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Aromaticity as a Quantitative Concept. 6. Aromaticity Variation with Molecular Environment

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The classical aromaticity of most heterocycles, and of some carbocycles such as azulene, increases with the polarity of the medium as shown by experimental and calculated bond lengths, aromaticity indices, and dipole moments.

Introduction

The first paper of this series[1] demonstrated, by principal component analysis, that 12 common quantitative criteria of aromaticity defined two independent scales of aromaticity which we labeled “classical” and “magnetic” aromaticity. In particular, geometrical criteria, and notably the Pozharskii and Bird aromaticity indices, were essentially “classical”, whereas magnetic criteria defined “magnetic” aromaticity. Subsequent papers refined the treatment for 16 familiar five- and six-membered monocyclic heterocycles[2] and extended it to benzo-fused derivatives,[3] and to less familiar monocycles.[4] We applied semiempirical methods to calculate aromaticity indices[5] and have summarized this work.[6]

Contemporaneously with and since our earlier work, there has been considerable activity, and various additional criteria for aromaticity were proposed.[7] The relationship between resonance energies, local aromaticity and electronic delocalization has been discussed,[18] and heteroaromaticities have been calculated by the AM1 method.[19] Ring current has again been estimated for 1-substituted pyridiniums[20] and further used to calculate the aromaticity of annulenes.[21] The extent of 6π aromaticity in four-membered rings was evaluated.[22] Wiberg calculated similar resonance energies for benzene, pyridine, and diazines.[23] A definitive monograph on aromaticity by Minkin, Glukhovtsev, and Simkin has appeared,[24] supplementing their comprehensive overview of heteroaromaticity[25,26] which updated our earlier overview.[27] Bird modified his index to be applicable to rings of all sizes,[28] has applied his method to bicyclics,[29] *N*-oxides,[30] and phosphorus and arsenic compounds,[31] and modified his index to measure steric[32] and tautomeric effects on aromaticity.[33] Hosmane and Liebman use the difference between $X(CH{=}CH_2)_2$ and $X(Ph)_2$ derivatives and the five- and six-membered rings as a measure of the aromaticity in such ring systems.[34,35] Parkanyi[36] proposed a new multilinear approach. Krygowski has refined his harmonic oscillator aromaticity index (HOMA) and investigated substituent effects on aromaticity.[37]

The suggestion that aromaticity is at least a two dimensional phenomenon has been widely accepted.[24,25,33,38] Jug and Koester[38] examined this concept in detail: they selected eight criteria and concluded that energetic and magnetic criteria dominate. However, in none of this previous work has attention been paid to the possible variation of the degree of aromaticity of a compound with the environment of the molecule. Indeed, this possibility

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(7) These criteria include the following: whether folding of a planar conjugated system is endothermic or exothermic,[8] the magnitude of rotational barriers about exocyclic $C-NMe_2$ bonds,[9] heats of protonation to give an sp^3-hybridized ring carbon,[10] $^{13}C-^{13}C$ spin couplings,[11] the concepts of relative and absolute hardness[12,13] and of conjugated circuits,[14] the tendency for “reversion to type” as suggested kinetically by transition state energies[15] or thermodynamically by the reversibility of protonation of enol ethers,[16] and integral bond lengths.[17]

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Table 1. Bond Lengths (Å) and Aromaticity Indices for Azulene

		formally double bonds					formally single bonds						ΔN	ΔN%	I
phase	technique	1–2	3–10	4–5	6–7	8–9	2–3	10–4	5–6	7–8	9–10	9–1	(Pozharskii)		(Bird)
gas	AM1	1.381	1.390	1.358	1.361	1.355	1.445	1.412	1.416	1.416	1.484	1.459	0.246	49.8	67.4
dioxane	AM1	1.382	1.396	1.363	1.362	1.360	1.444	1.407	1.417	1.417	1.483	1.458	0.234	52.2	68.9
water	AM1	1.384	1.397	1.361	1.363	1.362	1.444	1.412	1.414	1.413	1.482	1.456	0.228	53.4	69.5

seems not to have been previously addressed anywhere in the extensive literature on aromaticity.

