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On the Non-Classical Contribution in Lone Pair-π Interaction: IQA perspective

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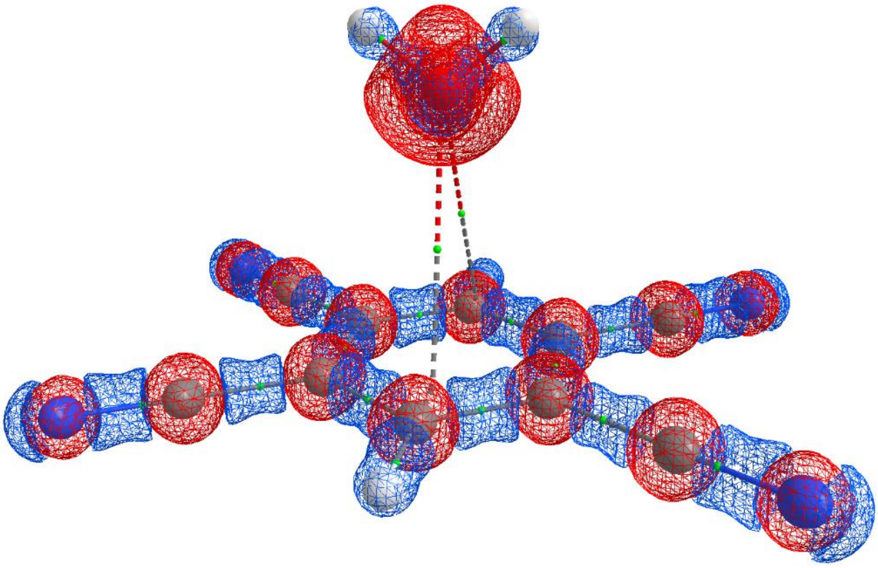
Abstract

In the present work the nature of lone pair-π interactions between water molecules and a number of π-rings with different substituents/hetero-atoms in the light of quantum chemical topology approaches is studied. The Quantum Theory of Atoms in Molecules (QTAIM) and Interacting Quantum Atoms (IQA) were employed for distinguishing the role of heteroatoms and electron withdrawing substituents in the complex formation between water and π-rings. Our IQA study identified three classes of water-π complexes on the basis of the relative role of electrostatics (classical) and exchange-correlation (non-classical) factors in the interaction energy between the oxygen of water (the lone pair donor) and the sp^2 atoms of the π-ring, i.e. the primary lp-π interaction. Considering both the primary and secondary (the rest of interatomic interactions except O_{water}-π-ring atoms) interactions demonstrates that the exchange-correlation is the dominant contributor in the binding energy. This proves a non-negligible contribution of non-classical factors in the stabilization of the lone pair-π complexes. However, in spite of relatively large contribution of the exchange-correlation, this part of the interaction energy is virtually counterbalanced by the deformation energy, i.e. the increase in atomic kinetic energy upon complexation. This finding clarifies why water-π interactions can be modelled by simple electrostatics without need to invoke quantum effects.

Graphical abstract



Most and least electrostatic repulsive parts of a complex presented by red and blue isosurfaces repulsive potential energy density

1. Introduction

Non-covalent interactions between Lewis bases and aromatic systems acting as Lewis acids are a major class of interactions in supramolecular chemistry and biochemistry.[1,2,3,4,5,6,7,8,9,10,11,12,13] Many experimental as well as theoretical studies in recent years have shown that π-systems with electronegative substituents, heteroatoms,[6,13,14,15,16,17,18,19,20,21,22] or protonated π-rings[23,3,4] (also known as π-acids) interact efficiently with various systems containing lone pairs of electrons (lp). Understanding the nature of such interactions has attracted attention of many researchers because of the significant role of lp-π interactions in various branches of chemistry.[2,3,5,6,24,25]

One of the outstanding examples of the lp-π interactions has been observed in Z-DNA. Egli and co-workers have demonstrated that the stability of the left-handed Z-DNA is related to the lp-π interaction between the oxygen lone-pair of the cytidine deoxyribose and the aromatic system of a guanine.[5] Comparing the interaction energy at MP2 level of theory to that of the HF demonstrates that correlation is a major contributor in the binding energy.[5]

Among various families of the lp-π complexes, the interaction of water with π-systems is particularly interesting.[1,3,4,12,18,26] Water plays a crucial role as the medium in all biological processes.[2] Accordingly, understanding the very nature of the water-π interactions is of great importance for all disciplines of science particularly those dealing with living systems. In spite of the pioneering work of Egli et. al.[5] on the nature of the lp-π interactions, numerous studies suggest that the electrostatic forces are the main source of stabilization for this interaction. In particular, the electrostatics has been suggested as the main source of stability for the complexes of water and its analogs, i.e. ethers and alcohols, with π systems containing "electron deficient" rings bearing either heteroatoms or electronegative substituents or both.[12,26,27,28,29,30] Originally Gallivan and Dougherty proposed that the lone pair-π interactions could be described exclusively by electrostatics, dominated by the forces between dipolar water and the quadrupole of the electron-deficient ring.[18] Electron-deficient rings show a positive electrostatic potential above and below their planes and a negative electrostatic potentials on the periphery of the rings. Besides, in some cases, different types of analyses predict a significant degree of *dispersion* contribution to the interaction energy.[12,22,28,30,31]

