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Solvatomorphism in (*E*)-2-(2,6-dichloro-4-hydroxybenzylidene)-hydrazinecarboximidamide

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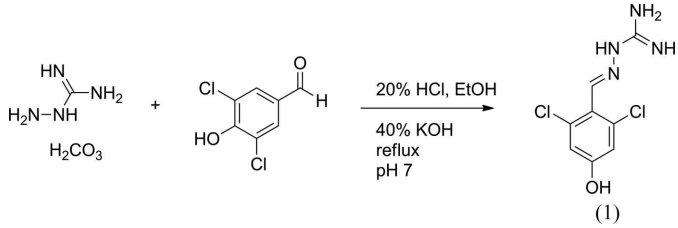
The structures of orthorhombic (*E*)-4-(2-{[amino(iminio)-methyl]amino}vinyl)-3,5-dichlorophenolate dihydrate, $C_8H_8Cl_2N_4O\cdot2H_2O$, (I), triclinic (*E*)-4-(2-{[amino(iminio)methyl]-amino}vinyl)-3,5-dichlorophenolate methanol disolvate, $C_8H_8Cl_2N_4O\cdot2CH_4O$, (II), and orthorhombic (*E*)-amino[(2,6-dichloro-4-hydroxystyryl)amino]methaniminium acetate, $C_8H_9Cl_2N_4O^+\cdot C_2H_3O_2^-$, (III), all crystallize with one formula unit in the asymmetric unit, with the molecule in an *E* configuration and the phenol H atom transferred to the guanidine N atom. Although the molecules of the title compounds form extended chains *via* hydrogen bonding in all three forms, owing to the presence of different solvent molecules, those chains are connected differently in the individual forms. In (II), the molecules are all coplanar, while in (I) and (III), adjacent molecules are tilted relative to one another to varying degrees. Also, because of the variation in hydrogen-bond-formation ability of the solvents, the hydrogen-bonding arrangements vary in the three forms.

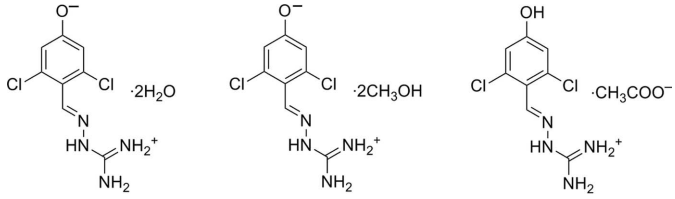
Comment

Solvatomorphism, the counterpart of polymorphism and sometimes called pseudopolymorphism, deals with systems with different crystal structures of the same substance associated with various amounts or types of solvent molecules (Brittain, 2010; Seddon, 2004; Desiraju, 2004; Bernstein, 2005; Nangia, 2006). Unlike polymorphs, solvatomorphs not only have different molecular arrangements but also possess diverse molecular compositions due to the presence of solvent molecules. Like polymorphism, solvatomorphism is also commonly observed in organics and is of great significance in pharmaceuticals and materials. (*E*)-2-(2,6-Dichloro-4-hydroxybenzylidene)hydrazinecarboximidamide, (1), is a metabolite of gaunabenz, an antiprion drug for the treatment of neurodegenerative disorders in mammals and also a potent tranquilizer



(1)

used to sedate horses (Fluck *et al.*, 1983). In this report, we describe three crystal structures of (1) which include two solvates, (I) and (II), and one acetate salt, (III) (Fig. 1).



(I) (II) (III)

Our analysis establishes that (I) is orthorhombic (space group *Pbca*) (Fig. 2), (II) is triclinic (space group $P\overline{1}$) (Fig. 3) and (III) is again orthorhombic (space group *Pbca*) (Fig. 4), with one formula unit in the asymmetric unit in each case. In the water, (I), and methanol, (II), solvates, (1) exists as a zwitterion with the phenol proton transferred to the guanidine N atom. In the acetate salt, (III), (1) is protonated by the acetic acid and is thus positively charged. The molecules in the three forms are all in the *E* configuration and are nearly flat.

