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ISOLATION OF A NEW XANTHONE AND 2-HYDROXYDIMETHYLTEREPHTHALATE FROM *SWERTIA PETIOLATA*

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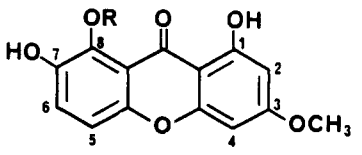
Swertia petiolata D. Don (Gentianaceae), a subspecies of an important Ayurvedic herb, *Swertia chirata,* is found in the alpine pastures of Kumaun Himalaya. This plant is not grazed by sheep but is known for its laxative and antimalarial properties in the folklore of the region. A previous chemical study (1) resulted in the isolation of 1,7-dihydroxy-3,8-dimethoxyxanthone [**1**], 8-*O*-glucosyl-1,7-dihydroxy-3-methoxyxanthone [**2**], ursolic acid, and β-sitosterol. In this note we describe the isolation of a new xanthone, 1,3-dihydroxy-5,8-dimethoxyxanthone [**3**], and 2-hydroxydimethylterephthalate [**6**] from an 80% MeOH extract of the same plant.

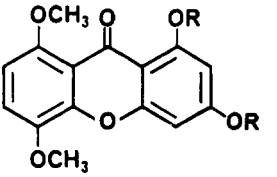
Compound **3**, mp 192.5–194.5°, molecular formula $C_{15}H_{12}O_6$ (ms), showed characteristic uv and ir absorptions (see Experimental) of a xanthone. That the xanthone nucleus was tetrasubstituted was established from the analysis of the ^{1}H-nmr spectrum that showed a pair of ortho (δ 7.38 and 7.14, each d, J=9.2 Hz) and of meta (δ 6.36 and 6.32, each d, J=1.5 Hz) coupled protons. Accordingly, the spectrum showed two hydroxyl (δ 13.12 and 5.97) and two methoxyl (δ 4.04 and 3.90) signals. That the two hydroxyl groups were on the same ring and oriented meta to each other was apparent from the ^{1}H-nmr spectrum of the derived diacetate **4** that showed downfield shifts for the meta coupled protons (δ 6.74 and 6.55) when compared with those of **3** (δ 6.36 and 6.32); the ortho coupled protons remained virtually unchanged. The presence of a chelated hydroxyl (δ 13.12) and a downfield methoxyl (δ 4.04) indicated that the peri-positions 1 and 8 are substituted, a fact consistent with the absence of proton signals around 8 ppm. On the basis of the above evidence the structure of the unknown was narrowed to either 1,3-dihydroxy-5,8-dimethoxyxanthone [**3**] or its isomer swertinin [**5**], mp 217° (2–4). Swertinin [**5**] is excluded by the melting point of **3** (192.5–194.5°) and from the observation that both the methoxyl groups of **3** exhibited large C_6H_6-induced upfield shifts (5) (see Experimental). An authentic sample of swertinin was unavailable.

The structure of the second crystalline compound, mp 92–92.5°, $C_{10}H_{10}O_5$, was shown to be **6**, the dimethyl ester of 2-hydroxyterephthalic acid on the basis of its spectral data and formation of a monoacetate **7**, mp 74.5°.

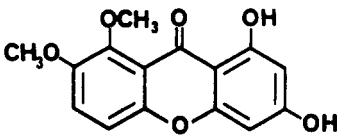
Compound **6** has been obtained previ-



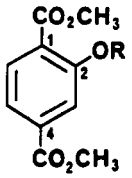
1 R=Me
2 R=glucosyl



3 R=H
4 R=Ac



5



6 R=H
7 R=Ac

ously by synthesis (6) but never to our knowledge as a natural product. We excluded the possibility that this substance is an artifact or an industrial contaminant by extracting the plant with cold EtOH instead of MeOH. The same 2-hydroxyterephthalic acid dimethyl ester [**6**] was isolated. Extraction of a fresh plant sample with hexane (distilled from glass) also furnished compound **6**. Its presence as a natural constituent of *S. petiolata* is, therefore, confirmed.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are corrected and were determined on a Thomas-Kofler hot stage apparatus equipped with a microscope and polarizer. Spectra were recorded on the following instruments: ir, Perkin-Elmer model 1420 spectrophotometer; ^{1}H nmr, JEOL FT model FX-90 Q; ms, Finnegan Quadrupole 4023 spectrometer.

PLANT MATERIAL.—The aerial parts of *S. petiolata* were collected in July 1985, at an altitude of 14,500 ft from the Pindari glaciers of Kumaun Himalaya, Uttar Pradesh, India; the plant was identified by Dr. G.S. Rawat, Department of Botany, Kumaun University, Nainital. A voucher specimen was deposited in the above department.

