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THE POSITION OF SUBSTITUENTS IN RING D OF THE ALKALOIDS MECAMBRIDINE, ORIENTALIDINE, AND OF THE ALKALOIDS PO-5, AND PO-4

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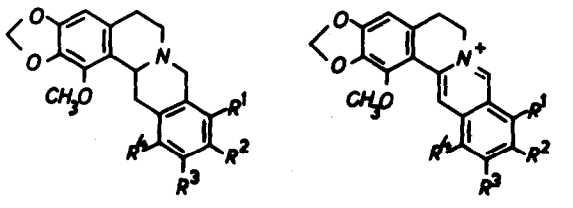
In recent studies, the tetrahydroprotoberberine structure was assigned to the alkaloids mecambridine (oreophiline) (1) (Ia) and orientalidine (bractavine) (2) (IIa) on the basis of NMR spectra. The skeleton of orientalidine was also determined on the basis of Hofmann's exhaustive methylation. The ultraviolet spectra of the dehydrogenated products of mecambridine and orientalidine showed to be identical with those of the alkaloids PO-5 (alkaloid R-K, alborine (3)) (IIIa) and PO-4 (IVa). The latter two alkaloids



Ia IIIa

$R^1 = -CH_2OH$; $R^2 = -OCH_3$; $R^3 = -OCH_3$; $R^4 = -H$

IIa IVa

$R^1R^2 = -CH_2-O-CH_2-O-$; $R^3 = -OCH_3$; $R^4 = -H$

Ib IIIb

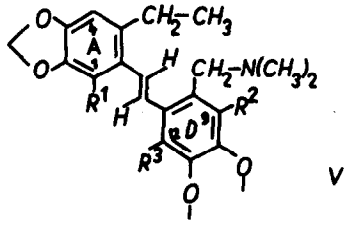
$R^1 = -H$; $R^2 = -OCH_3$; $R^3 = -OCH_3$; $R^4 = -CH_2OH$

IIb IVb

$R^1 = -H$; $R^2 = -OCH_3$; $R^3R^4 = -O-CH_2-O-CH_2$

are assigned (4) a pseudoprotoberberine structure where the auxochromic substituents of ring D are in the positions at C-10 and C-11. The position of the hydroxymethylene group in ring D of the alkaloids mecambridine, orientalidine, PO-5, and PO-4 could not be definitely established. The NMR spectra indicate (2) that this group is located at C-9 or C-12. For the location of the hydroxymethylene group at C-9, an analogy could not be found in the biogenesis of alkaloids derived from benzylisoquinoline alkaloids.

Studies (5) of the ultraviolet spectra of the second step of Hofmann's exhaustive methylation (stilbene derivative) of tetrahydroprotoberberine alkaloids, having various substituents in the aromatic rings A and D (V) show (particularly in products having a hydrogenated vinyl group on the first step of Hofmann's degradation) that in all these compounds the hydrogens at the ethylenic bridge are trans. The methoxyl or the hydroxymethylene group at C-9 does not affect the position of the ultraviolet band of longest wave-length. This band is affected by the substituents in the ortho-position to the

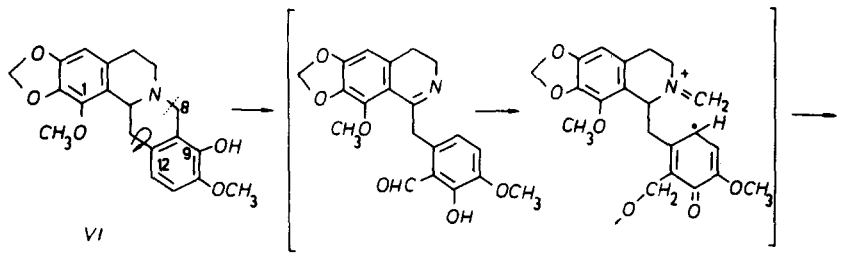


V

R^1 = -H or -OCH_3 R^2 = -H or -OCH_3 R^3 = -H or -CH_2O-

ethylenic bridge which connects the two aromatic nuclei. A comparison of the ultraviolet spectrum of dihydro-tetrahydroberberinebismethine (6) (λ_{max} 333nm, log ε 4.35) with those of dihydro-1-methoxycanadinebismethine (λ_{max} 308 nm, log ε 4.17) (Δ25 nm) and dihydrocoralydinebismethine (λ_{max} 326 nm, log ε 4.26) versus dihydro-1-methoxynorcoralydinebismethine (7) (λ_{max} 305 nm, log ε 4.25) (Δ21 nm) revealed that the hypsochromic displacement of the longest wave-length band is caused by the methoxyl group at C-1. A similar shift of the band of longest wave-length is displayed by dihydro-1-methoxycanadinebismethine versus dihydro-orientalidinebismethine (λ_{max} 289 nm, log ε 4.17)

(Δ19 nm) and 1-methoxycanadinebismethine (λ_{max} 314 nm, log ε 4.19) versus mecambridinebismethine (λ_{max} 288 nm, log ε 4.17) (Δ26 nm). A comparison of the ultraviolet spectrum of dihydro-tetrahydroberberinebismethine with that of dihydro-pseudotetrahydroepiberberinebismethine (8) (λ_{max} 333 nm, log ε 4.35) shows that the position of the maximum and the intensity of the bands of longest wave-length remain unchanged provided the substituent on the nucleus is situated at C-9 or C-11. It is concluded that the hypsochromic displacement of the longest wave-length band of orientalidine- and mecambridinebismethine is caused by some other substituent which is located in the ortho-position to the ethylenic bridge in ring D. This suggests that the hydroxymethylene group in ring D is not located at C-9 but at C-12, and the auxochromic substituents at C-10 and at C-11 (4). With this in view, mecambridine is assigned the structure Ib, orientalidine the structure IIb, the alkaloid PO-5 the structure IIIb, and the alkaloid PO-4 the structure IVb.



The position of the hydroxymethylene group at C-12 can also be explained along biogenetic pathways. Obviously, all the four alkaloids under investigation arise from the tetrahydroprotoberberine base VI by oxidative opening of the bond between the nitrogen and the C-8, by rotation of the ring D by 180° at C-13, and by new formation of a "berberine bridge" (9,10) between the nitrogen (ring B) and the rotated aromatic nucleus D.

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