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The influence of benzoate anion substituents on the crystal packing and hydrogen-bonding network of 9-aminoacridinium salts

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ABSTRACT

As a continuation of our recent work, we discuss the crystal structures of a series of salts with the 9-aminoacridinium cation and 3-chlorobenzoate, 4-chlorobenzoate and 3-hydroxybenzoate anions. The crystal structure of $[2(C_{13}H_{11}N_2^+)\cdot C_7H_5O_3^-\cdot Cl^-\cdot 2(H_2O)]$ is the first of all the known 9-aminoacridinium salts where mixed salts were obtained. Analysis of the hydrogen bonds in the crystal lattices of the title compounds shows that the ions are linked via N(amino)–H···O(carboxy) hydrogen bonds forming $R_2^2(8)$ or $R_2^4(16)$ hydrogen bond ring motifs. In the packing, there are also two kinds of hydrogen bond chain motif. The first, $C_4^2(16)$, in which 9-AA cations, a Cl^- anion and a water molecule are interlinked, and the second, C(7), in which aromatic carboxylic acid anions are connected directly. We also observed the influence of the different anions on the packing of the acridine skeletons in the crystal lattice.

1. Introduction

Having interesting antibacterial, antiprion, antitumor, and anti-inflammatory properties,[1] 9-aminoacridine (9-AA) derivatives are a group of amine bases capable of interacting with organic acids. The synthesis of these compounds and the analysis of the interactions between them are very useful in view of their importance in a wide range of different biological systems.[2]

In our investigations of new structural aspects of 9-aminoacridinium derivatives and as a continuation of our recent work,[3] we had intended to obtain its 3-chlorobenzoate (**1**), 4-chlorobenzoate (**2**), and 3-hydroxybenzoate (**3**) salts. To our surprise, however, compound **3** crystallized in the form of mixed salts: $2(C_{13}H_{11}N_2^+)\cdot C_7H_5O_3^-\cdot Cl^-\cdot 2(H_2O)$, represent an interesting object of research in the context of drug therapy[4] and crystal engineering.[5] In this paper we report on the synthesis and X-ray characterization of these compounds.

2. Results and discussion

2.1. 9-Aminoacridinium 3-chlorobenzoate (1)

Single-crystal X-ray diffraction measurements show that compound **1** crystallizes in the monoclinic $P2_1/c$ space group with the 9-AA cation and 3-chlorobenzoate anions in the asymmetric unit (Fig. 1S, Table 1S, Supplementary data). In the packing of the molecules in **1**, the crystal structure is stabilized via N–H···O and C–H···O hydrogen bonds and π–π stacking interactions (Tables 2S and 3S, Supplementary data). Analysis of the hydrogen bonds in the structure of **1** has shown that the inversely oriented cations and anions form a tetramer; these ions are linked via N(amino)–H···O(carboxy) hydrogen bonds in the crystal lattice and form an $R_2^2(8)$ hydrogen bond ring motif (Fig. 1a).[6]

In this motif amino groups from the cations and one O atom from the carboxy group in the anions participate in the hydrogen bonds. Additionally, the O(carboxy) atoms engaged in the formation of this motif also take part in weak C(acridine)–H···O(carboxy) hydrogen bonds that stabilize the tetramers. The tetramers in **1** are linked through an N(acridine)–H···O(carboxy) hydrogen bond, where the O atom is not involved in the formation of the $R_2^2(8)$ hydrogen bond ring motif (Fig. 1a). Analysis of the π–π interactions in **1** shows that the adjacent acridine skeletons are linked via π-stacking interactions in the *AB* arrangement to form a two-fold helical arrangement (Fig. 1b), in which the overlapping mode of neighboring cations shows that the adjacent acridine skeletons are rotated in-plane with respect to one another by approximately 135°. All the aromatic rings from the acridine skeletons participate in π–π interactions, forming a *zigzag* motif with centroid···centroid distances from 3.552 to 4.069 Å and a distance of 3.380 Å between the mean planes of the neighboring acridine skeleton. Analysis of the π–π interactions between the aromatic rings in the acid anions

