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Anion−Aromatic Bonding: A Case for Anion Recognition by π-Acidic Rings

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Abstract: The basis for unprecedented noncovalent bonding between anions and the aryl centroid of electron-deficient aromatic rings has been demonstrated by an ab initio study of the interaction between 1,3,5-triazine and the fluoride, chloride, and azide ion at the MP2 level of theory. Minima are also located corresponding to $C-H\cdots X^-$ hydrogen bonding, reactive complexes for nucleophilic attack on the triazine ring, and π-stacking interactions (with azide). Trifluoro-1,3,5-triazine also participates in aryl centroid complexation and forms nucleophilic reactive complexes with anions. This novel mode of bonding suggests the development of new cyclophane-type receptors for the recognition of anions.

Introduction

The practical scope for recognition and binding of anions is considerably narrower than that for cations.[1] One reason for this is because concentrations of negative potential are more accessible and manageable on the molecular scale than concentrations of positive potential. Thus while examples of electron wells abound in the form of easily manipulable heteroatom or π cloud arrays, localized electron deficits involve Lewis acidic sites (organomercury, tin, boron) which are less conveniently integrated into receptor design than the common nonmetals, and are generally incompatible with the only other vectorial noncovalent interaction relevant to anions, i.e., hydrogen bonding.

Simple ion pairing of anions with ammonium centers in macrocycles has been applied both on its own and in conjunction with hydrogen bonding to the effective complexation of halides and various oxyanions, and although several such macrocycles are cyclophanes, in no case does the aromatic π-system participate in the coordination.[2] Indeed, for complexation purposes aromatic rings are intuitively regarded as sources of electron density and are thus expected to interact repulsively with anions. However, Dougherty,[3] Besnard,[4] and Alkorta[5] and co-workers have recently produced theoretical evidence of electrostatic bonding between hexafluorobenzene and the heteroatom in molecules such as H_2O, HCN, and HF wherein the negative end of the dipole is directed toward the C_6 axis of the ring. Our interest in both the host−guest chemistry of cyclophanes[6] and anion recognition[7] led us to consider whether the more synthetically versatile yet still π-deficient 1,3,5-triazine ring (**1**) might also associate with anions, thereby possibly defining a new noncovalent design principle for their recognition.

Results and Discussion

The study of comparatively weak complexes is fraught with issues of reliability of theoretical methods, appropriateness of basis sets, and applicable corrections thereto. Looking to the literature involving π-deficient aromatics, Dougherty et al.[8] were able to reproduce the experimental benzene−hexafluorobenzene stacking geometry most reliably using the second-order Møller−Plesset energy correlation (MP2), and they also used this method in their investigation of the above-mentioned water−hexafluorobenzene complex.[3] Alkorta et al., in their study involving hexafluorobenzene,[5] considered both MP2 and the hybrid HF-density functional method Becke3LYP[9] to be more effective for weak complexes than methods without electron correlation. In our hands, DFT failed to locate minima previously confirmed with MP2, and we therefore felt the latter was the method of choice. We performed ab initio molecular orbital calculations at the MP2 level of theory with the 6-31+G* basis set, including counterpoise corrections for basis set superposition error (BSSE),[10] for the interaction of both 1,3,5-triazine (**1**) and

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(1) For an excellent recent review of anion recognition, see: Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486.

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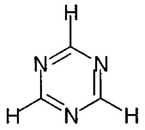

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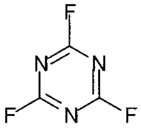

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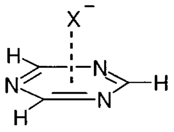

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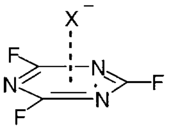

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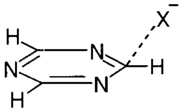

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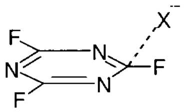

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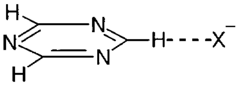

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a, X = Cl; **b**, X = F; **c**, X = N_3

trifluoro-1,3,5-triazine (**2**) with the chloride, fluoride, and azide anions, the results of which are summarized in Table 1.

