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Carbohydrate Research 337 (2002) 1047–1053

CARBOHYDRATE RESEARCH

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Note

Preparation and diastereomeric separation of an (*S*)- and (*R*)-1-(methoxycarbonyl)tridec-10-yl glucoside derivative, a precursor for a monosaccharide constituent of resin glycosides

Shigeru Kobayashi, Jun-ichi Furukawa, Tomoko Sakai, Nobuo Sakairi*

Division of Bioscience, Graduate School of Environmental Earth Science, Hokkaido University, Sapporo 060-0810, Japan

Received 18 June 2001; received in revised form 13 March 2002; accepted 25 March 2002

Abstract

The 6-*O*-mesyl derivative of phenyl 1-thio-β-D-glucopyranoside was prepared from D-glucose as a synthetic equivalent of a 6-deoxy-hexosyl donor. Racemic methyl 11-hydroxytetradecanoate (methyl convolvulinolate) was synthesized by Grignard reaction of propylmagnesium bromide with 10-undecenal followed by hydroboration. Both intermediates were coupled by NIS–TfOH-promoted glycosidation to give a mixture of two diasteromeric glucopyranosides, which were separated on a preparative scale by medium pressure chromatography. One of the products was identified as having the natural (*S*)-configuration by comparison of its ^{1}H NMR spectrum with an authentic sample prepared from the corresponding chiral hydroxyfatty acid.

Keywords: Resin glycosides; Convolvulinolic acid; 6-Deoxyhexose; Diastereomeric separation

1. Introduction

Resin glycosides are plant glycolipids, isolated mainly from such Convolvulaceae plants as morning glory. Numerous resin glycosides have been isolated and their structures determined spectroscopically.[1] Some of them have bioactivities such as cytotoxic activity against human breast cancer cell lines,[2] antimicrobial activity,[3] and controlling effects on plant growth.[4,5]

Resin glycosides frequently contain such deoxygenated hexopyranoses as D-quinovose, D-fucose, and L-rhamnose, and have optically active fatty acids such as jalapinolic acid [(*S*)-11-hydroxyhexadecanoic acid] and convolvulinolic acid[6] [(*S*)-11-hydroxytetradecanoic acid] as the aglycon. The most notable structural feature of resin glycosides is that one of the sugar hydroxyl groups is intramolecularly acylated with the carboxyl group in the aglycon moiety to form a macrolide structure.

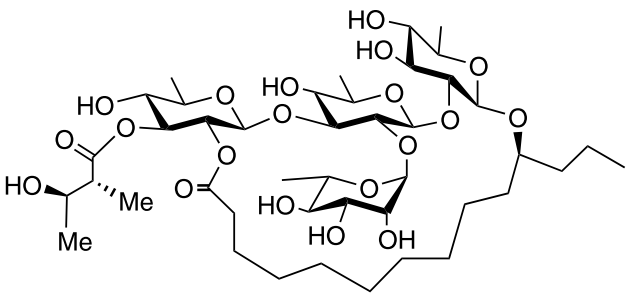
These features of bioactivity and structure have stimulated work on total synthesis of resin glycosides.[7,8] Our previous work on the total synthesis of calonyctin A2[8] (**1**) showed that a suitably protected (*S*)-1-(methoxycarbonyl)tridec-10-yl β-D-glucopyranoside (**2*S***) was one of the key intermediates. Although the aglycon moiety of **2*S*** has been prepared stereoselectivly from L-glutamic acid, the process requires 16 steps.[8] Schmidt and his co-workers used racemic jalapinonic acid in their total synthesis of a tetasaccharidic resin glycoside and they separated diasteromers at the final stage of the synthesis.[7a] Since a 2-*O*-glycosylated β-D-quinovose component appears at the reducing end of most resin glycosides, a concise preparation of **2*S*** would be useful for synthesizing various resin glycosides. We describe here the preparation of racemic methyl convolvulinolate and the separation of the desired (*S*)-isomer after coupling with a monosaccharide.

2. Results and discussion

Synthesis of two glycosyl donors **6** and **7** as precursors of a 6-deoxyhexoside unit is summarized in Scheme

* Corresponding author. Tel./fax: +81-11-706-2257.
E-mail address: nsaka@ees.hokudai.ac.jp (N. Sakairi).

