organic compounds

Hydrogen bonding in the anhydrous 1:1 proton-transfer compounds of isonipecotamide with nitro-substituted benzoic acids: the salts of the three isomeric mononitrobenzoic acids and of 3,5-dinitrobenzoic acid

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The structures of the anhydrous 1:1 proton-transfer compounds of isonipecotamide (piperidine-4-carboxamide) with the three isomeric mononitro-substituted benzoic acids and with 3,5-dinitrobenzoic acid, namely 4-carbamoylpiperidinium 2-nitrobenzoate, (I), 4-carbamoylpiperidinium 3-nitrobenzoate, (II), and 4-carbamoylpiperidinium 4-nitrobenzoate, (III), all $C_6H_{13}N_2O^+ \cdot C_7H_4NO_4^-$, and 4-carbamoylpiperidinium 3,5-dinitrobenzoate, $C_6H_{13}N_2O_8^+ \cdot C_7H_3N_2O_6^-$, (IV), respectively, have been determined at 200 K. All the salts form hydrogen-bonded structures, *viz.* three-dimensional in (I), two-dimensional in (II) and (III), and one-dimensional in (IV). Featured in the hydrogen bonding of three of these [(I), (II) and (IV)] is the cyclic head-to-head amide–amide homodimer motif [graph set $R_2^2(8)$] through a duplex N—H···O association, the dimer then giving structure extension *via* either piperidinium or amide H-atom donors and carboxylate O-atom and, in some examples [(II) and (IV)], nitro O-atom acceptors. In (I), the centrosymmetric amide–amide homodimers are expanded laterally through N—H···O hydrogen bonds *via* cyclic $R_4^2(8)$ interactions, forming ribbons which extend along the *c* cell direction. These ribbons incorporate the 2-nitrobenzoate cations through centrosymmetric cyclic piperidine–carboxylate N—H···O associations [graph set $R_4^4(12)$], giving interconnected sheets in the three-dimensional structure. In (II), in which no amide–amide homodimer is present, duplex piperidinium–amide N—H···O homomolecular hydrogen-bonding associations [graph set $R_2^2(14)$] give centrosymmetric head-to-tail dimers. Structure extension occurs through hydrogen-bonding associations between both the amide H-atom donors and carboxylate and nitro O-atom acceptors, as well as a three-centre piperidinium–carboxylate N—H···O,O′ cyclic $R_1^2(4)$ association, giving the two-dimensional network structure. In (III),

the centrosymmetric amide–amide dimers are linked through the two carboxylate O-atom acceptors of the anions *via* bridging piperidinium N—H···O,O′···H—N_{amide} hydrogen bonds, giving the two-dimensional sheet structure which features centrosymmetric cyclic $R_4^4(12)$ associations. In (IV), the amide–amide dimer is also centrosymmetric, with the dimers linked to the anions through amide–nitro N—H···O interactions. The piperidinium groups extend the structure into one-dimensional ribbons *via* N—H···$O_{carboxylate}$ hydrogen bonds. The structures reported here further demonstrate the utility of the isonipecotamide cation in molecular assembly. They also highlight the efficacy of the cyclic $R_2^2(8)$ amide–amide hydrogen-bonding homodimer motif in this process and provide an additional homodimer motif type in the head-to-tail $R_2^2(14)$ association.

