

TWO NEW XANTHONES FROM THE ROOT BARK OF *GARCINIA SUBELLIPTICA*

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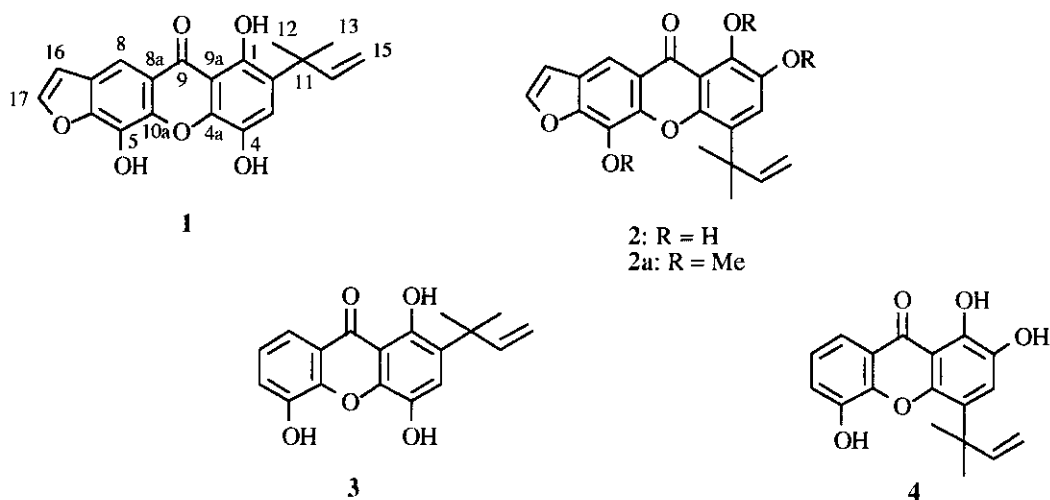
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Abstract --- From the root bark of *Garcinia subelliptica*, two new xanthenes named subelliptenones C (1) and D (2) were isolated in addition to two known xanthenes [12b-hydroxy-des-D-garcigerin (3) and globuxanthone (4)]. The structures were determined by analysis of nmr spectral data including 2D techniques.

In continuation of our works¹⁻³ oriented to reach for xanthone derivatives with bioactive potency in Guttiferaeous plants, we now report the isolation and characterization of two new xanthenes from the root bark of *G. subelliptica* Merr. (= *S. spicata* Hook. f.) (Clusiaceae) along with two known xanthenes.

The root bark of *G. subelliptica* collected in Okinawa, Japan was dried and ground, and successively extracted with *n*-hexane, benzene, acetone and 70% MeOH. The acetone extract suspended in water was partitioned with EtOAc. The EtOAc layer was repeatedly chromatographed on silica gel and Sephadex LH-20 to give four xanthenes (1-4).

Compound (1), subelliptenone C, obtained as a yellow amorphous, reacted positively to Gibbs and FeCl₃ reactions. The [M⁺] at *m/z* 352.0971 in the HRms corresponds to C₂₀H₁₆O₆. The uv and the ir spectrum were suggestive 1 to be a xanthone derivative. In the ¹H-nmr spectrum, a chelated hydroxyl (δ 13.01) and two aromatic singlet signals (δ 7.33 and 8.04) were observed in addition to two aromatic hydroxyl groups [δ 8.90 (2H, br s)]. The spectrum further showed the presence of a 1,1-dimethylallyl chain [δ 1.55 (6H, s, Me x 2),



5.01 (1H, dd, $J = 11, 1$ Hz, $-\text{CH}=\text{CH}_2$), 5.04 (1H, dd, $J = 18, 1$ Hz, $-\text{CH}=\text{CH}_2$) and 6.32 (1H, dd, $J = 18, 11$ Hz, $-\text{CH}=\text{CH}_2$) and a fused furan ring [δ 7.07 (1H, d, $J = 2$ Hz) and 7.97 (1H, d, $J = 2$ Hz)]. The presence of the fused furan ring was substantiated by the chemical shifts of methine carbons (δ 109.5 and 149.4) in the ^{13}C -nmr spectrum.⁴ All protonated carbons were assigned by CH COSY experiment (Table 1). In the HMBC spectrum of **1** (Figure 1), the chelated hydroxyl group was correlated to two quaternary aromatic carbons (δ 109.2 and 129.9), and one of which (δ 129.9) was further correlated to methyl signals (δ 1.55) of the 1,1-di-



