Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Brucine salts of L-α-hydroxy acids: brucinium hydrogen (*S*)-malate pentahydrate and anhydrous brucinium hydrogen (2*R*,3*R*)-tartrate at 130 K

Graham Smith,[a]* Urs D. Wermuth[b] and Jonathan M. White[c]

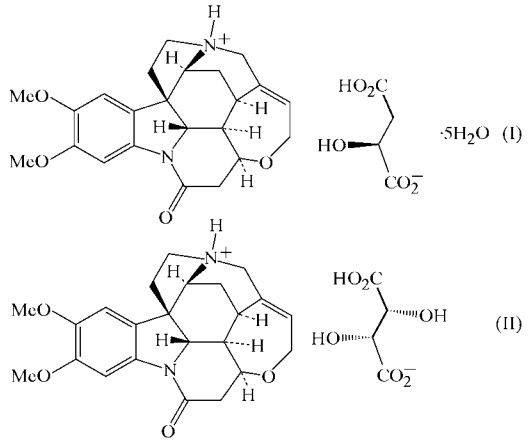
[a]School of Physical and Chemical Sciences, Queensland University of Technology, GPO Box 2434, Brisbane, Queensland 4001, Australia, [b]School of Science, Griffith University, Nathan, Queensland 4111, Australia, and [c]School of Chemistry, University of Melbourne, Parkville, Victoria 3052, Australia
Correspondence e-mail: g.smith@qut.edu.au

Received 24 March 2006
Accepted 10 May 2006
Online 24 May 2006

The structures of two brucinium (2,3-dimethoxy-10-oxostrychnidinium) salts of the α-hydroxy acids L-malic acid and L-tartaric acid, namely brucinium hydrogen (*S*)-malate pentahydrate, $C_{23}H_{27}N_2O_4^+\cdot C_4H_5O_5^-\cdot 5H_2O$, (I), and anhydrous brucinium hydrogen (2*R*,3*R*)-tartrate, $C_{23}H_{27}N_2O_4^+\cdot C_4H_5O_6^-$, (II), have been determined at 130 K. Compound (I) has two brucinium cations, two hydrogen malate anions and ten water molecules of solvation in the asymmetric unit, and forms an extensively hydrogen-bonded three-dimensional framework structure. In compound (II), the brucinium cations form the common undulating brucine sheet substructures, which accommodate parallel chains of head-to-tail hydrogen-bonded tartrate anion species in the interstitial cavities.

Comment

Although the crystal structures of the strychnine salts of both D-tartaric acid [strychninium hydrogen (2*S*,3*S*)-tartrate



trihydrate] and L-tartaric acid [bis(strychninium) (2*R*,3*R*)-tartrate hexahydrate] have been reported by Gould *et al.* (1987), surprisingly no brucinium tartrate salts are known. Although brucine is well known as an agent for the resolution of chiral species from enantiomeric mixtures of many organic molecule types, including α-hydroxy acids (Wilen, 1972), it is not considered the usual one for the simple series analogues, which include glyceric, malic and tartaric acids. However, the reported resolution of L-glyceric acid from a racemic mixture of the acid and the structure determination of its brucinium salt by Białońska *et al.* (2005) prompted us to attempt similar resolutions with malic and tartaric acids. We subsequently