Comment

The alicyclic amide piperidine-4-carboxamide (isonipecotamide, INIPA) (O'Neil, 2001) or any of its compounds previously had no structural representation in the crystallographic literature, prompting our investigation of the possible use of this Lewis base for the formation of crystalline proton-transfer compounds with organic acids. We have recently reported the crystal structures and hydrogen-bonding features of the anhydrous 1:1 salts with both picric acid and 3,5-dinitrosalicylic acid (two polymorphs, both picrates) (Smith & Wermuth, 2010b), as well the acetate (Smith & Wermuth, 2010a) and the 2:1 salt with biphenyl-4,4′-disulfonic acid (Smith *et al.*, 2010).
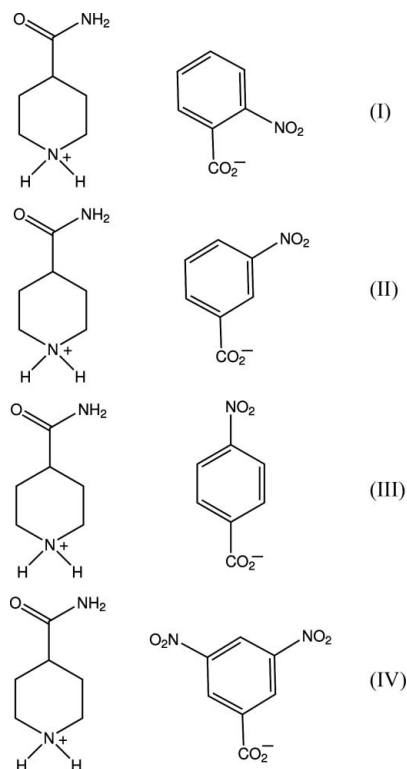
Among a number of 1:1 stoichiometric reactions of INIPA with aromatic acids in 50% aqueous ethanol, we also obtained
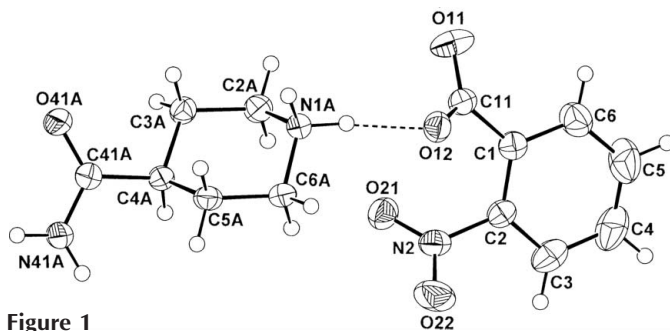
Figure 1
The molecular configuration and atom-naming scheme for the INIPA cation and 2-nitrobenzoate anion in (I). Displacement ellipsoids are drawn at the 50% probability level. The inter-ion hydrogen bond is shown as a dashed line.

Figure 3
The molecular configuration and atom-naming scheme for the INIPA cation and 4-nitrobenzoate anion in (III). Displacement ellipsoids are drawn at the 50% probability level. The inter-ion hydrogen bond is shown as a dashed line.
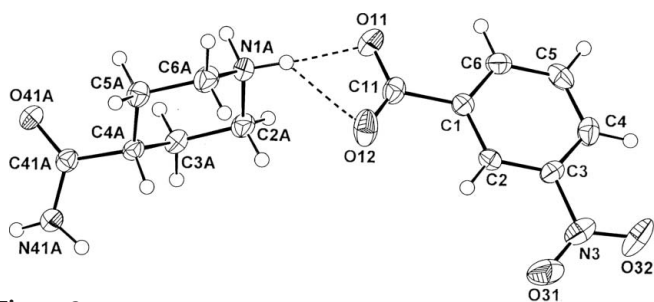

Figure 2
The molecular configuration and atom-naming scheme for the INIPA cation and 3-nitrobenzoate anion in (II). Displacement ellipsoids are drawn at the 50% probability level. Inter-ion hydrogen bonds are shown as dashed lines.
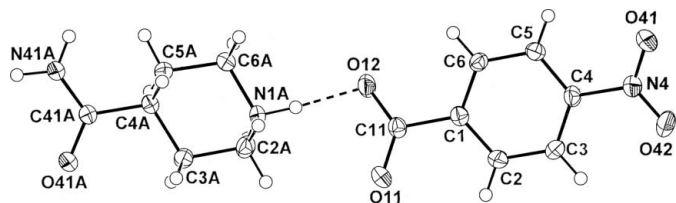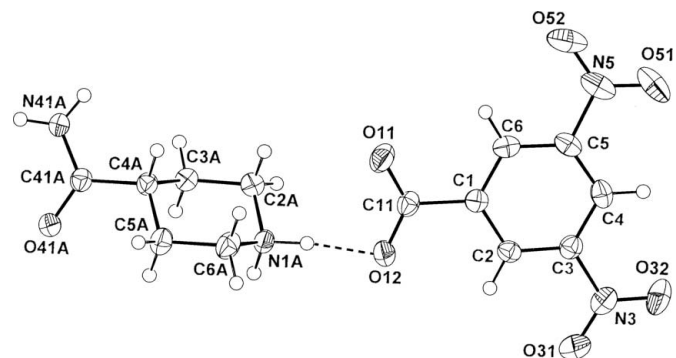

