

Dimeric supramolecular motifs of two carboxylate–guanidinium compounds

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Received 18 May 2010

Accepted 22 July 2010

Online 4 August 2010

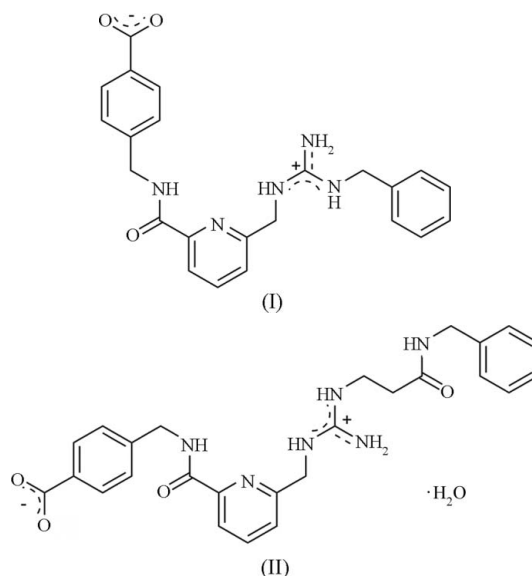
The structures of *N*-benzyl-*N'*-{6-[(4-carboxylatobenzyl)aminocarbonyl]-2-pyridylmethyl}guanidinium, C₂₃H₂₃N₅O₃, (I), and *N*-[2-(benzylaminocarbonyl)ethyl]-*N'*-{6-[(4-carboxylatobenzyl)aminocarbonyl]-2-pyridylmethyl}guanidinium monohydrate, C₂₆H₂₈N₆O₄·H₂O, (II), both form three-dimensional supramolecular hydrogen-bonded networks based on a dimeric primary synthon involving carboxylate–guanidinium linkages. The differences in the geometries and hydrogen-bonding connectivities are driven by the additional methylpropionamide group and water of crystallization of (II).

Comment

Guanidinium salts have been widely employed as motifs for carboxylate binding (Blondeau *et al.*, 2007; Fitzmaurice *et al.*, 2002) owing to a structural complementarity that results in well aligned hydrogen-bond donor and acceptor groups, and favourable electrostatic interaction in the ion pair. We have recently reported a pyridylguanidinium receptor in which two additional co-operative (amide) hydrogen-bond donors for carboxylate binding are incorporated, and in which the pyridine lone pair participates in intramolecular hydrogen bonding for preorganization of the binding motif (Fitzmaurice *et al.*, 2007). Entropy-driven binding of acetate has been achieved in this system in competitive solution-phase media, and we have now prepared analogous systems, (I) and (II), extended in structure to incorporate a tethered carboxylate terminus. We aim to develop a simple supramolecular model based on dimerization of zwitterions (I) and (II), in which the energetic contribution of individual intermolecular binding interactions to the overall self-assembly, driven primarily by the guanidinium–carboxylate binding, can be determined. The present study of dimeric self-association of (I) and (II) was undertaken in order to investigate the ion-pair interaction and other contributing intramolecular interactions

in the context of the overall assembly, and to inform monomer design.

The structure of (I) (Fig. 1) comprises an anionic benzoate group linked through a methylene group to a pyridinecarboxylic acid amide; this is in turn linked *via* another methylene group to a guanidinium cationic group terminated by a methylene-linked benzene ring. These four groups are individually essentially planar, with the three methylene groups acting as hinges, allowing the molecule to adopt a twisted conformation driven by steric and hydrogen-bonding influences. This can be described using the least-squares planes through the groups; the defined planes, the r.m.s. deviation from planarity (Å) and the atom with the maximum deviation from the plane are as follows: O1/O2/C1–C7, 0.097, O1 = 0.184 (2) Å; N1/N2/O3/C9–C14, 0.053, O3 = 0.095 (2) Å; N3/N4/N5/C16, 0.001, C16 = 0.001 (2) Å; C18–C23, 0.032, C18 = 0.05 (2) Å. The angles between adjacent planes are 77.33 (6), 87.22 (8) and 81.97 (9)°, respectively, and infer that the groups are mutually perpendicular.



