ABSTRACT

KINETICS AND EQUILIBRIA IN THE IONISATION OF CARBONYL AND NITRO COMPOUNDS

An Abstract of a thesis submitted to the
University of Stirling
for the degree of
Doctor of Philosophy

S. Grainger

Department of Chemistry
July 1974

ABSTRACT

In the first part isotope effects k_H/k_D for the racemisation of 3-bromocamphor catalysed by hydroxide ion in 15 to 70% by volume dimethyl sulphoxide (DMSO)-water at 25°C have been measured. The errors involved make interpretation difficult but the results are not inconsistent with a maximum isotope effect in the region of $\Delta pK = 0$.

The acid dissociation constant of 3-nitrocamphor has been determined and, with isotope effects k_H/k_D for its ionisation catalysed by a series of bases in water at 25°C, shows a clear maximum at $\Delta pK = 0$. In addition the Brönsted exponents for these reactions suggest the proton (deuteron) is approximately half transferred in the transition state.

In the second part, four series of substituted benzyl compounds [ethyl (α benzyl) acetoacetate, benzyl acetylacetone, benzoylacetone and benzyl malononitrile] have been prepared and Brönsted exponents measured by (a) variation of carboxylate anion catalyst and (b) variation of substrate within a series, with various fixed bases. These Brönsted exponents, generated in different ways, have been found to differ and are rationalised in terms of solvation or electrostatic interactions in the transition state.

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To my wife, Gwen.

CONTENTS

GENERAL INTRODUCTION

The kinetic and equilibrium studies of this thesis have in common the transfer of a proton from carbon acids. This unique cation is the only bare nucleus of any chemical importance under ordinary conditions. Its kinetics are comparatively simple and its small size considerably reduces any steric factors operating. On account of its low mass the isotopic mass ratios are high leading to large equilibrium and kinetic isotope effects. In addition the proton is more likely to give large deviations from classical mechanics, its De Broglie wavelength of 1 - 2Å at ordinary temperatures, being comparable to proton-transfer barriers.

The range of equilibrium constants and rates in which proton-transfers are involved is vast, from pK_A's of less than -11 for pentacyanopentadiene[1] to +50 for methane. The rates of transfer are equally diverse from the undetectable to diffusion controlled at 10^{10}-10^{11} dm^3 mol^{-1} s^{-1}. To cope with this range a host of experimental techniques have been developed both direct and indirect. In the present work rates have been determined directly by observing anion formation and tritium exchange and indirectly by anion scavenging using bromine and the rates of racemisation of optically active compounds.

The vast majority of proton transfer work has involved water as solvent. Though this may appear to complicate the system with the presence of hydrogen and hydroxide ions the complications involved in many non-dissociating solvents are far greater. A relatively new field is that of mixed solvents where highly basic and highly acidic media are used to set up acidity scales for correlation with kinetic studies.

Through the large body of data on rates and equilibria, proton-transfers have played a vital role in elucidating many problems of reaction kinetics, catalysis, salt effects and substituent effects.

A constantly recurring theme is that of selectivity, reactivity and the nature of the transition state. This centres around the Brönsted relationship[2] and primary kinetic isotope effects following predictions by Westheimer[3]. It is not unreasonable that there should exist a relationship between equilibrium and rate constants since the former is merely a ratio of rate constants for forward and reverse reactions. Similarly if we consider a compound becoming more reactive (say by substituent changes) it will eventually react with every reactant molecule it encounters. We can therefore expect an inverse relationship between selectivity and reactivity.

PART I

KINETIC HYDROGEN ISOTOPE EFFECTS IN SOME CAMPHOR DERIVATIVES

INTRODUCTION

Following the discovery of deuterium by Urey[4] and tritium by Rutherford[5] the use of isotope effects has become a powerful tool of mechanistic organic chemists. The values of k_H/k_D commonly lie between 1 and 10 though there are some notably higher values often in cases where steric hindrance makes an important contribution.

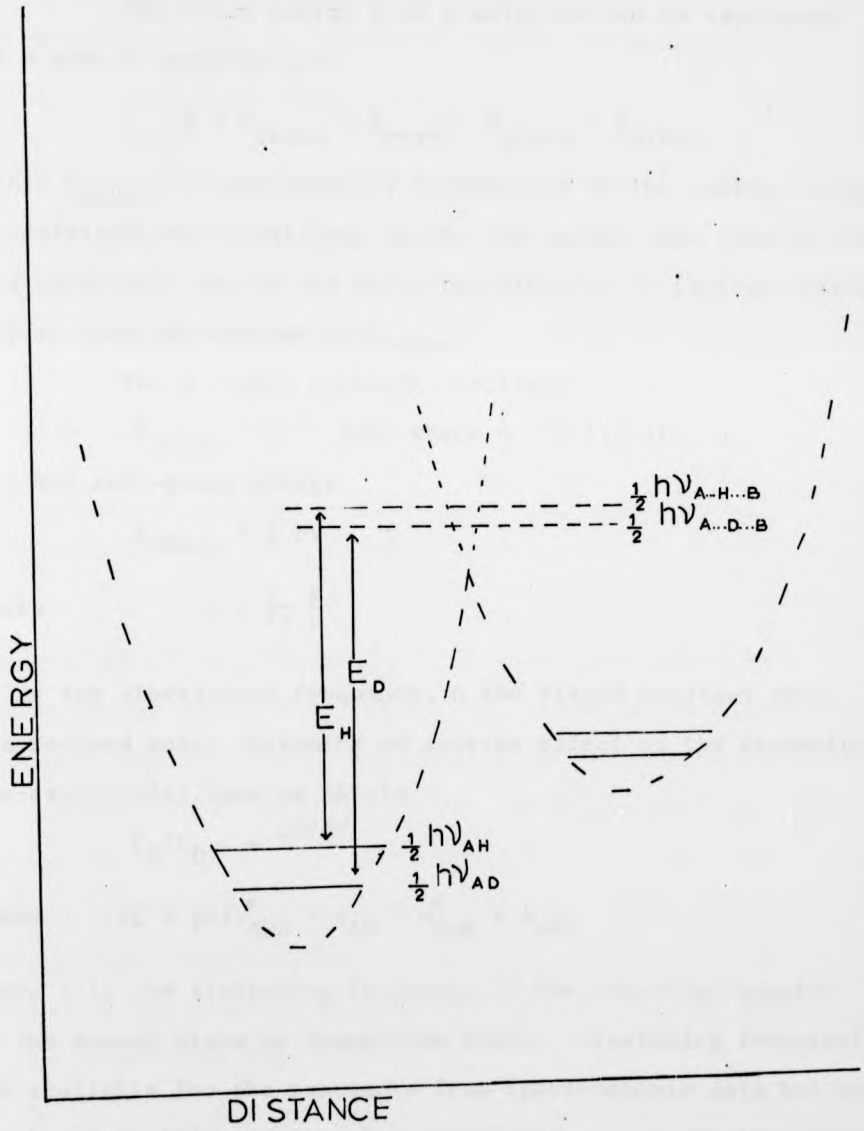
Kinetic hydrogen isotope effects are best considered within the framework of transition state theory. It is assumed that the reactants come together to form a transition state located at the top of an energy barrier to reaction which is at the summit of a pass connecting reactants and products. This transition state is considered as a normal molecule in equilibrium with reactants and products, except that one of its vibrations is replaced by an internal translation.

The proton transfer may be depicted by the interaction of two molecular potential-energy curves proposed by Horiuti and Polanyi[6] and by Bell[7] independently as in figure 1.

This now represents a section of a three-dimensional energy surface. Since the proton has no electrons, repulsion between it and the two bases is small, the only repulsion being between the two bases. Since the proton is considerably lighter than either of these the reaction can be considered approximately as proton movement between two fixed centres. The reaction coordinate now becomes some function of the distance of the proton from the substrate or base. The transition state is slightly lower than the point of intersection of the two curves due to resonance between the two valency states, but this is believed to be small[8] where charge transfer is involved. The minima of the curves are also slightly higher than those

FIG.I.
POTENTIAL ENERGY PROFILE
FOR THE REACTION

$AH + B = (A\text{----}H\text{----}B) = A + HB$



of the separate systems due to repulsive forces. Since all interatomic and intermolecular forces are largely independent of the nuclear mass of the species undergoing transfer, the same energy curve represents both proton and deuteron transfer.

The total energy E of a molecule can be expressed as a sum of contributions

$$E = E_{trans} + E_{rotn} + E_{vibrn} + E_{elect}$$

Since E_{elect} is approximately independent of the isotope being transferred and vibrational quanta are larger than translational and rotational quanta the major contribution to isotope effects arises from differences in E_{vibrn}.

For a simple harmonic oscillator

$$E_{vibrn} = (n + \tfrac{1}{2})h\nu \text{ where } n = 0,1,2 \text{ etc.}$$

and the zero-point energy

$$E_{vibrn} = \tfrac{1}{2} h\nu$$

where $$\nu = \frac{1}{2\pi}\frac{k}{\mu}$$

ν is the vibrational frequency, h the Planck constant and μ the reduced mass. Assuming no isotope effect on the Arrhenius pre-exponential term we obtain

$$k_H/k_D = e^{\Delta E/RT}$$

where $$\Delta E = \tfrac{1}{2}h(\nu^{*}_{ADB} - \nu_{AD} - \nu^{*}_{AHB} + \nu_{AH})$$

where ν is the stretching frequency of the subscript species in the ground state or transition state. Stretching frequencies are available for the reactants from spectroscopic data but not for the transition state. For carbon-hydrogen bonds this gives stretching frequencies of 2800 cm^{-1} and for deuterium 2100 cm^{-1}

corresponding to zero-point energies of 4150 cal mol^{-1} and 3000 cal mol^{-1} respectively, leading to an isotope effect k_H/k_D at 298K in typical carbon acids of approximately 7. Since no information is available for the transition state the simplest calculation assumes none of the zero-point energy is carried over to the transition state. In which case

$$\Delta E = \tfrac{1}{2} h(\nu_{AH} - \nu_{AD})$$

The stretching vibration then becomes a degree of translational motion. Isotope effects have been calculated (Table 1) on this basis for various bonds. From experimental observations this is

TABLE 1

Variation of calculated kinetic hydrogen isotope effects k_H/k_D at 298K with bond type[9]

Bond	N≡C-H	O-H	S-H	F-H	Cl-H	I-H
k_H/k_D	10.2	10.2	5.8	14.9	7.2	5.8

clearly over simplified as k_H/k_D on this basis would be approximately constant for all carbon acids and independent of the base used. Isotopic substitution must therefore affect the energy of the transition state. Although there are many vibrations in the initial and transition state most are largely unaffected by a change in the mass of the atom being transferred. We have however a bending vibration in the transition state whose frequency is dependent on the mass of the atom being transferred thus,

$$\begin{matrix} & \uparrow & \\ A & H & B \\ \downarrow & & \downarrow \end{matrix}$$

which is doubly degenerate, and a stretching vibration

$$\leftarrow A \ldots H \ldots B \rightarrow$$

in which H would move in all but a symmetrical transition state. It is therefore unlikely that the total zero-point energy of both stretching and bending vibrations would be lost in forming the transition state. Bigeleisen[10] however has calculated the maximum isotope effects based on this assumption as $k_H/k_D = 18$ and $k_H/k_T = 60$.

Prompted by observed isotope effects much smaller than the predicted maximum value Westheimer[11] first put forward a model which not only accounted for small isotope effects but predicted a variation with the acidic or basic strength of the reacting species and moreover predicted a maximum value for the isotope effect for a symmetrical transition state. In this case the proton is bound equally to A and B giving no motion to the proton in the stretching vibration above, and therefore a zero-point energy independent of its mass. This has the effect of reducing the isotope effect, due to zero-point energy differences, less in a symmetrical transition state than in an unsymmetrical one.

More quantitative treatments[12,13,14] are based on the linear three-centre model A .. H .. B and consider only the stretching vibrations for which the potential energy ν is given by,

$$2\Delta\nu = k_1(\Delta r_{AH})^2 + k_2(\Delta r_{BH})^2 + 2k_{12}\Delta r_{AH}\Delta r_{BH}$$

where k_1 and k_2 are stretching force constants and k_{12} an interaction force constant, r_{AH} and r_{AB} are the equilibrium internuclear distances and Δ represents the departure from equilibrium. In all these treatments the force constants are disposable parameters and as such have not been related to properties of the initial or final states. However very

extreme values of k_1 and k_2 are necessary (very unsymmetrical transition states) to produce isotope effects appreciably below the maximum.

More O'Ferrall[15,16] has calculated vibrational frequencies and the corresponding isotope effects for multi-centre models of assigned geometry and force constants for transition states varying from reactant to produce like. The stretching force constants and partial bond lengths to hydrogen were obtained from theoretical considerations, while the bending force constants were calculated from those of the reactants and products, in proportion of the bond order in the transition state to each.

Saunders[17] has shown that high bending frequencies in the transition state reduce the isotope effect and More O'Ferrall's[15,16] consideration of non-linear transition states has shown that low values of k_H/k_D are possible albeit in extreme cases.

A number of electrostatic models have been proposed[18,19,20] but are less sophisticated than that due to Bell et al.[21] This considers a proton (or deuteron) moving in the field of two rigid spherical electron distributions. This gives values of the isotope effect with and without tunnelling through a parabolic barrier. Both of these considerations give a maximum, though the former is considerably more pronounced. One important result is that the model suggests a variation of isotope effect with steric hindrance.

The concept of tunnelling has been reviewed by Caldin,[22] and is a consequence of quantum theory. The low mass of the proton imparts a considerable wave nature to the

particle, of wavelength comparable to the energy barrier width. By classical mechanics the probability of a particle of energy E surmounting a barrier of energy E' if E < E' is zero, and when E' < E unity. However according to the quantum theory the probability is a continuous function of E - E' (fig.2). Because of the relatively greater masses involved, deuteron and triton tunnelling is far less likely. Tunnelling therefore increases the rate of proton transfer more than that of deuteron or triton transfer. Further it has a greater effect in a thermoneutral reaction than in one which is exothermic or endothermic. This originates from the differing area available for tunnelling, which is at a maximum when $\Delta G = 0$. (Fig.3). We may therefore modify fig.1 to fig.4 on the grounds of transition state energy differences for different isotopes due to tunnel corrections, regardless of any other differences which may operate.

In summary of isotope effects it is probably true to say that the main effect is in zero point energies leading to k_H/k_D of approximately 7, while tunnelling is necessary to account for the magnitude of observed changes with ΔG and for some high values of k^H/k^D.

The Brönsted β and symmetry

A useful guide in visualising transition state structural models is due to Leffler[23,24]. The Leffler approximation states that the transition state bears the "greater resemblance to the less stable of the species (reactants or products) of a chemical equilibrium". Similar ideas by other authors[25,26] have led the transition states in uphill reactions to be considered as product-like and reactant-like

FIG.2.

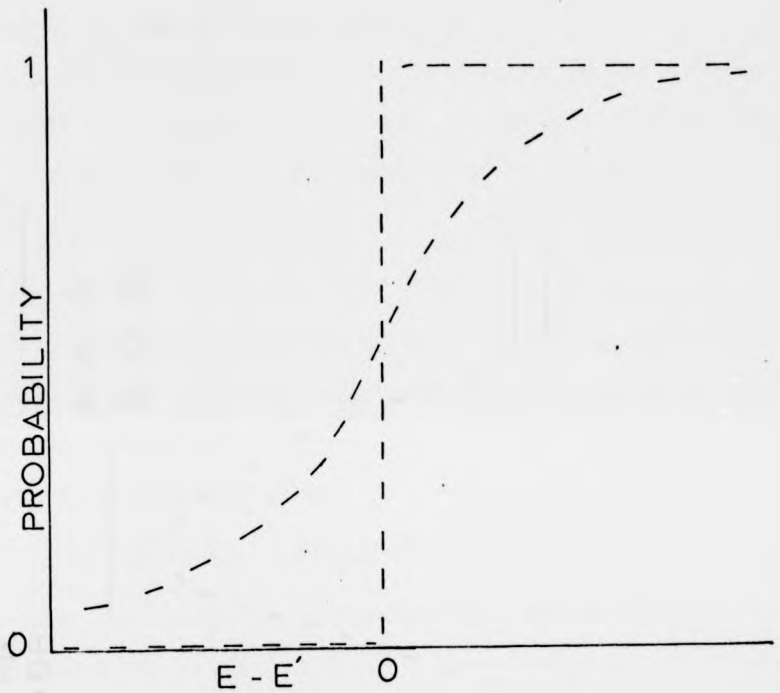


FIG.3.

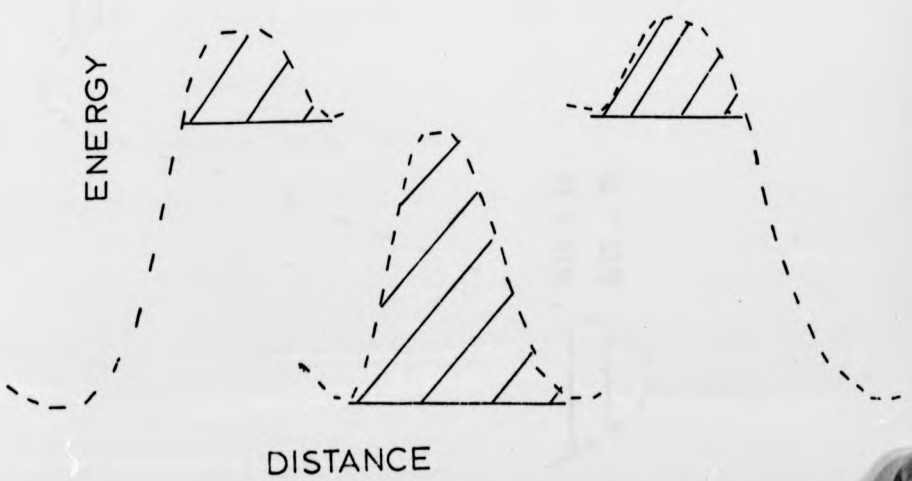
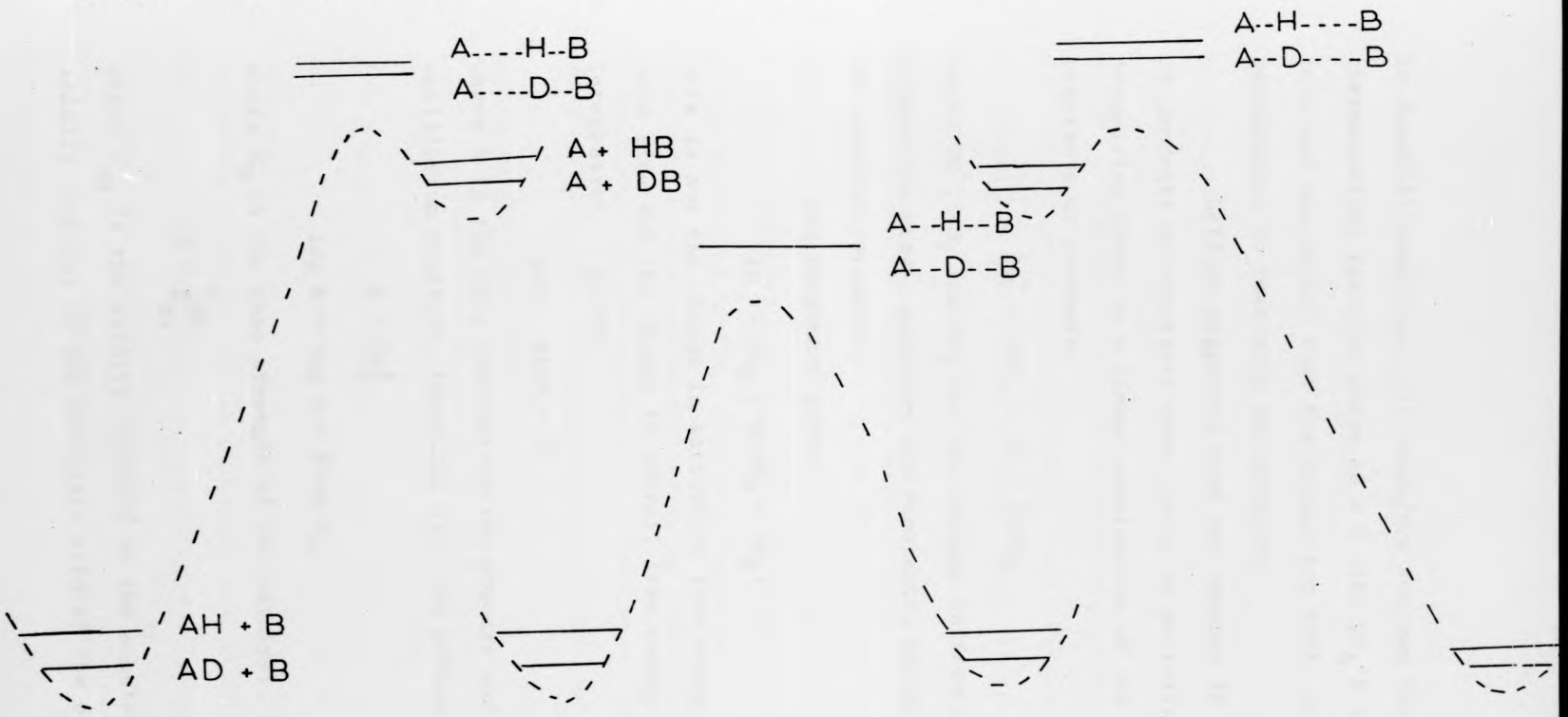


FIG.4. TUNNELLING AND TRANSITION STATE ENERGY



in downhill reactions. It therefore follows that in a thermoneutral reaction where $\Delta G = 0$ (the pK_A's of the acids involved are equal) that the transition state bears an equal resemblance to reactants and products.

Leffler suggested that any changes in free energy of products or reactants were likely to be reflected in the transition state as a linear combination of the changes to reactants or products.

$$\delta G^{\ddagger} = \beta \delta G_P + (1 - \beta)\delta G_R$$

where $\delta G^{\ddagger}$, δG_P and δG_R are the changes in free energy of transition state, products and reactants, while β is an extent of transfer parameter.

Rearrangement gives

$$\delta G^{\ddagger} - \delta G_R = \beta(\delta G_P - \delta G_R)$$

This is now the change in activation free energy on the left hand side and the change in overall free energy on the right. Integration gives:

$$\ln k = \beta \ln K + C$$

where k is the rate constant of the process and K the equilibrium constant, identical with the Brönsted relation

$$k = GK_B^{\beta}$$

$$\log k = \log G + \beta \log K_B$$

where K_B is the base strength of the catalyst, the relation being

$$K = \frac{K_{AH}}{K_{BH}}$$

where K_{AH} is the acidity constant of the substrate and K_{BH} the acidity constant of the conjugate acid of the catalyst.

Thus the extent of transfer parameter β and the Bronsted exponent can be equated.

However Kresge[27] has pointed out additional requirements. The extent of proton transfer may be represented by Z and for β to equal Z requires

$$\delta_R \Delta G^{*} = Z \delta_R \Delta G^{\circ}$$

where δ_R is a substituent stabilisation operator. This is obviously true at the two extremes where forward or reverse reactions are diffusion controlled but to be generally true requires the effect of the substituent on the free energy of the system to be linear in Z, a condition not unreasonable but by no means certain. There is the added complication that quantitative measures of symmetry or extent of reaction depend on the parameter chosen. We have the fraction of negative charge developed on the substrate, the value of the force constants between the hydrogen and the bases, the order of these bonds and the distances involved, all of which give different measures of symmetry or extent of reaction.

Review of Previous Work

Following Westheimer's predictions no evidence for a maximum of isotope effects is mentioned until 1965 when Kresge[28] drew together isotope effects, from various authors, for acid-catalysed hydrogen exchange of aromatic compounds. A plot of k_H/k_D against k_H gave a maximum but few of the pK values of the compounds concerned were known. Moreover those that were known indicated a maximum far removed from ΔpK = 0. However Longridge and Long[29] found the zero ΔpK position to have been misplaced and with their correction the maximum was in the region of ΔpK = 0.

More recent work by Challis and Millar[30] on aromatic hydrogen exchange in a reaction which they believe to be A-S_E-2 shows no maximum. Similarly E2 elimination from a series of substituted phenethyl bromides[31] has shown no maximum. However hydrogen atom transfer from labelled thiols with organic free radicals[32] shows a maximum in k_H/k_D with ΔH. Rising from 2 at ΔH = -25 kcal mol^{-1} to 6.5 in a symmetrical transition state and falling to 4.3 at ΔH = 18 kcal mol^{-1}. Only two different thiols are used in the study but the free radicals vary widely and only two points are available for positive ΔH values, one for each thiol and only one of these is near a curve for a symmetrical maximum about ΔH = 0. The other is well away from the curve and is misplotted in any case.

By far the most conclusive evidence has come from base catalysed proton transfer. It is clear in these investigations that it is desirable to keep structural changes in the substrate and base to a minimum while obtaining maximum changes in acidity differences. These somewhat contradictory requirements are satisfied by the use of aqueous dimethyl sulphoxide solutions of hydroxide ions.

There are three ways in which the symmetry of the transition state may be varied - (a) with fixed substrate the base is varied, (b) with fixed base the substrate is varied, or (c) both substrate and base are fixed and the solvent is varied. In (a) and (b) it is clearly difficult to change the substrate or base over wide acidities without involving gross changes in the reacting species.

The earliest well-established maximum involved k_H/k_D for the water catalysed bromination of a series of ketones[33] and

for the bromination of ethyl and methyl acetoacetate catalysed by six basic anions.[33] In addition there was a correlation between the magnitude of the isotope effect and the exponent β of the Brönsted relation between basic strength and catalytic power, suggesting both quantities depend on the position of the proton in the transition state. Later[34] isotope effects were measured for reactions between hydroxide ions and a series of nitro compounds plus 2-nitropropane and three bases. This now put four points at negative values of ΔpK.

$$\Delta pK = pK_{SH} - pK_{BH}$$

This work also confirmed a high value of k_H/k_D for 2,6-lutidene plus 2-nitropropane, a sterically hindered system, and illustrated the possibility of separate acid-base pairs having vertically displaced maxima with varying steric hindrance. This type of effect has recently been confirmed by Lewis[35] using 2,4,6-trimethylpyridine with methyl 4-nitrovalerate. Indeed the variations from a smooth curve exceed the experimental errors, presumably due to drastic modifications near to the reaction site. Bordwell[36] though has pointed out that the curve at negative values of ΔpK rests on the isotope effects for hydroxide ion on nitromethane, nitroethane and 2-nitropropane, where steric effects and secondary isotope effects may be important.

The Bell-Goodall plot at this stage was rather sparse from ΔpK -5 to +5. Dixon and Bruice[37] however have since studied nitroethane catalysed by ten primary amine bases (ΔpK -2.5 to +3). These results were widely scattered but showed a variation from 6 to 9 between the above limits, though the correlation with the Brönsted relation is poor and β was

0.55 and 0.59 for the proton and deuteron exchange respectively. A considerable number of points in the region -10 to +0.3 have been added by Bordwell[36] using deprotonation and dedeuteration of $ArCHMeNO_2$, $ArCH_2NO_2$ and $CH_2{:}CHCH_2NO_2$ with a few bases ranging in strength from hydroxide to pyridine. These again, however, deviate widely from a smooth curve. Work on the ionisation of nitroethane in highly basic media[38] gave a good smooth curve at negative values of ΔpK though β was rather high at 0.7. Measurements of proton and deuteron abstraction from tricarbomethoxymethane, propan-2-one-1-sulphonate ion and 2-acetylcyclohexanone[39] by a variety of bases lend general weight to the existence of a maximum but again are scattered. In addition general confirmation has been furnished by Lewis[35] and Keeffe[40]. The reactions of a series of nine bases with ethylnitroacetate[39] show a well pronounced maximum with a β again on the high side at 0.65.

While it is evident that a maximum exists the scatter is great, due largely to different classes of compounds and bases being used to construct different parts of the curve.

A possible solution to the problem is contained in the suggestion[41] that dipolar aprotic solvents may be used to alter the symmetry of the transition state. The H_- values of aqueous alkali solutions can be made to vary over more than 14 units by the addition of dimethyl sulphoxide.[42] This increased basicity results mainly from a gradual desolvation on the hydroxide ion.

The first isotope effect maximum[43] obtained by this method involved an elimination reaction; however objections have been raised[44] and the conclusions are somewhat doubtful.

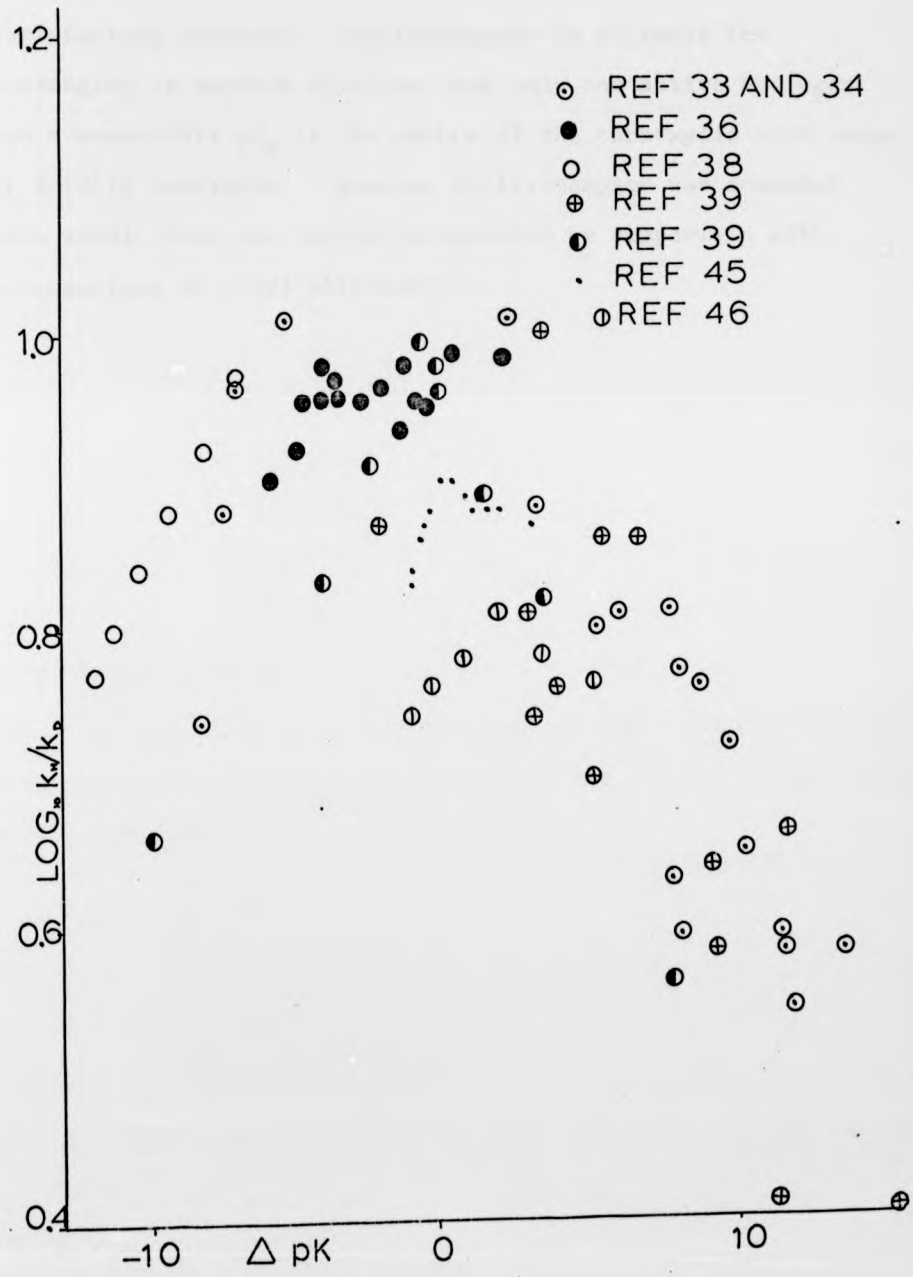
Two simple proton transfers have since been studied[45,46] and both give clearly pronounced maxima in the region of $\Delta pK = 0$, though in both cases the pK_A is inferred from kinetic and other considerations. Moreover both give logk versus H_- plots, which have been interpreted as Brönsted equivalents,[47] of slope 0.5. These results are summarised in figure 5.

