# **329.** *Reactions of the Alkyl-sulphate Ion. Part II. Kinetics and Mechanism of the Reaction with Phenoxide Ion and the Polar Effects of Substituents in the Phenol Nucleus.*

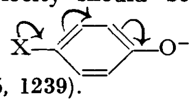
By G. H. Green and J. Kenyon.

The bimolecular nature of the reaction between alkyl-sulphate ion and phenoxide ion has been confirmed. The reaction takes place in the presence of hydroxide ion and, since this latter reacts with alkyl-sulphate ion at a rate comparable to that of phenoxide ion, it was necessary to derive kinetic expressions for the rate constants of two simultaneous second-order reactions. The reaction is entirely analogous to the corresponding reaction of alkyl halides with phenoxide ion except that, as it takes place between two similarly charged ions and not with an ion and a neutral molecule its velocity increases with increasing ionic concentration. The polar effects of nuclear substituents in the phenol are in the expected direction. Values for relative reactivities of phenols towards methylation by dimethyl sulphate by Hodgson and Nixon (*J.*, 1930, 2166) have been shown to be misleading owing to the superposition of two reaction mechanisms.

The alkylation of phenols with dialkyl sulphates occurs in two stages :

$$R_2SO_4 + PhO^- \longrightarrow RSO_4^- + PhOR \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$RSO_4^- + PhO^- \longrightarrow SO_4^{=} + PhOR \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

No direct evidence as to mechanism exists but indirect evidence that both stages are bimolecular, involving the phenoxide ion, is obtained from the similarity with the corresponding reactions of the alkyl halides and olefin oxides with phenoxide ion, both of which have been studied in considerable detail. By analogy, the velocity should be decreased by increasing accession of electrons on the α-carbon atom of the alkyl sulphate $R{\cdot}CH_2{\cdot}SO_4^-$ (cf. Woolf, *J.*, 1937, 1172). It is known that more stringent conditions are required with diethyl sulphate than with dimethyl sulphate (Cade, *Chem. Met. Eng.*, 1923, **29**, 319). Furthermore, the velocity should be increased by increasing electron accession to the phenolic oxygen atom  (cf. Goldsworthy, *J.*, 1926, 1254; Boyd *et al.*, *J.*, 1914, **105**, 2117; 1919, **115**, 1239).

In an attempt to verify the influence of nuclear substituents in phenol on its reactivity, Hodgson and Nixon (*J.*, 1930, 2166) examined the yields of anisoles produced from 19 phenols on reaction with dimethyl sulphate in aqueous medium under standard conditions. They fail, however, to explain numerous anomalous results : (i) the yield of *m*-tolyl ether is higher than that of the *p*-derivative, (ii) the yields of nitrophenyl ethers are the same as or only slightly less than that of anisole, (iii) the yields of chlorophenyl ethers are higher than that of anisole, (iv) the results for the di- and tri-substituted phenols appear unintelligible, (v) steric effects in the *ortho*-position are very small and absent altogether with *o*-cresol. In an attempt to interpret their results, two of their experiments were repeated, *viz.*, the methylation of phenol and of *p*-nitrophenol. On theoretical grounds these two phenols should show a considerable difference in reactivity. The experimental details given by Hodgson and Nixon are not very explicit and minor manipulations were used by us which may or may not have been carried out by them. Hodgson and Nixon obtained 65% of anisole and 55·5% of *p*-nitrophenyl methyl ether, whereas we obtained 87 and 61%, respectively. Although the duplication is not too satisfactory the values are in reasonably good relative agreement. During these experiments the following points emerged : (i) some unchanged phenol is carried over with anisole on steam-distillation from alkaline solution—though the quantity was not large enough to affect the yields materially in these cases, the presence of an *ortho*-substituent in the phenol considerably increases its volatility in steam, and if Hodgson and Nixon did not wash their steam-distillate with alkali, it may account, if only partly, for their relatively high yields of *ortho*-substituted anisoles; (ii) the sodium salts of the nitrophenols are relatively insoluble, and certainly less than 0·2 mole per 100 c.c. In the nitrophenol experiment, the greater part of the sodium salt remained undissolved during the initial 30 minutes' stirring in the cold. During the subsequent heating both the sodium salt and the unchanged dimethyl sulphate settled to the bottom of the vessel. This condition was equivalent to that used by Haworth and Lapworth (*J.*, 1923, **123**, 2986) and also by Hodgson and Nixon (*loc. cit.*) in which the phenol is heated with sodium carbonate and dimethyl sulphate in xylene, *i.e.*, in the absence of water. Under these conditions a different mechanism ensues, the reaction, according to Hodgson and Nixon, being facilitated by electron *recession* from the side chain. This in itself is sufficient to account for the high yields obtained with the nitrophenols and di*ortho*-polyhalogenophenols. It is thus obvious that the results give no true picture of the influence of nuclear substituents on the reactions under discussion.