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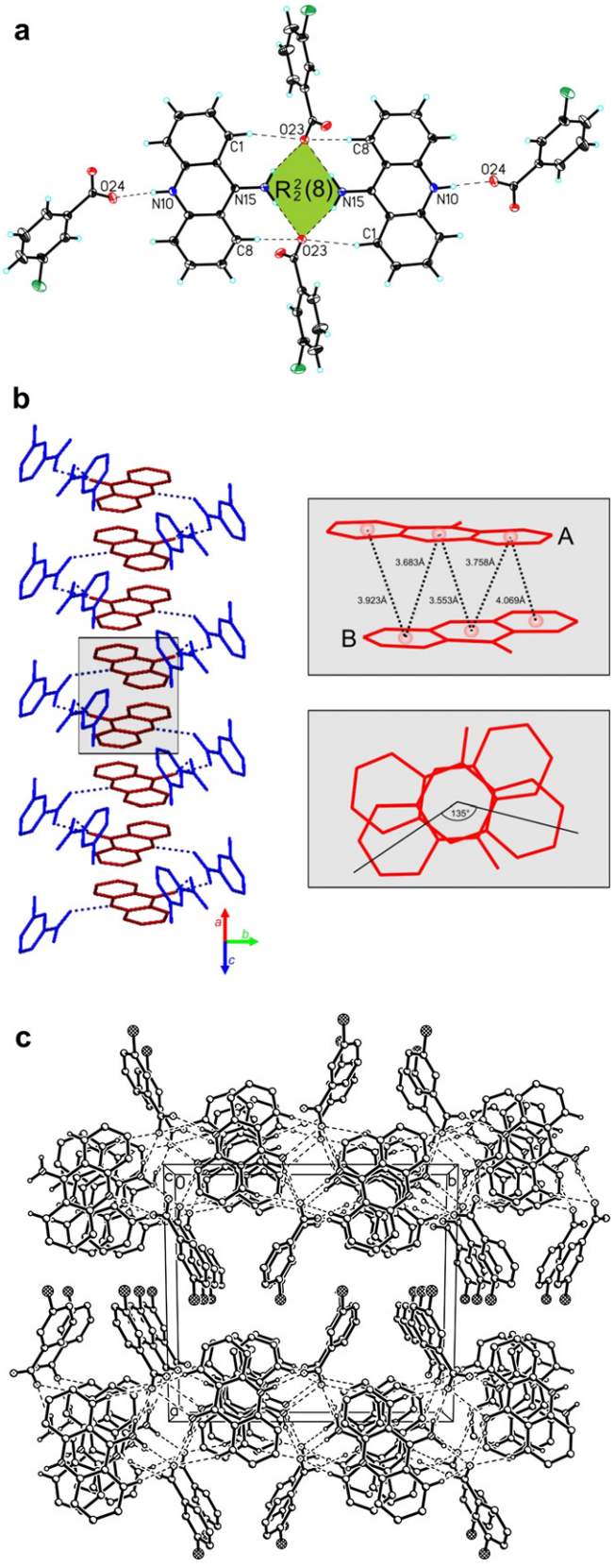

Fig. 1. Network of the intermolecular interactions in **1**: $R_2^2(8)$ hydrogen bond ring motif (a), π–π interactions (b) and crystal packing (c).

in **1** shows that the shortest centroid···centroid distance is 5.475 Å, which indicates that π-stacking interactions are absent. In the supramolecular architecture of **1**, there are columns forming separate layers (Fig. 1c).

2.2. 9-Aminoacridinium 3-chlorobenzoate (2)

Compound **2** forms triclinic crystals (*P*-1 space group) with the 9-AA cation, 4-chlorobenzoate anion and water molecule in the asymmetric unit (Fig. 2S, Table 1S, Supplementary data). The crystal structure of **2** is stabilized by N–H···O and O–H···O hydrogen bonds and π–π interactions (Tables 4S and 5S, Supplementary data). Analysis of the hydrogen bonds in the structure of **2** shows that the ions form tetramers and produce an $R_2^4(16)$ hydrogen bond ring motif (Fig. 2a). In this motif, the cations and anions are linked via N(amino)–H···O(carboxy) hydrogen bonds in the crystal lattice; in contrast to **1**, however, both O atoms from the carboxy group are involved in the formation of the hydrogen bond ring motif. In the crystal lattice of **2**, the tetramers are linked through an N(acridine)–H···O(water) and O(water)–H···O(carboxy) hydrogen bond (Fig. 2a). Incidentally, it is interesting to note that the tetramers are not stabilized through C(acridine)–H···O(carboxy) hydrogen bonds, as was observed in other structures from this group of compounds (e.g., compound **1**). Analysis of the π–π interactions in **2** shows that the 'head-to-tail' oriented neighboring acridine skeletons in **2** interact through π-stacking interactions in an *ABA* arrangement forming columns (Fig. 2b). In this arrangement, the π–π interactions with centroid···centroid distances from 3.417 to 3.824 Å and a distance of 3.346 Å between the mean planes of the neighboring acridine skeleton form a *zigzag* motif, as in **1**. In the overlapping mode of the neighboring acridine skeletons, adjacent cations are alternately shifted along the longest axis of the acridine skeletons for a distance of ~1.2 Å. Analysis of π–π interactions between the aromatic rings in the acid anions in **2** shows that the shortest centroid···centroid distance is 3.820 Å (Fig. 2c). This indicates that π-stacking interactions between the benzene rings from the acid anions are observed. In the supramolecular architecture of **2**, there are chains of $R_2^4(16)$ hydrogen bond ring motifs forming columns in a *staircase* motif. These columns are interlinked via π–π interactions between the aromatic rings in the anions (Fig. 2c).