One rather negative finding is due to Melander[48] where the methoxide catalysed racemisation of 2-methyl-3-phenylpropionitrile shows a change in k_H/k_D of only 1.2 to 1.5 in going from water to 98% (weight) dimethyl sulphoxide. This is to be expected as the transition state will be very asymmetrical in this "uphill" reaction, resembling the products.

To summarise the previous results we have a hybrid maximum involving many different compounds with different bases and independent maxima for the ionization of menthone,[46] phenylmethylacetophenone[45] and ethyl nitroacetate.[39] As previously mentioned, however, Bordwell[36] has suggested that β and k_H/k_D are either "a poor guide to the extent of proton transfer in the transition state, or that transition state structures vary but little over wide ΔpK ranges". This statement is based on (a) inaccuracy, (b) differing steric and tunnelling contributions, and (c) the possibility of prerate-limiting equilibria. These objections appear to apply only to the compound maximum and not to the results for menthone, phenylmethylacetophenone and ethyl nitroacetate.

The present investigation is aimed at a further study of isotope effects for both positive and negative values of ΔpK. Camphor derivatives are convenient, apart from being readily available, in that they are optically active at the

FIG.5.
COLLECTED ISOTOPE EFFECTS
VERSUS △ pK



reaction centre, an attraction for dimethylsulphoxide-water systems where scavenging using bromine is not possible. Kinetics by ^1H n.m.r. are of course possible but rarely of satisfactory accuracy. 3-nitrocamphor is suitable for scavenging in aqueous solution, has only one active hydrogen and a measurable pK_A in the centre of the carboxylic acid range of acidity constants. However 3-nitrocamphor was somewhat more acidic than was initially expected by comparison with nitroacetone or ethyl nitroacetate.

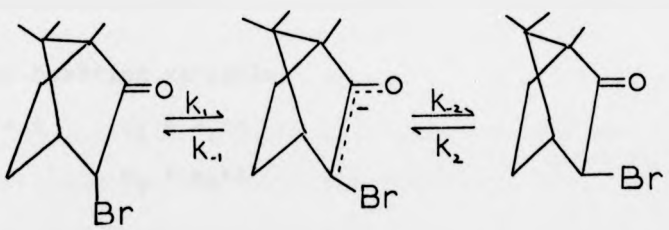
EXPERIMENTAL

Theory

The mechanism of base catalysed prototropy in the group -CH-C=O is clearly understood

$$B^- + -CH-C=O \underset{2}{\overset{1}{\rightleftharpoons}} BH + -C=C-O^-$$

It is now well proven that step 1 is rate determining.[49] If we consider 3-bromocamphor, there are three optically active centres but two of these are fixed and make this compound a derivative of D(+) camphor. We have



of concentrations C_1 C_- and C_2

where the two forms differ in stereochemistry at the α carbon. Under steady state conditions and where all k's are pseudo first-order rate constants

$$\frac{dc_1}{dt} = -k_1c_1 + k_{-1}c_-$$

$$\frac{dc_-}{dt} = -(k_{-1} + k_{-2})c_- + k_1c_1 + k_2c_2$$

$$\frac{dc_2}{dt} = -k_2c_2 + k_{-2}c_-$$

By the steady state approximation since the anion is very reactive

$$\frac{dc_-}{dt} = 0 \quad \text{or} \quad \frac{dc_1}{dt} + \frac{dc_2}{dt} = 0$$

and $$c_- = \frac{k_1c_1 + k_2c_2}{k_{-1} + k_{-2}}$$

therefore $$\frac{dc_1}{dt} = -k_1c_1 + k_{-1}\frac{(k_1c_1 + k_2c_2)}{k_{-1} + k_{-2}}$$

$$\frac{dc_2}{dt} = -k_2c_2 + k_{-2}\frac{(k_1c_1 + k_2c_2)}{k_{-1} + k_{-2}}$$

$$\frac{dc_1}{dt} = \frac{k_2k_{-1}c_2 - k_1k_{-2}c_1}{k_{-1} + k_{-2}} \text{ and } \frac{dc_2}{dt} = \frac{k_{-2}k_1c_1 - k_{-1}k_2c_2}{k_{-1} + k_{-2}}$$

Using $$\frac{dc_1}{dt} + \frac{dc_2}{dt} = 0$$

let at $t = 0$ $\quad c_1 \equiv a_1$

$\quad c_2 \equiv a_2$

Let x be the reaction variable

at $t = t$ $\quad c_1 = a_1 - x$

$\quad c_2 = a_2 + x$

$$\frac{dx}{dt} = \frac{k_1k_{-2}(a_1 - x) - k_2k_{-1}(a_2 + x)}{k_{-1} + k_{-2}}$$

At equilibrium

$$0 = \frac{k_1k_{-2}(a_1 - x_\infty) - k_2k_{-1}(a_2 + x_\infty)}{k_{-1} + k_{-2}}$$

$$\frac{dx}{dt} = \frac{k_1k_{-2}(x_\infty - x) - k_2k_{-1}(x - x_\infty)}{k_{-1} + k_2}$$

$$= \frac{k_1k_{-2} + k_2k_{-1}}{k_{-1} + k_{-2}}(x_\infty - x)$$

$$= k_{obs}(x_\infty - x)$$

where $$k_{obs} = \frac{k_1k_{-2} + k_2k_{-1}}{k_{-1} + k_{-2}}$$

However $k_{-1} >> k_{-2}$ [50] in camphor itself and is likely to be ever more so here where the bromine has been shown by N.M.R. to interact with the methyl group[51]

$$k_{obs} = \frac{k_1k_{-2} + k_2k_{-1}}{k_{-1}}$$

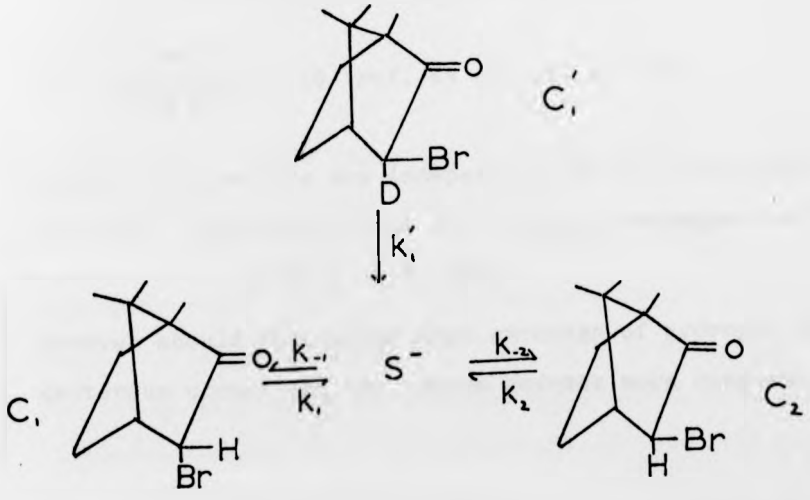
$$= k_2(\frac{k_1k_{-2}}{k_{-1}k_2} + 1)$$

$$= k_2(\frac{1}{K} + 1)$$

where $$K = \frac{k_{-1}k_2}{k_1k_{-2}} = \frac{[\text{ENDO Bromocamphor}]}{[\text{EXO Bromocamphor}]}$$

K is known to be large ($\approx$ 25) from specific rotation measurements[52,53] and is easily observed by ^{1}H n.m.r. In addition no variation in initial or final rotations was observed. Polarimetry therefore measures k_2.

For the deutero-compound we have



This will in general not give first order kinetics unless the formation of the two products are kinetically controlled, $\frac{c_2}{c_1} = \frac{k_{-2}}{k_{-1}}$ or equilibrium controlled, $\frac{c_2}{c_1} = k_{-2}k_1/k_{-1}k_2$.

It can be shown that both of these cases require $k_1 = k_2$. This is not unlikely in view of the results from 3-nitrocamphor. Strictly first order kinetics were always obtained.

For 3-nitrocamphor we have

$$SH + B^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} S^- + BH \xrightarrow[k_2]{Br_2} \text{Products}$$

The normal steady state treatment gives

$$-\frac{d[SH]}{dt} = \frac{k_1 k_2 [SH][B^-][Br_2]}{k_{-1}[BH] + k_2[Br_2]} = -\frac{d[Br_2]}{dt}$$

Since the rates observed are independent of bromine concentration

$$k_2[Br_2] >> k_{-1}[BH]$$

and $-d[SH]/dt = k_1[SH][B^-]$

Bromide ions are also present and we have the equilibrium

$$Br_2 + Br^- \rightleftharpoons Br_3^-$$

$$K = \frac{[Br_3^-]}{[Br_2][Br^-]} = 16 \text{ (ref. 54 and 55) at } 25^\circ C$$

However the results are independent of the particular brominating species. The deutero case is of course analogous so long as

$$k_2[Br_2] >> k_{-1}[BH]$$

However should this break down exchange of hydrogen for deuterium occurs and the system becomes more complex.

Instrumentation

Polarimetry was carried out on Perkin-Elmer model 141 polarimeter. This is a single beam instrument working on the optical null principle. The light beam of a sodium or mercury lamp is passed through one of five filters, whereby the proper wavelength interval is selected. This then passes through a calcite prism polariser which (apart from polarising the beam) oscillates the light to $\pm$ .7° at the mains frequency. The light then passes through a 10 cm water-jacketed cell with quartz end faces to the analyser and photomultiplier which converts the light signal into electrical signals. Of these the 50 cycle component is amplified and fed to drive the analyser to the null position (crossed polarising prisms). With a sample introduced these prisms will no longer be at 90° and the deviation is read on a mechanical counter. This signal also drives an endless potentiometer for automatic readings.

Temperature control was effected by a Grant SB2 thermostatic bath circulating water round the sample cell. The temperature of which was judged to be midway between that of the bath and the returning water (a difference of 0.3°C). Temperature control was to $\pm$ 0.1°C.

U.V. work was carried out using a Gilford 2400 or 2400S automatic recording spectrophotometer. This consists of deuterium and tungsten lamps, the light beam passing through a prism monochromator to the automatic sample handling system. This accommodates four cells (up to 1 cm) and cycles automatically at preset time intervals. The heart of the system is a photometer providing linear readings of absorbance from 0-3A. This being presented either as a four place digital indication

of absorbance or as a voltage proportional to absorbance which is fed to a pen recorder of continuously variable span in the range 0 to 3A. Temperature control was by means of a Grant SB2 thermostatic bath circulating water round the side plates of the sample compartment which incorporates a platinum resistance thermometer. This is referred to internal standards and periodically to a standard thermometer. Control is to $\pm$ 0.1°C.

Materials

The preparation of 3 bromo-(+)-camphor was by addition of bromine to D-(+)-camphor according to Ingersoll[56]. Recrystallisation from 95% ethanol gave a white solid m.p. 75°C, lit 76°C.[57] This is the endo bromocamphor as shown from the doublet at 5.5τ in ^{1}H n.m.r. Attempted separation of an equilibrated mixture of optical isomers by thin layer chromatography failed. The exo-bromo isomer was prepared from this by the method of Lowry,[52] consisting of equilibration in ethanol-ethoxide, acidification and fractional crystallisation, the less soluble endo-bromo isomer precipitating, while the exo-bromo isomer concentrates in the mother liquors. This procedure eventually gave a solid

$$\alpha^{20}_{546.1} = 39^\circ \text{ (c = 1.5g/100 ml in ethanol)}$$

compared with the endo isomer $\alpha^{20}_{546.1} = 162^\circ$ (c = 2.3g/100 ml in ethanol) lit 165° [57]. This material was then sublimed at 0-5°C 1 mm Hg.

$$\alpha^{20}_{546.1} = 43^\circ \text{ (c = 0.4 g/100 ml in ethanol)}$$

c.f. pure exo -40° [57]

$$\alpha^{20}_{365} = 367^\circ \text{ (c = 0.4 g/100 ml in ethanol)}$$

compared with the pure endo isomer $\alpha^{20}_{365} = 902^\circ$.

This as well as 'H n.m.r. and g.l.c. (15% carbowax on chromosorp W at 140°C) shows 60% exo-isomer.

For the deuterated material 10g of endo-bromocamphor were dissolved in 200 ml of dry dioxan and 100 ml of deuterium oxide (Fluorochem 99.77%D), a small amount of clean sodium metal was added and the solution kept at 80°C for one hour. Acidification and evaporation to dryness gave the deutero-compound. 'H n.m.r. showed no proto impurity. This procedure gives an equilibrium mixture of exo and endo isomers which were separated by g.l.c. using 10% carbowax on chromosorb W (Varian Autoprep 700) at 175°C. 'H n.m.r. after separation showed no proto impurity.

The 3-nitro-(+)-camphor was prepared by permanganate oxidation[58] of isonitrosocamphor prepared by the method of Claisen[59]. Recrystallisation from ethanol yielded the pure compound

m.p. 101 °C Lit 103°C [57]

α_D^{20} = -109° (c = 5g/100 ml in benzene) Lit -104° [58]

'H n.m.r. in deuterochloroform showed this to be 90% the endo-nitro isomer, however in dioxan it is completely endo and in acetonitrile 80% endo. The infra red spectrum shows nitro group absorption at 1560 and 1350 cm^{-1} and carbonyl absorption at 1720 cm^{-1}.

Deuterated 3-nitrocamphor was prepared by adding 5g of the proto-compound to 50 ml of deuterium oxide followed by sufficient sodium deuteroxide to dissolve the compound and then made acid with concentrated hydrochloric acid. This process was repeated and 'H n.m.r. showed no proto impurity.

A number of other preparations were carried out. The preparation of 3-cyano-(+)-camphor was attempted by forming the anion of camphor with sodamide, followed by reaction with ethyl formate[60] and hydroxylamine hydrochloride.[61] This was unsuccessful probably due to a very poor yield of anion. This was repeated using sodium naphthalide to form the anion.[62] Steam distillation and recrystallisation from ethanol gave 3-cyano-(+)-camphor.

m.p. 128°C Lit 127-8 [57]

α_D^{25} = 43° (c = 0.15 g/100 ml in ethanol)

α_{365}^{25} = 181° (" " " ")

At equilibrium

α_D^{25} = 155°

α_{365}^{25} = 865°

However this change in rotation was too small to be followed by polarimetry due to limited solubility in aqueous dimethyl-sulphoxide, e.g. in 15% volume DMSO-water a saturated solution gave a change of less than 0.04°. ^{1}H n.m.r. showed both isomers to be present in the ratio endo-cyano:exo-cyano = 11:1. Absorption of the anion in buffer solutions at 275 nm showed an approximate pK_A of 10.

D-ketopinic acid was prepared according to Bartlett[63] and brominated at C3 in acetic acid. Partial separation of the isomers was carried out as for 3-bromocamphor giving a 50/50 mixture of isomers at C3.

3,3'-dibromocamphor was prepared by bromination[58] of 3-bromocamphor and recrystallised from ethanol.

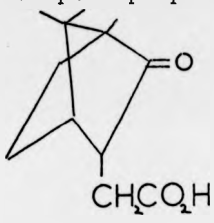
m.p. 57°C (Lit 60°C)[58]

The preparation of trans-π-bromo-3-nitrocamphor was according to Corey[64] and Lapworth.[65]

m.p. 142°C $\quad \alpha_D^{25} = 155^\circ$

However it was found that the isomers could not be separated as described in ref. 65.

The attempted preparation of



using sodiocamphor and ethyl bromoacetate followed by alkali hydrolysis always gave the disubstituted product (B.p. 80°C at 0.5 mm Hg) even with excess sodiocamphor.

Water was deionised and distilled from potassium permanganate. It was then boiled for 30 min. and cooled under nitrogen.

Dimethyl sulphoxide was purified according to Johnson[66] using molecular sieves, barium oxide, followed by distillation under reduced pressure.

Dioxan was dried with molecular sieves then refluxed with lithium aluminium hydride and distilled immediately before use.

Acetic acid, hydrochloric acid and sodium hydroxide solutions were prepared from B.D.H. volumetric ampoules.

Potassium chloride, glycine, benzoic acid, potassium dihydrogen phosphate and monochloroacetic acid were B.D.H. 'AnalaR' materials and were used without further purification though monochloroacetic acid solutions were titrated with standard alkali before use.

Dichloroacetic acid was distilled at 100°C and 20 mm Hg. Its solution was also titrated before use and the same solution used for buffer preparation.

DL-Mandelic acid was recrystallised from water.

m.p. 118 °C Lit 118[57]

Malonic acid was sublimed at 100°C, 10 mm Hg.

m.p. 137°C Lit 135.6°C [57]

Furoic acid was recrystallised from water and sublimed at 120°C 20 mm Hg.

m.p. 130°C Lit 133°C [57]

m-Nitrobenzoic acid was recrystallised from 50:50 petroleum ether, benzene.

m.p. 139°C Lit 140°C [57]

Cyanoacetic acid was recrystallised from methylene chloride-petrol (60-40).

m.p. 65-66°C Lit 66°C [57]

Lactic acid 'AnalaR' was distilled at 122°C 18 mm Hg.

All buffer solutions of varying concentrations were prepared by dilution of the most concentrated, with the ionic strength made up to 0.2 mol dm^{-3} by adding potassium chloride. The pH values were checked (glass electrode) and adjusted where necessary by addition of hydrochloric acid.

In the case of dichloroacetic, monochloroacetic and mandelic acids the concentration of anion was calculated by adding the hydrogen ion concentration to the concentration of alkali added, assuming an activity coefficient of 0.73.

Procedure

This consisted essentially of four procedures:

(a) The racemisation of 3-bromo-(+)-camphor in mixed solvents catalysed by hydroxide ion or various buffers.

(b) The bromination of 3-nitro-(+)-camphor catalysed by various carboxylate anions.

(c) The ionisation of 3-nitro-(+)-camphor catalysed by acetate anion followed by direct observation of the 3-nitro-(+)-camphor anion.

(d) The determination of the acidity constant of 3-nitro-+-camphor by observation of its anion in buffer solutions.

In the racemisation experiments all solutions were made up by volume. To a known volume of dimethyl sulphoxide 0.2 ml of 0.15 mol dm^{-3} (this is a minimum, used in highly aqueous media) 3-bromo-camphor in DMSO was added. The necessary amount of carbon dioxide-free water was added to give a total volume of 25 ml and the solution thermostated at 25°C. Sodium hydroxide solution was then added from a Hamilton syringe, the sample cell filled and the rotations observed with time. This gave changes in rotation of approximately 0.2°. In the initial experiments readings were taken manually, though later ones involved an automatic data acquisition system[67] designed in this department. Rate constants were calculated by a local version of the general least squares program LETAGROP VRID of Sillen.[68,69] For a kinetic expression of a given type this program can be used to determine the values of all the parameters which give the best fit to a set of experimental results; for example, for a simple first-order change the variation of the rotation r with time is given by

$$r = r_\infty - (r_\infty - r_o)e^{-kt}$$

and the values of r_∞, r_o and k are all treated as parameters whose best values are given by the program. This avoids the errors inherent in determining r_∞ though readings are needed over several half-lives. Further, estimates of r_o and r_∞ must be reasonable with errors on the intermediate points varying in a random manner.

In the bromination work to 2-3 ml of buffer containing 0.1 mol dm^{-3} potassium bromide, 10 µl of 0.05 mol dm^{-3} bromine in 1 mol dm^{-3} potassium bromide were added. The cell was then thermostated for five minutes, which also removed any impurities capable of rapid reaction with bromine. The absorbance was then measured at 330 nm and 4 µl of 0.07 mol dm^{-3} nitrocamphor in dioxan added on a small plastic stirrer to aid rapid mixing. The total fall in absorbance corresponded to 1 mole of bromine per mole of substrate being consumed and the rates were independent of bromine concentration. Using iodine instead of bromine gave no reaction.

In the case of the deuterated compound the stock solutions were in dioxan but a small amount of deuterium oxide was added in order that any racemisation should not introduce proto impurity.

For acetate catalysis the rates were checked by direct observation of the anion (317 nm). This was only carried out at one pH (5.75) which m eans that at equilibrium we have almost 100% anion and the back reaction is unimportant.

The pK_A of 3-nitrocamphor was obtained from observing the anion in standard phthalate buffers near its pK_A and in strong base. The absorption of the molecular species at this

wavelength is zero within experimental error.

Rate constants for this spectrophotometric work were obtained from the data by a plot of $\log_e(A_t - A_\infty)$ versus time where A represents the absorption at time t and infinity.

Results

In the following tables where particular runs have been duplicated the average rate constant is given.

As previously stated cyanocamphor showed too small a change in rotation for the available solubility to be useful, nor would it scavenge, showing no reaction with bromine.

The racemisation of 3-bromoketopinic acid in 40% vol dioxan solutions with approximately 0.5 mol dm^{-3} hydrochloric acid was very slow. It was therefore carried out at 90°C in sealed ampoules. However, the rotation did not change in a first-order manner, presumably due to decomposition, and work was discontinued.

The isomers of trans-π-bromo-3-nitrocamphor could not be separated though it would probably scavenge.

The bromination of 3-bromocamphor was first-order in bromine up to 6×10^{-3} mol dm^{-3} bromine. The product formation was also followed (ε = 834 at 245 nm, ε of 3-bromocamphor = 95) and showed the same behaviour.

The measurement of the pK_A of 3-bromocamphor was attempted by spectrophotometric observation of the anion in highly basic media. The solutions were degassed prior to mixing but results were irreproducible and showed changes with time, presumably due either to residual oxygen in the apparatus or to condensation of the anion.

In a single experiment with nitrocamphor the formation of the anion was observed at pH 5.6 from a mixture of endo and exo isomers. The last 10% of reaction was expanded to improve accuracy and the data treated[68,69] for two simultaneous first order reactions. This gave no improvement in standard deviation over a simple first-order treatment and it seems reasonable to conclude that both isomers are ionising at the same rate.

Acidification of a concentrated solution of the anion with hydrochloric acid precipitated nitrocamphor with endo:exo NO_2 = 28:1 and changed over 3 days in deuterochloroform to 18:1. The initial value is the ratio of exo:endo proton addition to the anion, assuming the precipitation is sufficiently rapid that no racemisation occurs.

Typical kinetic results are shown for racemisation and scavenging experiments.

TABLE 2

pK_A of 3-nitrocamphor at 25°C in aqueous solution, I = 0.1 mol dm^{-3}

pH of medium	absorbance	pK_A
14	1.300	-
0	0	-
3.00	0.370	3.40
3.30	0.562	3.42
3.40	0.636	3.42
3.50	0.750	3.36
3.60	0.781	3.42
4.00	1.025	3.43

Average pK_A = 3.42

The buffers used are phthalate taken from Robinson and Stokes.[70] The absorbances are at 317 nm with 1 x 10^{-4} mol dm^{-3} substrate in a 1 cm cell.

TABLE 3

Rates of racemisation of 3-bromocamphor in sodium hydroxide solutions at 25°C.

Vol % DMSO = 15

$10^4[\bar{O}H]$	20	40	80	160
$10^5\ k_H/s^{-1}$	102	212	432	857
$10^4[\bar{O}H]$	100	200	300	400
$10^5\ k_D/s^{-1}$	65	151	190	312

Vol % DMSO = 25

$10^4[\bar{O}H]$	20	40	70	
$10^5\ k_H/s^{-1}$	143	277	487	
$10^4[\bar{O}H]$	100	200	300	400
$10^5 k_D/s^{-1}$	88	202	296	394

Vol % DMSO = 35

$10^4[\bar{O}H]$	8	12	20	
$10^5\ k_H/s^{-1}$	73	117	203	
$10^4[\bar{O}H]$	100	200	300	400
$10^5\ k_D/s^{-1}$	129	276	399	578

Vol % DMSO = 45

$10^4[\bar{O}H]$	8	12	16	20
$10^5\ k_H/s^{-1}$	123	195	263	330
$10^4[\bar{O}H]$	100	200	300	400
$10^5\ k_D/s^{-1}$	235	500	715	980

Vol % DMSO = 50

$10^4[\bar{O}H]$	4	8	12		16
$10^5\ k_H/s^{-1}$	86	180	270		360
$10^4[\bar{O}H]$	100	150	200	250	300
$10^5\ k_D/s^{-1}$	330	500	630	840	1025

Vol % DMSO = 60

$10^4[\bar{O}H]$	2	4	6	8
$10^5\ k_H/s^{-1}$	79	210	308	428
$10^4[\bar{O}H]$	20	40	60	80
$10^5\ k_D/s^{-1}$	120	315	470	647

Vol % DMSO = 70

$10^4[\bar{O}H]$	1	2	3	4
$10^5\ k_H/s^{-1}$	107	307	513	707
$10^4[\bar{O}H]$	10	20	30	40
$10^5\ k_D/s^{-1}$	225	545	880	1190

TABLE 4

Values of $k^{OH} = k/[\bar{O}H]$ for racemisation of 3-bromocamphor at 25°C.

Vol % DMSO	$k_H^{OH}/s^{-1}mol^{-1}dm^3$	Standard Deviation	Intercept of Catalytic plot	Standard Deviation	$\log_{10}k_H^{OH}$
15	0.539	0.002	-0.00003	0.00002	-0.268
25	0.689	0.03	+0.00004	0.0001	-0.162
35	1.08	0.005	-0.00013	0.00001	0.033
45	1.72	0.01	-0.00013	0.00002	0.236
50	2.28	0.01	-0.00004	0.00001	0.358
60	5.72	0.1	-0.0003	0.00008	0.757
70	20.06	0.1	-0.0009	0.00003	1. 302

Vol % DMSO	$k_D^{OH}/s^{-1}mol^{-1}dm^3$	Standard Deviation	Intercept of Catalytic plot	Standard Deviation	$\log_{10}k_D^{OH}$
15	0.078	0.007	-0.00016	0.0002	-1.11
25	0.101	0.002	-0.00008	0.00006	-0.99
35	0.147	0.005	-0.00022	0.0001	-0.83
45	0.245	0.005	-0.00005	0.0001	-0.61
50	0.346	0.009	-0.0003	0.0002	-0.46
60	0.868	0.02	-0.0005	0.0001	-0.06
70	3.23	0.02	-0.00098	0.00006	0.51

TABLE 5

Racemisation of 3-bromocamphor in 15% vol DMSO with glycine catalysis $H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 9.0

$[H_2NCH_2CO_2^-]$	0.100	0.200	0.400
$10^4 k_H/s^{-1}$	1.28	1.57	2.03

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 4.0

$[H_2NCH_2CO_2^-]$	0.095	0.19	0.38
$10^4 k_H/s^{-1}$	0.792	0.967	1.32

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 2.3

$[H_2NCH_2CO_2^-]$	0.0875	0.175	0.353
$10^4 k_H/s^{-1}$	0.44	0.65	1.02

Average k_H(glycine) = 2.1×10^{-4} s^{-1} mol^{-1} dm^3

, TABLE 6

Racemisation of 3-bromocamphor in 20% (weight) dioxan at 25°C

$10^3[\bar{O}H]$	1.0	2.0	4.0	8.0
$10^5\ k_H/s^{-1}$	38.3	78.3	158	330

$$k_H^{OH} = 0.417\ s^{-1}\ mol^{-1}\ dm^3$$

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 9. 0

$[H_2NCH_2CO_2^-]$	0.095	0.190	0.380
$10^4\ k_H/s^{-1}$	0.907	1.08	1.41

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 4.0

$[H_2NCH_2CO_2^-]$	0.0857	0.178	0.358
$10^4\ k_H/s^{-1}$	0.507	0.640	0.917

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 2.3

$[H_2NCH_2CO_2^-]$	0.083	0.165	0.333
$10^4\ k_H/s^{-1}$	0.350	0.457	0.703

Average k_H(glycine) = $1.5 \times 10^{-4}\ s^{-1}\ mol^{-1}\ dm^3$

TABLE 7

Racemisation of 3-bromocamphor in 45% (weight) dioxan at 25°C

$10^4[\bar{O}H]$	10	20	40
$10^5\ k_H/s^{-1}$	45.0	93.3	192

$k_H^{OH} = 0.49\ s^{-1}\ mol^{-1}\ dm^3$

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 9.0

$[H_2NCH_2CO_2^-]$	0.072	0.145	0.289
$10^5\ k_H/s^{-1}$	3.07	3.82	5.47

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 4.0

$[H_2NCH_2CO_2^-]$	0.068	0.135	0.27
$10^5\ k_H/s^{-1}$	1.73	2.52	3.75

$H_2NCH_2CO_2^-/H_3^+NCH_2CO_2^-$ = 2.3

$[H_2NCH_2CO_2^-]$	0.063	0.125	0.25
$10^5\ k_H/s^{-1}$	1.30	1.92	3.20

Average k_H(glycine) = $1.03 \times 10^{-4}\ s^{-1}\ mol^{-1}\ dm^3$

Rates of bromination of 3-nitrocamphor.

