

## Theoretical Study of the Interaction between the Guanidinium Cation and Chloride and Sulfate Anions

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Received January 14, 2005

**Abstract:** The interactions between the guanidinium cation and the chloride and sulfate anions have been explored theoretically. As a basis for this study, the structure of the guanidinium cation has been reexamined and confirmed to possess a nonplanar propeller structure. Thus, computations at the MP2/6-31+G\* level yielded several guanidinium–chloride complexes in 1:1 and 2:1 stoichiometry, with the most stable being those in which the guanidinium cation(s) interact in pincerlike form with the spherical chloride anion. In the case of guanidinium–sulfate complexes, a large number of stable 1:1 dimers and 2:1 trimers were found at the same level of computation. The nature of all the interactions established has been analyzed by means of the AIMs and NBO approaches, and several correlations have been found between electron density at the bond critical points, hydrogen bond distances, and orbital interaction energies. The guanidinium moiety has been widely exploited as an anion receptor in supramolecular chemistry and bears relation to the arginine amino acid, which interacts with anionic substrates within proteins. Thus, the current study provides insight into the nature of the interactions involving the guanidinium cation within both abiotic and natural systems.

### Introduction

There is considerable current interest in the development of molecular and supramolecular systems that have the ability to bind, identify, and signal the presence of negatively charged ions.<sup>1</sup> The motivation behind such studies is the recognition that anions enjoy an important role in biology, medicine, and the environment.<sup>2</sup> In the field of molecular recognition, the guanidinium cation has proven to be an extremely effective motif (host) for binding anionic guests.<sup>3</sup> Strong noncovalent interaction between this host and guest species is derived from ion pairing and H-bonding (HB) contributions, and these interactions have been shown to be particularly effective even in competitive solvent systems such as water.<sup>4</sup> Several features allow the guanidinium group to effectively bind anions. First, a very high  $pK_a$  value of around 12–13 allows it to remain protonated over a wide pH range, including physiological pH. Furthermore, its geometrical orientation allows it to align well with anionic

groups, leading to a strong interaction. The incorporation of the guanidinium moiety into abiotic receptors is also driven in part by the recognition that the guanidinium group, in the form of the arginine amino acid, plays a crucial role in directing the formation of higher order structures in proteins through hydrogen-bonding as well as being a component found within enzymatic catalytic domains that bind anionic substrates.<sup>5</sup>

With the above concepts in mind, and in an effort to better understand those empirical contributions that lead to anion binding to the guanidinium cation, we undertook a theoretical study of the binding of the prototypical anions chloride (mononegative, spherical) and sulfate (dinegative, tetrahedral) to guanidinium. This empirical study provides a theoretical basis that might allow for better guanidinium receptor design and an impetus for our own formative structural studies into anion driven supramolecular chemistry.<sup>6</sup> Initial computational work focused on calculating the minimized structure of the guanidinium moiety itself. We then moved onto consider the interaction of chloride and sulfate anions with the guani-

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dinium cation in 1:1 (dimer) and 2:1 (trimer) host-to-guest stoichiometry, as these are the stoichiometries most commonly found within abiotic host–guest systems. A systematic search of the Cambridge Structural Database was also conducted to corroborate the results found via computational methods. Results from this study are presented herein.

## Methods

The geometry of the monomers (guanidinium cation and anion species) and host:guest complexes (guanidinium:anion) have been initially fully optimized with the Gaussian 98<sup>7</sup> program using the hybrid Hartree–Fock (HF) density functional theory (DFT) B3LYP/6-31G\* computational level.<sup>8</sup> These structures have been used as the starting point for the optimization at the second-order Møller–Plesset perturbation method (MP2),<sup>9</sup> with the 6-31+G\* basis set.<sup>10</sup> In the case of the guanidinium cation the MP2 method with the 6-31++G\*\* basis set<sup>11</sup> was also used for comparison purposes. The combination of DFT and MP2 methods has proven to be sufficient for an accurate description of HBs and is not computationally expensive. In the case of the dimers, the minimum nature of the complexes has been confirmed by frequency calculations at both the B3LYP/6-31G\* and MP2/6-31G\* levels, whereas the trimers frequency calculations have been performed at the B3LYP/6-31G\* level. Considering that the B3LYP and MP2 geometries were almost identical, B3LYP frequencies are enough to identify the trimers as minima.

The interaction energies have been calculated as the difference of the total energy of the complex and the sum of the isolated monomers. The interaction energies obtained in the majority of the cases were very high, and no basis set superposition error (BSSE) was calculated since, in those situations, such corrections should be irrelevant. The topological properties of the electron charge density have been studied using the atoms in molecules methodology (AIM) with the AIMPAC program package.<sup>12</sup> The natural bond orbital analysis was used to determine the nature of the interactions in the formation of the host:guest complexes. These calculations were performed with the NBO code implemented in Gaussian-98.<sup>13</sup> A search of the Cambridge Structural Database (CSD version 5.25 April 2004 Update)<sup>14</sup> for complexes of the guanidinium cation and chloride or sulfate anions was conducted employing the following restrictions: H-atoms were located, no disorder and a refinement (R-factor)  $\leq 6.0\%$ . All of the structures matching these criteria were examined manually and the following, deemed the most relevant to the current study, were fully analyzed and discussed in the text: guanidinium chloride (CSD refcode: GANIDC), guanidinium sulfate (CSD refcode: GUANSL01), and guanidinium bisulfate (CSD refcode: VETQIU).

