

A PRENYLATED BENZOPYRAN DERIVATIVE FROM *PEPEROMIA CLUSIIFOLIA*

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Key Word Index—*Peperomia clusiifolia*; Piperaceae; prenylated benzopyran.

Abstract—The structure of a new compound, clusifoliol, isolated from whole plants of *Peperomia clusiifolia* has been established as 3,4-dihydro-2,7-dimethyl-6-(3-methyl-2-butenyl)-2-(4-methyl-1,3-pentadienyl)-2H-1-benzopyran-5-ol by spectroscopic methods. © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

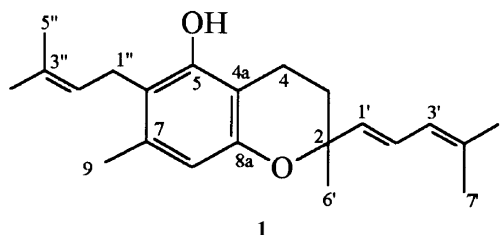
Within the Piperaceae, the genus *Peperomia* has received little phytochemical attention [1, 2], in contrast to the extensive studies of *Piper* compounds [3–5]. In this report, we describe the only metabolite isolated from *P. clusiifolia*, a creeping herb endemic to Jamaica and one of the more commonly occurring and abundant of the ca 40 *Peperomia* species growing on the island [6].

RESULTS AND DISCUSSION

Dried ground plants were extracted with hexane. The concentrated extract was subjected to repeated normal-phase silica gel column chromatography. This procedure yielded clusifoliol **1** as an oil (0.001%) C₂₂H₃₀O₂ which exhibited bands in the IR spectrum that indicated carbon-carbon double bonds (1649 and 1618 cm⁻¹) and a hydroxyl group (3439 cm⁻¹).

The presence of the 3-methyl-2-butenyl group attached to C-6 was inferred from a broad triplet ($J=7.1$ Hz) at δ 5.14 in the ¹H NMR spectrum. This was coupled to a pair of double-doublets ($J=14.9$, 7.1 Hz) at δ 3.25 and δ 3.36 for the allylic-benzylic methylene protons at C-1'' and showed HMBC cross-peaks to the carbon signals of two of the four vinylic methyl groups present in the compound. The proton signals of these methyl groups, as well as the C-1'' methylene, displayed cross-peaks to two other carbon signals in the side-chain at δ 123.25 (C-2'') and δ 130.3 (C-3'').

The C-1'' protons showed multiple-bond con-



nectivities to three aromatic carbons, viz: the oxygen-substituted position (C-5) at δ 152.2, the *ipso* carbon (C-6) at δ 135.0 and the methyl substituted carbon (C-7) at δ 120.0. The latter carbon correlated to the C-9 methyl protons and to the aromatic singlet (H-8) which, from its chemical shift (δ 6.14) and that of the directly bonded carbon (δ 107.7), was in an *ortho-para* relationship to two oxygen substituents, the *para*-substituent being at C-5. The aromatic proton also showed long-range connectivities to two other quaternary aromatic carbons, one oxygen-substituted (C-8a, δ 151.2), the other, *ortho* to two oxygen substituents (C-4a, δ 105.9). These biogenetically-informed assignments were corroborated by further cross-peaks (Table 1) and led to the formulation of the aromatic substitution pattern shown in **1**.

The 4-methyl-1,3-pentadienyl system attached to C-2 displayed a characteristic three-proton coupling pattern for H-1' (d , $J=15.5$ Hz), H-2' (dd , $J=15.4$, 10.6 Hz) and H-3' (d , $J=10.6$ Hz). The vicinally coupled H-3' signal showed multiple bond connectivities to the carbon signals of the remaining two vinylic methyl groups, C-5' and C-7'. The *trans*-coupled H-1' signal was indirectly correlated to the quaternary oxygen-substituted sp³ carbon C-2 (δ 75.9), thus establishing the point of attachment of the side-chain. HMBC cross-peaks also enabled the

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Table 1. NMR data of compound **1** (CDCl₃, *J* values given in Hz in parentheses)

