

Synthesis of ^{13}C -Labeled Possible Intermediates in the Biosynthesis of Phenylethanoid Derivatives, Cornoside and Rengyosides

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In order to clarify the biosynthetic pathway of $\text{C}_6\text{-C}_2$ unit compounds containing salidroside, cornoside, and rengyosides A and B in oleaceous plants, ^{13}C -labeled putative precursors, 4-hydroxyphenylethanol, salidroside and cornoside, were prepared.

Key words quinol glucoside; cornoside; cyclohexylethanoid; 4-hydroxyphenylethanol; salidroside; ^{13}C -labeled compound

In the course of phytochemical and biosynthetic studies on secoiridoid glucosides, we have been investigating the chemical constituents of several oleaceous plants.¹⁾ Oleaceae is a rich source of oleoside (1)-type secoiridoid glucosides, such as oleuropein (2) and ligstroside (3), which contain an esterified phenylethanol group in their molecules. In our search for glucoside constituents of the fresh leaves of *Abeliophyllum distichum* (Japanese name, Uchiwanoki) of this family, we have isolated a quinol-type phenylethanoid, cornoside (4) and three related compounds containing halleridone (5).¹⁾ On the other hand, Seya *et al.* have isolated the cyclohexylethanoids rengyosides A (6), B (7) and C (8), along with 4, 5 and salidroside (9) from the fruits of *Forsythia suspensa* of the same family, and have proposed a biosynthetic pathway leading from 4-hydroxyphenylethanol (10) *via* salidroside (9) and cornoside (4) to the above cyclohexylethanoids, based on their co-occurrence.²⁾ However, no unequivocal evidence for the biosynthesis of these aromatic and aliphatic $\text{C}_6\text{-C}_2$ compounds has so far been reported. Moreover, dihydro-cornoside (11), along with 4, 6, 7 and 9, was recently isolated from *Millingtonia hortensis* (Bignoniaceae) by Hase *et al.*³⁾ In the present paper, we describe the synthesis

of ^{13}C -labeled cornoside (4), rengyosides A (6), B (7) and salidroside (9), which are indispensable for experiments to confirm the proposed biosynthetic pathway. Additionally, the synthesis of 11 pertaining to the reduction process of 4 to 7 was examined.

Synthesis of ^{13}C -Labeled 4-Hydroxyphenylethanol (10) and Salidroside (9) We planned to introduce the ^{13}C -label into the C-8 position of $\text{C}_6\text{-C}_2$ compounds by carboxylation of a benzylmagnesium halide. Carbon dioxide (prepared from BaCO_3 and sulfuric acid) was passed into 4-methoxybenzylmagnesium chloride (prepared from 4-methoxybenzyl chloride and metallic Mg) in tetrahydrofuran (THF) to give the acid 12 in 75% yield based on BaCO_3 .^{4a-c)} Demethylation of 12 with BBr_3 gave 12a.⁵⁾ The attempted reduction of 12a with LiAlH_4 under several conditions was unsuccessful, but the methyl ester 12b obtained by methylation of 12a with HCl-MeOH was smoothly reduced with $\text{NaBH}_4\text{-H}_2\text{O}$ ⁶⁾ to give the desired alcohol 10 in 90% yield. Selective acetylation of 10 was performed with 1-acetyl-1*H*-1,2,3-triazolo[4,5-*b*]pyridine

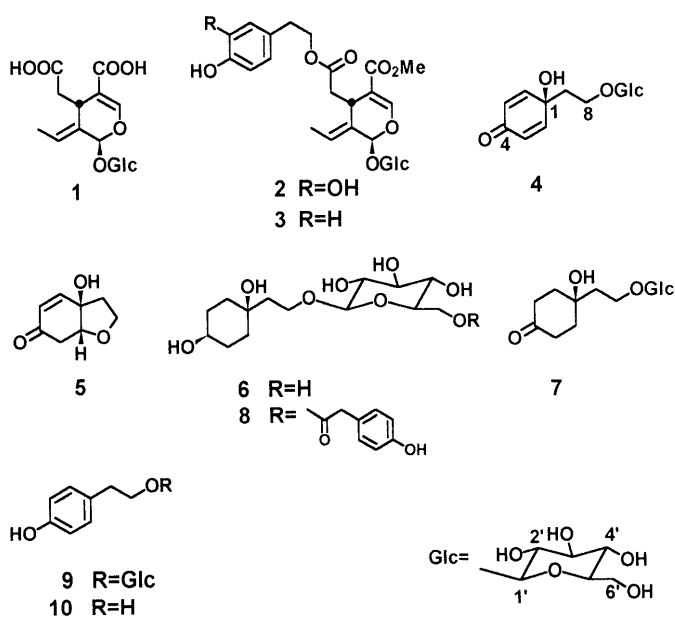


Fig. 1

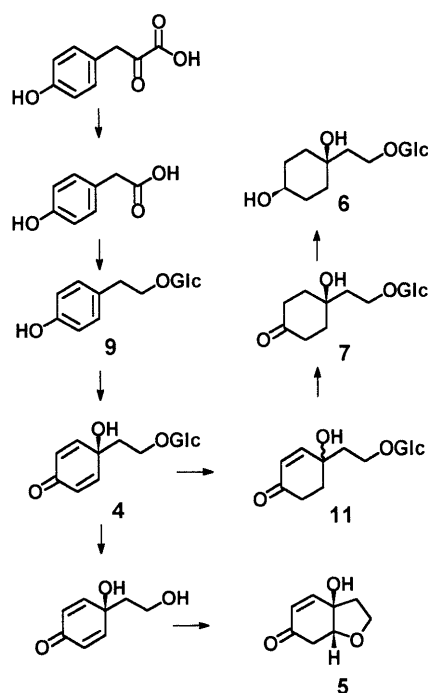
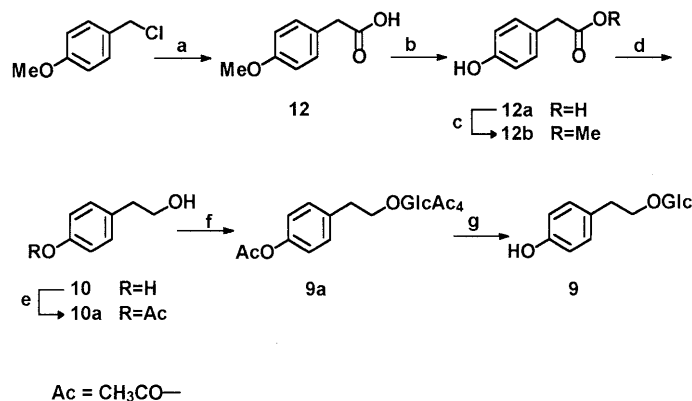


Chart 1

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a) i: Mg / THF, ii: CO₂; b) BBr₃, CH₂Cl₂, -78 °C; c) HCl / MeOH; d) NaBH₄ / H₂O
 e) 1-acetyl-1*H*-1,2,3-triazolo [4,5-*b*] pyridine / 0.1 N NaOH; f) 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide, Ag₂CO₃, Drierite, I₂ / Et₂O; g) NaOMe–MeOH

