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A simple synthesis of four stereoisomers of roseoside and their inhibitory activity on leukotriene release from mice bone marrow-derived cultured mast cells

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ABSTRACT

Four stereoisomers of roseoside (vomifoliol glucosides) were synthesized using glucose as a chiral resolving reagent. The four synthetic stereoisomers exhibited inhibitory activity on leukotriene release from mouse bone marrow-derived cultured mast cells (BMCMC). The (6*S*)-isomers of roseoside were about twice as active as (6*R*)-isomers.

1. Introduction

The tropical plant *Corchorus olitorius* L. (Tiliaceae), known as 'moroheiya' in Japanese, is used as a vegetable and is rich in vitamins and carotenoids. During a course of studies on the bioactive principles of medicinal foodstuffs, Yoshikawa and co-workers isolated corchoionosides A (**1**), B (**2**) and C [=(6*S*,9*S*)-roseoside (**3**)], and (6*S*,9*R*)-roseoside (**4**) from the leaves of Vietnamese *C. olitorius* L. (Fig. 1).[1] Corchoionosides A (**1**) and B (**2**), and (6*S*,9*R*)-roseoside (**4**) were found to exhibit inhibitory activity on the release of histamine from rat peritoneal exudate cells induced by an antigen–antibody reaction. However, the anti-histamine-release activites of corchoionoside C (**3**) and the (6*R*)-isomers of roseoside are unknown. Roseosides may be biosynthesized by oxidative cleavage of carotenoids, and 6*S*-isomer is the most commonly found among natural sources.[2] The only exception is (6*R*,9*R*)-roseoside (**5**), isolated from *Alangium premnifolium* by Otsuka.[2h] Although roseosides have been isolated from a wide variety of natural sources,[1,2] their biological functions and activities are unclear. In order to examine the anti-allergy activity of roseoside stereoisomers **3**, **4**, **5** and **6**, we investigated the synthesis of these four stereoisomers.

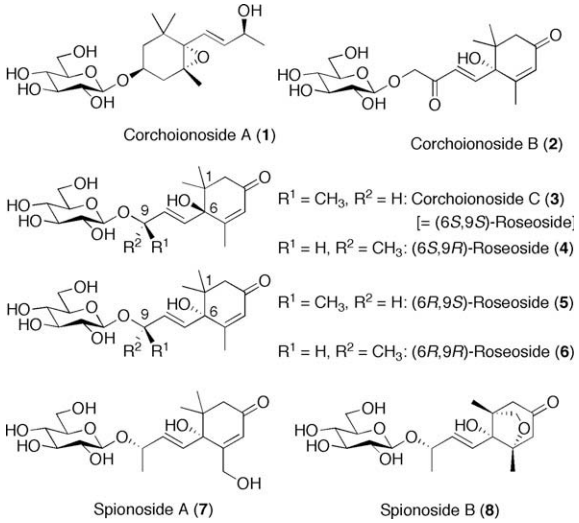

Figure 1. Structures of corchoionosides, roseosides and spionosides.

2. Results and discussion

Recently, Yamano and Ito reported the synthesis of four roseoside stereoisomers.[3] Their synthesis began with a chiral cyclohexanone derivative, and involved 19 steps via asymmetric transfer hydrogenation to construct the C-9 asymmetric center. We chose

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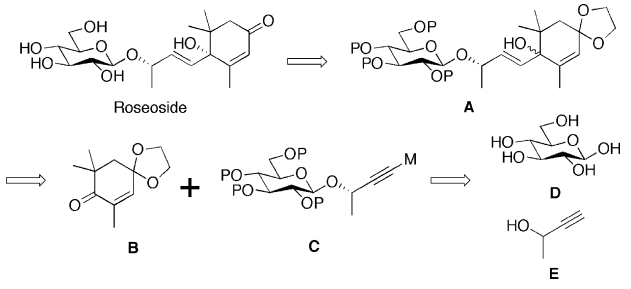
a different route for roseoside synthesis, which is summarized in Scheme 1. As the synthesis of the four stereoisomers was urgently required to allow investigation of the stereochemistry–biological activity relationship, we planned to separate each stereoisomer from a diastereomeric mixture. To construct the C-6 stereogenic center, the 1,2-addition of organo-metal reagent **C** to cyclohexenone **B** leads to a diastereomeric mixture of **A**, and the resulting diastereomers can be separated. Our plan was to resolve racemic 3-butyn-2-ol (**E**) by employing inexpensive D-glucose (**D**) as a chiral resolving agent and to separate the diastereomeric glucoside. Thus, commercially available 4-ketoisopholone, 3-butyn-2-ol and D-glucose were selected as the starting materials. This strategy was also expected to provide a method for the synthesis of spionosides A (**7**) and B (**8**) (Fig. 1), related natural products isolated from *Capparis spinosa* fruits.[2l]

Scheme 2 summarizes the synthesis of the key intermediate **14**. Glucosidation of (±)-**9**, catalyzed by silver trifluoromethanesulfonate (AgOTf), proceeded smoothly in the presence of silver carbonate[4] at −20 °C. Although the resulting β-glucoside **11**[5] was a diastereomeric mixture at C-2′ (1:1), the corresponding α-glucoside was not observed in ^{1}H NMR analysis. The acetyl groups of **11** were removed by treatment with KCN in MeOH[6] to give **12**. Protection of the 4- and 6-hydroxy groups as an isopropylidene acetal (**13**) and the 2- and 3-hydroxy groups as a tetraisopropyldisiloxanilidene (TIPDS) acetal gave **14**. Fortunately, the C-2′ diastereomers of **14** were easily separated by silica gel column chromatography at this stage to give (2′*R*)-**14** and (2′*S*)-**14**, respectively. The absolute configuration at C-2′ was confirmed by the comparison of the ^{1}H NMR spectra of both isomers with that of an authentic sample which was synthesized by using optically active 3-butyn-2-ol[(*S*)-**9**] as a starting material. A β-glucosidation reaction with 1.2 equivalent of (*S*)-**9** under the same conditions gave (2′*S*)-**11** in slightly lowered yield (71%), and (2′*S*)-**14** was synthesized in three steps by the method as described above (53%).

As shown in Scheme 3, segment coupling between **15**[7] and the lithium acetylide of **14**, and reduction of the triple bond with Red-Al, yielded the desired allyl alcohol **16**. After deprotection of TIPDS and the ethylene acetal groups of **16**, the diastereoselectivity of the segment coupling reaction was estimated to be approximately 55:45 by HPLC and ^{1}H NMR analysis regardless of the absolute configuration at the C-2′ position of **14**. This means that the slight diastereo induction observed (55:45) is due to the stereochemistry of the sugar moiety. Although it was impossible to determine the absolute configuration of each deprotected product, the isomers at the C-6 position of **17** were separable by MPLC for 9*S* isomers and preparative HPLC for 9*R* isomers. Deprotection of the acetonide group of the separated stereoisomers of **17** gave the four roseoside stereoisomers **3**, **4**, **5** and **6**, whose physical properties such as $[\alpha]_D$ values and ^{1}H and ^{13}C NMR spectra were in good accordance with the reported data.[1,2] The absolute configuration at C-6 generated by the segment coupling was determined by a comparison of the $[\alpha]_D$ values of the synthetic products with those of the reported data. Based on these stereochemical assignments, the (6*S*)-isomers were concluded to be the preferred isomers in the 1,2-addition reactions.