Figure 4
The molecular configuration and atom-naming scheme for the INIPA cation and 3,5-dinitrobenzoate anion in (IV). Displacement ellipsoids are drawn at the 50% probability level. The inter-ion hydrogen bond is shown as a dashed line.

good crystals of the anhydrous salts with the three isomeric mononitro-substituted benzoic acids and with 3,5-dinitrobenzoic acid, namely 4-carbamoylpiperidinium 2-nitrobenzoate, (I), 4-carbamoylpiperidinium 3-nitrobenzoate, (II), 4-carbamoylpiperidinium 4-nitrobenzoate, (III), and 4-carbamoylpiperidinium 3,5-dinitrobenzoate, (IV), and their structures and hydrogen-bonding modes are reported here. We have also recently determined the structures of a number of 1:1 proton-transfer salts of INIPA with aromatic dicarboxylic acids and heteroaromatic carboxylic acids (Smith & Wermuth, 2010c).

With the structures of (I)–(IV) (Figs. 1–4), proton transfer occurs to the hetero N atom of the piperidine ring, and the resulting group is subsequently involved in both hydrogen-bonded cation–anion interactions [single in (I), (III) and (IV), but asymmetric bidentate in (II)]. Featured in the hydrogen bonding of three of these [(I), (II) and (IV)] is the head-to-head cyclic amide–amide homodimer motif [graph set $R_2^2(8)$; Etter *et al.*, 1990], formed through a duplex N—H···O hydrogen-bonding association. Hydrogen-bonding extensions (Tables 1–4) result in structures which are three-dimensional in (I), two-dimensional in (II) and (III), and one-dimensional in (IV) (Figs. 5–8). The head-to-head amide hydrogen-bonding motif [the 'cyclic amide motif' (motif 23); Allen *et al.*, 1998] has a surprisingly low probability of formation among the total set of known amide structures, but when restricted to primary amides which have no competing functional substituent groups or other associative companion species, such as

molecules of solvation, the probability is much higher. No amide–amide dimers were found in any of the phenolate structures (Smith & Wermuth, 2010c), but in the biphenyl-4,4′-disulfonate salt there are two separate examples of the dimer involving the three independent INIPA cations, one centrosymmetric and the other noncentrosymmetric (Smith *et al.*, 2010).

In the structure of (I) (Fig. 1), the 2-nitrobenzoate salt, the centrosymmetric $R_2^2(8)$ INIPA cation amide–amide homodimers are extended laterally through N—H···O hydrogen bonds (Table 1), giving cyclic $R_4^2(8)$ interactions which are centred on crystallographic twofold rotation axes, forming ribbons which extend along the *c* cell direction at $a = 0, \frac{1}{2}$ (Fig. 5). These ribbons incorporate the cations through centrosymmetric cyclic piperidine–carboxylate N—H···O associations [graph set $R_4^4(12)$], giving interconnected sheets in the three-dimensional structure. The nitro group of the anion is unassociated, and both it and the carboxylate group are significantly rotated out of the plane of the benzene ring [torsion angles: C1—C2—N2—O22 = −131.60 (13)° and C2—C1—C11—O11 = −138.95 (14)°].

