A Theoretical ab initio Study of the Capacity of Several Binding Units for the Molecular Recognition of Anions

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Noncovalent bonding between anions and the π-cloud of electron-deficient aromatic rings has recently attracted considerable attention. Complexes of bromide with different electron-deficient aromatic rings and with other binding units based on hydrogen bonding (urea, thiourea and squaramide) have been studied and compared using high level B3LYP/6-31++G** ab initio and Molecular Interaction Potential with polarization (MIPp) calculations. Our findings reveal that electron-deficient aromatic rings are excellent candidates for constructing anion receptors and that the interaction strength can be modulated by the nature of the ring. Supporting experimental evidence has been obtained from X-ray structures retrieved from the Cambridge Structural Database.

Introduction

The supramolecular chemistry of anions[1,2] is a relatively undeveloped field in comparison with that of cations, in part because concentrations of positive potential are less accessible and manageable than concentrations of negative potential.[3] However, the design and synthesis of receptors capable of binding anionic guests is of considerable interest in the context of sensing and removal of environmental contaminants such as nitrate[4] or the radioactive pertechnate produced in the nuclear fuel cycle.[5] Synthetic receptors for anions are usually based on macrocyclic polyammonium/guanidinium,[6,7] amides,[8,9] urea/thiourea,[10,11] and functionalized calixarenes.[12,13] The binding of anions to neutral receptors is of special significance since it avoids the competing counterion complexes present if cationic hosts are used and improves selectivity due to the dominance of directional interactions,[14] which explains the high specificity of neutral anion binding proteins.[15]

The interaction of an anion with an electron-deficient aromatic ring, namely the anion−π interaction,[16] has attracted considerable attention in recent years.[17−23] It has been speculated[19,23] that electron-deficient aromatic rings can be used as new binding units for the molecular recognition of anions, although, at present, no anion receptor based on this interaction exists.

In this paper we report on a study, using high level ab initio calculations, of the binding capabilities of several aromatic rings (see Figure 1) with the bromide anion as the target, and we compare them with three molecules that have traditionally been used as binding blocks for building neutral anion receptors, namely urea,[10] thiourea[11] and squaramide,[24] each of which interacts with the anion through two hydrogen bonds. It is worth mentioning that we use two aromatic compounds that have not previously been studied as potential units for binding anions, namely 1,3,5-tricyanobenzene and 1,4,5,8,9,12-hexaazatriphenylene (HAT), and we compare them with two other aromatic rings, *s*-triazine and hexafluorobenzene, that have already been proposed as anion-binding units.[17,19] In addition, we have found experimental evidence for anion−π interactions involving these two new aromatic systems from the Cambridge Structural Database,[25] which is a reliable source of geometrical information.

Results and Discussion

Geometry optimizations[26] and energy calculations were done using the 6−31++G** basis set at the B3LYP level of theory by means of the Gaussian 98 program.[27] The binding energies of the complexes were obtained taking into account the basis set superposition error (BSSE) correction with the use of the counterpoise method[28] at the same level. Molecular polarizabilities ($\alpha_{\|}$) were computed at the B3LYP/6-31G* level of theory using the B3LYP/6-31++G** geometries. The quadrupole moments of **4** and **7** were computed using the CADPAC program[29] at the MP2/6-31G* level since previous studies[30] have demonstrated that quantitative results are obtained at this level of theory. The Merz−Kollman method[31] has been used to compute atomic charges.

