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HOMOISOFLAVONOIDS FROM *CAESALPINIA SAPPAN**

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Key Word Index—*Caesalpinia sappan*; Leguminosae; heartwood; homoisoflavonoids; flavonoids; brazilin.

Abstract—Three new homoisoflavonoids, 7-hydroxy-3-(4′-hydroxybenzylidene)-chroman-4-one, 3,7-dihydroxy-3-(4′-hydroxybenzyl)-chroman-4-one and 3,4,7-trihydroxy-3-(4′-hydroxybenzyl)-chroman were isolated from the dried heartwood of *Caesalpinia sappan*, together with the known compounds 4,4′-dihydroxy-2′-methoxychalcone, 8-methoxybonducellin, quercetin, rhamnetin and ombuin.

INTRODUCTION

A number of phenolic compounds have been isolated from *Caesalpinia sappan* L. [1–7]. In the course of our studies on homoisoflavonoids and related compounds, we have reported the isolation and structure elucidation of six homoisoflavonoids from the dried heartwood of *C. sappan* [1], which is known as Sappan Lignum among the oriental crude drugs. In the present paper, we report the isolation and structure assignment of three new homoisoflavonoids, 7-hydroxy-3-(4′-hydroxybenzylidene)-chroman-4-one (**2**), 3,7-dihydroxy-3-(4′-hydroxybenzyl)-chroman-4-one (**4**) and 3,4,7-trihydroxy-3-(4′-hydroxybenzyl)-chroman (**6**), and the known compounds 4,4′-dihydroxy-2′-methoxychalcone (**1**) [8], 8-methoxybonducellin (**8**) [9], quercetin (**9**), rhamnetin (**10**) and ombuin (**11**) from the same source.

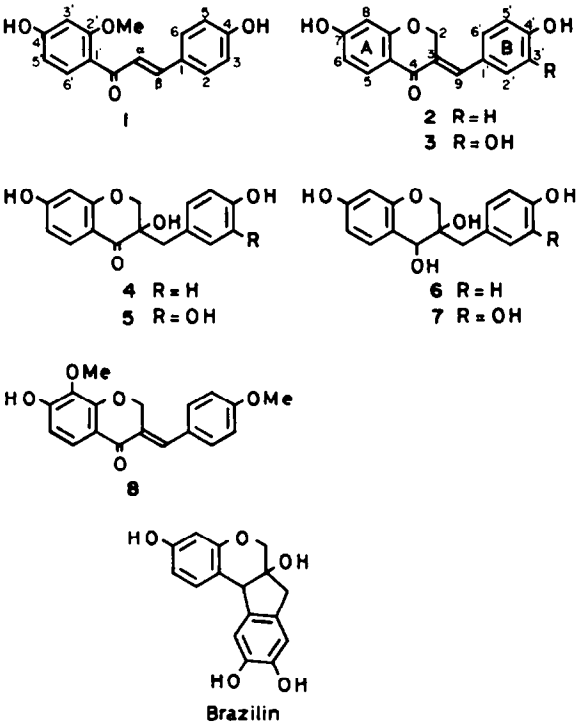
RESULTS AND DISCUSSION

Compound **1** was isolated as yellow needles and its molecular formula $C_{16}H_{14}O_4$ deduced from the high resolution mass spectrum. The physicochemical properties (Experimental) of **1** were identical with those of 4,4′-dihydroxy-2′-methoxychalcone [8].

The molecular formula of compound **2**, $C_{16}H_{12}O_4$, was determined from the high resolution mass spectrum. A ^{1}H NMR signal at δ7.80 (1H, *d*) was *ortho*-coupled (J = 8.8 Hz) to a one-proton doublet of doublets at δ6.53, which was further *meta*-coupled to a one-proton doublet (J = 2.2 Hz) at δ6.31. These signals could be assigned to the protons at C-5, C-6 and C-8, respectively. The long-range coupled (J = 1.8 Hz) signals at δ7.71 (1H, *t*) and δ5.35 (2H, *d*) were assigned to H-9 and H-2, respectively. These signals, assigned to H-2–H-9, closely resembled those of **3** [1] (summarized in Table 1). The pair of two-proton doublets (J = 9.0 Hz) at δ 6.88 and δ7.25 in the ^{1}H NMR spectrum of **2** showed the presence of a *para*-substituted aromatic ring. An *E*-orientation of the double bond at C-3 (C-9) was indicated by the position of the H-2 and H-9 proton signals at δ5.35 and δ7.71, respectively [10]. Compound **2** is therefore 7-hydroxy-3-(4′-hydroxybenzylidene)-chroman-4-one.

Compound **4** possesses the molecular formula $C_{16}H_{14}O_5$ (high resolution mass spectrum). The ^{1}H NMR signals, assigned to H-2–H-9, of **4** were very similar to those of **5** [1] (summarized in Table 1). The remaining resonances in the spectrum of **4** displayed the signals of typical *para*-substituted aromatic protons, whose pair of two-proton doublets (J = 8.9 Hz) at δ6.76 and δ7.09 were assignable to H-3′,5′ and H-2′,6′ of the B-ring, respectively. Compound **4** is therefore 3,7-dihydroxy-3-(4′-hydroxybenzyl)-chroman-4-one.

