Three New Compounds from *Securidaca inappendiculata*

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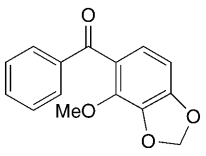
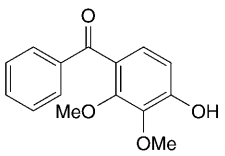
Three new compounds, 2-methoxy-3,4-(methylenedioxy)benzophenone (**1**), 4-hydroxy-2,3-dimethoxybenzophenone (**2**), and 3-hydroxy-4,6-dimethoxy-9*H*-xanthen-9-one (**3**), besides three known compounds were isolated from the roots of *Securidaca inappendiculata.* Their structures were established by spectroscopic means and X-ray crystallographic diffraction analysis. The biogenetic relationships among these six compounds are discussed.

Introduction. – *Securidaca inappendiculata* HASSK. is a traditional Chinese herbal medicine, belonging to the Polygalaceae family, mainly distributed in the south of China and the tropical regions of Asia [1]. The roots of *S. inappendiculata* are used as anti-inflammatory, antibacterial, and antirheumatism agent in China [2]. Pharmacological investigations have shown that the xanthones [3], as main components accumulated in *S. inappendiculata*, have many bioactivities including MAO inhibition, cytotoxic, anti-inflammatory, antitumor, antibacterial, antifungal, antioxidant, and tuberculostatic properties [4][5].

In the course of our search for natural antioxidants from *S. inappendiculata*, two new benzophenones **1** and **2** and a new xanthone **3**, along with three known compounds, 4-hydroxy-3-methoxybenzaldehyde (**4**), 4-hydroxy-3-methoxybenzoic acid (**5**) and 1,3,8-trihydroxy-4-methoxy-9*H*-xanthen-9-one (**6**), were isolated from the $CHCl_3$ extract of the roots of *S. inappendiculata*. According to the biosynthetic pathways to xanthones in higher plants, shikimate and acetate pathways form benzophenones or benzophenone-like intermediates, which then react intramolecularly to give xanthones; thus xanthones **3** and **6** could be derived from the benzophenone **2**. This paper describes the structure elucidation of the three new compounds **1**–**3** and a plausible biogenetic pathway for the formation of **1**–**3** and **6**.



1



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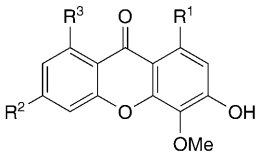
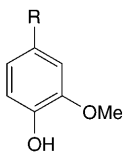


3 $R^1 = R^3 = H$, $R^2 = OMe$
6 $R^1 = R^3 = OH$, $R^2 = H$



4 R = CHO
5 R = COOH

Result and Discussion. – Compound **1**, obtained as colorless crystal, gave a molecular-ion peak at *m*/*z* 256 in the EI-MS, in accord with the molecular formula $C_{15}H_{12}O_4$

as determined by the HR-EI-MS, which was confirmed by the ^{13}C-NMR and DEPT spectra exhibiting signals for 15 C-atoms (*Table 1*[1])). Further spectral data (IR, HMQC, HMBC) and an X-ray crystal-structure analysis (*Fig. 1*) established the structure of 2-methoxy-(3,4-methylenedioxy)benzophenone (**1**).

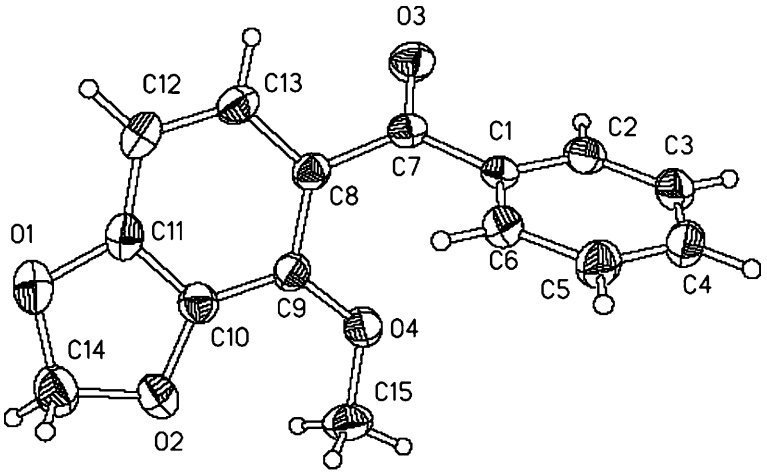


Fig. 1. *X-Ray single-crystal structure of* **1**[1])