Chart 2

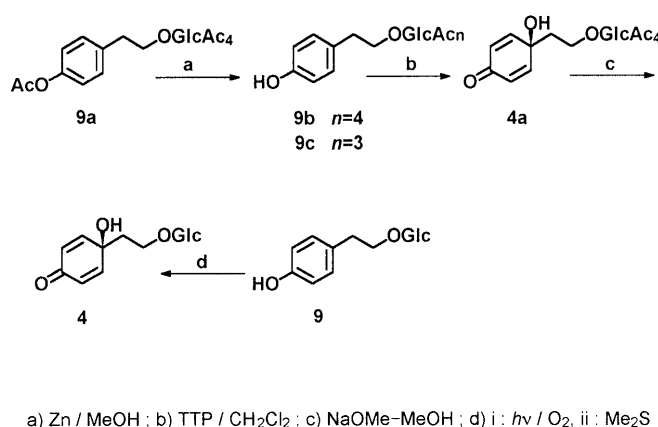


Chart 3

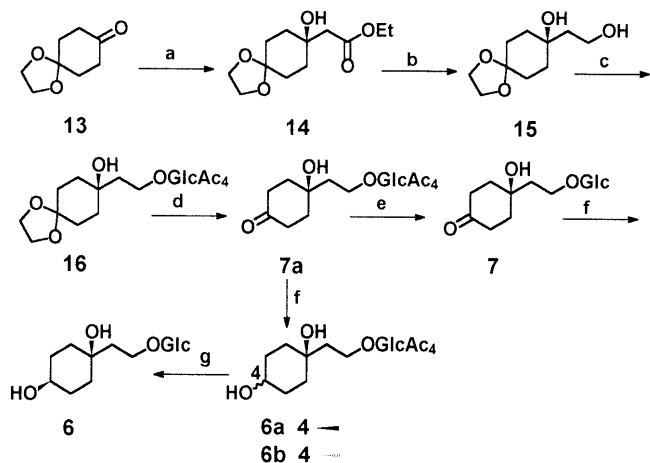
in aqueous NaOH⁷) to afford the desired monoacetate **10a** in 73% yield. The acetate **10a** was subjected to a König–Knorr reaction⁸) with 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide in the presence of Ag₂CO₃ to afford salidroside pentaacetate (**9a**). The configuration of the glycosidic linkage of **9a** was determined to be β from the coupling constant of the anomeric proton. **9a** was deacetylated with MeONa–MeOH⁹) to give salidroside (**9**) in the overall yield of 25% based on BaCO₃. Next, we carried out the same experiments using ¹³CO₂ instead of CO₂ and obtained [^{8-¹³C}]-4-hydroxyphenylethanol (**10**) (enrichment factor: 97.6%, calculated on the basis of EI-MS data) and [^{8-¹³C}]-salidroside (**9**), respectively.

Biomimetic Conversion of [^{8-¹³C}]-Salidroside (9**) to [^{8-¹³C}]-Cornoside (**4**)** In the biosynthesis of cornoside (**4**), salidroside (**9**) or its aglucone, 4-hydroxyphenylethanol (**10**), was supposed to be oxygenated to a quinol compound. Thus, we examined the oxygenation of salidroside (**9**) derivatives according to two methods. The tetraacetate **9b** prepared from the pentaacetate (**9a**) by treatment with zinc in MeOH¹⁰) was subjected to oxygenation with thallium triperchlorate (TTP) in CH₂Cl₂^{11a-c)} to give the quinol acetate **4a** in a low yield of 12%. On the other hand, the photosensitized oxygenation of **9b** in MeOH in the presence of Rose Bengal did

not proceed at all, whereas the oxygenation of **9** under the conditions described above gave the peroxide **4b**, without the formation of any by-product, and **4b** was subsequently reduced with dimethyl sulfide (Me₂S) to yield cornoside (**4**) in 49% isolated yield.¹²) By applying the latter procedure, [^{8-¹³C}]-salidroside (**9**) was converted to [^{8-¹³C}]-cornoside (**4**).

Synthesis of [^{7-¹³C}]-Rengyosides A (6**), B (**7**) and [^{7-¹³C}]-Dihydrocornoside (**11**)** Although the direct conversion of cornoside (**4**) into rengyoside B (**7**) via hydrogenation catalyzed by palladium on activated carbon has been reported,¹²) the yield of the product was unsatisfactory. Thus, we planned the preparation of ¹³C-labeled **7** by means of the Reformatsky reaction^{13a-c)} of a cyclohexanone derivative and ethyl bromoacetate. The condensation of 1,4-cyclohexanedione monoethyleneketal (**13**) with ethyl bromoacetate in the presence of zinc was examined in various solvents. The best yield (77%) of the desired ester **14** was obtained in dry benzene. On reduction of **14** with LiAlH₄ in dry THF,^{14a,b)} the alcohol **15** was formed in 83% yield. The glycosidation of **15** in a manner analogous to the preparation of salidroside (**9**) gave the ketal **16**, which was subjected to deprotection by *p*-toluenesulfonic acid (*p*-TsOH) in acetone¹⁵) to afford the corresponding ketone **7a**. This in turn gave rengyoside B (**7**) in 35% overall yield from the ketal **13** on decetylation with NaOH in acetone. [^{7-¹³C}]-Rengyoside B (**7**) was prepared as described above starting from [^{2-¹³C}]-ethyl bromoacetate and 1,4-cyclohexanedione monoethyleneketal (**13**).

In order to prepare rengyoside A tetraacetate (**6a**), rengyoside B tetraacetate (**7a**) was reduced with NaBH₄ in EtOH to give a separable mixture of two alcohols **6a** and **6b** in a ratio of 3:1. Their ¹H-NMR spectra showed different configurations of the newly generated hydroxy group at C-4 of **6a** and **6b**. It was concluded on the basis of the width of the H-4 signal that **6a** has the equatorial hydroxy group at C-4 [axial H-4 (*W*_{1/2} = 20 Hz) at δ 3.55–3.62] and **6b** the axial one [equatorial H-4 (*W*_{1/2} = 13 Hz) at δ 3.90–3.96] in accordance with the data reported previously.^{2,16)} However, the reduction of **7a** to



- a) Zn, BrCH₂CO₂Et / C₆H₆; b) LiAlH₄ / THF; c) 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl bromide, Ag₂CO₃, Drierite, I₂ / CHCl₃; d) *p*-TsOH / Me₂CO; e) 0.2 N NaOH-Me₂CO; f) NaBH₄ / EtOH; g) NaOMe-MeOH

Chart 4

the desired alcohol **6a** resulted in a poor yield of 27%, probably because **6a** was further hydrolyzed to more polar deacetylated compounds during the reaction. So, renyoside B (**7**) was reduced in the same way as above to give stereoselectively renyoside A (**6**) in quantitative yield; this product was identical with the deacetylated compound of **6a**. Next, [^{7-¹³C}]renyoside B (**7**) was reduced in the same way as above to give [^{7-¹³C}]renyoside A (**6**).

Finally, we tried to prepare a dihydro derivative of **4**, dihydrocornoside (**11**). Cornoside (**4**) was subjected to partial hydrogenation by using Pd/C to afford **11** in 39% yield as a diastereomeric mixture in a ratio of 1 : 1 as judged from the ¹H- and ¹³C-NMR spectra, along with renyoside B (**7**). [^{8-¹³C}]Cornoside (**4**) was subjected to the above hydrogenation to afford [^{8-¹³C}]dihydrocornoside (**11**). Feeding experiments with these ¹³C-labeled compounds are in progress.

Experimental

The melting points were measured on a Yanagimoto MP-32 micro-melting point apparatus and are uncorrected. Optical rotations were taken with a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a Hitachi Model 260-30 IR spectrophotometer. The NMR experiments were performed with a JEOL JNM-GX 500 or JNM-GSX 270 spectrometer, with tetramethylsilane as an internal standard. Mass spectra were recorded on a JEOL JMS-HX 100 instrument. For FAB-MS, glycerol was used as the matrix. For TLC, Silica gel 60 GF₂₅₄ was used and spots were visualized under UV light or by exposure to I₂ vapor or by spraying anisaldehyde-H₂SO₄ reagent followed by heating. For preparative TLC (PTLC), Silica gel 60 PF₂₅₄ was used and bands were detected under UV light or by exposure to I₂ vapor. For column chromatography, Silica gel BW-820 (Fuji Silysia Chemical Ltd.) and highly porous polymer Diaion SP207 (Mitsubishi Chemical Co. Ltd.) were used. Solvent ratios are expressed by volume. All extracts were dried over anhydrous MgSO₄.

