Chemical Studies on Crude Drug Processing. IX.[1] On the Constituents of Rehmanniae Radix. (3). Absolute Stereostructures of Rehmaionosides A, B, and C, and Rehmapicroside, Biologically Active Ionone Glucosides and a Monoterpene Glucoside Isolated from Chinese Rehmanniae Radix

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Following the characterization of the iridoid and iridoid glycoside constituents in Chinese Rehmanniae Radix, the dried root of *Rehmannia glutinosa* LIBOSCH. [Kan-jio in Japanese], we investigated the structures of biologically active ionone glucosides, rehmaionosides A, B, and C, and a monoterpene glucoside, rehmapicroside. Their absolute stereostructures were determined on the basis of chemical and physicochemical evidence, which included the result of application of the exciton chirality method to the allylic benzoyl derivatives.

Key words Rehmanniae Radix; *Rehmannia glutinosa*; ionone glucoside; monoterpene glucoside; rehmaionoside; rehmapicroside

As a part of our continuing chemical studies on the processing of Rehmanniae Radix,[3] we have investigated the chemical constituents of Chinese Rehmanniae Radix, whose botanical origin was identified as *Rehmannia glutinosa* LIBOSCH. (Scrophulariaceae). We have so far reported the isolation of four iridoids (rehmaglutins A,[4] B,[4] C,[1,5] and D[4]), a chlorinated iridoid glycoside (glutinoside[1,5]), three ionone glucosides [rehmaionosides A(**1**),[6] B(**2**),[6] and C(**3**)[5]], and a monoterpene glucoside [rehmapicroside (**10**)[6]], together with eight known glycosides. Among them, rehmaionosides A(**1**) and B(**2**) were found to induce contraction of the isolated bladder and urethral smooth muscle of mice.[7] We have described the absolute stereostructures of rehmaglutins A, B, C, and D, and glutinoside.[1,4,5]

This paper presents a full account of the structure elucidation of three ionone glucosides, rehmaionosides A(**1**), B(**2**), and C(**3**), and a monoterpene glucoside, rehmapicroside (**10**).[6]

Rehmaionosides A(1), B(2), and C(3) The infrared (IR) spectra of rehmaionosides A(**1**) and B(**2**) were very similar and showed absorption bands ascribable to hydroxyl and olefin functions. The liquid secondary ionization mass spectra (liquid SIMS) of **1** and **2** showed the same quasimolecular ion peaks at *m/z* 391 $(M+H)^+$, 413 $(M+Na)^+$, and 483 $(M+H+glycerol)^+$. The high-resolution liquid SIMS measurement of **1** and **2** revealed their molecular formula to be $C_{19}H_{34}O_8$.

Rehmaionoside C(**3**) was obtained as colorless prisms of mp 217—218 °C and the molecular formula $C_{19}H_{32}O_8$ was determined by elemental analysis. The ultraviolet (UV) and IR spectra of **3** showed absorption due to an enone function at 232 nm (ε 10700) and 1680 cm^{-1}, respectively. Reduction of **3** with $NaBH_4$ in methanol yielded rehmaionosides A(**1**) and B(**2**) in a 1 : 1 ratio, while **3** was obtained by oxidation of **1** and **2** with CrO_3 in pyridine. Acetylation of **3** with acetic anhydride and pyridine provided the pentaacetate (**3a**). The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **3a** showed signals assignable to four methyl groups, two olefinic protons, and a β-glucopyranosyl moiety. Hydrolysis of **3** with β-glucosidase afforded an aglycone (**5**), which was found to be identical with the synthetic ionone derivative (**5′**),[8] except for the sign of the specific rotation [**5**, $[\alpha]_D$ −54°; **5′**, $[\alpha]_D$ +55°]. Based on this evidence, the structure of the aglycone (**5**) was concluded to be the antipode of **5′**.

A detailed comparison of the ^{13}C-NMR data (Table 1) for **3** with those for **3a** and **5** led us to consider that the glucopyranosyl residue in **3** was attached to the 2′-hydroxyl group. Consequently, the structure of rehmaionoside C(**3**) has been determined to be as shown.

The plane structure of rehmaionoside C(**3**) was identical with that proposed for a dihydroxy-β-ionone glucoside which was isolated from *Aeginetia indica* L. var. *gracilis* NAKAI.[9] The physicochemical properties of **3** were found to be identical with those reported for the dihydroxy-β-ionone glucoside. Therefore, we concluded that the dihydroxy-β-ionone glucoside has the same absolute stereostructure as rehmaionoside C(**3**).

Next, the structures of rehmaionosides A(**1**) and B(**2**) were investigated. Treatment of **1** and **2** with 4.5% hydrogen chloride in dry methanol provided an epimeric mixture of the 2-methoxyl derivative (**4**), which gave the pentaacetate (**4a**) on usual acetylation. Comparison of the ^{13}C-NMR data (Table 1) for **4** with those of **4a** and the observation of a nuclear Overhauser effect (NOE) (14.1%) between 2-OCH_3 and 2-H substantiated the structure **4**. Methanolysis of **4** with 9% hydrogen chloride in dry methanol liberated **6**,[10] **7**[10] and methyl glucoside.

Hydrolysis of rehmaionoside A(**1**) and B(**2**) with β-glucosidase afforded **8** (from **1**) and **9** (from **2**), which were obtained in a 1 : 1 ratio from **5** by $NaBH_4$ reduction. Based on the above-mentioned evidence, the structures of rehmaionosides A(**1**) and B(**2**) were elucidated, except for the absolute stereostructure at the 2-position.

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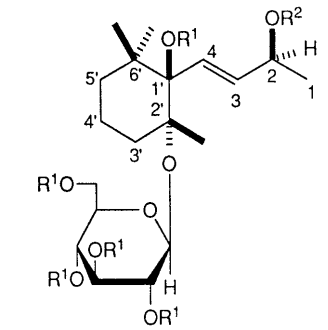
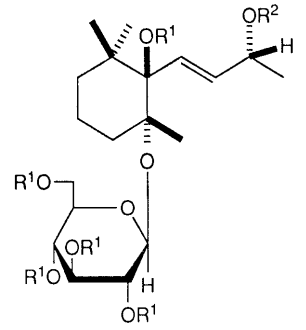


rehmaionoside A (**1**) : R^1=R^2=H

1a : R^1=Ac , R^2=H

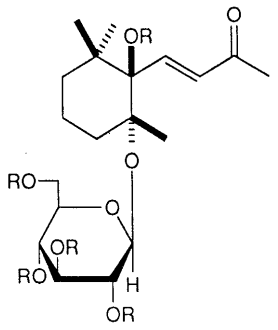
1b : R^1=Ac , R^2=Bz



rehmaionoside B (**2**) : R^1=R^2=H

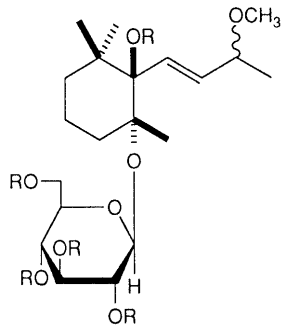
2a : R^1=Ac , R^2=H

2b : R^1=Ac , R^2=Bz



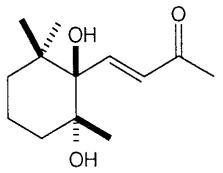
rehmaionoside C (**3**) : R=H

3a : R=Ac



4 : R=H

4a : R=Ac



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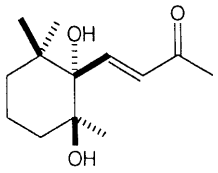

