ISOTOPE EFFECTS IN ACID-CATALYZED AROMATIC HYDROGEN EXCHANGE*

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Deuterium- or tritium-substituted aromatics undergo isotope exchange in fairly concentrated aqueous sulfuric acid media. The rate constant for this process is complex, being composed of that for the slow electrophilic attack, and the isotope effect on the breakup of the Wheland intermediate. Using experimental rate constant data for both deuterium and tritium exchange on the same substrate, the excess acidity method and the Swain–Schaad relationship, true protonation rate constants and isotope effects have been separated out for several positions in several simple aromatic substrates. Most of the electrophilic attack rate constants are described by a Hammett-type linear free energy relationship with a ρ^+ of $-6\cdot5$. The average observed deuterium isotope effect on Wheland intermediate breakup was $5\cdot3$. Using rate constants obtained at different temperatures, enthalpies and entropies of activation were also obtained for benzene, naphthalene and thiophene; the activation entropy averaged -8 cal mol^{-1} K^{-1}. Some evidence was found for general acid catalysis at the higher acidities.

INTRODUCTION

Aromatic hydrogen exchange, illustrated for benzene in reaction (1), is of fundamental interest, being the simplest possible electrophilic aromatic substitution. For this reason, among others, it has been the subject of extensive study.[1–14] Reaction (1) takes place at observable rates in moderately concentrated sulfuric and other acid media, and the mechanism is known to be the typical A-S_E2 one shown,[15] involving rate-determining proton transfer. Much success has attended the application of the excess acidity kinetic method[16,17] to other reactions in sulfuric acid,[18] and it can advantageously be applied to this process also.
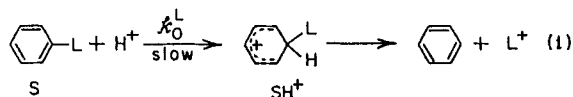
The observed pseudo-first-order rate constants of reaction (1) as a function of sulfuric acid concentration, k_ψ, can be equated with k_0^l, the medium-independent rate constant for the slow step, the activities a of the species involved and the activity coefficient of the transition state $f_{\neq}$ as shown in equation (2). Separating the activities into molar concentrations C and activity

coefficients f, rearranging and taking logarithms gives equation (3).

$$k_\psi C_S = k_0^l a_S a_{H^+}/f_{\neq} = k_0^l C_S C_{H^+} f_S f_{H^+}/f_{\neq} \qquad (2)$$

$$\log k_\psi - \log C_{H^+} = \log k_0^l + \log (f_S f_{H^+}/f_{\neq}) \qquad (3)$$

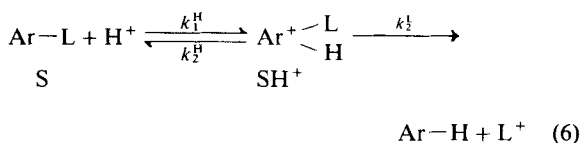$$\log (f_S f_{H^+}/f_{\neq}) = m^{\neq} \log (f_S f_{H^+}/f_{SH^+}) = m^{\neq} m^* X \qquad (4)$$

Regarding the activity coefficient term in equation (3), the excess acidity method makes the assumption that it is a linear function of an equivalent term describing equilibrium proton transfer to the same substrate, as shown in equation (4). The slope $m^{\neq}$, identical with Kresge et al.'s previously defined α-coefficient,[19] will have a value somewhere between zero and one, depending on how closely the transition state resembles (S + H$^+$) or (SH$^+$), i.e. it should reflect the degree of proton transfer,[19] at least to some extent. It has already been shown that terms such as $\log (f_S f_{H^+}/f_{SH^+})$ are linear in the excess acidity X[20] as shown in equation (4).[16] The slopes m^* depend on the type of substrate being protonated, with values of about $1\cdot0$ for primary aromatic amines, $0\cdot6$ for amides, $1\cdot4$ for thio compounds, and so on.[20] For carbocations such as SH$^+$, m^* is about $1\cdot8$.[21,22]

$$\log k_\psi - \log C_{H^-} = \log k_0^l + m^{\neq} m^* X \qquad (5)$$

Substitution of equation (4) into equation (3) produces the excess acidity equation (5) for reaction (1). The intercept at $X = 0$ (all activity coefficients unity), $\log k_0^l$, is the value in the standard state, infinite

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dilution in a hypothetical ideal 1 M acid solution,[20,23] which is the same as that used for pH measurements, facilitating comparisons between reactions that occur in the pH range and ones that occur in strong acid. Equation (5) has already been shown to give excellent linearity.[16,24]

$$Ar-L + H^+ \underset{k_{\bar{2}}^H}{\overset{k_1^H}{\rightleftharpoons}} Ar^{+} \underset{H}{\overset{L}{\diagdown}} \xrightarrow{k_2^L} $$