Of the materials purified for buffer solutions furoic acid and cyanoacetic acid gave a rapid reaction with bromine and lactic acid gave a slow reaction, but the rate

constants were irreproducible after the buffers had stood for a few days. Nitrobenzoic acid absorbed at 330 nm. No measurements are therefore reported for these buffer systems. No acid catalysis was detected. It is clear from Table 10 that under the conditions used the kinetics have the form

$$k(obs) = k_o + k[RCO_2^-]$$

TABLE 8

Rates of bromination of 3-nitrocamphor in acid solution at 25°C

k_H/s^{-1}	[HCl]
0.0463	0.2
0.0478	0.15
0.0499	0.125
0.0508	0.09
0.0488	0.05
0.0513	0.03
0.0521	0.009
0.0544	0.0045

There appears to be a general trend to increased rate with more dilute hydrochloric acid. This is unlikely to be hydroxide catalysis and may be negative salt effects since ionic strength was not kept constant.

TABLE 9

Carboxylate anion catalysed bromination of 3-nitrocamphor at 25°C

Dichloroacetate pH = 1.26 (I = 0.3 not 0.2 mol dm^{-3})

$10^2[RCO_2^-]$	6	12	18	24	30
$10^3 k_H/s^{-1}$	80	118	154	193	231
$10^3 k_D/s^{-1}$	17.0	23.5	28.0	33.7	40.4

Monochloroacetate pH = 2.40

$10^4[RCO_2^-]$	12.0	23.5	35.5	59.5
$10^3 k_H/s^{-1}$	49.3	52.9	56.9	64.8
$10^3 k_D/s^{-1}$	11.5	12.0	12.6	13.6

Mandelate pH = 3.335

$10^4[RCO_2^-]$	33	66	115	164
$10^3 k_H/s^{-1}$	78.0	104.0	137.0	172.5
$10^3 k_D/s^{-1}$	14.1	18.1	23.0	26.8

Benzoate pH = 4.59

$10^4[RCO_2^-]$	52	103	180	258
$10^3 k_H/s^{-1}$	129	197	308	398
$10^3 k_D/s^{-1}$	21.3	30.5	45.4	59.6

Acetate pH = 3.75

$10^4[RCO_2^-]$	3.3	6.6	16.5	33.0
$10^3 k_H/s^{-1}$	60.0	68.0	89.5	130
$10^3 k_D/s^{-1}$	12.8	13.6	16.8	22.2

TABLE 9 (contd.)

Acetate pH = 4.69

$10^4[RCO_2^-]$	16	32	85	169
$10^3 k_H/s^{-1}$	90	124	253	455

Acetate pH = 5.63 (by anion observation)

$10^4[RCO_2^-]$	39	53	70.5	88
$10^3\ k_H/s^{-1}$	131	171	210	250

Malonate pH = 5.70

$10^4[RCO_2^{2-}]$	5.0	10.0	17.4	25.0
$10^3 k_H/s^{-1}$	67	86	127	160
$10^3 k_D/s^{-1}$	16.1	19.6	27.1	32.0

Phosphate pH = 6.81

$10^4[HPO_4^{2-}]$	16.0	25.0	32.5	41.0
$10^3 k_H/s^{-1}$	328	488	625	760
$10^3 k_D/s^{-1}$	96	150	193	238

TABLE 10

Summary of rate constants for proton (deuteron) abstraction from 3-nitrocamphor by various bases in water at 25°C

Base	$k_H/s^{-1}mol^{-1}dm^3$	intercept/s^{-1}	$k_D/s^{-1}mol^{-1}dm^3$	intercept/s^{-1}	k_H/k_D
Dichloroacetate	0.63	0.043	0.098	0.0110	6.4
Monochloroacetate	3.29	0.045	0.415	0.0110	7.3
Mandelate	7.18	0.055	0.96	0.0115	7.5
Benzoate	13.38	0.060	1.87	0.013	7.2
Acetate pH 3.75	23.3	0.052	3.43	0.0116	6.8
Acetate pH 4.69	23.7	0.050	-	-	-
Acetate pH 5.63	23.9	0.044	-	-	-
Malonate	49	0.040	8.4	0.0117	5.8
Phosphate	176	0.050	52.0	0.006	3.4
Average intercepts		0.049		0.0108	
H_2O					4.5

Typical data from a racemisation experiment.
D-3-bromocamphor in 70% DMSO with 0.002M OH^- (Plotted in Fig. 6)
TABLE 11

Time sec^{-1}	Rotation*	$-\log_e(Rotation^*_\infty - Rotation^*_t)$
0	1.796	1.546
25	1.826	1.698
50	1.847	1.820
75	1.865	1.938
100	1.882	2.063
125	1.900	2.216
150	1.911	2.322
175	1.924	2.465
200	1.939	2.659
225	1.948	2.797
250	1.955	2.919
275	1.965	3.124
300	1.968	3.194
325	1.975	3.381
350	1.977	3.442
375	1.978	3.474
400	1.983	3.649
425	1.990	3.963
450	1.988	3.863
475	1.992	4.074
500	1.997	4.423
525	1.998	4.509
550	2.000	4.710
575	1.999	4.605
600	2.000	4.710
625	2.002	4.961
650	2.004	5.298
∞	2.009	

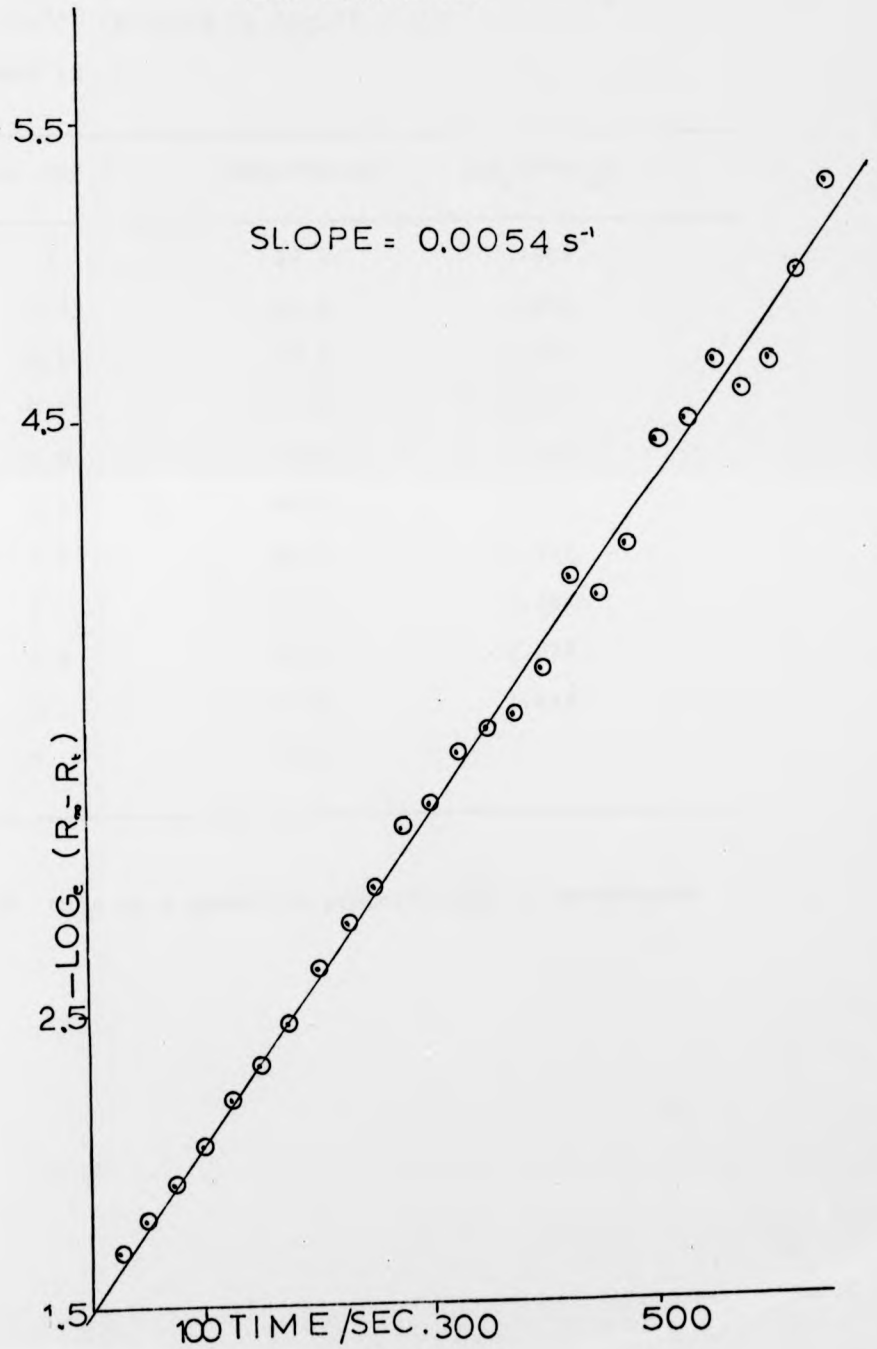
* This is a voltage proportional to rotation (see instrumentation). Readings were actually taken every 5 seconds.

Typical data from a racemisation experiment.
D-3-bromocamphor in 70% DMSO with 0.002M OH^- (Plotted in Fig. 6)
TABLE 11

Time sec^{-1}	Rotation*	$-\log_e(Rotation^*_\infty - Rotation^*_t)$
0	1.796	1.546
25	1.826	1.698
50	1.847	1.820
75	1.865	1.938
100	1.882	2.063
125	1.900	2.216
150	1.911	2.322
175	1.924	2.465
200	1.939	2.659
225	1.948	2.797
250	1.955	2.919
275	1.965	3.124
300	1.968	3.194
325	1.975	3.381
350	1.977	3.442
375	1.978	3.474
400	1.983	3.649
425	1.990	3.963
450	1.988	3.863
475	1.992	4.074
500	1.997	4.423
525	1.998	4.509
550	2.000	4.710
575	1.999	4.605
600	2.000	4.710
625	2.002	4.961
650	2.004	5.298
∞	2.009	

* This is a voltage proportional to rotation (see instrumentation). Readings were actually taken every 5 seconds.

FIG.6.
A TYPICAL RACEMISATION EXPERIMENT



Typical data for a scavenging experiment

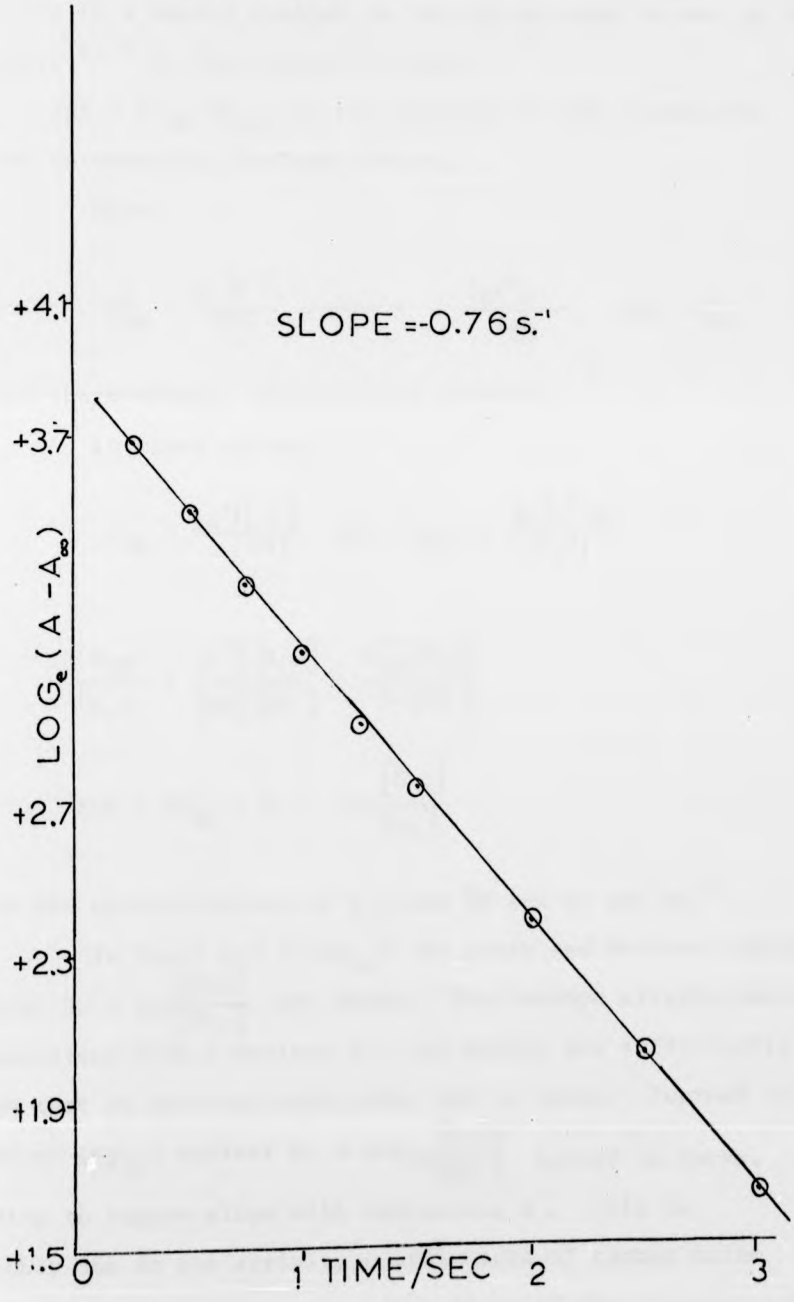
Bromination of 3-nitrocamphor in 0.0041M HPO_4^{2-} in water at 25°C (Plotted in fig.7)

TABLE 12

Time sec^{-1}	Absorbance*	$\log_e(A^*-A_\infty)$
0	98.0	3.862
0.25	90.5	3.691
0.5	83.6	3.502
0.75	77.5	3.299
1.0	73.0	3.117
1.25	69.0	2.923
1.5	66.0	2.747
2	61.3	2.388
2.5	58.0	2.028
3	55.6	1.648
∞	50.4	

* this is a quantity proportional to absorbance

FIG. 7.
A TYPICAL SCAVENGING EXPERIMENT.



DISCUSSION

(a) Ionisation of 3-bromocamphor by $\bar{O}H$ in DMSO-water mixtures.

We assume that 3-bromocamphor responds to changes in basicity in a manner similar to the amines used to set up the H_- scale[71,72] in DMSO-water mixtures.

$\Delta pK = pK_{SH} - pK_{H_2O}$ is the quantity we are interested in for interpreting isotope effects.

Then

$$K^{o}_{SH} = \frac{h_-[S^-]}{[SH]} \quad \text{where } h_- = \frac{a_{H^+} f_{S^-}}{f_{SH}} \quad \text{and} \quad K^{o}_{SH}$$

is the thermodynamic dissociation constant.

In mixed solvent

$$K_{SH} = \frac{[H^+][S^-]}{[SH]} \quad \text{and} \quad K_{H_2O} = \frac{[H^+][\bar{O}H]}{[H_2O]}$$

$$\frac{K_{SH}}{K_{H_2O}} = \frac{[S^-][H_2O]}{[SH][\bar{O}H]} = \frac{K^{o}_{SH}[H_2O]}{h_-[\bar{O}H]}$$

$$\Delta pK = pK^{o}_{SH} - H_- - \log\frac{[H_2O]}{[\bar{O}H]}$$

where the concentrations of H_2O and $\bar{O}H$ are in mol dm^{-3}.

In fig.8 and 9 $\log_{10}k$ for proto and deutero compounds against $H_- + \log\frac{[H_2O]}{[\bar{O}H]}$ are shown. The isotope effects are not inconsistent with a maximum but the errors are sufficiently large that no definite conclusion can be drawn. Further the plots of $\log_{10}k$ against $H_- + \log_{10}\frac{[H_2O]}{[\bar{O}H]}$ appear to curve, tending to higher slope with increasing H^-. This is probably due to the activity coefficients of carbon acids varying in a different manner from those of the nitrogen acids

TABLE 13

Ionisation of 3-bromocamphor by $\bar{O}H$ in DMSO-water mixtures

Vol % DMSO	Mole % DMSO	k_H/k_D	Standard Deviation	H_- for $[\bar{O}H]$ = 0.011 mol dm^{-3}	$H_- + \log_{10} \frac{[H_2O]}{[\bar{O}H]}$
15	4.3	6.9	0.6	-	-
25	7.8	6.8	0.4	12.6	16.2
35	12.0	7.4	0.3	13.2	16.7
45	17.2	7.0	0.2	13.9	17.3
50	20.2	6.6	0.2	14.3	17.7
60	27.6	6.6	0.3	15.15	18.5
70	37.06	6.2	0.1	16.15	19.4

used to set up the H_- scale. Similar effects have been noted before[73,74,75] in low DMSO concentrations. The slopes are 0.45 but would, at higher H_-, be somewhat greater. In 15% by volume DMSO, glycine (taking its pK_A in water) and hydroxide (by extrapolating H_- slightly) give a β of 0.57. In 20 and 40% by weight dioxan glycine and hydroxide give β's of 0.77 and 0.53 using the pK's of Harned[76] for glycine and calculating pK_{H_2O} from K_w.[77] Thus if we accept a maximum isotope effect at $H_- + \log[H_2O]/[\bar{O}H] = 17$ it is likely β would be in the region of 0.5 in these more basic media. An approximate extrapolation of the data in table 4 to water gives

$$k_H^{OH} = 0.4 \text{ s}^{-1} \text{ mol}^{-1} \text{ dm}^3$$

FIG.8.
BRÖNSTED PLOT FOR
3-BROMOCAMPHOR

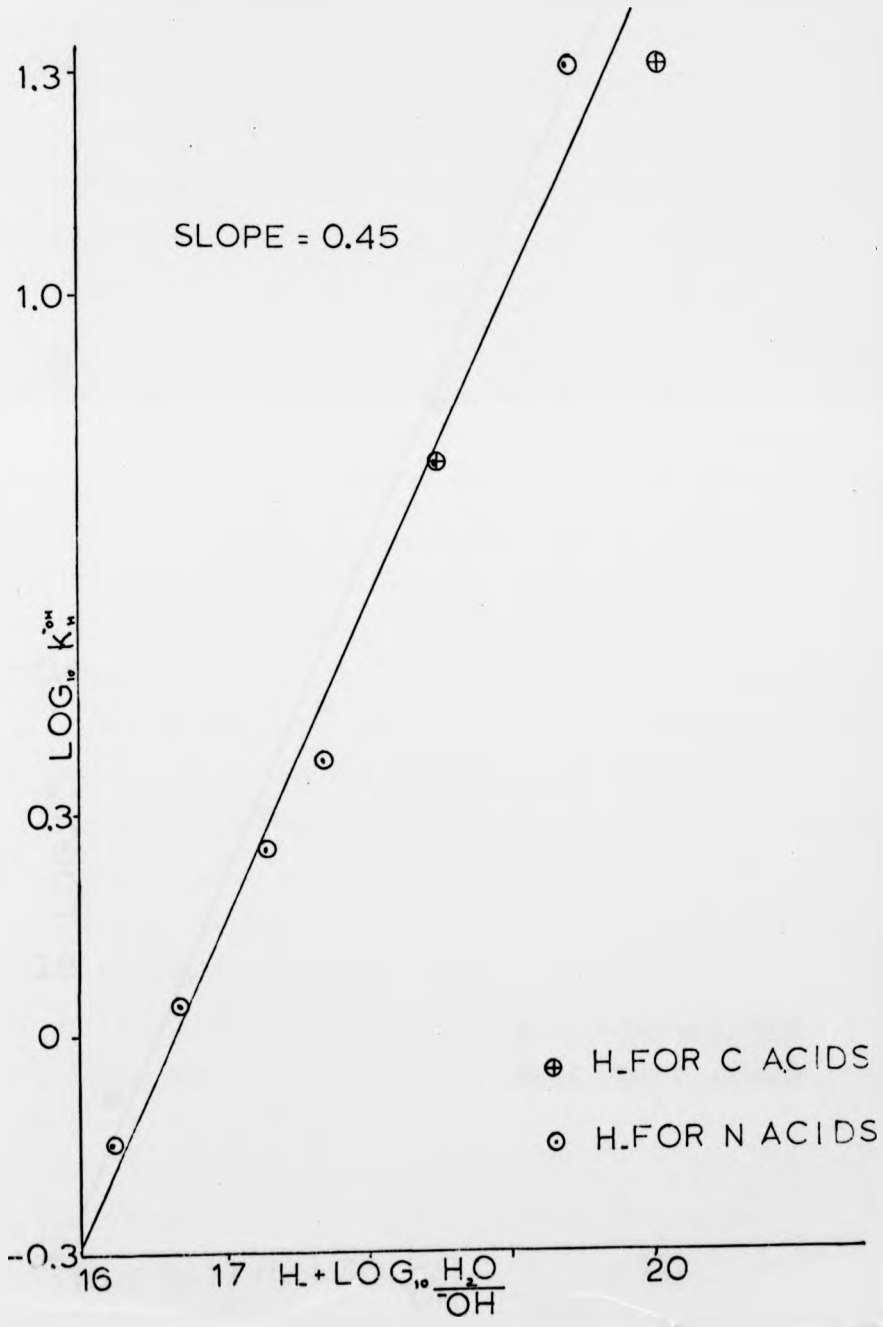


FIG.8.
BRÖNSTED PLOT FOR
3-BROMOCAMPHOR

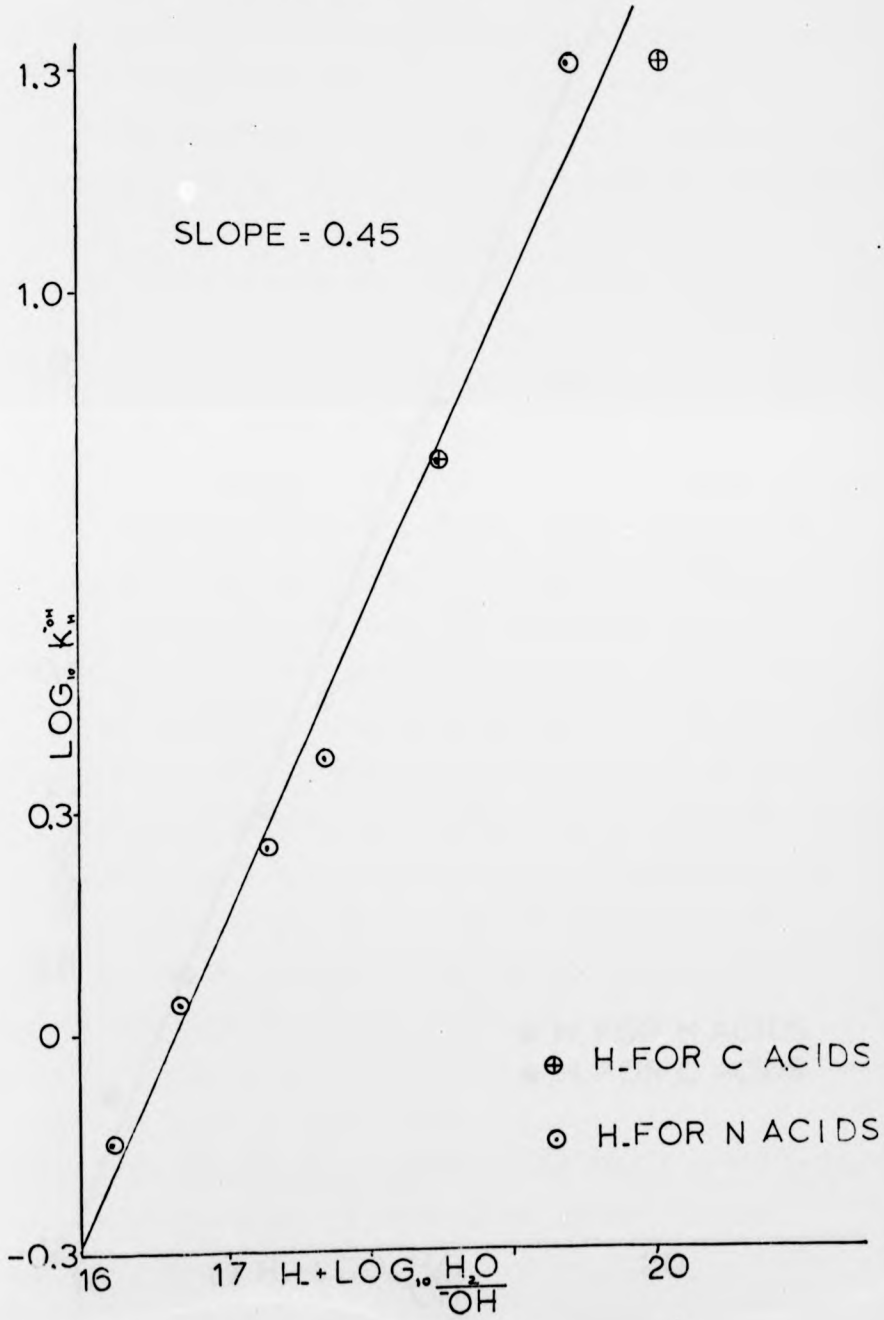
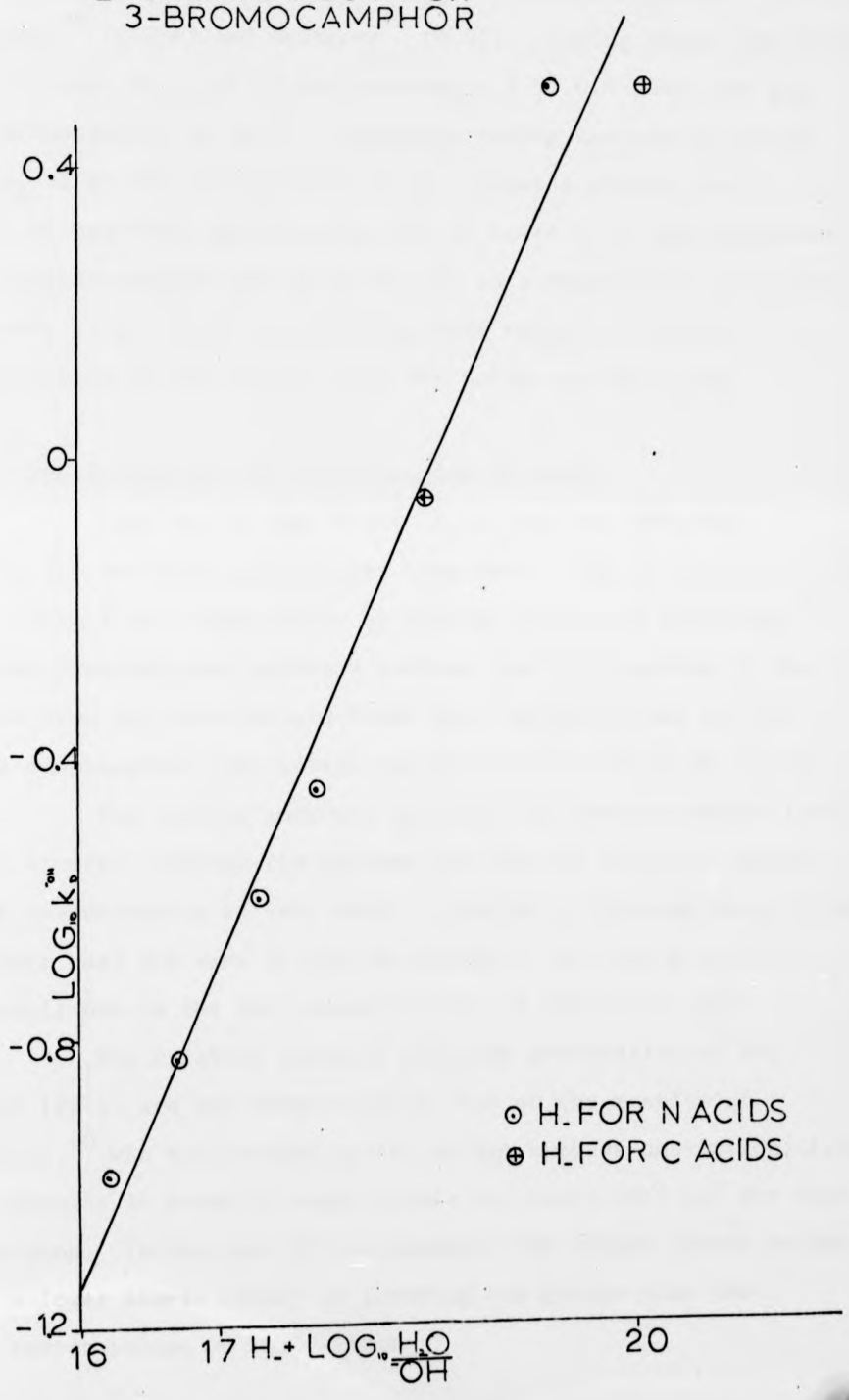


FIG. 9.
BRÖNSTED PLOT FOR
3-BROMOCAMPHOR



considerably larger than those of p-methoxyacetophenone[78] (0.025) acetone[79] (0.016) and menthone[74] (0.01). Taking these compounds all to have $pK_{A's}$ of 20 and assuming a β of 0.5 gives the pK_A of bromocamphor as 16-17. Similarly taking acetone as having a pK_A of 20 the introduction of an α bromine should give a fall of something greater than two pK units (c.f. acetylacetone and bromoacetylacetone) since we are in a relatively unreactive system, plus a small contribution from relief of steric interaction of the bromine with the bridge methyl group.

(b) The ionisation of 3-nitrocamphor in water.

Figs 10, 11 and 12 show k_H/k_D and the Brönsted plots for the proto and deutero compounds. The acidity constants are taken from a compilation by Kortüm, Vogel and Andrussow.[80] In the phosphate and malonate buffers the contribution to the rates from the mono-ionised forms are negligible and in the case of phosphate very little tri-ionised form will be present.

The acidity constant obtained for 3-nitrocamphor involves both isomers, however the extreme equilibrium position causes this correction to be very small. Similarly although many of the buffers used are very dilute the change in pH during reaction is small due to the low concentrations of substrate used.