With the exception of a water of crystallization the molecular structure of (II) (Fig. 2) differs from (I) solely in the

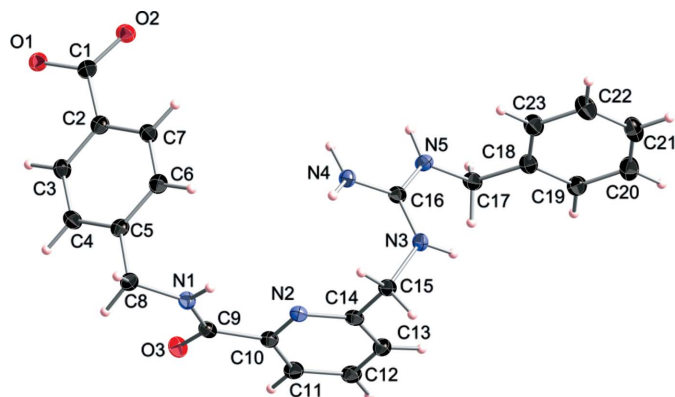


Figure 1

The molecular structure of (I). Displacement ellipsoids are drawn at the 35% probability level and H atoms are drawn with an arbitrary radius.

insertion of a methylpropionamide group before the terminal benzene ring. This additional group has a dramatic effect on the overall structure and geometry of the molecule. The least-squares planes, including the additional methylpropionamide group, are defined as previously as follows: O1/O2/C1–C7, 0.057, O1 = $-0.111(2)$ Å; N1/N2/O3/C9–C14, 0.036, C10 = $-0.059(2)$ Å; N3/N4/N5/C16, 0.004, C16 = $0.006(2)$ Å; C18/C19/N6/O4, 0.007, C19 = $-0.012(2)$ Å; C21–C26, 0.002, C26 = $-0.004(2)$ Å; these planes make angles of 67.43 (5), 4.11 (12), 73.16 (13) and 75.76 (10)°. It can be seen from these angles that the twist at the methylene group connecting the pyridinecarboxylic acid amide and the guanidinium group is now much smaller [dihedral angle = 4.11 (12)°], making the combined group essentially flat. The remaining two hinges revert to rotations approaching 90° [73.16 (13) and 75.76 (10)°], continuing the corkscrew-like twist of the molecule.

Both (I) and (II) exist as zwitterions with a formal negative charge associated with the carboxylate group and a formal positive charge with the guanidinium group. Analysis of the bond lengths shows the guanidinium unit to be in a resonance hybrid form, and in both (I) and (II) the differences between the bonds are within 3 s.u. of their values. In (I) the carboxylate group is clearly in its resonance hybrid form [O1–C1 = 1.263 (3) Å and O2–C1 = 1.264 (3) Å]. A similar case exists for (II), although a possible asymmetrical lengthening in favour of the stronger hydrogen-bond environment can be seen [O1–C1 = 1.254 (3) Å and O2–C1 = 1.261 (3) Å].

With their plethora of potential hydrogen-bond donors and acceptors it is unsurprising that both (I) and (II) form three-dimensional networks, and it is the interaction between the carboxylate and guanidinium groups that is responsible for the formation of a basic supramolecular building block (Figs. 3 and 4).

In (I), the guanidinium group is in the *trans* configuration [atom H93 is on the opposite side to the NH₂ group (N4)], so that it is an NH (N5) and an NH₂ (N4) group that participate in the carboxylate hydrogen bonding [N4···O2ⁱⁱⁱ and N5···O1ⁱⁱⁱ; symmetry code: (iii) $-x + 2, -y + 1, -z + 1$], whereas in (II) the group is in the *cis* form [both H atoms (H3 and H5) are on the opposite side from the NH₂ group (N4)] and both NH groups (N3 and N5) are oriented towards the

