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VEPRISINE AND N-METHYLPRESKIMMIANINE : NOVEL 2-QUINOLONES FROM VEPRIS LOUISII

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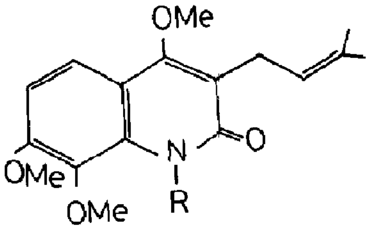
Summary: The structures of two new 2-quinolone alkaloids, N-methylpreskimmianine and veprisine (7,8-dimethoxy-N-methylflindersine) have been deduced from their spectra and confirmed by partial synthesis from known compounds.

Vepris louisii G. Gilb. is the only species of *Vepris* (Rutaceae) occurring in Cameroon[1]. As part of a continuing programme of study of Cameroonian Rutaceae, we have examined chemically the extracts of the stem bark of *Vepris louisii* and have isolated from the combined chloroform and hexane extracts lupeol and two new quinolone alkaloids. These alkaloids, N-methylpreskimmianine and veprisine have been identified and the present communication describes the evidence leading to their proposed structures.

N-methylpreskimmianine 1, $C_{18}H_{23}O_4N$, $M^{+\cdot}$ 317, colourless plates from n-hexane, m.p. 88-89° showed an infra-red absorption at 1638 cm^{-1} (2-quinolone) and the ultra-violet spectrum with λ_{max}^{EtOH} (εmax): 227 (26,000), 236 (23,400), 253 (10,600), 261,5 (11,000), 300 (6,600) 323 (7,300) and 335 nm (5,700) was typically that of a 2-quinolone[2]. No acid shift was observed. The ^1H NMR spectrum ($CDCl_3$) had three methoxyl absorptions at δ 3.93 (6H) and 3.85 (3H) and an N-methyl signal at δ 3.77 (3H). The presence of a dimethylallyl group was indicated by two vinylic methyl singlets at δ 1.79 and δ 1.66 and an olefinic triplet at δ 5.30 (1H) which was coupled to a two-proton doublet (J 7Hz) at δ 3.35. Two *ortho*-coupled aromatic protons appeared at δ 7.52 and δ 6.85 (J 9Hz) and the values of their chemical shifts indicated that they were H-5 and H-6 of a 2-quinolone[3,4]. These data are best accommodated by structure 1 which is also in accord with biogenetic considerations. Structure 1 has been confirmed by partial synthesis. Methylation of preskimmianine 2, previously totally synthesised[3], with methyl iodide and anhydrous potassium carbonate in acetone[5] gave 1 which must therefore be 7,8-dimethoxy-3-(γ,γ-dimethylallyl)-N-methyl-2-quinolone.

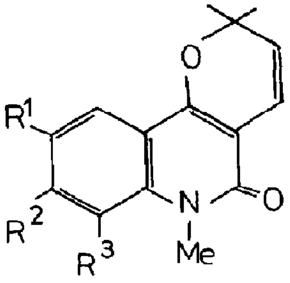
The second alkaloid for which we propose the name veprisine 3, $C_{17}H_{19}O_4$, $M^{+\cdot}$ 301 crystallised from n-hexane-benzene mixture as pale yellow needles and had m.p. 89-90°. The i.r. spectrum of 3 (νmax 1646 cm^{-1}) suggested a 2-quinolone[2] and its u.v. spectrum with λ_{max}^{EtOH} (εmax): 236 (32,000), 263 (16,300), 273 (14,600), 334 (10,600), 349 (12,800) and 364 nm (8,500) was similar to that of oricine 4[5]. The ^{1}H NMR spectrum of 3 showed bands for a 2,2-dimethylchromene {δ 1.49 (6H); δ 5.45 and 6.69 (1H doublets J 10Hz)}, an N-methyl (δ 3.76), two methoxyls {δ 3.93 (3H) and δ 3.90 (3H)} and two *ortho*-coupled aromatic protons {δ 7.67 and 6.85 (1H doublets, J 9Hz)}. The chemical shifts, δ 7.67, of the down-field doublet indicated that one of the aromatic protons was at C-5[3,4]. The above data suggested that veprisine was 7,8-dimethoxy-N-methyl-flindersine 3. This was readily confirmed by partial synthesis. N-methylpreskimmianine 1 was demethylated and cyclised by heating with concentrated hydrochloric acid. Dehydrogenation of the resulting dihydroveprisine 5 with dichloro dicyanobenzoquinone (D.D.Q) following the synthesis of oricine 4[5] then gave veprisine 3 identical with the natural sample.

The isolation of N-methylpreskimmianine and veprisine from *Vepris* may have some implications on the biosynthesis of quinoline alkaloids in the Rutaceae[3,6].



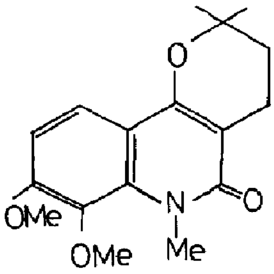
1 · R = Me

2 · R = H



3 · R1= H, R2= R3= OMe

4 · R1 = R2 = OMe, R3= H



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