

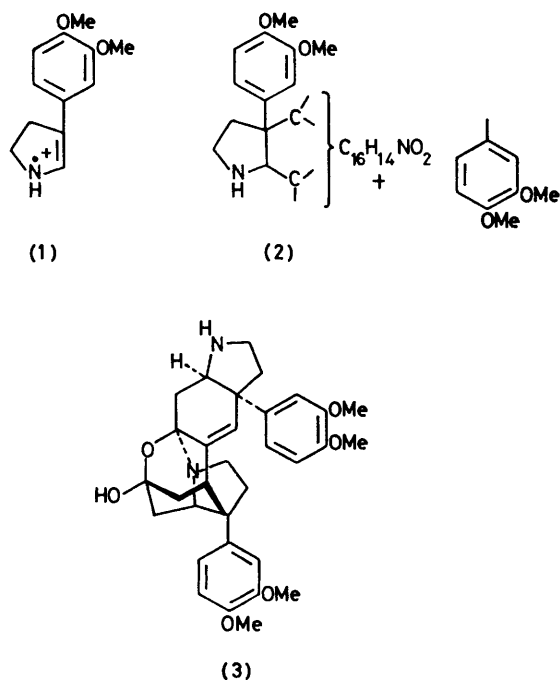
X-Ray Crystal and Molecular Structure of Channaine, an Unusual Alkaloid, Probably an Artefact from *Scelletium strictum*

By AMINA ABOU-DONIA, PETER W. JEFFS,* ANDREW T. MCPHAIL,* and RICHARD W. MILLER
(Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706)

Summary The structure of channaine (3), derived by spectral and single-crystal X-ray analyses, indicates that this alkaloid is probably an artefact which arises from the condensation of a pair of *N*-demethylmesembrenone (4) molecules during the isolation process.

ISOLATION of the alkaloid channaine from *Scelletium tortuosum* was first reported more than twenty years ago by Bodendorf and Krieger¹ who assigned to it the empirical formula $C_{16}H_{19/21}NO_3$ and determined from its i.r. spectrum that it contained OH and NH groups. Since that time the only mention of this compound in the literature appears in

Previous investigations of the alkaloids of *S. strictum* have afforded alkaloids belonging to a single ring system, *viz.* the mesembrine or 3a-aryloctahydroindole type.⁴ Channaine was obtained from the ether-insoluble non-phenolic alkaloid fraction by chromatography over alumina. Its ¹H n.m.r. spectrum showed general features which resembled the spectra of alkaloids of the mesembrine class. A multiplet at δ 6.96(6H) and four singlets at 3.98, 3.96, 3.95, and 3.94 indicated the presence of two veratryl units. The only other clearly assignable signal was a one-proton singlet at δ 5.70 (olefinic H). Its mass spectrum showed M^+ at m/e 546.2731 ($C_{32}H_{38}N_2O_6$; calc. 546.2728). Significantly, the base peak was at m/e 205.1096 and corresponded to the 3-arylpyrrolidinium fragment (*cf.* 1) which occurs characteristically as the major ion in the mass spectra of appropriately substituted 3a-aryloctahydroindole alkaloids of the mesembrine series.⁵ The u.v. spectrum provided supporting evidence for the presence of two isolated veratryl units, and the i.r. spectrum showed OH and NH absorptions while carbonyl absorptions were notably absent.



a review article² which cites briefly further unpublished work establishing that it was racemic and contained two aromatic methoxy groups in a veratryl chromophore but lacked any *N*-methyl or carbonyl functions. The review authors also made the intriguing comment that channaine might be a dimer with empirical formula $C_{16}H_{19}NO_3$. Since possession of a dimeric structure would place channaine into a new structural group, we have attempted to identify this base in the alkaloid fraction of *S. namaquense*. Although lengthy investigations of the alkaloids of this plant have resulted in the isolation of new bases representing four different ring systems,³ no evidence for the presence of channaine has been found. Recently we have re-examined the alkaloids of *S. strictum* and have isolated a racemic base with spectral and physical properties in accordance with those reported for channaine.