The study of reaction (1) is complicated by such factors as the immiscibility of the alkylating agent with water (unless methanol is used, in which interaction is far too vigorous at normal temperatures for kinetic study), and the presence of the side reaction with hydroxide ion. The former difficulty does not occur with reaction (2), and this process proceeds at a measurable velocity at temperatures of the order of 100°. The side reaction with hydroxide ion occurs at about the same rate as with phenoxide ion and must be allowed for. By employing a large excess (20-fold or more) of alkali over the phenol to ensure complete dissociation of the latter and a similar excess of alkyl sulphate, the amount of alkyl sulphate consumed by the phenoxide ion being very small compared with that consumed by hydroxide ion, it has been possible to evaluate the rate constants for the two simultaneous second-order reactions and so to study their kinetics.

## CALCULATIONS.

### *The rate constants for two simultaneous second-order reactions.*

*Equal* $CH_3{\cdot}SO_4Na$ *and* NaOH *Concentrations.*—

(*A*) $$CH_3{\cdot}SO_4Na + OH^- \xrightarrow{k'} CH_3{\cdot}OH + NaSO_4^-.$$

Let $$[CH_3{\cdot}SO_4Na] = [OH^-] = a$$

$$[CH_3{\cdot}OH] = [NaSO_4^-] = x \text{ after } t \text{ seconds.}$$

Then $$dx/dt = k'(a - x)^2$$

$$k' = x/[ta(a - x)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

$k'$ can be determined experimentally.

(*B*) $$CH_3{\cdot}SO_4Na + OPh^- \xrightarrow{k''} CH_3{\cdot}OPh + NaSO_4^-$$

If $[OH^-]$ is large compared with $[OPh^-]$, then the $CH_3{\cdot}SO_4Na$ consumed in reaction (*B*) will be negligible compared with that consumed in reaction (*A*), so that the $[CH_3{\cdot}SO_4Na]$ can be considered as $(a - x)$ throughout both reactions.

Let $$[OPh^-] = b$$

$$[CH_3{\cdot}OPh] = y \text{ after } t \text{ seconds.}$$

Then $$dy/dt = k''(a - x)(b - y)$$

Substituting for $(a - x)$ from equation $(a)$ and integrating, we have

$$k'' = \frac{k' \log b/(b - y)}{\log (1 + ak't)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

*Different* $CH_3{\cdot}SO_4Na$ *and* NaOH *Concentrations.*—

$$(A)\qquad CH_3{\cdot}SO_4Na + OH^- \xrightarrow{k'} CH_3{\cdot}OH + NaSO_4^-$$

Let $[CH_3{\cdot}SO_4Na] = a$ and $[OH^-] = p$

After $t$ seconds $[CH_3{\cdot}SO_4Na] = (a - x)$, and $[OH^-] = (p - x)$

Then $dx/dt = k'(a - x)(p - x)$

$$k' = \frac{1}{t(a - p)} . \ln \frac{p(a - x)}{a(p - x)} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (c)$$

$k'$ can be determined experimentally.

$$(B)\qquad CH_3{\cdot}SO_4Na + OPh^- \xrightarrow{k''} CH_3{\cdot}OPh + NaSO_4^-$$

If $[OH^-]$ is large compared with $[OPh^-]$, then the $CH_3{\cdot}SO_4Na$ consumed in reaction ($B$) will be negligible compared with that consumed in reaction ($A$), so that $[CH_3{\cdot}SO_4Na]$ can be considered as $(a - x)$ in both reactions.

