X-Ray Crystallographic Determination of the Structure of the Diterpenoid Alkaloid Denudatine

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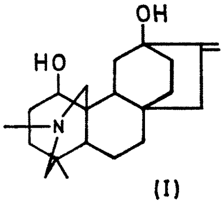
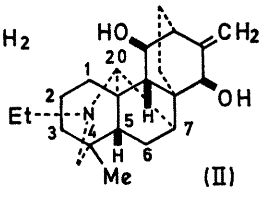
Summary Single-crystal *X*-ray diffraction studies of denudatine methiodide have shown that denudatine possesses an atisine-type skeleton with a C(7)–C(20) bridge: denudatine has a structure of the type which may serve as an intermediate in the biogenetic transformation of the atisine-type alkaloids to the aconitum-type alkaloids.

DENUDATINE, m.p. 248—249°, a diterpene alkaloid isolated from the roots provisionally identified as *Delphinium denudatum*, Wall (Ranunculaceae) was reported to have the molecular formula $C_{21}H_{33}NO_2$ (mol. wt. 331).[1] This compound was tentatively assigned structure (I) in 1961 on the basis of chemical and spectral evidence.[2,3] Since the evidence supporting (I) is not definite, a chemical correlation of denudatine with another of the diterpene alkaloids of known structure seemed advisable. However, preliminary spectral studies on an authentic sample of denudatine indicated the absence of an *N*-methyl group (n.m.r.) and a different molecular formula ($C_{22}H_{33}NO_2$), as evidenced by the mass spectrum (molecular ion at *m/e* 343). The structure of denudatine was determined by single-crystal *X*-ray analysis.



(I)

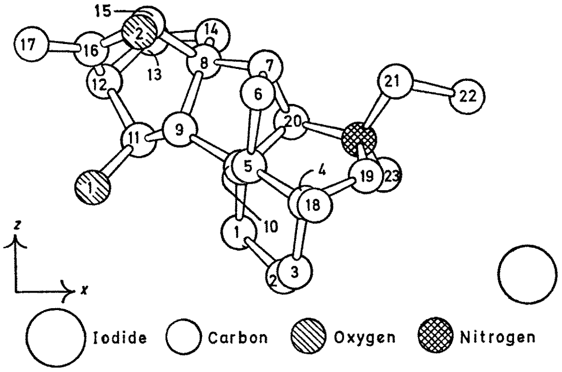


(II)

Denudatine methiodide was prepared and crystallized from 95% ethanol–pentan-3-one, m.p. 276—277° (with evolution of a gas): analysis satisfactory for $C_{23}H_{36}NO_2I$. The crystals were orthorhombic with unit cell dimensions of *a* 16·98 Å, *b* 7·86 Å, *c* 15·52 Å, $\alpha = \beta = \gamma = 90°$; $Z = 4$, $D_m = 1·53$ g./cm³., $D_c = 1·56$ g./cm³. (for $C_{23}H_{36}NO_2I$) as determined from precession photographs (Mo-K_α) $\lambda = 0·7107$ Å). The space group was uniquely determined as $P2_12_12_1$ by systematic absences. Intensity data were collected about the *b*-axis by the Weissenberg equi-inclination method using multiple film technique and Cu-K_α radiation ($\lambda = 1·5418$ Å). The intensities of the 1876 unique non-zero reflections which were used in the analysis were estimated visually with a standard intensity strip.

The structure was solved by the heavy-atom method.[4] After refinement to $R = 0·115$, the average estimated standard deviation of bond lengths was 0·04 Å and the average estimated standard deviation of bond angles was 2°. C–C bond lengths average 1·55 Å and C–N⁺ bond lengths average 1·52 Å.

A view of the structure projected on the *ac* plane is shown in the Figure. The correct structure of denudatine is now established as (II). The absolute configuration indicated is based on analogy with the other diterpene alkaloids.



FIGURE

Denudatine represents the first example of a C_{20}-diterpene alkaloid with an atisine skeleton possessing either an *N*-ethyl group or a C(7)–C(20) bridge. Both of these features are common in the *Garrya* alkaloids.[5] More importantly, denudatine has a skeleton of the type postulated by Wiesner[6] for an intermediate in the biogenetic transformation of the atisine-type alkaloids to the aconitum-type alkaloids.†

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† After this paper was written, work from another laboratory appeared also assigning structure (II) to denudatine.[7]

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