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NEOFLAVONOIDS FROM *DALBERGIA ODORIFERA*

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Key Word Index—*Dalbergia odorifera*; Leguminosae; neoflavonoids; 3′-hydroxy-melanettin; 3′-hydroxy-2,4,5-trimethoxydalbergiquinol.

Abstract—Two new neoflavonoids, 3′-hydroxymelanettin and 3′-hydroxy-2,4,5-trimethoxydalbergiquinol, were isolated from the heartwood of *Dalbergia odorifera*, together with the known compounds, dalbergin, melanettin, stevenin, 4-methoxydalbergione, and cearoin. The structures of the new compounds were established by spectral methods, especially 2D NMR. The ^{13}C assignments using HMQC and HMBC experiments were reported for all compounds. © 1997 Published by Elsevier Science Ltd

INTRODUCTION

The heartwood of *Dalbergia odorifera* T. Chen. (Leguminosae) has been used in traditional Chinese medicine to treat blood disorders, ischemia and inflammation [1]. Previous studies on this plant have resulted in the isolation of flavonoids and other phenolic constituents [2–4]. In our present investigation of the bioactive principles of this plant, two new neoflavonoids, 3′-hydroxymelanettin (**4**) and 3′-hydroxy-2,4,5-trimethoxydalbergiquinol (**5**), and five known neoflavonoids, dalbergin (**1**) [5], melanettin (**2**) [6], stevenin (**3**) [5], 4-methoxydalbergione (**6**) [7] and cearoin (**7**) [8] (see Fig. 1), were isolated from the heartwood for the first time. We report here the structural elucidation of the new compounds and ^{13}C NMR spectral assignments of all compounds obtained by NOESY, HMQC and HMBC experiments.

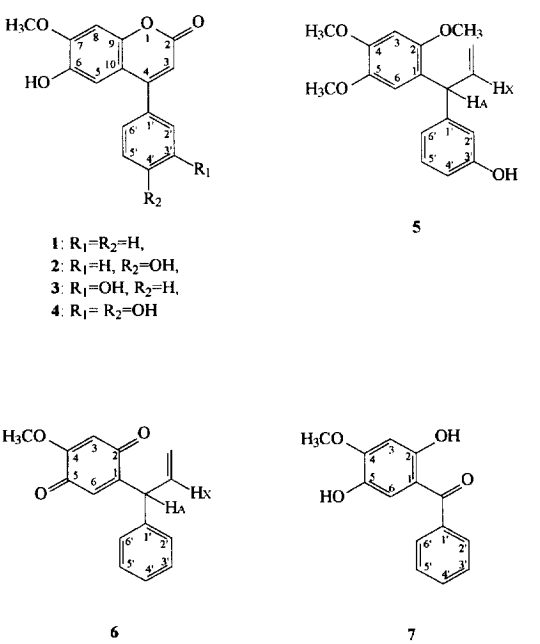

Fig. 1. The structures of **1–7**.

RESULT AND DISCUSSION

The UV, IR and ^1H NMR spectra of **1** closely resembled those reported for dalbergin [5]. However in further studies using NOESY, HMQC and HMBC experiments, we found that the previous ^1H [5] and ^{13}C [9] NMR spectra assignments were incorrect. In NOESY experiments we observed correlations between δ 7.08 and 3.86 and between δ 6.79 and 7.52 (Fig. 2). Thus, the two singlets of aromatic proton signals at δ 7.08 and δ 6.79 were assigned to the protons located at C-8 and C-5, respectively, and the methoxyl signal at δ 3.86 was located at C-7. According to the HMQC and HMBC experiments (Fig. 3), we have revised the assignments of the ^{13}C NMR spectrum (see Table 1) and confirm the structure of **1** as dalbergin.

Compounds **2** and **3** were identified by comparison of their UV and ^1H NMR spectral data as melanettin [6] and stevenin [5], respectively. The position of the methoxyl groups in the two compounds were confirmed by NOESY spectra.

