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A New Eudesmane Sesquiterpenoid Glycoside from *Lactuca Sativa* L *var. Anagustata*

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Abstract. Chemical reinvestigation of the methanolic extract of whole plant of *Lactuca sativa* L *var. anagustata* has now led to the isolation of one new eudesmane sesquiterpenoid glycoside which was elucidated by means of spectroscopic methods, including 2D-NMR experiments (^{1}H-^{1}H COSY, HMQC, HMBC, and NOESY) as 1*β*-*O*-*β*-D-glucopyranosyl-15-*O*-(*p*-methoxyphenylacetyl)-5*α*, 6*β*H-eudesma-3, 11(13)-dien-12, 6*α*-olide.

Introduction

Lactuca sativa L *var. anagustata*, which belongs to the genus of Lactuca (Compositae), also called "Chinese lettuce" or "wosun", is a cultivar of lettuce in China grown as a "stem-used type" vegetable which has also been used as a traditional medicine for stomach, which can stimulate digest, enhance appetite, and relieve inflammation [1]. Until now, several plants of this genus have been investigated chemically yielding sesquiterpene lactones, including a number of lactucin-type guaianolides [2-11], along with costus lactone-type guaianolides [12], germacranolides [13, 14] and some eudesmanolides [15].

Recently, we reported the isolation and structure elucidation of three new sesquiterpenes from *L. sativa* [15]. In this paper, we report the chemical reinvestigation of this species, which resulted in the isolation of one new eudesmane sesquiterpenoid glycoside (1) (see Fig. 1). Its structure was elucidated by HR-ESIMS, IR, and 1D- and 2D-NMR experiments.

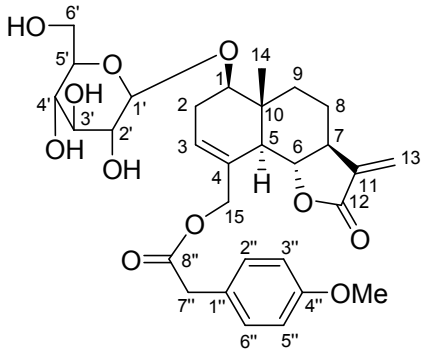

Fig. 1 Structure of compound 1

Materials and Methods

Materials. The whole plant of *L. sativa* L *var. anagustata* was collected from the Carrefour supermarket in Hangzhou city, Zhejiang province of China, and was identified by Prof. Xiao-Chuan Liu, School of Life Science, Zhejiang Sci-Tech University, China. A voucher specimen (No. 070901) has been deposited in the Department of Chemistry, Zhejiang Sci-Tech University, China.

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer Model 341 polarimeter. IR spectra were recorded on a Nicolet NEXUS 670 FTIR instrument. NMR spectra were measured on a Bruker AM-400 NMR spectrometer with TMS as an internal standard. HR-ESI-MS were obtained on a Bruker Daltonics APEX-II 47e spectrometer. Column chromatography was carried out on Si gel (200-300 mesh) and TLC on Si gel (GF254 10-40 μm), both supplied by Qingdao Marine Chemical Co.

Extraction and Isolation. The dried and powered stalks (3.5 kg) were extracted with methanol (12 L×3) at room temperature. The extracts were concentrated under reduced pressure to yield crude extract of methanol (220 g), which was suspended in water and successively extracted by petroleum ether, ethyl acetate and *n*-butanol. After evaporation of the solvents, a brown-red gum was obtained under reduced pressure. The *n*-BuOH extract (30 g) was subjected to repeated chromatography, eluting with a gradient of $CHCl_3$-MeOH (20:1-0:1, v/v) and six crude fractions were obtained. Fraction 3 was chromatographed on a silica gel column eluting with $CHCl_3$-MeOH (10:1) to give six fractions, in which subfraction 6 was further purified by repeated column chromatography ($CHCl_3$-CH_3OH-H_2O 10:1:0.1; EtOAc-EtOH-H_2O 20:1:05-10:1:0.5) to afford **1** (12 mg).