## Results and Discussion

**Guanidinium Cation.** For many years it was assumed that Y-conjugated molecules such as guanidinium were planar. Frenking<sup>15</sup> showed that guanidinium possesses a nonplanar minimum structure. In fact their calculations at the HF/6-31G\* level predicted a planar form of the guanidinium cation,

**Table 1.** Total Energy ( $E_T$ , au), Difference in Energy ( $\Delta E$ , kcal mol<sup>-1</sup>), ZPE and Frequencies for the Guanidinium Cation (G<sup>+</sup>) Calculated at the B3LYP/6-31G\*, MP2/6-31+G\*, and MP2/6-31++G\*\* Levels

B3LYP/6-31G*	$E_T$	$\Delta E$	imaginary frequencies
G <sup>+</sup> nonplanar	-205.7593033		0
G <sup>+</sup> planar	-205.7588422	0.29	1
MP2/6-31+G*	$E_T$	$\Delta E$	imaginary frequencies
G <sup>+</sup> nonplanar	-205.1307722		0
G <sup>+</sup> planar	-205.1297416	0.65	1
MP2/6-31++G**	$E_T$	$\Delta E$	imaginary frequencies
G <sup>+</sup> nonplanar	-205.1861055		0
G <sup>+</sup> planar	-205.1852451	0.54	3

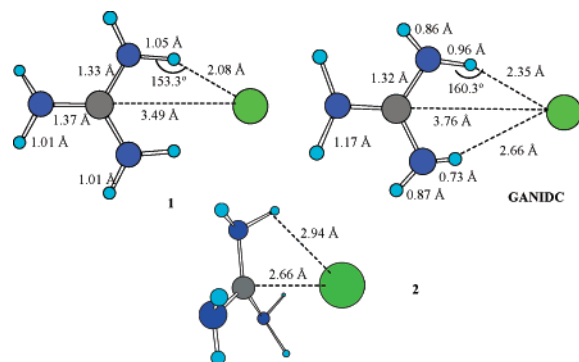
whereas at the MP2/6-31G\* level such a planar form showed one imaginary frequency. The energy minimum structure at the MP2/6-31G\* level had  $D_3$  symmetry with the NH<sub>2</sub> groups rotated by 15° and a difference in energy from the planar form of 0.4 kcal mol<sup>-1</sup>. To evaluate the interaction energy of the guanidinium–chloride and guanidinium–sulfate complexes and to analyze the behavior of DFT methods we have reinvestigated the nonplanarity of guanidinium at the B3LYP/6-31G\*, MP2/6-31+G\* and MP2/6-31++G\*\* levels.

In Table 1 the results obtained for the planar and nonplanar forms are presented. In all cases the nonplanar form was the minimum energy structure, whereas the planar structure showed one to three imaginary frequencies. The difference in energy obtained with respect to the planar form was 0.29, 0.65, and 0.54 kcal mol<sup>-1</sup> at the B3LYP/6-31G\*, MP2/6-31+G\*, and MP2/6-31++G\*\* levels, respectively.

The good performance of the B3LYP/6-31G\* method is noteworthy since the results obtained are very similar to those observed by Frenking at the MP2 level employing the same basis set ( $\Delta E_T = 0.4$  kcal mol<sup>-1</sup>, and one negative frequency for the planar form).<sup>16</sup> Frenking found that with inclusion of the ZPE corrections, the planar form was more stable than the nonplanar form by 0.2 kcal mol<sup>-1</sup>. At the three levels of computation employed within the current study similar results were obtained; however, ZPE corrections cannot be applied to structures that show imaginary frequencies, as these data would be meaningless.

Regarding the equilibrium structures at the three levels of computation, guanidinium shows  $D_3$  symmetry with the NH<sub>2</sub> groups rotated around the C–NH<sub>2</sub> bond by 14.5°, 16.9°, and 16.2°, respectively. The C–N bond lengths obtained in each case were the same for the planar and nonplanar forms and are very similar at the three levels of computation (B3LYP/6-31G\*: 1.337 Å, MP2/631+G\*: 1.336 Å, and MP2/6-31++G\*\*: 1.336 Å). As in the case reported by Frenking these C–N distances are in excellent agreement with experimental values derived from vibrational spectra and X-ray diffraction studies (1.33–1.35 Å).<sup>16</sup>

The nonplanar form of guanidinium may be viewed as a left- or right-handed propeller. We have followed the



**Figure 1.** MP2/6-31+G\* optimized structures of the two possible 1:1 guanidinium–chloride dimers, **1** and **2**, and the crystal structure of guanidinium chloride (GANIDC) as taken from the CSD.

transition between left- and right-handed propellers by a reaction coordinate in which the H–N–C–N dihedral angle was rotated from 15° (as observed in the minimum energy nonplanar structure) to –15° which would correspond to the mirror image structure. The structures with H–N–C–N = 15°, 10°, 5°, –5°, –10°, –15° are all minima, and the difference in energy between them is negligible. Only the planar structure (H–N–C–N = 0°) shows an imaginary frequency and a difference of energy of 0.24 kcal mol<sup>–1</sup> with respect to the nonplanar forms. Therefore, the planar form of guanidinium can be considered as the transition state between these two ‘propellers’, and the fact that this transition requires such a small amount of energy could explain the perception of guanidinium being planar.

**Guanidinium–Chloride Complexes.** Two possible interactions between the guanidinium and chloride anions with 1:1 stoichiometry were considered, and their optimized structures at the MP2/6-31+G\* level are shown in Figure 1. In one case the cation was looked as a pincerlike structure interacting with the spherical Cl<sup>–</sup> anion, whereas in the other, the cation was considered as a positively charged delocalized plane interacting with the Cl<sup>–</sup> anion in an orthogonal manner. Thus, complex **1** is similar to those observed in the crystal structure of guanidinium hydrochloride (GANIDC in Figure 1) and is at an energy minimum. The orthogonal dimer **2** (Figure 1) is a minimum as well.