In the present account, we try to solve this seemingly inconsistent picture in the light of the theory of Interacting Quantum Atoms (IQA)[32,33,34,35] performed within the framework of the Quantum Theory of Atoms in Molecules (QTAIM).[36] We aim to demonstrate why invoking electrostatics is sufficient for description of lp-π complexes in spite the fact that exchange-correlation, a quantum effect, has a prominent role in formation of lp-π complexes.[5] The most significant advantage of the IQA over conventional energy partitioning schemes is that neither an external reference nor an artificial intermediate state need to be involved.[33,34,35,37] It has been demonstrated that IQA can be successfully employed for probing the nature of different types of supramolecular interactions.[37,38] Since IQA analysis is performed within the framework of QTAIM, one can discriminate the role of individual atoms and interatomic interactions in the total electronic energy in 3-dimentional physical space of the electron density. Taking the latter advantage of the IQA one can distinguish the real lp-π interaction that is the interaction between the oxygen of water and sp^2 atoms of the π-rings from the rest of inter-atomic interactions in water-π complexes, i.e., interactions of water hydrogens with substituents of the π-rings.

To achieve this aim, we analysed the nature of the water lp-π interaction from the IQA perspective for selected aromatic systems bearing electron withdrawing substituents, containing electronegative atoms, as well as a protonated system, **Figure 1**. Besides the IQA, the electron density of the lone pair-π complexes is analysed by QTAIM and electron deformation density maps (EDD) to gain a complete picture of all electron density redistributions, causing the energy changes in the process of the lp-π bonding.[39,40]

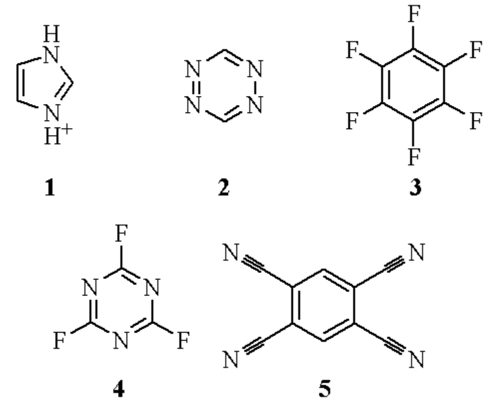


Figure 1. The Lewis structures of studied systems (**1**) imidazolium, (**2**) *s*-tetrazine, (**3**) hexafluorobenzene, (**4**) 2,4,6-trifluoro-1,3,5-triazine or cyanuric fluorid, and (**5**) 1,2,4,5-tetracyanobenzene.

2. Computational Details

All complexes were optimized by M06-2X meta-hybrid GGA functional, developed by Truhlar et al.,[41] combined with Dunning's aug-cc-pVTZ augmented triple-ζ basis set.[42] It has been demonstrated that this functional provides reasonable results for intermolecular interaction energies without any need for counterpoise correction.[41] In addition, it is known that BSSE has a very limited effect in real space properties computed in the context of QTAIM.[36,37] Therefore, in the present work we did not employed counterpoise correction. Frequency calculations were performed to confirm that the structures are local minima. It should be mentioned that the geometry of the **3**·H_2O has been previously studied theoretically and experimentally by Gallivan et. al.[18] and Amicangelo[22] et. al. and they had reported two and three binding motifs, respectively. One above and perpendicular to the ring centroid (*p*-

3·H_2O) having C_{2v} symmetry and two other tilted conformations that are closer to the periphery of the ring (t_1-**3**·H_2O and t_2-**3**·H_2O), both having Cs symmetries. These complexes differ slightly in the binding energy, ~ 0.1-0.2 kcal·mol^{-1}, which suggests that the potential energy surface for this complex is quite flat. We consider all structures in this study. Here binding energies are reported with respect to the unrelaxed fragments in the geometry of the complex. All calculations were performed by Gaussian 09.[43] Then IQA analyses were performed on the wave functions of the abovementioned complexes obtained at the same level of theory by AIMAll[44] program. In the framework of IQA, the binding energy ($E_{IQA}^{bind\ AB}$) is computed as the sum of the classical (electrostatic,), exchange-correlation (non-classical) (E_{XC}^{AB}), and deformation energies ($E_{Def}^{A/B}$) of the interacting fragments A and B, resulting from the electron/nuclei reorganization in each fragment influenced by the presence of the other fragment. An advantage of computing the binding energy with respect to the unrelaxed fragments is that the deformation energy can be attributed to the increase of the kinetic energy as is expected from virial theorem (no reorganization of nuclei).

$$E_{IQA}^{bind\ AB} = E_{Cl}^{AB} + E_{XC}^{AB} + E_{Def}^{A} + E_{Def}^{B} \qquad \text{Equation 1}$$

The exchange correlation and electrostatics contributions into the IQA binding energy originate from the variation of the "*potential energy*" of a molecule and are of equal importance.[37] We performed the IQA analysis for a number of molecules to have a standard set for the contributions of IQA energy components to the binding energy of some text book examples of ionic, covalent and polar covalent bonding, **Table 1**.

Table 1. IQA energy components and delocalization index (DI) for a number of molecules with ionic, covalent and polar covalent bonds.