Table 1. *^{1}H- and ^{13}C-NMR Data of Compounds* **1** *and* **2**[1]). δ in ppm, J in Hz.

	1		**2**	
	δ(C)[a])	δ(H)[b])	δ(C)[a])	δ(H)[b])
C(1)	126.2	–	124.0	–
C(2)	142.3	–	152.5	–
C(3)	136.8	–	140.4	–
C(4)	151.6	–	154.4	–
H–C(5)	102.8	6.61 (d, J=8.2)	111.5	6.72 (d, J=8.4)
H–C(6)	124.2	6.95 (d, J=8.2)	124.8	6.97 (d, J=8.4)
C(1′)	138.4	–	138.3	–
H–C(2′)(6′)	129.6	7.80 (d, J=7.8)	129.7	7.67 (d, J=8.0)
H–C(3′)(5′)	128.1	7.43 (t, J=7.5)	128.2	7.49 (t, J=7.7)
C(4′)	132.6	7.54 (d, J=7.3)	132.6	7.61 (d, J=7.5)
CO	195.1	–	194.7	–
MeO–C(2)	59.9	3.83 (s)	61.1	3.78 (s)
MeO–C(3)			60.2	
OCH_2O	101.5	6.01 (s)		3.60 (s)
OH–C(4)				10.01 (s)

[a]) Recorded at 100 MHz. [b]) Recorded at 400 MHz.

[1]) Arbitrary atom numbering; for systematic names see *Exper. Part.*

The ^{1}H-NMR spectrum of **1** (*Table 1*) showed the presence of a MeO (*s* at δ(H) 3.73) and a CH_2OCH_2 group (*s* at δ(H) 6.01), besides seven aromatic protons, the splitting pattern of the two aromatic protons at δ(H) 6.95 (*d*, $J=8.2$ Hz) and 6.61 (*d*, $J=8.2$ Hz) being typical of a 1,2,3,4-tetrasubstituted benzene ring (ring A), and the remaining five aromatic protons of ring B appearing as a *d* at δ(H) 7.80 ($J=7.8$ Hz) and two *t* at δ(H) 7.54 ($J=7.3$ Hz) and 7.43 ($J=7.5$ Hz). This suggested that ring A was substituted by the MeO and OCH_2O group and ring B was a symmetrical structure. The latter was confirmed by the overlapping signals in the ^{13}C-NMR spectrum at δ(C) 129.6 (C(2′), C(6′)) and 128.1 (C(3′), C(5′)). The HMBC spectrum of **1** (*Fig. 2*), displayed correlations of the aromatic-proton signals at δ(H) 6.95 (ring A) and 7.80 (ring B) with the C=O at δ(C) 195.1, elucidating the connection of the rings A and B *via* this C=O group. Furthermore, the aromatic proton at δ(H) 6.61 (ring A) correlated with the quaternary C-atoms at δ(C) 51.6 (C(4) and 136.8 (C(3)) which showed cross-peaks to the signal at δ(H) 6.01 (OCH_2O)[1]). The signal of the MeO group at δ(H) 3.83 correlated with the quaternary C-atom at δ(C) 42.3 (C(2)), suggesting that ring A of **1** was a 2-methoxy-3,4-(methylenedioxy)benzene moiety. The presence of the aromatic ring B was confirmed by the cross-peaks δ(H) 7.80/δ(C) 132.6 (C(4′)) and δ(H) 7.43/δ(C) 138.4 (C(1′)).

