J. Phys. Chem. A **2004,** *108,* 9423−9427 **9423**

Cation−π versus Anion−π Interactions: Energetic, Charge Transfer, and Aromatic Aspects

Carolina Garau, Antonio Frontera,* David Quiñonero, Pablo Ballester, Antoni Costa, and Pere M. Deyà*

Departament de Química, Universitat de les Illes Balears, Crta. de Valldemossa km 7.5,
07122 Palma de Mallorca, Baleares, Spain

Received: June 8, 2004; In Final Form: July 12, 2004

Several π-complexes of cations and anions with aromatic rings have been optimized at the MP2/6-31++G** level of theory. Different aspects of the cation−π interaction have been compared to those of anion−π, including changes in the aromaticity of the ring upon complexation, charge-transfer effects using the Merz−Kollman and "atoms-in-molecules" (AIM) charges, and the contribution of correlation and dispersion energies by comparing the complexation energies computed at the HF, B3LYP, and MP2 levels of theory. In this paper, we study three aromatic systems that allow direct comparisons, free from other influences, of the cation−π versus anion−π interactions, which are the 1,3,5-trifluorobenzene (**TFB**), *s*-triazine (**TAZ**), and 2,5-dichloropyrazine (**DCP**). These compounds are able to π-interact favorably with either anions or cations because of their very small quadrupole moments.

1. Introduction

Intermolecular interactions involving aromatic rings are important processes in both chemical and biological recognition. Their understanding is essential for the rational design of drugs and other new functional materials.[1] In particular, the interaction of a cation and an aromatic system, a cation−π interaction, is a strong interaction which plays a key role in molecular recognition.[2] Most studies have investigated the nature and energetics of cation−π interactions.[3] For example, Dougherty et al.[4] have reported that the preferential binding of cations to different aromatic compounds can be explained in terms of electrostatic considerations. Moreover, Cubero et al.[5] have demonstrated that the interaction is dominated by electrostatic and cation-induced polarization terms. Additionally, another study[6] concludes that the cation → benzene induction interaction (polarization) is more important for the Li^+/π and Na^+/π complexes than the electrostatic and that the contributions from dispersion and the benzene → cation induction are negligible. In cation−π interactions, the nature of the electrostatic component has been rationalized, giving emphasis to the function of the permanent quadrupole moment of benzene ($Q_{zz} = -8.45$ B (buckinghams), 1 B $= 3.336 \times 10^{-40}$ C m^2).[7] Regardless of whether the aromatic ring is substituted with electron-withdrawing groups, the quadrupole moment can invert its sign. For instance, the hexafluorobenzene (**HFB**) has a permanent quadrupole moment similar in magnitude to benzene (**BEN**) but of opposite sign ($Q_{zz} = +9.50$ B),[8] 1,3,5-trinitrobenzene (**TNB**) has a large and positive Q_{zz} (+20 B),[9] and 1,3,5-trifluorobenzene (**TFB**) has a very small Q_{zz} (+0.57 B).[10] We[11] and others[12] have recently demonstrated that these compounds can interact favorably with anions, and we have used the term anion−π interaction to define this new type of noncovalent interaction. This term was previously used by Schneider et al.[13] in their study of the interaction of sulfate anion with phenyl groups bearing ammonium substituents.[14] Our group has reported several studies of electron-deficient aromatic rings with anions[11,15] and the simultaneous interaction of aromatic rings with both anions and cations.[16] More recently, we have reported a topological study of the anion−π interaction in several complexes of aromatic compounds with positive quadrupole moments and Cl^-,[17] where we have shown that the electrostatic component of the interaction correlates with the magnitude of the Q_{zz} of the aromatic ring and the anion-induced polarization correlates with the molecular polarizability ($\alpha_{||}$) of the aromatic compounds. As for the cation−π interaction, these two contributions dominate the anion−π interaction, which are essentially equivalent in **HFB**; however, in molecules with a very positive Q_{zz} such as **TNB**, the interaction is basically electrostatic although the polarization is not negligible,[15a] and in molecules with a modest Q_{zz} and considerable molecular polarizabilities such as **TFB** the interaction is dominated by induction effects. The latter behavior explains the dual binding mode of **TFB**[15a] and other aromatic rings with small Q_{zz} values such as *s*-triazine (**TAZ**)[18] ($Q_{zz} = +0.90$ B)[19] and 2,5-dichloropyrazine (**DCP**) ($Q_{zz} = +1.47$ B), which are capable of π-interacting favorably with either anions or cations. All of these considerations indicate that the strength of the anion−π interaction and its contributions to the interaction energy (electrostatic, induction, dispersion, etc.) sharply depend on the Q_{zz} and $\alpha_{||}$ values of the aromatic compound.

