Three New Caged Prenylxanthones from *Garcinia bracteata*

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Three new caged prenylxanthones (xanthone = 9*H*-xanthen-9-one), named neobractatin (**1**), 3-*O*-methylneobractatin (**2**), and 3-*O*-methylbractatin (**3**), along with eight known compounds, were isolated from the twig of *Garcinia bracteata*. The structures of the new compounds were elucidated on the basis of 1D- and 2D-NMR experiments, including HMBC, HSQC, ^{1}H,^{1}H-COSY, and ROESY, as well as HR-MS analysis.

Introduction. – The plants of the genus *Garcinia* (Guttiferae) have been extensively investigated from the phytochemical and biological points of view. Xanthones [1][2], benzophenones [3], depsidones [4], flavonoids [5], biflavonoids [6], and triterpenes [7] have been isolated from African and southeast Asian species. *Garcinia bracteata* C. Y. WU ex Y. H. LI is distributed in the south of Yunnan and Guangxi Province of P. R. China [8]. Previous phytochemical investigations on *G. bracteata* resulted in the isolation of caged prenylxanthones and benzophenones [9][10]. Caged xanthones, having a rearranged skeleton, were mainly isolated from *Garcinia* species, such as *G. bracteata*, *G. cantleyana* [11], *G. gaudichaudii* [12], *G. hanburyi* [13], *G. morella* [14], and *G. scortechinii* [15]. As a part of our search for secondary metabolites from tropical plants, a careful investigation of the twigs of *G. bracteata* led to the isolation of three new caged prenylxanthones, neobractatin (**1**), 3-*O*-methylneobractatin (**2**), and 3-*O*-methylbractatin (**3**), together with five known caged prenylxanthones, bractatin (**4**) [9], isobractatin (**5**) [9], 1-*O*-methylisobractatin (**6**) [9], neoisobractatin A (**7**) [10], neoisobractatin B (**8**) [10] (*Fig. 1*), and three known 'classical' xanthones, gerontoxanthone I [16], morusignin I [17], and macluraxanthone [18]. The details of the isolation and structure elucidation of the new compounds, **1**–**3**, are reported in this article.

Results and Discussion. – Compound **1** was obtained as a yellow amorphous powder and showed an $[M+Na]^+$ peak at *m*/*z* 487.2085 (calc. 487.2096) in the HR-ESI-MS, corresponding to a molecular formula of $C_{28}H_{32}O_6$. The IR spectrum exhibited a broad band at 3425 cm^{-1} due to an OH group, and absorbtions at 1751 and 1637 cm^{-1} due an unconjugated C=O group and a chelated *ortho*-OH C=O group, respectively. The ^{1}H-NMR spectrum (*Table 1*) revealed the presence of a chelated OH group (δ(H) 12.67 (*s*)), an olefinic H-atom of an α,β-unsaturated C=O unit (δ(H) 7.15 (*d*, *J* = 7.0 Hz)), three coupled H-atoms (δ(H) 6.30 (*dd*, *J* = 10.0, 18.0), 4.81 (*d*, *J* = 18.0), and 4.69 (*d*, *J* = 10.0), which were assigned to three olefinic H-atoms of a 1,1-

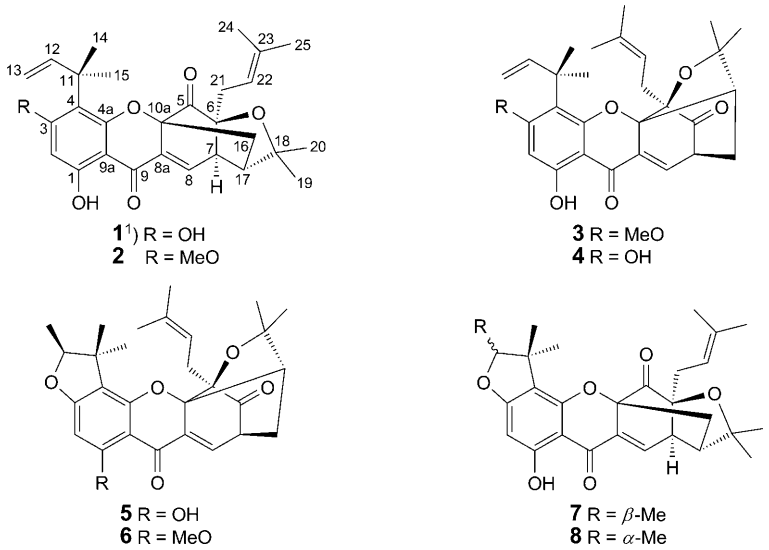

Fig. 1. *Structures of compounds* **1**–**8**

Table 1. *^{1}H-NMR Data of Compounds* **1**–**3**[1]). δ in ppm, J in Hz.