Results and Discussion

We now wish to point out that aromaticities are to be expected to, and do, vary in magnitude relatively, and in many cases absolutely, with molecular environment. We first illustrate this by considering benzene and azulene. Benzene, a centrosymmetric molecule with consequently no dipole moment, has a C–C bond length as determined by electron diffraction in the gas phase of 1.397 Å,[39] which is well within the experimental error of that found for the crystal by neutron diffraction of 1.398 Å:[40] this indicates that its geometry, and therefore aromaticity, is largely invariant with the medium.

Azulene (Figure 1), by contrast, has a dipole moment with the five-membered ring as the negative and the seven-membered ring as the positive pole. Microwave measurements have given 0.796 D as the gas phase dipole moment.[41] The dipole moment has also been measured in dioxane solution as 1.00 D.[42] Our calculations suggest that this difference is significant: the dipole moment is predicted, by AM1, to be 1.496 D in the gas phase and 1.757 D for solution in dioxane. Unfortunately, the microwave spectrum[41] and X-ray crystal structure determinations[43,44] of azulene do not give accurate bond lengths due to low ground state population (approximately 3% at 25 °C) and a disordered crystal, respectively. The bond lengths calculated by AM1 for azulene in the gas phase, in dioxane, and in water solution (at 20 °C) are shown in Table 1. It is immediately obvious that on average formally single bonds tend to become shorter as the dielectric constant is raised and formally double bonds tend to become longer. We can use the Pozharskii and Bird aromaticity criteria to express these variations quantitatively: The Pozharskii index $\Delta\bar{N}$ is the average of the fluctuations of all ring bonds, where n is the total number of differences between each possible pair of bond orders ΔN in the rings

$$\Delta\bar{N} = \frac{\sum \Delta N}{n} \tag{1}$$

The Bird index takes into account the degree of statistical uniformity of the bond orders of the ring, but uses the differences between the actual bond orders, N, and the arithmetic mean of these bond orders, N_o.

$$V = \frac{100}{N_o}\sqrt{\frac{\sum (N - N_o)^2}{n}} \tag{2}$$

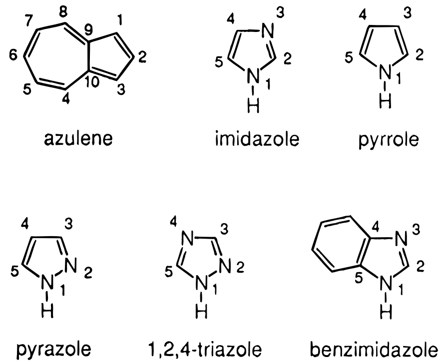

Figure 1. Structures and atom numbering convention used for compounds examined.

For azulene, ΔN% decreases from 53.4 to 49.8% from water to the gas phase, and the Bird index decreases from 69.5 to 67.4%. We therefore conclude that azulene is less aromatic in the gas phase than in media of higher dielectric constant.

Aromaticity variation with molecular environment is of particular significance in heterocyclic chemistry. Thus, in imidazole the two nitrogen atoms are of a fundamentally different type: the –NH– is an electron donor, whereas the –N= is an electron acceptor. Consequently, imidazole derivatives possess significant dipole moments (*cf.* Table 2). Imidazole itself has a measured dipole moment of 3.95 D in dioxane,[45] and a dipole moment of 3.67 D in the gas phase derived from microwave measurements.[46] We have now calculated, by AM1, the dipole moment for imidazole to be 3.60 D in the gas phase and 3.81 D in a medium of dielectric constant 2 (corresponding to dioxane), without any specific molecular solvation. The respective PM3 and *ab initio* SCF-calculated (6-31G* basis set) dipole moments in these two media are somewhat higher than the experimental values; however, identical relative shifts of the dipole moment values were obtained using any of the three methods. Therefore, the SCRF model describes reliably the polarization of imidazole in condensed media. When a water molecule (to act as a specific hydrogen bond acceptor toward the imidazole NH and to model the expected specific interaction with dioxane) is included together with the imidazole molecule in the solvent cavity, the AM1-calculated dipole moment increases to 4.15 D in satisfying agreement with the experimental values.