Let $[OPh^-] = b$

$[CH_3{\cdot}OPh] = y$ after $t$ seconds.

Then $dy/dt = k''(a - x)(b - y)$

Substituting for $(a - x)$ in equation ($c$) and integrating, we have

$$k'' = \frac{2{\cdot}303 \log b/(b - y)}{t(a - p) + \dfrac{2{\cdot}303}{k'} \log \dfrac{a - pe^{-k't(a-p)}}{(a - p)}} \quad . \; . \; . \; . \; . \; . \; . \quad (d)$$

In the limiting case when $a = p$, equation ($d$) becomes

$$k'' = \frac{k' \log b/(b - y)}{\log (1 + ak't)}$$

which is identical with equation ($b$).

## EXPERIMENTAL.

*Determination of Phenols.*—Phenols other than those containing an alkyl or alkoxy-group in the *ortho*- or *para*-position were determined with bromate–bromide reagent, anisoles, if present, being first removed by ethereal extraction of the alkaline phenol solution (cf. Ghaswalla and Donnan, *J.*, 1936, 1341). Phenol and *o*- and *p*-alkyl- and -alkoxy-phenols were determined colorimetrically by the method of Folin and Ciocalteu (*J. Biol. Chem.*, 1927, **73**, 627; Snell, "Colorimetric Methods of Analysis," Chapman and Hall, 1936, Vol. 2, p. 348). Anisoles do not interfere.

*Phenols Used.*—The m. p.s (or b. p.s) and percentage purity (by bromate–bromide titration) were: Phenol, m. p. 41°, purity 100·2%; guaiacol, m. p. 28·5°; *o*-cresol, m. p. 31°; *o*-chlorophenol, b. p. 173°, purity 100·2%; *o*-nitrophenol, m. p. 45—46°, purity 99·0%; *m*-methoxyphenol, b. p. 238°, purity 97·8%; *m*-ethoxyphenol, b. p. 138°/17 mm., purity 96·4%; *m*-cresol, b. p. 96—98°/20 mm., purity 98·9%; *m*-fluorophenol, b. p. 81°/16 mm., purity 91·0%; *m*-chlorophenol, m. p. 30—31°, purity 98·7%; *m*-nitrophenol, m. p. 95·5—96°, purity 99·4%; *p*-methoxyphenol, m. p. 52·5—53°; *p*-ethoxyphenol, m. p. 63·5—64°; *p*-cresol, m. p. 35°; *p*-*tert.*-amylphenol, m. p. 92—93°; *p*-fluorophenol, m. p. 45°, purity 100·5%; *p*-chlorophenol, m. p. 41·5—43°, purity 100·2%; *p*-bromophenol, m. p. 63·5°, purity 98·8%; *p*-iodophenol, m. p. 92°, purity 100·1%; *p*-nitrophenol, m. p. 112°, purity 100·4%; 3 : 5-dimethoxyphenol (phloroglucinol dimethyl ether), m. p. 35·5—36°, purity 99·5%.

*Stability of Phenols in Aqueous Alkali at* 100°.—No decomposition or oxidation of any of the phenols used was detected on heating them for one hour in 1·0N-sodium hydroxide at 100°.

*Metal Alkyl Sulphates.*—The preparation of the various metal alkyl sulphates and their quantitative determination have been described in Part I (*J.*, 1950, 1389). The same preparations were used.

*Determination of the Rate of Reaction of Alkyl-sulphate Ion with Phenoxide Ion.*—The determination of the constant $k'$ for the second-order reaction between alkyl-sulphate ion and hydroxide ion has already been described in Part I.

