Koniamborine, the First Pyrano[3,2-*b*]indole Alkaloid and Other Secondary Metabolites from *Boronella koniambiensis*

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Two new alkaloids, (−)-*cis*-1,2-dihydroxy-1,2-dihydromedicosmine (**3**) and koniamborine (**4**), have been isolated from *Boronella koniambiensis* aerial parts. Their structures have been established from NMR and mass data. Koniamborine is a novel type of alkaloid, which derives from the pyrano[3,2-*b*]indole basic skeleton, described for the first time from nature. 6-Methoxy-1-methylisatin, also present in the plant material, can be considered biogenetically as a degradation product of the fused pyrone ring of **4**.

The genus *Boronella* Baill., recently revised by Hartley, includes at least four species of rutaceous trees endemic to New Caledonia. The genus differs from the related *Boronia* Smith in having branchlets with articulated cortex and embryos with elliptic or suborbicular cotyledons.[1] *B. pancheri* Baill.[2] and *B. aff. verticillata* Baill.[3] were previously studied from a chemical point of view. Both species led to the isolation of coumarins and alkaloids derived biogenetically from anthranilic acid.[2,3] In a continuation of studies on the Rutaceae from the South Pacific area,[4,5] we report here the isolation and structure elucidation of the secondary metabolites of *B. koniambiensis* (Däniker) T. Hartley.

Fifteen compounds were isolated by fractionation of the dichloromethane extract of the aerial parts of *B. koniambiensis*. Two known alkaloids were identified, the furoquinolines evolitrine, widespread in the Rutaceae family, and medicosmine (**1**), previously isolated from *Medicosma cunninghamii* Hook. f.[6,7] Known neutral products included syringaldehyde, stigmast-4-en-3-one, benzamide, hexadecanamide, scopoletin, scoparone, auraptene, *O*-geranylosthenol,[8] the lignan dehydroxycubebin isolated for the first time as its *S*,*S*-(+)-enantiomer,[9] and the limonoid rutaevin previously isolated from *Euodia rutaecarpa* Benth.[10,11] The indole derivative 6-methoxy-1-methylisatin (**2**)[12] was isolated for the first time from a natural source. We report here the structure elucidation of the two novel compounds (−)-*cis*-1,2-dihydroxy-1,2-dihydromedicosmine (**3**) and koniamborine (**4**), which is the first alkaloid in nature deriving from the pyrano[3,2-*b*]indole skeleton (Figure 1).

Compound **2** was obtained as bright orange needles, mp 196 °C. Its empirical formula was established as $C_{10}H_9NO_3$ by HREIMS. The IR and UV spectra were suggestive of an isatin derivative. This skeleton was further confirmed by the ^{13}C NMR spectrum, which displayed the signals of one conjugated carbonyl carbon and one lactamic carbonyl carbon, three protonated aromatic carbons, two quaternary aromatic carbons, one OCH_3 carbon, and one NCH_3 carbon. The ^1H NMR spectrum showed an ABX system of three aromatic protons and two singlets each integrating for three protons corresponding to one OCH_3 and one NCH_3 group. The placement of the methoxy group at position 6 of the isatin nucleus was based on chemical shifts and coupling constants of the aromatic proton signals and HMBC correlation of the OCH_3 protons with C-6 and of H-4 with C-6, C-7a, and C-3. Additionally the NCH_3 protons were correlated with C-2 and C-7a, confirming the structure of **2** as 6-methoxy-1-methylisatin. Compound **2** had been previously described as a synthetic product with identical UV spectrum[12] and melting point,[6] but without any other reported data.

