# **199.** *Nucleophilic Reactivity. Part III.*[1] *The Significance of the Brönsted Relation, with Particular Reference to Acylation and Alkylation.*

By R. F. Hudson and G. Loveday.

The rates of reaction of a series of *para*-substituted phenols with ethyl chloroformate in 85% aqueous acetone at 0°, and with 3-bromopropanol in water at 61°, have been measured. The $pK_a$ values of the phenols were determined under these conditions, and the Brönsted relation was found to hold in both cases. The low exponents observed for alkylations and the high exponents usually observed for acylations are interpreted in terms of the transition-state structures by a simple electrostatic treatment, and the variation in the exponent with the leaving group is discussed. No *C*-alkylated products were obtained in the reaction of phenol and *p*-nitrophenol with 3-bromopropanol in water.

In the preceding paper, the reactivity constant $\rho_N$ of the Hammett $\rho$–$\sigma$-equation obtained for the reaction between substituted thiophenols and benzyl bromides by varying the substituent in the former was shown to increase linearly with the values of $\sigma_R$ for the substituents in the benzyl bromide. This was interpreted by identifying $\sigma_R$ with the charge density on the carbon atom in the transition state, and $\rho_N$ (or the analogous parameter $\alpha_N$ of the Brönsted equation) with the charge transfer from the nucleophile in the transition state. According to this interpretation, therefore, the value of $\rho_N$ (or $\alpha$) is determined by the transition-state structure and hence by the reaction mechanism.

To examine this relation further, we have compared the value of $\alpha$ in the Brönsted relation, $\log k = \alpha \, . \, pK_a + \text{Constant}$, for the reaction between a series of substituted phenols and ethyl chloroformate, $Cl{\cdot}CO_2Et + p\text{-}R{\cdot}C_6H_4{\cdot}O^- \longrightarrow p\text{-}R{\cdot}C_6H_4{\cdot}O{\cdot}CO_2Et + Cl^-$, with the value for the corresponding reaction of 3-bromopropanol, a typical alkylating agent, $HO{\cdot}[CH_2]_3{\cdot}Br + p\text{-}R{\cdot}C_6H_4{\cdot}O^- \longrightarrow p\text{-}R{\cdot}C_6H_4{\cdot}O{\cdot}[CH_2]_3{\cdot}OH + Br^-$. The bromopropanol was used to increase the solubility in water since the reactions were carried out in water, in order to compare the rates with the corresponding $pK_a$'s of the phenols under the conditions of the reaction.

In view of the report by Kornblum *et al.*[2] that certain benzyl and alkyl chlorides give high yields of the *C*-alkylated products in aqueous solution, the compositions of the products of the reactions of phenol and *p*-nitrophenol with 3-bromopropanol were studied. In both cases, the corresponding ether was found to be the main product, and no *C*-alkylated product was detected.

Good Brönsted plots were obtained for both reactions (Figure) giving values of $\alpha = 0{\cdot}22$ for the alkyl bromide, and 0·78 for the acyl chloride. The large differences cannot be attributed to the difference in the leaving groups, since Smith [3] obtained values of 0·20 for the reaction of carboxylate ions with the chloroacetate ion, and 0·195 for the corresponding reaction with the bromoacetate ion; it is considered to reflect the different transition-state structures, as discussed below.

Similar measurements have shown that the Brönsted relation is obeyed fairly accurately for various reactions of *p*-nitrophenyl acetate [4] and certain anhydrides [5] and phosphonyl compounds,[6,7] generally leading to high values for $\alpha$ (Table 1), compared with those normally obtained for alkylation.

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[1] Part II, preceding paper.

[2] Kornblum, Berrigan, and Noble, *J. Amer. Chem. Soc.*, 1960, **82**, 1257; Kornblum and Lurie, *ibid.*, 1959, **81**, 2705.

[3] Smith, *J.*, 1943, 521.

[4] Bruice and Lapinski, *J. Amer. Chem. Soc.*, 1958, **80**, 2265.

[5] Bender, *Chem. Rev.*, 1960, **60**, 63.

[6] Green, Sainsbury, Saville, and Stansfield, *J.*, 1958, 1583.

[7] Epstein, Rosenblatt, and Demek, *J. Amer. Chem. Soc.*, 1956, **78**, 341.

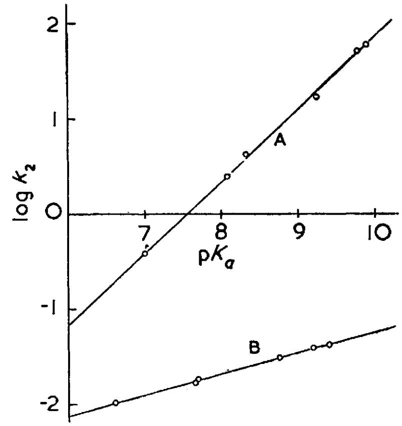
TABLE 1.