The relative rates of exo:endo protonation of the anion (28:1) are not surprising in view of the results of Tidwell,[50] who has studied cyclic bridge ketones and rationalised the results in terms of angle strain and non-bonded Van der Waals repulsion. In the case of nitrocamphor the single carbon bridge has a lower steric effect on incoming exo groups than the two carbon bridge on endo attack.

Fig. 13 shows the data on isotope effects for this work, menthone, ethyl nitroacetate and phenylmethylacetophenone each of which show a maximum. A clear maximum is evident for the camphor derivatives and both appear to fit quite well in a single curve, although the Brönsted slopes are slightly low at 0.43 and 0.46 this could be rationalised in terms of the effects discussed in part II. No explanation is offered for the fact that catalysis by water (not shown) falls below the line.

FIG. 10.
k_y/k_o VERSUS Δ pK FOR
3—NITROCAMPHOR

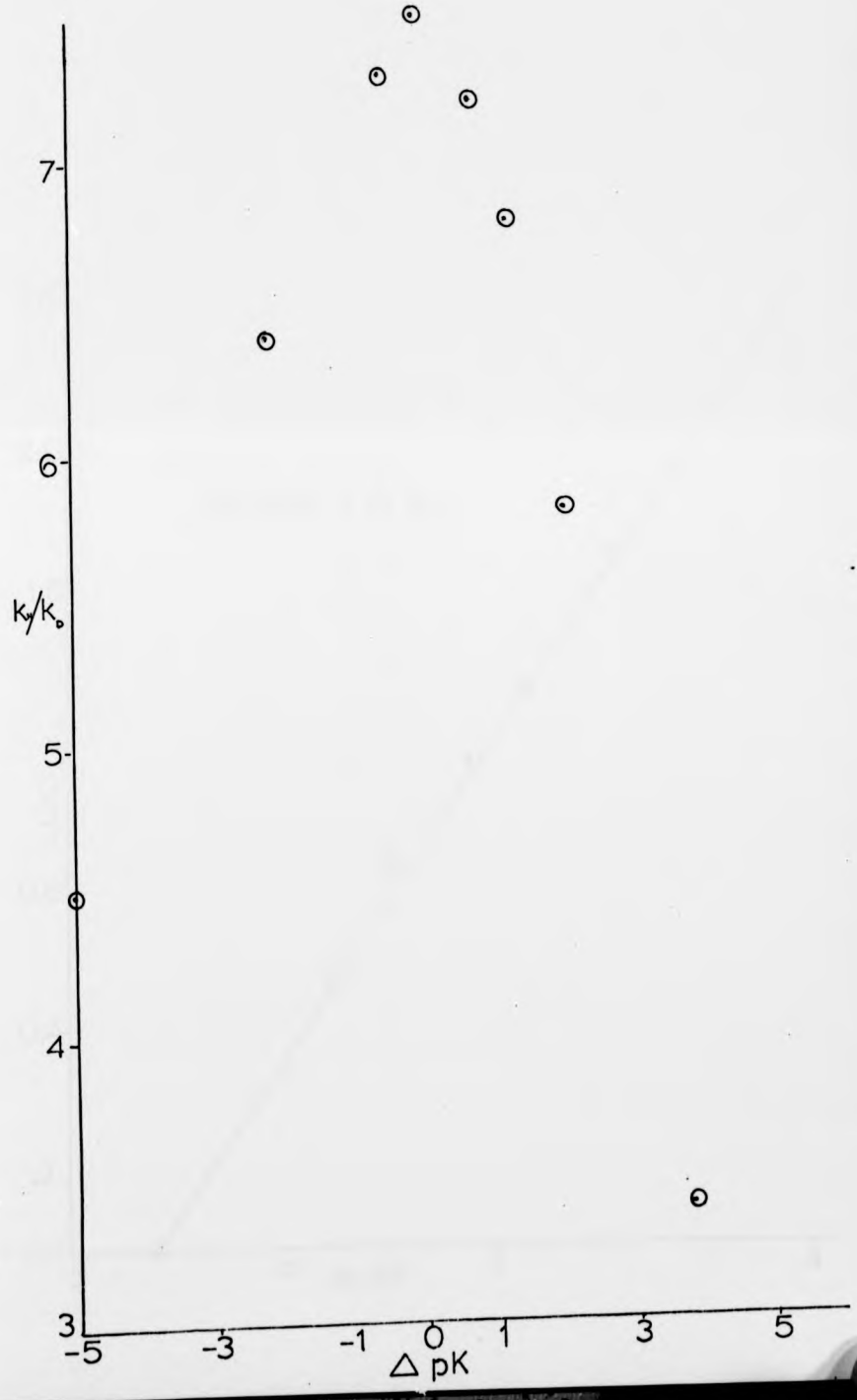


FIG.11.
BRÖNSTED PLOT FOR
3—NITROCAMPHOR

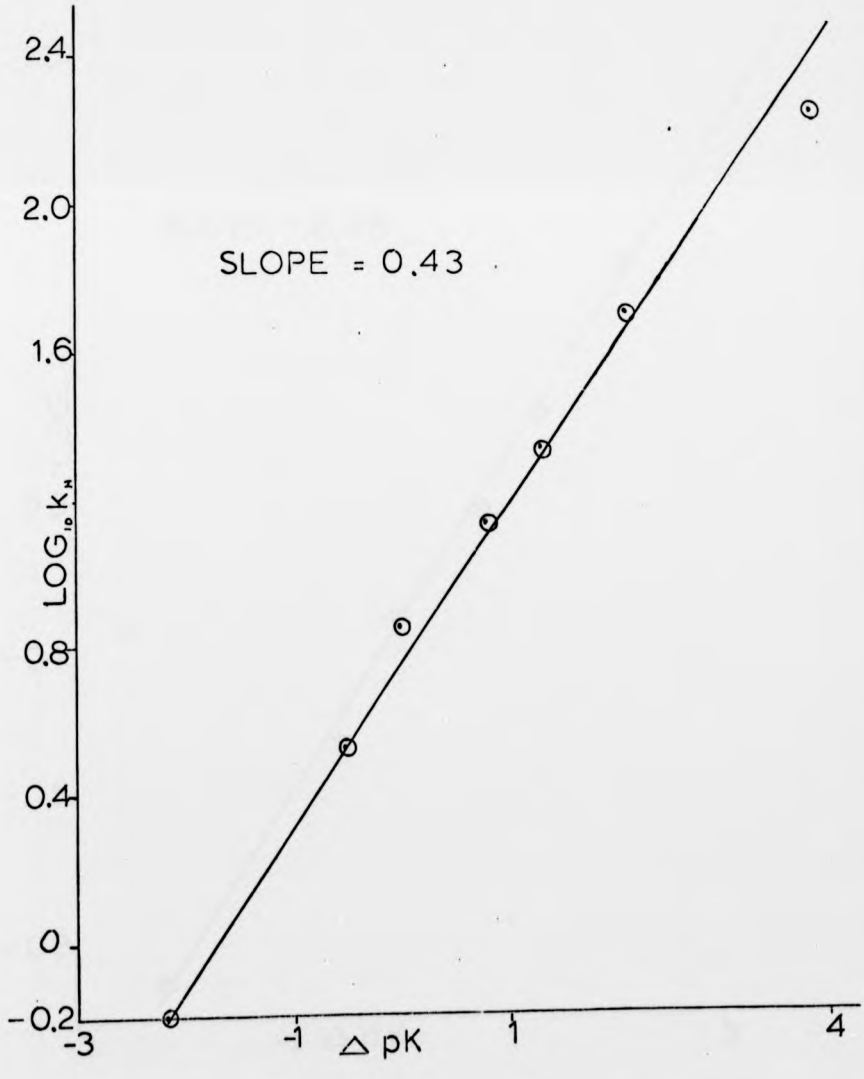


FIG.12.
BRÖNSTED PLOT FOR
3-NITROCAMPHOR

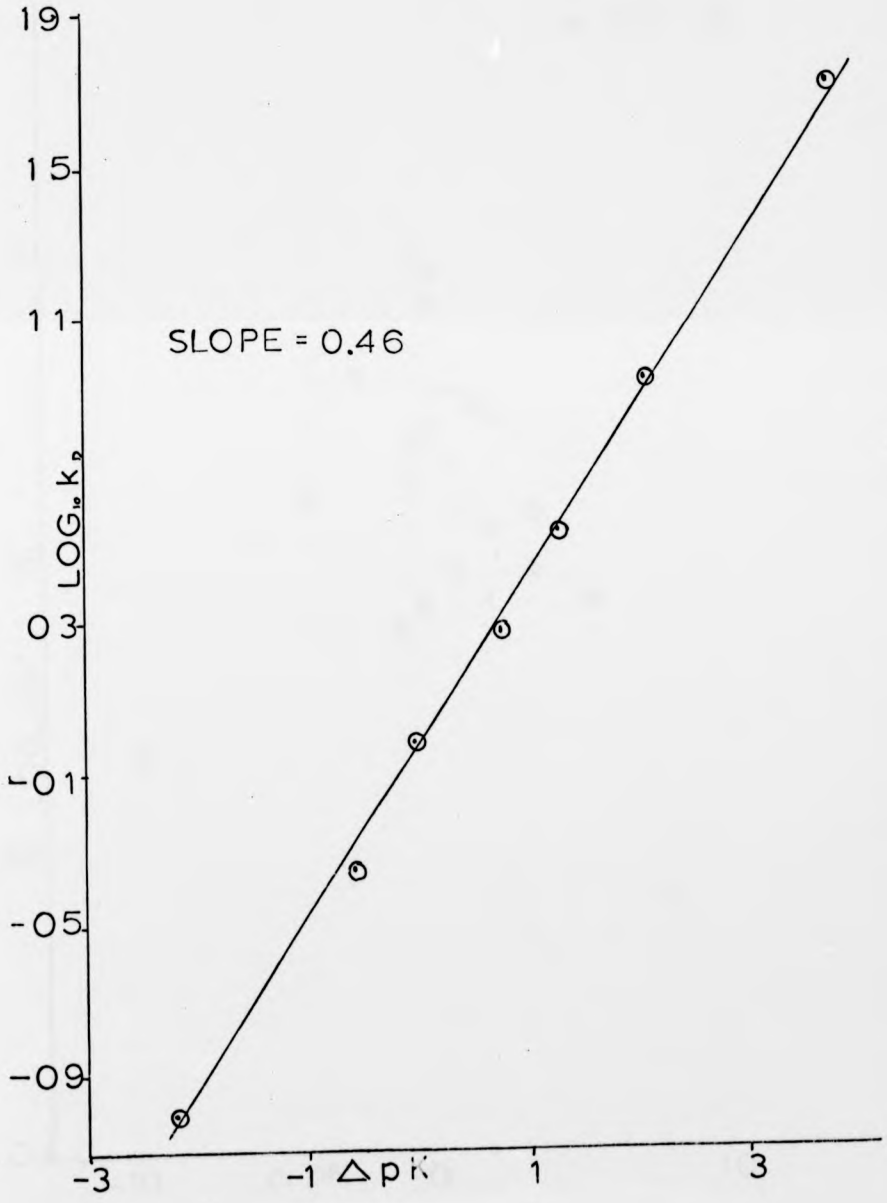
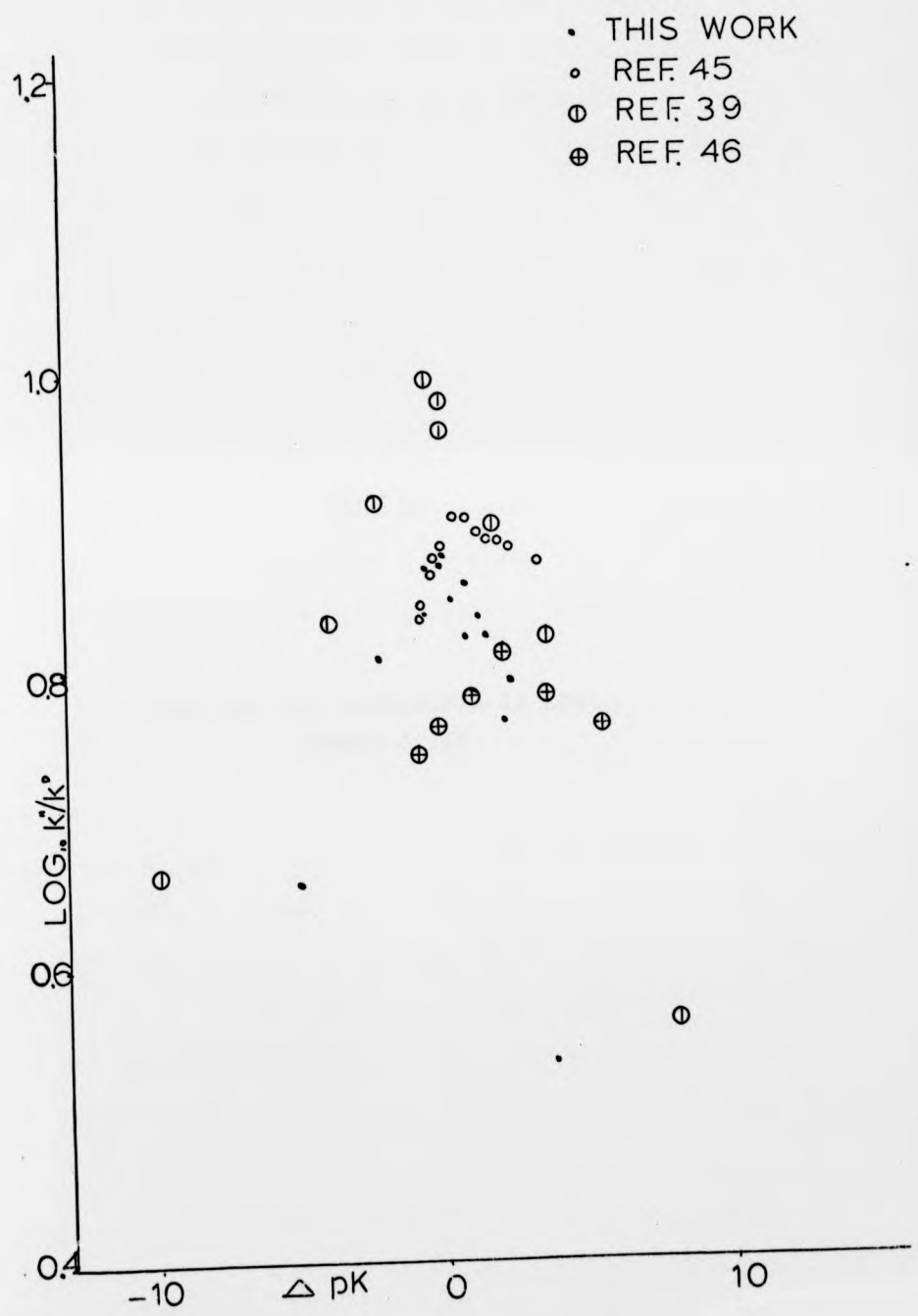


FIG.13.
COMPARISON OF THIS WORK WITH PREVIOUS MAXIMA



PART II

KINETICS AND EQUILIBRIA IN SOME CARBON ACIDS

INTRODUCTION

Theory

The Brönsted relation was put forward as an experimental observation by Brönsted and Pedersen[1] following their work on the base catalysed decomposition of nitramide. They were able to relate the reaction velocity (k) to the base strength of the catalyst (K_B) thus:-

$$k = G_B K_B^{\beta} \qquad \text{(i)}$$

$$\text{or} \quad k = G_B\left(\frac{1}{K_A}\right)^{\beta} \qquad \text{(ii)}$$

where K_A is the acidity constant of the conjugate acid of the base, G_B is a constant for a given reaction, temperature and solvent, and β is a constant for a reaction providing the base strength is not varied widely. β has commonly been found to lie between zero and unity.

This is modified on statistical grounds when comparing a mono and a dibasic acid. If all three acidic protons have an equal tendency to ionise the first K_A of the dibasic acid will be twice that of the mono-basic acid, since the anion may be formed by losing either of the protons. Similarly the catalytic constant of the dibasic acid will be twice that of the monobasic acid since the concentration of catalysing groups is effectively doubled. We must consider the dissociation constant and catalytic power per carboxyl group. This gives:-

$$k/q = G_B\left(p/qK_A\right)^{\beta} \qquad \text{(iii)}$$

where q is the number of equivalent sites where a proton may be attached to the catalysing base and f the number of equivalent protons available in the conjugate acid of the base. Similar corrections can be made for the number of equivalent acidic protons on the substrate.

We may rearrange (i) to logarithmic form

$$\log k = \log G_B + \beta \log K_B \qquad \text{(iv)}$$

If the base is now changed from B to B'

$$\log k - \log k' = \beta(\log K_B - \log K_{B'}) \qquad \text{(v)}$$

since $k = \frac{kT}{h} e^{-\frac{\Delta G^{\ddagger}}{RT}}$ and $\log K = -\frac{\Delta G^{o}}{RT}$

this is equivalent to

$$\Delta G^{\ddagger} - \Delta G^{\ddagger\prime} = \beta(\Delta G^{o} - \Delta G^{o\prime}) \qquad \text{(vi)}$$

$$\beta = \frac{\delta \Delta G^{\ddagger}}{\delta \Delta G^{o}} \qquad \text{(vii)}$$

where δ is a stabilisation operator.

β then represents the ratio of an effect on the free energy of activation and the overall free energy change. The Brönsted relation was the first linear free energy relationship and antedated the more general Hammett equation by more than a decade. It differs in that it relates the rate and equilibrium constants for the same process since K_A in (ii) may be replaced

by K_{SH}/K where K_{SH} is the acidity constant of the substrate and K the equilibrium constant of the catalysed reaction.

It was realised at an early date[1] that the rate of proton transfer from an acid to a base could not continue to increase in accordance with (i) indefinitely. As the base is made stronger and stronger the rate will become faster and faster until reaction occurs at every encounter and further increases in base strength will have no effect. ß will therefore equal zero. If on the other hand the base is continually made weaker its conjugate acid will become stronger and eventually the back reaction will become diffusion controlled and ß will be unity. These considerations led Brönsted and Pedersen to conclude that ß would vary regularly from zero to unity over a sufficient range of catalyst strength.

An interpretation of this on a molecular level has been proposed.[2,3] If we follow the treatment of part I and consider two intersecting potential-energy curves for the species SH (substrate) and BH (conjugate acid of the catalysing base), and consider only straight line configurations of SHB we have fig. 1. If we further consider only the proton to move in the reaction, the reaction coordinate becomes the distance of the proton from S or B.

The Brönsted relation can now be represented as in fig. 2.[4], where curve I represents $SH + B^-$, curve II S^- + BH and curve II' S^- + B'H where we have changed the catalysing base. The activation energy E^* is changed to $E^* + \delta E^*$ and the overall energy change E^o to $E^o + \delta E^o$. If the catalysing bases are similar it is reasonable to assume that curve II' is the same shape but vertically displaced from curve II. Then,

MOLECULAR BASIS OF THE
BRÖNSTED RELATION

FIG.1.

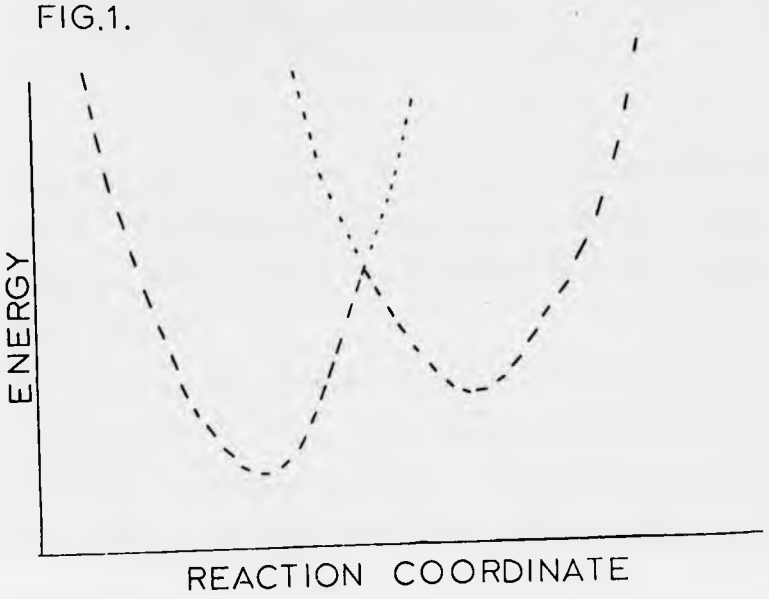
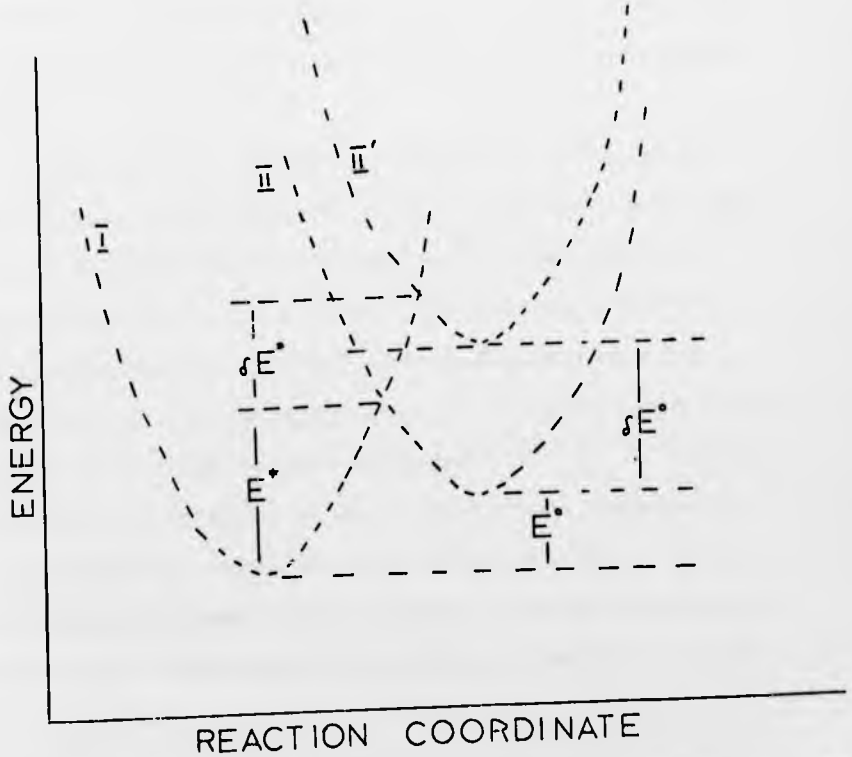


FIG. 2.



$$\delta E^{*} = \frac{|S_1|}{|S_1| + |S_2|} \delta E^{o} = \beta \delta E^{o}$$

where S_1 and S_2 are the slopes of the curves at the point of intersection. This strictly applies only at absolute zero and in practice δG^{*} and δH^{*} will both differ from δE^{o} as will δG^{*} and δH^{*} from δE^{*}.

The Brönsted relation is closely linked with Hammond's postulate.[5] It is intuitively obvious that if the transition state resembles reactants, changes in overall free energy will have no effect on the rate. The reverse is equally obvious: if the transition state resembles the products any change in ΔG^{o} will have an equal effect on ΔG^{*}. The quantitative extension of this by Leffler[6] however must assume a linearity between free energy and the extent of reaction in the transition state to yield the Brönsted relation.

Marcus[7] has derived a theory for outer-sphere electron transfer reactions in solution and this has been applied to atom and proton transfers.[8,9] This is not unreasonable as both the electron and hydrogen atom are simple free radicals, powerful reducing agents and the hydrogen atom is the conjugate acid of the solvated electron. This model is similar to that of Eigen[10,11,12,13,14] which considers proton transfer to be a three stage process of diffusion together, transfer, and diffusion apart. In the case of transfer between oxygen-oxygen, nitrogen-nitrogen or oxygen-nitrogen the transfer is rapid and the reaction is

diffusion controlled. Under these circumstances changes in base strength are of no consequence so long as the reaction remains diffusion controlled. For the reverse reaction the rate is directly proportional to K. At $\Delta pK = pK_{SH} - pK_{BH} = 0$ the rate is reduced by at least a factor of two, as the proton has an equal probability of going in either direction from the transition state. This is shown in fig.3. The only curvature occurring in a small region around $\Delta pK = 0$ in contrast to carbon acids where Brönsted exponents between zero and unity are commonly observed[15,16] to be linear over many pK_A units. In general the larger the rate constant at $\Delta pK = 0$ the ~~larger~~ shorter the range to which a linear approximation applies. This difference in rates is understandable in terms of a model put forward by Bell.[17]

To return to Marcus rate theory. The free energy of activation barrier is considered as a combination of an intrinsic barrier λ and the work done in preparing the reactants for transfer W^r. The intrinsic barrier λ is taken as the average of the barriers λ_s and λ_B.

$$SH + S^- \rightleftharpoons S^- + SH \qquad \lambda_s$$

$$BH + B^- \rightleftharpoons B^- + BH \qquad \lambda_B$$

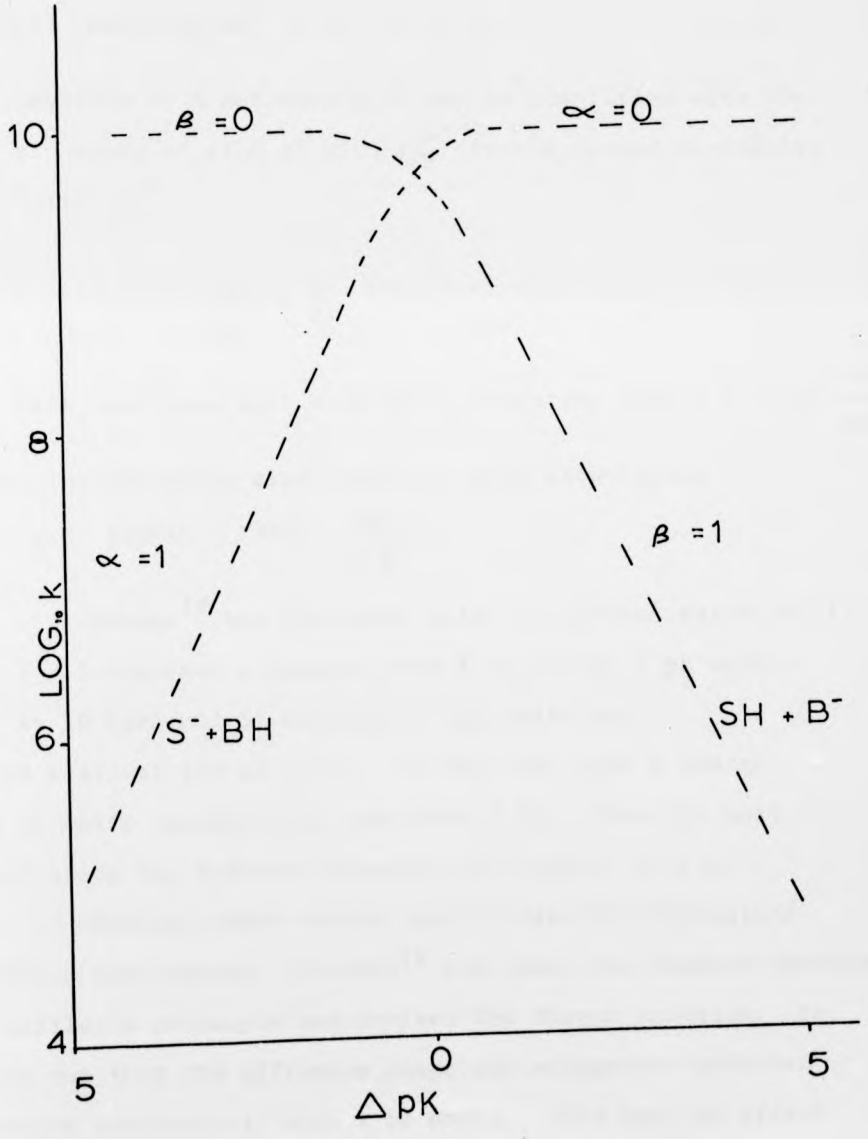
The theory then gives

$$\Delta G^* = W^r + \left(1 + \frac{\Delta G_R^{o'}}{4\lambda}\right)^2 \frac{\lambda}{}$$

where $\Delta G_R^{o'} = G^{o'} + W^p - W^r$

where W^p is analogous to W^r and $\Delta G^{o'}$ is the free energy of reaction under the experimental conditions. If it is assumed λ,

FIG. 3.
THE BRÖNSTED RELATION FOR TRUE ACIDS.



W^r and W^p remain constant for a series of catalysts.

$$\beta = d\Delta G^{*}/d\Delta G_R^{o'} = \tfrac{1}{2}(1 + \Delta G_R^{o'}/4\lambda)$$

For $\Delta G_R^{o'} = 0$ $\quad \beta = \frac{1}{2}$

Uphill reactions $G_R^{o'} > 0$ $\quad \beta > \frac{1}{2}$

Downhill reactions $\Delta G_R^{o'} < 0$ $\quad \beta < \frac{1}{2}$

The curvature of a Brönsted plot may be identified with the rate of change of α (or β) with $\Delta G_R^{o'}$ or the second derivative of ΔG^{*} with $\Delta G_R^{o'}$

$$\frac{d\beta}{d\Delta G_R^{o'}} = \frac{1}{8\lambda}$$

Thus fast reactions will show sharp curvature (small λ large $\frac{d\beta}{d\Delta G_R^{o'}}$) while intrinsically slow reactions will show little curvature (large λ small $\frac{d\beta}{d\Delta G_R^{o'}}$).

Kresge[18] has evaluated this for various values of λ. When λ = 1 kcal/mol α changes from 1 to 0 over 5 pK units, for λ= 10 kcal/mol it requires 55 pK units and λ = 20 kcal/mol 110 pK units. In the last case a change of 5 pK units changes α by less than 0.05. Thus for most carbon acids the Brönsted relation will appear linear.

Several other models lead to similar conclusions as Marcus rate theory. Murdoch[19] has taken the Hammond postulate and Leffler's principle and derived the Marcus equation. He points out that the diffusive steps can exaggerate Brönsted curvature particularly when λ is small. This has the effect

of making Brönsted plots for carbon acids tend towards those for 'normal' acids. This exaggerated curvature will tend to push in towards ΔpK = 0 more as the intrinsic barrier is reduced. Similarly making diffusion easier will have the same effect.