2.3. 9-Aminoacridinium 3-hydroxybenzoate (3)

Compound **3** crystallizes in the triclinic *P*-1 space group. The asymmetric unit of **3** consists of two 9-AA cations, 3-hydroxybenzoate and chlorate anions as well as two water molecules (Fig. 3S, Table 1S, Supplementary data). This structure is the first of all the known 9-aminoacridinium salts where mixed salts were obtained.[7] It is worth attention that the average deviations from planarity of the acridine skeleton are 0.015(2) and 0.027(2) Å, and the angle between the mean planes of the right- and left-hand halves of the acridine skeleton is equal to 1.5 and 3.7° in cations A and B, respectively. This shows above all that the presence of an aromatic carboxylic acid anion clearly influences the planarity of the acridine skeleton, which adopts the *butterfly* conformation,[8] especially in the case of cation B.

The crystal structure of **3** is stabilized by N–H···O, N–H···Cl, O–H···O, O–H···Cl, C–H···O, and C–H···Cl hydrogen bonds as well as π–π stacking (Tables 6S and 7S, Supplementary data). Analysis of the hydrogen bonds in **3** shows that the ions do not form tetramers in the crystal lattices, but produce two nearly perpendicularly aligned kinds of hydrogen bond chain motif. In the first, a $C_4^2(16)$ hydrogen bond chain motif, both A and B 9-aminoacridinium cations are linked via N(acridine)–H···Cl···H–N(amino) hydrogen bonds bifurcated on the chloride cation and N(acridine)–H···O···H–N

