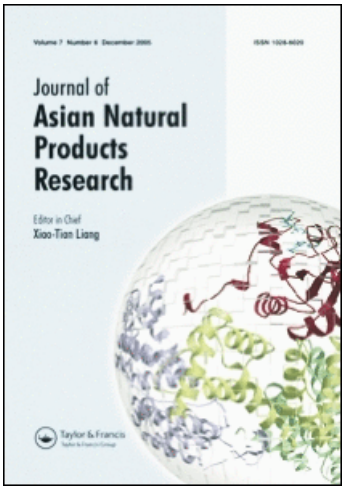

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Two new alkaloidal glycosides from the root bark of *Ailanthus altissima*

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Two new alkaloidal glycosides, canthin-6-one-5-*o*-β-D-xylopyranosyl- (1 → 6)-β-D-glucopyranoside (**1**) and canthin-6-one-1-*o*-β-D-xylopyranosyl- (1 → 6)-β-D-glucopyranoside (**2**) named ailantcanthinosides A and B, were isolated from the root bark of *Ailanthus altissima*. Their structures were elucidated by one-and two-dimensional ^{1}H NMR, ^{13}C NMR, FAB-MS, HRESI-MS spectra and chemical methods.

Keywords: *Ailanthus altissima* (Mill.); Simaroubaceae; Alkaloidal glucosides; Ailantcanthinoside A; Ailantcanthinoside B

1. Introduction

Ailanthus altissima (Mill.) Swingle is a large tree indigenous to India and South-east Asia, belonging to the Simaroubaceae. Its root bark is used in Chinese traditional medicine as a remedy for dyspepsia, dysentery, bronchitis, ophthalmia, snakebites under the name of 'chun pi' [1]. Previous reports on phytochemistry studies of this genus showed that it contains alkaloids [2–6], quassinoids [7–9], triterpenoid [10], steroid [11] and phenolic glycosides [12]. In this paper, we wish to report on the isolation and structural elucidation of two new alkaloidal glycosides from the root bark of *Ailanthus altissima*. Their structures have been established as canthin-6-one-5-*o*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (**1**) and canthin-6-one-1-*o*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (**2**), named ailantcanthinosides A and B.

2. Results and discussion

Ailantcanthinoside A (**1**) was obtained as a white powder from MeOH, mp 200–202°C, Positive reaction towards both Dragendorff's and Mayer's reagents as well as its acid

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solubility revealed the alkaloid nature of **1**. The IR spectrum exhibited strong absorptions for sugar (3389, 1049–1072 cm^{-1}), phenyl and α,β-unsaturated carbonyl groups (1606,1667 cm^{-1}) respectively, and its UV spectrum (225, 304, 343, 358, 376 nm) was very similar to that of canthin-6-one [3], HRESI-MS gave a $[M + 1]^+$ ion at *m/z* 531.1602 and $[M + Na]^+$ ion at *m/z* 553.1418 compatible with the molecular formula of $C_{25}H_{26}N_2O_{11}$. The ^1H NMR spectrum suggested the presence of one AX system at δ 7.80 and 8.80 (each 1H, d, $J = 5.2$ Hz) for H-1 and H-2 as well as four mutually coupled aromatic protons at δ 8.70 (1H, d, $J = 8.0$ Hz), 7.62 (1H, dt, $J = 1.5$, 8.0 Hz), 7.48 (1H, dt, $J = 1.5$, 8.0 Hz) and 8.10 (1H, d, $J = 8.0$ Hz), which were attributed to H-8, H-9, H-10, and H-11. One singlet at δ 8.20 (1H, s) was assigned to H-4. There were also two anomeric proton signals at δ 5.77 (1H, d, $J = 8.5$ Hz) and 4.97 (1H, d, $J = 8.5$ Hz), which indicated that the glycosyl linkage is β-configuration. The ^{13}C NMR and DEPT spectra of **1** showed 25 carbon signals including two methylenes, 16 methines, and seven quaternary carbons. Two of them were anomeric carbons at δ 102.5 and 105.6, respectively. The IR, ^1H NMR and ^{13}C NMR spectral data of **1** showed very similar features to those of canthin-6-one [3,13]. Acid hydrolysis of **1** produced xylose and glucose, identified by paper partition chromatography with authentic samples. The EI-MS of **1** showed an aglycone ion at *m/z* 236, an ion at *m/z* 208 and an another important ion at *m/z* 180 in its EI-MS, corresponding to the loss of 2C=O from the aglycone ion [236–56] [14,15]. By comparing the data of ^1H NMR and ^{13}C NMR of **1** with those of bruceacanthinoside, which had been isolated by Japanese researcher from the Indonesian medicine plant *Brucca javanica* (Simaroubaceae) [16], there was a similar distinct glycosylation effect at C-5, indicating that the position of sugars attachment with aglycone in **1** was the same as that of bruceacanthinoside, and the ^{13}C NMR spectra of **1** were in good agreement with 5-hydroxycanthin-6-one moiety of bruceacanthinoside, except for a β-D-xylopyranosyloxyl moiety at C-5 in place of a glucopyranosyloxyl. In order to confirm the structure of **1**, the 2D NMR experiments (^1H–^1H COSY, HMBC, HMQC and NOESY spectra) were performed. The HMBC spectrum showed long-range correlations of H-4/C-6; H-10/C-8; H-11/C-9; H-2, H-11/C-14; H-1, H-4/C-15 and H-2/ C-16, respectively. The correlations between δ 5.77 (H-1′ of glc.) and 152.6 (C-5 of aglycone), 4.86, 4.35 (H-6′ of glc.) and 105.6 (C-1″ of xyl.), suggesting that the structure of aglycone moiety of **1** was 5-hydroxycanthin-6-one [15], further confirmed that the glucose was connected to the C-5 of aglycone moiety, which was also supported by its NOE correlation between H-1′ and H-4, as well as the xylose unit was connected to the C-6′ of glucose, based on the glycosylation shift of C-6′ of the ^{13}C NMR at downfield ($\Delta\delta = -7.0$). Thus, the structure of **1** was elucidated as canthin-6-one-5-*o*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (**1**) (figure 2).

