



Counterintuitive interaction of anions with benzene derivatives

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Abstract

Ab initio calculations were carried out on complexes between 1,3,5-trinitrobenzene (TNB) and anions, where the anion is positioned over the ring along the C_3 axis. This study combines crystallographic and computational evidences to demonstrate an attractive interaction between the anion and the π -cloud of TNB. This interaction is rationalized based on the important role of the quadrupole moment of TNB and the anion-induced polarization. In addition, this study has been extended to 1,3,5-trifluorobenzene (TFB), which possesses a very small quadrupole moment. As a result, minimum energy complexes have been found between TFB and both anions and cations due to the stabilization obtained from the ion-induced polarization. © 2002 Elsevier Science B.V. All rights reserved.

1. Introduction

Non-covalent interactions play a fundamental role in many areas of modern chemistry. In particular cation– π interactions are strong non-covalent binding forces with a great importance in chemical [1] and biological systems [2]. Crystallographic studies provide much of the information on cation– π interactions and other non-bonded interactions that have attracted considerable attention in the last years such as improper hydrogen bonds [3,4], dihydrogen bonds [5,6] and other non-conventional hydrogen bonds [7]. Computational methods are incipient and incisive tools that provide insight into the non-covalent interactions

implicated in bimolecular complexes. A method that provides a rigorous criterion to determine which atoms are bonded in a molecule is the theory of atoms in molecules (AIM) [8], which has been successfully used to understand conventional [9] and unconventional [10] hydrogen bonds and cation– π interactions [11].

The cation– π interaction is, in general, equally dominated by electrostatic and cation-induced polarization [12]. The nature of the electrostatic component has been rationalized emphasizing the function of the permanent negative quadrupole (see Fig. 1) moment of benzene $Q_{zz} = -8.48$ B (buckinham, $1 \text{ B} = 3.336 \times 10^{-40} \text{ C m}^2$) [13]. The benzene–hexafluorobenzene favorable interaction has been studied, including the face-to-face stacking of its crystal structure [14]. A detailed analysis carried out by Williams stresses the important role of the large, permanent quadrupole of

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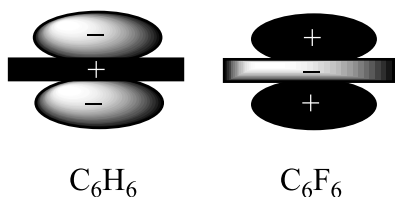


Fig. 1. Schematics of the quadrupole moments of benzene and hexafluorobenzene.

the two molecules, which are similar in magnitude but of opposite sign [15] ($Q_{zz}(\text{C}_6\text{F}_6) = +9.50 \text{ B}$). The importance of the quadrupole moment for understanding intermolecular interactions of aromatics has been rationalized before [16,17]. Several theoretical studies of the interaction of the π -cloud of C_6F_6 with several small electron donor molecules have been reported by Alkorta et al. [18] and Gallivan and Dougherty [19].

In this Letter, we report a preliminary study of interactions between anions and 1,3,5-trinitrobenzene (TNB, $Q_{zz} = +22 \text{ B}$) [20]. In these complexes the anion is positioned over the ring along the C_3 axis. This study combines crystallographic and computational evidences to demonstrate that anions can attractively interact with the π -cloud of the TNB and that the interaction is energetically favorable. Additionally we study the interaction of 1,3,5-trifluorobenzene (TFB) with ions. The quadrupole moment of TFB is very small ($Q_{zz} = +0.9 \text{ B}$). Accordingly, the interaction of TFB with ions will not be dominated by electrostatic interaction, instead it will be by the ion-induced polarization. Thus, the TFB should be able to form stable complexes with anions and cations due to the polarization contribution. The latter supposition has been confirmed by means of ab initio calculations.

