Available online at www.sciencedirect.com
SCIENCE DIRECT®
Phytochemistry 65 (2004) 939–944
PHYTOCHEMISTRY
www.elsevier.com/locate/phytochem

# Quaternary 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, Higashinada-ku, Kobe 658-8558, Japan*
[b]*Department of Botany, University of Nairobi, PO Box 30197 Nairobi, Kenya*
[c]*Department of Clinical Pharmacology, Kenyatta National Hospital, University of Nairobi, PO Box 19676 Nairobi, Kenya*

Received 12 August 2003; received in revised form 26 November 2003

**Abstract**

From the quaternary alkaloidal fraction of the bark and the root of *Xylopia parviflora* (Annonaceae), four isoquinoline alkaloids, xylopinidine, dehydrocoreximine, *N*, *N*-dimethylanomurine and *N*-methylphoebine were isolated along with the known compounds, pycnarrhine, lotusine, 6,7-dimethoxy-2-methyl-isoquinolinium salt, 1,2-dehydroreticuline, (−)-phellodendrine, (+)-tembetarine, (−)-litcubine, (+)-magnoflorine, tetradehydroreticuline, (−)-oblongine, (+)-menisperine, (+)-*N*-methylcorydine, stepharanine, (+)-xanthoplanine, dehydrodiscretine, jatrorrhizine and palmatine. 3,4-Dihydro-6,7-dimethoxy-2-methyl-isoquinolinium and *N*-methylpurpuerine were isolated as natural products for the first time. Their structures were determined on the basis of spectroscopic evidence.


*Keywords:* *Xylopia parviflora*; Annonaceae; Isoquinoline alkaloid

## 1. Introduction

*Xylopia parviflora* (Annonaceae) is a tall tree distributed in east Africa, a root of which decoction is taken by the Nyamwezi and coastal peoples for stomach disorders. It is also used by Nyamweji 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. Xylopia plants have bioactive components like alkaloids (Jossang et al., 1991, Harrigan et al., 1994a, Johns et al., 1968), acetogenins (Colman-Saizarbitoria et al., 1994), terpenes (Martins et al., 1998, Harrigan et al., 1994b) and essential oils (Brophy et al., 1998). The only previous chemical investigations of *X. parviflora* resulted in the isolation of an essential oil from its fruits (Jirovetz et al., 1997, Lamaty et al.,1989); however, a phytochemical study of other Xylopia genus species and pretest by use of Dragendorff's reagent suggested the presence of alkaloids. This present paper deals with the isolation and structural determination of various isoquinoline alkaloids, especially quaternary alkaloids, from the bark and the root of this plant.

## 2. Result and discussion

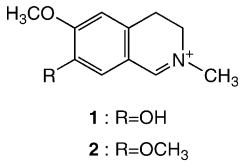
From the MeOH extract of the root and the bark, twenty-three quaternary alkaloids (**1**–**23**) were isolated as perchlorate derivatives. The root tissue gave pycnarrhine (**1**) (Menachery et al., 1986), 3,4-dihydro-6,7-dimethoxy-2-methyl-isoquinolinium (**2**) (Hughes et al., 1976), lotusine (**3**) (Koshiyama et al., 1970), 6,7-dimethoxy-2-methyl-isoquinolinium (**4**) (Wu et al., 1980), xylopinidine (**5**), 1,2-dehydroreticuline (**6**) (Borkowski et al., 1978), (−)-phellodendrine (**7**) (Nishiyama et al., 2000), (+)-tembetarine (**8**) (Kato et al., 1995), (−)-litcubine (**9**) (Lee et al., 1996), (+)-magnoflorine (**10**) (Moriyasu et al., 1994a), (−)-oblongine (**12**) (Moriyasu et al., 1994a), (+)-menisperine (**13**) (Moriyasu et al., 1994a), (+)-*N*-methylcorydine (**14**) (Marsaioli et al., 1979), stepharanine (**15**) (Nishiyama et al., 2000), dehydrocoreximine (**16**), (+)-xanthoplanine (**17**) (Moriyasu et al., 1994b), dehydrodiscretine (**18**) (Moriyasu et al., 1994b), jatrorrhizine (**19**), *N*-methylpurpuerine (**20**) (Ronsh et al., 1983), palmatine (**21**) (Moriyasu et al., 1994b), *N*,*N*-

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

0031-9422/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.phytochem.2003.12.010

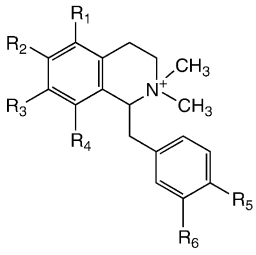
dimethylanomurine (**22**) and *N*-methylphoebine (**23**). The bark also gave **1**, **5**, **6**, **8**, **10**, tetradehydroreticuline (**11**) (Tanahashi et al., 2000), **12**, **13**, **17**, **18**–**20** and **23**. Alkaloids **1**, **3**, **4**, **6**–**15**, **17**–**19** and **21** were identified by comparison of their spectral data with those described in the literature or authentic samples. Compounds **5**, **16**, **22** and **23** were obtained as new compounds, and compounds **2** and **20** were isolated as natural products for the first time.

