NEW IRIDOID TRIMERS AND TETRAMERS FROM SEEDS OF EUCOMMIA ULMOIDESShoji YAHARA,^a Kimiyo KATO,^a Yoshihisa NAKAZAWA,^b Yoshihiro TODA,^c and Toshihiro NOHARA^{*,a}

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Four new iridoid glycosides, ulmoidosides A, B, C and D (1-4), were isolated from the seeds of Eucommia ulmoides. These compounds on alkaline hydrolysis provided a sole product, geniposidic acid (5). Their structures have been determined as an ester trimer (1) and a tetramer (3) bonding each other between C-11 and C-10 of geniposidic acid and as their respective 10-O-monoacetates (2 and 4) by spectral and chemical methods.

KEYWORDS Eucommia ulmoides; Eucommiaceae; iridoid trimer; iridoid tetramer; geniposidic acid oligomer; aucubin

Eucommiae Cortex, the barks of Eucommia ulmoides Oliv. (Eucommiaceae) is a Chinese crude drug used as a tonic and an antihypertensive medicine.¹⁾ Isolation and structure elucidation of several lignan glycosides and iridoids from the barks and leaves of this plant were reported previously by other groups.²⁾ As a part of our continuing chemical studies on the various glycosides, we have investigated the glycosides of the seeds of this plant. From the dil.MeOH extract, four new iridoid glycosides named ulmoidoside A (1, 0.30%), B (2, 0.10%), C (3, 0.03%) and D (4, 0.17%) were isolated along with a known compound, aucubin (1.7%). The structures of the new compounds were determined by spectral and chemical analysis.

Ulmoidoside A (1), $[\alpha]_D^{+7.5}$ (water), a white powder, showed IR absorptions due to the hydroxyl functions (3432 cm^{-1}) and α,β -unsaturated ester carbonyl groups (1698 and 1636 cm^{-1}), and UV absorptions with a maximum at 239 nm ($\log \epsilon\ 4.39$) due to the α,β -unsaturated carbonyl group. The negative FAB-MS of 1 exhibited a molecular peak at 1085 [M-H]^- , together with weak peaks at $m/z\ 922\text{ [M-gluc-H]}^-$, $729\text{ [M-m/z}\ 356\text{-H]}^-$ and $373\text{ [M-m/z}\ 356\times 2\text{-H]}^-$. The $^1\text{H-NMR}$ spectrum (Table I) of 1 showed characteristic peaks for iridoid glycoside; signals due to the olefinic protons at $\delta\ 7.61$ (2H, s), 7.36 (1H, s), 5.89 (1H, s), 5.86 (1H, s) and 5.85 (1H, s), hydroxymethyl protons at $\delta\ 4.90$ (4H, m), 4.33 (1H, d, $J=14\text{ Hz}$) and 4.22 (1H, d, $J=14\text{ Hz}$) and anomeric protons at $\delta\ 4.78$ (3H, br d, $J=8\text{ Hz}$). Moreover, the $^{13}\text{C-NMR}$ spectrum (Table II) of 1 displayed signals due to two α,β -unsaturated ester groups at $\delta\ 170.0$, 170.1 , 154.6×2 , 113.0 and 113.2 , an α,β -unsaturated carboxylic acid system at $\delta\ 174.8$, 151.4 and 116.7 and three β -glucopyranosyl anomeric carbons at $\delta\ 100.9\times 2$, 101.1 , suggesting that 1 should be the ester oligomer of iridoid glucoside. On alkaline treatment with 0.5 N NaOH , 1 afforded an iridoid glucoside (5), which was identified as geniposidic acid by comparison of $[\alpha]_D$ and $^1\text{H-}$ and $^{13}\text{C-NMR}$ spectra with the reported data.³⁾ A comparative study of the $^{13}\text{C-NMR}$ spectrum of 1 with that of 5 (salt) revealed that the chemical shifts assignable to the C-3, C-4 and C-11 in the b and c moieties, and C-10 in the a and b moieties in 1 were shifted to $\delta\ 154.6\times 2$; 113.0 and 113.2 ; 170.0 and 170.1 ; 64.2 and 64.3 , respectively. On the other hand, there was one unit of non-shifted carbon signals at $\delta\ 151.4$, 116.7 , 61.9 , 174.8 . Therefore, the structure of 1 could be represented as an ester trimer of geniposidic acid as shown in the formula.

