

129.6 (C-8), 133.1 (C-1'), 145.2 (C-8a), 145.5 (C-3'), 146.8 (C-4'), 152.5 (C-7 or C-5), 152.9 (C-5 or C-7), 158.7 (C-4), 162.8 (C-2); MS m/z (rel. int.) 330 $[M]^+$ (100), 302 $[M - CO]^+$ (13), 287 $[M - MeCO]^+$ (21), 259 $[M - MeCO - CO]^+$ (7); high resolution MS m/z (M^+): 330.0824 (calc. for $C_{17}H_{14}O_7$: 330.0739).

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GANSCHISANDRINE, A LIGNAN FROM *SCHISANDRA SPHENANTHERA*

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Key Word Index—*Schisandra sphenanthera*; Schisandraceae, lignan, ganschisandrine, 2S,5S-bis-(3,4-dimethoxyphenyl)-3R,4S-dimethyltetrahydrofuran

Abstract—The structure of ganschisandrine isolated from *Schisandra sphenanthera* was determined to be 2S,5S-bis-(3,4-dimethoxyphenyl)-3R,4S-dimethyltetrahydrofuran.

INTRODUCTION

In continuing our study on the chemical ingredients of *Schisandra sphenanthera*, a Chinese medicinal plant [1, 2], collected from Wudu district in Gansu province of China, we have isolated a novel lignan, ganschisandrine. The present work describes the assignment of structure 1 to the new lignan from a study of its spectra (largely by NMR).

RESULTS AND DISCUSSION

From physical constants and spectral data (see Experimental), it is apparent that ganschisandrine (1) is a tetrahydrofuran derivative, a stereoisomer of galbelgin [3], galgravin and veraguensin [4, 5]. From the 1H NMR (Table 1) and ^{13}C NMR (Table 2) data, magnetic non-equivalence of the α, α' -benzylic protons and β, β' -methyl protons of ganschisandrine suggests that one of the four substituents of the tetrahydrofuran ring is *trans* to the other three. The 2D NOESY spectrum of 1 showed correlations between the two methyl doublets (δ 0.63 and 1.02) and $H\alpha'$ signal (δ 4.67); the 2D-COSY spectrum of 1 showed that the $H\alpha$ (δ 5.46) coupled with the $H\beta$ (δ 2.5) and the $H\alpha'$ (δ 4.67) coupled with the $H\beta'$ (δ 2.5), clearly indicating that two methyl groups have the *cis* configuration and $H\alpha$ and $H\alpha'$ is at the same side of the two methyl groups, $H\alpha$ and $H\beta$ protons are in *cis*-position, $H\alpha'$ and $H\beta'$ are in *trans*-position.

The proton coupling constants ($J = 4.0$ and $J = 9.0$ Hz) show that the dihedral angles between $H\alpha$ and $H\beta$, $H\alpha'$ and $H\beta'$ should be *ca* 40 and 160°, respectively. Therefore, the tetrahydrofuran ring must be in 'twist envelope' conformation. It may be due to the mutual steric repulsion of three *cis*-substituents Ar- α , Me- β and Me- β' . The upfield shifted signal of Me- β is due to shielding effect of Ar- α and the downfield shifted signal of $H\alpha$ is caused by deshielded effect of Ar- α .

The ORD spectra of ganschisandrine (in MeOH, $[\phi]_{292} = +4130$ pk, $[\phi]_{241} = +14310$ pk) is similar to that of chicanine (in MeOH, $[\phi]_{296} = +5521$ pk, $[\phi]_{245} = +19000$ pk) [6]; both has a positive Cotton effect.

