

Studies on Orchidaceae Alkaloids

XXVII.* Quaternary Salts of the Dendrobine Type
from *Dendrobium nobile* Lindl.

KAJ HEDMAN and KURT LEANDER

Department of Organic Chemistry, University of Stockholm, Sandåsgatan 2,
S-113 27 Stockholm, Sweden

Five quaternary compounds, *N*-methyldendrobium iodide (I), *N*-isopentenyl-dendrobium bromide (II), dendrobine *N*-oxide (III), *N*-isopentenyl-dendroxinium chloride (IV), and *N*-isopentenyl-6-hydroxydendroxinium chloride (V) have been isolated from *Dendrobium nobile* Lindl. The configurations at the nitrogen atoms of II and III have been determined by synthesis.

The quaternary compounds *N*-methyldendrobium iodide (I)² and *N*-isopentenyl-dendrobium bromide (II)³ have been isolated from *Dendrobium nobile* Lindl. by Inubushi *et al.* Nothing has, however, been reported about the configuration at the nitrogen atom of II. In this communication we report the isolation of I and II as well as of dendrobine *N*-oxide (III), *N*-isopentenyl-dendroxinium chloride (IV), and *N*-isopentenyl-6-hydroxydendroxinium chloride (V) from *D. nobile*. The latter two compounds have previously been found in *D. friedricksianum* Lindl. and *D. hildebrandii* Rolfe.⁴ The configurations at the nitrogen atoms of II and III are shown to be those indicated in Fig. 1.

It is evident, from the IR and NMR spectra, that II contains an isopentenyl group. Since pyrolysis of II gave dendrobine (VI), II was considered to be either the *exo* or *endo* isomer of *N*-isopentenyl-dendrobium bromide. Alkylation of dendrobine (VI) with 1-bromo-3-methyl-2-butene gave a product (VII) which was distinguishable from II. A product identical with II was, however, obtained by methylation of *N*-isopentenyl-nordendrobine (X), which was obtained from nordendrobine (VIII) by alkylation to *N,N*-diisopentenyl-nordendrobium bromide (IX) followed by pyrolysis. As the reaction between the alkylation reagent and dendrobine (VI) or its derivative X preferably takes place from its sterically less hindered side, *i.e.* from the same side of the

* For number XXVI of this series, see Ref. 1.

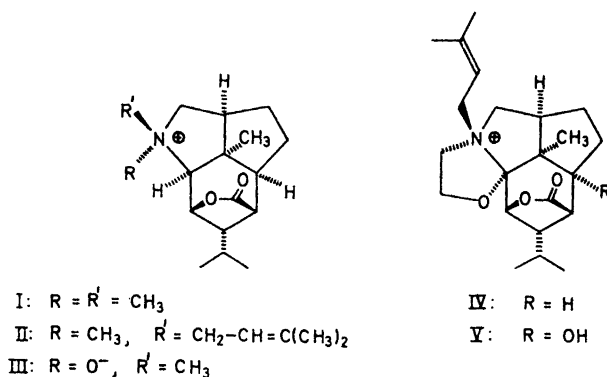


Fig. 1.

molecule as the isopropyl group is situated, it is evident that II has the configuration indicated in Fig. 1.

The *N*-oxide isolated from the plant was indistinguishable from a synthetic specimen of dendrobine *N*-oxide, obtained by reacting dendrobine (VI) with 3-chloroperbenzoic acid. For the same sterical reason discussed above, III should possess the configuration indicated in Fig. 1.

EXPERIMENTAL

All melting points are corrected. Mass spectra were measured on an LKB 9000 spectrometer (ionization energy 70 eV), and the optical rotations on a Perkin-Elmer 141 polarimeter. The IR spectra were recorded on a Perkin-Elmer 257 instrument, and the NMR spectra on a Varian A-60A spectrometer.