Ulmoidoside B (2), $[\alpha]_D^{+8.3}$, showed absorption bands at 3448 (OH), 1702 and 1636 cm^{-1}

Table I. ^1H -NMR Data for 1-5 ($\text{CD}_3\text{OD}+\text{D}_2\text{O}$)

	1	2	3	4	5
Ac		2.13 (3H, s)		2.11 (3H, s)	
H-6	2.15 (3H, m)	2.17 (3H, m)	2.14 (4H, m)	2.12 (4H, m)	2.11 (1H, dd, $\underline{J}=7, 17$)
H'-6, H-9	2.84 (2H, m)	2.83 (6H, m)	2.84 (8H, m)	2.80 (8H, m)	2.83 (2H, m)
H-5	3.20-3.55 (15H, m)	3.20-3.55 (15H, m)	3.19-3.55 (20H, m)	3.17-3.55 (20H, m)	3.17 (1H, dd, $\underline{J}=7, 7$)
glc H-2, 3, 4					3.40 (3H, m)
glc H-5					3.52 (1H, m)
glc H ₂ -6	3.69 (1H, d, $\underline{J}=12$)	3.71 (3H, d, $\underline{J}=12$)	3.71 (4H, d, $\underline{J}=12$)	3.68 (4H, d, $\underline{J}=12$)	3.69 (1H, dd, $\underline{J}=5, 12$)
	3.88 (3H, d, $\underline{J}=12$)	3.88 (3H, d, $\underline{J}=12$)	3.88 (4H, d, $\underline{J}=12$)	3.85 (4H, d, $\underline{J}=12$)	3.88 (1H, d, $\underline{J}=12$)
H ₂ -10	4.22 (1H, d, $\underline{J}=14$)c	4.90 (6H, m)	4.22 (1H, d, $\underline{J}=14$)c	4.75-4.95 (12H, m)	4.22 (1H, d, $\underline{J}=14$)
	4.33 (1H, d, $\underline{J}=14$)c		4.33 (1H, d, $\underline{J}=14$)c		4.32 (1H, d, $\underline{J}=14$)
	4.90 (4H, m)		4.90 (6H, m)		
glc H-1	4.78 (3H, d, $\underline{J}=8$)	4.77 (3H, d, $\underline{J}=8$)	4.80 (4H, d, $\underline{J}=8$)		4.78 (1H, d, $\underline{J}=8$)
H-1	5.18 (1H, d, $\underline{J}=7$)	5.20 (1H, d, $\underline{J}=7$)	5.19 (4H, d, $\underline{J}=7$)	5.12 (1H, d, $\underline{J}=7$)	5.17 (1H, d, $\underline{J}=7$)
	5.19 (1H, d, $\underline{J}=7$)	5.22 (1H, d, $\underline{J}=7$)	5.24 (2H, d, $\underline{J}=7$)	5.19 (3H, d, $\underline{J}=7$)	
	5.23 (1H, d, $\underline{J}=7$)	5.24 (1H, d, $\underline{J}=7$)			
H-7	5.85 (1H, s)	5.87 (1H, s)	5.85 (2H, s)	5.84 (3H, s)	5.84 (1H, s)
	5.86 (1H, s)	5.90 (1H, s)	5.89 (2H, s)	5.87 (1H, s)	
	5.89 (1H, s)	5.92 (1H, s)			
H-3	7.36 (1H, s)a	7.40 (1H, s)a	7.24 (1H, s)a'	7.33 (1H, s)a'	7.37 (1H, s)
	7.61 (2H, s)	7.61 (1H, s)	7.61 (3H, s)	7.57 (3H, s)	
		7.62 (1H, s)			

Table II. ^{13}C -NMR Data for 2-5 ($\text{CD}_3\text{OD}+\text{D}_2\text{O}$)

