# Bis-Iridoid Glucosides from *Abelia chinensis*

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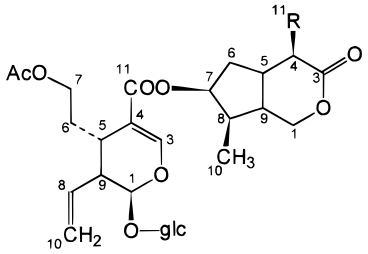
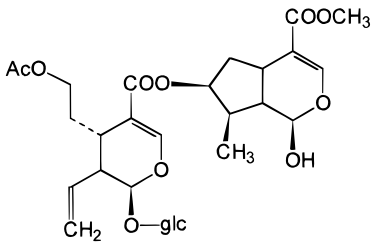
Seven bis-iridoid glucosides have been isolated from *Abelia chinensis* and were characterized by having a secoiridoid residue as unit A esterifying a $C_{10}$-iridoid or a $\delta$-lactone iridoid as unit B. Among these, compounds **1**−**3** are new and correspond to 7-*O*-acetyllaciniatoside IV, 7-*O*-acetyllaciniatoside V, and 7-*O*-acetylabelioside B, respectively. The structures of **1**−**3** were elucidated by spectral methods.

*Abelia chinensis* R. Br. (Caprifoliaceae) is an ornamental shrub of Chinese origin and has almost persistent leaves when grown in the temperate climate of Mediterranean Europe, where it is also cultivated.[1]

In the past, only one phytochemical study on the genus *Abelia* was reported,[2] describing the isolation of two bis-iridoid glucosides, abelioside A (identical to the previously isolated laciniatoside II[3]) and abelioside B, from *A. grandiflora* Rehd. The present paper reports on the isolation and structure elucidation of three new bis-iridoid glucosides (**1**−**3**), together with the known compounds sylvestroside III, laciniatoside II, sylvestroside II, and sylvestroside I, in order of increasing polarity, from *A. chinensis*.




**1** R = $COOCH_3$
**3** R = H




**2**

The aerial parts of *A. chinensis* were extracted and gave, after a preliminary purification, an EtOAc-soluble fraction, whose column chromatographic separation resulted in the isolation of seven compounds.

On the basis of its NMR data, the structure of a bis-iridoid glucoside was hypothesized for compound **1**. In fact, among the signals observed in its $^1$H and $^{13}$C NMR spectra, the resonances of two distinct parts, indicated as units A and B, could be identified. As unit A, compound **1** contained a secoiridoid moiety, almost identical to secologanic acid: the only significant differences were the low-field shift of $H_2$-7 ($\delta$ 4.09) and C-7 ($\delta$ 64.1), as a result of a deshielding effect due to an acetyl group ($^1$H NMR signal at $\delta$ 2.01; $^{13}$C NMR signals at $\delta$ 20.9 and 172.9). Furthermore, the carboxylic function at position 11 of unit A was linked through an ester bond to unit B. The remaining $^1$H and $^{13}$C NMR signals showed, for unit B, the structure of an iridoid $\delta$-lactone, characterized by a carbomethoxylic function. Unambiguous identification of all signals, obtained by 2D NMR spectra ($^{13}$C−$^1$H HETCOR and $^{13}$C−$^1$H COLOC experiments), enabled the assignment to **1** of a new structure as the 7-*O*-acetyl derivative of laciniatoside IV, a bis-iridoid glucoside previously isolated from *Dipsacus laciniatus* L.[3] Confirmation of the stereochemistry of the chiral centers present in the cyclopentane ring of unit B was obtained by NOE-difference NMR data, showing a OH-7$\beta$/Me-8$\beta$ configuration, consistent with the configuration of the same centers in laciniatoside IV.[3] Also, for the chiral carbon at position 4, a significant NOE interaction between H-4 and $H_\alpha$-6 (showing in turn a strong NOE with $H_\alpha$-7) and the absence of interaction between H-4 and H-5 allowed a COOMe-4$\beta$ configuration assignment, analogous to laciniatoside IV.[3] However, it is noteworthy that the acidic $\alpha$-dicarboxylic H-4 can easily be removed, when compound **1** is left in contact with polar solvents. The phenomenon has been observed in the $^1$H NMR spectrum of **1** in $CD_3OD$. When the spectrum was repeated after a few hours, the H-4 signal completely disappeared, owing to the exchange of the labile hydrogen with the deuterium of the solvent. Nevertheless, this continuous exchange seems not to affect the stereochemistry of C-4, with the −COOMe group remaining in a $\beta$-configuration, probably as a result of steric hindrance.

