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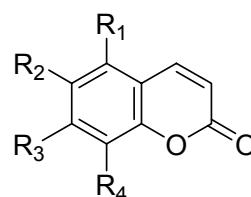
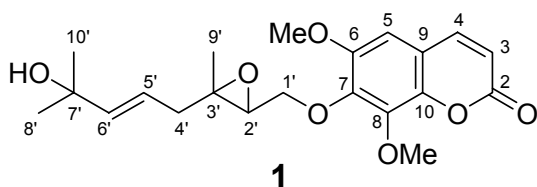
NEW COUMARINS FROM THE *AILANTHUS ALTISSIMA*

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Abstract – Two new coumarin derivatives were isolated together with three known coumarins, artelin (**3**), isofraxidin (**4**), and scoploetin (**5**) from the bark of *Ailanthus altissima* (Simaroubaceae). New coumarin derivatives were elucidated as terpenylated coumarins, named altissimacoumarin A (**1**) and altissimacoumarin B (**2**), respectively. *Trans*-Configuration of between C-2' and C-9' in compound (**1**) was clearly confirmed by NOESY experiments.

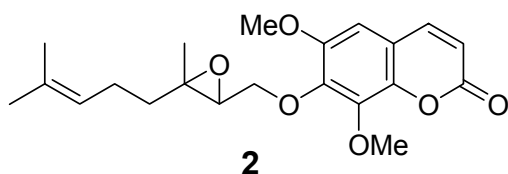
Ailanthus altissima is classified in the subfamily Simaroubaceae, which has been used for a treatment of colds and gastric diseases in Chinese traditional medicine.^{1,2} Previous researches revealed that *A. altissima* has many pharmacologically active constituents such as quassinoids,^{3,4} alkaloids⁵ and lipids.⁶ In continuing chemical studies on medicinal plants, we investigated the chemical constituents from this species. A methanol extract of the bark of *A. altissima* gave two new terpenylated coumarins, named altissimacoumarin A (**1**) and altissimacoumarin B (**2**) as well as three known coumarins, artelin (**3**), isofraxidin (**4**), and scoploetin (**5**).



3 R₁=R₂=R₃=R₄=OMe

4 R₁=H, R₂=R₄=OMe, R₃=OH

5 R₁=R₄=H, R₂=OMe, R₃=OH



The known compounds, artelin (**3**), isofraxidin (**4**), and scoploetin (**5**) were identified by comparison of their spectral data with literature data.^{7,8} The molecular formula of compound (**1**) was established as C₂₁H₂₆O₇ by HRMS ($m/z = 390.1677$) and DEPT results of ¹³C-NMR spectra. Base peak in MS fragment at m/z 222 [M-168]⁺ suggested the presence of a isofraxidin moiety. The lactonic group in coumarin skeleton was confirmed with a absorption at 1730 cm⁻¹ in IR spectrum. In the ¹H-NMR spectrum, the splitting patterns of a pair of doublets [δ 6.35 and 7.62 (each 1H, d, $J = 9.5$ Hz)], a one-proton singlet at δ 6.68 (1H, s), and two methoxy signals [δ 3.89 and 4.04 (each 3H, s)] were consistent with those of the isolated isofraxidin (**4**). Hence, the extra ten carbons in ¹³C-NMR spectrum were deduced the signals from terpenyl group. The terpenyl group was confirmed with ¹H-¹H COSY spectrum which revealed successive connectivities from C-1' to C-2' and from C-4' to C-6'. Unassigned connectivities of terpenyl group, C-4'/C-9' and C-2'/C-9', were determined on the basis of HMBC correlations (Figure 2). The proton at δ 3.24 and carbon at δ 60.5 suggested the presence of oxiran ring. Finally, the tertiary hydroxy group was confirmed with a absorption at 3450 cm⁻¹ in IR spectrum. This oxygenated terpenyl group was attached to the C-7 position because the H-1' proton resonating at δ 4.26 displayed HMBC connectivity with C-7. Thus, compound (**1**) was clearly defined as 7-(3',7'-dimethyl-7-hydroxy-2',3'-oxy-5-octenyl)oxyisofraxidin, named altissimacoumarin A. The *trans* configurations of the H-2' and H-9' were determined by 2D-NOESY experiments. NOE cross peaks were observed between H-2' and H-4', whereas NOE was not at H-2' and H-9'. Moreover, strong NOE cross peaks were observed between H-1' and H-9' (Figure 1).

