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Imidazolium-Based Dicationic Cyclophanes. Solid-State Aggregates with Unconventional $(C—H)^+\cdots Cl^-$ Hydrogen Bonding Revealed by X-ray Diffraction

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The first single-crystal X-ray crystallographic diffraction analysis of a dicationic heterophane showed a non-classic $(C—H)^+\cdots Cl^-$ hydrogen bond between the imidazolium rings and halide anions and the formation of unconventional charged assisted hydrogen bonds, which were the non-covalent forces driving the anion interactions shown by the dications 4·2X. Here is reported the halide-templated controlled synthesis and chemical response in basic media of 4·2X. Their structural properties were examined at the gas phase by electrospray ionization mass spectrometry in the negative-ion mode and in the solid-state by X-ray crystallography. Thus, the negative-ion ESI-MS response showed that the formation of non-covalent self-aggregates of macrocyclic dications is a consequence of hydrogen-bonded complexes with halide anions. Notably, X-ray diffraction of dication $4a·2Cl·2H_2O$ provides evidence for the H-bonding network, which has a crucial role in crystal packing. The solid-state aggregates showed that chloride anions and water molecules formed channels among dications $4a^+$.

Keywords: Charged cyclophanes; Hydrogen bonds; Anion recognition; Templated synthesis; Electrospray mass spectrometry; X-ray diffraction crystallography

INTRODUCTION

Anion recognition chemistry includes current developments on anion-templated synthesis and selective artificial anion receptors, especially positively charged systems [1–11]. For these cationic or oligocationic hosts, the driving forces for binding are electrostatic interactions or combinations with hydrogen bonding forces [12–16], i.e. N-H···anion bonds [1,17–19] and a novel type of charged hydrogen bonds $(C—H)^+\cdots$anion [10,17,18,20–25,29].

In the context of our current research on imidazolium-based frameworks cyclophanes **1·2X** and **2** have been studied [27] together with dicationic pincers **3·2X** (Fig. 1) [28]. Quaternary imidazolium units were selected due to their recognized chemical stability [20,26–33]. Dicationic $[1_4]$imidazoliophanes **4·2X** are simple prototypes for intermolecular interactions driven by unconventional $(C—H)^+\cdots X$ hydrogen bond. The significance of the hydrogen bonds in controlling the anion binding was observed in solution by ^1H NMR in polar solvents [29]. The '3 + 1' macrocyclization process is template-controlled by chloride anions [31,32] (Fig. 1). Dication **$4a·2Cl·2H_2O$** was the first reported example of a non-classical $(C—H)^+\cdots Cl^-$ hydrogen bond between the C—H of the imidazolium rings and chloride anions in the solid state [20]. From dicationic prototypes **4·2X**, a variety of imidazolium-linked scaffolds were investigated for anion binding driven by this new type of $(C—H)^+\cdots$halide hydrogen bond.

The present paper deals with significant aspects of simple imidazolium-based cyclophanes **4·2X**, such as halide template-directed '3 + 1' synthesis and the chemical response in basic media. The structural properties are discussed with the data gained in the solid state (X-ray crystallography) and the gas phase (electrospray ionization mass spectrometry in the negative-ion mode).

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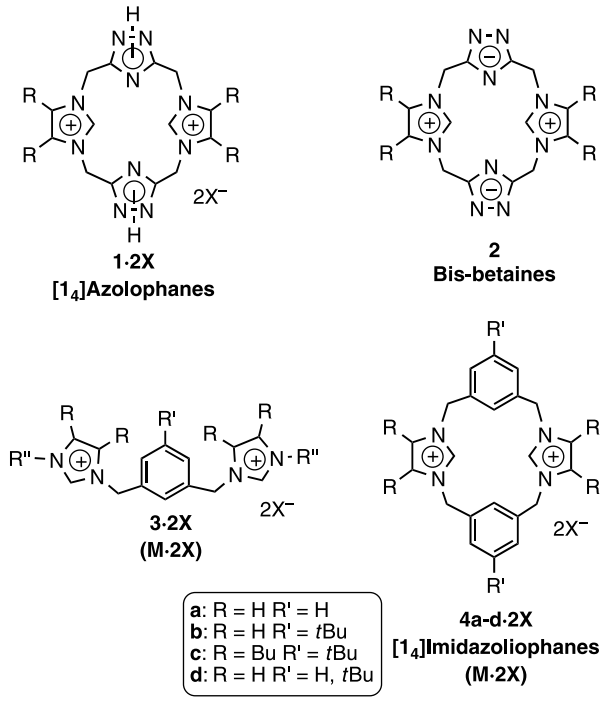


FIGURE 1 Imidazolium molecular motifs in [1$_4$]*meta*heterophane frameworks.

RESULTS AND DISCUSSION

The authors have already reported the results obtained for halide template-directed synthesis: the templated-controlled '3 + 1' macrocyclization reaction in the presence of chloride anions. When 5 molar equiv of TBA·Cl were added to the reaction, the yield improved to 83% for model dication **4a·2Cl**; competitive experiments indicate the relevance of both the condensation step and the chloride-templated closure step [31,32]. However, the '3 + 1' stepwise synthesis based on the coupling of protophane **5c** with 1,3-bis(bromomethyl)-5-*tert*-butylbenzene **6** was not anion-dependent and the macrocyclization reaction was governed by stereoelectronic control due to the *t*-butyl group in protophane **5c** (Scheme 1).