4-Methoxyphenylacetic Acid (12) 4-Methoxybenzyl chloride (5.7 ml, 42.0 mmol) was added dropwise to a stirred mixture of Mg (1.0 g, 42.0 mmol) and THF (84.0 ml) under argon over a period of 40 min at 20 °C, and stirring was continued for an additional 30 min. Carbon dioxide [generated from BaCO₃ (5.0 g, 25 mmol) and excess concentrated H₂SO₄] was passed into the reaction mixture over a period of 1.5 h at 10–25 °C with stirring. After acidification of the mixture by adding 1 N HCl, the residue obtained by removal of the solvent *in vacuo* was extracted

with Et₂O. The Et₂O layer was extracted with 2 N NaOH, and the aqueous layer was acidified with concentrated H₂SO₄ and extracted with Et₂O. The Et₂O layer was washed with brine, dried and concentrated *in vacuo* to give **12** (3.2 g, 75.0% based on BaCO₃). Compound **12** was identical with an authentic sample of 4-methoxyphenylacetic acid.

4-Methoxybenzyl chloride (5.7 ml, 42.0 mmol) and ¹³CO₂ generated from Ba¹³CO₃ (5.0 g, 25.0 mmol) (¹³C-enrichment 99%, CIL) were subjected to a Grignard reaction as described above to give [^{8-¹³C}]-**12** (3.1 g, 72.7%). [^{8-¹³C}]-**12**: ¹H-NMR (CDCl₃) δ : 3.58 (2H, d, ²J_{CH} = 7.6 Hz, H-7), 3.79 (3H, s, OCH₃), 6.86 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-3, -5), 7.19 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-2, -6). EI-MS (70 eV) *m/z*: 167 [M]⁺. ¹³C-enrichment factor: 97.8% (calculated on the basis of EI-MS data). The ¹³C-NMR spectrum of [^{8-¹³C}]-**12** exhibited a strongly enriched ¹³C signal arising from the carbonyl carbon of C-8 at 177.60. In the C-8-labeled compounds mentioned as follows, it was confirmed by examination of their ¹³C-NMR spectra that the C-8 carbon signals were enhanced.

4-Hydroxyphenylacetic Acid (12a) A solution of BBr₃ (4.2 ml, 44.4 mmol) in dry CH₂Cl₂ (34.0 ml) was added dropwise to a stirred solution of **12** (3.2 g, 19.3 mmol) in dry CH₂Cl₂ (50.0 ml) at -78 °C and the mixture was stirred for 30 min. After decomposition of the excess reagent by adding H₂O under ice-cooling, CH₂Cl₂ was removed *in vacuo* and the aqueous layer was extracted with Et₂O. The Et₂O layer was washed with brine, dried and concentrated *in vacuo* to give **12a** (2.7 g, 93.0%). **12a** was identical with an authentic sample of 4-hydroxyphenylacetic acid.

[^{8-¹³C}]-**12** (3.2 g) was demethylated in the same way as above to give [^{8-¹³C}]-**12a** (2.3 g, 85.6%). [^{8-¹³C}]-**12a**: ¹H-NMR (DMSO-*d*₆) δ : 3.42 (2H, d, ²J_{CH} = 7.5 Hz, H₂-7), 6.70 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-3, -5), 7.04 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-2, -6). EI-MS (70 eV) *m/z*: 153 [M]⁺.

Methyl 4-Hydroxyphenylacetate (12b) A solution of **12a** (2.7 g, 17.7 mmol) in MeOH (40 ml) was acidified with 3 drops of concentrated HCl and the mixture was refluxed for 30 min. After neutralization of the mixture with 10% aqueous NaHCO₃ under ice-cooling, the solution obtained by removal of MeOH *in vacuo* was extracted with Et₂O. The Et₂O layer was washed with brine, dried and concentrated *in vacuo* to give **12b** (2.8 g, 95.0%), which was identical with an authentic sample of methyl 4-hydroxyphenylacetate.

[^{8-¹³C}]-**12a** (3.2 g) was methylated in the same manner as described above to give [^{8-¹³C}]-**12b** (3.3 g, 94.4%). [^{8-¹³C}]-**12b**: ¹H-NMR (CDCl₃) δ : 3.56 (2H, d, ²J_{CH} = 7.9 Hz, H₂-7), 3.70 (3H, d, ³J_{CH} = 4.0 Hz, ¹³COOCH₃), 6.74 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-3, -5), 7.11 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-2, -6). EI-MS (70 eV) *m/z*: 167 [M]⁺.

4-Hydroxyphenylethanol (10) A stirred suspension of **12b** (2.8 g, 16.8 mmol) in H₂O (50.0 ml) was treated with NaBH₄ (4.7 g, 127.0 mmol) and stirring was continued for 8 h at room temperature. After decomposition of the excess reagent by adding 2 N HCl under ice-cooling, the mixture was extracted with Et₂O. The Et₂O layer was washed with brine, dried and concentrated *in vacuo*. The resulting residue was recrystallized from CHCl₃ to give 4-hydroxyphenylethanol (**10**) as colorless needles (2.1 g, 90.0%). This compound was identical with an authentic sample of 4-hydroxyphenylethanol.

[^{8-¹³C}]-**12b** (2.5 g) was reduced with NaBH₄ as described above to give [^{8-¹³C}]-4-hydroxyphenylethanol (**10**) (1.9 g, 91.0%). ¹H-NMR (CDCl₃) δ : 2.70 (2H, td, *J* = 7.0 Hz, ²J_{CH} = 5.0 Hz, H₂-7), 3.67 (2H, dt, ¹J_{CH} = 142.5 Hz, *J* = 7.0 Hz, H₂-8), 6.69 (2H, AA'BB' pattern, *J*_{ortho} = 8.3 Hz, H-3, -5), 7.02 (2H, AA'BB' pattern, *J*_{ortho} = 8.3 Hz, H-2, -6). EI-MS (70 eV) *m/z*: 139 [M]⁺.

4-O-Acetylphenylethanol (10a) A solution of 1-acetyl-1*H*-1,2,3-triazolo[4,5-*b*]pyridine (324.8 mg, 2.0 mmol) in dry THF (8.0 ml) was added dropwise to a solution of 4-hydroxyphenylethanol (**10**) (276.3 mg, 2.0 mmol) in 1 N NaOH (2.0 ml) and the mixture was stirred for 1 h at room temperature. After having been neutralized with 2 N HCl, the mixture was extracted with Et₂O. The Et₂O layer was washed with H₂O, dried and concentrated *in vacuo* to give the residue (282.6 mg), which was subjected to PTLC (CHCl₃:MeOH = 9:1) to yield 4-*O*-acetylphenylethanol (**10a**) as a colorless oil (263.2 mg, 73.0%). IR (neat) cm⁻¹: 3330, 1745, 1600. ¹H-NMR (CDCl₃) δ : 2.29 (3H, s, CH₃CO), 2.84 (2H, t, *J* = 6.7 Hz, H₂-7), 3.76–3.87 (2H, m, H₂-8), 7.02 (2H, AA'BB' pattern, *J*_{ortho} = 8.5 Hz, H-2, -6), 7.21 (2H, AA'BB' pattern, *J*_{ortho} = 8.5 Hz, H-3, -5). FAB-MS *m/z*: 181 [M+H]⁺.

[^{8-¹³C}]-**10** (2.1 g) was subjected to selective acetylation with 1-

acetyl-1*H*-1,2,3-triazolo[4,5-*b*]pyridine as described above to give [8-¹³C]-**10a** (1.98 g, 72.3%). ¹H-NMR (CDCl₃) δ: 2.29 (3H, s, CH₃CO), 2.85 (2H, td, *J* = 6.7 Hz, ²*J*_{CH} = 5.0 Hz, H₂-7), 3.82 (2H, br dt, ¹*J*_{CH} = 142.0 Hz, *J* = 7.0 Hz, H₂-8), 7.02 (2H, AA'BB' pattern, *J*_{ortho} = 8.2 Hz, H-2, -6), 7.21 (2H, AA'BB' pattern, *J*_{ortho} = 8.2 Hz, H-3, -5). FAB-MS *m/z*: 182 [M + H]⁺.