The HREI mass spectrum of **4** showed a $[M]^+$ peak

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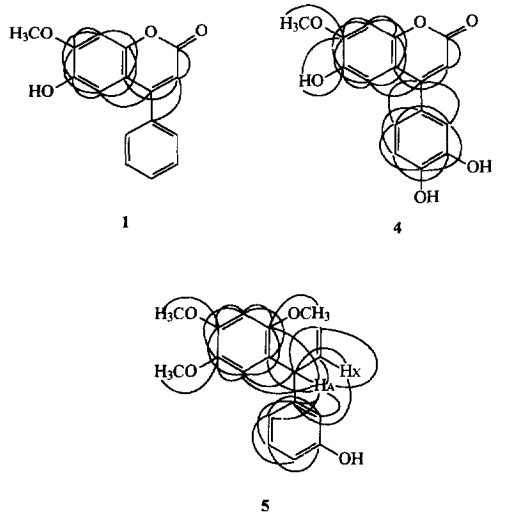

Fig. 2. The HMBC correlations of **1**, **4**, **5**.

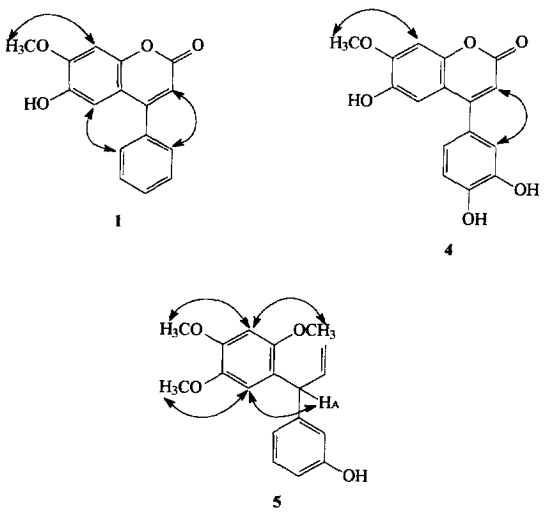

Fig. 3. The NOESY correlations of **1**, **4**, **5**.

at *m/z* 300.0633, consistent with the molecular formula of $C_{16}H_{12}O_6$. The UV spectrum was in close agreement with that of dalbergin, suggesting that **4** was also a neoflavonoid. The ^{1}H NMR spectrum showed three singlets at δ 6.05, 6.98 and 7.07 and an ABX-system at δ 6.79 (1H, *dd*, J = 8, 1.8 Hz), δ 6.86 (1H, *d*, J = 1.8 Hz), δ 6.88 (1H, *d*, J = 8 Hz), characteristic of the protons located at C-3, C-5, C-8, and the B ring of a neoflavonoid, respectively. Other signals were a methoxyl singlet at δ 3.87, three phenolic hydroxyls at δ 9.39, 9.43 and 9.52. The observed NOESY correlation depicted in Fig. 2, indicated that the methoxyl was located at C-7 (cross peaks H-8/OCH_3). From the above data, the structure of **4** was assigned as 3′,4′,6-trihydroxy-7-methoxyneoflavone i.e. 3′-hydroxymelanettin.

The HREI mass spectrum of **5** showed a $[M]^+$ peak at *m/z* 300.1369, consistent with the molecular formula of $C_{18}H_{20}O_4$. The IR and UV spectra of **5** were similar to those of *R*(+)-dalbergiphenol [8] and *R*-5-*O*-methyl latifolin [10]. The ^{1}H NMR spectrum showed the characteristic of a $>CH_A$-$CH_x = CH_2$-element at δ 4.92 (1H, *dd*, J = 17.1, 1.6 Hz, $= CH_{2trans}$) and δ 5.03 (1H, *d*, J = 6.7 Hz, C-H_A), δ 5.17 (1H, *dd*, J = 10.2, 1.6 Hz, $= CH_{2cis}$) and δ 6.22 (1H, *ddd*, J = 17.1, 10.2, 6.7 Hz, C-H_X), two singlets at δ 6.52 and 6.60 and three methoxyl signals at δ 3.70, 3.75 and 3.85, which were all in agreement with *R*(+)-dalbergiphenol [8] and *R*-5-*O*-methyl latifolin [10]. Thus, we suggest that the structure of **5** is similar to that of the *R*(+)-dalbergiphenol and *R*-5-*O*-methyl latifolin. Since the other signals showed an ABCX aromatic proton system at δ 6.62 (1H, *d*, J = 2 Hz), δ 6.64 (1H, *dd*, J = 8, 2 Hz) and δ 6.74 (1H, *d*, J = 8 Hz), δ 7.11 (1H, *dd*, J = 8, 8 Hz), we could confirm the position of the phenolic hydroxy group at C-3′. From the above data, we suggest **5** to be 3-(3-hydroxyphenyl)-3-(2,4,5-trimethoxy-phenyl)-prop-1-ene or 3′-hydroxy-2,4,5-trimethoxydalbergiquinol.

