Available online at www.sciencedirect.com
ScienceDirect
Chinese Chemical Letters 21 (2010) 943–946
CHINESE CHEMICAL LETTERS
www.elsevier.com/locate/cclet

Kansuinine J, a new macrocyclic diterpenoid from the roots of *Euphorbia kansui*

Jie Guo [a], Xin Fang [b], Ying Tong Di [b], Hui Ming Hua [a], Xiao Jiang Hao [b,*]

[a] *Department of Natural Products Chemistry, Shenyang Pharmaceutical University, Shenyang 110016, China*
[b] *State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, China*

Received 25 December 2009

Abstract

A new macrocyclic diterpenoid, named kansuinine J (**1**), was isolated from the roots of *Euphorbia kansui*. Its structure was characterized on the basis of spectroscopic analysis.

Keywords: *Euphorbia kansui*; Kansuinine J; Macrocyclic diterpenoid

Euphorbia kansui, an annual plant, distributes mainly in the northern China. It is well known as ''Gan Sui'' in traditional Chinese medicine for the treatment of edema, ascites, and tumor [1]. Previous phytochemical investigations on this species yielded a number of diterpenoid ingenol esters [2] and jatrophane diterpenoids [3]. In the course of our search for bioactive natural products from the roots of *E. kansui*, a new jatrophane diterpenoid, named kansuinine J (**1**) was isolated from the petroleum-soluble extracts of this plant. Herein we described the structure elucidation of kansuinine J (**1**).

Kansuinine J (**1**), was obtained as a colorless prism, $[\alpha]_D^{25}$ + 11.77 (*c* 0.29, $CHCl_3$). The molecular formula of **1** was determined to be $C_{35}H_{50}O_{15}$ by HR-ESI-MS spectrum for $[M+Na]^+$ at *m/z* 733.3034 (calcd. 733.3047), which indicated the presence of 11 degrees of unsaturation. The IR spectrum of **1** showed the absorptions of hydroxyl (3435 cm^{-1}) and carbonyl (1741 cm^{-1}) groups. The ^1H NMR and ^{13}C NMR spectra of **1** indicated the presence of six ester groups including five acetate groups [δ_H 1.99, 2.03, 1.96, 2.10, and 2.15, each 3H, s; δ_C 168.8, 169.2, 169.5, 170.2, 170.7 (CO), 22.0, 20.8, 20.4, 21.3, 21.2 (CH_3)], and one isopentanoate group [δ_H 1.13, d, 3H, J = 9.0 Hz; 0.82, t, 3H, J = 9.0 Hz; 2.40, q, 1H, J = 9.0 Hz; 1.45, dq, 1H, J = 16.0, 8.0, 2.0 Hz; 1.65, dq, 1H, J = 16.0, 8.0, 2.0 Hz; δ_C 175.8 (CO), 11.2 (CH_3), 26.5 (CH_2), 40.9 (CH), 16.4 (CH_3)], one ketone (δ_C 214.0), one exocyclic double bond (δ_H 5.20, 5.00, each H, s; δ_C 146.1, s; 106.2, t), which accounted for eight degrees of unsaturation. The remaining three degrees of unsaturation were assumed to be the presence of tricyclic system in **1**.

* Corresponding author.
E-mail address: haoxj@mail.kib.ac.cn (X.J. Hao).

1001-8417/$ – see front matter
doi:10.1016/j.cclet.2010.04.024

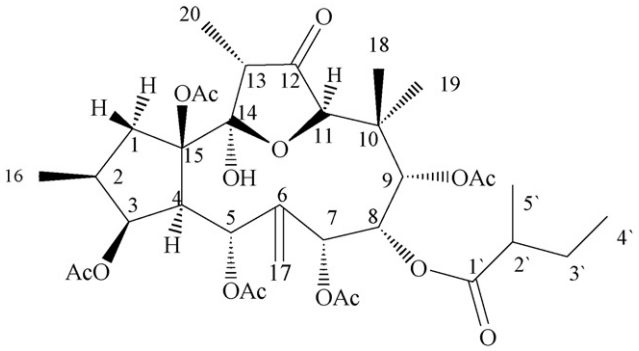

Fig. 1. Structure of kansuinine J (**1**).