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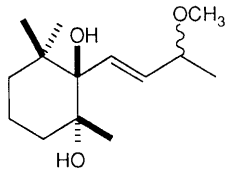
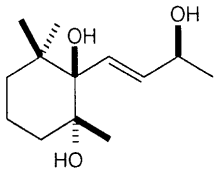


6 , **7**



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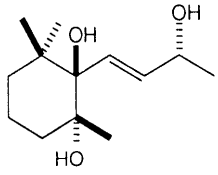

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Chart 1

Table 1. ^{13}C-NMR Data for **1**, **2**, **3**, **3a**, **4**, **4a**, **5**, **8**, and **9** (in Pyridine-d_5)

Carbon	1	2	3	3a	4	4a	5	8	9
1	24.8 (q)[a]	24.7 (q)	25.8 (q)	25.0 (q)	22.2 (q)	22.2 (q)	26.9 (q)	24.9 (q)	25.0 (q)
2	68.1 (d)	68.1 (d)	198.3 (s)	198.3 (s)	78.3 (d)	78.4 (d)	197.7 (s)	68.3 (d)	68.4 (d)
3	130.8 (d)	130.9 (d)	131.9 (d)	132.0 (d)	131.9 (d)	132.6 (d)	131.1 (d)	130.9 (d)	130.9 (d)
4	135.5 (d)	135.1 (d)	151.9 (d)	149.9 (d)	134.9 (d)	133.9 (d)	151.4 (d)	135.9 (d)	135.9 (d)
1′	79.4 (s)	79.1 (s)	79.7 (s)	83.9 (s)	79.4 (s)	84.1 (s)	79.8 (s)	79.1 (s)	79.1 (s)
2′	82.9 (s)	82.7 (s)	82.6 (s)	79.2 (s)	82.8 (s)	78.4 (s)	74.5 (s)	74.8 (s)	74.8 (s)
3′	32.0 (t)	32.0 (t)	32.0 (t)	32.6 (t)	31.6 (t)	32.0 (t)	36.5 (t)	37.0 (t)	37.0 (t)
4′	18.3 (t)	18.2 (t)	18.2 (t)	18.1 (t)	19.0 (t)	18.2 (t)	18.4 (t)	18.9 (t)	18.9 (t)
5′	36.9 (t)	36.7 (t)	36.6 (t)	36.0 (t)	36.9 (t)	36.4 (t)	36.8 (t)	37.2 (t)	37.3 (t)
6′	38.9 (s)	38.7 (s)	39.4 (s)	39.1 (s)	38.9 (s)	38.6 (s)	39.0 (s)	38.7 (s)	38.8 (s)
2′-CH_3	22.8 (q)	22.4 (q)	22.8 (q)	21.5 (q)	22.8 (q)	21.9 (q)	25.5 (q)	25.5 (q)	25.6 (q)
6′-CH_3	25.6 (q)	25.5 (q)	27.0 (q)	26.4 (q)	25.7 (q)	25.0 (q)	27.3 (q)	27.6 (q)	27.6 (q)
	27.8 (q)	27.6 (q)	27.6 (q)	27.6 (q)	27.8 (q)	27.7 (q)	27.6 (q)	27.6 (q)	27.7 (q)
1″	98.2 (d)	98.0 (d)	98.3 (d)	95.3 (d)	98.2 (d)	95.1 (d)			
2″	75.3 (d)	75.0 (d)	75.3 (d)	71.7 (d)	75.3 (d)	71.7 (d)			
3″	78.7 (d)	78.6 (d)	79.4 (d)	72.5 (d)	78.8 (d)	72.6 (d)			
4″	72.0 (d)	71.6 (d)	72.0 (d)	69.5 (d)	72.0 (d)	69.5 (d)			
5″	77.5 (d)	77.4 (d)	77.9 (d)	74.1 (d)	77.5 (d)	74.2 (d)			
6″	63.0 (t)	62.6 (t)	63.1 (t)	62.7 (t)	63.1 (t)	62.7 (t)			
–OCH_3					55.7 (q)	55.8 (q)			

a) The characterization of each carbon signal was based on INEPT (Insensitive Nuclei Enhanced by Polarization) and off-resonance experiments.

In order to elucidate the C2-configuration in **1** and **2**, the allylic benzoate exciton chirality method[11] was applied to **1b** and **2b**, which were prepared from rehmaionoside C pentaacetate (**3a**). Namely, reduction of **3a** with $NaBH_4$ in methanol yielded **1a** and **2a** in a 1 : 1 ratio. Benzoylation of **1a** and **2a** with benzoyl chloride in pyridine afforded the 2-benzoyl derivatives, **1b** (from **1a**) and **2b** (from **2a**), respectively. Since deacylation of **1b** and **2b** with 1% NaOMe in methanol regenarated **1** and **2**, the structures of **1b** and **2b** were corroborated.

The ^{1}H-NMR spectrum of **1b** in CD_3OD exhibited a signal due to benzoyloxy-bearing methine [δ 5.64, dq,

$J_{2,3}=6.1$ Hz, $J_{1,2}=6.4$ Hz]. The circular dichroism (CD) spectrum of **1b** in methanol gave a positive first Cotton effect at 226 nm (ε 13100). Consequently, the preferred configuration (**a**) around the 2-benzoyloxy-3-ene moiety in **1b** was presumed to be as shown in Fig. 1, and the 2*S* configuration in **1b** was determined.

On the other hand, the $J_{2,3}$ value in the ^{1}H-NMR spectrum of **2b** was 5.8 Hz and the CD spectrum of **2b** showed a negative first Cotton effect at 226 nm (ε -15200). Thus, the 2*R* configuration (**b**) in **2b** was concluded to be as shown in Fig. 1. Based on the above evidence, the absolute configurations of rehmaionosides A (**1**) and B (**2**) were determined to be as shown.

Rehmapicroside (10) Rehmapicroside (**10**) was obtained as colorless prisms of mp 127—129 °C. The IR spectrum of **10** showed absorption bands due to hydroxyl groups and an α, β-unsaturated carboxyl moiety at 3405, 1691, and 1637 cm^{-1}. The molecular formula $C_{16}H_{26}O_8$ was confirmed by the quasimolecular ion peaks at *m/z* 347 $(M+H)^+$, 369 $(M+Na)^+$, and 439 $(M+H+glycerol)^+$ in the liquid SIMS and by the elemental analysis measurement.

The ^{1}H- and ^{13}C-NMR spectra of **10** showed signals assignable to one olefinic methyl group, two tertiary methyl groups, a tetrasubstituted olefin moiety, an α,β-unsaturated carbonyl group, and a β-glucopyranosyl moiety. Ordinary acetylation of **10** yielded the tetraacetate (**10a**), while methylation of **10** with diazomethane in methanol gave the monomethyl ester (**10b**).

Methanolysis of **10** with 9% hydrogen chloride in dry methanol liberated a racemic 3-methoxyl derivative (**11**) and methyl glucoside. Hydrolysis of **10b** with β-glucosidase liberated an aglycone methyl ester (**12**), which gave the known enone (**13**)[12] by oxidation with CrO_3 in pyridine. Thus, the plane structure of rehmapicroside (**10**) was confirmed.

Finally, the absolute stereostructure of rehmapicroside (**10**) was determined by the application of the allylic benzoate exciton chirality method as described for rehmaionosides A (**1**) and B (**2**). Namely, benzoylation of an aglycone methyl ester (**12**) with benzoyl chloride in pyridine furnished the monobenzoate (**12a**). The CD spectrum of **12a** gave a positive first Cotton curve ($[\theta]_{229}$ +26500). Thus, the 3*R* configuration of **12a** was determined.

