Pergamon

0031-9422(94)00757-8

Phytochemistry, Vol. 38, No. 4, pp. 1009–1011, 1995

0031-9422/95 $9.50 + 0.00

SCHISANTHERINS P AND Q, TWO LIGNANS FROM *KADSURA COCCINEA*

JIA-SEN LIU* and LIANG LI

Shanghai Institute of Materia Medica, Academia Sinica, China

(*Received in revised form* 1 *August* 1994)

Key Word Index—*Kadsura coccinea*; Schisandraceae; seeds; lignans; schisantherin P, Q.

Abstract—Two new lignans, schisantherins P and Q, were isolated from the seeds of *Kadsura coccinea*. Their structures, including absolute configurations and conformations, were elucidated by spectroscopic analysis and chemical conversion.

INTRODUCTION

In previous papers we reported the isolation and structures of 10 new lignans: kadsulignans A, B [1], L, M, and N [2], schisantherins L, M, N, O, and acetylschisantherin L [3], from the seeds of *Kadsura coccinea*, an ethnomedicine used in the treatment of gastroenteric disorders and rheumatoid arthritis in southern China.

A continuing investigation of the extract led to isolation of a further two new dibenzocyclooctadiene lignans designated as schisantherins P (**1**) and Q (**2**). In the present paper we describe their isolation and structural elucidation, including absolute configurations and conformations of **1** and **2**.

RESULTS AND DISCUSSION

Schisantherins P (**1**) and Q (**2**) show a spectral feature of dibenzocyclooctadiene lignans in their ^{1}H NMR spectra. ^{1}H NMR spectral data revealed that both **1** and **2** possessed the same substituents, two methoxyls and two methylenedioxy groups, attached to the biphenyl rings. A NOE measurement result indicated that the two methoxyl substituents were at C-1 and C-14, whereas the two methylenedioxy groups were at C-2, C-3, and C-12, C-13 in light of no observable NOE enhancement at both H-4 and H-11 on irradiation of each methoxyl proton in **1** and **2**. The CD curve of **1** and **2** showed a negative Cotton effect around 255 nm, suggesting a *S*-configuration of biphenyl in both compounds.

The only structural difference between **1** and **2** lay in the conformation and oxidation level of the cyclooctadiene ring. The ^{1}H NMR, HR-mass and IR spectral data suggested the presence of 6,9-dihydroxyl substituents in **1** and 6-oxo, 9-hydroxyl moieties in **2**, these being verified by appropriate NOE measurements (Table 1). Furthermore, the NOE measurement results also elucidated the relative stereochemistry of **1** and **2**, and revealed the presence of a stable twist boat chair conformation in schisantherin P and a stable twist boat conformation in schisantherin Q as shown as structures **1** and **2**, respectively, because only the conformation assigned above can rationalize the NOE results (Table 1) of **1** and **2**. In addition, the IR spectrum of **2** showed a low frequency (1652 cm^{-1}) of carbonyl absorption, indicating that the carbonyl plane is conjugated to the benzene plane of the biphenyl system. If the carbonyl plane was not conjugated with that of the biphenyl system, an absorption at 1690 cm^{-1} would be expected [4–6]. This evidence provided further support for the presence of a 6-oxo substitution and a twist boat conformation in the molecule of **2**, because in the compound with a *S*-configuration of biphenyl, only the carbonyl located at the 6 position with a twist boat conformation allows the formation of a conjugation plane with the biphenyl system.

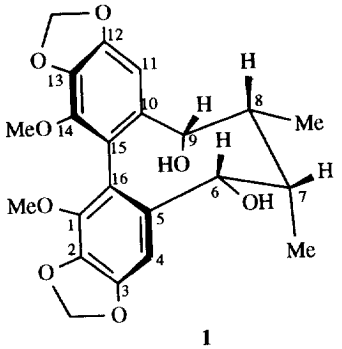
A chemical transformation provided indisputable evidence for the above proposed structures. Treatment of **1** and **2** with freshly prepared $AlCl_2H$ [7] afforded the same known compound, (−)-wuweizisu C (**3**) [8], allowing us unambiguously to assign structure **1** with the configuration of 6*S*,7*S*,8*R*,9*R*, and biphenyl S to schisantherin P and structure **2** with the configuration of 7*S*,8*R*,9*R*, and biphenyl S to schisantherin Q, respectively.

