Bicyclic Polyketide Lactones from Chinese Medicinal Ants, *Polyrhacis lamellidens*

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Two new bicyclic polyketide lactones, polyrhacitides A (**1**) and B (**2**), were isolated from Chinese medicinal ants, *Polyrhacis lamellidens*, which have been used as an effective therapeutic agent to treat rheumatoid arthritis and hepatitis in China. Their absolute structures were elucidated on the basis of spectroscopic analyses and chemical evidence. The occurrence of polyketides with similar structures in plants of the Lamiaceae, Lauraceae, and Staphyleaceae indicates their significance in the study of chemical ecology.

The Chinese medicinal ant *Polyrhacis lamellidens* Smith (Formicidae) is widely distributed in mainland China and has been used clinically as a folk medicine for treating rheumatoid arthritis and hepatitis in China.[1] We previously investigated the analgesic and anti-inflammatory effects of ethanol extracts of *P. lamellidens* and fractions obtained by solvent partition of the total extracts. The results demonstrated that extracts of *P. lamellidens* present remarkable analgesic and anti-inflammatory activities, which supported the traditional use of the medicinal ants in the treatment of various diseases associated with inflammation.[2] The diethyl ether fraction was found to have greater analgesic activity than the crude MeOH extract.[2] There are no reports of chemical studies of the secondary metabolites of this ant species, although a number of alkaloids[3] and peptides[4] were isolated from African and Australian ants. Herein, we describe the isolation and structural determination of polyrhacitides A (**1**) and B (**2**), two novel aliphatic polyketide lactones from the ether fraction of MeOH extracts of *P. lamellidens*.

Polyrhacitide A (**1**) was isolated as optically active ($[\alpha]^{15}_{D}$ +8.3), colorless needles. The molecular formula was established as $C_{18}H_{32}O_5$ on the basis of HREIMS ($[M - H_2O]^+$, *m/z* 310.2141) and ^{13}C NMR data (see Experimental Section). One of three degrees of unsaturation of **1** was attributed to an ester carbonyl on the basis of the IR absorption at 1729 cm^{-1} and the sp^2 carbon signal (δ 169.2) in the ^{13}C NMR spectrum. The remaining two degrees of unstaturation were attributed to two ring units in the molecule because no other unsaturated carbon signal was observed in the ^{13}C NMR spectrum. The NMR spectra exhibited five oxygenated methine signals (δ_C 72.6, 72.3, 72.2, 66.6, 66.0), one methyl group (δ_H 0.88; δ_C 14.1), and 11 methylene signals. Analyses of the cross-peaks in the $^1H-^1H$ COSY spectrum combined with information from the 1D NMR and HSQC spectra disclosed two partial structural units, shown by heavy lines in Figure 1. The HMBC correlation (Figure 1) between H-7 (δ 4.04, 1H, dddd, 3, 4, 10, 12) and C-3 (δ 66.0) demonstrated an ether linkage between C-3 and C-7. Furthermore, both H-2 (δ 2.90, 1H, d, 19; δ 2.82, 1H, dd, 5, 19) and H-5 (δ 4.89, 1H, ddd, 2, 4, 4) showed HMBC correlations with carbonyl C-1 (δ 169.2), suggesting a lactone structure in **1**. Finally, the HMBC correlations between the H_3-18 signal and C-16 and between H-12 and C-14 revealed a linear alkyl structure from C-12 to C-18. Taking the unsaturation degrees of **1** into account, both C-9 and C-11 were determined to be hydroxylated. Therefore, compound **1** was characterized as a bicyclic lactone having a hydroxylated alkyl group attached as shown in Figure 1.

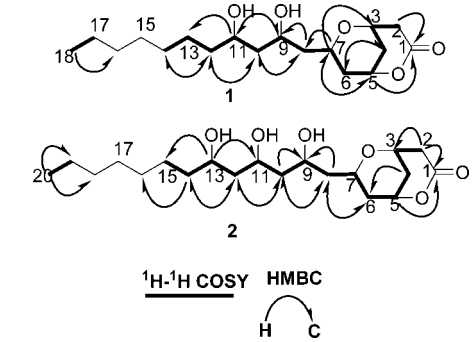
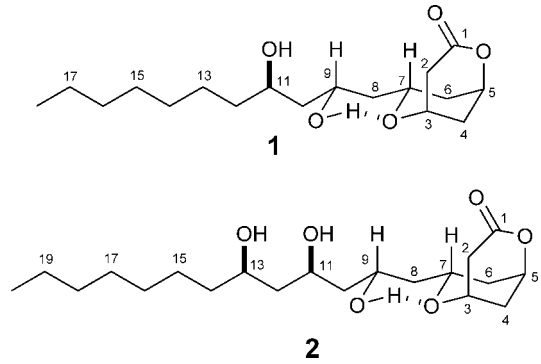


Figure 1. $^1H-^1H$ COSY and HMBC correlations in **1** and **2**.



