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Tautomeric Equilibria and Pi Electron Delocalization for Some Monohydroxyarenes—Quantum Chemical Studies†

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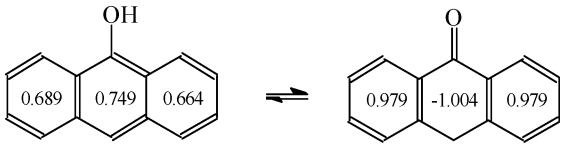


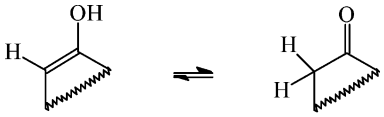
< 0.1 % gas phase ~100 %

~1 % water ~99 %

Keto−enol tautomeric interconversions and variations of the π-electron distribution were studied for 11 isolated monohydroxyarenes at the DFT(B3LYP)/6-311++G(2df,2p) level. For two monohydroxyarenes (phenol and 9-anthrol), the PCM model of solvation (water) was also applied to the DFT geometries. The geometry-based HOMA index was applied to estimate π-electron delocalization in the keto and enol tautomeric forms. Thermodynamic parameters of tautomeric interconversions (ΔE_T, ΔG_T, $T\Delta S_T$, pK_T) were calculated to estimate relative stabilities of individual tautomers and their percentage contents in the tautomeric mixtures. In almost all cases, the aromatic enol forms are strongly favored. An exception is 9-anthrol, which prefers its keto form. The resonance stabilization of this form comes from the central ring. Generally, aromaticity is the main factor that influences tautomeric equilibria in monohydroxyarenes. Hydration effect is considerably smaller and it does not change the tautomeric preference.

Introduction

It is well-known that monohydroxyarenes, classical examples of aromatic systems containing one *exo*-OH group, display keto−enol tautomerism similar to that observed in aliphatic open-chain and cyclic keto−enol systems.[1−3] During tautomeric interconversion, a proton is transferred from one conjugated site to the other conjugated site (i.e., from the *exo*-OH group to the ring carbon atom in the enol form or from the ring carbon to the *exo*-O-carbonyl atom in the keto form), and the migration of π electrons takes place in parallel.



enol keto

For the majority of cyclic and acyclic aliphatic derivatives, the keto forms are favored,[1,3] whereas monohydroxyarenes prefer the enol forms.[2,3] Only in some substituted and condensed phenols may this behavior be different due to additional internal effects, such as stabilities of functionalities, substituent effects, exceptional π-electron delocalization, and intramolecular H bonding.[2−5] Undoubtedly, in the case of aromatic systems, there is a problem of conjugation of the OH group to the aromatic system and of CO also being involved in conjugation with the

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π-electron system, which is not aromatic as a whole but may contain an aromatic part.

These differences in the tautomeric preferences for aliphatic and aromatic systems are usually discussed using energies of tautomerization (or tautomeric equilibrium constants), which qualitatively describe the relative stabilities of individual tautomers in tautomeric mixtures. High stability and preference of one tautomeric form in phenols are often explained by π-electron delocalization in the aromatic system. Katritzky and co-workers showed that the aromatic stabilization energy (25 $\pm$ 5 kcal mol^{-1}) of unsubstituted phenol (enol form) is considerably higher than the energy of tautomeric interconversion from the enol to the keto form (13 $\pm$ 3.5 kcal mol^{-1}).[6]

The aim of this paper is to analyze the variation of π-electron distribution during the keto−enol tautomerism in various monohydroxyarenes, such as unsubstituted phenol, 1- and 2-naphthols, 1-, 2-, and 9-anthrols, and 1-, 2-, 3-, 4-, and 9-phenanthrols. For our analysis, the HOMA index (Harmonic Oscillator Model of Aromaticity)[7] was selected and applied to geometrical parameters calculated (Gaussian 03)[8] for isolated tautomers using the DFT(B3LYP) method and the 6-311++G-(2df,2p) basis set.[9] The DFT method with the B3LYP functional has been successfully applied to study the keto−enol tautomerism in acyclic systems, and it has been shown recently that the computed energy of tautomerization is even in better agreement with the experimental one than that estimated at the G1 and G2 levels.[10] The HOMA index is the geometry-based measure of π-electron delocalization recommended by Schleyer[11] as an upright measure of aromaticity. Among various descriptors of aromaticity (geometric, energetic, and magnetic) proposed in the literature, the HOMA index describes the π-electron delocalization in tautomeric systems (both cyclic and acyclic) very well.[3] Transition states of the tautomerization processes were not considered here.

Because it is well-known that tautomeric equilibria are strongly dependent on solvent polarity for cyclic hydroxypyridine/pyridone[3,12,13] as well as for acyclic keto−enol tautomeric systems (e.g., malonaldehyde and acetylacetone) able to form a quasi ring built of the π-electron chain with a H bond involved,[3,12,14] we also investigated the solvation (water) effect on tautomeric equilibria for two monohydroxyarenes (phenol and 9-anthrol) for which some experimental data are available.

A number of methods have been proposed in the literature for modeling solute−solvent interactions by computations.[15] Generally, two principal strategies are used: classical ensemble treatments and quantum chemical continuum models. The classical treatments are mainly represented by molecular dynamics simulations,[16] Monte Carlo statistical methods,[17] free energy perturbations,[18] and Langevin dipole models.[19] Currently, these methods are standard tools for investigations of biomolecules.[20] The quantum chemical approaches are based on the Onsanger reaction field theory.[21] They are incorporated into the ab initio schemes as self-consistent reaction field models. Included among them are the simplest reaction field model, which uses a spherical cavity.[22] The model is based on the methodology developed by Rivail, Rinaldi, and co-workers,[23] which uses an ellipsoidal cavity, the polarizable continuum model (PCM) developed by Tomasi and co-workers,[15b,h,24] and

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its modified versions isodensity PCM and self-consistent isodensity PCM,[25] which use the solute cavity defined by a set of overlapping spherical atoms having an approximate radii (e.g., 20% greater than the standard van der Waals radii[25]). The surface potential can be calculated by numerical or analytical differentiation, and solute−solvent interactions take a mutual polarization of solute and solvent into account in a self-consistent way. All these methods model the solvent as a continuum of the dielectric constant. The quantum chemical methods may be used for small molecules and for large complexes. For our analysis of hydration effect on tautomeric equilibria in monohydroxyarenes, we chose the PCM method, which has been successfully applied for tautomeric systems.[26] We used the recent version of the PCM model[24g] (with the default values of the scaled van der Waals radii of the constituent atoms), implemented for a variety of the quantum-chemical methods (including DFT) in the Gaussian 03 program.[8]

