k_{AcOH}/k_{AcOD}	$\frac{ko(AcOH)^c}{ko(AcOD)}$	k_{HCL}/k_{DCL} [a]	k_{HCL}/k_{DCL} [b]
X=m-NO_2	0.697	0.460	0.947	1.096
m-Br	0.975	0.499		
m-F	0.649	0.422	0.724	0.866
m-Meo	1.960	0.668		
H	1.283	0.779	0.565	0.690
p-Me	0.650	0.336	0.561	0.649
p-Meo	1.529	0.646	0.5819	0.623
Acylal	3.038	2.595		
Dimethyl			0.292	0.326

a: Catalytic coefficients from slopes of k_{obs} vs. [HCl] and [DCl]

b: k_{obs} values taken at [HCl] and [DCl] = 0.001 M

c: values corrected for acid concentration i.e. $k_o = k_{int}/a_{H_3O^+}$ or $a_{D_3O^+}$

TABLE 139

Primary Deuterium Isotope Effects for Substituted (Y) -Benzaldehyde Phenyl Methyl Acetals.

	k_{AcOH}/k_{AcOD}	$\frac{ko(AcOH)}{ko(AcOD)}$ [d]	k_{HCl}/k_{DCl} [a]	k_{HCl}/k_{DCl} [b]
Y=m-NO_2	1.060	0.348		
m-F			0.627	0.661
m-Meo	1.112	0.093		
H	1.283	0.779	0.565	0.690
p-Me	3.513	0.374		0.970[c]
p-Meo	2.199	0.667	0.802	0.825

a: catalytic coefficients from slopes of k_{obs} vs [HCl] and [DCl]

b: k_{obs} values taken at [HCl] and [DCl] at 0.001 M

c: value relatively uncertain since it was not done for other values of [HCl] and [DCl]

d: values corrected for acid concentration i.e. $k_o = k_{int}/a_{H_3O^+}$ or $a_{D_3O^+}$

TABLE 140

Log $(k_{int}/a_{H_3O^+})$ for Benzaldehyde Substituted (X) - Phenyl Methyl Acetals.

	Chloro-acetic A.	Formic A.	β-Chloro-propionic A.	Acetic A.	Pivalic A.	Deutero-acetic A.
X=m-NO_2	1.3230	1.2680	1.6136	1.7785	2.0276	2.1156
m-Br	1.4040	1.1981	1.6076	1.4159	1.5229	1.7180
m-F	1.2909	1.3234	1.5371	1.4315	1.4578	1.8059
m-MeO	1.5863	1.5923	1.6666	1.6537	1.6485	1.8290
H	1.6433	1.5731	1.8051	1.6862	1.6927	1.7946
p-Me	1.8160	1.6664	1.8779	1.7545	1.8024	2.2289
p-MeO	1.8599	1.8597	2.2608	1.9322	1.8964	2.1220

TABLE 141

Log ($k_{int}/a_{H_3O^+}$) for Substituted (Y) - Benzaldehyde Phenyl Methyl Acetals.

	Chloro-acetic A.	Formic A.	β-Chloro-propionic A.	Acetic A.	Pivalic A.	Deutero-acetic A.
Y=m-NO_2	0.2548	0.1744	0.2178	0.2469	0.2275	0.7051
m-F	0.9588	0.9060	1.0069	0.9904	0.9692	
m-MeO	1.5524	1.4622	1.5515	1.5558	1.4765	
H	1.6433	1.5731	1.8051	1.6862	1.6927	1.7946
p-Me	1.9984	2.0922	2.4063	1.7199	2.0648	2.1477
p-MeO	2.4060	2.3504	2.7105	2.6210	2.7014	2.7967

Yukawa-Tsuno L.F.E.R.

The following tables indicate the dependence of k_{HA}, for the general acid catalysed hydrolysis of substituted-benzaldehyde phenyl methyl acetals, on the compound substituent constant $[\sigma + r(\sigma^+ - \sigma)]$ of the substrate, according to the Yukawa-Tsuno L.F.E.R.[127]

$$\log k/k_o = \rho[\sigma + r(\sigma^+ - \sigma)]$$

The values for σ are those described earlier,[155] and the following values of σ^+ were used:[166]

m - NO_2	0.662	H	0.000
m - F	0.337	p-Me	-0.306
m - MeO	0.047	p-MeO	-0.764

The value of 0.50 has been used for r in the above equation, resulting in the following $[\sigma + 0.5\ (\sigma^+ - \sigma)]$ constants:

m - NO_2	0.686	H	0.000
m - F	0.337	p-Me	-0.236
m - MeO	0.031	p-MeO	-0.516

TABLE 142

The Chloroacetic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

$[\sigma + 0.5 (\sigma^+ - \sigma)]$	log k_{HA} obs	log k_{HA} calc	residual
0.686	$\bar{2}.2940$	$\bar{2}.3076$	$+1.3632 \times 10^{-2}$
0.337	$\bar{1}.1631$	$\bar{1}.0381$	-1.2501×10^{-1}
0.081	$\bar{1}.4770$	$\bar{1}.5590$	$+8.1983 \times 10^{-2}$
0.000	$\bar{1}.5764$	$\bar{1}.7238$	$+1.4739 \times 10^{-1}$
-0.236	0.3286	0.2040	-1.2461×10^{-1}
-0.516	0.7671	0.7737	$+6.6035 \times 10^{-3}$

$\rho = -2.035$ C.C. $= 9.92 \times 10^{-1}$

S.d. $= 0.129$ (6.32%)

TABLE 143

The Formic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

$[\sigma + 0.5 (\sigma^+ - \sigma)]$	log k_{HA} obs	log k_{HA} calc	residual
0.686	$\bar{3}.1690$	$\bar{3}.2522$	$+8.3177 \times 10^{-2}$
0.337	$\bar{2}.2541$	$\bar{2}.1430$	-1.1111×10^{-1}
0.081	$\bar{2}.9388$	$\bar{2}.7964$	-1.4237×10^{-1}
0.000	$\bar{2}.3724$	$\bar{1}.0032$	$+1.3073 \times 10^{-1}$
-0.236	$\bar{1}.5616$	$\bar{1}.6056$	$+4.3964 \times 10^{-2}$
-0.516	0.3247	0.3203	-4.4409×10^{-3}

$\rho = -2.552$ C.C. $= 9.95 \times 10^{-1}$

S.d. $= 0.128$ (5.02%)

TABLE 144

The β-Chloropropionic Acid Catalysed Hydrolysis of Substituted Benzaldehyde Phenyl Methyl Acetals

$[\sigma + 0.5(\sigma^+ - \sigma)]$	log k_{HA}obs	log k_{HA}calc	residuals
0.686	$\bar{3}$.0434	$\bar{3}$.0526	$+9.2067 \times 10^{-3}$
0.337	$\bar{3}$.9920	$\bar{3}$.9272	-6.4764×10^{-2}
0.081	$\bar{2}$.5643	$\bar{2}$.5638	$+4.4971 \times 10^{-3}$
0.000	$\bar{2}$.6370	$\bar{2}$.7718	$+3.4791 \times 10^{-2}$
-0.236	$\bar{1}$.3713	$\bar{1}$.3632	-3.0692×10^{-3}
-0.516	0.0906	0.0649	-2.5661×10^{-2}

$\rho = -2.506$

C.C. = 9.99×10^{-1}

S.d. = 0.059 (2.33%)

TABLE 145

The Acetic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

$[\sigma + 0.5(\sigma^+ - \sigma)]$	log k_{HA}obs	log k_{HA}calc	residual
0.686	$\bar{4}$.4242	$\bar{4}$.4274	$+3.2435 \times 10^{-3}$
0.337	$\bar{3}$.3395	$\bar{3}$.3344	-5.1443×10^{-3}
0.081	$\bar{3}$.9340	$\bar{3}$.9996	$+1.5593 \times 10^{-2}$
0.000	$\bar{2}$.1106	$\bar{2}$.2101	$+9.9435 \times 10^{-2}$
-0.236	$\bar{1}$.0332	$\bar{2}$.8234	-2.1435×10^{-1}
-0.516	$\bar{1}$.4493	$\bar{1}$.5510	$+1.0166 \times 10^{-1}$

$\rho = -2.599$

C.C. = 9.95×10^{-1}

S.d. = 0.137 (5.26%)

TABLE 146

The Pivalic Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals.

$[\sigma + 0.5\ (\sigma^{+}-\sigma)]$	log k_{HA} obs	log k_{HA} calc	residual
0.686	$\bar{5}.8685$	$\bar{4}.0201$	$+1.5153 \times 10^{-1}$
0.337	$\bar{3}.1939$	$\bar{3}.0124$	-1.8154×10^{-1}
0.081	$\bar{3}.8608$	$\bar{3}.7402$	-1.2058×10^{-1}
0.000	$\bar{3}.8793$	$\bar{3}.9705$	$+9.1218 \times 10^{-2}$
-0.236	$\bar{2}.6502$	$\bar{2}.6415$	-8.6831×10^{-3}
-0.516	$\bar{1}.3696$	$\bar{1}.4376$	$+6.8007 \times 10^{-2}$

$\rho = -2.843$

C.C. = 9.94×10^{-1}

S.d. = 0.153 (5.38%)

Graph 10

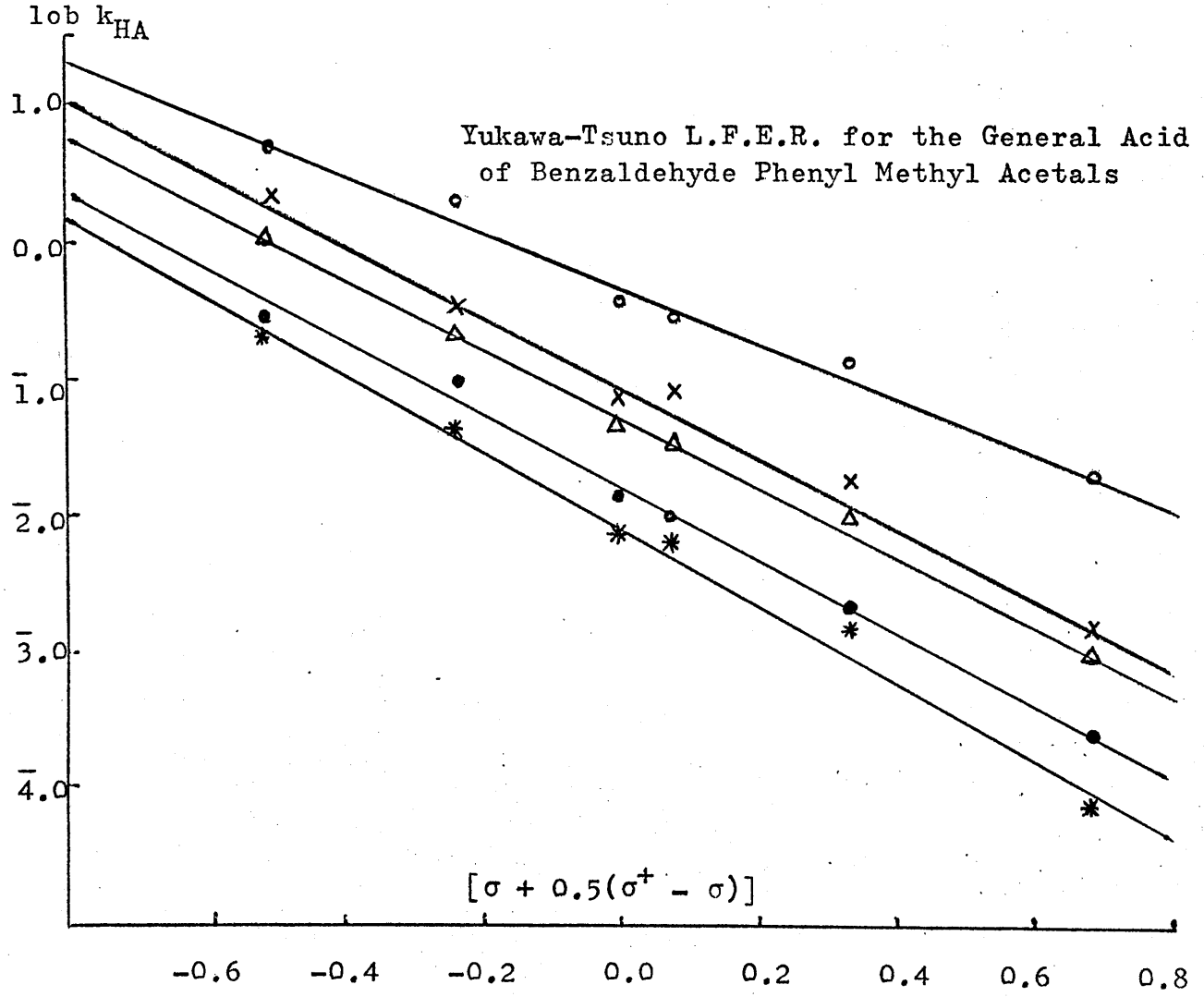

lob k_{HA}
1.0
0.0
$\bar{1}.0$
$\bar{2}.0$
$\bar{3}.0$
$\bar{4}.0$
Yukawa-Tsuno L.F.E.R. for the General Acid Catalysed Hydrolysis
of Benzaldehyde Phenyl Methyl Acetals
$[\sigma + 0.5(\sigma^+ - \sigma)]$
-0.6
-0.4
-0.2
0.0
0.2
0.4
0.6
0.8

