

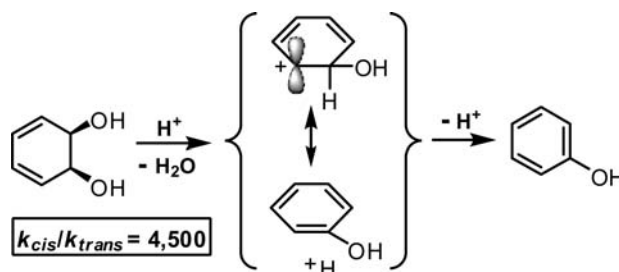
Hyperaromatic Stabilization of Arenium Ions

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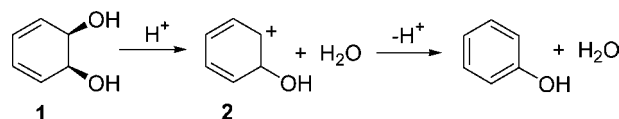
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ABSTRACT



Benzene-*cis*- and *trans*-1,2-dihydrodiols undergo acid-catalyzed dehydration at remarkably different rates: $k_{cis}/k_{trans} = 4500$. This is explained by formation of a β -hydroxycarbocation intermediate in different initial conformations, one of which is stabilized by hyperconjugation amplified by an aromatic no-bond resonance structure ($\text{HOC}_6\text{H}_6^+ \leftrightarrow \text{HOC}_6\text{H}_5 \text{H}^+$). MP2 calculations and an unfavorable effect of benzoannulation on benzenium ion stability, implied by $\text{p}K_{\text{a}}$ measurements of -2.3 , -8.0 , and -11.9 for benzenium, 1-naphthalenium, and 9-phenanthrenium ions, respectively, support the explanation.

Arene-*cis*-1,2-dihydrodiols are products of bacterial oxidation of aromatic molecules by microorganisms such as *Pseudomonas putida* containing dioxygenase enzymes.¹ A characteristic reaction they undergo is acid-catalyzed dehydration to form phenol as illustrated for benzene-*cis*-1,2-dihydrodiol **1** in Scheme 1.² The mechanism of this reaction is similar to that of the dehydration of alcohols, with initial formation of a carbocation (arenium ion) intermediate **2**. However, in contrast to most alcohols, the rate-determining step is formation rather than reaction of the carbocation. This is because loss of a proton to form an aromatic product or the alternative hydride rearrangement (NIH shift)³ are both rapid reactions.

Scheme 1. Dehydration of *cis*-Benzene-1,2-dihydrodiol

The *trans*-isomers of arene dihydrodiols are not accessible by bacterial oxidation, but they are accessible by synthesis.⁴ Comparison of rate constants for the 1,2-dihydrodiols of benzene shows that the *cis*-isomer is 4500 times as reactive as the *trans*. This is a surprising result because one expects the two isomers to react via a common carbocation intermediate (**2**) and to do so at similar rates. Thus, it is unlikely

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that a greater stability of the *trans* than *cis* reactant can account for more than a factor of 2 or 3 in the observed difference in reactivity.^{5,6}

Remarkably, the magnitude of the rate difference depends on the aromaticity of the ring formed in the dehydration product. Values of k_{cis}/k_{trans} for *vic*-dihydrodiols of benzene, naphthalene, and phenanthrene are compared in Figure 1, and it can be seen

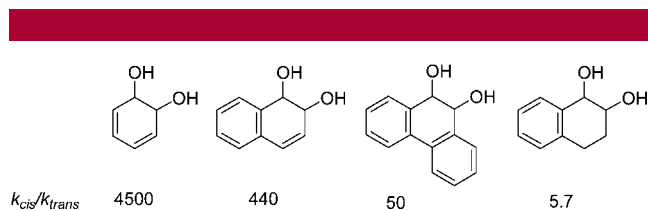


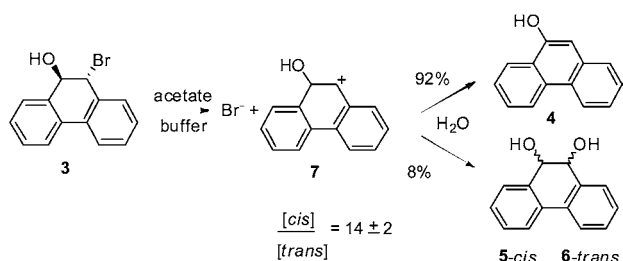
Figure 1. *Cis/trans* reactivity ratios for arene dihydrodiols.

that this ratio decreases to 440 for the naphthalene-1,2-dihydrodiols and to 50 for the phenanthrene-9,10-dihydrodiols. For the dihydrodiol of the nonaromatic double bond of 3,4-dihydronaphthalene, k_{cis}/k_{trans} drops to 5.7 (of which a factor of 1.5 stems from the difference in stabilities of the *cis* and *trans* reactants). The ratios are not appreciably affected by replacement of hydroxy by methoxy groups.⁶

Nucleophilic Trapping of β -Hydroxycarbocations. A corollary of these results is that generating an arenium ion independently and trapping it with water to give dihydrodiols in the back reaction should yield a much higher proportion of the *cis*-dihydrodiol than its more stable *trans* isomer.