Isolation of the quaternary salts. Fresh plants of *Dendrobium nobile* Lindl. (3 kg) were extracted with methanol (10 l). The extract was concentrated to 1 l, acidified with hydrochloric acid and washed with carbon tetrachloride (5×0.2 l). The aqueous solution was made alkaline with sodium hydrogen carbonate, extracted with ether (5×0.3 l), neutralised, and finally evaporated to dryness. The residue was extracted with ethanol (4×0.2 l) until negative to the Dragendorff reagent. The combined ethanol extracts were concentrated and filtered through a column of Dowex 1-X4 (Cl^- , 3×30 cm) irrigated with water. The eluate was evaporated to dryness and chromatographed on neutral alumina (5×70 cm) using ethanol as eluent.

The first fraction contained dendrobine *N*-oxide (III, 50 mg).

Material from the second fraction (500 mg) was crystallised from acetone-ether containing a small amount of ethanol. The precipitate (100 mg) was recrystallised from ethanol giving *N*-isopentenyl-6-hydroxydendrobium chloride (V, 50 mg), indistinguishable (IR, NMR, TLC, m.p. and optical rotation) from an authentic sample. Material (270 mg) from the mother liquor from the first crystallisation (acetone-ether) was subjected to countercurrent distribution using the system butanol-water (phases, 5 ml each). After 24 distributions, the fractions 1-8 contained pure *N*-isopentenyl-dendrobium chloride (60 mg), which was converted into its bromide (II) by filtration through a column of Dowex 1-X4 (Br^-). The combined fractions 9-15 (190 mg), which contained mixtures of II, IV, and V, were redistributed, giving II in a total yield of 150 mg. Fractions 16-24, which consisted mainly of IV, were crystallised from acetone-ether containing a small amount of ethanol and gave *N*-isopentenyl-dendrobium chloride (IV,

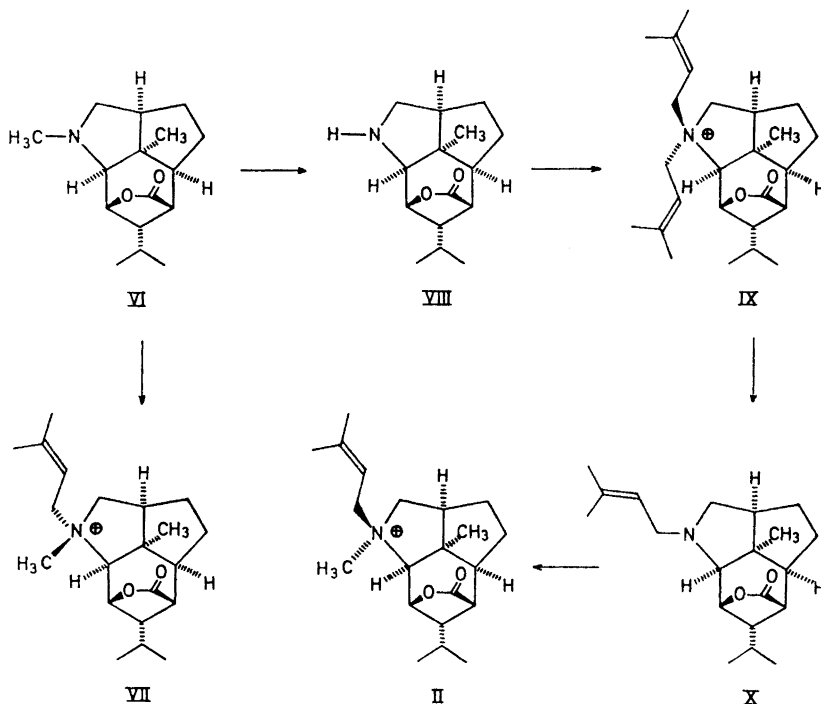


Fig. 2.

50 mg) indistinguishable (IR, NMR, TLC, m.p. and optical rotation) from an authentic sample.

