Medicinal Foodstuffs. XVI.[1] Sugar Beet. (3): Absolute Stereostructures of Betavulgarosides II and IV, Hypoglycemic Saponins Having a Unique Substituent, from the Roots of *Beta vulgaris* L.

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Received June 21, 1999; accepted August 23, 1999

The absolute stereostructures of betavulgaroside II having a dioxolane-type substituent and betavulgaroside IV having an acetal-type substituent, which were isolated from the roots of *Beta vulgaris* L. (sugar beet, Chenopodiaceae) and exhibited hypoglycemic activity on glucose-loaded rats, were determined by the chemical correlations of betavulgarosides II and IV with a known saponin, momordin I. In these chemical correlations, the α-L-arabinopyranosyl moiety of momordin I was converted to a dioxolane-type substituent of betavulgaroside II or to an acetal-type substituent of betavulgaroside IV. Additionally, the 2′-diastereoisomer of betavulgaroside IV was synthesized from momordin I, and four acetal-type substituent analogues were also synthesized from L- and D-arabinose.

Key words *Beta vulgaris*; sugar beet; betavulgaroside absolute stereostructure; hypoglycemic effect; medicinal foodstuff; momordin Ic chemical correlation

The Chenopodiaceae plant *Beta vulgaris* L. (sugar beet) has been widely cultivated in European and North American countries and the roots have been used industrially as a raw material for sugar. The fresh roots and leaves of this plant are also used as a vegetable and food garnish in Japanese-style dishes. In traditional Chinese medicine, the roots of sugar beet have been listed as a medicinal herb, which has been known to exhibit sedative and emmenagogue-like effects.

As part of our continuing studies of antidiabetogenic constituents from medicinal foodstuffs,[2] we have found that the saponin fractions from the roots and leaves of sugar beet show a potent inhibitory effect on the increase in serum glucose levels in glucose-loaded rats. From the saponin fractions, we have isolated nine triterpene oligoglycosides called betavulgarosides I—IX with a unique substituent, acetal-type and dioxolane-type substituents,[3] which were presumed to be biosynthesized through the oxidative degradation of a terminal monosaccharide moiety.[4] Among those saponins, oleanen-28-oic acid 3-monodesmosides such as betavulgarosides II (**2**) and IV (**4**) were found to show potent hypoglycemic activity, while oleanen-28-oic acid 3,28-bisdesmosides such as betavulgarosides I (**1**) and III (**3**) lacked the activity.[3] Furthermore, the structural requirements for the activity and the modes of action of the saponins for hypoglycemic activity were clarified.[5] The structures of betavulgarosides were elucidated on the basis of chemical and physicochemical evidence, except for the stereostructure of their substituents. In this paper, we describe the elucidation of the absolute stereostructure of the acetal-type substituent in **4** by means of chemical correlation with a known saponin, momordin I (**5**), which was isolated from several natural medicines: for example, the fruits of *Kochia scoparia* L.[6] and the roots of *Momordica cochinchinensis* SPRENG.[7] In this chemical correlation, **5** was initially transformed to the 2″-diastereoisomer (**18**) of betavulgaroside IV derivative (**19**), then the acetal-type substituent having the 1″(*S*) and 2″(*R*)-configurations in **4** was synthesized from the α-L-arabinopyranosyl moiety of **5** *via* the α-L-ribopyranosyl derivative (**23**). In addition, the absolute stereostructures of **2** were chemically characterized by synthesis of the dioxolane-type substituent in **2** from the diglycoside moiety of **5**.[8]

Syntheses of Acetal-Type Substituent Analogues By detailed ^{1}H-NMR and ^{13}C-NMR examination using various two dimensional (2D) NMR analytical methods, we have reported the planar structure of the acetal-type substituent composed of a tartronaldehydic acid and glycolic acid, which bonded at the 3′-hydroxyl group of the 3-*O*-β-D-glucopyranosiduronic acid moiety in **4**. In order to chemically confirm the planar structure of the acetal-type substituent, four acetal-type substituent analogues were synthesized for L- and D-arabinose. Methyl α-L-arabinopyranoside (**8**), which was selectively obtained by methanolysis of L-arabinose with 9% hydrogen chloride in dry methanol, was converted to the dialdehyde derivative (**9**) through the following procedures: 1) protection of the 3- and 4-hydroxyl groups with isopropylidene group, 2) silylation of the 2-hydroxyl group with *tert*-butyldimethylsilyl (TBDMS) group, 3) removal of the isopropylidene group, and 4) oxidative cleavage of the 3,4-diol moiety with lead tetraacetate [$Pb(OAc)_4$]. Further oxidation of **9** with sodium chlorite ($NaClO_2$) and sulfamic acid (NH_2SO_3H) in 75% aqueous 1,4-dioxane proceeded with removal of the 2-TBDMS group to provide the 1*S*,2*S*-analogue, which was converted to the dimethyl ester (**10**) by diazomethane methylation. On the other hand, methyl β-L-arabinopyranoside (**11**) was prepared by the glycosidation of methanol with *O*-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl) trichloroacetimidate[9] in the presence of boron trifluoride etherate followed by deacetylation. The β-anomer (**11**) was transformed to the methyl ester (**13**) of the 1*R*,2*S*-analogue *via* the dialdehyde derivative (**12**). The methyl esters (**14**, **15**) of the 1*R*,2*R*- and the 1*S*,2*R*-analogues were also synthesized from D-arabinose in a similar manner as above. Comparison of the ^{1}H-NMR and ^{13}C-NMR spectra for four acetal-type substituent analogues (**10**, **13**, **14**, **15**) with those for **3** and **4** led us to confirm the planar structure of the acetal-type substituent composed of a tartronaldehydic acid and glycolic

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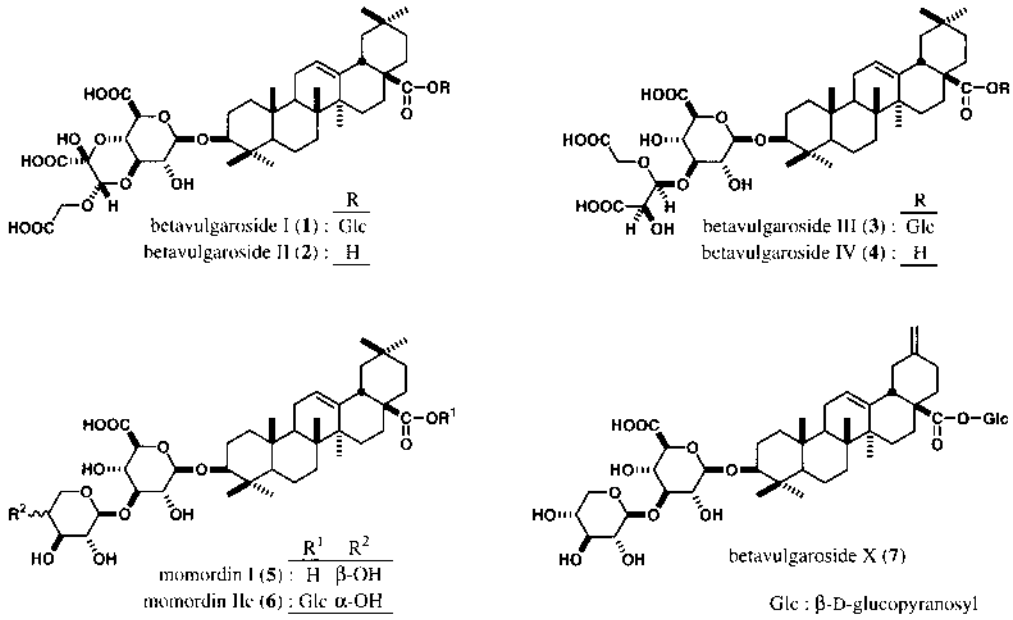

