Highly Oxygenated Monoterpene Acylglucosides from *Spiraea cantoniensis*

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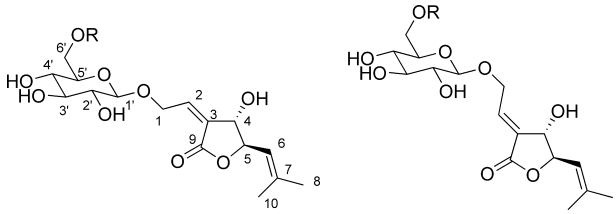
Received October 30, 2009

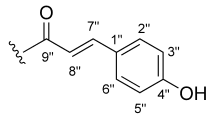
Six new monoterpene acylglucosides named kodemariosides A−F (**1**−**6**) were isolated from the leaves and flowers of *Spiraea cantoniensis*. Their absolute structures including a highly oxygenated monoterpene aglycon part were determined by NMR experiments and chemical derivatization.

In recent years, in the search for effective intestinal α-glucosidase inhibitors from natural sources, much attention has been paid to the development of physiological functional foods and lead compounds for use as potential antidiabetic agents.[1] In the course of a continuing search for such inhibitors from cultivated temperate plants from Japan, we have isolated three flavonol acylglycosides from the flowers of *Spiraea cantoniensis* Lour. (Rosaceae) as rat intestinal maltase inhibitors.[2] *S. cantoniensis* is an ornamental deciduous shrub. There have been only a few reports on the chemical constituents of this plant,[3−5] but no distinctive medicinal usage is so far known. During the isolation of the active principles above,[2] we also found a series of novel monoterpene acylglucosides (**1**−**6**) in the less active fractions from the flowers and leaves of this plant. In this article, we describe the isolation and structural determination of **1**−**6** from *S. cantoniensis*.

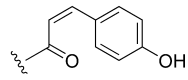


1: R = *E*-*p*-coumaroyl
2: R = *Z*-*p*-coumaroyl
5: R = *E*-caffeoyl

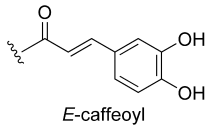
3: R = *E*-*p*-coumaroyl
4: R = *Z*-*p*-coumaroyl
6: R = *E*-caffeoyl



E-*p*-coumaroyl



Z-*p*-coumaroyl



E-caffeoyl

Results and Discussion

Flowers of *S. cantoniensis* were extracted and fractionated by a series of chromatographic steps to yield three new monoterpene acylglucosides, named kodemariosides A (**1**), E (**5**), and F (**6**). A further search for related compounds in the leaves of this plant resulted in the isolation of **1** and its three stereoisomers, kodemariosides B (**2**), C (**3**), and D (**4**).

