THE PRIMARY HYDROGEN KINETIC ISOTOPE EFFECT IN THE ELIMINATION FROM 2-PHENETHYL SYSTEMS.

A thesis presented in partial fulfilment of the
requirements for the degree of Master of
Science with Honours in Chemistry at
Massey University.

John Leslie Woodhead
1974

ABSTRACT

The primary kinetic isotope effects for the base-catalysed E2 elimination from a series of substituted 2-phenethyl bromides and 2-phenethyldimethylsulphonium bromides in dimethyl sulphoxide-water as solvent at 20° have been measured. A broad maximum in the isotope effect was observed for the 2-phenethyl bromides. The Hammett ρ value for each reaction series at 20° has also been determined and both were large and positive. Arrhenius plots using the k_H/k_D ratios for each of the p-MeO substituted compounds at 20°, 30° and 40° were carried out to determine the importance of proton tunnelling in these reactions. The usefulness of the primary kinetic isotope effect as a measure of proton position in the E2 transition states for these reactions is discussed.

ACKNOWLEDGEMENTS

I am grateful to Dr L.F. Blackwell for the guidance and assistance he provided. I would also like to thank Prof. R. Hodges for carrying out the mass spectral analyses and Mr A. Trow for the n.m.r. spectra. The modified least-squares computer programme used to calculate the second-order rate constants was compiled by Mr A.K.H. MacGibbon.

TABLE OF CONTENTS

Table of contents (contd.)

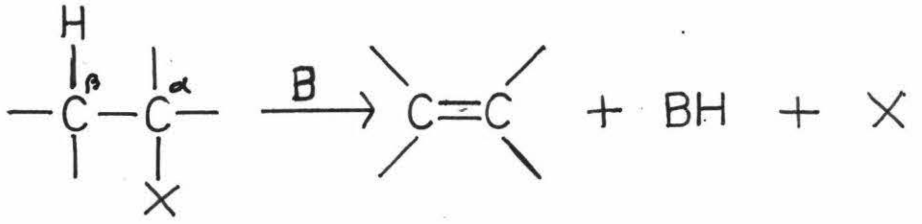
LIST OF FIGURES

1. INTRODUCTION

In recent years a considerable amount of data has been published concerning primary hydrogen kinetic isotope effects and their application to the elucidation of transition state symmetry in E2 elimination reactions. This has given rise to much theoretical speculation over the meaning attached to the observed trends. However, despite the quantity of data available, conflicting views have developed over the interpretation of the results. The work presented in this thesis is an attempt to resolve some of the uncertainty which surrounds this area of chemistry.

1.1 β-elimination reactions

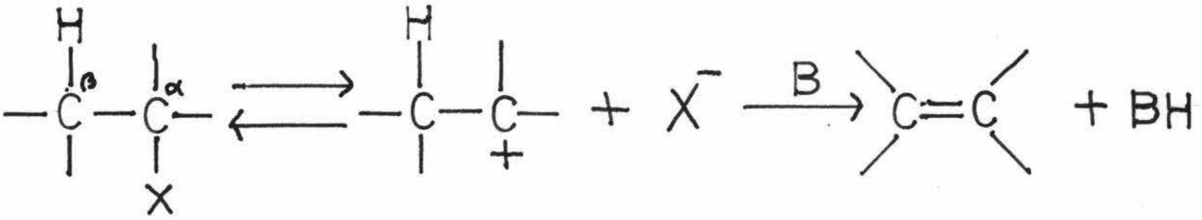
β-elimination reactions can be defined as those reactions in which two atoms or groups on adjacent carbon atoms are split off with consequent formation of a new carbon-carbon multiple bond. The overall reaction for the elimination of HX can be written as follows,



where B represents the base and X the leaving group. There are three basic types of mechanism for β-elimination reactions.

1.1.1 E1 mechanism

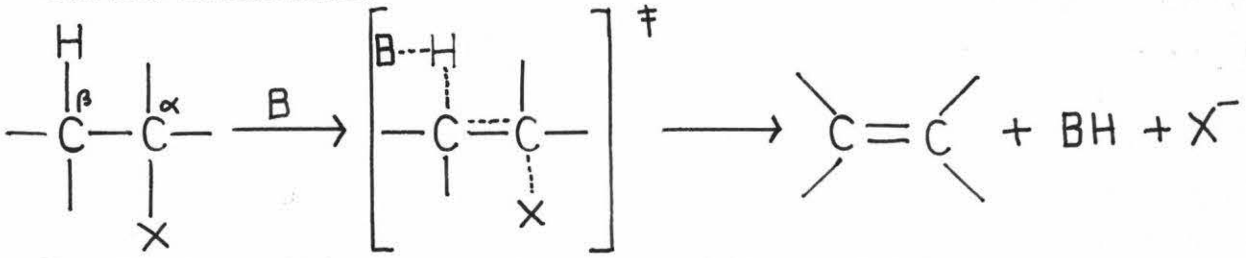
The C-H and C-X bonds are broken in separate steps. The first step involves reversible formation of a carbonium ion intermediate, while the second step involves irreversible loss of a β-proton to a base or solvent molecule.



The reaction kinetics are first order overall.

1.1.2

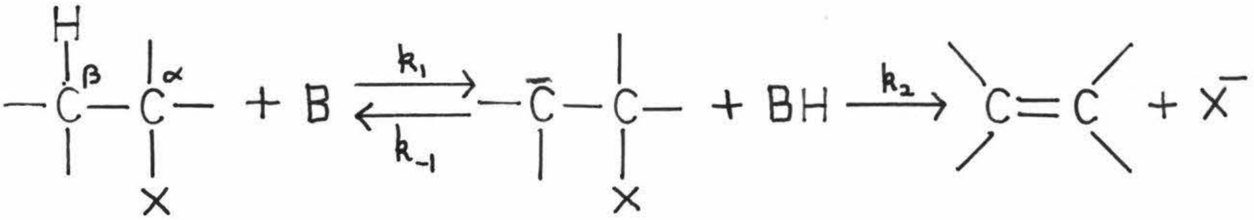
The C-H and C-X bonds are ruptured in the same step in a concerted mechanism.



In the transition state both the C-H and C-X bonds are partially broken, while the B-H and carbon-carbon double bonds are partially formed. The reaction kinetics are second order.

1.1.3 Elcb mechanism

This mechanism involves initial proton abstraction from the β-carbon to form a carbanion intermediate, followed by rupture of the C-X bond in a second step.



There are two possibilities within this mechanism. These are reversible carbanion formation ($k_1 \gg k_2$) and irreversible carbanion formation ($k_1 \ll k_2$).

1.2 Variable E2 transition state theories

In 1927 Ingold[1] raised the possibility that C-H and C-X bond breaking may not occur to equal extends in the E2 transition state. However, for many years afterwards the degree of rupture of these two bonds was treated as equal in the transition state, that is fully synchronous breaking was assumed to occur. In 1956 Cram[2] published evidence for varying E2 transition state geometry, which implied differences in the relative extents of C-H and C-X bond breaking and also in carbon-carbon double bond formation. Subsequently, there has been additional evidence to support the view that although the E2 mechanism is concerted it does not have to be entirely synchronous.

Bunnett (1962)[3] developed a 'variable transition state' theory to account for experimental observations in E2 reactions. He proposed a whole spectrum of transition states which differ in the relative extents of C-X and C-H bond rupture.

1.2.1 El-like transition state

This lies on one side of the transition state spectrum where C-X bond breaking is more advanced than C-H bond breaking. There is little double bond character in this transition state and the β-carbon has a partial positive charge. The transition state in this case approaches that for the first step of the El mechanism but differs from it in that the base is involved.

1.2.2 Elcb-like transition state

This transition state lies on the other side of the spectrum and involves a larger degree of C-H bond rupture than C-X bond rupture. The β-carbon therefore has a partial negative charge and again there is little double bond character. This transition state approaches that for the first step of the Elcb mechanism.

1.2.3 Central transition state

This transition state is intermediate between the two transition state extremes. The C-H and C-X bonds have equal degrees of rupture and considerable development of double bond character is proposed.

Thornton[4] has proposed a theory which predicts the effects of substituent changes on the geometry of the E2 transition state. He also proposes a whole spectrum of transition states but these differ from the Bunnett theory in that they range from 'reactant-like' to 'product-like'. For a 'reactant-like' transition state there is little double bond character and little rupture of either the C-H and C-X bonds, whereas a 'product-like' transition state has much double bond character with extensive rupture of both the C-H and C-X bonds. However, there is disagreement between some of the predictions based on the Thornton theory and those of the Bunnett theory.

More O'Ferrall (1970)[5] suggested that the progress of β-elimination reactions could be represented by a potential energy surface, with C-H distance along one axis and C-X distance along the other axis.

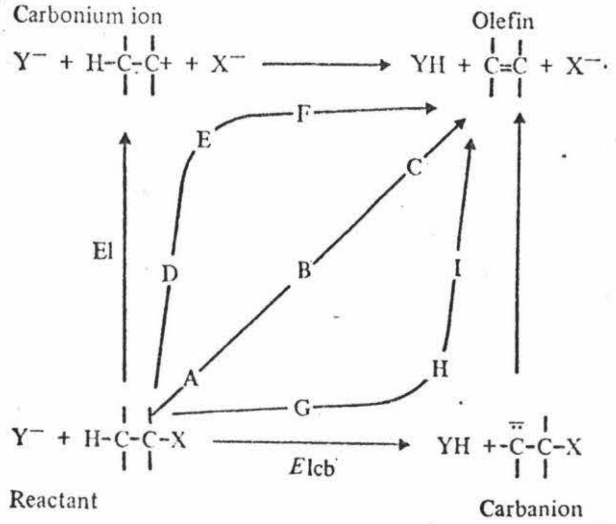
A schematic representation of the possible E2 mechanisms has been adapted from the potential surface diagrams of O'Ferrall by Fry[6] (Figure 1). The Elcb mechanism is represented by movement along the horizontal C-H axis from the reactant origin to the carbanion, followed by vertical movement to the olefin. Vertical movement from the origin along the C-X axis to the carbonium ion followed by horizontal movement to the product represents the El mechanism. Diagonal movement corresponds to simultaneous breaking of the C-H and C-X bonds and represents the synchronous E2 mechanism. A whole spectrum of central transition states ranging from reactant-like to product-like can occur along the diagonal, one of which is represented by (B). An El-like transition state can be represented by (E) and an Elcb-like transition state by (H). This approach can be used to predict the effect changes in leaving group, substituents, and reaction conditions will have on transition state structure.

1.3 Primary hydrogen kinetic isotope effect

For reactions in which a hydrogen bond is broken in the rate determining step different rates of reaction are observed if deuterium is substituted for hydrogen. This occurs because the mass difference between H and D atoms gives rise to a larger activation energy for the breaking of the deuterium bond compared to the hydrogen bond, hence giving a slower reaction rate for the deuterated compound. Proton transfer occurs in the rate determining step for all E2 reactions, hence a kinetic isotope effect should be observed in all cases. From theoretical considerations, based on the loss of stretching vibrational frequency for the C-H and C-D bonds in the transition state, the primary kinetic isotope effect expressed as a k_H/k_D rate ratio should be approximately 6.9[7]. However, there are many experimental observations which show considerable variation in the kinetic isotope effect with values both greater and less than the theoretical value. Westheimer[8] proposed a theory

Figure 1.

Adapted More O'Ferrall potential surface diagram.



(From Fry, A., Chem.Soc.Rev., 1, 189 (1972)) to explain low k_h/k_D ratios which was based on a simple linear three-centre model for the transition state. This theory predicts that the maximum isotope effect will only be observed for symmetrical transition states, with a progressive decrease in the k_H/k_D ratio as the transition state becomes more asymmetrical. Thus, for a reaction which involves the transfer of a proton to a base in the rate determining step, the k_H/k_D ratio should be a maximum when the proton is half-transferred in the transition state, and show lower values when the proton is either closer to the base or to the substrate. Theoretical predictions based on multi-centre models[9,10] also suggest that a maximum will be observed when the proton is about half-transferred in the transition state but there is no general agreement over the size of this maximum.

Bell (1966)[11] suggested that information about transition state symmetry could be obtained indirectly. For the transfer of a proton from an acidic substrate (SH) to a base (B) it was considered reasonable to assume that the transition state symmetry could be related to the expression,

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

where $pK_{(SH)}$ refers to the acid strength of the substrate and $pK_{(BH)}$ refers to the acid strength of the conjugate acid of the base. When $\Delta pK = 0$ the proton should be half-transferred and so the transition state is symmetrical. For this case the k_H/k_D ratio should be at its maximum value. If ΔpK has a positive or negative value, the transition state should be asymmetrical with a consequent lower than maximum kinetic isotope effect. Therefore, in theory a plot of k_H/k_D versus ΔpK for such a system should produce a 'bell-shaped' curve with the k_H/k_D ratio passing through a maximum when $\Delta pK = 0$. An apparent maximum has experimentally been observed for proton removal from nitroalkanes[12], but this data has been criticised by Bordwell[13] as being inconclusive. Bordwell maintains that either k_H/k_D is relatively insensitive to transition state symmetry or that the transition state symmetry does not appreciably change over wide ranges of ΔpK in systems studied so far.

1.3.1 Proton tunnelling

From the quantum mechanical viewpoint the wave nature of the proton suggests that there is a finite probability that some protons with less energy than the required activation energy can still react by tunnelling through the energy barrier. The probability for tunnelling by a deuteron is much less than for a proton, hence the k_H/k_D ratio can be larger than the theoretical maximum because of tunnelling effects. Bell (1970)[14] has suggested that the kinetic isotope effect is in fact primarily determined by proton tunnelling, thus allowing changes in the k_H/k_D ratio to occur even though the proton position may remain unchanged over a wide ΔpK range.

The importance of proton tunnelling can be determined by considering the Arrhenius parameters for the reaction. From a plot of log (k_H/k_D) versus (I/T) (where T is absolute temperature) the difference in activation energies for the proton and deuteron $(E_a^D - E_a^H)$ can be calculated from the slope. The intercept gives the value of log (A_H/A_D). Proton tunnelling probably occurs if the value for $(E_a^D - E_a^H)$ is appreciably greater than the theoretical maximum value based on loss of stretching vibration of the C-H and C-D bonds in the transition state[15]. Proton tunnelling is also indicated if the A_D/A_H ratio is significantly greater than unity.

1.4 Hammett equation

The effect of meta or para substituents in a benzene ring on sidechain reactions has been correlated by the Hammett equation. The original form of the equation was,

$$\log \frac{k}{k_o} = \rho\sigma$$

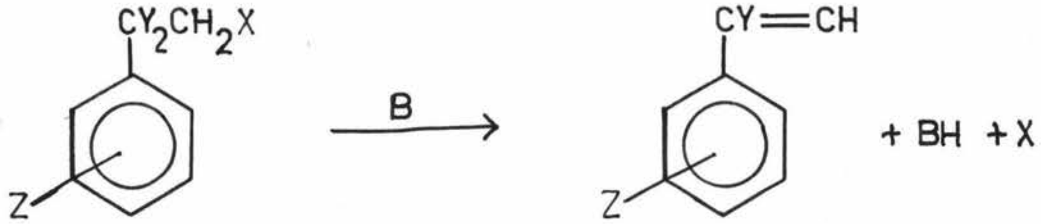
where k is the rate constant for the sidechain reaction of a meta- or para-substituted benzene derivative, k_o is the rate constant for the unsubstituted benzene derivative, σ is a substituent constant which is dependent on the substituent and its position in the benzene ring, and ρ is a reaction constant which is dependent on the nature of the substrate, on the reaction itself, and on the reaction conditions. A negative value for ρ indicates that the reaction involves the development positive charge in the transition state as it is assisted by electron releasing substituents. A positive ρ value indicates the development of negative charge in the transition state for the rate determining step.