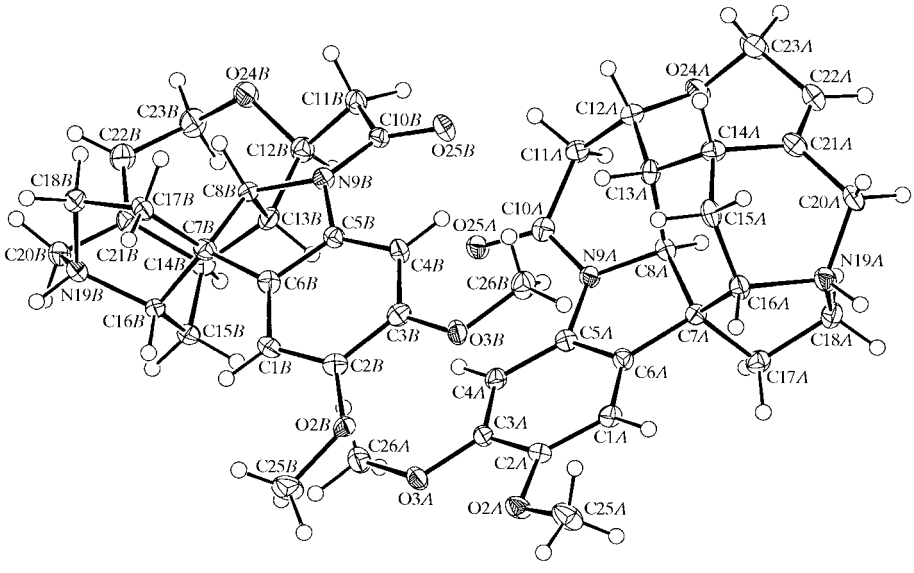


Figure 1
The molecular configuration and atom-numbering scheme for the two independent brucinium cations (*A* and *B*) in the asymmetric unit in (I). Non-H atoms are shown as 40% probability displacement ellipsoids.

 DOI: 10.1107/S0108270106017288

obtained crystals of brucinium hydrogen L-malate pentahydrate, (I), by simple refluxing of brucine with D,L-malic acid in 50% ethanol–water. The resolution of D,L-tartaric acid was not as successful under these conditions, so the reaction with L-tartaric acid was completed in 50% 2-propanol–water. The use of 2-propanol rather than ethanol was also to test the observation of Sada *et al.* (1998) that this solvent promoted the crystallization of brucinium carboxylates, often with incorporation of 2-propanol molecules of solvation. However, with our preparation, the well formed clusters of crystals obtained were found to have no molecules of solvation, giving brucinium hydrogen L-tartrate, (II). The structures of both (I) and (II) are reported here.

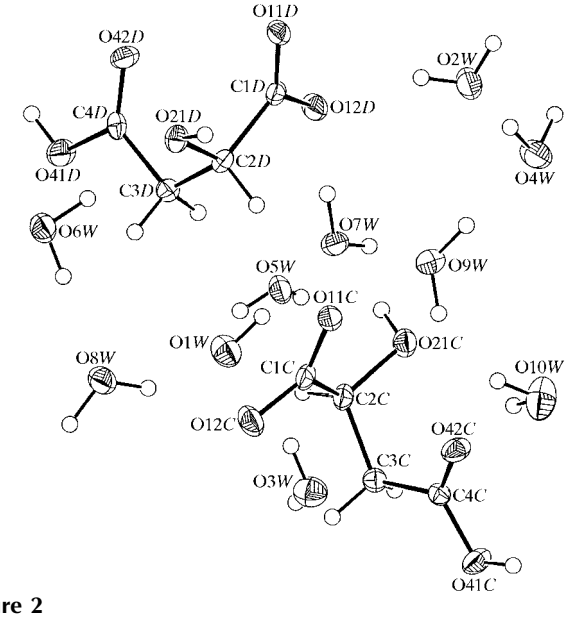


Figure 2
The molecular configuration and atom-numbering scheme for the two L-malate anions (*C* and *D*) and the ten water molecules of solvation in (I). Non-H atoms are shown as 40% probability displacement ellipsoids.