$$S \qquad\qquad SH^+$$

$$Ar-H + L^+ \quad (6)$$

$$k_0^L = k_1^H/(1 + k_2^H/k_2^L) \qquad (7)$$

$$\log k_0^D = \log k_1^H - \log(1 + k_2^H/k_2^D) \qquad (8)$$

$$\log k_0^T = \log k_1^H - \log[1 + (k_2^H/k_2^D)^{1\cdot442}] \qquad (9)$$

However, k_0^L is complex [see reaction (6)]; use of the steady-state approximation on SH^+ shows that the previously defined k_0^L is a combination of the true protonation rate constant, k_1^H, and the isotope effect on the breakup of the Wheland intermediate SH^+, k_2^H/k_2^L, as shown in equation (7). Thus, if results are available for both deuterium and tritium exchange from the same substrate, it should be possible to obtain k_2^H/k_2^D from the predicted small difference in intercepts by applying the Swain–Schaad relationship,[25] that $k^H/k^T = (k^H/k^D)^{1\cdot442}$, to equation (7). Thus equations (8) and (9) apply to deuterium and tritium exchange, respectively, and $\log k_1^H$ and k_2^H/k_2^D can be obtained. To simplify matters the additional, probably very good, assumption can be made that $f_{\neq}$ is the same for both deuterium and tritium exchange, i.e. that the same $m^{\neq}$ slope applies to both. This assumption is readily tested, and this was done; if true it means that isotope effects do not change with acidity.[26]

$$\log k_1^H = 10\cdot3188 + \log T$$

$$- \frac{\Delta G^{\neq}}{R\theta \ln 10} + \frac{\Delta H^{\neq}}{R\theta \ln 10}\left(\frac{T-\theta}{T}\right) \quad (10)$$

In a a number of cases, results at several temperatures T are available,[1-8] in which case $\log k_1^H$ can be expanded according to equation (10), which is based on equations given by Clarke and Glew.[22,27] This gives the activation parameters $\Delta G^{\neq}$ and $\Delta H^{\neq}$ applicable at the standard temperature θ of 25 °C; $\Delta S^{\neq}$ is then available using $\Delta G^{\neq} = \Delta H^{\neq} - \theta \Delta S^{\neq}$. (Formulation in terms of ΔG and ΔH is preferred because these parameters are not strongly correlated, and hence can be reliably separated,[22,27] whereas ΔH and ΔS are correlated in an isokinetic relationship.)[28] Substitution of equation (10) into equation (8) or equation (9) and substituting the result into equation (5) gives an equation which can be solved as a multiple linear regression using standard techniques.[29] In this case the isotope effect obtained will be an average over all the temperatures studied.[30]
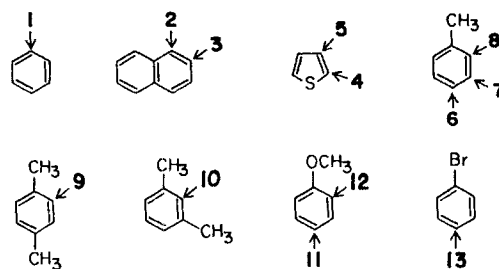
Scheme 1

The eight compounds in the study are given in Scheme 1, viz. benzene, naphthalene, thiophene, toluene, p- and m-xylene, anisole and bromobenzene. As indicated in Scheme 1, in this paper bold numerals are used to indicate the position of exchange in the molecule, rather than the molecule itself; for instance, 6 refers to exchange at the para position of toluene and 7 to exchange at the meta position. Both deuterium and tritium exchange results were used for all eight compounds, and results at several temperatures are available for the first three.

DATA AND CALCULATIONS

The numerical data used were obtained from the following sources. The exchange of tritium out of tritiated benzene in aqueous sulfuric acid at 25, 35, 45 and 55 °C, followed using a scintillation counting technique, was reported by Johnson's group;[1] the 25 °C data are in excellent agreement with earlier results obtained by Eaborn and Taylor[2] and Olsson and Russell,[3] as can be seen from Figure 2. Also in agreement are deuterium-exchange results obtained by Olsson and Russell,[3] but not the earlier values reported by Gold and Satchell,[4] which were not used for the analysis in this paper. Tritium exchange at the α- and β-positions of naphthalene at four temperatures was also studied by Johnson's group;[1] deuterium exchange at these positions was studied by Stevens and Strickler[5] at five different temperatures, using mass spectrometry. Butler and Hendry[6] studied the exchange of tritium out of the 2- and 3-positions of thiophene at several temperatures; a correction to some of the numerical data was subsequently reported.[7] Olsson studied both deuterium- and tritium-exchange in this substrate at 25 °C.[8]

Tritium exchange at 25 °C at the ortho, meta and para positions in toluene has been studied by Eaborn and Taylor,[2] Olsson[8] and Baker et al.,[9] and deuterium exchange at 25 °C at the same sites by Olsson[8] and Gold and Satchell;[10] all the results are in excellent agreement, as can be seen from Figure 1. Deuterium and tritium exchange results at 25 °C for both p- and m-xylene were reported by Olsson.[8] Deuterium exchange at 25 °C at

the *ortho* and *para* positions of anisole was studied by Satchell,[12] and both deuterium and tritium exchange at these sites by Russell and Olsson.[11] Deuterium and tritium exchange results at the *para* position of bromobenzene at 25 °C were also reported by Olsson.[13] Gold and Satchell studied the deuterium exchange of *p*-methyl-, *p*-chloro- and *p*-nitrophenol at 25 °C.[14]

