

Experimental and Theoretical Study of Aromaticity Effects in the Solid State Architecture on Squaric Acid Derivatives

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Supporting Information



ABSTRACT: In this manuscript, the aromaticity of the four-membered ring in squaric acid derivatives and, particularly, how it changes when it participates in noncovalent interactions are studied combining experimental observations and theoretical analysis using the nucleus independent chemical shift (NICS). Moreover, the ability of the squaric acid and its derivatives to establish hydrogen bonds, $\pi - \pi$ stacking, and other π -interactions (anion $-\pi$, lone pair $-\pi$, and C-H/ π) is related to the increase in the aromaticity of the ring. In addition, several squaric acid derivatives (*benzamh*)(*sqah*)·H₂O (**1**), (*pipropamh*₂)(*sqa*)·2H₂O (**2**), (*deamh*)(*deamsqa*) (**3**), (*phpetamh*)(*sqah*)·(**4**), (*amsqa*)(*sqa*) (**5**), (and *benzamh*)(*benzamsqa*)·H₂O (**6**) where *benzam* = benzylamine; *sqah*₂ = squaric acid; *deamsqah* = diethylamidosquaric acid; *pipropam* = 3,3'-(piperazine-1,4-diyl)bis(propan-1-amine); *deam* = diethylamine *phpetam* = *p*-hydroxiphenylethylamine and *benzamsqah* = benzylamidosquaric acid) were synthesized and characterized by single crystal X-ray diffraction analyses.

1. INTRODUCTION

The cyclic oxocarbon acids $(C_n O_n H_2)$ and their conjugated bases, the oxocarbon dianions $(C_n O_n)^{2-}$, have been widely investigated both theoretically and experimentally due to their highly functionalized and interesting structures.¹ In their pioneering work, West et al.² recognized cyclic oxocarbon dianions as aromatic systems and suggested that they constitute a series of aromatic compounds. The latter generalization has been reinvestigated by others and questioned for the oxocarbons in general,³ although there are arguments in favor of aromaticity in the smallest members of the oxocarbon dianions series, the deltate and squarate dianions.⁴ It should be mentioned that squaramides have recently attracted attention in several fields such as catalysis,⁵ host-guest chemistry,⁶ and transmembrane transport.⁷ It is a useful supramolecular synthon to generate interesting architectures in the solid state.⁸ Actually, the utilization of squarate and hydrogen squarate salts is common in crystal engineering⁹ and organic material research.¹⁰

Some of us have recently studied⁸ the electrostatic compression phenomenon¹¹ in order to explain the face-to-face π -stacked architectures shown by a series of zwitterionic

squaric acid/squaramide compounds. The aim of this contribution is to extend the knowledge about the forces that govern these specific π -stacked assemblies by combining X-ray characterization and computational analysis of several squarate and amidosquarate salts (see Scheme 1). In particular, we focus our attention to analyze if the aromatic character of the fourmembered ring influences the solid state architecture of these mono and dianion salts directing the type of noncovalent interactions. Previously, a very interesting experimental and theoretical investigation focused on alkaline squarate salts $[M_2(C_4O_4)]$ (M = Li, Na, K, and Rb) was reported devoted to correlate the structures, vibrational analysis, and aromaticity.¹² In that work, the significant role of hydrogen bonding interactions to water molecules was examined, and it was shown that aromaticity and hydrogen bonds are the most important forces driving the interactions in the solid structures of squarate ions. In the present work, we examine the propensity of squaramide,

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Scheme 1. Squarate and Amidosquarate Salts 1-6 Studied in This Work



hydrogen squarate, and squarate salts in the solid state to establish interactions that are typical of aromatic compounds¹³ (stacking interactions,¹⁴ ion– π ,¹⁵ C–H/ π ,¹⁶ etc.). As far as our knowledge extends, this type of analysis has not been previously performed in the literature, especially the ability of the fourmembered ring to participate in anion– π (or lone pair– π) and C–H/ π interactions. This ability can be understood as an experimental consequence of the aromaticity of the fourmembered ring, which is an experimentally nonmeasurable property.

We have also studied by means of density functional theory (DFT) calculations the aromatic character of squaric acid and its derivatives. Moreover, we have studied changes in the aromatic character of the ring upon complexation with hydrogen bond donors, acceptors, and both simultaneously. An increase in the aromatic character of the four-membered ring upon complexation can be related to its ability to concurrently form other types of noncovalent interactions in the solid state involving the π -system of the ring. We have used the Cambridge Structural Database¹⁷ and the new crystal structures reported herein to analyze this topic. Finally, among the known criteria for aromaticity, we have used Schleyer's¹⁸ nucleus independent chemical shift (NICS) because it does not require the use of complicated equations and fictitious reference systems.^{1a}

2. EXPERIMENTAL AND THEORETICAL METHODS

2.1. Materials and Measurements. All chemicals used were reagent grade and used as received from Sigma-Aldrich.

2.2. Synthesis. Synthesis of 1. Compound 1 was prepared from a 1:1 mixture of squaric acid (2.01 g, 17.6 mmol) and benzilamine (1.89 g, 17.6 mmol) in water (25 mL). The suspension was refluxed for 3 h, and the solution was slowly cooled to r.t. The resulting crystals were filtered, washed with acetone (2×5 mL), and dried under a vacuum overnight. The yield was 97%. Single crystals of 1 were analyzed by single X-ray diffraction.

