Bioactive Constituents from Chinese Natural Medicines. XXIX.[1] Monoterpene and Monoterpene Glycosides from the Roots of *Rhodiola sachalinensis*

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A new monoterpene, sachalol, and three new monoterpene glycosides, sachalosides VI, VII, VIII, were isolated from Rhodiolae Radix, the roots of *Rhodiola sachalinensis*. The absolute stereostructures of new monoterpenes were elucidated on the basis of chemical and physicochemical evidence including the application of the modified Mosher's method.

Key words Rhodiolae Radix; *Rhodiola sachalinensis*; Crassulaceae; monoterpene; sachalol; sachaloside

In the course of our characterization studies on bioactive constituents from Chinese natural medicines,[2—11] we have reported the isolation and structure elucidation of two new monoterpene glycosides, sachalosides I and II, two new flavonol bisdesmosides, sachalosides III and IV, a new cyanogenic glycoside, sachaloside V, from the roots of *Rhodiola sachalinensis* A. BOR. (Crassulaceae) together with 34 known constituents.[12] As a continuation of the characterization studies on *R. sachalinensis*, we have isolated a new monoterpene, sachalol (**1**), and three monoterpene glycosides, sachalosides VI—VIII (**2**—**4**). In this paper, we describe the isolation and absolute stereostructure elucidation of these new monoterpenes (**1**—**4**).

Isolation of Sachalol and Sachalosides VI—VIII The roots of *R. sachalinensis* were extracted with methanol under reflux as previously reported. The methanolic extract (14.6% from the roots) was partitioned into an EtOAc–H_2O mixture to furnish an EtOAc-soluble fraction (3.5%) and aqueous layer. The aqueous layer was further extracted with *n*-BuOH to give *n*-BuOH and H_2O-soluble fractions (4.4%, 6.5%, respectively). The EtOAc-soluble fraction was subjected to normal-phase and reverse-phase column chromatographies, and finally HPLC to give sachalol (**1**, 0.00074%). The *n*-BuOH-soluble fraction was also subjected to Diaion HP-20 column chromatography (H_2O→MeOH) to give the water- and methanol-eluted fractions (0.8%, 3.5%, respectively). The methanol-eluted fraction was subjected to normal- and reversed-phase column chromatographies, and finally HPLC to give sachalosides VI (**2**, 0.0011%), VII (**3**, 0.00038%), and VIII (**4**, 0.00028%).

Sachalol (**1**) was obtained as a colorless viscous oil with a negative optical rotation ($[\alpha]_D^{25}$ −7.2° in $CHCl_3$). The IR spectrum of **1** showed absorption bands at 3339 and 1655 cm^{-1} ascribable to hydroxyl and olefin functions. In the positive-ion chemical ionization (CI)-MS of **1**, a quasimolecular ion peak was observed at *m/z* 173 $(M+H)^+$, and the high-resolution (HR) CI-MS analysis revealed the molecular formula of **1** to be $C_{10}H_{20}O_2$. The ^1H-NMR ($CDCl_3$) and ^{13}C-NMR (Table 1) spectra of **1**, which were assigned by various NMR experiments,[13] showed signals assignable to three methyls [δ 0.96 (3H, d, J=6.8 Hz, H_3-10), 1.65, 1.75 (3H each, both s, H_3-8, 9)], a methylene bearing an oxygen function [δ 3.63 (1H, m, H-1a), 3.76 (1H, m, H-1b)], a methine bearing an oxygen function [δ 3.41 (1H, m, H-4)], an olefinic proton [δ 5.17 (1H, t, J=6.8 Hz, H-6)], two methyl-

Table 1. ^{13}C-NMR (150 MHz) Data for Sachalol (**1**, $CDCl_3$) and Sachalosides VI—VIII (**2**—**4**, CD_3OD)

Position	1	2	3	4
1	60.6	69.4	66.4	66.7
2	35.9	33.1	121.7	121.6
3	36.2	36.4	142.0	142.0
4	75.6	76.9	37.7	41.1
5	33.4	33.5	30.3	23.5
6	120.2	122.5	78.8	44.3
7	135.6	133.7	73.8	71.4
8	18.0	18.1	24.9[a]	29.2
9	26.0	26.1	25.8[a]	29.2
10	16.7	16.3	16.5	16.5
1′		104.5	102.8	102.3
2′		75.1	75.1	75.0
3′		78.0	78.1	78.0
4′		71.6	71.7	71.7
5′		77.9	78.0	76.9
6′		62.8	62.8	69.5
1″				105.2
2″				72.4
3″				74.2
4″				69.5
5″				66.7

a) May be interchangeable within the same column.