With the one exception noted above, all the data for a given position in a given compound were amalgamated and treated together, regardless of source. The basic equation fitted was equation (5), using a computer program based on a multiple linear regression routine given by Bevington.[29] The values of X and log C_{H^+} used in equation (5) were taken from Cox and Yates[20] and adjusted to the temperature of measurement, if necessary, as before.[22,31] Preliminary line-fitting showed that the $m^{\neq}$ slope was, well within experimental error, the same for both deuterium and tritium exchange, for the same position in the same molecule. Because of this, a slightly modified program was written that enabled two lines with the same slope but different intercepts to be fitted simultaneously. Solving equations (8) and (9) provided values of log k_1^H and k_2^H/k_2^D from the different intercepts. Data at several temperatures were accommodated by expanding log k_1^H according to equation (10) and solving, using as variables X and $(T - \theta)/T$. Points which did not fall within the data set, to 95% confidence, were disregarded, using a test based on t-statistics; these points are indicated by parentheses in Table 1 and Figures 2–4. The computer program provided errors on the calculated coefficients; all the errors given in Tables 1–3 are standard deviations.

The σ^+ values used for Figure 6 are from Hammett,[32] with additional literature values for naphthalene[33] and thiophene.[34] The *p*-nitrophenol data in Figure 7 were separated into two components using the curve-fitting routine used before[31] for this type of analysis.

RESULTS

The results of applying equation (5) to the available 25 °C experimental data[2,8-10] for **6** and **7**, exchange at the *para* and *meta* positions of toluene, are shown in Figure 1. Three conclusions can be drawn: (a) the assumption made earlier about $m^{\neq}$ being the same for both deuterium and tritium exchange is amply justified, since a very high degree of parallelism is apparent; (b) deuterium and tritium exchange do in fact give different intercepts, justifying the analysis in the Introduction; and (c) results obtained by different groups of workers[2,8-10] are in excellent agreement with one another, which justifies treating all of the experimental results as equally valid, as was done here. Point (a) above means that for this reason the isotope effects truly are independent of acidity, in contrast to the slight but real differences found for another reaction, the hydration of 9-thiabicyclo[3.3.1]non-1-ene.[26]
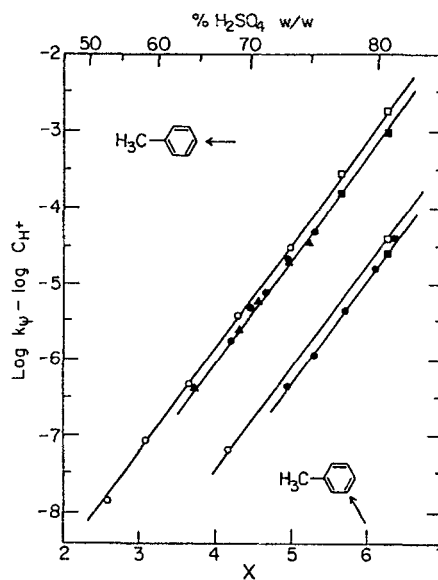

Figure 1. Excess acidity plots according to equation (5) for **6** and **7**, the deuterium (open symbols) and tritium exchange (filled symbols) of toluene at 25 °C. □, Ref. 8; ○, Ref. 10; ●, Ref. 2; ■, Ref. 8; ▲, Ref. 9

In Figure 2 the experimental data for **1**, attack on a ring position of benzene,[1-4] are plotted against X. The tritium exchange lines at different temperatures are parallel because temperature-corrected[31] values of X and log C_{H^+} were used in the analysis, ensuring that the resulting $\Delta H^{\neq}$ and $\Delta S^{\neq}$ contain only contributions from the reaction of interest, and not from the variation of X and log C_{H^+} with temperature. Olsson and Russell's deuterium exchange results[3] are parallel to the tritium exchange data, but Gold and Satchell's early results[4] are not. Because of the high degree of parallelism shown in Figure 1 and elsewhere, the conclusion was drawn that the latter results are in error, and they were not used in the analysis in this paper.

The exchange at the α- and β-positions of naphthalene,[1,5] **2** and **3**, is illustrated in Figures 3 and 4. These reactions are slow under the conditions used, particularly for the deuterium exchange,[5] and experimental scatter is apparent, particularly for **3**. Nevertheless, the large quantity of data compensates for this to some extent, and a high degree of parallelism is still apparent. In contrast, exchange at the 2- and 3-positions of thiophene,[6-8] **4** and **5**, illustrated in Figure 5, is fast, and is conveniently measurable in more dilute sulfuric acid media than those used for **1–3**. In Figure 5 the $m^{\neq}m^*$ slopes are defined by 25·0 and 1·9 °C data, and the short line segments drawn through the single points obtained at intermediate temperatures illustrate the
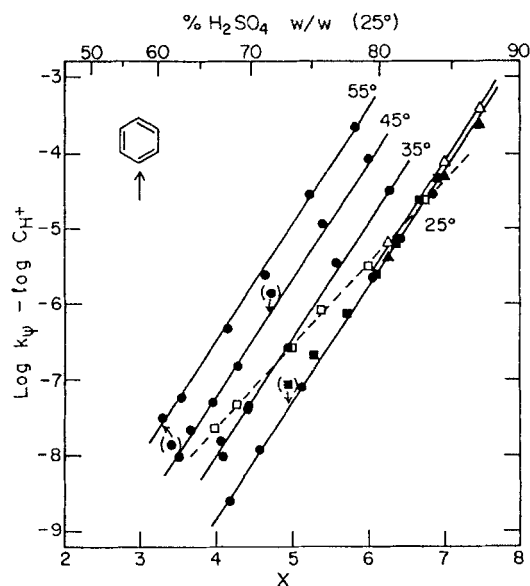
Figure 2. Excess acidity plots for **1**, the deuterium (open symbols) and tritium exchange (filled symbols) of benzene at several temperatures. □, Ref. 4; △, Ref. 3; ●, Ref. 1; ■, Ref. 2; ▲, Ref. 3

