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Anion−π Interactions in Four-Membered Rings

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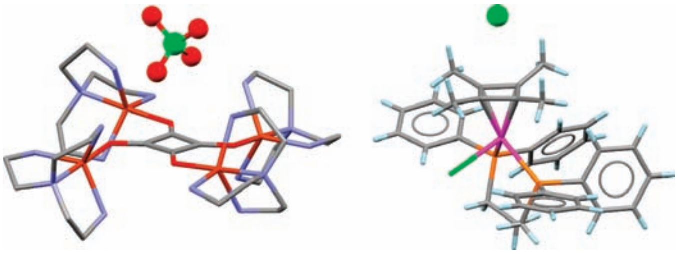
ABSTRACT



In this study, the importance of anion−π interactions in four-membered rings has been evidenced. Two kinds of rings have been found to be suitable for participation in anion−π interactions: first, in different salts of cyclobuten-1,2-dione derivatives and, second, in η^4-cyclobutadiene complexes with transition metals.

The chemistry of noncovalent interactions is a highly active interdisciplinary field. It has decisive implications in biology, chemistry, physics, and engineering.[1] Noncovalent contacts involving aromatic rings such as $\pi-\pi$,[2] cation−π,[3] and C−H/π[4] interactions are widely recognized as stabilizing interactions for many systems, including biomolecules, molecular recognition, and supramolecular assemblies. During the past five years, a new type of supramolecular bonding force is being considered by the scientific community, i.e., the anion−π interaction with electron−deficient aromatic rings.[5] It has been clearly evidenced by theoretical[6] and experimental studies.[7] This new field of supramolecular chemistry has been widely developed, and some significant new examples of anion−π binding associations are now increasingly described in the literature.[8]

The anion−π interaction has been recently reviewed.[5] There are many examples that state the importance of this interaction in the solid state. Many of these examples involve a more or less electron−deficient six-membered ring. An

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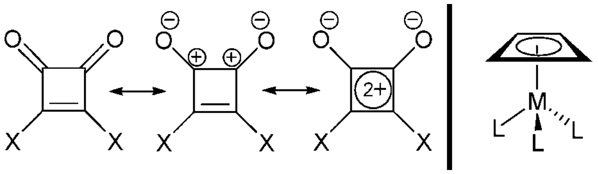
increasing number of examples have been also observed in five-membered rings as, for instance, the imidazole ring.[9]

In this paper, we demonstrate the importance of anion−π interactions in four-membered rings. As far of our knowledge extends, this is the first study that deals with anion−π interactions in this type of rings. Previous studies have provided evidence of the aromatic character of cyclobutene-1,2-diones and its derivatives due to the partial contribution of a resonance structure (see Scheme 1), which leads to an electron-deficient aromatic ring.[10] The simplest four-membered ring, cyclobutadiene, is not a good candidate to participate in anion−π interactions since it is antiaromatic and it is not electron deficient. However, an additional possibility to envisage anion−π interaction in four-membered rings using cyclobutadiene is taking advantage of its aromatization when it is η^4-coordinated to a transition metal (see Scheme 1, right).[11]

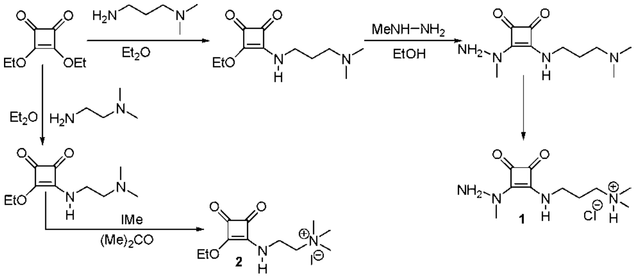
Scheme 1. (Left) Resonance Forms of Cyclobutene-1,2-dione Derivatives. (Right) η^4 Coordination of Cyclobutadiene with a Transition Metal



We have divided this manuscript into three parts that illustrate the importance of anion−π interactions in four-membered rings from different approaches. First, we report the synthesis and solid-state characterization of two derivatives of cyclobutene-1,2-dione that exhibit relevant anion−π interactions. Second, a search on the Cambridge Structural Database[12] gives a global view of the types of four-membered rings that are appropriate to participate in anion−π interactions. Third, a theoretical study using high level ab initio calculations that confirms the noncovalent interaction, which is characterized energetically and geometrically at the RI-MP2/aug-cc-pVTZ level of theory.