Next, the biological activites of the four stereoisomers of roseoside were compared based on an inhibition assay of leukotriene release from mouse bone marrow-derived cultured mast cells (BMCMC).[8] In this study we chose to employ a simpler anti-leukotriene release assay rather than an anti-histamine release assay. Table 1 shows the rate of inhibition of leukotriene release from BMCMC using 100 mM of roseoside, as measured by a commercially available CAST ELISA kit. The (6*S*)-isomers (**3** and **4**) were found to be about twice as active as the (6*R*)-isomers (**5** and **6**).



Scheme 1. Retrosynthetic analysis of roseosides.

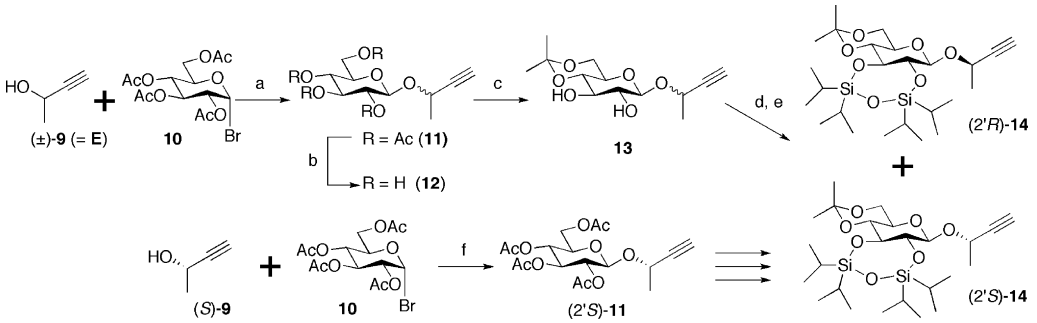
3. Conclusion

A simple and practical synthesis of the four stereoisomers of roseoside, **3**, **4**, **5** and **6**, was achieved. The overall yield of the four roseoside stereoisomers was 10–13% for 10 synthetic steps from D-glucose. By using **14** as a common intermediate, related natural products such as spionosides A (**7**) and B (**8**),[2l] isolated from *C. spinosa*, would also be synthesized in similar manners. An anti-leukotriene release assay of the four roseoside stereoisomers gave interesting results that the (6*S*)-isomers were about twice as active as the (6*R*)-isomers. This result indicates that the structure of cyclohexenone portion of roseoside is important in its activity. Because most of naturally occurring roseosides have 6*S* configuration, natural food sources containing roseosides could act as functional foods with anti-allergy activity.

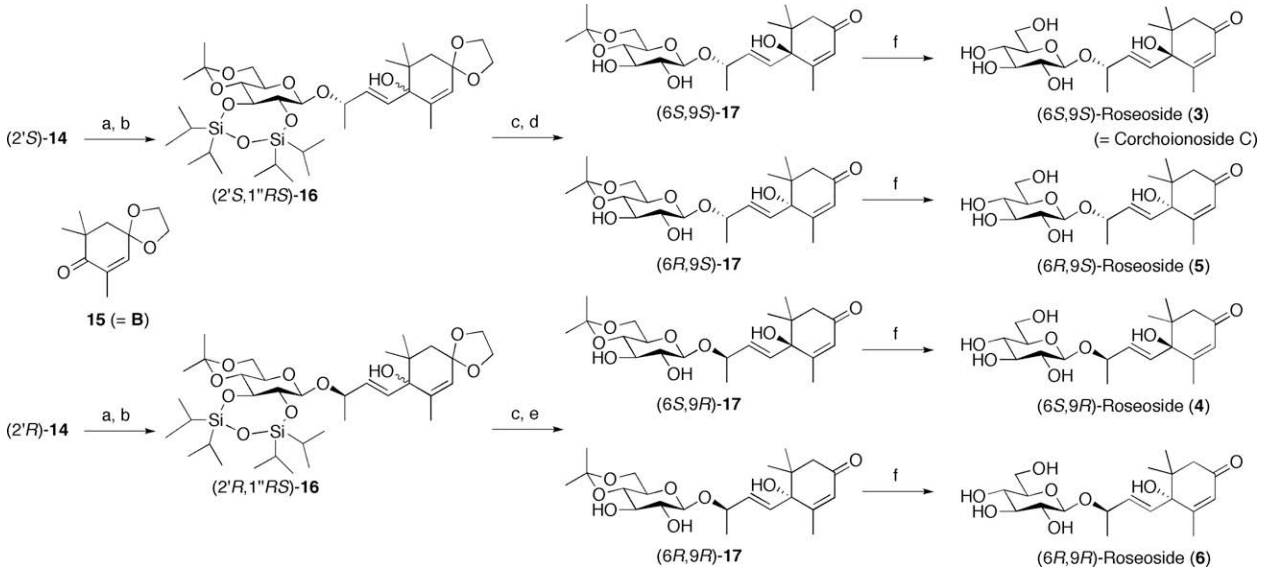
4. Experimental

4.1. General

Optical rotations were recorded by JASCO DIP-140. IR spectra were measured with a Shimadzu IR-4100 spectrometer. NMR spec-



Scheme 2. Synthesis of the key intermediates (2′*R*)- and (2′*S*)-**14**. Reagents, conditions and yields: (a) (±)-**9**, AgOTf, Ag_2CO_3, CH_2Cl_2, MS 4A, −20 °C to r.t. (80%); (b) KCN, MeOH, 55 °C (quant.); (c) dimethoxypropane, PPTS, THF (87%); (d) $TIPDSCl_2$, imidazole, THF; (e) SiO_2 chromatog. [44% for (2′*R*)-**14** and 44% for (2′*S*)-**14**]; (f) (−)-**9**, AgOTf, Ag_2CO_3, CH_2Cl_2, MS 4A, −20 °C to r.t. (71%).



Scheme 3. Synthesis of the four stereoisomers of roseoside. Reagents, conditions and yields: (a) *n*-BuLi, THF, −78 °C, then **15** [94% for (2′*S*)-isomer and 97% for (2′*R*)-isomer]; (b) Red-Al, THF, −10 °C to r.t. [86% for (2′*S*)-**16** and 74% for (2′*R*)-**16**]; (c) TBAF, THF, H_2O then AcOH, Et_2O, H_2O [quant. for (2′*S*)-**17** and 94% for (2′*R*)-**17**]; (d) MPLC separation; (e) HPLC separation; (f) PPTS, EtOH, H_2O [quant. for (6*S*,9′*S*)-**3**, 99% for (6*R*,9′*S*)-**5**, 99% for (6*S*,9′*R*)-**4** and 96% for (6*R*,9′*R*)-**6**].