TABLE 147

The Hydrochloric Acid Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals 0.001 M HCl

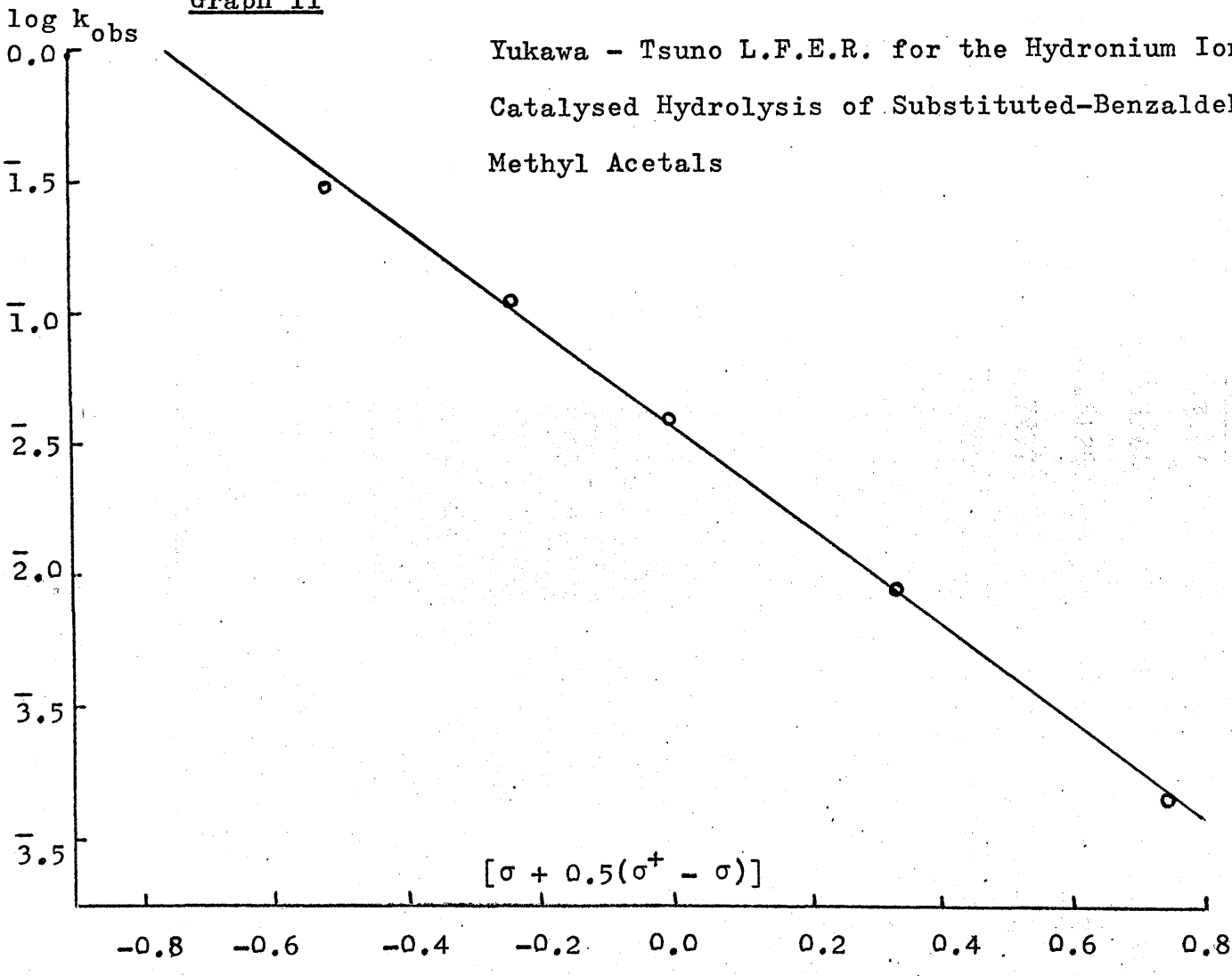
$[\sigma^+ + 0.5 (\sigma^+ - \sigma)]$	log k obs	log k calc	residual
0.686	$\bar{3}.1617$	$\bar{3}.2271$	$+6.5362 \times 10^{-2}$
0.337	$\bar{3}.9503$	$\bar{3}.9026$	-4.7666×10^{-2}
0.000	$\bar{2}.6126$	$\bar{2}.5550$	-5.7623×10^{-2}
-0.236	$\bar{1}.0410$	$\bar{1}.0118$	-2.9190×10^{-2}
-0.516	$\bar{1}.4847$	$\bar{1}.5538$	$+6.9116 \times 10^{-2}$

$\rho = -1.936$

C.C. $= 9.98 \times 10^{-1}$

S.d. $= 0.076$ (3.93%)

Graph 11



Yukawa - Tsuno L.F.E.R. for the Hydronium Ion Catalysed Hydrolysis of Substituted-Benzaldehyde Phenyl Methyl Acetals

TABLE 148

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals [0.001 M HCl]

$[\sigma + 0.5 (\sigma + - \sigma)]$	$\log k_{obs}$	$\log k_{calc}$	residual
0.686	$\bar{2}.3094$	$\bar{2}.2639$	-4.5498×10^{-2}
0.337	$\bar{2}.3941$	$\bar{2}.4487$	$+5.4575 \times 10^{-2}$
0.000	$\bar{2}.6126$	$\bar{2}.6271$	$+1.4495 \times 10^{-2}$
-0.236	$\bar{2}.7497$	$\bar{2}.7520$	$+2.3424 \times 10^{-3}$
-0.516	$\bar{2}.9262$	$\bar{2}.9003$	-2.5915×10^{-2}

ρ = -0.529

C.C. = 9.88×10^{-1}

S.d. = 0.047 (3.89%)

TABLE 149

The Hydrochloric Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals[0.001 M HCl].

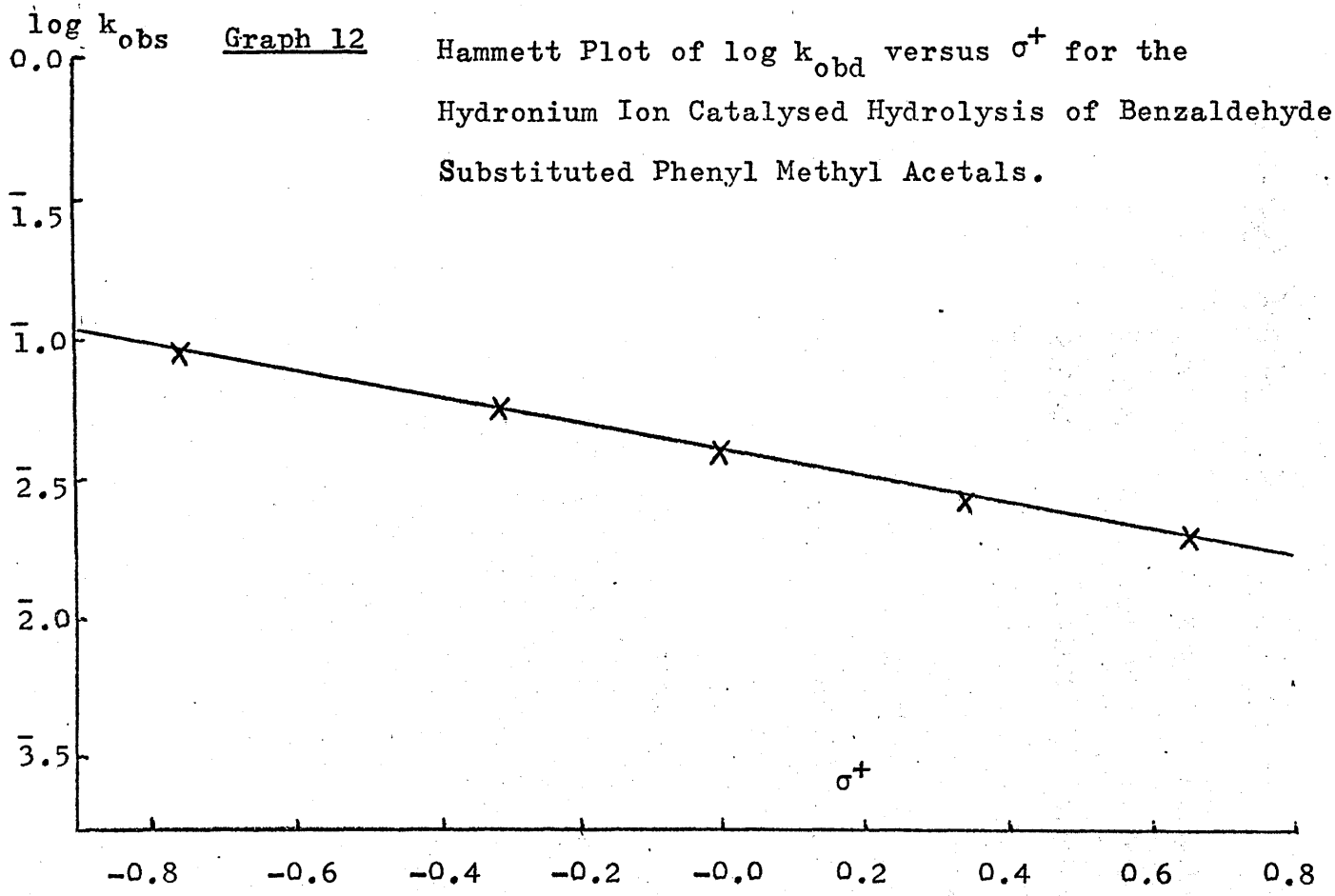
The σ^+ substituent constants used are those described earlier[166] for the equation:

$$\log k/k_o = \rho \sigma^+$$

σ^+	$\log k_{obs}$	$\log k_{calc}$	residual
0.662	$\bar{2}.3094$	$\bar{2}.2913$	-1.7626×10^{-2}
0.337	$\bar{2}.3941$	$\bar{2}.4391$	$+4.5047 \times 10^{-2}$
0.000	$\bar{2}.6126$	$\bar{2}.5920$	-2.0639×10^{-2}
-0.306	$\bar{2}.7497$	$\bar{2}.7307$	-1.3932×10^{-2}
-0.764	$\bar{2}.9262$	$\bar{2}.9384$	$+1.2200 \times 10^{-2}$

ρ = -0.453 C.C. = 9.94×10^{-1}

S.d. = 0.029 (6.57%)



Graph 12

Hammett Plot of log k_{obd} versus σ^+ for the Hydronium Ion Catalysed Hydrolysis of Benzaldehyde Substituted Phenyl Methyl Acetals.