Values of the Brönsted coefficient α for reactions of nucleophiles with alkylating, acylating, and phosphorylating agents in water.

| Compound | Nucleophile | α | Ref. | Compound | Nucleophile | α | Ref. |
|---|---|---|---|---|---|---|---|
| $MeO{\cdot}SO_3^-$ | $R{\cdot}C_6H_4{\cdot}O^-$ | 0·16 | *a* | *p*-$NO_2{\cdot}C_6H_4{\cdot}COCl$ | $R{\cdot}C_6H_4{\cdot}O^-$;<br>$R{\cdot}C_5H_4N$ | 0·80 | *f* |
| $Cl{\cdot}CH_2{\cdot}CO_2^-$ | $R{\cdot}CO_2^-$ | 0·20 | *b* | | | | |
| $Br{\cdot}[CH_2]_3{\cdot}OH$ | $R{\cdot}C_6H_4{\cdot}O^-$ | 0·22 | *c* | $Ac_2O$ | $R{\cdot}C_5H_4N$ | 0·92 | *g* |
| | | | | $Et_2N{\cdot}P({:}O)(CN){\cdot}OEt$ | $R_2C{:}N{\cdot}O^-$ | 0·50 | *b* |
| $\overline{CH_2{\cdot}CH_2{\cdot}O}$ | ,, | 0·32 | *d* | $(EtO)_2P({:}O){\cdot}O{\cdot}P({:}O)(OEt)_2$ | ,, | 0·70 | *h* |
| $2,4\text{-}(NO_2)_2C_6H_3Cl$ | ,, | 0·50 | *e* | $Me{\cdot}POF{\cdot}OPr^i$ | $R{\cdot}CO{\cdot}NH{\cdot}O^-$ | 0·82 | *h* |
| $Cl{\cdot}CO_2Et$ | ,, | 0·78 | *c* | ,, | $R{\cdot}C_6H_4(OH){\cdot}O^-$ | 0·90 | *i* |

(*a*) Green and Kenyon, *J.*, 1950, 1595. (*b*) Smith, *J.*, 1943, 521. (*c*) Present results. (*d*) Goldsworthy, *J.*, 1926, 1254. (*e*) Miller, Parker, Leahy, and Liveris, *Austral. J. Chem.*, 1956, 382. (*f*) Bruice and Lapinski, *J. Amer. Chem. Soc.*, 1958, **80**, 2265. (*g*) Gold and Jefferson, *J.*, 1953, 1409. (*h*) Green, Saville, Sainsbury, and Stansfield, *J.*, 1958, 1583. (*i*) Epstein, Rosenblatt, and Demek. *J. Amer. Chem. Soc.*, 1956, **78**, 341.

The difference is attributed to the large charge on the carbonyl-carbon atom, and is illustrated by a simple electrostatic argument of the kind originally proposed by Ri and Eyring,[8] as follows. Consider the $S_N2$ transition state to be symmetrical owing to the similar electronegativities of the groups N and X, and to be formed by a stretching of the C–X bond requiring energy $E_1$ to give the bond $\overset{\delta+}{C}$—$\overset{\delta-}{C}$, followed by interaction with the nucleophile:



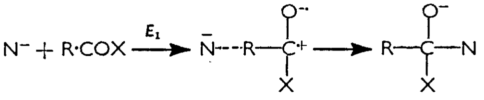
Plot of log. *k* against p$K_a$ for reaction of various phenols with (A) ethyl chloroformate and (B) 3-bromopropanol.

$$N^- + R{\cdot}CH_2{\cdot}X \xrightarrow{E_1} \bar{N} \quad \overset{\frac{1}{2}+}{R{\cdot}CH_2}\text{—}\overset{\frac{1}{2}-}{X} \longrightarrow \overset{\frac{1}{2}-}{N}\text{—}\underset{R}{\overset{H\ \ H}{C}}\text{—}\overset{\frac{1}{2}-}{X}$$

(I) (II)

We assume also that the N–C distance ($r$) in the transition state is the mean of the covalent and ionic radii, *i.e.*, $r_1 = \frac{1}{2}(r_{C-X} + r_{C^+X^-}) \approx r_{C-X} + 0{\cdot}4$ Å.

The transition state for acylation is assumed to be similar to that of the *sp*³-hybridised intermediate,[9] and is imagined to be formed in a similar way to the $S_N2$ transition state, *viz.*:



$$N^- + R{\cdot}COX \xrightarrow{E_1} \bar{N}\text{---}R\text{—}\underset{X}{\overset{O^-}{C^+}} \longrightarrow R\text{—}\underset{X}{\overset{O^-}{C}}\text{—}N$$

(I′) (II′)

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[8] Ri and Eyring, *J. Chem. Phys.*, 1940, **8**, 433.

