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# Hyperaromatic Stabilization of Arenium Ions: Acid-Catalyzed Dehydration of 2-Substituted 1,2-Dihydro-1-naphthols

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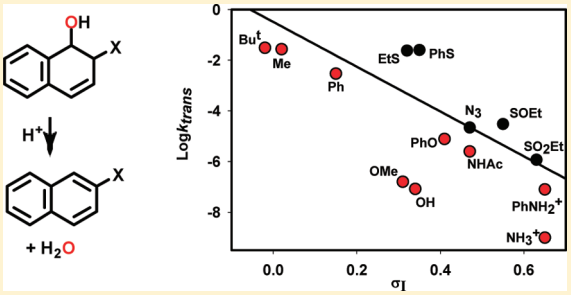
Supporting Information

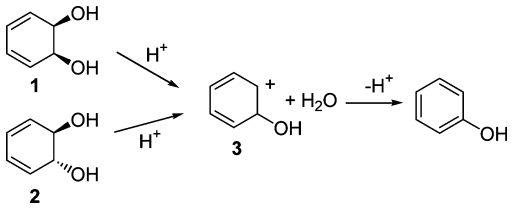
**ABSTRACT:** Rate constants for acid-catalyzed dehydration of *cis*-2-substituted 1,2-dihydro-naphthols are well correlated by the Taft relationship log $k = -0.49 - 8.8\sigma_I$, with minor negative deviations for OH and OMe. By contrast the *trans* substituents show a poor correlation with $\sigma_I$ and in most cases react more slowly than their *cis* isomers. The behavior is consistent with rate-determining formation of a 2-substituted carbocation (naphthalenium ion) intermediate that for *cis* reactants possesses a 2-C−H bond suitably oriented for hyperconjugation with the charge center. For the *trans* isomers the 2-substituent itself is oriented for hyperconjugation in the initially formed conformation of the cation. It is argued that $k_{cis}/k_{trans}$ rate ratios for substituents (Me, 8.4; Bu$^t$, 12.7; Ph, 3.8; $NH_3^+$, 160; OH, 440) reflect their hyperconjugating ability relative to hydrogen. Faster reactions of *trans* isomers are observed for substitutents known (RS, $N_3$) or suspected (EtSO, $EtSO_2$) of stabilizing the cation by a $\pi$ or $\sigma$ neighboring group effect. The good Taft correlation is taken to indicate that *cis* substuents are reacting normally, differentiated only by their inductive effects. The slower reactions of the *trans* isomers are the judged to be "abnormal". This is confirmed by comparing effects of *cis* and *trans* $\beta$-OH substituents on the reactivities of dihydro phenols, naphthols, and phenanthrols. Whereas $k_H/k_{OH}$ for *cis* substituents varies by less than 8-fold and is consistent with the influence of an inductive effect of the OH group ($k_H/k_{OH} \approx 2000$), $k_H/k_{OH}$ for the *trans* substituents varies by 3 orders of magnitude, reflecting the additional influence of the lesser hyperconjugating ability of a C−OH bond compared to a C−H bond. The magnitude and variation of this difference is consistent with C−H hyperconjugation conferring aromatic character on the arenium ions




## INTRODUCTION

*Cis* and *trans* benzene dihydrodiols differ markedly in their reactivity toward acid-catalyzed dehydration to form phenol.[1,2] As shown in a previous paper[1] and summarized in Scheme 1, the

**Scheme 1**




*cis* isomer **1** is 4,500 times more reactive than the *trans* **2** despite both reactions proceeding with rate-determining formation of what apparently is the same carbocation intermediate **3**.

This difference in reactivity is linked to the aromaticity of the phenolic product, as is shown by reduced values of $k_{cis}/k_{trans}$ = 440 and 50, respectively, for dehydration of naphthalene (1,2) and phenanthrene (9,10) dihydrodiols.[1,2] It is complemented by stereoselective attack of nucleophiles on the $\beta$-hydroxy arenium ion intermediate to give *cis* product. Thus in the reverse of the carbocation-forming step, attack of water on the cation yields almost exclusively *cis*-dihydrodiol (as shown in the case of the 10-hydroxy-9-phenanthrenonium ion).

That much was demonstrated in the earlier paper. The interpretation of the behavior offered there was that in their reactions with acid *cis* and *trans* dihydrodiols lead initially to different conformations of the $\beta$-hydroxy carbocation intermediate **3**. In the conformation formed from the *cis* isomer **4** a $\beta$-C−H bond occupies an axial position with respect to the charge center of the carbocation and is optimally oriented for hyperconjugation. This conformation of the carbocation was deemed more stable than that formed from the *trans* isomer in which a $\beta$-C−OH bond is oriented axially. It was suggested that the C−H hyperconjugation was amplified compared with non-arenium carbocations by the contribution of an aromatic valence bond structure **5b**[3] to the most important resonance forms representing the ions (**5a** ↔ **5b**). This is supported by computational results and calculations of ring currents for arenium ions described in a following paper.[4]

An obvious question arises that will be addressed in the present paper. What is the consequence of extending the range of 2-substituents from hydroxyl to other possibilities that can be envisaged? This can be established by measuring rate constants

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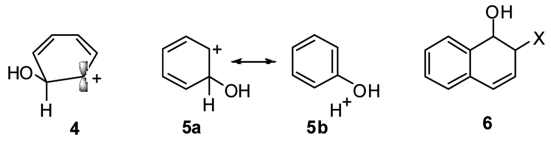


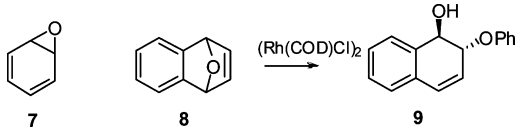

for dehydration of a series of *cis* and *trans* 2-substituted-1,2-dihydro-1-naphthols (**6**) including substituents (X in **6**) alkyl, phenyl, alkoxy, phenoxy, alkyl- and phenyl-thio, phenylsulphonyl, azido, amido, and ammonio. The choice of dihydro-1-naphthols as substrates rather than the corresponding dihydrophenols is dictated by their more straightforward synthesis.

In principle hyperconjugation is not the only explanation of the high *cis*/*trans* rate ratios for arene dihydrodiols. In the Discussion we consider briefly (and reject) three other possibilities. A further issue addressed is whether the high rate ratios arise from an abnormally high reactivity of the *cis* isomer or low reactivity of the *trans*. We find that rate constants for the acid-catalyzed dehydration of *cis* isomers of 2-substituted-1,2-dihydronaphthols (**6**) show a good Taft correlation[5,6] when plotted against inductive substituent constants ($\sigma_I$ or $\sigma^*$). By contrast no such correlation exists for the *trans* isomers most of which react more slowly than their *cis* counterparts. These results suggest that *cis* substituents may be considered to react normally and that it is the slow reaction of the *trans* 2-substituents, especially of oxygen susbtituents 2-HO or 2-MeO, that is "abnormal". The logic of this view is confirmed by a comparison of the reactivities of arene dihydrodiols and structurally related alcohols lacking a $\beta$-hydroxyl group.

## RESULTS

**Synthesis of 2-Substituted 1,2-Dihydro-1-naphthols.** The principal routes for synthesis of 2-substituted 1,2-dihydronaphthols were as follows. *Trans* isomers were prepared by nucleophilic ring opening of naphthalene oxide (**7**, Scheme 2),[7,8]

**Scheme 2**




including with alkyl lithium reagents.[9] For azide and sulfur nucleophiles[9] further functionalization to an amino group and amide or sulfoxide and sulfone was possible. The phenyl derivative was obtained from copper-catalyzed reaction of phenyl magnesium bromide with naphthalene-1,4-*endo*-oxide **8**.[10] *trans*-2-Phenoxy-1,2-dihydro-1-naphthol **9** was obtained by reaction of phenol with the same *endo* oxide with $(Rh(COD)Cl)_2$ as catalyst.[11]

For *cis* substituents a methoxy derivative was prepared by alkylation of the *cis*-dihydrodiol. For alkyl and phenyl derivatives the naphthalene-1.4-*endo*-oxide **7** was reacted with the corresponding alkyl or phenyl lithium.[12] The *cis*-2-phenoxy substrate was prepared by cross-coupling of the *cis*-dihydrodiol with $PhBF_3K$ in the presence of copper acetate.[13] For most other substituents the products came from nucleophilic displacement of bromide from the *trans*-bromohydrin of 1,2-dihdydronaphthalene[9] followed by benzylic bromination (with protection of the OH group by acetylation) and reaction with sodium methoxide as in Scheme 3.[14] Again azide or sulfur nucleophiles were converted to amine and amide or sulfoxide and sulfone.