Compounds **6** and **7** were identified by comparison of their ^{1}H NMR spectra with those in the literature data as 4-methoxydalbergione [7] and cearoin [8], respectively. These and all the other structures and ^{13}C NMR data assignments (Table 1) were confirmed using HMQC and HMBC (Fig. 3) experiments.

EXPERIMENTAL

General. Commercially available, processed heartwood of *Dalbergia odorifera* T. Chen. (Leguminosae) was purchased from the local market and authenticity was confirmed by Prof. Chung-Chuan Chen of China Medical College. A voucher specimen is deposited in the herbarium of the School of Pharmacy, China Medical College, Taiwan, Republic of China. IR spectra were measured in KBr. Mps were uncorr. Silica gel 60 (E. Merck), Sephadex LH-20 (Sigma), Diaion HP-20 (Mitsubishi) were used for CC.

Isolation of constituents. The heartwood of *D. odorifera* (10 kg) was extracted exhaustively with MeOH (20 l × 5). The concd MeOH extract (fr. A, 1150 gm) was suspended in H_2O and partitioned successively with EtOAc and *n*-BuOH to afford frs B (850 gm), C (30 gm) and D (135 gm, H_2O layer). Fr. B (180 gm) was chromatographed on a silica gel column eluted with a gradient of *n*-hexane–EtOAc to give frs I–VI. These frs were chromatographed successively on silica gel eluted with CH_2Cl_2, Sephadex LH-20 eluted with MeOH and Diaion HP-20 eluted with MeOH–H_2O to afford **1**–**7**.

Dalbergin (**1**). Yellow prisms (MeOH), mp 210–211°, R_f 0.59 (CH_2Cl_2–MeOH, 10:1). IR [5], UV [5], $[M]^+$ 268. ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.86 (3H, *s*, 7-OCH_3), 6.16 (1H, *s*, H-3), 6.79 (1H, *s*, H-5), 7.08 (1H, *s*, H-8), 7.52 (5H, *m*, H-2′–6′), 9.43 (1H, *s*, 6-OH). ^{13}C NMR (50 MHz, DMSO-d_6): Table 1.

3′-Hydroxymelanettin (**4**). White powder (MeOH): mp 297–299°. R_f 0.442 (CH_2Cl_2–MeOH, 10:1). UV λ_{max}^{MeOH} nm (log ε): 235 sh (4.274), 256 (4.063), 296 sh (3.934), 346 (4.179). EIMS *m/z* (rel. int.): 300 $[M]^+$ (76), 272 (68), 257 (63), 187 (12), 155 (16), 136 (14),

Table 1. ^{13}C NMR chemical shifts of compounds **1** [9], **2**–**5**, **6** [8], **7** [8]

