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Alkaloids of *Ochrosia poweri* Bail. The Stereochemistry of Poweridine and the Identity of Elliptamine and Reserpiline

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Abstract

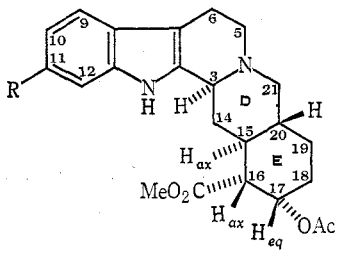
The alkaloid poweridine from *Ochrosia poweri* Bail. has been shown to have the same relative configuration as yohimbine. Elliptamine, previously obtained from *O. poweri*, has been identified as reserpiline.

A study of the proton and ^{13}C nuclear magnetic resonance spectra of the alkaloid poweridine, isolated previously from the leaves of *Ochrosia poweri* Bail.,[1] has shown that this alkaloid has the same relative stereochemistry as yohimbine, and subject only to the assumption that C 15–H has the α-configuration usual for this type of alkaloid, the absolute structure can be given as (1). The main structural features of poweridine have already been established.[1] It has been shown to give 7-methoxyyobyrine on selenium dehydrogenation, and the acid formed by alkaline hydrolysis reacts with ethyl chloroformate to give a β-lactone in the same way as yohimbic acid is converted into yohimbic acid lactone.[2] The formation of a β-lactone under these conditions indicates that the carboxyl group and the hydroxy group are *cis*, and that the hydroxy group is axial.

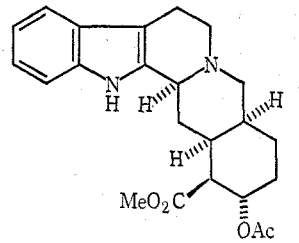
The p.m.r. spectrum of poweridine ($CDCl_3$ solution) shows a narrow multiplet at δ 5·42 for C 17–H, similar to that found for C 17–H (δ 5·40) in the spectrum of *O*-acetylyohimbine (2). The narrow multiplet for C 17–H indicates that all couplings to C 17–H are small and specifically excludes any possibility that C 17–H is axial because there is no large *trans*-diaxial coupling. The signal from C 16–H is a doublet of doublets (δ 2·35; J 11, 2 Hz), and irradiation at the C 17–H signal collapses the C 16–H signal to a doublet (J 11 Hz). The large coupling between C 15–H and C 16–H indicates that these protons have a *trans*-diaxial configuration.

Confirmation for these stereochemical assignments and for the close relationship of poweridine (1) and *O*-acetylyohimbine (2) has been obtained by a comparison of their ^{13}C n.m.r. spectra and also those of *O*-acetyl-α-yohimbine (*O*-acetylrauwolscine) (3), yohimbine and reserpine (4). Chemical shift data for these alkaloids are listed in Table 1, together with probable assignments based on single frequency off-resonance proton decoupled (SFORD) spectra, and on chemical shift data for indole alkaloids

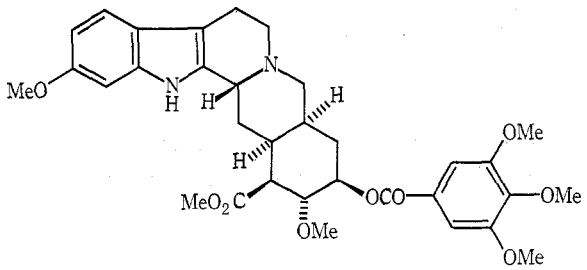
[1] Doy, F. A., and Moore, B. P., *Aust. J. Chem.*, 1962, **15**, 548.
[2] Diassi, P. A., and Dylion, C. M., *J. Amer. Chem. Soc.*, 1958, **80**, 3746.



(1) R = MeO
(2) R = H



(3)



(4)

Table 1. Chemical shift data from ^{13}C n.m.r. spectra

Carbon atom	Multiplicity[A]	Yohimbine	Reserpine	Ajmalicine	Tetrahydroalstonine	Serpentine
C2	s	129·5	134·4	134·7	134·2	130·7
C3	d	60·0	59·9	60·0	60·2	54·0
C5	t	52·9	52·8	52·9	53·4	49·3
C6	t	21·8	21·6	21·9	21·6	17·0
C7	s	108·0	108·1	108·5	108·3	108·3
C8	s	121·5	127·6	127·6	127·4	122·5
C9	d	118·6	118·2	118·2	118·1	118·6
C10	d	108·9	121·4	121·4	121·4	109·2
C11	d	152·2 (s)	119·4	119·5	119·4	156·5 (s)
C12	d	95·4	110·9	110·8	111·0	95·6
C13	s	133·2	136·2	136·2	136·4	136·6
C14	t	30·0	29·9	31·7	27·4	29·9
C15	d	37·0	36·9	36·9	36·6	34·3
C16	d	51·2	51·0	52·6	52·0	52·0
C17	d	69·7	69·7	69·1	69·2	78·0
C18	t	34·1	33·9	34·5	31·0	78·2 (d)
C19	t	24·1	23·9	23·4	24·8	24·5
C20	d	40·2	39·9	40·9	38·4	32·5
C21	t	61·2	61·0	61·5	60·4	52·0
C22	s	172·3	172·4	175·5	172·8	172·9
CO_2CH_3	q	51·8	51·9			
$OCOCH_3$	s	170·0	170·1		170·0	
$OCOCH_3$	q	21·0	21·0		21·0	
OCH_3	q	55·8				56·0