The molecular electrostatic potential (MEP) maps of **1** (Figure 1a) and **2** (Figure 1b) clearly indicate an area of positive charge concentrated on the C_3 axis of the ring, similar to that demonstrated in Alkorta's comparison of C_6F_6 with benzene.[5] In seeking to locate aryl centroid−anion structures **3**, we first optimized with the anions starting near the proposed minimum, and indeed the predicted interaction was demonstrated for **1** with chloride and azide (Figure 2a). The fluoride−aryl centroid complex on the other hand was characterized by the presence of a negative vibrational frequency (16.8i), and represented a shallow inflection point on a surface connected to a second geometry, i.e the "attack" structure **5b** (Figure 2b).[11] This new minimum was suggestive of a reactant complex, with the halide "attacking" close to the Bürgi−Dunitz trajectory.[12] The C···F distance in **5b** (1.5 Å) is only slightly longer than a typical C_{sp^3}−fluorine bond, and the attendant lengthening of the C−N bonds and the considerable stabilization of **5b** relative to the other triazine complexes in Table 1 all point to a strong σ-complex. However, a much looser complex of this general description is also observed between azide and **1** (i.e, **5c**), which more closely resembles the off-axis water−hexafluorobenzene minimum described by Dougherty.[3] No such structure involving chloride could be found.

Optimization from geometries close to another anticipated minimum, i.e., that involving a C−H···X^- hydrogen bonding interaction, resulted in the observation of complexes with all three anions (**7a**−**c**). The H-bonds are of a good quality, with short X···C distances and X···H−C angles at or near 180° (Figure 2c). The energies of these interactions are comparable in magnitude to those of conventional hydrogen bonds,[13] and although the participation of ions in gas-phase chemistry inevitably leads to bond energies which seem exaggerated vis-à-vis familiar solution values, they may still be relevant to chemistry in the interior of a receptor.

Finally, the azide anion was also found to participate in an apparent $\pi-\pi$ stacking interaction with **1**, i.e., **8** (Figure 2d). The close approach of the two fragments (2.8 Å mean interplanar distance) is consistent with the substantial complexation energy calculated for **8** (Table 1).

Although in regards to receptor design trifluorotriazine **2** is a functional dead-end, we thought it apt to consider the extent to which further electron withdrawal in the triazine system would enhance complexation. As can be seen in Table 1, even stronger anion complexes of the same kind as those described for **1** could generally be located for **2**. The energies and close contacts in the aryl centroid complexes **4** in particular are comparable to alkali cation−π complexes of benzene calculated at the same level of theory.[14] Fluoride shows a strong π-type interaction with **2** (**4b**) which, like **3b**, is distinguished by a single negative frequency (−33.0i), the animation of which connects it to the analogous "attack" structure **6b**. Complex **6b** differs from the other "attack" structures in Table 1 in that it is symmetric about the F···C···F "reaction center", i.e., a Meisenheimer complex of the incipient S_NAr reaction.[15] The cesium salt of **6b** has been observed experimentally.[16]

We chose two representative complexes, i.e., the aryl−centroid and H-bonding complexes of **1** with chloride (**3a** and **7a**, respectively), for evaluation with the highly accurate Complete Basis Set method CBS-Q.[17] While the structures of the optimized complexes change very little, the complexation energies, -6.2 kcal mol^{-1} for **3a** and -8.7 kcal mol^{-1} for **7a**, fall between the uncorrected and counterpoise corrected MP2 values. This seems reasonable in the light of suggestions that MP2 BSSE energies may in fact be overestimated in some cases.[8,18]

As expected, the energy of these interactions falls off sharply with increasing polarity of the medium. Using Tomasi's polarized continuum solvent model,[19] simple comparison of (uncorrected) MP2 single point energies of the chloride−triazine complex (**3a**) in the gas phase (−8.5), heptane (−0.4), chloroform (2.1), ethanol (2.8), and finally water (3.2 kcal mol^{-1})

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[11] Optimization in Gaussian 98 using the "tight" convergence option did not affect the negative frequency, although the imposition of C_{3v} symmetry caused it to shift to a low positive value (5.3 cm^{-1}).

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Table 1. MP2/6-31+G*//MP2/6-31+G* Energies (kcal mol^{-1}) and Noncovalent Bond Distances (Å) and Angles (deg) for Complexes of Triazine (**1**) and Trifluorotriazine (**2**) with Chloride, Fluoride, and Azide Ion

