

[Chem. Pharm. Bull.]
[33(10)4275—4280(1985)]

Sweet and Bitter Principles of the Chinese Plant Drug, Bai-Yun-Shen: Revision of the Assignment of the Source Plant and Isolation of Two New Diterpene Glycosides

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(Received February 22, 1985)

The assignment of the source plant of the Chinese plant drug "Bai-Yun-Shen" as *Salvia digitaloides* DIELS (Labiatae), was revised to *Phlomis betonicoides* DIELS of the same family. From roots of this plant, a sweet glycoside named phlomisioside-I (5) and a bitter glycoside named phlomisioside-II (6) were isolated. The aglycone of both compounds was proved to be baiyunol (7, furano-labdane-type diterpene), the aglycone of baiyunoside (1), which has already been isolated as the sweet principle from this plant drug. The structures of 5 and 6 were elucidated as the 3-*O*- α -rhamnopyranosyl-(1 $\rightarrow$ 2)- β -glucopyranoside and the 3-*O*-sophoroside of 7, respectively.

Keywords—Bai-Yun-Shen; Chinese plant drug; *Phlomis betonicoides*; Labiatae; sweet glycoside; bitter glycoside; phlomisiosides-I, II; labdane-type diterpene glycoside; baiyunoside; baiyunol

In our studies on the sweet principles of Chinese plants,¹⁻³⁾ isolation and structure elucidation of a sweet diterpene glycoside named baiyunoside (1) from the Chinese medicinal plant drug, "Bai-Yun-Shen," have been reported as a communication to the editor of this Bulletin.⁴⁾ Three bitter iridoid glucosides, shanzhiside methyl ester (2), its 8-*O*-acetate (3) and 6-*O*-syringyl-8-*O*-acetyl-shanzhiside methyl ester (4) were also isolated from the same drug.⁴⁾

At that time, the source plant of this crude drug was reported as *Salvia digitaloides* DIELS (Labiatae). However, further botanical investigation led to the revision of the assignment of the source plant to *Phlomis betonicoides* DIELS (Labiatae). This paper reports the isolation and structure determination of two additional diterpene glycosides from this crude drug and presents full experimental details concerning 1—4 as well.

A suspension of a methanolic extract of the roots collected in Yunnan, China, was washed with ether and then chromatographed on highly porous polymer to give a glycoside mixture which was subjected to repeated chromatography, affording 1, 2, 3, 4 and two new glycosides named phlomisiosides-I (5) and -II (6) in yields of 0.23, 0.03, 0.28, 0.19, 0.01 and 0.01%, respectively. The structure determination of 1 and 4 as well as the identification of 2 and 3 have already been reported.⁴⁾

On enzymic hydrolysis, both 5 and 6 yielded an acid-unstable aglycone which was identical with baiyunol (7) previously obtained from 1 by the same treatment. The structure elucidation of 7 has been reported already.⁴⁾ The determination of the absolute configuration of 7 (normal type) has been achieved by elucidation of the chirality of the 3-equatorial hydroxyl group,⁴⁾ the experimental details are described in the experimental part of this paper. The carbon-13 nuclear magnetic resonance (¹³C-NMR) signals due to the aglycone moiety of 5 and 6 (Table I) were found to be almost identical with those of 1, indicating that both compounds are also glycosides of 7.

Acid hydrolysis of **5** gave glucose and rhamnose and the electron impact-mass spectra (EI-MS) of its peracetate exhibited fragment ions at m/z 561 ((Glc-Rha)-Ac₆) and 273 (terminal Rha-Ac₃). The ¹³C-NMR signals due to the sugar moiety of **5** (Table I) were observed at almost the same positions as those of saponin E (**8**) obtained from leaves of *Hovenia dulcis*,⁵⁾ leading to the formulation of this compound as 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl baiyunol.