A-B	$E_{bind–DFT}$	$E_{bind–IQA}$	E_{int}	E_{XC}	E_{Cl}	%E_{xc}	E_{Def} (A)[a]	E_{Def} (B)	**DI**
NaCl	–98.3/*–132.9*	–98.5/*–133.1*	–144.4	– 27.2	– 117.2	18.8	115.3/*– 3.2*	–69.4/*14.5*	0.2535
CH_3F	–121.5	–121.4	–392.4	–168.1	–224.3	42.8	219.6	51.4	0.7910
Ethane	–113.5	–113.3	–195.9	–217.1	21.2	110.8[b]	41.3	41.3	1.0157
NH_3-BH_3	–45.0	–45.0	–187.5	–111.0	–76.5	59.2	103.2	39.3	0.3260

a. Component A is the cation in the ionic (heterolytic) bond dissociation.

b. Electrostatics is repulsive for this molecule accordingly the contribution of the exchange-correlation in binding energy is larger than the binding energy itself.

As one may infer on the basis of **Table 1**, the relative contribution of the exchange-correlation energy to the total binding energy is a good measure of covalency/ionicity. In fact, the more the covalency, the higher the relative contribution of the exchange-correlation in the binding energy.

To obtain an insight towards the charge reorganization during the complexation and assess the delocalization index, DI, topological analyses were performed as well. The delocalization index, δ(A↔B), is a quantitative tool in the context of QTAIM, which measures the magnitude of the electron sharing between any pair (neighboring or non-neighboring) of atomic basins A and B.[45,46,47] In other word, DI is a unique measure of covalency and a direct probe for measuring the bond order between any atomic pair. It has been suggested that the DI as a covariance of the electron population between two basins, is intimately linked to the exchange-correlation energies.[48,49]

Professional package of AIMAll was used to perform QTAIM and IQA analyses.[44] Proaim and Promega-1st order approaches were employed for integration of atomic basins. Accuracy of integration procedure was guaranteed by keeping the absolute error in computation of the total QTAIM basin energy below 0.6 kcal.mol^{-1} compared to the DFT energies. Furthermore, the average of absolute error in the IQA analysis, which stems from an inherent inaccuracy of the second order density matrix, obtained from the DFT computation, is about 0.6 kcal.mol^{-1}[50,37,51].

3. Results and Discussion

3.1. Electron density in π-space of the model systems 1-5

The so-called π-acids are generally considered to be electron deficient π-systems. However, recently Wheeler and Bloom by studying the electrostatic potential maps (ESP) proposed that π-acids are not actually π-electron deficient.[52] The number of π-electrons in these π-acids can be used to demonstrate this proposal *quantitatively*. Comparing the number of π-electrons in the atomic basins of different π-system, Figure 1, with those of benzene suggests that π-acids are not π-electron deficient; see Table 2. In fact, π-rings with electronegative substituents/heteroatoms have denser π-electron clouds, which are tightly associated with their π-rings. This is consistent with the fact that substituents like fluoride are in fact π-electron donor. Therefore, the π-electron density is pushed more towards the ring centre in hexafluorobenzene, compared to benzene. Besides, nitrogen heteroatoms keep their π-electrons more tightly in their atomic basin compared to less electronegative carbon atoms. A system such as benzene has a relatively extended π-system that is not accumulated right above the carbon atoms but can extend to the basin of hydrogen atoms, where there is no *p*-electron to limit the extension of the π-electron density by repulsion.. This view is consistent with the recent proposal of Wheeler et. al.[52]

Table 2. QTAIM-derived number of π-electrons in each atomic basin and the total value for π-systems investigated in this study. See Figure 1 for numbering.

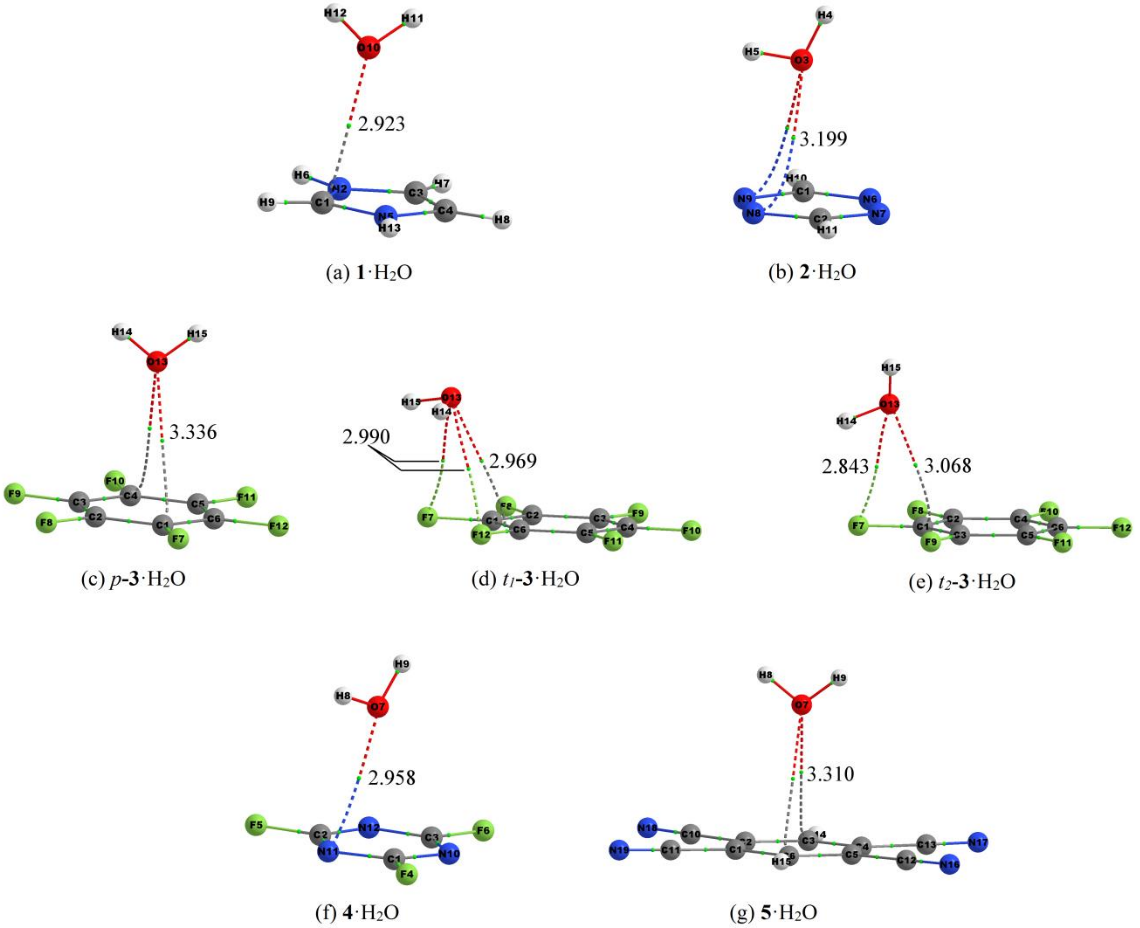
Molecule	Atom	Π	π_{tot}
Benzene	C	0.9691	5.8143
1	C1	0.7321	5.9119
	N2/3	1.6546	
	C3/4	0.9353	
2	C	0.7020	5.9595
	N	1.1389	
3	C	1.0005	6.0028
4	C	0.6049	6.0970
	N	1.4275	
5	C(CN)	0.9965	5.8177