At this point, competitive experiments were set up between protophanes **5a** and **5c** and 1,3-bis(bromomethyl)-*tert*-butylbenzene **6** in both the absence and the presence of **TBA·Br** (Scheme 2). The ratio of the macrocycles **4c·2Br** and **4d·2Br** formed from the ^{1}H NMR analysis is shown in Scheme 2 and the results support the idea of conformationally biasing assistance of the reaction leading to **4c·2Br**, not being anion-controlled. Similar behavior was observed in the '3 + 1' approach leading to the *N*-benzhydryl macrocyclic dications, precursors of azolophanes **1·2X** [27]. The enhancement induced by bromide anions for the formation of **4d·2Br** suggests a clear anion-template influence for this macrocycle.

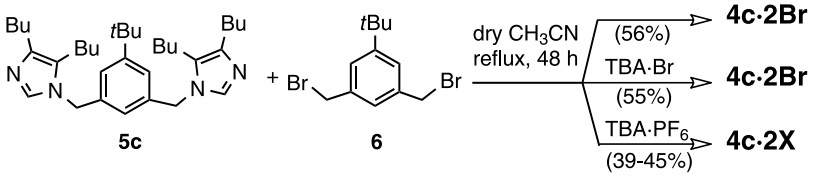
Transformation of model dications **4a–c·2X** into the corresponding ureophanes was examined, since imidazolium subunit(s) on a variety of imidazolium-linked azolate betaines and azolyl salts, cyclophanes and pincers, e.g. **1·2X** to **4·2X** have proved stable and no formation of byproducts through generation of imidazol-2-ylidenes (NHC) has been detected to date [26–30]. From literature reports on benzimidazole pseudobases [34], preparation of imidazol-2-ylidenes [35] and transformations under basic conditions of 2,2′-diimidazolium [36] and 2,2′-dibenzimidazolium salts located in either open-chain or macrocyclic systems [37,38], four methods were selected: Method A [34] KOH-H_2O/MeCN; Method B [35] (i) *t*-BuOK/THF, (ii) *air*; Method C [37] (i) 1,1′,3,3′-tetramethylguanidine/MeCN-DMF, (ii) *air*; Method D [37,38] (i) HNa/MeCN, (ii) *air* (Scheme 3).

The chemical response of the *imidazolium rings* under basic reaction of dications **4a–c·2X** showed that in no instance was formation of products, through generation of carbenes such as ureophanes, detected (Scheme 3). Products of alteration or decomposition were observed by ^{1}H NMR and TLC, and these were not further investigated.

STRUCTURAL STUDIES

Electrospray ionisation mass spectrometry is a consolidated as a innovative analytical technique, which normally involves the use of positive-ion ESI experiments [39]. Recent negative-ion ESI-MS studies expand the current capacities of the negative-ion mode [40–43]. Positive-ion electrospray ionization mass spectrometry was used for characterizing imidazoliun-based frameworks, with prime examples derived from [1$_4$]*meta*heterophanes **1·2X** (**MH$_2$·2X**), **2** and **4·2X** (**M·2X**) [27,33,44,45].

In the negative-ion mode ESI-MS experiments azolophanes **1·2X** were examined [44] together with a set of [{imidazolio}methyl] azolate betaines **B** and



SCHEME 1 "3 + 1" Convergent synthesis of **4c·2Br**.

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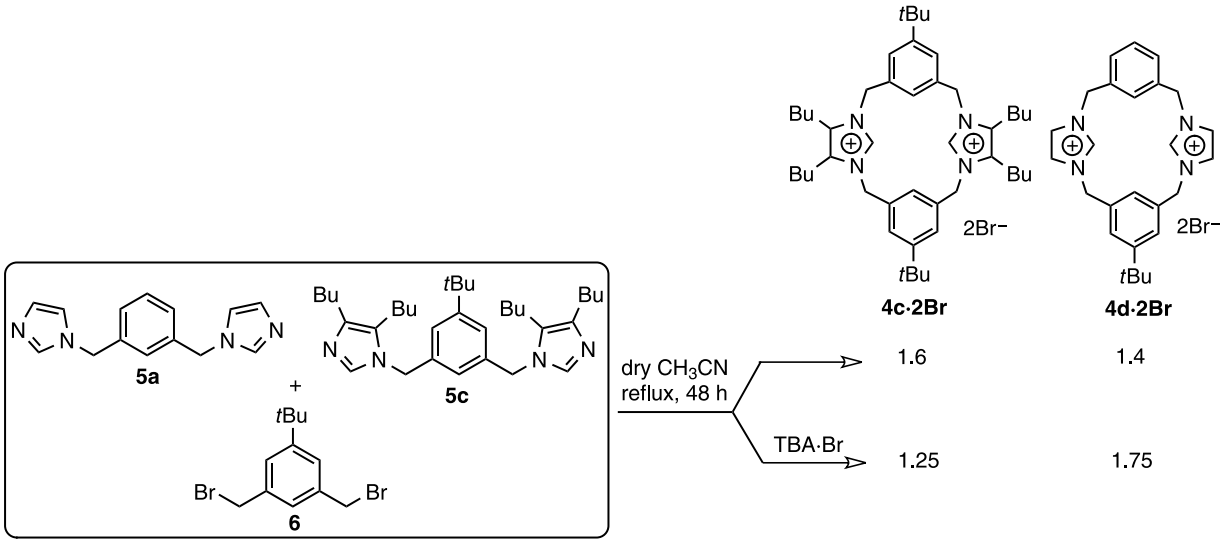

SCHEME 2 Competitive experiments combining trinuclear protophanes **5a** and **5c** and bis(bromomethyl)-*tert*-butylbenzene **6** to build [1_4]imidazoliophanes **4c·2Br** and **4d·2Br**, showing the ratio of the macrocycles formed.