Synthesis of 2. Compound 2 was prepared from a 1:1 mixture of squaric acid (0.50 g, 4.4 mmol) and 1,4-bis(3-aminopropyl)piperazine (0.44 g, 2.2 mmol) in water (10 mL). The yield was 80%. Single crystals of 2 were analyzed by single X-ray diffraction.

Synthesis of 3. Compound 3 was prepared from a 1:1 mixture of squaric acid (0.20 g, 1.7 mmol) and diethylamine (1.28 g, 17.5 mmol) in water (10 mL). The suspension was stirred for 4 h, and the solid was recrystallized in water at 70 °C by slowly cooling to 5-8 °C. Single crystals of 3 were filtered and analyzed by single X-ray diffraction.

Synthesis of 4. Compound 4 was prepared analogously to 1 from a 1:1 mixture of squaric acid (1.09 g, 9.6 mmol) and tyramine (0.94 g,

8.7 mmol) in water (25 mL). Single crystals of 4 were separated by filtration and analyzed by single X-ray diffraction.

Synthesis of 5. Compound 5 was obtained from a 1:1 mixture of squaric acid (0.10g, 0.88 mmol) and 3,4-bis(2-dimethylamino-ethylamino)-cyclobut-3-ene-1,2-dione (0.23 g, 0.88 mmol) in water (10 mL). The suspension was stirred for 4 h, and it was cooled to r.t. The needle shaped crystals of 5 were filtered and analyzed by single X-ray diffraction.

Synthesis of **6**. Compound **6** was prepared from a 1:2 mixture of squaric acid (0.21 g, 17.6 mmol) and benzilamine (1.89 g, 17.6 mmol) in water (6 mL). The suspension was refluxed for 3 h, and the solution was slowly cooled to r.t. Some crystals appeared after 3 days at r.t. and one prismatic crystal was analyzed by single X-ray diffraction.

2.3. X-ray Crystallographic Analysis. Single crystal X-ray diffraction intensity data of the title complexes were collected using a MAR345 diffractometer with an image plate detector, equipped with graphite monochromated Mo K α radiation ($\lambda = 0.71073$ Å). Lorentz-polarization and empirical absorption correction SADABS¹⁹ were applied. The structure of the title compounds were solved by direct method and refined by the full-matrix least-squares technique on F² with anisotropic thermal parameters to describe the thermal motions of all non-hydrogen atoms using the programs SHELXS97 and SHELXL97,²⁰ respectively. All calculations were carried out using PLATON²¹ and WinGX system Ver-1.64.²² All hydrogen atoms were located from difference Fourier map and refined isotropically. A summary of crystal data and relevant refinement parameters is given in Table 1.

2.4. Theoretical Methods. The energies of all compounds and complexes included in this study were optimized at the M06-2X/6-311+G* level of theory within the program Gaussian-09.23 NICS values were obtained at the same level of theory by calculating the absolute NMR shielding using the GIAO method²⁴ at the ring centers, at 0.5 and 1.0 Å above them in order to reduce the local shielding of nearby σ -bonds which complicates the analysis for small rings. The maximum diatropic ring current effect for benzene is in the center of the ring but is offset by the paratropic contribution of the C-H and C–C $\sigma\text{-bonds}.$ These paratropic effects decrease more rapidly than the diatropic ones away from the center. Therefore, NICS values above the ring minimize the paratropic effect and give a more reliable indication of aromaticity. As it is mentioned below, the NICS value computed at 0.5 Å above the ring centroid is used for the discussion of the results. We have selected this distance because the protonated squaric acid derivatives have their maximum value of NICS at 0.5 Å, and then it decreases rapidly at higher distances (see Table 2). In contrast, for the rest of compounds (neutral and anionic) the variation of the value of NICS from 0.5 to 1 Å is very small. Therefore, the utilization of NICS(0.5) values is a good compromise to deal simultaneously with protonated, neutral, and anionic squaric acid derivatives.

