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A LIGNAN FROM *PIPER CHABA* STEMS†

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Abstract—A new lignan, epimers of [8*R*,8′*R*]-9-hydroxy,3,4-dimethoxy,3′,4′-methylene dioxy-9,9′ epoxy lignan, was isolated from the chloroform-soluble fraction of a crude alcoholic extract of *Piper chaba*. Its proposed structure was established from NMR and mass spectral evidences. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Earlier work [1, 2] on the aerial parts of *Piper chaba* resulted in the isolation of piperine, sylvatine, piperlonguminine, β-sitosterol and an alkaloid, piplartine. A recent review [3] on the biological activities of lignans of common occurrence in the genus *Piper*, prompted us to look for the presence of lignans/neolignans in *P. chaba*. We report herein, the isolation and structural elucidation of a new lignan from the aerial parts of *P. chaba*.

RESULTS AND DISCUSSION

The IR spectrum of **1** showed absorption bands at 3400, 1032 cm^{-1} (hydroxyl), 1610, 1450 cm^{-1} (aromatic) and 930 cm^{-1} (methylenedioxy). It analyzed for $C_{21}H_{24}O_6$ (EI mass spectrum *m/z* 372 $[M]^+$). The ^1H and ^{13}C NMR spectra (Tables 1 and 2) of **1** indicated that the compound was a dibenzyl butyrolactol [4–7]. The ^1H NMR spectrum (Table 1) showed an ABX-pattern of aromatic proton signals (δ 6.43–δ 6.77), two sharp singlets (δ 3.82, 3.83) due to aryl methoxyl groups and a broad singlet (δ 5.94) for a methylene dioxy group, revealing the presence of 1,3,4 trisubstituted phenyl systems, as in the case of cubebin [6]. The ^1H NMR spectrum further showed two sets of carbinol protons, due to epimers at δ 3.57 and 4.11, and δ 3.76 and 4.01, and a hemiacetal proton at δ 5.23, revealing the presence of a lactol ring system. This was further supported by ^{13}C NMR chemical shifts [8, 9] at δ 42.8 (45.9), 52.1 (53.1), 72.6 (72.2) and 98.8 (103.6).

Careful comparison of the ^{13}C NMR spectral data of the aromatic carbon resonances of **1** are in good agreement with those reported [9, 12] for 1,3,4 trisubstituted phenyl systems possessing methylenedioxy and dimethoxyl groups in two different ring systems.

Table 1. ^1H NMR spectral data of compound **1** in $CDCl_3$ (TMS)

Proton	α [**1a**] δH (*J* = Hz)	β [**1b**] δH (*J* = Hz)
H-2	6.43 (*d*, *J* = 1.5)	6.43 (*d*, *J* = 1.5)
H-5	6.70 (*d*, *J* = 7.8)	6.70 (*d*, *J* = 7.8)
H-6	6.49 (*dd*, *J* = 7.8, 1.5)	6.49 (*dd*, *J* = 7.8, 1.5)
H_2-7	2.61–2.78 (*m*)	2.47–2.65 (*m*)
H-8	1.97 (*m*)	2.15 (*m*)
H-9	5.23 (*m*)	5.23 (*m*)
H-2′	6.44 (*d*, *J* = 1.8)	6.44 (*d*, *J* = 1.8)
H-5′	6.77 (*d*, *J* = 8.2)	6.77 (*d*, *J* = 8.2)
H-6′	6.51 (*dd*, *J* = 8.2, 1.8)	6.51 (*dd*, *J* = 8.2, 1.8)
H_2-7′	2.67–2.80 (*m*)	2.45–2.65 (*m*)
H-8′	2.43 (*m*)	2.18 (*m*)
H_2-9′	4.11 (*t*, *J* = 8)	4.01 (*dd*, *J* = 7.0, 8.5)
	3.57 (*t*, *J* = 8)	3.76 (*m*)
OMe	3.82 (*s*)	3.83 (*s*)
OCH_2-O	5.94 (*br s*)	5.94 (*br s*)

Thus, correlating all the spectral evidence from ^1H, ^{13}C NMR and ^1H–^1H COSY spectra, the structure of **1** could be deduced as 9-hydroxy-3,5-dimethoxy,3′-4′ methylenedioxy-9,9′-epoxy lignan.

