Brucinium 2-carboxy-6-nitrophthalate dihydrate: the 1:1 proton-transfer compound of brucine with 3-nitrophthalic acid

In the title compound (systematic name: 2,3-dimethoxy-10-oxostrychnidinium 2-carboxy-6-nitrophthalate dihydrate), \( \text{C}_{23}\text{H}_{27}\text{N}_{2}\text{O}_{4}^+\text{C}_8\text{H}_4\text{NO}_6^-\text{H}_2\text{O} \), the carboxylic acid and carboxylate groups of the hydrogenphthalate anions form head-to-tail catemeric chains of strong intermolecular O—H···O hydrogen bonds [O—H···O distance = 2.563 (5) Å] along the \( 2_1 \) screw axis parallel to the \( a \) axis. The chains further associate with the water molecules, forming sheet structures parallel to (010). The protonated N atom at the 19-position of the brucine molecule forms a peripheral intermolecular hydrogen bond with the carboxylate group of the anion.

Comment

The alkaloids brucine and strychnine have been employed on a hit-or-miss basis for enantiomeric separation of racemic mixtures of chiral organic compounds since the time of Fischer (1899), while the crystal structures of their compounds with chiral organic compounds have allowed determination of the absolute configuration, based on the known absolute configuration of the parent strychnine (Peerdeman, 1956). These structures include the original Fischer-type proton-transfer compounds with \( N \)-benzoyl protected amino acids (Gould & Walkinshaw, 1984; Gould et al., 1985). Although regarded mainly as agents for complex formation with chiral molecules, brucine and strychnine give complexes equally well with achiral species, the formation and separation process being clearly identified as one of molecular recognition (Gould & Walkinshaw, 1984; Gould et al., 1985; Dijksma et al., 1998; Oshikawa et al., 2002; Bálońska & Ciunik, 2004a). Brucine commonly forms regular undulating parallel-chain host structures, which extend along \( 2_1 \) screw axes in the crystal structure (Gould & Walkinshaw, 1984; Dijksma et al., 1998), whereas with strychnine, such regularity is not usually found. The compatible guest species occupy the interstitial cavities and hydrogen-bond with the brucine host structure, while water or other molecules of solvation may also be accommodated in the channels. Thus the solvates of brucine, such as brucine—ethanol—water (1/1/2) (Glover et al., 1985), brucine—propan-2-ol—water (1/1/2) (Bálońska & Ciunik, 2004b) and brucine—acetone (1/1) (Bálońska & Ciunik, 2004b), may be considered as host–guest compounds.

Our particular interest lies in the hydrogen bonding in proton-transfer compounds of achiral aromatic carboxylic acids with Lewis bases, and both brucine and strychnine (\( pK_{a2} = 11.7 \)) presented interesting possibilities for a molecular recognition study. A limited number of crystal structures of proton-transfer compounds of mostly brucine with achiral carboxylic acids have been reported, e.g. with fumaric and maleic acids (brucine) (Dijksma et al., 1998), 4-hydroxy-
benzoic acid (brucine) (Sada et al., 1998), 3-nitrobenzoic acid (brucine) (Oshikawa et al., 2002) and 2,2'-dimethoxy-1-oxonaphthalene-4-carboxylic acid (brucine) (Cheung et al., 1999). Similar proton-transfer brucine compounds with 2,2'-bis(3-phenyl-1-naphthol)phosphoric acid (Bao et al., 1996), and 4-nitrophenol (Guo et al., 2001) and 8-aminonaphthalene-2-sulfonic acid (strychnine) (Smith, Wermuth, Healy & Young, 2005), have also been reported. Oshikawa et al. (2002) observed that brucine had a recognitive affinity for the meta-substituted nitro-, chloro- and bromo-substituted benzoic acids but not the ortho- or para-isomers. This fact prompted us to look at the reactions of substituted salicylic acids. We subsequently prepared and established the crystal structures of the brucinium compounds with 5-nitrosalicylic acid, 3,5-dinitrosalicylic acid and 5-sulfosalicylic acid (Smith, Wermuth, & Healy, 2005), as well as those of the strychninium compounds with 5-nitrosalicylic acid and 3,5-dinitrosalicylic acid (Smith, Wermuth & White, 2005).

3-Nitrophthalic acid (NPA) may be considered a special example of a meta-substituted benzoic acid and has been reported to a limited extent from structural studies on its proton-transfer compounds, e.g. the 3-nitrohydrogenphthalates of 3-iodoaniline (Glidewell et al., 2005) and 4-iodoaniline (Glidewell et al., 2003b) (both 1:1), and the (1:1) piperazine salt (Guo, 2004), in which the phthalate is dianionic. We therefore reacted 3-nitrophthalic acid with brucine in 50% ethanol–water, resulting in the formation of large orange–yellow crystals of the title compound, (I). No crystalline product was given in a parallel reaction with strychnine.