3. RESULTS AND DISCUSSION

3.1. Preliminary Theoretical Study. We have first studied the effect of both protonation and deprotonation of squaric

Table 1. Crystal Data	and Structure Refineme	nt Parameters for 1–6				
structure	(1)	(2)	(3)	(4)	(5)	(9)
empirical formula	$C_{22}H_{24}N_2O_9$	$C_{18}H_{34}N_4O_{11}$	$C_{12}H_{22}N_2O_3$	$C_{12}H_{10}NO_4$	$C_{16}H_{24}N_4O_7$	$C_{36}H_{38}N_4O_7$
formula weight	460.43	482.49	242.32	251.23	384.39	638.70
temperature (K)	293(2)	293(2)	105(2)	293(2)	110(2)	293(2)
wavelength (Å)	0.710730	0.710730	0.710730	0.710730	0.710730	0.710730
crystal system	monoclinic	monoclinic	monoclinic	orthorhombic	monoclinic	orthorhombic
space group	C2/c	C2/c	$P2_1/c$	$P22_{1}2_{1}$	$P2_1/c$	Pbca
a, b, c (Å)	23.793(11)	18.512(11)	7.041(4)	6.019(4)	10.737(6)	23.15(2)
	9.123(2)	7.339(3)	12.717(5)	7.217(3)	11.931(5)	10.354(10)
	10.925(4)	16.768(8)	16.156(7)	26.878(13)	16.323(7)	29.282(10)
$\alpha, \beta, \gamma \text{ (deg)}$	90.00	00.06	90.00	90.00	90.00	90.00
	102.60(2)	102.90(2)	104.25(3)	90.00	119.13(3)	90.00
	90.00	00.06	90.00	90.00	90.00	90.00
volume $(Å^3)$	2314.3(15)	2220.6(19)	1402.1(11)	1167.6(11)	1826.5(16)	7018.0(10)
Z, density (calc) (Mg/m ³)	4, 1.321	4, 1.443	4, 1.148	4, 1.429	4, 1.398	8, 1.209
absorption coefficient (mm ⁻¹)	0.104	0.120	0.082	0.050	0.111	0.085
F(000)	968	1032	528	528	816	2704
crystal size (mm ³)	$0.02 \times 0.09 \times 0.09$	$0.02 \times 0.1 \times 0.1$	$0.1 \times 0.09 \times 0.08$	$0.2 \times 0.1 \times 0.1$	$0.2 \times 0.1 \times 0.1$	$0.2 \times 0.19 \times 0.08$
θ range for data collection (deg)	1.75 to 30.61	2.26 to 29.66	2.06 to 32.34	1.51 to 30.43	2.17 to 32.49	1.39 to 32.58
limiting indices	$\begin{array}{l} 31 \leq h \leq 31, -12 \leq k \leq 11, \\ -12 \leq l \leq 14 \end{array}$	$-25 \le h \le 25, \\ -9 \le k \le 9, -20 \le l \le 20$	$9 \le h \le 9, -18 \le k \le 18, -23 \le l \le 23$	$-6 \le h \le 7, -7 \le k \le 8, -36 \le l \le 36$	$-12 \le h \le 16,$ $-17 \le k \le 17, -21 \le l \le 21$	$\begin{array}{l} -34 \leq h \leq 33, -13 \leq k \leq 13, \\ -44 \leq l \leq 37 \end{array}$
reflections collected/ unique	10061/3048 [R(int) = 0.0279]	7470/2430 [R(int) = 0.0254]	12749/4065 [R(int) = 0.0414]	7054/2313 [R(int) = 0.0317]	13716/5911 [R(int) = 0.0637]	32155/8532 [R(int) = 0.0898]
completeness to $ heta$ (%)	98.6	96.4	99.4	85.8	99.4	88.5
absorption correction	empirical	none	empirical	none	empirical	empirical
max and min transmission	0.99 and 0.98	0.99 and 0.98	0.99 and 0.98	0.99 and 0.98	0.90 and 0.89	099 and 0.98
refinement method	full-matrix least-squares on ${ m F}^2$	full-matrix least-squares on F^2	full-matrix least-squares on F^2	full-matrix least-squares on F^2	full-matrix least-squares on F^2	full-matrix least-squares on F^2
data/parameters	3048/3/153	2430/0/171	4065/6/158	2313/1/202	5911/13/279	8532/23/394
goodness-of-fit on F^2	1.129	1.104	1.113	1.123	0.877	0.923
final R indices $[I > 2\sigma(I)]$	$R_1 = 0.0516, wR_2 = 0.1456$	$R_1 = 0.0444, wR_2 = 0.1146$	$R_1 = 0.0593, wR_2 = 0.1604$	$R_1 = 0.0503, wR_2 = 0.1378$	$R_1 = 0.0550, wR_2 = 0.1258$	$R_1 = 0.0568, wR_2 = 0.1316$
R indices (all data)	$R_1 = 0.0557, wR_2 = 0.1485$	$R_1 = 0.0487, wR_2 = 0.1184$	$R_1 = 0.0803, wR_2 = 0.1742$	$R_1 = 0.0540, wR_2 = 0.1508$	$R_1 = 0.1477, wR_2 = 0.1513$	$R_1 = 0.1908, wR_2 = 0.1639$
largest diff peak and hole (e.Å ⁻³)	0.244 and -0.277	0.264 and -0.179	0.247 and -0.282	0.334 and -0.527	0.194 and -0.277	0.311 and -0.324
centroid–centroid distance (Å)	3.71	4.05		3.33	3.63 and 3.95	3.44
CCDC	987591	987592	987593	987594	987595	987596