K. S. Kim et al. have recently reported[20] theoretical investigations on anion−π interactions, focusing their attention on a quantitative estimation of the individual interaction energy components. They have also compared the anion−π with the cation−π interaction in terms of the magnitudes of several contributions to the total interaction energies, and they have found that dispersion energies are more important in anion−π than in cation−π complexes.

In this manuscript, we report a theoretical ab initio study where we compare several important aspects of both anion−π and cation−π interactions which have not been considered before, as their different behavior in the change in the aromaticity of the ring upon complexation, the change in the electron charge density topology upon complexation, etc. We also compute the contribution of the dispersion energy in both

---

* Corresponding author. E-mail: toni.frontera@uib.es.

10.1021/jp047534x CCC: $27.50

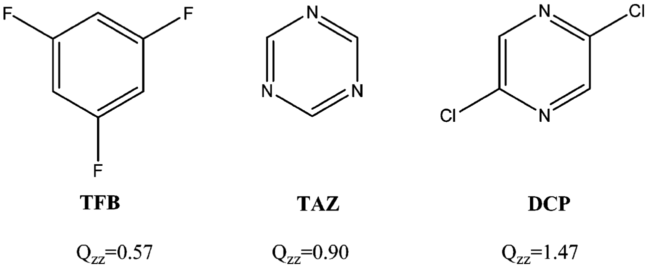

Figure 1. 1,3,5-Trifluorobenzene (**TFB**), *s*-triazine (**TAZ**), and 2,5-dichloropyrazine (**DCP**) and their corresponding quadrupole moments (Q_{zz}) in buckinghams.

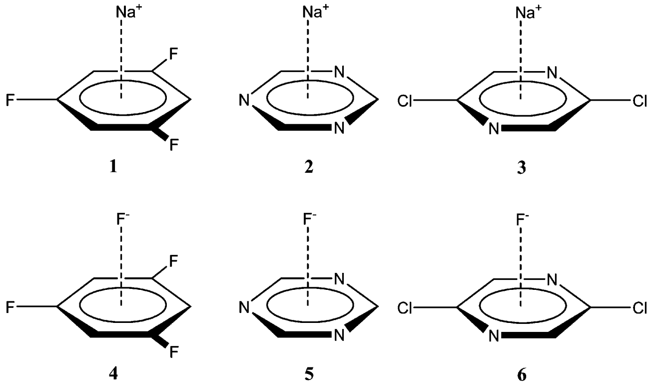

Figure 2. Cation−π and anion−π complexes **1**−**6**.

cation−π and anion−π interactions using a methodology which is based on the fact that the B3LYP method does not take into account dispersion effects, and, thus, its contribution can be roughly estimated as the difference between the MP2 and the B3LYP interacting energies.[21] It is worth mentioning that we compare the anion−π to the cation−π interaction using the same series of aromatic compounds, that is, **TFB**, **TAZ**, and **DCP**, which are able to interact favorably with both anions and cations (see Figure 1). In contrast with other works,[20,22] this direct comparison using the same aromatic ring is free from other influences; for instance, when comparing **BEN**−cation complexes with **HFB**−anion complexes, the absolute values of the quadrupole moment are similar but not equal and the molecular polarizabilities of the aromatic rings are different ($\alpha_{||}$(**BEN**) = 41.5 au and $\alpha_{||}$(**HFB**) = 37.7 au); therefore, the individual contributions to the total interaction energy are not only due to the ion, but they are also influenced by the nature of the ring.

2. Computational Methods

The geometries of all of the complexes included in this study were fully optimized at the MP2/6-31++G** level of theory using the Gaussian 98 program.[23] The interaction energy was calculated at the same level with and without correction for the basis set superposition error (BSSE) using the Boys−Bernardi counterpoise technique.[24] The vibrational frequencies at the MP2 level were also calculated for the optimized geometries, indicating that only one structure is a genuine minimum (**TFB**···Na$^+$). Previous studies have shown[11,12,15,20] that, in contrast to other halogen anions, the true minimum in the F$^-$ anion−π complexes with a variety of aromatics is the nucleophilic attack of the anion to one carbon atom of the ring. However, because the aim of this study is to compare the anion/cation recognizing ability of the π-systems and to analyze different aspects of the interaction, we concentrate on the geometries where the ion is located along the main symmetry axis.