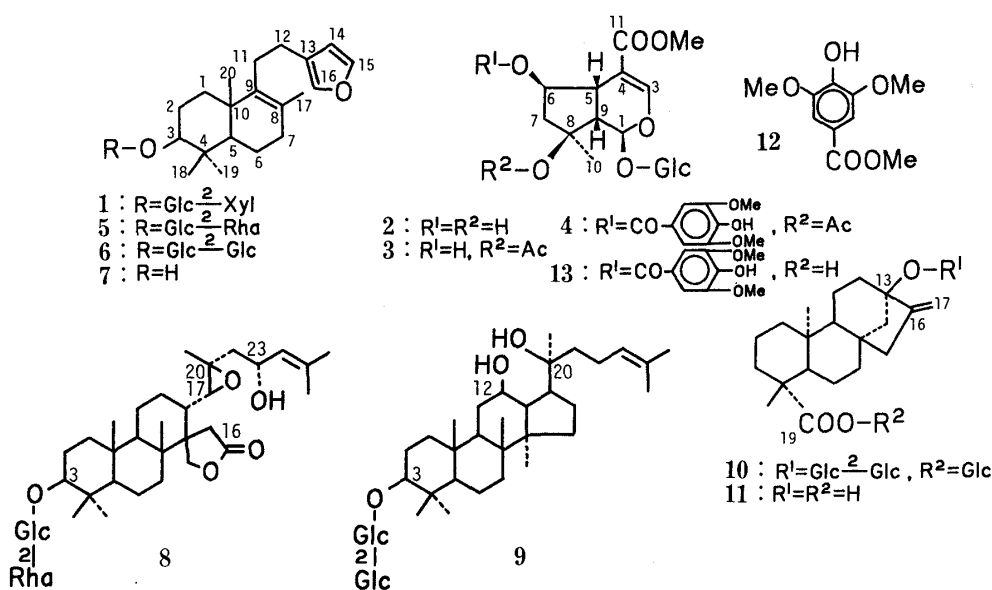
On acid hydrolysis, **6** afforded glucose. The EI-MS of peracetylated **6** showed fragment ions at m/z 619 ((Glc-Glc)-Ac₇) and 331 (terminal Glc-Ac₄). The ¹³C resonances of the sugar moiety of **6** (Table I) were found to be almost superimposable on those of 20(*S*)-ginsenoside-Rg₃ (**9**).⁶⁾ It follows that **6** can be formulated as 3-*O*-β-sophorosyl baiyunol. The coupling constants of two anomeric proton signals of **6** (see Experimental) supported this formulation. Partial synthesis of **6** was achieved by glycosylation of **7** with acetobromosophorose prepared from sophorose, which was obtained from stevioside (**10**) by mild acid hydrolysis.

Like **1**, **5** tastes sweet and its sweetness persists for more than 1 h, while **6** tastes bitter. In

TABLE I. ¹³C-NMR Chemical Shifts of **1** and **5**—**9** (δ from TMS in C₅D₅N)

Carbon		1	5	6	7	8	9
Aglycone moiety	1	35.3	35.5	35.3	35.5		
	2	27.2	27.4	27.2	29.2		
	3	89.3	89.0	89.3	78.1		
	4	38.7 ^{a)}	38.7 ^{a)}	38.7 ^{a)}	39.1 ^{a)}		
	5	51.6	51.7	51.6	51.4		
	6	18.9	19.0	19.0	19.5		
	7	34.0	34.0	34.0	34.1		
	8	126.5 ^{b)}	126.5 ^{b)}	126.6 ^{b)}	126.6 ^{b)}		
	9	139.9	140.0	140.0	140.1		
	10	39.6 ^{a)}	39.6 ^{a)}	39.6 ^{a)}	39.5 ^{a)}		
	11	29.0	29.0	29.0	29.2		
	12	26.1	26.1	26.1	26.1		
	13	126.1 ^{b)}	126.1 ^{b)}	126.1 ^{b)}	126.1 ^{b)}		
	14	111.5	111.5	111.5	111.4		
	15	143.3	143.3	143.3	143.3		
	16	139.0	139.1	139.1	139.1		
	17	19.0	19.0	19.0	19.2		
	18	28.0	29.0	28.4	28.7		
	19	16.0	17.2	16.8	16.5		
	20	20.2	20.3	20.1	20.3		
Sugar moiety		(Glc)	(Glc)	(Glc)		(Glc)	(Glc)
Inner-	1	105.0	105.4	105.1		105.3	104.8
	2	83.8	80.0	83.4		79.7	82.9
	3	78.3 ^{c)}	77.8 ^{c)}	78.4 ^{c)}		77.7	77.8 ^{a)}
	4	71.4 ^{d)}	72.5	71.5 ^{d)}		72.2	71.4
	5	78.1 ^{c)}	78.1 ^{c)}	78.2 ^{c)}		78.1	77.7
	6	62.6	62.8	62.8		62.9	62.6
Terminal-		(Xyl)	(Rha)	(Glc)		(Rha)	(Glc)
	1	106.8	101.7	106.0		101.6	105.5
	2	76.5	72.1	77.1 ^{c)}		72.2	76.6
	3	77.9	72.5	78.0		72.2	77.7 ^{a)}
	4	71.0 ^{d)}	74.2	71.7 ^{d)}		74.0	71.4
	5	67.4	69.6	78.0 ^{c)}		69.5	77.8 ^{a)}
	6		18.7	62.8		18.6	62.6