Crystal Growth & Design

Table 2. Computed NICS (ppm) at the M06-2X/6-311+G* Level of Theory for Compounds 7-15

compound	NICS(0)	NICS(0.5)	NICS(1)
7	-1.9	-5.9	-5.0
8	-2.3	-6.4	-5.4
9	-0.3	-5.7	-5.4
10	-7.2	-10.0	-6.6
11	-8.1	-10.0	-6.2
12	-6.8	-10.2	-6.9
13	0.8	-5.6	-6.0
14	1.4	-4.8	-5.3
15	-0.7	-5.4	-5.1
benzene	-7.4	-9.6	-10.4

acid derivatives (compounds 7-9, see Scheme 2) on their aromatic character, and the results are gathered in Table 2. For comparison purposes and to make the discussion tractable, we have included the NICS value of benzene at the same level. It has previously assigned the convention that if a molecule has less than half of the magnitude of NICS value in comparison to that of benzene (NICS(0.5) = -9.6 ppm), it is not aromatic.²⁵ In Table 2, we have included the NICS values at several distances, and it can be clearly observed that the NICS computed at the ring center is clearly affected by paratropic effects in the four-membered rings. In addition, the computation of NICS at 1 Å is not adequate for the four-membered rings since the ring current diatropic effect vanishes. Therefore, the NICS(0.5) values will be used for the discussion of aromaticity in the squaric acid and its derivatives. The NICS values computed for the neutral compounds 7-9 indicate that they are moderately aromatic, in agreement with previous results.¹ The di-O-protonated compounds 10–12 are aromatic (approximately equal to benzene) because the 2e-aromatic resonance form is predominant (see right of Scheme 2). In

contrast the squarate dianion (13) and monoanions 14 and 15 are moderately aromatic. In fact compound 14 has exactly the half NICS value compared to benzene, thus indicating a very modest aromatic character. The squarate dianion exhibits a complete equalization of the C–C bonds due to equal population of the four resonance forms shown at the bottom of Scheme 2. The aromatic resonance form has a strong charge separation and consequently is likely not important. These anionic compounds are clear examples where structural criteria for aromaticity based either on bond length (e.g., Julg²⁶ aromaticity index) or on bond order considerations (e.g., Bird²⁷ and Jug²⁸ indexes) are not adequate since they predict high aromatic character for squarate dianion. It should be also emphasized that the aromatic resonance form of squarate dianion can be stabilized electrostatically by the countercation and/or hydrogen bonding interactions and, consequently, increasing the relative importance of this resonance form.

We have also computed a series of dimers and trimers based on squaric acid and squaramide in order to investigate the influence of the hydrogen bonding on the aromatic character. They are represented in Scheme 3, and the NICS(0.5) values are summarized in Table 3. From the inspection of the results, some interesting issues arise. First, in the squaric acid dimer (16), the aromatic character of ring A decreases (H-bond donor) and, conversely, it increases in ring B (H-bond acceptor), which is in agreement with the expectation taking into account that the di-O-protonated squaric acid is as aromatic as benzene and that the squarate dianion is only moderately aromatic. Second, for squaramide both rings increase their aromatic character in the dimer (17) compared to the monomer. A likely explanation is that ring A upon complexation reduces the delocalization of the lone pair of electrons on nitrogen into the ring, and, consequently, the aromaticity of the ring increases. This result agrees with the experimental hydrogen bond acceptor/donor dual character of squaramide

Scheme 2. Compounds 7–15 Studied in This Work and Resonance Forms of a Generic Di-O-protonated Compound and Squarate Dianion 13







compound	А	В	С
16	-5.1(0.8)	-6.6 (-0.7)	
17	-7.2 (-0.8)	-7.2 (-0.8)	
18	-5.2 (-0.4)	-5.2 (-0.4)	
19	-5.3 (0.6)	6.8 (-0.9)	-6.1(-0.2)
20	-7.4 (-1.0)	-7.6 (-1.2)	-7.7 (-1.3)
21	-4.6 (1.3)	-4.6 (1.3)	-7.1 (-1.5)

^{*a*}The NICS variation with respect to the monomers 7-15 is indicated in parentheses.

derivatives, acting as binding units in several receptors for both anions and cations. We have also examined the dimer of the



monoanion 14, which also increases its aromatic character in the self-assembled dimer 18. Third, the central ring C of the squaric acid trimer (19), which simultaneously participates in hydrogen bonding interactions as donor and acceptor, very modestly increases its aromatic character compared to 10. Remarkably, the central ring C of the squaramide trimer (20) significantly increases its aromaticity. Therefore, the simultaneous participation of the squaramide in H-bonding interactions as donor and acceptor contributes to increase the aromaticity of the four-membered ring, confirming previous results observed for dimer 17. Finally, the central ring in trimer 21 significantly increases its aromatic character with respect to the naked dianion (13); therefore, the squarate dianion is also expected to form π -interactions in the solid state.