	1	2	3	4	5 (C-11 COONa)
C-1	98.4a	98.4a	98.1a'	98.3a'	98.6
	99.0	99.1x2	99.0x2	99.0x2	
	99.2		99.3	99.2	
C-3	151.4a	152.0a	149.6a'	151.5a'	151.9
	154.6x2	154.7x2	154.7x3	154.7x3	
C-4	113.0	112.9x2	112.9	112.8x3	116.2
	113.2	115.9a	113.0	116.3a'	
	116.7a		113.2		
			118.9a'		
C-5	36.6	36.5	36.5x2	36.4x2	37.0
	36.9	36.7	36.8	36.5x2	
	37.1	36.8	37.2		
C-6	40.4	40.5x3	40.4	40.4x4	40.2
	40.6x2		40.5x2		
			40.6		
C-7	129.7c	132.5x2	129.8c	132.3x3	130.1
	132.3	132.8	132.5x3	132.9	
	132.5				
C-8	139.7	139.4	139.5	139.1x2	144.0
	139.8	139.5	139.6x2	139.4x2	
	144.7c		144.5c		
C-9	47.6	47.8	47.5	47.6	47.7
	48.2	48.1	48.1x2	47.9x2	
	48.5	48.3	48.7	48.4	
C-10	61.9c	64.2	61.9c	64.3x2	61.8
	64.2	64.6x2	64.3x2	64.6x2	
	64.3		64.4		
C-11	170.0	170.2x2	170.1	170.0x3	174.5
	170.1	174.5a	170.2x2	174.7a'	
	174.8a		177.2a'		
glc C-1	100.9x2	101.0x3	100.9x2	100.9x2	100.7
	101.1		101.0x2	101.0x2	
glc C-2	75.2x3	75.1x3	75.1x4	74.8x4	74.9
glc C-3	78.5x3	78.5x3	78.5x4	78.2x4	78.2
glc C-4	71.8x3	71.7x3	71.7x4	71.4x4	71.6
glc C-5	78.0	78.0x3	78.0x4	77.7x4	77.8
	78.1x2				
glc C-6	62.9	63.0x3	63.0x4	62.8x4	62.6
	63.1x2				
Ac		21.9		22.1	
		174.8		175.1

(α,β -unsaturated ester) in the IR spectrum. In the negative FAB-MS, there was a molecular ion peak at m/z 1127 $[M-H]^-$ along with other fragment ions at m/z 771 $[M-H-m/z\ 356]^-$, 729 $[m/z\ 771-CH_2CO]^-$, 415 $[M-H-m/z\ 356 \times 2]^-$ and 373 $[m/z\ 415-CH_2CO]^-$ and its spectrum had a pattern similar to that of 1. The 1H -NMR spectrum of 2 showed the presence of an acetyl group at δ 2.13 and other signals were analogous to those of 1. Comparison of the 1H - and ^{13}C -NMR spectra of 2 with those of 1 disclosed that the chemical shifts due to the terminal C-10 position (hydroxymethyl) in 2 was shifted to δ_H 4.90 (m) and δ_C 64.2 (t), thus the acetyl group was attached to the terminal hydroxymethyl moiety (C-10) in 1. Therefore, the structure of 2 was concluded to be 10-O-acetylulmoidoside A.

Ulmoidoside C (3), $[\alpha]_D +9.5^\circ$, showed absorption bands similar to those of 1 in the IR (3432, 1702, 1636 cm^{-1}) and the UV 236 nm (log ϵ 4.51) spectra. The negative FAB-MS exhibited a molecular ion peak at m/z 1441 $[M-H]^-$ along with fragment ions at m/z 1085 $[M-H-m/z\ 356]^-$, 729 $[M-H-m/z\ 356 \times 2]^-$, 373 $[M-H-m/z\ 356 \times 3]^-$, suggesting that 3 was an ester tetramer of iridoid glycoside. On alkaline hydrolysis, 3 afforded 5. The 1H - and ^{13}C -NMR spectra of 3 showed peaks very similar to those of 1, except peaks in the ester part. Therefore, the structure of 3 was characterized as an ester tetramer of geniposidic acid as shown in the formula.

Ulmoidoside D (4), $[\alpha]_D +15.4^\circ$, showed the IR, UV and 1H - and ^{13}C -NMR spectra similar to those of 2. In the negative FAB-MS, a molecular ion peak at m/z 1483 $[M-H]^-$, together with other fragment ions at m/z 1127 $[M-m/z\ 356-H]^-$, 1085 $[m/z\ 1127-CH_2CO]^-$, 771 $[M-m/z\ 356 \times 2-H]^-$, 729 $[m/z\ 771-CH_2CO]^-$, 415 $[M-m/z\ 356 \times 3-H]^-$ and 373 $[m/z\ 415-CH_2CO]^-$ was observed, therefore the structure of 4 was determined to be the monoacetate of 3 as shown in the formula. This is the first report of the isolation of the ester trimer and tetramer of the iridoid glucoside from the plant.

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