Table 1
Inhibitory effects of the roseoside four stereoisomers (100 mM) on leukotriene release from BMCMC (means ± S.E., $n = 3$)

	Inhibition rate (%)
(6*S*,9*S*)-**3**	70.3 ± 7.5
(6*S*,9*R*)-**4**	67.4 ± 6.3
(6*R*,9*S*)-**5**	36.7 ± 8.4
(6*R*,9*R*)-**6**	22.9 ± 12.3

tra were recorded with a Jeol JNM-A400 spectrometer operating at 400 MHz for the ^{1}H NMR spectra and at 100 MHz for ^{13}C NMR spectra. Chemical shifts are reported as ppm relative to $CHCl_3$ or CH_3OH measured from the solvent resonance (^{1}H NMR; $CHCl_3$: 7.26 ppm or CH_3OH: 3.30 ppm, ^{13}C NMR; $CDCl_3$: 77.0 ppm or CD_3OD: 49.0 ppm). The elemental compositions were analyzed on a J-Science MICROCORDER JM10. Column chromatography was carried out with silica gel (Wakogel C-200). Medium pressure chromatography was carried out with silica gel (Wakogel C-500 HG) and YAMAZEN YFLC-600A as a pump. Preparative HPLC was carried out with Develosil 30-5 as a column and Shimadzu LC-6AD as a pump.

4.1.1. (2′*RS*)-3′-Butyn-2′-yl-(2,3,4,6-tetra-*O*-acetyl)-β-D-glucopyranoside (11)

Powdered MS 4A (6 g) was dried at 140 °C under reduced pressure for 1 day in a two necked flask. To the flask were added dry silver carbonate (2.53 g, 9.17 mmol) prepared by azeotoropic removal of water with toluene, silver trifluoromethanesulfonate (222 mg, 860 μmol) and dry CH_2Cl_2 (30 ml) under Ar atmosphere. After cooling to −15 °C, freshly distilled (±)-3-butyn-2-ol (**9**, 1.57 ml, 20.0 mmol) was added, and the mixture was stirred for 30 min. To the mixture was added the solution of bromide (**10**, 1.17 g, 2.85 mmol) in dry CH_2Cl_2. The reaction mixture was allowed to warm to room temperature, and stirred for 1 day. The mixture was filtered through a Celite pad, and the filtrate was washed with sat. $NaHCO_3$ aq. The aqueous phase was extracted with $CHCl_3$ and the combined organic phase was washed with brine and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by column chromatography with hexane/EtOAc (2:1) to give (2′*RS*)-**11** (911 mg, 80%) as a colorless amorphous solid. $[\alpha]_D^{22}$ +2.8 ($c = 1.0$, $CHCl_3$); IR (film): υ_{max} (cm^{-1}) = 3279 (s), 2943 (s), 2112 (w), 1739 (s), 1233 (s), 1159 (s), 1051 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.46$ (d, $J = 6.8$ Hz, 3H), 2.00–2.10 (m, 12H), 2.46, 2.50 (d, $J = 2.4$ Hz, 1H), 3.73 (ddd, $J = 2.4$, 5.4, 9.3 Hz, 1H), 4.13 (dd, $J = 2.4$, 12.2 Hz, 1H), 4.26 (dd, $J = 5.4$, 12.2 Hz, 1H), 4.54 (dq, $J = 2.4$, 6.8 Hz, 1 H), 4.77, 4.85 (d, $J = 7.8$ Hz, 1H), 4.99 (dd, $J = 7.8$, 9.8 Hz, 1H), 5.08 (dd, $J = 9.3$, 9.8 Hz, 1H), 5.22 (dd, $J = 9.3$, 9.3 Hz, 1H). Found: C, 54.01%, H, 6.01%. Calcd for $C_{18}H_{24}O_{10}$: C, 53.99%, H, 6.04%.

4.1.2. (2′*S*)-3′-Butyn-2′-yl-(2,3,4,6-tetra-*O*-acetyl)-β-D-glucopyranoside (11)

(2′*S*)-**11** was prepared from **10** and 1.2 eq. of (*S*)-**9** in the same manner just as described above (71%). $[\alpha]_D^{22}$ −47.6 ($c = 1.00$, $CHCl_3$); IR (film): υ_{max} (cm^{-1}) = 3279 (s), 2943 (s), 2112 (w), 1739 (s), 1233 (s), 1159 (s), 1051 (s). ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.44$ (d, $J = 6.8$ Hz, 3H), 2.00, 2.02, 2.05 and 2.08 (s × 4, 12 H), 2.46 (d, $J = 2.4$ Hz, 1H), 3.73 (ddd, $J = 2.4$, 5.4, 9.3 Hz, 1H), 4.13 (dd, $J = 2.4$, 12.2 Hz, 1H), 4.26 (dd, $J = 5.4$, 12.2 Hz, 1H), 4.59 (dq, $J = 2.4$, 6.8 Hz, 1H), 4.77 (d, $J = 7.8$ Hz, 1H), 4.99 (dd, $J = 7.8$, 9.3 Hz, 1H), 5.08 (dd, $J = 9.3$, 9.3 Hz, 1H), 5.24 (dd, $J = 9.3$, 9.3 Hz, 1H). Found: C, 53.99%, H, 6.04%. Calcd for $C_{18}H_{24}O_{10}$: C, 53.99%, H, 6.04%.

4.1.3. (2′*RS*)-3′-Butyn-2′-yl-β-D-glucopyranoside (12)

To a stirred solution of (2′*RS*)-**11** (2.35 g, 5.87 mmol) in MeOH (50 ml) was added KCN (191 mg, 2.93 mmol) at 55 °C. The mixture was stirred for 3 h and the solvent was removed by evaporation. The residue was chromatographed on silica gel (45 g, $CHCl_3$/MeOH = 5:1) to give 1.36 g of (2′*RS*)-**12** (quant.) as a colorless amorphous solid. $[\alpha]_D^{22}$ −13.1 ($c = 1.0$, MeOH); IR (film): υ_{max} (cm^{-1}) = 3405 (br.s, OH), 3279 (w), 2934 (m), 2112 (w), 1079 (s). ^{1}H NMR (CD_3OD, 400 MHz): $\delta = 1.41$, 1.44 (d, $J = 6.8$ Hz, 3H), 2.84, 2.86 (d, $J = 2.4$ Hz, 1H), 3.18 (m, 1H), 3.23–3.39 (m, 3H), 3.61–3.68 (m, 1H), 3.86–3.92 (m, 1H), 4.41, 4.68 (d, $J = 7.8$ Hz, 1H), 4.62, 4.75 (dq, $J = 2.4$, 6.8 Hz, 1H). Found: C, 51.74%, H, 6.95%. Calcd for $C_{10}H_{16}O_6$: C, 51.72%, H, 6.94%.

4.1.4. (2′*S*)-3′-Butyn-2′-yl-β-D-glucopyranoside (12)

In the same manner just as described above, (2′*S*)-**12** was prepared from (2′*S*)-**11** (91%). $[\alpha]_D^{22}$ −194.1 ($c = 1.20$, MeOH); IR

(film): υ_{max} (cm^{-1}) = 3405 (br.s, OH), 3279 (w), 2934 (m), 2112 (w), 1079 (s). ^1H NMR (CD_3OD, 400 MHz): δ = 1.44 (d, J = 6.3 Hz, 3H), 2.86 (d, J = 2.4 Hz, 1H), 3.18 (dd, J = 7.8, 7.8 Hz, 1H), 3.25–3.39 (m, 3H), 3.64 (m, 1H), 3.90 (dd, J = 1.4, 11.7 Hz, 1 H), 4.60 (d, J = 7.8 Hz, 1H), 4.75 (dq, J = 2.4, 6.8 Hz, 1H). Found: C, 51.57%, H, 6.69%. Calcd for $C_{10}H_{16}O_6$: C, 51.72%, H, 6.94%.