In general the initial mixture was N. with respect to metal alkyl sulphate and alkali, and approx. 0·05N. with respect to phenol. The sodium hydroxide and potassium hydroxide were carbonate-free and all solutions were made up with carbon dioxide-free water. The anhydrous metal alkyl sulphate was weighed rapidly into a beaker and transferred with water to a graduated flask, followed by the required quantities of standard 4N-alkali and phenol. Aliquots (10 ml.) were pipetted into the reaction-tubes. Alternatively, 5 ml. each of two separate solutions of 2·00N-metal alkyl sulphate and approx. 0·1N-phenol in 2·00N-alkali were used. The reaction was carried out at 100° under conditions identical with those used in the determination of $k'$ (*q.v.*). The reaction was arrested by plunging the tubes into cold running water. Two or three tubes were taken at zero time for the determination of the initial hydroxide ion concentration by titration with 0·5N-hydrochloric acid to phenolphthalein. The phenol did not interfere, except with the nitrophenols, for which it was necessary to carry out a parallel reaction with the nitrophenol absent. Tubes were also withdrawn at zero time and at intervals for determination of the residual phenol.

Owing to the relatively rapid reduction of the methyl-sulphate ion concentration owing to the side reaction with hydroxide ion, the reaction could not usefully be prolonged beyond 4 hours, by which time it had become very slow indeed. This meant that even in the most favourable cases (*e.g.*, the *p*-alkoxyphenols) only 60% of the phenol had reacted, with phenol itself 50%, down to the exceedingly unreactive *o*- and *p*-nitrophenols reacting to the extent of only 2 and 4% respectively. In these last two cases the rate constant is based on the amount which had reacted at one time interval only, *viz.*, 240 minutes. In all other cases the mean value at 4 or more time intervals has been taken. The reaction between ethyl-sulphate ion and phenoxide ion was carried out over 6 hours, in which time some 25% of the phenol had reacted. The detailed results of two typical experiments using equations (*b*) and (*d*) are given in Tables I and II respectively. The complete results are summarised in Tables III and IV.

### TABLE I.

*Rate of reaction of sodium methyl sulphate with phenol in aqueous alkaline solution at* 100° (*equivalent methyl-sulphate and hydroxide ion concentrations*).

Initial concns. of reactants: $[NaOH]$ and $[CH_3{\cdot}SO_4Na] = 1{\cdot}000$, $[\text{phenol}] = 0{\cdot}05$.
Phenol determined by Folin and Ciocalteu's method.
0·05N-HCl $\equiv$ residual NaOH at zero time = 18·8 ml.: $a = 0{\cdot}923$.

| Time (mins.). | Residual phenol (mg.). | $\frac{b}{b-y}$. | $60ak't$. | $10^5 k'' = \frac{k' \log b/(b-y)}{\log(1+60ak't)}$. |
|---|---|---|---|---|
| 0 | 45·76 | — | — | — |
| 20 | 41·88 | 1·093 | 0·1262 | (6·7) |
| 40 | 39·38 | 1·162 | 0·2524 | 7·5 |
| 61 | 36·76 | 1·254 | 0·3850 | 7·6 |
| 85 | 34·84 | 1·313 | 0·5364 | 7·2 |
| 115 | 32·16 | 1·423 | 0·7257 | 7·3 |
| 145 | 29·92 | 1·529 | 0·9152 | 7·4 |
| 175 | 28·58 | 1·601 | 1·104 | 7·2 |
| 205 | 26·90 | 1·702 | 1·294 | 7·4 |
| 240 | 24·80 | 1·845 | 1·515 | 7·5 |
| | | | Mean | 7·4 |

Notes: (1) $k' = 11{\cdot}35 \times 10^{-5}$ (see Part I).
(2) Owing to expansion of the reaction solution on heating the true volume of the solution is 10·17 ml. (see Part I).

### TABLE II.

*Rate of reaction of sodium methyl sulphate with phenol in aqueous alkaline solution at* 100° (*non-equivalent methyl-sulphate and hydroxide ion concentrations*).

Initial reaction mixture: 5 ml. of solution $A$ + 5 ml. of solution $B$ (solution $A$: 1·044N-NaOH, 0·50M-$Na_2SO_4$, 0·10N-phenol; solution $B$: 2·000N-$CH_3{\cdot}SO_4Na$).
Phenol determined by bromate–bromide method.