Chart 1

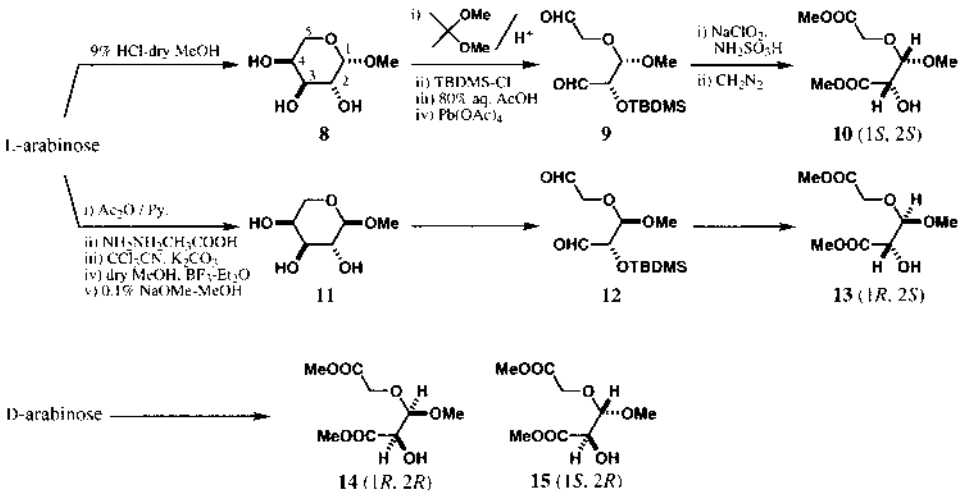

Chart 2

acid, but no evidence for the stereostructure of an acetal-type substituent in **3** and **4** was obtained.

Synthesis of the 2″-Diastereoisomer of Betavulgaroside IV Although four possible stereostructures were considered for the acetal-type substituent of **4**, we have presumed at the beginning that it might be the same configuration as the 1″- and 2″-positions of the terminal monosaccharides in momordin IIc (**6**) and betavulgaroside X (**7**), which coexisted with **3** and **4** in sugar beet. Consequently, we carried out the synthesis of the 2″-diastereoisomer (**18**) with a 1″(*S*),2″(*S*)-configuration from the α-L-arabinopyranosyl moiety in **5**.

Since the absolute configurations of the component monosaccharides in **5** were not characterized, **5** was treated with 5% aqueous sulfuric acid–dioxane (1 : 1) to give the monosaccharides, which were determined to be D-glucuronic acid and L-arabinose by GLC analysis[10] of their condensates with L-cysteine methyl ester. Momordin I (**5**), thus the confirmed absolute stereostructure, was subjected to methylation with diazomethane and subsequent acetonization of the 3″- and 4″-*cis*-dihydroxyl moiety with 2,2-dimethoxypropane to provide the acetonide (**16**), quantitatively. After protection of other hydroxyl groups in **16** with chloromethyl methyl ether (MOM-Cl), the acetonide group was removed by treatment with 80% aqueous acetic acid to furnish the diol (**17**) in 86% yield. Oxidative cleavage of the 3″ and 4″-dihydroxyl moiety in **17** with $Pb(OAc)_4$ gave a dialdehyde, which was oxidized with $NaClO_2$ and NH_2SO_3H followed by diazomethane methylation to give the 2″-diastereoisomer (**18**) in 35.4% yield. On the other hand, diazomethane methylation of **4** furnished the tetramethyl ester, which was protected with MOM-Cl to give 2′,2″,4′-tri-*O*-methoxymethylbetavulgaroside IV tetramethyl ester (**19**).

In the positive-ion FAB-MS spectra of **18** and **19**, a common quasimolecular ion peak was observed at *m/z* 1005 $(M+Na)^+$, and the molecular formula of both **18** and **19** was determined to be $C_{51}H_{82}O_{18}$ by high-resolution MS measure-

