Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Pseudopolymorphism in brucine: brucine–water (1/2), the third crystal hydrate of brucine

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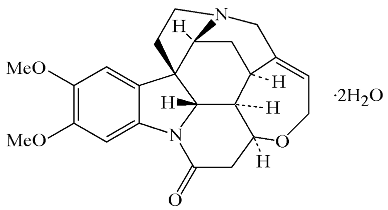
Received 20 May 2007
Accepted 2 July 2007
Online 26 July 2007

The structure of a third pseudopolymorphic hydrate of brucine, brucine–water (1/2) [systematic name: 2,3-dimethoxystrychnidin-10-one–water (1/2)], $C_{23}H_{26}N_2O_4\cdot 2H_2O$, has been determined at 130 K. The asymmetric unit comprises two independent brucine molecules and four water molecules of solvation. The four water molecules form uncommon cyclic hydrogen-bonded homomolecular $R_4^4(8)$ tetramer rings, which then form primary hydrogen-bonded chain substructures extending down the 2_1 screw axis in the unit cell. The two brucine molecules are linked peripherally to these substructures by either single $O-H\cdots N_{brucine}$ or asymmetric three-centre $O-H\cdots O_{brucine}$ hydrogen bonds.

Comment

The common crystalline form of the alkaloid brucine is a tetrahydrate [brucine–water (1/4)], and we have completed the structure determination of this and another pseudopolymorphic hydrate, brucine–water (1/5.25), obtained from the attempted preparation of a brucine adduct with urea (Smith *et al.*, 2006*a*). Other crystallographically characterized brucine



(I)

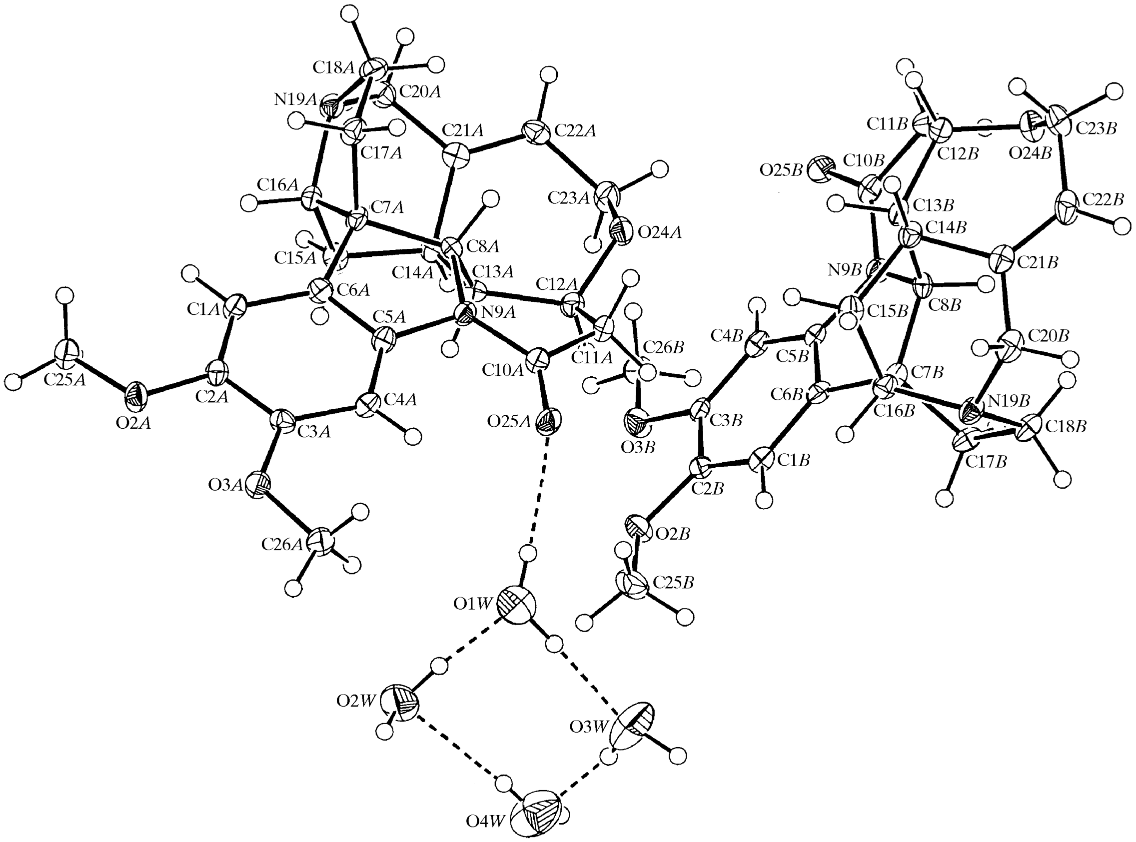


Figure 1
The molecular configuration and atom-numbering scheme for the two brucine molecules (*A* and *B*) and the four water molecules of solvation in the asymmetric unit in (I). The hydrogen bonding in the cyclic $R_4^4(8)$ tetrameric water units and the intra-unit hydrogen bonds are shown as dashed lines. Non-H atoms are shown as 40% probability displacement ellipsoids.