2. Theoretical methods

The geometry of all the complexes included in this study was fully optimized at the Hartree–Fock level using the 6-31++G** basis set [21]. The binding energies were calculated at the same level with and without correction for the basis set superposition error (BSSE) using the Boys–Bernardi

counterpoise technique [22] and the differences found are small, except for the interaction of TNB with bromide (see Table 1). Neither the number nor the quality of the critical points (CP) change upon inclusion of electron correlation effects [23]. In one case (complex **2**) we have extended our calculation to MP2/6-31++G** and the interaction energy (BSSE corrected) was only 2 kcal/mol lower in energy than the obtained at HF/6-31++G** and the equilibrium distance was very similar (2.50 Å), see Table 1. Moreover, the number of CPs obtained using the correlated wavefunction in complex **2** was the same than using the uncorrelated (HF) one and the values of the charge density at the CPs obtained from both wavefunctions were similar.

No symmetry constrains have been imposed and in all cases the minimum nature of the complexes has been confirmed by frequency calculations at the same level, except for the TNB $\cdots\text{F}^-$ complex. In this case the minimum corresponds to the nucleophilic attack of the fluoride to one of the carbon atoms bonded to a hydrogen atom. The TNB $\cdots\text{F}^-$ complex has been calculated assuming a C_{3v} symmetry and it shows two imaginary frequencies. Similar behavior has been observed before in complexes between hexafluorobenzene and fluoride [24].

Topological properties of CPs originated upon complexation of TNB and TFB with ions were determined using Bader's theory of AIMs. The electronic density analysis was performed using the program AIMPAC [25]. Some basic concepts of Bader's topology analysis follow (see [8] for a more comprehensive treatment). The presence of a path linking two nuclei in an equilibrium structure implies that the two atoms are bonded to one another and it is characterized by the bond critical point, i.e. the point of minimum electron charge density (ρ) along the bond path, but maximum along the directions perpendicular to the bond path. The curvature, the second derivative of ρ , is negative at a maximum and positive at a minimum. The rank of a critical point, denoted by ω , is the number of non-zero curvatures. Its signature, denoted by σ , is the sum of their algebraic signs. The critical point is labeled by giving the duo of values (ω, σ). The CPs of electron charge distribution for molecules

Table 1

Interaction energies (HF/6-31++G**) with (E_{BSSE} , kcal/mol) and without (E , kcal/mol) the BSSE correction, equilibrium distances (R_c , Å) and selected electron density topological properties for the complexes of TNB with anions and for the complexes of TFB with sodium cation and fluoride

Compound	E	E_{BSSE}	R_c	CP ^a	n	$10^2\rho$	$10^2\nabla^2\rho$
TNB...H ⁻	-20.56	-20.34	2.86	(3, -1)	3	0.729	1.423
(1)				(3, +1)	3	0.707	1.485
				(3, +3)	1	0.598	2.001
TNB...F ⁻	-29.08	-28.25	2.54	(3, -1)	3	1.219	5.054
(2)	-29.91 ^b	-26.22 ^b	2.50 ^b	(3, +1)	3	1.155	5.053
				(3, +3)	1	0.836	4.949
TNB...Cl ⁻	-20.09	-19.60	3.27	(3, -1)	3	0.703	2.030
(3)				(3, +1)	3	0.673	2.041
				(3, +3)	1	0.540	2.217
TNB...Br ⁻	-24.06	-17.24	3.39	(3, -1)	3	0.722	1.862
(4)				(3, +1)	3	0.682	1.878
				(3, +3)	1	0.548	2.146
TFB...Na ⁺	-9.19	-8.75	2.64	(3, -1)	3	0.731	3.299
(5)				(3, +1)	3	0.704	3.272
				(3, +3)	1	0.610	3.003
TFB...F ⁻	-6.46	-5.99	2.91	(3, -1)	3	0.654	2.599
(6)				(3, +1)	3	0.642	2.657
				(3, +3)	1	0.507	2.632

^a The electron density (ρ) and its Laplacian ($\nabla^2\rho$) in atomic units at the critical points (CP) originated upon complexation are given, as well as the total number (n) of each CP in the complex.