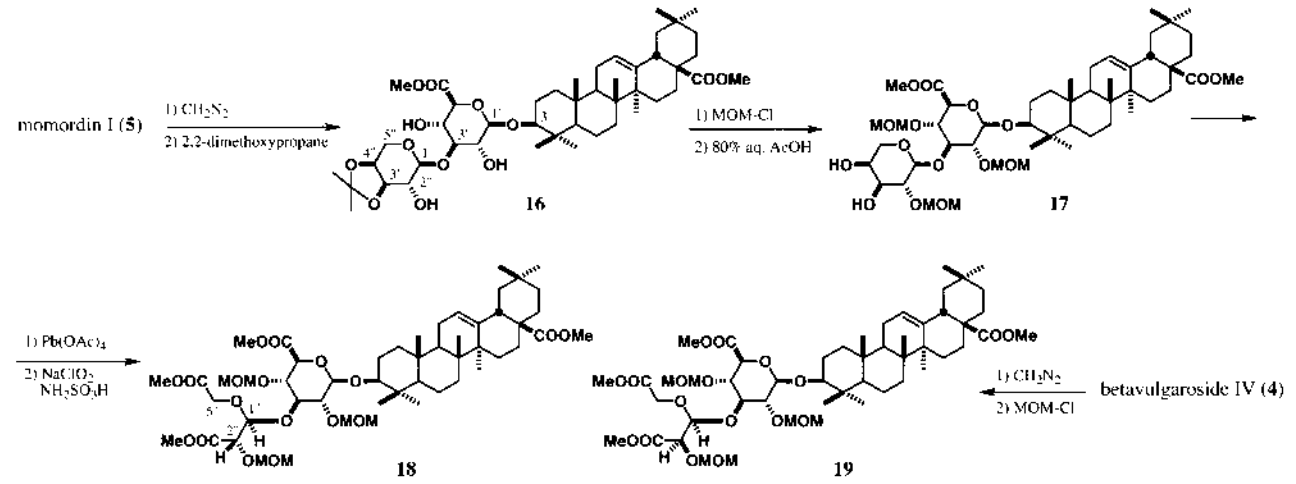

Chart 3

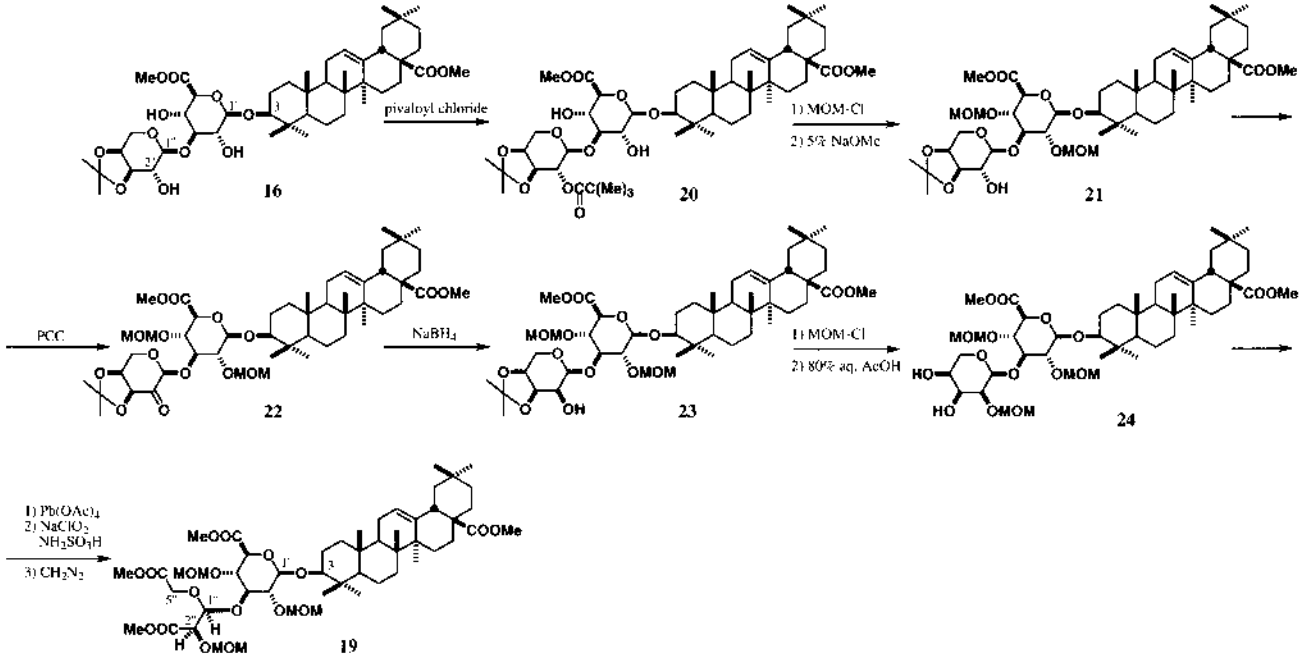

Chart 4

ment. The IR and ^{1}H-NMR ($CDCl_3$) spectra of **18** and **19** strongly resembled each other, except for the proton signals due to their acetal-type substituents [**18**: δ 4.31 (d, J=4.6 Hz, 2″-H), 5.35 (d, J=4.6 Hz, 1″-H); **19**: δ 4.50 (d, J=3.3 Hz, 2″-H), 5.50 (d, J=3.3 Hz, 1″-H)]. On the basis of this evidence, the possibility of a 1″(*S*),2″(*S*)-configuration could be ruled out from the absolute stereostructures of the acetal-type substituent in **4**.

Absolute Stereostructure of Betavulgaroside IV Next, the synthesis of **19** with the 1″(*S*),2″(*R*)-configuration was carried out from the α-L-ribopyranosyl derivative (**23**). The 2″-hydroxyl group of the terminal D-xylose moiety in the 3″,4″-acetonide (**16**) was presumed to be less hindered than the 2′- and 4′-hydroxyl groups of the inner D-glucuronic acid moiety, which were adjacent to the sapogenol and the 3′-sugar parts. After several preliminary experiments under a mild acylation condition, the 3″,4″-acetonide (**16**) was subjected to selective acylation with pivaloyl chloride in the presence of dimethylaminopyridine (DMAP) in pyridine at 0 °C to give the 2″-pivaloyl derivative (**20**) in 78% yield. In the positive-ion FAB-MS spectrum of **20**, a quasimolecular ion peak was observed at *m/z* 939 $(M+Na)^+$ and its molecular formula was determined to be $C_{51}H_{80}O_{14}$ which indicated it as a monopivaloyl derivative. The position of the pivaloyl group in **20** was clarified by the examination of its ^{1}H-NMR data. Thus, the ^{1}H-NMR spectrum of **20** showed the presence of a 2″-pivaloyl α-D-arabinopyranosyl moiety [δ 1.19 (9H, s, pivaloyl methyls), 4.64 (d, J=6.1 Hz, 1″-H), 4.98 (t-like, J=*ca.* 6 Hz, 2″-H)] together with a β-D-glucopyranosyl moiety [δ 4.31 (d, J=7.0 Hz, 1′-H)] and the sapogenol part.

After protection of the 2′- and 4′-hydroxyl groups in **20** with a methoxymethyl (MOM) group, the 2″-pivaloyl group was removed by treatment with 5% sodium methoxide (NaOMe) in methanol to give **21** in 60% yield. Oxidation of

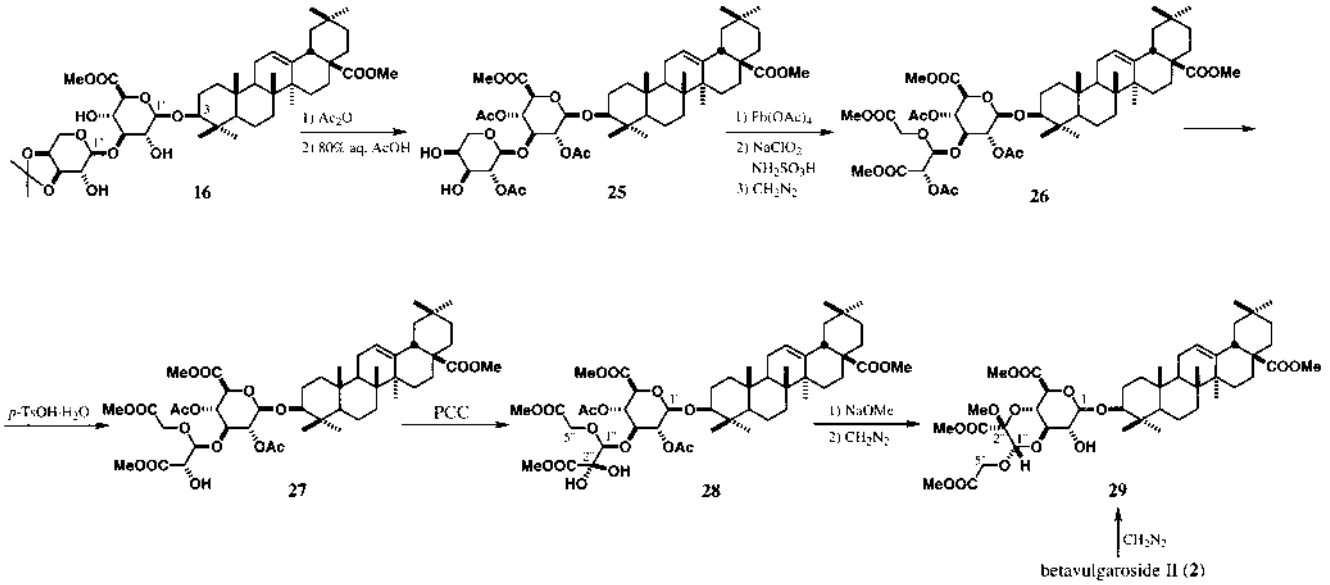

Chart 5

21 with pyridinium chlorochromate (PCC) in benzene furnished an unstable ketone (**22**), which was immediately treated with sodium borohydride ($NaBH_4$) in methanol to yield the α-L-ribopyranosyl derivative (**23**) in 53% yield. The stereostructure of the α-L-ribopyranosyl moiety in **23** was characterized by comparison of the anomeric proton signals in the ^{1}H-NMR data ($CDCl_3$) for **23** [δ 4.40 (d, J=7.6 Hz, 1′-H) and 5.02 (d, J=3.9 Hz, 1″-H)] with those for **21** [δ 4.38 (d, J=7.6 Hz, 1′-H) and 4.46 (d, J=7.9 Hz, 1″-H)]. The 2″-hydroxyl group of **23** was protected with a MOM group and then the isopropylidene group was removed with an acid treatment to give the 3″- and 4″-dihydroxyl derivative (**24**) in 86% yield. Finally, the diol (**24**) was converted to **19** through the following successive reactions as described in the case of **18**: 1) $Pb(OAc)_4$ cleavage of the 3″- and 4″-dihydroxyl moiety giving a dialdehyde derivative; 2) oxidation of the aldehyde group to the dicarboxyl derivative; 3) diazomethane methylation. Since synthetic **19** has been identified by comparison of its physical data with those of an authentic sample derived from **4**, the absolute stereostructure of **4** was determined as shown.

