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TWO NEW OXINDOLE ALKALOIDS ISOLATED FROM HAMELIA PATENS JACQ.

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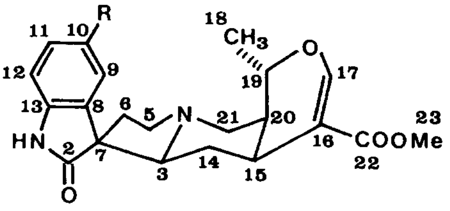
Summary. Two new oxindole alkaloids of the heteroyohimbane type have been isolated from Hamelia Patens Jacq. Their structures correspond to that of isopteropodine with -OH and $-OCH_3$ groups at C-10.

Continuing our study of Hamelia Patens Jacq.[1], we report in this communication the isolation and structure of two new oxindole alkaloids, which we propose to name palmirine (I) and rumberine (II). Following the usual procedure[1], the aerial part of Hamelia Patens Jacq. was refluxed in ethanol, yielding a crude extract of alkaloids. Chromatography of this extract on Kieselgel 60, using varying proportions ob benzene and ethyl acetate, gave in the medium polarity fractions a crystalline product, the new oxindole alkaloid palmirine (I), $C_{22}H_{26}N_2O_5$, m.p. 101-102° (methanol/water), $[\alpha]_D^{20}$ -56.5°. From the fractions eluted using pure ethyl acetate a second oxindole alkaloid, rumberine (II), was obtained in the same manner, $C_{21}H_{24}N_2O_5$, m.p. 188-189° (cyclohexane), $[\alpha]_D^{20}$ -48.0°.

(I) R = OCH_3
(II) R = OH
(III) R = H



Palmirine is an oxindole alkaloid of the heteroyohimbane type[2]. Its IR spectrum (Nujol) shows the following characteristic bands : 3300 cm^{-1} (-$\underline{NH}$), 1720 cm^{-1} (-$\underline{CO}$·OR) and 1690 cm^{-1} (-$\underline{CO}$·NH-). UV spectrum (ethanol) : λ_{max} 312 nm (ε 2,990), 255 nm (ε 24,900) and 220 nm (ε 30,900). Its mass spectrum exhibits a molecular ion at m/e 398 (83 %) and a fragmentation pattern characteristic of heteroyohimbanic alkaloids [3,4] : m/e 223 (100 %), 208 (48 %), 189 (18 %), 180 (36 %), 174 (37 %), 160 (36 %), 69 (57 %). The peak at m/e 180 has stereochemical importance and is characteristic of this type of oxindole alkaloids with <u>allo</u> or <u>epiallo</u> configuration and an α-C-19 methyl group[5]. The masses of all the fragment ions containing the oxindole moiety are 30 units (-OMe) greater than the corresponding ones in the mass spectrum of isopteropodine (III)[3,4]. The ^{1}H-NMR spectrum (acetone-d_6) of palmirine shows the following signals : δ1.42 (3H, doublet, J=7 Hz), 3.54 (3H, singlet), 3.72 (3H, singlet), 4.38 (1H, multiplet), 6.7-7.0 (3H, ABC system), 7.37 (1H, singlet) and 9.24 (1H, broad singlet which disappeared after shaking the NMR sample with D_2O). This spectrum is very similar to that of isopteropodine[1,6], except for the aromatic region and the singlet at δ3.72 (Ar-O$\underline{Me}$). The analysis of the ABC system given by the three aromatic protons yielded the following results : δ_A 6.82, δ_B 6.74, δ_C 6.94, J_{AB}= 8.35, J_{AC} = 0.30, J_{BC} = 2.55 . These values are fully in accordance with the presence of the methoxy group at C-10. The ^{13}C-NMR spectrum of palmirine (see Table 1) provides additional evidence for the C-10 substitution, since the ^{13}C chemical shifts of carbon atoms C-8 to C-13 are in accordance with those of 5-methoxy-oxindole[7]. Furthermore, a comparison of the ^{13}C-NMR spectra of palmirine and of isopteropodine reveals an excellent agreement of the chemical shifts of all the carbon atoms in rings C, D and E and clearly confirms that <u>both compounds have the same stereochemistry in these three rings</u>.

Table 1. ^{13}C-NMR Spectra of Palmirine (I) and Isopteropodine (III).
(δ_C, ppm ; $CDCl_3$)

Carbon atom	I	III	Carbon atom	I	III
C-2	181.0	180.7	C-14	34.9	34.7
C-3	71.3	70.9	C-15	30.7	30.7
C-5	54.1	53.8	C-16	110.0	109.5
C-6	30.3	30.0	C-17	155.1	154.4
C-7	57.6	56.7	C-18	18.6	18.5
C-8	133.8	133.2	C-19	72.3	71.8
C-9	111.9	124.0	C-20	38.2	37.8
C-10	156.0	121.0	C-21	53.6	53.3
C-11	112.2	127.2	C-22	167.6	166.9
C-12	109.9	109.3	C-23	51.0	50.7
C-13	135.3	139.5	$\underline{CH_3}$O-Ar	55.7	

Rumberine (II) is another oxindole alkaloid belonging to the heteroyohimbane type and is related to palmirine. Its IR spectrum (Nujol) shows the following characteristic bands : 3300 cm^{-1} (broad band, -$\underline{NH}$ and -$\underline{OH}$), 1720 cm^{-1} (-$\underline{CO}$·OR) and 1690 cm^{-1} (-$\underline{CO}$·NH-). UV spectrum (ethanol) : λ_{max} 312 nm (ε 2,900), 255 nm (ε 18,100) and 227 nm (ε 12,600). Its mass spectrum exhibits a molecular ion at m/e 384 (90 %) as well as the fragmentation pattern characteristic of heteroyohimbanic alkaloids[3,4] : m/e 223 (100 %), 208 (53 %), 180 (47 %), 146 (37 %) , 69 (80 %). The ^{1}H-NMR spectrum (acetone-d_6) of rumberine is practically identical to that of palmirine, except for the absence of the methoxy signal at δ3.72 and the appearance of a phenolic signal at δ7.20, which disappeared on the addition of D_2O to the NMR sample : δ1.40 (3H, doublet, J=7 Hz), 3.56 (3H, singlet), 4.40 (1H, multiplet), 6.7-7.1 (3H, ABC system), 7.39 (1H, singlet). The analysis of the ABC system given by the three aromatic protons yielded the following results : δ_A 6.71, δ_B 6.63, δ_C 6.88, J_{AB} = 8.30, J_{AC} = 0.40, J_{BC} = 2.52 . These data confirm the presence of the hydroxyl group at C-10. Owing to the small amount of sample isolated to date, it has not yet been possible to obtain a ^{13}C-NMR spectrum of rumberine. However, all the available spectrometric data are fully consistent with structure II.

These two alkaloids are, to our knowledge, the first examples found in nature of oxindole alkaloids of the heteroyohimbane type monosubstituted at the C-10 position with either an -OH or an -OMe group. Until now, all the monosubstituted alkaloids of this type reported in the literature are substituted at either the C-9 or the C-11 position[2,8].

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