

Studies on *Orchidaceae* Alkaloids III*The Alkaloids in *Dendrobium primulinum* Lindl. and *Dendrobium chrysanthum* Wall.

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Two alkaloids, hygrine (I) and the hitherto unknown 5,7-dimethyl-octahydroindolizine (II), were isolated from *Dendrobium primulinum* Lindl. 2,4-Dimethyl-6-propylpyridine (III) was synthesized in order to identify one of the products from selenium dehydrogenation of II. I was also found to be the only alkaloid in *Dendrobium chrysanthum* Wall.

Several species of the genus *Dendrobium* contain appreciable amounts of alkaloids. One of the major alkaloids, dendrobine, has been found in *Dendrobium nobile* Lindl.²⁻⁸ and *Dendrobium linawianum* Rehb. f.⁵ In *D. nobile* the additional alkaloids nobiline⁷ and dendramine⁸ together with a quaternary ammonium compound⁸ have been reported. In *D. primulinum* Lindl. we have found two alkaloids of another type, *i.e.* hygrine (I) and the hitherto unknown 5,7-dimethyl-octahydroindolizine (II). I was identified as hygrine by the melting point of the picrate and the mass spectrum (Fig. 1) of the base; both being identical with those of an authentic sample.** Hygrine was also found to be the only alkaloid in *Dendrobium chrysanthum* Wall.

The elementary analysis and mass spectrum of II indicate that the molecular formula is C₁₀H₁₉N. II does not decolorize bromine solution at room temperature and the IR and NMR spectra show no alkene bands. The molecule therefore contains two rings. The NMR spectrum of II shows two C—CH₃ doublets, τ 8.99 ($J = 6.0$ c/s) and τ 9.11 ($J = 5.0$ c/s), which in the methiodide of II have been shifted to τ 8.69 ($J = 6.0$ c/s) and τ 9.03 ($J = 5.0$ c/s). The singlet at 1385 cm⁻¹ in the IR spectrum indicates the presence of two methyl groups attached to different tertiary carbon atoms. The absence of N—H bands in the IR and NMR spectra and the absence of bands in the NMR

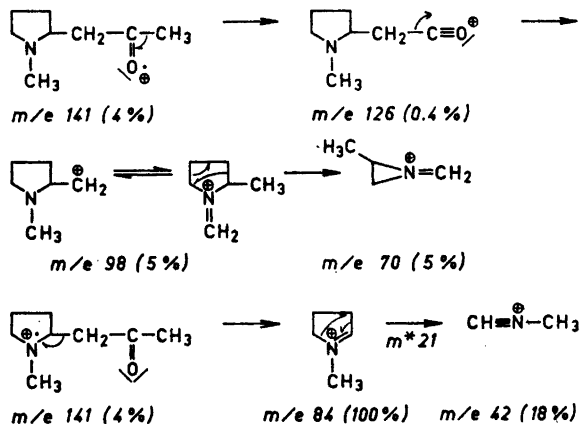
* Number II of this series see Ref. 1.

** Obtained from Dr. Theodor Schuchardt, München.

spectrum due to CH_3 groups attached to N or CH_2 , indicate the presence of a bridgehead nitrogen. The methiodide of II gives *one* N— CH_3 band in the NMR spectrum at τ 7.04 (3H). (*cf.* Ref. 9) II can thus be postulated as a dimethyl-octahydroindolizine.

In order to prove the site of the methyl groups, the base was subjected to selenium dehydrogenation. The main product after this reaction is 2,4-dimethyl-6-propylpyridine (III). The identity of III has been verified by comparison of mass spectrum, NMR spectrum, UV spectrum, and hydrochloride of III with those of a synthetic product obtained by reacting the mono-lithium compound of 2,4,6-trimethylpyridine with ethyl iodide. The methyl groups are thus situated in the 5 and 7 positions and II is 5,7-dimethyl-octahydroindolizine.

The mass spectrum of I (Fig. 1) shows the expected fragmentation (Scheme 1).



Scheme 1

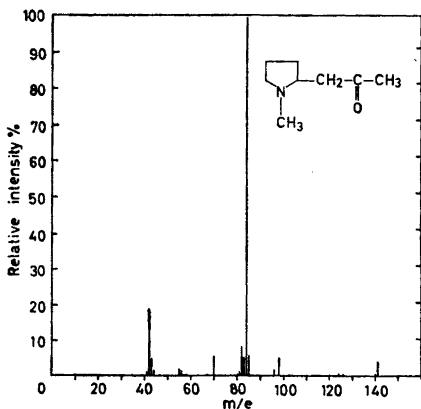
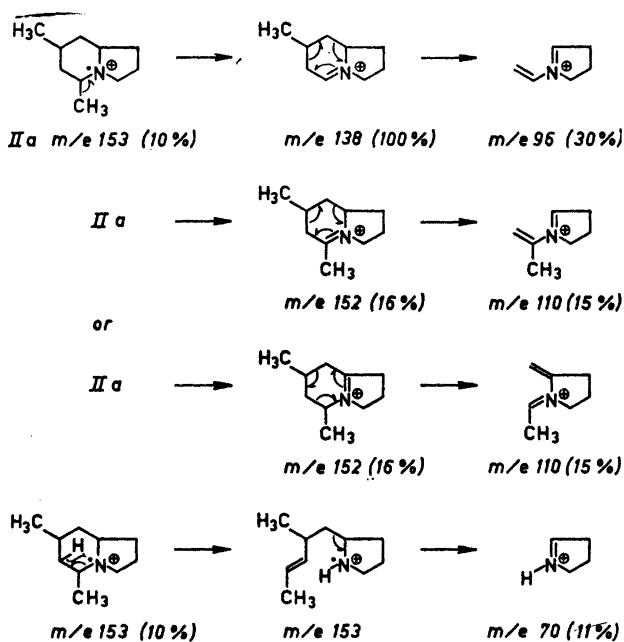


