Pergamon

0031-9422(94)00938-4

Phytochemistry, Vol. 39, No. 2, pp. 469–471, 1995

0031-9422/95 \$9.50 + 0.00

DEHYDROPLEIOCARPINE ALKALOIDS FROM *KOPSIA PROFUNDA*

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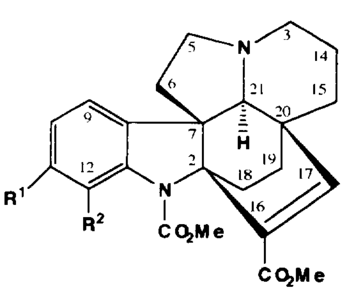
(*Received* 5 *September* 1994)

Key Word Index—*Kopsia profunda*; Apocynaceae; indole alkaloids.

Abstract—Several new alkaloids of the pleiocarpine type, namely N_1-methoxycarbonyl-12-hydroxy-$\Delta^{16,17}$-kopsinine, N_1-methoxycarbonyl-11,12-methylenedioxy-$\Delta^{16,17}$-kopsinine *N* (4) oxide and N_1-methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine *N* (4) oxide, in addition to N_1-methoxycarbonyl-11,12-methylenedioxy-$\Delta^{16,17}$-kopsinine, N_1-methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine and kopsinine have been isolated from the leaves and stem of *Kopsia profunda*.

INTRODUCTION

As part of our studies on Malaysian *Kopsia* species [1–7] we investigated the alkaloidal composition of *Kopsia profunda* Markgraf and reported the presence of N_1-methoxycarbonyl-11,12-methylenedioxy-$\Delta^{16,17}$-kopsinine (**1**) and N_1-methoxycarbonyl-12-methoxy-$\Delta^{16,17}$-kopsinine (**2**) as the major alkaloids present in the stem extract. We now report the full alkaloidal composition of the stem as well as leaf extracts including the occurrence of several new alkaloids (**3**–**5**). The alkaloidal composition of the leaf and stem was found to be similar, both leaf and stem ethanol extracts gave alkaloids **1**–**6** although the relative yields of the various alkaloids in the stem and leaf extracts are different (see Experimental). N_1-Methoxycarbonyl-12-hydroxy-$\Delta^{16,17}$-kopsinine (**3**) is a new alkaloid, differing from **1** and **2** in the nature of the aromatic substituent. The mass spectrum of **3** shows $[M]^+$ at *m/z* 410 consistent with the molecular formula $C_{23}H_{26}N_2O_5$, i.e. where an OMe function has been replaced by OH when compared with **2** ($C_{24}H_{28}N_2O_5$). This is confirmed by the ^1H NMR spectrum which showed that the aromatic methoxy signal is now absent and has been replaced by a singlet attributable to a phenolic OH at δ10.83 (disappears on deuteration). The presence of an OH function is further supported by the observation of a broad absorption band in the IR spectrum at *ca* 3400 cm^{-1} and by the presence of only three aromatic protons in the ^1H NMR spectrum (Table 1). The coupling pattern of the aromatic protons (δ6.82, *d*, $J = 7$ Hz, H-9; 7.00, *t*, $J = 7$ Hz, H-10; 6.79, *d*, $J = 7$ Hz, H-11), taken with the observed aromatic carbon resonances (Table 2), support the assignment of **3** as the 12-hydroxy congenor of **1** and **2**. Compounds **4** and **5** coeluted on column chromatography and could not be resolved by preparative TLC since the R_fs were similar in a variety of solvent systems tested. Eventually **4** and **5** were separated by repeated fractional recrystallization (diethyl ether–acetone) and were readily deduced to be the *N*-oxides of the alkaloids **1** and **2**, respectively, from the spectral data, in particular the characteristic downfield shifts of the carbon resonances for carbons 3,5 and 21 when compared to those of **1** and **2**. Further confirmation was provided by the ready reduction (ferrous sulphate) of **4** and **5** to **1** and **2**, respectively. Alkaloids **1**–**5** are members of the small group of dehydropleiocarpine alkaloids, of which only kopsidasine[8] and kopsijasmine [9] represent previously known examples.



	R^1	R^2	
1	O — CH_2 — O		
2	H	OMe	
3	H	OH	
4	O — CH_2 — O,		N(4)→O
5	H	OMe,	N(4)→O

EXPERIMENTAL

Plant material. Collected from Terengganu, Malaysia, and voucher specimens (KL3636) are deposited at the Herbarium, Department of Chemistry, University of Malaya and at Rijksherbarium, Leiden.