TABLE 150

log k_{HA} versus pKa of leaving group for the Formic Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl Acetals.

pKa (leaving group)	log k_{HA} obs	log k_{HA} calc.	residual
8.40	$\bar{1}$.3754	$\bar{1}$.3894	$+1.4012 \times 10^{-2}$
9.03	$\bar{1}$.2902	$\bar{1}$.1896	-1.006×10^{-1}
9.28	$\bar{2}$.9749	$\bar{1}$.1103	$+1.3541 \times 10^{-1}$
9.65	$\bar{1}$.0577	$\bar{2}$.9930	-6.4734×10^{-2}
9.98	$\bar{2}$.8724	$\bar{2}$.8883	$+1.5904 \times 10^{-2}$

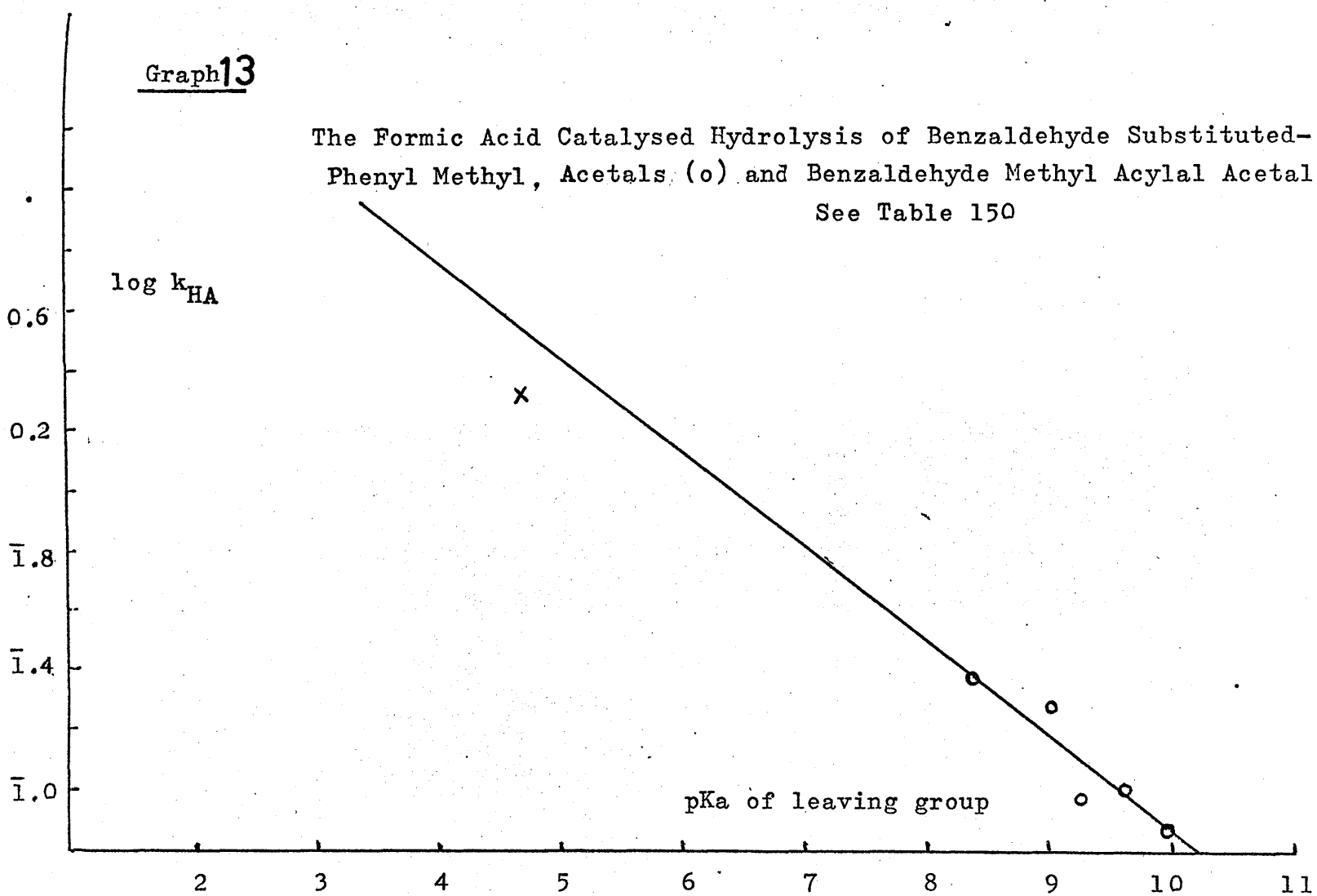
slope = -0.317

C.C. = 9.04

S.d. = 0.087 (27.38%)

Graph 13

The Formic Acid Catalysed Hydrolysis of Benzaldehyde Substituted-Phenyl Methyl, Acetals (o) and Benzaldehyde Methyl Acylal Acetal (x)
See Table 150



K I N E T I C E X P E R I M E N T A L

KINETIC EXPERIMENTAL

Solutions and Buffers

'AnalaR' grade chemicals were used in the preparation of all the buffered and other solutions. Pivalic acid was distilled and chloroacetic and β-chloropropionic acids were recrystallised from hot ligroin before use. Formic acid was standardised against 0.1N sodium hydroxide and found to be 89.95% pure.. The buffered solutions were prepared using standard B.D.H. carbonate-free sodium hydroxide solution for neutralisation, except for acetate buffers, where fused anhydrous sodium acetate was used. The solutions were all made up with degassed, deionised water, and for buffer catalysis the stock buffer solutions were diluted with stock potassium chloride at the same ionic strength. Diluted HCl and DCl solutions were also maintained at constant ionic strength by the addition of potassium chloride. These solutions, 0.001N to 0.0002N HCl and DCl, were titrated against standardised N/10 NaOH using a Radiometer Copenhagen Equipment, Type SBR2/SBU1/TTA3. All solutions contained 10^{-4} M E.D.T.A. which had no effect upon the observed rate constant but stabilised the products. All the stock solutions of acetals, and the aqueous dioxan buffers were prepared with Merck 'spectrograde' dioxan, which was stored in brown bottles

in a refrigerator.

pH Measurements

The pH of all buffer solutions was measured at the temperature of the kinetic experiment with either a Radiometer TTT1 titrator with expansion scale, or a Radiometer Model 26 pH Meter, with an external temperature compensator. A Radiometer type G202C glass electrode was used with a type K401 calomel electrode. The pH meter was standardised against commercial standard buffers complying to BS 1647, 1961.

Deuterated buffers

D_2O was obtained from Koch-Light, DCl and d_1-deuteroacetic acid from CIBA, and d_4-deuterated methanol from CIBA and Prochem. Fused anhydrous sodium acetate was used to prepare deuteroacetic acid buffers, and dried KCl used to adjust ionic strengths. The purity of the deuterated solutions were determined by adding a known quantity of pure dioxan and measuring the quantity of H_2O by n.m.r., which was always <1%.

Spectrophotometric rate determinations

Rate constants with $t_{1/2} < 15$ minutes were determined on a Zeiss PMQ II spectrophotometer, and those with $t_{1/2} > 15$ minutes on a Cary Model 14 spectrophotometer. A Unicam SP300 spectrophotometer was used only for preliminary determinations. The cell block of the Zeiss

PMQII was kept constant to $\pm 0.005C^{o}$ by an efficient electronic relay system. The Cary Model 14 was fitted with an automatic five cell compartment, and constant temperature maintained with a Lauda electronic thermostatting bath which kept both cell block and reference cell holder to $\pm 0.03C^{o}$. In each spectrophotometer the temperatures were always checked in the cell block with an N.P.L. calibrated thermometer before and after each run.

10 mm Spectrosil quartz U.V. cells were used, and 2.5 mls of the buffer were added about 30 minutes before commencement of the run to allow temperature equilibration. 25 µls of the stock dioxan solution of the substrate were injected into the buffer so that all reported rate constants for aqueous solutions relate to 1% dioxan. 40 mm thick-walled Spectrosil quartz U.V. cells were implemented when using Benzaldehyde m-Bromophenyl Methyl Acetal substrate since the solubility of this compound was considerably less than that of the others. A three cell thermostatted block was made in the Chemistry Department, University of Glasgow by Mr. A. Hislop to accommodate the 40 mm cells in the Zeiss PMQII cell compartment. After addition of the substrate to buffer, the cells were shaken and a nominal time lapse allowed, depending on the reaction rate, to allow the temperature to re-equilibrate.

The output from the spectrophotometers was fed to a Solartron Compact Data Logger which digitised the absorbance or transmittance readings and fed them on five-channel paper tape through a Creed punch at convenient time intervals. About three half lines were taken; with about thirty values contained in the first.

The first-order rate constants were determined from the equation

$$A[t] = A[\infty] - (A[\infty]-A[o]\ e^{-kt}),$$

where $A[\infty]$, $A[o]$ and k are adjustable parameters, using a generalised least-squares program, written by Dr. B. Capon, utilising the procedure of Wentworth[146] and Derming,[147] although laterally an adjustment was made to the standard deviation calculation procedure of the former. The slopes and intercepts of plots of k_{obs} against buffer concentration were also determined by a generalised least-squares procedure, and the Hammett and Brønsted plots by a linear least-squares procedure. Evaluation was performed on an English Electric KDF9 computer.

PREPARATIVE EXPERIMENTAL

PREPARATIVE EXPERIMENT

Nuclear Magnetic Resonance (N.M.R) spectra were obtained from a Varian T-60 60MHz spectrometer unless otherwise stated. The 100 MHz spectra were obtained from a Varian HA-100 spectrometer. Chemical shifts were measured downfield from internal T.M.S. and are quoted in Hz. The integration value of each peak is given in brackets.

Infrared (I.R.) spectra were performed either on a Unicam SP200, SP1000 or a Perkin-Elmer 257 Grating Infrared Spectrometer. The following abbreviations are used:

sh = sharp; st = strong; m = medium; w = weak;

def = deformation; str = stretch; skel = skeletal.

Gas Liquid Chromatographs (G.L.C) were obtained from a Pye Argon Chromatograph.

abbreviations: sens = sensitivity; F.R = argon gas flow-rate; C.S = chart speed; R_T = retention time.

Mass Spectral(M.S.) analysis were performed on an A.E.I. MS.12 Mass Spectrometer. Abbreviations: R.A = relative abundance; M/e = mass charge.

Elemental analysis were determined by Mr. J. Cameron of the University of Glasgow, except for fluorine-containing compounds which were determined by: Mikroanalytisches Laboratorium, Beller, Göttingen, W. Germany

Preparative Experimental

The preparation of the mixed aromatic methyl aryl acetals and S-Aryl Thioacetals cited in this work employed the general procedures described below. In most cases certain modifications were adopted and these will be described in detail in the appropriate parts of this section.

Preparation of Dialkyl Acetals by the "Trialkyl Orthoformate" method

$$Ar\ CHO + HC(OR)_3 \xrightarrow[H^+]{ROH} Ar\ CH(OR)_2 + HCO_2R$$

This procedure is described by Fife and Jao.[68]

Preparation of -Chloro Aryl Methyl Ethers.

$$Ar\ CH(OR)_2 \xrightarrow[\text{or } SOCl_2]{CH\ CO.Cl} Ar\ CH(OR)Cl + \begin{matrix} CH_3CO_2R \\ \text{or} \\ RCl^{-}SO_2 \end{matrix}$$

This procedure is described by Straus,[148] Anderson and Capon[94] and reviewed by Summers.[149]

Preparation of mixed Aromatic Methyl Aryl Acetals

$$Ar\ CH(OR)Cl \xrightarrow[DMF]{\bar{O}Ar} Ar\ CH(OMe)OAr$$

This procedure is described by Anderson and Capon.[94]

Preparation of mixed Aromatic Methyl S-Aryl Thioacetals.

$$Ar\ CH(OR)Cl \xrightarrow[DMF]{SAr} Ar\ CH(OMe)SAr'$$

This procedure is described by Fife and Anderson.[95]

An alternative route to the synthesis of dimethyl acetals is the method of Hassner, Wiederkehr and Kascheves,[150] and to the synthesis of α-methoxy carbonium ions by Davis and Williams.[151]

PREPARATION OF SUBSTITUTED BENZALDEHYDE DIMETHYL ACETALS

Equimolar quantities of substituted benzaldehyde and trimethyl orthoformate were mixed in an excess of absolute methanol. A drop of methane sulphonic acid was added as catalyst. The reaction mixture was then allowed to stand for 24 hours at room temperature, after which time anhydrous potassium carbonate was added to neutralise the acid. After suction filtration the solution was fractionally distilled to yield the desired dimethyl acetal.

Although commercially obtained aldehydes were used in the reactions they were rigorously tested for isomeric impurity, usually by G.L.C.

The following substituted benzaldehyde dimethyl acetals were synthesised by this procedure.

m-Nitrobenzaldehyde Dimethyl Acetal

B.Pt. 107-109°C (36 mm) Fluorescent yellow/green oil yield 80%.

N.M.R.($CDCl_3$): 202Hz, singlet (6)...methoxyl protons
329Hz, singlet (1)...acetal proton
428-503Hz. multiplet(4)..aromatic protons

I.R.(neat)νcm^{-1}: 3080 w(aromatic CH str); 2940 m(CH_3 str); 2830m.sh(acetal CH str); 1610 (aromatic C=C str); 1580w.sh(N=O str); 1400n 1520st (assymetric CH def); 1340st (symmetric CH_3def) 1105, 1070, 1050, 980 (acetal C-O-C-O-C str); 880, 835, 830m., 740, 715 st.sh. 670,(arometic skel)

T.L.C: Neutral alumina with tertiary solvent 20% ether; 40% benzene: 40% (40-60) Pet. Ether, R_f=0.45. Iodine stain.

U.V. The compound absorbed at 700 nanometers which indicated, as did the fluorescence, that the nitro group had been at least partially reduced to the nitroso.

Analysis: Theoretical: C- 54.82%; H- 5.62%; N- 7.10%.
Found: C- 54.75%; H- 5.59%; N- 6.86%.

m-Bromobenzaldehyde Dimethyl Acetal.

