Synthesis of Four Possible Intermediates after Secologanin on the Biosynthesis of the Oleoside-, 10-Hydroxyoleoside- and Ligustaloside-Type Glucosides in Oleaceous Plants[1a,b]

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To examine the biosynthetic pathway from secologanin to three types of secoiridoid glucosides characteristic of oleaceous plants, synthesis of two respective stereoisomers at C-8 of 8,10-epoxysecologanin and -secoxyloganin was established and their deuterium-labeled analogues were prepared.

Key words synthesis; epoxysecologanin; epoxysecoxyloganin; oleoside; 10-hydroxyoleoside; ligustaloside

Oleaceous plants contain a wide variety of secoiridoid glucosides,[2] *e.g.* oleuropein (**1**),[3,4] jasminin (**2**)[5] (oleoside-type), and 10-acetoxyoleuropein (**3**)[6] (10-hydroxyoleoside-type). In the course of our continuing examinations of the iridoid glucosides of oleaceous plants, we have isolated, along with 10-hydroxyoleuropein (**4**), ligustalosides A (**5**) and B (**6**)[7] which are secoiridoid glucosides with an aldehyde group at C-10 (ligustaloside-type). The systematic explanation of the biosynthesis of these three types of glucosides led us propose a pathway from secologanin (**7**) *via* epoxide (**8a**) as depicted in Chart 1. The configuration at C-8 of epoxide (**8a**) was presumed to be based on the *E* configuration of the ethylidene group in oleoside-type glucosides, and this was in agreement with the configuration formed by *trans* elimination of the corresponding (8*S*)-hydroxy derivative in the chemical reaction.[4] Another important clue for the stereochemistry was provided by the isolation of 8-epikingiside (**9**) with the same configuration (8*S*) as that of **8a** from a few plants of this family.[8] Since oleaceous secoiridoid glucosides usually have a carboxy group at C-7 which forms an ester linkage with various alcohols, however, carboxylic acid (**10a**), the oxidation derivative at C-7 of the epoxide (**8a**) also was assumed to be another putative intermediate in this pathway.

Based on the above presumption, the (*S*)-isomer **8a** or **10a** seemed to best satisfy the stereochemical requirement. However, in order to examine the stereospecificity of this pathway, the stereoisomers (**8b**, **10b**) were also prepared to be used for the feeding experiments.

We report here the syntheses of (8*S*)-8,10-epoxysecologanin (**8a**) and its oxidative derivative at C-7, (8*S*)-8,10-epoxysecoxyloganin (**10a**), and their (8*R*)-isomers (**8b**, **10b**). The preparation of their deuterium-labeled analogues is described.

Synthesis of 8,10-Epoxysecologanin (8) and 8,10-Epoxysecoxyloganin (10) Taking into consideration the presence of the epoxy ring and the glucosidic linkage in the target compounds (**8**, **10**), *o*-nitrophenylethylene acetal[9] which could be removed readily by light irradiation under neutral condition was selected for the protection of the aldehyde group in secologanin tetraacetate (**7a**). Protection of the aldehyde in **7a** with *o*-nitrophenylethylene glycol gave a mixture of two stereoisomeric acetals **11**. Based on the intensity of the anomeric signals of the glucose moiety observed at δ 4.85 (1H, J=8.0 Hz) and 4.86 (1H, J=8.0 Hz) in the ^{1}H-NMR spectrum of **11**, the ratio of the two isomers[10] in this mixture was estimated to be 1 : 1. The mixture was used for further reaction without separation for a series of reactions leading to epoxide (**15**). This mixture was subjected to oxidation with OsO_4 to give diol **12**, which was then tosylated to afford tosylate **13**. Treatment of **13** with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) gave a separable mixture of two stereoisomeric epoxides (**14a**, **14b**) in a ratio of 1 : 1. Deprotection of the two compounds by photolysis yielded aldehydes **15a** and **15b**, respectively. The configurations at C-8 of these two isomers could not be determined from their ^{1}H-NMR spectra, so we tried to solve the problem by elucidating