Extraction and isolation. Extraction of plant material was carried out in the usual manner which has been described previously [1]. The alkaloids were isolated by

Table 1. ^{1}H NMR spectral data for **1**–**5** (270 MHz, CDCl$_3$)

H	**1**	**2**	**3**	**4**	**5**
3	2.96–3.06 *m*	2.91–3.04 *m*	3.00–3.10 *m*	3.72–3.90 *m*	3.75–3.84 *m*
	2.96–3.06 *m*	2.91–3.04 *m*	3.00–3.10 *m*	3.54 *td* (13, 4)	3.55 *td* (13, 4)
5	2.40–2.62 *m*	2.32–2.58 *m*	2.40–2.60 *m*	3.00–3.26 *m*	3.03–3.24 *m*
	2.66 *t* (8)	2.62 *t* (8)	2.69 *t* (8)	3.00–3.26 *m*	3.03–3.24 *m*
6	1.54–1.72 *m*	1.60–1.72 *m*	1.58–1.96 *m*	2.25–2.50 *m*	2.44 *ddd* (14, 12, 8)
	2.40–2.62 *m*	2.32–2.58 *m*	2.40–2.60 *m*	2.57 *dd* (14, 7)	2.67 *dd* (14, 8)
9	6.75 *d* (7.5)	6.85 *dd* (7.5, 1.5)	6.82 *d* (7)	7.68 *d* (8)	7.84 *d* (7)
10	6.52 *d* (7.5)	6.92 *t* (7.5)	7.00 *t* (7)	6.59 *d* (8)	7.04 *t* (7)
11	—	6.74 *dd* (7.5, 1.5)	6.79 *d* (7)	—	6.86 *d* (7)
14	1.18–1.37 *m*	1.10–1.30 *m*	1.10–1.34 *m*	1.80–2.14 *m*	1.75–2.08 *m*
	1.75–1.94 *m*	1.76–1.90 *m*	1.58–1.96 *m*	1.80–2.14 *m*	1.75–2.08 *m*
15	1.54–1.72 *m*	1.44–1.58 *m*	1.58–1.96 *m*	1.44–1.76 *m*	1.35–1.70 *m*
	1.75–1.94 *m*	1.76–1.90 *m*	1.58–1.96 *m*	1.80–2.14 *m*	1.75–2.08 *m*
17	6.83 *s*	6.76 *s*	6.86 *s*	6.58 *s*	6.56 *s*
18	1.43 *td* (13, 3)	1.36 *td* (13, 3)	1.43 *td* (13, 3)	1.66–1.76 *m*	1.35–1.70 *m*
	2.03 *dt* (13, 3)	1.96 *dt* (13, 3)	1.99–2.14 *m*	1.80–2.14 *m*	1.75–2.08 *m*
19	1.18–1.37 *m*	1.10–1.30 *m*	1.10–1.34 *m*	1.44–1.76 *m*	1.35–1.70 *m*
	1.18–1.37 *m*	1.10–1.30 *m*	1.10–1.34 *m*	1.44–1.76 *m*	1.35–1.70 *m*
21	3.24 *s*	3.16 *s*	3.32 *s*	3.63 *s*	3.62 *s*
–OCH$_2$O–	5.92 *d* (1.5)	—	—	5.96 *br s*	—
	5.95 *d* (1.5)				
Ar-OMe	—	3.78 *s*	—	—	3.85 *s*
Ar-OH	—	—	10.83 *s*	—	—
OMe	3.73 *s*	3.68 *s*	3.75 *s*	3.78 *s*	3.78 *s*
OMe	3.77 *s*	3.72 *s*	3.82 *s*	3.82 *s*	3.82 *s*

Table 2. ^{13}C NMR spectral data for **1**–**5** (67.8 MHz, CDCl$_3$)