	1[a])[b])	**2**[c])[d])	**3**[c])[d])
HO–C(1)	12.67 (*s*)	12.77 (*s*)	13.27 (*s*)
CH(2)	5.97 (*s*)	6.08 (*s*)	6.11 (*s*)
MeO–C(3)		3.79 (*s*)	3.76 (*s*)
H–C(7)	3.77 (*dd*, *J* = 5.0, 7.0)	3.72 (*dd*, *J* = 5.0, 7.0)	3.48 (*dd*, *J* = 5.0, 7.0)
H–C(8)	7.15 (*d*, *J* = 7.0)	7.16 (*d*, *J* = 7.0)	7.47 (*d*, *J* = 7.0)
H–C(12)	6.30 (*dd*, *J* = 10.0, 18.0)	6.32 (*dd*, *J* = 10.0, 18.0)	6.14 (*dd*, *J* = 10.0, 18.0)
CH_2(13)	4.81 (*d*, *J* = 18.0),	4.86 (*d*, *J* = 18.0),	4.75 (*d*, *J* = 10.0),
	4.69 (*d*, *J* = 10.0)	4.75 (*d*, *J* = 10.0)	4.69 (*d*, *J* = 18.0)
Me(14)	1.53 (*s*)[e])	1.60 (*s*)[e])	1.69 (*s*)[e])
Me(15)	1.51 (*s*)[e])	1.57 (*s*)[e])	1.62 (*s*)[e])
H_a–C(16)	2.30 (*d*, *J* = 14.0)	2.51 (*d*, *J* = 13.0)	2.49 (*d*, *J* = 9.0)
H_b–C(16)	1.84 (*dd*, *J* = 10.0, 14.0)	1.78 (*dd*, *J* = 10.0, 13.0)	
H_a–C(17)	2.20 (*dd*, *J* = 5.0, 10.0)	2.16 (*dd*, *J* = 5.0, 10.0)	2.32 (*dd*, *J* = 5.0, 13.0)
H_b–C(17)			1.31 (*dd*, *J* = 9.0, 13.0)
Me(19)	1.21 (*s*)	1.33 (*s*)	1.22 (*s*)
Me(20)	1.25 (*s*)	1.35 (*s*)	1.65 (*s*)[e])
CH_2(21)	2.27 (*dd*, *J* = 8.0, 14.0),	2.48 (*dd*, *J* = 8.0, 14.0),	2.64–2.62 (*m*)
	1.84 (*dd*, *J* = 8.0, 14.0)	2.06 (*dd*, *J* = 8.0, 14.0)	
H–C(22)	4.90 (*t*, *J* = 8.0)	5.01 (*t*, *J* = 8.0)	4.37 (*t*, *J* = 8.0)
Me(24)	1.63 (*s*)	1.72 (*s*)	1.39 (*s*)
Me(25)	1.52 (*s*)[e])	1.58 (*s*)[e])	1.08 (*s*)

[a]) Recorded in (D_6)DMSO. [b]) Recorded at 400 MHz. [c]) Recorded in $CDCl_3$. [d]) Recorded at 500 MHz. [e]) Signals may be exchanged.

[1]) Arbitrary atom numbering. For systematic names, see *Exper. Part*.