*cis*- and *trans*-Naphthalene-1,2,3,4-tetrahydro-1,2-diols (**13** and **14** below) were prepared by reduction of the corresponding 1,2-dihydrodiols.[15]

**Kinetic and Product Analyses.** Rate constants $k_{obs}$ ($s^{-1}$) for acid-catalyzed dehydration of the *cis* and *trans* 2-substituted 1,2-dihydronaphthols were measured in aqueous solution by monitoring the change in UV spectrum accompanying formation of the aromatic product. Examples of changes in UV spectra are shown in Figure S1 in Supporting Information. The presence of an OH group rendered most of the reactants soluble in water at spectrophotometrically measurable concentrations. However, in some instances the products precipitated and first order rate constants had to be extrapolated from measurements in aqueous organic solvent mixtures as described in the Supporting Information.

Second-order rate constants were obtained from a plot of $k_{obs}$ against acid concentration for measurements at low acid concentrations. For less reactive substrates rate constants measured in concentrated solutions of $HClO_4$ were extrapolated to water by plotting $\log(k_{obs}/[H^+])$ against the solvent acidity parameter $X_o$.[16] Examples of these plots for *cis* and *trans* 2-$NH_3^+$ and 2-PhO substituents are shown in Figure 1.

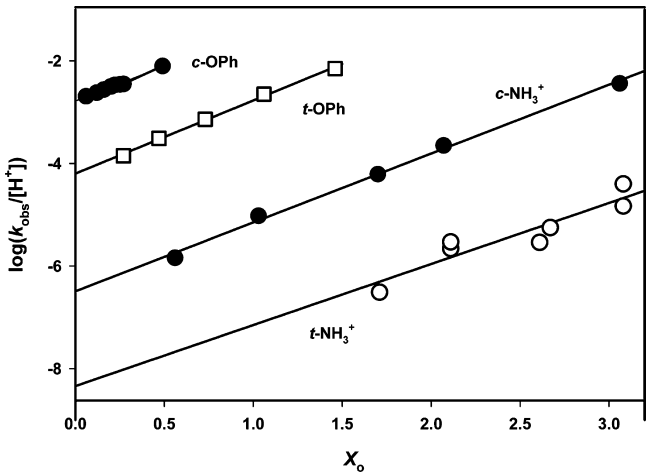
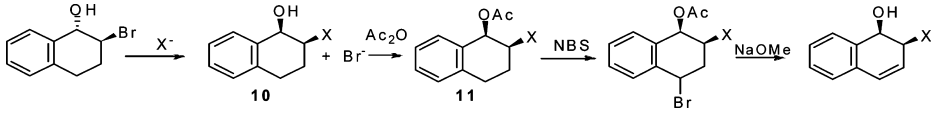



**Figure 1.** Plots of logs of second order rate constants against $X_o$ for the acid-catalyzed dehydration of *cis*- and *trans*-2-phenoxy- and 2-amino-1,2-dihydro-1-naphthols in aqueous $HClO_4$.

For 2-substituents such as H, alkyl, Ph, PhSO, $PhSO_2$, and $NH_3^+$ both *cis* and *trans* reactants gave a single 2-substituted naphthalene as product. However, where a 2-substituent, such as HO, MeO, or PhO, was capable of reacting itself, two products were obtained corresponding to the rate constants $k_a$

**Scheme 3**





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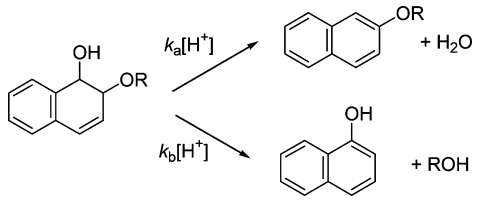
and $k_b$ shown in Scheme 4. It was then necessary to use a product analysis to extract the desired rate constant ($k_a$) for formation

**Scheme 4**




of the 2-substituted product. Product analyses employed HPLC or GC measurements, and a value of $k_a$ was obtained by combining the ratio of product concentrations ($\equiv k_a/k_b$) with the measured second order rate constant ($k_a + k_b$). As the 2-position is more reactive than the 1- position, the fraction of desired product was quite small, in the range of 1−5%, and these rate constants are generally less precise than those based on substrates yielding a single product. Table 1 includes measured rate constants and product proportions as well as conditions of analyses. 2-Azido and 2-PhS or 2-EtS substituents led to dehydration products only. However, these substituents also gave partial rearrangement, with formation of 1- as well as 2-substituted naphthalene products.[4] For the *cis* isomers it seems likely that the rearrangement must follow formation of the *β*-hydroxynaphthalenium ion intermediate and thus does not affect its rate of formation. In the case of the *trans* isomers rearrangement probably accompanies formation of the carbocation. Thus the sulfur substituents were unique among 2-substituents in leading to faster reactions for the *trans* than for the *cis* isomers, and this is sensibly attributed to neighboring group participation. The *trans* 2-azido substrate reacts at the same rate rather than faster than its *cis* isomer. However, it is sufficiently unusual for the *trans* isomer not to be slower than the *cis* that it is reasonable to infer in this case also that the rearrangement occurs in the rate-determining carbocation-forming step of the reaction and leads to an acceleration of the unassisted rate. A more detailed discussion of the rearrangement of these substrates is postponed to a later paper.[4] However, product analyses for rearranging substituents are summarized in Table S1 of the Supporting Information.

Rate constants for *cis* and *trans* isomers of the 2-substituted-1,2-dihydronaphthols are summarized in Table 2 together with $\sigma_I$ values for the substituents.[17,18] Where possible values of $\sigma_I$ are based on the ionization of quinuclidinium ions[18] insofar as the neutralization of a positive charge in the equililibrium would seem to make them more appropriate for a carbocation reaction than values based on the ionization of substituted acetic acids. There appears to be no general relationship between the two sets of $\sigma_I$. However, for oxygen, sulfur, and elctronegative nitrogen substituents (OMe, SMe, $SO_2Me$, and NHAc) $\sigma_I$ for the quinuclidinium ions is on average larger by 0.05 log units than a value based on the ionization of acetic acids. For nitrogen and sulfur substituents for which only an acetic acid based $\sigma_I$ is available, 0.05 is added to $\sigma_I$ to provide a more consistent scale of substituent constants. The effect of this on the quality of correlations between log $k$ and $\sigma_I$ is small.

There are more *trans* than *cis* substituents in Table 2 because the synthesis of the *trans* isomers lends itself to preparation of a range of substituted amino groups. Also included among the *trans* but not *cis* substituents is an acetamido group. The corresponding *cis* substitutent was prepared, but dehydration of the dihydronaphthol was pre-empted by N−O rearrangement of the acetyl group. Acyl rearrangements also complicated attempts to measure substituent effects of acetoxy and benzoyloxy substituents and details of the behavior of these derivatives will also be reported elsewhere.

Also shown in Table 2 are ratios of rate constants for *cis* and *trans* substituents. For the least reactive substituents, rate constants in water are extrapolated from their $X_o$ dependence in concentrated solutions of $HClO_4$. In the case of $NH_3^+$ as a leaving group these dependences differ by a small amount, with slopes of plots of log $k_2$ against $X_o$ having values $m^*$ = 1.34 and 1.18 for the *cis* and *trans* isomers, respectively. A conseqence is that values of $k_{cis}/k_{trans}$ depend on the acid concentration. However, as seen in Figure 1 measurements for the *trans* isomer show significant scatter. The difference in $m^*$ values may not be real therefore. Consequently the value of $k_{cis}/k_{trans}$ = 160 given in the table corresponds to an average over the acid concentration range for which both rates were measured. This is larger than the ratio $k_{cis}/k_{trans}$ = 60 from rate constants extrapolated to zero acid concentration and smaller than the previously reported value of 310.[2]

**Tetrahydronaphthalene Diols.** Rate constants $k_{cis}$ and $k_{trans}$ for carbocation formation from *cis*- and *trans*-1,2-dihydroxy-1,2,3,4-tetrahydronaphthalene (**12** and **13**) were derived from measurements of rate and equilibrium constants, $k_{obs}$ and $K_{eq}$, for acid-catalyzed equilibration of the isomers by the method described by Whalen[21] and the ratios $x$ of *cis*/*trans* tetrahydrodiol products formed in the solvolysis of *cis*- and *trans*-1-chloro-2-hydroxy-1,2,3,4-tetrahydronaphthalenes **14**.[22] The analysis assumes that equilibration and partitioning occur via a *β*-hydroxycarbocation intermediate ($R^+$) as shown in Scheme 5. Consistently with this, the *cis*- and *trans*-chlorohydrins yield the same ratios of products. The measured constants may be expressed in terms of the microscopic rate constant of Scheme 5, $k_{cis}$, $k_{trans}$, and $k_{-1}/k_2$ (= $x$ = 3.5),[1] as shown in eqs 1−3.