Results and Discussion

Geometry-Based HOMA Index. To describe quantitatively the π-electron delocalization in various π-electron systems and to define their aromatic nature, numerous theories were formulated. Various numerical measures of π-electron delocalization (classified as geometric, energetic, and magnetic indices of aromaticity) were proposed.[7c,27,28] An analysis of the relations between these descriptors of π-electron delocalization and tautomeric equilibria in selected acyclic and cyclic systems revealed that the geometric index (HOMA) describes the π-electron delocalization in both acyclic and cyclic systems very well.[3] The magnetic parameter (NICS, nucleus-independent chemical shift) can mostly be applied to cyclic π-electron systems. In acyclic as well as in cyclic tautomeric systems closed by an intramolecular H bond, the NICS index seems not to distinguish π-electron delocalization. Among various energetic criteria, the energy of tautomerization (ΔE_T or ΔG_T) and the tautomeric equilibrium constant (pK_T) give information not only about tautomeric preferences in the tautomeric mixture but also about the differences in the stabilities of tautomeric forms. They are thus related to changes in π-electron delocalization in individual tautomers. For this reason, we chose the HOMA index and the thermodynamic parameters of tautomeric interconversion to describe the relation between tautomeric equilibria and π-electron delocalization in various monohydroxyarenes.

The geometry-based HOMA index[7] was defined using bond lengths as shown by eq 1, where n is the number of bonds taken into account, α is a normalization constant, R_{opt} is the optimum bond length assumed for a full electron delocalized system, and R_i ($i = 1, 2, ..., n$) are the real bond lengths; HOMA = 1 for the system with all bonds equal to the optimal values (with complete π-electron delocalization) and HOMA $\leq$ 0 for nonaromatic and anti-aromatic (nondelocalized) systems. In tautomeric systems, where a proton is transferred from an sp^3 to an sp^2 atom, the negative values of HOMA result most often from the fact that in such cases double bonds are substantially shorter and the single bonds are substantially longer than those that were used for reference bonds in the procedure of the R_{opt} estimation.[7]

$$\mathrm{HOMA} = 1 - \alpha/n\Sigma(R_{opt} - R_i)^2 \qquad (1)$$

For all monohydroxyarenes, the total HOMA index for the whole molecule was used in two ways. First, when all bonds CC and CO were taken into account in the calculation, irrespective of the hybridization state of the ring carbon atom (that was bound to two hydrogen atoms (CH_2)) or of the oxygen atom in the *exo*-OH group. Second, when the bonds with atoms in an sp^3 state of hybridization are not taken into account (e.g., oxygen-sp^3 in the OH group of the enol form and ring carbon-sp^3 in the keto form). This was labeled as HOMA(sp^2). The total HOMA(sp^2) values are given in parentheses in all schemes. The partial HOMA indices were also calculated for individual rings of all tautomers.

Unsubstituted Phenol. For unsubstituted phenol (P_1), three intramolecular proton transfers corresponding to the keto−enol interconversions are possible (Scheme 1), two 1,3- and one 1,5-proton shifts. They lead to two identical 2,4-cyclohexadienones (P_2 and P_4) and one 2,5-cyclohexadienone (P_3), respectively. Katritzky and co-workers,[6a] considering 2,4-cyclohexadienone for the keto form and using the tautomeric equilibrium constants for the enolization process in this form and additionally in cyclohexanone in aqueous solution ($pK_T = -9.5 \pm 2.5$ and 5.4 ± 0.4, respectively), estimated the aromatic resonance energy difference between tautomeric forms of phenol. The value

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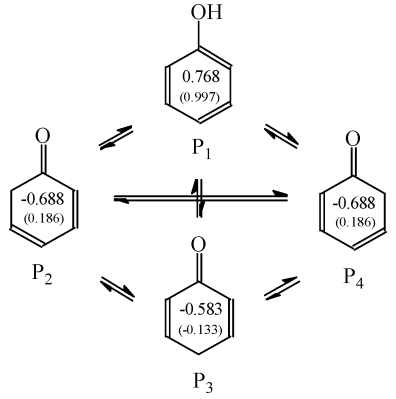
SCHEME 1. Tautomeric Equilibria in Unsubstituted Phenol and HOMA Indices Estimated at the DFT(B3LYP)6-311++G(2df,2p) Level for the Whole Keto and Enol Forms[a]



[a] The estimates include C-sp^3 and O-sp^3 atoms for the keto and enol forms, respectively, and for the corresponding fragments without C-sp^3 in the keto and O-sp^3 in the enol form (HOMA(sp^2) given in parenthesis).

TABLE 1. Thermodynamic Parameters (ΔE_T, ΔG_T, $T\Delta S_T$, and pK_T) for the $P_1 \rightleftharpoons P_i$ Tautomeric Interconversions in Unsubstituted Phenol (Scheme 1) and Percentage Contents of the Keto Forms (% P_i)[a]

equilibria	phase	ΔE_T[b,c]	ΔG_T[b,c]	$T\Delta S_T$[b,c]	pK_T	% P_i
$P_1 \rightleftharpoons P_2$	gas	18.26	17.46	0.80	12.80	2×10^{-11}
$P_1 \rightleftharpoons P_3$		17.14	16.88	0.26	12.37	4×10^{-11}
$P_1 \rightleftharpoons P_2$	water	20.21	19.45	0.77	14.26	5×10^{-13}
$P_1 \rightleftharpoons P_3$		18.21	17.88	0.33	13.11	8×10^{-12}

[a] Calculated in the gas phase and in aqueous solution at the DFT(B3LYP)/6-311++G(2df,2p) and PCM//DFT(B3LYP)/6-311++G(2df,2p) levels, respectively, at 298.15 K [b] In kcal mol^{-1}. [c] Zero-point vibrational energy is included. Scaled by the empirical factor of 0.9464.

obtained (25 ± 5 kcal mol^{-1}) was close to that estimated for simple aromatic hydrocarbons (30−50 kcal mol^{-1}).[6b,c,7c,27,29] In this way, they confirmed quantitatively higher stability of phenol (enol form) than its keto tautomers.

Our DFT calculations performed for isolated molecules showed that the keto forms (P_2−P_4) have higher energies than phenol (P_1) by 17−18 kcal mol^{-1} (Table 1), and among the keto forms, 2,5-cyclohexadienone (P_3) is slightly more stable than 2,4-cyclohexadienones (P_2 and P_4) in the gas phase. The contributions of cyclohexadienones in the gaseous tautomeric mixture are exceptionally small ($<10^{-10}$%). This observation is consistent with earlier literature HF, MP2, and B3LYP results.[30] However, Shiner et al.,[31] on the basis of measurements of the gas-phase acidities and the heats of formation of both keto forms, suggested that the 2,4-cyclohexadienone is more stable than 2,5-cyclohexadienone by a few kilocalories per mole.

