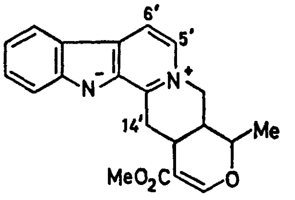
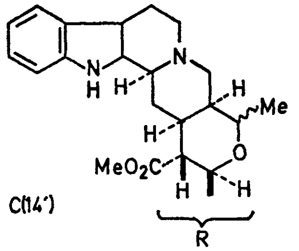
X-Ray Crystallographic Determination of the Structure of the Alkaloid Serpentinine

By Hiroshi Irie, Kazuo Ishizuka, Shizu Kawashima, Norio Masaki, Kenji Osaki, Tetsuro Shingu, and Shojiro Uyeo*
(*Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan*)
and Hidehiko Kaneko and Shunsuke Naruto
(*Research Laboratory, Dainippon Pharmaceutical Co., Ltd., Osaka, Japan*)

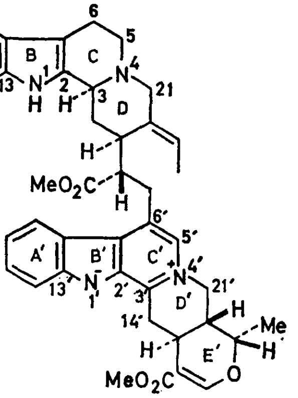
Summary The structure of the alkaloid serpentinine, $C_{42}H_{44}N_4O_5$, from *Rauwolfia* species, has been elucidated by *X*-ray crystallographic studies of its dihydrobromide dihydrate.

In a recent review article Gorman, *et al.*[1] discussed the structure of serpentinine, a bisindole alkaloid isolated from *Rauwolfia serpentina* Benth. and other related species, and suggested the partial structure (Ib) which differs from that (Ia) advanced previously[2] by one (H.K.) of us, in one of the positions which link the two heteroyohimbane units in the molecule. Because of the inconclusive nature of the chemical and spectral data, it was decided to elucidate the structure of this alkaloid by *X*-ray crystallographic analysis of serpentinine dihydrobromide dihydrate, which crystallised from ethanol in yellow prisms elongated along the *a*-axis with developed (001), m.p. 280—290° (decomp.), D_m 1·437 g cm^{-3}, D_c 1·437 g cm^{-3}. These single crystals are orthorhombic, space group $P2_12_12_1$, with four formula units of $C_{42}H_{44}N_4O_5,2HBr,2H_2O$ in a unit cell of dimensions a = 19·16(2), b = 20·57(2), c = 10·35(1) Å. 2995 independent reflections from equi-inclination Weissenberg photographs taken along the a and c axes with Cu-K_α radiation were measured visually. The structure was solved by the heavy-atom method and refined by least-squares methods to an R-factor of 13·1% at present. Further refinements are in progress. The absolute configuration was determined by the comparison of Bijvoet pairs on the Weissenberg films. The molecular structure so derived is shown in the Figure, where all the atoms excluding hydrogen are shown by the perspective drawing along the *a*-axis. Rings A′, B′, and C′ are nearly coplanar with the C (14′) and C (21′) atoms, and rings D′ and E′ are half-chair shaped. On the other hand, rings A and B are coplanar with C(3) and C(6), while ring C is in the half-chair and ring D in the boat conformation. All four nitrogen atoms in the molecule of the hydrobromide make close contact with bromine atoms in the crystal. Closest nitrogen–bromine interatomic distances and the bromine–nitrogen–carbon angles are presented in the Table.

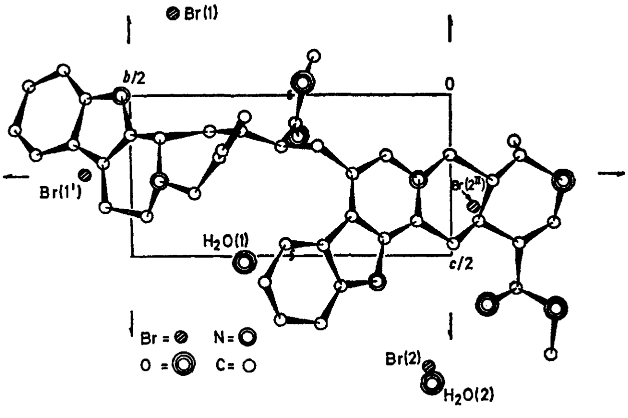




(Ia) R(without stereochemistry) at C(14′)
(Ib) R at either C(5′) or C(6′)



(II)



Figure

Interatomic distances and angles involving the nitrogen atoms

Distances

N(1) ··· Br(1) ..	3·40 Å	N(1′) ··· Br(2) ..	3·26 Å
N(4) ··· Br(1I) ..	3·18 Å	N(4′) ··· Br(2II)	3·69 Å

Angles

Br(1) ··· N(1) ··· C(2)	113°	Br(2) ··· N(1′) ··· C(2′)	136°
Br(1) ··· N(1) ··· C(13)	136°	Br(2) ··· N(1′) ··· C(13′)	116°
Br(1I) ··· N(4) ··· C(3)	104°	Br(2II) ··· N(4′) ··· C(3′)	79°
Br(1I) ··· N(4) ··· C(5)	107°	Br(2II) ··· N(4′) ··· C(5′)	99°
Br(1I) ··· N(4) ··· C(21)	105°	Br(2II) ··· N(4′) ··· C(21′)	98°

We interpret these results as indicating that in the crystals of the hydrobromide, N(1), N(1′), and N(4) take part in hydrogen bonding, while N(4′) is the planar tetracovalent cation to which no hydrogen atom is attached. Since N(4) is not linked to any adjacent carbon atoms by a double bond, we can rule out the possibility that the free serpentinine base contains a carbinolamine grouping. Therefore the structure of serpentinine, $C_{42}H_{44}N_4O_5$, is now represented by formula (II). The u.v., i.r., and n.m.r. spectra and chemical properties of the alkaloid are compatible with this formula.

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[1] A. A. Gorman, M. Hesse, H. Schmid, P. G. Waser, and W. H. Hopff, 'The Alkaloids,' Vol. 1, The Chemical Society, London, 1971, p. 287.

[2] H. Kaneko, *J. Pharm Soc.* (*Japan*), 1960, **80**, 1357, 1362, 1365, 1370, 1374, 1378, 1382.