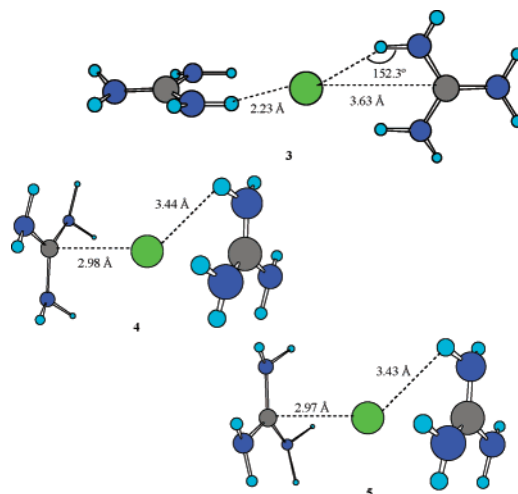
Aspects of the geometry and nature of the interactions in dimer **1** are in agreement with those found in the crystal structure, GANIDC. The N–H···Cl distances and angles suggest the existence of hydrogen bond (HB) interactions. In complex **2**, the C···Cl distance suggests an ionic interaction, and the N–H···Cl distance is too long to correspond to a HB, even though there is a clear ionic attraction of the H atoms toward the Cl anion (the H atoms bend toward the chloride ion). Details of hydrogen bond interactions within GANIDC as derived from the CSD are brought together within Table 2 for comparison.

With regard to the existence of possible trimers, i.e. 2:1 host-to-guest complexes, they were constructed with consideration given to the computed structures of dimers **1** and **2** (see trimers **3–5** in Figure 2). Thus, the addition of a second guanidinium group to the dimer **1** yielded trimer **3**, whose MP2/6-31+G\* optimized structure is shown in Figure

**Table 2.** Hydrogen Bond Parameters within Guanidinium Chloride (GANIDC), Guanidinium Sulfate (GUANSL01), and Guanidinium Bisulfate (VETQIU) as Derived from the CSD<sup>14</sup>

D–H···A <sup>a</sup>	D–H/Å	d(H···A)/Å	d(D···A)/Å	<(DH···A)/°
GANIDC				
N1–H1···Cl <sup>i</sup>	0.86	2.43	3.256	160.1
N1–H2···Cl <sup>ii</sup>	0.96	2.35	3.272	160.3
N2–H3···Cl <sup>iii</sup>	0.73	2.66	3.357	160.5
N2–H4···Cl <sup>iii</sup>	0.87	2.41	3.256	163.6
N3–H5···Cl <sup>iii</sup>	1.16	2.23	3.348	159.9
N3–H6···Cl <sup>i</sup>	1.17	2.26	3.328	149.7
GUANSL01				
N1–H1···O2	0.86	2.25	3.036	150.9
N1–H2···O2 <sup>iv</sup>	0.86	2.26	3.036	150.9
N2–H3···O3 <sup>v</sup>	0.86	2.23	2.975	145.0
N2–H4···O1 <sup>vi</sup>	0.86	2.11	2.914	154.8
N3–H5···O3 <sup>vii</sup>	0.86	2.45	3.157	140.1
N3–H6···O3 <sup>viii</sup>	0.86	2.45	3.157	140.1
N4–H7···O2 <sup>ix</sup>	0.86	2.05	2.899	169.3
N4–H8···O4 <sup>x</sup>	0.86	2.02	2.865	165.9
N5–H9···O3 <sup>x</sup>	0.86	2.11	2.957	163.0
N5–H10···O2 <sup>vi</sup>	0.86	2.10	2.955	169.8
N6–H11···O1 <sup>ix</sup>	0.86	2.08	2.928	169.3
N6–H12···O1 <sup>xi</sup>	0.86	2.19	2.981	152.3
VETQIU				
N1–H1···O4 <sup>xii</sup>	0.86	2.18	2.951	149.5
N1–H2···O2 <sup>xiii</sup>	0.86	2.47	3.207	144.1
N2–H3···O2 <sup>xiii</sup>	0.86	2.23	3.020	152.8
N2–H4···O3	0.86	2.21	2.962	145.5
N3–H5···O4 <sup>xi</sup>	0.86	2.28	3.030	145.2

<sup>a</sup> Symmetry codes: i = 1/2+x, y, 1/2–z; ii = x, 1/2–y, 1/2+z; iii = 1/2–x, 1/2+y, z; iv = 1/4–x, 5/4+y, –5/4+z; v = –1/4+x, 1/4–y, 5/4+z; vi = 1/2–x, 1–y, 1/2+z; vii = x, y, 1+z; viii = 1–x, 1/2+y, –1/2–z; ix = 1/4–x, –3/4+y, 3/4+z; x = –1/2+x, 1/2–y, –1–z; xi = 1/4+x, –1/4+y, 1/4–z; xii = 1–x, –1–y, 1–z; xiii = –1+x, y, z.