a—d) These assignments may be interchanged in each column. Glc, β-D-glucopyranosyl; Xyl, β-D-xylopyranosyl; Rha, α-L-rhamnopyranosyl.



Glc: β -D-glucopyranosyl, Xyl: β -D-xylopyranosyl, Rha: α -L-rhamnopyranosyl

Chart 1

studies on sweet diterpene glycosides, **10** and related glycosides of steviol (**11**),⁷⁾ it has been mentioned that the replacement of a glucosyl unit by a rhamnosyl unit results in a decrease of sweetness. However, the present finding that with regard to glycosides of **7**, the glucosyl-glucoside (**6**) is bitter and the xylosyl-glucoside (**1**) and rhamnosyl-glucoside (**5**) are sweet, indicates the complexity of the structure-sweetness relationship of the diterpene glycosides.

Experimental

General Procedures—Melting points were determined on a Yanaco micro hot stage and are uncorrected. Ultraviolet (UV) spectra were taken on a Shimadzu UV 200S or UV 202 spectrometer. Optical rotations were measured with a Union automatic digital polarimeter PM-101 at 15–24 °C. Nuclear magnetic resonance (NMR) spectra were recorded on JEOL FX-100, GX-270 or Hitachi R-40 spectrometers (internal standard: tetramethylsilane (TMS)), at 99.55, 270 or 90 MHz for ¹H-NMR, and at 25.00 or 67.80 MHz for ¹³C-NMR. Mass spectra (MS) were taken on a JEOL JMS-01SG-2. For gas liquid chromatography (GLC), a Shimadzu GC-4A or GC-6A (detection by hydrogen flame ionization detector (FID); carrier gas, N₂) was used. For column chromatography, Kieselgel 60 (70–230 mesh) (Merck), LiChroprep RP-8 (40–63 μ m, Merck) and Diaion HP-20 an MCI-Gel CHP-20P (Mitsubishi Chem. Ind. Co., Ltd.) were used. All solvent systems for chromatography were homogeneous.

Acetylation for MS: A solution of a few mg of glycoside in 5–6 drops of C₅H₅N and Ac₂O was allowed to stand for 3 h at room temperature. The reaction mixture was concentrated to dryness by blowing N₂ gas over it and the residue was subjected to MS.

Acid Hydrolysis of Glycosides and Identification of Resulting Monosaccharides: A few mg of glycoside was heated with 4% HCl in H₂O–dioxane (1:1) (1 ml) in a sealed microtube at 100 °C for 5 h. The reaction mixture was concentrated to dryness by blowing N₂ gas over it. The residue was heated with 10 drops of *N*-trimethylsilylimidazole in a sealed microtube at 80 °C for 3 h. The reaction mixture was diluted with H₂O and then extracted with *n*-C₆H₁₄. The hexane layer was washed with H₂O and concentrated to dryness by blowing N₂ gas over it. A solution of the residue in *n*-C₆H₁₄ was subjected to GLC analysis.⁸⁾

Plant Material of Bai-Yun-Shen—*Phlomis betonicoides* DIELS was collected at Lijiang, Yunnan, China (1982). The specimen was unambiguously identified by Prof. Chen-yih Wu, the former Director of Kunming Institute of Botany, Academia Sinica. A specimen has been deposited at the Herbarium of the Kunming Institute of Botany, Academia Sinica.

