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Studies on Orchidaceae Alkaloids

XXIX.* The Absolute Configuration of Dendroprimine, an Alkaloid from *Dendrobium primulinum* Lindl.

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Dendroprimine (I), 5,7-dimethyloctahydroindolizine, is converted by three successive Hofmann reactions into (+)-4-methylnonane, from which the absolute configuration of I is deduced. The CD curves of *R*(−)-1,2-dimethylpyrrolidine and (+)2*S*-methyl-1-(1-methyl-2*R*-pyrrolidyl)pentane (IV), a degradation product of dendroprimine (I), are compared.

In 1965 Lüning and Leander[2] reported the isolation from *Dendrobium primulinum* Lindl. of a 5,7-dimethyloctahydroindolizine (I), for which we now propose the name dendroprimine. The alkaloid was later shown to have the 5,7-*cis*,9-*trans* configuration.[3] In this communication we report a determination of the absolute configuration of dendroprimine (I) by degradation of I to *S*(+)-4-methylnonane.

Hofmann degradation of dendroprimine methiodide (II) followed by hydrogenation gave the dihydromethine base IV. Pyrolysis of the methohydroxide of IV afforded three isomeric components (VI, VII, VIII) in the ratio 1:6:6, the structures of which were established by mass spectrometry. The IR absorptions of VII and VIII at 966 and 968 cm^{-1}, respectively, indicate that their double bonds have the *trans* configuration.

Hydrogenation of a mixture of VII and VIII gave the dihydro compound (IX). Hofmann degradation of the methohydroxide of IX, followed by hydrogenation of the resulting alkene, gave (+)-4-methylnonane. Levene and Marker [4] have synthesised (+)-4-methylnonane and shown that it has the same absolute configuration as (+)-methylhexane. As the latter has been correlated with

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

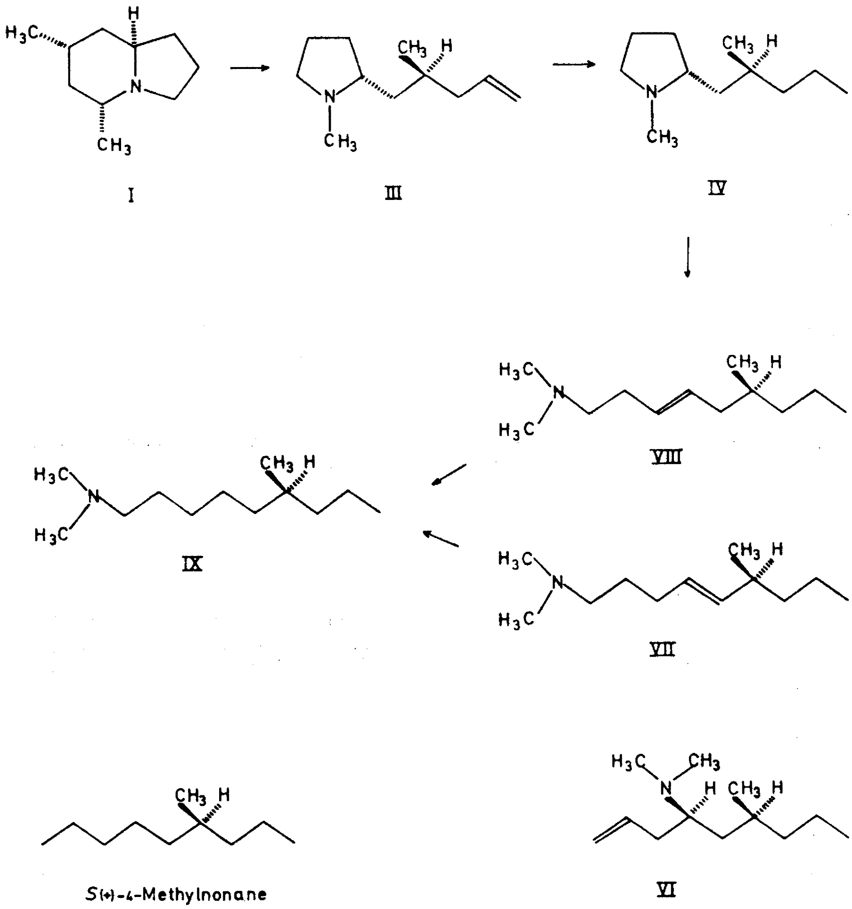

Fig. 1. Degradation of dendroprimine (I) to $S(+)$-4-methylnonane.

$(-)$-shikimic acid, of known absolute configuration, $(+)$-4-methylnonane can be assigned the 4*S* configuration.

Comparison of the CD curve (Fig. 2) of IV with that of $R(-)$-1,2-dimethylpyrrolidine (X),[6] derived from $S(-)$-proline, indicates that IV has the *R* configuration at the pyrrolidine ring.

Dendroprimine (I) can thus be formulated as (5*R*,7*S*,9*R*)-5,7-dimethyloctahydroindolizine.

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, the NMR spectra on a Varian A-60A spectrometer, and the CD spectra on a Cary 60 spectropolarimeter.

