Flavonoids from the Resin of *Dracaena cochinchinensis*

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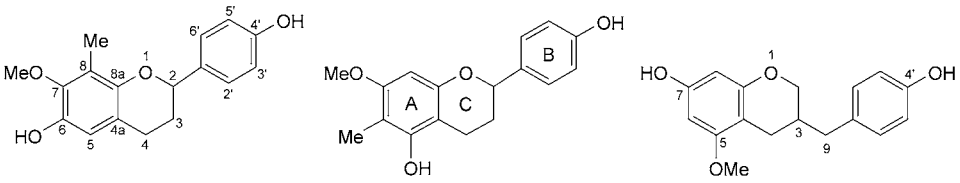
Chemical investigation of the red herbal resin of *Dracaena cochinchinensis* resulted in the isolation of three new configurationally isomeric flavonoids: 6,4′-dihydroxy-7-methoxy-8-methylflavane (= 3,4-dihydro-2-(4-hydroxyphenyl)-7-methoxy-8-methyl-2*H*-[1]benzopyran-6-ol; **1**), 5,4′-dihydroxy-7-methoxy-6-methylflavane (= 3,4-dihydro-2-(4-hydroxyphenyl)-7-methoxy-6-methyl-2*H*-[1]benzopyran-5-ol; **2**), and 7,4′-dihydroxy-5-methoxyhomoisoflavane (= 3,4-dihydro-3-[(4-hydroxyphenyl)methyl]-5-methoxy-2*H*-[1]benzopyran-7-ol; **3**). Their structures were identified by means of detailed spectral analysis.
In addition, thirteen known compounds were isolated from *D. cochinchinensis:* 7-hydroxy-4′-methoxyflavane (**4**), 2,4,6-trimethoxy-4′-hydroxydihydrochalcone (**5**), 2,4-dimethoxy-4′-hydroxydihydrochalcone (**6**), 7,8-(methylenedioxy)-4′-hydroxyhomoisoflavane (**7**), 4′,7-dihydroxy-8-methylflavane (**8**), 2,6-dimethoxy-4,4′-dihydroxydihydrochalcone (**9**), 2-methoxy-4,4′-dihydroxydihydrochalcone (**10**), 7-methoxy-6,4′-dihydroxyhomoisoflavane (**11**), 2-methoxy-4,4′-dihydroxychalcone (**12**), 4′,7-dihydroxyflavane (**13**), 7,4′-dihydroxyhomoisoflavane (**14**), 7,4′-dihydroxyhomoisoflavone (**15**), and 7,4′-dihydroxyflavone (**16**). Compounds **7**, **8**, **9**, **14**, and **15** have been isolated for the first time from this type of herbal source.

Introduction. – The red resin of *Dracaena cochinchinensis* S. C. CHEN (Agavaceae), a raw material of Chinese Dragon's Blood, is commonly used in traditional Chinese medicine for the treatment of traumatic and visceral hemorrhages [1]. The original plant of this herb material is native to the tropic region of Southwest China, from which steroidal glycosides and flavonoids have been isolated [2–5]. Chemical studies have revealed that the resin mainly contains phenolic compounds, as well as some steroids and aliphatic acids [6–11]. In the case of the red resin of *D. cochinchinensis*, phenol derivatives are the main constituents.

As a part of our continuing studies on Chinese Dragon's Blood, a total of 16 flavonoids (**1**–**16**) have been isolated, including three new ones: 6,4′-dihydroxy-7-methoxy-8-methylflavane (**1**), 5,4′-dihydroxy-7-methoxy-6-methylflavane (**2**), and 7,4′-dihydroxy-5-methoxyhomoisoflavane[1]) (**3**). Here, we describe the isolation and characterization of the new compounds **1**–**3**, which were identified by means of spectroscopic methods.

Results and Discussion. – The $CHCl_3$ extract of the resin of *D. cochinchinensis* was subjected to repeated column chromatography (CC) on *a*) silica gel, *b*) *Sephadex LH-20* gel, *c*) *CHP-20* gel, and *d*) *RP-18* gel, affording, besides **1**–**3**, the known flavonoids **4**–**16**. The latter were identified, based on comparison with literature data, as 7-

[1]) For systematic names, see the *Exper. Part*.



1 **2** **3**

hydroxy-4′-methoxyflavane (**4**) [7], 2,4,6-trimethoxy-4′-hydroxydihydrochalcone (**5**) [12], 2,4-dimethoxy-4′-hydroxydihydrochalcone (**6**) [13], 7,8-(methylenedioxy)-4′-hydroxyhomoisoflavane (**7**) [14], 4′,7-dihydroxy-8-methylflavane (**8**) [13], 2,6-dimethoxy-4,4′-dihydroxydihydrochalcone (**9**) [15], 2-methoxy-4,4′-dihydroxydihydrochalcone (**10**) [12], 7-methoxy-6,4′-dihydroxyhomoisoflavane (**11**) [7], 2-methoxy-4,4′-dihydroxychalcone (**12**) [11], 4′,7-dihydroxyflavane (**13**) [9], 7,4′-dihydroxyhomoisoflavane (**14**) [13], 7,4′-dihydroxyhomoisoflavone (**15**) [13], and 7,4′-dihydroxyflavone (**16**) [14].

