

Phenolic Compounds of Dragon's Blood from *Dracaena draco*

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Three new compounds, 2,4,4'-trihydroxydihydrochalcone (**1**), 3-(4-hydroxybenzyl)-5,7-dimethoxychroman (**2**), and 7-hydroxy-3-(4-hydroxybenzyl)chromone (**3**), were isolated from the resin "Dragon's blood" obtained from *Dracaena draco* along with 18 known compounds. The structures of **1**, **2**, and **3** were determined using MS and NMR techniques.

As part of our research on natural phenolic compounds, the red resin "Dragon's blood" from *Dracaena draco* L. (Dracaenaceae) is being studied anew^{1,2} and has yielded 21 compounds: a phenylpropanoid, four chalcones, six flavonoids, nine homoisoflavonoids, and 3,4,5-trimethoxycinnamyl alcohol. Eighteen of these compounds are already known.

Thirteen of these compounds had not previously been isolated from this plant. Their structures were confirmed by comparison of the ¹H NMR and mass spectra data with published values. Camarda et al.² give tentatively the position of the methyl and the methoxyl for the compound (2*S*)-4',5-dihydroxy-7-methoxy-8-methylflavan. By means of a NOESY experiment, we have made the definitive assignment since there exists a clear interaction between the methyl and methoxyl groups and between the latter and H-6.

The new compounds were identified as 2,4,4'-trihydroxydihydrochalcone (**1**), 3-(4-hydroxybenzyl)-5,7-dimethoxychroman (**2**), and 7-hydroxy-3-(4-hydroxybenzyl)chromone (**3**).

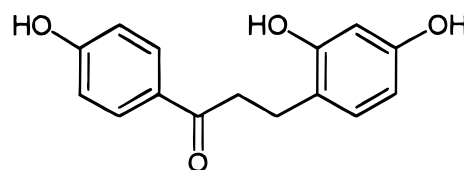
The molecular formula C₁₆H₁₂O₄ for **1** was deduced from HREIMS data in combination with the ¹H and ¹³C NMR spectra (Table 1). The dominant peaks in the mass spectrum, at *m/z* 121 and 123, revealed the presence of monohydroxybenzyl and a dihydroxytropilium ions from α and β cleavage,^{5,15} respectively. The ¹H NMR spectrum of **1** was similar to that of louterin C,⁵ except that there was no proton signal for the 6-OMe group. This result, in conjunction with the molecular formula, suggested that **1** was 2,4,4'-trihydroxydihydrochalcone. Analysis of the HMQC and HMBC spectra allowed complete ¹³C NMR assignments for **1** (Table 1). A literature search¹⁶ led us to the said substance but did not provide physical and spectroscopic data, which we are therefore now reporting for the first time.

Compound **2** differs from 7-hydroxy-3-(4-hydroxybenzyl)chroman² in the oxygenation and methylation patterns of ring A. The HREIMS of **2** showed the [M]⁺ at *m/z* 300.1259, matching the molecular formula C₁₈H₂₀O₄. Its IR spectrum gave absorption bands for a hydroxyl (3300 cm⁻¹) and an aromatic ring (2918, 2849, 1514 cm⁻¹). The MS displayed characteristic homoisoflavan ion fragments at *m/z* 107 and 193. The ion fragment at *m/z* 107 revealed the presence of

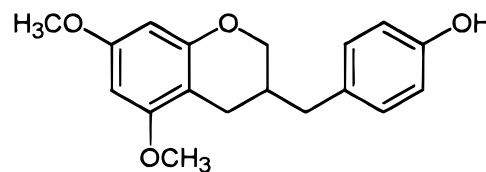
Table 1. NMR Assignments for **1** in C₅D₅N