The synthetic route to compounds **1** and **2** is shown in Scheme 2. Compound **1** was synthesized by condensation at room temperature of $N,^1N^1$-dimethylpropane-1,3-diamine and diethyl squarate, followed by a second condensation with methyl hydrazine. During the purification procedure, compound **1** was obtained as chlorhydrate. Compound **2** was synthesized by condensation of $N,^1N^1$-dimethylethane-1,2-diamine and diethyl squarate, followed by exhaustive methylation with methyl iodide.[13] For both compounds, suitable crystals for X-ray crystallography were obtained and resolved (see the Supporting Information for experimental details). They exhibit interesting noncovalent interactions that are highlighted in Figure 1. In compound **1**, the chloride anion establishes an anion−π interaction with the squaramide ring. The anion is located over the ring plane at 3.55 Å. In addition, it establishes several nonconventional $\mathrm{C{-}H\cdots Cl}$ hydrogen bonds (HB) with the α hydrogen atoms of two trialkylammonium groups and one conventional hydrogen bond with the N−H group (see Figure 1). In compound **2**, the iodide anion establishes a strong $\mathrm{N{-}H\cdots I^-}$ hydrogen bond with the N−H group of the squaramide ring. It also interacts with the positively charged $-\mathrm{N^+Me_3}$ group, com-

Scheme 2. Synthetic Route to **1** and **2**



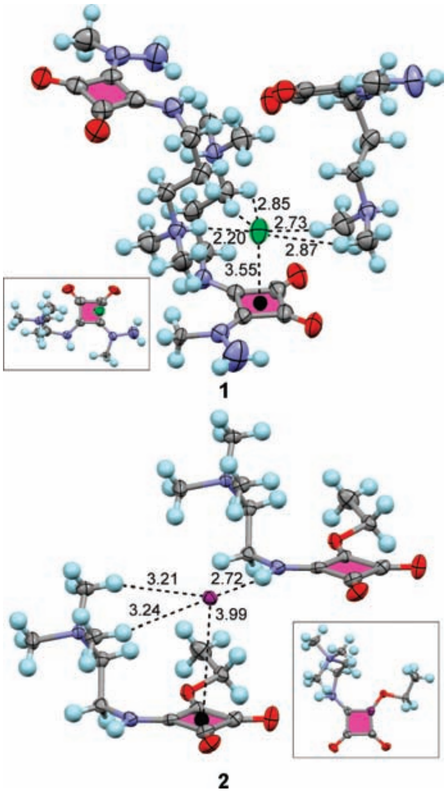


Figure 1. ORTEP representation of X-ray structures **1** (up) and **2** (down). Thermal ellipsoids are plotted at the 50% probability level.

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bining the C−H···I$^-$ hydrogen bonds with the electrostatic interaction. Finally, the iodide anion is further stabilized interacting with the four-membered ring, at 3.99 Å from the center of the ring. It is located over one carbon of the ring that belongs to one C═O group at 3.82 Å; see the on-top representation of Figure 1.

