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A topological analysis of charge density in complexes between derivatives of squaric acid and ammonium cation

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Abstract

A topological analysis of the electron charge density in complexes between derivatives of squaric acid and ammonium cation has been carried out. There are excellent relationships between either the charge density or its associated Laplacian at the ring critical point originated upon complexation and both geometric and energetic parameters. There is a remarkable influence of the substituents attached to the four-membered ring on the charge density at the ring critical point. © 2001 Elsevier Science B.V. All rights reserved.

1. Introduction

Supramolecular chemistry bears on the organized entities of higher complexity that results from the association of two or more chemical species held together by intermolecular forces [1]. Molecular receptors are organic structures held mainly by covalent bonds, which are able to bind selectively ionic or molecular substrates (or both) by means of various intermolecular interactions, leading to an assembly formed by two or more species [2]. Molecular recognition is defined by the energy involved in the binding of a substrate by a given receptor molecule. It implies a pattern recognition process through a structurally well-defined set of intermolecular interactions.

Molecular modeling techniques based on high-level *ab initio* calculations have become incipient and incisive tools that provide insight into the molecular recognition process for simple molecular receptors. These techniques help us in getting a deeper understanding of the intermolecular forces involved in the binding process that finally account for the molecular recognition features of the receptor.

In non-polar organic solvents, the so-called strong or conventional hydrogen bond [3] (O,N)–H···(O,N), an electrostatic force with some covalent character, is probably the most important directional intermolecular force used for supramolecular construction. The hydrogen bond can be successfully studied by means of the topological properties of the electron charge density (ρ) using the theory of ‘atoms in molecules’ [4,5]. Although there are some examples where this method has not given a correct interpretation of the bond pattern [6,7], it has been satisfactorily

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used to study the formation of hydrogen bonds in a great variety of molecular complexes [4,8–10]. This theory has also provided new insights in to non-conventional hydrogen bonds [11] and cation– π interactions [12]. These studies are usually based on various properties (ρ , $\nabla\rho$, $\nabla^2\rho$) obtained at the bond critical points. The topology of the electron density yields a reliable mapping of the molecule, i.e., atoms, bonds and structure, and provides the basis for a theory of structural stability.

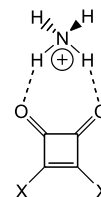
Our group has used squaramide as a binding block in the construction of tripodal receptors [13,14]. The tripodal receptors were assayed in the molecular recognition of ammonium cations [15], and choline containing phospholipids [16]. Our findings revealed that the squaramide unit (3,4-diamino-3-cyclobutene-1,2-dione), theoretically [17–19] and experimentally [15] has a remarkable hydrogen bond acceptor character. In this Letter we report our theoretical studies on the interaction of ammonium cation (hydrogen bond donor) with a series of derivatives of squaric acid (hydrogen bond acceptor). Particularly, the existence of relationships among the topological properties at the ring critical points (instead of the more commonly used bond critical points) originated upon binding and the energetic and geometric characteristics of the complexes formed. These relationships make clear the influence of the substituents attached to the four-membered ring on the geometric and energetic features of the complexes.

2. Computational methods

Some basic concepts of Bader's topology analysis follows (see [4,5] 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 critical points of electron charge distribution for molecules at energetically stable configurations are all rank 3 ($\omega = 3$). For instance, a bond critical point denoted as (3, –1) has two associated curvatures of ρ , denoted as λ_1 and λ_2 , negative 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 ellipticity, defined as $\varepsilon = [\lambda_1/\lambda_2 - 1]$, provides a measure of the extent at which the electron charge density is accumulated in a given plane. For example, the ellipticity for C–C bond in ethane is $\varepsilon = 0.0$ (symmetrical bond), in ethene is $\varepsilon = 0.45$, in benzene is $\varepsilon = 0.23$. The remaining two stable critical points 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).

A series of complexes of ammonium cation with derivatives of squaric acid (see Fig. 1) has been studied. The geometry of all complexes was fully optimized at the Hartree–Fock level using the 6-31G** basis set by using GAUSSIAN 98 program




- | | |
|----------------------|-------------------------|
| 1: X=F | 9: X=SMe |
| 2: X=OH | 10: X=NHNH ₂ |
| 3: X=H | 11: X=NMe ₂ |
| 4: X=PH ₂ | 12: X=OOH |
| 5: X=NH ₂ | 13: X=OMe |
| 6: X=Me | 14: X=Cl |
| 7: X=NHMe | 15: X=SiH ₃ |
| 8: X=SH | |

Fig. 1. Ammonium cation complexes 1–15.