Generation of arenium ions derived from benzene or naphthalene 1,2-dihydrodiols leads almost exclusively to aromatic products. However, as shown in Scheme 2, aqueous

Scheme 2. Aqueous Solvolysis of Phenanthrene Bromohydrin



solvolysis of phenanthrene-9,10-bromohydrin **3** forms 8% of 9,10-dihydrodiols in addition to the predominant 9-hydroxyphenanthrene **4**. The ratio of *cis*- to *trans*-dihydrodiols (**5** and **6**) was found to be 14 ± 2 (Table S1, Supporting Information (SI)).

This measurement confirms that trapping of the 9-hydroxyphenanthrenium ion **7** leads to predominant formation of the

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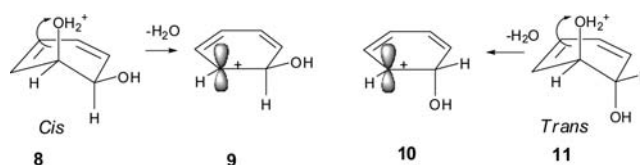
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less stable *cis* product (Scheme 2). The *cis/trans* ratio of **14** is significantly lower than $k_{cis}/k_{trans} = 50$ for carbocation formation. This would imply $50/14 = 3.6$ as the ratio of stabilities of *trans* and *cis* reactants. This ratio seems a little large, but it is difficult to exclude formation of some *trans* product from reaction of an epoxide intermediate,^{6,7} and generation of the carbocation from solvolysis of the monochloroacetate ester of the phenanthrene-9,10-*cis*-dihydrodiol (**5-cis**) led to no detectable fraction of *trans*-dihydrodiol, implying a *cis/trans* ratio >20 for this reactant (Table S2, SI).

The implication of these results is that, in the case of phenanthrene, the ratio of *cis* to *trans* products substantially matches the rate constant ratio for reaction of the *cis*- and *trans*-dihydrodiols (allowing for their difference in thermodynamic stabilities). This strongly suggests that the same would be true of the much higher rate ratios in the case of benzene and naphthalene (4500 and 440) if their carbocations could be similarly trapped. Direct measurements for carbocations derived from dihydrodiols of nonaromatic double bonds, such as dihydronaphthalene, consistently give small trapping ratios favoring the *cis* product. This was demonstrated for the 1,2-dihydrodiols of 6-methoxy-1,2-dihydronaphthalene and 5-methoxyindene by Whalen.⁵

Hyperconjugation. What is the explanation of this behavior? We believe it lies in the formation of different initial conformations of carbocations from *cis*- and *trans*-dihydrodiol precursors. For example, from the *cis*-isomer of (*O*-protonated) benzene-1,2-dihydrodiol **8**, a carbocation is formed with a conformation **9** in which a pseudoaxial β -C–H bond is optimally aligned for hyperconjugation with a p-orbital of the carbocation. In this conformer, the β -OH group is in a pseudoequatorial position. For carbocation formation from the *trans*-benzene dihydrodiol (**11**) we suppose that the positions of the β -OH and H are reversed and that hyperconjugation of a C–OH bond in the resultant carbocation **10** is much less favorable than that of a C–H bond. The differentiation depends on the protonated hydroxyl leaving group (OH_2^+) departing from a pseudoaxial position in the diol reactant. This is an expected constraint arising from the requirement of efficient overlap of the developing p-orbital of the carbocation with the π -bonds or benzene rings of the arenium ion intermediate.⁸ It implies that the *trans*-1,2-dihydrodiol **11** will react from its diaxial rather than diequatorial conformation (Scheme 3).