^b Values in italics correspond to MP2/6-31++G** level.

at energetically stable configurations are all rank 3 ($\omega = 3$). For instance, a bond critical point denoted as (3, -1) has two negative associated curvatures of ρ , denoted as λ_1 and λ_2 , and one positive denoted as λ_3 . In a bond with cylindrical symmetry, λ_1 and λ_2 are of equal magnitude. However, if the density is preferentially accumulated in a given plane along the bond path (for example a bond with π character) λ_1 and λ_2 are not of equal magnitude. The remaining two stable CPs occur as a consequence of particular geometrical arrangements of bond paths and they define the remaining elements of molecular structure, i.e. rings (3, +1) and cages (3, +3).

The contributions to the total interaction energy have been computed using the Molecular Interaction Potential with polarization (MIPp) [26], which is a powerful tool for the prediction of binding properties of aromatic compounds [12,27]. MIPp is an improved generalization of the MEP where three terms contribute to the interaction energy, (i) an electrostatic term identical to the MEP [28], (ii) a classical dispersion–repulsion term, and (iii) a polarization term derived from

perturbational theory [29]. Therefore, it provides a natural partitioning of the interaction energy into intuitive components. Calculation [30] of the MIPp of TNB and TFB interacting with F⁻ or Na⁺ (see Table 2) was performed using the HF/6-311+G* geometries and wavefunctions. In the calculations the F⁻ and Na⁺ were considered as classical non-polarizable particles.

We have used the Nucleus Independent Chemical Shift (NICS) [31] criterion to evaluate the aromaticity of TNB and TFB upon complexation. This method is based on the negative of the magnetic shielding computed at the center of the ring. Significantly 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(1.0) (1 Å above the plane of the ring) essentially reflects π effects and is a better indicator of the ring current than the value at the center. NICS were computed at GIAO-HF/6-31++G** [32] level of theory.

Table 2
Contributions to the total interaction energy (kcal/mol) calculated for TNB interacting with F⁻ and TFB interacting with F⁻ and Na⁺ at several distances (Å) from the center of the ring using MIPp

Distance	E_c				E_p				E_{vw}				E_t			
	TNB/F ⁻	TNB/F ⁻	TFB/Na ⁺	TFB/Na ⁺	TNB/F ⁻	TNB/F ⁻	TFB/Na ⁺	TFB/Na ⁺	TNB/F ⁻	TNB/F ⁻	TFB/Na ⁺	TFB/Na ⁺	TNB/F ⁻	TNB/F ⁻	TFB/Na ⁺	TFB/Na ⁺
1.5	-47.44	-13.41	13.41	-45.37	-51.29	-45.37	-45.37	-45.37	1023.82	1044.66	81.53	81.53	925.09	985.87	49.57	49.57
2.0	-33.20	-3.83	3.83	-25.73	-29.57	-25.73	-25.73	113.11	117.08	8.51	8.51	50.34	87.52	-13.39	-13.39	-13.39
2.5	-26.16	-1.89	1.89	-14.46	-16.92	-14.46	-14.46	11.94	12.96	0.67	0.67	-31.14	-3.38	-11.90	-11.90	-11.90
3.0	-21.22	-1.56	1.56	-8.30	-9.93	-8.30	-8.30	0.20	0.49	-0.13	-0.13	-30.94	-9.37	-6.87	-6.87	-6.87
3.5	-17.25	-1.46	1.46	-4.97	-6.08	-4.97	-4.97	-0.84	-0.75	-0.14	-0.14	-24.17	-7.17	-3.65	-3.65	-3.65
Minimum ^a	-24.03	-1.59	2.64	-20.42	-13.61	-9.25	-20.42	4.23	1.37	3.33	3.33	-33.41	-9.47	-14.44	-14.44	-14.44

^a Distance where the MIPp energy value is minimum (2.7 Å for TNB/F⁻, 2.9 Å for TNB/F⁻ and 2.2 Å for TFB/Na⁺).