Table 1

Interaction energies (E , kcal/mol), equilibrium distances (R_e , Å), critical points (CP) originated upon complexation, distances from the nitrogen atom of the ammonium cation to the CP (r_{cp} , Å), charge electron densities (ρ , a.u.) and its associated Laplacian ($\nabla^2\rho$, a.u.)

	Complex	E	R_e	CP	r_{cp}	$10^3 \rho$ (cp)	$10^2 \nabla^2 \rho$ (cp)
X = F	1	−21.4	2.94	(3, −1)	1.65	21.40	6.600
				(3, +1)	1.73	4.457	2.605
X = OH	2	−28.9	2.87	(3, −1)	1.62	25.81	7.987
				(3, +1)	1.69	5.106	3.052
X = H	3	−27.2	2.91	(3, −1)	1.64	23.52	7.257
				(3, +1)	1.71	4.769	2.824
X = PH ₂	4	−28.9	2.88	(3, −1)	1.63	25.09	7.760
				(3, +1)	1.69	5.058	3.002
X = NH ₂	5	−39.7	2.82	(3, −1)	1.60	30.20	9.460
				(3, +1)	1.66	5.736	3.496
X = Me	6	−32.4	2.86	(3, −1)	1.62	26.38	8.182
				(3, +1)	1.69	5.205	3.112
X = NHMe	7	−42.6	2.79	(3, −1)	1.59	32.28	10.219
				(3, +1)	1.66	6.006	3.653
X = SH	8	−26.6	2.89	(3, −1)	1.63	24.65	7.606
				(3, +1)	1.70	4.973	2.956
X = SMe	9	−30.5	2.85	(3, −1)	1.62	26.92	8.391
				(3, +1)	1.69	5.307	3.153
X = NHHN ₂	10	−37.2	2.81	(3, −1)	1.60	30.51	9.591
				(3, +1)	1.67	5.766	3.495
X = NMe ₂	11	−42.5	2.78	(3, −1)	1.58	32.96	10.495
				(3, +1)	1.66	6.115	3.72
X = OOH	12	−29.6	2.87	(3, −1)	1.62	25.63	8.002
				(3, +1)	1.70	5.155	3.017
X = OMe	13	−33.8	2.83	(3, −1)	1.61	28.23	8.840
				(3, +1)	1.69	5.459	3.259
X = Cl	14	−22.3	2.93	(3, −1)	1.65	2.193	6.757
				(3, +1)	1.72	4.557	2.674
X = SiH ₃	15	−29.5	2.88	(3, −1)	1.63	2.539	7.857
				(3, +1)	1.69	5.092	3.012

package [20]. Interaction energies (energy difference between complex and reactants, denoted as E) were determined at the HF/6-31G** level, without correction for the basis set superposition error. Previous studies have demonstrated that reliable quantitative results are obtained at this level of theory [21,22]. Topological properties of critical points were determined using Bader's theory of atoms in molecules. The electronic density analysis was performed using the program AIM-PAC¹.

3. Results and discussion

The interaction energies and equilibrium distances for complexes **1–15** are given in Table 1. The analysis of the critical points for the interaction of squaric acid derivatives with ammonium cation showed the presence of two (3, −1) critical points, which connect two hydrogen atoms of the ammonium cation with the two carbonyl oxygen atoms of the squaric ring (see Fig. 2). The Laplacian of the (3, −1) critical points is positive (see Table 1) because interactions between closed-shell systems, such as hydrogen bond interactions, are characterized by low values of ρ and positive values of $\nabla^2\rho$. The sign of the Laplacian is

¹ Available from Prof. R.F.W. Bader's Laboratory, McMaster University, Hamilton, Ont., Canada L8S 4M1.