Without considering the participation of the solvent molecules, all three forms show the same *C*(11) hydrogen-bonding

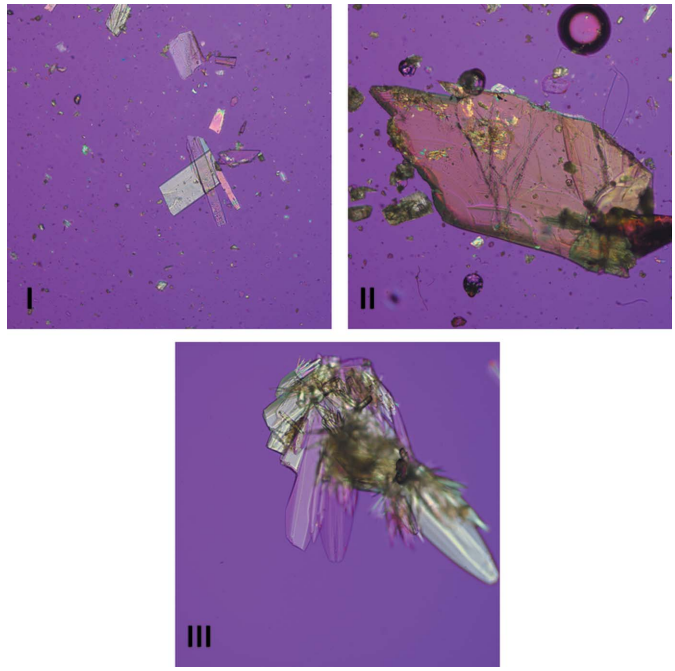


Figure 1
Representative crystals of (I), (II) and (III).

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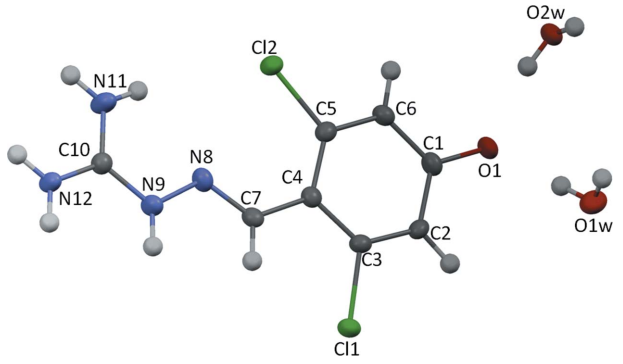

Figure 2
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

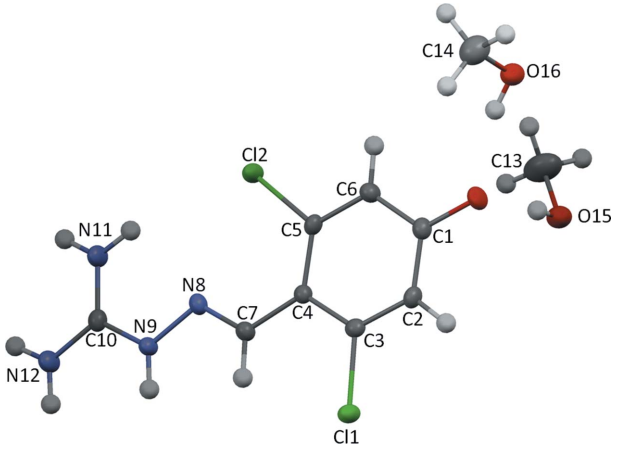

Figure 3
The molecular structure of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

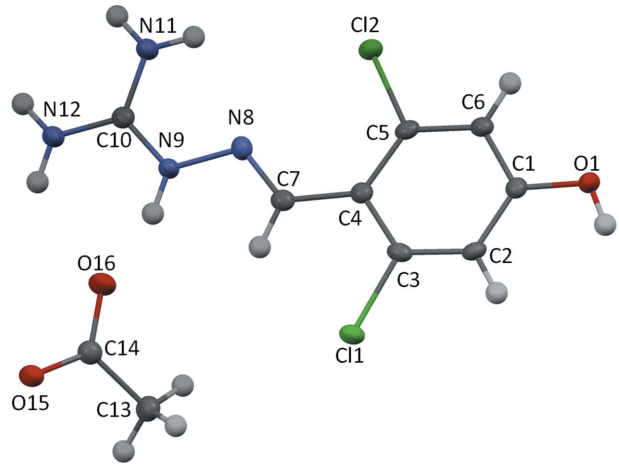

Figure 4
The molecular structure of (III), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