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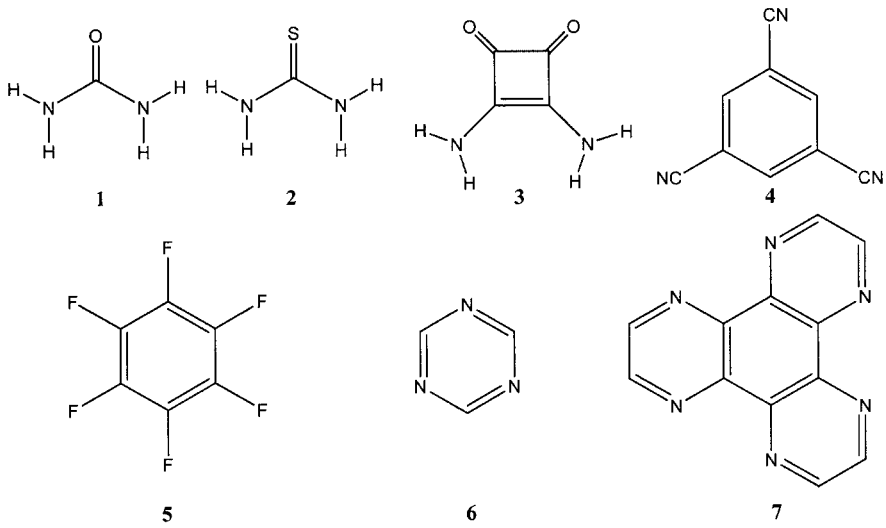

Figure 1. Urea (**1**), thiourea (**2**), squaramide (**3**), 1,3,5-tricyanobenzene (**4**), hexafluorobenzene (**5**), s-triazine (**6**) and 1,4,5,8,9,12-hexaazatriphenylene (HAT, **7**)

The B3LYP/6-31++G** optimized geometries of complexes **1**−**7** with bromide, including the values of some relevant distances and angles, are presented in Figure 2, and the binding energies are presented in Table 1. The geometrical characteristics of the urea, thiourea and squaramide complexes (**1**−**3**) are similar; all three binding units interact

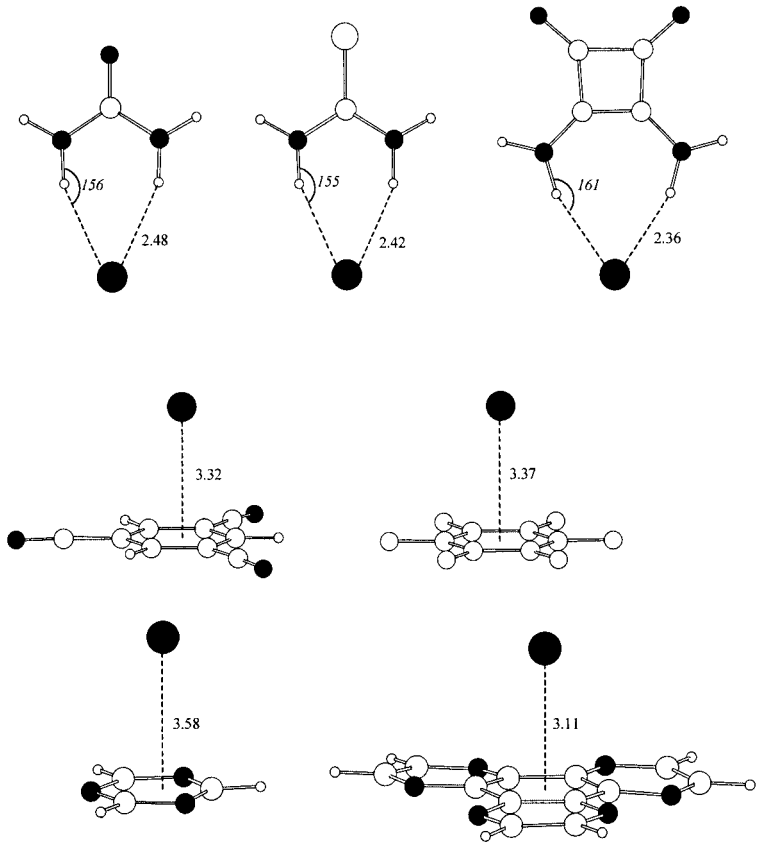

Figure 2. B3LYP/6-31++G** optimized complexes of **1**−**7** with bromide; angles (in italics) are in ° and distances in Å

Table 1. Complexation energies with and without BSSE correction (E and E_{BSSE}, kcal/mol), equilibrium distances (R_e, Å) and bromide Merz−Kollman charge (q, e) computed for complexes **1**−**7** with bromide, and the dipole moment (μ, Debye) and molecular polarizabilities parallel to the main symmetry axis ($\alpha_{\|}$, a.u.) for compounds **1**−**7** at the B3LYP/6-31++G** level of theory