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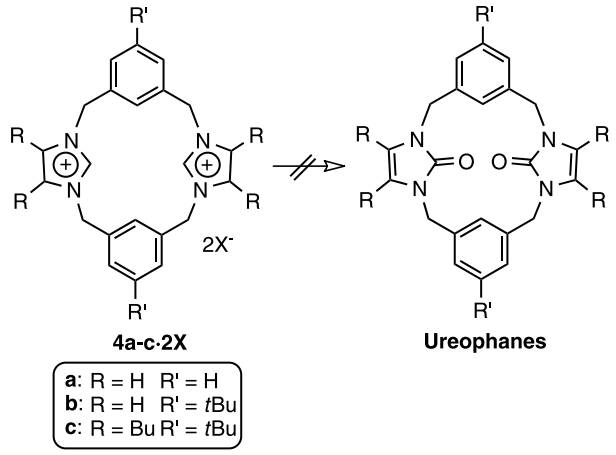

Experiment 1, **Method A**

4a·2PF6 ⟶ Alteration or decomposition products

Experiment 2, **Method B**

4b·2PF6 ⟶ Alteration or decomposition products

Experiment 3, **Method C**

4a·2Cl ⟶ **4a·2Cl**

Experiment 4, **Method D**

4a·2Cl ⟶ Alteration or decomposition products

SCHEME 3 Chemical response of dications **4a–c·2X**. *Reagents and Conditions*. Method A: (i) 10 eq KOH-H_2O/MeCN, rt 3h; (ii) reflux 3 days. Method B: (i) Sublimate *t*-BuOK/THF/N_2, 5h, (ii) *air*, reflux 16h. Method C: (i) 1,1′,3,3′-tetramethylguanidine/dry MeCN-DMF, (ii) *air*, rt 24h, 80°C 21h. Method D: (i) HNa/dry MeCN, Ar, rt 4h (ii) *air*, rt 18h.

their corresponding salts **BH·X** [30]. The negative-ion ESI responses displayed peaks attributable to non-covalent self-aggregates: further study to confirm this was restricted to instrumental limitation. Under the same experimental conditions [30,44], dications **4a,c,d·2Cl** (**M·2Cl**) displayed different ionic species due to proton-mediated ion-molecule reactions and non-covalent interactions, which produced several polymolecular self-assemblies with chloride anions and the most characteristic species corresponding to the singly charged ions $[M + 3Cl]^-$, $[2M + 5Cl]^-$ and $[3M + 7Cl]^-$. Use of a different mass spectrometer led to similar results: the negative-ion response between dications **4a·2Cl** and **4a·2PF$_6$** revealed that in **4a·2Cl** (**M·2Cl**) a variety of self-assembled aggregates were produced, whereas, on changing the counteranion, dication **4a·2PF$_6$** (**M·2PF$_6$**) displayed a peak at *m/z* 145 from a PF_6^- anion due to the lack of hydrogen bonding between the hexafluorophosphate counteranions and dications $(\mathbf{4a})^{2+}$ (Fig. 2). Moreover, macrocycle **4b·2Cl** gave clean spectra and the base peak corresponds to the single charged ion $[M + 3Cl]^-$ (Fig. 3). The negative-ion ESI-MS response of dications **4a·2Cl**, **4a·2PF$_6$** and **4b·2Cl** shows that the formation of non-covalent self-aggregates in the gas phase is a consequence of hydrogen-bonded complexes with chloride anions.

^{1}H NMR spectroscopy studies indicated the importance of imidazolium units as motifs for anion recognition of **4·2X** and complexation studies with the model dication **4c·2PF$_6$** using several tetrabutylammonium salts (TAB·X) in polar solvents (CD_3CN and DMSO-d_6 were performed. The best association constant (*Ka*) was observed for the complex of **4c·2PF$_6$** and TBA·CH_3CO_2 in DMSO-d_6 [29].

One of the relevant aspects of model imidazolium-based cyclophanes **4·2X** is the solid-state aggregates

