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THE STRUCTURE OF HYPOGNAVINOL

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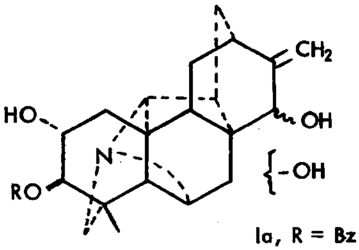
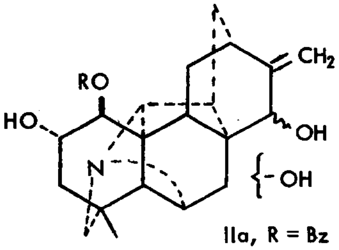
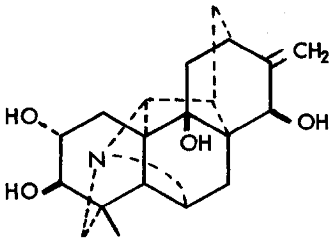
Hypognavine ($C_{27}H_{31}NO_5$), a diterpene ester alkaloid isolated from certain plants of *Aconitum sanyoense* Nakai, yields as its alkaline hydrolysis product, hypognavinol ($C_{20}H_{27}NO_4$), m.p. 307-308°.[1-6] In the previous work the structure of hypognavine was assigned as either Ia or IIa and hypognavinol as Ib or IIb. The similarities in the properties of hypognavinol and anhydroignavinol (III) and our recent determination of the structure of the latter prompted further investigation of the structure of hypognavinol. Since NMR spectral examination of hypognavinol was unsuccessful in differentiating between structures Ib and IIb, we undertook determination of this structure by single crystal X-ray analysis.



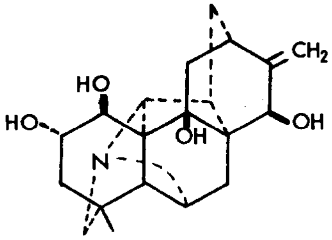
Ia, R = Bz
Ib, R = H



IIa, R = Bz
IIb, R = H



III

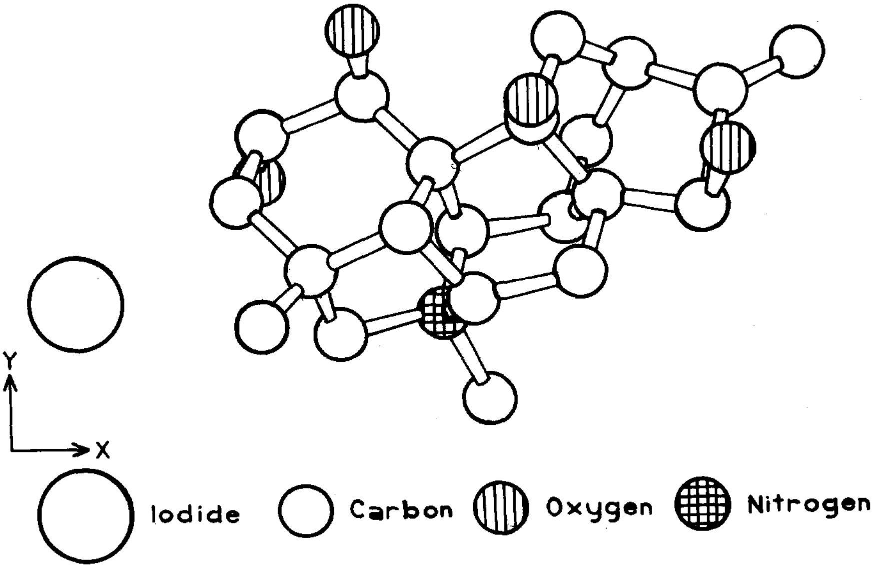


IV

Hypognavinol methiodide, m.p. 309-310°, was prepared in absolute methanol and recrystallized from a methanol/3-pentanone solvent system. The crystals were orthorhombic with unit cell dimensions of $a = 13.69$ Å, $b = 14.41$ Å, $c = 10.00$ Å, $\alpha = \beta = \gamma = 90°$, $Z = 4$, $D_m = 1.64\ g/cm^3$, and $D_c = 1.64\ g/cm^3$ (for $C_{21}H_{30}NO_4I$) as determined from precession photographs (Mo-K$_\alpha$, $\lambda = 0.7107$ Å). The space group was uniquely determined as $P2_12_12_1$ by systematic absences. Intensity data were collected on an Enraf-Nonius automated diffractometer using Cu-K$_\alpha$ radiation ($\lambda = 1.5418$ Å). Lorentz and polarization corrections were made on the 1935 unique non-zero reflections measured and considered to be above background radiation. No absorption corrections were made on the data.

The structure was solved by the heavy atom method[8]. After refinement to R=0.087, the average estimated standard deviation of bond lengths was 0.02 Å and the average estimated standard deviation of bond angles was 1.2°. C-C bond lengths average 1.54 Å, C-N$^+$ bond lengths average 1.53 Å, and C-OH bond lengths average 1.43 Å.

A view of the resulting structure projected on the ab plane is shown in the Figure. The correct structure of hypognavinol is now established as IV. The hydroxyl group previously unassigned is thus shown to reside at C(9). The assignment of the ester function of hypognavine at C-1 (or C-3) in the previous work was based on steric arguments.[4,6] A careful examination of models suggests, however, that the steric difference between a benzoyl group on the β-C(1)-hydroxyl or on the α-C(2)-hydroxyl would be slight. The hydroxyl at position C(9) increases the steric hinderance in the region of the C(1)-hydroxyl and makes this position less favorable than otherwise as the site of the benzoyl group. The location of the benzoyl group in hypognavine therefore remains in doubt. The absolute configuration indicated is based on analogy with the other diterpene alkaloids.



Figure

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