[9] Ref. 5, p. 59.

For simplicity we shall assume that the energies of the states (I) and (II) and of (I′) and (II′) are similar, *i.e.*, that the N–C bond energies in the transition states may be given by the electrostatic interaction in (I) and (I′). If the charge on the nucleophile N is $Z$ and on the carbon atom is $\delta$, then $\Delta E^* = E_1 + Z\delta/r_1D$. For the combination of a proton with $N^-$, the heat of reaction $\Delta H$ is given similarly by $\Delta H = Z/r_0D$.

Combination of the two equations gives $\Delta E^* = (r_0/r_1)\delta \,.\, \Delta H$ + Constant, or $\log k = (r_0/r_1)\delta \,.\, pK_a$ + Constant. Thus, from $r_0$ and $r_1$ for the H–O and C–O bond, respectively, and the assumed transition-state structures (I) and (I′), computed values of $(r_0/r_1)\delta$ can be compared with the experimental values of the Brönsted $\alpha$ (see Table 2).

TABLE 2.

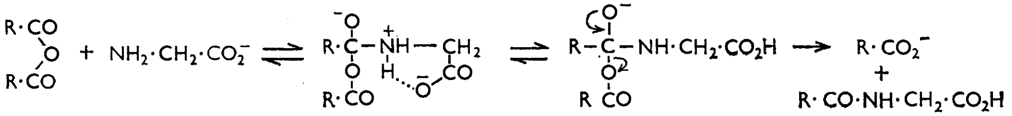
Calculated and observed values of the Brönsted parameter $\alpha$.

| Reaction | $r_1$ (Å) | $\alpha$ (Calc.) | $\alpha$ (Obs.) |
|---|---|---|---|
| $S_N2$ | 1·83 | 0·25 | 0·22 |
| $S_{NH}$ * | 1·36 | 0·36 | 0·47 † |
| $S_{NC=O}$ | 1·42 | 0·70 | 0·78 |

* General base-catalysis, *i.e.*, nucleophilic attack on hydrogen.
† Value given by Jencks and Carriuolo, *J. Amer. Chem. Soc.*, 1961, **83**, 1743.

This simple model of a substitution leads to values of $\alpha$ comparable with the experimental values, and illustrates the general relation between the value of $\alpha$ and the charge density at the reaction centre. A value of $\alpha$ for a general base-catalysed hydrolysis is also included in the Table, the transition state again being taken to be symmetrical, *i.e.*, $N^- + H{-}X{-}\phi \longrightarrow \overset{\frac{1}{2}-}{N}{—}H{—}\overset{\frac{1}{2}-}{X}{-}\phi$. The calculated value is similar to that recently found [10] for the base-catalysed hydrolysis of esters (0·47), which is considerably lower than that normally obtained for nucleophilic displacement at the carbonyl centre (Table 1).

This kind of catalysis may explain the low values of $\alpha$ obtained for the reactions of $\alpha$-amino-acids in the ionised form with 2,4-dinitrophenyl acetate [11] and with certain anhydrides.[12] As shown by the data summarised in Table 7 of ref. 5, these values lie within the range 0·38—0·55, whereas all other values for acylation, including reactions of other amines with these acylating agents, give values of 0·8—1·1. It is now well established that amines react with esters to give relatively stable addition products, the rate-determining decomposition of which involves general base-catalysis.[13] Similarly the hydrolysis of anhydrides is subject to similar catalysis by carboxylate ions.[14] These considerations suggest that the low values of $\alpha$, observed only when $\alpha$-amino-acids are used as nucleophiles, may be due to an internal base-catalysed mechanism as follows:



Many examples of internally catalysed hydrolyses of esters and anhydrides are now known.[5]

*The Effect of the Leaving Group*.—As previously mentioned, small changes in the electronegativity of the leaving group probably have little effect on the magnitude of $\alpha$. Thus the similarity in the values [3] for chloroacetate and bromoacetate ions has already been

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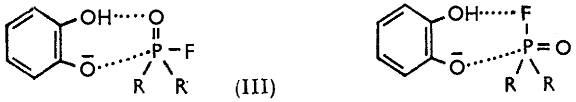
[10] Jencks and Carriuolo, *J. Amer. Chem. Soc.*, 1961, **83**, 1743.
[11] Brouwer, van der Vlugt, and Havinga, *Proc. K. Ned. Akad. Wetenschap.*, 1958, *B*, **61**, 141.
[12] Bartlett and Jones, *J. Amer. Chem. Soc.*, 1957, **79**, 2153.
[13] Bunnett and Davis, *J. Amer. Chem. Soc.*, 1960, **82**, 665; Jencks and Carriuolo, *ibid.*, p. 675.
[14] Kilpatrick, *J. Amer. Chem. Soc.*, 1928, **50**, 2891; Butler and Gold, *Proc. Chem. Soc.*, 1960, 15.

noted, and the present value of 0·78 for ethyl chloroformate is close to the mean value of 0·8 given by Bruice and Lapinski for *p*-nitrophenyl acetate.[4] Bender [5] has pointed to the relatively high value for phenyl acetate, but this may be due to the use of a high temperature for the reaction (109°; cf. 25° for *p*-nitrophenyl acetate).