**Table 1. Rate Constants and Product Fractions for Reactions of *cis*- and *trans*-2-Hydroxy and 2-Methoxy-1,2-dihydro-1-naphthols in Aqueous $HClO_4$ at 25° C**

| substituents | $[H^+]$ (M) | rxn time (h) | $k_{obs}$ ($M^{-1}$ $s^{-1}$) | rxn at 1-posn (%) | rxn at 2-posn (%) | $k_a$ ($M^{-1}$ $s^{-1}$)[a] | $k_b$ ($M^{-1}$ $s^{-1}$)[b] |
|---|---|---|---|---|---|---|---|
| *cis*-1,2-OH | 0.1 | 5 | $1.48 \times 10^{-3}$ | 4.7 | 95.3 | $7.0 \times 10^{-5}$ | $1.41 \times 10^{-3}$ |
| *trans*-1,2-OH | 2.0 | 15 | $4.00 \times 10^{-6}$ | 3.8 | 96.2 | $1.5 \times 10^{-7}$ | $3.85 \times 10^{-6}$ |
| *cis*-1-HO-2-MeO | 0.1 | 10 | $8.30 \times 10^{-4}$ | 3.2 | 96.8 | $2.7 \times 10^{-5}$ | $8.00 \times 10^{-4}$ |
| *trans*-1-HO-2-MeO | 2.0 | 15 | $2.00 \times 10^{-6}$ | 4.3 | 95.7 | $8.4 \times 10^{-8}$ | $1.91 \times 10^{-6}$ |
| *cis*-1-HO-2-PhO | 0.5 | 10 | $1.61 \times 10^{-3}$ | 4.0 | 76.0 | $6.4 \times 10^{-5}$ | $1.22 \times 10^{-3}$ |
| *trans*-1-HO-2-PhO | 2.0 | 10 | $6.26 \times 10^{-5}$ | 4.0 | 96.0 | $2.5 \times 10^{-6}$ | $6.01 \times 10^{-5}$ |

[a]Rate constant for loss of OH from the 1-position. [b]Rate constant for loss of OH or OMe from the 2-position.


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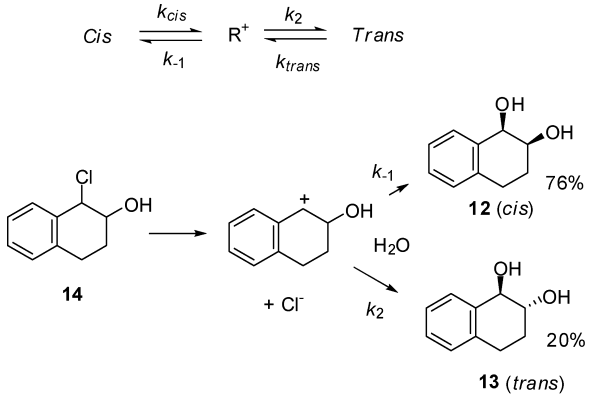
**Table 2. Rate Constants ($M^{-1}$ $s^{-1}$) for Acid-Catalyzed Dehydration of 2-Substituted *cis*- and *trans*-1,2-Dihydro-1-naphthols 6 at 25 °C[a]**

| substituent | $\sigma_I$ | $k_{cis}$ | $k_{trans}$ | $k_{cis}/k_{trans}$ |
|---|---|---|---|---|
| H | 0 | 0.35 | 0.35 | 1.0 |
| Me | 0.02 | 0.228 | $2.70 \times 10^{-2}$ | 8.4 |
| $Bu^t$ | −0.02 | 0.392 | $3.09 \times 10^{-2}$ | 12.7 |
| Ph | 0.15 | 0.013 | $2.97 \times 10^{-3}$ | 3.8 |
| NHAc | 0.29 | | $7.78 \times 10^{-6}$ | |
| OH | 0.31 | $6.96 \times 10^{-5}$ | $1.57 \times 10^{-7}$ | 440 |
| OMe | 0.34 | $2.65 \times 10^{-5}$ | $8.4 \times 10^{-8}$ | 315 |
| OPh | 0.42 + 0.05 | $6.4 \times 10^{-5}$ | $2.5 \times 10^{-6}$ | 26 |
| SEt | 0.31[b] | | $2.4 \times 10^{-2}$ | |
| SPh | 0.30 + 0.05 | $4.25 \times 10^{-4}$ | $2.5 \times 10^{-2}$ | 0.017 |
| $N_3$ | 0.42 + 0.05 | $2.50 \times 10^{-5}$ | $2.18 \times 10^{-5}$ | 1.2 |
| SOEt | 0.50[c] + 0.05 | | $3.01 \times 10^{-5}$ | |
| $SO_2Et$ | 0.59[d] + 0.05 | | $1.17 \times 10^{-6}$ | |
| $SO_2Ph$ | 0.55[e] + 0.05 | $9.8 \times 10^{-7}$ | | (∼1.0)[f] |
| $NH_2Ph^+$ | 0.60[g] + 0.05 | | $8.00 \times 10^{-8}$ | |
| $NH_3^+$ | 0.60 + 0.05 | $3.16 \times 10^{-7}$ | $4.6 \times 10^{-9}$ | (160)[h] |
| $NMe_2H^+$ | 0.70 + 0.05 | | $1.4 \times 10^{-9}$ | |

[a]Values of $\sigma_I$ for the first six substituents are based on the ionization of quinuclidinium ions.[17,18] Except as indicated the others are based on the ionization of substituted acetic acids[17] with +0.05 correction . [b]Value for SMe from ionization of quniuclidinium ions. [c]Estimated value for SOMe;[19] cf ref 17. [d]Value for $SO_2Me$. [e]Value reported by Exner[20] (ref 17) [f]Approximate value based on comparison with *trans* $SO_2Et$ substituent. [g]Value for $NH_2Me^+$ corrected by = +0.05, the difference in $\sigma_I$ between $CH_3$ and $PhCH_2$. [h]Average value in acid concentration range of measurements (5.5−8.0 M $HClO_4$).

**Scheme 5**




$$x = k_{-1}/k_2 \quad (1)$$

$$K_{eq} = \frac{k_{cis}k_2}{k_{trans}k_{-1}} = \frac{k_{cis}/k_{trans}}{x} \quad (2)$$

$$k_{obs} = \frac{k_{cis}[H^+]}{(1+x)} + \frac{xk_{trans}[H^+]}{(1+x)} \quad (3)$$

Equilibration of the *cis*- and *trans*-1,2-dihydroxy-1,2,3,4-tetrahydronaphthalenes (**12** and **13**) at 25 °C required fairly concentrated acid, in the range 2.5−4.5 M $HClO_4$. It was accompanied by formation of 10% 2-tetralone (formed to the extent of 4% in the solvolysis of **14**) and an unknown product, perhaps from a pinacol rearrangement. A first-order kinetic analysis was based on the relative concentrations of *cis* and *trans* isomers only, for which HPLC measurements are shown in Table S2 in Supporting Information. Figure S2 in Supporting Information shows that this leads to some discrepancy in rate constants between *cis* and *trans* reactants. However, the difference is not greater than 50% and has a fairly minor effect on the estimated reactivities of *cis* and *trans* diol isomers. Moreover the value of $k_{cis}/k_{trans}$ is given independently of the rate measurements as $K_{eq}x = 5.7$. Similar measurements in an earlier paper[1] for equilibration of acenaphthylene dihydrodiols showed a discrepancy of only 10% between values of $K_{eq}$ and $k_{obs}$ determined as described here and by taking explicit account of a competing reaction of the dihydrodiols to form acenaphthenone. In practice $k_{cis}$ and $k_{trans}$ were determined at each acid concentration (Table S3 in Supporting Information) and extrapolated to dilute acid by plotting log $k$ against $X_o$ (Figure S3 in Supporting Information) to give $k_{cis} = 1.2 \pm 0.6 \times 10^{-5}$ $M^{-1}$ $s^{-1}$ and $k_{trans} = 2.1 \times 10^{-6}$. The value of $x$ was assumed to be independent of acid concentration.

## DISCUSSION

**Alternative Explanations of High *cis/trans* Reactivity Ratios.** As outlined in the introduction, the greater reactivity of *cis* than *trans* isomers of arene dihydrodiols may be attributed to the superior hyperconjugating ability of an axially oriented C−H compared with C−OH bond $\beta$ to the charge center of an arenium ion intermediate (e.g., **4**). However, other explanations can be considered. Thus it is conceivable that reaction of the *cis* arene dihydrodiol is promoted by a hydride rearrangement accompanying breaking of the $C-OH_2^+$ bond to yield not a $\beta$-hydroxycarbocation as intermediate but the more stable rearranged $\alpha$-hydroxycarbocation, e.g., **15**. Further possibilites are that the *cis*-dihydrodiols are accelerated by a neighboring group interaction from the $\beta$-hydroxy group or that the *cis*-OH group provides intramolecular solvation of the departing $OH_2^+$ group in the transition state as in **16**.