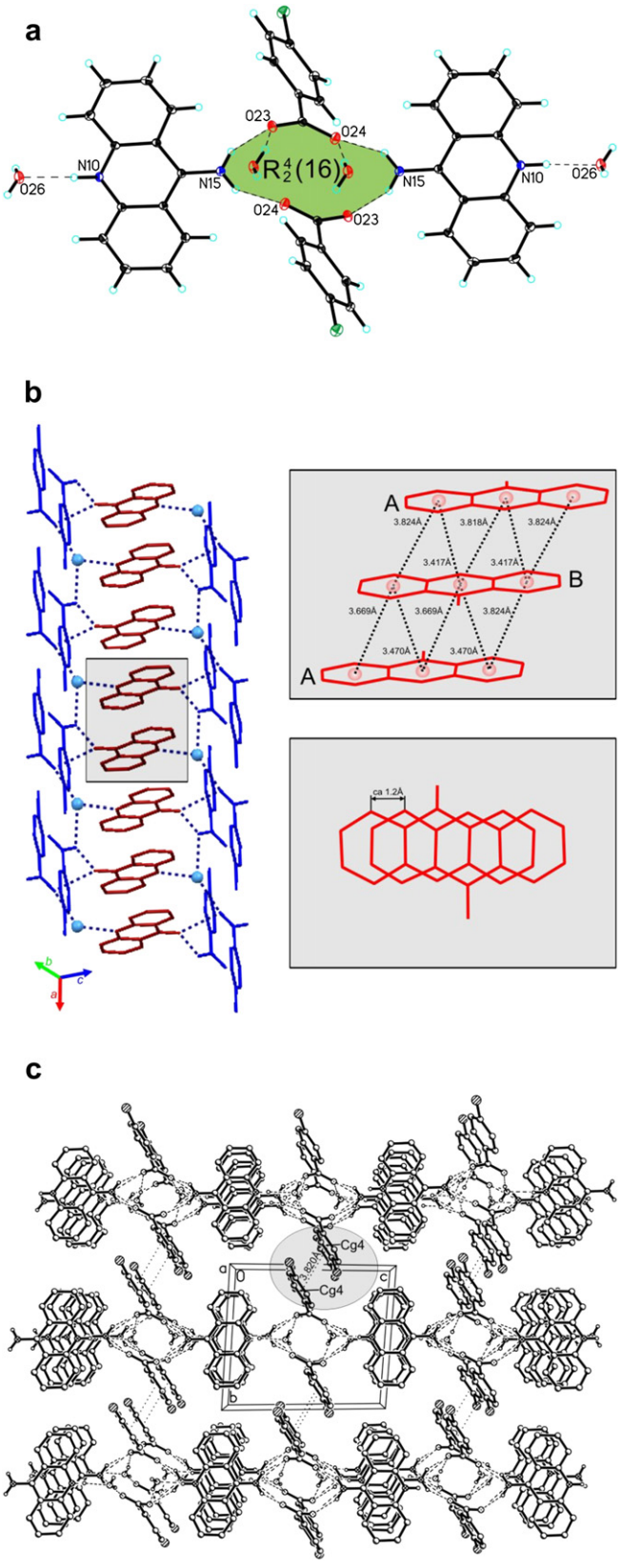

Fig. 2. Network of the intermolecular interactions in **2**: $R_2^4(16)$ hydrogen bond ring motif (a), π–π interactions (b) and the crystal packing (c).

(amino) hydrogen bonds bifurcated on the O atom of the water molecule (Fig. 3a). In the second, a C(7) hydrogen bond chain motif, the neighboring 3-hydroxybenzoate anions interact via an O (hydroxy)–H···O(carboxy) hydrogen bond (Fig. 3b). In the crystal packing, these chains are linked by N(amino)–H···O(carboxy), N (amino)–H···O(water), O(water)–H···O(carboxy), O(water)–H···O (hydroxy), O(water)–H···Cl, and C(benzene)–H···Cl hydrogen bonds, as shown in Fig 3c. In the crystal lattice of **3**, the neighboring