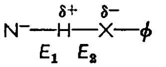
(III)

Large changes in α have, however, been observed for reactions of organophosphorus compounds,[6] the value increasing with the electronegativity $x_y$ of the displaced group (Table 3) which increases the positive charge on the phosphorus atom. The value of α is further increased when the charge transfer from the nucleophile is assisted by hydrogen bonding to the phosphonyl group, as in the reaction with substituted catechols [7] (cf. III).

When the displaced group is highly conjugated, and the changes in the inductive effect are relatively small, a different effect is observed. As the conjugation energy in the displaced group increases, the effective electron affinity increases, so that a symmetrical transition state cannot be assumed. The effect may be represented by comparing two reactions, producing a non-conjugated group (IV) and a highly conjugated group (V), respectively, as follows:

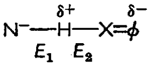
TABLE 3.

| | $NEt_2\cdot P{:}O(CN)\cdot OEt$ | $[(EtO)_2P(O)]_2O$ | $Me\cdot POF\cdot OPr$ |
|---|---|---|---|
| $x_y$ | 2·5 | 3·5 | 4·0 |
| α | 0·5 | 0·7 | 0·8 |



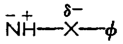
$N^{-}\underset{E_1}{—}\overset{\delta+}{H}\underset{E_2}{—}\overset{\delta-}{X}—\phi$

(IV)



$N^{-}\underset{E_1}{—}\overset{\delta+}{H}\underset{E_2}{—}\overset{\delta-}{X{=}\phi}$

(V)



$\overset{-\,+}{NH}—\overset{\delta-}{X}—\phi$

(IVA)

In the first case the interaction energy $E_2 > E_1$; so the transition state is not reached. Thus an increase in the bond-forming energy, represented by closer approach of H to N produced by an increase in δ, is necessary to reach the energy barrier. This is represented by structure (IVA), where $\overset{-\,+}{NH}$ represents complete bond formation in terms of the model used above. In the second case, $E_1 > E_2$, *i.e.*, the transition state has already been reached for a reduced N–H interaction energy. Thus the value of α will decrease with the ease of ionisation of the pseudo-acid, as demonstrated by the decrease with p$K_a$ observed for the base-catalysed halogenation of ketones: [5] $B^- + H\cdot CH_2\cdot COR \longrightarrow BH + [CH_2\cdot COR]^-$.

The values of 1·31, 1·075, and 0·914 given by Bender [5] for the reactions of pyridines with phenyl, *p*-nitrophenyl, and 2,4-dinitrophenyl acetate also decrease with increases in conjugation in the displaced group.

It is interesting that the α-value for a nitroparaffin, *e.g.*, nitromethane, is greater than the value for a ketone of comparable basicity.[15] This is interpreted on the present views by the increased inductive effect of the nitrogen atom in the group $O{=}\underset{|}{N^{+}}—O^{-}$, superimposed on the effect of conjugation in the displaced group.

These examples are introduced to illustrate the scope of the simple electrostatic interpretation of the reaction parameter, and its use in describing transition-state structures.

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[15] Bell and Lindwell, *Proc. Roy. Soc.*, 1940, *A*, **176**, 88; Bell, Gelles, and Moller, *ibid.*, 1949, *A*, **198**, 308.

## EXPERIMENTAL

*Preparation of Materials.*—3-Bromopropanol, prepared (73%) by the action of anhydrous hydrogen bromide on trimethylene glycol [16] at $-5°$, had b. p. 71—72°/15 mm., $n_D^{17}$ 1·4848.

*p*-Hydroxyacetophenone was prepared by the action of anhydrous aluminium chloride on phenyl acetate. The mixture was steam-distilled and the product crystallised from benzene–light petroleum (b. p. 60—80°), to give a solid, m. p. 109—109·5° (yield, 50%).

Phenol, b. p. 91—92°/24 mm., *p*-cresol, b. p. 102—104°/20 mm., and *p*-chlorophenol, b. p. 216—217°, were purified by distillation.

*m*-Nitrophenol, recrystallised from water and from light petroleum (b. p. 80—100°), had m. p. 95·5—96°.