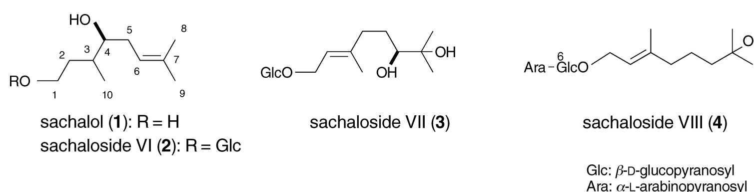

Chart 1

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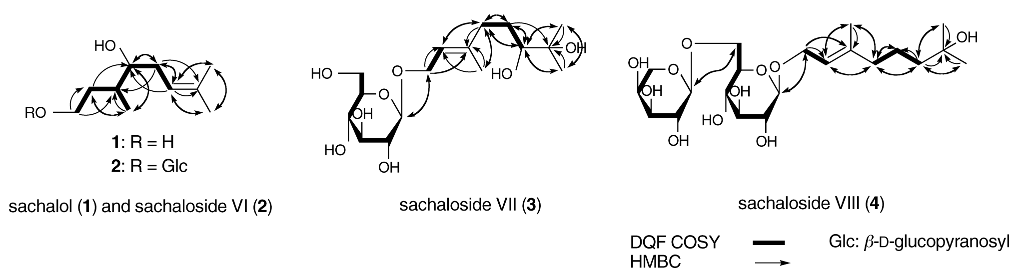

Fig. 1

ene [δ 1.63 (2H, m, H_2-2), 2.19 (2H, m, H_2-5)], a methine [δ 1.73 (1H, m, H-3)]. As shown in Fig. 1, the double quantum filter correlation spectroscopy (DQF COSY) experiment on **1** indicated the presence of partial structures written in bold lines, and in the heteronuclear multiple-bond correlations (HMBC) experiment, long-range correlations were observed between the following protons and carbons: H-1 and C-2, 3; H-2 and C-4, 10; H-4 and C-5, 10; H-5 and C-3, 4, 6, 7; H-6 and C-4, 5, 7, 8, 9; H-8 and C-9; H-9 and C-8; H-10 and C-2, 3, 4. These results supported that the plane structure of **1** was the same as that of (3*S*,4*R*)-3,7-dimethyl-6-octene-1,4-diol, which was synthesized by Umemura and Mori.[14] Next, the configuration at 4-position in **1** was characterized by the application of the modified Mosher's method. Namely, the 1-pivaloyl ester (**1a**), which was derived from **1** upon reaction with pivaloyl chloride in pyridine, gave the (*S*)-2-methoxy-2-trifluromethylphenylacetic acid (MTPA) ester (**1b**) by treatment with (−)-2-methoxy-2-trifluoromethylphenylacetyl choloride [(−)-MTPACl] in pyridine. In addition, the (*R*)-MTPA ester (**1c**) was obtained from **1a** using (+)-MTPACl in pyridine. As shown in Fig. 2, the signals due to protons attached to the 5, 6, 8 and 9-positions in the (*S*)-MTPA ester (**1b**) were observed at higher fields compared with those of the (*R*)-MTPA ester (**1c**) [$\Delta\delta$: negative], while the signals due to protons on the 1, 2, 3 and 10-positions in **1b** were observed at lower fields compared with those of **1c** [$\Delta\delta$: positive]. Thus, the absolute configuration at the 4-position in **1** was determined to be *S*. On the basis of this evidence, the structure of sachalol was elucidated to be (3ξ,4*S*)-3,7-dimethyl-6-octene-1,4-diol (**1**).[15]