Kresge[20] has developed a model based on intersecting parabola of different curvature, but as he has pointed out[18] it is unlikely that the assumptions of equal and constant curvature needed to simplify to Marcus theory will be upheld. In this case the linear dependence of α on ΔE gives way to a complex sigmoid relationship, and though these are straight over a considerable portion, the slope differs from that of simple Marcus theory. B.E.B.O. methods,[21] extended B.E.B.O. by Marcus,[22] and a method based on a modified SATO potential energy surface to describe the proton transfer,[23] all give the same results with a straight portion of slope which is too high. However, all predict curved Brönsted plots, the curvature increasing as λ decreases.

Brönsted β and the position of the Transition State

If we take the Brönsted relation in the form,

$$\beta = \frac{\delta \Delta G^{*}}{\delta \Delta G^{o}}$$

with the usual notation and consider this with Leffler's principle[6]

$$\delta G^{*} = \alpha \delta G_{P}^{o} + (1 - \alpha)\delta G_{R}^{o}$$

where G^{*}, G_{P}^{o} and G_{R}^{o} are the free energies of transition state

products and reactants respectively and α the degree of proton transfer in the transition state. As written α has a value of unity for close resemblance to products and zero for resemblance to reactants, and represents the order of the bond being formed between proton and base catalyst or the fraction of negative charge acquired by the substrate. This is equivalent to:-

$$\delta\Delta G^{*} = \alpha\delta\Delta G^{o}$$

which is represented in fig.4 and 5, where x represents the difference in energy of curves I and II for a particular α. Leffler's principle states that the plot of x against α is a straight line. Clearly if this is the case β represents the extent of proton transfer in the transition state. It is evident that any change in the system which affects one of of these free energy quantities without producing a corresponding change in the other will result in a deviation. One can imagine a case in which a deviation of the above type could be linear with ΔG^{o} thus would still produce a straight line of logk against pK but in which there is no correspondence between β and α.

The effects discussed by Murdoch[19] will give rise to a similar case in which the slope is only partially derived from chemical factors and distorted by diffusion contributions. However this is more likely to be of importance in oxygen and nitrogen acids where λ is small and should affect transfers from carbon acids only in the case of cyanocarbon and sulphonyl-carbon acids.

If we consider this in the light of Marcus rate theory[7] the expression

LEFFLER'S APPROXIMATION

FIG.4.

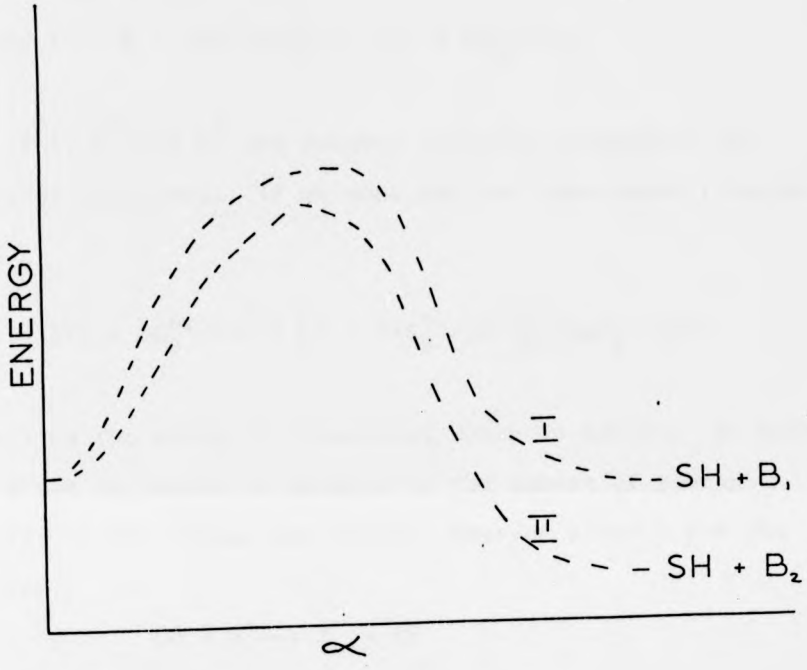
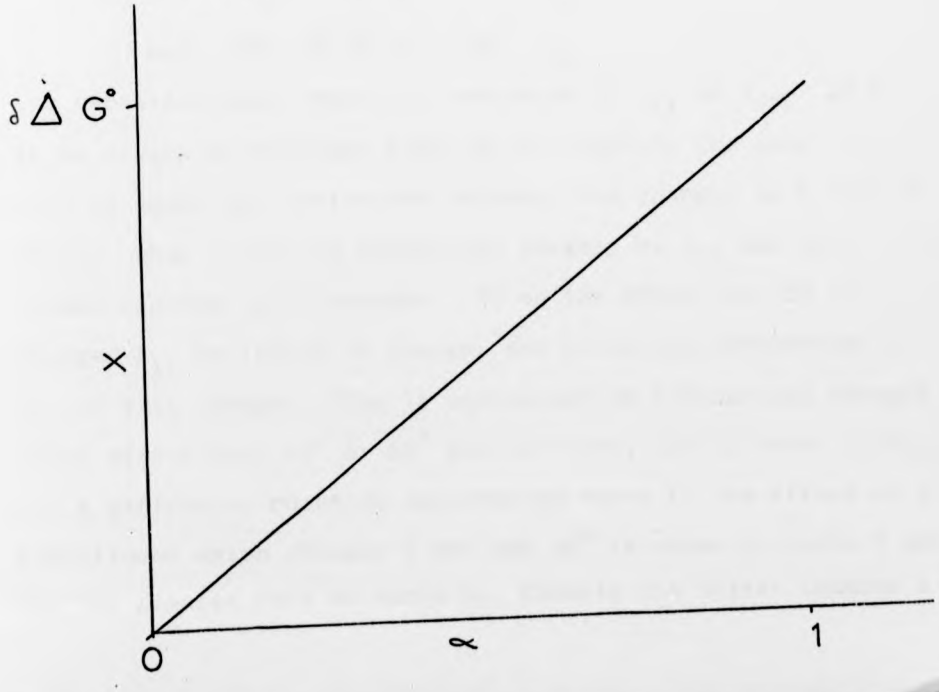


FIG. 5.



$$\Delta G^{\ddagger} = W^{r} + \left(1 + \frac{\Delta G_R^{o\prime}}{4\lambda}\right)^2 \lambda$$

reduces to $\beta = d\Delta G^{\ddagger}/d\Delta G_R^{o\prime} = \frac{1}{2}(1 + \Delta G_R^{o\prime}/4\lambda)$

only if λ, W^r and W^P are assumed constant throughout the series of catalysts. If we consider the case where λ varies[24] then:

$$\beta = \tfrac{1}{2}(1 + \Delta G_R^{o\prime}/4\lambda) + \left[1 - (\Delta G_R^{o\prime}/4\lambda)^2\right]\frac{d\lambda}{dY}/(d\Delta G_R^{o\prime}/dY)$$

where Y is the group in a reactant which is varied. In this case β can no longer be equated to the extent of proton transfer in the transition state. However since λ for the reaction

$$SH + B^- \longrightarrow S^- + BH$$

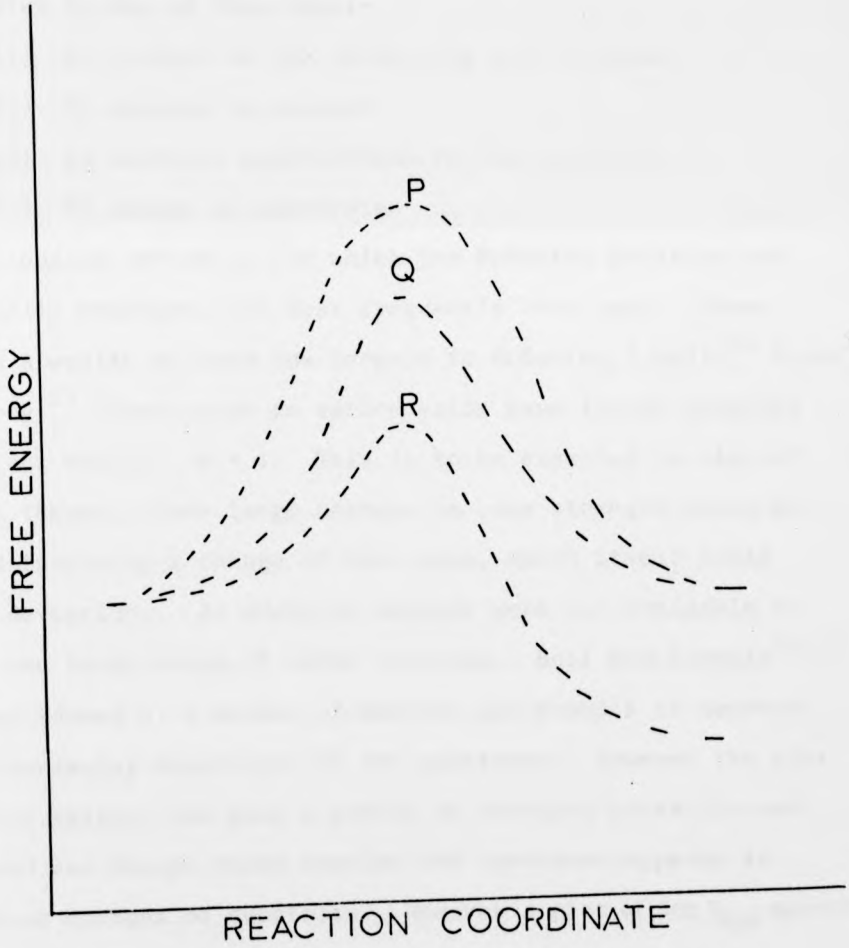
is the average for the exchange reactions

$$SH + S^- \rightleftharpoons S^- + SH \quad \lambda_{11}$$

and $$BH + B^- \rightleftharpoons B^- + BH \quad \lambda_{22}$$

its variation will depend on variation in λ_{11} or λ_{22}. If B is an oxygen or nitrogen base, as is commonly the case, λ_{22} will be small and variations arising from changes in B will be small. Thus λ will be determined largely by λ_{11} and will remain constant as B changes. If on the other hand SH is changed λ_{11} is likely to change, and since this determines λ, it too will change. This is equivalent to introducing changes which affect only ΔG^{o} or $\Delta G^{\ddagger}$ but not both, and is shown in fig.6.[24] For a particular reaction depicted by curve P, the effect of a substituent which changes λ but not ΔG^{o} is shown by curve Q and and the reverse case by curve R. Clearly the latter induces a

FIG.6.
DEVIANT BRÖNSTED RELATIONSHIPS
AND MARCUS THEORY



correlation between position of the transition state and ΔG^{o}, while the former does not.

Review of Previous Work

It has been suggested that changes in free energy of reaction used to generate Brönsted relationships may be generated in any of four ways:-

(1) By changes in the catalysing acid or base

(2) By changes in solvent

(3) By isotopic substitution in the substrate

(4) By change of substrate

Traditionally method 1, for which the Brönsted relation was originally proposed, has most frequently been used. There exists a wealth of data due largely to Brönsted,[1] Bell,[25] Eigen[26] and Long.[27] Early work on carbon acids gave linear Brönsted relations with $0 < \beta < 1$. This is to be expected in view of Marcus theory, since large changes in base strength would be needed involving a change of Base type, which itself could cause deviations. In addition methods were not available to cover the large range of rates involved. Bell and Lidwell[28,29] however looked at a series of ketones and found β to decrease with increasing reactivity of the substrate. However the plot of rates against ΔpK gave a series of straight lines for each compound and though these overlap the curvature appears to come from changes of substrate. However a plot of log K_{H_2O} against pK_A of substrate is distinctly curved.

In the work on carbon acids systematic deviations were noticed. The most striking is that for the decomposition of

nitramide with differently charged bases,[30,31] where dipositive, neutral, negative and dinegative catalysts define four parallel straight lines separated by a factor of 20 in reactivity. This is also observed in the hydrolysis of ethyl vinyl ether[32] where neutral carboxylic acids and positive amino acids define two parallel lines though the plots are poor. These are presumably cases of transition state interactions, of equal magnitude for a particular series of bases, moving the plots vertically. In the case of nitramide the base is removing a proton from a neutral substrate and generating a negative charge. This will be partially realised in the transition state and electrostatic interaction with the charge on the base will stabilise or destabilise the transition state relative to that for a neutral base.

Dipolar groups in the catalyst are also able to produce this effect as shown by Kresge's[33] work, in which eight vinyl ethers are hydrolysed by seven neutral carboxylic acids. Acids containing polar groups (e.g. cyano, methoxy) show consistent deviations i.e. always positive or negative. This highlights the danger of taking a few widely differing bases, for instance differently charged bases catalysing the nitramide decomposition could give positive, negative or zero slope, depending on charge and pK_A.

Steric hindrance can also reduce the rate while leaving the acidity unaffected,[34,35,36] and an effect in the opposite direction has been noted[37] where both species of the transition state are large. This results in hydrophobic bonding and stabilisation. Prompted by systematic deviations, Pfluger[38] suggested that Brönsted plots could be obtained using bases which are normally deviant by redefining their acidity, though this has been little used.

In nucleophilic displacements those nucleophiles possessing an unshared pair of electrons adjacent to the nucleophilic atom have been observed to show large positive deviations of log k_{rate} in the Brönsted plot. This is the so-called "α effect"[39] and has been rationalised in several ways.[40] However it has been found not to apply, at least for nitroethane, in proton transfer reactions.[40]

It has been recognised for some time that hydronium and hydroxide ions do not conform to Brönsted relations based on other catalytic species,[41] frequently appearing as poor catalysts. This is unfortunate as these species are often at the extremes of pK_A in a Brönsted plot and may appear to indicate curvature. The problem may well be one of assigning acid and base strengths to the ions in aqueous solution. Both involve the concentration of the solvent whereas other acids involve only dilute solution solute species.

For a non solvent-derived acid

$$HA + H_2O = H_3O^+ + A^-$$

$$K_{HA} = \frac{[H_3O^+][A^-]}{[HA]}$$

where the concentration of water is omitted by convention. However for H_3O^+ and H_2O

$$H_3O^+ + H_2O = H_3O^+ + H_2O$$

$$K_{H_3O^+} = \frac{[H_3O^+][H_2O]}{[H_3O^+]}$$

$$H_2O + H_2O = \bar{O}H + H_3O^+$$

$$K_{H_2O} = \frac{[H_3O^+][\bar{O}H]}{[H_2O]}$$

It has been suggested[42] that the concentration of monomeric water should be used. Since water is extensively hydrogen bonded the fraction of free molecules is small and forms a relatively dilute solution. This reduces $[H_2O]$ below 55 molar, lowers $K_{H_3O^+}$, and raises K_{H_2O}. The problem has also been discussed in terms of Brönsted plot curvature[43] and electrostatic interactions,[44] but these cannot account for both positive and negative deviations. Long[45] has suggested that in the ionisation of carbon acids the back reaction with water, for a hydroxide catalysed forward reaction, will be retarded on the basis of hydrogen-bond considerations. Kresge[46] has suggested that hydronium and hydroxide ions are more strongly solvated than other catalysts and that desolvation would increase the free energy of activation. This would apply only where the substrate cannot hydrogen-bond to water (carbon-acids) and the GROTTHUSS chain mechanism is not operating. The reverse case (nitrogen and oxygen acids) might be expected to show positive deviations, where hydronium and hydroxide ions have the advantage of the Grotthuss chain mechanism. Data collected by Kresge[47] bears this out quite well. In summary of the work on carbon acids (excluding cyano and sulphonyl carbon acids) it is probably fair to say these show little curvature in agreement with Marcus theory, except in cases where the substrate is also changed, e.g. the compilation by Bell.[48]

If we consider now cyano-carbon acids where much work has been done by Long,[49] a value of $\beta = 0.98$ was observed for malononitrile with a variety of bases giving ΔpK 2 to 14 with a reverse rate of 10^8 s^{-1} mol^{-1} dm^3 for general acids and 3×10^9 for the hydronium ion. In addition a low primary kinetic

isotope effect (k_H/k_T = 1.6) was observed. Sulphonyl-activated carbon acids appear similar[50,51] with β's of 1 and low isotope effects. This behaviour resembles that of oxygen and nitrogen acids[10-14] suggesting that there is little shift of charge away from carbon, and that their acidity is the result of an inductive stabilisation.[52] This leads, in accordance with Marcus theory to β's of zero and unity over large pK ranges with a short transition region.

The second method of obtaining Brönsted correlations has been used in a number of cases[53] with dimethyl sulphoxide-water mixtures using the H_- acidity function[54]. However it has been suggested[55] that this is not valid, the rate increase arising from destabilisation of reactants and products relative to the transition state, with no necessary change in the equilibrium. This will be considered later with its implications for Brönsted correlations in aqueous solution.

Isotopic substitution has been little used.[56,57,58,59] Albery[58] has studied 3-diazobutan-2-one with acetic and formic acid isotopically substituted and found this α to agree with α obtained by conventional means. Davies[59] has found β derived from deuterium substitution in 2-nitropropane with acetate and hydroxide ions as bases, to differ from that found conventionally. Owing to the scarcity of data in this field it is impossible to make generalisations.

Changes in substrate have to a certain degree already been considered e.g. the compilation by Bell,[48] and these appear normal and straightforward. However the discovery of a Brönsted exponent greater than unity by Bordwell[60] and Schechter[61] in the reaction of substituted 1-phenyl-1 nitroethanes with

hydroxide ion and the analogous reaction of substituted 1-phenyl-2-nitropropanes altered the situation. Bordwell[62] later studied phenylnitromethanes with hydroxide ion and various amine bases with the same result. Attention was also drawn to data for the acidity constants of nitromethane,[63] nitroethane[63] and 2-nitropropane[64] and the rates of reaction of these substances with hydroxide ion[65] which give a negative value of the Brönsted exponent. Hibbert[51] has added to this for a series of sulphones giving $\alpha = 1.1 \pm 0.1$.

In each of these series the substance held constant is water, hydroxide or an amine which is therefore taken to be the substrate. The catalyst and substrate roles are therefore reversed. This distinction is somewhat arbitrary except when considered in the light of Marcus theory, which assumes the intrinsic barrier λ for the process to be an average of those for the exchange reactions

$$SH + B^- \rightleftharpoons S^- + BH \qquad \lambda_{12}$$
$$SH + S^- \rightleftharpoons S^- + SH \qquad \lambda_{11}$$
$$BH + B^- \rightleftharpoons B^- + BH \qquad \lambda_{22}$$

λ_{12} is an average of λ_{11} and λ_{22}. Since λ_{11} is large it is in the main responsible for determining λ_{12}, any changes of λ_{11} are reflected in λ_{12}. Thus where the pseudo acid is changed there are likely to be changes in the intrinsic barrier unlike the reverse case where the oxygen or nitrogen base is varied.

Kresge[66] has put forward a different interpretation of this in terms of substitution effects. Since

$$\beta = \frac{\delta \Delta G^{\ddagger}}{\delta \Delta G^{\circ}}$$

any substitution effects must apply both to the transition state and reactants or products. If this is not the case fig.5 becomes

fig.7 or 8, where fig.7 gives a β between the 'true' value and 1 while fig.8 gives β > 1. In cases where the oxygen or nitrogen base has been varied the position of the equilibrium has always been more sensitive to substitution changes than have the rates k_1 and k_{-1}. This is a consequence of the fact that structural changes in these acids affect k_1 and k_{-1} in an opposite manner. However when the equilibrium constant and rate constant are no longer linked by the Brönsted relationship k_1 and k_{-1} may be affected in the same manner giving β > 1. In the series nitromethane, nitroethane and 2-nitropropane proton abstraction by hydroxide ion is retarded by increased methyl substitution but abstraction by the nitronate anion of a proton from water is even more retarded, giving a negative β for the forward rate.

Kresge[67] has pointed out that there are likely to be interactions in the transition state of bimolecular reactions which do not appear in the initial or final states. Union of the reactants to form the transition state may create forces which cannot be present before they come together or after they part. He considers the reaction,

$$HO^- + H - \overset{R}{\underset{|}{C}}Me - NO_2 = \overset{\delta-}{HO} \ldots H \ldots \overset{R}{\underset{|}{C}}Me \ldots \overset{\delta-}{NO_2} =$$

$$HO - H + \overset{R}{\underset{|}{C}}Me = NO_2^-$$

where the effect of R on the free energy change ΔG° is ${}_\delta{}_R\Delta G^\circ$ and arises from electrical interaction of R with the negatively charged nitro group

$${}_\delta{}_R\Delta G^\circ = I_{R,NO_2^-}$$

TRANSITION STATE INTERACTIONS AND THE BRÖNSTED RELATION

FIG.7.

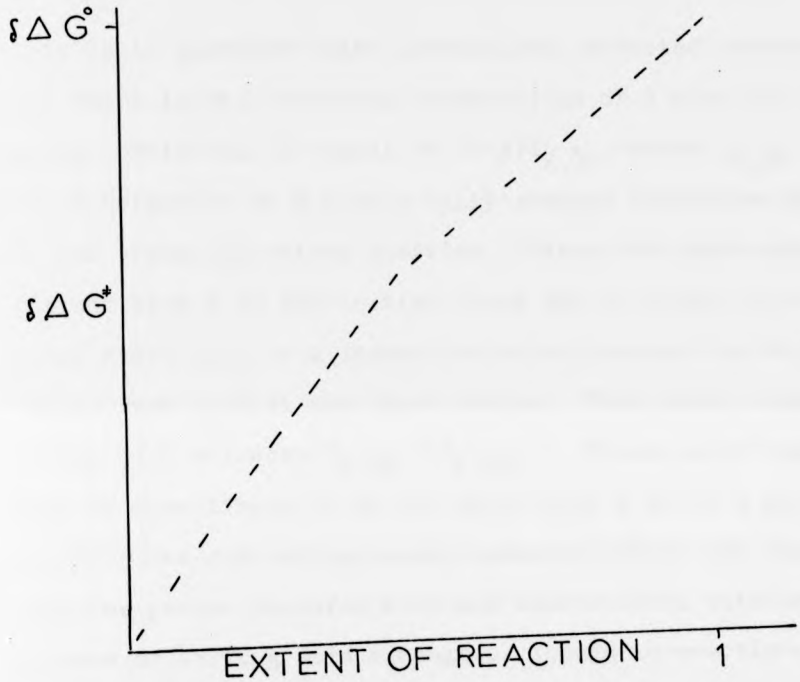
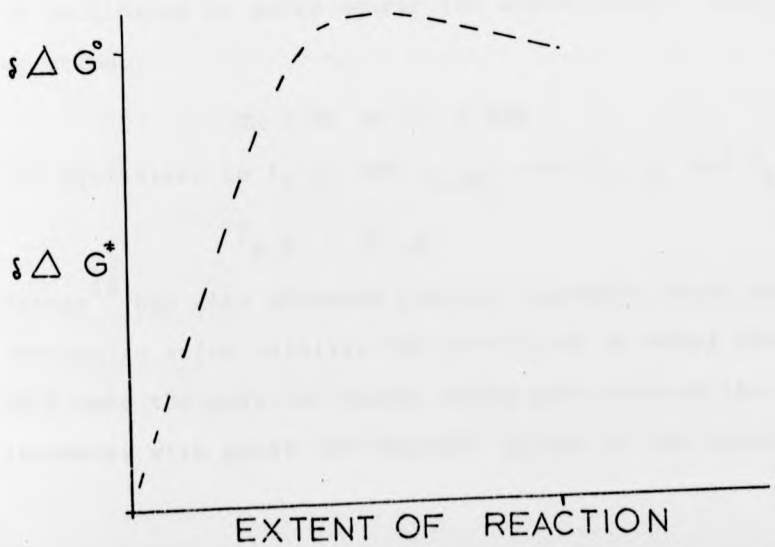


FIG.8.



In the transition state if x is the fraction of negative charge transferred

$$\delta_R \Delta G^{\ddagger} = x I_{R,NO_2^-}$$

This is in agreement with conventional Brönsted theory but there is the additional interaction of R with the hydroxide group. This will be equal to $(1-x)I_{R,\bar{O}H}$, where $I_{R,\bar{O}H}$ is the interaction of R with a fully charged hydroxide ion situated in its transition-state position. Since this hydroxide ion is distant from R in the initial state and no longer exists in the final state this is a transition-state interaction which is absent from initial and final states. This model leads to values of $\beta > 1$ when $I_{R,\bar{O}H} > I_{R,NO_2^-}$. Kresge also suggests that this is more likely to be the case where R is on a pseudo acid in which the activating groups commonly remove the negative charge from the proton transfer site and substituents introduced for the purpose of varying acid strength. Though interactions can still occur when R is on an oxygen or nitrogen base these are likely to be small since the charge either remains on the atom where it originated or moves nearer the substituent. Thus for the reaction,

$$SH + RB^- \rightleftharpoons S^- + RBH$$

the equivalent to $I_{R,\bar{O}H}$ and I_{R,NO_2^-} are I_{S^-,B^-} and I_{R,B^-} thus.

$$I_{R,B^-} > I_{S^-,B^-}.$$

Kresge[68] has also advanced similar arguments where various carboxylic acids catalyse the hydrolysis of vinyl ethers. In this case the positive charge being generated on the vinyl ether interacts with polar (or dipolar) groups in the catalyst.

Obviously any interaction which is present in every case will have no visible effect and only those present in some catalysts and not others will be apparent. It seems reasonable that these interactions could act through the charges present as pointed out by Kresge.[69] This would predict in nitramide decomposition the observed order of parallel Brönsted lines for differently charged bases. He further suggests that in flexible systems attractive interactions (energy lowering) would bring the interacting groups closer together and augment the effect, whereas repulsive interactions will push the interacting groups apart and minimise the effect. Although if these effects are considered as essentially inductive effects on the charge there would be a balance between minimising the charge repulsion and keeping the species sufficiently close together to minimise the activation energy. It is not unreasonable that effects such as this should parallel acidity constants, leading to a trend in the magnitude of transition state interactions.

The aims of the present work are to extend the work of Bordwell and Kresge in compounds where substitution is distant from the reaction centre, and in particular to study the magnitude of deviations with the acidity of the substrate and charge of the base. The compounds used were chosen on the criteria:-

(a) ability to scavenge

(b) pK_A's are measurable

(c) proton transfer occurs at an accessible rate

(d) substituents in the substrates are distant from the reaction centre.

EXPERIMENTAL

Theory

Kinetics were followed by one of two techniques:-

(a) Scavenging of the anion with bromine

(b) Tritium exchange.

The former has been discussed previously and will not be mentioned here.

In the detritiation experiments, results are obtained in the form of a measured count per minute (c.p.m.) as a function of time, the c.p.m. being directly proportional to the radioactivity remaining in the ketone. Since this is a tracer technique back reaction involving the substrate anion is with hydrogen not tritium and the rate expression takes the form,

$$\text{Rate} = \frac{d[S\text{-}T]}{dt} = k_B^T [S\text{-}T][B] = k^T[S\text{-}T]$$

where k^T is the pseudo first-order rate constant for detritiation. This integrates to,

$$\ln \frac{[S\text{-}T_o]}{[S\text{-}T_t]} = k^T t + C$$

where $[S\text{-}T]_t \propto (\text{c.p.m.})_t$

$[S\text{-}T]_o$ being incorporated into the integration constant and $[S\text{-}T]_\infty$ or $(\text{c.p.m.})_\infty$ is zero.

Thus for first-order kinetics a plot of $\log_{10}(\text{c.p.m.})_t$ versus time(t) gives a straight line the slope of which is related to k_B^T by

$$k_B^T = -\text{slope} \times \frac{2.303}{[B]}$$

Instrumentation

Scavenging experiments were carried out using a Gilford 2400 or 2400S and have already been discussed.

Tritium is a very weak β emitter (E_{max} = 18.6 KeV) with a half life of 12 years. Since the introduction of liquid scintillation counting its analysis has become a routine matter. The method consists of dissolving the radioactive sample in a solution comprising a scintillation solvent and solute. In the scintillation process the energy of an ionising particle is converted into light-energy with wavelengths that can be detected by a photomultiplier tube assembly. The solvent (toluene in this case) absorbs the energy of the ionising particle and transfers it to the solute (2,5-diphenyloxazole in this case). The fluorescence of the excited solute molecule represents the scintillation emission of the binary solution. A secondary solute may be used if the wavelength distribution of the scintillation emission is not matched to the photomultiplier response.

The assay of radioactive samples in the present study was carried out in an Intertechnique S.L.30 liquid scintillation spectrometer. The scintillator is viewed with two photomultiplier tubes operating in coincidence to reduce background counts due to thermionic emission at the photocathode. The coincidence technique ensures that only simultaneous pulses, occurring in both photomultipliers within a certain coincidence resolving time, are recorded. The electronic pulses from the anode of the photomultiplier are fed to electronic circuits for amplification, pulse-amplitude analysis and data recording.

Materials

Water was deionised and distilled from potassium permanganate. It was then boiled for 30 min and cooled under nitrogen.

Acetic acid, hydrochloric acid and sodium hydroxide solutions were prepared from B.D.H. volumetric ampoules.

Potassium chloride, Benzoic acid, Pyridine and Monochloroacetic acid were BDH 'AnalaR' materials and were used without further purification, though monochloroacetic acid solutions were titrated with standard alkali before use.

3-Chloropropionic acid was recrystallised from cyclohexane, 2-chloropropionic acid was distilled at 83°C 12 mm Hg. Propionic acid was distilled at 140°C.

Toluene used in the tritium work was BDH "sulphur free".

All buffer solutions were prepared by adding sodium hydroxide to the acid and the concentration varied by dilution of this solution, made up to an ionic strength of 0.2 mol dm^{-3} by addition of potassium chloride. The pH values were checked (glass electrode) and adjusted in the diluted buffers by addition of HCl where necessary. In the case of monochloroacetic and 2-chloropropionic acids the concentration of basic buffer component was corrected by adding to it the hydrogen ion concentration assuming an activity coefficient of $f_{\pm} = 0.72$.

The other compounds consisted of three series of substituted benzyl groups attached to the acidic carbons of:-

(a) Ethyl acetoacetate
(b) Acetylacetone
(c) Malononitrile.

In addition a series of substituted benzoylacetones were prepared.

The benzyl derivatives were prepared by two general methods:

(1) Reaction of the active methylene compound with one equivalent of potassium hydroxide and one equivalent of substituted benzyl chloride or bromide in acetal according to Weizmann.[70] The reaction products were acidified and extracted with ether followed by distillation or recrystallisation etc. as given under individual compounds.