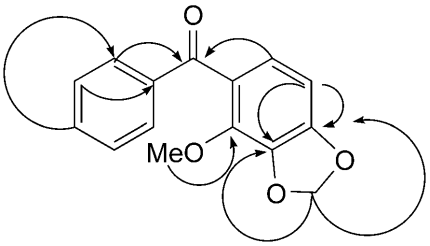


Fig. 2. *Selected H → C HMBC correlations of* **1**

Compound **2**, obtained as a colorless powder, was assigned a molecular formula $C_{15}H_{14}O_4$, as determined by HR-EI-MS (M^+ at m/z 258.09077) as well as by its ^{13}C-NMR and DEPT data. The spectral data were similar to those of **1**.

Comparison of the ^{1}H- and ^{13}C-NMR spectra of **2** (see *Table 1*) with those of **1** revealed the presence of two MeO groups at δ(H) 3.78 (*s*) and 3.60 (*s*) and an OH group at δ(H) 10.01 (*s*) in **2** instead of a MeO and CH_2-OCH_2 group in **1**. The IR absorptions of **2** at 3222 (OH) and 1634 cm^{-1} (C=O) were consistent with the proposed structure. The HMBC spectrum showed the correlations δ(H) 6.97/δ(C) 152.5 (C(2)) and 154.4 (C(4)), δ(H) 6.72/δ(C) 140.4 (C(3)) and 124.0 (C(1)), δ(H) 10.01 (OH)/δ(C) 140.4 (C(3)), δ(H) 3.60 (MeO)/δ(C) 152.2 (C(2)), and δ(H) 3.78 (MeO)/δ(C) 140.4 (C(3)).

Compound **3**, obtained as yellow needles, had a molecular formula $C_{15}H_{12}O_5$, as deduced from the molecular-ion peak at m/z 272.06847 in the HR-EI-MS and from ^{1}H- and ^{13}C-NMR data (*Table 2*). In the IR spectrum, the characteristic absorptions of a xanthone were observed at 3396 (OH), 1660 (conjugated C=O), and 1621 and 1476 cm^{-1} (aromatic moieties).

The ^{1}H-NMR spectrum of **3** (*Table 2*) showed an OH group at δ(H) 9.49 (*s*), two aromatic MeO groups at δ(H) 3.83 (*s*) and 3.87 (*s*), a three-proton spin system at δ(H) 7.52 (*d*, $J=3.0$ Hz), 7.40 (*dd*, $J=9.1$, 3.0 Hz), and 7.54 (*d*, $J=9.0$ Hz), and an *AB* system at δ(H) 7.27 (*d*, $J=9.1$ Hz) and 7.38 (*d*, $J=9.1$ Hz). The ^{13}C-NMR spectrum indicated the presence of two aromatic MeO (δ 55.6 and 61.0) and a C=O group (δ 174.9), and that C(1) (δ 113.5) and C(8) (δ 119.1) where unsubstituted. The HMBC experiment of **3** revealed the following long-range correlations: δ(H) 7.27/δ(C) 115.7 (C(9a)) and 146.8 (C(3)), δ(H) 7.38/δ(C) 144.9 (C(4)), δ(H) 9.49 (OH)/δ(C)123.9 (C(2)) and 144.9 (C(4)), δ(H) 3.83 (MeO)/δ(C) 144.9 (C(4)), δ(H) 3.87 (MeO)/δ(C) 155.4 (C(6)), δ(H) 7.40/δ(C) 121.8 (C(8a)), and δ(H) 7.54/δ(C) 155.4 (C(6)).