Salidroside Pentaacetate (9a) A solution of **10a** (4.2 g, 23.3 mmol) in dry Et₂O (120.0 ml) was stirred, and Ag₂CO₃ (12.8 g, 46.4 mmol) and Drierite (33.0 g) were added to it at room temperature. After 10 min, 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide (19.2 g, 46.6 mmol) and I₂ (680 mg) were added to the mixture and stirring was continued for 14 h in the dark. The insoluble material was filtered off through a Celite layer, which was washed with Et₂O. The combined filtrate and washings were concentrated *in vacuo* to give the residue (16.0 g), which was purified by silica gel column chromatography (C₆H₆:Et₂O = 4:1) to afford **9a** as a colorless oil (6.2 g, 70.0%). IR (neat) cm⁻¹: 1765, 1740, 1500. ¹H-NMR (CDCl₃) δ: 1.91, 2.00, 2.08, 2.17, 2.28 (15H, each s, CH₃CO), 2.86 (1H, br ddd, *J* = 14.5, *ca.* 7.0, *ca.* 6.0 Hz, H-7a), 2.92 (1H, br ddd, *J* = 14.5, 8.0, *ca.* 7.0 Hz, H-7b), 3.65 (1H, ddd, *J* = 9.5, 8.0, 6.6 Hz, H-8a), 3.68 (1H, ddd, *J* = 9.5, 4.6, 2.5 Hz, H-5'), 4.13 (1H, ddd, *J* = 9.5, 6.8, 6.0 Hz, H-8b), 4.20 (1H, dd, *J* = 12.0, 2.5 Hz, H-6'a), 4.26 (1H, dd, *J* = 12.0, 4.6 Hz, H-6'b), 4.48 (1H, d, *J* = 8.0 Hz, H-1'), 4.99 (1H, dd, *J* = 9.5, 8.0 Hz, H-2), 5.08 (1H, t, *J* = 9.6 Hz, H-4'), 5.18 (1H, t, *J* = 9.5 Hz, H-3'), 6.99 (2H, AA'BB' pattern, *J*_{ortho} = 8.6 Hz, H-2, -6), 7.20 (2H, AA'BB' pattern, *J*_{ortho} = 8.6 Hz, H-3, -5). FAB-MS *m/z*: 511 [M + H]⁺.

A solution of [8-¹³C]-**10a** (1.9 g) was prepared in dry Et₂O (60 ml), and Ag₂CO₃ (5.8 g) and Drierite (15.0 g) were added to it. 2,3,4,6-Tetra-*O*-acetyl- α -D-glucopyranosyl bromide (8.7 g) and I₂ (308 mg) were added to the solution, and the mixture was worked-up as described above to yield [8-¹³C]-**9a** (3.0 g, 75.0%). ¹H-NMR (CDCl₃) δ: 1.91, 2.00, 2.08, 2.17, 2.28 (15H, each s, CH₃CO), 2.82–2.95 (2H, m, H₂-7), 3.66 (1H, dddd, ¹*J*_{CH} = 143.2 Hz, *J* = 9.5, 7.9, 6.6 Hz, H-8a), 3.68 (1H, ddd, *J* = 9.5, 4.6, 2.5 Hz, H-5'), 4.13 (1H, dddd, ¹*J*_{CH} = 143.2 Hz, *J* = 9.5, 6.8, 6.0 Hz, H-8b), 4.20 (1H, dd, *J* = 12.0, 2.5 Hz, H-6'a), 4.25 (1H, dd, *J* = 12.0, 4.6 Hz, H-6'b), 4.48 (1H, dd, *J* = 8.0 Hz, ³*J*_{CH} = 4.5 Hz, H-1'), 4.98 (1H, dd, *J* = 9.5, 8.0 Hz, H-2'), 5.08 (1H, t, *J* = 9.6 Hz, H-4'), 5.18 (1H, t, *J* = 9.5 Hz, H-3'), 6.99 (2H, AA'BB' pattern, *J*_{ortho} = 8.6 Hz, H-2, -6), 7.20 (2H, AA'BB' pattern, *J*_{ortho} = 8.6 Hz, H-3, -5). FAB-MS *m/z*: 512 [M + H]⁺.

Salidroside (9) Methanolic NaOMe (0.1 N, 4.3 ml) was added to a solution of **9a** (401.2 mg, 0.86 mmol) in dry MeOH (4.2 ml) and the mixture was stirred for 1 h at room temperature. After neutralization of the mixture by adding Amberlite IR 120B (H⁺ form), the resin was filtered off and washed with MeOH. The combined filtrate and washings were concentrated *in vacuo* to give a syrupy residue, which was recrystallized from *n*-hexane–EtOH to give colorless needles (251.1 mg, 97.7%) of **9**. [α]_D²³ –40.6° (*c* = 0.65, H₂O) [lit.,¹²] [α]_D²⁰ –30.0° (*c* = 1.78, H₂O)]. mp 163–165.5 °C. IR (KBr) cm⁻¹: 3250, 1610, 1510. ¹H-NMR (CD₃OD) δ: 2.81 (1H, br ddd, *J* = 14.0, 8.0, *ca.* 7.0, H-7a), 2.84 (1H, dt, *J* = 14.0 Hz, 7.0 Hz, H-7b), 3.17 (1H, dd, *J* = 9.0, 8.0 Hz, H-2'), 3.24 (1H, ddd, *J* = 9.5, 5.5, 2.0 Hz, H-5'), 3.27 (1H, t, *J* = 9.5 Hz, H-4'), 3.34 (1H, t, *J* = 9.0 Hz, H-3'), 3.67 (1H, dd, *J* = 11.6, 5.5 Hz, H-6'a), 3.69 (1H, ddd, *J* = 9.0, 8.0, 6.5 Hz, H-8a), 3.85 (1H, dd, *J* = 11.6, 2.0 Hz, H-6'b), 4.02 (1H, ddd, *J* = 9.0, 8.0, *ca.* 7.0 Hz, H-8b), 4.28 (1H, d, *J* = 8.0 Hz, H-1'), 6.68 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-3, -5), 7.06 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-2, -6). FAB-MS *m/z*: 301 [M + H]⁺.

Methanolic NaOMe (0.1 N, 29.5 ml) was added to a solution of [8-¹³C]-**9a** (3.0 g) in dry MeOH (30.0 ml) and the mixture was deacetylated as described above to give [8-¹³C]-**9** (1.65 g, 93.5%). ¹H-NMR (CD₃OD) δ: 2.81 (1H, m, H-7a), 2.84 (1H, m, H-7b), 3.17 (1H, dd, *J* = 9.0, 8.0 Hz, H-2'), 3.25 (1H, ddd, *J* = 9.5, 5.5, 2.0 Hz, H-5'), 3.28 (1H, t, *J* = 9.5 Hz, H-4'), 3.34 (1H, t, *J* = 9.0 Hz, H-3'), 3.66 (1H, dd, *J* = 11.6, 5.5 Hz, H-6'a), 3.69 (1H, dddd, ¹*J*_{CH} = 143.5 Hz, *J* = 9.0, 8.0, 6.5 Hz, H-8a), 3.86 (1H, dd, *J* = 11.6, 2.0 Hz, H-6'b), 4.02 (1H, dddd, ¹*J*_{CH} = 143.5 Hz, *J* = 9.0, 8.0, *ca.* 7.0 Hz, H-8b), 4.28 (1H, dd, *J* = 8.0 Hz, ³*J*_{CH} = 4.2 Hz, H-1'), 6.68 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-3, -5), 7.06 (2H, AA'BB' pattern, *J*_{ortho} = 8.8 Hz, H-2, -6). FAB-MS *m/z*: 302 [M + H]⁺.