Deviations from the Hammett correlation can occur when there is direct resonance interaction between the benzene ring para-substituents and the sidechain. Different standard reaction series can be used to allow for the effects of these interactions. When a sidechain can donate electrons by resonance interaction (+ M) to a benzene ring that contains a para (- M) substituent, then the reactivities can be better correlated by the σ^- parameters based on the ionization of anilines as the standard reaction series.

For β-elimination reactions a substituted benzene ring on either the α-carbon or β-carbon can be used to obtain a Hammett plot by varying the substituents. The ρ value so determined gives an indication of whether the transition state is positively or negatively charged, and hence gives some information on the relative extents of C-H and C-X bond breaking in the transition state.

1.5 Elimination from 2-phenethyl systems

The 1,2-elimination of HX from 2-phenethyl compounds under basic conditions can be written in the following general form,



where Z = meta- or para-substituent, Y = H or D, and X represents the leaving group. The elimination exhibits second order kinetics and reported ρ values are positive, thus it appears that the E2 transition state is carbanionic in character. It has been found[16] that as the leaving group becomes progressively poorer along the series X = Br, OTs, $\overset{+}{S}Me_2$ and $\overset{+}{N}Me_3$ the ρ values for elimination in ethanol-ethoxide increase, being +2.14, +2.27, +2.75 and +3.77

respectively. This trend indicates that the transition state is becoming more carbanionic and thus would be expected to be accompanied by an increase in the ratio of C-H to C-X bond breaking. The kinetic isotope effect has been measured for this series and the k_H/k_D ratios observed were 7.11, 5,66, 5.07 (at 30°) and 2.98 (at 50°) respectively[16]. These figures have been commonly interpreted as indicating an increasing degree of proton transfer to the eliminating base as the transition state becomes more carbanionic in agreement with the variable transition state theory. However, there is disagreement about what these figures mean as regards to the extent of the proton transfer because of the inherent ambiguity in isotope effects which are smaller than the maximum.

It should also be possible to alter the character of the transition state by keeping the leaving group constant and varying the β-aryl substituent, as this would be expected to affect the acidity of the β-hydrogens. If the isotope effect is reflecting the extent of proton transfer it would be expected that it would either increase, decrease, or perhaps exhibit a maximum as the aryl substituent became progressively more electron-withdrawing. Blackwell et al[17] have studied the effect of substituents on the k_H/k_D ratio for the elimination from a series of substituted 2-phenethyl bromides in _tert_-butyl alcohol with _tert_-butoxide base. The aryl substituents for the series were Z = _p_-MeO, H, _p_-Cl, _m_-Br, _m_-NO_2 and _p_-NO_2. However, no significant change in the magnitude of the isotope effect was observed.

A study of the change in the kinetic isotope effect caused by increasing the dimethyl sulphoxide (DMSO) concentration in the _tert_-butoxide catalysed elimination from 2-phenethyl bromide has been carried out by Cockerill et al[18]. Again, no change was observed in the isotope effect as the DMSO concentration was increased. Cockerill[19] has studied the effect of varying DMSO concentrations on the hydroxide ion catalysed elimination from 2-phenethyldimethylsulphonium bromide in water. Significant changes in the isotope effect were observed when the DMSO concentration was varied from 0% to 84%. Over this range the k_H/k_D ratio increased to a maximum then decreased again. The ρ value for this reaction was found to be positive with a value of 2.11 in water at 50°, but this value increased rapidly as DMSO was added until a solvent composition of 20% DMSO was reached. The ρ value showed little further change as more DMSO was added after this point.

1.6 Present work

It was decided to study substituent effects on the k_H/k_D ratio for hydroxide ion catalysed elimination from substituted 2-phenethyldimethylsulphonium bromides in DMSO-water in the hope of observing a maximum in the isotope effect. A maximum in the isotope effect for the unsubstituted compound had previously been observed by Cockerill, as noted on page 9 , but he did not carry out any substituent effect studies. The effect of substituent changes on the 2-phenethyl bromides in this system was also studied in order to determine whether substituent effects on the k_H/k_D ratio depend on the base-solvent system and/or the leaving group. The solvent composition used was 50.2 mole % DMSO because, according to the work of Cockerill, this appears to be where the k_H/k_D ratio is at a maximum for 2-phenethyldimethylsulphonium bromide. It was expected that any changes in k_H/k_D caused by changes in the β-aryl substituent would be more apparent if the size of the isotope effects themselves were large rather than small.

2 EXPERIMENTAL

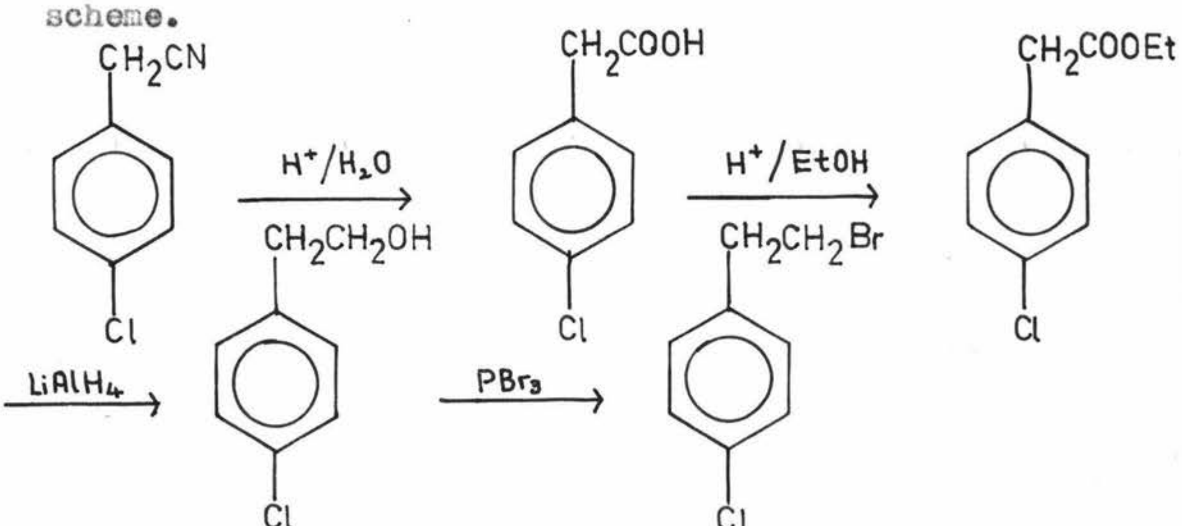
All melting-points and boiling-points are uncorrected. Unless otherwise stated, the reference melting-points, boiling-points and refractive indices are listed in Heilbron and Bunbury's 'Dictionary of Organic Compounds' or Weast's (Ed) 'Handbook of Chemistry and Physics'. The reference values are given in brackets after the measured values. The infra-red spectra were measured on a Beckman IR-20 infra-red spectrophotometer. A JEOL JNM C-60HL High Resolution n.m.r. spectrometer was used to record the n.m.r. spectra. Mass spectral data was recorded on an AEI MS-9 High Resolution mass spectrometer.

2.1 Preparation of non-deuterated compounds

The 2-phenethyl bromides were prepared from either the benzyl cyanide or the phenylacetic acid. The 2-phenethyldimethylsulphonium bromides were prepared from the corresponding 2-phenethyl bromides.

2.1.1 Preparation of 2-(p-chlorophenyl)ethyl bromide

2-(p-chlorophenyl)ethyl bromide was prepared from p-chlorobenzyl bromide according to the following synthetic scheme.



p-chlorophenylacetic acid

Acid hydrolysis of p-chlorobenzyl cyanide was used to prepare p-chlorophenylacetic acid.

Procedure[20]

p-chlorobenzyl cyanide (50 g) was added to a mixture of water (50 cm^3), concentrated sulphuric acid (50 cm^3) and glacial acetic acid (50 cm^3). The mixture was refluxed for 120 minutes then poured into excess water (500 cm^3) to form a fluffy white crystalline solid. The crude product was filtered, washed with water, and dried in a vacuum dessicator. The product was recrystallized from ethanol/water to give white needle-like crystals, m.p. 104-105° (lit. 105-106°). The yield was 76%.

2-(p-chlorophenyl)ethanol

The reduction of the acid to the alcohol was carried out by the initial conversion of the acid to the ethyl ester followed by reduction of the ester by lithium aluminium hydride ($LiAlH_4$) to form the alcohol. The reduction of the ester requires at least 0.5 moles of $LiAlH_4$ per mole of ester. The reducing agent was used in excess of the minimum requirement to allow for impurities present in the ester and also for any water present in the diethyl ether solvent.

Procedure

p-chlorophenylacetic acid (35 g) was dissolved in ethanol (300 cm^3) followed by the addition of concentrated sulphuric acid (10 cm^3). The mixture was refluxed for 2 hours then 200 cm^3 of the ethanol were removed by distillation, followed by the addition of water (300 cm^3) after the solution was allowed to cool. The solution was extracted with diethyl ether (4 x 100 cm^3) and the combined ether extracts washed with water (100 cm^3), dried over magnesium sulphate, and then the ether was removed on a rotary evaporator. The crude ester was a pale yellow liquid (30 g). An infra-red analysis showed the absence of a carboxylic -OH peak, indicating that the acid had been successfully converted to the ethyl ester. The crude ester was used in the reduction step without further purification.

Lithium aluminium hydride (5.7 g) was then suspended in sodium-dried diethyl ether (200 cm^3). The ethyl ester (30 g) from the previous step was dissolved in sodium-dried diethyl ether (50 cm^3) and added dropwise to the diethyl ether/lithium aluminium hydride mixture which was cooled over ice. Stirring was carried out during the addition. The mixture was refluxed for 2 hours under anhydrous conditions, then cooled over iced water. Wet diethyl ether was then added dropwise to decompose the unreacted lithium aluminium hydride. The decomposition was completed by dropwise addition of water. The white solid residue which formed was filtered off from the ether layer, washed with diethyl ether (2 x 100 cm^3), then discarded. The combined ether layers were dried over magnesium sulphate, then the ether was removed to yield a yellow liquid residue (25 g). An infra-red analysis showed a very strong -OH peak at 3400 cm^{-1} and no carbonyl peak, thus it was assumed that only 2-(p-chlorophenyl) ethanol was present in significant quantity. The n.m.r. spectrum was consistent with structure and so the crude product was used in the bromination step without further purification.

2-(p-chlorophenyl) ethyl bromide

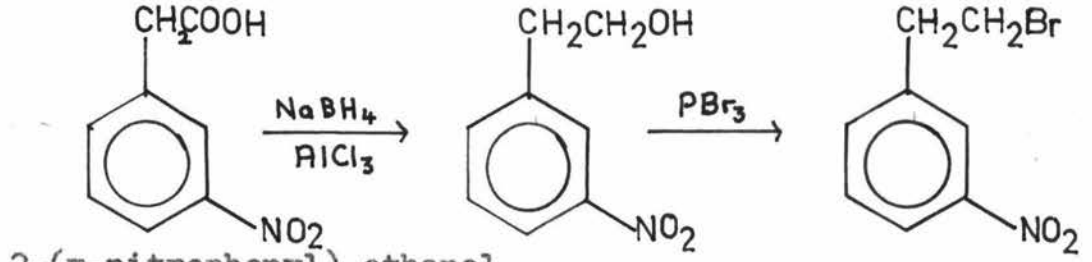
Bromination of 2-(p-chlorophenyl) ethanol with PBr_3 by a method similar to that of Rupe[21] was used to prepare 2-(p-chlorophenyl) ethyl bromide.

Procedure

Phosphorous tribromide (10 cm^3) was added dropwise to the 2-(p-chlorophenyl) ethanol (25 g) from the previous step. The mixture was cooled over ice during the addition. Refluxing was carried out for 2 hours over a water bath at 90°. The reaction mixture was then poured into iced water (80 cm^3) and extracted with diethyl ether (4 x 50 cm^3). The combined ether extracts were washed with 5% sodium hydroxide (50 cm^3) followed by water (2 x 50 cm^3), then dried over magnesium sulphate. The ether was removed (rotary evaporator) and an infra-red analysis of the crude product showed complete disappearance of the -OH peak. The product was distilled under reduced pressure to give a clear liquid, b.p. 84-85°/1.3 mm (lit.[22] 86.5°/1.6 mm) and n_D^{21} 1.5681 (lit.[22] n_D^{25} 1.5697). The yield was 60%, calculated from the amount of p-chlorophenylacetic acid originally used. The structure of the product was confirmed by n.m.r.

2.1.2 Preparation of 2-(m-nitrophenyl) ethyl bromide

The synthetic scheme for the preparation of 2-(m-nitrophenyl) ethyl bromide from m-nitrophenylacetic acid is as follows:



2-(m-nitrophenyl) ethanol

Reduction of m-nitrophenylacetic acid was carried out using sodium borohydride with aluminium trichloride as a catalyst. Reduction of the nitro-group would occur if $LiAlH_4$ was used as the reducing agent.

Procedure[23]

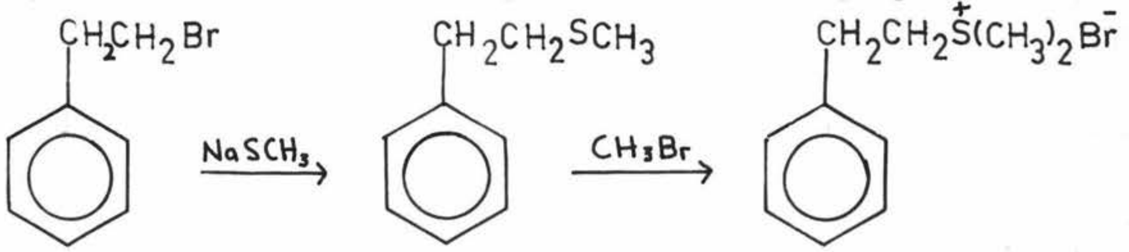
m-nitrophenylacetic acid (10 g) was dissolved in 95 cm^3 of anhydrous diglyme (freshly distilled and stored over sodium wire) then sodium borohydride (4.6 g) added. Aluminium trichloride (1.5 g) was dissolved in 12 cm^3 of anhydrous diglyme and slowly added to the above mixture. Fluka aluminium trichloride was used as this did not need to be sublimed. The reaction mixture was heated for 3 hours between 50^o and 60^o. Excess sodium borohydride was then decomposed with cold dilute hydrochloric acid and the solution extracted with diethyl ether (3 x 100 cm^3). The ether extracts were washed with 5% potassium hydroxide (50 cm^3) to remove unreacted acid, then dried over magnesium sulphate. The ether and remaining diglyme were removed on a rotary evaporater to yield an orange-yellow oil (8 g). An infra-red spectrum showed an -OH peak at 3400 cm^{-1}, but no carbonyl peak, indicating the presence of the alcohol. The nitro doublet was present at 1520 cm^{-1} and 1340 cm^{-1}. The n.m.r. spectrum was also consistent with structure. The crude alcohol was used in the next step without further purification.

2-(m-nitrophenyl) ethyl bromide

Phosphorous tribromide (5 g) was reacted with the 2-(m-nitrophenyl)ethanol (8 g) from the previous step using the same procedure as described for the preparation of 2-(p-chlorophenyl)ethyl bromide. The yield was 56% of 2-(m-nitrophenyl)ethyl bromide, b.p. 128-130°/0.4 mm (lit.[17] 136-138°/0.5 mm). The refractive index was n_D^{20} 1.5849 (lit.[17] n_D^{22} 1.5852). The infra-red spectrum showed disappearance of the alcohol -OH peak, and the n.m.r. spectrum was consistent with the structure of the product.

2.1.3 Preparation of 2-phenethyldimethylsulphonium bromide

2-phenethyl bromide was converted to 2-phenethyldimethylsulphonium bromide according to the following synthetic scheme.