C	**1**	**2**	**3**	**4**	**5**
2	71.7	72.3	71.4	71.1	71.6
3	47.2	47.2	47.1	64.3	64.3
5	50.2	50.2	50.0	64.7	64.7
6	38.7	37.8	38.2	35.9	35.1
7	62.8	63.4	62.9	63.1	63.6
8	133.9	140.7	140.1	133.6	138.0
9	115.0	114.9	117.7	119.1	118.4
10	103.7	124.5	126.7	104.4	125.0
11	148.7	112.8	113.3	149.3	113.6
12	124.1	148.7	145.5	123.5	147.5
13	134.9	134.9	134.8	137.0	136.9
14	16.1	16.1	16.0	20.6	20.5
15	25.7	25.8	26.0	24.7	24.8
16	[a]	130.1	126.1	131.1	129.6
17	143.2	143.2	143.6	138.7	138.6
18	33.8	33.8	33.7	32.2	32.1
19	32.1	31.9	32.0	31.6	31.6
20	38.2	37.9	38.7	40.7	40.5
21	69.3	69.4	68.9	84.1	83.5
–OCH$_2$O–	100.4	—	—	100.6	—
ArOMe	—	56.5	—	—	56.5
OMe	51.8	51.8	51.9	52.3	52.2
OMe	52.5	52.2	53.3	52.7	52.5
$\underline{C}O_2Me$	165.9	165.9	166.0	165.4	165.3
$N\underline{C}O_2Me$	153.3	153.8	156.0	153.4	153.9

[a] Not observed.

CC, prep. TLC and HPLC on silica gel. Solvent systems used for CC were CHCl$_3$ with increasing MeOH gradient and Et$_2$O with increasing EtOAc gradient. Solvent systems used for prep. TLC and HPLC were Et$_2$O–EtOAc (5:1) and 3% MeOH–CHCl$_3$, respectively. The yields (g kg^{-1}) of the alkaloids isolated were as follows: stem alkaloids, **1** (0.095), **2** (0.056), **3** (0.009), **4** (0.023), **5** (0.036) and **6** (0.023); leaf alkaloids, **1** (0.225), **2** (0.102), **3** (0.025), **4** (0.125), **5** (0.10) and **6** (0.6).

N$_1$-*Methoxycarbonyl*-12-*hydroxy*-$\Delta^{16,17}$-*kopsinine* (**3**). $[\alpha]_D$ − 121° (CHCl$_3$; *c* 0.04). UV (EtOH), λ_{max} nm (log ε): 218 (3.98), 248 (3.61), 290 (3.13). EIMS (probe) 70 eV, *m/z* (rel. int.): 410 $[M]^+$ (100), 374 (3), 351 (6), 329 (3), 218 (3), 143 (7), 138 (5), 109 (6) and 107 (5). HREIMS, $[M]^+$ found 410.1826, calcd for $C_{23}H_{26}N_2O_5$ 410.1842. ^{1}H and ^{13}C NMR: see Tables 1 and 2, respectively.

N$_1$-*Methoxycarbonyl*-11,12-*methylenedioxy*-$\Delta^{16,17}$-*kopsinine* N (4) *oxide* (**4**). $[\alpha]_D$ − 125° (CHCl$_3$; *c* 0.06). UV (EtOH), λ_{max} nm (log ε): 224 (4.29), 245 (3.88), 290 (2.97). FABMS nitrobenzylalcohol (NBA), *m/z*: found 455.14 $[MH]^+$ calcd for $C_{24}H_{26}N_2O_7 + H$ 455.18. ^{1}H and ^{13}C NMR: see Tables 1 and 2, respectively.

N$_1$-*Methoxycarbonyl*-12-*methoxy*-$\Delta^{16,17}$-*kopsinine* N (4) *oxide* (**5**). Mp 244–245°. $[\alpha]_D$ − 163° (CHCl$_3$; *c* 0.15). UV (EtOH), λ_{max} nm (log ε): 217 (4.42), 250 (3.99), 288 (3.30). FABMS (NBA) *m/z* found 441.16 $[MH]^+$, calcd for $C_{24}H_{28}N_2O_6 + H$ 441.20. ^{1}H and ^{13}C NMR: see Tables 1 and 2, respectively.

N_1-*Methoxycarbonyl*-11,12-*methylenedioxy*-$\Delta^{16,17}$-*kopsinine* (**1**) [1]. $[\alpha]_D$ $-180°$ ($CHCl_3$; *c* 0.17).

N_1-*Methoxycarbonyl*-12-*methoxy*-$\Delta^{16,17}$-*kopsinine* (**2**) [1]. $[\alpha]_D$ $-75°$ ($CHCl_3$; *c* 0.23).

Acknowledgement—We thank the University of Malaya and IRPA (04-07-04-139) for financial support of this work.

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