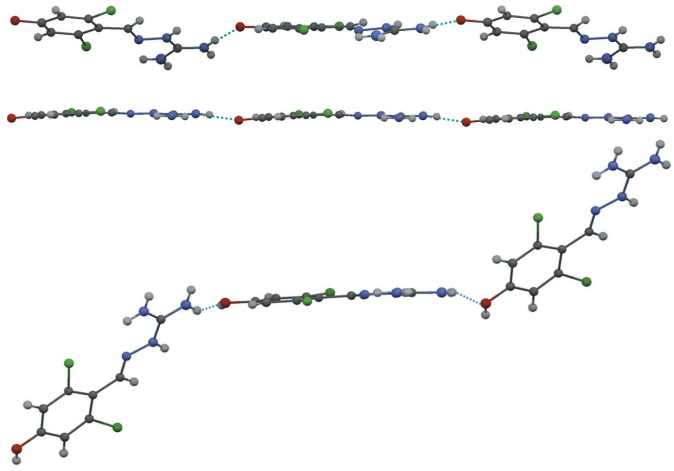

Figure 5
Crystal packing of (I) (top), (II) (middle) and (III) (bottom) without considering the solvent molecules and acetate counter-ion.

pattern in the graph-set concept (Bernstein *et al.*, 1995), *i.e.* one-dimensional chains based on the hydrogen bond between the phenol O atom and a guanidine NH group [for example, N12—H12*B*···O1^{i} in (I); symmetry code: (i) x, $-y+\frac{1}{2}$, $z+\frac{1}{2}$] (Tables 1–3). The relative positions of the molecules in the chains differ, however, with molecules in the chain of (II) in the same plane, and molecules in the chains of (I) and (III) tilted toward each other to different degrees as indicated by the dihedral angles between the arene rings on adjacent molecules in the three forms: *ca* 22° for (I), 0° for (II) and 55° for (III) (Fig. 5).

Since compound (1) is associated with different guest molecules in the three forms, the packing is distinct in each case because of different hydrogen-bonding patterns. In (I), there are two equivalents of water, and water is both a hydrogen-bond donor and acceptor (Fig. 6). When acting as a hydrogen-bond donor, one water molecule (O1*W*) forms hydrogen bonds with both O1 of the host molecule and O2*W* of the other water molecule [O1*W*—H2*W*1···O2*W*^{iii}; symmetry code: (iii) $x-\frac{1}{2}$, $-y+\frac{1}{2}$, $-z+1$] (Table 1); while serving as a hydrogen-bond acceptor, O1*W* accepts H atoms from both N11 and N12 from the guanine group of the host molecule [N11—H11*A*···O1*W*^{ii} and N12—H12*A*···O1*W*^{ii}; symmetry code: (ii) $-x+1$, $y-\frac{1}{2}$, $-z+\frac{3}{2}$]. When the second water molecule (O2*W*) acts as a hydrogen-bond donor, it links two adjacent host molecule chains through hydrogen bonds with O1; when it works as a hydrogen-bond acceptor, it forms hydrogen bonds with the other water molecule and N9—H9 of the host molecule (N9—H9···O2*W*^{i}). Overall, the crystal structure can be viewed as parallel one-dimensional chains of the host molecules along the *a* axis bridged by water molecules.

Form (II) contains two equivalents of another solvent molecule, *i.e.* methanol. The O—H group of methanol similarly participates in hydrogen bonds as both a donor and acceptor (Fig. 7). The first methanol molecule connects two adjacent chains by using the O15—H15 group as a hydrogen-bond donor to O1 of the host molecule from one chain and meanwhile utilizing O15 as a hydrogen-bond acceptor to accept H atoms from both N9 and N12 of the host molecule from another chain [N9—H9···O15^{i} and N12—H12*B*···O15^{i}; symmetry code: (i) $-x+2$, $-y+2$, $-z+1$] (Table 2). The second methanol molecule forms hydrogen bonds with O1 as a

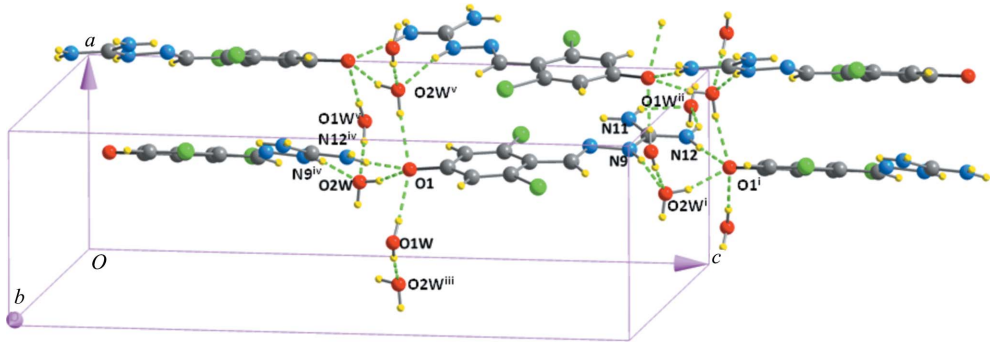

Figure 6
The crystal packing of (I); for details of symmetry codes see Table 1. Additionally: (iv) $x, -y+\frac{1}{2}, z-\frac{1}{2}$; (v) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$.