Figure 1. CSD search results for squaramide (top) and squaric acid (bottom), and partial views of some X-ray structures retrieved from the search. The CSD codes are indicated. Distances in Å.

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Figure 2. CSD search results for mono squarate anion and partial views of some X-ray structures retrieved from the search. The CSD codes are indicated. Distances in Å.

We have examined the Cambridge Structural Database, to learn the solid state features of squaric acid. In particular we focused our study on analyzing the noncovalent interactions involving the four-membered ring and comparing them to the typical aromatic interactions $(\pi - \pi, \text{ ion} - \pi, \text{ C} - \text{H}/\pi)$. This type of analysis that relates the aromaticity to the ability to form anion- π , lone pair- π , and C-H/ π interactions is unprecedented and can be understood as an experimental confirmation of the aromaticity of the four-membered ring. We have performed several searches that have been restricted to only organic compounds; therefore, organometallic compounds have not been considered. The results and some examples are shown in Figures 1-3, and we have divided the searches into neutral, anionic, and dianionic systems. For squaric acid, we have found 15 X-ray structures in the CSD, and in only two of them the π -system of the four-membered ring is a mere spectator. In the rest of structures, it participates in typical aromatic π -interactions, including $\pi - \pi$ stacking (8 hits), lp(anion) - π (3 hits), and C–H/ π (1 hit) interactions. Some selected examples for each type of binding are shown in Figure 1 (bottom). For the squaramide search, a similar result is found since in only 5 of a total of 31 structures the four-membered ring does not participate in π -interactions. The rest of structures present interesting assemblies in the solid state dominated by a combination of H-bonds and π -interactions (π - π , C-H/ π , and $lp(anion)-\pi$). This result agrees well with the theoretical study (vide supra) that showed a significant increase in the aromatic character of the squaramide ring when it participates in H-bonding interactions as donor and acceptor, which is the case of the WECCAK structure (Figure 1).

The results for the monoanionic search are presented in Figure 2. A significant number of structures have been found (78), and in most of them the squarate ring participates in π - π stacking interactions. As an example, the ODEZOO structure is shown in Figure 2 that forms in the solid state the self-assembled dimer that we have previously studied theoretically. As aforementioned, the aromatic character of this dimer (18) increases with respect to the monomer (14) and likely increases the ability to establish short π - π interactions as observed in ODEZOO structure (3.23 Å). The number of structures that form C-H/ π and lp(anion)- π interactions is lower (7 and 10, respectively), and two selected examples are shown in Figure 2. It should be emphasized that only in four structures the fourmembered ring does not establish any type of π -interaction.

Finally, the results for the dianionic search are gathered in Figure 3. In this case we have found 51 structures, and in only 12 of those the ring does not participate in π -interactions. In 26 structures the ring participates in π - π interactions. It should be



Figure 3. CSD search results for squarate dianion and partial views of some X-ray structures retrieved from the search. The CSD codes are indicated. Distances in Å.

noted the importance of this result, since a strong electrostatic repulsion between the dianionic squarate moieties is expected. Obviously, the counterions also play a prominent role in the final structure. Relevant examples are included in Figure 3, and in all cases the squarate forms a three-component assembly resembling complex **20** studied above. In this complex, ring **C** (squarate dianion) increased its aromatic character significantly. Therefore, the ability of this ring, even in its formal dianionic form, to participate in $\pi - \pi$ interactions is related to its aromatic character.

3.2. Description of Squaric Acid Derivatives 1–6. We have synthesized and characterized six new squaric salts. The structural analysis of five out of the six new compounds reveals well-defined crystal architectures through $\pi - \pi$ stacking in combination with charge-assisted hydrogen bonding interactions as expected. The packing motif is similar to the ones presented by our previously published⁸ zwitterionic squaramido compounds and consists of a variety of electrostatically compressed assemblies. In an effort to correlate the solid state architecture of compounds 1-6 and the aromaticity of the fourmembered ring, we have performed further theoretical



Figure 4. Solid state structures of compounds 1-6 with indication of the NICS(0.5) values.