An intramolecular hydrogen bond between the ether oxygen at C-7 and the OH group at C-9 was deduced from the following observations. First, the IR absorption at 3315 cm^{-1} of **1** suggested the existence of a hydrogen-bonded OH group. Second, the coupling constants of 10 Hz for $J_{H\text{-}8a,H\text{-}7}$ and $J_{H\text{-}8a,H\text{-}9}$ and of 3 Hz for $J_{H\text{-}8b,H\text{-}7}$ and $J_{H\text{-}8b,H\text{-}9}$ indicated a six-membered ring in a chair conformation, formed by an intramolecular hydrogen bond between 9-OH and the ether oxygen at C-7. Upon acetylation of **1** to **1a**, the values of $J_{H\text{-}8a,H\text{-}7}$, $J_{H\text{-}8a,H\text{-}9}$, $J_{H\text{-}8b,H\text{-}7}$, and $J_{H\text{-}8b,H\text{-}9}$ in the acetylated **1** (**1a**) changed to 7, 7, 5, and 5 Hz, respectively (Figure 2), indicating that the six-membered ring had been disrupted by acetylation of the C-9 OH group. A six-membered ring with chair conformation resulted from the intramolecular hydrogen bond, as indicated by the NOE correlations between H_{ax}-6 (1.64, 1H, ddd, 4, 12, 14) and H_{ax}-8 (1.73, 1H, dt, 14, 10) and between H_{eq}-6 (2.04, 1H, dd, 4, 14) and H_{eq}-8 (1.58, 1H, dt, 14, 3) observed in the NOESY spectrum of **1**. Therefore, a *syn* configuration of C-7 and C-9 was established by the existence of the intramolecular hydrogen bond described above. This type of intramolecular hydrogen bond was reported in a synthetic fragment of maitotoxin by Kishi et al.[5] The relative configuration between C-5 and C-7 was also elucidated to be *syn*

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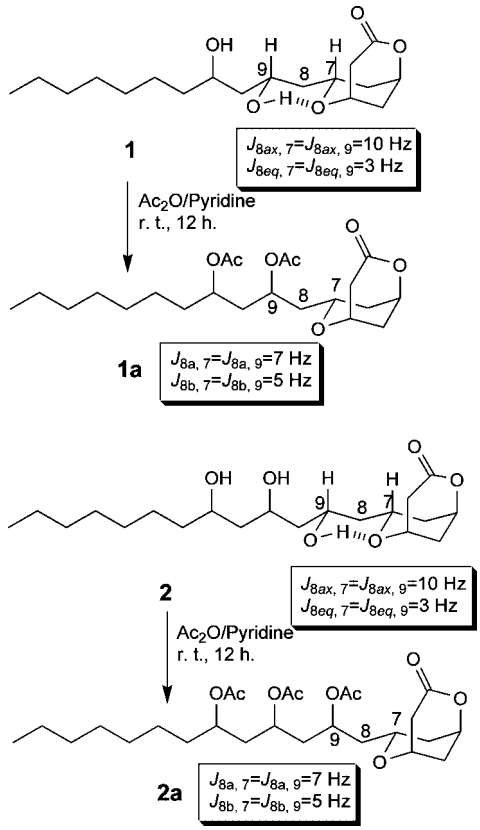

Figure 2. Acetylation of compounds **1** and **2**.

based on an axial orientation of H-7*ax* (1H, dddd, 3, 4, 10, 12) and equatorial orientations of both H-5*eq* (1H, ddd, 2, 4, 4) and H-3*eq* (1H, br s) on a six-membered ring (C7−C6−C5−C4−C3−O) with a chair conformation.