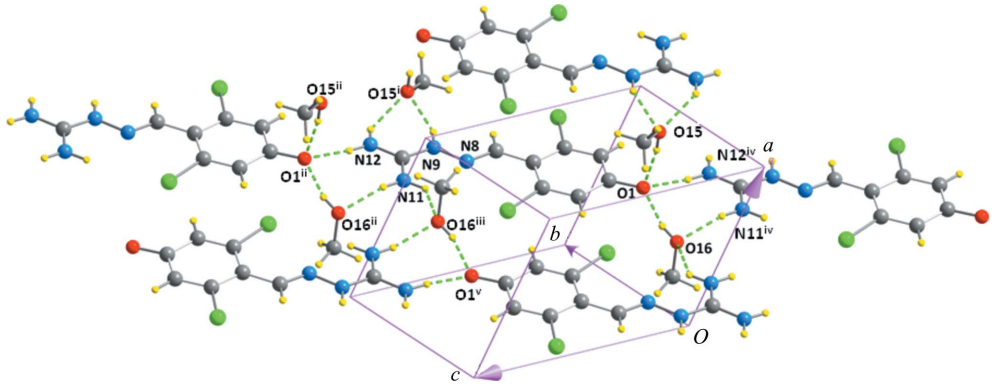

Figure 7
The crystal packing of (II); for details of symmetry codes see Table 2. Additionally: (iv) $x, y-1, z-1$; (v) $x+1, y+1, z+1$.

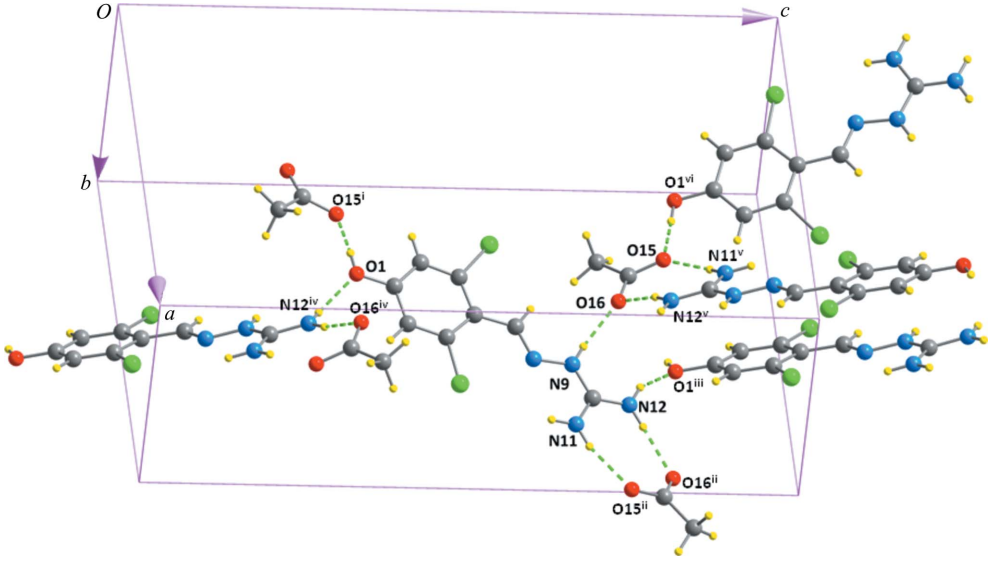

Figure 8
The crystal packing of (III); for details of symmetry codes see Table 3. Additionally: (iv) $x, -y+\frac{1}{2}, z-\frac{1}{2}$; (v) $-x+2, y-\frac{1}{2}, -z+\frac{3}{2}$; (vi) $-x+\frac{3}{2}, -y, z+\frac{1}{2}$.

donor and N11 as an acceptor [N11—H11*A*···O16^{ii}; symmetry code: (ii) $x, y+1, z+1$]. Similar to (I), the crystal structure of (II) also can be considered as parallel one-dimensional chains of (1) linked by methanol molecules.

