

### 344. Alkylation of Phenoxide Ions

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Rates of alkylation of a series of *meta*- and *para*-substituted sodium phenoxides have been measured in azeotropic ethanol using methyl iodide (at 35.1°) and ethyl or isopropyl iodide (45°) as substrates. There are slight differences in the electron demand and in the extent of resonance interaction in the transition state with the different alkyl iodides.

THE Hammett equation<sup>1</sup> is an inductive-effect relationship and differences in the extent of resonance interaction in going from reactant to transition (or final) state are a major cause of deviation from the precise linear correlation.<sup>2</sup> For a particular reaction series such differences, which are properly measured not by the exaltation of the substituent constants ( $\bar{\sigma} - \sigma$ ), but rather by the free-energy term<sup>3</sup>  $2.3 RT\rho(\bar{\sigma} - \sigma^0)$ , provide useful information about the electron distribution in the transition state.\* Equilibrium protonation of phenoxide ions (dissociation of phenols) was one of the first reactions in which exaltation of substituent constants resulting from resonance effects was observed. Hammett<sup>1</sup> himself cited the anomalous  $\sigma$  value for the *p*-nitro-group, derived from the dissociation constant of *p*-nitrophenol. We now report rates of alkylation of phenoxide ions with methyl, ethyl, and isopropyl iodides. It was anticipated that there would be more resonance interaction between the aryl group and the attached oxygen atom in the transition state of the alkylation than in the corresponding phenol and, as a consequence,

\* Taft's symbolism<sup>2</sup> is followed:  $\bar{\sigma} = 1/\rho (\log k/k_0)$ ;  $\sigma^0$  values are inductive constants and for *meta*-substituted phenyl groups are means of a narrow range of  $\sigma$  values. For *para*-substituted phenyl groups  $\sigma^0$  values are obtained from ionisation of phenylacetic acids and related reactivities.

<sup>1</sup> Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 193.

<sup>2</sup> Taft, *J. Phys. Chem.*, 1960, **64**, 1805.

<sup>3</sup> van Bekkum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.

there would be a smaller decrease in resonance interaction in going from phenoxide ion to transition state than from phenoxide ion to phenol. In addition, any change in the transition state resulting from a change in the alkylating agent was expected to be reflected in changes in  $\rho$  and in the resonance interaction energies.

## EXPERIMENTAL

*Phenols.*—*m*-Cresol, b. p. 64°/0.5 mm., *m*-hydroxyacetophenone, m. p. 95°, *p*-hydroxyacetophenone, m. p. 108°,  $\beta$ -naphthol, m. p. 122°, phenol, m. p. 40.5°, and *m*-bromo-, m. p. 32.5°, *m*-nitro-, m. p. 96°, and *p*-nitro-phenol, m. p. 114°, were commercial products. *p*-Cyanophenol, m. p. 111°, was prepared (cf. ref. 4) from *p*-hydroxybenzaldehyde. *p*-Nitrosophenol, m. p. 139° (decomp.) (Found: C, 58.7; H, 3.7; N, 11.1; O, 26.2. Calc. for C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub>: C, 58.5; H, 4.1; N, 11.4; O, 26.0%) was obtained by nitrosation<sup>5</sup> of phenol.

*Reagents.*—Ethanol (96%) was distilled successively from sulphuric acid and from aqueous sodium hydroxide and finally fractionated. Methyl iodide was washed with water, dilute sodium carbonate, water, dilute sodium thiosulphate, and water. After being dried over calcium chloride and for a short period over phosphorus pentoxide it was distilled twice. The middle fraction, b. p. 43°, was collected and stored over mercury. Ethyl and isopropyl iodides were purified similarly. Sodium ethoxide solution was prepared by dissolving freshly cut sodium in the purified ethanol and was standardised against constant-boiling hydrochloric acid. AnalaR reagents were used for the Volhard titrations.