B.Pt. 128-132°C (760mm) Clear Oil.

Yield 76%.

N.M.R.($CDCl_3$): 200Hz.singlet(6)...methoxyl protons

322Hz,singlet(1)...acetal proton

424-462Hz,multiplet(4).aromatic protons

I.R.(Neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 m.sh.(CH_3str); 2820 m.sh(acetal CH str); 1590 w, 1570 m.sh (aromatic C=C str); 1470m (assymmetric CH_3def); 1350 st.sh.(symmetric CH_3def); 1105, 1090, 1060, 1005, 990 st (acetal C-O-C-O-C str); 880, 790, 730, 685, 665 (aromatic skel)

G.L.C. 1% OV-17 (100°C); sens x10; volts x1500; F.R.=44 mls/min; C.S=15 inch/hr; T_R=6.4mins.

T.L.C. Silica withbinary solvent 95% (60-80) Pet. Ether: 5% methanol; R_F=0.65. Iodine stain.

Analysis: Theoretical: C- 46.75%; H- 4.72%

Found: C- 46.03%; H- 4.39%

Although this compound did not analyse well there were no traces of aldehydic impurity.

m-Chlorobenzaldehyde Dimethyl Acetal.

B.Pt. 126-128°C (760 mm) Clear Oil

Yield 87.5%.

N.M.R. ($CDCl_3$): 200Hz, singlet (6)...methoxyl protons

321Hz, singlet (1)...acetal proton

434-450Hz, multiplet(4)..aromatic protons

I.R.(neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 m.(CH_3str); 2850 w(acetal CH str); 1600 st. 1580m.sh. (aromatic C=C str); 1480 m.sh(assymmetric CH_3def);1360 st.sh(symmetric CH_3def); 1110, 1090, 1070, 1060, 995 sh (acetal C-O-C-O-C str); 885m, 800, 750, 695 st.sh (aromatic skel)

G.L.C; 1% S.E.-30 (135°C); sens x 3; volts x1500; F.R.=60 mls/min; C.S.=12 inch/hr; T_R =6.5 mins.

T.L.C: Silica with binary solvent 95% (60-80) Pet. Ether: 5% methanol; R_F=70; Iodine stain.

m-Fluorobenaldehyde Dimethyl Acetal

B.Pt. 130-132°C (760 mm) Clear oil

Yield 84%

N.M.R. ($CDCl_3$): 200Hz, singlet (6)...methoxyl protons

323Hz, singlet (1)...acetal proton

410-460Hz, multiplet (4).aromatic protons

I.R.(near)νcm^{-1} 3050 w/aromatic CH str); 2950 m(CH_3str); 2850m.sh(acetal CH str); 1600, 1495st.sh (aromatic C=C str); 1460 st.sh(asymmetric CH_3def); 1360 m(symmetric CH_3def); 1140m, 1100, 1030, 1060 st, 1000 m.sh (acetal C-O-C-O-C str); 890, 830m, 790 st, 700 m, 680 w.sh(aromatic skel)

T.L.C. Silica with binary solvent 95% Pet. Ether (60-80), 5% methanol; R_F=0.60; Iodine stain

m-Anisaldehyde Dimethyl Acetal

B.Pt. 74-76 mm(0.2mm) Clear Oil

Yield 70%

N.M.R. ($CDCl_3$): 200 Hz, singlet (6)....acetalmethoxyl protons

228 Hz, singlet (3)....aromatic methoxyl protons

320 Hz, singlet (1)....acetal proton

403-424 Hz, multiplet (4)..aromatic protons

I.R.(neat)νcm^{-1}: 3050 w(aromatic CH str); 2940 st.(CH_3str) 2825 st(acetal CH str); 1605, 1585 st. (aromatic C=C str); 1485, 1450 st. (assymmetric CH_3def); 1350 st(symmetric CH_3def); 1100, 1075, 1045, 980(acetal C-O-C-O-C str); 860, 800 m, 770, 695 m (aromatic skel)

Analysis: Theoretical: C- 65.91%; H- 7.74%

Found: C- 65.77%; H- 7.71%

Benzaldehyde Dimethyl Acetal.

B.Pt. 102-104°C(40 mm) Clear Oil

Yield 60%.

N.M.R.($CDCl_3$): 201 Hz, singlet (6)...methoxyl protons

324 Hz, singlet (1)...acetal proton

435-455 Hz, multiplet (5).aromatic protons

N.M.R.(M/2 solution in CD_3OD); 100 MHz. 328HZ, singlet (6)...methoxy protons

534Hz, singlet (1)...acetal proton

725-750Hz, multiplet(5)..aromatic protons

I.R(neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 m (CH_3str); 2850 w.sh. (acetal CH str); 1465m (assymmetric CH def); 1355 m (symmetric CH_3def); 1115 st, 1075 m, 1055 st, 1040 m.sh (acetal C-O-C-O-C str); 770; 730 m.sh (aromatic skel)

G.L.C. 1% S.E -30 (110°C); sens x3; volts x1500; F.R=48 mls/min; C.S=12 inch/hr.

T_R =7.5 mins.

T.L.C. Silica with binary solvent 30% ether: 70% (60-80) Pet. Ether; R_F=0.70; Iodine Stain.

Analysis: Theoretical: C- 71.02%; H- 7.95%

Found: C- 70.84%; H- 7.79%

p-Tolualdehyde Dimethyl Acetal

B.Pt. 128-130°C (760mm) Clear Oil

Yield 55%

N.M.R. ($CDCl_3$): 142 Hz, singlet (3)...aromatic methyl group protons

200 Hz, singlet (6)...methoxyl protons

323 Hz, singlet (1)...acetal proton

424-447 Hz, multiplet(4)..aromatic protons

I.R.(neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 st(CH_3str); 2840 m(acetal CH str); 1905 m(mono-substd. aromatic str); 1620, 1520 m.sh. (aromatic C=C str); 1450 m.b(assymmetric CH_3def); 1360 st.b(symmetric CH_3def); 1105, 1090, 1060 st, 1015 m, 980 st.sh. (acetal C-O-C-O-C str); 920, 820, 790 st 770, 720 m.sh (aromatic skel)

G.L.C: 5% carbowax (100°C); sens x10; volts x1500; F.R=45 mls/min; C.S = 15 inch/hour

R_T = 8 mins.

T.L.C: Silica with binary system 40% ether: 60% (60-80) Pet. Ether; R_F=0.35; Iodine stain

Analysis: Theoretical: C- 72.26%; H- 8.49%

Found: C- 72.02%; H- 8.33%

p-Anisaldehyde Dimethyl Acetal

B.Pt. 134-138°C Clear Oil

Yield 48%

N.M.R. ($CDCl_3$): 200 Hz, singlet (6) ....acetal methoxyl protons

229 Hz, singlet (3).... aromatic methoxyl protons

321 Hz, singlet (1).... acetal proton

407-447 Hz, multiplet(4)... aromatic protons showing very strong para splitting

I.R. (neat)νcm^{-1}: 3050 w(aromatic CH str); 2930 m (CH_3 str); 2825 (acetal CH str); 1603 st, 1510 m.sh (aromatic C=C str); 1480, 1430 m.sh. (asymmetric CH_3 def); 1360 m.sh (symmetric CH_3 def); 1105, 1075, 1055 1040, 990 st (acetal C-O-C-O-C str); 835, 790 st, 760 w(aromatic skel)

T.L.C: Silica with binary solvent 95% Pet.Ether (60-80): 5% methanol; R_F=0.5; Iodine stain.

Analysis: Theoretical: C- 65.91%; H- 7.74%.

Found: C- 65.98%; H- 7.57%.

PREPARATION OF SUBSTITUTED α-CHLORO BENZYL METHYL ETHERS.

Substituted Benzaldehyde Dimethyl Acetal (0.5m) was mixed with an excess of freshly distilled acetyl chloride (0.8m) and thionyl chloride (0.1m) in a flask equipped with a nitrogen inlet and reflux condenser. The reaction evolved heat for several minutes, after which it was allowed to stand in a water bath at 65°C. for up to 1 hour depending on the acetal. The excess acetyl and thionyl chlorides were removed in vacuo at room temperature and the residue used directly into the next stage of the reaction.

With one exception, viz. α-chloro benzylmethyl ether, the residue was not distilled since frequently this was found to reduce the overall yield of the extremely reactive α-chloro ether by breaking it down to aldehyde.

α-Chloro benzylmethylether..B.Pt. 71-72°C(0.1mm)

This boiling point compares favourably with that of Straus and Heinz (71-72°C 0.1mm)[148] but not that of Anderson and Capon (68-70°C 1.0mm)[94] although the N.M.R. spectrum of this compound compared favourably with that of the latter. A proton attached to carbon bearing one phenyl group, one methoxyl and one chlorine should have, according to Shodery's rules, a value of 375 Hz. The

value found by Anderson and Capon was 382 Hz, and by the author 378 Hz.

Identification of the α-Cl-ethers was then by N.M.R. and I.R.spectra. The significant feature in the N.M.R. spectrum was the downfield shift of the acetal proton from around Hz.322 to Hz.378, which also served to indicate quantitatively the amount of unreacted dimethyl acetal.

The following substituted α-Chloro Benzyl Methyl Ethers were prepared by this general procedure. All were yellow liquids.

α-Chloro-m-NitrobenzylMethyl Ether.

N.M.R. (neat): 225 Hz, singlet (3)....methoxyl protons

401 Hz, singlet (1)....α-chloroether proton

444-501 Hz, multiplet (4)..aromatic protons

α-Chloro-m-Bromobenzyl Methyl Ether

I.R. (neat)νcm^{-1}: 3050 w(aromatic Ch str); 2950 w(CH_3str); 1580 m.sh.(aromatic C=C str); 1410 m.sh (asymmetric CH_3 def); 1360 w(symmetric CH_3 def); 1300 m. 960 st, 800 m, 710st.sh.

α-Chloro-m-FluorobenzylMethyl Ether

N.M.R. (neat): 217 Hz, singlet (3)....methoxyl protons

390 Hz, singlet (1)....α-Chloro ether proton.

403-450 Hz, multiplet (4)..aromatic protons

I.R.(neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 w(CH_3 str); 1590 st.sh(aromatic C=C str); 1450 m (asymmetric CH_3 def); 1390 v.w. (symmetric CH_3 def); 980 st. 800 m, 710 st.sh.

α-Chloro-Benzyl Methyl Ether

B.Pt. 71-72° 0.1 mm

N.M.R(neat): 209 Hz, singlet (3)....methoxyl protons

378 Hz, singlet (1)....α-Chloro-ether proton

423-456 Hz, multiplet(5)...aromatic protons

I.R.(neat)νcm^{-1}: 3050 v.w (aromatic CH str); 2950 v.w. (CH_3 str); 1590, 1580 w.sh (aromatic C=C str); 1450m(asymmetric CH_3 def); 1245 m, 1200 1110s, 980 m, 830, 750 m, 700 st.sh.

α-Chloro-p-Methylbenzyl Methyl Ether

N.M.R.(neat): 130 Hz, singlet (3)....aromatic methyl group protons

206 Hz, singlet (3)....methoxyl protons

383 Hz, singlet (1)....α-Chloro-ether proton

414-462 Hz, multiplet(4)...aromatic protons

I.R.(neat)νcm^{-1}: 3050 v.w(aromatic CH str); 2950 w (CH_3 str); 1600 st. sh.(aromatic C=C str) 1450 w.b(asymmetric CH_3 def); 1390m.sh (symmetric CH_3 def); 1300 m. 1200, 1170 st.sh, 860, 820, 770 st.sh.

α-Chloro-m-Methoxybenzyl Methyl Ether

N.M.R ($CDCl_3$): 218 Hz, singlet (3)....acetal methoxyl group protons

228 Hz, singlet (3)....aromatic methoxyl group protons

335 Hz, singlet (1)....α-chloro ether proton

412-448Hz, multiplet(4)...aromatic protons

I.R.(neat)νcm^{-1}: 3050 w(aromatic Ch str); 2930 m(CH_3str); 1598, 1585 (aromatic C=C str); 1485, 1450 m(asymmetric CH_3 def); 1350 m (symmetric CH_3 def); 1269, 1150, 1040, 860, 770, 695.

α-Chloro-p-Methoxybenzyl Methyl Ether

I.R (neat)νcm^{-1}: 3050 w(aromatic CH str); 2960 w(CH_3str); 1600, 1520 st.sh(aromatic C=C str); 1460 w(asymmetric CH_3 def); 1360 v.w. (symmetric CH_3 def); 1269, 1170 st.sh. 1040, 960, 860, 840 m, 750 st.sh.