The molecular formula of compound **1** (kodemarioside A) was assigned as $C_{25}H_{30}O_{11}$ by HRFDMS. The ^{1}H NMR spectrum (Table 1) showed signals characteristic of *trans*-*p*-coumaroyl [δ_H 6.88 and 7.56 (each 2H, d, J = 8.7 Hz) and δ_H 6.39 and 7.63 (each 1H, d, J = 16.0 Hz)] and glucose [δ_H 4.41 (1H, d, J = 7.7 Hz), 3.24 (1H, dd, J = 8.7, 7.7 Hz), 3.44 (1H, dd, J = 8.8, 8.7 Hz), 3.39 (1H, dd, J = 9.2, 8.8 Hz), 3.57 (1H, ddd, J = 9.2, 5.9, 2.1 Hz), 4.28 (1H, dd, J = 11.9, 5.9 Hz), and 4.54 (1H, dd, J = 11.9, 2.1 Hz)] moieties. The COSY spectrum supported the presence of these two substructures. The ^{1}H NMR spectrum also showed a pair of nonequivalent oxymethylene protons at δ_H 4.82 and 4.85 (each 1H, ddd, J = 16.0, 5.6, 2.1 Hz) coupled with an olefinic proton at δ_H 6.54 [1H, dt, J = 5.6 (t), 2.1 (d) Hz]. This olefinic proton gave a long-range allyl correlation with an oxymethine proton at δ_H 4.51 [1H, dq, J = 5.1 (d), 2.1 (q) Hz], which was coupled with another oxymethine at δ_H 4.89 (1H, dd, J = 9.1, 5.1 Hz). The latter oxymethine was further coupled with an olefinic proton at δ_H 5.21 [1H, dsep, J = 9.1 (d), 1.4 (sep) Hz]. Finally, this second olefinic proton had an allyl coupling with signals of two methyl groups at δ_H 1.76 (6H, d, J = 1.4 Hz). This proton sequence of (O)-CH_2-CH═C-CH(O)-CH(O)-CH═$C(CH_3)_2$ was confirmed by the corresponding COSY cross-peaks. The ^{13}C NMR data (Table 2), including the DEPT spectrum, showed two methyls (δ_C 18.5 and 25.8), two oxymethines (δ_C 75.1 and 82.7), one oxymethylene (δ_C 66.2), two olefinic methines (δ_C 122.4 and 142.3), two quaternary olefinic carbons (δ_C 131.4 and 141.0), and an ester carbonyl (δ_C 168.5) as well as the coumaroyl [δ_C 127.0 and 160.5 (each C), δ_C 115.5, 116.6, 131.0, and 145.6 (each CH), and δ_C 167.6 (CO)] and the glucose [δ_C 71.2, 74.6, 75.1, 77.7, and 104.1 (each CH) and δ_C 64.2 (CH_2)] carbons. The ester carbonyl at δ_C 168.5 showed HMBC correlation peaks with the olefinic proton at δ_H 6.54 and the oxymethine at δ_H 4.89, consistent with being in a γ-lactone ring. Thus, the aglycon part of **1** was indicated to be 3-hydroxy-2-hydroxyethylidene-6-methylhept-5-en-1,4-olide. The additional key HMBC correlations between the oxymethylene protons (δ_H 4.82 and 4.85) and the anomeric carbon of glucose (δ_C 104.1) and between the glucose methylene protons (δ_H 4.28 and 4.54) and the *p*-coumaroyl carbonyl (δ_C 167.6) clearly indicated that the lactone aglycon is glucosylated at the side chain hydroxymethylene and that the C-6 hydroxy group on the glucose is esterified with the *trans*-*p*-coumaric acid. The planar structure of **1** was thus confirmed. The relative configuration was deduced from the NOESY spectrum. The NOE peak between the olefin (δ_H 6.54) and the oxymethine (δ_H 4.51) protons revealed the *Z*-configuration of the exocyclic double bond. The additional NOE correlation appeared between the oxymethine at δ_H 4.51 and the olefin proton at δ_H 5.21 and was supportive of the *trans*-

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10.1021/np900699e
Published on Web 03/23/2010

Table 1. ^{1}H NMR Spectroscopic Data for Compounds **1**−**6** (acetone-d_6)