There are arguments against each of these possibilities. Hydride rearrangement is excluded because application of the azide clock to determing the stability of the carbocation intermediate shows that a $\beta$-OH group decreases its stability compared with a parent arenium ion, rather than increasing it, as would be the case for formation of an $\alpha$-hydroxycarbocation.[23] Hydride rearrangement does indeed occur and has been well characterized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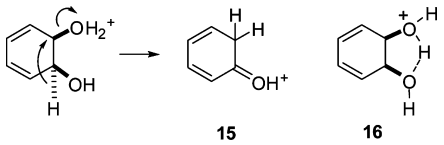



15 16

as the NIH shift.[24] However, the rearrangement follows rather than precedes formation of the carbocation intermediate (e.g., **3**).[25]

Neighboring group participation, if it occurred, would be expected to be more important for the *trans* dihydrodiol than the *cis*, as indeed is shown below to be true of neighboring EtS and PhS groups. There is no evidence of participation by *cis* substituents. A major contribution from intramolecular solvation by an OH group has little or no precedent in aqueous media and would not explain the dependence of the *cis*/*trans* rate ratio on the aromaticity of the phenolic product of the reaction.

**Taft Correlation of *cis* Substituents.** We turn to the question of whether ratios of rate constants for *cis* and *trans* substituents other than OH are consistent with their relative hyperconjugating abilities. However, before considering rate constant ratios it is instructive to consider *cis* substituents only. Figure 2 shows a Taft plot of log *k* versus $\sigma_I$ for *cis*-2-substituted

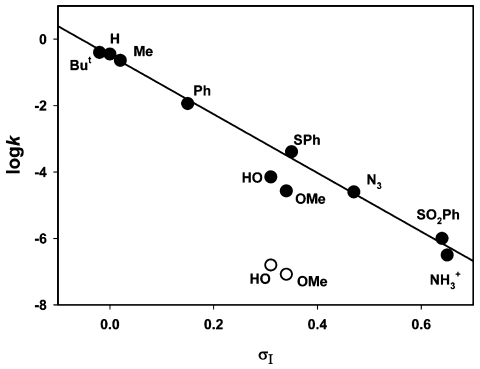



**Figure 2.** Plot of log *k* against $\sigma_I$ for acid-catalyzed dehydration of 2-substituted-1,2-dihydronaphthols (**6**) in aqueous solution at 25 °C. The filled circles represent *cis* substituents, and the open circles represent *trans* substitutents.

1,2-dihydro-1-naphthols **6** (also shown in the preliminary communication of the present results).[2] The good correlation observed strongly suggests that these substituents are behaving "normally" in the sense that they are displaying an expected inductive effect on the reaction rate This impression is reinforced by the reasonable magnitude of $\rho_I = -8.8$ for a reaction involving development of a positive charge at the $\beta$-carbon atom. The value may be compared with $\rho_I = -7.0$, estimated from $\rho^* = -3.14$, for the protonation of 2-substituted alkylamines ($XCH_2NH_3^+$).[26]

The correlation line in Figure 2 was calculated without including the *cis*-2-hydroxy and -methoxy substituents. These show small negative deviations from the line, which are almost certainly outside the error limits of the measured rate constants. This is true despite the errors being significantly greater than normal because the predominant reaction monitored is that of the 2-HO or 2-MeO groups, with dehydration involving the 1-OH groups accounting for less than 5% of the reaction (Scheme 4).

In Figure 2 the *cis* substituents are shown as filled circles. Also shown as open circles are rate constants for the *trans* 2-HO and MeO substituents. These show much larger negative deviations from the correlation line than their *cis* isomers, with $k_{cis}/k_{trans}$ = 440 for the 2-OH substituent and 416 for the 2-MeO substituent. The implication that the *cis* substituents are behaving normally and that the *trans*-substituted dihydrodiols are reacting 'abnormally' slowly is further reinforced.

How do the oxygen substituents compare with other *trans* subsituents? A full range of *trans* 2-substituted 1,2-dihydo-1-naphthols is shown in Figure 3, again as a plot of log *k* versus $\sigma_I$.

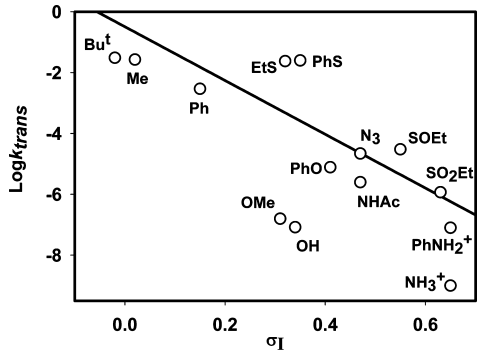
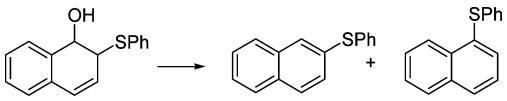



**Figure 3.** Plot of log *k* for acid-catalyzed dehydration of *trans*-2-substituted 1,2-dihydro-1-naphthols (**6**) against $\sigma_I$. The line represents the correlation of log *k* with $\sigma_I$ for *cis* isomers.

In the majority of cases the *trans* dihydrodiols react more slowly than their *cis* isomers. This can be seen from their falling below the correlation line shown in the figure, which is based not on the *trans* substituents themselves but on the *cis* substituents from Figure 2. Only in the case of the sulfur substituents, PhS and EtS, is a significantly faster reaction for the *trans* isomer observed. For these substituents rearrangement occurs, with the formation of a 1- as well as 2-substituted naphthalene product (Scheme 6). It is reasonable to infer therefore that these reactions

**Scheme 6**




are accelerated by neighboring group participation. The same conclusion can be drawn for the azido substituent, which also shows rearrangement. In this case the rate constants for the *cis* and *trans* isomers are similar. However as the rate of the *trans* would have been expected to be lower than that of the *cis*, there is still a strong indication that participation by the azido group accelerates the reaction.

It is clear that there is no satisfactory correlation between log *k* and $\sigma_I$ for *trans* substituents. As already noted most substituents apart from azido and thio react more slowly than their *cis* isomers. Although none show as large a negative deviation from the *cis* correlation line as HO or MeO, there is a broad downward trend in rate constants with increasing electronegativity, and for the most electronegative substituent $NH_3^+$ $k_{cis}/k_{trans}$ = 160 most closely approaches that for the OH (440). It is a little surprising that the electronegative groups EtSO and $EtSO_2$ yield rate constants for *trans* isomers close to the *cis* correlation line. No rearrangement is observed in these cases and, while this does not rule out participation, reaction at the sulfonyl oxygen is made unlikely by the relatively slower reactions of *trans* acetoxy and benzoyloxy substituents possessing a more nucleophilic carbonyl group, for which $k_{cis}/k_{trans} \approx 20$.[23]


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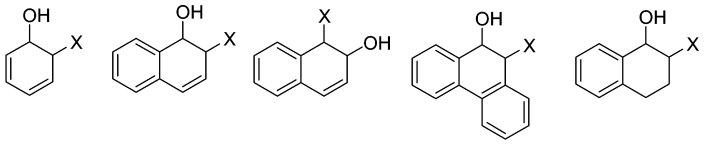
**Chart 1**



| | | | | | |
|---|---|---|---|---|---|
| $k_H$ ($M^{-1}s^{-1}$) | 180 | 0.35 | 1.8 | $3.5 \times 10^{-3}$ | $2.8 \times 10^{-3}$ |
| $k_H/k_{OH}$ (*cis*) | 3,270 | 5,000 | 1280 | 1590 | 650 |
| $k_H/k_{OH}$ (*trans*) | $1.50 \times 10^7$ | $1.75 \times 10^6$ | $4.67 \times 10^5$ | $8.4 \times 10^4$ | 3700 |
| $k_{cis}/k_{trans}$ | 4,500 | 440 | 366 | 50 | 5.7 |

Participation by a lone pair on sulfur in the case of the sulfoxide or an unexpectedly large $\sigma$ interaction by the carbon sulfur bonds remain possibilities.

A further obvious candidate for participation is the amido group. This deviates negatively from the correlation line but by a much smaller amount than oxygen or ammonium substituents. Also apparent is that phenoxy and anilinium substituents show less negative deviations than hydroxyl and alkoxy on the one hand or ammonium or alkyl ammonium on the other. The reason for this is not clear but may be associated with the presence of the phenyl group.