As in the case of compound **1**, the $^1$H and $^{13}$C NMR spectra of **2** indicated the characteristic structure of a bis-iridoid. In particular, besides the signals of an acetoxysecologanic acid moiety as unit A, the resonances of a $C_{10}$-iridoid aglucon were observed. The chemical shift and the coupling constants in the $^1$H NMR spectrum of the latter part were consistent with those of a loganin aglucon moiety (loganetin),[4] in which the low-field shift value of H-7 ($\delta$ 5.21) accounted for the esterification of the hydroxyl at position 7 by the carboxyl group of the acetoxysecologanic acid. This observation, together with further confirmation

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obtained by $^{13}C-^{1}H$ HETCOR and $^{13}C-^{1}H$ COLOC data, allowed the structure 7-*O*-acetyllaciniatoside V to be assigned to **2**.[3,5]

The same A unit of compounds **1** and **2** was apparent from the $^{1}H$ and $^{13}C$ NMR spectra of **3**, with the acetoxysecologanic acid esterifying in this case an iridoid $\delta$-lactone unit. The whole structure was identical to that of the previously isolated bis-iridoid abelioside B, apart from the presence of an acetyl group linked to the primary alcoholic group at position 7 of unit A. Therefore, this new compound was assigned as 7-*O*-acetylabelioside B. Since the parent compound of abelioside B was obtained as a pentaacetate derivative, after acetylation,[2] this leaves in doubt the actual occurrence of the unacetylated compound in *Abelia* extracts.

The remaining bis-iridoid glucosides isolated from *A. chinensis* were the known compounds sylvestroside III,[6] laciniatoside II,[3] sylvestroside II,[6] and sylvestroside I[6] and were all identified by comparison with authentic samples.

## Experimental Section

**General Experimental Procedures.** Optical rotations were measured on a JASCO DIP-370 polarimeter. IR spectra were obtained on a Shimadzu IR-470 spectrophotometer. NMR spectra were recorded on a Bruker AM 500 spectrometer ($^{1}H$ and $^{13}C$ NMR spectra in $CD_3OD$, using TMS as internal standard). FABMS were run on a VG7070 EQ-HF mass spectrometer, equipped with its own FAB source, using *m*-nitrobenzyl alcohol (NBA) as matrix.

HPLC analysis was performed on a Hewlett-Packard HP 1090 instrument, equipped with a diode array detector ($\lambda$ 230 nm), using a Lichrospher RP-18 column (Merck, 125-4, 5 $\mu$m), and a $H_2O-MeCN$ (7:3) mixture as mobile phase (flow 1 mL/min). TLC analysis was performed on Si gel $SiF_{254}$ (Merck) and visualized with the spray reagents 2 N $H_2SO_4$ or vanillin (3 g of vanillin, 4 mL of HCl, 100 mL of MeOH).

**Plant Material.** *A. chinensis* R. Br. (whole plant, 250 g) was collected in the botanical garden of Università "La Sapienza", Dipartimento di Biologia Vegetale, Rome, Italy, where voucher specimens are deposited (RO General Herbarium).

**Extraction and Isolation.** Fresh aerial parts of the plant were exhaustively extracted with 95% EtOH at room temperature, and the extract was evaporated in vacuo. The residue was partitioned between $H_2O$ and cyclohexane to remove chlorophylls, and then the $H_2O$ phase was extracted with EtOAc. The EtOAc fraction was subsequently submitted to column chromatographic separation on $SiO_2$. Elution with $CH_2Cl_2-MeOH$ (8:2) gave, in order, pure compounds **1**−**3** and the four known compounds sylvestroside III (90 mg), laciniatoside II (106 mg), sylvestroside II (93 mg), and sylvestroside I (116 mg). The separation was monitored by HPLC and TLC analysis.