The bond lengths of substituted heteroaromatic compounds and other molecular systems are known to be affected by the solvent reaction field.[47–51] Measured and

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Table 2. Experimental Dipole Moments for Azoles (Gas Phase and Dioxane Solutions) and Calculated Dipole Moments for the Gas Phase and for Solution in Dioxane without and with specific Solvation

	experimental dipole moments					AM1-calculated dipole moments (D)					PM3-calculated dipole moments (D)					6-31G*-calculated dipole moment (D)		
	gas phase		dioxane															
	D	ref	D	ref	δ D	gas	dioxane	dioxane (SS)	δ (g−d)	δ (g−d*)	gas	dioxane	dioxane (SS)	δ (g−d)	δ (g−d*)	gas	dioxane	δ (g−d)
pyrrole	1.74	62	2.11	45	0.37	1.950	2.076	2.429	0.126	0.479	2.181	2.312	2.654	0.131	0.473	1.898	2.143	0.245
pyrazole	2.21	63	2.44	45	0.23	2.106	2.229	2.449	0.123	0.343	2.370	2.511	2.707	0.141	0.337	2.424	2.698	0.274
imidazole	3.67	46	3.95	45	0.28	3.598	3.814	4.149	0.216	0.335	3.862	4.095	4.426	0.233	0.331	3.864	4.297	0.403
1H-1,2,4-triazole	2.73	64	3.32	65	0.59	2.733	2.895	3.147	0.162	0.414	2.980	3.160	3.418	0.180	0.438	2.989	3.303	0.314
benzimidazole	3.26	66	3.97	65	0.71	3.136	3.356	3.768	0.220	0.632	3.268	3.546	3.852	0.278	0.584			

Table 3. Experimental and Calculated Bond Lengths (Å) and Values of Derived Aromaticity Indices for Imidazole

			formally double bonds		formally single bonds					
phase	technique	specif solv	2−3	4−5	1−2	3−4	5−1	Δ*N* (Pozharskii)	Δ*N*% (Pozharskii)	*I* (Bird)
gas	AM1	n	1.351	1.408	1.400	1.394	1.395	0.210	57.2	84.0
	6-31G*	n	1.289	1.350	1.349	1.372	1.372	0.323	34.1	58.8
dioxane	AM1	n	1.353	1.409	1.399	1.394	1.393	0.203	58.6	85.2
	6-31G*	n	1.291	1.350	1.348	1.372	1.370	0.319	35.0	59.6
dioxane	AM1	y	1.354	1.411	1.397	1.393	1.391	0.193	60.6	87.1
water	AM1	n	1.356	1.411	1.397	1.393	1.389	0.191	61.0	87.7
	6-31G*	n	1.294	1.351	1.345	1.374	1.367	0.314	36.0	60.7
water	AM1	y	1.355	1.411	1.397	1.391	1.390	0.190	61.2	87.8
water	AM1	y[a]	1.356	1.412	1.399	1.389	1.392	0.192	60.8	87.8
gas	MW[d]		1.314	1.364	1.364	1.382	1.377	0.290	40.9	75.6
crystal	neutron[c]		1.316	1.357	1.337	1.367	1.362	0.256	47.8	83.6[d]

[a] Two water molecules involved in specific solvation: one as H-acceptor, one as H-donor. [b] Reference 46. [c] Reference 52. [d] Lit. value 79.[28]

Table 4. Experimental and Calculated Bond Lengths (Å) and Values of Derived Aromaticity Indices for Pyrrole

			formally double bonds	formally single bonds				
phase	technique	specif solv	2−3[a]	1−2[b]	3−4	Δ*N* (Pozharskii)	Δ*N*% (Pozharskii)	*I* (Bird)
gas	AM1	n	1.402	1.392	1.435	0.243	50.4	82.3
	6-31G*	n	1.362	1.358	1.426	0.265	45.9	66.4
dioxane	AM1	n	1.402	1.391	1.435	0.240	51.0	82.7
	6-31G*	n	1.362	1.358	1.426	0.265	45.9	66.4
dioxane	AM1	y	1.404	1.390	1.434	0.231	52.8	84.1
water	AM1	n	1.403	1.390	1.435	0.234	52.2	83.7
	6-31G*	n	1.361	1.359	1.427	0.271	44.6	65.5
water	AM1	y	1.405	1.389	1.433	0.226	54.0	85.1
gas	MW[c]	n	1.382	1.370	1.417	0.239	51.3	85.6[d]