Fig. 1.

The mass spectra of II (Fig. 2) and III (Fig. 3) can easily be rationalized according to current ideas (Scheme 2).



Scheme 2

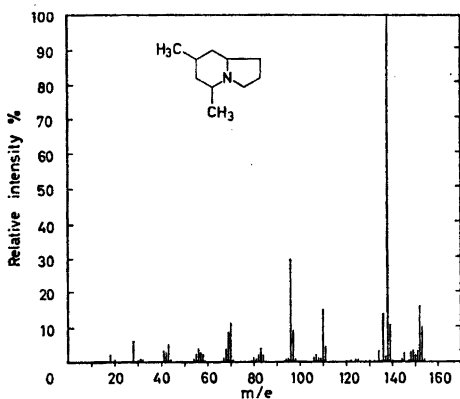


Fig. 2.

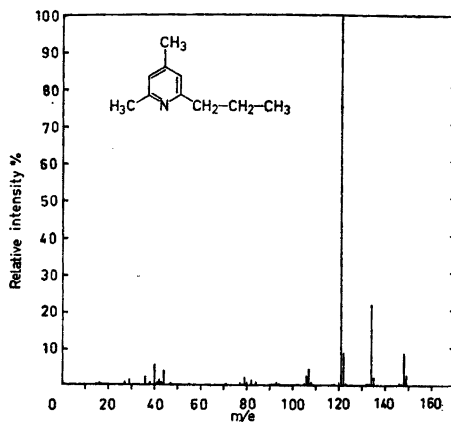
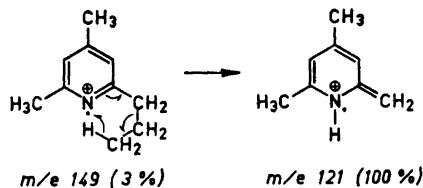


Fig. 3.

The base peak in the mass spectrum of III can be explained as illustrated in Scheme 3.

The present data are not sufficient to deduce the stereochemistry of II, although two papers recently have appeared dealing with the conformational and configurational aspects of octahydroindolizine, octahydroquinolizines,



Scheme 3

and their quaternary salts.^{9,10} Work is being continued on the stereochemistry of II.

EXPERIMENTAL *

6.0 kg of fresh plants of *Dendrobium primulinum* Lindl. were minced with methanol (20 l). The mixture was allowed to stand 24 h at 2°C, filtered and evaporated *in vacuo* to almost dryness. The residue was extracted with 3 × 25 ml 0.5 N HCl and the acidic aqueous solution filtered. The filtrate was extracted fifteen times with chloroform-ethanol 3/2 (v/v). During this process the acidic solution was successively made alkaline by the addition of 4 N sodium hydroxide. The combined chloroform-ethanol solutions were dried over anhydrous sodium sulphate and evaporated *in vacuo* to leave a few ml of a dark brown oil. The oil was chromatographed on basic alumina. Elution with ether afforded a pale yellow liquid containing the alkaloids. Thin layer chromatography and gas chromatography showed the ether solution and a fresh sample of the plant to contain the same two alkaloids. These were separated by gas chromatography using a column (width 8 mm, length 2.9 m) of 20% SE-52 on 60–80 mesh Chromosorb W HMDS at 130°C. Measurements of the areas enclosed by the peaks on the gas chromatogram showed that the alkaloids were present in the ratio 3 (first peak, I) to 1 (second peak, II).

I (*Hygrine*). n_D^{25} 1.4547; $[\alpha]_D -0.7^\circ$ (c 1.1, CHCl₃); molecular weight 141 (mass spectrometry); IR spectrum: $\nu_{\max}^{\text{CCl}_4}$ 1720(s) cm⁻¹; NMR (in CDCl₃): 6.8–8.8 τ (9H); 7.73 τ (3H) singlet; 7.86 τ (3H) singlet. (Found: C 68.0; H 10.1; N 10.0. C₈H₁₅NO requires: C 68.1; H 10.7; N 9.9). *Hydrochloride*, colourless needles from ethanol, m.p. 132–133°C. (Found: C 54.0; H 9.02; N 7.92. C₈H₁₆ClNO requires: C 54.1; H 9.07; N 7.89). *Picrate*, yellow prisms from ethanol, m.p. 149–151°C. (cf. Ref. 11).

