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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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 antidiabeticogenic 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 these saponins, oleanen-28-oic acid 3-monodesmosides such as betavulgarosides II (2) and IV (4) were found to show potent hypoglycemic activity, while olean-28-oic acid 3,28-bidesmosides such as betavulgarosides I (1) and III (3) lacked the activity.5) Furthermore, the structural requirements for the activity and the modes of action of the saponins for hypoglycemic activity were clarified.6) 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 Monordicia cochinensis 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(5)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 1H-NMR and 13C-NMR examination using various two-dimensional (2D) NMR analytical methods, we have reported the planar structure of the acetal-type substituent composed of a tartronaldheydic acid and glycolic acid, which was bonded to the 3'-hydroxyl group of the 3-β-β-glucopyrano-siduronic 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 methanolyis 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 (TBDSM) 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 (NaClO3) and sulfamic acid (NH2SO3H) in 75% aqueous 1,4-dioxane proceeded with removal of the 2-TBDS group to provide the 15,2S-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) trichloroacetimidate9) in the presence of boron trifluoride etherate followed by deacetylation. The β-anomer (11) was transformed to the methyl ester (13) of the 18,2S-analogue via the dialdehyde derivative (12). The methyl esters (14, 15) of the 1R,2R- and the 1S,2R-analogues were also synthesized from d-arabinose in a similar manner as above. Comparison of the 1H-NMR and 13C-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 tartronaldheydic acid and glycolic...
acid, but no evidence for the stereostructure of an acetal-type substituent in 3 and 4 was obtained.

**Synthesis of the 2′-Diastereoisomer of Betavalgaroside 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 Ic (6) and betavalgaroside 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 α-D-glucuronic acid and α-L-arabinose by GLC analysis(16) 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 NaClO₂ and NH₄SO₄ 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-methoxymethylbetavalgaroside 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 C₅₆H₇₈O₁₈ by high-resolution MS measure-
ment. The IR and 1H-NMR (CDCl₃) 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 this basis of 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 Betavagalgaroside 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 α-xylose moiety in the 3'',4''-acetetone (16) was presumed to be less hindered than the 2'- and 4'-hydroxyl groups of the inner α-glucoronic acid moiety, which were several preliminary experiments under a mild acylation condition, the 3'',4''-acetetone (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 C₅₁H₈₇O₄₄ which indicated it as a monopivaloyl derivative. The position of the pivaloyl group in 20 was clarified by the examination of its 1H-NMR data. Thus, the 1H-NMR spectrum of 20 showed the presence of a 2''-pivaloyl α-α-arabinoxyranosyl 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-α-glucopyranosyl moiety [δ 4.31 (d, J=7.0 Hz, 1''-H)] and the sapogenol part.

After protection of the 2'α- 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
with pyridinium chlorochromate (PCC) in benzene furnished an unstable ketone (22), which was immediately treated with sodium borohydride (NaBH₄) in methanol to yield the α-l-rubropapsyl moiety (23) in 53% yield. The stereostructure of the α-l-rubropapsyl moiety in 23 was characterized by comparison of the anomic proton signals in the ¹H-NMR data (CDCl₃) 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''-hydroxy 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''-dihydroxy 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''-dihydroxy 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 1**

