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PENTOUREGINE, AN APORPHINE ALKALOID WITH A METHYLENEOXY BRIDGE FROM *GUATTERIA OUREGOU**

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Key Word Index—*Guatteria ouregou*; Annonaceae; methyleneoxy-bridged aporphine alkaloid; pentouregine.

Abstract—Pentouregine, isolated from the leaves of *Guatteria ouregou*, is the first aporphine alkaloid with a 1,11-methyleneoxy bridge found in an Annonaceae. Its structure has been elucidated by means of spectral analysis.

INTRODUCTION

Only a few aporphinoids with a methyleneoxy bridge bonding C-1 to C-11 are known. To date, they have been reported mostly from *Thalictrum* species (Ranunculaceae) and, in one case, from a species of *Phellodendron* (Rutaceae) [1–3]. The first reported methyleneoxy-bridged aporphinoids were the phenanthrene thaliglucine (**1**) from *Thalictrum rugosum* [4], and the related aporphines thalphenine (**2**), *N*-demethylthalphenine (**3**) and bisnorthalphenine (**4**) from other *Thalictrum* species [5–7]. Some alkaloids of this type have exhibited significant antimicrobial activity [8].

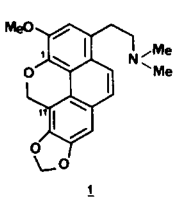
Pentouregine (**5**), a minor alkaloid isolated from the leaves of the Guianese Annonaceous tree *Guatteria ouregou*, belongs to this small group of aporphine alkaloids. Its structural elucidation is described in the present paper.

RESULTS AND DISCUSSION

Pentouregine was obtained only in an amorphous form. It analysed for $C_{18}H_{17}NO_3$, and gave a negative optical rotation, indicative of a 6a-*R* configuration which is contrary to all known methyleneoxy-bridged aporphines [1, 2]. The presence of a phenolic group was deduced from a bathochromic shift in the UV spectrum upon addition of base. The ^{1}H NMR spectrum exhibited two doublets (2H) at δ4.94 and 5.15 (J = 13.5 Hz), which is a diagnostic feature of methyleneoxy-bridged aporphines [1, 2]. The ^{1}H NMR spectrum further indicated a methoxyl singlet at δ3.79 and a multiplet centred at δ6.97 typical of H-8, H-9, and H-10 in an 11-substituted aporphinic D-ring. The absence of any signal for H-3 (near δ6.6) and H-11 (near δ8.0) was also noted. The mass spectrum of pentouregine exhibited significant ions at *m/z* 295 $[M]^+$, 294 $[M-1]^+$ (100%), 280 $[M-15]^+$ and 266 $[M-29]^+$, characteristic of a noraporphine alkaloid. The presence of OH and NH groups was supported by acetylation (Ac_2O–pyridine) which gave *N,O*-diacetylpentouregine (**6**) (^{1}H NMR: two additional three protons singlets at δ2.23 and 2.38, for NAc and OAc groups, respectively; IR: two carbonyl bands at 1635 and 1760 cm^{-1}, for amide and ester, respectively).

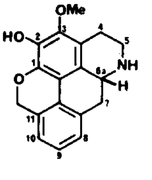
The above spectral data led to two possible isomeric structures, **5** or **7**, for pentouregine, differing in placement of the hydroxyl at C-2 or C-3. The presence of a phenolic hydroxyl at C-3 in an aporphine can be deduced from the bathochromic and hyperchromic effects exhibited near 315 nm in the UV spectrum in basic solution [9]. These effects have been clearly observed in the cases of 3-hydroxynuciferine and 3-hydroxynornuciferine, two other aporphines isolated from *G. ouregou* leaves [10]. For pentouregine, only a very small hyperchromic effect was observed, inadequate for a 3-hydroxyl substitution and ruling out structure **7**.

The structure for pentouregine was definitely established as **5** by means of careful examination of the mass spectrum of its diacetyl derivative **6**. Achenbach *et al.* [11] have shown that mass spectra of 3-methoxy *N*-acetylnoraporphines exhibit a major ion (*a*) at $[M-72]^+$, derived by McLafferty rearrangement and retro-

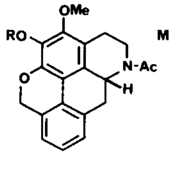


1

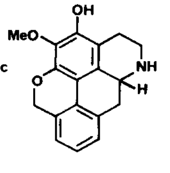
2: R= $(Me)_2$ (quaternary)
3: R= Me
4: R= H



5: Pentouregine



6: R= Ac
8: R= Et



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* Part 59 in the series "Alkaloids of the Annonaceae". For part 58 see: Cortes, D., Ramahatra, A., Cavé, A., De Carvalho Bayma, J. and Dadoun, H. (1985) *J. Nat. Prod.* **48**, 254.

Diels–Alder elimination, and also two ions (*c* and *d*) at $[M-32]^+$ and $[M-74]^+$ ($[M-32-42]^+$) which can be derived through the route indicated in Scheme 1. The ion *b* $[a-42]^+$ is also observed. If, on the other hand, the 3-substituent is a phenolic, the mass spectrum of the *N,O*-diacetate reveals two additional characteristic ions (*e* and *f*), at $[M-59]^+$ and $[M-101]^+$, as well as one corresponding to *d*, but at $[M-102]^+$. The 3-methoxy substituent of pentouregine was clearly indicated by its mass spectral fragmentations (Scheme 1), and structure **5** was also supported by the mass spectrum of the *N*-acetyl-*O*-ethyl derivative **8**, again ruling out the possibility of a 3-hydroxy group.