*p*-Nitrophenol, recrystallised twice from water, had m. p. 113—114°.

*Rate Measurements.*—(a) *Reactions in water.* The solutions were prepared by adding a weighed amount of the appropriate phenol to water. Sodium hydroxide was added with stirring to bring the pH of the solution to the required value. The solution was then made up to 500 ml., and 200 ml. were transferred to the reaction cell in a thermostat bath at 61°. The glass and calomel electrodes were connected to a Pye automatic titrator, and the solenoid-operated burette was fitted in place. About 10 drops of the substrate were added from a Lunge Rey weight-pipette, a stop-clock was started, and the rate of reaction followed by withdrawing 5 ml. portions of the reaction mixture at known times and estimating the liberated bromide by the Volhard method. The volume of alkali added was noted at each time, and the appropriate correction made to the volume of the sample. The reaction mixture was stirred continuously by a high-speed centrifugal stirrer.

(b) *Reactions in acetone–water.* Distilled water was added to acetone (75 ml.), then a weighed quantity of the phenol was added, followed by sodium hydroxide solution until the required pH was reached. The solution was then diluted to 500 ml., and 200 ml. were pipetted into a 350-ml. beaker held in a Dewar vessel containing a stirred ice–water mixture. The pH of the solution was controlled by the Pye automatic titrator, 10-ml. samples were withdrawn at regular intervals, and unchanged ethyl chloroformate was extracted with ether. The aqueous layer was then titrated for chloride by the Volhard method.

*Evaluation of the Rate Constants.*—For both reactions good first-order plots were obtained by plotting the first-order reaction in the form $2{\cdot}303 \log_{10} (V_\infty - V_t) = -k_1t$, where $V_\infty$ is the volume of the final titration and $V_t$ the volume titrated at time $t$. The second-order rate constant $k_2$ was obtained by using the following equation, $k_2 = \{(k_1)_N - (k_1)_0\}/[N^-]$ where $(k_1)_N$ is the first-order rate constant obtained in the presence of the phenol, and $k_0$ is the first-order rate constant in the solvent alone. The concentration of phenol in the ionised form, $[N^-]$, was obtained from the appropriate p$K_a$ determined under the conditions of the experiment, *i.e.*, $[N^-] = K_a[\text{PhOH}]/1 + K_a$, where [PhOH] is the stoicheiometric concentration of the phenol calculated from the weight added.

*Determination of the* p$K_a$'s *of the Phenols.*—An $\sim$0·05N-solution of the phenol was prepared by dissolving a weighed portion in freshly distilled water in a 250-ml. flask. The phenol was partly neutralised with freshly prepared, carbonate-free sodium hydroxide solution, and the mixture was diluted to 250 ml.; 200-ml. of this solution were allowed to reach thermal equilibrium in the thermostat bath, and the pH was measured by means of a glass electrode. The p$K_a$ values were calculated from the Henderson equation, and the average of determinations at 20%, 40%, and 60% neutralisation was taken.

The p$K_a$ values of the phenols at 0° in acetone–water (85% of water plus 15% of acetone by volume) were measured by dissolving a weighed amount of the phenol in the solvent and allowing the solution to reach thermal equilibrium. Nitrogen was passed through the solution continuously. The p$K_a$ was calculated from the measured pH of the solution, the average of three determinations with different initial concentrations of phenol being taken in each case.

*Results.*—Results are in Tables 4—7.

*Products.*—(a) 3-*Bromopropanol and phenol.* 40% Sodium hydroxide solution was added with stirring to a solution of phenol (10 g.) in water (1 l.) until the pH reached 9·5. 3-Bromopropanol (5 g.) was added, and the mixture was shaken and left at 61° for 72 hr. The pH was kept at 9·5 by the addition of sodium hydroxide solution, controlled by the automatic titrator.

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[16] Bogart and Slocum, *J. Amer. Chem. Soc.*, 1924, **46**, 765.

TABLE 4.

Pseudo-unimolecular rate constants, $k_1$, and second-order rate constants, $k_2$, for the reaction of *para*-substituted phenols $R \cdot C_6H_4 \cdot OH$ with 3-bromopropanol in water at 61° and pH 9·5.