C(H)	0.9159

Surveying Table 2 shows higher π-populations for all π-systems investigated here comparing to benzene. The π-acidity (attraction of electrons in the π-space) of these systems seems to arise from the deficiency in σ-space, not the π-electrons. Even the electron density of the tetracyanobenzene, **5**, remains comparable with that of benzene and no real π-electron deficiency is observed.

3.2. QTAIM and EDD analyses; patterns of electron density redistribution

The magnitude of charge variation in atomic basins for our model systems, Figure 2, upon complexation is summarized in Table 3.



(a) **1**·H$_2$O (b) **2**·H$_2$O

(c) *p*-**3**·H$_2$O (d) t_1-**3**·H$_2$O (e) t_2-**3**·H$_2$O

(f) **4**·H$_2$O (g) **5**·H$_2$O

Figure 2. Molecular graphs corresponding to the minimum energy structures of the studied model systems; (a) **1**·H_2O (b) **2**·H_2O (c) *p*-**3**·H_2O (d) t_1-**3**·H_2O (e) t_2-**3**·H_2O (f) **4**·H_2O (g) **5**·H_2O.

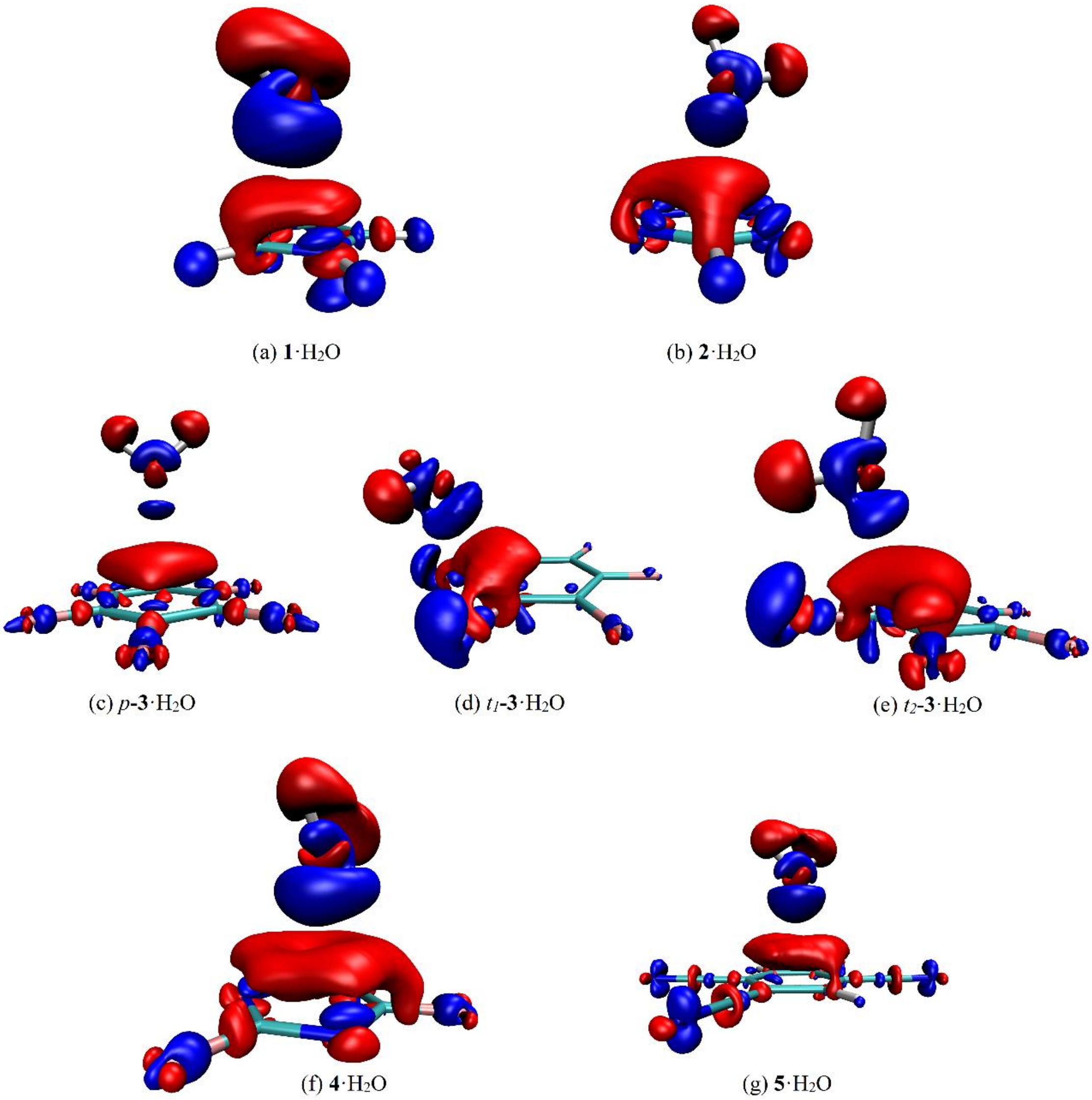
Scrutinizing Table 3 reveals general features of charge redistribution in water-π complexes. The magnitude of the charge redistribution in water molecule suggests that in all cases water hydrogens loose electrons and oxygen gains; this is a clear sign of polarization of water towards the ring. This is an evidence for an electrostatic component of water-π bonds. Inspecting the charge of free water molecule with that of the complexed water reveals a slight charge-transfer from water to the π-systems (except *p*-**3**·H_2O). The charge-transfer strengthens the electrostatic interaction further. (Results for comparison of charge variations in three motifs of complex **3** are listed in Table S1)

