

Absolute Configuration of the Indole Alkaloid (–)-Mehranine Hydrobromide

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Abstract. The structure including the absolute configuration of the indole alkaloid (–)-mehranine hydrobromide ($1 \cdot \text{HBr}$) has been assigned by X-ray analysis. This result gave

the possibility to assign the absolute configurations of some related alkaloids.

The stereochemistry of (–)-mehranine isolated from *Tabernaemontana divaricata* (L.) R. Br. ex Roem. & Schult. (Apocynaceae) has been tentatively assigned assuming that it has a common biogenetic origin with the other indole alkaloids found in this plant [1]. Unfortunately, the configuration at C-2 was not specified in the published formula. We isolated this indole alkaloid and the related new compounds 3-oxo-mehranine, $14\alpha,15\beta$ -dihydroxy-*N*-methylasspidospermine, tabernaebovine and methylenebismehranine from *Tabernaemontana bovina* Lour. [2, 3]. The enantiomeric (+)-mehranine has been isolated from *Ervatamia coronaria* Stapf (Apocynaceae) [4]. We have studied the stereochemistry of (–)-mehranine, a key structure for the assignments of the absolute configurations of some related indole alkaloids.

Results and Discussion

The steric structure including the absolute configuration of (–)-mehranine hydrobromide ($1 \cdot \text{HBr}$) has been established by X-ray analysis. A perspective drawing of the final X-ray model is shown in Figure 1. The hydrobromide of **1** crystallizes in the space group $P2_12_12_1$ with four formula units per unit cell. Additionally the unit cell contains four molecules of methanol and two water molecules which are disordered statistically. The protonated mehranine cations and the bromide anions are well separated. The crystal structure determination shows that the addition of HBr to mehranine leads to the protonation of the nitrogen N(4), which is more basic than the indole nitrogen N(1). The bond lengths and angles are within the expected range. The torsion angles of the two five-membered and the two six-membered rings are given in

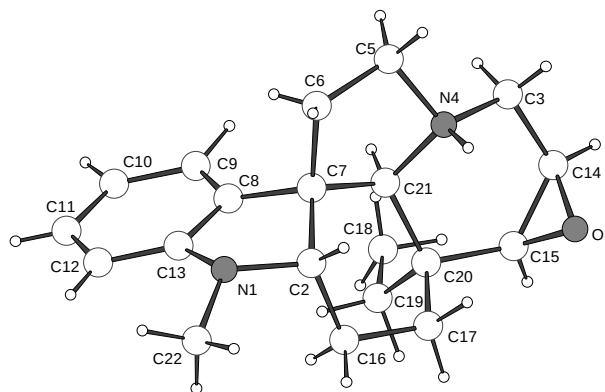


Fig. 1 Molecular structure of compound **1**·HBr

Table 1. The observed values indicate that the five-membered rings N(1)–C(2)–C(7)–C(8)–C(13) and N(4)–C(5)–C(6)–C(7)–C(21) adopt an envelope conformation. The six-membered ring C(2)–C(7)–C(21)–C(20)–C(17)–C(16) exhibits a slightly distorted chair conformation. Due to the steric requirements of the epoxide ring C(14)–O(1)–C(15) the six-membered ring N(4)–C(21)–C(20)–C(15)–C(14)–C(3) shows an irregular twist conformation.

A packing diagram of mehranine hydrobromide is shown in Figure 2. There are no unusually short contacts between the protonated mehranine molecules. The most important inter-molecular interaction arises from a hydrogen bridge which is formed between the proton bonded to N(4) and the oxygen atom of the methanol molecule [N–H: 89(4) pm, H···O:

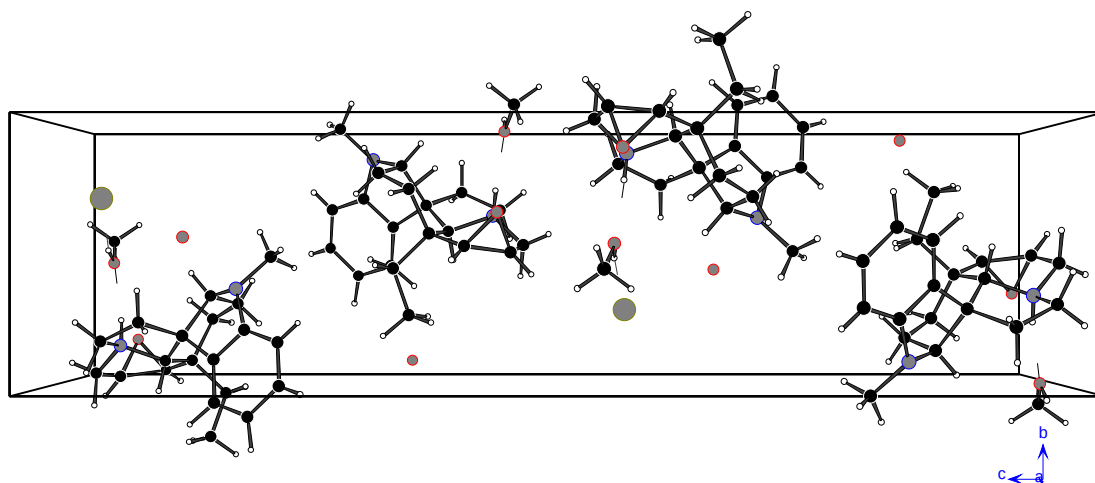
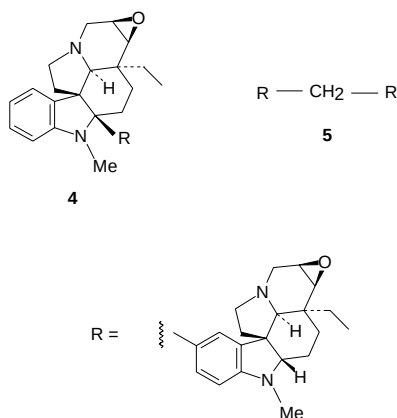
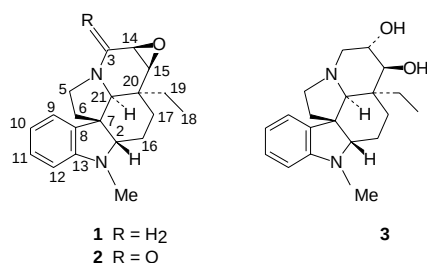