The UV spectrum of compound **2** resembled that of pycnarrhine (**1**), suggesting that **2** was a simple isoquinoline alkaloid. Its $^{1}H$ and $^{13}C$ NMR spectral features were also very similar to those of **1**, except an additional two methoxyl groups. The HMBC correlations and NOE experiment (Fig. 1) indicated that its structure was elucidated as shown. **2** was previously reported as a synthetic compound (Hughes et al., 1976) but not as naturally occurring.



**1** : R=OH

**2** : R=$OCH_3$



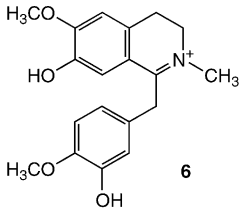
**3** : $R_1$, $R_4$, $R_6$=H, $R_2$, $R_5$=OH, $R_3$=$OCH_3$

**5** : $R_1$, $R_4$=H, $R_2$, $R_6$=OH, $R_3$, $R_5$=$OCH_3$

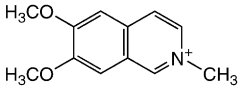
**8** : $R_1$, $R_4$=H, $R_2$, $R_5$=$OCH_3$, $R_3$, $R_6$=OH

**12** : $R_1$, $R_2$, $R_6$=H, $R_3$=$OCH_3$, $R_4$, $R_5$=OH

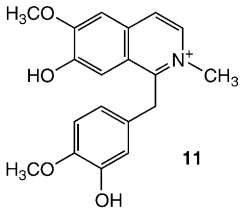
**22** : $R_1$, $R_2$, $R_3$, $R_5$=$OCH_3$, $R_4$, $R_6$=H



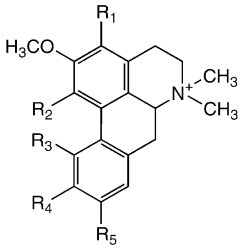
**6**



**4**



**11**



**10** : $R_1$, $R_5$=H, $R_2$, $R_3$=OH, $R_4$=$OCH_3$

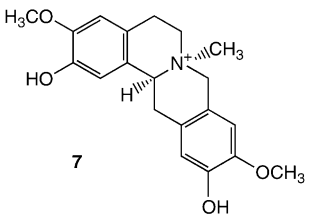
**13** : $R_1$, $R_5$=H, $R_2$, $R_4$=$OCH_3$, $R_3$=OH

**14** : $R_1$, $R_5$=H, $R_2$=OH, $R_3$, $R_4$=$OCH_3$

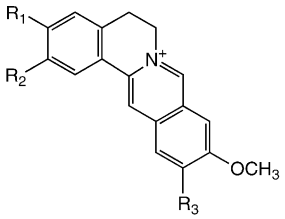
**17** : $R_1$, $R_3$=H, $R_2$, $R_4$=$OCH_3$, $R_5$=OH