The structure determination of (I) confirmed the presence of two independent brucinium cations (*A* and *B*) (Fig. 1), two hydrogen L-malate anions (*C* and *D*, having the expected *S* configuration and being conformationally similar; Table 1) and ten water molecules of solvation (Fig. 2) in the crystallographic asymmetric unit. In (I), as well as in (II) (Fig. 3), the atom-numbering scheme for the brucine cage follows the original Robinson convention employed for strychnine (Holmes, 1952). In both (I) and (II), this gives the overall Cahn–Ingold–Prelog absolute configuration for the protonated brucinium species as C7(*S*), C8(*S*), C12(*S*), C13(*R*), C14(*R*), C16(*S*) and N19(*S*). In the hydrogen malate anions in (I), the carboxylic acid group adjacent to the α-hydroxy group is preferentially deprotonated on the basis of its decreased pK_a value compared with the C4 carboxylic acid group (Tapscott, 1982). This is consistent with observations for other hydrogen malates, *e.g.* ammonium hydrogen (*S*)-malate (Versichel *et al.*, 1978).

The isolation of the enantiomeric L-malate salt of (I) represents a facile resolution from D,L-malic acid using brucine, which has not previously been considered among recognized resolving agents for this acid. More commonly, 1-phenylethylamine or cinchonine have been the agents of choice for the resolution of both D- and L-malic acid, while both of these, as well as quinine, have been used for D-malic acid resolution (McKenzie *et al.*, 1923; Newman, 1981). The structures of the three configurational isomers 1-phenylethylaminium D-, L- and DL-malate have been reported (Turkington *et al.*, 2004). In (I), the cations, anions and water molecules form an extensively hydrogen-bonded three-dimensional framework structure (Fig. 4 and Table 2). This structure is in many respects [*viz.* space group (*P*1), unit-cell dimensions and contents] similar to the structures of both

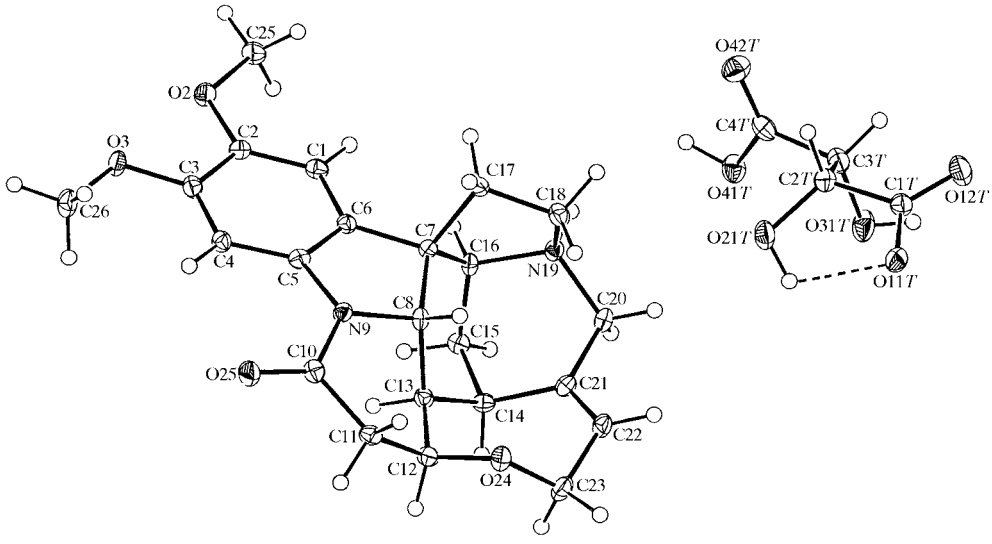


Figure 3
The molecular configuration and atom-numbering scheme for the brucinium cation and the hydrogen L-tartrate anion in (II). The intramolecular hydroxy–carboxyl O—H···O hydrogen bond in the tartrate anion is shown as a broken line. Non-H atoms are shown as 40% probability displacement ellipsoids.

brucinium L-glycerate 4.75-hydrate (Białońska *et al.*, 2005) and brucinium citrate pentahydrate (Smith *et al.*, 2005). In brucine compounds generally, the brucine species commonly form regular undulating parallel or antiparallel host sheet substructures built from partially overlapping head-to-tail molecular associations (Gould & Walkinshaw, 1984; Dijksma, Gould, Parsons, Taylor & Walkinshaw, 1998; Białońska & Ciunik, 2004). However, in (I), there is no such directional substructuring, although, as with the L-glycerate and citrate compounds, there is significant structuring within the guest cavity, including numerous cyclic and extended-chain water–water and water–anion hydrogen-bonding interactions. In addition, in (I), there are brucine N^+—H···O(malate) interactions (four-centred in *A* and three-centred in *B*) and malate O—H···O (brucine) host–guest interactions.