**Figure 2.** MP2/6-31+G\* optimized structures of the 2:1 guanidinium–chloride trimers **3–5**.

**2.** The N–H···Cl distances and angles to both guanidinium moieties are the same and indicative of a HB.

At the MP2 level of theory, the dimer resulting from the interaction of the Cl anion with the H atoms (complex **1**) is more stable than the C···Cl one (complex **2**) by 10.60 kcal mol<sup>–1</sup> (see Table 3). This difference in energy is extremely

**Table 3.** Total Energies ( $E_T$ , au) and Interaction Energies ( $E_i$ , kcal mol<sup>-1</sup>) for the Guanidinium (G<sup>+</sup>)–Chloride Complexes Calculated at the MP2/6-31+G\* Computational Level

	$E_T$	$E_i$
G <sup>+</sup> ...Cl (1)	−664.9761235	−109.32
G <sup>+</sup> ...Cl (2)	−664.9592279	−98.71
G <sup>+</sup> ...Cl...G <sup>+</sup> (3)	−870.1729693	−150.78

**Table 4.** Electron Density and Laplacian at the BCP (au) of the HB Found in the Guanidinium (G<sup>+</sup>)–Chloride Dimers and Trimers Optimized at the MP2/6-31+G\* Level<sup>a</sup>

	X...Cl	$\rho(\text{BCP})$	$\nabla^2\rho(\text{BCP})$	$d(\text{X}...Cl)$	$\angle \text{NH}...Cl$
G <sup>+</sup> ...Cl (1)	C...Cl			3.49	
	H...Cl	0.0369	0.0892	2.08	153.3
G <sup>+</sup> ...Cl (2)	C...Cl	0.0307	0.0742	2.63	
	H...Cl			3.13	78.5
G <sup>+</sup> ...Cl...G <sup>+</sup> (3)	C...Cl			3.63	
	H...Cl	0.0235	0.0713	2.23	152.3

<sup>a</sup> The interaction distances (Å) and N–H...Cl angles (°) are also shown.

high, and, therefore, dimer **2** will be probably nonexistent in the gas phase. However, the relevance of orthogonal interactions have been recently put into perspective by Diederich et al.,<sup>17</sup> and, hence, we consider that the characterization of this dimer **2** still deserves some attention, since this type of approach could be present in other related systems such as supramolecular systems or highly sterically hindered guanidiniums.

In the case of the trimers, only complex **3** should be considered since trimers **4** and **5** show six imaginary frequencies, and when they were further optimized they evolved to complex **3** (see Figure 2). The MP2 interaction energies, gathered together in Table 3, are clustered from ca. 98 to 109 kcal mol<sup>-1</sup> for the dimers **1** and **2** and ca. 151 kcal mol<sup>-1</sup> for trimer **3**, showing that the interactions within all these complexes are extremely strong. In the case of dimer **1**, the minimized structure is consistent with that found in the crystal structure of guanidinium chloride (GANIDC).

The AIM analysis of these complexes shows electron density values around 10<sup>-2</sup> au and positive Laplacians at the bond critical points (BCP), indicating HB or ionic interactions between the chloride and the electron acceptor atoms (H or C, respectively), Table 4. The position of the BCP is approximately in the middle of the interaction distance only in the case of dimer **2**. Short interaction distances, where the BCP is much closer to the H atom than to the chloride, are found in **1** and **3** and correspond to the large value of the electron density at the BCP as shown in Table 4. The value of the electron density at the BCP depends on the interaction distance as has been shown previously for other systems.<sup>18</sup>

Thus, the shorter the distance is the larger the electron density at the BCP. In all cases the electron density values found correspond to strong HB (complexes **1** and **3**) or strong ‘closed-shell’ interactions (complex **2**). Two ring critical points (RCP) have been found for the dimer **1** and its corresponding trimer **3** (see Table 4). No BCP was found

**Table 5.** Charge Transfer (e), Dipole Moment Enhancement, and Orbital Interaction Energy (kcal mol<sup>-1</sup>) Calculated for the Guanidinium (G<sup>+</sup>)–Chloride Complexes at the B3LYP/6-31+G\* Level with the NBO Method

	charge transfer	$\Delta\mu$	H...Cl	$E(2)$
G <sup>+</sup> ...Cl (1)	0.231	11.54	H...Cl	28.31
G <sup>+</sup> ...Cl (2)	0.251	4.60	H...Cl	137.67
G <sup>+</sup> ...Cl...G <sup>+</sup> (3)	0.098		H...Cl	9.09

between the chloride and the H atoms in dimer **2**, which is in agreement with the small N–H...Cl angles found, which are incompatible with the formation of a HB.

The dipole moment enhancement, charge transfer, and nature of the interaction using the NBO method at the B3LYP/6-31+G\* level are gathered together in Table 5. Large dipole moment enhancement and charge transfer (from the chloride toward the guanidinium cation) are due to the formation of the complexes and are observed in those cases where the Cl...C(H,C) distances are short and in both dimers and trimer.

The NBO analysis (Table 5) shows the formation of a very strong ionic Cl–C bond, with over 80% contribution from the chloride, in complex **2** ( $d(\text{Cl}...C) = 2.66$  Å). The molecular orbital responsible for this bond shows the important contribution of the *p*-orbitals of the chloride and the carbon atoms. In dimer **1** and trimer **3**, a lone pair from the chloride interacts with antibonding N–H orbitals, from one or two guanidiniums respectively, which is typical of HB interactions.

**Guanidinium–Sulfate Complexes.** The crystal structure of guanidinium sulfate (GUANSL01) was retrieved from the CSD. It shows an arrangement of guanidinium molecules surrounding each sulfate anion (see Figure 3) with typical S–O...H–N hydrogen bond distances ranging from 2.02 and 2.45 Å. The hydrogen bond interactions within GUANSL01 are brought together in Table 2. Using this structure as a basis, different dimers were considered, and the final MP2 optimized structures are shown in Figure 3.