Sachaloside VI (**2**), obtained as a colorless viscous oil with a negative optical rotation ($[\alpha]_D^{27}$ −23.9° in MeOH), showed absorption bands at 3586, 1643 and 1032 cm^{-1} assignable to hydroxyl, olefin, and ether functions in the IR spectrum. The molecular formula, $C_{16}H_{30}O_7$, was determined from the positive-ion fast atom bombardment (FAB)-MS at *m/z* 335 $(M+H)^+$ and by HR-FAB-MS measurement. Acid hydrolysis of **2** with 1.0 M aqueous HCl liberated D-glucose, which was identified by HPLC analysis using an optical rotation detector.[3,7,12] Enzyme hydrolysis of **2** with β-glucosidase liberated sachalol (**1**). The ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (Table 1) spectra[13] of **2** showed signals assignable to a sachalol moiety [δ 0.90 (3H, d, *J*=6.9 Hz, H_3-10), 1.40, 1.87 (1H each, both m, H_2-2), 1.60, 1.68 (3H each, both s, H_3-8, 9), 1.68 (1H, m, H-3), 2.07, 2.19 (1H each, both m, H_2-5), 3.38 (1H, m, H-4), 3.55, 3.97 (1H each, both m, H_2-1), 5.22 (1H, t, *J*=6.8 Hz, H-6)], together with a β-D-glucopyranosyl moiety [δ 4.23 (1H, d, *J*=7.5 Hz, H-1′)]. The structure of **2** was characterized by means of DQF COSY and HMBC experiments. As shown in Fig. 1, long-range correlations in the HMBC experiment on **2** were observed between the following proton and carbons: H-1 and C-2, 3, 1′; H-2 and C-4, 10; H-4 and C-5, 10; H-5 and C-3, 4, 6, 7; H-6 and C-4, 5, 7, 8, 9; H-8 and C-9; H-9 and C-8; H-10 and C-2, 3, 4; H-1′ and C-1. Furthermore, comparison of the ^{13}C-NMR data of **2** with those of **1** indicated the presence of a glycosylation shift around the 1-position. On the basis of this evidence, the structure of sachaloside VI was elucidated to be (3ξ,4*S*)-3,7-dimethyl-6-octene-1,4-diol 1-*O*-β-D-glucopyranoside (**2**).[15]

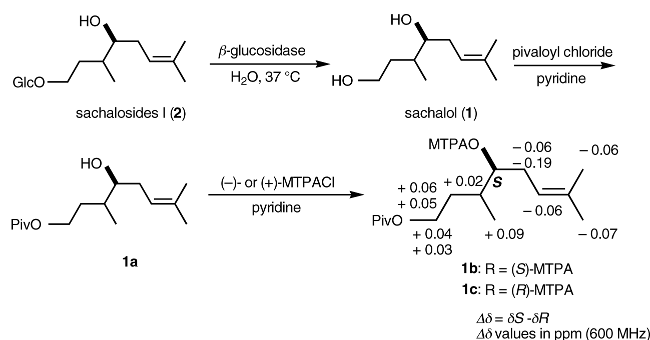

Fig. 2

Sachaloside VII (**3**), obtained as a colorless viscous oil with a negative optical rotation ($[\alpha]_D^{27}$ −44.0° in MeOH), showed absorption bands at 3567, 1636 and 1040 cm^{-1} assignable to hydroxyl, olefin, and ether functions in the IR spectrum. The molecular formula, $C_{16}H_{30}O_8$, was determined from the positive-ion FAB-MS at *m/z* 373 $(M+Na)^+$ and by HR-FAB-MS measurement. The acid hydrolysis of **3** liberated D-glucose, which were identified by HPLC analysis.[3,7,12] The enzymatic hydrolysis of **3** afforded a known monoterpene, (*S*)-3,7-dimethyloct-2*E*-en-1,6,7-triol.[16] The ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (Table 1) spectra[13] of **3** showed signals assignable to a monoterpene aglycon moiety [δ 1.13, 1.17, 1.71 (3H each, both s, H_3-8, 9, 10), 1.39, 1.75 (1H each, both m, H_2-5), 2.08, 2.29 (1H each, both m, H_2-4), 3.24 (1H, m, H-6), 4.25 (1H, dd, *J*=7.6, 12.0 Hz, H-1a), 5.34 (1H, dd, *J*=6.4, 12.0 Hz, H-1b), 5.43 (1H, t like, *J*=*ca.* 7 Hz, H-2)], together with an β-D-glucopyranosyl moiety [δ 4.28 (1H, d, *J*=7.7 Hz, H-1′)]. As shown in Fig. 1, long-range correlations in the HMBC experiment on **3** were observed between the following proton and carbon pairs: H-1 and C-2, 3, 1′; H-2 and C-4; H-4 and C-2, 3, 5, 6, 10; H-5 and C-4, 6, 7; H-6 and C-4, 5, 8, 9; H-8, 9 and C-6, 7; H-10 and C-2, 3, 4; H-1′ and C-1. Finally, comparison of the ^{13}C-NMR data of **3** with those of (*S*)-3,7-dimethyloct-2*E*-en-1,6,7-triol indicated the presence of a glycosylation shift around the 1-position. On

the basis of this evidence, the structure of sachaloside VII was elucidated to be (*S*)-3,7-dimethyloct-2*E*-en-1,6,7-triol 1-*O*-β-D-glucopyranoside (**3**).