Ailantcanthinoside B (**2**), a white amorphous powder from EtOH, mp 186–188°C, gave a positive Dragendorff's test, and displayed an intense green fluorescence in organic solvents. The IR spectrum showed absorption bands assignable to sugar moiety (3428–3301 and 1069–1043 cm^{-1}), α,β-unsaturated carbonyl group (1674 cm^{-1}) [14] of the amide function as well as the phenyl group (1604 cm^{-1}), and its UV spectrum (225, 358, 376 nm) was also quite similar to that of **1**, suggesting that **1** and **2** contained a similar structure skeleton. The molecular formula $C_{25}H_{26}N_2O_{11}$ was determined from its quasi-molecular ion peak $[M + Na]^+$ at *m/z* 553.2, and 531.3 $[M + H]^+$ of FAB-MS spectroscopy with ^1H NMR and ^{13}C NMR data. Its ^1H NMR, ^{13}C NMR, and DEPT spectral data inferred that **2** and **1** were isomers. The EI-MS of **2** showed a molecular ion of the aglycone at *m/z* 236 and a fragment

ion at *m/z* 208 corresponding to the loss of C=O from the aglycone ion[236–28] [14,15]. The ^{1}H NMR spectrum of **2** showed one AX systems at δ 7.98 and 6.87 (each 1H, d, $J = 10.0$ Hz) for H-4, H-5 as well as four mutually coupled aromatic protons at δ 8.81 (1H, d, $J = 8.0$ Hz), 7.61 (1H, dt, $J = 1.5$, 8.0 Hz), 7.37 (1H, dt, $J = 1.5$, 8.0 Hz) and 8.49 (1H, d, $J = 8.0$ Hz), which were attributed to H-8, H-9, H-10 and H-11, respectively. One singlet at δ 9.31 (1H, s) was assigned to H-2, two anomeric proton signals at δ 6.03 (1H, d, $J = 7.5$ Hz) and 4.95 (1H, d, $J = 7.5$ Hz) were attributable to β-glycosidic linkages. The ^{13}C NMR spectrum of **2** showed two anomeric carbon signals at δ 102.7 and 105.9. Finally, acid hydrolysis of **2** also produced xylose and glucose, identified by paper partition chromatography with authentic samples, and an aglycone. The ^{13}C NMR and DEPT spectra of the aglycone showed the presence of seven sp^2 CH and seven quaternary carbons in which one was a carbonyl at δ 160.0 and its mass spectral pattern also resembled to that reported for canthinones [14–16]. All the ^{1}H NMR and ^{13}C NMR spectral data and MS fragmentation pattern of the aglycone were in good agreement with those reported for the 1-hydroxycanthin-6-one [14]. A combination of NMR experiments (COSY, HMBC, HMQC, ^{1}H and ^{13}C DEPT spectra) determined the assignments of all protons and carbons. The connectivities of the glucose with xylose unit and sugars with the aglycone moiety were established on the basis of HMBC correlations between δ 6.03 (1H,d, $J = 7.5$ Hz, H-1′ of β-D-glc.) and 150.7 (C-1 of aglycone), 4.84, 4.40 (H-6′ of glc.) and 105.9 (C-1″ of xyl.), thus suggesting that glucose was connected to the C-1 of aglycone and the xylose unit was connected to C-6′ of glucose. Additionally, the NOESY spectrum showed the presence of the strong NOE correlation between H-1′ and H-2. By comparing ^{1}H NMR and ^{13}C NMR spectral data of aglycone moiety of **2** with 1-hydroxycanthin-6-one, there was a distinct glycosylation effect at C-1 ($\Delta\delta = +2.40$) and an aromatic *ortho* glycosylation effect at H-2 ($\Delta\delta = +0.61$), respectively. Based on the above spectral analysis, the structure of **2** was determined to be canthin-6-one-1-*o*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside (**2**) (figure 2).