proton	**1**	**2**	**3**	**4**	**5**	**6**
1	4.85 ddd (16.0, 5.6, 2.1) 4.82 ddd (16.0, 5.6, 2.1)	4.83 ddd (16.0, 5.6, 2.1) 4.75 ddd (16.0, 5.6, 2.1)	4.68 ddd (16.0, 5.7, 1.2) 4.62 ddd (16.0, 5.7, 1.2)	4.64 ddd (16.0, 5.6, 1.2) 4.57 ddd (16.0, 5.6, 1.2)	4.84 ddd (16.0, 5.5, 2.0) 4.80 ddd (16.0, 5.5, 2.0)	4.69 ddd (16.2, 5.4, 1.5) 4.62 ddd (16.2, 5.4, 1.5)
2	6.54 dt [5.6 (t), 2.1 (d)]	6.53 dt [5.6 (t), 2.0 (d)]	6.84 dt [5.7 (t), 3.2 (d)]	6.82 m	6.53 dt [5.5 (t), 2.2 (d)]	6.83 m
4	4.51 dq [5.1 (d), 2.1 (q)]	4.48 m	4.75 m	4.72 m	4.50 m	4.78 m
5	4.89 dd (9.1, 5.1)	4.87 dd (9.1, 4.9)	4.95 dd (9.1, 3.2)	4.94 dd (9.1, 3.2)	4.89 dd (8.9, 5.2)	4.96 dd (9.1, 3.2)
6	5.21 dsep [9.1 (d), 1.4 (sep)]	5.19 dsep [9.1 (d), 1.5 (sep)]	5.12 dsep [9.1 (d), 1.5 (sep)]	5.12 dsep [9.1 (d), 1.4 (sep)]	5.21 dsep [8.9 (d), 1.4 (sep)]	5.13 dsep [9.1 (d), 1.5 (sep)]
8	1.76 d (1.4)	1.74 brs	1.72 d (1.5)	1.72 d (1.2)	1.73 d (1.4)	1.73 d (1.4)
10	1.76 d (1.4)	1.74 brs	1.74 d (1.5)	1.75 d (1.2)	1.76 d (1.4)	1.75 d (1.4)
1′	4.41 d (7.7)	4.39 d (7.9)	4.46 d (7.6)	4.43 d (7.9)	4.41 d (7.6)	4.43 d (7.9)
2′	3.24 dd (8.7, 7.7)	3.22 dd (8.9, 7.9)	3.27 dd (8.6, 7.6)	3.25 dd (8.9, 7.9)	3.24 m	3.28 dd (8.5, 7.9)
3′	3.44 dd (8.8, 8.7)	3.42 dd (9.1, 8.9)	3.44 dd (8.9, 8.6)	3.43 dd (9.0, 8.9)	3.44 m	3.45 dd (8.9, 8.5)
4′	3.39 dd (9.2, 8.8)	3.35 dd (9.8, 9.1)	3.39 dd (9.1, 8.9)	3.36 dd (9.5, 9.0)	3.39 m	3.41 dd (9.1, 8.9)
5′	3.57 ddd (9.2, 5.9, 2.1)	3.54 ddd (9.8, 5.9, 2.2)	3.59 ddd (9.1, 5.9, 2.1)	3.56 ddd (9.5, 5.9, 2.2)	3.56 m	3.59 ddd (9.1, 5.7, 2.2)
6′	4.54 dd (11.9, 2.1) 4.28 dd (11.9, 5.9)	4.48 dd (11.8, 2.2) 4.25 dd (11.8, 5.9)	4.49 dd (12.1, 2.1) 4.28 dd (12.1, 5.9)	4.46 dd (12.1, 2.2) 4.24 dd (12.1, 5.9)	4.53 dd (11.9, 2.0) 4.28 dd (11.9, 5.7)	4.49 dd (11.9, 2.2) 4.29 dd (11.9, 5.7)
2″	7.56 d (8.7)	7.72 d (8.6)	7.53 d (8.5)	7.72 d (8.6)	7.18 d (2.0)	7.16 d (2.0)
3″	6.88 d (8.7)	6.81 d (8.6)	6.87 d (8.5)	6.81 d (8.6)		
5″	6.88 d (8.7)	6.81 d (8.6)	6.87 d (8.5)	6.81 d (8.6)	6.85 d (8.4)	6.85 d (8.4)
6″	7.56 d (8.7)	7.72 d (8.6)	7.53 d (8.5)	7.72 d (8.6)	7.06 dd (8.4, 2.0)	7.04 dd (8.4, 2.0)
7″	7.63 d (16.0)	6.86 d (12.8)	7.62 d (16.0)	6.86 d (12.8)	7.56 d (16.0)	7.56 d (16.0)
8″	6.39 d (16.0)	5.81 d (12.8)	6.37 d (16.0)	5.80 d (12.8)	6.32 d (16.0)	6.31 d (16.0)

Table 2. ^{13}C NMR Spectroscopic Data for Compounds **1**−**4** (acetone-d_6)

carbon	**1**	**2**	**3**	**4**
1	66.2	66.2	66.8	66.7
2	142.3	142.3	140.5	140.5
3	131.4	131.3	132.1	132.1
4	75.1	75.0	72.6	72.6
5	82.7	82.7	83.0	83.1
6	122.4	122.2	122.4	122.4
7	141.0	141.1	140.8	140.7
8	25.8	25.8	25.7	25.7
9	168.5	168.6	169.8	169.9
10	18.5	18.5	18.4	18.4
1′	104.1	103.9	103.9	103.8
2′	74.6	74.5	74.5	74.4
3′	77.7	77.6	77.5	77.5
4′	71.2	71.0	71.0	71.0
5′	75.1	74.8	75.1	74.9
6′	64.2	64.1	64.1	64.0
1″	127.0	127.1	126.8	127.1
2″(6″)	131.0	133.6	131.0	133.6
3″(5″)	116.6	115.7	116.6	115.7
4″	160.5	159.7	160.7	159.7
7″	145.6	144.4	145.7	144.4
8″	115.5	116.3	115.2	116.3
9″	167.6	167.0	167.7	167.0

configuration of the hydroxy group and the 2-methyl-1-propenyl substituents on the lactone ring (Figure 1).