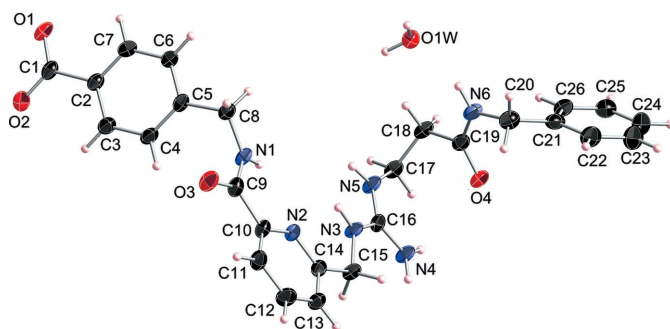


Figure 2

The molecular structure of (II). Displacement ellipsoids are drawn at the 35% probability level and H atoms are drawn with an arbitrary radius.

carboxylate group [N3···O1ⁱ and N5···O1ⁱ; symmetry code: (i) $-x - 1, -y, -z$; see Tables 1 and 2 for details]. In (I), both carboxylate O atoms hydrogen bond to separate H atoms of the guanidinium group, but the interaction is not planar, with the amine group twisting away below the plane of the carboxylate group (the angle between the least-squares planes through each group is 42.76°). The (inversion) symmetry-related interactions complete a dimer or 34-membered ring (N4···O2ⁱⁱⁱ and N5···O1ⁱⁱⁱ), as depicted in Fig. 3.

In (II), the approach of the carboxylate and guanidinium units is characterized by a single bifurcated hydrogen bond from O1ⁱ to N3 and N5. The hydrogen-bonding environment of the carboxylate unit is now very different from that in (I), with atom O1 acting as a receptor in three hydrogen bonds, two from the guanidinium unit (N3···O1ⁱ and N5···O1ⁱ) and one from the amide group of the pyridinecarboxylic acid amide group (N1···O1ⁱ; see Fig. 4).

Additionally, the benzoate rings are arranged parallel in (II), such that π - π interactions become relevant; the separation between the C2–C7 and C2ⁱ–C7ⁱ centroids is 3.662 Å, with the perpendicular distance between the least-squares planes through each benzene ring being 3.372 Å, as depicted with a dashed line in Fig. 4. It is possible that the π - π interaction

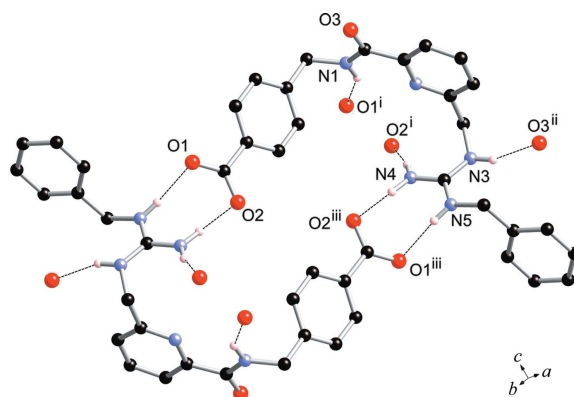


Figure 3

The dimeric primary synthon in (I), showing the extended hydrogen-bonding environment. H atoms not involved in significant close contacts have been omitted for clarity. [Symmetry codes: (i) $-x - 1, y, z$; (ii) $-x - \frac{1}{2}, -y + \frac{1}{2}, z + \frac{1}{2}$; (iii) $-x + 2, -y + 1, -z + 1$.]

