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VEPRISILONE, A PRENYLATED 2-QUINOLONE, AND LIMONIN FROM *VEPRIS LOUISII*

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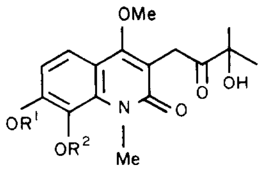
Key Word Index—*Vepris louisii*; Rutaceae; trunk bark; prenylated 2-quinolone alkaloid; veprisilone; limonoid; limonin.

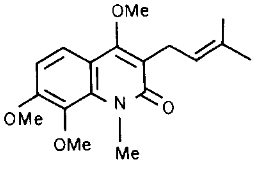
Abstract—A new 2-quinolone alkaloid, veprisilone, isolated from the trunk bark of *Vepris louisii* has been characterized as 3-(3-hydroxy-3-methyl-2-oxobutyl)-4,7,8-trimethoxy-1-methyl-2-quinolone from spectral and chemical data. Limonin was also identified in the extracts.

INTRODUCTION

The bark of *Vepris louisii* is a rich source of isoprenoid quinoline alkaloids and to date three alkaloids of this class have been isolated and their structures elucidated [1, 2]. The present communication describes the structure of one more base, for which we propose the name veprisilone, which was isolated together with the limonoid, limonin, from the neutral components of the MeOH extracts of the trunk bark of this plant.



1 $R^1 = R^2 = Me$
2 $R^1 + R^2 = CH_2$



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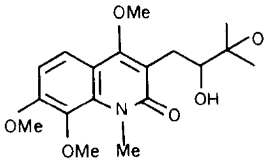

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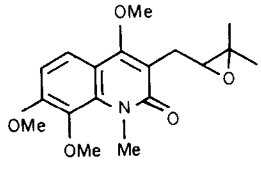

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RESULTS AND DISCUSSION

Veprisilone **1**, $C_{18}H_{23}O_6N$ (M^+ 349) was optically inactive and nonphenolic. Its UV spectrum in neutral and in acid solution was consistent with that of a 2-quinolone [3] and resembled that of *N*-methylpreskimmianine **3** [1]. This was confirmed by IR absorption at 1640 cm^{-1} (2-quinolone carbonyl). The IR spectrum furthermore showed hydroxylic (3490 cm^{-1}) and carbonyl (1710 cm^{-1}) absorptions. The ^{1}H NMR spectrum of **1** was almost identical with that of hydroxylunidonine **2** [4] in the lowfield region, showing signals attributable to two *ortho*-coupled aromatic protons. Four resonances for methyls bonded to electronegative atoms (N or O) were also present. The appearance of a six-proton singlet at δ1.50, a two-proton singlet at δ3.93 and a one-proton D_2O-exchangeable broad singlet at δ4.42 was consistent with a 3-hydroxy-3-methyl-2-oxobutyl residue. The presence of this substituent was further indicated by the mass spectrum which showed a prominent peak (61%) at $(M^+ - 87)^+$ (loss of $C_4H_7O_2$). On the basis of these spectral data, structure **1** was assigned to veprisilone. The proposed structure was confirmed by chemical correlation of veprisilone with *N*-methylpreskimmianine (**3**). $NaBH_4$ reduction of **1** gave a product which was identical in all respects (NMR, UV, mp, IR, mass spectrum) with 3-(2,3-dihydroxy-3-methylbutyl)-4,7,8-trimethoxy-1-methyl-2-quinolone (**4**) obtained by peracid oxidation [8] of **3**. Quinolone alkaloids with the 3-hydroxy-3-methyl-2-oxobutyl group are very rare. To our knowledge, only one previous example, hydroxylunidonine (**2**) [4], isolated from *Ptelea trifoliata* is known. Veprisilone thus constitutes the second member and its co-occurrence with **3** would suggest its derivation from **3** by oxidation of the side-chain probably via the epoxide intermediate (**5**) [5].

The second component of the neutral fraction was identified as limonin [6] from spectral data and by direct comparison with an authentic specimen. This is the first report of limonin from the genus *Vepris*, although a related limonoid, veprisone, has been previously identified in *V. bilocularis* [7].

EXPERIMENTAL

^{1}H NMR spectra were measured at 100 MHz. Mps are uncorr. Analytical TLC was done on Si gel GF 254. Si gel 60 (70–230 mesh, Merck) was used for CC. MS were measured at 70 eV by direct inlet.

Plant material. The trunk bark of *V. louisii* G. Gilbert was collected in Dec. 1979 near Ngola in the Eastern Province of Cameroon and identified by Mr Mpom Benoît (National

Herbarium, Yaoundé). Confirmation of identification was carried out by the National Herbarium, Yaoundé, where a voucher sample is deposited under the Cipher RL. No. 3637.