EXTRACTION AND ISOLATION OF CONSTITUENTS.—The aerial parts of shade-dried *S. petiolata* (500 g) were pulverized and extracted with 80% MeOH (2 liters) for 48 h. The extract was concentrated in vacuo and then was partitioned between 1:1 $CHCl_3$ and H_2O (400 ml). The $CHCl_3$ layer was separated and concentrated, and the residue was extracted with petroleum ether (60–80°, 200 ml). The petroleum ether concentrate was chromatographed on a column of Si gel G (Glaxo, 60–120 mesh); elution with petroleum ether-C_6H_6, 99:1 and 19:1, afforded compounds **6** (200 mg, mp 82–83° from MeOH) and **3** (60 mg, mp 180–181° from MeOH), respectively.

To exclude the possibility of compound **6** being an artifact, another plant sample was extracted with cold EtOH. This extract upon workup also furnished compound **6**.

The aerial parts of *S. petiolata* (2.6 g) were percolated with glass-distilled hexane at room temperature for 24 h. The extract was concentrated in vacuo, and the resulting gum (48 mg) was purified by preparative tlc (silica, 1 mm, C_6H_6-EtOAc, 19:1) to afford 4 mg of crude 2-hydroxydimethylterephthalate [**6**]. The ^{1}H-nmr spectrum of this material agreed with that of a sample of **6** isolated by MeOH extraction. Recrystallization of the isolate from EtOAc-hexane gave **6**, mp 91–92°.

PROPERTIES OF 1,3-DIHYDROXY-5,8-DIMETHOXYXANTHONE [**3**].—Recrystallization of crude **3** from EtOAc/hexane gave mp 192.5–194.5°; eims *m/z* 288 ($C_{15}H_{12}O_6$); uv (MeOH) 220, 224, 305, 376 nm; ir (KBr) 3360, 2950, 2860, 1650, 1610, 1470, 1435, 1320, 1300, 1210, 1160, 1100, 1060, 825 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 13.12 (1H, s, exchanged with D_2O, OH at C-1), 7.38 and 7.14 (each 1H, d, J=9.2 Hz, H-6 and H-7), 6.36 and 6.32 (each 1H, d, J=1.5 Hz, H-2 and H-4), 5.97 (1H, br, exchanged with D_2O, OH at C-3), 4.04 and 3.90 (each 3H, s, OMe); ^{1}H nmr (C_6H_6) δ 7.01 and 6.67 (each 1H, d, J=9.2 Hz, H-6 and H-7), 6.38 and 6.20 (each 1H, d, J=2.2 Hz, H-2 and H-4), 3.59 and 3.11 (each 3H, s, OMe).

PREPARATION OF 1,3-DIACETOXY-5,8-DIMETHOXYXANTHONE [**4**].—A mixture of **3** (4 mg), 0.5 ml of pyridine, and 0.5 ml of Ac_2O was stirred at room temperature overnight. Excess reagents were evaporated in vacuo to yield **4** (5 mg). ^{1}H nmr ($CDCl_3$) δ 7.34 and 7.14 (each 1H, d, J=9.2 Hz), 6.74 and 6.55 (each 1H, d, J=2.2 Hz), 3.90 (6H, s, OMe), 2.47 and 2.35 (each 3H, Ac).

PROPERTIES OF 2-HYDROXYDIMETHYLTEREPHTHALATE [**6**].—Recrystallization of crude **6** from EtOAc/hexane gave material with mp 92–92.5° [lit. (6) 92–93°]; ir (KBr) 3400, 1750, 1675, 1620 cm^{-1}; eims *m/z* 210 ($C_{10}H_{10}O_5$); ^{1}H nmr δ 10.74 (1H, exchanged with D_2O, OH at C-2), 7.89 (1H, d, J=7.9 Hz, H-6), 7.62 (1H, d, J=1.3 Hz, H-3), 7.50 (1H, dd, J=7.9, 1.3 Hz, H-5), 3.97 and 3.92 (each 3H, s, CO_2Me).

PREPARATION OF 2-ACETOXYDIMETHYLTEREPHTHALATE [7].—A mixture of 19 mg of **6**, 0.5 ml of pyridine, and 0.5 ml of Ac_2O was stirred at room temperature overnight. Usual work-up followed by crystallization from EtOAc/hexane gave 14 mg of **7**, mp 74.5–75° [lit. (6) 76°]; ir (Nujol) 1755, 1730, 1710 cm^{-1}; ^1H nmr δ 8.08 (1H, d, J=7.9, H-6), 7.93 (1H, dd, J=7.9, 1.8 Hz, H-5), 7.77 (1H, d, J=1.8 Hz, H-3), 3.94 and 3.90 (each 3H, s, CO_2Me) and 2.36 (3H, s, OAc).

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