Pergamon

PII: S0031-9422(96)00362-7

Phytochemistry, Vol. 43, No. 4, pp. 897–902, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0031-9422/96 $15.00 + 0.00

ALKALOIDS FROM ROOT BARK OF *STRYCHNOS PANGANENSIS*

JEAN-MARC NUZILLARD, PHILIPPE THÉPENIER, MARIE-JOSÉ JACQUIER, GEORGES MASSIOT, LOUISETTE LE MEN-OLIVIER* and CLÉMENT DELAUDE†

Faculté de Pharmacie (U.R.A. au C.N.R.S. no. 492) 51, rue Cognacq Jay, 51096 Reims Cedex, France;
†Institut de Chimie-B_6, Université de Liège, Sart Tilman, Belgium

(*Received* 11 *April* 1996)

Key Word Index—*Strychnos panganensis*; Loganiaceae; root bark; indole alkaloids; NMR.

Abstract—Twelve alkaloids, seven of which are new, have been isolated from the root bark of *Strychnos panganensis* collected in Tanzania. The known alkaloids are matopensine, 16-(*S*)-*E*-isositsirikine, 12-hydroxy-11-methoxydiaboline, *N*-desacetylretuline and *N*-desacetylisoretuline. The novel alkaloids are *N*-desacetylspermostrychnine, 12-hydroxy-11-methoxy-nor-*C*-fluorocurarine, 12-hydroxy-11-methoxy-*N*-acetylmon-*C*-fluorocurarimine and four dimeric alkaloids, panganensines R, S, X and Y. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Strychnos panganensis Gilg is an African species growing in east Africa (Kenya, Tanzania and Mozambique) and at the northernmost point of Madagascar. It is a scandent or scrambling shrub or liane found in lowland rain forests, gallery forests or thickets in coastal evergreen bushland. It is used in traditional medicine, internally for chest complaints [1]. The leaves have been screened for alkaloids [2] but only traces were found. There is no other phytochemical or pharmacological information on this species available in the literature. For this reason, as part of our chemotaxonomic study of *Strychnos* species from the African continent, we report herein our results on the alkaloid content of the root bark of *S. panganensis*.

RESULTS AND DISCUSSION

Alkaloids were extracted in the usual fashion; 780 g of powdered roots bark yielded 6.6 g of crude alkaloid mixture (8.5 g kg^{-1}), which was purified by medium pressure liquid chromatography and TLC. From this mixture, 12 alkaloids were separated. They are, in order of elution from silica gel: matopensine (**1**) (2.6% of alkaloids), 16-(*S*)-*E*-isositsirikine (**2**) (0.2%), panganensine R (**3**) (0.3%), panganensine S (**4**) (3%), 12-hydroxy-11-methoxy-*N*-acetyl-nor-C-fluorocurarimine (**5**) (2.2%), 12-hydroxy-11-methoxy-nor-C-fluorocurarine (**6**) (1.2%), *N*-desacetylisoretuline (**7**) (24%), *N*-desacetylspermostrychnine (**8**) (0.6%), 12-hydroxy-11-methoxydiaboline (**9**) (0.3%), *N*-desacetylretuline (**10**) (1%), panganensine X (**11**) (0.5%) and panganensine Y (**12**) (0.7%). Alkaloids **1**, **2**, **7**, **9** and **10** were identified by direct comparison with compounds previously isolated in our laboratory from *Strychnos* species and kept in our collections [3–6].

The UV and IR spectra of compound **6**, are similar to those of nor-C-fluorocurarine [7]. M_r (*m/z* 338) was determined by mass spectrometry; the $[M]^+$ analysed for $C_{20}H_{22}N_2O_3$ (measured 338.1629; calculated 338.1630). This formula is in agreement with a nor-C-fluorocurarine augmented by a methoxyl group and an oxygen atom. The ^1H NMR spectrum of **6** is superimposable on that of nor-C-fluorocurarine except in the aromatic region where only two protons appear at δ 6.79 and 6.54 as an AB system ($J = 7.9$ Hz). Proton H-9 was identified through its coupling with C-7 (HMBC). The other aromatic proton is thus H-10. Quaternary carbons C-11 and C-12 were identified by their coupling with H-9 and H-10, respectively. Moreover, C-11 is coupled with the aromatic methoxyl protons (δ 3.85). These data suggest that **6** is 12-hydroxy-11-methoxy-nor-C-fluorocurarine. The carbon chemical shifts of the indole nucleus are in agreement with those reported for 12-hydroxy-11-methoxydiaboline from *S. staudtii* [6].