To determine the relative configuration of the 9,11-diol of **1**, the acetonide derivative (**1b**) of **1** was prepared. The chemical shift of the acetal carbon and the large difference in chemical shifts of the two isopropylidene methyl carbons (Figure 3) indicated a *syn* relationship between C-9 and C-11.[6]

Compound **1** was also converted to 11-mono-(*R*)- and (*S*)-MTPA esters (**1c**, **1d**), 9,11-di-(*R*)- and (*S*)-MTPA esters (**1e**, **1f**), and 9-mono-(*R*)- and (*S*)-MTPA esters (**1g**, **1h**) for determination of the absolute configuration. Application of MTPA esters **1c**, **1d** and **1g**, **1h** to the modified Mosher's method,[7] respectively, indicated *R*-configurations for both C-9 and C-11 in **1** (Figure S1, Supporting Information). Thus, the absolute configuration of **1** was established as 3*S*, 5*R*, 7*R*, 9*R*, 11*R*.

Polyrhacitide B (**2**) was isolated as an optically active ($[\alpha]^{15}_{D}$ +7.2), white powder. Its molecular formula ($C_{20}H_{36}O_6$), two carbons more than **1**, was established on the basis of HREIMS ($[M - 2H_2O]^+$, *m*/*z* 336.2299) and ^{13}C NMR data. Comparison of its NMR data with those of **1** disclosed that chemical shifts of proton and carbon signals due to most of the groups were in good agreement with those of **1**, except for additional signals of a methylene and a hydroxylated methine. Assignment of the NMR signals for **2**, with the aid of $^1H-^1H$ COSY, HMQC, and HMBC experiments, established the gross structure of **2**. The intramolecular hydrogen bond between the C-9 OH and the C-7 oxygen was confirmed on the basis of analyses of the coupling constants of H-7, H-8, and H-9 of **2** and its acetylated product **2a**.

To determine the relative configurations of the three OH groups in **2**, two acetonide derivatives (**2b**, **2c**) were synthesized (Figure 3). The ^{13}C NMR data of acetal and isopropylidene methyl carbons in both **2b** and **2c** indicated a *syn* relationship between the C-9 and C-11 as well as C-11 and C-13.[6] Application of the MTPA esters

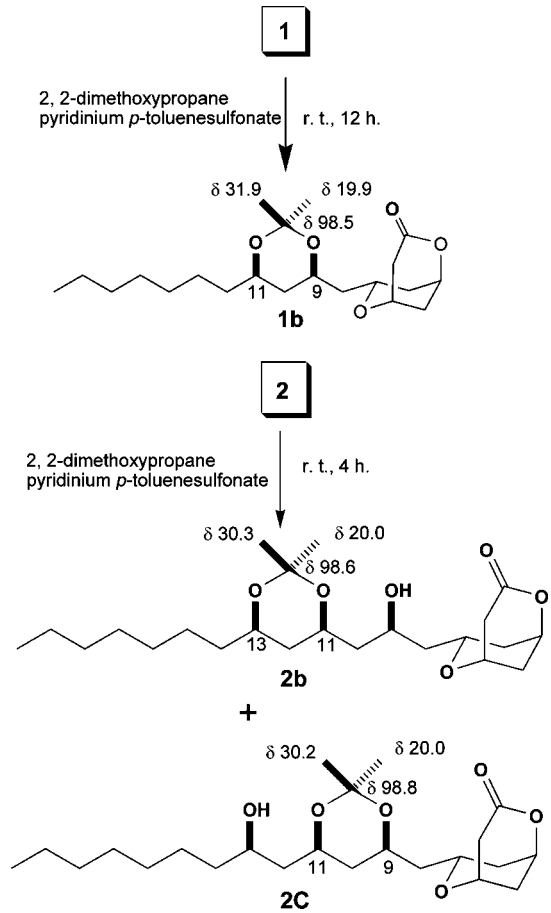

Figure 3. Synthesis of the acetonides of polyrhacitides A (**1**) and B (**2**).

(**2d**, **2e**) of the 11,13-*syn* acetonide (**2b**) to the modified Mosher's method[7] led to the conclusion of an *R* configuration at C-9 (Figure S1, Supporting Information). Therefore, the absolute configuration of **2** was determined to be 3*S*, 5*R*, 7*R*, 9*R*, 11*R*, and 13*R*.

