

## TOTAL SYNTHESIS OF (+)-GALANOLACTONE

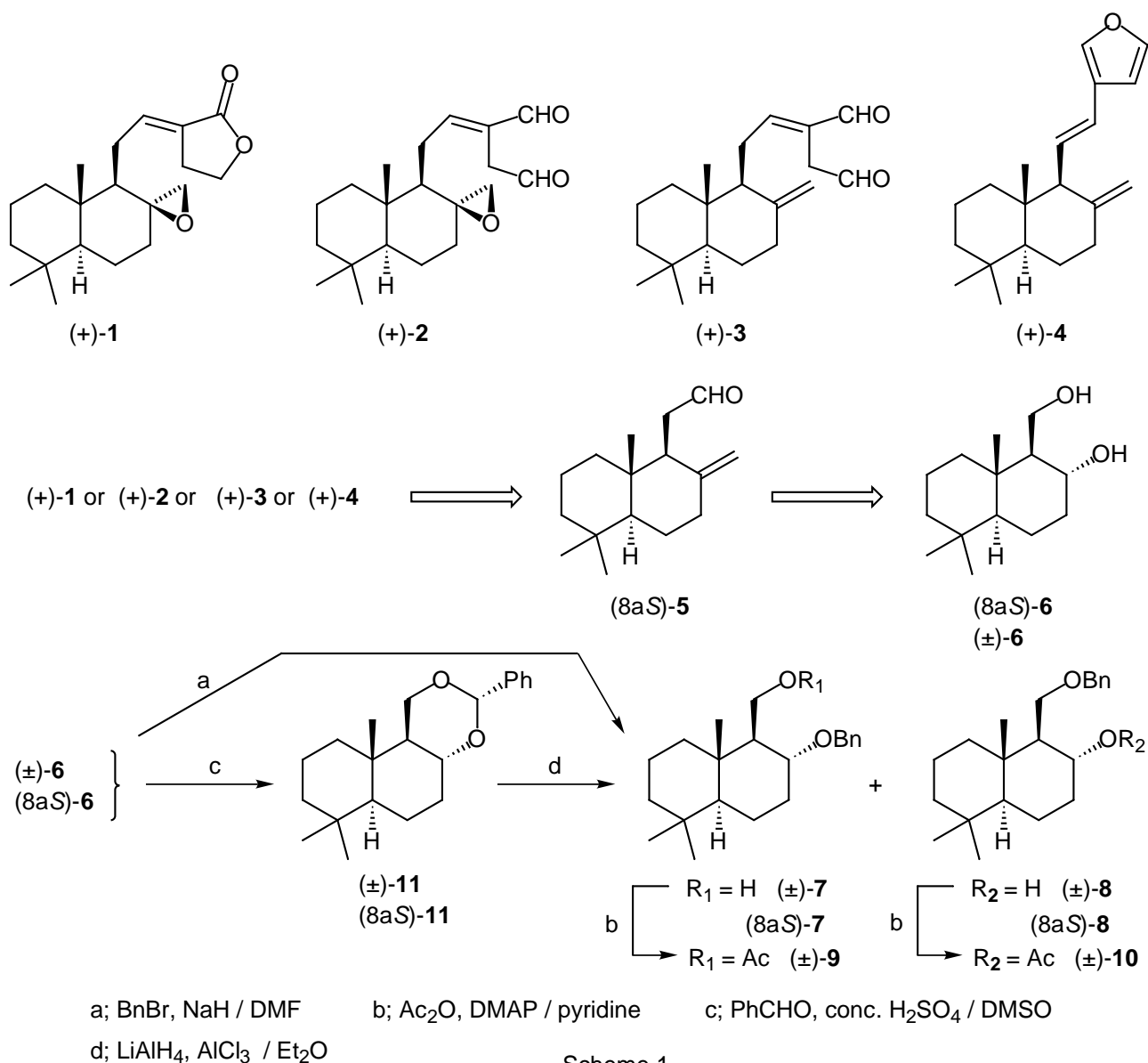
Masako Nozawa, Eriko Ono, and Hiroyuki Akita\*