Compound **3** was obtained as a colorless amorphous solid. Its empirical formula was deduced as $C_{17}H_{17}NO_5$ by HREIMS. The aromatic part of the ^1H NMR spectrum, which exhibited two pairs of doublets at 7.03 and 7.65 ppm (J = 3 Hz) and 7.24 and 7.88 ppm (J = 8 Hz), was closely related to that of medicosmine (**1**)[7] (Figure 1). At higher field, the expected three 3H singlets corresponding to the Ar-OCH_3 and the $C(CH_3)_2$ groups were also observed at 4.42, 1.49, and 1.39 ppm, respectively. Nevertheless, dramatic differences with the spectrum of medicosmine were observed for the resonances attributable to the protons of the dihydropyran ring. Indeed, a set of four signals, two of them exchangeable with D_2O, between 3.35 and 5.40 ppm was typical for the 1,2-dihydroxy-1,2-dihydropyran system previously encountered in the related pyranofuroquinoline *cis*-1,2-dihydroxy-1,2-dihydroacronydine.[13] The ^{13}C NMR and DEPT spectra of **3** were also very similar to those of medicosmine, showing seven aromatic quaternary carbons, four protonated aromatic carbons, two aliphatic oxygenated methines, one quaternary oxygenated aliphatic carbon, and one carbon corresponding to a methoxy group. The most important difference was observed for the two oxygenated methines, which in the case of medicosmine were replaced by two protonated olefinic carbons. In the HMBC spectrum (Figure 2), important correlations that indicated the similarity with the medicosmine skeleton were those of the two furan protons with the aromatic C-7a and C-10a, H-6 with C-11a and C-4a, and H-5 with C-11b and C-6a. The fusion of the pyran ring at positions 4a and 11b on the furanoquinoline skeleton, as in the case of medicosmine, was confirmed from the HMBC correlations of H-1 with C-4a, C-11a, and C-3 on one hand and of the homobenzylic H-2 with C-11b and the two methyl carbons

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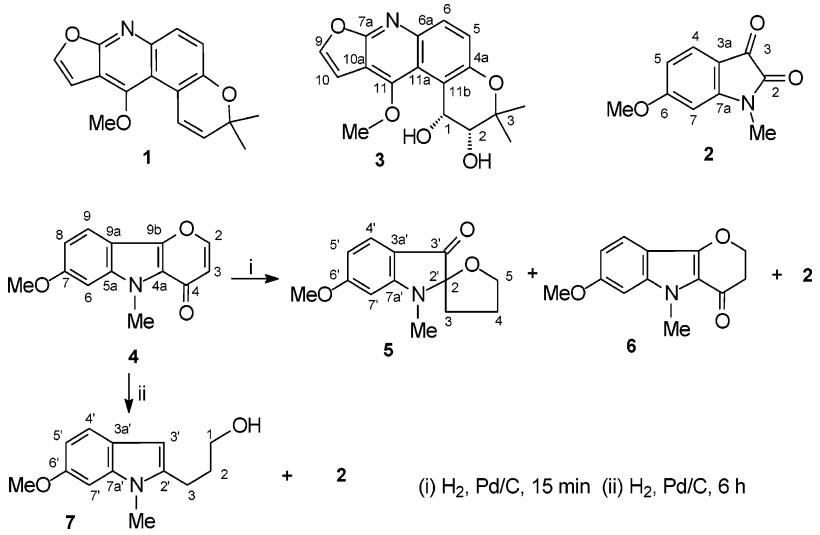

Figure 1. Structures of isolated compounds **1**−**4** and catalytic hydrogenation reactions of **4**. Compound **3** is depicted in a relative configuration.

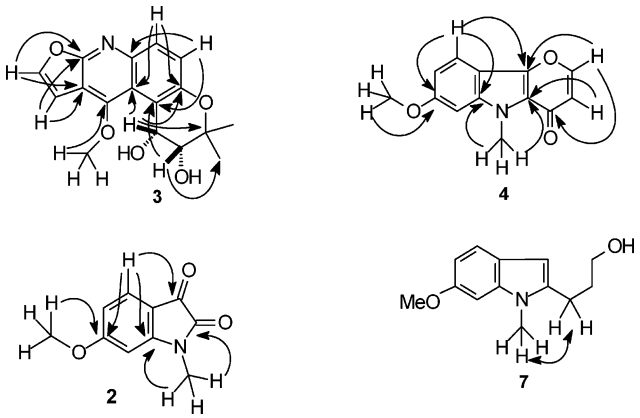

Figure 2. HMBC (→) correlations of **2**, **3**, and **4** and NOESY correlations (↔) for **7**.