Salidroside Tetraacetate (9b) Activated zinc¹⁷⁾ (114.0 g) was added to a solution of **9a** (8.4 g, 16.4 mmol) in MeOH (100 ml) and the mixture was stirred for 4.2 h at room temperature. The zinc was filtered off through a Celite layer. The Celite layer was washed successively with CHCl₃ and MeOH. The combined filtrate and washings were concentrated *in vacuo* to give the residue, which was subjected to column chromatography (C₆H₆:Et₂O = 1:1) on silica gel to afford **9b** (3.3 g,

43.3%) and **9c** (2.4 g, 34.2%), each as a colorless oil. **9c** was identified as the 3'-deacetylated derivative of **9b** (¹H-NMR, FAB-MS). Compound **9b**: IR (neat) cm⁻¹: 3310, 2910, 1740, 1700. ¹H-NMR (CDCl₃) δ: 1.92, 1.99, 2.02, 2.09 (12H each s, CH₃CO), 2.80 (1H, br ddd, *J* = 14.0, *ca.* 7.0, *ca.* 6.0 Hz, H-7a), 2.83 (1H, dt, *J* = 14.0, 7.5 Hz, H-7b), 3.62 (1H, dt, *J* = 9.5, 7.5, H-8a), 3.67 (1H, ddd, *J* = 9.6, 5.0, 2.5 Hz, H-5'), 4.08 (1H, ddd, *J* = 9.5, 7.0, 6.0 Hz, H-8b), 4.13 (1H, dd, *J* = 12.3, 2.5 Hz, H-6'a), 4.26 (1H, dd, *J* = 12.0, 5.0 Hz, H-6'b), 4.48 (1H, d, *J* = 8.0, H-1'), 4.99 (1H, dd, *J* = 9.5, 8.0 Hz, H-2'), 5.08 (1H, t, *J* = 9.6 Hz, H-4'), 5.18 (1H, t, *J* = 9.5 Hz, H-3'), 6.74 (2H, AA'BB' pattern, *J*_{ortho} = 8.3 Hz, H-3, -5), 7.05 (2H, AA'BB' pattern, *J*_{ortho} = 8.3 Hz, H-2, -6). FAB-MS *m/z*: 469 [M + H]⁺. Compound **9c**: ¹H-NMR (CDCl₃) δ: 1.93, 2.08, 2.12 (9H, each s, CH₃CO), 2.78 (1H, ddd, *J* = 14.0, 7.0, 6.0 Hz, H-7a), 2.82 (1H, dt, *J* = 14.0, 7.5 Hz, H-7b), 3.50 (1H, ddd, *J* = 9.6, 5.0, 2.5 Hz, H-5'), 3.58 (1H, t, *J* = 9.5 Hz, H-3'), 3.61 (1H, ddd, *J* = 9.5, 7.5, 7.0 Hz, H-8a), 4.07 (1H, ddd, *J* = 9.5, 7.0, 6.0 Hz, H-8b), 4.32 (1H, dd, *J* = 12.1, 2.1 Hz, H-6'a), 4.45 (1H, d, *J* = 8.0, H-1'), 4.47 (1H, dd, *J* = 12.1, 4.3 Hz, H-6'b), 4.92 (1H, dd, *J* = 9.5, 8.0 Hz, H-2'), 5.03 (1H, t, *J* = 9.5 Hz, H-4'), 6.74 (2H, AA'BB' pattern, *J*_{ortho} = 8.5 Hz, H-3, -5), 7.04 (2H, AA'BB' pattern, *J*_{ortho} = 8.5 Hz, H-2, -6). FAB-MS *m/z*: 427 [M + H]⁺.

Corsinide Tetraacetate (4a) A solution of **9b** (3.0 g, 6.4 mmol) was prepared in CH₂Cl₂ (140.0 ml), and to it were added H₂O (140.0 ml) and TTP (1.0 mmol), which was prepared from Ti₂O₃ (3.0 g) and 60% HClO₄ (50.0 ml). The mixture was vigorously stirred for 15 min and the CH₂Cl₂ layer was separated and washed successively with saturated aqueous NaHCO₃, H₂O and brine, and concentrated *in vacuo*. The residue (1.0 g) was purified by silica gel column chromatography (C₆H₆:Et₂O = 1:1) to give **4a** as a colorless oil (358.0 mg, 11.5%). IR (neat) cm⁻¹: 3420, 3300, 1760, 1665, 1650, 1625. ¹H-NMR (CDCl₃) δ: 2.00–2.07 (2H, m, H₂-7), 2.01, 2.04, 2.06, 2.10 (12H, each s, CH₃CO), 3.70 (1H, ddd, *J* = 10.2, 7.0, 5.5 Hz, H-8a), 3.71 (1H, ddd, *J* = 9.6, 5.0, 2.5 Hz, H-5'), 4.09 (1H, ddd, *J* = 10.2, 7.0, 5.5 Hz, H-8b), 4.18 (1H, dd, *J* = 12.5, 2.5 Hz, H-6'a), 4.25 (1H, dd, *J* = 12.5, 5.0 Hz, H-6'b), 4.52 (1H, d, *J* = 8.0, H-1'), 5.00 (1H, dd, *J* = 9.5, 8.0 Hz, H-2'), 5.09 (1H, t, *J* = 9.6 Hz, H-4'), 5.21 (1H, t, *J* = 9.5 Hz, H-3'), 6.13–6.19 (2H, m, H-3, -5), 6.87–6.92 (2H, m, H-2, -6). FAB-MS *m/z*: 485 [M + H]⁺.

Corsinide (4) A (Photooxygenation of **9**): A mixture of **9** (100 mg, 0.33 mmol) and Rose Bengal (9.4 mg) in MeOH (28.0 ml) was irradiated under a halogen lamp (Ushio, JPD 100V-500 WC) in a Pyrex reactor with bubbling O₂ for 3 h at 20 °C. The reaction mixture was treated with Me₂S (0.062 ml, 0.83 ml) with stirring for 4 h and then concentrated *in vacuo* to give a residue (158.8 mg), which was purified by PTLC (C₆H₆:EtOAc:EtOH:H₂O = 1:4:1:0.5) to yield **4** as a powder (52.1 mg, 49.4%) and recovered **9** (38.7 mg).

B (Zemplén Deacetylation of 4a): Methanolic NaOMe (0.1 N, 1.8 ml) was added to a solution of **4a** (40.3 mg, 0.077 mmol) in dry MeOH (2.0 ml) and the mixture was worked-up as described above. The product (28.5 mg) was purified by PTLC (CHCl₃:MeOH:H₂O:AcOH = 10:7:2:0.1) to give **4** (14.8 mg, 61.1%), which was identical with an authentic sample of corsinide. [α]_D²³ –19.1° (*c* = 0.99, EtOH) [lit.,¹¹] [α]_D²⁰ –20.3° (*c* = 1.13, EtOH), lit.,¹²] [α]_D²⁰ –10.5° (*c* = 0.42, MeOH)]. FAB-MS *m/z*: 315 [M – H][–].

