Pergamon

PII: S0031-9422(96)00856-4

Phytochemistry, Vol. 45, No. 1, pp. 133–136, 1997

0031-9422/97 $17.00+0.00

THREE XANTHONES FROM *POECILONEURON PAUCIFLORUM* AND *MAMMEA ACUMINATA*

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(*Received* 7 *October* 1996)

Key Word Index—*Poeciloneuron pauciflorum*; *Mammea acuminata*; Guttiferae; 1,6-dihydroxy-7-methoxyxanthone; 1,6-dihydroxy-7-methoxyxanthone 6-*O*-β-D-glucoside; 2,7-dihydroxyxanthone.

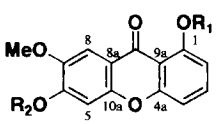
Abstract—From the stem of *Poeciloneuron pauciflorum*, two new xanthones (1,6-dihydroxy-7-methoxyxanthone and 1,6-dihydroxy-7-methoxyxanthone 6-*O*-β-D-glucoside) in addition to 12 known compounds (1,5-dihydroxy-, 1,5-dihydroxy-3-methoxy-, 1,7-dihydroxy-, 1-hydroxy-7-methoxy-, 2-methoxy-, 4-methoxy-, 1,4,5-trihydroxy-, 1,3,5-trihydroxy-, 1,3,6-trihydroxy-7-methoxy-, 1,3,7-trihydroxy-, 3-hydroxy-2-methoxyxanthone and (−)-epicatechin) were isolated. From the aerial parts (stems and bark) of *Mammea acuminata*, a new xanthone (2,7-dihydroxyxanthone) was isolated in addition to two known xanthones (1,5-dihydroxy- and 5-hydroxy-1-methoxyxanthone) and (−)-epicatechin. The structures were established by spectral analysis and total synthesis in case of 1,6-dihydroxy-7-methoxyxanthone.

INTRODUCTION

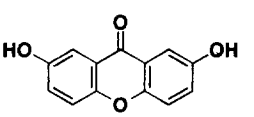
Two genera *Poeciloneuron* and *Mammea* are classified in the same subfamily of Calophylloideae (Guttiferae) as *Calophyllum* and *Mesua*. A rare species of *Poeciloneuron pauciflorum* Bedd. is an endemic plant in India. Based on available literature, almost no phytochemical research work has been carried out on this plant. The genus *Mammea* is well-known to produce coumarin derivatives [1–3] and simply oxygenated xanthones [4]. In our previous papers, we reported the chemical investigation and structural determination of new furanoxanthones (acuminols A and B) in *M. acuminata* Kosterm [5]. In continuation of our studies [6–8], oriented to obtain biologically active compounds and influenced by a chemotaxonomic interest in the family, we investigated the chemical constituents in *P. pauciflorum* and *M. acuminata*.

RESULTS AND DISCUSSION

Stem of *Poeciloneuron pauciflorum* collected in India was dried and ground, and extracted successively with benzene, acetone and 70% methanol. The acetone extract was repeatedly chromatographed on Si and Sephadex LH-20 to give compounds **1**–**14**. Stems and bark of *Mammea acuminata* collected in Indonesia were extracted and purified in same manner as *P. pauciflorum* to give **3** and **14**–**16**.



1 : R_1 = H, R_2 = H
2 : R_1 = H, R_2 = Glc
17 : R_1 = Me, R_2 = H



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Compound **1**, a pale yellow amorphous solid, reacted positively to $FeCl_3$ and Gibbs tests. The HREIMS showed the molecular ion at *m/z* 258.0518 corresponding to $C_{14}H_{10}O_5$. An absorption band at 1647 cm^{-1} in the IR spectrum showed the presence of a conjugated carbonyl group. Its UV spectral data suggested that **1** was a xanthone derivative. The signals of three aromatic protons [δ 6.76, 7.01 (1H each, *dd*, *J* = 8.3, 1.0 Hz) and 7.65 (1H, *t*, *J* = 8.3 Hz)] in an ABC system due to a 1,2,3-trisubstituted benzene ring, a methoxyl [δ 3.91 (2H, *s*)] and hydroxyl groups [δ 10.99 (1H, *br s*) and 12.92 (1H, *s*, chelated)] were observed in the ^1H NMR spectrum, in addition to two