Table 3. The difference in atomic-basin charges induced by complexation, Δq, in atomic units.

		C	N	H_π^*	F	O	H_W^*	Water
1·H_2O	C1	+0.0189	–	0.0098	–	–0.0408	+0.0474	+0.0066
	C3/4	+0.0016	–	–0.0110	–	–	–	
	N2/5		+0.008	–0.0062	–	–	–	
2·H_2O	C1/2	+0.0134		–0.0073	–	–0.0146	+0.0170	+0.0024
	N6/7	–	+0.0014	–	–	–	–	
	N8/9	–	–0.0087	–	–	–	–	
***p*-3·H_2O**	C1/4	+0.0092	–	–	–0.0036	–0.0156	+0.0152	-0.0004
	C2/3/5/6	+0.0035	–	–	–0.0045	–	–	
4·H_2O	C1/2	+0.0069	–	–	–0.0054	–0.0190	+0.0252	+0.0062
	C3	+0.0018	–	–	–0.0051	–	–	
	N10/12	–0.0075	+0.0009	–	–	–	–	
	N11	–0.0075	–0.0075	–	–	–	–	
5·H_2O	C-H	+0.0143	–	–0.0053	–	–0.0244	+0.0252	+0.0008
	C-CN**	+0.0099	–	–	–	–	–	
	C-**C**N**	–0.0013	–	–	–	–	–	
	C-C**N****	–	–0.0125	–	–	–	–	

* H_π and H_w correspond to hydrogen atom of the ring and sum of both hydrogen atoms of water molecule, respectively.
** The bold font in C-CN fragment corresponds to the analyzed atom.

Among the studied complexes, water hydrogens in complex **1**·H_2O show the largest charge reorganization between hydrogen and oxygen of water upon complexation. This is due to the ionic character of **1**, i.e. the imidazolium ion, which polarizes water significantly. The charge of hydrogens of the rings, fluorine atoms, and nitrogens of the nitryl groups increases upon complexation. This is evidence in favour of the role of the σ-framework of the π-systems, i.e. the substituents of the system, in the complexation process. This observation is in line with a previous suggestion by Houk and Wheeler on the role of the σ-framework of the π-systems in anion-π bonding, a subset of lone-pair bonding interactions.[53] Upon complexation, the electron density of a π-system polarizes towards the edge of the molecule, i.e. the substituents and hydrogen atoms on the σ-framework of the system. This increases the electron population of all atoms in the periphery of the ring, including hydrogen atoms. Furthermore, the variation in the charge density of ring endocyclic atoms, i.e. carbon and nitrogen heteroatoms, is relatively small and does not follow a unique trend. EDD maps depicted in Figure 3, provide a qualitative picture of the charge variation in our model systems upon complexation with water. Evidently, in all cases water molecules are polarized towards the π-systems (c.f. QTAIM charge analysis). Besides, polarization of π-systems towards the periphery can be seen in Figure 3.



(a) **1**·H_2O (b) **2**·H_2O

(c) *p*-**3**·H_2O (d) t_1-**3**·H_2O (e) t_2-**3**·H_2O

(f) **4**·H_2O (g) **5**·H_2O

Figure 3. EDD maps of studied complexes (a) **1**·H_2O (b) **2**·H_2O (c) *p*-**3**·H_2O (d) t_1-**3**·H_2O (e) t_2-**3**·H_2O (f) **4**·H_2O (g) **5**·H_2O. Red and blue iso-surfaces represent -0.0005 au decrease and +0.0005 au increase in the electron density, respectively.

