2,3-Dimethoxy-10-oxostrychnidinium 3-carboxybenzoate trihydrate: the 1:1 proton-transfer compound of brucine with isophthalic acid

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The structure of the title, compound $C_{23}H_{27}N_2O_4^+ \cdot C_8H_5O_4^- \cdot 3H_2O$, has been determined at 130 K. The hydrogen isophthalate anions and the water molecules (one of which is disordered over two approximately equal sites) associate through extensive hydrogen-bonded interactions, including those with the common undulating brucinium cation layer substructures, forming a three-dimensional framework structure.

Comment

The Strychnos alkaloids strychnine and brucine have mostly been used to resolve enantiomorphic mixtures of chiral compounds, and the number of crystal structures of both salts and adducts of strychnine and brucine with such compounds reflects this. However, these alkaloids form salts equally well with achiral acids, but as with the chiral compounds, formation of good crystalline products is largely a hit-or-miss process. Oshikawa *et al.* (2002) observed the selectivity of brucine for *meta*-substituted benzoic acids, so we have continued that investigative theme, preparing and characterizing a number of brucine compounds with substituted benzoic acid analogues. Structurally characterized examples include the brucinium salts with 3-nitrophthalic acid (Smith, Wermuth *et al.*, 2005), and 5-nitrosalicylic acid, 3,5-dinitrosalicylic acid and 5-sulfo-salicylic acid (Smith *et al.*, 2006a). Strychnine demonstrated a lesser tendency to form crystalline salts with this same acid series but did give good crystals with 5-nitrosalicylic acid and 3,5-dinitrosalicylic acid (Smith, Wermuth & White, 2005).

(I)

We also reacted isophthalic acid (1,3-benzenedicarboxylic acid) in a 1:1 stoichiometric ratio with both brucine and strychnine in 80% propan-2-ol–water, this solvent being employed instead of the 80% ethanol–water used in our normal preparative procedure. This was also done to test the observation by Sada *et al.* (1998) that the use of propan-2-ol promotes the crystallization of brucinium carboxylate compounds, often with incorporation of propan-2-ol solvent
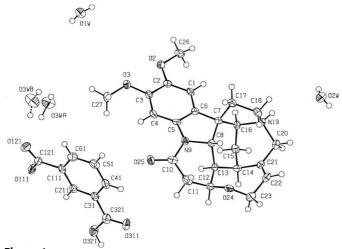
Figure 1
The asymmetric unit of (I), with the atom-numbering scheme. Molecules O3WA (site occupancy factor 0.57) and O3WB (site occupancy factor 0.43) represent two disordered sites for water molecule 3. Displacement ellipsoids are shown at the 40% probability level.

molecules. However, the product from our reaction of isophthalic acid with brucine was a hydrate, (I), and its structure is reported here. The parallel reaction employing strychnine gave no crystalline product.

In compound (I), protonation occurs, as expected, at N19 of the brucine cage (Fig. 1). Setting the absolute configuration for (I) according to that determined for the parent strychnine (Peerdeman, 1956) gives the overall Cahn–Ingold–Prelog stereochemistry of the cation as C7(S), C8(S), C12(S), C13(R), C14(R), C16(S), N19(S). The brucinium cations form into the previously described undulating sheet host substructures (Gould & Walkinshaw, 1984; Białońska & Ciunik, 2004a,b), with a dimeric repeat period along the direction of propagation (the a cell dimension) of 12.4560 (9) Å and a brucine molecule offset angle (α; Smith *et al.*, 2006b) of *ca* 120 ° (Fig. 2). These values are consistent with those for similarly structured brucine compounds (*e.g.* Gould & Walkinshaw, 1984; Smith, Wermuth *et al.*, 2005). The hydrogen isophthalate anions and the three water molecules {one of which is disordered over two close sites, O3WA [site occupancy factor 0.57 (2)] and O3WB [site occupancy factor 0.43 (2)]}, occupy the interstitial spaces in the substructure and are hydrogen-bonded to it through both the brucine aminium and carbonyl groups (Table 1), giving a three-dimensional framework structure. Interactions include a strong hydrogen bond between the carboxylic acid group of the anion (O321) and a water molecule (O1W), and a cyclic water···water association involving O2W across a twofold rotation axis.

Experimental

The title compound, (I), was synthesized by heating 1 mmol quantities of brucine tetrahydrate and isophthalic acid (1,3-benzene-dicarboxylic acid) in propan-2-ol–water (80:20, 50 ml) for 10 min under reflux. After concentration to *ca* 30 ml, partial room-temperature evaporation of the hot-filtered solution gave large colourless prisms (m.p. 454.6–457.6 K).
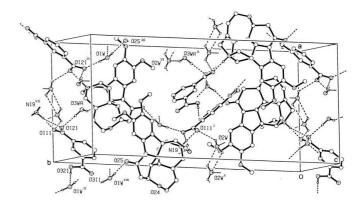

Figure 2
A perspective view of the packing of (I) in the unit cell. Hydrogen-bonding associations are shown as broken lines. Interactions for the disordered water molecule O3WB have been omitted. [See Table 1 for symmetry codes (i)–(vi); (vii) $-x + \frac{1}{2}, y + \frac{1}{2}, -z + 1$; (viii) $x - 1, y, z$; (ix) $-x + 1, -y + 1, z - 1$; (x) $x + \frac{1}{2}, -y + \frac{3}{2}, -z + 1$.]

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

D—H···A	D—H	H···A	D···A	D—H···A
N19—H19···O111^i	0.91 (3)	1.73 (3)	2.629 (3)	173 (4)
N19—H19···O121^i	0.91 (3)	2.57 (4)	3.217 (3)	129 (3)
O321—H321···O1W^{ii}	0.92 (6)	1.73 (6)	2.646 (3)	178 (7)
O1W—H11W···O25^{iii}	0.90 (3)	1.95 (3)	2.818 (3)	162 (4)
O1W—H12W···O121^{iv}	0.90 (3)	1.95 (3)	2.841 (3)	179 (4)
O2W—H21W···O111^i	0.85 (5)	2.19 (5)	2.780 (4)	126 (5)
O2W—H22W···O2W^v	0.85 (6)	2.42 (6)	2.817 (5)	110 (5)
O3WA—H31W···O121	0.91 (6)	1.91 (6)	2.822 (10)	178 (8)
O3WA—H32W···O2W^{vi}	0.90 (7)	1.85 (7)	2.705 (7)	157 (6)
O3WB—H33W···O121	0.90 (7)	1.77 (7)	2.667 (10)	179 (5)
O3WB—H34W···O2W^{vi}	0.89 (7)	1.86 (7)	2.752 (11)	179 (5)

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

H atoms potentially involved in hydrogen-bonding interactions were located by difference methods and their positional and isotropic displacement parameters were refined. Other H atoms were included in the refinement in calculated positions, with C—H(aromatic) = 0.95 Å and C—H(aliphatic) = 0.98–1.00 Å, and treated using a riding model, with $U_{iso}(H) = 1.2U_{eq}(C)$. The atom-numbering scheme employed for the brucinium cation cage in (I) follows the original Robinson convention for strychnine (Holmes, 1952). The absolute configuration determined for the parent strychnine (Peerdeman, 1956) was invoked.

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 1999); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997) in *WinGX* (Farrugia, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997) in *WinGX*; molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *PLATON*.

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