CHEM. RES. CHINESE U. 2006, 22(3), 400—402

New Xanthones from *Polygala crotalarioides*

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Received May 18, 2005

Keywords *Polygala crotalarioides*; Polygalaceae; Xanthones
Article ID 1005-9040(2006)-03-400-03

Introduction

Xanthones are secondary metabolites commonly occurring in a few higher plant families, fungi and lichen. Their high taxonomic value in such families and their pharmacological properties, including *in vitro* cytotoxicity, *in vivo* antitumour activity, antifungal, antibacterial, antiinflammatory properties[1] and aldose reductase inhibitory activity[2] have provoked great interest. The discovery of the antidiabetic activity of some axnthones' from Swertiaceae has prompted us to undertake a more broadly search for novel xanthones from plants of Polygalaceae[3]. The phytochemical investigation has not been performed on this plant up to now. Herein we report the isolation and structure elucidation of two new xanthones (compounds **1** and **2**) and three known xanthones (compound **3**, **4** and **5**).

Experimental

1 General Experimental Procedures

The melting points were measured on a Kofler block and uncorrected. The UV spectra were recorded in MeOH on a UV-2100 spectrophotometer. The NMR spectra were obtained on a Brucker AM-400 MHz spectrometer. The general ^{1}H NMR data were determined at 400 MHz, and the ^{13}C NMR data were measured at 100.6 MHz. The FAB-MS and EI-MS spectra were recorded with a ZAB-HS mass spectrometer and a VG Autospec-3000 spectrometer. Silica gel (200—300 mesh and 300—400 mesh) and D-101 resin were used for column chromatography.

2 Plant Material

The roots of *Polygala crotalarioides* Buch. Ham. ex. DC. were collected in Linchang, Yunnan Province, China, in August 1999. The botanical identification was made by CHENG Shu-kun, professor of Kunming Institute of Botany, Chinese Academy of Sciences, where a voucher specimen was deposited.

3 Extraction and Isolation

The air-dried root sample of *Polygala crotalarioides* (2.8 kg) was powdered and extracted four times with 80% ethanol (in volume fraction) at boiling. The extract was evaporated ($\leqslant$55 ℃) to dryness under reduced pressure and the residue was dissolved in water (4000 mL). The aqueous solution was extracted with ethyl acetate and *n*-butanol to give the ethyl acetate fraction (62.0 g) and the *n*-butanol fraction (473.0 g), respectively. The ethyl acetate residue (31.0 g) was chromatographed on a silica gel column eluted with $CHCl_3$-MeOH with a volume ratio gradient from 100:1 to 25:1 to give fractions A—F.

Fraction B (2.5 g) was chromatographed on a silica gel column eluted with $CHCl_3$-MeOH (50:1—10:1, volume ratio) and petroleum ether (60—90 ℃)-acetone (15:1—5:1, volume ratio) repeatedly to give compounds **1** (150 mg) and **2** (87 mg). Fraction C (5.6 g) was subjected to a silica gel column eluted with $CHCl_3$-MeOH (30:1—10:1) and petroleum ether (60—90 ℃)-acetone (10:1—3:1) to give compounds **3** (115 mg), **4** (50 mg) and **5** (350 mg).

Results and Discussion

1 Identification

Compound **1**, obtained as yellow needles, shows a molecular ion peak at *m/z* 288 $[M]^+$ in the EI-MS spectrum. The ^{13}C NMR data and DEPT spectral data of compound **1** are indicative of a pentasubstituted xanthone, having one methylenedioxy moiety (δ 103.4, t, —O—CH_2—O—) and three hydroxyl groups; its mo-

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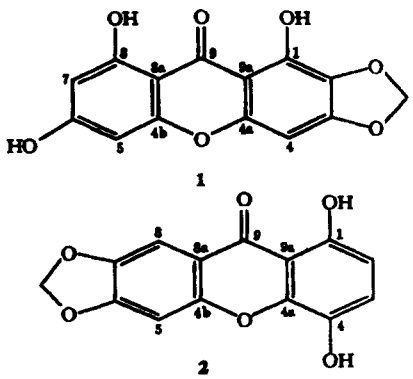
lecular formula $C_{14}H_8O_7$ can be derived from the HREI-MS spectrum of compound **1** (288.0263, calc. 288.0271). The IR and UV spectra also show the characteristic absorption of xanthone. The carbonyl carbon signal at δ 184.5 in the ^{13}C NMR spectrum of compound **1** indicates a double chelated carbonyl structure, that is, two hydroxyl groups are attached to positions C1 and C8[4] of compound **1** (Scheme 1). This result accords with the absence of proton signals in low field in the ^1H NMR spectra. The three singlet peaks of aromatic protons (sometimes *meta* coupling also shows singlet peak) show only *meta* substitution, which corresponds to the presence of 6-substituted hydroxyl. The oxygen atoms at positions 1, 2, 3, rather than 1, 2, 4 or 1, 3, 4, of another aromatic ring can be deduced by the low value (δ 131.2) for C2 in the ^{13}C NMR spectrum[5]. Therefore, compound **1** can be identified as 1,6,8-trihydroxy-2,3-methylenedioxy-xanthone, which is a new natural product.