3.3. IQA analysis

The IQA analysis can provide a detailed picture of all energy components contributing in the bonding energy. Furthermore, IQA can reveal the role of every single atom in bonding. Here, we will identify the source of attraction and repulsion between water and individual atoms in the π-systems.

3.3.1. Components of the Binding Energy.

In a bond formation process two factors are in favour of the bond formation; the electrostatic attraction between nuclei-electrons, which usually surpasses the nuclear-nuclear and electron-electron repulsion, and the electronic exchange-correlation, a non-classical factor that lowers the electron-electron repulsion more than what is expected from a classical model. On the other hand, reorganization of electrons and nuclei upon bonding needs a primary energy that is called deformation or promotion energy. Previous studies have shown that the exchange-correlation energy is closely related to the delocalization index for different systems.[49] Recalling that the delocalization index is a measure of the bond order, one may state that the exchange-correlation energy is a measure of the contribution of the quantum effects on the electron sharing or covalency. The sum of the exchange-correlation and electrostatics contributions in IQA analysis defines the interaction energy within the framework of IQA. Binding energies obtained from DFT and IQA calculations as well as IQA interaction energies of the studied systems are summarized in Table 4.

Surveying Table 4 shows notable interaction energies for all structures, Figure 2. The **1**·H_2O complex that is formed between a positively charged imidazolium and water, has the largest interaction energy among studied complexes. The interaction energy is partly compensated by the positive deformation energies of the interacting fragments originating from the charge reorganization upon complexation.

Comparing the exchange-correlation with the electrostatic components indicates a bigger contribution of the exchange-correlation term, associated with electron sharing in all complexes. It seems that the exchange-correlation plays the main role in the lone pair-π interaction. It is interesting to note that even in the case of **1**·H_2O system, the electrostatic component is less important than the exchange-correlation contribution into the interaction energy, although the contribution of the electrostatics is notably more important here compared to other model systems. The larger contribution from the electrostatic part is expected from the positively charged imidazolium that polarizes the water molecule more efficiently than neutral π-systems. Accordingly, our analysis suggests a more prominent contribution from non-classical factors for lone-pair-π interactions compared to the electrostatics. The magnitudes of the delocalization indices, listed in Table 4, between water and the π-systems are comparable with those of strong (covalent) hydrogen bonds.[54,55] However, one should keep in mind that the lp-π interaction belongs to multi-center class of interactions and individual atom-atom delocalization indices are notably smaller.

Table 4. The binding energy ($E_{bind–DFT}$ and $E_{bind–IQA}$), the interaction energy (E_{int}), and individual components of the interaction energy, i.e. the exchange-correlation (E_{XC}), electrostatic potential (E_{Cl}), and deformation energies [E_{Def} (H_2O) and E_{Def} (π)] for each fragment upon complexation as well as the total delocalization index (DI) between water (w) and π-system (lp-acceptor) for **1-5**. All the energy components are in kcal.mol^{-1} and DI is in au.

	$E_{bind–DFT}$	$E_{bind–IQA}$	E_{int}	E_{XC}	E_{Cl}	E_{Def} (H_2O)	E_{Def} (π)	DI
1·H_2O	–9.1	–9.2	–24.6	–15.3	–9.3	8.7	6.7	0.1556
2·H_2O	–4.0	–4.4	–20.1	–16.1	–4.0	8.1	7.6	0.1643
***p*–3·H_2O**	–3.3	–2.0	–15.9	–13.0	–2.9	6.6	7.1	0.1372
***t*$_1$–3·H_2O**	–3.4	–3.2	–18.9	–15.5	–3.4	8.5	7.2	0.1597
***t*$_2$–3·H_2O**	–3.6	–4.3	–18.2	–15.3	–2.9	8.0	5.9	0.1525
4·H_2O	–5.4	–6.0	–23.1	–17.8	–5.3	9.1	8.0	0.1775
5·H_2O	–5.1	–4.4	–19.9	–13.6	–6.3	7.5	8.0	0.1458

Our results do not parallel the previous studies based on the energy decomposition schemes[28] which suggest predominant role of the electrostatic components in the lp-π interaction with some contribution of dispersion energy. The reason for such disagreement between the IQA and other energy decomposing methods has been discussed by Pendás et al.[37] regarding the nature of hydrogen bond. Orbital-based energy decomposition schemes do not clearly separate the exchange-correlation, a factor that lowers the potential energy, and the kinetic energy, which increases the IQA atomic energies. It should be mentioned that here the exchange-correlation contribution in the IQA is virtually cancelled out by the deformation energy (increase in kinetic energy) of the interacting fragments. Accordingly, the electrostatic component seems to be the predominant contributor into the interaction energy as the other energy decomposing methods suggest. It must be noted that cancelling the exchange-correlation with the deformation energy does not mean that the complexes do not benefit from some degrees of electron sharing that is of non-classical origin.

3.3.2. Decomposing the interaction energy into the interatomic contributions.

The lp-π interaction is the sole interaction between the oxygen atom and the sp^2 atoms of the π-ring. However, in conventional chemical analyses separating the interaction of the oxygen with sp^2 atoms of the π-ring from those of hydrogens or substituents of the π-ring is not possible. Fortunately, IQA analysis provides a straightforward approach for this purpose within the 3D space. To elucidate the role of the oxygen and the hydrogen atoms of water in the lone pair-π interaction separately, the interaction energies decomposed within the context of QTAIM methodology are analyzed in this section. We label the interaction of the oxygen and all sp^2 atoms of the π-ring (O...π) as the primary interaction from now on and E_{int}^{prim} represents its interaction energy. The other interactions between the rests of the atoms in the complex are called the secondary interactions characterized by the secondary interaction energy, E_{int}^{sec}. Atomic contributions in the IQA interaction energy, for each atomic basin as well as primary (O...π with E_{int}^{prim}), secondary (with E_{int}^{sec}), and the fragment-based (with E_{int}^{Tot}) values are summarized in Table 5.