The ^{13}C NMR and DEPT spectra of **1** suggested that the skeleton consisted of 20 carbons: one ketone, one exocyclic double bond, four methyls, one methylene, nine methines, and three quaternary carbons, which exhibited resonances closely related to a jatrophane skeleton [3] (Fig. 1).

The structure of kansuinine J (**1**) was further elucidated by means of ^{1}H-^{1}H COSY, HMQC and HMBC experiments. HMBC correlations of H-1, H-16, to C-2 (δ_C 38.9) and H-1, H-3, H-5, to C-15 (δ_C 90.5) suggested the presence of a similar five-membered ring as kansuinine A [4]. Furthermore, in the HMBC spectrum a series of correlations between H-5 and H-11 (Fig. 2) and the surrounding carbons via two or three bonds, confirmed an identical C-5 to C-11 partial structure and esterification in the positions of C-5, C-7, C-9, and C-15 as in kansuinine **A**. It was obvious that the structures of kansuinine J (**1**) and kansuinine A were based on the same parent system and differed only in the esterification. The absence of benzoate signals and the presence of the signals of an isopentanoate group indicated the replacement of the benzoate unit with an isopentanoate group. The position of this substitution at C-8 was established from the HMBC correlation of H-8 to the carbonyl signal at δ_C 175.8. Correlations of H-11, H-13, and H-20 to the carbonyl signal at δ_C 214.0 indicated that a ketone group should be located at C-12. The position of hemiketal (δ_C 106.2) was assigned to C-14 based on its HMBC correlations with H-1, H-4, H-13, and H-20, while ether linkage between C-14 and C-11 could be assigned by the correlations from H-11 (δ_H 4.08) to C-12, and H-13 (δ_H 2.28, q, J = 8.5 Hz) to C-14 and C-15 (Table 1).

The relative stereochemistry of kansuinine J (**1**) was established by the comparison the ^{1}H and ^{13}C NMR data with kansuinine A, and was confirmed by ROESY experiment. The very similar chemical shifts between these two compounds suggested that both compounds not only share a same skeleton but also exhibit an identical relative configuration. The ROSEY correlations and ^{1}H NMR coupling constants of H-1, H-3, and H-4 of **1** are quite resembling to those of kansuinine A with a *trans*-fused AB ring junction [5], which suggested the same configurations of C-2, C-3, C-4, and C-15. The zero coupling constant between H-4 and H-5 demonstrated that the 6,17-exomethylene group was parallel to the plane of the macrocycle as described for jatrophanes [6] and a β-oriented H-5 pointed inward into the macrocycle. ROSEY correlations between H-4/H-7, H-7/H-11, and H-11/Me-19 indicated that

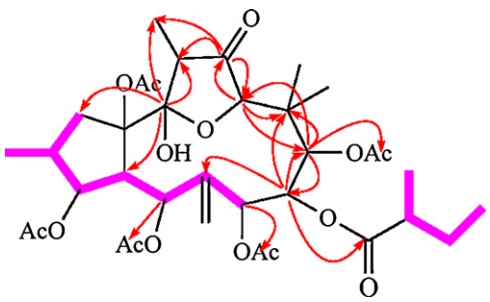

Fig. 2. The diagnostic ^{1}H-^{1}H COSY (—) and selected HMBC (H → C) correlations of **1**.

Table 1
NMR spectral data of kansuinine J (**1**) ($CDCl_3$, TMS, δ, J = Hz).