Values of $k_{cis}/k_{trans}$ for different substituents are summarized in Table 2. Again allowing for neighboring group or other special effects it seems at least plausible that these correlate with the hyperconjugative capacity of the 2-substituent. For the *cis*-substituted compounds a hydrogen atom is favorably disposed for hyperconjugation in the initial conformation of the $\beta$-hydroxynaphthalenium ion intermediate and the rates for different 2-substituents are differentiated by their inductive effects only. For the *trans* compounds the rate reflects both an inductive effect and the hyperconjugative ability of the 2-substituent. The implied hyperconjugative order is H > Ph > alkyl > $R_3N^+$ > RO. The rather small negative deviations of *trans*-alkyl substituents from the *cis* correlation line in Figure 3 are consistent with their hyperconjugative ability being less than but comparable with that of hydrogen.[4] More generally, it seems reasonable that hyperconjugative stabilization of a carbocation should decrease with increasing electronegativity of a substituent, with RO and $R_3N^+$ being particularly unfavorable.

It is possible that the observed order of *cis*/*trans* reactivity ratios is also influenced by mild neighboring group effects of *trans* substituents, e.g., rendering the phenyl group more reactive than might have been expected because a favorable $\pi$-interaction with the positive charge partly overrides its unfavorable inductive effect. However, with the exception perhaps of phenoxy and anilinium, a combination of inductive effects with participation by $\sigma$, n, and $\pi$ electrons would seem to offer a reasonable explanation of the overall pattern of *trans* substituent effects. The high reactivities of the *trans* sulfoxide and sulfonyl groups remain a puzzle but may also find an explanation within this framework.

***trans*-$\beta$-Oxygen Substituents React "Abnormally" Slowly.** An implication of Figures 1 and 2 is that most *trans* substituents, and especially the oxygen substituents, are reacting "abnormally" slowly. The higher reactivity of the *cis*-substituted compounds may be considered "normal" in the sense that the influence of the substituents is described by a Taft correlation reflecting only their inductive effects. For *trans* substituents there is no Taft correlation because the rates are affected not only by inductive effects but also substituent-dependent hyperconjugative effects (or for some substituents neighboring group effects). The hyperconjugative effects are characteristically less activating than in the case of the *trans* C–H group, which influences all *cis*-substituted compounds.

The influence of an "extra" rate-retarding effect as a result of the poor hyperconjugation of a *trans* C–OH group is corroborated by a comparison between the reactivities of the *cis* and *trans* dihydrodiols and the corresponding substrates lacking a $\beta$-oxygen substituent. In Chart 1 below, the kinetic effects of *cis* and *trans* $\beta$-hydroxyl groups are compared based on measurements in a previous paper[1] for the dihydrodiols and earlier papers for the corresponding alcohols or "arene hydrates" lacking the $\beta$-OH substituent.[27,28]

The substrates in the chart are arranged so that the aromaticity of the product of dehydration decreases from left to right. Included are dihydrodiols and hydrates (with X = OH and H, respectively) of benzene, naphthalene, phenanthrene, and dihydronaphthalene. The two naphthalene derivatives correspond to reaction of the 1- or 2-hydroxyl group. Because the 2-OH is more reactive than the 1-OH, the rate constant for the 2-hydroxy-1,2-dihydronaphthalenes are the more accurate. However, as can be seen, with $k_{cis}/k_{trans}$ = 366 and 440, respectively, there is little difference between the values, especially allowing for potential errors for reaction of the 1-hydroxy group.

For the *cis*-dihydrodiols in Chart 1 the influence of the OH group, as expressed by the ratio of rate constants for unsubstituted and substituted substrates, $k_H/k_{OH}$, varies by less than 8-fold, with no obvious trend between its upper and lower limits. Significantly the average value of $k_H/k_{OH}$ = 2000 is close to the expected inductive effect of an OH reported for solvolysis reactions of substrates with tosylate or chloride leaving groups for which neighboring group participation is inhibited by constraining the oxygen within a bicyclic structure such as **17**.[22,29]

**17**

By contrast, for the *trans*-dihydrodiols the magnitude of $k_H/k_{OH}$ decreases by a factor of 4000-fold in going from the dihydrodiol of benzene ($k_H/k_{OH} = 1.5 \times 10^7$) at one extreme to that of the nonaromatic double bond of dihydronaphthalene (3700) at the other. There is a clear implication that in this case the OH is exerting an effect over and above that of an inductive effect. This is consistent with an unfavorable effect upon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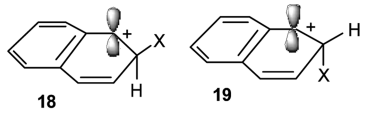
carbocation formation arising from replacement of a $\beta$-axial C−H bond optimally oriented for hyperconjugation in the conformation of the carbocation from a *cis*-dihydrodiol (**18**) with a C−OH bond for a carbocation formed (initially) from a *trans*-dihydrodiol (**19**). For the *cis*-dihydrodiols and the parent alcohol or hydrate lacking a $\beta$-OH substituent there is no such inhibition of C−H hyperconjugation.

## CONCLUSIONS

In summary, the comparison of *cis*- and *trans*-substituted dihydrodiols in Figures 1 and 2 confirm (a) that the rate of acid-catalyzed dehydration is strongly inhibited when a $\beta$-oxygen substituent is present in a *trans* configuration and (b) that for substituents other than oxygen the reduction in rate reasonably reflects the hyperconjugating ability of the substituent. The second conclusion is complicated by the intervention of neighboring group effects from n or $\pi$ electrons (as opposed to hyperconjugating $\sigma$ electrons)




*cis*-diol X = OH *trans*-diol X = OH
hydrate X = H hydrate X = H

for some substituents and a lack of independent evidence for the effectiveness of $\sigma$ or n electron participation in the case of sulfone or sulfoxide substitutents. The first conclusion is confirmed by comparison of rate constants for *cis* and *trans* arene dihydrodiols with those of their 2-deoxy counterparts the arene hydrates (Chart 1)

Regrettably no simple synthetic pathway to 2-substituents that would lead to a greater degree of hyperconjugation than hydrogen substituents, such as $SiMe_3$ or *spiro*-cyclopropyl was found. However, in a further paper[4] the effects of these substituents are examined computationally, and further evidence for hyperaromatic stabilization of arenium ions, including the influence of benzoannelation and the role of hyperconjugation in electrophilic aromatic substitution, is described.

## EXPERIMENTAL SECTION

**General.** $^1$H and $^{13}$C NMR spectra were measured on 300 and 500 MHz NMR spectrometers. UV−vis spectra and kinetic measurements were recorded on a spectrophotometer equipped with an automatic cell changer thermostatted at 25 ± 0.1 °C. HPLC measurements were made with an HPLC system equipped with dual wavelength absorbance detection.

**Materials.** Naphthalene-1,2-oxide[7,8] and1-hydroxy-1,2-dihydronaphthalene with *trans* methyl, phenyl,[10] *tert*-butyl,[30] azido, methoxy, ethylthio, ethylsufoxy, ethylsulfonyl[10] hydroxy,[1,31] and phenoxy[11] 2-substituents and *cis* methyl, *tert*-butyl, and phenyl 2-substituents[12] were prepared by previously reported methods. *cis*-Naphthalene-1,2-dihydrodiol was available from fermentation.[1,2] The NMR spectra of the *trans* ethylsulfoxy and ethlsulfonyl derivatives indicated the presence of ca. 5% of the positional isomer from opening of naphthalene-1,2-oxide. The following compounds were prepared for the first time or by new methods.

***trans*-1-Hydroxy-2-phenylthio-1,2-dihydronaphthalene (6, X = *trans*-PhS).** To a solution of NaOH (0.24 g, 6.0 mmol) in water (10 mL) was added phenylthiol (0.56 g, 5.09 mmol). The mixture was stirred for 10 min and the resulting solution transferred to a round-bottom flask (50 mL) containing naphthalene oxide (7, 0.15 g, 1.04 mmol). Stirring was continued for 5 h at room temperature and the product extracted with ether (3 × 25 mL). The extracts were dried over $Na_2SO_4$ and the solvent evaporated under reduced pressure to yield a cream colored liquid (0.19 g, 73%):; $^1$H NMR ($CDCl_3$) $\delta$ 2.0 (d, $J$ = 6.6, OH), 4.19 (t, $J$ = 4.2 Hz, 1H), 4.75 (dd, $J$ = 6.0, 3.9 Hz, 1H), 6.07 (dd, $J$ = 9.3, 5.1 Hz, 1H), 6.58 (dd, $J$ = 9.6 Hz, 1H), 7.13−7.6 (m, 9H). The NMR spectrum indicated the presence of ca. 5% of a positional isomer.