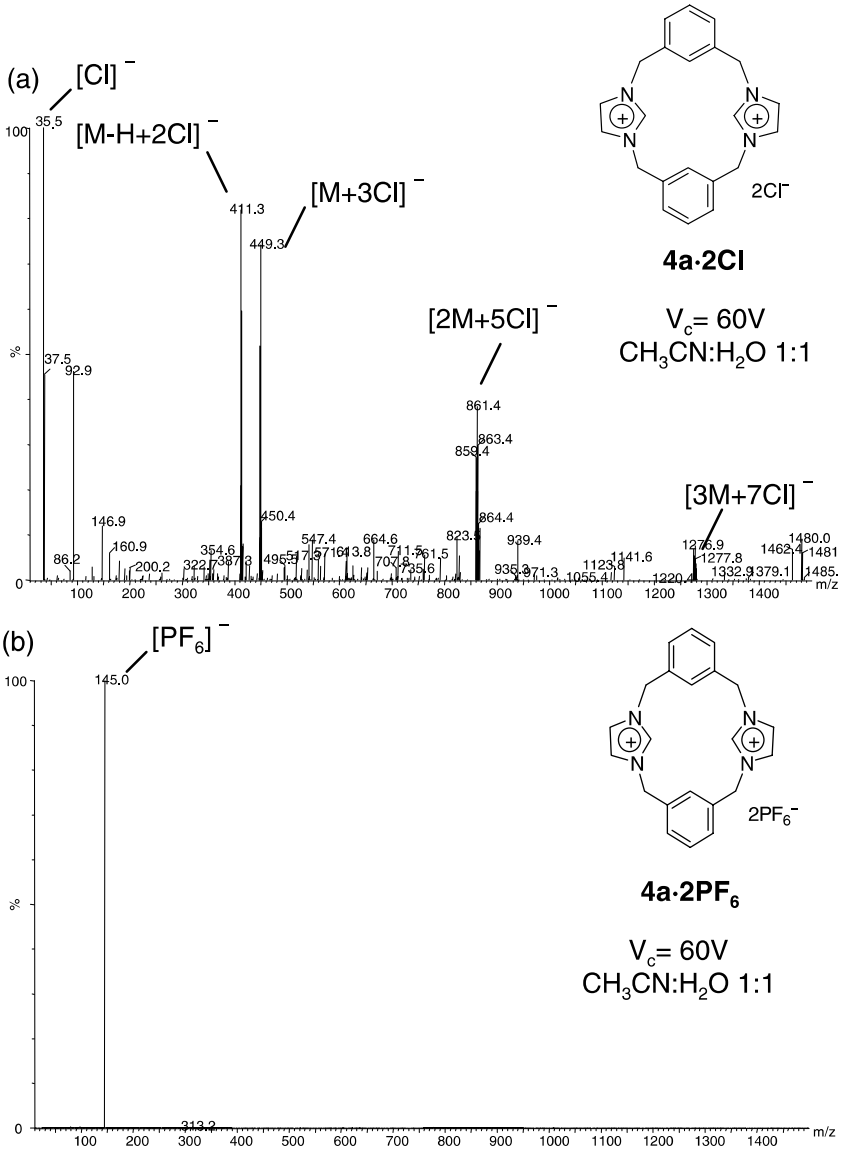

FIGURE 2 Negative-ion ESI-MS of **4a·2Cl** and **4a·2PF$_6$**.

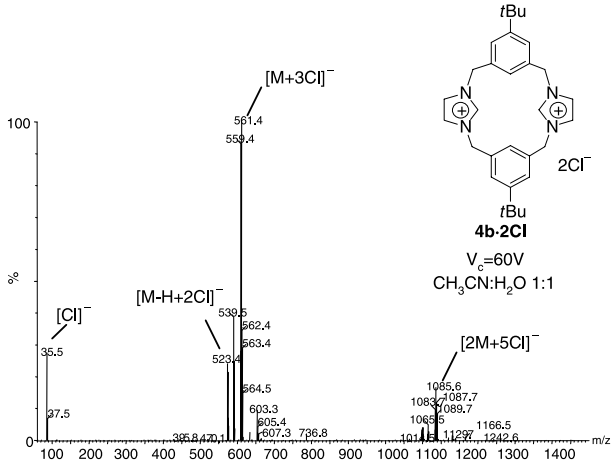

FIGURE 3 Negative ion ESI-MS of **4b·2Cl**.

with unconventional C—H···Cl$^-$ hydrogen bonds observed by X-ray crystallography. Among the whole palette of hydrogen bonds [17], the first non-classic (C—H)$^+$···Cl$^-$ hydrogen bonds between quaternary imidazolium rings and the counteranions were observed for dicationic imidazoliophane **4a·2Cl·2H$_2$O** in the solid state [20,45,46]. Thereafter, a variety of quaternary imidazolium-linked frameworks were reported for anion recognition driven by (C-H)$^+$···X$^-$ hydrogen bonds [10,17,18,21–25]. The imidazolium units represent the main structural motifs for intermolecular interactions driven by hydrogen bonds in which the chloride counteranions have been noncovalently bound to the dicationic framework and, in addition, the C—H···O hydrogen bonds with water play a role in governing the conformations of the solid-state aggregates. In this connection, Steiner has pointed out that hydrogen

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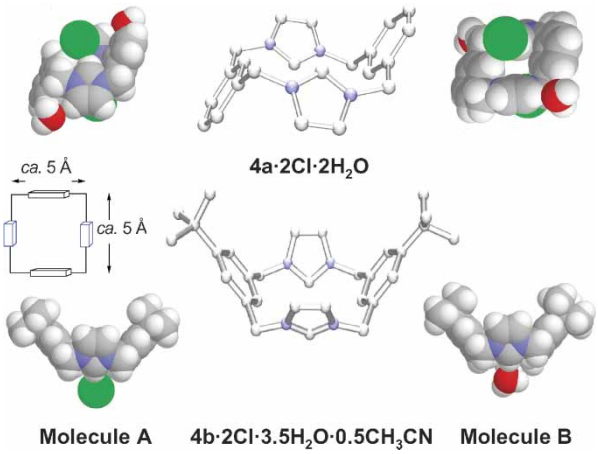

FIGURE 4 Molecular shape of dications **4a·2Cl·2H$_2$O** and **4b·2Cl·3.5H$_2$O·0.5CH$_3$CN**.

bonds from C—H groups to halides ions are only rarely discussed in the literature, even though stronger C—H donors had CH···Hal$^-$ distributions of a similar shape as O/N-H donors had and can be analyzed in the same way. As for (NN)Csp^2-H fragment, the mean C—H··· Cl$^-$ distance of 2.54 Å was found [19]. Within NH···Hal$^-$ bonds, it should be mentioned the calix[4]pyrroles reported by Sessler and co-workers as chloride anion receptors [19,48] and also showing imidazolium inclusion in both the confused and regular forms [17,18].

