A Novel Bis-indole Alkaloid. *X*-Ray Crystal Structure Determination of Borreverine and its Rearrangement Product on Diacetylation

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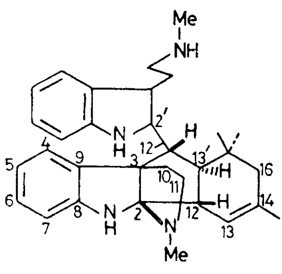
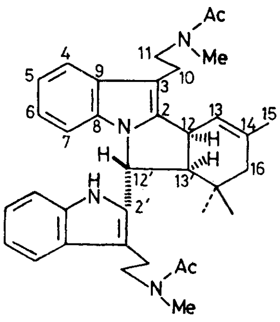
Summary Borreverine is a novel bis-indole alkaloid isolated from *Borreria verticillata* (Rubiaceae), diacetylation of which gives a rearrangement product; the molecular structures of both compounds were established by *X*-ray diffraction analyses.

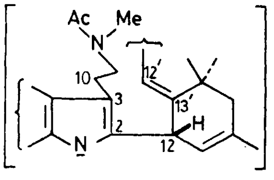
We report the elucidation of the structure of the bis-indole alkaloid borreverine (I) extracted from *Borreria verticillata* (Rubiaceae) which also contains the indole alkaloid borrerine.[1] The molecular formula of borreverine, $C_{32}H_{40}N_4$, m.p. 193 °C, $[\alpha]_D^{20}$ 0° ($CHCl_3$), M^+ 480·3254, has been established by mass spectroscopy (high resolution), *m/e* (% relative abundance) 480 ($M^{+\cdot}$; 24), 437 (100), 393 (12), 271 (18), 264 (17), 250 (25), 205 (18), 198 (35), 196 (50), 185 (32), 182 (39), and 172 (87). The u.v. spectrum, λ_{max} (EtOH) 225 (log ε 4·78) 285 (4·40), and 295 (4·40) nm, is in accord with an indole–dihydroindole chromophore.



(I)



(II)



(III)

The ^1H n.m.r. spectrum ($CDCl_3$, Me_4Si) displays signals at δ 0·32 (3H, s), 0·90 (3H, s), 1·70 (3H, s), 5·60 (1H, s), 2·53 (3H, s), 2·56 (3H, s), 1·40 and 4·20 (exchangeable with D_2O), and 6—7·70 (8 ArH).

Initially, we examined crystals of borreverine and its dimethiodide. Neither compound gave crystals suitable for *X*-ray diffraction analyses. Borreverine was converted into its diacetyl derivative, m.p. 272—274 °C, $[\alpha]_D^{20}$ 0°, M^+ 564. Good crystals were grown and the complete structure and stereochemistry of this derivative were determined. The molecular structure of diacetylborreverine (II) is shown in Figure 1.

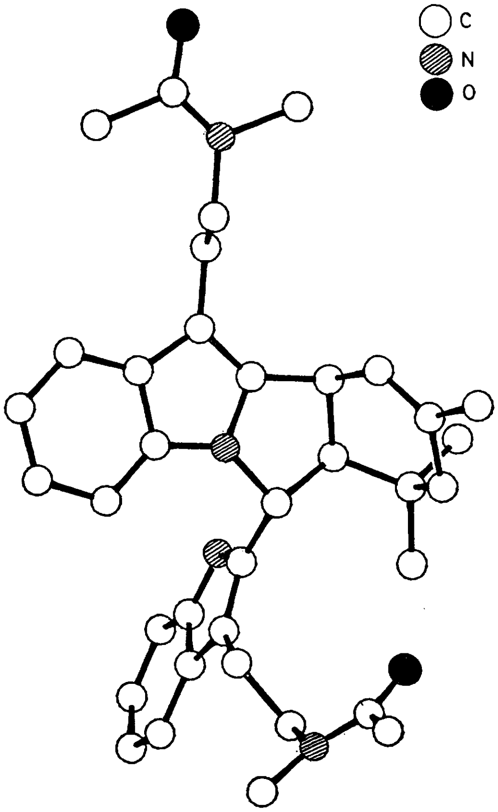


Figure 1. Molecular structure of diacetylborreverine (II).