A similar situation was found in aqueous solution. Hydration effect on energies of tautomerization is considerably smaller (ca. 1−2 kcal mol^{-1}) than the aromatic resonance energy difference between tautomeric forms (25 ± 5 kcal mol^{-1}),[6a] and thus, the tautomeric preference does not change in phenol. Application of the PCM model[24] of solvation (water) to geometries of the keto and enol forms of phenol optimized at the DFT(B3LYP)/6-311++G(2df,2p) level confirmed the fact that the keto forms (P_2−P_4) have higher energies than the enol form (P_1) by 18−20 kcal mol^{-1} (Table 1). The PCM model does not change the relative stabilities of the keto forms; 2,5-cyclohexadienone (P_3) is slightly more stable than 2,4-cyclohexadienones (P_2 and P_4). The tautomeric equilibrium constant estimated for 2,4-cyclohexadienone → phenol enolization in aqueous solution (p$K_T = -14$) is almost the same as that (p$K_T = -13$) found in the gas phase. Our PCM//DFT(B3LYP) results are consistent with earlier estimations of Katritzky and co-workers[6a] as well as with the experiment of Capponi and Gut,[32] who generated 2,4-cyclohexadienone by flash photolysis and, investigating the kinetics of the 2,4-cyclohexadienone → phenol enolization process in acidic and neutral aqueous solutions, they found the equilibrium constant (p$K_T = -13 \pm 1$) as being only slightly greater than that estimated by Katritzky and co-workers. All these observations indicate that from a physicochemical point of view the keto forms of phenol could be neglected in the tautomeric mixture. However, they are frequently invoked as reactive intermediates in many reactions, such as the Reimer−Tiemann and Kolbe−Schmitt reactions and electrophilic substitution.[2]

Analysis of the total HOMA indices estimated for the DFT geometries of the whole keto and enol tautomeric conjugated systems, built of seven heavy atoms, six carbons, and one oxygen, clearly shows that the transfer of the proton from the *exo*-OH group to the *endo*-(ring)-carbon atom destroys aromaticity of the ring and strongly destabilizes the keto form in comparison to the enol one. The total HOMA indices are negative for the keto forms (<−0.5), whereas the total HOMA index is positive for the enol form (0.768). Ionization of the system does not change this behavior.[33] The ionized system (deprived of one electron) prefers the enol form (phenol) similarly as the neutral one. As shown by Bouchoux and co-workers,[33] the energies of the ionized keto forms (radical cations of 2,4- and 2,5-cyclohexadienones) are considerably larger than that of the ionized enol form (radical cation of phenol) by more than 30 kcal mol^{-1} at the B3LYP/6-311++G(d,p) level. There is also no particular change in the total HOMA indices estimated for the B3LYP/6-311++G(d,p) geometries.[3] The total HOMA indices are negative for the ionized keto forms, and they are highly positive for the ionized enol form (0.703). This observation indicates how important aromaticity is in the system that even ionization does not change significantly the π-electron delocalization. It is important also to say that excluding bonds with sp^3 hybridized atoms raise up the HOMA(sp^2) index significantly for all cases (the data in parentheses). Interestingly, if the chain of conjugated π electrons is not branched (P_2 and P_4), the HOMA(sp^2) index is significantly greater than that for another case (P_3). The NICS index calculated according to Schleyer procedure[28] for phenol (−10.79) is strongly negative, typically as that for other aromatic systems, whereas this index is positive for the keto forms (P_2 and P_4, +5.14 and P_3, +3.19), indicating only their loss of aromaticity.

Naphthols. Naphthols (Scheme 2) containing two condensed phenyl rings display intramolecular proton transfers (keto−enol

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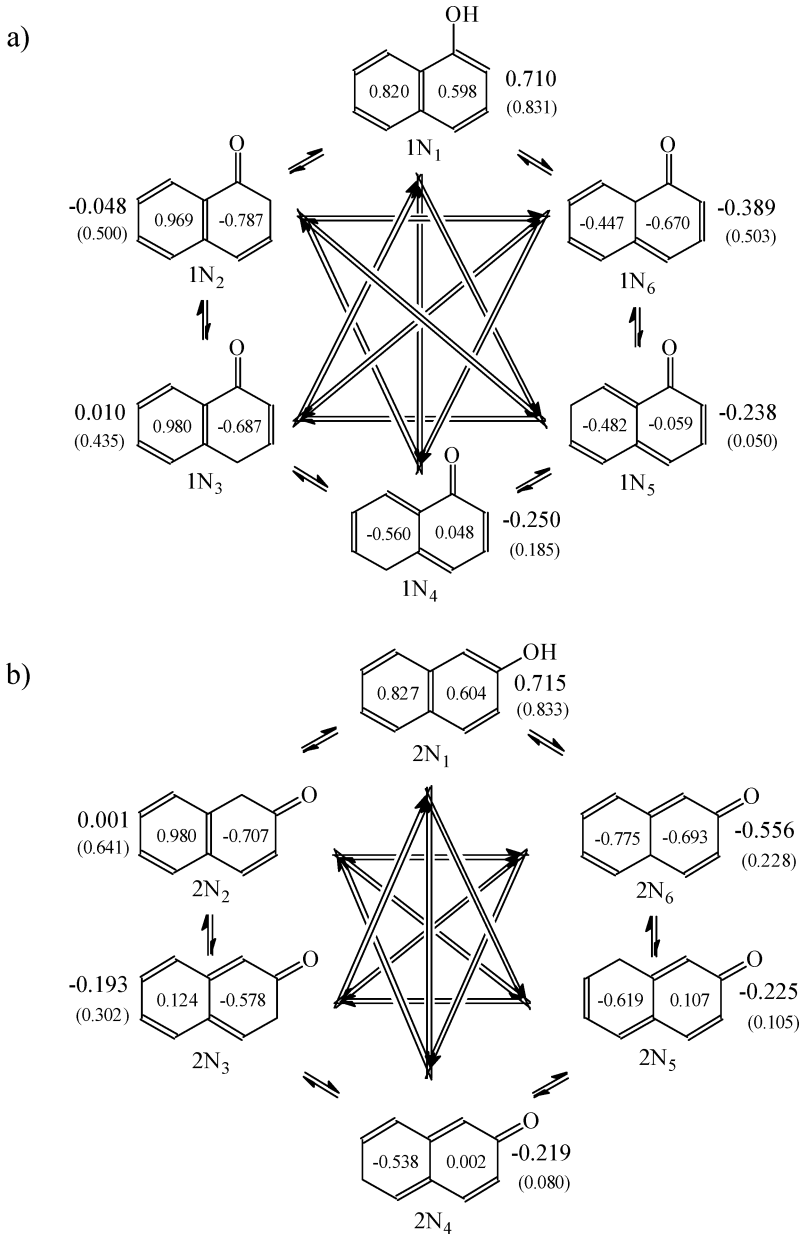
SCHEME 2. Tautomeric Equilibria in 1- (a) and 2-Naphthol (b) and HOMA Indices Estimated at the DFT(B3LYP)6-311++G(2df,2p) Level for the Individual Rings and for the Whole Molecule of the Keto and Enol Forms[a]



[a] The estimates include C-sp^3 and O-sp^3 atoms for the keto and enol forms, respectively, and for the corresponding fragments without C-sp^3 in the keto and O-sp^3 in the enol form (HOMA(sp^2) given in parenthesis).

interconversions) similar to those in unsubstituted phenol (Scheme 1). One difference is that the *exo*-OH group may be bonded to two different positions (1 and 2), and the proton of this group may be shifted not only to the carbon atoms of the phenyl ring possessing the OH group but also to the carbon atoms of the other condensed ring.