Suppose that the temperature of the reaction mixture be raised to 100° without any reaction taking place. Then when allowance is made for expansion, the concentrations of the reactants become

$$[NaOH] = 0{\cdot}522 \times 10{\cdot}00/10{\cdot}17 = 0{\cdot}513 = p'$$
$$[CH_3{\cdot}SO_4Na] = 1{\cdot}000 \times 10{\cdot}00/10{\cdot}17 = 0{\cdot}983 = a'.$$

0·5N-HCl = residual NaOH at zero time = 9·85 ml.: $p = 0{\cdot}484$.

Hence drop in $[NaOH]$ = drop in $[CH_3{\cdot}SO_4Na]$ from commencement of the reaction to zero time $= (p' - p) = 0{\cdot}513 - 0{\cdot}484 = 0{\cdot}029 = c$.

Hence $[CH_3{\cdot}SO_4Na]$ at zero time $= (a' - c) = 0{\cdot}983 - 0{\cdot}029 = 0{\cdot}954 = a$.

| Time (mins.). | Ml. of 0·1N-Br = residual phenol $(b-y)$. | $\frac{b}{b-y}$. | $2{\cdot}303 \log b/(b-y)$ $(A)$. | $60t(a-p)$ $(B)$. | $(C)$.* | $10^5 k'' = \frac{A}{B+C}$. |
|---|---|---|---|---|---|---|
| 0 | 28·35 | — | — | — | — | — |
| 20 | 26·3 | 1·077 | 0·07508 | 564·0 | 568·0 | 6·6 |
| 50 | 23·5 | 1·206 | 0·1877 | 1410 | 1481 | 6·1 |
| 90 | 20·4 | 1·390 | 0·3294 | 2538 | 2576 | 6·4 |
| 140 | 17·8 | 1·593 | 0·4657 | 3949 | 3846 | 6·0 |
| 200 | 16·5 | 1·718 | 0·5416 | 5640 | 5458 | (4·9) |
| | | | | | Mean | 6·3 |

* $C = \frac{2{\cdot}303}{k'} \log \frac{a - pe^{-60tk'(a-p)}}{a-p}$.
$k' = 11{\cdot}35 \times 10^{-5}$.

TABLE III.

*Second-order rate constants for the reaction between metal alkyl sulphates and phenoxide ion in aqueous solution at* 100°.

Initial phenol concn. approx. 0·05M. in all cases except in Expt. 1D where it was 0·025M.

| Expt. | Metal alkyl sulphate. | Initial concn. | Alkali. | Initial concn. | $k'' \times 10^5$. |
|---|---|---|---|---|---|
| 1A | $CH_3{\cdot}SO_4Na$ | 1·00 | NaOH | 1·00 | 7·4 |
| 1B | ,, | ,, | ,, | ,, | 7·4 |
| 1C | ,, | ,, | ,, | 0·50 | 6·6 — 4·9 * |
| 1D | ,, | ,, | ,, | ,, | 7·4 — 5·6 * |
| 2 | $CH_3{\cdot}SO_4K$ | ,, | KOH | 1·00 | 6·8 |
| 3 | $C_2H_5{\cdot}SO_4Na$ | ,, | NaOH | ,, | 1·37 |

* The total ionic concentration (Σ [ion] × change) was adjusted to 4·00 by the addition of 0·25M-$Na_2SO_4$.

TABLE IV.

*Second-order rate constants for the reaction between sodium methyl sulphate and phenoxide ions in aqueous solution at* 100°.

Initial concns. : [NaOH] = 1·00, [$CH_3{\cdot}SO_4Na$] = 1·00, [phenol] = approx. 0·05M.

