Two New 3-Methoxy-4-quinolone Alkaloids from the Bark of Sarcomeliche megistophylla

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Two new alkaloids, megistonine I (1) and megistonine II (2), were isolated from the bark of Sarcomeliche megistophylla. Their structures, which are derived from the 3-methoxy-4-quinolone basic skeleton, were elucidated on the basis of MS and extensive NMR studies.

Key words quinolone; alkaloid; Sarcomeliche megistophylla; Rutaceae

*Sarcomeliche megistophylla* Hartley (Rutaceae) is a small to medium sized tree, 8—12 m high, characterized by its large (up to 34 cm long) pubescent leaves. Hartley described it as endemic to the region of Nouméa, New Caledonia. Recently, we described the chemical constituents of its leaves and the major alkaloids of the bark. In a continuation of our studies of the genus *Sarcomeliche* we report here the isolation and structural elucidation of two new quinolone alkaloids, megistonine I (1) and megistonine II (2), isolated from the ether extract of the bark of *Sarcomeliche megistophylla*.

Megistonine I (1) was obtained as a yellow amorphous compound. The empirical formula was determined by HRMS to be C_{16}H_{23}NO_4. The UV spectrum was suggestive of a quinolone derivative. A typical hypsochromic shift observed upon the addition of acid gave evidence of a 4-quinolone basic skeleton. In the aromatic region of the ^1H-NMR spectrum, two ortho-coupled signals, at 8.17 and 6.98 (each 1H, d, J=8.8 Hz), were associated with the A ring of a substituted-4-quinolone. A broad singlet at 10.5 was indicative of one phenolic OH group. At a higher field, typical signals accounted for one 1,1-dimethylallyl side chain, two OMe groups and one NMe group. The ^13C-NMR spectrum showed two carbonyl resonances, at 173.7 and 163.5 ppm, the former confirming the presence of the 4-quinolone system and the latter characterizing a methyl ester group. Further information on the structure of 1 was obtained from the long range C–H correlations in the ^1H-detected heteronuclear multibond connectivity (HMBC) spectrum (Fig. 2). Three bond correlations observed between the 3H-singlet of the NMe group and two quaternary aromatic carbons (δ 144.7, 140.5) permitted the assignment of C-8α and C-2, respectively. The methylene protons of the side chain, at δ 3.53, showed a correlation with the 8α-quaternary carbon on one hand, and the oxygenated aromatic carbon C-7 at δ 160.3, on the other hand. These observations permitted location of the 1,1-dimethylallyl side chain at C-8 of the quinolone A ring. Additionally, a three bond correlation between the signal of the tertiary C-3 at δ 140.2 and the 3H-singlet of the OMe ether group placed this latter at position 3 and, consequently, the COOH group at position 2 and the phenolic hydroxyl group at position 7. Therefore, the structure of this new alkaloid was depicted as 1. This structure was in full agreement with the chemical shift effects observed for C-2 and C-3, when compared with the homologous signals of 1-methyl-4-quinolone-2,3-dicarboxylic acid esters.

Megistonine II (2) was obtained as a yellow amorphous compound with the molecular formula C_{16}H_{23}NO_5. The UV spectrum was similar to that of 1. Comparison of the ^1H- and ^13C-NMR data of 2 with those of 1 indicated that the 1,1-dimethylallyl side chain in 1 was replaced by a methoxy group in 2. The position of the methoxy group was further confirmed by the HMBC spectrum in which the 3H-singlet of the OMe at δ 3.77 had a three bond correlation with C-8, at δ 134.9. The other cross peaks were essentially similar to those observed in the HMBC spectrum of 1, except those referring to the 1,1-dimethylallyl side chain. Consequently, structure 2 was attributed to this new natural product for which we propose the trivial name megistonine II.