Chemical Correlation of Betavulgaroside II with Momordin I Previously, we have reported the stereostructure of **1** and **2** on the basis of chemical and physicochemical evidence.[3] This time, the absolute stereostructures of **1** and **2** were confirmed by the chemical transformation of the dioxolane-type substituent in **2** from the α-L-arabinopyranosyl moiety in **5**. After acetylation of the acetonide derivative (**16**) with acetic anhydride in the presence of DMAP, the isopropylidene group was removed by acid treatment to give the 3″,4″-dihydroxyl derivative (**25**) in 85% yield. The $Pb(OAc)_4$ cleavage of **25** furnished the dialdehyde, which was then subjected to an oxidation reaction with $NaClO_2$ and NH_2SO_3H followed by diazomethane methylation to provide the triacetate (**26**) in 63% yield. Among the three acetoxyl groups of **26**, the 2″-acetoxyl group of the tartronaldehydic acid moiety is expected to be more unstable than the other two acetoxyl groups of the D-glucuronic acid moiety. After a preliminary experiment using various acid or alkaline conditions, selective deacetylation of **26** with *p*-toluene sulfonic acid in methanol–chloroform (4 : 1) at 40 °C was found to furnish the diacetate (**27**) in 55% yield. The ^{1}H-NMR spectrum ($CDCl_3$) of **27** showed signals due to a methyl 2′,4′-di-*O*-acetyl-β-D-glucopyranosiduronate moiety [δ 2.06, 2.09 (both s, acetyl methyls), 3.94 (d, J=9.9 Hz, 5′-H), 4.10 (dd, J=9.2, 9.6 Hz, 3′-H), 4.46 (d, J=8.0 Hz, 1′-H), 5.04 (dd, J=8.0, 9.2 Hz, 2′-H), 5.14 (dd, J=9.6, 9.9 Hz, 4′-H)] together with an acetal-type substituent [δ 4.17, 4.38 (ABq, J=16.5 Hz, 5″-H_2), 4.31 (br d, J=*ca.* 9 Hz, 2″-H), 5.01 (br s, 1″-H)]. Oxidation of **27** with PCC yielded an unstable product (**28**).[11] The ketal structure (**28**) was presumed on the basis of the positive-ion FAB-MS data of **28**, which showed a sole quasimolecular ion peak at *m/z* 973 $(M+Na)^+$. The oxidation product (**28**) was subjected to deacetylation with 0.1% NaOMe in methanol followed by diazomethane methylation to give **29** in 29% yield. The synthetic **29** was identical with an authentic betavulgaroside II pentamethyl ester.

Experimental

The following instruments were used to obtain physical data: Melting points, Yanagimoto micro-melting point apparatus MP-500D (values are uncorrected); specific rotations, Horiba SEPA-300 digital polarimeter (l=5 cm); IR spectra, Shimadzu FTIR-8100 spectrometer; FAB-MS and high-resolution MS, JEOL JMS-SX 102A mass spectrometer; ^{1}H-NMR spectra, JEOL EX-270 (270 MHz) and JNM LA-500 (500 MHz) spectrometer; ^{13}C-NMR spectra, JEOL EX-270 (68 MHz) and JNM LA-500 (125 MHz) spectrometer with tetramethylsilane as an internal standard.

The following experimental conditions were used for chromatography: ordinary-phase silica gel column chromatography, Silica gel BW-200 (Fuji Silysia Chemical, Ltd., 150—350 mesh); reversed-phase silica gel column chromatography, Chromatorex ODS DM1020T (Fuji Silysia Chemical, Ltd., 100—200 mesh); TLC, pre-coated TLC plates with Silica gel $60F_{254}$ (Merck, 0.25 mm) (ordinary phase) and Silica gel RP-18 $60F_{254}$ (Merck, 0.25 mm) (reversed phase); reversed-phase HPTLC, pre-coated TLC plates with Silica gel RP-18 $60WF_{254S}$ (Merck, 0.25 mm); detection was achieved by spraying with 1% $Ce(SO_4)_2$–10% aqueous H_2SO_4 and heating.

Preparation of Methyl Arabinoside A solution of L-arabinose (Nakalai Tesque, 50 mg) in 9% HCl–dry MeOH (5 ml) was stirred at 80 °C for 3 h. The reaction mixture was neutralized with IRA-400 (OH^- form). Removal of the solvent under reduced pressure gave the crude product, which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (5 : 1)] to give methyl β-L-arabinopyranoside (**8**, 40 mg, 73.2%). Methyl α-

D-arabinopyranoside (**11**) was also prepared from D-arabinose (Nakalai Tesque) by the procedure described above. Compounds **8** and **11** were identified by TLC, $[\alpha]_D$ values, and ^{1}H- and ^{13}C-NMR spectral comparisons with authentic samples.[12)]

A solution of L-arabinose (5.0 g) in dry pyridine (16 ml) was treated with Ac_2O (8 ml), and the whole mixture was stirred at 50 °C for 10 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave tetra-*O*-acetyl-L-arabinose (quant.). A solution of tetra-*O*-acetyl-L-arabinose (2.0 g) in dry *N*,*N*-dimethylformamide (DMF, 10 ml) was treated with $NH_2NH_2 \cdot CH_3COOH$ (709 mg, 1.2 eq), and the whole mixture was stirred at room temperature (25 °C) for 3 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave the crude product, which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (5 : 1)] to give 2,3,4-tri-*O*-acetyl-L-arabinose (0.56 g) and tetra-*O*-acetyl-L-arabinose (1.28 g) was recovered. A solution of 2,3,4-tri-*O*-acetyl-L-arabinose (550 mg) in dry CH_2Cl_2 (5.0 ml) was treated with CCl_3CN (1.4 ml, 5 eq) in the presence of K_2CO_3 (550 mg, 2 eq), and the whole mixture was stirred at room temperature (25 °C) for 4 h. The reaction mixture was poured into brine and the whole was extracted with AcOEt. The AcOEt extract was washed brine, then dried over Na_2SO_4. Removal of the solvent under reduced pressure gave *O*-(2,3,4-tri-*O*-acetyl-α-L-arabinosyl)trichloroacetimidate (762 mg, 91.0%). A solution of L-arabinosyl imidate (760 mg) was treated with dry MeOH (1.0 ml) and $BF_3 \cdot Et_2O$ (80 ml) and the whole mixture was stirred at room temperature (25 °C) for 15 min. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product, which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (3 : 1)] to give a methyl 2,3,4-tri-*O*-acetyl-α-L-arabinopyranoside (420 mg, 80.2%). A solution of a methyl 2,3,4-tri-*O*-acetyl-α-L-arabinopyranoside (420 mg) in 0.1% NaOMe–MeOH (5.0 ml) was stirred at room temperature (25 °C) for 1 h. The reaction mixture was neutralized with Dowex HCR W2 (H^+ form). Removal of the solvent under reduced pressure gave methyl α-L-arabinopyranoside (**8**, 230 mg, 97.0%). Methyl α-D-arabinopyranoside was also prepared from D-arabinose by the procedure described above. Methyl α-L- and D-arabinopyranosides were identified by comparison of their physical data ($[\alpha]_D$ values, positive-ion FAB-MS, and ^{1}H- and ^{13}C-NMR spectra) with reported values.[13)]

Syntheses of Acetal-Type Substituent Analogues (10, 13, 14, 15) A solution of **8** (50 mg) in dry DMF (4.0 ml) was treated with 2,2-dimethoxypropane (0.065 ml, 2 eq) in the presence of *p*-TsOH (2 mg) and the whole mixture was stirred at room temperature (25 °C) for 3 h. The reaction mixture was neutralized with IRA-400 (OH^- form). Removal of the solvent under reduced pressure gave the acetonide (60.1 mg, 96.6%), a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.37, 1.57, 3.54 (3H, all s, 3, 4, 1-OMe), 3.92 (2H, m, 5-H_2), 3.77 (1H, m, 2-H), 4.17 (1H, dd, J=5.8, 6.1 Hz, 3-H), 4.22 (1H, ddd, J=2.2, 2.4, 5.8 Hz, 4-H), 4.72 (1H, d, J=3.7 Hz, 1-H).

