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A NEW PHLOROGLUCINOL DIMER FROM *MALLOTUS PALLIDUS*

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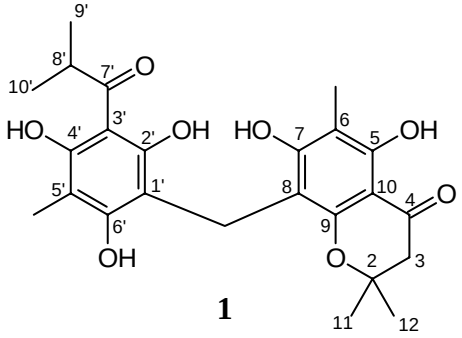
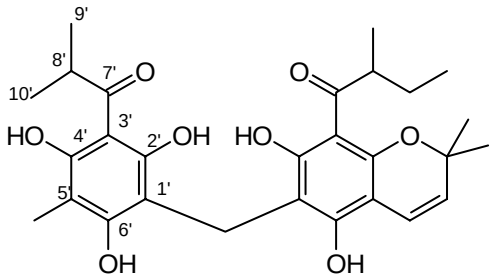
Abstract – A phytochemical investigation of an EtOAc extract of the leaves of *Mallotus pallidus* led to the isolation of a new phloroglucinol dimer, mallopallidusol (**1**), along with five known compounds.

The genus *Mallotus* (Euphorbiaceae) is known to produce a variety of complex phenolic compounds such as phloroglucinols,[1-3] tannins,[4] coumarins,[5] chalcones[6] and benzopyrans.[7] *Mallotus pallidus* (Airy Shaw) Airy Shaw, formerly known as *M. philippensis* (Lam.) Mull.Arg. var. *pallida* Airy Shaw, is a shrub growing in southwestern Thailand.[8] As part of our continuing studies on naturally occurring phenolics,[9, 10] a chemical investigation of an EtOAc extract of the leaves of this plant was initiated, and this led to the isolation of a new dimeric phloroglucinol derivative named mallopallidusol (**1**), along with the known compounds *β*-sitosterol,[11] epifriedelanol,[12] friedelin,[13] kaempferol[14] and isoscopoletin.[15]

Compound (**1**) was obtained as yellow needles. The HR-ESI-MS (negative ion mode) spectrum of **1** exhibited an ion peak for $[M-H]^+$ at *m/z* 443.1699 (cacld for $C_{24}H_{27}O_8$ *m/z* 443.1706), suggesting a molecular formula of $C_{24}H_{28}O_8$. UV absorptions at 230, 305 and 336 nm were indicative of aromaticity, and IR bands were observed at 3400 (OH), and 1639 (C=O) cm^{-1}. The ^{13}C-NMR and DEPT spectral data (Table 1) indicated the presence of twelve aromatic quaternary carbons, six of which were oxygenated, suggesting a bis-aryl structure for **1**.[3]



1



2

The ^{1}H NMR resonances at δ 3.92 (1H, m, H-8′), 1.16 (6H, d, *J* = 6.8 Hz, H_3-9′ and H_3-10′), 2.09 (3H, s, Me-5′) and 3.78 (2H, s, Ar-CH_2-Ar) and the ^{13}C NMR signals at δ 105.6 (C-1′), 160.0 (C-2′), 103.3 (C-3′), 156.2 (C-4′), 101.6 (C-5′), 159.6 (C-6′), 211.1 (C-7′), 9.3 (C-8′), 19.3 (C-9′ and C-10′), 15.9 (Ar-CH_2-Ar) and 7.5 (Me-5′) were