Figure 5. Crystal structure of the dianions 2 (a) and 5 (b) showing centroid-centroid distances (water molecules not shown).

calculations. We have specially focused our attention on the interplay between H-bonding interactions in the molecular plane (σ -interactions) and the aromaticity of the ring and, consequently, π -interactions. As described above, both dianions (2 and 5) and monoanions 1, 4, and 6 participate in $\pi - \pi$ stacking interactions, and, concurrently, several hydrogen bonds are also present. Obviously the final solid state architecture is dominated by an intricate combination of interactions, and we have analyzed some of them. In Figure 4 we represent the six salts with indication of the NICS(0.5) values. Interestingly all compounds exhibit higher aromatic character than the isolated mono- and dianions 13-15 as a consequence of the interaction with the counterion. Moreover, the squaramide ring in compound 5 is also more aromatic than compound 8 (-6.4 ppm, see Scheme 2 and Table 2) as a consequence of the $\pi - \pi$ stacking interaction with squaric acid dianion.

The crystal structure of the dianion **2** shows a distorted electrostatically compressed assembly of disquarates in a zigzag fashion with a centroid—centroid distance of 4.05 Å. Squarate dianions are bridged with others from equivalent assemblies via strong H-bonds with water molecules (see Figure 5). On the other hand, **5** forms discrete assemblies of two squaramides and two disquarate rings establishing two different π – π stacking interactions between them, with a centroid—centroid distance 3.95 Å for the squaramide-squarate and 3.63 Å for squaramide—squaramide interactions. Strong charge-assisted NH…O interactions between both kind of rings are also established.

Squarate dianions are bridged with disquaramide molecules via strong H-bonds with water molecules.

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In compound 1, the squarate monoanions form infinite chains by means of O···H–O interactions as previously reported²⁹ that are interconnected through parallel displaced $\pi-\pi$ interactions with a centroid–centroid distance of 3.71 Å. CH– π interactions between aromatic hydrogens and monosquarate ring are also observed with a centroid–aromatic hydrogen distance of 3.39 Å (see Figure 6). In this case water molecules establish strong H-bonds simultaneously with both monoanions and benzilammonium cations.

Similarly, in compound 4 infinite chains are also formed (see Figure 7); however the donor-acceptor hydrogen bonding groups are in a less frequent³⁰ relative position 1,3 than the 1,2 position in compound 1 (see Figure 6b). In this compound the stacked four-membered rings display a centroid-centroid distance of 3.33 Å, and strong H-bonds are formed between phenol and squarate groups.

In compound 3 we observe two different $C-H/\pi$ interactions (centroid-alkyl hydrogen distances of 3.32 and 3.40 Å, respectively) and a strong H-bond between the anionic oxygen atom and the protonated amine; however, no $\pi-\pi$ stacking interactions are established (see Figure 8).

Finally, in compound 6, stacked dimers of the monoanion with a centroid–centroid distance of 3.44 Å are formed. Interestingly, the usual self-complementary squaramide/ squaramide interaction through H-bonding is formed in a non-coplanar fashion (see Figure 9).

Figure 6. Crystal structure of 1 showing centroid-centroid distance (a) and H-bonding chains (b) (water molecules not shown).



Figure 7. Crystal structure of 4 showing centroid-centroid distance (a) and H-bonding chains (b).



Figure 8. Crystal structure of 3 showing centroid-alkyl hydrogen distances.

We have evaluated theoretically the trimers shown in Figure 10 that are used as models for the H-bonded infinite



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Figure 9. Crystal structure of **6** showing centroid–centroid distances (water molecules not shown).

chains formed by the squarate monoanions in compounds 1 and 4. It can be observed that the central squarate presents a NICS value of -5.3 ppm in the model of 1 and -5.7 ppm in the model of 4. The NICS value (see Table 1) for compound 14 (squarate monoanion) is -4.8 ppm, indicating that the formation of the infinite chain increases the aromaticity of the ring and the ability to establish $\pi - \pi$ interactions, as corroborated by the solid state architecture of both compounds. We have also analyzed the NICS value in a model of compounds 3 and 6, where the amidosquarate anion forms a strong H-bond with the ammonium counterion and concurrently establishes a C-H/ π interaction. The NICS value slightly increases from -5.4 to -5.6 ppm upon formation of the hydrogen bond in agreement with previous results. In order to validate the models used for 3 and 6, we have also performed calculations using the solid state geometries of these salts and evaluated the NICS(0.5) values in the absence and presence of the counterion (see Figure 10, right). The results using the crystallographic coordinates also indicate a significant increase in the aromatic character of the ring if the countercation is included in the calculation, thus confirming the strong influence of the ammonium cations on the aromaticity of the ring in the X-ray structures.



Figure 10. M06-2X/6-311+G* optimized structures of several theoretical models and X-ray structures of compounds 3 and 6. The NICS values (ppm) of some four-membered rings are indicated.