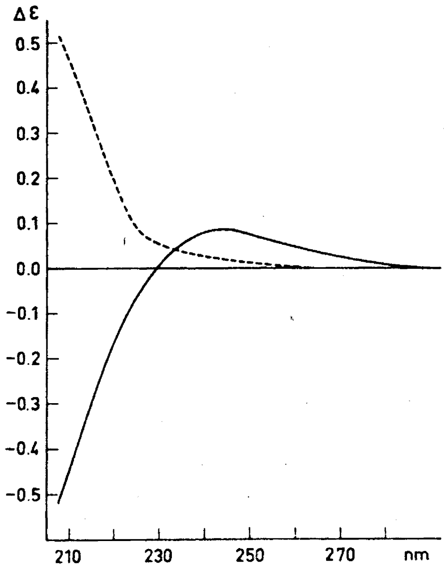

Fig. 2. CD curves of IV (———) and *R*(−)-1,2-dimethylpyrrolidine (− − −) in methanol.

Hofmann degradation of dendroprimine methiodide (II). A solution of II [2] (0.510 g), $[\alpha]_D^{23}$ +1.9° (*c* 10, methanol), in methanol−water (20 ml, 1:1) was shaken vigorously with freshly prepared silver oxide (1.5 g) for 45 min. After filtration, the solution was evaporated to dryness and the residue was pyrolysed at 90°/20 torr. The methine base (III) obtained, which was gas chromatographically pure, was collected as a colourless oil (0.200 g, 70 %), $[\alpha]_D^{25}$ +101° (*c* 0.48, methanol). IR spectrum: σ_{max} ($CHCl_3$) 1647(m), 997(m), 918(s) cm^{-1}. NMR spectrum ($CDCl_3$) τ: 3.8−5.2 (m, 3 H), 6.6−7.1 (m, 1 H), 7.68 (s, 3 H), 7.5−8.9 (m, 11 H), 8.9−9.3 (m, 3 H). Pertinent mass spectral peaks *m/e* (rel. intensity): M^+ 167 (2), 152 (1), 124 (5), 110 (1), 98 (1), 97 (3), 94 (2), 84 (100), 82 (4), 70 (2). The *methiodide* of III was crystallised from acetone−ether, m.p. 122.5−125°. (Found: C 46.5; H 7.74; I 41.2; N 4.70. Calc. for $C_{12}H_{24}IN$: C 46.6; H 7.82; I 41.0; N 4.53.)

Hydrogenation of III. Hydrogenation of III over Adams catalyst in methanol (25°, 1 atm., 12 h) produced the dihydromethine base IV, $[\alpha]_D^{22}$ +103° (*c* 0.36, methanol). NMR spectrum ($CDCl_3$) τ: 6.7−7.1 (m, 1 H), 7.68 (s, 3 H), 7.6−9.0 (m, 13 H), 9.0−9.3 (m, 6 H). Pertinent mass spectral peaks *m/e* (rel. intensity): M^+ 169 (1), 124 (1), 98 (1), 94 (3), 84 (100), 82 (3), 70 (1). The methiodide (V) of the dihydromethine base IV was crystallised from ethyl acetate−acetone, m.p. 132.5−134°. (Found: C 46.6; H 7.90; I 40.8; N 4.72. Calc. for $C_{12}H_{26}IN$: C 46.5; H 8.12; I 40.9; N 4.52.)

Hofmann degradation of V. The methiodide V (1.15 g) was transformed into the hydroxide as described above. Pyrolysis of the hydroxide at 95−110°/60 torr gave three components (0.60 g, VI, VII and VIII) in the ratio 1:6:6, which were separated by preparative gas chromatography.

Compound VI. Pertinent mass spectral peaks *m/e* (rel. intensity): M^+ 183 (1), 182 (1), 181 (2), 167 (2), 142 (100), 140 (5), 100 (5), 98 (25), 95 (7), 87 (7), 85 (20), 84 (27), 83 (30), 73 (5), 72 (40).

Compound VII. IR spectrum: σ_{max} (CS_2) 968(s) cm^{-1}. NMR spectrum ($CDCl_3$) τ: 4.4−4.7 (m, 2 H), 7.76 (s, 6 H), 7.5−8.9 (m, 11 H), 8.9−9.2 (m, 6 H). Pertinent mass spectral peaks *m/e* (rel. intensity): M^+ 183 (3), 168 (1), 140 (3), 95 (2), 84 (2), 71 (4), 67 (2), 58 (100).

Compound VIII. IR spectrum: σ_{max} (CS_2) 966 cm^{-1}. Pertinent mass spectral peaks *m/e* (rel. intensity): M^+ 183 (0.2), 182 (0.3), 181 (0.2), 110 (0.6), 84 (0.8), 58 (100).

Conversion of VII and VIII to R(+)-4-methylnonane. Hydrogenation of a mixture of VII and VIII (0.40 g) over Adams catalyst (25°, 1 atm., 12 h) in methanol (10 ml) gave the dihydro compound IX. The methiodide of IX was treated with silver oxide and the hydroxide pyrolysed at 90°/220 torr. The resulting alkene was hydrogenated as above over Adams catalyst in ether – acetic acid (1:1). The alkane obtained was purified by preparative gas chromatography, giving 4-methylnonane as a colourless oil, $[\alpha]_D^{24}$ + 1.76° (*c* 4.3, methanol) indistinguishable (GLC, MS) from an authentic sample.

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