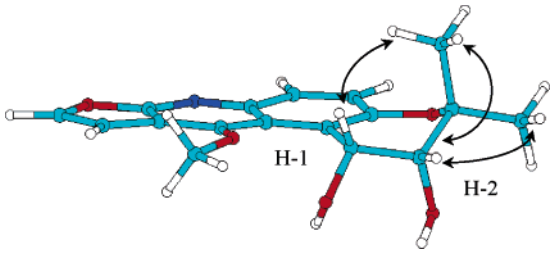

Figure 3. Lower energy conformation for compound **3** and selected NOE correlations.

on the other hand. All the above findings permitted the structure of this compound to be depicted as 1,2-dihydroxy-1,2-dihydromedicosmine. The conformational behavior and the relative configuration of the pyran ring were established using *J*-values and NOEs derived from the 2D NOESY spectrum as well as with molecular mechanics calculations. Based on the coupling constant between H-1 and H-2 (J = 5 Hz) a *trans* pseudo-diaxial conformation could be excluded. However, the *trans* pseudo-diequatorial or the *cis* configuration is compatible with this coupling constant. The clear NOE correlation (Figure 3) between H-2 and both methyls of the pyran ring and of H-1 with one of the methyls are in complete agreement with the *cis* configuration.[14] Finally, computational conformation analysis was performed using molecular mechanics calculations, and these conclusions were in good agreement with the above experimental results. First, low-energy conformations of compound **2** were generated using the Low-Mode/Monte Carlo[15] search protocol with the MM2 force field as it is implemented in the molecular modeling software Macromodel 6.5.[16] After a 5000-step search, the conformer with the lowest energy was found to adopt a conformation in which the pyran ring is half-chair and C-2 is below and C-3 is above the plane formed by the four other atoms of the D-ring. Consequently, the structure of compound **3** was determined as *cis*-1,2-dihydroxy-1,2-dihydromedicosmine. The small quantity of isolated material did not permit definition of the absolute configuration of compound **3**.

Koniamborine (**4**) was obtained as whitish needles, mp 142 °C. The molecular formula was determined as $C_{13}H_{11}NO_3$ on the basis of HREIMS analysis. The UV spectrum displayed absorptions at 242, 264, 279, and 322 nm, associated with a conjugated aromatic chromophore. A strong band at 1632 cm^{-1} in the IR spectrum was indicative of a conjugated keto group. Other characteristic bands were at 1586 (C=C) and 1231 cm^{-1} (aromatic ether). The ^1H NMR spectrum exhibited two methyl singlets at 3.89 and 4.12 ppm. Two sets of signals appeared at lower field. The first one, at 6.70 (d, J = 2 Hz), 6.83 (dd, J = 8, 2 Hz), and 7.69 (d, J = 8 Hz) ppm, accounted for a 1,2,4-trisubstituted aromatic ring. The second one was a pair of doublets at 6.32 and 7.72 ppm (J = 6 Hz), typical of the protons at C-2 and C-3 of a fused pyran-4-one subunit. The ^{13}C NMR and DEPT spectra demonstrated the presence of two methyls, five sp^2 methines, and six sp^2 quaternary carbons. Two-dimensional multiple pulse experiments permitted unambiguous assignment of the different resonances. Two signals at 30.9 and 55.3 ppm characterizing an N-CH_3 and an O-CH_3 showed HMQC correlations at δ_H 4.12 and 3.89 ppm, respectively. Of particular interest were the ^3J HMBC correlations (Figure 2) observed between (i) the N-CH_3 protons and the quaternary carbons at 123.1 (C-4a) and 138.6 ppm (C-5a), (ii) H-3 and C-4a at 123.1 ppm, (iii) H-2 and C-9b (144.8 ppm) and C-4 (170.7 ppm), and (iv) the aromatic doublet at 7.69 ppm and the quaternary carbons at 138.6 (C-5a) and 144.8 ppm (C-9b). These data determined the structure of koniamborine as 7-methoxy-5-methyl-4,5-dihydropyrano[3,2-*b*]indol-4-one (**4**). The positions of the substituents on the pyrano[3,2-*b*]indol-4-one basic core were further confirmed by the following correlations observed in the two-dimensional NOESY spectrum: H-2/H-3; 5-NMe/H-6; H-6/7-OMe; 7-OMe/H-8; H-8/H-9. In addition, the ^1H and ^{13}C NMR data of **4** were in full

agreement with those previously published for the related synthetic 5-benzyl-4,5-dihydropyrano[3,2-*b*]indol-4-one.[17]