| Phenol. | $k'' \times 10^5$. | Phenol. | $k'' \times 10^5$. |
|---|---|---|---|
| Phenol | 7·4, 7·4 | *p*-Methoxyphenol | 10·1 |
| Guaiacol | 6·7 | *p*-Ethoxyphenol | 10·95 |
| *o*-Cresol | 6·7 | *p*-Cresol | 9·3 |
| *o*-Chlorophenol | 3·0 | *p*-*tert*.-Amylphenol | 10·5 |
| *o*-Nitrophenol | 0·25 | *p*-Fluorophenol | 7·2 |
| *m*-Methoxyphenol | 6·0 | *p*-Chlorophenol | 5·45 |
| *m*-Ethoxyphenol | 6·0 | *p*-Bromophenol | 5·3, 5·3 |
| *m*-Cresol | 8·3 | *p*-Iodophenol | 5·1 |
| *m*-Fluorophenol | 4·3 | *p*-Nitrophenol | 0·5 |
| *m*-Chlorophenol | 4·2 | 3 : 5-Dimethoxyphenol | 5·2 |
| *m*-Nitrophenol | 2·6 | | |

*Accuracy of the Results.*—Where duplicate runs were carried out the results were in excellent agreement. A number of other experiments (not reported here), in which the mean value of $k''$ is based on only three values, also confirmed the reproducibility of the results. In general the error of the mean is certainly not greater than 5% for the less reactive phenols and considerably less for the more reactive ones.

*Influence of Electrolyte on the Reaction.*—Various amounts of anhydrous sodium sulphate were added to 10-ml. portions of a solution containing 1·00N-sodium hydroxide, 1·00N-sodium methyl sulphate, and 0·10N-phenol. After 60 minutes' heating at 100° the residual phenol was determined and approximate values for the rate constant were calculated. The values obtained rose steadily from $8{\cdot}22 \times 10^{-5}$ with no added sodium sulphate to $8{\cdot}63 \times 10^{-5}$ in the presence of 2·0N-sodium sulphate.

*Repetition of Some Experiments of Hodgson and Nixon.*—Methyl sulphate (12 ml.) was added to a stirred solution of the phenol (0·1 mole) in sodium hydroxide (50 ml.; 10%), and the stirring continued for 30 minutes. The mixture was transferred to a 250-ml. flask, slowly warmed to 100° in a water-bath (20 minutes), and kept there for 30 minutes. The mixture was distilled in a current of steam until no more anisole came over, then for a further 10 minutes. The anisole was taken up in ether, the ethereal extract washed once with 4% sodium hydroxide solution, the ether evaporated on the steam-bath, and the anisole placed in a steam-oven for 1 hour. After this time no smell of ether was detectable. Yields : anisole, 9·4 g. (87%); *p*-nitroanisole, 9·3 g. (61%).

## DISCUSSION.

The absence in all cases of any upward or downward trend in the rate constants calculated from equation (*b*) for two simultaneous second-order reactions confirms the bimolecular nature of the reaction between alkyl-sulphate ion and phenoxide ion. When equation (*d*) was used, however, the value of $k''$ tended to fall as the reaction proceeded. Since $k''$ as calculated from this equation is extremely sensitive to small errors in the values of the alkyl-sulphate and hydroxide ion concentrations, it is possible that a refinement in experimental technique may overcome this anomaly. It is extremely unlikely that the divergence is serious enough to throw doubt upon the postulated bimolecular nature of the mechanism.

The reaction, being between two ions of like charge, is accelerated by increasing ionic concentration (see also Part I). No attempt has been made to investigate the matter thoroughly. The accelerating effect of sodium ions appears to be slightly greater than that of potassium ions.

The fall in reaction velocity on passing from methyl to ethyl is due to increasing accession of electrons to the α-carbon atom. The ratio of the rates is approximately 5 : 1, in reasonable agreement with ratio of 4 : 1 obtained by Woolf (*loc. cit.*) for the relative rates of reaction of methyl and ethyl iodides with sodium eugenoxide in ethyl alcohol at 50°. Comparison of the rates of reaction of the two alkyl sulphates with hydroxide and with phenoxide ions (see Table V) reveals the interesting fact that, contrary to expectation, sodium ethyl sulphate reacts more readily with the latter. A partial distribution of the negative charge over the benzene ring would render phenoxide less reactive than hydroxide ion. The reason for this anomaly is not known.

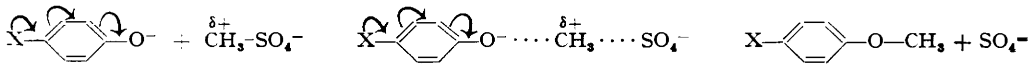
TABLE V.

