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Xanthone and dihydroisocoumarin from *Montrouziera sphaeroidea*

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Abstract

A xanthone, montrouxanthone and a dihydroisocoumarin, montroumarin were isolated from the stem bark of *Montrouziera sphaeroidea* Pancher Ex Planchon et Triana [Guttiferae], along with two known compounds. Their structures were elucidated on the basis of spectroscopic analyses. This is the first report of the analysis of chemical constituents of *Montrouziera* species.

Keywords: *Montrouziera sphaeroidea*; Guttiferae; Xanthone; Dihydroisocoumarin; Lignan; Montrouxanthone; Montroumarin

1. Introduction

In our previous papers (Ito, Miyamoto, Rao & Furukawa, 1996; Ito, Miyamoto, Nakayama, Kawai, Rao & Furukawa, 1997) on biologically active natural products from tropical medicinal plants, the isolation and structural elucidation of a dibenzofuran, a depsidone, and some new xanthones from *Calophyllum panciflorum* A.C. Smith, *Garcinia assigu* Lantb., *Garcinia dulcis* (Roxb.) Kurz., and *Garcinia latissima* Miq. belonging to the Guttiferae were reported. This paper describes the isolation and structural elucidation of two new compounds, a xanthone named montrouxanthone (**1**) and a dihydroisocoumarin named montroumarin (**3**) from the acetone extract of *Montrouziera sphaeroidea* belonging to the same family, Guttiferae, collected in New Caledonia.

2. Results and discussion

The acetone extract of the dried stem bark of the plant was subjected successively to silica gel column chromatography and preparative TLC to give **1** and **3** along with 4-(3′,7′-dimethylocta-2′,6′-dienyl)-1,3,5-trihydroxy-9H-xanthen-9-one (**4**) (Sordat-Diserens, Rogers, Sordat & Hostettmann, 1992) and kaerophyllin (**5**) (Mikaya, Turabelidze, Kemertelidze & Wulfson, 1981; Gonzalez, Estevez-Reyes, Mato & Estevez-Braun, 1990).

Montrouxanthone (**1**) was obtained as a yellow oil. The molecular formula was determined as $C_{23}H_{24}O_6$ by high-resolution (HR)-MS. The UV spectrum was similar to that of ugaxanthone (**2**), (Locksley, Moore & Scheinmann, 1966) indicating the presence of a 1,3,5,6-tetraoxygenated xanthone chromophore. The IR spectrum exhibited bands at ν_{max} 3544, 3332 (*br*), 3220 (*br*), and 1649 cm^{-1} due to hydroxyl and carbonyl groups, respectively. In the ^{1}H-NMR spectrum, a 1H singlet occurred at δ 6.30 was assigned to H-2, two AB-type protons at δ 7.74 and 6.96 (each 1H, d, J = 8.8 Hz) assignable to H-8 and H-7, respectively, appeared in addition to a chelated hydroxyl group proton signal at δ 12.98. The remaining signals at δ 5.29 (1H, *m*), 5.04 (1H, *m*), 3.58 (2H, *d*, J = 6.6 Hz), 2.11 (2H, *m*), 2.09 (2H, *m*), 1.87, 1.64, 1.58 (each 3H, *s*) in the ^{1}H-NMR spectrum, suggested a geranyl moi-

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ety. This was supported by two characteristic ions at m/z 327 and 273 arising from loss of [$^{\cdot}C_5H_9$] and [$^{\cdot}C_9H_{15}$], respectively, from the molecular ion in the EIMS. The appearance of a nuclear Overhauser effect (nOe) enhancement between the H-1′ (δ 3.58) and 3′-Me (δ 1.87) proton signals further suggested that xanthone (**1**) contained a geranyl moiety [–CH_2CH=$C(CH_3)$–CH_2CH_2CH=$C(CH_3)_2$] in the molecule. The location of the geranyl moiety was confirmed by ^{1}H-detected heteronuclear multiple bond connectivity (HMBC) spectrum. A hydrogen bonded proton at δ_H 12.98 showed C–H long-range correlation with a carbon resonance at δ_C 98.99 (C-2), which was also found to be attached to a proton at δ_H 6.30 (*s*, H-2). Further, C–H long-range correlations were detected between a carbon resonance at δ_C 105.08 (C-4) and a singlet at δ_H 6.30 (H-2), and between a carbon resonance at δ_C 105.08 (C-4) and the side chain proton at H-1′ (δ_H 3.85). These data, coupled with the presumed presence of an oxygenated group at C-3 based on biogenetic considerations, indicated the presence of the geranyl moiety at C-4. Other observed long-range correlations are shown by arrows in Fig. 1. On the basis of these results, the structure of montrouxanthone is proposed as **1**.