Sachaloside VIII (**4**), obtained as a colorless viscous oil with a negative optical rotation ($[\alpha]_D^{27}$ $-36.8°$ in MeOH), showed absorption bands at 3503, 1647 and 1040 cm^{-1} assignable to hydroxyl, olefin, and ether functions in the IR spectrum. The molecular formula, $C_{21}H_{38}O_{11}$, was determined from the positive-ion FAB-MS at *m/z* 489 $(M+Na)^+$ and by HR-FAB-MS measurement. The acid hydrolysis of **4** liberated L-arabinose and D-glucose,[3,7,12] while enzyme hydrolysis of **4** with naringinase liberated a known monoterpene, *E*-3,7-dimethyloct-2-en-1,7-diol.[17] The ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (Table 1) spectra[13] of **4** showed signals assignable to a monoterpene aglycon moiety [δ 1.17 (6H, s, H_3-8, 9), 1.69 (3H, s, H_3-10), 1.50 (2H, m, H_2-5), 2.04 (2H, t, J=6.9 Hz, H_2-4), 1.49 (2H, m, H-6), 4.20 (1H dd, J=7.6, 12.4 Hz, H-1a), 4.35 (1H dd, J=6.9, 12.4 Hz, H-1b), 5.38 (1H, t like, J=*ca.* 7 Hz, H-2)], together with a β-D-glucopyranosyl moiety [δ 4.29 (1H, d, J=8.2 Hz, H-1′)] and an α-L-arabinopyranosyl moiety [δ 4.31 (1H, d, J=6.8 Hz, H-1″)]. The proton and carbon signals due to the 1-*O*-glycoside moiety in the ^{1}H- and ^{13}C-NMR spectra of **4** were similar to those of sachaloside I.[12] As shown in Fig. 1, long-range correlations in the HMBC experiment on **4** were observed between the following proton and carbon pairs: H-1 and C-2, 3, 1′; H-2 and C-4, 10; H-4 and C-2, 5, 6, 10; H-5 and C-4; H-6 and C-4, 5, 7, 8, 9; H-8, 9 and C-6, 7; H-10 and C-2, 3, 4; H-1′ and C-1; H-6′ and C-1″; H-1″ and C-6′. Comparison of the ^{13}C-NMR data of **4** with those of *E*-3,7-dimethyloct-2-en-1,7-diol and methyl β-D-glucopyranoside indicated the presence of glycosylation shifts around the 1- and 6′-positions. On the basis of this evidence, the structure of sachaloside VIII (**4**) was elucidated to be *E*-3,7-dimethyloct-2-en-1,7-diol 1-*O*-α-L-arabinopyranosyl(1→6)-β-D-glucopyranoside.

Experimental

General Experimental Procedures The following instruments were used to obtain physical data: specific rotations, Horiba SEPA-300 digital polarimeter (l=5 cm); IR spectra, Shimadzu FTIR-8100 spectrometer; EI-MS, CI-MS, HR-EI-MS, and HR-CI-MS, JEOL JMS-GCMATE mass spectrometer; FAB-MS and HR-FAB-MS, JEOL JMS-SX 102A mass spectrometer; ^{1}H-NMR spectra, JEOL EX-270 (270 MHz), JNM-LA500 (500 MHz), and JEOL ECA-600K (600 MHz) spectrometers; ^{13}C-NMR spectra, JEOL EX-270 (68 MHz) JNM-LA500 (125 MHz), and JEOL ECA-600K (150 MHz) spectrometers with tetramethylsilane as an internal standard; HPLC detector, Shimadzu RID-6A refractive index detector; and HPLC column, YMC-Pack ODS-A (YMC, Inc., 250×4.6 mm i.d.) and (250×20 mm i.d.) columns were used for analytical and preparative purposes, respectively.

