Thermodynamic Acidity Constants of *ortho*-Substituted Benzenethiols

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Thermodynamic acidity constants for a series of *ortho*-substituted benzenethiols have been measured in water at 25 °C by an e.m.f.–spectrophotometric method. Analysis of the substituent effects in terms of free energy relationships suggests that the dominant substituent interaction is electronic. Other minor effects appear to operate for the alkyl, methoxy-, and methylthio-substituents, while intramolecular hydrogen bonding is important for *o*-nitrobenzenethiol.

RECENTLY we have reported thermodynamic acidity constants for a series of *meta*- and *para*-substituted benzenethiols in both water[1] and aqueous methanol[2] at 25 °C. The compounds chosen represented a wide range of substituent effects. We now report the effects of similar substituents upon the thermodynamic acidity constants of *ortho*-substituted benzenethiols and discuss the observed results in terms of free energy relationships. Previously only a few acidity constant data were available[3] for this class of compounds.

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EXPERIMENTAL

The following benzenethiols were synthesized from the appropriate anilines as described in the literature: *o*-methyl-,[4] *o*-methoxy-,[5] *o*-ethoxy-,[6] *o*-chloro-,[7] *o*-bromo-,[8] 2,6-dimethyl-,[9] and *o*-methylthio-.[10] The *o*-nitro-compound [11] was prepared by reduction of the disulphide with glucose in alkaline ethanolic solution. All thiols were purified prior to use, checked by titration,[12] and stored under argon. Only thiols found to be >99% pure were used in the experiments. The solutions of benzenethiols used in the spectrophotometer were flushed with argon to prevent formation of insoluble oxidation products.[1]

Thermodynamic acidity constants, on the molality scale, were calculated from equation (1), where the ratio of

$$\mathrm{p}K_a = \mathrm{p}(a_{\mathrm{H}}\gamma_{\mathrm{Cl}}) - \log(m_{\mathrm{A^-}}/m_{\mathrm{AH}}) \qquad (1)$$

deprotonated to protonated benzenethiol was determined spectrophotometrically in aqueous buffer solution, and the acidity function values, $\mathrm{p}(a_{\mathrm{H}}\gamma_{\mathrm{Cl}})$, of the buffers used, are known [13] with great precision. We have previously shown [1] that the e.m.f. spectrophotometric method provides, for aromatic thiols, an accuracy of $\pm 0{\cdot}005$ pK_a units.

A Beckman model DU manual spectrophotometer thermostatted to 25 ± 0·1 °C was used for absorbance measurements by following the procedure previously described.[1]

For 2,6-dimethylbenzenethiol we have assumed simple additivity of the substituent effect in order to evaluate an appropriate σ_0^-. The pK_a of *o*-nitrobenzenethiol was omitted from our correlation calculations because of its anomalous behaviour. The table lists our pK_a values at 25 °C, together with relevant experimental details.

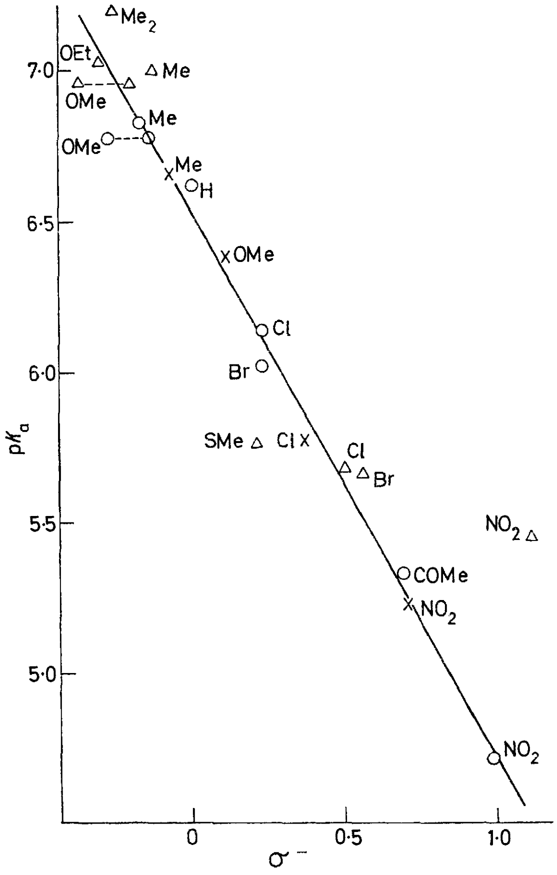
Thermodynamic pK_a values and experimental conditions of measurements. Molality of benzenethiols in all cases *ca.* 10^{-4}

