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ISOTOPE EFFECTS IN AROMATIC BROMINATION REACTIONS

KINETIC ISOTOPE EFFECTS IN AROMATIC BROMINATION REACTIONS

by

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SCOPE AND CONTENTS:

Both bromodeprotonation and bromodesulphonation occur during aqueous bromination of sodium p-methoxybenzenesulphonate, A, and potassium 1-methylnaphthalene-4-sulphonate, B. Extensive kinetic studies reported here suggest that bromodesulphonation of A proceeds by a two-step process with Br_2 as the brominating species, but do not completely exclude Br^+ (or H_2OBr^+) acting in either a one- or two-step process. For B, the kinetic data can be interpreted by either a one- or two-step process with Br_2 as the brominating species. Kinetic sulphur isotope effects have been measured for the bromodesulphonation of A and B and found to vary with bromide-ion concentration, thus strongly supporting the two-step process involving molecular bromine. The kinetic results for the bromodeprotonation of A cannot distinguish between a one- and two-step process involving Br_2; the two-step mechanism has been confirmed by the observation of a variation in kinetic hydrogen isotope effect with bromide-ion concentration.

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GENERAL INTRODUCTION

In electrophilic aromatic substitution an atom or group attached to an aromatic ring is replaced by some other atom or group which becomes bound to the ring by an electron pair originating in the aromatic molecule. The displaced entity is usually hydrogen, although reactions in which such groups as -COOH, $-SO_2OH$ and -COR are eliminated are also well known. In recent years there has been a great deal of interest in the mechanism of this important class of reactions and a large number of studies have been directed to the problem of establishing the identity of the actual attacking species in each of the various reaction types and also to the question of elucidating the detailed pathway of the substitution process itself.

Two different reaction pathways have been proposed:

Mechanism I One-Step Process

$$ArH + X_2 + (B) \rightleftharpoons \text{transition state} \longrightarrow ArX + X^- + H^+(B)$$

Mechanism II Two-Step Process

$$ArH + X_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \overset{+}{Ar}\!\!<\!\!\begin{matrix} H \\ X \end{matrix} + X^-$$

$$\overset{+}{Ar}\!\!<\!\!\begin{matrix} H \\ X \end{matrix} + (B) \xrightarrow{k_3} ArX + H^+(B)$$

Here, X_2 is the electrophile, B is the base which may or may not participate in a rate-determining step, and ArH is the aromatic substrate. In

the one-step process the potential-energy curve for reaction system would have a maximum corresponding to the single transition state intervening between reactants and products, while in the two-step mechanism this curve would have a small depression, corresponding to the high-energy intermediate $\mathrm{Ar}\langle^{H}_{X}$, and two maxima, one associated with the transition state for the formation of this intermediate and the other with the transition state for its destruction.

Whereas ordinary kinetic studies have frequently provided valuable information on the nature of the electrophilic species involved in a reaction, they have been of limited value in shedding light on the detailed mechanism of the substitution process itself. One of the most fruitful approaches to the solution of this latter problem has been found in the study of kinetic isotope effects. Melander (1,2) in the year 1950, and later others (3,4,5), have reported that in aromatic nitration and bromination the rate of substitution is the same whether hydrogen or one of its isotopes is displaced from the aromatic nucleus. These zero isotope effects were interpreted in terms of the two-step process with the rate-determining step being the formation of an intermediate in which the bond to the isotopic hydrogen is still intact. The subsequent observation of a small isotope effect in aromatic sulphonation (6,7,8) was taken to mean that in this reaction the overall rate is determined in part by the step involving rupture of the carbon-hydrogen bond.

In the year 1955, Hammond (9) in an important paper, argued that the observation of a zero or very small isotope effect means only that the carbon-hydrogen bond is not significantly weakened in the transition state of the rate-determining step and that such a result can also be

interpreted in terms of a single-step process. In other words, as de la Mare and Ridd (10) have expressed it, a zero isotope effect does not require that the complex $Ar\overset{H}{\underset{X}{<}}$ be a normal chemical species; it may be only an unstable configuration along the reaction path. There is, however, one way in which kinetic isotope effects may provide unambiguous support for the two-step mechanism: this is by the demonstration of a variation in the magnitude of the isotope effect with a change in the concentration of X^-, if such a species is formed in the reaction, or of B, if the reaction shows base catalysis. Changes in the concentration of either of these species would be expected to influence the relative rates of return of an intermediate to reactant and of decomposition to product and hence would affect the extent to which the latter step (in which there is carbon-hydrogen bond rupture) contributes to the overall reaction rate. Only two successful applications of this criterion have been reported to date.

Zollinger (11) in 1955 observed a variation in hydrogen isotope effect with change in concentration of base in the coupling reaction of p-chlorodiazobenzene with 2-naphthol-6,8-disulphonic acid. This important result provided the first unambiguous evidence for the formation of a meta-stable intermediate in an electrophilic aromatic substitution process. Shortly after, Grovenstein and Ropp (12) were able to demonstrate the operation of the two-step mechanism in the bromodecarboxylation of 3,5-dibromo-4-hydroxybenzoic acid by their observation that the magnitude of the carbon isotope effect in the reaction can be varied by changing the bromide-ion concentration.

All attempts to achieve a variation in the magnitude of the hydrogen isotope effect in ordinary halogenation reactions by varying the concentration of halide ion have been unsuccessful. Grimison and Ridd (13) observed a normal isotope effect, unaffected by changes in halide-ion concentration, in the iodination of glyoxaline by molecular iodine, while a similar result has been obtained by Berliner (14) in the iodination of anisole with iodine monochloride. These results can be accommodated by either a one- or two-step mechanism with hypoiodous acidium ion as the iodinating species or by a two-step mechanism in which molecular halogen (I_2 or ICl) acts as the electrophile. Finally, Berliner and Schueller (15) have observed a small isotope effect, invariant with bromide-ion concentration, in the bromination of diphenyl.

A halogenation reaction in which the two-step mechanism would appear to have been established is the bromodesulphonation of aromatic sulphonates in aqueous medium.

$$ArSO_2O^- + Br_2 \longrightarrow ArBr + Br^- + SO_3$$

Cannell (16) obtained spectroscopic as well as kinetic evidence for the rapid formation of a relatively stable quinoid intermediate in the bromination of sodium 3,5-dibromo-4-hydroxybenzenesulphonate. With less reactive substrates (17), sodium p-methoxybenzenesulphonate, sodium 3,5-dibromo-4-aminobenzenesulphonate and the disodium salt of 3,5-dinitro-4-hydroxybenzenesulphonic acid, the suppression of reaction rate by bromide ion was interpreted in terms of the two-step mechanism with molecular bromine as the electrophile, although, as will be demonstrated by the work to be reported in this thesis, the kinetic results

may also be accommodated by a one- or two-step process in which hypobromous-acidium ion is the halogenating species. Finally, with the least reactive compound studied, potassium 1-methylnaphthalene-4-sulphonate, Cannell found no depression of rate by bromide ion, a result which can be accommodated by either a one- or a two-step mechanism with molecular bromine as the brominating agent.

The first part of the work to be reported in this thesis has been devoted to a study of kinetic sulphur isotope effects in the bromodesulphonation reaction. The reactants chosen for this investigation were sodium p-methoxybenzenesulphonate, for which ordinary rate studies leave an ambiguity with respect to both the nature of the electrophile and the reaction pathway, and potassium 1-methylnaphthalene-4-sulphonate, for which the lack of rate depression by bromide ion allows no distinction between the one- and two-step processes. The approach has been to reinvestigate the kinetics of the two reactions and then to measure the $S^{32}:S^{34}$ isotope effect at various concentration of bromide ion.

In preliminary rate studies on sodium p-methoxybenzenesulphonate it was found that the bromodesulphonation reaction is accompanied by a competing process of bromodeprotonation in which a hydrogen ortho to the methoxy group is replaced by bromine. This reaction, which Cannell had apparently completely overlooked, becomes increasingly important at the higher bromide-ion concentrations. (At 0.1 M bromide-ion concentration it constitutes about 50 per cent of the total bromination process.) By determining sulphate yields as well as total reaction rates it was found possible to obtain accurate rate constants for each of the two competing processes. Since the reaction is carried out in water in which the

substrate is soluble, even at the very high bromide-ion concentrations, the bromination of sodium p-methoxybenzenesulphonate appeared to be an exceptionally suitable system for attempting to obtain unambiguous evidence in support of the two-step mechanism for ordinary bromination. The second part of the work reported in this thesis has been devoted to a study of the kinetic hydrogen isotope effect in this reaction at different bromide-ion concentrations.

HISTORICAL INTRODUCTION

A - Isotope Effects

Discovery, Theory and Application

Following the discovery of isotopes (18), there was considerable speculation concerning the possibility that isotopic species might possess differences in chemical reactivity. With the discovery of deuterium (19) in 1932 and of the heavy isotopes of carbon (20), nitrogen (21), and oxygen (22) in the period 1928-1930, it became possible to investigate systems possessing a large percentage mass difference. Urey and Rittenberg (23) in 1933, using the methods of statistical mechanics, calculated from spectroscopic data the equilibrium constants for a number of isotopic exchange reactions involving hydrogen and deuterium, for example,

$$H_2 + D_2 \rightleftharpoons 2HD$$

The calculated equilibrium constant for this reaction at 25°C is 3.28, which differs markedly from the value 4 expected on the basis of purely statistical considerations and is in perfect agreement with the value 3.28 obtained experimentally (24). Close agreement between calculated and experimental constants has been found for other reactions involving hydrogen and deuterium (25,26).

Theoretical calculations were later extended to exchange reactions involving the isotopes of other light elements, such as lithium, carbon,

oxygen, and nitrogen, and gave isotopic exchange constants differing slightly from the statistical values (27). For example, in the system

$$1/2\ CO_2^{16} + H_2O^{18} \rightleftharpoons 1/2\ CO_2^{18} + H_2O^{16}$$

calculation predicts an equilibrium constant of 1.044 at 0°C, whereas if there were no isotopic fractionation between the two chemical species this constant would be unity. The experimental value for the reaction at 0°C was later found to be 1.046 (28). Similar agreement has been obtained for a variety of other exchange reactions and can be seen in a tabulation of calculated and experimental isotopic exchange constants appearing in an important review by Urey (26).

Since an exchange process involves two opposing unidirectional reactions, the discovery of exchange isotope effects showed that isotopic molecules may react at different rates. Isotope effects arising from a difference in reaction rates of isotopic species are referred to as kinetic isotope effects and were observed for reactions involving the hydrogen isotopes shortly after the discovery of deuterium. For example, the early investigation by Reitz (29) using heavy water and deuteroacetone shed light on the detailed mechanism of the enolisation of acetone while the observation of Westheimer and Nicolaides (30) that 2-deuteropropanol-2 is oxidised about one-sixth as fast as ordinary isopropyl alcohol aided in the elucidation of the mechanism of chromic acid oxidation of alcohols.

Carbon isotope effects in an unidirectional process were not observed until 1948 when Stevenson and co-workers reported their study on the dissociation of C^{13} labelled propane (31). They found that the probability for dissociation by electron impact in the mass spectrometer

of the C-C bonds of propane-1-C^{13} was decreased by approximately 12 per cent for the C^{12}-C^{13} bond and increased by nearly 7 per cent for the C^{12}-C^{12} bond, as compared with ordinary propane. Also, in the pyrolysis of propane-1-C^{13}, it was found (32) that there was an 8 per cent more frequent rupture of the C^{12}-C^{12} bonds than of C^{12}-C^{13} bonds.

Carbon isotope effects then attracted the interest of many workers. Yankwich and Calvin (33) found that for the molecule $HOOC^{12}$-$C^{12}H_2$-$C^{14}OOH$, there is a 12 per cent more frequent rupture of a C^{12}-C^{12} bond than of a C^{12}-C^{14} bond. This is an intramolecular isotope effect of 12 per cent. Two different groups, Bigeleisen and Friedman (34), and Lindsay, Bourns and Thode (35), carried out a carbon-13 isotope effect study with malonic acid containing the natural abundances of carbon isotopes and, using the mass spectrometer for measurement of the isotopic ratios, observed an intramolecular carbon-13 isotope effect of 2.0 and 2.5 per cent, respectively. These carbon-13 results can be compared with the theoretical value of 2.0 per cent calculated according to the method given by Bigeleisen for carbon-14 (36).

A controversy arose in this early work on carbon isotope effects since the theory predicts that a carbon-14 effect should be very close to twice the carbon-13 value (37). Yankwich et al. (38) re-examined the malonic acid system using malonic acid containing one per cent carbon-14 as well as the one per cent natural abundance of carbon-13 and measuring the isotopic ratios mass spectrometrically. The isotope effects were found to be 5.5 and 2.9 per cent for carbon-14 and carbon-13, respectively. The ratio of these effects is 1.9 which agrees well with the theoretical prediction of 2.0. The discrepancy in the early results can be attributed to impurities in the substrate which caused appreciable errors in

the counting technique. Thus, the malonic acid system serves to point up the likely dangers associated with carbon isotope effect studies using labelled compounds.

Since an isotope effect of considerable magnitude in an unidirectional process will occur only if the rate-determining step involves a significant change in the degree of bonding of the isotopic atom in question, the study of isotopic fractionation has important application in the field of reaction mechanisms. Although such applications have mainly involved the isotopes of hydrogen, the last decade has seen a number of interesting studies using the isotopes of carbon, oxygen, nitrogen and sulphur. For further discussion the reader is referred to reviews by Thode (39), Craig (40), Ropp (41), Silverman (42), Bigeleisen (43), Melander (44), and Bourns (80).

The general theory of isotope effects in unidirectional processes is outlined below.

According to classical statistical mechanics, kinetic energy follows the equipartition law and the distribution of the molecules in space is given by the Boltzmann equation. No isotope effects, therefore, are to be expected in equilibrium processes. Classical theory would allow, however, very small isotope effects in unidirectional reactions of higher order than one, because the collision numbers for molecules are a function of their mass. As has already been indicated, isotope effects of considerable magnitude do occur in both equilibrium and rate processes; hence these effects must be quantum phenomena.

The energy, E, of a molecule may be considered to be the sum of two independent terms, the translational energy, E_{tr}, and the internal

energy, E_{int}. The latter may be further expressed as a sum of electronic energy, E_e, rotational energy, E_r, and vibrational energy, E_v. Thus,

$$E = E_{tr} + E_{int} = E_{tr} + E_e + E_r + E_v$$

According to quantum mechanics all of these are quantized. The source of isotope effects must be one of these energies. The translational energy levels are so closely spaced that they may be considered as continuous and hence classical. The electronic ground states for isotopic molecules are almost identical and in most chemical reactions the electrons are all in their respective ground states. The electronic energy difference, therefore, cannot be considered as a source of isotope effects. Further, except for hydrogen compounds and at very low temperatures, one can consider the rotational energy level distribution to be classical since the product 'kT' is large. Thus, the vibrational energy is the only internal energy to be affected by quantum considerations and it is the source of chemical isotope effects.

A theory of chemical isotope effects in unidirectional processes has been developed by Bigeleisen (45) using only the hypotheses of the absolute rate theory. According to this theory, for reactions in which A_1, B, C, ... react to give P_1, and A_2, B, C, ... give P_2, where A_1 and A_2 are isotopic molecules, one can express the rate constants as follows:

$$k_1 = K_1 \frac{C_1^{\ddagger}}{C_{A_1} C_B \cdots} \left(\frac{kT}{2\pi m_1^{\ddagger}}\right)^{1/2} \frac{1}{\delta_1} \qquad (1)$$

$$k_2 = K_2 \frac{C_2^{\ddagger}}{C_{A_2} C_B \cdots} \left(\frac{kT}{2\pi m_2^{\ddagger}}\right)^{1/2} \frac{1}{\delta_2} \qquad (2)$$

where K_1 and K_2 are transmission coefficients, $\ddagger$ indicates the activated complex, m^* is the effective mass of the activated complex moving along the reaction co-ordinate, and δ is the length of the top of the potential energy barrier along the reaction co-ordinate. Since the electronic structure and hence the forces which hold the atoms together are nearly independent of changes in mass caused by isotopic substitution, the potential-energy surface for isotopic molecules are essentially identical, or at least sufficiently so to allow the assumption that $\delta_2/\delta_1 = 1$. Furthermore, there are theoretical reasons for believing that the transmission coefficients should be independent of isotopic mass. Hence

$$\frac{k_1}{k_2} = \frac{C_{A_2}}{C_{A_1}} \cdot \frac{C_1^{\ddagger}}{C_2^{\ddagger}} \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \qquad (3)$$

The concentrations of the various molecular species in equation 3 may be replaced by the complete partition functions, Q. Thus

$$\frac{k_1}{k_2} = \frac{Q_{A_2}}{Q_{A_1}} \cdot \frac{Q_1^{\ddagger}}{Q_2^{\ddagger}} \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \qquad (4)$$

Bigeleisen and Mayer (45a) have expressed the ratio of the partition functions for isotopic molecules in terms of a function f, which is defined as

$$f = \frac{Q_2}{Q_1} \cdot \prod_i \left(\frac{m_{1i}}{m_{2j}}\right)^{3/2} , \qquad (5)$$

where the m_j's refer to the masses of the isotopic atoms in the isotopic molecules. Using this new "partition function" one can now express the ratio of the rate constants for isotopic molecules by equation 6,

$$\frac{k_1}{k_2} = \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \cdot \frac{f}{f^\ddagger}, \qquad (6)$$

the terms involving the isotopic atomic masses having cancelled. It has been shown (45a) that the quantity f is a function of molecular vibrations only and takes the form

$$f = \frac{s_1}{s_2} \prod_i^{3n-6} \frac{u_i}{u_i + \Delta u_i} \cdot e^{\Delta u_i/2} \cdot \frac{1 - e^{-(u_i + \Delta u_i)}}{1 - e^{-u_i}} \qquad (7)$$

where $u_i = \frac{h\nu_i}{kT}$ (h = Planck's constant, k = Boltzmann constant, T = absolute temperature and ν_i = fundamental vibration frequency) and refers to the heavier isotopic molecule, $u_i + \Delta u_i$ is the corresponding term for the lighter molecule, and the s quantities are symmetry numbers which indicate the number of indistinguishable positions for the isotopic molecules in question. The product in equation 7 is taken over all of the 3n - 6 fundamental vibrational frequencies of the molecule. A similar expression may be written for $f^\ddagger$, only in this case one of the vibrational modes is now imaginary and corresponds to motion along the coordinate of decomposition. Substituting for f and $f^\ddagger$ in equation 6 leads to

$$\frac{k_1}{k_2} = \frac{s_1}{s_2} \cdot \frac{s_2^\ddagger}{s_1^\ddagger} \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \frac{\prod_i^{3n-6} \frac{u_i}{u_i + \Delta u_i} \cdot e^{\Delta u_i/2} \cdot \frac{1 - e^{-(u_i + \Delta u_i)}}{1 - e^{-u_i}}}{\prod_i^{3n'-6} \frac{u_i'}{u_i' + \Delta u_i'} \cdot e^{\Delta u_i'/2} \cdot \frac{1 - e^{-(u_i' + \Delta u_i')}}{1 - e^{-u_i'}}} \qquad (8)$$

Further simplification of equation 8 depends upon whether it is to be applied to light or heavier isotopes as will be shown below.

Light Isotope Simplification Hydrogen and Deuterium

Making $u_i = u_{D_i}$ and $\Delta u_i = u_{H_i} - u_{D_i}$, equation 8 becomes

$$\frac{k^H}{k^D} = \left(\frac{m_D^*}{m_H^*}\right)^{1/2} \left(\frac{s_H/s_H^\ddagger}{s_D/s_D^\ddagger}\right) \frac{\prod_i^{3n-6} \frac{u_{D_i}}{u_{H_i}} \cdot e^{\frac{u_{H_i} - u_{D_i}}{2}} \cdot \frac{1 - e^{-u_{H_i}}}{1 - e^{-u_{D_i}}}}{\prod_i^{3n-6} \frac{u_{D_i}^\ddagger}{u_{H_i}^\ddagger} \cdot e^{\frac{u_{H_i}^\ddagger - u_{D_i}^\ddagger}{2}} \cdot \frac{1 - e^{-u_{H_i}^\ddagger}}{1 - e^{-u_{D_i}^\ddagger}}} \qquad (9)$$

It can be assumed that all fundamental vibrational modes which do not involve important motion of the isotopically substituted hydrogen are the same in the initial and transition states and hence cancel out in the quotient involving the frequency terms. There are left three vibrations in the initial state (one stretching and two bending modes) and two bending modes in the transition state. The vibrational frequencies of most bonds to hydrogen are > 1000 cm^{-1} and therefore, at ordinary temperatures, e^{-u_i} terms for the initial state are very small relative to unity. If there is no change in the two bending frequencies in going from the initial state to the transition state, the terms for these frequencies in the transition state also cancel the corresponding terms in the initial state. Equation 9 then becomes

$$\frac{k^H}{k^D} = \left(\frac{s_H/s_H^\ddagger}{s_D/s_D^\ddagger}\right)\left(\frac{m_D^*}{m_H^*}\right)^{1/2} \cdot \frac{u_{D_i}}{u_{H_i}} \cdot e^{\frac{u_{H_i} - u_{D_i}}{2}} \qquad (10)$$

Now, in equation 10, u_i refers only to the stretching frequency which is lost in going from the initial to the transition state. Since in almost any molecule H - X, $m_H \ll m_X$ it follows that

$$\frac{u_{D_i}}{u_{H_i}} \approx \left(\frac{m_H^*}{m_D^*}\right)^{1/2}$$

Therefore, equation 10 reduces to

$$\frac{k^H}{k^D} = \left(\frac{s_H/s_H^\ddagger}{s_D/s_D^\ddagger}\right) \cdot e^{\frac{u_{H_i} - u_{D_i}}{2}} \qquad (11)$$

If, however, the bending frequencies of the bond being broken approach zero in the transition state a different simplification can be made.

Firstly, $$\lim_{u_i^\ddagger \to 0} \frac{1 - e^{-u_{H_i}^\ddagger}}{1 - e^{-u_{D_i}^\ddagger}} = \frac{u_{H_i}^\ddagger}{u_{D_i}^\ddagger}$$

Secondly, $$\lim_{u_i^\ddagger \to 0} e^{\frac{u_{H_i}^\ddagger - u_{D_i}^\ddagger}{2}} = 1$$

Equation 9, now becomes,

$$\frac{k^H}{k^D} = \left(\frac{s_H/s_H^\ddagger}{s_D/s_D^\ddagger}\right)\left(\frac{m_D^*}{m_H^*}\right)^{1/2} \prod_i^3 \frac{u_{D_i}}{u_{H_i}} \cdot e^{\frac{u_{H_i} - u_{D_i}}{2}} \qquad (12)$$

The product $\prod_i^3 \frac{u_{D_i}}{u_{H_i}}$ is made up of 3 terms. Out of these, namely that corresponding to a stretching motion, cancels $\left(\frac{m_D}{m_H}\right)^{1/2}$, while the two bending frequency ratios together give m_H/m_D. Also, it can be shown by resolution into series that the product

$$\prod_i^3 e^{\frac{u_{H_i} - u_{D_i}}{2}}$$

can be written as a sum

$$\sum_i^3 e^{\frac{u_{H_i} - u_{D_i}}{2}} .$$

Hence equation 12 becomes

$$\frac{k^H}{k^D} = \left(\frac{s_H/s_H^\ddagger}{s_D/s_D^\ddagger}\right) \cdot \frac{m_H}{m_D} \cdot \sum_i^3 e^{\frac{u_{H_i} - u_{D_i}}{2}} \qquad (13)$$

In equations 11 and 13 the frequencies of the deuterated compound, if unknown, can be calculated from the corresponding frequencies in the lighter molecule making use of the relationship,

$$\frac{u_{H_i}}{u_{D_i}} = \frac{\nu_H}{\nu_D} = \left(\frac{m_D}{m_H}\right)^{1/2} \qquad (14)$$

Equation 11 predicts $k^H/k^D \backsim 7$ at room temperature for C - H bond rupture and many C - H isotope effects are close to this figure (46). Equation 13 predicts $k^H/k^D > 7$ and higher values are indeed observed in many reactions.

There is a further factor, namely quantum mechanical tunnelling through the energy barrier, which may contribute to the hydrogen isotope effect. This factor is known as the "tunnell effect" and has been treated theoretically by Bell (47) and by Johnston (48). The only reaction where its contribution has been satisfactorily demonstrated is in the fluoride-ion catalysed bromination of 2-carbethoxycyclopentanone (49,50) although it may also be important in other reactions (51,52).

In many reactions, the observed deuterium isotope effect has been found to be less than that calculated using the preceding assumptions. The usual explanation offered for low k^H/k^D values in reactions in which a bond to the isotopic atom is broken in the rate-determining step is that the bond is only partially broken in the transition state for this step. In a recent review (53) Westheimer has argued that such a statement has no theoretical basis and is in violation of the absolute reaction rate theory. It will be interesting to see to what extent this point of view is accepted.

Heavy Isotope Simplification

For all isotopes other than those of hydrogen Δu_i is very much smaller than u_i. Resolution into series of each of the three quantities appearing in the product terms of equation 8, and neglecting in these series terms of second and higher order, leads to the following approximations:

$$\frac{u_i}{u_i + \Delta u_i} \approx 1 - \frac{\Delta u_i}{u_i} ; \quad e^{\Delta u_i/2} \approx 1 + \frac{\Delta u_i}{2}$$

and $$\frac{1 - e^{-(u_i + \Delta u_i)}}{1 - e^{-\Delta u_i}} \approx 1 + \frac{\Delta u_i}{e^{u_i} - 1}$$

Substituting these into equation 8, multiplying and again neglecting second- and third-order terms gives

$$\frac{k_1}{k_2} = \frac{s_1}{s_2} \cdot \frac{s_2'}{s_1'} \cdot \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \frac{\prod_i^{3n-6} \left[1 + \left(\frac{1}{2} - \frac{1}{u_i} + \frac{1}{e^{u_i} - 1}\right) \Delta u_i\right]}{\prod_i^{3n'-6} \left[1 + \left(\frac{1}{2} - \frac{1}{u_i'} + \frac{1}{e^{u_i'} - 1}\right) \Delta u_i'\right]} \qquad (15)$$

Defining a function $G(u_i) = \frac{1}{2} - \frac{1}{u_i} + \frac{1}{e^{u_i} - 1}$ and substituting into equation 15,

$$\frac{k_1}{k_2} = \frac{s_1}{s_2} \cdot \frac{s_2'}{s_1'} \cdot \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \frac{\prod_i^{3n-6} \left[1 + G(u_i)\, \Delta u_i\right]}{\prod_i^{3n'-6} \left[1 + G(u_i')\, \Delta u_i'\right]} \qquad (16)$$

The product term in equation 16 can be written as a sum by i fold multiplication and the rejection of terms of second and higher powers. Equation 16 thus becomes

$$\frac{k_1}{k_2} = \frac{s_1}{s_2} \cdot \frac{s_2'}{s_1'} \cdot \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \frac{\left[1 + \sum_i^{3n-6} G(u_i)\, \Delta u_i\right]}{\left[1 + \sum_i^{3n'-6} G(u_i')\, \Delta u_i'\right]} \qquad (17)$$

which as a first approximation can be written as

$$\frac{k_1}{k_2} = \frac{s_1}{s_2} \cdot \frac{s_2^{\ddagger}}{s_1^{\ddagger}} \cdot \left(\frac{m_2^*}{m_1^*}\right)^{1/2} \left[1 + \sum_i^{3n-6} G(u_i)\,\Delta u_i - \sum_i^{3n'-6} G(u_i^{\ddagger})\,\Delta u_i^{\ddagger}\right] \quad (18)$$

This is the basic equation, known as the Bigeleisen equation, utilised for the calculation of isotope effects of heavier atoms.

The quantity in the square brackets of equation 18 gives a quantitative measure of the energy differences in the initial and transition states and is sometimes referred to as the free energy factor. Assuming that all molecules are in their ground states, the first summation in this factor refers to the zero point energy differences for the two isotopic molecules in their initial states and the second to the corresponding differences in the transition state. The quantity $(m_2^*/m_1^*)^{1/2}$ is known as the effective mass term and arises from the effect of isotopic mass upon the rate with which a reacting molecule passes over the energy barrier.

According to Slater (54), in an unimolecular process, the effective mass of the reacting molecule may be taken as the reduced mass of an imaginary diatomic molecule composed of the atoms which form the bond undergoing change in the rate-controlling step. The effective mass term is then equal to square root of the ratio of the reduced mass for the two isotopic diatomic molecules. This is expressed as,

$$\left(\frac{m_2^*}{m_1^*}\right)^{1/2} = \left(\frac{\mu_2}{\mu_1}\right)^{1/2} \quad (19)$$

where μ's correspond to the reduced masses. The calculation of the effective mass term by equation 19 involves the assumption that, for the rupture of a particular bond in a polyatomic molecule, the reaction

co-ordinate involves only motion of the atoms associated with this bond. Bigeleisen (pages 28-31 of Ref. 43), however, has more recently suggested that the reduced masses should be calculated from the masses of the entire molecular fragments on each side of the bond being broken. Quite recently, Wolfsberg (55) has discussed this problem in relation to the rupture of the A - B bond in the molecule R - A - B - R'. If as the A - B bond is lengthened, the R - A and B - R' bonds simultaneously shorten, then, Wolfsberg proposes, it would be reasonable to use the Slater method for the calculation of the effective mass term. If, however, the force constant of the A - B bond is much smaller than that of the other bonds, the normal mode of decomposition will be one which takes apart the centers of mass of the RA and R'B fragments. In this case, the masses of these separating fragments should be used in the calculation of the mass term.

A relationship has been derived (56) for the calculation of $(m_2^3/m_1^3)^{1/2}$ in three-center reactions. This expression takes into account the relative extent of bond breaking to the extent of bond making.

To evaluate the free energy factor precisely one must know all the fundamental vibrational frequencies of isotopic reactants and transition states. A complete vibrational analysis for polyatomic reactants has rarely been achieved and the vibrational frequencies of the transition state are, of course, unknown. Nevertheless, equation 18 can be used for the calculation of isotope effects provided that certain simplifying assumptions are made. Firstly, all frequencies other than the stretching frequency of the bond being broken are considered to remain unchanged in going from the initial state to the transition state and hence the

terms involving these frequencies cancel. Secondly, the force constant of the bond being broken is taken as zero in the transition state and hence $G(u_i^{\ddagger})\ \Delta u_i^{\ddagger} = 0$. Equation 18 then becomes

$$\frac{k_1}{k_2} = \frac{s_1}{s_2} \cdot \frac{s_2^{\ddagger}}{s_1^{\ddagger}} \cdot \left(\frac{m_2}{m_1}\right)^{1/2} \left[1 + G(u_s)\ \Delta u_s\right] \qquad (20)$$

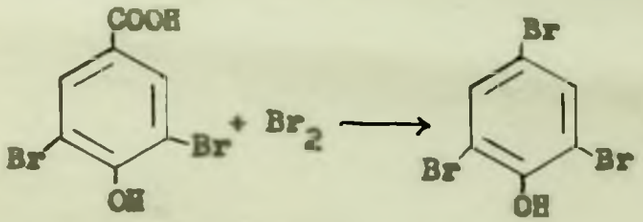
where u_s refers to the stretching frequency of the bond being broken.