Methyl 2-phenethyl sulphide

Methyl 2-phenethyl sulphide has been prepared by Steffa and Thornton from 2-phenethyl bromide[24]. This method involves heating a solution of sodium hydroxide in ethanol with methanethiol (CH_3SH) to form the sodium salt of methanethiol ($NaSCH_3$). The bromide is then added dropwise and the mixture refluxed. Steffa and Thornton used commercial CH_3SH which is contained in a phial. However, CH_3SH has a low b.p. (6.2°), therefore it was decided that this reactant could be handled more conveniently by producing it <u>in situ</u> in the gas phase and bubbling it through the solution of sodium hydroxide in ethanol. This solution was cooled over ice so that the CH_3SH condensed into the liquid phase as it bubbled through. The CH_3SH was passed through in excess to ensure that no unreacted sodium hydroxide remained, as this could cause the elimination of the methyl sulphide produced after the addition of the bromide. The number of moles of sodium hydroxide used to produce the $NaSCH_3$ was equal to the number of moles of the

2-phenethyl bromide to be reacted. This was to prevent an excess of $NaSCH_3$ building up which could give rise to side reactions.

CH_3SH was produced in situ by heating the methylisothiouronium salt of methanethiol in aqueous sodium hydroxide[25]. The CH_3SH produced was passed up through a reflux condenser and then carried by a gas line into the sodium hydroxide/ethanol solution. Excess CH_3SH was trapped by passing it into a gas jar containing 1 M sodium hydroxide. The methylisothiouronium salt was prepared from a mixture of thiourea, water and dimethyl sulphate[26].

Procedure

To prepare the methylisothiouronium salt of methanethiol, thiourea (76 g), water (50 cm^3) and dimethyl sulphate (63 g) were warmed together until the thiourea dissolved. The mixture was then boiled vigorously and the liquid distilled off until a thick slurry was produced. Water (10 cm^3) and ethanol (100 cm^3) were added and the mixture was allowed to cool. The solid was filtered off and the crystals dried in a vacuum dessicator to yield 98 g of the methylisothiouronium salt of methanethiol (m.p. 240-245°). To 80 cm^3 of 20% sodium hydroxide solution were added 56 g of the methylisothiouronium salt of methanethiol and the mixture heated to produce methanethiol. The gas was bubbled through a solution of sodium hydroxide (4.3 g) in ethanol (100 cm^3) which was cooled over ice. This solution was then heated and 2-phenylethyl bromide (20 g) was added dropwise. The reaction mixture was refluxed for 0.5 hours. The ethanol was removed by distillation under reduced pressure, water (200 cm^3) added and the mixture extracted with diethyl ether (4 x 100 cm^3). The combined ether extracts were dried over magnesium sulphate. The ether was removed (rotary evaporator) to yield a yellow liquid (13 g) which had a characteristic sulphide smell. The infra-red spectrum showed that the 2-phenethyl bromide had reacted to form a different compound, and so the crude product was used in the methylation step without further purification.

2-phenethyldimethylsulphonium bromide

The method of Saunders and Williams[22] was used to prepare 2-phenethyldimethylsulphonium bromide from methyl 2-phenethyl sulphide. This method involves dissolving methyl 2-phenethyl sulphide and methyl bromide (CH_3Br) in nitromethane and allowing the mixture to stand at room temperature. The solvent is then removed to yield 2-phenethyldimethylsulphonium bromide. CH_3Br has a low boiling-point (3.56°), thus it was decided to produce it in situ by heating a mixture of sodium bromide, conc. H_2SO_4, and methanol[27]. The CH_3Br evolved was bubbled through a solution of methyl 2-phenethyl sulphide in nitromethane which was cooled over ice to cause the CH_3Br to condense on contact. The CH_3Br was passed through in considerable excess to ensure maximum yields of the product. The excess CH_3Br is easily removed owing to its low boiling point. For every 100 g of sodium bromide used approximately 0.8 to 0.9 moles of CH_3Br are produced.

Procedure

Methyl bromide was generated by slowly adding concentrated sulphuric acid (25 g) to methanol (20 g) cooled over ice. The mixture was shaken during the addition. Sodium bromide (30 g) was suspended in the mixture which was then heated over a water bath at 50°. The methyl bromide gas produced was dried by passing it through concentrated sulphuric acid in a gas jar. The temperature of the water bath was increased when the rate of gas evolution began to decrease, and heating was terminated when the mixture became a thick slurry. The dried methyl bromide was bubbled through a solution of the methyl 2-phenethyl sulphide (13 g) from the previous step in nitromethane (180 cm^3), cooled over ice. The reaction flask was then loosely stoppered and allowed to stand at room temperature for 2 days. The nitromethane was removed at room temperature (rotary evaporator) to leave crude white crystals. The product was recrystallized from ethanol/ether to give white crystals (15 g) of 2-phenethyldimethylsulphonium bromide, m.p. 136-137° (lit.[22] 135-135.5°). The yield, determined from the amount of 2-phenethyl bromide originally used in the previous step, was 57%. The n.m.r. spectrum of the product using D_2O was solvent was consistent with structure.

The following substituted 2-phenethyldimethylsulphonium bromides were prepared by the methods previously outlined from the corresponding substituted 2-phenethyl bromides. The 2-(p-chlorophenyl)ethyl bromide used was prepared as described on page 10 while the remaining 2-phenethyl bromides were supplied by Dr L.F. Blackwell. The intermediate methyl 2-phenethyl sulphides prepared were recognisable by their characteristic smell. An infra-red analysis was carried out on both the reactant bromide and the crude sulphide to determine whether reaction had occurred. The infra-red results combined with the characteristic smell were used as confirmation that the sulphide had been formed, and so the crude sulphides were used in the methylation step withou further purification. The 2-phenethyldimethylsulphonium bromides were purified by recrystallization from ethanol/diethyl ether until a constant melting-point was obtained. An n.m.r. analysis of the sulphonium salts was carried out using D_2O as the solvent and all the chemical shifts and integrals were consistent with the structure of the products. A mass spectral analysis was carried out on the products which had not previously been reported in the literature to confirm structure and purity. Yields of the sulphonium salts were calculated on the basis of the corresponding 2-phenethyl bromides being the starting compounds, with the 2-phenethyl sulphides being regarded as intermediates.

2.1.4 Preparation of 2-(p-chlorophenyl)ethyldimethylsulphonium bromide

2-(p-chlorophenyl)ethyldimethylsulphonium bromide was prepared from 2-(p-chlorophenyl)ethyl bromide (15 g) to give fine plate-like white crystals (11.7 g), m.p. 125-126° (lit[22] 126-126.5°) yield 62%.

2.1.5 Preparation of 2-(p-methoxyphenyl)ethyldimethylsulphonium bromide

An 83% yield of 2-(p-methoxyphenyl)ethyldimethylsulphonium bromide (5.5 g) was obtained from 2-(p-methoxyphenyl)ethyl bromide (5 g). The white crystals of the product had a m.p. of 130-131° (lit.[22] 133-133.5°).

2.1.6 Preparation of 2-(m-bromophenyl)ethyldimethylsulphonium bromide

2-(m-bromophenyl)ethyl bromide (2 g) was converted to white crystals of 2-(m-bromophenyl)ethyldimethylsulphonium bromide (1.1 g) in 45% yield, m.p. 142-144°. The mass spectrum showed a molecular ion peak at M/e 229.9765 which corresponds to $C_9H_{11}BrS$. This is consistent with loss of CH_3Br from $C_{10}H_{14}Br_2S$.

2.1.7 Preparation of 2-(p- nitrophenyl)ethyldimethylsulphonium bromide

2-(p-nitrophenyl)ethyldimethylsulphonium bromide (3.1 g) was prepared from 2-(p-nitrophenyl)ethyl bromide (6 g) to give a 41% yield of pale yellow crystals of the product, m.p. 125-126°. The mass spectrum showed a molecular ion peak at M/e 197.0644. This is consistent with the formula $C_9H_{11}NO_2S$ which corresponds to loss of CH_3Br from $C_{10}H_{14}BrNO_2S$.

2.1.8 Preparation of 2-(p-acetylphenyl)ethyldimethylsulphonium bromide

White crystals of 2-(p-acetylphenyl)ethyldimethylsulphonium bromide (3.2 g), m.p. 119-120° (lit.[22] 121-121.5°), were prepared from 2-(p-acetylphenyl)ethyl bromide (4 g) in 63% yield.

2.1.9 Attempted preparation of 2-(m-nitrophenyl)ethyldimethylsulphonium bromide

An attempt was made to convert 2-(m-nitrophenyl)ethyl bromide (2 g) into 2-(m-nitrophenyl)ethyldimethyl sulphonium bromide. However, it appeared that dimerization occurred because an ultra-violet spectrum of the product in 50.2% DMSO showed two peaks and the mass spectrum indicated the presence of higher molecular weight material than that expected for the product.

2.2 Preparation of deuterated compounds

2.2.1 Deuteration procedure

Deuteration in the 2-position of the 2-phenethyl compounds was carried out at the phenylacetic acid stage.

Method I

The phenylacetic acid was converted to the sodium salt by reaction with a slight excess of sodium hydroxide, this neutralization being carried out in water. The water was then taken off, the solid dried, and then it was redissolved in a small amount of D_2O. The solution was then refluxed under anhydrous conditions for a few days. The D_2O was then removed, fresh D_2O added, and the refluxing repeated. This procedure was continued until a satisfactory amount of deuterium had been incorporated into the α-position of the phenylacetic acid salt. The phenylacetic acid was reformed by acidification of the salt with conc. HCl.

Method II

This method was adapted from a procedure used by Belanger *et al*[28]. A solution containing the phenylacetic acid in 1M concentration and a 0.63 M sodium hydroxide concentration in D_2O was heated at 85° under anhydrous conditions for 48 hours. Conc. HCl was then added to precipitate out the deuterated phenylacetic acid. This procedure was found to be more satisfactory than that of method I as it gave a higher degree of deuteration in a shorter period of time.

2.2.2 Preparation of 2-(*p*-methoxyphenyl)ethyl-2,2-d_2 bromide.

p-methoxyphenylacetic acid -α,α,-d_2

Method I was used to deuterate *p*-methoxyphenylacetic acid in the α,α-position.

Procedure

p-methoxyphenylacetic acid (20 g) was neutralized with sodium hydroxide (5 g) in water (50 cm^3). The water was removed (rotary evaporator) and the sodium salt of the acid which contained the excess sodium hydroxide was dried in a vacuum dessicator. The sodium salt was dissolved in deuterium oxide (20 cm^3) and refluxed for 4 days under anhydrous conditions. The deuterium oxide was then removed and the salt dried. The refluxing procedure was repeated with deuterium oxide (15 cm^3) for 5 days, and again with a further quantity of deuterium oxide (10 cm^3) for 4 days. The acid was precipitated out by the addition of concentrated hydrochloric acid (20 cm^3), then filtered off, followed by recrystallization from water. The yield of p-methoxyphenylacetic acid-α,α-d_2 was 86% (17 g), m.p. 85-86° (lit. 86-86.5°). The mass spectrum of the product showed 1.68 D atoms/mol.

2-(p-methoxyphenyl)ethanol-2, 2-d_2

p-methoxyphenylacetic acid-α,α-d_2 (17 g) was reduced by lithium aluminium hydride to 2-(p-methoxyphenyl)ethanol-2, 2-d_2 by the method previously described for the preparation of 2-(p-chlorophenyl)ethanol. A 12 g yield of the crude liquid product was obtained. The infra-red spectrum of the product showed a very strong -OH peak at 3400 cm^{-1}. The n.m.r. spectrum was consistent with structure and so the crude product was used in the bromination step without further purification.

2-(p-methoxyphenyl)ethyl-2,2-d_2 bromide

The 2-(p-methoxyphenyl)ethanol-2,2-d_2 from the previous step was converted to 2-(p-methoxyphenyl)ethyl-2,2-d_2 bromide with phosphorous tribromide, as previously described for the preparation of 2-(p-chlorophenyl)ethyl bromide. The infra-red spectrum of the crude product showed almost complete disappearance of the -OH peak at 3400 cm^{-1}. The product was distilled under reduced pressure to give 2-(p-methoxyphenyl) ethyl-2,2-d_2 bromide (12 g), b.p. 147-149°/18 mm (lit[17] 144-146°/18 mm). The yield was 55% calculated from the amount of p-methoxyphenylacetic acid-α,α-d_2 originally used. The n.m.r. spectrum was consistent with structure. The mass spectral analysis showed 1.68 D atoms/mol.

2.2.3 Preparation of 2-phenethyl-2,2-d_2 bromide.

Phenylacetic acid-α,α-d_2

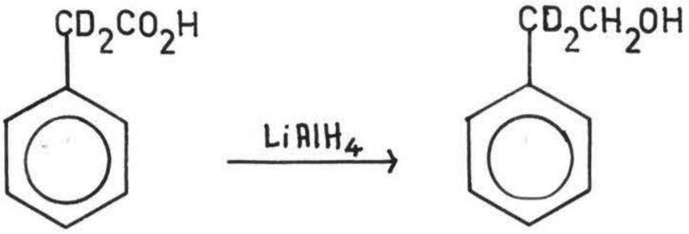
Phenylacetic acid was deuterated at the α,α-position by method II.

Procedure

Phenylacetic acid (26 g) was neutralized with a solution of sodium hydroxide (8 g) in water (50 cm^3) to give sodium phenylacetate. The water was removed and the sodium salt dried to yield 30 g. of white crystals. The sodium phenylacetate was then dissolved in 195 cm^3 of deuterium oxide containing sodium hydroxide (5 g). The solution was heated at 85° under anhydrous conditions for 48 hours then allowed to cool. The deuterated phenylacetic acid was then precipitated out of the solution with concentrated hydrochloric acid (25 cm^3), filtered off, and recrystallized from hot water. The yield was 96% of phenylacetic acid-α,α-d_2 (25 g), m.p. 76-77 (lit. 77°). The n.m.r. spectrum (in deuteroacetone) showed absence of the methylene protons, indicating almost complete α,α- deuteration.

2-phenylethanol-2,2-d_2

The phenylacetic acid was reduced directly to the alcohol by lithium aluminium hydride using the method of Nystrom and Brown[29]. This reduction does not involve the initial conversion of the acid to the ethyl ester.



Procedure

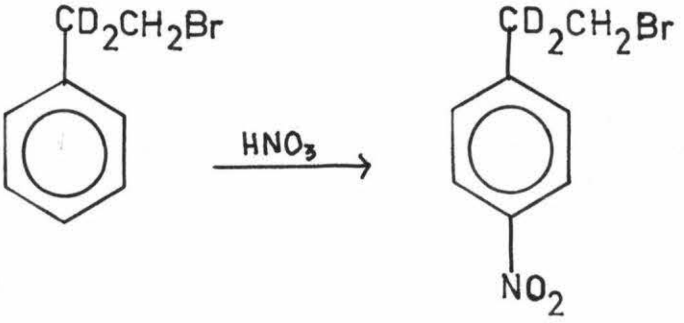
Lithium aluminium hydride (10 g) was suspended in sodium-dried diethyl ether (300 cm^3). Phenylacetic acid-α,α-d_2 (25 g) was dissolved in sodium-dried diethyl ether (200 cm^3) and added dropwise to the above suspension at such a rate, with stirring, to produce gentle refluxing. After the addition was completed, the reaction mixture was refluxed for one hour under anhydrous conditions. The mixture was then cooled over ice. Excess lithium aluminium hydride was decomposed by the dropwise addition of wet diethyl ether, followed by the dropwise addition of water. Ten per cent sulphuric acid (250 cm^3) was added (cooling) to produce a clear solution. The ether layer was drawn off and the aqueous layer extracted with diethyl ether (200 cm^3). The combined ether extracts were washed with water (200 cm^3), 5% sodium bicarbonate (100 cm^3), and again with water (200 cm^3). The ether layer was dried over magnesium sulphate and then the solvent removed to give the crude alcohol (20 g). The infra-red spectrum of the product showed a very strong -OH peak (3400 cm^{-1}) and no carbonyl peak. The n.m.r. spectrum was also consistent with the structure of the product. The 2-phenylethanol-2,2-d_2 was used in the bromination step without further purification.