PREPARATION OF MIXED AROMATIC METHYL ARYL ACETALS

Benzaldehyde Phenyl Methyl Acetal

Phenol (0.1 mole) in dried Dimethyl formamide (10 mls) was added slowly to a cooled stirred suspension of sodium hydride (0.1 mole) in dried dimethyl formamide contained in a flask equipped with an efficient reflux condenser. It was important to remove the hydrocarbon suspension from the sodium hydride as it proved a difficult contaminant to remove at a later stage. When the evolution of hydrogen had ceased, α-chloro-benzyl methyl ether was added dropwise to the solution, which was then allowed to warm to room temperature and left for 40 minutes.

After this period the reaction mixture was poured into 2% sodium carbonate and extracted with ether. Subsequent washings were with N/10 sodium hydroxide (to remove unreacted phenol), water (to remove residual dimethyl formamide), and sodium bisulphite (to remove any aldehyde). After drying over anhydrous potassium carbonate and evaporating the solvent in vacuo, a viscous oil remained containing about 70-80% of the mixed acetal.

The crude material was distilled in a molecular distillation apparatus under high vacuum using a mercury difussion pump. An analytically pure sample was obtained by repeated distillation taking, in each case, about four centre cuts, therefore reducing drastically the yield.

The pure sample had no dimethyl acetal impurity (N.M.R., and G.L.C.) and had B.Pt. 118-120°C 0.1 mm. Clear Oil.

N.M.R.($CDCl_3$): 201 Hz, singlet (3)....methoxyl protons
366 Hz, singlet (1)....acetal proton
400-460 Hz, multiplet(9)...aromatic protons

N.M.R (M/2 Solution in CD_3OD) 100 MHz.
332 Hz, singlet (3)....methoxyl group protons
609 Hz, singlet (1)....acetal proton.
684-760 Hz, multiplet(9)...aromatic protons

I.R.(neat)ν cm^{-1}: 3100 w(aromatic CH str); 2930 m(CH_3str) 2830 m(acetal CH str); 1600s, 1592s (aromatic C=C str) 1475 m(asymmetric CH_3 def); 1360s (symmetric CH_3 def); 1110m, 1095s, 1050, 1040, 1020 st.sh, 990m(acetal C-O-C-O-C str), 780 st.sh, 720 st.sh (aromatic skel)

G.L.C: 1% S.E-30 (110°C); sens x 3; volts x 1500
F.R. = 48 mls/min; C.S.=12 inches/hour
R_F = 11mins
Impurities in the other fractions were at R_T = 7.5 mins (coincidental with authentic dimethyl acetal sample), and R_T = 17.25 mins (thought to be the benzaldehyde diphenyl acetal).

T.L.C: Silica with tertiary solvent system 20% ether; 40% benzene; 40% (40-60) Pet. Ether. R_F 0.85.

Mass Spectrum:

M/e	R.A(%)	ion type
214	8.5	molecular ion (M^+)
183	22.1	M^+ minus OCH_3
121	100	M^+ minus OPh
91	73.1	$C_7H_7^+$
65	58.0	$C_5H_5^+$

Analysis: Theoretical: C- 78.48%; H- 6.59

Found: C- 78.51%; H- 6.72

The following benzaldehyde substituted phenyl methyl and substituted benzaldehyde phenyl methyl acetals were prepared by this general procedure.

It should be noted that the molecular distillation apparatus used could not accommodate an internal thermometer, and consequently all temperatures quoted from this apparatus are related to oil bath temperatures. These distillations which employed a short path semi-micro apparatus were measured by an internal thermometer and this will be registered beside the quoted boiling point. In general, preparative chromatography was applied unsuccessfully to the acetals quoted below. All but the more unreactive were consistently broken down either in G.L.C. column packings or neutral alumina and silica media.

Benzaldehyde m-Nitrophenyl Methyl Acetal

B.Pt. 170° 174°C 4 x 10^{-2} torr. Clear oil(internal thermometer)

N.M.R. ($CDCl_3$): 202 Hz, singlet (3)....methoxyl protons

366 Hz, singlet (1)....acetal proton

400-470 Hz, multiplet(9)...aromatic protons

I.R. (neat)ν cm^{-1}: 3050 w(aromatic CH str); 2950 m (CH_3 str); 2850 m (acetal CH str); 1595 st (aromatic C=C str); 1550 shoulder (N=O str); 1470 st.sh (asymmetric CH_3 def); 1360 m (symmetric CH_3 def); 1110, 1090, 1085, 1010, 1000, 940 (acetal C-O-C-O-C str); 880 m(C-N str); 790,780, 710, 690 (aromatic skel).

Benzaldehyde m-Bromophenyl Methyl Acetal

B.Pt. 114 - 118°C 9×10^{-2} torr. Clear Oil.

N.M.R. ($CDCl_3$): 201 Hz, singlet (3)....methoxyl protons
361 Hz, singlet (1)....acetal proton
410-470 Hz, multiplet (9)..aromatic protons

I.R.(neat)νcm^{-1}: 3100 w(aromatic CH str); 2950 m. (CH_3 str); 2850 m (acetal CH str); 1590 st(aromatic C=C str); 1470 st.sh (asymmetric CH_3 def); 1350 m(symmetric CH_3 def); 1120, 1100, 1070, 1020, 1000, 940 (acetalC-O-C-O-C str); 900, 870, 790, 710 st.sh.(aromatic skel).

Analysis: Theoretical: C- 57.34%;H- 4.44%
Found: C- 57.67%;H- 4.65%

Benzaldehyde m-Fluorophenyl Methyl Acetal

B.Pt. 82-88°C (0.1 mm) Clear Oil (internal thermometer)

N.M.R. ($CDCl_3$): 203 Hz, singlet (3).... methoxy protons

366 Hz, singlet (1).... acetal proton

386-460 Hz, multiplet(9)... aromatic protons

N.M.R.(M/2 solution in CD_3OD)100 MHz.

334 Hz, singlet (3).... methoxy protons

614 Hz, singlet (1).... acetal proton

652-770 Hz, multiplet(9)... aromatic protons

I.R.(neat)ν cm^{-1}: 3020 w(aromatic CH str); 2950 w(CH_3 str); 2850 w.sh(acetal CH str); 1610, 1590 st.sh. (aromatic C=C str); 1490, 1450 sh. (asymmetric CH_3 def). 1360 (symmetric CH_3 def); 1130, 1090, 1070, 1020, 1000 (acetal C-O-C-O-C str); 920, 960, 780, 700 (aromatic skel.)

G.L.C: 1% OV-17 (235°C); sens x 10; volts x1500; F.R= 40 mls/min; C.S=12 inches/hour; T_R = 13 mins.

Analysis: Theoretical: C-72.41%; H-5.44%; F - 7.95%

Found: C-72.22%; H-5.45%; F - 8.20%

Benzaldehyde m-Methoxyphenyl Methyl Acetal

B.Pt. 140-145°C (1 x 10^{-4} torr) Clear Oil

N.M.R ($CDCl_3$): 203 Hz, singlet(3)....acetal methoxy protons

216 Hz, singlet(3)....aromatic methoxy protons

365 Hz, singlet(1)....acetal proton

385-460 Hz, multiplet(9)..aromatic protons

I.R.(neat)ν cm^{-1}: 3050 (aromatic CH str); 2930m(CH str); 2830 (acetal CH str); 1585 st(aromatic C=C str); 1480, 1445 m (asymmetric CH_3def); 1340 m (symmetric CH def); 1070, 1040, 1010, 980 st (acetal C-O-C-O-C str); 330 m, 750, 695 st (aromatic skel).

Analysis: Theoretical: C-73.75%; H-6.60%

Found: C-73.94%; H-6.66%.

Benzaldehyde p-Methylphenyl Methyl Acetal

B.Pt. 100-106°C 1.5×10^{-2} torr. Clear oil (internal thermometer)

N.M.R.($CDCl_3$): 137 Hz, singlet (3)....aromatic methyl group protons

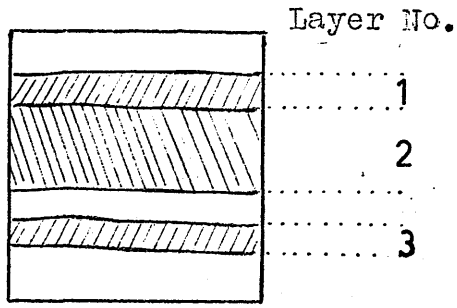
203 Hz, singlet (3)....methoxy protons

364 Hz, singlet (1)....acetal proton

410-460 Hz, multiplet(9)...aromatic protons

I.R.(neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 w(CH_3str); 2820 w.sh.(acetal CH str); 1610, 1590 m.sh. (aromatic C=C str); 1510, 1460 st.sh. (asymmetric CH_3 def); 1360 sh. (symmetric CH_3 def); 1100, 1035, 1030 1010, 1000, 940 (acetal C-O-C-O-C str); 830, 760, 710 str. sh. (aromatic skel).

T.L.C. The crude mixed acetal was distilled after work up to produce four fractions of which the highest boiling (120-130°C 0.8 mm) was plated on neutral alumina (0.5 mm) with 100% Petroleum Ether (40-60) as solvent. Iodine spray stained the plate as shown below:-



Layer No. 2 was collected and distilled to give two fractions.

Fraction No.1) 97 - 100°C 1.5×10^{-1} torr.

2)100 - 106°C 1.5×10^{-2} torr.

Fraction No. 2 was found to be analytically pure.

Analysis: Theoretical: C- 78.92%; H- 7.06%.

Found: C- 78.74%; H- 7.13%.

Benzaldehyde p-Methoxyphenyl Methyl Acetal

B.Pt. 160°C 1 x 10^{-4} torr. Clear Oil.

N.M.R.($CDCl_3$): 204 Hz, singlet (3)..acetal methoxy group protons

224 Hz, singlet (3)..aromatic methoxy group protons

360 Hz, singlet (1)..acetal proton

402-456 Hz, multiplet(9).aromatic protons

N.M.R.(M/2 solution in CD_3OD); 100 MHz.

334 Hz, singlet (3)..acetal methoxy group protons

594 Hz, singlet (1)..acetal proton

670-757 Hz, multiplet(9).aromatic protons

I.R.(neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 m.sh (CH_3 str); 2850 m.sh. (acetal CH str) 1595, 1575 st.sh. (aromatic C=C str.) 1460 m(asymmetric CH_3 def); 1360 m (symmetric CH_3 def); 1100, 1095, 1040 1010, 930 (acetal C-O-C-O-C str); 900w 840, 770, 710 st.sh.(aromatic skel)

Analysis: Theoretical: C-73.75%; H- 6.60%

Found: C-73.54%; H- 6.63%

m-Nitrobenzaldehyde Phenyl Methyl Acetal

B.Pt. 95-100°C 1 x 10^2 torr Yellow oil (internal thermometer)

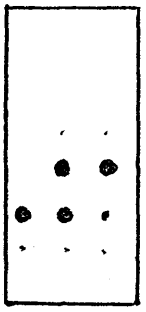
N.M.R. ($CDCl_3$): 204 Hz, singlet (3)....methoxy protons
372 Hz, singlet (1)....acetal proton
410-510 Hz, multiplet (9)..aromatic protons

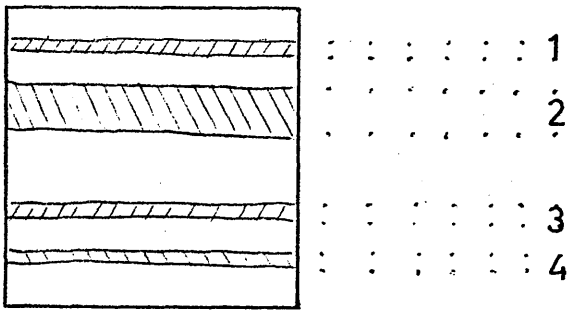
I.R. (neat) ν cm^{-1}: 3050 w(aromatic CH str); 2950 w(CH_3 str); 2850 (acetal CH str); 1600 m, 1530 st.sh. (aromatic C=C str); 1490 m.sh (asymmetric CH_3 def); 1350d (symmetric CH_3 def. and C-NO_2 str); 1100, 1080, 1040, 1000, 990 m.sh. (acetal C-O-C-O-C str); 900, 820, 760, 740, 720, 700 (aromatic skel.)

G.L.C: 1% C.E.-301 (165.4°C); sens x 10; volts x1250; F.R. = 51 mls/min; C.S.=10 mm/hour; R_T =12.5 mins

T.L.C: Preparative chromatography was possible with this compound because of its relative stability. 200 mgs. of impure material was plated on 0.5 mm silica using the tertiary solvent system 10% ether: 20% benzene: 70% (40-60) Pet.Ether U.V.and iodine spray stained the plate as shown below:

analytical preparative layer No.