With the structure of the 3-nitrobenzoate salt, (II) (Fig. 2), in which no INIPA amide–amide dimer is present, a different homomolecular head-to-tail cyclic dimer is present involving the $R_2^2(14)$ duplex piperidinium–amide N—H···O hydrogen-bonding association (Fig. 6). This dimer has precedence in a single example among the known INIPA structures in the picrate (Smith & Wermuth, 2010b). In (II), structure extension occurs through hydrogen-bonding associations between both
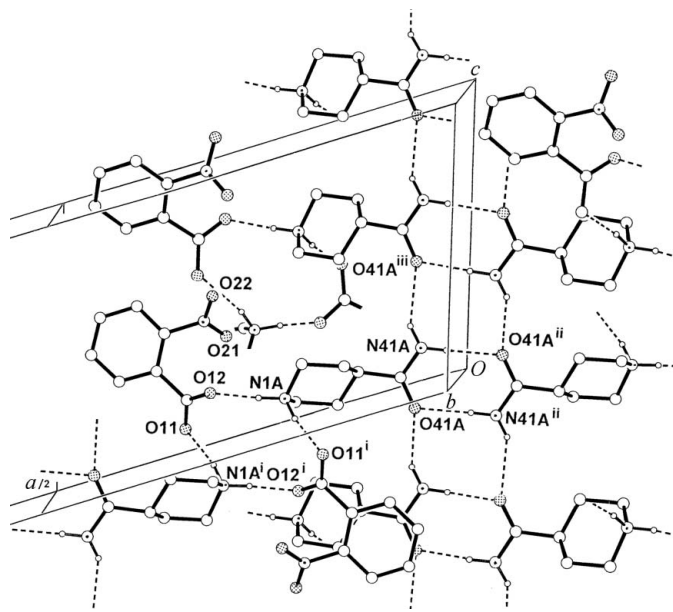
Figure 5
A view of the partial unit cell of (I), viewed down the approximate *b* cell direction, showing the centrosymmetric $R_2^2(8)$ hydrogen-bonded INIPA amide–amide homodimers and their lateral extension into ribbon structures along *c* at *a* = 0, and their further extensions through the 2-nitrobenzoate anions. Hydrogen bonds are shown as dashed lines and non-associative H atoms have been omitted. (For symmetry codes, see Table 1.)
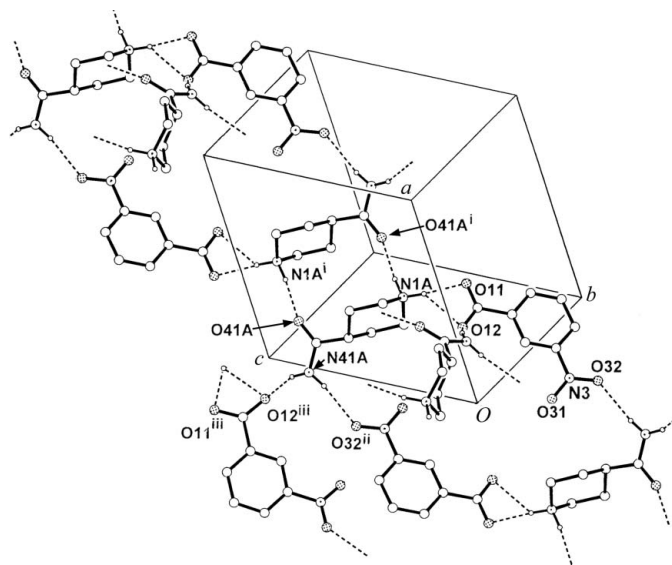

Figure 6
A perspective view of the two-dimensional hydrogen-bonded network structure of (II), showing the centrosymmetric head-to-tail cyclic $R_2^2(14)$ hydrogen-bonded piperidinium–amide associations in the INIPA cationic dimer and the structure extensions. Hydrogen bonds are shown as dashed lines and non-associative H atoms have been omitted. (For symmetry codes, see Table 2.)

amide H-atom donors and the carboxylate and nitro O-atom acceptors, and between the second piperidinium H-atom donor and the carboxylate O-atom acceptors of the anion, in an asymmetric three-centre cyclic $R_1^2(4)$ mode (Table 2). This results in the two-dimensional structure, which also features
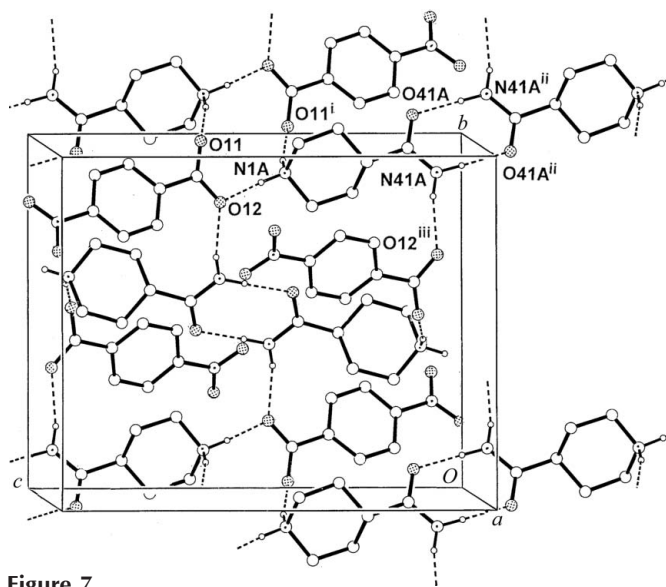

