Pergamon

PII: S0031-9422(96)00496-7

*Phytochemistry*, Vol. 43, No. 6, pp. 1385–1387, 1996

0031-9422/96 $15.00 + 0.00

# ALKALOIDS FROM *KOPSIA PAUCIFLORA*

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(*Received* 10 *May* 1996)

**Key Word Index**—*Kopsia* spp.; Apocynaceae; stem; indole alkaloids.

**Abstract**—Two new indole alkaloids, 12-methoxy-10-demethoxykopsidasinine and (+)-19-oxoeburnamine, in addition to 10 known alkaloids, were obtained from the stem extract of *Kopsia pauciflora*. The structures of the new alkaloids were established by spectral methods. Copyright © 1996 Elsevier Science Ltd

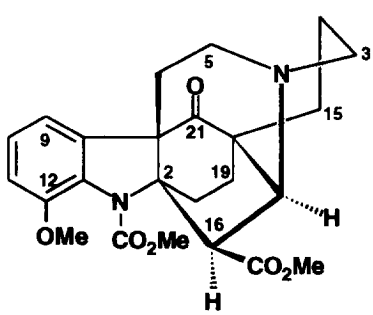
## INTRODUCTION

The genus *Kopsia* comprises some 30 species, distributed mainly over Southeast Asia, China and India [1, 2]. In continuation of our studies on Malaysian *Kopsia* species [3–11], we investigated the alkaloidal composition of the stem extract of *Kopsia pauciflora*, a species indigenous to North Borneo, and wish to report the presence of two new alkaloids. A previous study of the alkaloids of trunk-bark of this species yielded several eburnane-type alkaloids and some bisindoles of the pleiomutine type [12].

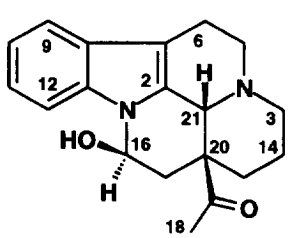
## RESULTS AND DISCUSSION

Extraction of the alkaloids in the usual manner, followed by extensive chromatography of the crude mixture, gave the following alkaloids, viz kopsinine (**1**), (−)-eburnamine (**2**), (+)-isoeburnamine (**3**), (+)-eburnamonine (**4**), norpleiomutine (**5**), *N*-methoxy carbonyl- 12-methoxy-$\Delta^{16,17}$-kopsinine (**6**), *N*-methoxy carbonyl-11,12-dimethenedioxykopsinaline (**7**), kopsamine *N*-oxide (**8**), *N*-methoxycarbonyl-11,12-dimethoxykopsinaline (**9**), *N*-methoxycarbonyl-12-methoxykopsinaline (**10**), 12-methoxy-10-demethoxykopsidasinine (**11**) and (+)-19-oxoeburnamine (**12**). The last two are new alkaloids.

Compound **11** was isolated as a light yellow oil, $[\alpha]_D$ −115° ($CHCl_3$, *c* 0.114). Its mass spectrum showed a $[M]^+$ at *m/z* 440, corresponding to the formula $C_{24}H_{28}N_2O_6$, with other major peaks at *m/z* 408 $[M - OMe - H]^+$ 380 $[M - CO_2Me - H]^+$ and 353 $[M - CO_2Me - CH_2 = CH_2]^+$. The UV spectrum was typical of a dihydroindole chromophore, while the IR spectrum revealed the presence of three carbonyl absorptions at 1745, 1726, and 1692 $cm^{-1}$, corresponding to ester, ketone and urethane functions, respectively. The $^1H$ NMR spectrum (Table 1) accounted for a total of 28 hydrogens, and the coupling pattern and chemical shifts of the aromatic protons were consistent with 12-methoxyl substitution [3, 11]. This is also supported by examination of the aromatic carbon chemical shifts. Three methoxyl absorptions were observed at $\delta$ 3.72, 3.74 and 3.83, attributable to ester, urethane and aromatic methoxyl groups, respectively. Another immediately distinguishable feature of the proton spectrum was a pair of AB doublets at $\delta$ 3.94 and 3.52 with $J = 9.5$ Hz, due to an isolated CHCH unit. Further analysis of the proton spectrum required application of COSY, which revealed the remaining fragments to be made up of two $CH_2CH_2$