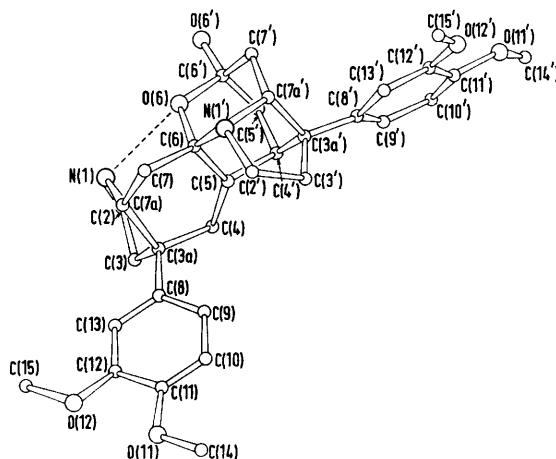
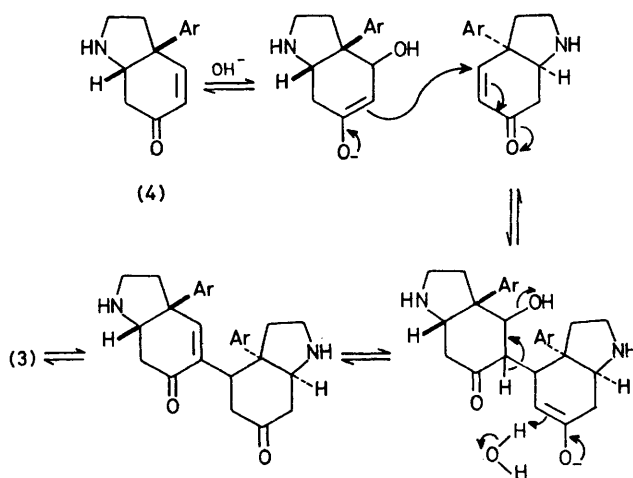


FIGURE. Molecular structure and conformation of one enantiomer of channaine; the broken line denotes an intramolecular N-H...O hydrogen bond.

Partial structure (2) could be derived from spectral data but lack of material precluded further chemical studies. Elucidation of the structure of channaine (Figure) as the racemate of (3) was achieved by X-ray analysis of the hexahydrate, m.p. 180–181 °C, single crystals of which were obtained by slow evaporation of a solution of channaine in ethyl acetate. *Crystal data*: $C_{32}H_{38}N_2O_6 \cdot 6H_2O$, monoclinic, space group $P2_1/c$, $a = 16.412(8)$, $b = 7.745(4)$, $c = 26.925(13)$ Å, $\beta = 111.22(3)^\circ$, $U = 3190.4$ Å³, $D_c = 1.36$ g cm⁻³, $Z = 4$. The crystal structure was solved by use of MULTAN⁶ and difference Fourier syntheses. Least-squares refinement of atomic positional and thermal

(anisotropic C, N, O; fixed H contributions) parameters has reduced R to 0.075 over 3167 statistically significant [$I > 2.0\sigma(I)$] reflections measured on an Enraf-Nonius CAD-3 automated diffractometer (θ - 2θ scans; Ni-filtered $\text{Cu-K}\alpha$ radiation).†

Nearly all *Scelletium* alkaloids are obtained in optically active form, the principal exception being the base mesembrenone which is isolated as the racemate. However, if mesembrenone were produced in the plant as a single enantiomer, the isolation conditions employed would result in racemization.⁴ The formation of channaine from *N*-demethylmesembrenone (4) can be readily explained by the sequence shown in the Scheme.⁷ That channaine is obtained as the racemate suggests that it is an artefact, its formation taking place under the conditions of isolation and/or chromatography during which the natural base (–)-*N*-demethylmesembrenone (as yet undetected) is racemized prior to undergoing the condensations and reactions in the Scheme. The stereochemistry revealed by the *X*-ray study indicates that channaine is formed by condensation of two molecules of (4) possessing the same absolute stereochemistry, *i.e.* (+)(+) and (–)(–). The formation of the spiroaminol-hemiacetal rings and the intramolecular N(1)–H···O(6) hydrogen bond obviously confer considerable stability and are important in shifting the equilibria towards channaine since mesembrenone shows no evidence of undergoing a similar condensation under comparable conditions.



SCHEME

We thank the Egyptian Government for a fellowship to A. A.-D. while on leave from the Department of Pharmacognosy, Alexandria University.

(Received, 14th August 1978; Com. 888.)

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

¹ K. Bodendorf and W. Krieger, *Arch. Pharm.*, 1957, **290**, 441.

² A. Popelak and G. Lettenbauer, 'The Alkaloids,' ed. R. H. F. Manske, Vol. 9, Academic Press, New York, 1967.

³ P. W. Jeffs, P. A. Luhan, A. T. McPhail, and N. H. Martin, *Chem. Comm.*, 1971, 1446; T. M. Capps, K. D. Hargrave, P. W. Jeffs, and A. T. McPhail, *J.C.S. Perkin II*, 1977, 1098.

⁴ P. W. Jeffs, G. Ahmann, H. F. Campbell, D. S. Farrier, G. Ganguli, and R. L. Hawks, *J. Org. Chem.*, 1970, **35**, 3512; P. E. J. Kruger and R. R. Arndt, *J. S. African Chem. Inst.*, 1971, 235.

⁵ N. H. Martin, D. Rosenthal, and P. W. Jeffs, *Org. Mass Spectrometry*, 1976, **11**, 1.

⁶ G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

⁷ For an intramolecular analogue of the Michael reaction see *e.g.* S. Swaminathan, J. P. John, and S. Ramachandran, *Tetrahedron Letters*, 1962, 729.