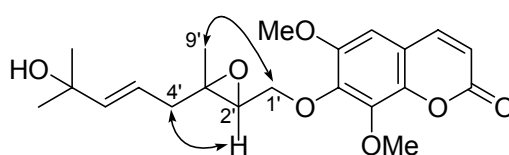
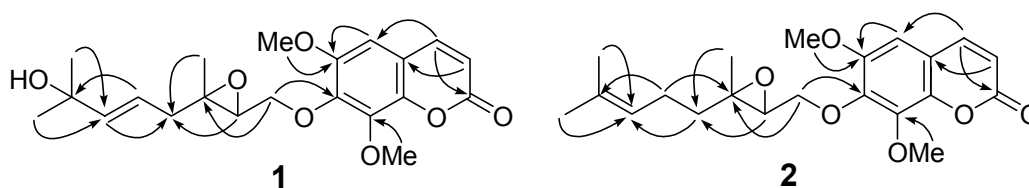


Figure 1 Selected NOE correlations of **1**

Compound (**2**) was found to have the molecular formula of C₂₁H₂₆O₆ from HRMS ($m/z = 374.1730$) and DEPT results of ¹³C-NMR spectra. Base peak in MS fragment at m/z 222 [M-152]⁺ suggested the presence of a isofraxidin moiety which showed same pattern of ¹H- and ¹³C-NMR data with compound **1**. The terpenyl group was also determined on the basis of ¹H-¹H COSY and HMBC correlations (Figure 2). The proton at δ 3.21 and carbon at δ 60.8 suggested the presence of oxiran ring in terpenyl group. This oxygenated terpenyl group was attached to the C-7 position because the H-1' proton resonating at δ 4.25 displayed HMBC connectivity with C-7. Thus, compound (**2**) was clearly defined as 7-(3',7'-dimethyl-2',3'-epoxygeranyl)oxyisofraxidin, named altissimacoumarin B; it showed optical activity with $[\alpha]_D^{20} +18.2^\circ$ (c , 0.50, CHCl₃).

Figure 2 Important HMBC correlations of **1** and **2**Table 1. The ^1H - and ^{13}C -NMR spectral data of **1** and **2** (CDCl_3)

Position	1		2	
	^1H	^{13}C	^1H	^{13}C
2	-	160.7 s	-	160.7 s
3	6.35 (1H, d, 9.5)	115.9 d	6.34 (1H, d, 9.5)	115.8 d
4	7.62 (1H, d, 9.5)	143.7 d	7.66 (1H, d, 9.5)	143.7 d
5	6.68 (1H, s)	104.3 d	6.67 (1H, s)	104.2 d
6	-	150.6 s	-	150.6 s
7	-	143.0 s	-	145.1 s
8	-	141.9 s	-	141.9 s
9	-	115.2 s	-	115.1 s
10	-	143.3 s	-	143.3 s
1'	4.26 (2H, dd, 2.1, 5.6)	72.6 t	4.25 (2H, m)	72.9 t
2'	3.24 (1H, t, 5.6)	60.0 d	3.21 (1H, t, 6.1)	60.9 d
3'	-	60.5 s	-	60.8 s
4'	2.34 (2H, m)	41.1 t	1.66 (1H, m) 1.53 (1H, m)	38.7 t
5'	5.65 (1H, m)	125.7 d	2.08 (2H, dd, 12.9, 25.7)	23.9 t
6'	5.65 (1H, m)	137.9 d	5.10 (1H, m)	123.8 d
7'	-	82.3 s	-	132.4 s
8'	1.32 (3H, s)	24.5 q	1.61 (3H, s)	18.0 q
9'	1.26 (3H, s)	17.4 q	1.25 (3H, s)	17.1 q
10'	1.32 (3H, s)	24.6 q	1.68 (3H, s)	26.0 q
6-OMe	3.89 (3H, s)	56.8 q	3.90 (3H, s)	56.7 q
8-OMe	4.04 (3H, s)	62.2 q	4.05 (3H, s)	62.2 q