2-phenethyl-2,2-d_2 bromide

The method previously described for the preparation of 2-(p-chlorophenyl)ethyl bromide was used to convert the 2-phenylethanol-2,2-d_2 (19 g) from the above step to 2-phenethyl-2,2-d_2 bromide (23 g), b.p. 76-78°/3 mm (lit.[30] 100-102°/18 mm), and n_D^{20} 1.5533 (lit.[30] n_D^{23} 1.5537). The yield was 79% based on the phenylacetic acid -$\alpha,\alpha d_2$ being the starting material. The infra-red spectrum of the product showed complete disappearance of the -OH peak at 3400 cm^{-1}. The n.m.r. spectrum was consistent with structure. A mass spectral analysis showed 1.90 D atoms/mol.

2.2.4 Preparation of 2-(p-nitrophenyl)ethyl-2,2-d_2 bromide.

Nitration of 2-phenethyl-2,2-d_2 bromide with fuming nitric acid in acetic acid/acetic anhydride was used to prepare 2-(p-nitrophenyl)ethyl-2,2-d_2 bromide.

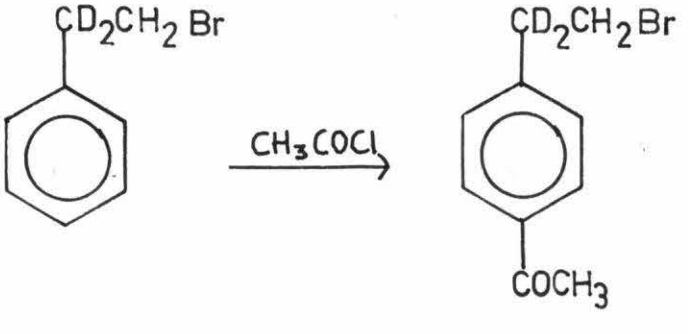


Procedure[31]

Fuming nitric acid (9 g) was added dropwise to a mixture of acetic acid (8 g) and acetic anhydride (14 g) cooled to -5° over ice/salt mixture. 2-phenethyl-2,2-d_2 bromide (12 g) was very slowly added dropwise with stirring. The temperature was kept below 0° during the addition. Stirring was continued for 2 hours (at 0°) then the reaction mixture was poured into a suspension of sodium bicarbonate (18 g) in ice/water mixture (20 cm^3). After bubbling had ceased, the yellow product was extracted into benzene (3 x 100 cm^3), then washed with water (50 cm^3), 5% sodium bicarbonate (50 cm^3), followed by water again (50 cm^3). The benzene layer was dried over magnesium sulphate, and then the solvent was removed to yield crude yellow crystals. The product was recrystallized from hexane to give 2-(p-nitrophenyl)ethyl-2,2-d_2 bromide (8 g), m.p. 69-70° (lit.[17] 68-69°). The yield was 53%. The n.m.r. spectrum (in deuterochloroform) was consistent with structure. A mass spectral analysis of the product showed 1.90 D atoms/mol.

2.2.5 Preparation of 2-(p-acetylphenyl)ethyl-2,2-d_2 bromide

A Friedel-Crafts acylation reaction was used to prepare 2-(p-acetylphenyl)ethyl-2,2-d_2 bromide from 2-phenethyl-2,2-d_2 bromide.



Procedure[31]

A mixture of aluminium trichloride (6.7 g), carbon disulphide (24.3 cm^3) and acetyl chloride (3.8 cm^3) was cooled over an ice bath. 2-Phenethyl-2,2-d_2 bromide (10 g) in acetyl chloride (7.7 cm^3) was added as fast as possible with stirring. The mixture was stirred over the ice bath until no further hydrogen chloride was given off (3 hours). The reaction product was decomposed with a mixture of concentrated hydrochloric acid and crushed ice. The carbon disulphide layer was removed and the aqueous layer was extracted with benzene (2 x 100 cm^3). The combined benzene and carbon disulphide layers were washed with dilute hydrochloric acid (50 cm^3), water (50 cm^3), and 10% sodium hydroxide (50 cm^3), followed by water again (100 cm^3). The solvent was removed (rotary evaporator) and the product was twice fractionally distilled under reduced pressure. The yield was 56% of 2-(*p*-acetylphenyl)ethyl-2,2-d_2 bromide (7 g), b.p. 128-130°/0.3 mm (lit.[31] 117-118°/0.1) and n_D^{22} 1.5735 (lit.[31] n_D^{25} 1.5724. The n.m.r. spectrum was consistent with structure. The mass spectrum showed 1.90 D atoms/mol.

The following deuterated 2-phenethyldimethylsulphonium bromides were prepared from the corresponding deuterated 2-phenethyl bromides by the methods described for the non-deuterated sulphonium salts. The 2-(p-chlorophenyl)ethyl-2,2-d_2 and 2-(m-bromophenyl)ethyl-2,2-d_2 bromides were supplied by Dr L.F. Blackwell while the remainder were prepared as described above. The comments on page 17 regarding the preparation of the non-deuterated sulphonium salts also apply to the following preparations.

2.2.6 Preparation of 2-phenethyldimethylsulphonium-2,2-d_2 bromide

2-phenethyldimethylsulphonium-2,2-d_2 bromide (1 g), m.p. 135-136° (lit.[30] 136.5-137°), was prepared from 2-phenethyl-2,2-d_2 bromide (1.5 g) in 53% yield. The mass spectrum showed 1.90 D atoms/mol.

2.2.7 Preparation of 2-(p-methoxyphenyl)ethyldimethylsulphonium-2,2-d_2 bromide

2-(p-methoxyphenyl)ethyl-2,2-d_2 bromide (9 g) was converted to 2-(p-methoxyphenyl)ethyldimethylsulphonium-2,2-d_2 bromide (8 g) in 70% yield. The m.p. of the product was 130-131° (lit.[22] 133-135.5°). The mass spectrum showed the presence of 1.68 D atoms/mol.

2.2.8 Preparation of 2-(p-chlorophenyl)ethyldimethylsulphonium-2,2-d_2 bromide

A 64% yield of 2-(p-chlorophenyl)ethyldimethylsulphonium-2,2-d_2 bromide (2.5 g) was obtained from 2-(p-chlorophenyl)ethyl-2,2-d_2 bromide (3 g, 1.86 D atoms/mol.). The product m.p. was 125.5-126° (lit.[22] 126-126°).

2.2.9 Preparation of 2-(m-bromophenyl)ethyldimethylsulphonium-2,2-d_2 bromide

2-(m-bromophenyl)ethyldimethylsulphonium-2,2-d_2 bromide (1.5 g) m.p. 141-142°, was prepared from 2-(m-bromophenyl)ethyl-2,2-d_2 bromide (2 g) in 50% yield. A mass spectral analysis showed 1.88 D atoms/mol.

2.2.10 Preparation of 2-(p-acetylphenyl)ethyldimethylsulphonium-2,2-d_2 bromide

2-(p-acetylphenyl)ethyldimethylsulphonium-2,2-d_2 bromide (4 g), m.p. 119-120° (lit.[22] 121-121.5°), was prepared from 2-(p-acetylphenyl)ethyl-2,2-d_2 bromide (5 g) in 63% yield. The mass spectrum showed 1.90 D atoms/mol.

2.2.11 Attempted preparation of 2-(p-nitrophenyl)ethyldimethylsulphonium-2,2-d_2 bromide

An attempt was made to prepare 2-(p-nitrophenyl)ethyldimethylsulphonium-2,2-d_2 bromide from 5 g of 2-(p-nitrophenyl)ethyl-2,2-d_2 bromide. However, the product would not crystallize out from ethanol/diethyl ether, probably owing to impurities. The product was therefore dissolved in water, washed with diethyl ether, and the water layer boiled for 10 minutes with decolourizing charcoal. The charcoal was filtered off, the water removed (rotary evaporator), and the resultant crystals dried in a vacuum dessicator. The product was then recrystallized from diethyl ether/ethanol to yield 2 g of pale yellow crystals, m.p. 124-125°. However, although the mass spectrum of the product confirmed the structure, exchange had occurred between hydrogen and deuterium atoms at the 2,2-position so that the extent of deuteration was only 1.08 D atoms/mol. This level of deuteration is not high enough to be able to determine a k_2^D value for the E2 elimination reaction.

3 KINETICS

3.1 Purification of solvents

3.1.1 Dimethyl sulphoxide (DMSO)

Dimethyl sulphoxide (Ajax Unilab.) was twice distilled under reduced pressure from calcium hydride, and stored in a stoppered flask.

$$n_D^{20} = 1.4790 \text{ (lit. } n_D^{20} = 1.4795)$$

3.1.2 H_2O

Deionized water was distilled from alkaline potassium permanganate, and stored in a stoppered glass bottle.

3.2 Preparation of standard sodium hydroxide solution

Sodium hydroxide solution (1M) was prepared from standard concentrate (BDH.CVS ampoule) diluted with distilled water to the specified volume. Base concentrations were checked periodically with standard hydrochloric acid using bromocresol green-methyl red as indicator.

3.3 Preparation of base solutions

Heat is evolved when DMSO and water are mixed, therefore stock base solutions containing both the required mole percentage of DMSO and the required sodium hydroxide concentration for a given kinetic run were prepared beforehand. All the solutions were made up at 20°. The correct volume of standard 1M sodium hydroxide to give the required concentration when diluted to a total volume of 100 cm^3 was added to a 100 cm^3 volumetric flask. Distilled water was then added to give a total weight of 20 g including the weight of water present in the sodium hydroxide solution. The solution was then made up to 100 cm^3 with DMSO and reweighed. The mole percentage of DMSO was 50.2 calculated from the respective weights of water and DMSO in the solution. The base solutions were stable at room temperature for at least two weeks.

3.4 Preparation of solvent

Distilled water (20 g) was added to a 100 cm^3 volumetric flask and then made up to 100 cm^3 with DMSO to give a DMSO content of 50.2 mole %.

3.5 General kinetic procedure

The rate of styrene production by pseudo-first order kinetics was followed spectrophotometrically at 260 nm for all substrates except p-Ac (280 nm) and p-NO_2 (310 nm). An attempt was made to follow the elimination from 2-(m-nitrophenyl) ethyl bromide. However, in 50.2% DMSO, the substrate peak (275 nm) was too close to the m-nitro sytrene peak (260 nm) for either the production of the styrene or the disappearance of the substrate to be followed spectrophotometrically.

The excess of base over substrate was at least in the ratio of 20 to 1. It was found that the derived second order rate constants were independent of base concentration over at least a 10-fold base concentration range. Reactions with a half-life of one minute or greater were followed on a Unicam SP 500 Spectrophotometer, while those with shorter half-lives were measured using a Durrum-Gibson D-110 stopped flow spectrophotometer. Both the 2-phenethyl bromides and the 2-phenethyldimethylsulphonium bromides appear to be essentially completely converted into the corresponding styrenes[17,19].

3.5.1 Unicam SP 500 procedure

The reactions were followed in a stoppered cell in the thermostatted cell compartment (±0.1°) of the instrument. Stock substrate solutions, containing substrate concentrations of approximately 0.02 M, were prepared in 10 cm^3 quantities using 50.2 mole % DMSO solvent. These substrate solutions were stable over a period of several months. Two cells were each filled with the base solution (2 cm^3) required for the kinetic run and placed in the cell compartment, which was held at the required temperature by the circulation of water from a constant temperature bath. The cells were left standing in the compartment for at least 10 minutes so that thermal equilibrium was attained. An aliquot of the required stock substrate solution (0.05 cm^3) was then pipetted into one of the cells, giving a final substrate concentration of approximately 10^{-4} M, and the reaction mixture thoroughly stirred with a small glass stirrer. The other cell was used as the reference blank. Initially, an attempt was made to record the spectrophotometric changes for all kinetic runs against time using the Direct Readout mode onto a Unicam SP 22 chart recorder. However, it was found for reactions with a half-life of less than two minutes and for following the smaller optical density changes which occur after the second half-life that the reproducibility suffered. Hence, for the faster reactions and for those in which readings after two half-lives were required in the rate constant calculations, the Null Balance mode and a stopwatch were used to measure percentage transmission against time. The infinity readings were recorded for the reactions after at least ten half-lives had elapsed. The infinity value was found to be very stable in all cases.

3.5.2 Durrum-Gibson D-110 procedure

Equal volumes of substrate and base solutions were used in the mixing chamber of the stopped-flow instrument, therefore both solutions are diluted by half. However, the light path-length of the reaction cuvette is twice that of the SP 500 instrument, therefore the same substrate concentrations as used in the SP 500 reaction cells (i.e. approximately 10^{-4} M) were used for the stopped-flow spectrophotometer. The base and substrate solutions were allowed to reach thermal equilibrium for 15 minutes in the drive syringes of the instrument which were immersed in water circulating through a heat exchanger in a constant temperature water bathh. The temperature was kept to within ±0.2° of the required value. The instrument was then actuated and the optical density changes were recorded against time on a Hewlett-Packard 141 B storage oscilloscope. The traces were photographed with an Asahi Pentax camera and the negatives were traced onto graph paper using a Leitz Valoy II enlarger. The optical density versus time values for the reaction were read off from the graph paper.

3.6 Treatment of results

The integrated pseudo-first order rate equation is,

$$\log (C_{\infty} - C_t) = - \frac{k_{\psi}}{2.303} \cdot t + \log C_{\infty}$$

where C_{∞} is the product concentration at time = infinity, C_t is the product concentration at time t, and k_{ψ} is the pseudo-first order rate constant. From Beer's law the concentration is directly proportional to optical density for a constant light path length, therefore the above rate equation can be written as,

$$\log (D_{\infty} - D_t) = - \frac{k_{\psi}}{2.303} \cdot t + \log D_{\infty}$$

where D is the optical density and the subscripts t and ∞ have their usual meanings. The pseudo-first oder rate constants were obtained from a least squares plot of $\log (D_{\infty} - D_t)$ versus t, the slope of the plot giving the value of $- k_{\psi}/2.303$. The second order rate constants (k_2) were obtained by dividing the k_{ψ} value by the base concentration. In cases where percentage transmission (T %) was measured, these values were converted to optical density by the equation,

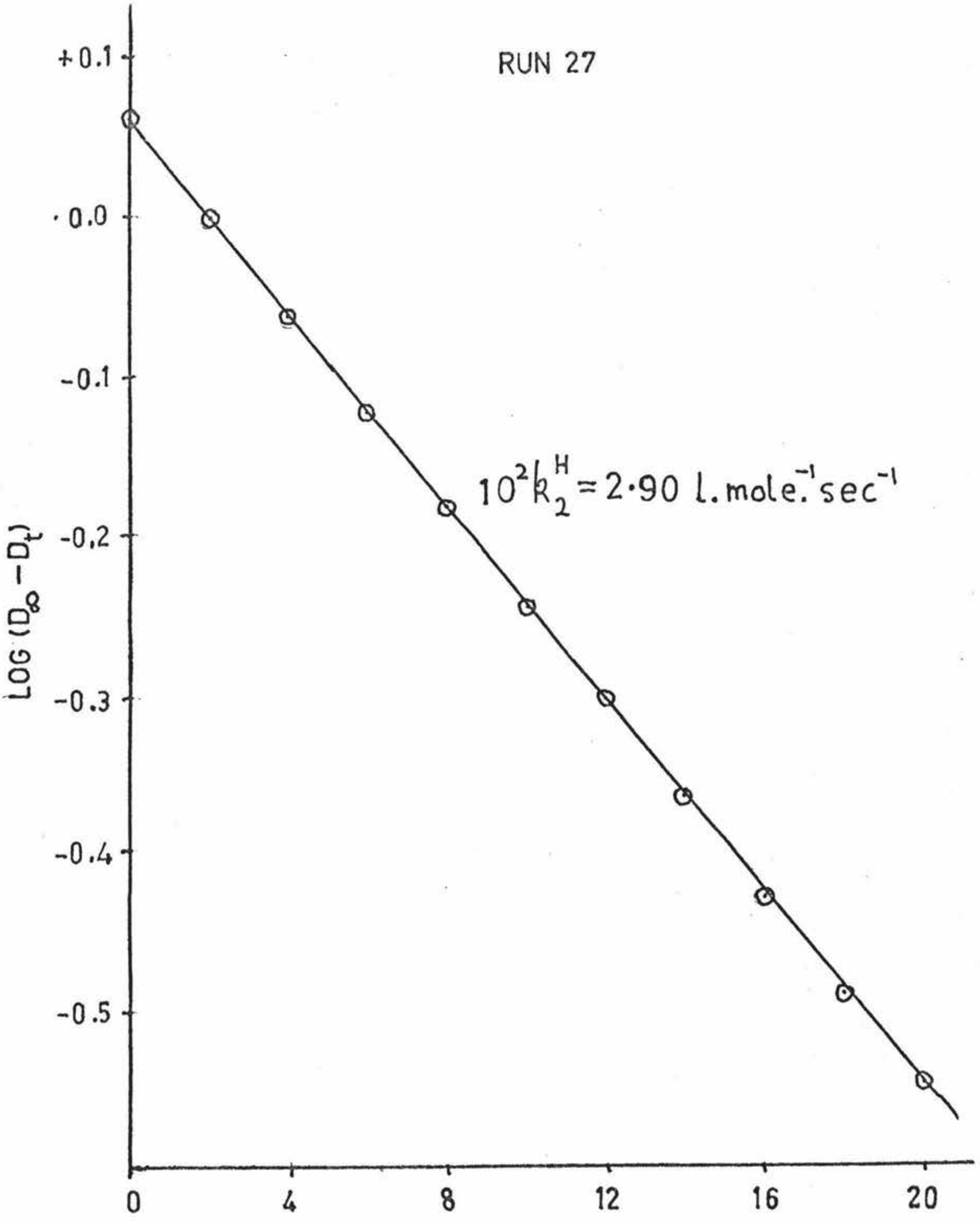
$$D = 2 - \log T\%.$$

Computations were carried out using a least squares fit programme on a B 6700 computer.

