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TWO SECOLIGNANS FROM *PEPEROMIA DINDIGULENSIS*

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Key Word Index—*Peperomia dindigulensis*; Piperaceae; secolignans; peperomins A, B, E and F.

Abstract—Peperomins E and F, two new secolignans have been isolated from the aerial parts of *Peperomia dindigulensis*, along with the known compounds peperomins A and B. © 1998 Published by Elsevier Science Ltd. All rights reserved

INTRODUCTION

Many plants belonging to the genus *Piper* have been investigated and shown to contain homolignols, dimers of phenylpropanoids and olefinic or alkyl isobutylamides, which have insecticidal activity [1]. So far, only six species of the genus *Peperomia* have been investigated. Of these, *P. japonica* (Taiwan) and *P. glabella* (Venezuela) yielded some novel secolignans [2, 3]. In a programme directed at the chemical characterisation of *Peperomia* species endemic to India, we present here our work on *P. dindigulensis*, a large succulent herb growing on wet rocks at elevations of 2000–4000 ft in peninsular India. From the aerial parts of this species, peperomins A and B earlier reported from *P. japonica* and two new compounds, peperomins E and F, were isolated and characterised.

RESULTS AND DISCUSSION

The ^{1}H and ^{13}C NMR of peperomin E indicated a skeleton similar to that of peperomin A isolated previously from *P. japonica* [2]. The main difference was the replacement of a secondary methyl group by an exocyclic methylene group, as shown by the ^{1}H NMR signals at δ_H 6.15 (*d*, J = 2 Hz) and 4.94 (*d*, J = 1.7 Hz). The presence of an exocyclic methylene in peperomin E was also confirmed by irradiation experiments. Irradiation of the proton at C-3 gave sharp singlets for the exocyclic methylene protons (disappearance of allylic coupling). The IR data also confirmed the α,β-unsaturated five-membered lactone system. All NMR assignments for peperomin E were confirmed by homo and heterocosy experiments.

The stereochemistry at position 3 in peperomin E was assigned as *S* based on the ORD curve, where a positive curve at 265 nm was followed by a negative curve at 238 nm, as in peperomins A–C [2]. Thus, peperomin E was assigned structure **1**.

Peperomin F had the molecular formula $C_{24}H_{26}O_{10}$, as determined by HR mass spectral data. IR peaks at 1738 and 1260 cm^{-1} showed the presence of an ester carbonyl. ^{1}H and ^{13}C NMR data indicated the presence of a skeleton similar to that of the known peperomins A, B and E, but there was no secondary methyl or exocyclic methylene group. The ^{1}H NMR spectrum of peperomin F showed the presence of a primary acetate group CH_2–O–$COCH_3$, a hemiacetal proton and a hydroxyl proton exchangeable with D_2O. The aromatic region of the spectrum showed a substitution pattern similar to that of peperomin E. Acetylation of peperomin F gave a compound which showed the presence of two acetyl methyls and an additional carbonyl in the ^{13}C NMR spectrum; the hemiacetal proton shifted downfield by 0.8 ppm. Thus, the presence of a secondary hydroxyl group, part of a hemiacetal system and an acetoxymethyl group instead of a secondary methyl group found in peperomin A could be deduced. Structure **2** is proposed for peperomin F. It was difficult to assign the relative stereochemistry on the basis of NMR data at 200 MHz, because there was considerable overlapping of the signals for the protons at C-3, C-4, C-5 and C-6. However, data obtained at 400 MHz showed better resolved peaks and J values

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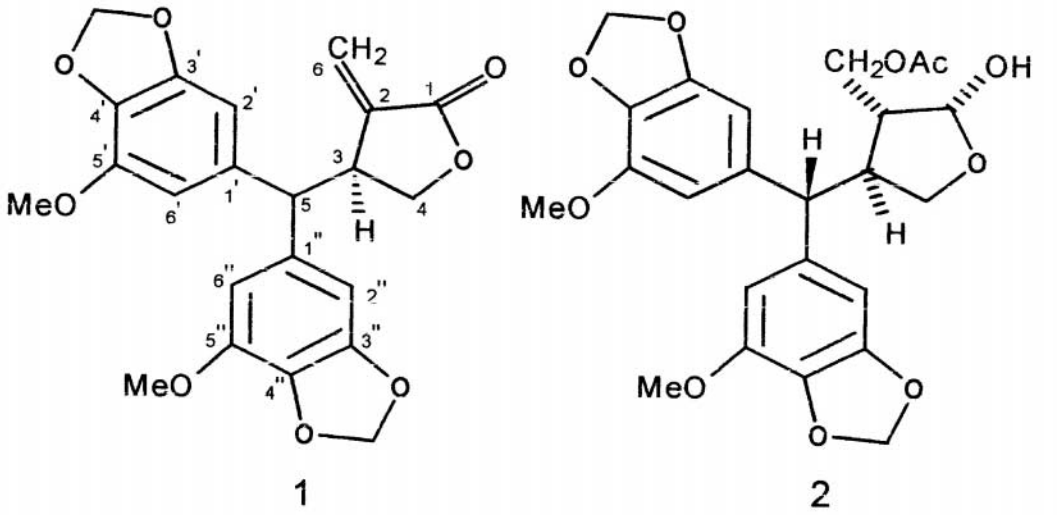

could be determined easily on the basis of which relative stereochemistry could be assigned for the three centres C-1, C-2 and C-3.