The absolute configuration of the aglycon part of **1** was determined by the advanced Mosher method[6] as follows. Tannase hydrolysis of **1** directly yielded the aglycon **7**. All attempts for direct MTPA esterification of **1** by MTPA chloride-pyridine or MTPA-DCC-DMAP, however, failed. The *in situ* NMR analysis of the reaction solution indicated the initial appearance of a mono-MTPA ester on OH-1 and the subsequent rapid dehydration of OH-4, probably after esterification, to a conjugated triene product due to an easily dehydrating 3-hydroxy-1,5-diene system of **7**. Removal of the *exo*-double bond conjugated with the lactone carbonyl by a nucleophilic addition of thiophenol gave a diastereomeric mixture of 2-phenylthio compounds (**8a** and **8b**). Both products showed a similar coupling constant between H-3 and H-4, of 9.1 Hz for **8a** and 10.1 Hz for **8b**, and an NOE enhancement between H-3 and H-5. The relative configuration of C-3 and C-4 was inferred as being *trans* in **8a** and **8b**, and hence, they are apparent C-2 epimers of each other. The major product, **8a**, was successively esterified with 1 molar (*S*)-MTPA chloride to give the 1-*O*-(*R*)-MTPA ester, **9**. Finally, careful esterification of the OH-4 group of **9** with (*R*)- or (*S*)-MTPA yielded the 1*R*,4*R*-di-MTPA ester (**10R**) or the 1*R*,4*S*-di-MTPA ester (**10S**), respectively, in an NMR tube. *In situ* NMR analysis clearly indicated the difference in chemical shifts of both diesters, as shown in Figure 2. Consequently, the absolute configuration of C-4 in **1** was deduced to be *S*.

Compound **2** (kodemarioside B) gave the same molecular formula, $C_{25}H_{30}O_{11}$, as that of **1**. The ^{1}H NMR spectrum was similar to that in **1** except for low-field signals arising from the *p*-coumaroyl portion. A pair of olefinic doublets at δ_H 5.81 and 6.86 (J = 12.8 Hz) were observed in **2** in place of the *trans*-double bond signals at δ_H 6.39 and 7.63 (J = 16.0 Hz) in **1**. This higher field doublet pair with a relatively small coupling constant compared to the *trans*-*p*-coumaroyl side chain was characteristic of a *cis*-*p*-coumaroyl residue. The other parts of the molecule, including the monoterpene aglycon and the sugar unit, were in accordance with those in **1**. Hence, **2** was concluded to be a *cis*-*p*-coumaroyl analogue of **1**.

Compound **3** (kodemarioside C) also gave a molecular formula of $C_{25}H_{30}O_{11}$. In the NMR spectrum, the signals of a *trans*-*p*-coumaroylglucose unit were consistent with those in **1**. However,

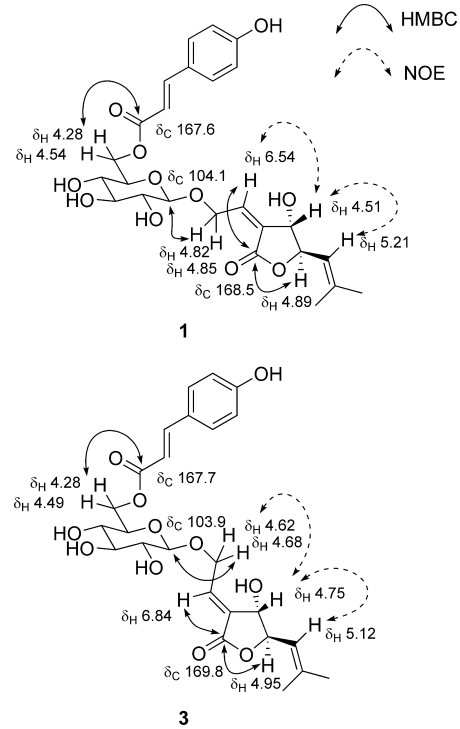

Figure 1. Key HMBC and NOE correlations for **1** and **3**.

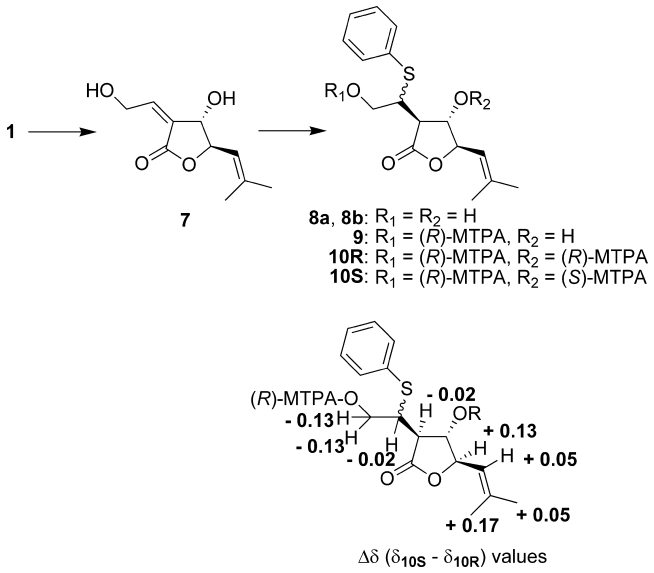

Figure 2. Determination of the absolute configuration of **1**.

