THE STRUCTURE OF CELAGLAUMIN

—— ANTITUMOR PRINCIPLE OF *Celastrus glaucophyllus*

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Since pronounced antitumor activity displayed by maytansine and triptolide from the plants of *Celastraceae* was discovered, scientists investigated and screened the plants of *Celastraceae* phytochemically and pharmacologically, hoping to discover new antitumor compounds. Four sesquiterpene esters were isolated from the acetone extract of the root barks of *Celastrus glaucophyllus* Rehd. et Wils. by using chromatography on aluminum oxide and silica gel. Their structures were elucidated on the basis of UV, IR, HRMS, ^{1}H-NMR, ^{13}C-NMR and 2D-NMR as well as chemical methods. They are all new compounds. In this note, two of them are reported. Compound **1** (celaglaumin) showed antitumor activity against L_{1210} and P-388. IC_{50} (μg/ml): L_{1210} 2.11; P-388 4.12.

Celaglaumin was obtained as colourless crystals, m. p. 222—223°C, $(\alpha)_D^{20}$-48.5 (c 0.2, $CHCL_3$). The molecular formula, $C_{36}H_{44}O_{10}$, was determined by means of high resolution mass spectrometry (calcd. for $C_{36}H_{44}O_{10}$: 636.2934. Found: 636.2867). Its UV spectrum (MeOH) showed λ_{max} at 282(log ε 3.2), 274(3.25), 232(4.4) nm. The IR spectrum (KBr) showed absorption for hydroxyl(3500 cm^{-1}, br.), esters(1740 cm^{-1}, br.) and aromatic rings(1600, 1588, 1500 cm^{-1}), m/z: 636(M^+), 621([M — CH_3]$^+$), 515([M—$C_7H_5O_2$]$^+$), 105([C_7H_5O]$^+$). From ^{1}H-NMR and ^{13}C-NMR spectra and the result of methanolysis, celaglaumin was suggested to contain two benzoates, one acetate and one 2-methylbutyrate, the skeleton of this molecule belonged to the β-dihydroagarofurane type[1,2].

In the ^{1}H-NMR of celaglaumin, H-9 appeared as singlet. A similar case was reported in the past[3]. Perhaps this is due to the effect of the substituents in the ring to make the dihedral angle between H-8 and H-9 adjacent to 90°.

In the NOESY of celaglaumin, we observed the cross peaks between H-8 and H-7, H-8

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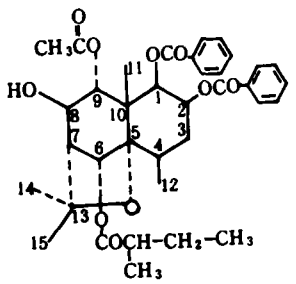
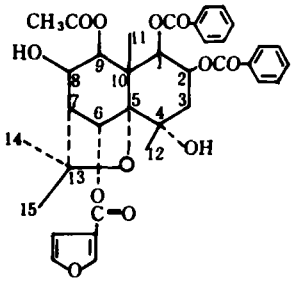
and 8-OH, H-8 and OAc, H-9 and OAc, H-6 and H-9, H-6 and H-7, H-6 and H-12, and the protons of the benzene ring and H-12. Between the protons of two benzene rings, cross peaks were also observed. Therefore, celaglaumin was determined as 1β-benzoyl, 2β-benzoyl, 6α-2-methyl-butyryl, 8β-hydroxyl, and 9α-acetyl β-dihydroagarofurane (**1**) (Fig. 1).



1



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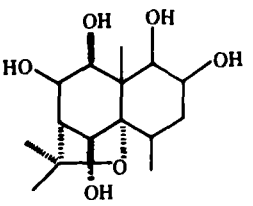