The molecular ion peak was not detected in the EI mass



*Part 1 in the series "Homoisoflavonoids and Related Compounds".

Table 1. ^{1}H NMR data (100 MHz) for compounds 2–7*

Compound (solvent)	H-2	H-4	H-5	H-6	H-8	H-9	H-2′	H-3′	H-5′	H-6′
2	5.35(*d*)	—	7.80(*d*)	6.53(*dd*)	6.31(*d*)	7.71(*t*)	7.25(*d*)	6.88(*d*)	6.88(*d*)	7.25(*d*)
(CD_3OD)	J = 1.8		J = 8.8	J = 2.2, 8.8	J = 2.2	J = 1.8	J = 9.0	J = 9.0	J = 9.0	J = 9.0
3	5.39(*d*)	—	7.83(*d*)	6.55(*dd*)	6.34(*d*)	7.68(*t*)		—	6.60–7.00(3H, *m*)	
(CD_3OD)	J = 1.8		J = 8.9	J = 2.2, 8.9	J = 2.2	J = 1.8				
4	4.05(*d*)	—	7.74(*d*)	6.63(*dd*)	6.47(*d*)	2.90(*s*)	7.08(*d*)	6.77(*d*)	6.77(*d*)	7.08(*d*)
(acetone-d_6)	4.21(*d*)		J = 8.8	J = 2.2, 8.8	J = 2.2		J = 8.9	J = 8.9	J = 8.9	J = 8.9
	J = 11.5									
5	4.05(*d*)	—	7.73(*d*)	6.64(*dd*)	6.48(*d*)	2.85(*s*)	6.81(*d*)	—	6.76(*d*)	6.56(*dd*)
(acetone-d_6)	4.23(*d*)		J = 8.8	J = 2.2, 8.8	J = 2.2		J = 2.0		J = 8.0	J = 2.0, 8.0
	J = 11.5									
6	3.65(*dd*)	4.22(*d*)	7.11(*d*)	6.43(*dd*)	6.27(*d*)	2.66(*s*)	7.02(*d*)	6.69(*d*)	6.69(*d*)	7.02(*d*)
(CD_3OD)	J = 1.3, 10.5	J = 1.3	J = 8.2	J = 2.2, 8.2	J = 2.2		J = 8.8	J = 8.8	J = 8.8	J = 8,8
	3.89(*d*)									
	J = 10.5									
7†	3.67(*dd*)	4.21(*d*)	7.09(*d*)	6.41(*dd*)	6.26(*d*)	2.57(*d*)	6.69(*d*)	—	6.66(*d*)	6.50(*dd*)
(CD_3OD)	J = 1.2, 10.6	J = 1.2	J = 8.2	J = 2.3, 8.2	J = 2.3	2.63(*d*)	J = 2.0		J = 8.0	J = 2.0, 8.0
	3.88(*d*)					J = 14.0				
	J = 10.6									

*Chemical shifts are given in δ (ppm) relative to TMS. Coupling constants are given in Hz.
†This compound was observed at 400 MHz.

spectrum of **6**, but a $[M-H_2O]^+$ ion at m/z 270 was observed. A similar phenomenon was observed in the EI mass spectrum **7** [1]. Comparison of the ^{1}H NMR spectrum of **6** with those of **4** and **7** (summarized in Table 1) revealed the structure of **6** as 3,4,7-trihydroxy-3-(4′-hydroxybenzyl)-chroman.

Compound **8** was obtained as a yellow gum, showing a $[M]^+$ for $C_{18}H_{16}O_5$ at m/z 312 in the mass spectrum. The physical and spectral properties (Experimental) of **8** were identical with those of 8-methoxybonducellin [9]. Compound **8** is therefore 7-hydroxy-8-methoxy-3-(4′-methoxybenzylidene)-chroman-4-one.

Compounds **9**, **10** and **11** were identical with the authentic specimens of quercetin, rhamnetin and ombuin, respectively.

Compounds **1** and **8–11** have never been isolated from this plant before.

The biogenetic pathway from sappanchalcone (3,4,4′-trihydroxy-2′-methoxychalcone) [3] to brazilin, a well known main component of this plant, via compounds **3**, **5** and **7** was confirmed [1, 3, 11]. The compounds reported in this paper were biogenetically synthesized via a similar pathway to these compounds, that is from compound **1** → **2** → **4** to **6**. But compound **6** will not cyclize to form a brazilin type compound, because of the lack of an oxygen-function at C-3′ [11].

