Available online at www.sciencedirect.com
ScienceDirect
Phytochemistry 67 (2006) 2671–2675
PHYTOCHEMISTRY
www.elsevier.com/locate/phytochem

Secondary and tertiary isoquinoline alkaloids from *Xylopia parviflora*

Yumi Nishiyama [a,*], Masataka Moriyasu [a], Momoyo Ichimaru [a], Kinuko Iwasa [a], Atsushi Kato [a], Simon G. Mathenge [b], Patrick B. Chalo Mutiso [b], Francis D. Juma [c]

[a] *Natural Medicinal Chemistry, Kobe Pharmaceutical University, 4-19-1, Motoyamakita-machi, Higashinada-ku, Kobe 658-8558, Japan*
[b] *Department of Botany, University of Nairobi, P.O. Box 30197, Nairobi, Kenya*
[c] *Department of Clinical Pharmacology, Kenyatta National Hospital, University of Nairobi, P.O. Box 19676, Nairobi, Kenya*

Received 14 February 2006; received in revised form 27 May 2006
Available online 11 September 2006

Abstract

From the secondary and tertiary alkaloidal fractions of the root and the bark of *Xylopia parviflora* (Annonaceae), the isoquinoline alkaloids, 10,11-dihydroxy-1,2-dimethoxynoraporphine and parvinine were isolated, along with 39 known alkaloids. Their structures were determined on the basis of analysis of spectroscopic data.

Keywords: *Xylopia parviflora*; Annonaceae; Isoquinoline alkaloids

1. Introduction

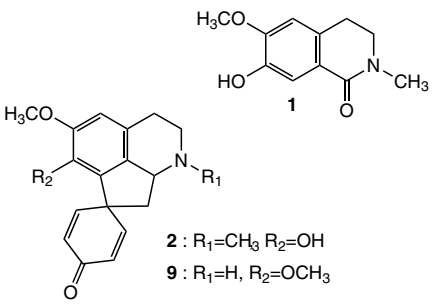
Xylopia parviflora Spruce. (Annonaceae) is a tall tree distributed in east Africa, whose root decoction is taken by the Nyamwezi and coastal peoples for stomach disorders. According to the natives, it is also used by Nyamwezi women for barrenness. Other medicinal uses include insertion of root pieces into nostrils for headache relief, and its bark is also used for analgesic and antispasmodic purposes (Chalo Mutiso, Private communication). Since *Xylopia* plants are known to have various bioactive components (Harrigan et al., 1994; Colman-Saizarbitoria et al., 1994), a fuller examination of the constituents of this plant was warranted. In a previous paper (Nishiyama et al., 2004), the isolation and structural elucidation of 23 quaternary isoquinoline alkaloids were reported from the root and the bark of this plant. In a continuing investigation of the secondary and tertiary alkaloidal constituents, 41 alkaloids, including two new compounds, were obtained through a combination of preparative ion-pair HPLC using sodium perchlorate and preparative TLC. This paper describes the isolation and structural determination of the two new alkaloids.

2. Results and discussion

From the MeOH extract of the root and the bark, the secondary and tertiary alkaloidal fractions (BE fraction) were dissolved in diethyl ether. The alkaloids insoluble in diethyl ether were extracted with chloroform to obtain the BC fraction. The BE fraction of the root gave 32 alkaloids, and the bark fraction gave 25 alkaloids, as shown in Table 1. The BC fraction of the root afforded two alkaloids, and the bark gave six alkaloids, as shown in Table 1. Some quaternary alkaloids reported as constituents of this plant (Nishiyama et al., 2004), (+)-*N*-methylphoebine, (+)-*N*-methyl purpuerine and (−)-*N*,*N*-dimethyl anomurine, were contained in the BC fraction of the root. Alkaloids **1**–**3**, **5**–**35**, and **37**–**41** were identified by comparison of their spectroscopic data with those described in the literature, or with authentic samples, or by analysis of their various 2D NMR and MS data. Alkaloids **4** and **36** were obtained as new compounds.

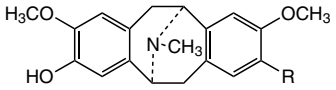
* Corresponding author. Tel./fax: +81 78 441 7543.
E-mail address: nisiyama@kobepharma-u.ac.jp (Y. Nishiyama).