signals from the monoterpene aglycon part were slightly but obviously different. The nonequivalent methylene protons (H-1) of δ_H 4.82 and 4.85 in **1** were shifted to higher fields of δ_H 4.62 and 4.68, whereas the exocyclic olefin proton (H-2) at δ_H 6.54 in **1** was shifted to δ_H 6.84. This chemical shift change would be expected to arise from an *E*-configuration of the exocyclic double bond in **3** compared with the *Z*-geometry in **1**. The olefinic proton, H-2, was deshielded by the lactone carbonyl in **3**, while the nonequivalent methylene protons, H-1, were affected in **1**. This chemical shift change was consistent with a similar *E*−*Z* pair of tuxpanolide−isotuxpanolide.[7] The *E*-configuration of the double bond was confirmed by the presence of a correlation peak between H-1 (δ_H 4.62 and 4.68) and H-4 (δ_H 4.75) in the NOESY spectrum (Figure 1). The structure of **3** was thus determined to be an *E*-aglycon analogue of **1**.

Compound **4** (kodemarioside D), $C_{25}H_{30}O_{11}$, was also found to be an isomer of compounds **1**−**3**. The NMR spectrum of **4** showed characteristic profiles of both **2** and **3** in contrast to **1**. Hence, the structure of **4** was deduced to be a *cis*-*p*-coumaroyl *E*-aglycon analogue of **1**.

Compound **5** (kodemarioside E) was assigned a molecular formula of $C_{25}H_{30}O_{12}$, which is one oxygen greater than those of **1**−**4**. The major difference in the NMR spectra of **5** and **1** was in the aromatic region of the phenolic acid part of the molecule. The characteristic pair of doublets at δ_H 6.88 and 7.56 (J = 8.7 Hz each) in **1** was replaced with a typical 1,2,4-trisubstituted pattern at δ_H 6.85 (d, J = 8.4 Hz), 7.06 (dd, J = 8.4, 2.0 Hz), and 7.18 (d, J = 2.0 Hz) in **5**. The residual signals of the NMR spectra of **1** and **5** were nearly identical. Hence, the structure of **5** was concluded to be a caffeoyl analogue of **1**.

Compound **6** (kodemarioside F) was found to be an isomer of **5**, having a molecular formula of $C_{25}H_{30}O_{12}$. In a similar manner to **5**, a comparison of the NMR spectra of **6** with those of **3** revealed its structure as a caffeoyl analogue of **3**.

Isolates **1**−**6** are novel acylglucosides based on a highly oxidized monoterpene aglycon. The maltase-inhibitory activity was found to be lower, 15% and 43% inhibition at 1 mM for **1** and **5**, respectively, than the previously identified flavonol glycosides,[2] whereas the activity of the other isolates has not yet been determined. It was reported that *S. cantoniensis* contains monoterpene ketone glucosides.[5] In addition, a closely related monoterpene derivative, prunioside A, has been isolated from *Spiraea prunifolia*.[8,9] A prunioside A aglycon showed an inhibition of NO production in stimulated macrophage-like cells.[8] More recently, it is interesting that a similar monoterpene lactone glucoside, sibiskoside, has been found in *Sibiraea angustata*, of the same family as a plant affording an antiobesity compound.[10]

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. NMR spectra were recorded on a Bruker AMX500 instrument (^{1}H, 500 MHz; ^{13}C, 125 MHz). Chemical shifts were determined relative to residual signals of acetone-d_6 (δ_H 2.04 ppm, δ_C 29.8 ppm) or chloroform-*d* (δ_H 7.24 ppm) as a solvent. Field desorption (FD) and fast-atom bombardment (FAB) mass spectra were determined using a JEOL SX102A instrument. Column chromatography was performed with silica gel (Wakogel C-300, 300 mesh). HPLC was run on a JASCO PU-980 instrument equipped with a UV detector. Preparative TLC was carried out on precoated silica gel plates (0.5 mm thickness, Merck).