position	δ_C (mult) ^a	δ_H (mult, <i>J</i> in Hz)	HMBC
1	119.68 s		3, 5
2	157.82 s		6
3	104.22 d	7.02 (d, 1.53)	5
4	158.66 s		6
5	107.02 d	6.79 (dd, 1.53, 8.19)	3
6	131.42 d	7.30 (d, 8.19)	
1'	129.59 s		3', 5'
2'	131.27 d	8.17 (d, 8.37)	
3'	116.14 d	7.16 (d, 8.37)	
4'	163.54 s		2', 6'
5'	116.14 d	7.16 (d, 8.37)	
6'	131.27 d	8.17 (d, 8.37)	
α	36.68 t	3.54 (t, 7.91)	β
β	26.12 t	3.43 (t, 7.91)	6, α
CO	198.80 s		2', 6', β
OH		11.31, 12.15	

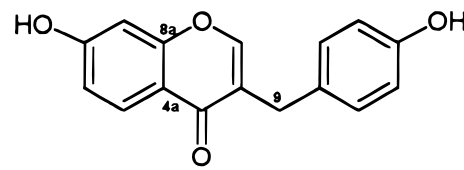
^a Multiplicities were obtained from DEPT experiments.



1



2



3

a hydroxybenzyl group, and the ion at *m/z* 193, the presence of two methoxyl groups on ring A. The ¹H NMR spectra (Table 2) of **2** and 7-hydroxy-3-(4-hydroxybenzyl)chroman² were very similar, but that of **2** showed two methoxy singlets at δ 3.72 and 3.73, located at C-5 and C-7, two

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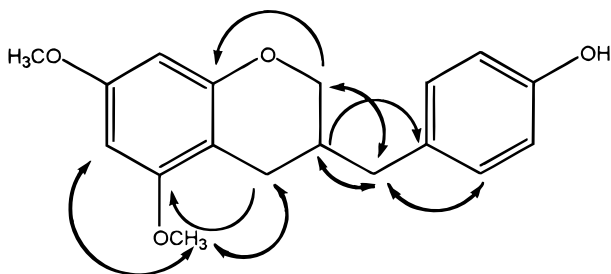
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Table 2. ^1H NMR δ , mult (J in Hz) Data of **2**^a and **3**^b

proton	compound	
	2	3
H-2	3.71 dd (8.60, 10.18) 4.08 dd (2.51, 10.18)	7.91s
H-3	2.20 m	
H-4	2.18 m 2.67 dd (3.45, 14.43)	
H-5		7.96 d (8.74)
H-6	6.00 d (2.30)	6.99 dd (2.35, 8.74)
H-8	6.02 d (2.30)	6.88 d (2.35)
H-9	2.57 d (7.11)	3.68 s
H-2', H-6'	7.04 d (8.37)	7.20 d (8.52)
H-3', H-5'	6.75 d (8.37)	6.82 d (8.52)
OMe	3.72 s	
OMe	3.73 s	
OH	4.66 br	9.64 br, 8.18 br

^a Spectra were recorded in CDCl_3 . ^b Spectra were recorded in $(\text{CD}_3)_2\text{CO}$.

**Figure 1.** Correlations of **2**. Double-headed arrows indicate NOESY, and single-headed arrows indicate HMBC correlations.

doublets at δ 6.00 and 6.02, assigned to H-6 and H-8, and two 2-proton doublets at δ 6.75 and 7.04, assigned to H-5'/H-3' and H-6'/H-2', respectively. This homoisoflavan^{17,18} can thus be defined as 3-(4-hydroxybenzyl)-5,7-dimethoxychroman (**2**), which was confirmed by ^{13}C NMR, NOESY, and HMBC spectra (Figure 1).

The HREIMS of **3** indicated a molecular formula of $\text{C}_{15}\text{H}_{14}\text{O}_4$. The mass fragmentation pattern and the ^1H NMR of **3** (Table 2) were almost identical with those of 5,7-dihydroxy-3-(4-hydroxybenzyl)chromone.¹¹ ^1H , ^{13}C , and HMBC spectral data showed that the hydroxyl groups of **3** were attached to C-7 and C-4'. Hence, the structure 7-hydroxy-3-(4-hydroxybenzyl)chromone is proposed for **3**.