**11**




**12**

Table 1. $^1$H and $^{13}$C NMR spectral data for compounds **11** and **12***

| Position | **11** | | **12** | |
|---|---|---|---|---|
| | $\delta_H$ | $\delta_C$ | $\delta_H$ | $\delta_C$ |
| 2 | — | 71.1 | — | 131.5 |
| 3 | 2.80 *m* | 54.5 | 2.36 *m* | 44.0 |
| | 2.90 *m* | | 2.49 *m* | |
| 5 | 2.76 *ddd* (13, 6, 1.5) | 44.3 | 3.22 *m* | 50.6 |
| | 2.98 *br dd* (13, 6) | | 3.22 *m* | |
| 6 | 1.56 *m* | 33.6 | 2.49 *m* | 16.8 |
| | 3.72 *m* | | 2.95 *m* | |
| 7 | — | 63.1 | — | 106.6 |
| 8 | — | 134.5 | — | 128.7 |
| 9 | 7.37 *dd* (7.8, 1) | 117.5 | 7.49 *dd* (6, 2) | 118.2 |
| 10 | 7.04 *dd* (8.3, 7.8) | 124.8 | 7.16 *m* | 120.4 |
| 11 | 6.85 *dd* (8.3, 1) | 113.1 | 7.19 *m* | 121.6 |
| 12 | — | 148.5 | 7.71 *dd* (6, 2) | 112.0 |
| 13 | — | 129.6 | — | 136.7 |
| 14 | 2.30 *m* | 29.0 | 1.43 *m* | 22.6 |
| | 2.36 *m* | | 1.43 *m* | |
| 15 | 1.21 *m* | 14.8 | 0.93 *br td* (13, 5) | 24.9 |
| | 1.31 *m* | | 2.04 *br d* (13) | |
| 16 | 3.94 *d* (9.5) | 49.2 | 5.62 *dd* (9, 5) | 76.3 |
| 17 | 3.52 *d* (9.5) | 66.7 | 1.70 *dd* (14, 9) | 42.0 |
| | | | 2.30 *m* | |
| 18 | 1.38 *m* | 30.0 | 2.36 *s* | 25.6 |
| | 1.84 *m* | | | |
| 19 | 1.33 *m* | 29.2 | — | 210.3 |
| | 1.53 *br dd* (9, 4) | | — | |
| 20 | — | 47.6 | — | 51.7 |
| 21 | — | 213.7 | 4.67 *s* | 54.8 |
| $CO_2$Me | 3.72 *s* | 51.8 | — | — |
| $CO_2$Me | — | 171.0 | — | — |
| NCO$_2$Me | 3.74 *s* | 52.3 | — | — |
| NCO$_2$Me | — | 152.9 | — | — |
| Ar-OMe | 3.83 *s* | 56.3 | — | — |

*$CDCl_3$, 270 MHz; assignments based on COSY and HETCOR.

and one $CH_2CH_2CH_2$. The presence of the relatively low-field pair of AB doublets, together with the observation of an unusually low-field ketonic carbon resonance ($\delta_C$ 213.7), are features reminiscent of the rare kopsidasinine-type skeleton [13, 14] and, in fact, comparison of the spectral data for compound **11** with that of kopsidasinine [13] and 10-demethoxykopsidasinine [14] confirms that **11** is 12-methoxy-10-demethoxykopsidasinine.