Figure 7
The two-dimensional hydrogen-bonded network structure of (III), showing the centrosymmetric hydrogen-bonded amide–amide dimers and their extensions *via* the carboxylate groups of the anions, in a perspective view of the unit cell. Hydrogen bonds are shown as dashed lines and non-associative H atoms have been omitted. (For symmetry codes, see Table 3.)
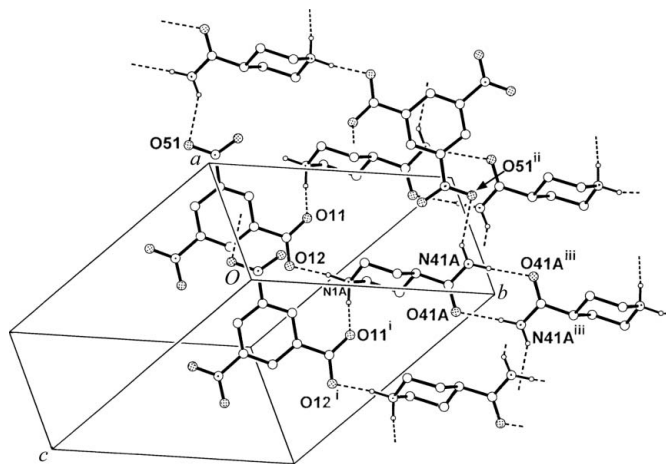

Figure 8
A perspective view of the one-dimensional hydrogen-bonded ribbon structure of (IV), formed by extension of the INIPA amide–amide dimers through both amide and piperidinium N—H⋯O interactions. Hydrogen bonds are shown as dashed lines and non-associative H atoms have been omitted. (For symmetry codes, see Table 4.)

large cyclic rings $[R_4^4(30)]$. The carboxylate group of the anion is approximately coplanar with the benzene ring, while the nitro group is rotated slightly out of the plane [torsion angles C2—C1—C11—O11 = −174.27 (16)° and C2—C3—N3—O32 = −167.65 (16)°].

In the structure of the 4-nitrobenzoate salt, (III) (Fig. 3), the centrosymmetric $R_2^2(8)$ amide–amide dimers are linked through the two carboxylate O-atom acceptors of the anions *via* bridging amide–carboxylate N—H⋯O and piperidinium–carboxylate N—H⋯O hydrogen bonds, giving the two-dimensional sheet structure. Within this structure are centro-symmetric $R_4^4(12)$ associations (Fig. 7). The nitro group is

unassociated. Both the carboxylate and nitro groups of the anion in (III) are rotated slightly out of the plane of the benzene ring [torsion angles: C2—C1—C11—O12 = −163.01 (12)° and C3—C4—N4—O41 = 169.40 (12)°].

In the 3,5-dinitrobenzoate salt, (IV), the amide–amide dimer is also centrosymmetric but with the dimers linked to the anions through amide–nitro N—H···O interactions (Table 4), the second nitro group (at C3) being unassociated. The piperidinium groups extend the structure into one-dimensional ribbons *via* N—H···O$_{carboxylate}$ hydrogen bonds (Fig. 8). The carboxylate group of the anion in (IV) is approximately coplanar with the benzene ring [torsion angle C2—C1—C11—O11 = 175.83 (15)°], while the nitro groups are either close to coplanar [C2—C3—N3—O32 = −178.67 (16)°] or rotated slightly out of the plane [C4—C5—N5—O52 = 168.85 (16)°].

With the INIPA cations in (I)–(IV), the conformation of the amide group is variable [minimum torsion angle C3A/C5A—C4A—C41A—O41A = −15.24 (19)° in (I), 35.9 (2)° in (II), 14.2 (3)° in (III) and −27.3 (2)° in (IV)]. However, the largest value is associated with the structure of (II), where no amide–amide homodimer is formed.

The structures reported here demonstrate the utility of the INIPA cation as a synthon with previously unrecognized potential for structure-assembly applications, in many cases facilitated through the formation of the robust cyclic head-to-head amide–amide hydrogen-bonded dimer association.

