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THE EMDE DEGRADATION OF ISORHOEADINE DERIVATIVES

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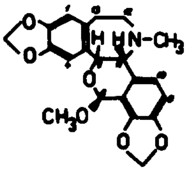
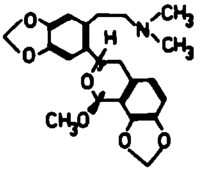
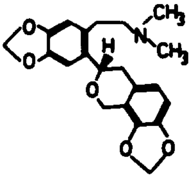
On the basis of ORD data, the absolute configuration 5R,11R was assigned[1] to rhoeadine alkaloids and the configuration 5S,11R to isorhoeadine alkaloids. The stereochemical relationship between the OCH_3 group at C-6 and the hydrogen atom at C-5 was derived from PMR and kinetic studies[2]. The proposed absolute configuration[1] was confirmed[3] by application of the aromatic chirality method. The absolute configuration of rhoeadine (I) 5R,11R and 6S was inferred from X-ray analysis of N-methylrhoeagenine iodide[4].

Recently, we have reported[5] the Emde degradation of methiodides of rhoeadine (B/D cis, $I.CH_3I$) and of rhoeagenine diol ($VI.CH_3I$) which gave the compounds III and X from rhoeadinemethiodide and the compounds VIII and X from


I, 5R
II, 5S


III, 5S
IV, 5R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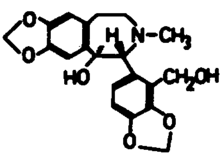
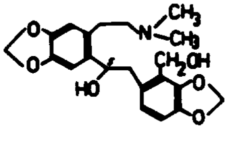
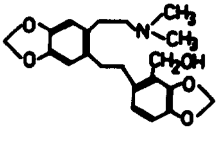

VI, 5R
VII, 5S


VIII, 5S
IX, 5R


X

rhoeagenine diol methiodide. Since our results were not in agreement with those reported in ref.[6], we undertook to study analogous reactions of isorhoeadine derivatives.

An aqueous suspension of isorhoeadinemethiodide (B/D trans, II.CH_3I) was treated with sodium amalgame (3%) and the mixture left standing for 24 h at room temperature. Column chromatography on alumina gave the main reaction product IV which could not be crystallized ($[\alpha]_D^{24}$ +39° in methanol). The more polar fraction afforded the optically inactive substance X, m.p. 134-135°, which was identical with the minor product of the Emde degradation of rhoeadinemethiodide[5]. The PMR spectrum of the compound IV provided confirmatory evidence[2] of the trans-arrangement of the OCH_3 group at C-6 and H-5 (4.95dd, $/J_{AX} + J_{BX}/ = 15$ Hz, 1H (H-5); 5.93s, 1H (H-6)) (ref. 7). The CD spectrum of the compound IV (297 nm ($\Delta\varepsilon$ +2.72), 280 (-1.64), 243 (-4.42), 228 (+1.01), 203 (+12.96), 195 (-13.82), EtOH) is a mirror image of the spectrum of the compound III (ref. 5, fig. 1). If we suppose that the contribution of the methoxyl group at C-6 to the CD of the substances III and IV is negligible[8], then both substances have the same conformation of the ring D, though with reverse helicity. A further verification of the size of the contribution of the methoxyl group to the CD was carried out by the Emde degradation of 6-demethoxyrhoeadinemethiodide[9] which afforded, in addition to the compound X, the substance V, m.p. 125-127°, $[\alpha]_D^{24}$ -85° in methanol. In the region of 270 - 300 nm (^1L_b transition), the CD spectrum of the compound V (294 nm ($\Delta\varepsilon$ -2.24), 278 (+1.22), 248 (-0.56), 241 (+0.32), 230 (-0.55), 210 (+7.45), 203 (-14.9), EtOH) is virtually the same as that of the compound III (fig. 1).

The Emde degradation of the rhoeagenine diol methiodide (VI.CH_3I) yielded[5] the optically active diol VIII with only one center of chirality at C-5 and the compound X. The Emde degradation of isorhoeagenine diol methiodide (VII.CH_3I) gave, in addition to the substance X, the substance IX, m.p. 135-136°, $[\alpha]_D^{24}$ -110° in methanol whose PMR spectrum is identical with that of the compound VIII. The CD spectrum of the compound IX (296 nm ($\Delta\varepsilon$ -1.97), 242 (-4.54), 205 (-7.75), EtOH) is a mirror image (fig. 2) of the spectrum of the substance VIII.

The CD spectra of the studied compounds show that the alkaloids of the rhoeadine and isorhoeadine series differ by their configuration at C-5. Hence, on the basis of the chemically determined relative configuration of the alkaloids I and II and in view of the known absolute configuration of rhoeadine (I) (ref. 4), the definite absolute configuration 5S,11R and 6S has been assigned to isorhoeadine (II).

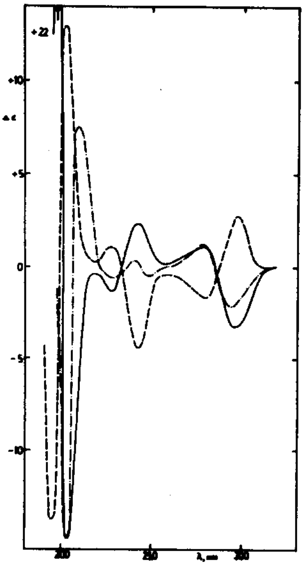


Fig. 1. CD spectra of compounds III (——), IV (- - -), and V (-.-.-)

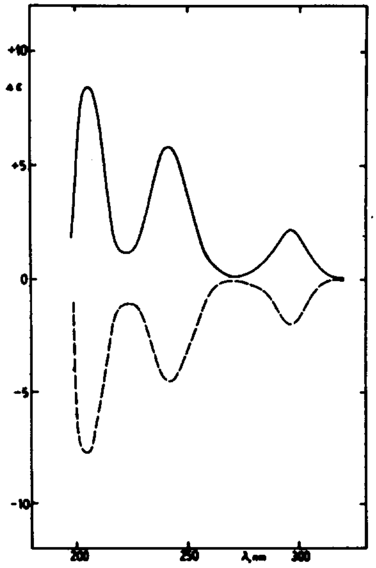


Fig. 2. CD spectra of compounds VIII (——) and IX (- - -)

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