Analytical plate: I = authentic dimethyl acetal intermediate

M = mixture of I and P to test separation

P = product (crude reaction mixture)

Solvent system: 20% ether; 40% benzene; 40% (40-60) Pet. ether.

For better resolution the preparative plate was run twice in a solvent system the polarity of which was half that of the analytical plate.

Preparative plate: layer No. 1 ....9 mgs unidentifiable product

2 ....109 mgs mixed acetal

3 ....dimethyl acetal

4 ....unidentifiable material

Analysis: analysis of layer No. 2

Theoretical: C- 64.91%; H- 5.25%; N- 5.36%

Found: C- 64.86%; H- 5.05%; N- 5.40%.

analysis of distilled product ($90-100^{\circ}C$ 1 x 10^{-2} torr)

Found: C- 64.73%; H- 5.00%. N- 5.55%.

Mass Spectrum: For line diagram see end of this Section.

M/e.	R.A.(%)	ion type
259	10.5	Molecular ion (M^+)
228	14.0	M^+ minus OCH_3
166	100	M^+ minus OPh
120	97.0	M^+ minus (OPh+ NO_2)
91	66.5	$C_7H_7^+$
65	81.5	$C_5H_5^+$

m-Bromobenzaldehyde Phenyl Methyl Acetal

B.Pt. 135 - 140°C (2×10^{-3} torr) Yellow oil

N.M.R.($CDCl_3$): 202 Hz, singlet (3) ....methoxy protons
364 Hz, singlet (1) ....acetal proton
412-468 Hz, multiplet (9)...aromatic protons

I.R. (neat)νcm^{-1}: 3050 w(aromatic CH str); 2950 m (CH_3 str); 2850 (acetal CH str); 1600 st.sh (aromatic C=C str); 1495 st.sh. (asymmetric CH_3 def); 1360 m(symmetric CH_3 def); 1100, 1080, 1040, 1020, 1000 st. (acetal C-O-C-O-C str); 900, 840m, 800, 760, 700 st.sh. (aromatic skel.)

G.L.C: 1% OV-17 (100°C); volts x1500; sens x10; F.R=44 mls/min; C.S.=15 inches/hour; $T_R = 8.2$ mins.

T.L.C: Silica plate using binary solvent system 3% methanol: 97% (60-80) Pet.Ether R_F 0.5. Iodine stain.

Analysis: Theoretical: C- 57.35%; H- 4.47%.
Found: C- 57.48%; H- 4.59%.

m-Fluorobenzaldehyde Phenyl Methyl Acetal

B.Pt. 160-165 5×10^{-5} torr. Yellow oil.

N.M.R ($CDCl_3$): 203 Hz, singlet (3)...methoxy protons
365 Hz, singlet (1)...acetal proton
404-448 Hz, multiplet(9)..aromatic protons

I.R.(neat)νcm^{-1}: 3080 m(aromatic CH str); 2950 m (CH_3 str); 2850 m(acetal CH str); 1610 1590 st.(aromatic C=C str); 1495, 1450 st. (asymmetric CH_3 def); 1360 m (symmetric CH_3 def); 1110, 1100, 1080, 1040, 1020, 995 (acetal C-O-C-O-C str); 890, 800, 780, 700 st. (aromatic skel)

Analysis: Theoretical: C- 72.41%; H- 5.44%; F- 7.95%
Found: C- 70.03%; H- 5.82%; F- 8.8%.

Although the analysis figures were poor, there was no trace of either dimethyl or diphenyl acetal contaminant.

m-Methoxybenzaldehyde Phenyl Methyl Acetal

B.Pt. 140-145°C (1 x 10^{-4} torr)

N.M.R($CDCl_3$); 204 Hz, singlet (3)....acetal methoxy protons

226 Hz, singlet (3)....aromatic methoxy protons

363 Hz, singlet (1)....acetal proton

405-450 Hz, multiplet (9)..aromatic protons

I.R.(neat) ν cm^{-1}: 3040 (aromatic CH str); 2938 m (CH_3 str); 2830 sh(acetal CH str); 1588 st.(aromatic C=C str); 1480, 1450m (asymmetric CH_3 def); 1345 m (symmetric CH_3 str); 1070, 1025; 1008 990m (acetal C-O-C-O-C str); 860m, 750, 690 st(aromatic skel).

Analysis: Theoretical: C- 73.75%; H- 6.60%

Found : C- 72.75%; H- 6.61%.

Although slightly impure there were no traces of either dimethyl or diphenyl acetals.

p-Tolualdehyde Phenyl Methyl Acetal

B.Pt. 90-95°C 5×10^{-5} torr. Clear oil.

N.M.R. ($CDCl_3$): 140 Hz, singlet (3)....aromatic methyl group proton

202 Hz, singlet (3)....methoxy protons

365 Hz, singlet (1)....acetal proton

416-456 Hz, multiplet(9)...aromatic protons

I.R.(neat)νcm^{-1}: 3040 (aromatic CH str); 2940 m (CH_3 str); 2840 m.sh.(acetal CH str); 1600 (aromatic C=C str); 1495 st. 1460w (asymmetric CH_3 def); 1355 m(symmetric CH_3 def); 1090, 1035, 1018, 990 st. (acetal C-O-C-O-C str); 810, 755st, 695 (aromatic skel)

G.L.C: 1% OV-17 (125°C); volts x1500; sens x10; F.R = 29 mls/min; C.S.=12 inches/hour; T_R = 31mins.

Preparative chromatography was attempted since there was good separation of the mixed and dimethyl acetals on the column (ΔR_T = 4 mins)

50 mgs. of an impure distillate produced two fractions, the first having the same composition as the distillate, the second about 90% pure in mixed acetal. Further purification by this technique was unsuccessful.

T.L.C: Grade I Neutral Alumina with the tertiary solvent system 10% ether; 20% benzene, 70% (40_60) Pet. Ether, $R_F = 0.85$
Iodine stain.

Analysis: Theoretical: C- 78.92%; H-7.06%.
Found: C- 78.62%; H-7.14%.

An analytically pure sample which gave only one peak on G.L.C. was obtained from repeated molecular distillations.

Mass Spectrum:

M/e	R.A(%)	ion type
no molecular ion apparent		
197	0.4	M + minus OCH_3
135	100.0	M^+ minus OPh
91	98.5	$C_7H_7^+$
65	97.9	$C_5H_5^+$

p-Anisaldehyde Phenyl Methyl Acetal

B.Pt. 125-130°C 8 x 10^{-5} torr. Pale yellow oil

N.M.R. ($CDCl_3$):

202 Hz, singlet (3)....acetal methoxy protons

228 Hz, singlet (3)....aromatic methoxy protons

361 Hz, singlet (1)....acetal proton

402-456 Hz, multiplet (9)..aromatic protons

I.R.(neat)νcm^{-1}:

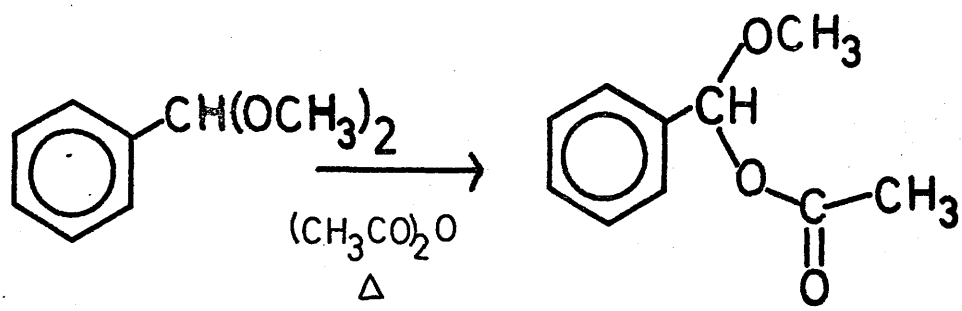
3050 w(aromatic CH str); 2950 st. (CH_3 str); 2860 m(acetal CH str); 1600 w (aromatic C=C str); 1460 st.sh. (asymmetric CH_3 def); 1375 m.sh. (symmetric CH_3 def); 1190, 1160, 1135, 1105, 1090, 1000 (acetal C-O-C-O-C str); 840 w, 725 m(aromatic skel).

Analysis:

Theoretical: C- 73.75%; H- 6.60%.

Found: C- 73.54%; H- 6.63%.

Preparation of Benzaldehyde Methyl Acetal Acylal[38] (α-methoxy, α-acetoxy toluene).



Benzaldehyde dimethyl acetal (0.1 mole) and acetic anhydride (0.2 moles) were heated under reflux until all of the dimethyl acetal appeared to have reacted (t.l.c on silica using 25% ether, 75% (40-60) pet. ether), which was after 24 hours. The heating was continued for a further 12 hours after which the excess acetic anhydride was distilled off at atmospheric pressure. The residue was fractionally distilled under reduced pressure to yield the product in about 90% yield.

B.Pt. 67 - 68°C 0.3mm Clear Oil

N.M.R.($CDCl_3$): 128 Hz, singlet (3)....acetoxy methyl protons

212 Hz, singlet (3)....acetal methoxy protons

400 Hz, singlet(1).... acylal proton

433-453 Hz, multiplet (5). aromatic protons

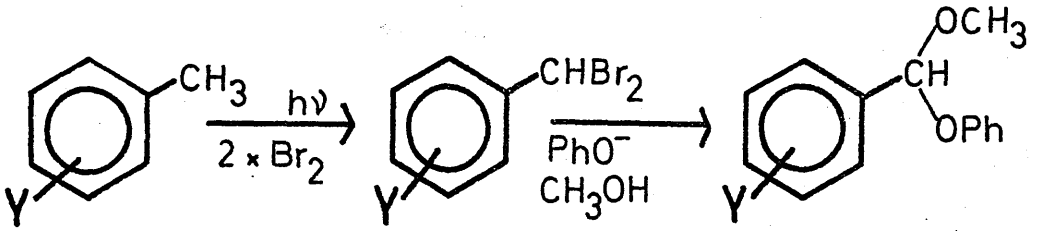
I.R.(neat) cm^{-1}: 3050 w(aromatic CH str); 3025; 2990 w; 2930 m.sh. (CH_3 str); 2830 (methine CH str) 1870 (acetoxy C=O str); 1495 w (aromatic C=C str); 1450 (asymmetric CH_3 def); 1370 st.sh. (symmetric CH_3 def); 1275; 1100 st; 1140 sh, 1010, 990, 940, 890 st, (C-O-C-O-C str);750, 695 st.sh (aromatic skel.)

Analysis: Theoretical: C- 66.66%; H- 6.66%.

Found: C- 66.46%; H- 6.55%.

Preparation of m-Nitrobenzaldehyde Phenyl Methyl Acetal via m-Nitrobenzalbromide. J4,152

An alternative route to the synthesis of substituted benzaldehyde phenyl methyl acetals which was attempted is shown by the reaction scheme.



I. 6.85 g(0.05m) of freshly distilled m-Nitrotoluene in 800 mls. carbon tetrachloride was placed in a 500 ml. three-necked flask filled with reflux condenser and nitrogen inlet. The solution was stirred continuously with a 500 watt tungsten/mercury lamp approximately 2 cms from the flask, which was enveloped in tin foil.

The solution gently refluxed while 15g(0.10m) of Bromine in 80 mls carbon tetrachloride was added over three hours, such that a red colour persisted in the solution. After this period the flask was allowed to cool to 45°C. and immersed in a dry ice-acetone bath. Before immersion the solution was turbid and therefore

made the addition of petroleum ether unnecessary.

The solution was suction filtered to produce 2.64g (0.0g moles: 18% yield) of a cream coloured solid, and a residual yellow oil containing none of the desired product.

Solid (needles) M.Pt. 94-95°C. (crude).

The solid was extremely insoluble in all organic solvents tried. Hot acetone fractionally dissolved the solid 144 mgs.into three fractions, of which the major one (122 mgs) was not soluble M.Pt. 96-97°C.

I.R.(nujol mull) cm^{-1}: 1618 m(aromatic C C str); 1530 st.sh. (asymmetric NO_2 def); 1350 st.sh. (symmetric NO_2 def); 1105, 918, 830, 724w; 705 m.sh.

G.L.C: (an extremely dilute solution in acetone.)

1% C.E-301 (165.4°C); volts x1250; sens x10; F.R.= 51 mls/min; C.S.= 10mm/min; T_R =25.5 mins with slight impurity at T_R=7 mins.

II. Sodium (0.3 g; 0.017 moles) was added to dry methanol in a 100ml round bottomed flask with efficient reflux condenser and nitrogen inlet. Phenol (1.39g; 0.017 moles) in dried methanol (5 mls) was added dropwise, followed by the m-Nitrobenzalbromide (0.017 moles). The solution refluxed violently of its own accord for about one hour. The reaction was warmed gently and followed by t.l.c. (silica with 50% ether: 50% (40-60) pet. ether, with iodine stain). After 12 hours the reaction mixture was worked up in the same manner as the other mixed acetals.