Furthermore, the absolute stereostructure of **10** was substantiated by its partial synthesis from α-ionone. The enone methyl ester (**13**), which was prepared from α-ionone,[13] was treated with $NaBH_4$ in methanol to afford racemic **12**. Glycosidation of racemic **12** with 1-bromo-2,3,4,6-tetra-*O*-acetylglucopyranose and $Hg(CN)_2$ and subsequent deacetylation reaction gave the 3-epimeric mixture, which was further subjected to high-performance liquid chromatographic (HPLC) purification to provide **10b** (30% yield from **13**) and the diastereoisomer (**14**, 31%). Hydrolysis of **10b** with 10% KOH in aqueous methanol furnished rehmapicroside (**10**, 69%).

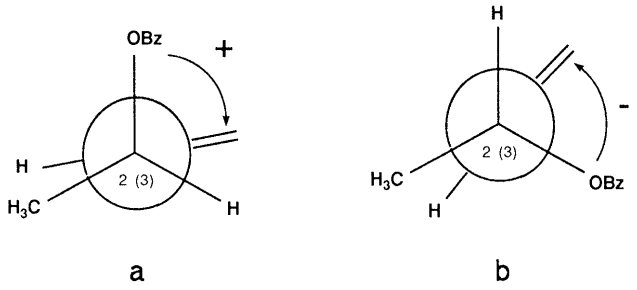

Fig. 1

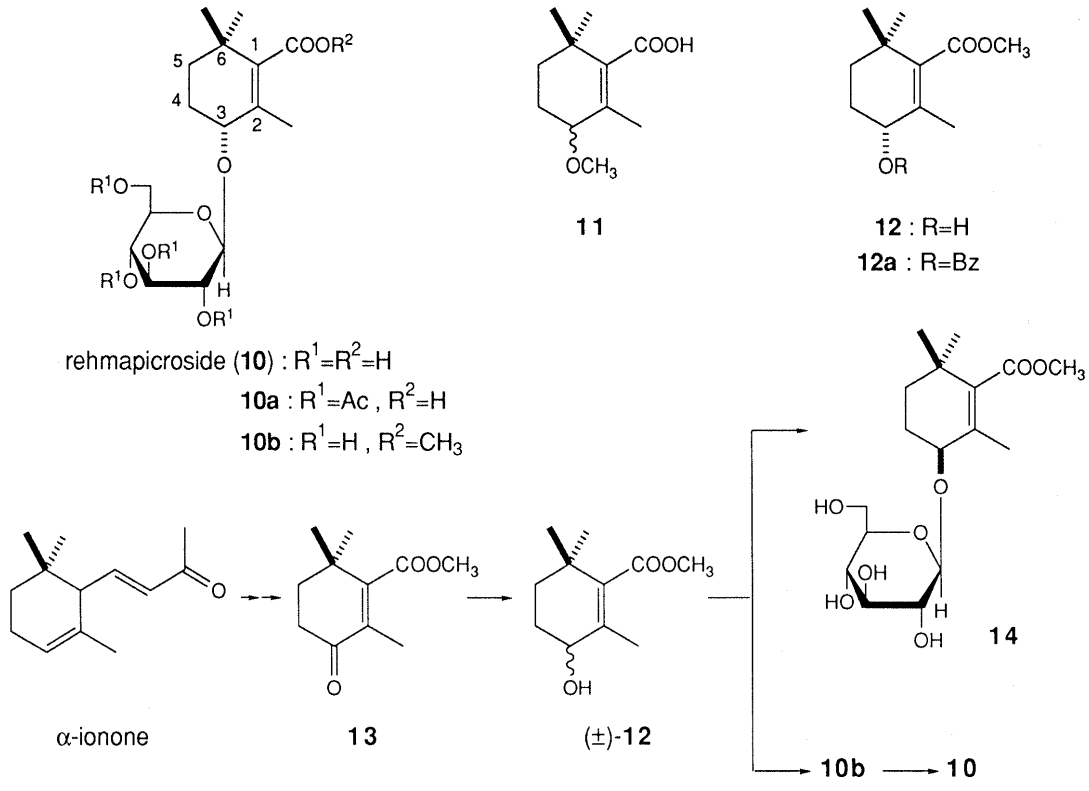

Chart 2

Table 2. ^{13}C-NMR Data for **10**, **10a**, **10b**, **11**, **12**, and **14** (in Pyridine-d_5)

Carbon	10	10a	10b	11	12	14
1	140.5 (s)	142.0 (s)	139.1 (s)	141.0 (s)	137.4 (s)	138.9 (s)
2	129.8 (s)	128.9 (s)	132.6 (s)	130.8 (s)	135.9 (s)	133.3 (s)
3	73.1 (d)	76.4 (d)	73.1 (d)	77.8 (d)	68.1 (d)	74.7 (d)
4	24.0 (t)	25.3 (t)	24.2 (t)	23.6 (t)	29.4 (t)	24.3 (t)
5	33.7 (t)	33.8 (t)	34.0 (t)	34.8 (t)	35.2 (t)	34.0 (t)
6	32.7 (s)	33.5 (s)	33.3 (s)	33.5 (s)	33.8 (s)	33.4 (s)
1-COO–	171.7 (s)	170.2 (s)	170.2 (s)	172.3 (s)	170.7 (s)	170.3 (s)
2-CH_3	17.9 (q)	18.5 (q)	18.2 (q)	18.4 (q)	18.3 (q)	18.5 (q)
	26.9 (q)	27.0 (q)	27.1 (q)	27.6 (q)	27.8 (q)	27.2 (q)
6-CH_3	27.9 (q)	28.7 (q)	28.0 (q)	28.7 (q)	28.3 (q)	28.4 (q)
1′	100.9 (d)	99.7 (d)	101.4 (d)			107.1 (d)
2′	74.1 (d)	72.1 (d)	74.7 (d)			75.3 (d)
3′	77.2 (d)	72.1 (d)	78.0 (d)			78.1 (d)
4′	71.2 (d)	69.3 (d)	71.6 (d)			71.7 (d)
5′	77.2 (d)	73.5 (d)	78.0 (d)			78.3 (d)
6′	62.1 (t)	62.4 (t)	62.7 (t)			62.9 (t)
–OCH_3			50.8 (q)	56.5 (q)	50.9 (q)	50.9 (q)

Based on the above evidence, the absolute configuration of rehmapicroside (**10**) was determined to be as shown.

Experimental

The instruments used to obtain physical data and the experimental conditions for chromatography were the same as described in our previous paper.[1)]

Rehmaionosides A(1), B(2), C(3), and Rehmapicroside (10) Rehmaionoside A(**1**): Hygroscopic amorphous powder, $[\alpha]_D^{20}$ −49.3° (c=1.03, MeOH). *Anal.* Calcd for $C_{19}H_{34}O_8 \cdot 2H_2O$: C, 53.51; H, 8.98. Found: C, 53.36; H, 8.91. High-resolution liquid SIMS: Calcd for $C_{19}H_{35}O_8$ $(M+H)^+$: 391.233. Found: 391.234. IR (KBr): 3400, 2924, 1633, 1075, 1021 cm^{-1}. ^{1}H-NMR (90 MHz, pyridine-d_5) δ: 1.20 (3H, s, 6′-α-CH_3), 1.41 (3H, d, J=6 Hz, 1-CH_3), 1.61, 1.73 (3H each, both s, 2′,6′-β-CH_3), 5.11 (1H, d, J=7 Hz, 1″-H), 6.36 (1H, dd, J=6, 16 Hz, 3-H), 6.87 (1H, d, J=16 Hz, 4-H). ^{13}C-NMR: see Table 1. Liquid SIMS (Xe^+, glycerol matrix) m/z: 391 $(M+H)^+$, 413 $(M+Na)^+$, 483 $(M+H+glycerol)^+$.