Scheme 1 Structures of compounds 1 and 2.

Compound **2** is amorphous yellow powder, the EI-MS {[M]$^+$ at *m/z* 272} and ^{13}C NMR spectra including DEPT spectral data of compound **2** are indicative of a tetrasubstituted xanthone with a methylenedioxy moiety (δ103.1, t, —O—CH_2—O—) and two hydroxyl groups; the HREI-MS spectrum of compound **2** (272.0323, calc. 272.0321) gives its molecular formula $C_{14}H_8O_6$. The IR and UV spectra also shows the characteristic absorption of xanthone. The signal at δ 181.8 indicates a free hydroxyl group at C1 or C8, which is chelated with the carbonyl group[4] (Scheme 1). The down field singlet at δ 7.97 of H8 in the ^1H NMR spectrum suggests that the positions of *ortho* and *meta* of C8 are substituted, and the di-*ortho*-substitutuent (C6 and C7) must be methylenedioxyl. The *ortho*-coupled AB system at δ 7.43 (1H, d, J = 8.4 Hz, H3) and δ 7.53 (1H, d, J = 8.4 Hz, H2) shows that another hydroxyl group is substituted at the C4 position. The absence of an NaOAc-induced shift in the UV spectrum also confirms the above inference[6]. Hence, the structure of compound **2** can be determined as 1,4-dihydroxy-6,7-methylenedioxy xanthone, which is also a new natural product.

2 Spectral Data

Compound **1**: 1,6,8-trihydroxy-2,3-methylenedioxy xanthone, $C_{14}H_8O_7$, yellow needles, m. p. 280—282 ℃; EI-MS, *m/z*: 288 [M]$^+$ (84), 272, 259, 230; HR-MS, *m/z*: 288.0263, (calc. 288.0271); IR (KBr), $\tilde{\nu}_{max}$/cm^{-1}: 3471, 2924, 1638, 1618, 1500, 1480, 1274 1177; UV (MeOH), λ_{max}/nm: 209.0, 239.5, 259.5, 324.0, 345.0; ^1H NMR (400 MHz, C_5D_5N): 86.12 (2H, s, —O—CH_2—O—), 6.59 (1H, s, H4), 6.62 (1H, s, H5), 6.68 (1H, s, H7); The ^{13}C NMR (100.6 MHz, C_5D_5N) data are shown in Table 1.

Table 1 ^{13}C NMR data for compounds 1 and 2

C	1	2
1	154.5 s	155.5 s
2	131.2 s	125.3 d
3	159.0 s	119.3 d
4	89.9 d	150.8 s
4a	153.8 s	143.4 s
4b	156.0 s	155.5 s
5	95.1 d	89.4 d
6	167.8 s	157.5 s
7	99.8 d	155.5 s
8	163.4 s	108.7 d
8a	104.8 s	121.0 s
9	184.5 s	181.8 s
9a	102.0 s	105.5 s
OCH_2O	103.4 t	103.1 t

Compound **2**: 1,4-dihydroxy-6,7-methylnedioxy xanthone, $C_{14}H_8O_6$, amorphous yellow powder, m. p. 234—236 ℃, EI-MS, *m/z*: 272 [M]$^+$ (80), 253, 215, 193; HR-MS, *m/z*: 272.0323, (calc. 272.0321); IR (KBr), $\tilde{\nu}_{max}$/cm^{-1}: 3386, 2922, 1677, 1490, 1287, 1228; UV (MeOH), λ_{max}/nm: 204.0, 250.0, 259.5, 326.0; + NaOAc: 203.5, 248.5, 254.0, 299.5 329.0. ^1H NMR (400 MHz, C_5D_5N), δ: 7.97 (1H, s, H8), 7.53 (1H, d, J = 8.4 Hz, H2), 7.43 (1H, d, J = 8.4 Hz, H3), 6.65 (1H, s, H5), 6.11 (2H, s, —O—CH_2—O—); ^{13}C NMR (100.6 MHz, C_5D_5N) data are listed in Table 1.