Table 2. *^{1}H- and ^{13}C-NMR Data for Compound* **3**. δ in ppm, J in Hz

	δ(C)[a])	δ(H)[b])
H–C(1)	113.5	7.27 (*d*, *J* = 9.1)
H–C(2)	123.9	7.38 (*d*, *J* = 9.1)
C(3)	146.5	–
C(4)	144.9	–
C(4a)	149.4	–
C(10a)	149.7	–
H–C(5)	105.8	7.52 (*d*, *J* = 3.0)
C(6)	155.4	–
H–C(7)	123.9	7.40 (*dd*, *J* = 9.1, 3.0)
H–C(8)	119.1	7.54 (*d*, *J* = 9.0)
C(8a)	121.8	–
C(9a)	115.7	–
C=O	174.9	–
MeO–C(4)	61.0	3.83
MeO–C(6)	55.6	3.87
OH–C(3)	–	9.49

[a]) Recorded at 100 MHz. [b]) Recorded at 400 MHz.

The discovery of the simple benzophenones as natural products is useful for the understanding of the biogenetic pathways to xanthones in higher plants. This involves the condensation of shikimate- and acetate-derived moieties to form benzophenones or benzophenone-like intermediates, which then react intramolecularly to form xanthones [6]. To date, only several benzophenones and *C*-glucosides were found in *Mangifera indica* L. [7], *Gnidia involucrata* STEUT. ex A. RICH. [8], and *Hypericum annulatum* [9]. This is the first report of the occurrence of two simple benzophenones isolated from the plant family of the Polygalaceae. A plausible biosynthetic pathway of the formation of **1**–**3** and **6** from **4** *via* **5** is given in the *Scheme*.

Experimental Part

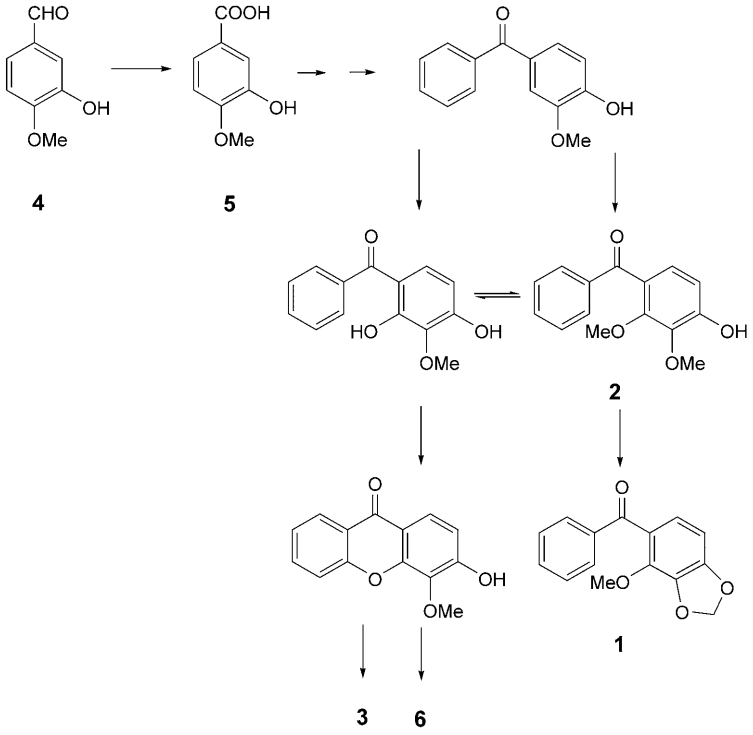
General. M.p.: uncorrected; *XRC-1* apparatus. Optical rotations: *Jasco-DIP-370* digital polarimeter. CC = Column chromatography. IR spectra: *Bio-Rad-FTS-135* spectrometer; KBr pellets; in cm^{-1}. 1D- and 2D-NMR Spectra: *Bruker-AM-400* spectrometer; δ in ppm, *J* in Hz. MS and HR-MS: *VG-AutoSpec-3000* spectrometeter; 70 eV for EI; in *m*/*z* (rel. %).

Plant Material. The roots of *Securidaca inappendiculata* HASSK. were collected in Xishuang-banna, Yunnan Province, China, in May 2004. The plant was identified by Mr. *Jingyun Cui* (Xishuangbanna Institute of Botany, Chinese Academy of Sciences), and a voucher specimen was deposited in the Herbarium of the College of Chemistry & Molecular Engineering, Peking University.