DOI: 10.1107/S0108270107032295

pseudopolymorphs include anhydrous brucine, brucine–acetone (1/1) and brucine–2-propanol–water (1/1/2) (Białońska & Ciunik, 2004*a*), and brucine–ethanol–water (1/1/2) (Glover *et al.*, 1985). The 2-propanol–water and ethanol–water solvates are isomorphous.

In a number of these solvate structures, as well as in the proton-transfer compounds of brucine, it has been recognized (Gould & Walkinshaw, 1984; Białońska & Ciunik, 2004*b*; Smith *et al.*, 2006*a*,*b*) that the brucine species form regular undulating parallel or antiparallel host sheet substructures, accommodating the guest molecules in the interstitial cavities. Thus, molecules of solvation are similarly incorporated and associated through hydrogen bonding. In the orthorhombic $P2_12_12_1$ or monoclinic $P2_1$ examples, the presence of a *ca* 12.5 Å unit-cell repeat along a crystallographic 2_1 screw axis was reasonably indicative of this characteristic substructure, *e.g.* in brucine–2-propanol–water (1/1/2) (12.37 Å; Białońska & Ciunik, 2004*a*) and brucine–ethanol–water (1/1/2) (12.34 Å; Glover *et al.*, 1985) (both $P2_12_12_1$), or in the proton-transfer example brucinium D-glucuronate (12.7 Å, $P2_1$; Dijksma *et al.*, 1998). In examples where the *ca* 12.5 Å/$P2_1$ cell parameter/space group combination is not found, the characteristic structuring is usually absent, *e.g.* brucine–acetone (1/1) (7.14 Å, $P2_1$) in the present set of brucine solvates (see Table 2); brucine–water (1/4) (11.53 Å, $P2_12_12_1$), in which the structure is present, is the exception. On the basis of this generalization, the structure of the monoclinic dihydrate, *viz*. brucine–water (1/2), (I), obtained from the attempted preparation of a brucine–diethanolamine adduct in 95% ethanol, was not expected to have the structuring (with a *b* cell length of *ca* 7.45 Å; $P2_1$). This type of structuring was in fact not found, distinguishing the structure from those of brucine–water (1/4) and brucine–water (1/5.25) (Smith *et al.*, 2006*a*).

In (I), the asymmetric unit comprises two independent brucine molecules and four water molecules of solvation. The two brucine molecules (*A* and *B*; Fig. 1) have the overall Cahn–Ingold–Prelog absolute configuration [C7(*R*), C8(*S*), C12(*S*), C13(*R*), C14(*R*), C16(*S*)], as found in strychnine (Peerdeman, 1956). Because of the rigid nature of the brucine molecular cage, both molecules, as expected, are conformationally identical, including the methoxy substituents at C2 and C3, which in all brucine structures lie essentially in the plane of the benzene ring. In the efflorescent brucine–water (1/5.25) structure, the asymmetric unit also comprises two independent brucine molecules together with 10.5 molecules of solvent water, some of these having split-occupancy sites. However, unlike this structure, in which one set of brucine molecules forms the common undulating sheet substructure, in (I) there is no such structuring. Instead, the water molecules dominate the structure assembly, forming uncommon cyclic hydrogen-bonded tetramer units (graph set $R_4^4(8)$; Etter *et al.*, 1990; Bernstein *et al.*, 1995) (Figs. 2 and 3). These are analogous to the cyclic water pentamer units found in the structure of brucinium L-glycerate 4.75-hydrate (Białońska *et al.*, 2005). In (I), O—H···O—H···O associations (O4*W*—H42*W*···O3*W*$^{\rm i}$; symmetry code as in Table 1) link the tetramers into chain structures which form down the 2_1 screw axis in the unit cell (Fig. 2).

