complementary values at the 6 site. This was allowed for by use of suitable restraints during the refinement [with C—Br set to 1.885 (5) and C—Cl to 1.720 (5) Å]. Compound (2) crystallized in the monoclinic system; space groups *C2/c* or *Cc* were indicated by the systematic absences; *C2/c* was assumed, and confirmed by the analysis. A difference map showed the methyl H atoms as a torus of density and these H atoms were allowed for by placing six H atoms with 0.5 occupancy around the methyl C atom with appropriate geometry constraints. Compound (3) crystallized in the orthorhombic system; space group $P2_12_12_1$ was indicated by the systematic absences. In all three compounds, H atoms were treated as riding atoms (C—H 0.93 and 0.96, N—H 0.86 Å). Compounds (1) and (3) are chiral; the analysis of (1) showed that it was best treated as a racemic twin [Flack (1983) parameter 0.46 (4)], while in the case of (3), the analysis unequivocally established the chirality of the crystal studied [Flack (1983) parameter −0.02 (2)].

For all compounds, data collection: *CAD-4-PC* (Enraf–Nonius, 1992); cell refinement: *SET*4 and *CELDIM* in *CAD-4-PC*; data reduction: *DATRD*2 in *NRCVAX*96 (Gabe *et al.*, 1989); program(s) used to solve structures: *NRCVAX*96; program(s) used to refine structures: *NRCVAX*96 and *SHELXL*97 (Sheldrick, 1997); molecular graphics: *NRCVAX*96, *ORTEP*II (Johnson, 1976) and *PLATON* (Spek, 1998); software used to prepare material for publication: *NRCVAX*96, *SHELXL*97 and *PRPCIF*97 (Ferguson, 1997).

We are indebted to Dr J. F. Gallagher and Dublin City University for funds to purchase the X-ray tube used in the data collections. While no direct support for this work was provided by NSERC Canada, we do acknowledge that organization for partially funding the 1992 upgrade of the CAD-4 diffractometer.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1221). Services for accessing these data are described at the back of the journal.

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(−)-Tetrahydropalmatine Monohydrate

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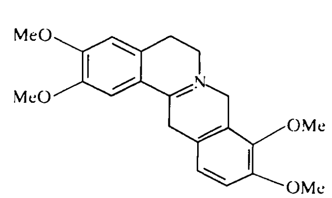
Abstract

The title compound, $C_{21}H_{25}NO_4.H_2O$, was isolated from the rhizome of *Stefania rotunda* L. of Vietnam and its structure elucidated. An *S* configuration was found at the asymmetric C13 atom of the (−)-enantiomer. The water molecule generates infinite helically arranged molecular columns around the screw axes in the *z* direction through intermolecular hydrogen bonds.

Comment

Tetrahydropalmatine, (1), is an alkaloid of the protoberberine type which can be isolated from different plants (Glasby, 1975; Ribár *et al.*, 1993). The sample used for this study was isolated from the Vietnamese plant *Stefania rotunda* L. (Menispermaceae family), which grows wild among limestone rocks at Cuc Phuong National Park. It is used in Vietnamese folk medicine for its activity against insomnia, stomach-ache, headache, asthma and fever. The main alkaloid, (−)-tetrahydropalmatine, is preserved for neuroasthenia and psychoses. Since the chemical identity of (−)-tetrahydropalmatine was originally not known, its X-ray structure was elucidated.



(1)

The structure of the racemic form, (±)-tetrahydropalmatine, is reported in the literature (Ribár *et al.*, 1993), together with the non-racemic form of isocorypalmine (Ribár *et al.*, 1992), which lacks the fourth methoxy group but has a hydroxy substituent instead on C16. Entry CASSEU in the Cambridge Structural Database (CSD; Allen & Kennard, 1993) with the compound designation corydalis B (Zhuli *et al.*, 1983) agrees with the title compound, however, the absolute configuration is opposite to that found here and no H-atom parameters (except for one water H atom) are reported in the CSD, so that no hydrogen-bonding interactions can be discussed.

The molecular structure of (−)-tetrahydropalmatine is shown in Fig. 1, together with the atomic numbering scheme. As judged from the Flack (1983) parameter being close to zero for the enantiomer shown in Fig. 1 and close to 1 for the opposite enantiomer, there is evidence from this X-ray analysis that (−)-tetrahydropalmatine has an *S* configuration at the asymmetric C13 atom. This absolute configuration is compatible with that assigned chemically by Corrodi & Hardegger (1956). Since these authors have assigned the *R* configuration to the (+)-enantiomer of tetrahydropalmatine and to (+)-isocorypalmine, the representation of isocorypalmine in the paper of Ribár *et al.* (1992), where the *S* enantiomer is displayed, refers then to (−)-isocorypalmine.