Montroumarin (**3**) was obtained as a colorless oil having a molecula formula of $C_{15}H_{12}O_4$. The spectral data of **3** showed the presence of a hydroxyl group (3599, 3300 cm^{-1}), a benzene ring (1627, 1512 cm^{-1}; 203, 228 sh, 268, 300 nm) and a δ-lactone carbonyl group (1668 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra (see Section 3) and the results of the ^{1}H-detected heteronuclear multiple quantum coherence (HMQC) spectrum are described as follows: These showed signals assignable to a monosubstituted benzene ring, a hydroxyl group proton [δ_H 9.52], two broad 1H-singlets [δ_H 6.36; δ_C 107.58, δ_H 6.30; δ_C 102.08] due to protons on another benzene ring, a methine group [δ_H 5.66 (1H, *dd*, J = 12.0, 3.3 Hz); δ_C 80.97] bearing an oxgen atom, methylene protons [δ_H 3.28 (1H, *dd*, J = 16.5, 12.0 Hz), 3.15 (1H, *dd*, J = 16.5, 3.3 Hz); δ_C 35.52] which were coupled with the methine proton at δ_H 5.66, a lactone carbonyl group [δ_C 170.52] in addition to an intramolecularly hydrogen-bonded hydroxyl group proton at δ_H 11.22. In the HMBC spectrum, the hydrogen-bonded proton at δ_H 11.22 showed C–H three-bond correlations with the carbon signals at δ_C 102.08 (C-7). A quatanery carbon at δ_C 101.86 (C-8a) correlated with one of the methylene protons at δ_H 3.15 (H-4) and with two broad 1H-singlets at δ_H 6.36 (H-5) and 6.30 (H-7). The methine proton resonance at δ_H 5.66 was correlated with a carbon signal at δ_C 127.18 (C-2′, 6′) on the non-substituted phenyl group in the HMBC spectrum. From these spectral data and further HMBC results shown by arrows in Fig. 2, structure **3** for montroumarin is proposed. The determination of the absolute configuration of 3-substituted dihydroisocoumarins by CD spectroscopy was studied by Snatzke et al. in 1983 (Hill, 1986; Antus, Snatzke & Steinke, 1983). Applications of this method 3-phenyldihydroisocoumarins have been reported (Hashimoto, Tori & Asakawa, 1987). From the analysis of the CD spectrum of **3**, which showed a negative Cotton effect at 253 nm and a positive Cotton effect at 233 nm, the absolute configuration at C-3 of **3** was concluded to be **S**. Montroumarin (**3**) has been synthesized by Sakai et al. (1974). However this is the first report of **3** from a natural source.

Other compounds isolated from the acetone extract were characterized as 4-(3′,7′-dimethylocta-2′,6′-dienyl)-1,3,5-trihydroxy-9H-xanthen-9-one (**4**) (Sordat-Diserens et al., 1992) and kaerophyllin (**5**) (Mikaya et al., 1981; Gonzalez et al., 1990) by comparisons of the ^{1}H-NMR, IR, UV, and MS data with those reported

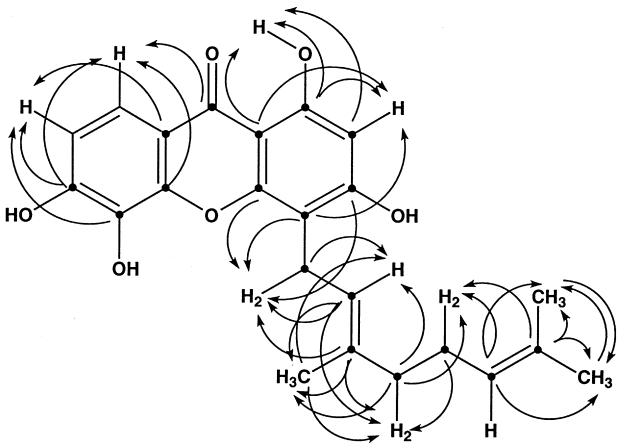


Fig. 1. C–H long-range correlations in the HMBC spectrum of Montrouxanthone (**1**) in $CDCl_3$.