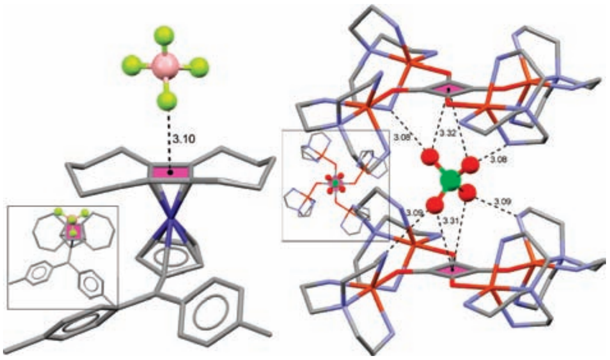

Figure 2. Partial views of X-ray structures ZEQRES (right) and REPXEP (left).

The discovery of these unprecedented anion−π interactions in these compounds, which are characterized by the presence of a small four-membered ring, drove us to search additional examples in the Cambridge Structural Database (CSD) in an effort to generalize the existence of the interaction in these rings. Crystal structures are very rich in information and often reveal effects that had not been noticed by the original authors. The CSD is a convenient and reliable storehouse for geometrical information. The utility of small-molecule crystallography and the CSD in analyzing geometrical parameters and nonbonding interactions has been clearly established.[14] In exploring the CSD, we found 59 structures in which noncovalent π interactions are present between atoms such as F, Cl, Br, O, and S bearing a negative charge and four-membered rings. Two selected examples (REPXEP[15] and ZEQRES[16]) that exemplify the nature of four-membered rings that are well suited to participate in anion−π interactions are depicted in Figure 2. In the ZEQRES structure, the anion establishes two anion−π interactions with two rings. In addition, hydrogen-bonding interactions with the neighborig −NH$_2$ groups further stabilize the anion. In the REPXEP structure, the anion also interacts with several aromatic hydrogen atoms of neighboring molecules, which are not shown for the sake of clarity. Other interesting examples are included in the Supporting Information. From the search we learn that in all cases the four-membered ring is either a derivative of 1,2-cyclobutendione or a cyclobutadiene coordinated to a transition metal. The former are more abundant than the latter. Only four structures involving cyclobutadiene are present in the CSD. In contrast, a considerable number (55 hits) of structures related to 1,2-cyclobutendione (squarate, squaramide, and thiosquarate derivatives) exhibit interesting anion−π interactions. This fact can be considered additional evidence for the proposed aromatic character of oxocarbons[10] since the aromatic resonance structure (see Scheme 1) implies an electron-deficient aromatic ring.

The geometries of all complexes studied in this work were fully optimized at the RI-MP2(full)/aug-cc-pVTZ level of theory using the TURBOMOLE program.[17] The binding energies were calculated with correction for the basis set superposition error (BSSE) by using the Boys−Bernardi counterpoise technique.[18] The optimization of the complexes has been performed imposing C_{2v} symmetry for complexes **6**−**9** and C_2 for complexes **10** and **11** (see Figure 3).

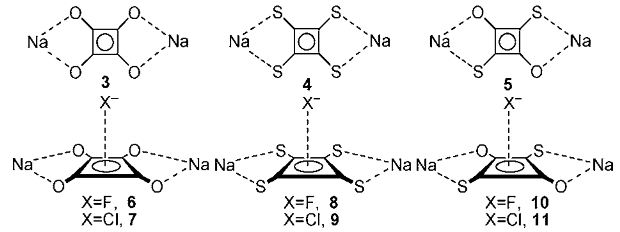

Figure 3. Schematic representation of model compounds **3** and **4** and complexes **6**−**11**.

We have analyzed computationally the anion−π binding affinity of squarate and thiosquarate salts. We have found several X-ray structures in the CSD, which are shown in Figure 4. It can be appreciated that in the thiosquarate salt (KDTSQM[19]) one sulfur atom is located over the center of the ring establishing an anion−π interaction. In addition, the CEZFUI[20] structure is characterized by the presence of an anion−π interaction involving one sulfur atom. The lithium squarate salt (NAZDAU[21]) forms a parallel displaced stacking where the oxygen atom is located over one carbon atom of the four-membered ring.