A solution of the acetonide (60 mg) in dry DMF (4 ml) was treated with *tert*-butyldimethylsilyl chloride (TBDMS-Cl, 80.0 mg, 4 eq) in the presence of imidazole (133.2 mg, 3 eq), and the whole mixture was stirred at room temperature (25 °C) for 12 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave the silyl derivative (80.7 mg, 86.2%), a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.10, 0.12 (3H each, both s, TBDMS), 1.55 (9H, s, TBDMS), 1.36, 1.52, 3.41 (3H, all s, 3, 4, 1-OMe), 3.74 (1H, ddd, J=1.0, 3.3, 6.6 Hz, 4-H), 3.92 (2H, br s, 5-H_2), 4.12 (1H, t, J=6.6 Hz, 3-H), 4.20 (1H, br d, 2-H), 4.55 (1H, d, J=3.4 Hz, 1-H).

A solution of the silyl derivative (60 mg) in 80% aq. AcOH (10 ml) was stirred at room temperature (25 °C) for 2 h. Removal of the solvent under reduced pressure gave a crude product which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (10 : 1)] to give the diol (29 mg, 41.1%), a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.10, 0.12 (3H each, both s, TBDMS), 0.92 (9H, s, TBDMS), 3.41 (3H, all s, 1-OMe), 3.74 (1H, dd, J=1.7, 12.5 Hz, 4-H), 3.93 (1H, m, 5-H_2), 3.90 (1H, m, 3-H), 3.93 (2H, m, 5-H_2), 4.20 (1H, m, 2-H), 4.67 (1H, d, J=2.9 Hz, 1-H).

A solution of the diol (29 mg) in dry benzene (3 ml) was treated with $Pb(OAc)_4$ (46.2 mg, 1 eq), and the whole mixture was stirred at 5 °C for 10 min. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. $NaHCO_3$ and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave the dialdehyde (**9**, 17.8 mg, 61.8%), a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.10, 0.12 (3H each, both s, TBDMS), 0.93 (9H, s, TBDMS), 3.47 (3H, all s, 1-OMe), 4.20 (1H, dd, J=1.0, 4.0 Hz, 2-H), 4.24 (2H, br s, 5-H_2), 4.24 (1H, d, J=4.0 Hz, 1-H), 9.68 (1H, d, J=1.0 Hz, 3-H), 9.71 (1H, br s, 4-H).

A solution of **9** (17 mg) in 1,4-dioxane–H_2O (3 : 1, v/v, 4 ml) was treated with $NaClO_2$ (23.3 mg, 4 eq) and NH_2SO_3H (12.9 mg, 2 eq), and the whole mixture was stirred at room temperature (25 °C) for 3 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product. A solution of crude product in MeOH (0.5 ml) was treated with CH_2N_2 (5 ml) and the whole mixture was stirred at room temperature (25 °C) for 30 min. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (10 : 1)] to give **10** (11.6 mg, 81.2%). **13**, **14**, and **15** were also prepared from methyl β-D-arabinopyranoside, methyl α-L-arabinopyranoside, and methyl α-D-arabinopyranoside by the procedure described above.

10: Colorless oil, $[\alpha]_D^{25}$ +6.0° (c=0.1, MeOH). IR (KBr): 3475, 1746 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_8H_{14}O_7Na$ $(M+Na)^+$: 245.0637. Found: 245.0637. ^{1}H-NMR (pyridine-d_5) δ: 3.55, 3.62, 3.73 (3H each, all s, 1, 3, 4-OMe), 4.63 (2H, s, 5-H_2), 4.81 (1H, d, J=5.6 Hz, 2-H), 5.19 (1H, d, J=5.6 Hz, 1-H). ^{13}C-NMR (pyridine-d_5) δ_C: 51.5, 51.8, 55.9 (3, 4, 1-OMe), 64.3, 73.5, 104.7, 172.4, 170.9 (5, 2, 1, 3, 4-C). Positive-ion FAB-MS *m/z*: 223 $(M+Na)^+$.

13: Colorless oil, $[\alpha]_D^{25}$ −7.6° (c=0.1, MeOH). IR (KBr): 3470, 1746 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_8H_{15}O_7$ $(M+H)^+$: 223.0817. Found: 223.0824. ^{1}H-NMR (pyridine-d_5) δ: 3.54, 3.62, 3.73 (3H, all s, 1, 3, 4-OMe), 4.63 (2H, s, 5-H_2), 4.81 (1H, d, J=5.3 Hz, 2-H), 5.19 (1H, d, J=5.3 Hz, 1-H). ^{13}C-NMR (pyridine-d_5) δ_C: 51.6, 51.8, 55.9 (3, 4, 1-OMe), 64.3, 73.5, 104.7, 172.4, 170.9 (5, 2, 1, 3, 4-C). Positive-ion FAB-MS *m/z*: 223 $(M+Na)^+$.

14: Colorless oil, $[\alpha]_D^{25}$ +10.5° (c=0.1, MeOH), IR (KBr): 3486, 1752, 1737 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_8H_{15}O_7$ $(M+H)^+$: 223.0817. Found: 223.0824. ^{1}H-NMR (pyridine-d_5) δ: 3.55, 3.62, 3.74 (3H, all s, 1, 3, 4-OMe), 4.50, 4.60 (2H, ABq, J=16.2 Hz, 5-H_2), 4.87 (1H, d, J=5.3 Hz, 2-H), 5.24 (1H, d, J=5.3 Hz, 1-H). ^{13}C-NMR (pyridine-d_5) δ_C: 51.6, 51.8, 54.8 (3, 4, 1-OMe), 64.4, 73.2, 104.0, 172.6, 170.7 (5, 2, 1, 3, 4-C). Positive-ion FAB-MS *m/z*: 223 $(M+Na)^+$.

15: Colorless oil, $[\alpha]_D^{25}$ −7.1° (c=0.1, MeOH). IR (KBr): 3479, 1752, 1737 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_8H_{14}O_7Na$ $(M+Na)^+$: 245.0637. Found: 245.0627. ^{1}H-NMR (pyridine-d_5) δ: 3.53, 3.62, 3.73 (3H, all s, 1, 3, 4-OMe), 4.50, 4.59 (2H, ABq, J=16.2 Hz, 5-H_2), 4.87 (1H, d, J=5.2 Hz, 2-H), 5.23 (1H, d, J=5.2 Hz, 1-H). ^{13}C-NMR (pyridine-d_5) δ_C: 51.6, 51.8, 54.8 (3, 4, 1-OMe), 64.4, 73.2, 104.1, 172.7, 170.7 (5, 2, 1, 3, 4-C). Positive-ion FAB-MS *m/z*: 223 $(M+Na)^+$.

Acid Hydrolysis of 5 A solution of **5** (2 mg each) in 5% H_2SO_4–1,4-dioxane (1 : 1, v/v, 1 ml) was heated under reflux for 1 h. After cooling, the reaction mixture was neutralized with Amberlite IRA-400 (OH^- form) and the resin was filtered. After removal of the solvent *in vacuo* from its filtrate, the residue was passed through a Sep-Pak C_{18} cartridge with H_2O and MeOH. The H_2O eluate was concentrated and the residue was treated with L-cysteine methyl ester hydrochloride (2 mg) in pyridine (0.02 ml) at 60 °C for 1 h. After reaction, the solution was treated with *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (0.01 ml) at 60 °C for 1 h. The supernatant was then subjected to GLC analysis to identify the derivatives of D-glucuronic acid (i) and D-xylose (ii) from **5**. GLC conditions: column, Supelco SPR^{TM}-1, 0.25 mm (i.d.)×30 m; column temperature, 230 °C; t_R, i, 24.2 min; ii, 19.3 min.