4.1.5. (2′*RS*)-3′-Butyn-2′-yl-(4,6-*O*-isopropylidene)-β-D-glucopyranoside (13)

To a stirred solution of (2′*RS*)-**12** (174 mg, 768 μmol) in dry THF (5 ml) were added 2,2-dimethoxypropane (4.00 ml, 32.6 mmol) and a catalytic amount (ca. 10 mg) of pyridinium *p*-toluenesulfonate at 0 °C under Ar. The solution was stirred for 1 day at room temperature and the reaction was quenched with Et_3N. The solution was concentrated in vacuo, and the residue was purified by column chromatography (6 g, $CHCl_3$) to give 177 mg of (2′*RS*)-**13** (87%) as a colorless amorphous solid and the recovered starting material (2′*RS*)-**12** (14 mg, 8%). $[\alpha]_D^{22}$ −0.3 (c = 1.0, MeOH); IR (film): υ_{max} (cm^{-1}) = 3435 (br.s, OH), 2993 (s), 2889 (s), 2112 (s), 1267–1010 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.44 (s, 3H), 1.49–1.51 (m, 6H), 2.49, 2.51 (d, J = 2.0 Hz, 1H), 2.62 (br.s, 1H), 2.83 (br.s, 1H), 3.24–3.32 (m, 1H), 3.42–3.92 (m, 5H), 4.54, 4.70 (d, J = 7.8 Hz, 1H), 4.58, 4.63 (dq, J = 2.0, 6.8 Hz, 1H). Found: C, 57.33%, H, 7.40%. Calcd for $C_{13}H_{20}O_6$: C, 57.34%, H, 7.40%.

4.1.6. (2′*S*)-3′-Butyn-2′-yl-(4,6-*O*-isopropylidene)-β-D-glucopyranoside (13)

In the same manner just as described above, (2′*S*)-**13** was prepared from (2′*S*)-**12** (70%). $[\alpha]_D^{22}$ −72.7 (c = 0.60, $CHCl_3$). IR (film): υ_{max} (cm^{-1}) = 3435 (br.s, OH), 2993 (s), 2889 (s), 2112 (s), 1267–1010 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.44 (s, 3H), 1.50 (d, J = 6.3 Hz, 3H), 1.51 (s, 3 H), 1.56 (s, 3H), 2.45 (d, J = 2.0 Hz, 1H), 2.49 (d, J = 2.0 Hz, 1H), 2.60 (d, J = 2.0 Hz, 1H), 3.32 (ddd, J = 5.4, 10.8, 10.8 Hz, 1H), 3.48 (m, 1 H), 3.60 (dd, J = 9.2, 9.2 Hz, 1H), 3.73 (ddd, J = 2.0, 10.8, 10.8 Hz, 1H), 3.79 (dd, J = 10.8, 10.8 Hz, 1H), 3.93 (dd, J = 5.4, 10.8 Hz, 1H), 4.63 (dq, J = 2.0, 6.8 Hz, 1H), 4.70 (d, J = 7.8 Hz, 1H). Found: C, 57.53%, H, 7.62%. Calcd for $C_{13}H_{20}O_6$: C, 57.34%, H, 7.40%.

4.1.7. (2′*R*)- and (2′*S*)-3′-Butyn-2′-yl-[2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)-4,6-*O*-isopropylidene]-β-D-glucopyranoside (14)

To a stirred solution of (2′*RS*)-**13** (1.97 g, 7.23 mmol) and imidazole (2.22 g, 32.6 mmol) in dry THF (45 ml) was added 1,3-dichrolo-1,1,3,3-tetraisopropyldisiloxane (2.78 ml, 8.68 mmol) at 0 °C under Ar. The reaction mixture was stirred for 12 h at room temperature and the mixture was poured into water. The aqueous phase was extracted with ether and the combined organic phases were washed with brine and dried with Na_2SO_4. After concentration in vacuo, the residue was chromatographed on silica gel (120 g, hexane/EtOAc = 190:1) to give 1.62 g (44%) of (2′*R*)-**14** and 1.63 g (44%) of (2′*S*)-**14** as colorless solids.

Properties of (2′*R*)-isomer: $[\alpha]_D^{22}$ −13.4 (c = 0.98, $CHCl_3$). IR (film): υ_{max} = 3256 cm^{-1} (s), 2945–2867 (s), 2122 (s), 1090 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.87–1.11 (m, 28H), 1.37 (s, 3H), 1.45 (s, 3H), 1.46 (d, J = 6.8 Hz, 3 H), 2.44 (d, J = 2.4 Hz, 1H), 3.25 (ddd, J = 5.4, 9.8, 10.3 Hz, 1H), 3.54 (m, 2H), 3.66 (dd, J = 7.8, 8.8 Hz, 1H), 3.79 (dd, J = 10.3, 10.7 Hz, 1H), 3.93 (dd, J = 5.4, 10.7 Hz, 1H), 4.49 (dq, J = 2.4, 6.8 Hz, 1H), 4.52 (d, J = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 12.2, 12.8, 12.9, 16.9, 17.1 (×2), 17.2 (×2), 17.3, 19.0, 22.1, 29.0, 62.3, 66.5, 67.4, 71.3, 72.9, 73.0, 74.8, 76.0, 77.9, 80.5, 83.5, 99.3, 102.9. Found: C, 58.30%, H, 9.00%. Calcd for $C_{25}H_{46}O_7Si_2$: C, 58.32%, H, 9.01%.

Properties of (2′*S*)-isomer: $[\alpha]_D^{22}$ −71.7 (c = 1.00, $CHCl_3$). IR (film): υ_{max} = 3311 cm^{-1} (s), 2992–2869 (s), 2134 (w), 1091 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.01–1.08 (m, 28H), 1.37 (s, 3H), 1.45 (d, J = 6.3 Hz, 3H), 1.46 (s, 3H), 2.38 (d, J = 2.0 Hz, 1H), 3.25 (ddd, J = 5.4, 9.8, 10.7 Hz, 1H), 3.52 (m, 2H), 3.69 (dd, J = 8.3, 8.8 Hz, 1H), 3.76 (dd, J = 10.3, 10.7 Hz, 1H), 3.91 (dd, J = 5.4, 10.7 Hz, 1H), 4.60 (dq, J = 2.0, 6.3 Hz, 1H), 4.70 (d, J = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 12.1, 12.8 (×2), 16.9, 17.0 (×2), 17.2, 17.3 (×2), 18.9, 22.0, 29.0, 62.2, 63.4, 66.9, 71.3, 73.1, 73.3, 74.4, 75.4, 77.1, 80.5, 82.8, 99.9, 100.6. Found: C, 58.32%, H, 9.01%. Calcd for $C_{25}H_{46}O_7Si_2$: C, 58.32%, H, 9.01%.