*Second-order rate constants for the reaction of sodium alkyl sulphates with hydroxide and phenoxide ions in aqueous solution at* 100°.

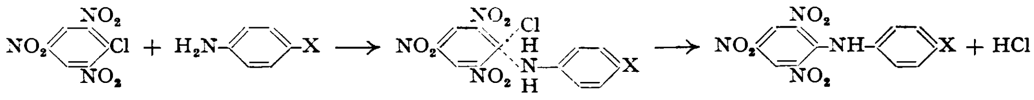
| | $10^5k$ for reaction with | |
|---|---|---|
| Alkyl sulphate. | $OH^-$.* | $OPh^-$. |
| Sodium methyl ........................................ | 11·35 | 7·4 |
| Sodium ethyl .......................................... | 1·05 | 1·37 |

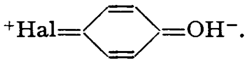
* From Part I.

*Influence of Nuclear Substituents.*—The influence of nuclear substituents in the phenol is in the expected direction, except for those in the *ortho*-position where considerable steric effects are apparent. This is in contrast to the results of Boyd *et al.* (*loc. cit.*) who did not find appreciable steric hindrance in their reaction of phenoxide ions with ethylene and propylene oxides (except the nitro-group); also the dissociation constants of the *ortho*-substituted phenols are normal (Dippy, Evans, Gordon, Lewis, and Watson, *J.*, 1937, 1421). In the *meta*- and *para*-positions the influence of the substituent is determined solely by the relative magnitude of the inductive and tautomeric effects. It is observed (Table IV) that the reaction rates of the *p*-halogeno-substituted phenols diminish in the order H > F > Cl > Br > I; the tautomeric electron-release effects (+*T*) of the halogens diminish in the same order, whereas their inductive effects (−*I*) become more negative in the reverse order. To explain this co-ordination of tautomeric effect with reaction rate it is necessary to consider the electron movements during the course of the reaction. The initial, transitional, and final states of the reactants are as follows :



The formation of the transitional state is facilitated by the localisation of the negative charge on the phenolic oxygen atom; the formation of the final state requires the localisation of both negative charges on the $SO_4$ group. *Both* these conditions will be facilitated by electron release from the group X. In only a few other cases has complete inversion of the relative reactivities of the *para*-halogens been observed in reactions facilitated by electron accession to the side chain, and all but one are unimolecular and have one rate-determining stage only. The only bimolecular reaction reported to show complete inversion is that between chloronitrobenzenes and substituted anilines in dilute alcohol (Linke, *Ber.*, 1923, **56**, 848). Although *p*-fluoroaniline was not included there is no reason to doubt that it will fall into line. The reaction may be formulated :



Here again, *both* stages are facilitated by electron release from the group X: (*a*) the attack of the amino-nitrogen atom on the positive nuclear carbon atom, and (*b*) the release of the negatively charged chlorine ion. It may be expected that the reaction of phenoxide ion with dialkyl sulphates, alkyl halides, ethylene oxides, etc., will also exhibit the inverted order of reactivity for the *p*-halogeno-compounds. The inverted order is also to be found in the dissociation constants of phenols, benzoic acids, phenylacetic acids, and phenylboric acids (Dippy, *Chem. Reviews*, 1939, **25**, 151). In these cases the predominant influence is the mesomeric (+*M*) portion of the tautomeric effect reflected in the resonance of the molecule due to a contribution of the quinonoid form, *e.g.*, .

In the case of the phenoxide ion, the oxygen atom already possesses six free electrons and resonance of this type cannot be expected. It must, therefore, be the electromeric ($+E$) effect acting in the initial and transitional states which assists the reaction between phenoxide ion and alkyl sulphate. Summing up we have:

Forces affecting equilibrium constant $-I + M$
Forces affecting reaction constant $-I + E$

If log $k$ for the reaction is plotted against log $K$ for the equilibrium (see Table VI and figure) the points for the substituted phenols lie on a straight line, whereas phenol itself lies considerably off the line. It has been pointed out by Dippy and Watson (*J.*, 1936, 436) that the operation of electromeric effects can cause a divergence from the linear relation between log $k$ and log $K$.

