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STRUCTURE OF A NEW XANTHONE FROM *Securidaca inappendiculata*

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*A new xanthone (**1**, 1,7-dihydroxy-2-methoxyxanthone), in addition to the known metabolites 1,7-dihydroxyxanthone (**2**), 24(*R*)-stigmast-7,22 (E)-dien-3α-ol (**3**), and 1,7-dimethoxyxanthone (**4**), was isolated from the roots of* Securidaca inappendiculata. *Compounds **1–4** were evaluated by anti-HIV assay and **1–3** showed anti-HIV-1inhibitory activity* in vitro.

Key words: *Securidaca inappendiculata*, xanthones, anti-HIV assay.

We previously reported the isolation of xathone and benzophenone compounds from the roots of *Securidaca inappendiculata* [1]. In continuation of these investigations, a study of xanthones from the $CHCl_3$-soluble portion of the extract was begun.

The dried roots of this plant collected in the Xishuangbanna (Yunnan province, PRC) in May 2004 were extracted with ethanol (95%) at room temperature. The combined alcohol extracted was evaporated in vacuum. The condensed solution was diluted with water and successively treated with chloroform and *n*-butanol. The solvents were removed to afford chloroform (60 g) and *n*-butanol (390 g) fractions.

The chloroform extract (60 g) was chromatographed over a silica-gel column separately with gradient elution by petroleum–acetone (100:1–1:9). There were xanthones in the petroleum–acetone (20:1–10:1) fractions. All the fractions were combined to obtain 1.7 g. This fraction was evaluated by anti-HIV assay *in vitro* and the EC_{50} value of this fraction was 1 mg/mL. So, this fraction was subjected repeatedly to column chromatography over silica gel H eluting with petroleum–acetone (15:1) to afford compounds **1–4**. The structure of the new compound was established, and the known metabolites were identified using spectral methods, including 2D NMR spectroscopy and mass spectrometry.

Compound **1**, obtained as yellow needles, has the molecular formula $C_{14}H_{10}O_5$, as deduced from the molecular-ion peak at *m/z* 258.05280 in the HR-EI-MS and from ^{1}H- and ^{13}C NMR data (Table 1). In the IR spectrum, the characteristic absorptions of a xanthone were observed at 3451 (OH), 1650 (conjugated C=O), and 1620, 1576, 1499, and1465 (aromatic moieties).

According to ^{13}C NMR, compound **1** contains a methoxy group, five methines, and eight quaternary C atoms (Table 1). Of these, **1** contains a methoxy group [δ 56.7 ppm and 3.84 (3H, s) in the ^{13}C and ^{1}H NMR, respectively]; five methines [δ 105.7 (C-4), 107.6 (C-8), 119.2 (C-5), 121.9 (C-3) and 125.7 (C-6) and 7.02 (1H, d, J = 9.0 Hz, H-4), 7.44 (1H, d, J = 3.0 Hz, H-8), 7.51 (1H, d, J = 9.3 Hz, H-5), 7.53 (1H, d, J = 9.0 Hz, H-3) and 7.35 (1H, dd, J = 9.3, 3.0 Hz, H-6) in the HMQC spectrum, respectively]; a carbonyl carbon [δ 182.1 (C) ppm in the ^{13}C NMR]; seven quaternary C atoms [δ 108.1 (C-8b), 119.7 (C-8a), 141.8 (C-2), 149.3 (C-4a), 149.5 (C-1), 149.6 (C-4b), 153.8 (C-7) ppm in the ^{13}C NMR, respectively]; a chelated OH group [δ 12.71 ppm (1H, s) in the ^{1}H NMR], and an OH group [δ 10.04 ppm (1H, s) in the ^{1}H NMR].

HMBC experiment on **1** revealed the following long-range correlations (Fig. 1): 1-OH [δ 12.71 ppm] and C-8b, C-1 and C-2 [δ 108.1, 149.5 and 141.8]; 2-MeO [δ 3.84] and C-2 [δ 141.8]; H-3 [δ 7.53] and C-1 [δ 149.5]; H-4 [δ 7.02] and C-8b, C-2 and C-4a [δ 108.1, 141.8 and 149.3]; H-5 [δ 7.51] and C-8a [119.7]; H-6 [δ 7.35] and C-4a [δ 149.6]; 7-OH [δ 10.04] and C-8 and C-6 [δ 107.6 and 125.7], H-8 [δ 7.44] and C=O [δ 182.1].

Thus, the structure of **1** was established as 1,7-dihydroxy-2-methoxyxanthone.