*Kinetics.*—Reactions with ethyl iodide were carried out in a flask fitted with a side-arm and separate neck. Sodium ethoxide solution (50 ml., 0.1M) was placed in the main bulb and phenol (1% excess) was added. Excess of phenol was used to reduce alcoholysis of the phenoxide. Ethyl iodide solution (50 ml., 1M) was placed in the side-arm and the vessel was immersed in a thermostat-bath at 45.0° ± 0.1°. After temperature equilibrium had been attained (15 min.) the solutions were mixed. At appropriate intervals aliquots (10 ml.) were withdrawn, added to benzene (50 ml.), and the benzene solution extracted with water (2 × 10 ml.). The aqueous extracts were acidified with 6N-nitric acid (5 ml.) and analysed for iodide by the Volhard method. The foregoing procedure proved unsatisfactory for runs with the more volatile methyl iodide which tended to distil from the side-arm into the main bulb during the period allowed for temperature equilibration. For runs with this iodide the reaction mixture was prepared at ambient temperature. Eight aliquots (10 ml.) were pipetted into separate glass vials fitted with polythene caps and the vials placed in a water-bath maintained at 35.1° ± 0.1°. After 15 min., and then at appropriate intervals, the contents of a vial were transferred to a separatory funnel containing benzene (50 ml.) and the iodide extracted and analysed as described above. The two methods gave equivalent results. The second method was also used for reactions involving isopropyl iodide, run at 45.0°.

## RESULTS

Runs were followed to at least 60% reaction and the rate constants were evaluated from second-order rate plots. At least three runs were carried out for each compound and individual rate constants agreed to ± 3%. Mean rate constants are shown in Table I.

TABLE I  
Alkylation of substituted phenoxide ions (0.048M); 10<sup>4</sup> *k* (l. mole<sup>-1</sup> sec.<sup>-1</sup>)

| X = H | At 35.1° with methyl iodide  |                                   |                |                |                |              |                           |                           |                           |
|-------|------------------------------|-----------------------------------|----------------|----------------|----------------|--------------|---------------------------|---------------------------|---------------------------|
|       | <i>m</i> -Me                 | 3,4-C <sub>4</sub> H <sub>4</sub> | <i>m</i> -COMe | <i>p</i> -COMe | <i>p</i> -CN   | <i>p</i> -NO | <i>m</i> -NO <sub>2</sub> | <i>p</i> -NO <sub>2</sub> |                           |
| 5.1   | 6.8                          | 5.8                               | 2.2            | 0.68           | 0.50           | 10           | 0.81                      | 0.22                      |                           |
| H     | At 45° with ethyl iodide     |                                   |                |                |                |              |                           |                           |                           |
|       | <i>m</i> -Me                 | 3,4-C <sub>4</sub> H <sub>4</sub> | <i>m</i> -Br   | <i>m</i> -COMe | <i>p</i> -COMe | <i>p</i> -CN | <i>p</i> -NO              | <i>m</i> -NO <sub>2</sub> | <i>p</i> -NO <sub>2</sub> |
| 5.2   | 7.3                          | 4.5                               | 2.4            | 2.2            | 1.16           | 0.75         | 11                        | 0.90                      | 0.30                      |
| H     | At 45° with isopropyl iodide |                                   |                |                |                |              |                           |                           |                           |
|       | <i>m</i> -Me                 | 3,4-C <sub>4</sub> H <sub>4</sub> | <i>m</i> -COMe | <i>p</i> -COMe | <i>p</i> -CN   | <i>p</i> -NO | <i>m</i> -NO <sub>2</sub> | <i>p</i> -NO <sub>2</sub> |                           |
| 1.61  | 2.2                          | 1.68                              | 0.75           | 0.32           | 0.29           | 2.8          | 0.37                      | 0.151                     |                           |

<sup>4</sup> Culbertson, Carpenter, and Neilsen, *Proc. Iowa Acad. Sci.*, 1930, **37**, 248.

<sup>5</sup> Bridge, *Annalen*, 1893, **85**, 277.