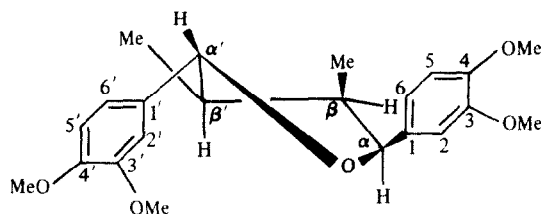


Table 1 ^1H NMR data of ganschisandrine

H	Chemical shifts (ppm)	H-H coupling constants
α	5.46 (d)	$J(\alpha, \beta) = 9$ Hz
α'	4.67 (d)	$J(\alpha', \beta') = 4$ Hz
β		
β'	2.5 (m), 2H	
(β -Me)	0.63 (d)	$J(\beta, \beta\text{-Me}) = 7$ Hz
(β' -Me)	1.02 (d)	$J(\beta', \beta'\text{-Me}) = 6$ Hz
(-OMe)	3.83 (s), 3H	
	3.80 (s), 3H	
	3.78 (s), 3H	
2	6.89 (d)	$J(2, 6) = 1.6$ Hz
2'	6.88 (d)	$J(2', 6') = 1.6$ Hz
5	6.85 (d)	$J(5, 6) = 8$ Hz
5'	6.85 (d)	$J(5', 6') = 8$ Hz
6	6.93 (dd)	$J(5, 6) = 8$ Hz $J(2, 6) = 1.6$ Hz
6'	6.93 (dd)	$J(5', 6') = 8$ Hz $J(2', 6') = 1.6$ Hz

The assignments are extracted from the 2D COSY and 2D NOESY spectra.

The absolute configuration of chicanine has been established as 2*S*-(3-methoxy-4-hydroxyphenyl)-3*R*,4*S*-dimethyl-5*S*-(3,4-methylenedioxyphenyl) tetrahydrofuran [6]. Therefore, ganschisandrine is 2*S*,5*S*-bis(3,4-dimethoxyphenyl)-3*R*,4*S*-dimethyltetrahydrofuran (1).

EXPERIMENTAL

Plant material. *Schisandra sphenanthera* Rehd. et Wils collected from Wudu district in Gansu province of China, authenticated by Prof. Ru-neng Zhao (Department of Pharmacy, Lanzhou Medical College, Lanzhou, China) and the voucher specimen was deposited in the Department of Biology of Lanzhou University.

Isolation. The air-dried powdered fruits (2 kg) were successively extracted with petrol, Et_2O and MeOH. The Et_2O extract was chromatographed on a 3×60 cm column packed with 250 g of silica gel (20–30 μ) and eluted successively with petrol, petrol–10% Me_2CO , petrol–25% Me_2CO and petrol–40% Me_2CO to give fractions P-1 (0.45 g), P-2 (0.15 g), P-3 (0.5 g), P-4

(1.2 g). The P-2 fraction was rechromatographed on a 1.5×25 cm column packed with 20 g of silica gel (40 μ) and eluted with petrol containing increasing amounts of EtOAc (15–50%) to give crude ganschisandrine (70 mg) which was crystallized from *n*-hexane–ether to give ca 50 mg of white flakes.

Physical and spectral data. Ganschisandrine $\text{C}_{22}\text{H}_{28}\text{O}_5$ (Found: 372.1927, requires 372.1936), mp 114–115° uncorr. (*n*-hexane–ether). $[\alpha]_{\text{D}}^{20} + 173.1$ (CHCl_3 ; *c* 0.26). UV $\lambda_{\text{max}}^{\text{CHCl}_3}$ nm: 206, 233, 280 IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1592.5 (s), 1513.1 (s) (Ar–) EIMS (direct insert probe), 70 eV, *m/z* (rel. int.). 372 $[\text{M}]^+$ (32), 206 $[\text{M} - \text{PhCHO}]^+$ (100), 194 (15), 191 $[\text{M} - \text{PhCHO} - \text{Me}]^+$ (96), 175 (52), 166 (27), 138 (20), 91 (18) and 77 (25). ^1H NMR and ^{13}C NMR (400 MHz, CDCl_3) see Tables 1 and 2. ORD (in MeOH), $[\phi]_{292} = +4130\text{pk}$, $[\phi]_{241} = +14310\text{pk}$

Acknowledgement—The financial support of the National Scientific Foundation and Laboratory of Applied Organic Chemistry of Lanzhou University Research Fund is gratefully acknowledged.

