# Crystal Structure of the Diterpene Alkaloid Hetidine

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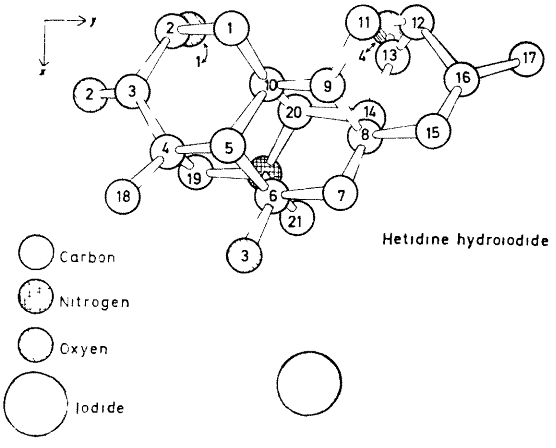
*Summary* Treatment of hetidine with methyl iodide in $Me_2N{\cdot}CHO$ gave hetidine hydroiodide, whose structure has been determined as (I) by single-crystal *X*-ray diffraction studies: hetidine has structure (II).

HETIDINE, a diterpene alkaloid isolated[1] recently in very small amounts from the very strong basic fraction of the roots of *Aconitum heterophyllum* Wall has an analysis corresponding to $C_{21}H_{27}NO_4$, and shows: m.p. 218—221°; $\nu_{max}$ (KBr) 3520, 3460 (OH), 1700 (C=O), 1665 and 920 cm$^{-1}$ ($C{=}CH_2$); $\lambda_{max}$ 209 ($\epsilon$ 5200); n.m.r. $\tau$ 8·80 (3H, s, $CCH_3$), 7·52 (3H, s, $N{-}CH_3$), 5·17 and 5·07 p.p.m. ($C{=}CH_2$): mass spectrum *m/e* 357 ($M^+$; calc. 357·5). Due to the very small amount of hetidine available, the structure of this alkaloid was determined by single crystal *X*-ray diffraction studies on a heavy atom derivative. Upon prolonged treatment with methyl iodide in $Me_2N{\cdot}CHO$ hetidine afforded a crystalline derivative, m.p. 305—307°; $\nu_{max}$ (KBr) 3600—2700, 1723 (C=O), and 923 cm$^{-1}$ ($C{=}CH_2$); n.m.r. $\tau$ = 8·39, 7·08, and 5·0 p.p.m.; *m/e* 358. The molecular weight of this derivative, determined from the volume of the unit cell and the density of the crystal measured by the flotation method,[2] suggested that the product is hetidine hydroiodide, rather than the methiodide. Recrystallization of the sample from acetonitrile gave a crystal suitable for *X*-ray analysis.

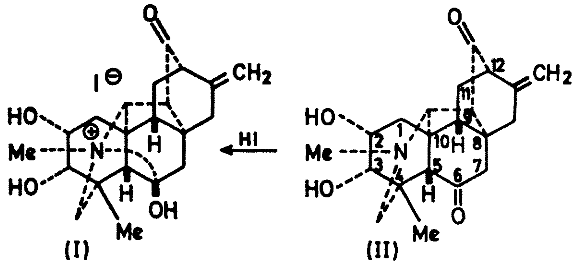


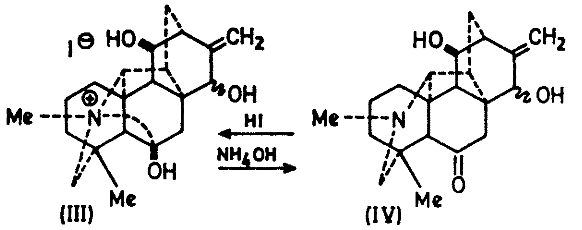
FIGURE

Unit cell dimensions were determined from precession photographs (Mo-$K_\alpha$, $\lambda$ = 0·7107 Å) as *a* 16·566, *b* 11·887, *c* 10·196 Å, $\alpha = \beta = \gamma = 90°$; $Z = 4$, $D_m$ 1·59, $D_c$ 1·60 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. (Cu-$K_\alpha$, $\lambda$ = 1·5148 Å). Intensities were estimated visually with a standard intensity strip. In all, 1230 unique non-zero reflections were used in the analysis.

The structure was solved by the heavy-atom method[3] and refined to $R$ = 13·6%. A view of the structure projected on the *ab* plane is shown in the Figure. The average estimated standard deviation of bond lengths is approximately 0·07 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 accepted values for alkaloids.[4]

The structure of the product is thus established as the hydroiodide (I). Its formation parallels results with other alkaloids,[5] where prolonged treatment with methyl iodide and $Me_2N{\cdot}CHO$ affords a hydroiodide. Hetidine may be assigned structure (II) by analogy with the relationship known to exist between pseudokobusine methiodide (III) and the derived *N*-methyl ketone (IV).[6] The chemical shift value of the *C*-methyl protons in (II) are at slightly higher field than in (I), probably due to the absence of the bond between the nitrogen atom and the C(6)-hydroxyl group. Hetidine (II), upon treatment with pyridine and acetic anhydride afforded an amorphous diacetate, $\tau$ 8·49, 8·0, 7·96, and 7·62 p.p.m.; *m/e* at 441. Molecular models indicate that the proximity of the nitrogen atom and the carbonyl group at C(6) facilitate formation of a N–C–OH bond on treatment with hydroiodic acid.





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