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

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Two new alkaloids, megistonine I (1) and megistonine II (2), were isolated from the bark of *Sarcomelicope 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; *Sarcomelicope megistophylla*; Rutaceae

Sarcomelicope 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[1] described it as endemic to the region of Nouméa, New Caledonia. Recently, we described the chemical constituents of its leaves[2,3] and the major alkaloids of the bark.[4] In a continuation of our studies of the genus *Sarcomelicope*[5—12] 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 *Sarcomelicope megistophylla*.

Megistonine I (**1**) was obtained as a yellow amorphous compound. The empirical formula was determined by HR-MS to be $C_{18}H_{21}NO_5$. 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.[13,14] In the aromatic region of the ^{1}H-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 disubstituted-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 *O*Me groups and one *N*Me group. The ^{13}C-NMR spectrum showed two carbonyl resonances, at δ 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 ^{1}H-detected heteronuclear maltibond connectivity (HMBC) spectrum (Fig. 2). Three bond correlations observed between the 3H-singlet of the *N*Me group and two quaternary aromatic carbons (δ 144.7, 140.5) permitted the assignment of C-8a and C-2, respectively. The methylene protons of the side chain, at δ 3.53, showed a correlation with the 8a-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 *O*Me ether group placed this latter at position 3 and, consequently, the $COOCH_3$ 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.[5,15]

Megistonine II (**2**) was obtained as a yellow amorphous compound with the molecular formula $C_{14}H_{15}NO_6$. The UV spectrum was similar to that of **1**. Comparison of the ^{1}H- and ^{13}C-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 *O*Me 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 *Orixa*

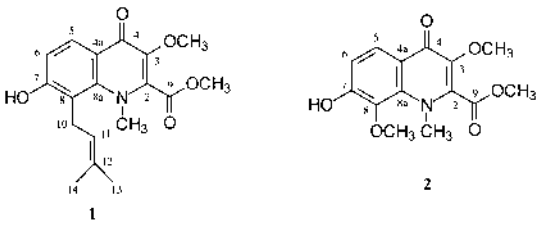

Fig. 1. Structures of Megistonine I (**1**), Megistonine II (**2**)

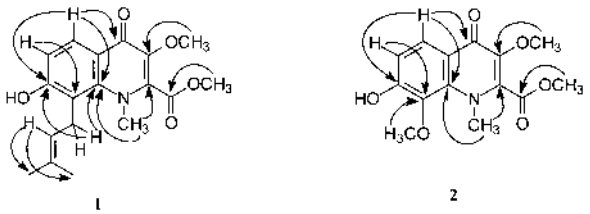

Fig. 2. Selected HMBC Correlations for Megistonine I (**1**) and Megistonine II (**2**)

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japonica, which also belongs to the Rutaceae family.[14)]

Experimental

General Experimental Procedures UV spectra were recorded in spectroscopic 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. EI-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 Nouméa (New Caledonia) in May 1984. A voucher sample (Pusset-Chauviere 261) is deposited in the herbarium of the Centre ORSTOM at Nouméa, New Caledonia.

Extraction and Isolation Extraction of the alkaloids was as described.[4)] The ether bark 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_2Cl_2/MeOH (99 : 1) to afford megistonine I (7 mg) and megistonine II (5 mg).

Megistonine I (**1**): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 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 ($CDCl_3$, 50 MHz) δ: 173.7 (C-4), 163.5 (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 λ_{max} (MeOH) nm (log ε): 243 (3.91), 267 (sh.), 335 (3.48). UV λ_{max} (MeOH+HCl) nm (log ε): 258 (4.07), 315 (3.48). HRMS *m/z*: 331.1415 (Calcd for $C_{18}H_{21}NO_5$: 331.1419); MS-DCI *m/z*: 332 $[M+H]^+$; EI *m/z* (rel.int.): 331 (90), 316 (100).

Megistonine II (**2**); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 10.6 (1H, br s, HO-C7), 8.16 (1H, d, J=8.8 Hz, H-5), 7.92 (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) δ: 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). UV λ_{max} (MeOH) nm (log ε): 241 (3.99), 268.5 (3.85), 337.5 (3.53). UV λ_{max} (MeOH+HCl) nm (log ε): 257 (4.05), 317 (3.53). HR-MS *m/z*: 293.0897 (Calcd for $C_{14}H_{15}NO_6$: 293.0899); MS-DCI *m/z*: 294 $[M+H]^+$; EI *m/z* (rel.int.): 293 (60), 278 (100), 260 (20), 248 (30), 234 (18), 218 (50).

References and Notes

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