3. Results and discussion

Table 1 reports the energies and equilibrium distances corresponding to the interaction of TNB with a series of anions. The exploration of the CPs in the complexes revealed the presence of three (3, -1) and three (3, +1) CPs symmetrically distributed.

The bond CPs connect the anion with the three carbon atoms bonded to nitro groups and the ring CPs are located along the line connecting the anion with the non-substituted carbon atoms (see Fig. 2). The Laplacian of the bond CPs is positive, indicating a depletion of the electron density, as is common in closed-shell interactions [8]. Finally, the interaction is further described by the presence of a cage CP located over the TNB along the C₃ axis, connecting the anion with the center of the ring. We have found an interesting relationship between the interaction energy (E_{BSSE}) and the electronic density at the cage CP that it is formed upon complexation ($r = 0.97$). An analogous relationship has been reported for complexes between benzene and several cations [12]. This relationship between the density at the cage CP and the interaction energy has been used to extend the concept of bond order to ion- π interactions.

It is evident that without the results of crystallographic experiments, molecular modeling would at best have been a highly speculative activity. Crystal structures are so rich in information that reveal effects that had not been noticed by the original authors. The Cambridge Structural Database (CSD) [33] is a convenient and reliable storehouse for geometrical information. The utility of small-molecule crystallography and the CSD in analyzing geometrical parameters and non-bonded interactions has been clearly established [34]. Exploring the CSD, we have found 271 fragments where non-covalent π -interactions are present between lone pair electrons of electronegative atoms and TNB derivatives, using the following criteria: (i) the interacting atom with TNB derivatives was either S, N, O, F, Cl, Br or I, (ii) the type of non-bonded contact was either intramolecular or intermolecular, (iii) the non-bonded contact was defined using distance criteria, i.e. less than the sum of van der Waals radii, (iv) to store a hit a

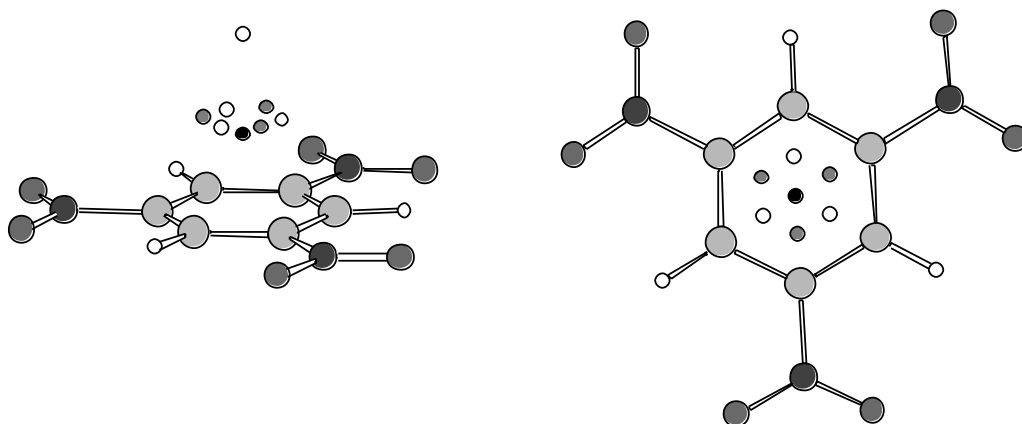


Fig. 2. Schematic representation of the location of the three (3, -1) (grey circles) and three (3, +1) (white circles) CPs, and of the (3, +3) (black circle) CP originated from the interaction of TNB with H^+ . For clarity, the hydride anion has been omitted in the on-top representation (right side).

non-bonded contact must exist between the interacting atom and all six carbon atoms of the aromatic ring. Ten of the 271 fragments were π -interactions between anions and TNB derivatives. In Fig. 3 we show the crystal structure of a 2,4,6-trinitrobenzenesulfonate salt, where the anion- π interaction is evident (CSD reference

CXMETN10). The distance between the O^- and the ring-centroid is 2.97 Å. We also show a very interesting X-ray structure where the lone pair of a nitrogen atom of a cycl[3,2,2]azine is located approximately equidistant from the ring-centroids of two TNB molecules (see Fig. 3, CSD reference CAZTBZ01).