The variation of rate constant with ionic strength (= initial concentration of phenoxide) was investigated for the reaction of sodium *m*-nitrophenoxide with ethyl iodide at 45°. Results are given in Table 2. A plot of  $\log k$  against  $I$  was linear and had slope  $-2.8$  and intercept ( $-\log k$  at  $I = 0$ )  $4.091$  corresponding to  $10^5 k = 12.3$  l. mole<sup>-1</sup> sec.<sup>-1</sup>.

TABLE 2  
Ethylation of *m*-nitrophenoxide at 45°

|                |      |      |     |     |     |     |
|----------------|------|------|-----|-----|-----|-----|
| $10^5 I$ ..... | 1.0  | 1.9  | 2.9 | 4.3 | 5.1 | 7.6 |
| $10^5 k$ ..... | 11.6 | 11.5 | 9.6 | 9.5 | 8.9 | 7.7 |

#### DISCUSSION

Goldsworthy<sup>6</sup> and Benkeser *et al.*<sup>7</sup> measured rates of ethylation of substituted phenoxide ions. In each case the range of substituent constants investigated was too limited to be of use for the purposes of the present investigation. Neither set of results is directly comparable with ours since measurements were made at a different temperature and in absolute ethanol. Segaller<sup>8</sup> studied the effect of variation of temperature and of solvent on the reaction of sodium phenoxide with a series of alkyl halides. If our value for the rate of methylation of sodium phenoxide at 35.1° is corrected to 45° using Segaller's value of the temperature coefficient, the relative rates of alkylation of sodium phenoxide with alkyl iodides are MeI:EtI:PrI, 11:3:1. This is in satisfactory agreement with Segaller's rate ratio, determined under slightly different conditions (absolute ethanol, 42.5°), of 12:3:1. There is conflict as to whether the increased positive inductive effect resulting from increased alkyl substitution on the  $\alpha$ -carbon atom facilitates or retards nucleophilic substitution.<sup>9</sup> It seems likely, however, that increasing steric hindrance to the approach of the nucleophilic phenoxide anion resulting from increasing alkyl substitution makes a major contribution to the observed rate order.<sup>10</sup> The fact that the introduction of both an  $\alpha$ -methyl group and an  $\alpha$ -halogen atom results in a reduction of the S<sub>N</sub>2 reactivity of methyl halides<sup>11</sup> points to the importance of steric-hindrance effects in these systems.

From the regression line fitted to the  $\log k$  against  $\sigma^\circ$  data for the *meta*-substituted and unsubstituted compounds, the reaction constants ( $\rho$ ), correlation coefficients ( $r$ ), and intercepts with the ordinate ( $\log k_0$ ) listed in Table 3 were obtained.

TABLE 3  
Alkylation of phenoxide ions

| Substrate | Temp. | $\rho$ | $r$   | $-\log k_0$ |
|-----------|-------|--------|-------|-------------|
| MeI ..... | 35.1° | -1.172 | 0.999 | 3.263       |
| EtI ..... | 45    | -1.125 | 0.993 | 3.243       |
| PrI ..... | 45    | -0.975 | 0.995 | 3.767       |

The  $\rho$  values are about one third of the magnitude of that for dissociation of phenols in the same solvent (3.141).<sup>3</sup> The implication is that the alkyl-oxygen bond is less than half formed in the transition state. If bond formation were almost complete  $\rho$  would be close to  $-3$ .

For the methylation the value of  $\rho$  corrected to 45° by assuming an inverse temperature dependence,<sup>12</sup> is  $-1.16$ . The decrease in  $\rho$  with increasing alkyl substitution at the  $\alpha$ -carbon is indicative of a concomitant decrease in the difference in charge on the phenoxide oxygen between initial and transition states. Such a result seems reasonable since

<sup>6</sup> Goldsworthy, *J.*, 1926, 1254.

<sup>7</sup> Benkeser, De Boer, Robinson, and Saure, *J. Amer. Chem. Soc.*, 1956, **78**, 682.

<sup>8</sup> Segaller, *J.*, 1913, 1154, 1421; 1914, 106, 112.

<sup>9</sup> Streitwieser, *Chem. Rev.*, 1956, **56**, 587.