The third fraction contained *N*-methyldendrobinium chloride (100 mg), which was converted into its iodide (I) by filtration through a column of Dowex 1-X4 (I⁻).

N-Methyldendrobinium iodide (I). Crystallisation of I from acetone-ether afforded needles, m.p. 245–246° (lit.² m.p. 253°, uncorrected), $[\alpha]_D^{23} -29^\circ$ (c 1.0, methanol). Crystallisation of I from acetone gave prisms, m.p. 235–238°. IR spectrum: σ_{\max} (CHCl₃) 1785 cm⁻¹. NMR spectrum (CDCl₃) τ : 4.65 (q, 1 H, $J_1 = 3.0$ Hz, $J_2 = 5.0$ Hz), 5.70 (d, 1 H, $J = 3.0$ Hz), 6.05 (s, 3 H), 6.17 (s, 3 H), 8.25 (s, 3 H), 8.70 (d, 3 H, $J = 6$ Hz), 8.98 (d, 3 H, $J = 6$ Hz). I was indistinguishable (IR, NMR, TLC, m.p. and optical rotation) from an authentic sample of *N*-methyldendrobinium iodide, obtained by reacting dendrobine (VI) with methyl iodide.

N-Isopentenylidendrobinium bromide (II). II did not crystallise, $[\alpha]_D^{23} -33^\circ$ (c 1.4, methanol). IR spectrum: σ_{\max} (CHCl₃) 1787 (s), 1670 (w) cm⁻¹. NMR spectrum (CDCl₃) τ : 6.30 (s, 3 H), 8.07 (s, broad, 6 H), 8.23 (s, 3 H), 8.71 (d, 3 H, $J = 5$ Hz), 8.99 (d, 3 H, $J = 5$ Hz). Pyrolysis of II at 160° gave dendrobine (VI), indistinguishable (MS, TLC, GLC and optical rotation) from an authentic sample.

Dendrobine N-oxide (III). Crystallisation of III from acetone-ether afforded needles, m.p. 160–180° (dec.), $[\alpha]_D^{23} -34^\circ$ (c 0.27, methanol). (Found: C 64.4; H 9.25; O 21.8. Calc. for C₁₆H₂₅NO₃·H₂O: C 64.6; H 9.15; O 21.5.) Suzuki *et al.*⁵ reported m.p. 150° (dec.) and $[\alpha]_D -37.76^\circ$ (ethanol) for a compound with the composition C₁₆H₂₅NO₃·H₂O₂. IR spectrum: σ_{\max} (CHCl₃) 1785 (s) cm⁻¹. NMR spectrum (CDCl₃) τ : 5.02 (q, 1 H, $J_1 = 3.0$ Hz, $J_2 = 5.0$ Hz), 6.62 (s, 3 H), 8.28 (s, 3 H), 8.95 (d, 3 H, $J = 6$ Hz), 8.97 (d, 3 H, $J = 6$ Hz). III was indistinguishable (IR, NMR, TLC, m.p. and optical rotation) from an

authentic sample of dendrobine *N*-oxide, obtained by reacting dendrobine (VI) with 3-chloroperbenzoic acid according to a general procedure for the synthesis of amine oxides given by Craig and Purushothaman.⁶