Extraction and Separation of Glycosides—The dried roots (500 g) were powdered and extracted with hot MeOH, and the MeOH extract was concentrated to dryness. The resulting extract (128 g) was suspended in H₂O and then washed with Et₂O. The aqueous solution was chromatographed on a column of Diaion HP-20 (2500 ml) and elution was carried out with H₂O, 60% MeOH, 80% MeOH and MeOH successively. The fractions eluted with 60% and 80% MeOH were combined and subjected to chromatography on silica gel. Elution with CHCl₃–MeOH–H₂O

(44:10:1, 30:10:1 and then 15:10:1) provided three fractions (Fr. 1—Fr. 3 in order of elution).

Fr. 1 was subjected to chromatography on a silica gel column (CHCl_3 –MeOH– H_2O (50:10:1)), on a reverse-phase column (LiChroprep RP-8, 55% MeOH) and again on a silica gel column (EtOAc–EtOH– H_2O (80:8:1)) to give **4** (yield 0.19%): a white powder, $[\alpha]_D^{24} - 71.0^\circ$ ($c=1.0$, MeOH). Anal. Calcd for $\text{C}_{26}\text{H}_{34}\text{O}_{15} \cdot 1/3\text{H}_2\text{O}$: C, 52.70; H, 5.90. Found: C, 52.67; H, 5.73. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 276 (3.8), 221 (4.2). $^1\text{H-NMR}$ (in $\text{C}_5\text{D}_5\text{N}$) δ : 1.71 (s, 10-H), 1.93 (s, acetyl H_3), 3.60 (s, C-11- COOCH_3), 3.83 (s, $-\text{OCH}_3 \times 2$), 5.36 (d, $J=7.2$ Hz, anomeric H of Glc), 5.93 (br s, 6-H), 6.31 (d, $J=3.6$, 1-H), 7.69 (s, aromatic H $\times 2$), 7.74 (d, $J=1.2$ Hz, 3-H).

Chromatography of Fr. 2 on MCI-gel CHP-20P (40% MeOH and then 50% MeOH) afforded **3** (yield, 0.28%): a white powder, $[\alpha]_D^{26} - 84.8^\circ$ ($c=1.3$, MeOH). Anal. Calcd for $\text{C}_{19}\text{H}_{28}\text{O}_{12} \cdot 1/2\text{H}_2\text{O}$: C, 49.89; H, 6.39. Found: C, 50.13; H, 6.37. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 234 (4.0). $^1\text{H-NMR}$ (in $\text{C}_5\text{D}_5\text{N}$) δ : 1.65 (s, 10- H_3), 1.88 (s, acetyl H_3), 2.15 (dd, $J=5.4$, 15.0 Hz, 5-H), 2.54 (dd, $J=1.0$, 15.1 Hz, 9-H), 3.53 (br s, H-7), 3.60 (s, C-11- COOCH_3), 5.32 (d, $J=7.2$, anomeric H of Glc), 6.43 (d, $J=1.5$, 1-H), 7.68 (s, 3-H). This product was identified by comparison of the $^{13}\text{C-NMR}$ spectrum and other physical data with those of an authentic sample (**3**) isolated from *Barleria prionitis* L.⁹⁾

Fr. 3 was chromatographed on silica gel (EtOAc–EtOH– H_2O (11:2:1)) and further purified by chromatography on a silica gel column (CHCl_3 –MeOH– H_2O (44:10:1)) and on a reverse-phase column (LiChroprep RP-8, 30% MeOH) to give **2** (yield, 0.03%): a white powder, $[\alpha]_D^{22} - 123.3^\circ$ ($c=3.8$, MeOH). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 236 (3.9), which was identified by comparison of the $^{13}\text{C-NMR}$ spectrum and other physical data with those of an authentic sample.¹⁰⁾

The first fraction eluted with MeOH in the first chromatography of the MeOH extract on Diaion HP-20 (*vide supra*) was chromatographed on a reverse-phase column (LiChroprep RP-8, 75% MeOH) to give **6** (yield, 0.01%) and a mixture of **1** and **5**. The latter was subjected to high performance liquid chromatography (HPLC), giving **1** and **5** in yields of 0.23% and 0.01%, respectively. HPLC conditions: column, Lichrosorb Si 60 $5\mu\text{m}$ (Merck), 7.5 mm i.d. $\times$ 30 cm; mobile phase, CHCl_3 –EtOH– H_2O (50:13:1, homogeneous); flow rate, 2.0 ml/min; RI detector, Toyo Soda RI-8.