Experimental Section

General Experimental Procedures. Melting points were determined on an Ernst Leitz GMBH Wetzlar apparatus and are uncorrected. Optical rotations were measured using a Perkin-Elmer model 241. UV spectra were recorded using a JASCO model V-560 spectrophotometer. IR spectra were recorded using a Bruker model IFS-55 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained on a Bruker model AMX-500 spectrometer with standard pulse sequences, operating at 500 MHz in ^1H and 125 MHz in ^{13}C . CDCl_3 , $(\text{CD}_3)_2\text{CO}$, $\text{C}_5\text{D}_5\text{N}$, and $\text{DMSO}-d_6$ were used as solvents, and TMS was used as internal standard. EIMS were taken on a Micromass model Autospect (70 eV) spectrometer. Column chromatography (CC) was carried out on silica gel (70–230 mesh, Merck). Fractions obtained from CC were monitored by TLC (silica gel 60 F_{254}), and PTLC was carried out on silica gel 60 PF₂₅₄+366 plates (20 × 20 cm, 1 mm thick).

Plant Material. The red resin Dragon's blood, from *Dra-caena draco*, was collected in Balayo, Anaga, Tenerife, Canary Islands, Spain, in June 1998. The plant material was identified by Prof. Lázaro Sánchez-Pinto. A voucher specimen (TFMC-8914) is deposited at the Museo de la Naturaleza y el Hombre, Cabildo Insular de Tenerife, Canary Islands, Spain.

Table 3. ^{13}C NMR δ , mult^a Data of **2**^b and **3**^c

carbon	compound	
	2	3
2	69.5 t	152.6 d
3	33.7 d	124.5 s
4	25.1 t	175.5 s
4a	102.9 s	114.0 s
5	158.6 s	114.6 d
6	93.0 d	127.1 d
7	159.2 s	162.2 s
8	91.15 d	102.1 d
8a	155.7 s	156.7 s
9	37.3 t	30.00 t
1'	131.7 s	130.3 s
2'	130.0 d	129.8 d
3'	115.1 d	115.1 d
4'	153.8 s	155.8 s
5'	115.1 d	115.1 d
6'	130.0 d	129.8 d
OMe	55.19 q	
OMe	55.26 q	

^a Multiplicities were obtained from DEPT experiments. ^b Spectra were recorded in CDCl_3 . ^c Spectra were recorded in $(\text{CD}_3)_2\text{CO}$.