<sup>10</sup> de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3200.

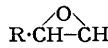
<sup>11</sup> Hine, "Physical Organic Chemistry," McGraw-Hill, New York, 1956, p. 154.

<sup>12</sup> Fischer and Vaughan, *J. Chem. Phys.*, 1957, **27**, 976.

increasing alkyl substitution would tend to make the  $\alpha$ -carbon less positive (or more negative) in the transition state and hence reduce the extent of acceptance of electrons from the nucleophilic oxygen. Thus, increased alkyl substitution results in increased  $S_N1$  character in the transition state.

Effective  $\sigma$  values ( $\bar{\sigma}$ ) and resonance interaction energy differences ( $2.3 RT_p(\bar{\sigma} - \sigma^0)$ ) for *para*-substituted aryl groups are given in Table 4, together with mean values derived from reaction of phenoxides with ethylene and propylene oxides and mean values from dissociation of phenols.<sup>3</sup>

TABLE 4  
 $\bar{\sigma}$  Values for  $p$ -C<sub>6</sub>H<sub>4</sub>X from phenoxide reactions

| Substrate  | MeI  | EtI  | PrI  | RI (mean) | R-CH-CH <sub>2</sub><br> | H <sup>+</sup> |
|--|------|------|------|-----------|--|----------------|
| X = NO <sub>2</sub> .....  | 1.19 | 1.12 | 1.08 | 1.13      | 1.08   | 1.19           |
| X = COMe .....   | 0.77 | 0.61 | 0.74 | 0.71      | —  | 0.80           |
| X = CN .....   | 0.88 | 0.78 | 0.79 | 0.82      | 0.79   | 0.91           |
| Resonance interaction energy differences (kcal. mole <sup>-1</sup> ) |      |      |      |           |  |                |
| X = NO <sub>2</sub> .....  | 0.62 | 0.49 | 0.37 | 0.49      | 0.48   | 1.41           |
| X = COMe .....   | 0.52 | 0.25 | 0.40 | 0.39      | —  | 0.90           |
| X = CN .....   | 0.32 | 0.15 | 0.14 | 0.20      | 0.18   | 0.71           |

The  $\bar{\sigma}$  values for the alkylations are only slightly smaller than those for equilibrium protonation (dissociation). However, the resonance energy differences reveal that *ca.* one third of the additional resonance interaction in the substituted phenoxide is lost in the transition state of the alkylation reaction, a result which confirms the earlier conclusion that the C-O bond is not nearly completely formed in the transition state. The tendency for the resonance terms to decrease with increasing alkyl substitution at the  $\alpha$ -carbon also points to a parallel decrease in the extent of C-O-bond formation in the transition state. The close similarity in the magnitudes of the resonance energy contributions derived from the reactions of phenoxides with alkyl halides and with oxirans implies that C-O bond formation in the transition state of both reactions has progressed to a similar extent.

The mean  $\bar{\sigma}$  value for the *p*-nitrosophenyl group, derived from the alkylations, is  $-0.22$ . Runs with *p*-nitrosophenoxide gave curved plots and there was some masking of the end-points of the Volhard titrations. However, in spite of these complications, which made results for this substituent rather less accurate than the rest, the  $\bar{\sigma}$  value derived from the alkylation is certainly significantly different from the value derived from dissociation of phenols<sup>13</sup> (1.63). *p*-Nitrosophenoxide ion is alkylated about 100 times faster than would be predicted from its dissociation constant. This high rate of alkylation can be attributed to reaction at the nitroso-group. Reaction of nitrosophenoxides with alkylating agents has long been known to give the quinone oxime ether rather than the nitrosophenol ether.<sup>14</sup>

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<sup>13</sup> Fickling, Fischer, Mann, Packer, and Vaughan, *J. Amer. Chem. Soc.*, 1959, **81**, 4226.

<sup>14</sup> Pechmann and Seel, *Ber.*, 1898, **31**, 296; Veibel and Simesen, *ibid.*, 1930, **63**, 2476.