EXPERIMENTAL

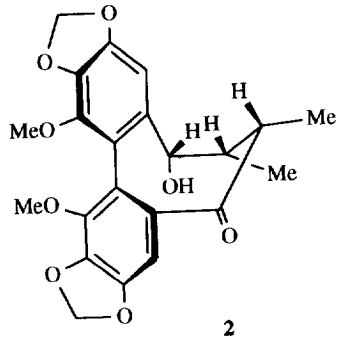
Mps: uncorr. Silica gel: Quingdao Haiyang Chemicals Co. HPTLC plates: Yantai Institute of Chemical Technology. For the collection and identification of plant materials see ref. [3]. The voucher specimen is deposited in the herbarium of Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China.

Extraction and preliminary separation. For the procedures of extraction and preliminary fractionation of Parts A, B, C, and D see ref. [3].

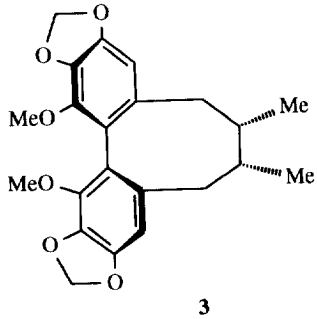
*Author to whom all correspondence should be addressed.
Present address: SynPhar Laboratories Inc., 4290–91A Street, Edmonton, Alberta, Canada T6E 5V2.



1



2



3

Table 1. NOE enhancements* of compounds **1** and **2**

Compound	Irradiation (δ)	Observation (δ)	NOE enhancement (%)
1	H-4 (6.90)	H-6β (4.64)	0
	H-6β (4.64)	H-4 (6.90)	0
	H-11 (6.28)	H-9β (4.57)	13
	H-9β (4.57)	H-11 (6.28)	10
		H-8β (2.00)	0
	Me-7α (0.88)	H-4 (6.90)	13
		H-7β (2.10)	21
		H-6β (4.64)	0
		H-8β (2.00)	0
	Me-8α (1.18)	H-9β (4.57)	10
		H-8β (2.00)	20
		H-7β (2.10)	10
		H-11 (6.28)	0
2	H-11 (6.34)	H-9β (4.74)	13
	H-9β (4.74)	H-11 (6.34)	12
		H-8β (1.95)	20
	Me-7α (0.95)	H-7β (2.79)	25
		H-8β (1.95)	10
		H-4 (7.42)	0
	Me-8α (0.88)	H-9β (4.74)	6
		H-8β (1.95)	28
		H-11 (8.34)	0

*No NOE enhancement of H-4 and H-11 was observed on irradiation of each methoxyl protons in compounds **1** and **2**.

Schisantherin P (**1**). Part B was chromatographed over silica gel (200–300 mesh) eluting with petrol–Me_2CO (10:1). The later frs were rechromatographed over silica gel again using C_6H_6–EtOAc (8:1) to provide **1** (1.85 g, 0.026%), recrystallized from MeOH, mp 107–108°; $[\alpha]_D$ + 7.98° (MeOH; *c* 1.290); UV λ_{max}^{MeOH} nm (log ε): 214 (4.56), 252 (3.93, sh), 282 (3.53); IR ν_{max}^{KBr} cm^{-1}: 3460, 1620; ^1H NMR ($CDCl_3$, 400 MHz): δ0.88 (3H, *d*, *J* = 7.3 Hz, Me-7α), 1.18 (3H, *d*, *J* = 7.2 Hz, Me-8α), 2.00 (1H, *m*, H-8β), 2.10 (1H, *m*, H-7β), 3.84 (3H, *s*, OMe), 3.97 (3H, *s*, OMe), 4.57 (1H, *s*, H-9β), 4.64 (1H, *d*, *J* = 0.8 Hz, H-6β), 5.30 (1H, *s*, OH), 5.94 (2H, *s*, OCH_2O), 5.97 (2H, *s*, OCH_2O), 6.28 (1H, *s*, H-11), 6.90 (1H, *s*, H-4); HR-MS *m/z* (rel. int.): 416.1503 ($[M]^+$, calcd for $C_{22}H_{24}O_8$, 416.1471) (57), 399.1424 $[M - OH]^+$ (22), 398.1366 $[M - H_2O]^+$ (100), 380.1279 $[M - H_2O - H_2O]^+$ (4), 233.0853 $[C_{13}H_{13}O_4]^+$ (33); CD $\Delta\varepsilon$(nm) in MeOH: − 16.4 (201), 0 (215), + 14.2 (225), + 12.2 (234), 0 (242), − 16.5 (256).