In 1-naphthol ($1N_1$), two 1,3- and one 1,5-proton shifts leading to three keto forms $1N_2$, $1N_6$, and $1N_3$, respectively, are similar to those in unsubstituted phenol. The proton of the *exo*-OH group is transferred to the carbons of the phenyl ring containing this group. However, two other 1,5-proton shifts leading to two additional keto forms, $1N_4$ and $1N_5$, are typical for condensed monohydroxyarenes. The proton of the *exo*-OH group is transferred to the carbons of the condensed ring (without the OH group).

In 2-naphthol ($2N_1$), the situation is analogous. Two 1,3- and one 1,5-proton shifts leading to three keto forms $2N_2$, $2N_3$, and $2N_6$, respectively, are similar to those in unsubstituted phenol. The proton of the *exo*-OH group is transferred to the carbons of the phenyl ring with this group. However, two other proton transfers, 1,5- and 1,7-proton shifts leading to two additional keto forms $2N_5$ and $2N_4$, respectively, are typical for condensed monohydroxyarenes. The proton of the *exo*-OH group is transferred to the carbons of the condensed ring.

Although the proton shifts are different in 1- and 2-naphthols, six tautomeric forms, one enol form, and five keto forms are possible for both monohydroxyarenes. Among them, the enol forms ($1N_1$ and $2N_1$) are favored (Table 2). However, both naphthols have slightly lower aromatic character (total HOMA 0.710 and 0.715, respectively, estimated for the whole tauto-

TABLE 2. Thermodynamic Parameters (ΔE_T, ΔG_T, $T\Delta S_T$, and pK_T) for the $N_1 \rightleftharpoons N_i$ Tautomeric Interconversions in Naphthols (Scheme 2) and Percentage Contents of the Keto Forms (% N_i)[a]

equilibria	ΔE_T[b,c]	ΔG_T[b,c]	$T\Delta S_T$[b,c]	pK_T	% N_i
$1N_1 \rightleftharpoons 1N_2$	8.93	8.23	0.71	6.03	9×10^{-5}
$1N_1 \rightleftharpoons 1N_3$	9.10	8.66	0.43	6.35	4×10^{-5}
$1N_1 \rightleftharpoons 1N_4$	33.04	31.98	1.06	23.43	4×10^{-22}
$1N_1 \rightleftharpoons 1N_5$	29.97	29.46	0.51	21.59	3×10^{-20}
$1N_1 \rightleftharpoons 1N_6$	37.00	36.67	0.33	26.88	1×10^{-25}
$2N_1 \rightleftharpoons 2N_2$	9.11	7.98	1.13	5.85	1×10^{-4}
$2N_1 \rightleftharpoons 2N_3$	29.36	28.27	1.08	20.72	2×10^{-19}
$2N_1 \rightleftharpoons 2N_4$	28.22	27.80	0.43	20.38	4×10^{-19}
$2N_1 \rightleftharpoons 2N_5$	30.26	29.34	0.92	21.51	3×10^{-20}
$2N_1 \rightleftharpoons 2N_6$	41.40	40.95	0.46	30.02	1×10^{-28}

[a] Calculated in the gas phase at the DFT(B3LYP}/6-311++G(2df,2p) at 298.15 K. [b] In kcal mol^{-1}. [c] Zero-point vibrational energy is included. Scaled by the empirical factor of 0.9464.

meric conjugated system, built of 11 heavy atoms: 10 carbons, and 1 oxygen) than unsubstituted phenol (total HOMA 0.768, estimated in the analogous way). Similar behavior has been observed for hydrocarbons. The HOMA index of naphthalene (0.827) is lower than that of benzene (0.974).[7c] Interestingly, excluding the CO bond (to OH group) increases the HOMA-(sp^2) values for both $1N_1$ (0.831) and $2N_1$ (0.833) to the value of HOMA for naphthalene itself. This follows the rule found for monosubstituted benzenes that substituent effect on the aromaticity of the ring is very weak.[34] Again, in all these cases, HOMA(sp^2) values are higher than those for the calculation carried out including sp^3 hybridized atoms (total HOMA). Important to say is that HOMA(sp^2) values for whole molecules are the highest for cases in which one ring is of Kekule structure for benzene: $1N_2$, $1N_3$, and $2N_2$, or the chain conjugated with carbonyl group is long as in $1N_6$, $2N_3$.

The difference in the aromatic character of the condensed rings in naphthols and of the single ring in phenol may partially explain why some nonaromatic keto forms, $1N_2$ and $1N_3$ of 1-naphthol and $2N_2$ of 2-naphthol, are more important in the tautomeric mixtures than the keto forms, P_2-P_4, in tautomeric phenol. The percentage contents of $1N_2$, $1N_3$, and $2N_2$ (with total HOMA indices of -0.048, 0.010, and 0.001, respectively, estimated for the whole molecules) are higher than 1×10^{-5}% (Table 2), whereas those of the keto forms, P_2-P_4, of phenol are smaller than 1×10^{-10}% (Table 1). Interestingly, for these important keto forms of naphthols ($1N_2$, $1N_3$, and $2N_2$), the partial HOMA indices of the condensed phenyl rings (without the OH group) increase almost to unity (0.969, 0.980, and 0.980, respectively) in comparison to those in the enol forms (0.820 in $1N_1$ and 0.827 in $2N_1$). The high aromatic character of these condensed rings seems to be sufficient to strongly increase the percentage contents of $1N_2$, $1N_3$, and $2N_2$ in tautomeric naphthols in comparison to those of P_2-P_4 in tautomeric phenol.

The partial HOMA indices of the less-important keto forms ($1N_4-1N_6$ and $2N_3-2N_6$) estimated for the individual rings as well as for the whole naphthol molecules are negative or close to zero, indicating high localization of π electrons (Scheme 2). Their percentage contents (ranging from 1×10^{-28}% to 5×10^{-19}%) are even smaller than those of the keto forms of phenol P_2-P_4 (ca. $1-3 \times 10^{-11}$%). This means that from the physicochemical point of view the nonaromatic less-important keto forms of naphthols ($1N_4-1N_6$ and $2N_3-2N_6$) can be neglected in the tautomeric mixtures.