Plant Material. *Spiraea cantoniensis* was cultivated, collected in May (flowers) and September (leaves) 2004 in an experimental field in Tsukuba, Japan, and identified by one of the authors (A.H.). A voucher specimen (No. 0131-79TS) is deposited in the Tsukuba Division, Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation, Tsukuba, Japan.

Extraction and Isolation. Dried flowers (6.5 g) of *S. cantoniensis* were extracted with 50% MeOH. The aqueous methanol extracts were partitioned with water and ethyl acetate. The ethyl acetate-soluble part (0.38 g) was chromatographed with silica gel and eluted by a stepwise mixture of chloroform−methanol (10:0, 10:1, 8:1, 6:1, 4:1, 2:1) containing 1% formic acid. The chloroform−methanol (4:1) eluate (0.25 g) was rechromatographed with silica gel (chloroform−methanol, 3:1, containing 1% formic acid) to yield 15 fractions. Fractions 4−6 were combined (0.09 g) and further purified by preparative HPLC (column: Inertsil PREP-ODS 20 × 250 mm, mobile phase: 27.5% MeCN in water containing 0.1% TFA, flow rate: 5.0 mL/min, detection: UV 254 nm) to yield **5** (t_R 28 min, 3.4 mg) and **1** (t_R 40 min, 5.0 mg). A larger scale fractionation of the dried flowers (100 g) was conducted in a similar manner. Half of the ethyl acetate-soluble part of the 50% methanol extract (3.0 g) was chromatographed over silica gel (chloroform−methanol). One-fifth of the amount (0.2 g) of the chloroform−methanol (6:1) eluate was further fractionated by preparative HPLC (column: Inertsil PREP-ODS 20 × 250 mm ×2 (serial connection), mobile phase: 20% MeCN in water, flow rate: 7.0 mL/min for 0−30 min and 5.0 mL/min for 30−110 min, detection: UV 254 nm) to yield **6** (t_R 82 min, 2.3 mg).

Dried leaves (50 g) of *S. cantoniensis* were extracted with 50% MeOH. The aqueous methanol extracts were partitioned with water and ethyl acetate. The ethyl acetate-soluble part (2.4 g) was chromatographed with silica gel and eluted using a stepwise mixture of chloroform−methanol (10:0, 10:1, 8:1, 6:1, 4:1, 2:1) containing 1% formic acid. The chloroform−methanol (6:1) eluate (0.48 g) was purified by preparative HPLC (column: Inertsil PREP-ODS 20 × 250 mm, mobile phase: 27.5% MeCN in water, flow rate: 5.0 mL/min, detection: UV 254 nm) and yielded **3** (t_R 38 min, 17 mg), **1** (t_R 44 min, 90 mg), **4** (t_R 53 min, 10 mg), and **2** (t_R 58 min, 30 mg).

Kodemarioside A (1): yellow gum; $[\alpha]^{23}_D$ −10 (*c* 0.31, MeOH); ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FDMS *m*/*z* 506 $[M]^+$; HRFDMS *m*/*z* 506.1767 $[M]^+$ (calcd for $C_{25}H_{30}O_{11}$, 506.1788).

Kodemarioside B (2): yellow gum; $[\alpha]^{23}_D$ +8 (*c* 0.21, MeOH); ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FDMS *m*/*z* 506 $[M]^+$; HRFDMS *m*/*z* 506.1790 $[M]^+$ (calcd for $C_{25}H_{30}O_{11}$, 506.1788).

Kodemarioside C (3): yellow gum; $[\alpha]^{23}_D$ −10 (*c* 0.49, MeOH); ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FDMS *m*/*z* 506 $[M]^+$; HRFDMS *m*/*z* 506.1776 $[M]^+$ (calcd for $C_{25}H_{30}O_{11}$, 506.1788).

Kodemarioside D (4): yellow gum; $[\alpha]^{23}_D$ +5 (*c* 0.20, MeOH); ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FDMS *m*/*z* 506 $[M]^+$; HRFDMS *m*/*z* 506.1794 $[M]^+$ (calcd for $C_{25}H_{30}O_{11}$, 506.1788).

Kodemarioside E (5): yellow gum; $[\alpha]^{23}_D$ −9 (*c* 0.17, MeOH); ^{1}H NMR data, see Table 1; FDMS *m*/*z* 522 $[M]^+$; HRFABMS (positive) *m*/*z* 523.1825 $[M + H]^+$ (calcd for $C_{25}H_{31}O_{12}$, 523.1815).