[8-¹³C]-**9** (100.0 mg) was photooxygenated followed by reduction with Me₂S as described above to give [8-¹³C]-**4** (47.5 mg, 45.0%). ¹H-NMR (CD₃OD) δ: 2.04 (2H, td, ²*J*_{CH} = 7.0 Hz, *J* = 6.5 Hz, H₂-7), 3.13 (1H, dd, *J* = 9.0, 8.0, H-2'), 3.26 (1H, t, *J* = 9.0 Hz, H-4'), 3.33 (1H, t, *J* = 9.0 Hz, H-3'), 3.62 (1H, ddt, ¹*J*_{CH} = 141.5 Hz, *J* = 10.0, 6.5 Hz, H-8a), 3.64 (1H, dd, *J* = 12.0, 5.5 Hz, H-6'a), 3.84 (1H, dd, *J* = 12.0, 2.0 Hz, H-6'b), 3.99 (1H, ddt, ¹*J*_{CH} = 145.5 Hz, *J* = 10.0, 6.5 Hz, H-8b), 4.21 (1H, dd, *J* = 8.0 Hz, ³*J*_{CH} = 4.0 Hz, H-1'), 6.11 (1H, dd, *J* = 10.0, 2.0 Hz, H-3 or -5), 6.12 (1H, dd, *J* = 10.0, 2.0 Hz, H-3 or -5), 7.02 (2H, d, *J* = 10.0 Hz, H-2, -6). FAB-MS *m/z*: 318 [M + H]⁺.

Reformatsky Reaction of 1,4-Cyclohexanedione Monoethylene Ketal (13) and Ethyl Bromoacetate One-tenth of a solution of ethyl bromoacetate (0.36 ml, 3.2 mmol) in dry C₆H₆ (2.4 ml) was added to a stirred mixture of activated zinc (251.0 mg, 3.8 mg atom) and dry C₆H₆ (1.5 ml) at room temperature under argon. After 15 min, the remaining solution of ethyl bromoacetate was added dropwise and the whole was refluxed for 30 min. It was then the ice-cooled, and a solution of the ketal **13** (500 mg, 3.2 mmol) in dry C₆H₆ (3.2 ml) was added dropwise over a period of 15 min. The reaction mixture was refluxed for 3 h, quenched with ice-water, and filtered through Celite. The residue obtained through concentration of the filtrate *in vacuo* was extracted with Et₂O. The Et₂O layer was washed with brine, dried and concentrated *in vacuo*. The

resulting residue (706.0 mg) was purified by PTLC (C_6H_6 : Et_2O =1:1) to afford the ester **14** as a pale yellow oil (603.7 mg, 77.3%). IR (neat) cm^{-1} : 3450, 1720. 1H -NMR ($CDCl_3$) δ : 1.28 (3H, t, J =7.0 Hz, OCH_2CH_3), 1.59 (2H, m, H-2eq, -6eq), 1.68 (2H, td, J =13.0, 4.5 Hz, H-2ax, -6ax), 1.79 (2H, m, H-3eq, -5eq), 1.95 (2H, td, J =13.0, 4.5 Hz, H-3ax, -5ax), 2.49 (2H, s, H₂-7), 3.88—3.99 (4H, m, OCH_2CH_2O), 4.18 (2H, q, J =7.0 Hz, OCH_2CH_3). EI-MS m/z : 244 [M]⁺. HR-EI-MS m/z : 244.1307 (Calcd for $C_{12}H_{20}O_5$: 244.1311).

A solution of [2- ^{13}C]ethyl bromoacetate (1.0 g, 6.0 mmol) (^{13}C -enrichment 99%, Aldrich) and the ketal **13** (935.0 mg, 6.0 mmol) in dry C_6H_6 (3.5 ml) was added dropwise to a mixture of activated zinc (470.0 mg, 7.2 mg atom) and dry C_6H_6 (3.5 ml) under argon. The mixture was refluxed for 3 h and worked-up according to the same procedure as described above to give the product (1.32 g), which was purified by PTLC to afford [7- ^{13}C]-**14** (191.2 mg, 13.6%). The low yield may have been due to insufficient drying of [2- ^{13}C]ethyl bromoacetate. 1H -NMR ($CDCl_3$) δ : 2.49 (2H, d, J_{CH} =125.0 Hz, H₂-7). FAB-MS m/z : 246 [$M+H$]⁺. ^{13}C -enrichment factor: 97.2% (calculated on the basis of FAB-MS data). The ^{13}C -NMR spectrum of [7- ^{13}C]-**14** exhibited a strongly enriched ^{13}C signal arising from the methyl carbon of C-7 at δ 45.24. In the C-7 labeled compounds mentioned below, it was confirmed by examination of their ^{13}C -NMR spectra that the C-7 carbon signals were enhanced.

Reduction of the Ester 14 A solution of **14** (500.0 mg, 2.1 mmol) in dry THF (7.0 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (116.0 mg, 3.0 mmol) in dry THF under argon, and the mixture was stirred for 30 min at room temperature. After decomposition of the excess reagent by adding H_2O under ice-cooling, the mixture was concentrated *in vacuo* and the residue was extracted continuously with CH_2Cl_2 . The crystalline residue obtained by the removal of the solvent *in vacuo* was recrystallized from Et_2O to give colorless needles (346.0 mg, 83.8%) of the alcohol **15**. mp 57.5—69.7 °C. IR (KBr) cm^{-1} : 3360, 2940. 1H -NMR ($CDCl_3$) δ : 1.59 (2H, m, H-2eq, -6eq), 1.63 (2H, td, J =13.0, 4.5 Hz, H-2ax, -6ax), 1.73 (2H, t, J =6.0 Hz, H₂-7), 1.78 (2H, m, H-3eq, -5eq), 1.90 (2H, td, J =13.0, 4.5 Hz, H-3ax, -5ax), 3.88 (2H, m, H₂-8), 3.92—3.99 (4H, m, OCH_2CH_2O). FAB-MS m/z : 203 [$M+H$]⁺. HR-FAB-MS m/z : 203.1203 (Calcd for $C_{10}H_{16}O_4$: 203.1205).

[7- ^{13}C]-**14** (270.0 mg) was reduced with $LiAlH_4$ (62.6 mg) as described above to give a residue (240.2 mg), which was purified by PTLC ($CHCl_3$: $MeOH$ =19:1) to yield [7- ^{13}C]-**15** (214.9 mg, 96.4%). 1H -NMR ($CDCl_3$) δ : 1.73 (2H, dt, J_{CH} =124.5 Hz, J =5.6 Hz, H₂-7). FAB-MS m/z : 204 [$M+H$]⁺.

Glycosidation of the Alcohol 15 A mixture of **15** (260.0 mg, 1.3 mmol), Ag_2CO_3 (1.3 g, 4.7 mmol) and Drierite (52.1 g) in dry $CHCl_3$ (50.0 ml) was stirred for 10 min. After addition of 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide (593.0 mg, 1.7 mmol) and I_2 , the mixture was stirred for 22 h. The crude product (894.0 mg) obtained by work-up in the usual way was then subjected to column chromatography on silica gel with $CHCl_3$ - $MeOH$ (46:1) as an eluent to give **16** as a colorless oil (336.0 mg, 49.0%) and recovered **15** (122.0 mg, 47.0%). IR (neat) cm^{-1} : 3495, 2940, 1760, 1720. 1H -NMR ($CDCl_3$) δ : 1.54—1.64 (4H, m, H-2, -6), 1.70 (2H, m, H₂-7), 1.75—1.84 (2H, m, H-3eq, -5eq), 1.92 (2H, m, H-3ax, -5ax), 2.00, 2.02, 2.04, 2.09 (12H, each s, CH_3CO), 3.70 (1H, ddd, J =9.6, 4.5, 2.5 Hz, H-5'), 3.68—3.72 (1H, ddd, J =10.0, 6.0, 5.0 Hz, H-8a), 3.90—3.97 (4H, m, OCH_2CH_2O), 4.12 (1H, ddd, J =10.0, 6.0, 5.0 Hz, H-8b), 4.16 (1H, dd, J =12.5, 2.5 Hz, H-6'a), 4.26 (1H, dd, J =12.5, 4.5 Hz, H-6'b), 4.52 (1H, d, J =8.0 Hz, H-1'), 4.98 (1H, dd, J =9.5, 8.0 Hz, H-2'), 5.09 (1H, t, J =9.6 Hz, H-4'), 5.21 (1H, t, J =9.5 Hz, H-3'). FAB-MS m/z : 533 [$M+H$]⁺. HR-FAB-MS m/z : 533.2150 (Calcd for $C_{24}H_{37}O_{13}$: 533.2159).