Fig. 2 Molecular arrangement of alkaloid 1·HBr in the crystal

188(4) pm]. A second weak hydrogen bridge can be observed between the hydroxy group of the methanol molecule and the bromide ion [O··H: 79(7) pm, H··Br: 249(7) pm].

From this result the absolute configurations of 3-oxo-mehranine (2) and 14 α ,15 β -dihydroxy-*N*-methylasspidospermine (3) have been deduced by comparison of their circular dichroism spectra with that of 1 [2], those of tabernaevovine (4) and methylenebismehranine (5) by biogenetic considerations [3].

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Scheme 1

Table 1 Selected torsion angles (°) of the indole alkaloid (–)-mehranine (1·HBr)

N(1)–C(2)–C(7)–C(8)	–33.0(4)
C(2)–C(7)–C(8)–C(13)	22.0
C(7)–C(8)–C(13)–N(1)	–2.0(5)
C(8)–C(13)–N(1)–C(2)	–21.0(5)
C(13)–N(1)–C(2)–C(7)	33.9(4)
N(4)–C(5)–C(6)–C(7)	–25.6(5)
C(5)–C(6)–C(7)–C(21)	1.0(5)
C(6)–C(7)–C(21)–N(4)	23.8(4)
C(7)–C(21)–N(4)–C(5)	–40.4(4)
C(21)–N(4)–C(5)–C(6)	40.9(4)
C(2)–C(7)–C(21)–C(20)	30.3(5)
C(7)–C(21)–C(20)–C(17)	–36.9(5)
C(21)–C(20)–C(17)–C(16)	52.9(5)
C(20)–C(17)–C(16)–C(2)	–63.4(5)
C(17)–C(16)–C(2)–C(7)	53.3(5)
C(16)–C(2)–C(7)–C(21)	–36.8(5)
N(4)–C(21)–C(20)–C(15)	–34.1(4)
C(21)–C(20)–C(15)–C(14)	2.9(6)
C(20)–C(15)–C(14)–C(3)	1.3(7)
C(15)–C(14)–C(3)–N(4)	25.5(6)
C(14)–C(3)–N(4)–C(21)	–57.3(5)
C(3)–N(4)–C(21)–C(20)	64.4(4)

Experimental

(–)-Mehranine (1)

m.p. 102–104 °C (from Me₂CO). [α]_D²⁴ –48.4° (CHCl₃, *c* 1.02), lit. [1]: [α]_D –49° (CHCl₃).

(–) Mehranine monohydrobromide (1·HBr)

Equivalent amounts of 1 and 48% HBr were united in MeOH, the solvents evaporated *in vacuo* and the residue crystallized from Me₂CO–MeOH; *m.p.* 160–163 °C.

Crystal data of (–) mehranine monohydrobromide

C₂₀H₂₇BrN₂O, *M* = 391.36, *T* 293(2)° K, λ 0.71073 Å, orthorhombic, space group P 2₁2₁2₁, with *a* = 7.7021(12), *b* =

8.354(2) and $c = 32.135(6)$ Å, $\alpha = \beta = \gamma = 90^\circ$, $Z = 4$, volume $2067.8(7)$ Å³, $D_c = 1.260$ g cm^{–3}, absorption coefficient 2.003 mm^{–1}, $F(000)$ 784, Θ range for data collection 2.52 to 26.03° , index ranges $-8 \leq h \leq 8$, $-10 \leq k \leq 10$, $-39 \leq l \leq 39$, 13297 collected reflections, 3822 independent reflections [$R(\text{int}) = 0.0991$], refinement method full-matrix least-squares on F^2 , data/restraints/parameters 3822/0/344, goodness-of-fit on F^2 0.957, final R indices [$I > 2\sigma(I)$] $R_1 = 0.0425$, $wR_2 = 0.0730$, R indices (all data) $r_1 = 0.0821$, $wR_2 = 0.0830$, absolute structure parameter $-0.016(12)$, largest difference peak and hole 0.401 and -0.218 e.Å^{–3}.

The atomic co-ordinates for this work are available on request from the director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this paper.

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