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Fig. 1

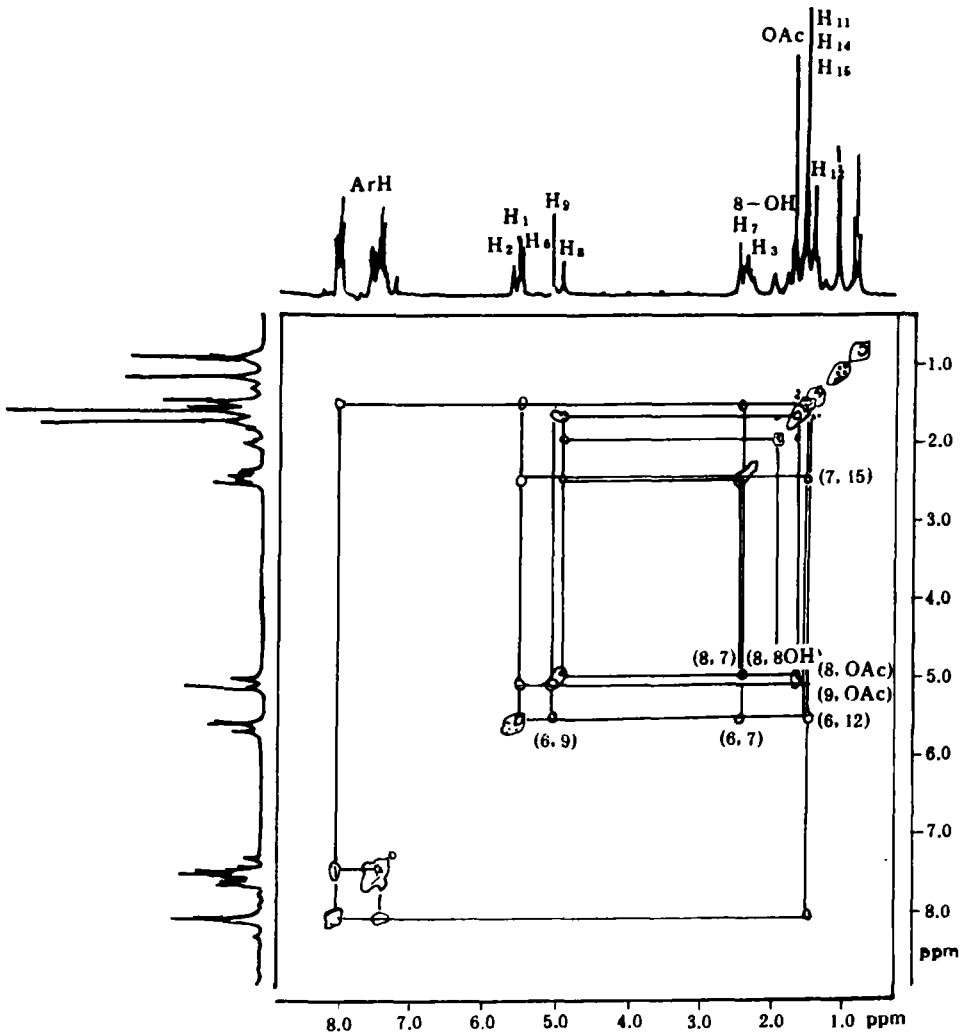

Fig. 2. The NOESY of celaglaumin.

Methanolysis of celaglaumin: Fifty mg of celaglaumin was dissolved in 0.5-ml methanol and 2-ml freshly prepared MeONa/MeOH was added. This solution was set aside at room temperature overnight. The reaction products were separated with preparative TLC (developing with $CHCL_3$-MeOH 9 : 1) to obtain about 20 mg of (**3**) 90 MHz ^{1}H-NMR (C_5D_5N): 3.7—5.0(5H, m, 5 CHOH), 2.11, 2.03, 1.95(each 3H, s, H-11, H-14 and H-15), 2.01(3H, d, J=8 Hz, H-12); m/z : 302(M^+), 287($[M-CH_3]^+$), 251($[M-CH_3-2H_2O]^+$), 233($[M-CH_3-3H_2O]^+$), 195, 145, 59, 43.

The UV, IR and ^{1}H-NMR of compound **2** are very similar to the compounds reported in our previous paper[4], but in the ^{1}H-NMR of compound **2** we can observe the signals of a furan group (6.71, 7.50, 7.97). The mass spectrum of compound **2** also proves the presence of furan (m/z, 95), λ_{max}(EtOH); 280(log ε 3.2), 274(3.3), 232(4.5); ν_{max}(KBr): 3500 (br., OH), 1740 (br., RCOO−), 1600 1588, 1500 (s, Ar) cm^{-1}; m/z: 647($[M-CH_3]^+$), 629($[M-CH_3-H_2O]^+$), 525($[M-CH_3-C_7H_6O_2]^+$), 105($[C_7H_5O]^+$), 95($[C_5H_3O_2]^+$); ^{1}H-NMR(400 MHz, $CDCL_3$): 5.55(1H, d, J=3.7Hz, H-1), 5.78(1H, dd, J=3.7, 6.5Hz, H-2), 2.25(2H, m, H-3), 5.58(1H, d, J=3.0 Hz, H-6), 2.62(1H, d, J=3.0 Hz, H-7), 4.95(1H, d, J=5.4 Hz, H-8), 5.09(1H, d, J=5.4Hz, H-9), 5.16 (1H, s, 8-OH), 3.32(1H, s, 4-OH), 1.90(3H, s, CH_3CO), 1.80, 1.68, 1.65 1.57(each 3H, s, H-11, H-12, H-14 and H-15); and 6H, m, 7.3—7.7; 4H, m, 8—8.1 (the signals of a benzoyl group). So compound **2** was determined as: 1β-benzoyl, 2β-benzoyl, 4α-hydroxyl, 6α-furanoyl, 8β-hydroxyl, and 9β-acetyl β-dihydroagarofurane(**2**, celaglausin).

Table 1

The ^{1}H and ^{13}C-NMR Spectral Data of Celaglaumin

Position	^{13}C-NMR Chemical Shift	^{1}H-NMR Chemical Shift	Position	^{13}C-NMR Chemical Shift	^{1}H-NMR Chemical Shift
1	71.4	5.56 d(3.8)	14	26.0	1.55 s
2	69.5	5.65 m	15	31.4	1.56 s
3	26.6	2.36 m	OCO	169.4	
4	41.7	1.75 m	CH_3	20.7	1.70 s
5	91.6		OCO	175.8	
6	76.4	5.52 d(3.6)	CH	33.2	2.39 m
7	55.2	2.49 dd(3.6, 3.0)	CH_3	16.7	1.13 d(7)
8	77.0	4.97 d(3.0)	CH_2	26.6	
9	73.2	5.08 s	CH_3	11.6	0.88 t(7.3)
10	48.9		Ar	128-133(12 C)	7.3-7.7(6H, m)
11	20.4	1.54 s	CO	164.9	8.0-8.1(4H, m)
12	19.1	1.41 d(8.5)		164.7	
13	82.3				

Notes: Solvent in $CDCL_3$. Values in parentheses are coupling constants in Hz. Chemical shift in ppm is relative to internal TMS.

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