Compound **1**, obtained as a colorless amorphous powder, with an $[\alpha]_D^{26}$ value of 0.00 (MeOH), had the molecular formula $C_{17}H_{18}O_4$, as determined by EI-MS (M^+ signal at *m/z* 286) and HR-ESI-MS ($[M+Na]^+$ signal at *m/z* 309.1099 ($C_{17}H_{18}NaO_4^+$; calc. 309.1102)). The structure of **1** was established by ^{1}H-NMR, ^{13}C-NMR (*Tables 1* and *2*, resp.), HMQC, HMBC, ^{1}H,^{1}H-COSY, and NOESY experiments as 6,4′-dihydroxy-7-methoxy-8-methylflavane (= 3,4-dihydro-2-(4-hydroxyphenyl)-7-methoxy-8-methyl-2*H*-[1]benzopyran-6-ol).

Table 1. *^{1}H-NMR Data for Compounds* **1**–**3**. At 400 MHz in CD_3OD; δ in ppm, *J* in Hz.

	1	**2**	**3**
H–C(2)	4.82 (br. *d*, *J* = 8.4, 1 H)	4.80 (*dd*, *J* = 2.2, 13.2, 1 H)	3.99 (*dd*, *J* = 10.4, 1.6, 1 H), 3.59 (*dd*, *J* = 10.4, 8.1, 1 H)
H–C(3)	2.07 (*m*, 1 H), 1.89 (*m*, 1 H)	1.71 (*m*, 1 H), 1.94 (*m*, 1 H)	2.06 (*m*, 2 H)
H–C(4)	2.85 (*m*, 1 H), 2.61 (*m*, 1 H)	2.44 (*m*, 1 H), 2.51 (*m*, 1 H)	2.56 (*m*, 1 H), 2.09 (*m*, 1 H)
H–C(5)	6.40 (*s*, 1 H)	–	–
H–C(6)	–	–	5.95 (*d*, *J* = 2.0)
H–C(8)	–	6.02 (*s*, 1 H)	5.85 (*d*, *J* = 2.0)
H–C(9)	–	–	2.48 (*m*)
H–C(2′,6′)	7.20 (*d*, *J* = 8.6)	7.21 (*d*, *J* = 8.5)	6.70 (*d*, *J* = 8.6)
H–C(3′,5′)	6.77 (*d*, *J* = 8.6)	6.77 (*d*, *J* = 8.5)	6.97 (*d*, *J* = 8.6)
Me	2.07 (*s*)	1.96 (*s*)	–
MeO	3.69 (*s*)	3.70 (*s*)	3.68 (*s*)

A total of 16 signals were observed in the ^{13}C-NMR (DEPT) spectrum of **1** (*Table 2*), including five quaternary C-atoms, seven CH, two CH_2, one MeO, and one Me group. The spectrum showed the presence of twelve aromatic C-atoms (δ_C 100–165), together with an oxygenated CH (δ_C 78.9) and two CH_2 (δ_C 31.7 and 26.6) groups, indicating a flavane skeleton. In addition, Me and MeO signals (δ_C 9.7 and 61.1, resp.) were observed.

Table 2. *^{13}C-NMR Data for Compounds* **1**–**3**. Assignments are based on HMBC and ROESY experiments. At 100.5 MHz in CD_3OD; δ in ppm.

	1	**2**	**3**
C(2)	78.9	78.5	70.2
C(3)	31.7	30.7	34.8
C(4)	26.6	20.5	25.6
C(4a)	120.6	103.3	102.6
C(5)	114.6	155.0	159.6
C(6)	146.5	104.9	92.0
C(7)	148.2	157.1	157.1
C(8)	118.7	92.0	96.0
C(8a)	144.5	155.5	156.0
C(9)	–	–	37.8
C(1′)	135.1	134.7	134.1
C(2′)	128.6	128.2	130.5
C(3′)	116.5	116.0	115.7
C(4′)	158.3	157.8	156.6
C(5′)	116.5	116.0	115.7
C(6′)	128.6	128.2	130.5
Me	9.7	8.1	–
MeO	61.1	55.6	55.3

