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### THREE NEW *ENT*-KAURANE DITERPENOIDS FROM THE SEEDS OF *PHARBITIS NIL*

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**Abstract** – Three new *ent*-kaurane diterpenoids, 7 $\beta$ , 16 $\beta$ , 17-trihydroxy *ent*-kauran 18-(6 $\beta$ )-olide (**1**), methyl 6 $\beta$ , 7 $\beta$ , 16 $\beta$ , 17-tetrahydroxy *ent*-kauran-18-oate (**2**) and 6 $\beta$ , 7 $\beta$ , 16 $\beta$ , 17-tetrahydroxy *ent*-kauran-18-oic acid (**3**), together with thirteen known compounds, were isolated from the seeds of *Pharbitis nil* (Convolvulaceae). The identification and structural elucidation of these compounds were based on 1D- and 2D-NMR spectral data analysis. The absolute configuration of **1** was determined by a convenient Mosher ester procedure carried out in NMR tube.

## INTRODUCTION

Pharbitidis Semen, the seeds of 'morning-glory' *Pharbitis nil* CHOISY (Convolvulaceae), has been used as a crude purgative drug in Korean traditional medicine. Previous phytochemical studies of this herb found that gibberellins and their glycosides were abundant secondary metabolites in this herb.<sup>1-4</sup> Its major constituent is known to be an ether-insoluble resin glycoside with resinous purgative principles.<sup>5-7</sup> Pharbitidis Semen has anti-gastric cancer and anti-fungal activities.<sup>8,9</sup> In the course of our continuing search for potential lead compounds for drug development from Korean medicinal plant sources, we performed a phytochemical investigation of this herb. Column chromatographic purification of the CHCl<sub>3</sub>-soluble fraction of the EtOH extract of this source led to the isolation of three new kaurane diterpenes (**1-3**), together with thirteen known compounds (**4-16**). The structures of known compounds were determined to be ethyl caffeate (**4**),<sup>10</sup> *p*-coumaric acid ethyl ester (**5**),<sup>11</sup> ferulic acid ethyl ester (**6**),<sup>12</sup>

scopoletin (**7**),<sup>13</sup> crenulatin (**8**),<sup>14</sup> convolvulinolic acid (**9**),<sup>15</sup> (12*S*, 13*S*) 12, 13-dihydroxyoctadec-*cis*-9-enoic acid (**10**),<sup>16</sup> 9-oxooctadec-*cis*-12-enoic acid (**11**),<sup>17</sup> 9-hydroxyoctadec-*cis*-12-enoic acid (**12**),<sup>18</sup> (2*R*)-2-*O*-(9-oxooctadec-*cis*-12-enoyl) glycerol (**13**),<sup>17</sup> (2*R*)-2-*O*-(9-hydroxyoctadec-*cis*-12-enoyl) glycerol (**14**),<sup>18</sup> (9*S*, 10*E*, 12*Z*)-hydroxyoctadeca-10, 12-dienoic acid (**15**)<sup>19</sup> and trilinolein (**16**)<sup>20</sup> by comparing their spectroscopic data with those in the literatures. All the isolated known compounds (**4-8**, **10-16**) except **9** were reported from this source for the first time.