The structure of koniamborine was further confirmed by a thorough study of its hydrogenation products. When koniamborine (**4**) was subjected to palladium-catalyzed hydrogenation for a short time (15 min), racemic spiroindolin-3-one **5**, resulting from the rearrangement of an intermediate benzylic alcohol, was obtained as major product. This compound was accompanied by two minor products, 2,3-dihydrokoniamborine (**6**), isolated in minute amounts, and 6-methoxy-1-methylisatin (**2**), arising from the loss of the substituent at position 2 of **5**. A longer reaction time (6 h) led to the fully opened 3-(6-methoxy-1-methyl-1*H*-indol-2-yl)propan-1-ol (**7**), which was also accompanied by smaller amounts of 6-methoxy-1-methylisatin (**2**).

The empirical formula of **5** was determined as $C_{13}H_{15}NO_3$ by HREIMS analysis. The set of aromatic signals observed in the ^{1}H NMR spectrum, comprising a doublet (J = 8 Hz) at 7.48 ppm, a double doublet (J = 8, 2 Hz) at 6.29 ppm, and a doublet (J = 2 Hz) at 6.07 ppm, was typical for a 6-methoxyindolin-3-one.[18] Two methyl singlets at 3.88 and 2.89 ppm accounted for an aromatic methoxy and an N-CH_3 group, respectively. The important shielding of the latter, compared to the corresponding resonance of **4**, provided additional evidence for the lack of the 2,3-double bond. Finally, a series of three *gem*-coupled methylene signals, at 4.20 and 4.13, 2.31 and 2.12, and 2.22 and 2.03 ppm, indicated the presence of a 2,2-disubstituted tetrahydrofuran unit. Thus, the structure of **5** was established as 6′-methoxy-1′-methyl-4,5-dihydro-3*H*-spiro-[furan-2,2′-indol]-3′(1′*H*)-one.

The empirical formula of **6** was determined as $C_{13}H_{13}NO_3$ by HREIMS analysis. The ^{1}H NMR spectrum of **6** was very similar to that of **4**. The only major difference was observed in the signals attributable to the protons at C-2 and C-3, which appeared as two proton triplets (J = 6.5 Hz) at 4.62 and 2.75 ppm, respectively. Consequently, the structure of compound **6** was determined as 7-methoxy-5-methyl-2,3-dihydropyrano[3,2-*b*]indol-4(5*H*)-one.

The molecular formula of **7** was determined by HREIMS as $C_{13}H_{17}NO_2$. The ^{1}H NMR spectrum displayed typical aromatic and methyl signals associated with a 2-substituted 6-methoxy-1-methyl-1*H*-indole.[19] Signals corresponding to a hydroxypropyl chain appeared as a quintet and two triplets, each integrating for 2H, at 2.01, 2.86, and 3.80 ppm, respectively. A strong ^3J HMBC correlation between the triplet at 2.86 ppm and the typical signal of C-3 at 98.7 ppm on one hand and a NOESY correlation of the same triplet with the N-Me singlet, on the other hand, confirmed the position of attachement of the side chain at C-2′. Therefore, the structure of 3-(6-methoxy-1-methyl-1*H*-indol-2-yl)propan-1-ol was attributed to **7**.

The structures of **5** and **7**, with a three-carbon unit attached at the carbon α to the nitrogen, unambiguously confirm the mode of fusion of the pyrone ring onto the indole nucleus in the novel natural alkaloid and consequently the pyrano[3,2-*b*]indole basic core of koniamborine (**4**).

The biosynthesis of the pyrano[3,2-*b*]indol-4-one skeleton of koniamborine, described here for the first time from nature, most probably involves condensation of an anthranilic acid unit, which gives rise to the indole moiety of the alkaloid, with acetyl units, leading to the fused pyrone system. In agreement with this hypothesis, anthranilate and acetate have been previously demonstrated to be the precursors of several series of alkaloids typical to rutaceous plants, exemplified by quinolones and acridones.[20] Interestingly, anthranilic acid is also directly implied in the biogenetic origin of other indole derivatives containing a single nitrogen atom present in Rutaceae, such as the carbazole and pyranocarbazole alkaloids encountered in *Murraya* L., *Glycosmis* Correa, and *Clausena* Burm. f. species.[21] The simultaneous isolation of koniamborine (**4**) and 6-methoxy-1-methylisatin (**2**) from *Boronella koniambiensis* should also be emphasized, since the latter compound can be considered to arise biogenetically from the degradation of the fused pyrone ring of **4**.