Figure 4. Excess acidity plots for **3**, the deuterium (open symbols, Ref. 5) and tritium exchange (filled symbols, Ref. 1) at the β-position of naphthalene at several temperatures. For clarity the x-axis is offset for the tritium exchange data

Figure 3. Excess acidity plots for **2**, the deuterium (open symbols, Ref. 5) and tritium exchange (filled symbols, Ref. 1) at the α-position of naphthalene at several temperatures. For clarity the x-axis is offset for the tritium exchange data
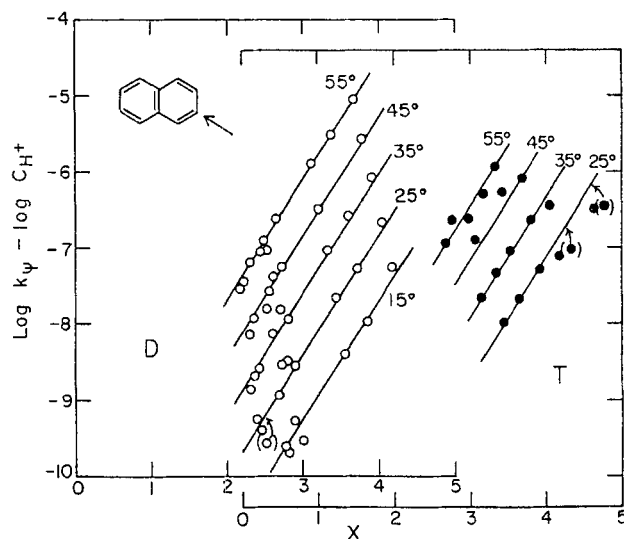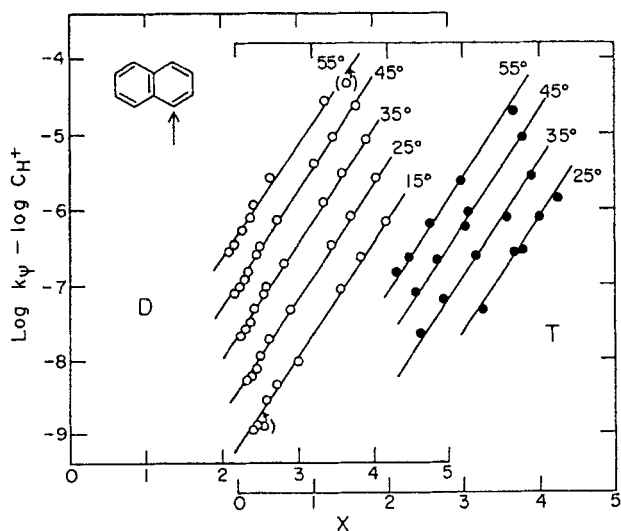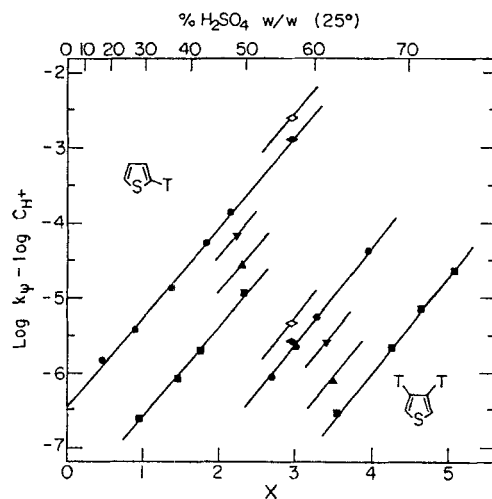

Figure 5. Excess acidity plots for **4** and **5**, the deuterium (open symbols, Ref. 8) and tritium exchange (filled symbols, Refs 6–8) of thiophene at several temperatures. ●, $25\cdot0\,^{\circ}C$, Ref. 6; ◆, $24\cdot6\,^{\circ}C$, Ref. 8; ▼, $17\cdot9\,^{\circ}C$, Ref. 6; ▲, $9\cdot7\,^{\circ}C$, Ref. 6; ■, $1\cdot9\,^{\circ}C$, Ref. 6, with a correction in Ref. 7

Table 1. Standard-state hydrogen isotope exchange rate constants and slopes for the aromatic substrates in Scheme 1