0008-6215/02/$ - see front matter
PII: S0008-6215(02)00092-7



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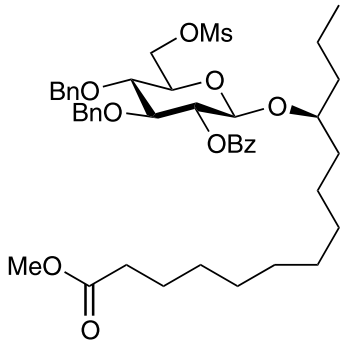
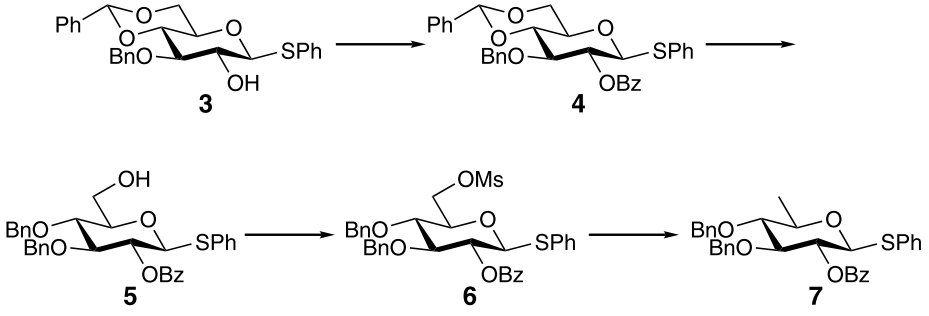


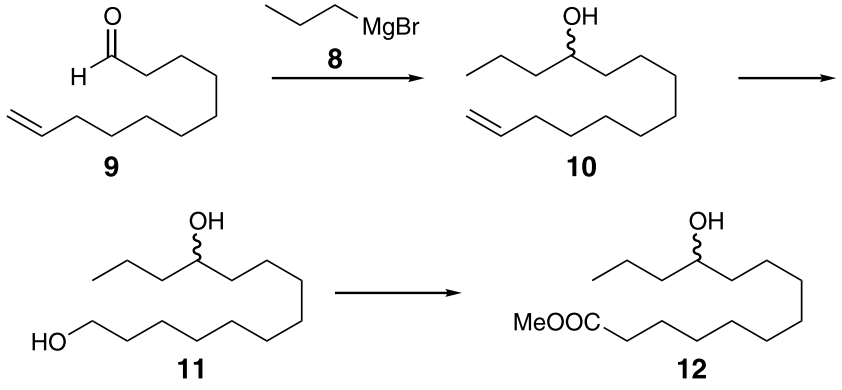
2S

1. The known phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[9] (**3**) was benzoylated to give the 2-benzoate **4**, from which the benzylidene acetal was removed by reductive cleavage. After considering many reagent systems for the reduction,[10] we succeeded in preparing the desired 6-hydroxyl derivative **5** by using borane·dimethylamine complex–boron trifluoride etherate as reported by Kusumoto.[11] This reagent system in dichloromethane at −20 °C allowed regioselective reduction of the *O*-benzylidene group without affecting other protecting groups. The yield of the 4-*O*-benzyl derivative **5** was 77%, and the free hydroxyl group was mesylated in pyridine to give the glycosyl donor **6** in 89% yield. Because the mesylate **6** was unstable, freshly prepared material whose purity was confirmed by both ^{1}H and ^{13}C NMR spectroscopy was used for the next reaction. The mesyloxy group in **6** was reduced with sodium borohydride in DMF at 70 °C to give the stable deoxy derivative **7** in 62% yield. Both the mesylate **6** and the 6-deoxy derivative **7** were used as glycosyl donors for the next glycosidation.

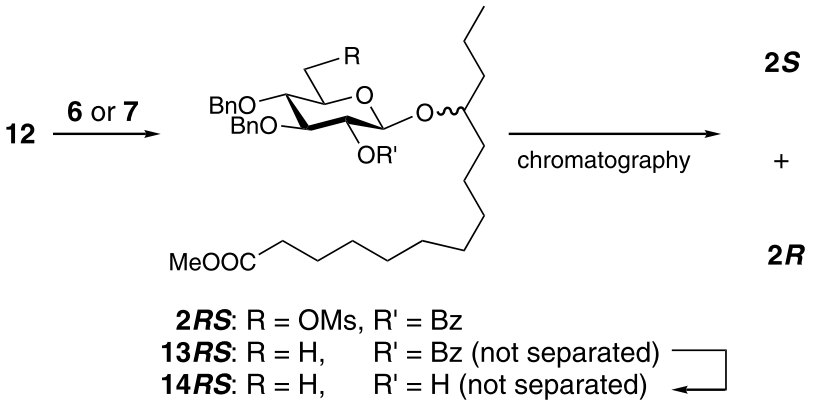
Synthesis of the racemic aglycon moiety, methyl 11-hydroxydecanoate (**12**), was initiated by a Grignard reaction of propylmagnesium bromide **8** with 10-undecenal **9**. In order to introduce a primary hydroxyl group, the resulting tetradecen-4-ol **10** was subjected to hydroboration with borane·tetrahydrofuran complex with a subsequent oxidative workup (Scheme 2). Selective oxidation of the primary hydroxyl group of the resulting tetradecan-1,11-diol **11** was next achieved by a two-phase reaction in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl, free radical (TEMPO) as the



Scheme 1.



Scheme 2.



Scheme 3.