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-arabinofuranosyl 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''-diol derivative (25) in 85% yield. The Pb(OAc)₄ cleavage of 25 furnished the dialdehyde, which was then subjected to an oxidation reaction with NaClO₄ and NH₄SO₄ 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 tarrtonaldeydic acid moiety is expected to be more unstable than the other two acetoxyl groups of the α-glucuronic acid moiety. After a preliminary experiment using various acid or alkaline conditions, selective deacylation 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 ¹H-NMR spectrum (CDCl₃) of 27 showed signals due to a methyl 2',4'-di-O-acetyl-β-¿-glucopyranosiduronic 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 acetate-type substituent [δ 4.17, 4.38 (ABq, J=16.5 Hz, 5''-H), 4.31 (br d, J=ca. 9 Hz, 2''-H), 5.01 (brs, 1''-H)]. Oxidation of 27 with PCC yielded an unstable product (28).³³ The ketol 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 deacylation 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; ¹H-NMR spectra, JEOL EX-270 (270 MHz) and JNM LA-500 (500 MHz) spectrometers; ¹³C-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 60F₂₅₄ (Merck, 0.25 mm) (ordinary phase) and Silica gel RP-18 60F₂₅₄ (Merck, 0.25 mm) (reversed phase); reversed-phase HPTLC, pre-coated TLC plates with silica gel RP-18 60F₂₅₄ (Merck, 0.25 mm); detection was achieved by spraying with 1% Ce(SO₄)₃–10% aqueous H₂SO₄ 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 (8:1)] to give methyl β-¿-arabinofuranoside (8, 40 mg, 73.2%). Methyl α-
A solution of \( \alpha \)-arabinoside (5.0 g) in dry pyridine (16 ml) was treated with AcO (8 ml), and the whole mixture was stirred at 50°C for 10h. 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-\( \alpha \)-arabinose (quant.). A solution of tetra-O-acetyl-\( \alpha \)-arabinose (2.0 g) in dry N,N-dimethylformamide (DMF, 10 ml) was treated with \( \text{NH}_2\text{NH}_2\cdot\text{HCl} \) (709 mg, 1.2 eq.), and the whole mixture was stirred at room temperature (25°C) for 3h. 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 (\( \eta \)-hexane-AcOEt (5:1) to give 2,3,4-tri-O-acetyl-\( \alpha \)-arabinose (0.36 g) and tetra-O-acetyl-\( \alpha \)-arabinose (1.28 g) was recovered. A solution of 2,3,4-tri-O-acetyl-\( \alpha \)-arabinose (550 mg) in dry \( \text{CH}_2\text{Cl}_2\) (5.0 ml) was treated with \( \text{CCL}_3\text{CN} \) (1.4 ml, 5 eq.) in the presence of \( \text{K}_2\text{CO}_3 \) (550 mg, 2 eq.), and the whole mixture was stirred at room temperature (25°C) for 4h. The reaction mixture was poured into brine and the whole was extracted with AcOEt. The AcOEt extract was washed with brine, then dried over NaSO\(_4\). Removal of the solvent under reduced pressure gave a product, which was purified by normal-phase silica gel column chromatography (\( \eta \)-hexane-AcOEt (3:1) to give a methyl 2,3,4-tri-O-acyl-\( \alpha \)-arabinose (92 mg). A solution of methyl 2,3,4-tri-O-acyl-\( \alpha \)-arabinopyranoside (420 mg) in 0.1% NaOMe-MeOH (5.0 ml) was stirred at room temperature (25°C) for 1h. The reaction mixture was neutralized with Dowex HCR W2 (H\(^+\) form). Removal of the solvent under reduced pressure gave methyl \( \alpha \)-arabinopyranoside (8, 230 mg, 97.0%). Methyl 4-\( \alpha \)-arabinopyranoside was also prepared from \( \alpha \)-arabinoside by the procedure described above. Methyl 2-\( \alpha \)- and 3-\( \alpha \)-arabinopyranosides were identified by comparison of their physical data (\( \nu \)\text{O} values, positive-ion FAB-MS, and \( \eta \)-NMR spectra) and reported values.15

**Syntheses of Acretyl-Substituted 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 \( \text{p-TsOH} \) (2 mg) and the whole mixture was stirred at room temperature (25°C) for 3h. The reaction mixture was neutralized with IRA-400 (OH\(^-\) form). Removal of the solvent under reduced pressure gave the acetamide (60 mg, 97.6%), a colorless oil. 

**Acid Hydrolysis of 5**

A solution of the acetamide (60 mg) in dry DMF (4 ml) was treated with tert-butylidimethylsilyl chloride (TBDMSCl, 0.80 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 12h. 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. 