Results and Discussion

Compound 1, $[\alpha]^{20}_{D}$: +39 (*c* 0.12, EtOH), was isolated as a yellow gum. The molecular formula was determined to be $C_{30}H_{38}O_{11}$ by HR-ESIMS (*m/z* = 597.2309, calcd. for $[C_{30}H_{38}O_{11}+Na]^+$: 597.2312) requiring 12 degrees of unsaturation. Its IR spectrum showed the presence of hydroxyl (3409 cm^{-1}), *α*-methylene-*γ*-lactone (1755, 1615 cm^{-1}), and phenyl (1598, 1509, 1455 cm^{-1}) groups.

Table 1 ^1H and ^{13}C NMR data of 1 in CD_3OD (400 MHz for ^1H and 100 MHz for ^{13}C)

Position	**1**	
	δ_H (mult[a], *J* in Hz)	δ_C (mult)[a]
1	3.63 (dd, 10.0, 5.6)	80.8 (d)
2	2.30 (om)/1.89 (om)	32.1 (t)
3	5.71 (br s)	128.9 (d)
4	-	133.0 (s)
5	2.42 (d, 10.0)	48.8 (d)
6	3.42 (dd, 10.0, 10.0)	80.9 (d)
7	2.26 (om)	50.1 (d)
8	1.88 (om)/1.39 (om)	20.5 (t)
9	1.99 (m)/1.35 (om)	33.8 (t)
10	-	39.6 (s)
11	-	139.3 (s)
12	-	170.6 (s)
13	6.02 (d, 2.4)/5.40 (d, 2.4)	116.6 (t)
14	0.77 (s)	11.4 (q)
15	4.64 (d, 12.0)/4.50 (d, 12.0)	67.3 (t)
1′	4.13 (d, 7.6)	105.2 (d)
2′	2.85 (m)	73.9 (d)
3′	3.12 (m)	76.2 (d)
4′	3.33 (m)	69.4 (d)
5′	4.30 (m)	76.7 (d)
6′	3.69 (dd, 12.0, 2.4)/3.50 (dd, 12.0, 6.0)	61.2 (t)
1″	-	125.9 (s)
2″	7.12 (d, 8.4)	130.3 (d)
3″	6.76 (d, 8.4)	113.6 (d)
4″	-	158.1 (s)
5″	6.76 (d, 8.4)	113.6 (d)
6″	7.12 (d, 8.4)	130.3 (d)
7″	3.47 (br s)	40.6 (t)
8″	-	171.3 (s)
OCH_3	3.80 (s)	55.9 (q)

[a] Multiplicity: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; o, overlapped.