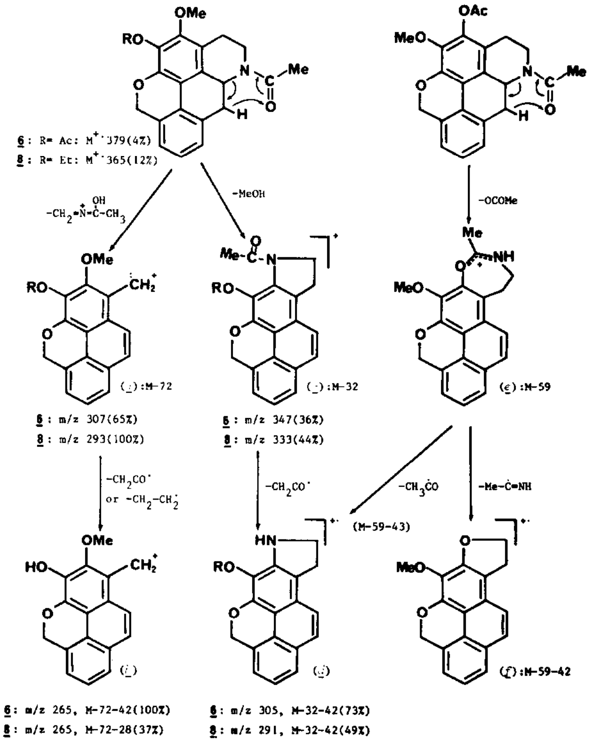
Thus, pentouregine (**5**) is the first aporphine alkaloid with a methyleneoxy bridge found in an Annonaceae. It is also the first example of this rare structural type bearing a substituent on C-3, but unsubstituted at C-9 and C-10, and also the first with the 6a-*R* configuration.

EXPERIMENTAL

UV spectra were obtained in EtOH and IR spectra in films. ^{1}H NMR spectra were run at 90 MHz or 250 MHz; chemical shifts are in δ units, with TMS as int. standard. EIMS were recorded at 70 eV.

Plant material. Leaves of *G. ouregou* Dun. were collected in French Guiana, near Cabassou, during November 1979. Voucher specimens are kept under reference Moretti 1085 (Herbarium ORSTOM, Cayenne).

Extraction and isolation of alkaloid. Dried, powdered, leaves (1.18 kg) were extracted in a Soxhlet, first by petrol (bp 40–60°) and then with CH_2Cl_2 after alkalinization with 10% aq. NH_4OH. The CH_2Cl_2 extract, treated using a procedure previously reported [12], yielded 4.63 g of crude alkaloids (0.39%) which were partitioned into phenolic and nonphenolic bases. The phenolic alkaloids were subjected to CC over silica gel 60. Elution with CH_2Cl_2–MeOH (97:3) afforded pentouregine which was further purified (20 mg, 0.4% of crude alkaloids) by prep. TLC using CH_2Cl_2–EtOAc–MeOH–NH_4OH (20:20:10:1) as eluent.



Scheme 1. Mass spectral fragmentation of the diacetyl (**6**) and *N*-acetyl-*O*-ethyl (**8**) derivatives of pentouregine.

Pentouregine (**5**). Isolated as an amorphous powder; $C_{18}H_{17}NO_3$ ($[M]^+$ *m/z* 295); $[\alpha]_D$ $-61°$ (*c* 0.14, EtOH). UV λ_{max} nm (log ε): 224 (4.31), 284 (4.14), 303 sh (3.98); (+NaOH): 223 (4.37), 264 (4.15), 290 (4.07), 307 sh (4.02). ^{1}H NMR (90 MHz, $CDCl_3$–CD_3OD, 1:1): δ3.79 (3H, *s*, 3-OMe), 4.94 and 5.15 (2H, AB *q*, *J* = 13.5 Hz, OCH_2), 6.97 (3H, *m*, H-8, H-9, H-10). EIMS *m/z* (rel. int.): 295 (64) $[M]^+$, 294 (100), 280 (14), 278 (14), 266 (55), 251 (12), 235 (9).

N,O-*Diacetylpentouregine* (**6**). Treatment of **5** (5 mg) with Ac_2O–pyridine (room temp, 15 hr) and subsequent work-up gave compound **6** (quant yield) as an amorphous powder; $C_{22}H_{21}NO_5$ ($[M]^+$ *m/z* 379). IR ν_{max} cm^{-1}: 1760 (C=O ester), 1635 (C=O amide). ^{1}H NMR (250 MHz, $CDCl_3$): δ2.23 (3H, *s*, NAc), 2.38 (3H, *s*, OAc), 3.78 (3H, *s*, 3-OMe), 5.06 and 5.18 (2H, AB *q*, *J* = 13.5 Hz, OCH_2), 7.11 (3H, *m*, H-8, H-9, H-10). EIMS *m/z* (rel. int.): 379 (4) $[M]^+$, 347 (36) [*c*], 337 (5) $[M-42]^+$, 308 (14), 307 (65) [*a*], 306 (21), 305 (73) [*d*], 266 (42), 265 (100) [*b*], 250 (42); no detectable peak at 320 [*e*] or 278 [*f*].

N-*Acetyl*-O-*ethylpentouregine* (**8**). Pentouregine (**5**, 1.5 mg) in MeOH was treated (2 days, room temp) with excess $C_2H_5N_2$. After evapn, treatment of the residue with Ac_2O–pyridine by the usual procedure gave compound **8** in quantitative yield; $C_{22}H_{23}NO_4$ ($[M]^+$ *m/z* 365). EIMS *m/z* (rel. int.): 365 (12) $[M]^+$, 333 (44) [*c*], 293 (100) [*a*], 291 (49) [*d*], 265 (37) [*b*].

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