Scheme 3. Conformations of the β -Hydroxybenzenium Ion



If the stabilization of the carbocation arises from more favorable C–H than C–OH hyperconjugation, why should this depend on the stability of the π -bond formed in the

product, which should have no influence on the stabilities of either the dihydrodiol reactants or the arenium ion intermediates? A simple explanation is that it depends on the stability of the valence bond structures associated with hyperconjugation treated as “no-bond resonance”. As illustrated for the β -hydroxybenzenium ion **2a** in Figure 2,

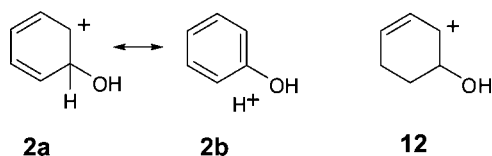


Figure 2. “No-bond resonance” of the 2-hydroxybenzenium ion **2**; cyclo-2-hydroxycyclohexen-5,6-yl cation **12**.

the contributing no-bond valence structure **2b** includes a benzene (phenol) ring. It is thus understandable that the stereochemical constraint (implied by the *cis/trans* rate ratio) tracks the aromatic stabilization of the final product because this mirrors the structure contributing to the resonance.

The supposed order of stabilities of different conformations of arenium ions is reproduced by MP2 calculations (6-311+G** or 6-31G*) summarized in Table S5 (SI). In practice, only one conformation corresponding to a minimum energy, in which the β -C–H bond is pseudoaxial (as in **9**), is identified by the calculations. However, constraining dihedral angles to give a structure close to that in which a β -OH group rather than a β -H atom occupies a pseudoaxial position (as in **10**) increases the energy by 8.8, 6.0, and 4.3 kcal mol⁻¹, respectively, for benzenium, 1-naphthalenium, and 9-phenanthrenium ions bearing a hydroxyl group β to the carbocation center. For the cation **12** derived from reaction of the dihydrodiol of 1,3-cyclohexadiene, the difference is 0.4 kcal. Comparison of hyperconjugating groups gives the expected order of stabilization H₃Si > H > CH₃ > OH > F.⁶ An independent estimate of magnetic ring currents⁹ suggests a value for the benzenium ion close to half that for benzene.¹⁰

The above energy differences imply that the transition states and carbocation conformations (e.g., **10**) formed from the arene-*trans*-dihydrodiols are exceptionally unstable. This is confirmed and the alternative possibility that the *cis*-conformation is unusually reactive ruled out, by a Taft correlation for dehydration of 2-substituted 1,2-dihydro-1-naphthols **13** shown in Figure 3. The filled circles refer to *cis*-substituents, and these form a good correlation ($\rho_1 = 8.8$) with small but distinct deviations for hydroxy and methoxy groups. The open circles represent *trans*-hydroxy and -methoxy groups, and these show pronounced negative deviations consistent with the interpretation offered above.

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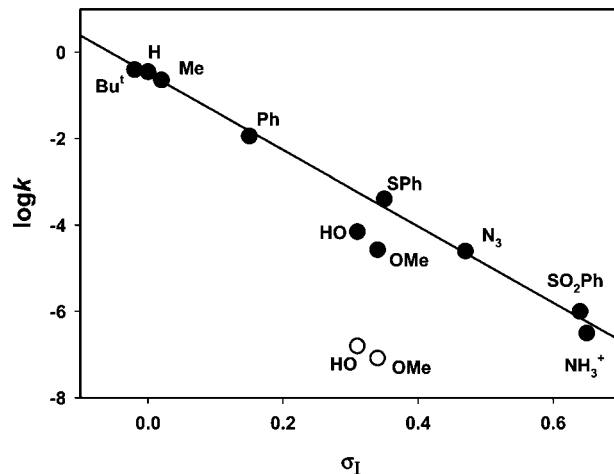
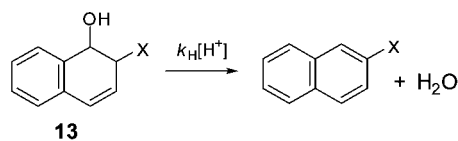


Figure 3. Taft plot of $\log k$ versus σ_1 ($\log k = -0.49 - 8.84\sigma_1$) for the acid-catalyzed dehydration of *cis* (filled circles) and *trans* (open circles) 2-substituted 1,2-dihydro-1-naphthols in aqueous solution at 25 °C; rate constants are listed in Table S4 (SI).