Compound **5** displayed non-characteristic UV and IR spectra. Its structure was established by means of its mass and NMR spectra and by comparison with those of **6**. In the mass spectrum, the $[M]^+$ (100%) at *m/z* 379 analysed for $C_{22}N_{25}N_3O_3$ (measured 379.1892, calculated 379.1896). The peak at *m/z* 121 is typical of an akuammicine skeleton [8]. Analysis of COSY, HMQC and HMBC data allowed us to delineate in **5** most of the structure of **6**, especially for the aromatic part. The doublet at δ 7.45 was identified as H-17 by its

---

*Author to whom correspondence should be addressed.

coupling with C-2 and C-15 (HMBC); the chemical shift is not compatible with an aldehyde group. Its proton-coupling partner ($J = 8.8$ Hz) is a doublet at δ 11.5, which is not directly bound to a carbon atom, as shown by the HMQC map. Therefore, it must be an imino proton. This is confirmed by the shift of C-17 (δ 130.3) compared with its counterpart in **6** (δ 187.9). The additional methyl group at δ 2.25 (^{1}H) and δ 23.9 (^{13}C) is part of an acetyl group (C=O at δ 168.8). The latter is bound to N_a, as inferred from the lack of an NH signal. The chromophore of a vinylogous amidine is rare and, to the best of our knowledge, has not been encountered in an open-chain situation.

Compound **8** is a new compound whose structure was determined by comparison of its spectra with those of spermostrychnine [9]. The mass spectra of both compounds displayed the same ions for the piperidine par (*m/z* 166) and for the desacylated indole nucleus (*m/z* 130 and 144); differences were observed between the $[M]^+$ (*m/z* 296 vs. *m/z* 338) and on the presence of desacylated fragments (*m/z* 199 vs. *m/z* 241). The UV spectrum of **8** shows the characteristic absorptions of an indoline chromophore and its IR spectrum lacks an amide carbonyl resonance at 1650 cm^{-1}. Moreover, its ^{1}H NMR spectrum does not exhibit any methyl resonance at δ 2.4. The structure was confirmed by acetylation of **8** into a compound identical (TLC and UV, ^{1}H NMR and mass spectrum) with spermostrychnine.

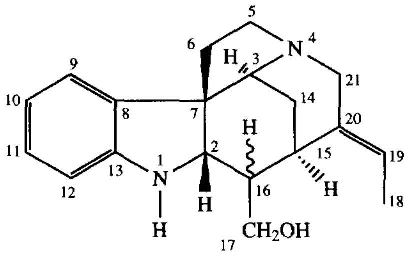
Compounds **3**, **4**, **11** and **12** are dimeric alkaloids. Examination of their ^{13}C NMR spectra shows that all of these molecules possess 38 carbon atoms. Their UV spectra are characteristic of an indoline chromophore. ^{1}H and ^{13}C analyses, including 2D COSY, HMBC and HMQC data, indicate that they are formed by attachment of two strychnane sub-units. One of the sub-units has an unusual oxidation pattern characterized by a C_{20}–C_{21} double bond, as revealed by the presence of a singlet H-21 olefinic signal in the ^{1}H NMR spectrum. The absolute configurations of the asymmetric centres at C-2, C-3, C-7 and C-15 are assumed to be identical to those in strychnane-type alkaloids. The relative configuration at C-2 and C-16 was deduced from the value of the coupling constant between H-2 and H-16. Its value is close to 6 Hz in *N*-desacetylretuline (16*S*) and close to 9.5 Hz in *N*-desacetylisoretuline (16*R*) [10].

Compounds **3** and **4** exhibit almost identical spectral features. Their molecular formula was established as $C_{38}H_{44}N_4O_2$ by HR mass spectrometry (measured 588.3491 and 588.3475; calculated 588.3464). The mass spectra displayed the ions for the indole nucleus (*m/z* 130 and 144) and an important ion at *m/z* 294. The occurrence of a cyclic ether was supported by the $H_{17'}$–$C_{19'}$ HMBC correlation. The corresponding monomer, **8**, is also present in the title plant. From analysis of the ^{1}H NMR spectrum the other monomeric unit was shown to be **7**, also found in the plant. The linkage between the sub-units is situated between C-18 and C-21′. This is supported by long-range couplings between C-19 and H-21′ and C-20′ and H-18. The geometry of the C_{18}–C_{19} double bond is *trans*, as proved by the high value of the vicinal coupling constant (15.4 Hz). Protons H-20′ and H-21′ in **3** are both axial, as revealed by their vicinal coupling constant (*ca* 10 Hz). Identical coupling constants were evaluated in **4** from traces in the HMQC spectrum; therefore, the *N*-desacetylisoretuline unit is equatorial. The only differences between panganensines R and S lies in the absolute configuration at C-19′. In panganensines R, (19′-[*R*]), the ROESY spectrum shows a correlation between H-21′ and H-18′, thus providing that H-19′ is α. Conversely, in panganensine S, (19′-[*S*]), a ROESY correlation is observed between H-21′ and H-19′.

