Tetrahedron Letters No. 56, pp. 4859-4861, 1970. Pergamon Press. Printed in Great Britain.

SYNTHETIC STUDIES OF DENDROBINE I[+)]

SYNTHESIS OF THE SKELETON OF DENDROBINE

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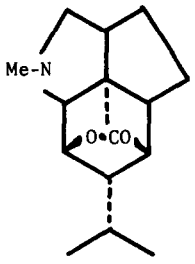
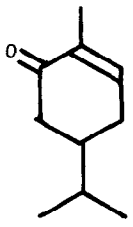
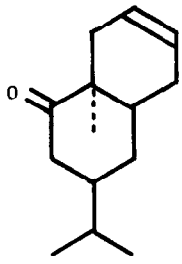
Dendrobine (I), a main alkaloid of Dendrobium nobile Lindl, was first isolated by Suzuki in 1932[1)] and its structure was established by the three groups[2,3,4)]. In this paper we described a synthesis of the molecular skeleton of dendrobine. Carvotanacetone (III), which prepared from carvone, was condensed with butadiene in benzene solution in the presence of aluminium chloride to afford the adduct IV, bp 105-106°/0.6 mm, ν^{neat} 1710 cm^{-1}, δppm (CCl_4): 5.58(2H broad s), 1.17(3H, s), 0.91(6H, d, J=7 Hz), in 60 % yield. The compound IV was converted by the Prevost's method[5)] to cis-diol V, bp 150-170°/0.001 mm, ν^{neat} 3400, 1710, 1060 cm^{-1}, δ ppm (CCl_4): 0.91 (6H, d, J=7 Hz), 1.23(3H, s), 3.77(2H, broad s), in 50 % yield. Cleavage of the diol V with periodic acid in THF-water solution at room temperature and subsequent treatment with acetic acid and piperidine in benzene solution at 60° afforded αβ-unsaturated aldehyde VI, which was purified by silica gel chromatography, bp 110-120°/0.1 mm, ν^{neat} 1710, 1680, 1610, 2720 cm^{-1}, δ ppm (CCl_4): 0.92(6H, d, J=7 Hz), 1.25(3H, s), 6.83(1H, broad s), 9.55(1H, s), in 40-50 % yield.[6)] The compound VI was hydrogenated in the presence of platinum oxide in ethanol at room temperature. The reduction products were oxidized with chromic trioxide in acetic acid and followed by esterification with diazomethane to give the stereoisomeric mixture of ketoesters, bp 149-154°/0.1 mm, ν^{neat} 1710, 1740 cm^{-1}, in 50 % yield based on VI. The ketoester VII and VIII were separated by preparative gaschromatography (carvowax 20M, 170°) and the conformational assignment to each isomer was made on the basis of NMR spectra; the compound VII showed signals at 0.91(6H, d, J=7 Hz), 1.25(3H, s) ppm(CCl_4) and the compound VIII shwed at 0.88(6H, d, J=7 Hz), 1.10(3H, s) ppm. The isomer having a methyl signal at a lower field than the other should be trans isomer and the another isomer should have cis substituent at C_1 and C_8. This conclusion was supported additionaly by the fact that the compound VIII was isomerized to the compound VII by treatment with sodium in boiling methanol. The isomer VII was ketalized with ethylene



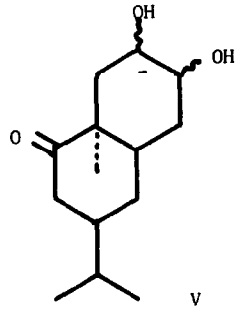
I



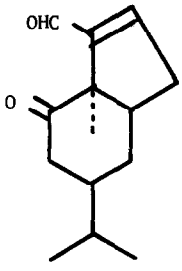
III



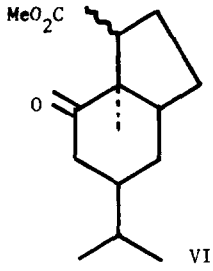
IV



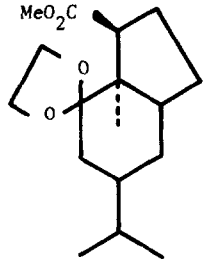
V



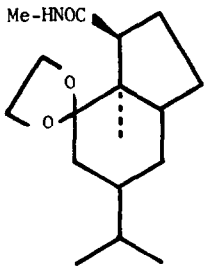
VI



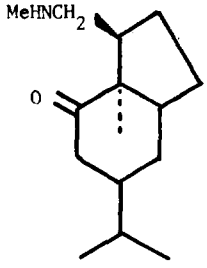
VII,VIII



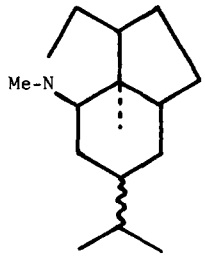
IX



X



XI



II

glycol using p-toluensulfonic acid and ethyl orthoformate as a catalyst to give a compound IX, bp 140-150°/0.1 mm, ν^{neat} 1740 cm^{-1}, δ ppm (CCl_4): 0.87(6H, d, J=7 Hz), 1.10(3H, s), 3.67(4H, s), 3.90(3H, s), in 90 % yield. Treatment of the ketal ester IX with 30 % methylamine in ethanol solution at 100° gave a crude amide X. Reduction of the amide X with lithium aluminum hydride in tetrahydrofuran and subsequent treatment with dilute hydrochloric acid gave an amino ketone XI, bp 150-160°/0.1 mm (bath temp.), ν^{neat} 1710 cm^{-1}, in 30 % yield based on IX. The hydrogenolysis of the compound XI in the presence of platinum oxide in ethanol at 200° under 50 atm. afforded an isomeric mixture of amine II, bp 100-120°/0.1 mm (bath temp.), ν^{neat} 2820 cm^{-1}, δ ppm ($CDCl_3$): 0.90(6H, d, J=7 Hz), 1.09(3H, s), 2.20(3H, s), in 57 % yield. One of the isomers showed peaks at 221(M^+ 22), 220(46), 206(24), 178(100), 150(9), 136(5), 135(6), 109(8), 108(16), 96(37) by the GC-mass spectrum and the other isomer showed essentially the identical spectrum but slightly different in intensity.

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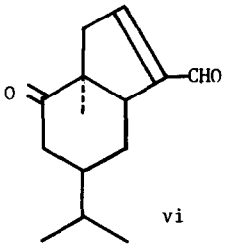
6) Another possible isomer vi could not be isolated as a pure form.



vi