From the present single-crystal X-ray diffraction analyses of two macrocyclic dications [46], relevant aspects should be mentioned. Their molecular shapes are shown in Fig. 4: Dication **4a** assumes a chair-like conformation in contrast with the cone-like arrangement observed for **4b**. However, both dications **4a** and **4b** have similar molecular cavity dimensions, a square of 5 Å side**,** close to those observed for macrocyclic bis-betaines **2** and related systems [27].

For dication **4a·2Cl·2H$_2$O**, the non-covalent interactions with the chloride ions are based on multicentered (C—H)$^+$···Cl bonds established between the Cl$^-$ ion with the aromatic hydrogen bonds on the *m*-xylyl spacer and the acidic hydrogen atom of the imidazolium ring which is the shortest hydrogen bond interaction (2.54(2)Å, $\theta = 157(1)°$) consistent with the complexing ability of chloride anions; there are, in addition, weak interactions with water. The chloride anions occupy an outer position above and below the main plain defined by the methylene spacer groups (see later). For the X-ray diffraction analysis of **4b·2Cl·3.5H$_2$O·0.5CH$_3$CN**, many different crystals were used but crystals deteriorated so fast that, in consequence, the final refinement values were inappropriate for a detailed discussion of noncovalent interactions.

For the X-ray analysis of **4a·2Cl·2H$_2$O**, a perspective molecular diagram of dication **4a** is shown in Fig. 5 and selected nonbonding parameters related

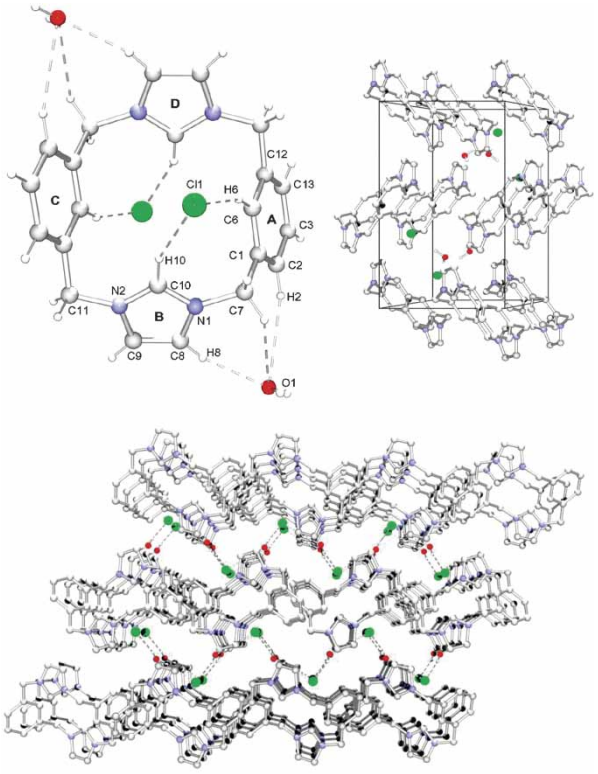

FIGURE 5 Imidazolium-based dication **4a·2Cl·2H$_2$O**: Molecular structure showing non-classic (C-H)$^+$···Cl$^-$ hydrogen bonds; crystal packing showing a channel disposition of the chloride anions and the water molecules among the dicationic framework.

to the molecular shape as well as the H-bonding interactions are listed in Tables I and II. Since the molecule is a centrosymmetric structure, the experimental asymmetric unit contains a half molecule of dication **4a** and one chloride anion and one water molecule, matched by an equivalent subunit generated by symmetry. The atom numbering diagram used for the X-ray data [47] is not the same as the IUPAC numbering system for the NMR data. Significant nonbonding distances [Å] concern both the (C—H)$^+$···Cl$^-$ interactions and the molecular shape adopted by the dicationic framework that may be described by the macrocyclic cavity dimensions, the spatial arrangement within the four rings which constitute the walls of the dicationic framework and their inclination with respect to the reference plane. The weighted least-squares reference plane defined by C7, C11, C7a, and C11a methylene carbon atoms are C7·····C1 = 4.954(3)Å and C(7)·····C(11a) = 4.996(3)Å, with the cavity dimensions being a square of ca. 5 Å side (Table I).

A relevant point relating to the structural shape of dication **4a** is the position of the corresponding counteranions within the molecule: the two chloride anions are located above and below the reference plain (plane E). The chloride counteranion is bicentered between the acidic hydrogen atom on the imidazolium ring, i.e. H10, which is the shortest

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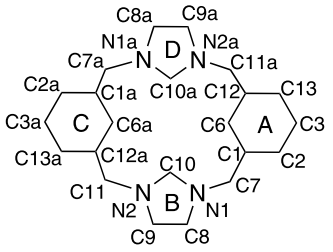
TABLE I Selected X-ray crystallographic data for macrocycle **4a·2Cl·2H$_2$O**.[a,b]



C7...C11 Å[c]	4.964	Cl1...A Å[f]	5.151	A–E [°][d]	117.6	A...C Å[e]	6.781
C11...C7a Å[c]	4.996	Cl1...B Å[f]	4.558	B–E [°][d]	50.8	A...B Å[e]	4.578
C7...C7a Å[c]	6.571	Cl1...C Å[f]	4.247	A–B [°][d]	110.3	A...D Å[e]	4.604
C11...C11a Å[c]	7.486	Cl1...D Å[f]	4.468			B...D Å[e]	6.192
C3...C3a Å[c]	9.115						
C6...C6a Å[c]	4.964						
C10...C10a Å[c]	4.628						