In the 1:1 organic acetate salt (III), compound (1) is protonated at O1. Both O atoms of the acetate act as hydrogen-bond acceptors (Fig. 8). O15 accepts hydrogen bonds from O1 and N11 from different cations [O1—H1···O15^{i} and N11—H11*A*···O15^{ii}; symmetry codes: (i) $-x+\frac{3}{2}, -y, z-\frac{1}{2}$; (ii) $-x+2, y+\frac{1}{2}, -z+\frac{3}{2}$] and O16 also accepts hydrogen bonds from N9 and N12 of two different cations (N9—H9···O16 and N12—H12*A*···O16^{ii}). Thus, one acetate

anion bridges three chains through hydrogen bonding with one cation in each chain. These undulating chains also run parallel in space.

Attempts were made to obtain good-quality crystals of an unsolvated and/or a neutral form of (1) without success. A Cambridge Structural Database (CSD, version 5.32; Allen, 2002) search resulted in six structurally related hits, none of which was found to form multiple solvates. Among them, the complex chloro(β-resorcylidene aminoguanidine)copper(II) tetrahydrate (refcode RIYMIV; Onuska *et al.*, 1996) is similar to (III) with the O atom protonated and a hydrogen bond existing between the O atom and a guanine N atom, leading to one-dimensional chains. In *N*-(2,4-dimethoxybenzylideneamino)guanidinium dihydrogenphosphate (refcode DAYHOB; Dinçer *et al.*, 2005), 7-amino-5-(*p*-tolyl)-4-phenyl-2-(*p*-methoxyphenyl)-3,4-dihydroimidazo[1,5-*b*]pyridazine (refcode LORRAL; Kolos *et al.*, 1999), 2,4,6-trimethoxybenzylideneaminoguanidinium chloride (refcode MELBIO; Bats & Hoffmann, 2000) and (4-methoxy-3-nitrobenzylideneamino)guanidinium chloride (refcode RIGKOI; Ring *et al.*, 2007), the corresponding O atom is methylated. The chain structure is replaced by a dimer based on two hydrogen bonds between methoxy O and guanine N atoms [graph-set notation $R_2^2(22)$] in DAYHOB, and no hydrogen bonds form between the corresponding atoms in the other three compounds. In 2-methyl-4-hydroxybenzaldehyde 2-imidazolin-2-yl-hydrazone hydrochloride monohydrate (refcode FAJHED; Atfani *et al.*, 1986), the O atom is protonated as in (III), and the two N atoms in the guanine group are integrated into a five-membered ring. Again, a one-dimensional chain similar to that in (III) is observed. Thus, it seems this hydrogen-bonding motif is a common feature of (*E*)-2-(4-hydroxybenzylidene)hydrazinecarboximidamides and is likely due to the relatively high strength of the N—H···O interaction.

Our work has thus shown that compound (1) can form at least two solvated crystalline forms and salt formation with acids should be expected as indicated by the existence of an acetate salt. Owing to the presence of different solvents or acids, the crystals have diverse packing and hydrogen-bond arrangements.

Experimental

Compound (1) was synthesized according to a modified literature procedure (Li *et al.*, 2010; Holzer *et al.*, 1992; Gug *et al.*, 2010). To a solution of HCl (20%, 1 ml) in ethanol (17 ml) was added 2,6-dichloro-4-hydroxybenzaldehyde (0.5g, 2.62 mmol), followed by the slow addition of a solution of aminoguanidine bicarbonate in H_2O (3 ml). After liberation of CO_2, the solution was heated to reflux and then cooled to room temperature. An aqueous solution of 40% KOH (8.5 ml) was then added and the solution was refluxed for 10 min. Afterward, the solution was left stirring overnight at room temperature. To quench the reaction, the pH was adjusted to 7 using 5 *M* NaOH. $NaHCO_3$ (15 ml) and dichloromethane (15 ml) were added and the mixture was stirred for 30 min. The product precipitated as an orange powder. Crystals of (I), (II) and (III) were grown from solutions of (1) in acetone, methanol and acetic acid, respectively.