The brucine molecules in (II) form the previously described parallel-mode substructures, which in (II) extend along the *a* direction in the unit cell, with a dimeric repeat of *ca* 12.27 Å and a chain offset angle α (Smith *et al.*, 2006) of *ca* 118° (Fig. 5). These values compare with 12.66 Å and 123°, respectively, in the similar parallel-mode brucinium D-glucuronate structure (Dijksma, Gould, Parsons & Walkinshaw, 1998). The inter-sheet cavities accommodate the hydrogen tartrate anion species, which form parallel chain structures through head-to-tail cyclic $R_2^2(9)$ hydrogen-bonding interactions (Table 4). These associations incorporate an intramolecular tartrate O21*T*(hydroxy)—H···O11*T*(carboxyl) hydrogen bond (Table 4). The chains are linked peripherally to the brucinium cation substructure through O(hydroxy)—H···O(carbonyl) and N^+(brucine)—H···O(carboxyl) interactions, giving a three-dimensional cage structure. The tartrate chains in (II) are similar to the succinate chain substructure found in strychnidinium hydrogen succinate (Maurin *et al.*, 2006). In this analysis, the accepted 2*R*,3*R* absolute configuration is confirmed for the L-tartrate residue, which also adopts an extended conformation (Table 3).

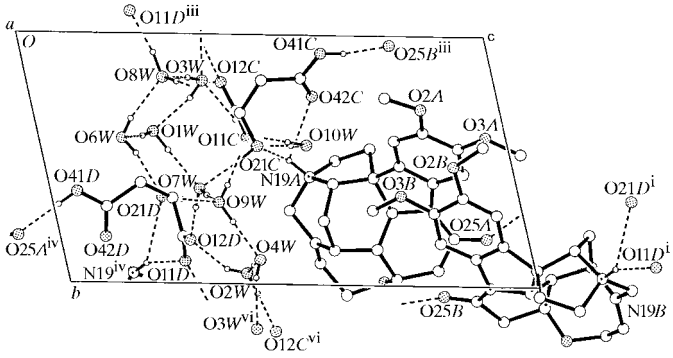


Figure 4
The packing of (I), viewed down the *a* axial direction, showing hydrogen-bonding interactions as broken lines. Non-interactive H atoms have been omitted. For symmetry codes, see Table 2.

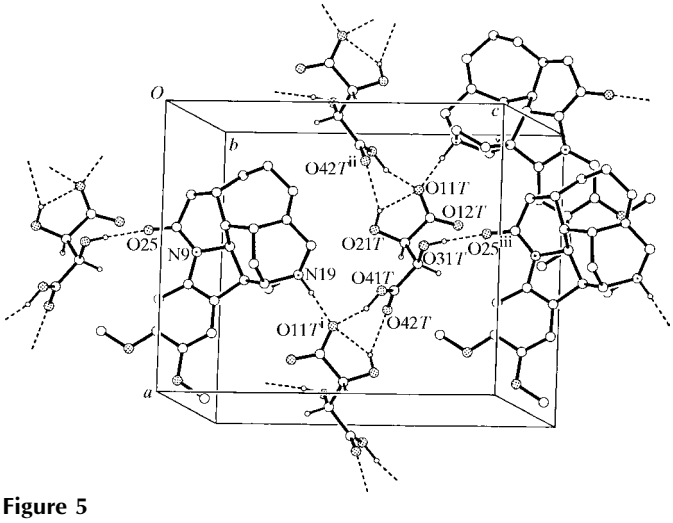


Figure 5
A perspective view of the packing of (II), viewed approximately down the *b* axial direction. Non-interactive H atoms have been omitted. For symmetry codes, see Table 4.