Extraction and Isolation. The powdered resin (6.4 g) was dissolved in MeOH, silica gel (20 g) was added, and after the solvent had been removed in vacuo, the extract was subjected to silica gel chromatography eluting with *n*-hexane and increasing amounts of EtOAc, to give six fractions. Fraction 2 [*n*-hexane–EtOAc (4:1)], containing crude homoisoflavanoids, was subjected to column chromatography using Sephadex LH-20 and *n*-hexane– CH_2Cl_2 –MeOH (2:1.5:0.5) as eluent to give 3-(4-hydroxybenzyl)-7,8-methylenedioxychroman⁹ (16 mg) and **2** (2 mg). Compounds (2*S*)-3',7'-dihydroxy-4'-methoxy-8-methylflavan⁷ (2 mg), (2*S*)-4',7'-dihydroxy-3'-methoxy-8-methylflavan² (6 mg), (2*S*)-4',7'-dihydroxy-8-methylflavan⁸ (10 mg), and 7-hydroxy-3-(4-hydroxybenzyl)-8-methoxychroman⁹ (8 mg) were obtained from fraction 3 by Sephadex LH-20 chromatography [*n*-hexane– CH_2Cl_2 –MeOH (2:1:1)] and/or preparative TLC [CHCl_3 –MeOH (15:1)]. Compounds xenognosin³ (12 mg), (2*S*)-4',7'-dihydroxy-3'-methoxyflavan⁹ (7 mg), (2*S*)-4',5'-dihydroxy-7-methoxy-8-methylflavan² (6 mg), 5,7-dihydroxy-3-(4-hydroxybenzyl)-chromone¹¹ (6 mg), 7-hydroxy-3-(4-hydroxybenzyl)-chroman² (14 mg), and 5,7-dihydroxy-3-(4-hydroxybenzyl)-chroman-4-one¹² (20 mg) were isolated from fraction 4 by repeated preparative TLC [CHCl_3 –MeOH (15:1)]. Sephadex LH-20 chromatography [*n*-hexane– CH_2Cl_2 –MeOH (1:1:1)] and/or preparative TLC [CHCl_3 –MeOH (10:1)] of fractions 5 and 6 gave isoliquiritigenin⁴ (14 mg), lourerin C⁵ (12 mg), liquiritigenin¹⁰ (20 mg), and 7-hydroxy-3-(4-hydroxybenzyl)chroman-4-one² (15 mg), **1** (3 mg), 4,4'-dihydroxy-2'-methoxychalcone⁶ (8 mg), **3** (3 mg), 10-hydroxy-11-methoxydracaenone¹³ (20 mg), and 3,4,5-trimethoxycinnamyl alcohol¹⁴ (5 mg).

2,4,4'-Trihydroxydihydrochalcone (1): amorphous; UV (EtOH) λ_{max} (log ϵ) 220.8 (4.20), 263.2 nm (3.99), 280.9 nm (4.12); IR (film) ν_{max} 3288 (OH), 2960, 1650, 1600, 1514, 1455, 1370, 1243, 1167, 1103, 972 cm^{-1} ; ^1H and ^{13}C NMR, see Table 1; EIMS (70 eV) m/z 258 [$\text{M}]^+$ (55), 240 (61), 239 (100), 164 (8), 152 (5), 148 (18), 146 (11), 136 (23), 123 (67), 121 (87), 109 (12); HREIMS m/z 258.0808 (calcd for $\text{C}_{15}\text{H}_{14}\text{O}_4$, 258.0892).

3-(4-Hydroxybenzyl)-5,7-dimethoxychroman (2): colorless needles (MeOH–EtOAc); mp 127–129 °C; $[\alpha]_{\text{D}}^{25} +73.1^\circ$ (c 0.026, CHCl_3); UV (EtOH) λ_{max} (log ϵ) 227.2 nm (3.44), 277.4 nm (3.72); IR ν_{max} (film) 3300 (OH), 2918, 2849, 2489, 1540, 1514, 1487, 1475, 1355, 1214, 1089, 1071, 925, 781 cm^{-1} ; ^1H and ^{13}C NMR, see Tables 2 and 3; EIMS (70 eV) m/z 300 [$\text{M}]^+$ (100), 206 (11), 193 (37), 192 (52), 191 (29), 167 (21), 138 (10), 133 (6), 107 (30); HREIMS m/z 300.1259 (calcd for $\text{C}_{18}\text{H}_{20}\text{O}_4$, 300.1361).

7-Hydroxy-3-(4-hydroxybenzyl)chromone (3): colorless needles (MeOH–EtOAc); mp 179–181 °C; UV (EtOH) λ_{max} (log ϵ) 241.4 nm (3.45), 249.6 nm (3.46), 297.6 (3.25), 305.8 (3.20); IR ν_{max} (film) 3308 (OH), 2923, 2852, 1628, 1594, 1456, 1241, 1171, 1099, 1028, 808 cm^{-1} ; ^1H and ^{13}C NMR, see Tables 2

and 3; EIMS (70 eV) m/z 268 $[M]^+$ (100), 251 (11), 239 (8), 137 (67), 131 (11); HREIMS m/z 268.0745 (calcd for $C_{16}H_{12}O_4$, 268.0754).

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