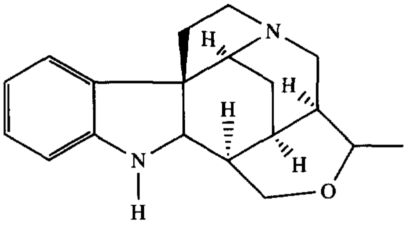
Compounds **11** and **12** correspond with the molecular formula $C_{38}H_{46}N_4O_2$, as derived from their HR mass spectra (measured 590.3633 and 590.3590; calculated 590.3620). The spectra displayed characteristic ions from *N*-desacetylretuline for the piperidine part (*m/z* 166) and for the indole nucleus (*m/z* 130 and 144). Their C_{20}–C_{21} double bonds occur within a *N*-desacetylretuline unit (H-2; *d*, *J ca* 6.5 Hz). The H-2′ proton signals are superimposed on other signals and their analysis was carried out on HMQC traces. They were determined as doublets with *J ca* 9 Hz, in agreement with the desacetylisoretuline unit type. The linkage between the units is situated between C-19 and C-10′. This is indicated by long-range couplings between C-19 and H-9′, C-19 and H-11′, C-10′ and H-19, and C-10′ and H-18. Panganensines X and Y correspond with the two possible configurations at C-19. However, it has not been possible to assign them for each molecule.

Apart from the ubiquitous sitsirikine, all the alkaloids of *S. panganensis* are of the retuline-diaboline type. The Wieland–Gumlich aldehyde is missing from the list, but its dimeric form, matopensine, is present as the sole dimeric alkaloid with a centrosymmetrical carbon skeleton. The four dimeric alkaloids were at one time thought to be elaborated forms of the matopensines; formulae of this type could certainly have been published for these compounds without the detailed analyses allowed by HMBC and HMQC experiments. Carbon by carbon examination of these alkaloids showed the presence of extra C–C bonds on C-21, ruling out matopensine-type structures. Oxidation of C-21 may occur at a late biosynthetic stage at the *N*-oxide level or early in a cathenamine-like environment. The formation of bonds between C-21′ and C-18, on the one hand, and C-19 and C-10′, on the other, does not break any fundamental rule of alkaloid organic chemistry.

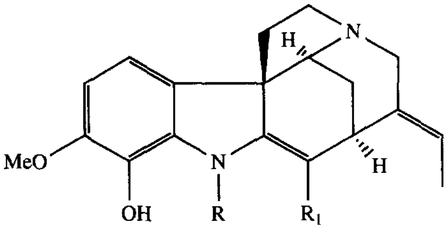
The isolation of **5**, a vinylogous amidine, remains an isolated and mysterious case. Our laboratory has displaced alkaloids from their salts with ammonia (the 'usual technique of extraction') for many years and never been able to isolate such compounds of reaction of ammonia with carbonyl groups. The case of **5** is special because the starting functionality is not a vinylogous amide, as in nor-*C*-fluorocurarine. The presence of an N_a-acetyl group presumably enhances the reactivity of the aldehyde part of the molecule. The stability of **5** is, however, surprising, as it exists solely in the *E*-form.



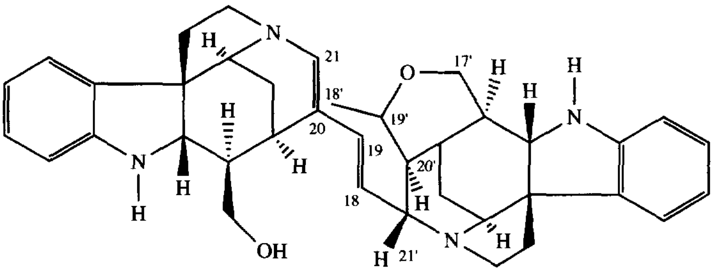
7 16aH
10 16bH



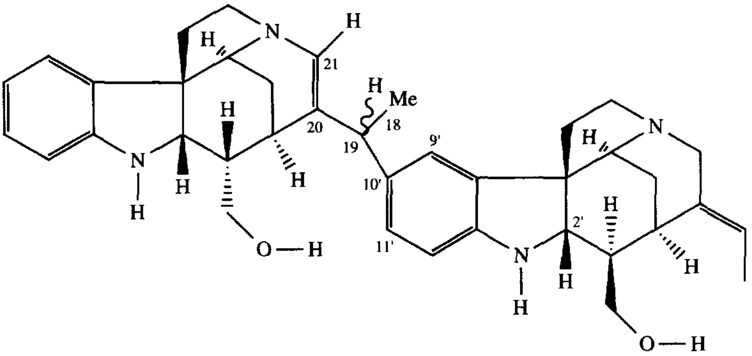
8



	R	R_1
6	H	$-\mathrm{C}\genfrac{}{}{0pt}{}{\nearrow\mathrm{O}}{\searrow\mathrm{H}}$
5	Ac	$-\mathrm{C}\genfrac{}{}{0pt}{}{\nearrow\mathrm{NH}}{\searrow\mathrm{H}}$



3, 4



11, 12

EXPERIMENTAL

General. Plant material was collected in Tanzania at Dar es Salam, near the University. A Herbarium specimen is deposited in the Brussels National Botanical garden under ref. HB 5533. ^1H and ^{13}C NMR were recorded at 300 and 75 MHz, respectively.