1: a white powder, $[\alpha]_D^{26} + 13.8^\circ$ ($c=2.50$, MeOH). Anal. Calcd for $\text{C}_{31}\text{H}_{48}\text{O}_{11} \cdot \text{H}_2\text{O}$: C, 60.57; H, 8.20. Found: C, 60.42; H, 8.19. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 213 (3.8). EI-MS (peracetate) m/z : 81 and 95 (furan ring), 890 (M^+), 547 ((Glc–Xyl)– Ac_6), 259 (terminal Xyl– Ac_3). $^1\text{H-NMR}$ (in $\text{C}_5\text{D}_5\text{N}$) δ : 0.97, 1.13, 1.35 (s each, 18-, 19- and 20- H_3), 1.60 (s, 17- H_3), 3.35 (dd, $J=5.2$, 11.0 Hz, 3-H), 4.93 (d, $J=6.0$ Hz, anomeric H of Glc), 5.25 (d, $J=6.0$ Hz, anomeric H of Xyl), 6.52 (br dd, 14-H), 7.57 (br dd, 16-H), 7.63 (t, $J=1.8$ Hz, 15-H). On mineral acid hydrolysis, **1** yielded glucose and xylose.

5: a white powder, $[\alpha]_D^{16} - 7.7^\circ$ ($c=2.3$, MeOH). Anal. Calcd for $\text{C}_{32}\text{H}_{50}\text{O}_{11} \cdot 1/3\text{H}_2\text{O}$: C, 62.32; H, 8.28. Found: C, 62.34; H, 8.32. EI-MS (peracetate) m/z : 81 and 95 (furan ring), 561 ((Glc–Rha)– Ac_6), 273 (terminal Rha– Ac_3). $^1\text{H-NMR}$ (in $\text{C}_5\text{D}_5\text{N}$) δ : 0.93, 1.22, 1.31 (s each, 18-, 19- and 20- H_3), 1.60 (s, 17- H_3), 1.74 (s, 6- H_3 of Rha), 3.43 (dd, $J=4.0$, 13.1 Hz, 3-H), 4.99 (d, $J=7.3$ Hz, anomeric H of Glc), 6.52 (br dd, 14-H), 6.61 (br s, anomeric H of Rha), 7.56 (br dd, 16-H), 7.64 (t, $J=1.8$ Hz, 15-H). On mineral acid hydrolysis, **5** yielded glucose and rhamnose.

6: a white powder, $[\alpha]_D^{15} + 15.4^\circ$ ($c=2.3$, MeOH). Anal. Calcd for $\text{C}_{32}\text{H}_{50}\text{O}_{12} \cdot 1/3\text{H}_2\text{O}$: C, 58.52; H, 8.19. Found: C, 58.64; H, 8.19. EI-MS (peracetate) m/z : 81 and 95 (furan ring), 331 (terminal Glc– Ac_4), 619 ((Glc–Glc)– Ac_7). $^1\text{H-NMR}$ (in $\text{C}_5\text{D}_5\text{N}$) δ : 0.95, 1.16, 1.36 (s each, 18-, 19- or 20- H_3), 1.73 (s, 17- H_3), 3.40 (dd, $J=4.5$, 11.3 Hz, 3-H), 4.98 (d, $J=7.0$, anomeric H of inner Glc), 5.41 (d, $J=7.3$ Hz, anomeric H of terminal Glc), 6.54 (br dd, 14-H), 7.59 (br dd, 16-H), 7.67 (t, $J=1.8$ Hz, 15-H). On mineral acid hydrolysis, **6** yielded glucose.

Enzymic Hydrolysis of 1, 5 and 6—A solution of a glucoside, **1**, **5** or **6** (1 g), and crude hesperidinase (1 g; Tanabe Pharm. Inc. Co., Ltd., Osaka, Japan)¹¹⁾ in H_2O (100 ml) was incubated at 37°C for 24 h. Additional crude hesperidinase (500 mg) was added and the reaction mixture was further incubated for an additional 12 h. The reaction mixture was concentrated to dryness and the residue was subjected to chromatography on silica gel; elution with benzene–acetone (4:1) gave **7** in a yield of 50–60% from each glycoside.