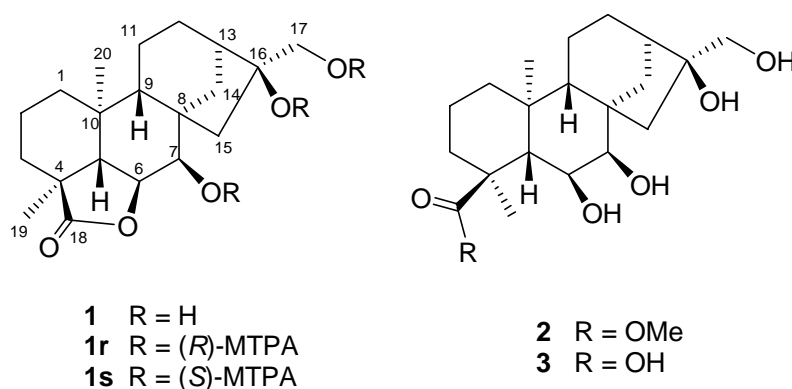


Figure 1. The structures of the isolated compounds (**1-3**) from *P.nil*

## RESULTS AND DISCUSSION

Compound **1** was obtained as a colorless gum, whose molecular formula was determined to be C<sub>20</sub>H<sub>30</sub>O<sub>5</sub> from the [M + H]<sup>+</sup> peak at m/z 351.2173 (calcd. for C<sub>20</sub>H<sub>31</sub>O<sub>5</sub>: 351.2172) in the high resolution-electron impact (HR-EI) MS spectrum. The IR spectrum indicated that **1** possessed hydroxyl (3413 cm<sup>-1</sup>) and  $\gamma$ -lactone (1757 cm<sup>-1</sup>) groups. The <sup>1</sup>H-NMR spectrum (Table 1) of **1** displayed signals for presence of two tertiary methyl groups at  $\delta_{\text{H}}$  = 1.15 and 1.25 and one hydroxymethylene group at  $\delta_{\text{H}}$  = 3.36 (d, *J* = 11.0 Hz) and 3.44 (d, *J* = 11.0 Hz), adjacent to the quaternary carbon. The <sup>13</sup>C-NMR and distortionless enhancement by polarization transfer (DEPT) experiments revealed that **1** displayed 20 carbon signals, composed of two methyls, eight methylenes, five methines, and five quaternary carbons. The <sup>13</sup>C-NMR resonances were similar to those of the related *ent*-kaurane  $\gamma$ -lactone diterpenes, *ent*-7 $\beta$ -hydroxykaurenolide,<sup>21</sup> except for the replacement of double bond for C-16 and C-17 with hydroxylated carbons at  $\delta_{\text{C}}$  = 80.4 ppm (C-16) and  $\delta_{\text{C}}$  = 70.6 ppm (C-17) in **1**, suggesting that **1** was to be *ent*-kaurane derivative. The *ent*-kaurane skeleton of **1** was also confirmed on the basis of the coupling constants (*J*<sub>5,6</sub> = 11.5 Hz and *J*<sub>6,7</sub> = 2.0 Hz) observed in the <sup>1</sup>H-NMR spectral data, NOESY correlations (H-6/H-20), and no NOESY correlations (H-5/H-6, H-5/H-20) (Figure 2).

The HMBC spectrum confirmed the position of the two hydroxyl groups at C-16 and C-17; The signals of H-17 ( $\delta_{\text{H}}$  = 3.36 and 3.44) correlated with C-13 ( $\delta_{\text{C}}$  = 42.3), C-15 ( $\delta_{\text{C}}$  = 49.5) and C-16 ( $\delta_{\text{C}}$  = 80.4). The

$\gamma$ -lactone function was located at C-4/C-6 from the HMBC correlations between H-19 ( $\delta_{\text{H}} = 1.25$ ) and C-18 ( $\delta_{\text{C}} = 185.9$ ), and H-5 ( $\delta_{\text{H}} = 2.33$ ) and C-18 ( $\delta_{\text{C}} = 185.9$ ) (Figure 2). And the signal of H-7 ( $\delta_{\text{H}} = 3.80$ ) correlated with C-6 ( $\delta_{\text{C}} = 80.0$ ), C-8 ( $\delta_{\text{C}} = 51.9$ ) and C-9 ( $\delta_{\text{C}} = 55.8$ ) in the HMBC experiment, allowing a hydroxyl group to be at C-7. The relative stereochemistry of **1** was assigned on the basis of the  $J$  values in the  $^1\text{H}$ -NMR spectrum and the NOESY experiment (Figure 2). The coupling constants of H-6 (dd,  $J_{5,6} = 11.5$  Hz and  $J_{6,7} = 2.0$  Hz) and H-7 (d,  $J_{6,7} = 2.0$  Hz) observed in the  $^1\text{H}$ -NMR spectrum in **1** were very similar with those of H-6 (dd,  $J_{5,6} = 11.5$  Hz and  $J_{6,7} = 2.5$  Hz) and H-7 (d,  $J_{6,7} = 2.5$  Hz) in 6 $\beta$ ,7 $\beta$ -dihydroxykaurenoic acid.<sup>22</sup> Thus, the configurations of H-6 and H-7 were determined to be  $\alpha$ -orientation, and also the  $\gamma$ -lactone group to be  $\beta$  disposition. These configurations could be confirmed in the NOESY correlations between H-5/H-1 $_{\text{ax}}$ , H-5/H-3 $_{\text{ax}}$ , between H-6/H-20, between H-19/H-3 $_{\text{eq}}$ , H-19/H-20 and between H-20/H-14 $_{\text{ax}}$ , which also suggested the  $\alpha$ -orientation of CH<sub>3</sub>-19 and CH<sub>3</sub>-20 (Figure 2). In addition, a correlation between H-17/H-13 in the NOESY spectrum confirmed that the configuration of OH group at C-16 was  $\beta$  form. Thus, the structure of **1** was determined to be 7 $\beta$ , 16 $\beta$ , 17-trihydroxy *ent*-kauran 18-(6 $\beta$ )-olide. The absolute configuration of **1** was determined by a convenient Mosher ester procedure carried out in NMR tube.<sup>23</sup> Analysis of the chemical shift differences between the (*R*)- and (*S*)-MTPA ester derivatives (**1r** and **1s**, respectively) ( $\delta_{\text{S}} - \delta_{\text{R}}$ ) of **1** (Figure 4) showed that the absolute stereostructures at C-7 and C-16 of **1** were to be *R*- and *S*-configuration, respectively.