**20** : $R_1$, $R_2$, $R_4$, $R_5$=$OCH_3$, $R_3$=H

**23** : $R_1$, $R_2$=$OCH_3$, $R_4$, $R_5$=$OCH_2O$, $R_3$=H

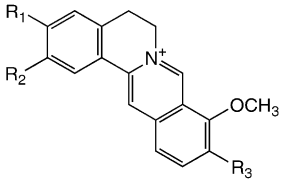


**7**



**16** : $R_1$=$OCH_3$, $R_2$, $R_3$=OH

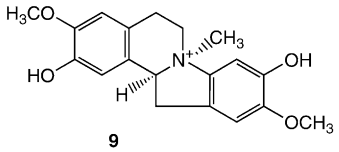
**18** : $R_1$=OH, $R_2$, $R_3$=$OCH_3$



**15** : $R_1$=$OCH_3$, $R_2$, $R_3$=OH

**19** : $R_1$=OH, $R_2$, $R_3$=$OCH_3$

**21** : $R_1$, $R_2$, $R_3$=$OCH_3$



**9**

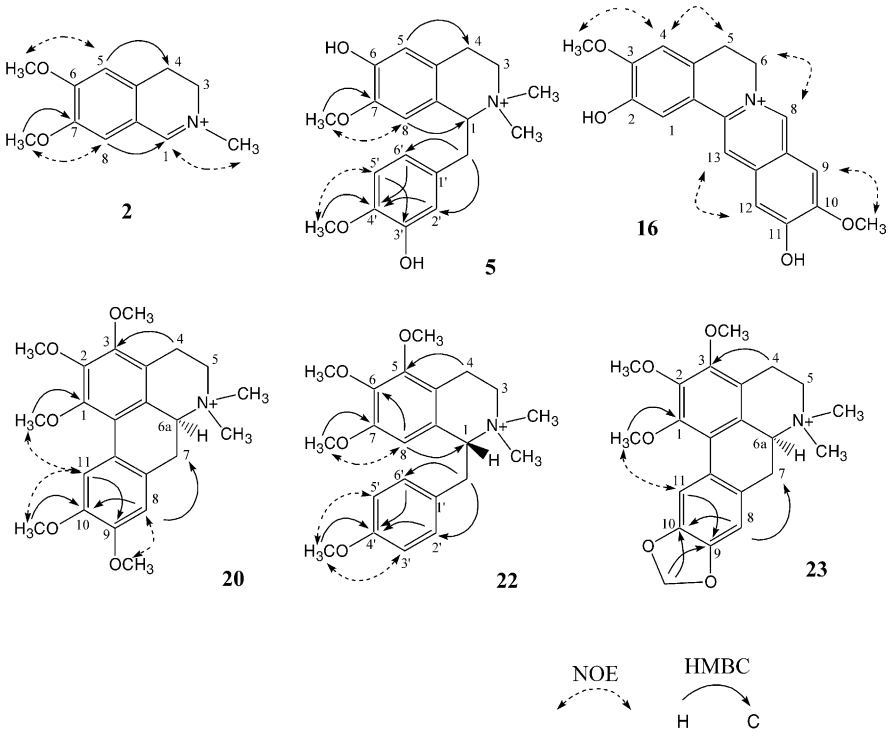



Fig. 1. HMBC and NOE interactions observed for **2**, **5**, **16**, **20**, **22** and **23**.

Compound **5**, termed xylopinidine, was obtained as colorless amorphous powder, having a molecular formula of $C_{20}H_{26}NO_4$. The UV, $^1H$ and $C^{13}$ NMR spectra of **5** (Table 1) resembled these of (+)-tembetarine (**8**), suggesting that **5** was a 6,7,3′,4′-tetrasubstituted tetrahydrobenzylisoquinoline alkaloid. Measuring its various 2D-NMR spectra provided further support for the structure of this compound. All methyl, methylene and methine protons and carbons were assigned from analysis of the $^1H$-$^1H$ COSY, HMQC and HMBC spectra. The presence of two singlet protons ($\delta$ 5.88 and 6.74) and an HMBC correlation (Fig. 1) from one of the protons ($\delta$ 5.88) to C-1 ($\delta$ 73.79), and from another proton ($\delta$ 6.74) to C-4 ($\delta$ 23.98) revealed that they were bound to C-8 and C-5, respectively. An HMBC correlation was also observed from H-$\alpha$ ($\delta$ 3.00 and 3.78) to two aromatic carbons ($\delta$ 117.77 and 122.19), and the presence of three aromatic protons combined with C-2′, C-5′ and C-6′ was noted having an ABX spin system. Therefore, two methoxyl and two hydroxyl groups are substituents at C-6, C-7, C-3′ and C-4′. From the HMBC and NOE experiments, signals at $\delta$ 3.42 and 3.83 were assigned to two methoxyl groups on C-7 and C-4′, respectively; hence two hydroxyl groups must bind to C-6 and C-3′. Accordingly, the structure of the new compound was elucidated as shown. The optical rotation of **5** (sodium D line) was near zero, indicating that it has either a very small optical rotation or is near racemic. The CD spectrum of **5**, however, showed no Cotton effect, suggesting that it is racemic.

Compound **22** was obtained as an amorphous powder, having a molecular formula of $C_{22}H_{30}NO_4$, and its UV, $^1H$ and $^{13}C$ NMR spectra (Table 1) suggested that it was also a tetrahydrobenzylisoquinoline alkaloid. The

Table 1
$^{13}C$ NMR spectral data for compounds **5** in acetone-*d*6 and **22** in $CDCl_3$ (125 MHz)

| C | 5 | 22 |
|---|---|---|
| 1 | 73.79 | 72.66 |
| 3 | 55.70 | 54.92 |
| 4 | 23.98 | 19.29 |
| 4a | 121.89 | 113.15 |
| 5 | 115.56 | 150.78 |
| 6 | 147.67[a] | 141.80 |
| 7 | 146.50 | 152.28 |
| 8 | 112.69 | 107.56 |
| 8a | 121.89 | 124.39 |
| α | 38.17 | 37.58 |
| 1′ | 129.41 | 125.90 |
| 2′ | 117.77 | 131.30 |
| 3′ | 147.74[a] | 114.34 |
| 4′ | 147.85[a] | 159.18 |
| 5′ | 112.54 | 114.34 |
| 6′ | 122.19 | 131.30 |
| N-$CH_3$ | 51.54 | 51.10 |
| N-$CH_3$ | 52.94 | 51.76 |
| 5-$OCH_3$ | | 60.69[a] |
| 6-$OCH_3$ | | 60.89[a] |
| 7-$OCH_3$ | 55.84 | 55.64 |
| 4′-$OCH_3$ | 56.38 | 55.34 |