Table 1. ^{13}C NMR spectral data of **1**, **2**, **15** and **17**

Carbon	1*	2*	15*	17*
1	160.8	160.8	109.7	160.0
2	109.7	109.9	154.5	106.1
3	136.1	136.6	124.8	134.4
4	106.8	107.4	120.2	109.5
5	104.6	103.1	120.2	102.3
6	155.5†	153.8	124.8	153.5†
7	146.3	146.9	154.5	145.9
8	102.7	104.6	109.7	105.9
9	180.1	180.4	171.5	173.5
4a	155.6	155.8	151.0	157.3
8a	111.6	113.3	122.5	114.5
9a	107.6	106.9	122.5	111.3
10a	152.3†	146.9	151.0	150.4†
1′		99.5		
2′		73.0		
3′		76.6†		
4′		69.4		
5′		77.1†		
6′		60.6		
OMe-C-1				56.1
OMe-C-7	55.9	55.9		55.8

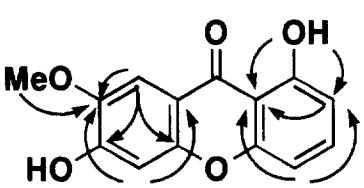
* Measured in DMSO-d_6.
† Interchangeable.

aromatic protons [δ 6.95 and 7.47 (1H each, *s*)]. These spectral data indicated that the structure of **1** was either 1,6-dihydroxy-7-methoxyxanthone or 1,7-dihydroxy-6-methoxyxanthone. An NOE was observed in the aromatic proton at δ 7.47 when the methoxyl group was irradiated, supporting that the proton was assignable to H-8. Therefore, **1** was preferably considered to be 1,6-dihydroxy-7-methoxyxanthone. To clarify the structure, **1** was synthetically prepared by demethylation [9] of 6-hydroxy-1,7-dimethoxyxanthone (**17**) which was synthesized by condensation of 2,6-dimethoxybenzoyl chloride with 2,4-dihydroxy-1-methoxybenzene. Both physical data agreed well. Thus, **1** was confirmed to be 1,6-dihydroxy-7-methoxyxanthone. The ^{13}C NMR spectral assignment of **1** and **17** (Table 1) was accomplished with the aid of CH COSY and HMBC spectrum (Fig. 1).

Compound **2**, a pale yellow amorphous solid, also reacted positively to $FeCl_3$ and Gibbs tests. Its UV absorptions were closely similar to those of **1**, indicating that **2** was a xanthone. Although the ^1H and ^{13}C NMR spectral data were characteristic for 1,6-dihydroxy-7-methoxyxanthone (**1**), the presence of a glucose was revealed by the ^{13}C NMR spectral analysis (Table 1), which was supported by a signal based on an anomeric proton [δ 5.24 (1H, *d*, J = 7.3 Hz)] in the ^1H NMR spectrum. A molecular ion peak at m/z 420 in the EIMS spectrum was faintly observed, but a fragment ion peak at m/z 258 corresponding to the aglycone was observed as a base peak, which substantiated that **2** was a β-*O*-glucoside of **1**. In the ^1H NMR spectrum, the presence of a chelated hydroxyl group [δ 12.79 (1H, *s*)] was shown, and an NOE was observed at the aromatic proton [δ 7.54 (1H, *s*)] when the methoxyl group [δ 3.91 (3H, *s*)] was irradiated. Furthermore, the other aromatic proton assigned to H-5 [δ 7.36 (1H, *s*)] was shifted in a lower field (+0.41 ppm) compared with that of **1** (δ 6.95) caused by glycosylation shift [10]. Thus the glucose moiety was located at C-6 of the xanthone. Consequently the structure of **2** was concluded to be 1,6-dihydroxy-7-methoxyxanthone 6-*O*-β-D-glucoside.

Compound **15**, a yellow amorphous solid, gave a molecular ion peak at m/z 228.0415 in the HREIMS corresponding to $C_{13}H_8O_4$. The ^1H NMR spectrum showed signals of a 1,2,4-trisubstituted benzene ring [δ 7.35 (*dd*, J = 9.0, 2.9 Hz), 7.47 (*d*, J = 9.0 Hz) and 7.61 (*d*, J = 2.9 Hz)] and a hydroxyl group [δ 8.79 (*br s*)]. The ^{13}C NMR spectrum (Table 1) showed the presence of a carbonyl group (δ 171.5), the signal strength of which was significantly attenuated. Taking these data and UV absorptions into account, **1** was suggested to be a xanthone with a symmetrical axis in the structure. Then, the number of hydroxyl group and hydrogen were duplicated. The structure for **15** was supposed to be 2,7-dihydroxyxanthone. When the ^1H and ^{13}C NMR spectral data of **15** were compared with those of 2-hydroxyxanthone, which has a partially similar structure and was previously isolated from this plant [5], both spectral data agreed completely. Therefore, **15**, 2,7-dihydroxyxanthone.