The proton on C-5 was a large doublet (J = 12.3 Hz) similar to that in other peperomins and a similar configuration at C-5 and C-3 can be assumed, with the C-3 proton as α. The proton at C-3 was a complex multiplet due to coupling with protons at C-2, C-4 and C-5. The J value of the proton at C-2 due to coupling with the proton at C-3 was 6.4 Hz, which was similar to the value reported for other peperomins and, hence, gave the same configuration, with the C-2 proton β. Investigation of the geometry of peperomin F acetate using PCMODEL [4] indicated that in the structure of minimum energy, the dihedral angle H1–C1–C2–H2 was found to be 39.8°, wherein a coupling constant of 5–6 Hz is expected. But the appearance of the C-1 proton as a singlet showed the absence of coupling with the C-2 proton. This could be attributed to the presence of the OAc function at C-1 *anti* to the C-2 proton, thus showing the β-orientation of the C-1 proton [5]. The dihedral angle H2–C2–C3–H3 was found to be 45°, consistent with the observed J value. Thus, the structure of peperomin F was assigned as **2**.

Peperomins A, B and E were tested for their antifeedant activity on three phytophagous pests,

Table 1. ^{1}H NMR spectral data of peperomins E and F and peperomin F acetate

H	Peperomin E*	Peperomin F*	Peperomin F acetate*	Peperomin F acetate†	Peperomin F acetate‡
1	–	5.45 *s*	6.24 *s*	6.20 *s*	6.76 *s*
2	–	2.45 *m*	2.50 *m*	2.45 *ddd* (J = 4.3, 9.8, 6.4 Hz)	2.67 *ddd* (J = 4.2, 6.4, 10.4 Hz)
3	3.7 *m*	3.57 *m*	3.45 *m*	3.42 *m*	3.58 *m*
4a	3.99 *dd* (J = 4.1, 9.4 Hz)	3.57 *m*	3.60 *m*	3.63 *dd* (J = 8.6, 9.4 Hz)	3.68 *dd* (J = 8.3, 9.3 Hz)
4b	4.32 *dd* (J = 7.3, 9.4 Hz)	3.82 *m*	3.85 *m*	3.88 *t* (J = 8.6 Hz)	4.08 *t* (J = 8.3 Hz)
5	3.65 *d* (J = 11.5 Hz)	3.57 *m*	3.61 *d* (J = 11.8 Hz)	3.58 *d* (J = 12.3 Hz)	3.50 *d* (J = 12.1 Hz)
6a	6.15 *d* (J = 2.0 Hz)	4.08 *dd* (J = 4.6, 11.1 Hz)	4.1 *dd* (J = 4.6, 11.2 Hz)	4.1 *dd* (J = 4.3, 11.3 Hz)	4.29 *dd* (J = 4.2, 11.2 Hz)
6b	4.94 *d* (J = 1.7 Hz)	3.96 *m*	4.0 *m*	3.98 *dd* (J = 11.4, 9.8 Hz)	4.08 *dd* (J = 11.2, 10.4 Hz)
2′,2″	6.37, 6.43 *d* (J = 1.5 Hz)	6.38, 6.43 *d* (J = 1.5 Hz)	6.37, 6.43 *d* (J = 1.5 Hz)	6.37, 6.42 *d* (J = 1.5 Hz)	6.34 *d* (J = 1.5 Hz)
6′,6″	6.50, 6.60 (J = 1.5 Hz)	6.49, 6.60 *d* (J = 1.5 Hz)	6.47, 6.60 *d* (J = 1.5 Hz)	6.46, 6.60 *d* (J = 1.5 Hz)	6.56 *d* (J = 1.5 Hz)
OCH_3	3,88, 3.89, *s* (3H each)	3.88, 3.89, *s* (3H each)	3.90, 3.91, *s* (3H each)	3.86 *s* (6H)	3.45, 3.49 *s* (3H each)
O–CH_2–O	5.92, *s* (4H)	5.92, *s*, 5.90 *dd* (J =1.3, 3.4 Hz)	5.94, *s*, 5.90 *dd* (J =1.3, 3.7 Hz)	5.89, 5.88 *q* (J = 1.4)	5.25, 5.27 *q* (J = 1.4 Hz)
$OCOCH_3$	–	1.91 *s* (3H)	2.03, 2.11, *s* (3H each)	2.32, 2.1, *s* (3H each)	1.67, 1.54, *s* (3H each)

*In $CDCl_3$ at 200 MHz.
†In $CDCl_3$ at 400 MHz.
‡In C_6D_6 at 400 MHz.

