

Polyester Type Sesquiterpene Alkaloids from *Euonymus japonica* (Structures of euojaponine-D, -F, -G, -J and -K)

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Abstract □ Five new sesquiterpene alkaloids, euojaponine-D, -F, -G, -J, and -K were isolated from the root bark of *Euonymus japonica* Thunb. and their structures were elucidated by various spectroscopic methods.

Keywords □ *Euonymus japonica*, Celastraceae, euojaponine, alkaloid, sesquiterpene, two-dimensional NMR.

Our previous papers^{1,2)} described the structure elucidations of some polyester type sesquiterpene alkaloids which were isolated from *Euonymus japonica* Thunb. and designated as euojaponine-A, -C, -I, -L and -M³⁾. Present paper describes the structures of new sesquiterpene alkaloids which were isolated in our continuing studies on the same plant and designated as euojaponine-D(1), -F(2), -K(3), -G(4) and -J(5).

The alkaloids in this paper have wilfordic acid as their dibasic acid moiety which links to sesquiterpe-

ne nucleus by cyclodiester bonds. And they have characteristics of having a number of acyl groups such as acetyl, benzoyl and/or nicotinoyl groups in the molecule. Linking sites of acyl groups to sesquiterpene moiety were determined unambiguously by the help of ¹H-¹³C long range COSY spectra. All the proton and carbon NMR peaks were assigned with ¹H-¹H COSY, ¹H-¹³C COSY and DEPT spectra as shown in Table I and Table II.

EXPERIMENTAL METHODS

Table I. ¹H-NMR spectral data of euojaponines (300MHz, CDCl₃)

No. of Proton	1	2	3	4	5
1	5.97 (d 3.5)	5.95 (d 3.8)	5.82 (d 3.7)	6.23 (d 4.0)	6.02 (d 3.5)
2	5.25 (dd 3.5,3.0)	5.25 (dd 3.8,2.7)	4.03 (dd 3.7,2.7)	5.66 (ddd 4.0,2.0,1.0)	4.12 (dd 3.5,2.0)
3	5.05 (d 3.0)	5.00 (d 2.7)	5.07 (d 2.7)	5.08 (d 2.0,1.0)	5.08 (d 2.5,1.0)
4				2.86 (qdd 8.0,1.0,1.0)	2.75 (qd 8.0,1.0)
5	5.39 (d 3.0)	6.96 (brs)	6.97 (brs)	6.68 (brs)	6.58 (d 1.0)
6	2.46 (d 4.5)	2.36 (d 4.0)	2.33 (d 4.0)	2.48 (d 4.0)	2.45 (dd 4.0, 1.0)
7	5.51 (dd 5.0,4.5)	5.53 (dd 5.7,4.0)	5.53 (dd 6.0,4.0)	5.58 (dd 6.0,4.0)	5.58 (dd 5.5,4.0)

8	5.40 (d 5.0)	5.42 (d 5.7)	5.51 (d 6.0)	5.48 (d 6.0)	5.42 (d 5.5)
11	4.70, 5.35 (ABq 13.5)	4.65, 5.41 (ABq 13.4)	4.79, 5.54 (ABq 13.5)	4.58, 5.64 (ABq 13.0)	4.75, 5.50 (ABq 13.2)
12	1.90 (d 1.0)	1.58 (d 1.0)	1.34 (d 1.2)	1.36 (d 8.0)	1.33 (d 8.0)
14	1.70(s)	1.70(s)	1.67(s)	1.70(s)	1.65(s)
15	3.77, 5.92 (ABq 13.0)	3.78, 5.75 (ABq 12.0)	3.79, 5.70 (ABq 11.9)	3.63, 5.63 (ABq 11.5)	3.63, 5.52 (ABq 11.5)
4'*	8.53	8.33	8.29	8.28	8.23
5'*	7.48	7.28	7.26	7.25	7.24
6'*	8.82	8.76	8.72	8.74	8.72
7'	3.13 (m)	2.95 (ddd 11.6,6.8,5.6)	3.79 (ddd 13.7,6.3,5.5)	3.03 (ddd 13.5,6.0,4.5)	3.06 (ddd 13.5,6.5,5.5)
	4.14 (m)	3.95 (ddd 11.6,9.9,5.9)	3.86 (ddd 13.7,9.4,6.5)	3.86 (ddd 13.5,6.0,4.5)	3.73 (ddd 13.5,10.0,6.5)
8'	1.93 (m)	1.98 (m)	1.97 (m)	2.01 (m)	2.02 (m)
	2.45 (m)	2.38 (m)	2.18 (m)	2.23 (m)	2.29 (m)
9'	2.35(m)	2.41(m)	2.36(m)	2.32(m)	2.29(m)
10'	1.22 (d 7.0)	1.20 (d 6.8)	1.12 (d 7.0)	1.18 (d 7.0)	1.13 (d 6.5)
2-Ac	2.14	2.14	(OH)	2.18	(OH)
5-Ac	(OH)	2.18	2.17	(Nic)	2.21
7-Ac	2.12	2.13	2.12	2.16	2.15
8-Ac	1.41	1.42	1.41	1.41	1.44
11-Ac	2.22	2.32	2.29	2.23	2.24
(1-Bz)**					
<i>ortho</i>	7.82	7.83	7.95	7.80	8.02
<i>meta</i>	7.38	7.40	7.40	7.33	7.45
<i>para</i>	7.54	7.53	7.54	7.52	7.58
(5-Nic)***					
2''				9.29	
4''				8.35	
5''				7.47	
6''				8.85	