The k_2^H values were calculated from the optical density measurements for the first 2 half-lives of the reaction of the non-deuterated substrates. An example plot for 2-(p-methoxyphenyl)ethyl bromide at 20° (NaOH = 0.04 M) is shown in Fig.2. The measurements from which this plot was determined are as follows:

Figure 2.

Plot of log (D_∞-D_t) vs. time for 2-(p-methoxyphenyl)ethyl bromide at 20°.



Run 27

t (min.)	D_t	$\log (D_\infty - D_t)$
0	0.215	0.059
2	0.365	-0.002
4	0.495	-0.063
6	0.606	-0.123
8	0.703	-0.182
10	0.793	-0.246
12	0.863	-0.304
14	0.928	-0.365
16	0.987	-0.428
18	1.036	-0.490
20	1.076	-0.547
∞	1.360	

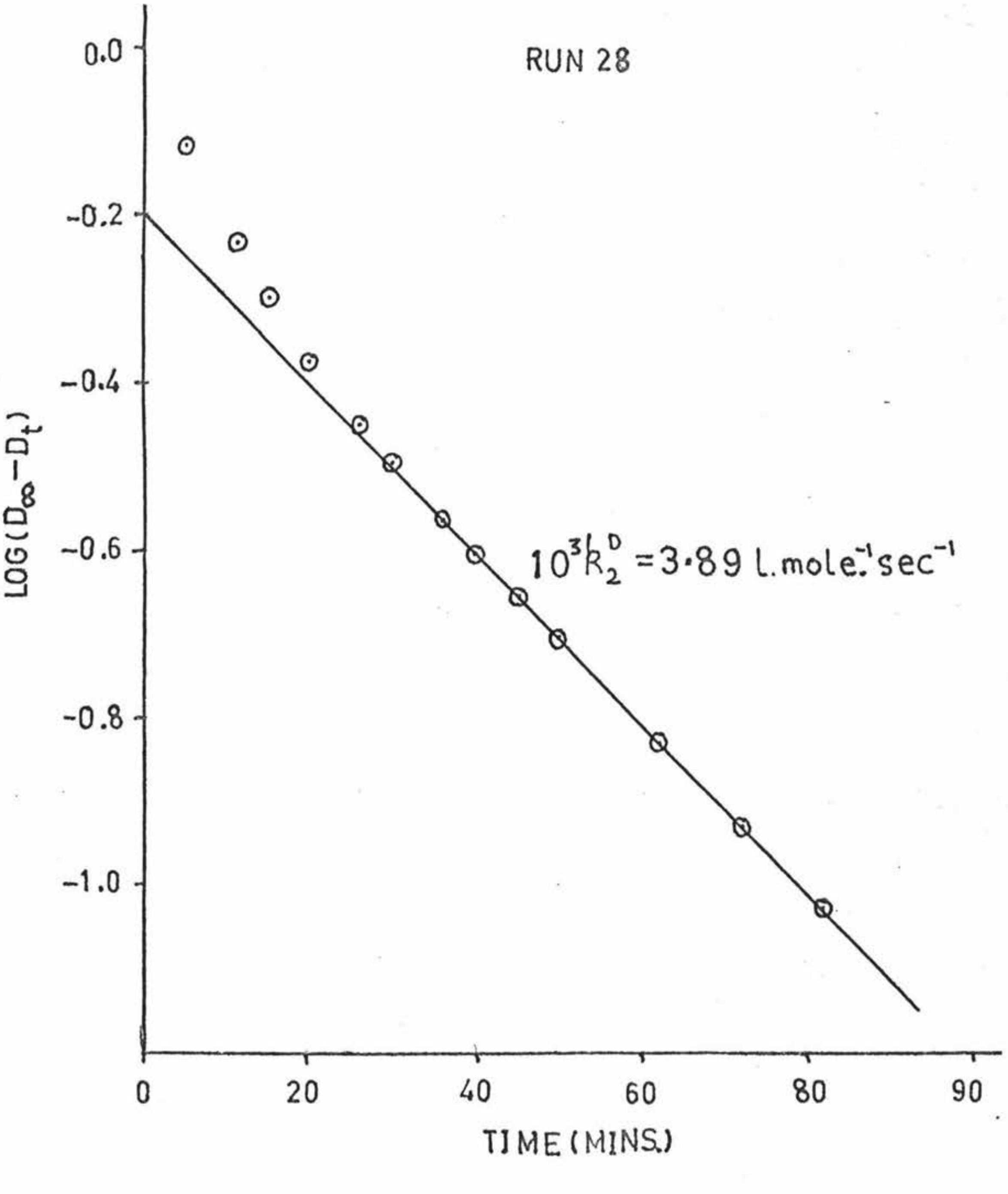
In the case of the deuterated substrates the presence of some of the non-deuterated compound caused initial curvature of the $\log (D_\infty - D_t)$ versus t plots. Therefore, only the optical density values for the deuterated substrate which were recorded after at least 8 half-lives for the non-deuterated substrate had elapsed were used to determine k_2^D. The example plot (Fig.3) for 2-(p-methoxyphenyl)ethyl-2,2-d_2 bromide (20°, NaOH = 0.1 M) shows the effect that non-deuterated material has on the slope of the $\log (D_\infty - D_t)$ versus t plot for deuterated substrates, as indicated by the initial steep curve before the plot becomes linear. The values which were used in this plot are as follows:

Run 28

t (min.)	D_t	$\log (D_\infty - D_t)$
5	0.411	-0.114
11	0.597	-0.234
15	0.680	-0.301
20	0.757	-0.374
26	0.824	-0.449
30	0.860	-0.495
36	0.907	-0.564
40	0.932	-0.606
45	0.959	-0.656

Figure 3.

Plot of log $(D_\infty - D_t)$ vs. time for 2-(p-methoxyphenyl)ethyl-2,2-d_2 bromide at 20°.



Run 28 (Contd.)

t (min.)	D_t	$\log (D_\infty - D_t)$
50	0.983	-0.706
62	1.032	-0.830
72	1.063	-0.932
82	1.085	-1.022
∞	1.180	

The Hammett ρ values for the 2-phenethyl bromides and the 2-phenethyldimethylsulphonium bromides were calculated from a least squares plot of $\log k_2^H$ versus σ. The procedure which was used is discussed more fully in Section 5.2.

4 RESULTS

The results of the reaction kinetics for both the deuterated and non-deuterated versions of each compound on the following pages are headed by the name of the non-deuterated compound. The kinetic results for the non-deuterated substrate are sub-headed by Y = H, while those for the deuterated substrate are sub-headed by Y = D. An example table showing about ten time and optical density measurements is given for one run of each substrate at each temperature, whereas only the k_2 values are given for any other runs at the same temperature used to calculate the mean k_2 value. In the case of the deuterated substrates only the optical density measurements which were recorded after 8 half-lives for the non-deuterated substrate had elapsed are shown. The k_2^H/k_2^D ratio for each pair of deuterated and non-deuterated substrates is given at the bottom of the page beneath the corresponding tables of results. Summaries of the k_2 values and the k_2^H/k_2^D ratios follow the tables of results.

4.1 2-phenethyldimethylsulphonium bromide

Y = H

Run 1

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0	0.070
4	0.175
8	0.261
12	0.340
16	0.405
20	0.468
24	0.513
28	0.556
32	0.952
34	0.609
∞	0.800

$10^2\ k_2^H = 3.29$ l.mol.$^{-1}$ sec.$^{-1}$

Y = D

Run 4

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0	0.633
20	0.660
40	0.686
60	0.710
70	0.721
80	0.733
90	0.740
110	0.760
130	0.775
150	0.791
∞	0.920

$10^3\ k_2^D = 4.44$ l.mol.$^{-1}$ sec.$^{-1}$

Run No.	$10^2 k_2^H$ l.mole^{-1}.sec.$^{-1}$
2	3.31
3	3.24

Run No.	$10^3 k_2^D$ l.mole^{-1}.sec.$^{-1}$
5	4.45

Mean $10^2 k_2^H = 3.28 \pm 0.03$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^3 k_2^D = 4.44 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 7.39 \pm 0.09$$

4.2 <u>2-(p-methoxyphenyl)dimethylsulphonium bromide</u>

Y = H

Run 6

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0	0.012
20	0.105
40	0.191
60	0.268
80	0.337
100	0.398
120	0.450
140	0.497
200	0.612
240	0.668
∞	0.870

$10^3 k_2^H = 5.04$ l.mole.$^{-1}$sec.$^{-1}$

Y = D

Run 19

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0	0.717
60	0.735
120	0.755
180	0.772
240	0.788
300	0.801
420	0.833
540	0.857
660	0.876
780	0.896
∞	1.080

$10^4 k_2^D = 7.29$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^3 k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
7	4.91
8	4.93

Run No.	$10^4 k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
18	7.23

Mean $10^3 k_2^H = 4.96 \pm 0.05$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^4 k_2^D = 7.26 \pm 0.03$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 6.83 \pm 0.10$$

2-(p-methoxyphenyl)ethyldimethylsulphonium bromide (Contd.)

Y = H

Run 70

NaOH = 0.1 M, temp = 30°

time (mins.)	D_t
0	0.095
2	0.266
4	0.417
6	0.548
8	0.664
10	0.770
12	0.857
14	0.947
16	1.013
∞	1.550

$10^2k_2^H = 1.05$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
71	1.07

Y = D

Run 72

NaOH = 0.1 M, temp = 30°

time (mins.)	D_t
0	1.139
4	1.170
8	1.202
12	1.228
16	1.252
21	1.283
26	1.313
31	1.348
36	1.368
∞	1.820

$10^3k_2^D = 1.90$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^3k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
73	1.86

Mean $10^2k_2^H = 1.06 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^3k_2^D = 1.87 \pm 0.02$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 5.64 \pm 0.11$$

2-(*p*-methoxyphenyl)ethyldimethylsulphonium bromide (Contd.)

Y = H

Run 74

NaOH = 0.04 M, temp = 40°

time (mins.)	D_t
0	0.086
2	0.293
4	0.469
6	0.620
8	0.750
10	0.854
12	0.947
14	1.022
16	1.097
∞	1.440

$10^2k_2^H$ = 3.54 l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
75	3.54

Y = D

Run 76

NaOH = 0.04 M, temp = 40°

time (mins.)	D_t
0	1.452
4	1.484
8	1.513
12	1.538
16	1.562
21	1.587
26	1.609
31	1.627
36	1.656
41	1.676
46	1.695
∞	1.920

$10^3k_2^D$ = 6.54 l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^3k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
77	6.81

Mean $10^2k_2^H = 3.54 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^3k_2^D = 6.61 \pm 0.14$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 5.30 \pm 0.12$$

4.3 2-(*p*-chlorophenyl)ethyldimethylsulphonium bromide

Y = H

Run 11

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0.0	0.155
0.5	0.250
1.0	0.330
1.5	0.396
2.0	0.448
2.5	0.502
3.0	0.543
3.5	0.582
4.0	0.612
4.5	0.642
5.0	0.668
∞	0.860

$10\ k_2^H = 2.16$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10\ k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
9	2.05
10	2.10

Y = D

Run 12

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0	0.338
4	0.435
8	0.476
12	0.515
16	0.545
20	0.573
24	0.600
28	0.622
32	0.640
36	0.658
∞	0.790

$10^2\ k_2^D = 2.57$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2 k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
13	2.59

Mean $10\ k_2^H = 2.10 \pm 0.04$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^2 k_2^D = 2.58 \pm 0.02$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 8.14 \pm 0.22$$

4.4 2-(*m*-bromophenyl)ethyldimethylsulphonium bromide

Y = H

Run 14

NaOH = 0.01 M, temp = 20°

time (secs.)	D_t
0	0.183
30	0.302
60	0.396
90	0.475
120	0.543
150	0.600
180	0.648
210	0.690
240	0.720
270	0.752
300	0.777
∞	0.930

$10\ k_2^H = 5.26$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10\ k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
15	5.28

Y = D

Run 16

NaOH = 0.01 M, temp = 20°

time (mins.)	D_t
0	0.573
2	0.602
4	0.623
8	0.667
12	0.705
16	0.738
20	0.765
24	0.788
28	0.808
30	0.817
∞	0.930

$10^2\ k_2^D = 6.36$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2\ k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
17	6.23

Mean $10\ k_2^H = 5.27 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^2 k_2^D = 6.29 \pm 0.06$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 8.38 \pm 0.10$$

4.5 2-(p-acetylphenyl)ethyldimethylsulphonium bromide

Y = H

Run 53

NaOH = 0.05 M, temp = 20°

time (secs.)	D_t
0.0	0.120
0.2	0.180
0.4	0.232
0.6	0.280
0.8	0.320
1.0	0.357
1.2	0.390
1.4	0.420
1.6	0.447
1.8	0.468
∞	0.650

k_2^H = 11.97 l.mole.$^{-1}$sec.$^{-1}$

Run No.	k_2^H l.mole.$^{-1}$sec.$^{-1}$
50	12.03
52	11.73

Y = D

Run 55

NaOH = 0.05 M, temp = 20°

time (secs.)	D_t
0	0.135
2	0.160
4	0.175
6	0.190
8	0.203
10	0.218
12	0.230
14	0.235
16	0.243
18	0.250
∞	0.310

k_2^D = 1.19 l.mole.$^{-1}$sec.$^{-1}$

Run No.	k_2^D l.mole.$^{-1}$sec.$^{-1}$
56	1.30

Mean k_2^H = 11.9 ± 0.1 l.mole.$^{-1}$sec.$^{-1}$

Mean k_2^D = 1.24 ± 0.05 l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 9.60 \pm 0.48$$