3. Experimental

3.1 General experimental procedures

Melting points were measured on Kofler microscope (Reichert) and are uncorrected. The UV spectra were recorded on a Shimadzu UV-260 spectrophotometer. ^{1}H, ^{13}C and 2D NMR spectra were scanned on a Bruker AM 400 FT-NMR and an INOVA-500 spectrometer with pyridine-d_5 as solvent and with TMS as internal standard. FAB-MS and ESI-MS were obtained on a VG-ZAB-HS and a Bruker APEX™ II spectrometer, respectively. Silica gel (300–400 mesh) was used for column chromatography and silica gel GF_{254} for TLC. Spots were detected on TLC under UV light or by heating after spraying with 5% H_2SO_4 in ethanol and by spraying Dragendorff's reagent.

3.2 Plant material

Ailanthus altissima was collected at Lingtai county, Gansu province of China. The original plant was identified by Professor Ru-Neng Zhao, College of Pharmacy, Lanzhou University. A voucher specimen (No. W10) is deposited in the Laboratory of Natural

Products, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou, China.

3.3 Extraction and isolation of alkaloidal glycosides

The air-dried and powdered root bark of *A. Altissima* (3.5 kg) was exhaustively extracted with methanol at room temperature. The extract was concentrated under reduced pressure. The residue was suspended in H_2O and partitioned with $H_2O/CHCl_3$ (1:5) to divide the $CHCl_3$-soluble fraction (40 g) and H_2O-soluble fraction. Then, the H_2O-soluble fraction was extracted with EtOAc and n-BuOH to obtain the EtOAc-soluble fraction (30 g) and n-BuOH-soluble fraction (40 g), respectively. The n-BuOH-soluble extract (40 g) was desugared with absolute ethanol firstly, then subjected to column chromatography on silica gel eluting with a gradient of $CHCl_3$/MeOH (9:1 to 5:1) as developing solvent to obtain ten fractions (monitored by TLC analysis). Ailantcanthinosides A (**1**) (25 mg) and B (**2**) (35 mg) were obtained from fractions 7 and 6, respectively.

3.3.1 Ailantcanthinoside A (1): canthin-6-one-5-*o*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside. White amorphous powder, mp 200–202°C. UV λ_{max} (pyridine, nm): 225, 304,343, 358, 376; IR (KBr, cm^{-1}): 3389 (OH), 1667 (C=O), 1639, 1606, 1591, 1569, 1444, 1289, 1270, 1238, 1072, 1049; HRESI-MS $m/z = 531.1602$ $[M + 1]^+$ (calcd for $C_{25}H_{27}N_2O_{11}$ $[M + H]^+$, 531.1609); $m/z = 553.1418$ $[M + Na]^+$ (calcd for $C_{25}H_{26}N_2O_{11}Na$ $[M + Na]^+$, 553.1429); EI-MS (rel. int.): 236 ($M-C_6H_{10}O_5-C_4H_8O_4$, 100), 208 (236-CO, 4.5), 180 (236-2CO, 33). ^1H NMR, ^{13}C NMR: see table 1.