[7- ^{13}C]-**15** (140.0 mg) was glycosidated with 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide (365.0 mg) as described above to give [7- ^{13}C]-**16** (137.7 mg, 37.3%) and recovered [7- ^{13}C]-**15** (60.2 mg, 43.1%). 1H -NMR ($CDCl_3$) δ : 1.70 (2H, dm, J_{CH} =ca. 140 Hz, H₂-7), 3.68—3.73 (1H, dddd, J =10.0, 6.0, 5.0 Hz, J_{CH} =2.0 Hz, H-8a), 4.12 (1H, dddd, J =10.0, 6.0, 5.0 Hz, J_{CH} =2.0 Hz, H-8a). FAB-MS m/z : 534 [$M+H$]⁺.

Rengyoside B Tetraacetate (7a) A solution of **16** (101.0 mg, 0.2 mmol) in Me_2CO (5.0 ml) was treated with *p*-TsOH· H_2O (10.0 mg, 0.053 mmol) and the mixture was stirred for 18 h. After addition of H_2O (3.0 ml) to the solution, the mixture was neutralized with saturated aqueous $NaHCO_3$ under ice-cooling, concentrated *in vacuo* and extracted with $CHCl_3$. The $CHCl_3$ layer was worked-up in the usual way to give the residue (111.0 mg), which was subjected to PTLC (Et_2O : Me_2CO =9:1).

The main product yielded **7a** as colorless needles (65.0 mg, 69.8%) on recrystallization from Et_2O . mp 132.5—134.0 °C. IR (KBr) cm^{-1} : 3420, 1750, 1740, 1690. 1H -NMR ($CDCl_3$) δ : 1.72 (2H, tt, J =13.0, 4.0 Hz, H-2ax, -6ax), 1.87 (2H, t, J =6.0 Hz, H₂-7), 2.02, 2.04, 2.06, 2.10 (12H, each s, CH_3CO), 2.22 (2H, br ddd, J =ca. 15.0, 5.0, 3.0 Hz, H-3eq, -5eq), 2.75 (1H, br dd, J =13.5, 5.6 Hz, H-3ax or -5ax), 2.80 (1H, br dd, J =13.5, 5.6 Hz, H-5ax or -3ax), 3.73 (1H, ddd, J =9.6, 4.5, 2.5 Hz, H-5'), 3.76 (1H, ddd, J =11.5, 6.0, 5.0 Hz, H-8a), 4.18 (1H, ddd, J =11.5, 6.0, 5.0 Hz, H-8b), 4.18 (1H, J =12.5, 2.5 Hz, H-6'a), 4.26 (1H, J =12.5, 4.5 Hz, H-6'b), 4.53 (1H, d, J =8.0 Hz, H-1'), 5.00 (1H, dd, J =9.5, 8.0 Hz, H-2'), 5.10 (1H, t, J =9.6, H-4'), 5.23 (1H, t, J =9.5 Hz, H-3'). FAB-MS m/z : 489 [$M+H$]⁺.

p-TsOH· H_2O (19.9 mg) was added to a solution of [7- ^{13}C]-**16** (200.7 mg) in Me_2CO (10.0 ml) and worked-up as described above to yield [7- ^{13}C]-**7a** (139.2 mg, 75.2%). 1H -NMR ($CDCl_3$) δ : 1.88 (2H, dt, J_{CH} =125.0 Hz, J =6.0 Hz, H₂-7), 3.75 (1H, br dddd, J =11.5, 6.0, 5.0 Hz, J_{CH} =ca. 3.0 Hz, H-8a), 4.18 (1H, br dddd, J =11.5, 6.0, 5.0 Hz, J_{CH} =ca. 3.0 Hz, H-8b). FAB-MS m/z : 490 [$M+H$]⁺.

Rengyoside B (7) 0.2 N NaOH (13.09 ml) was added to a solution of **7a** (300.0 mg, 0.61 mmol) in Me_2CO (9.0 ml) and the mixture was stirred for 4 h at room temperature. After having been neutralized with 0.1 N HCl under ice-cooling, the mixture was evaporated *in vacuo* to give a residue, which was subjected to PTLC (Et_2O : Me_2CO =9:1). The residue obtained from the main band was subjected to column chromatography on SP207 and eluted successively with H_2O and $MeOH$. The $MeOH$ eluate was concentrated *in vacuo* to give **7** as a colorless oil (164.8 mg, 83.8%). $[\alpha]_D^{25}$ -17.6° (c =0.46, $EtOH$) [lit.²⁾ $[\alpha]_D$ -10.4° (c =0.28, $EtOH$)]. IR (neat) cm^{-1} : 3250, 2925, 1700. 1H -NMR ($CDCl_3$) δ : 1.85 (2H, br dt, J =13.0, 5.0 Hz, H-2ax, -6ax), 1.90 (2H, t, J =7.0 Hz, H₂-7), 2.02 (2H, br d, J =13.0 Hz, H-2eq, -6eq), 2.20 (2H, br dt, J =15.0, 4.0 Hz, H-3ax, -5eq), 2.63—2.72 (2H, m, H-3eq, -5ax), 3.15 (1H, dt, J =9.5, 8.0 Hz, H-2'), 3.65 (1H, dd, J =11.5, 5.0 Hz, H-6'a), 3.76 (1H, dt, J =10.5, 7.0 Hz, H-8a), 3.86 (1H, dd, J =11.5, 1.5 Hz, H-6'b), 4.13 (1H, dt, J =10.5, 7.0 Hz, H-8b), 4.27 (1H, d, J =8.0 Hz, H-1'). FAB-MS m/z : 321 [$M+H$]⁺.

A solution of [7- ^{13}C]-**7a** (121.2 mg) in Me_2CO (5.3 ml) was treated with 0.2 N NaOH (3.6 ml) and the mixture was stirred for 4 h at room temperature. It was treated in the same manner as described above to give [7- ^{13}C]-**7** (50.3 mg, 63.3%). 1H -NMR ($CDCl_3$) δ : 1.90 (2H, dt, J_{CH} =126.0 Hz, J =7.0 Hz, H₂-7), 3.75 (1H, dtd, J =10.5, 7.0 Hz, J_{CH} =2.5 Hz, H-8a), 4.12 (1H, dtd, J =10.5, 7.0 Hz, J_{CH} =2.5 Hz, H-8b). FAB-MS m/z : 322 [$M+H$]⁺.