The contributions to the total interaction energy have been computed using the molecular interaction potential with polarization (MIPp),[25] which is an improved generalization of the MEP where three terms contribute to the interaction energy: (i) an electrostatic term identical to the MEP,[26] (ii) a classical dispersion-repulsion term, and (iii) a polarization term derived from perturbational theory.[27] Calculation of the MIPp of **TFB**, **TAZ**, and **DCP** interacting with Na$^+$ and F$^-$ was performed using the HF/6-311+G* wave function of the aromatic rings by means of the MOPETE-98 program.[28] The ionic van de Waals parameters for F$^-$ and Na$^+$ were taken from the literature.[18,29]

The HF method does not include electron correlation; therefore, its contribution to the total interaction energy can be estimated as the difference between the interacting energy of the complexes computed at the MP2(full)//MP2 and HF//MP2 levels of theory. Additionally, the dispersion interactions are not given by the DFT B3LYP level of theory but are given at the MP2 level; thus, the difference between MP2(full)//MP2 and B3LYP//MP2 interacting energies can be considered as an approximate contribution of the dispersion term to the total interacting energy.[21] It should be emphasized that this a qualitative estimation of the dispersive interaction energy.

We have used the nucleus-independent chemical shift (NICS)[30] criterion to evaluate the aromaticity of **TFB**, **TAZ**, and **DCP** upon complexation. This method is based on the negative of the magnetic shielding computed at the center of the ring. Significant negative values imply aromaticity (diatropic ring current), and positive values correspond to antiaromaticity (paratropic ring current). NICS at the geometrical center of the ring is influenced by the local (paratropic) effects arising mainly from the σ bonds. NICS(1) (1 Å above the plane of the ring) essentially reflects π effects, and it is a better indicator of the ring current than the value at the center. NICS values were computed at the GIAO-HF/6-31++G**[31] level of theory using the MP2 optimized structures.

The topological analysis of the electron charge density performed for **TFB**, **TAZ**, and **DCP**, and for complexes **1**−**6**, was determined using Bader's theory of AIM.[32] The electronic density analysis was performed using the AIMPAC program[33] at the HF/6-31++G** level of theory. The AIM charges were evaluated using the AIM2000 program.[34]

The quadrupole moment of **DCP** was computed using the CADPAC program[35] at the MP2/6-31G* level because previous studies[10] have demonstrated that quantitatively correct values are obtained at this level of theory.

3. Results and Discussion

First of all, the selection of the complexes studied in this manuscript (see Figure 2) deserves an explanation. As stated in the Introduction, we have chosen three aromatic systems with small (**DCP** and **TAZ**) or very small (**TFB**) Q_{zz} values that allow us to make direct comparisons between cation−π and anion−π interactions, that is, to study their differences only on the basis of the nature of the interacting ion. Additionally, the interacting ions are Na$^+$ and F$^-$, which are isoelectronic, and, consequently, their complexes with the aromatic compound are also isoelectronic.

In a previous study on the nature of anion−π interactions, Kim et al.[20] conclude that the total interaction energies of anion−π complexes are comparable to those of cation−π complexes. This is true for the systems studied in that work, that is, **BEN** complexes with cations and **HFB** complexes with anions, but it cannot be generalized. The same is applicable to the conclusion that the largest contributions in anion−π

TABLE 1: Interaction Energies at the MP2/6-31++G Level of Theory with the BSSE Correction (E_{BSSE}, kcal/mol), Equilibrium Distances (R_e, Å), and the Contribution of Correlation (E_{corr}, kcal/mol) and Dispersion (E_{dis}, kcal/mol) Terms to the Total Interaction Energy, Merz−Kollman and AIM Charges (q, e) of the Ion (Na$^+$, F$^-$), Electron Charge Density at the (3,+3) Cage Critical Point (ρ, au) Originated upon Complexation, the Variation upon Complexation of the Electron Charge Density at the Aromatic C−C or C−N (3,−1) Bond Critical Point ($\Delta\rho$, au), and the Variation (ΔNICS(1), ppm) upon Complexation of the NICS Computed at 1.0 Å below the Aromatic Ring (Opposite to the Ion) for Complexes 1−6**