Table 2. ^{13}C NMR data of ganschisandrine

C	Chemical shifts (ppm)	C	Chemical shifts (ppm)
α^*	84.77	3	149.10
α'	85.96	3'	148.66
β	47.56	4	148.44
β'	43.45	4'	147.74
β -Me	9.47	5	118.50
β' -Me	11.86	5'	118.07
1	135.66	6	109.32
1'	133.23	6'	109.02
2	109.32	-OMe	55.87
2'	109.20		55.92

The assignments are made partly on the basis of DEPT technique

*The α , α' , β , β' , 1, 1', 2, 2' . . and 6,6' carbon chemical shifts may be interchanged.

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CHALCONES FROM *HUMULUS LUPULUS*

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Key Word Index—*Humulus lupulus*, Moraceae, plant chemistry, isoxanthohumol, xanthohumol, 3'-(isoprenyl)-2',4-dihydroxy-4',6'-dimethoxychalcone, 2',6'-dimethoxy-4,4'-dihydroxychalcone

Abstract—Extracts of *Humulus lupulus* yielded two known compounds, isoxanthohumol and xanthohumol, and two new chalcones, 3'-(isoprenyl)-2',4-dihydroxy-4',6'-dimethoxychalcone and 2',6'-dimethoxy-4,4'-dihydroxychalcone. Their structures were established by spectral methods.

INTRODUCTION

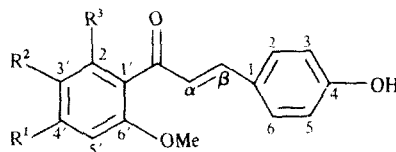
Two new chalcone derivatives—3'-(isoprenyl)-2',4-dihydroxy-4',6'-dimethoxy chalcone and 2',6'-dimethoxy-4,4'-dihydroxychalcone, together with two already known compounds: isoxanthohumol and xanthohumol [1, 2] were isolated from hop cone extract. The structures of the isoxanthohumol and xanthohumol were determined by comparing their spectra with those of references, while the new compounds were identified mainly by their ¹H NMR and MS spectra.

RESULTS AND DISCUSSION

The MS spectra of xanthohumol (3) and isoxanthohumol (4) showed a similar fragmentation pattern and the same molecular formula C₂₁H₂₂O₅ ([M]⁺ *m/z* 354), although the *R_f* values on TLC differed. These similarities in the MS of the two compounds provided the necessary information for the determination of their chemical structures. The MS spectrum of 3, which was cyclized to 4 by electron impact, exhibited exactly the same fragmentation pattern as 4 due to retro-Diels-Alder

rearrangement. The ¹H NMR and other spectra of 3 and 4 were identical with those reported for iso- and xanthohumol, respectively, which were synthesized [3] and isolated from hops [1, 2].

3'-(isoprenyl)-2',4-dihydroxy-4',6'-dimethoxychalcone (1) mp 152–153° [M]⁺ at *m/z* 368 (C₂₂H₂₄O₅) closely resembled xanthohumol in its UV, IR and MS spectral characteristics. The IR spectrum showed a hydroxyl band at 3350 cm⁻¹ and a α,β-unsaturated carbonyl group at 1610 cm⁻¹. It had a UV maximum at 370 nm, which shifted to 446 nm on the addition of sodium methoxide, confirming the presence of the phenolic hydroxy group.



1 R¹ = OMe, R² = CH₂CH=CHMe₂, R³ = OH

2 R¹ = OH, R² = H, R³ = OMe

3 R¹ = OH, R² = CH₂CH=CHMe₂, R³ = OH

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