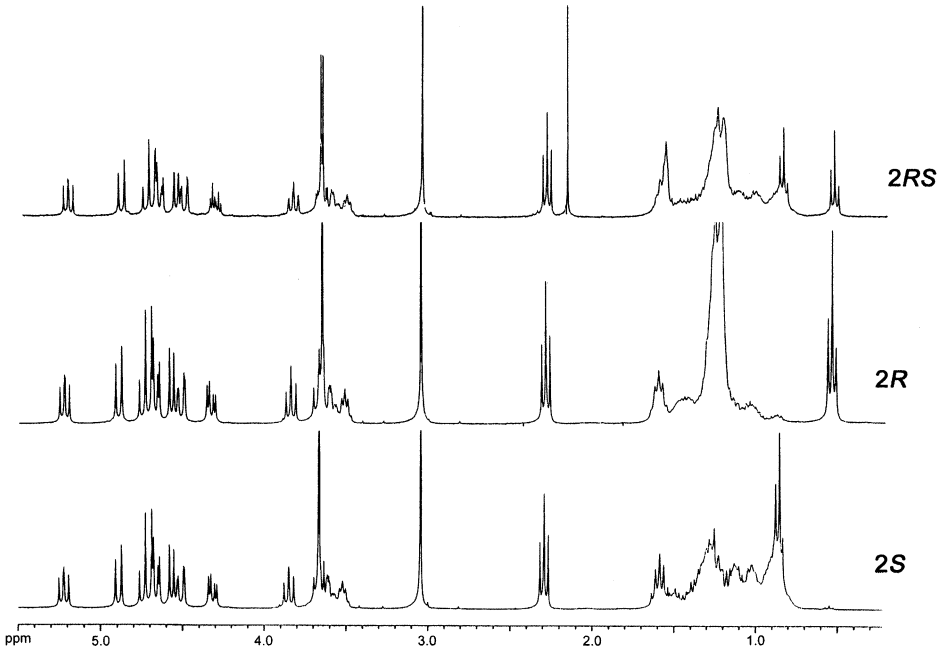


Fig. 1. ^{1}H NMR spectra of compounds **2*R***, **2*S***, and **2*RS***.

catalyst.[12] Thus, **11** was treated with TEMPO and *N*-chlorosuccinimide (NCS) in CH_2Cl_2–phosphate buffer containing tetrabutylammonium chloride as the phase-transfer catalyst to give an aldehyde intermediate, which was further oxidized by sodium chlorite to the carboxylic acid. After treatment with diazomethane in diethyl ether, the racemic methyl ester **12** was isolated in 76% overall yield.

Having prepared both glycosyl donors **6** and **7**, the racemic acceptor **12**, glycosidation and subsequent separation of the resulting diastereomers were examined next. At first, the deoxy donor **7** and methyl tetradecanoate **12** were reacted in the presence of methyl trifluoromethanesulfonate (4.5 equiv) as a promoter, giving the 6-deoxygenated *O*-glycoside **13*RS*** in 89% yield as a mixture of diastereomers. Zemplén deacylation of **13*RS*** gave the 2-unprotected derivatives **14*RS*** (Scheme 3). Unexpectedly, neither spectroscopic nor chromatographic differences were observed between both pairs of diastereomers, **13*RS*** and **14*RS***. Next, we examined the glycosidation using the more labile 6-*O*-mesyl thioglycoside **6**. On treatment of **12** and freshly prepared **6** in CH_2Cl_2 with *N*-iodosuccinimide (NIS)–TfOH,[13] the reaction proceeded smoothly to give the β-glycoside **2*RS*** as a mixture of diastereomers in 83% yield. The stable *O*-glycosides thus obtained were found to be separable by medium pressure chromatography on a column of silica gel, using hexane–acetone as the eluant. The isolated yields of the faster- and slower-moving products were 29 and 32%, respectively, together with 20% of the recovered mixture. In order to determine their absolute configuration, we also synthesized the corresponding enantiomerically pure *S*-isomer **2*S*** by similar glycosylation of

methyl (*S*)-11-hydroxytetradecanoate.[8] As shown in the ^{1}H NMR spectrum of the products **2*R*** and **2*S*** (Fig. 1), all peaks due to protons of the glucose residue and H-11, the chiral center, are found to be superposable. However, protons of the terminal *C*-methyl groups of the aglycon moieties of the faster- and slower-moving products were observed at δ 0.551 and 0.860 as triplets, respectively. Comparing the spectra to that of an authentic sample, we concluded that the latter, namely, the slower-moving product, was the natural **2*S*** type. This upfield shift of the methyl group of the faster-moving product **2*R*** is probably due to the shielding effect of the benzene ring of the 2-*O*-benzoyl group.

In summary, we have developed a synthesis of the β-D-glycoside **2*S*** with the *S* configuration by preparation of racemic methyl convolvulinolate, glycosidation of the 6-*O*-mesyl donor, and separation of the diastereomers. Compound **2*S*** may be regarded as a key and common intermediate for synthesis of various resin glycosides.