4. CONCLUSIONS

In this manuscript, the aromatic character of the fourmembered ring in squaric acid derivatives and, principally, how it changes when it participates in noncovalent interactions have been studied theoretically using the nucleus independent chemical shift (NICS). Moreover, the aromaticity in these rings has been also studied using an unprecedented criterion, which is the analysis of the noncovalent interactions involving the ring in the solid state that has been performed using the Cambridge Structural Database. Apart from confirming the previously observed ability of the four-membered ring to participate in π -stacking interactions, it should be emphasized the significant number of structures where the ring participated in ion- π and $C-H/\pi$ interactions that has not been previously analyzed in detail. Moreover, several squaric acid derivatives have been synthesized and characterized by single crystal X-ray diffraction analyses to further analyze this topic and confirm the ability of the squaric acid derivatives to establish hydrogen bonds and $\pi - \pi$ stacking interactions in the solid state.

ASSOCIATED CONTENT

Supporting Information

Experimental characterization and X-ray crystallographic information files (CIF) of the synthesized squaric acid derivatives are available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Korkmaz, U.; Bulut, A. J. Mol. Struct. 2013, 1050, 61–68.
(b) Korkmaz, U.; Uçar, I.; Bulut, A.; Büyükgüngör, O. Struct. Chem.
2011, 22, 1249–1259. (c) Frontera, A.; Deyà, P. M.; Quiñonero, D.; Garau, C.; Ballester, P.; Costa, A. Chem.—Eur. J. 2002, 8, 433–438.

(d) von Ragué Schleyer, P.; Najafian, K.; Kiran, B.; Jiao, H. J. Org. Chem. 2000, 65, 426–431 and references cited therein.

(2) West, R.; Niu, H.-Y.; Powell, D. L.; Evans, M. V. J. Am. Chem. Soc. 1960, 82, 6240.

(3) (a) Aihara, J. J. Am. Chem. Soc. 1981, 103, 1633. (b) Jug, K. J. Org. Chem. 1983, 48, 1344.

(4) Semmingsen, D.; Groth, P. J. Am. Chem. Soc. 1987, 109, 7238.

(5) (a) Sun, W.; Hong, L.; Zhu, G.; Wang, Z.; Wei, X.; Ni, J.; Wang, R. Org. Lett. 2014, 16, 544. (b) Wang, X.-B.; Li, T.-Z.; Sha, F.; Wu, X.-Y. Eur. J. Org. Chem. 2014, 739. (c) Kumar, V.; Mukherjee, S. Chem. Commun. 2013, 49, 11203–11205. (d) Yang, K. S.; Nibbs, A. E.; Turkmen, Y. E.; Rawal, V. H. J. Am. Chem. Soc. 2013, 135, 16050–16053. (e) Kasaplar, P.; Rodriguez-Escrich, C.; Pericas, M. A. Org. Lett. 2013, 15, 3498–3501. (f) Kasaplar, P.; Riente, P.; Hartmann, C.; Pericas, M. A. Adv. Synt. Catal. 2012, 354, 2905–2910.

(6) (a) Elmes, R. B. P.; Turner, P.; Jolliffe, K. A. Org. Lett. 2013, 15, 5638–5641. (b) Bera, K.; Namboothiri, I. N. N. Chem. Commun. 2013, 49, 10632–10634. (c) Jin, C.; Zhang, M.; Wu, L.; Guan, Ya.; Pan, Y.; Jiang, J.; Lin, C.; Wang, L. Chem. Commun. 2013, 49, 2025–2027. (d) Lopez, C.; Sanna, E.; Carreras, L.; Vega, M.; Rotger, C.; Costa, A. Chem.—Asian J. 2013, 8, 84–87. (e) Soberats, B.; Martinez, L.; Sanna, E.; Sampedro, A.; Rotger, C.; Costa, A. Chem.—Eur. J. 2012, 18, 7533–7542. (f) Amendola, V.; Fabbrizzi, L.; Mosca, L.; Schmidtchen, F.-P. Chem.—Eur. J. 2011, 17, 5972.

(7) Busschaert, N.; Kirby, I. L.; Young, S.; Coles, S. J.; Horton, P. N.; Light, M. E.; Gale, P. A. Angew. Chem., Int. Ed. 2012, 51, 4426–4430.
(8) (a) Portell, A.; Prohens, R. Cryst. Growth Des. 2014, 14, 397.
(b) Portell, A.; Alcobe, X.; Lawson Daku, L. M.; Cerny, R.; Prohens, R. Powder Diffraction 2013, 28, S470–S480. (c) Portell, A.; Font-Bardia, M.; Prohens, R. Cryst. Growth Des. 2013, 13, 4200–4203. (d) Prohens, R.; Portell, A.; Alcobe, X. Cryst. Growth Des. 2012, 12, 4548–4553.

(9) (a) Kolev, T.; Seidel, R. W.; Mayer-Figge, H.; Spiteller, M.; Sheldrick, W. S.; Koleva, B. B. Spectrochim. Acta 2009, A72, 502-509.
(b) Kolev, T.; Mayer-Figge, H.; Seidel, R. W.; Sheldrick, W. S.; Spiteller, M.; Koleva, B. B. J. Mol. Struct. 2009, 919, 246-254.
(c) Ivanova, B.; Spiteller, M. Spectrochim. Acta 2010, A77, 849-855.
(d) Georgopoulos, S. L.; Edwards, H. G. M.; De Oliveira, L. F. C. Spectrochim. Acta 2013, A111, 54-61.