The brucine molecules are linked peripherally to these water structures by hydrogen bonds; there is a single linear interaction with a nitrogen acceptor of a *B* molecule (O2*W*—H22*W*···N19*B*$^{\rm i}$), as well as an asymmetric three-centred interaction with the carbonyl O-atom acceptor of an *A* molecule [O2*W*—H12*W*···O25*A* and O3*W*$^{\rm vii}$—H32*W*···O25*A*; symmetry code: (vii) $-x + 1, y + \frac{1}{2}, -z$]. The second carbonyl O

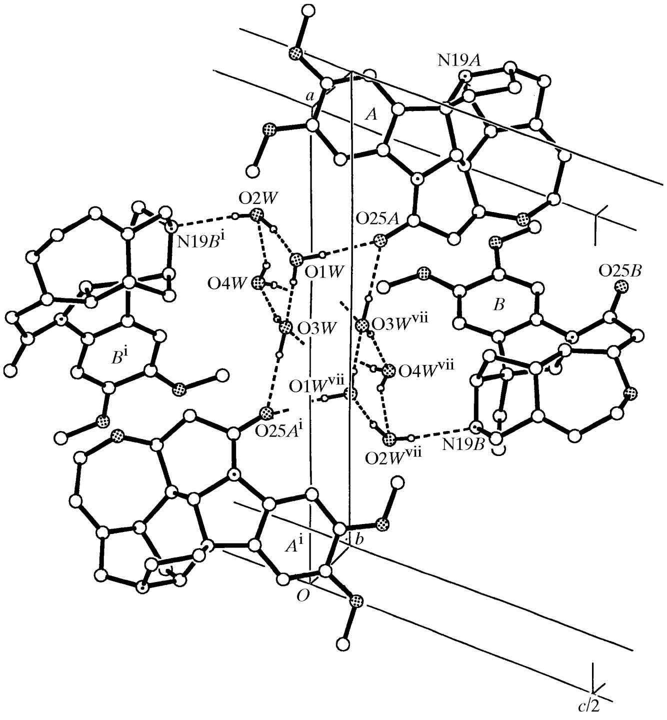


Figure 2

A perspective view of the intermolecular hydrogen bonding in the water chain structure of (I), extending approximately down the *b* axial direction. Non-associative H atoms have been omitted. [Symmetry code: (vii) $-x + 1, y + \frac{1}{2}, -z$; for other symmetry codes, see Table 1.]

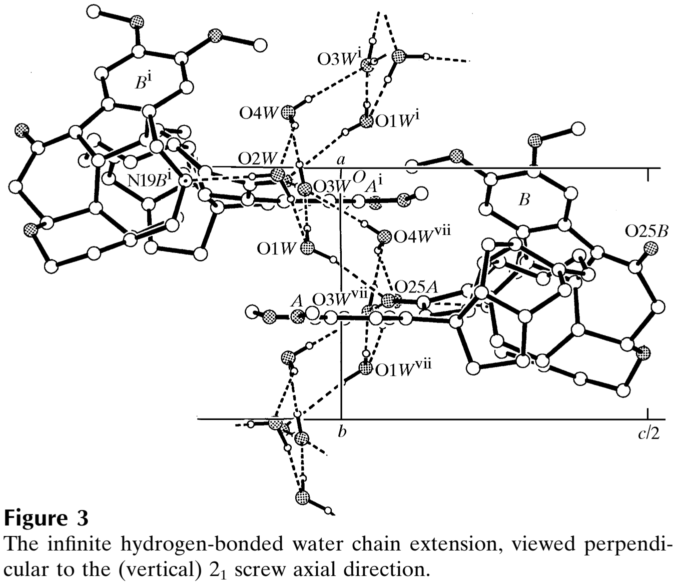


Figure 3

The infinite hydrogen-bonded water chain extension, viewed perpendicular to the (vertical) 2_1 screw axial direction.

atom of molecule *B* (O25*B*) and atom N19*A* of molecule *A* are unassociated except for some weak C—H···O and C—H···N interactions. Unlike the structures of both of the other brucine hydrates (Smith *et al.*, 2006*a*), there are no water–methoxy O—H···O interactions in (I).

It can be assumed that formation of different pseudopolymorphic solvates of brucine depends not only upon solvent composition (Bernstein, 1987; Kumar *et al.*, 1999) but, in the case of the pure hydrates, also upon the presence of additional non-incorporated but structure-influencing solute components, *e.g.* diethanolamine in the case of (I) and urea in brucine–water (1/5.25).

Experimental

Brucine dihydrate, (I), was obtained from the attempted preparation of a 1:1 brucine–diethanolamine adduct by refluxing 0.1 mmol quantities of brucine tetrahydrate and diethanolamine in 40 ml of 50% ethanol–water for 10 min. Colourless prismatic crystals were obtained after total room-temperature evaporation of the solvent.