An illustration of the use of equation 20 is provided by the unimolecular decomposition of trichloroacetate ion. Using a C^{12}-C^{12} vibrational frequency of 900 cm^{-1} (57) and a temperature of 70.4°C, the free energy factor becomes equal to 1.020. The effective mass term can be calculated as the square root of the ratio of the reduced masses of C^{13}-C^{12} bond to the C^{12}-C^{12} bond (Slater hypothesis) and is 1.020. Thus, $k^{12}/k^{13} = 1.020 \times 1.020 = 1.040$, i.e., an isotope effect of 4 per cent. This is to be compared with the value, 1.0338 ± 0.0007, obtained experimentally at this temperature (58).

It is apparent from the foregoing discussion that the derivation of equation 20, and also the evaluation of reduced-mass and free-energy terms, involve gross approximations. It might appear, therefore, that we are a long way from being able to make any sort of precise theoretical evaluation of the magnitude of an isotope effect to be expected in any given reaction. Despite such approximations, however, rather good agreement has been found between experimental and calculated results in a wide variety of reactions involving isotopes of heavier elements. Some representative examples are shown in Table I.

TABLE I

SOME REPRESENTATIVE INTERMOLECULAR ISOTOPE EFFECTS

Reaction	Isotopes Compared	t(°C)	$(k_l/k_h - 1)100$ Exp.	$(k_l/k_h - 1)100$ Calc.	Ref.
$CH_2(COOH)_2 \xrightarrow{H_2SO_4} CO_2 + CH_3COOH$	C^{12}/C^{13}	137	3.4	3.5	59
$Cl_3C-COO^- + H_2O \xrightarrow{OH^-} CHCl_3 + HCO_3^-$	C^{12}/C^{13}	70	3.4	4.0	58
	C^{12}/C^{13}	20	4.5	4.4	12
$CH_3CH_2\overset{+}{N}(Me)_3 + OH^- \longrightarrow CH_2=CH_2 + (Me)_3N + H_2O$	N^{14}/N^{15}	60	1.7	2.6	60
$C_6H_5CH_2CNO_2 \xrightarrow{-OEt^-} C_6H_5CHO + NO_2^-$	N^{14}/N^{15}	30	2.0	3.8	61
$(CH_3)_3C-\overset{+}{S}(CH_3)_2 + H_2O \longrightarrow (CH_3)_3C-OH + (CH_3)_2S + H^+$	S^{32}/S^{34}	25	1.8	1.6	62
$n\text{-}C_6H_{13}\underset{SO_2O^-}{CHOH} \longrightarrow n\text{-}C_6H_{13}\text{-}CHO + HSO_3^-$	S^{32}/S^{34}	25	1.4	1.5	63

Role of Kinetic Isotope Effects in Reaction Mechanism Studies

The foregoing theoretical treatment has shown that an isotope effect of appreciable magnitude can only be expected if a bond associated with the isotopic atom is being broken in the rate-determining step of the reaction. It is true that secondary isotope effects may sometimes arise from the rupture of a bond not associated with the isotopic atom, but such effects are of much smaller magnitude. For example, in the acetolysis of cyclopentanol and cyclopentanol-1-d tosylates, which involves formation of the carbonium ion in the rate-determining step, k^H/k^D was found to be 1.15 (64); and in the formation of 2,4-dinitrophenylhydrazone of acetophenone-β-C^{14}, k^{14}/k^{12} = 1.0085 was observed (65). A detailed treatment of secondary isotope effects is available elsewhere (44).

Most of the applications of kinetic isotope effect studies to reaction mechanism questions reported to date have involved the isotopes of hydrogen since only with this element are the rate differences sufficiently large for measurement by ordinary kinetic methods or simple radioisotopic-assay techniques. Although the isotope effects associated with the heavier elements, carbon, oxygen, nitrogen, and sulphur, are very much smaller, in the range of 1 - 10 per cent, it nevertheless is now possible, using the modern mass spectrometer, to measure these within precision limits not greatly exceeding those normally obtained in hydrogen isotope effect studies. For example, a 2 - 5 per cent C^{13} or a 1 - 2 per cent S^{34} or N^{15} isotope effects are readily measured to the nearest ±0.1 per cent or better. The results of such studies can therefore be used with confidence to determine

whether or not a bond to the isotopic atom is being broken in the rate-determining step. Furthermore, it is usually possible to use compounds of natural isotopic abundance and hence to avoid time-consuming isotopic labelling.

B - Kinetic Isotope Effects and Role of Intermediates in Electrophilic Aromatic Substitution

General

This section of the thesis presents a critical review of kinetic isotope effects in electrophilic aromatic substitution and the role of such studies in the elucidation of the mechanism of this reaction. In this review emphasis will be given to the diazo coupling reaction and to halogenation (including bromodecarboxylation), the former because it was in this reaction that the formation of a meta-stable intermediate was first unambiguously demonstrated and the latter because of the subject of this thesis. The section concludes with a discussion of the bromodesulphonation reaction, including a critical examination of Cannell's kinetic work (16,17) and the basis for applying kinetic sulphur isotope effect studies to the solution of the unsolved questions relating to reaction mechanism.

The first kinetic hydrogen isotope effect study was reported in 1950 by Melander (1,2) who showed that in the nitration of benzene, toluene, bromobenzene and naphthalene, the isotopes hydrogen and tritium are replaced by the nitro group at very nearly the same rate, i.e., $k^H/k^T \simeq 1$. (A similar result was found for bromination, as will be discussed later.) Shortly after, Bonner *et al*. (3) carried out a deuterium isotope effect

study on the nitration of nitrobenzene and found that the rates of reaction of the labelled and unlabelled compounds are identical within experimental error, $k^H/k^D \simeq 1$. Lauer and Noland (4) obtained the same result in the nitration of monodeuterobenzene.

The absence of a hydrogen isotope effect was interpreted by Melander (2) in terms of a two-step mechanism,

$$ArH + NO_2^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \overset{+}{Ar}\!<\!\begin{matrix}H\\NO_2\end{matrix}$$

$$\overset{+}{Ar}\!<\!\begin{matrix}H\\NO_2\end{matrix} + B \xrightarrow{k_3} ArNO_2 + H^+B$$

in which the rate-determining step is the formation of a true intermediate in which the C - H bond is still intact. It was argued that the alternative one-step mechanism,

$$ArH + NO_2^+ + B \rightleftharpoons \text{transition state} \longrightarrow ArNO_2 + BH^+ ,$$

would be expected to give rise to an isotope effect since the C - H bond is now being broken in the rate-determining step and the difference in zero-point energies for the C - H and C - D bonds should therefore be less in the transition state than is in the reactant.

In contrast to the results obtained in nitration reactions, isotope effects have been observed for aromatic sulphonation. Berglund-Larsson and Melander (6,7) found a small isotope effect for the sulphonation of bromobenzene at 0^o, namely, $k^H/k^T = 2.5$ and $k^H/k^D = 1.49$. More recently, Brand et al. (8) have observed isotope effects, k^H/k^D, of 1.6 to 2.0 in the sulphonation of nitrobenzene and several para-substituted phenyltrimethylammonium ions. These results

have been interpreted in terms of the two-step mechanism in which the rate of return of the intermediate to reactants is appreciable compared to its rate of decomposition into products, i.e., the second step (k_3) is partially rate-controlling.

The significance, in relation to a reaction mechanism, of the observation of a zero isotope effect requires very careful consideration. Hammond, in an important paper (9) appearing in 1955, has argued that the absence of a measurable hydrogen isotope effect in aromatic substitution does not necessarily require that the C - H bond remains intact in the rate-determining step of the reaction. What is really shown is that the zero-point energies associated with the bending and stretching of the C - H bond are not changed significantly in going from reactants to the transition state. One way in which this may come about, of course, is through the formation in a rate-determining step of a true intermediate, $\overset{+}{\mathrm{Ar}}\!<\!\overset{\mathrm{H}}{\underset{\mathrm{Z}}{}}$. Not excluded, however, is reaction in a single step, the transition state for which is reached before the C - H bond has lost an appreciable part of its zero-point energy. Similarly, the observation of a small isotope effect, as in sulphonation, may be interpreted, as Melander has done, in terms of the two-step mechanism with decomposition of the intermediate rate-determining. Alternatively, it may be accommodated by a one-step process involving a transition state in which the C - H bond is only slightly weakened.

It is of interest to note that Melander (page 112 of Ref. 44) in his recent book, "Isotope Effects on Reaction Rates", admits to the validity of Hammond's argument. He points out, however, that a one-step process involving a transition state in which the C - H bond is

still essentially intact would require, if one considers the reverse reaction, that the gain in energy resulting from the formation of an essentially normal C - H bond never completely balances the loss in energy due to the stretching of the carbon-substituent bond. This, Melander suggests, seems entirely improbable and he therefore favours the two-step mechanism. It should be pointed out, however, that this argument does not take into account that these are not the only bond changes involved in the substitution process; bonds to solvent molecules are being formed or broken and these changes will contribute to the energy requirements of the process. The author of this thesis takes the view that a knowledge of the magnitude of an isotope effect in an electrophilic aromatic substitution reaction, although important in that it can provide an indication of the extent of bond rupture in the transition state, is of no value in answering the question as to whether or not a true intermediate is involved in the process.

In the light of these conclusions it is fruitful to consider the potential-energy profiles for reaction occurring with and without an isotope effect (page 39 of Ref. 10). When a normal isotope effect is observed, the C - H bond must be significantly weakened in the highest-energy state which the reaction achieves in going from reactants to product. The change in potential energy along the reaction co-ordinate may either follow the solid line in Fig. 1, if the reaction were to proceed in a single step, or the dotted line, if the transition state were to be preceded in the reaction path by a meta-stable intermediate. When no isotope effect is observed, it may be concluded that C - H bond rupture has made little progress in the state corresponding to

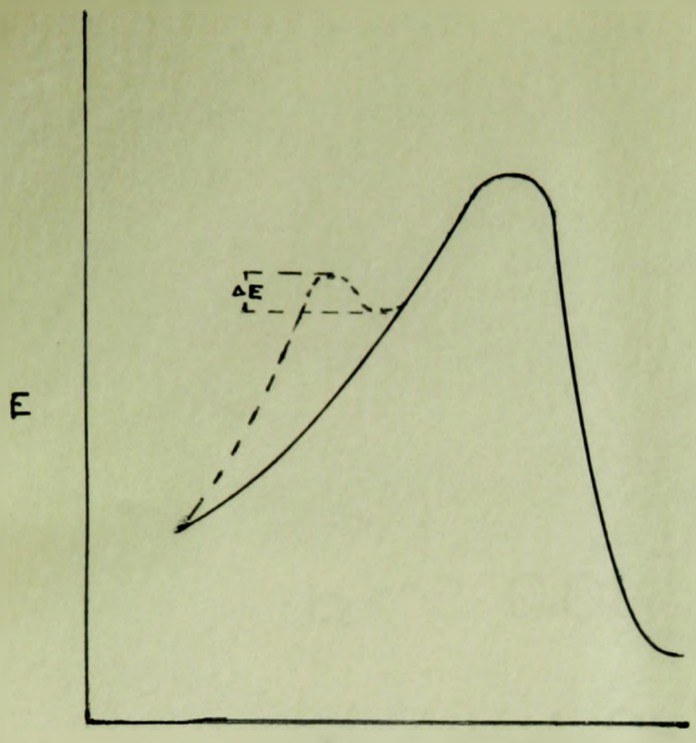


Fig. 1

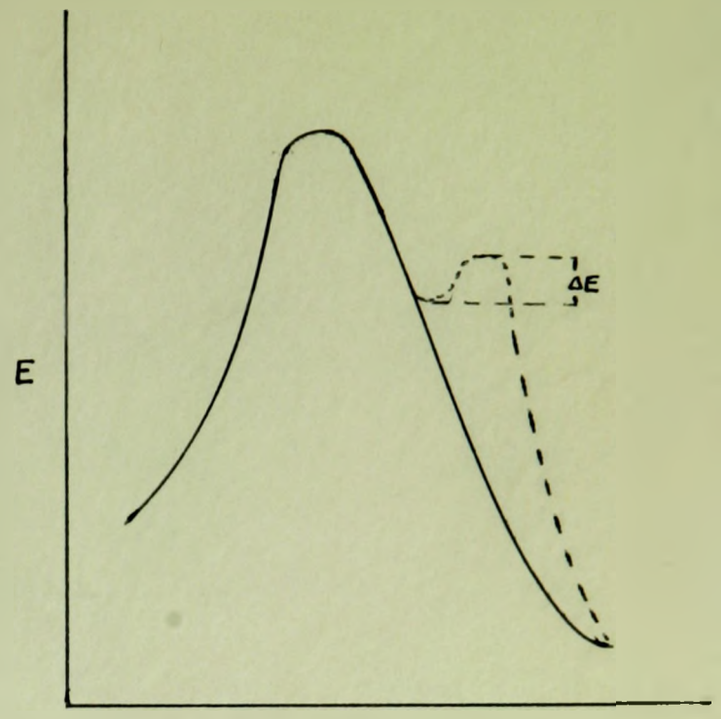


Fig. 2

highest energy along the reaction path. Whether this state is followed by an intermediate (dotted line in Fig. 2) or proceeds directly to products (full line in Fig. 2) has no bearing on the matter. It is worthy of note as Zollinger (66) has pointed out, that the question of whether or not an intermediate exists in any reaction is immaterial when its stability (ΔE in Figs. 1 and 2) is less than 0.5 kcal $mole^{-1}$ since it would be largely bypassed as a result of the thermal vibrations in the system.

Although a knowledge simply of the magnitude of the isotope effect under a given set of reaction conditions cannot establish whether or not a true intermediate is involved, the observation of a variation in the magnitude of the effect with changes in the concentration of certain reacting species can. Let us consider first the two-step mechanism in which a base is included in the transition state for the proton-expulsion step:

$$ArH + Z^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Ar\langle^{H}_{Z}$$

$$Ar\langle^{H}_{Z} + B \xrightarrow{k_3} ArZ + BH^+$$

Application of the steady-state treatment leads to the rate expression,

$$\frac{d[ArZ]}{dt} = \frac{k_1 k_3}{k_2 + k_3[B]} [ArH][Z^+][B] \qquad (21)$$

When $k_2 \gg k_3[B]$, that is, when the intermediate is essentially in equilibrium with reactants, equation 21 becomes

$$\frac{d[ArZ]}{dt} = \frac{k_1 k_3}{k_2} [ArH][Z^+][B] \qquad (22)$$

The reaction is then subject to base catalysis and can be expected to show a normal isotope effect. On the other hand, if the reverse situation applies, i.e., $k_2 \ll k_3[B]$, equation 21 reduces to

$$\frac{d[ArZ]}{dt} = k_1[ArH][Z^+] \qquad (23)$$

The reaction is now no longer subject to base catalysis and the rate-determining step does not involve the breaking of the C - H bond. Under these conditions there should be no isotope effect other than, possibly, a very small secondary isotope effect* associated with the formation of the intermediate.

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*Secondary isotope effects of a small magnitude have been reported in the following aromatic substitution reactions: (i) the bromination of diphenyl (15): $k^H/k^D = 1.15$ and (ii) in the nitration of benzene and toluene: $k^H/k^D = 0.87$. (67)

It can thus be seen that in a reaction following the two-step mechanism a change in the concentration of some basic reagent may cause a change in the magnitude of the isotope effect. In the one-step process, however, $ArH + Z^+ + B \rightleftharpoons$ transition state $\longrightarrow ArZ + H^+B$, for which the rate expression is

$$\frac{d[ArZ]}{dt} = k[ArH][Z^+][B], \qquad (24)$$

the magnitude of the isotope effect, whether it be small or large, will be independent of changes in the concentration of B. This criterion, accompanied by ordinary kinetic studies, has been applied by Zollinger to the study of the mechanism of diazo-coupling reaction (as will be discussed later).

A similar criterion can, in principle, be used if the reaction is one in which there is produced from the electrophile some species whose concentration may be varied by pre-addition, for example halide ion from molecular halogen. In the two-step mechanism, as before,

$$ArH + X_2 \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} \overset{+}{Ar}\!<\!\overset{H}{X} + X^-$$

$$\overset{+}{Ar}\!<\!\overset{H}{X} + (B) \xrightarrow{k_3'} ArX + H^+(B)$$

Application of the steady-state treatment leads to the rate expression,

$$\frac{d[ArX]}{dt} = \frac{k_1'k_3'}{k_2'[X^-] + k_3'}[ArH][X_2] \qquad (25)$$

At X^- concentration sufficiently low such that $k_2'[X^-] \ll k_3'$, equation 25 becomes

$$\frac{d[ArX]}{dt} = k_1' [ArH][X_2] \qquad (26)$$

In this case the rate-determining step will be the formation of the intermediate, $\overset{+}{Ar}\!<^{H}_{X}$, in which the C - H bond is still intact. No isotope effect (other than a possible secondary) would, therefore, be expected. As the concentration of X^- is increased to make $k_2'[X^-] \simeq k_3'$, there will be a partial return of the intermediate to reactants relative to its decomposition into products. The rupture of the C - H bond will then be partially rate determining and an appreciable isotope effect should be observed. Finally, at very high X^- concentration, such that $k_2'[X^-] \gg k_3'$, equation 25 becomes

$$\frac{d[ArX]}{dt} = \frac{k_1' k_3'}{k_2'[X^-]} [ArH][X_2] \qquad (27)$$

In this case the intermediate formed will be essentially in equilibrium with the reactants and the supture of the C - H bond is fully rate determining. Under these conditions a normal isotope effect should be observed.

It can be seen, therefore, that the magnitude of the isotope effect can be expected to vary with changes in concentration of X^-. On the other hand, for a one-step mechanism

$$ArH + X_2 + (B) \rightleftharpoons \text{transition state} \longrightarrow ArX + X^- + (B)H^+$$

the rate expression is

$$\frac{d[ArX]}{dt} = k [ArH][X_2][B] \qquad (28)$$

It follows from the latter that the magnitude of the isotope effect (small or large) should be invariant with changes in concentration of X^-.

To date, this criterion has been successfully applied in only one reaction, namely, the bromodecarboxylation of 3,5-dibromo-4-hydroxybenzoic acid. Attempts to apply it to ordinary halogenations, specifically iodination and bromination, so far have been unfruitful. It will be seen later that this criterion can, in principle, be used also to distinguish between the halogenating species X_2 and X^+ (or H_2OX^+) in the halogenation reaction.

Diazo Coupling

The first application of the "variable kinetic isotope effect test" for the formation of a meta-stable intermediate in an electrophilic aromatic substitution was reported by Zollinger in 1955 (11; see also reviews 66,68) in his study of the mechanism of the diazo coupling reaction. This important work will be presented in some detail.

Normally the diazo coupling reaction is not catalysed by bases and shows no hydrogen isotope effect. When, however, the attack of the diazo component on the aromatic substrate is sterically hindered owing to the presence of substituents in close proximity to the seat of displacement, the reaction is found to be strongly catalysed by a variety of bases, for example pyridine. The rates of these base-catalysed reactions are not linearly dependent upon the concentration of base as would, of course, be required if the reaction were to proceed by a

single-step mechanism. Instead, the form of the catalysis is entirely compatible with the two-step mechanism,

$$ArH + Ar'N_2^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Ar\overset{H}{\underset{N=N-Ar'}{<}}^+$$

$$Ar\overset{H}{\underset{N=N-Ar'}{<}}^+ + B \xrightarrow{k_3} Ar-N=N-Ar' + B^+H$$

for which, as discussed in the previous section (page 28) the relationship between rate and concentration of base is given by the equation

$$-\frac{d[ArH]}{dt} = \frac{k_1 k_3}{k_2 + k_3[B]}[B][ArH][Ar'N_2^+] \qquad (29)$$

Zollinger observed that the coupling reactions whose rates are subject to base catalysis, unlike the uncatalyzed reactions, exhibit an isotope effect. The magnitude of the isotope effect, however, decreases with increasing strength or concentration of the catalyzing base, as is shown in Table II.

These results are entirely in accordance with the predictions of the two-step mechanism. In the presence of a weak base, such as water, the intermediate is essentially in equilibrium with reactants, that is $k_2 \gg k_3[B]$ and a normal isotope effect is exhibited. Addition of a stronger base, for example pyridine, causes an increase in the rate of the forward reaction, that is, an increase in $k_3[B]$ relative to k_2, and a smaller isotope effect results.

By studying the variation in the observed rates and isotope effects with changes in the concentration of pyridine, Zollinger was able to calculate the isotope effect for the step involving the rupture

TABLE II

KINETIC ISOTOPE EFFECTS FOR THE COUPLING OF p-CHLORODIAZOBENZENE WITH 2-NAPHTHOL-6,8-DISULPHONIC ACID IN THE PRESENCE OF DIFFERENT BASES

(Temperature = 10°C)

Base	Concentration of Base (moles/litre)	k^H/k^D	k_3^H/k_3^D
Water	55.6	6.55	6.58
Pyridine	0.0232	6.01	6.16
Pyridine	0.905	3.62	6.67
			Mean 6.4 ± 0.3

of the C - H bond, that is, k_3^H/k_3^D. That this quantity is essentially independent of the nature and concentration of the base (see last column in Table II) is further support for the interpretation given for the reaction.

The two-step mechanism accounts also for the relationship between the magnitude of the observed isotope effects and the structure of the reactants. Normally $k_2 \ll k_3 [H_2O]$ and no isotope effect is observed. Steric strain in the reaction intermediate, however, would be expected to promote the expulsion of the bulky diazo group at the expense of proton loss and, when k_2 assumes a value comparable to $k_3[H_2O]$, an isotope effect will be associated with the process. The importance of this structural factor is revealed by the data for the first three reactions shown in Table III.

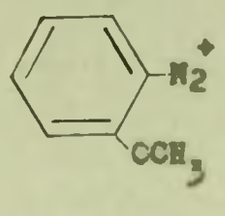
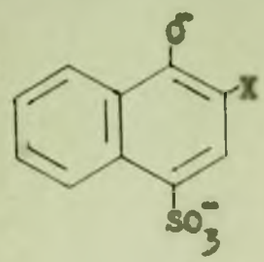
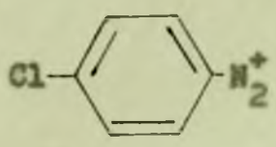
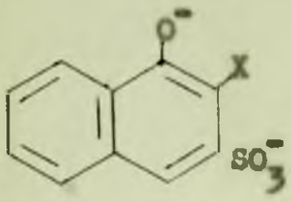
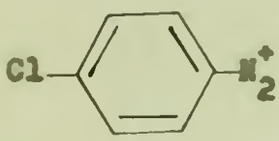
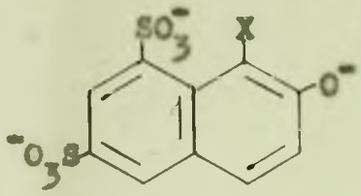
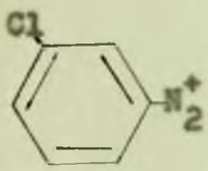
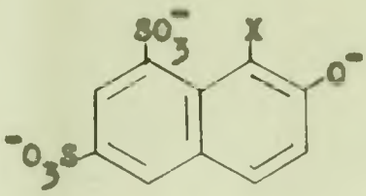
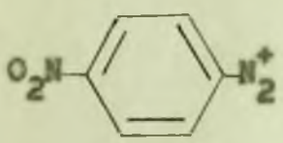
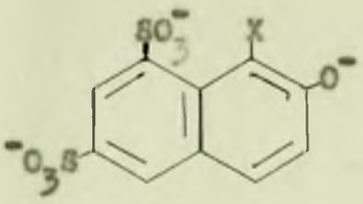
Further, the presence of electron-withdrawing substituents might be expected to have the opposite effect, namely to promote proton loss relative to expulsion of the diazo group. Thus, in a reaction system showing an isotope effect, an increase in the electron-withdrawing tendency of substituents on one of the reactants might be expected to cause a lowering of the observed effect. The influence of this structural factor is found in the last four entries in Table III.

Kidd and co-workers (69,70) have recently reported the results of kinetic isotope effect studies in the coupling reaction of heterocyclic compounds. Neither indole nor glyoxaline in their coupling with p-nitrobenzenediazonium ion or diazotised sulphanilic acid, respectively, show any difference in the reaction rates of the deuterated and undeuterated compounds. Apparently, in these systems, as one might have predicted, steric strain in the reaction intermediate is of minor importance.

TABLE III

KINETIC ISOTOPE EFFECTS IN AZO COUPLING REACTIONS IN AQUEOUS SOLUTION AND IN THE ABSENCE OF ADDED BASE

(Temperature = 10°C)

Diazo Component	Coupling Component X = H,D	k^H/k^D
		≤ 1.0
		3.0
		6.55
		5.48
		4.78

Iodination

Extensive experimental data on the kinetics of this reaction are available and some kinetic isotope effect studies have been made in an effort to shed light on the detailed mechanism of this reaction. In the discussion which follows it is of interest to enquire whether the substitution takes place through a preformed I^+ or its hydrate H_2OI^+ (hypoiodous-acidium ion), or whether the iodine is conveyed to the nucleus by a carrier such as I_2, HOI or even by I_3^-. At the onset it should be pointed out that at the present time no experimental evidence is available to distinguish between I^+ and H_2OI^+ as the iodinating species and no such distinction is implied in the following discussion.

To begin with, Painter and Soper (71) studied the kinetics of the iodination of phenol by iodine in water and obtained results which could be fitted to the following rate equations:

$$-\frac{d[I_2]}{dt} = \frac{k[PhO^-][I_2]}{[I^-]} \qquad (30)$$

$$-\frac{d[I_2]}{dt} = \frac{k[PhOH][I_2]}{[H^+][I^-]} \qquad (31)$$

Berliner (72,73) later studied the kinetics of iodination in an attempt to distinguish between undissociated phenol and phenoxide ion as the reacting species. The rate of iodination of phenol was found to be very much more rapid than that of aniline. This is consistent with phenoxide ion as the reacting form since, by the electronic theory, the relative rates of substitution should follow the sequence: $PhO^- > Ph.NH_2 > Ph.OH$. The mechanism favoured by Painter and Soper, and also by Berliner, which accounts for the suppression of rate by iodide ion, involves I^+ (or H_2OI^+) as the iodinating species in either a one- or two-step process:

Mechanism I Iodinating species I^+ (or H_2OI^+)

$$ArOH \underset{}{\overset{K_1}{\rightleftharpoons}} ArO^- + H^+$$

$$I_2 + H_2O \overset{K_2}{\rightleftharpoons} H_2OI^+ + I^-$$

(a) Two Step

$$ArO^- + H_2OI^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \begin{matrix} H \\ I \end{matrix}\!\!>\!\overset{+}{Ar} - O^- + H_2O$$

$$\begin{matrix} H \\ I \end{matrix}\!\!>\!\overset{+}{Ar} - O^- \xrightarrow{k_3} I - Ar - O^- + H^+$$

(b) One Step

$$H_2OI^+ + Ar - O^- \overset{k_4}{\rightleftharpoons} \text{transition state} \longrightarrow I - Ar - O^- + H^+$$

Steady-state treatment, assuming equilibrium between I_2 and H_2OI^+, yields for I (a)

$$\text{rate} = K_1K_2 \cdot \frac{k_1k_3}{k_2 + k_3} \cdot \frac{[ArOH]\,[I_2]}{[H^+]\,[I^-]} \qquad (32)$$

while for I (b) the rate expression is

$$\text{rate} = K_1K_2k_4 \cdot \frac{[ArOH]\,[I_2]}{[H^+]\,[I^-]} \qquad (33)$$

These kinetic forms are identical to that observed by Painter and Soper and by Berliner (equation 31).

Berliner extended his kinetic studies to iodination by iodine chloride of p-chloroaniline (74), 2,4-dichlorophenol and anisole (75) in aqueous hydrochloric acid. He observed inverse dependence of rate on both $[H^+]$ and $[Cl^-]$, which is compatible with either form of mechanism I (but with $[Cl^-]$ replacing $[I^-]$ in the denominator of equations 32 and 33).

There is, however, a further mechanism which can account for the iodination kinetics. This mechanism was first proposed by Grovenstein and Henderson to account for the kinetic results of bromodecarboxylation (see page 52) and involves a two-step process with molecular I_2 (or ICl) as the iodinating species.

Mechanism II Iodinating species I_2 or ICl

$$ArOH \underset{}{\overset{K_1'}{\rightleftharpoons}} ArO^- + H^+$$

$$ArO^- + I_2 \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} \begin{matrix} H \\ I \end{matrix}\!\!>\!\overset{+}{Ar} - O^- + I^-$$

$$\begin{matrix} H \\ I \end{matrix}\!\!>\!\overset{+}{Ar} - O^- \xrightarrow{k_3'} Ar\!<\!\begin{matrix} O^- \\ I \end{matrix} + H^+$$

Steady-state treatment gives

$$\text{rate} = K_1' \frac{k_1' k_3' [ArOH][I_2]}{[k_2'[I^-] + k_3'][H^+]} \qquad (34)$$

when $k_2'[I^-] \gg k_3'$ (i.e., the intermediate $\begin{matrix} H \\ I \end{matrix}\!\!>\!\overset{+}{Ar} - O^-$ is essentially in equilibrium with reactants), equation 34 reduces to

$$\text{rate} = K_1' \frac{k_1' k_3'}{k_2'} \frac{[ArOH][I_2]}{[H^+][I^-]} \qquad (35)$$

which is again of the same kinetic form as observed experimentally by Painter and Soper and by Berliner.

It is clear from the foregoing discussion that the kinetic results are accommodated by the following three possibilities:

Mechanism I a, the two-step process, involving I^+ (or H_2OI^+) as the reacting species, with either the formation or decomposition of the intermediate rate determining;

Mechanism I b, the one-step process with I^+ (or H_2OI^+) as the reacting species, and

Mechanism II, the two-step process involving I_2 as the reacting species, with the decomposition of the intermediate rate determining.

It is of value to discuss the kinetic isotope effect studies which have been made recently in an effort to shed light on this question. Grovenstein and Kilby (76) observed that iodination of 2,4,6-trideuterophenol in acetate buffer resulted in an isotope effect, k^H/k^D, of 3.97. This result which establishes that C - H bond is being broken in the rate-determining step is consistent with either mechanism I a or mechanism II provided that in either case the decomposition of the intermediate is rate determining. It is also consistent with mechanism I b, a one-step process involving I^+ (or H_2OI^+) as the reacting species, provided that in the transition state of this process there is considerable C - H bond loosening (Hammond (9)).

Analogous studies were made by Shilov and Weinstein (77,78) on the iodination of several aromatic amines, amino-carboxylic acids and amino-sulphonic acids. The values of k^H/k^D obtained varied for no apparent reasons from 1 to 4 with the nature of the aromatic substrate. Although these observations are not fruitful with respect to mechanism, the authors favour as the iodinating species a complex of iodine and the amine because of the third-order kinetics observed (second order for amine and first order for iodine). Berliner (79) has also observed an

isotope effect, $k^H/k^D \simeq 4$, in the iodination of anisole by ICl in glacial acetic acid under conditions in which the kinetic order with respect to ICl is two.