(2) By reaction of the sodium salt of the active methylene compound with the substituted benzyl halide (usually bromide) in dry ether or benzene. The sodium salts were prepared from one equivalent of sodium ethoxide and refluxed with the benzyl halide for 24 hours. The mixture was then acidified, the ether layer removed, evaporated and distilled or recrystallised as given under individual compounds.

All preparations were carried out without regard for maximum yield and no yields are therefore quoted. All ^{1}H n.m.r. spectra are in accordance with the structures.

Ethyl(benzyl)acetoacetate.

Method 1. Distilled 156-8^{o}C 12 mm Hg. (Lit 156-160 13 mm Hg)[70]

Ethyl(4-nitrobenzyl)acetoacetate.

Method 2. Purified by preparative thin layer chromatography on silica plates with 80% ether-petrol. This gave a pale yellow solid which was recrystallised from 50% benzene-petrol m.p. 43^{o}C (Lit 43-45^{o}C)[71]

Ethyl(3-methyl benzyl)acetoacetate.

Method 2. Distilled at 116-117^{o}C 0.8 mm Hg. 110-112 0.25 mm Hg[73]

Ethyl(4-chlorobenzyl)acetoacetate.

Method 2. Distilled at 123°C 4 mm Hg (Lit 190-7°C 18 mm Hg)[72]

Ethyl(4-methoxybenzyl)acetoacetate

The 4-methoxybenzyl bromide was prepared from the corresponding alcohol[75] and distilled at 130°C 16 mm Hg

Lit 130° 16 mm Hg.[74]

Method 2. Distilled 145°C 0.05 mm Hg (Lit 172°C 0.25 mm Hg)[76]

Ethyl(4-cyanobenzyl)acetoacetate.

4-cyanobenzyl bromide was prepared by bromination of p-tolunitrile.[77]

Method 2 was used and the product purified by column chromatography on silica with 50% ether-petrol. This gave a colourless oil which solidified on standing. Infrared spectroscopy (neat liquid) showed C≡N stretching at 2220 cm^{-1} and carbonyl absorption at 1720 and 1740 cm^{-1}. This is believed to be a new compound.

Benzylacetylacetone.

Method 2. Distilled at 125°C 3.25 mm Hg (Lit 110-12°C 2 mm Hg)[78]

4-nitrobenzyl acetylacetone

Method 2. Purified by preparative thin layer chromatography on silica plates with 80% ether-petrol. This gave an oil which solidified on standing and was recrystallised from ethanol.

m.p. 82°C.

4-Methoxbenzyl acetylacetone.

Method 2. Distilled 166°C 0.7 mm (Lit 174-6°C 1 mm Hg)[79]

4-cyanobenzyl acetylacetone.

Method 2. The product was purified by column chromatography on silica with 50% ether-petrol. This gave a colourless solid which was recrystallised from 70% ethanol-water m.p. 38-40°C. This is believed to be a new compound. Infra-red spectroscopy (nujol mull) showed C≡N stretching at 2215 cm^{-1}.

4-Chlorobenzyl acetylacetone.

Method 1. Distilled 164°C 1.5 mm Hg.

4-Chlorobenzyl malononitrile.

Method 1. The crude product was sublimed 150°C 2 mm Hg. m.p. 86-9 (Lit 89°C)[80]

4-nitrobenzyl malononitrile.

Method 2. The product was recrystallised from 90% methanol-water but still contained some 4-nitrobenzyl bromide. This was removed by thin layer chromatography (silica plates, ether) and the product recrystallised from 90% methanol-water. m.p. 150°C. This is believed to be a new compound. Infra-red spectroscopy showed weak C≡N at 2260 cm^{-1} and strong NO_2 bands at 1350 and 1520 cm^{-1}.

Benzyl malononitrile.

The above preparations (in particular of 4-chlorobenzyl malononitrile) were far from satisfactory in yield, the condensation step appears to decompose malononitrile. The parent compound was therefore prepared via diethyl benzyl malonate[81] and benzyl malondiamide[82] to benzyl malononitrile.[80] The product was recrystallised from aqueous methanol m.p. 90°C (Lit 79°C,[80] 91°C.[83])

4-cyanobenzyl malononitrile.

Prepared by the same method as benzyl malononitrile. The ester, diethyl(4-cyanobenzyl)malonate, was distilled at 219°C 1 mm Hg but the final product would not distil off phosphorus pentoxide[80] and was extracted with ether. Recrystallisation from aqueous methanol gave the final material
m.p. 118°C.
This is believed to be a new compound. Infra-red spectroscopy showed a weak C≡N at 2260 cm^{-1} and a stronger band at 2240 cm^{-1}.

Benzoylacetone.

Commercial material was recrystallised from 90% aqueous methanol m.p. 56°C (Lit 58°C)[84]

p-Nitrobenzoylacetone.

This was prepared by the method of Barry[85] involving reaction between the copper complex of acetylacetone and p-nitrobenzoyl chloride in chloroform at room temperature. Recrystallisation from methanol gave the compound
m.p. 112°C (Lit 112-114)[85]

p-Methylbenzoylacetone.

This was prepared by reaction of the sodium salt of p-methylacetophenone on ethyl acetate. Distillation at 160°C 10 mm Hg gave the material. Lit 132°C 15 mm Hg[86]

p-Methoxybenzoylacetone.

This was prepared according to Sabnis.[87]
m.p. 57-8°C (Lit 53°C)[87]

p-Chlorobenzoylacetone.

Prepared as p-methoxybenzoylacetone.
m.p. 71-2°C (Lit 72-3)[88]

p-Cyanobenzoylacetone.

Prepared as p-methoxybenzoylacetone. The material was recrystallised from ethanol and carbon tetrachloride. m.p. 89°C. This is believed to be a new compound. Infra-red spectroscopy showed C≡N stretch at 2240 cm^{-1}.

Ethyl (α phenyl) acetoacetate was prepared according to Wong[89] and distilled at 125°C 4 mm Hg Lit 129°C 7 mm Hg[89]
Commercial phenylacetone was distilled at 87°C 6 mm Hg
Lit 86-87°C 6 mm Hg[74]
The preparation of benzyl nitroacetone was attempted from the sodium salt of nitroacetone[90] and benzyl bromide in ether. Proton n.m.r. of the crude material showed an acidic triplet but attempted recrystallisation from methanol gave an oil which would not crystallise and n.m.r. now showed no acidic protons. The compound was judged to be unstable and work was discontinued.

Procedure

(a) Kinetics by Scavenging

To 2 ml of the appropriate buffer solution plus 0.2 ml of 1 mol dm^{-3} potassium bromide, 5 µl (10 µl in the benzoylacetone series) of 0.02 mol dm^{-3} bromine in 1 mol dm^{-3} potassium bromide were added. The cell was thermostated at 25°C and 3 µl of 0.02 mol dm^{-3} substrate in acetonitrile were added. The disappearance of tribromide ion was followed at 300 nm giving a fall in absorption from approximately 0.24 to 0.15 O.D. All rates were observed to be independent of bromine concentration.

In the case of benzoylacetone two moles of bromine are taken up per mole of substrate and it has been shown[91] that the second bromine atom goes in half as fast as the first one. As a result of this the observed rate constant is equal to that of the second bromine entering the substrate molecule, and the observed rate constants have been doubled to give the rates of ionisation of SH_2.

For the malononitrile series difficulty was encountered with scavenging. The kinetic experiments were therefore carried out as follows. To 3 ml of buffer containing 0.1 mol dm^{-3} potassium bromide, 25 µl of 0.44 mol dm^{-3} bromine in potassium bromide solution were added to give $[Br_2] = 5 \times 10^{-3}$. The cells were thermostated at 25°C and 20 µl of 0.1 mol dm^{-3} substrate in acetonitrile added to give $[SH] = 6 \times 10^{-4}$ mol dm^{-3}. This gives a fall in optical density at 380 nm from approximately 1.8 to 1.6. No work was done below pH5 because of this scavenging difficulty, and above pH5 the rates of bromine uptake were independent of bromine concentration.

The results were analysed by the LETAGROP VRID of Sillen[92,93] for a first order curve plus a linear decrease in absorbance. This linear decrease was negligible in the

malononitrile series and has been commented on before for diketones.[91] The previous work[91] considered th is to be due to decomposition of the bromination product and further reaction with bromine of the decomposition products, but it could also be bromination in other parts of the molecule or simple evaporation of bromine from the cell. In all cases (allowing for the linear decrease) the calculated quantity of bromine is consumed. No acid catalysis was detected.

(b) Kinetics by tritium exchange

Approximately 100 mg of compound were dissolved in 1 ml of dry dioxan and 1 µl of 5 Ci cm^{-3} tritiated water were added. This was left at least 24 hours at room temperature in the case of the malononitriles, and several days at 50°C for the acetylacetone series. Sodium sulphate was added and a small amount of this solution (approximately 2 µl) were added to 20 ml of thermostated buffer or acid solution. 1 ml aliquots were taken at appropriate time intervals. These aliquots were added to 10 ml of toluene plus 2,5 diphenyloxazole (7g per litre), over 10 ml of water. This was shaken, the toluene separated, dried, and 5 ml counted for an appropriate time. The first-order rate constants were obtained from a plot of $\log_e$ c.p.m. versus time. Several infinity values were checked and found to be negligible.

(c) pK_A determinations

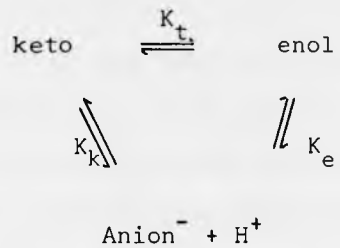
This was carried out spectrophotometrically by observing the anion absorption at 287, 309 and 233 nm for the ethyl acetoacetate, acetylacetone and malononitrile series respectively. In solutions of potassium hydroxide this absorption decreased slowly with time and a slight extrapolation

was necessary. A constant concentration (1×10^{-4} mol dm^{-3} for the malononitriles, 5×10^{-5} mol dm^{-3} for ethyl acetoacetate and acetylacetone series) of substrate was added to a series of standard buffer solutions,[94] 1 mol dm^{-3} potassium hydroxide, 0.1 mol dm^{-3} potassium hydroxide and 0.1 mol dm^{-3} hydrochloric acid. Where there was no absorption by molecular species the acidity constants were obtained from a plot of observed optical density versus observed optical density divided by activity of hydroxide ion (calculated from K_w and the known pH's). This gives a slope of $-K_w/K'_{SH}$ where $K'_{SH} = [S^-][H_3O^+] f_{H_3O^+}/[SH]$. In cases where the uncharged molecule absorbs the above procedure was carried out to give an approximate pK_A and the procedure repeated subtracting the absorption of the molecular species from the observed total absorption. All acidity constants were corrected for the activity coefficients of the substrate anions by subtracting log f_i, determined from

$$- \log f_i = \frac{Az^2\sqrt{I}}{1 + Ba_i\sqrt{I}}$$

where A = 0.51 $mol^{-\frac{1}{2}}$ $dm^{3/2}$, B = 0.33×10^8 cm^{-1} $mol^{-\frac{1}{2}}$ $dm^{3/2}$ and $a_i = 5 \times 10^{-8}$ cm. The ionic strength varied slightly through the range of buffer solutions and an average was taken for the buffer solutions used in each particular pK_A determination.

The acidity constants were also corrected for enol content. We have



and determine

$$K' = [S^-][H^+] / [\text{Keto} + \text{Enol}]$$
$$= K_k/(K_T + 1)$$

(d) Enol-Content Determinations

To 3 ml of solution containing 0.1 mol dm^{-3} hydrochloric acid and 0.1 mol dm^{-3} potassium bromide, 5 µl of a solution of known substrate concentration (approximately 0.02 mol dm^{-3}) in dioxan (freshly distilled from lithium aluminium hydride) were added. This was followed by 10 µl of 0.02 mol dm^{-3} bromine. Observing the tribromide ion at 330 nm the chart drive was started as the bromine was added and the first order curve extrapolated back to zero time. The linear loss of bromine at the end of reaction was also extrapolated to zero time. Substitution of pure dioxan for substrate solutions provided a blank and the enol content was taken as the ratio of bromine consumed immediately to that consumed in the reaction less that consumed by linear decrease.

A second method was based on liberation of iodine from potassium iodide.

To 10 ml of a solution containing 0.09 mol dm^{-3} hydrochloric acid and 0.1 mol dm^{-3} potassium bromide 20 µl of a solution of known substrate concentration (approximately 0.1 mol dm^{-3}) in dioxan were added. This was followed by 200 µl of 0.05 mol dm^{-3} bromine in 1 mol dm^{-3} potassium bromide and immediately by 100 µl of 10% (volume) aqueous allyl alcohol. 1 ml of this solution was mixed with 1 ml of 0.2 mol dm^{-3} potassium iodide and the iodine which is liberated determined spectrophotometrically at 353 nm with $\varepsilon_{I_3^-} = 2.49 \times 10^4$ mol^{-1} dm^3 cm^{-1} and K for the equilibrium,

$$I_2 + I^- = I_3^-$$

$$K = 714 \text{ mol}^{-1}\text{dm}^{+3}$$

The amount of iodine liberated in the same procedure using pure dioxan in place of a substrate solution was subtracted from each determination as was the absorption due to substrate, though this was negligible in all but one case.

RESULTS

In the following tables where particular runs have been duplicated the average rate constant is given.

Ethyl α phenylacetoacetate in 0.2 mol dm^{-3} acetate buffer of pH 4.75 gave an instantaneous reaction with bromine. Scavenging of phenylacetone with iodine gave k_{AcO^-} of 3×10^{-5} s^{-1} mol^{-1} dm^3, for acetone[95] k_{AcO^-} is 1.5×10^{-5} min^{-1} mol^{-1} dm^3 a factor of 360 allowing for the number of protons. Ethyl acetoacetate[96] has k_{AcO^-} = 29 min^{-1} mol^{-1} dm^3 and if the phenyl group has the same effect (a factor of 180 allowing for the number of protons) the reaction in 0.1 mol dm^{-3} AcO^- would have a half life of < 0.1s.

Typical kinetic results are shown for scavenging and detritiation experiments, and a typical acidity constant determination is given.

The rates were found to obey the expression $k = k_o + k_B[B]$.

TABLE 1

Rate of bromination of Ethyl (α benzyl) acetoacetate at 25°C

Monochloroacetate

10^2 $[RCO_2^-]$	2.05	4.10	5.50	6.85
10^5 k/s^{-1}	5.1	9.5	12.3	15.3

2 Chloropropionate

10^2 $[RCO_2^-]$	3.20	4.70	6.30	7.90
10^4 k/s^{-1}	2.26	2.73	3.03	3.42

3 Chloropropionate

10^2 $[RCO_2^-]$	1.20	2.40	3.60	4.80	6.00
10^4 k/s^{-1}	1.43	2.00	3.08	3.82	4.72

Benzoate

10^2 $[RCO_2^-]$	1.8	3.65		7.3	9.1
10^4 k/s^{-1}	1.33	2.50		6.16	7.17

Acetate

10^2 $[RCO_2^-]$	1.80	3.60	5.45	7.30	9.10
10^4 k/s^{-1}	2.83	5.42	8.05	9.75	12.83

Propionate

10^2 $[RCO_2^-]$	1.80	3.60	5.45	7.30	9.10
10^4 k/s^{-1}	4.16	6.92	9.66	12.67	15.80

TABLE 2

Rates of bromination of substituted ethyl (α benzyl) acetoacetate at 25°C with acetate catalysis

pMeO

10^2 $[AcO^-]$	2.7	5.4	8.1	10.8	13.5
10^4 k/s^{-1}	4.33	7.75	11.40	13.50	17.30

pMe

10^2 $[AcO^-]$	2.7	5.4	8.1	10.8	13.5
10^4 k/s^{-1}	6.67	8.83	12.80	16.00	18.80

m-Me

10^2 $[AcO^-]$	2.7	5.4	8.1	10.8	13.5
10^4 k/s^{-1}	2.50	6.16	10.00	12.60	18.10

pCl					
10^2 $[AcO^-]$		3.60	5.45	7.3	9.1
10^4 k/s^{-1}		7.75	11.80	14.50	19.00

p-CN					
10^2 $[AcO^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	8. 5	15.8	24.0	31.0	35.5

pNO_2					
10^2 $[AcO^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	12.0	22.0	32.3	42.8	51.8

Enol content determinations of substituted Ethyl (α benzyl) acetoacetates at 25°C in aqueous solutions.

Within experimental error no enol was found to be present.

TABLE 3

Acidity constant determinations on substituted Ethyl (α benzyl) acetoacetates at 25°C in aqueous solution.

Substituent	pK_A'	I mol^{-1} dm^3	-log f_i	pK_A
p-MeO	11.72	0.13	0.17	11.89
p-Me	11.71	0.13	0.17	11.88
m-Me	11.70	0.13	0.17	11.87
p-H	11.64	0.13	0.17	11.81
p-Cl	11.42	0.09	0.15	11.57
p-CN	11.08	0.09	0.15	11.23
p-NO_2	10.91	0.09	0.15	11.06

TABLE 4

Summarised data for ethyl (α benzyl) acetoacetate catalysed by various bases at 25°C

Base	pK_A of conjugate acid	10^3 k/s^{-1} mol^{-1} dm^3	$-\log_{10}k$
Monochloroacetate	2.86	2.14	2.67
2-chloropropionate	2.96	2.35	2.63
3-chloropropionate	4.00	6.98	2.16
Benzoate	4.21	8.53	2.07
Acetate	4.75	14.35	1.84
Propionate	4.87	15.74	1.80

These results are shown in Fig.9.

TABLE 5

Summarised data for substituted ethyl (α benzyl) acetoacetates catalysed by acetate at 25°C

Substituent	pK_A	k s mol dm^{-3} x 10^2	$-\log_{10}k$
pMeO	11.89	1.18	1.93
pMe	11.88	1.24	1.91
mMe	11.87	1.39	1.86
pH	11.81	1.44	1.84
pCl	11.57	1.98	1.70
pCN	11.23	3.70	1.43
pNO_2	11.06	4.98	1.30

These results are shown in Fig.10.

TABLE 4

Summarised data for ethyl (α benzyl) acetoacetate catalysed by various bases at 25°C

Base	pK_A of conjugate acid	10^3 k/s^{-1} mol^{-1} dm^3	$-\log_{10}k$
Monochloroacetate	2.86	2.14	2.67
2-chloropropionate	2.96	2.35	2.63
3-chloropropionate	4.00	6.98	2.16
Benzoate	4.21	8.53	2.07
Acetate	4.75	14.35	1.84
Propionate	4.87	15.74	1.80

These results are shown in Fig.9.

TABLE 5

Summarised data for substituted ethyl (α benzyl) acetoacetates catalysed by acetate at 25°C

Substituent	pK_A	k s mol dm^{-3} x 10^2	$-\log_{10}k$
pMeO	11.89	1.18	1.93
pMe	11.88	1.24	1.91
mMe	11.87	1.39	1.86
pH	11.81	1.44	1.84
pCl	11.57	1.98	1.70
pCN	11.23	3.70	1.43
pNO_2	11.06	4.98	1.30

These results are shown in Fig.10.

FIG.9.
BRÖNSTED PLOT OF ETHYL(∝BENZYL) ACETOACETATE CATALYSED BY VARIOUS BASES

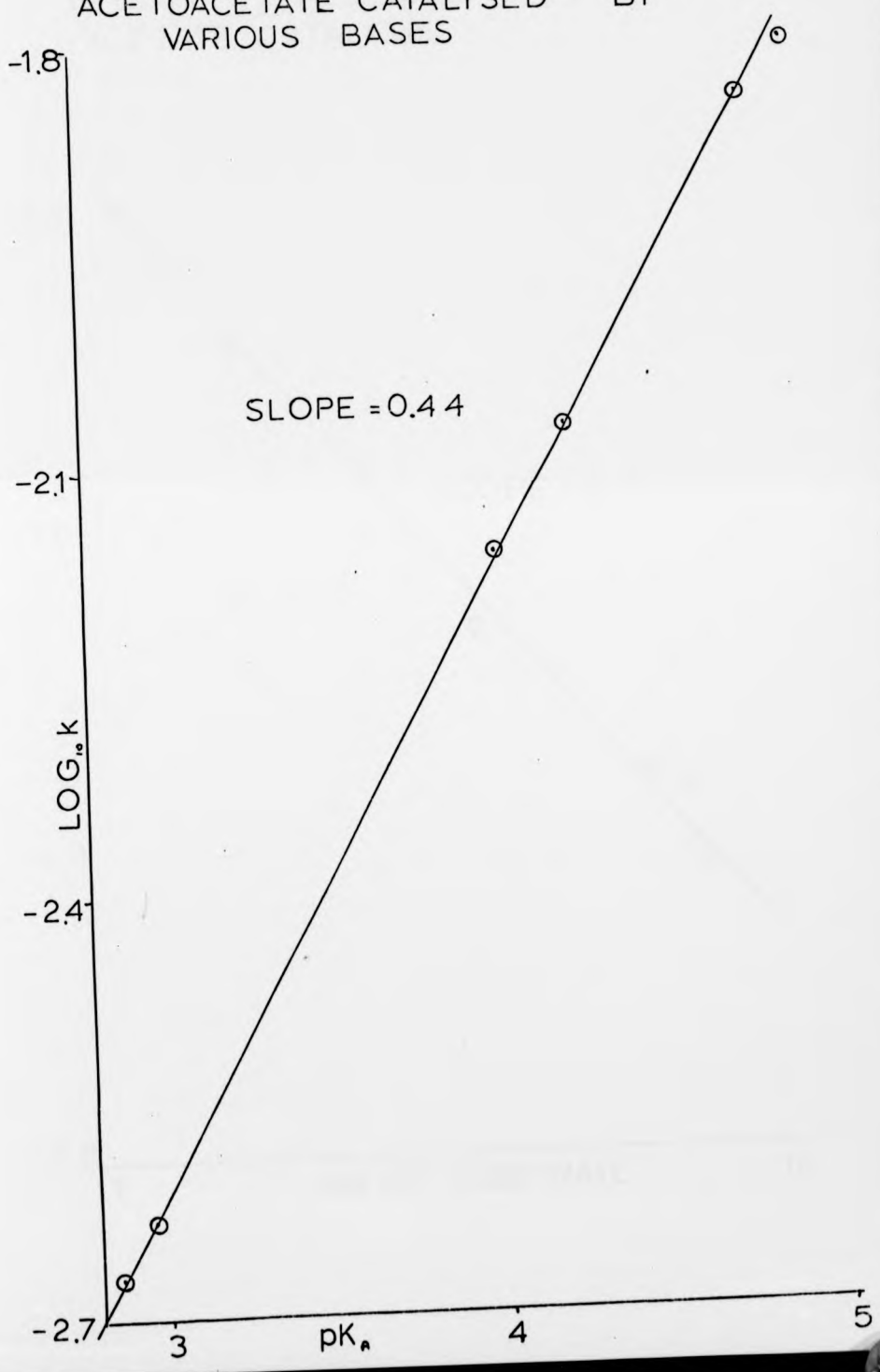


FIG 10
BRÖNSTED PLOT OF SUBSTITUTED ETHYL (∝ BENZYL) ACETOACETATES WITH ACETATE CATALYSIS.

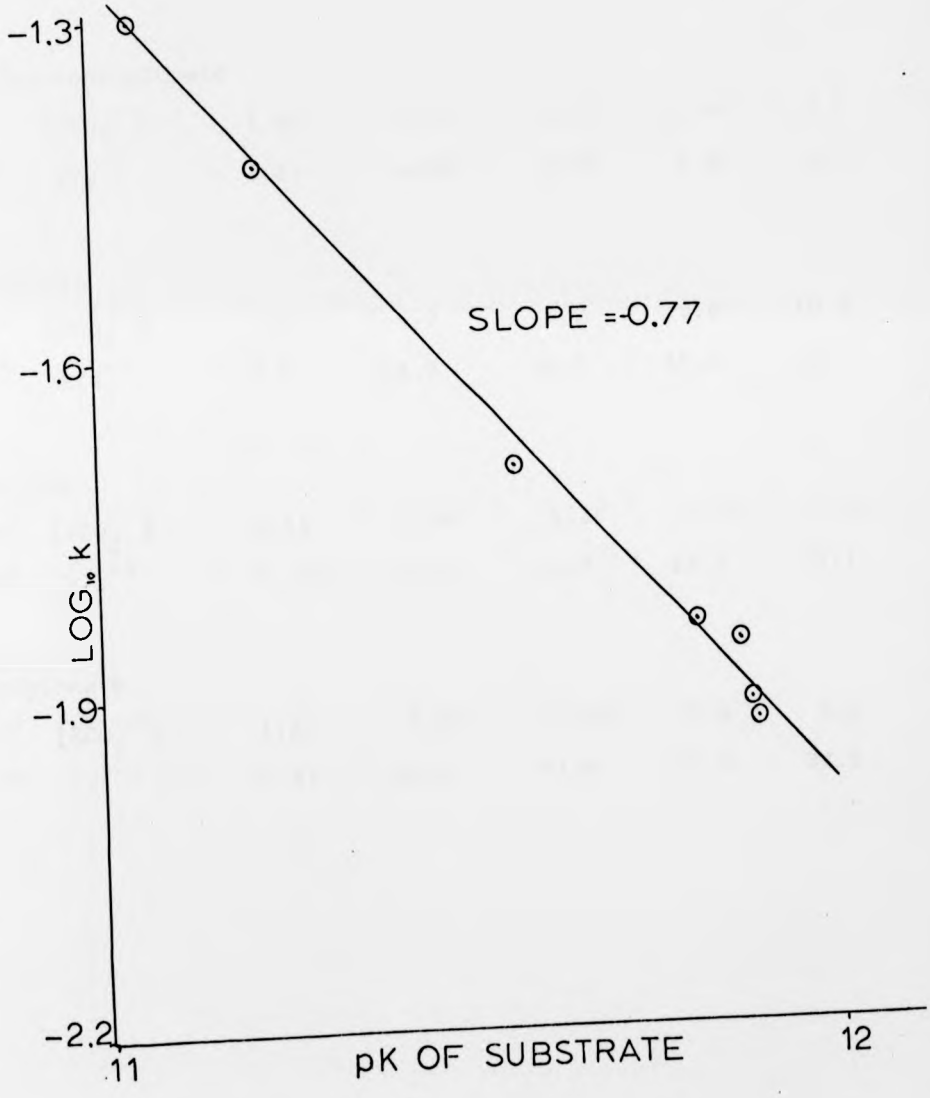


TABLE 6

Rates of bromination of benzyl acetylacetone with various base catalysts at 25°C

Monochloroacetate					
10^2 $[RCO_2^-]$	1.65	3.30	5.00	6.65	8.30
10^4 k/s^{-1}	2.55	3.22	3.95	4.80	5.40
2-chloropropionate					
10^2 $[RCO_2^-]$	1.63	3.25	4.80	6.50	8.1
10^4 k/s^{-1}	3.13	4.08	4.42	5.35	6.43
Benzoate					
10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	9.0	11.0	14.5	19.0	23.3
Acetate					
10^2 $[RCO_2^-]$	1.45	2.90	4.35	5.80	7.25
10^4 k/s^{-1}	7. 67	12.0	16.2	21.3	24.2
Propionate					
10^2 $[RCO_2^-]$	1.82	3.63	5.45	7.3	9.1
10^4 k/s^{-1}	6.33	15.3	21.0	27.3	32.5

TABLE 7

Rates of bromination of substituted-benzyl acetylacetones at 25°C with acetate catalysis

p-MeO

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	8.50	14.2	20.3	24.0	29.5

pCl

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	8.33	15.6	23.8	30.0	41.8

p-CN

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	18.3	31.8	40.2	68.5	84.7

p-NO_2

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	23.8	42.2	63.0	80.8	103.0

TABLE 8

Enol determinations of substituted-benzyl acetylacetones at 25°C in aqueous solution.

Substituent	% Enol
pMeO	18
H	15
P-Cl	15
p-CN	15
p-NO_2	15

TABLE 9

Acidity constant determinations on substituted-benzyl acetylacetone at 25°C in aqueous solution

Substituent	pK_A'	I / mol^{+1} dm^{-3}	$-\log f_i$	$\log (K_T + 1)$	pK_A
pMeO	10.50	0.11	0.16	0.086	10.57
p-H	10.40	0.11	0.16	0.071	10.49
p-Cl	10.16	.11	0.16	0.071	10.25
p-CN	9.60	.11	0.16	0.071	9.69
pNO_2	9. 47	.11	0.16	0.071	9.54

TABLE 10

Summarised data for benzyl acetylacetone catalysed by various bases at 25°C

Base	pK_A of conjugate acid	10^3 k/s^{-1} mol^{-1} dm^3	$-\log_{10}k$
Monochloroacetate	2.86	4.48	2.35
2-chloropropionate	2.96	4.93	2.31
Benzoate	4.21	19.0	1.72
Acetate	4.75	29.1	1.54
Propionate	4.87	34.8	1.46

This is shown in Fig.11.

TABLE 11

Summarised data for substituted-benzyl acetylacetones catalysed by acetate at 25°C

Substituent	pK_A	10^3k/s^{-1} mol^{-1} dm^3	$-\log_{10}k$
pMeO	10.57	25.9	1.59
pH	10.49	29.1	1.54
pCl	10.25	40.2	1.40
pCN	9.69	85.7	1.07
pNO_2	9.54	99.1	1.00

These results are shown in Fig.12.