Extraction and separation. Dried powdered root bark (780 g) was wetted with 470 ml NH_4OH half diluted in H_2O and lixiviated with 20 l EtOAc. The organic soln was extracted with 2% H_2SO_4 and the resulting acidic soln basified with NH_4OH and extracted with $CHCl_3$. The extract was dried (Na_2SO_4) and evapd to dryness under red. pres. to yield 6.6 g crude alkaloid mixt. The alkaloid mixt. (6.6 g) was fractionated on Merck silica gel H-60 (900 g) (elution pressure 10 bar) with $CHCl_3$–MeOH mixts of increasing polarity obtained through a gradient generator. After 1.5 l dead vol., 25 ml frs were collected (500 frs) and the column was washed with 8 l MeOH. Compound **1** was in frs 127–169, **2** and **3** were in frs 127–145, **4** in frs 132–162, **6** and **5** in frs 163–199 (this last compound was also in frs 150–500 and in the MeOH residue) and the major alkaloid, **7**, in frs 266–500 and in the MeOH residue. Compounds **8**, **9**, **10**, **11** and **12** were in the MeOH residue and were isolated by prep. TLC (Whatman PK6 F254) with $CHCl_3$–MeOH–NH_4OH (90:9:1).

12-*Hydroxy*-11-*methoxy-nor*-C-*fluorocurarine* (**6**). Grey–yellow Ce^{4+} reaction. $[\alpha]_D = -688°$ ($CHCl_3$; *c* 0.47). UV λ_{max}^{MeOH} nm: 213, 240, 267, 372. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3296, 3003, 1636, 1549, 1505, 1464, 1370, 1267, 1153, 1080, 754. MS *m/z* (rel. int.): 338.1629 $([M]^+$, (85), calc. for $C_{20}H_{22}N_2O_3$: 338.1630), 323 (28), 309 (14), 295 (18), 282 (10), 268 (26), 252 (8), 240 (10), 218 (20), 202 (8), 169 (9), 149 (12), 121 (100), 106 (12), 82 (34), 69 (24). ^1H NMR: δ 10.8 (1H, *s*), 9.3 (1H, *s*), 6.79 (1H, *d*, $J = 7.9$ Hz, H-9), 6.54 (1H, *d*, $J = 7.9$ Hz, H-10), 5.42 (1H, *q*, $J = 7.4$ Hz, H-19), 4.10 (1H. *br s*, H-3), 4.01 (1H, *br d*, $J = 16.7$ Hz, H-21), 3.85 (3H, *s*, Ar-OMe), 3.7 (1H, *br s*, H-15), 3.33 (1H, *dt*, $J = 4.4$, 11.9 Hz, H-5), 3.06 (1H, *dd*, $J = 6.6$, 12.3 Hz, H-5), 2.95 (1H, *d*, $J = 15.8$ Hz, H-21), 2.58 (1H, *dt*, $J = 1.7$, 13.6 Hz, H-14′), 2.42 (1H, *dt*, $J = 6.5$, 12.3 Hz, H-6′), 1.83 (1H, *dt*, $J = 5.3$, 12.3 Hz, H-6), 1.31 (1H, *dt*, $J = 2.2$, 14.1 Hz, H-14). ^{13}C NMR: δ 187.9 (C-17), 170.5 (C-2), 148.0 (C-11), 139.1 (C-20), 132.2 (C-12), 131.0 (C-8), 129.9 (C-13), 121.1 (C-19), 111.5 (C-16), 110.9 (C-9), 105.6 (C-10), 62.0 (C-3), 58.7 (C-7), 57.0 (C-21), 56.5 (OMe), 55.9 (C-5), 45.9 (C-6), 31.5 (C-15), 30.3 (C-14), 13.2 (C-18).

12-*Hydroxy*-11-*methoxy*-N-*acetyl-nor*-C-*fluorocurarimine* (**5**). Yellow Ce^{4+} reaction. $[\alpha]_D = -478°$ ($CHCl_3$; *c* 0.65). UV λ_{max}^{MeOH} nm: 217, 243, 264, 353. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3013, 1695, 1628, 1496, 1253, 1082, 756. MS *m/z* (rel. int.): 379.1892 $([M]^+$ (100), calc. for $C_{22}H_{25}N_3O_3$: 379.1896), 364 (22), 336 (9), 320 (14), 305 (23), 293 (9), 277 (16), 265 (16), 252 (7), 236 (9), 190 (15), 164 (36), 149 (27), 121 (40), 109 (32), 97 (38), 83 (47), 69 (76). ^1H NMR: δ 11.5 (1H, *br d*, N-H), 7.45 (1H, *d*, $J = 8.8$ Hz, H-17), 6.83 (1H, *d*, $J = 8.0$ Hz, H-9), 6.68 (1H, *d*, $J = 8.0$ Hz, H-10), 5.55 (1H, *br q*, $J = 7.0$ Hz, H-19), 4.05 (1H, *br s*, H-3), 3.98 (1H, *dq*, $J = 15.8$, 1.7 Hz, H-21), 3.9 (3H, *s*, OMe), 3.6 (1H, *br s*, H-15), 3.4, (1H, *dt*, $J = 5.1$, 12.7 Hz, H-5), 3.2 (1H, *dd*, $J = 6.2$, 12.3 Hz, H-5′), 3.0 (1H, *dd*, $J = 15.8$, 2.1 Hz, H-21′), 2.55 (1H, *dt*, $J = 6.4$, 12.6 Hz, H-6), 2.45 (1H, *ddd*, $J = 2.3$, 4.1, 14.1 Hz, H-14), 2.25 (3H, *s*, Ac), 1.7 (1H, *br d*, $J = 7.0$ Hz, H-18), 1.5 (1H, *dd*, $J = 5.0$, 12.1 Hz, H-6′), 1.35 (1H, *dt*, $J = 13.9$ Hz, H-14). ^{13}C NMR: δ 184.1 (C-2), 168.8 (CO), 147.4 (C-11), 140.3 (C-13), 139.2 (C-20), 139.2 (C-8), 137.6 (C-12), 130.3 (C-17), 122.5 (C-19), 113.9 (C-16), 110.7 (C-9), 108.1 (C-10), 64.2 (C-7), 62.8 (C-3), 58.0 (C-5), 57.3 (C-21), 56.6 (OMe), 41.6 (C-6), 35.7 (C-15), 29.3 (C-14), 23.9 [Me(Ac)], 13.8 (C-18).

