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A New Triterpenoid from the Leaves of *Eucommia ulmoides* OLIV.

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A new triterpenoid called ulmoidol was isolated from the leaves of *Eucommia ulmoides* OLIV. On the basis of spectroscopic analysis, the structure was elucidated as 11α,12α-epoxy-2α,3β-dihydroxy-24-nor-urs-4(23)-en-28,13β-olide.

Key words *Eucommia ulmoides*; triterpenoid; ulmoidol

Eucommia ulumoides OLIV. (Eucommiaceae) is distributed in the midstream of the Yangtze River and in southern China. The bark of this crude drug has long been used as an antihypertensive, diuretic, sedative, tonic and a nourishing medicine in China. Extensive studies have been reported on its pharmacological and chemical characteristics.[1-7] Namba *et al.* reported chemical and pharmacological findings on the application of leaves of this crude drug in tea.[8-10] We also reported that the leaves contained geniposidic acid and syringaresinol diglucoside,[11] that when treated for commercial tea they were comprised of seven iridoids,[12] and that the water extract possessed antihypertensive action.[13] We report here the isolation and structural elucidation of a new triterpenoid called ulmoidol.

A methanol extract of the leaves (927.9 g) was partitioned between water and benzene, and the organic layer (5.5 g) was taken up and subjected to Sephadex LH-20 column chromatography eluted with benzene and gradiently mixed with MeOH to afford eleven fractions. Fraction 3 (496.5 mg) was further purified by silica gel columm chromatograpy ($CHCl_3$: MeOH = 10 : 1 → MeOH) to give three fractions. Subsequent chromatographies of fr. 1 (324.6 mg) using Sephadex LH-20 (H_2O → MeOH) and silica gel provided **1** (19.4 mg) as a white amorphous powder, showing $[\alpha]_D$ +48.0° ($CHCl_3$). The high resolution-electron impact (HR-EI) mass spectrum of **1** displayed a molecular ion at *m/z* 470.3036 consisting of a molecular formula $C_{29}H_{42}O_5$. A peak at *m/z* 470 due to $[M]^+$ was observed in the EI-MS. Its IR spectrum showed absorptions due to an epoxide (935 cm^{-1}) together with a hydroxy (3421 cm^{-1}), a γ-lactone (1778 cm^{-1}) and a double bond (1652 cm^{-1}) group.

The ^1H-NMR spectrum exhibited signals due to the protons of five methyl groups at δ 0.88 (3H, s), 1.00 (3H, d, J=6.0 Hz), 1.10 (3H, s), 1.14 (3H, s), 1.22 (3H, d, J=5.9 Hz), four oxygen-bearing methine protons, at δ 2.97 (1H, d, J=3.7 Hz), 3.18 (1H, br s), 3.63 (1H, m), 3.88 (1H, d, J=7.9 Hz) and two exomethylene protons at δ 4.79 (1H, br s), 5.22 (1H, br s). The ^1H–^1H chemical shift correlation spectroscopy (COSY) experiment revealed that the signals at δ 3.88 and 3.63 correlated with those at δ 4.79 and 5.22.

The ^{13}C-NMR (complete decoupling (COM), distortionless enhancement by polarization transfer (DEPT)) spectrum indicated signals due to one ester carbonyl carbon at δ 178.1, one oxygen-bearing quaternary carbon at δ 88.0, four oxygen-bearing methine carbons at δ 77.1, 72.1, 55.2, 53.7, two exomethylene carbons at δ 147.1, 104.4, four quaternary carbons at δ 44.1, 40.5, 40.4, 37.0, five methine carbons at δ 59.6, 48.6, 48.1, 39.2, 36.5, seven methylene carbons at δ 45.2, 30.3, 29.5, 28.8, 25.8, 21.7, 19.1, five methyl carbons at δ 19.0, 18.5, 16.3, 15.4, 14.6. The heteronuclear multiple quantum coherence (HMQC) and heteronuclear multiple bond correlation (HMBC) experiments made assignments of the respective proton and carbon signals as shown in Fig. 1. Especially, the correlations of Hax-1 → C-2; Heq-1 → C-2/C-5/C-10; H-3 → C-2/C-4/C-23; H-11 → H-9; H-12 → C-13/C-14/C-18; H-

Table 1. ^{13}C and ^1H Assignments and ^1H–^{13}C Long range Correlations of **1** by ^1H–^1H COSY, HMQC and HMBC Experiments (in $CDCl_3$)

C	δ_H	δ_C	Cross peak C in HMBC spectrum
1	1.32 (m)	45.2 t	2
	2.28 (dd, 4.6, 12.8)		2, 3, 5, 10
2	3.63 (m)	72.1 d	
3	3.88 (d, 7.9)	77.1 d	2, 4, 23
4		147.1 s	
5	1.66 (m)	48.6 d	4, 6, 10
6	1.53 (m)	19.1 t	5
	1.66 (m)		5, 10
7	1.25 (m)	28.8 t	6
	1.37 (m)		6, 8, 14
8		40.4 s	
9	1.75 (br s)	48.1 d	1, 5, 8, 11, 14, 25, 26
10		37.0 s	
11	3.18 (br s)	53.7 d	9, 10
12	2.97 (d, 3.7)	55.2 d	11, 13, 14
13		88.0 s	
14		40.5 s	
15	1.13 (m)	25.8 t	8, 14, 16, 17, 27
	1.70 (m)		27
16	1.39 (br dd, 5.8, 13.4)	21.7 t	14, 15, 18, 22
	2.15 (ddd, 5.9, 13.4, 13.4)		15, 17, 18, 28
17		44.1 s	
18	1.79 (br d, 11.6)	59.6 d	12, 13, 14, 16, 17, 19, 22, 28, 29
19	1.66 (br s)	36.5 d	13, 17, 18, 20, 21
20	0.99 (m)	39.2 d	19, 30
21	1.62 (m)	29.5 t	17
22	1.83 (m)	30.3 t	16, 17, 18, 20
23	4.79 (br s)	104.4 t	3, 4
	5.22 (br s)		3, 4, 5
24			
25	0.88 (s)	14.6 q	1, 5, 9, 10
26	1.10 (s)	19.0 q	7, 8, 9, 14
27	1.14 (s)	15.4 q	8, 13, 14, 15
28		178.1 s	
29	1.22 (d, 5.9)	16.3 q	18, 19, 20
30	1.00 (d, 6.0)	18.5 q	19, 20, 21