dimethylprop-2-en-1-yl, and an olefinic H-atom of 3-methylbut-2-en-1-yl (δ(H) 4.90 (*t*, $J = 8.0$)). The ^{13}C-NMR spectrum (*Table 2*) exhibited 28 C-atom signals which were sorted by a DEPT experiment as those of six Me, three CH_2, and six CH groups, and of thirteen quaternary C-atoms (including two C=O C-atom signals at δ(C) 199.9 and 177.9, resp.). In the ^{1}H-NMR spectrum, characteristic signals at δ(H) 3.77 (*dd*, $J = 5.0$, 7.0, H–C(7))[1]), 2.20 (*dd*, $J = 5.0$, 10.0, H–C(17)), and 1.84 (*dd*, $J = 10.0$, 14.0, H_b–C(16)) were discernible. Together with the presence of three O-bearing quaternary C-atom signals at δ(C) 83.6 (C(18)), 83.6 (C(10a)), and 78.9 (C(6)), and the evidence of correlations between CH_2(16) and C(5), C(7), C(8a), C(10a), and C(17), correlations between H–C(17) with C(6), C(7), C(16), and C(18) in the HMBC spectrum (*Fig. 2*) led to the assumption that **1** was a caged prenylxanthone, resembling 1-*O*-methylneobractatin [9], isolated from the same species, except for an OH group instead of a MeO group at C(1). The C-atom signals at δ(C) 162.1 (C(1)) and 177.9 (C(9)) of compound **1** appeared at more down-field than those of 1-*O*-methylneobractatin (160.5 and 175.0, resp.) [9], due to the HO–C(1) chelated with C(9)=O in **1**. Moreover, the HMBCs (*Fig. 2*) of HO–C(1) (δ(H) 12.67 (*s*)) with C(1) (δ(C) 162.1), C(2) (97.1), and C(9a) (δ(C) 100.5) also ascertained the presence of an OH group at C(1). ROESY Correlations (*Fig. 3*) were detected between H–C(7), H–C(17), Me(19), H–C(8), CH_2(21), and H–C(22), indicating that H–C(7) and Me(19) have the same orientation as the isoprenyl chain at C(6). Therefore, compound **1** was elucidated as neobractatin.

Table 2. *^{13}C-NMR Data of Compounds* **1**–**3**[1]). δ in ppm.

	1[a])[b])	**2**[c])[d])	**3**[c])[d])		**1**[a])[b])	**2**[c])[d])	**3**[c])[d])
C(1)	162.1	163.8	164.0	CH_2(13)	106.2	106.0	106.5
CH(2)	97.1	93.9	97.1	Me(14)	28.3	29.3	30.8
C(3)	167.0	168.1	168.1	Me(15)	27.4	28.9	27.9
C(4)	112.6	114.9	113.5	CH_2(16) or CH(16)	32.0	32.7	49.4
C(4a)	159.1	158.4	159.1	CH_2(17) or CH(17)	41.4	42.4	26.5
C(5)	199.9	199.6	84.9	C(18)	83.6	83.6	83.1
C(6)	78.9	79.3	204.1	Me(19)	26.5	26.7	29.2
CH(7)	44.5	44.8	47.4	Me(20)	29.2	29.6	31.2
CH(8)	135.5	134.0	134.0	CH_2(21)	30.1	30.2	28.8
C(8a)	133.2	134.8	133.3	CH(22)	117.6	117.4	118.0
C(9)	177.9	178.7	180.0	C(23)	135.4	136.1	135.1
C(9a)	100.5	102.0	101.5	Me(24)	17.9	18.1	16.9
C(10a)	83.6	83.6	91.4	Me(25)	25.7	25.8	25.5
C(11)	40.1	41.2	41.4	*Me*O–C(3)		55.4	55.3
CH(12)	151.0	151.4	150.7				

[a]) Recorded in (D_6)DMSO. [b]) Recorded at 100 MHz. [c]) Recorded in $CDCl_3$. [d]) Recorded at 125 MHz.

Compound **2**, a yellow amorphous powder, was shown to have the molecular formula $C_{29}H_{34}O_6$ on the basis of its HR-ESI-MS (*m/z* 501.2254 ($[M + Na]^+$; calc. 501.2253)). The ^{1}H- and ^{13}C-NMR (*Tables 1* and *2*), HSQC, and HMBC spectra indicated that the structure of **2** was similar to that of **1**, except for the presence of a