Experimental

The title compounds were synthesized by heating together for 10 min under reflux piperidine-4-carboxamide (isonipecotamide) (1 mmol) with 2-nitrobenzoic acid (1 mmol) [for (I)], 3-nitrobenzoic acid (1 mmol) [for (II)], 4-nitrobenzic acid (1 mmol) [for (III)] or 3,5-dinitrobenzoic acid (1 mmol) [for (IV)] in 50% ethanol–water (50 ml). After concentration to *ca* 30 ml, partial room-temperature evaporation of the hot-filtered solutions gave colourless needles of (I) (m.p. 429 K), colourless prisms of (II) and (III) (m.p. 452 and 537–539 K, respectively), and yellow plates of (IV) (m.p. 473–475 K).

Compound (I)

Crystal data

$C_6H_{13}N_2O^+ \cdot C_7H_4NO_4^-$	$V = 2897.0\ (5)\ Å^3$
$M_r = 295.30$	$Z = 8$
Monoclinic, $C2/c$	Mo $K\alpha$ radiation
$a = 29.035\ (3)\ Å$	$\mu = 0.11\ mm^{-1}$
$b = 9.7660\ (9)\ Å$	$T = 200\ K$
$c = 10.5779\ (12)\ Å$	$0.50 \times 0.26 \times 0.12\ mm$
$\beta = 105.020\ (12)°$	

Table 1
Hydrogen-bond geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N1A—H11A···O11^i	0.941 (17)	1.848 (17)	2.7759 (17)	168.3 (17)
N1A—H12A···O12	0.951 (18)	1.792 (17)	2.7380 (17)	172.5 (13)
N41A—H41A···O41A^{ii}	0.90 (2)	2.00 (2)	2.8978 (19)	174.6 (15)
N41A—H42A···O41A^{iii}	0.878 (16)	2.313 (16)	3.0914 (17)	147.8 (13)

Symmetry codes: (i) $-x+\frac{1}{2}, -y+\frac{3}{2}, -z$; (ii) $-x, -y+1, -z$; (iii) $x, -y+1, z+\frac{1}{2}$.

Data collection

Oxford Gemini-S Ultra CCD area-detector diffractometer	9784 measured reflections
Absorption correction: multi-scan (*CrysAlis Pro*; Oxford Diffraction, 2009)	2832 independent reflections
	2076 reflections with $I > 2\sigma(I)$
$T_{min} = 0.940$, $T_{max} = 0.980$	$R_{int} = 0.029$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.035$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.087$	
$S = 0.93$	
2832 reflections	$\Delta\rho_{max} = 0.15\ e\ Å^{-3}$
206 parameters	$\Delta\rho_{min} = -0.17\ e\ Å^{-3}$

Compound (II)

Crystal data

$C_6H_{13}N_2O^+ \cdot C_7H_4NO_4^-$	$V = 1358.5\ (2)\ Å^3$
$M_r = 295.30$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 14.2504\ (15)\ Å$	$\mu = 0.11\ mm^{-1}$
$b = 6.8276\ (5)\ Å$	$T = 200\ K$
$c = 15.4580\ (17)\ Å$	$0.30 \times 0.20 \times 0.15\ mm$
$\beta = 115.410\ (13)°$	

Data collection

Oxford Gemini S Ultra CCD area-detector diffractometer	9250 measured reflections
Absorption correction: multi-scan (*CrysAlis Pro*; Oxford Diffraction, 2009)	2669 independent reflections
	1982 reflections with $I > 2\sigma(I)$
$T_{min} = 0.948$, $T_{max} = 0.980$	$R_{int} = 0.026$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.038$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.093$	
$S = 1.04$	
2669 reflections	$\Delta\rho_{max} = 0.21\ e\ Å^{-3}$
206 parameters	$\Delta\rho_{min} = -0.20\ e\ Å^{-3}$

Compound (III)

Crystal data

$C_6H_{13}N_2O^+ \cdot C_7H_4NO_4^-$	$V = 1392.1\ (2)\ Å^3$
$M_r = 295.30$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 7.5371\ (6)\ Å$	$\mu = 0.11\ mm^{-1}$
$b = 12.4216\ (12)\ Å$	$T = 200\ K$
$c = 15.0911\ (13)\ Å$	$0.30 \times 0.18 \times 0.15\ mm$
$\beta = 99.848\ (7)°$	