School of Pharmaceutical Sciences, Toho University, 2-2-1 Miyama, Funabashi,  
Chiba 274-8510, Japan

**Abstract** - Regioselective monobenylation of the chemoenzymatically prepared chiral decalin-type diol ((8a*S*)-**6**) via the benzylidene acetal ((8a*S*)-**11**) afforded the primary alcohol ((8a*S*)-**7**), from which total synthesis of (+)-galanolactone (**1**) was achieved and formal syntheses of (+)-(*E*)-8 $\beta$ (17),12-labddiene-15,16-dial ((+)-**3**) and (+)-coronarin E (**4**) were carried out.

Labdane-type diterpenoids are one of the main groups in terpenoid natural products. Galanolactone ((+)-**1**) and (*E*)-8 $\beta$ (17),12-labddiene-15,16-dial ((+)-**3**) were isolated from *Alpinia galanga* (Zingiberaceae) together with (*E*)-8(17) - epoxyabd-12-ene-15,16-dial ((+)-**2**) and these compounds exhibited the cytotoxic and antifungal activities.<sup>1</sup> Recently, ((+)-**1**) is reported to exhibit anti-5HT (serotonin) effect<sup>2</sup> and the inhibitory effect of (+)-**2** against cholesterol biosynthesis is also reported.<sup>3</sup> Coronarin E ((+)-**4**) has been isolated from the rhizomes of the Brazilian medical plant *Hedychium coronarium* (Zingiberaceae).<sup>4</sup> Total syntheses of **1**<sup>5</sup> and **2**<sup>6</sup> as racemic form<sup>5,6</sup> in multiple steps and conversion of natural sclareol into (+)-**1**,<sup>7</sup> (+)-**3**<sup>7</sup> and (+)-**4**<sup>8</sup> are reported. In connection with our synthetic study of decalin-type chiral synthon ((8a*S*)-**6**) based on enzymatic function and its application to terpenoid synthesis, the synthesis of labdane-type diterpenoids possessing biological activities has aroused our interest. (8a*S*)-Decahydro-5,5,8a-trimethyl-2-methylene-1-naphthalenealdehyde (**5**) appears to be an important intermediate for the synthesis of these labdane-type diterpenoids and could be synthesized from the chemoenzymatic reaction product ((8a*S*)-**6**) reported previously by us.<sup>9</sup> We now report the total synthesis of (+)-**1** and the formal syntheses of (+)-**3** and (+)-**4** from the chemoenzymatic product ((8a*S*)-**6**).