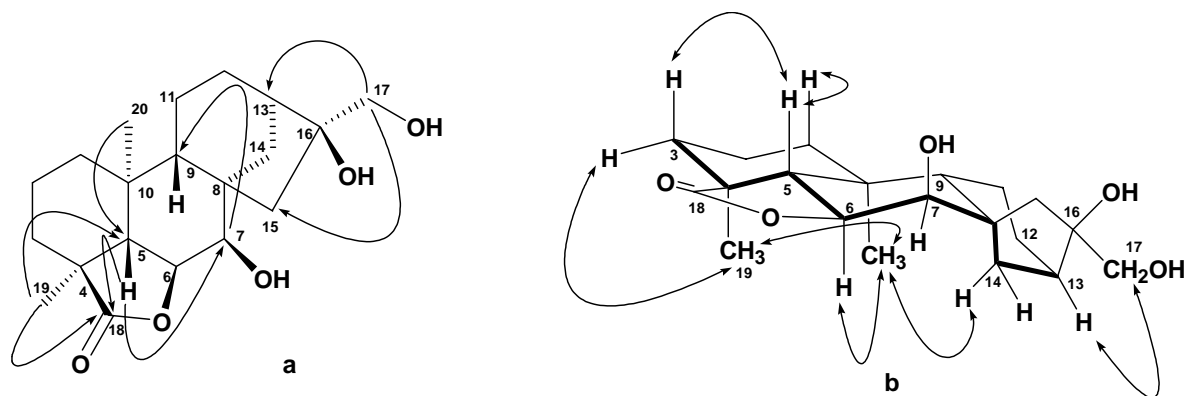


Figure 2. Key HMBC (↷) (a) and NOESY (↔) (b) correlations of **1**

Compound **2** was obtained as a colorless gum, whose molecular formula was determined to be C<sub>21</sub>H<sub>34</sub>O<sub>6</sub> from the [M + Na]<sup>+</sup> peak at  $m/z$  405.2265 (calcd. for C<sub>21</sub>H<sub>34</sub>O<sub>6</sub>Na: 405.2253) in the positive-ion high resolution (HR)-FAB-MS spectrum. The IR spectrum indicated that **2** possessed hydroxyl (3421 cm<sup>-1</sup>) and ester (1642 cm<sup>-1</sup>) groups. The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectral data (Table 1) of **2** were very similar to those of **1**, except for the presence of a methoxy group ( $\delta_{\text{C}} = 52.8$ ) at C-18 in **2**. This suggested that C-4/C-6  $\gamma$ -lactone function of **1** was broken into methylester functionality in **2**. The position of the

methoxy group was also confirmed to be at C-18 from the HMBC correlation between methoxy proton ( $\delta_{\text{H}} = 3.69$ ) and C-18 ( $\delta_{\text{C}} = 180.4$ ), as shown in Figure 3. A correlation between H-19/OCH<sub>3</sub>, H-19/H-20 in the NOESY spectrum confirmed that the methyl group at C-19 was  $\alpha$  form. In addition, the stereochemistry of **2** was assigned to be same as that of **1** on the basis of the NOESY experiment and the  $J$  values in the <sup>1</sup>H-NMR spectrum (Figure 3). Thus, the structure of **2** was determined to be methyl 6 $\beta$ , 7 $\beta$ , 16 $\beta$ , 17-tetrahydroxy *ent*-kauran-18-oate. The compound **2** could be detected by TLC analysis in the 50% ethanol extract of the source, which implied that **2** was not an artifact.