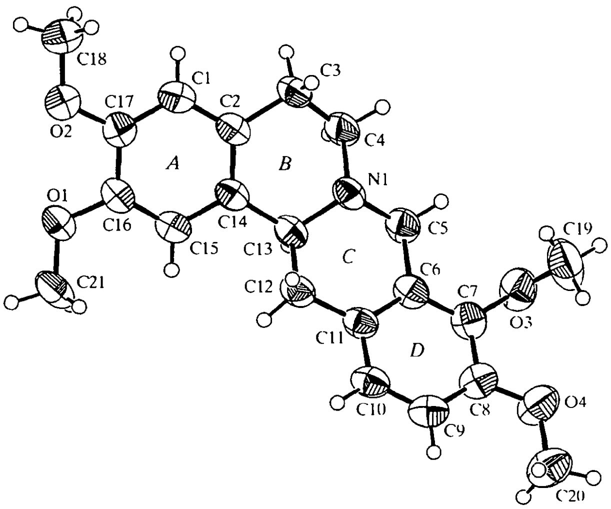


Fig. 1. The molecular structure of the title compound (50% probability) showing the chosen numbering scheme (*ORTEP*II; Johnson, 1976).

All bond lengths and angles in the title compound are in the expected ranges and need no further discussion.

In the molecule, which consists mainly of the tetracyclic ring system *A*–*D*, both rings *A* and *D* are planar with average deviations from the least-squares planes of σ = 0.01 Å for ring *A* and σ = 0.004 Å for ring *D*. The dihedral angle *A*/*D* is 32.6 (4)°.

Normally, methoxy groups linked to a phenyl ring have their C and O atoms also in the ring plane. This holds for the title molecule in three of the four cases; the O3—C19 group is rotated out of plane, indicated by a torsion angle C19—O3—C7—C6 of 104.2 (3)°, thus avoiding steric hindrance with the adjacent methylenic C5 atom.

The ring conformations of the two non-planar rings *B* and *C* can be described by the Cremer–Pople ring-puckering parameters (Cremer & Pople, 1975; Luger & Bülow, 1983). Ring *C* is in a pure half-chair conformation, with the adjacent ring atoms N1 and C13 above and below the plane of the remaining four atoms, respectively. For ring *B*, a half-chair conformation also dominates (N1 and C4 as out-of-plane atoms), however, there is a tendency towards an envelope form, with C4 as the out-of-plane atom.

The overall molecular geometry is characterized by two major planes (I: ring *A* plus atoms C3, C13, O2, C18, O1 and C21; II: ring *D* plus atoms C5, C12, O3, O4 and C20), which contain all non-H atoms except N1, C4 and C18. The average deviation from the least-squares planes of I and II are σ = 0.035 Å for I and σ = 0.010 Å for II, and the I/II angle is 32.0 (3)°.

Except from some minor discrepancies, the above-described molecular geometry is practically the same as was found for the racemic form of tetrahydropalmatine,

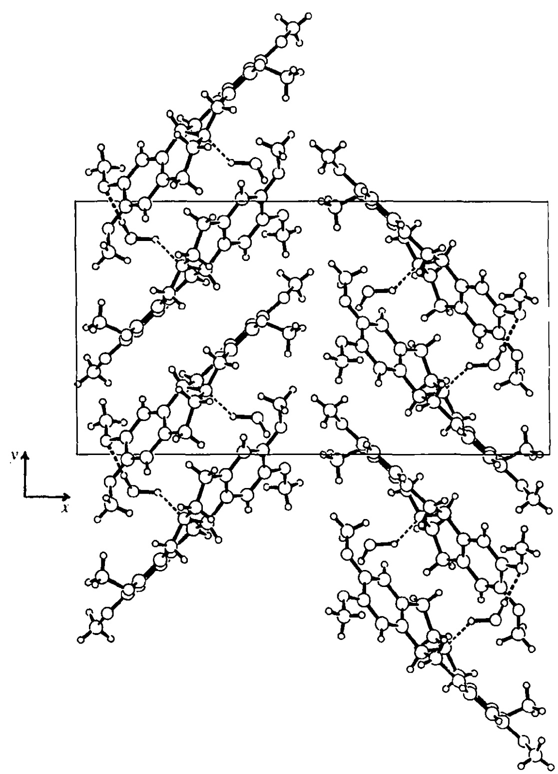


Fig. 2. Packing illustration in a projection of the lattice onto the *xy* plane (*SCHAKAL*88; Keller, 1988).