The ^{13}C NMR and DEPT spectra (Table 1) of 1 clearly exhibited 30 carbon signals, which were classified as two methyls, seven methylenes, fourteen methines, and seven quaternary carbons. Typical signals for a *p*-methoxyphenylacetate moiety (δ_H 3.47, 2H, br s, H-7″; 3.80, 3H, s, OMe; 6.76, 2H, d, J = 8.4 Hz, H-3″, 5″ and 7.12, 2H, d, J = 8.4 Hz, H-2″, 6″; δ_C 40.6, t, C-7″; 55.9, q, OMe; 113.6, d, C-3″, 5″; 130.3, d, C-2″, 6″; 125.9, s, C-1″; 158.1, s, C-4″ and 171.3, s, C-8″) and a *β*-glucopyranoside moiety (δ_H 4.13, d, 1H, J = 7.6 Hz, H-1′; 2.85-4.30, m, 6H, H-2′, 3′, 4′, 5′, 6′; δ_C 105.2, d, C-1′; 73.9, d, C-2′; 76.2, d, C-3′; 69.4, d, C-4′; 76.7, d, C-5′ and 61.2, t, C-6′) were readily recognized from the NMR spectra [16]. The remaining signals indicated that the aglycone was a eudesmane-type sesquiterpene lactone, which was further confirmed by typical quaternary carbon signal resonance at δ_C 39.6 (C-10) in the ^{13}C NMR spectrum [17]. Accordingly, the ^{1}H and ^{13}C NMR spectra of 1 closely resembled those of known compound 1*β*-*O*-*β*-D-glucopyranosyl-15-*O*-(*p*-hydroxyphenylacetyl)-5*α*, 6*β*H-eudesma-3, 11(13)-dien-12, 6*α*-olide [16] with the exception of the appearance of a methoxy group (δ_H 3.80, 3H, s; δ_C 55.9, q), which assigned to be attached at *p*-methoxyphenylacetate moiety. The attachment of glucose to the hydroxyl at C-1 was deduced from the HMBC experiment which showed a long-rang correlation between H-1 (δ_H 3.63, dd, J = 10.0, 5.6 Hz) and C-1′ (δ_C 105.2) (see Fig. 2). The position of *p*-methoxyphenylacetate group was fixed at C-15 by the HMBC experiment which showed the cross-peaks between H_2-15 (δ_H 4.64, d, J = 12.0 Hz and 4.50, d, J = 12.0 Hz) and the ester carbonyl (δ_C 171.3, C-8″).

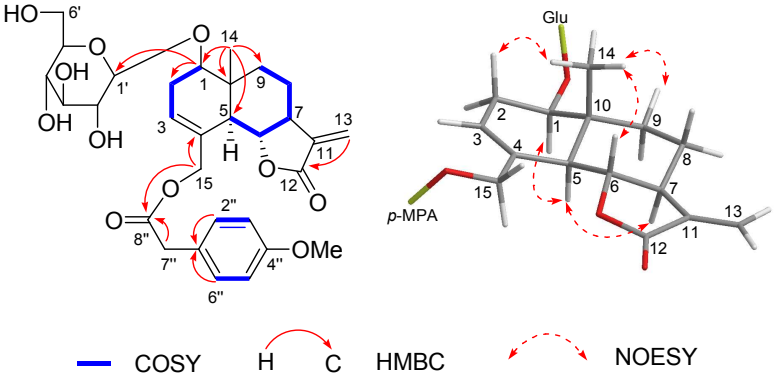

Fig. 2 ^{1}H-^{1}H COSY and HMBC (left) and NOESY correlations of 1

The large coupling constants observed for H-1 with H-2 ($J_{1\alpha,\,2\beta}$ = 10.0 Hz), and H-6 ($J_{6\beta,\,5\alpha} = J_{6\beta,\,7\alpha}$ = 10.0 Hz) allowed the assignment of the relative stereochemistry for H-1 as *α*-oriented and that of the lactone group at C-6 and C-7 as *trans*-fused. Furthermore, the chemical shift value of the methyl group at δ_C = 11.4 ppm is typical for eudesmanolides having *α*-methyl group at C-11, which was also confirmed by NOESY correlations of H_3-14 with H-6, and H-5 with H-1 and H-7. Therefore, the structure of 1 was identified as 1*β*-*O*-*β*-D-glucopyranosyl-15-*O*-(*p*-methoxyphenylacetyl)-5*α*, 6*β*H-eudesma-3, 11(13)-dien-12, 6*α*-olide.

Conclusions

Chemical reinvestigation on *L. sativa* L *var. anagustata* has resulted in one new eudesmane-type sesquiterpenoid glycoside, which possesses a potential anti-tumor active *α*-methylene-*γ*-lactone group [18], was elucidated by means of spectroscopic methods as 1*β*-*O*-*β*-D-glucopyranosyl-15-*O*-(*p*-methoxyphenylacetyl)-5*α*, 6*β*H-eudesma-3, 11(13)-dien-12, 6*α*-olide.

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