The novel alkaloid koniamborine (**4**) as well as the major metabolites medicosmine, (+)-dehydroxycubebin, and *O*-geranylosthenol were evaluated for their cytotoxic activity against the L1210 cancer cell line and showed IC_{50} at 38.2, 48.0, 72.1, and 15.7 μM, respectively.

From a chemotaxonomic point of view, the isolation from *B. koniambiensis* of the rare pyranofuroquinoline alkaloid medicosmine and the limonoid rutaevin, which had been previously isolated from *Medicosma* J. D. Hook. and *Euodia* J. R. & G. Forst. species, respectively, is particularly interesting. Indeed, the genus *Boronella* is currently considered to belong to a lineage otherwise comprised of *Myrtopsis* Engl., *Euodia*, *Brombya* F. Muell., and *Medicosma*.[1]

Experimental Section

General Experimental Procedures. Optical rotations were measured with a Perkin-Elmer 341 polarimeter. UV spectra were recorded on a Shimadzu-160A spectrophotometer. The IR spectra were obtained on a Perkin-Elmer Paragon 500 instrument. NMR spectra were recorded on Bruker DRX 400 and Bruker AC 200 spectrometers [^{1}H (400 MHz) and ^{13}C (50 MHz)]; chemical shifts are expressed in ppm downfield to TMS. The 2D NMR experiments were performed using standard Bruker microprograms. EIMS were determined on a HP-6890 spectrometer, FABMS were obtained using a ZAB HF instrument, and HREIMS and HRFABMS were obtained on a AEI MS-902 mass spectrometer. Liquid chromatography was performed on columns containing Si gel 60 Merck (40−63 μm).

Plant Material. Aerial parts of *B. koniambiensis* were collected on August 10, 1999, in Koniambo Mountains, New Caledonia. A voucher sample (LIT 0907) is retained in the Herbarium of the Centre IRD of Nouméa, New Caledonia. The plant material was identified by one of the authors (M.L.).

Extraction and Isolation. Dried pulverized aerial parts of *B. koniambiensis* (1.5 kg) were extracted by percolation with CH_2Cl_2 (3 × 2 L). The solvent was removed under reduced pressure to give a crude extract (24.6 g). An aliquot (5.5 g) was subjected to silica gel liquid vacuum chromatography, using a stepwise gradient elution of EtOAc in cyclohexane, collecting 300 mL fractions. Fractions of similar composition were pooled on the basis of TLC analysis. Further purifications by column chromatography on silica gel 20−45 μm performed with cyclohexane/CH_2Cl_2/MeOH mixtures of increasing polarity yielded successively rutaevin (25 mg), *O*-geranylosthenol (32 mg), *S*,*S*-(+)-dehydroxycubebin (235 mg), stigmast-4-en-3-one (12 mg), auraptene (20 mg), 6-methoxy-1-methylisatin (17 mg), medicosmine (600 mg), scoparone (5 mg), scopoletin (5 mg), evolitrine (10 mg), syringaldehyde (8 mg), koniamborine (550 mg), (−)-*cis*-1,2-dihydroxy-1,2-dihydromedicosmine (3 mg), benzamide (5 mg), and hexadecanamide (7 mg).

Medicosmine (1): colorless needles; UV, IR, MS, and ^{1}H NMR identical with the data previously published;[6,7] ^{13}C NMR ($CDCl_3$) δ 27.1 (2 × CH_3), 59.3 (OCH_3), 74.4 (C-3), 104.3 (C-10), 105.2 (C-10a), 114.1 (C-11b), 115.2 (C-11a), 122.3 (C-5), 122.6 (C-1), 127.1 (C-2), 129.2 (C-6), 142.4 (C-6a), 143.5 (C-9), 150.6 (C-4a), 158.0 (C-11), 161.8 (C-7a).

