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ELEGANTINE, A NEW OXINDOLE ALKALOID FROM VINCA ELEGANTISSIMA HORT[1].

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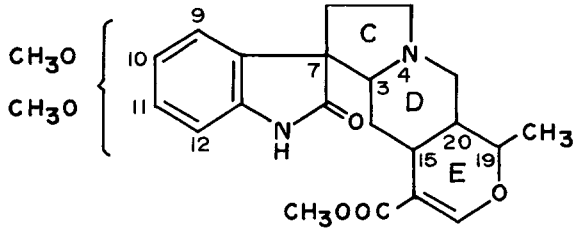
Vinca major Linn. var. Vinca elegantissima Hort. (N.O. Apocynaceae) is a comparatively rare herb growing in the Nilgiri Hills of Southern India and does not appear to have been investigated so far. We now wish to report the isolation and structure elucidation of a new oxindole alkaloid, elegantine, $C_{23}H_{28}N_2O_6$, m.p. 202-204°, from the whole plant which also yielded reserpinine. Lupeol and β-amyrine (both in their free state and as acetate) besides β-sitosterol have also been encountered in the petroleum ether extract.

The total crude alkaloids from the benzene extract of the whole plant (2.5 kg.) were taken up in 10% acetic acid and thoroughly extracted first at ~pH 3 by benzene (Fraction A) and then at pH 9 by methylene chloride. Fraction A after usual work up was repeatedly chromatographed in a column of silica gel or better over acid washed alumina. Initial benzene eluates yielded an alkaloid, crystallizing out of acetone in plates, m.p. 240-241° (decom.), $[\alpha]_D$ -130° (c. 0.505); B.HCl, m.p. 244-246° (decom.), the identity of which with reserpinine was established through IR comparison and mass spectral fragmentation pattern. The crude mixture of alkaloids eluted with benzene-methylene chloride (9:1) after repeated chromatography and crystallizations from alcohol, acetone or methanol yielded elegantine in white needles.

The UV spectrum of elegantine showed $\lambda_{max.}^{EtOH}$ at 228 nm(log ε 4.57) and $\lambda_{max.}^{0.1N\ NaOH}$ at 227(log ε 4.79), 278(log ε 3.75) and 288(log ε 3.42)nm. The IR spectrum of the base in nujol showed characteristic carbonyl absorptions at 1716 and 1614 cm^{-1} for conjugated ester-enolether system and bands at 1670 and 3200 cm^{-1} for an amide grouping. The spectrum is very similar to that of the pentacyclic oxindole alkaloid, carapanaubine. The mass spectral fragmentation

pattern of the compound exhibiting peaks at m/e 428(M^+, base peak), 413(M-15), 411(M-17; characteristic for oxindoles), 399(M-29), 398, 397(M-31), 224, 223 (characteristic of the pentacyclic oxindoles), 222, 219, 208, 206, 205, 204, 190, 180, 69 is virtually the same as that of carapanaubine[2] with slight difference in the relative peak intensities.

The 100 MHz NMR spectrum of elegantine in $CDCl_3$ with TMS as internal standard confirmed the presence of 28 protons in the molecule. A lowfield CH_3 doublet at 1.40 ppm (C_{18}-CH_3; $J_{CH_3/H}$=6Hz) and a one-proton octet at 4.35 ppm (C_{19}-H) showed the heterocyclic nature of ring E[3] in elegantine. Other important signals appear at 3.63 (3H, $COOCH_3$), two singlets at 3.86 and 3.88 (two Ar-OCH_3), two doublets at 6.56 and 6.93 (two ortho Ar-H, J=8Hz), a sharp singlet at 7.44 (one olefinic H) and a broad signal at 7.66 (deshielded NH) ppm. The NMR spectrum is also very similar to that of carapanaubine except the signals for aromatic protons. All the above spectral data can be accommodated in structure I for elegantine, with three possible arrangements of the OCH_3 groups at 9, 10 or 9,12 or 11,12 positions.



I

The chemical shift of the C_{18}-CH_3 doublet in the NMR spectrum has been shown to be diagnostic of the nature of the D/E ring junction in pentacyclic oxindole bases[3]. Elegantine, with a C_{18}-CH_3 doublet at 1.40 ppm must have a <u>cis</u> D/E ring junction (usually between 1.23 and 1.40 ppm), rather than <u>trans</u> which is expected to show the CH_3 shift between 1.10 and 1.14 ppm. Also, the C_{19}-H in elegantine appears as an octet at 4.35 ppm ($J_{CH_3/H}$=6Hz; $J_{19H/20\ H}$=11Hz). This high coupling constant of 11Hz between the C_{19}-H and C_{20}-H is indicative of a <u>trans</u> diaxial relationship between them as in uncarine C and uncarine E[3].

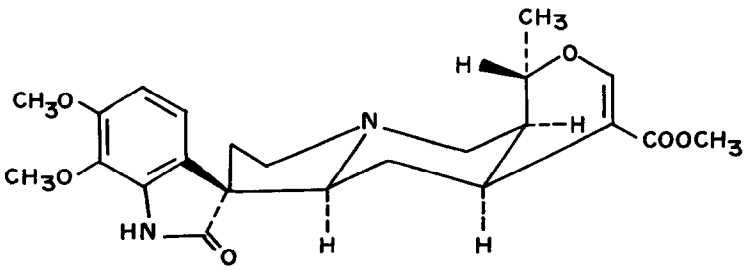
The C_{15}-H could be assigned an α(axial)configuration which has been shown to be always the case with all the alkaloids having normal corynane skeleton[4]. Consequently, both the C_{18}-CH_3 and C_{20}-H should have α-configuration.

The stereochemistry at C_3 and C_7 now remains to be ascertained. Elegantine undergoes a facile mercuric acetate oxidation in ~70 seconds indicating[5] a trans diaxial relationship between the C_3-H and N_4-lone pair orbital, i.e. a trans C/D ring junction. Furthermore, the predominant formation of elegantine (TLC) on reduction of the oxidation product either by Zn/AcOH or by $NaBH_4$ is consistent with C_3-αH and hence allo configuration for the compound.

The very fast mercuric acetate oxidation and low basicity as evidenced by its extraction with benzene from acid solution at pH ~3 (cf. uncarine E[4b, 6]) pointed to the anti relationship between the N_4-lone pair and the oxindole carbonyl[7b]. The aromatic proton signal at lower field (6.93 ppm) could be assigned to C_9-H due to its proximity to N_4-lone pair. The downfield shift of the C_9-H in anti oxindole alkaloids, viz., herbaline, isocarapanaubine, rauvoxine and rauvanine-oxindole A are reported respectively at 6.97, 6.90, 7.02 and 6.92 ppm while in the syn series such as carapanaubine, rauvoxinine and rauvanine-oxindole B, the same signal appear at 6.76, 6.71 and 6.75 ppm respectively[8].

The above NMR evidence also suggests that any OCH_3 group in elegantine should be located at positions other than C_9. Therefore, the presence of two ortho aromatic protons (NMR) could then be only accommodated if the OCH_3 groups are located at positions 11 and 12.

All the foregoing observations led to the complete structure and stereochemistry of elegantine as II.



II

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