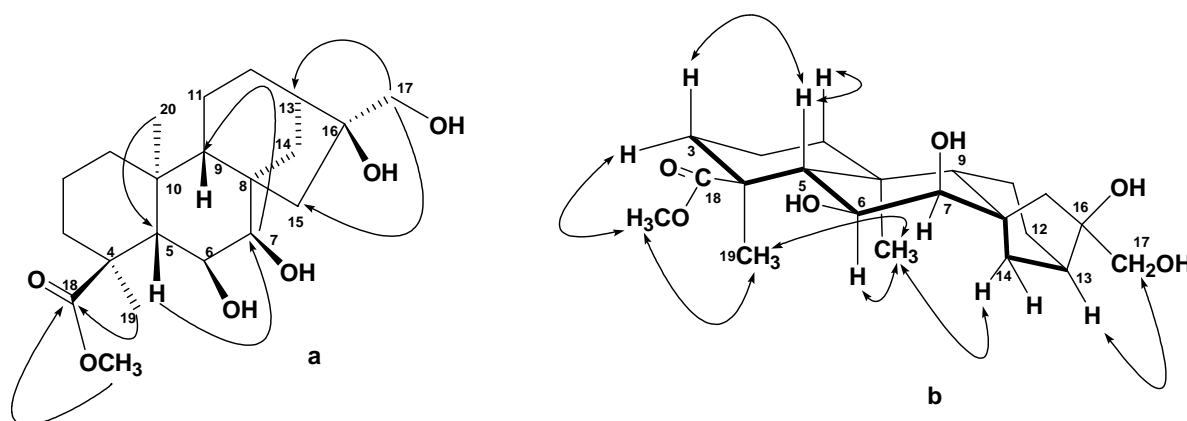


Figure 3. Key HMBC (↷) (a) and NOESY (↔) (b) correlations of **2**

Compound **3** was obtained as a colorless gum, whose molecular formula was determined to be C<sub>20</sub>H<sub>32</sub>O<sub>6</sub> from the [M + Na]<sup>+</sup> peak at  $m/z$  391.2122 (calcd. for C<sub>20</sub>H<sub>32</sub>O<sub>6</sub>Na: 391.2097) in the positive-ion high resolution (HR)-FAB-MS spectrum. The IR spectrum indicated that **3** possessed hydroxyl (3357 cm<sup>-1</sup>) and ester (1661 cm<sup>-1</sup>) groups. The <sup>1</sup>H- and <sup>13</sup>C-NMR spectral data (Table 1) of **3** were very similar to those of **2**, except for the absence of a methoxy group at C-18 in **3**. The stereochemistry of **3** was assigned to be same as that of **2** on the basis of the NOESY experiment and the  $J$  values in the <sup>1</sup>H-NMR spectrum. Thus, the structure of **3** was determined to be 6 $\beta$ , 7 $\beta$ , 16 $\beta$ , 17-tetrahydroxy *ent*-kauran-18-oic acid. The kaurenolides, diterpene lactones, are biosynthetically related to the gibberellin plant hormones.<sup>24,25</sup> Michael *et al.*<sup>26</sup> reported that *ent*-kaura-6, 16-dien-19-oic acid was incorporated, after incubation with the mutant (B1-41a), into 7 $\beta$ -hydroxykaurenolide via *ent*-6 $\beta$ , 7 $\alpha$ -dihydroxykaur-16-en-19-oic acid. Possible biosynthetic routes from *ent*-kaura-6, 16-dien-19-oic acid to 7 $\beta$ -hydroxykaurenolide were also studied.<sup>26</sup> Thus, we assumed that the compounds **2** and **3** could be the precursors of **1**.