Data collection

Oxford Gemini-S Ultra CCD area-detector diffractometer	14612 measured reflections
Absorption correction: multi-scan (*CrysAlis Pro*; Oxford Diffraction, 2009)	2727 independent reflections
	2279 reflections with $I > 2\sigma(I)$
$T_{min} = 0.952$, $T_{max} = 0.980$	$R_{int} = 0.042$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.035$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.095$	
$S = 1.14$	
2727 reflections	$\Delta\rho_{max} = 0.21\ e\ Å^{-3}$
206 parameters	$\Delta\rho_{min} = -0.19\ e\ Å^{-3}$

Table 2
Hydrogen-bond geometry (Å, °) for (II).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1A—H11$A\cdots$O41A^i	0.97 (2)	1.88 (2)	2.7933 (19)	157 (2)
N1A—H12$A\cdots$O11	0.93 (2)	1.88 (3)	2.7587 (19)	156 (2)
N1A—H12$A\cdots$O12	0.93 (2)	2.36 (2)	3.0599 (19)	132 (2)
N41A—H41$A\cdots$O32^{ii}	0.863 (19)	2.213 (19)	3.068 (2)	171.1 (13)
N41A—H42$A\cdots$O12^{iii}	0.91 (2)	1.98 (2)	2.844 (2)	159 (2)

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

Table 3
Hydrogen-bond geometry (Å, °) for (III).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1A—H11$A\cdots$O11^i	0.938 (15)	1.933 (15)	2.8503 (15)	165.4 (14)
N1A—H12$A\cdots$O12	0.936 (18)	1.808 (17)	2.7278 (15)	167.0 (14)
N41A—H41$A\cdots$O41A^{ii}	0.949 (19)	1.940 (19)	2.8833 (16)	172.3 (14)
N41A—H42$A\cdots$O12^{iii}	0.882 (16)	2.078 (16)	2.9401 (15)	165.5 (14)

Symmetry codes: (i) $-x, -y+2, -z+1$; (ii) $-x, -y+2, -z$; (iii) $x, -y+\frac{3}{2}, z-\frac{1}{2}$.

Compound (IV)

Crystal data

$C_6H_{13}N_2O^+\cdot C_7H_3N_2O_6{}^-$	$\gamma = 100.772\ (8)°$
$M_r = 340.30$	$V = 767.04\ (14)$ Å^3
Triclinic, $P\bar{1}$	$Z = 2$
$a = 5.7159\ (5)$ Å	Mo $K\alpha$ radiation
$b = 11.9970\ (12)$ Å	$\mu = 0.12$ mm^{-1}
$c = 12.6447\ (10)$ Å	$T = 200$ K
$\alpha = 111.370\ (8)°$	$0.30 \times 0.25 \times 0.15$ mm
$\beta = 99.504\ (7)°$	

Data collection

Oxford Gemini-S Ultra CCD area-detector diffractometer	9445 measured reflections
	2996 independent reflections
Absorption correction: multi-scan (*CrysAlis Pro*; Oxford Diffraction, 2009)	2279 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.029$
$T_{min} = 0.967, T_{max} = 0.980$	

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.040$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.092$	
$S = 1.05$	
2996 reflections	$\Delta\rho_{max} = 0.16$ e Å^{-3}
233 parameters	$\Delta\rho_{min} = -0.21$ e Å^{-3}

H atoms involved in hydrogen-bonding interactions were located in difference electron-density maps and were freely refined. The

Table 4
Hydrogen-bond geometry (Å, °) for (IV).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1A—H11$A\cdots$O11^i	0.947 (18)	1.925 (18)	2.822 (2)	157.4 (15)
N1A—H12$A\cdots$O12	0.96 (2)	1.74 (2)	2.696 (2)	173 (2)
N41A—H41$A\cdots$O51^{ii}	0.87 (2)	2.37 (2)	3.141 (2)	147.5 (18)
N41A—H42$A\cdots$O41A^{iii}	0.89 (2)	1.99 (2)	2.877 (2)	175.8 (17)

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

other H atoms were included in calculated positions and refined using a riding-model approximation, with aromatic C—H = 0.93 Å and aliphatic C—H = 0.97–0.98 Å, and with $U_{iso}(H) = 1.2U_{eq}(C)$.

For all compounds, data collection: *CrysAlis Pro* (Oxford Diffraction, 2009); cell refinement: *CrysAlis Pro*; data reduction: *CrysAlis Pro*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008) within *WinGX* (Farrugia, 1999); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *PLATON*.

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