Anthrols. Anthrols contain three condensed phenyl rings and one *exo*-OH group. This group may be bonded to the ring carbon atom at three different positions: 1, 2, and 9. As derivatives of monohydroxyarenes, anthrols display keto−enol interconversions similar to those in unsubstituted phenol and naphthols. The proton of the *exo*-OH group may be shifted to the carbon atoms of the phenyl ring possessing this group or to those of the other condensed rings. As shown earlier for naphthols, the proton transfers from the OH group to the carbon atoms of the condensed rings lead to nonaromatic and less-important keto forms. These forms may be neglected in tautomeric naphthols. Taking this observation into account, we considered for anthrols only the proton transfers from the OH group to the carbons of the phenyl ring containing this group, that is, one 1,3- and one 1,5-proton shift for 1-anthrol ($1A_1$) leading to two keto forms ($1A_2$ and $1A_3$, respectively), two 1,3-proton shifts for 2-anthrol ($2A_1$) leading to two keto forms ($2A_2$ and $2A_3$), and one 1,5-proton shift for 9-anthrol ($9A_1$) leading to one keto form ($9A_2$). Tautomeric equilibria selected in this way are given in Scheme 3.

DFT calculations show evidence that the enol forms ($1A_1$ and $2A_1$) are favored only for the 1- and 2-anthrols (Table 3). Both anthrols have slightly lower aromatic character than that of unsubstituted phenol similar to what has been found for naphthols. The total HOMA indices (0.677 and 0.665, respectively) estimated for the whole tautomeric conjugated systems, built of 15 heavy atoms: 14 carbons, and 1 oxygen, are smaller than that of unsubstituted phenol (total HOMA, 0.768, estimated in the analogous way). Similar behavior has been observed for hydrocarbons: anthracene (HOMA, 0.710) and benzene (HOMA, 0.974).[7c]

Similar to the case of naphthalene, the HOMA(sp^2) values for the systems with exclusion of sp^3 hybridized atoms are significantly larger than those for the other ones. Again, in tautomers with a unit of naphthalene $1A_2$, $1A_3$, $2A_2$, $2A_3$, and with two benzene rings as in $9A_2$, the HOMA(sp^2) values are relatively high (HOMA(sp^2) > 0.4).

It is also interesting to mention here that the percentage contents of one keto form ($2A_3$) is very small (1×10^{-22}%). This form may be neglected in tautomeric 2-anthrol. Negligible percentage contents of $2A_3$ may be explained by a strong decrease of the partial HOMA indices of each phenyl ring in $2A_3$ (partial HOMA close to zero or negative) in comparison to those in $2A_1$ (partial HOMA of 0.5−0.8). As described above, similar behavior is observed for the keto forms of unsubstituted phenol (P_2-P_4) and the less-important keto forms of naphthols ($1N_4-1N_6$ and $2N_3-2N_6$). For other keto forms of 1- ($1A_2$ and $1A_3$) and 2-anthrol ($2A_2$), only the phenyl rings with the O atom lose their aromaticity (partial HOMA negative). The other condensed rings in $1A_2$, $1A_3$, and $2A_2$ are highly aromatic. Their partial HOMA indices increase to about 0.8 in comparison to those of the enol forms $1A_1$ and $2A_1$. This increase of aromaticity of the condensed rings in the keto forms $1A_2$, $1A_2$, and $2A_2$ may explain their particularly high percentage contents ($>1 \times 10^{-3}$%) in the tautomeric mixtures. However, this is insufficient to change the tautomeric preferences in 1- and 2-anthrols from the enol to the keto forms.

Quite a different situation takes place in 9-anthrol. Although its enol form ($9A_1$) has aromatic character (total HOMA of 0.674, estimated for the whole molecule) similar to those of the other anthrols, the less aromatic keto form $9A_2$ (total HOMA of 0.262, estimated in similar way) predominates in the

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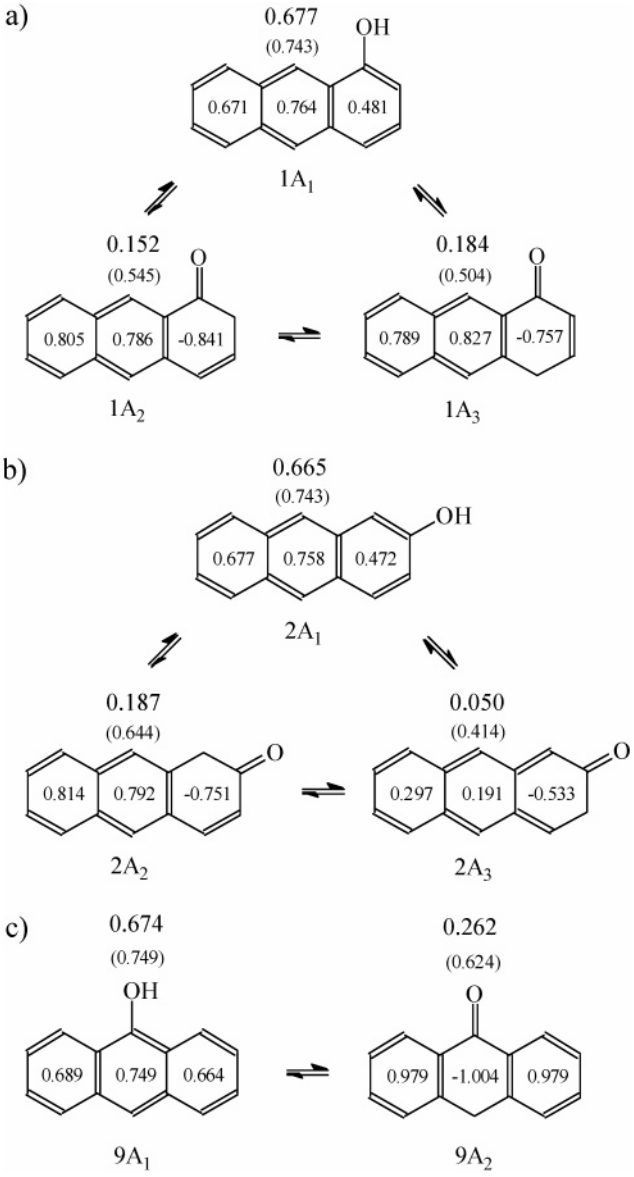
SCHEME 3. Tautomeric Equilibria in 1- (a), 2- (b), and 9-Anthrol (c), Limited to the Phenyl Ring Containing the *exo*-OH Group, and HOMA Indices Estimated at the DFT(B3LYP)6-311++G(2df,2p) Level for the Individual Rings and for the Whole Molecule of the Keto and Enol Forms[a]



[a] The estimates include C-sp^3 and O-sp^3 atoms for the keto and enol forms, respectively, and for the corresponding fragments without C-sp^3 in the keto and O-sp^3 in the enol form (HOMA(sp^2) given in parenthesis).