Crystal data

$C_{23}H_{26}N_2O_4\cdot 2H_2O$
$M_r = 430.49$
Monoclinic, $P2_1$
$a = 15.178$ (2) Å
$b = 7.4496$ (12) Å
$c = 19.751$ (3) Å
$\beta = 112.397$ (3)°
$V = 2064.8$ (5) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm^{-1}
$T = 130$ (2) K
0.50 × 0.15 × 0.10 mm

Data collection

Bruker SMART CCD detector diffractometer
9011 measured reflections
3936 independent reflections
3072 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.064$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.048$
$wR(F^2) = 0.090$
$S = 0.87$
3936 reflections
559 parameters
1 restraint
H atoms parameters constrained
$\Delta\rho_{\max} = 0.20$ e Å^{-3}
$\Delta\rho_{\min} = -0.21$ e Å^{-3}

H atoms potentially involved in hydrogen-bonding interactions were generally located by difference Fourier methods. Some of the H atoms of the water molecules could not be located and were included in the refinement at calculated sites dictated by the assumed hydrogen-bonding geometry, and their positional and isotropic displacement parameters were refined. However, because of the poor reflection–parameter ratio, these were fixed in the final refinement cycles. Brucine H atoms were included at calculated positions (aromatic C—H = 0.95 Å and aliphatic C—H = 0.98–1.00 Å) and treated as riding, with $U_{\rm iso}$(H) values of $1.2U_{\rm eq}$(C). The absolute configuration determined for the parent strychnine (Peerdeman, 1956) was invoked. Friedel pairs were averaged for the data used in the refinement.

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 1999); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics:

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*W*—H11*W*···O3*W*	0.93	1.86	2.785 (6)	170
O1*W*—H12*W*···O25*A*	0.87	2.11	2.960 (4)	168
O2*W*—H21*W*···O1*W*	0.91	1.90	2.815 (5)	175
O2*W*—H22*W*···N19*B*$^{\rm i}$	0.77	2.02	2.781 (4)	170
O3*W*—H31*W*···O4*W*	0.81	2.00	2.785 (7)	164
O3*W*—H32*W*···O25*A*$^{\rm i}$	0.89	1.90	2.794 (4)	179
O4*W*—H41*W*···O2*W*	0.73	2.13	2.843 (7)	164
O4*W*—H42*W*···O3*W*$^{\rm i}$	0.73	2.55	3.210 (6)	151
C4*A*—H4*A*···O25*A*	0.95	2.39	2.930 (4)	115
C4*B*—H4*B*···O25*B*	0.95	2.43	2.923 (4)	112
C22*A*—H22*A*···O25*B*$^{\rm ii}$	0.95	2.57	3.327 (4)	137
C26*B*—H30*B*···O24*A*$^{\rm iii}$	0.98	2.56	3.107 (4)	115
C17*A*—H31*A*···O3*A*$^{\rm iv}$	0.99	2.44	3.324 (4)	149
C20*B*—H35*B*···N19*A*$^{\rm v}$	0.99	2.58	3.525 (4)	159
C15*A*—H38*A*···O3*A*$^{\rm vi}$	0.99	2.44	3.164 (4)	129

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

Table 2
Comparative unit-cell data for the pseudopolymorphic brucine solvates.

Cell parameters	Brucine	Brucine·$2H_2O$	Brucine·$4H_2O$	Brucine·$5.25H_2O$	Brucine·EtOH·$2H_2O$	Brucine·^{i}PrOH·$2H_2O$	Brucine–acetone
a (Å)	7.992 (2)	15.178 (2)	7.555 (2)	23.351 (5)	7.723 (1)	7.9297 (3)	12.765 (3)
b (Å)	12.704 (3)	7.4496 (12)	11.531 (3)	12.200 (3)	12.337 (1)	12.3289 (7)	7.1360 (14)
c (Å)	9.471 (2)	19.751 (3)	26.492 (8)	16.972 (4)	25.212 (2)	25.1631 (10)	13.686 (3)
α (°)	90	90	90	90	90	90	90
β (°)	99.68 (3)	112.397 (3)	90	96.202 (4)	90	90	114.35 (3)
γ (°)	90	90	90	90	90	90	90
V (Å^3)	947.9 (4)	2064.7 (6)	2307.9 (11)	4806.7 (19)	2403 (1)	2460.06 (19)	1135.8 (4)
Z	2	4	4	8	4	4	2
Space group	$P2_1$	$P2_1$	$P2_12_12_1$	$C2$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
Reference	*a*	*b*	*c*	*c*	*d*	*a*	*a*

Notes: (*a*) Białońska & Ciunik (2004*a*); (*b*) this work; (*c*) Smith *et al.* (2006*a*); (*d*) Glover *et al.* (1985).

PLATON (Spek, 2003); software used to prepare material for publication: *PLATON*.

The authors acknowledge financial support from the School of Physical and Chemical Sciences (Queensland University of Technology), the School of Biomolecular and Physical Sciences (Griffith University) and the School of Chemistry (University of Melbourne).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GA3057). Services for accessing these data are described at the back of the journal.

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