TWO NEW SPIROBENZYLISOQUINOLINE ALKALOIDS FROM *RUPICAPNOS AFRICANA* (LAM.) POMEL

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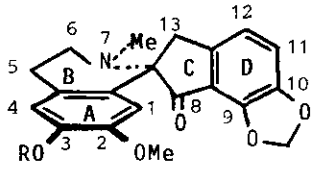
Abstract- Two new spirobenzylisoquinolines, (+)-isoparfumine and (+)-africanine, have been isolated from *Rupicapnos africana* (Lam.) Pomel and identified spectroscopically.

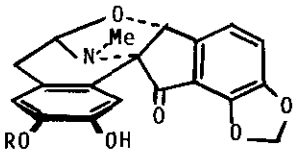
The spirobenzylisoquinolines are a group of alkaloids that have hitherto been isolated almost exclusively from the genera *Fumaria* and *Corydalis*[1]. As part of our work on the isolation and identification of Fumarioideae alkaloids[2] we have recently studied specimens of *Rupicapnos africana* (Lam.) Pomel collected in the Sierra del Chorro (Málaga) which as well as the known isoquinolines protopine, aobamidine and coptisine[3] were found to contain two new spirobenzylisoquinolines that we have named (+)-isoparfumine (1) and (+)-africanine (3).

(+)-Isoparfumine (1) was obtained as a white, crystalline, optically active substance, mp 206-208ºC (MeOH), $[\alpha]_D^{25}$ +54º (c= 0.792, $CHCl_3$). Its UV spectrum, with absorptions at λ_{max}(EtOH) (log ε) 210(4.30), 234(4.35), 260(4.60), 293(sh) and 350(3.47) nm, λ_{max}($EtOH+OH^-$) 300 and 350 nm and a band in its IR spectrum at λ_{max} ($CHCl_3$) 1710 cm^{-1} were typical of an 8-ketospirobenzylisoquinoline[1,4]. The IR spectrum also displayed a band at 3500 cm^{-1} (OH). The molecular formula $C_{20}H_{19}O_5N$, obtained by elemental analysis, was confirmed by MS, in which the molecular ion appeared at m/z 353 (52%). In addition, the fragment (M^+-29) characteristic of an 8-ketospirobenzylisoquinoline[5] was observed at 324 (100%). The pmr data (80 MHz, acetone-d_6, δ) suggested structure (1) for (+)-isoparfumine in view of the singlets at 2.28 (3H, NMe), 3.52 (3H, OMe), 6.15 (2H, OCH_2O), 6.26 (1H, H-1), 6.59 (1H, H-4) and an AB centred at 6.93 and 7.20 ppm (J= 7.9 Hz, H-12 and H-11 respectively). Further support for this assignment was obtained by O-methylation of (+)-isoparfumine with diazomethane, which afforded (+)-parfumidine (2)[2], whose identity with an authentic specimen was proved by direct comparison (IR, NMR, tlc). Finally, the methoxy group of (+)-isoparfumine was placed at C-2 on the basis of its appearance at 3.52 ppm, as it is known that in an 8-ketospirobenzylisoquinoline a methoxy group at C-2 should appear at 3.50-3.65 whereas at C-3 appears at 3.70-3.94 ppm[1].

(+)-Africanine (3) was obtained as a white, crystalline, optically active substance, mp 237ºC (MeOH), $[\alpha]_D^{25}$ +22º (c= 0.322, $CHCl_3$). Its molecular formula



1 R=H
2 R=Me



3 R=Me
4 R=Ac

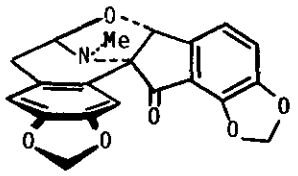


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Table 1. PMR and n.O.e. data for (+)-africanine 3 and (+)-africanine acetate 4