## EXPERIMENTAL

**General.** All melting points were determined on a Gallenkamp melting point apparatus and uncorrected.

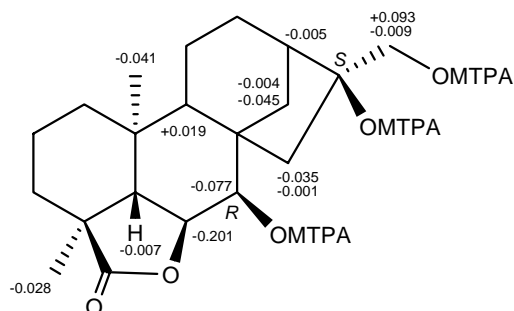


Figure 4. Values of  $\delta_S - \delta_R$  (data obtained in pyridine- $d_5$ ) of the MTPA esters of **1**.

Optical rotations were measured on a Jasco P-1020 polarimeter in MeOH. IR spectra were recorded on a Bruker IFS-66/S FT-IR spectrometer. EI and HR-EI mass spectra were recorded on a JEOL SX102 mass spectrometer. FAB and HR-FAB mass spectra were obtained on a JEOL JMS700 mass spectrometer. NMR spectra, including NOESY, DEPT and HMBC experiments, were recorded on a Varian UNITY INOVA 500 NMR spectrometer operating at 500 MHz ( $^1\text{H}$ ) and 125 MHz ( $^{13}\text{C}$ ), respectively, with chemical shifts given in ppm ( $\delta$ ) using TMS as an internal standard. Preparative HPLC used a Gilson 306 pump with Shodex refractive index detector. Silica gel 60 (Merck, 70-230 mesh and 230-400 mesh) and RP- $\text{C}_{18}$  silica gel (Merck, 230-400 mesh) was used for column chromatography. Merck precoated Silica gel F<sub>254</sub> plates and RP-18 F<sub>254s</sub> plates were used for TLC. Spots were detected on TLC under UV light or by heating after spraying with 10 %  $\text{H}_2\text{SO}_4$  in  $\text{C}_2\text{H}_5\text{OH}$  (v/v). The packing material for molecular sieve column chromatography was Sephadex LH-20 (Pharmacia Co.). Low pressure liquid chromatography was carried out over a Merck Lichroprep Lobar<sup>®</sup>-A Si 60 (240×10 mm) or a Lichroprep Lobar<sup>®</sup>-A RP-18 (240×10 mm) column with a FMI QSY-0 pump (ISCO).

**Plant material.** The seeds of *P. nil* were purchased from Kyungdong herbal market, Seoul, Korea, in July 2006. A voucher specimen (SKKU 2006-7) was deposited in the herbarium of the College of Pharmacy, Sungkyunkwan University, Suwon, Korea.

**Extraction and isolation.** The dried seeds (10 kg) were extracted with 50% EtOH three times at rt. The resultant ethanolic extracts (1.4 kg) were suspended in distilled water (7.2 L) and then successively partitioned with *n*-hexane,  $\text{CHCl}_3$ , EtOAc and *n*-BuOH, yielding 10 g, 7 g, 10 g and 550 g, respectively. The  $\text{CHCl}_3$  soluble fraction (7 g) was chromatographed on a RP- $\text{C}_{18}$  silica gel (230-400 mesh, 300 g), eluting with gradient solvent system of MeOH/ $\text{H}_2\text{O}$  (4:1, 9:1 and 1:0). According to TLC analysis, five crude fractions (fr. A - E) were collected. Fr. B (1.0 g) was chromatographed further on a RP- $\text{C}_{18}$  silica gel (230-400 mesh, 150 g), eluting with gradient solvent system of MeOH/ $\text{H}_2\text{O}$  (3:2, 4:1, 9:1 and 1:0) to

