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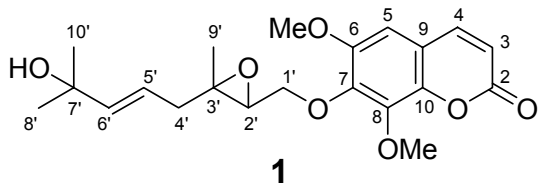
NEW COUMARINS FROM THE *AILANTHUS ALTISSIMA*

Seon Woo Hwang,[a] Jong Rok Lee,[b] Jun Lee,[a] Hyun Sook Kwon,[a] Min Suk Yang,[a] and Ki Hun Park *,[a]

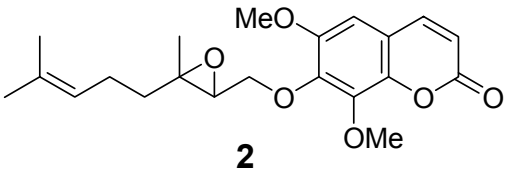
[a]Division of Applied Life Science, Gyeongsang National University, Jinju 660-701, Korea, [b]Research Center of Biomedical Resources of Oriental Medicine, Daegu Haany University, Daegu 706-828, Korea; E-mail: khpark@gsnu.ac.kr

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] alkaloids[5] 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**).



1



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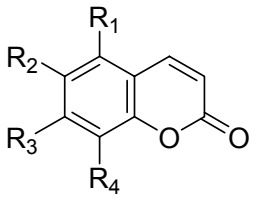

3 $R_1=R_2=R_3=R_4=OMe$

4 $R_1=H$, $R_2=R_4=OMe$, $R_3=OH$

5 $R_1=R_4=H$, $R_2=OMe$, $R_3=OH$

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 $C_{21}H_{26}O_7$ by HRMS (*m/z* = 390.1677) and DEPT results of ^{13}C-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 ^{1}H-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 ^{13}C-NMR spectrum were deduced the signals from terpenyl group. The terpenyl group was confirmed with ^{1}H-^{1}H 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).

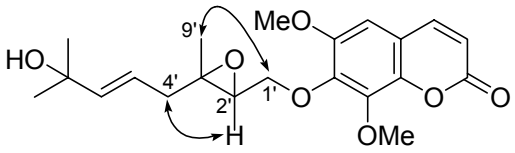

Figure 1 Selected NOE correlations of **1**

Compound (**2**) was found to have the molecular formula of $C_{21}H_{26}O_6$ from HRMS (*m/z* = 374.1730) and DEPT results of ^{13}C-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 ^{1}H- and ^{13}C-NMR data with compound **1** . The terpenyl group was also determined on the basis of ^{1}H-^{1}H 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° (*c*, 0.50, $CHCl_3$).

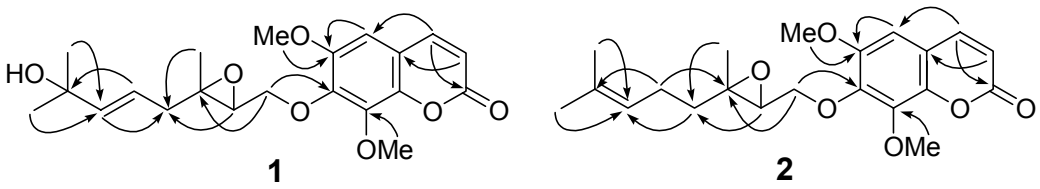

Figure 2 Important HMBC correlations of **1** and **2**

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

Position	***1***		***2***	
	^{1}H	^{13}C	^{1}H	^{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. ^{1}H and ^{13}C-NMR spectra along with 2D-NMR spectral data were obtained on a Bruker AM 500 (^{1}H-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×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° (*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 $[M]^+$ (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 $C_{21}H_{26}O_7$ 390.1679); ^{1}H- and ^{13}C-NMR (see Table **1**).

Altissimacoumarin B (2): $[\alpha]_D^{20}$ +18.2° (*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 $[M]^+$ (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 $C_{21}H_{26}O_6$ 374.1729); ^{1}H- and ^{13}C-NMR (see Table **1**).

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