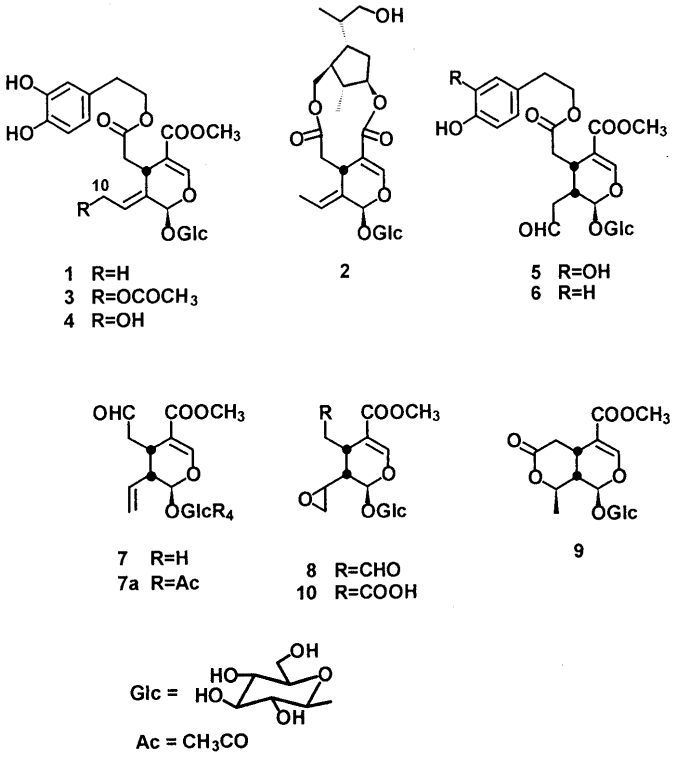

Fig. 1

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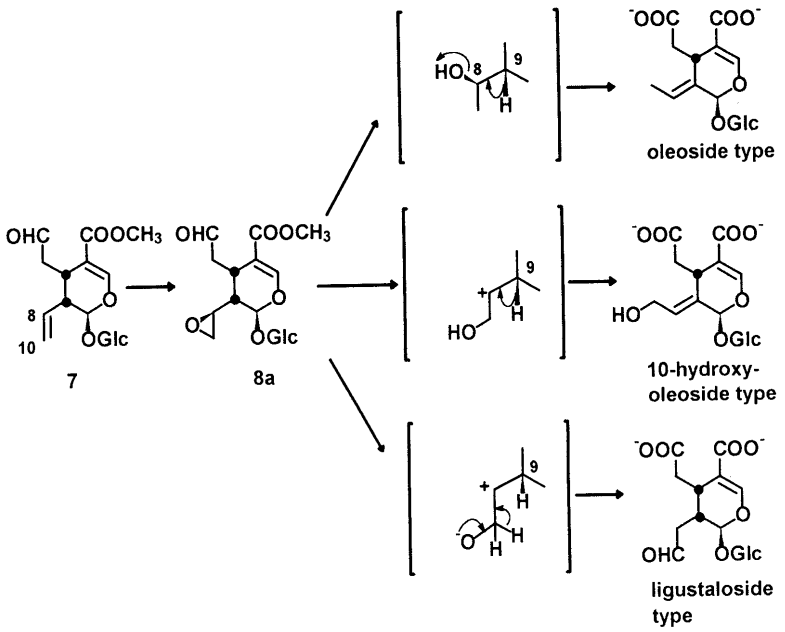
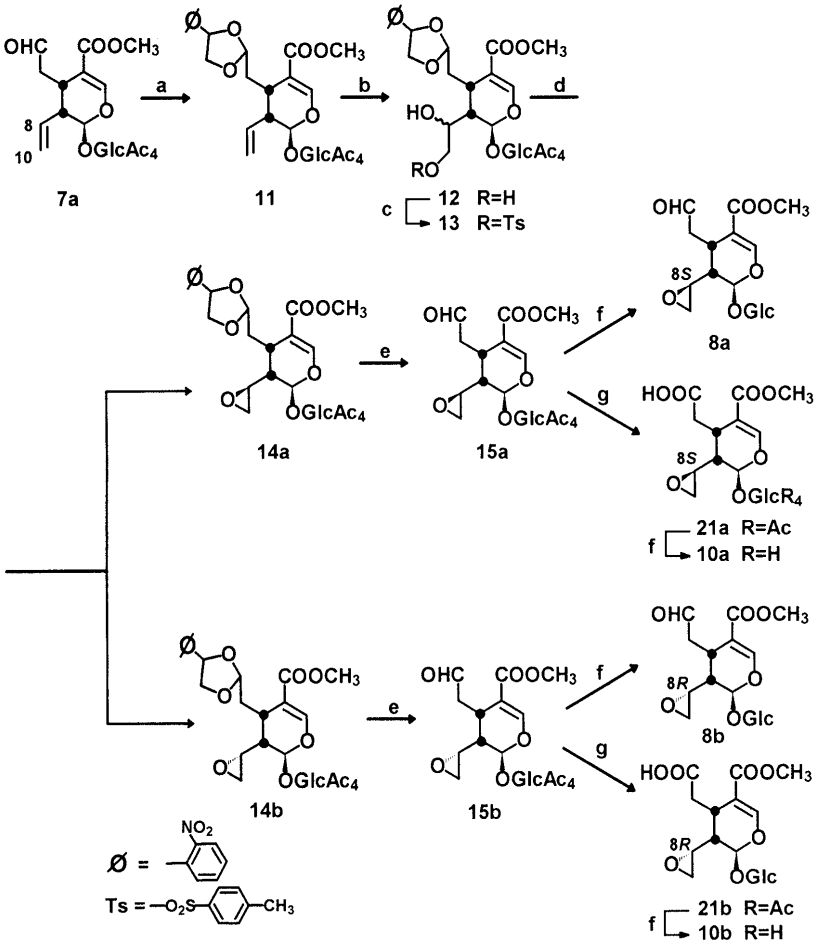
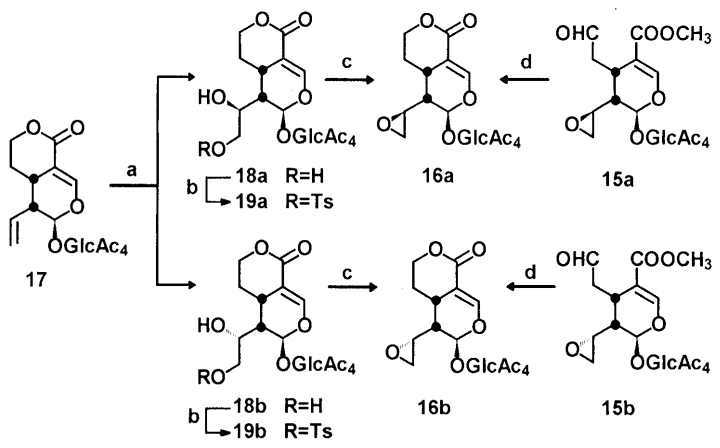


Chart 1



a) *o*-nitrophenylethylene glycol, *p*-TsOH / benzene; b) i: OsO_4, *N*-methylmorpholine-*N*-oxide / acetone-*tert*-BuOH-H_2O, ii: aqueous $NaHSO_3$; c) *p*-TsCl, molecular sieves / pyridine d) DBN / benzene; e) hν / benzene; f) NaOMe / MeOH; g) Jones reagent / acetone

Chart 2



a) i: OsO_4, *N*-methylmorpholine-*N*-oxide / acetone-*tert*-BuOH-H_2O, ii: aqueous $NaHSO_3$; b) *p*-TsCl, molecular sieves / pyridine; c) DBN / benzene; d) $NaBH_4$ / EtOH, 0 °C

Chart 3

the relationship of the two isomers **15a** and **15b** to two epimers (**16a**, **16b**) of 8,10-epoxysweroside tetraacetates,[11,12] in which the stereochemistry at C-8 was established. Conversion of **15a** and **15b** into **16a** and **16b** was achieved by the reduction with $NaBH_4$, respectively.

The authentic samples **16a** and **16b** were prepared from sweroside tetraacetate (**17**). Compound **17** was dihydroxylated with OsO_4 to give a separable mixture of epimeric diols **18a** and **18b**.[13] **18a** was converted to monotosylate **19a** which was treated with DBN to give the epoxide **16a** as colorless needles, mp 158—159 °C, whose chemophysical data were in agreement with those reported previously on (8*S*)-8,10-epoxysweroside tetraacetate.[12] **18b** was derived in the same way *via* tosylate **19b** to epoxide **16b** (colorless needles, mp 199—200 °C), the chemophysical data of which were identical with those reported on (8*R*)-8,10-epoxysweroside tetraacetate.[11,12] Thus, it was concluded that **15a** was (8*S*)-8,10-epoxysecologanin tetraacetate and **15b** was its (8*R*)-epimer. Zemplén reaction of **15a** and **15b** gave the target compounds **8a** and **8b**, respectively. Further, Jones oxidation of **15a** and **15b** followed by Zemplén reaction gave (8*S*)-8,10-epoxysecoxyloganin (**10a**) and (8*R*)-8,10-epoxysecoxyloganin (**10b**), respectively.

Synthesis of [8-^{2}H,10]-Epoxysecologanin (8) and [8-^{2}H,10]-Epoxysecoxyloganin (10) As a preliminary experiment of the radioisotopic labelling, attempts to prepare compounds **15a** and **15b** labeled with deuterium on C-8 were made. The ketone **20**, which was obtained by Jones oxidation of tosylate **13**, was subjected to NaB^2H_4 reduction in dioxane to afford [8-^{2}H]-tosylate **13**. This compound was then treated with DBN followed by photolysis as described above to give [8-^{2}H]-epoxyaldehydes (**15a**, **15b**) in a ratio of 2:1. In the ^{1}H-NMR spectrum of [8-^{2}H]-**15a** and **15b**, three signals due to H-9, H_2-10 of each compound lost the coupling with H-8 (see Experimental), indicating deuterium-labeling at C-8. Accordingly, the synthetic method of 8-labeled 8,10-epoxides was established. Syntheses of tritium labeled epoxides **8a**, **8b**, **10a** and **10b**, and experiments on their administration will be reported elsewhere.