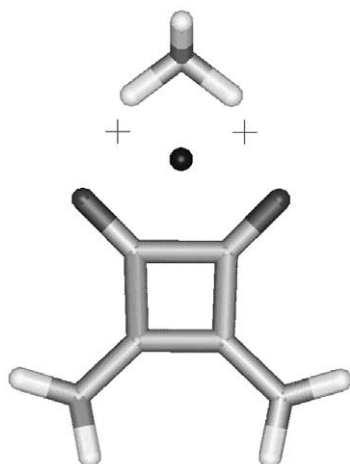


Fig. 2. Schematic representation of the location of the two $(3, -1)$ (crosses) and the $(3, +1)$ (circle) critical point originated from the complexation of the ammonium cation with squaramide.

determined by the positive curvature of ρ along the interaction line, leading to a relative depletion of charge in the interatomic surface [4,23]. Furthermore, it is also observed the presence of one $(3, +1)$ ring critical point, placed approximately in the middle of the ring that it is formed upon complexation of the ammonium cation with squaric acid derivatives (see Fig. 2). The values of the density and its associated Laplacian at the ring critical points are given in Table 1. We have found interesting relationships between the electronic density at the ring critical point that it is formed upon complexation, the interaction energy (E) and the equilibrium distance (R_e) of the complexes. In particular, there is an excellent correlation between the equilibrium distance ($H_4N \cdots O = C$) and either the value of the charge density (ρ) or the value of the Laplacian ($\nabla^2\rho$) at the ring critical point. $r^2 = 0.99$ for both regressions, as shown in Fig. 3. Moreover, there is a good correlation between the interaction energy (E) of the complexes and either ρ or $\nabla^2\rho$ at the ring critical point. $r^2 = 0.96$ and $r^2 = 0.97$, respectively (see Fig. 3). In addition, there is also an acceptable correlation between the location of the ring critical point (r_{cp}) and the equilibrium distance (R_e), $r^2 = 0.95$. It is remarkable that the large influence of the substitu-

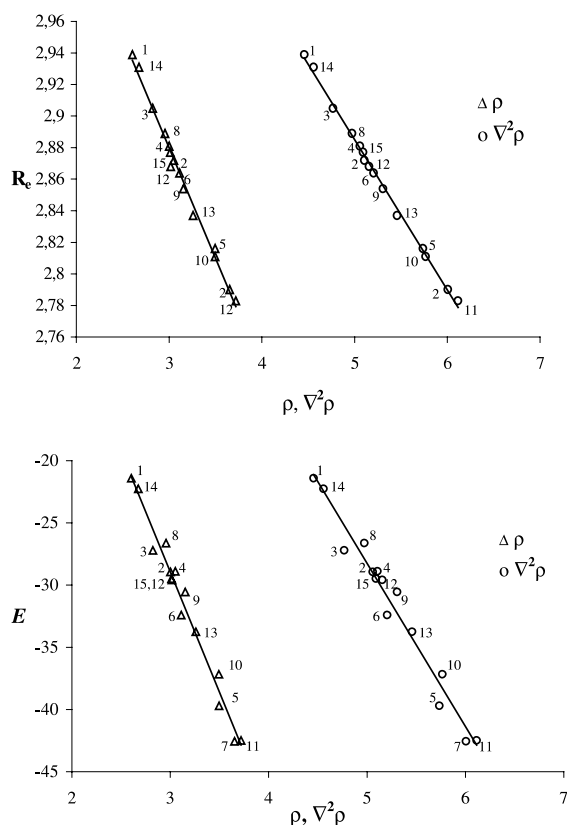
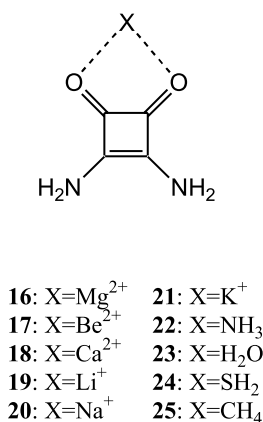


Fig. 3. Plots of the regression between the electron density and its associated Laplacian (a.u.) at the $(3, +1)$ critical point and the interaction energy (kcal/mol) (bottom), and the equilibrium distance (Å) (top) for the 1–15 complexes.

ents attached to the four-membered ring over the charge density and the interaction energies. This confirms the large differences in resonance and electron-withdrawing effects for the different substituents employed. In consequence, the hydrogen bond accepting character of the squaric acid derivative can be modulated by choosing adequate substituents.