As a model of the squarate and thiosquarate salts we have used the compounds shown in Figure 3. We have studied computationally their π−interaction ability toward F$^-$ and Cl$^-$ anions.

In Table 1 we summarize the binding energies without and with the basis set superposition error (BSSE) correction (*E* and

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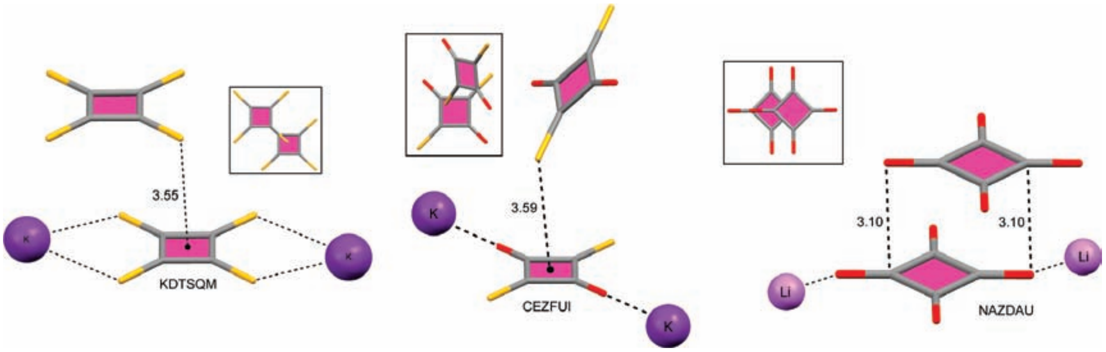

Figure 4. Partial views of several X-ray structures.

Table 1. Binding Energies without and with the BSSE Correction (E and E_{BSSE}, kcal/mol, respectively) and Equilibrium Distances (R_e, Å) at the RI-MP2/aug-cc-pVTZ Level of Theory for Complexes **6**−**11** Are Summarized

complex	E	E_{BSSE}	R_e
6 (**3** + F^-)	−7.27	−4.66	2.596
7 (**3** + Cl^-)	−6.09	−2.99	3.160
8 (**4** + F^-)	−10.00	−5.49	2.319
9 (**4** + Cl^-)	−6.23	−2.68	3.050
10 (**5** + F^-)	−11.17	−7.43	2.425
11 (**6** + Cl^-)	−8.10	−4.13	3.029

E_{BSSE}, respectively) and equilibrium distances (R_e) of complexes **6**−**11** at the RI-MP2/aug-cc-pVTZ level of theory. The energetic features of the complexes clearly indicate that the interaction of anions with squarate and thiosquarate salts is favorable. The equilibrium distances are shorter in complexes **8** and **9**, where the interaction is established with the thiosquarate ring. A likely explanation is that the repulsion between the O/S atoms and the interacting anion is smaller in complexes **8** and **9** than in **6** and **7**. The most favorable complexes are **10** and **11**, in agreement with the experimental X-ray geometries of (thio)squarate salts (see Figure 4), as deduced by the directionality of the anion−π interaction in the CEZFUI structure.

In summary, the results reported in this paper stress the significance of the anion−π interaction in four-membered rings, which has not been previously described in the literature. We have evidenced it by reporting the synthesis and X-ray characterization of two new squaramide salts that exhibit interesting anion−π interactions in the solid state. A search in the CSD has provided further evidence on the importance of this interaction in four-membered rings. It has been also used to generalize the interaction in cyclobutene-1,2-dione derivatives and in η^4-cyclobutadiene complexes with transition metals. In addition, a high level ab initio investigation on squarate and thiosquarate salts have provided computational support for the experimental observations.

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Supporting Information Available: CCDC 720233 and CCDC 720232 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Experimental details, Cartesian coordinates of optimized structures, AIM analysis, and the list of X-ray structures retrieved from the CSD. This material is available free of charge via the Internet at http://pubs.acs.org.

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