4.6 2-(p-nitrophenyl)ethyldimethylsulphonium bromide

Run 86

NaOH = 0.05 M, temp = 20°

time (secs.)	D_t
0.00	0.045
0.01	0.088
0.02	0.137
0.03	0.175
0.04	0.217
0.06	0.285
0.08	0.338
0.10	0.384
0.12	0.422
0.14	0.455
∞	0.625

k_2^H = 175.8 $l.mole.^{-1}sec.^{-1}$

Run No.	k_2^H $l.mole.^{-1}sec.^{-1}$
87	178.3
88	176.1

Mean k_2^H = 176.7 ± 1.0 $l.mole.^{-1}sec.^{-1}$

4.7 2-phenylethyl bromide

Y = H

Run 20

NaOH = 0.05 M, temp = 20°

time (mins.)	D_t
0.0	0.228
0.5	0.307
1.0	0.375
1.5	0.434
2.0	0.482
2.5	0.524
3.0	0.565
3.5	0.597
4.0	0.625
5.0	0.676
6.0	0.714
∞	0.863

$10^2\ k_2^H$ = 7.97 l.mole.$^{-1}$sec.^{01}

Run No.	$10^2 k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
21	8.16
22	8.37

Y = D

Run 24

NaOH = 0.05 M, temp = 20°

time (mins.)	D_t
0	0.582
4	0.622
8	0.654
12	0.678
16	0.703
20	0.726
24	0.747
28	0.765
32	0.780
36	0.799
∞	0.910

$10^3\ k_2^D$ = 9.55 l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^3\ k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
23	9.42
25	9.70

Mean $10^2\ k_2^H$ = 8.17 ± 0.10 l.mole.$^{-1}$sec.$^{-1}$

Mean $10^3\ k_2^D$ = 9.56 ± 0.01 l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 8.54 \pm 0.19$$

4.8 2-(*p*-methoxyphenyl)ethyl bromide

Y = H

Run 26

NaOH = 0.04 M, temp = 20°

time (mins.)	D_t
0	0.223
2	0.370
4	0.496
6	0.607
8	0.699
10	0.788
12	0.854
14	0.917
16	0.967
18	1.027
20	1.060
∞	1.330

$10^2\ k_2^H = 2.94$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2\ k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
27	2.90

Y = D

Run 28

NaOH = 0.1 M, temp = 20°

time (mins.)	D_t
0	0.860
2	0.879
4	0.893
6	0.907
8	0.921
10	0.932
20	0.983
32	1.032
42	1.063
52	1.085
∞	1.180

$10^3\ k_2^D = 3.89$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^3\ k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
29	3.85

Mean $10^2\ k_2^H = 2.92 \pm 0.02$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^3\ k_2^D = 3.87 \pm 0.02$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 7.55 \pm 0.09$$

2-(*p*-methoxyphenyl)ethyl bromide (Contd.)

Y = H

Run 78

NaOH = 0.04 M, temp = 30°

time (mins.)	D_t
0	0.135
1	0.314
2	0.471
3	0.609
4	0.726
5	0.827
6	0.914
7	0.975
8	1.050
9	1.102
∞	1.400

$10^2\ k_2^H = 6.63$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2\ k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
79	6.54

Y = D

Run 80

NaOH = 0.04 M, temp = 30°

time (mins.)	D_t
0	1.122
4	1.153
10	1.203
14	1.234
18	1.253
22	1.275
26	1.294
31	1.315
36	1.334
46	1.364
∞	1.480

$10^2\ k_2^D = 1.03$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2\ k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
81	1.02

Mean $10^2\ k_2^H = 6.59 \pm 0.04$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^2\ k_2^D = 1.03 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 6.40 \pm 0.09$$

2-(*p*-methoxyphenyl)ethyl bromide (Contd.)

Y = H

Run 82

NaOH = 0.02 M, temp = 40°

time (mins.)	D_t
0	0.126
1	0.294
2	0.434
3	0.554
4	0.658
5	0.740
6	0.815
7	0.873
8	0.921
∞	1.190

$10\ k_2^H = 1.44$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10\ k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
83	1.42

Y = D

Run 84

NaOH = 0.02 M, temp = 40°

time (mins.)	D_t
0	1.125
2	1.142
4	1.155
6	1.169
8	1.180
10	1.191
12	1.202
19	1.237
29	1.272
∞	1.385

$10^2\ k_2^D = 2.41$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2\ k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
85	2.42

Mean $10\ k_2^H = 1.43 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^2 k_2^D = 2.41 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 5.93 \pm 0.07$$

4.9 2-(p-chlorophenyl)ethyl bromide

Y = H

Run 30

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0.0	0.101
0.5	0.197
1.0	0.277
1.5	0.340
2.0	0.393
2.5	0.437
3.0	0.471
3.5	0.503
4.0	0.527
∞	0.655

$10\ k_2^H = 3.04\ \text{l.mole.}^{-1}\text{sec.}^{-1}$

Run No.	$10\ k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
31	3.03
32	2.97

Y = D

Run 33

NaOH = 0.02 M, temp = 20°

time (mins.)	D_t
0	0.815
2	0.863
4	0.903
6	0.947
8	0.983
12	1.051
16	1.107
20	1.154
24	1.195
28	1.228
∞	1.415

$10^2\ k_2^D = 3.49\ \text{l.mole.}^{-1}\text{sec.}^{-1}$

Run No.	$10^2 k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
34	3.43
35	3.34

Mean $10\ k_2^H = 3.01 \pm 0.03\ \text{l.mole.}^{-1}\text{sec.}^{-1}$

Mean $10^2 k_2^D - 3.42 \pm 0.05\ \text{l.mole.}^{-1}\text{sec.}^{-1}$

$$\frac{k_2^H}{k_2^D} = 8.81 \pm 0.21$$

4.10 2-(*m*-bromophenyl)ethyl bromide

Y = H

Run 36

NaOH = 0.01 M, temp = 20°

time (mins.)	D_t
0.0	0.163
0.5	0.282
1.0	0.384
1.5	0.465
2.0	0.530
2.5	0.585
3.0	0.633
3.5	0.670
4.0	0.699
∞	0.875

$10\ k_2^H = 5.85$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10\ k_2^H$ l.mole.$^{-1}$sec.$^{-1}$
37	5.86
38	5.80

Y = D

Run 39

NaOH = 0.01 M, temp = 20°

time (mins.)	D_t
0	0.572
2	0.599
4	0.623
6	0.646
8	0.666
12	0.701
16	0.735
20	0.762
24	0.783
∞	0.920

$10^2 k_2^D = 6.40$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10^2 k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
41	6.30

Mean $10\ k_2^H = 5.84 \pm 0.02$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10^2 k_2^D = 6.35 \pm 0.05$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 9.19 \pm 0.10$$

4.11 2-(*p*-acetylphenyl)ethyl bromide

$Y = H$

Run 64

NaOH = 0.05 M, temp = 20°

time (secs.)	D_t
0.00	0.083
0.25	0.133
0.50	0.175
0.75	0.215
1.00	0.250
1.50	0.315
2.00	0.365
2.50	0.408
3.00	0.443
3.50	0.472
∞	0.625

$k_2^H = 7.22$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	k_2^H l.mole.$^{-1}$sec.$^{-1}$
65	7.63

$Y = D$

Run 66

NaOH = 0.05 M, temp = 20°

time (secs.)	D_t
0	0.366
1	0.381
2	0.393
3	0.403
5	0.423
10	0.466
15	0.500
20	0.528
25	0.551
30	0.570
∞	0.663

$10\ k_2^D = 7.64$ l.mole.$^{-1}$sec.$^{-1}$

Run No.	$10\ k_2^D$ l.mole.$^{-1}$sec.$^{-1}$
68	7.62

Mean $k_2^H = 7.43 \pm 0.20$ l.mole.$^{-1}$sec.$^{-1}$

Mean $10\ k_2^D = 7.63 \pm 0.01$ l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 9.74 \pm 0.27$$

4.12 2-(p-nitrophenyl)ethyl bromide

$Y = H$

Run 58

NaOH = 0.05 M, temp = 20°

time (secs.)	D_t
0.0	0.010
0.5	0.095
1.0	0.165
1.5	0.225
2.0	0.275
2.5	0.324
3.0	0.363
3.5	0.400
4.0	0.430
5.0	0.483
∞	0.645

k_2^H = 54.3 l.mole.$^{-1}$sec.$^{-1}$

Run No.	k_2^H l.mole.$^{-1}$sec.$^{-1}$
59	52.4

$Y = D$

Run 61

NaOH = 0.05 M, temp = 20°

time (secs.)	D_t
0.0	0.440
0.5	0.467
1.0	0.492
1.5	0.513
2.0	0.532
2.5	0.547
3.0	0.560
3.5	0.573
4.0	0.583
5.0	0.599
∞	0.645

k_2^D = 6.01 l.mole.$^{-1}$sec.$^{-1}$

Run No.	k_2^D l.mole.$^{-1}$sec.$^{-1}$
63	6.26

Mean k_2^H = 53.3 ± 0.9 l.mole.$^{-1}$sec.$^{-1}$

Mean k_2^D = 6.14 ± 0.12 l.mole.$^{-1}$sec.$^{-1}$

$$\frac{k_2^H}{k_2^D} = 8.68 \pm 0.31$$

4.13 Summary of rate constants

4.13.1 2-phenethyldimethylsulphonium bromides

Z	Y	Temp. °C	$10^3 k_2$ l.mole.$^{-1}$sec.$^{-1}$
p-MeO	H	20	4.96 ± 0.05
p-MeO	H	30	10.6 ± 0.1
p-MeO	H	40	35.4 ± 0.1
H	H	20	32.8 ± 0.3
			$10 k_2$
p-Cl	H	20	2.10 ± 0.04
m-Br	H	20	5.27 ± 0.01
			k_2
p-Ac	H	20	11.9 ± 0.1
p-NO_2	H	20	176.7 ± 1.0
			$10^4 k_2$
p-MeO	D	20	7.26 ± 0.03
p-MeO	D	30	18.7 ± 0.2
p-MeO	D	40	66.1 ± 1.4
H	D	20	44.4 ± 0.1
			$10^2 k_2$
p-Cl	D	20	2.58 ± 0.02
m-Br	D	20	6.29 ± 0.06
p-Ac	D	20	124.2 ± 5.15

4.13.2 2-phenethyl bromides

Z	Y	Temp. °C	$10^2 k_2$ l.mole.$^{-1}$sec.$^{-1}$
p-MeO	H	20	2.92 ± 0.02
p-MeO	H	30	6.59 ± 0.04
p-MeO	H	40	14.3 ± 0.1
H	H	20	8.17 ± 0.10

Z	Y	Temp. °C	10 k_2 l.mole.$^{-1}$sec.$^{-1}$
p-Cl	H	20	3.01 ± 0.03
m-Br	H	20	5.84 ± 0.02
			k_2
p-Ac	H	20	7.43 ± 0.20
p-NO_2	H	20	53.3 ± 0.9
			10^3 k_2
p-MeO	D	20	3.87 ± 0.02
p-MeO	D	30	10.3 ± 0.1
p-MeO	D	40	24.1 ± 0.1
H	D	20	9.56 ± 0.01
			10^2 k_2
p-Cl	D	20	3.42 ± 0.05
m-Br	D	20	6.35 ± 0.05
			10 k_2
p-Ac	D	20	7.63 ± 0.01
p-NO_2	D	20	61.4 ± 1.2

4.14 Summary of kinetic isotope effects

4.14.1 2-phenethyldimethylsulphonium bromides

Z	Temp. °C	k_2^H/k_2^D
p-MeO	20	6.83 ± 0.10
p-MeO	30	5.64 ± 0.11
p-MeO	40	5.30 ± 0.12
H	20	7.39 ± 0.09
p-Cl	20	8.14 ± 0.22
m-Br	20	8.38 ± 0.10
p-Ac	20	9.60 ± 0.48

4.14.2 2-phenethyl bromides

Z	Temp. °C	k_2^H/k_2^D
p-MeO	20	7.55 ± 0.09
p-MeO	30	6.40 ± 0.09
p-MeO	40	5.93 ± 0.07
H	20	8.54 ± 0.19
p-Cl	20	8.81 ± 0.21
m-Br	20	9.19 ± 0.10
p-Ac	20	9.74 ± 0.27
p-NO_2	20	8.68 ± 0.31

5 DISCUSSION

5.1 Accuracy of results

The derived second order rate constants were reproducible to within ±2%. However, although it appeared to be sufficient to use the readings obtained for the first two half-lives when calculating the rate constants for non-deuterated substrates, it was found that the readings for the second and third half-lives were required in the case of the deuterated substrates to maintain good reproducibility. This was because the deuterated substrates all contained some non-deuterated material which contributed to the initial spectrophotometric changes observed. To enable reliable rate constants for the deuterated compounds to be calculated the absorbance or transmittance values were only recorded after the equivalent of 8 half-lives for the non-deuterated substrate (ca. one half-life for the deuterated reaction). This time interval ensures that all the non-deuterated material has disappeared. Reproducibility of k_H/k_D values was adversely affected if less than the above time interval was allowed, especially in cases where the degree of deuteration was less than 1.9 atoms D per molecule.

Although it was found that the second order rate constants could be reproduced over at least a 10-fold base concentration range, wherever possible the same base concentration was used for both the non-deuterated and deuterated kinetic runs for each substrate to minimize errors in the k_H/k_D ratio.

It was found, when the aforementioned precautions were taken, that the k_H/k_D ratios were reproducible to better than ±3%.

5.2 The Hammett Plot

It was found that for Z = p-MeO the Hammett σ gave a better correlation than the σ^0 value in the case of both X = Br and X = SMe_2^+, hence the regression line was calculated using rather than σ^0 values for all substituents. Both Hammett plots were set up using the log k_2^H values for Z = p-MeO, H, p-Cl and m-Br at 20°. The Hammett plot for X = Br is shown in Fig.4, and for X = $\overset{+}{S}Me_2$ in Fig.5. The σ values for each substituent, along with the corresponding log k_2^H values for both the leaving groups, are shown in Table I.