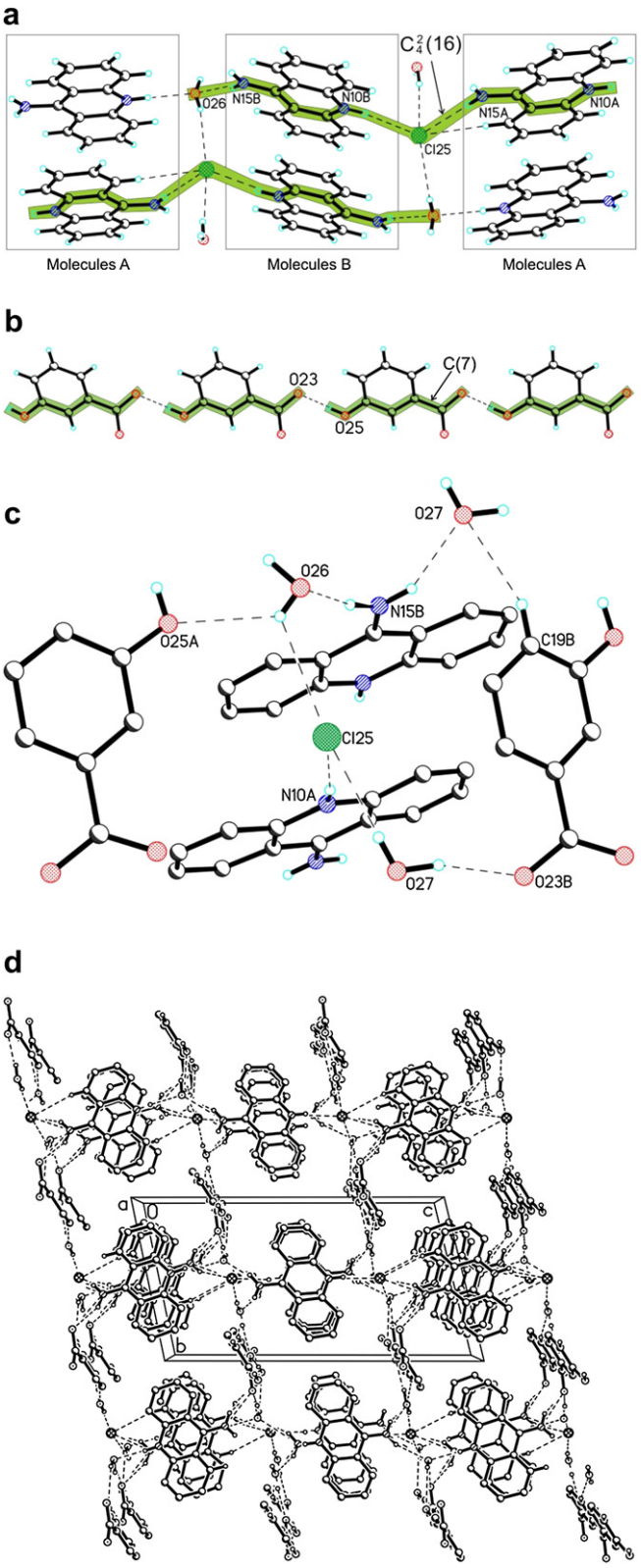

Fig. 3. Network of the intermolecular interactions in **3**: $C_4^2(16)$ hydrogen bond chain motif (a), C(7) hydrogen bond chain motif (b), connection between $C_4^2(16)$ and C(7) hydrogen bond chain motifs (c), and crystal packing (d).

acridine skeletons are linked by π–π interactions in the *ABA* arrangement forming alternately aligned columns of molecules A and B (Figs. 3a and 4).

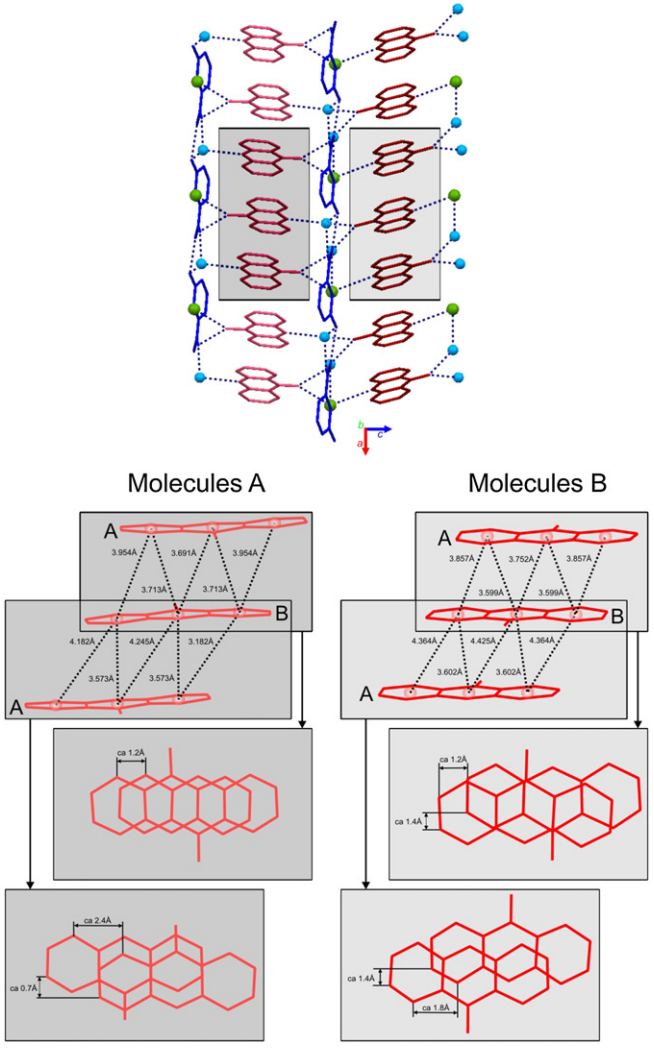

Fig. 4. Geometry of the π–π interactions in **3**.

In the *ABA* arrangement of molecules A, all the aromatic rings from the acridine skeletons participate in π–π interactions, forming a *zigzag* motif with centroid···centroid distances from 3.573 to 4.182 Å and a distance of 3.450 Å between the mean planes of the neighboring acridine skeleton. In this arrangement, the overlapping mode of the neighboring cations shows that they are alternately shifted toward each other for a distance of ~1.4 Å and ~1.2 Å along the shortest and longest axis of the acridine skeletons, respectively, in the *AB* sequence and shifted for a distance of ~1.4 Å and ~1.8 Å along the shortest and longest axis of the acridine skeletons, respectively, in the *BA* sequence. Molecules of B are also packed in the *ABA* arrangement with centroid···centroid distances from 3.602 to 4.364 Å and a distance of 3.520 Å between the mean planes of the neighboring acridine skeleton. However, there are differences between the overlapping modes of the neighboring cations. In the *AB* sequence, the adjacent cations are alternately shifted along the longest axis of the acridine skeletons for a distance of ~1.2 Å, whereas in the *BA* sequence, the overlapping mode of neighboring cations shows that they are alternately shifted along the shorter axis by a distance of ~0.7 Å and along the longer axis of the acridine skeleton by a distance of ~2.4 Å. In the crystal lattice of **3**, there are networks of chains forming columns (Fig. 3c). The presence of chains in the crystal packing is the reason of lack of π-stacking interactions between the aromatic rings in the anions.