It is interesting to point out that megistonine I (1) and megistonine II (2) are the second examples of natural 4-quinolones oxygenated in position 3. To the best of our knowledge there is only one previous account describing a natural compound of this type, i.e., japonine (1-methyl-2-phenyl-3,6-dimethoxy-4-quinolone), isolated from *Orixia*

![Fig. 1. Structures of Megistonine I (1), Megistonine II (2)](image1.png)

![Fig. 2. Selected HMBC Correlations for Megistonine I (1) and Megistonine II (2)](image2.png)

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japonica, which also belongs to the Rutaceae family.\(^{14}\)

**Experimental**

**General Experimental Procedures**  UV spectra were recorded in spectrophotometric grade MeOH on a Shimadzu-160A spectrophotometer. NMR spectra were recorded on Bruker DRX 400 and Bruker AC 200 spectrometers \(^{1}H\) (400 and 200 MHz) and \(^{13}C\) (50 MHz), and chemical shifts are expressed in ppm downfield to TMS. The 2D NMR experiments were performed using standard Bruker microprograms. El-MS spectra were determined on a HP-6890 and HR-MS on an AEI MS-902 spectrometer.

**Plant Material**  The plant material was collected at Noumäa (New Caledonia) in May 1984. A voucher sample (Pusset-Chauvière 261) is deposited in the herbarium of the Centre ORSTOM at Noumäa, New Caledonia.

**Extraction and Isolation**  Extraction of the alkaloids was as described.\(^{16}\) The ether extract was chromatographed over a column containing Si gel (Merck 0.04–0.06 mm; flash) using a cyclohexane/EtOAc gradient to give 7 fractions. Fraction 6 was submitted to flash chromatography on silica gel with CH\(_2\)Cl\(_2\)/MeOH (99:1) to afford megitonine I (7 mg) and megitonine II (5 mg).

Mejitonine I (1): \(^{1}H\)-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 10.5 (1H, br s, HO-C7), 8.17 (1H, d, \(J=8.8\) Hz, H-5), 6.98 (1H, d, \(J=8.8\) Hz, H-6), 5.27 (1H, t, \(J=8.3\) Hz, H-11), 3.99 (3H, s, OMe-C9), 3.92 (3H, s, OMe-C3), 3.65 (3H, s, NMe), 3.53 (2H, d, \(J=8.3\) Hz, H-10), 1.76 (6H, s, H-13, 14). \(^{13}C\)-NMR (CDCl\(_3\), 100 MHz) \(\delta\): 173.7 (C-4), 163.2 (C-9), 160.3 (C-7), 144.7 (C-8a), 140.5 (C-2), 140.2 (C-3), 135.1 (C-12), 126.2 (C-5), 122.8 (C-4a), 122.0 (C-11), 114.5 (C-6), 114.2 (C-8), 61.1 (OMe-C3), 53.2 (OMe-C9), 42.5 (NMe), 27.4 (C-10), 25.7(C-13), 18.2 (C-14). UV \(\lambda_{max}\) (MeOH) nm (log e): 243 (3.91), 267 (sh), 335 (3.48). HRMS m/z: 331.1415 (Calcd for C\(_{15}\)H\(_{16}\)N\(_{2}\)O\(_{4}\): 331.1419; MS-DCI m/z: 322 [M+H]\(^{+}\); El m/z (rel.int.): 331 (90), 316 (100).

Megotimine II (2): \(^{1}H\)-NMR (CDCl\(_3\), 400 MHz) \(\delta\): 10.6 (1H, br s, HO-C7), 8.16 (1H, d, \(J=8.8\) Hz, H-5), 7.02 (1H, d, \(J=8.8\) Hz, H-6), 4.02 (3H, s, OMe-C9), 3.93 (3H, s, OMe-C3), 3.84 (3H, s, NMe), 3.77 (3H, s, OMe-C8). \(^{13}C\)-NMR (CDCl\(_3\), 50 MHz) \(\delta\): 172.6 (C-4), 163.3 (C-9), 153.3 (C-7), 140.2 (C-2), 140.1 (C-3), 135.2 (C-8a), 134.9 (C-8), 123.9 (C-5), 123.8 (C-4a), 113.6 (C-6), 62.0 (OMe-C8), 60.9 (OMe-C3), 53.3 (OMe-C9), 39.4 (NMe).

**References and Notes**