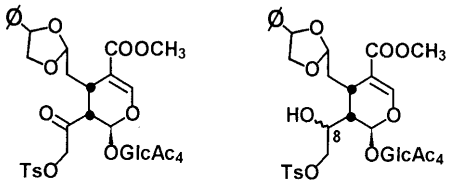


Fig. 2

Experimental

Melting points were measured on Yanagimoto microapparatus and are uncorrected. Optical rotations were taken with a Union PM 101 automatic digital polarimeter. UV spectra were recorded on a Hitachi Model 323 S spectrophotometer, and IR spectra on a Hitachi Model 260-30 IR spectrophotometer. NMR spectra were taken on a JEOL JNM FX-200 unless otherwise noted or JEOL JNM-GX 500 with tetramethylsilane as the internal standard. FAB-MS spectra were recorded on a JEOL JMS-HX 100 mass spectrometer using 3-nitro-benzyl alcohol unless otherwise noted or glycerol as the matrix. Column chromatography was performed on Silica gel 60 (70—230 mesh, Merck) and on highly porous polymer Diaion HP-21 (Mitsubishi Chemical Industries). For TLC, Silica gel 60 GF_{254} (Merck) was used and spots were visualized by irradiation under UV light, or by exposure to I_2 vapor. For preparative TLC (PTLC), Silica gel 60 PF_{254} (Merck) was used and bands were detected under UV light. The ratios of solvents are expressed by volume. All extracts were dried over anhydrous $MgSO_4$.

Acetal 11 *p*-TsOH (230 mg) was added to a solution of **7a** (4.4 g), which was prepared from secologanin (7) with pyridine-Ac_2O, and *o*-nitrophenylethylene glycol (1.5 g) in dry benzene (500 ml), and the mixture was heated under reflux for 2 h with a Dean–Stark separator. It was then washed successively with saturated aqueous $NaHCO_3$ and brine, dried and concentrated *in vacuo*. The residue (5.5 g) was chromatographed on silica gel (66 g) column with $CHCl_3$ as an eluent, and 200 ml of each fraction was collected. Fractions 2—4 were combined and concentrated *in vacuo* to give acetal **11** (4.3 g, 75%) as a pale yellow powder. UV λ_{max}^{EtOH} nm (log ε): 228 (4.16), 262 inf (3.83). IR ν_{max}^{KBr} cm^{-1}: 1760, 1710, 1630, 1530. ^{1}H-NMR ($CDCl_3$) δ: 1.91—2.10 (12H, each s, $-OCOCH_3$), 2.40—2.60 (2H, m, H_2-6), 2.80—2.88 (1H, m, H-9), 2.88—3.18 (1H, m, H-5), 3.60—3.84 (5H, m, 5′-H, $-CO_2CH_3$, $-C_6H_4CHCHH-O-$), 4.15— 4.80 (3H, m, H_2-6′, $-C_6H_4CHCHH-O-$), 4.80, 4.85 (1H, each d, J=8.0, H-1′), 4.95—5.80 (9H, m, H-1, -7, -8, -2′, -3′, -4′, H_2-10, $-C_6H_4CH-O-$), 7.43—8.10 (4H, m, arom. H), 7.38, 7.39 (1H, each s, H-3). FAB-MS *m/z*: 722 $(M+H)^+$. *Anal.* Calcd for $C_{33}H_{39}NO_{17}$: C,

54.92; H, 5.45; N, 1.94. Found: C, 54.94; H, 5.42; N, 1.89.

Diol 12 A solution of *N*-methylmorpholine-*N*-oxide·$2H_2O$ (160 mg) in H_2O (10 ml) was added to a solution of **11** (730 mg) in acetone (50 ml) under argon. To the stirred solution was added dropwise a solution of OsO_4 (30 mg) in *tert*-BuOH (1 ml) and the mixture was stirred for 96 h at room temperature in the dark. After addition of 10% aqueous $NaHSO_3$ (1 ml), stirring was continued for an additional 1 h at room temperature. The solution was then diluted with H_2O (50 ml), neutralized with 1 N HCl, and extracted with $CHCl_3$ (50 ml × 4). The $CHCl_3$ layer was washed successively with brine, H_2O and dried. Removal of the solvent *in vacuo* gave the residue (633 mg), which was chromatographed on silica gel (20 g) column, and eluted successively with benzene–Et_2O (9 : 1) (150 ml) and Et_2O (100 ml). Fractions of 10 ml were collected. Fractions 14—33 were combined and concentrated *in vacuo* to give diol **12** (234.8 mg, 31%) as a white powder. UV λ_{max}^{EtOH} nm (log ε): 235 (4.19), 264 inf (3.80). IR ν_{max}^{KBr} cm^{-1}: 3480, 1755, 1705, 1640, 1530. ^{1}H-HMR ($CDCl_3$) δ: 1.70—1.98 (2H, m, H_2-6), 2.01—2.10 (12H, each s, –$OCOCH_3$), 2.26—2.64 (1H, m, H-9), 3.18—3.30 (1H, m, H-5), 3.58—4.02 (8H, m, H-8, -5′, H_2-10, –CO_2CH_3, –C_6H_4CHCHH–O–), 5.02—5.64 (6H, m, H-1, -7, -2′, -3′, -4′, –C_6H_4CH–O–), 4.10—4.80 (3H, m, H_2-6′, –C_6H_4CHCHH–O–), 4.94, 4.96 (1H, each d, *J* = 8.0 Hz, H-1′), 7.41, 7.42 (1H, each s, H-3), 7.43—8.08 (4H, m, arom. H). FAB-MS *m/z*: 756 $(M+H)^+$. *Anal.* Calcd for $C_{33}H_{41}NO_{19}$: C, 52.45; H, 5.47; N, 1.85. Found: C, 52.32; H, 5.42; N, 1.89. Fractions 1—3 were identified as the starting material (267 mg).

Tosylate 13 *p*-TsCl (130 mg) and freshly activated molecular sieves type 4A (500 mg) were added to a solution of **12** (497 mg) in dry pyridine (20 ml). After stirring for 40 h at room temperature in the dark, the mixture was filtered through a Celite layer, and the layer was washed with $CHCl_3$ (75 ml). The combined filtrate and washings were diluted with H_2O (100 ml), and extracted with $CHCl_3$ (100 ml × 4). The $CHCl_3$ layer was washed successively with 1 N HCl, saturated aqueous $NaHCO_3$ and H_2O, dried and concentrated *in vacuo*. The resulting residue (422 mg) was subjected to PTLC ($CHCl_3$: MeOH = 50 : 1, 3 developments) to give tosylate **13** (413.8 mg, 69%) as a white powder. UV λ_{max}^{EtOH} nm (log ε): 226 (4.37), 271 sh (3.60). IR ν_{max}^{KBr} cm^{-1}: 3480, 1755, 1705, 1640. ^{1}H-NMR ($CDCl_3$) δ: 1.60—1.98 (2H, m, H_2-6), 2.02—2.10 (12H, each s, –$OCOCH_3$), 2.24—2.63 (4H, m, H-9, arom. CH_3), 3.02—3.18 (1H, m, H-5), 3.47—3.82 (5H, m, H-5′, –CO_2CH_3, –C_6H_4CHCHH–O–), 4.01—4.78 (6H, m, H-8, H_2-10, -6′, –C_6H_4CHCHH–O–), 4.94—5.63 (7H, m, H-1, -7, -1′, -2′, -3′, -4′, –C_6H_4CH–O–), 7.38, 7.40 (1H, each s, H-3), 7.24—8.18 (8H, m, arom. H). FAB-MS *m/z*: 910 $(M+H)^+$. *Anal.* Calcd for $C_{40}H_{47}NO_{21}S$: C, 52.80; H, 5.21; N, 1.54. Found: C, 52.69; H, 5.19; N, 1.60.