FIG.11.
BRÖNSTED PLOT OF BENZYL ACETYLACETONE CATALYSED BY VARIOUS BASES

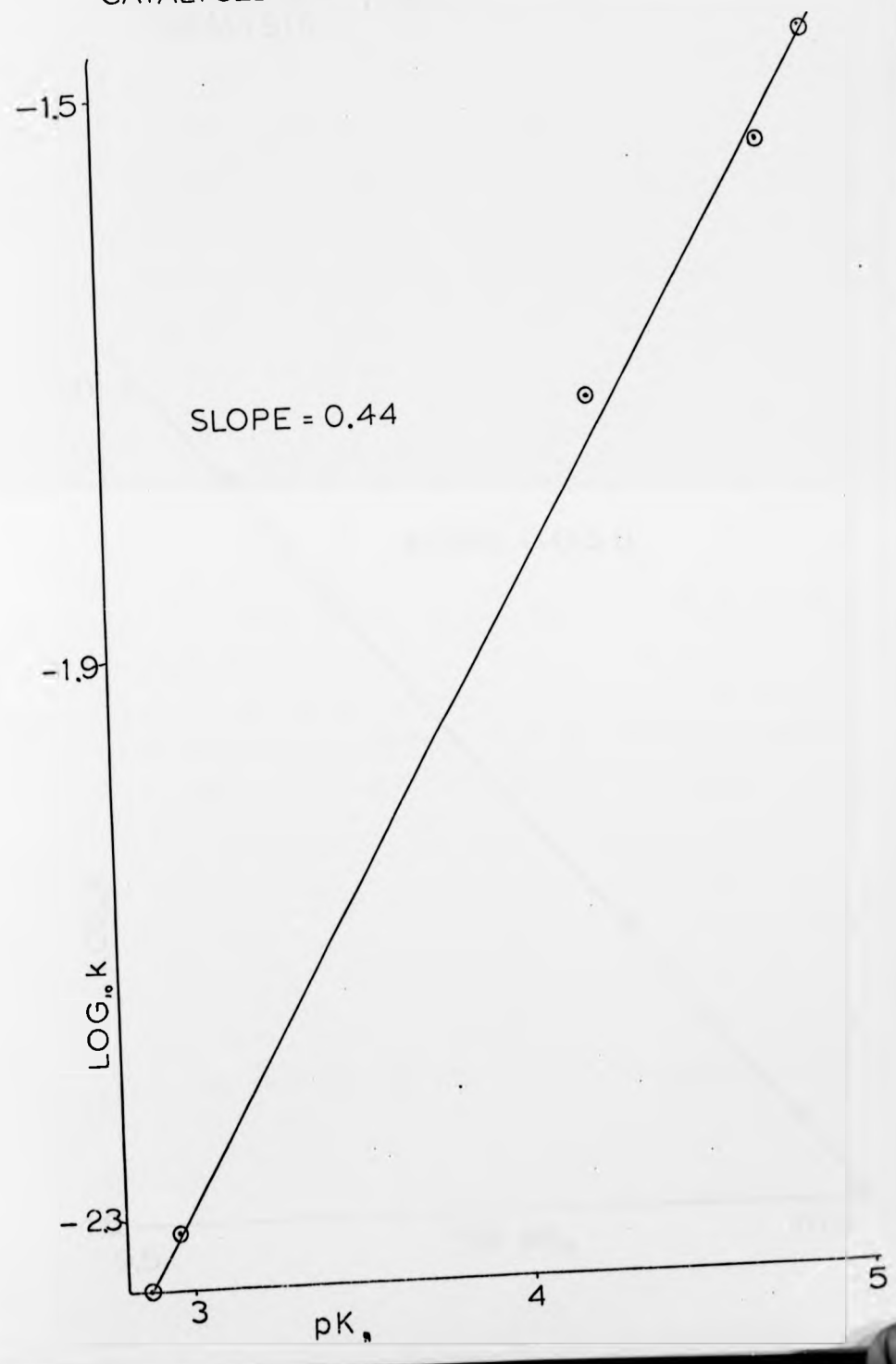


FIG.12.
BRÖNSTED PLOT OF SUBSTITUTED BENZYL ACETYLACETONE WITH ACETATE CATALYSIS

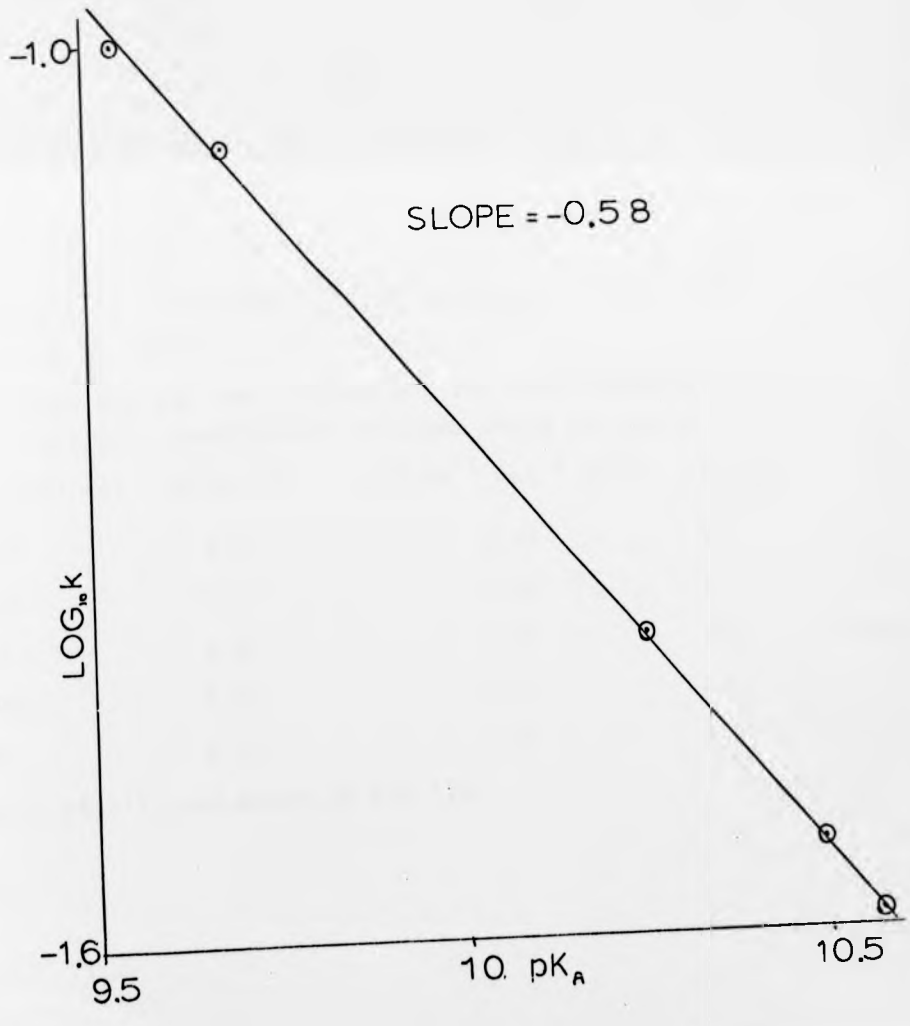


TABLE 12

Rates of detritiation of substituted-benzyl acetylacetones at 25°C

(a) Water catalysis

Substituent	$[H^+]$	10^5 k/s^{-1}	5 + $\log_{10}$k	pK_A
pMeO	0.001	1.19	0.075	10.57
p-H	0.001	1.47	0.167	10.49
p-Cl	0.001	1.79	0.253	10.25
p-CN	0.001	3.26	0. 513	9.69
p-NO_2	0.001	3.90	0.591	9.54
p-H	0.01	1.45	0.161	10.49

These results are shown in Fig. 13.

TABLE 13

(b) Pyridine catalysis. $[Pyridine]_{total}$ = 0.2 mol dm^{-3}

Buffer ratio = 1.

Only one run was carried out for each compound and the catalytic coefficient obtained using the water rates above.

Substituent	10^4k/s^{-1}	10^3k/s^{-1} mol^{-1} dm^{+3}	-$\log_{10}$k	pK_A
pMeO	3.43	3.31	2.48	10.57
p-H	4.27	3.81	2.42	10.49
pCl	5.25	5.07	2.30	10.25
p-CN	9.05	8.72	2.06	9.69
pNO_2	9.70	9.31	2.03	9.54

These results are shown in Fig. 14.

FIG.13.
BRÖNSTED PLOT OF SUBSTITUTED BENZYL ACETYLACETONES WITH WATER CATALYSIS

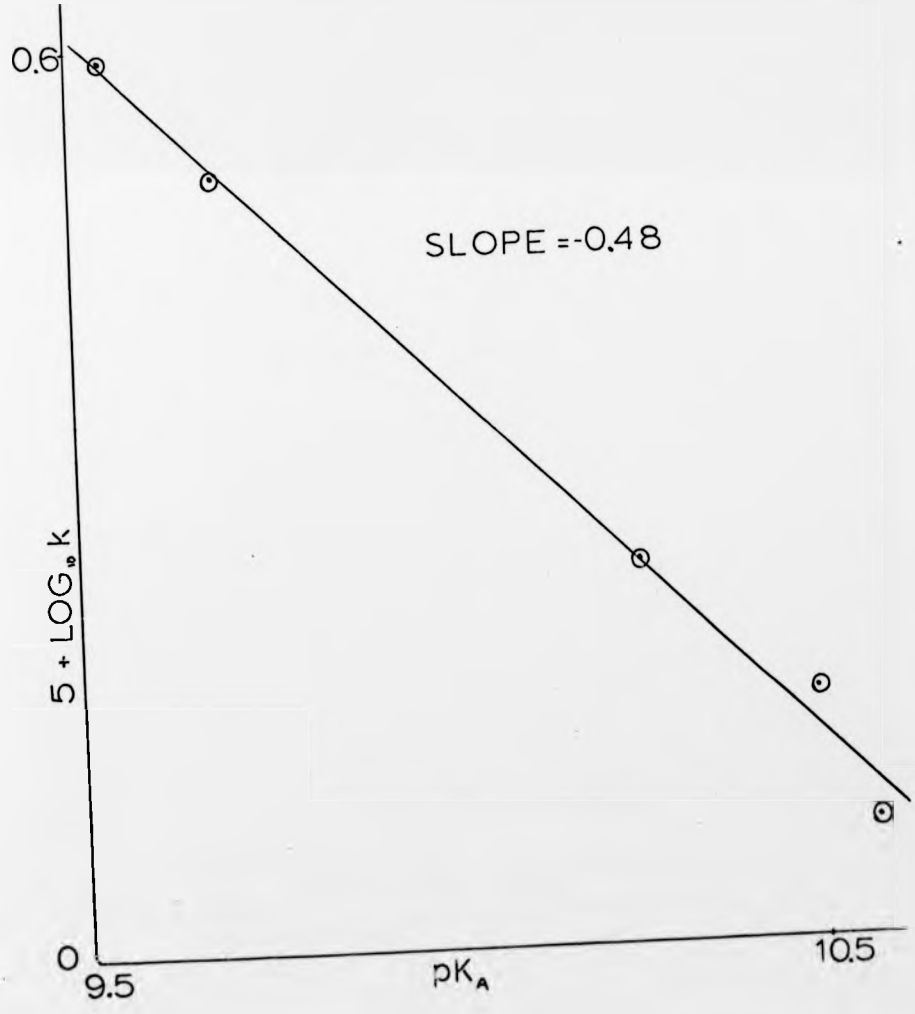
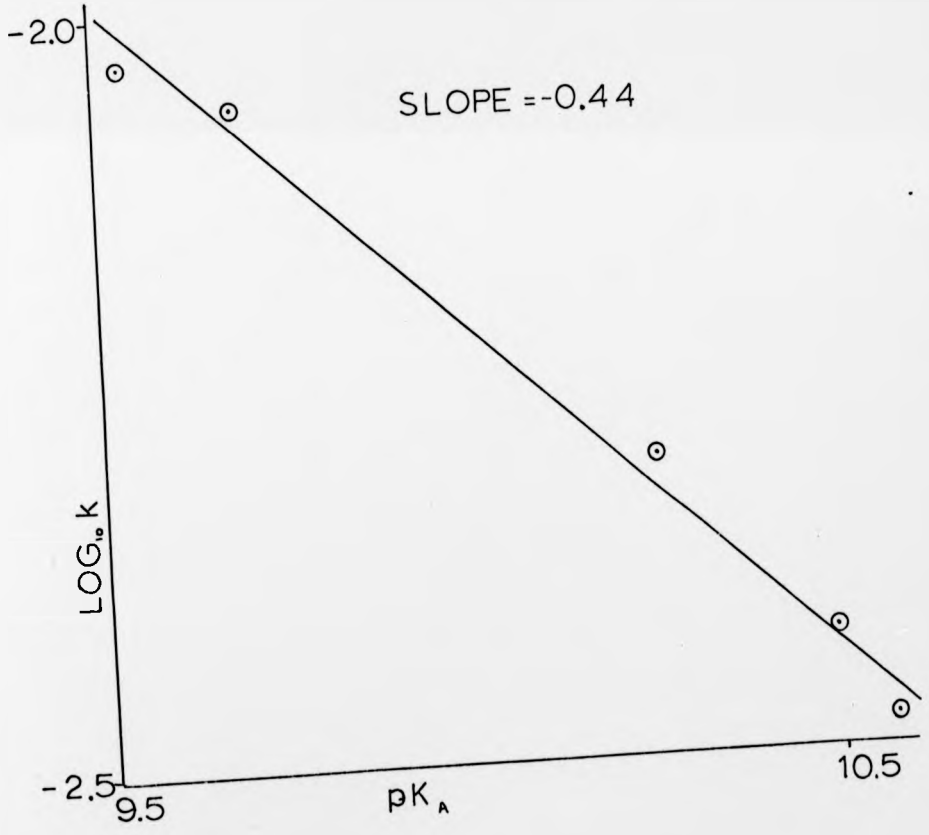


FIG.14.
BRÖNSTED PLOT OF SUBSTITUTED BENZYL ACETYLACETONES WITH PYRIDINE CATALYSIS



Bromination of Benzoylacetone.

We have

$$SH_2 + Br_2 \xrightarrow{k_1} SHBr + Br$$

$$SHBr + Br \xrightarrow{k_2} SBr_2 + Br$$

where k_1 and k_2 are pseudo first-order rate constants. This would not give simple first-order kinetics in general unless (a) $k_2 >> k_1$ or (b) $k_1 = 2k_2$. However first-order kinetics have been observed[91] and the rate of bromination of mono-brominated benzoylacetone has been measured in this work and previously,[91] by adding one equivalent of bromine to a solution of the anion, followed by more bromine. This gives an observed rate equal to that for bromination of benzoylacetone, where two equivalents of bromine are taken up.

We thus have

$$SH_2 + Br_2 \xrightarrow{2k_1} SHBr + Br$$

$$SHBr + Br_2 \xrightarrow{k_1} SBr_2 + Br$$

where k_1 is a pseudo first order rate constant.

$$\frac{d[Br_2]}{dt} = 2k_1[SH_2] + k_1[SHBr]$$

$$= k_1\{2[SH_2] + [SHBr]\}$$

$$[Br_2] - [Br_2]_\infty = 2[SH_2] + [SHBr]$$

$$\frac{d[Br_2]}{dt} = k_1\{[Br_2] - [Br_2]_\infty\}$$

The observed first-order rate constants are therefore doubled to

give the rate of ionisation of SH_2.

Rates of bromination of Benzoylacetone with various base catalysts at 25°C.

This work has been done by Bell[91] giving β of 0.52.

TABLE 14

Rates of bromination of substituted benzoylacetones with acetate catalysis at 25°C

p-MeO						
10^3	$[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^3	k/s^{-1}	8.0	11.5	16.8	21.6	26.4

pMe						
10^3	$[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^3	k/s^{-1}	11.0	20.0	30.0	40.0	50.4

p-H						
10^3	$[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^3	k/s^{-1}	31.2	46.0	55.2	75.2	91.6

p-Cl						
10^3	$[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^3	k/s^{-1}	29.2	58.4	74.8	96.0	130.8

p-CN						
10^3	$[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^3	k/s^{-1}	72.0	100.0	188.0	264.0	260.0

pNO_2						
10^3	$[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^3	k/s^{-1}	184	232	312	392	452

TABLE 15

Enol determinations of substituted benzoylacetones in aqueous solution at 25°C

Substituent	% Enol
pMeO	10
pMe	45
pH	48
pCl	56
pCN	61
pNO_2	75

TABLE 16

Summarised data for substituted benzoylacetones at 25°C catalysed by acetate

Substituent	pK_A'/(ref.99)	$\log_{10}(K_T+1)$	pK_A	$k/s^{-1}mol^{-1}dm^3$	$\log_{10}k/s^{-1}mol^{-1}$
pMeO	9.21	0.05	9.16	1.188	0.075
pMe	8.99	0.26	8.73	2.532	0.403
pH	8.71	0.28	8.43	3.668	0.564
PCl	8.42	0.36	8.06	6.000	0.778
pCN	7.75*	0.41	7.34	14.24	1.154
pNO_2	7.57	0.60	6.97	17.56	1.245

* This value is from a plot of $\log_{10} K/K_o$ versus σ using $\sigma = 0.660$[97]

These results are shown in Fig.15.

FIG.15.
BRÖNSTED PLOT OF SUBSTITUTED BENZOYLACETONES WITH ACETATE CATALYSIS.

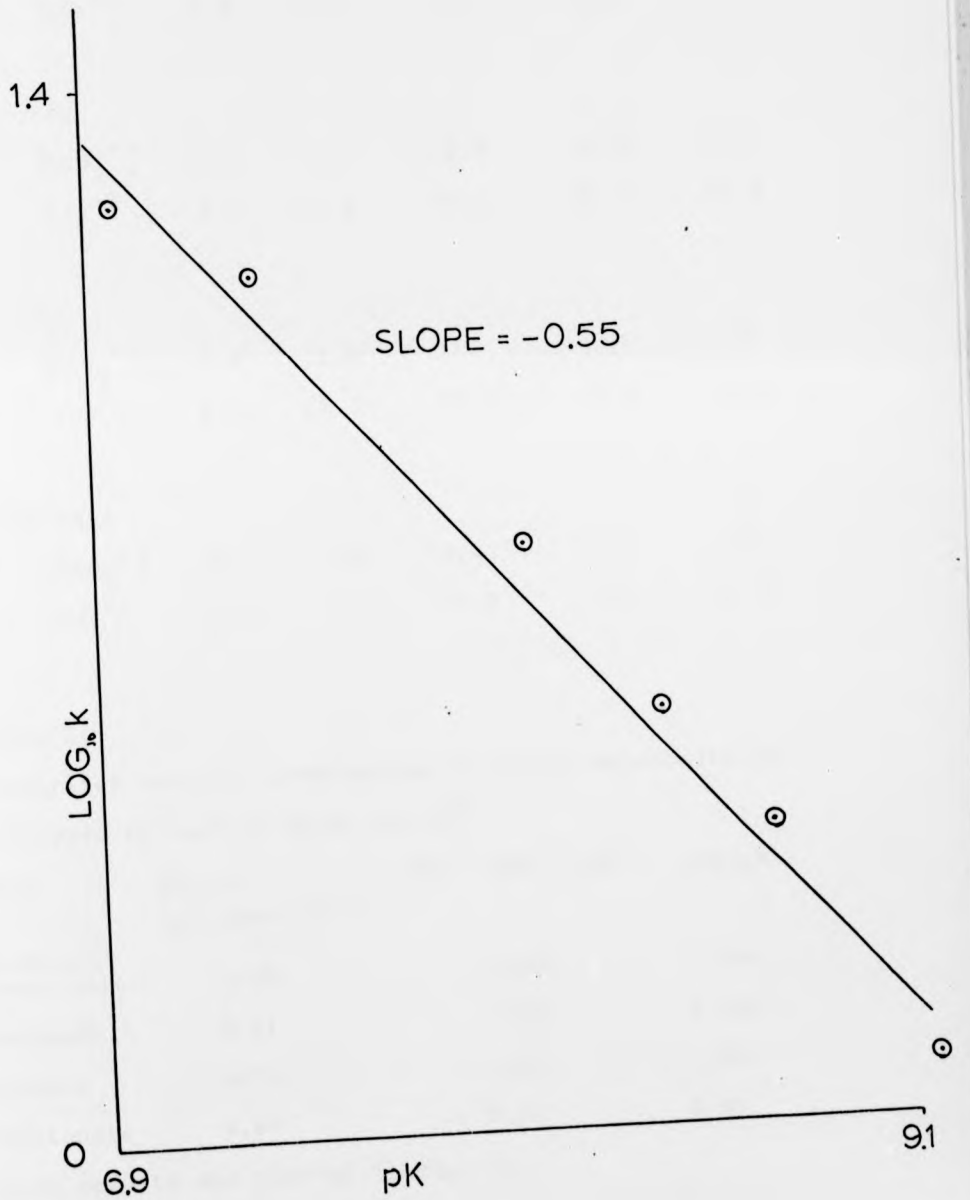


TABLE 17

Rate of bromination of benzyl malononitrile catalysed by various bases at 25°C

3-chloropropionate

10^2 $[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^2 k/s^{-1}	9.3	16.9	21.2	23.8	30.4

Benzoate

10^2 $[RCO_2^-]$	4.0	8.0	12.0	16.0	20.0
10^2 k/s^{-1}	8.5	17.1	20.7	30.5	40.7

Acetate

10^2 $[RCO_2^-]$	0.8	1.6	2.4	3.2	4.0
10^2 k/s^{-1}	6.1	14.7	17.2	23.9	29.9

Propionate

10^2 $[RCO_2^-]$	0.8	1.6	2.4	3.2	4.0
10^2 k/s^{-1}	10.1	17.7	25.9	32.5	37.0

TABLE 18

Summarised data for bromination of benzyl malononitrile catalysed by various bases at 25°C

Base	pK_A of Conjugate Acid	k/s^{-1} mol^{-1} dm^3	$\log_{10}k$
3-Chloro-propionate	4.00	1.256	0.099
Benzoate	4.21	1.933	0.286
Acetate	4.75	7.33	0.865
Propionate	4.87	8.71	0.94

These results are plotted in Fig. 16.

FIG 16
BRÖNSTED PLOT OF BENZYL MALONONITRILE CATALYSED BY VARIOUS BASES

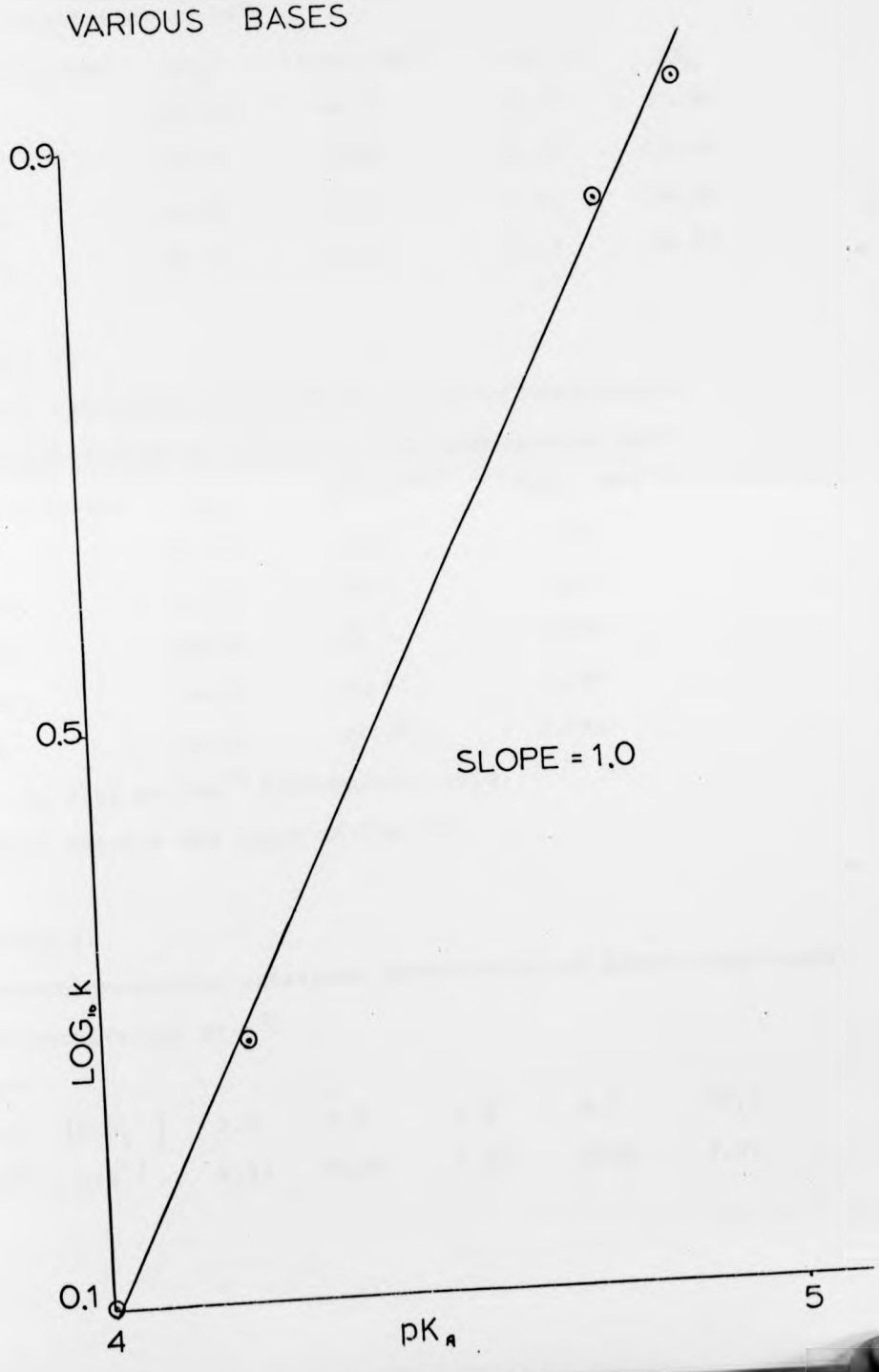


TABLE 19

Acidity constant determination of substituted-benzyl malononitriles at 25°C

Substituent	pK_A'	I/mol dm^{-3}	-log f_i	pK_A
pH	11.63	0.13	0.17	11.80
pCl	11.34	0.09	0.15	11.49
pCN	10.81	0.09	0.15	10.96
pNO_2	10.72	0.09	0.15	10.87

TABLE 20

Water catalysed detritiations of substituted-benzyl malononitriles at 25°C in 0.001M hydrochloric acid

Substituent	pK_A	$10^4 k/s^{-1}$	$-\log_{10} k/s^{-1}$
pH	11.80	27.0	2.569
pCl	11.49	38.3	2.417
pCN	10.96	86.7	2.062
pNO_2	10.87	91.4	2.039
pH	11.80	26.0*	2.585

* in 0.01 mol dm^{-3} hydrochloric acid

These results are shown in Fig. 17.

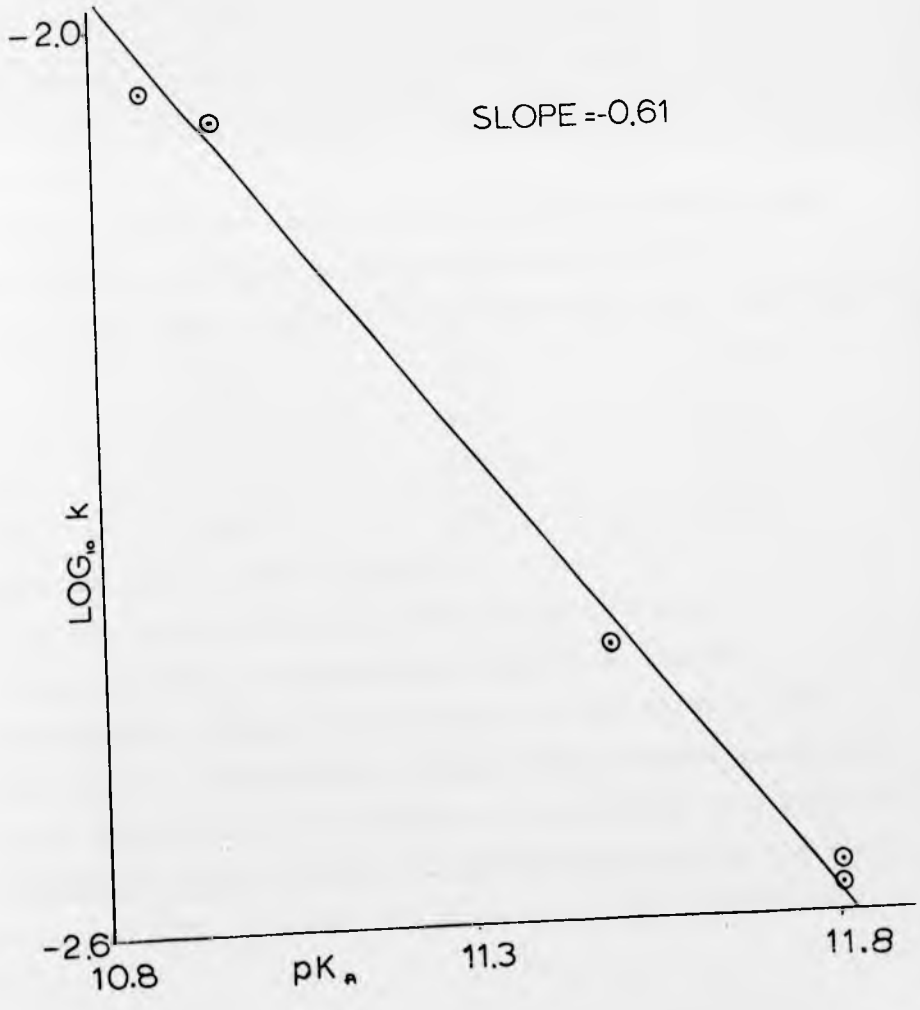
TABLE 21

Monochloroacetate catalysed detritiation of substituted-benzyl malononitriles at 5°C

p-H

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	4.17	4.83	5.83	7.00	7.92

FIG.17.
BRÖNSTED PLOT OF SUBSTITUTED BENZYL MALONONITRILES CATALYSED BY WATER



p-Cl

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	5.58	7.25	8.83	10.75	12.33

p-CN

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	19.8	20.7	33.3	32.1	39.5

p-NO_2

10^2 $[RCO_2^-]$	2.0	4.0	6.0	8.0	10.0
10^4 k/s^{-1}	19.8	27.5	33.3	39.5	46.8

TABLE 22

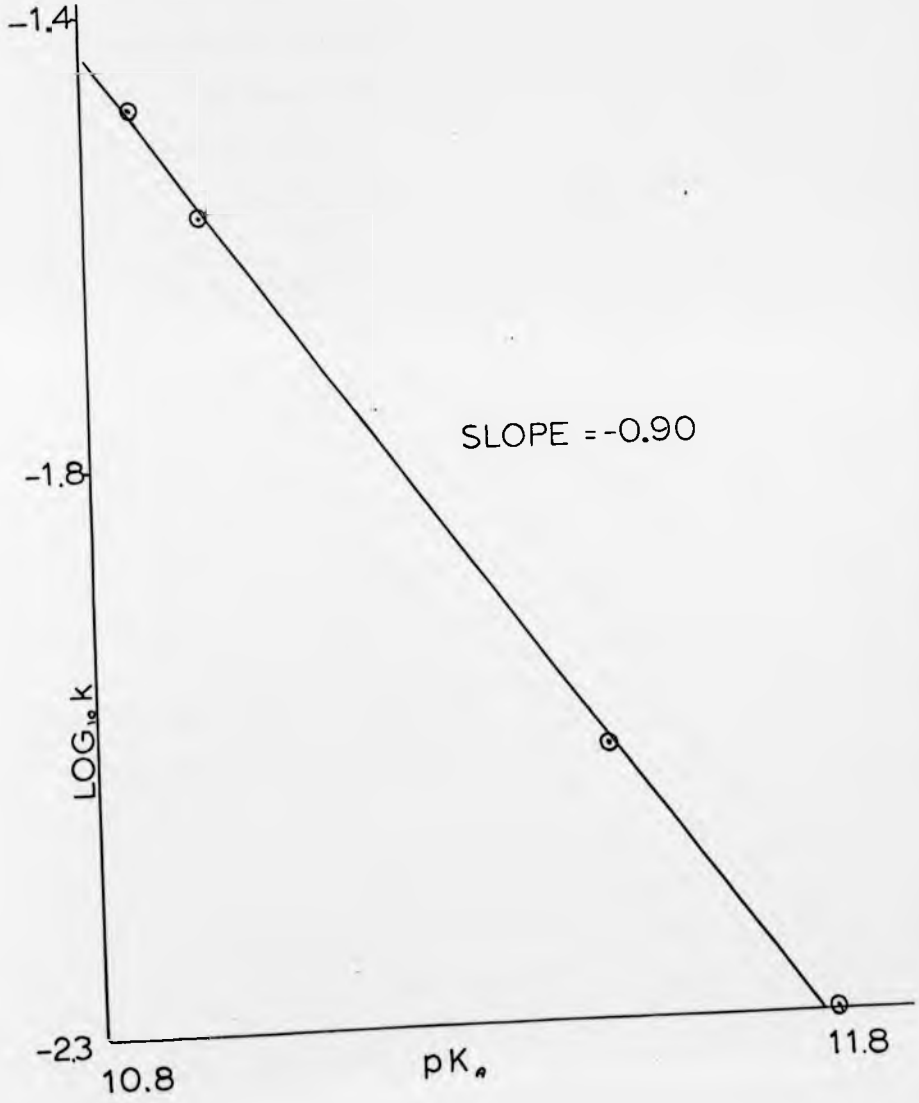
Summarised data for substituted-benzyl malononitriles with detritiation catalysed by Monochloroacetate at 5°C

Substituent	pK_A at 25°C	10^4 $k/s^{-1}mol^{-1}dm^3$	$-\log_{10}$ k/s^{-1} mol^{-1} dm^3
pH	11.80	49.2	2.308
pCl	11.49	85.9	2.066
pCN	10.96	271.0	1.567
pNO_2	10.87	328	1.484

These results are shown in Fig. 18.