N-*Desacetylspermostrychnine* (**8**). Yellow–orange Ce^{4+} reaction. $[\alpha]_D = -120°$ ($CHCl_3$; *c* 0.48). UV λ_{max}^{MeOH} nm: 210, 245, 301. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3298, 1606, 1485, 1248, 1103, 752. MS *m/z* (rel. int.): 296.1891 $[M]^+$ (70), calc. for $C_{19}H_{24}N_2O$: 296.1888), 281 (5), 199 (47), 166 (100), 154 (16), 144 (46), 130 (27), 122 (27), 70 (50). ^1H NMR: δ 7.1 (2H, *m*, H-9, H-11), 6.8 (1H, *t*, $J = 8$ Hz, H-10), 6.6 (1H, *d*, $J = 8$ Hz, H-12), 3.9 (1H, *d*, $J = 11.2$ Hz, H-17), 3.7 (1H, *d*, $J = 9$ Hz, H-2), 3.6 (1H, *dd*, $J = 11.2$, 2 Hz, H-17′), 3.55 (1H, *dq*, $J = 3$, 7 Hz, H-19), 3.35 (1H, *t*, $J = 3.5$ Hz, H-3), 3.2 (1H, *ddd*, $J = 7.5$, 10.5, 12 Hz, H-5), 3.05 (1H, *dd*, $J = 6$, 12 Hz, H-2), 2.85 (1H, *ddd*, $J = 3$, 9, 12 Hz, H-5′), 2.5 (1H, *dt*, $J = 13$, 7.5 Hz, H-6), 2.3 (1H, *t*, $J = 12$ Hz, H-21), 2.0 (1H, *dt*, $J = 13.5$, 3.5 Hz, H-14), 1.8 (1H, *m*, H-6), 1.75 (1H, *m*, H-20), 1.7 (1H, *m*, H-15), 1.6 (1H, *dt*, $J = 13.5$, 3.5 Hz, H-14), 1.35 (1H, *m*, H-16), 1.15 (3H, *d*, $J = 7$ Hz, Me-18). ^{13}CNMR: δ 149 (C-13), 134.0 (C-8), 127.6 (C-11), 122.6 (C-9), 122.0 (C-10), 109.6 (C-12), 76.0 (C-19) 71.5 (C-17), 68.4 (C-2), 61.4 (C-3), 54.7 (C-5), 53.3 (C-7), 48.7 (C-21), 43.8 (C-6), 42.9 (C-16), 37.2 (C-20), 30.5 (C-15), 27.3 (C-14), 17.7 (C-18).

Acetylation of N-*desacetylspermostrychine* (**8**). Compound **8** (10 mg, 0.03 mmol) was dissolved in dry CH_2Cl_2 (3 ml) and 4.8 μl (0.045 mmol) of Ac_2O with 3.6 mg (0.03 mmol) of DMAP were added. After 24 hr at room temp., the mixt. was washed with 10% aq. $CuSO_4$, made alkaline with NH_4OH and extracted with $CHCl_3$. After drying and evapn, the crude product, purified by silica gel CC, gave spermostrychnine (6 mg), identified by TLC, MS and ^1H NMR.