3. Experimental

General procedures.—Melting points were determined in a capillary with a Yamato melting-point apparatus (model MP-21) and are uncorrected. Optical rotations were determined with a Horiba Sepa-300 polarimeter. ^{1}H NMR (300.13 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded with a Bruker ASX-300 spectrometer for solutions in $CDCl_3$. Chemical shifts (δ) are given in ppm relative to internal Me_4Si. TLC and HPTLC were performed using precoated glass plates of Silica Gel 60 F_{254} (E. Merck, Darmstadt, Germany) with layer thicknesses of 0.25 and 0.2 mm, respectively. The spots were visualized under a UV lamp at 254 nm and by spraying 5% aq H_2SO_4 followed by heating on a hot plate for a few minutes. Column chromatography and medium-pressure column chromatography were performed on Silica Gel 60 (230–400 mesh) and on LiChroprep Si-60 (E. Merck, Darmstadt, Germany), respectively. Molecular sieves 4 Å were activated at 160–180 °C under diminished pressure prior to use.

*Phenyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-*D*-glucopyranoside* (**4**).—To a solution of phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D- glucopyranoside[9] (**3**, 9.20 g, 20.43 mmol) in pyridine (100 mL), benzoyl chloride (7.1 mL, 61.0 mmol) was added dropwise. The mixture was stirred at rt for 12 h, quenched with ice–water, and extracted with $CHCl_3$. The extract was successively washed with 2 M HCl, aq satd $NaHCO_3$, and brine, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a column of silica gel using 30:1 toluene–EtOAc to give the 2-benzoate **4** (10.84 g, 94%) as a white solid; mp 178.0–179.6 °C ($CHCl_3$–hexane); $[\alpha]_D$ +37.5° (*c* 1.16, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.03–7.08 (m, 20 H, 4 C_6H_5), 5.60 (s, 1 H, Ph*CH*), 5.29 (dd, 1 H, $J_{1,2}$ 10.05, $J_{2,3}$ 8.31 Hz, H-2), 4.85 (d, 1 H, H-1), 4.81 (d, 1 H, *J* 11.9 Hz, 1/2 PhCH_2), 4.66 (d, 1 H, 1/2 PhCH_2), 4.42 (dd, 1 H, *J* 5.10 Hz, H-6), 3.89 (t, 1 H, $J_{2,3}$ 8.31 Hz, H-3), 3.88–3.77 (m, 2 H, H-4,6), 3.61–3.53 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$) δ 165.60 [*C*(O)Ph], 101.85 (Ph*C*HO_2), 87.56 (C-1), 81.99 (C-2), 74.82 (Ph*C*H_2), 71.16 (C-5), 69.16 (C-6); Anal. Calcd for $C_{33}H_{30}O_6S$: C, 71.46; H, 5.45; S, 5.78. Found: C, 71.46; H, 5.53; S, 5.71.

*Phenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-*D*-glucopyranoside* (**5**).—To a solution of **4** (3.013 g, 5.43 mmol) and borane·dimethylamine complex (2.9 g, 27 mmol) in dry CH_2Cl_2 (200 mL) was added dropwise boron trifluoride etherate (3.4 mL, 27.1 mmol) with stirring at 0 °C under nitrogen. The mixture was stirred at the same temperature for 30 min, poured slowly into ice-cold aq $NaHCO_3$ with vigorous stirring, and extracted with $CHCl_3$. The extract was successively washed with 2 M HCl, aq satd $NaHCO_3$, and brine, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a column of silica gel using 5:1 hexane–EtOAc to give the 3,4-di-*O*-benzyl derivative **5** (2.324 g, 76.9%) as a white solid; mp 108.6–110.2 °C (EtOH); $[\alpha]_D$ +43.1° (*c* 0.64, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.05–7.09 (m, 20 H, 4 C_6H_5), 5.27 (dd, 1 H, $J_{1,2}$ 9.72, $J_{2,3}$ 9.36 Hz, H-2), 4.85 (d, 1 H, *J* 10.98 Hz, 1/2 PhCH_2), 4.83 (d, 1 H, H-1), 4.74 (d, 1 H, 1/2 PhCH_2), 4.65 (d, 2 H, 1/2 PhCH_2), 3.95–3.89 (m, 1 H, H-6), 3.86 (t, 1 H, *J* 9.00 Hz, H-3), 3.77–3.70 (m, 1 H, H-6), 3.69 (t, 1 H, *J* 9.00 Hz, H-4), 3.53–3.48 (m, 1 H, H-5), 1.97 (t, 1 H, *J* 6.90 Hz, 6-OH); ^{13}C NMR ($CDCl_3$) δ 165.17 [*C*(O)Ph], 83.99 (C-2), 75.31 (Ph*C*H_2), 75.15(Ph*C*H_2), 72.46 (C-5), 62.01 (C-6); Anal. Calcd for $C_{33}H_{32}O_6S$: C, 71.20; H, 5.79; S, 5.76. Found: C, 71.23; H, 5.87; S, 5.71.

*Phenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-mesyl-1-thio-β-*D*-glucopyranoside* (**6**).—To a solution of **5** (2.07 g, 3.72 mmol) in pyridine (30 mL) mesyl chloride (0.87 mL, 11 mmol) was added dropwise with stirring at 0 °C. The mixture was stirred at 0 °C for 2 h, quenched with crushed ice, and extracted with $CHCl_3$. The extract was successively washed with 2 M HCl, aq satd $NaHCO_3$, and brine, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a column of silica gel using 15:1 toluene–EtOAc to give the unstable 6-mesylate **6** (2.10 g, 88.9%); ^{1}H NMR ($CDCl_3$) δ 8.05–7.12 (m, 20 H, 4 C_6H_5), 5.27 (t, 1 H, $J_{1,2} = J_{2,3}$ 9.56 Hz, H-2), 4.87 (d, 1 H, *J* 10.89 Hz, 1/2 PhCH_2), 4.83 (d, 1 H, H-1), 4.74 (d, 1 H, 1/2 PhCH_2), 4.66 (d, 1 H, 1/2 PhCH_2), 4.64 (d, 1 H, 1/2 PhCH_2), 4.50 (dd, 1 H, $J_{5,6}$ 1.46, $J_{6,6}$ 11.44 Hz, H-6), 4.32 (dd, 1 H, H-6), 3.88 (t, 1 H, $J_{2,3} = J_{3,4}$ 8.71 Hz, H-3), 3.70–3.63 (m, 1 H, H-5), 3.63 (t, 1 H, $J_{4,5}$ 8.69 Hz, H-4), 3.00 (s, 3 H, OSO_2CH_3); ^{13}C NMR ($CDCl_3$) δ 165.12 [*C*(O)Ph],

86.29 (C-1), 84.01 (C-2), 75.45 (Ph*C*H_2), 75.24 (Ph*C*H_2), 72.21 (C-5), 68.29 (C-6), 37.84 ($OSO_2C$$H_3$). Because this compound was unstable, satisfactory elemental analysis data were not obtained, and freshly prepared material was used for the next step.

Phenyl 2-O-benzoyl-3,4-di-O-benzyl-6-deoxy-1-thio-β-D-glucopyranoside (**7**).—To a solution of **6** (408 mg, 0.64 mmol) in DMF (20 mL) was added $NaBH_4$ (242 mg, 6.4 mmol). The mixture was heated at 70 °C and stirred at for 6 h, quenched with crushed ice, and extracted with $CHCl_3$. The extract was successively washed with aq 10% NH_4Cl, aq satd $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a column of silica gel using 15:1 toluene–EtOAc to give the 6-deoxy derivative **7** (216 mg, 62.1%) as an amorphous solid; $[\alpha]_D$ +53.1° (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.05–7.11 (m, 20 H, 4 C_6H_5), 5.26 (t, 1 H, $J_{1,2} = J_{2,3}$ 9.5 Hz, H-2), 4.86, 4.66 (d, 1 H, *J* 11.2 Hz, Ph*C*H_2), 4.76 (d, 1 H, H-1), 4.72, 4.61 (d, 1 H, Ph*C*H_2), 3.80 (t, 1 H, $J_{3,4}$ 9.1 Hz, H-3), 3.56–3.50 (m, 1 H, H-5), 3.34 (t, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 1.39 (d, $J_{5,6}$ 6.0 Hz, 3 H, H-6); ^{13}C NMR ($CDCl_3$) δ 165.7 [*C*(O)Ph], 86.6 (C-1), 84.6 (C-2), 76.4 (Ph*C*H_2), 75.9 (Ph*C*H_2), 73.2 (C-5), 18.6 (C-6); HRMS (FAB) *m*/*z* for $C_{33}H_{33}O_5S$ $[M+H]^+$, Calcd: 541.2049; Found: 541.2026.

1-Tetradecen-11-ol (**10**).—A solution of 1-brompropane (22.9 g, 0.186 mol) in dry Et_2O (50 mL) was added dropwise to a stirred mixture of dry Et_2O (50 mL) and magnesium ribbon (4.14 g, 0.169 mol) under nitrogen. After cooling at −20 °C, a solution of 10-undecenal **9** (20.3 g, 0.124 mol) in Et_2O was added dropwise to the resulting mixture and stirred for 1 h. The mixture was quenched with 2 M HCl and extracted with Et_2O. The extract was successively washed with satd $NaHCO_3$ and brine, dried (Na_2SO_4), and evaporated. Column chromatography of the residue on silica gel using 15:1 toluene–EtOAc gave the alcohol **10** (17.0 g, 64.6%); ^{1}H NMR ($CDCl_3$) δ 5.81 (m, 1 H, =CH), 4.95 (m, 2 H, =CH_2), 3.61 (m, 1 H, CH-11), 2.04 (q, 2 H, *J* 7.00 Hz, CH_2-3), 1.68–1.20 (m, 18 H,), 0.929 (t, 3 H, *J* 6.90 Hz, CH_3-14); ^{13}C NMR ($CDCl_3$) δ 139.82 (*C*H=CH_2), 114.69 (*C*H_2=CH), 72.31 (C-11), 14.71 (C-14); MS (FD): $C_{14}H_{28}O$ (M) for 212.21; Found: *m*/*z* 211 $[M-H]^+$.