Experimental

The two title compounds were synthesized by heating 1 mmol quantities of either D,L-malic acid for (I) or L-tartaric acid for (II) and brucine tetrahydrate in 50 ml of either 50% ethanol–water for (I) or 50% 2-propanol–water for (II) for 10 min under reflux. Compound (I) was obtained as colourless plates (m.p. 493.5–495.8 K), while (II) was obtained as clusters of colourless prisms (m.p. 522.4–523.6 K), after partial room-temperature evaporation of the solvent.

Compound (I)

Crystal data

$C_{23}H_{27}N_2O_4^+\cdot C_4H_5O_5^-\cdot 5H_2O$
M_r = 618.63
Triclinic, *P*1
a = 9.2915 (10) Å
b = 9.4337 (9) Å
c = 16.9287 (17) Å
α = 76.401 (2)°
β = 88.716 (2)°
γ = 82.104 (2)°
V = 1428.5 (3) Å^3
Z = 2
D_x = 1.438 Mg m^{-3}
Mo *K*α radiation
μ = 0.12 mm^{-1}
T = 130 (2) K
Plate, colourless
0.40 × 0.35 × 0.05 mm

Data collection

Bruker CCD area-detector diffractometer
φ and ω scans
7141 measured reflections
5034 independent reflections
4397 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 25.0°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.072
S = 0.90
5034 reflections
772 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0367P)^2 + 0.2077P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.005
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Table 1
Selected torsion angles (°) for (I).

O11*C*—C1*C*—C2*C*—O21*C*	1.1 (4)	O11*D*—C1*D*—C2*D*—O21*D*	6.6 (4)
O11*C*—C1*C*—C2*C*—C3*C*	125.0 (3)	O12*D*—C1*D*—C2*D*—O21*D*	−175.7 (3)
O12*C*—C1*C*—C2*C*—O21*C*	179.3 (3)	O12*D*—C1*D*—C2*D*—C3*D*	−54.2 (4)
O12*C*—C1*C*—C2*C*—C3*C*	−56.8 (4)	O11*D*—C1*D*—C2*D*—C3*D*	128.1 (3)
C1*C*—C2*C*—C3*C*—C4*C*	−62.9 (4)	C1*D*—C2*D*—C3*D*—C4*D*	−57.5 (4)
O21*C*—C2*C*—C3*C*—C4*C*	62.7 (4)	O21*D*—C2*D*—C3*D*—C4*D*	66.7 (4)
C2*C*—C3*C*—C4*C*—O41*C*	−169.1 (3)	C2*D*—C3*D*—C4*D*—O42*D*	9.0 (5)
C2*C*—C3*C*—C4*C*—O42*C*	11.8 (5)	C2*D*—C3*D*—C4*D*—O41*D*	−171.8 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N19A—H19A···O11C	0.99	1.86	2.742 (4)	147
N19A—H19A···O21C	0.99	2.36	3.117 (4)	133
N19A—H19A···O42C	0.99	2.59	3.097 (4)	112
N19B—H19B···O11D^{i}	0.92	1.89	2.759 (4)	156
N19B—H19B···O21D^{i}	0.92	2.51	3.129 (4)	124
O21C—H21C···O7W	0.90	1.79	2.689 (4)	180
O21D—H21D···O9W^{ii}	0.90	1.82	2.719 (4)	180
O41C—H41C···O25B^{iii}	0.93	1.73	2.645 (3)	168
O41D—H41D···O25A^{iv}	0.89	1.75	2.647 (3)	179
O1W—H11W···O7W	0.90	1.93	2.826 (4)	176
O1W—H12W···O6W^{v}	0.91	1.91	2.811 (4)	171
O2W—H21W···O12D	0.84	1.90	2.731 (4)	171
O2W—H22W···O12C^{vi}	0.89	1.83	2.721 (4)	175
O3W—H31W···O8W^{v}	0.93	1.82	2.743 (5)	173
O3W—H32W···O1W	0.86	1.96	2.805 (4)	167
O4W—H41W···O3W^{vi}	0.90	1.95	2.845 (4)	179
O4W—H42W···O2W	0.90	1.82	2.712 (5)	180
O5W—H51W···O11C	0.90	1.76	2.659 (4)	179
O5W—H52W···O3W^{ii}	0.85	2.06	2.880 (4)	164
O6W—H61W···O8W	0.91	1.90	2.808 (4)	179
O6W—H62W···O21D	0.91	1.89	2.799 (5)	179
O7W—H71W···O12D	0.90	1.76	2.664 (4)	179
O7W—H72W···O9W	0.87	1.92	2.764 (4)	161
O8W—H81W···O11D^{iii}	0.94	1.76	2.690 (4)	168
O8W—H82W···O12C	0.86	1.92	2.768 (4)	169
O9W—H91W···O5W^{v}	0.90	1.84	2.738 (4)	179
O9W—H92W···O4W	0.92	1.76	2.653 (4)	162
O10W—H10W···O5W^{v}	0.91	1.92	2.795 (5)	160
O10W—H13W···O21C	0.90	1.94	2.844 (4)	180
C3D—H31D···O7W	0.97	2.60	3.459 (5)	148