Panganensine R (**3**). Orange Ce^{4+} reaction. $[\alpha]_D = +66°$ ($CHCl_3$; *c* 0.28). UV λ_{max}^{MeOH} nm: 207, 247, 292. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3327, 1631, 1606, 1485, 1250, 1136, 1059, 752. MS *m/z* (rel. int.): 588.3491 $([M]^+$ (10), calc. for $C_{38}H_{44}N_4O_2$: 588.3464), 294 (82), 249 (23), 164 (34), 144 (100), 130 (45). ^1H NMR: δ 7.10 (2H, H-9′, H-11′), 7.05 (2H, H-9, H-11), 6.80 (1H, *t*, $J = 7.5$ Hz, H-10′), 6.75 (1H, *t*, $J = 7.4$ Hz, H-10), 6.65 (1H, *d*, $J = 7.9$ Hz, H-12′), 6.60 (1H, *t*, $J = 7.8$ Hz, H-12), 6.20 (1H, *d*, $J = 15.4$ Hz, H-19), 6.15 (1H, *s*, H-21), 5.35 (1H, *dd*, $J = 8.9$, 15.2 Hz, H-18), 4.05 (1H, *br s*, H-3′), 3.95 (1H, H-19′), 3.85 (1H, H-17′), 3.80 (1H, H-2′), 3.60 (1H, *br s*, H-3), 3.55 (2H, H-17), 3.55 (1H, H17′), 3.50 (1H, H-5), 3.40 (1H, H-5′), 3.30 (1H, *dd*, $J = 4.4$, 9.75 Hz, H-5′), 3.25 (1H, H-5), 3.15 (1H, *t*, $J = 10.1$ Hz, H-21′), 2.96 (1H, *d*, $J = 10.2$ Hz, H-2), 2.80 (1H, *br s*, H-15), 2.57 (1H, H-6′), 2.46 (1H, H-6), 2.14 (1H, H-14′), 2.12 (1H, *br s*, H-15′), 2.10 (1H, H-14), 1.90 (1H, H-6′), 1.85 (1H, *td*, $J = 2.5$, 13.3 Hz, H-14), 1.75 (1H, H-16), 1.54 (1H, *dd*, $J = 3.5$, 11.3 Hz, H-20′), 1.37 (1H, *m*, H-16′), 1.25 (3H, *d*, $J = 6.8$ Hz, H-18′). ^{13}C NMR: δ 150.3 (C-13), 149.1 (C-13′), 143.2 (C-21), 140.6 (C-19), 131.2 (C-8′, C-8), 128.6 (C-11′), 127.9 (C-11), 122.3 (C-9′), 121.6 (C-9), 119.8 (C-10′), 118.8 (C-10), 113.2 (C-20), 110.1 (C-12′, C-12), 69.5 (C-19′), 67.0 (C-21′), 66.9 (C-2′), 66.2

(C-2), 63.5 (C-17), 62.4 (C-17′), 60.5 (C-3′), 58.0 (C-3), 55.4 (C-7), 52.7 (C-7′), 50.4 (C-5′), 50.1 (C-5), 48.9 (C-16), 42.2 (C-20′), 42.0 (C-6′), 40.6 (C-6), 40.3 (C-6′), 29.6 (C-14), 25.6 (C-15), 25.4 (C-14′), 23.3 (C-15′), 16.0 (C-18′).

Panganensine S (**4**). Orange Ce^{4+} reaction. $[\alpha]_D$ = +71° ($CHCl_3$; *c* 1.58). UV λ_{max}^{MeOH} nm: 206, 248, 295. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3350, 1633, 1606, 1483, 1464, 1242, 1217, 765. MS *m/z* (rel. int.): 588.3475 ($[M]^+$ (47), calc. for $C_{38}H_{44}N_4O_2$: 588.3464), 570 (55), 491 (8), 348 (13), 294 (60), 249 (21), 210 (29), 168 (28), 144 (100), 130 (60), 83 (77). ^1H NMR: δ 7.05 (2H, H-11, H-11′), 7.02 (2H, H-9, H-9′), 6.77 (1H, *t*, *J* = 6.5 Hz, H-10′), 6.74 (1H, *t*, *J* = 6.5 Hz, H-10), 6.62 (1H, *d*, *J* = 7.0 Hz, H-12′), 6.59 (1H, *d*, *J* = 7.0 Hz, H-12), 6.10 (1H, *s*, H-21), 6.08 (1H, *d*, *J* = 15.4 Hz, H-19), 5.35 (1H, *dd*, *J* = 8.8, 15.8 Hz, H-18), 3.90 (1H, *d*, *J* = 11.4 Hz, H-17′), 3.75 (1H, *d*, *J* = 9.2 Hz, H-2′), 3.72 (1H, *br s*, H-3′), 3.70 (1H, *br s*, H-3), 3.65 (1H, H-17′), 3.65 (1H, H-17′), 3.55 (1H, H-17), 3.50 (1H, H-19′), 3.45 (1H, H-5), 3.30 (1H, H-5′), 3.20 (1H, H-5), 3.15 (1H, H-5′), 3.10 (1H, H-21′), 2.95 (1H, *d*, *J* = 10.5 Hz, H-2), 2.50 (1H, H-6′), 2.45 (1H, H-6), 2.30 (1H, *br s*, H-15), 2.15 (1H, H-14′), 2.10 (1H, H-14), 1.90 (1H, H-14), 1.85 (1H, H-6′), 1.80 (1H, *br s*, H-15), 1.75 (1H, H-16), 1.75 (1H, H-20′), 1.70 (1H, H-6), 1.70 (1H, H-14′), 1.35 (1H, *br d*, *J* = 7.9 Hz, H-16′), 1.15 (3H, *d*, *J* = 7 Hz, H-18′). ^{13}C NMR: δ 150.3 (C-13), 149.3 (C-13′), 141.4 (C-21), 139.3 (C-19), 132.4 (C-8′), 131.4 (C-8), 128.1 (C-11′), 127.9 (C-11), 121.7 (C-9′, C-9), 119.5 (C-10′), 118.8 (C-10), 110.0 (C-12′, C-12), 78.5 (C-19′), 71.7 (C-17′), 67.3 (C-2′), 66.1 (C-2), 63.8 (C-17), 63.4 (C-21′), 60.2 (C-3′), 58.1 (C-3), 55.4 (C-7), 53.5 (C-7′), 50.5 (C-5′), 50.3 (C-5), 48.9 (C-16), 42.7 (C-20′), 42.2 (C-16′), 41.5 (C-6′), 40.7 (C-6), 31.8 (C-15′), 27.0 (C-14), 26.6 (C-14′), 25.5 (C-15), 21.5 (C-18′).