| $[Br \cdot [CH_2]_3 \cdot OH]$ (mole l.$^{-1}$) | R | [ArOH] | $[R \cdot C_6H_4 \cdot O^-]$ calc. $[ArO^-]$ (calc.) | $10^4k_1$ (min.$^{-1}$) | Mean $10^4k_1$ | $10^2k_2$ (l. mole$^{-1}$ min.$^{-1}$) | Mean $10^2k_2$ |
|---|---|---|---|---|---|---|---|
| 0·0153 | ($H_2O$) | — | — | 4·43 | 4·40 | — | — |
| 0·0166 | ($H_2O$) | — | — | 4·37 | | | |
| 0·0160 | Me | 0·125 | 0·070 | 27·10 | 27·10 | 4·15 | 4·17 |
| 0·0148 | ,, | 0·125 | 0·070 | 27·10 | | | |
| 0·0121 | ,, | 0·076 | 0·042 | 18·60 | 18·50 | 4·19 | |
| 0·0136 | ,, | 0·076 | 0·042 | 18·40 | | | |
| 0·0121 | H | 0·081 | 0·054 | 25·90 | 25·8 | 3·89 | 3·93 |
| 0·0121 | ,, | 0·081 | 0·054 | 25·70 | | | |
| 0·0137 | ,, | 0·150 | 0·100 | 44·00 | 44·0 | 3·96 | |
| 0·0187 | Cl | 0·046 | 0·039 | 16·10 | 16·1 | 3·00 | 3·02 |
| 0·0145 | ,, | 0·046 | 0·039 | 16·10 | | | |
| 0·0151 | ,, | 0·054 | 0·046 | 18·30 | 18·2 | 3·03 | |
| 0·0126 | ,, | 0·054 | 0·046 | 18·10 | | | |
| 0·0141 | Ac | 0·046 | 0·045 | 12·7 | 12·7 | 1·86 | 1·86 |
| 0·0137 | ,, | 0·046 | 0·045 | 12·6 | | | |
| 0·0096 | *m*-$NO_2$ | 0·052 | 0·051 | 13·2 | 13·3 | 1·74 | 1·74 |
| 0·0103 | ,, | 0·052 | 0·051 | 13·3 | | | |
| 0·0128 | *p*-$NO_2$ | 0·057 | 0·057 | 10·5 | 10·5 | 1·07 | 1·07 |
| 0·0130 | ,, | 0·057 | 0·057 | 10·4 | | | |

TABLE 5.

p$K_a$ values for *meta*- and *para*-substituted phenols in water at 61°.

| [ArOH] (mole l.$^{-1}$) | 0·1N-NaOH added (ml.) | pH | $\log_{10}$ [Salt]/[ArOH] | p$K_a$ * | Mean p$K_a$ |
|---|---|---|---|---|---|
| p-*Cresol* | | | | | |
| 0·054 | 25·26 | 8·79 | −0·60 | 9·39 | 9·40 |
| 0·033 | 33·38 | 9·23 | −0·18 | 9·41 | |
| 0·011 | 15·9 | 9·56 | −0·18 | 9·41 | |
| *Phenol* | | | | | |
| 0·040 | 19·85 | 8·59 | −0·60 | 9·19 | 9·20 |
| 0·024 | 22·41 | 9·03 | −0·18 | 9·21 | |
| 0·029 | 43·12 | 9·38 | 0·18 | 9·20 | |
| p-*Chlorophenol* | | | | | |
| 0·009 | 4·43 | 8·12 | −0·60 | 8·72 | 8·76 |
| 0·011 | 10·66 | 8·62 | −0·18 | 8·80 | |
| 0·011 | 16·44 | 8·93 | 0·18 | 8·75 | |
| p-*Hydroxyacetophenone* | | | | | |
| 0·005 | 2·70 | 7·08 | −0·60 | 7·68 | 7·68 |
| 0·009 | 8·65 | 7·48 | −0·18 | 7·66 | |
| 0·011 | 16·10 | 7·86 | 0·18 | 7·68 | |
| m-*Nitrophenol* | | | | | |
| 0·022 | 10·93 | 7·12 | −0·60 | 7·72 | 7·66 |
| 0·022 | 21·88 | 7·49 | −0·18 | 7·67 | |
| 0·020 | 30·15 | 7·78 | 0·18 | 7·60 | |
| p-*Nitrophenol* | | | | | |
| 0·036 | 17·98 | 5·98 | −0·60 | 6·58 | 6·60 |
| 0·045 | 45·12 | 6·42 | −0·18 | 6·60 | |
| 0·049 | 73·32 | 6·79 | 0·18 | 6·61 | |

* The three values for each substance are for 20%, 40%, and 60% neutralisation, respectively.

TABLE 6.