In the ^{1}H-NMR spectrum, the *s* at δ_H 6.40, assigned to H–C(5) by means of a HMBC interaction with C(4) at δ_C 26.6 (*Figure*), indicated that the flavane ring *A* had three neighboring substituents. HMBC Correlations of H–C(5) with three oxygenated C-atoms (δ_C 148.2, 146.5, and 144.5) indicated oxygenations in both 6- and 7-positions, so that the Me group (δ_C 9.7) was at C(8). In the ROESY spectrum of **1**, the upfield Me H-atoms (δ_H 2.07) were correlated with the MeO H-atoms (δ_H 3.69), indicating that the MeO group was attached at C(7) (*Figure*). The *AA′BB′* spin system at δ_H 7.20 (*d*, $J = 8.60$ Hz, 2 H) and 6.77 (*d*, $J = 8.60$ Hz, 2 H) indicated that the remaining OH group was in 4′-position (ring *B*).

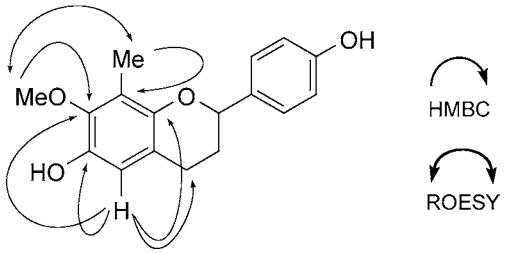


Figure. *Selected HMBC and ROESY correlations observed for flavane* **1**

Compound **2** showed the same molecular formula ($C_{17}H_{18}O_4$) as **1**, as deduced by EI-MS (M^+ at *m/z* 286) and HR-ESI-MS ($[M+Na]^+$ signal at *m/z* 309.1113 ($C_{17}H_{18}NaO_4^+$; calc. 309.1102)), and also gave rise to similar MS fragmentation patterns. From the spectral data, compound **2** – a regioisomer of **1** – was identified as 5,4′-dihydroxy-7-methoxy-6-methylflavane (= 3,4-dihydro-2-(4-hydroxyphenyl)-7-methoxy-6-methyl-2*H*-[1]benzopyran-5-ol).

The ^{1}H- and ^{13}C-NMR spectral features (*Tables 1* and *2*) of **2** were closely related to those of **1**, showing the occurrence of a flavane skeleton with a 4′-OH substituted ring *B*, and ring *A* containing a Me (δ_C 8.1, δ_H 1.96) and a MeO group (δ_C 55.6, δ_H 3.70). However, significant differences were observed for ring-*A* ^{13}C-NMR

chemical shifts, δ_C values of 155.0, 157.1, and 155.5 (three oxygenated quaternary C-atoms) indicating that **2** had two oxy groups at C(5) and C(7), and a methine group (δ_C 92.0) at C(8). Thus, the upfield Me group at δ_C 8.1 was deduced to be at C(6). In the HMBC spectrum (data no shown), correlations of H–C(4) (δ_H 2.51) with C(8a), of H–C(8) (δ_H 6.02) with C(8a) and C(7), and of the MeO H-atoms at δ_H 3.70 with C(7) were observed.

Compound **3** was also shown to have the molecular formula $C_{17}H_{18}O_4$ according to HR-ESI-MS ($[M+Na]^+$ signal at *m/z* 309.1101 (calc. 309.1102)). From the spectral data, the structure of **3** was determined to be 7,4′-dihydroxy-5-methoxy-homoisoflavane (= 3,4-dihydro-3-[(4-hydroxyphenyl)methyl]-5-methoxy-2*H*-[1]benzopyran-7-ol).

The homoisoflavane skeleton of compound **3** was indicated by the ^{13}C-NMR signals of two CH_2 (δ_C 25.6, 37.8), one OCH_2 (δ_C 70.2), one CH (δ_C 34.8), and twelve aromatic C-atoms. In addition, there was a MeO group (δ_C 55.3) present in ring *A*. In the ^{1}H-NMR spectrum, an *AA′BB′* spin system (δ_H 6.97, 6.70 (2*d*, *J* = 8.6 Hz each, 2 × 2 H) indicated a 4′-OH substituent in ring *B*. In addition, two *meta*-coupling H-atom resonances (δ_H 5.95 and 5.85 (2*d*, *J* = 2.0 Hz each, 2 × 1 H), together with the typical ^{13}C-NMR chemical shifts of flavonoids (δ_C 159.6, 157.1, and 156.0) suggested a 5,7-dioxy-substituted ring *A*. In the HMBC spectrum of **3** (data not shown), the MeO (δ_H 3.68) and H–C(4) (δ_C 2.09, 2.56) resonances were both correlated with C(5) (δ_C 159.6).