Epoxides 14a and 14b To a solution of **13** (79.2 mg) in dry benzene (5 ml) was added DBN (0.059 ml) and the mixture was stirred for 20 h at room temperature in the dark. After successive washings with 1 N HCl, brine and H_2O, the benzene layer was dried and concentrated *in vacuo* to give the residue (64.1 mg), which was subjected to PTLC (benzene : EtOAc = 5 : 1, 8 developments). Of the three bands, the least polar one yielded epoxide **14b** (19.5 mg, 30%) and the second polar one gave **14a** (20.2 mg, 32%) as a white powder, respectively. The most polar one was identified as the starting material (1.3 mg).

14a: UV λ_{max}^{EtOH} nm (log ε): 228 (4.13), 260 inf (3.76). IR ν_{max}^{KBr} cm^{-1}: 1760, 1710, 1630, 1530. ^{1}H-NMR ($CDCl_3$) δ: 1.60—1.90 (2H, m, H_2-6), 2.00—2.10 (12H, each s, –$OCOCH_3$), 2.48—2.90 (3H, m, H-8, H_2-10), 3.10—3.40 (2H, m, H-5, -9), 3.60—3.88 (5H, m, H-5′, –CO_2CH_3, –C_6H_4CHCHH–O–), 4.00—4.84 (3H, m, H_2-6′, –C_6H_4CHCHH–O–), 4.95—5.75 (7H, m, H-1, -7, -1′, -2′, -3′, -4′, –C_6H_4CHO–), 7.30—8.16 (5H, m, H-3, arom. H). FAB-MS *m/z*: 738 $(M+H)^+$. *Anal.* Calcd for $C_{33}H_{39}NO_{18}$: C, 53.73; H, 5.33; N, 1.90. Found: C, 53.65; H, 5.30; N, 1.91.

14b: UV λ_{max}^{EtOH} nm (log ε): 227 (4.13), 258 sh (3.75). IR ν_{max}^{KBr} cm^{-1}: 1755, 1710, 1630, 1530. ^{1}H-NMR ($CDCl_3$) δ: 1.50—1.80 (2H, m, H_2-6), 1.92—2.10 (12H, each s, –$OCOCH_3$), 2.64—2.96 (3H, m, H-8, H_2-10), 3.00—3.30 (2H, m, H-5, -9), 3.64—3.92 (5H, m, H-5′, –CO_2CH_3, –C_6H_4CHCHH–O–), 4.02—4.81 (3H, m, H_2-6′, –C_6H_4CHCHH–O–), 4.90—5.70 (7H, m, H-1, -7, -1′, -2′, -3′, -4′, –C_6H_4CH–O–), 7.40—8.18 (5H, m, H-3, arom. H). FAB-MS *m/z*: 738 $(M+H)^+$. *Anal.* Calcd for $C_{33}H_{39}NO_{18}$: C, 53.73; H, 5.33; N, 1.90. Found: C, 53.65; H, 5.30; N, 1.91.

Epoxy-aldehydes 15a and 15b A solution of **14a** (20.1 mg) in benzene (2.5 ml) was stirred at intervals of 10 cm under irradiation through a high-pressure mercury lamp (λ_{max} 365 nm, 500 W, Eikosha Co., Ltd.) in a Pyrex filter for 1 h at room temperature. Removal of the solvent *in vacuo* gave a residue, which was purified by PTLC (benzene : EtOAc = 7 : 3, 4 developments) to afford epoxy-aldehyde **15a** (9.3 mg, 57%) as a white powder. $[\alpha]_D^{14}$ −67.50° (*c* = 0.800, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 233 (3.98). IR ν_{max}^{KBr} cm^{-1}: 1760, 1705, 1630. ^{1}H-NMR ($CDCl_3$) δ: 1.81 (1H, ddd, *J* = 8.0, 6.0, 4.0 Hz, H-9), 1.94, 2.01, 2.03, 2.10 (12H, each s, –$OCOCH_3$), 2.56 (1H, dd, *J* = 5.0, 3.0 Hz, H-10a), 2.73—2.81 (1H, m, H-8), 2.78 (2H, m, H-10b, ddd, *J* = 17.6, 8.0, 1.1 Hz, H-6a), 3.05 (1H, ddd, *J* = 17.6, 5.5, 1.1 Hz, H-6b), 3.39 (1H, dddd, *J* = 8.0, 6.0, 5.5, 1.8 Hz, H-5), 3.71 (3H, s, –CO_2CH_3), 3.74 (1H, ddd, *J* = 9.5, 4.4, 2.6 Hz, H-5′), 4.16 (1H, dd, *J* = 12.5, 2.6 Hz, H-6′a), 4.29 (1H, dd, *J* = 12.5, 4.4 Hz, H-6′b), 4.89 (1H, d, *J* = 8.1 Hz, H-1′), 5.01 (1H, dd, *J* = 9.2, 8.1 Hz, H-2′), 5.11 (1H, dd, *J* = 9.5, 9.2 Hz, H-4′), 5.23 (1H, t, *J* = 9.2 Hz, H-3′), 5.38 (1H, d, *J* = 4.0 Hz, H-1), 7.43 (1H, d, *J* = 1.8 Hz, H-3), 9.78 (1H, t like, *J* = 1.1 Hz, H-7). FAB-MS *m/z*: 573 $(M+H)^+$. *Anal.* Calcd for $C_{25}H_{32}O_{15}$: C, 52.45; H, 5.63. Found: C, 52.65; H, 5.55.

14b (18.4 mg) was deprotected as described above to give **15b** (8.4 mg, 59%) as a white powder. $[\alpha]_D^{14}$ −62.59° (*c* = 0.735, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 232 (3.94). IR ν_{max}^{KBr} cm^{-1}: 1760, 1710, 1630. ^{1}H-NMR ($CDCl_3$) δ: 1.81 (1H, ddd, *J* = 9.0, 6.0, 2.6 Hz, H-9), 1.91, 2.01, 2.03, 2.10 (12H, each s, –$OCOCH_3$), 2.52 (1H, ddd, *J* = 17.6, 8.0, 1.8 Hz, H-6a), 2.53 (1H, dd, *J* = 5.0, 2.8 Hz, H-10a), 2.73 (12H, ddd, *J* = 9.0, 4.0, 2.8 Hz, H-8), 2.82 (1H, dd, *J* = 5.0, 4.0 Hz, H-10b), 3.38 (1H, dddd, *J* = 8.0, 6.0, 5.5, 2.2 Hz, H-5), 3.70 (3H, s, –CO_2CH_3), 3.75 (1H, ddd, *J* = 9.5, 4.8, 2.6 Hz, H-5′), 4.13 (1H, dd, *J* = 12.5, 2.6 Hz, H-6′a), 4.30 (1H, dd, *J* = 12.5, 4.8 Hz, H-6′b), 4.90 (1H, d, *J* = 8.1 Hz, H-1′), 5.01 (1H, dd, *J* = 9.2, 8.1 Hz, H-2′), 5.09 (1H, dd, *J* = 9.5, 9.2 Hz, H-4′), 5.23 (1H, t, *J* = 9.2 Hz, H-3′), 5.58 (1H, d, *J* = 2.6 Hz, H-1), 7.48 (1H, d, *J* = 2.2 Hz, H-3), 9.75 (1H, t like dd, *J* = 1.8, 1.5 Hz, H-7). FAB-MS *m/z*: 573 $(M+H)^+$. *Anal.* Calcd for $C_{25}H_{32}O_{15}$: C, 52.45; H, 5.63. Found: C, 52.63; H, 5.70.