Rehmaionoside B(**2**): Hygroscopic amorphous powder, $[\alpha]_D^{20}$ −54.2° (c=3.06, MeOH). *Anal.* Calcd for $C_{19}H_{34}O_8 \cdot 2H_2O$: C, 53.51; H, 8.98. Found: C, 53.72; H, 8.93. High-resolution liquid SIMS: Calcd for $C_{19}H_{35}O_8$ $(M+H)^+$: 391.233. Found: 391.235. IR (KBr): 3400, 2926, 1631, 1074, 1020 cm^{-1}. ^{1}H-NMR (90 MHz, pyridine-d_5) δ: 1.18 (3H, s, 6′α-CH_3), 1.41 (3H, d, J=6 Hz, 1-CH_3), 1.57, 1.69 (3H each, both s, 2′,6′β-CH_3), 5.14 (1H, d, J=7 Hz, 1″-H), 6.33 (1H, dd, J=6, 16 Hz, 3-H), 6.83 (1H, d, J=16 Hz, 4-H). ^{13}C-NMR: see Table 1. Liquid SIMS (Xe^+, glycerol matrix) m/z: 391 $(M+H)^+$, 413 $(M+Na)^+$, 483 $(M+H+glycerol)^+$.

Rehmaglutin C(**3**): mp 217—218 °C (colorless prisms from MeOH), $[\alpha]_D^{24}$ −59.4° (c=0.28, MeOH). *Anal.* Calcd for $C_{19}H_{32}O_8$: C, 58.75; H, 8.30. Found: C, 58.44; H, 8.34. UV λ_{max}^{MeOH} nm (ε): 232 (10700). IR (KBr): 3270, 1680, 1059 cm^{-1}. ^{1}H-NMR (90 MHz, pyridine-d_5) δ: 1.10 (3H, s, 6′α-CH_3), 1.58, 1.65 (3H each, both s, 2′,6′β-CH_3), 2.25 (3H, s, 1-CH_3), 5.05 (1H, d, J=7 Hz, 1″-H), 6.86 (1H, d, J=17 Hz, 3-H), 7.96 (1H, d, J=17 Hz, 4-H). ^{13}C-NMR: see Table 1.

Rehmapicroside (**10**): mp 127—129 °C (colorless prisms from MeOH), $[\alpha]_D^{24}$ +8.5° (c=0.66, MeOH). High-resolution liquid SIMS: Calcd for $C_{16}H_{27}O_8$ $(M+H)^+$: 347.171. Found: 347.172. IR (KBr): 3405, 1691, 1637, 1073 cm^{-1}. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 1.24, 1.35 (3H, each, both s, 6α,6β-CH_3), 1.87 (3H, s, 2-CH_3), 3.98 (1H, ddd, J=2, 6, 9 Hz, 5′-H), 4.01 (1H, dd, J=8, 9 Hz, 2′-H), 4.22 (1H, dd, J=9, 9 Hz, 4′-H). 4.29 (1H, dd, J=9, 9 Hz, 3′-H), 4.37 (1H, dd, J=6, 12 Hz, 6′-H), 4.45 (1H, br s, 3-H), 4.56 (1H, dd, J=2, 12 Hz, 6′-H), 4.96 (1H, d, J=8 Hz, 1′-H). ^{13}C-NMR: see Table 2. Liquid SIMS (Xe^+, glycerol matrix) m/z: 347 $(M+H)^+$, 369 $(M+Na)^+$, 439 $(M+H+glycerol)^+$.

$NaBH_4$ Reduction of Rehmaionoside C(3) A solution of **3** (10 mg) in MeOH (1 ml) was treated with $NaBH_4$ (6 mg) and the mixture was stirred at room temperature (23 °C) under an N_2 atmosphere for 20 min, then neutralized with Dowex 50 W × 8 (H^+ form). The resin was removed by filtration. After removal of the solvent from the filtrate under reduced pressure, the product was purified by HPLC [Zorbax ODS, MeOH–H_2O (3 : 2)] to yield **1** (5 mg) and **2** (5 mg). These products were shown to be identical with authentic rehmaionosides A and B, which were isolated above from Chinese Rehmanniae Radix, by TLC [Silica gel 60 F_{254} pre-coated TLC (ordinary phase TLC): $CHCl_3$–MeOH–H_2O (65 : 35 : 10, lower phase), n-BuOH–AcOEt–H_2O (4 : 1 : 5, upper phase); silanized silica gel 60 F_{254} pre-coated TLC (reversed phase TLC): MeOH–H_2O (1 : 1)] and IR (KBr) comparisons.

CrO_3 Oxidation of Rehmaionoside A(1) A solution of **1** (7 mg) in pyridine (1.0 ml) was treated with CrO_3 (21 mg)-pyridine (0.5 ml) and the mixture was stirred at room temperature (23 °C) under an N_2 atmosphere for 3 h. The reaction mixture was treated with isopropyl alcohol (1.0 ml) and stirred for 3 h as above, then filtered to remove the inorganic precipitate. Concentration of the filtrate under reduced pressure yielded a product (11 mg), which was purified by column chromatography [SiO_2 200 mg, $CHCl_3$–MeOH–H_2O (10 : 3 : 1, lower phase)] to provide **3** (5 mg). This product was shown to be identical with authentic rehmaionoside C obtained from Chinese Rehmanniae Radix by TLC [ordinary phase TLC: $CHCl_3$–MeOH–H_2O (7 : 3 : 1, lower phase), $CHCl_3$–MeOH (10 : 1) and $CHCl_3$–n-BuOH (1 : 1)], IR (KBr), and ^{1}H-NMR (90 MHz, pyridine-d_5) comparisons.

CrO_3 Oxidation of Rehmaionoside B(2) A solution of **2** (8 mg) in pyridine (1.0 ml) was treated with CrO_3 (21 mg)-pyridine (0.5 ml) and the mixture was stirred at room temperature (23 °C) under an N_2 atmosphere for 3 h. Isopropyl alcohol (1.0 ml) was added and the mixture was stirred, then filtered as described in connection with the oxidation of **1**. Concentration of the filtrate under reduced pressure yielded a product (13 mg), which was purified by column chromatography [SiO_2 200 mg, $CHCl_3$–MeOH–H_2O (10 : 3 : 1, lower phase)] to furnish **3** (6 mg). This was shown to be identical with authentic rehmaionoside C by TLC (as described above), IR (KBr), and ^{1}H-NMR (90 MHz, pyridine-d_5) comparisons.

Acetylation of Rehmaionoside C(3) A solution of **3** (13 mg) in pyridine (1.0 ml) was treated with Ac_2O (1.0 ml) and the mixture was stirred at room temperature (19 °C) under an N_2 atmosphere for 12 h. It was then poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 2 N HCl, aqueous saturated $NaHCO_3$, and brine, and then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave **3a** (20 mg).