Kodemarioside F (6): yellow gum; $[\alpha]^{23}_D$ −6 (*c* 0.22, MeOH); ^{1}H NMR data, see Table 1; FDMS *m*/*z* 522 $[M]^+$; HRFDMS *m*/*z* 522.1755 $[M]^+$ (calcd for $C_{25}H_{30}O_{12}$, 522.1737).

Tannase Hydrolysis of 1. To a solution of **1** (145 mg, 0.287 mmol) in water (30 mL) was added tannase (150 mg, 41 units/mg, Sigma). The mixture was stirred at 30 °C for 48 h. The reaction mixture was

extracted with EtOAc, and the extract was purified by silica gel preparative TLC (R_f = 0.30, hexane−EtOAc−formic acid, 50:50:1) to give an aglycon, **7** (25 mg, 44%). **7**: colorless oil; ^{1}H NMR (acetone-d_6) δ 1.72 (6H, d, J = 1.3 Hz, H-8,10), 4.58 [1H, ddt, J = 5.3 (d), 2.2 (t), 1.8 (d) Hz, H-4], 4.75 (1H, ddd, J = 16.0, 5.6, 2.2 Hz, H-1b), 4.81 (1H, ddd, J = 16.0, 5.9, 1.8 Hz, H-1a), 4.96 (1H, dd, J = 9.1, 5.3 Hz, H-5), 5.22 [1H, dsep, J = 9.1 (d), 1.3 (sep) Hz, H-6], 6.64 (1H, ddd, J = 5.9, 5.6, 2.2 Hz, H-2); FDMS m/z 199 $[M + H]^+$; HRFDMS m/z 199.0953 $[M + H]^+$ (calcd for $C_{10}H_{15}O_4$, 199.0971).

Thiophenol Addition of 7. To **7** (5.8 mg, 29 μmol) was added thiophenol (10 μL, 97 μmol, 3.3 equiv) in EtOAc (10 drops). After 30 min at room temperature, the reaction mixture was directly separated by silica gel preparative TLC (chloroform−MeOH, 19:1). **8a** (R_f 0.40, 4.0 mg, 44%) and **8b** (R_f 0.26, 2.4 mg, 27%) were obtained as oils. **8a**: colorless oil; ^{1}H NMR (chloroform-*d*) δ 1.80 (3H, s, H-10), 1.82 (3H, s, H-8), 2.97 (1H, dd, J = 9.1, 2.5 Hz, H-3), 3.78 (1H, ddd, J = 3.4, 2.5, 2.0 Hz, H-2), 3.81 (1H, dd, J = 10.3, 2.0 Hz, H-1b), 3.91 (1H, dd, J = 10.3, 3.4 Hz, H-1a), 4.18 (1H, dd, J = 9.1, 8.3 Hz, H-4), 4.87 (1H, dd, J = 9.1, 8.3 Hz, H-5), 5.27 (1H, d, J = 9.1 Hz, H-6), 7.31 [3H, m, PhS (H-3,4,5)], 7.55 [2H, d, J = 7.1 Hz, PhS (H-2,6)]; FDMS m/z 308 $[M]^+$. **8b**: colorless oil; ^{1}H NMR (chloroform-*d*) δ 1.77 (3H, s, H-10), 1.80 (3H, s, H-8), 3.07 (1H, dd, J = 10.1, 3.9 Hz, H-3), 3.70 (1H, ddd, J = 6.9, 5.2, 3.9 Hz, H-2), 3.89 (1H, dd, J = 12.1, 6.9 Hz, H-1b), 4.01 (1H, dd, J = 12.1, 5.2 Hz, H-1a), 4.43 (1H, dd, J = 10.1, 8.1 Hz, H-4), 4.81 (1H, dd, J = 8.6, 8.1 Hz, H-5), 5.22 (1H, d, J = 8.6 Hz, H-6), 7.29 [1H, t, J = 7.6 Hz, PhS (H-4)], 7.32 [2H, t, J = 7.6 Hz, PhS (H-3,5)], 7.49 [2H, d, J = 7.6 Hz, PhS (H-2,6)]; FDMS m/z 308 $[M]^+$.