Table I

Z	σ	log k_2^H (X = Br)	log k_2^H (X = $\overset{+}{S}Me_2$)
p-MeO	−0.268	−1.535	−2.304
H	0.000	−1.088	−1.484
p-Cl	+0.226	−0.521	−0.678
m-Br	+0.391	−0.234	−0.278
p-Ac	+0.516	+0.871	+1.076
p-NO_2	+0.778	+1.727	+2.248

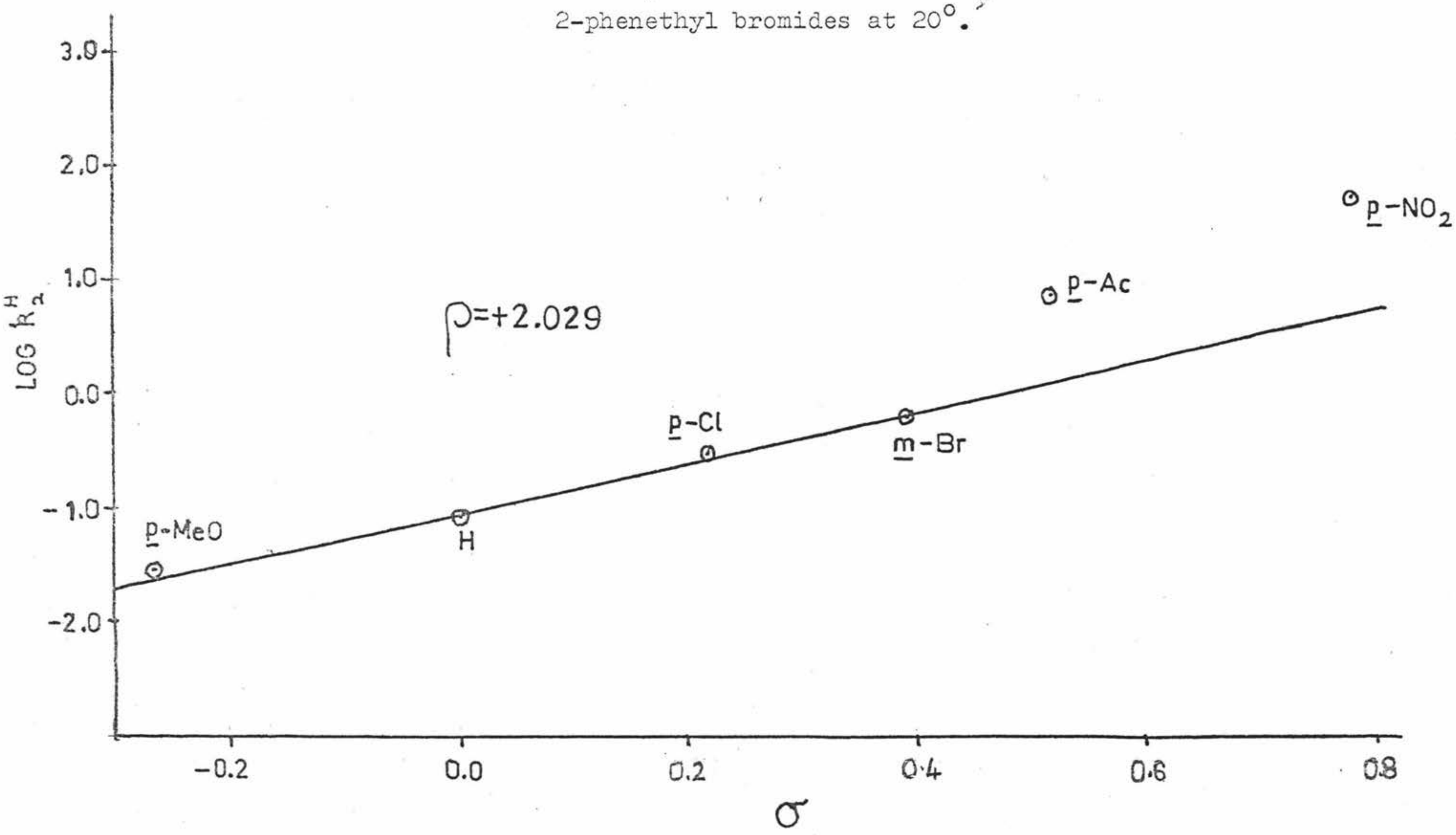
For X = Br the calculated ρ value was 2.029 ± 0.012 with a correlation coefficient (r) of 0.998, whereas for X = $\overset{+}{S}Me_2$ the ρ value was 3.126 ± 0.037 and r was 0.996. In the case of both X = Br and X = $\overset{+}{S}Me_2$ the points for Z = p-Ac and Z = p-NO_2 lie above the regression line and give derived σ values of +0.965 and +1.386 respectively for X = Br and +0.817 and +1.192 for X = $\overset{+}{S}Me_2$. These enhanced σ values are close to the σ^- values for each substituent.

5.3 Discussion of Hammett results

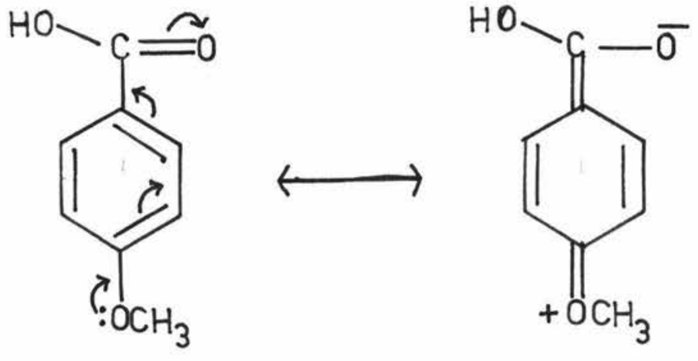
The ρ values observed for X = Br and X = $\overset{+}{S}Me_2$ are both fairly large and positive. These values indicate the development of negative charge at the β-carbon atom in the transition state for the E2 elimination reaction. Thus, there must be a greater degree of C–H than C–X bond breaking in the transition state for both leaving groups. Both transition states can be considered to have a considerable degree of carbonionic character. The exalted σ values for Z = p-Ac and Z = p-NO_2 are consistent with the development of a large degree of negative charge in these transition states. The observation that the Hammett σ value rather than the σ^0 value for Z = p-MeO gives a better correlation could be an indication of significant double bond character in these two transition states.

Figure 4.

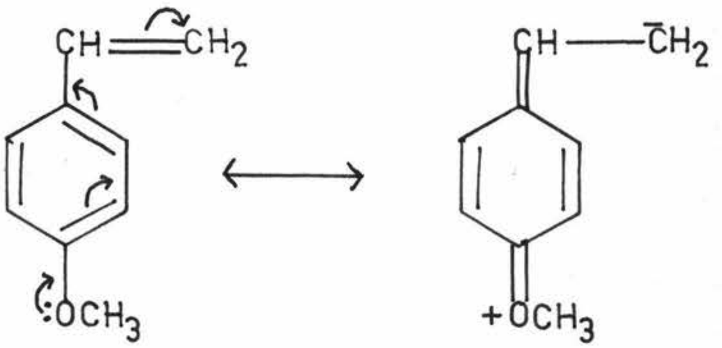
Hammett plot for elimination from 2-phenethyl bromides at 20°.



The Hammett σ allows for conjugation with a double bond and by implication the transition state for Z = p-MeO would involve a similar interation. This is shown as follows,



p-MeO benzoic acid

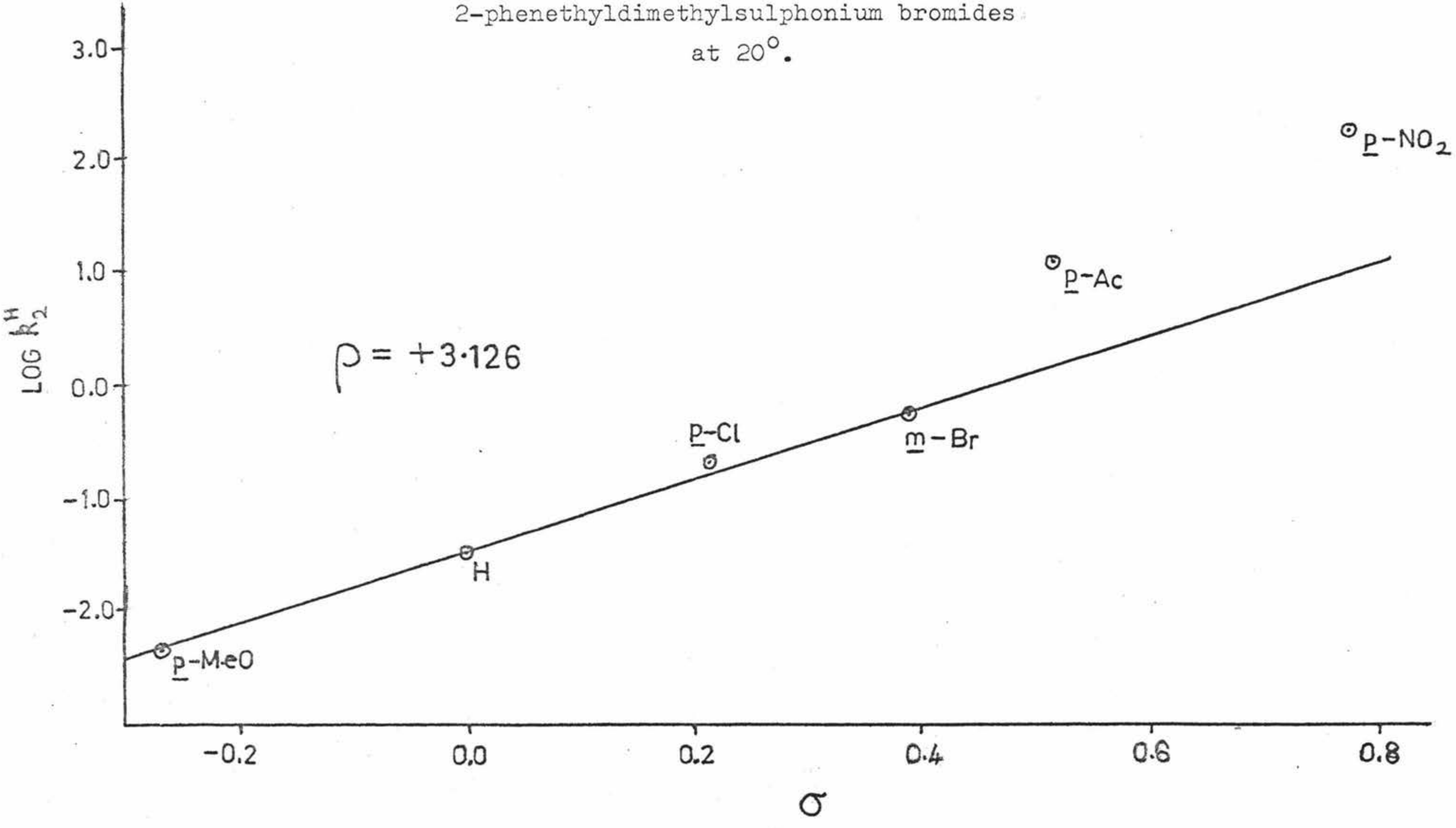


p-MeO styrene

An inspection of the k_2^H values (p.49) for the unsubstituted compound in the case of both X = Br and X = $\overset{+}{S}Me_2$ shows that the rate of elimination for the bromide is faster than for the dimethylsulphonium bromide. Therefore, X = Br is a better leaving group in this solvent-base system than X = $\overset{+}{S}Me_2$. The lower ρ value for X = Br indicates that this transition state has a lower C-H/C-X bond breaking ratio than for the poorer leaving group (X = $\overset{+}{S}Me_2$), that is, it is less carbanionic. These results are similar to those obtained in related 2-phenethyl systems. For the elimination from 2-arylethyl compounds with sodium ethoxide in ethanol[16] it has been shown that as the leaving group becomes progressively poorer (as indicated by the relative reaction rates for the unsubstituted compounds) the ρ value becomes increasingly positive. Cockerill[32] also has shown for the elimination from substituted 2-phenethyl arenesulphonates in t- butoxide - t-butanol that the ρ value for each leaving group, determined

Figure 5.

Hammett Plot for elimination from
2-phenethyldimethylsulphonium bromides
at 20°.



by changing the substituent in the phenethyl benzene ring, became increasingly positive as the leaving group became poorer.

5.4 The kinetic isotope effects

The primary isotope effect values observed are summarized on page 50 and are listed in order of increasing electron-withdrawing power of the 2-phenyl substituents. All of the k_H/k_D ratios observed at 20° for both the 2-phenethyl bromides and the 2-phenethyldimethylsulphonium bromides are high compared to those expected from theoretical[10] considerations. The k_H/k_D values have not been corrected for any secondary isotope effect arising from the presence of the second deuterium atom, but experimental evidence[30] appears to suggest that this effect would be very small.

Another possible reason for the high k_H/k_D values could be proton tunnelling. The Arrhenius parameters for 2-(p-methoxyphenyl)ethyl bromide and 2-(p-methoxyphenyl)ethyldimethylsulphonium bromide were calculated (see Table II) in order to determine whether proton tunnelling was an important factor.

Table II

X	Z	$(E_a^D - E_a^H)$ kJ. mol^{-1}	A_H/A_D
Br	p-MeO	9.5 ± 0.4	0.15
$\overset{+}{S}Me_2$	p-MeO	9.7 ± 0.6	0.13

The k_H/k_D ratios for the above substrates at 20°, 30° and 40° were used in the Arrhenius plots. The slope of the best straight line which could be drawn through the three points of the log k_H/k_D versus I/T plot was used to determine the $(E_a^D - E_a^H)$ value from the relation,

$$\text{slope} = (E_a^D - E_a^H)/2.303\ R$$

and the intercept was used to determine the A_H/A_D ratio from the expression,

$$\text{intercept} = \log A_H/A_D$$

Both the $(E_a^D - E_a^H)$ values are significantly greater than the theoretical[15] maximum value of 5.1 to 5.5 kJ. mol^{-1}, indicating that proton tunnelling is probably important in these reactions. The A_H/A_D ratio in both cases is considerably less than the classical limit of unity, and also significantly less than the possible extreme theoretical limit of 0.5[33]. This observation provides further evidence for the existence of proton tunnelling for Z = p-MeO. It is assumed that a similar situation exists for the other substrates.

5.5 Discussion of isotope effects

5.5.1 Substituent effects

A similar trend is observed in the k_H/k_D ratios as the β-aryl substituents become more electron-withdrawing for both the leaving groups studied (p 50). The values tend to be lower for the dimethylsulphonium salts compared to the corresponding bromides. There appears to be a rise in k_H/k_D values from Z = p-MeO to Z = p-Ac for both X = Br and X = $\overset{+}{S}Me_2$. In the case of X = Br there is a slight, but significant, drop in k_H/k_D from Z = p-Ac to Z = p-NO_2. No kinetic isotope effect value was obtained for Z = p-NO_2 in the case of X = $\overset{+}{S}Me_2$ for the reasons outlined in the experimental section. Thus, in the case of the 2-phenethyl bromides at least, a maximum in the k_H/k_D ratio appears to occur as the β-aryl substituent becomes more electron-withdrawing, providing the high value for p-Ac can be regarded as reliable. However, there is no reason to doubt this value. The electron-withdrawing power of the β-aryl substituent should be proportional to the Δ pK parameter of Bell[11,17]. If this is the case then a fairly large change in transition state symmetry would be expected as Z is changed from p-MeO to p-NO_2. Hence the maximum observed for X = Br appears to be a broad one as the change in the k_H/k_D ratio along the series is not very great. The significance of the changes in the k_H/k_D ratio caused by a systematic change in the substituents and the meaning to be attached to the observed maximum is however far from obvious.

5.5.2 Interpretation of the substituent effects

If we assume that the isotope effect does give an indication of proton position in the transition state, then a picture of the transition state can be built up based purely on the experimental evidence, and compared with current theories of the effect of substituent changes on transition state structure. There have been no data reported in the literature regarding the effect of substituents on the k_H/k_D ratio for the elimination from 2-phenethyldimethylsulphonium bromides. However, Thornton[24] has measured the secondary isotope effects, as expressed by the k_{DO^-}/k_{HO^-} ratio, for the elimination from 2-phenethyltrimethylammonium ions in water. The theoretical values[24] for this isotope effect are 1.88 for complete proton transfer to the base in the transition state and 1.37 if the proton is half-transferred. Values lower than 1.37 indicate that the proton is less than half-transferred in the transition state.

For the unsubstituted compound a value of 1.79 is reported, indicating more than 50% transfer of the β-proton to the base. However, a smaller value of 1.73 was observed for Z = p-Cl, indicating that the proton was not as extensively transferred to the base for the more electron-withdrawing substituent. The nitrogen isotope effect (for elimination in ethanol-ethoxide solutions) in the case of Z = p-Cl[34] is less than for the unsubstituted compound, indicating that there is less C-N bond rupture as the substituent becomes more electron-withdrawing. Thus, it appears that both C-H and C-X bond rupture decreases as the substituent becomes more electron-withdrawing, suggesting movement towards a more reactant-like transition state. Some unpublished results[35] concerning the effect of substituents on the primary kinetic isotope effect for this elimination show that along the series Z = p-MeO, H, p-Cl and p-CF_3 the k_H/k_D ratios are 2.64, 3.23, 3.48 and 4.15 respectively. (These eliminations were carried out in ethanol-ethoxide at 40°). Since the secondary isotope effects[24] are greater than 1.37, the increase in the k_H/k_D ratio observed along the above series must indicate decreasing C-H bond rupture as the substituents become more electron-withdrawing.