For clarity, other *trans*-substituents are not included in the figure. For 2-alkyl and 2-aryl substituents, the *trans* isomer is less reactive than the *cis*, but the ratios of rate constants are much smaller than for OH or OMe (Me, 8.4; Bu', 12.7; Ph, 3.8). This is consistent with the groups exerting a stabilizing hyperconjugative effect which, however, is less than that of hydrogen. Other *trans*-substituents such as EtS, PhS, and N₃ show positive deviations consistent with neighboring group participation. Only protonated 2-amino substituents exhibit *cis/trans* rate ratios comparable to (and perhaps surprisingly smaller than) OH or OMe; e.g., for NH₃⁺, $k_{cis}/k_{trans} = 315$.⁶

Evidence for “aromaticity-enhanced” stabilization of arenium ions by hyperconjugation is not confined to stereochemical comparisons. It comes also from measurements of thermodynamic stabilities. These stabilities are conveniently expressed by the equilibrium constant K_R , which relates the stability of an ion (ArH⁺) to that of its formal hydrolysis product (ArHOH) as shown in eqs 1 and 2.



$$K_R = \frac{[\text{ArHOH}][\text{H}^+]}{[\text{ArH}^+]} \quad (2)$$

Values of $\text{p}K_R$ ($-\log K_R$) for the benzenium, 1-naphthalenium, and 9-phenanthrenium ions are shown under the relevant structures in Figure 4. It is apparent that $\text{p}K_R$ decreases along the series from -2.3 to -8.0 to -11.6 .¹¹ This implies a decrease in stability of nearly ten powers of ten in going from protonated benzene to protonated phenanthrene.

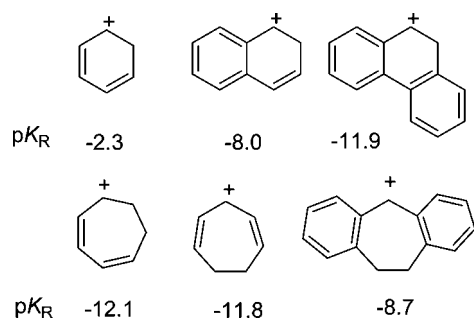


Figure 4. Influence of benzoannellation on carbocation stability (cycloheptadienyl charges indicate sites of reaction with water).

This might not seem remarkable. However, solvolysis of substrates yielding benzylic carbocations normally occurs more readily than that of those yielding structurally comparable allylic cations.¹² This difference in reactivity is opposite to that expected from the effect of benzoannellation on the stability of the benzenium ion.

The unusual stability of the benzenium ion is confirmed by comparison with the cycloheptadienyl cation in Figure 4.⁶ The difference in pK_R for these two ions, -2.3 and -12.1 , seems too large to be accounted for by a difference in strain energies but is consistent with a difference of aromatic from nonaromatic hyperconjugation. Moreover, as indicated by the inferred values of pK_R above,¹³ for the cycloheptadienyl cation benzoannellation does increase its stability (pK_R decreases from -11.8 to -8.7).

Electrophilic Aromatic Substitution. The benzenium ion (cyclohexadienyl cation, protonated benzene) is the parent Wheland intermediate of electrophilic aromatic substitution and is itself implicated in aromatic hydrogen isotope exchange.¹⁴ Stabilization of this ion by hyperconjugation associated with significant aromatic character was originally envisaged by Mulliken in 1953.¹⁵ Perhaps because the magnitude of this stabilization was later thought to be overestimated,¹⁶ and certainly because experimental implications were lacking or overlooked, the notion remained largely dormant for 40 years. There is no mention of it in Dewar's monograph on hyperconjugation in 1964¹⁷ or Taylor's account of electrophilic aromatic substitution in 1990,¹⁴ while a discussion by Ahira in 1980¹⁸ attracted only two citations.

Hyperconjugation was invoked in the 1960s to account for the high reactivity of trimethylsilylbenzene toward protodesilylation and the much greater reactivity with acid

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of benzene bound to tin, germanium, and lead.^{14,19} Here the hyperconjugation is for C–Si, C–Sn, C–Ge, and C–Pb bonds. These indeed are much more effective than C–H.^{20,21} Yet no serious suggestion of an aromatic component to the stabilization was entertained.

In 1993, Schleyer provided computational evidence for the aromatic character of σ – π electron delocalization in the phenonium and benzenium ions.²² Subsequent studies, including calculations of aromaticity indices for cyclopentadienes substituted at the methylene group with Si, Sn, and Ge substituents,²³ have identified him as a consistent advocate of hyperconjugative aromaticity. His conclusions have not escaped criticism^{24,25} but are emphatically endorsed by the present results.

In view of its theoretical and experimental significance, it seems appropriate to characterize aromatic hyperconjugation by the term “hyperaromaticity”. This implies an analogy between hyperconjugation and hyperaromaticity on the one hand and homoconjugation and homoaromaticity on the other.²⁶ The term would seem to be consistent with Mulliken's original definition of hyperconjugation²⁷ as “conjugation over and above that usually recognized”. It remains remarkable that so apparently important a concept should only now find extensive experimental support.

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Supporting Information Available: Experimental procedures, kinetic measurements, and tables of rate constants and product ratios (S1–S4) and of computational details (Table S5). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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