0031-9422/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.phytochem.2006.07.011

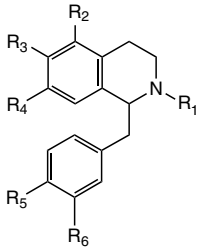


1

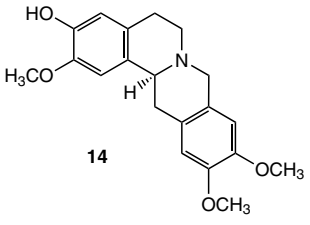
2 : R_1=CH_3 R_2=OH
9 : R_1=H, R_2=OCH_3



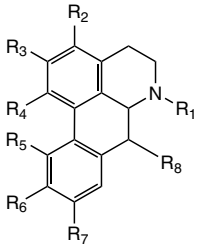
3 : R_1=OH
12 : R_1=OCH_3



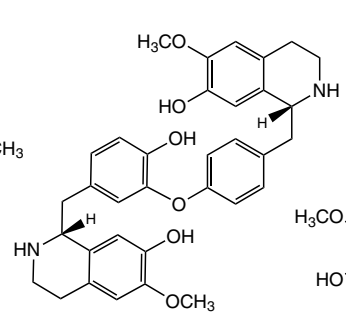
6 : R_1, R_2, R_6=H, R_3=OCH_3, R_4, R_5=OH
7 : R_1=CH_3, R_2, R_6=H, R_3=OCH_3, R_4, R_5=OH
10 : R_1=CH_3, R_2=H, R_3, R_6=OH, R_4, R_5=OCH_3
11 : R_1=CH_3, R_2=H, R_3, R_5=OCH_3, R_4, R_6=OH
16 : R_1=CH_3, R_2=H, R_3, R_5, R_6=OCH_3, R_4=OH
17 : R_1=CH_3, R_2=H, R_3, R_4, R_5=OCH_3, R_6=OH
19 : R_1, R_2, R_6=H, R_3, R_5=OCH_3, R_4=OH
26 : R_1, R_2, R_6=H, R_3, R_4, R_5=OCH_3
28 : R_1, R_6=H, R_2=OH, R_3, R_4, R_5=OCH_3
34 : R_1, R_6=H, R_2, R_3, R_4, R_5=OCH_3
36 : R_1, R_6=H, R_2, R_3=OCH_2O, R_4, R_5=OCH_3



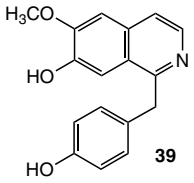
14



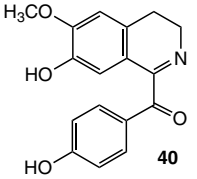
4 : R_1, R_2, R_7, R_8=H, R_3, R_4=OCH_3, R_5, R_6=OH
5 : R_1, R_2, R_5, R_8=H, R_3, R_7=OH, R_4, R_6=OCH_3
8 : R_1=CH_3, R_2, R_5, R_8=H, R_3, R_7=OH, R_4, R_6=OCH_3
13 : R_1=CH_3, R_2, R_5, R_8=H, R_3, R_6=OCH_3, R_4, R_7=OH
15 : R_1, R_2, R_7, R_8=H, R_3, R_4, R_6=OCH_3, R_5=OH
18 : R_1, R_2, R_5, R_8=H, R_3, R_4, R_6=OCH_3, R_7=OH
20 : R_1, R_2, R_6, R_8=H, R_3, R_4=OCH_2O, R_5=OH, R_7=OCH_3
21 : R_1=CH_3, R_2, R_5, R_8=H, R_3, R_4, R_6=OCH_3, R_7=OH
22 : R_1, R_7, R_8=H, R_2, R_3, R_4, R_6=OCH_3, R_7=OH
23 : R_1, R_2, R_5, R_6, R_8=H, R_3, R_4=OCH_2O, R_7=OH
24 : R_1, R_2, R_5, R_6, R_7=H, R_3, R_4=OCH_2O, R_8=OH
25 : R_1, R_2, R_5, R_8=H, R_3, R_4, R_6, R_7=OCH_3
27 : R_1=CH_3, R_2, R_5, R_8=H, R_3, R_4, R_6, R_7=OCH_3
29 : R_1, R_5, R_8=H, R_2=OH, R_3, R_4=OCH_3, R_6, R_7=OCH_2O
30 : R_1, R_2, R_5, R_8=H, R_3, R_4=OCH_3, R_6, R_7=OCH_2O
31 : R_1, R_5, R_8=H, R_2, R_3, R_4, R_6, R_7=OCH_3
32 : R_1, R_2, R_5, R_6, R_7, R_8=H, R_3, R_4=OCH_2O
33 : R_1=CH_3, R_5, R_8=H, R_2, R_3, R_4, R_6, R_7=OCH_3
35 : R_1, R_2, R_5, R_6, R_8=H, R_3, R_4=OCH_2O, R_7=OCH_3
37 : R_1, R_5, R_8=H, R_2, R_3, R_4=OCH_3, R_6, R_7=OCH_2O
38 : R_1=CH_3, R_2, R_7, R_9=H, R_3, R_6=OCH_3, R_4, R_5=OH