C	1	2	3	4	C	5	6	7
C-2	160.85	160.39	160.67	160.99	C-1	123.20	151.02	111.77
C-3	111.70*	110.28	111.22	110.59	C-2	151.24	186.84	160.09*
C-4	155.55*	155.03	155.45	155.72	C-3	98.34	108.42	99.91
C-5	110.75*	110.62	110.61	111.11	C-4	148.17	159.67	153.80*
C-6	143.96*	143.34	143.74	143.79	C-5	142.99	182.52	137.71
C-7	152.35*	151.67	152.14	152.12	C-6	113.58	132.13*	116.70
C-8	100.91	100.43	100.76	100.89	C-1′	145.23	141.05	138.23
C-9	148.83*	148.33	148.62	148.83	C-2′	115.38	129.29	128.74
C-10	111.32*	111.06	111.12	111.49	C-3′	155.43	129.36	128.31
C-1′	135.72	125.76	136.81	126.68	C-4′	112.91	127.64*	131.44
C-2′	128.71	129.76	115.21	145.81	C-5′	129.17	129.36	128.31
C-3′	129.24	115.48	157.74	116.26	C-6′	120.89	129.29	128.74
C-4′	129.95	158.67	116.67	147.41	$C\text{-}H_A$	46.89	48.11	—
C-5′	129.24	115.48	130.30	120.26	$C\text{-}H_X$	140.13	138.93	—
C-6′	128.71	129.76	119.12	116.08	CH_2	116.09	117.88	—
7-OCH_3	56.57	56.04	56.40	56.55	C=O	—	—	200.03
					2-OCH_3	56.80	—	—
					4-OCH_3	56.07	56.64	56.36
					5-OCH_3	56.66	—	—

* Signals revised.

127 (15), 115 (36), 114 (18), 113 (27), 102 (14), 87 (16), 77 (34), 69 (100), 63 (41), 53 (36), 51 (35). HRMS: Found 300.0633 ($C_{16}H_{12}O_6$), require 300.0634. ^1H NMR (300 MHz, DMSO-d_6) δ 3.87 (3H, *s*, 7-OCH_3), 6.05 (1H, *s*, H-3), 6.79 (1H, *dd*, $J = 8$, 1.8 Hz, H-6′), 6.86 (1H, *d*, $J = 1.8$ Hz, H-2′), 6.88 (1H, *d*, $J = 8$ Hz, H-5′), 6.98 (1H, *s*, H-5), 7.07 (1H, *s*, H-8), 9.39 (1H, *s*, 3′-OH), 9.43 (1H, *s*, 6-OH), 9.52 (1H, *s*, 4′-OH). ^{13}C NMR (75.4 MHz, DMSO-d_6): Table 1.

3′-Hydroxy-2,4,5-trimethoxydalbergiquinol (**5**). White crystals (MeOH–H_2O), mp 124–126°, R_f 0.76 (CH_2Cl_2–MeOH, 10:1). $[\alpha]_D$ −39.4° ($CHCl_3$, *c* 0.06). UV λ_{max}^{MeOH} nm (log ε): 229 sh (4.02), 284 (3.69). EIMS *m/z* (rel. int.): 300 $[M]^+$ (100), 285 (19), 269 (30), 254 (10), 253 (22), 224 (17), 181 (21), 176 (15), 168 (30), 165 (15), 153 (23), 152 (12), 138 (10), 131 (40), 127 (19), 115 (20), 107 (43), 77 (42), 69 (41), 63 (24). HRMS: Found 300.1369 ($C_{18}H_{20}O_4$), require 300.1361. ^1H NMR (300 MHz, $CDCl_3$) δ 3.71 (3H, *s*, 2-OCH_3), 3.75 (3H, *s*, 4-OCH_3), 3.75 (3H, *s*, 5-OCH_3), 4.92 (1H, *dd*, $J = 17.1$, 1.6 Hz, $= CH_{2trans}$), 5.03 (1H, *d*, $J = 6.7$ Hz, $C\text{-}H_A$), 5.17 (1H, *dd*, $J = 10.2$, 1.6 Hz, $= CH_{2cis}$), 6.22 (1H, *ddd*, $J = 17.1$, 10.2, 6.7 Hz, $C\text{-}H_X$), 6.52 (1H, *s*, H-3), 6.62 (1H, *d*, $J = 2$ Hz, H-2′), 6.64 (1H, *dd*, $J = 8$, 2 Hz, H-4′), 6.66 (1H, *s*, H-6), 6.74 (1H, *d*, $J = 7.6$ Hz, H-6′), 7.11 (1H, *dd*, $J = 8$, 7.6 Hz, H-5′). ^{13}C NMR (75.4 MHz, $CDCl_3$): Table 1.

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