compound	E_{BSSE}	R_e	E_{corr}	E_{dis}	q (MK)	q (AIM)	$10^3\rho$ (au) (3,+3)	$\Delta\rho$ (au) (3,−1)	ΔNICS(1)
TFB···Na$^+$ (**1**)	−8.21	2.552	−3.21	−1.48	0.81	0.95	6.103	−0.004	0.89
TZN···Na$^+$ (**2**)	−2.59	2.696	−2.18	−1.53	0.85	0.97	4.178	−0.003	0.55
DCP···Na$^+$ (**3**)	−2.87	2.617	−4.85	−2.99	0.82	0.97	4.360	−0.003[a]	0.99
TFB···F$^-$ (**4**)	−7.77	2.748	−4.04	−2.51	−0.87	−0.99	5.069	0.002	−0.28
TZN···F$^-$ (**5**)	−9.70	2.592	−4.14	−2.64	−0.85	−0.98	7.073	0.002	0.04
DCP···F$^-$ (**6**)	−13.88	2.508	−5.66	−3.46	−0.81	−0.98	7.608	0.003[a]	−0.67

[a] This value corresponds to the C−C bond critical point of the pyrazine; see text.

TABLE 2: Contributions to the Total Interaction Energy (kcal/mol) Calculated Using MIPp for the TFB, TAZ, and DCP Compounds Interacting with Na$^+$ and F$^-$ at the Distance (d, Å), Where the MIPp Is Minimum, from the Center of the Ring along the Main Symmetry Axis[a]

compound	E_e	E_p	E_{vw}	E_t	d (Å)	E_{BSSE}	R_e
TFB···Na$^+$	1.83	−13.81	2.15	−9.83	2.54	−8.21	2.552
TAZ···Na$^+$	5.58	−7.84	−0.01	−2.28	2.81	−2.59	2.696
DCP···Na$^+$	7.00	−11.39	0.34	−4.05	2.71	−2.87	2.617
TFB···F$^-$	−1.59	−9.15	1.26	−9.47	2.91	−7.77	2.748
TAZ···F$^-$	−5.63	−7.93	2.34	−11.22	2.80	−9.70	2.592
DCP···F$^-$	−6.52	−10.44	2.72	−14.23	2.79	−13.88	2.508

[a] For comparison purposes, the interacting energies (E_{BSSE}, kcal/mol) and equilibrium distances (R_e, Å) corresponding to MP2 optimized complexes are included.

complexes are electrostatic and induction, because these contributions sharply depend on the Q_{zz} and $\alpha_{||}$ values of the aromatic system and this is correct only for **HFB** complexes with anions, but this is not correct, for instance, for **TNB** complexes where the largest contribution is electrostatic or **TFB** complexes where the induction energy dominates the interaction. To solve this inherent problem, the present study details an investigation of the interaction of Na$^+$ and F$^-$ with several π-systems, focusing our attention on the differences that the interaction of an anion or a cation induces in the same aromatic compound, such as energetic, charge transfer, aromaticity, and electron density.

3.1. Energetic Results. Table 1 reports the total interacting energies and equilibrium distances of complexes **1**−**6** at the MP2/6-31++G** level of theory. In all cases, the interacting energies are negative, indicating that the interaction is favorable; that is, the complexes are energetically stable. Some interesting features can be learned from the inspection of the interaction energies and equilibrium distances depending on the aromatic system. The **TFB** interacts more favorably with the sodium cation than with the fluoride anion, whereas **TAZ** and **DCP** behave in the opposite manner. Additionally, the **TFB** complex with Na$^+$ (**1**) has an equilibrium distance shorter than that of the **TFB** complex with F$^-$ (**4**), while **TAZ** and **DCP** complexes behave in the opposite manner. It should be mentioned that cations have smaller van der Waals radii than anions and they are expected to have shorter equilibrium distances. Furthermore, **TFB** complexes **1** and **4** have very similar interacting energies (−8.21 and −7.77 kcal/mol, respectively), and **TAZ** and **DCP** complexes have very dissimilar interacting energies depending on the interacting ion. A likely explanation for these results is that the **TFB** is the only aromatic system that has an almost negligible Q_{zz}, and, accordingly, the electrostatic repulsion when it is interacting with Na$^+$ is very small, allowing the approximation of the cation at a distance of 2.552 Å, close to the value obtained for the **BEN**···Na$^+$ complex at the same level (2.429 Å[22]). As is further discussed below, this short distance allows the cation to polarize the π-cloud of **TFB** in an effective way and to improve the interaction, in comparison with complexes **2** and **3**, where the equilibrium distances are longer due to the electrostatic repulsion with the small but positive values of $\mathbf{Q_{zz}}$ of **TAZ** and **DCP**.