Aliphatic polyketides such as **1** and **2** are unusual in ants, although the aromatic polyketides mellein and 2,4-dihydroxyacetophenone were isolated from the Australian ponerine ant.[8] Polyrhacitides **1** and **2** have a bicyclic lactone structure in the molecule formed by intramolecular addition of an OH group to an α,β-unsaturated lactone. Similar polyketides having bicyclic lactones, and their precursors, have been isolated from the plants of *Cryptocarya* and *Ocotea* (Lauraceae),[9] *Syncolostemon* (Lamiaceae),[10] *Iboza* (Lamiaceae),[11] and *Euscaphis* (Staphyleaceae).[12]

Experimental Section

General Experimental Procedures. Melting points were determined on a micromelting point hot stage apparatus (Yanagimoto) and are uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a JASCO FT-IR-230 spectrometer. ^1H and ^{13}C NMR spectra were obtained with the following instruments: Varian Unity plus 500, Varian Gemini 300 at 500 and 300 MHz for ^1H and 125 and 75 MHz for ^{13}C, respectively. Coupling constants are expressed in Hz, and chemical shifts are given on a δ (ppm) scale with tetramethylsilane as an internal standard. HRESIMS were recorded on a Q-TOF mass spectrometer (Bruker Daltonics, MA). EIMS were obtained on a JEOL JMS DX-303 spectrometer. Column chromatography was performed with Kieselgel 60 (70–230 mesh, Merck), MCI-gel CHP 20P (75–150 mm, Mitsubish Chemical Co.), and Chromatorex ODS (100–200 mesh, Fuji Silysia Chemical Ltd.). TLC was performed on precoated Kiesegal 60 F_{254} plates (0.2 mm thick, Merck), and spots were detected by spraying 10% sulfuric acid reagent.

Animal Material. Ants, *Polyrhachis lamellidens* (2.0 kg), were purchased from Jinling Ants Therapy Research Center, Nanjing, China.

The ants were identified by Professor Jian Wu of Chinese Academy of Forestry, Beijing, China.

Extraction and Isolation. MeOH extracts of the ants (2 kg) were partitioned between Et_2O and H_2O. The Et_2O layer (90 g) was fractionated by chromatography over silica gel ($CHCl_3$−MeOH−H_2O, 100:0:0–90:10:1–70:30:5). A fraction (16.4 g) eluted with $CHCl_3$−MeOH−H_2O (90:10:1) was further subjected to chromatography over MCI-gel CHP 20P (0%−100% MeOH). The 80–90% eluent was chromatographed over silica gel ($CHCl_3$−MeOH−H_2O, 100:0:0–90:10:1) and Chromatorex ODS (60–80% MeOH) to afford polyrhacitide A (**1**, 56.2 mg) and polyrhacitide B (**2**, 19.2 mg).

Polyrhacitide A (1): colorless needles; mp 65–68 °C; $[\alpha]^{15}_D$ +8.3 (*c* 0.6, MeOH); IR (neat) ν_{max} (cm^{-1}) 3421, 3315 (hydrogen-bonded OH), 2923, 2854, 1729, 1454, 1340, 1201, 1087 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.89 (1H, ddd, J = 2, 4, 4 Hz, H-5), 4.41 (1H, br s, H-3), 4.09 (1H, dddd, J = 3, 3, 9, 10 Hz, H-9), 4.04 (1H, dddd, J = 3, 4, 10, 12 Hz, H-7), 3.83 (1H, m, H-11), 2.90 (1H, d, J = 19 Hz, H-2a), 2.82 (1H, dd, J = 5, 19 Hz, H-2b), 2.04 (1H, ddd, J = 2, 4, 14 Hz, H-4a), 2.04 (1H, dd, J = 4, 14 Hz, H-6*eq*), 1.95 (1H, ddd, J = 2, 4, 14 Hz, H-4b), 1.73 (1H, dt, J = 14, 10 Hz, H-8*ax*), 1.64 (1H, ddd, J = 4, 12, 14 Hz, H-6*ax*), 1.58 (1H, J = dt, 14, 3 Hz, H-8*eq*), 1.54, (1H, m, H-10b), 1.52 (1H, m, H-10a), 1.44 (2H, m, H-12), 1.40 (1H, m, H-13a), 1.29 (7H, m, H-13b, H-14, H-15, H-16, H-17), 0.88 (3H, t, J = 7 Hz, H-18); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.4 (C, C-1), 72.6 (CH, C-5), 72.3 (CH, C-9), 72.2 (CH, C-11), 66.6 (CH, C-7), 66.0 (CH, C-3), 43.3 (CH_2, C-10), 43.0 (CH_2, C-8), 37.8 (CH_2, C-12), 37.2 (CH_2, C-6), 36.4 (CH_2, C-2), 31.8 (CH_2, C-16), 29.6 (CH_2, C-14), 29.5 (CH_2, C-4), 29.3 (CH_2, C-15), 25.4 (CH_2, C-13), 22.6 (CH_2, C-17), 14.1 (CH_3, C-18); EIMS m/z 328 $[M]^+$, 310 $[M - H_2O]^+$; HREIMS m/z 310.2141 $[M - H_2O]^+$ (calcd for $C_{18}H_{30}O_4$, 310.2144).