41



39



40

Alkaloid **4** was obtained as an amorphous powder, having a molecular formula of $C_{18}H_{19}NO_4$ (HR-SIMS), and its UV spectrum resembled that of norisocorydine (**15**), suggesting that **4** had the same 1,2,10,11-substitution of an aporphine alkaloid. Its ^{1}H NMR spectroscopic features were also closely similar to those of **15**, except for the presence of only two methoxy groups. The ^{1}H NMR spectrum displayed a singlet for an aromatic proton at δ 6.71, two doublets for *o*-coupled protons at δ 6.92 and 7.02, and two singlets for methoxy groups at δ 3.69 and 3.92. The HMBC correlations from H-8 (δ 7.02) to C-7 (δ 37.63) and C-10 (δ 147.97) and an NOE experiment (Fig. 1) indicated that its structure was as shown. The absolute configuration of C-6a was determined to be in the *S* form, because the HPLC analysis of **4** with a CD detector showed a negative Cotton effect at 280 nm and a positive Cotton effect at 240 nm (Ringdahl et al., 1981). Accordingly, **4** was (*S*)-10,11-dihydroxy-1,2-dimethoxynoraporphine, the *N*-H derivative of (*S*)-suaveoline (aporphine type) (Barger et al., 1939; Guinaudeau et al., 1975). This alkaloid might

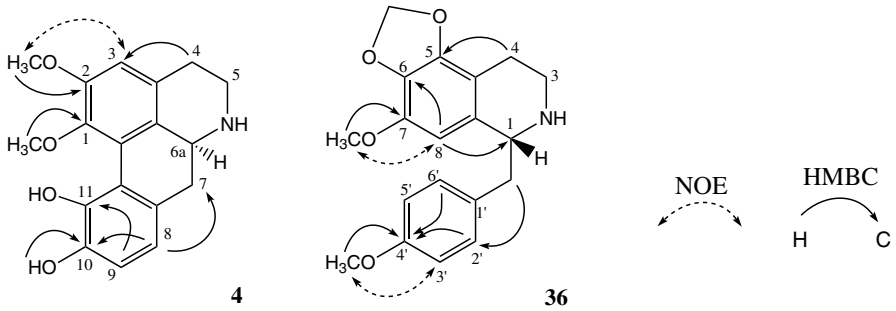
Table 1
Alkaloids from the root and the bark of *Xylopia parviflora*