3.3.2 Ailantcanthinoside B (2): canthin-6-one-1-*o*-β-D-xylopyranosyl-(1 → 6)-β-D-glucopyranoside. White amorphous powder, mp 186–188°C. UV λ_{max} (pyridine, nm): 225, 358, 376; IR (KBr, cm^{-1}): 3428, 3301 (OH), 1674 (C=O), 1634, 1604, 1240, 1069, 1043; FAB-MS $m/z = 531.3$ $[M + H]^+$; EI-MS (rel. int.): 236 ($M-C_6H_{10}O_5-C_4H_8O_4$, 100), 208 (236-CO, 43.3). ^1H NMR, ^{13}C NMR: see table 2.

3.3.3 1-Hydroxycanthin-6-one (aglycone of 2). It was crystallised from Et_2O/EtOH, mp 196–198°C, UV λ_{max} (MeOH, nm): 221, 252, 272, 361, 377, 404; IR (KBr, cm^{-1}): 3428, 3300, 1674, 1633, 1600, 1510, 1440, 830, 790, 754; ^1H NMR (400 MHz, pyridine-d_5): δ 6.86 (1H, d, $J = 9.6$ Hz, H-5), δ 7.54 (1H, dd, $J = 1.5$, 8.0 Hz, H-10), δ 7.64 (1H, dd, $J = 1.5$, 8.0 Hz, H-9), δ 8.51 (1H, d, $J = 8.0$ Hz, H-11), δ 8.79 (1H, s, H-2), δ 8.94 (1H, d, $J = 8.0$ Hz, H-8). ^{13}C NMR: δ153.1 (C-1), δ 136.1 (C-2), δ 139.6 (C-4), δ 125.7 (C-5), δ 160.4 (C-6), δ 117.0 (C-8), δ 129.0 (C-9), δ 125.7 (C-10), δ 124.6 (C-11), δ 124.9 (C-12), δ 138.6 (C-13), δ 115.7 (C-14), δ 134.9 (C-15), δ 134.3 (C-16); MS m/z (rel. int.): 236 (M^+, 100), 208 (44), 181 (9).

3.3.4 Acid hydrolysis of 1 and 2. To **1** (18 mg) was added 10 ml of 1 M HCl/MeOH solution and allowed to stand at room temperature for 48 h. MeOH was then evaporated under reduced pressure. The residue was suspended in water and extracted with EtOAc. The aqueous layer was neutralised with $NaHCO_3$, evaporated to dryness, and identified by

Table 1. NMR data of **1** in C_5D_5N (500 MHz).

No.	δ_C	δ_H *(J in Hz)*	*HMBC (observed)*
1	114.6	7.80 d, 5.2	H-2
2	146.0	8.80 d, 5.2	H-1
4	117.3	8.20 s	
5	152.8		H-4, H-1′
6	155.6		H-4
8	117.3	8.70 d, 8.0	H-10
9	130.6	7.62 dt, 1.5, 8.0	H-11
10	126.8	7.48 dt, 1.5, 8.0	H-8
11	124.1	8.10 d, 8.0	H-9
12	125.6		H-1,H-8, H-10
13	139.4		H-9, H-11
14	129.3		H-2, H-11
15	128.3		H-1, H-4
16	137.2		H-2
1′	102.5	5.77 d, 8.5	H-3′
2′	74.2	4.13 m	H-4′
3′	77.6	4.15 m	H-5′
4′	71.1	4.27 m	H-6′
5′	74.8	4.31 m	H-3′
6′	69.4	4.86 (d, 11.5) 4.35 m	H-1″
1″	105.6	4.97 d, 8.5	H-6′, H-4″
2″	74.9	4.13 brd	H-4″
3″	77.9	4.14 brd	H-5″
4″	71.1	4.29 m	H-2″
5″	66.7	3.66 (t, 12.0), 4.34 m	

Table 2. NMR data of **2** in C_5D_5N (400 MHz).

No.	δ_C	δ_H *(J in Hz)*	*HMBC*
1	150.7		H-1′
2	135.8	9.31 s	
4	139.4	7.98 d, 10.0	
5	125.9	6.87 d, 10.0	
6	160.0		H-4
8	116.7	8.81 d, 8.0	H-10
9	129.7	7.61 dt, 1.5, 8.0	H-11
10	125.6	7.37 dt, 1.5, 8.0	H-8
11	125.3	8.49 d, 8.0	H-9
12	124.0		H-8, H-10
13	138.7		H-9, H-11
14	118.2		H-2, H-11
15	133.4		H-4
16	131.3		H-5, H-2
1′	102.7	6.03 d, 7.5	H-3′
2′	74.8	4.46 m	H-4′
3′	77.6	4.42 m	H-5′
4′	71.0	4.20 m	H-6′
5′	78.1	4.40 m	H-3′
6′	69.6	4.84 (d, 8.5) 4.40 m	H-1″
1″	105.9	4.95 d, 7.5	H-6′, H-4″
2″	74.9	4.04 dd, 7.5,8.5	H-4″
3″	78.5	4.12 dd, 7.5,8.5	H-5″
4″	71.0	4.30 m	H-2″
5″	67.1	3.61 (t, 11.0), 4.26 m	H-4″