As has been emphasized before, the simple observation of a kinetic isotope effect cannot distinguish between mechanisms I and II. There is, however, one criterion which in principle should distinguish mechanism II from other possibilities. This is the variation of the observed isotope effect with halide-ion concentration. Inspection of mechanism II shows us that as the concentration of iodide ion (or Cl^-, as the case may be) is decreased the rate of reversal of step 2 becomes smaller and smaller relative to the rate of step 3. Eventually then, a stage should be reached whereby $k_2' [I^-] \ll k_3'$ and the isotope effect should have disappeared. On the other hand, in mechanisms I a or I b, the isotope effect should be independent of iodide-ion concentration, since iodide ion is formed in a pre-equilibrium step not involving aromatic substrate. Actual attempts made in using the criterion of variation in isotope effect with halide-ion concentration are discussed below.

Ridd et al. (81) studied the rate of iodination of glyoxaline as a function of iodide-ion concentration. Their kinetic results could be accommodated by either mechanisms, I (a or b) or II. A comparison of the reaction rates of glyoxaline and 2,4,5-trideuteroglyoxaline at 0.01M iodide-ion concentration gave an isotope effect $k^H/k^D = 4.4$ which remained unchanged even at very low iodide-ion concentration ($\not>$ 0.0005M) (13,70). Although this result strongly supports mechanism I (a or b) involving I^+ (or H_2OI^+) as the iodinating species, it does not completely

eliminate mechanism II with I_2 as the iodinating species. The possibility of mechanism II exists because, even at the lowest iodide-ion concentration used, the rate of reversal of the intermediate could still be faster than proton loss ($k_2' [I^-] \gg k_3'$) and hence C - H bond rupture still be fully rate-determining. More recently, Berliner (14) has observed an isotope effect, k^H/k^D, of 3.8 for the iodination of anisole, a value which remained unchanged even at the very low chloride-ion concentrations. The same ambiguity, therefore, with respect to mechanism exists in the iodination of anisole as in the iodination of glyoxaline. Thus, to date, no unambiguous distinction between mechanisms I (a or b) and II for the iodination reaction would appear to have been provided.

Bromination

Kinetic studies on bromination have been somewhat more extensive than those on iodination. As in iodination, it is theoretically possible for any bromine-containing species to behave as a brominating agent, and the most obvious ones that suggest themselves are Br_2, HOBr, Br^+ (or H_2OBr^+), or even Br_3^-. Often the object of a kinetic study is to ascertain which of these halogenating species is active under the particular experimental conditions. The influence of the solvent, pH, catalysts, and electrolytes, particularly bromide ions, on the rate of reaction may indicate which brominating agent or agents attack the aromatic nucleus. As in iodination, however, no experimental data is available to distinguish between Br^+ and H_2OBr^+ (hypobromous-acidium ion) as the brominating species and no such distinction is implied in the following discussion.

Francis (82) in 1925 found that the bromination of *p*-nitrophenol by bromine water takes place about 1000 times more rapidly than bromination by hypobromous acid at pH3, and he suggested (wrongly) that the free ion Br^+ might be the effective halogenating agent in bromine water. Fourteen years later, Shilov and Kanjaev (83) made the important discovery that hypobromous acid, in the presence of a strong acid such as perchloric acid, is a much more active brominating agent than bromine water. They found that the bromination of anisole-*p*-sulphonic acid by acidified hypobromous acid follows the rate equation, rate = $k\,[ArH]\,[HOBr]\,[H^+]$. Since $[HOBr]\,[H^+] \propto [H_2OBr^+]$ and water is in constant excess, the authors favoured brominium ion, Br^+, as the brominating species.

The identity of the brominating species in brominations by bromine water was considered by Wilson and Soper (84) in their study on the bromination of benzene and *o*-nitroanisole in the presence of excess bromide ion. The reaction was found to follow the rate law

$$-\frac{d\,[Br_2]_t}{dt} = k_{obs}\,[Br_2]_t\,[ArH] \qquad (36)$$

where k_{obs} is the observed second-order rate constant and $[Br_2]_t$ is the total titratable bromine. Taking into account the equilibrium,

$$Br_2 + Br^- \underset{}{\overset{K}{\rightleftharpoons}} Br_3^-$$

equation 36 may be rewritten as follows:

$$-\frac{d\,[Br_2]_t}{dt} = k_{obs}\left[[Br_2]_f + [Br_3^-]\right]\,[ArH] \qquad (37)$$

where $[Br_2]_f$ is the concentration of free uncomplexed bromine. Now the rate law required for a bimolecular reaction of molecular bromine with the aromatic compound is:

$$-\frac{d[Br_2]_t}{dt} = k_{Br_2}[Br_2]_f[ArH] \qquad (38)$$

where k_{Br_2} is the specific rate constant for bromination by molecular bromine. Taking into account the equilibrium with tribromide ion, equation 38 can be written as follows:

$$-\frac{d[Br_2]_t}{dt} = k_{Br_2}\frac{[Br_2]_f + [Br_3^-]}{1 + K[Br^-]}[ArH] \qquad (39)$$

It can be seen that the observed rate law, equation 37, and that required for bromination by molecular bromine, equation 39, are the same provided

$$k_{obs}\left[1 + K[Br^-]\right] = k_{Br_2} \qquad (40)$$

or, in other words, provided that the product $k_{obs}\left[1 + K[Br^-]\right]$ remains constant as the concentration of bromide ion is varied. As this was found to be the case, Wilson and Soper concluded that molecular bromine is the active brominating species in bromine water.

Derbyshire and Waters (85) have directly compared the reactivity of sodium p-anisate towards hypobromous acid and molecular bromine by carrying out brominations in aqueous solution in the presence of bromide ion. Under these conditions, because of the equilibrium

$$HOBr + H^+ + Br^- \rightleftharpoons Br_2 + H_2O,$$

bromination by HOBr and Br_2 may proceed concurrently. It was found that molecular bromine is about 2000 times more active than HOBr, which further confirms the conclusion drawn above that Br_2 is the only significant brominating agent in bromine water.

There is kinetic evidence that molecular bromine can also be a brominating species in reactions carried out in non-aqueous solvents. Thus, observations by Bradfield et al. (86,87) on the bromination of

aromatic ethers in 50 per cent and 75 per cent aqueous acetic acid, by Robertson (88) on the bromination of aromatic hydrocarbons in glacial acetic acid and by Berliner and Beckett (89) on the bromination of naphthalene in 50 per cent aqueous acetic acid provide supporting evidence for molecular bromine as the active electrophile.

The accelerating influence of mineral acids on the rate of reaction between hypobromous acid and aromatic compounds (82,84) suggests that under acidic conditions HOBr is transformed into an active cationic species, Br^+ (or H_2OBr^+) which serves as a powerful brominating agent. More recently, this has been unambiguously confirmed in other systems by de la Mare et al. (90) and by Branch et al. (91) for bromination of a variety of aromatic compounds in water, aqueous dioxane, and aqueous-acetic acid.

The inclusion of Br_3^- as a possible brominating agent is surprising in that one would not expect a negative ion to function as an electrophilic species. Berliner and Beckett (89), however, in their work on the bromination of naphthalene in 50 per cent aqueous acetic acid ascribed a small activity to this anion. Also pertinent in this connection is the work of Bartlett and Tarbell (92) on the kinetics of bromine addition to stilbene in methanolic solution in which they ascribe a small activity to the tribromide ion. It has been suggested by Bell and Ramsden (93) and also earlier by Alexander (94) that the activity of Br_3^- as a brominating agent could be appreciable for bromination of aromatic amines and of phenoxide ions.

A number of kinetic isotope effect studies on aromatic bromination have been made, particularly within the past few years, and these have

provided some insight into the detailed mechanism of the substitution process itself. In contrast to aromatic iodination, bromination normally proceeds without any appreciable isotope effect. As early as 1950, Melander (2) demonstrated the absence of a deuterium isotope effect in the iodine-catalysed bromination of benzene. De la Mare, Dunn and Harvey (5) carried out a bromination study of benzene and hexadeutero-benzene by aqueous hypobromous acid containing perchloric acid in aqueous dioxane and found that the two substrates react at rates which are the same within experimental error. On the basis of these results, the reaction can be considered to proceed either by a two-stage process, with the second step faster than its reversal ($k_3 \gg k_2 [Br^-]$), or by a one-step process with insignificant C - H bond stretching. In harmony with Hammond's postulate, the least categorical statement that can be made is that the breaking of the C - H bond has not made significant progress in the rate-determining step of the reaction.

A few aromatic brominations have been found to exhibit hydrogen isotope-effects of a small magnitude. Thus, Zollinger (66) observed $k^H/k^D \simeq 2$ in the bromination of 2-naphthol-6,8-disulphonic acid, while Farrell and Mason (95) have observed an effect of similar magnitude in the bromination of dimethylaniline in water. Also, more recently, Baciocchi et al. (96) in their study on the bromination of 3-bromodurene and 3-bromo-6-deuterodurene observed an isotope effect, k^H/k^D, of 1.4. A year ago, Myhre (97) reported a normal tritium isotope effect, k^H/k^T, of 10 in the bromination of 1,3,5-tritertiarybutylbenzene.

The existence of an isotope effect in the bromination of these more complex compounds, and not of the simpler substrates, can be readily understood in terms of the two-step mechanism,

$$ArH + Br_2 \rightleftharpoons \overset{+}{Ar}\overset{H}{\underset{Br}{<}} + Br^-$$

$$\overset{+}{Ar}\overset{H}{\underset{Br}{<}} \longrightarrow ArBr + H^+,$$

since an increased steric crowding at the reaction centre would be expected to favour the return of the intermediate to reactant relative to its conversion to product. (Compare Zollinger's work on diazo coupling, page 31.) It is surprising to note in this connection that no isotope effect is observed in the nitration of 1,3,5-tri-t-butylbenzene (97). Berliner (79) has advanced similar steric reasons for the fact that isotope effects are less frequently encountered in aromatic brominations than in iodinations. He suggests that this difference may be either due to a less rapid proton loss from the intermediate containing the less electronegative iodine or to a more rapid return to reactants of the sterically crowded (iodine-containing) intermediate.

From the foregoing discussion, it can be said that in aromatic brominations exhibiting an isotope effect the same ambiguity with respect to mechanism arises as in the iodination of phenol and aromatic amines (76,77,78). Again, as with iodinations, the only conclusive means of establishing the two-step mechanism with molecular bromine as the brominating species is to demonstrate a variation of the isotope effect with change in bromide-ion concentration.

An attempt to observe such a variation, if it exists, has recently been made by Berliner and Schueller (15) who studied the bromination of 4,4'-dideuterobiphenyl and biphenyl in 50 per cent aqueous acetic acid. At 0.1M bromide-ion concentration, this reaction showed an isotope effect, k^H/k^D, of 1.15. If this effect is a primary

one an increase in its magnitude to 1.3 should be observed at 0.2M bromide-ion concentration. Surprisingly, the magnitude of the isotope effect was found to be invariant with change in concentration of bromide ion. This result can be interpreted in two ways:

(a) the reaction proceeds by the two-step mechanism with the formation of the intermediate rate determining (in this case the 15 per cent isotope effect is a secondary one);

(b) the reaction proceeds in one step through a transition state in which the C - H bond is only slightly weakened.

Thus to date, as in iodination, there is no unambiguous evidence to distinguish between one- and two-step mechanisms for aromatic bromination. Furthermore, in the case of reactions showing a normal hydrogen isotope effect, it has not been possible to distinguish between Br_2 and Br^+ (or $H_2O\,Br^+$) as the brominating species.

Recently, Bell and Rawlinson (98) reported a thorough kinetic study of the bromination of a series of anisoles in water. For anisole, at an ionic strength of 0.5M, the product $k_{obs}[1 + K[Br^-]]$ (see equation 40) showed a small decrease of about 10 per cent with increasing bromide-ion concentration over the range from 0.1 to 0.5M. For o-bromoanisole, at an ionic strength of 1.51M, this product showed a marked decrease of about 60 per cent over the range of bromide-ion concentration from 0.06 to 1.5M. Bell attributes such a decrease to a kinetic salt effect arising from the increase in concentration of sodium bromide, which replaces sodium perchlorate, at a constant ionic strength. It could also be due, as the authors admit (98), to inaccuracies in the value of K, the equilibrium constant for tribromide-ion formation since this constant has not been measured at the ionic strength used in the kinetic study.

A decrease of about 11 per cent in the magnitude of $k_{obs}\left[1 + K\left[Br^-\right]\right]$ with increasing concentration of bromide ion was observed by Grovenstein and Henderson (99) for the bromination of 2,6-dibromophenol in 80 per cent aqueous acetic acid at an ionic strength of 0.3M in a range of bromide-ion concentration from 0.1 to 0.3M. These authors also attribute such a decrease to salt effects but admit the alternate possibility of a two-step mechanism in which there is a partial return of the intermediate to reactants at the expense of its decomposition into products. Cannell (17) has also observed a decrease of about 25 per cent in the value of $k_{obs}\left[1 + K\left[Br^-\right]\right]$ for the bromination of o-methoxybenzoic acid in water at an ionic strength of 0.15M in a range of bromide-ion concentration from 0.0025 to 0.15M.

From the foregoing discussion of the effect of added bromide ion on the product $k_{obs}\left[1 + K\left[Br^-\right]\right]$, one is led to consider the following mechanisms, both involving molecular bromine as the brominating agent.

(i) The reaction involves a one-step process, and the observed decrease in the product, $k_{obs}\left[1 + K\left[Br^-\right]\right]$, is due solely to salt effects;

(ii) The reaction involves a two-stage process and the decrease in the product, $k_{obs}\left[1 + K\left[Br^-\right]\right]$, is either due to a salt effect, or to partial return of the intermediate to reactants, or to a combination of the two.

Again, as in iodination, the only way to resolve this question is to demonstrate (if possible) a variation in kinetic hydrogen isotope effect with bromide-ion concentration. Such a variation in isotope effect would be taken as a strong support for the two-step process.

Chlorination

In chlorination, the possible halogenating species are Cl^+, cations derived from these by co-ordination with a neutral nucleophilic species (e.g., H_2OCl^+), and molecular chlorine. In iodination and bromination, no attempt has been made to distinguish between X^+ and H_2OX^+ as halogenating agents. de la Mare *et al.* (100), however, have been able to shed light on this problem in the case of aromatic chlorinations in acidified aqueous solutions of HOCl.

For aromatic compounds of moderate or low reactivity, it was found that

$$\text{rate} = k\,[ArH]\,[HOCl][H^+]$$

and for compounds of high reactivity,

$$\text{rate} = k\,[HOCl]\,[H^+]$$

This situation is clearly analogous to that in nitration (see Ch. 5, ref. 10) and must mean that in the chlorination of highly reactive aromatic compounds, the active chlorinating species is formed in a rate-determining step. This is strong evidence for Cl^+ rather than H_2OCl^+ as the chlorinating species. Further evidence for Cl^+ as an intermediate in chlorination has been provided by the measurement of reaction rate in deuterium oxide. It was found (101) that the rate of chlorination of methyl-p-tolyl ether by acidified hypochlorous acid is faster by a factor of about two in deuterium oxide than in ordinary water.

The remainder of the discussion in the present section on chlorination has its emphasis on molecular chlorine as the chlorinating agent. Strong evidence in support of Cl_2 as the chlorinating species has been obtained in many reactions. Most of the kinetic studies have been carried out in acetic acid as solvent.

Orton and Bradfield (102) studied the chlorination of phenolic ethers in 99 per cent acetic acid under strictly anhydrous conditions. The reaction was shown to have the kinetic form,

$$-\frac{d[Cl_2]}{dt} = k_2[ArH][Cl_2] \qquad (41)$$

The second-order rate constant, k_2, was found to be little affected by the addition of HCl, which strongly indicates that molecular chlorine is the electrophilic species. Robertson et al. (103), studied the effect of added electrolytes on the rate of chlorination of naphthalene and of m-xylene in anhydrous acetic acid. The rate of reaction was found to be accelerated by all electrolytes and the catalysis is, in fact, reasonably closely related to the degree of ionisation of the electrolyte. Anticatalysis either by acetate ions, by chlroide ions or by hydrogen chloride was not observed. These results rule out the possibility of reaction through Cl^+, $ClOAcH^+$, or ClOAc, and fit perfectly with the view that molecular chlorine is the chlorinating agent. The small amount of catalysis by electrolytes and the increase in rate found on addition of water to the solvent can be attributed to the fact that the transition state of the reaction involves polarisation of both the chlorine molecule and the aromatic compound. The transition state is more polar than the starting materials with the result that the reaction is facilitated by increase in ionising power of the environment (103,104).

Recently, Baciocchi et al. (96) have reported that 3-bromodurene and 3-bromo-6-deuterodurene react with molecular chlorine in acetic acid at very nearly the same rate. This zero isotope effect is to be compared with $k^H/k^D = 1.4$ found (96) in the bromination of these reactants. It would appear from this result, and from studies on bromination and iodination discussed earlier, that the magnitude of the isotope effect depends on the type of halogenation reaction, and usually follows the sequence, iodination > bromination > chlorination. Steric crowding in an intermediate, which can influence the relative rate of its return to reactants and decomposition to product, would, as previously discussed, account for such a trend.

Bromodecarboxylation

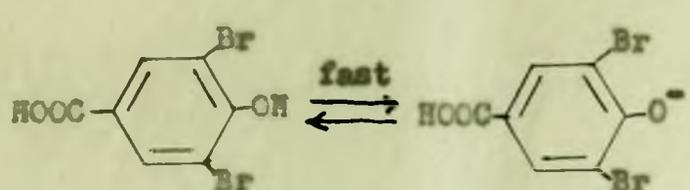
The direct replacement by bromine of a carboxyl group attached to an aromatic ring

$$ArCO_2H + Br_2 \longrightarrow Ar - Br + CO_2 + HBr$$

is a process known as bromodecarboxylation. This reaction is very common with aromatic carboxylic acids in which the carboxyl group is attached to a position which is ortho or para with respect to an electron releasing substituent. Thus, salicylic acid has been reported (105) to react with bromine to form dibromosalicylic acid, which in turn may undergo replacement of the carboxyl group by bromine to give tribromophenol. p-Hydroxybenzoic acid has been found to behave similarly on bromination (106) and iodination (107). Also, analogous halodecarboxylations have been reported for p-aminobenzoic acid (108), anthranilic acid (109), pyrrole-α-carboxylic acids (110) and α-furoic acids (111).

Grovenstein and Henderson (99) have carried out a thorough kinetic study of the bromodecarboxylation of 3,5-dibromo-4-hydroxy and 3,5-dibromo-2-hydroxybenzoic acids in 70 to 80 per cent acetic acid at 20°C. At constant hydrogen-ion and bromide-ion concentrations, both compounds undergo bromination to give tribromophenol at a rate proportional to the stoichiometric concentration of bromine and the aromatic substrate. The apparent second-order rate constants, k_{obs}, so obtained were found to vary with hydrogen- and bromide-ion concentrations. After correcting k_{obs} for conversion by the bromide ion of much of the bromine to unreactive Br_3^-, the corrected second-order rate constants, k°, still diminished with increasing bromide-ion concentration. Both hydrogen-ion and bromide-ion dependencies of rate can be explained by either of the following mechanisms, I and II, involving brominating agents Br_2 and H_2OBr^+, respectively.

Mechanism I Brominating Species Br_2



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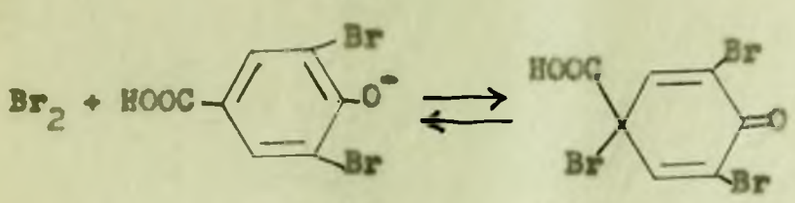

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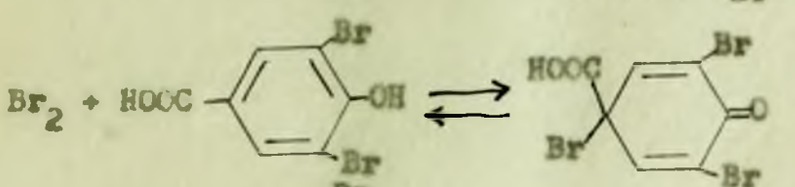

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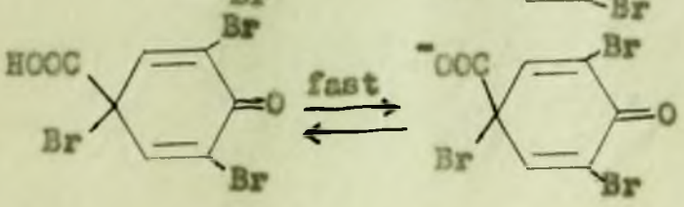

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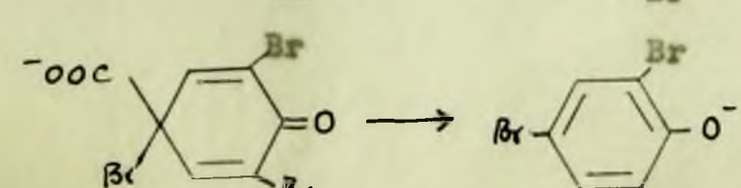
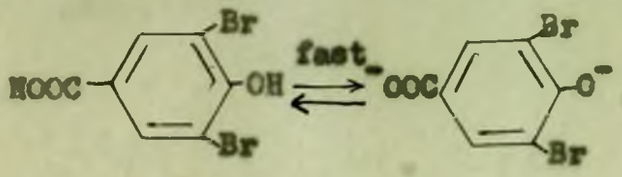


5

The rate expression for mechanism I (see page 575, Ref. 99) requires that, at constant hydrogen-ion concentration, a plot of $1/k^{\circ}[H^+]^2$ versus $[Br^-]$ should give a straight line. This was indeed observed for both 3,5-dibromo-4-hydroxy- and 3,5-dibromo-2-hydroxybenzoic acids.

Mechanism II Brominating Species H_2OBr^+

$$Br_2 + H_2O \overset{\text{fast}}{\rightleftharpoons} H_2OBr^+ + Br^- \qquad 6$$



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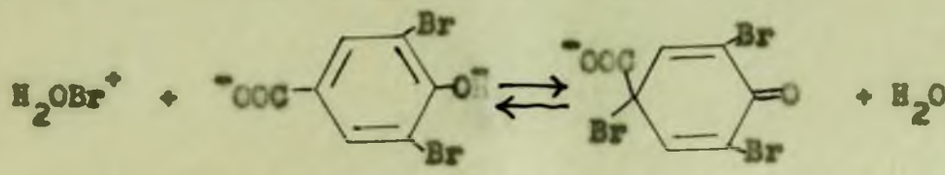

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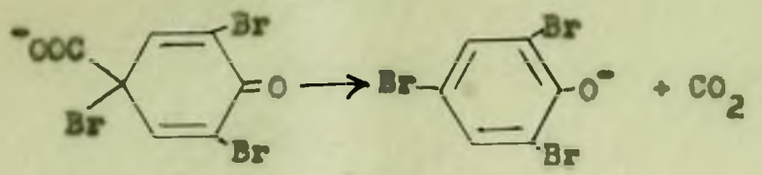

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The rate expression for mechanism II (see page 573, Ref. 99) requires that rate should be inversely proportional to the bromide-ion concentration and to the square of the hydrogen-ion concentration. The inverse squared hydrogen-ion dependence of rate was observed for both 3,5-dibromo-4-hydroxy- and 3,5-dibromo-2-hydroxybenzoic acids, while the inverse bromide-ion dependence was observed only for the former. It would appear then that mechanism II is eliminated as the reaction pathway for the bromodecarboxylation of 3,5-dibromo-2-hydroxybenzoic aicd, but that the kinetic results permit no distinction between the two mechanisms for the reaction of 3,5-dibromo-4-hydroxybenzoic acid.

As a means of distinguishing these two mechanisms for the bromodecarboxylation of 3,5-dibromo-4-hydroxybenzoic acid, Grovenstein and Kopp (12) have measured the kinetic carbon isotope effect as a function of bromide-ion concentration. It is important to note that this is the first and only successful application of this criterion of reaction mechanism for aromatic halogenation reported to date.

Inspection of mechanism II shows that a carbon isotope effect can be expected if step 9 is rate determining and no appreciable effect if the slow step is 8. In either case, however, the magnitude of the isotope effect should be independent of bromide-ion concentration. In mechanism I the rate-controlling steps, in the absence of bromide ion, are 2 and 3 and hence essentially every molecule of the quinoid intermediate formed will proceed to products. No carbon isotope effect would therefore be expected under these conditions. As the bromide-ion concentration is increased, the rate of return of the intermediate relative to its conversion into products will start to become significant, with the result that decomposition of the intermediate (which involves rupture of the C - C bond) becomes partially rate controlling. This should give rise to an appreciable isotope effect. Finally, in the presence of high bromide-ion concentration, the intermediate will be essentially in rapid, reversible equilibrium with the reactants, with the result that the decomposition of the intermediate is fully rate determining. Under these conditions a normal isotope effect should be observed.

The results obtained by Grovenstein and Kopp are tabulated in Table IV. From this table it is seen that in the absence of additional solutes bromodecarboxylation occurs with a ratio k^{12}/k^{13} of 1.002 ± 0.003

TABLE IV

KINETIC CARBON ISOTOPE EFFECTS FOR THE BROMODECARBOXYLATION OF 3,5-DIBROMO-4-HYDROXYBENZOIC ACID IN 80 PER CENT ACETIC ACID

(Temperature = 20.5 ± 0.5°)

Reagent Concentration	Per Cent Reaction (Range Represented)	k^{12}/k^{13}
None	12.5 - 25	1.000
	75 - 100	1.005
	13 - 26	1.000
	13 - 26	1.004
	75 - 100	1.002
		Mean 1.002 ± 0.003
0.3M HBr	0 - 10	1.046
	10 - 23.5	1.045
	23.5 - 37	1.045
	37 - 47.5	1.044
		Mean 1.045 ± 0.001
0.3M $HClO_4$	0 - 9	1.005
	0 - 20	1.006
	20 - 50	1.012
	79 - 100	1.019

or essentially unity. However, in the presence of 0.3M HBr this ratio becomes 1.045. That this result is not due solely to increase in hydrogen-ion concentration of the solution was shown by the fact that at 0.3M $HClO_4$ the observed ratio k^{12}/k^{13} is very much smaller than 1.045. Thus, the variation of the magnitude of carbon isotope effect due to change in bromide-ion concentration unambiguously confirms mechanism I for the bromodecarboxylation of 3,5-dibromo-4-hydroxybenzoic acid.

At 0.3M $HClO_4$, as the reaction progresses, there is a gradual rise in the ratio k^{12}/k^{13} from 1.005 to 1.019. This was accounted for on the basis that the added hydrogen ion and the bromide ion developed during the course of the reaction aid the reversal of the intermediate to reactants (step 3) compared to its conversion into products. In other words the contribution of the C - C bond rupture to the rate-controlling step becomes more and more important.

The carbon isotope effect study carried out by Grovenstein and Kopp is unique in the sense that they have demonstrated unambiguously the presence of a non-isolable, meta-stable intermediate in the bromodecarboxylation reaction of 3,5-dibromo-4-hydroxybenzoic acid. In the absence of HBr, this intermediate passes rapidly to the products of substitution without appreciable reversion to the reactants. In the presence of 0.3M perchloric acid after some 50 per cent reaction, sufficient bromide ion has been formed for this intermediate to partition approximately equally between reactants and products. Finally, in the presence of 0.3M hydrobromic acid, most of the intermediate formed reverts to reactants and a relatively small portion goes to the products;

i.e., the intermediate is essentially in equilibrium with respect to the reactants. That the isotope fractionation factor k^{12}/k^{13} has reached its maximum value under such conditions is confirmed by the fact that the experimental value, $k^{12}/k^{13} = 1.045$, compares favourably with the calculated value of 1.044 for a reaction involving rate-determining C - C bond rupture.

Bromodesulphonation

A reaction that is analogous to bromodecarboxylation is the direct replacement by bromine of the sulphonate group in aromatic sulphonates:

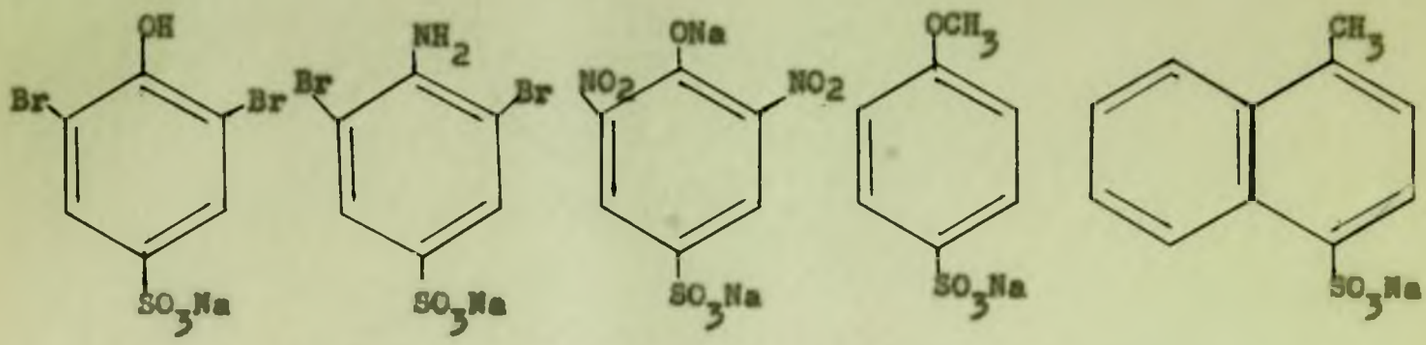
$$Ar - SO_3^- + Br_2 \longrightarrow Ar - Br + SO_3 + Br^-$$

This reaction, known as bromodesulphonation, is shown by aromatic sulphonates which have the sulphonate group in a position ortho or para to powerful electron-releasing groups in the aromatic ring. Thus, previous investigators (112 - 116) have found that the reaction is greatly facilitated by ortho or para amino, methoxy, hydroxy and even alkyl substituents. When these groups are meta to the sulphonate group, however, they do not promote bromodesulphonation. A great many sulphonates have been bromodesulphonated, practically all reactions having been carried out in aqueous solution.

For a given sulphonate, depending on the nature and position of the substituents on the ring, there results either a bromosulphonic acid (by ordinary bromination), an aryl bromide (by bromodesulphonation), or a mixture of both. Analogous reactions have been reported with chlorine as a desulphonating agent (117), but not with iodine. That the bromodesulphonation reaction does not proceed by a free-radical mechanism

is indicated by the fact that alkylbenzenesulphonates undergo bromination on the aromatic ring and not on the side chain (118).

The first mechanistic study of bromodesulphonation was made by Cannell (16,17), who in 1957 reported for a number of compounds (I to V) a rather thorough investigation of the kinetics of the process and, in particular, of the effect of added bromide ion on the reaction rate.