1,11-Tetradecanediol (**11**).—To a solution of alcohol **10** (10.2 g, 0.0480 mol) in dry tetrahydrofuran (150 mL) was added a 1 M solution of borane in tetrahydrofuran (44 mL, 0.044 mol) at 0 °C under nitrogen. The solution was stirred at 0 °C for 2 h, and quenched by careful addition of aq tetrahydrofuran. Aqueous NaOH (2 M, 16 mL) and 30% aq H_2O_2 (10.5 mL) was successively added to the mixture. The mixture was stirred at 45 °C for 30 min and, extracted twice with Et_2O. The combined extracts were washed with brine, dried (Na_2SO_4), and evaporated. Column chromatography of the residue on silica gel using (5:1→3:1) toluene–EtOAc gave 1,11-tetradecanediol **11** (8.7 g, 78%); ^{1}H NMR ($CDCl_3$) δ 3.64 (t, 2 H, $J_{3,4}$ 6.60 Hz, CH_2-1), 3.61 (m, 1 H, CH-11), 1.64–1.28 (m, 22 H), 0.929 (t, 3 H, *J* 6.75 Hz, CH_3-14); ^{13}C NMR ($CDCl_3$) δ 72.34 (C-11), 63.69 (C-1), 14.72 (C-14). MS (FD): $C_{14}H_{30}O_2$ (M) for 230.22; Found: *m*/*e* 229 $[M-H]^+$, 213 $[M-OH]^+$, 194 $[M-H_2O]^+$; HRMS (FAB) *m*/*z* for $C_{14}H_{29}O$ $[M-OH]^+$, Calcd: 213.2218; Found: 213.2206.

Methyl 11-hydroxytetradecanoate (**12**).—A solution of the diol **11** (4.34 g, 18.8 mmol) in CH_2Cl_2 (40 mL) and 0.5 M carbonate buffer (pH 8.6, 40 mL) was vigorously stirred at rt. To the mixture was added tetra-*n*-butylammonium chloride (522 mg, 18.8 mmol), 2,2,6,6,-tetramethylpiperidin-1-yloxy radical (TEMPO, 294 mg, 18.8 mmol), and *N*-chlorosuccinimide (3.77 g, 28.2 mmol). The mixture was stirred for 1.5 h, and partitioned between CH_2Cl_2 and water. The organic layer was washed with brine twice, and evaporated below 30 °C under diminished pressure. To a solution of the residue in *t*-butyl alcohol (80 mL) was added 2-methyl-2-butene (30 mL), water (80 mL), and $Na_2HPO_4 \cdot 12\ H_2O$ (3.5 g, 9.8 mmol). To the resulting mixture, stirred vigorously at rt, was added $NaClO_2$ (80%, 3.5 g, 31 mmol), and the mixture was stirred for 1 h, extracted with $CHCl_3$. The extract was washed with 1 M HCl three times and with water twice, and evaporated. The residue was dissolved in Et_2O (50 mL), and an ethered solution of CH_2N_2, generated from methyl nitrosomethylguanidine, was added to the solution. The solution was allowed to stand for 2 h, quenched with AcOH, washed successively with aq $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a column of silica gel with 20:1 toluene–EtOAc to give methyl 11-hydroxytetradecanoate (**12**, 3.7 g, 76%) as a white solid; mp 41.4–42.0 °C (EtOAc–hexane); ^{1}H NMR ($CDCl_3$), δ 3.67 (s, 3 H, $CO_2C$$H_3$), 3.60 (m, 1 H, CH-11), 2.30 (t, 2 H, *J* 7.54 Hz, CH_2-2), 1.28–1.64 (m, 20 H), 0.93 (t, 3 H, *J* 6.84 Hz, CH_3-14); ^{13}C NMR ($CDCl_3$) δ 174.25 [*C*(O)OCH_3], 71.52 (C-11), 17.42 [C(O)O*C*H_3], 14.02 (C-14); Anal. Calcd for $C_{15}H_{30}O_3$: C, 69.72; H, 11.70. Found: C, 69.60; H, 11.61.