Subsequently, it became apparent that the u.v. mass, and ^{13}C n.m.r. spectra of borreverine were not compatible with a formula corresponding to (II) and that conversion into the diacetyl derivative must have been accompanied by a rearrangement of the parent compound. Eventually it was possible to obtain single crystals of borreverine itself. Prismatic crystals grown from methanol decayed to a powder within a few seconds, probably owing to loss of solvent of crystallization. A crystal, sealed in a thin-walled capillary with a drop of mother liquor, maintained its integrity during the data collection. *X*-ray diffraction analysis of borreverine revealed the unexpected formula (I).

Crystal data: Diacetylborreverine (II): $C_{36}H_{44}N_4O_2$, $M = 564$, monoclinic, space group $P2_1/n$, $Z = 4$, $a = 10{\cdot}156(1)$, $b = 13{\cdot}703(2)$, $c = 22{\cdot}623(2)$ Å, $\beta = 94{\cdot}85(7)°$. Borreverine hydrate methanol solvate (I): $C_{32}H_{40}N_4,CH_4O,1{\cdot}5H_2O$,† $M = 546$, monoclinic, space group $P2_1/c$, $Z = 4$, $a = 17{\cdot}501(6)$, $b = 10{\cdot}195(4)$, $c = 18{\cdot}409(5)$ Å, $\beta = 94{\cdot}96(2)°$. Single-crystal X-ray diffraction data were measured with a Philips PW 1100 diffractometer using θ–2θ scan techniques with graphite monochromated Cu-K_α radiation. The structures were solved by conventional direct methods.[2] The least-squares refinements based on 3038 (I) and 2375 (II) observed reflections resulted in R factors of 0·06 (I) and 0·10 (II). The molecular structure of the racemic alkaloid borreverine (I) is shown in Figure 2.‡

This alkaloid, which has a novel structure, is derived formally from the dimerization of two 2-isopropenyl-N-methyltryptamine residues. The acetylation of borreverine, followed by this rearrangement probably proceeds *via* an intermediate such as (III) formed through the successive breaking of bonds C(2)–N_b and C(3)–C(12′) [assisted by the indole ring of (I)]. The intermediate (III) would then undergo an internal rotation about the C(2)–C(12) single bond, before cyclization.

We thank Mr. Mohamed Damak for the preparation of crystals of borreverine.

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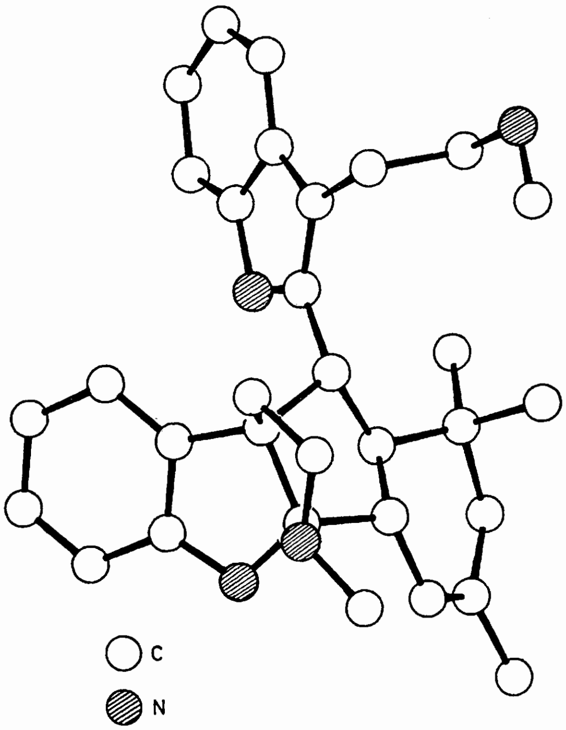

FIGURE 2. Molecular structure of borreverine (I).

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† To account for a substantial peak in the difference map calculated near the end of the refinement, the presence of a second molecule of water was postulated. The oxygen atom was introduced with an occupancy factor of 0·5.

‡ 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 communication.

[1] J. Pousset, J. Kerharo, G. Maynart, X. Monseur, A. Cavé, and R. Goutarel, *Phytochemistry*, 1973, **12**, 2308.
[2] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.