I II III IV V

For the reaction of sodium 3,5-dibromo-4-hydroxybenzenesulphonate (I), in which the sulphonate group is <u>para</u> to the highly activating hydroxyl group, both kinetic and spectral studies provided evidence for the existence of a relatively long-lived quinoid-type intermediate whose decomposition is the rate-determining step in the bromodesulphonation reaction.

For the less highly activated sulphonates, sodium 3,5-dibromo-4-aminobenzenesulphonate (II), disodium 3,5-dinitro-4-hydroxybenzenesulphonate (III), sodium p-methoxybenzenesulphonate (IV), and potassium 1-methylnaphthalene-4-sulphonate (V), where no such intermediate could be detected spectroscopically, Cannell found that, with the exception of V, the rate of reaction, as measured by the rate of disappearance of bromine, decreased with increasing bromide-ion concentration by an

amount greater than that due to the conversion of Br_2 to the unreactive Br_3^-. It was found that, at constant bromide-ion concentration, the bromodesulphonation reaction of II, III, IV, and V showed second-order kinetics, first in the stoichiometric concentration of bromine, as determined by titration with thiosulphate, and first in stoichiometric concentration of aryl sulphonate:

$$-\frac{d[B]}{dt} = k_{obs}[B][Ar - SO_3^-] \qquad (42)$$

where $[B]$ is the concentration of bromine, i.e., $[Br_2] + [Br_3^-]$, $[Ar - SO_3^-]$ is the concentration of sulphonate and k_{obs} is the observed specific reaction rate constant. The rate of bromination was depressed by added bromide ion as would be expected from the decrease in the concentration of free bromine due to the formation of tribromide ion:

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

for which the equilibrium constant, K, is expressed as

$$K = \frac{[Br_3^-]}{[Br^-][Br_2]} .$$

Now the kinetic expression for a second-order reaction between free bromine and the aryl sulphonate has the form:

$$-\frac{d[Br_2]}{dt} = k[Br_2][Ar - SO_3^-] \qquad (43)$$

where $[Br_2]$ is the concentration of free bromine and k is the specific reaction rate constant. Taking into account the equilibrium involving tribromide ion, equation 43 becomes

$$-\frac{d[Br_2]}{dt} = -\frac{d[B]}{dt} = \frac{k}{1 + K[Br^-]}[B][Ar - SO_3^-] \qquad (44)$$

Since in any given kinetic experiment the concentration of bromide ion is effectively constant, the term $k/1 + K[Br^-]$ will be constant and will be equal to the experimentally observed rate constant, k_{obs}, of equation 42. In other words, the quantity $k_{obs}[1 + K[Br^-]]$ should be a constant and it was indeed found to be so for the bromination of potassium 1-methylnaphthalene-4-sulphonate (V). But for the other three sulphonates studied (II, III and IV), the depression in rate caused by bromide ion was considerably greater than that predicted by equation 44.

The depression in the rate caused by bromide ion over and above that which can be attributed to tribromide ion formation was accounted for by Cannell by the following mechanism (Mechanism A) involving the formation of a quinoid intermediate, $\overset{+}{Ar}\!<\!\begin{matrix}Br\\SO_3^-\end{matrix}$:

Mechanism A

$$Ar - SO_3^- + Br_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \overset{+}{Ar}\!<\!\begin{matrix}Br\\SO_3^-\end{matrix} + Br^-$$

$$\overset{+}{Ar}\!<\!\begin{matrix}Br\\SO_3^-\end{matrix} \xrightarrow{k_3} Ar - Br + SO_3$$

Applying the steady-state treatment to this mechanism, the following kinetic expression can be derived:

$$-\frac{d[B]}{dt} = \frac{1}{1 + K[Br^-]} \cdot \frac{k_1 k_3}{k_2[Br^-] + k_3} \cdot [B][Ar - SO_3^-] \qquad (45)$$

from which it follows that

$$k_{obs} = \frac{k_1 k_3}{k_2 [Br^-] + k_3} \cdot \frac{1}{1 + K [Br^-]} \qquad (46)$$

or

$$\frac{1}{k_{obs}[1 + K [Br^-]]} = \frac{k_2}{k_1 k_3} [Br^-] + \frac{1}{k_1} \qquad (47)$$

According to equation 47, for a series of kinetic experiments at different bromide-ion concentrations, a plot of $\left\{ k_{obs} [1 + K [Br^-]] \right\}^{-1}$ versus $[Br^-]$ should give a straight line whose slope is $k_2/k_1 k_3$ and whose intercept, at $[Br^-] = 0$, is $1/k_1$. Such a linear relationship was indeed observed by Cannell for sodium 3,5-dibromo-4-aminobenzenesulphonate (II) and sodium p-methoxybenzenesulphonate (IV), over a range of bromide-ion concentrations from zero to 0.15M. For disodium 3,5-dinitro-4-hydroxybenzenesulphonate (III), sufficient kinetic measurements were not made to establish this linear relationship, although the depression in rate by added bromide ion was close to that observed for II.

For potassium 1-methylnaphthalene-4-sulphonate as previously stated, Cannell found that there was no sufficient depression in rate by added bromide ion beyond that which could be accounted for by the equilibrium between Br_2 and Br_3^-. In other words, the bromination rate was in accordance with equation 44. This observation can be accounted for either by a two-step mechanism with $k_3 \gg k_2[Br^-]$ or by a one-step process. Indeed, Cannell himself states that "the kinetics require only a transition state and it is not necessary to propose a reaction intermediate". A one-step process for V does not, in fact, seem unreasonable since the quinoid configuration, stabilised by hyperconjugation only, would be expected to possess a higher energy than in

the case of the more highly activated systems II, III and IV and might, therefore, not correspond to a potential energy minimum along the reaction co-ordinate curve.

It is most important to note that a depression in rate with increasing bromide-ion concentration can be accommodated fully as well by another mechanism not considered by Cannell. This mechanism (Mechanism B) is analogous to that proposed by Painter and Soper (page 36) for the iodination of phenols and aromatic amines, and involves Br^+ (or H_2OBr^+) as the brominating species.

Mechanism B

$$Br_2 + H_2O \underset{}{\overset{K'}{\rightleftharpoons}} H_2OBr^+ + Br^-$$

$$H_2OBr^+ + Ar - SO_3^- \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} Ar\overset{Br}{\underset{SO_3^-}{}}{}^+ + H_2O$$

$$Ar\overset{Br}{\underset{SO_3^-}{}}{}^+ \xrightarrow{k_3'} Ar - Br + SO_3$$

Applying the steady-state treatment, the following rate equation can be derived:

$$-\frac{d\ B}{dt} = \frac{K'}{1 + K\ Br^-} \cdot \frac{k_1'k_3'}{k_2' + k_3'} \cdot \frac{[B]\ [Ar - SO_3^-]}{[Br^-]} \qquad (48)$$

where K' and k_2' include the concentration of the solvent water. It follows, therefore, that, at constant bromide-ion concentration:

$$k_{obs} = \frac{K'k_1'k_3'}{(k_2' + k_3')\ [1 + K\ [Br^-]]\ [Br^-]} \qquad (49)$$

If instead of the two-step process involving the quinoid intermediate, $\overset{+}{Ar}<^{Br}_{SO_3^-}$, the brominating species Br^+ (or H_2OBr^+) were to give product directly in a single step having a rate constant k_4 (as previously considered for iodination, page 37), an equation similar to 49, namely,

$$k_{obs} = \frac{K'k_4}{[1 + K[Br^-]][Br^-]} \qquad (49a)$$

would be followed. In either case one would expect a straight line relationship for the plot of k_{obs} versus $1/[1 + K[Br^-]][Br^-]$.

Since the two mechanisms A and B lead to quite different rate expressions it might be expected that kinetic studies would distinguish between them. Examination of equation 45, however, shows that under the circumstance $k_2[Br^-] \gg k_3$, mechanism A leads to a rate expression

$$-\frac{d[B]}{dt} = \frac{k_1k_3}{k_2[1 + K[Br^-][Br^-]} [B][ArSO_3^-]$$

and hence, like mechanism B, will give a straight line plot of k_{obs} versus $1/[1 + K[Br^-]][Br^-]$. Now when the rate data for compounds II and III were analysed by Cannell in terms of mechanism A there was obtained a k_2/k_3 ratio such that $k_2[Br^-]$ is large relative to k_3, even at quite low bromide-ion concentrations. It is therefore not surprising for the present author to find that Cannell's data for these compounds give a good linear plot of k_{obs} versus $1/[1 + K[Br^-]][Br^-]$, and hence do not distinguish between the two mechanisms.

The data obtained by Cannell for sodium p-methoxybenzene-sulphonate, on the other hand, when fitted to equation 47 gave a k_2/k_3 ratio of only 22 and, therefore, $k_2[Br^-] \not\gg k_3$ at low bromide-ion

concentrations. Hence, reaction by mechanism A would not be expected to give a straight line in a plot of k_{obs} versus $1/[1 + K[Br^-]][Br^-]$. Indeed, such a plot of Cannell's data was found by the present author to be distinctly non-linear and the result was considered at the time to provide support for the two-step mechanism with molecular bromine as the brominating species.

Unfortunately it was disclosed in our early studies that Cannell's kinetic data on sodium p-methoxybenzenesulphonate (IV) are unreliable, as he has overlooked the important fact that bromination of IV results in two competing reactions, bromodesulphonation and bromodeprotonation, the latter resulting in the substitution of bromine for a hydrogen atom ortho to the methoxy group. As will be seen later in this thesis, even at zero bromide-ion concentration as much as twelve per cent of the bromine consumed is by bromodeprotonation, and at 0.1M bromide-ion concentration this reaction accounts for about fifty per cent of the total reaction. It can be concluded, therefore, that a plot of k_{obs} versus $\{[1 + K[Br^-]][Br^-]\}^{-1}$ (where k_{obs} is the rate constant for disappearance of Br_2) is meaningless in terms of reaction mechanism for the bromination of sodium p-methoxybenzenesulphonate.

In summary then, it may be concluded that for the three compounds, II, III and IV whose bromodesulphonation rates are suppressed by bromide ion, Cannell's kinetic studies do not provide a means of distinguishing between a two-stage mechanism with Br_2 as the brominating agent and a one- or two-stage mechanism with Br^+ (or H_2OBr^+) as the brominating agent. In other words, exactly the same ambiguity would appear to exist here as in the iodination of phenol where a suppression of rate by iodide ion could be interpreted in terms of either one of two mechanisms.

A distinction between mechanisms A and B can be made by measuring the kinetic sulphur isotope effect as a function of bromide-ion concentration. The basis of the kinetic isotope effect approach is outlined in the following paragraphs.

From the kinetic equation 46 derived for mechanism A, which involves molecular bromine as the brominating species, the ratio of the rate constants for the light and heavy sulphur isotopes, k^{32}/k^{34}, is given by the equation:

$$(k^{32}/k^{34})_{obs} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{k_3^{32}}{k_3^{34}} \cdot \frac{k_2^{34}[Br^-] + k_3^{34}}{k_2^{32}[Br^-] + k_3^{32}} \qquad (50)$$

At zero or very low bromide-ion concentration, this becomes

$$(k^{32}/k^{34})_{obs} = k_1^{32}/k_1^{34}$$

The observed isotope effect is, therefore, a measure of the relative rates with which the two isotopic species form a quinoid intermediate. Since this step does not involve the rupture of a C - S bond, the isotope effect can be expected to be small or zero ($k_1^{32}/k_1^{34} \simeq 1$).

At bromide-ion concentrations sufficiently high such that $k_2[Br^-] \gg k_3$,

$$(k^{32}/k^{34})_{obs} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{k_2^{34}}{k_2^{32}} \cdot \frac{k_3^{32}}{k_3^{34}}$$

This expression now includes a rate-constant ratio, k_3^{32}/k_3^{34}, for the step in which a C - S bond is being ruptured and the isotope effect (a primary one) should be of normal magnitude. Thus, it can be seen that for reaction by mechanism A the isotope effect can be varied from

zero to normal magnitude by changing the concentration of bromide ion. In other words, the isotope effect should be dependent on the concentration of bromide ion.

From the kinetic equation 49 derived for mechanism B, which involves Br^+ (or H_2OBr^+) as the brominating species, the ratio of the rate constants for light and heavy sulphur isotopes, k^{32}/k^{34}, is given by the equation:

$$(k^{32}/k^{34})_{obs} = \frac{k_1'^{32}}{k_1'^{34}} \cdot \frac{k_3'^{32}}{k_3'^{34}} \cdot \frac{k_2'^{34} + k_3'^{34}}{k_2'^{32} + k_3'^{32}} \qquad (51)$$

Since the bromide-ion concentration, $[Br^-]$, does not appear in this expression, the isotope effect should be independent of it. If $k_3' \gg k_2'$, the isotope effect will be zero or very small; if $k_3' \ll k_2'$, the effect will be a normal one, but in either case the isotope effect will be independent of bromide-ion concentration. Similarly, for a one-step bromination with Br^+ (or H_2OBr^+) as the brominating species:

$$(k^{32}/k^{34})_{obs} = k_4^{32}/k_4^{34}$$

This also should give rise to an isotope effect whose magnitude is independent of bromide-ion concentration. Thus the observation of an isotope effect varying with bromide-ion concentration could be considered as unequivocal evidence against mechanism B and would provide strong support for mechanism A.

As mentioned before, Cannell's kinetic results for potassium 1-methylnaphthalene-4-sulphonate (V) show that $k_{obs}[1 + K[Br^-]]$ is nearly a constant in the range of bromide-ion concentrations from zero to 0.15M. Such an observation (as seen in the bromination of

o-nitroanisole, 2,6-dibromophenol, anisoles etc.; see page 47) clearly eliminates Br^+ (or H_2OBr^+) as the brominating species and supports either a one-step process or a two-step process with $k_2 [Br^-] \ll k_3$, both involving Br_2 as the brominating species. Kinetic sulphur isotope effect measurements might here also be expected to shed some light on this question of mechanism for the bromodesulphonation reaction of V. The basis of the isotope effect study that was made is outlined below.

If the reaction is step-wise, with the formation of the intermediate being rate determining, then

$$(k^{32}/k^{34})_{obs} = k_1^{32}/k_1^{34}$$

and the isotope effect should be zero or very close to it (at the most a few-tenths of a per cent). On the other hand, if the reaction involves a single-step, then of course the C - S bond is being ruptured in the process and a sulphur isotope effect should result. It is true that the magnitude of this effect would be determined by the extent of bond rupture in the transition state and, conceivably, this could be such as to give rise to only a very small effect. If this result were observed, then no distinction could be drawn between the two mechanisms, although one would have gained a valuable insight into the extent to which bond rupture has proceeded in the highest energy state along the reaction coordinate. On the other hand, if a normal sulphur isotope effect were to be found for this system, say of the order of one to two per cent, this would clearly eliminate the two-stage mechanism and provide strong evidence in support of the one-step process.

EXPERIMENTAL

General Discussion

When the work of this thesis was initiated it appeared that Cannell's kinetic results had provided strong evidence in support of the two-step mechanism for the bromodesulphonation of sodium 3,5-dibromo-4-aminobenzenesulphonate (II), disodium 3,5-dinitro-4-hydroxybenzenesulphonate (III), and sodium p-methoxybenzenesulphonate (IV), whose reaction rates are dependent on the concentration of bromide ion. His data, however, could not establish the mechanism of bromodesulphonation of potassium 1-methylnaphthalene-4-sulphonate (V). In order to use kinetic sulphur isotope effects as a criterion to distinguish between one- and two-step mechanisms for the bromodesulphonation of this latter compound, it was felt necessary first to test this tool by applying it to the bromodesulphonation of a compound which appeared on the basis of kinetic results to proceed through a two-stage mechanism.

Of the three compounds, II, III, and IV, whose rates of bromination are suppressed by bromide ion beyond that attributable to Br_3^- formation, sodium p-methoxybenzenesulphonate (IV), seemed to be the most suitable for this test for the following reasons. Firstly, its reaction rate in the absence of bromide ion is sufficiently low to permit the use of concentrations convenient for the isotope effect experiments and, furthermore, the bromide ion developed during the course of the reaction does not significantly affect the constancy of the rate constant, at

least during the extent of reaction chosen for the study. Secondly, the ratio k_2/k_3 is of reasonable magnitude, namely 22 (as found by Cannell), to achieve the required condition $k_2[Br^-] \gg k_3$ at attainable concentrations of bromide ion.

Initially, it was assumed that Cannell's kinetic results on sodium p-methoxybenzenesulphonate were reliable, and hence provided sound evidence for the two-step mechanism with Br_2 as the brominating species. Preliminary quantitative experiments involving the determination of sulphate yield in the partial bromodesulphonation of sodium p-methoxybenzenesulphonate disclosed the surprising fact that this yield is considerably less than expected on the basis of the quantity of bromine consumed. This suggested that the bromination of sodium p-methoxybenzenesulphonate results in two concurrent reactions, bromodesulphonation and bromodeprotonation, the latter being the ordinary halogenation of the benzene ring in a position <u>ortho</u> to the methoxy group. This was further confirmed by product analysis: by isolating separately from the reaction both p-bromoanisole and sodium 3-bromo-4-methoxybenzenesulphonate, these being, respectively, the bromodesulphonated and bromodeprotonated products.

Furthermore, it was established that these two competing reactions are of the same kinetic order by the observation that, at a given bromide-ion concentration, the ratio of the yield of sulphate to the total amount of bromine consumed is independent of the ratio of the two reactants or the extent of total reaction. Since these two competing reactions are of the same kinetic order, it is therefore possible to evaluate their individual rate constants simply from a

knowledge of the total rate of bromination and the yield of sulphate (as related to the total amount of bromine consumed). This being the case, it was decided to make a careful reinvestigation of the kinetics of bromination of sodium p-methoxybenzenesulphonate with the determination of not only the total rate of bromination but also the yield of sulphate at different bromide-ion concentrations. The range of bromide-ion concentrations studied was from zero to 0.5M compared to Cannell's range of zero to 0.15M.

When the new kinetic data for the bromodesulphonation reaction of sodium p-methoxybenzenesulphonate was analyzed, it was found that, although the results favour a two-step mechanism involving Br_2 as the brominating species, a one- or two-step mechanism with Br^+ (or H_2OBr^+) as the brominating species cannot be completely eliminated. It now became apparent that a study of kinetic sulphur isotope effect as a function of bromide-ion concentration for sodium p-methoxybenzene-sulphonate was desirable in order to confirm the mechanism of the bromodesulphonation of this compound and was not, as originally intended, to be simply a test of reaction mechanism criterion.

When attention was turned to potassium 1-methylnaphthalene-4-sulphonate, the compound for which Cannell had found no rate dependence on the concentration of bromide ion and for which it was hoped that kinetic sulphur isotope effect measurements might distinguish between the one- and two-step processes, again it was found that bromination results in two competing reactions, bromodeprotonation and bromo-desulphonation. Furthermore, there were strong indications that Cannell's salt was far from being of sufficient purity for reliable

kinetic measurements. Consequently, with this compound, also, the sulphur isotope effect investigation was preceded by a careful kinetic study involving determination of total bromination rates and yield of sulphate at different bromide-ion concentrations. These results revealed that, contrary to Cannell's findings, the rate of the bromodesulphonation reaction is indeed suppressed somewhat by added bromide ion, although not to an extent that cannot be reasonably attributed to a salt effect. Nevertheless, this result suggested the desirability of studying the kinetic isotope effect, not just at one bromide-ion concentration as had been originally intended, but at different concentrations, with the view to obtaining strong supporting evidence for the two-step mechanism through a variation of the magnitude of the effect with changes in the concentration of this ion.

It will be recalled that, although in the last few years a large number of hydrogen isotope effect studies have been made for ordinary aromatic halogenation, no successful effort to bring about a variation in the magnitude of the effect by varying halide-ion concentration has been reported. In other words, there is to date no unambiguous evidence for the two-stage mechanism in aromatic halodeprotonation reactions. Presumably one of the reasons for this is the low solubility of the organic compounds and of halide ions in the solvents chosen.

It seemed to the present author that the bromination of sodium p-methoxybenzenesulphonate might provide an excellent reaction in which to attempt to achieve this kinetic isotope effect test of the mechanism of bromodeprotonation. It is true that the bromodeprotonation reaction

is one of two competing processes, but its contribution to the overall rate can readily be assessed if the specific reaction rate constant for total bromination and the yield of sulphate are precisely known. Furthermore, because of the solubilizing action of the sulphonate group in the solvent water, wide variations in the bromide-ion concentration can be achieved. Encouragement for this attempt was found in the results of the rate studies of bromodeprotonation which showed a small, but definite, depression in rate with increasing bromide-ion concentration. It was recognised that this could be due to a salt effect (98), but it at least suggested the possibility that perhaps one is dealing here with a system involving some reversion of the quinoid intermediate to the reactants at the expense of its decomposition into products.

The experimental part is developed in the following way. First, the methods adopted in the preparation of all the starting materials and the product analysis are described. Next, the procedures used in the quantitative study, namely, the kinetics of bromination and sulphate-yield determination are dealt with. Finally, the preparation of samples of sulphur dioxide for isotope abundance measurements is given.

Preparation of Compounds

Introduction

Sodium p-methoxybenzenesulphonate and potassium 1-methylnaphthalene-4-sulphonate have been prepared by sulphonating anisole and α-methylnaphthalene, respectively. The usual method employed in sulphonation has been to sulphonate the aromatic compound by means of concentrated sulphuric acid. One of the disadvantages in using concentrated sulphuric acid as a sulphonating agent is that it yields more than one

substitution product. Chlorosulphonic acid is also an effective sulphonating agent, however, and under suitable conditions its attack yields only the para-sulphonic acid. Fieser et al. (119) used chlorosulphonic acid in the sulphonation of α-methylnaphthalene; their procedure was an improvement on a similar method adopted by Veseley and Stursa (120). Fieser's procedure, also used by Steiger (121) in the sulphonation of α-methylnaphthalene, was employed in the present work for the sulphonation of anisole, 2,4,6-trideuteroanisole and α-methylnaphthalene.

Several attempts were made to prepare sodium o, o'-deuterated-p-methoxybenzenesulphonate, by direct exchange between sodium p-methoxybenzenesulphonate and deuterosulphuric acid. The results were unsuccessful and it was concluded that the sulphonic acid group has a pronounced deactivating effect in the exchange of hydrogen atoms on the benzene ring. A similar conclusion was reached by Ingold et al. (122) after their unsuccessful attempts to deuterate benzenesulphonic acid by direct exchange with deuterosulphuric acid. An alternative method, is to prepare 2,4,6-trideuteroanisole first and then sulphonate it under conditions such that there would be no exchange in the ortho positions. The preparation of 2,4,6-trideuteroanisole can be accomplished in two ways: either by the methylation of 2,4,6-trideuterophenol or by the deuteration of anisole itself. For economic and practical reasons, the method adopted by Brown et al. (123), involving direct exchange between anisole and deuteroacetic acid (CH_3COOD) using sulphuric acid as catalyst, was found to be most suitable. This method has a distinct advantage over the direct exchange of anisole with deuterosulphuric acid,

in the following respects: the deuterium source (D_2O) needed for the operations is much less; the yield of deuteroanisole is greater; and the exchange is exclusively in the 2,4,6 positions of anisole, as desired.

For the preparation of potassium 1-methylnaphthalene-4-sulphonate, direct sulphonation of α-methylnaphthalene by means of chlorosulphonic acid as used by Cannell (17) was first tried. The sulphonate obtained after several recrystallisations showed, however, unsteady rate constants when the rate of bromination was measured and hence was impure. It was found necessary, therefore, to employ a different method for purifying potassium 1-methylnaphthalene-4-sulphonate. Of the two purification methods tried for this purpose, only one proved to be successful.

The unsuccessful method was to convert the sulphonate into the p-toluidine salt, repeatedly recrystallise the p-toluidine salt to constant melting point, and then to convert it back to the sulphonate. Although this method yielded a p-toluidine derivative of melting point (234.8 - 235.8°C), much higher than that reported by Cannell (227 - 229°C), after its reconversion to the sulphonate the material still showed unsteady rate constants.

The second method was to convert the sulphonate into the sulphonyl chloride, repeatedly recrystallise the sulphonyl chloride to constant melting point, and then convert it back to the sulphonate. Despite such an elaborate procedure the final product obtained was found to be only 93 per cent pure, as indicated by the data on complete bromodesulphonation. This material, however, did show steady rate

constants and was used subsequently for the quantitative work. There was evidence that the 7 per cent impurity is an unreactive isomer of the desired compound, probably potassium 1-methylnaphthalene-5-sulphonate.

Reagents

Anisole: Eastman Kodak White Label. This was dried and fractionally distilled; the middle fraction, boiling at 153-153.5°C, was collected.

α-Methylnaphthalene: L. Light & Co., England. This material was claimed to be 99 per cent pure.

Chlorosulphonic acid: B. D. H. Laboratory Reagent Grade. This was distilled twice before use.

Carbon tetrachloride: Mallinckrodt Analytical Reagent. This was dried and fractionally distilled; the middle fraction, boiling at 76.5 - 77°C, was collected.

Phosphorus pentachloride: Mallinckrodt Analytical Reagent.

Potassium hydroxide: B. D. H. Analar Reagent.

Deuterium oxide: This was obtained from Dr. R. H. Tomlinson, McMaster University. The material, claimed to be 99.4 per cent pure, came from Oak Ridge National Laboratory, Tennessee.

Deuterosulphuric acid: This was obtained from Dr. E. A. Robinson, McMaster University. The material was prepared by distilling sulphur trioxide into deuterium oxide and later adjusting the freezing point to 14.21°C (the freezing point of pure deuterosulphuric acid) with deuterium oxide.

Acetic anhydride: Fisher Certified Reagent Grade. This was fractionally distilled through a long column and the middle fraction, boiling at 139.5 - 140.5°C, was collected. This procedure was to ensure that the substance was free of moisture and acetic acid.

Preparation of 2,4,6-Trideuteroanisole

The deuteroacetic acid (CH_3COOD) that was required was prepared by treating acetic anhydride (325 ml; 3.45 mole) with deuterium oxide (63 ml; 3.45 mole). The mixture was heated under reflux for ten hours, taking every precaution to exclude moisture. To the resulting deuteroacetic acid was added deuterosulphuric acid (4 ml) as catalyst.

Anisole (25 g; 0.23 mole) was treated with deuteroacetic acid (160 ml; 2.76 mole) in a 500 ml round-bottomed flask whose upper neck was constricted for vacuum sealing. The system was frozen by means of liquid nitrogen and the flask was evacuated. With the stopcock closed, the contents were allowed to thaw and were then frozen again by means of liquid nitrogen. The system was again evacuated and then the flask was sealed off. The flask, enclosed in a copper wire net, was immersed in an oil bath at 90 ± 0.1°C for 48 hours. At the end of this period the flask was removed and well cooled. It was then opened and its contents were carefully poured on to chipped ice. In the meantime, 320 ml of 9M sodium hydroxide solution were cooled in ice. The solution in chipped ice was then slowly poured into the alkali solution with constant stirring, keeping the system well-cooled. When the entire solution was added the final pH was about 8.

The separated anisole was extracted with ether in many portions and the combined extracts were repeatedly washed with water until the washings were neutral to litmus. The ether extract was then dried thoroughly with anhydrous sodium sulphate and the ether was finally removed by vacuum distillation. The recovered anisole was further subjected to two similar exchanges, using each time 120 ml (2.07 mole)

of deuteroacetic acid. The alkali used for neutralisation after these exchanges was 240 ml of 9M sodium hydroxide. In each of the three exchanges there was approximately 25 - 30 per cent loss of anisole, the major loss being almost certainly due to its destruction on prolonged heating with the acid. The anisole finally obtained was distilled over metallic sodium and the distillate boiling at 153 - 153.5°C was collected. The final yield was 9 g, which is about 36 per cent of the starting material.

An NMR spectrum of the deuteroanisole in carbon tetrachloride (the solution was ∿ 25 per cent by weight) is shown in Fig. 4 and that of ordinary anisole obtained under similar conditions in Fig. 3. It can be seen that the multiple spectrum of the five hydrogens of the benzene ring in ordinary anisole is completely replaced by a single sharp peak (of 3,5-meta protons) in the deuteroanisole. The latter peak has two-thirds the area of that of the methyl protons, showing that the anisole is essentially completely deuterated in the 2,4,6 positions.

Preparation of Sodium p-Methoxybenzenesulphonate

Freshly distilled anisole (218 ml; 2 mole) and carbon tetrachloride (600 ml) were placed in a two-litre, three-necked round-bottomed flask. The flask was provided with a sturdy mercury-sealed stirrer of tantalum wire or glass disc, an inlet for a dropping funnel containing chlorosulphonic acid (117 ml; 1.8 mole), and another outlet attached to a drying tube packed with fused calcium chloride. An auxiliary connection was made to this drying tube to lead off the hydrogen chloride that is produced.