The following experimental materials were used for chromatography: normal-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); Diaion HP-20 column chromatography (Nippon Rensui); TLC, precoated TLC plates with Silica gel $60F_{254}$ (Merck, 0.25 mm) (ordinary phase) and Silica gel RP-18 F_{254S} (Merck, 0.25 mm) (reversed phase); reversed-phase HPTLC, precoated TLC plates with Silica gel RP-18 WF_{254S} (Merck, 0.25 mm); and detection was achieved by spraying with 1% $Ce(SO_4)_2$–10% aqueous H_2SO_4 followed by heating.

Plant Material The dried roots of *R. sachalinensis* were collected at Jilin and Heilongjiang provinces of China in 2005 and identified by one of authors (M.Y.). A voucher of the plant is on file in our laboratory (2006. China-06).

Extraction and Isolation The methanolic extract (1457 g, 14.6%) was obtained from dried roots of *R. sachalinensis* (10.0 kg) as reported previously.[12] The aliquot (1395 g) from the extract was partitioned into an EtOAc–H_2O (1 : 1, v/v) mixture to furnish an EtOAc-soluble fraction (336 g, 3.5%) and an aqueous phase. The aqueous phase was further extracted with *n*-BuOH to give an *n*-BuOH-soluble fraction (418 g, 4.4%) and an H_2O-soluble fraction (620 g, 6.5%). The *n*-BuOH-soluble fraction (366 g) was subjected to Diaion HP-20 column chromatography (4.0 kg, H_2O→MeOH) to give H_2O- and MeOH-eluted fractions 65.9 g, 0.8% and 290.7 g, 3.5%), respectively. The EtOAc fraction (139 g) was subjected to ordinary-phase silica gel column chromatography [3.0 kg, $CHCl_3$→$CHCl_3$–MeOH (20 : 1)→$CHCl_3$–MeOH–H_2O (15 : 3 : 1, lower layer→10 : 3 : 1, lower layer→7 : 3 : 1, lower layer)→MeOH] to give six fractions [Fr. 1 (18.0 g), Fr. 2 (38.7 g), Fr. 3 (19.8 g), Fr. 4 (13.1 g), Fr. 5 (15.1 g), Fr. 6 (17.4 g)]. Fraction 2 (16.8 g) was subjected to ordinary-phase silica gel column chromatography [450 g, *n*-hexane–EtOAc (20 : 1→10 : 1→5 : 1→2 : 1→1 : 1, v/v)→$CHCl_3$–MeOH–H_2O (20 : 3 : 1, lower layer)] to give eight fractions [Fr. 2-1 (117 mg), Fr. 2-2 (1681 mg), Fr. 2-3 (4256 mg), Fr. 2-4 (2233 mg), Fr. 2-5 (217 mg), Fr. 2-6 (2385 mg), Fr. 2-7 (3549 mg), Fr. 2-8 (1005 mg)]. Fr. 2-7 (3549 mg) was subjected to reversed-phase silica gel column chromatography [180 g, MeOH–H_2O (50 : 50→60 : 40→70 : 30→90 : 10, v/v)→MeOH] to give seven fractions [Fr. 2-7-1 (866 mg), Fr. 2-7-2 (483 mg), Fr. 2-7-3 (37 mg), Fr. 2-7-4 (175 mg), Fr. 2-7-5 (107 mg), Fr. 2-7-6 (89 mg), Fr. 2-7-7 (166 mg)]. Fr. 2-7-2 (483 mg) was further purified by HPLC [MeOH–H_2O (55 : 45, v/v)] to give sachalol (**1**, 21.3 mg). The MeOH-eluted fraction (188.8 g) was subjected to ordinary-phase silica gel column chromatography [3.0 kg, $CHCl_3$–MeOH–H_2O (15 : 3 : 1, lower layer→10 : 3 : 1, lower layer→7 : 3 : 1, lower layer→6 : 4 : 1, v/v/v)→MeOH] to give seven fractions [Fr. 1 (428 mg), Fr. 2 (1.8 g), Fr. 3 (60.5 g), Fr. 4 (13.4 g), Fr. 5 (16.6 g), Fr. 6 (12.6 g), Fr. 7 (64.1 g)]. Sachalosides I—V was obtained from Fr. 4 and Fr. 6 as reported previously.[12] Fraction 3 (60.5 g) was subjected to reversed-phase silica gel column chromatography [1.5 kg, MeOH–H_2O (10 : 90→20 : 80→30 : 70→40 : 60→50 : 50→60 : 40→70 : 30, v/v)→MeOH] to give 11 fractions [Fr. 3-1 (12.1 g), Fr. 3-2 (3.4 g), Fr. 3-3 (2.3 g), Fr. 3-4 (822 mg), Fr. 3-5 (572 mg), Fr. 3-6 (26.5 g), Fr. 3-7 (956 mg), Fr. 3-8 (221 mg), Fr. 3-9 (347 mg), Fr. 3-10 (626 mg), Fr. 3-11 (356 mg)]. Fr. 3-7 (956.3 mg) was separated by HPLC [MeOH–H_2O (45 : 55, v/v)] to give sachaloside VI (**2**, 61.9 mg). Fraction 5 (15.1 g) was subjected to reversed-phase silica gel column chromatography [450 g, MeOH–H_2O (20 : 80→30 : 70→50 : 50→70 : 30→90 : 10, v/v)→MeOH] to afford nine fractions [Fr. 5-1 (142 mg), Fr. 5-2 (5021 mg), Fr. 5-3 (860 mg), Fr. 5-4 (761 mg), Fr. 5-5 (6560 mg), Fr. 5-6 (212 mg), Fr. 5-7 (381 mg), Fr. 5-8 (386 mg), Fr. 5-9 (143 mg)]. Fraction 5-3 (860 mg) was separated by HPLC [MeOH–H_2O (20 : 80, v/v)] to give sachaloside VII (**3**, 20.5 mg). Fraction 6 (11.6 g) was subjected to reversed-phase silica gel column chromatography [400 g, MeOH–H_2O (20 : 80→30 : 70→50 : 50→70 : 30→90 : 10, v/v)→MeOH] to afford ten fractions [Fr. 6-1 (1308 mg), Fr. 6-2 (813 mg), Fr. 6-3 (2004 mg), Fr. 6-4 (761 mg), Fr. 6-5 (586 mg), Fr. 6-6 (2039 mg), Fr. 6-7 (491 mg), Fr. 6-8 (2255 mg), Fr. 6-9 (787 mg), Fr. 6-10 (218 mg)]. Fraction 6-5 (586 mg) was separated by HPLC [MeOH–H_2O (25 : 75, v/v)] to give sachaloside VIII (**4**, 15.5 mg).