**7-*O*-Acetyllaciniatoside IV (1)**: white amorphous powder (9 mg); $[\alpha]^{20}_{D}$ −27.2° (*c* 0.20, MeOH); IR (KBr) $\nu_{max}$ 1750, 1700, 1630 $cm^{-1}$; $^{1}H$ NMR ($CD_3OD$, 500 MHz) unit A, $\delta$ 7.49 (1H, s, H-3), 5.76 (1H, ddd, $J$ = 17.4, 10.7 and 9.0 Hz, H-8), 5.54 (1H, d, $J$ = 6.6 Hz, H-1), 5.27 (2H, m, $H_2$-10), 4.70 (1H, d, $J$ = 7.8 Hz, H-1′), 4.09 (2H, m, $H_2$-7), 3.90 (1H, dd, $J$ = 12.0 and 2.0 Hz, H-6′a), 3.66 (1H, dd, $J$ = 12.0 and 6.2 Hz, H-6′b), 3.36 (1H, t, $J$ = 9.0 Hz, H-3′), 3.28 (2H, m, H-5′ and H-4′), 3.19 (1H, dd, $J$ = 9.0 and 7.8 Hz, H-2′), 2.85 (1H, q-shaped m, H-5), 2.66 (1H, q-shaped m, H-9), 2.01 (3H, s, Ac), 2.00 (1H, m, H-6a), 1.82 (1H, dq, $J$ = 14.0 and 6.2 Hz, H-6b); unit B, $\delta$ 5.25 (1H, sharp m, H-7), 4.43 (1H, dd, $J$ = 11.6 and 6.0 Hz, H-la), 4.17 (1H, dd, $J$ = 11.6 and 9.2 Hz, H-1b), 3.78 (3H, s, $OCH_3$), 3.68 (1H, d, $J$ = 9.4 Hz, H-4), 3.05 (1H, q-shaped m, H-5), 2.36 (1H, m, H-9), 2.16 (1H, m, H-6a), 2.04 (1H, m, H-8), 1.61 (1H, ddd, $J$ = 13.6, 9.5 and 3.0 Hz, H-6b), 1.03 (3H, d, $J$ = 6.6 Hz, $H_3$-10); $^{13}C$ NMR ($CD_3OD$, 125 MHz) unit A, $\delta$ 172.9 (*C*$OCH_3$), 168.1 (C-11), 153.9 (C-3), 135.6 (C-8), 119.6 (C-10), 111.5 (C-4), 100.2 (C-1′), 97.8 (C-1), 78.4 (C-5′), 78.0 (C-3′), 74.7 (C-2′), 71.6 (C-4′), 64.1 (C-7), 62.8 (C-6′), 45.4 (C-9), 31.2 (C-5), 30.1 (C-6), 20.9 (CO*C*$H_3$); unit B, $\delta$ 171.9 (C-3), 170.3 (C-11), 80.1 (C-7), 70.8 (C-1), 53.1 ($OCH_3$), 52.4 (C-4), 43.4 (C-9), 42.4 (C-8), 39.1 (C-6), 37.8 (C-5),13.5 (C-10); FABMS $m/z$ $[M + Na]^+$, 651 [628 + 23]; *anal.* C 55.54%, H 6.48%, calcd for $C_{29}H_{40}O_{15}$, C 55.41%, H 6.41%.

**7-*O*-Acetyllaciniatoside V (2):** white amorphous powder (11 mg); $[\alpha]^{20}_{D}$ −17.4° (*c* 0.20, MeOH); IR (KBr) $\nu_{max}$ 1750, 1700, 1640 $cm^{-1}$; $^{1}H$ NMR ($CD_3OD$, 500 MHz) unit A, $\delta$ 7.50 (1H, s, H-3), 5.78 (1H, ddd, $J$ = 17.8, 10.5 and 8.2 Hz, H-8), 5.54 (1H, d, $J$ = 6.6 Hz, H-1), 5.26 (2H, m, $H_2$-10), 4.71 (1H, d, $J$ = 7.8 Hz, H-1′), 4.08 (2H, m, $H_2$-7), 3.90 (1H, dd, $J$ = 12.0 and 2.2 Hz, H-6′a), 3.66 (1H, dd, $J$ = 12.0 and 6.0 Hz, H-6′b), 3.36 (1H, t, $J$ = 9.0 Hz, H-3′), 3.29 (2H, m, H-5′ and H-4′), 3.20 (1H, dd, $J$ = 9.0 and 7.8 Hz, H-2′), 2.87 (1H, q-shaped m, H-5), 2.67 (1H, q-shaped m, H-9), 2.01 (3H, s, Ac), 2.00 (1H, m, H-6a), 1.81 (1H, dq, $J$ = 14.0 and 6.2 Hz, H-6b); unit B, $\delta$ 7.45 (1H, m, H-3), 5.21 (1H, t-shaped m, H-7), 4.91 (1H, bd, $J$ = 5.8 Hz, H-1), 3.70 (3H, s, $OCH_3$), 3.09 (1H, q-shaped m, H-5), 2.33 (1H, m, H-6a), 2.12 (1H, m, H-8), 1.87 (1H, m, H-9), 1.62 (1H, m, H-6b), 1.07 (3H, d, $J$ = 6.6 Hz, $H_3$-10); $^{13}C$ NMR ($CD_3OD$, 125 MHz) unit A, $\delta$ 173.0 (*C*$OCH_3$), 168.2 (C-11), 153.7 (C-3), 135.7 (C-8), 119.6 (C-10), 111.7 (C-4), 100.1 (C-1′), 97.8 (C-1), 78.4 (C-5′), 78.0 (C-3′), 74.7 (C-2′), 71.6 (C-4′), 64.2 (C-7), 62.7 (C-6′), 45.3 (C-9), 31.3 (C-5), 30.1 (C-6), 20.8 (CO*C*$H_3$); unit B, $\delta$ 169.7 (C-11), 153.9 (C-3), 111.7 (C-4), 97.0 (C-1), 78.2 (C-7), 51.7 ($OCH_3$), 48.6 (C-9), 41.8 (C-8), 40.8 (C-6), 33.7 (C-5), 14.4 (C− 10); FABMS $m/z$ $[M + Na]^+$, 651 [628 + 23]; *anal.* C 55.50%, H 6.46%, calcd for $C_{29}H_{40}O_{15}$, C 55.41%, H 6.41%.