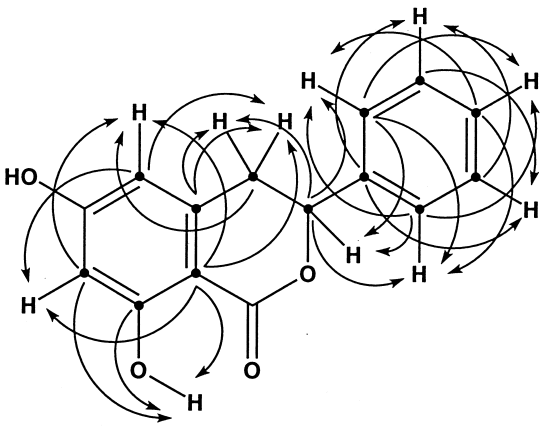
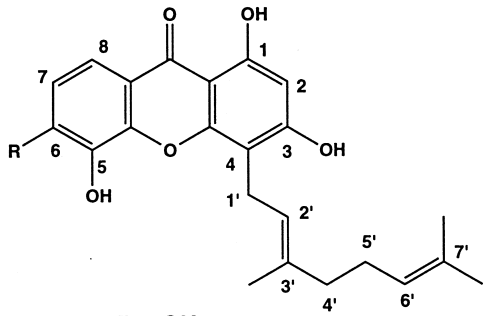
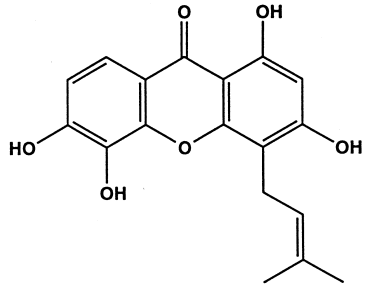
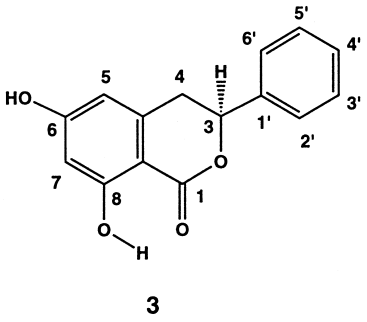
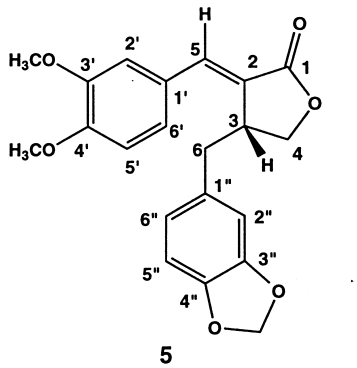


Fig. 2. C–H long-range correlations in the HMBC spectrum of Montroumarin (**3**) in acetone-d_6.









in the literature (Sordat-Diserens et al., 1992; Mikaya et al., 1981; Gonzalez et al., 1990).

3. Experimental

3.1. General

^{1}H-NMR (400 and 600 MHz), ^{13}C-NMR (150 MHz), NOE, HMQC, and HMBC (J = 8 Hz) spectra: in $CDCl_3$ (unless otherwise stated) with TMS as international standard. UV spectra: in MeOH; IR spectra: in $CHCl_3$. TLC: Kieselgel 60 F_{254} (Merck). Optical rotations: in $CHCl_3$ at 25°C.

3.2. Plant material

The plant material used in this study, *Montrouziera sphaeroidea* Pancher Ex Planchon et Triana (Guttiferae) was collected at "Montagne des sources", New Caledonia, in December 1995. A voucher specimen (LIT0070) is preserved in the herbarium of the Medicinal Plants Laboratory of the C.N.R.S., Noumea, New Caledonia.

3.3. Extraction and separation

The dried stem bark (1.5 kg) of *M. sphaeroidea* was extracted with acetone. The acetone extract was evaporated under reduced pressure to give an oily residue (78.2 g), which was subjected to silica gel chromatography with hexane–acetone (10:1, 3:1, 2:1, 1:1, 1:2), acetone, and MeOH, successively as eluants. The hexane–acetone (2:1) eluate was further subjected to silica gel column chromatography eluted with hexane, hexane–acetone (4:1, 3:1, 3:2, 1:1), CH_2Cl_2– MeOH (3:1), MeOH, successively, to give 7 fractions. Fraction 2 was subjected to preparative silica gel TLC (PTLC) developed with hexane-EtOAc (7:3) to afford 4-(3′,7′dimethylocta-2′,6′-dienyl)-1,3,5-trihydroxy-9H-xanthen-9-one (**4**) (2.3 mg). Fraction 3 was subjected to PTLC developed with CH_2Cl_2-acetone (50:1) to afford kaerophyllin (**5**) (2.1 mg) and Montroumarin (**3**) (6.0 mg). Fraction 5 was further subjected to PTLC with hexane-iso-Pr_2O (1:4) and hexane–acetone (4:1) as developing solvents to obtain montrouxanthone (**1**) (6.0 mg).