After vacuum evaporation of the solid solvent, a yellow viscous oil (0.56g) was left which was partially dissolved in 10mls. ethyl acetate and the most soluble fraction (247 mgs) plated on silica with 20% ether; 40% benzene; 40% (40-60) petroleum ether. Although the oil contained a high percentage of m-nitrobenzaldehyde dimethyl acetal, distillation produced 10 mgs of m-nitrobenzaldehyde phenyl methyl acetal.

B.Pt. 90-100°C (1×10^{-2} torr)

Physical constants as before.

The dependence of this type of reaction on carbonium ion stability and nucleophilic concentration has been adequately discussed.[33,61] Because of these considerations and the low yield obtained this general procedure was not adopted.

Preparation of substituted Benzaldehyde S-Phenyl Methyl Thioacetal.

The preparative method is very similar to that of the mixed alkyl aryl acetals and is fully described by Fife and Anderson[95] benzene thiol is condensed with the appropriate substituted α-chloro benzyl methyl ether.

Tolualdehyde S-Phenyl Methyl Thioacetal

B.Pt. 108 - 110°C 0.04 mm

N.M.R. ($CDCl_3$): 138 Hz, singlet (3).....aromatic methyl protons

208 Hz, singlet(3).....methoxy protons

340 Hz, singlet (1).....thioacetal proton

424-456 Hz, multiplet (9)...aromatic protons

I.R. (neat) cm^{-1}: 3060 m(aromatic CH str); 2830 m(CH_3 str); 2820m.sh.(thioacetal CH str); 1615 w. 1575 m(aromatic C=C str); 1475, 1435s. (asymmetric CH_3 def); 1330vw, (symmetric CH_3 def); 1095, 1080, 1060, 1020 st.sh. 995wsh, 960 m,(thioacetal C-O-C-S-C str); 815, 780m, 740, 720, 637, 660 (aromatic skel)

Analysis: Theoretical: C- 73.77%. H- 6.55%.

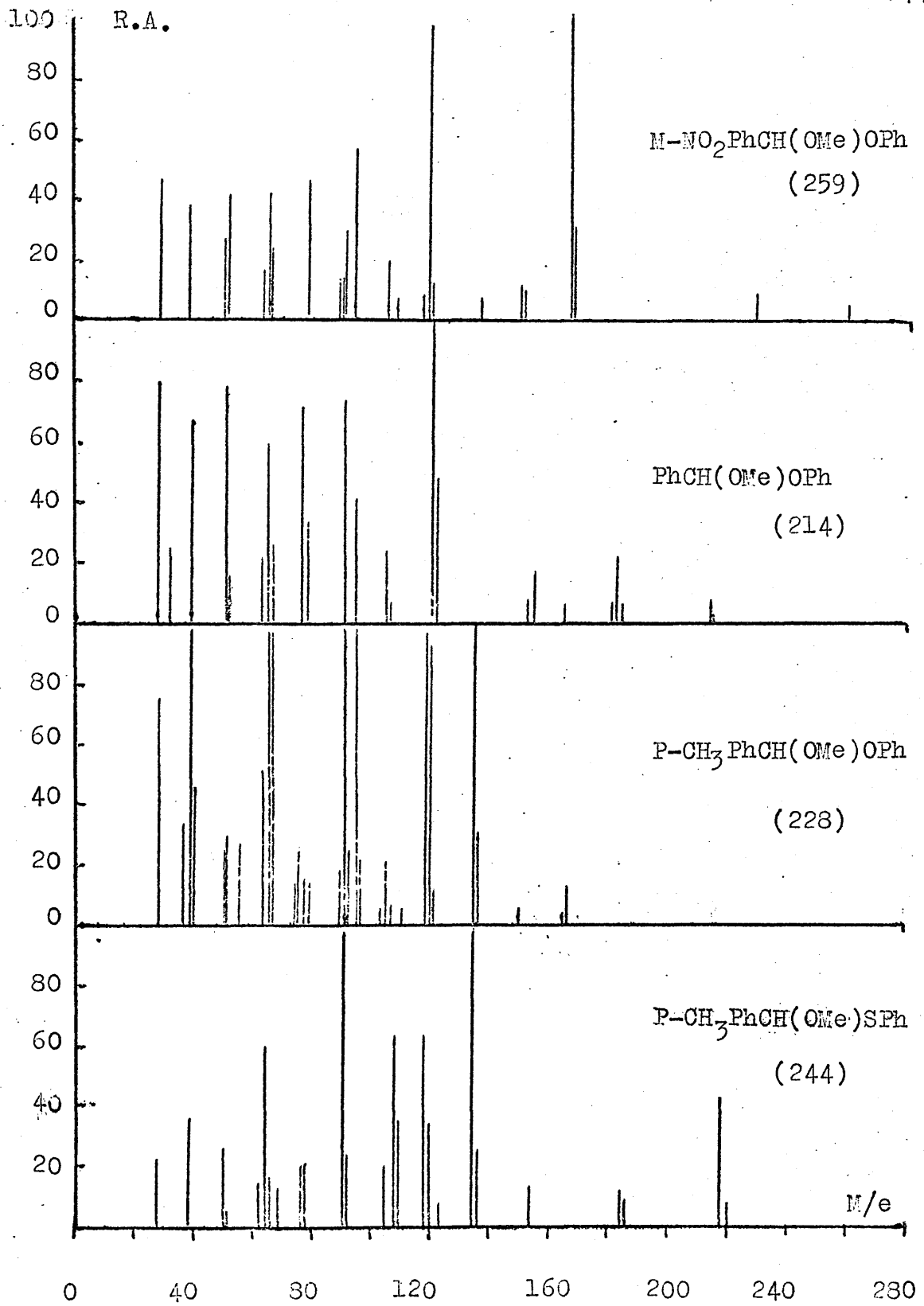
Found: C- 72.89%. H- 6.26%

Mass Spectrum:

M/e	R.A.	ion type
No molecular ion apparent.		
213	-	M^+ minus OCH_3
135	100	M^+ minus SPh
91	98.5	$C_7H_7^+$
65	59.1	$C_5H_5^+$

Mass Spectral Analysis of Substituted Y -Benzaldehyde Phenyl Methyl Acetals

Y= M - NO (259)		Y = H(214)		Y= P - Me(228)		Y= P - Me (Thiophenyl) (244)	
M/e	RA	M/e	RA	M/e	RA	M/e	RA
259	4.5	214	8.5	228	-	244	-
228	9.0	184	6.8	197	0.4	218	43.1
167	29.9	183	22.1	167	3.7	186	10.2
166	100	181	6.8	166	14.0	185	13.1
151	9.0	155	17.0	150	5.9	154	13.9
150	10.4	122	47.6	136	32.0	136	27.0
120	12.7	121	100	135	100	135	100
119	97.1	105	20.4	121	13.2	120	35.1
105	19.4	94	40.8	120	92.8	119	64.3
94	56.0	91	73.1	119	98.5	109	62.9
91	27.9	78	34.0	105	22.1	105	20.5
78	44.8	77	71.0	91	98.5	92	14.6
66	23.2	66	25.5	79	14.7	91	98.5
65	40.3	65	58.0	75	25.0	78	21.9
51	40.3	51	76.5	66	97.9	77	21.9
38	36.6	39	66	65	97.9	66	17.5
28	45.5	28	80	63	52	65	59.1
				51	41.2	63	16.1
				39	98.5	51	27.0
				28	75.8	39	36.5
						28	22.6


100
R.A.
80
60
40
20
0
M-NO2PhCH(OMe)OPh
(259)
PhCH(OMe)OPh
(214)
P-CH3PhCH(OMe)OPh
(228)
P-CH3PhCH(OMe)SPh
(244)
M/e
0
40
80
120
160
200
240
280

R E F E R E N C E S

REFERENCES

1) see W.P. Jencks "Catalysis in Chemistry and Enzymology" 1969, McGraw-Hill Book Co.

2) D.C. Phillips et al, Nature, 196 , 1173.

3) B. Capon, Biochemie, 53, 145 (1971)

4) J.A. Rupley, Proc. Roy. Soc., (B) 167, 416 (1967)

5) see B. Capon, Chem. Revs., 69, 407 (1969)

6) L.N. Johnson and D.C.Phillips, Nature, 206, 761 (1965)

7) D.C. Phillips et al, Proc. Roy. Soc., (B) 167, 378 (1967)

8) F.Steitz et al, J. Mol. Biol. 46, 337 (1969)

9) M.F.Perutz, Proc. Roy. Soc., (B) 167, 448 (1967)

10) J.C. Kendrew, Brookhaven Symp. Biol., 15, 216 (1962)

M.F.Perutz, J.Mol. Biol., 13, 646 (1965)

11) E.H. Cordes et al, J.Phys. Chem., 73, 1898 (1969) and references therein.

12) D.E. Koshland Jr., et al., Fed. Proc., 21, 1031 (1962)

13) C.A.Vernon, Proc. Roy. Soc., (B), 167, 389 (1967)

14) D.C. Phillips, Scientific American, 215, 78 (1966)

D.C. Phillips et al, Nature, 206, 757 (1965)

15) M.A. Raftery and T. Rand-Meir, Biochemistry, 7, 3231 (1968)

16) B.M. Dunn and T.C. Bruice, J. Amer. Chem. Soc., 92, 2410 (1970).

17) R. Lumry, Enzymes, 1, 157 (1959)

18) W.P. Jencks in "Current Aspects of Biochemical Energetics" (New York, Academic Press) 1966, p.273.

19) D.E. Koshland Jr., J. Theoret. Biol., 2, 85 (1962); Advan, Enzymol., 22, 45 (1960)

20) B. Capon, unpublished observations.

21) F.W.Dahlquist and M.A. Raftery, Biochemistry, 7, 3269 (1968)

22) D.R. Storm and D.E.Koshaland Jr., Proc. Nat. Acad. Sci., U.S.A. 66, 445 (1970); Chem. Brit., 6, 372 (1970)

23) B. Capon, J. Chem. Soc., (B) 1207 (1971)

24) D.E.Koshland, Biol. Rev. Cambridge Phil. Soc., 28, 416 (1953)

25) D.E.Koshland in "The Mechanism of Enzyme Action" (Editors, W.D. McElroy and B. Glass), John Hopkins Press, Baltimore, Md., 1954.

26) K. Wallenfels and E. Bernt, Annalen, 584, 63 (1953)

27) G. Leger, Biochim. Biophys. Acta., 151, 728 (1968)

28) J.A. Thoma and J. Wakim, J. Theoret. Biol., 19, 297 (1968)

29) E.H. Fisher and E.A.Steir, Enzymes, 4, 313 (1960)

30) M.L. Bender and R. Breslow, "Comprehensive Biochemistry", 2, 38 (editors M. Florkin and E.H. Stortz), Elsevier, Amsterdam (1962)

31) F.C. Mayer and J. Larner, J. Amer. Chem. Soc., 81, 133 (1959)

32) G. Lowe, Proc. Roy. Soc., (B), 167, 448 (1967)

33) B.Capon and D. Thacker, J. Chem. Soc., (B), 1322 (1967)

34) B. Capon et al, J. Chem. Soc., (B), 1038 (1969)

35) T.C. Bruice and D. Piszkiewicz, J. Amer.Chem. Soc., 90, 2156 (1968)

36) B. Capon and N.C. Smith, Chem. Comm., 523 (1965)

37) M.I. Page, Ph.D. Thesis, Univ. of Glasgow, Scotland (1970)

38) E. Anderson, Ph.D. Thesis, Univ. of Leicester, England (1968)

39) G. Lowe, Proc. Roy. Soc. (B), 167, 431 (1967)

40) D. Piszkiewicz and T.C.Bruice, J. Amer. Chem. Soc., 89 6237 (1967)

41) R.L. Nath and H.N. Rydon, Biochem. J., 57, 1 (1954)

42) S.Matsubara, J.Biochem. (Tokyo), 49, 242 (1961)

43) G. Lowe et al., Biochem J., 104, 893 (1967)

44) A.N. Hall, S.Hollingshead and H.N. Rydon, Biochem. J., 84, 390 (1962)

45) M.R.J. Morgan, Biochem J., 102, 45P (1967)

46) F. Van Wunendaele and K.C.DeBruyne, Carbohyd. Res., 14, 189 (1970)

47) R.B. Dunlop, G.A. Ghanim, and E.H. Cordes, J.Phys. Chem., 73, 1398 (1969)

48) J.G.Voet and R.H. Abeles, J. Biol. Chem.,245, 1020 (1970)

49) D.E. Koshland Jr., and K.E.Heet, Ann. Rev. Biochemistry, 37, 359 (1963)

50) M.L. Bender and F.J. Kezdy, Ann. Rev. Biochemistry, 34, 49 (1965)

51) B. Capon, Tet. Letts., 14, 911 (1963)

52) B. Capon and M.I. Page, unpublished observations.