Compound	E	E_{BSSE}	R_e	$\alpha_{\|}$	μ	q (MK, e)
1···Br^-	−25.63	−21.23	2.48	23.95	4.5	−0.911
2···Br^-	−31.94	−27.22	2.42	34.24	5.6	−0.867
3···Br^-	−39.82	−34.39	2.36	37.87	8.5	−0.823
4···Br^-	−21.03	−13.57	3.32	37.74	0.0	−0.864
5···Br^-	−13.73	−9.40	3.37	37.97	0.0	−0.874
6···Br^-	−5.64	−2.99	3.58	30.12	0.0	−0.925
7···Br^-	−15.08	−5.17	3.11	54.03	0.0	−0.769

with bromide by means of two hydrogen bonds. The urea and thiourea complexes have very similar Br^-···H−N distances and angles. However, the computed binding energy of the thiourea complex (E_{BSSE}) is 6 kcal/mol more favorable than that of the urea complex. A likely explanation is that the charge transfer from the anion to thiourea is more significant than that for urea. The E_{BSSE} of the squaramide complex is about 7 kcal/mol lower than that of the thiourea complex and 13 kcal/mol lower than that of urea. In this case, the difference is probably due to the combination of two effects. First, the geometrical features of the two hydrogen bonds are better in squaramide (greater angle and shorter distance, see Figure 2) and, second, the charge transfer from bromide to squaramide is larger. When comparing the binding units **1**−**3**, based on hydrogen bonds, with **4**−**7**, based on anion−π interactions, several observations can be made. First, the computed binding energies are smaller for the **4**−**7** complexes than for the **1**−**3** complexes; however it should be mentioned that the latter interact with the anions through two hydrogen bonds and the aromatic ring provides just one π-interaction. Second, the charge transfer computed for thiourea and squaramide complexes is similar to that computed for the aromatic complexes except the *s*-triazine complex, which shows a very small binding energy and a large equilibrium distance as a consequence of its small quadrupole moment (Q_{zz} = 0.90 B). Third, 1,3,5-tricyanobenzene (Q_{zz} = 19.53 B) shows a significant binding energy that is higher than hexafluorobenzene and comparable to thiourea when account is taken of the number of interactions.

Special mention should be made of the HAT molecule which, in spite of having a negative quadrupole moment (Q_{zz} = −8.53 B), is able to form stable complexes with anions. This is probably due to its high molecular polarizability ($\alpha_{\|}$ = 54.03 au); the value computed for benzene at the same level is $\alpha_{\|}$ = 21.01 au. In order to verify this hypothesis we carried out a Molecular Interaction Potential with polarization[32] (MIPp) calculation which is a powerful tool for predicting the binding properties of aromatic compounds.[33] MIPp is an improved generalization of the Molecular Electrostatic Potential (MEP),[34] in which three terms contribute to the interaction energy: 1) an electrostatic term identical to the MEP, 2) a classical dispersion-repulsion term, and 3) a polarization term derived from perturbation theory.[35] It therefore provides a natural partitioning of the interaction energy into intuitive components. We performed the MIPp calculation for the interaction of HAT with Br^- by using the HF/6-31++G** wavefunction, and explored the electrostatic (E_e), polarization (E_p) and van der Waals (E_{vw}) interaction energies when a bromide anion approaches a HAT molecule perpendicular to the center of the central aromatic ring. The MIPp minimum is found at 3.35 Å with the following results: E_p = −10.25 kcal/mol, E_e = 0.22 kcal/mol and E_{vw} = −0.16 kcal/mol, indicating that the interaction is clearly dominated by the polarization term. The same calculation for **4** ($\alpha_{\|}$ = 37.74 au) gives a totally different situation; the MIPp minimum is found 3.40 Å from the center of the ring with the following partition energies: E_p = −7.34 kcal/mol, E_e = −12.36 kcal/mol and E_{vw} = 0.18 kcal/mol. In this case the interaction is dominated by both electrostatic and polarization contributions.