1-(Methoxycarbonyl)tridec-10-yl 2-O-benzoyl-3,4-di-O-benzyl-6-deoxy-β-D-glucopyranoside (**13*RS***).—A suspension of methyl 11-hydroxytetradecanoate **12** (126 mg, 0.49 mmol), phenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-deoxy-1-thio-β-D-glucopyranoside (**7**, 222 mg, 0.41 mmol), and molecular sieves 4 Å (100 mg) in CH_2Cl_2 (5.2 mL) was stirred under nitrogen for 30 min at rt. Methyl triflate (207 μL, 1.8 mmol) was added to the mixture. After 24 h, the suspension was neutralized with pyridine and filtered through a Celite pad. The filtrate was diluted with $CHCl_3$, washed successively with aq $Na_2S_2O_3$, aq $NaHCO_3$, and brine, dried (Na_2SO_4), and evaporated. The residue was subjected

to chromatography on a column of silica gel with 5:1 hexane–EtOAc, giving the β-glycoside **13*RS*** (251 mg, 89%) as an amorphous solid; ^{1}H NMR ($CDCl_3$), δ 8.02–7.12 (m, 15 H, 3 C_6H_5), 5.23 (dd, 1 H $J_{1,2}$ 8.02, $J_{2,3}$ 8.69 Hz, H-2), 4.87 (d, 1 H, J 10.88 Hz, 1/2 PhCH_2), 4.73 (d, 1 H, 1/2 PhCH_2), 4.64 (d, 1 H, 1/2 PhCH_2), 4.61 (d, 1 H, 1/2 PhCH_2), 4.49 (d, 1 H, H-1), 3.76 (t, 1 H, $J_{2,3} = J_{3,4}$ 8.73 Hz, H-3), 3.67, 3.66 (s × 2, 3 H, COOCH_3), 3.47 (m, 1 H, H-5), 3.34 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.27 Hz, H-4), 2.29 (t, 2 H, J 7.52 Hz, OCOCH_2), 1.63–0.85 (m, 23 H, 10 CH_2, H-6), 0.88, 0.57 (t × 2, 3 H, J 7.12 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 174.83 [C(O)OCH$_3$], 165.56 [C(O)Ph], 101.14 (C-1), 75.71 (CH$_2$Ph), 75.36 (CH$_2$Ph); HRMS (FAB) m/z for $C_{42}H_{56}O_8Na$ $[M + Na]^+$, Calcd: 711.3872; Found: 711.3881.

*(*S*)-1-(Methoxycarbonyl)tridec-10-yl 3,4-di-*O*-benzyl-6-deoxy-β-*D*-glucopyranoside* (**14**).—To a solution of monosaccharide derivative **13** (786 mg, 1.1 mmol) in MeOH (20 mL) was added 3 M NaOMe (0.5 mL). The solution was heated at 40 °C, stirred for 2 days, and neutralized by Amberlite IR-120B (H^+ form). The resin was filtered and washed with MeOH and the filtrate and the washings were combined and concentrated. Column chromatography of the residual syrup with 25:1 toluene–EtOAc as eluant gave the 2-OH derivative **14*RS*** (516 mg, 77%) as an amorphous solid; ^{1}H NMR ($CDCl_3$) δ 7.40–7.16 (m, 10 H, 2 C_6H_5), 4.95 (d, 1 H, J 11.3 Hz, 1/2CH_2Ph), 4.88 (d, 1 H, 1/2CH_2Ph), 4.82 (d, 1 H, 1/2 CH_2Ph), 4.63 (d, 1 H, 1/2 CH_2Ph), 4.25 (d, 1 H, J 7.2 Hz, H-1), 3.66 (s, 3 H, CO_2Me), 3.63–3.47 (m, 3 H, CHO, H-2, H-3), 3.43–3.39 (m, 1 H, H-5), 3.20 (t, 1 H, J 8.8 Hz, H-4), 2.30 (t, 2 H, J 7.3 Hz, CH_2CO_2), 1.63–1.27 (m, 23 H, 10 CH_2, H-6), 0.90 (t, 3 H, J 7.1 Hz, CH_3); Anal. Calcd for $C_{35}H_{52}O_7$: C, 71.89; H, 8.96. Found: C, 71.67; H, 8.79.