Position[a]	Log k_0^{D} [b]	Log k_0^{T} [b]	$m^{\neq}m^{*}$ [b]	$\pm \sigma_y$ [c]	N [d]
1	$-14\cdot89 \pm 0\cdot11$	$-15\cdot01 \pm 0\cdot09$	$1\cdot54 \pm 0\cdot01$	$0\cdot08$	41(3)
2	$-11\cdot79 \pm 0\cdot05$	$-12\cdot20 \pm 0\cdot06$	$1\cdot53 \pm 0\cdot02$	$0\cdot07$	66(2)
3	$-13\cdot18 \pm 0\cdot11$	$-13\cdot47 \pm 0\cdot14$	$1\cdot59 \pm 0\cdot04$	$0\cdot13$	66(3)
4	$-6\cdot15 \pm 0\cdot07$	$-6\cdot45 \pm 0\cdot04$	$1\cdot20 \pm 0\cdot02$	$0\cdot05$	13
5	$-9\cdot41 \pm 0\cdot13$	$-9\cdot77 \pm 0\cdot13$	$1\cdot29 \pm 0\cdot04$	$0\cdot06$	12
6	$-11\cdot28 \pm 0\cdot06$	$-11\cdot47 \pm 0\cdot06$	$1\cdot36 \pm 0\cdot01$	$0\cdot05$	19
7	$-12\cdot86 \pm 0\cdot11$	$-13\cdot06 \pm 0\cdot12$	$1\cdot35 \pm 0\cdot02$	$0\cdot04$	8
8	$-11\cdot21 \pm 0\cdot08$	$-11\cdot46 \pm 0\cdot07$	$1\cdot36 \pm 0\cdot01$	$0\cdot04$	8
9	$-10\cdot62 \pm 0\cdot04$	$-10\cdot83 \pm 0\cdot04$	$1\cdot37 \pm 0\cdot01$	$0\cdot01$	6
10	$-8\cdot80 \pm 0\cdot11$	$-9\cdot03 \pm 0\cdot11$	$1\cdot32 \pm 0\cdot03$	$0\cdot02$	4
11	$-8\cdot35 \pm 0\cdot05$	$-8\cdot68 \pm 0\cdot08$	$1\cdot27 \pm 0\cdot02$	$0\cdot05$	9
12	$-8\cdot64 \pm 0\cdot05$	$-9\cdot00 \pm 0\cdot08$	$1\cdot26 \pm 0\cdot02$	$0\cdot03$	7
13	$-14\cdot55 \pm 0\cdot12$	$-14\cdot80 \pm 0\cdot12$	$1\cdot34 \pm 0\cdot02$	$0\cdot01$	4

[a] Position of exchange; numbering as in Scheme 1.
[b] Slopes and intercepts of equation (5); see Figures 1–5.
[c] Root-mean-square deviation between experimental points and fitted lines.
[d] Number of data points. Any rejected by the computer program used as being off the best regression lines are in parentheses, both here and in Figures 2–4.

goodness of fit of equation (10). For all the reactions studied the analysis given in the Introduction works exceptionally well.

All of the equation (5) slopes and intercepts, those illustrated in Figures 1–5 and those for the other systems studied, are given in Table 1, together with the errors found and other statistical information. In Table 2 are collected the k_2^{H}/k_2^{D} values (isotope effects on Wheland intermediate breakup), the true protona-

tion rate constants (partial rate factors) as log k_1^{H}, values of $m^{\neq}$ (obtained by dividing the observed $m^{\neq}m^{*}$ slopes by $1\cdot8$)[21,22,24] and rate constants relative to that for benzene, the slowest reaction observed. In Figure 6 log k_1^{H} and $m^{\neq}$ are illustrated in the form of a linear free energy relationship against σ^{+}. Table 3 reports the activation parameters for those compounds for which rate data at several temperatures were available.

Table 2. Isotope effects, log k_1^{H} and $m^{\neq}$ values for the aromatic substrates in Scheme 1

Position[a]	k_2^{H}/k_2^{D} [b]	Log k_1^{H} [c]	$m^{\neq}$ [d]	Rel. rate[e]	σ^{+} [f]
1	$2\cdot4 \pm 1\cdot8$	$-14\cdot36 \pm 0\cdot26$	$0\cdot86$	1	$0\cdot00$
2	$9\cdot8 \pm 3\cdot6$	$-10\cdot76 \pm 0\cdot15$	$0\cdot85$	$4\cdot0 \times 10^3$	$-0\cdot45$
3	$5\cdot4 \pm 4\cdot6$	$-12\cdot38 \pm 0\cdot33$	$0\cdot88$	95	$-0\cdot28$
4	$5\cdot9 \pm 2\cdot3$	$-5\cdot31 \pm 0\cdot16$	$0\cdot67$	$1\cdot1 \times 10^9$	$-0\cdot79$
5	$7\cdot5 \pm 6\cdot6$	$-8\cdot48 \pm 0\cdot36$	$0\cdot72$	$7\cdot6 \times 10^5$	$-0\cdot52$
6	$3\cdot3 \pm 1\cdot5$	$-10\cdot65 \pm 0\cdot16$	$0\cdot76$	$5\cdot1 \times 10^3$	$-0\cdot31$
7	$3\cdot5 \pm 2\cdot9$	$-12\cdot20 \pm 0\cdot30$	$0\cdot75$	140	$-0\cdot07$
8	$4\cdot4 \pm 2\cdot3$	$-10\cdot47 \pm 0\cdot20$	$0\cdot75$	$7\cdot8 \times 10^3$	$-0\cdot31$
9	$3\cdot9 \pm 0\cdot9$	$-9\cdot93 \pm 0\cdot09$	$0\cdot76$	$2\cdot7 \times 10^4$	$-0\cdot38$
10	$4\cdot1 \pm 3\cdot1$	$-8\cdot09 \pm 0\cdot28$	$0\cdot73$	$1\cdot9 \times 10^6$	$-0\cdot62$
11	$6\cdot8 \pm 2\cdot9$	$-7\cdot45 \pm 0\cdot17$	$0\cdot70$	$8\cdot1 \times 10^6$	$-0\cdot78$
12	$7\cdot5 \pm 3\cdot4$	$-7\cdot71 \pm 0\cdot18$	$0\cdot70$	$4\cdot5 \times 10^6$	$-0\cdot78$
13	$4\cdot7 \pm 3\cdot8$	$-13\cdot79 \pm 0\cdot31$	$0\cdot75$	$3\cdot7$	$0\cdot15$