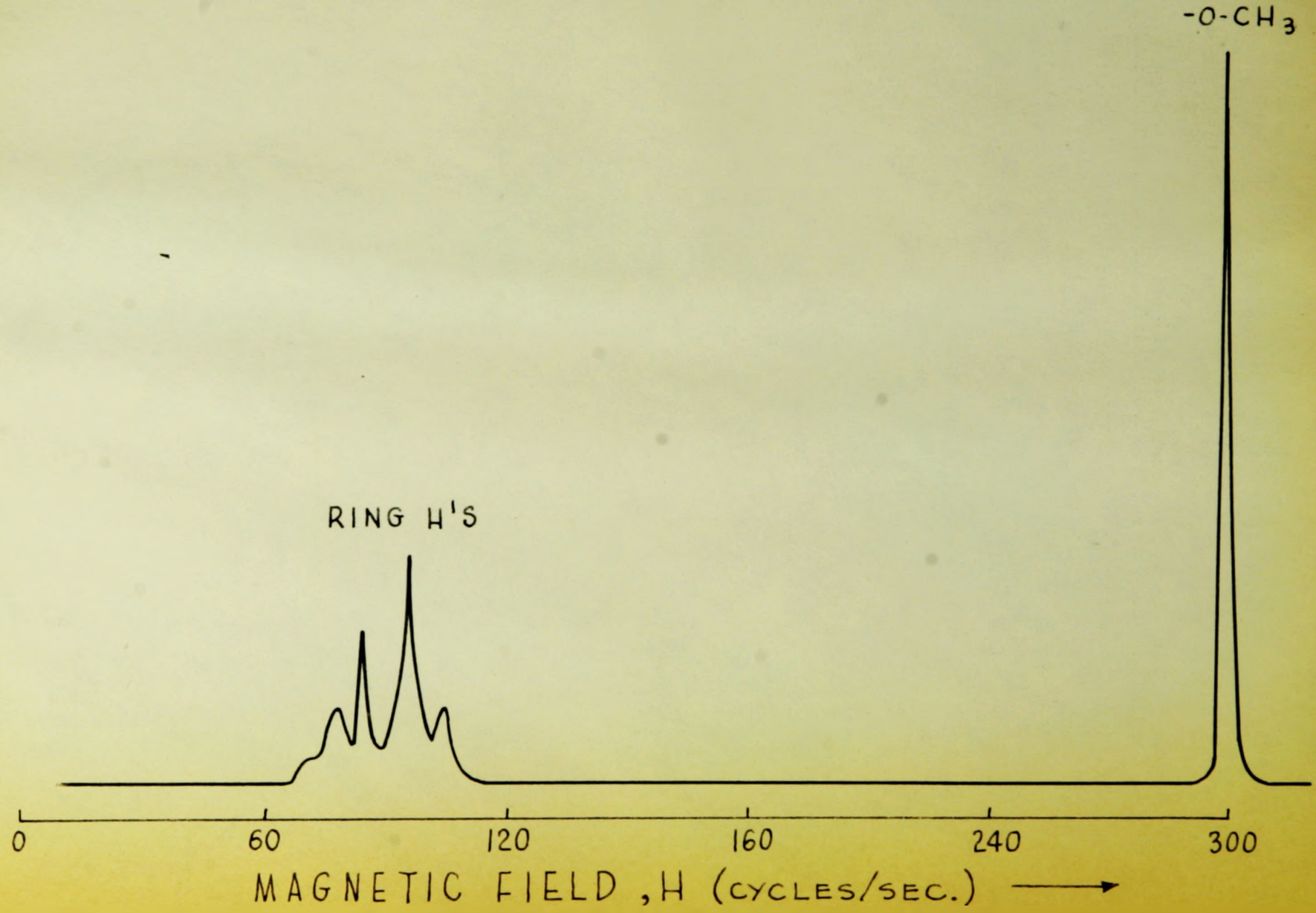


FIG.3. PROTON NMR SPECTRUM OF ANISOLE AT 60 MC./SEC. IN CCL_4

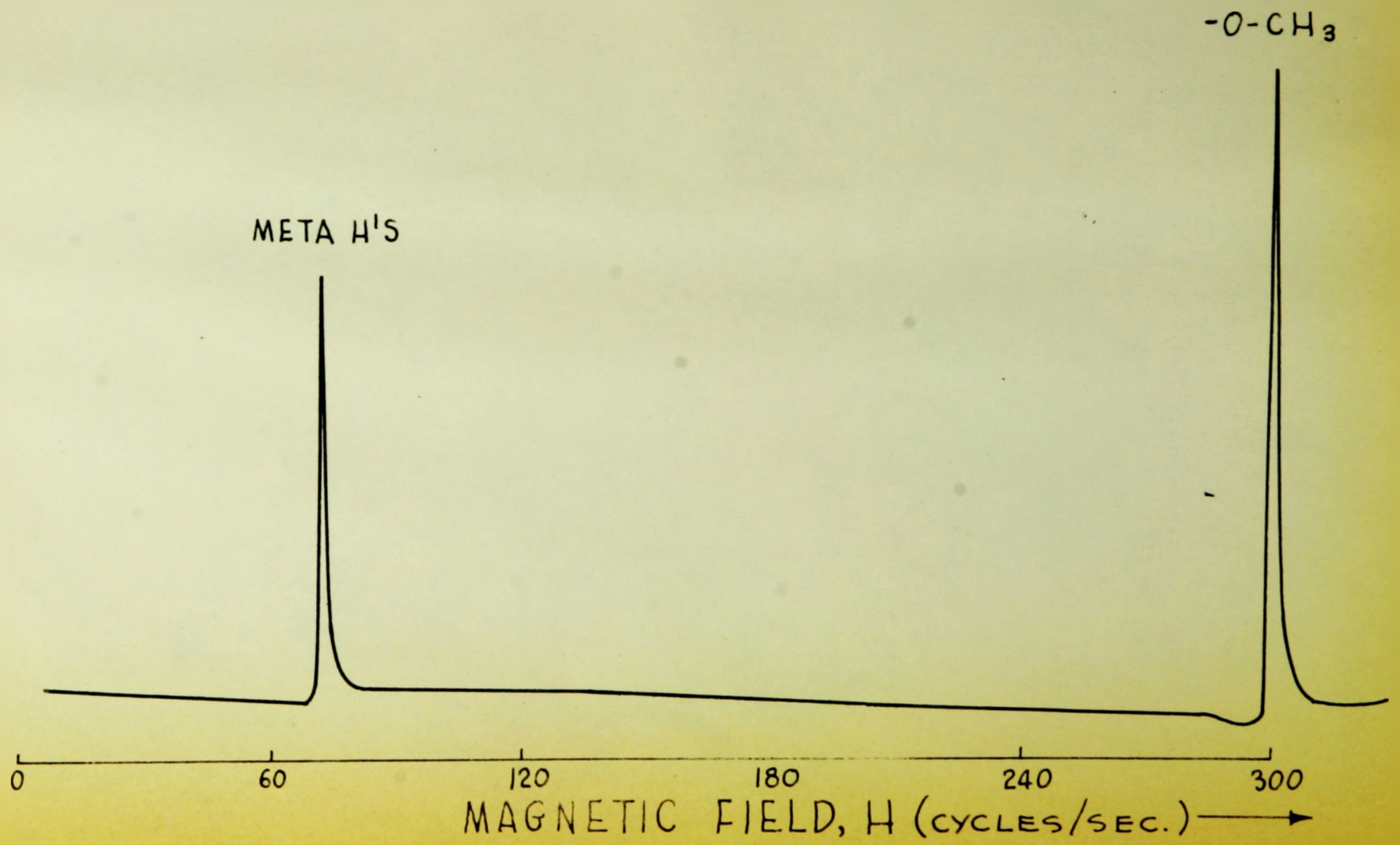


FIG. 4. PROTON NMR SPECTRUM OF 2,4,6-TRIDEUTEROANISOLE AT 60 Mc/SEC. IN CCl_4.

The flask was cooled to a temperature close to -20°C and the contents kept stirred efficiently. The acid was then added drop by drop at a rate such that 1 1/2 - 2 hours was taken for complete addition, the temperature being kept at about -20°C. This slow addition of acid was necessary to keep the reaction fully under control. After some time, when the sulphonic acid began to separate as a solid, the rate of stirring was increased in order to keep the contents vigorously stirred. After the addition of the acid, the stirring was continued until the evolution of hydrogen chloride ceased. The flask was then allowed to warm to room temperature. Enough distilled water was then added to dissolve all the sulphonic acid. The aqueous layer was separated, washed twice with fresh carbon tetrachloride to remove any unreacted anisole, and then filtered from any insoluble material. The clear aqueous solution was carefully neutralised with saturated sodium carbonate solution to a pH of 7 to 8 and then concentrated by evaporation to the crystallization stage. After the solution was cooled to room temperature, further separation of the salt was allowed to take place by cooling to ice-cold temperature.

The separated sulphonate was sucked dry, dried in a vacuum desiccator, and finally in an oven at 110°C. This gave a yield of 180 g. Qualitative tests showed the presence of traces of chloride but no sulphate. The sulphonate was crystallized once more from water and then twice from aqueous ethanol. Cannell's kinetic experiment on the rate of bromination (Expt. 26, page 2935 of Ref. 17) was repeated on this sulphonate. A steady rate constant, 0.0253 l $mole^{-1}$ sec^{-1} compared to Cannell's value, 0.0254 l $mole^{-1}$ sec^{-1}, was obtained. The

purity of the sulphonate was further established by estimating the yield of sulphate, gravimetrically, on complete bromodesulphonation. In several experiments, yields in the range 99.6 - 99.9 per cent were obtained in remarkable agreement with the theoretical yield of 100 per cent.

Preparation of Sodium o,o'-deuterated-p-methoxybenzenesulphonate

The procedure used for the sulphonation of 2,4,6-trideutero-anisole was essentially the same as that used for the sulphonation of ordinary anisole. However, to obtain the best yield of the final labelled sulphonate, the procedure had to be modified, particularly in some of the final steps. This procedure was first carried out on ordinary anisole in order to check the purity and yield of the sulphonate. After this modified procedure was found to be efficient, it was carefully applied to the labelled anisole.

2,4,6-Trideuteroanisole (9 g; 0.083 mole) was sulphonated with chlorosulphonic acid (9.3 g; 0.08 mole) in 30 ml of carbon tetrachloride as solvent, using the procedure described previously. The sulphonic acid was filtered and freed from any unreacted anisole by washing it with carbon tetrachloride. The solid acid was then carefully added to an ice-cold saturated solution of sodium carbonate with constant stirring such that when all the sulphonic acid was added the pH of the solution was about 7 to 8. The solution was then vacuum distilled at 50°C to remove water. The dry solid left behind was then extracted with 80 per cent ethanol in three portions of 100 ml, 50 ml, and 50 ml. The combined ethanol extracts were vacuum distilled and

the solid obtained was found to be almost free from inorganic impurities. It was then subsequently recrystallised twice from aqueous ethanol.

Fig. 6 shows the NMR spectrum of the deuterated sulphonate in deuterium oxide (the solution was 5 per cent by weight) and Fig. 5 the spectrum of the unlabelled sulphonate obtained under similar conditions. The spectrum of the unlabelled sulphonate consists of two doublets of the ortho and meta protons of the benzene ring. In the deuterated sulphonate the ortho doublet has completely disappeared and the meta doublet has coalesced into a single sharp peak. The latter peak has two-thirds the area of that of the methyl protons, showing that the sulphonate is essentially completely deuterated in 2,6 positions.

Preparation of Potassium 1-Methylnaphthalene-4-sulphonate

The method used for sulphonation of α-methylnaphthalene was essentially the same as that used for ordinary anisole and the reagents and amounts were as follows: chlorosulphonic acid (130 ml; 2 mole); α-methylnaphthalene (284 ml; 2 mole); and carbon tetrachloride (600 ml). The crude sulphonate, 338 g, being impure, was once more recrystallized before its conversion into the sulphonyl chloride described below.

Perfectly dried potassium 1-methylnaphthalene-4-sulphonate (250 g), free from inorganic impurities, was treated with phosphorus pentachloride (250 g) in a round-bottomed flask and the mixture stirred efficiently. The flask was warmed on a water bath continuously with vigorous stirring for 2 - 3 hours and then finally allowed to cool. The sulphonyl chloride formed was repeatedly washed with water to remove all the inorganic salts. After drying in a vacuum desiccator it was subjected to repeated recrystallisations from benzene-petroleum

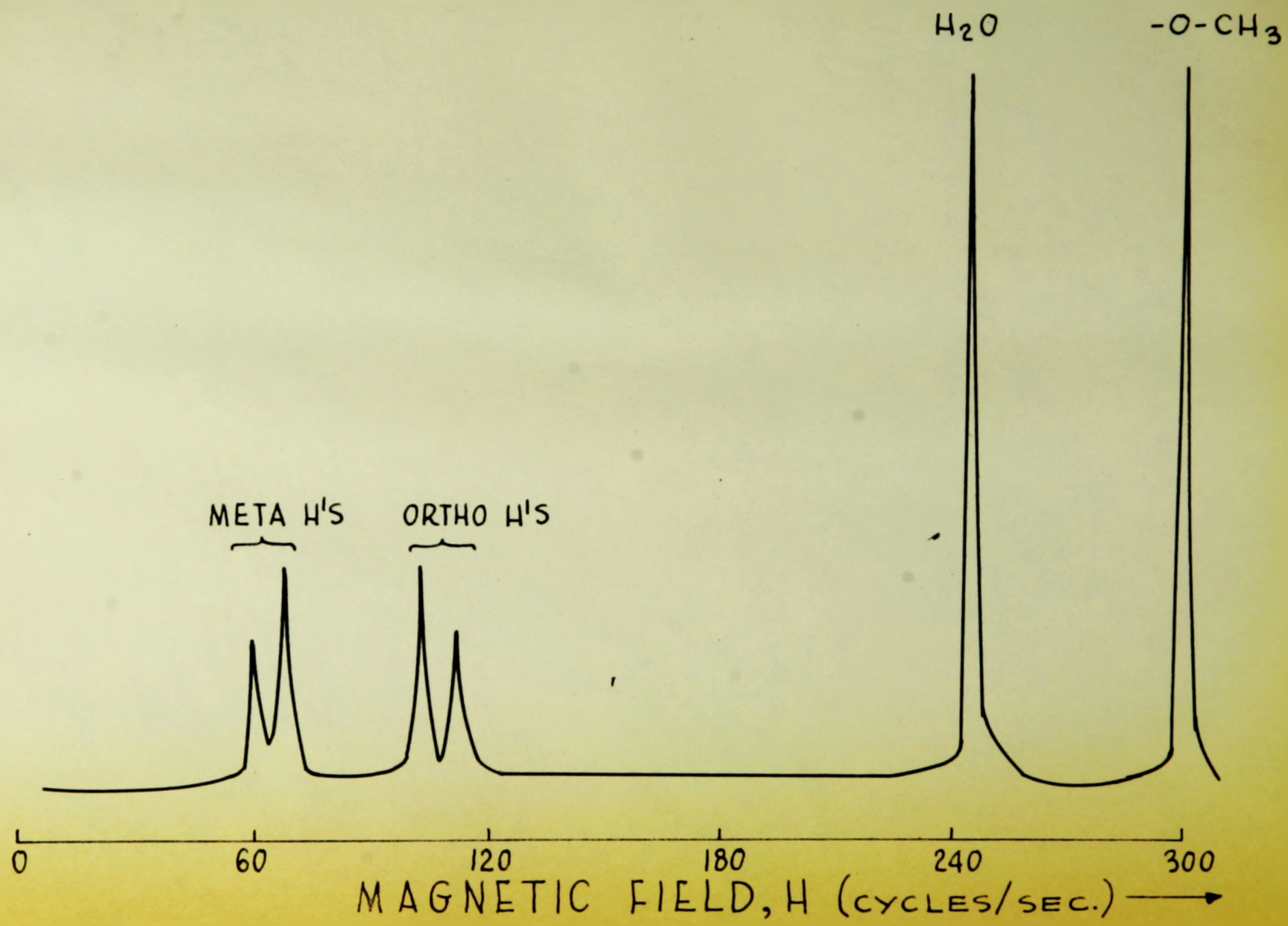


FIG. 5. PROTON NMR SPECTRUM OF SODIUM p-METHOXYBENZENESULPHONATE AT 60 Mc/SEC. IN D_2O.

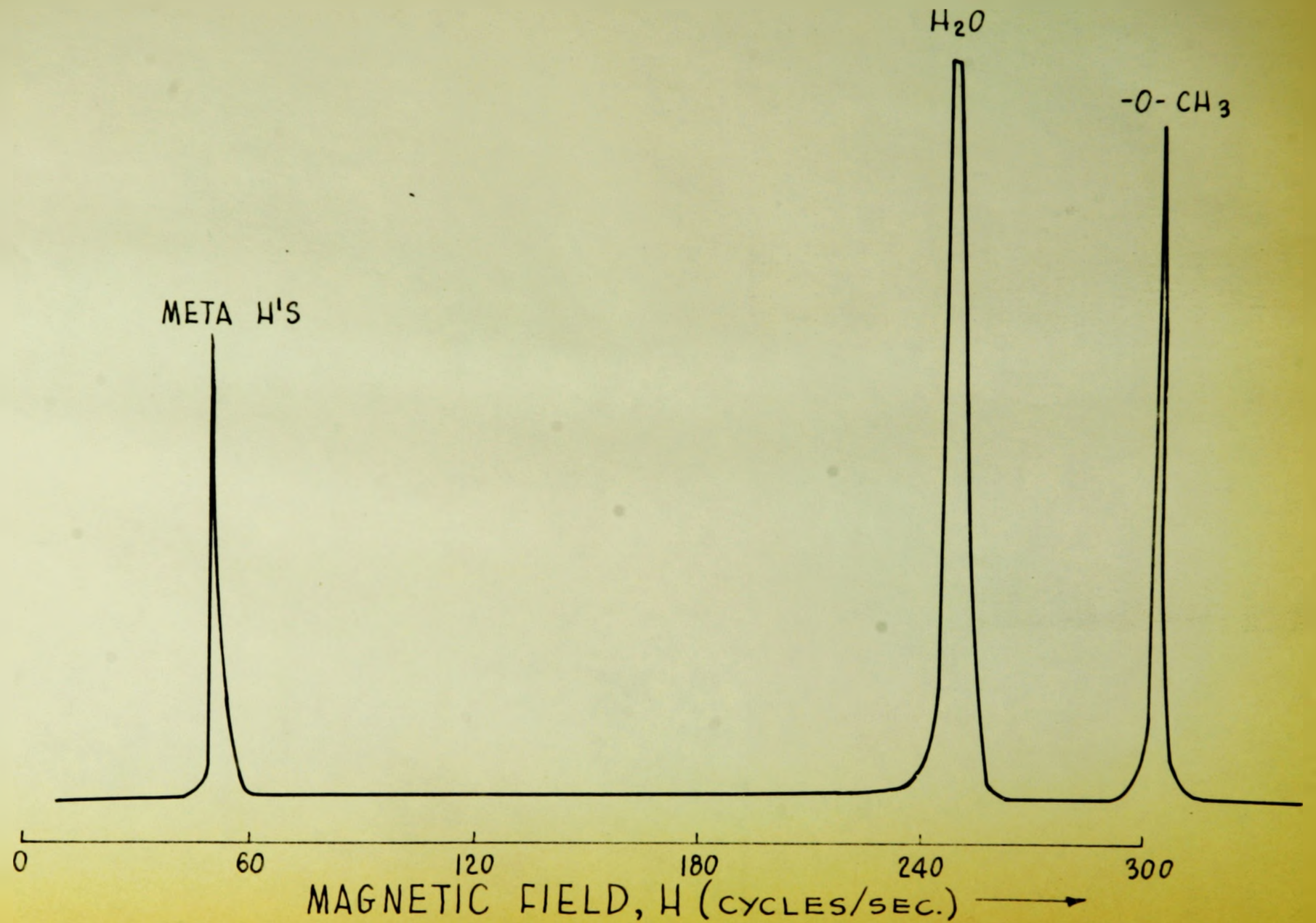


FIG. 6. PROTON NMR SPECTRUM OF SODIUM
Q, Q'-DEUTERATED-P-METHOXYBENZENESULPHONATE AT
60 Mc./SEC. IN D_2O.

ether (B.P. 40 - 60°) until there was no change in the melting point between two successive recrystallisations. A final yield of 78 g of the sulphonyl chloride melting very sharply at 81°C (lit. (124), m.p. 81°C) was obtained. A derivative of this sulphonyl chloride, to characterize it, was prepared as follows: A hot solution of 1.2 g of the sulphonyl chloride in a little alcohol was treated with one gram of aniline, refluxed for an hour, and then allowed to cool. On acidification with dilute hydrochloric acid, the anilide precipitated. This, after recrystallization from dilute acetic acid, gave pure colourless flakes of m.p. 157.5 - 158°C; lit. (124), m.p. 158°C.

The sulphonyl chloride was converted back into potassium 1-methylnaphthalene-4-sulphonate as follows: Potassium hydroxide (43 g) was dissolved in 50 per cent ethanol (500 ml), and the sulphonyl chloride (78 g) was refluxed in this solution for three hours. This solution after treatment with decolourising carbon was filtered through a hot water funnel and the sulphonate was allowed to crystallize. This product was then recrystallized twice from aqueous ethanol. The question of the purity of this material and of the material prepared initially by the method used by Cannell is discussed in the following.

A number of kinetic experiments were first performed on material prepared and purified by the method of Cannell the conditions used being identical to those of Expts. 29 and 30 reported in his paper (page 2935, Ref. 17). It was found that although the rate constants obtained from initial rates agreed fairly closely with Cannell's values there was a serious fall off in rate-constant values as the reaction progressed. Nor could satisfactory results be obtained with material

"purified" through the p-toluidine salt. On the other hand, the product obtained from the sulphonyl chloride purification procedure described above gave perfectly steady rate constants throughout the course of a kinetic run. It is of interest to note that the rate constant obtained for this material under the conditions of Cannell's experiment No. 29 was 0.0511 l mole^{-1} sec^{-1}, which is to be compared to Cannell's reported value of 0.0985 l mole^{-1} sec^{-1}. Since there seems little doubt that the salt used in the present study was of considerably higher purity than that used by Cannell, it is this author's view that no reliance can be placed on his rate constants for this compound.

In spite of the elaborate purification procedure, the purity of the salt used in the present work left something to be desired. The yields of sulphate obtained by "complete" bromodesulphonation in the presence of excess bromine at room temperature ranged from 92.6 - 93.1 per cent of the theoretical, suggesting that the salt contained approximately 7 per cent impurity. Since bromodesulphonations in a sealed tube at 210°C for 8 days yielded sulphate in yields of 99.4 - 99.9 per cent it would appear that the impurity is an unreactive isomer, probably potassium 1-methylnaphthalene-5-sulphonate. Its presence, although introducing some error in the rate studies, should have no effect on the kinetic isotope effect results.

Product Analysis in the Bromination of Sodium p-Methoxybenzenesulphonate

Two separate aqueous solutions of 400 ml each, one containing sodium p-methoxybenzenesulphonate (13.55 g; 0.064 mole) and the other bromine (0.064 mole) and sodium bromide (0.4 mole) were cooled

to 0°C and then thoroughly mixed. The resulting solution was maintained at this temperature for about 3 hours to permit the bromination to proceed to completion. At the end of the reaction, the bromodesulphonated product, p-bromoanisole, was extracted with carbon tetrachloride. After distilling off the carbon tetrachloride, crude p-bromoanisole (2.45 g; 0.013 mole) was obtained in a yield corresponding to about 20 per cent of the initial sulphonate. The product was identified by converting it to a derivative, p-methoxybenzoic acid (m.p. 183.5 - 184°C), which gave no depression in melting point on admixture with an authentic sample of this acid (m.p. 183.5 - 184°C).

After removing p-bromoanisole, the clear aqueous solution containing sodium 3-bromo-4-methoxybenzenesulphonate (the bromodeprotonated product) was first neutralised with solid sodium carbonate to a pH of 7. The solution was concentrated to about 125 ml by heating at its boiling point and, when still hot, was saturated with sodium chloride before being allowed to cool. The solid which separated was filtered and dried. Its weight (15.1 g; 0.051 mole) corresponded in yield to about 80 per cent of the initial sulphonate on the assumption that only one nuclear position is substituted by bromine. It was recrystallised twice from water before being converted to its sulphonamide by the procedure described in the following paragraph.

The dry salt was treated with phosphorus pentachloride (6.0 g) and the mixture heated under reflux for about three hours on a steam bath. The cooled mass was extracted twice with dry benzene (35 ml each time) and the benzene extract was added slowly with stirring to 40 ml of concentrated ammonia solution. The benzene was removed by evaporation

on a water bath and the residual solid was recrystallised twice from water to give a product whose melting point (139.5 - 140°) agreed with the literature value (139 - 140°C (125)) for 3-bromo-4-methoxybenzenesulphonamide. The identity of the compound was further established by its infra red spectra and by the lack of any melting point depression on admixture with an authentic sample of the sulphonamide.

The authentic sample of 3-bromo-4-methoxybenzenesulphonamide was prepared as follows: o-bromoanisole (1.0 g) was converted to 3-bromo-4-methoxybenzenesulphonyl chloride by sulphonation at 0°C with chlorosulphonic acid (5 g). The sulphonyl chloride was taken up in benzene and converted to the sulphonamide by the procedure described in the preceding paragraph.

Kinetics

Introduction

Total Bromination Rates

The rate of bromination of sodium p-methoxybenzenesulphonate, sodium o,o'-deuterated-p-methoxybenzenesulphonate and potassium 1-methylnaphthalene-4-sulphonate were measured using the technique adopted by Cannell. Samples of the reacting solution were withdrawn at regular time intervals, the reaction was quenched by means of an iodide solution and the liberated iodine titrated with sodium thiosulphate using starch as the indicator. The concentrations of sulphonate and bromine were varied but kept, essentially, in the molar ratio of 4:1 in order to reduce the possibility of any dibromination. The reactions were carried out at constant acidity and ionic strength adjusted by means of perchloric acid and sodium perchlorate, respectively.

The rate of bromination of sulphonate follows a second-order rate equation which can be expressed as follows:

$$-\frac{d[B]}{dt} = -\frac{d[A]}{dt} = k\,[Br_2]\,[A] \qquad (52)$$

where k is the second-order rate constant, [A] is the concentration of sulphonate, [B] is the total concentration of bromine (true bromine plus tribromide ion) which corresponds to the iodine liberated from the solution and $[Br_2]$ is the concentration of free bromine. In a given experiment the bromide-ion concentration is essentially constant and, incorporating the equilibrium

$$Br_2 + Br^- \underset{}{\overset{K}{\rightleftharpoons}} Br_3^-$$

in equation 52, the rate expression can be written:

$$-\frac{d[B]}{dt} = \frac{k}{1 + K[Br^-]}[B][A_o - (B_o - B)] \qquad (53)$$

where A_o and B_o refer to the initial concentrations of sulphonate and bromine, respectively. Equation 53 shows that the reaction is first order in titrable bromine, [B], and with an observed rate constant, k_{obs}, given by

$$k_{obs} = \frac{k}{1 + K[Br^-]}$$

Equation 53 may also be written as

$$-\frac{d[B]}{dt} = k_{obs}[B][A_o - (B_o - B)] \qquad (54)$$

Equation 54 on integration, gives the rate equation 54a used to calculate k_{obs} in a given experiment.

$$k_{obs} \cdot t = \frac{2.303}{(A_o - B_o)} \log \left[\frac{A_o - B_o + B}{B}\right]\left[\frac{B_o}{A_o}\right] \qquad (54a)$$

A precise evaluation of k_{obs} was made by the least-square plot of $\log \frac{A_o - B_o + B}{B}$ versus t. From the slope of this plot and its statistical

deviation, as calculated by the method described elsewhere (126), the rate constant with its precision was calculated.

A knowledge of the equilibrium constant K for bromine tribromide-ion equilibrium is necessary in order to calculate the factor, $1 + K[Br^-]$, which enters into calculation of the total rate. Cannell used a value 19.6 for K at 0°C, a value taken from the literature (127) for an ionic strength considerably different from that used in the present work. A redetermination of K for the ionic strength used in this work was not found necessary as Schaife and Tyrrel (128) have recently precisely determined its value for the same ionic strength at different temperatures and, moreover, their experimental conditions involved the same salts as those used in the present work, namely, sodium bromide and sodium perchlorate. Their experimental values of K are shown in Table V.

TABLE V

EXPERIMENTAL EQUILIBRIUM CONSTANTS
(Schaife and Tyrrel)

(Ionic Strength = 0.5M)

Temperature (°C)	5	25	35
K_{expt} (l mole^{-1})	19.97	16.20	14.78

From the values of K_{expt} at different temperatures, the quantity "ΔH" was calculated by means of the expression

$$-\Delta H = \frac{2.303\ RT_1T_2}{(T_2 - T_1)} \log \frac{K_1}{K_2} \qquad (55)$$

and are tabulated in Table VI.

TABLE VI

EVALUATION OF ΔH FROM K_{expt} AT DIFFERENT TEMPERATURES

Temperature Range for calc. of ΔH ($^{\circ}C$)	$-\Delta H$ (cal.) calc.
5 - 25	1724
5 - 35	1707
25 - 35	1670
	Mean 1700

Using this value of 1700 cal. for $-\Delta H$ and substituting into equation 55 an equilibrium constant, K, at $0^{\circ}C$ was calculated from each of the K_{expt} values given in Table V.

TABLE VII

EQUILIBRIUM CONSTANT K FOR TRIBROMIDE ION FORMATION AT $0^{\circ}C$

Temperature ($^{\circ}C$)	K_{expt} (1 $mole^{-1}$)	"K" calc. at $0^{\circ}C$ (1 $mole^{-1}$)
5	19.97	21.13
25	16.20	21.06
35	14.78	21.09
		Mean 21.09

The value of K equal to 21.09 (1 $mole^{-1}$) at $0^{\circ}C$ has been used in the present work.

Resolution of Total Bromination Rates into Bromodesulphonation and Bromodeprotonation Rates

Since both bromodesulphonation and bromodeprotonation reactions are found to be of the same kinetic order (first order with respect to sulphonate and first order with respect to bromine), the resolution of the total bromination rate into individual rates of these two competing reactions can be achieved from a knowledge of the yield of sulphate and the amount of bromine consumed. For determining the yield of sulphate, extensive preliminary experiments were done to establish that the sulphate formed in the reaction could be quantitatively recovered and estimated gravimetrically as barium sulphate with a good degree of precision and without significant interference by foreign ions. For the sulphate-yield results to be kinetically meaningful it was essential that only one molecule of bromine is consumed per molecule of sulphonate, or, in other words, that there is no dibromination. In order to avoid any possibility of dibromination during the course of the reaction the following procedure was adopted: the molar ratio of sulphonate to bromine was always kept 4:1 and the reaction was allowed to proceed only until about 12 per cent of the sulphonate is consumed. The acidity and ionic strengths were the same as in kinetic experiments. However, to obtain sufficient barium sulphate ($\sim$70 mg) for gravimetric estimation and for conversion to sulphur dioxide for isotopic analysis, the concentrations of sulphonate and bromine were changed with changing bromide-ion concentration since the extent of bromodesulphonation reaction is strongly dependent upon the concentration of this ion.

In these partial bromination reactions, knowing the total amount of bromine consumed (as found by difference between the initial concentration and the concentration when the reaction was stopped) and the corresponding yield of sulphate formed (as found gravimetrically), the percentage of bromodesulphonation (as related to the total amount of bromine consumed) is calculated by:

$$\text{per cent bromodesulphonation} = \frac{\text{moles of sulphate formed} \times 100}{\text{moles of bromine consumed}}$$

If x is the per cent bromodesulphonation, the per cent bromodeprotonation will be (100 - x); knowing these two percentages, the total bromination rate is then resolved as follows. If k_{obs} is the specific reaction rate constant for total bromination, then $k_{obs} \cdot \frac{x}{100}$ and $k_{obs} \cdot \frac{100 - x}{100}$ will be the rate constants for bromodesulphonation and bromodeprotonation reactions, designated as k^{S}_{obs} and k^{H}_{obs}, respectively.

Evaluation of Deuterium Isotope Effect in Bromodeprotonation of Sodium p-Methoxybenzenesulphonate

For the evaluation of bromodedeuteration rates in the bromination of sodium o,o'-deuterated-p-methoxybenzenesulphonate, the labelled material, being short in quantity, was not used for estimating the yield of sulphate. However, the ratio, k^{H}/k^{D}, can be obtained from a knowledge of the total bromination rates of the labelled and unlabelled sulphonates and the per cent yield of sulphate from the unlabelled compound only. Thus, if $(k_{obs})_H$ and $(k_{obs})_D$ are the rate constants for the total bromination of unlabelled and labelled sulphonates, respectively, then

$$\frac{(k_{obs})_H}{(k_{obs})_D} = \frac{k^S + k^H}{k^S + k^D} = \frac{k^S/k^H + 1}{k^S/k^H + k^D/k^H}$$

or

$$\frac{k^H}{k^D} = \frac{\frac{(k_{obs})_H}{(k_{obs})_D}}{(k^S/k^H)\left[1 - \frac{(k_{obs})_H}{(k_{obs})_D}\right] + 1} \qquad (56)$$

where, k^S, k^H, and k^D are the rate constants for bromodesulphonation, bromodeprotonation, and bromodedeuteration, respectively. In deriving this equation the assumption is made that the rate constant, k^S, for bromodesulphonation is unaffected by deuterium substitution. Since k^S/k^H is known from the sulphate yield data for the unlabelled compound, the isotope effect k^H/k^D can be readily evaluated.