[a] CCDC deposition codes GOCYUS (102466) and GOCZAZ (102467). [b] X-ray atom numbering diagram. [c] Most relevant intermolecular distances. [d] Dihedral angles between the weighted least-squares planes. Plane A: C1-C2-C3-C13-C12-C6, Plane B: N1-C10-N2-C9-C8, Plane C: C1a-C2a-C3a-C13a-C12a-C6a, Plane D: N1a-C10a-N2a-C9a-C8a, Plane E: C7-C11-C7a-C11a. [e] Distance between the indicated planes. [f] Distance between the chloride anion and the indicated plane.

TABLE II Hydrogen-bonding geometry [Å or °]

D–H	d(D–H)	d(H...A)	< DHA	d(D...A)	A
C10–H10	0.976	2.538	156.7	3.456	Cl1
C6–H6	1.005	2.811	162.3	3.781	Cl1
C8–H8	0.973	2.225	158.9	3.153	O1
C2–H2	0.972	2.751	154.4	3.652	O1
C7–H7	0.990	2.826	135.1	3.596	O1

hydrogen bond interaction and a *m*-xylyl hydrogen atom, i.e. H6. The H···Cl$^-$ distances (Å) and (C—H)$^+$··· Cl$^-$ angles (°) are H6···Cl1 = 2.81(2)Å, angle 162.(1)° and H10···Cl1 = 2.54(2)Å, angle 157.(1)°; for the *weak* interactions with water, the C—H···O hydrogen bonding connects the trifurcated acceptor O1 with the cationic ring, as shown in Fig. 5 (Tables I and II).

The unit cell packing of dication **4a·2Cl·2H$_2$O** contains two independent cations together with their associated anions and four water molecules located in a channel fashion. The hydrogen bond networks help to sustain the crystal lattice and forming channels that extend through the crystal: the chloride anions and the water molecules are located among the dicationic imidazolium-based framework in a channel disposition, as shown in Figs. 5 and 6. On examination of the crystal packing, intermolecular π-π stacking interactions between the *m*-xylyl aromatic rings also help sustain the crystal lattice: the rings are positioned at an interplanar distance of 3.59 Å and engaged in a parallel displaced pattern, whereas the interplanar separations between the imidazolium rings are in the range of 5 Å to 8.5 Å.

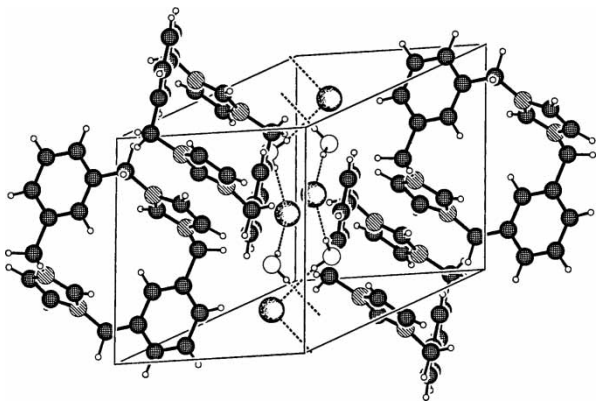


FIGURE 6 Crystal packing of dication **4a·2Cl·2H$_2$O**.

For the X-ray analysis of **4b·2Cl·3.5H$_2$O·0.5CH$_3$CN**, several sets of data were measured and many different crystals, but as crystals deteriorated fast, it was difficult to find reliable solutions for the ordered fragments. The disordered Cl$^-$ anions and solvent atoms were unidentifiable in most of the collected data. In the end, a physically and chemically acceptable solution was reached, refined to a reasonable point that took into consideration both the presence of structural disorder and rapid crystal deterioration; the best recorded data were then refined to $R_1 = 0.1032$ and $wR_2 = 0.2512$. The asymmetric unit contains two crystallographically independent dications (**4b**), molecule **A** and molecule **B**, their four associated chloride anions together with seven water molecules and one solvent molecule (acetonitrile) (Fig. 7). Molecule **A** tended to form a three-centered hydrogen bond with one of the chlorine counteranions Cl2 and molecule **B** preferred to hydrogen bond to an included water molecule. Although both **A** and **B** molecules displayed uncommon multi-centered acceptor hydrogen bond arrangements mainly due to the presence of hydrogen donor-rich imidazolium rings, these similar complexing patterns show how sensitive the (C—H)$^+$···*Acceptor* hydrogen bond is to structural changes within the imidazolium-based framework.

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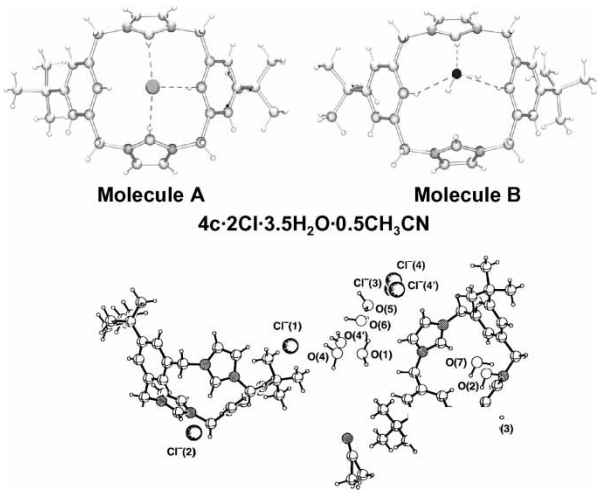

FIGURE 7 Dicationic macrocycle **4b·2Cl·3.5H_2O·0.5CH_3CN**.