[a] Position of exchange; numbering as in Scheme 1.
[b] Isotope effect for Wheland intermediate breakup; see equation (8).
[c] True protonation partial rate factor; see equation (8).
[d] Probable extent of proton transfer at the transition state; see text.
[e] Relative to benzene.
[f] Naphthalene, values from Ref. 33; thiophene, values from Ref. 34; otherwise from Ref. 32.
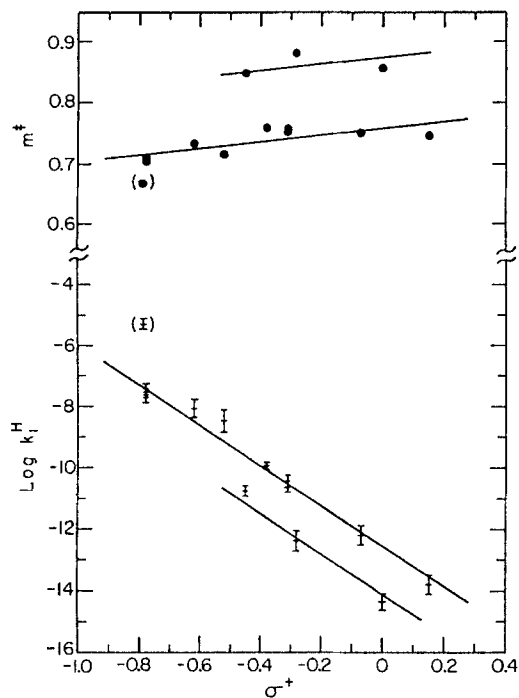
Figure 6. Linear free-energy relationship plot against σ^+ for the $\log k_1^H$ (lower lines) and $m^{\neq}$ (upper lines) data in Table 2. From left to right the positions of exchange are **2, 3, 1** (three-point lines) and **4, 11** and **12, 10, 5, 9, 6** and **8, 7, 13** (ten-point lines)
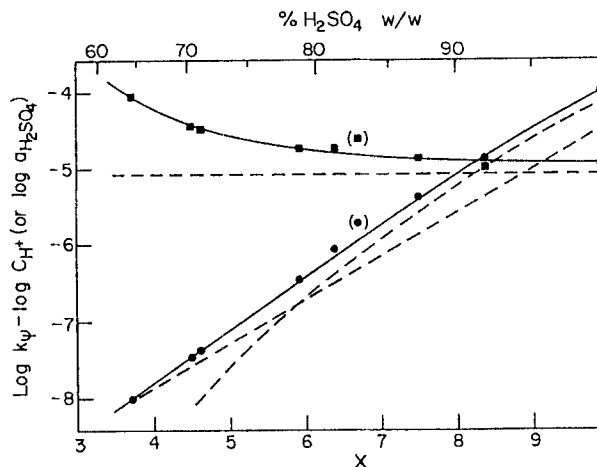

Figure 7. Excess acidity plots for the deuterium exchange of p-nitrophenol at 25 °C, indicating possible general acid catalysis (see text). Plotted against X are (circles) $\log k_\psi - \log C_H^+$ and (squares) $\log k_\psi - \log a_{H_2SO_4}$. Data from Ref. 14

In Figure 7, some deuterium exchange results obtained by Gold and Satchell for p-nitrophenol[14] are shown as an excess acidity plot. These data are not well correlated by equation (5) (although data on p-methyl- and p-chlorophenol in the same paper are),[16] but are better explained as two simultaneous reactions, one of which is the reaction (1)/equation (5) process (lower dashed straight line) in which proton transfer is from solvated 'H$^+$' and the other of which involves proton transfer from undissociated sulfuric acid molecules, dominant in media more concentrated than about 80% (w/w)[35] (curved dashed line). The observed points

Table 3. Activation parameters for the isotope exchanges of benzene, naphthalene and thiophene