3a: mp 183—184 °C (colorless needles from acetone), $[\alpha]_D^{20}$ −56.2° (c=1.00, MeOH). *Anal.* Calcd for $C_{29}H_{42}O_{13}$: C, 58.19; H, 7.07. Found: C, 57.88; H, 7.19. UV λ_{max}^{MeOH} nm (ε): 228 (16600). IR (KBr): 1751, 1674, 1241, 1036 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.00 (6H), 2.01, 2.02, 2.04 (3H each) (all s, OAc × 5) and others as given in Table 2. ^{13}C-NMR (22.5 MHz, pyridine-d_5) δ_C: 20.4 (4C), 20.8 (1C) and others as given in Table 1.

Enzymatic Hydrolysis of Rehmaionoside C(3) A solution of **3** (11 mg) in water (1.5 ml) was treated with β-glucosidase (42 mg, from almond, Sigma) and the mixture was stirred at 37 °C for 72 h. It was then diluted with water and the whole was extracted with AcOEt. The AcOEt extract was washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the product was purified by column chromatography [SiO_2 500 mg, benzene–acetone (6 : 1)] to furnish **5** (4 mg).

5: mp 115—116 °C (colorless prisms from benzene), $[\alpha]_D^{25}$ −53.6° (c=0.10, EtOH). High-resolution MS: Calcd for $C_{13}H_{22}O_3$ (M^+) 226.157. Found: 226.154. IR ($CHCl_3$): 3600, 3450, 1670, 1620 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.83, 1.13, 1.23 (3H each, all s, 2′,6′α,6′β-CH_3), 2.31 (3H, s, 1-CH_3), 6.34, 7.33 (1H each , both d, J=16 Hz, 3,4-H). ^{13}C-NMR: see Table 1.

Acid Treatment of Rehmaionoside A(1) A solution of **1** (11 mg) in dry MeOH (1.0 ml) was treated with 9% HCl–dry MeOH and the mixture was stirred at room temperature (23 °C) under an N_2 atmosphere for 8 h, then neutralized with Dowex 1 × 2 (OH^- form) and filtered. Removal of the solvent from the filtrate under reduced pressure gave a product (13 mg), which was purified by column chromatography [SiO_2 500 mg, $CHCl_3$–MeOH (10 : 1)] to furnish **4** (8 mg).

4: mp 166—168 °C (colorless prisms from acetone), $[\alpha]_D^{20}$ −60.2° (c=0.23, MeOH). *Anal.* Calcd for $C_{20}H_{36}O_8 \cdot H_2O$: C, 56.86; H, 9.07. Found: C, 56.55; H, 8.98. IR (KBr): 3391, 2929, 1598, 1036 cm^{-1}. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 1.20 (3H, d, J=6 Hz, 1-CH_3), 1.25, 1.68, 1.73 (3H each, all s, 2′,6′α,6′β-CH_3), 3.29 (3H, s, 2-OCH_3), 3.72 (1H dq, J=6, 8 Hz, 2-H), 5.12 (1H, d, J=9 Hz, 1″-H), 6.00 (1H, dd,

$J=8$, 16 Hz, 3-H), 6.72 (1H, d, $J=16$ Hz, 4-H). ^{13}C-NMR: see Table 1. MS *m/z* (%): 226 (M^+, 1), 208 (M^+-H_2O, 13).

Acid Treatment of Rehmaionoside B(2) A solution of **2** (35 mg) in dry MeOH (1.0 ml) was treated with 9% HCl–dry MeOH (1.0 ml) and the mixture was stirred at room temperature (23 °C) under an N_2 atmosphere for 8 h, then worked up as described above for the acid treatment of **1**. The product (39 mg) was purified by column chromatography [SiO_2 1 g, $CHCl_3$–MeOH (10 : 1)] to furnish **4** (29 mg), which was identical with an authentic sample obtain from acid treatment of 1 by TLC [ordinary phase TLC; $CHCl_3$–MeOH (10 : 1), benzene–acetone (2 : 1), *n*-hexane–AcOEt (1 : 1)], and ^{1}H-NMR (500 MHz, pyridine-d_5) comparisons.

Acetylation of 4 A solution of **4** (12 mg) in pyridine (0.5 ml) was treated with Ac_2O (0.5 ml) and the mixture was stirred at room temperature (23 °C) under an N_2 atmosphere for 8 h, then poured into ice-water. The whole was extracted with AcOEt. The AcOEt extract was worked up as described above for the acetylation of **3** to furnish **4a** (18 mg).

4a: mp 111—113 °C (colorless prisms from acetone), $[\alpha]_D^{18}$ −81.5° ($c=0.42$, MeOH). *Anal.* Calcd for $C_{30}H_{46}O_{13}$: C, 58.62; H, 7.54. Found: C,58.18; H, 7.79. IR ($CHCl_3$): 2934, 1751, 1600, 1035 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.84, 1.03, 1.14, (3H each, all s, 2′,6′α,6′β-CH_3), 1.25 (3H, d, $J=6$ Hz, 1-CH_3), 1.99 (3H), 2.02, 2.03 (6H each) (all s, OAc × 5), 3.28 (3H, s, 2-OCH_3), 3.75 (1H, dq, $J=6$, 8 Hz, 2-H), 4.68 (1H, d, $J=7$ Hz, 1″-H), 5.46 (1H, dd, $J=8$, 16 Hz, 3-H), 6.14 (1H, d, $J=16$ Hz, 4-H). ^{13}C-NMR (22.5 MHz, pyridine-d_5) δ_C: 20.4 (2C), 20.5 (2C), 20.8 (1C) and others as given in Table 1.

Methanolysis of 4 A solution of **4** (10 mg) in 9% HCl–dry MeOH (1.0 ml) was stirred at room temperature (24 °C) under an N_2 atmosphere for 15 h, then neutralized with Ag_2CO_3 and filtered. Removal of the solvent from the filtrate under reduced pressure furnished a product, which was purified by column chromatography [SiO_2 1 g, benzene–acetone (10 : 1)] to give **6** (2 mg), **7** (3 mg), and a methyl glucoside mixture. The methyl glucoside mixture was dissolved in pyridine (0.1 ml) and treated with *N,O*-bis(trimethylsilyl)tri-fluoroacetamide (BSTFA, 0.2 ml) for 1 h. The product was then analyzed by GLC to identify the trimethylsilyl (TMS) derivatives of methyl α- and β-glucopyranoside. GLC: 5% SE-52 on Uniport HP (60—80 mesh); 3 mm × 2 m glass column; column temperature 170 °C; N_2 flow rate 40 ml/min; t_R: TMS-methyl glucopyranoside 10 min 35 s, 11 min 31 s.

6: mp 93—94 °C (colorless needles from MeOH), $[\alpha]_D^{18}$ −73.6° ($c=0.12$, MeOH). High-resolution MS: Calcd for $C_{14}H_{24}O_2$ (M^+-H_2O) 224.177; $C_{13}H_{22}O_2$ (M^+−MeOH): 210.162; $C_{13}H_{20}O$ (M^+-H_2O−MeOH): 192.152. Found: 224.176, 210.162, 192.152. IR ($CHCl_3$): 3360, 2930, 1600, 1074 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.88, 1.13, 1.21, (3H each, all s, 2′,6′α,6′β-CH_3), 1.29 (3H, d, $J=6$ Hz, 1-CH_3), 3.30 (3H, s, OCH_3), 3.84 (1H, dq, $J=6$, 8 Hz, 2-H), 5.59 (1H, dd, $J=8$, 16 Hz, 3-H), 6.14 (1H, d, $J=16$ Hz, 4-H). MS *m/z* (%): 224 (M^+-H_2O, 0.1), 210 (M^+−MeOH, 11), 192 (M^+-H_2O−MeOH, 5). CI-MS *m/z* (%): 225 [(M^+-H_2O), 22], 211 [(M^+−MeOH), 100], 193 [(M^+-H_2O−MeOH), 57].