Monoacetonide (16) An ice-cold solution of **5** (500 mg) in MeOH (3.0 ml) was treated with ethereal diazomethane (*ca.* 10 ml) until the yellow color persisted. The solution was stirred at room temperature (25 °C) for 30 min, then the solvent was removed under reduced pressure to furnish a residue. The residue was purified by normal-phase silica gel column chromatography [50 g, $CHCl_3$–MeOH (20 : 1)] to give momordin I dimethyl ester (quant.), which was found to be identical to an authentic sample. A solution of momordin Ic dimethyl ester (500 mg) in dry DMF (15.0 ml) was treated with 2,2-dimethoxypropane (0.3 ml) in the presence of *p*-TsOH·H_2O (5.0 mg) and the whole mixture was stirred at room temperature (25 °C) for 30 min. The reaction mixture was neutralized with IRA-400 (OH^- form). Removal of the solvent under reduced pressure gave a crude product which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (5 : 2)] to give the isopropylidene derivative (**16**, quant.).

16: Colorless fine crystals from $CHCl_3$–MeOH, mp 159—160 °C, $[\alpha]_D^{24}$ +27.4° (c=0.1, $CHCl_3$). High-resolution positive-ion FAB-MS: Calcd for $C_{46}H_{72}O_{13}Na$ $(M+Na)^+$: 855.4871. Found: 855.4862. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.71, 0.81, 0.92, 1.00, 1.11 (3H each, all s, *tert*-CH_3×5), 0.90 (6H, s, *tert*-CH_3×2), 1.36, 1.55 (3H each, both s, isopropylidene), 2.84 (1H, dd, J=4.2, 13.4 Hz, 18-H), 3.16 (1H, dd, J=5.2, 11.3 Hz, 3-H), 3.62, 3.82 (3H each, both s, OMe×2), 4.12 (1H, dd-like, 2″-H), 4.34 (1H, d, J=8.3 Hz, 1′-H), 4.39 (1H, d, J=7.6 Hz, 1″-H), 5.28 (1H, br s, 12-H). Positive-ion FAB-MS m/z: 855 $(M+Na)^+$.

Conversion from 16 to 17 A solution of **16** (300 mg) in dry pyridine (5.0 ml) was treated with *N*,*N*-diisopropylethylamine (2.3 ml, 16 eq) in the presence of chloromethyl ether (1.1 ml, 16 eq) and the whole mixture was stirred at 50 °C for 12 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [6.0 g, *n*-hexane–AcOEt (1 : 1)] to furnish the MOM derivative (330 mg, 90.0%). A solution of the MOM derivative in 80% aq. AcOH (10.0 ml) was stirred at 40 °C for 4 h. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [6.0 g, *n*-hexane–AcOEt (1 : 2)] to furnish **17** (280 mg, 90%).

17: A white powder. ^{1}H-NMR ($CDCl_3$) δ: 0.71, 0.80, 0.92, 0.97, 1.11 (3H each, all s, *tert*-CH_3), 0.90 (6H, s, *tert*-CH_3), 2.86 (1H, dd-like, 18-H), 3.10 (1H, dd, J=4.9, 11.0 Hz, 3-H), 3.30, 3.42, 3.45 (3H each, all s, MOM-Me), 3.62, 3.79 (3H each, both s, OMe), 4.41 (1H, d, J=7.9 Hz, 1′-H), 4.62 (1H, d, J=6.6 Hz, 1″-H), 5.27 (1H, br s, 12-H).

Conversion from 17 to 18 A solution of **17** (62 mg) in dry benzene (4.0 ml) was treated with $Pb(OAc)_4$ (32 ml, 1 eq) and the whole mixture was stirred at 5 °C for 30 min. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. $NaHCO_3$ and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product. A solution of crude product in 1,4-dioxane–H_2O (4: 1, v/v, 1 ml) was treated with $NaClO_2$ (23 ml, 4 eq) in the presence of NH_2SO_3H (12 mg, 2 eq) and the whole mixture was stirred at room temperature (25 °C) for 30 min. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product. An ice-cold solution of crude product in MeOH (1.0 ml) was treated with ethereal diazomethane (*ca.* 5 ml) until the yellow color persisted. The solution was stirred at room temperature (25 °C) for 30 min, then the solvent was removed under reduced pressure to furnish a residue. The residue was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (3 : 1)] to give **18** (22.6 mg, 35%).

18: Colorless fine crystals, mp 88—90 °C, $[\alpha]_D^{25}$ +34.6° (c=0.1, MeOH). IR (KBr): 1754, 1736, 1157, 1032 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.70, 0.79, 0.92, 0.97, 1.11 (3H each, all s, *tert*-CH_3), 0.89 (6H, s, *tert*-CH_3), 2.85 (1H, dd-like, 18-H), 3.11 (1H, dd, J=5.0, 11.2 Hz, 3-H), 3.28, 3.37, 3.40 (3H each, all s, MOM-Me), 3.62, 3.73, 3.75, 3.78 (3H each, all s, OMe), 4.31 (1H, d, J=4.6 Hz, 2″-H), 4.33, 4.41 (2H, ABq, J=16.5 Hz, 5″-H_2), 4.42 (1H, d, J=7.9 Hz, 1′-H), 5.27 (1H, br s, 12-H), 5.35 (1H, d, J=4.6 Hz, 1″-H). Positive-ion FAB-MS m/z: 1005 $(M+Na)^+$.

Conversion from 4 to 19 A solution of **4** (7 mg) in MeOH (3 ml) was treated with CH_2N_2 (10 ml) and the whole mixture was stirred at room temperature (25 °C) for 30 min. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (1 : 1)] to give a tetramethyl ester (3 mg, 42.9%). A solution of tetramethyl ester (2.5 mg) in dry CH_2Cl_2 (0.5 ml) was treated with *N*,*N*-diisopropylethylamine (0.02 ml) in the presence of chloromethyl ether (0.02 ml) and the whole mixture was stirred under reflux for 8 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [*n*-hexane–AcOEt (2 : 1)] to furnish **19** (2.6 mg, quant.).

19: Colorless fine crystals, mp 86—88 °C, $[\alpha]_D^{25}$ +14.3° (c=0.1, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{51}H_{82}O_{18}Na$ $(M+Na)^+$: 1005.5399. Found: 1005.5380. IR (KBr): 1755, 1732, 1156, 1030 cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.71, 0.79, 0.92, 0.96, 1.11 (3H each, all s, *tert*-CH_3×5), 0.90 (6H, s, *tert*-CH_3×2), 2.85 (1H, dd-like, 18-H), 3.10 (1H, dd, J=4.9, 11.2 Hz, 3-H), 3.29, 3.40, 3.44 (1H each, all s, MOM×3), 3.62, 3.73, 3.76, 3.79 (3H each, all s, OMe×4), 4.38, 4.44 (2H, ABq, J=16.5 Hz, 5″-H_2), 4.38 (1H, d, J=6.6 Hz, 1′-H), 4.50 (1H, d, J=3.3 Hz, 2″-H), 5.27 (1H, br s, 12-H), 5.50 (1H, d, J=3.3 Hz, 1″-H). Positive-ion FAB-MS m/z: 1005 $(M+Na)^+$.

Pivaloylation of 16 A solution of **16** (417 mg) in dry pyridine (10.0 ml) was treated with trimethylacetyl chloride (3.12 ml, 3 eq) in the presence of DMAP (10.0 mg), and the whole mixture was stirred at 0 °C for 3 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [0.5 g, *n*-hexane–AcOEt (3 : 1)] to furnish **20** (305 mg, 78%).

20: Colorless fine crystals, mp 208—210 °C, $[\alpha]_D^{25}$ +21.3° (c=0.1, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{51}H_{80}O_{14}Na$ $(M+Na)^+$: 939.5446. Found: 939.5432. IR (KBr): 3424, 1757, 1744, 1711, 1140 cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.67, 0.77, 0.88, 0.95, 1.07 (3H each, all s, *tert*-CH_3×5), 0.86 (6H, s, *tert*-CH_3×2), 1.19 (9H, s, pivaloyl), 1.31, 1.52 (3H each, both s, isopropylidene), 2.81 (1H, dd, J=4.2, 13.4 Hz, 18-H), 3.11 (1H, dd, J=4.3, 11.3 Hz, 3-H), 3.58, 3.76 (3H each, both s, OMe×2), 4.31 (1H, d, J=7.0 Hz, 1′-H), 4.64 (1H, d, J=6.1 Hz, 1″-H), 4.98 (1H, t-like, J=*ca.* 6 Hz, 2″-H), 5.23 (1H, br s, 12-H). Positive-ion FAB-MS m/z: 939 $(M+Na)^+$.