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

D—H···A	D—H	H···A	D···A	D—H···A
N9—H9···O2W^{i}	0.88	1.99	2.863 (3)	169
N11—H11A···O1W^{ii}	0.88	2.05	2.829 (3)	147
N11—H11B···Cl2	0.88	2.96	3.817 (3)	166
N12—H12A···O1W^{ii}	0.88	2.13	2.888 (3)	143
N12—H12B···O1^{i}	0.88	1.98	2.854 (3)	175
O1W—H1W1···O1	0.84 (2)	1.96 (2)	2.800 (3)	178 (4)
O1W—H2W1···O2W^{iii}	0.80 (2)	1.97 (2)	2.751 (3)	166 (3)
O2W—H1W2···O1	0.82 (2)	1.83 (2)	2.616 (3)	158 (3)
O2W—H2W2···O1^{iii}	0.82 (2)	2.00 (2)	2.819 (3)	171 (3)

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

Compound (I)

Crystal data

$C_8H_8Cl_2N_4O\cdot 2H_2O$
M_r = 283.12
Orthorhombic, *Pbca*
a = 6.8802 (1) Å
b = 16.7892 (4) Å
c = 21.9240 (5) Å
V = 2532.51 (9) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.52 mm^{-1}
T = 90 K
0.40 × 0.10 × 0.03 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.820, T_{max} = 0.985
5390 measured reflections
2898 independent reflections
1692 reflections with $I > 2\sigma(I)$
R_{int} = 0.061

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.142
S = 1.05
2898 reflections
167 parameters
6 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.66 e Å^{-3}
$\Delta\rho_{min}$ = −0.41 e Å^{-3}

Compound (II)

Crystal data

$C_8H_8Cl_2N_4O\cdot 2CH_4O$
M_r = 311.17
Triclinic, $P\overline{1}$
a = 7.0255 (1) Å
b = 10.0683 (2) Å
c = 11.7580 (2) Å
α = 112.3416 (8)°
β = 93.9597 (9)°
γ = 107.4271 (9)°
V = 718.02 (2) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.46 mm^{-1}
T = 90 K
0.40 × 0.30 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.837, T_{max} = 0.913
6495 measured reflections
3269 independent reflections
2673 reflections with $I > 2\sigma(I)$
R_{int} = 0.027

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.095
S = 1.06
3269 reflections
176 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O15—H15···O1	0.84	1.83	2.6640 (18)	171
O16—H16···O1	0.84	1.83	2.6464 (17)	163
N9—H9···O15^{i}	0.88	2.02	2.8109 (18)	149
N12—H12A···O1^{ii}	0.88	1.89	2.7665 (19)	173
N12—H12B···O15^{i}	0.88	2.23	2.969 (2)	142
N11—H11A···O16^{ii}	0.88	1.99	2.8596 (19)	167
N11—H11B···O16^{iii}	0.88	2.57	3.1702 (19)	127

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

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O15^{i}	0.84	1.70	2.5336 (19)	175
N9—H9···O16	0.88	1.91	2.730 (2)	153
N11—H11A···O15^{ii}	0.88	2.04	2.900 (2)	167
N12—H12A···O16^{ii}	0.88	1.96	2.828 (2)	168
N12—H12B···O1^{iii}	0.88	2.05	2.868 (2)	153

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

Compound (III)

Crystal data

$C_8H_9Cl_2N_4O^+\cdot C_2H_3O_2^-$
M_r = 307.14
Orthorhombic, *Pbca*
a = 15.9630 (1) Å
b = 7.4060 (2) Å
c = 21.7930 (3) Å
V = 2576.41 (8) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.51 mm^{-1}
T = 90 K
0.40 × 0.20 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.821, T_{max} = 0.950
5505 measured reflections
2952 independent reflections
2375 reflections with $I > 2\sigma(I)$
R_{int} = 0.020

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.100
S = 1.09
2952 reflections
174 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}

For (II) and (III), H atoms were found in difference Fourier maps and were subsequently placed in idealized positions, with O—H = 0.84 Å, N—H = 0.88 Å, Csp^2—H = 0.95 Å and Csp^3—H = 0.98 Å for methyl H atoms. For (I), H atoms, except for those of the water molecules, were found in difference Fourier maps and were subsequently placed in idealized positions, with N—H = 0.88 Å, Csp^2—H = 0.95 Å and Csp^3—H = 0.98 Å for methyl H atoms. For (I), the water H atoms were refined with restraints of O—H = 0.82 (2) Å and H···H = 1.30 (3) Å. Isotropic displacement parameters for all H atoms were fixed at U_{iso}(H) = 1.5U_{eq}(parent atoms) for hydroxy and methyl H atoms and 1.2U_{eq}(parent atoms) for all others.

For all compounds, data collection: *COLLECT* (Nonius, 1998); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXL97* and local procedures.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ3285). Services for accessing these data are described at the back of the journal.

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