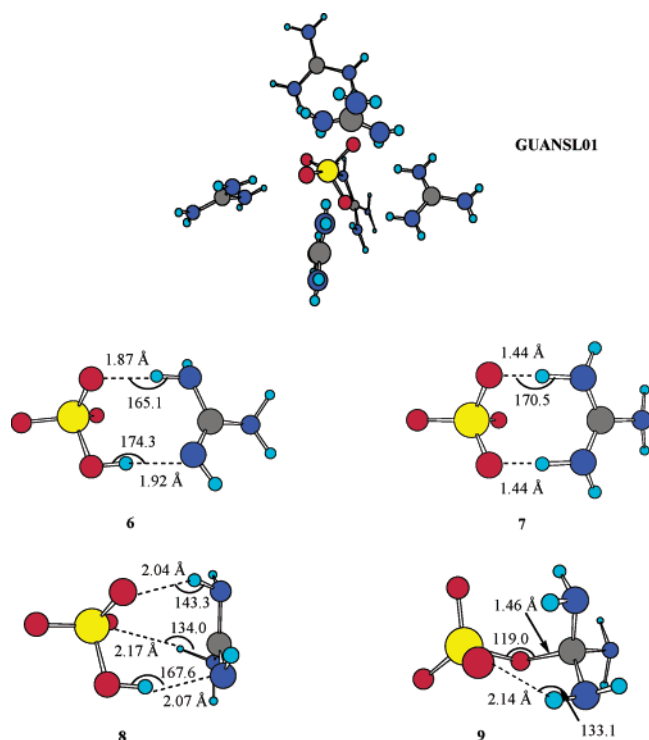
In the first approximation, a proton transfer from one of the N–H groups to the sulfate oxygen atom occurred yielding a guanidine–bisulfate complex, **6**, possessing a double HB interaction and no negative frequencies. Furthermore, it was possible to optimize structure **7** where no proton transfer has occurred, yielding a complex between the sulfate anion and the guanidinium cation, but this complex showed one negative frequency.

In the case of a dimer with two N–H groups interacting with one O atom, when undergoing optimization, a change in the configuration occurred yielding a guanidine–bisulfate complex, **8**, with three HBs and no negative frequencies.

When considering a putative C...O orthogonal interaction between both ions, after optimization a new bond appeared between the C atom of the cation and an O atom of the sulfate anion to give compound **9**. This molecule **9** occurs at an energy minimum with no negative frequencies.

The O...H distances within the optimized structure **6** are shorter than those found within the crystal structure of guanidinium sulfate (GUANSL01) and guanidinium bisulfate





**Figure 3.** MP2/6-31+G\* optimized structures of the 1:1 guanidinium-sulfate dimers 6–9 and crystal structure of guanidinium sulfate (GUANSL01) as derived from the CSD.

**Table 6.** Total Energies (au) and Interaction Energies (kcal mol<sup>-1</sup>) for the Guanidinium (G<sup>+</sup>), Guanidine (G)-Sulfate, Bisulfate Complexes Calculated at the MP2/6-31+G\* Computational Level

	$E_T$	$E_I$
G $\cdots$ HSO <sub>4</sub> (6)	-903.2088034	-15.27
G $\cdots$ HSO <sub>4</sub> (8)	-903.2188189	-21.56
G <sup>+</sup> -OSO <sub>3</sub> (9)	-903.2094419	
G <sup>+</sup> $\cdots$ SO <sub>4</sub> $\cdots$ G <sup>+</sup> (10)	-1108.5093054	-327.84
G <sup>+</sup> $\cdots$ HSO <sub>4</sub> $\cdots$ G (11)	-1108.5110424	-122.87
G <sup>+</sup> $\cdots$ SO <sub>4</sub> $\cdots$ G <sup>+</sup> (12)	-1108.5068796	-326.32
G <sup>+</sup> $\cdots$ SO <sub>4</sub> $\cdots$ G <sup>+</sup> (13)	-1108.5072762	-326.57
G <sup>+</sup> -OSO <sub>3</sub> $\cdots$ G <sup>+</sup> (14)	-1108.5028902	-102.08
G <sup>+</sup> -OSO <sub>3</sub> $\cdots$ G <sup>+</sup> (15)	-1108.5055215	-103.73

(VETQIU, see Table 2), although the O $\cdots$ H distances found for the optimized structures 8 and 9 are closer to those observed in the solid-state structures (between 2.04 and 2.17 Å).<sup>19</sup> These short HB distances and the occurrence of proton transfer is most probably a consequence of the mismatch in charge between the dinegative anion and the monocation within the 1:1 species and the desire for the system to offset this situation.

The total energies of these structures at the MP2/6-31+G\* level and the interaction energies are presented in Table 6. Thus, the most stable dimer is 8, being 6.28 kcal mol<sup>-1</sup> more stable than 6. The presence of an extra N-H $\cdots$ O HB interaction in complex 8 could justify the additional stability. The difference in energy between 6 and 8 is quite high, but structure 6 is the most related to that found in the crystal structure, and, thus, subsequent analyses of the interactions established within both complexes will be performed.