Compounds **3**–**14** and **16** were identified as 1,5-dihydroxy- (**3**), 1,5-dihydroxy-3-methoxy- (**4**), 1,7-dihydroxy- (**5**), 1-hydroxy-7-methoxy- (**6**), 2-methoxy- (**7**), 4-methoxy- (**8**), 1,4,5-trihydroxy- (**9**), 1,3,5-trihydroxy- (**10**), 1,3,6-trihydroxy-7-methoxy- (**11**), 1,3,7-trihydroxy- (**12**), 3-hydroxy-2-meth-



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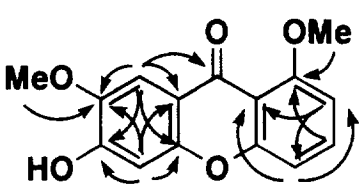

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Fig. 1. HMBC (J = 10 Hz) spectrum of **1** and **17**.

oxyxanthone (**13**), (−)-epicatechin (**14**) and 5-hydroxy-1-methoxyxanthone (**16**), respectively, by spectroscopic analysis.

EXPERIMENTAL

Plant material. Stem of *P. pauciflorum* was collected in Tamil Nada, India, in June 1995, and stem with bark of *M. acuminata* was also collected in Indonesia, in October, 1994. Both voucher specimens are deposited in the Herbarium of Gifu Pharmaceutical University.

Extraction and isolation. The dried and ground stem of *P. pauciflorum* (850 g) was extracted successively with C_6H_6 (21 × 24 hr × 3) (residual wt after conc: 3 g), Me_2CO (21 × 24 hr × 3) (25 g) and 70% MeOH (21 × 24 hr × 3) (25 g) under reflux. The Me_2CO extract (17 g) was subjected to Si CC eluted with $CHCl_3$–MeOH system to give 11 frs (frs 1–11). Fr. 2 ($CHCl_3$ 100%) was chromatographed on Sephadex LH-20 eluted with Me_2CO to give four fractions (frs 2-1–2-4). Fr. 2-1 was further purified by PTLC (*n*-hexane–Me_2CO 50:1) to isolate **6** (1 mg), **7** (2 mg) and **8** (1 mg). Fr. 2-2 was also separated by PTLC (*n*-hexane–Me_2CO 20:1) to give **3** (1 mg), **4** (1 mg) and **5** (1 mg). Fr. 2-4 was purified in the same manner (*n*-hexane–EtOAc 15:1) to give **1** (1 mg) and **13** (1 mg). Fr. 3 [$CHCl_3$–MeOH (50:1)] was further chromatographed on Sephadex LH-20 (Me_2CO) to give **9** (2 mg). Fr. 4 (25:1) was repeatedly purified by PTLC with three solvent systems [*n*-hexane–EtOAc–MeOH (8:2:1), C_6H_6–Me_2CO (15:1) and $CHCl_3$–MeOH (50:1)] to isolate **10** (1 mg), **11** (1 mg) and **12** (1 mg). Fr. 7 [$CHCl_3$–MeOH (5:1)] was chromatographed on Sephadex LH-20 (acetone) to give **14** (6 mg) and **2** (2 mg).

The dried and ground aerial parts (stem and bark) of *M. acuminata* (600 g) were extracted successively with C_6H_6 (21 × 24 hr × 3) (27 g), Me_2CO (21 × 24 hr × 3) (18 g) and 70% MeOH (21 × 24 hr × 3) (50 g) under reflux. The Me_2CO extract (3 g) was subjected to Si CC eluted with a $CHCl_3$–MeOH system. The $CHCl_3$–MeOH (20:1) eluent was repeatedly purified by PTLC with three solvent systems [*n*-hexane–EtOAc–MeOH (8:2:1), C_6H_6–Me_2CO (20:1) and $CHCl_3$–MeOH (40:1)] to give **3** (1 mg), **14** (5 mg), **15** (2 mg) and **16** (1 mg).

Compound **1** (*1,6-dihydroxy-7-methoxyxanthone*). A pale yellow amorphous solid. HREIMS *m/z* 258.0518 for $C_{14}H_{10}O_5$ (calcd 258.0528); EIMS *m/z* (rel. int.): 258 (M^+, 100), 243 (45), 224 (8), 215 (26), 187 (19), 149 (4), 129 (4); IR ν^{KBr} cm^{-1}: 3350, 2900, 1647, 1585; UV λ^{MeOH} nm: 205, 221, 250, 261sh, 269sh, 290, 311sh, 368; ^1H NMR (400 MHz, DMSO-d_6) δ: 3.91 (3H, *s*, OMe-C-7), 6.76 (1H, *dd*, *J* = 8.3, 1.0 Hz, H-2), 6.95 (1H, *s*, H-5), 7.01 (1H, *dd*, *J* = 8.3, 1.0 Hz, H-4), 7.47 (1H, *s*, H-8), 7.65 (1H, *t*, *J* = 8.3 Hz, H-3), 10.99 (1H, *br s*, OH-C6), 12.92 (1H, *s*, OH-C-1).