Isomerization of the 2″-Hydroxyl Group in 21 A solution of **20** (450 mg) in dry pyridine (10.0 ml) was treated with *N*,*N*-diisopropylethylamine (4.28 ml, 25 eq) in the presence of chloromethyl ether (1.87 ml, 25 eq), and the whole mixture was stirred at 40 °C for 8 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (10 : 1)] to furnish the MOM derivative (444 mg, 90.0%). A solution of the MOM derivative (184 mg) in 5% NaOMe–MeOH (10 ml) was stirred at 40 °C for 2 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product. An ice-cold solution of crude product in MeOH (2 ml) was treated with ethereal diazomethane (*ca.* 10 ml) until the yellow color persisted. The solution was stirred for 30 min, then the solvent was removed under reduced pressure to furnish a residue. The residue was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (5 : 1)] to give **21** (111 mg, 66%).

21: Colorless fine crystals, mp 128—130 °C, $[\alpha]_D^{25}$ +80.9° (c=0.1, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{50}H_{80}O_{15}Na$ $(M+Na)^+$: 943.5395. Found: 943.5371. IR (KBr): 3459, 1754, 1730, 1125 cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.72, 0.79, 0.92, 0.95, 1.11 (3H each, all s, *tert*-CH_3×5), 0.90 (6H, s, *tert*-CH_3×2), 1.35, 1.52 (3H each, both s, isopropylidene), 2.85 (1H, dd, J=3.3, 13.2 Hz, 18-H), 3.11 (1H, dd, J=4.9, 10.3 Hz, 3-H), 3.28, 3.40 (3H each, both s, MOM×2), 3.61, 3.78 (3H each, both s, OMe×2), 4.38 (1H, d, J=7.6 Hz, 1′-H), 4.46 (1H, d, J=6.1 Hz, 1″-H), 5.27 (1H, br s, 12-H). Positive-ion FAB-MS m/z: 943 $(M+Na)^+$.

Conversion from 21 to 23 A solution of **21** (10 mg) in dry benzene (1.0 ml) was treated with PCC (9.4 mg, 4 eq), and the whole mixture was stirred under reflux for 2 h in an N_2 atmosphere. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product (**22**). A solution of crude product (**22**) was added to dry MeOH (1.0 ml) treated with $NaBH_4$ (0.3 mg, 4 eq) and the whole mixture was stirred at room temperature (25 °C) for 30 min. The reaction mixture was poured into acetone and ice-water, then the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (5 : 1)] to furnish **23** (5.3 mg, 53%).

23: Colorless fine crystals, mp 122—124 °C, $[\alpha]_D^{25}$ +10.7° (c=0.1, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{50}H_{80}O_{15}Na$ $(M+Na)^+$: 943.5395. Found: 943.5386. IR (KBr): 3467, 1754, 1734, 1078 cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.72, 0.80, 0.93, 0.96, 1.11 (3H each, all s, *tert*-CH_3×5), 0.90 (6H, s, *tert*-CH_3×2), 1.36, 1.51 (3H each, both s, isopropylidene), 2.85 (1H, dd-like, 18-H), 3.11 (1H, dd, J=5.0, 11.2 Hz, 3-H), 3.28, 3.43 (3H each, both s, MOM×2), 3.61, 3.77 (3H each, both s, OMe×2), 3.87 (1H, m, 2″-H), 4.40 (1H, d, J=7.6 Hz, 1′-H), 5.02 (1H, d, J=3.9 Hz, 1″-H), 5.27 (1H, br s, 12-H). Positive-ion FAB-MS m/z: 943

$(M+Na)^+$.

Conversion from 23 to 24 A solution of **23** (16 mg) in dry CH_2Cl_2 (2 ml) was treated with *N*,*N*-diisopropylethylamine (33 ml, 25 eq) in the presence of chloromethyl ether (74 ml, 25 eq), and the whole mixture was stirred at 50 °C for 12 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave the MOM derivative. A solution of the MOM derivative in 80% aq. AcOH (2.0 ml) was stirred at 50 °C for 30 min. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (1 : 2)] to furnish **24** (13.8 mg, 86%).

24: A white powder. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.71, 0.79, 0.92, 0.96, 1.11 (3H each, all s, *tert*-$CH_3\times5$), 0.90 (6H, s, *tert*-$CH_3\times2$), 2.86 (1H, dd-like, 18-H), 3.11 (1H, dd, J=4.9, 11.0 Hz, 3-H), 3.30, 3.41, 3.45 (3H each, all s, MOM×2), 3.62, 3.79 (3H each, all s, OMe×2), 4.39 (1H, d, J=7.9 Hz, 1′-H), 4.95 (1H, br s, 1″-H), 5.27 (1H, br s, 12-H).

Conversion from 24 to 19 A solution of **24** (6.5 mg) in dry benzene (1.0 ml) was treated with $Pb(OAc)_4$ (3.1 ml, 1 eq), and the whole mixture was stirred at 5 °C for 30 min. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. $NaHCO_3$ and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product. A solution of crude product in 1,4-dioxane–H_2O (4 : 1, v/v, 1 ml) was treated with $NaClO_2$ (2.3 ml, 4 eq) in the presence of NH_2SO_3H (1.3 mg, 2 eq), and the whole mixture was stirred at room temperature (25 °C) for 30 min. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product. An ice-cold solution of crude product in MeOH (1.0 ml) was treated with ethereal diazomethane (*ca.* 5 ml) until the yellow color persisted. The solution was stirred at room temperature (25 °C) for 30 min, then the solvent was removed under reduced pressure to furnish a residue. The residue was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (3 : 1)] to give **19** (2.0 mg, 29.0%), which was identified by TLC, $[\alpha]_D$ values, positive-ion FAB-MS, and ^{1}H-NMR spectral comparisons with authentic samples.

Conversion from 16 to 25 A solution of **16** (259.0 mg) in dry pyridine (6.0 ml) was treated with Ac_2O (3.0 ml) in the presence of DMAP (11.0 mg, 0.3 eq) and the whole mixture was stirred at 40 °C for 12 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [5.0 g, *n*-hexane–AcOEt (2 : 1)] to give the acetate (310.3 mg, quant.). A solution of the acetate (51.0 mg) in 80% aq. AcOH (3.0 ml) was stirred at 40 °C for 4 h. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. $NaHCO_3$ and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–acetone (1 : 1)] to give **25** (41.3 mg, 85%).

25: Colorless fine crystals, mp 188—190 °C, $[\alpha]_D^{23}$ +3.3° (c=0.1, $CHCl_3$). High-resolution positive-ion FAB-MS: Calcd for $C_{49}H_{74}O_{16}Na$ $(M+Na)^+$: 941.4875. Found: 941.4877. IR (KBr) : 3475, 1751, 1736, 1067, 1038 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.71, 0.73, 0.90, 0.92, 1.10 (3H each, all s, *tert*-$CH_3\times5$), 0.89 (6H, s, *tert*-$CH_3\times2$), 2.07, 2.09, 2.13 (3H each, all s, OAc×3), 2.85 (1H, dd, J=4.2, 13.8 Hz, 18-H), 3.07 (1H, dd, J=5.6, 10.9 Hz, 3-H), 3.62, 3.74 (3H each, both s, OMe×2), 3.97 (1H, d, J=9.9 Hz, 5′-H), 4.47 (1H, d, J=8.0 Hz, 1′-H), 4.61 (1H, d, J=4.3 Hz, 1″-H), 4.78 (1H, dd, J=4.3, 6.2 Hz, 2″-H), 5.09 (1H, dd-like), 5.12 (1H, dd-like) (2′ or 4′-H), 5.27 (1H, dd-like, 12-H). Positive-ion FAB-MS *m/z*: 941 $(M+Na)^+$.

