

Acid-catalysed Aromatisation of Benzene *cis*-1,2-dihydrodiols: a Carbocation Transition State poorly stabilised by Resonance

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Acid-catalysed dehydration of 3-substituted benzene *cis*-1,2-dihydrodiols exhibits a Hammett plot with $\rho = -8.2$, consistent with reaction *via* a benzenonium ion-like intermediate; however, correlation of +M resonance substituents such as Me and MeO by σ_p rather than σ^+ constants indicates a marked imbalance between resonance and inductive stabilisation of the transition state.

Development of microbial methods for oxidation of aromatic hydrocarbons has made available an extensive range of arene dihydrodiols.¹ In the presence of acids these diols undergo dehydration and aromatisation to form phenols.² Here we describe the influence of structure upon reactivity for dehydration of a series of previously prepared³ and new (X = PhS, PhSO and PhSO₂) monosubstituted benzene *cis*-1,2-dihydrodiols **1**.

Earlier studies,² and analogy with similar reactions of arene oxides and arene hydrates,^{4,5} suggest that the rate-determining step in the dehydration reaction is generation of a carbocation intermediate **2** as shown in Scheme 1. This may be followed either by a hydride (NIH) shift to form a cyclohexadienone, which tautomerises to the phenolic product,⁶ or by direct formation of the phenol *via* deprotonation of the carbocation.

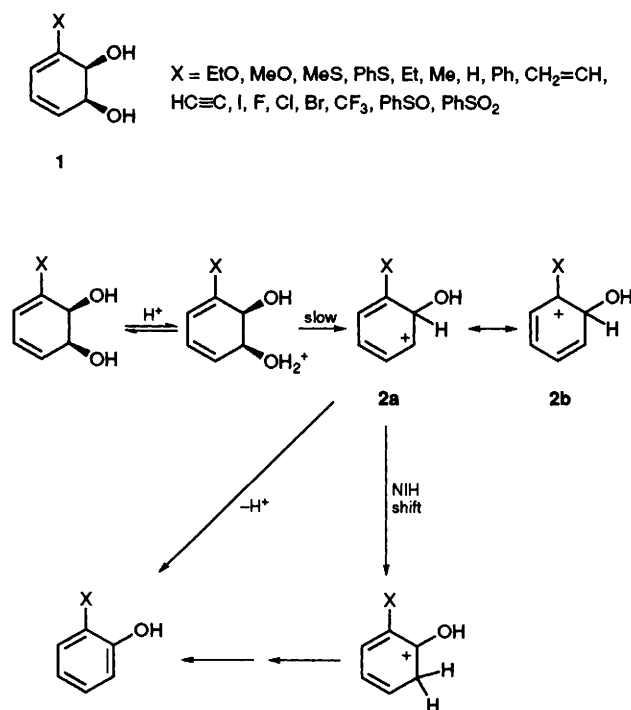
Depending on the substituent, aromatisation of the benzene dihydrodiols occurs smoothly in dilute or concentrated solutions of aqueous acid. The reaction is conveniently monitored spectrophotometrically and reaction rates show a first-order dependence upon H⁺ and substrate concentrations. For the least reactive diols rate constants have to be extrapolated from strongly acidic media based on their correlation with the X-acidity function,⁷ but methoxy, ethoxy and methylthio

substituted diols react in acetic acid buffers (without buffer catalysis). The overall variation in reactivities is greater than 10⁷-fold.

Rate constants, together with proportions of *o*- and *m*-phenol products determined by GCMS, are shown in Table 1. In most cases the *o*-phenol predominates. Only for the strongly electron-withdrawing substituent CF₃ is a substantial amount of the *m*-isomer found.

From Scheme 1 it can be seen that the carbocation **2** is structurally related to a benzenonium ion intermediate of electrophilic aromatic substitution. It is stabilised by +M resonance substituents (*cf.* resonance structure **2b**) which should lead to *o*-product. For electronegative substituents analogy with *m*-directing effects in aromatic substitution suggests that the carbocation **3** should be favoured over **2** because it has no valence bond resonance structure with a positive charge next to the X-substituent. The product is then a *m*-phenol. Interestingly, halogens decrease the rate of dehydration but favour product formation from the resonance-stabilised carbocation **2**. This is consistent with their role in electrophilic aromatic substitution as deactivating but *o*- and *p*-directing substituents. However the strongly electron withdrawing phenyl sulfonyl substituent (PhSO₂) which lacks a lone pair also yields mainly *o*-product.

Fig. 1 shows a Hammett plot for the dehydration reaction leading to *o*-phenols. The rate constants plotted are measured



Scheme 1

Table 1 Rate constants for acid-catalysed aromatisation of 3-substituted benzene *cis*-1,2-dihydrodiols **1** in HClO₄ (aq) at 25 °C

Substituent	10 ² <i>k</i> / dm ³ mol ⁻¹ s ⁻¹	<i>o</i> -Phenol (%) ^a	σ _p	σ _p ⁺
EtO	1250	91	-0.24	-0.82
MeO	1110	99	-0.268	-0.78
MeS	200	>98	0.0	-0.60
Et	149	>98	-0.15	-0.30
Me	152	98	-0.12	-0.31
PhS	45	>98	0.13	-0.45
H	11	— ^b	0	0
Ph	4.5	70	0.05	-0.18
CH ₂ =CH	2.6	79	-0.08	—
F	0.64	91	0.062	-0.07
HC≡C	0.32	91	0.23	0.18
I	0.31	— ^c	0.18	0.14
Cl	0.26	99	0.227	0.11
Br	0.16	94	0.232	0.15
CF ₃	0.0033	9	0.54	0.53
PhSO	0.0019	78	0.46	0.50
PhSO ₂	0.00043	77	0.70	0.70

^a Measured by GC-MS analysis of reaction products at 0.1 or 0.5 mol dm⁻³ HCl, except for less reactive substrates where higher acid concentrations were used. ^b Rate constant statistically corrected for the presence of two equivalent hydroxy groups. ^c Taken as 90.

