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CITRANS AND CYCLOLS FROM *CLUSIA MULTIFLORA**

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Key Word Index—*Clusia multiflora*; Guttiferae; fruits; citrans; cyclols; prenylated benzophenones; nemorosonol.

Abstract—From an extract of fruits of *Clusia multiflora*, a new prenylated benzophenone and two pairs of regioisomeric cytriylidene derivatives of 2,4,6-trihydroxybenzophenone were isolated. The structures have been established by high field 2D NMR techniques. Nemorosonol A, a known polyisoprenylated-modified benzophenone, was also found in the same extract.

INTRODUCTION

During earlier studies on the genus *Clusia*, we isolated from the fruits a number of polyisoprenylated derivatives of 2,4,6-trihydroxy benzophenone with a fully substituted phoroglucinol nucleus [1–6]. Continuing our chemosystematic investigation, we have now examined the fruits of the Colombian species, *C. multiflora* and isolated the citrans, **2** and **3**, the cyclols, **4** and **5**, and the chromene **8**. By contrast with the previously found compounds, these pigments contain a free aromatic proton in the acetate-derived A ring. This paper deals with the structural elucidation of this new representative among the benzophenones from the genus *Clusia*.

RESULTS AND DISCUSSION

In addition to a mixture of sesquiterpenes [7] and the known nemorosonol A, **1** [2, 5], CC of the fruit extract of *Clusia multiflora* yielded the pairs of regioisomers **2** and **3**, **6** and **7** and the compound **8**.

Common features of the isolated new pigments were UV, NMR data and a fragment ion at *m/z* 105 in the EI mass spectrum consistent with structures derived from 2,4,6-trihydroxybenzophenone, as well as a molecular formula, $C_{23}H_{24}O_4$, which requires three further cycles or unsaturations for the non-aromatic framework. Besides, all were optically inactive and exhibited in the ^{1}H NMR spectra a signal near δ6.0 for a lone aromatic proton. The ^{1}H and ^{13}C parameters of the regioisomers **2** and **3**, named clusiacitran A and B, respectively, are collected in Table 1. The assignment of each NMR signal to the pertinent proton and carbon was achieved by HETCOR measurements [8], while that of the quaternary carbons followed from the long-range HETCOR spectra [9]. Apart from the signals due to the benzophenone moiety, both regioisomers exhibited in the ^{13}C NMR spectra those for two methines, three methyls, three methylenes and two quaternary carbons.

The absence of any signals for further unsaturations suggested a tricyclic structure for the terpene-derived part of the molecules. Moreover, among the most significant ^{1}H NMR signals were those appearing as broad triplets at δ2.67 and 2.79, respectively, which may be attributed to benzylic protons. Cumulatively, the above findings suggested for the terpenoid moiety a tricyclic cytrylidene framework, like in rubranine [10] and in deoxybruceol [11], and the structures **2** and **3** for the two regioisomers. Long-range connectivities from their NMR spectra (Table 1) were decisive in assigning structure **2** to clusiacitran A, mp 212–214° and structure **3** to clusiacitran **B**, mp 219–221°.

Chemical confirmation was provided by acid-catalysed ring-opening [10], which yielded quantitatively **4** and **5** from **2** and **3**, respectively. The main differences in the ^{1}H NMR spectra were the signals attributed to the hydroxyls (see Experimental) and to the aliphathic methyl. Of note, the methyl signal for **5** was found at δ0.68 (δ1.39 for **4**) lying above the aromatic B ring and within its shielding cone.

The ^{1}H and ^{13}C assignments for the second pair of regioisomers **6** and **7**, named clusiacyclol A and **B**, respectively, are reported in Table 2. Relating to the terpenoid portion, both compounds exhibited in their ^{13}C NMR spectra signals for three methines, three methyls, two methylenes and two quaternary carbons, which again require a tricyclic structure. Comparison of the spectral data with those of cannabicyclol [12], eriobrucinol [13] and its regioisomers [14] define a common framework of the terpenoid part. In agreement with the

*Part 10 in the series 'Chemistry of the *Clusia* genus'. For part 9 see ref. [1]. Preliminary results presented at III Encuentro Nacional de Fitoquimica, Cali, Colombia, November 1992.