Reagents

Sodium bromide: Mallinckrodt Analytical Reagent. Dried at 110 - 120°C before use.

Sodium perchlorate: Fisher Purified Chemical. Recrystallised once from water and dried at 120°C for prolonged periods before use.

Potassium iodide: B. D. H. Analar Reagent.

Barium chloride: B. D. H. Analar Reagent.

Starch: Merck Reagent.

Perchloric acid: Nichols Chemical Corporation "Reagent Grade".

Bromine: B. D. H. Analar Reagent.

Distilled water: Boiled to free it from dissolved air and carbon dioxide.

Sodium thiosulphate: B. D. H. Analar Reagent.

Potassium iodate: Mallinchrodt Analytical Reagent. Dried before use.

Sodium p-methoxybenzenesulphonate: The salt prepared as described earlier was dried thoroughly at 110°C before use.

Sodium o,o'-deuterated-p-methoxybenzenesulphonate: The salt prepared as described earlier was dried thoroughly at 110°C before use.

Potassium 1-methylnaphthalene-4-sulphonate: The salt prepared as described earlier was dried thoroughly at 110°C before use.

Experimental Details

Bromination Rates

All solutions of appropriate concentrations were made by direct weighing of the chemical using distilled water as solvent. A stock solution of bromine (app. 0.1M) was made in water. A stock solution of sodium thiosulphate (app. 0.1N) was made and standardised against potassium iodate solution. This thiosulphate solution was used periodically to obtain more dilute standard solutions of thiosulphate, as required. The acidity of the reaction system was kept constant at 0.02M and adjustments to the various ionic strengths, 0.5, 1.0 and 2.0M, were made using sodium perchlorate.

Two solutions, A and B, were prepared of concentrations such that on mixing equal volumes the desired concentration was obtained.

Solution A contained: Sulphonate - 0.008M

Sodium perchlorate - as needed

Solution B contained: Bromine ≃ 0.002M

Perchloric acid - 0.04M

Sodium bromide - as needed.

Solutions A and B, 125 ml each, were pipetted out separately into 250 ml and 500 ml round-bottomed flasks, respectively, provided with ground-glass steppers. The flasks were kept immersed in a thermostat containing a mixture of ice and water kept vigorously stirred. From time to time both solutions were shaken to attain the temperature of the bath ($0^{\circ}C$). After a lapse of at least three hours, the initial concentration of bromine in solution B was first determined before mixing. This was done by pipetting out 10 ml of solution B, by means of a fast-delivery pipette (calibrated before use) also cooled to $0^{\circ}C$, into 10 ml of 2 per cent aqueous potassium iodide. The liberated iodine was titrated with 0.001N sodium thiosulphate solution using starch as indicator towards the end of the titration. An equal volume of solution A was rejected to compensate for the loss of volume in B.

The two solutions were then mixed. At appropriate intervals of time, a 10-ml sample of the solution was run into 10 ml of 2 per cent aqueous potassium iodide and the liberated iodine was titrated immediately with standard thiosulphate solution. About twelve to sixteen points were taken in each experiment. It was also shown by conducting blank experiments that the loss of bromine by volatilization was negligible over the time interval necessary to conduct an experiment. The normality of the sodium thiosulphate solution was periodically checked by titration against standard potassium iodate solution.

In the case of sodium p-methoxybenzenesulphonate (both deuterated and undeuterated) the rate of bromination in the absence of added bromide ion was too fast for the above technique to be used and hence a slight modification had to be employed. Separate 10-ml portions of solutions A and B were mixed together for each point taken. The

initial concentration of bromine was determined by using samples of solution B as blanks from time to time. The loss of bromine by volatilisation was found to be insignificant over the time interval necessary to conduct an experiment.

Sulphate Yields

The concentrations of sulphonate and bromine used varied from 0.004 to 0.016M and 0.001 to 0.004M, respectively. The amount of solutions A and B taken was varied from 250 to 375 ml as desired. The reaction was allowed to proceed for a duration of time (calculated from the rate constant) at which approximately 50 per cent of bromine would be consumed (i.e., about 12 per cent reaction with respect to sulphonate). At the end of this time period, the reaction was quenched by addition of 10 ml of 25 per cent aqueous potassium iodide (also cooled to $0^{\circ}C$).

After determining the amount of iodine liberated, the quenched solution was quantitatively transferred to a beaker. The acidity of the solution was made 0.05M by means of perchloric acid and necessary amount of barium chloride solution was added to make the entire solution 0.01M with respect to Ba^{++}. The solution was then digested on a steam bath for 3 to 4 hours to make the barium sulphate coarse. The supernatant was then filtered through a quantitative filter paper and finally the barium sulphate was quantitatively transferred into the filter paper. The precipitate was freed of inorganic ions by necessary washings with water. After drying, the filter paper with the precipitate was ignited in a crucible and the weight of barium sulphate was determined. Each determination of sulphate was made in duplicate and the per cent bromodesulphonation was calculated as described earlier.

Complete bromodesulphonation reactions of sodium p-methoxybenzenesulphonate and potassium 1-methylnaphthalene-4-sulphonate were carried out to establish that the sulphonates are quantitatively bromodesulphonated being given sufficient time and also to provide the sulphate needed for determination of the sulphur isotopic ratio in the reactant. The complete bromodesulphonation results served also as a criterion of purity for the material. As already discussed under the section "Preparation of Compounds", sodium p-methoxybenzenesulphonate gave a quantitative yield of sulphate when brominated in the presence of excess bromine at room temperature whereas the yield from potassium 1-methylnaphthalene-4-sulphonate was only 93 per cent. The latter compound, however, was shown to be quantitatively desulphonated under drastic conditions, which, as stated previously, establishes that the material present as impurity could only be another sulphonic acid.

The complete bromodesulphonation reaction at room temperature was performed as follows. A 0.01M sulphonate solution was prepared in water and 100 ml of this solution was taken in a 250 ml Erlenmeyer's flask provided with ground glass stopper. A solution of bromine was prepared by mixing 0.5 to 1 ml of liquid bromine in 25 ml of water. This solution was added carefully to the sulphonate solution and the contents were uniformly mixed. Thus the concentration of bromine was kept at least ten times greater than that of sulphonate. The system was allowed three to four days during which period the bromodesulphonation reaction would be complete. At the end of this time the solution was processed as follows.

The excess bromine was first removed on a steam bath and the organic product was removed from the aqueous solution by extraction with carbon tetrachloride. The organic extract was washed several times with water and the washings combined with the aqueous solution and transferred to a beaker. The acidity of the solution was made 0.05M by means of perchloric acid and barium chloride solution was added to make the solution 0.01M with respect to Ba^{++}. The barium sulphate was digested on a steam bath and was then estimated gravimetrically as described before. The experiments were repeated several times.

The complete bromodesulphonation of potassium 1-methylnaphthalene-4-sulphonate under drastic conditions was carried out as follows. Twenty-five millilitres of a 0.02M aqueous solution of the sulphonate and from one-half to one millilitre of liquid bromine were placed in a pyrex tube (35 cm in length and 100 ml capacity), which was then sealed and introduced into a furnace maintained at 210°C. After 8 days at this temperature the tube was opened, and the sulphate formed was precipitated as barium sulphate and weighed as previously described. These experiments also were repeated several times.

Evaluation of Kinetic Sulphur Isotope Effects

Introduction

In the bromodesulphonation reaction, there is a carbon-sulphur bond cleavage resulting in the displacement of the sulphonate group as sulphur trioxide which in the aqueous medium is immediately converted to sulphate ion. When a sulphur isotope effect is associated with the reaction the difference in the S^{32}/S^{34} ratios in the reactant and product

is a function of the extent of reaction, it being at a maximum initially and decreasing to zero for complete conversion to product. For an infinitesimally small extent of reaction, the isotope effect is given directly by the quotient of the isotopic ratio for the atom in question in the product and in the reactant. In practice, however, the reaction is allowed to proceed to some known extent of reaction, usually around 10 to 15 per cent, and the isotope effect is calculated using an expression which is given later in this thesis.

In order to obtain the S^{32}/S^{34} ratio for the reactant the bromodesulphonation of the sulphonate was carried to completion and the resulting sulphate ion was then quantitatively precipitated as barium sulphate which was converted to sulphur dioxide for mass spectrometric analysis. The sulphate ion produced in the partial reactions was similarly converted, following quenching, to barium sulphate and thence to sulphur dioxide.

The conversion of sulphur of barium sulphate to sulphur dioxide involved the following steps. The barium sulphate samples were first reduced to hydrogen sulphide using a mixture of hydrochloric, hypophosphorus and hydriodic acids and the hydrogen sulphide was then precipitated as cadmium sulphide. The cadmium sulphide was converted to silver sulphide and the latter was burned to sulphur dioxide using a high-vacuum technique.

Experimental Details

Reagents

Hydriodic acid (d. 1.7): B. D. H. Analar'

Hydrochloric acid (conc.): B. D. H. Analar'

Hypophosphorus acid (conc.): B. D. H. Laboratory Reagent.

Acetic acid (glacial): B. D. H. Analar.

Silver nitrate: Merck Reagent.

Potassium thiocyanate: Merck Reagent.

Barium chloride: B. D. H. Analar.

Conversion of Barium Sulphate to Silver Sulphide

The reducing solution was prepared by mixing hydriodic acid (500 ml), hydrochloric acid (816 ml) and hypophosphorous acid (245 ml). Sulphur impurities were removed by boiling the solution gently for 40 - 50 minutes. The absorbent for hydrogen sulphide consisted of cadmium acetate (62.5 g) dissolved in solution of water (2 l) and glacial acetic acid (500 ml).

A sample of barium sulphate, 60 to 90 mg according to the sample availability, was accurately weighed and placed in flask A (Fig. 7) and 50 ml of the reducing solution added. Trap B was filled with distilled water and trap C with 100 ml of the absorbing solution of cadmium acetate. A stream of nitrogen gas was passed through the apparatus at a moderate rate. The contents of flask A were brought to a gentle boil by heating with the flame of a bunsen burner. The intensity of the flame was such that at least one-half hour elapsed before the onset of boiling. The contents of flask A were refluxed gently for a period of one-half hour and then boiled vigorously for a similar period of time. The barium sulphate dissolved in the reducing solution and the evolved hydrogen sulphide was swept through the system to trap C where it was precipitated as cadmium sulphide.

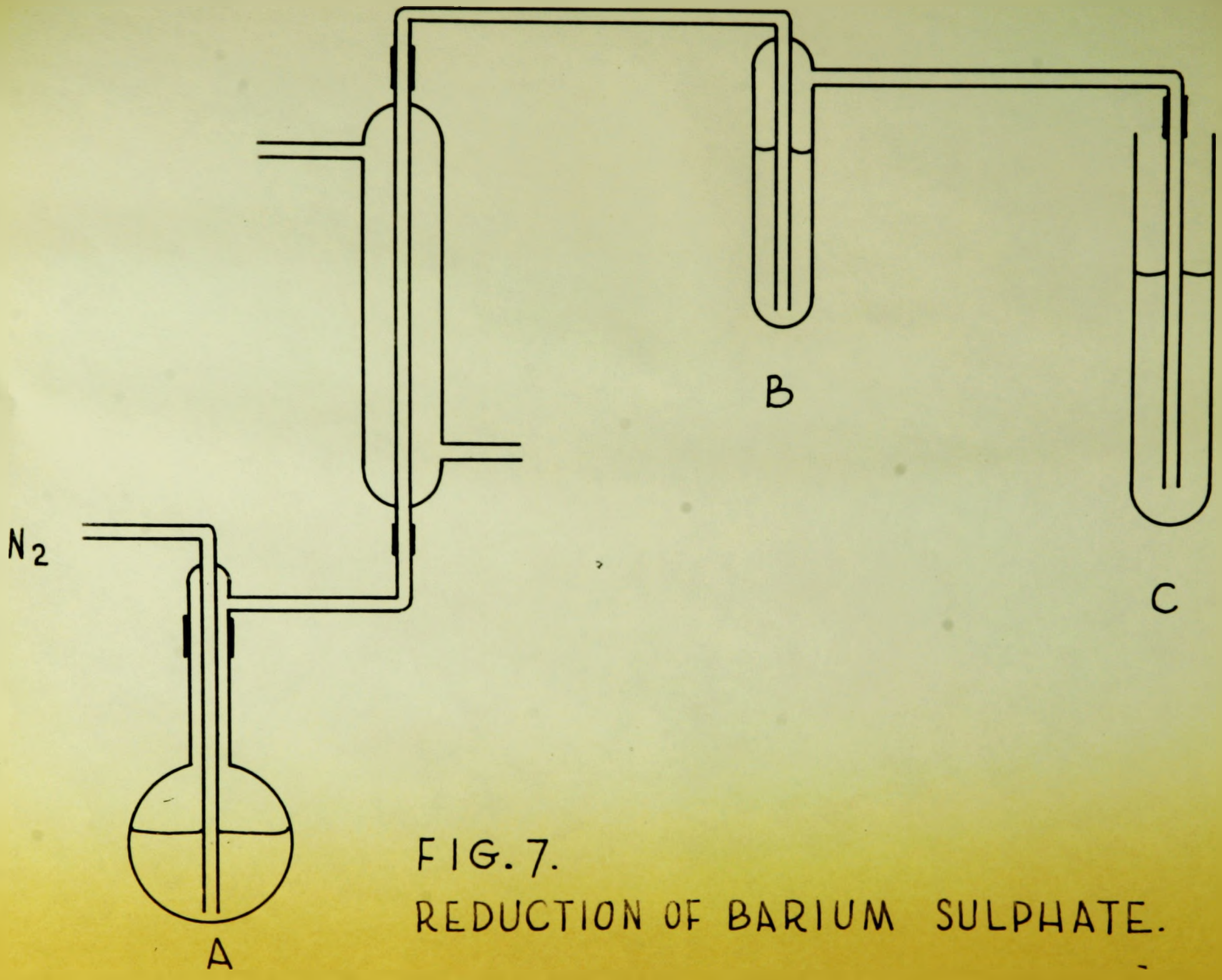


FIG. 7.
REDUCTION OF BARIUM SULPHATE.

At the end of the heating period, trap C and its bubbler were detached from the line and the cadmium sulphide was converted to silver sulphide by the addition of 25 ml of a standardized solution (0.1N) of silver nitrate. The silver sulphide was digested on a steam bath and then collected by filtration on to a small piece of glass wool. The precipitate was washed with a small amount of dilute ammonium hydroxide solution to remove silver ions, then with distilled water and finally was dried.

The quantitativeness of the conversion of barium sulphate to silver sulphide was determined in every case by titration with potassium thiocyanate of the excess silver nitrate in the filtrate from the silver sulphide filtration. In no case was the consumption of silver ions less than 99 per cent of the theoretical based on the weight of barium sulphate used.

Oxidation of Silver Sulphide to Sulphur Dioxide

The silver sulphide was converted to sulphur dioxide by burning it in a stream of purified oxygen gas using a method developed by Thode's group (129) in the McMaster laboratories. The sulphur dioxide thus formed is purified and collected using a high-vacuum system illustrated in Fig. 8. The detailed procedure used in the present investigation is as follows.

The entire bulk of the silver sulphide sample was separated from most of the glass wool on which it had been collected and was placed in a small stainless steel boat to which was attached a stainless steel wire. This boat was carefully pushed to the mid-point of the quartz tube Q. The remaining portion of the line had been previously

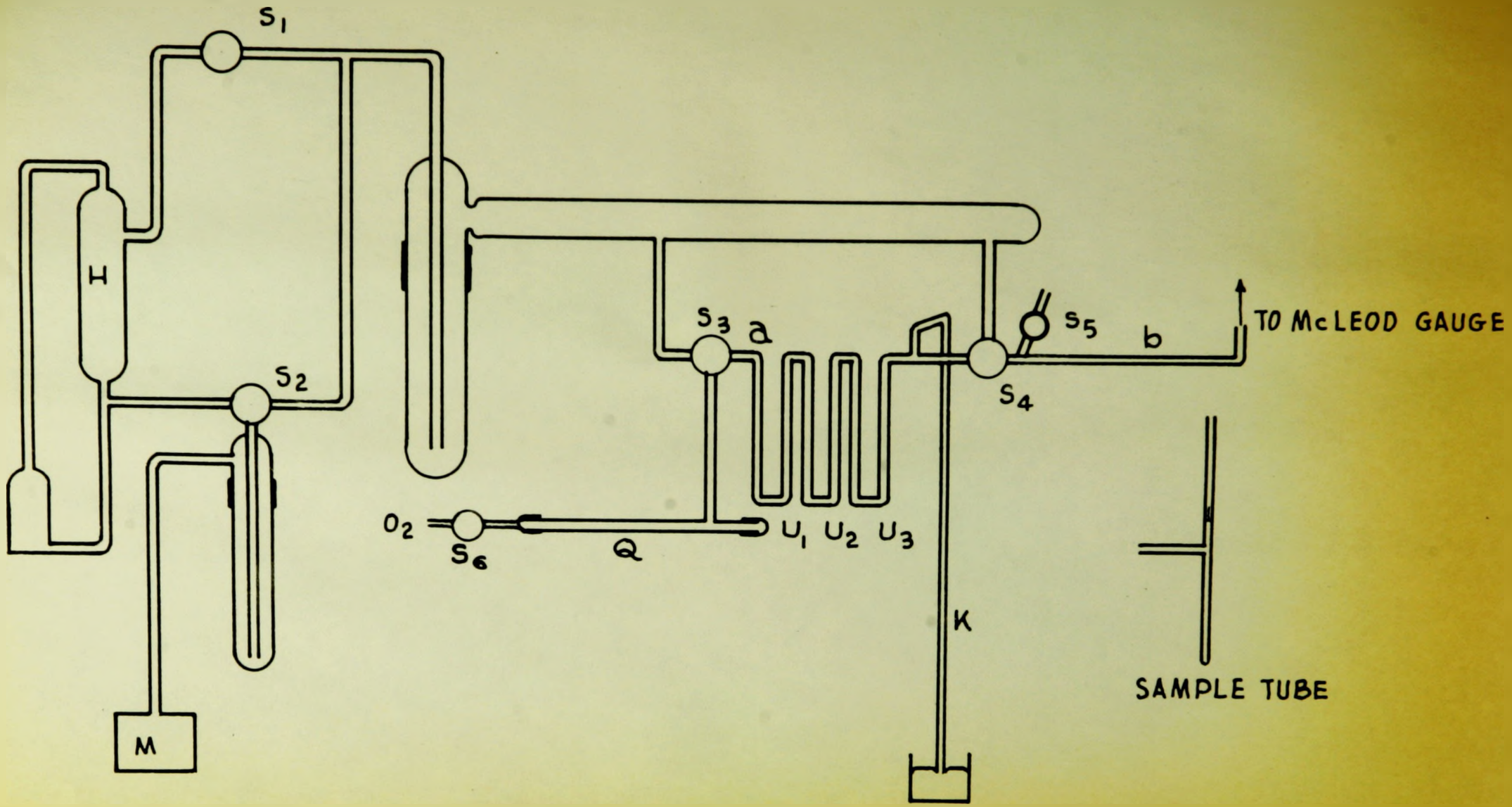


FIG. 8.

SULPHUR DIOXIDE SAMPLE LINE.

evacuated to a pressure of 10^{-6} mm of mercury as determined by the McLeod gauge. The two-way stopcock, S_1, was turned so that the mercury diffusion pump was bypassed. Stopcock S_3 was slowly turned so as to connect arm a with the quartz tube Q thus evacuating the latter. After the initial surge of air accompanying this operation had been eliminated by the mechanical pump M, stopcock S_1 was turned to introduce the mercury diffusion pump M. The entire line was then evacuated until the McLeod gauge registered a pressure of 10^{-6} mm of mercury, this operation requiring approximately ten minutes. As the line was pumped down, the entire system was thoroughly flamed with a hand torch.

When a satisfactory vacuum was attained, stopcocks S_3 and S_4 were adjusted so as to connect the quartz tube Q with the U-tubes and the bank of sample tubes, b, and to isolate this whole section of the line from the rest of the manifold. Stopcock S_6 was then very slowly opened and purified oxygen gas* was passed into the quartz tube and traps. When the pressure within this section had reached atmospheric, as indicated by the manometer K, stopcock S_5 was opened and the oxygen, sweeping through the quartz tube and traps, was led out of the system through a long column of silica gel. A constant rate of flow of oxygen at about 0.2 litres per minute was maintained.

With the U-tubes U_1 and U_3 immersed in liquid oxygen (liquid oxygen was used instead of liquid air in order to avoid the condensation of oxygen gas), the flame of a hand torch (burning oxygen/gas mixture) of strong intensity (about 1000°C) was played on the central portion of

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*Oxygen was purified by passage through a train arranged in the following order: a sulphuric acid trap, a column packed with ascarite and dehydrite, a flow meter and finally a spiral trap immersed in liquid oxygen.

the quartz tube Q directly below the boat. The sulphide sample glowed and the resulting sulphur dioxide was swept in the oxygen stream into the U-traps where it condensed. After the heating was over (about 2 - 3 minutes), the tube Q was swept by the oxygen for about five minutes. Stopcocks S_5 and S_6 were then closed and S_1 was turned so as to bypass the mercury diffusion pump H. Stopcock S_4 was opened very slowly to the U-traps and the system was again evacuated. In this way all gases present in the combustion tube were passed through the cold U-traps thus insuring complete condensation of the sulphur dioxide. Stopcock S_1 was then turned to readmit the mercury diffusion pump and the line was evacuated to a pressure of 10^{-6} mm of mercury. Stopcocks S_3 and S_4 were turned to isolate the U-traps and the surrounding dewars of liquid oxygen around U_1 and U_3 were removed. This served to free any oxygen entrapped in the solid sulphur dioxide. The liquid oxygen trap was replaced around U_2 and, after the sulphur dioxide had again solidified, the stopcock S_4 was opened, connecting the U-tubes with the manifold. This second condensation under a very much reduced pressure of oxygen would entrap a negligible amount of this gas in the solid sulphur dioxide.

The U-traps were again isolated, the liquid oxygen trap was removed and the tube U_2 was allowed to come to room temperature. After noting the manometer reading to have an approximate idea of the amount of sulphur dioxide formed, the gas was freed from moisture as follows. All the sulphur dioxide was condensed in U_2 by means of liquid air. The stopcock S_4 was turned so that arms a and b directly connected and isolated from rest of the system. The liquid-air trap around U_2 was quickly replaced by dry-ice acetone and the sulphur dioxide was distilled

into one of the sample tubes on b surrounded by liquid air. Any moisture was thus retained in U_2. About ten minutes were given for this distillation. Stopcock S_4 was then closed, U_2 was allowed to warm up to room temperature and the latter was again surrounded by dry-ice acetone. Stopcock S_4 was turned to connect a and b for 2 minutes to allow last traces of sulphur dioxide to dirtill into the sample tube. Finally, the stopcock S_4 was turned so that the arm b was bypassed, the dry-ice acetone trap was removed and the U-traps were directly connected to the vacuum manifold. The U-traps were flamed as the line was pumped down.

Final purification of the sulphur dioxide from carbon dioxide invariably present was accomplished at a temperature of melting ethyl chloride (-138°C) at which carbon dioxide has appreciable vapour pressure. The stopcock S_4 was turned so that the U-traps and arm, b, were directly connected and isolated from rest of the manifold. The liquid-air trap surrounding the sample tube was removed and the sulphur dioxide was distilled in U_2 which was surrounded by solid-liquid ethyl chloride slurry. When all the sulphur dioxide has condensed in U_2 the stopcock S_4 was turned to connect the U-traps to the vacuum manifold for about 2 to 3 minutes so as to remove the carbon dioxide. The U-traps were isolated, the ethyl chloride bath was removed and U_2 was allowed to warm up to room temperature. The sulphur dioxide was again condensed in U_2 by ethyl chloride bath and, by turning S_4, the traps were further evacuated for about 30 seconds. Finally the sulphur dioxide was distilled into one of the sample tubes, attached to arm b, surrounded by liquid air. After about 60 seconds, the tube was sealed off from the line. The sample was now ready for mass spectrometric analysis.

Mass Spectrometric Measurements of the S^{32}/S^{34} Ratios

The relative abundances of the sulphur isotopes were measured using a 6-inch, 90-degree, simultaneous collection mass spectrometer similar to that described by Wanless and Thode (130). This was a high-precision instrument capable of measuring changes of isotopic ratios with a precision of ±0.02 per cent. The conventional collector of a single beam instrument had been modified to permit simultaneous collection and measurement, by means of a null method, of ion currents due to masses 64 and 66. The collection system is so constructed that only ion currents of these two masses strike the collector electrodes. A magnetic valve system permits rapid switching from standard gas to unknown thereby reducing the time required for analysis and making the rapid comparison of samples possible.

The analytical procedure for determining the isotope ratio of the unknown gas compared to the standard gas is as follows. The ion current produced by the mass-66 beam was amplified and applied to a put-and-take potentiometer. Some fraction of the current from the put-and-take potentiometer was balanced against the separately amplified current from the mass-64 beam and the balance point was recorded on a Minneapolis Honeywell Brown Electronik Recorder. Since the position of balance will vary depending on the ratio of isotopes present in the sample, a shift of the balance point will be a measure of the 64/66 ratio relative to a standard sample. The ion current from mass 64 was used as a reference voltage and was adjusted to the same value for both the standard and the sample by changing the gas pressure of the sample until the peak height of mass 64, measured on single collection,

was identical with that of the standard. The instrument was switched to simultaneous collection operation, the put-and-take potentiometer was adjusted to give a balance near the centre of the recorder chart and the displacement of the null point of the sample from that of the standard was measured. The average of six displacements was used to calculate the per cent change in the isotope ratio of the sample relative to the standard. This gave the value of the 64/66 ratio.

The S^{32}/S^{34} ratio in the sulphur dioxide samples was calculated from the ratio of the masses 64 and 66 as determined by the ion currents arising from the various SO_2^+ species. Neglecting contributions from molecules containing two or more of the heavy isotopes the mass spectrometric ratio 64/66 may be equated as follows.

$$\frac{64}{66} = \frac{S^{32}O_2^{16}O^{16}}{S^{34}O_2^{16}O^{16} + S^{32}O_2^{16}O^{18}}$$

Now the probability of occurrence of $S^{34}O_2^{16}O^{16}$ as compared with that of $S^{32}O_2^{16}O^{16}$ is given simply by the S^{34}/S^{32} ratio of the sample. However, since there are two atoms of oxygen in a molecule of sulphur dioxide, the probability of occurrence of the species $S^{32}O_2^{16}O^{18}$ compared to $S^{32}O_2^{16}O^{16}$ is twice the O^{18}/O^{16} ratio. The 64/66 ratio may therefore be expressed in terms of the relative abundance of the sulphur and oxygen isotopes as follows.

$$\frac{64}{66} = \frac{1}{S^{34}/S^{32} + 2O^{18}/O^{16}}$$

The O^{18}/O^{16} ratio has previously been determined by Thode (131) for the tank oxygen and has the value 0.00208. The S^{32}/S^{34} ratios reported in this thesis are all relative to a value of 22.225 for meteoritic sulphur, as

employed by Thode's group. On this scale the S^{32}/S^{34} ratio for the standard sample with which all other samples were compared in the mass spectrometric analysis is 22.140 (64/66 = 20.273).

Calculation of Kinetic Isotope Effects

The following expression has been derived by Stevens and Attree (132) for the calculation of a kinetic isotope effect for a reaction in which there is no complication of competing processes:

$$k^{32}/k^{34} = \frac{\ln (1 - f)}{\ln (1 - rf)} \qquad (57)$$

where $r = (S^{32}/S^{34})$ reactant/(S^{32}/S^{34})product, and f is the mole fraction of the reactant which has undergone reaction*. In the present study an estimate of f is made difficult because of the competing reaction of bromodeprotonation. It cannot be taken simply as the mole fraction of reactant which has been consumed since the bromodeprotonation component of the total reaction proceeds without sulphur isotopic fractionation. Nor is a suitable value of f given by the mole fraction of the reactant which has undergone bromodesulphonation only since part of the reactant is being simultaneously removed by the bromodeprotonation process. A satisfactory approximation of f, however, may be made by considering that an amount of reactant, corresponding to the bromodeprotonation component, is actually withdrawn from the system before the bromodesulphonation reaction gets underway. If a is the initial amount of reactant in moles, x is the amount of reactant in moles which has

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*Strictly speaking, f in equation 57 is the mole fraction of S^{32} which has undergone reaction. Because of the relative insensitivity of k^{32}/k^{34} to small variations in f it is entirely satisfactory to consider f to be the mole fraction of the <u>total</u> reactant (S^{32} plus S^{34} species) which has reacted. This is the quantity which, of course, is actually measured in determining the amount of reactant consumed or product formed.

undergone bromination (bromodesulphonation plus bromodeprotonation), and p is the fraction of the total reaction which is the bromodeprotonation process, then xp is the amount of reactant consumed by bromodeprotonation, and (a - xp) is the amount of reactant remaining. An estimate of f is then given by the following expression

$$f \backsim \frac{x(1 - p)}{a - xp} \qquad (58)$$

where (1 - p) is the fraction bromodesulphonation. This may be rewritten as

$$f \backsim \frac{f'(1 - p)}{1 - f'p} \qquad (59)$$

where f' = x/a, the mole fraction of reactant which has undergone bromination. For the small conversions of sulphonate used in the present investigation (10 - 15 per cent) the error introduced by using this approximation is negligible.

An example of the calculation of a kinetic isotope effect is as follows:

$(S^{32}/S^{34})_{reactant} = 22.149$; $(S^{32}/S^{34})_{product} = 22.532$;

$f' = 13.7$, $p = 0.792$ and $f = 3.19$

$$k^{32}/k^{34} = \frac{\ln(1 - f)}{\ln(1 - rf)} = \frac{\ln(1 - 3.19)}{\ln(1 - \frac{22.149}{22.532} \times 3.19)}$$

$$= 1.0180$$

RESULTS AND DISCUSSION

Bromodesulphonation of Sodium p-Methoxybenzenesulphonate

In the present work and also earlier in Cannell's study, it was found that the rate of bromination of sodium p-methoxybenzene-sulphonate is depressed by added bromide ion by an amount much greater than that can be ascribed to Br_3^- formation alone. As discussed earlier (page 60), this additional depression in rate by bromide ion is in accord with two different mechanisms, involving different substituting agents. In mechanism A, proposed by Cannell, the brominating species is Br_2 which reacts with the sulphonate in a two-step process; in mechanism B, not considered by Cannell, the brominating agent is Br^+ (or H_2OBr^+) which reacts with the sulphonate in either a one- or two-step process.