3.4. Montrouxanthone (*1*)

Yellow oil, UV λ_{max} nm: 202, 237 (sh), 252, 285, 326; IR ν_{max} cm^{-1}: 3544, 3332 (*br*), 3220 (*br*), 1649, 1589; HR-MS m/z 396.1538 ([M$^+$], calculated for $C_{23}H_{24}O_6$: 396.1570); EIMS m/z (rel. int.): 396 [M$^+$](18), 327 (37), 311 (12), 285 (11), 273 (100), 257 (10). ^{1}H-NMR spectral data (600 MHz, $CDCl_3$): δ 12.98 (1H, *s* OH-1), 7.74 (1H, *d*, J = 8.8 Hz, H-8), 6.96 (1H, *d*, J = 8.8 Hz, H-7), 6.30 (1H, *s*, H-2), 5.29 (1H, *m*, H-2′), 5.04 (1H, *m*, H-6′), 3.58 (2H, *d*, J = 6.6 Hz, H-1′), 2.11 (2H, *m*, H-5′), 2.09 (2H, *m*, H-4′), 1.87 (3H, *s*, 3′-CH_3), 1.64 (3H, *s*, 7′-CH_3); 1.58 (3H, *s*, 7′-

CH_3; ^{13}C-NMR spectral data (150 MHz, $CDCl_3$): δ 180.54 (C-9), 161.71 (C-1 & C-3), 154.20 (C-4a), 149.42 (C-6), 145.12 (C-10a), 138.66 (C-3′), 132.20 (C-7′), 130.36 (C-5), 123.56 (C-6′), 121.46 (C-2′), 118.28 (C-8), 114.13 (C-8a), 112.59 (C-7), 105.08 (C-4), 103.25 (C-9a), 98.99 (C-2), 39.57 (C-4′), 26.31 (C-5′), 25.62, (7′-CH_3), 21.90 (C-1′), 17.70 (7′-CH_3),16.32 (3′-CH_3).

3.5. Montroumarin (**3**)

Colorless oil, $[\alpha]_D$ +68° ($CHCl_3$, c0.057). UV λ_{max} nm: 203, 228 (sh), 268, 300; IR ν_{max} cm^{-1}: 3599, 3300 (*br*), 1668, 1627, 1512; HR-MS *m*/*z* 256.0745 ([M^+], calculated for $C_{15}H_{12}O_4$: 256.0735); EIMS *m*/*z* (rel. int.): 256 [M^+](100), 238 (54), 210 (70), 181 (21), 165 (102); ^{1}H-NMR spectral data (600 MHz, acetone-d_6): δ 11.22 (1H, *s*, OH-8), 9.52 (1H, *br*, OH-6), 7.55 (2H, *d*, *J* = 7.3 Hz, H-2′, 6′), 7.44 (2H, *t*, *J* = 7.3 Hz, H-3′, 5′), 7.39 (1H, *t*, *J* = 7.7 Hz, H-4′), 6.36 (1H, *br s*, H-5), 6.30 (1H, *br s*, H-7), 5.66 (1H, *dd*, *J* = 12.0, 3.3 Hz, H-3), 3.28 (1H, *dd*, *J* = 16.5, 12.0 Hz, H-4), 3.15 (1H, *dd*, *J* = 16.5, 3.3 Hz, H-4); ^{13}C-NMR spectral data (150 MHz, acetone-d_6): δ 170.52 (C-1), 165.41 (C-8 or C-6), 165.34 (C-6 or C-8), 143.09 (C-4a), 139.90 (C-1′), 129.44 (C-3′, 5′), 129.38 (C-4′), 127.18 (C-2′, 6′), 107.58 (C-5), 102.08 (C-7), 101.86 (C-8a), 80.97 (C-3), 35.52 (C-4); CD curve: $[\theta]_{273}$ + 10255, $[\theta]_{253}$-1199, $[\theta]_{233}$ +21625.

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