species	$E_{(MP2+ZPE)}$	$E_{(MP2+ZPE-BSSE)}$	r, θ
triazine + chloride π (**3a**)	−8.3	−4.8	3.2, 90.0[a]
triazine + fluoride π (**3b**)	−12.1[b]	−9.2	2.6, 90.0
triazine + azide π (**3c**)	−7.6	−4.5	2.8, 90.0
triazine + fluoride “attack” (**5b**)	−25.0	−18.5	1.5, 106.6[c]
triazine + azide “attack” (**5c**)	−9.0	−5.9	2.8, 97.0
triazine + chloride H-bond (**7a**)	−9.6	−7.4	3.4, 180.0[d]
triazine + fluoride H-bond (**7b**)	−18.4	−16.5	2.8, 180.0
triazine + azide H-bond (**7c**)	−8.0	−6.5	3.1, 175.0
triazine + azide “stack” (**8**)	−10.6	−6.4	2.8[e]
F_3triazine + chloride π (**4a**)	−19.7	−14.8	3.0, 90.0
F_3triazine + fluoride π (**4b**)	−27.7[b]	−24.0	2.4, 90.0
F_3triazine + azide π (**4c**)	−17.9	−13.9	2.6, 90.0
F_3triazine + chloride “attack” (**6a**)	−22.1	−11.1	1.9, 107.9
F_3triazine + fluoride “attack” (**6b**)	−56.1	−48.8	1.4, 108.2
F_3triazine + azide “attack” (**6c**)	−27.0	−17.5	1.5, 109.1
F_3triazine + azide “stack” (**9**)	−20.0	−14.3	2.7[e]

[a] The r and θ values in π complexes represent the $X^-\cdots$aryl centroid distance and the angle of the $X^-\cdots$aryl centroid axis to the plane of the ring, respectively. [b] Stationary point with one imaginary frequency. [c] The r and θ values in “attack” complexes represent the $X^-\cdots C$ distance and the mean $X^-\cdots C{-}N$ “attack” angle, respectively. [d] The r and θ values in H-bond complexes represent the $X^-\cdots C$ distance and the $X^-\cdots H{-}C$ angle, respectively. [e] The r value represents the mean distance of the N atoms in the azide fragment to the plane of the ring.

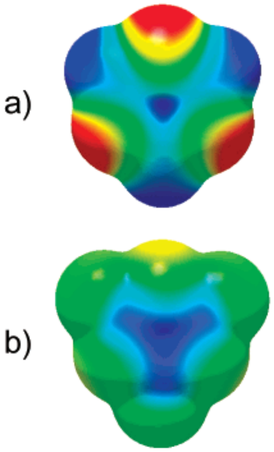

Figure 1. Calculated 6-31+G*//6-31+G* electrostatic potential surfaces for (a) 1,3,5-triazine and (b) trifluoro-1,3,5-triazine. Electrostatic potential surface energies range from −15 (red) to +15 (blue) kcal mol^{-1} for 1,3,5-triazine and −35 (red) to +35 (blue) kcal mol^{-1} for trifluoro-1,3,5-triazine.

suggests that the practical manifestation of these forces will most likely be in the context of anion containment.

To our knowledge, this is the first theoretical demonstration of an interaction between a formally negatively charged species and the π system of an aromatic ring, and complex energies on the order of those shown in Table 1 suggest that the aryl centroid−anion bond should be applicable as noncovalent design principle, and the triazine ring incorporated as a new anion recognition module in cyclophane chemistry.

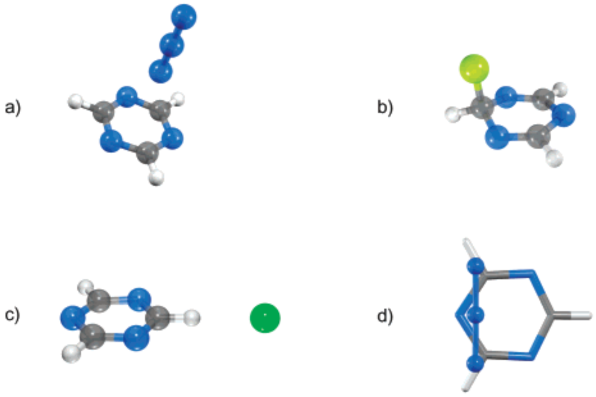

Figure 2. Modeled representations of (a) the triazine−azide aryl centroid complex **3c**; (b) the triazine−fluoride “attack” complex **5b**; (c) the triazine−chloride H-bonding complex **7a**; and (d) the triazine−azide “stack” complex **8**.

Methods

All calculations were performed with the Gaussian 98 program (revision A-9)[20] with default optimization procedures. Symmetry was disabled in all calculations by use of the nosymm keyword. Frequency calculations were performed at the same level of theory as the optimizations (MP2/6-31+G*) to determine zero-point energy (ZPE) corrections, which were applied unscaled. Counterpoise corrections were calculated for optimized structures by using the method of Boys and Bernardi.[10] CBS-Q calculations were performed according to the method of Petersson et al.[17]

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Supporting Information Available: Cartesian coordinates of MP2/6-31+G* optimized geometries of all complexes appearing in this study (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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