7: colorless needles, mp 85.5 – 86°C (from $n\text{-C}_6\text{H}_{14}$), $[\alpha]_D^{21} + 64.0^\circ$ ($c=1.47$, CHCl_3). Anal. Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_2 \cdot 1/3\text{H}_2\text{O}$: C, 77.87; H, 10.02. Found: C, 77.85; H, 10.01. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 212 (3.9). EI-MS m/z : 302 (M^+), 98 and 95 (furan ring). $^1\text{H-NMR}$ (in CDCl_3) δ : 0.81, 0.97, 1.02 (s each, 18-, 19- and 20- H_3), 1.60 (s, 17- H_3), 3.25 (dd, $J=6.0$, 10.8 Hz, 3-H), 6.30 (br dd, 14-H), 7.23 (br dd, 16-H), 7.35 (t, $J=1.8$ Hz, 15-H).

Modified Horeau's Method¹²⁾ for 7 (Determination of Absolute Configuration of 7)—A solution of 7 mg of **7** and 12 μl of ($\pm$)-2-phenylbutyric acid anhydride in dry pyridine was allowed to stand in a sealed microtube at room temperature for 20 h, then 12 μl of (+)-(*R*)- α -phenylethylamine was added. After standing for 30 min, the mixture was concentrated to dryness by blowing N_2 gas over it. The residue was extracted with a small amount of EtOAc and the solution was subjected to GLC analysis (dual FID; carrier gas, N_2 2.1 kg/cm²; column packed with 2% SE-30, 2 m $\times$ 3 mm; isothermal 200°C ; injection and detector temperatures, 250°C). The relative proportions of the amides of (–)-(*R*)- and (+)-(*S*)- α -phenylbutyric acid were calculated from the areas of their peaks. Subtraction of the corresponding value from the reaction for cyclohexanol gave the increment of the percentage area representing the (–)-(*R*)-acid: +6.7%.

Synthesis of 6—A solution of **10** (10 g) in 20 ml of 36% HCl was stirred vigorously for 8–10 min and the reaction mixture was diluted with H_2O (500 ml). The mixture was neutralized with Amberlite IRA-400 resin and

concentrated to dryness. The residue was subjected to chromatography on silica gel; elution with CHCl_3 -MeOH- H_2O (8:5:1) gave 2.5 g of sophorose (yield, 59%). Acetylation of sophorose with Ac_2O -pyridine in the usual way afforded sophorose peracetate. A solution of sophorose peracetate (2 g) in 5 ml of dry CH_2Cl_2 was treated with 10 ml of 30% HBr-AcOH at 0°C . After being stirred for 5 h at 4°C , the reaction mixture was poured into 20 ml of CH_2Cl_2 . The organic layer was washed with ice water, dried over Na_2SO_4 , and concentrated to dryness to give acetobromosophorose as a solid. A solution of **7** (40 mg), acetobromosophorose (100 mg) and $\text{Hg}(\text{CN})_2$ (40 mg) in toluene was boiled under reflux for 4 h. After addition of 50 mg of acetobromosophorose and 20 mg of $\text{Hg}(\text{CN})_2$, the reaction mixture was refluxed continuously for an additional 3 h, then concentrated to dryness at 40°C . The residue was deacetylated with 20 ml of 3% KOH-MeOH under stirring at room temperature for 2 h and the resulting precipitate was removed by filtration. The filtrate was neutralized with Amberlite IR-120-B resin and concentrated to dryness. The crude product was purified by chromatography on silica gel, and elution with CHCl_3 -MeOH- H_2O (30:10:1) afforded 35 mg of **6**: a white powder, $[\alpha]_D^{16} + 16.3^\circ$ ($c=0.5$, MeOH), which was identified by comparison of the ^{13}C -NMR spectrum with that of an authentic sample.