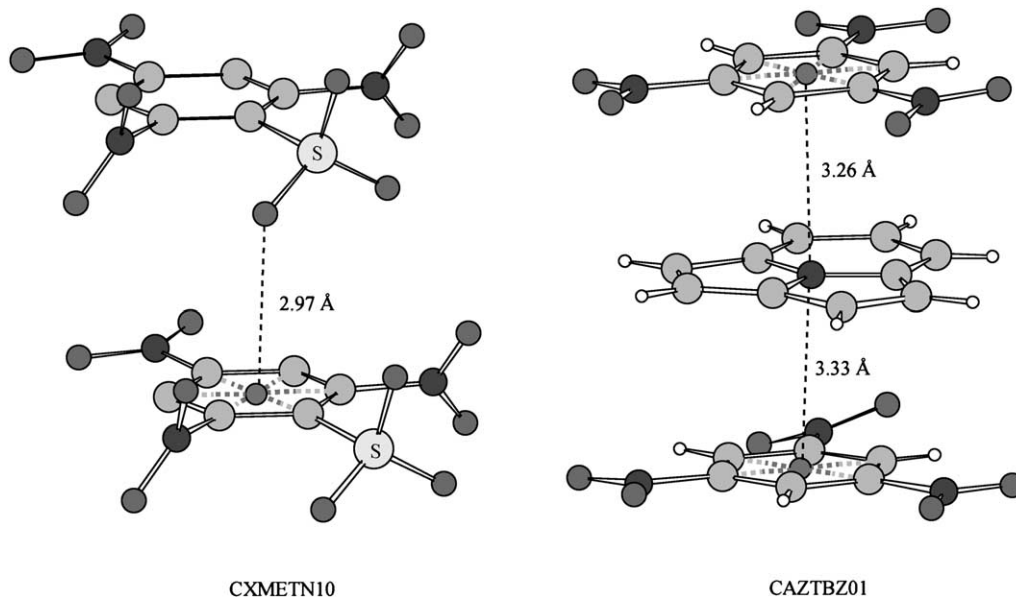


Fig. 3. Partial view of X-ray structure of (*R*)-((3*S*)-3-amino-3-carboxypropyl)(carboxymethyl)methylsulfonium 2,4,6-trinitrobenzenesulfonate (CXMETN10) and cycl(3.2.2)azine 1,3,5-trinitrobenzene (CAZTBZ01). Distances are in Å.

In order to analyze the physical nature of the anion– π interaction and whether polarization is important, we have computed its contribution to the total interaction energy using the recently developed MIPp. We have explored the electrostatic (E_e), polarization (E_p), Van der Waals (E_{vw}) and total (E_t) interaction energies when a F^- approaches a TNB molecule perpendicular to the center of the aromatic ring. The results in Table 2 point out that the main contributions to the total energy are the electrostatic and the polarization components and that the latter is significant in the 2.0–2.5 Å range. The importance of the electrostatic effect in TNB complexes has been confirmed evaluating its interaction with a cation (Na^+). We have not found any minimum energy complex between TNB and Na^+ in the potential energy surface. Moreover, if the sodium cation is fixed at 2.6 Å over the ring along the C_3 axis, the resulting interaction energy is large and positive (+13.3 kcal/mol at HF/6-31++G**).