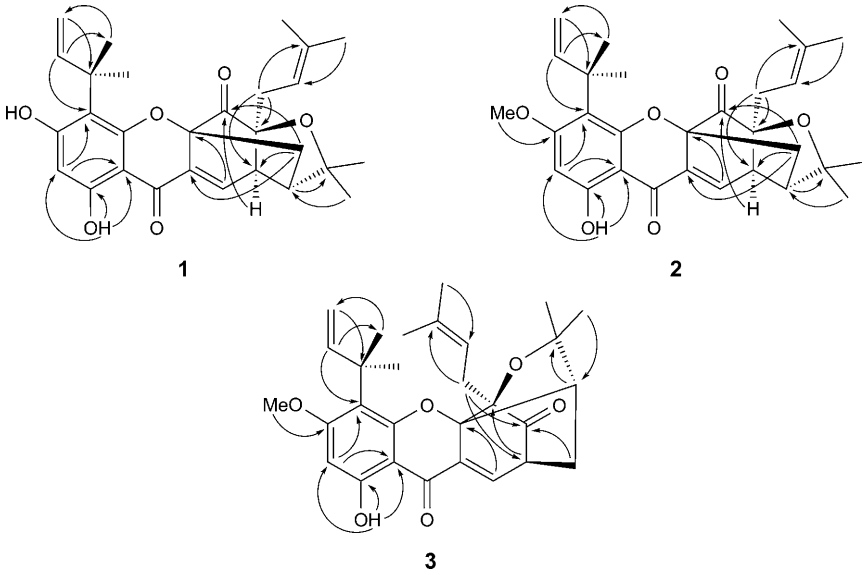

Fig. 2. *Key HMBCs* (H → C) *of compounds* **1**–**3**

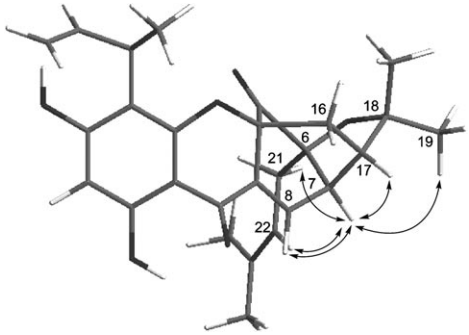

Fig. 3. *Key ROESY correlations* (H ↔ H) *of compound* **1**

MeO group (δ(H) 3.79 (*s*); δ(C) 55.4) in **2** instead of the phenolic OH group in compound **1**. The key HMBC correlation (*Fig. 2*) of MeO (δ(H) 3.79) with C(3) (δ(C) 168.1) indicated that the MeO group is located at C(3). Thus, the structure of **2** was deduced as 3-*O*-methylneobractatin.

Compound **3** was isolated as a yellow amorphous powder with the same molecular formula $C_{29}H_{34}O_6$ as **2**, deduced from the HR-ESI-MS (*m*/*z* 501.2264 ($[M+Na]^+$; calc. 501.2253)). The NMR spectra (*Tables 1* and *2*) of **3** suggested that its structure was very similar to that of **2**. The main difference between the structures was the different position of the unconjugated C=O. Correlations from H_b–C(17) (δ(H) 1.31) to the C=O (δ(C) 204.1), and from H_b–C(16) (δ(H) 1.78) to the C=O (δ(C) 199.6) were

observed in the HMBC spectrum of **3** and **2**, respectively (*Fig. 2*), which indicated that oxo group in **3** is located at C(6), *i.e.*, C(6)=O. Hence, compound **3** is an isomer of **2**, and its structure was established as 3-*O*-methylbractatin.

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Experimental Part

General. Column chromatography (CC): silica gel (SiO_2; 200–300 mesh; *Qingdao Marine Chemical Inc.*, P. R. China), SiO_2 *H* (10–40 μm; *Qingdao Marine Chemical Inc.*), *Lichroprep RP-18* gel (40–63 μm; *Merck*, D-Darmstadt), *MCI* gel (75–150 μm; *Mitsubishi Chemical Corporation*, Japan), and *Sephadex LH-20* (*Pharmacia*). Fractions were monitored by TLC, and spots were visualized by heating SiO_2 plates sprayed with 10% H_2SO_4/EtOH. Optical rotations: *Jasco DIP-370* digital polarimeter. UV Spectra: *Shimadzu-UV-2401A* spectrophotometer in MeOH solns.; λ_{max} (log ε) in nm. IR Spectra: *Bio-Rad-FTS-135* spectrometer in KBr pellets; $\tilde{\nu}$ in cm^{-1}. 1D- and 2D-NMR Spectra: *Bruker-AM-400* and -*DRX-500* spectrometers; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *VG-Auto-Spec-3000* spectrometer with glycerol as matrix for FAB; *API-QSTAR-Pulsar-1* spectrometer for HR-ESI; in *m*/*z* (rel. %).