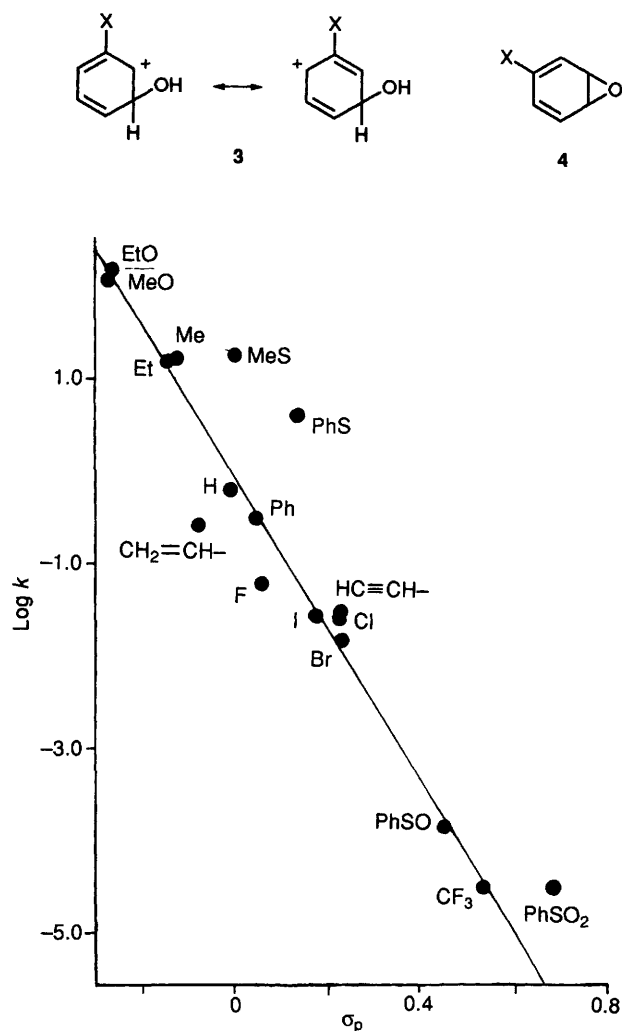


Fig. 1 Plot of $\log k$ vs. σ_p for the dehydration of 3-substituted benzene *cis*-1,2-dihydrodiols in aqueous HClO_4 at 25 °C

values multiplied by the fraction of *o*-product obtained. By analogy again with electrophilic aromatic substitution one expects a large negative ρ and that +M resonance substituents will show enhanced reactivity correlated by σ^+ constants.

In practice the best straight line through the points gives $\rho = -8.2$, which compares with ρ s in the range -2.5 to -12 for electrophilic aromatic substitution.⁸ Remarkably, however the plot is based not on σ^+ constants but on σ_p (from the ionisation of substituted benzoic acids). Even the strongly electron donating methoxy and ethoxy substituents are correlated by σ_p , despite the fact that for $\rho = -8.2$ they are nearly 10,000-fold less reactive than expected on the basis of their σ^+ values.[†] Closer inspection of Fig. 1 reveals a significant dispersion of +M substituents. Thus, fluoro and vinyl deviate negatively while the more polarisable methylthio and phenylthio show positive deviations. Nevertheless the small amount of resonance is confirmed by the value of $r = 0.3$ ($\rho = -7.0$) from application of the Yukawa-Tsuno equation⁹ $\{\log k_X/k_H = \rho[\sigma^0 + r(\sigma^+ - \sigma^0)]\}$.

The most likely explanation of the weak influence of resonance is that there is an imbalance in the development of resonance and inductive effects at the transition state.¹⁰ In electrophilic aromatic substitution attack of OH^+ to form the benzenonium ion **2** would allow direct development of positive charge adjacent to the substituent in the transition state (as in **2b**). However, in the present reaction the charge is developed at a ring carbon remote from the substituent and efficient π -electron interaction requires that five carbon atoms of the benzenonium ion ring lie in a plane (cf. **2a**). Since there

should be no geometric restriction on inductive effects, lack of planarity would imply a 'lag' in the development of resonance effects at the transition state. In the intermediate relaxation of the structure allows the charge to be localised mainly on the substituent and greater resonance stabilisation becomes possible.

Interestingly, in acid-catalysed ring-opening of 4-substituted benzene oxides **4** to form *p*-substituted phenols Bruice and Kasperek¹¹ found a similarly large negative ρ (-7.2), but that the rate constants are correlated by σ^+ . Although the only +M substituent used was methyl, this result is consistent with a more efficient relay of resonance in a transition state where planarity of only three ring carbon atoms linking the positive charge and substituent is required.

In conclusion the utility of the structure-reactivity relationship in Fig. 1 for predicting the stability of benzene dihydrodiols as a function of pH may be noted. This is pertinent to their survival under conditions of enzyme-catalysed formation and isolation and of reactions leading to further functionalisation such as peracid oxidation to epoxides or (for thio substituents) *S*-oxides. Had resonance effects in their aromatisation reactions been larger it is doubtful whether the highly reactive alkoxybenzene dihydrodiols could have been isolated.

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Footnote

[†] In practice use of σ^+ leads to a smaller ρ and thus smaller deviations.

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