Two New Alkaloids from the Bark of *Sarcomelicope megistophylla*

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Two new alkaloids, megistophylline I (**1**) and megistophylline II (**2**), were isolated from the bark of *Sarcomelicope megistophylla*. Their structures have been elucidated on the basis of MS and NMR data.

Sarcomelicope megistophylla Hartley (Rutaceae) is a small to medium-sized tree, 8−12 m high, easily recognized by its large (up to 34 cm long) pubescent leaves. Hartley[1] described it as endemic to the region of Néaoua, New Caledonia. Recently we described chemical constituents of its leaves.[2,3] In a continuation of our studies of the genus *Sarcomelicope*,[4] we report here a phytochemical study of the bark of *S. megistophylla*. Two new acridone alkaloids, megistophylline I (**1**) and megistophylline II (**2**), were isolated from the ether and dichloromethane bark extracts. The structure of the two novel alkaloids was deduced from ^{1}H and ^{13}C NMR spectral data and by interpretation of COSY 45°, COSY−LR, DEPT 135°, HMQC, HMQC−TOCSY, and HMBC experiments.

Megistophylline I (**1**) was obtained as a colorless amorphous compound, and its empirical formula was determined by HRMS as $C_{21}H_{23}NO_5$. The UV spectrum was suggestive of an acridone derivative. The ^{1}H NMR spectrum indicated four aromatic protons associated with a nonsubstituted ring A in an acridone-derived skeleton, one 1,1-dimethylallyl side chain, two OMe groups, one *N*Me group, and one hydrogen-bonded phenolic OH group. The ^{13}C NMR confirmed the above observations and showed the presence of two carbonyl groups. One (δ 178.1) is included in the quinolone skeleton, and the second corresponds to a conjugated ketone (δ 186). The ^{1}H and ^{13}C NMR values observed were closely related to those previously reported for a compound obtained by m-CPBA oxidation of glycocitrine.[5] The only significant differences were the absence of the proton at C-2 and the presence of a methoxy group. These data were consistent with significant chemical shift differences observed for the signals of C-1, C-2, and C-3. Further information on the structure of **1** was obtained from the long-range C−H correlations in the HMBC spectrum (Figure 1). Three-bond correlations between the two methylene protons at δ 3.18 and 2.93 and the 4a-tertiary carbon at δ 155.0, on one hand, and the ketonic carbonyl group at δ 186.0, on the other hand, permitted placement of the 1,1-dimethylallyl side chain at C-4 and the carbonyl group at C-3 of the acridone ring C. Finally, observation of three bond correlations between the strongly deshielded hydrogen-bonded hydroxyl at δ 16.22 and the 9a-quaternary carbon at δ 109.2 placed the phenolic hydroxyl group at C-1. Consequently, structure **1** was attributed to this new natural product for which we propose the trivial name megistophylline I. The absolute configuration of the chiral center at C-4 could not be determined, due to the small amount of product isolated.

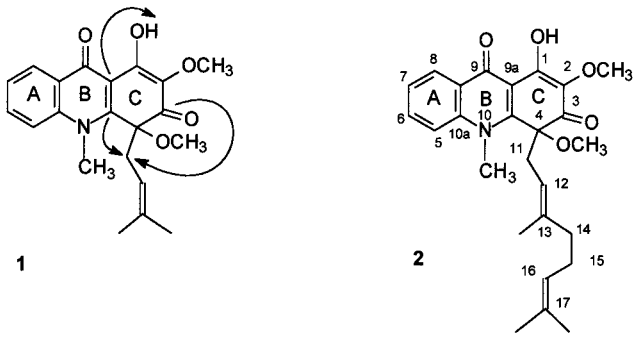

Figure 1. Selected HMBC correlations for megistophylline I (**1**) and megistophylline II (**2**).

Megistophylline II (**2**) was obtained as a colorless amorphous compound with the empirical formula $C_{26}H_{31}NO_5$. 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 geranyl group in **2**. The presence of the geranyl group was further confirmed by the EIMS spectrum, where two prominent fragment ions (*m/z* 368 and 301) were observed. Finally, the HMBC spectrum exhibited the same cross signals as those observed in **1**.