In (I), the expected proton transfer to N19 of the brucine ring occurs (Fig. 1). The introduction of a new chiral centre at N19 (S) gives for the brucinium cations the overall Cahn–Ingold–Prelog configuration (Eliel, 1962) as C7(S), C8(S), C12(S), C13(R), C14(R), C16(S), N19(S), common to all proton-transfer compounds of both brucine and strychnine. The brucinium donor group (N19) then forms a single cation–anion hydrogen bond (Table 1) with one of the carboxylate O-atom acceptors of the deprotonated acid group at C2 of the hydrogenphthalate anion. These anions form a two-dimensional hydrogen-bonding network parallel to (010) (Figs. 2 and 3) comprising primary head-to-tail catemeric hydrogen-bonded carboxylic acid–carboxylate chains along the a axis (O11P—H11P ... O22P; for symmetry code, see Table 1), together with water–carboxylate and water–water interactions. There are no intermolecular associations involving O-atom acceptors of the nitro group or the second carboxylic acid O atom (O12P). The brucinium cations are peripherally attached to the hydrogen-bonded sheet structures via an N—H...O hydrogen bond. The organic cations
and anions lie approximately parallel to the (001) plane. This is consistent with the perfect cleavage of (I) across the prism axis (c axis).

Within the anion in (I), the structural features are similar to those found in the known 3-nitrophthalate salts (Glidewell et al., 2003a, 2005). The deprotonated C2 carboxylate group is approximately perpendicular to the benzene ring [C1P–C2P–C21P–O22P = 102.1 (5)°], while the C1 carboxylic acid group is essentially coplanar [C2P–C1P–C11P–O11P = 178.3 (4)°]. However, unlike the parent acid (Glidewell et al., 2003a), where the C3 nitro group is also almost coplanar with the benzene ring, in (I) this group is inclined [C2P–C3P–N31P–O32P = 152.3 (5)°].

**Experimental**

The title compound (I) was synthesized by heating 1 mmol quantities of brucine and 3-nitrophthalic acid (NPA) in 50% ethanol–water (50 ml) for 10 min under reflux. After concentration to ca 30 ml, partial room-temperature evaporation of the hot-filtered solution gave yellow–orange pseudo-hexagonal prisms of (I) (m.p. 491.4–494.4 K).

**Crystal data**

C24H16N6O8•C8H4NO6•2H2O

M_r = 641.62

Orthorhombic, P2_12_12_1

a = 12.7001 (14) A

b = 32.015 (5) A

c = 7.3041 (19) A

V = 2969.8 (10) A^3

Z = 4

D_x = 1.435 Mg m^{-3}

Data collection

Rigaku AFC-7R diffractometer

ω/2θ scans

Absorption correction: none

5089 measured reflections

3974 independent reflections

2953 reflections with F^2 > 2σ(F^2)

R_int = 0.028

Refinement

Refinement on F^2

R[F^2 > 2σ(F^2)] = 0.065

wR(F^2) = 0.179

S = 1.17

3974 reflections

424 parameters

H atoms treated by a mixture of independent and constrained refinement

H atoms involved in hydrogen-bonding interactions were located in difference-density maps, but with the exception of atoms H11P and H19 their positional and isotropic displacement parameters were not refined. Other H atoms were positioned geometrically and treated as riding in the refinement, with Uiso(H) = 1.2Ueq(C) (C–H = 0.95–0.98 Å and O–H = 0.89–1.01 Å). The atom-numbering scheme (Fig. 1) follows the original Robinson convention (Holmes, 1952). Friedel-pair reflections were merged, since the anomalous scattering effect was negligible. The absolute configuration determined for the parent strychnine (Peerdeman, 1956) was invoked, giving for the protonated species the overall Cahn–Ingold–Prelog absolute stereochemistry [C7(S), C8(S), C12(S), C13(R), C14(R), C16(S), N19(S)].

Data collection: MSC-AFCF Diffractometer Control Software (Molecular Structure Corporation, 1999); cell refinement: MSC-AFCF Diffractometer Control Software; data reduction: TEXSAN for Windows (Molecular Structure Corporation, 1999); program(s) used to solve structure: SIR92 (Altomare et al., 1994); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: PLATON (Spek, 2003); software used to prepare material for publication: PLATON.

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**References**