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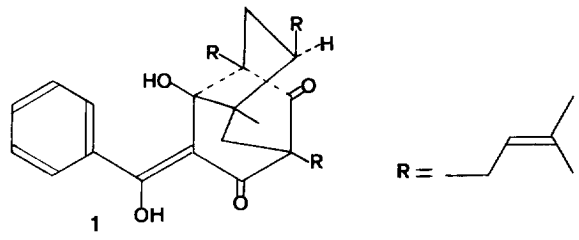
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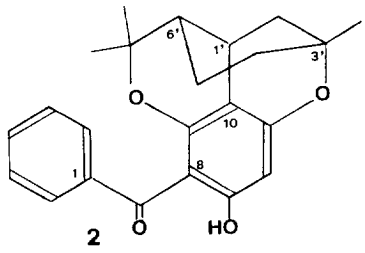
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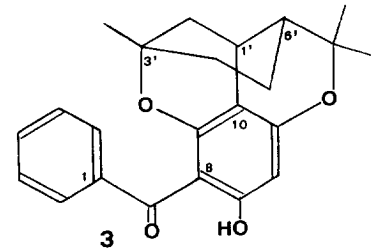
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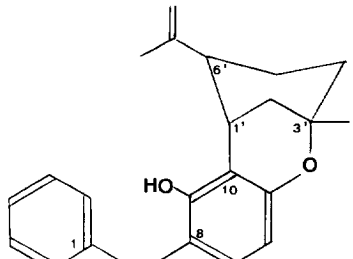
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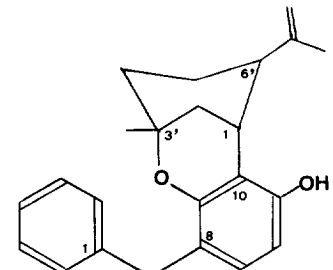
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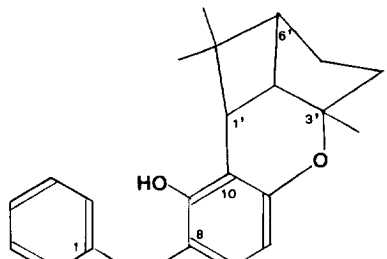
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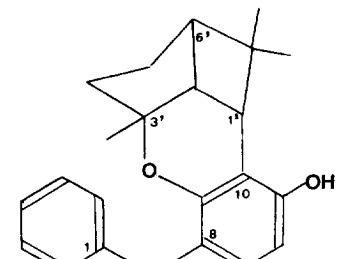
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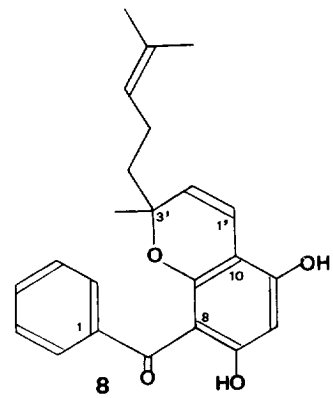
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Table 1. NMR spectral data of **2** and **3***

H/C	2 δ_H	2 δ_C	3 δ_H	3 δ_C	**2** and **3** Long-range C–H connectivities
1	—	142.0	—	141.8	
2, 6	7.60 *m*	127.6	7.60 *m*	127.8 *m*	
3, 5	7.40†	127.2	7.40†	127.3	
4	7.40†	130.2	7.40†	130.4	
7	—	198.2	—	199.0	H-2, 6
8	—	107.2	—	105.4	H-12, OH-13
9	—	159.3	—	158.3	H-1′
10	—	107.8	—	106.9	H-1′, H-2′, H-12
11	—	163.3	—	163.5	H-12, H-1′
12	6.11 *s*	97.3	6.08 *s*	98.2	OH-13
13	—	164.3	—	164.5	H-12, OH-13
13OH	12.69 *s*	—	12.52 *s*	—	
1′	2.67 *br t*	27.5	2.79 *br t*	27.3	H-2′
2′	2.20 *dd* (13, 4)	34.7	2.00†	34.7	Me-10′
	1.82 *dd* (13, 2)		1.73 *dd* (13, 2)		
3′	—	76.2	—	75.8	Me-10′
4′	1.90 *m*	37.5	1.63 *m*	37.6	Me-10′
	1.42 *m*		1.30†		
5′	1.20 *m*	21.7	1.30†	21.8	
	0.80 *m*		0.83 *m*		
6′	2.0 *m*	45.7	2.00†	45.7	Me-8′
7′	—	85.7	—	85.3	Me-8′, Me-9′, H-1′
8′	1.17 *s*	29.0	1.53 *s*	29.5	Me-9′
9′	0.60 *s*	23.4	1.09 *s*	24.2	Me-8′
10′	1.37 *s*	28.6	0.75 *s*	27.6	

*In $CDCl_3$. ^1H (300 MHz), ^{13}C (75 MHz). Coupling constants (in Hz) in parentheses.
†Overlapped multiplets.

long-range connectivities, structure **6** is assigned to clusiacyclol A and structure **7** to clusiacyclol B. Clusiacitrans A (**2**) and B (**3**), and clusiacyclols A (**4**) and B (**5**) are new cytriylidene derivatives, the first ones of a benzophenone.