***trans*-1-Hydroxy-2-amino-1,2-dihydronaphthalene (6, X = *trans*-$NH_2$).** To a solution of *trans*-1-hydroxy-2-azido-1,2-dihydronaphthalene[9] (**6**, X = *trans*-$N_3$, 0.2 g, 1.06 mmol) in anhydrous THF (10 mL) was added a mixture of zinc powder (0.6 g, 9.17 mmol) and cobalt chloride hexahydrate (3.0 g, 12.6 mmol) under a nitrogen atmosphere. After 45 min TLC showed complete loss of starting material. Dilution with THF (15 mL), removal of salts by filtration through Celite and evaporation of the filtrate gave a crude product, which was purified by column chromatography to yield a pale red liquid (0.16 g, 93.1%): $^1$H NMR ($CD_3OD$) $\delta$ 3.28 (td, $J$ = 3.23, 1.61 Hz, 3H, OH and $NH_2$), 3.9−3.94 (td, $J$ = 11.5, 2.46 Hz, 1H), 4.8 (b, 1H), 5.94 (dd, $J$ = 9.8, 2.44 Hz, 1H), 6.64 (dd, $J$ = 9.8, 2.45 Hz, 1H), 7.14−7.52 (m, 4H); $^{13}$C NMR ($CD_3OD$) 54.7, 70.9, 124.8, 126.7, 128.5, 128.5, 130.3, 131.9, 136.3; $m/z$ (ES); 162.1 $(M + H)^+$, 146; HRMS = 162.0919 (calculated for $[M + H^+]^+$, $C_{10}H_{11}NO$), 162.0926 (observed).

***trans*-*N*-(1-Hydroxy-1,2-dihydronaphthalen-2-yl)-acetamide (6, X = *trans*-NHCOMe).** To a mixture of dry powdered ZnO (0.015 g, 0.2 mmol) and acetic anhydride (0.04 g, 0.39 mmol) was added *trans*-1-hydroxy-2-amino-1,2-dihydronaphthalene (0.05 g, 0.31 mmol). The reaction was complete (TLC) after 1 h of vigorous stirring. The solid mass (ZnO) was triturated with methanol (20 mL) and the methanol extract dried with sodium bicarbonate followed by anhydrous sodium sulfate. The methanol was evaporated and the crude product purified by preparative TLC (20% ethyl acetate in pentane, 1% MeOH) to give a solid (0.03 g, 58%): $^1$H NMR ($CDCl_3$) $\delta$ 2.04 (s, 3H, $CH_3$), 3.28 (b, 1H, OH), 4.7 (d, 1H), 4.81−4.86 (m, 1H,), 5.68 (b, 1H, N−H), 5.78 (dd, $J$ = 9.63, 3.45 Hz, 1H), 6.53 (dd, $J$ = 9.63, 1.79 Hz, 1H) 7.09−7.54 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.3, 52.9, 73.2, 125.9, 126.7, 126.8, 128.4, 128.5, 129.9, 131.5, 135.9, 171.5; HRMS = 204.1025 (calculated for $[M + H^+]^+$, $C_{12}H_{14}NO_2$), 204.1020 (observed).

***trans*-1-Hydroxy-2-phenylamino-1,2-dihydronaphthalene (6, X = *trans*-$PhNH_2$).** To a solution of NaOH (0.24 g, 6.0 mmol) in water (10 mL) was added aniline (1.55 g, 16.6 mmol). After stirring for 10 min the solution was transferred to a round-bottom flask (50 mL) containing naphthalene oxide[7,8] (0.2 g, 1.36 mmol). Stirring was continued for 75 h at room temperature followed by extraction with EtOAc (3 × 25 mL) and drying over $Na_2SO_4$. The solvent was evaporated under reduced pressure and the crude product purified by column chromatography to yield a cream-colored solid (20 mg, 14% yield): $^1$H NMR ($CDCl_3$) $\delta$ 2.34 (s, 1H, OH), 3.64 (s, 1H, NH), 4.3 (d, $J$ = 6, 1H), 4.8 (d, $J$ = 7.2 Hz, 1H), 6.03 (dd, $J$ = 9.6, 3.6 Hz, 1H), 6.5 (d, $J$ = 9.9 Hz, 1H), 6.7−7.49 (m, 9H); HRMS = 238.1232 (calculated for $[M + H^+]^+$, $C_{16}H_{16}NO$), 238.1235 (observed).[32]

***trans*-1-Hydroxy-2-dimethylamino-1,2-dihydronaphthalene (6, X = *trans*-$NMe_2$).** To a solution of naphthalene oxide[7,8] (7, 0.15 g, 1.04 mmol) in MeOH (10 mL) and water (10 mL) were added dimethylamine (0.11 g, 2.18 mmol) and sodium hydroxide (87 mg, 2.18 mmol). The solution was stirred for 24 h at 30−35 °C, extracted with $CHCl_3$ (2 × 20 mL) and dried over $Na_2SO_4$. The solvent was removed under reduced pressure to yield a crude product which was purified by column chromatography (ethyl acetate, cyclohexane, $CHCl_3$) to give a light brown liquid (0.04 g, 21%): $^1$H NMR ($CDCl_3$) $\delta$ 2.41−2.36 (m, 6H), 3.13−2.77 (m, 1H, OH), 3.44 (td, $J$ = 11.76, 2.44 Hz, 1H), 4.84 (d, $J$ = 11.76 Hz, 1H), 6.08 (dd, $J$ = 9.93, 2.39 Hz, 1H), 6.55 (dd, $J$ = 9.93, 2.47 Hz, 1H), 7.07 (t, 1H), 7.36−7.14 (m, 2H), 7.62−7.54 (m, 1H); $^{13}$C NMR $\delta$ 41.3, 67.5, 68.7, 124.4, 124.9, 126.3, 127.6, 128.0, 129.8, 132.0, 137.4; $m/z$ (GC−MS) 171.1 (Found: C, 76.01; H, 7.8; N 7.2; $C_{12}H_{15}NO$ requires C, 76.16; H 7.99; N 7.4)

***cis*-1-Hydroxy-2-phenylthio-1,2,3,4-tetrahydronaphthalene (10, X = PhS).** To a stirred solution of (±)-*trans*-1-hydroxy-2-bromo-1,2,3,4-tetrahydronaphthalene[9] (9.5 g, 41.8 mmol) in DMF (50 mL) was added sodium thiophenolate (6.1 g, 46.2 mmol). The mixture was stirred for 15 h at 25 °C followed by dilution with water (150 mL) and extraction with EtOAc (3 × 75 mL). The EtOAc was washed with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water (4 × 50 mL) and the aqueous portion re-extracted (2 × 25 mL). The combined organic phases were dried over $Na_2SO_4$ and the solvent evaporated under reduced pressure to yield a crude product which was purified by crystallizing from cyclohexane to give a colorless solid (4.2 g, 39%): mp 85−87 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.0−2.3 (m, 2H), 2.76 (d, $J$ = 3.2 Hz, 1H), 2.9 (m, 1H), 3.1 (m, 1H), 3.65 (td, $J$ = 11.2, 3.09 Hz, 1H), 4.6 (s, 1H), 7.1−7.5 (m, 9H); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.8, 28.6, 52.0, 67.8, 126.2, 127.4, 128.2, 128.8, 29.2, 130.0, 132.03, 133.8, 135.7, 136.4; $m/z$ (GC−MS) 256.1 (Found: C, 74.87; H, 6.24; S, 12.46; $C_{16}H_{16}OS$ requires C, 74.96; H, 6.29; S, 12.51); HRMS = 257.1000 (calculated for $[M + H^+]^+$, $C_{16}H_{16}OS$), 257.0994 (observed).

***cis*-1-Acetoxy-2-phenylthio-1,2,3,4-tetrahydronaphthalene (11, X = PhS).** To *cis*-1-hydroxy-2-phenylthio-1,2,3,4-tetrahydronaphthalene (**10**, X = PhS, 3.5 g, 13.6 mmol) in dry pyridine (15 mL) was added acetic anhydride (2.1 mL, 20.4 mmol). The mixture was stirred for 20 h at room temperature, after which water (50 mL) was added and the pH adjusted to 5−6 using 10% hydrochloric acid (v/v) at 5−10 °C. The aqueous phase was extracted with $CHCl_3$ (3 × 75 mL) and the extracts washed with water (2 × 50 mL) and saturated NaCl solution (20 mL). The solvent was evaporated under reduced pressure to yield an oil (3.8 g, 93%): $^1$H NMR ($CDCl_3$) $\delta$ 2.07 (s, 3H), 2.09−2.35 (m, 2H), 2.88 (q, 1H), 3.06 (q, 1H), 3.60 (td, $J$ = 11.33, 3.50 Hz, 1H) 6.20 (d, $J$ = 3.07 Hz, 1H), 7.05−7.54 (m, 9H); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.0, 25.0, 26.6, 49.0, 70.3, 126.3, 127.2, 128.6, 128.9, 129.0, 130.0, 132.2, 134.1, 134.6, 136.1, 170.5; $m/z$ (ES) 299.1 $(M + H)^+$ (Found: C, 72.1; H, 5.9; S, 10.1; $C_{18}H_{18}O_2S$ requires C, 72.45; H, 6.08; S, 10.7); HRMS = 321.0925 (calculated for $[M + Na^+]^+$, $C_{18}H_{18}O_2S$), 321.0911 (observed).