**Acid hydrolysis 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 30min, then the solution was removed under reduced pressure to furnish a residue. The residue was purified by normal-phase silica gel column chromatography (\( \eta \)-hexane-AcOEt (5:2) to give the isopropylidene derivative (16), which was found to be identical to an authentic sample. A solution of \( \alpha \)-methyl 1,3-dimethyl ester (500 mg in dry DMF (15.0 ml) was treated with 2,2-dimethoxypropane (0.3 ml) in the presence of \( \text{p-TsOH} \) (H\(_2\text{O}\) (5.0 mg) and the whole mixture was stirred at room temperature (25°C) for 30min. 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 (\( \eta \)-hexane-AcOEt (5:2) to give the isopropylidene derivative (16), quant.);
16: Colorless fine crystals from CHCl₃–MeOH, mp 159–160°C, [α]D²⁰ +27.4° (c=0.1, CHCl₃). High-resolution positive-ion FAB-MS: Calculated for C₁₅H₁₀O₄Na (M+Na⁺): 585.4871. Found: 585.4862. 1H-NMR (270 MHz, CDCl₃), δ: 0.71, 0.81, 0.92, 1.00, 1.11 (3H each, all s, tert-CH₂-X), 0.59 (6H, s, tert-CH₃), 2.16 (3H, s, Me), 5.31–5.33 (2H, m), 5.37 (1H, dd, J=4.6, 1H-1'), 6.76 (1H, dd, J=4.6, 1H-1'), 7.03 (1H, d, J=4.6, 1H-1'), 4.38 (1H, d, J=6.6 Hz, 1H-2'), 4.50 (1H, d, J=3.3 Hz, 2H-2'), 5.27 (1H, s, 12-H), 5.50 (1H, d, J=3.3 Hz, 1H'), 9.65 (1H, br s, MeOH). 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 trimethylchlorosilane (3.12 ml, 3 eq) in the presence of DMAP (10.0 mg), and the 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 NaHCO₃, and brine, then dried over MgSO₄. Removal of the solvent under reduced pressure gave a product which was purified by normal-phase silica gel chromatography (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 [n-hexane–AcOEt (1:2)] to furnish 17 (280 mg, 90%).

17: A white powder. 1H-NMR (270 MHz, CDCl₃), δ: 0.71, 0.80, 0.82, 0.97, 1.11 (3H each, all s, tert-CH₂), 0.59 (6H, s, tert-CH₃), 2.09 (1H, dd, 1H-2'), 1.30 (7H, dd, J=5.0, 7.0 Hz, 1H), 2.23 (3H, s, Me), 3.15–3.26 (2H each, all s, MOM-Me), 3.60 (4H, OMe), 4.41 (1H, d, J=7.9 Hz, 1H'), 4.46 (1H, d, J=6.6 Hz, 1H), 5.27 (1H, brs, 12-H).

Conversion from 17 to 18 A solution of 17 (62 mg) in dry benzene (4.0 ml) was treated with Pbr(OAc)₂ (32 ml, 1 eq) and the mixture was warmed 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 NaHCO₃ and brine, then dried over MgSO₄. Removal of the solvent under reduced pressure gave a crude product. A solution of crude product in 1,4-dioxane–H₂O (4:1, v/v, 1 ml) was treated with NaClO (23.3 mg, 0.2 eq) in the presence of NH₄Cl (12 mg, 2 eq) and the 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 MgSO₄. Removal of the solvent under reduced pressure gave a product. An ice-cold solution of crude product in MeOH (1.0 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 [n-hexane–AcOEt (3:1)] to give 18 (22.6 mg, 35%).

18: Colorless fine crystals, mp 88−89°C, [α]D²⁰ +34.6° (c=0.1, MeOH). IR (KBr): 1754, 1736, 1157, 1032 cm⁻¹. 1H-NMR (CDCl₃), δ: 0.70, 0.79, 0.97 (3H each, all s, tert-CH₂), 0.59 (6H, s, tert-CH₃), 2.86 (1H, dd, 1H-2'), 2.68 (3H, s, Me), 2.85 (1H, dd, 1H-3'), 3.11 (1H, dd, J=5.0, 11.2 Hz, 3H), 3.28, 3.37 (3H each, all s, OMe), 4.31 (1H, d, J=4.6 Hz, 2H'), 4.33, 4.41 (2H, ABq, J=16.5 Hz, 5'H'), 4.42 (1H, d, J=7.9 Hz, 1H'), 5.27 (1H, brs, 12-H), 5.35 (1H, d, J=4.6 Hz, 1H'), 9.98 ppm (1H, brs, MeOH). 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 CH₃ONO₂ (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 CHCl₃ (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 sat. aq NaHCO₃ and brine, then dried over MgSO₄. 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, [α]D²⁰ +14.3° (c=0.1, MeOH). High-resolution positive-ion FAB-MS: Calculated for C₁₅H₁₀O₄Na (M+Na⁺): 593.5395. Found: 593.5386. IR (KBr): 3467, 1754, 1736, 1078 cm⁻¹. 1H-NMR (270 MHz, CDCl₃), δ: 0.70, 0.79, 0.92, 1.01 (3H each, all s, tert-CH₂), 0.59 (6H, s, tert-CH₃), 2.88 (1H, dd, 1H-2'), 3.09 (1H, dd, J=4.9, 11.2 Hz, 3H), 3.29, 3.40 (1H each, all s, OMe), 3.62, 3.73, 3.76, 3.79 (3H each, all s, OMe×4), 4.38, 4.42 (2H, ABq, J=16.5 Hz, 5'H') ppm. Positive-ion FAB-MS m/z: 593.5395 (M+Na⁺).
lution of crude product in MeOH (5 ml) was treated with ethereal diisopropylamine (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–AcOEt (1:1)] to give 26 (69.2 mg, 63%).