[a] Values with the same superscript are interchangeable.

doublets at $\delta$ 6.80 and 6.90 (each 2H, *d*, $J = 8.5$ Hz) were assigned to 3′, 5′ and 2′, 6′-H of a *p*-substituted benzene moiety, with the singlet proton signal at $\delta$ 5.61 (HMBC correlation to C-1 also observed) to the proton at C-8, as well as the signals at $\delta$ 3.42, 3.77, 3.83, and 3.93 being correlated with the four methoxyl groups at C-7, C-4′, C-5, and C-6, using NOE and HMBC spectral analysis (Fig. 1). Accordingly, **22** was *N*,*N*-dimethylanomurine. The absolute configuration of C-1 was determined to be in the *R* form, because the HPLC analysis of **22** with a CD detector gave a negative Cotton effect at 280 and 240 nm (Moriyasu et al., 1997).

Compound **16** was isolated as pale yellow crystalline solid, mp. 243–247 °C, having a molecular formula of $C_{19}H_{18}NO_4$. The UV and $^1$H NMR spectra of **16** resembled those of dehydrodiscretine (**18**), suggesting it to be a 2,3,10,11-substituted pseudoprotoberberine alkaloid. Its $^1$H NMR spectrum demonstrated six singlets for aromatic protons at $\delta$ 7.00, 7.38, 7.52, 7.59, 8.34, and 9.20, two signals for aromatic methoxyl groups at $\delta$ 3.96 and 4.09, and two triplets for methylenes at $\delta$ 3.22 and 4.75 ($J = 6.5$ Hz). The NOE experiment (Fig. 1) suggested that **16** was dehydrocoreximine. This was confirmed by comparison of spectral data of coreximime obtained from **16** by reduction with $NaBH_4$, as well as with that described in the literature (Ohiri et al., 1983).

Compound **23** was isolated as an amorphous powder, and its HR-SIMS established the composition $C_{22}H_{26}NO_5$. It showed a UV maxima at 283 and 309 nm. Its $^1$H NMR spectrum demonstrated two singlets for aromatic protons at $\delta$ 7.75 and 6.88, three resonances corresponding to aromatic methoxyl groups at $\delta$ 3.77, 3.96, and 3.97, and two doublets for a methylenedioxyl group at $\delta$ 5.98 and 5.99 ($J = 1.5$ Hz). The singlet proton at $\delta$ 7.75 appeared downfield for an aromatic hydrogen. Taken together, these findings suggested that this compound is an aporphine alkaloid. HMBC correlations (ex. from the proton at $\delta$ 6.88 to C-7) and a NOE experiment (Fig. 1) indicated that **23** was the *N*-methyl derivative of phoebine. The absolute configuration of C-6a was determined to be in *S* form, since the HPLC analysis of **23** with CD detection gave a negative Cotton effect at 280 nm and a positive Cotton effect at 240 nm (Ringdahl et al., 1981).

Compound **20** had an UV spectra which resembled that of **23**. Other spectral data [$^1$H and $^{13}$C NMR (Table 2)] also suggested **20** was a 1,2,3,9,10-substituted aporphine alkaloid. HMBC correlations (ex. from the proton at $\delta$ 6.99 to C-7) and a NOE experiment (Fig. 1) indicated that **20** was *N*-methylpurpuerine. The absolute configuration of C-6a was also determined to be in the *S* form, because the HPLC analysis of **20** with CD detection gave a negative Cotton effect at 280 nm and a positive Cotton effect at 240 nm (Ringdahl et al., 1981). **20** was previously known as a synthetic compound (Ronsh et al., 1983) but not as naturally occurring.

Table 2
$^{13}$C NMR spectral data for compounds **20** and **23** in $CDCl_3$ (125 MHz)

| C | **20** | **23** |
|---|---|---|
| 1 | 151.27 | 151.48 |
| 2 | 146.95[c] | 146.89[c] |
| 3 | 149.66[c] | 149.81[c] |
| 3a | 118.04 | 117.74 |
| 4 | 19.52 | 19.52 |
| 5 | 61.75 | 61.76 |
| 6a | 70.36 | 70.20 |
| 7 | 29.05 | 29.71 |
| 7a | 122.91[b] | 121.85[b] |
| 8 | 111.84 | 108.71 |
| 9 | 148.81 | 147.08[d] |
| 10 | 148.49 | 147.75[d] |
| 11 | 111.14 | 108.39 |
| 11a | 123.47[b] | 123.31[b] |
| 11b | 123.73[b] | 124.12[b] |
| 11c | 121.93 | 124.08[b] |
| N-$CH_3$ | 43.44 | 43.42 |
| N-$CH_3$ | 54.34 | 54.27 |
| 1-$OCH_3$ | 60.72[a] | 60.75[a] |
| 2-$OCH_3$ | 60.89[a] | 60.9[a] |
| 3-$OCH_3$ | 61.06[a] | 61.00[a] |
| 9-$OCH_3$ | 56.12 | |
| 10-$OCH_3$ | 56.12 | |
| $OCH_2O$ | | 101.33 |