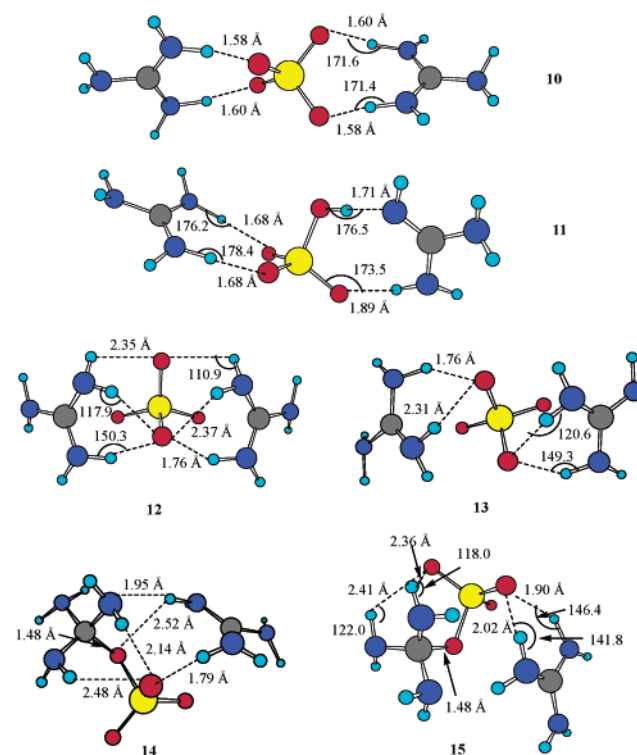
Compound 9 cannot be compared with complexes 6 and 8 since is a monomer and will not be further discussed.

In the case of the trimers, the starting systems were built from the optimized dimers, and the MP2 optimized structures are shown in Figure 4. Thus, complex 10, which was formed by the double interactions observed in the GUANSL01 crystal structure, shows no negative frequencies, and no proton transfer occurred. Considering dimer 6, in which proton transfer did occur, trimer 11 was built and optimized, showing no negative frequencies at the B3LYP/6-31G\* level. It was not possible to obtain any complexes as a result of a double proton transfer (a putative 1:2 sulfuric acid-guanidine complex).

Two symmetrical trimers were obtained. One of them, 12, is at a minimum energy at the B3LYP/6-31G\* level, and in this structure one of the O atoms participates in two HB interactions whereas another participates in four. As well, trimer 13 was found to be an energy minimum at the B3LYP level. Finally, two quite irregular dimer complexes, 14 and 15 (derived from compound 9), were optimized and displayed no negative frequencies.

The total and interaction energies of these complexes are shown in Table 6. In general, these trimers exhibit very large interaction energies and larger still when all of the species involved are charged. This could indicate that a high electrostatic component is involved in the interactions within the trimers

At the MP2 level, the difference in stability among the trimers is small. The most stable of these complexes is 11, which is 1.09, 2.61, and 2.36 kcal mol<sup>-1</sup> more stable than 10 (which is a similar complex but lacks the proton resulting from transfer), 12, and 13, respectively. Complexes 6, 8, and



**Figure 4.** MP2/6-31+G\* optimized structures of the 2:1 guanidinium-sulfate trimers 10–15.

**Table 7.** Electron Density and Laplacian at the BCP (au) of the HB Found in Guanidinium ( $G^+$ ), Guanidine (G)-Sulfate, Bisulfate Complexes Optimized at the MP2/6-31+G\* Level<sup>a</sup>

	DH...A	$\rho(\text{BCP})$	$\nabla^2\rho(\text{BCP})$	$d(\text{H}\cdots\text{A})$	$\angle\text{DH}\cdots\text{A}$
$G\cdots\text{HSO}_4$ ( <b>6</b> )	NH...O	0.0322	0.0984	1.87	165.1
	OH...N	0.0305	0.0891	1.92	174.3
$G\cdots\text{HSO}_4$ ( <b>8</b> )	NH...O	0.0232	0.0736	2.04	143.3
	NH...O	0.0174	0.0601	2.17	134.0
	OH...N	0.0223	0.0654	2.07	167.6
	NH...O	0.0603	0.1807	1.58	171.8
$G^+\cdots\text{SO}_4\cdots G^+$ ( <b>10</b> )	NH...O	0.0565	0.1745	1.60	171.5
	NH...O	0.0480	0.1498	1.68	176.2
	NH...O	0.0481	0.1482	1.68	178.4
	NH...O	0.0282	0.0943	1.89	173.5
$G^+\cdots\text{HSO}_4\cdots G$ ( <b>11</b> )	OH...N	0.0493	0.1285	1.71	176.5
	NH...O	0.0423	0.1293	1.76	150.3
	NH...O	0.0153	0.0540	2.34	111.0
	NH...O	0.0118	0.0540	2.37	117.9
$G^+\cdots\text{SO}_4\cdots G^+$ ( <b>12</b> )	NH...O	0.0423	0.1299	1.76	149.2
	NH...O	0.0161	0.0538	2.31	120.6
$G^+-\text{OSO}_3\cdots G^+$ ( <b>13</b> )	C-O <sup>b</sup>	0.2298	-0.4981	1.48	118.6
	NH...O <sup>b</sup>	0.0122	0.0442	2.48	119.1
	NH...O <sup>b</sup>	0.0209	0.0734	2.14	119.4
	NH...O	0.0381	0.1202	1.79	156.3
	NH...O	0.0128	0.0438	2.52	102.1
	NH...N	0.0311	0.0830	1.95	164.1
$G^+-\text{OSO}_3\cdots G^+$ ( <b>14</b> )	C-O <sup>b</sup>	0.2282	-0.4847	1.48	118.2
	NH...O <sup>b</sup>	0.0123	0.0427	2.41	122.0
	NH...O <sup>b</sup>	0.0114	0.0456	2.36	118.0
	NH...O	0.0310	0.0942	1.90	146.4
	NH...O	0.0245	0.0768	2.02	141.8
	NH...O	0.0245	0.0768	2.02	141.8

<sup>a</sup> The interaction distances (Å) and D-H...A angles (°) are also shown. <sup>b</sup> Interactions within the  $\text{H}_6\text{N}_3\text{C}-\text{OSO}_3^-$  molecule.