EXPERIMENTAL

Extraction and isolation. The dried heartwood of *C. sappan* L. (Sappan Lignum) (500 g), purchased in Tokyo, was extracted with MeOH (3 days at room temp. × 3). The MeOH extract (48.9 g) was repeatedly subjected to CC on silica gel, Sephadex LH-20 or Polyamide as described previously [1]. The minor components reported in this paper were isolated by repeated CC on Sephadex LH-20 (MeOH) and silica gel, and prep. TLC of the remaining fractions after separation of the previously reported compounds. Various ratios of the solvent mixtures [$CHCl_3$–MeOH, C_6H_6–Me_2CO, hexane–Me_2CO] were used on a silica gel column and in TLC and afforded the **1** (26 mg), **2** (8 mg), **4** (5 mg), **6** (210 mg), **8** (4 mg), **9** (12 mg), **10** (6 mg) and **11** (5 mg).

The R_f values of the compounds **1–8** are as follows: solvent mixtures (A) $CHCl_3$–MeOH (9:1), (B) C_6H_6–Me_2CO (4:1), (C) C_6H_6–Me_2CO (7:3), (D) hexane–Me_2CO (3:2), (E) hexane–Me_2CO (1:1); **1** [0.43 (A), 0.26 (B), 0.43 (C), 0.22 (D), 0.44 (E)], **2** (0.42, 0.33, 0.48, 0.27, 0.50), **3** (0.34, 0.16, 0.33, 0.16, 0.36), **4** (0.38, 0.27, 0.43, 0.23, 0.45), **5** (0.28, 0.11, 0.27, 0.14, 0.33), **6** (0.24, 0.12, 0.29, 0.15, 0.34), **7** (0.11, 0.04, 0.11, 0.08, 0.20), **8** (0.79, 0.59, 0.68, 0.50, 0.70).

Compound **1**. Yellow needles ($CHCl_3$), mp 210–212°, UV λ_{max}^{MeOH} nm (log ε): 349 (3.90), 235 (4.04); EIMS (70 eV) m/z: 270.0865 ($[M]^+$; calcd for $C_{16}H_{14}O_4$: 270.0890) (100%), 269 (22), 255 (32), 253 (16), 242 (17), 164 (53), 151 (83), 147 (37), 137 (25), 121 (28), 120 (17), 119 (20), 108 (18), 107 (34), 91 (18), 65 (23); ^{1}H NMR (100 MHz in acetone-d_6): δ 3.92 (3H, *s*, OMe), 6.53 (1H, *dd*, J = 2.2, 8.5 Hz, H-5′), 6.60 (1H, *d*, J = 2.2 Hz, H-3′), 6.91 (2H, *d*, J = 8.8 Hz, H-3 and 5), 7.44 (1H, *d*, J = 16.2 Hz, H-α), 7.50–7.68 (4H, *m*, H-β, 2, 6 and 6′). These data agreed with lit. values [8].

Compound **2**. Yellow needles (Me_2CO–hexane), mp 248–249°; UV λ_{max}^{MeOH} nm (log ε): 369 (4.58), 323 (sh, 4.46), 239 (4.34); EIMS (70 eV) m/z: 268.0731 ($[M]^+$; calcd for $C_{16}H_{12}O_4$: 268.0733) (74%), 267 (34), 151 (38), 138 (51), 137 (100), 132 (64), 131 (89), 103 (31), 77 (56).

Compound **4**. $[\alpha]_D^{25}$ +11.9° (MeOH, *c* 0.21); UV λ_{max}^{MeOH} nm (log ε): 310 (3.55), 275 (3.92), 227 (4.14); EIMS (70 eV) m/z: 286.0847 ($[M]^+$; calcd for $C_{16}H_{14}O_5$: 286.0841) (16%), 179 (100), 151 (22), 137 (80), 123 (23), 121 (23), 108 (61), 107 (98), 105 (30), 95 (28), 77 (73).

Compound **6**. Colourless needles (Me_2CO–hexane), mp 182–183°; $[\alpha]_D^{25}$ +54.5° (MeOH, *c* 0.77); UV λ_{max}^{MeOH} nm (log ε): 284 (3.74), 278 (3.80), 223 (4.37); EIMS (70 eV) m/z: 270 ($[M-H_2O]^+$, 7%), 164 (100), 163 (40), 147 (12), 102 (98), 77 (42).

Compound **8**. UV λ_{max}^{EtOH} nm (log ε): 348 (4.23), 328 (sh, 4.20), (EtOH–NaOAc): 388 (4.22), 318 (4.15), 270 (3.89),

(EtOH–NaOAc–H_3BO_3): 348 (4.22), 328 (sh, 4.20); EIMS (70 eV) *m/z*: 312 ([M]$^+$, 50%), 167 (56), 146 (100), 138 (37), 131 (31), 123 (17), 115 (11), 103 (43), 95 (16), 77 (23); ^{1}H NMR (100 MHz in acetone-d_6): δ 3.84 (3H, *s*, OMe), 3.89 (3H, *s*, OMe), 5.49 (2H, *d*, J = 1.8 Hz, H-2), 6.66 (1H, *d*, J = 8.8 Hz, H-6), 7.08 (2H, *d*, J = 9.0 Hz, H-3′ and 5′), 7.45 (2H, *d*, J = 9.0 Hz, H-2′ and 6′), 7.63 (1H, *d*, J = 8.8 Hz, H-5), 7.73 (1H, *t*, J = 1.8 Hz, H-9). These data agreed with lit. values [9].

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