(10) (a) Qin, C.; Numata, Y.; Zhang, S.; Yang, X.; Islam, A.; Zhang, K.; Chen, H.; Han, L. *Adv. Funct. Mater.* **2014**, DOI: 10.1002/ adfm.201303769. (b) Dega-Szafran, Z.; Dutkiewicz, G.; Kosturkiewicz, *Z. J. Mol. Struct.* **2012**, *1029*, 28–34. (c) Barczyński, P.; Dega-Szafran, Z.; Katrusiak, A.; Szafran, M. J. *Mol. Struct.* **2012**, *1018*, 28–34.

(11) Braga, D.; Bazzi, C.; Grepioni, F.; Novoa, J. J. New J. Chem. 1999, 23, 577–579.

(12) Stéfanos L. Georgopoulos, S. L.; Diniz, R.; Yoshida, M. I.; Speziali, N. L.; Dos Santos, N. F.; Junqueira, G. M. A.; de Oliveira, L. F. C. J. Mol. Struct. **2006**, 794, 63–70.

(13) Meyer, E. A.; Castellano, R. K.; Diederich, F. Angew. Chem., Int. Ed. 2003, 42, 1210–1250.

(14) (a) Hunter, C. A.; Sanders, J. K. M. J. Am. Chem. Soc. 1990, 112, 5525–5534. (b) Burley, S. K.; Petsko, G. A. Science 1985, 229, 23–28.
(c) Kim, K. S.; Tarakeshwar, P.; Lee, J. Y. Chem. Rev. 2000, 100, 4145–4185.

(15) (a) Ma, J. C.; Dougherty, D. A. Chem. Rev. **1997**, *97*, 1303–1324. (b) Kim, K. S.; Lee, J. Y.; Lee, S. J.; Ha, T.-K.; Kim, D. H. J. Am. Chem. Soc. **1994**, *116*, 7399–7400. (c) Schottel, B. L.; Chifotides, H. T.; Dunbar, K. R. Chem. Soc. Rev. **2008**, *37*, 68–83. (d) Hay, B. P.; Bryantsev, V. S. Chem. Commun. **2008**, 2417–2428. (e) Frontera, A.; Gamez, P.; Mascal, M.; Mooibroek, T. J.; Reedijk, J. Angew. Chem., Int. Ed. **2011**, *50*, 9564–9583.

(16) (a) Nishio, M.; Hirota, M.; Umezawa, Y. In The $C-H/\pi$ Interaction: Evidence, Nature, Consequences; Wiley-VCH: New York, 1998. (b) Nishio, M. CrystEngComm **2004**, 6, 130–156. (c) Seth, S. K.; Sarkar, D.; Roy, A.; Kar, T. CrystEngComm **2011**, 13, 6728–6741.

(17) Allen, F. H. Acta Crystallogr. 2002, B58, 380-388.

(18) von Ragué Schleyer, P.; Maerker, C.; Dransfeld, A.; Jiao, H.; van Eikema Hommes, N. J. R. J. Am. Chem. Soc. **1996**, 118, 6317.

(19) SADABS; Bruker AXS: Madison, Wisconsin, USA, 2004. SAINT, Software Users Guide, Version 6.0; Bruker Analytical X-ray Systems: Madison, WI, 1999. Sheldrick, G. M. SADABS v2.03: Area-Detector Absorption Correction; University of Göttingen: Germany, 1999. Saint +, Version 7.60A and SADABS, V. 2008-1; Bruker AXS: Madison, WI, 2008.

(20) Sheldrick, G. M. Acta Crystallogr. 2008, A64, 112-122.

(21) Spek, A. L. J. Appl. Crystallogr. 2003, 36, 7-13.

(22) Farrugia, L. J. J. Appl. Crystallogr. 1999, 32, 837-838.

(23) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision D.01; Gaussian, Inc.: Wallingford CT, 2009.

(24) Wolinski, K.; Hinto, J. F.; Pulay, P. J. Am. Chem. Soc. 1990, 112, 8251.

(25) Jemmis, E. D.; Kiran, B. Inorg. Chem. 1998, 37, 2110.

(26) Julg, A.; Francois, P. Theor. Chim. Acta. 1967, 7, 249.

(27) (a) Bird, C. W. Tetrahedron 1985, 41, 1409. (b) Bird, C. W. Tetrahedron 1986, 42, 89.

(28) Jug, K. J. Org. Chem. 1983, 48, 1344.

(29) Braga, D.; Grepioni, F. Chem. Commun. 1998, 911.

(30) Bertolasi, V.; Gilli, P.; Ferretti, V.; Gilli, G. Acta Crystallogr. 2001, B57, 591.