We have extended our study to the interaction properties of TFB. Striking and interesting is the fact that TFB is able to form minimum complexes with both anions and cations (see Table 1). Similarly to TNB, three (3, –1) and three (3, +1) CPs symmetrically distributed are originated upon complexation of TFB with Na^+ (**5**) and with F^- (**6**). The Laplacian of the (3, –1) CPs is positive indicating the closed shell nature of the interaction. In addition a cage CP is generated and analogously to TNB complexes, the greater the density at the cage CP the greater the interaction energy (see Table 1).

The interaction energy of complex **5** (TFB... Na^+) is –9.19 kcal/mol, slightly lower

than the previously reported by Cubero et al. [12] at HF/6-31G** (–12.4 kcal/mol). In addition, the formation of complex **6** (TFB... F^-) is also favored, and the computed binding energy is –6.46 kcal/mol. A likely explanation for the latter result lies in the polarization contribution to the total binding energy which is critical. In Table 2 we report the E_e , E_p and E_{vw} and E_t interaction energies derived from MIPp calculations when either Na^+ or F^- approaches a TFB molecule along the C_3 axis. The quadrupole moment of TFB is very small ($Q_{zz} = 0.9$ B) and consequently the electrostatic contribution is small (1–2 kcal/mol in absolute value) in the 2.0–3.0 Å range for the interaction with either Na^+ or F^- (see Table 2). In contrast, the polarization term dominates the interaction and is the responsible of the unusual behavior of TFB which is able to interact with anions and cations favorably. The minimum E_t predicted by the MIPp method for the interaction of TFB with F^- is –9.47 kcal/mol at an equilibrium distance of 2.9 Å. These values compare satisfactorily with the computed binding energy of the optimized complex structure ($E = -6.46$ kcal/mol, $R_e = 2.91$ Å). The predicted minimum MIPp energy for the interaction with Na^+ is –14.4 kcal/mol (see Table 2) at an equilibrium distance of 2.2 Å. In this case the MIPp method overestimates the binding energy approximately in 5 kcal/mol. However, the computed MIPp energy at 2.5 Å is in agreement with the computed binding energy for the optimized complex ($E = -9.19$ kcal/mol, $R_e = 2.64$ Å).

Finally, the last point we have examined is the variation of the degree of aromaticity of TNB and TFB upon complexation. Table 3 reports the

Table 3

NICS values in ppm at the geometrical center of the ring and 1.0 Å below (NICS(1.0)) the aromatic ring opposite to the ion) for TNB and TFB complexes with ions

Compound	NICS	NICS(1.0)	Δ NICS ^a	Δ NICS(1.0) ^a
TNB	–13.05	–12.09	–	–
TFB	–14.54	–11.47	–	–
TNB... H^-	–13.97	–12.82	–0.92	–0.73
TNB... Cl^-	–13.18	–12.26	–0.13	–0.17
TNB... Br^-	–13.38	–12.53	–0.33	–0.44
TFB... F^-	–15.20	–11.86	–0.66	–0.39
TFB... Na^+	–13.22	–10.46	1.32	1.01

^a Δ NICS = NICS(complexed) – NICS(free).

NICS computed values at the ring centers and 1 Å below in order to reduce the local shielding of nearby σ -bonds. In all TNB complexes the variation in the degree of aromaticity is very small (0–1 ppm) indicating that the interaction of the anion with the π -cloud of TNB does not affect the aromaticity of the ring. This is probably due to the small charge transference from the anion to TNB, for instance, in complex **3**, the amount of charge [35] transferred is 0.14 e. The same behavior is observed for TFB complexes **5** and **6**, where the change in the degree of aromaticity is very small.

In summary, the results derived from crystallographic structures and theoretical calculations reported in this study reveal the existence of counterintuitive interactions between TNB and anions. This non-bonded interaction has been studied using a topological analysis of the electron density and MIPp calculations. The interaction of ions with TFB, characterized by a very small Q_{zz} , is dominated by the ion-induced polarization term. The latter turns out as essential to explain the minimum energy TFB complexes **5** and **6**.

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