The correlation and dispersion energies are in all cases more negative for anion−π complexes than for the corresponding cation−π complexes. The computed value of dispersion energy obtained for complex **5** is significantly lower in energy than the previously reported value by Kim et al.[20] using the symmetry adapted perturbation theory (SAPT) calculation, which is −5.94 kcal/mol. The computed values of E_{corr} are significant for all complexes, indicating the importance of taking into account correlation effects when studying noncovalent interactions involving aromatic rings.

3.2. Molecular Interaction Potential with Polarization (MIPp) Analysis. We have analyzed the physical nature of the cation/anion−π interaction in these systems, evaluating it using the energetic partition scheme of the MIPp. We have explored the electrostatic (E_e), polarization (E_p), van der Waals (E_{vw}), and total (E_t) interaction energies when the ion (Na$^+$ or F$^-$) approaches the aromatic molecules (**TFB**, **TAZ**, and **DCP**) perpendicular to the center of the ring along the main symmetry axis. In Table 2, we summarize the contribution of the three terms and the total energy at the point along the symmetry axis where the MIPp is minimum, and we also present the MP2 interacting energies and equilibrium distances (R_e) of the optimized complexes for comparison purposes. It is worth mentioning that the MIPp energies are computed from the wave function of the single aromatic compounds **TFB**, **TAZ**, and **DCP** interacting with the corresponding ions considered as classical particles; therefore, the changes in the geometry of the ring in the complex are not accounted in MIPp calculations. The results present in Table 2 point out that the performance of MIPp calculations is notable, giving results comparable to MP2 in both energies and equilibrium distances. The results also confirm the aforementioned assumption that the negligible Q_{zz} value of **TFB** allows the approximation of Na$^+$ to the center of the ring. In this case, the MIPp minimum is located at 2.54 Å from the ring center, very close to the MP2 optimized distance of 2.55 Å. For the interaction of Na$^+$/F$^-$ with **TFB**, the smallest

TABLE 3: Molecular Polarizabilities Parallel to the Principal Symmetry Axis ($\alpha_{\|}$, au), Quadrupole Moments (Q_{zz}, buckinghams), Nucleus-Independent Chemical Shifts (NICS(1), ppm), and the Density at the Bond Critical Point (ρ, au) Computed for the TFB, TAZ, and DCP Compounds

compound	$\alpha_{\|}$ (au)	Q_{zz}	NICS(1)	ρ (3,−1)
TFB	38.79	0.57[a]	−11.77	0.335
TAZ	30.34	0.90[b]	−9.95	0.368
DCP	44.32	1.47[c]	−11.11	0.333[d]

[a] From ref 10. [b] From ref 19. [c] This work. [d] This value corresponds to the C−C aromatic bond of the pyrazine ring; see text.

contribution to the total interaction energy is the electrostatic term, and the polarization term is large and negative and clearly dominates the interaction. For the interaction of **TFB** with F$^-$, the MIPp minimum is located at 2.91 Å because of its larger van der Waals radius, and, as a result, the polarization term is smaller in comparison with the Na$^+$ complex. For the **TAZ** and **DCP** systems, the interaction is dominated by the polarization term; however, in both molecules the electrostatic term is not negligible, and it is responsible for the considerable difference in energy between the cation−π (positive contribution) and the anion−π interaction (negative contribution).

Finally, the molecular polarizabilities of **TFB**, **TAZ**, and **DCP** are presented in Table 3, ensuing the following trend **DCP** > **TFB** > **TAZ**, in agreement with the observed trend for the contribution of the polarization term in their anion−π complexes which are comparable due to their similar distances (*d*, Table 2).