Epoxy-lactones 16a and 16b A solution of $NaBH_4$ (2 mg) in EtOH (1 ml) was added dropwise to a stirred solution of **15a** (22.8 mg) in EtOH (1 ml) under ice-cooling and the mixture was stirred for 2 h at room temperature. After decomposition of the excess reagent by adding two drops of AcOH under ice-cooling, the mixture was diluted with H_2O (5 ml) and extracted with $CHCl_3$ (5 ml × 4). The $CHCl_3$ layer was washed successively with saturated aqueous $NaHCO_3$ and H_2O, dried and concentrated *in vacuo*. The residue (19.4 mg) was subjected to PTLC ($CHCl_3$: MeOH = 50 : 1) to yield colorless needles (14.1 mg, 65%) of epoxy-lactone **16a** on recrystallization from EtOH. mp 158—159 °C. $[\alpha]_D^{13}$ −150.08° (*c* = 0.653, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 241 (3.92). IR ν_{max}^{KBr} cm^{-1}: 1755, 1740, 1710 sh, 1620. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.70 (1H, ddd, *J* = 9.0, 6.5, 2.0 Hz, H-9), 1.95—2.07 (2H, m, H_2-6, covered with acetyl group), 1.98, 2.01, 2.04, 2.10 (12H, each s, –$OCOCH_3$), 2.60 (1H, dd, *J* = 4.5, 2.5 Hz, H-10a), 2.74 (1H, ddd, *J* = 9.0, 4.0, 2.5 Hz, H-8), 2.80 (1H, dd, *J* = 4.5, 4.0 Hz, H-10b), 2.94 (1H, dtd, *J* = 12.5, 6.0, 2.5 Hz, H-5), 3.75 (1H, ddd, *J* = 9.5, 4.0, 2.0 Hz, H-5′), 4.16 (1H, dd, *J* = 12.5, 2.0 Hz, H-6′a), 4.30 (1H, dd, *J* = 12.5, 4.0 Hz, H-6′b), 4.34 (1H, ddd, *J* = 12.5, 11.5, 2.5 Hz, H-7ax), 4.54 (1H, ddd, *J* = 11.5, 4.5, 2.0 Hz, H-7eq), 4.90 (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* = 9.5 Hz, H-4′), 5.24 (1H, t, *J* = 9.5 Hz, H-3′), 5.43 (1H, d, *J* = 2.0 Hz, H-1), 7.57 (1H, d, *J* = 2.5 Hz, H-3). FAB-MS *m/z*: 543 $(M+H)^+$. *Anal.* Calcd for $C_{24}H_{30}O_{14}$: C, 53.14; H, 5.57. Found: C, 53.08; H, 5.62. This compound was identical with (8*S*)-8,10-epoxysweroside tetraacetate derived from sweroside tetraacetate (**17**) (mixed mp, IR and ^{1}H-NMR).

15b (20.1 mg) was reduced with $NaBH_4$ (2 mg) as described above and PTLC followed by recrystallization of the crude product (16.2 mg) gave colorless needles (13.6 mg, 71%) of epoxy-lactone **16b**. mp 199—200 °C. $[\alpha]_D^{13}$ −150.99° (*c* = 0.404, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 242 (3.98). IR ν_{max}^{KBr} cm^{-1}: 1755, 1710, 1630. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.67 (1H, ddd, *J* = 9.5, 5.5, 2.0 Hz, H-9), 1.83 (1H, dddd, *J* = 12.5, 5.5, 3.2, 2.5 Hz, H-6eq), 1.88 (1H, qd, *J* = *ca.* 12.5, 4.5 Hz, H-6ax), 1.98, 2.01, 2.03, 2.10 (12H, each s, –$OCOCH_3$), 2.57 (1H, dd, *J* = 5.2, 2.5 Hz, H-10a), 2.72 (1H, ddd, *J* = 9.5, 4.0, 2.5 Hz, H-8), 2.88 (1H, dd, *J* = 5.2, 4.0 Hz, H-10b), 2.96 (1H, dtd, *J* = 12.5, 5.5, 2.5 Hz, H-5), 3.77 (1H, ddd, *J* = 9.5, 4.5, 2.0 Hz, H-5′), 4.12 (1H, dd, *J* = 12.5, 2.0 Hz, H-6′a), 4.31 (1H, dd, *J* = 12.5, 4.5 Hz, H-6′b), 4.34 (1H, td, *J* = 11.5, 3.2 Hz, H-7ax), 4.50 (1H, ddd, *J* = 11.5, 4.2, 2.5 Hz, H-7eq), 4.93 (1H, d, *J* = 8.0 Hz, H-1′), 4.98 (1H, dd, *J* = 9.5, 8.0 Hz, H-2′), 5.07 (1H, t, *J* = 9.5 Hz, H-4′), 5.25 (1H, t, *J* = 9.5 Hz, H-3′), 5.66 (1H, d, *J* = 2.0 Hz, H-1), 7.62 (1H, d, *J* = 2.5 Hz, H-3). FAB-MS *m/z*: 543 $(M+H)^+$. *Anal.* Calcd for $C_{24}H_{30}O_{14}$: C, 53.14; H, 5.57. Found: C, 53.21; H, 5.47. This compound was identical with (8*R*)-8,10-epoxysweroside tetraacetate derived from sweroside tetraacetate (**17**) (mixed mp, IR and ^{1}H-NMR).

Preparation of Epoxides 16a and 16b from Sweroside Tetraacetate (17) i) Diols **18a** and **18b**: In the same way as described above for the preparation of **12**, **17** (300 mg) was dihydroxylated with *N*-methylmorpholine-*N*-oxide (140 mg) in acetone and OsO_4 (20 mg) in *tert*-BuOH for 6 d. The crude product (260 mg) was subjected to PTLC (Et_2O: MeOH = 95 : 5, 4 developments). Of the two major bands, the less polar one gave a residue (38.3 mg), which yielded on recrystallization from Et_2O–MeOH, colorless needles (36.4 mg, 11%) of diol **18a**. mp 109—110 °C (lit.,[13] mp 111—113 °C). $[\alpha]_D^{11}$ −142.05° (c = 0.352, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 243 (3.92). IR ν_{max}^{KBr} cm^{-1}: 3425, 1750, 1700, 1620. ^{1}H-NMR ($CDCl_3$) δ: 1.93, 1.99, 2.01, 2.08 (12H, each s, $-OCOCH_3$), 2.24 (1H, td, J = 6.0, 1.9 Hz, H-9), 2.92—3.08 (1H, m, H-5), 3.72 (1H, ddd, J = 9.9, 4.3, 2.5 Hz, 5′-H), 3.56—3.68 (3H, m, H-8, H_2-10), 4.10 (1H, dd, J = 12.5, 2.5 Hz, H-6′a), 4.29 (1H, dd, J = 11.0, 2.5 Hz, H-7a), 4.33 (1H, dd, J = 12.5, 4.3 Hz, H-6′b), 4.50 (1H, dt, J = 11.0, 3.0 Hz, H-7b), 4.86 (1H, d, J = 8.0 Hz, H-1′), 4.98 (1H, dd, J = 9.3, 8.0 Hz, H-2′), 5.08 (1H, dd, J = 9.6, 9.3 Hz, H-4′), 5.23 (1H, t, J = 9.3 Hz, H-3′), 5.51 (1H, d, J = 1.9 Hz, H-1), 7.52 (1H, d, J = 2.6 Hz, H-3). FAB-MS m/z: 561 $(M+H)^+$. *Anal.* Calcd for $C_{24}H_{32}O_{15}$: C, 51.43; H, 5.75. Found: C, 51.23; H, 5.87.