Rates of reaction of ethyl chloroformate at pH 8·0 at 0°.

| $[Cl\cdot CO_2Et]$ (mole l.$^{-1}$) | ArOH | [ArOH] (calc.) | $[ArO^-]$ (calc.) | $10^4k_1$ (min.$^{-1}$) | Mean $10^4k_1$ | $k_2$ (l. mole$^{-1}$ min.$^{-1}$) | Mean $k_2$ |
|---|---|---|---|---|---|---|---|
| 0·0088 | ($H_2O$) | — | | 23·5 | 23·2 | — | — |
| 0·0109 | ,, | — | | 23·1 | | | |
| 0·0245 | ,, | — | | 23·2 | | | |
| 0·0119 | ,, | — | | 23·0 | | | |
| 0·0119 | ,, | — | | 23·2 | | | |
| 0·0159 | ,, | — | | 23·2 | | | |
| 0·0159 | ,, | — | | 23·2 | | | |
| 0·0127 | *p*-Cresol | 0·075 | 9·5 | 555·0 | 553·9 | 55·6 | 55·7 |
| 0·0105 | ,, | 0·075 | | 552·7 | | | |
| 0·0100 | ,, | 0·033 | 4·2 | 259·1 | 258·1 | 55·8 | |
| 0·0094 | ,, | 0·033 | | 257·1 | | | |
| 0·0124 | PhOH | 0·055 | 8·5 | 451·4 | 452·6 | 50·4 | 50·2 |
| 0·0113 | ,, | 0·055 | | 453·7 | | | |
| 0·0108 | ,, | 0·024 | 3·7 | 207·2 | 206·9 | 49·9 | |
| 0·0116 | ,, | 0·024 | | 206·5 | | | |
| 0·0121 | *p*-$Cl\cdot C_6H_4\cdot OH$ | 0·072 | 37·9 | 653·0 | 653·0 | 16·6 | 16·55 |
| 0·0106 | ,, | 0·036 | 19·0 | 338·7 | 337·0 | | |
| 0·0101 | ,, | 0·036 | | 335·2 | | 16·5 | |
| 0·0123 | *m*-$NO_2\cdot C_6H_4\cdot OH$ | 0·011 | 35·6 | 162·4 | 161·8 | 3·89 | 4·13 |
| 0·0119 | ,, | 0·011 | | 161·2 | | | |
| 0·0128 | ,, | 0·006 | 17·4 | 95·3 | 95·5 | 4·15 | |
| 0·0136 | ,, | 0·006 | | 95·8 | | | |
| 0·0131 | ,, | 0·068 | 216·2 | 955·7 | 957·6 | 4·32 | |
| 0·0139 | ,, | 0·068 | | 959·5 | | | |
| 0·0132 | ,, | 0·034 | 107·7 | 479·0 | 478·0 | 4·14 | |
| 0·0145 | ,, | 0·034 | | 477·1 | | | |
| 0·0158 | *p*-$Ac\cdot C_6H_4\cdot OH$ | 0·013 | 58·5 | 166·6 | 167·0 | 2·46 | 2·47 |
| 0·0121 | ,, | 0·013 | | 167·3 | | | |
| 0·0109 | ,, | 0·007 | 31·5 | 105·9 | 106·1 | 2·47 | |
| 0·0153 | ,, | 0·007 | | 106·2 | | | |

*In water–acetone* (85 : 15).

| $[Cl\cdot CO_2Et]$ (mole l.$^{-1}$) | ArOH | [ArOH] (calc.) | $[ArO^-]$ (calc.) | $10^4k_1$ (min.$^{-1}$) | Mean $10^4k_1$ | $k_2$ (l. mole$^{-1}$ min.$^{-1}$) | Mean $k_2$ |
|---|---|---|---|---|---|---|---|
| 0·0121 | *p*-$NO_2\cdot C_6H_4\cdot OH$ | 0·058 | 522·5 | 233·0 | 232·2 | 0·40 | 0·38 |
| 0·0104 | ,, | 0·058 | | 231·5 | | | |
| 0·0112 | ,, | 0·014 | 125·5 | 68·6 | 68·4 | 0·36 | |
| 0·0104 | ,, | 0·014 | | 68·1 | | | |

*Reactions at* pH 7.

| $[Cl\cdot CO_2Et]$ (mole l.$^{-1}$) | ArOH | [ArOH] (calc.) | $[ArO^-]$ (calc.) | $10^4k_1$ (min.$^{-1}$) | Mean $10^4k_1$ | $k_2$ (l. mole$^{-1}$ min.$^{-1}$) | Mean $k_2$ |
|---|---|---|---|---|---|---|---|
| 0·0132 | ($H_2O$) | — | — | 16·00 | 15·80 | — | — |
| 0·0132 | ,, | — | — | 15·70 | | | |
| 0·0148 | ,, | — | — | 16·10 | | | |
| 0·0148 | ,, | — | — | 15·40 | | | |
| 0·0108 | PhOH | 0·110 | 1·6 | 102·1 | 101·8 | 49·4 | 49·4 |
| 0·0085 | ,, | 0·110 | | 101·4 | | | |

TABLE 7.

p$K_a$ of *meta*- and *para*-substituted phenols in water–acetone (85 : 15) at 0°.