Frac.	Alkaloid	Root	Bark	Ref.
	Thalifoline (**1**)		○	Doskotch et al. (1969)
	(−)-*N*-Methylcrotsparine (**2**)		○	Bhakuni et al. (1970)
	(−)-Bisnorargemonine (**3**)	○		Ohiri et al. (1983a)
	(+)-10,11-Dihydroxy-1,2-dimethoxynoraporphine (**4**)	○		
	(+)-Norboldine (**5**)	○		Guinaudeau et al. (1975)
	(+)-Coclaurine (**6**)	○	○	Johns et al. (1967)
	(−)-*N*-Methylcoclaurine (**7**)	○		Tomita et al. (1965)
	(+)-Boldine (**8**)	○		Guinaudeau et al. (1975)
	(+)-Stepharine (**9**)	○	○	Nishiyama et al. (2000)
	Protosinomenine (**10**)		○	Jossang et al. (1983)
	(+)-Reticuline (**11**)	○	○	Ichimaru et al. (1997)
	(−)-Norargemonine (**12**)	○		Slavik et al. (1971)
	(+)-Isoboldine (**13**)	○	○	Guinaudeau et al. (1975)
	(−)-Discretine (**14**)	○	○	Ohiri et al. (1983b)
	(+)-Norisocorydine (**15**)	○	○	Guinaudeau et al. (1975)
	(+)-Codamine (**16**)		○	Brochmann-Hanssen et al. (1965)
	(+)-Laudanidine (**17**)	○	○	Wu et al. (1977)
	(+)-Laurotetanine (**18**)	○	○	Guinaudeau et al. (1975)
	(+)-4′-*O*-Methylcoclaurine (**19**)	○	○	Tomita et al. (1965)
BE	(−)-Calycinine (**20**)	○	○	Guinaudeau et al. (1983)
	(+)-*N*-Methyllaurotetanine (**21**)	○	○	Guinaudeau et al. (1975)
	(+)-Noroconovine (**22**)	○		Guinaudeau et al. (1979)
	(−)-Anolobine (**23**)	○	○	Ichimaru et al. (1997)
	(−)-Michelalbine (**24**)	○		Guinaudeau et al. (1975)
	(+)-Norglaucine (**25**)	○	○	Guinaudeau et al. (1975)
	(+)-*O*-Methylarmepavine (**26**)	○	○	Tomita et al. (1965)
	(+)-Glaucine (**27**)	○	○	Guinaudeau et al. (1975)
	(+)-Anomuricine (**28**)	○		Leboeuf et al. (1981)
	(+)-1,2-Dimethoxy-3-hydroxy-9,10-methylenedioxynoraporphine (**29**)	○		Guinaudeau et al. (1988)
	(+)-Nornantenine (**30**)		○	Guinaudeau et al. (1975)
	(+)-Norpurpuerine (**31**)	○	○	Guinaudeau et al. (1975)
	(−)-Anonaine (**32**)	○		Ichimaru et al. (1997)
	(+)-Purpuerine (**33**)	○	○	Guinaudeau et al. (1975)
	(+)-Anomurine (**34**)	○		Tomita et al. (1965)
	(−)-Xylopine (**35**)	○	○	Guinaudeau et al. (1975)
	(+)-Parvinine (**36**)	○	○	
	(+)-Norphoebine (**37**)	○	○	Guinaudeau et al. (1988)
	(+)-Coclaurine (**6**)	○	○	Johns et al. (1967)
	(+)-Reticuline (**11**)		○	Ichimaru et al. (1997)
BC	(+)-Corytuberine (**38**)	○	○	Guinaudeau et al. (1975)
	Yuzirine (**39**)		○	Kimura et al. (1983)
	Longifolonine (**40**)		○	Bick et al. (1981)
	(+)-Lindoldhamine (**41**)		○	Guinaudeau et al. (1986)

be named norsuaveoline, but another one in the indole alkaloid series (Majumdar et al., 1972), was improperly named suaveoline and norsuaveoline (its NH type) (Nasser et al., 1984) in addition to the aporphine type. Alkaloid **4** was not given any name.

Alkaloid **36**, named parvinine, was obtained as a colorless amorphous powder, having a molecular formula of $C_{19}H_{21}NO_4$ (HR-SIMS). The UV and ^1H NMR spectra of **36** resembled those of (+)-anomurine (**34**), suggesting that **36** was a 5,6,7,4′-tetrasubstituted tetrahydrobenzylisoquinoline alkaloid. Measuring various 2D NMR spectra provided further support for the structure of this alkaloid. All of the methyl, methylene, methine protons and carbons were assigned from the ^1H–^1H COSY, HMQC, and HMBC spectra. The presence of a singlet proton (δ 6.34) and an HMBC correlation (Fig. 1) from this proton to C-1 (δ 57.09) revealed that this proton was correlated with C-8. From the NOE experiments, the correlations were observed between a methoxy group (δ 3.85) and H-8, and between another methoxy group (δ 3.80) and H-3′,5′ (δ 6.87). The two methoxy groups could be placed on C-7 and C-4′. Hence, the methylenedioxy group must be located at C-5 and C-6. Accordingly, the structure of the new alkaloid was elucidated as **36**. The absolute configuration of C-1 was determined as *R*, because the HPLC analysis of **36** with a CD detector showed negative Cotton effects at 280 and 240 nm (Moriyasu et al., 1997).