Extraction and Isolation. The dried roots of *Securidaca inappendiculata* HASSK (5.9 kg) were extracted with 95% EtOH (3×7 l) at r.t. After evaporation of the EtOH the residue was suspended in H_2O and extracted with $CHCl_3$ and BuOH. The $CHCl_3$ extract (60 g) was subjected to CC (silica gel (200–300 mesh), petroleum ether/Me_2CO 95 : 5 → 9 : 1): *Fractions 1–4*. *Fr. 1* was resubjected to CC *Sephadex LH-20*, MeOH): *Fr. 1.1* and *1.2*. *Fr. 1.1* was isolated separated by CC (silica gel *H*, petroleum ether/Me_2CO): **1** (861 mg) and **2** (437 mg). *Fr. B* was repeatedly subjected to CC (silica gel *H*, petroleum ether/Me_2CO 20 : 1; then *Sephadex LH-20*, Me_2CO): **3** (23 mg), **4** (9 mg), **5** (13 mg), and **6** (8 mg).

2-Methoxy-3,4-(methylenedioxy)benzophenone (= *(4-Methoxy-1,3-benzodioxol-5-yl)phenylmethanone*; **1**). Colorless crystal (MeOH). $[\alpha]_D^{20} = 0$ ($c = 0.50$, $CHCl_3$). M.p. 81.5°. UV (MeOH): 251, 243, 283, 357. ^{1}H- and

Scheme. *Plausible Biosynthetic Pathway of the Formation Compounds* **1**–**3** *and* **6**



^{13}C-NMR: *Table 1*, EI-MS (70 eV): 256 (70), 239 (25), 179 (100), 164 (35). HR-EI-MS: 256.07512 ($C_{15}H_{12}O_4^+$; calc. 256.07356).

Crystallographic Data of **1**[2]). Data were collected at 293 K on a *Nonius-Kappa-CCD* area detector by using graphite-monochromated MoK_a radiation (*Bruker D8 Discover*). Colorless block. Empirical formula $C_{15}H_{12}O_4$, M_r 256.25. Crystal system: triclinic. space group H-M '$P\bar{1}$'. Unit-cell dimensions: $a=6.7279(2)$, $b=8.6893(2)$, $c=10.8003(3)$ Å; $\alpha=93.3460(10)$, $\beta=104.7360(10)$, $\gamma=90.861(2)^\circ$; $V=609.29(3)$ Å^3; $Z=2$, $D_{calc.}=1.397$ g/cm^3; $\mu=0.102$ mm^{-1}, $F(000)=268$.

4-Hydroxy-2,3-dimethoxybenzophenone (*=(4-Hydroxy-2,3-dimethoxyphenyl)phenylmethanone*; **2**). Colorless powder. $[\alpha]_D^{20}=0$ ($c=0.10$, $CHCl_3$). M.p. 62.5°. UV (MeOH): 250, 242, 282, 341. IR (KBr): 3222, 1634, 1597, 1576, 1466, 1450, 1323, 1301, 1211. ^{1}H- and ^{13}C-NMR: *Table 1*. EI-MS (70 eV): 258 (85), 241 (60), 209 (30), 181 (100), 167 (30). HR-EI-MS: 258.09077 ($C_{15}H_{14}O_4^+$; calc. 258.08921).

*3-Hydroxy-4,6-dimethoxy-9*H*-xanthen-9-one* (**3**). Yellow needles. $[\alpha]_D^{20}=0$ ($c=1.00$, $CHCl_3$). UV (MeOH): 237, 266, 318, 380. IR (KBr): 3396, 1660, 1621, 1476, 1432, 1296, 1205. ^{1}H- and ^{13}C-NMR: *Table 2*. EI-MS (70 eV): 272 (75), 254 (100), 229 (60), 198 (45). HR-EI-MS: 272.06859 ($C_{15}H_{12}O_5^+$; calc. 272.06847).

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