Compound **12** was obtained as an amorphous powder, $[\alpha]_D$ + 83° ($CHCl_3$, c 0.058). Its mass spectrum showed a $[M]^+$ at *m/z* 310, corresponding to the formula $C_{19}H_{22}N_2O_2$ with other major peaks at *m/z* 292 $[M - H_2O]^+$, 267 $[M - MeCO]^+$ and 249 $[M - H_2O - MeCO]^+$. The strong *m/z* 249 peak (base) is typical of eburnane-type compounds, such as eburnamine, isoeburnamine, eburnamenine and 16-*O*-alkyleburnamine derivatives [9, 10] and corresponds with loss of water followed by loss of the 20-ethyl side-chains in these compounds. The occurrence of the same peak in **12** afforded the first indication that it was the 20-acetyl congenor of eburnamine. This was supported by both the $^1$H and $^{13}$C NMR spectral data (Table 1), which showed the spectra of **12** to be essentially similar to that of eburnamine except for replacement of the signals due to the 20-ethyl group by an acetyl group ($\delta_{H\text{-}18}$ 2.36; $\delta_{C\text{-}19}$ 210.3; $\delta_{C\text{-}18}$ 25.6). Compound **12** is, therefore, 19-oxoeburnamine. The configuration at C-20 and C-21 was assumed to follow that of the other eburnan-type compounds occurring in the plant, viz **2**, **3** and **4**, assuming that they share a common biogenetic origin. The configuration of the remaining stereocentre, viz position 16 can be deduced from the coupling constants for H-16 ($\delta$ 5.62, *dd*, $J = 9$ and 5 Hz), which is diagnostic of eburnan-type compounds belonging to the eburnamine series (16-$\beta$OH), as opposed to those of the diastereomeric isoeburnamine or epieburnamine series (16-$\alpha$OH; $J = 4$ and 2 Hz) [9]. From the preceding considerations, the structure and absolute configuration is as shown for **12**.

## EXPERIMENTAL

*Plant material.* This was collected in Sabah, Malaysia. Herbarium voucher specimens are deposited at the Herbarium of the Sabah Forest Department, Sandakan, Sabah, Malaysia.

*Extraction and isolation.* Extraction of alkaloids was carried out in the usual manner [11] to give a total crude alkaloid yield of *ca* 1.8 g kg$^{-1}$ for the stem. Alkaloids were isolated by CC and centrifugal TLC on silica gel. Solvent systems used for CC were $CHCl_3$ – MeOH and $Et_2O$ – EtOAc. Solvent systems used for centrifugal TLC were $Et_2O$, $Et_2O$ – EtOAc (3:1), $Et_2O$ – hexane (2:1), $CHCl_3$ and 3% MeOH – $CHCl_3$. The yields (g kg$^{-1}$) of the alkaloids from the stem extract were: **1** (0.204), **2** (0.016), **3** (0.008), **4** (0.002), **5** (0.006), **6** (0.016), **7** (0.028), **8** (0.088), **9** (0.017), **10** (0.003), **11** (0.006) and **12** (0.002).

12-Methoxy-10-demethoxykopsidasinine (**11**). $[\alpha]_D$ −115° ($CHCl_3$, *c* 0.114). UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 216 (4.30), 249 (3.82), 280 (2.98), 287 (3.04). EIMS (probe) 70 eV, *m/z* (rel. int.): 440 $[M]^+$ (97), 408 (100), 380 (31), 353 (15), 122 (39), 109 (41). $^1$H and $^{13}$C NMR: Table 1.

(+)-19-*Oxoeburnamine* (**12**). $[\alpha]_D$ +83° ($CHCl_3$, *c* 0.058). UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 202 (3.81), 229 (4.0), 282 (3.39), 292 (3.25). EIMS (probe) 70 eV, *m/z* (rel. int.): 310 $[M]^+$ (10), 292 (22), 277 (7), 267 (12), 249 (100), 239 (6), 221 (10), 206 (9), 193 (12). $^1$H and $^{13}$C NMR: Table 1.

*Acknowledgments*—We thank the University of Malaya and IRPA for financial support of this work, and Dr K. M. Wong, Leopold Madani and Julius Kulip of the Sabah Forest Department for assistance during the collection of plant material.

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