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O–H Bond Strengths and One-electron Reduction Potentials of Multisubstituted Phenols and Phenoxyl Radicals. Predictions Using Free Energy Relationships

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General equations for the empirical determination of relative O–H bond strengths and one-electron reduction potentials of multisubstituted phenols and phenoxyl radicals are derived. The derivations are based on data from direct and indirect measurements of phenolic O–H bond strengths, and one-electron reduction potential measurements using electrochemical and radiation chemical methods. The resulting equations are $\Delta D(\text{O–H}) = -1.97 + 29.87\ \Sigma\sigma^+$ (kJ mol)$^{-1}$ and $E^\circ = 0.79 + 0.34\ \Sigma\sigma^+$ (V *vs.* NHE) where $\Sigma\sigma^+$ is the sum of the Brown substituent values ($\sigma_o{}^+ = 0.66\ \sigma_p{}^+$, $\sigma_m{}^+$ and $\sigma_p{}^+$). The conditional relationship $\sigma_o{}^+ = 0.66\ \sigma_p{}^+$ is also derived in this work.

The antioxidant activity of substituted phenols can be ascribed to the relatively low bond dissociation enthalpy of the O–H bond. Recently, values of the latter have been measured for a few *para*-substituted phenols in benzene by means of a direct calorimetric method, photoacoustic spectroscopy.[1] Measurements of one-electron reduction potentials have been carried out employing radiation chemical[2] or electrochemical[3] methods. When combined with the corresponding phenolic acidities, bond strengths were derived according to eqn. (1)

$$D(\text{O–H}) = 96.48\ E^\circ + 5.703\ \text{p}K_a + C \quad (\text{kJ mol}^{-1}) \qquad (1)$$

where C depends on the solvent but not on the substituent. Eqn. (1) follows from thermochemical cycles, and these have been described in ref. 4 as well as in a series of papers by Bordwell *et al.*[5–7] Underlying eqn. (1) is the assumption that ΔS°_1 and the difference in solvation between phenol and phenoxyl radical are almost unaffected by the substituent. The similar response to substituents of directly[1] or indirectly[2,3] determined relative bond dissociation energies substantiates this assumption.

Substituent effects on O–H bond strengths and reduction potentials have been found to follow linear relationships for 4-substituted phenols[1–3] and phenoxyl radicals.[2,3]

The question of whether the effects of multiple substitution of phenols and phenoxyl radicals are additive or not has never been satisfactorily answered, although some attempts to find constants for *ortho* and *meta* substituents[8] have been made.

To the best of our knowledge no general equation for calculating relative O–H bond strengths for multisubstituted phenols has been published. In this work we present general equations for predictions of O–H bond strengths and one-electron reduction potentials for multisubstituted phenols and phenoxyl radicals based on the experimental results of refs. 1–3 and 8–12.

Brown σ^+ values are used throughout this work since they seem to best reflect the effects of substituents on bond strengths.

Results and Discussion

The pK_as and the one-electron reduction potentials are linearly transferable between DMSO and water, thus making it possible to compare data obtained in the different solvents.

In order to determine *ortho*, *meta* and *para* (Fig. 1) substituent effects independently we plotted relative O–H bond strength[1,2,3] versus σ_p^+[13] for *ortho* and *para* substituted phenols and *versus* σ_m^+[14] for *meta* substituted phenols.

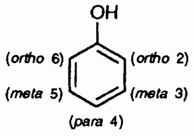

Fig. 1

Linear relationships were found for all three cases following eqn. (2) for *ortho* substitution, eqn. (3) for *meta* substitution and eqn. (4) for *para* substitution (kJ mol^{-1}).

$$\Delta D(\text{O–H}) = -1.38 + 18.87\,\sigma_p^+;\ R^2 = 0.98 \qquad (2)$$

$$\Delta D(\text{O–H}) = -0.75 + 28.33\,\sigma_m^+;\ R^2 = 0.97 \qquad (3)$$

$$\Delta D(\text{O–H}) = -1.34 + 30.67\,\sigma_p^+;\ R^2 = 0.96 \qquad (4)$$

A linear correlation between *ortho* and *para* substituent effects on phenols has previously been reported.[15] However, voluminous substituents deviated from this correlation.[16] We therefore exclude 2-*tert*-butyl and 2,6-di-*tert*-butyl substituted phenols from the following treatment. The factor by which σ_p^+ must be multiplied in order to get a value for σ_o^+ is derived from a comparison of *ortho* and *para* effects on O–H bond strengths[2,3] of phenols and on one-electron reduction potentials of phenoxyl radicals.[2,9] Since we aim to derive an empirical relationship, we simply take the factor as the mean of the ratios between *ortho* and *para* effects, excluding ratios for substituents with σ_p^+ values close to zero. This gives us a conditional σ_o^+ scale for phenols which is characterized by eqn. (5). As an example of a

$$\sigma_o^+ = 0.66\,\sigma_p^+ \qquad (5)$$

conditional σ_o^+ value we take the value for MeO which we calculate to be -0.52. We note that this figure differs significantly from -0.67, the corresponding value found in the literature.[17] Almost the same value, -0.53, was calculated when only *ortho* effects of six different *ortho*-MeO substituted phenols were taken into account.[9] In Fig. 2 we plot the O–H bond strength[1,2,3] *versus* the sum of substituent constants (denoted $\Sigma\sigma^+$) and from the equation of the resulting least squares fit we obtain the general equation (6). When combined with eqn. (1)

$$\Delta D(\text{O–H}) = -2.0 + 29.9\,(\sigma_{o2}^+ + \sigma_{m3}^+ + \sigma_{p4}^+ + \sigma_{m5}^+ + \sigma_{o6}^+) \quad (\text{kJ mol});\ R^2 = 0.96 \qquad (6)$$