[a–c]Values with the same superscript are interchangeable

## 3. Experimental

### 3.1. General

Melting points were determined by a Yanaco MP-500D micro melting point apparatus and are uncorrected. IR spectra were obtained on a Shimadzu FTIR-8200 IR spectrometer, UV spectra were recorded on Shimadzu UV-2500PC spectrophotometer. SIMS and HR-SIMS were obtained with a Hitachi M-4100 spectrometer, glycerol was used as the matrix. Optical rotations were measured on a JASCO DIP-370 digital polarimeter and CD spectra on Shimadzu-AVIV 62 A DS circular dichroism spectrometer. $^1$H (500 and 300 MHz) and $^{13}$C (125 MHz) NMR experiments were performed on a Varian VXR-500 (500 MHz) and Varian Gemini-300 spectrometer and a chemical shifts were referenced to internal TMS. HPLC conditions were follows: column, Cosmosil AR-II ODS, 6×150 mm, Nacalai tesque (20×250 mm for preparative); mobile phase, $CH_3CN$ (MeOH for repreparative): 0.2M 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).

### 3.2. Plant material

The root and bark tissues of *Xylopia parviflora* were collected in the Kwale district in Kenya. This plant was

identified and authenticated by two of the authors, Mr. S. G. Mathenge and Mr. P. B. Chalo Mutiso. Voucher specimens of this plant were deposited both in Kobe Pharmaceutical University and University of Nairobi.

### 3.3. Extraction and isolation

Dried root and bark tissues of *X. parviflora* (each 370 g and 210 g) were finely cut and individually extracted with hot MeOH. The resulting MeOH extracts were individually evaporated under reduced pressure and each residue (41 g and 31 g), respectively, was reextracted with 2.5% aq. tartaric acid. Each acidic solution was subjected to conventional isolation methods for secondary and tertiary alkaloids (each 570 mg and 1350 mg), using ion-pair extraction with sodium perchlorate for quaternary alkaloids (each 440 mg and 170 mg) as devised in our laboratory (Moriyasu et al., 1993). The quaternary alkaloid fractions was then subjected to ion-pair preparative HPLC, and re-preparative HPLC using another solvent, supplied as necessary. The root tissue gave 22 alkaloids as perchlorates, **1** (1.2 mg), **2** (3.8 mg), **3** (1 mg), **4** (1.4 mg), **5** (4.1 mg), **6** (6.4 mg), **7** (2.9 mg), **8** (9.8 mg), **9** (2.5 mg), **10** (32.2 mg), **12** (12.2 mg), **13** (3.9 mg), **14** (3.8 mg), **15** (2.2 mg), **16** (1.2 mg), **17** (3.3 mg), **18** (2.1 mg), **19** (3.4 mg), **20** (3.3 mg), **21** (1 mg), **22** (4.7 mg) and **23** (3.5 mg). The bark tissue gave thirteen alkaloid as perchlorates, **1** (1 mg), **5** (4.4 mg), **6** (13.5 mg), **8** (12 mg), **10** (42.4 mg), **11** (1.4 mg), **12** (16.9 mg), **13** (4.6 mg), **17** (2.1 mg), **18** (7.5 mg), **19** (2.1 mg), **20** (4.7 mg) and **23** (3.8 mg).

### 3.4. Spectral data of compounds

#### 3.4.1. 3,4-dihydro-6,7-dimethoxy-2-methyl-isoquinolinium (2) perchlorate

Colorless crystalline. Mp. 184.5–187.5 °C, HR-SIMS: 206.1176 (206.1180 calcd for $C_{12}H_{16}NO_2$). UV $\lambda_{max}^{MeOH}$ nm (log $\epsilon$): 248 (3.92), 309 (3.59), 361 (3.52). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1664, 1647, 1607, 1572, 1524, 1468, 1346, 1300, 1123, 1090. $^1$H NMR (500 MHz, acetone-$d_6$): $\delta$ 3.36 (2H, *t*, $J$ = 8.0 Hz, $H_2$-4), 3.88, 4.02 (each 3H, *s*, $OCH_3$ × 2), 3.92 (3H, *s*, N-$CH_3$), 4,20 (2H, *t*, $J$ = 8.0 Hz, $H_2$-3), 7.22 (1H, *s*, H-5), 7.46 (1H, *s*, H-8), 9.03 (1H, *s*, H-1). $^{13}$C NMR (125 MHz, acetone-$d_6$): $\delta$ 25.70 (C-4), 47.68 (N-$CH_3$), 50.46 (C-3), 56.56, 56.96 ($OCH_3$-7, $OCH_3$-6), 112.18 (C-5), 115.95 (C-8), 118.06 (C-8a), 133.36 (C-4a), 149.82 (C-7), 158.62 (C-6), 165.97 (C-1).