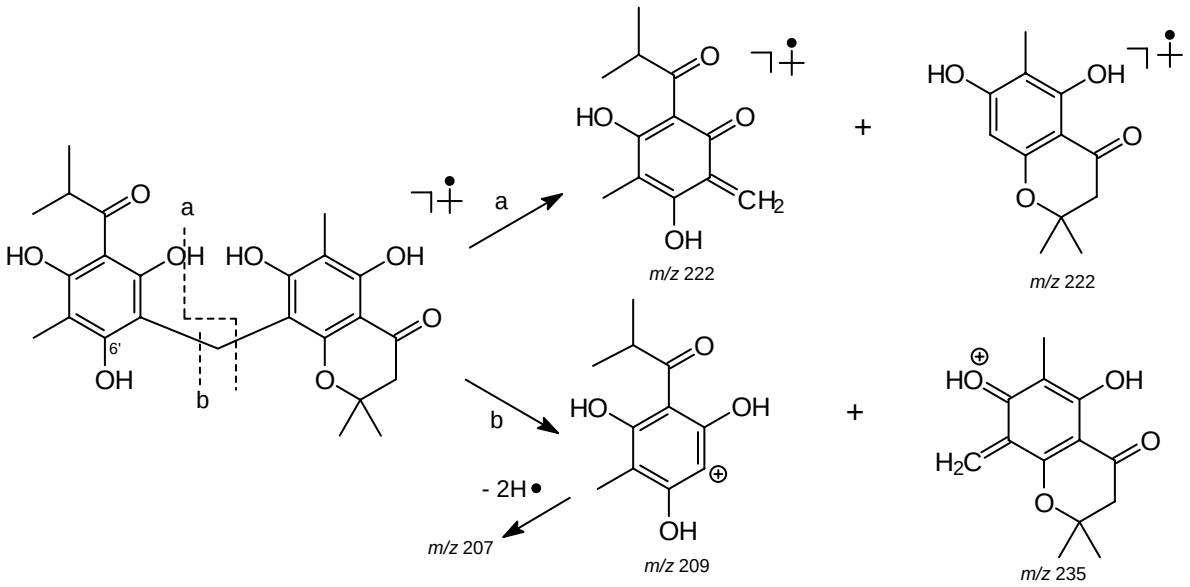
reminiscent of a 2,4,6-trihydroxy-3-isobutyryl-5-methylbenzyl moiety, a phloroglucinol-related partial structure of mallotophilippen A (**2**).[16] This was supported by ions at *m/z* 222, 209 and 207 in the EIMS (Scheme 1) spectrum.[1]

Table 1 NMR spectral data of **1** as compared with those of **2**

No.	**1**		**2**[a]	
	δ_H (*J*, Hz)	δ_C	δ_H (*J*, Hz)	δ_C
2		81.1	-[b]	-
3	2.77 s	47.8	-	-
4		195.2	-	-
5		160.2	-	-
6		106.2	-	-
7		162.8	-	-
8		105.0	-	-
9		153.5	-	-
10		101.3	-	-
11	1.61 s	26.6	-	-
12	1.61 s	26.6	-	-
Me-6	2.03 s	7.3	-	-
OH-5	12.17 s		-	-
Ar-CH_2-Ar	3.78 s	15.9	3.78 s	15.9
1′		105.6		106.3
2′		160.0		162.2
3′		103.3		104.5
4′		156.2		155.3
5′		101.6		101.9
6′		159.6		160.2
7′		211.1		211.2
8′	3.92 m	39.3	3.94 m	39.2
9′	1.16 d (6.8)	19.3	1.19 d (6.7)	19.3
10′	1.16 d (6.8)	19.3	1.19 d (6.7)	19.3
Me-5′	2.09 s	7.5	2.09 s	7.5
OH-2′	15.50 br s		16.20 s	

[a]From reference 16; [b]Not applicable.