Atom	^1H	^{13}C	^1H-^1H COSY	HMBC	ROESY
1α	2.64 dd (16.5, 8.0)	39.8	H-1β, H-2	C-2, 3, 4, 14, 15	H-3, 20
1β	2.24 dd (16.5, 8.0)		H-1α	C-2, 14, 15, 16	H-16
2	2.09 m	38.9	H-1α, 3, 16	C-3	H-16
3	5.60 s	74.2	H-2, 4	C-2, 15, CO (δ 170.2)	H-1α
4	2.89 br s	51.6	H-3, 5	C-6, 14, 15	H-7
5	6.08 s	69.5	H-4, 17α	C-3, 4, 6, 7, 15, CO (δ 168.8)	H-8
6		146.1			
7	6.32 s	68.8	H-17α, 17β	C-6, 8, 9, CO (δ 170.7)	H-5, 11
8	5.78 s	70.2		C-6, 9, 10, CO (δ 175.8)	H-5, 18
9	4.94 s	82.2		C-8, 10, 11, 18, 19, CO (δ 169.5)	H-18, 19
10		41.6			
11	4.08 s	77.2		C-9, 10, 12, 18, 19	H-7, 19
12		214.0			
13	2.28 q (8.5)	50.9	H-20	C-12, 14, 15, 20	H-18, 20
14		106.2			
15		90.5			
16	0.92 d (8.0)	13.2	H-2	C-1, 2, 3	H-1β, 3
17α	5.20 s	106.2	H-5, 7	C-5, 6	
17β	5.00 s		H-7		
18	1.24 s	18.7		C-9, 10, 11, 19	H-8, 13
19	1.10 s	22.0		C-9, 10, 11, 18	H-9, 11, 2′
20	1.28 d (8.5)	9.1	H-13	C-12, 13, 14	H-1α
Acetyl					
3-COMe	2.10 s	170.2		CO (δ 170.2)	H-16
		21.3			
5-COMe	1.99 s	168.8		CO (δ 168.8)	
		20.8			
7-COMe	2.15 s	170.7		CO (δ 170.7)	
		21.2			
9-COMe	1.96 s	169.5		CO (δ 169.5)	
		22.0			
15-COMe	2.03 s	169.2		CO (δ 169.2)	
		20.4			
8-COiPe					
1′		175.8			
2′	2.40 q (8.5)	40.9	H-5′	C-5′, 3′, 4′, CO (δ 175.8)	H-19
3′α	1.45 dq (16.0, 8.0, 2.0)	26.5	H-3′β, 4′	C-2′, 5′, 4′, CO (δ 175.8)	
3′β	1.64 dq (16.0, 8.0, 2.0)		H-3′α, 4′	C-2′, 5′, 4′, CO (δ 175.8)	
4′	0.82 t (9.5)	11.2	H-3′α, 3′β	C-2′, 3′	
5′	1.13 d (9.0)	16.4	H-2′	C-2′, 3′, CO (δ 175.8)	H-9

500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR.

H-7, H-11, and Me-19 are α-oriented and then Me-18 adopted an β-orientation. The ROSEY correlation of Me-18 with H-13 indicated the Me-20 to be α-orientation. A combination of ROSEY correlations from H-7 to H-8, H-8 to H-9 as well as Me-18, H-9 to Me-18 and Me-19, together with the zero ^3J (H-7 to H-8 and H-8 to H-9) coupling constant was best interpreted by designating of H-8 and H-9 as β-form. All of the above analyses led to the structural elucidation of Kansuinine J (**1**).

Kansuinine J (**1**) is one of the most highly esterified Euphorbiaceae diterpenoid identified up to date, and its isopentanoate group has been reported in jatrophane diterpenes for the first time. The isolated compound is additional member of the small group of jatrophane diterpenoids, which is considered to be the most important taxonomic members in this family.

Acknowledgments

This work was financially supported by grants from the Ministry of Science and Technology (Nos. 2009CB940900 and 2009CB522300).

References

[1] Pharmacopoeia Commission of People's Republic of China. The Pharmacopoeia of the People's Republic of China, Part 1, Chemical Industry Publishing House, Beijing, 2005, p. 60.
[2] F.T. Halaweish, S. Kronberg, J.A. Rice, J. Chem. Ecol. 29 (2002) 1073.
[3] L.G. Liu, J.C. Meng, R.X. Tan, Planta Med. 68 (2002) 244.
[4] Q. Pan, Z.D. Min, Chin. Chem. Lett. 13 (2002) 1178.
[5] S. Yamamura, S. Kosemura, Y. Saito, Tetrahedron Lett. 22 (1981) 5315.
[6] B.X. Ma, T.Z. Fang, J. Nat. Prod. 60 (1997) 134.