

Two New Phenolic Glycosides from the Roots of *Rhododendron molle*

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Abstract: Two new phenolic glycosides, everninic acid methyl ester-2-O- β -D-xylopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside **1** and 7-hydroxy-5-methoxyphthalide-7- β -D-xylopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside **2** were isolated from the roots of *Rhododendron molle* G. Don. Their structures were determined by spectral evidence including 2D NMR techniques.

Keywords: *Rhododendron molle*, Ericaceae, everninic acid methyl ester-2-O- β -D-xylopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside, 7-hydroxy-5-methoxyphthalide-7- β -D-xylopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside.

Rhododendron molle G. Don (Ericaceae) has long been used in China for insecticidal and medicinal purposes¹. Many diterpenes and phenolic compounds have been isolated from the fruits and flowers of this plant before^{2,3}. However, chemical constituents of the plant roots were never reported. As a part of our study on the active principles of traditional Chinese medicines, we investigated the chemical constituents of the roots of *R. molle*. Two new phenolic glycosides **1** and **2** were isolated. This paper describes the isolation and structure elucidation of **1** and **2**.

Compound **1** was obtained as amorphous powder, possessing a molecular formula of C₂₁H₃₀O₁₃ by FABMS data (m/z 513 [M+Na]⁺, 491 [M+H]⁺) in conjunction with its ¹H and ¹³C NMR data (**Table 1**). The IR spectrum showed the absorption bands of hydroxyl (3470 cm⁻¹), aromatic (1608, 1496 cm⁻¹) and ester carbonyl (1710, 1045 cm⁻¹) groups. Acidic hydrolysis of **1** afforded D-glucose and D-xylose, detected by co-TLC with authentic samples. The ¹H NMR spectrum showed the signals for a pair of meta-coupled aromatic protons (δ_{H} 6.51, d; 7.24, d, each 1H $J = 2$ Hz), an aromatic methyl (δ_{H} 2.32, s, 3H) and two methoxyls (δ_{H} 3.73, s; 3.86, s, each 3H). Besides one D-glucose and one D-xylose units, the ¹³C NMR and DEPT spectra revealed 10 carbons, representing a 1, 2, 4, 6-tetra-substituted aromatic ring (δ_{C} 118.18 s, 157.46 s, 101.58 d, 161.90 s, 110.18 d, 138.22 s), a methyl (δ_{C} 19.93 q), a methoxyl (δ_{C} 55.46 q) and a benzoic acid methyl ester (δ_{C} 168.8 s, 51.95 q). The substituted pattern as 2-glycosyl-4-methoxyl-6-methyl benzoic acid methyl ester (everninic methyl ester) was deduced by HMBC experiment (**Table 2**), in which the important correlation was observed between H-1' of D-glucose (δ_{H} 5.47) to C-2 (δ_{C} 157.46), suggesting that the D-glucose should be connected to C-2 with β -configuration due to larger coupling

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constant ($J_{1,2} = 7.6$ Hz). The selected HMBC correlation was shown in **Figure 2**. The NOESY correlation between H-3/OCH₃ (3.73, s, 3H), H-3/H-1', H-5/OCH₃ (3.73, s, 3H), H-5/H-9 (2.32, s, 3H) also confirmed the above deduction (**Figure 1**). In comparison of ¹H and ¹³C NMR data of sugar moiety in **1** with that of methyl-β-D-glucopyranoside⁴, the downfield shift of C-6' was observed due to glycosylation, indicating that D-xylose should be linked to C-6' of the D-glucose. The HMBC spectrum showed the cross peak between H-1'' (δ_{H} 4.90, d) of xylose and C-6' (δ_{C} 70.20 t) of glucose, confirming the 1→6 linkage of the D-xylose to the D-glucose. The β-configuration of D-xylose was also suggested by coupling constant of the anomeric proton (δ_{H} 4.90, d, $J_{1'',2''} = 7.5$ Hz). Thus compound **1** was elucidated as evernicic acid methyl ester-2-O-β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside.

Compound **2** was obtained as amorphous powder, possessing a molecular formula of C₂₀H₂₆O₁₃ by FABMS data (m/z 497 [M+Na]⁺, 474 [M+H]⁺) and its ¹H and ¹³C NMR data (**Table 1**). The IR spectrum showed absorption bands for hydroxyl (3587, 3338 cm⁻¹), aromatic (1612, 1494 cm⁻¹) and α,β-unsaturated γ-lactone carbonyl (1726 cm⁻¹) groups. Acidic hydrolysis of **2** afforded D-glucose and D-xylose, detected by co-TLC with authentic samples. There were striking resemblances between ¹H and ¹³C NMR data (**Table 1**) of sugar moiety in **2** and **1**, indicating that **2** also contained a β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl group. Besides sugar moiety, ¹H, ¹³C NMR and DEPT data of **2** revealed the signals for a 1, 2, 3, 5 tetra-substituted aromatic ring (δ_{H} 6.51, s, 7.22, s, each 1H; δ_{C} 151.80 s, 107.42 s, 158.06 s, 102.91 d, 166.83 s, 100.24 d), a methoxyl (δ_{H} 3.79, s, 3H; δ_{C} 56.10 q), oxygenated methylene (δ_{H} 5.13, s, 2H; δ_{C} 68.77 t) and a α,β-unsaturated γ-lactone carbonyl (δ_{C} 168.83 s). On the basis of various 2D NMR techniques, the aglycone was determined as 7-hydroxyl-5-methoxyphthalide and sugar moiety connected to 7-hydroxyl group. The important HMBC correlation (**Table 2**) was observed between H-4/C-5, H-4/C-8, H-4/C-3, H-6/C-7, H-6/C-8, OCH₃/C-5 and H-1'/C-7, respectively. The selected HMBC correlation were shown in **Figure 2**. The NOESY correlation between H-4/OCH₃ (3.79, s, 3H), H-4/H-3 (5.13, s, 2H), H-6/OCH₃ (3.79, s, 3H) and H-6/H-1' were also observed (**Figure 1**). Thus, compound **4** was elucidated as 7-hydroxy-5-methoxyphthalide-7-β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside. All the ¹H and ¹³C NMR signals were unambiguously assigned by 2D NMR experiments.