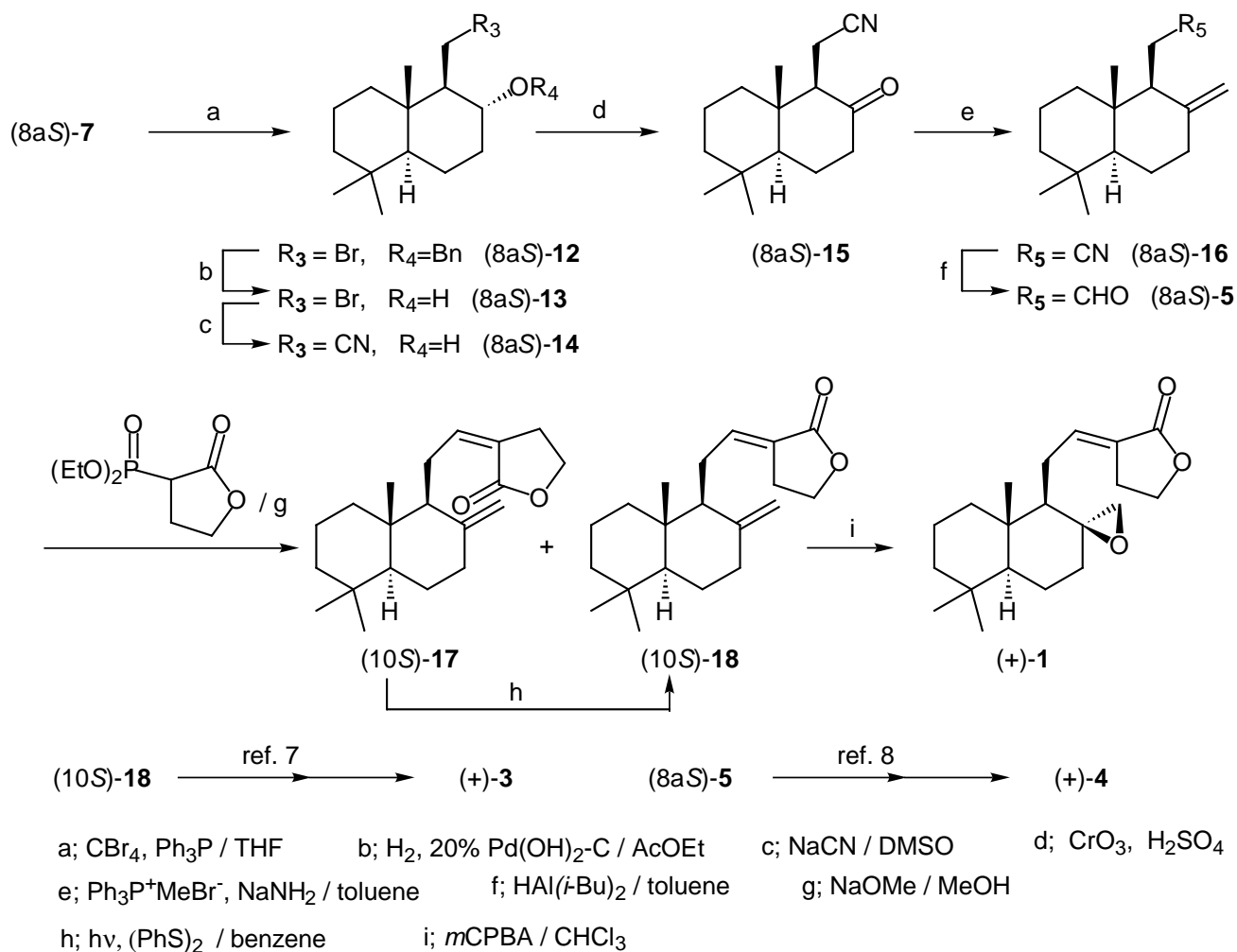
In the synthesis of (8a*S*)-**5** from (8a*S*)-**6**, the regioselective protection of two hydroxyl groups of (8a*S*)-**6** is necessary. As a model experiment, direct benzylation of ( $\pm$ )-**6** using one equivalent of benzyl bromide gave the monobenzyl ethers (( $\pm$ )-**7**) (7% yield) and (( $\pm$ )-**8**) (37% yield). The structure of both monobenzyl ethers (( $\pm$ )-**7**) and (( $\pm$ )-**8**) was confirmed by derivation to the corresponding acetates (( $\pm$ )-**9**) and (( $\pm$ )-**10**), respectively. This drawback could be overcome by the regioselective and reductive cleavage of acetal bond of benzylideneacetal (**11**). Treatment of ( $\pm$ )-**6** with benzaldehyde in the presence of a catalytic amount of conc. H<sub>2</sub>SO<sub>4</sub> afforded the benzylidene acetal (( $\pm$ )-**11**) exclusively in 94% yield. Benzylideneacetals have the useful property that one of the two C-O bonds can be selectively cleaved. The direction of cleavage is dependent on steric and electronic factors as well as on the nature of the reducing agent. When ( $\pm$ )-**11** was treated with various kinds of reducing agent in the presence of Lewis acid, the results are