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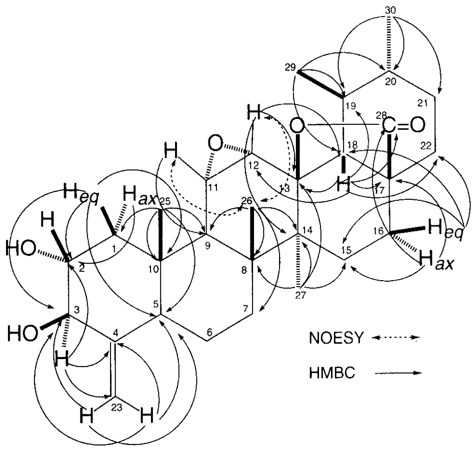
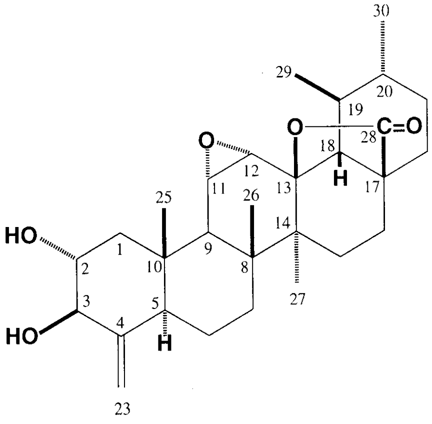


Fig. 1. HMBC and NOESY Correlations of **1**



18→C-12/C-13/C-17/C-19/C-22/C-28; H_2-23→C-3/C-4/C-5; H_3-25→C-1/C-9; H_3-29→C-18/C-20; H_3-30→C-19/C-21 suggested the presence of dihydroxy groups at C-2 and C-3, an exomethylene group at C-4, an epoxy group between C-12 and C-13, a γ-lactone composed of C-13, C-17, C-18 and C-28, and two secondary methyl groups at C-19 and C-20, thus constructing the plain structure of a 24-nor-urs-4(23)-ene derivative for compound **1**. The methylation of **1** with CH_2N_2 in ether gave no reaction product. The coupling constant (J=7.9 Hz) of H-3 indicated a *trans*-diaxial orientation for H_β-2 and H_α-3, although the conformation of A-ring is a little distorted owing to the sp^2-C at C-4. Moreover, a nuclear Overhauser spectroscopy (NOESY) between H-11 or H-12 and H_3-26 suggested the configuration of a 11α,12α-epoxide. Therefore, the structure of new triterpenoid **1** was determined to be 11α,12α-epoxy-2α,3β-dihydroxy-24-nor-urs-4(23)-en-28,13β-olide, and was termed ulmoidol.

Experimental

The optical rotations were measured on a JASCO DIP-360 automatic digital polarimeter. ^{1}H- and ^{13}C-NMR spectra were measured on a JEOL α-500 MHz spectrometer and chemical shifts were given on a δ (ppm) scale with tetramethylsilane as an internal standard. EI-MS was measured on a JEOL DX-303HF spectrometer. Column chromatograph was carried out on Kieselgel 60 (230—400 mesh, Merck), Sephadex LH-20 (Pharmacia), TLC was performed on pre-coated Kieselgel 60 F254 plates (Merck).

Extraction and Isolation The dried leaves (928 g) of *Eucommia ulmoides* were extracted with MeOH and evaporated to give a residue (51.9 g), which was partitioned between benzene and water. The organic layer was evaporated to provide a residue (5.5 g), which was then chromatographed using Sephadex LH-20 (solvent: benzene : MeOH = 10 : 1→MeOH), silica gel (solvent: $CHCl_3$: MeOH = 50 : 1→MeOH), $CHCl_3$: MeOH : H_2O = 9 : 2 : 0.1, benzene : acetone = 3 : 1→MeOH, to give ulmoidol (**1**, 19 mg).

Ulmoidol (1) A white amorphous powder, $[\alpha]_D^{30}$ +48.0° (c=1.0, $CHCl_3$). FT-IR ν_{max}^{KBr} cm^{-1}: 3421 (OH), 1778 (γ-lacton), 1652 (C=C), 935 (epoxide). HR-EI (m/z): 470.3036 (M^+, $C_{29}H_{42}O_5$; 470.3032). EI-MS (m/z): 470 $[M]^+$. ^{1}H-NMR (in $CDCl_3$) δ: 0.88 (3H, s, H-25), 1.10 (3H, s, H-26), 1.14 (3H, s, H-27), 1.00 (3H, d, J=6.0 Hz, H-30), 1.22 (3H, d, J=5.9 Hz, H-29), 2.15 (1H, ddd, J=5.9, 13.4, 13.4 Hz, H-16), 2.28 (1H, dd, J=4.6, 12.8 Hz, H-1), 2.97 (1H, d, J=3.7 Hz, H-12), 3.18 (1H, br s, H-11), 3.63 (1H, m, H-2), 3.88 (1H, d, J=7.9 Hz, H-3), 4.79 (1H, br s, H*a*-23), 5.22 (1H, br s, H*b*-23).

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