The present and previous (Nishiyama et al., 2004) results confirmed the structures of many isoquinoline alkaloids contained in *X. parviflora*. The root and the bark of this plant have been used as medicine mainly for analgesic purpose. A study of the potential analgesic activity of these



4 36

Fig. 1. HMBC and NOE interactions observed for **4** and **36**.

alkaloids is now in progress by acetic acid-induced abdominal writhing response and formalin-induced licking response in mice.

3. Experimental

3.1. General

Melting points were determined using a Yanaco MP-500D micro melting point apparatus and are uncorrected. IR spectra were obtained on a Shimadzu FT-IR-8200 IR spectrometer, UV spectra were recorded on a Shimadzu UV-2500PC spectrophotometer. SIMS and HR-SIMS were obtained with a Hitachi M-4100 spectrometer; glycerol was used as the matrix. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR experiments were performed on a Varian VXR-500 (500 MHz) spectrometer with chemical shifts referenced to internal TMS. HPLC conditions were as follows: column, Cosmosil AR-II ODS, 6 × 150 mm, Nacalai tesque (20 × 250 mm for preparative HPLC); mobile phase, CH_3CN: 0.2 M sodium perchlorate (trace $HClO_4$): 2.0 mL/min (9.0 mL/min for preparative); detection, photodiode array detector (991J, Waters) and CD detector (JASCO CD-2095 Plus). TLC conditions were as follows: TLC plate, Merck 5715 Si-gel plate (Merck 5744 for preparative); mobile phase, $CHCl_3$/MeOH/NH_3 aq (9 mL/1 mL/2 drops or 8 mL/2 mL/2 drops).

3.2. Plant material

The root and bark of *X. parviflora* were collected in the Kwale district of Kenya in 1997 and 2000. The plant was identified and authenticated by Mr. S. G. Mathenge and Mr. P. B. Chalo Mutiso, two of the authors. Voucher specimens of this plant were deposited both in the laboratory of Kobe Pharmaceutical University (2000, No. 3) and the herbarium of University of Nairobi (No. 00/3).