Panganensine X (**11**). Yellow–orange Ce^{4+} reaction. $[\alpha]_D$ = +14° ($CHCl_3$; *c* 0.18). UV λ_{max}^{MeOH} nm 220, 247, 300. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3356, 1651, 1608, 1487, 1464, 1055, 754. MS *m/z* (rel. int.): 590.3633 ($[M]^+$ (25), calc. for $C_{38}H_{46}N_4O_2$: 590.3620), 575 (18), 422 (7), 368 (12), 314 (18), 296 (72), 264 (17), 199 (34), 166 (100), 144 (93), 130 (82), 97 (48). ^1H NMR: δ 7.05 (1H, *d*, *J* = 7.4 Hz, H-9), 7.02 (1H, *t*, *J* = 7.6 Hz, H-11), 6.94 (1H, *d*, *J* = 7.8 Hz, H11′), 6.92 (1H, *s*, H-9′), 6.76 (1H, *t*, *J* = 7.3 Hz, H-10), 6.60 (1H, *d*, *J* = 7.9 Hz, H-12), 6.59 (1H, *d*, *J* = 7.9 Hz, H-12′), 5.63 (1H, *s*, H-21), 5.50 (1H, *q*, *J* = 6.6 Hz, H-19′), 3.70 (1H, *dd*, *J* = 5.2, 10.3 Hz, H-17′), 3.65 (1H, *d*, *J* = 6.6 Hz, H-2), 3.53 (1H, H-17′), 3.50 (1H, H-3), 3.45 (2H, H-2′, H-21′), 3.42 (1H, H-17), 3.27 (1H, H-5), 3.25 (2H, H-19, H3′), 3.23 (1H, H-17), 3.17 (1H, H-5), 3.13 (1H, H-5′), 3.00 (1H, *br d*, *J* = 13.6 Hz, H-21′), 2.80 (1H, *ddd*, *J* = 3.2, 8.7, 12.1 Hz, H-5′), 2.70 (1H, *br q*, *J* = 3 Hz, H-15′), 2.50 (1H, *dt*, *J* = 13.7, 8.3 Hz, H-6′), 1.98 (1H, H-14), 1.94 (3H, H-14′, H-6, H-6), 1.80 (1H, H-6′), 1.79 (1H, H-16′), 1.78 (1H, H-15), 1.71 (2H, H-16, H-14′), 1.64 (1H, H-14), 1.58 (3H, *dd*, *J* = 1.6, 6.7 Hz, H-18′), 1.37 (3H, *d*, *J* = 7.1 Hz, H-18). ^{13}C NMR: δ 150.1 (C-13), 147.2 (C-13′), 137.2 (C-8), 136.1 (C-10′), 135.1 (C-20′), 133.6 (C-8′), 131.1 (C-21), 127.5 (C-11), 127.1 (C-11′), 127.0 (C-20), 121.5 (C-9), 121.2 (C-9′), 120.9 (C-19′), 119.5 (C-10), 109.8 (C-12′), 109.5 (C-12). 72.0 (C-2′), 67.1 (C-17′), 64.0 (C-17), 63.6 (C-2), 62.1 (C-3), 61.9 (C-3′), 58.1 (C-21′), 54.4 (C-7), 53.4 (C-7′), 53.9 (C-5), 53.5 (C-5′), 48.3 (C-16′), 45.3 (C-16), 43.8 (C-19), 42.9 (C-6′), 29.7 (C-15′), 29.2 (C-15), 28.3 (C-14′), 23.6 (C-14), 20.1 (C-18), 12.8 (C-18′).