6-Methoxy-1-methylisatin (2): bright orange needles (cyclohexane/EtOAc), mp 196 °C (lit.[6] 195−197 °C); UV identical with the data previously published;[12] IR ($CHCl_3$) ν_{max} 3023,

2940, 1740, 1623, 1506, 1463, 1377, 1259, 1178, 1099, 848, 836 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.19 (3H, s, NCH_3), 3.90 (3H, s, OCH_3), 6.35 (1H, d, J = 2 Hz, H-7), 6.54 (1H, dd, J = 8, 2 Hz, H-5), 7.57 (1H, d, J = 8 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 26.1 (N*C*H_3), 56.1 (O*C*H_3), 97.1 (C-7), 107.9 (C-5), 111.0 (C-3a), 127.8 (C-4), 154.0 (C-7a), 159.6 (C-2), 168.3 (C-6), 180.6 (C-3); EIMS *m/z* 191 $[M]^+$, 163, 135, 134; HREIMS *m/z* 191.0584 (calcd for $C_{10}H_9NO_3$, 191.0582).

(−)-*cis*-1,2-Dihydroxy-1,2-dihydromedicosmine (3): amorphous solid; $[\alpha]_D$ −5° ($CHCl_3$, *c* 0.1). UV (MeOH) λ_{max} 245, 300, 312, 342, 357 nm; IR ($CHCl_3$) ν_{max} 3619, 3019, 1581, 1516, 1211, 1048, 734, 669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (3H, s, C−CH_3), 1.49 (3H, s, C−CH_3), 3.35 (1H, d, D_2O exch., J = 9 Hz, O*H*-2), 3.77 (1H, d, D_2O exch., J = 3 Hz, O*H*-1), 3.90 (1H, dd, J = 9, 5 Hz, H-2), 4.42 (3H, s, O−CH_3), 5.40 (1H, dd, J = 5,3 Hz, H-1), 7.03 (1H, d, J = 3 Hz, H-10), 7.24 (1H, d, J = 8 Hz, H-5), 7.65 (1H, d, J = 3 Hz, H-9), 7.88 (1H, d, J = 8 Hz, H-6); ^{13}C NMR ($CDCl_3$) δ 20.1 (*C*H_3), 26.3 (*C*H_3), 61.5 (O*C*H_3), 63.4 (C-1), 73.1 (C-2), 77.5 (C-3), 104.0 (C-10), 106.1 (C-10a), 115.4 (C-11b), 119.3 (C-11a), 124.2 (C-5), 130.8 (C-6), 144.1 (C-9), 145.5 (C-6a), 150.6 (C-4a), 157.2 (C-11), 162.3 (C-7a); EIMS *m/z* 315 $[M]^+$, 297, 282, 269, 254, 239, 228, 222, 212; HRFABMS *m/z* 316.1183 (calcd for $[C_{17}H_{17}NO_5 + H]^+$, 316.1185).

Koniamborine (4): whitish needles (cyclohexane/EtOAc); mp 142 °C; UV (MeOH) λ_{max} (log ϵ) 242 (3.83), 264 (3.96), 279 (3.83), 322 (4.21) nm; IR ($CHCl_3$) ν_{max} 3009, 2938, 1632, 1586, 1569, 1453, 1359, 1284, 1231, 1135, 947, 816 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.89 (3H, s, O−CH_3), 4.12 (3H, s, N−CH_3), 6.32 (1H, d, J = 6 Hz, H-3), 6.70 (1H, d, J = 2 Hz, H-6), 6.83 (1H, dd, J = 8, 2 Hz, H-8), 7.69 (1H, d, J = 8 Hz, H-9), 7.72 (1H, d, J = 6 Hz, H-2); ^{13}C NMR ($CDCl_3$) δ 30.9 (N−*C*H_3), 55.3 (O−*C*H_3), 91.3 (C-6), 108.6 (C-9a), 111.6 (C-8), 115.0 (C-3), 120.1 (C-9), 123.1 (C-4a), 138.6 (C-5a), 144.8 (C-9b), 151.3 (C-2), 160.3 (C-7), 170.7 (C-4); EIMS *m/z* 229 $[M]^+$, 228, 214, 186, 185; HREIMS *m/z* 229.0733 (calcd for $C_{13}H_{11}NO_3$, 229.0739).