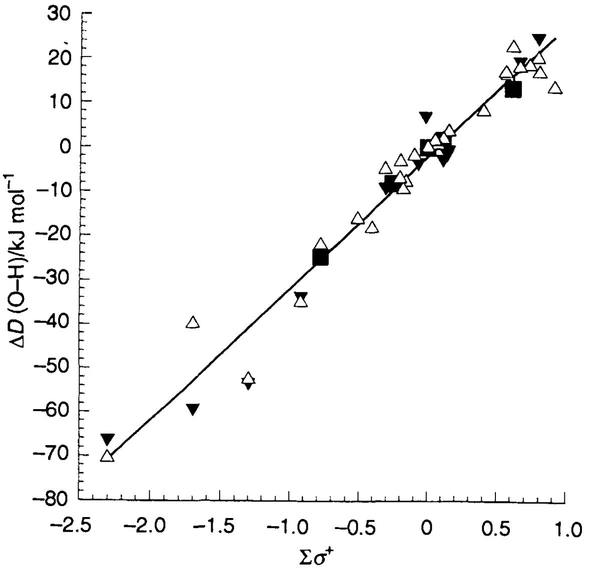

Fig. 2

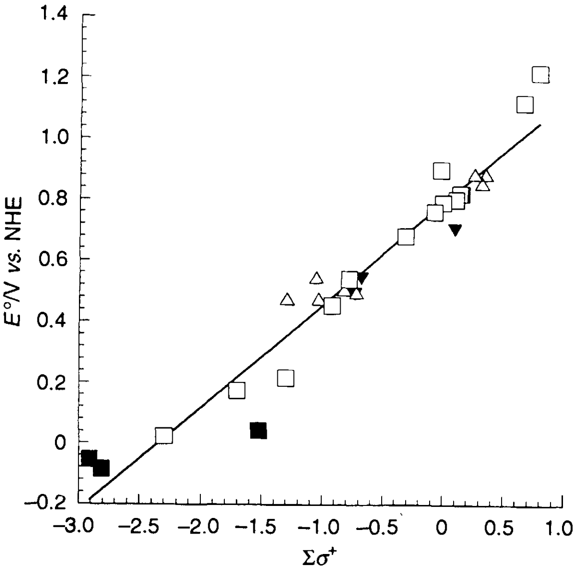

Fig. 3

and if the pK_a of the corresponding phenol is known, eqn. (6) can be used to calculate the one-electron reduction potential of phenoxyl radicals. An equation for predicting one-electron reduction potentials in a given solvent can, of course, also be derived directly from experimental data.

In Fig. 3 we plot the one-electron reduction potentials[2,8-11,18] in aqueous solution for mono- and multi-substituted phenoxyl radicals against the sum of the substituent constants (denoted $\Sigma\sigma^{+}$). The resulting general equation [eqn. (7)] can

$$E^{\circ} = 0.79 + 0.34(\sigma_{o2}^{+} + \sigma_{m3}^{+} + \sigma_{p4}^{+} + \sigma_{m5}^{+}\ {}^{+}+ \sigma_{o5}^{+}) \quad (\text{V } vs. \text{ NHE});\ R^2 = 0.94 \qquad (7)$$

thus be used to predict phenoxyl radical reduction potentials in aqueous solution. When studying the kinetics of hydrogen abstraction reactions, *e.g.* in the context of antioxidant activity, eqn. (6) should be used, the more so since the relative O–H bond strength is essentially invariant with the solvent. Obviously, by the same token, eqn. (7) is of a more limited usefulness. However, for estimations of rate constants for outer-sphere electron transfer reactions involving phenolates or phenoxyl radicals eqn. (7) combined with the Marcus equation can be very useful. Thus, for example, in ref. 19 it was shown that the rate constant of the reaction between molecular oxygen and variously substituted phenolate anions was uniquely predicted by the Marcus equation with the one-electron oxidation potential of the phenolate as the parameter. The effects of multiple-substitution are treated as being additive in the derivation of eqns. (6) and (7), *i.e.* the effects of all substituents are superimposable. For phenols and phenoxyl radicals this assumption seems to be correct within experimental error. However, in ref. 20 the general equation (8) for prediction of

$$E^{\circ} = 2.2 + 0.8\,(\sigma_{p1}^{+} + \sigma_{p4}^{+}) + 0.4\sigma_{p1}^{+}\sigma_{p4}^{+} \qquad (8)$$

one-electron reduction potentials of 1,4-substituted benzene radical cations is given. This empirical equation was derived taking experimental and estimated values of one-electron reduction potentials for a number of 1,4-substituted benzene radical cations into account. As can be seen the equation contains a cross-interaction constant[21] of 0.4, indicating that additivity cannot be taken for granted in general.

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