Since the acidity constants above are at 25°C and the kinetics at 5°C, a correction was applied as follows: Two phosphate buffers of pH values 11.40 and 11.80 at 25°C were prepared. The anions of benzyl malononitrile and p-nitro-benzyl malononitrile were observed as previously in 0.1 mol dm^{-3} hydrochloric acid, 1.0 mol dm^{-3} sodium hydroxide and the above buffers at 5°C. Although the pH values of the buffers are

FIG.18.
BRÖNSTED PLOT OF SUBSTITUTED BENZYL MALONONITRILES CATALYSED BY MONOCHLOROACETATE.



unknown the differences in pK_A between the two compounds are available. This gave ΔpK_A = 0.86 and 0.84 as opposed to 0.93 at 25°C. This has the effect of increasing β from 0.9 to 0.98.

TABLE 23

A typical detritiation experiment.

The detritiation of benzyl malononitrile in 0.01 mol dm^{-3} hydrochloric acid at 25°C

time/s	c.p.m. x 10^{-5}	$\log_e$ c.p.m.
120	143	4.963
505	55	4.007
790	25.6	3.243
869	20.6	3.025
976	15.8	2.760
1104	11.2	2.416
1238	7.91	2.068
1355	5.90	1.775
1527	3.75	1.322

These results are shown in Fig. 19.

-Slope = rate constant = 0.0026 s^{-1}

FIG. 19.
A TYPICAL DETRITIATION EXPERIMENT

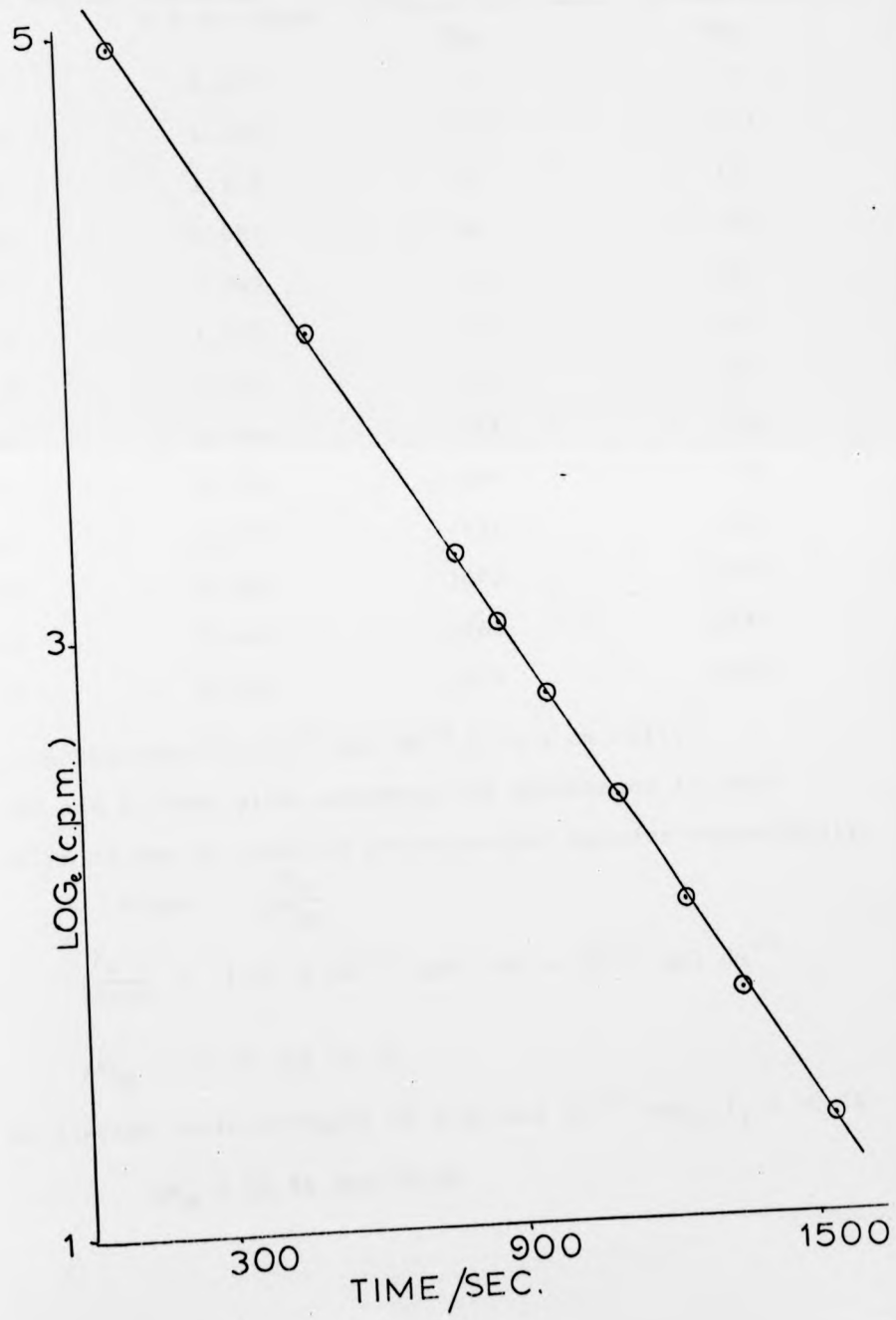


TABLE 24

A typical pK_A determination

p-nitrobenzyl malononitrile

pH of medium	Observed* O.D at 233nm	Observed OD-0.147 a^-_{OH}	OD due to anion a^-_{OH}
1	0.147	-	-
13.82	1.128	1.5	1.7
12.88	1.113	16	18
12.00	1.088	94	107
11.80	1.049	143	163
11.60	1.011	217	246
11.40	0.947	318	361
11.20	0.884	468	526
11.00	0.777	630	717
10.80	0.672	832	953
10.60	0.569	1060	1256
10.40	0.465	1266	1533
10.20	0.349	1275	2240

* approximately 7×10^{-5} mol dm^{-3} in a 1 cm cell.

Fig.20 and 21 show plots assuming the absorbance in acid solution is due to impurity and molecular species respectively.

$$\text{Slope} = -\frac{K_w}{K'_{SH}}$$

$$K'_{SH} = -\frac{K_w}{\text{slope}} = 1.89 \times 10^{-11} \text{ and } 2.00 \times 10^{-11} \text{ mol dm}^{-3}$$

$$pK'_{SH} = 10.72 \text{ and } 10.70$$

At an average ionic strength of 0.09 mol dm^{-3} $\log_{10} f_i = -0.15$

$$pK_A = 10.85 \text{ and } 10.83$$

FIG. 20.
A TYPICAL pK_a DETERMINATION.
1) assuming absorption in acid solution is due to impurity.

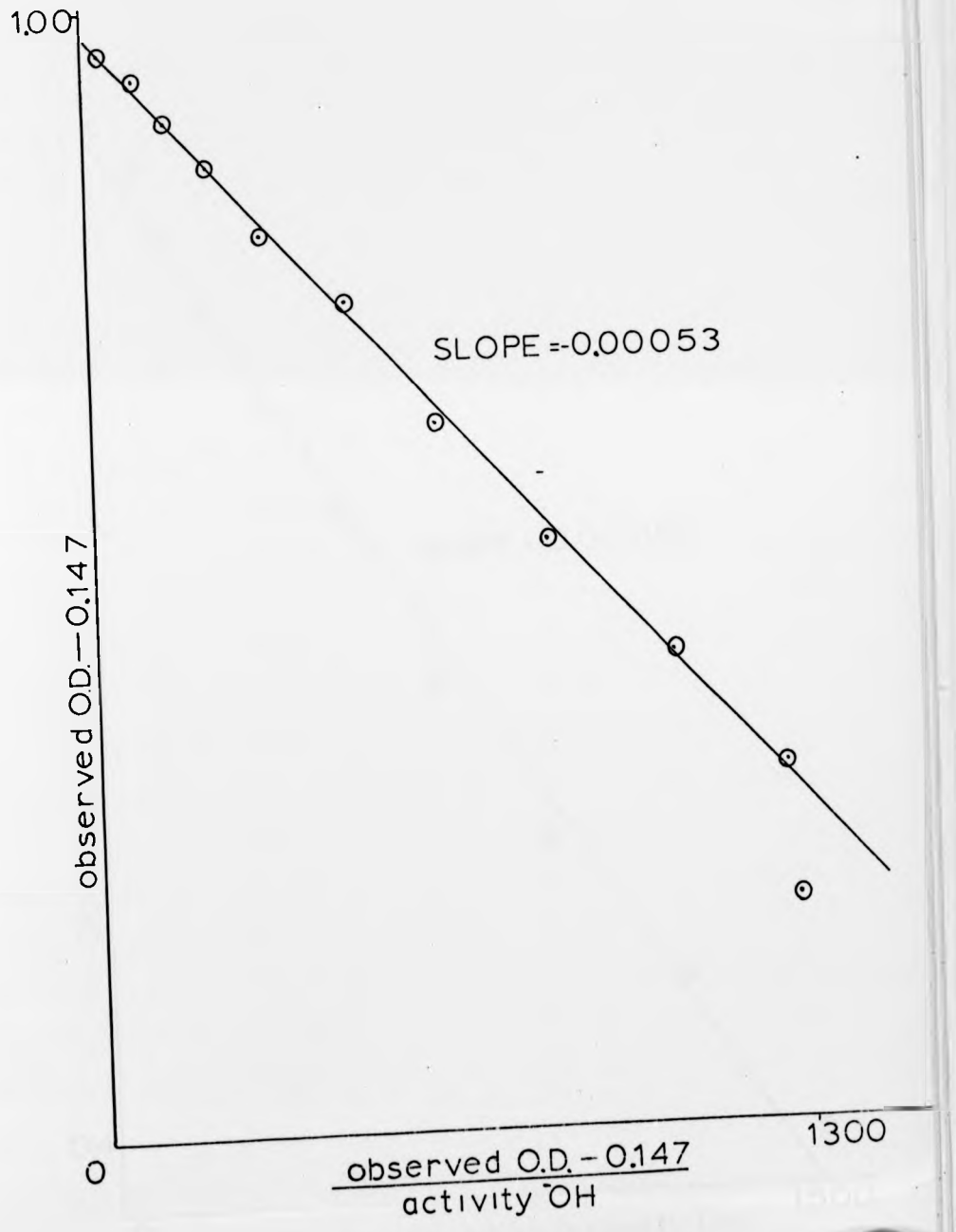


FIG. 21.

A TYPICAL pK_a DETERMINATION.

2) assuming in acid solution the observed absorption is due to molecular species.

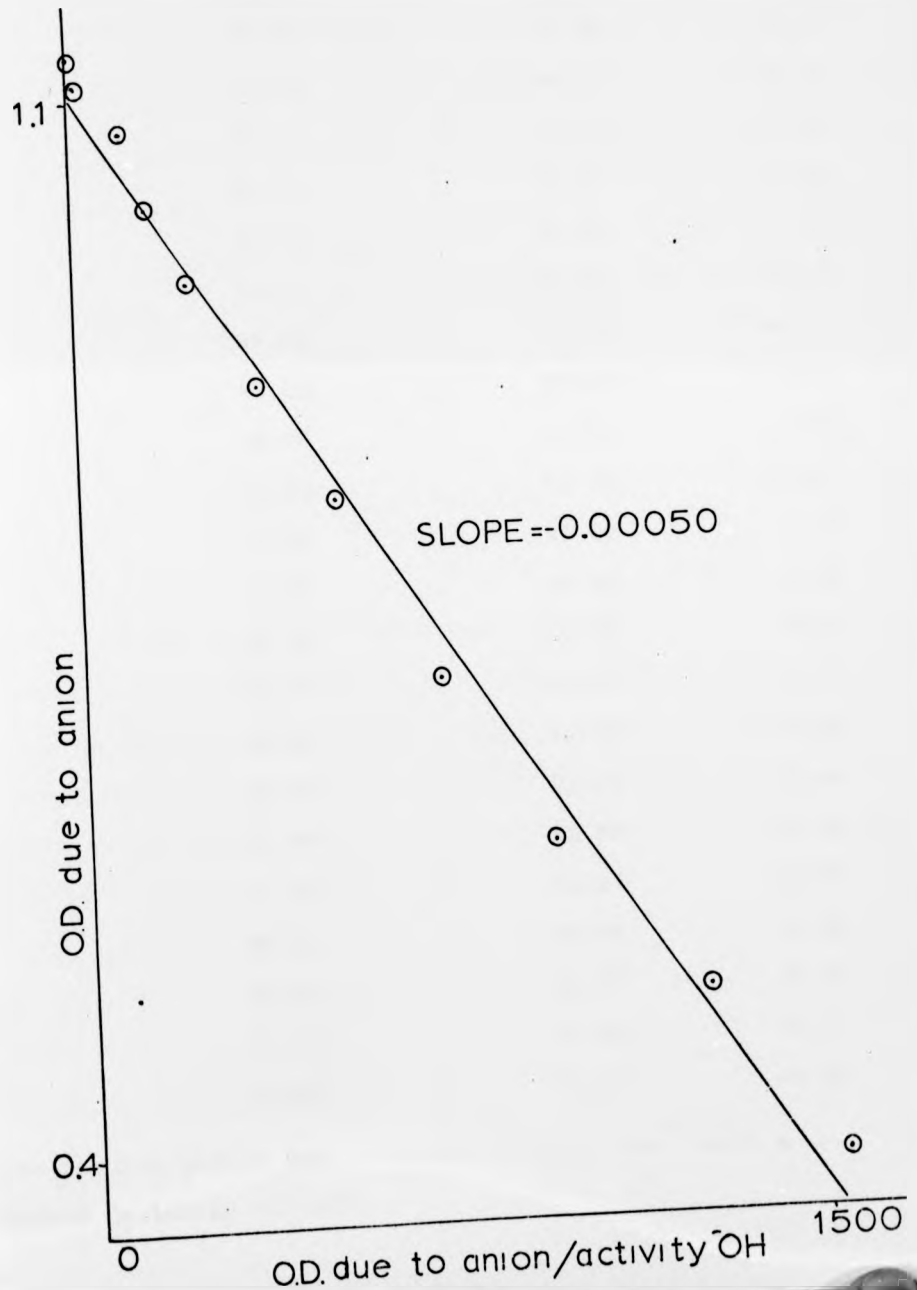


TABLE 25

Typical data from scavenging experiments.

p-Nitrobenzyl acetylacetone catalysed by 0.1 mol dm^{-3} acetate ions.

Time/min	Experimental Chart Reading	Calculated Chart Reading	Deviation
0	79.00	78.72	-0.28
0.5	70.00	70.40	0.39
1.0	64.00	64.17	0.16
1.5	59.50	59.48	-0.02
2.0	56.00	55.91	-0.09
2.5	53.40	53.18	-0.22
3.0	51.20	51.05	-0.15
3.5	49.50	49.37	-0.12
4.0	48.00	48.02	0.02
4.5	46.90	46.91	0.009
5.0	46.00	45.98	-0.02
5.5	45.00	45.17	0.17
6.0	44.30	44.46	0.16
6.5	43.80	43.82	0.02
7.0	43.20	43.23	0.03
7.5	42.60	42.68	0.08
8.0	42.20	42.16	-0.04
8.5	41.70	41.65	-0.04
9.0	41.20	41.17	-0.03
9.5	40.60	40.69	0.08
10.0	40.10	40.22	0.12
10.5	39.90	39.76	-0.14
11.0	39.40	39.30	-0.10

These results give a rate constant of 0.615 min^{-1} with a standard deviation of 0.01.

DISCUSSION

TABLE 26

Summarised Brönsted exponents

Reactant 1	Reactant 2	Varied reactant	Brönsted exponent
Ethyl (α benzyl) acetoacetate	Carboxylate anions	2	0.44
Ethyl (α benzyl) acetoacetate	Acetate	1	0.77
Benzyl acetylacetone	Carboxylate anion	2	0.44
Benzyl acetylacetone	Acetate	1	0.58
Benzyl acetylacetone	Water	1	0.48
Benzyl acetylacetone	Pyridine	1	0.44
Benzoylacetone	Carboxylate anions	2	0.52
Benzoylacetone	Acetate	1	0.55
Benzyl malononitrile	Carboxylate anions	2	1.00
Benzyl malononitrile	Water	1	0.61
Benzyl malononitrile	Monochloroacetate	1	0.98

We may consider first the reactions involving malononitrile. From the known acidity constants, of the compounds, and the conjugate acids of the base catalysts we may calculate the equilibrium constant of the catalysed reaction, and knowing the forward rates calculate the rates of the back reactions.

TABLE 27

Rates of reverse reaction $S^- + HA \longrightarrow SH + A^-$

Malononitrile anion	Acid	$k/s^{-1}\ mol^{-1}\ dm^3$
Benzyl	Acetic	8×10^7
Benzyl	Benzoic	8×10^7
Benzyl	Monochloroacetic	4×10^7
p-nitrobenzyl	Monochloroacetic	4×10^7
Benzyl	Hydronium	3×10^9
p-nitrobenzyl	Hydronium	3×10^8

The values of $4 \times 10^7\ s^{-1}\ mol^{-1}\ dm^3$ assume a factor of four in the forward rates due to these being at 5°C not 25°C and an isotope effect k_H/k_T of 2. The values of $3 \times 10^9\ s^{-1}\ mol^{-1}\ dm^3$ and $8 \times 10^8\ s^{-1}\ mol^{-1}\ dm^3$ also assumes an isotope effect $k_H/k_T = 2$. The velocity constants for reaction of malononitrile anions with carboxylic acids are close to those found by Long[98] of $1 \times 10^8\ s^{-1}\ mol^{-1}\ dm^3$. Since these are independent of the acid strength of the catalyst we obtain a Brönsted exponent for the forward reaction of unity, and since the velocity constants for the back reactions are determined by physical considerations the values of β have no chemical significance. The velocity constants for the back reactions with hydronium ions are not constant and rise to that given by Long[98] of $3 \times 10^9\ s^{-1}\ mol^{-1}\ dm^3$. It is reasonable that hydronium ions should have higher diffusion controlled limits since the Grotthus chain mechanism may operate, although all of these velocity constants are approximately a factor of ten below those normally expected for diffusion control.[99] Long[98] has suggested this may be due to an activation

energy barrier (in addition to that due to diffusion) arising from restructuring of solvation shells in carbon acids, but which is unnecessary in oxygen and nitrogen acids where transfer may occur through the solvent shell. However one might have expected this to affect the ratio of "diffusion controlled" limits for general acids and hydronium ion, which remains constant between carbon and nitrogen (or oxygen) acids at 40. Since the rate constants for hydronium ion back reactions vary, reaching Long's "diffusion limit" only in the fastest case, the value of $\beta = 0.6$ is probably a better guide to transition state symmetry than the values of unity obtained for "traditional" Brönsted slopes. Although this value is no doubt affected by diffusion control, it is reasonable in view of the overall free energy change.

If we now turn to the other reactions and write the Brönsted relation in the form:

$$\beta = \frac{\delta_R \Delta G^*}{\delta_R \Delta G^\circ}$$

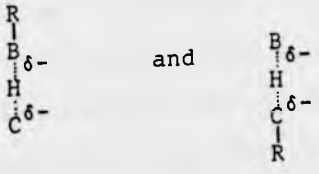
The differing values of β obtained by different methods point to interactions affecting only ΔG^* or ΔG° and not both. As has been stated previously this is likely in a bimolecular reaction where two reactants come together in the transition state and are likely to interact, whereas this is not possible in the initial or final states where they are separated. Moreover it is necessary that any additional interaction in the transition state be linear with ΔpK otherwise no Brönsted correlation would exist. Kresge[100] has considered this in

terms of polar interactions of substituents and as outlined in the review of previous work gives the equation

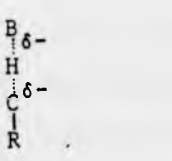
$$\beta = \left[xI_{R,NO_2^-} + (1-x)I_{R,\bar{O}H} \right] / I_{R,NO_2^-}$$

for the reaction of hydroxide with an R substituted nitro compound, where I_{R,NO_2^-} is the effect of R on a fully charged nitro group, $I_{R,\bar{O}H}$ the interaction of R on a fully charged hydroxide group and x the degree of proton transfer. In order that the Brönsted relation should work $I_{R,\bar{O}H}$ has to be zero, then $\beta = x$. A slightly different way of viewing this is to consider the transition-state interaction to be electrostatic in origin between the charge on the base and the charge on the acidic carbon of the substrate in the transition state. In the case of pseudo acids it is evident most of the charge will reside on whatever activating group is present and although this can interact with the charge on the base it will be at a greater distance and the interaction that less powerful. Hence greater removal of charge from the acidic carbon will result in an effectively lower charge on the substrate at least insofar as charge interactions are concerned.

If we now consider the Brönsted exponents for ethyl (α benzyl) acetoacetate with a series of carboxylate anions, and acetate ion for substituted ethyl (α benzyl) acetoacetates we have in the transition state the arrangements:-



and



respectively

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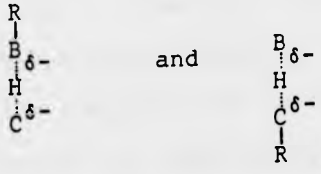


and

respectively

In both cases the charge interaction is transition state destabilising, leading to reduced rates of reaction. In the first reaction where the base catalyst is changed, say from monochloroacetate to propionate, there will be a greater localisation of charge on the oxygen of the base in the case of propionate than monochloroacetate where the chlorine attracts charge away from those parts of the base molecule near to the substrate. This results in a greater destabilisation of the transition state (and hence slower rates than in the absence of this effect) in reaction with propionate than with monochloroacetate. Thus Brönsted exponents obtained by this "traditional method" are lower than the "true" Brönsted exponent. Turning to the second reaction where the substrate is altered and the base is acetate ion, there will be a greater concentration of charge on the acidic carbon atom in ethyl (α benzyl) acetoacetate than in ethyl (p-nitrobenzyl) acetoacetate where some of the charge is leaked to the p-nitro group. Thus the reduction in rate of the former will be greater than in the latter (both compared to the rates in the absence of charge interaction). This has the effect of increasing the Brönsted exponent obtained by this method over the "true" exponent. Moreover as the substrate becomes more acidic as in the series ethyl (α benzyl) acetoacetate, benzylacetylacetone and benzoylacetone this effect will become less important since there is less negative charge on the acidic carbon atom. Consequently the two β values approach each other as observed. In the case of water or pyridine catalysis on benzylacetylacetone we have a positive charge developing on the incoming base in the transition state and the interaction with the negative charge on the carbon acid has

a stabilising effect on the transition state. As before this interaction is greater for benzylacetylacetone than p-nitrobenzyl acetylacetone causing a reduction in the Brönsted exponent from the "true" exponent, though not in this case below that measured by base catalyst variation. It is worth mentioning that in these last two reactions the rates are those of detritiation, and while it is unlikely the isotope effect would change at these extreme values of ΔpK, if it did this would be to higher k_H/k_T as ΔpK approached zero. Thus going from benzylacetylacetone to p-nitrobenzylacetylacetone k_H/k_T increases giving a Brönsted slope higher for hydrogen rates than tritium rates.

A rather different interpretation of these results involves the effects of solvation.[55] If we accept that the change in acidity of a compound on introducing substituents is only partly due to inductive and mesomeric effects and partly to solvation differences as has been suggested largely by Ritchie et al,[101] then this is a factor which does not vary monatonically with extent of reaction. It is generally accepted that solvation effects are far larger on ions than neutral molecules and largest for ions in which the charge is localised. If we consider a reaction occurring in the gas phase and transfer it to a solvent then for a reaction of the type

$$AH + B^- \rightleftharpoons A^- + BH.$$

the main changes in energy will be in reactants and products where we have a localised charge, rather than in the transition state where the charge is spread over A and B. Ritchie[101b,101d] has found that substituent effects are less in protic solvents due to hydrogen bonding than in aprotic solvents and Kebarle[101f] has

found the ΔpK between dichloroacetic acid and acetic acid in the gas phase to be 15 as opposed to 3.5 in water. Since these solvent changes are having a relatively small effect on the energy of the transition state the Brönsted relation must break down.

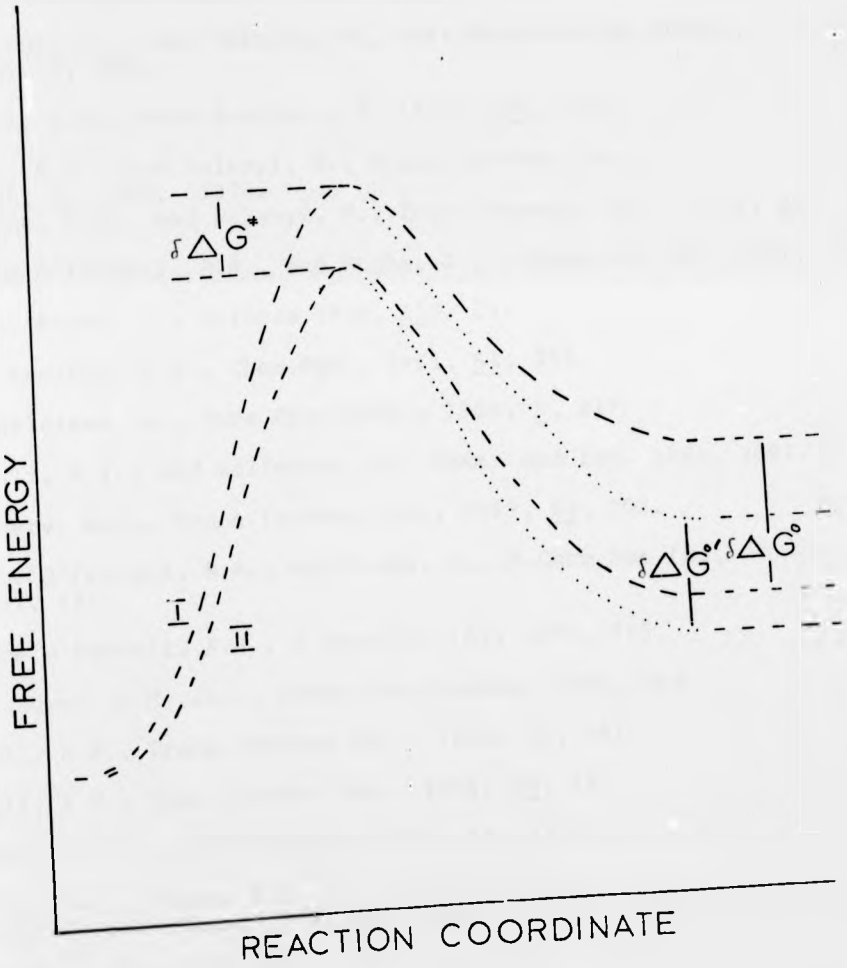
If we consider ethyl (α benzyl) acetoacetate and ethyl (p-nitrobenzyl) acetoacetate with acetate anion in the gas phase and in water we have fig.22. Where curve I is the former and curve II the latter, the dashed lines representing the gas phase and the dotted lines in water. For simplicity the curves in the two phases have been moved relative to each other to align reactants, and the solvent has been shown as having no effect on the transition state. Then:

$$\beta = \frac{\delta \Delta G^{\ddagger}}{\delta \Delta G^{o}}$$

but we are using $\delta \Delta G^{o'}$. We have the problem of not using the free energy changes we require. Thus for changes of substrate β is too high and considering the diagram from right to left we have the equivalent of a fixed substrate and a differing base catalyst giving β too low. Moreover this compression of pK's will increase as the charge on the substrate anion becomes more localised, i.e. less acidic, giving greater deviations in say ethyl (α benzyl) acetoacetate than in benzoylacetone as is observed.

It is not possible from the results to decide between these two explanations and indeed it seems likely that both could be operating.

FIG.22.
SOLVATION EFFECTS AND THE BRÖNSTED RELATION.



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