***cis*-1-Hydroxy-2-phenylthio-1,2-dihydronaphthalene (6, X = *cis*-PhS).** *cis*-1-Acetoxy-2-phenylthio-1,2,3,4-tetrahydronaphthalene (**12**, X = PhS, 1.0 g, 3.35 mmol) was dissolved in $CCl_4$ (30 mL) and *N*-bromosuccinimide (0.59 g, 3.35 mmol) and a catalytic quantity of AIBN added. The mixture was heated under reflux with stirring (ca. 70 °C). When reaction was complete (1.5 h, by $^1$H NMR), the mixture was cooled to room temperature and filtered to remove succinimide. Removal of the solvent under reduced pressure gave an oil which was dissolved in THF (15 mL) and cooled to 0−5 °C. A 1.0 M solution of DIBAL-H (11.1 mL, 11.2 mmol, 1.0 M solution in THF) was added slowly over 45 min. The resultant reaction mixture was stirred for 30 min at 0−5 °C and quenched with 1.0 M HCl at −10 °C (the final pH of the mixture is 5−6) followed by extraction with ethyl acetate (3 × 25 mL). The combined organic phases were dried over $Na_2SO_4$ and the solvent removed under reduced pressure to give an oil, which was dissolved in DMSO (75 mL). Tetrabutylammonium fluoride hydrate (1.75 g, 6.7 mmol) was added and the suspension stirred for 4 h at 25 °C, followed by dilution with water (150 mL) and extraction into EtOAc (3 × 100 mL). The EtOAc was washed with water (6 × 100 mL), dried and the solvent evaporated under reduced pressure to yield a crude product which was purified by preparative TLC (30% ethyl acetate in pentane) to give a cream-colored solid (0.2 g, 24%): $^1$H NMR ($CDCl_3$) $\delta$ 2.9 (d, $J$ = 10.3 Hz, OH), 4.09 (t, $J$ = 5.85 Hz, 1H), 5.06 (dd, $J$ = 10.2, 6.1 Hz, 1H), 6.12 (dd, $J$ = 9.5, 5.6 Hz, 1H), 6.46 (d, $J$ = 9.5 Hz, 1H), 6.9 (d, $J$ = 7.4 Hz, 1H), 7.1−7.3 (m, 7H), 7.55 (d, $J$ = 7.5 Hz, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 52.2, 69.1, 125.1, 125.9, 126.2, 127.5, 127.8, 128.3, 128.5, 129.1, 132.1, 132.9, 133.3, 136.5; $m/z$ (ES) 255 $(M + H)^+$; HRMS = 255.0844 (calculated for $[M + H^+]^+$, $C_{16}H_{14}OS$), 255.0838 (observed).

***cis*-1-Hydroxy-2-phenylsulfonyl-1,2-dihydronaphthalene (6, X = *cis*-PhSO$_2$).** To an ice-cold solution of *cis*-1-hydroxy-2-phenylthio-1,2-dihydronaphthalene (**6**, X = *cis*-PhS, 40 mg, 0.157 mmol) in $CHCl_3$ (10 mL) was added *m*-chloroperbenzoic acid (54 mg, 0.31 mmol) over 15 min with stirring. The reaction mixture was allowed to come to room temperature and stirred for 2 h. When the starting material had been consumed (TLC), undissolved benzoic acid was removed by filtration and the solvent evaporated under reduced pressure. The crude product was purified by column chromatography (ethyl acetate/pentane mixtures) to yield the product as a light brown liquid (25 mg, 56%): $^1$H NMR ($CDCl_3$) $\delta$ 4.15 (t, $J$ = 5.64 Hz, 1H), 5.21 (m, $J$ = 5.97 Hz, 1H), 6.07 (dd, $J$ = 9.56, 5.51 Hz, 1H), 6.53 (d, $J$ = 9.54, Hz, 1H), 6.65 (d, $J$ = 7.36, Hz, 1H), 7.05 (t, $J$ = 7.64 Hz, 1H), 7.21−7.27 (m, 3H), 7.42 (t, $J$ = 7.32, Hz, 1H), 7.52 (d, $J$ = 7.58 Hz, 1H), 7.59 (d, $J$ = 7.53 Hz, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 64.9, 68.7, 118.5, 124.9, 126.6, 127.9, 128.0, 129.1, 129.5, 131.2, 133.6, 134.0, 135.6, 136.4; $m/z$ (ES) 309.1 $(M + Na)^+$; HRMS = 309.0561 (calculated for $[M + Na^+]^+$, $C_{16}H_{14}O_3S$), 309.0563 (observed).

***cis*-1-Hydroxy-2-azido-1,2,3,4-tetrahydronaphthalene (10, X = N$_3$).** To a stirred solution of (±)- *trans*-1-hydroxy-2-bromo-1,2,3,4-tetrahydronaphthalene (10.5 g, 46.2 mmol) in DMF (30 mL) was added sodium azide (3.3 g, 50.7 mmol). Stirring was continued for 20 h at 75 °C and the mixture then cooled to 25 °C and diluted with water (150 mL). The products were extracted with chloroform (3 × 150 mL) and the combined organic layers washed with water (5 × 100 mL) and dried over sodium sulfate. The solvent was removed to yield a crude product, which was crystallized in cyclohexane to give an off-white solid (4.5 g, 51% yield): mp 82−85 °C; $^1$H NMR ($CDCl_3$) $\delta$ 1.95−2.44 (m, 2H and OH), 2.84 (m, 1H), 3.04 (td, $J$ = 17.25, 5.78 Hz, 1H), 3.90 (td, $J$ = 9.67, 3.11 Hz, 1H), 4.78 (d, $J$ = 2.77 Hz, 1H), 7.07−7.19 (m, 1H), 7.18−7.35 (m, 2H), 7.55−7.36 (m, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.7, 26.7, 61.7, 69.3, 126.5, 128.3, 128.6, 129.3, 135.3, 135.8; $m/z$ (ES) 190.1$(M + H)^+$; IR $\upsilon$ ($cm^{-1}$) 1454, 3434 (Found: C, 63.4; H, 5.79; N, 22.17; $C_{10}H_{11}N_3O$ requires C, 63.48; H, 5.86; N, 22.21).

***cis*-1-Acetoxy-2-azido-1,2,3,4-tetrahydronaphthalene (11, X = N$_3$).** To a stirred solution of (±) *cis*-1-hydroxy-2-azido-1,2,3,4-tetrahydronaphthalene (**11**, X= $N_3$, 3.0 g, 15.8 mmol) in pyridine (15 mL) was added acetic anhydride (6.0 mL, 58.8 mmol) at room temperature. The mixture was stirred at 25 °C for a further 20 h, cooled to 5 °C and the pH adjusted to 5−6 with 10% hydrochloric acid. After extraction with chloroform (3 × 50 mL) the combined organic layers were washed with water (3 × 50 mL) and dried over sodium sulfate. The solvent was removed to yield an off white solid (3.0 g 82%): $^1$H NMR ($CDCl_3$) $\delta$ 2.2 (s, 3H), 2.8−2.95 (m, 2H), 3.08 (td, $J$ = 7.27, 5.43 Hz, 2H), 3.83 (td, $J$ = 10.14, 3.10 Hz, 1H), 6.18 (d, $J$ = 3.13 Hz, 1H), 7.1−7.36 (m, 4H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 170.5, 135.9, 132.8, 129.6, 128.7, 128.7, 126.5, 70.6, 58.8, 26.8, 23.3, 21.1; $m/z$ (EI) 232.1$(M + H)^+$; IR $\upsilon$ ($cm^{-1}$) 1454, 3434 (Found: C, 62.2; H, 5.61; N, 17.93; $C_{12}H_{13}N_3O_2$ requires C, 62.3; H, 5.67; N, 18.1).