Position[a]	$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta S^{\neq}$ (cal mol^{-1} k^{-1})
1	$34 \cdot 6 \pm 0 \cdot 6$	-8 ± 2
2	$30 \cdot 0 \pm 0 \cdot 3$	-7 ± 1
3	$33 \cdot 2 \pm 0 \cdot 6$	-4 ± 3
4	$21 \cdot 0 \pm 0 \cdot 5$	-13 ± 2
5	$26 \cdot 8 \pm 1 \cdot 0$	-8 ± 4

[a] Position of exchange; numbering as in Scheme 1.

are the sum of these two processes (circles, full line). Examination of the upper set of lines in Figure 7 (squares), in which $\log k_\psi - \log a_{H_2SO_4}$[36] is plotted against X, shows that the sulfuric acid process becomes increasingly dominant at higher acidities, trending to the horizontal dashed line limit at 100% acid. Thus is seen the onset of catalysis by the general acid H_2SO_4, in addition to that due to the general acid 'H$^+$.' Behaviour like this has been seen before, in the Wallach rearrangement of azoxybenzene to p-hydroxyazobenzene,[35] and in other reactions.[37] General acid catalysis by HSO_4^- (and H_3PO_4) has been observed previously in the tritium exchange of 1,3-dimethoxy[4-^{3}H]benzene, by comparing reaction rates obtained in sulfuric and phosphoric acids with those measured in monobasic acids.[38] The curvature in Figure 7 is probably not due to a complicating oxygen protonation, since in this case curvature would also be observed for p-methyl- and p-chlorophenol, but it is not.[16]

DISCUSSION

The true protonation rate constants for reaction (1), separated from the isotope effect on the breakup of the Wheland intermediate, are plotted as a linear free energy relationship (LFER) in Figure 6 (lower half). It is arguable whether or not this is a reasonable plot to make, since reaction (1) involves loss of aromaticity, which is not the situation for which the Hammett equation was originally derived.[39] Nevertheless, LFERs are often applied to aromatic substitutions,[39] and Figure 6 makes an interesting visual presentation of the results. The majority of these fall on two parallel lines,

with a slope (ρ^+) of $-6 \cdot 5 \pm 0 \cdot 3$ and a correlation coefficient of $0 \cdot 99$. The three points that form a line of their own are **1–3**, exchange in benzene and naphthalene, which can be regarded as not having substituents or heteroatoms. All of the other points (**4–13**) represent exchange in thiophene or substituted compounds. Exchange at the 2-position of thiophene **4** is off on its own, which might be due to the σ^+ value used[34] not being applicable to this process.

Two parallel lines are drawn through the data points in Figure 6. This is not done for any theoretical reason, but because it is the only reasonable correlation that is statistically consistent with the data. The tabulated standard deviations on the points are illustrated as error bars in Figure 6. Drawing a single line or curve through all the points leaves several which are more than two standard deviations away from it. The data are better than this. A referee has commented that 'the lower part of Figure 6 can easily be regarded as a single, non-linear curve, with a positive second derivative, and reasonable scatter.' If this were so, explanation in terms of the current theories of physical organic chemistry[40] would be straightforward. But since it is not, the reason why **1–3** form a line of their own is not clear. However, it is worth commenting that of the many studies which have been made of the Hammett equation, for instance of the separation of polar, steric and resonance effects,[41] few if any seem to have considered something so basic as the very presence or absence of a substituent as being important. It is not unheard of for the parent phenyl compound to be off the line in an LFER; a very recent example arises in the formation of vinyl cations from $YC_6H_4C{\equiv}CCF_3$ in sulfuric acid media, the unsubstituted compound exhibiting anomalous behaviour.[24]

The protonation of substituted benzenes has been studied in the gas phase,[42,43] and ρ^+ values of -17 to -18 can be estimated from the resulting basicities or proton affinities. The value of $-6 \cdot 5$ observed here is about a third of that, which probably represents a reasonable attenuation due to solvation. Typical solution values for other electrophilic aromatic substitutions range from $-2 \cdot 4$ to $-12 \cdot 1$.[39]

Values of $m^{\neq}$ (or α_A)[44] are listed in Table 2. These are obtained from the observed slopes by dividing them all by $1 \cdot 8$, the m^* for carbocation formation,[21,22] and should reflect to some extent the degree of proton transfer at the transition state,[19,44] although the true situation is probably more complex.[40] (Values of m^* for the specific substrates used are not available, but they should not differ much from $1 \cdot 8$ or from one another.)[24] Two values have been reported previously. The $m^{\neq}$ of $0 \cdot 70$ obtained for **11** agrees fairly well with the α_A measured by Kresge *et al.*[44] in perchloric acid media, $0 \cdot 71 \pm 0 \cdot 02$. However, the value of $0 \cdot 86$ obtained for **1** is lower than Kresge *et al.*'s calculated value of $0 \cdot 93 \pm 0 \cdot 04$. The latter value is based on the

assumption that the H_C acidity function applies to benzene in perchloric acid,[44] and the former on the assumption that $m^* = 1 \cdot 8$ for this compound in sulfuric acid; considering that both of these assumptions are untested, a 10 per cent discrepancy is probably still good agreement.