[a] And 4−5. [b] And 1−5. [c] Reference 62. [d] Lit. value 85.[28]

calculated bond lengths for imidazole in various environments are given in Table 3, together with the Pozharskii and Bird aromaticity indices derived from them. Values derived from AM1 and 6-31G* bond lengths for both of these indices increase successively on progressing from the gas phase to dioxane, to dioxane with specific solvation, to water, and to water with a single specific solvation, and finally to water with two specifically solvating water molecules. There are especially large increases in the aromaticity indices derived from experimental bond lengths in going from the gas phase to the crystal, presumably because of the very strong association in the crystal where the H-bonds are evidently near symmetrical, indicating a very strong H-bonding interaction. In the crystal, imidazole exists as roughly linear ribbons of molecules hydrogen bonded between N(1) and N(3) as determined by neutron diffraction.[52] This hydrogen bonding imparts negative character to N(1) and positive character to N(3), so in the crystal, each molecule is in a highly polar environment. Clearly imidazole is considerably more aromatic in a medium of high dielectric constant: as compared to the gas phase the formally single bonds all become significantly shorter and the formally double bonds lengthen somewhat (cf. Table 3), in qualitative agreement with experimental results. We conclude that the aromaticity of imidazole increases significantly with the polarity of the medium.

Table 2 also presents the experimental and AM1- and 6-31G*-calculated dipole moments for pyrrole, pyrazole, and 1*H*-1,2,4-triazole and AM1 dipole moments for benzimidazole for comparison with those for imidazole, discussed above. All of these heterocycles show significantly higher measured dipole moments in the solution than in gas phase. In the case of all heterocycles studied, the increases in dipole moments predicted by the semiempirical methods are also in good quantitative agreement with the increases determined experimentally, provided the dioxane model with specific solvation is followed: for pyrrole 0.37 *vs* 0.48 (AM1) or 0.47 (PM3), for pyrazole 0.23 *vs* 0.34 (AM1 or PM3), for 1,2,4-triazole 0.59 *vs* 0.41 (AM1) or 0.44 (PM3), and for benzimidazole 0.71 *vs* 0.63 (AM1) or 0.58 (PM3).

Tables 4−7 compare the experimental bond lengths, in the gas phase and in the crystal lattice, with those calculated theoretically for media of various dielectric constant. For pyrrole (Table 4), the importance of specific hydration is demonstrated: according to both criteria, water is less effective without this than dioxane is with

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Table 5. Experimental and Calculated Bond Lengths (Å) and Values of Derived Aromaticity Indices for Pyrazole

phase	technique	specif solv	formally dobule bonds		formally single bonds			ΔN	$\Delta N\%$	I
			2–3	4–5	1–2	3–4	1–5	(Pozharskii)		(Bird)
gas	AM1	n	1.359	1.402	1.333	1.446	1.398	0.184	62.4	91.8
	6-31G*	n	1.302	1.363	1.330	1.413	1.341	0.194	60.4	76.8
dioxane	AM1	n	1.360	1.403	1.333	1.446	1.398	0.183	62.6	92.0
	6-31G*	n	1.303	1.363	1.330	1.412	1.341	0.193	60.7	77.0
dioxane	AM1	y	1.361	1.405	1.332	1.445	1.396	0.177	63.8	93.2
water	AM1	n	1.361	1.404	1.333	1.445	1.397	0.180	63.2	92.6
	6-31G*	n	1.304	1.364	1.331	1.410	1.340	0.190	61.2	77.4
water	AM1	y	1.363	1.406	1.332	1.443	1.394	0.174	64.6	94.1
water	AM1	y[a]	1.365	1.408	1.332	1.442	1.393	0.170	65.3	94.8
gas	MW[63]		1.332	1.374	1.351	1.417	1.360	0.198	59.7	91.9
crystal	neutron[63]		1.337	1.389	1.352	1.371	1.328	0.210	57.2	92.5[b]