26. A white powder. H-NMR (CDCl₃, 270 MHz) δ 0.70, 0.72, 0.92, 1.11 (3H each, s, tert-CH₃-H), 0.89 (9H, s, tert-CH₂), 2.03, 2.12, 2.14 (3H each, s, OMe×2), 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), 4.44 (1H, dd, 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', 5'-H), 5.27 (1H, dd, like-12-H).

Decaytation of 26: A solution of 26 (10 mg) in MeOH–CHCl₃ (4:1, v/v) was treated with P-TOSOH·H₂O (4.6 mg, 0.006 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 28 (6.9 mg, 55%) and 26 (1.8 mg, 12%). *(conversion yield)

27. Colorless fine crystals, mp 179–181°C (C₂H₅OH) 0.13 (v = 0.1, CHCl₃). High-resolution positive-ion FAB-MS: Calcd for C₀₆H₁₀O₃·H₂O: 957.4683. Found: 957.4683. IR (KBr) 3429, 1758, 1736, 1637 cm⁻¹. H-NMR (CDCl₃, 270 MHz) δ 0.70, 0.72, 0.92, 1.11 (3H each, all s, tert-CH₃-H), 0.89 (9H, s, tert-CH₂), 2.06, 2.09 (3H each, both s, OMe×2), 2.85 (1H, dd, like-12-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), 4.31 (1H, brd, J = ca. 9 Hz, 2'-H), 4.46 (1H, dd, 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 N₂ atmosphere. The reaction mixture was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was washed with sat. aq. NaHCO₃, and then dried over MgSO₄. 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%).

28. A white powder. H-NMR (CDCl₃, 270 MHz) δ 0.70, 0.72, 0.92, 1.11 (3H each, all s, tert-CH₃-H), 0.89 (9H, s, tert-CH₂), 2.07, 2.10 (3H each, both s, OMe×2), 2.85 (1H, dd, like-12-H), 3.05 (1H, dd, like-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), 4.45 (1H, d, J = 7.9 Hz, 1'-H), 5.02 (1H, s, 1'-H), 5.03 (1H, dd, like-12-H), 5.12 (1H, dd, 2'-H), 5.27 (1H, dd, like-12-H). Positive-ion FAB-MS m/z: 973 (M+Na)⁺.

Decaytation of 28: A solution of 28 (3.7 mg) in 0.1% NaOMe–MeOH (8.0 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 (C₂H₅OH) 0.19 (v = 0.12, MeOH). IR (KBr): 3520, 1755, 1046 cm⁻¹. High-resolution positive-ion FAB-MS: Calcd for C₀₆H₁₀O₃·H₂O·Na (M+Na)⁺: 885.4613. Found: 885.4600. H-NMR (CDCl₃, 270 MHz) δ 0.71, 0.83, 0.93, 1.01, 1.12 (3H each, all s, tert-CH₃-H), 0.50 (9H, s, tert-CH₂), 2.96 (1H, dd, like-12-H), 3.19 (1H, dd, J = 4.9, 10.8 Hz, 3-H), 3.27 (2H, s, OMe×2), 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), 4.43 (1H, dd, J = 7.5 Hz, 1'-H), 4.48 (1H, s, 1'-H), 5.28 (1H, dd, like-12-H). Positive-ion FAB-MS m/z: 885 (M+Na)⁺.

References and Notes


8) This work was partly reported in our preliminary communication:


11) Since the positive-ion FAB-MS of 27 showed the quasimolecular ion peak at m/z 973 (M+Na)+, the ketone (27) partly existed as the ketal form.