give five subfractions (fr. B1 - B5). Fr. B1 (90 mg) was purified by silica gel Lobar<sup>®</sup>-A Si 60 (240×10mm) column (hexane/CHCl<sub>3</sub>/EtOAc, 2:1:2) to afford **7** (5 mg) and **8** (6 mg) and was purified by preparative reversed-phase HPLC, using a solvent system of 30% MeCN to yield **3** (20 mg). Fr. B2 (550 mg) was chromatographed on a Sephadex LH-20 (150 g, Pharmacia Co.), using a solvent system of 100% MeOH, and purified by preparative reversed-phase HPLC, using a solvent system of 60% MeOH to yield **4** (50 mg). Fr. B3 (130 mg) was purified further by preparative reversed-phase HPLC, using a solvent system of 60% MeOH to obtain **1** (23 mg). Fr. B4 (60 mg) was purified by preparative reversed-phase HPLC, using a solvent system of 40% MeCN to obtain **2** (5 mg), **5** (14 mg) and **6** (20 mg), respectively. Fr. C (400 mg) was chromatographed on a RP-C<sub>18</sub> silica gel (230-400 mesh, 100 g), eluting with a gradient solvent system of MeCN/H<sub>2</sub>O (3:2, 4:1, 9:1 and 1:0) to give seven main fractions (fr. C1 - C7). Fr. C6 (70 mg) was purified by Lobar<sup>®</sup>-A RP-18 (240×10 mm) column (55% MeCN), and purified further by preparative reversed-phase HPLC, using a solvent system of 55% MeCN to obtain **10** (30 mg). Fr. C7 (30 mg) was chromatographed on a Sephadex LH-20 (150 g, Pharmacia Co.), using a solvent system of CH<sub>2</sub>Cl<sub>2</sub>/MeOH (1:1), to obtain **9** (8 mg). Fr. D (600 mg) was chromatographed on a Sephadex LH-20 (150 g, Pharmacia Co.), using a solvent system of 100% MeOH to give two main fractions (fr. D1 - D2), and Fr. D1 (400 mg) was rechromatographed on a RP-C<sub>18</sub> silica gel (230-400 mesh, 100 g), eluting with a gradient solvent system of MeCN/H<sub>2</sub>O (7:3, 9:1 and 1:0) to give six subfractions (fr. D11 - D16). Fr. D11 (25 mg) was purified further by preparative HPLC, using a solvent system of *n*-hexane/EtOAc (2:1) to yield **15** (6 mg) and **16** (4 mg). Fr. D12 (65 mg) was purified further by preparative HPLC, using a solvent system of *n*-hexane/EtOAc (2:3) to obtain **14** (30 mg). Fr. D13 (40 mg) was purified further by preparative HPLC, using a solvent system of *n*-hexane/EtOAc (1:1) to obtain **13** (6 mg). Fr. D14 (200 mg) was purified further by preparative HPLC, using a solvent system of *n*-hexane/EtOAc (5:2) to yield **12** (40 mg). Finally, fr. D16 (50 mg) was purified by preparative HPLC, using a solvent system of *n*-hexane/EtOAc (5:2) to obtain **11** (30 mg).

**7β, 16β, 17-Trihydroxy *ent*-kauran 18-(6β)-olide (1).** colorless gum.  $[\alpha]_D^{25} -20.2^\circ$  (c 0.25, MeOH); IR (KBr)  $\nu_{\max}$  cm<sup>-1</sup>: 3413, 2935, 1757, 1463, 1182 1095, 1009, 1616; EI-MS *m/z* (rel. int.) = 350 ([M]<sup>+</sup>, 2), 332 (10), 319 (35), 273 (28), 166 (28), 137 (28), 109 (100); HR-EI-MS *m/z* = 351.2173 [M + H]<sup>+</sup> (calcd for C<sub>20</sub>H<sub>31</sub>O<sub>5</sub>: 351.2172); <sup>1</sup>H- and <sup>13</sup>C-NMR: see Table 1.

**Methyl 6β, 7β, 16β, 17-tetrahydroxy *ent*-kauran-18-oate (2).** colorless gum.  $[\alpha]_D^{25} -41.0^\circ$  (c 0.15, MeOH); IR (KBr)  $\nu_{\max}$  cm<sup>-1</sup>: 3421, 1642, 1550, 1033, 668; Positive-ion HR-FAB-MS *m/z* = 405.2265 [M + Na]<sup>+</sup> (calcd. for C<sub>21</sub>H<sub>34</sub>O<sub>6</sub>Na: 405.2253); <sup>1</sup>H- and <sup>13</sup>C-NMR: see Table 1.