The main chemical-shift differences between the carbon resonances of the two epimers were observed at δ 98.8 and 33.6 (**1a**), and at δ 103.6 and 39.1 (**1b**), whereas the corresponding proton signals were observed at δ 3.57 and 4.11 (**1a**), and 3.76 and 4.01 (**1b**). Several lignans with lactol rings have been reported previously as mixtures of epimers in solution [4, 5].

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Table 2. ^{13}C NMR spectral data of compound **1** in $CDCl_3$ (TMS)

Carbon	α-isomer (**1a**)	DEPT	β-isomer (**1b**)
1	132.9	C	132.7
2	111.8	CH	111.7
3	148.8	C	148.7
4	147.7	C	147.3
5	111.3	CH	111.2
6	120.5	CH	120.9
7	33.6	CH_2	39.1
8	52.1	CH	53.1
9	98.8	CH	103.6
1′	133.3	C	134.5
2′	109.3	CH	109.1
3′	147.5	C	147.2
4′	145.7	C	145.5
5′	108.1	CH	108.0
6′	121.7	CH	121.6
7′	38.7	CH_2	38.4
8′	42.8	CH	45.9
9′	72.6	CH_2	72.2
OCH_3	55.8	CH_3	55.8
OCH_3	55.7	CH_3	55.7
OCH_2O	100.8	CH_2	100.8

The stereochemistry at the chiral centres (8,8′) and the orientation of the hydroxyl group at C-9 could be established from coupling constants and ^{13}C NMR chemical shifts. The upfield shift of C-7 ($-\delta$ 5.50) and C-9 ($-\delta$ 4.8) in the major isomer, in comparison with the β-isomer (minor), could only be explained by the α-configuration [8] of the hydroxyl group at C-9. The appearance of envelopes of benzylic protons at δ 2.45–2.80 and methine protons at δ 1.97–2.43, arises only when the stereochemistry at C-8, C-8′ is *trans* [9], whereas for the *cis*-isomer [10], these protons generally appear as multiplet at δ 12.1–3.3. Non-equivalence of H-9′ protons also supported the *trans*-configuration [9, 11] in both isomers of **1**.

The ^1H, ^{13}C spectral data and ^1H–^1H COSY analysis were in full agreement with **1** being a mixture of α- and β-isomers. Thus, the α-isomer (**1a**) and β-isomer (**1b**) were unambiguously assigned as [8*R*,8′*R*]-9α-hydroxy-3,4-dimethoxy-3′,4′-methylenedioxy 9,9′-epoxy lignan and [8*R*,8′*R*]-9β-hydroxy-3,4-dimethoxy-3′,4′-methylenedioxy-9,9′-epoxy lignan, respectively.

EXPERIMENTAL

MS were recorded at 70 eV. ^1H and ^{13}C NMR were recorded on a Bruker WM 400 MHz and ^1H–^1H COSY on Bruker DRX-300 MHz equipped with an aspect 2000 computer. CC: silica gel (60–120 mesh). Flash CC: EF-10 (EYELA) A.S.C. silica-gel (230–400 mesh) (SISCO).

Plant material

Stem parts of *P. chaba* Hunter (11.5 kg) were collected from Hooghly, West Bengal, India, in 1994. A voucher specimen (12361) is deposited in the herbarium of the Institute.

Extraction and isolation

Dried and powdered stems were extracted with EtOH (2 × 2.5 l). The EtOH extracts were combined and concd *in vacuo* to give a crude extract (87 g). This was fractionated into hexane- and $CHCl_3$-sol. The $CHCl_3$-sol frs. fr. was chromatographed using hexane, hexane–benzene, benzene and EtOAc solvent systems. Frs (100 ml each) eluted with EtOAc were combined after monitoring by TLC [silica gel; benzene–MeOH, 24:1 to give a lignan-containing fr. LA-1. Repeated flash CC of fr. LA-1, followed by semi-prep. HPLC on ODS-2, MeOH–H_2O (9:1), afforded **1** (20 mg) as a viscous oil. IR (neat) max: 3400 cm^{-1}, 2935, 1610, 1515, 1450, 1270, 1032, 930 cm^{-1}. EIMS (70 eV); *m/z* 372 $[M]^+$, 354 $[M-H_2O]^+$, 219, 194, 177, 151 (ion-*a*), 135 (ion-*b*), 121, 84 (base peak). ^1H and ^{13}C NMR: Tables 1 and 2, respectively.

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