Experimental Part

General. Column chromatography (CC): silica gel (200–300 mesh; *Qingdao*), *CHP-20P* gel (*MCI*), *Sephadex LH-20* and *FUJI* (*ODS*) gel (*Mitsubishi Chemical Co.*). TLC: precoated plates (*Qingdao*), eluent: MeOH/$CHCl_3$ 1:9. M.p.: *XRC-1* apparatus. UV Spectra: *UV-210A* spectrophotometer (company apparatus); λ_{max} in nm (log ε). IR Spectra: *Bio-Rad FTS-135* spectrometer; in cm^{-1}. NMR Spectra: *Bruker AM-400* or *DRX-500* spectrometers, in CD_3OD; δ values in ppm (rel. to the residual solvent signal), *J* in Hz. EI-MS: *Autospec-3000* mass spectrometer; in *m/z* (rel. %). HR-ESI-MS: *API Qstar Pulsa* spectrometer.

Plant Material. The red resin of *Dracaena cochinchinensis* was purchased from *Weihe Pharmaceutical Factory* (Yunnan, China). A sample was deposited in our laboratory. Identification of the extract was supported by an HPLC comparison with an authentic sample.

Extraction and Isolation. The red resin (1.0 kg) of *D. cochinchinensis* was ground and successively extracted with $CHCl_3$, AcOEt, and MeOH. The $CHCl_3$ extract (90 g) was subjected to CC (SiO_2; $CHCl_3$, $CHCl_3$/MeOH 20:1, 10:1, 10:2, then MeOH): Fractions *Fr. 1–6* (based on TLC evaluation). *Fr. 1* (20.0 g) was subjected to repeated CC (SiO_2; $CHCl_3$/MeOH) to yield the pure compounds **4** (2.0 g), **5** (3.0 g), **6** (14.0 g), and **7** (56 mg). *Fr. 2* (3.0 g) was subjected to CC (1. SiO_2; $CHCl_3$/MeOH; 2. *Sephadex LH-20* gel) to yield the pure compounds **1** (50 mg), **2** (20 mg), **8** (10 mg), and **9** (25 mg). *Fr. 3* (2.0 g) was also subjected to repeated CC (SiO_2, *Sephadex LH-20* gel, *ODS* gel), affording the pure compounds **10** (140 mg), **3** (100 mg), **11** (15 mg), and **12** (50 mg). Finally, *Fr. 4* (4.5 g) was purified by CC (SiO_2, *CHP-20P* gel, *Sephadex LH-20* gel) to yield the pure compounds **13** (200 mg), **14** (1.0 g), **15** [8] (520 mg), and **16** (90 mg).

*3,4-Dihydro-2-(4-hydroxyphenyl)-7-methoxy-8-methyl-2*H*-[1]benzopyran-6-ol* (**1**). Amorphous solid. $[\alpha]_D^{26} = 0.00$ (*c* = 0.2, MeOH). UV (MeOH): 207 (2.6), 284 (0.4), 396 (0.006). IR (KBr): 3433 (br., OH), 2933 (CH), 1374, 1041, 887. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. EI-MS: 286 (65, M^+), 269 (25), 253 (16), 180 (73), 167 (100), 151 (33), 137 (55), 120 (70), 107 (51), 91 (25), 83 (10), 67 (11). HR-ESI-MS: 309.1099 ($[M+Na]^+$, $C_{17}H_{18}NaO_4^+$; calc. 309.1102).

*3,4-Dihydro-2-(4-hydroxyphenyl)-7-methoxy-6-methyl-2*H*-[1]benzopyran-5-ol* (**2**). Colorless crystals (MeOH). M.p. 155–156°. $[\alpha]_D^{26} = 0.00$ (*c* = 0.2, MeOH). UV (MeOH): 211 (3.07), 275 (0.24). IR (KBr): 3433 (br., OH), 2933 (CH), 1374, 1041, 887. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. EI-MS: 286 (48, M^+), 269 (2), 255 (1), 180 (3), 166 (15), 138 (50), 121 (54), 109 (21), 91 (100), 78 (35), 69 (30). HR-ESI-MS: 309.1113 ($[M+Na]^+$, $C_{17}H_{18}NaO_4^+$; calc. 309.1102).

*3,4-Dihydro-3-[(4-hydroxyphenyl)methyl]-5-methoxy-2*H*-[1]benzopyran-7-ol* (**3**). Amorphous solid. $[\alpha]_D^{26} = +24.45$ (*c* = 0.2, MeOH). UV (MeOH): 209 (2.56), 224 (1.77), 281 (0.54). IR (KBr): 3587 (br., OH), 3287, 2916, 1600, 1512, 1237, 1151, 1029, 852. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. EI-MS: 286 (92, M^+), 161 (12), 148 (67), 133 (26), 123 (35), 107 (100), 73 (6), 55 (13). HR-ESI-MS: 309.1101 ($[M+Na]^+$, $C_{17}H_{18}NaO_4^+$; calc. 309.1102).

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