3.3. Extraction and isolation

Dried roots and bark of *X. parviflora* (370 g and 210 g, respectively) were finely cut and extracted with hot MeOH (each 3 L, refluxed for 5 h) three times. The resulting MeOH extracts were evaporated under reduced pressure and the residue (41 g and 31 g, respectively) was re-extracted with 2.5% tartaric acid. Each acidic solution was subjected to conventional methods for the isolation of secondary and tertiary alkaloids, and gave Et_2O soluble fractions (BE fraction: 570 mg and 1350 mg, respectively), and $CHCl_3$ soluble fractions (BC fraction: 270 mg and 315 mg, respectively). The quaternary alkaloid fractions were examined and reported previously (Nishiyama et al., 2004). The secondary and tertiary alkaloidal fractions were subjected to ion–pair preparative HPLC system, and preparative TLC, applied as necessary. The BE fraction of the roots (570 mg) gave 32 alkaloids as free bases, **3** (1.5 mg), **4** (5.0 mg), **5** (3.0 mg), **6** (17.1 mg), **7** (2.6 mg), **8** (4.6 mg), **9** (1.0 mg), **11** (27.7 mg), **12** (3.4 mg), **13** (3.0 mg), **14** (3.5 mg), **15** (3.5 mg), **17** (6.6 mg), **18** (6.8 mg), **19** (3.1 mg), **20** (1.5 mg), **21** (2.5 mg), **22** (1.3 mg), **23** (9.6 mg), **24** (4.4 mg), **25** (3.5 mg), **26** (8.8 mg), **27** (8.5 mg), **28** (3.0 mg), **29** (1.8 mg), **31** (4.4 mg), **32** (8.6 mg), **33** (5.3 mg), **34** (4.7 mg), **35** (4.9 mg), **36** (4.5 mg), and **37** (17.2 mg). The BE fraction of the bark (520 mg) gave 25 alkaloids as free bases, **1** (1.8 mg), **2** (0.7 mg), **6** (24.2 mg), **9** (1.0 mg), **10** (3.3 mg), **11** (50.0 mg), **13** (7.8 mg), **14** (1.9 mg), **15** (1.3 mg), **16** (1.0 mg), **17** (4.4 mg), **18** (7.3 mg), **19** (3.4 mg), **20** (1.6 mg), **21** (2.3 mg), **23** (5.0 mg), **25** (2.2 mg), **26** (8.4 mg), **27** (11.8 mg), **30** (7.7 mg), **31** (2.2 mg), **33** (1.2 mg), **35** (8.8 mg), **36** (3.6 mg), and **37** (6.2 mg). The BC fraction of the roots (270 mg) gave **6** (1.0 mg), **38** (4.0 mg), *N*-methylpurpuerine (4.3 mg), *N*,*N*-dimethylanomurine (4.7 mg), and *N*-methylphoebine (2.6 mg). The BC fraction of the bark gave **6** (9.4 mg), **11** (3.6 mg), **38** (12.1 mg), **39** (3.8 mg), **40** (3.0 mg), and **41** (3.9 mg).

3.4. Spectroscopic data of alkaloids

3.4.1. (+)-10,11-Dihydroxy-1,2-dimethoxynoraporphine (4)

Colorless amorphous powder. $[\alpha]_D^{22}$: +57° (MeOH, *c* 0.46), SIMS(*m*/*z*): 314 $[M+H]^+$, 297, 282. HR-SIMS: 314.1387 (314.1391 calcd for $[C_{18}H_{19}NO_4+H]$). UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 266 (4.09), 273 (sh), 306 (3.85). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH, NH), 1634, 1597, 1464, 1437, 1375. ^{1}H NMR (500 MHz, $CDCl_3$): 2.52 (1H, br. t, $J = 13.5$ Hz, HA-7), 2.70 (1H, m, HA-4), 2.81 (1H, dd,

$J = 13.5$, 4.0 Hz, HB-7), 3.00 (2H, m, HA-5, HB-4), 3.36 (1H, m, HB-5), 3.69 (3H, s, OCH_3-1), 3.76 (1H, br. dd, $J = 13.5$, 4.0 Hz, H-6a), 3.92 (3H, s, OCH_3-2), 6.71 (1H, s, H-3), 6.92 (1H, d, $J = 8.0$ Hz, H-9), 7.02 (1H, dd, $J = 8.0$, 0.5 Hz, H-8). ^{13}C NMR (125 MHz, $CDCl_3$): δ 29.03 (C-4), 37.63 (C-7), 42.80 (C-5), 53.75 (C-6a), 56.11 ($O\underline{C}H_3$-2), 62.09 ($O\underline{C}H_3$-1), 112.03 (C-3), 114.42 (C-9), 118.49 (C-11b), 124.57 (C-3a), 125.14 (C-11a), 125.19 (C-8), 129.21 (C-11c), 130.08 (C-7a), 141.79 (C-1), 142.07 (C-11), 147. 97 (C-10), and 148.79 (C-2).

3.4.2. (+)-Parvinine (**36**)