* *J* values of pyridinic protons of wilfordic acid

4'(dd, 7.8-8.1, 1.8-2.0)

5'(dd, 7.8-8.1, 4.8-4.9)

6'(dd, 4.8-4.9, 1.8-2.0)

** *J* values of benzoyl groups*ortho*(dd, 8.5, 1.4-1.5)*meta*(dd, 8.5, 7.5-8.0)*para*(dd, 7.5-8.0, 1.4-1.5)*** *J* values of nicotinoyl group

2''(d, 1.5)

4''(ddd, 8.0, 1.5, 1.5)

5''(dd, 8.0, 5.0)

6''(dd, 5.0, 1.5)

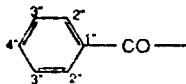
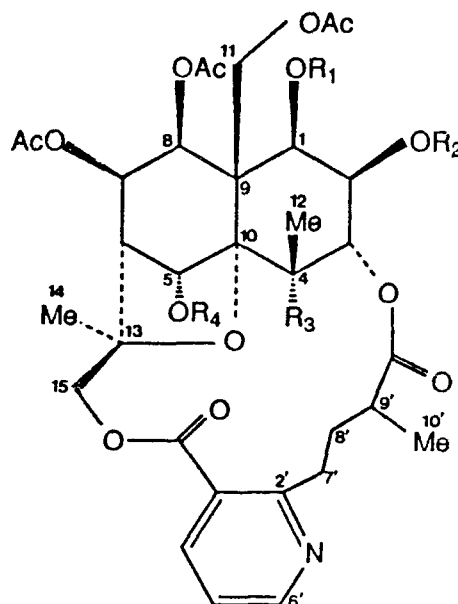


Table II. ^{13}C -NMR spectral data of euojaponines (75 MHz, CDCl_3)

No. of	1	2	3	4	5
1	73.47	73.53	75.46	73.68	76.20
2	69.90	69.78	70.64	72.51	71.28
3	75.03	75.86	78.16	74.54	76.01
4	71.89	69.88	69.81	36.92	37.08
5	74.12	73.76	73.95	74.20	74.42
6	52.38	51.03	50.98	50.45	50.36
7	69.13	68.95	68.97	68.83	69.04
8	71.76	71.54	71.86	71.38	72.05
9	51.19	52.46	52.80	50.86	51.21
10	92.82	93.85	94.14	90.66	91.25
11	60.99	60.21	60.55	60.64	60.84
12	23.40	22.65	22.67	12.28	15.18
13	85.22	84.60	84.24	83.00	82.68
14	18.03	17.87	17.87	18.15	18.08
15	71.24	70.44	70.33	69.29	69.57
2'	165.03	163.97	163.72	162.95	162.69
3'	123.86	124.51	124.58	124.97	125.87
4'	138.72	139.09	138.71	138.81	138.48
5'	121.24	121.30	121.09	121.10	120.95
6'	153.46	152.76	152.96	152.35	152.39
7'	32.95	33.12	33.22	32.56	32.88
8'	33.43	33.28	33.40	33.21	33.26
9'	38.10	38.36	38.54	37.41	37.70
10'	19.08	18.83	18.57	19.20	18.89
11'	175.24	175.03	175.75	175.88	176.23
12'	168.85	166.62	169.06	168.95	169.07
2-Ac	20.93*	20.88	(OH)	20.95	(OH)
5-Ac	(OH)	22.57*	21.46	(Nic)	21.39
7-Ac	20.91*	20.95*	20.94	21.12	20.96
8-Ac	19.90	19.92	19.98	19.87	19.98
11-Ac	21.49	22.38	21.57	21.38	21.45
1-CO	168.34*	164.77	165.00	164.83	165.05
2-CO	167.00*	170.00*	(OH)	163.76	(OH)
5-CO	(OH)	168.37*	169.87	165.71	166.12
7-CO	169.86	169.84*	170.05	170.47	170.08
8-CO	169.86	168.91	169.06	169.59	169.93
11-CO	169.86	170.33	170.18	170.01	170.00
(1-Bz)					
<i>ipso</i>	130.00	129.21	129.31	129.09	129.36
<i>ortho</i>	129.45	129.46	129.64	129.49	129.69
<i>meta</i>	128.36	128.46	128.50	128.46	128.55