**11** are the only ones with a noncharged monomer (guanidine), and this may be the reason for the relatively lower interaction energies. However, the interaction energies of these complexes are smaller than those of the complexes with all charged monomers (guanidinium and sulfate). Again, a highly attractive polar interaction cannot be dismissed.

In terms of the electron density analysis, several HB have been identified for the dimers based on the values of the electron density (around  $10^{-2}$  au), the Laplacian (all positive), and bond distances and angles (see Table 7).

Thus, in the guanidine-bisulfate complex **6**, two strong intermolecular HB have been identified, with large electron density values and short HB distances. One of these HB is established between the N-H of the guanidine and one of the O atoms of the bisulfate, with the other between the N of the guanidine and the O-H of the bisulfate. In complex **8**, three different BCP have been identified, and by considering the values of the electron density and the medium HB distances ( $\sim 2$  Å), all of them correspond to medium strength HBs. In addition to S-O...H-N and O-H...N interactions (similar to those seen in **6**), a third S-O...H-N interaction is established. This explains the larger interaction energy found for **8** compared with **6**.

Four BCP were found for trimers **10** and **11** (see Table 7 and Figure 4). In the case of **10** two of the BCP are symmetrical with short H...O distances and a very large  $\rho$ -(BCP), which corresponds to two very strong HBs. Trimer

**11** exhibits three strong O...H HBs and one strong N...H HB, all with short bond distances and large electron density values at their BCPs. The symmetrical trimer **12** shows a total of six medium-to-strong HB interactions (three on each side of the symmetry plane) involving two  $\text{NH}_2$  groups from each guanidinium cation (see Figure 4 and Table 7). Trimer **13** is also symmetrical and shows one strong and one medium HB involving two of the  $\text{NH}_2$  groups of each guanidinium cation (see Table 7). Finally, **14** and **15** exhibit a complicated network of inter- and intramolecular interactions in which different BCPs were found. Their electron densities and interaction bond distances are characteristic of medium-to-strong HBs (see Figure 4 and Table 7). In complexes **14** and **15** a BCP was found between the C atom of the guanidinium and one of the O atoms of the sulfate moiety. The  $\rho(\text{BCP})$  values were very high, and the Laplacian of those  $\rho(\text{BCP})$  was always negative, clearly indicating the covalent nature of those bonds.

As in our previous work<sup>18</sup> an excellent logarithmic correlation was found between the HB distances and the  $\rho$ -(BCP) values for each of the HB interactions in both dimer and trimer species. Considering all of the N-H...O, N-H...N, and O-H...N interactions found within the present study the following relationship was derived:  $d(\text{H}\cdots\text{X}) = -0.53\text{Ln}(\rho(\text{BCP})) + 0.06$  ( $R^2 = 0.97$ ,  $n = 25$ ). This equation not only ratifies the strong dependence between  $\rho(\text{BCP})$  and the HB distance but also allows for the prediction of  $\rho(\text{BCP})$  values if a certain HB distance is known.

With regard to the NBO analysis, both the charge transferred and the orbital interaction energies were calculated for each interaction found within the complexes (see Table 8).

Strong charge transfer is observed ( $\sim 10^{-1}$  e) in those complexes in which each of the interacting species is charged and compares with a charge transfer of around  $\sim 10^{-2}$  e for those complexes in which one of the interacting species is neutral (complexes **6**, **8**, and **11**). This observation corroborates the high  $E_1$  found in the former complexes (all charged) and indicates that a significant electrostatic force is present and that the HBs are not the only forces responsible for the interactions.

In terms of the orbital interaction energy ( $E(2)$ ) calculated, the NBO analysis shows that in all the N-H...O HBs observed, a lone pair of one of the O atoms of the sulfate or bisulfate anions interacts with antibonding N-H orbitals (from one or two guanidinium molecules). In the case of the O-H...N and N-H...N connections the interaction takes place between a lone pair of one of the N atoms and the antibonding O-H or N-H orbitals, respectively. All of the antibonding molecular orbitals show a very large contribution from the  $p$ -orbitals based on the N and C atoms. All of the computed  $E(2)$  values are in agreement with the medium-to-strong nature of the HB interactions and considering the different nature of the HBs found within these complexes, it is logical that the values are spread over a wide range (from 0.37 to 48.98 kcal mol<sup>-1</sup>).

The strength of any HB is indicated by considering the electron density in the BCP, and this value should correlate with the orbital interaction energy, which itself gives an idea

**Table 8.** Charge Transfer (e) and Orbital Interaction Energy (kcal mol<sup>-1</sup>) Calculated for the Guanidinium (G<sup>+</sup>), Guanidine (G)-Sulfate, Bisulfate Complexes at the B3LYP/6-31+G\* Level with the NBO Method