Figure 1 Long range correlations in the HMBC spectrum of **1** and **2**

methylallyl group. In the ^1H -nmr spectrum, an nOe was observed between the methyl groups (δ 1.55) and one of the aromatic protons [δ 7.33 (1H, s)]. In addition, the aromatic proton (δ 7.33) gave cross peaks to three aromatic carbons with an *O*-function (δ 137.4, 143.0 and 154.2) in the HMBC spectrum. Therefore, **1** was a 1,4-dihydroxy-2-(1,1-dimethylallyl-2-propenyl)xanthone derivative. Compared with the ^{13}C -nmr spectral data

of subelliptenone A,¹ which has a same partial structure as **1**, the data based on the partial structure were superimposed each other. The positions of the furan ring and another non-chelated hydroxyl group were determined as follows. As another aromatic proton at δ 8.04 was shifted to a lower field in the ^1H -nmr spectrum, the proton was deshielded by an adjacent carbonyl group and assignable to H-8. The chemical shifts of the quaternary carbons with an *O*-function found at δ 132.3, 143.0 and 148.6 the ^{13}C -nmr spectrum further suggested the partial structure to be a 1,2,3-trioxygenated benzene, which was confirmed by HMBC spectrum. Therefore, the furan ring was fused at C-7 through oxygen at C-6 and the non-chelated hydroxyl group was substituted at C-4. The structure of subelliptenone C was thus characterized as **1**.

Compound (**2**), subelliptenone D, obtained as a yellow amorphous, also reacted positively to Gibbs and FeCl_3 reactions. The data on the $[\text{M}^+]$ at m/z 352.0959 corresponding to $\text{C}_{20}\text{H}_{16}\text{O}_6$, the ir and the uv spectrum suggested that **2** was also a xanthone derivative and is an isomer of **1**, which was supported by the ^1H -nmr spectrum showing the presence of a chelated hydroxyl (δ 12.90), two non-chelated hydroxyl groups [δ 8.60 and 9.21 (1H each, br s)] and two aromatic protons [δ 7.39 and 8.05 (1H each, s)] as well as the presence of a 1,1-dimethylallyl group [δ 1.67 (6H, s, Me x 2), 5.06 (1H, dd, $J = 11, 1$ Hz, $-\text{CH}=\text{CH}_2$), 5.21 (1H, dd, $J = 18, 1$ Hz, $-\text{CH}=\text{CH}_2$), 6.43 (1H, dd, $J = 18, 11$ Hz, $-\text{CH}=\text{CH}_2$)] and a fused furan ring [δ 7.10, 8.00 (1H each, d, $J = 2$ Hz)]. An nOe was observed between the methyl groups (δ 1.67) of the 1,1-dimethylallyl group and one of the aromatic protons (δ 7.39) which gave cross peaks to three quaternary carbons with an *O*-function (δ 140.2, 147.4 and 148.4) in the HMBC spectrum (Figure 1), which indicated the presence of a 1,3,4-trioxygenated benzene moiety different from **1**. In the ^1H -nmr of a trimethyl ether (**2a**) derived from **2** by usual methylation, an nOe was observed between one of the methoxyl groups (δ 3.94) and an aromatic proton [δ 7.53 (1H, s)]. A possible partial structure of **2** was then either a 1,2-dihydroxy-4-(1,1-dimethyl-2-propenyl)- or a 1,4-dihydroxy-2-(1,1-dimethyl-2-propenyl)xanthone. Compared the ^1H -nmr and ^{13}C -nmr spectral data of **2** with those of subelliptenone B,¹ the 1,2-dihydroxy-4-(1,1-dimethyl-2-propenyl)xanthone derivative is preferable to another. On the other hand, the positions of the furan ring and the non-chelated hydroxyl group were determined not only by the comparison of ^1H -nmr and ^{13}C -nmr of **1**, and by the HMBC spectrum. Subsequently, the structure of subelliptenone D was designated as **2**. This is the first isolation of furanoxanthones from the natural resources.