Sachalol (**1**): Obtained as colorless viscous oil; $[\alpha]_D^{25}$ $-7.2°$ (c=1.25, $CHCl_3$); IR (Film) ν_{max} 3339, 2928, 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.96 (3H, d, J=6.8 Hz, H_3-10), 1.63 (2H, m, H_2-2), 1.65, 1.75 (3H each, both s, H_3-8, 9), 1.73 (1H, m, H-3), 2.19 (2H, m, H_2-5), 3.41 (1H, m, H-4), 3.63 (1H, m, H-1a), 3.76 (1H, m, H-1b), 5.17 (1H, t, J=6.8 Hz, H-6); ^{13}C-NMR data see Table 1; positive-ion CI-MS *m/z* 173 $[M+H]^+$; HR-CI-MS *m/z* 173.1541 (Calcd for $C_{10}H_{20}O_2$ $[M+H]^+$, 173.1545).

Sachaloside VI (**2**): Obtained as colorless viscous oil; $[\alpha]_D^{27}$ $-23.9°$ (c=2.98, MeOH); IR (Film) ν_{max} 3586, 1643, 1032 cm^{-1}; ^{1}H-NMR (CD_3OD, 600 MHz) δ 0.90 (3H, d, J=6.9 Hz, H_3-10), 1.40, 1.87 (1H each, both m, H_2-2), 1.60, 1.68 (3H each, both s, H_3-8, 9), 1.68 (1H, m, H-3), 2.07, 2.19 (1H each, both m, H_2-5), 3.38 (1H, m, H-4), 3.55, 3.97 (1H each, both m, H_2-1), 4.23 (1H, d, J=7.5 Hz, H-1′), 5.22 (1H, t, J=6.8 Hz, H-6); ^{13}C-NMR data see Table 1; positive-ion FAB-MS *m/z*: 335 $[M+H]^+$; HR-FAB-MS *m/z*: 335.2077 (Calcd for $C_{16}H_{30}O_7$ $[M+H]^+$, 335.2069).