[A] Observed multiplicity of signal in SFORD spectrum; exceptions are indicated within brackets in chemical shift columns.

cited in a recent review of ^{13}C n.m.r. spectroscopy.[3] The very close coincidence in chemical shifts in the spectra of poweridine and *O*-acetylyohimbine, apart from the shifts of the carbon atoms associated with the C 11 methoxy group, indicate the close similarity of the two compounds. In particular, the C 3 configuration (axial H) is the same in poweridine, *O*-acetylyohimbine and *O*-acetyl-α-yohimbine as shown by the C 3 chemical shift at $60 \cdot 0 \pm 0 \cdot 2$ p.p.m. whereas in reserpine, with C 3–H equatorial, the C 3 resonance is at 54·0 p.p.m. The change in configuration at C 3 in reserpine, in which a bulky axial substituent replaces the axial hydrogen of the other compounds, is reflected in the upfield shifts of the sterically perturbed γ-carbon atoms, viz, C 5, C 15 and C 21. Similarly the configuration at the D/E ring junction is the same in poweridine and *O*-acetylyohimbine with the chemical shifts of C 20 ($40 \cdot 0 \pm 0 \cdot 2$ p.p.m.) and C 15 ($37 \cdot 0 \pm 0 \cdot 1$ p.p.m.) being identical. A change in configuration at C 20 from an axial hydrogen in poweridine to an equatorial hydrogen and hence bulky axial substituent in *O*-acetyl-α-yohimbine is again reflected in the shift of the C 20 resonance and the two sterically perturbed γ-carbons (C 14 and C 18). The similarity in shifts of the A ring signals of poweridine with those of reserpine confirm the position of the methoxyl group as C 11.

Re-examination of the alkaloid elliptamine,[1,4] isolated as a crystalline picrate from *O. poweri* and *O. elliptica*, has shown that this alkaloid is identical with reserpiline.

Experimental

General

N.m.r. spectra were measured in $CDCl_3$ solutions and chemical shifts are referred to $SiMe_4$ (δ 0·00). The proton spectra were measured on a Varian HA100 spectrometer operating at 100 MHz and the carbon spectra on a Varian CFT 20 spectrometer operating at 20 MHz and locked to the deuterium signal in the solvent, $CDCl_3$. The single frequency off-resonance spectra were recorded with the decoupling frequency approximately 1000 Hz upfield from the $SiMe_4$ signal.

Poweridine

P.m.r. spectrum: δ 3·80, 3H, s, OMe; 3·68, 3H, s, CO_2Me; 2·07, 3H, s, OCOMe; 7·32, 1H, d, *J* 8 Hz, C 9–H; 6·73, doublet of doublets, *J* 8, 2 Hz, C 10–H; 6·79, 1H, d, *J* 2 Hz, C 12–H; 5·42, multiplet, all couplings small, C 17–H; 2·35, doublet of doublets, *J* 11, 2 Hz, C 16–H. Mass spectrum: 426 (M^+ and base peak, 100%), 368 (10), 366 (10), 214 (14), 200 (16), 199 (24), 176 (12).

Elliptamine

Elliptamine picrate[4] was obtained as orange-red solvated crystals, m.p. 170°, from aqueous methanol, and non-solvated crystals, m.p. 215–216° from anhydrous methanol. (Literature m.p. reserpiline picrate, 173°.) The n.m.r. spectrum indicated a close relationship to isoreserpiline, and comparison of the mass spectra confirmed that the two bases were isomeric (M^+ at *m/e* 412) and very clearly similar in structure. The molecular ion peak at *m/e* 412 was consistent with the molecular formula $C_{23}H_{28}N_2O_5$ previously deduced from microanalytical data. The free base yielded a crystalline oxalate, m.p. 244–245° (dec.) (literature m.p. reserpiline oxalate, 244–245°), which had an i.r. spectrum identical with that recorded for reserpiline oxalate.[5]

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[3] Wenkert, E., Bindra, J. S., Chong, C.-J., Cochran, D. W., and Schell, F. M., *Accounts Chem. Res.*, 1974, **7**, 46.
[4] Douglas, B., Kirkpatrick, J. L., Moore, B. P., and Weisbach, J. A., *Aust. J. Chem.*, 1964, **17**, 246.
[5] 'Physical Data of Indole and Dihydroindole Alkaloids' 4th Edn (Eli Lilly & Co.: Indianapolis 1960).