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

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Received October 28th, 1998

Keywords: Natural products, Alkaloids, Indole alkaloid, Conformation analysis, (–)-Mehranine

Abstract. The structure including the absolute configuration of the indole alkaloid (–)-mehranine hydrobromide (1·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-oxomehranine, 14α,15β-dihydroxy-*N*-methylaspidospermine, 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.

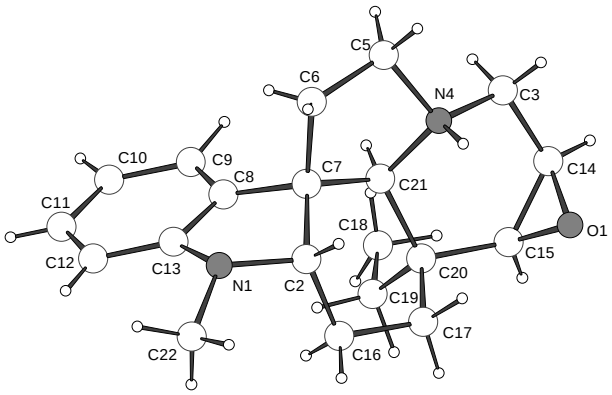


Fig. 1 Molecular structure of compound **1**·HBr

Results and Discussion

The steric structure including the absolute configuration of (–)-mehranine hydrobromide (**1**·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 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:

  1436-9966/99/34101-69 $ 17.50 + .50/0

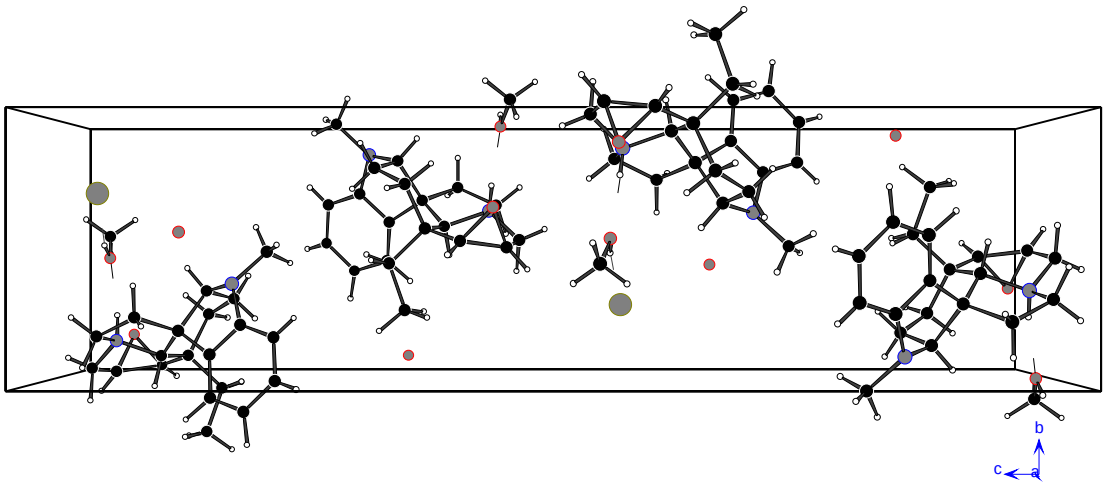
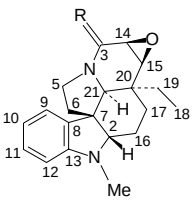


Fig. 2 Molecular arrangement of alkaloid **1**·HBr in the crystal

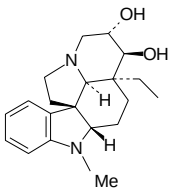
188(4) pm]. A second weak hydrogen bridge can be observed between the hydroxy group of the methanol molecule and the bromide ion [O-H: 79(7) pm, H···Br: 249(7) pm].

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

We thank the Volkswagenstiftung and the Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie, Bonn, for financial support. One of us (T.P.L.) is indebted to the Deutscher Akademischer Austauschdienst for a grant.



1 R = H_2
2 R = O



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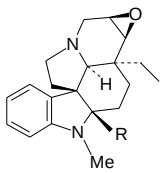

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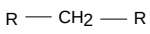

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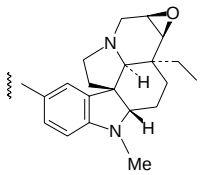
R =



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 Me_2CO). $[\alpha]_D^{24}$ –48.4° ($CHCl_3$, *c* 1.02), lit. [1]: $[\alpha]_D$ –49° ($CHCl_3$).

(–) 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 Me_2CO–MeOH; *m.p.* 160–163 °C.

Crystal data of (–) mehranine monohydrobromide

$C_{20}H_{27}BrN_2O$, M = 391.36, T 293(2)° K, λ 0.71073 Å, orthorhombic, space group P $2_12_12_1$, with a = 7.7021(12), b =

8.354(2) and c = 32.135(6) Å, $\alpha = \beta = \gamma = 90°$, Z = 4, volume 2067.8(7) $Å^3$, 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 < = h < = 8, –10 < = k < = 10, –39 < = l < = 39, 13297 collected reflections, 3822 independent reflections [R(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 [$I > 2\sigma(I)$] R1 = 0.0425, wR2 = 0.0730, R indices (all data) r1 = 0.0821, wR2 = 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.

References

[1] Toh-Seok Kam, S. Anuradha, Phytochemistry **1995**, *40*, 313
[2] Trinh Phuong Lien, H. Ripperger, A. Porzel, K. Merzweiler, Tran Van Sung, G. Adam, Phytochemistry **1998**, *49*, 1457
[3] Trinh Phuong Lien, C. Kamperdick, Tran Van Sung, G. Adam, H. Ripperger, Phytochemistry, in press
[4] Atta-ur-Rahman, A. Muzzafar, N. Daulatabadi, Z. Naturforsch., Teil B **1983**, *38*, 1700

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