4.1.8. (1″*RS*,2′*R*)-4′-(4″,4″-Ethylenedioxy-1″-hydroxy-2″,6″,6″-trimethyl-2″-cyclohexen-1″-yl)-3′-butyn-2′-yl-[2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)-4,6-*O*-isopropylidene]-β-D-glucopyranoside

To a stirred solution of (2′*R*)-**14** (726 mg, 1.41 mmol) in dry THF was added slowly 1.60 M *n*-BuLi in hexane (1.06 ml, 1.69 mmol) at −78 °C under Ar. After stirring for 20 min, a solution of **15** (332 mg, 1.69 mmol) in dry THF (10 ml) was added dropwise to the mixture. The reaction mixture was allowed to warm to room temperature and stirred for 5 h. The mixture was poured into water and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried with Na_2SO_4. After concentration in vacuo, the residue was chromatographed on silica gel (35 g, hexane/EtOAc = 10:1) to give 947 mg (94%) of the title compound as a colorless amorphous solid. $[\alpha]_D^{23}$ −10.1 (c = 0.98, $CHCl_3$). IR (film): υ_{max} = 3448 cm^{-1} (br.m, OH), 2946–2869 (s), 1092 (s), 834 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.95–1.09 (m, 34 H), 1.13, 1.14 (s, 2H), 1.37 (s, 3H), 1.44 (d, J = 1.0 Hz, 3H), 1.45 (s, 3H), 1.89, 1.90 (d, J = 1.0 Hz, 3H), 3.10, 3.24 (ddd, J = 5.4, 9.8, 10.2 Hz, 1H), 3.45–3.54 (m, 2H), 3.65, 3.66 (dd, J = 8.3, 8.8 Hz, 1 H), 3.75 (dd, J = 10.2, 10.7 Hz, 1H), 3.89–3.97 (m, 5H), 4.50–4.55 (m, 2H), 5.36 (br.s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 12.0, 12.2, 12.8, 12.9, 16.9, 17.1, 17.2, 17.3, 17.4, 19.0, 22.0, 22.1 (×2), 22.7, 22.8, 25.1, 25.4, 25.5, 29.0, 39.2, 43.4, 62.3, 63.7, 64.1, 64.2, 67.1, 67.2, 67.5, 72.8, 72.9, 74.3, 78.1, 85.1, 85.7, 85.8, 99.2, 102.9, 103.0, 104.8, 123.4, 123.5, 126.2, 140.0, 140.1. Found: C, 60.81%, H, 8.79%. Calcd for $C_{36}H_{62}O_{10}Si_2$: C, 60.81%, H, 8.79%.

4.1.9. (1″*RS*,2′*S*)-4′-(4″,4″-Ethylenedioxy-1″-hydroxy-2″,6″,6″-trimethyl-2″-cyclohexen-1″-yl)-3′-butyn-2′-yl-[2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)-4,6-*O*-isopropylidene]-β-D-glucopyranoside

In the same manner just as described above, (1″*RS*,2′*S*)-isomer was prepared from 1.29 g (2.51 mmol) of (2′*S*)-**14** to give 1.73 g (97%) of the title compound as a colorless amorphous solid. $[\alpha]_D^{23}$ −60.9 (c = 0.13, $CHCl_3$). IR (film): υ_{max} = 3466 cm^{-1} (br.w, OH), 2946–2869 (s), 1093 (s), 834 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.94–1.10 (m, 34H), 1.13, 1.14 (s, 2H), 1.38 (s, 3H), 1.42, 1.44 (d, J = 2.0 Hz, 3H), 1.46 (s, 3H), 1.90 (br.d, J = 1.5 Hz, 3H), 3.25 (m, 1H), 3.52 (t, J = 7.8 Hz, 1H), 3.53 (dd, J = 9.3, 9.8 Hz, 1H), 3.68 (m, 1H), 3.75 (br.t, J = 10.7 Hz, 1H), 3.90–3.97 (m, 5H), 4.67–4.71 (m, 2H), 5.37 (br.s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.9, 12.2, 12.7, 12.8, 16.9, 17.1, 17.3, 17.4, 19.0, 22.0, 22.8, 25.2, 25.5, 29.0, 39.1, 41.7, 43.5, 62.2, 62.3, 62.9, 63.0, 63.7, 64.1, 64.3, 66.8, 66.9, 67.1, 73.1, 73.2, 74.4, 84.8, 86.1, 99.2, 99.3, 100.1, 100.4, 104.7, 123.5, 126.3, 140.02, 140.13. Found: C, 60.81%, H, 8.80%. Calcd for $C_{36}H_{62}O_{10}Si_2$: C, 60.81%, H, 8.79%.

4.1.10. (1″*RS*,2′*R*,3′*E*)-4′-(4″,4″-Ethylenedioxy-1″-hydroxy-2″,6″,6″-trimethyl-2″-cyclohexen-1″-yl)-3″-buten-2′-yl-[2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)-4,6-*O*-isopropylidene]-β-D-glucopyranoside [(1″*RS*,2′*R*,3′*E*)-16]

To a stirred solution of (1″*RS*,2′*R*)-isomer of the above compound (2.20 g, 3.09 mmol) in dry THF (40 ml) was added a solution of 65 wt% Red-Al in toluene (2.79 ml, 9.30 mmol), diluted with dry THF (10 ml), at 0 °C under Ar. After stirring for 4 h, the reaction was quenched with careful addition of water and saturated Rochelle salt solution. The mixture was stirred for 30 min at room temper-

ature and the aqueous phase was extracted with EtOAc. The combined organic phase was washed with brine and dried with Na_2SO_4. After concentration in vacuo, the residue was chromatographed on silica gel (77 g, hexane/EtOAc = 10:1) to give 1.89 g (86%) of **16** as a colorless amorphous solid. $[\alpha]_D^{23}$ −60 (c = 0.08, $CHCl_3$). IR (film): υ_{max} = 3504 cm^{-1} (br.m, OH), 2946–2869 (s), 1670 (w), 1091 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.86–1.08 (m, 34H), 1.25, 1.27 (d, J = 2.0 Hz, 3H), 1.36 (s, 3H), 1.44 (s, 3H), 1.64, 1.67 (d, J = 1.5 Hz, 3 H), 1.70 (dd, J = 1.5, 14.2 Hz, 1H), 1.88, 1.90 (br.d, J = 14.2 Hz, 1H), 3.13 (m, 1H), 3.47–3.53 (m, 2H), 3.63 (dd, J = 8.3, 8.8 Hz, 1H), 3.72 (m, 1H), 3.84–4.02 (m, 5H), 4.23 (m, 1H), 4.33, 4.34 (d, J = 7.8 Hz, 1H), 5.40 (m, 1H), 5.64, 5.65 (d, J = 15.6 Hz, 1H), 5.72, 5.74 (dd, J = 2.4, 15.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 12.1, 12.2, 12.3, 12.9, 16.9, 17.1, 17.2, 17.4, 17.9, 18.0, 18.8, 19.0, 21.3, 21.5, 22.8, 23.1, 24.1, 24.8, 28.9, 38.6, 41.1, 44.7, 49.7, 62.3, 63.7, 63.9, 64.5, 67.3, 72.9, 73.0, 77.8, 78.2, 78.4, 99.2, 99.3, 102.4, 102.8, 104.9, 123.7, 126.9, 127.0, 130.1, 132.5, 132.6, 133.7, 133.8, 141.7. Found: C, 60.63%, H, 9.05%. Calcd for $C_{36}H_{64}O_{10}Si_2$: C, 60.63%, H, 9.05%.