The more polar one gave a residue (50.7 mg), which yielded colorless needles (48.7 mg, 15%) of diol **18b** on recrystallization from Et_2O–MeOH. mp 92—93 °C (lit.,[13] mp 92—93 °C). $[\alpha]_D^{11}$ −108.70° (c = 0.092, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 246 (3.81). IR ν_{max}^{KBr} cm^{-1}: 3450, 1760, 1740 sh, 1710, 1622. ^{1}H-NMR ($CDCl_3$) δ: 1.68—1.84 (2H, m, H_2-6), 1.94, 1.99, 2.02, 2.08 (12H, each s, $-OCOCH_3$), 2.14 (1H, t like, H-9), 2.84—3.04 (1H, m, H-5), 3.72 (1H, ddd, J = 9.6, 4.5, 2.5 Hz, H-5′), 3.44—3.70 (3H, m, H-8, H_2-10), 4.15 (1H, dd, J = 12.5, 2.5 Hz, H-6′a), 4.31 (1H, dd, J = 12.5, 4.5, H-6′b), 4.49 (1H, dt like, H-7), 4.90 (1H, d, J = 8.0 Hz, H-1′), 4.99 (1H, dd, J = 9.3, 8.0 Hz, H-2′), 5.08 (1H, dd, J = 9.6, 9.3 Hz, H-4′), 5.24 (1H, t, J = 9.3 Hz, H-3′), 5.81 (1H, d, J = 2.0 Hz, H-1), 7.64 (1H, d, J = 2.5 Hz, H-3). FAB-MS m/z: 561 $(M+H)^+$. *Anal.* Calcd for $C_{24}H_{32}O_{15}$: C, 51.43; H, 5.75. Found: C, 51.30; H, 5.67.

ii) Tosylates **19a** and **19b**: In the same way as described above for the preparation of **13**, **18a** (63 mg) in dry pyridine (1 ml) was tosylated with *p*-TsCl (21.6 mg) and molecular sieves type 4A (100 mg). After stirring for 40 h, *p*-TsCl (10.3 mg) was added to the mixture and stirred for further 15 h and worked-up as described above. PTLC (1st; Et_2O : MeOH = 19 : 1, 2nd; $CHCl_3$: MeOH = 50 : 1, 3 developments) followed by recrystallization from EtOH of the crude product (100 mg) gave colorless needles (56.2 mg, 70%) of tosylate **19a**. mp 87—88 °C. $[\alpha]_D^{11}$ −96.93° (c = 0.619, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 227 (4.28), 240 inf (3.96), 271 inf (2.78). IR ν_{max}^{KBr} cm^{-1}: 3475, 1750, 1710, 1620. ^{1}H-NMR ($CDCl_3$) δ: 1.80—1.95 (2H, m, H_2-6), 1.95, 2.01, 2.04, 2.10 (12H, each s, $-OCOCH_3$), 2.28 (1H, td, J = 6.5, 1.5 Hz, H-9), 2.48 (3H, s, arom. CH_3), 3.00 (1H, m, H-5), 3.77 (2H, ddd, J = 9.6, 4.5, 2.0 Hz, H-5′, and m, H-8), 4.10—4.24 (3H, m, H-7a, H_2-10), 4.14 (1H, dd, J = 12.5, 2.0 Hz, H-6′a), 4.32 (1H, dd, J = 12.5, 4.5 Hz, H-6′b), 4.45 (1H, dt, J = 11.0, 3.0 Hz, H-7b), 4.84 (1H, d, J = 8.0 Hz, H-1′), 4.96 (1H, dd, J = 9.3, 8.0 Hz, H-2′), 5.08 (1H, dd, J = 9.6, 9.3 Hz, H-4′), 5.24 (1H, t, J = 9.3 Hz, H-3′), 5.51 (1H, d, J = 1.5 Hz, H-1), 7.36 (2H, AA′BB′ pattern, J_{ortho} = 8.3 Hz, arom. H), 7.47 (1H, d, J = 2.5 Hz, H-3), 7.78 (2H, J_{ortho} = 8.3 Hz, arom. H). FAB-MS m/z: 715 $(M+H)^+$. *Anal.* Calcd for $C_{31}H_{38}O_{17}S$: C, 52.10; H, 5.36. Found: C, 52.08; H, 5.29.

Likewise, diol **18b** (62 mg) was tosylated with pyridine (1 ml)–*p*-TsCl (22.9 mg) as described above and the crude product (100 mg) was subjected to PTLC followed by recrystallization from EtOH to give colorless needles (52.3 mg, 66%) of tosylate **19b**. mp 92 °C. $[\alpha]_D^{11}$ −109.30° (c = 0.677, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 227 (4.26), 240 inf (3.94), 271 inf (3.00). IR ν_{max}^{KBr} cm^{-1}: 3500, 1750, 1710, 1620. ^{1}H-NMR ($CDCl_3$) δ: 1.95, 2.00, 2.04, 2.09 (12H, each s, $-OCOCH_3$), 2.47 (3H, s, arom. CH_3), 2.85—3.04 (1H, m, H-5), 3.75 (1H, ddd, J = 10.0, 4.5, 2.5 Hz, H-5′), 3.80 (1H, dd, J = 7.5, 3.0 Hz, H-8), 3.93—4.21 (3H, m, H-7a, H_2-10), 4.18 (1H, dd, J = 12.6, 2.0 Hz, H-6′a), 4.30 (1H, dd, J = 12.6, 4.5 Hz, H-6′b), 4.44 (1H, dt, J = 11.0, 3.0 Hz, H-7b), 4.86 (1H, d, J = 8.0 Hz, H-1′), 4.96 (1H, dd, J = 9.3, 8.0 Hz, H-2′), 5.07 (1H, dd, J = 10.0, 9.3 Hz, H-4′), 5.23 (1H, t, J = 9.3 Hz, H-3′), 5.75 (1H, d, J = 1.9 Hz, H-1), 7.36 (2H, AA′BB′ pattern, J_{ortho} = 8.3 Hz, arom. H), 7.59 (1H, d, J = 2.6 Hz, H-3), 7.78 (2H, AA′BB′ pattern, J_{ortho} = 8.3 Hz, arom. H). FAB-MS m/z: 715 $(M+H)^+$. *Anal.* Calcd for $C_{31}H_{38}O_{17}S$: C, 52.10; H, 5.36. Found: C, 52.21; H, 5.48.

iii) Epoxides **16a** and **16b**: Tosylate **19a** (28.7 mg) in dry benzene (1 ml) was epoxidated with DBN (0.021 ml) under stirring for 15 h as described above. The crude product (23.1 mg) was subjected to PTLC ($CHCl_3$: MeOH = 50 : 1, 4 developments) followed by recrystallization from EtOH to give (8*S*)-8,10-epoxysweroside tetraacetate (**16a**) (13.0 mg, 60%) as colorless needles.

Tosylate **19b** (30.4 mg) was treated with DBN (0.025 ml) as described above and purification of the product (32.8 mg) gave (8*R*)-8,10-epoxysweroside tetraacetate (**16b**) (13.0 mg, 56%).