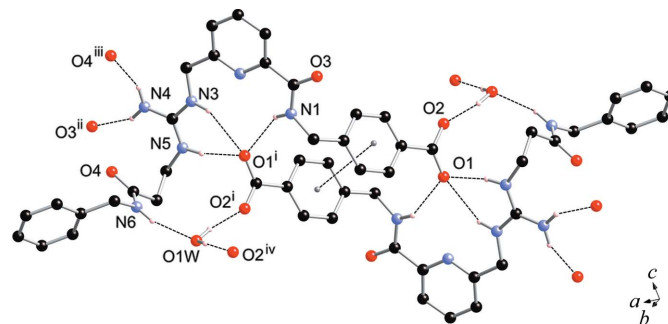


Figure 4

The dimeric primary synthon in (II), showing the extended hydrogen-bonding environment. H atoms not involved in significant close contacts have been omitted for clarity. π - π interactions are depicted using a dashed line between ring centroids. [Symmetry codes: (i) $-x - 1, -y, -z$; (ii) $x + 1, y, z$; (iii) $-x + 1, -y + 1, -z + 1$; (iv) $x + 1, y + 1, z$.]

arises from the changed geometry of the guanidinium-carboxylate interaction compared to that in (I), but more likely the π - π interaction provides a co-operative driving force for this offset ion-pair interaction in combination with the hydrogen bonding from the propionamide group to the water molecule (N6 \cdots O1W) described below.

For the packing of (I), the dimer rings are stacked *via* other hydrogen bonds [N4 \cdots O2ⁱ and N1 \cdots O1; symmetry code: (i) $x - 1, y, z$] to form a one-dimensional molecular chain structure along the *a* axis. In the structure, guanidinium-carboxylate hydrogen-bonded pairs are connected *via* N4 \cdots O2ⁱ hydrogen bonds. A herringbone-like arrangement is also observed when the structure is viewed down the *c* axis. The supramolecular structure of (II) is punctuated by hydrogen-bonded rings formed around a centre of symmetry *via* two water molecules and two O atoms of two separate carboxylate groups [O1W \cdots O2ⁱ and O1W \cdots O2^{iv}; symmetry code: (iv) $x + 1, y + 1, z$]. The water molecules also act as acceptors in hydrogen bonds to the methyl propionamide groups (N6 \cdots O1W) such that the rings connect four individual molecules.

As a general point, hydrogen-bond interactions between a guanidinium and carboxylate group often form a subunit characterized by linear bidendate interactions. However, it is often observed that other competitive interactions can force a nonplanar geometry for this unit (*e.g.* Zafar *et al.*, 2002). Preliminary searches of the Cambridge Structural Database (Allen, 2002) for such interactions show a wide range of geometries and will be the subject of a subsequent study.

Experimental

Full synthetic procedures for the stepwise preparation of (I) and (II) from ethyl 6-[[bis(*tert*-butoxycarbonyl)amino]methyl]pyridine-2-carboxylate will be reported elsewhere. Single crystals were obtained by slow diffusion of a 40 mM solution of each in MeOH with CH₂Cl₂ for (I) and with Et₂O for (II).

Compound (I)

Crystal data

C ₂₃ H ₂₃ N ₅ O ₃	$V = 1999.10 (12) \text{ \AA}^3$
$M_r = 417.46$	$Z = 4$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 8.1826 (3) \text{ \AA}$	$\mu = 0.10 \text{ mm}^{-1}$
$b = 18.1530 (7) \text{ \AA}$	$T = 120 \text{ K}$
$c = 13.4723 (4) \text{ \AA}$	$0.15 \times 0.1 \times 0.1 \text{ mm}$
$\beta = 92.601 (2)^\circ$	

Table 1

Hydrogen-bond geometry ($\text{\AA}, ^\circ$) for (I).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1-H91 \cdots O1 ⁱ	0.89	2.17	2.904 (3)	140
N3-H93 \cdots O3 ⁱⁱⁱ	0.89	1.92	2.762 (3)	158
N4-H94A \cdots O2 ⁱⁱⁱ	0.97	1.92	2.894 (3)	177
N4-H94B \cdots O2 ⁱ	0.90	2.06	2.934 (3)	167
N5-H95 \cdots O1 ⁱⁱⁱ	0.86	2.03	2.863 (3)	162

Symmetry codes: (i) $x - 1, y, z$; (ii) $x - \frac{1}{2}, -y + \frac{1}{2}, z + \frac{1}{2}$; (iii) $-x + 2, -y + 1, -z + 1$.