4.1.11. (1″*RS*,2′*S*,3′*E*)-4′-(4″,4″-Ethylenedioxy-1-hydroxy-2″,6″,6″-trimethyl-2″-cyclohexen-1″-yl)-3′-buten-2′-yl-[2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)-4,6-*O*-isopropylidene]-β-D-glucopyranoside [(1″*RS*,2′*S*,3′*E*)-16]

In the same manner just as described above, (2′*S*)-isomer was prepared from 1.48 g (2.08 mmol) of (1″*RS*,2′*S*)-isomer to give 1.10 g (74%) of (1″*RS*,2′*S*,3′*E*)-**16** as a colorless amorphous solid. $[\alpha]_D^{23}$ −11.1 (c = 0.32, $CHCl_3$). IR (film): υ_{max} = 3503 cm^{-1} (br.m, OH), 2947–2869 (s), 1670 (w), 1092 (s), 834 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.86–1.20 (m, 34H), 1.23, 1.25 (d, J = 3.9 Hz, 3H), 1.35 (s, 3H), 1.43 (s, 3H), 1.63, 1.67 (d, J = 1.0 Hz, 3H), 1.72 (br.d, J = 14.2 Hz, 1H), 1.86, 1.88 (d, J = 14.2 Hz, 1H), 3.11 (ddd, J = 4.9, 10.3, 10.7 Hz, 1H), 3.48–3.52 (m, 2H), 3.58 (m, 1H), 3.75 (ddd, J = 3.0, 10.3, 10.7 Hz, 1H), 3.86–3.98 (m, 5H), 4.32–4.37 (m, 1H), 4.34 (d, J = 7.3 Hz, 1H), 5.36, 5.38 (br.s, 1H), 5.57–5.64 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 11.9, 12.2, 12.8 (×2), 16.9, 17.1, 17.2, 17.3,18.0, 19.0, 22.1 (×2), 22.8, 23.1, 24.1, 24.8, 25.1, 29.0, 38.5, 38.6, 44.8 (×2), 62.3, 63.7, 63.9, 64.5, 66.8, 66.9, 67.0, 73.1, 74.4, 77.1, 77.4, 78.2, 78.4, 99.2 (×2), 100.2, 100.7, 104.8, 123.7, 123.8, 127.1, 131.6, 131.8, 133.1, 133.7, 133.8, 141.5, 141.7. Found: C, 60.62%, H, 9.04%. Calcd for $C_{36}H_{64}O_{10}Si_2$: C, 60.63%, H, 9.05%.

4.1.12. (6*R*,9*R*)- and (6*S*,9*R*)-9-(4′,6′-*O*-Isopropylidene-β-D-glucopyranosyl)oxy-6-hydroxy-3-oxo-α-ionol (17)

To a stirred solution of (1"*RS*,2′*R*,3′*E*)-**16** (1.89 g, 2.65 mmol) in THF (28 ml) was added a mixture of 1 M TBAF in THF (11.1 ml, 11.1 mmol), THF (8 ml) and water (1 ml) at 0 °C. After stirring for 12 h, the mixture was poured into sat. $NaHCO_3$ aq. and the aqueous phase was extracted with EtOAc. The combined organic phases wrer washed with brine and dried with Na_2SO_4. After concentration in vacuo, the residue was chromatographed on silica gel (100 g, hexane/EtOAc = 1:5) to give crude material. The obtained crude material was dissolved in ether (100 ml) and water (1 ml) and acetic acid (20 ml) was successively added at room temperature. After stirring for 24 h, the reaction mixture was poured into sat. $NaHCO_3$ aq. and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried with Na_2SO_4. After concentration in vacuo, the residue was chromatographed on silica gel (90 g, hexane/EtOAc = 1:5) to give a diastereomeric mixture of **17** (1.13 g, quant.). The ratio of the isomers was estimated to be 55:45 by ^1H NMR analysis. Preparative HPLC separation (rate: 8.0 ml/min, hexane/EtOH = 8:1, R_t[(6*S*,9*R*)-**17**] = 108.0 min, R_t[(6*R*,9*R*)-**17**] 124.7 min) gave pure (6*S*,9*R*)-**17** (201 mg) and (6*R*,9*R*)-**17** (264 mg) as well as the diastereomeric mixture (660 mg).

Properties of (6S,9R)-isomer: Colorless amorphous solid, $[\alpha]_D^{22}$ +80.9 (c = 1.07, $CHCl_3$). IR (film): υ_{max} = 3503 cm^{-1} (br.m, OH), 2947–2869 (s), 1670 (w), 1092 (s), 834 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.01 (s, 3H), 1.08 (s, 3H) 1.31 (d, J = 6.3 Hz, 3H), 1.43 (s, 3H), 1.50 (s, 3H), 1.88 (d, J = 1.0 Hz, 3H), 2.24 (d, J = 16.6 Hz, 1H), 2.41 (d, J = 16.6 Hz, 1H), 3.22 (ddd, J = 5.4, 9.8, 10.3 Hz, 1H), 3.45 (dd, J = 7.8, 8.8 Hz, 1H), 3.57 (dd, J = 9.3, 9.8 Hz, 1H), 3.66 (dd, J = 8.8, 9.3 Hz, 1H), 3.75 (dd, J = 10.3, 10.7 Hz, 1H), 3.83 (dd, J = 5.4, 10.7 Hz, 1H), 4.34 (sep, J = 6.3 Hz, 1H), 4.40 (d, J = 7.8 Hz, 1H), 5.75 (d, J = 15.6 Hz, 1H), 5.83 (dd, J = 6.3, 15.6 Hz, 1H), 5.91 (br.s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.9, 19.0, 21.2, 22.8, 24.1, 29.0, 30.9, 41.2, 49.6, 62.0, 65.9, 67.4, 73.0, 73.5, 74.6, 99.8, 102.1, 127.1, 130.3, 133.6162.2, 197.8. Found: C, 61.95%, H, 8.04%. Calcd for $C_{22}H_{34}O_8$: C, 61.95%, H, 8.04%.

Properties of (6R,9R)-isomer: Colorless amorphous solid, $[\alpha]_D^{22}$ −125.0 (c = 1.03, $CHCl_3$). IR (film): υ_{max} = 3503 cm^{-1} (br.m, OH), 2947–2869 (s), 1670 (w), 1092 (s), 834 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.99 (s, 3H), 1.07 (s, 3 H), 1.32 (d, J = 6.4 Hz, 3H), 1.43 (s, 3H), 1.50 (s, 3H), 1.89 (d, J = 1.5 Hz, 3H), 2.23 (d, J = 17.1 Hz, 1H), 2.44 (d, J = 17.1 Hz, 1H), 3.21 (ddd, J = 5.4, 9.3, 10.3 Hz, 1H), 3.43 (dd, J = 7.8, 8.8 Hz, 1H), 3.56 (t, J = 9.3 Hz, 1H), 3.65 (dd, J = 8.8, 9.3 Hz, 1H), 3.74 (dd, J = 10.3, 10.7 Hz, 1H), 3.83 (dd, J = 5.4, 10.7 Hz, 1H), 4.34 (sep, J = 6.4 Hz, 1H), 4.39 (d, J = 7.8 Hz, 1H), 5.75 (d, J = 15.6 Hz, 1H), 5.83 (dd, J = 6.4, 15.6 Hz, 1H), 5.60 (d, J = 1.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.0, 19.4, 21.3, 22.8, 24.1, 29.0, 30.9, 41.2, 49.7, 62.0, 67.5, 73.0, 73.5, 74.7, 99.8, 101.7, 102.3, 126.9, 130.3, 133.6, 165.3, 199.2. Found: C, 61.96%, H, 8.05%. Calcd for $C_{22}H_{34}O_8$: C, 61.95%, H, 8.04%.