[a] Two water molecules involved in specific solvation. [b] Lit. value 90.[28]

Table 6. Experimental and Calculated Bond Lengths (Å) and Values of Derived Aromaticity Indices for 1*H*-1,2,4-Triazole

phase	technique	specif solv	formally double bonds		formally single bonds			ΔN	$\Delta N\%$	I
			2–3	4–5	1–2	3–4	1–5	(Pozharskii)		(Bird)
gas	AM1	n	1.365	1.351	1.335	1.406	1.407	0.166	66.1	92.4
	6-31G*	n	1.297	1.294	1.341	1.355	1.329	0.202	58.8	74.7
dioxane	AM1	n	1.366	1.352	1.334	1.407	1.406	0.167	65.9	92.4
	6-31G*	n	1.299	1.294	1.340	1.354	1.328	0.197	59.8	75.5
dioxane	AM1	y	1.368	1.355	1.333	1.404	1.404	0.158	67.7	94.5
water	AM1	n	1.366	1.354	1.332	1.406	1.406	0.167	66.0	92.7
	6-31G*	n	1.303	1.294	1.339	1.352	1.327	0.188	61.6	76.9
water	AM1	y	1.369	1.356	1.330	1.402	1.403	0.159	67.6	94.8
water	AM1	y[a]	1.371	1.357	1.330	1.401	1.401	0.153	68.8	96.0
gas	MW[64]		1.328	1.280	1.381	1.354	1.375	0.288	41.2	76.57
crystal	X-ray[55]		1.325	1.334	1.360	1.366	1.334	0.131	73.2	101.8[b]

[a] Two water molecules involved in specific solvation. [b] Lit. value 100.[28]

Table 7. Experimental and Calculated Bond Lengths (Å) and Values of Derived Aromaticity Indices for the Five-Membered Ring of Benzimidazole

phase	technique	specif solv	formally double bonds		formally single bonds			ΔN	$\Delta N\%$	I
			2–3	7a–3a	1–2	3–3a	1–7a	(Pozharskii)		(Bird)
gas	AM1	n	1.341	1.455	1.408	1.411	1.399	0.186	62.0	88.1
dioxane	AM1	n	1.343	1.457	1.408	1.413	1.397	0.184	62.5	88.9
dioxane	AM1	y	1.345	1.458	1.405	1.412	1.394	0.174	64.5	91.1
water	AM1	n	1.344	1.458	1.405	1.412	1.397	0.176	64.1	90.4
water	AM1	y	1.347	1.459	1.403	1.411	1.394	0.165	66.3	92.9
water	AM1	y[a]	1.350	1.458	1.402	1.411	1.395	0.159	67.6	93.9
gas	MW[66]		1.316	1.382	1.370	1.373	1.379	0.330	32.6	68.5
crystal	X-ray[64]		1.315	1.398	1.361	1.390	1.376	0.250	48.9	82.0

[a]Two water molecules involved in specific solvation.

it. Both the Bird and Pozharskii indices increase by *ca.* 3 units going from gas phase to water with specific hydration. No crystal structure is available for pyrrole.

For pyrazole (Table 5), the aromaticity indices based on AM1- and 6-31G*-calculated bond lengths increase from the gas phase to the condensed phases as expected, by amounts which are in line with those found for imidazole and pyrrole. However, the experimental bond lengths give only a small increase on going from the gas phase to the crystal for the Bird index and show a decrease for the Pozharskii index. The origin of this can be traced to the apparent increase in the length of the 1,2-bond in going from the gas to the crystal. Crystal structure studies[54] have shown that in the solid state pyrazole exists in long helical chains, hydrogen bonded through N(1)–H(1)···N(2). As for imidazole, these hydrogen bonding interactions increase the polarity of the environment experienced by individual pyrazole molecules.

For 1*H*-1,2,4-triazole (Table 6), the aromaticity indices based on the calculated bond lengths again show the expected increases. Now the situation is reversed from pyrazole, because the measured bond lengths show massive increases in the aromaticity indices from gas phase to crystal. Crystal studies[55] once again show strong hydrogen bonding between H(1) and N(4), with the molecules arranged in corrugated sheets.