Aldehydes 8a and 8b Methanolic NaOMe (1 N, 0.01 ml) was added to a solution of **15a** (31.6 mg) in dry MeOH (0.2 ml) and the mixture was stirred for 30 min at room temperature. After neutralization of the mixture by adding Amberlite IR-120 B (H^+ form), the resin was filtered off. The filtrate was concentrated *in vacuo* to give a residue (26.2 mg), which was purified by PTLC ($CHCl_3$: MeOH = 5 : 1, 5 developments) to yield a white powder (16.8 mg, 75%) of (8*S*)-8,10-epoxide **8a**. $[\alpha]_D^{18}$ −136.59° (c = 0.410, MeOH). UV λ_{max}^{MeOH} nm (log ε): 231 (4.08). IR ν_{max}^{KBr} cm^{-1}: 3380, 1710, 1635. ^{1}H-NMR (CD_3OD) δ: 1.74 (1H, ddd, J = 8.0, 5.0, 2.0 Hz, H-9), 1.85 (1H, ddd, J = 12.0, 6.4, 1.0 Hz, H-6a), 2.60 (1H, dd, J = 4.5, 2.5 Hz, H-10a), 2.84 (1H, dd, J = 4.5, 3.5 Hz, H-10b), 3.01 (1H, ddd, J = 12.0, 4.8, 1.2 Hz, H-6b), 3.70 (3H, s, $-CO_2CH_3$), 4.70 (1H, d, J = 7.0 Hz, H-1′), 5.63 (1H, d, J = 2.0 Hz, H-1), 7.54 (1H, d, J = 2.0 Hz, H-3), 9.72 (1H, t like, H-7). FAB-MS (glycerol) m/z: 403 $(M-H)^-$. *Anal.* Calcd for $C_{17}H_{24}O_{11} \cdot 1/2H_2O$: C, 49.39; H, 6.10. Found: C, 49.42; H, 5.98.

Aldehyde **15b** (15.0 mg) was worked-up as described above to give a white powder (9.8 mg, 93%) of (8*R*)-8,10-epoxide **8b**. $[\alpha]_D^{18}$ −120.00° (c = 0.175, MeOH). UV λ_{max}^{MeOH} nm (log ε): 233 (4.02). IR ν_{max}^{KBr} cm^{-1}: 3350, 1690, 1620. ^{1}H-NMR (CD_3OD) δ: 1.70 (1H, ddd, J = 7.5, 5.0, 2.0 Hz, H-9), 2.63 (1H, dd, J = 4.5, 2.5 Hz, H-10), 3.69 (3H, s, $-CO_2CH_3$), 4.67 (1H, d, J = 7.0 Hz, H-1′), 5.62 (1H, d, J = 4.5 Hz, H-1), 7.57 (1H, d, J = 1.2 Hz, H-3), 9.73 (1H, t like, H-7). FAB-MS m/z: 405 $(M+H)^+$. *Anal.* Calcd for $C_{17}H_{24}O_{11} \cdot 1/2H_2O$: C, 49.39; H, 6.10. Found: C, 49.21; H, 6.00.

Acids 21a and 21b Jones reagent (0.02 ml) was added dropwise to a stirred solution of **15a** (25.4 mg) in acetone (1.0 ml) under ice-cooling and stirring was continued for 25 min. After decomposition of the excess reagent by adding a drop of MeOH, the reaction mixture was diluted with H_2O (4.0 ml) and extracted with $CHCl_3$ (5 ml × 4). The $CHCl_3$ layer was washed with brine, dried and concentrated *in vacuo*. The residue (22.1 mg) was purified by PTLC ($CHCl_3$: EtOAc = 5 : 2, 2 developments) to give acid **21a** (15.2 mg, 58%) as a white powder. $[\alpha]_D^{18}$ −77.61° (c = 0.335, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 232 (3.96). IR ν_{max}^{KBr} cm^{-1}: 3450, 1740, 1720, 1630. ^{1}H-NMR ($CDCl_3$) δ: 1.87 (1H, ddd, J = 8.0, 5.0, 4.0 Hz, H-9), 1.94, 2.01, 2.03, 2.11 (12H, each s, $-OCOCH_3$), 2.59 (1H, dd, J = 4.2, 2.4 Hz, H-10a), 2.70 (1H, dd, J = 10.8, 8.0, H-6a), 2.82 (1H, dd, J = 4.2, 3.2 Hz, H-10b), 2.86 (1H, ddd, J = 8.0, 3.2, 2.4 Hz, H-8), 3.12 (1H, dd, J = 10.8, 4.5 Hz, H-6b), 3.28 (1H, dddd, J = 8.0, 5.0, 4.5, 2.0 Hz, H-5), 3.72 (3H, s, $-CO_2CH_3$), 3.75 (1H, ddd, J = 9.0, 4.0, 2.0 Hz, H-5′), 4.16 (1H, dd, J = 11.5, 2.0 Hz, H-6′a), 4.29 (1H, dd, J = 11.5, 4.0 Hz, H-6′b), 4.90 (1H, d, J = 7.2 Hz, H-1′), 5.01 (1H, dd, J = 8.8, 7.2 Hz, H-2′), 5.11 (1H, d, J = 8.8, 8.2 Hz, H-4′), 5.23 (1H, dd, J = 9.0, 8.2 Hz, H-3′), 5.41 (1H, d, J = 4.0 Hz, H-1), 7.42 (1H, d, J = 2.0 Hz, H-3). FAB-MS m/z: 589 $(M+H)^+$. *Anal.* Calcd for $C_{25}H_{32}O_{16}$: C, 51.02; H, 5.48. Found: C, 50.97; H, 5.20.

15b (23.1 mg) was oxidized as described above to give acid **21b** (10.5 mg, 44%) as a white powder. $[\alpha]_D^{18}$ −54.01° (c = 0.500, $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 229 (3.59). IR ν_{max}^{KBr} cm^{-1}: 3450, 1750, 1740. ^{1}H-NMR ($CDCl_3$) δ: 1.86 (1H, ddd, J = 9.0, 6.0, 2.7 Hz, H-9), 1.91, 2.00, 2.03, 2.10 (12H, each s, $-OCOCH_3$), 2.45 (1H, dd, J = 16.5, 10.0, H-6a), 2.52 (1H, dd, J = 5.0, 2.9 Hz, H-10a), 2.75 (1H, ddd, J = 9.1, 4.0, 2.9 Hz, H-8), 2.81 (1H, dd, J = 5.0, 4.0 Hz, H-10b), 3.18 (1H, dd, J = 16.5, 4.9 Hz, H-6b), 3.71 (3H, s, $-CO_2CH_3$), 4.12 (1H, dd, J = 12.5, 2.9 Hz, H-6′a), 4.30 (1H, dd, J = 12.5, 4.5 Hz, H-6′b), 4.90 (1H, d, J = 8.1 Hz, H-1′), 5.00 (1H, dd, J = 9.5, 8.1 Hz, H-2′), 5.09 (1H, t, J = 10.0 Hz, H-4′), 5.22 (1H, t, J = 10.0 Hz, H-3′), 5.57 (1H, d, J = 2.7 Hz, H-1), 7.44 (1H, d, J = 2.0 Hz, H-3). FAB-MS m/z: 589 $(M+H)^+$. *Anal.* Calcd for $C_{25}H_{32}O_{16}$: C, 51.02; H, 5.48. Found: C, 51.22; H, 5.35.