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

Compound (II)

Crystal data

$C_{23}H_{27}N_2O_4^+\cdot C_4H_5O_6^-$
M_r = 544.55
Orthorhombic, $P2_12_12_1$
a = 12.2719 (7) Å
b = 13.5151 (8) Å
c = 14.3814 (9) Å
V = 2385.2 (2) Å^3
Z = 4
D_x = 1.516 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.12 mm^{-1}
T = 130 (2) K
Block, colourless
0.45 × 0.25 × 0.20 mm

Data collection

Bruker CCD area-detector diffractometer
φ and ω scans
15054 measured reflections
3088 independent reflections
2514 reflections with $I > 2\sigma(I)$
R_{int} = 0.047
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.071
S = 0.91
3088 reflections
368 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0258P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 3
Selected torsion angles (°) for (II).

O11T—C1T—C2T—O21T −16.1 (2)	O21T—C2T—C3T—C4T 59.5 (2)
O12T—C1T—C2T—C3T 39.8 (2)	C1T—C2T—C3T—O31T 63.1 (2)
O12T—C1T—C2T—O21T 164.62 (17)	O31T—C3T—C4T—O41T 4.4 (2)
O11T—C1T—C2T—C3T −140.97 (17)	O31T—C3T—C4T—O42T −175.57 (18)
C1T—C2T—C3T—C4T −173.82 (15)	C2T—C3T—C4T—O41T −117.85 (18)
O21T—C2T—C3T—O31T −63.5 (2)	C2T—C3T—C4T—O42T 62.2 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
N19—H19···O11T^{i}	0.952 (19)	1.662 (19)	2.606 (2)	170.4 (17)
O21T—H21T···O11T	0.92 (3)	2.33 (3)	2.687 (2)	102.8 (19)
O21T—H21T···O42T^{ii}	0.92 (3)	2.28 (3)	3.118 (2)	151 (2)
O31T—H31T···O25^{iii}	0.87 (3)	2.04 (3)	2.833 (2)	152 (2)
O41T—H41T···O11T^{i}	0.98 (2)	1.61 (2)	2.5415 (19)	157 (2)