Synthesis of **1**. A soln containing 2,6-dimethoxybenzoic acid (850 mg, 4.7 mmol) in $SOCl_2$ (1.5 g) was heated under reflux for 2 hr. After evapn of $SOCl_2$, the reaction mixture was dissolved in dried ether (200 ml), and to the soln 2,4-dihydroxy-1-methoxybenzene (650 mg, 4.71 mmol) and $AlCl_3$ (1 g, 7.5 mmol) were added. After the mixt. was stirred at room temp for 12 hr, the solvent was removed under reduced pressure, and the residue was poured into dilute HCl. The acidified suspension was extracted with EtOAc, and the organic solvent was evapd. The resulting residue was treated with 20% NaOH (20 ml) under reflux for 2 hr. The reaction mixt. was purified by Si CC (C_6H_6–Me_2CO 10:1) to give **17** (170 mg).

Compound **17**. An amorphous solid. EIMS *m/z* (rel. int.): 272 (M^+, 100), 255 (18), 243 (46), 227 (26), 226 (35), 211 (7), 199 (13), 171 (13), 136 (5), 115 (8); UV λ^{MeOH} nm: 209sh, 217, 247, 257sh, 269sh, 286, 308, 359; ^1H NMR (400 MHz, DMSO-d_6) δ: 3.87 (3H, *s*, OMe-C-7), 3.89 (3H, *s*, OMe-C-1), 6.87 (1H, *s*, H-5), 6.95 (1H, *dd*, *J* = 8.3, 1.0 Hz, H-2), 7.08 (1H, *dd*, *J* = 8.3, 1.0 Hz, H-4), 7.43 (1H, *s*, H-8), 7.66 (1H, *t*, *J* = 8.3 Hz, H-3), 10.58 (1H, *br s*, OH-C-6). To a solution containing **17** (55 mg, 0.20 mmol) in CH_2Cl_2 (100 ml) cooled at −25 °, BCl_3 (1 ml) was added. The reaction mixt. was left at room temp for 1 hr. The reaction mixt. was partitioned with H_2O, and the organic layer was evapd. The residue was subjected to Si CC (C_6H_6–Me_2CO 20:1) to give **1** (10 mg).

Compound **2** (*1,6-dihydroxy-7-methoxyxanthone* 6-O-*β*-D-*glucoside*). A pale yellow amorphous solid. EIMS *m/z* (rel. int.): 420 (M^+, 1), 258 (100), 243 (38), 238 (12), 215 (17), 187 (11), 129 (5); UV λ^{MeOH} nm: 209, 235, 248, 260sh, 268, 288, 311sh, 369; ^1H NMR (400 MHz, DMSO-d_6) δ: 3.17–3.71 (sugar protons), 3.91 (3H, *s*, OMe-C-7), 4.54, 5.02, 5.06 and 5.35 (1H each, sugar OH), 5.24 (1H, *d*, *J* = 7.3 Hz, H-1′), 6.80 (1H, *dd*, *J* = 8.3, 1.0 Hz, H-2), 7.06 (1H, *dd*, *J* = 8.3, 1.0 Hz, H-4), 7.36 (1H, *s*, H-5), 7.54 (1H, *s*, H-8), 7.69 (1H, *t*, *J* = 8.3 Hz, H-3), 12.79 (1H, *s*, OH-C-1).

Compound **15** (*2,7-dihydroxyxanthone*). A yellow amorphous solid. HREIMS *m/z* 228.0415 for $C_{13}H_8O_4$ (calcd 228.0422); EIMS *m/z* (rel. int.): 228 (M^+, 100), 200 (8), 171 (6), 115 (7); UV λ^{MeOH} nm: 206, 238, 258, 319, 375; ^1H NMR (400 MHz, acetone-d_6) δ: 7.35 (2H, *dd*, *J* = 9.0, 2.9 Hz, H-3, 6), 7.47 (2H, *d*, *J* = 9.0 Hz, H-4, 5), 7.61 (2H, *d*, *J* = 2.9 Hz, H-1, 8), 8.79 (2H, *br s*, OH-C-2, 7).

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