Compounds (**3**) and (**4**) were determined by the spectral analysis to be 12b-hydroxy-des-D-garcigerin⁵ and globuxanthone,⁶ respectively, which have been already isolated from the heartwood of the same plant.⁷

Table 1. ^{13}C -Nmr spectral data on compounds (1-4)

carbon No.	1	2	3	4
1	154.2	147.4	153.5	147.4 ^{c)}
2	129.9	140.2	129.8	140.0
3	123.7	123.4	123.4	123.4
4	137.4	126.8	137.0	126.9
5	132.3	132.0	147.0	147.7
6	148.6	148.3	122.0	120.9
7	127.8	126.9	125.2	124.4
8	108.7	108.7	116.8	116.2
9	184.9	184.9	183.9	184.1
4a	143.0 ^{a)}	148.4	142.2	146.9 ^{c)}
8a	111.5 ^{b)}	111.4	121.9	121.5
9a	109.2	109.6	109.4	110.2
10a	143.0 ^{a)}	144.5	145.8	146.7
11	41.6	41.3	41.1	41.0
12	29.8	29.6	29.3	27.7
13	29.8	29.6	29.3	27.7
14	148.2	148.9	148.1	148.5
15	111.5 ^{b)}	111.5	111.5	111.1
16	109.5	109.0		
17	149.4	149.2		

All compounds were measured in acetone- d_6 . a) and b): overlapping. c): interchangeable. All carbons were assigned by the aid of CH COSY, COLOC and HMBC spectrum.

EXPERIMENTAL

Plant material. Root bark of *G. subelliptica* cultivated in the Botanical Garden of the University of Ryukyu was collected in April, 1993. The voucher specimens are deposited in the Herbarium of Gifu Pharmaceutical University.

Extraction and isolation. The dried and ground root bark (2.8 kg) was successively extracted with *n*-hexane (5 l x 3), benzene (4 l x 3), acetone (4 l x 3) and 70%MeOH (5 l x 3) each for 24 hr at room temperature. After each solvent was removed, the resulting acetone extract (135 g) was suspended into water (1.5 l) and partitioned with EtOAc (1.5 l x 3) and *n*-BuOH (1.2 l x 3) successively. The EtOAc soluble extract (90 g) was chromatographed on Si CC eluted with benzene-acetone system. A benzene-acetone (10 : 1) eluent was further purified by vacuum liquid chromatography on Si with *n*-hexane-EtOAc system to give nine fractions. Compounds 2 (5 mg) [Fr. 5 (7 : 1)] and 3 (8 mg) [Fr. 6 (7 : 1)] were purified by recrystallization. Fr. 3 (10 : 1) and Fr. 7 (7 : 1) were further chromatographed on Sephadex LH-20 eluted with acetone to give 4 (6 mg) and 1 (4 mg), respectively.

Compound (1) (subelliptenone C). An yellow amorphous; hrms m/z 352.0971 (Calcd 352.0947 for $\text{C}_{20}\text{H}_{16}\text{O}_6$); Elms m/z (rel. int.): 352 (M^+ , 84), 337 (100), 319 (22), 316 (20), 297 (21), 177 (6), 161 (8), 147 (9); uv λ (nm, MeOH) (log ϵ): 230 (4.06), 264 (4.40), 340 (3.47), 418 (3.45), +NaOMe: 276, 320sh, 375,

+NaOAc: 275, 310sh, 366, 438, +NaOAc/H₃BO₃: 271, 320sh; ir ν (cm⁻¹, KBr): 3450, 2975, 1645, 1610; ¹H-nmr (400 MHz, acetone-*d*₆) δ : 1.55 (6H, s, Me-12, 13), 5.01 (1H, dd, *J* = 11, 1 Hz, H-15Z), 5.04 (1H, dd, *J* = 18, 1 Hz, H-15E), 5.04 (1H, dd, *J* = 18, 11 Hz, H-14), 7.07 (1H, d, *J* = 2 Hz, H-16), 7.33 (1H, s, H-3), 7.97 (1H, d, *J* = 2 Hz, H-17), 8.04 (1H, s, H-8), 8.90 (2H, br s, OHs), 13.01 (1H, s, C1-OH).

Compound (2) (subelliptenone D). An yellow amorphous; HRms *m/z* 352.0959 (Calcd 352.0947 for C₂₀H₁₆O₆); EIms *m/z* (rel. int.): 352 (M⁺, 100), 336 (53), 321 (80), 319 (99), 311 (18), 295 (20), 291 (43), 281 (20), 177 (8), 161 (13), 149 (10), 105 (12), 77 (13); uv λ (nm, MeOH) (log ϵ): 239sh, 270 (4.77), 295sh, 310sh, 415 (3.75), +NaOMe: 251, 288, 365sh, +NaOAc: 276 351sh, +NaOAc/H₃BO₃: 271; ir ν (cm⁻¹, KBr): 3560, 3440, 2960, 1635, 1605, 1585; ¹H-nmr (400 MHz, acetone-*d*₆) δ : 1.67 (6H, s, Me-12, 13), 5.06 (1H, dd, *J* = 11, 1 Hz, H-15Z), 5.21 (1H, dd, *J* = 18, 1 Hz, H-15E), 6.43 (1H, dd, *J* = 18, 11 Hz, H-14), 7.10 (1H, d, *J* = 2 Hz, H-16), 7.39 (1H, s, H-3), 8.00 (1H, d, *J* = 2 Hz, H-17), 8.05 (1H, s, H-8), 8.60, 9.21 (1H each, br s, OHs), 12.90 (1H, s, C1-OH).