Panganensine Y (**12**). Orange Ce^{4+} reaction. $[\alpha]_D$ = +34° ($CHCl_3$; *c* 0.48). UV λ_{max}^{MeOH} nm 208, 247, 301. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3377, 1257, 1606, 1487, 1055, 754. MS *m/z* (rel. int.): 590.3590 ($[M]^+$ (58), calc. for $C_{38}H_{46}N_4O_2$: 590.3620), 575 (45), 545 (13), 422 (9), 401 (33), 379 (12), 314 (15), 296 (53), 249 (22), 199 (32), 166 (100), 144 (77), 130 (53). ^1H NMR: δ 7.01 (1H, *br d*, *J* = 7.4 Hz, H-9), 6.95 (1H, *dt*, *J* = 1.2, 7.7 Hz, H-11), 6.84 (1H, *dd*, *J* = 1.5, 7.9 Hz, H-11′), 6.82 (1H, *s*, H-9′), 6.70 (1H, *dd*, *J* = 0.7, 7.6 Hz, H-10), 6.56 (1H, *d*, *J* = 7.6 Hz, H-12), 6.49 (1H, *d*, *J* = 7.7 Hz, H-12′), 5.75 (1H, *s*, H-21), 5.40 (1H, *q*, *J* = 6.7 Hz, H-19′), 3.71 (1H, *d*, *J* = 6.9 Hz, H-2), 3.63 (1H, *dd*, *J* = 6.2, 10.3 Hz, H-17′), 3.55 (1H, *br s*, H-3′), 3.50 (1H, H-17′), 3.48 (1H, H-21′), 3.47 (1H, H-17), 3.42 (1H, *d*, *J* = 9 Hz, H-2′), 3.30 (4H, H-19, H-5a, H-5b, H-17), 3.27 (1H, H-3), 3.20 (1H, *ddd*, *J* = 8.0, 10.1, 11.5 Hz, H-5′), 3.03 (1H, *br d*, *J* = 13.6 Hz, H-21′), 2.78 (1H, *ddd*, *J* = 3.1, 8.6, 11.9 Hz, H-5′), 2.68 (1H, *br q*, *J* = 3.2 Hz, H-15′), 2.48 (1H, *dt*, *J* = 13.5, 8.1 Hz, H-6′), 2.00 (2H, H-6), 1.94 (1H, H-14′), 1.90 (1H, H-14), 1.83 (1H, H-16), 1.78 (1H, H-6′), 1.76 (1H, H-16′), 1.68 (1H, H-14′), 1.63 (1H, H-15), 1.60 (3H, *dd*, *J* = 1.9, 6.75 Hz, H-18′), 1.56 (1H, H-14), 1.30 (3H, *d*, *J* = 7 Hz, H-18). ^{13}C NMR: δ 150.2 (C-13), 147.5 (C-13′), 137.1 (C-10′), 136.9 (C-8), 134.3 (C-20′), 133.0 (C-8′), 130.7 (C-21), 127.5 (C-11), 127.0 (C-11′), 126.2 (C-20), 121.5 (C-19′, C-9), 120.9 (C-9′), 119.4 (C-10), 109.8 (C-12′), 109.7 (C-12), 71.8 (C-2′), 66.6 (C-17′), 64.7 (C-17), 63.7 (C-2), 61.8 (C-3, C-3′), 57.7 (C-21′), 54.5 (C-7), 53.7 (C-7′), 53.5 (C-5), 53.3 (C-5′), 48.2 (C-16′), 45.1 (C-16), 42.2 (C-19), 42.1 (C-6′), 40.6 (C-6), 28.9 (C-15′), 28.4 (C-15), 27.9 (C-14′), 23.1 (C-14), 20.7 (C-18), 12.7 (C-18′).

REFERENCES

1. Bisset, N. G. (1970) *Lloydia* **33**, 201.
2. Bisset, N. G. and Phillipson, J. D. (1971) *J. Nat. Prod.* **34**, 1.
3. Massiot, G., Massoussa, B., Jacquier, M. J., Thépenier, P., Le Men-Olivier, L., Delaude, C. and Verpoorte, R. (1988) *Phytochemistry* **27**, 3993.
4. Massiot, G., Massoussa, B., Thépenier, P., Jacquier, M. J. and Le Men-Olivier, L. (1983) *Heterocycles* **20**, 2339.
5. Thépenier, P., Jacquier, M. J., Henin, J., Massiot, G., Le Men-Olivier, L. and Delaude, C. (1990) *Phytochemistry* **29**, 2384.

6. Thépenier, P., Jacquier, M. J., Massiot, G., Le Men-Olivier, L. and Delaude, C. (1988) *Phytochemistry* **27**, 657.
7. Verpoorte, R., Verzijl, M. J. and Baerheim-Svendsen, A. (1982) *Planta Med.* **44**, 21.
8. Budzikiewicz, H., Wilson, J. M., Djerassi, C., Lévy, J., Le Men, J. and Janot, M.-M. (1963) *Tetrahedron* **19**, 1265.
9. Massiot, G., Thépenier, P., Jacquier, M. J., Henin, J., Le Men-Olivier, L. and Delaude, C. (1991) *Phytochemistry* **30**, 3449.
10. Tavernier, D., Anteunis M. J. O., Tits, M. and Angenot, L. J. G. (1978) *Bull. Soc. Chim. Belg.* **87**, 595.