where O3—C19 was also the only out-of-plane methoxy group and where an interplanar angle between rings *A* and *D* of 25.8 (1)° was reported. In the racemic form, both non-planar rings were in pure half-chair conformations. An even closer agreement is seen if a comparison with isocorypalmine (Ribár *et al.*, 1992) is made. Here, the dihedral angle *A*/*B* [33.8 (1)°] is similar to that found in (1) and both non-planar rings have the same conformation, *i.e.* ring *C* is half-chair and ring *B* has a form intermediate between envelope and half-chair as in the title molecule.

The solvent water molecule is a donor of two hydrogen bonds. One acceptor is the N1 atom [O1*W*···N1 2.893 (4), H12*W*···N1 2.04 (2) Å and O1*W*—H12*W*···N1 128.3 (2)°] and the second is the methoxy O1 atom of a molecule symmetry related by the screw axis in the *z* direction [O1*W*···O1^i 3.054 (4), H11*W*···O1^i 1.94 (2) Å and O1*W*—H11*W*···O1^i 158.4 (2)°; symmetry code: (i) $\frac{1}{2}-x$, $2-y$, $\frac{1}{2}+z$]. In this way, infinite helically arranged molecular columns are generated around the screw axes at $(x,y) = (\frac{1}{4},0)$, ...; $(\frac{3}{4},\frac{1}{2})$, ... There is no interhelical interaction. In the racemic form of the title molecule, which lacks any solvent, only van der Waals interactions in the crystal lattice were discussed.

Experimental

Rhizomes of *Stefania rotunda* L. were collected in Cuc Phuong National Park, Ninh Binh Province, Vietnam, during March 1996. A voucher specimen is deposited in the herbarium of the Institute of Ecology and Biological Resources, NCST, Vietnam. Fresh rhizomes of *Stefania rotunda* L. were extracted with 95% EtOH by percolation. The EtOH extract was evaporated to dryness under reduced pressure and the residue taken up in 5% aqueous HCl. After alkalization with concentrated NH_4OH, the aqueous solution was extracted with $CHCl_3$ and the solvent removed *in vacuo* to yield a mixture of alkaloids. The crude base mixture was chromatographed on a silica-gel column; elution was started with CH_2Cl_2 and then continued with a CH_2Cl_2/MeOH mixture. Fractions were collected and grouped after monitoring by TLC. Alkaloids were detected by UV and after spraying with Dragendoff's reagent. Fractions were treated separately and their alkaloid content was purified by flash column chromatography and preparative TLC on silica gel.

Crystal data

$C_{21}H_{25}NO_4.H_2O$	Cu $K\alpha$ radiation
$M_r = 373.44$	$\lambda = 1.54180$ Å
Orthorhombic	Cell parameters from 136 reflections
$P2_12_12_1$	$\theta = 25$–$40°$
$a = 22.322$ (5) Å	$\mu = 0.736$ mm^{-1}
$b = 11.801$ (3) Å	$T = 293$ (2) K
$c = 7.425$ (1) Å	Sheet
$V = 1955.9$ (7) Å^3	0.80 × 0.40 × 0.15 mm
$Z = 4$	Yellow
$D_x = 1.268$ Mg m^{-3}	
D_m not measured	

Data collection

Stoe MicroVAX-controlled four-circle diffractometer	2804 reflections with $F_o > 4\sigma(F_o)$
$\omega/2\theta$ scans	$R_{int} = 0.019$
Absorption correction: Gaussian (Hall & Stewart, 1987)	$\theta_{max} = 67.99°$
$T_{min} = 0.734$, $T_{max} = 0.897$	$h = 0 \rightarrow 26$
3984 measured reflections	$k = -14 \rightarrow 14$
3524 independent reflections	$l = 0 \rightarrow 8$
	3 standard reflections frequency: 90 min intensity decay: 3%

Refinement

Refinement on F^2	$\Delta\rho_{max} = 0.150$ e Å^{-3}
$R[F^2 > 2\sigma(F^2)] = 0.039$	$\Delta\rho_{min} = -0.137$ e Å^{-3}
$wR(F^2) = 0.117$	Extinction correction: *SHELXL*93
$S = 1.166$	Extinction coefficient: 0.0015 (2)
3518 reflections	Scattering factors from *International Tables for Crystallography* (Vol. C)
249 parameters	Absolute structure: Flack (1983)
H atoms: see below	Flack parameter = 0.0 (3)
$w = 1/[\sigma^2(F_o^2) + (0.0287P)^2 + 0.7793P]$ where $P = (F_o^2 + 2F_c^2)/3$	
$(\Delta/\sigma)_{max} = 0.003$	