TABLE VI.

*Relation between log* K *and log* k *for* p-*halogenophenols.*

| Substituent. | $10^{10}K$.* | $11 + \log K$. | $10^5k$. | $5 + \log k$. |
|---|---|---|---|---|
| — | 0·32 | 0·5051 | 7·4 | 0·8692 |
| *p*-F | 0·26 | 0·4150 | 7·2 | 0·8573 |
| *p*-Cl | 1·32 | 1·1206 | 5·45 | 0·7364 |
| *p*-Br | 1·55 | 1·1903 | 5·3 | 0·7243 |
| *p*-I | 2·19 | 1·3404 | 5·1 | 0·7076 |

* $K$ is the dissociation constant in 30% ethanol at 25° (Bennett, Brooks, and Glasstone, *J.*, 1935, 1821). Since the relative dissociation constants of acids are generally independent of both medium and temperature, it is permissible to compare reaction velocities in one medium with dissociation constants in another medium and at a different temperature (Dippy, *Chem. Reviews*, 1939, **25**, 151).

The present reaction provides an addition to the list of benzene side-chain reactions which obey the simple law $\log K = \log K^\circ + \rho\sigma$ where $\rho$ = reaction constant, $\sigma$ = substitution constant, and $K$ and $K^\circ$ = rate constants for substituted and unsubstituted reactants respectively (Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 184; *J. Amer. Chem. Soc.*, 1937, **59**, 96). By using Hammett's value of $\sigma$, values of $\rho$ have been calculated and are given in Table VII. The large divergence of the *p*-fluoro- and *p*-nitrophenols may be due to experimental error—the former owing to the very small difference in rate with unsubstituted phenol, and the latter to the difficulty of measuring its very slow reaction rate with accuracy.

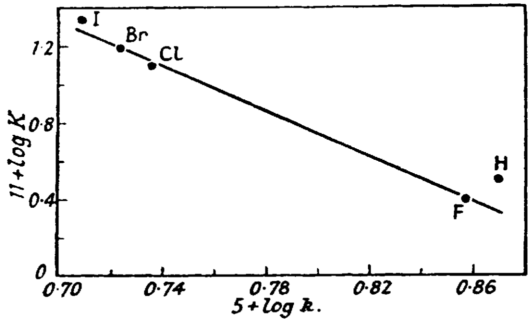


TABLE VII.

*Calculated values of* ρ *for the reaction between substituted phenoxide ions and sodium methyl sulphate.*

| Substituent. | σ. | ρ. | Substituent. | σ. | ρ. |
|---|---|---|---|---|---|
| *p*-OMe | −0·268 | 0·520 | *p*-Cl | 0·227 | 0·585 |
| *p*-OEt | −0·25 | 0·682 | *p*-Br | 0·232 | 0·624 |
| *p*-Me | −0·170 | 0·584 | *p*-I | 0·276 | 0·586 |
| *m*-Me | −0·069 | 0·723 | *m*-F | 0·337 | 0·700 |
| *p*-F | 0·62 | (0·180) | *m*-Cl | 0·373 | 0·658 |
| *m*-OMe | 0·115 | 0·791 | *m*-$NO_2$ | 0·710 | 0·640 |
| *m*-OEt | 0·15 | 0·606 | *p*-$NO_2$ | 1·27 | (0·921) |

Mean $\rho$ 0·642.

*General Considerations.*—Since sodium methyl sulphate reacts with phenoxide and hydroxide ions at roughly the same rate it is obviously of advantage in using this reagent as a methylating agent to maintain the hydroxide ion concentration at as low a level as possible consistent with keeping the phenol dissociated. Highest yields based on the methylating agent and most rapid reaction will be obtained when the alkali is added slowly to a boiling strong solution of phenol and sodium methyl sulphate so that the solution is maintained *just* alkaline all the time. Sodium salts are preferred to the corresponding potassium salts on account of their more rapid reaction and greater solubility.

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