Two New Secobisbenzylisoquinoline Alkaloids from the Leaves of *Anisocycla jollyana*

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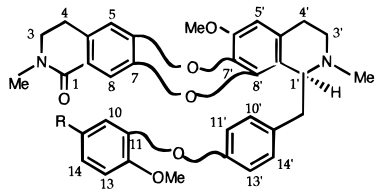
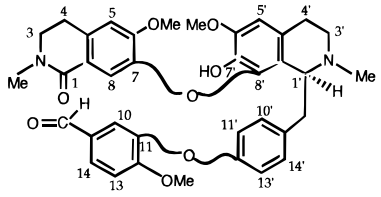
Two new *seco*-dibenzylisoquinolines, (−)-secojollyanine (**1**) and (−)-secohomoaromaline (**3**), were isolated from the leaves of *Anisocycla jollyana* together with the known alkaloid (−)-*O*-methylpunjabine (**2**). Their structures and stereochemistry were determined by chemical and spectrometric methods.

A previous phytochemical study on the leaves of *A. jollyana* Diels (Menispermaceae) has shown that this species contains numerous alkaloids belonging to the dibenzylisoquinoline and aporphine groups.[1] On continuation of our exhaustive phytochemical investigation on this species, we now report the isolation and structure elucidation of two new secobisbenzylisoquinoline alkaloids, (−)-secojollyanine (**1**) and (−)-secohomoaromaline (**3**), isolated from the leaves along with the known alkaloid, (−)-*O*-methylpunjabine (**2**).



1 R=CH_2OH
2 R=CHO



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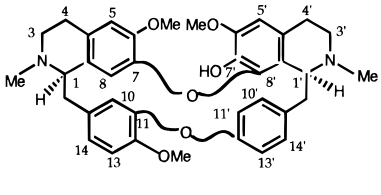

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The MeOH extract of *A. jollyana* leaves was fractionated by column chromatography on Si gel and on Al_2O_3 and by preparative TLC on Si gel yielding alkaloids **1** (0.030%), **2** (0.190%), and **3** (0.036%) which were isolated as colorless needles. The "seco" nature of these compounds was postulated on the basis of their EIMS which did not exhibit molecular peaks and which generated a base peak at *m/z* 365 for **1** and **2** and at *m/z* 397 for **3**; these base peaks result from the known benzylic cleavage of *seco*-dibenzylisoquinoline alkaloids.[2,3] Corroborating this hypothesis, **1**−**3** showed IR bands at 1600 and 1650 cm^{-1}, typical of a tertiary δ-lactam linkage.[4] Treatment of **1** and **2** with concentrated $HNO_3-H_2SO_4$ (1:9) gave a blue coloration, suggesting the presence of a dibenzo-*p*-dioxin system related to a structure with three diaryl ether bridges;[5] this reaction was negative for **3**.

Table 1. ^{1}H-NMR Data for Alkaloids **1** and **3**[a]

	alkaloid	
proton	**1**	**3**
H-5	6.73 s	6.71 s
H-5′	6.31 s	6.50 s
H-8	7.45 s	7.29 s
H-10	7.01 d (1.9)	7.38 d (1.9)
H-10′	7.21 d (8.6)	7.13 d (8.5)
H-11′	6.90 d (8.6)	6.82 d (8.5)
H-13	6.95 d (8.2)	7.07 d (8.3)
H-13′	6.90 d (8.6)	6.82 d (8.5)
H-14	7.08 dd (8.2, 1.9)	7.60 dd (8.3, 1.9)
H-14′	7.21 d (8.6)	7.13 d (8.5)
2-CONMe	3.08 s	3.08 s
N-2′ Me	2.42 s	2.29 s
6-OMe		3.95 s
6′-OMe	3.84 s	3.87 s
12-OMe	3.86 s	3.95 s
$ArCH_2OH$	4.57 s	
CHO		9.78 s

[a] Recorded at 250 MHz in $CDCl_3$; chemical shifts are given in δ units (downfield from TMS); *J* values are given in parentheses and reported in Hz.