Mechanism A

$$ArSO_3^- + Br_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \overset{+}{Ar}\!\!<^{Br}_{SO_3^-} + Br^-$$

$$\overset{+}{Ar}\!\!<^{Br}_{SO_3^-} \xrightarrow{k_3} ArBr + SO_3$$

This leads to the kinetic relationship

$$k^s_{obs} = \frac{k_1 k_3}{k_2[Br^-] + k_3} \cdot \frac{1}{1 + K[Br^-]}$$

or,

$$\left\{k^s_{obs}\left[1 + K[Br^-]\right]\right\}^{-1} = \frac{k_2}{k_1 k_3}[Br^-] + \frac{1}{k_1} \qquad (60)$$

Mechanism B

$$Br_2 + H_2O \underset{}{\overset{K'}{\rightleftharpoons}} H_2OBr^+ + Br^-$$

Two-step

$$H_2OBr^+ + ArSO_3^- \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} \overset{+}{Ar}\begin{matrix}Br\\SO_3^-\end{matrix} + H_2O$$

$$\overset{+}{Ar}\begin{matrix}Br\\SO_3^-\end{matrix} \xrightarrow{k_3'} ArBr + SO_3$$

One-step

$$H_2OBr^+ + ArSO_3^- \underset{}{\overset{k_4}{\rightleftharpoons}} \text{Transition State} \longrightarrow ArBr + SO_3 + H_2O$$

The following kinetic relationships are obtained for mechanism B: for a two-step process

$$k^s_{obs} = \frac{K'k_1'k_3'}{(k_2' + k_3')} \cdot \frac{1}{[1 + K[Br^-]][Br^-]} \qquad (61)$$

and, for one-step

$$k^s_{obs} = K'k_4 \cdot \frac{1}{[1 + K[Br^-]][Br^-]} \qquad (62)$$

Equation 60 requires that a plot of $\left\{k^s_{obs}\left[1 + K\left[Br^-\right]\right]\right\}^{-1}$ versus $[Br^-]$ should be a straight line. Cannell reported that a plot of $\left\{k_{obs}\left[1 + K\left[Br^-\right]\right]\right\}^{-1}$ versus $[Br^-]$, where k_{obs} is the rate constant for disappearance of bromine, is linear over the range of bromide-ion concentration from zero to 0.15M and he considered that this result constituted strong evidence in support of mechanism A.

It was found in the present work that the bromination of sodium p-methoxybenzenesulphonate results in two concurrent reactions, bromodesulphonation and bromodeprotonation. The latter reaction was apparently

overlooked by Cannell who had interpreted his kinetic results on the assumption that bromodesulphonation is the only reaction. If the rate of bromodeprotonation were to be less sensitive to bromide-ion concentration than that of bromodesulphonation, then the former reaction would become increasingly competitive at the higher bromide-ion concentrations. This occurrence of the bromodeprotonation reaction would be expected to destroy the linear relationship of $\left\{k_{obs}\left[1 + K[Br^-]\right]\right\}^{-1}$ with respect to $[Br^-]$. By carefully replotting Cannell's data, it was found by the present author that significant deviations from a straight line actually do occur at the higher range of bromide-ion concentrations, 0.1 to 0.15M.

That the two competing reactions are of the same kinetic order was concluded from the following observations. In Cannell's study and also in the present work, the observed second-order rate constants for total bromination, k_{obs}, were independent of the molar ratio of sulphonate to bromine. In addition, it was found in the present work that at a given bromide-ion concentration, the ratio of the yield of sulphate to the total amount of bromine consumed was the same irrespective of the ratio of the two reactants or the extent of reaction. Some of these results are given below.

Molar Ratio Sulphonate:Bromine	Per Cent Reaction of Sulphonate	$[Br^-]$ mole/l	Per Cent Sulphate Yield
2:1	44.5	0.5	20.4
	10.3	0.5	20.9
4:1	13.5	0.5	20.8

Since the two competing reactions are of the same kinetic order, it was possible to resolve the total bromination rate, k_{obs}, into a bromodesulphonation rate, k^{S}_{obs}, and a bromodeprotonation rate, k^{H}_{obs}, (see page 93). The results of a series of kinetic experiments and the sulphate-yield determinations carried out at bromide-ion concentrations ranging from zero to 0.5M, under conditions of constant ionic strength and acidity, are given in Table VIII.

It can be seen from this table that the amount of bromodeprotonation increases as the bromide-ion concentration is increased. A plot of $\left\{k_{obs}\left[1 + K\left[Br^{-}\right]\right]\right\}^{-1}$ versus $\left[Br^{-}\right]$ over a range of bromide-ion concentration from zero to 0.5M is shown in Fig. 9. (Points drawn by open squares.) It can be seen that, as expected, the points at the higher bromide-ion concentrations deviate considerably from a straight line. On the other hand, a plot of $\left\{k^{S}_{obs}\left[1 + K\left[Br^{-}\right]\right]\right\}^{-1}$ versus $\left[Br^{-}\right]$ (Fig. 9, points shown by open circles) shows excellent linearity over the range of bromide-ion concentrations used. (There is a small deviation in the point at $\left[Br^{-}\right]$ = 0.5M, but this can be attributed to experimental error in the determination of the very low yield of sulphate at this high bromide-ion concentration.) Interpreting this linear relationship in terms of mechanism A, the slope of the straight line is k_2/k_1k_3 and its intercept at $\left[Br^{-}\right]$ = 0 is $1/k_1$. From these two quantities the ratio k_2/k_3 may be calculated and is found to have the value 66. This is to be compared with the value 22 obtained by Cannell from a plot of $\left\{k_{obs}\left[1 + K\left[Br^{-}\right]\right]\right\}^{-1}$ versus $\left[Br^{-}\right]$ in the range of $\left[Br^{-}\right]$ from zero to 0.15M, on the assumption that bromodesulphonation is the only reaction.

TABLE VIII

KINETIC DATA FOR THE BROMINATION OF SODIUM p-METHOXYBENZENESULPHONATE AT 0°C

(Ionic Strength = 0.5M
Rate Constants Expressed in Litres/Mole-Sec)

$[Br^-]$ mole/l	Per Cent Sulphate Yield	k_{obs}	k^H_{obs}	k^S_{obs}	$k^S_{obs}[1 + K[Br^-]]$
0	88.2	0.538 ± 0.0041[a]	0.0630	0.475	0.475
0.03	65.9	0.177 ± 0.0012	0.0600	0.117	0.191
0.07	53.0	0.0800 ± 0.0006	0.0380	0.0420	0.104
0.1	47.4	0.0549 ± 0.0005	0.0289	0.0260	0.0808
0.2	36.0	0.0219 ± 0.0002	0.0140	0.00790	0.0412
0.3	29.2	0.0132 ± 0.0001	0.00935	0.00385	0.0282
0.4	24.1	0.00910 ± 0.00008	0.00691	0.00219	0.0207
0.5	20.8	0.00674 ± 0.00004	0.00534	0.00140	0.0162

[a] Precision limits are calculated from the standard deviation of slope of the least square plot of $\log_{10} \frac{A_o - B_o + B}{B}$ versus t.

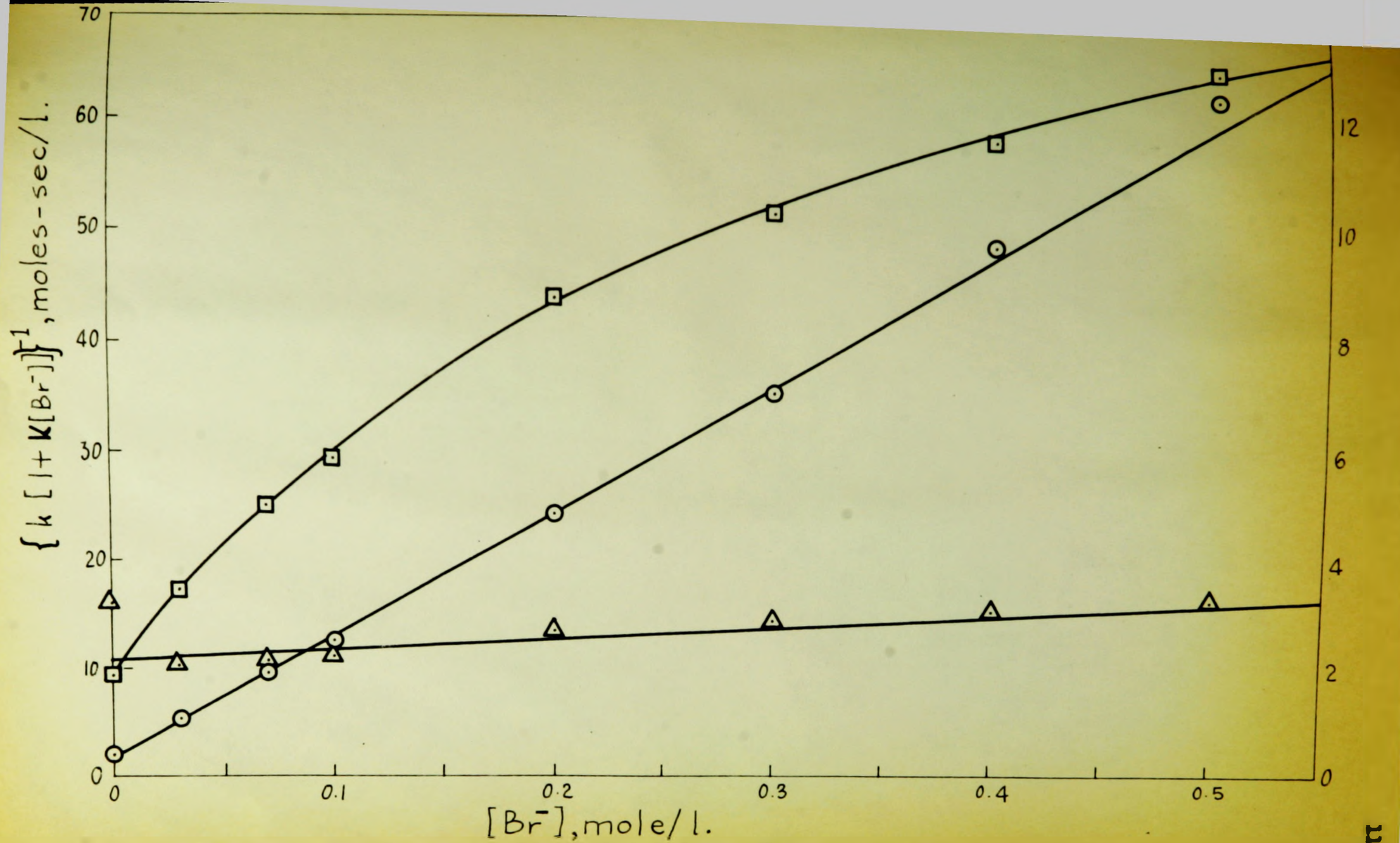

FIG. 9. PLOT OF RATE CONSTANTS, CORRECTED FOR Br_3^- EFFECT, FOR THE TOTAL BROMINATION, BROMODESULPHONATION, AND BROMODEPROTONATION OF SODIUM P-METHOXYBENZENESULPHONATE VERSUS $[Br^-]$.
⊡, $k = k_{obs}$ (RIGHT-HAND ORDINATE); ⊙, $k = k^{S}_{obs}$ (LEFT-HAND ORDINATE); △, $k = k^{H}_{obs}$ (LEFT-HAND ORDINATE).

(The remaining plot in Fig. 9, points shown by open triangles, refers to the bromodeprotonation reaction of sodium p-methoxybenzenesulphonate and will be discussed later.)

Inspection of equations 61 and 62 shows that mechanism B also predicts a straight line for the plot $\left\{k^{s}_{obs}\left[1 + K\left[Br^{-}\right]\right]\right\}^{-1}$ versus $\left[Br^{-}\right]$, but, unlike mechanism A, requires a zero intercept*. The fact that a small but experimentally real intercept has been observed in the latter plot for the bromodesulphonation of sodium p-methoxybenzenesulphonate (Fig. 9) might be considered to exclude mechanism B for this compound. It is the opinion of the present author, however, that one would not be justified in completely eliminating mechanism B simply on the basis of this very small intercept.

The usual way to see whether mechanism B is operative or not is to test the linearity of k^{s}_{obs} versus $\left\{\left[1 + K\left[Br^{-}\right]\right]\left[Br^{-}\right]\right\}^{-1}$, as required by the relationships of equations 61 and 62. For sodium p-methoxybenzenesulphonate a plot of k^{s}_{obs} versus $\left\{\left[1 + K\left[Br^{-}\right]\right]\left[Br^{-}\right]\right\}^{-1}$ is shown in Fig. 10, where it can be seen that over the range of bromide-ion concentrations, 0.5 to 0.1M, the points fit perfectly well to a straight line. At bromide-ion concentration of 0.03M and 0.07M, deviations from linearity were observed, the deviation being quite considerable for the point corresponding to $\left[Br^{-}\right]$ = 0.03M. (It was not

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*A more rigorously derived kinetic expression for mechanism B, which takes into account the very small amount of titratable bromine which is in the form H_2OBr^{+}, actually does require an intercept for this plot. It can be shown, however, that this intercept is equal to the product of the slope and K', the equilibrium constant for H_2OBr^{+} formation. Since the slope is approximately 120 and K' has a value of 10^{-20} (135), the intercept required by mechanism B is obviously quite insignificant.

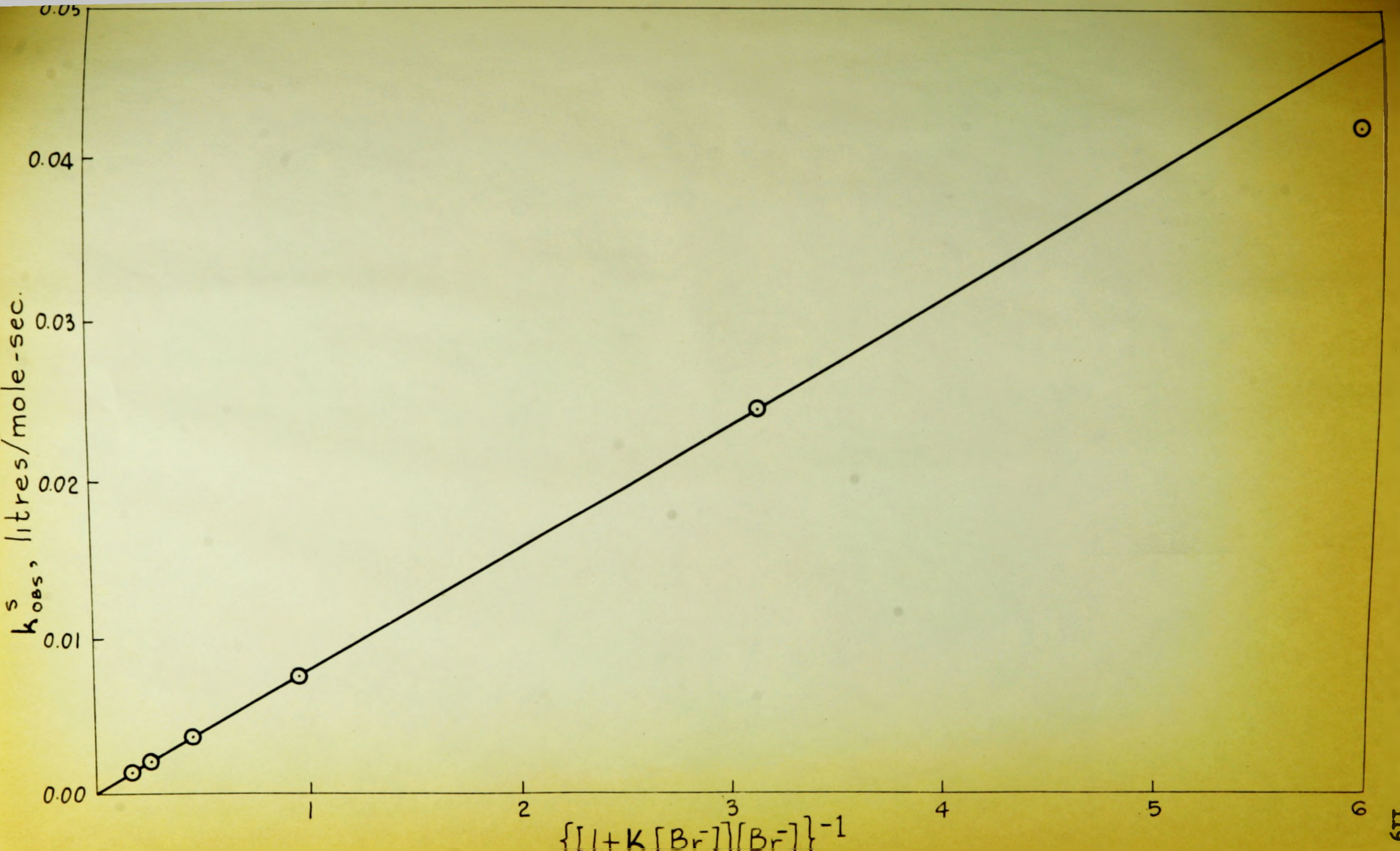


FIG. 10. PLOT OF RATE CONSTANTS, $k^s_{obs.}$, FOR THE BROMODESULPHONATION OF SODIUM P-METHOXYBENZENESULPHONATE VERSUS $\{[1+k[Br^-]][Br^-]\}^{-1}$.

convenient to include the latter point in the plot of Fig. 10 because of the relatively large value of $\left\{\left[1 + K\left[Br^-\right]\right]\left[Br^-\right]\right\}^{-1}$, namely 20.4.)

These deviations from linearity appear exactly where one would expect them for reaction by mechanism A with a k_2/k_3 ratio of 66. When the bromide-ion concentration is above 0.1M, $k_2\left[Br^-\right]$ is sufficiently large relative to k_3 to cause the kinetic points to fit a straight line within the limits of experimental error. Below 0.1M, however, the product $k_2\left[Br^-\right]$ starts to assume a value comparable to k_3 and deviations from linearity become apparent. The kinetic results, therefore, clearly favour mechanism A over B. Strong supporting evidence, however, is desirable and this has been sought through a kinetic sulphur isotope effect study of the reaction.

An inspection of mechanism B for the bromodesulphonation reaction reveals that the sulphur isotope effect should be independent of the bromide-ion concentration, since the bromide ion is formed in a pre-equilibrium which has nothing to do with the substitution step. For a two-step process in mechanism B,

$$\left[\frac{k^{32}}{k^{34}}\right]_{obs} = \frac{k_1'^{32}}{k_1'^{34}} \cdot \frac{k_3'^{32}}{k_3'^{34}} \cdot \frac{k_2'^{34} + k_3'^{34}}{k_2'^{32} + k_3'^{32}} \qquad (51)$$

and the observed isotope effect will depend on the relative magnitudes of k_3' and k_2'. If $k_3' \gg k_2'$, the effect will be zero (or close to it) and if $k_3' \ll k_2'$, the effect will be a normal one. Also, for a one-step process in mechanism B an isotope effect of appreciable magnitude can be expected since C - S bond rupture is involved in the rate-determining step.

For mechanism A, it follows from equation 60 that

$$\left[\frac{k^{32}}{k^{34}}\right]_{obs} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{k_3^{32}}{k_3^{34}} \cdot \frac{k_2^{34}\,[Br^-] + k_3^{34}}{k_2^{32}\,[Br^-] + k_3^{32}} \qquad (50)$$

It can be seen that this expression includes $[Br^-]$ and hence the magnitude of the isotope effect, $(k^{32}/k^{34})_{obs}$, can be expected to depend on the concentration of bromide ion. At zero or very small bromide-ion concentrations, $(k^{32}/k^{34})_{obs}$ is equal to k_1^{32}/k_1^{34}, which is a ratio of the rates with which the two isotopic species form an intermediate in which the C - S bond is still intact. No isotope effect (other than a small secondary one) can, therefore, be expected. As the bromide-ion concentration is increased, the intermediate will start to revert to reactants at the expense of its decomposition into products. The rupture of the C - S bond is then partially rate determining and an isotope effect will start to be associated with the reaction. Finally, at bromide-ion concentrations sufficiently high such that $k_2\,[Br^-] \gg k_3$, the ratio $(k^{32}/k^{34})_{obs}$ is given by the expression

$$\left[\frac{k^{32}}{k^{34}}\right]_{obs} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{k_2^{34}}{k_2^{32}} \cdot \frac{k_3^{32}}{k_3^{34}} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{k_3^{32}}{k_3^{34}}$$

where k_1^{32}/k_1^{34} is the equilibrium sulphur isotope effect for the reversible formation of the intermediate. This expression now includes the rate-constant ratio, k_3^{32}/k_3^{34}, for the step in which a C - S bond is being broken, and the observed isotope effect should be of considerable magnitude, namely of the order of 1.5 to 2 per cent. Thus, for mechanism A, the isotope effect can be expected to vary with changing bromide-ion concentration.

Kinetic sulphur isotope effects have been determined for the bromodesulphonation of sodium p-methoxybenzenesulphonate at three different initial bromide-ion concentrations: zero, 0.03 and 0.5M. In a reaction with no added bromide ion, the concentration of this ion will have reached 5×10^{-4} M during the 12 per cent reaction (with respect to sulphonate) used in the isotope effect experiments. This means that if mechanism A is operative, the ratio of the rate of reversion of the intermediate to its rate of conversion to product, $k_2 [Br^-]/k_3$, will on the average be only $66 \times 0.00025 = 0.0165$. For all practical purposes, then, one can consider that the intermediate proceeds only to product; that is the formation of the intermediate is rate determining. At $[Br^-] = 0.03$M, rate reverse/rate forward = $k_2 [Br^-]/k_3 = 66 \times 0.03 = \sim 2$; i.e., of every three intermediates formed, two revert to reactant and one proceeds to product. Finally, at $[Br^-] = 0.5$M, rate reverse/rate forward = $k_2 [Br^-]/k_3 = 66 \times 0.5 = 33$; under these conditions the intermediate should be essentially in equilibrium with reactants and a normal isotope effect can be expected.

The sulphur isotope abundance of the reactant and of the product formed in the various partial reactions are given in Table IX. Each sulphur isotopic ratio reported in this table is for barium sulphate produced in a separate bromodesulphonation experiment, either complete or partial. The ratios for the product of the complete reactions are averaged and the mean combined with the individual isotopic ratios obtained for the product of the partial reactions to give the $(S^{32}/S^{34})_{partial} \div (S^{32}/S^{34})_{complete}$ values recorded in the right-hand column of Table IX. These quotients are then substituted

TABLE IX

MASS SPECTROMETRIC RESULTS FOR THE BROMODESULPHONATION REACTION OF SODIUM p-METHOXYBENZENESULPHONATE

Expt. No.	Reaction	f'[a]	f[b]	S^{32}/S^{34}	$\frac{(S^{32}/S^{34})_{partial}}{(S^{32}/S^{34})_{complete}}$
ES-SI-1	Complete			22.152	
ES-SI-2				22.139	
ES-SI-3				22.200	
ES-SI-5				22.129	
ES-SI-6				22.124	
				Mean 22.149 ± 0.027[c]	
ES-SII-1	Partial at $[Br^-]$ = 0	0.125	0.112	22.245	1.0043
ES-SII-3		0.116	0.104	22.196	1.0021
ES-SII-4		0.144	0.129	22.182	1.0015
ES-SII-5		0.148	0.133	22.232	1.0037
ES-SII-6		0.150	0.135	22.225	1.0034
ES-SIII-2	Partial at $[Br^-]$ = 0.03M	0.129	0.0889	22.391	1.0109
ES-SIII-3		0.131	0.0904	22.431	1.0127
ES-SIII-4		0.160	0.112	22.435	1.0129
ES-SIV-1	Partial at $[Br^-]$ = 0.5M	0.144	0.0338	22.521	1.0168
ES-SIV-2		0.146	0.0345	22.489	1.0154
ES-SIV-3		0.146	0.0345	22.543	1.0178
ES-SIV-4		0.137	0.0319	22.532	1.0173

[a] f' is the mole fraction of the reactant which has undergone bromination.

[b] f is the corrected mole fraction of the reactant which has undergone bromodesulphonation (see page 111).

[c] The limit shown is the standard deviation.

into equation 57 (page 110), along with the corresponding f values, for the calculation of the kinetic isotope effects, k^{32}/k^{34}, recorded in Table X. The individual k^{32}/k^{34} ratios at a given bromide-ion concentration are averaged and the standard deviation calculated.

Inspection of Table X reveals that the kinetic isotope effect does indeed increase with an increase in the concentration of bromide ion. These results completely eliminate mechanism B and are readily interpretable in terms of mechanism A, the two-step process with molecular bromine as the electrophilic agent. Thus, at very low bromide-ion concentration, the rate-determining step is the formation of the quinoid intermediate in which the C - S bond is still intact. The isotope effect, which is a measure of the rate ratio k_1^{32}/k_1^{34} is 1.0032. At bromide-ion concentration of 0.5M, the rupture of the C - S bond is fully rate determining and a normal isotope effect of 1.0173 is observed. At intermediate bromide-ion concentration of 0.03M the rupture of the C - S bond is partially rate determining and the isotope effect is 1.0127.

It is of interest to evaluate the ratio k_3^{32}/k_3^{34}, the isotope effect for the step involving C - S bond rupture, using equation 50 and the experimentally observed isotope effects at the different bromide-ion concentrations.

$$\left[\frac{k^{32}}{k^{34}}\right]_{obs} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{k_3^{32}}{k_3^{34}} \cdot \frac{k_2^{34}[Br^-] + k_3^{34}}{k_2^{32}[Br^-] + k_3^{32}} \qquad (50)$$

This calculation requires an assumption concerning the value of k_2^{32}/k_2^{34}. Since the quinoid intermediate is a high-energy species it seems reasonable to assume that the transition state for the first step more closely

TABLE X

KINETIC SULPHUR ISOTOPE EFFECTS FOR THE BROMODESULPHONATION OF SODIUM p-METHOXYBENZENESULPHONATE AT 0°C

Expt. No.	$[Br^-]$ mole/l	k^{32}/k^{34}	k_3^{32}/k_3^{34}
ES-SII-1	0	1.0045	
ES-SII-3		1.0023	
ES-SII-4		1.0017	
ES-SII-5		1.0041	
ES-SII-6		1.0037	
		Mean 1.0032 ± 0.0012[a]	
ES-SIII-2	0.03	1.0113	
ES-SIII-3		1.0133	
ES-SIII-4		1.0136	
		Mean 1.0127 ± 0.0009[a]	1.0143
ES-SIV-1	0.5	1.0171	
ES-SIV-2		1.0160	
ES-SIV-3		1.0181	
ES-SIV-4		1.0178	
		Mean 1.0173 ± 0.0008[a]	1.0145

[a]The limits shown are standard deviations.

resembles this intermediate than it does the reactant. This being so, the ratio k_2^{32}/k_2^{34} should be considerably closer to unity than is the ratio k_1^{32}/k_1^{34} for which the value 1.0032 has been observed. It would seem reasonable, therefore, to assume $k_2^{32} = k_2^{34}$, in other words, that there is no significant isotope effect for the reverse reaction within the limits of the present measurements. With this assumption then, it follows from equation 50 that

$$\left[\frac{k^{32}}{k^{34}}\right]_{obs} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{\frac{k_3^{32}}{k_3^{34}} \cdot \frac{k_2^{32}}{k_2^{32}} \cdot [Br^-] + 1}{\frac{k_2^{32}}{k_3^{32}} \cdot [Br^-] + 1} \qquad (63)$$

In equation 63, $k_1^{32}/k_1^{34} = 1.0032$, the isotope effect measured at zero bromide-ion concentration; and $k_2^{32}/k_3^{32} = 66$, a value obtained from the slope and intercept of the plot for $\left\{k^a_{obs}\left[1 + K\,[Br^-]\right]\right\}^{-1}$ versus $[Br^-]$ in Fig. 9. Equation 63 reduces to

$$\left[\frac{k^{32}}{k^{34}}\right]_{obs} = 1.0032 \cdot \frac{\frac{k_3^{32}}{k_3^{34}} \cdot 66 \cdot [Br^-] + 1}{66 \cdot [Br^-] + 1} \qquad (64)$$

In this equation, $(k^{32}/k^{34})_{obs}$ is the measured isotope effect at a particular bromide-ion concentration and hence the only unknown quantity, k_3^{32}/k_3^{34}, can be calculated. The latter values are given in Table X.

The significant point which comes out of this calculation is that exactly the same value, within experimental error, is obtained for the k_3^{32}/k_3^{34} ratio by substituting into equation 64 the observed kinetic isotope effect at the two different bromide-ion concentrations, 0.03M and 0.5M. This internal self-consistency of the results, when inter-

preted in terms of mechanism A, lends further support to this mechanism for the reaction. It is of interest to note also that the value 1.014 obtained for k_3^{32}/k_3^{34} corresponds closely to the theoretical value, 1.016, for a transition state in which there is complete carbon-sulphur bond rupture.

It is of some significance that there is a small, but certainly real, isotope effect in the formation of the quinoid intermediate. Since the C - S bond remains intact in this process one might have expected a zero isotope effect. It might, therefore, be argued that the isotope effect observed at zero bromide-ion concentration results from a slight reversion of the intermediate as a consequence of the bromide-ion developed during the course of the reaction. That this is not so, and that the effect is quite definitely a secondary one, can be shown by the method of successive approximations as follows.

(a) Assuming $k_1^{32}/k_1^{34} = 1$ (i.e., there is no secondary isotope effect in the formation of the quinoid intermediate as one would have expected), equation 63 is used to calculate k_3^{32}/k_3^{34} from the experimental data: $[Br^-] = 0.5$, $(k^{32}/k^{34})_{obs} = 1.0173$. The value of k_3^{32}/k_3^{34} so obtained is 1.0178.

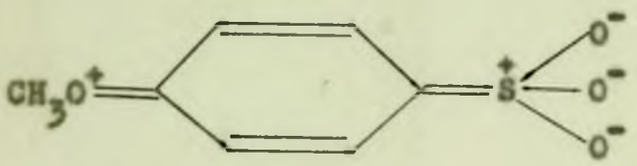
(b) This value of k_3^{32}/k_3^{34} is substituted in equation 63 to calculate k_1^{32}/k_1^{34} using the experimental data: $[Br^-] = 0.00025M$ (average bromide-ion concentration developed during the course of the reaction in the partial run in which there is no added bromide ion); $(k^{32}/k^{34})_{obs} = 1.0032$. The value of k_1^{32}/k_1^{34} so obtained, which should be somewhat better than the initially assumed value of unity, is 1.0030.

(c) Now, using $k_1^{32}/k_1^{34} = 1.0030$, procedure (a) is repeated and a value of 1.0147 is obtained for k_3^{32}/k_3^{34}.

(d) Procedure (b) is again repeated using $k_3^{32}/k_3^{34} = 1.0147$. The value of k_1^{32}/k_1^{34} so obtained is 1.0030, identical with the result from operation (b).

Thus, through this series of operations, k_1^{32}/k_1^{34} finally assumes a constant value 1.0030 which is not significantly different from the observed effect 1.0032, obtained in the absence of added bromide ion. This effect is clearly a secondary one associated with the step for the formation of the intermediate.

It is not unreasonable that a small secondary isotope effect should be associated with the step involving formation of the intermediate. The sulphonate group in the initial state is capable of conjugative interaction with the benzene ring.