7: mp 74—75 °C (colorless needles from MeOH), $[\alpha]_D^{15}$ −42.6° ($c=0.10$, MeOH). High-resolution MS: Calcd for $C_{13}H_{22}O_2$ (M^+−MeOH): 210.162; $C_{13}H_{20}O$ (M^+−MeOH−H_2O) 192.152. Found: 210.164, 192.153. IR ($CHCl_3$): 3360, 2930, 1600, 1075 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.83, 1.17, 1.26, (3H each, all s, 2′,6′α,6′β-CH_3), 1.29 (3H, d, $J=5$ Hz, 1-CH_3), 3.30 (3H , s, OCH_3), 3.86 (1H, dq, $J=5$, 8 Hz, 2-H), 5.58 (1H, dd, $J=8$, 16 Hz, 3-H), 6.15 (1H, d, $J=16$ Hz, 4-H).

Enzymatic Hydrolysis of 1 with β-Glucosidase A solution of **1** (16 mg) in H_2O (2.5 ml) was treated with β-glucosidase (20 mg) and the mixture was stirred at 37 °C for 72 h, then diluted with H_2O. The whole was extracted with AcOEt. The AcOEt extract was worked up as described above in connection with the enzymatic hydrolysis of **3**. The product was purified by column chromatography [SiO_2 500 mg, benzene–acetone (5 : 1)] to furnish **8** (8 mg).

8: mp 88—90 °C (colorless needles from benzene), $[\alpha]_D^{28}$ −26.4° ($c=0.14$, MeOH). High-resolution MS: Calcd for $C_{13}H_{22}O_2$ (M^+-H_2O): 210.162; $C_{13}H_{20}O$ (M^+-2H_2O): 192.152. Found: 210.163, 192.154. IR ($CHCl_3$): 3610, 3445, 2933, 1600 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.84, 1.13, 1.18, (3H each, all s, 2′,6′α,6′β-CH_3), 1.31 (3H, d, $J=7$ Hz, 1-CH_3), 4.44 (1H, ddq, $J=1$, 5, 7 Hz, 2-H), 5.77 (1H, dd, $J=5$, 16 Hz, 3-H), 6.15 (1H, dd, $J=1$,16 Hz, 4-H). ^{13}C-NMR: see Table 1.

Enzymatic Hydrolysis of 2 A solution of **2** (15 mg) in H_2O (2.5 ml) was treated with β-glucosidase (20 mg) and the mixture was stirred at 37 °C for 72 h. Work-up as described above in connection the enzymatic hydrolysis of **3** furnished a product, which was purified by column chromatography [SiO_2 500 mg, benzene–acetone (5 : 1)] to give **9** (7 mg).

9: mp 111—113 °C (colorless needles from benzene), $[\alpha]_D^{28}$ −39.6° ($c=0.42$, MeOH). High-resolution MS: Calcd for $C_{13}H_{22}O_2$ (M^+-H_2O): 210.162; $C_{13}H_{20}O$ (M^+-2H_2O) 192.152. Found: 210.162, 192.153. IR (KBr): 3610, 3445, 2933, 1600 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.87, 1.16, 1.17 (3H each, all s, 2′,6′α,6′β-CH_3), 1.32 (3H, d, $J=6$ Hz, 1-CH_3), 4.44 (1H, dq, $J=6$, 6 Hz, 2-H), 5.78 (1H, dd, $J=6$, 16 Hz, 3-H), 6.14 (1H, d, $J=16$ Hz, 4-H). ^{13}C-NMR: see Table 1.

$NaBH_4$ Reduction of 5 A solution of **5** (10 mg) in MeOH (1.0 ml) was treated with $NaBH_4$ (12 mg) and the mixture was stirred at room temperature (25 °C) under an N_2 atmosphere for 10 min, then worked up as described above in connection with the $NaBH_4$ reduction of **3**. The reaction products were purified by HPLC [Zorbax ODS (9.4 mm × 20 cm), MeOH–H_2O (3 : 2)] to furnish **8** (5 mg) and **9** (5 mg), which were identical with authentic samples obtained from the enzymatic hydrolysis of **1** and **2**, respectively, by TLC [ordinary-phase TLC: $CHCl_3$–MeOH (20 : 1), benzene–acetone (3 : 1); reversed-phase TLC: MeOH–H_2O (1 : 1)], IR ($CHCl_3$) and ^{1}H-NMR ($CDCl_3$) comparisons.

$NaBH_4$ Reduction of 3a A solution of **3a** (21 mg) in MeOH (1.5 ml) was treated with $NaBH_4$ (12 mg) and the mixture was stirred at room temperature (28 °C) under an N_2 atmosphere for 30 min. Work-up as described above in connection with the $NaBH_4$ reduction of **3** furnished a product, which purified by HPLC [Zorbax ODS (9.4 mm × 20 cm), MeOH–H_2O (2 : 1)] to furnish **1a** (10 mg) and **2a** (10 mg).

1a: mp 106—108 °C (colorless needles from benzene), $[\alpha]_D^{27}$ −67.3° ($c=0.24$, MeOH). *Anal.* Calcd for $C_{29}H_{44}O_{13}$: C, 57.99; H, 7.38. Found: C, 58.41; H, 7.15. IR (KBr): 3350, 1751, 1596, 1242, 1036 cm^{-1}. ^{1}H-NMR (90 MHz, acetone-d_6) δ: 0.83, 1.01, 1.21 (3H each, all s, 2′,6′α,6′β-CH_3),1.21 (3H, d, $J=6$ Hz, 1-CH_3), 1.94 (3H), 2.00 (12H) (both s, OAc × 5), 4.92 (1H, d, $J=8$ Hz, 1″-H), 5.75 (1H, dd, $J=6$, 16 Hz, 3-H), 6.12 (1H, d, $J=16$ Hz, 4-H).

2a: mp 96—98 °C (colorless prisms from benzene), $[\alpha]_D^{27}$ −71.4° ($c=0.42$, MeOH). *Anal.* Calcd for $C_{29}H_{44}O_{13}$: C, 57.99; H, 7.38. Found: C, 58.22; H, 7.52. IR ($CHCl_3$): 3470, 1751, 1596, 1239, 1034 cm^{-1}. ^{1}H-NMR (90 MHz, acetone-d_6) δ: 0.81, 1.00, 1.23 (3H each, all s, 2′,6′α,6′β-CH_3),1.22 (3H, d, $J=6$ Hz, 1-CH_3), 1.94 (3H), 2.01 (12H) (both s, OAc × 5), 5.74 (1H, dd, $J=6$, 16 Hz, 3-H), 6.13 (1H, d, $J=16$ Hz, 4-H).

Benzoylation of 1a A solution of **1a** (3 mg) in pyridine (0.4 ml) was treated with benzoyl chloride (0.015 ml) and the mixture was stirred at room temperature (30 °C) under an N_2 atmosphere for 8 h, then poured into ice-water. The whole was extracted with AcOEt. The AcOEt extract was washed with 2 N HCl, aqueous saturated $NaHCO_3$, and brine, and then dried over $MgSO_4$. After removal of the solvent under reduced pressure, the product was purified by column chromatography [SiO_2 1 g, benzene–AcOEt (4 : 1)] to furnish **1b** (3 mg).