II (*5,7-Dimethyl-octahydroindolizine*) is a colourless oil with a characteristic smell, has no UV absorption above 230 m μ and does not decolourize bromine solution at room temperature. n_D^{25} 1.4732; $[\alpha]_D -38^\circ$ (c 1.00, CHCl₃); molecular weight 153 (mass spectrometry); IR spectrum: $\nu_{\max}^{\text{CCl}_4}$ 1385(s) cm⁻¹ singlet; NMR (in CDCl₃): 8.99 τ (3H) doublet ($J = 6.0$ c/s); 9.11 τ (3H) doublet ($J = 5.0$ c/s). (Found: C 77.2; H 12.4; N 9.10. C₁₀H₁₉N requires: C 78.3; H 12.5; N 9.14). *Hydrochloride*, m.p. 194–195°C. (Found: C 63.0; H 10.7; N 7.16. C₁₀H₂₀ClN requires: C 63.3; H 10.6; N 7.39). *Methiodide*, m.p. 263–264°C. (Found: N 4.36. C₁₁H₂₂IN requires: N 4.74). NMR (in D₂O): 5.8–6.9 τ (4H); 7.04 τ (3H) singlet; 7.5–8.6 τ (9H); 8.69 τ (3H) doublet ($J = 6.0$ c/s); 9.03 τ (3H) doublet ($J = 5.0$ c/s). *Hydrobromide*, m.p. 206–207°C.

Selenium dehydrogenation of II. A mixture of 100 mg II and 200 mg powdered selenium was heated under argon in a sealed tube at 300 ± 10°C for 18 h. Gas chromatography ** of the resulting pale yellow liquid showed the presence of two components at retention times of 7.5 and 18.5 (III) min. The compounds were separated by gas chromatography and III was showing to have the following properties. Molecular weight 149 (mass spectro-

* All melting points are corrected.

** An aluminium column (2.9 m × 8 mm) was packed with 20% SE-52 on 60–80 mesh Chromosorb W HMDS. The column was kept at 170°C. Carrier gas He, at a flow-rate of 30 ml/min was used.

metry); UV spectrum: $\lambda_{\max}^{\text{hexane}}$ 214 μ ; 263.6 μ ; 267.2 μ ; 271.0 μ ; NMR (in CCl_4): 3.37 τ (2H) singlet; 7.40 τ (2H) triplet ($J = 7.5$ c/s); 7.61 τ (3H) singlet; 7.79 τ (3H) singlet; 8.0–8.6 τ (2H) multiplet; 9.06 τ (3H) triplet ($J = 6.5$ c/s). *Hydrochloride*, m.p. 52–54°C.

2,4-Dimethyl-6-propylpyridine. Phenyllithium * (0.050 mole) in 65 ml of ether was added dropwise under reflux over a period of 30 min to a solution of 6.1 g (0.050 mole) of 2,4,6-trimethylpyridine in 150 ml of ether. The resulting reddish-brown liquid was treated with a solution of 7.8 g (0.050 mole) of ethyl iodide in 50 ml of ether. The reaction mixture was heated under reflux for 30 min, water was added and the ether layer was separated. After drying over anhydrous sodium sulphate, the ether solution was passed through basic alumina and freed of solvent. Separation of the components was performed by preparative gas chromatography using the same conditions as described under *Selenium dehydrogenation of II*. Estimated ** yield of 2,4-dimethyl-6-propylpyridine ca. 50 %. n_D^{25} 1.4913; molecular weight 149 (mass spectrometry); UV spectrum: $\lambda_{\max}^{\text{hexane}}$ 215 μ (ϵ 3700); 263.6 μ (ϵ 3200); 266.9 μ (ϵ 3000); 271.0 μ (ϵ 2800); NMR (in CCl_4): 3.39 τ (2H) singlet; 7.39 τ (2H) triplet ($J = 7.5$ c/s); 7.61 τ (3H) singlet; 7.80 τ (3H) singlet; 8.0–8.6 τ (2H) multiplet; 9.06 τ (3H) triplet ($J = 6.5$ c/s). (Found: C 80.2; H 9.96; N 9.49. $\text{C}_{10}\text{H}_{15}\text{N}$ requires: C 80.5; H 10.1; N 9.38). *Hydrochloride*, m.p. 54–56°C. (Found: Cl 19.1. $\text{C}_{10}\text{H}_{15}\text{N}$ requires: Cl 19.1).

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* The concentration of the phenyllithium solution was determined as follows: an aliquot of the solution was hydrolyzed in distilled water and the hydrolysate titrated with hydrochloric acid. A second aliquot of the same size was run into dry methyl iodide. After 2 min the mixture was treated with distilled water and titrated as before. The difference between the two titration values represents the concentration of phenyllithium.

** Estimated from the gas chromatogram.