3. Conclusion

In summary, as a continuation of our recent work, we discuss the crystal structures of a series of salts with the 9-aminoacridinium cation and the 3-chlorobenzoate (**1**), 4-chlorobenzoate (**2**), and 3-hydroxybenzoate (**3**) anions. The structure of **3** is the first of all the known 9-aminoacridinium salts where mixed salts were obtained. Conformational analysis of the 9-aminoacridinium skeleton suggests that the aromatic carboxylic acid anions affect the planarity of the 9-AA skeleton, especially in compound **3**, which adopts an evident butterfly conformation. Analysis of the hydrogen bonds in the crystal lattices of the title compounds shows that the cations and anions form tetramers (**1** and **2**) or chains (**3**). In the tetramers, the ions are linked via N(amino)–H···O(carboxy) hydrogen bonds forming $R_2^2(8)$ (**1**) or $R_2^4(16)$ (**2**) hydrogen bond ring motifs. In the packing of **3**, there are two kinds of hydrogen bond chain motif. The first, $C_4^2(16)$, in which 9-AA cations, a Cl^- anion and a water molecule are interlinked, and the second, C(7), in which aromatic carboxylic acid anions are connected directly. We also observed the influence of the different anions on the packing of the acridine skeletons in the crystal lattice. The 9-AA cations are π–π stacked in the *AB* (**1**) or *ABA* (**2** and **3**) arrangement to form a two-fold helical arrangement (**1**) or columns (**2** and **3**). Analysis of the π–π interactions between the aromatic rings of anions indicates that π-stacking interactions are observed only in the packing of molecules **2**.

4. Experimental

4.1. General

The synthesis of compounds **1**, **2**, and **3** is described in Supplementary data. Single crystals of **1**–**3** were grown by slow evaporation of an ethanol solution.

4.2. Crystal structure determination

Good-quality single-crystal specimens of **1**, **2**, and **3** were selected for the X-ray diffraction experiments at T=295(2) K. They were mounted with epoxy glue at the tip of glass capillaries Diffraction data were collected on an Oxford Diffraction Gemini R ULTRA Ruby CCD diffractometer with Cu*K*α (λ=1.54184 Å) (for **1**) and Mo Kα (λ=0.71073 Å) (for **2** and **3**) radiation. In all cases, lattice parameters were obtained by least-squares fit to the optimized setting angles of the collected reflections by means of *CrysAlis CCD*[9] Data were reduced by using *CrysAlis RED* software with applying multi-scan absorption corrections (Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm). The structural resolution procedure was made using the *SHELXS-97* package solving the structures by direct methods and carrying out refinements by full-matrix least-squares on F^2 using *SHELXL-97* program.[10] All H-atoms bound with aromatic C-atoms were placed geometrically and refined using a riding model with C–H=0.93 Å and U_{iso}(H)=1.2 U_{eq}(C). All H-atoms bound with N-atoms were placed geometrically and refined using a riding model with N–H=0.86 Å and U_{iso}(H)=1.5 U_{eq}(N). The all amino $-NH_2$ groups were assumed to be planar-trigonal and coplanar with the mean planes of acridinium skeleton. All H-atoms from the water molecules were located in a difference Fourier map and refined freely with U_{iso}(H)=1.5 U_{eq}(O). All interactions demonstrated were found by *PLATON* program.[11]

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data

Center as supplementary publication no. CCDC-794396 (**1**), CCDC-794397 (**2**), and CCDC-794398 (**3**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

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Supplementary data

Electronic Supplementary Information (ESI) available: experimental details; crystal, and structure refinement data for **1**, **2**, and **3**; figures; hydrogen bonds and π–π interactions geometry. ESI and crystallographic data in CIF or other electronic format can be found. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.02.083. These data include MOL files and InChiKeys of the most important compounds described in this article.

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