The data presented in Table 7 for benzimidazole refer to the five-membered ring of this compound. The aromaticity indices derived from calculated bond lengths show increases of some magnitude. Larger increases are again found for those derived from the experimental bond lengths. Crystal structure studies[56] have shown chains of benzimidazole molecules strongly associated by hydrogen bonds, indicating that these molecules are experiencing a polar environment.

For the first time, we have shown that the degree of aromaticity of a molecule is dependent on the environment of the molecule. These results suggest that care should be taken in comparing levels of aromaticity for different molecules in different environments and, especially, in different phases.

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Experimental Section

Quantum-Chemical Method of Calculation. The semiempirical quantum-chemical calculations were performed using Dewar's Austin Model 1 (AM1)[57] parameterization. The computer program MOPAC 6.0 was modified by us with the inclusion of the multicavity self-consistent reaction field (MCa SCRF) code to account for the combined specific hydrogen-bonding and dielectric environmental effects on the molecular electronic structure in solutions. The MCa SCRF method has been described in detail elsewhere,[58,59] and therefore we present only the essentials here. The interaction of a charge and higher electrical moments of a charge distribution in a spherical cavity, with the corresponding reaction fields localized in the center of the cavity, does not depend on the position of charge or (point) multipole centers in this cavity.[60] Therefore it is possible to divide a hydrogen-bonded molecular complex between two or more spherical cavities that embed solute and solvent molecules, respectively, and meet each other along the hydrogen bond(s). Assuming the classical Born−Kirkwood−Onsager charge density expansion[60] for each of these fragments, the total energy of the solute in a dielectric medium can be expressed as a sum of terms that correspond to the energies arising from the interaction of the partial charge and the electric moments of a molecular fragment with the reaction field of its own and reaction fields of other fragments, as well as from the interaction between the reaction fields of different fragments. Terms in these expansions proportional to the charge reaction field coefficients, Γ_X^{o}, and to the dipole reaction field coefficients, Γ_X, can be referred to as the first-order reaction field energies, terms proportional to the squares or cross-terms of Γ_X^{o} and Γ_X as the second-order energies.

$$\Gamma_X^{\mathrm{o}} = \frac{\epsilon - 1}{2\epsilon a_X} \tag{3}$$

$$\Gamma_X = \frac{2(\epsilon - 1)}{(2\epsilon + 1)a_X^3} F_X \tag{4}$$

In eqs 3 and 4, a_X denotes the cavity radius for a given molecular fragment X, ϵ is the macroscopic dielectric constant of the medium, and F_X is the factor accounting for the gauge independency of the dipole moment of the fragment. In the framework of the one-electron approximation, the corresponding quantum-mechanical extension of the total energy of a solute−solvent molecular complex has the following form, up to the dipole term, of