tautomeric mixture (99.9%). This is consistent with the earlier results of Kresge[35] and separately of More O'Ferrall and co-workers,[36] who suggested that resonance stabilization of the keto form comes from the central ring. Indeed, our ab initio calculations indicate that the partial HOMA index of the central ring (when six carbons and one oxygen were taken into account) decreases from the positive value of 0.749 in $9A_1$ to the negative value of -1.004 in $9A_2$ (Scheme 3c). On the other hand, the partial HOMA indices of both side phenyl rings increase from 0.689 and 0.664 in $9A_1$ to 0.979 in $9A_2$. This means that higher aromaticity of these phenyl rings in $9A_2$ than in $9A_1$ as well as higher stability of the carbonyl than the OH group may decide about the tautomeric preference in 9-anthrol. General behavior derived on the basis of the NICS index is the same. The NICS index estimated for the central ring in $9A_1$ is also more negative (-13.94) than those for the side rings (-8.33 and -8.14). In $9A_2$, this index is positive ($+4.64$) for the cental ring due to loss of its aromaticity, and it is negative (-9.39) for the aromatic side rings.

TABLE 3. Thermodynamic Parameters (ΔE_T, ΔG_T, $T\Delta S_T$, and pK_T) for the $A_1 \rightleftharpoons A_i$ Tautomeric Interconversions in Anthrols (Scheme 3) and Percentage Contents of the Keto Forms (% A_i)[a]

equilibria	phase	ΔE_T[b,c]	ΔG_T[b,c]	$T\Delta S_T$[b,c]	pK_T	% A_i
$1A_1 \rightleftharpoons 1A_2$	gas	5.19	4.49	0.71	3.29	5×10^{-2}
$1A_1 \rightleftharpoons 1A_3$		6.22	5.72	0.50	4.19	6×10^{-3}
$2A_1 \rightleftharpoons 2A_2$		5.42	4.58	0.85	3.36	4×10^{-2}
$2A_1 \rightleftharpoons 2A_3$		34.33	32.73	1.60	23.99	1×10^{-22}
$9A_1 \rightleftharpoons 9A_2$		−3.88	−4.23	0.35	−3.10	99.9
$9A_1 \rightleftharpoons 9A_2$	water	−2.17	−2.61	0.45	−1.91	98.8

[a] Calculated at 298.15 K in the gas phase at the DFT(B3LYP)/6-311++G(2df,2p) level and also in aqueous solution for 9-anthrol at the PCM//DFT(B3LYP)/6-311++G(2df,2p) level. [b] In kcal mol^{-1}. [c] Zero-point vibrational energy is included. Scaled by the empirical factor 0.9464.

The tautomeric equilibrium constant calculated at the PCM//DFT(B3LYP)/6-311++G(2df,2p) level for the keto−enol interconversion $9A_2 \rightarrow 9A_1$ in aqueous solution (pK_T = 1.91) is close to that (pK_T = 2.10) measured by More O'Ferrall and co-workers.[36] It is also not very much larger than that (pK_T = 3.10) estimated at the DFT(B3LYP)/6-311++G(2df,2p) level for the isolated tautomeric mixture in the gas phase. Not very different pK_T values found in aqueous solution and in the gas phase show additionally that hydration has a small effect on the contribution of the keto form in the tautomeric mixture (99% in aqueous solution and almost 100% in the gas phase). This may be explained by the fact that polar water has amphiprotic properties. Interacting as a weak base with the acidic enol form and as a weak acid with the basic keto form, it slightly changes their relative stabilities. This behavior may be completely different for solvents of potential basic properties that can stabilize the enol form and for solvents of potential acidic properties that can stabilize the keto form.[12] Low pK_T values observed in both phases (p$K_T \leq 3$) indicate additionally that both forms (anthrone and anthrol) may be observed experimentally.[37]

Phenanthrols. Phenanthrols (Scheme 4) contain also three phenyl rings and one *exo*-OH group similarly as anthrols, but the rings are differently condensed and, thus, the OH group may take five different positions: 1, 2, 3, 4, and 9. These differences lead to changes in π-electron distribution and in percentage of the contents of tautomeric mixtures.

Taking into account the observation that transfers of the proton from the OH group to the carbon atoms of the condensed phenyl rings lead to nonaromatic and less-important keto forms, we selected for phenanthrols only the proton transfers from the OH group to the carbon atoms of the phenyl ring containing this group, that is, one 1,3- and one 1,5-proton shift for 1- ($1PA_1$)

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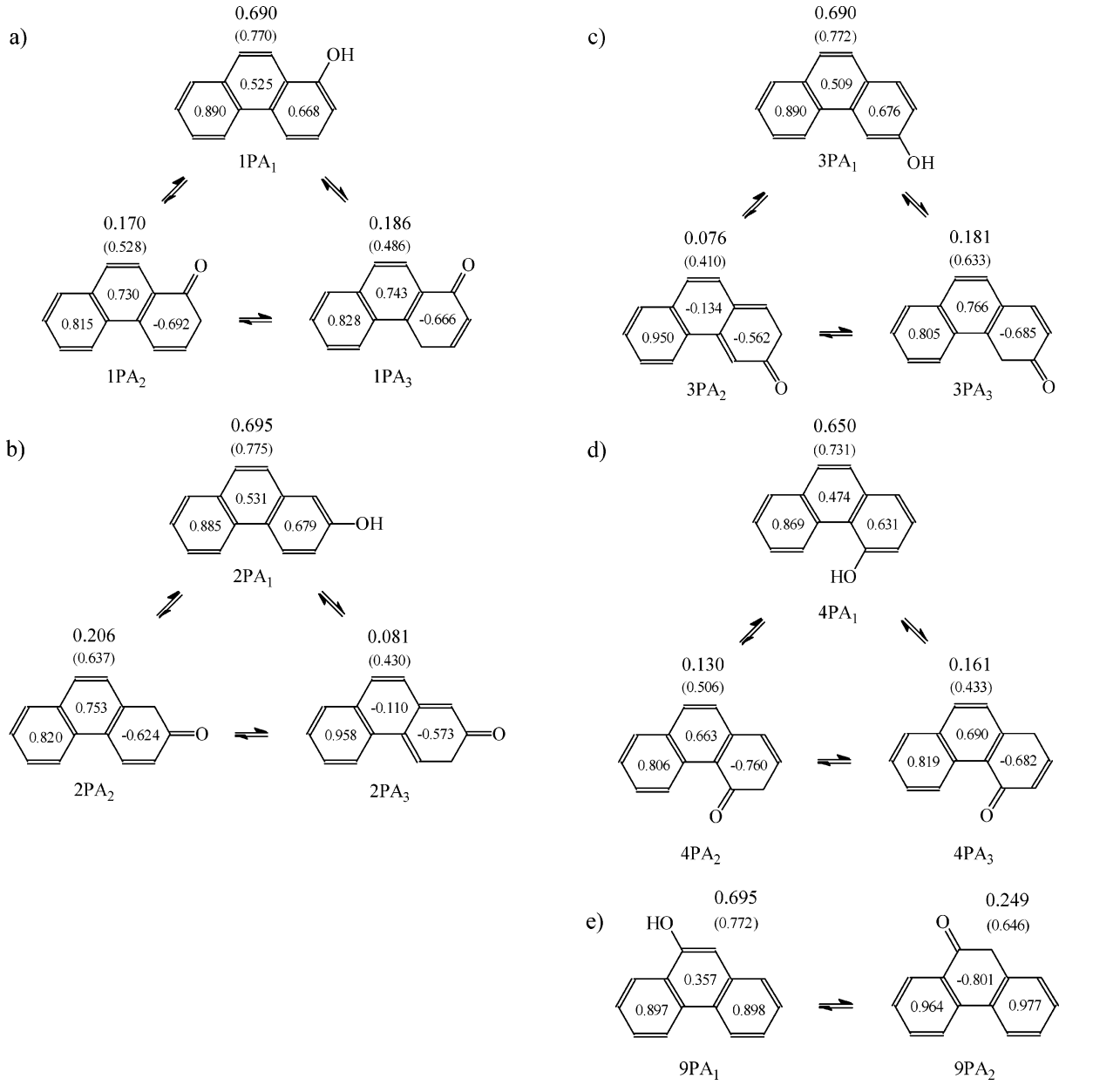
(36) McCann, G. M.; McDonnell, C. M.; Magris, L.; More O'Ferrall, R. A. *J. Chem. Soc., Perkin Trans. 2* **2002**, 784.
(37) (a) Mills, S. G.; Beak, P. *J. Org. Chem.* **1985**, *50*, 1216. (b) Powell, M. F. *J. Org. Chem.* **1987**, *52*, 56. (c) Freiermuth, B.; Hellrung, B.; Perterli, S.; Schultz, M. F.; Wintgens, D.; Wirz, J. *Helv. Chim. Acta* **2001**, *84*, 3796. (d) Abraham, R. J.; Mobli, M.; Smith R. J. *Magn. Reson. Chem.* **2003**, *41*, 26.