Table

entry	reducing reagents conditions	(±)-11	+	(±)-7	+	(±)-8	+	(±)-6	products (%)
1	HAl( <i>i</i> -Bu) <sub>2</sub> / THF	(±)-11							(±)-11(96%)
2	NaBH <sub>3</sub> CN / TiCl <sub>4</sub> / MeCN			(±)-7+		(±)-8		(±)-6	(±)-7+ (±)-8 (33%, (±)-7 : (±)-8 = 1: 5.5) (±)-6 (43%)
3	LiAlH <sub>4</sub> / BF <sub>3</sub> ·Et <sub>2</sub> O / Et <sub>2</sub> O	(±)-11		(±)-7+		(±)-8		(±)-6	(±)-11(62%) (±)-7+ (±)-8 (8%, (±)-7 : (±)-8 = 1: 1.2) (±)-6 (29%)
4	LiAlH <sub>4</sub> / AlCl <sub>3</sub> / Et <sub>2</sub> O			(±)-7+		(±)-8			(±)-7+ (±)-8 (99%, (±)-7 : (±)-8 = 17:1)

shown in Table. In case of using LiAlH<sub>4</sub> (1 eq)-AlCl<sub>3</sub> (4 eq) system<sup>10</sup> as shown in entry 4, chemical yield (99%) and regieselectivity ((±)-7 : (±)-8 = 17 : 1) were found to be extremely high. This result was applied for the following chiral synthesis. Treatment of (8aS)-6 with benzaldehyde in the presence of a catalytic amount of conc. H<sub>2</sub>SO<sub>4</sub> afforded the acetal ((8aS)-11) exclusively in 98% yield, which was



Scheme 2

reduced with a mixed reducing reagent ( $\text{LiAlH}_4$  (1 eq)- $\text{AlCl}_3$  (4 eq)) to provide selectively primary alcohol ((8aS)-7) (93% yield) along with a small amount of secondary alcohol ((8aS)-8) (5% yield). Conversion of (8aS)-7 into the keto nitrile ((8aS)-15) via bromination ((8aS)-12; 98% yield), reduction ((8aS)-13; 99% yield), CN substitution ((8aS)-14; 97% yield) and oxidation ((8aS)-15; 96% yield) was reported by us.<sup>11</sup> The Wittig olefination of (8aS)-15 with  $\text{Ph}_3\text{P}=\text{CH}_2$  provided the *exo* olefin ((8aS)-16) in 96% yield, which was reduced with diisobutylaluminum hydride (Dibal-H) to give the desired ((8aS)-5) in 92% yield. Coupling of the aldehyde ((8aS)-5) with the anion of diethylphosphono-2-butyrolactone afforded the isomeric lactones ((10S)-17) (*Z*-form, 26% yield) and ((10S)-18) (*E*-form, 59% yield). While the nOe enhancement (2.6%) between 12-H ( $\delta$  6.17) and one of 14-methylene ( $\delta$  1.78) protons of (10S)-17 was indicated, no nOe enhancement between 12-H ( $\delta$  6.72) and 14-H ( $\delta$  2.85) of (10S)-18 was observed. Isomerization of (10S)-17 to (10S)-18 was effected by irradiation in the presence of diphenyl disulfide<sup>12</sup> and 91% conversion yield of 18 was obtained. By applying the reported procedure,<sup>7</sup> epoxidation of exomethylene at C(8) of (10S)-18 with an excess of *m*-chloroperbenzoic acid (*m*CPBA) at 0°C gave (+)-galanolactone (1) (19% yield, mp 126°C,  $[\alpha]_D^{27} +30.0^\circ$  (c=0.75,  $\text{CHCl}_3$ )) whose spectral data were identical with those (mp 125.5-126°C,  $[\alpha]_D^{27} +28.0^\circ$  (c=0.26,  $\text{CHCl}_3$ ), and <sup>1</sup>H-NMR) of natural (+)-1.

Conversion of (10*S*)-**18** into (+)-(*E*)-8 $\beta$ (17),12-labddiene-15,16-dial ((+)-**3**) *via* reduction followed by Swern oxidation was already achieved.<sup>7</sup> The above-mentioned aldehyde ((8*aS*)-**5**) was also led to (+)-coronarin E (**4**) *via* treatment with 3-furyllithium followed by dehydration.<sup>8</sup>

In conclusion, regioselective monobenylation of the chemoenzymatically prepared diol ((8*aS*)-**6**) *via* the benzylidene acetal ((8*aS*)-**11**) afforded the primary alcohol ((8*aS*)-**7**), from which total synthesis of (+)-galanolactone (**1**) was achieved and formal syntheses of (+)-(*E*)-8 $\beta$ (17),12-labddiene-15,16-dial ((+)-**3**) and (+)-coronarin E (**4**) were carried out.