3.3. Topological Properties of the Electron Charge Density, Aromatic, and Charge-Transfer Analyses. In Table 1, we compare some interesting aspects of cation−π and anion−π complexes. For instance, we have measured the degree of the charge-transfer effect in these systems to determine the atomic charges of complexes **1**−**6** using the Merz−Kollman (MK) method,[36] which has been demonstrated to provide high-quality charges.[37] In general, the computed charge transfer in absolute value is very similar for all complexes, ranging from 0.1 to 0.2 *e*. To analyze the charge transfer from another quantum chemical approach, we have computed the atomic charges of the interacting ion in complexes **1**−**6** obtained upon integration of the electron density in the basin of the Na$^+$ and F$^-$ (AIM charges). The results based on AIM methodology indicate that the charge transfer is almost negligible for all complexes (<0.03 *e*). The disagreement between the AIM and electrostatic potential derived charges methods has been observed before for other systems and has been discussed in the literature.[36,38,39]

A common feature of all compounds upon complexation of the ion is the formation of a cage critical point, located along the line connecting the ion with the center of the ring. It has been demonstrated[17,40] that the electron charge density at the cage critical point in cation/anion−π interactions can be used as a measure of the strength of the interaction. The values of the charge density computed at the cage critical point (ρ (3,+3)) for complexes **1**−**6** are present in Table 1. Inspection of the results indicates that there is a relationship between the interaction energy and the electron charge density at the cage critical point. In Figure 3, we represent the plot of the regression between ρ (3,+3) and the interaction energy (E_{BSSE}) for complexes **1**−**6**, with a regression coefficient $r = 0.945$. It is worth mentioning the relevance of this relationship, because it includes both cation−π and anion−π complexes and allows for dealing simultaneously with both interactions.

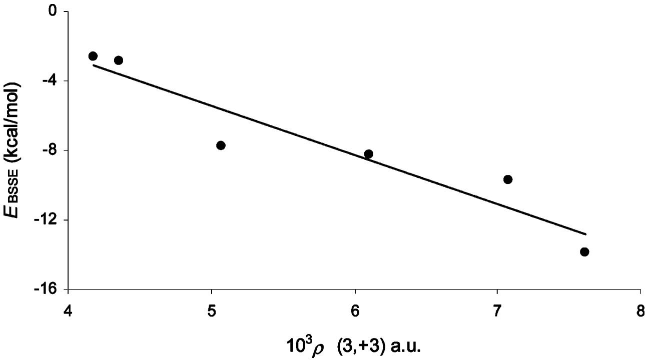

Figure 3. Plot of the regression between the density at the cage critical point and the interaction energy for complexes **1**−**6**.

An interesting feature that has been studied is the variation of the electron charge density measured at the six bond critical points of the aromatic rings upon complexation of the ion. Because the electron density at the bond critical point provides a measure of the bond order, it can be reasonably assumed that the induced change in electron density at the bond critical point upon complexation gives a measure of the variation in the strength of the bond. The computed charge density values for **TFB** and **TAZ** at the six bond critical points of the ring are present in Table 3 (ρ (3,−1)), and its variation upon complexation ($\Delta\rho$ (3,−1)) are present in Table 1. **TFB** and **TAZ** complexes have C_{3v} symmetry, and consequently the six bond critical points of the ring are equivalent; however, the **DCP** has C_{2v} symmetry, and it has three different types of bond critical points in the ring, so in this case only the corresponding values of ρ and $\Delta\rho$ at the bond critical point of the C−C aromatic bond are shown in Tables 1 and 3. It should be mentioned that the $\Delta\rho$ values computed for the rest of the bond critical points of the **DCP** ring (C−N bonds) behave the same. Curiously, the computed $\Delta\rho$ values are negative for the cation−π complexes **1**−**3**, indicating a reduction in the strength of the aromatic bonds upon complexation. On the contrary, the values are positive for anion−π complexes **4**−**6**, indicating an increase in the strength of the aromatic bonds upon complexation. Latter findings can be related, first, with the charge transfer (MK) from the aromatic ring to the cation (**1**−**3**) and from the anion to the aromatic ring (**4**−**6**) and, second, with the results of the variation in the aromaticity of the ring induced upon complexation, which are present in Table 1. The cation−π complexes give a positive variation of the NICS, indicating a diminution in the aromaticity of the ring upon complexation of the cation. In contrast, the variation in the aromaticity upon complexation of the anions is negligible in complex **5** and negative in complexes **4** and **6**, indicating a gain in the aromaticity of the ring in anion−π complexes, in agreement with previous studies on complexes of **HFB**[22] and **TNB**[15a] with anions.