Mono-(*R*)-MTPA Esterification of 8a. To **8a** (5.9 mg, 19.2 μmol) in MeCN (10 drops) and pyridine (5 drops) was added (*S*)-(+)-MTPA chloride (15 μL, 60 μmol, 3.1 equiv). After 3 h at room temperature, the reaction mixture was directly separated by silica gel preparative TLC (hexane−EtOAc, 2:1). The mono-(*R*)-MTPA ester **9** (R_f 0.40, 3.6 mg, 36%) was obtained as an oil. **9**: colorless oil; ^{1}H NMR (chloroform-*d*) δ 1.77 (3H, s, H-10), 1.81 (3H, s, H-8), 2.90 (1H, dd, J = 8.6, 3.2 Hz, H-3), 3.53 (3H, s, MTPA-OMe), 3.77 (1H, ddd, J = 5.3, 3.3, 3.2 Hz, H-2), 3.83 (1H, dd, J = 8.6, 7.8 Hz, H-4), 4.24 (1H, dd, J = 11.3, 3.3 Hz, H-1b), 4.73 (1H, dd, J = 8.9, 7.8 Hz, H-5), 4.94 (1H, dd, J = 11.3, 5.3 Hz, H-1a), 5.08 (1H, d, J = 8.9 Hz, H-6), 7.31 [3H, m, PhS (H-3,4,5)], 7.43 [3H, m, MTPA-Ph (H-3,4,5)], 7.52 [2H, m, PhS (H-2,6)], 7.61 [2H, m, MTPA-Ph (H-2,6)]; FDMS m/z 524 $[M]^+$.

***In Situ* (*R*)- and (*S*)-MTPA Esterification of 9.** The (*R*)-monoester **9** (0.8 mg, 1.4 μmol) was reacted with (*R*)-(+)-MTPA (1.0 mg, 4.3 μmol, 3.1 equiv), dicyclohexylcarbodiimide (DCC, 1.0 mg, 4.9 μmol, 3.5 equiv), and 4-dimethylaminopyridine (DMAP, 1.0 mg, 8.2 μmol, 5.9 equiv) in 0.3 mL of chloroform-*d* in an NMR tube for 2 h. (*R*,*R*)-Diester (**10R**): ^{1}H NMR (chloroform-*d*) δ 1.50 (3H, s, H-10), 1.75 (3H, s, H-8), 3.10 (1H, dd, J = 7.1, 4.2 Hz, H-3), 3.38 and 3.45 (each 3H, s, MTPA-OMe), 3.76 (1H, ddd, J = 9.3, 5.4, 4.2 Hz, H-2), 4.24 (1H, dd, J = 11.6, 9.3 Hz, H-1b), 4.70 (1H, dd, J = 11.6, 5.4 Hz, H-1a), 4.80 (1H, dd, J = 9.4, 5.9 Hz, H-5), 5.23 (1H, d, J = 9.4 Hz, H-6), 5.62 (1H, dd, J = 7.1, 5.9 Hz, H-4), 7.30−7.50 (15H, m, 2MTPA-Ph,PhS).

In the same manner, **9** was reacted with (*S*)-(−)-MTPA, DCC, and DMAP in 0.3 mL of chloroform-*d* in an NMR tube for 2 h. (*R*,*S*)-Diester (**10S**): ^{1}H NMR (chloroform-*d*) δ 1.67 (3H, s, H-10), 1.80 (3H, s, H-8), 3.08 (1H, dd, J = 7.3, 4.1 Hz, H-3), 3.42 and 3.43 (each 3H, s, MTPA-OMe), 3.74 (1H, ddd, J = 8.9, 5.7, 4.1 Hz, H-2), 4.11 (1H, dd, J = 11.3, 8.9 Hz, H-1b), 4.57 (1H, dd, J = 11.3, 5.7 Hz, H-1a), 4.93 (1H, dd, J = 9.4, 5.9 Hz, H-5), 5.28 (1H, d, J = 9.4 Hz, H-6), 5.64 (1H, dd, J = 7.3, 5.9 Hz, H-4), 7.25−7.45 (15H, m, 2MTPA-Ph,PhS).

Maltase-Inhibition Assay. Compounds **1** and **5** were evaluated in a maltase-inhibition assay, according to a previous protocol.[2] Pentagalloylglucose was used as a positive control (80% inhibition at 1 mM).[11]

Acknowledgment. The authors thank Mr. K. Watanabe and Dr. E. Fukushi, GC-MS and NMR Laboratory, Faculty of Agriculture, Hokkaido University, for their skillful measurements of mass spectra.

Note Added after ASAP Publication: This paper was published on the Web on Mar 23, 2010, with an error regarding configuration at the end of the third paragraph in the Results and Discussion section. The corrected version was reposted on Apr 9, 2010.

Supporting Information Available: ^{1}H NMR and ^{13}C NMR (in part) spectra of kodemariosides A−F (**1**−**6**) and the derivatives are available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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NP900699E