Seven known acridones, melicopicine,[6,7] melicopine,[8] melicopidine,[8,9] normelicopidine,[10,11] normelicopine,[12] arborinine,[13] and 1,2,3-trimethoxy-10-methylacridone;[3,6] three pyranoacridones, acronycine,[6,14] 12-demethylacronycine,[12] and noracronycine;[15] two furoquinolines, dictamnine[9] and acronycidine;[16] one pyranocoumarin, seselin;[17] and the alkaloid fareanine[18] were also obtained. The two new alkaloids, as well as fareanine,[18] are acridone-derived secondary metabolites characterized by a highly oxygenated C-ring. Compounds with such high oxidation levels belonging to the same series were previously isolated only from *Medicosma fareana*[18] and *Sarcomelicope dogniensis*.[4] Megistophylline II (**2**), is the first example of a C-geranyl acridone. Interestingly, the isolation of 3-geranyloxy-1-hydroxy-4-methoxy-10-methylacridone from *Sarcomelicope leiocarpa*[19] bark was the only previous record of a natural acridone bearing an *O*-geranyl substituent.

Experimental Section

General Experimental Procedures. Optical rotations were measured with a Perkin−Elmer 341 polarimeter. NMR spectra were recorded on Bruker DRX 400 and Bruker AC 200

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spectrometers [^{1}H (400 and 200 MHz) and ^{13}C (50 MHz)]; chemical shifts are expressed in parts per million (ppm) downfield to TMS. The 2D NMR experiments were performed using standard Bruker microprograms. EIMS, HP-6890; HRMS, AEI MS-902 spectrometer.

Plant Material. Plant material was collected at Néaoua (New Caledonia) in May 1984. Herbarium samples (Pusset−Chauviere 261) are deposited in the herbaria of the Centre ORSTOM of Nouméa, New Caledonia.

Extraction and Isolation of Alkaloids. Dried, pulverized bark of *Sarcomelicope megistophylla* (1 kg) was basified with NH_4OH and extracted with ether (4 × 2 L) and repeated with CH_2Cl_2 (4 × 2 L). The residue of the CH_2Cl_2 extract was washed with 1N HCl. The aqueous solutions were basified with NH_4OH to pH 10 and extracted with CH_2Cl_2 (3 × 1 L). After drying over Na_2SO_4, the organic solvent was removed in vacuo to give a crude alkaloid mixture (14 g), which was subjected to vacuum liquid chromatography (VLC) over S gel using an EtOAc−hexane gradient to give six fractions.

Fractions 2−3 were chromatographed (with a cyclohexane−EtOAc gradient, Si gel 0.015−0.04 mm) to afford 1.2 g melicopicine[6,7] and 0.8 g acronycine.[6,14] Fraction 4 was chromatographed to afford 1.2 g melicopidine,[8,9] 1.8 g melicopine,[8] 0.7 g normelicopidine,[10,11] 0.6 g normelicopine,[12] and 2.4 g acronycine.[6,14] Fraction 5 was chromatographed to afford 150 mg 1,2,3-trimethoxy-10-methylacridone,[3,6] 20 mg megistophylline I (**1**), 10 mg megistophylline II (**2**), and 5 mg fareanine. Using the same procedure as above, the residue of the ether extract afforded 30 mg dictamine,[9] 300 mg melicopicine,[6,7] 10 mg noracronycine,[15] 9 mg seseline,[17] 0.13 g melicopidine,[8,9] 13 mg melicopine,[8] 90 mg acronycine,[6,14] 30 mg acronycidine,[16] 30 mg 12-demethylacronycine,[12] 70 mg normelicopidine,[10,11] 50 mg normelicopine,[12] 60 mg arborinine,[13] and 40 mg 1,2,3-trimethoxy-10-methylacridone.[3,6] All the compounds isolated were identified by comparison of their spectral (NMR, MS, and UV) and chromatographic data with those of authentic samples.