$$\begin{aligned} E_{\mathrm{tot}} = \langle\varphi|\mathbf{H}|\varphi\rangle = {} & \langle\varphi|\mathbf{H_o}|\varphi\rangle + \sum_{\mathrm{A}}\Gamma_{\mathrm{A}}\langle\varphi|\mu_{\mathrm{A}}|\varphi\rangle\langle\varphi|\mu_{\mathrm{A}}|\varphi\rangle + \sum_{\mathrm{A}}\Gamma_{\mathrm{A}}^{\mathrm{o}} \\ & \langle\varphi|\mathbf{P_A}|\varphi\rangle\langle\varphi|\mathbf{A}_{\mathrm{A}}|\varphi\rangle + \sum_{\mathrm{A}}\sum_{\mathrm{B}\neq\mathrm{A}}\Gamma_{\mathrm{A}}\langle\varphi|\mu_{\mathrm{A}}|\varphi\rangle\langle\varphi|\mu_{\mathrm{B}}|\varphi\rangle/R_{\mathrm{AB}}^2 + \\ & \sum_{\mathrm{A}}\sum_{\mathrm{B}\neq\mathrm{A}}\Gamma_{\mathrm{A}}^{\mathrm{o}}\langle\varphi|\mathbf{P_A}|\varphi\rangle\langle|\mathbf{P_B}|\varphi\rangle/R_{\mathrm{AB}} + \\ & \sum_{\mathrm{A}}\sum_{\mathrm{B}\neq\mathrm{A}}\Gamma_{\mathrm{A}}\langle\varphi|\mu_{\mathrm{A}}|\varphi\rangle\langle\varphi|\mathbf{P_B}|\varphi\rangle/R_{\mathrm{AB}}^2 + \\ & \sum_{\mathrm{A}}\sum_{\mathrm{B}\neq\mathrm{A}}\Gamma_{\mathrm{B}}^{\mathrm{o}}\langle\varphi|\mu_{\mathrm{A}}|\varphi\rangle\langle\varphi|\mathbf{P_B}|\varphi\rangle/R_{\mathrm{AB}}^2 + \\ & \sum_{\mathrm{A}}\sum_{\mathrm{B}\neq\mathrm{A}}\Gamma_{\mathrm{A}}\Gamma_{\mathrm{B}}\langle\varphi|\mu_{\mathrm{A}}|\varphi\rangle\langle\varphi|\mu_{\mathrm{B}}|\varphi\rangle/R_{\mathrm{AB}}^3 + \\ & \sum_{\mathrm{A}}\sum_{\mathrm{B}\neq\mathrm{A}}\Gamma_{\mathrm{A}}^{\mathrm{o}}\Gamma_{\mathrm{B}}^{\mathrm{o}}\langle\varphi|\mathbf{P_A}|\varphi\rangle\langle\varphi|\mathbf{P_B}|\varphi\rangle/R_{\mathrm{AB}} + \\ & \sum_{\mathrm{A}}\sum_{\mathrm{B}\neq\mathrm{A}}\Gamma_{\mathrm{A}}\Gamma_{\mathrm{B}}^{\mathrm{o}}\langle\varphi|\mu_{\mathrm{A}}|\varphi\rangle\langle\varphi|\mathbf{P_B}|\varphi\rangle/R_{\mathrm{AB}}^2 \end{aligned} \tag{5}$$

where $\mathbf{H_o}$ is the reaction field-unperturbed Hamiltonian of the system of the solute (A) and solvent (B) molecule(s), R_{AB} is the distance between the centers of the respective spherical cavities, μ_{A} and μ_{B} represent the dipole moment operators of the molecular fragments A and B, and $\mathbf{P_A}$ and $\mathbf{P_B}$ are the projection operators of the partial charge on fragments A and B to the total molecular wave function $|\phi\rangle$, respectively. The $\mathbf{P_A}$ and $\mathbf{P_B}$ operators can be defined following one of the possible LCAO MO charge partitioning schemes in the molecule. Mulliken charges have been used in the present application. The Hartree−Fock-type equations derived from the variational functional for the total energy E can then be solved iteratively using the SCRF procedure.

Also, the calculations were performed for four heterocycles (pyrrole, pyrazole, imidazole, and 1,2,4-triazole) using *ab initio* SCRF method with the 6-31G* basis set in the framework of the Gaussian 94 program.[68]

In the present calculations, various systems with different solvation were considered. These correspond to the isolated heterocycles (gas phase) and to the heterocycles embedded into dielectric media with the dielectric permittivity of dioxane (2.209), benzene (2.284), and water (80.0). If applicable, we have also considered heterocycles embedded into the same media and solvated by one or two water molecules acting as the hydrogen-bonding acceptor (analog of a dioxane molecule) or hydrogen-bonding donor, respectively. The cavity radii of molecular fragments, a_{o}, were calculated from the mass densities ρ and molecular masses MW of the compounds as[61]

$$a_{\mathrm{o}} = \left(\frac{3\mathrm{MW}\rho}{4\pi N_{\mathrm{A}}}\right)^{1/3}$$

with the following numerical values: $a_{\mathrm{o}} = 3.13$ Å in the case of pyrrole; $a_{\mathrm{o}} = 3.09$ Å in the case of pyrazole, imidazole, and 1,2,4-triazole molecules; $a_{\mathrm{o}} = 3.69$ Å in the case of azulene; and $a_{\mathrm{o}} = 3.73$ Å in the case of benzimidazole. For all structures studied, full optimization of geometry was performed.

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