Figure 1 Significant NOESY correlation for **1** and **2**

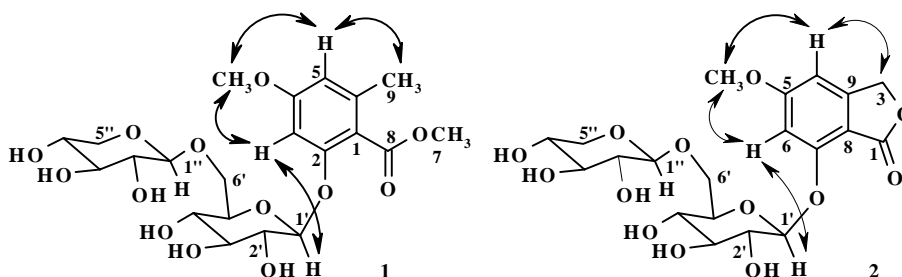


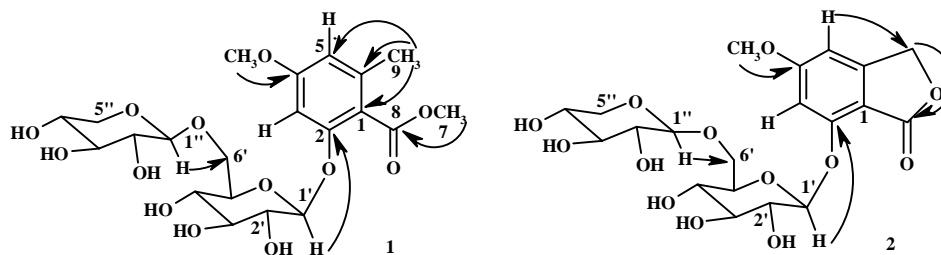
Table 1 ^1H and ^{13}C NMR spectra data of **1-2** in pyridine- d_5 ^a

No. C	δ_{H} (J, Hz)		δ_{C}	
	1	2	1	2
1			118.18 s	168.83 s
2			157.46 s	
3	7.24 (d, 2)	5.13 (s)	101.28 d	68.77 t
4		6.51 (s)	161.90 s	100.24 d
5	6.51 (d, 2)		110.18 d	166.91 s
6		7.22 (s)	138.22 s	102.91 d
7	3.86 (s)		51.95 q	158.06 s
8			168.76 s	107.42 s
9-CH ₃	2.32 (s)		19.93 q	151.80 s
OMe	3.73 (s)	3.79 (s)	55.46 q	56.10 q
Glc-1'	5.47 (d, 7.6)	5.78 (d, 7.3)	103.58 d	101.80 d
2'	4.18 (m)	4.36 (m)	74.79 d	74.28 d
3'	4.27 (m)	4.30 (m)	78.39 d	78.53 d
4'	4.23 (m)	4.23 (m)	71.06 d	71.00 d
5'	4.20 (m)	4.35 (m)	77.46 d	77.57 d
6'	4.77 (m), 4.30 (m)	4.78 (m), 4.33 (m)	70.20 t	69.95 t
Xly-1''	4.90 (d, 7.6)	4.90 (d, 7.6)	106.11 d	106.16 d
2''	4.00 (dd, 7.6, 8.5)	4.02 (dd, 7.6, 8.5)	74.93 d	74.94 d
3''	4.12 (t, 8.5)	4.11 (t, 8.5)	78.20 d	78.22 d
4''	4.19 (m)	4.23 (m)	71.20 d	71.07 d
5''	4.30 (m), 3.63 (m)	4.30 (m), 3.61 (m)	67.11 t	67.13 t

a. ^1H NMR recorded at 500 MHz and ^{13}C NMR at 125 MHz

Table 2 HMBC correlation for **1** and **2**

No. H	1	2	No. H	1	2
3	C-4, C-2, C-1, C-5	C-8, 4, 1	3'	C-2', C-4'	C-2', C-4'
4		C-8, 6, 5, 3	4'	C-6'	C-6'
5	C-1, C-3, C-4, C-9		5'		
6		C-5, 7, 8, 4	6'	C-5', C-1''	C-5', C-1''
7	C-8		Xly-1''	C-6'	C-6'
9	C-1, C-5, C-6		2''	C-1'', 3''	C-1'', 3''
OMe	C-4	C-5	3''	C-4'', 2''	C-4'', 2''
Glc-1'	C-2, C-5'	C-7	4''		
2'	C-1', C-3'	C-4', 3', 1'	5''	C-1'', 4''	C-1'', 4''

Figure 2 Significant HMBC (H-C) correlation for **1** and **2****Acknowledgment**

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