Acetylation of 2—Acetylation of **2** (127 mg) with Ac_2O (2 ml)-pyridine (2 ml) in the usual way afforded a crude product, which was chromatographed on silica gel with CHCl_3 -MeOH (30:1) to give the hexaacetate of **2** (49 mg): colorless needles, mp 181 – 182°C (from Et_2O), $[\alpha]_D^{23} - 118.3^\circ$ ($c=0.55$, CHCl_3), ^1H -NMR (in CDCl_3) δ : 1.50, 1.88, 1.97 and 2.00 (3H each, s), 2.03 (6H, s), 2.10 (3H, s), 2.26 (1H, m), 3.09 (2H br s), 3.72 (3H, s), 4.27 (2H, m), 5.89 (1H, d, $J=1.9$ Hz) and 7.41 (1H, d, $J=1.0$ Hz) and the pentaacetate of **2** (55 mg): colorless needles, mp 175 – 176°C (from Et_2O), $[\alpha]_D^{23} 105.2^\circ$ ($c=1.0$, CHCl_3), ^1H -NMR (in CDCl_3) δ : 1.32, 1.92, 2.00, 2.03, 2.09 and 2.10 (3H each, s), 2.67 (1H, dd, $J=9.4$, 3.0 Hz), 3.21 (1H, d, $J=9.4$ Hz), 3.70 (3H, s), 4.24 (2H, m), 5.42 (1H, d, $J=3.0$ Hz) and 7.37 (1H, d, $J=1.2$ Hz), both of which were identified by comparison of the ^1H -NMR spectra and other physical data with those of authentic samples.¹³⁾

Alkaline Hydrolysis of 3—A solution of **3** (103 mg) in 3 ml of 0.1 N NaOH-MeOH was allowed to stand for 19 h at room temperature. The solution was neutralized with Amberlite MB-3 resin and then concentrated to dryness. The crude product was purified by chromatography on a reverse-phase column (RP-8, 45% MeOH) to give 74 mg of **2**, which was identified by comparison of the ^{13}C -NMR spectrum and $[\alpha]_D$ with those of an authentic sample.

Alkaline Hydrolysis of 4—A solution of 181 mg of **4** in 1.5 ml of 1 N NaOH-MeOH was allowed to stand at room temperature for 4 d. After being neutralized with DOWEX 50W- $\times 8$ resin, the reaction mixture was concentrated to dryness. The residue was subjected to chromatography on a silica gel column (CHCl_3 and then CHCl_3 -MeOH- H_2O (30:10:1)) to give methyl syringate (**12**) (32 mg) and an iridoid (55 mg). Compound **12** was identified by comparison of the MS and NMR data with those of an authentic sample, which was derived from syringic acid by the usual treated with CH_2N_2 . The iridoid was methylated with CH_2N_2 to give 59 mg of **2** which was identified by comparison of the ^{13}C -NMR spectrum with that of an authentic sample.

12: colorless prisms (from $n\text{-C}_6\text{H}_{14}$), mp 107 – 108°C . EI-MS m/z : 212 (M^+), 181 ($[\text{M}-\text{OMe}]^+$). ^1H -NMR (in CDCl_3) δ : 3.91 (3H, s, OMe), 3.95 (6H, s, OMe $\times 2$), 7.35 (2H, s, aromatic H).

2: a white powder, $[\alpha]_D^{22} - 124.5^\circ$ ($c=0.8$, MeOH).

Alkaline Partial Hydrolysis of 4—A solution of **4** (150 mg) in 3 ml of 0.1 N NaOH-MeOH was allowed to stand at room temperature for 4 d. After being neutralized with Amberlite MB-3 resin, the solution was concentrated to dryness. The crude product was purified by chromatography on a reverse-phase column (LiChroprep RP-8) with 45% MeOH to afford 120 mg of **13**: a white powder, $[\alpha]_D^{22} - 117.3^\circ$ ($c=1.1$, MeOH). Anal. Calcd for $\text{C}_{26}\text{H}_{34}\text{O}_{15}$: C, 50.16; H, 6.15. Found: C, 50.17; H, 5.90. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 275 (3.9), 221 (4.3).

Acknowledgement We are grateful to Prof. Chen-yih Wu, the former Director of Kunming Institute of Botany, Academia Sinica, for the taxonomical identification and for valuable advice. We are also grateful to Prof. Hiroyuki Inouye, Kyoto University, for his valuable advice and for supplying samples of the iridoid glucosides. This study was supported by a Grant (in 1983) from Yamada Science Foundation, Osaka.

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