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

H atoms potentially involved in hydrogen-bonding interactions were generally located by difference methods or, in the case of (I), where the water H atoms could not be located by difference methods, positioned in their probable interactive sites. For (II), both positional and isotropic displacement parameters for the interactive H atoms were refined. However, for (I), because of the low reflection/refined parameter ratio, the interactive H atoms were fixed in the final cycle of refinement. Other brucine and hydroxy H atoms in both (I) and (II) were included at calculated positions (aromatic C—H = 0.93 Å and aliphatic C—H = 0.96–1.00 Å) and treated as riding [U_{iso}(H) = 1.2U_{eq}(C)]. In both structures, Friedel pairs were averaged for the data used in the refinements. The absolute configuration determined for the parent strychnine (Peerdeman, 1956) was invoked.

For both compounds, data collection: *SMART* (Bruker, 2000); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1999); 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*.

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

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3010). Services for accessing these data are described at the back of the journal.

References

Białońska, A. & Ciunik, Z. (2004). *CrystEngComm*, **6**, 276–279.
Białońska, A., Ciunik, Z., Popek, T. & Lis, T. (2005). *Acta Cryst.* C**61**, o88–o91.
Bruker (1999). *SAINT*. Version 6.02. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2000). *SMART*. Version 5.55. Bruker AXS Inc., Madison, Wisconsin, USA.
Dijksma, F. J. J., Gould, R. O., Parsons, S., Taylor, J. & Walkinshaw, M. D. (1998). *Chem. Commun.* pp. 745–746.
Dijksma, F. J. J., Gould, R. O., Parsons, S. & Walkinshaw, M. D. (1998). *Acta Cryst.* C**54**, 1948–1951.
Farrugia, L. J. (1999). *J. Chem. Crystallogr.* **32**, 837–838.
Gould, R. O., Taylor, P., Walkinshaw, M. D. & Bruins Slot, H. J. (1987). *Acta Cryst.* C**43**, 2405–2410.
Gould, R. O. & Walkinshaw, M. D. (1984). *J. Am. Chem. Soc.* **106**, 7840–7842.
Holmes, H. L. (1952). *The Alkaloids*, Vol. II, edited by R. F. H. Manske & H. L. Holmes, p. 514. New York: Academic Press.
McKenzie, A., Plenderleith, H. J. & Walker, N. (1923). *J. Chem. Soc.* **123**, 2875–2880.
Maurin, J. K., Lis, T., Zawadzka, A. & Czarnocki, Z. (2006). *Acta Cryst.* E**62**, o694–o696.

Newman, P. (1981). *Optical Resolution Procedures for Organic Compounds.* Vol. 2, Part I, pp. 66–67. Riverdale, New York: Optical Resolution Information Centre, Manhattan College.
Peerdeman, A. F. (1956). *Acta Cryst.* **9**, 824.
Sada, K., Yoshikawa, K. & Miyata, M. (1998). *Chem. Commun.* pp. 1763–1764.
Sheldrick, G. M. (1997). *SHELXL97* and *SHELXS97*. University of Göttingen, Germany.
Smith, G., Wermuth, U. D., Healy, P. C. & White, J. M. (2006). *Acta Cryst.* C**62**, o203–o207.
Smith, G., Wermuth, U. D. & White, J. M. (2005). *Acta Cryst.* C**61**, o621–o624.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Tapscott, R. E. (1982). *Transition Metal Chemistry*, Vol. 8, edited by G. A. Melson & B. N. Figgis, pp. 253–429. New York: Marcel Dekker.
Turkington, D. E., Ferguson, G., Lough, A. J. & Glidewell, C. (2004). *Acta Cryst.* C**60**, o617–o622.
Versichel, W., Van de Mieroop, W. & Lenstra, A. T. H. (1978). *Acta Cryst.* B**34**, 2643–2645.
Wilen, S. H. (1972). *Tables of Resolving Agents and Optical Resolutions*, edited by E. N. Eliel, pp. 68–71. London: University Notre Dame.