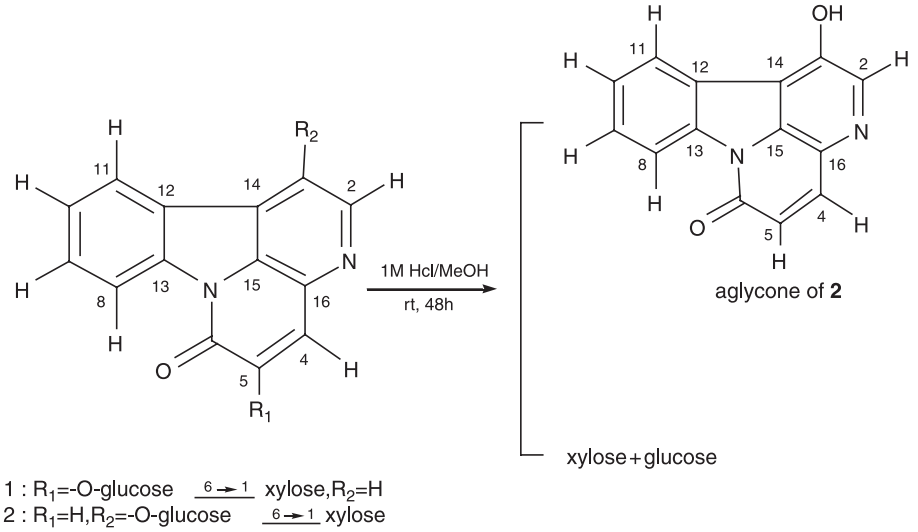

Figure 1. Acid hydrolysis of **1** and **2**.

paper chromatography with glucose and xylose authentic samples, using EtOAc/pyridine/H_2O (12:5:4) as developing solvent. And the aglycone of **1** was not obtained.

2 (25 mg) was hydrolysed in the same way as **1**. The EtOAc solution of **2** was evaporated to dryness and the residue was chromatographed on silica gel by gradient elution with $CHCl_3$/MeOH (20:1, ca. 500 ml) to obtain an aglycone (8 mg), which was identified by the ^1H and ^{13}C NMR spectra and by comparison of the spectral data (NMR, MS) with those reported for 1-hydroxycanthin-6-one [14] (figure 1).

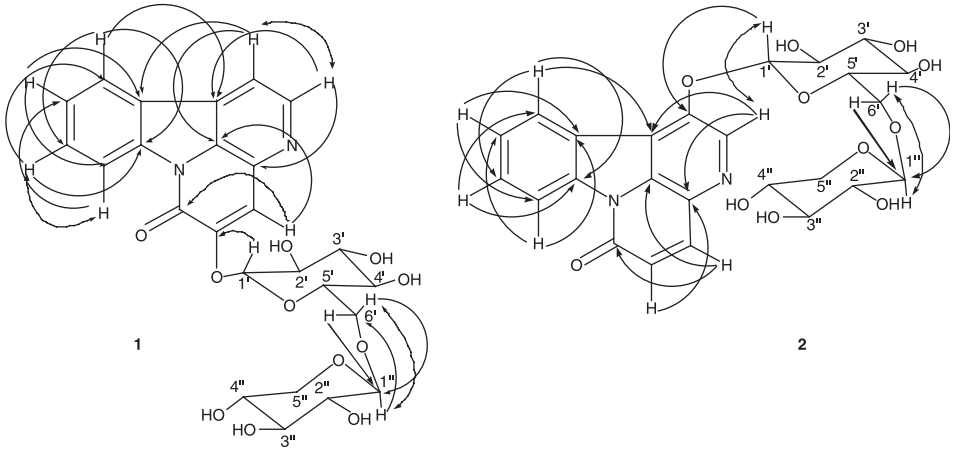

Figure 2. The important HMBC (→) and NOESY (↔) correlations of compounds **1** and **2**.

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