<i>para</i>	133.34	133.43	133.53	133.47	133.59
(1-Nic)					
2''				151.06	
3''				125.64	
4''				137.32	
5''				123.62	
6''				154.07	

* exchangeable in each column



	R ₁	R ₂	R ₃	R ₄
1	COPh	Ac	OH	H
2	COPh	Ac	OH	Ac
3	COPh	H	OH	Ac
4	COPh	Ac	H	nicotinoyl
5	COPh	H	H	Ac

The root bark (8kg) of *Euonymus japonica* Thunb. collected in December, 1987 at Mt. Naejang, Korea was powdered and extracted with MeOH (45 L) and concentrated to give a residue (900g). The residue was partitioned between Et₂O and H₂O, and the Et₂O layer was concentrated (80g) and dissolved in MeOH (2 L) and then treated with Pb(OH)Ac aq. solution in order to remove phenolic compounds as precipitate. The precipitate was filtered off and washed with MeOH, and the filtrate was concentrated to give a residue of alkaloidal mixture (11g).

The alkaloidal mixture was chromatographed on silica gel (420g) developed successively with *n*-hexane/EtOAc/*iso*-PrOH (100:100:2 and 100:300:3). Fr. 1-5 (1.5 g), Fr. 6 (400 mg), Fr. 7-9 (1.0 g), Fr. 10-11 (1.1 g), Fr. 12 (1.9 g), Fr. 13 (1.1 g), Fr. 14 (780 mg) and Fr. 15-17 (1.4 g). Fr. 12 was chromatographed on silica gel with CHCl₃/MeOH (30:1) to give fr. 12-1 and fr. 12-2. Fr. 12-1 was chromatographed on silica gel with Benzene/EtOAc (2:1) to yield euojaponine-D, -F, -G containing fractions (fr. D, fr. F and fr. G). Fr. D and fr. F were further purified by semi-preparative HPLC[RP-18 column, MeOH/H₂O (gradient)] to give euojaponine-D (18 mg) and euojaponine-F (164 mg). Fr. G was chromatographed on alumina with Benzene/EtOAc (2:1) and euojaponine-G was crystallized in EtOH (18 mg). Fr. 12-2 was chromatographed on silica gel with CHCl₃/MeOH (50:1→10:1) to give fr. J and fr. K. Fr. J and fr. K was further purified by semi-preparative HPLC[RP-18 column, MeOH/H₂O (65:35)] to yield euojaponine-J (12 mg) and euojaponine-K (160 mg).

Euojaponine-D (1). C₄₁H₄₇NO₁₇, Mp 253 °; UV λ_{max} (CH₃CN), nm (ε): 229 (18600), 268 (3900); SIMS *m/z*: 826[M+]⁺, 848[M+Na]⁺; ¹H-NMR (Table I). ¹³C-NMR (Table II).

Euojaponine-F (2). C₄₃H₄₉NO₁₈, Mp 142 °; UV λ_{max} (EtOH), nm (ε): 231 (18900), 272 (3800); SIMS *m/z*: 868 [M+H]⁺; ¹H-NMR (Table I). ¹³C-NMR (Table II).

Euojaponine-K (3). C₄₁H₄₇NO₁₇, Mp 188 °; UV λ_{max} (CH₃CN), nm (ε): 229 (20000), 268 (4000); SIMS *m/z*: 826 [M+H]⁺, 848 [M+Na]⁺; ¹H-

NMR (Table I). ¹³C-NMR (Table II).

Euojaponine-G (4). C₄₇H₅₀N₂O₁₇, Mp 143 °; UV λ_{max} (EtOH), nm (ε): 227 (18600), 265 (5700); SIMS *m/z*: 915 [M+H]⁺; ¹H-NMR (Table I). ¹³C-NMR (Table II).

Euojaponine-J (5). C₄₁H₄₇NO₁₆, Mp 243 °; UV λ_{max} (EtOH), nm (ε): 229 (15500), 270 (3400); SIMS *m/z*: 810 [M+H]⁺; ¹H-NMR (Table I). ¹³C-NMR (Table II).

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