The $m^{\neq}$ values are illustrated as a function of substituent in the upper half of Figure 6; they mirror the LFER in the lower half fairly well, with the corresponding points off the line, and so on. They agree with intuition in that the slower reactions have later transition states, e.g. proton transfer is about 85 per cent complete for **1**, **2** and **3**, but only about 70–75 per cent complete for others. The lines trend upwards with a slope of $0 \cdot 05 \pm 0 \cdot 02$, correlation coefficient $0 \cdot 75$; this is reminiscent of the slight upward trend in the α_A vs substrate pK_a graph given by Kresge *et al.*[44]

Figure 6 illustrates a basic problem. In order to use the Hammett LFER, the assumption is made that the position of the transition state (TS) along the reaction coordinate does not change with substituent, only the extent of charge dispersal varying.[39] However, Figure 6 indicates that the position of the TS (the degree of proton transfer) *is* substituent dependent, at least in this case. (This can be referred to as the reactivity–selectivity principle: fast reaction, early TS, unselective; slow reaction, late TS, selective)[39,45] We have investigated this situation for reactions in sulfuric acid recently.[24,46] Reactions involving initial protonation at oxygen or sulfur tend to have substituent-dependent $m^{\neq}$ values (or, putting this another way, ρ varies with acidity).[46] Three out of four reactions involving carbon protonation, however, have substituent-independent $m^{\neq}$ values.[24] In the reaction under consideration here, small systematic variations in m^* with substituent could well remove all the observed variation too; unfortunately, the equilibrium protonation of the substrates could not be studied. More theoretical work in this area is needed; in particular, it would be useful to know what interpretation to place upon the slope of $0 \cdot 05 \pm 0 \cdot 02$ quoted above. Values of $m^{\neq}$ or $m^*m^{\neq}$ are already LFER slope parameters,[47] and the theoretical meaning of the slope of a plot of these in another LFER is, at present, obscure.

The isotope effects on Wheland intermediate breakup [SH^+ in reaction (1)] are given in the first column of Table 2. The errors on these are high, which is not surprising considering that they are obtained from the results of different workers using different techniques at different times. The results in Table 2 will also contain contributions due to both primary and secondary isotope effects. The elegant work by Kresge and Chiang[48] on hydrogen exchange in 1,3,5-trimethoxybenzene in perchloric acid shows that secondary isotope effects are important. However, in this work there is insufficient experimental information to permit a reliable separation into primary and secondary

effects, and the relatively high experimental error makes such an attempted separation difficult in any case. Overinterpretation is therefore not warranted. Still, some points can be made.

No correlation is apparent between the k_2^H/k_2^D values in Table 2 and either log k_1^H or $m^\neq$ in Table 2.

Averaging all 13 values in Table 2 gives a k_1^H/k_2^D value of $5 \cdot 3 \pm 2 \cdot 1$. Application of Marcus theory to the protonation of benzene leads to an estimated primary deuterium isotope effect of $2 \cdot 43$,[49] which is very close (probably fortuitously) to the $2 \cdot 4$ in Table 2. However, there will be secondary isotope effects to be added to the primary ones, and a value of $5 \cdot 3$ does not seem at all unreasonable as an average. One of the values in Table 2 is significantly higher than this, however, i.e. protonation at the α-position of naphthalene, 2; in fact it is twice as large as that for 3, β-position protonation. This difference is likely to be real, since the same groups of workers studied both positions.[1,5] The reason for it is not clear; the two positions differ in that steric interference is possible between the 1- and 8-positions in naphthalene, but how or why this would affect the primary isotope effect on Wheland intermediate breakup, when the hydrogens of concern are out-of-plane anyway, is by no means clear.

The activation parameters in Table 3 show that the rate differences between the different substrates are a function of different enthalpies of activation, since the five $\Delta S^\neq$ values in Table 3 are essentially all the same, except for 4, averaging -8 ± 3 cal mol^{-1}k^{-1} (intriguingly, 4 is also off the lines in Figure 6). The small negative entropies of activation could mean that the solvation requirements of SH$^+$ are almost counterbalanced by the release of water molecules solvating H$^+$, at the transition state. The values in Table 3 refer to the standard state, not to any particular acid solution, so they sometimes differ considerably from those reported in the original papers,[1,5,6] usually as a function of acidity, because all effects due to the change of acidity function, etc., with temperature are absent in this work. We submit that the values reported here are more reliable.

The relative rates in Table 2 are mostly, but not entirely, in accord with expectation. For instance, 7, *meta* attack on toluene, is 140 times faster than 1, attack on a ring position of benzene, but about 50 times slower than attack at the *ortho* or *para* positions (see Figure 1). Also, 2 is faster than 3, 4 is faster than 5 (1500 times), 10 is faster than 9, and so on. However, in toluene, *ortho* attack (8) is $1 \cdot 5$ times faster than *para* attack (6), but in anisole the opposite is true, *para* attack (11) being $1 \cdot 8$ times faster than *ortho* attack (12). Electron-donating substituents speed up the rate (see Figure 6), but 13, *para* attack on bromobenzene, is nearly four times faster than 1, attack on a ring position of benzene. A bromine substituent is generally regarded as being deactivating,[50] which does not appear to

be true for this simplest of all possible electrophilic aromatic substitutions.

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