An Unusual Rearrangement of a Hetisine Derivative

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Summary Lithium aluminium hydride reduction of a hetisine derivative affords a novel rearrangement product whose structure has been determined by single-crystal *X*-ray diffraction studies.

KOBUSINE, a diterpene alkaloid occurring in several Japanese *Aconitum* species, was assigned either structure (I) or (II) on the basis of chemical studies in 1959.[1] In a subsequent communication structure (I) was assigned to kobusine without the presentation of clear evidence to eliminate (II).[2] Because of the obvious relationship of kobusine to hetisine (III), whose structure has been determined by *X*-ray diffraction studies,[3] a chemical correlation of the two compounds appeared desirable.

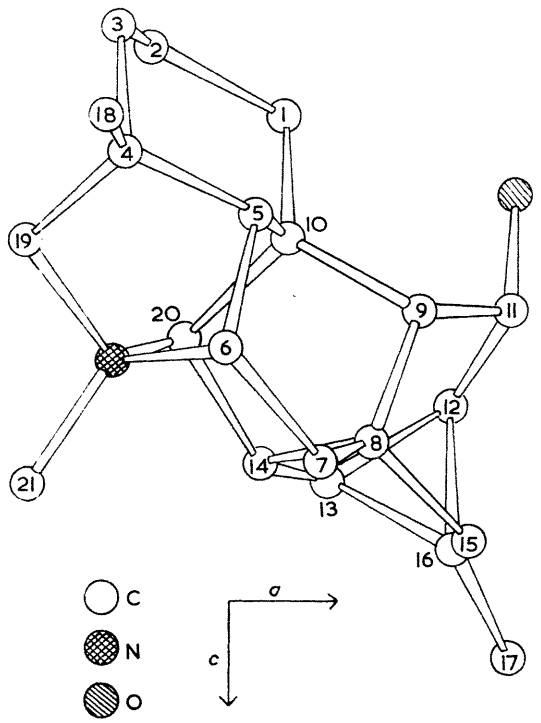
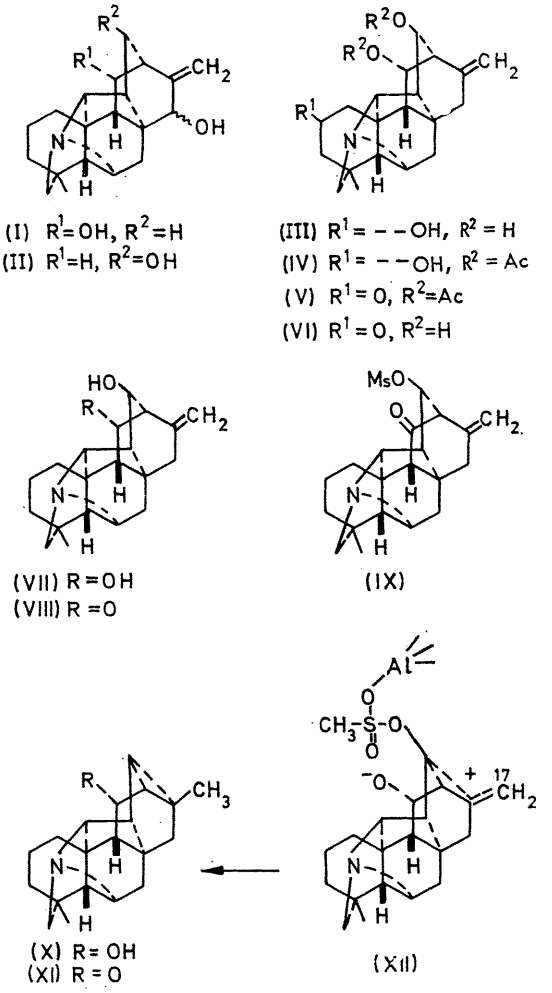


FIGURE. *A projection of the structure of the cyclopropyl derivatve* (X) *on to the* ac *plane. The position of the iodide ion is not shown.*

The correlation route involved oxidation of hetisine diacetate (IV)[4] to the keto-diacetate (V), saponification of (V) to (VI), and Wolff–Kishner reduction of (VI) to 2-deoxyhetisine (VII). Selective Sarett oxidation of the latter afforded (VIII), which was converted into the mesylate (IX). Presumably, reduction of (IX) with $LiAlH_4$ and introduction of an allylic hydroxy-group should have produced kobusine (I). However, hydride reduction of (IX) produced an interesting rearrangement product whose chemical and spectral data are in good agreement with the cyclopropyl structure (X). The n.m.r. spectra of the product [δ 0·93 (s, C-CH_3), 1·18 p.p.m. (s, CCH_3)] and of its acetate [δ 0·95 (s, CCH_3), 1·2 (s, CCH_3), 2·03 (s, OCOCH_3), 5·19 p.p.m. (d, *J* 8 Hz., C*H*OAc] indicate that two tertiary methyl groups are present and that vinyl protons have disappeared. The new methyl signal at δ 1·18 p.p.m. was considerably more deshielded than any of the tertiary methyl groups previously encountered in the hetisine series. Alcohol (X) was oxidized with chromic acid to a ketone (XI), m.p. 139—141°; ν_{max} 1680 cm.$^{-1}$; λ_{max} (EtOH) 204 (ε 5400), 277·5 nm. (ε 54); *m/e* 295, with spectral properties consistent with that of a ketone α to a cyclopropyl ring.



The structure of the cyclopropyl derivative (X) was determined by single-crystal *X*-ray analysis. Compound (X) was converted into the methiodide and crystallized from methanol–acetone. The orthorhombic crystals were block-like and elongated about the *b*-axis. Unit-cell dimensions were determined from precession photographs (Mo-K_α, $\lambda = 0{\cdot}7107$ Å) as *a* 15·870, *b* 7·685, *c* 16·031 Å, $\alpha = \beta = \gamma = 90°$; $Z = 4$, D_m 1·42 g./cm.^{3}, D_c 1·49 g./cm.^{3} Systematic absences established the space group uniquely as $P2_12_12_1$. Intensity data were collected around the *b*-axis

by use of the multiple-film technique and Cu-K_α radiation ($\lambda = 1{\cdot}5418$ Å). Intensities were estimated visually with a standard intensity strip. In all, 954 unique non-zero reflections were used in the analysis.

The structure was solved by the heavy-atom method[5] and refined to $R = 0{\cdot}10$. A view of the structure projected on the *ac* plane is shown in the Figure. The average estimated standard deviation of bond lengths is approximately 0·06 Å and average estimated standard deviation of bond angles is about 3·5°. C–C bond lengths average 1·55 Å, in good agreement with the accepted value. C–N bond lengths average 1·56 Å which agrees favourably with $C(sp^3)$–N^+ bond lengths found in other alkaloids.[6]

The structure of the anomalous reaction product is thus established as the cyclopropyl compound (X). Its formation can be rationalized in terms of an intermediate such as (XII) in which some species of aluminium, such as hydride or oxide, co-ordinates with one of the mesylate oxygens providing at least partial ionization. Hydride attack on (XII) could then occur at C-17 to afford the cyclopropyl derivative (X). This reaction represents the first reported example of this type of skeletal rearrangement among the diterpene alkaloids, though homoallylic carbonium-ion rearrangements have ample precedents in other systems.[7]

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