The final pigment, namely clusiachromene C (**8**), displayed *inter alia* in the NMR spectra signals attributable to a chromene and to an isoprenyl group (see Experimental). The orientation of the chromene ring, as depicted in structure **8**, was chosen from the presence of signals for a chelated hydroxyl (δ12.50) and for a shielded aliphatic methyl (δ0.96) in the NMR spectrum.

EXPERIMENTAL

Plant material. Fruits of *C. multiflora* H. B. Kunth were collected in the National Park of Purace (Colombia) and identified by Dr R. Jaramillo (Instituto de Ciencias Naturales, Univerisdad Nacional de Colombia, Bogotà). Voucher specimens are deposited in the Nacional Herbarium of Colombia under the cipher 236663.

Extraction and fractionation. Roughly ground fresh fruits (1 kg) were extracted with petrol (bp 60–80°) in a Soxhlet. A portion (10 g) of the residue (125 g) was fractionated on silica gel by CC using mixts of petrol–EtOAc and 7 frs collected: Ml (1 g; petrol); M2 (1.8 g; petrol–EtOAc, 99:1); M3 (800 mg; 99:1); M4 (1.8 g; 97:3); M5 (900 mg; 19:1); M6 (1.5 g; 9:1) and M7 (1.2 g; EtOAc). M2 and M3 contained 3-ketoeuphane, friedlin, euphol [7] and nemorosonol A, **1**. The latter showed identical spectral data to published values [5] and its identity was confirmed by co-TLC with an authentic sample. Successive recrystallization from $CHCl_3$ and EtOAc of M4 gave a mixt. (1:2) of clusiacitrans A and B (500 mg), which could be sepd by additional CC (silica gel, benzene). Clusiacyclol A (50 mg) was obtained from M5 by CC (silica gel, benzene–EtOAc, 99:1) and recrystallization. Finally, purification of M6 by CC (silica gel, benzene–EtOAc, 49:1) yielded clusiacyclol B (120 mg) and clusiachromene C (30 mg).

Clusiacitran A (**2**). $C_{23}H_{24}O_4$, mp 212–215° (EtOAc). $[\alpha]_D = 0$ ($CHCl_3$; *c* 0.3). UV λ_{max}^{MeOH} 314 nm, + $AlCl_3$ 340 nm. NMR data in Table 1; EIMS (probe) 70 eV, *m/z* (rel. int.): 364 $[M]^+$ (45), 349 (13), 321 (5), 283 (14), 282 (31), 281 (100), 243 (6), 203 (16), 165 (7), 105 (33), 91 (6), 77 (29), 69 (13).

Clusiacitran B (**3**). $C_{23}H_{24}O_4$, mp 219–221° (EtOAc). $[\alpha]_D$, UV and EIMS like **2**. NMR data in Table 1.

Cleavage of clusiacitrans. Compounds **2** and **3** (50 mg) in HOAc (2 ml) were refluxed for 2 hr and the solvent evapd. CC purification (silica gel, benzene or benzene–EtOAC, 19:1, respectively) and recrystallization (CH_2Cl_2–heptane) yielded **4** from **2** and **5** from **3**. Compound **4**, $C_{23}H_{24}O_4$, mp 150–151°. ^1H NMR (300 MHz, $CDCl_3$)

Table 2. NMR spectral data of **6** and **7***

H/C	6 δ_H	6 δ_C	7 δ_H	7 δ_C	Long-range C–H connectivities
1	—	140.1	—	143.1	
2, 5	7.6–7.5	129.2	7.5–7.3	127.6	
3, 5	7.6–7.5	127.9	7.5–7.3	126.8	
4	7.6–7.5	132.2	7.5–7.3	129.7	
7	—	197.3	—	200.7	
8	—	104.4	—	106.4	H-12, OH-13
9	—	158.9	—	156.4	
9/11OH	10.12 *s*	—	5.72 *br s*	—	H-1′
10	—	104.5	—	103.4	H-1′
11	—	161.6	—	162.2	H-12, H-1′
12	5.96 *s*	97.8	6.01 *s*	95.8	OH-13
13	—	161.6	—	164.2	H-12, OH-13
13OH	12.80 *s*	—	12.45 *s*	—	
1′	3.06 *d* (9)	35.5	2.95 *d* (9)	35.6	Me-8′, Me-9′
2′	2.58 *dd* (9, 7)	37.3	2.39 *dd* (9, 7)	37.1	Me-10′
3′	—	84.8	—	84.1	Me-10′
4′	1.94 *dt* (12, 7)	38.9	1.81 *m*	37.8	
	1.62 *m*		1.63 *ddd* (13, 7, 6)		
5′	1.70 *m*	25.7	1.43 *m*	25.8	
6′	2.41 *t* (7)	46.5	2.29 *t* (7)	45.9	Me-8′, Me-9′
7′	—	39.0	—	38.9	Me-8′, Me-9′
8′	1.35	33.6	1.32 *s*	33.6	Me-9′
9′	0.82 *s*	17.8	0.81 *s*	17.7	Me-8′
10′	1.41	27.5	0.68 *s*	26.4	

*See footnotes in Table 1.