Colorless amorphous powder. $[\alpha]_D^{22}$: +20° ($CHCl_3$, *c* 0.28), SIMS(*m*/*z*): 328 $[M + H]^+$, 206, 121. HR-SIMS: 328.1552 (328.1548 calcd for $[C_{19}H_{21}NO_4 + H]$). UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 278 (3.36), 284 (sh). IR ν_{max}^{KBr} cm^{-1}: 3400 (NH), 1647, 1610, 1510, 1464, 1383, 1248. ^1H NMR (500 MHz, $CDCl_3$): 2.65 (2H, br. t, $J = 6.0$ Hz, H_2-4), 2.88 (1H, dd, $J = 14.0$, 9.5 Hz, HA-α), 2.91 (1H, dd, $J = 12.5$, 6.0 Hz, HA-3), 3.14 (1H, dd, $J = 14.0$, 4.5 Hz, HB-α), 3.21 (1H, td, $J = 12.5$, 6.0 Hz, HB-3), 3.80 (3H, s, OCH_3-4′), 3.85 (3H, s, OCH_3-7), 4.09 (1H, dd, $J = 9.5$, 4.5 Hz, H-1), 5.96 (2H, s, OCH_2O), 6.34 (1H, s, H-8), 6.87 (2H, d-like, $J = 9.0$ Hz, H-3′, 5′), 7.16 (2H, d-like, $J = 9.0$ Hz, H-2′, 6′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.04 (C-4), 39.78 (C-3), 41.63 (C-α), 55.27 ($O\underline{C}H_3$-4′), 56.70 ($O\underline{C}H_3$-7), 57.09 (C-1), 101.40 ($O\underline{C}H_2O$), 105.23 (C-8), 110.82 (C-4a), 114.07 (C-3′, 5′), 130.32 (C-2′, 6′), 130.66 (C-1′), 132.83 (C-8a), 133.09 (C-6), 141,76 (C-7), 146.32 (C-5), and 158.34 (C-4′).

Acknowledgements

Our thanks go to Dr. M. Sugiura, Dr. A. Takeuchi, and Dr. K. Saiki (Kobe Pharmaceutical University) for the NMR and MS measurements.

References

Barger, G., Sargent, L.J., Brown, C.J., Cox, E.G., 1939. Alkaloids of *Artabotrys suaveolens*. J. Chem. Soc., 991–997.

Bhakuni, D.S., Satish, S., Dhar, M.M., 1970. The alkaloids of *Croton sparsiflorus*. Phytochemistry 9, 2573–2580.

Bick, I.R.C., Sévenet, T., Sinchai, W., Skelton, B.W., White, A.H., 1981. Alkaloids of *Cryptocarya longifolia*: X-ray crystal structure of thalifoline and longifolonine. Aust. J. Chem. 34, 195–207.

Brochmann-Hanssen, E., Nielsen, B., Utzinger, G.E., 1965. Opium alkaloids II. Isolation and characterization of codamine. J. Pharm. Sci. 54, 1531–1532.

Chalo Mutiso, P.B. (Private communication).

Colman-Saizarbitoria, T., Gu, Z.M., McLaughlin, J.L., 1994. Two new bioactive monotetrahydrofuran annonaceous acetogenins from the bark of *Xylopia aromatica*. J. Nat. Prod. 57, 1661–1669.

Doskotch, R.W., Schiff Jr., P.L., Beal, J.L., 1969. Alkaloids of *Thalictrum-X*. Two new alkaloids from *T. minus var. adiantifolium:* noroxyhydrastinine and thalifoline. Tetrahedron 25, 469–475.

Guinaudeau, H., Leboeuf, M., Cavé, A., 1975. Aporphine alkaloids. Lloydia 38, 275–338.

Guinaudeau, H., Leboeuf, M., Cavé, A., 1979. Aporphine alkaloids. II. J. Nat. Prod. 42, 325–360.

Guinaudeau, H., Leboeuf, M., Cavé, A., 1983. Aporphinoid alkaloids, III. J. Nat. Prod. 46, 761–835.

Guinaudeau, H., Freyer, A.J., Shamma, M., 1986. Spectral characteristics of the bisbenzylisoquinoline alkaloids. Nat. Prod. Rep., 477–488.

Guinaudeau, H., Leboeuf, M., Cavé, A., 1988. Aporphinoid alkaloids, IV. J. Nat. Prod. 51, 389–474.

Harrigan, G.G., Gunatilaka, A.A.L., David, G.I., Chan, G.W., Johnson, R.K., 1994. Isolation of bioactive and other oxoaporphine alkaloids from two annonaceous plants, *Xylopia aethiopica* and *Miliusa cf. banacea*. J. Nat. Prod. 57, 68–73.