The FABMS of **1** was characterized by a molecular ion at *m/z* 609 [MH^+] which supported a molecular formula $C_{36}H_{36}N_2O_7$ and by a fragment at *m/z* 244 corresponding to the lower part of the molecule. The ^{1}H-NMR spectrum of **1** in $CDCl_3$ (Table 1) exhibited one *N*-methyl singlet at δ 2.42 and one lactam *N*-methyl at δ 3.08, two methoxy singlets at δ 3.84 and 3.86, a 2H singlet at δ 4.57 which was assigned to an $ArCH_2OH$ group, two 1H singlets at δ 6.31 and 6.73 attributed, respectively, to H-5′ and H-5, and one deshielded 1H singlet at δ 7.45 attributed to the H-8 adjacent to the lactam function as observed in other *seco*-dibenzylisoquinoline alkaloids.[2,3,6] In addition, this spectrum showed two 2H doublets at δ 6.90 and 7.21 due to the 1,4-disubstituted benzene ring system (A_2B_2, J_{AB} = 8.6 Hz, respectively, H-11′, 13′ and H-10′, H-14′) and, finally, three protons belonging to the 1,2,4-trisubstituted benzene ring system (ABX system) at δ 6.95 (1H, d, J_{AB} = 8.2 Hz, H-13), 7.01 (1H, d, J_{BX} = 1.9 Hz, H-10), and 7.08 (1H, dd, J_{AB} = 8.2, 1.9 Hz, H-14).[2,3,6,7] The NMR and MS data of **1** were in complete agreement

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with those reported for *O*-methylpunjabine, a *seco*-dibenzylisoquinoline alkaloid belonging to the isotrilobine group; the only difference consisted in the replacement of the aldehyde function by an alcohol group.[6] Finally, $NaBH_4$ reduction of **1** provided compound **2**. On the basis of all collected experimental results, we propose, for this new alkaloid, named (−)-secojollyanine, structure **1** with the same configuration as (−)-*O*-methylpunjabine.

The known alkaloid **2** was identified to be (−)-*O*-methylpunjabine by direct comparison of its spectral data with those previously reported.[6]

The FABMS of **3** was characterized by a molecular ion at *m/z* 639 [MH^+] which supported a molecular formula $C_{37}H_{38}N_2O_8$ and by a fragment at *m/z* 242 corresponding to the lower part of the molecule. The ^{1}H-NMR spectrum (Table 1) showed common features with compound **1**, a 3H singlet at δ 2.29 due to an *N*-methyl group, a 3H singlet at δ 3.08 attributable to a lactam *N*-methyl, and two 2H doublets at δ 6.82 and 7.13 (A_2B_2 aromatic system, J_{AB} = 8.5 Hz, H-11′, 13′ and H-10′, H-14′), and three protons belonging to a ABX aromatic system at δ 7.07 (1H, d, J = 8.3 Hz, H-13), 7.38 (1H, d, J = 1.9 Hz, H-10), and 7.60 (1H, dd, J = 8.3, 1.9 Hz, H-14). In addition, this spectrum showed a 6H singlet due to two methoxyl groups at δ 3.95 located on the C-6 and C-12 positions and an additional methoxy group at δ 3.87 located on the C-6′ position;[7] it also exhibited three 1H singlets at δ 6.50, 6.71, and 7.29 attributed to H-5′, H-5, and H-8, respectively, as in maroumine.[7]

Evidence in favor of the presence of an aldehyde function in **3** was confirmed by the existence of a deshielded signal at δ 9.78 in the ^{1}H-NMR spectrum and by an additional band at 1690 cm^{-1} in the IR spectrum. The UV spectrum of **3** presented two maxima which showed, after alkalinization, bathochromic shifts suggesting a phenolic nature for **3**; the low values of these shifts ($\Delta \leq 1$ nm) indicated that the hydroxyl group was not para to the aromatic aldehyde;[2,8] therefore, the hydroxyl group must be at the 7′-position of the benzylisoquinoline moiety. The absence of a MeO signal upfield at about δ 3.65 in the ^{1}H-NMR spectrum supported this hypothesis which was further confirmed by treatment of **3** with CH_2N_2 in Et_2O; this methylation yielded a derivative in which the signal of the fourth methoxy group was indeed observed in upfield at about δ 3.65.[2,7] On the basis of these data, a *seco*-dibenzylisoquinoline structure with a "head to head" linkage was assumed for **3**. Finally, to confirm our hypothesis, homoaromaline **4**, which was also isolated from the plant,[1] was treated with potassium permanganate in acetone. The derivative obtained was identical, by TLC and ^{1}H-NMR, with the naturally occuring alkaloid **3**.[2] Therefore, the configuration of **3** at C1′ must be 1′*S*. We named this alkaloid (−)-secohomoaromaline.