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TABLE 1. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) Chemical Shifts (δ, ppm) in NMR of **1**

C atom	δ_H	δ_C	C atom	δ_H	δ_C
1		149.5	5	7.51 (d, J = 9.3)	119.2
2		141.8	6	7.35 (dd, J = 9.3, 3.0)	125.7
3	7.53 (d, J = 9.0)	121.9	7		153.8
4	7.02 (d, J = 9.0)	105.7	8	7.44 (d, J = 3.0)	107.6
4a		149.3	8a		119.7
4b		149.6	8b		108.1
C=O		182.1	OCH_3	3.84 (s)	56.7
1-OH	12.71 (s)		7-OH	10.04 (s)	

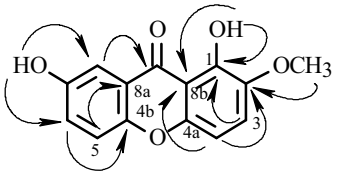

Fig. 1. Structure and important HMBC correlation of **1** (H → C).

EXPERIMENTAL

Melting point were determined on an XRC-1 apparatus and uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. IR spectra were taken as KBr pellets on a BIO-RAD FTS-135 spectrometer. MS and HRMS were measured with a VG AUTO.SPCE-3000 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer in DMSO at 26°C.

Column chromatography was performed either on silica gel (200–300 mesh, Qingdao Marine Chemical Inc, China) or on silica gel H (60 μ; Qingdao Marine Chemical Inc, China). Spots of TLC were detected by spraying with 5% H_2SO_4 followed by heating.

Compound 1 [1,7-dihydroxy-2-methoxyxanthone], yellow needles; mp 241–242°C, ^{1}H and ^{13}C NMR data are given in Table 1. IR (KBr, ν_{max}, cm^{-1}): 3451, 1650, 1620, 1576, 1499, 1465, 1380, 1297, 1174, 1047. HR-EIMS *m/z*: 258.05280 calcd for $C_{14}H_{10}O_5$ 258.05282, EI-MS (*m/z*): 258 $[M]^+$, 243 [M-15].

Compound 2 [1,7-dihydroxyxanthone], yellow needles; IR (KBr, ν_{max}, cm^{-1}): 3304, 1640, 1600, 1580, 1480, 1465. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 12.73 (1H, s, 1-OH), 6.78 (1H, dd, J = 8.1, 0.8, H-2), 7.71, (1H, t, J = 8.3, H-3), 7.02 (1H, dd, J = 8.3, 0.8, H-4), 7.54 (1H, d, J = 9.1, H-5), 7.44 (1H, dd, J = 9.0, 3.0, H-6), 7.62 (1H, d, J = 3.0, H-8). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 181.7 (C-9), 161.0 (C-1), 155.9 (C-3), 154.2 (C-4a), 149.4 (C-4b), 137.3 (C-3), 125.7 (C-6), 120.5 (C-8a), 119.5 (C-5), 109.7 (C-2), 108.0 (C-4), 107.9 (C-8), 107.2 (C-8b) [2].

Compound 3 [24(*R*)-stigmast-7,22 (*E*)-dien-3α-ol], $C_{29}H_{48}O$, amorph., mp 150–152°C, [α] +15° (*c* 0.4, $CHCl_3$), ^{1}H NMR (400 MHz, C_5D_5N, δ, ppm, J/Hz): 0.54 (3H, s, Me-18), 0.78 (3H, d, J = 7.0, Me-26), 0.81 (3H, t, J = 7.2, Me-29), 0.85 (3H, d, J = 6.5, Me-27), 1.03 (3H, d, J = 6.5, Me-21), 3.35 (1H, m, H-3), 5.18 (1H, m, H-7), 5.21 (1H, dd, J = 16.0, 7.0, H-23), 5.32 (1H, dd, J = 16.0, 7.0, H-22). ^{13}C NMR (100 MHz, C_5D_5N, δ, ppm): 139.6 (C-8), 138.0 (C-22), 129.6 (C-23), 117.2 (C-7), 70.3 (C-3), 55.8 (C-17), 55.6 (C-14), 51.3 (C-24), 49.0 (C-9), 43.1 (C-13), 40.4 (C-5), 40.2 (C-20), 39.6 (C-12), 37.0 (C-1), 34.4 (C-10), 33.9 (C-4), 31.8 (C-25), 29.4 (C-6), 28.4 (C-16), 27.6 (C-2), 25.5 (C-28), 23.1 (C-15), 21.0 (C-21), 19.2 (C-26), 12.5 (C-19), 12.6 (C-29), 12.0 (C-18) [3].

Compound 4 [1,7-dimethoxyxanthone], $C_{15}H_{12}O_4$, yellow needles; mp 152–154°C, ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.39 (1H, dd, J = 7.1, 2.0, H-2), 6.05 (1H, br.s, H-3), 7.36 (1H, dd, J = 7.1, 2.0, H-4), 7.21 (1H, d, J = 9.2, H-5), 7.29 (1H, dd, J = 9.1, 3.0, H-6), 7.16 (1H, d, J = 3.1, H-8) [4].

Biological Assay. Compounds **1–4** were tested for anti-HIV-1 activity following [5], and compounds **1–3** showed anti-HIV-1 activity. The EC_{50} value were 0.79, 1.00, and 3.48 μg/mL, respectively. The test for anti-HIV-1 activity was carried out by the Laboratory of Virus and Pharmacology in Beijing University of Technology, China.

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