6-O-Benzoylgomisin O, a New Lignan from the Fruits of Schizandra chinensis

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6-*O*-BENZOYLGOMISIN O, A NEW LIGNAN FROM THE FRUITS OF *SCHIZANDRA CHINENSIS*

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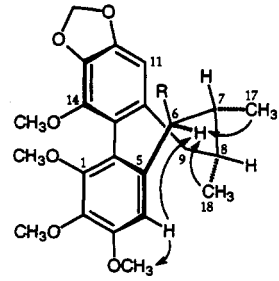
ABSTRACT.—A new dibenzocyclo-octadiene lignan, 6-*O*-benzoylgomisin O [**1**] was isolated from the fruits of *Schizandra chinensis* together with 5-hydroxymethyl-2-furaldehyde, protocatechuic acid, and sorbic acid. The structure of **1** was determined by spectral analysis.

The fruits of *Schizandra chinensis* Baill. (Schizandraceae) have been used as a tonic and an anti-aging drug in traditional Chinese medicine (1). Sesquiterpenoids (2,3) and lignans (4–12) have been isolated from this drug. Our previous studies have demonstrated that gomisin A, gomisin B, and schizandrin isolated from this drug exhibited Ca^{++}-antagonistic activity on the guinea pig taenia coli (13). In our continuing research on this drug, a new lignan, 6-*O*-benzoylgomisin O [**1**], and three known compounds, 5-hydroxymethyl-2-furaldehyde (14), protocatechuic acid, and sorbic acid, were isolated from *S. chinensis*. This paper describes the isolation and structural elucidation of the new lignan **1**.

The ir spectrum of **1** indicated that it is a dibenzocyclo-octadiene lignan (4–12) possessing a benzoyloxy group (1715 cm^{-1}). The cd spectrum indicated that the compound has an *S*-biphenyl configuration (5, 12, 15). The ^{1}H-nmr spectrum showed the presence of two secondary methyls (δ 0.83 and 0.99, doublet for each), a benzylic methylene (δ 2.19–2.28), and a benzylic methine (δ 5.92) with a benzoyloxy group. A methylenedioxy moiety (δ 5.89), two aromatic protons (δ 6.47 and 6.74) and four methoxyls (δ 3.51, 3.55, 3.86, and 3.89) were also associated wth the aromatic rings. The ^{1}H-nmr spectral data of **1** were very similar to those published for gomisin O [**2**] (6) except for the presence of five aromatic protons (δ 7.27–7.62) and a benzylic methine proton at δ 5.92 (d, J=7.5 Hz), which indicated that the benzoyloxy group is linked at C-6 in this compound.

When the ^{13}C-nmr spectrum of **1** was compared with those of **2** and epigomisin O (7), which possess a boat conformation and twist-boat-chair conformation of the cyclo-octadiene ring respectively, the data of **1** exhibited a closer similarity to those of **2**, especially at C-17 and C-18.

Finally, the structure of **1**, including the conformation of the cyclo-octadiene ring, was confirmed by nOe measurements as shown in Figure 1. Irradiation of H-4 at δ 6.74 enhanced the signals at δ 3.89 (OCH_3-3) and 5.92 (H-6) by 6% and 8%, respectively. Irradiation of H-11 at δ 6.47 did not affect the signals of any methoxyl group. Irradiation of the methyl groups at δ 0.99 and 0.83 en-



1 R=$OCOC_6H_5$
2 R=OH

FIGURE 1. NOe Observations for **1**.

hanced the signal at δ 5.92 (H-6) by 2% and 4%, respectively.

On the basis of the above results, the structure of 6-*O*-benzoylgomisin O was assigned as **1**, with a boat conformation of the cyclo-octadiene ring.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The ir spectra were recorded on a Biorad Ft-ir spectrometer. The cd spectrum was recorded using a Jasco-710 CD polarimeter. ^{1}H- and ^{13}C-nmr spectra were taken on a Bruker AM-300WB (300 MHz) Ft-nmr instrument. Hreims and eims were obtained on JEOL SX-102A and JEOL JMS-HX100 spectrometers, respectively. Protocatechuic acid and sorbic acid were purchased from Sigma Chemical Company.

PLANT MATERIAL.—The fruits of *Schizandra chinensis* were purchased from a market in Taipei, under the direction of Mr. M.T. Kao, National Research Institute of Chinese Medicine, where voucher specimens are maintained.