This conjugation is destroyed in the formation of the intermediate, resulting in some C - S bond weakening. Evidence in support of such conjugative interaction of the sulphonate group with the aromatic ring has been obtained in studies on the acid strength of naphthylammonium ions (133), $\bar{O}_3SC_{10}H_6\overset{+}{N}H_3$, and of substituted benzenesulphonic acids (134). It is to be noted that the very small secondary isotope effects associated with the elements of higher atomic number usually are not detectable. To the author's knowledge, the only other example reported to date is a secondary C^{14} effect in the formation of 2,4-dinitrophenylhydrazone of acetophenone-β-C^{14} (65).

As discussed earlier in the Historical Introduction (page 63) kinetic data cannot distinguish between mechanisms A and B for the bromodesulphonation of sodium 3,5-dibromo-4-aminobenzenesulphonate and disodium 3,5-dinitro-4-hydroxybenzenesulphonate since a plot of k_{obs} versus $\left\{\left[1 + K\,[Br^-]\right][Br^-]\right\}^{-1}$ is linear. The evidence obtained in the present work for the operation of mechanism A in the bromodesulphonation of sodium p-methoxybenzenesulphonate strongly suggests that this mechanism is being followed also in the reaction of these more reactive compounds.

Bromodesulphonation of Potassium 1-Methylnaphthalene-4-Sulphonate

Preliminary kinetic studies on the bromination of potassium 1-methylnaphthalene-4-sulphonate revealed that this compound, like sodium p-methoxybenzenesulphonate, undergoes competing bromodesulphonation and bromodeprotonation reactions. The latter reaction had been overlooked by Cannell in his kinetic study of the bromination of this compound. Furthermore, there was reason for believing that the salt on which Cannell performed his measurements was quite impure. For these reasons, a careful reinvestigation of the bromination kinetics, including the determination of sulphate yields, was made over a range of bromide-ion concentrations from zero to 0.5 M. The results are given in Table XI.

It can be seen from this table that the product $k^s_{obs}\left[1 + K\,[Br^-]\right]$ is not strictly constant but shows a decrease of about 33 per cent over the range of bromide-ion concentration studied. Similar small decreases in $k_{obs}\left[1 + K\,[Br^-]\right]$ have been observed by others in certain bromodeprotonation processes (98,99) and have been attributed to a salt effect

TABLE XI

KINETIC DATA ON THE BROMODESULPHONATION OF POTASSIUM 1-METHYLNAPHTHALENE-4-SULPHONATE AT 0°C
(Rate Constants Expressed in Litres/Mole-Sec)

Ionic Strength M	$[Br^-]$ mole/l	Per Cent Sulphate Yield	k_{obs}	k^a_{obs}	$k^a_{obs}\left[1 + K[Br^-]\right]$
0.5	0	89.7	0.103 ± 0.0008[a]	0.0924	0.0924
	0.1	88.5	0.0304 ± 0.00022	0.0269	0.0836
	0.25	80.1	0.0143 ± 0.00007	0.0115	0.0721
	0.4	76.8	0.00887 ± 0.00004	0.00681	0.0643
	0.5	75.5	0.00709 ± 0.00003	0.00535	0.0618
2.0[b]	0	88.8	0.321 ± 0.0032	0.321	
	2.0	59.6	0.00267 ± 0.000024	0.00159	

[a] Precision limits are calculated from the standard deviation of slope of the least square plot of $\log_{10} \frac{A_o - B_o + B}{B}$ versus t.

[b] Kinetics investigated for isotope effect study at high ionic strength.

resulting from the replacement by sodium bromide of some inert salt used to maintain constant ionic strength at the different bromide-ion concentrations. Clearly, this very small depression in rate by bromide ion eliminates any form of mechanism with Br^+ (or H_2OBr^+) serving as the brominating species (see equations 61 and 62), but it is consistent with either the one- or two-step mechanism with Br_2 as the attacking agent. As stated in an earlier section a one-step process does not seem too unreasonable here since a species having the quinoid configuration, stabilised by hyperconjugation only, might be expected to have a higher energy in this reaction than in the more highly activated systems studied and, therefore, might not correspond to a potential energy minimum along the reaction co-ordinate curve.

If the bromodesulphonation reaction of potassium 1-methylnaphthalene-4-sulphonate does proceed by the one-step mechanism then the small decrease in $k^s_{obs}\left[1 + K\left[Br^-\right]\right]$ with increasing bromide-ion concentration must be due entirely to the salt effect. On the other hand, if the reaction is proceeding in two steps through a quinoid intermediate then the decrease in $k^s_{obs}\left[1 + K\left[Br^-\right]\right]$ would be due in part or in all to the return of this intermediate to reactant as the bromide-ion concentration is increased. The fact that a plot of $\left\{k^s_{obs}\left[1 + K\left[Br^-\right]\right]\right\}^{-1}$ versus $\left[Br^-\right]$ (Fig. 11*) is linear lends support to the two-step mechanism, although the possibility that a salt effect could take a similar form is not excluded. Interpreting the decrease of $k^s_{obs}\left[1 + K\left[Br^-\right]\right]$ solely in terms of a return of

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*The scale chosen for this plot is the same as in the bromodesulphonation of sodium p-methoxybenzenesulphonate in order to allow visual comparison of the effect of bromide ion on rate in the two systems.

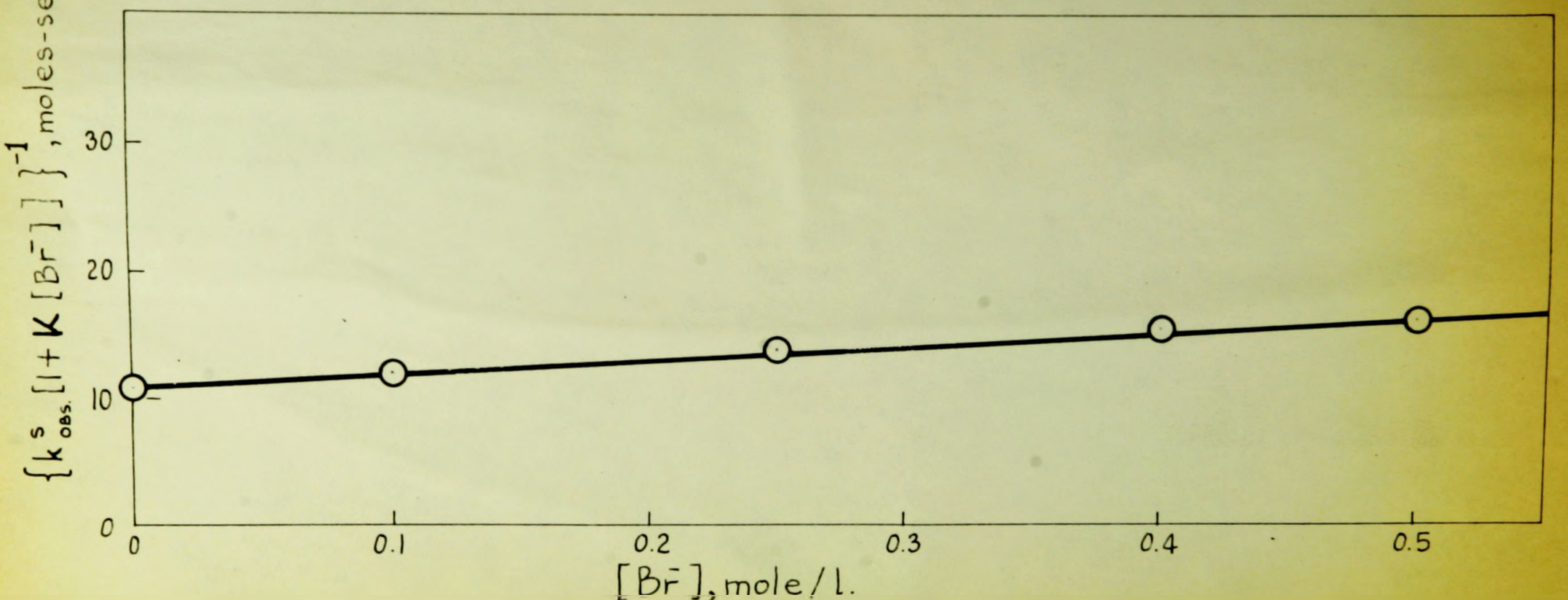

FIG.11. PLOT OF RATE CONSTANTS, CORRECTED FOR Br_3^- EFFECT, FOR THE BROMODESULPHONATION OF POTASSIUM 1-METHYLNAPHTHALENE-4-SULPHONATE VERSUS $[Br^-]$.

an intermediate to reactant, the slope and intercept of the line in Fig. 11 gives a value of 1.1 for k_2/k_3, the ratio of the rate constants for the reverse and forward reactions involving this intermediate.

It was hoped that a study of the kinetic sulphur isotope effect in this reaction would distinguish between the two mechanisms. Since the ratio $k_2/k_3 = 1.1$, if real, is extremely small compared to the value 66 obtained for sodium p-methoxybenzenesulphonate, the magnitude of the sulphur isotope effect one might expect for a two-step mechanism should be small even at quite high bromide-ion concentrations. If this effect, however small, is found to vary significantly with bromide-ion concentration then this result would be very strong evidence in support of the two-step mechanism. On the other hand, a small effect whose magnitude is independent of bromide-ion concentration allows no distinction between the two possibilities. The depression in $k^s_{obs}\left[1 + K\left[Br^-\right]\right]$ would in this case be entirely due to the salt effect and the reaction could be proceeding either by a two-step mechanism, in which k_3 is always much greater than $k_2\left[Br^-\right]$, or by a one-step mechanism involving a transition state with little C - S bond rupture. Finally, the observation of a normal isotope effect, 1 - 2 per cent, which is independent of bromide-ion concentration, would clearly eliminate the two-step mechanism and would provide strong evidence in support of a concerted process.

In Table XII are given the sulphur isotope abundances of barium sulphate produced in two kinds of "complete" bromodesulphonation reactions, one carried out at room temperature and giving a 93 per cent yield of barium sulphate and the other performed under drastic

TABLE XII

MASS SPECTROMETRIC RESULTS FOR THE PRODUCT OF COMPLETE BROMODESULPHONATION OF POTASSIUM 1-METHYLNAPHTHALENE-4-SULPHONATE

Expt. No.	Reaction Conditions	S^{32}/S^{34} Individual Values	Mean
E'S-SI-3	Room Temperature	22.236	
E'S-SI-4		22.216	
E'S-SI-5		22.213	
E'S-SI-8		22.188	
E'S-SI-9		22.202	
			22.211 ± 0.019[a]
E'S-SI-1	Sealed Tube 210°C	22.200	
E'S-SI-2		22.193	
E'S-SI-6		22.219	
E'S-SI-7		22.213	
			22.206 ± 0.012[a]
		Overall Mean	22.209 ± 0.014[a]

[a]The limits shown are standard deviations.

conditions in a sealed tube and producing close to the theoretical yield of product. It can be seen from this table that the sulphur isotopic ratios of the barium sulphate produced in two kinds of "complete" bromodesulphonations are identical to well within experimental error. This shows that the seven per cent impurity, which it will be recalled is considered to be an unreactive isomer of potassium 1-methlnaphthalene-4-sulphonate, has the same sulphur isotopic abundance as the compound in question.

In Table XIII are given the isotopic abundance ratios for the sulphur of the barium sulphate produced in partial reactions carried out at bromide-ion concentrations ranging from zero to 2.0M and at two different ionic strengths. These ratios were each divided by the mean value obtained for the products of complete reaction and the resulting quotients were separately used for the calculation of the isotope effect values k^{32}/k^{34} given in the last column of the table. The individual k^{32}/k^{34} ratios obtained in experiments conducted at the same bromide-ion concentration and ionic strength were then averaged.

Initial experiments were carried out at a constant ionic strength of 0.5M and at bromide-ion concentrations ranging from zero to 0.5M. These were the conditions used in the sodium p-methoxybenzne-sulphonate study. Inspection of Table XIII reveals that over this range of bromide-ion concentration the isotope effects are small and show a variation which is barely beyond experimental error. There is, however, a strong suggestion of a small increase in the isotope effect with increasing bromide-ion concentration, but the change is too small to be meaningful as a mechanistic criterion.

TABLE XIII

KINETIC SULPHUR ISOTOPE EFFECTS FOR THE BROMODESULPHONATION OF POTASSIUM 1-METHYLNAPHTHALENE-4-SULPHONATE AT 0°C

Expt. No.	$[Br^-]$ mole/l	Ionic Strength mole/l	f'[a]	f[b]	s^{32}/s^{34}	$\frac{(s^{32}/s^{34})_{partial}}{(s^{32}/s^{34})_{complete}}$[c]	k^{32}/k^{34}
E'S-SII-1	0	0.5	0.0954	0.0864	22.235	1.0012	1.0013
E'S-SII-2	0	0.5	0.0988	0.0895	22.244	1.0016	1.0015
							Mean 1.0014
E'S-SII'-1	0	2.0	0.201	0.184	22.227	1.0008	1.0011
E'S-SII'-2	0	2.0	0.200	0.183	22.262	1.0024	1.0025
E'S-SII'-3	0	2.0	0.184	0.168	22.258	1.0022	1.0026
E'S-SII'-4	0	2.0	0.184	0.169	22.274	1.0029	1.0032
							Mean 1.0023 ± 0.0008[d]
E'S-SIV-1	0.25	0.5	0.112	0.0917	22.259	1.0022	1.0026
E'S-SIV-2	0.25	0.5	0.111	0.0908	22.272	1.0028	1.0032
							Mean 1.0029
E'S-SIII-1	0.5	0.5	0.111	0.0862	22.292	1.0038	1.0043
E'S-SIII-2	0.5	0.5	0.105	0.0811	22.262	1.0024	1.0030
E'S-SIII-3	0.5	0.5	0.201	0.159	22.269	1.0027	1.0028
E'S-SIII-4	0.5	0.5	0.201	0.159	22.306	1.0044	1.0046
							Mean 1.0037 ± 0.0008[d]
E'S-SV-4	2.0	2.0	0.0542	0.0332	22.350	1.0064	1.0069
E'S-SV-5	2.0	2.0	0.0544	0.0333	22.399	1.0085	1.0088
E'S-SV-2	2.0	2.0	0.112	0.0771	22.383	1.0078	1.0081
E'S-SV-3	2.0	2.0	0.114	0.0786	22.366	1.0071	1.0075
E'S-SV-1	2.0	2.0	0.236	0.169	22.346	1.0062	1.0066
E'S-SV-1(D)	2.0	2.0	0.236	0.169	22.365	1.0070	1.0079
							Mean 1.0076 ± 0.0007[d]

[a] f' is the mole fraction of the reactant which has undergone bromination.
[b] f is the corrected mole fraction of the reactant which has undergone bromodesulphonation (see page 111).
[c] $(s^{32}/s^{34})_{complete}$ = 22.209 - see Table XII.
[d] The limits shown are standard deviations.

These results obviously made it necessary to go to a higher bromide-ion concentration. Since in doing so the ionic strength of the medium would also change, it was necessary first to demonstrate that a change in ionic strength alone does not significantly influence the magnitude of the isotope effect. That this is indeed the case can be seen from Table XIII by comparing the results obtained at the two ionic strengths in the absence of added bromide ion. The difference in the mean k^{32}/k^{34} ratios does not exceed experimental error.

Having established this point, a series of isotope effect measurements were made at $[Br^-]$ = 2.0M. The mean value so obtained, 1.0076* ± 0.0007, is significantly different from the value, 1.0023 ± 0.0008, found at zero bromide ion and the same ionic strength. This result amply confirms the trend suggested by the earlier experiments and, in the opinion of this author, clearly establishes the two-step mechanism for the bromodesulphonation of potassium 1-methylnaphthalene-4-sulphonate.

Both the magnitude and variation in the isotope effects given in Table XIII show that the decrease in $k^a_{obs}\left[1 + K\,[Br^-]\right]$ with $[Br^-]$ (see Table XI) is not entirely due to the return of the intermediate to reactants. Thus, if the number 1.1 obtained from the plot in Fig. 11 were the true value for the ratio k_2/k_3, then at $[Br^-]$ = 0.5M, one intermediate returns to reactant to two going forward and the isotope effect should have increased considerably over the value obtained in

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*It is of interest to note that the same isotope effect, within the precision of measurement, is obtained at $[Br^-]$ = 2.0M at widely different extents of reaction, f. This establishes that the impurity present in the salt causes no complication in the experiments.

the absence of added bromide ion. At $[Br^-] = 2.0M$, the observed isotope effect should have nearly reached a normal value. Clearly, therefore, much of the depression in $k^s_{obs}\left[1 + K\,[Br^-]\right]$ is due to the salt effect.

It is possible by substitution into equation 63 to estimate from the isotope effect results the true value of the k_2/k_3 ratio. In this equation

$$\left[\frac{k^{32}}{k^{34}}\right]_{obs} = \frac{k_1^{32}}{k_1^{34}} \cdot \frac{\frac{k_3^{32}}{k_3^{34}} \cdot \frac{k_2^{32}}{k_3^{32}} \cdot [Br^-] + 1}{\frac{k_2^{32}}{k_3^{32}} \cdot [Br^-] + 1} \qquad (63)$$

k_1^{32}/k_1^{34} is 1.0023, the isotope effect at zero bromide-ion concentration, while the ratio k_3^{32}/k_3^{34} can to a first approximation be considered to be the same as that found in the reaction of sodium p-methoxybenzene-sulphonate, namely 1.0144. These ratios when combined in equation 63 with the observed isotope effect at 2.0M bromide ion gave a value of 0.29 for the k_2/k_3 ratio. That some reliance can be placed in the k_2/k_3 ratio calculated in this way, and in the assumption that $k_3^{32}/k_3^{34} \simeq 1.014$, is shown by the agreement between the isotope effects obtained experimentally at the other bromide-ion concentrations, 0.25 and 0.5M, and the values calculated by substitution of the k_2/k_3, k_1^{32}/k_1^{34} and k_3^{32}/k_3^{34} values into equation 63. At 0.25M bromide ion the experimentally observed isotope effect is 1.0029, the calculated value 1.0032; at 0.5M bromide ion the corresponding values are 1.0037 and 1.0041. It can be inferred, therefore, that nearly 75 per cent of the depression in the quantity $k^s_{obs}\left[1 + K\,[Br^-]\right]$ by bromide ion results from the salt effect.

Bromodeprotonation of Sodium p-Methoxybenzenesulphonate

The rate constants, k^H_{obs}, for the bromodeprotonation reaction of sodium p-methoxybenzenesulphonate, at various bromide-ion concentrations, evaluated from the rate constants for total bromination, k_{obs}, and sulphate-yield results (see Table VIII) are given in Table XIV. It can be seen that the product, $k^H_{obs}\left[1 + K\,[Br^-]\right]$, is not strictly a constant but diminishes by a considerable amount (~37 per cent) over a range of bromide-ion concentration, zero to 0.5M. This result is strictly incompatible with any form of mechanism involving Br^+ (or H_2OBr^+) as the brominating species (see equations 61 and 62, page 113), but can be accommodated readily by a one- or two-step mechanism with Br_2 as the brominating agent.

The question which now arises is whether the decrease in $k^H_{obs}\left[1 + K\,[Br^-]\right]$ is purely a salt effect resulting from the replacement of sodium perchlorate by sodium bromide as the bromide-ion concentration is increased (at constant ionic strength), or whether it is due, at least in part, to the return of a reaction intermediate to reactant. The fact that a plot of $\left\{k^H_{obs}\left[1 + K\,[Br^-]\right]\right\}^{-1}$ versus $[Br^-]$ is linear (see Fig. 9*) is certainly in accordance with the two-step mechanism in which the depression of rate with increasing bromide ion results from the return of the intermediate.

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*The deviation from linearity of the point at $[Br^-] = 0$ in this plot is undoubtedly due to the large experimental error in the value used for per cent bromodeprotonation. At $[Br^-] = 0$, the sulphate yield is 88 ± 1 per cent, hence bromodeprotonation is 12 ± 1 per cent.

TABLE XIV

KINETIC DATA ON THE BROMODEPROTONATION OF SODIUM p-METHOXYBENZENESULPHONATE AT 0°C

(Ionic Strength = 0.5M
Rate Constants expressed in litres/mole-sec)

$[Br^-]$ mole/l	k^H_{obs}	$k^H_{obs}\left[1 + K[Br^-]\right]$
0	0.0630	0.0630
0.03	0.0600	0.0980
0.07	0.0380	0.0940
0.1	0.0289	0.0898
0.2	0.0140	0.0731
0.3	0.00935	0.0685
0.4	0.00691	0.0652
0.5	0.00534	0.0616

$$ArH + Br_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Ar\overset{H}{\underset{Br}{<}} + Br^-$$

$$Ar\overset{+}{\underset{Br}{<}}\overset{H}{} \xrightarrow{k_3} ArBr + H^+$$

On the other hand, Bell and Rawlinson (98) have found a similar depression of rate in the aqueous bromination of anisole and have attributed it entirely to the salt effect.

The answer to this question may be provided through a study of kinetic hydrogen isotope effect at different bromide-ion concentrations. If the depression in $k^H_{obs}\left[1 + K\left[Br^-\right]\right]$ is due entirely to a salt effect, no change in the kinetic isotope effect should occur with changing bromide-ion concentration. If this result were to be observed, then no distinction could be made between a one-step mechanism and a two-step mechanism in which the rate of decomposition of the intermediate is fast relative to its return to reactant at all experimentally realisable bromide-ion concentrations, i.e., $k_3 \gg k_2\left[Br^-\right]$. If, however, any significant part of the depression of $k^H_{obs}\left[1 + K\left[Br^-\right]\right]$ is due to the return of an intermediate to reactant, then this should manifest itself in an increase in k^H/k^D with increasing concentration of bromide ion. This observation would provide the strongest possible evidence for the two-step mechanism.

As described in the experimental section of this thesis, the kinetic isotope effect, k^H/k^D, may be evaluated from a knowledge of the total bromination rate constants for the undeuterated and deuterated compounds, i.e., $(k_{obs})_H$ and $(k_{obs})_D$, respectively, and the ratio of the rate constants for bromodesiphonation and bromodeprotonation, k^S/k^H.

The results of this investigation are given in Table XV, where it can be seen that there is a definite increase in the isotope effect with increasing bromide-ion concentration. The two-step mechanism is thus established.

Now if the depression in $k^H_{obs}\left[1 + K\,[Br^-]\right]$ were due entirely to a return of the intermediate to reactant, then the slope of this line in Fig. 9 is k_2/k_1k_3 and the intercept is $1/k_1$. From these a value of 1.2 is calculated for the ratio k_2/k_3. That this value is much too high is evident from the small value of the isotope effect and its relative insensitivity to changes in bromide-ion concentration. Thus, if this ratio were correct, then at $[Br^-]$ = 2.0M, for every seven molecules of the intermediate formed, five would return to reactant and only two would proceed to product. This is approaching an equilibrium condition between reactant and intermediate and would be expected to give rise to an isotope effect, k^H/k^D, of several fold.

It is possible to obtain an estimate of the true k_2/k_3 ratio, and with it the quantity k^H_3/k^D_3, the isotope effect for the C - H bond rupture step, by a trial and error substitution into equation 65* so as to obtain the best fit to the experimental values of k^H/k^D at the different bromide-ion concentrations.

$$\frac{k^H}{k^D} = \frac{k^H_1}{k^D_1} \cdot \frac{\frac{k^H_3}{k^D_3} \cdot \frac{k^H_2}{k^H_3} \cdot [Br^-] + 1}{\frac{k^H_2}{k^H_3} \cdot [Br^-] + 1} \qquad (65)$$

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*The corresponding equation for the sulphur isotope effect in the bromodesulphonation reaction is derived on page 126.

TABLE XV

KINETIC HYDROGEN ISOTOPE EFFECTS FOR THE BROMODEPROTONATION REACTION OF SODIUM p-METHOXYBENZENESULPHONATE AT 0°C

(Rate Constants expressed in litres/mole-sec)

Ionic Strength M	$[Br^-]$ mole/l	[a] $(k_{obs})_H \times 10^3$	[a] $(k_{obs})_D \times 10^3$	[b] $\left(\frac{k^S}{k^H}\right)_H$	k^H/k^D Found	k^H/k^D Calc.
0.5	0	538 ± 4	536 ± 4	7.47	1.01 ± 0.02[c]	1.00
	0.1	54.9 ± 0.5	54.4 ± 0.2	0.901	1.02 ± 0.02	1.02
	0.5	6.76 ± 0.035	6.42 ± 0.02	0.263	1.07 ± 0.01	1.08
1.0	0.5	9.44 ± 0.03	8.94 ± 0.04	0.241	1.07 ± 0.01	1.08
	1.0	4.24 ± 0.026	3.67 ± 0.018	0.119	1.18 ± 0.02	1.16
2.0	2.0	3.04 ± 0.012	2.34 ± 0.012	0.0417[d]	1.31 ± 0.02	1.31

[a] Precision limits are calculated from the standard deviation of slope of the least square plot of $\log_{10} (A_o - B_o + B)/B$ versus t.

[b] $(k^S/k^H)_H$ = per cent bromodesulphonation/per cent bromodeprotonation for the undeuterated sulphonate.

[c] Estimated maximum overall error based upon variation in the $(k^S/k^H)_H$ and rate constant values.

[d] The sulphate yield at $[Br^-]$ = 2.0M was estimated to be 4 per cent. An accurate experimental determination was not possible at this concentration of salt.

In deriving this equation the reasonable assumption is made that the isotope effect for the return of the intermediate to reactants, k_2^H/k_2^D, is unity. The term k_1^H/k_1^D, which is the ratio of the observed rate constants at zero bromide ion concentration is, as seen from Table XV, also unity. This procedure leads to $k_2/k_3 = 0.027$ and $k_3^H/k_3^D = 7.0$. The fit to the experimental data obtained by substitution of these values into equation 65 can be seen by comparing the last two columns in Table XV*.

The value for k_2/k_3 of 0.027 obtained from the isotope effect results is to be compared to the value 1.2 obtained on the assumption that the depression in $k^H_{obs}[1 + K[Br^-]]$ with $[Br^-]$ (Fig. 9) is due entirely to an increasing return of the intermediate to reactants as the bromide-ion concentration is increased. Clearly, therefore, almost all this depression in rate is the result of the salt effect. Indeed, it was fortunate that there was sufficient return of the intermediate to give a fruitful result in the application of the isotope effect test for the two-step mechanism.

It is of interest to note that the isotope effect for the second step, k_3^H/k_3^D, is 7.0. This is about the value to be expected for C - H bond rupture in a reaction at 0°C.

Finally, attention should be drawn to the fact that the ratio k_1^H/k_1^D, which is the ratio of the rates of formation of the intermediate from the two isotopic compounds and is given by k^H/k^D at $[Br^-] = 0$,

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*It is recognised that the k_2/k_3 ratio will not be entirely independent of ionic strength. The fact, however, that the isotope effect at two ionic strengths for $[Br^-] = 0.5M$ is the same within the limits of measurement indicates that the k_2/k_3 ratio is rather insensitive to changes in ionic strength.

is unity within the precision of about $\pm$0.02. The absence of a significant secondary isitope effect in this reaction is to be compared with the result obtained by de la Mare *et al*. (5) for the bromination of benzene, $k^H/k^D = 0.97 \pm 0.04$, and that found by Berliner and Schueller (15) in the bromination of diphenyl, $k^H/k^D = 1.15 \pm 0.01$. It is suggested that the similar rate of formation of the intermediate in the bromodeprotonation of undeuterated and deuterated sodium p-methoxybenzenesulphonate is a consequence of a fortuitous cancellation in the transition state of the effect of hyperconjugation and of the rehybridization of the carbon orbitals from sp^2 to sp^3 (15).

SUMMARY

1. The bromination of sodium p-methoxybenzenesulphonate results in two concurrent reactions, bromodesulphonation and bromodeprotonation, the latter increasing in amount as the bromide-ion concentration is raised. In the bromination of the less reactive potassium 1-methylnaphthalene-4-sulphonate, these two competing reactions also occur, but bromodeprotonation takes place to a relatively small extent.

2. A reinvestigation of the kinetics of bromination and a determination of sulphate yields for both of these compounds over a range of bromide-ion concentration, zero to 0.5M, has been made in order to assess the individual rates of bromodesulphonation and bromodeprotonation. The kinetic data for the bromodesulphonation of sodium p-methoxybenzenesulphonate favour a two-step mechanism with molecular bromine as the brominating agent but are not considered to completely eliminate a one- or two-step process involving Br^+ (or H_2OBr^+). In the case of potassium 1-methylnaphthalene-4-sulphonate, the kinetics allow either a one- or two-step process with molecular bromine as the brominating species.

3. Kinetic sulphur isotope effects have been measured for the bromodesulphonation of sodium p-methoxybenzenesulphonate at different bromide-ion concentrations. The observed effects are: at $[Br^-] = 0$, 0.3 per cent; at $[Br^-] = 0.03M$, 1.3 per cent; at $[Br^-] = 0.5M$, 1.7 per cent. These results confirm the two-step mechanism favoured by

the kinetic data and allow the rejection of the alternate mechanism with Br^+ (or H_2OBr^+) as the brominating species. A similar study of potassium 1-methylnaphthalene-4-sulphonate gave the following results: at $[Br^-]$ = 0, 0.2 per cent; at $[Br^-]$ = 0.25M, 0.3 per cent; at $[Br^-]$ = 0.5M, 0.4 per cent; at $[Br^-]$ = 2.0M, 0.8 per cent. These results establish the two-step mechanism for this compound and completely eliminate the alternate one-step process.

4. In the case of sodium p-methoxybenzenesulphonate a secondary sulphur isotope effect of 0.3 per cent has been observed for the formation of the meta-stable intermediate. This result is accounted for in terms of conjugative interaction of the sulphonate group with the aromatic ring in the initial state. Also, the observed isotope effects at different bromide-ion concentrations enabled the calculation of the isotope effect for the step involving carbon-sulphur bond rupture and the value obtained, 1.4 per cent, compares favourably with the theoretical value of 1.6 per cent.

5. The kinetic data for the bromodeprotonation of sodium p-methoxybenzenesulphonate do not distinguish between a one- and two-step mechanism with molecular bromine as the brominating species. The two-step mechanism was confirmed by the observation of a variation in kinetic hydrogen isotope effect, k^H/k^D, with changing bromide-ion concentration: at $[Br^-]$ = 0, k^H/k^D = 1.01; at $[Br^-]$ = 0.5M, k^H/k^D = 1.07; at $[Br^-]$ = 1.0M, k^H/k^D = 1.18; at $[Br^-]$ = 2.0M, k^H/k^D = 1.31. This work is of special significance in that it constitutes the first study establishing a meta-stable intermediate in the ordinary halodeprotonation reaction.

6. The isotope effect study for the bromodesulphonation of potassium 1-methylnaphthalene-4-sulphonate and bromodeprotonation of sodium p-methoxybenzenesulphonate strongly establish that in these reactions the small depression in rate produced by bromide ion, beyond that due to tribromide-ion formation, arises mainly from a salt effect and only a small amount of this depression is caused by return of the intermediate to reactant.

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