4. Conclusions

It is clear that the strength of cation−π and anion−π interactions strongly depends on the magnitude of the quadrupole moment and molecular polarizability of the aromatic system and direct comparisons between the strength of both interactions should be performed using the same aromatic compound.

The conclusions that can be drawn from this study are listed below:

(1) Molecules with negligible Q_{zz} values can interact favorably with either cations or anions, and it is expected that the strength of the interaction would be comparable, especially if the ionic van der Waals radii are similar.

(2) In general, the contributions of dispersion and correlation terms to the total interaction energies are small, and they are more important in anion−π than in cation−π complexes.

(3) The density at the cage critical point generated upon complexation of the ion is a useful parameter for measuring the strength of the interaction, even when comparing cation−π to anion−π complexes.

(4) A gain in the aromaticity of the ring is observed upon complexation of the anion, and the contrary is observed for the cation. This behavior agrees with the observed variation in the strength of the bonds of the ring upon complexation of the ion, measured using the computed electron charge density at the bond critical points of the ring, which is negative for cation−π complexes and positive for anion−π complexes.

Acknowledgment. We thank the DGICYT and Conselleria d'Innovació i Energia (Govern Balear) of Spain (projects BQU2002-04651 and PRDIB-2002GC1-05, respectively) for financial support. We thank the Centre de Supercomputació de Catalunya (CESCA) for computational facilities. C.G. thanks the MECD for a predoctoral fellowship. A.F. thanks the MCyT for a "Ramón y Cajal" contract.

References and Notes

(1) Meyer, E. A.; Castellano, R. K.; Diederich, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1210.

(2) (a) Dougherty, D. A. *Science* **1996**, *271*, 163. (b) Sussman, J. L.; Harel, M.; Frolow, F.; Oefner, C.; Goldman, A.; Tolker, L.; Silman, I. *Science* **1991**, *253*, 872.

(3) (a) Zhu, W.-L.; Tan, X.-J.; Shen, J. H.; Luo, X. M.; Cheng, F.; Mok, P. C.; Ji, R. Y.; Chen, K.-X.; Jiang, H. L. *J. Phys. Chem. A* **2003**, *107*, 2296. (b) Felder, C.; Jiang, H.-L.; Zhu, W.-L.; Chen, K.-X.; Silman, I.; Botti, S. A.; Sussman, J. L. *J. Phys. Chem. A* **2001**, *105*, 1326. (c) Zhu, W.-L.; Tan, X.-J.; Puah, C. M.; Gu, J. D.; Jiang, H. L.; Chen, K.-X.; Felder, C.; Silman, I.; Sussman, J. L. *J. Phys. Chem. A* **2000**, *104*, 9573. (d) Kim, D.; Hu, S.; Tarakeshwar, P.; Kim, K. S.; Lisy, J. M. *J. Phys. Chem. A* **2003**, *107*, 1228. (e) Mo, Y.; Subramanian, G.; Gao, J.; Ferguson, D. M. *J. Am. Chem. Soc*. **2002**, *124*, 4832. (f) Nicholas, J. B.; Hay, B. P.; Dixon, D. A. *J. Phys. Chem. A* **1999**, *103*, 1394.

(4) Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303.

(5) Cubero, E.; Luque, F. J.; Orozco, M. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 5976.

(6) Tsuzuki, S.; Yoshida, M.; Uchimaru, T.; Mikami, M.; Tanabe, K. *J. Phys. Chem. A* **2001**, *105*, 769.

(7) Luhmer, M.; Bartik, A.; Dejaegere, A.; Bovy, P.; Reisse, J. *Bull. Soc. Chim. Fr.* **1994**, *131*, 603.

(8) Williams, J. H. *Acc. Chem. Res*. **1993**, *26*, 593.

(9) Heard, G. L.; Boyd, R. J. *J. Phys. Chem. A* **1997**, *101*, 5374.

(10) Hernandez-Trujillo, J.; Vela, A. *J. Phys. Chem*. **1996**, *100*, 6524.

(11) Quiñonero, D.; Garau, C.; Rotger, C.; Frontera, A.; Ballester, P.; Costa, A.; Deyà, P. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 3389.

(12) (a) Alkorta, I.; Rozas, I.; Elguero, J. *J. Am. Chem. Soc*. **2002**, *124*, 8593. (b) Mascal, M.; Armstrong, A.; Bartberger, M. *J. Am. Chem. Soc*. **2002**, *124*, 6274.