Conversion from 25 to 26 A solution of **25** (103.0 mg) in dry benzene (8.0 ml) was treated with $Pb(OAc)_4$ (99.0 mg, 2 eq), and the whole mixture was stirred at 5 °C for 10 min. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. $NaHCO_3$ and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a dialdehyde (105.7 mg). A solution of dialdehyde (105.7 mg) in 1,4-dioxane–H_2O (4 : 1, v/v, 10 ml) was treated with $NaClO_2$ (104.0 mg, 5 eq) in the presence of NH_2SO_3H (112.0 mg, 5 eq), and the whole mixture was stirred at room temperature (25 °C) for 30 min. The reaction mixture was neutralized with IRA-400 (OH^- form). Removal of the solvent under reduced pressure gave a crude product. An ice-cold solution of crude product in MeOH (5 ml) was treated with ethereal diazomethane (*ca.* 10 ml) until the yellow color persisted. The solution was stirred at room temperature for 30 min, then the solvent was removed under reduced pressure to furnish a residue. The residue was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–acetone (3 : 1)] to give **26** (69.2 mg, 63%).

26: A white powder. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.70, 0.72, 0.92, 1.11 (3H each, all s, *tert*-$CH_3\times4$), 0.89 (9H, s, *tert*-$CH_3\times3$), 2.03, 2.12, 2.14 (3H each, all s, OAc×3), 2.85 (1H, dd, J=3.7, 13.6 Hz, 18-H), 3.05 (1H, dd, J=5.6, 10.2 Hz, 3-H), 3.62, 3.73, 3.74, 3.76 (3H each, all s, OMe×4), 3.93 (1H, d, J=9.6 Hz, 5′-H), 4.12 (1H, dd, J=9.2, 10.3 Hz, 3′-H), 4.19, 4.28 (2H, ABq, J=16.1 Hz, 5″-H_2), 4.44 (1H, d, J=7.9 Hz, 1′-H), 5.09 (1H, dd, J=7.9, 10.3 Hz, 2′-H), 5.11—5.20 (3H, m, 4′, 2″, 3″-H), 5.27 (1H, dd-like, 12-H).

Deacetylation of 26 A solution of **26** (10 mg) in MeOH–$CHCl_3$ (4 : 1, v/v, 2.0 ml) was treated with p-TsOH·H_2O (4.6 mg, 1.6 eq), and the whole mixture was stirred at 40 °C for 20 h. Removal of the solvent under reduced pressure gave a crude product which was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (1 : 1)] to give **27** (6.9 mg, 55%*) and **26** (1.8 mg, 12%). (*: conversion yield)

27: Colorless fine crystals, mp 179—181 °C, $[\alpha]_D^{26}$ −1.3° (c=0.1, $CHCl_3$). High-resolution positive-ion FAB-MS: Calcd for $C_{49}H_{74}O_{17}Na$ $(M+Na)^+$: 957.4824. Found: 957.4843. IR (KBr): 3453, 1758, 1736, 1037 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.70, 0.72, 0.92, 1.11 (3H each, all s, *tert*-$CH_3\times4$), 0.89 (9H, s, *tert*-$CH_3\times3$), 2.06, 2.09 (3H each, both s, OAc×2), 2.85 (1H, dd-like, 18-H), 3.05 (1H, dd-like, 3-H), 3.62, 3.74, 3.77, 3.77 (3H each, all s, OMe×4), 3.94 (1H, d, J=9.9 Hz, 5′-H), 4.10 (1H, dd, J=9.2, 9.6 Hz, 3′-H), 4.17, 4.38 (2H, ABq, J=16.5 Hz, 5″-H_2), 4.31 (1H, br d, J=*ca.* 9 Hz, 2″-H), 4.46 (1H, d, J=8.0 Hz, 1′-H), 5.01 (1H, br s, 1″-H), 5.04 (1H, dd, J=8.0, 9.2 Hz, 2′-H), 5.14 (1H, dd, J=9.6, 9.9 Hz, 4′-H), 5.27 (1H, dd-like, 12-H). Positive-ion FAB-MS *m/z*: 957 $(M+Na)^+$.

PCC Oxidation of 27 A solution of **27** (10 mg) in dry benzene (3.0 ml) was treated with PCC (25.0 mg, 10 eq), and the whole mixture was stirred under reflux for 30 min under an N_2 atmosphere. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. $NaHCO_3$ and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product which was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (1 : 1)] to furnish **28** (4.9 mg, 44.0%).

28: A white powder. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.70, 0.72, 0.92, 1.11 (3H each, all s, *tert*-$CH_3\times4$), 0.89 (9H, s, *tert*-$CH_3\times3$), 2.07, 2.10 (3H each, both s, OAc×2), 2.85 (1H, dd-like, 18-H), 3.05 (1H, dd, J=5.3, 10.9 Hz, 3-H), 3.62, 3.74, 3.77, 3.84 (3H each, all s, OMe×4), 3.90 (1H, d, J=9.9 Hz, 5′-H), 3.94 (1H, dd, J=9.2, 9.2 Hz, 3′-H), 4.02, 4.72 (2H, ABq, J=17.1 Hz, 5″-H_2), 4.45 (1H, d, J=7.9 Hz, 1′-H), 5.02 (1H, s, 1″-H), 5.05 (1H, dd-like, 2′-H), 5.12 (1H, dd, J=9.2, 9.9 Hz, 4′-H), 5.27 (1H, dd-like, 12-H). Positive-ion FAB-MS *m/z*: 973 $(M+Na)^+$.

Deacetylation of 28 A solution of **28** (3.7 mg) in 0.1% NaOMe–MeOH (0.8 ml) was stirred at 40 °C for 6 h. The reaction mixture was neutralized with Dowex HCR W2 (H^+ form). Removal of the solvent under reduced pressure gave a crude product. An ice-cold solution of crude product in MeOH (2 ml) was treated with ethereal diazomethane (*ca.* 10 ml) until the yellow color persisted. The solution was stirred at room temperature (25 °C) for 30 min, then the solvent was removed under reduced pressure to furnish a residue. The residue was purified by normal-phase silica gel column chromatography [1.0 g, *n*-hexane–AcOEt (1 : 1)] to give **29** (1.0 mg, 29%).

29: Colorless fine crystals, mp 200—202 °C, $[\alpha]_D^{25}$ +87.1° (c=0.12, MeOH). IR (KBr): 3520, 1755, 1046 cm^{-1}. High-resolution positive-ion FAB-MS: Calcd for $C_{46}H_{70}O_{15}Na$ $(M+Na)^+$: 885.4613. Found: 885.4600. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.71, 0.83, 0.93, 1.01, 1.12 (3H each, all s, *tert*-$CH_3\times5$), 0.90 (6H, s, *tert*-$CH_3\times2$), 2.86 (1H, dd-like, 18-H), 3.19 (1H, dd, J=4.9, 10.8 Hz, 3-H), 3.27 (3H, s, 2″-OMe), 3.62, 3.73, 3.79, 3.84 (3H each, all s, OMe×4), 4.05—4.13 (3H, m), 4.19, 4.31 (2H, ABq, J=16.5 Hz, 5″-H_2), 4.43 (1H, d, J=7.5 Hz, 1′-H), 4.88 (1H, s, 1″-H), 5.28 (1H, dd-like, 12-H). Positive-ion FAB-MS *m/z*: 885 $(M+Na)^+$.

References and Notes

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