EXPERIMENTAL

Plant materials. Bark materials of *Ailanthus altissima* Swingle were collected in Jinju (Korea) and identified by Prof. Myong Gi Chung. A voucher specimen (*S. W. Hwang & M. S. Yang 022*) of this raw material is deposited at Herbarium of the Gyeongsang National University (GSNU).

General experimental procedures. Optical rotations were obtained using a Perkin-Elmer polarimeter. IR spectra were recorded on a Bruker IFS66 and UV spectra were measured on a Beckman DU650 spectrophotometer. ^1H and ^{13}C -NMR spectra along with 2D-NMR spectral data were obtained on a Bruker AM 500 (^1H -NMR at 500 MHz, ^{13}C -NMR at 125 MHz) spectrometer in CDCl_3 solution. EIMS and HREIMS spectra were recorded on a JEOL JMS-700 instrument operated at 70eV.

Extraction and Isolation. The air-dried bark (2 kg) of *A. altissima* was extracted with MeOH (10 L \times 3) at rt for 72 h. The combined extract was concentrated *in vacuo* to afford a brown gum (120 g), which was partitioned with chloroform and water. The chloroform layer was washed with brine, dried over Na_2SO_4 , and then concentrated to give a thickish residue (36 g). The residue was chromatographed

on a silica gel (500 g) column eluted with a gradient of 100% chloroform to 100% MeOH to afford 72 fractions (F1-F72, each 250 mL). F 25-32 were combined and applied to a silica gel column, eluted with hexane-ethyl acetate mixtures of increasing polarity (49 : 1 → 1 : 1, each 50 mL), to give 40 subfractions (A1-A40). Fractions A21-A25 were further purified with silica gel chromatography eluting with hexane and ethyl acetate (9 : 1 → 1 : 1) to afford compound **(1)** (10 mg, $R_f=0.32$, hexane-ethyl acetate = 1 : 1), **3** (18 mg, $R_f=0.71$, hexane-ethyl acetate = 1 : 1), and **4** (15 mg, $R_f=0.45$, hexane-ethyl acetate = 1 : 1). Fractions A26-A29 were further purified with silica gel chromatography eluting with chloroform and acetone (49 : 1 → 1 : 1) to afford compound **(2)** (28 mg, $R_f=0.75$, chloroform-acetone = 9 : 1) and **5** (15 mg, $R_f=0.42$, chloroform-acetone = 9:1).

Altissimacoumarin A (1): $[\alpha]_D^{20} +11.1^\circ$ (c , 0.50, CHCl_3); UV λ_{max} : 223, 293, 333, 339 nm (MeOH); IR ν_{max} (KBR) cm^{-1} : 3436, 1732 nm; EIMS: $m/z = 390$ $[\text{M}]^+$ (4.8), 372 (7.5), 222 (100), 207 (14), 179 (7.5), 150 (11.2), 107 (22.1); HREIMS: $m/z = 390.1677$ (calcd for $\text{C}_{21}\text{H}_{26}\text{O}_7$ 390.1679); ^1H - and ^{13}C -NMR (see Table 1).

Altissimacoumarin B (2): $[\alpha]_D^{20} +18.2^\circ$ (c , 0.50, CHCl_3); UV λ_{max} : 225, 293, 339, 395 nm (MeOH); IR ν_{max} (KBR) cm^{-1} : 1732, 1565, 1458 nm; EIMS: $m/z = 374$ $[\text{M}]^+$ (7.5), 252 (9.2), 222 (100), 221 (10.2), 207 (9.9), 150 (5.2), 135(10.2); HREIMS: $m/z = 374.1730$ (calcd for $\text{C}_{21}\text{H}_{26}\text{O}_6$ 374.1729); ^1H - and ^{13}C -NMR (see Table 1).

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