Acids 10a and 10b Methanolic NaOMe (1 N, 0.03 ml) was added to a solution of **21a** (10.7 mg) in dry MeOH (0.5 ml) and the mixture was stirred for 30 min at room temperature. The reaction mixture was treated in the usual manner and the resulting crude product (9.2 mg) was purified by PTLC ($CHCl_3$: MeOH = 85 : 15, 2 developments) to give a white powder (7.3 mg, 96%) of acid **10a**. $[\alpha]_D^{18}$ −89.52° (c = 0.190, MeOH). UV λ_{max}^{MeOH} nm (log ε): 235 (3.95). IR ν_{max}^{KBr} cm^{-1}: 3400, 1710, 1690, 1630. ^{1}H-NMR (CD_3OD) δ: 1.78 (1H, ddd, J = 8.0, 5.0, 4.8 Hz, H-9), 2.58 (1H, dd, J = 15.0, 8.0 Hz, H-6a), 2.63 (1H, dd, J = 4.5, 2.0 Hz, H-10a),

2.79 (1H, dd, J=4.5, 3.5, H-10b), 2.92 (1H, ddd, J=8.0, 3.5, 2.0 Hz, H-8), 3.70 (3H, s, $-CO_2CH_3$), 4.65 (1H, d, J=7.5 Hz, H-1′), 5.65 (1H, d, J=4.8 Hz, H-1), 7.47 (1H, d, J=1.2 Hz, H-3). FAB-MS (glycerol) m/z: 421 $(M+H)^+$. *Anal.* Calcd for $C_{17}H_{24}O_{12}\cdot 1/2H_2O$: C, 47.55; H, 5.87. Found: C, 47.82; H, 5.66.

21b (9.5 mg) was deacetylated with methanolic NaOMe (1 N, 0.02 ml) and worked-up as described above to give a white powder (5.0 mg, 74%) of acid **10b**. $[\alpha]_D^{14}$ −48.92° (c=0.450, MeOH). UV λ_{max}^{MeOH} nm (log ε): 232 (3.50). IR ν_{max}^{KBr} cm^{-1}: 3400, 1720, 1710. ^{1}H-NMR (CD_3OD) δ: 1.73 (1H, ddd, J=9.0, 6.1, 4.0 Hz, H-9), 2.54 (1H, dd, J=16.0, 8.9 Hz, H-6a), 2.57 (1H, dd, J=4.6, 2.5 Hz, H-10a), 2.79 (1H, dd, J=4.6, 4.0, H-10b), 3.20 (1H, dd, J=16.0, 5.0 Hz, H-6b), 3.69 (3H, s, $-CO_2CH_3$), 4.68 (1H, d, J=8.0 Hz, H-1′), 5.66 (1H, d, J=4.0 Hz, H-1), 7.52 (1H, d, J=2.0 Hz, H-3). FAB-MS (glycerol) m/z: 421 $(M+H)^+$. *Anal.* Calcd for $C_{17}H_{24}O_{12}\cdot 1/2H_2O$: C, 47.55; H, 5.87. Found: C, 47.42; H, 5.95.

Ketone 20 Jones reagent (1 ml) was added dropwise to a solution of **13** (187.6 mg) in acetone (4 ml) under ice-cooling and the mixture was stirred for 20 h in the dark. The reaction mixture was worked-up in the usual way and the product (172.1 mg) was subjected to PTLC ($CHCl_3$: MeOH = 50 : 1). Of the two major bands, the band around Rf 0.45 gave ketone **20** (116.4 mg, 62%) as a white powder and the band around Rf 0.03 afforded the starting material (19.4 mg). UV λ_{max}^{EtOH} nm (log ε): 227 (4.37), 256 inf (3.83), 274sh (3.74). IR ν_{max}^{KBr} cm^{-1}: 1755, 1740 sh, 1640, 1530. ^{1}H-NMR ($CDCl_3$) δ: 2.00—2.10 (12H, each s, $-OCOCH_3$), 2.44 (3H, s, arom. CH_3), 3.12—3.34 (1H, m, H-5), 3.44—3.84 (5H, m, H-5′, $-CO_2CH_3$, $-C_6H_4CHCH\underline{H}-O-$), 4.08—4.86 (3H, m, H_2-6′, $-C_6H_4CH-C\underline{H}H-O-$), 4.92—5.72 (7H, m, H-1, -7, -1′, -2′, -3′, -4′, $-C_6H_4C\underline{H}-O-$), 7.30—8.16 (9H, m, H-3, arom. H). FAB-MS m/z: 909 $(M+H)^+$. *Anal.* Calcd for $C_{40}H_{45}NO_{21}S$: C, 52.92; H, 5.00; N, 1.54. Found: C, 52.89; H, 4.86; N, 1.63.

Reduction of Ketone 20 with $NaBH_4$ A solution of $NaBH_4$ (6.3 mg) in H_2O (1 ml) was added to a stirred solution of **20** (101.4 mg) in dioxane (2.5 ml) and stirring was continued for 30 min at room temperature. The reaction mixture was worked-up in the usual way and the crude product (92.5 mg) was subjected to PTLC ($CHCl_3$: MeOH = 50 : 1, 2 developments). Of the two major bands, the more polar one gave tosylate **13** (63.1 mg, 62%) and the less polar one the starting material (9.6 mg).

Reduction of Ketone 20 with NaB^2H_4 Followed by Photolysis A solution of NaB^2H_4 (20 mg) in H_2O (5 ml) was added dropwise to a solution of **20** (300 mg) in dioxane and the mixture was worked-up as described above to give tosylate [8-^{2}H]-**13** (118.8 mg, 40%). To a solution of [8-^{2}H]-**13** (135 mg) in dry benzene (10 ml) was added DBN (0.1 ml) and stirring was continued for 20 h at room temperature. The reaction mixture was washed successively with 1 N HCl, brine and H_2O, dried and concentrated *in vacuo*. The residue (110.2 mg) was subjected to PTLC (benzene : EtOAc = 5 : 1, 8 developments). Of the two major bands, the more polar one gave [8-^{2}H]-**14a** (47.5 mg, 43%) and the less polar one afforded [8-^{2}H]-**14b** (27.1 mg, 25%).

A solution of [8-^{2}H]-**14a** in benzene (6 ml) was irradiated with a high pressure mercury lamp for 1 h at room temperature at intervals of 10 cm with stirring. The reaction product was purified by PTLC (benzene : EtOAc = 7 : 3) to yield aldehyde [8-^{2}H]-**15a** (22.1 mg, 60%). Only the proton signals which were changed through the introduction of deuterium were shown. ^{1}H-NMR ($CDCl_3$) δ: 1.81 (1H, dd, J=6.0, 4.0 Hz, H-9), 2.56 (1H, d, J=5.0 Hz, H-10a), 2.78 (1H, d, J=5.0 Hz, H-10b). FAB-MS m/z: 574 $(M+H)^+$.

Likewise, a solution of [8-^{2}H]-**14b** in benzene (3 ml) was irradiated as described above to afford aldehyde [8-^{2}H]-**15b** (12.4 mg, 59%). ^{1}H-NMR ($CDCl_3$) δ: 1.81 (1H, dd, J=6.0, 2.6 Hz, H-9), 2.51 (1H, d, J=5.0 Hz, H-10a), 2.82 (1H, d, J=5.0 Hz, H-10b). FAB-MS m/z: 574 $(M+H)^+$.

References and Notes

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