Acetylation of 1. A solution of **1** (2 mg) in Ac_2O (0.5 mL) and pyridine (0.5 mL) was kept at room temperature overnight. H_2O (5 mL) and Et_2O (5 mL) were added to the reaction mixture. The dried (Na_2SO_4) Et_2O layer was evaporated *in vacuo* to give **1a** (2 mg): white powder; $[\alpha]^{20}_D$ +4.6 (*c* 0.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.04 (1H, m, H-9), 4.88 (1H, m, H-11), 4.86 (1H, ddd, J = 2, 4, 4 Hz, H-5), 4.32 (1H, br s, H-3), 3.88 (1H, ddt, J = 12, 7, 5 Hz, H-7), 2.88 (1H, d, J = 19 Hz, H-2a), 2.75 (1H, dd, J = 6, 19 Hz, H-2b), 2.10, 2.04 (each 3H, s, acetyls), 1.98, 1.91 (each 1H, m, H_2-4), 1.98 (1H, m, H-6a), 1.85 (2H, dt, J = 14, 7 Hz, H-8b, H-10b), 1.75 (1H, dt, J = 14, 6 Hz, H-10a), 1.69 (1H, dt, J = 14, 5 Hz, H-8a), 1.56 (1H, ddd, J = 2, 12, 14 Hz, H-6b), 1.52 (1H, m, H-12a), 1.25 (11H, m, H-12b, H_2-13, H_2-14, H_2-15, H_2-16, H_2-17), 0.88 (3H, d, J = 7 Hz, H_3-18); EIMS m/z 352 $[M - Ac - H_2O]^+$ (20), 310 $[M - Ac \times 2\text{-}H_2O]^+$ (50), 292 $[M - Ac \times 2\text{-}H_2O \times 2]^+$ (100), 271 (18), 211 (42), 193 (70), 183 (50), 167 (45), 155 (95), 141 (100); positive HRESIMS m/z 435.2321 (calcd for $C_{22}H_{36}O_7Na$, 435.2353).

Acetonide of 1. To a solution of **1** (6 mg) in CH_2Cl_2 (0.5 mL) were added 2,2-dimethoxypropane (0.1 mL) and pyridinium *p*-toluenesulfonate (2 mg), and the mixture was kept at room temperature overnight. The solution was subsequently evaporated *in vacuo*, and the residue was purified by silica gel column chromatography (CC) with *n*-hexane−EtOAc (3:1–1:1) to yield acetonide **1b** (5.5 mg): white powder; $[\alpha]^{20}_D$ +6.5 (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.90 (1H, br s, H-5), 4.35 (1H, br s, H-3), 4.01, 3.81, 3.94 (each 1H, m, H-7, 9, 11), 2.82 (2H, m, H_2-2), 1.37, 1.28 (each 3H, s, isopropylidene-Me), 0.88 (3H, t, J = 7 Hz, H_3-18); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7 (C-1), 98.5 (isopropylidene quaternary carbon), 73.0 (C-5), 65.8 (C-3), 69.0, 65.4, 62.3 (C-7, 9, 11), 42.4, 36.9, 36.8, 36.5 × 2 (C-2, 6, 8, 10, 12), 31.9 (C-16), 30.3 (isopropylidene-Me), 29.9, 29.6, 29.3 (C-4, 14, 15), 25.1 (C-13), 22.7 (C-17), 19.9 (isopropylidene-Me), 14.2 (C-18); EIMS m/z 368 $[M]^+$ (1), 353 $[M - CH_3]^+$ (100), 310 (30), 293 (25), 183 (50), 163 (30), 141 (100); positive HRESIMS m/z 391.2418 (calcd for $C_{21}H_{36}O_5Na$, 391.2455).