Plant Material. The twigs of *G. bracteata* were collected from Xishuangbanna, Yunnan Province, P. R. China, in August 2008, and authenticated by Prof. *Guo-Da Tao*, Xishuangbanna Tropical Botanical Garden. A voucher specimen (No. 20080801) was deposited with the ethnobotany research group of Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried twigs of *G. bracteata* (6.5 kg) were powdered and then extracted with 95% EtOH (3 × 20 l) at r.t. The combined solns. were concentrated to dryness under vacuum. The crude extract was suspended in H_2O and successively extracted with petroleum ether (PE) and AcOEt. The combined PE extracts were evaporated to give a deep-brown gum (154 g), which was separated on a SiO_2 column, eluted with a gradient of PE/AcOEt 95:5–40:60 to afford six fractions, *Frs. A–F. Fr. C* (8.6 g) was further chromatographed (SiO_2; PE/AcOEt 4:1) to provide **1** (35 mg), **4** (65 mg), and five subfractions, *Frs. C1–C5*. *Fr. C2* was purified by reversed-phase (RP) CC (*RP-18*; MeOH/H_2O 7:3–9:1) to give **5** (28 mg) and **2** (22 mg). *Fr. C3* was subjected to *RP-18* CC (MeOH/H_2O 6:4–8:2) to afford **6** (32 mg) and **3** (26 mg). *Fr. D* (3.5 g) was fractionated by CC (SiO_2; PE/AcOEt 3:1), followed by *Sephadex LH-20* (MeOH), to provide **7** and **8** (mixture, 42 mg). *Fr. E* (6.5 g) was divided into three subfractions by CC (SiO_2; $CHCl_3$/MeOH 30:1): *Frs. E1–E3*. *Fr. E1* was further purified by CC (*RP-18*; MeOH/H_2O 7:3) to yield gerontoxanthone I (19 mg) and morusignin I (26 mg). *Fr. E3* was purified by CC (*Sephadex LH-20*; MeOH) to provide macluraxanthone (11 mg).

Neobractatin (=*(+)-(3*R*,3a*S*,10a*R*,11a*R*)-9-(1,1-Dimethylprop-2-en-1-yl)-2,3,3a,11a-tetrahydro-6,8-dihydroxy-2,2-dimethyl-11a-(3-methylbut-2-en-1-yl)-3,10a-methano-10a*H*-furo[3,2-*b*]xanthene-5,11-dione*; **1**). Yellow amorphous power. $[\alpha]_D^{27} = +9.4$ (*c* = 0.24, MeOH). UV: 208 (4.59), 346 (4.19). IR: 3425, 2920, 1751, 1637, 1592. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. FAB-MS (pos.): 465 ($[M+H]^+$). HR-ESI-MS: 487.2085 ($[M+Na]^+$, $C_{28}H_{32}NaO_6^+$; calc. 487.2096).

3-O-*Methylneobractatin* (=*(+)-(3*R*,3a*S*,10a*R*,11a*R*)-9-(1,1-Dimethylprop-2-en-1-yl)-2,3,3a,11a-tetrahydro-6-hydroxy-8-methoxy-2,2-dimethyl-11a-(3-methylbut-2-en-1-yl)-3,10a-methano-10a*H*-furo[3,2-*b*]xanthene-5,11-dione*; **2**). Yellow amorphous power. $[\alpha]_D^{26} = +5.4$ (*c* = 0.17, MeOH/$CHCl_3$). UV: 237 (4.19), 348 (4.28). IR: 3432, 2923, 1751, 1634, 1588. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. ESI-MS: 501 ($[M+Na]^+$). HR-ESI-MS: 501.2254 ($[M+Na]^+$, $C_{29}H_{34}NaO_6^+$; calc. 501.2253).

3-O-*Methylbractatin* (=*(−)-(1*S*,3a*R*,5*R*)-11-(1,1-dimethylprop-2-en-1-yl)-3,3a,4,5-tetrahydro-8-hydroxy-10-methoxy-3,3-dimethyl-1-(3-methylbut-2-en-1-yl)-1,5-methano-1*H*,7*H*-furo[3,4-*d*]xanthene-7,13-dione*; **3**). Yellow amorphous power. $[\alpha]_D^{26} = -1.3$ (*c* = 0.44, MeOH). UV: 217 (4.51), 354 (4.15). IR: 3443, 2930, 1736, 1637, 1581. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. ESI-MS: 501 ($[M+Na]^+$). HR-ESI-MS: 501.2264 ($[M+Na]^+$, $C_{29}H_{34}NaO_6^+$; calc. 501.2253).

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