#### 3.4.2. Xylopinidine (5) perchlorate

Colorless amorphous powder. $[\alpha]_D^{22°}$: 0° (MeOH, *c* 0.36), HR-SIMS: 344.1850 (344.1860 calcd for $C_{20}H_{26}NO_4$). UV $\lambda_{max}^{MeOH}$ nm (log $\epsilon$): 282 (3.68). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3197(OH), 1647, 1616, 1595, 1514, 1443. $^1$H NMR (500 MHz, acetone-$d_6$): $\delta$ 3.00 (1H, *dd*, $J$ = 10.0, 12.5 Hz, $H_A$-α), 3,26 (2H, *m*, $H_2$-4), 3.37 (3H, *s*, N-$CH_3$), 3.42 (3H, *s*, $OCH_3$-7), 3.64 (3H, *s*, N-$CH_3$), 3.78 (1H, *br dd*, $J$ = 3.5, 12.5 Hz, $H_B$-α), 3.83 (3H, *s*, $OCH_3$-4′), 3.85 (1H, *m*, $H_A$-3), 4.10 (1H, *ddd*, $J$ = 7.5, 11.5, 13.0 Hz, $H_B$-3), 4.82 (1H, *dd*, $J$ = 3.5, 10.0 HZ, H-1), 5.88 (1H, *s*, H-8), 6.54 (1H, *dd*, $J$ = 2.0, 8.0 Hz, H-6′), 6.66 (1H, *d*, $J$ = 2.0 Hz, H-2′), 6,74 (1H, *s*, H-5), 6.89 (1H, *d*, $J$ = 8.0 Hz, H-5′). For $^{13}$C NMR: Table 1. CD: No cotton effects (MeOH, *c* 0.21).

#### 3.4.3. Dehydrocoreximine perchlorate (16)

Pale yellow crystalline solid. Mp. 243–247 °C. HR-SIMS: 324.1255 (324.1234 calcd for $C_{19}H_{18}NO_4$). UV $\lambda_{max}^{MeOH}$ nm (log $\epsilon$): 222 (4.23), 292 (4.54), 320 (4.48), 380 (4.11). IR $\nu_{max}^{KBr}$ $cm^{-1}$ : 3400 (OH), 1612, 1576, 1522, 1495, 1456, 1385, 1285, 1215. $^1$H NMR (500 MHz, $CD_3OD$) $\delta$ 3.22 (2H, *t*, $J$ = 6.5 Hz, $H_2$-5), 3.96 (3H, *s*, $OCH_3$-3), 4.09 (3H, *s*, $OCH_3$-10), 4.75 (2H, *t*, $J$ = 6.5 Hz, $H_2$-6), 7.00 (1H, *s*, H-4), 7.38 (1H, *s*, H-1), 7.52 (1H, *s*, H-12), 7.59 (1H, *s*, H-9), 8.34 (1H, *s*, H-13), 9.20 (1H, *s*, H-8).

#### 3.4.4. Preparation of coreximin from dehydrocoreximine (16)

A crude sample mainly containing dehydrocoreximine (**16**) (5 mg) was dissolved in MeOH, and $NaBH_4$ added slowly stirring. After refluxing for 30 min, the mixture was diluted with water, then neutralized to pH 7 with 5% aq. HCl. This solution was evaporated under reduced pressure and the residue (water solution) was basified with $NaHCO_3$, and extracted with $CHCl_3$ (3 × 20 ml). The $CHCl_3$ exracts were combined, dried (anhydr $NaSO_4$), filtered and evaporated in vacuo to leave a residue (3.4 mg). The residue was subjected to preparative TLC ( $CHCl_3$/MeOH/$NH_3$aq = 9 ml/1 ml/2 drops ), to afford coreximine (1.1 mg) as a colorless amorphous powder. HR-EIMS: 327.1466 (327.1470 calcd for $C_{19}H_{21}NO_4$). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.86 (3H, *s*, $OCH_3$), 3.88 (3H, *s*, $OCH_3$), 6.55 (1H, *s*, H-12), 6.59 (1H, *s*, H-4), 6.71 (1H, *s*, H-9), 6.82 (1H, *s*, H-1).