In relation with the structural effect, it should be mentioned that Baker *et al.* [49,50] have reported a tricationic imidazolium-based cyclophane formed by two mesytilene rings triple-bridged by three imidazolium rings **M·3Br·2H_2O** and that X-ray diffraction analysis revealed that in each molecule the three bromide anions formed a hydrogen bond with two water molecules and no anionic species are trapped within the imidazoliophane.

CONCLUSIONS

Dicationic [1_4]imidazoliophanes **4·2X** are simple prototypes for examination of the intermolecular interactions driven by hydrogen bonds, in which the halide counteranion, i.e. X = Cl, was non-covalently bound to the macrocyclic framework and, in addition, the ability to bind halide anions was exploited during their synthesis. The chemical responses of *imidazolium* rings for dications **4a-c·2X** in basic media were examined and the putative formation of products through generation of imidazol-2-ylidenes (NHC), e.g. ureophanes, was not detected. Their distinctive structural facets were examined in the gas phase by electrospray ionization mass spectrometry in negative-mode experiments and in the solid-state by X-ray crystallography of **4a·2Cl·2H_2O** and **4b·2Cl·3.5H_2O·0.5CH_3CN**.

On the whole, the simple imidazolium-based cyclophanes **4·2X** can be considered models for intermolecular anion interactions driven by hydrogen bonds since there is good parallelism between the experimental trends observed in the solid state, in the gas phase by negative-ion ESI-MS and in solution by ^{1}H NMR complexation studies. Notably, the single-crystal X-ray diffraction analysis of dication **4a·2Cl·2H_2O** typified the first example of a non-classic $(C—H)^+\cdots Cl^-$ hydrogen bond between the imidazolium rings and chloride anions —the shortest hydrogen bond interaction was H10···Cl1 (2.54 Å, θ = 157°). Efforts are currently being directed towards the use of imidazolium-linked systems for processes controlled by hydrogen bonding networks.

EXPERIMENTAL SECTION

General Methods

^{1}H NMR: Varian Gemini 200 and Varian Gemini 300 spectrometers (200 MHz and 300 MHz). NMR spectra were determined in dimethylsulfoxide-d_6 or chloroform-*d*, and chemical shifts are expressed in parts per million (δ) relative to the central peak of dimethylsulfoxide-d_6 or chloroform-*d* at 298 K. TLC was performed on Merck pre-coated 60 F_{254} silica gel plates in the solvent system methanol-ammonium chloride 2M-nitromethane (6:3:1) as developing solvent; and the spots were located with UV light and developed with a 10% aqueous solution of potassium iodide or 3% aqueous solution of hexachloroplatinic acid. When a rotary evaporator was used, the bath temperature was 25°C. In general, the compounds were dried overnight at 25°C in a vacuum oven.

Materials

1,1′,3,3′-Tetramethylguanidine and tetrabutylammonium salts were purchased from commercial sources. Macrocycles **4a-c·2X** [29,45], protophanes **5a,c** [29,45], and 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**6**) [51] were prepared as described in the literature.

Macrocycle 4c·2Br. Anion Template Effect

Experiment 1

A stirred solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**6**, 0.31 g, 0.96 mmol) in dry acetonitrile (50 mL) was added dropwise to a solution of protophane **5c** (0.5 g, 0.96 mmol) in dry acetonitrile (150 mL) at 25°C under nitrogen, and the mixture was then maintained in a bath at about 85°C for 48 h (Scheme 1). The solvent was removed in a rotary evaporator, and the solid residue was triturated with dry acetone (25 mL) and filtered to give macrocycle **4c·2Br** (0.45 g, 56%) as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.90–0.97 (m, 12 H), 1.35–1.48 (m, 36 H), 2.55–2.62 (m, 8 H), 5.48 (s, 8 H), 6.42 (s, 2 H), 7.32 (s, 4 H), 10.75 (s, 2 H) ppm.

Experiment 2

A stirred solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**6**, 0.31 g, 0.96 mmol) in dry acetonitrile (50 mL) was added dropwise to a solution of protophane **5c** (0.5 g, 0.96 mmol) and 5 molar equiv of tetrabutylammonium bromide (1.5 g, 4.8 mmol)

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in dry acetonitrile (150 mL) at 25°C under nitrogen, and the mixture was then maintained in a bath at about 85°C for 48 h (Scheme 1). The solvent was removed in a rotary evaporator, and the solid residue was triturated with dry acetone (25 mL) and filtered to give macrocycle **4c·2Br** (0.44 g, 55%) as a white solid.

Experiment 3

A stirred solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**6**, 61 mg, 0.19 mmol) in dry acetonitrile (14 mL) was added dropwise to a solution of protophane **5c** (0.1 g, 0.19 mmol) and 5 molar equiv of tetrabutylammonium hexafluorophosphate (0.31 g, 0.95 mmol) in dry acetonitrile (25 mL) at 25 °C under nitrogen, and the mixture was then maintained in a bath at about 85°C for 48 h (Scheme 1). The solvent was removed in a rotary evaporator, and the solid residue was triturated with dry acetone (10 mL) and filtered to give macrocycle **4c·2X** (71 mg, 39–45%) as a white solid.