4.1.13. (6*R*,9*S*)- and (6*S*,9*S*)-9-(4′,6′-*O*-Isopropylidene-β-D-glucopyranosyl)oxy-6-hydroxy-3-oxo-α-ionol (17)

In the same manner as described above, (1″*RS*,2′*S*,3′*E*)-**16** (942 mg, 1.32 mmol) was converted to a diastereomeric mixture of **17** (528 mg, 94%). The ratio of the isomers was estimated to be 55:45 by ^1H NMR analysis. MPLC separation of the diastereomers (rate: 4 ml/min., toluene/THF = 10:1 to 3:1) gave pure (6*R*,9*S*)-**17** (72 mg) and (6*S*,9*S*)-**17** (72 mg) as well as the diastereomeric mixture (380 mg).

Properties of (6 S,9*S*)-isomer: Colorless amorphous solid, $[\alpha]_D^{22}$ +54.1 (c = 1.00, $CHCl_3$). IR (film): υ_{max} = 3447 cm^{-1} (br.w, OH), 2972 (s), 1654 (s), 841 (s), 998 (s). ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.99 (s, 3H), 1.07 (s, 3H), 1.32 (d, J = 6.4 Hz, 3H), 1.42 (s, 3H), 1.49 (s, 3H), 1.91 (s, 3H), 2.26 (br.d, J = 17.1 Hz, 1H), 2.49 (br.d, J = 17.1 Hz, 1H), 3.18 (m, 1H), 3.45 (br.dd, J = 7.8, 8.3 Hz, 1H), 3.56 (m, 2H), 3.78 (dd, J = 10.3, 10.7 Hz, 1H), 3.89 (dd, J = 5.4, 10.7 Hz, 1H), 4.32 (d, J = 7.8 Hz, 1H), 4.41 (sep, J = 6.4 Hz, 1H), 5.75 (dd, J = 6.4, 15.6 Hz, 1H), 5.87 (d, J = 15.6 Hz, 1H), 5.91 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.0, 21.1, 22.0, 23.0, 24.2, 29.0, 30.9, 41.1, 49.6, 62.0, 74.5, 75.5, 77.2, 77.6, 79.8, 100.4, 127.0, 131.3, 132.1,167.1, 201.3. Found: C, 61.96%, H, 8.04%. Calcd for $C_{22}H_{34}O_8$: C, 61.95%, H, 8.04%.

Properties of (6R,9S)-isomer: Colorless amorphous solid, $[\alpha]_D^{22}$ −134.9 (c = 1.00, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.03 (s, 3H), 1.09 (s, 3H), 1.32 (d, J = 6.3 Hz, 3H), 1.43 (s, 3H), 1.50 (s, 3H), 1.89 (d, J = 1.5 Hz, 3H), 2.27 (br.d, J = 17.1 Hz, 1H), 2.43 (br.d, J = 17.1 Hz, 1H), 3.21 (m, 1H), 3.47 (t, J = 7.8 Hz, 1H), 3.59 (m, 2H), 3.80 (dd, J = 10.3, 10.7 Hz, 1H), 3.91 (dd, J = 5.4, 10.7 Hz, 1H), 4.35 (d, J = 7.8 Hz, 1H), 4.41 (sep, J = 6.3 Hz, 1H), 5.71 (dd, J = 6.3, 16.1 Hz, 1H), 5.85 (d, J = 16.1 Hz, 1H), 5.91 (br.s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.8, 19.0, 22.0, 22.9, 24.3, 29.0, 41.0, 49.6, 62.0, 67.4, 73.0, 73.7, 74.5, 77.2, 99.8, 100.2, 127.2, 132.3, 132.6, 167.3, 201.2. Found: C, 61.96%, H, 8.05%. Calcd for $C_{22}H_{34}O_8$: C, 61.95%, H, 8.04%.

4.1.14. (6*S*,9*S*)-Roseoside (=corchoionoside C) (3)

To a solution of (6*S*,9*S*)-**17** (72 mg, 169 μmol) in EtOH (1 ml) and water (0.5 ml) was added a catalytic amount (ca. 2 mg) of

pyridinium *p*-toluenesulfonate at room temperature. The reaction mixture was stirred for 16 h at room temperature and at 50 °C for 6 h. After cooling to room temperature, Et_3N was added to the mixture. The solvent was removed by evaporation, and the residue was chromatographed on silica gel (27 g, $CHCl_3$/MeOH = 10:1) to give 65 mg (quant.) of **3** as a colorless amorphous solid. $[\alpha]_D^{22}$ +60.4 (c = 0.96, MeOH), lit.[2l] $[\alpha]_D^{20}$ +31.2 (c = 2.0, MeOH), lit.[3] $[\alpha]_D^{25}$ +74.0 (c = 0.96, MeOH). IR (film): υ_{max} = 3430 cm^{-1} (br.s, OH), 2970–2928 (m), 1654 (s), 1073 (s), 1036 (s). ^1H NMR (CD_3OD, 400 MHz): δ = 0.95 (s, 3H, 11-CH_3), 0.97 (s, 3H, 12-CH_3), 1.22 (d, J = 6.3 Hz, 3H, 10-CH_3), 1.87 (d, J = 1.5 Hz, 3H, 13-CH_3), 2.10 (d, J = 17.1 Hz, 1H, 2-C*H*H), 2.54 (d, J = 17.1 Hz, 1H, 2-CH*H*), 3.06–3.38 (m, 4H, 2′,3′,4′,5′-CH), 3.56 (dd, J = 6.3, 11.7 Hz, 1H, 6′-C*H*H), 3.78 (dd, J = 2.0, 11.7 Hz, 1H, 6′-CH*H*), 4.20 (d, J = 7.8 Hz, 1H, 1′-CH), 4.46 (m, 1H, 9-CH), 5.63 (dd, J = 7.3, 15.6 Hz, 1H, 8-CH), 5.80 (s, 1H, 4-CH), 5.91 (d, J = 15.6 Hz, 1H, 7-CH). ^{13}C NMR (CD_3OD, 100 MHz): δ = 19.6 (C-13), 22.2 (C-10), 23.5 (C-11), 24.7 (C-12), 42.4 (C-1), 50.8 (C-2), 62.8 (C-6′), 71.7 (C-4′), 74.6 (C-9), 74.9 (C-2′), 78.2 (C-5′), 78.4 (C-3′), 80.0 (C-6), 101.2 (C-1′), 127.1 (C-4), 133.7 (C-8), 133.8 (C-7), 167.1 (C-5), 201.3 (C-3). Found: C, 59.06%, H, 7.83%. Calcd for $C_{19}H_{30}O_8$: C, 59.05%, H, 7.83%.

