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THE ABSOLUTE CONFIGURATION OF THE RHOEADINE ALKALOIDS[1]

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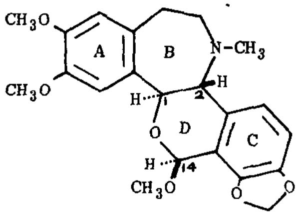
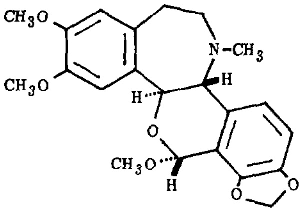
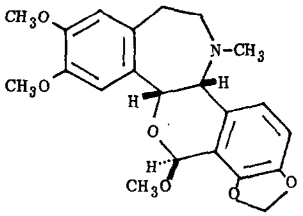
The rhoeadine alkaloids are dextrorotatory bases found only in Papaver species (Papaveraceae); three typical examples being (+)-glaudine, (+)-epiglaudine and (+)-oreodine.[2] The relative stereochemistry at C-1 and C-2 was obtained from nmr coupling constants,[3] while the relative stereochemistry at C-14 was derived through nmr and kinetic studies.[4] It was also established that when glaudine is treated with very dilute acid in methanol, isomerization at C-14 occurs to give epiglaudine. Stronger acid epimerizes irreversibly epiglaudine (B/D trans) to oreodine (B/D cis),[5] while isomerization again occurs at C-14.



(+)-Glaudine



(+)-Epiglaudine

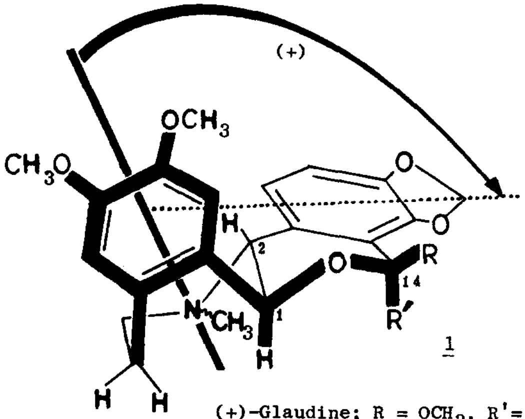


(+)-Oreodine

We now wish to report that application of the aromatic chirality method[6] to the above three alkaloids leads to the absolute configurations indicated.

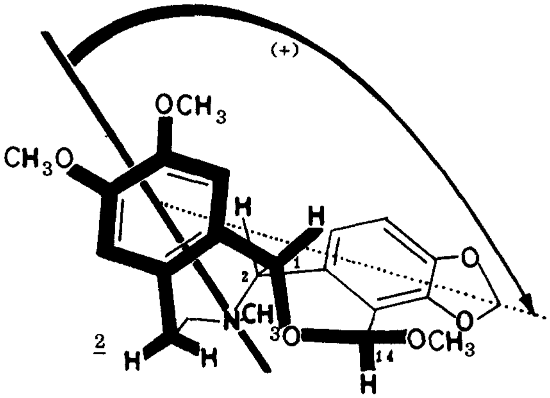
All the rhoeadine alkaloids show characteristic uv maxima at about 290 (A→L_b), 240 (A→L_a) and 200 nm (A→B). As shown in the Table, the 290 and 240 nm uv bands are associated with positive and negative cd extrema respectively. In spite of the rather strong uv absorptions in these two regions ($\log \epsilon \approx 3.9$), chromophoric interactions leading to exciton splitting is not observed in the cd spectra due to the relatively long distance between the two chromophores.

In contrast, a Davydov splitting[7] was observed in the allowed A→B transition band ($\log \epsilon \approx 5.0$); this was more clearly observed in n-hexane than in ethanol solution due to better transmission. The first Cotton effect was definitely positive in each of the three cases, so that the two chromophores interact as depicted in expressions 1 and 2 (positive chirality), thus establishing the absolute configuration. The chiral center at C-14 can be safely regarded as exerting negligible influence on the split Cotton effects.



1

(+)-Glaudine; R = OCH_3, R'= H
(+)-Epiglaudine; R = H, R'= OCH_3



2

(+)-Oreodine

Since all the rhoeadine alkaloids are strongly dextrorotatory and their relative configurations are known,[4] it follows that they must all possess the absolute configurations depicted above. The determination of the configurations of the rhoeadines also clearly indicates that acid catalyzed transformation of an epiglaudine to an oreodine analog (trans→cis B/D) proceeds through isomerization at C-1 rather than at C-2.[8] The following classification can now be made for the rhoeadine bases:[2,4]

(a) Glaudine Analogs: Isorhoeadine, papaverrubine A, papaverrubine B, papaverrubine D, alpinine and papaverrubine G.

(b) Epiglaudine Analogs: Isorhoeagenine, isorhoeagenine-α-D-glucoside, glaucamine, epipapaverrubine B, N-methyl-14-O-desmethylepiporphyroxine, papaverrubine C, alpinigenine and O-methylalpinigenine.

(c) Oreodine Analogs: Rhoeadine, rhoeagenine, dubirheine, papaverrubine E, oreogenine and papaverrubine F.

Table

CD Data at Room Temperature

Compound	CD Extrema, nm (Δε)	
	Split Cotton Effect[a]	Normal Cotton Effect[b]
(+)-Glaudine	195 (-5.00), 207 (+7.25)	222 (+5.7), 250 (-2.0), 290 (+5.3)
(+)-Epiglaudine	193 (-7.5), 207 (+9.4)	250 (-1.3), 270 (+5.7)
(+)-Oreodine	197 (-10.0), 207 (+12.5)	238 (-3.00), 288 (+3.9)

a. In hexane.

b. In absolute ethanol.

References

1. This research was supported by grants NIH HE-12971 (M.S.) and NIH CA-11572 (K.N.).
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