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THIAZINEDIONE FROM *XANTHIUM STRUMARIUM*

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Key Word Index—*Xanthium strumarium*; Compositae; fruit; Xanthii Fructus; phenolic; thiazinedione; xanthiazone; 7-hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzo[1,4]thiazine-3,5-dione.

Abstract—From the aqueous acetone extract of burweed fruit, a new thiazinedione and four known phenolic compounds were isolated. The phenolics were identified as caffeic acid, potassium 3-*O*-caffeoyl quinate, 1,5-di-*O*-caffeoylquinic acid and 1,3,5-tri-*O*-caffeoylquinic acid. Based on 2D-NMR experiments and X-ray analysis, the thiazinedione was determined to be 7-hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzo[1,4]thiazine-3,5-dione and named xanthiazone. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Xanthii Fructus refers to the fruit of *Xanthium strumarium* (Compositae) commonly known as burweed or cocklebur. In traditional Chinese medicine, it is used for sinusitis, headache due to rheumatism and skin pruritus [1, 2]. In previous studies on *X. strumarium*, carboxyatractyloside, xanthanol, isoxanthanol, hydroquinone, alkaloids [3, 4], and caffeoylquinic acids [5] were identified. Our chemical investigation of Xanthii Fructus has resulted in the isolation of a novel compound **1**, along with four phenolics (**2**–**5**).

RESULTS AND DISCUSSION

By using a combination of high-porous polystyrene, polydextran, silica gel and reverse-phase column chromatography in various solvent systems, five compounds were isolated from the aq. acetone extract of Xanthii Fructus. The following four known compounds were identified: caffeic acid (**2**), potassium 3-*O*-caffeoyl quinate (**3**), 1,5-di-*O*-caffeoylquinic acid (**4**) [6, 7] and 1,3,5-tri-*O*-caffeoylquinic acid (**5**) [5], based on ^{1}H, DEPT, ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY, COLOC experiments, and X-ray analysis.

Compound **1** is a colorless cubic crystal (MeOH), mp 159–161° and the positive FABMS afforded an $[M+H]^+$ peak at m/z 240. The ^{1}H NMR spectrum of **1** exhibited singlet signals at δ 6.38 (1H), 4.32 (2H), 3.47 (2H) and 1.36 (6H) together with a D_2O exchangeable signal at δ 9.34. DEPT experiments with **1** showed the presence of two methylenic carbons (δ 28.7 and 59.4), a trisubstituted olefinic carbon (δ 120.1), six quarternary carbons (δ 42.0, 130.0, 141.1, 162.6, 170.3 and 175.3) and methyl carbons at δ 26.9. In addition, the ^{1}H-^{13}C COSY spectrum examination indicated a correlation between the signals at δ 1.36 (6H) and δ 26.9 suggesting that the compound has two methyl groups. Therefore, **1** contained an skeleton with eleven carbons.

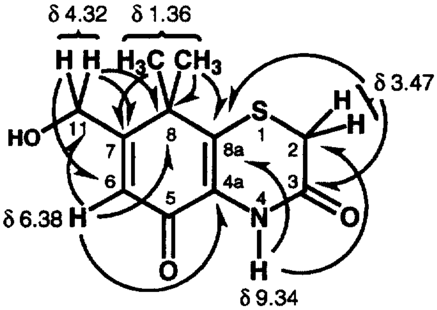

Fig. 1. COLOC correlation of compound **1**.

The COLOC spectrum showed correlations between H-Me$_2$ (δ 1.36)/C-7 (δ 170.3), C-8 (δ 42.0) and C-8a (δ 141.1); H-2 (δ 3.47)/C-3 (δ 162.6) and C-8a (δ 141.1); H-11 (δ 4.32)/C-6 (δ 120.1), C-7 (δ 170.3) and C-8 (δ 42.0); H-6 (δ 6.38)/C-4a (δ 130.0), C-8 (δ 42.0) and C-11 (δ 59.4); H-N (δ 9.34)/C-2 (δ 28.7) and C-8a (δ 141.1). These correlations showed that the hydroxymethyl group was linked to C-7, the dimethyl group was substituted at C-8 while the methylene group neighbored upon the carbonyl C-3 (Fig. 1).