Sachaloside VII (**3**): Obtained as colorless viscous oil; $[\alpha]_D^{27}$ $-44.0°$ (c=0.84, MeOH); IR (Film) ν_{max} 3567, 1636, 1040 cm^{-1}; ^{1}H-NMR (CD_3OD, 600 MHz) δ: 1.13, 1.17, 1.71 (3H each, both s, H_3-8, 9, 10), 1.39, 1.75 (1H each, both m, H_2-5), 2.08, 2.29 (1H each, both m, H_2-4), 3.24 (1H, m, H-6), 4.25 (1H, dd, J=7.6, 12.0 Hz, H-1a), 4.28 (1H, d, J=7.7 Hz, H-1′), 5.34 (1H, dd, J=6.4, 12.0 Hz, H-1b), 5.43 (1H, t like, J=*ca.* 7 Hz, H-2); ^{13}C-NMR data see Table 1; positive-ion FAB-MS: *m/z* 373 $[M+Na]^+$; HR-FAB-MS *m/z*: 373.1844 (Calcd for $C_{16}H_{30}O_8Na$ $[M+Na]^+$, 373.1838).

Sachaloside VIII (**4**): Obtained as colorless viscous oil; $[\alpha]_D^{27}$ $-36.8°$ (c=0.79, MeOH); IR (Film) ν_{max} 3503, 1647, 1040 cm^{-1}; ^{1}H-NMR (CD_3OD, 600 MHz) δ: 1.17 (6H, s, H_3-8, 9), 1.69 (3H, s, H_3-10), 1.50 (2H,

m, H_2-5), 2.04 (2H, t, J=6.9 Hz, H_2-4), 1.49 (2H, m, H-6), 4.20 (1H dd, J=7.6, 12.4 Hz, H-1a), 4.35 (1H dd, J=6.9, 12.4 Hz, H-1b), 4.29 (1H, d, J=8.2 Hz, H-1′), 4.31 (1H, d, J=6.8 Hz, H-1″), 5.38 (1H, t like, J=*ca.* 7 Hz, H-2); ^{13}C-NMR data see Table 1; positive-ion FAB-MS *m/z* 489 $[M+Na]^+$; HR-FAB-MS *m/z* 489.2317 (Calcd for $C_{21}H_{38}O_{11}Na$ $[M+Na]^+$, 489.2312).

Acid Hydrolysis of 2—4 Solution of **2**—**4** (each 1.0 mg) in 1 M HCl (2.0 ml) were each heated under reflux for 3 h. After cooling, each reaction mixture was neutralized with Amberlite IRA-400 (OH^- form) and filtrated, and the solution was partitioned with EtOAc to give two layers. The aqueous layer was evaporated and then subjected to HPLC analysis using Kaseisorb LC NH_2-60-5 column (4.6 mm×250 mm i.d., Tokyo Kasei Co., Ltd., Tokyo, Japan) and an optical rotation detector (Shodex OR-2, Showa Denko Co., Ltd., Tokyo, Japan) with CH_3CN–H_2O [(75 : 25, v/v), 0.5 ml/min]. D-Glucose and L-arabinose were confirmed by comparison of the retention time with the authentic samples (Wako Pure Chemicals Ltd., Osaka, Japan); t_R: 13.8 min (D-(+)-glucose, positive optical rotation); t_R: 12.3 min (L-(+)-arabinose, positive optical rotation).

Enzymatic Hydrolysis of 2 and 3 with β-Glucosidase Solution of **3** (5.5 mg) in H_2O (2.0 ml) was treated with β-glucosidase (from Almond, Oriental yeast Co., Ltd., Japan, 1 unit) and the solution was stirred at 37 °C for 24 h. After EtOH was added to the reaction mixture, the solvent was removed under reduced pressure and the residue was purified by HPLC [MeOH–H_2O (45 : 55, v/v)] to furnish (*S*)-3,7-dimethyloct-2*E*-en-1,6,7-triol (2.7 mg, 90%). Through a similar procedure, enzymatic hydrolysis of **2** (7.2 mg) was carried out to afford sachalol (**1**, 3.1 mg, 82%). The obtained compound, (*S*)-3,7-dimethyloct-2*E*-en-1,6,7-triol, was identified by comparison of their physical data ($[\alpha]_D$, ^{1}H-NMR, ^{13}C-NMR, MS) with reported values.

Enzymatic Hydrolysis of 4 with Naringinase Solution of **4** (6.7 mg) in 0.1 M acetate buffer (pH 3.8, 2.0 ml) was treated with naringnase (Sigma Chemical Co., 2 units), and the solution was stirred at 40 °C for 24 h. After EtOH was added to the reaction mixture, the solvent was removed under reduced pressure and the residue was purified by HPLC [MeOH–H_2O (45 : 55, v/v)] to furnish *E*-3,7-dimethyloct-2-en-1,7-diol (1.2 mg, 49%). The obtained compound, *E*-3,7-dimethyloct-2-en-1,7-diol, was identified by comparison of their physical data (^{1}H-NMR, ^{13}C-NMR, MS) with reported values.