charge transfer			<i>E</i> (2)	
G...HSO <sub>4</sub> (6)	SO <sub>4</sub> H → G	0.00541	N-H...O	9.71
			O-H...N	15.50
G...HSO <sub>4</sub> (8)	SO <sub>4</sub> H → G	0.01085	N-H...O	6.10
			O-H...N	2.86
G <sup>+</sup> ...SO <sub>4</sub> ...G <sup>+</sup> (10)	SO <sub>4</sub> H → G <sup>+</sup>	0.15584	N-H...O	37.22
			N-H...O	26.87
G <sup>+</sup> ...HSO <sub>4</sub> ...G (11)	SO <sub>4</sub> H → G	0.0579	N-H...O	27.35
			O-H...N	8.56
G <sup>+</sup> ...SO <sub>4</sub> ...G <sup>+</sup> (12)	SO <sub>4</sub> → G <sup>+</sup>	0.11638	O-H...N	39.61
			N-H...O	13.38
G <sup>+</sup> ...SO <sub>4</sub> ...G <sup>+</sup> (13)	SO <sub>4</sub> H → G	0.00541	N-H...O	1.96
			N-H...O	0.96
G <sup>+</sup> ...SO <sub>4</sub> ...G <sup>+</sup> (13)	SO <sub>4</sub> → G <sup>+</sup>	0.11731	N-H...O	9.71
			N-H...O	21.29
G <sup>+</sup> -OSO <sub>3</sub> ...G <sup>+</sup> (14)	G <sup>+</sup> -OSO <sub>3</sub> → G <sup>+</sup>	0.12488	N-H...O <sup>a</sup>	2.68
			N-H...O <sup>a</sup>	2.11
G <sup>+</sup> -OSO <sub>3</sub> ...G <sup>+</sup> (15)	G <sup>+</sup> -OSO <sub>3</sub> → G <sup>+</sup>	0.11143	N-H...O <sup>a</sup>	0.84
			N-H...O <sup>a</sup>	12.76
G <sup>+</sup> -OSO <sub>3</sub> ...G <sup>+</sup> (15)	SO <sub>4</sub> → G <sup>+</sup>	0.11731	N-H...O	0.37
			N-H...O	19.00
G <sup>+</sup> -OSO <sub>3</sub> ...G <sup>+</sup> (15)	SO <sub>4</sub> → G <sup>+</sup>	0.11731	N-H...O <sup>a</sup>	1.11
			N-H...O <sup>a</sup>	1.52
G <sup>+</sup> -OSO <sub>3</sub> ...G <sup>+</sup> (15)	SO <sub>4</sub> → G <sup>+</sup>	0.11731	N-H...O	7.33
			N-H...O	11.32
G <sup>+</sup> -OSO <sub>3</sub> ...G <sup>+</sup> (15)	SO <sub>4</sub> → G <sup>+</sup>	0.11731	N-H...O	21.29
			N-H...O	21.29

<sup>a</sup> Interactions within the H<sub>6</sub>N<sub>3</sub>C-OSO<sub>3</sub><sup>-</sup> molecule.

of the nature of the bond. We first observed such a correlation in previous studies.<sup>20</sup> Thus, all of the *E*(2) orbital energy values were correlated to those of the corresponding  $\rho(\text{BCP})$ , and the following relationship was found:  $E(2) = 815.92\rho(\text{BCP}) - 11.46$  ( $R^2 = 0.90$ ,  $n = 25$ ). As before, two different trends were observed in the linear plot, and therefore two separate correlations were established. One correlation was found for those interactions involving N as the HB acceptor, and the following relationship was established:  $E(2) = 1310.60\rho(\text{BCP}) - 24.26$ ,  $R^2 = 0.99$ ; it must be mentioned that there were only four cases to be considered. The other correlation took into account the remaining 21 cases in which an O atom was the HB acceptor, and this yielded the following relationship:  $E(2) = 763.63\rho(\text{BCP}) - 10.65$ ,  $R^2 = 0.92$ .

## Conclusions

From our computations at a higher level of theory, it may be concluded that the structure of the guanidinium cation is not planar but can be perceived as two interchangeable mirror image propellers passing through a planar transition state with a very small cost of energy. In this case, DFT calculations performed similarly to other higher and more expensive levels of computation.

Structures of minimum energy have been found for the guanidinium-chloride and guanidinium-chloride-guanidinium dimer and trimer complexes. The geometrical, AIM and NBO analysis of these complexes indicated the presence

of strong HB between two H of the guanidinium cations and the chloride anion in a pincerlike disposition. The interactions observed in the dimer are in agreement with the crystal structures found in the CSD, and this kind of arrangement might be anticipated within a putative crystal structure of the trimer.

In the case of the sulfate-guanidinium dimers and trimers, several energy minima have been localized, and in all the cases numerous HB interactions have been found to be formed between both charged species making very strongly bound complexes. The tetrahedral disposition of the sulfate anion opens a wide range of possible interactions. This is reflected by the complex crystal structure found in the CSD where a unique sulfate molecule is surrounded by six guanidinium cations each one interacting in a different way with the dianion. Thus, compounds bearing guanidinium cations would be able to form a variety of very stable complexes with this anion, which augurs well for its future use in structural supramolecular chemistry.<sup>21</sup>

Computations yielded compound **9**, which is a gem-triamine that has, to the best of our knowledge, no known precedent within the literature. However, as a theoretical tool, it gives a good idea of all the possibilities of how the two ionic species may potentially interact.

In general, the interaction energies of all these dimers and trimers are extremely large, while the electron densities at the BCP and the *E*(2) values are those expected for a HB. This could indicate that in these charged complexes a large polar contribution is being added to that of the formation of HBs resulting in extremely strong interactions. Furthermore, we have verified that a correlation exists between the electron density in the BCP and the orbital interaction energy and that this gives an idea of both the nature and strength of any HB.

**Acknowledgment.** Funds from the Irish Higher Education Authorities Program for Research in Third Level Institutions (PRTL) through the Centre for Synthesis and Chemical Biology supported this research. We also thank Prof. Jose Elguero, Dr. Raj S. Chari, and Dr. Anthea C. Lees for helpful discussions.

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CT050009X