(*R*)- and (*S*)-MPTA Esters of 1. A solution of **1** (3.8 mg), dicyclohexylcarbodiimide (8 mg), 4-dimethylaminopyridine (4 mg), and (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (9 mg) in CH_2Cl_2 (1 mL) was left to stand at room temperature overnight. The resulting mixture was subjected to silica gel CC with *n*-hexane−EtOAc (5:1–2:1) to give 11-mono-(*R*)-MTPA ester **1c** (1.1 mg), 9,11-di-(*R*)-MTPA ester **1e** (2 mg), and 9-mono-(*R*)-MTPA ester **1g** (0.5 mg). Using (*S*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid gave 11-mono-(*S*)-MTPA ester **1d** (0.8 mg), 9,11-di-(*S*)-MTPA ester **1f** (2 mg), and 9-mono-(*S*)-MTPA ester **1h** (0.5 mg) (Figure S1, Supporting Information).

Polyrhacitide B (2): white powder; $[\alpha]^{15}_D$ +7.2 (*c* 0.6, MeOH); IR (neat) nmax (cm^{-1}) 3450, 3342 (hydrogen-bonded OH), 2925, 2856, 1733, 1454, 1328, 1201, 1093 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.89 (1H, ddd, J = 2, 4, 4 Hz, H-5), 4.41 (1H, br s, H-3), 4.12 (1H, m, H-11), 4.10 (1H, dddd, J = 3, 3, 9, 10 Hz, H-9), 4.04 (1H, dddd, J = 3, 4, 10, 12 Hz, H-7), 3.86 (1H, ddd, J = 5, 7, 12 Hz, H-13), 2.90 (1H, d, J = 19 Hz, H-2a), 2.82 (1H, dd, J = 5, 19 Hz, H-2b), 2.04 (1H, dd, J = 4, 14 Hz, H-6*eq*), 2.04 (1H, ddd, J = 2, 4, 14 Hz, H-4a), 1.95 (1H, ddd, J = 2, 4, 14 Hz, H-4b), 1.73 (1H, dt, J = 14, 10 Hz, H-8*ax*), 1.65 (1H, ddd, J = 4, 12, 14 Hz, H-6*ax*), 1.61 (1H, m, H-10a), 1.58 (1H, dt, J = 14, 3 Hz, H-8*eq*), 1.53 (2H, m, H-12), 1.48 (2H, m, H-10b, H-14a), 1.41 (1H, m, H-14b), 1.39 (1H, m, H-15b), 1.29 (7H, m, H-15b, H-16, H-17, H-18, H-19), 0.88 (3H, t, J = 7 Hz, H-20); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.2 (C, C-1), 73.2 (CH, C-11), 72.5 (CH, C-5), 72.5 (CH, C-13), 72.3 (CH, C-9), 66.9 (CH, C-7), 66.1 (CH, C-3), 43.9 (CH_2, C-10), 43.5 (CH_2, C-12), 42.8 (CH_2, C-8), 38.0 (CH_2, C-14), 37.2 (CH_2, C-6), 36.5 (CH_2, C-2), 31.8 (CH_2, C-18), 29.7 (CH_2, C-16), 29.5 (CH_2, C-4), 29.3 (CH_2, C-17), 25.4 (CH_2, C-15), 22.7 (CH_2, C-19), 14.1 (CH_3, C-20); EIMS m/z 372 $[M]^+$, 354 $[M - H_2O]^+$, 336 $[M - H_2O \times 2]^+$; HREIMS m/z 336.2299 $[M - H_2O \times 2]^+$ (calcd for $C_{20}H_{32}O_4$, 336.2301).

Acetylation of 2. Compound **2** (1 mg) was acetylated in a manner similar to that of **1** to give triacetate **2a** (1 mg): white powder; $[\alpha]^{20}_D$ +10.4 (*c* 0.1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.04 (1H, m, H-9), 4.95 (1H, m, H-11), 4.88 (1H, m, H-13), 4.86 (1H, m, H-5), 4.32 (1H, br s, H-3), 3.88 (1H, J = 12, 7, 5 Hz, H-7), 2.88 (1H, d, J = 19 Hz, H-2a), 2.75 (1H, dd, J = 6, 19 Hz, H-2b), 2.10, 2.04, 2.02 (each 3H, s, acetyls), 1.98, 1.91 (each 1H, m, H_2-4), 1.98 (1H, m, H-6a), 1.88 (2H, m, H_2-10), 1.85 (2H, dt, J = 14, 7 Hz, H-8b, H-12b), 1.75 (1H, dt, J = 14, 6 Hz, H-12a), 1.69 (1H, dt, J = 14, 5 Hz, H-8a), 1.56 (1H, ddd, J = 2, 12, 14 Hz, H-6b), 1.52 (1H, m, H-14a), 1.25 (11H, m, H-14b, H_2-15, H_2-16, H_2-17, H_2-18, H_2-19), 0.88 (3H, d, J = 7 Hz, H_3-20); EIMS m/z 498 $[M]^+$ (0.2), 480 $[M - H_2O]^+$ (0.5), 438 $[M - Ac - H_2O]^+$ (10), 378 (60), 336 (25), 318 (100), 297 (20), 180 (25), 141 (85); positive HRESIMS m/z 521.2713 (calcd for $C_{26}H_{42}O_9Na$, 521.2721).