**6 $\beta$ , 7 $\beta$ , 16 $\beta$ , 17-Tetrahydroxy *ent*-kauran-18-oic acid (3).** colorless gum.  $[\alpha]_D^{25}$  -58.6° (c 0.25, MeOH); IR (KBr)  $\nu_{\max}$   $\text{cm}^{-1}$ : 3357, 2948, 1661, 1453, 1033, 671; Positive-ion HR-FAB-MS  $m/z = 391.2122$   $[\text{M} + \text{Na}]^+$  (calcd. for  $\text{C}_{20}\text{H}_{32}\text{O}_6\text{Na}$ : 391.2097);  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR: see Table 1.

**Preparation of the (R)- and (S)-MTPA Ester Derivatives of 1 by a Convenient Mosher Ester Procedure.** Compound **1** (0.6mg) in deuterated pyridine (1.0 mL) was transferred into clean NMR tube. (S)-(+)- $\alpha$ -Methoxy- $\alpha$ -(trifluoromethyl)phenylacetyl chloride (10  $\mu\text{L}$ ) was added into the NMR tube immediately under a  $\text{N}_2$  gsa stream, and then the NMR tube was shaken carefully to mix the sample and MTPA chloride evenly. The reaction NMR tube was permitted to stand at room temperature. After overnight, the reaction was completed to afford the (R)-MTPA ester derivative (**1r**) of **1**. In manner described for **1r**, (S)-MTPA ester derivative of **1** (**1s**) was obtained. The  $^1\text{H}$ -NMR spectra of **1r** and **1s** were measured with the reaction NMR tubes directly.

**1.** (500 MHz, pyridine- $d_5$ ):  $\delta$  4.461 (1H, dd,  $J = 11.5, 2.0$  Hz, H-6), 4.131 (1H, d,  $J = 2.0$  Hz, H-7), 3.864 (1H, d,  $J = 11.0$  Hz, H-17a), 3.799 (1H, d,  $J = 11.0$  Hz, H-17b), 2.787 (1H, d,  $J = 11.5$  Hz, H-5), 2.571 (1H, m H-13), 2.518 (1H, m, H-11a), 2.458 (1H, m, H-3a), 2.457 (1H, m, H-2a), 2.162 (1H, m, H-12a), 2.096 (1H, m, H-1a), 1.964 (1H, m, H-15a), 1.962 (1H, m, H-3b), 1.943 (1H, m, H-14a), 1.622 (1H, m, H-15b), 1.610 (1H, m, H-12b), 1.558 (1H, m, H-2b), 1.556 (1H, m, H-11b), 1.554 (1H, m, H-14b), 1.430 (1H, m, H-9), 1.299 (3H, s, H-19), 1.033 (3H, s, H-20), 0.825 (1H, m, H-1b).

**1r.** (500 MHz, pyridine- $d_5$ ):  $\delta$  5.833 (1H, d,  $J = 2.0$  Hz, H-7), 4.703 (1H, d,  $J = 11.0$  Hz, H-17a), 4.621 (1H, dd,  $J = 11.5, 2.0$  Hz, H-6), 4.385 (1H, d,  $J = 11.0$  Hz, H-17b), 2.763 (1H, d,  $J = 11.5$  Hz, H-5), 2.423 (1H, m H-13), 2.410 (1H, m, H-11a), 2.273 (1H, m, H-3a), 2.272 (1H, m, H-2a), 2.104 (1H, m, H-12a), 2.080 (1H, m, H-1a), 1.994 (1H, m, H-3b), 1.957 (1H, m, H-15a), 1.934 (1H, m, H-14a), 1.584 (1H, m, H-12b), 1.572 (1H, m, H-15b), 1.548 (1H, m, H-2b), 1.546 (1H, m, H-11b), 1.496 (1H, m, H-14b), 1.380 (1H, m, H-9), 1.029 (3H, s, H-19), 1.018 (3H, s, H-20), 0.825 (1H, m, H-1b).