SCHEME 4. Tautomeric Equilibria in 1- (a), 2- (b), 3- (c), 4- (d), and 9-Phenanthrol (e), Limited to the Phenyl Ring Containing the *exo*-OH Group, and HOMA Indices Estimated at the DFT(B3LYP)6-311++G(2df,2p) Level for the Individual Rings and for the Whole Molecule of the Keto and Enol Forms[a]



[a] The estimates include C-sp^3 and O-sp^3 atoms for the keto and enol forms, respectively, and for the corresponding fragments without C-sp^3 in the keto and O-sp^3 in the enol form (HOMA(sp^2) given in parenthesis).

and 4-phenanthrols ($4PA_1$), leading to the corresponding pairs of their keto forms ($1PA_2$, $1PA_3$ and $4PA_2$, $4PA_3$), two 1,3-proton shifts for 2- ($2PA_1$) and 3- phenanthrols ($3PA_1$), leading to the corresponding pairs of their keto forms ($2PA_2$, $2PA_3$ and $3PA_2$, $3PA_3$), and one 1,5-proton shift for 9-phenanthrol ($9PA_1$), leading to one keto form ($9PA_2$).

Our DFT calculations performed for phenanthrols indicate that the enol forms ($1PA_1$, $2PA_1$, $3PA_1$, $4PA_1$, and $9PA_1$) are favored independently on the position of the OH group (Table 4). All enol forms have similar aromatic character as those of anthrols. The total HOMA indices for phenanthrols $1PA_1$, $2PA_1$, $3PA_1$, $4PA_1$, and $9PA_1$ (0.65−0.70), estimated for the whole tautomeric conjugated enol forms, are almost the same as those of anthrols $1A_1$, $2A_1$, and $9A_1$ (0.67−0.68). They are also higher than those of the corresponding keto forms (<0.25). Similarly as in the case of anthols, the keto tautomers exhibit high HOMA-(sp2) values if a naphthalene unit formed in the tautomer $1PA_2$, $1PA_3$, $2PA_2$, $3PA_3$, $4PA_2$, and $4PA_3$ or in two benzene rings separated by the ring with $COCH_2$ unit in the keto form $9PA_2$.

Some general analogy as well as some differences between phenanthrols and anthrols when going from the enol to the keto forms is also observed in variations of the partial HOMA indices of individual rings and in changes of the percentage contents of the keto forms in tautomeric mixtures. In phenanthrols, aromatic character of two condensed phenyl rings strongly increases the percentage contents of the keto forms (ca. 10^{10}−10^{15} times) in comparison to the keto forms possessing only one aromatic ring. In anthrols, this increase is even higher (ca.

TABLE 4. Thermodynamic Parameters (ΔE_T, ΔG_T, $T\Delta S_T$, and pK_T) for the $PA_1 \rightleftharpoons PA_i$ Tautomeric Interconversions in Phenanthrols (Scheme 4) and Percentage Contents of the Keto Forms (% PA_i)[a]

equilibria	ΔE_T[b,c]	ΔG_T[b,c]	$T\Delta S_T$[b,c]	pK_T	% PA_i
$1PA_1 \rightleftharpoons 1PA_2$	11.53	10.68	0.85	7.83	1×10^{-6}
$1PA_1 \rightleftharpoons 1PA_3$	10.65	10.48	0.17	7.68	2×10^{-6}
$2PA_1 \rightleftharpoons 2PA_2$	12.12	10.74	1.38	7.87	1×10^{-6}
$2PA_1 \rightleftharpoons 2PA_3$	24.69	23.60	1.10	17.30	5×10^{-16}
$3PA_1 \rightleftharpoons 3PA_2$	24.61	23.59	1.02	17.29	5×10^{-16}
$3PA_1 \rightleftharpoons 3PA_3$	10.98	10.45	0.53	7.66	2×10^{-6}
$4PA_1 \rightleftharpoons 4PA_2$	10.20	8.92	1.28	6.54	3×10^{-5}
$4PA_1 \rightleftharpoons 4PA_3$	10.43	9.85	0.57	7.22	6×10^{-6}
$9PA_1 \rightleftharpoons 9PA_2$	4.23	3.79	0.44	2.78	0.2

[a] Calculated in the gas phase at the DFT(B3LYP)/6-311++G(2df,2p) at 298.15 K. [b] In kcal mol^{-1}. [c] Zero-point vibrational energy is included. Scaled by the empirical factor 0.9464.

$\geq 10^{20}$ times), because less-important keto forms have solely nonaromatic rings. However, an increase of aromaticity of the marginal phenyl rings in $9PA_2$ (partial HOMA almost close to unity) seems to be insufficient to change the tautomeric preference in 9-phenanthrol as it takes place in the case of 9-anthrol. The contribution of the keto form $9PA_2$ (0.2%) in the tautomeric mixture is considerably smaller than that of $9A_2$ (99.9%).