(13) Schneider, H.-J.; Yatsimirski, A. *Principles and Methods in Supramolecular Chemistry*; Wiley: New York, 2000.

(14) (a) Schneider, H.-J.; Werner, F.; Blatter, T. *J. Phys. Org. Chem*. **1993**, *6*, 590. (b) Schneider, H.-J.; Blatter, T.; Palm, B.; Pfingstag, U.; Rudiger, V.; Theis, J. *J. Am. Chem. Soc*. **1992**, *114*, 7004.

(15) (a) Quiñonero, D.; Garau, C.; Frontera, A.; Ballester, P.; Costa, A.; Deyà, P. M. *Chem. Phys. Lett*. **2002**, *359*, 486. (b) Garau, C.; Quiñonero, D.; Frontera, A.; Ballester, P.; Costa, A.; Deyà, P. M. *Chem. Phys. Lett*. **2003**, *370*, 7. (c) Garau, C.; Frontera, A.; Quiñonero, D.; Ballester, P.; Costa, A.; Deyà, P. M. *Chem. Phys. Lett*. **2003**, *382*, 534.

(16) Garau, C.; Quiñonero, D.; Frontera, A.; Ballester, P.; Costa, A.; Deyà, P. M. *New J. Chem.* **2003**, *27*, 211.

(17) Garau, C.; Frontera, A.; Quiñonero, D.; Ballester, P.; Costa, A.; Deyà, P. M. *ChemPhysChem* **2003**, *4*, 1344.

(18) Garau, C.; Quiñonero, D.; Frontera, A.; Ballester, P.; Costa, A.; Deyà, P. M. *Org. Lett*. **2003**, *5*, 2227.

(19) Doerksen, R. J.; Thakkar, A. J. *J. Phys. Chem. A* **1999**, *103*, 10009.

(20) Kim, D.; Tarakeshwar P.; Kim, K. S. *J. Phys. Chem. A* **2004**, *108*, 1250.

(21) Rappé, A. K.; Bernstein, E. R. *J. Phys. Chem. A* **2000**, *104*, 6117.

(22) Garau, C.; Frontera, A.; Quiñonero, D.; Ballester, P.; Costa, A.; Deyà, P. M. *Chem. Phys. Lett*. **2004**, *392*, 85.

(23) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Forestman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(24) Boys, S. B.; Bernardi, F. *Mol. Phys*. **1970**, *19*, 553.

(25) (a) Orozco, M.; Luque, F. J. *J. Comput. Chem*. **1993**, *14*, 587. (b) Luque, F. J.; Orozco, M. *J. Comput. Chem*. **1998**, *19*, 866.

(26) Scrocco, E.; Tomasi, J. *Top. Curr. Chem*. **1973**, *42*, 95.

(27) Francl, M. M. *J. Phys. Chem*. **1985**, *89*, 428.

(28) Luque, F. J.; Orozco, M. MOPETE-98 computer program, Universitat de Barcelona, Barcelona, 1998.

(29) Åqvist, J. *J. Phys. Chem*. **1990**, *94*, 8021.

(30) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317.

(31) Wolinski, K.; Hinton, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251.

(32) Bader, R. F. W. *Atoms in Molecules. A Quantum Theory*; Clarendon: Oxford, 1990.

(33) Available from Prof. R. F. W. Bader's Laboratory, McMaster University, Hamilton, Ontario, Canada L8S 4M1.

(34) Biegler-König, F.; Schönbohm, J. AIM2000 computer program v. 2.0, http://www.aim2000.de.

(35) CADPAC computer program, University of Cambridge.

(36) Besler, B. H.; Merz, K. M.; Kollman, P. A. *J. Comput. Chem*. **1990**, *11*, 431.

(37) Sigfridson, E.; Ryde, U. *J. Comput. Chem*. **1998**, *19*, 377.

(38) Wiberg, K. B.; Rablen, P. *J. Comput. Chem*. **1993**, *14*, 1504.

(39) Gross, K. C.; Seybold, P. G.; Hadad, C. M. *Int. J. Quantum Chem*. **2002**, *90*, 445.

(40) Cubero, E.; Orozco, M.; Luque, F. J. *J. Phys. Chem. A* **1999**, *103*, 315.