ortho-Substituents	pK_a ±0·005 at 25 °C	Buffer table no.[a]	Ionic strength (molality) of the buffer	λ_{max} of base form (nm)
2,6-Me_2	7·377	11	0·04	261
OEt	7·063	11	0·04	264
Me	6·995	11	0·04	262
OMe	6·890	11	0·04	264
H	6·6151	11	0·04	263
SMe	5·754	10	0·041	271
Cl	5·675	10	0·041	267
Br	5·659	10	0·041	267
NO_2	5·453	10	0·041	261

[a] These numbers refer to the buffer table number of ref. 13.

DISCUSSION

Because the Hammett equation is not considered appropriate to *ortho*-substituents, other correlations [14–17] have been proposed; and of these that by Tribble and Traynham,[17] involving σ_0^- values has been chosen here because their defining system is as close as possible to that under examination. Their σ_0^- values are derived from measurements of chemical shifts of the OH group in *ortho*-substituted phenols in dimethyl sulphoxide and are claimed to represent electronic effects of *ortho*-substituents in the absence of steric effects.



Hammett plot for the thermodynamic acidity constants of substituted thiophenols; △ = *ortho*, × = *meta*, ○ = *para*

A correlation of our pK_a values of the *ortho*-, *meta*-, and *para*-substituted benzenethiols in terms of a combined Hammett assessment is highly linear (see Figure) and our $\rho_{m,p}$ value [1] does not differ, within experimental error, from the present $\rho_{o,m,p}$ value ($-1{\cdot}80$; $r = 0{\cdot}973$). This indicates that acid dissociation in *ortho*-substituted benzenethiols is also essentially governed by electronic effects.

No σ_0^- value has been reported for the *o*-nitro-substituent. A value of 1·20 [17] relates to a different

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solvent[18] but does not fit our present plot. The anomalously high pK_a value of *o*-nitrobenzenethiol is probably due to intramolecular hydrogen bonding. A comparison of the effects of nitro-substituents on benzenethiols and phenols shows that ΔpK_a (*ortho* — *para*) in water is 0·738 units for benzenethiols and only 0·067 units for phenols. Analogous ΔpK_a differences were found in ethanol–water mixtures.[3b] This greater hydrogen bonding ability for benzenethiols can be attributed to the more favourable position[19] and greater acidity of the mercapto-group as compared to the hydroxy-group. This proposal is further supported by the evidence[20] that intramolecular interaction is stronger in *o*-aminobenzenethiol than in *o*-aminophenol.

The non-conformity of the effect of the *ortho*-methoxy-substituent was expected. Its σ_0^- value is questionable because the reference compound is probably not free of residual intramolecular interaction.[17] However, another σ_0^- value, calculated by Tribble and Traynham[17] from previously reported data,[18] gives a much better correlation on our pK_a *vs.* σ^- plot.

It is known[21] that the methoxy-substituent is not free of specific solvent effects which can influence its ability to interact mesomerically with the reaction centre. This could explain the low pK_a value, not only for *o*-methoxy-, but also for *p*-methoxy-benzenethiol. This same explanation could further apply to the methylthio-substituent.

The small positive deviation of the *o*-alkylbenzenethiols can be attributed to steric inhibition of solvation of the anion, for this effect has previously been observed for the bulky *ortho*-t-butyl substituent.[3f]

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