Table 1. *Selected geometric parameters (Å, °)*

C4—N1	1.465 (3)	C17—O2	1.371 (3)
N1—C5	1.462 (4)	C18—O2	1.418 (4)
N1—C13	1.475 (3)	C19—O3	1.431 (5)
C7—O3	1.383 (3)	C20—O4	1.425 (4)
C8—O4	1.361 (4)	C21—O1	1.422 (4)
C16—O1	1.375 (3)		
N1—C4—C3	110.0 (2)	N1—C5—C6	112.1 (2)
C5—N1—C4	109.7 (2)	N1—C13—C14	112.2 (2)
C5—N1—C13	109.8 (2)	N1—C13—C12	107.5 (2)
C4—N1—C13	111.1 (2)		

Table 2. *Puckering parameters (Å, °) (Cremer & Pople, 1975) of the six-membered B and C rings*

Ring	Q, q_2	θ	Φ, φ_2	Type†
B	0.513 (4)	51.28 (1)	321.36 (5)	*H*←*E*
C	0.538 (5)	50.11 (1)	215.24 (5)	*H*

† *H* = half-chair and *E* = envelope.

H atoms were refined with a riding model, except for the water H atoms, H11*W* and H12*W*.

Data collection: *DIF*4 (Stoe & Coe, 1990*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1990*b*). Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976) and *SCHAKAL*88 (Keller, 1988). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1224). Services for accessing these data are described at the back of the journal.

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Methylxanthines. II.† Anhydrous Theobromine

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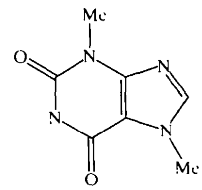
Abstract

Clear crystals of anhydrous theobromine (3,7-dihydro-3,7-dimethyl-1*H*-purine-2,6-dione, $C_7H_8N_4O_2$) were grown by vacuum sublimation and the structure determined. The melting point of anhydrous theobromine has been determined as 620 (1) K. Two molecules in the asymmetric unit form a pseudo-centrosymmetric dimer and pack to form a layered structure of two-dimensional hydrogen-bonded networks.

† Part I: Ebisuzaki *et al.* (1997).

Comment

Theobromine (3,7-dimethylxanthine) is the principal alkaloid in the cocoa bean and is known to contribute to the stimulating effect of chocolate. The structure of theobromine has, until now, been determined only when the molecule has been used as a ligand for a metal complex (Crowston *et al.*, 1986), as a theobrominium counter-ion (Herbstein & Kapon, 1975, 1979), or as part of a molecular complex (Shefter *et al.*, 1971). As part of our research on methylxanthines (Ebisuzaki *et al.*, 1997), we report the crystal structure of pure anhydrous theobromine, (I).



(I)

Anhydrous theobromine crystallizes with two molecules in the asymmetric unit. The two molecules form a nearly planar pseudo-centrosymmetric hydrogen-bonded dimer. The asymmetric unit and labeling scheme are shown in Fig. 1. In this paper, the molecule which has the unprimed atom labels is referred to as molecule *A*; the primed atom labels belong to molecule *B*. The intramolecular bond lengths and angles are given in Table 1, and are unremarkable. Individual bond lengths and angles agree well with expected values (Allen *et al.*, 1987) as well as with the values obtained from the previously determined structure of the 2:1

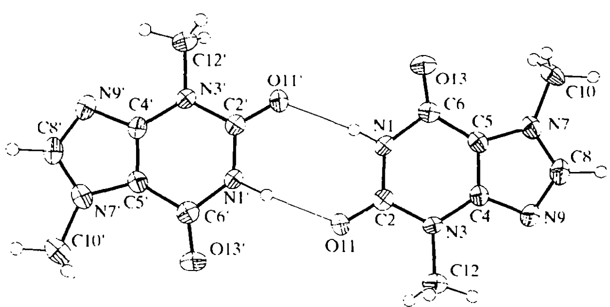


Fig. 1. *ORTEPII* (Johnson, 1976) drawing of the title molecule, showing the asymmetric unit and the labelling scheme. Non-H-atom displacements ellipsoids are drawn at the 50% probability level. H atoms are drawn as circles with a small arbitrary radius, for clariy.