***cis*-1-Hydroxy-2-azido-1,2-dihydronaphthalene (6, X = *cis*-N$_3$).** *cis*-1-Acetoxy-2-azido-1,2,3,4-tetrahydronaphthalene (**11**, X = $N_3$, 0.5 g, 2.16 mmol) was dissolved in dry $CCl_4$ (20 mL) and *N*-bromosuccinimide (0.38 g, 2.16 mmol) and a catalytic quantity of AIBN added. The mixture was heated under reflux (ca. 70 °C) and on completion of the reaction (1.5 h, by $^1$H NMR), cooled to room temperature and filtered to remove succinimide. Removal of the solvent under reduced pressure gave the crude bromo compound as an oil, which was dissolved in dry THF (25 mL) cooled to 0 °C and sodium methoxide (0.23 g, 4.32 mmol) added. The mixture was stirred for 3 h at 0 °C and left overnight in a freezer. Cold diethyl ether (15 mL) was added and salts removed by filtration through Celite. The filtrate was quickly washed with cold water (20 mL) and dried over $Na_2SO_4$ followed by evaporation under reduced pressure. The crude product was purified by preparative TLC (20% ethyl acetate in pentane) to yield an off-white solid (0.1 g, 33%): mp 75−77 °C; $^1$H NMR ($CDCl_3$) $\delta$ 2.27 (d, $J$ = 9.83 Hz, 1H), 4.15 (t, $J$ = 5.13 Hz, 1H), 4.89 (dd, $J$ = 9.71, 5.11 Hz, 1H), 6.07 (dd, $J$ = 9.57, 5.17 Hz, 1H), 6.78 (d, $J$ = 9.57 Hz, 1H), 7.15 (m, 1H), 7.3 (m, 2H), 7.57 (d, $J$ = 7.23 Hz, 1H); $^{13}$C NMR ($CDCl_3$) 59.6, 70.2, 122.0, 125.8, 127.0, 128.4, 129.0, 131.4, 132.1, 135.8; HRMS = 188.0824 (calculated for $[M + H^+]^+$, $C_{10}H_9N_3O$), 188.0832 (observed).

***cis*-1-Hydroxy-2-amino-1,2-dihydronaphthalene (6, X = *cis*-NH$_2$).** To a solution of *cis*-1-hydroxy-2-azido-1,2-dihydronaphthalene[9] (**6**, X = *cis*-$N_3$, 0.05 g, 0.26 mmol) in anhydrous THF (5 mL) was added a mixture of zinc powder (0.17 g, 2.67 mmol) and cobalt chloride hexahydrate (0.76 g, 3.2 mmol) under a nitrogen atmosphere. After 45 min TLC showed that starting material had been consumed and the reaction mixture was diluted with 15 mL of THF and filtered. Evaporation of the filtrate gave a crude product which was purified by flash column chromatography (EtOAc/hexane, MeOH) to yield a light brown oil (0.035 g, 81%): $^1$H NMR ($CD_3OD$) $\delta$ 3.49 (t, 1H), 3.54−3.58 (m, 3H, OH and $NH_2$), 4.58 (d, $J$ = 5.04 Hz, 1H), 5.91 (dd, $J$ = 9.64,


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3.85 Hz, 1H), 6.51 (dd, $J$ = 9.63, 1.56 Hz, 1H), 7.08−7.42 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 62.8, 71.8,127.5, 128.4, 128.8, 129.0, 129.2, 131.6, 133.6, 137.3; $m/z$ (ES) 162.1 $(M + H)^+$; HRMS = 162.0919 (calculated for $[M + H^+]^+$, $C_{10}H_{11}NO$), 162.0920 (observed).

***cis*-1-Hydroxy-2-methoxy-1,2-dihydronaphthalene (6, X = *cis*-MeO).** To a solution of *cis*-1,2-dihydroxy-1,2-dihydronaphthalene (**6**, X = *cis*-OH, 0.5 g 3.08 mmol) in DMF (20 mL) was added sodium hydride (0.15 g, 6.25 mmol) followed by (slowly over ten minutes) dimethyl sulfate (0.77 g 6.2 mmol). The mixture was stirred for 20 h at room temperature and quenched with 1 mL of acetic acid followed by dilution with water (50 mL). It was extracted with diethyl ether (2 × 50 mL) and the ether washed with water, dried ($Na_2SO_4$) and evaporated to yield a mixture of *cis*-dimethoxy-dihydronaphthalene and two methoxy hydroxy regioisomers which was purified and separated by column chromatography (diethylether-hexane mixture) to give the desired product (0.08 g, 18%):. $^1$H NMR ($CDCl_3$) $\delta$ 2.6 (b, 1H), 3.45 (s, 3H), 4.00 (t, $J$ = 4.4 Hz, 1H) 4.78 (b, 1H) 6.08 (dd, $J$ = 9.6, 3.9 Hz, 1H), 6.59, (dd, $J$ = 9.6 Hz, 1H), 7.1−7.55 (m, 4H); $m/z$ (GC−MS) 156 ($M - H_2O$) (Found C 74.32, H 6.99; $C_{11}H_{12}O_2$ requires C 74.98, H 6.86). The discrepancy in the microanalysis is consistent with the presence of residual diethyl ether in the analytical sample.

***cis*-1-Hydroxy-2-phenoxy-1,2-dihydronaphthalene (6, X = *cis*-PhO).** A suspension of $PhBF_3^-K^+$ (0.34 g, 1.85 mmol), Cu-$(OAc)_2{\cdot}H_2O$ (0.02 g, 0.10 mmol),[12] DMAP (0.030 g, 0.24 mmol) and powdered 4 Å molecular sieves (0.5 g) in $CH_2Cl_2$ (15.0 mL) were stirred for 5 min at room temperature and *cis*-naphthalene-1,2-dihydrodiol[1] (0.2 g, 1.23 mmol) added. The reaction flask was sealed with a rubber septum and the mixtured stirred under an atmosphere of oxygen (delivered via a balloon) for 15 h at 35−40 °C. The reaction mixture was filtered through Celite and concentrated under reduced pressure to afford the crude product which was purified by column chromatography (EtOAc and pentane mixtures) to give a white crystalline solid (0.2 g, 69%): $^1$H NMR ($CDCl_3$) $\delta$ 5.40 (ddd, $J$ = 9.11, 3.37, 1.26 Hz, 1H), 5.62 (d, $J$ = 9.11 Hz, 1H), 6.00 (dd, $J$ = 9.90, 3.39 Hz, 1H), 6.50 (d, $J$ = 9.89 Hz, 1H), 7.12 (m, 1H), 7.37−7.3 (m, 4H), 7.47−7.43 (m, 1H), 7.55 (m, 1H), 7.84−7.82 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 73.5, 74.5, 124.7, 127.4, 127.7, 128.5, 129.2, 130.1, 130.7, 131.1, 131.4, 134.9; $m/z$ (100%) 239 $(M + H)^+$; HRMS = 238.09935 (calculated for $[M + H^+]^+$, $C_{16}H_{14}O_2$), 238.0994 (observed).

***trans*-1,2-Dihydroxy-1,2,3,4,-tetrahydronaphthalene 13.** Pd/C (10%, 10 mg) was added to *trans*-1,2-dihydroxy-1,2-dihydronaphthalene[31] (0.2 g, 6.1 mmol) in methanol (25 mL) and the mixture stirred under a hydrogen atmosphere for 5 h. After consumption of the reactant (TLC), the mixture was filtered through Celite and the filtrate concentrated under reduced pressure to yield a colorless solid which was crystallized from dichloromethane (0.14 g, 70%); $^1$H NMR ($CDCl_3$) $\delta$ 1.9 − 2.1 (m, 1H), 2.1−2.2 (m, 1H), 2.69−2.86 (m, 1H), 2.98 (m, 1H), 3.82 (ddd, $J$ = 11.4, 8.0, 3.65 Hz, 1H), 4.7 (d, $J$ = 8.0 Hz, 1H), 7.1−7.45 (m, 4H).[33]

***cis*-1,2-Dihydroxy-1,2,3,4,-tetrahydronaphthalene 12.** This product was prepared from *cis*-1,2-dihydroxy-1,2-dihydronaphthalene[1] by the method described for its *trans* isomer **13**. It was isolated as a colorless solid (85 mg, 84%) $^1$H NMR ($CDCl_3$) $\delta$ 1.9 (m, 2H), 2.36 (bs, 2H), 2.7−3.0 (m, 2H), 4.0 (td, $J$ = 9.8, 3.5 Hz, 1H), 4.7 (d, $J$ = 3.6 Hz, 1H), 7.1−7.45 (m, 4H).[15,34]

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Measurements of rate constants, selected UV spectra, product analyses, HPLC analysis of equilibration of *cis*- and *trans*-1,2-dihydroxy-1,2,3,4-tetrahydronaphthalenes, NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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