Extraction and separation. Powdered trunk bark (6 kg) was extracted successively with *n*-hexane, $CHCl_3$ and MeOH. The MeOH extract was concd and suspended in 7% HCl. Extraction with $CHCl_3$ gave a dark gum (18 g) after removal of solvent. The crude extract was chromatographed on Si gel and the column eluted with *n*-hexane–Et_2O to give traces of *N*-methylpreskimmianine and veprisine [1]. Further elution with Et_2O–$CHCl_3$ (3:1) yielded successively veprisilone (**1**) (200 mg), limonin (3 g) and a dark unidentified gum.

Veprisilone, [3-(3-*hydroxy*-3-*methyl*-2-*oxobutyl*)-1-*methyl*-4,7,8-*trimethoxy*-2-*quinolone*] (**1**). Prisms (from EtOAc), mp 135–136°; ν_{max} cm^{-1}: 3496, 1710, 1640, 1600, 1500, 1450, 1355, 1260, 1070, and 810; λ_{max}^{EtOH} nm: 336 (ϵ 9000), 323 (11 600), 302 (11 600), 261 (18 000), 253 (17 500), 237 (37 500) and 227 (39 000); $\lambda_{max}^{MeOH-HCl}$: as above; ^{1}H NMR (100 MHz, $CDCl_3$): δ1.5 (6H, *s*), 3.8 (3H, *s* =N–Me), 3.92 (9H, *s*, 3 × OMe), 3.93 (2H, *s*, ArC$\underline{H}_2$), 4.42 (1H *br s*, exchangeable D_2O, OH), 6.91 (1H, *d*, $J = 9$ Hz, H-6) and 7.55 (1H, *d*, $J = 9$ Hz, H-5); MS *m/z* (rel. int.): 349 (M^+, 31), 334 ($M^+ - Me$, 4), 331 ($M^+ - H_2O$, 2), 290 ($M^+ - C_3H_7O$, 20), 263 ($M^+ - C_4H_6O_2$, 100), 262 ($M^+ - C_4H_7O_2$, 61), 248 (M^+ – side chain, 81), 59 ($Me_2C^+ = OH$, 22). Found: C, 62.10; H, 6.52; N, 3.80, $C_{18}H_{23}NO_6$ requires: C, 61.88; H, 6.64; N, 4.01%.

Peracid oxidation of N-*methylpreskimmianine* (**3**). **3** (250 mg) in $CHCl_3$ (50 ml) was stirred with 3-chloroperbenzoic acid (350 mg; 85%). After standing 2 hr at room temp. the soln was shaken successively with 2M NaOH and H_2O, then dried and evaporated to give crude 3-(2,3-dihydroxy-3-methylbutyl)-4,7,8-trimethoxy-1-methyl-2-quinolone (**4**). Chromatographic purification (Si gel, EtOAc) yielded pure **4** (183 mg), mp 114–116°, ν_{max}^{KBr} cm^{-1}: 3540 (non-bonded OH), 3270 (bonded OH), 1622 (chelated 2-quinolone C=O), 1585, 1500, 1480, 1360, 1080, 1040 and 900; λ_{max}^{EtOH} nm: 336 (ϵ 9700) 323 (12 100), 303 (10 900), 262 (18 300), 254 (17 500), 236 (37 800) and 227 (40 000): ^{1}H NMR 100 MHz, $CDCl_3$): δ1.31 [6H, *s*, $Me_2C(OH)$], 2.65 [1H, *br s* disappeared on deuteration, Me_2 C-O$\underline{H}$), 2.67 (1H, *dd*, $J = 13.5$ and 2 Hz, benzylic H), 3.05 (1H, *dd*, $J = 13.5$ and 2 Hz, benzylic H), 3.58 (1H, *dt*, $J = 10$ and 2 Hz, -C$\underline{H}$-OH), 3.81 (3H, *s*, N-Me), 3.92 (3H, *s*, OMe) 3.98 (6H, *s*, 2 × OMe), 5.18 (1H, *d*, $J = 2$ Hz, exchangeable D_2O, OH), 6.95 (1H, *d*, $J = 9$ Hz, H-6) and 7.55 (1H, *d*, $J = 9$ Hz, H-5). MS *m/z* (rel. int.): 351 (M^+, trace), 336 ($M^+ - Me$, 2), 333 ($M^+ - H_2O$, 4), 292 ($M^+ - C_3H_2O$, 100), 263 (M^+ – side-chain, 15), 262 (24), 248 (24), 59 (4). Found: C, 61.72; H, 7.03; N, 4.18: $C_{18}H_{25}O_6N$ requires: C, 61.52; H, 7.17; N, 3.99%.

$NaBH_4$ *reduction of veprisilone* (**2**). 2 (100 mg) was dissolved in MeOH (10 ml) and $NaBH_4$ (25 mg) was added gradually. The reaction mixture was stirred at room temp. for 1 hr. Evaporation and chromatographic separation (Si gel, EtAOc) afforded **4** as prisms from EtOAc–*n*-hexane, identical with an authentic sample synthesized from *N*-methylpreskimmianine.

Limonin crystallized from $CHCl_3$–MeOH, mp 296–298° (lit. [9] 298°), $[\alpha]_D^{21}$ −123° (Me_2CO). The IR spectrum of the isolate and reference limonin were superimposable, and a mmp showed no depression.

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