The high aromatic character of the condensed phenyl rings without the OH group in the other important keto forms $1PA_2$, $1PA_3$, $2PA_2$, $3PA_3$, $4PA_2$, and $4PA_3$ (partial HOMA 0.66−0.83) has a smaller effect on their contribution in the tautomeric mixtures (1×10^{-6} to 3×10^{-5}%) than that in the corresponding anthrones $1A_2$, $1A_3$, and $2A_2$ ($>1 \times 10^{-3}$%). This may be explained by the fact that the partial HOMA indices of the central rings of these phenanthrols ($1PA_1$, $2PA_1$, $3PA_1$, and $4PA_1$) strongly increase when going from the enol to the keto forms, whereas the partial HOMA indices of the marginal aromatic rings slightly decrease. In the case of anthrols ($1A_1$ and $2A_1$), aromaticity of both condensed rings without the OH group increase in the keto forms $1A_2$, $1A_3$, and $2A_2$. Only the phenyl rings with the O atom lose their aromaticity (partial HOMA negative) in phenanthrones in a similar way as that in anthrones. On the other hand, the percentage contents of the less-important keto forms $2PA_3$ and $3PA_2$ ($6-7 \times 10^{-16}$%) is higher than those of $2A_3$ (1×10^{-22}%). This may be explained by the fact that although the partial HOMA indices of the central ring as well as the marginal ring with the O atom decrease in $2PA_3$ and $3PA_2$ to negative values, the other marginal ring gains its aromaticity (partial HOMA $\geq$ 0.95), whereas all rings in $2A_3$ lose their aromaticity (partial HOMA negative or close to zero).

Conclusions

Although aromaticity, with its high π-electron delocalization on the whole tautomeric system in the enol forms, plays an important role and decides about tautomeric preferences in a majority of monohydroxyarenes, other internal effects such as stability of functionalities and high π-electron delocalization in individual rings of condensed systems also influence tautomeric equilibria in the gas phase, particularly in the case when tautomeric equilibrium constants are not very different from unity. This behavior is strongly marked in 9-anthrol and 9-phenanthrol. The keto form of 9-anthrol ($9A_2$ in Scheme 3) is favored in the tautomeric mixture (99.9%), whereas in 9-phenanthrol, the enol form ($9A_1$ in Scheme 4) predominates. The contribution of its keto form ($9PA_2$) in the tautomeric mixture is considerably smaller (0.2%). The greater stability of the keto form of 9-anthrol ($9A_2$) than its enol form ($9A_1$) is consistent with the Clar rule (higher number of full aromatic sextets in the molecule and a more stable structure).[38] In the case of $9A_2$, one can assign two full aromatic sextets, whereas only one in $9A_1$.

Generally, the enol forms possess aromatic character (HOMA $\geq$ 0.5 for the total system as well as for the individual rings). Electron delocalization in the keto forms, in particular aromatic character of the condensed rings, strongly depends on the position of the *exo*-OH group. If the keto form represents a situation in which the resulting C=C double bond is a point bond with another fused ring (e.g., in $1N_2$, $1N_3$, $2N_2$, $1A_2$, $1A_3$, $2A_2$, $1PA_2$, $1PA_3$, $2PA_2$, $3PA_3$, $4PA_2$, $4PA_3$, and $9PA_2$), then the fused ring represents high aromatic character (HOMA(sp2) > 0.6). If the resulting double bond(s) is directed to the individual carbon(s) in a fused ring (e.g., in $2N_3$, $2A_3$, $2PA_3$, and $3PA_2$), then the fused ring exhibits low aromatic properties (HOMA close to zero or negative).

As shown for phenol and 9-anthrol, hydration has only a small effect on the tautomeric equilibria in monohydroxyarenes. When going from the gas phase to aqueous solution, the Gibbs free energies of tautomerization vary by less than 2 kcal mol^{-1}. This is not sufficient to change the tautomeric preference, even for an exceptional case of monohydroxyarene, 9-anthrol, for which ΔG_T is very low [−4.23 kcal mol^{-1} in the gas phase at the DFT(B3LYP)/6-311++(2df,2p) level and −2.61 kcal mol^{-1} in aqueous solution at the PCM//DFT(B3LYP)/6-311++(2df,2p) level]. The contribution of anthrone (keto form) in the tautomeric mixture is almost 100% in the gas phase and 99% in aqueous solution. In the case of phenol, the contribution of the more stable enol form is 100% in both phases, and the keto form can be neglected. Aromaticity of the enol form plays here the principal role.

Computational Details

The geometries of the keto−enol tautomers of unsubstituted phenol (Scheme 1), 1- and 2-naphthols (Scheme 2), 1-, 2-, and 9-anthrols (Scheme 3), and 1-, 2-, 3-, 4-, and 9-phenanthrols (Scheme 4) were optimized at the DFT(B3LYP)/6-311++G(2df,2p) level,[9] and vibrational frequencies were calculated using the Gaussian 03 program.[8] At the same level of theory, thermodynamic parameters, such as electronic energy (ΔE_T), Gibbs free energy (ΔG_T), entropy term ($T\Delta S_T$), and tautomeric equilibrium constants (pK_T), were calculated for each tautomeric interconversion, and the percentage contents of individual tautomers in the tautomeric mixtures were estimated. The PCM model[24] of solvation, implemented in the Gaussian 03 program[8] by default, was applied to geometries of the keto and enol forms of phenol and 9-anthrol optimized at the DFT(B3LYP)/6-311++G(2df,2p) level. To obtain the molecular cavity, the simple united atom topological model applied on atomic radii of the UHF force field was used. Only one value of the dielectric constant ($\epsilon = 78.39$) corresponding to water (polar solvent) was considered. To estimated the thermodymanic parameters (ΔE_T, $T\Delta S_T$, ΔG_T, and pK_T) and the percentage contents of the keto forms in water, the same thermal corrections as those found for isolated molecules were used. The zero-point vibrational energy and thermal corrections to the Gibbs free energy were scaled using the empirical factor 0.9464 (vacuum). This factor was derived

(38) (a) Clar, E. *Polycyclic Hydrocarbons*; Academic Press: London, 1964; Vol. 1 & 2. (b) Clar, E. *The Aromatic Sextet*; Wiley: London, 1972.

on the basis of experimental IR data for phenol[39] and its calculated vibrational frequencies. The same scaling factor was used for all derivatives.

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(39) Bist, H. D.; Brand, J. C. D.; Williams, D. R. *J. Mol. Spectrosc.* **1967**, *24*, 402.

Supporting Information Available: Complete details of computational results (atom coordinates and energies) at the DFT-(B3LYP)/6-311++G(2df,2p) and parameters of the PCM method. This material is available free of charge via the Internet at http://pubs.acs.org.

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