Compound **3**: 1,7-dihydroxy-2,3-dimethoxy xanthone, $C_{15}H_{12}O_6$, amorphous yellow powder; m. p. 245—246 ℃, EI-MS, *m/z*: 288 [M]$^+$ (100), 273 [M − 15] (100), 259 [M − 29] (15), 245 [M − 15 − 28] (65), 202 (23), 174 (20), 136 (18); UV

(MeOH), λ_{max}/nm: 241.0, 261.5 and 308.0. ^{1}H NMR(400 MHz, C_5D_5N): δ: 3.85(3H, s, 3-OCH_3), 3.97(3H, s, 2-OCH_3), 6.12(1H, s, 7-OH), 6.58(1H, s, H4), 7.45(1H, d, J=9.1 Hz, H5), 7.55(1H, dd, J=9.1 and 2.9 Hz, H6), 8.01(1H, d, J=2.9 Hz, H8)[6]. ^{13}C NMR(100.6 MHz, C_5D_5N): δ: 153.9(s, C1), 132.2(s, C2), 160.6(s, C3), 91.3(d, C4), 119.4(d, C5), 125.5(d, C6), 155.6(s, C7), 109.1(d, C8), 181.6(s, C9), 154.7(s, C4a), 150.2(s, C4b), 121.4(s, C8a), 104.4(s, C9a)[5].

Compound 4: 1,3,6-trihydroxyly-2,7-dimethoxy xanthone, $C_{15}H_{12}O_7$, amorphous yellow powder; m.p. 231—233 ℃, EI-MS, m/z: 304 [M]$^+$(100), 289 [M-15](97), 275 [M-29](20), 261 [M-15-28](98), 246 [M-15-15-28](60), 218(25). UV (MeOH), λ_{max}/nm: 206.0, 241.0, 254.5, 323.0, 356.0; + NaOAc: 240.0, 254.0, 323.0, 368.0. ^{1}H NMR(400 MHz, C_5D_5N): δ: 3.75(3H, s, 7-OMe), 3.86(3H, s, 2-OMe) 6.77(1H, s, H4), 7.16(1H, s, H5), 7.81(1H, s, H8), 13.2 (1H, s, 1-OH); ^{13}C NMR(100.6 MHz, C_5D_5N), δ: 153.8(s, C1), 131.8(s, C2), 155.3(s, C3), 94.9 (d, C4), 103.9(d, C5), 153.4(s, C6), 146.9(s, C7), 105.4(d, C8), 180.5(s, C9), 159.5(s, C4a), 156.3(s, C4b), 112.4(s, C8a), 103.2(s, C9a)[7].

Compound 5: 6,8-dihydroxy-1,2,3-trimethoxy xanthone, $C_{16}H_{14}O_7$, amorphous yellow powder; m.p. 164—166 ℃, EI-MS, m/z: 318 [M]$^+$(75), 303 [M-15](100), 288 [M-15-15](25), 275 [M-15-28](45), 257(20), 245(25), 204(35), 167(33). UV, λ_{max}/nm: 209.0, 240.0, 313.0, 352.0; + NaOAc: 208.0, 240.0, 357.5. ^{1}H NMR (400 MHz, C_5D_5N), δ: 3.84(3H, s, 3-OMe), 4.00 (6H, s, 1, 2, —OMe), 6.26(1H, d, J=2.0 Hz, H5), 6.29(1H, d, J=2.0 Hz, H7), 6.70(1H, s, H4), 13.4(1H, s, 8-OH); ^{13}C NMR(100.6 MHz, C_5D_5N), δ: 152.4(s, C1), 137.4(s, C2), 154.4 (s, C3), 97.0(d, C4), 92.1(d, C5), 166.0(s, C6), 98.9(d, C7), 163.7(s, C8), 180.2(s, C9), 155.4(s, C4a), 156.9(s, C4b), 109.0(s, C8a), 103.6(s, C9a)[8].

References

[1] Hostettmann K., Hostettmann M., *Methods in Plant Bio-chemistry, Vol. 1*, Academic Press, London, 1989, 493

[2] Mao S. L., Liao S. X., Wu J. H., *Acta Pharmaceutica Sinica*, 1997, *32*, 360

[3] Basnet P., *Plant Med.*, 1994, *60*, 507

[4] Sluis W. G., Labadie R. P., *Phytochemistry*, 1985, *24*, 2601

[5] Pinheiro T. R., Filho V. C., Santos A. R. S., *et al.*, *Phytochemistry*, 1998, *48*, 725

[6] Mequita Lins A. A., Barros Correa De D., Gottlieb O. R., *et al.*, *Anal. Chim. Acta*, 1968, *42*, 311

[7] Ikeya Y., Sugama K., Okada M., *et al.*, *Phytochemisty*, 1991, *30*, 2061

[8] Fujita T., Liu D. Y., Ueda S., *et al.*, *Phytochemistry*, 1992, *31*, 3997