Megistophylline I (1): $[\alpha]^{25}_D$ +32.9° (*c* 0.26, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 301 (3.95), 342 (3.88), 407 (sh) nm; IR (KBr) ν_{max} 3350, 1630, 1580, 1520, 1480 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 16.22 (1H, s, HO-1), 3.84 (3H, s, CH_3O-2), 3.23 (3H, s, CH_3O-4), 7.85 (1H, d, J = 8.3 Hz, H-5), 7.94 (1H, td, J = 8.3, 1.5 Hz, H-6), 7.65 (1H, t, J = 8.3 Hz, H-7), 8.57 (1H, dd, J = 8.3, 1.5 Hz, H-8), 4.52 (3H, s, N−CH_3), 2.93 (1H, dd, J = 14.5, 8.3 Hz, H-11a), 3.18 (1H, dd, J = 14.5, 8.3 Hz, H-11b), 4.78 (1H, t, J = 8.3 Hz, H-12), 1.38 (3H, s, CH_3-13), 1.64 (3H, s, CH_3-13); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 164.0 (C-1), 132.3 (C-2), 60.0 (CH_3O-2), 186.0 (C-3), 85.5 (C-4), 53.5 (CH_3O-4), 155.0 (C-4a), 116.4 (C-5), 134.4 (C-6), 126.2 (C-7), 126.5 (C-8), 124.7 (C-8a), 178.1 (C-9), 109.2 (C-9a), 141.2 (C-10a), 37.1 (N−CH_3), 40.0 (C-11), 114.0 (C-12), 137.8 (C-13), 26.0 (CH_3-13), 17.0 (CH_3-13); HRMS found 369.15762 (calcd 369.15762); EIMS *m*/*z* (rel int) [M]$^+$ 369 (22), 301 (30), 286 (100), 272 (20).

Megistophylline II (2): $[\alpha]^{25}_D$ +11.26°(c 0.10, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 301 (4.36), 338 (3.88), 404 (sh) nm; IR (KBr) ν_{max} 3350, 1632, 1580, 1520, 1480 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 16.20 (1H, s, HO-1), 3.85 (3H, s, CH_3O-2), 3.23 (3H, s, CH_3O-4), 7.85 (1H, d, J = 8.3 Hz, H-5), 7.92 (1H, td, J = 8.3, 1.5 Hz, H-6), 7.65 (1H, t, J = 8.3 Hz, H-7), 8.55 (1H, dd, J = 8.3, 1.5 Hz, H-8), 4.52 (3H, s, N−CH_3), 2.97 (1H, dd, J = 14.5, 8.3 Hz, H-11a), 3.09 (1H, dd, J = 14.5, 8.3 Hz, H-11b), 4.81 (1H, t, J = 8.3 Hz, H-12), 1.34 (3H, s, CH_3-13), 1.83 (2H, br s, H-14), 1.83 (2H, br s, H-15), 4.93 (1H, br s, H-16), 1.62 (3H, s, CH_3-17), 1.51 (3H, s, CH_3-17); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 165.0 (C-1), 132.6 (C-2), 60.0 (CH_3O-2), 186.2 (C-3), 85.8 (C-4), 54.2 (CH_3O-4), 155.1 (C-4a), 116.5 (C-5), 134.4 (C-6), 125.9 (C-7), 126.8 (C-8), 124.0 (C-8a), 178.2 (C-9), 108.0 (C-9a), 141.4 (C-10a), 37.3 (N−CH_3), 39.4 (C-11), 114.0 (C-12), 141.5 (C-13), 16.0 (CH_3-13), 39.6 (C-14), 26.2 (C-15), 123.3 (C-16), 131.8 (C-17), 25.9 (CH_3-17), 17.3 (CH_3-17); HRMS found 437.2202 (calcd 437.2202); EIMS *m*/*z* (rel int) [M]$^+$ 437 (12), 368 (10), 301 (30), 286 (100), 272 (20), 258 (20), 242 (24).

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