**7-*O*-Acetylabelioside B (3):** white amorphous powder (32 mg); $[\alpha]^{20}_{D}$ −46.2° (*c* 0.80 MeOH); IR (KBr) $\nu_{max}$ 1750, 1700, 1620, 1240 $cm^{-1}$; $^{1}H$ NMR ($CD_3OD$, 500 MHz) unit A, $\delta$ 7.46 (1H, s, H-3), 5.76 (1H, ddd, $J$ = 17.4, 10.0 and 8.5 Hz, H-8), 5.54 (1H, d, $J$ = 6.6 Hz, H-1), 5.25 (2H, m, $H_2$-10), 4.69 (1H, d, $J$ = 7.8 Hz, H-1′), 4.08 (2H, m, $H_2$-7), 3.90 (1H, dd, $J$ = 12.0 and 2.4 Hz, H-6′a), 3.66 (1H, dd, $J$ = 12.0 and 6.0 Hz, H-6′b), 3.34 (1H, t, $J$ = 9.0 Hz, H-3′), 3.27 (2H, m, H-5′ and H-4′), 3.19 (1H, dd, $J$ = 9.0 and 7.8 Hz, H-2′), 2.85 (1H, q-shaped m, H-5), 2.66 (1H, q-shaped m, H-9), 2.01 (3H, s, Ac), 2.00 (1H, m, H-6a), 1.81 (1H, dq-shaped m, $J$ = 14.0 and 6.2 Hz, H-6b); unit B, $\delta$ 5.21 (1H, sharp m, H-7), 4.41 (1H, dd, $J$ = 12.0 and 4.4 Hz, H-la), 4.19 (1H, dd, $J$ = 12.0 and 4.0 Hz, H-1b), 2.88 (1H, m, H-5), 2.74 (1H, dd, $J$ = 15.2 and 6.8 Hz, H-4a), 2.37 (1H, dd, $J$ = 15.2 and 4.4 Hz, H-4b), 2.22 (1H, m, H-9), 2.13 (1H, ddd, $J$ = 14.4, 8.0 and 1.5 Hz, H-6a), 2.04 (1H, m, H-8), 1.46 (1H, ddd, $J$ = 14.4, 10.2 and 4.0 Hz, H-6b), 1.03 (3H, d, $J$ = 6.6 Hz, $H_3$-10); $^{13}C$ NMR ($CD_3OD$, 125 MHz) unit A, $\delta$ 172.9 (*C*$OCH_3$), 168.2 (C-11), 153.7 (C-3), 135.6 (C-8), 119.6 (C-10), 111.6 (C-4), 100.1 (C-1′), 97.8 (C-1), 78.5 (C-5′), 78.1 (C-3′), 74.7 (C-2′), 71.6 (C-4′), 64.1 (C-7), 62.8 (C-6′), 45.4 (C-9), 31.2 (C-5), 30.0 (C-6), 20.9 (CO*C*$H_3$); unit B, $\delta$ 176.3 (C-3), 79.9 (C-7), 69.8 (C-1), 43.9 (C-9), 41.9 (C-8), 40.0 (C-6), 35.1 (C-4), 34.2 (C-5), 13.4 (C-10); FABMS $m/z$ $[M + Na]^+$, 593 [570 + 23]; *anal.* C 56.94%, H 6.76%, calcd for $C_{27}H_{38}O_{13}$, C 56.84%, H 6.71%.

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