Competitive Experiments Combining Protophanes 5a and 5c and 1,3-bis(bromomethyl)-5-*tert*-butylbenzene 6

Experiment 1

A stirred solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**6**, 61 mg, 0.19 mmol) in dry acetonitrile (14 mL) was added dropwise to a solution of protophane **5a** (46 mg, 0.19 mmol) and protophane **5c** (0.1 g, 0.19 mmol) in dry acetonitrile (25 mL) at 25°C under nitrogen, and the mixture was then maintained in a bath at about 85°C for 48 h (Scheme 2). The solvent was removed in a rotary evaporator, and the solid residue was triturated with dry acetone (10 mL) and filtered. According to the ^{1}H NMR analysis, the reaction mixture composition led to the formation of macrocycles **4c·2Br**:**4d·2Br** in the proportion of 1.6:1.4. **4c·2Br** ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.67–0.72 (m, 12 H), 0.82–0.86 (m, 8 H), 1.07–1.14 (m, 8 H), 1.34 (s, 18 H), 2.21–2.26 (m, 8 H), 5.50 (s, 8 H), 6.45 (s, 2 H), 7.70 (s, 4 H), 9.40 (s, 2 H) ppm. **4d·2Br** ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.31 (s, 9 H), 5.42 (s, 4 H), 5.43 (s, 4 H), 6.72 (s, 1 H), 7.02 (s, 1 H), 7.56–7.60 (m, 5 H), 7.82 (s, 4 H), 9.36 (s, 2 H) ppm.

Experiment 2

A stirred solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**6**, 61 mg, 0.19 mmol) in dry acetonitrile (14 mL) was added dropwise to a solution of protophane **5a** (46 mg, 0.19 mmol), protophane **5c** (0.1 g, 0.19 mmol) and 5 molar equiv of tetrabutylammonium bromide (0.31 g, 0.95 mmol) in dry acetonitrile (25 mL) at 25°C under nitrogen, and the mixture was then maintained in a bath at about 85°C for 48 h (Scheme 2). The solvent was removed in a rotary evaporator, and the solid residue was triturated with dry acetone (10 mL) and filtered. According to the ^{1}H NMR analysis, the reaction mixture composition led to the formation of macrocycles **4c·2Br**:**4d·2Br** at the proportion of 1.25:1.75.

Attempted Preparation of Ureophanes

Experiment 1. Method A

A suspension of macrocycle **4a·2PF$_6$** (100 mg, 0.16 mmol) and finely powdered 85% potassium hydroxide (21 mg, 0.32 mmol) in dry acetonitrile (20 mL) was vigorously stirred at room temperature for 3 h and at reflux temperature for 3d. The suspension was cooled and filtered, and the solution was evaporated to dryness to obtain alteration or decomposition products.

Experiment 2. Method B

A solution of sublimate potassium *tert*-butoxide (121 mg, 1.08 mmol) in dry THF (20 mL) was added dropwise to a suspension of macrocycle **4b·2PF$_6$** (200 mg, 0.27 mmol) in dry THF (80 mL), under an atmosphere of nitrogen. After the reaction mixture was stirred at room temperature for 5 h, the mixture was heated at reflux temperature and dry air was bubbled through for 16 h. The resulting suspension was evaporated to dryness to obtain alteration or decomposition products.

Experiment 3. Method C

A suspension of macrocycle **4a·2Cl** (186 mg, 0.45 mmol) and 1,1′,3,3′-tetramethylguanidine (0.5 mL, 3.99 mmol) in a dry mixture of acetonitrile and dimethylformamide (5 mL, 1:1) was stirred at reflux temperature and dry air was bubbled through for 21 h. The reaction mixture was cooled and evaporated to dryness to recover macrocycle **4a·2Cl**.

Experiment 4. Method D

A mixture of macrocycle **4a·2Cl** (200 mg, 0.48 mmol) in dry acetonitrile (35 mL) was added dropwise to a suspension of NaH (288 mg, 12 mmol) in dry acetonitrile (20 mL). After the reaction mixture was stirred at room temperature for 4 h, dry air was bubbled through for 18 h. The resulting suspension was evaporated to dryness to obtain alteration or decomposition products.

Electrospray Ionization Mass Spectrometry

The negative-ion ESI-MS experiments were first performed on a VGQuattro mass spectrometer from Micromass Instruments, as previously described

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[30,44]. Then, negative-ion ESI-MS analyses were recorded on a ZQ mass spectrometer from Waters-Micromass. Electrospray interface (pneumatically assisted) under the following conditions: the nebulizing nitrogen gas flow was 30 L h^{-1} and drying nitrogen 250 Lh^{-1}, source temperature 80°C with a capillary voltage of −2.5 kV and the cone voltage varied from 20 V to 80 V depending on the experiment. The eluent flowing through the probe was CH_3CN:H_2O (1:1, v/v) at a flow rate of 100 μL min^{-1}. Spectra were scanned at a rate of 1.5 s over the mass range *m/z* 10–1500 and were recorded and processed using the MassLynx software, version 4.0. Mass calibration was performed with a NaCsI mixture standard solution.

Single-crystal X-ray Diffraction Analysis

Registration no. CCDC 182/1132 contains the supplementary crystallographic data for this paper. *Imidazoliophanes* **4a·2Cl·2H_2O** and **4b·2Cl·3.5 H_2O·0.5CH_3CN**: CCDC deposition numbers 102466 and 102467.

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