#### 3.4.5. N-methylpurpuerine (20)

Colorless crystalline solid. Mp. 187.5–190.0 °C; $[\alpha]_D^{22°}$: +25.1° (MeOH, *c* 0.51), HR-SIMS: 400.2114 ( 400.2123 calcd for $C_{23}H_{30}NO_5$). UV $\lambda_{max}^{MeOH}$ nm (log $\epsilon$): 281 (4.01), 303 (4.00). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1608, 1514, 1460, 1418, 1398, 1267. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 2.97 (1H, *t*, $J$ = 13.5 Hz, $H_A$-7), 3,14 (2H, *m*, $H_2$-4), 3.17 (3H, *s*, N-$CH_3$), 3.38 (1H, *dd*, $J$ = 4.0, 13.5 Hz, $H_B$-7), 3.54 (1H, *m*, $H_A$-5), 3.56 (3H, *s*, N-$CH_3$), 3.76 (3H, *s*, $OCH_3$-1), 3.90 (3H, *s*, $OCH_3$-10), 3.94 (3H, *s*, $OCH_3$-9), 3.97, 3.98 (each 3H, *s*, $OCH_3$-2, 3), 4.11 (1H, *m*, $H_B$-5), 4.29 (1H, *dd*, $J$ = 4.0, 13.5 Hz, H-6a), 6.99 (1H, *s*, H-8), 7.87 (1H, *s*, H-11). For $^{13}$C NMR spectral analysis, see Table 2.

*3.4.6. N,N-Dimethylanomurine (**22**)*

Colorless amorphous powder. $[\alpha]_D^{22^\circ}$: −26.3 ° (MeOH, *c* 0.32), HR-SIMS : 372.2148 (372.2173 calcd for $C_{22}H_{30}NO_4$). UV $\lambda_{max}^{MeOH}$ nm (log $\epsilon$): 277 (3.49), 283 (3.47). IR $\nu_{max}^{KBr}$ $cm^{-1}$; 1636, 1514, 1497. $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 2.85 (1H, *dd*, *J* = 10.0, 13.0 Hz, $H_A$-α), 3.00 (1H, *m*, $H_A$-4), 3.11 (1H, *m*, $H_B$-4), 3.25 (3H, *s*, N-$CH_3$), 3.42 (3H, *s*, $OCH_3$-7), 3.55 (3H, *s*, N-$CH_3$), 3.62 (1H, *dd*, *J* = 4.0, 13.0 Hz, $H_B$-α), 3.66 (2H, *m*, $H_2$-3), 3.77 (3H, *s*, $OCH_3$-4′), 3.83, 3.93 (each 3H, *s*, $OCH_3$-5, 6), 4.71 (1H, *dd*, *J* = 4.0, 10.0 HZ, H-1), 5.61 (1H, *s*, H-8), 6.80 (2H, *d*, *J* = 8.5 Hz, H-3′, 5′), 6.90 (2H, *d*, *J* = 8.5 Hz, H-2′, 6′). For $^{13}C$ NMR spectral analysis, see Table 1.

*3.4.7. N-Methylphoebine (**23**)*

Colorless amorphous powder. $[\alpha]_D^{22^\circ}$: +37.1 ° (MeOH, *c* 0.70), HR-SIMS: 384.1828 (384.1809 calcd for $C_{22}H_{26}NO_5$). UV $\lambda_{max}^{MeOH}$ nm (log $\epsilon$): 283 (4.03), 309 (4.02). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1647, 1608, 1514, 1460. $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 2.94 (1H, *t*, *J* = 13.5 Hz, $H_A$-7), 3.14 (2H, *m*, $H_2$-4), 3.17 (3H, *s*, N-$CH_3$), 3.26 (1H, *dd*, *J* = 3.5, 13.5 Hz, $H_B$-7), 3.53 (1H, *m*, $H_A$-5), 3.56 (3H, *s*, N-$CH_3$), 3.77 (3H, *s*, $OCH_3$-1), 3.96, 3.97 (each 3H, *s*, $OCH_3$-2, 3), 4.15 (1H, *td*, *J* = 3.0, 13.0 Hz, $H_B$-5), 4.27 (1H, *dd*, *J* = 3.5, 13.5 Hz, H-6a), 5.98, 5.99 (each 1H, *d*, *J* = 1.5 Hz, -$OCH_2O$-), 6.88 (1H, *s*, H-8), 7.75 (1H, *s*, H-11). For $^{13}C$ NMR spectral analysis, see Table 2.

## Acknowledgements

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

## References

Borkowski, P.R., Horn, J.S., Rapoport, H., 1978. Role of 1,2-dehydroreticulinium ion in the biosynthetic conversion of reticuline to thebaine. J. Am. Chem. Soc. 100, 276–281.

Brophy, J.J., Goldsack, R.J., Forster, P.I., 1998. The essential oils of the Australiane species of Xylopia (Annonaceae). J. Essent. Oil Res. 10, 469–472.

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.