Reduction of Rengyoside B Tetraacetate (7a) $NaBH_4$ (17.8 mg, 0.47 mmol) was added to a solution of **7a** (460.0 mg, 0.94 mmol) in $EtOH$ (15.0 ml) and the mixture was stirred for 30 min at room temperature. It was worked-up in the usual way to give the product (205.2 mg), which was subjected to column chromatography on silica gel with Et_2O . Fractions of 10 ml were collected. Fractions 40—99 were concentrated *in vacuo* to give **6b** as a white powder (40.9 mg, 8.9%). 1H -NMR ($CDCl_3$) δ : 1.43—1.53, 1.68—1.95 (10H, m, H-2, 3, 5, 6, 7), 2.00, 2.03, 2.06, 2.10 (12H, each s, CH_3CO), 3.66—3.75 (2H, m, H-8a, -5'), 3.90—3.96 (1H, m, $W_{1/2}$ =13.0 Hz, H-4), 4.13 (1H, ddd, J =10.0, 6.5, 5.0 Hz, H-8b), 4.17 (1H, dd, J =12.5, 2.5 Hz, H-6'a), 4.26 (1H, dd, J =12.5, 4.5 Hz, H-6'b), 4.52 (1H, d, J =8.0 Hz, H-1'), 4.98 (1H, dd, J =9.5, 8.0 Hz, H-2'), 5.09 (1H, t, J =10.0 Hz, H-4'), 5.21 (1H, t, J =9.5 Hz, H-3'). FAB-MS m/z : 491 [$M+H$]⁺. The residue obtained from Fractions 100—145 was recrystallized from $AcOEt$ to afford **6a** as colorless needles (125.8 mg, 27.2%). mp 125.5—127.0 °C. IR (KBr) cm^{-1} : 3380, 2930, 1740. 1H -NMR ($CDCl_3$) δ : 1.28—1.38, 1.63—1.82 (10H, m, H-2, 3, 5, 6, 7), 2.01, 2.03, 2.05, 2.10 (12H, each s, CH_3CO), 3.55—3.62 (1H, m, $W_{1/2}$ =20 Hz, H-4), 3.68—3.71 (2H, m, H-8a, -5'), 4.11 (1H, ddd, J =10.0, 6.5, 5.0 Hz, H-8b), 4.16 (1H, dd, J =12.5, 2.5 Hz, H-6'a), 4.26 (1H, dd, J =12.5, 4.5 Hz, H-6'b), 4.51 (1H, d, J =8.0 Hz, H-1'), 4.98 (1H, dd, J =9.5, 8.0 Hz, H-2'), 5.09 (1H, t, J =10.0 Hz, H-4'), 5.21 (1H, t, J =9.5 Hz, H-3'). FAB-MS m/z : 491 [$M+H$]⁺.

Rengyoside A (6) A (Reduction of 7): $NaBH_4$ (6.6 mg, 0.2 mmol) was added to a solution of **7** (113.4 mg, 0.35 mmol) in $EtOH$ (5.0 ml) and the mixture was stirred for 30 min at room temperature. The mixture was worked-up in the usual way to give the product (164.6 mg), which was purified through PTLC ($CHCl_3$: $MeOH$: H_2O : $AcOH$ =7:3:0.5:0.1) to yield **6** (114.6 mg, 100%) as a syrupy compound.

B (Zemplén Deacetylation of 6a): Methanolic $NaOMe$ (0.1 N, 2.0 ml) was added to a solution of **6a** (125.8 mg, 0.26 mmol) in dry $MeOH$ (2.0 ml). After having been stirred for 40 min at room temperature, the

mixture was worked-up in the usual way to give **6** (87.7 mg, 100%). $[\alpha]_D^{23} -13.5^\circ$ ($c=0.46$, EtOH) [lit., 12 $[\alpha]_D^{23} -13.3^\circ$ ($c=0.35$, MeOH)]. IR (neat): 3300, 2900. $^1\text{H-NMR}$ (CD_3OD) δ : 1.37–1.46, 1.59–1.76 (8H, m, H-2, 3, 5, 6), 1.75 (1H, dt, $J=14.0$, 7.0 Hz, H-7a), 1.78 (1H, dt, $J=14.0$, 7.0 Hz, H-7b), 3.14 (1H, $J=9.0$, 8.0 Hz, H-2'), 3.48–3.55 (1H, m, $W_{1/2}=20.0$ Hz, H-4), 3.65 (1H, dd, $J=12.0$, 5.5 Hz, H-6'a), 3.70 (1H, dt, $J=10.0$, 7.0 Hz, H-8a), 3.86 (1H, dd, $J=12.0$, 1.5 Hz, H-6'b), 4.07 (1H, dt, $J=10.0$, 7.0 Hz, H-8b), 4.25 (1H, d, $J=8.0$ Hz, H-1'). FAB-MS m/z : 321 $[\text{M}-\text{H}]^-$.

A solution of $[7-^{13}\text{C}]-7$ (30.0 mg) in EtOH (2.0 ml) was reduced with NaBH_4 (1.7 mg) according to procedure A to give $[7-^{13}\text{C}]-6$ (29.5 mg, 97.4%). $^1\text{H-NMR}$ (CDCl_3) δ : 1.76 (1H, ddt, $^1J_{\text{CH}}=125.0$ Hz, $J=14.0$, 7.0 Hz, H-7a), 1.77 (1H, ddt, $^1J_{\text{CH}}=125.0$ Hz, $J=14.0$, 7.0 Hz, H-7b), 3.70 (1H, dtd, $J=10.0$, 7.0 Hz, $^2J_{\text{CH}}=2.5$ Hz, H-8a), 4.13 (1H, dtd, $J=10.0$, 7.0 Hz, $^2J_{\text{CH}}=2.5$ Hz, H-8b). FAB-MS m/z : 322 $[\text{M}-\text{H}]^-$.

Partial Hydrogenation of Cornoside (4) A solution of **4** (41.1 mg, 0.13 mmol) in EtOH (1.5 ml) was hydrogenated in the presence of 5% Pd-C (4.1 mg) and the suspension was stirred for 2.5 h at room temperature with monitoring by TLC (AcOEt: MeOH: H₂O = 10: 1.5: 0.5). The catalyst was filtered off and washed with MeOH, then the filtrate and washings were combined and concentrated *in vacuo*. The resulting residue (36.8 mg) was subjected to PTLC (AcOEt: MeOH: H₂O = 10: 1.5: 0.5, 4 developments). Of the three major bands, the most polar one gave **7** (7.5 mg, 39.4%), and the less polar one gave **11** as a colorless oil (7.3 mg, 38.6%), which was a diastereomeric mixture in a ratio of 1:1 as judged from the ^1H - and ^{13}C -NMR data. The least polar one was identified as the starting material (22.3 mg). Compound **11**: $[\alpha]_D^{15} -12.1^\circ$ ($c=1.12$, MeOH). IR (neat) cm^{-1} : 3330, 3300. $^1\text{H-NMR}$ (CD_3OD) δ : 1.946–2.046 (2H, m, H-6a), 2.025–2.103 (4H, m, H-7), 2.188–2.260 (2H, m, H-6b), 2.471, 2.473 (each 1H, ddd, $J=17.0$, 11.5, 5.0 Hz, H-5ax), 2.550, 2.552 (each 1H, ddd, $J=17.0$, 6.5, 5.0 Hz, H-5eq), 3.154, 3.156 (each 1H, dd, $J=9.0$, 7.5 Hz, H-2'), 3.64 (3H, m, H-5', 6'a), 3.772, 3.780 (each 1H, dt, $J=10.0$, 6.0 Hz, H-8a), 3.86 (2H, br dd, $J=12.0$, ca. 1.0 Hz, H-6'b), 4.135, 4.141 (each 1H, dt, $J=10.0$, 6.0 Hz, H-8b), 4.277, 4.297 (each 1H, d, $J=7.5$ Hz, H-1'), 5.86 (2H, d, $J=10.0$ Hz, H-3), 6.958, 6.960 (each 1H, dd, $J=10.0$, 1.0 Hz, H-2). FAB-MS m/z : 319 $[\text{M}+\text{H}]^+$.

$[8-^{13}\text{C}]-4$ (475 mg) was hydrogenated over 5% Pd-C (48 mg) with stirring for 3.5 h as described above to give $[8-^{13}\text{C}]-11$ (15.4 mg, 7.0%), $[8-^{13}\text{C}]-7$ (37.4 mg, 17.0%), and 224.6 mg of the starting material. $^1\text{H-NMR}$ (CD_3OD) δ : 3.772, 3.780 (each 1H, ddt, $^1J_{\text{CH}}=142.5$ Hz, $J=10.0$, 6.0 Hz, H-8a), 4.135, 4.141 (each 1H, ddt, $^1J_{\text{CH}}=145.0$ Hz, $J=10.0$, 6.0 Hz, H-8b), 4.270, 4.280 (each 1H, dd, $J=7.5$ Hz, $^3J_{\text{CH}}=1.0$ Hz, H-1'), FAB-MS m/z : 320 $[\text{M}+\text{H}]^+$.

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