Spodoptera litura, *Rhaphidopalpa foveicollis* and *Atractomorpha crenulata*; the results obtained are summarised in Table 1.

EXPERIMENTAL

Aerial parts of *P. dindigulensis* Miq. were collected from Yercaud, Tamilnadu, India, during January, 1997. A voucher specimen (BDV 506) is deposited in the Herbarium, Department of Botany, Bharathidasan University. Plant material was shade-dried (4.3 kg) and extracted ×3 with EtOH. The combined extracts on removal of solvent *in vacuo* gave a residue (270 g), which was suspended in 2 l of H_2O and extracted with *n*-hexane, $CHCl_3$ and EtOAc (each 2 l) and the solvents removed *in vacuo*. The $CHCl_3$ fraction (17 g) was redissolved in solvent and treated with charcoal and filtered to remove chlorophylls. The residue obtained after removal of solvent (10 g) was chromatographed over silica gel eluting with *n*-hexane–EtOAc mixt. The eluants from 50% EtOAc (frs 26–49) were rechromatographed to obtain pure compounds. Frs 26–34 on further CC using benzene–EtOAc 97:3 yielded peperomins E and A.

Peperomin E

Yield 300 mg, m.p. 140°. $[\alpha]_D$ +2.7° ($CHCl_3$; *c* 0.7). UV λ_{max} nm (log ε): 221 (4.32), 254 (4.04), 280 (3.65). IR ν_{max} cm^{-1} 1760, 1634, 1570, 1453. ^1H and ^{13}C NMR: Tables 2 and 3. HRMS $C_{22}H_{20}O_8$, 412.116233 (obs.), 412.115818 (calcd); base peak $C_{17}H_{15}O_6$, 315.087495 (obs.), 315.086863 (calcd).

Table 2. ^{13}C NMR spectral data of peperomins E and F and peperomin F acetate (50 MHz δ values in $CDCl_3$)

C	Peperomin E	Peperomin F	Peperomin F acetate
1	170.7	101.0	101.4
2	135.8	46.0	45.1
3	42.4	42.0	42.3
4	69.6	71.6	72.6
5	55.3	50.3	50.1
6	125.2	60.9	60.4
1′,1″	134.3 (×2)	133.9 (×2)	134.1 (×2)
2′,2″	101.5, 101.9	100.8, 101.0	100.7, 100.8
3′,3″	149.2, 149.5	149.1, 149.2	149.3, 149.4
4′,4″	136.0, 136.1	137.3, 138.3	137.0, 137.9
5′,5″	143.4, 143.6	143.3,143.5	143.4, 143.6
6′,6″	108.4, 108.8	106.8, 107.2	107.1, 107.7
OCH_2O-	102.0 (×2)	101.3 (×2)	100.7, 100.8
OCH_3-	56.8, 56.9	56.7, 56.8	56.9, 57.0
$OCOCH_3$	–	23.8	20.8, 21.4
$OCOCH_3$	–	170.9	170.6, 171.2

Table 3. Antifeedant activity of peperomins (AI_{50})

Insect species	Azadirachtin A	Peperomin A	Peperomin B	Peperomin E
Spodoptera litura	10.2	47.15	54.67	33.01
Raphidopalpa foveicollis	15.5	36.20	37.70	25.90
Atractomorpha crenulata	13.6	42.17	35.00	24.90

AI_{50} is the concentration of the compound in μg cm of leaf disc that gives an estimated antifeedant index of 50%. Calculations are based on probit analysis.

Peperomin A

Yield 350 mg, m.p. 145–146° (lit. 143–145° [2]).

Frs 37–42 on concn and recrystallisation from MeOH–H_2O gave peperomin B. Yield 300 mg, m.p. 145° (lit. 143–145° [2]).

Frs. 43–49 on further CC using $CHCl_3$–MeOH (49:1) gave peperomin F. Yield 50 mg, m.p. 170°. $[\alpha]_D$ −41.17° ($CHCl_3$; *c* 0.17). UV λ_{max} nm (log ε): 253 (2.912), 278 (2.630). IR ν_{max} cm^{-1} 3040, 1738, 1633, 1505, 1232; ^1H and ^{13}C NMR: Tables 2 and 3. HRMS $C_{24}H_{26}O_{10}$, 474.152960 (obs.), 474.152597 (calcd); base peak $C_{17}H_{15}O_6$, 315.086443 (obs.), 315.086863 (calcd).

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