EXTRACTION AND ISOLATION.—The ground fruit materials (3 kg) were extracted with 95% EtOH and the extract was concentrated *in vacuo* and fractionated into EtOAc- and MeOH-soluble fractions. The EtOAc-soluble fraction was chromatographed on a Si gel column. The following fractions were eluted in order with the indicated solvent system: fraction 1 [*n*-hexane-EtOAc (30:1)], fraction 2 [*n*-hexane-EtOAc (20:1)], fraction 3 [*n*-hexane-EtOAc (10:1)], fraction 4 [*n*-hexane-EtOAc (2:1)], and fraction 5 (Me_2CO). Repeated chromatography of fraction 4, first by cc [Si gel, *n*-hexane-Me_2CO (8:1)] and then by hplc [Cosmosil 5C-18Ar, 8×250 mm; CH_3CN-H_2O (7:3), 2 ml/min], gave **1** (10 mg). Fraction 5 was further chromatographed on a Si gel column with $CHCl_3$-Me_2CO (4:1) to yield 5-hydroxymethyl-2-furaldehyde, protocatechuic acid, and sorbic acid.

6-*O*-*Benzoylgomisin O* [**1**].—Amorphous powder; $[\alpha]^{25}D$ −41.39° (c=1.06, $CHCl_3$); cd Δε (MeOH) (nm) −2.74 (203.1), +2.47 (222.5), −1.24 (242.0), −0.56 (250.2), −0.31 (255.8), +0.51 (270.0); ir ν max (KBr) 1715, 1699, 1614, 1590, 1274, 1110 cm^{-1}; eims *m/z* 520 (M^+, 100), 398 (42), 105 (68), 77 (24); hreims *m/z* 520.2092 (calcd for $C_{30}H_{32}O_8$, 520.2097); ^{1}H nmr ($CDCl_3$) δ 0.83 (3H, d, J=6.9 Hz, 8-CH_3), 0.99 (3H, d, J=6.9 Hz, 7-CH_3), 2.02–2.15 (2H, m, H-7 and H-8), 2.19–2.28 (2H, m, H-9), 3.51 (3H, s, -OCH_3), 3.55 (3H, s, -OCH_3), 3.86 (3H, s, 2-OCH_3), 3.89 (3H, s, 3-OCH_3), 5.89 (2H, s, -OCH_2O-), 5.92 (1H, d, J=7.5 Hz, H-6), 6.47 (1H, s, H-11), 6.74 (1H, s, H-4), 7.27–7.62 (5H, m, Ph-CO-); ^{13}C nmr ($CDCl_3$) δ 14.2 (C-18), 19.2 (C-17), 36.5 (C-8), 36.8 (C-9), 37.5 (C-7), 55.9 (OCH_3), 59.0 (OCH_3), 60.5 (OCH_3), 60.8 (OCH_3), 81.5 (C-6), 100.6 (OCH_2O), 102.4 (C-11), 110.6 (C-4), 121.7 (C-15), 123.1 (C-16), 132.2 (C-13), 134.4 (C-10), 135.4 (C-5), 141.8 (C-14 and C-2), 148.7 (C-12), 151.7 (C-1), 152.0 (C-3), benzoyl moiety [127.9 (C-3′ and C-5′), 129.6 (C-2′ and C-6′), 130.3 (C-1′), 132.6 (C-4′), 165.4 (C=O)].

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LITERATURE CITED

1. H.Y. Hsu and W.G. Peacher, "Chinese Herb Medicine and Therapy." Oriental Healing Arts Institute, Los Angeles, p. 176 (1976).
2. Y. Ohta and H. Hirosa, *Tetrahedron Lett.*, 1251 (1968).
3. Y. Ohta and H. Hirosa, *Tetrahedron Lett.*, 2483 (1968).
4. H. Taguchi and Y. Ikeda, *Chem. Pharm. Bull.*, **23**, 3296 (1975).
5. Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.*, **27**, 1383 (1979).
6. Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.*, **27**, 2695 (1979).
7. Y. Ikeya, H. Taguchi, H. Sasaki, K. Nakajima, and I. Yosioka, *Chem. Pharm. Bull.*, **28**, 2414 (1980).
8. Y. Ikeya, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.*, **28**, 2422 (1980).
9. Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.*, **28**, 3357 (1980).
10. Y. Ikeya, H. Taguchi, I. Yosioka, Y. Iitaka, and H. Kobayashi, *Chem. Pharm. Bull.*, **27**, 1395 (1979).
11. Y. Ikeya, N. Ookawa, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.*, **30**, 3202 (1982).
12. Y. Ikeya, H. Taguchi, and I. Yosioka, *Chem. Pharm. Bull.*, **30**, 3207 (1982).
13. C.C. Chen, Y.L. Huang, S.M. Chen, H.T. Chen, Y.P. Chen, and H.Y. Hsu, *J. Taiwan Pharm. Assoc.*, **39**, 255 (1987).
14. S. Nishibe, S. Hisada, and I. Inagaki, *Chem. Pharm. Bull.*, **21**, 1155 (1973).
15. Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.*, **26**, 3257 (1978).

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