Table 5. Inter-atomic interaction energy, contributions of inter-atomic exchange-correlation energy, electrostatic contribution, and delocalization index as well as primary (E_{int}^{prim}), secondary (E_{int}^{sec}), and fragment-based (E_{int}^{Tot}) for complexes **1**·H_2O–**5**·H_2O. Energy in kcal·mol^{-1} and DI in au.

Molecule	**A…B**	**E*inter–atomic***	**E*XC***	**E*Cl***	**DI**
1·H_2O	O…C1	–155.9	–3.2	–152.7	0.0284
	O…C3/4	–56.4	–1.6	–54.8	0.0174
	O…N2/5	+156.1	–4.2	+160.3	0.0414
$\boldsymbol{E_{int}^{prim}}$		**+43.5**	**–14.8**	**+58.3**	**0.1460**
	O…H9	–21.7	–0.2	–21.5	0.0019
	O…H7/8	–16.0	0.0	–16.0	0.0004
	O…H6/13	–57.3	0.0	–57.3	0.0004
	H_W^*… R	+100.2	–0.3	+100.5	0.0061
$\boldsymbol{E_{int}^{sec}}$		**–68.1**	**–0.5**	**–67.6**	**0.0096**
$\boldsymbol{E_{int}^{Tot}}$		**–24.6**	**–15.3**	**–9.3**	**0.1556**
2·H_2O	O…C1/2	–139.2	–2.2	–137.0	0.0214
	O…N6/7	+64.8	–2.0	+66.8	0.0218
	O…N8/9	+69.5	–3.5	+73.0	0.0337
$\boldsymbol{E_{int}^{prim}}$		**–9.8**	**–15.4**	**+5.6**	**0.1537**
	O…H10/11	–9.4	–0.1	–9.3	0.0009
	H_W^*… R	+8.5	–0.5	+9.0	0.0088
$\boldsymbol{E_{int}^{sec}}$		**–10.3**	**–0.7**	**–9.6**	**0.0106**
$\boldsymbol{E_{int}^{Tot}}$		**–20.1**	**–16.1**	**–4.0**	**0.1643**
***p*–3·H_2O**	O…C1/4	–73.1	–2.1	–71.0	0.0212
	O…C2/3/5/6	–71.8	–2.0	–69.8	0.0199
$\boldsymbol{E_{int}^{prim}}$		**–433.4**	**–12.2**	**–421.2**	**0.1220**
	O…F	+67.4	–0.1	+67.5	0.0017
	H_W^*… R	+13.1	–0.2	+13.3	0.0051
$\boldsymbol{E_{int}^{sec}}$		**+417.5**	**–0.8**	**+418.3**	**0.0152**

$\boldsymbol{E_{int}^{Tot}}$		**–15.9**	**–13.0**	**–2.9**	**0.1372**
4·H$_2$O	O…C1/2	–240.1	–2.1	–238.0	0.0187
	O…C3	–222.1	–1.1	–221.0	0.0107
	O…N10/12	+143.7	–3.1	+146.8	0.0316
	O…N11	+153.0	–5.2	+158.2	0.0481
$\boldsymbol{E_{int}^{prim}}$		**–261.9**	**–16.7**	**–245.2**	**0.1594**
	O…F4/5	+76.8	–0.3	+77.1	0.0044
	O…F6	+69.8	0.0	+69.8	0.0012
	H_W^*… R	+15.4	–0.5	+15.9	0.0081
$\boldsymbol{E_{int}^{sec}}$		**+238.8**	**–1.1**	**+239.9**	**0.0181**
$\boldsymbol{E_{int}^{Tot}}$		**–23.1**	**–17.8**	**–5.3**	**0.1775**
5·H$_2$O	O…C-H	–11.7	–2.1	–9.6	0.0223
	O…C-CN	–11.7	–2.1	–9.6	0.0213
$\boldsymbol{E_{int}^{prim}}$		**–70.2**	**–12.6**	**–57.6**	**0.1298**
	O…H14/15	–11.0	0.0	–11.0	0.0010
	O…C(CN)	–83.4	0.0	–83.4	0.0016
	O…N(CN)	*+95.6*	*–0.1*	*+95.7*	0.0005
	H_W^*… R	+23.5	–0.6	+24.1	0.0056
$\boldsymbol{E_{int}^{sec}}$		**+50.3**	**–1.0**	**+51.3**	**0.0160**
$\boldsymbol{E_{int}^{Tot}}$		**–19.9**	**–13.6**	**–6.3**	**0.1458**

* R and H_W correspond to sum of all atoms of the π-system (lp-acceptor) and hydrogen atoms of water molecule, respectively.

In all complexes the primary interaction, that is the interaction between the water oxygen and all *sp*^{2} atoms of the lp-acceptor, is favourable except for **1**·H$_2$O. Considering just the primary interaction, three types of complexes are distinguishable.