Acetonides of 2. Compound **2** (12 mg) was treated in the same way as described for **1** to give a mixture of acetonides **2b** and **2c** (4:1, 10 mg) as a white powder: ^1H NMR (500 MHz, $CDCl_3$) for **2b**, δ 4.89 (1H, ddd, J = 2, 4, 4 Hz, H-5), 4.38 (1H, br s, H-3), 4.09 (1H, m, H-11), 3.99 (2H, m, H-7, 9), 3.81 (1H, m, H-13), 2.90 (1H, d, J = 19 Hz, H-2a), 2.78 (1H, dd, J = 5, 19 Hz, H-2b), 2.08 (1H, m, H-6a), 2.04, 1.94 (each 1H, ddd, J = 2, 4, 14 Hz, H-4a, H-4b), 1.74 (1H, dt, J = 14, 10 Hz, H-8a),1.67 (1H, m, H-10a), 1.64 (1H, m, H-6b), 1.56 (1H, m, H-8b), 1.50 (1H, m, H-12a), 1.48 (1H, m, H-10b), 1.45, 1.38 (each 3H, s, isopropylidene-Me), 1.18 (1H, dt, J = 20, 12, 12 Hz, H-12b), 0.88 (3H, t, J = 7 Hz, H_3-20); ^{13}C NMR (75 MHz, $CDCl_3$) for **2b**, δ 169.6 (C-1), 98.6 (isopropylidene quaternary carbon), 72.5 (C-5), 69.0, 68.9, 68.8 (C-9, 11, 13), 66.0 (C-7), 65.2 (C-3), 43.3, 43.0, 37.2, 37.0, 36.5, 36.4 (C-2, 6, 8, 10, 12, 14), 31.9 (C-18), 30.3 (isopropylidene-Me), 29.7, 29.6, 29.3 (C-4, 16, 17), 25.0 (C-15), 22.7 (C-19), 20.0 (isopropylidene-Me), 14.2 (C-20); for **2c**: δ 169.7 (C-1), 98.8 (isopropylidene quaternary carbon), 73.0 (C-5), 71.9, 70.5, 62.2 (C-9, 11, 13), 65.8 (C-7), 65.3 (C-3), 42.9, 42.1, 37.7, 37.2, 36.91, 36.87 (C-2, 6, 8, 10, 12, 14), 31.9 (C-18), 30.2 (isopropylidene-Me), 29.8, 29.7, 29.4 (C-4, 16, 17), 25.5 (C-15), 22.7 (C-19), 20.0 (isopropylidene-Me), 14.2 (C-20); MS data for the mixture of **2b** and **2c**, EIMS m/z 412 $[M]^+$ (2), 397 $[M - CH_3]^+$ (98), 336 (10), 297 (10), 209 (15), 155 (30), 141 (80); positive HRESIMS m/z 435.2701 (calcd for $C_{23}H_{40}O_6Na$, 435.2717).

(*R*)- and (*S*)-MPTA Esters of 2b. A solution of **2b** (3 mg), dicyclohexylcarbodiimide (6 mg), 4-dimethylaminopyridine (4 mg), and (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (8 mg) in CH_2Cl_2 (1 mL) was kept at room temperature overnight. The resulting mixture was purified by silica gel CC with *n*-hexane−EtOAc (3:1–1:1) to give *R*-MTPA ester **2d** (2.8 mg). Using (*S*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid gave **2e** (2.6 mg).

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Supporting Information Available: Figure S1, determination of absolute configurations of **1** and **2** by the modified Mosher's method. This material is available free of charge via the Internet at http://pubs.acs.org.

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