Schisantherin Q (**2**). Part C was chromatographed over silica gel eluting with petrol–Et_2O (5:1, 2:1, 1:1). The frs eluted by petrol–Et_2O (2:1) were combined and rechromatographed over silica gel (200–300 mesh) using petrol–Et_2O (5:1) to give **2** (35 mg, 0.00049%), recrystallized from MeOH, mp 173–175°; UV λ_{max}^{MeOH} nm (log ε): 215 (4.52), 240 (4.44), 292 (3.98), 330 (3.69, sh); IR ν_{max}^{KBr} cm^{-1}: 3490, 1652, 1610; ^1H NMR ($CDCl_3$, 400 MHz): δ0.88 (3H, *d*, *J* = 7.3 Hz, Me-8α), 0.95 (3H, *d*, *J* = 7.0 Hz, Me-7α), 1.95 (1H, *m*, H-8β), 2.79 (1H, *m*, H-7β),

3.76 (3H, *s*, OMe), 3.85 (3H, *s*, OMe), 4.74 (1H, *s*, H-9β), 5.90 (1H, *br s*, OH), 6.01 (2H, *s*, OCH_2O), 6.02 (2H, *s*, OCH_2O), 6.34 (1H, *s*, H-11), 7.42 (1H, *s*, H-4); HR-MS *m/z* (rel. int.): 414.1286 ($[M]^+$, calcd for $C_{22}H_{22}O_8$, 414.1315) (100), 384.1246 $[C_{21}H_{20}O_7]^+$ (8); CD $\Delta\varepsilon$(nm) in MeOH: − 71.7 (209), 0 (219), + 65.3 (230), 0 (243), − 8.2 (252), 0 (262), + 8.8 (286), 0 (310), − 8.8 (340).

(−)-*Wuweizisu C* (**3**). Compound **1** (20 mg) in dry Et_2O (5 ml) was added to an Et_2O solution of $AlCl_2H$ (1 mmol) freshly prepared from $LiAlH_4/AlCl_3$ [7] and reacted at room temperature for 1.5 hr. The reaction was quenched by adding H_2O (10 ml) and then the mixt. was extracted with Et_2O. The ext. was purified by CC over silica gel, affording **3** (15 mg), which was identical with an authentic sample (mmp, ^{1}H NMR, IR, MS, CD) [8]. Similarly, **2** was reduced in the same manner to afford the identical product.

Acknowledgements—Financial support was provided by the National Natural Science Foundation of China. The authors are grateful to Prof. Yu-Hu Liu (Huanan Institute of Botany, Academia Sinica, China) for the botanical identification of materials investigated, and to the Department of Analytical Chemistry, Shanghai Institute of Materia Medica, Academia Sinica, China, for UV, IR, NMR, MS and CD measurements.

REFERENCES

1. Liu, J.-S., Li, L. and Yu, H.-G. (1989) *Can. J. Chem.* **67**, 682.
2. Liu, J.-S. and Li, L. (1994) *Phytochemistry* **38**, 241.
3. Liu, J.-S. and Li, L. (1993) *Phytochemistry* **32**, 1293.
4. Gottlieb, H. E., Mervic, M. and Ghera, E. (1982) *J. Chem. Soc., Perkin Trans. 1* 2353.
5. Mervic, M. and Ghera, E. (1977) *J. Am. Chem. Soc.* **99**, 7673.
6. Liu, J.-S. and Zhou, H.-X. (1991) *Acta Chim. Sin.* **49**, 412.
7. Brewster, J. H., Bayer, H. O. and Osman, S. F. (1964) *J. Org. Chem.* **29**, 110.
8. Chen, Y.-Y., Shu, Z.-B. and Li, L.-N. (1976) *Sci. Sin.* **19**, 276.