**1s.** (500 MHz, pyridine- $d_5$ ):  $\delta$  5.756 (1H, d,  $J = 2.0$  Hz, H-7), 4.684 (1H, d,  $J = 11.0$  Hz, H-17a), 4.420 (1H, dd,  $J = 11.5, 2.0$  Hz, H-6), 4.478 (1H, d,  $J = 11.0$  Hz, H-17b), 2.756 (1H, d,  $J = 11.5$  Hz, H-5), 2.418 (1H, m H-13), 2.410 (1H, m, H-11a), 2.273 (1H, m, H-3a), 2.274 (1H, m, H-2a), 2.105 (1H, m, H-12a), 2.070 (1H, m, H-1a), 1.993 (1H, m, H-3b), 1.956 (1H, m, H-15a), 1.930 (1H, m, H-14a), 1.590 (1H, m, H-12b), 1.544 (1H, m, H-11b), 1.537 (1H, m, H-15b), 1.536 (1H, m, H-2b), 1.451 (1H, m, H-14b), 1.399 (1H, m, H-9), 1.001 (3H, s, H-19), 0.977 (3H, s, H-20), 0.825 (1H, m, H-1b).

## ACKNOWLEDGEMENTS

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Table 1.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR chemical shifts of **1–3** ( $\delta$  in ppm, 500 MHz for  $^1\text{H}$  and 125 MHz for  $^{13}\text{C}$ , in  $\text{CD}_3\text{OD}$ )

Position	<b>1</b>		<b>2</b>		<b>3</b>	
	$\delta_{\text{H}}$ (multi, $J = \text{Hz}$ )	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (multi, $J = \text{Hz}$ )	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (multi, $J = \text{Hz}$ )	$\delta_{\text{C}}$
1	0.97, m 1.73, m <sup>b)</sup>	39.6	0.93, m 1.78, m <sup>b)</sup>	41.9	0.92, m 1.75, m <sup>b)</sup>	41.9
2	1.56, m <sup>b)</sup> 2.12, m	17.8	1.54, m <sup>b)</sup> 2.13, m	19.6	1.54, m <sup>b)</sup> 2.12, m	19.5
3	1.83, m <sup>b)</sup> 2.08, m	25.5	1.81, m <sup>b)</sup> 2.10, m	41.0	1.81, m <sup>b)</sup> 2.09, m	40.9
4		42.0		45.6		45.3
5	2.33, (d, 11.5) <sup>a)</sup>	49.1	1.88, m <sup>b)</sup>	50.8	1.90, m <sup>b)</sup>	50.9
6	4.35, (dd, 11.5, 2.0)	80.0	4.24, (dd, 11.5, 2.5)	72.2	4.27, (dd, 11.5, 2.5)	72.4
7	3.80, (d, 2.0)	78.8	3.35, (d, 2.0)	83.4	3.36, (d, 2.0)	83.0
8		51.9		49.6		49.6
9	1.32, m	55.8	1.30, m	52.0	1.27, m	52.5
10		40.5		41.8		41.8
11	1.53, m <sup>b)</sup> 1.90, m <sup>b)</sup>	19.3	1.54, m <sup>b)</sup> 1.84, m <sup>b)</sup>	20.2	1.54, m <sup>b)</sup> 1.85, m <sup>b)</sup>	20.1
12	1.56, m <sup>b)</sup> 1.89, m <sup>b)</sup>	27.8	1.55, m <sup>b)</sup> 1.88, m <sup>b)</sup>	28.4	1.55, m <sup>b)</sup> 1.89, m <sup>b)</sup>	29.2
13	2.12, m	42.3	2.01, m	42.0	2.03, m	42.0
14	1.50, m <sup>b)</sup> 1.78, m <sup>b)</sup>	37.9	1.48, m <sup>b)</sup> 1.77, m <sup>b)</sup>	38.0	1.49, m <sup>b)</sup> 1.77, m <sup>b)</sup>	38.1
15	1.54, m <sup>b)</sup> 1.82, m <sup>b)</sup>	49.5	1.52, m <sup>b)</sup> 1.79, m <sup>b)</sup>	49.4	1.52, m <sup>b)</sup> 1.79, m <sup>b)</sup>	49.5
16		80.4		80.5		80.5
17	3.36, (d, 11.0) 3.44, (d, 11.0)	70.6	3.43, (d, 11.5) 3.35, (d, 11.5)	70.7	3.43, (d, 11.0) 3.35, (d, 11.0)	70.6
18		185.9		180.4		182.3
19	1.25, s	29.8	1.43, s	32.6	1.45, s	33.1
20	1.15, s	18.0	0.89, s	17.2	1.02, s	17.1
OMe			3.69, s	52.8		

<sup>a)</sup> Coupling constants ( $J$  in Hz) are given in parentheses.

<sup>b)</sup> Overlapped signals.

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