Methylation of 2. To a DMF solution containing **2** (3 mg), CH₃I (5 mg) and K₂CO₃ (0.5 g) were added and the solution was heated for 3 h under reflux. The reaction mixture was poured into water and then extracted with EtOAc. After evaporation of the organic layer, the residue was chromatographed on Si to give a trimethyl ether (**2a**) (2 mg), as a pale yellow oil; HRms *m/z* 394.1400 (Calcd 394.1416 for C₂₃H₂₂O₆); EIms *m/z* (rel. int.): 394 (100), 379 (84), 365 (41), 351 (13), 349 (18), 348 (16), 333 (13), 319 (7), 283 (5), 279 (4), 191 (5), 167 (8), 149 (33), 105 (7), 91 (10); uv λ (nm, MeOH): 235sh, 260, 290sh, 386; ir ν (cm⁻¹, KBr): 2925, 2840, 1650, 1620; ¹H-nmr (400 MHz, acetone-*d*₆) δ : 1.72 (6H, s, Me-12, 13), 3.90 and 4.31 (3H each, s, OMe x 2), 3.94 (3H, s, OMe at C3), 5.07 (1H, dd, *J* = 11, 1 Hz, H-15Z), 5.13 (1H, dd, *J* = 18, 1 Hz, H-15E), 6.43 (1H, dd, *J* = 18, 11 Hz, H-14), 7.11 (1H, d, *J* = 2 Hz, H-16), 7.53 (1H, s, H-3), 8.01 (1H, d, *J* = 2 Hz, H-17), 8.14 (1H, s, H-8).

Compound (3) (12b-hydroxy-des-D-garcigerin). An orange amorphous; EIms *m/z* (rel. int.): 312 (M⁺, 73), 297 (100), 279 (18), 271 (17), 269 (14), 257 (24), 137 (7), 121 (8); uv λ (nm, MeOH): 249, 266, 316, 408; ir ν (cm⁻¹, KBr): 3350, 2970, 1640, 1605, 1585; ¹H-nmr (400 MHz, acetone-*d*₆) δ : 1.54 (6H, s, Me-12, 13), 5.00 (1H, dd, *J* = 11, 1 Hz, H-15Z), 5.01 (1H, dd, *J* = 18, 1 Hz, H-15E), 6.31 (1H, dd, *J* = 18, 11 Hz, H-14), 7.30 (1H, t, *J* = 8 Hz, H-7), 7.34 (1H, s, H-3), 7.35 (1H, dd, *J* = 8, 2 Hz, H-6), 7.71 (1H, dd, *J* = 8, 2 Hz, H-8), 8.70 (1H, br s, OH), 12.85 (1H, s, C1-OH).

Compound (4) (gulobuxanthone). Orange needles, mp 137-138°C (*n*-hexane-EtOAc); EIms *m/z* (rel. int.): 312 (88), 297 (25), 279 (100), 257 (8), 251 (47), 137 (7), 115 (6), 73 (12); uv λ (nm, MeOH): 247, 266, 298sh, 313sh, 405; ir ν (cm⁻¹, KBr): 3500, 3400, 2950, 1650, 1590; ¹H-nmr (400 MHz, acetone-*d*₆) δ : 1.65 (6H, s, Me-12, 13), 5.04 (1H, dd, *J* = 11, 1 Hz, H-15Z), 5.18 (1H, dd, *J* = 18, 1 Hz, H-15E), 6.39 (1H, dd, *J* = 18, 11 Hz, H-14), 7.25 (1H, t, *J* = 8 Hz, H-7), 7.38 (1H, dd, *J* = 8, 2 Hz, H-6), 7.40 (1H, s, H-3), 7.70 (1H, dd, *J* = 8, 2 Hz, H-8), 8.80 (1H, br s, OH), 12.72 (1H, s, C1-OH).

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