*(*S*)-1-(Methoxycarbonyl)tridec-10-yl* (**2*S***) *and (*R*)-1-(methoxycarbonyl)tridec-10-yl 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-mesyl-β-*D*-glucopyranoside* (**2*R***).—A suspension of methyl 11-hydroxytetradecanoate (**12**, 70 mg, 0.27 mmol), phenyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-6-*O*-mesyl-1-thio-β-D-glucopyranoside (**6**, 201 mg, 0.317 mmol), *N*-iodosuccinimide (106 mg, 0.471 mmol), and molecular sieves 4 Å (100 mg) in CH_2Cl_2 (3 mL) was stirred under nitrogen for 30 min and cooled to −20 °C. Trifluoromethanesulfonic acid (3 μL) was added to the mixture. After 20 min, the wine-red colored suspension was made neutral with pyridine and filtered through a Celite pad. The filtrate was diluted with $CHCl_3$, washed successively with aq $Na_2S_2O_3$, aq $NaHCO_3$, and brine, dried (Na_2SO_4), and evaporated. The residue was subjected to chromatography on a column of silica gel with 5:1 hexane–EtOAc, giving a 1:1 diastereomeric mixture of the β-glycoside **2*RS*** (204 mg, 83%), estimated by ^{1}H NMR analysis. The mixture was subjected to medium-pressure column chromatography using (10:1 → 6:1) hexane–acetone to give the syrupy (*R*)-isomer **2*R*** (73 mg, 29%) as the first fraction; $[\alpha]_D$ +17.4° (*c* 0.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.02–7.14 (m, 15 H, 3 C_6H_5), 5.23 (t, 1 H, J 8.10, J 9.24 Hz, H-2), 4.90 (d, 1 H, J 10.86 Hz, 1/2 PhCH$_2$), 4.75 (d, 1 H, 1/2 PhCH$_2$), 4.68 (d, 1 H, 1/2 PhCH$_2$), 4.67 (d, 1 H, 1/2 PhCH$_2$), 4.57 (d, 1 H, $J_{1,2}$ 8.04 Hz, H-1), 4.51 (dd, 1 H, $J_{5,6a}$ 1.52, $J_{6a,6b}$ 11.33 Hz, H-6a), 4.33 (dd, 1 H, $J_{5,6b}$ 4.32 Hz, H-6b), 3.85 (t, 1 H, $J_{2,3} = J_{3,4}$ 8.99 Hz, H-3), 3.71–3.56 (m, 1 H, H-5), 3.67 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.75 Hz, H-4), 3.65 (s, 3 H, COOCH_3), 3.52 (m, 1 H, OCH), 3.05 (s, 3 H, OSO_2CH_3), 2.29 (t, 2 H, J 7.52 Hz, OCOCH_2), 1.63–0.85 (m, 20 H, 10 × CH_2), 0.551 (t, 3 H, J 7.12 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 174.83 [C(O)OCH$_3$], 165.56 [C(O)Ph], 101.38 (C-1), 83.13 (C-2), 75.69 (CH$_2$Ph), 75.64 (CH$_2$Ph), 73.52 (C-5), 69.01 (C-6), 18.36 [C(O)OCH$_3$], 14.41 (C-14); Anal. Calcd for $C_{43}H_{58}O_{11}S$: C, 65.96; H, 7.47; S, 4.10. Found: C, 65.83; H, 7.40; S, 4.18.

Further elution of the column with 6:1 hexane–acetone gave a mixture of **2*R*** and **2*S*** (53 mg, 20%) and the pure (*S*)-isomer **2*S*** (78 mg, 32%) as a syrup; $[\alpha]_D$ +26.6° (*c* 0.344 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.02–7.14 (m, 15 H, 3 C_6H_5), 5.22 (t, $J_{1,2}$ 8.15, $J_{2,3}$ 9.44 Hz, 1 H, H-2), 4.89 (d, 1 H, J 10.86 Hz, 1/2 PhCH_2), 4.74 (d, 1 H, 1/2 PhCH_2), 4.67 (d, 1 H, 1/2 PhCH_2), 4.66 (d, 1 H, 1/2 PhCH_2), 4.56 (d, 1 H, H-1), 4.51 (dd, 1 H, $J_{5,6a}$ 1.79, $J_{6a,6b}$ 11.36 Hz, H-6), 4.31 (dd, 1 H, $J_{5,6b}$ 4.40 Hz, H-6), 3.85 (t, 1 H, $J_{2,3} = J_{3,4}$ 9.45 Hz, H-3), 3.67 (s, 3 H, COOCH_3), 3.69–3.56 (m, 2 H, H-4, H-5), 3.52 (m, 1 H, OCH), 3.05 (s, 3 H, OSO_2CH_3), 2.29 (t, 2 H, J 7.53 Hz, OCOCH_2), 1.61–0.84 (m, 20 H, 10 × CH_2), 0.860 (t, 3 H, J 7.10 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 174.81 [C(O)OCH$_3$], 165.49 [C(O)Ph], 101.43 (C-1), 83.15 (C-2), 75.67 (CH$_2$Ph), 73.48 (C-5), 69.04 (C-6), 18.99 [C(O)OCH$_3$], 14.63 (C-14); Anal. Calcd for $C_{43}H_{58}O_{11}S$: C, 65.96; H, 7.47; S, 4.10. Found: C, 65.83; H, 7.40; S, 4.18.

The (*S*)-isomer **2*S*** was also synthesized by coupling optically active methyl (*S*)-11-hydroxytetradecanoate[8] (11 mg, 0.042 mmol) with thioglycoside **6** (43 mg, 0.067 mmol) using NIS (18 mg, 0.081 mmol) and TfOH (3 μL) under the same conditions, in 46% yield, and its ^{1}H and ^{13}C NMR spectra were identical with those already described.

Acknowledgements

This work was supported by Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science, Sports, and Culture of Japan (No. 0924010) and by Research Fellowship to J.F. of the Japan Society for the Promotion of Science (JSPS). We would like to thank Ms A. Maeda and Ms S. Oka (Center for Instrumental Analysis, Hokkaido Univer-

sity) for elemental analysis and recording mass spectra measurement, respectively.

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