Table 2

Hydrogen-bond geometry ($\text{\AA}, ^\circ$) for (II).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1-H1 \cdots O1 ⁱ	0.88	2.32	3.084 (3)	145
N3-H3 \cdots O1 ⁱ	0.88	2.46	3.180 (3)	139
N4-H4A \cdots O3 ⁱⁱⁱ	0.88	2.03	2.847 (3)	154
N4-H4B \cdots O4 ⁱⁱⁱ	0.88	2.04	2.856 (3)	154
N5-H5 \cdots O1 ⁱ	0.88	1.91	2.770 (3)	167
N6-H6 \cdots O1W	0.88	2.03	2.884 (3)	163
O1W-H1W \cdots O2 ⁱ	0.86	1.88	2.734 (3)	169
O1W-H2W \cdots O2 ^{iv}	0.85	2.00	2.844 (3)	170

Symmetry codes: (i) $-x - 1, -y, -z$; (ii) $x + 1, y, z$; (iii) $-x + 1, -y + 1, -z + 1$; (iv) $x + 1, y + 1, z$.

Data collection

Bruker-Nonius KappaCCD diffractometer	16252 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	3519 independent reflections
$T_{\min} = 0.986, T_{\max} = 0.991$	2719 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.078$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.060$	280 parameters
$wR(F^2) = 0.132$	H-atom parameters constrained
$S = 1.08$	$\Delta\rho_{\text{max}} = 0.27 \text{ e \AA}^{-3}$
3519 reflections	$\Delta\rho_{\text{min}} = -0.28 \text{ e \AA}^{-3}$

Compound (II)

Crystal data

C ₂₆ H ₂₈ N ₆ O ₄ ·H ₂ O	$\gamma = 117.818 (4)^\circ$
$M_r = 506.56$	$V = 1286.03 (18) \text{ \AA}^3$
Triclinic, $P\bar{1}$	$Z = 2$
$a = 11.0848 (9) \text{ \AA}$	Mo $K\alpha$ radiation
$b = 11.5591 (7) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$c = 11.9676 (11) \text{ \AA}$	$T = 120 \text{ K}$
$\alpha = 99.956 (5)^\circ$	$0.2 \times 0.17 \times 0.06 \text{ mm}$
$\beta = 98.908 (3)^\circ$	

Data collection

Bruker-Nonius KappaCCD diffractometer	20604 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	5835 independent reflections
$T_{\min} = 0.982, T_{\max} = 0.994$	4304 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.049$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.077$	334 parameters
$wR(F^2) = 0.145$	H-atom parameters constrained
$S = 1.12$	$\Delta\rho_{\text{max}} = 0.31 \text{ e \AA}^{-3}$
5835 reflections	$\Delta\rho_{\text{min}} = -0.24 \text{ e \AA}^{-3}$

C-bound H atoms were identified in a difference map and subsequently placed in idealized positions and refined using a riding model (aromatic C-H = 0.95 \AA and methylene C-H = 0.99 \AA). N-bound H atoms were located in the difference map and their coordinates set as riding on their parent atoms. For all C- and N-bound atoms, the displacement parameters were set at 1.2 times U_{eq} of the parent atom. In (II), the H atoms of the water molecule were clearly visible in the difference map as the two highest residual density peaks. Their coordinates were initially restrained using distance restraints [O-H = 0.84 (2) \AA and H \cdots H = 1.37 (2) \AA] and then fixed during the final refinement cycles; displacement parameters were constrained to 1.5 times those of the parent O atom. Also in (II), a void of 76 \AA^3 exists

around a centre of symmetry at $(\frac{1}{2}, 1, \frac{1}{2})$, but no significant residual electron density was observed in this region.

For both compounds, data collection: *COLLECT* (Hooft, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *CrystalMaker* (CrystalMaker, 2005); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *publCIF* (Westrip, 2010).

We thank the Higher Education Commission of Pakistan for funding of MIA under the split PhD programme.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: UK3023). Services for accessing these data are described at the back of the journal.

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