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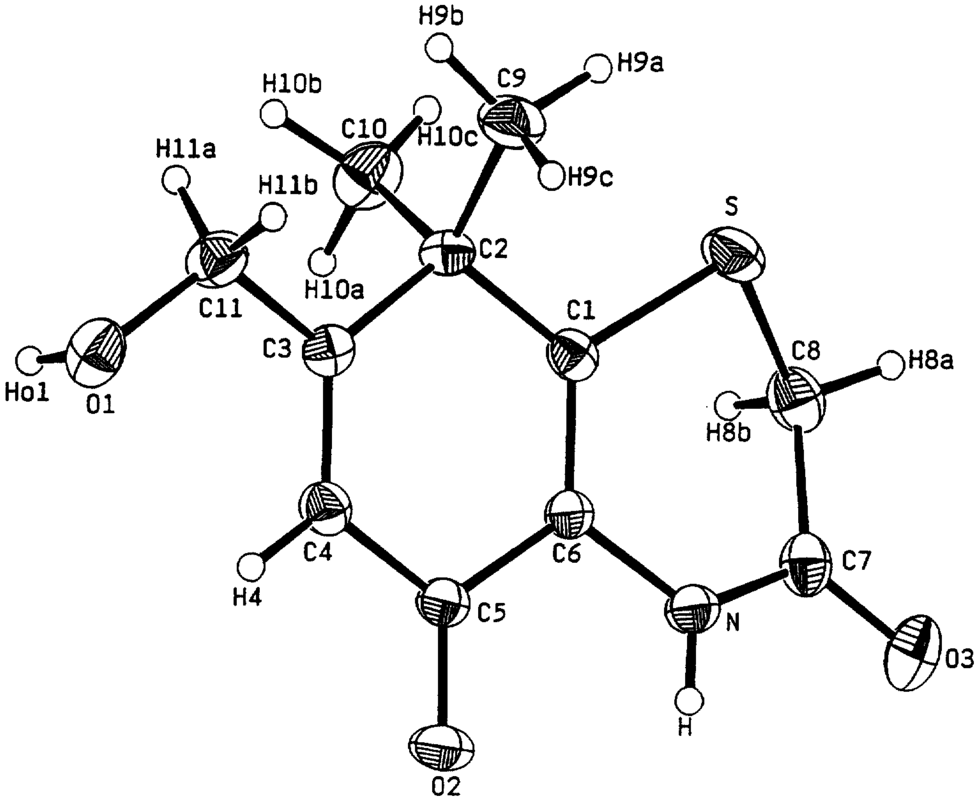


Fig. 2. An ORTEP diagram of compound **1**.

Results from an X-ray diffraction analysis of a single crystal of **1** confirmed the proposed structure and its stereochemistry. An ORTEP diagram of **1** is shown in Fig. 2. Based on these findings **1** was characterized as a 7-hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzo[1,4]thiazine-3,5-dione and named xanthiazone.

EXPERIMENTAL

General experimental procedures

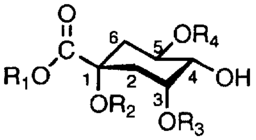
Mp: uncorr; ^{1}H and ^{13}C NMR: at 300 MHz and 75 MHz, respectively, TMS as int. standard; FABMS: Jeol JMS–HX 110; X-ray crystallography: CAD4 Kappa Axis single crystal XRD; TLC was performed on a precoated Kieselgel 60 F_{254} plates (Merk) and detection was achieved by spraying with 10% H_2SO_4 followed by heating (for thiazine) and $FeCl_3$ reagent (for phenolics). The Xanthii Fructus were purchased from Kang–Yuan Chinese Medicine Co. in Taipei, and were identified by Dr. Hsien-Chang Chang, Brion Research Institute of Taiwan.