N-Isopentenylnordendrobine (X). Nordendrobine^{5,7} (VIII, 70 mg), sodium carbonate (100 mg) and 1-bromo-3-methyl-2-butene (200 mg) were heated in methanol at 60° for 1 h. The mixture was filtered and evaporated to dryness, leaving crude *N,N*-diisopentenyl-dendrobium bromide (IX). Without purification IX was heated at 160° for 15 min. The reaction mixture was filtered through neutral alumina (0.5 × 3 cm) using ether as eluent. The first fraction consisted of *N*-isopentenylnordendrobine (X, 50 mg) which did not crystallise, $[\alpha]_D^{23} - 74^\circ$ (*c* 1.4, chloroform). IR spectrum: σ_{\max} (CHCl₃) 1772 (s), 1670 (w) cm⁻¹. NMR spectrum (CDCl₃) τ : 4.63 (t, 1 H, *J* = 7 Hz, further coupled), 5.18 (q, 1 H, *J*₁ = 3.0 Hz, *J*₂ = 4.5 Hz), 6.59 (d, 2 H, *J* = 7 Hz, further coupled), 7.17 (d, 1 H, *J* = 3.0 Hz), 8.27 (s, broad, 6 H), 8.60 (s, 3 H), 9.02 (d, 3 H, *J* = 6 Hz), 9.07 (d, 3 H, *J* = 6 Hz). Mass spectrum *m/e* (rel. intensity): M⁺ 317 (17), 302 (24), 274 (44), 260 (10), 249 (35), 221 (28), 206 (100), 193 (10), 190 (13), 150 (60), 82 (85), 69 (75), 55 (15), 41 (93).

endo-*N*-Isopentenyl-dendrobium bromide (II). A solution of *N*-isopentenylnordendrobine (X, 40 mg) and methyl iodide (100 mg) in acetone (3 ml) was heated at 50° for 1 h. The mixture was evaporated to dryness and filtered through a column of Dowex 1-X4 (Br⁻) irrigated with water. The bromide, which did not crystallise, was obtained in a quantitative yield, $[\alpha]_D^{23} - 31^\circ$ (*c* 2.2, methanol), indistinguishable (IR, NMR, TLC) from the natural product.

exo-*N*-Isopentenyl-dendrobium bromide (VII). A solution of dendrobine (VI, 150 mg) and 1-bromo-3-methyl-2-butene (100 mg) in acetone (3 ml) was heated at 50° for 30 min. Addition of ether (3 ml) gave crystalline VII (200 mg), m.p. 140–150° (dec.), $[\alpha]_D^{23} - 42^\circ$ (*c* 0.78, methanol). (Found: C 61.3; H 8.23; O 7.75. Calc. for C₂₁H₃₄BrNO₂: C 61.2; H 8.32; O 7.76.) IR spectrum: σ_{\max} (CHCl₃) 1787 (s), 1667 (w) cm⁻¹. NMR spectrum (CDCl₃) τ : 6.57 (s, 3 H), 8.02 (s, broad, 6 H), 8.25 (s, 3 H), 8.69 (d, 3 H, *J* = 6 Hz), 8.97 (d, 3 H, *J* = 6 Hz).

Acknowledgements. We are indebted to Prof. Yasuo Inubushi (Kyoto) for valuable information concerning *N*-isopentenyl-dendrobium bromide. We thank Dr. Björn Lünig for his interest and Dr. Ragnar Ryhage for measuring the mass spectra. Financial support from *Hierta-Retzzius stipendiefond* and from the *Swedish Natural Science Research Council* is gratefully acknowledged.

REFERENCES

1. Lindström, B., Lünig, B. and Siirala-Hansén, K. *Acta Chem. Scand.* **25** (1971) 1900.
2. Inubushi, Y., Ishii, H., Yasui, B., Konita, T. and Harayama, T. *Chem. Pharm. Bull. (Tokyo)* **12** (1964) 1175.
3. Inubushi, Y. *Personal communication*.
4. Hedman, K., Leander, K. and Lünig, B. *Acta Chem. Scand.* **25** (1971) 1142.
5. Suzuki, H., Kaimatsu, I. and Ito, K. *J. Pharm. Soc. Japan* **54** (1934) 801.
6. Craig, I. C. and Purushothaman, K. K. *J. Org. Chem.* **35** (1970) 1721.
7. Inubushi, Y., Sasaki, Y., Tsuda, Y., Yasui, B., Konita, T., Matsumoto, J., Katarao, E. and Nakano, J. *Tetrahedron* **20** (1964) 2007.

Received February 18, 1972.