Pivaloylation of 1 Solution of **1** (4.0 mg, 0.023 mmol) in pyridine (1.0 ml) was treated with pivaloyl chloride (20 μl, 0.161 mmol) and the mixture was stirred at rt for 6 h. The reaction mixture was poured into water (1.0 ml) and the whole was extracted with EtOAc (5 ml). The EtOAc extract was successively washed with H_2O and brine, then dried over Na_2SO_4 powder and filtered. Removal of the solvent from the filtrate under reduced pressure furnished a residue, which was purified by normal-phase silica gel column chromatography [*n*-hexane–EtOAc (2 : 1, v/v)] to give **1a** (4.3 mg, 72%).

Compound **1a**: Obtained as colorless viscous oil; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 1.20 (9H, s, $(C\underline{H}_3)_3CCOO$), 0.97 (3H, d, J=7.0 Hz, H_3-10), 1.63 (2H, m, H-2), 1.65, 1.74 (3H each, both s, H_3-8, 9), 1.73 (1H, m, H-3), 2.17 (2H, m, H-5), 3.44 (1H, m, H-4), 3.65 (1H, m, H-1a), 3.77 (1H, m, H-1b), 5.17 (1H, t like, J=*ca.* 7.0 Hz, H-6); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ 15.7 (C-10), 18.0 (C-8), 26.0 (C-9), 27.2 [$(\underline{C}H_3)_3CCOO$], 33.4 (C-5), 36.1 (C-3), 36.2 (C-2), 38.7 [$(CH_3)_3\underline{C}COO$], 63.0 (C-1), 75.3 (C-4), 120.2 (C-6), 135.6 (C-7), 178.7 [$(CH_3)_3C\underline{C}OO$]; positive-ion CI-MS *m/z*: 257 $[M+Na+H]^+$; HR-CI-MS *m/z*: 257.2109 (Calcd for $C_{15}H_{29}O_3Na$ $[M+Na+H]^+$, 257.2117).

Preparation of the (*S*)- and (*R*)-MTPA Esters, 1b and 1c, with MTPA-Cl Solution of **1a** (1.7 mg, 0.0066 mmol) in pyridine (1.0 ml) was treated with (−)-MTPA-Cl (0.01 ml, 0.066 mmol), and the mixture was stirred at rt for 6 h. The reaction mixture was poured into water (1.0 ml) and the whole was extracted with EtOAc (6 ml). The EtOAc extract was washed with H_2O and brine, then dried over Na_2SO_4 powder and filtered. Removal of the solvent from the filtrate under reduced pressure furnished a residue, which was purified by normal-phase silica gel column chromatography [*n*-hexane–EtOAc (3 : 1, v/v)] to give (*S*)-MTPA ester derivative (**1b**, 2.0 mg, 64%). Using a similar procedure, (*R*)-MTPA ester derivative (**1c**, 1.5 mg, 58%) was obtained from **1a** (1.4 mg, 0.0055 mmol).

(*S*)-MTPA Ester **1b**: ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.97 (3H, d, J=6.7 Hz, H_3-10), 1.20 (9H, s, $(C\underline{H}_3)_3CCOO$), 1.40 (1H, m, H-2a), 1.55, 1.63 (3H each, both s, H_3-8, 9), 1.85 (1H, m, H-2b), 1.94 (1H, m, H-3), 2.21 (1H, m, H-5a), 2.24 (1H, m, H-5b), 4.06 (1H, m, H-1a), 4.12 (1H, m, H-1b), 4.98 (1H, t, J=7.0 Hz, H-6).

(*R*)-MTPA Ester **1c**: ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 0.88 (3H, d, J=8.0 Hz, H_3-10), 1.20 (9H, s, ($C\underline{H}_3)_3CCOO$), 1.34 (1H, m, H-2a), 1.61, 1.70 (3H each, both s, H_3-8, 9), 1.80 (1H, m, H-2b), 1.92 (1H, m, H-3), 2.27 (1H, m, H-5a), 2.43 (1H, m, H-5b), 4.02 (1H, m, H-1a), 4.09 (1H, m, H-1b), 5.04 (1H, m, H-6).

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