Extraction and isolation

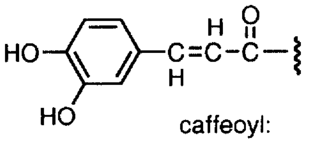
Commercial Xanthii Fructus (6 Kg) were chopped into small pieces and an extract × 3 was obtained using 70% aq. Me_2CO at room temp. The extract, after removal of the Me_2CO by evapn and filtration of the ppt, was fractionated with CC on a Diaion HP-20, eluted with H_2O–MeOH with increasing MeOH content to afford 3 fractions. Fr. 1 was subjected to a Cosmosil C-18 OPN column with 20% aq. MeOH and further purified by Sephadex LH-20 eluted with EtOH to give **3** (220 mg). The fr. 2 was chromatographed on Sephadex LH-20 with 60% aq. MeOH, and with acetone to afford **2** (260 mg) and **4** (1.8 g). Chromatography of the fr. 3 on Sephadex LH-20 (60% aq. MeOH) gave 2 frs (3–I and 3–II). Rechromatography of fr 3–I on MCI-gel CHP 20P with 50% aq. MeOH and on silica gel with CH_2Cl_2-MeOH (12:1→9:1) yielded **1** (407 mg). Purification of fr 3–II on Sephadex LH-20 with acetone resulted in **5** (200 mg).

Xanthiazone: 7-Hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzo[1,4]*thiazine-3,5-dione* (1)

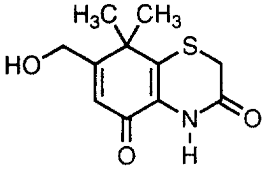
Colorless cubic crystals (MeOH), mp 159–161°; Positive-ion FAB MS *m/z*: 240 $[M + H]^+$; Found: C, 55.08; H, 5.29; N, 5.84. $C_{11}H_{13}O_3SN$ requires: C, 55.23; H, 5.44; N, 5.86%. ^{1}H NMR (DMSO): δ 9.34 (1H, *s*, NH), 6.38 (1H, *s*, H-6), 4.32 (2H, *s*, H-11), 3.47 (2H, *s*, H-2), 1.36 (6H, *s*, Me × 2). ^{13}C NMR (DMSO): δ 175.3 (-CO-), 170.3 (C-7), 162.6 (-CO-), 141.1 (C-8a),



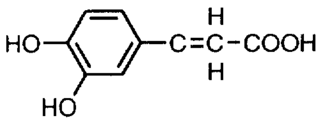
	R_1	R_2	R_3	R_4
5	H	caffeoyl	caffeoyl	caffeoyl
4	H	caffeoyl	H	caffeoyl
3	K	H	caffeoyl	H



caffeoyl:



1



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130.0 (C-4a), 120.1 (C-6), 59.4 (C-11), 42.0 (C-8), 28.7 (C-2), 26.9 (Me × 2).

X-ray crystallography of **1**

The space group was determined to be the monoclinic C 2/c. Crystal size: 0.1 × 0.40 × 0.40 mm. Unit cell dimensions: $a = 15.413$ (6), $b = 12.112$ (4), $c = 15.117$ (5) Å. Data were collected at 298.0 K and a total of 1997 reflections measured. The other crystallographic data, bond distances and angles have been deposited with the Cambridge Crystallographic Center.

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REFERENCES

1. Chiu, N.-Y. and Chang, K.-H., in *The Illustrated Medicinal Plants of Taiwan*, Vol. 1. Southern Materials Center, Inc., Taipei, 1987, p. 233.
2. Huang, K.-C., in *The Pharmacology of Chinese Herbs*. CRC Press, Boca Raton, 1993, p. 160.
3. Hsu, H.-Y., Chen, Y.-P. and Hong, M., in *Chemistry of Chinese Herb Drugs*, Vol. 2. Brion Research Institute, Taipei, 1979, p. 859.
4. Chang, H.-M. and But, P. P.-H., in *Pharmacology and Applications of Chinese Materia Medica*, Vol. 1. World Scientific, Singapore, 1986, p. 589.
5. Ageta, I., Goto, S., Hatano, T., Nishibe, S. and Okuda, T., *Phytochemistry*, 1993, **33**, 508.
6. Morishita, H., Iwahashi, H. and Osaka, N., Kido, R., *J. Chromatogr.*, 1984, **315**, 253.
7. Merfort, I., *Phytochemistry*, 1992, **31**, 2111.