1b: Colorless oil, $[\alpha]_D^{27}$ −21.9° ($c=0.33$, MeOH). High-resolution liquid SIMS: Calcd for $C_{36}H_{49}O_{14}$ $(M+H)^+$: 705.312 Found: 705.310. UV λ_{max}^{MeOH} nm (ε): 228 (14100). CD (MeOH): $[\theta]^{25}$ (nm) +13100 (226) (pos. max.). IR (KBr): 2935, 1753, 1716, 1600, 1272, 1034 cm^{-1}. ^{1}H-NMR (500 MHz, CD_3OD) δ: 0.78, 0.90, 1.16 (3H each, all s, 2′,6′α,6′β-CH_3), 1.47 (3H, d, $J=6$ Hz, 1-CH_3), 1.97, 1.99, 2.00 (3H each), 2.01 (6H) (all s, OAc × 5), 5.65 (1H, dq, $J=6$, 6 Hz, 2-H), 5.80 (1H, dd, $J=6$, 16 Hz, 3-H), 6.34 (1H, d, $J=16$ Hz, 4-H), 7.50 (2H, dd, $J=7$, 8 Hz), 7.61 (1H, t, $J=7$ Hz), 8.03 (2H, d, $J=8$ Hz) (benzoyl).

Benzoylation of 2a A solution of **2a** (2 mg) in pyridine (0.4 ml) was treated with benzoyl chloride (0.015 ml) and the mixture was stirred at room temperature (30 °C) under an N_2 atmosphere for 8 h. Work-up as described above in connection with the benzoylation of **1a** furnished a product, which was purified by column chromatography [SiO_2 1 g, benzene–AcOEt (4 : 1)] to give **2b** (2 mg).

2b: Colorless oil, $[\alpha]_D^{27}$ −45.9° ($c=0.24$, MeOH). High-resolution liquid SIMS: Calcd for $C_{36}H_{49}O_{14}$ $(M+H)^+$: 705.312. Found: 705.311. UV λ_{max}^{MeOH} nm (ε): 229 (13000). CD (MeOH): $[\theta]^{25}$ (nm): −15200 (226) (neg. max.). IR ($CHCl_3$): 2935, 1753, 1728, 1600, 1272, 1040 cm^{-1}. ^{1}H-NMR (500 MHz, CD_3OD) δ: 0.79, 0.94, 1.19 (3H each, all s, 2′,6′α,6′β-CH_3), 1.47 (3H, d, $J=6$ Hz, 1-CH_3), 1.93, 1.97, 2.00 (3H each), 2.01 (6H) (all s, OAc × 5), 5.65 (1H dq, $J=6$, 6 Hz, 2-H), 5.85 (1H, dd, $J=6$, 16 Hz, 3-H), 6.34 (1H, d, $J=16$ Hz, 4-H), 7.50 (2H, dd, $J=8$, 8 Hz), 7.63 (1H, t, $J=8$ Hz), 8.05 (2H, d, $J=8$ Hz) (benzoyl).

Deacylation of 1b A solution of **1b** (3 mg) in 1% NaOMe–MeOH (0.5 ml) was stirred at room temperature (27 °C) under an N_2 atmosphere for 30 min and neutralized with Dowex 50 W × 8 (H^+ form). The resin

was removed by filtration. After removal of the solvent from the filtrate under reduced pressure, the product was purified by column chromatography [SiO_2 100 mg, $CHCl_3$–MeOH–H_2O (7:3:1)] to furnish **1** (1 mg), which was identical with rehmaionoside A obtained from Chinese Rehmanniae Radix in terms of TLC (as described above for the $NaBH_4$ reduction of **3**) and HPLC [Zorbax ODS, MeOH–H_2O (3:2)] behavior.

Deacylation of 2b A solution of **2b** (3 mg) in 1% NaOMe–MeOH (0.5 ml) was stirred at room temperature (27 °C) under an N_2 atmosphere for 30 min and neutralized with Dowex 50 W × 8 (H^+ form). Work-up of the reaction mixture as described above for the deacylation of **1b**, gave a product, which was purified by column chromatography [SiO_2 100 mg, $CHCl_3$–MeOH–H_2O (7:3:1, lower phase)] to furnish **2** (1 mg); this was identical with authentic rehmaionoside B obtained from Chinese Rehmanniae Radix in terms of TLC (as described above) and HPLC (as described above) behavior.

Acetylation of Rehmapicroside (10) A solution of **10** (16 mg) in pyridine (1.0 ml) was treated with Ac_2O (1.0 ml) and the mixture was stirred at room temperature (23 °C) under an N_2 atmosphere for 2 h, then poured into ice-water. The whole was extracted with AcOEt. Work-up of the AcOEt extract as described above in connection with the acetylation of **3** furnished **10a** (22 mg).

10a: mp 146—148 °C (colorless prisms from Et_2O), $[\alpha]_D^{20}$ +15.8° (c=0.36, $CHCl_3$). *Anal.* Calcd for $C_{24}H_{34}O_{12}$: C, 56.03; H, 6.66. Found: C, 56.28; H, 6.47. IR ($CHCl_3$): 1746, 1698, 1239, 1030 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.13, 1.14 (3H each, both s, 6α,6β-CH_3), 1.81 (3H, s, 2-CH_3), 2.01, 2.08 (3H each), 2.04 (6H) (all s, OAc × 4), 3.71 (1H, ddd, J=2, 5, 10 Hz, 5′-H), 3.96 (1H, br s, 3-H), 4.17 (1H, dd, J=2, 12 Hz, 6′-H), 4.22 (1H, dd, J=5, 12Hz, 6′-H), 4.56 (1H, d, J=8 Hz, 1′-H), 4.96 (1H, dd, J=8, 10 Hz, 2′-H), 5.08 (1H, dd, J=10, 10 Hz, 4′-H), 5.22 (1H, dd, J=10, 10 Hz, 3′-H). ^{13}C-NMR (22.5 MHz, pyridine-d_5) δ_C: 20.4 (4C, CH_3CO– × 4) and others as given in Table 2.

Methylation of Rehmapicroside (10) with Diazomethane A solution of **10** (29 mg) in MeOH (15 ml) was treated with an excess of CH_2N_2–ether and the mixture was left to stand for 12 h. Removal of the solvent from the reaction mixture furnished **10b** (30 mg).

10b: White amorphous powder, $[\alpha]_D^{20}$ +5.8° (c=0.67, MeOH). High-resolution liquid SIMS: Calcd for $C_{17}H_{29}O_8$ $(M+H)^+$: 361.186. Found: 361.187. IR (KBr): 3400, 1722, 1071 cm^{-1}. ^{1}H-NMR (90 MHz, CD_3OD) δ: 1.06 (6H, s, 6α,6β-CH_3), 1.71 (3H, s, 2-CH_3), 3.72 (3H, s, –$COOCH_3$), 4.34 (1H, d, J=7 Hz, 1′-H). ^{13}C-NMR: see Table 2.

Methanolysis of Rehmapicroside (10) A solution of **10** (25 mg) in 9% HCl–dry MeOH (2 ml) was heated under reflux for 2 h, then neutralized with Ag_2CO_3, and filtered. Work-up of the filtrate as described above in connection with the methanolysis of **6** furnished a product, which was purified by column chromatography [SiO_2 1 g, $CHCl_3$–MeOH (10:1)] to give **11** (11 mg) and a methyl glucoside mixture (10 mg).

A solution of the methyl glucoside mixture (2 mg) in pyridine (0.1 ml) was treated with BSTFA (0.2 ml) for 1 h. The product was analyzed by GLC (as described above for the methanolysis of **6**) to identify TMS-methyl α- and β-glucopyranoside.