	3 ($CDCl_3$+ TFA-d_1)		4 ($CDCl_3$)	
Proton	δ	n.O.e.(%)[a]	δ	n.O.e.(%)[a]
H-1	6.46(s)	H-13 (1.1)	6.62(s)	H-13 (1.7)
H-4	6.78(s)	OMe (6.7)	6.88(s)	OMe (9)
H-5	3.54(m)	H-6 (5.3); H-4 (2.1)	2.9-3.7 (m)	(b)
H-6	4.32(m)	H-5 (2.9), N-Me (3.8)		
H-11	7.25(d,J=7.8)*	(b)	7.14 (d,J=8)	(c)
H-12	7.23(d,J=7.8)*	(b)	7.13 (d,J=8)	(c)
H-13	6.05 (s)	H-1 (3.4)	5.39 (br s)	H-1(4),H-12(3.8)
N-Me	3.32 (s)	(b)	2.77 (s)	(c)
OMe	3.89 (s)	H-4 (3.7)	3.82 (s)	H-4 (3.6)
OCH_2O	6.28(d,J=1)	(b)	6.20 (d,J=1)	(b)
	6.26(d,J=1)	(b)	6.18 (d,J=1)	(b)
OAc	----------	----------	2.22 (s)	(b)

(a) Protons shown are the ones which experience enhancement upon pre-irradiation of the proton indicated in Column 1.
(b) non-irradiated signal.
(c) no n.O.e. was observed.

$C_{20}H_{17}O_6N$ was established by high resolution MS (Found:367.1044±0.0018; Calcd.:367.1056) and fragments were also observed at 335 (50%) and 321 (100%). An intense absorption band in its IR spectrum at ν_{max}(KBr) 1710 cm^{-1}, which is typical of a conjugated carbonyl in a five-member ring, its UV spectrum, with absorption maxima at λ_{max}(EtOH) (log ε) 206 (4.29), 233 (4.42), 259(sh, 4.00), 290 (3.62) and 346 (3.26) revealed the presence of an 8-ketospirobenzylisoquinoline skeleton[1,4] in its structure. Upon addition of base its UV spectrum suffered a bathochromic shift to λ_{max}(EtOH+OH^-) 310 and 350 nm, indicating the phenolic nature of the alkaloid. Further support was obtained from its treatment with Ac_2O/Py, which afforded a simple compound. Its PMR (250 MHz, $CDCl_3$, δ) (2.22 ppm, s,

3H, -CO-CH_3) showed it to be monoacetylated.

The PMR spectrum (250 MHz, $CDCl_3$,δ) of (+)-africanine (3) exhibited signals at 2.75 (s, 3H, NMe), 3.20-3.60 (broad signals, 3H), 3.88 (s, 3H, OMe), 5.32 (s, 1H, HCO), 5.54 (br s, 1H, OH), 6.18 and 6.21 (AB dd, J= 1.0 Hz, OCH_2O) and 6.48 (s, 1H, H-1), 6.77 (s,1H, H-4) and 7.14 (s, 2H, H-11 and H-12). All the above spectroscopic data were very similar to those of densiflorine (5)[6], the only significant difference being the presence in (+)-africanine of a singlet at 3.88 (OMe) and 5.54 (OH) instead of the singlet at 5.93 ppm (OCH_2O) in densiflorine (5)[6]. Hence the only structural difference between the two alkaloids is the presence in (+)-africanine of methoxy and hydroxy groups in ring A instead of the methylendioxy group of densiflorine. The position of the methoxy singlet (3.79 ppm) places the methoxy group at C-3 (see argument for (+)-isoparfumine (1) above).

Upon addition of one drop of deuterated trifluoroacetic acid (TFA-d_1) to a $CDCl_3$ solution of (+)-africanine, sharper signals for protons H-5 and H-6 were observed, along with a significant downfield shift of the H-6, H-13 and N-Me signals (see Table 1). Assignments of all the resonances were confirmed by nuclear Overhauser effect experiments (n.O.e.). In table 1 PMR data for (+)-africanine acetate are also given. Specially relevant is the n.O.e. observed for protons H-1 and H-12 after saturation of H-13, which are those expected for the spiro structure (4). Thus structure (3) is established for (+)-africanine, making it the second known sample of a spirobenzylisoquinoline alkaloid with an oxygen bridge between C-6 and C-13.

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