Position	¹³ C	¹ H	HMBC*
2	75.9		4, 1'', 2'', 6''
3	31.4	1.73, <i>m</i> [#] 1.91, <i>ddd</i> (13.3, 5.9, 5.9)	4, 6''
4	17.2	2.49, <i>ddd</i> (16.3, 9.7, 6.2) 2.62, <i>ddd</i> (16.3, 5.6, 5.6)	
4a	105.9		4, 8
5	152.2		4, 1''
6	135.0		9, 1''
7	120.0		8, 9, 1''
8	107.7	6.14, <i>s</i>	9
8a	151.2		4, 8
9	19.3	2.20, <i>s</i>	8
1''	134.2	5.55, <i>d</i> (15.5)	3'', 6''
2''	125.1	6.36, <i>dd</i> (15.4, 10.6)	3''
3''	124.5	5.76, <i>d</i> (10.6)	1'', 2'', 5'', 7''
4''	135.1		2'', 5'', 7''
5''	18.2	1.64, <i>s</i>	3'', 7''
6''	27.5	1.40, <i>s</i>	
7''	26.0	1.73, <i>s</i>	3'', 5''
1''	25.0	3.25, <i>dd</i> (14.9, 7.1) 3.36, <i>dd</i> (14.9, 7.1)	2''
2''	123.3	5.14, <i>t</i> (7.1)	5'', 1'', 4''
3''	130.3		5'', 1'', 4''
4''	17.9	1.77, <i>s</i>	5'', 2''
5''	25.9	1.64, <i>s</i>	2'', 4''

* Protons correlating with carbon resonance; [#]obscured.

identification of the remaining two substituents on this carbon as the C-6' methyl group and the C-3-C-4 methylene chain. The presence of this latter sequence of coupled protons was inferred from COSY correlations between the C-3 homoallylic and C-4 benzylic protons. Linkage to the aromatic ring of the benzylic group and the oxygen attached to the sp³ carbon at positions 4a (δ 105.9) and 8a (δ 151.2) respectively, led the structure of clusifoliol **1**. The observed two and three-bond ¹H-¹³C connectivities (Table 1) ruled out all other isomeric possibilities.

Clusifoliol **1** is likely of mixed acetate and mevalonate biosynthetic origin, and contains the somewhat unusual 4-methyl-1,3-pentadienyl side-chain. It is closely related to the prenylated diphenols, piperogalin, grifolin and grifolic acid, recently reported from *P. galioides* [1].

EXPERIMENTAL

General

EIMS were obtained at 70 eV. IR was determined for a film on NaCl discs and UV for an EtOH soln. NMR were recorded at 200 and 500 MHz for ¹H and 125 MHz for ¹³C; samples were dissolved in CDCl₃, with TMS as int. standard. Adsorption CC was performed on silica gel 60 (230–400 mesh) and TLC on

pre-coated silica gel 60 F₂₅₄ plates. Spots were visualized under UV and by spraying with 4% phosphomolybdic acid in 5% H₂SO₄, followed by heating.

Plant material. Whole plants of *P. clusiifolia* Jacq. were collected in Hellshire Hills, St. Catherine, Jamaica, in February 1996. A voucher specimen is lodged in the Herbarium at the University of the West Indies, Mona, Jamaica.

Extraction and isolation. Dried whole plants (400 g) were ground and extracted by cold percolation with hexanes. Evapn of the solvent *in vacuo* yielded a gum (20 g), a portion (10 g) of which was chromatographed (gradient elution with Me₂CO-hexane). The frs eluted with 5% Me₂CO were rechromatographed, again using a Me₂CO-hexane gradient. Clusifoliol **1** (200 mg) was obtained from frs eluted with 2% Me₂CO-hexane.

Compound 1. Oil. [α]_D +160.0° (c 0.01, EtOH). IR ν_{max} 3439, 1649, 1618, 1093 cm⁻¹. UV λ_{max} nm (log ε) 210 (5.60), 238 (4.41)+KOH nm (log ε) 212 (5.65), 240 (4.60). EIMS *m/z* (rel. int.): 326 [M]⁺ (100), 311 (17), 270 (28), 205 (62), 189 (59), 107 (87); HRMS *m/z* 326.2254 (calcd for C₂₂H₃₀O₂ 326.2246). ¹H (500 MHz) and ¹³C (125 MHz) NMR, see Table 1.

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