In the first type of complexes (**1**·H$_2$O) primary electrostatic force (+58 kcal·mol^{-1}) is the dominant and destabilizing. The attractive electrostatic interactions between the oxygen of water and carbons of the ring are overcompensated by the large repulsive electrostatic interactions between the oxygen and the negatively charge nitrogen atoms (c.f. Table 5 and S2). The only source of stabilization in the primary interaction is the exchange-correlation (-14 kcal·mol^{-1}) which is fairly large but not large enough to compensate for the electrostatic repulsion. It should be explicitly mentioned that the secondary interaction between water oxygen and hydrogen atoms of the ring makes the complexation of water and imidazolium stable. This interaction is favourable particularly in terms of electrostatic contribution (-67 kcal·mol^{-1}). However, still the overall role of exchange-correlation (-15 kcal·mol^{-1}) is more prominent than the electrostatics (-9 kcal·mol^{-1}).

In the second class of complexes, represented by **2**·H_2O, the primary exchange-correlation component (-15 kcal·mol^{-1}) is dominant and electrostatic component (classical) is just weakly destabilizing for the primary interaction. So, one can state that the net source of stabilization is the exchange-correlation (-16 kcal·mol^{-1}) not the classical electrostatic interactions (-4 kcal·mol^{-1}).

In the third class, the primary interaction mainly benefits from the attractive electrostatic force. This applies to complexes **3-5**·H_2O. Nevertheless, the secondary interaction in all complexes of this family has an unfavourable contribution from the electrostatics that offsets the favourable attractive primary electrostatic interaction. As a results, the exchange-correlation contribution dominates the total interaction energy, E_{int}^{Tot}. The results of the decomposed interaction energy into the interatomic contributions for t_1–**3**·H_2O and t_2–**3**·H_2O are listed for comparison in Table S3.

In all cases, except those for t_1–**3**·H_2O and t_2–**3**·H_2O thoroughly discussed in Supporting Information, the main part of the total exchange-correlation energy originates, as expected, from the primary interaction (E_{int}^{prim}) Furthermore, all the exchange-correlation values correlate linearly with the DI values in the frame of QTAIM, Table 5 and Figure 4. In fact, as mentioned above, the DI as a covariance of the electron population between two basins is intimately linked to the exchange-correlation energies (c.f. Figure 4).

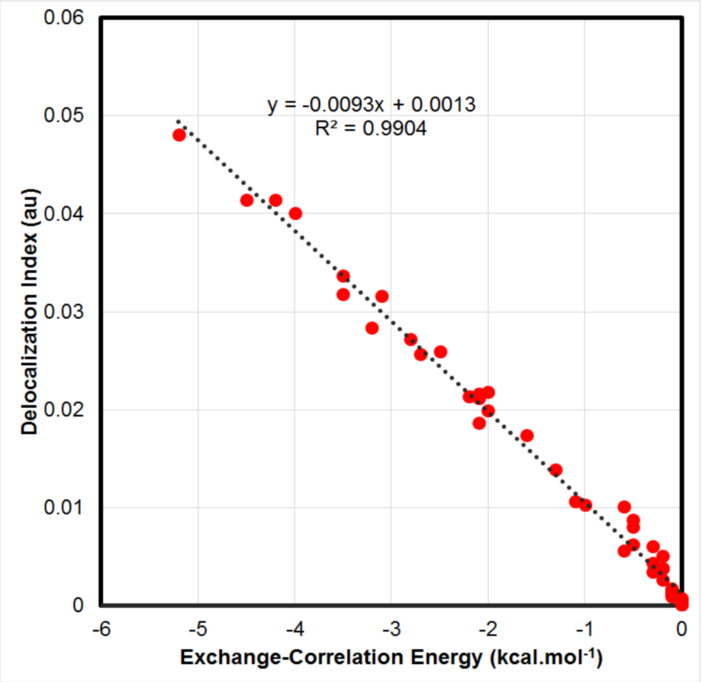


Figure 4. The plot of delocalization indices value versus exchange-correlation contribution in the IQA binding energy.

4. Conclusion

In the present account, we studied the nature of the lone pair-π interaction in a group of water-π complexes by using the IQA approach. We found three classes of complexes on the basis of the relative contributions of the electrostatics and exchange-correlation energy components in the primary interactions between water and the π-ring, i.e. the interaction between water oxygen and *sp*^{2} hybridized atoms of the π-ring. Although in one class of complexes the primary interaction benefits mainly from the electrostatics, it is effectively balanced by the secondary electrostatics of almost the same magnitude but opposite sign; therefore, the exchange-correlation plays the dominant role in the total stabilization of the complexes. This is in contrast with the previous studies based on the alternative energy decomposition schemes[28] and MESP,[29] which predicted the electrostatic component to be the major stabilizing factor in the lone pair-π interactions.

Decomposition of the IQA interaction energy into atomic contributions reveals that the electrostatic contribution is locally very strong. Whereas the positively charged carbon atoms in heterocyclic and/or fluorinated systems attract strongly the oxygen atom of water, the electronegative atoms (nitrogen, fluorine) repel the same oxygen atom. However, the net energy effect of the electrostatic push-pull phenomenon is much smaller than the overall contribution of the exchange-correlation in the water-π complexes investigated here.

As the exchange-correlation contribution is virtually compensated for by the deformation contribution, the remaining classical electrostatic term can be easily covered by the contemporary force-fields used in biomolecular simulations. The mutual compensation between E_{XC} and E_{Def} can be related to the huge success of MD and simulations employing classic/non-polarizable force fields. Besides, this explains how simple models based on electrostatics (MESP) can successfully predict the binding energy without considering the exchange-correlation.

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