Ichimaru, M., Moriyasu, M., Nishiyama, Y., Kato, A., Juma, F.D., Nganga, J.N., Ogeto, J.O., 1997. Studies on African medicinal plants. Alkaloidal constituents of *Uvaria acuminata* and *U. lucida*. Nat. Med. 51, 272–274.

Johns, S.R., Lamberton, J.A., Sioumis, A.A., 1967. 1-Benzyl-1,2,3,4-tetrahydroisoquinoline alkaloids from *Alseodaphne archboldiana* (ALLEN) kostermans (family Lauraceae). Aust. J. Chem. 20, 1729–1735.

Jossang, A., Leboeuf, M., Cabalion, P., Cavé, A., 1983. Alkaloids from Annonaceae XLV: Alkaloids of *Polyalthia nitidissima*. Planta Med. 49, 20–24.

Kimura, I., Kimura, M., Yoshizaki, M., Yanada, K., Kadota, S., Kikuchi, T., 1983. Neuromuscular blocking action of alkaloids from Japanese crude drug "Shin-I" (Flos Magnoliae) in frog skeletal muscle. Planta Med. 48, 43–47.

Leboeuf, M., Legueut, C., Cavé, A., Desconclois, J.F., Forgacs, P., Jacquemin, H., 1981. Alkaloids of Annonaceae XXIX. Alkaloids of *Annona muricata* L. Planta Med. 42, 37–44.

Majumdar, S.P., Potier, P., Poisson, J., 1972. Structure of suaveoline, a new alkaloid from *Rauwolfia suaveolens*. (Apocynaceae). Tetrahedron Lett. 16, 1563–1566.

Moriyasu, M., Ichimaru, M., Nishiyama, Y., Kato, A., 1997. (R)-(+)-Isotembetarine, a quaternary alkaloid from *Zanthoxylum nitidium*. J. Nat. Prod. 60, 299–301.

Nasser, A.M.A.G., Court, W.E., 1984. Stem bark alkaloids of *Rauwolfia caffra*. J. Ethnopharmacol. 11, 99–117.

Nishiyama, Y., Moriyasu, M., Ichimaru, M., Iwasa, K., Kato, A., Mathenge, S.G., Chalo Mutiso, P.B., Juma, F.D., 2000. Secondary and tertiary isoquinoline alkaloids from *Monodora junodii*. Nat. Med. 54, 338–341.

Nishiyama, Y., Moriyasu, M., Ichimaru, M., Iwasa, K., Kato, A., Mathenge, S.G., Chalo Mutiso, P.B., Juma, F.D., 2004. Quaternary isoquinoline alkaloids from *Xylopia parviflora*. Phytochemistry 65, 939–944.

Ohiri, F.C., Verpoorte, R., Svendsen, A.B., 1983a. Tertiary phenolic alkaloids from *Chasmanthera dependens*. Planta Med. 49, 17–19.

Ohiri, F.C., Verpoorte, R., Svendsen, A.B., 1983b. ^1H NMR chemical shift values for aromatic protons in 2,3,9,10- and 2,3,10,11-tetrasubstituted tetrahydroberberine alkaloids. Planta Med. 49, 162–164.

Ringdahl, B., Chan, R.P.K., Craig, J.V., 1981. Circular dichroism of aporphines. J. Nat. Prod. 44, 80–85.

Slavik, J., Slavikova, L., 1971. Alkaloids of the Papaveraceae. XLV. Phenolic non-quaternary alkaloids from the roots of three *Eschscholtzia* species. Collect. Czech. Chem. Commun. 36, 2067–2069.

Tomita, M., Shingu, T., Fujitani, K., Furukawa, H., 1965. Studies on the alkaloids of Menispermaceous plants. CCXVI. Nuclear magnetic resonance spectra of benzylisoquinoline derivatives. (1) *N*-Methylcoclaurine type bases. Chem. Pharm. Bull. 13, 921–926.

Wu, J., Beal, J.L., Wu, W., Doskotch, R.W., 1977. Alkaloids of *Thalictrum.* XXIV. Isolation and identification of alkaloids from the tertiary phenolic fraction of *Thalictrum revolutum* Tops. Lloydia 40, 593–601.