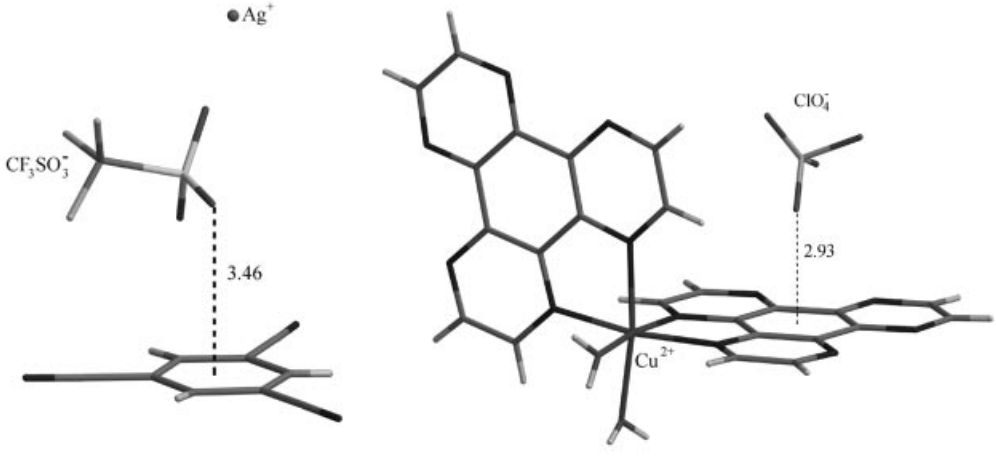

Figure 3. X-ray structures zabqey[36] (left) and xubpep[37] (right) retrieved from the CSD, which show anion−π interactions [zabqey = (tricyanobenzene)silver trifluoromethanesulfonate, xubpep = bis(HAT-*N*,*N*′)copper(II) diperchlorate]; distances are in Å

In order to find experimental evidence of interactions between anions and the aromatic rings of 1,3,5-tricyanobenzene (**4**) and HAT (**7**) derivatives we looked at crystallographic structures as they have been successfully used to study a wide variety of noncovalent interactions, including anion−π interactions.[17] We explored the CSD, searching for evidence of anion−π interactions, and we found 22 fragments where noncovalent interactions are present between anions or electron pairs of electronegative atoms and the π-cloud of 1,3,5-tricyanobenzene derivatives. In addition, we found 186 fragments for HAT derivatives that correspond to 29 X-ray structures. As examples, in Figure 3 we show one selected crystal structure for each aromatic compound.

Additional experimental evidence of the potential use of these systems as building blocks for constructing anion receptors can be obtained from the interesting work of Kitagawa's group.[38] They used a HAT derivative, namely 2,3,6,7,10,11-hexacyano-1,4,5,8,9,12-hexaazatriphenylene, [HAT-$(CN)_6$], to build up a copper(I) complex which exhibits its anion-trapping behavior in both the solid state and in solution. This HAT-$(CN)_6$ compound can be viewed as a combination of two of the compounds studied here, HAT and 1,3,5-tricyanobenzene, and it takes advantage of the presence of electron-withdrawing cyano groups and the high molecular polarizability of the extended π-system that clearly contributes to the anion-trapping behavior of this system. In Figure 4 the X-ray structure published by Kitagawa's group, retrieved from the CSD, is shown. The interaction of the $CF_3SO_3^-$ anion with the π-cloud of the aromatic system is clear and confirms that HAT-based systems are appropriate to perform effective anion−π interactions.

Figure 4. X-ray structure of jebyaq retrieved from the CSD where the anion-trapping behavior of the cationic moiety $[(Cu\text{-}dppe)_3\{HAT\text{-}(CN)_6\}]^{2+}$ is shown [dppe = 1,2-bis(diphenylphosphanyl)ethane], anion = $CF_3SO_3^-$; hydrogen atoms have been omitted for clarity

Conclusion

In summary, we have proposed two new binding units that can be used for the molecular recognition of anions, and we have compared their capabilities with several binding units based on hydrogen bonds that have been widely used for the construction of anion receptors, and with other aromatic rings that have already been proposed as binding units for anion recognition. The HAT molecule has a negative Q_{zz} comparable to benzene and, surprisingly, is able to interact favorably with bromide due to its high polarizability. Finally, crystallographic structures confirm that 1,3,5-tricyanobenzene and HAT aromatic rings are suitable binding units for interaction with anions.

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