Catalytic Hydrogenation of Koniamborine. (a) To a solution of **4** (20 mg, 0.09 mmol) in MeOH (2 mL) was added 10% Pd/C (10 mg). The suspension was stirred under H_2 (1 atm) for 15 min at room temperature. The mixture was filtered through Celite and evaporated under reduced pressure. Flash chromatography (cyclohexane/Me_2CO, 4:1 v/v) afforded successively 6′-methoxy-1′-methyl-4,5-dihydro-3*H*-spiro[furan-2,2′-indol]-3′(1′*H*)-one (**5**) (9.5 mg, 47%), 2,3-dihydrokoniamborine (**6**) (1.0 mg, 10%), and 6-methoxy-1-methylisatin (**2**) (3.0 mg, 18%). (b) A similar experiment was performed for 6 h at room temperature. After the usual workup, flash chromatography (cyclohexane/Me_2CO, 3:2 v/v) gave successively 6-methoxy-1-methylisatin (**2**) (2.5 mg, 15%) and 3-(6-methoxy-1-methyl-1*H*-indol-2-yl)propan-1-ol (**7**) (8 mg, 42%).

6′-Methoxy-1′-methyl-4,5-dihydro-3*H*-spiro[furan-2,2′-indol]-3′(1′*H*)-one (5): amorphous solid; ^1H NMR ($CDCl_3$) δ 2.03 (1H, ddd, J = 13, 7, 4 Hz, H-3a), 2.12 (1H, m, H-4a), 2.22 (1H, ddd, J = 13, 8, 4.5 Hz, H-3b), 2.31 (1H, m, H-4b), 2.89 (3H, s, N−CH_3), 3.88 (3H, s, O−CH_3), 4.13 (1H, ddd, J = 14, 7.5, 1 Hz, H-5a), 4.20 (1H, ddd, J = 14, 6, 3 Hz, H-5b), 6.07 (1H, d, J = 2 Hz, H-7′), 6.29 (1H, dd, J = 8, 2 Hz, H-5′), 7.48 (1H, d, J = 8 Hz, H-4′); EIMS *m/z* 233 $[M]^+$, 205, 204, 177, 176; HREIMS *m/z* 233.1051 (calcd for $C_{13}H_{15}NO_3$, 233.1052).

2,3-Dihydrokoniamborine (6): amorphous solid; ^1H NMR ($CDCl_3$) δ 2.75 (2H, t, J = 6.5 Hz, CH_2-3), 3.92 (3H, s, O−CH_3), 3.97 (3H, s, N−CH_3), 4.62 (2H, t, J = 6.5 Hz, CH_2-2), 6.60 (1H, d, J = 2 Hz, H-6), 6.75 (1H, dd, J = 8, 2 Hz, H-8), 7.56 (1H, d, J = 8 Hz, H-9); EIMS *m/z* 231 $[M]^+$, 215, 188, 187; HREIMS *m/z* 231.0892 (cacld for $C_{13}H_{13}NO_3$, 231.0895).

3-(6-Methoxy-1-methyl-1*H*-indol-2-yl)propan-1-ol (7): amorphous solid; ^1H NMR ($CDCl_3$) δ 2.01 (2H, quintet, J = 7 Hz, CH_2-2), 2.86 (2H, t, J = 7 Hz, CH_2-3), 3.65 (3H, s, N−CH_3), 3.80 (2H, t, J = 7 Hz, CH_2-1), 3.89 (3H, s, O−CH_3), 6.22 (1H, s, H-3′), 6.77 (1H, dd, J = 8, 2 Hz, H-5′), 6.78 (1H, d, J = 2 Hz, H-7′), 7.43 (1H, d, J = 8 Hz, H-4′); ^{13}C NMR ($CDCl_3$) δ 23.3 (C-3), 29.1 (N−*C*H_3), 31.6 (C-2), 55.3 (O−*C*H_3), 62.5 (C-1), 93.3 (C-7′), 98.7 (C-3′), 109.1 (C-5′), 120.4 (C-4′), 122.1 (C-3′a), 138.8 (C-7′a), 139.7 (C-2′), 155.9 (C-6′); EIMS *m/z* 219 $[M]^+$, 186, 175, 174; HREIMS *m/z* 219.1264 (cacld for $C_{13}H_{17}NO_2$, 219.1259).

Molecular Mechanics Calculations. All calculations were performed on a R5000 Silicon Graphics workstation. For the molecular mechanics calculations the MM2 force field was used as it is implemented in the Macromodel 6.5 program.[15] The Truncated Conjugate Gradient (TNCG) minimization method with an energy convergence criterion of 0.01 kcal mol^{-1} was also used for geometry optimization.

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