Harrigan, G.G., Bolzani, V.da S., Gunatilaka, A.A.L., Kingston, D.G.I., 1994a. Kaurane and trachylobane diterpenes from *Xylopia aethiopica*. Phytochemistry 36, 109–113.

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

Hughes, D.W., Holland, H.L., McLean, D.B., 1976. $^{13}C$ magnetic resonance spectra of some isoquinoline alkaloids and related model compounds. Can. J. Chem. 54, 2252–2260.

Jirovetz, L., Buchbauer, G., Ngassoum, M.B., 1997. Investigation of the essential oils from the dried fruits of *Xylopia aethiopica* (West African "Peppertree") and *Xylopia parviflora* from Cameroon. Ernaehrung (Vienna) 21 (7/8), 324–325.

Johns, S.R., Lamberton, J.A., Sioumis, A.A., 1968. Alkaloids of *Xylopia papuana*. Aust. J. Chem. 21, 1383–1386.

Jossang, A., Lebceuf, M., Cave, A., Pusset, J., 1991. Alkaloids of the Annonaceae. 96. Dehydroxylopine and dehydrocorytenchine, novel isoquinoline alkaloids from *Xylopia vieillardi*. J. Nat. Prod. 54, 466–472.

Kato, A., Moriyasu, M., Ichimaru, M., Nishiyama, Y., Juma, F.D., Nganga, J.N., Mathenge, S.G., Ogeto, J.O., 1995. Examination of alkaloidal constituents of *Zanthoxylum usambarense* by a combination of ion-pair extraction and ion-pair chromatography using sodium perchlorate. Phytochem. Anal. 6, 89–95.

Koshiyama, H., Ohkuma, H., Kawaguchi, H., Hsu, H., Chen, Y., 1970. Isolation of 1-(*p*-hydroxybenzyl)-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline (demethylcoclaurine), an active alkaloid from *Nelumbo nucifera*. Chem. Pharm. Bull. 18, 2564–2568.

Lamaty, G., Menut, C., Bessiere, J.M., Zollo, P.H., Amvam, F., 1989. The essential oil of *Xylopia parviflora* (A. Rich) Benth. from Cameroon. J. Essent. Oil Res. 1, 247–248.

Lee, S., Chen, C., Huang, F., Chen, C., 1996. Two dibenzopyrrocoline alkaloids from *Litsea cubeba*. J. Nat. Prod. 59, 80–82.

Marsaioli, A.J., de Reis, F.A.M., Magalhaes, A.F., Ruveda, E.A., 1979. $^{13}C$ NMR analysis of aporphine alkaloids. Phytochemistry 18, 165–169.

Martins, D., Osshiro, E., Roque, N.F., Marks, V., Gottlieb, H.E., 1998. A sesquiterpene dimer from *Xylopia aromatica*. Phytochemistry 48, 677–680.

Menachery, M.D., Lavanier, G.L., Wetherly, M.L., 1986. Simple isoquinoline alkaloids. J. Nat. Prod. 49, 745–778.

Moriyasu, M., Ichimaru, M., Nishiyama, Y., Kato, A., 1993. The acquisition of alkaloids from plant materials by a combination of ion-pair extraction and preparative ion-pair HPLC using sodium perchlorate. Bunseki Kagaku 42, 659–665.

Moriyasu, M., Ichimaru, M., Nishiyama, Y., Kato, A., 1994a. Isolation of alkaloids from plant materials by the combination of ion-pair extraction and preparative ion-pair HPLC using sodium perchlorate. I Magnoliae cortex. Natural Medicines 48, 282–286.

Moriyasu, M., Ichimaru, M., Nishiyama, Y., Kato, A., 1994b. Isolation of alkaloids from plant materials by the combination of ion-pair extraction and preparative ion-pair HPLC using sodium perchlorate. II Sinomeni Caulis et Rhizoma. Natural Medicines 48, 287–290.

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

Nishiyama, Y., Moriyasu, M., Sonoda, M., Ichimaru, M., Iwasa, K., Kato, A., Mathenge, S.G., Juma, F.D., 2000. Isoquinoline alkaloids from *Monodora junodii*. Natural Medicines 54, 42.

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

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

Ronsch, H., Preiβ, A., Schreiber, K., Fernandez de Cordoba, H., 1983. Structure elucidation and carbon-13 NMR of the new aporphine alkaloid 3-hydroxyglaucine. Liebigs Annalen der Chemie 744–752.

Tanahashi, T., Su, Y., Nagakura, N., Nayeshiro, H., 2000. Quaternary isoquinoline alkaloids from *Stephania cepharantha*. Chem. Pharm. Bull. 48, 370–373.

Wu, J., Beal, J.L., Wu, W., Doskotch, R.W., 1980. Alkaloids of thalictrum. XXXII. Isolation and identification of alkaloids from *Thalictrum revolutum* DC. fruit. J. Nat. Prod. 43, 270–277.