| [ArOH] (mole l.$^{-1}$) | pH | p$K_a$ | Mean p$K_a$ | [ArOH] (mole l.$^{-1}$) | pH | p$K_a$ | Mean p$K_a$ |
|---|---|---|---|---|---|---|---|
| p-*Cresol* | | | | m-*Nitrophenol* | | | |
| 0·055 | 5·58 | 9·90 | 9·89 | 0·032 | 4·89 | 8·29 | 8·33 |
| 0·028 | 5·73 | 9·91 | | 0·016 | 5·09 | 8·38 | |
| 0·014 | 5·86 | 9·86 | | 0·008 | 5·21 | 8·32 | |
| *Phenol* | | | | p-*Nitrophenol* | | | |
| 0·044 | 5·59 | 9·82 | 9·80 | 0·046 | 4·20 | 7·06 | 7·00 |
| 0·022 | 5·72 | 9·77 | | 0·023 | 4·32 | 7·01 | |
| 0·011 | 5·89 | 9·82 | | 0·012 | 4·42 | 6·92 | |
| p-*Chlorophenol* | | | | | | | |
| 0·047 | 5·28 | 9·23 | 9·25 | | | | |
| 0·024 | 5·42 | 9·22 | | | | | |
| 0·012 | 5·61 | 9·29 | | | | | |

The mixture, when cool, was extracted with ether (5 × 100 ml.). The extracts were dried ($MgSO_4$) and evaporated to a residue (5·2 g.) which gave 3 peaks on the vapour-phase chromatograph. Distillation through a spinning-band column gave fractions (I) (0·4 g.), b. p. 115—116°/14 mm., (II) (0·4 g.), b. p. 116—141°/14 mm., (III) (4·1 g.), b. p. 141—143°/14 mm. Fraction (I) gave only one peak on vapour-phase chromatography and had the same retention time as trimethylene glycol. Benzoylation gave crystals, m. p. 56—57° (lit., m. p. 57—57·5°). Fraction (II) gave 3 peaks, corresponding respectively to trimethylene glycol, the oxidation product of phenol (proved by repeating the reaction in the absence of 3-bromopropanol), and fraction (III). Fraction (III) gave only one peak; its infrared spectrum showed a strong hydroxyl and aromatic ether (8·13 $\mu$) absorption; the b. p. corresponds to that of 3-hydroxypropyl phenyl ether (lit.,[17] 160°/25 mm.); $n_D^{20}$ 1·5295 (lit., $n_D^{20}$ 1·5293). It gave the 3,5-dinitrobenzoate m. p. 100—101°, having no infrared hydroxyl adsorption [Found: *M*, 340·2 (by saponification). Calc. for $C_{16}H_{14}N_2O_7$: *M*, 346].

The aqueous solution remaining after the ether-extraction was acidified and extracted 5 times with ether. These ethereal solutions were dried ($MgSO_4$) and evaporated, giving a solid. A benzene solution gave one peak only with the same retention time as that of phenol, and an infrared spectrum identical with that of phenol. The *p*-nitrobenzoate obtained directly from the solid had m. p. 126·5—127·5°, and after recrystallisation, m. p. 127—128° (lit., m. p. 127°).

(b) 3-*Bromopropanol and* p-*nitrophenol.* A solution of *p*-nitrophenol (14 g.) in water (1 l.) at pH 9·5 was allowed to react with 3-bromopropanol (5 g.) as described above. Ether-extraction was carried out in the same way, the ethereal solution was washed twice with sodium hydroxide solution, and the washings were added to the aqueous solution remaining after the ether-extraction The ethereal solution was dried ($MgSO_4$), and evaporated Distillation of the residue (5·3 g.) gave trimethylene glycol (2·0 g.), b. p. 114—115°/14 mm. (dibenzoate, m. p. 57—58°). Further distillation gave at 165—167°/0·2 mm. 3-hydroxypropyl *p*-nitrophenyl ether (3·0 g.), m. p. 48·5—50° (lit.,[18] m. p. 48—49°). It was only sparingly soluble in sodium hydroxide solution, showing the absence of a phenolic group, and the solution was colourless. The infrared spectrum showed a strong absorption hydroxyl and aromatic ether (8·02 $\mu$) [Found: N (Kjeldahl), 7·0. Calc. for $C_9H_{11}NO_4$: N, 7·1%]. Treatment of the solid with constant-boiling hydriodic acid gave *p*-nitrophenol, characterised by the infrared spectrum.

The aqueous solution and washings were acidified and extracted with ether (2 × 100 ml.). The extract was dried ($MgSO_4$) and evaporated, leaving *p*-nitrophenol, m. p. and mixed m. p. 113·5—115°. A solution of it in ether gave only one peak, with the correct retention time. The infrared spectrum was also correct. The acetate had m. p. 82—83° (lit., 81—82°).

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