11: Colorless oil, $[\alpha]_D^{20}$ 0 (c=0.50, $CHCl_3$). High-resolution MS: Calcd for $C_{11}H_{18}O_3$ (M^+): 198.126. Found: 198.127. IR ($CHCl_3$): 2924, 2816, 1685, 1078 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.14, 1.16 (3H each, both s, 6α,6β-CH_3), 1.83 (3H, s, 2-CH_3), 3.39 (3H, s, OCH_3), 3.56 (1H, t, J=5 Hz, 3-H). ^{13}C-NMR: see Table 2. MS (%) m/z: 198 (M^+, 23), 183 ($M^+ - CH_3$, 35).

Enzymatic Hydrolysis of 10b with β-Glucosidase A solution of **10b** (25 mg) in H_2O (15 ml) was treated with β-glucosidase (50 mg) and the mixture was stirred at 37 °C for 10 h. Work-up of the reaction mixture as described above in connection with the enzymatic hydrolysis of **3** furnished a product, which was purified by column chromatography [SiO_2 1 g, benzene–acetone (5:1)] to give **12** (13 mg).

12: Colorless oil, $[\alpha]_D^{20}$ +53.8° (c=0.24, $CHCl_3$). High-resolution MS: Calcd for $C_{11}H_{18}O_3$ (M^+): 198.126. Found: 198.128. IR (KBr): 3420, 1718, 1216, 1059 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.08, 1.10 (3H each, both s, 6α,6β-CH_3), 1.76 (3H, s, 2-CH_3), 3.76 (3H, s, $COOCH_3$), 3.92 (1H, br t, J=5 Hz, 3-H). ^{13}C-NMR: see Table 2.

CrO_3 Oxidation of 12 A solution of **12** (10 mg) in pyridine (0.5 ml) was treated with CrO_3 (20 mg)–pyridine (0.5 ml) and the mixture was stirred at room temperature (28 °C) for 1 h, then poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 2 N HCl, aqueous saturated $NaHCO_3$, and brine, and then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product, which was purified by column chromatography [SiO_2 500 mg, n-hexane–AcOEt (10:1)] to furnish **13** (8 mg).

13: Colorless oil, High-resolution MS: Calcd for $C_{11}H_{16}O_3$ (M^+): 196.110. Found: 196.108. UV λ_{max}^{EtOH} nm (ε): 228 (11100). IR ($CHCl_3$): 2942, 1714, 1667, 1234 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.24 (6H, s, 6α,6β-CH_3), 1.72 (3H, s, 2-CH_3), 3.83 (3H, s, $COOCH_3$). MS (%) m/z: 196 (M^+, 47), 181 ($M^+ - CH_3$, 9).

Benzoylation of 12 A solution of **12** (10 mg) in pyridine (1.0 ml) was treated with benzoyl chloride (0.082 ml) and the mixture was stirred at room temperature (28 °C) under an N_2 atmosphere for 1 h, then poured into ice-water. The whole was extracted with AcOEt. After work-up of the AcOEt extract as described above in connection with the benzoylation of **1a**, the product was purified by column chromatography [SiO_2 500 mg, benzene] to furnish **12a** (10 mg).

12a: Colorless oil, $[\alpha]_D^{20}$ +50.6° (c=0.47, $CHCl_3$). High-resolution MS: Calcd for $C_{18}H_{22}O_4$ (M^+): 302.152. Found: 302.153. UV λ_{max}^{EtOH} nm (ε): 229 (14600). CD (EtOH): $[\theta]^{25}$ (nm): +36500 (239) (pos. max). IR ($CHCl_3$): 1717, 1595, 1268, 1101 cm^{-1}. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.13, 1.17 (3H each, both s, 6α,6β-CH_3), 1.69 (3H, s, 2-CH_3), 3.79 (3H, s, $COOCH_3$), 5.47 (1H, t, J=5 Hz, 3-H), 7.42—7.62 (3H, m), 8.00—8.16 (2H, m) (benzoyl). MS (%) m/z: 302 (M^+, 2), 271 (M^+ – MeOH, 53), 197 ($M^+ - C_6H_5CO$, 18), 105 (C_6H_5CO, 100).

$NaBH_4$ Reduction of 13 A solution of **13** [6.8 g, prepared from α-ionone (20 g)[13]] in methanol (150 ml) was treated with $NaBH_4$ (7 g) and the mixture was stirred at 0 °C under an N_2 atmosphere for 20 min, then treated with acetone and poured into ice water. The whole was extracted with AcOEt. The AcOEt extract was worked up to give racemic **12** (6.7 g).

Glycosidation of Racemic 12 Followed by Alkaline Hydrolysis A solution of 1-bromo-2,3,4,6-tetraacetylglucose (5.91 g) in benzene (40 ml) was added to a stirred solution of racemic **12** (810 mg) and $Hg(CN)_2$ (6.12 g) in benzene (70 ml)–dioxane (35 ml) under an N_2 atmosphere. The reaction mixture was heated under reflux for 5 h and then poured into ice-water. The whole was extracted with AcOEt and the AcOEt extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure furnished the glycosidation product (7.2 g), which was dissolved in 0.5% NaOMe–MeOH (70 ml). This solution was stirred at room temperature (24 °C) for 15 min, then neutralized with Dowex 50 W × 8 (H^+ form) and filtered. After removal of the solvent from the filtrate, the product was purified by column chromatography [SiO_2 100 g, $CHCl_3$–MeOH (10:1)] and HPLC [Zorbax ODS, MeOH–H_2O (1:2)] to furnish **10b** (430 mg) and **14** (448 mg). **10b** was found to be identical with an authentic sample obtained from rehmapicroside (**4**) by TLC [ordinary-phase TLC: $CHCl_3$–MeOH–H_2O (7:3:1, lower phase), n-BuOH–AcOEt–H_2O (4:1:5, upper phase); reversed-phase TLC: MeOH–H_2O (1:1)], IR (KBr) and ^{1}H-NMR (pyridine-d_5) comparisons.

14: Hygroscopic amorphous powder, $[\alpha]_D^{20}$ +16.4° (c=0.84, MeOH). High-resolution liquid SIMS: Calcd for $C_{17}H_{29}O_8$: 361.186. Found: 361.188. IR (KBr): 3400, 1719, 1158, 1065 cm^{-1}. ^{1}H-NMR (90 MHz, CD_3OD) δ: 1.04 (6H, s, 6α,6β-CH_3), 1.75 (3H, s, 2-CH_3), 3.73 (3H, s, $COOCH_3$), 4.40 (1H, d, J=7 Hz, 1′-H). ^{13}C-NMR: see Table 2.

Alkaline Hydrolysis of 10b A solution of **10b** (50 mg) in MeOH (1.0 ml) was treated with 10% KOH (1 ml) and the mixture was stirred at 60 °C for 12 h, then neutralized with Dowex 50 W × 8 and filtered. After removal of the solvent from the filtrate, the product was purified by column chromatography [SiO_2 5 g, $CHCl_3$–MeOH–H_2O (65:35:10, lower phase)] to furnish **10** (33 mg), which was identical with authentic rehmapicroside by TLC [ordinary-phase TLC: $CHCl_3$–MeOH–H_2O (65:35:10, lower phase), n-BuOH–AcOH–H_2O (4:1:5, upper phase), reversed-phase TLC: MeOH–H_2O (1:1)], IR (KBr), ^{1}H-NMR (pyridine-d_5) and ^{13}C-NMR (pyridine-d_5) comparisons.

References and Notes

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