If the principle that the proton is less transferred for the more electron-withdrawing substituents can be applied to the elimination from 2-phenethyldimethylsulphonium bromides and 2-phenethyl bromides in 50.2% DMSO, as seems reasonable, then the observed trend in the primary k_H/k_D ratios for these substrates must indicate transition states in which the proton is more than half-transferred and which becomes more reactant-like as the substituents change from Z = p-MeO to Z = p-Ac. However, the k_H/k_D ratio observed for Z = p-NO_2 and X = Br is lower than for Z = p-Ac, although the p-NO_2 substituent is more electron-withdrawing. An explanation for this result could be that the proton is now closer to the β-carbon than to the base (i.e. less than half-transferred) and so the k_H/k_D ratio begins to decrease. However, Bronsted correlations using substituted phenoxide bases in ethanol for 2-phenethyl bromides[36] show that $\beta = 0.54$ when Z=H and $\beta = 0.67$ when Z = p-NO_2, indicating that the proton is in fact closer to the base for the p-NO_2 compound than for the unsubstituted compound. Therefore, the decrease in the k_H/k_D ratio observed when Z is changed from p-Ac to p-NO_2 seems to be caused by the proton now being closer to the base for Z = p-NO_2 so that C-H bond breaking has increased rather than continued to decrease.

5.6 Nature of the E2 transition state

Thus, the experimental results for X = Br indicate that the transition state for the p-methoxy compound involves considerable proton transfer to the base. It is carbanionic, as indicated by the positive ρ value, and it also has a significant amount of double bond character, as indicated by the need for the exalted Hammett σ constant for this substituent. As the substituents become more electron-withdrawing up to Z = p-Ac the extent of proton transfer in the transition state decreases, probably along with a decrease in C-Br bond rupture. Thus, there is uncertainty as to whether there is a change in carbanionic character of the transition state for these substituents as it is not known whether the decrease in C-H bond breaking is greater or less than that for the C-Br bond. However, for Z = p-NO_2 the proton now becomes more transferred to the base again, hence C-H bond breaking is increased. It would be expected[32] that theC-Br bond breaking would continue to decrease, giving an increase in the C-H/C-X bond breaking ratio and hence an increase in carbanion character for the p-NO_2 compound. The changes in transition state structure described for the X = Br series from Z = p-MeO to Z = p-Ac should also apply to the X = $\overset{+}{S}Me_2$ series. Although it was not possible to measure k_H/k_D for the p-NO_2 substituent in the case of X = $\overset{+}{S}Me_2$ it is assumed that the result would be similar to that observed for X = Br.

If the above conclusions are accepted then the observed maximum results from complex transition state behaviour as the substituents are varied, rather than from the proton passing through a half-transferred position.

5.7 Comparison of the results with theoretical predictions

The picture of the E2 transition state which has been formed using the experimental observations appears to be consistent with the More O'Ferrall theoretical treatment[5]. The positive ρ values observed for the 2-phenethyl bromides and the 2-phenethyldimethylsulphonium bromides in 50.2% DMSO indicate a carbanionic transition state (i.e. C-H bond breaking is more advanced than C-X bond breaking). Thus, the E2 transition states will lie somewhere to the right of the diagonal line (which represents equal C-H and C-X bond rupture) on the modified More O'Ferrall diagram (Fig.1). The experimental evidence obtained also suggests that the transition states lie to the right of a vertical line through the centre of the diagram which would represent a half-broken C-H bond. This is because the proton appears to be more than half-transferred in all transition states. It is predicted[4] that an increase in the electron-withdrawing power of substituents on the β-carbon will produce a more reactant-like transition state, resulting in a decrease in both C-H and C-X bond breaking. However, according to Bunnett[3] electron-withdrawing substituents will also stabilize any carbanionic character in the transition state. The More O'Ferrall approach predicts that this latter effect will act across rather than along the reaction coordinate and tend to pull the transition state towards greater carbanionic character. If this 'perpendicular' effect was considered alone then an increase in C-H bond length would be predicted along the series for X = Br from Z = p-MeO to Z = p-NO_2, along with a decrease in C-Br bond length. However, if the effects along the reaction coordinate (i.e. 'parallel') are considered in conjunction with the 'perpendicular' effects then it can be seen that they reinforce each other with regard to C-X bond length, but work in opposition when the C-H bond is considered. It appears from the experimental results, for both X = Br and X = $\overset{+}{S}Me_2$, that the 'parallel' effect which tends to make the transition state more reactant-like by stabilizing the product (and hence decreasing the C-H bond length) overrides the 'perpendicular' effect from Z = p-Meo to Z = p-Ac, giving a net decrease in C-H bond breaking. However, the extreme electron-withdrawing nature of the p-NO_2 substituent could be expected to stabilize the carbanionic nature of the transition state to a greater degree than it stabilizes the product, resulting in a net increase, rather than a decrease, in C-H bond rupture. This would explain the decrease in k_H/k_D ratio observed for X = Br when the Z substituent is changed from p-Ac to p-NO_2 and is also consistent with the increase in the Bronsted coefficient (β) for the p-NO_2 substituent. On this basis, a similar result would be expected for the $\overset{+}{S}Me_2$ leaving group. It should be noted that the principle that the proton is least transferred to the base for the most electron-withdrawing substituents only applies to situations in which the 'parallel' effect is most important.

A change to a poorer leaving group is predicted to make the transition state more product-like by stabilizing the reactants, and also to make it more carbanionic by tending to stabilize a potential carbanion intermediate. The 'parallel' effect should increase both C-H and C-X bond breaking, whereas the 'perpendicular' effect should increase C-H bond breaking but decrease C-X bond breaking. The overall effect on the transition state should be to increase C-H bond breaking but to tend to cancel any change in C-X bond rupture, giving a net increase in the C-H/C-X bond breaking ratio. This prediction is in accordance with the larger ρ value recorded for the X = $\overset{+}{S}Me_2$ reaction series compared to the X = Br series, which indicates increased carbanionic character for the sulphonium salt transition state. It is also consistent with the decrease in k_H/k_D ratio in going from X = Br to X = $\overset{+}{S}Me_2$ (8.54 to 7.39) for the unsubstituted substrate. The prediction that there will probably be little change in C -X bond rupture as the leaving group becomes poorer is supported by the sulphur[37] and nitrogen[36] isotope effects for X = $\overset{+}{S}Me_2$ and X = $\overset{+}{N}Me_3$ respectively.

Thus, there seems to be a reasonable degree of consistency between the experimental observations, their empirical interpretation, and the theoretical predictions for the elimination from 2-phenethyl systems. The assumption that the primary kinetic isotope effect is an indicator of proton position in the transition state therefore seems to have some validity. However, the interpretation of the results is complicated by the existence of little understood factors such as proton tunnelling and coupling of atomic motions in multicentre reactions. These factors help to determine the size of the isotope effect but may be unrelated to the position of the proton in the transition state. Some of the difficulties which need to be resolved are discussed in the next section.

5.8 Criticism of kinetic isotope effects

The theoretical maximum primary kinetic isotope effect which can be observed according to the simple 3-centre model of Westheimer[8] is approximately 7.0. However, as has been noted, there have been many values higher than this maximum reported in the literature. The multi-centre model of Katz and Saunders[10] predicts that the isotope effects observed will be lower than those of the 3-centre model, but a maximum is still predicted to occur when the proton is half-transferred to the base. This multi-centre model takes into account the coupling of the proton transfer motion with other atomic vibrations in the transition state, and is based on the reaction of hydroxide ion with the ethyldimethylsulphonium ion. Thus, it is structurally related to the transition states which would occur for the 2-phenethyldimethylsulphonium bromides. An important point which arises from the above model is the possibility that the size of the k_H/k_D ratio for a given extent of proton transfer can vary as the E2 transition state varies from E1-like to E1cb-like. The possibility that the degree of coupling of the C-H motion with other atomic vibrations can also affect the size of the k_H/k_D ratio tends to make one wary of comparing isotope effects obtained from different substrates or even from the same substrate in different solvent-base systems. For example, in the substituent effect studies for substituted 2-phenethyldimethylsulphonium bromides in 50.2% DMSO at 20° the k_H/k_D ratios cover a range from 6.83 to 9.60. However, Cockerill[19] found that the maximum k_H/k_D ratio he could observe in the DMSO-H_2O system for the unsubstituted compound was 6.85 at 30°. Even allowing for the increase in the k_H/k_D ratio when the temperature is decreased to 20°, the maximum for the unsubstituted sulphonium salt is considerably less than the value of 9.60 observed for the p-Ac compound. It is disturbing to find that the highest possible isotope effect value which apparently can be observed for one member of a reaction series (and is taken as the point where the proton is about half-transferred) is less than some of the k_H/k_D values observed for other members of the same series. This appears to be inconsistent with the assumption that the same maximum value should be observed when the proton is half-transferred for all members of a particular reaction series, even if the maximum can vary between different reaction series.

As has been noted, proton tunnelling appears to be present in the system studied. This increases the difficulty of interpreting the kinetic isotope effect values in terms of transition state structure. There appear to be differences of opinion as to the effect proton tunnelling has on the shape of the maximum in the isotope effect. Bell et al[14] have even claimed that the isotope effects are primarily determined by the tunnel correction. He has proposed an electrostatic model which predicts a maximum in the isotope effect along a reaction series although the position of the proton may remain unchanged.

Finally, the application of kinetic isotope effects to the determination of transition state structure in E2 reactions is hindered by the fact that the theoretical predictions of the shape of the maximum differ, even in the absence of the tunnelling correction. Willi et al[38] predicted that the maximum can range from being relatively sharp to being very broad, the latter case giving rise to high k_H/k_D values even when the C-H bond is considerably less than or greater than 50% broken. More O'Ferrall et al[9] have stated that the maximum is more likely to be sharp rather than broad, although it is recognised that the shape cannot be conclusively determined from their multi-centre model. Therefore, the interpretation of the effect of different substituents on the k_H/k_D ratio is subject to considerable reservation, because if the maximum in the kinetic isotope effect is broad, as is the case in this study, then relatively small changes in k_H/k_D ratio could indicate quite large changes in proton position. However, the opposite will be the case if the maximum is fairly sharp.

5.9 Conclusion

The results obtained in this study tend to suggest that if the substituents are varied systematically along a reaction series then a systematic variation in the primary kinetic isotope effect can be observed for E2 reactions. This could be an indication that the symmetry of the transition state is changing owing to the substituent effects, but such an interpretation cannot be accepted without reservation because of the presence of conflicting opinions regarding the meaning of the kinetic isotope effect. Further doubt arises from there being no common agreement on how changes in the structure of the reactants, solvent, or reaction conditions in E2 reactions will alter the character of the transition state. Therefore, it becomes a case of attempting to resolve one uncertainty with another. Work in this field has tended to be disjointed with no apparent attempt to completely resolve a given system. This has given rise to much speculation using incomplete data. In this respect, the system used in this study appears to hold promise as an ideal system with which to obtain a considerable amount of information about the relationship between isotope effects and transition state structure for E2 reactions. The substituent effect can be studied as in this thesis, while the base strength can be dramatically changed by altering the DMSO content of the solvent to study the effect of the base. The effect of a range of different leaving groups can be observed subject to their solubility in the DMSO-water system. A study of substituent effects on the elimination from 2-phenethyltrimethylammonium salts in this system could prove interesting. The trimethylammonium ion is a much poorer leaving group than either the bromide or dimethylsulphonium ion leaving groups and so the transition state would be expected to be considerably more carbanionic, as indicated by the large positive ρ value[16]. If the substituent effect on the k_H/k_D ratio was studied for a given leaving group at different DMSO percentages then a great deal of information may be obtained about the effect of changes in transition state structure on the k_H/k_D ratio.

It is felt that until a fairly exhaustive study on a particular system similar to that suggested above is carried out then no definite conclusions can be made. It appears that a considerable amount of coordinated data has yet to be accumulated before the present speculation in this area can be given more substance.

REFERENCES

1. Hanhart, W., and Ingold, C.K., J.Chem.Soc., 997 (1927).
2. Cram, D.J., Greene, F.D., and De Puy, C.H., J.Amer.Chem. Soc., 78, 790 (1956).
3. Bunnett, J.F., Angew. Chem., 74, 731 (1962).
4. Thornton, E.R., J.Amer.Chem.Soc., 89, 2915 (1967).
5. More O'Ferrall, R.A., J.Chem.Soc. (B), 274 (1970).
6. Fry, A.,
7. Bigeleisen, J., J.Chem.Phys., 17, 675 (1949).
8. Westheimer, F.H., Chem.Rev., 61, 265 (1961).
9. More O'Ferrall, R.A., and Kouba, J., J.Chem.Soc. (B), 985, (1967).
10. Katz, A.M., and Saunders, W.H. jnr. J.Amer.Chem.Soc., 91, 4469 (1969).
11. Bell, R.P., and Goodall, D.M., Proc.Roy.Soc.,A, 294, 273 (1966).
12. Bell, R.P., and Cox, B.G., J.Chem.Soc. (B), 783 (1971).
13. Bordwell, F.G., J.Amer.Chem.Soc., 93, 512 (1971).
14. Bell, R.P., Sachs, W.H., and Tranter, R.L., Trans.Faraday Soc., 66, 1995 (1970).
15. Caldin, E.F., Chem.Rev. 69, 138 (1969).
16. Bunnett, J.F., Surveys Progr.Chem., 5, 53 (1969).
17. Blackwell, L.F., Buckley, P.D., Jolley, K.W., and MacGibbon, A.K.H., J.Chem.Soc., 169 (1973).
18. Cockerill, A.F., Rottschaefer, S., and Saunders, W.H. jnr, J.Amer.Chem.Soc., 89, 901 (1967).
19. Cockerill, A.F., J.Chem.Soc. (B), 964 (1967).
20. Vogel, A.I., 'Elementary Practical Organic Chemistry, Part 1: Small Scale Preparations,' Longmans, London, (1966), p.342.
21. Rupe, H., Annalen, 395, 114 (1912).
22. Saunders, W.H., and Williams, R.A., J.Amer.Chem.Soc., 79, 3714 (1957).
23. Foerst, W., 'Newer Methods of Preparative Organic Chemistry', Vol. IV, Academic Press, New York, p.271.
24. Steffa, L.J., and Thornton, E.R., J.Amer.Chem.Soc., 89, 6149 (1967).
25. Shildneck, P.R., and Windus, W., Org.Syntheses, 14, 54 (1934).

26. Shildneck, P.R., and Windus, W., Org.Syntheses, 12, 52 (1932).
27. Smith, L.I., Org.Syn.Coll. Vol., 2, 248 (1943).
28. Belanger, P., Atkinson, J.G., and Stuart, R.S., Chem.Comm., 1067 (1969).
29. Nystrom, R.F., and Brown., W.G., J.Amer.Chem.Soc., 69, 2548 (1947).
30. Saunders, W.H. jnr., and Edison, D.H., J.Amer.Chem.Soc., 82, 138 (1960).
31. Foreman, E.L., and McElvain, S.M., J.Amer.Chem.Soc., 62, 1435 (1940).
32. Banger, J., Cockerill, A.F., and Davies, G.L.O., J.Chem.Soc. (B), 498 (1971).
33. Bell, R.P., 'The Proton in Chemistry,' Cornell University Press, Ithaca, New York (1959), chapter XI.
34. Bourns, A.N., and Smith, P.J., Proc.Chem.Soc., 366 (1964).
35. Bourns, A.N., and Smith, P.J., Private Communication (1973).
36. Hudson, R.F., and Klopman, G., J.Chem.Soc., 5 (1964).
37. Saunders, W.H. jnr., Cockerill, A.F., Asperger, S., Klasinc, L., and Stefanovic, D., J.Amer.Chem.Soc., 88, 848 (1966).
38. Willi, A.V., and Wolfsberg, M., Chem.Ind. (London), 2097 (1964).