53) T.C. Bruice and D. Piszkiewicz, J. Amer. Chem. Soc., 89, 3568 (1967)

54) O. Smidsrød, A.Haug, and B. Larsen, Acta. Chem. Scand., 20, 1026 (1966)

55) J.B.Howard and A.N. Glazer, J. Biol. Chem., 244, 1399 (1969)

56) B. Capon and M.I. Page, Chem. Comm., 1443 (1970)

57) C.A. Vernon, Proc. Roy. Soc. (B), 167, 431 (1967)

58) L.L. Schalegar and F.A.Long, Advan. Phys. Org. Chem, 1 (1963)

59) E.H. Cordes, Advan. Phys. Org. Chem., 4, 1 (1967)

60) J.N. BeMiller, Adv. Carbohydrate Chem., 22, 25 (1961)

61) C.K. Ingold, "Structure and Mechanism in Organic Chemistry" Cornell Univ. Press, Ithaca, N.Y., 1953.

62) R.P. Bell, "The Proton in Chemistry", Cornell Univ. Press, New York, 1959.

63) J.F. Bunnett, "Technique of Organic Chemistry", Vol. VIII, Part 1, 2nd editn.,

64) T.H. Fife and L.H. Brod, J. Amer.Chem. Soc., 92, 1631 (1970)

65) J.M. O'Gorman and H.J. Lucas, J.Amer.Chem. Soc., 72, 5489 (1950)

66) J.D. Drumheller and L.J. Andrews, J. Amer. Chem. Soc. 77, 3290 (1955)

67) N.A. Bourns et al, Can. J. Chen., 34, 123 (1956)

68) T.H. Fife and L.K. Jao, J. Org. Chem., 30, 1492 (1965)

69) J.C. Speck Jr. et al., J. Amer. Chem. Soc., 87, 4979 (1965)

70) L.L. Schalegar and F.A.Long, Adv. Phys. Org. Chem., 2, 93 (1964)

71) E. Whalley, Adv. Phys. Org. Chem., 2,

72) F.A. Long, Ann. N.Y. Acad. Sci., 84, 596 (1960)

73) C.A. Bunton and V.J. Shiner Jr., J. Amer. Chem. Soc., 83, 3207) (1961)

74) T.H. Fife and L.H. Brod, J. Org. Chem., 33, 4136 (1968)

75) G. Lowe et al, Biochem. J., 104, 393 (1967)

76) T.H. Fife and L.K. Jao, J. Amer. Chem. Soc., 91, 4081 (1969)

77) T.H. Fife and L. Hagopian, J. Org. Chem., 31, 1772 (1966)

78) P. Salomaa and A. Kankoanpera, Acta. Chem. Scand., 15, 871 (1961)

79) P. Salomaa, Ann. Univ. Turku, Ser. A. 46 (1961)

80) A. Kankaanpera, ibid, 95 (1966)

81) A.Kankaanpera and K. Mikki, Suomen Kem. B42, 343, (1969)

82) M.S. Newman and R.J. Harper Jr., J. Amer. Chem. Soc., 80 6350, (1958)

83) J.A. Orvik, Ph.D. Thesis, Univ. of Washington, U.S.A.(1967)

84) T.H. Fife, J. Amer. Chem. Soc., 89, 3223 (1967)

85) P. Watts, J. Chem. Soc. (B), 543, (1968)

86) O. Cedar, Arkiv, Kemi, 6, 523, (1954)

87) N.A. Hughes, A. Grodski and R. Fannucci, J. Amer Chem.Soc. 90, 4958 (1968)

88) A.Kankaanpera, Suomen Kem., B.43, 133 (1970)

89) B. Capon and M.C.Smith, J. Chem. Soc. (B), 1031 (1969)

90) G.A.Hammont, J. Amer. Chem. Soc., 77, 334 (1955)

91) C.D. Ritchie and W.F.Sager, Progr. Phys. Org. Chem., 2, 323 (1964)

92) A.J. Kresge and R.J. Preto, J. Amer. Chem. Soc., 87, 4593 (1965)

93) C.A. Bunton and R.H. DeWolfe, J. Org. Chem., 30, 1371 (1965)

94) E. Anderson and B.Capon, J. Chem. Soc., 1033 (1969)

95) T.H. Fife and E. Anderson, J. Amer. Chem. Soc.,92, 5464 (1970).

96) G.E.Lienhard and W.P.Jencks, J. Amer. Chem. Soc., 88, 3982 (1966)

97) A. Albert and E.P. Serjeant, "Ionization Constants of Acids and Bases", Methuen & Co. Ltd.(1962)

98) A. Kankaanpera and M.Lahti, Acta. Chem. Scand., 23, 2465 (1969)

99) E. Anderson and T.H. Fife, J. Amer. Chem. Soc., 91, 7163 (1969).

100) R.H. DeWolfe et al., J. Org. Chem., 34, 843,(1969)

101) H.C. Brown, Chem. Soc., Spec. Publ., 16, 140 (1962)

102) F.A.Long and D.McIntyre, J. Amer. Chem. Soc., 76, 3240, 3243 (1954)

103) C.A. Bunton and J.D. Reinheimer, J. Phys. Chem., 74, 4457 (1970)

104) M. Eigen, Discuss Faraday Soc., 39, 7 (1965)
Proceeds of 5th Nobel Symposium, p.245.

105) V. Gold and D.C.A. Waterman, J. Chem. Soc.(B), 840 (1968)

106) D.L. Martin and F.J.C. Rossotti, Proc. Chem. Soc., 60 (1959)

F.J.C. Rossotti, Nature, 188, 936 (1960)

107) H. Kwart and M.B. Price, J. Amer. Chem. Soc., 82, 5123 (1960)

108) P. Salomaa, A. Kankaanpera and M. Lahti, J. Amer. Chem. Soc. 93, 2084 (1971)

109) A.J. Kresge et al, J. Amer. Chem. Soc., 93, 413 (1971)

110) J.N. Brønsted and K.J.Pederson, Z.Phys. Chem., 108, 185 (1924)

111) see ref. 156

J.E. Leffler and E. Grunwold "Rates and Equilibria of Organic Reactions", Wiley, New York, N.Y. (1963) p.24.

112) Loudon and Noyce, J. Amer. Chem. Soc., 91, 1433 (1969)

R.H. Marcus, J.Phys. Chem., 72, 891 (1968); J. Amer. Chem.Soc. 91, 7224 (1969)

113) R.P. Bell, Discuss. Faraday Soc., 39, 16 (1965)

114) J. Bigeleisen and M. Wolfsberg, Advan. Chem. Phys. 1, 15 (1958)

115) see V. Gold, Chem. Brit., 292 (1970) and references cited therein.

116) R.P. Bell "Acid-Base Catalysis", Oxford Univ. Press, London, Chpt. IV.

117) K.B. Wiberg, Chem. Rev., 55, 713 (1955)

118) E.H. Cordes et al., J. Org. Chem., 34, 22 (1969)

119) F.H. Westheimer, Chem. Rev., 61, 265 (1961)

120) see R.A.More O'Ferrall and J. Korba, J. Chem. Soc. (B), 985, (1967)

R.A.More O'Ferrall, J. Chem. Soc.(B), 785 (1970)

121) F.G. Bordwell and W.J. Boyle Jr., J.Amer. Chem. Soc., 93, 512 (1971)

122) F.G. Bordwell et al., J. Amer. Chem. Soc., 91, 4002 (1969) 92, 5926 (1970)

123) S.B. Hanna, C. Jermini and H. Zollinger, Symposium on Isotope Effects, Univ. of York (July 1969); Tet. Letts. 51, 4415 (1969)

124) J.E. Dixon and T.C. Bruice, J. Amer. Chem. Soc., 92, 905 (1970)

125) R.P. Bell and D.M. Goodall, Proc. Roy. Soc., Ser. A, 294 273 (1966)

126) L.P. Hammett "Physical Organic Chemistry", McGraw-Hill Book Co., N.Y., (1940)pp404.

127) Y.Yukawa and Y. Tsuno, Bull. Chem. Soc., Japan, 32, 971 (1959)

128) M.M.Kreevoy and R.W.Taft Jr. J. Amer. Chem. Soc., 77, 5590 (1955)

M.M. Kreevoy, C.R. Morgan and R.W. Taft Jr., J. Amer.Chem.Soc 82, 3064 (1960)

129) B. Capon, M.J. Perkins and C.W. Rees, "Organic Reaction Mechanisms" (1965) Interscience, London.

130) P. Wells, Chem. Revs., 63, 171,(1963)

131) M.I. Page, Leicester Chem. Revs., 9, 31 (1968)

132) R.W.Taft Jr., J. Amer. Chem. Soc., 79, 1045 (1957)

133) H.C. Brown and Y. Okamoto, J.Amer. Chem.Soc., 80, 4979 (1958)

134) H. Van Bekkum , P.E. Verkade and B.M. Webster, Rec. Trav. Chim. Phys., 78, 815 (1959)

135) J.O. Schreck, J.Chem. Ed. 48, 103 (1971)

136) R.P. Bell and P.G. Evans, Proc.Roy. Soc. (London), 291A 297 (1966)

137) see ref. 37.

138) H.A. Scheraga et al., J. Amer Chem. Soc., 86, 3444 (1964)

139) J.M. Sayer and W.P. Jencks, J.Amer. Chem. Soc., 91, 6353 (1969)

140) E.H. Cordes et al., J.Amer. Chem. Soc., 12, 3002 (1971)

141) A. Kankaanpera and M.Lahti, Suomen Kem. (B), 43, 75 (1970)

142) R.E. Pincock, Accounts Chem. Res., 2, 97 (1969) and references therein.

143) see M.M. Kreevay and J.M. Williams, J.Amer. Chem. Soc., 90, 6809 (1968)

144) J.N.Brønsted and W.F.K. Wynne-Jones, Trans. Faraday Soc. 76, 4379 (1954)

145) R.H. DeWolfe and R.M. Roberts, J. Amer. Chem. Soc., 76, 4379 (1954)

146) W.E. Wentworth, J.Chem.Ed., 42, 96 (1965)

147) W.E.Deming, "Statistical Adjustment of Data", J. Wiley & Sons, Inc., New York (1962)

148) F. Strauss and H. Heinz, Annalen., 493, 191 (1932)

F. Strauss and H.J.Weber, ibid, 498, 101 (1932)

149) L. Summers, Chem. Rev., 55, 301 (1955)

150) A.Hassner et al., J. Org. Chem., 35, 1962 (1970)

151) B.Davis and D.H.Williams, J. Org. Chem., 35, 2033 (1970)

152) E.L. Eliel and D.A.Rivard, J.Org. Chem., 1252 (1952)

153) M.M. Kreevay and R.W.Taft, J.Amer. Chem. Soc., 77, 3146 (1955)

154) A. Kankaanpera and M. Lahti, Suomen Kem. (B), 43, 105 (1970)

155) K.B. Wiberg, "Physical Organic Chemistry", p.281 (1963).

156) C.G. Swain et al., J.Amer. Chem. Soc., 87, 1553 (1965)

157) G.Kortum, W.Vogel and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution", Butterworths, London (1961).

158) V. Gold and D.C.A. Waterman, J.Chem.Soc.(B) 849 (1968)

159) B. Capon and D. Thacker, J.Chem.Soc.(B), 185 (1967)

160) see W.P. Jencks and Leinhard, J.Amer.Chem.Soc., 88, 3993 (1966)

161) E.D. Hughes and C.K. Ingold, J.Chem.Soc., 4, 29 (1965)

162) R. Fuchs and A. Nisbet, J.Amer.Chem.Soc., 81, 2371 (1959)

163) P. Haberfield, ibid, 93, 2091 (1971)

164) W.F.K. Wynne-Jones, Trans.Faraday Soc., 34, 245 (1938)

165) E. Anderson and T.H. Fife, J.Amer.Chem.Soc., 93, 1701 (1971)

166) Y. OKamoto and H.C. Brown, J.Org.Chem., 22, 485 (1957)

167) T.H. Fife and L.K. Jao, J.Amer.Chem.Soc., 91, 4217 (1969)

168) see E.G. Sander and W.P. Jencks, ibid, 90, 4377 (1968)

169) C.G. Swain, ibid, 74, 4108 (1952)

170) D.G. Williams et al., J.Org.Chem., 29, 1041 (1964)