The above-mentioned results reveal the relationship between the properties at the ring critical point and the geometrical and energetic characteristics of the ammonium complexes. We have also examined the properties of complexes involving other types of cations (either hydrogen-bonded or not) and complexes involving hydrogen-bonded neutral molecules (see Fig. 4). Interaction energies and equilibrium distances for the interaction of

Fig. 4. Squaramide complexes **16–25**.

squaramide with Mg²⁺, Be²⁺, Ca²⁺, Li⁺, Na⁺, K⁺, NH₄⁺, NH₃, H₂O, SH₂ and CH₄ are summarized in Table 2. There is a strong relationship between the interaction energy (E) and the electron density (ρ) at the ring critical point formed upon complexation ($r^2 = 0.98$, see Fig. 5). A similar result

is obtained when the Laplacian of the electron density is studied ($r^2 = 0.95$). The computed ellipticities of the charge density at the (3, −1) critical point of the C–N bond in squaramide complexes are listed in Table 2. There is a correlation between the interaction energy and the ellipticity of C–N bond, $r^2 = 0.93$. The Be²⁺-squaramide complex (**17**) has the highest interaction energy, and the highest value of ellipticity determined for the C–N bond ($\epsilon = 0.149$). Similarly, the CH₄-squaramide complex (**25**) has the lowest interaction energy and the lowest value of the ellipticity for the C–N bond ($\epsilon = 0.011$). Therefore, the double bond character of the C–N bond, as a measure of the π -electron donation from the nitrogen atom to the carbonyl oxygen atom of squaramide, is important in complexes that have large interaction energies. This reasoning is confirmed by means of the computed C–N Wiberg bond indices [24] (WBI) for the squaramide complexes (see Table 2). The C–N WBI of complex **17** (Be²⁺-squaramide, $E = -295.9$ kcal/mol) is 1.476 indicating delocalization of the lone pair of the nitrogen atom whereas the

Table 2

Interaction energies (E , kcal/mol), equilibrium distances (R_e , Å), critical points (CP) originated upon complexation, distances from the heavy atom of the interacting compound to the CP (r_{cp} , Å), charge electron densities (ρ , a.u.) and its associated Laplacian ($\nabla^2\rho$, a.u.), Wiberg bond indexes (WBI) and ellipticities (ϵ) associated with the C–N bond of squaramide complexes

Comp.	Complex	E	R_e	WBI	ϵ	CP	r_{cp}	$10^2 \rho$ (cp)	$10 \nabla^2 \rho$ (cp)
NH ₄ ⁺	5	−39.7	2.82	1.216	0.052	(3, −1)	1.60	3.017	0.946
						(3, +1)	1.66	0.574	0.350
Mg ²⁺	16	−179.9	1.98	1.395	0.115	(3, −1)	0.85	4.796	3.857
						(3, +1)	1.11	1.979	0.922
Be ²⁺	17	−295.9	1.55	1.476	0.149	(3, −1)	0.53	9.927	7.964
						(3, +1)	0.92	4.292	1.893
Ca ²⁺	18	−122.6	2.36	1.394	0.093	(3, −1)	1.16	3.656	1.991
						(3, +1)	1.44	1.316	0.702
Li ⁺	19	−64.2	2.01	1.246	0.069	(3, −1)	0.53	2.348	1.727
						(3, +1)	0.91	1.109	0.685
Na ⁺	20	−49.9	2.36	1.227	0.059	(3, −1)	1.31	1.926	1.204
						(3, +1)	1.24	0.781	0.511
K ⁺	21	−37.2	2.77	1.210	0.051	(3, −1)	1.39	1.546	0.704
						(3, +1)	1.63	0.576	0.359
NH ₃	22	−4.0	3.47	1.135	0.014	(3, −1)	1.92	0.655	0.262
						(3, +1)	2.02	0.179	0.102
H ₂ O	23	−7.2	3.16	1.141	0.017	(3, −1)	1.73	1.129	0.394
						(3, +1)	1.82	0.280	0.168
H ₂ S	24	−4.1	3.75	1.138	0.014	(3, −1)	2.25	0.803	0.266
						(3, +1)	2.29	0.165	0.088
CH ₄	25	−1.3	3.88	1.131	0.011	(3, −1)	2.18	0.317	0.135
						(3, +1)	2.27	0.085	0.052

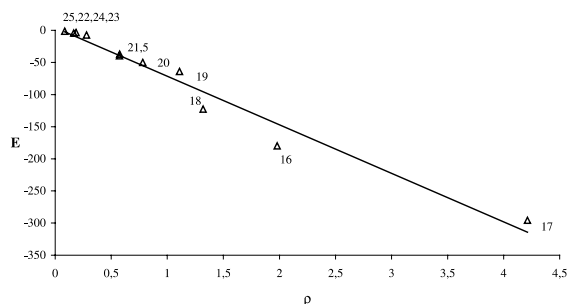


Fig. 5. Plot of the regression between the electron density (a.u.) and the interaction energy (kcal/mol) for the **5** and **16–25** complexes.