The second aryl unit was derived from a methylated phloroglucinol having a prenyl side-chain oxidized and cyclized to form a chroman-4-one structure, as indicated by the ^{1}H NMR signals at δ 1.61 (6H, s, H_3-11 and H_3-12), 2.03 (Me-6), 2.77 (2H, s, H_2-3), and 12.17 (OH-5), and the ^{13}C NMR resonances at δ 81.1 (C-2), 47.8 (C-3), 195.2 (C-4),160.2 (C-5), 106.2 (C-6), 162.8 (C-7), 105.0 (C-8), 153.5 (C-9), 101.3 (C-10), 26.6 (C-11 and C-12) and 7.3 (Me-6).[7] This was corroborated by the ions at *m/z* 235 and 222 in the EIMS spectrum (Scheme 1).[1] The downfield shift of OH-5 at δ 12.17 was due to its H-bonding with the C-4 carbonyl. HMBC correlations were observed from OH-5 to C-5, C-6 and C-10; H_2-3 to C-2, C-4 and C-10; H_3-11 and H_3-12 to C-2 and C-3; Me-6 to C-5, C-6 and C-7. Finally, the two phloroglucinol monomers were linked through a methylene bridge as shown by the HMBC correlations of the methylene protons (Ar-CH_2-Ar) at δ 3.78 with the C-7, C-8, C-9, C-1′ C-2′, and C-6′carbons. Thus, **1** was determined as 8-(2,4,6-trihydroxy-3-isobutyryl-5-methylbenzyl)-5,7-dihydroxy-2,2,6-trimethyl-chroman-4-one and named mallopallidusol.



Scheme 1 Mass fragmentation of **1**

EXPERIMENTAL

Melting points were measured on a Fisher-Johns melting point apparatus. IR spectra were recorded as KBr discs on a JASCO FT/IR-300E spectrophotometer, and UV spectra were measured on a Thermospectronic UV-1 spectrophotometer. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on a Bruker DPX 500 spectrometer. EIMS spectra were obtained with a Fison Micromass VG Platform II mass spectrometer and HR-ESI-MS was taken on a Micromss LCT mass spectrometer.

Plant Material The leaves of *M. pallidus* were collected from Prachuap Khiri Khan Province, Thailand, in August 2001 and the voucher specimen No BKF110693 has been deposited at the Royal Forest Department, Ministry of Agriculture and Cooperatives, Bangkok, Thailand.

Extraction and Isolation The air dried and ground leaves (1.2 kg) were extracted with hexane (3 X 6L) and ethyl acetate (3 X 6L) at rt for 24 h. Removal of the organic solvent under reduced pressure left a hexane extract (40 g) and an ethyl acetate extract (20 g). The ethyl acetate extract (20 g) was subjected to vacuum column chromatography (silica gel), using gradient elution with *n*-hexane-ethyl acetate system (10-100 %). Nine major fractions (I-IX) were obtained on the basis of TLC monitoring of the individual fractions. Fraction V (688 mg) was fractionated on a Sephadex LH-20 column, eluted with MeOH-CH_2Cl_2 (1:1) to afford fractions V1-V4. Fraction V3 (63 mg) was refractionated on a Sephadex LH-20 column using MeOH as eluent to give **1** (2 mg). Chromatographic separations (silica gel and sephadex LH-20) of the remaining fractions afforded protocatechuic acid (125 mg), β-sitosterol (15 mg), epifriedelanol (8 mg), friedelin (19 mg), kaempferol (13 mg) and isoscopoletin (2 mg).

8-(2,4,6-trihydroxy-3-isobutyryl-5-methylbenzyl)-5,7-dihydroxy-2,2,6-trimethyl-chroman-4-one (mallopallidusol) (**1**). Yellow needles; mp 208-209 ºC; IR (KBr) ν_{max} 3400, 3101, 2973, 2930, 1639, 1610, 1452, 1371, 1328, 1291, 1198, 1144, 1125, 1053, 1021, 754 cm^{-1}; UV (EtOH) λ_{max} (log ε) : 231 (4.2), 305 (4.3), 336 (4.4) nm; ^{1}H (500

MHz) and ^{13}C (125 MHz) NMR in $CDCl_3$ see Table 1; HR-ESI-MS (negative ion mode) 443.1699 $[M-H]^+$ (cacld for $C_{24}H_{27}O_8$, 443.1706); EIMS *m/z* (rel. int.) 444 $[M]^+$ (5), 235 (18), 222 (55), 209 (2), 207 (84), 179 (43), 167 (96), 138 (23), 83 (44), 77 (21), 69 (71), 57 (42), 55 (100).

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