δ:11.04 and 9.0 (*ss*; OH-9, OH-13), 7.62–7.45 (*m*, C_6H_5), 5.93 (*s*, H-12), 4.70, 4.43 (*br ss*, H_2-8′), 3.44 (*br s*, H-1′), 2.22 (*m*, H-6′), 2.04–1.45 (*m*; $3 \times H_2$), 1.83 (*br s*, Me-9′), 1.39 (*s*, Me-10′). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 197.3 (C-7), 164.3, 160.0, 159.9 (C-13, C-11, C-9), 148.2 (C-7′), 140.2 (C-1), 131.9 (C-4), 128.9 (C-2, C-6), 128.0 (C-3, C-5), 109.5 (C-8′), 103.7, 103.5 (C-10, C-8), 95.5 (C-12), 76.3 (C-3′), 48.1 (C-1′), 39.1, 37.3, 22.7 (C-2′, C-4′, C-5′), 29.8 (C-6′), 28.5 (C-10′), 23.0 (C-9′). EIMS (probe) 70 eV, *m/z* (rel. int.): 364 $[M]^+$ (19), 349 (5), 321 (5), 281 $[M-C_6H_{11}]^+$ (100), 203 (12), 105 (17), 77 (19). Compound **5**, $C_{23}H_{24}O_4$, mp 174–175°. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.13 (*s*, OH-13′), 7.55–7.33 (*m*, C_6H_5), 6.14 (*br s*, OH-11), 5.95 (*s*, H-12), 4.80, 4.59 (*br ss*, H_2-8′), 3.29 (*br s*, H-1′), 2.26, 2.22 (*dt*, $J = 11.7$, 3.4, 3.4 Hz; H_2-6′), 2.0–1.45 (*m*, $3 \times H_2$), 1.79 (*br s*, Me-10′), 0.68 (*s*, Me-10′). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.1 (C-7), 163.4, 161.0, 159.2 (C-13, C-11, C-9), 148.9 (C-7′), 142.8 (C-1), 139.1 (C-4), 127.5 (C-2, C-6), 127.2 (C-3, C-5), 111.0 (C-8′), 104.6 (C-8), 101.9 (C-10), 95.1 (C-12), 75.7 (C-3′), 47.9 (C-1′), 38.6, 36.8, 22.6 (C-2′, C-4′, C-5′), 31.6 (C-6′), 27.4 (C-10′), 22.5 (C-9′). EIMS like **6**.

Clusiacyclol A (**6**). $C_{23}H_{24}O_4$, mp 136–138° (EtOAc) $[\alpha]_D = 0$ ($CHCl_3$; *c* 0.3). NMR data in Table 2.

Clusiacyclol B (**7**). $C_{23}H_{24}O_4$, mp 178–180° (Me_2CO–petrol) $[\delta]_D = 0$ ($CHCl_3$, *c* 0.3). NMR data in Table 2.

Clusiachromene C. $C_{23}H_{24}O_4$, oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.50 (*s*, OH-13), 7.50–7.35 (*m*, C_6H_5), 6.52 (*d*, $J = 10$ Hz, H-1′), 6.10 (*br s*, OH-11), 5.94 (*s*, H-12), 5.24 (*d*, $J = 10$ Hz, H-2′), 4.87 (*br t*, $J = 7$ Hz, H-6′), 1.67 (*m*, H_2-5′), 1.63, 1.49 (*br ss*; Me-8′, Me-9′), 1.30–1.05 (*m*, H_2-4′), 0.96 (*s*, Me-10′). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.6 (C-7), 164.6, 158.9, 156.7 (C-13, C-11, C-9), 142.7 (C-7′), 131.6 (C-1), 130.2 (C-4), 127.6 (C-2, C-5), 127.0 (C-3, C-6), 123.9, 123.8 (C-6′, C-2′), 116.3 (C-1′), 105.4, 101.9 (C-10, C-8), 95.8 (C-12), 80.4 (C-3′), 40.8 (C-4′), 25.9, 25.6 (Me-8′, Me-10′), 22.5 (C-5′), 17.6 (Me-19′).

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