C–N WBI for complex **25** (CH_4 -squaramide, $E = -1.41$ kcal/mol) is 1.131 indicating a negligible electron donation from the nitrogen atom.

It is worthy to note the relevance of the above-mentioned relationships because they cover a wide range in the interaction energy (from -1 to -300 kcal/mol) and they allow for treating simultaneously the interaction of squaramide with both cations (either hydrogen-bonded or not) and hydrogen-bonded neutral molecules.

4. Conclusions

The results reported in this study demonstrate the influence of the substituents attached to the four-membered ring on the electron density and on the interaction energy of the complexes between ammonium cation and C_4 -pseudooxocarbons. The existence of the ring critical point, present in all complexes studied, permits to detect relationships between energetic and geometrical parameters and the charge density at the ring critical point. Actually, the topological arrangement detected for the interaction of squaramide with ammonium cation can also be appropriated for other cations, either hydrogen-bonded or not, and even to neutral molecules.

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References

- [1] J.-M. Lehn, *Angew. Chem. Int. Ed. Eng.* 27 (1998) 89.
- [2] G.W. Gokel (Ed.), *Advances in Supramolecular Chemistry*, vol. 3, Jai Press, Greenwich, 1993.
- [3] G.A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford University Press, New York, USA, 1997.
- [4] R.F.W. Bader, *Chem. Rev.* 91 (1991) 893.
- [5] R.F.W. Bader, *Atoms in Molecules. A Quantum Theory*, Oxford University Press, Oxford, UK, 1990.
- [6] S.T. Howard, J.A. Platts, *J. Phys. Chem.* 99 (1995) 9027.
- [7] J.A. Platts, S.T. Howard, B.R.F. Bracke, *J. Am. Chem. Soc.* 118 (1996) 2726.
- [8] U. Koch, P.L.A. Popelier, *J. Phys. Chem.* 99 (1995) 9747.
- [9] P.L.A. Popelier, *J. Phys. Chem. A* 102 (1998) 1873.
- [10] F.J. Luque, et al., *J. Phys. Chem. A* 102 (1998) 6690.
- [11] I. Alkorta, I. Rozas, J. Elguero, *Chem. Soc. Rev.* 27 (1998) 163.
- [12] E. Cubero, M. Orozco, F.J. Luque, *J. Phys. Chem. A* 103 (1999) 315.
- [13] P. Ballester, et al., *Tetrahedron Lett.* 35 (1994) 3813.
- [14] R. Prohens, et al., *Tetrahedron Lett.* 39 (1998) 1063.
- [15] S. Tomàs, et al., *J. Org. Chem.* 61 (1996) 9394.
- [16] S. Tomàs, et al., *Angew. Chem. Int. Ed.* 38 (1999) 2208.
- [17] D. Quiñonero, A. Frontera, P. Ballester, P.M. Deyà, *Tetrahedron Lett.* 41 (2000) 2001.
- [18] D. Quiñonero, et al., *Theor. Chem. Acc.* 104 (2000) 50.
- [19] D. Quiñonero, et al., *Chem. Phys. Lett.* 326 (2000) 247.
- [20] M.J. Frisch, et al., *GAUSSIAN 98*, Revision A.7, Gaussian, Inc., Pittsburgh, PA, 1998.
- [21] R.J. Boyd, S.C. Choi, *Chem. Phys. Lett.* 120 (1985) 80.
- [22] R.J. Boyd, S.C. Choi, *Chem. Phys. Lett.* 129 (1986) 62.
- [23] R.F.W. Bader, H. Essen, *J. Chem. Phys.* 80 (1984) 1943.
- [24] K.B. Wiberg, *Tetrahedron* 24 (1968) 1083.