Experimental Section

General Experimental Procedures. UV spectra were recorded on a Shimadzu UV-265 FS spectrophotometer. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. EIMS and FABMS were, respectively, recorded with a VG Micromass 7070 F apparatus (70 eV) and with an AEI MS902S (glycerol as matrix). All NMR spectra were recorded at 250 MHz for ^{1}H-NMR on a Brüker WP 250 spectrometer, using TMS as internal reference. Si gel 60 (E. Merck, Darmstadt, Germany) and neutral Al_2O_3 (M. Woelm, Eschwege, Germany) were used for column chromatography, and Si gel 60 PF_{254} (E. Merck, Darmstadt, Germany, layer thickness 1.0 mm) was used for TLC. The TLC chromatograms were visualized under UV at 254 nm and/or sprayed with Dragendorff's and potassium iodoplatinate reagents.

Plant Material. Leaves of *A. jollyana* were collected in 1992 near Kivuza/Kiasi-Kole, in the province of Bas-Zaire (Zaire), and identified by Mr. Bavukinina-Ngoma and Mr. Menavanza, Institut de Recherches en Sciences de la Santé, Kinshasa, Zaire. A voucher specimen has been deposited in the Herbarium of the Institut de Recherches en Sciences de la Santé, Kinshasa, Zaire (ref no. 124).

Extraction and Isolation. Powdered dry leaves (300 g) were extracted exhaustively with MeOH (3 L) by percolation. The MeOH extract was evaporated to dryness under reduced pressure, and the residue was taken up with 5% aqueous HCl (2 × 100 mL). After filtration, the solution was extracted several times with petroleum ether (300 mL). After alkalinization with aqueous 25% NH_4OH, the aqueous phase was extracted five times with $CHCl_3$ (5 × 50 mL). The combined $CHCl_3$ extracts were washed with H_2O and dried on anhydrous Na_2SO_4 and then evaporated to dryness, yielding the alkaloidal fraction (6 g). A part of this extract (1 g) was chromatographed on a column packed with neutral Al_2O_3 with a mixture of $CHCl_3$−MeOH (4:1). The less polar tertiary bases were further separated on a Si gel column (70−200 mesh, 100 g) eluted with $CHCl_3$ containing increasing amounts of MeOH; the final purification was achieved by preparative TLC on Si gel, using the following mobile phase: $CHCl_3$−MeOH−NH_4OH 25% (38.5:1.5:0.2). This procedure allowed the isolation of two new alkaloids **1** (15 mg) and **3** (18 mg) along a known base *O*-methylpunjabine (95 mg).

(−)-Secojollyanine (1): colorless needles; UV λ max (MeOH) nm (log ϵ) 218 (4.7), 283 (3.9); $[\alpha]^{20}_D$ −8.4° (c = 2.0, $CHCl_3$); IR λ max ($CHCl_3$) cm^{-1} 1600 and 1650 (lactam); EIMS *m/z* (rel int) $[M]^+$ 365 (100), 244 (4); FABMS *m/z* [MH^+] 609 (100), 365 (90), 264 (50); ^{1}H-NMR ($CDCl_3$, 250 MHz) see Table 1.

(−)-Secohomoaromaline (3): colorless needles; UV λ max (MeOH) nm (log ϵ) 226 (4.6), 268 (4.2); UV λ max (MeOH + KOH) nm (log ϵ) 227 (4.6), 269 (4.2); $[\alpha]^{20}_D$ −5.4° (c = 5.3, $CHCl_3$); IR λ max ($CHCl_3$) cm^{-1} 1600 and 1650 (lactam), 1690 (C=O aldehyde); EIMS *m/z* (rel int) $[M]^+$ 397 (100), 242 (5); FABMS *m/z* [MH^+] 639 (100), 245 (5); ^{1}H-NMR ($CDCl_3$, 250 MHz) see Table 1.

Reduction of (−)-Secojollyanine (1). Compound **1** (7 mg) was dissolved in MeOH (10 mL), and the solution was treated with $NaBH_4$ (20 mg). The mixture was stirred for 2 h and then worked up to afford **2** (TLC, ^{1}H-NMR, MS).

Oxidation of (+)-Homoaromaline (4). Homoaromaline (**4**) (40 mg) was dissolved in 60 mL of Me_2CO, and $KMnO_4$ (100 mg) in 65 mL of Me_2CO was added dropwise over 30 min with stirring. After one night, the reaction mixture was filtered, the solvent evaporated, and the residue purified by preparative TLC to

afford 5 mg of amorphous compound identical with natural product **3**.

Methylation of 3. Compound **3** (10 mg) was dissolved in MeOH and excess CH_2N_2 in Et_2O added. The mixture was allowed to stand for 24 h. Workup afforded a compound which exhibited a fourth MeO group at δ 3.65 in the ^{1}H-NMR spectrum.

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