4.1.15. (6*S*,9*R*)-Roseoside (4)

In the same manner as described above, (6*S*,9*R*)-**17** (201 mg, 169 μmol) was converted to **4** (180 mg, 99%). $[\alpha]_D^{22}$ = +116.2 (c = 1.02, MeOH), lit.[2a] $[\alpha]_D$ +112 (c = 1.19, MeOH), lit.[3] $[\alpha]_D^{19}$ +109.4 (c = 0.96, MeOH). IR (film): υ_{max} = 3409 cm^{-1} (br.s, OH), 2972–2931 (m), 1655 (s), 1075 (s), 1036 (s). ^1H NMR (CD_3OD, 400 MHz): δ = 0.98 (s, 6H, 11,12-CH_3), 1.23 (d, J = 6.4 Hz, 3H, 10-CH_3), 1.87 (d, J = 1.5 Hz, 3H, 13-CH_3), 2.10 (d, J = 17.1 Hz, 1H, 2-C*H*H), 2.47 (d, J = 17.1 Hz, 1H, 2-CH*H*), 3.10–3.32 (m, 4H, 2′,3′,4′,5′-CH), 3.58 (dd, J = 5.4, 11.7 Hz, 1H, 6′-C*H*H), 3.80 (dd, J = 2.0, 11.7 Hz, 1H, 6′-CH*H*), 4.29 (d, J = 7.3 Hz, 1H, 1′-CH), 4.37 (m, 1H, 9-CH), 5.80–5.82 (m, 3H, 4,7,8-CH). ^{13}C NMR (CD_3OD, 100 MHz): δ = 19.5 (C-13), 21.2 (C-10), 23.4 (C-11), 24.7 (C-12), 42.4 (C-1), 50.6 (C-2), 62.8 (C-6′), 71.6 (C-4′), 75.2 (C-2′), 77.3 (C-9), 77.9 (C-5′), 78.0 (C-3′), 80.0 (C-6), 102.7 (C-1′), 127.1 (C-4), 131.5 (C-7), 135.2 (C-8), 167.2 (C-5), 201.2 (C-3). Found: C, 59.06%, H, 7.82%. Calcd for $C_{19}H_{30}O_8$: C, 59.05%, H, 7.83%.

4.1.16. (6*R*,9*S*)-Roseoside (5)

In the same manner as described above, (6*R*,9*S*)-**17** (72 mg, 170 μmol) was converted to **5** (66 mg, quant.). $[\alpha]_D^{22}$ −137.4 (c = 0.80, MeOH), lit.[3] $[\alpha]_D^{26}$ −157.5 (c = 0.80, MeOH). IR (film): υ_{max} = 3410 cm^{-1} (br.s, OH), 2971–2929 (m), 1653 (s), 1071 (s), 1035 (s). ^1H NMR (CD_3OD, 400 MHz): δ = 0.97 (s, 6H, 11,12-CH_3), 1.20 (d, J = 6.3 Hz, 3H, 10-CH_3), 1.84 (d, J = 1.6 Hz, 3H, 13-CH_3), 2.10 (d, J = 17.1 Hz, 1H, 2-C*H*H), 2.47 (d, J = 17.1 Hz, 1H, 2-CH*H*), 3.10–3.28 (m, 4H, 2′,3′,4′,5′-CH), 3.56 (dd, J = 5.9, 12.2 Hz, 1H, 6′-C*H*H), 3.80 (dd, J = 2.0, 12.2 Hz, 1H, 6′-CH*H*), 4.24 (d, J = 7.8 Hz, 1H, 1′-CH), 4.46 (m, 1H, 9-CH), 5.63 (dd, J = 7.8, 15.6 Hz, 1H, 8-CH), 5.79 (s, 1H, 4-CH), 5.89 (d, J = 15.6 Hz, 1H, 7-CH). ^{13}C NMR (CD_3OD, 100 MHz): δ = 19.4 (C-13), 22.2 (C-10), 23.4 (C-11), 24.8 (C-12), 42.3 (C-1), 50.6 (C-2), 62.9 (C-6′), 71.7 (C-4′), 74.7 (C-9), 75.0 (C-2′), 78.1 (C-5′), 78.2 (C-3′), 80.0 (C-6), 100.9 (C-1′), 127.2 (C-4), 133.8 (C-8), 134.1 (C-7), 166.9 (C-5), 201.1 (C-3). Found: C, 59.05%, H, 7.83%. Calcd for $C_{19}H_{30}O_8$: C, 59.05%, H, 7.83%.

4.1.17. (6*R*,9*R*)-Roseoside (6)

In the same manner as described above, (6 R,9*R*)-**17** (264 mg, 619 μmol) was converted to **6** (230 mg, 96%). $[\alpha]_D^{22}$ −101.3 (c = 0.79, MeOH), lit.[2h] $[\alpha]_D^{22}$ −74.0 (c = 0.23, MeOH), lit.[3] $[\alpha]_D^{19}$ −116.0 (c = 0.79, MeOH). IR (film): υ_{max} = 3400 cm^{-1} (br.s, OH), 2972–2931 (m), 1653 (s), 1076 (s), 1035 (s). ^1H NMR (CD_3OD, 400 MHz): δ = 0.93 (s, 3H, 11-CH_3), 0.96 (s, 3H, 12-CH_3), 1.23 (d, J = 6.3 Hz, 3H, 10-CH_3), 1.85 (d, J = 1.5 Hz, 3H, 13-CH_3), 2.08 (d, J = 17.1 Hz, 1H, 2-C*H*H), 2.45 (d, J = 17.1 Hz, 1H, 2-CH*H*), 3.22 (m, 4H, 2′,3′,4′,5′-CH), 3.58 (dd, J = 5.4, 11.7 Hz, 1H, 6′-C*H*H), 3.74 (dd, J = 2.4, 11.7 Hz, 1H, 6′-CH*H*), 4.29 (d, J = 7.8 Hz, 1H, 1′-CH), 4.37 (m, 1H, 9-CH), 5.78 (m, 2H, 7,8-CH), 5.80 (br.s, 1H, 4-CH). ^{13}C NMR (CD_3OD, 100 MHz): δ = 19.7 (C-13), 21.2 (C-10), 23.4 (C-11), 24.6 (C-12), 42.4 (C-1), 50.7 (C-2), 62.5 (C-6′), 71.3 (C-4′), 75.1 (C-2′), 76.9 (C-9), 77.8 (C-5′), 77.9 (C-3′), 79.9 (C-6), 102.5 (C-1′), 127.0 (C-4), 131.6 (C-7), 135.0 (C-8), 167.3 (C-5), 201.2 (C-3). Found: C, 59.05%, H, 7.83%. Calcd for $C_{19}H_{30}O_8$: C, 59.05%, H, 7.83%.

5. Cell culture and stimulation[8]

Femoral bone marrow cells derived from male ICR (Nippon SLC) mice were cultured in IL-3-containing medium (10 ng/ml) for more than 8 weeks to generate >95% pure populations of bone marrow-derived cultured mast cell (BMCMC). BMCMC were incubated with 1 mg/ml of anti-DNP mouse IgE (SPE-7, Sigma Aldrich) for 6 h with or without 100 mM of roseoside. For FceRI cross-linking, cells were further incubated with antigen, 10 ng/ml of DNP-HSA for 30 min.

6. Measurements of leukotrienes

Amounts of leukotoriens in BMCMC culture supernatants were measured by using commercial kit (Buhlman CAST ELISA kit).

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