## Experimental

All melting points were measured on a Yanaco MP-3S micro melting point apparatus and are uncorrected. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded on JEOL EX 400 spectrometer in CDCl<sub>3</sub>. Carbon substitution degrees were established by DEPT pulse sequence. IR spectra were recorded a JASCO FT/IR-300 spectrophotometer. Fast atom bombardment mass spectrometry (FAB-MS) were obtained with a JEOL JMS-SX 102 A instrument (matrix: *m*-nitrobenzyl alcohol (NBA)). Optical rotations were measured with a JASCO DIP-370 digital polarimeter. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.

**(1*S*\*, 2*R*\*, 4*aS*\*, 8*aS*\*)-2-Benzoyloxydecahydro-5,5,8*a*-trimethyl-1-naphthylmethanol (( $\pm$ )-**7**) and (1*R*\*, 2*R*\*, 4*aS*\*, 8*aS*\*)-1-Benzoxymethyl-2-hydroxy-decahydro-5,5,8*a*-trimethylnaphthalene (( $\pm$ )-**8**)** A mixture of ( $\pm$ )-**6** (452 mg, 2 mmol) and 55% NaH (96 mg, 2.2 mmol) in DMF (3 mL) was stirred for 30 min at rt. A solution of benzyl bromide (342 mg, 2 mmol) in DMF (1 mL) was added to the above reaction mixture and the whole mixture was stirred for 1 h at rt. The reaction mixture was diluted with saturated brine and extracted with ether. The organic layer was dried over MgSO<sub>4</sub> and evaporated to give a residue which was chromatographed on silica gel (20 g, n-hexane-AcOEt=10:1) to give ( $\pm$ )-**7** (45 mg, 7%) as crystals and ( $\pm$ )-**8** (215 mg, 37%) as a colorless oil, respectively. Recrystallization of the former from n-hexane gave ( $\pm$ )-**7** as colorless plates. ( $\pm$ )-**7**: mp 67 °C; IR (KBr): 3479 cm<sup>-1</sup> (OH); <sup>1</sup>H NMR :  $\delta$  0.75 (3H, s), 0.79 (3H, s), 0.88 (3H, s), 0.90~1.58 (9H, m), 1.71~1.85 (2H, m), 2.30~2.36 (1H, m), 3.39 (1H, d, *J*=11 Hz, OH), 3.59 (1H, dd, *J*= 8, 11 Hz), 3.64 (1H, dt, *J*=5, 11 Hz), 3.78 (1H, t, *J*=11 Hz), 4.44 (1H, d, *J*=11.5 Hz), 4.70 (1H, d, *J*=11.5 HZ), 7.26~7.37 (5H, m). *Anal.* Calcd for C<sub>21</sub>H<sub>32</sub>O<sub>2</sub> : C, 79.70; H, 10.19. Found: C, 79.98; H, 10.04. FAB MS *m/z*: 317 (M<sup>+</sup>+1). ( $\pm$ )-**8**: IR (neat): 3480 cm<sup>-1</sup> (OH); <sup>1</sup>H NMR :  $\delta$  0.81 (3H, s), 0.81 (3H, s), 0.88 (3H, s), 0.91~1.75 (11H, m), 2.05~2.12 (1H, m), 3.61 (1H, t, *J*=9 Hz), 3.82 (1H, dt, *J*=5, 10.5 Hz), 3.85 (1H, dd, *J*=3, 9 Hz), 4.05 (1H, br s), 4.51 (2H, s), 7.26-7.36 (5H, m). *Anal.* Calcd for C<sub>21</sub>H<sub>32</sub>O<sub>2</sub> : C, 79.70; H, 10.19. Found: C, 79.73; H, 10.08. FAB MS *m/z*: 317 (M<sup>+</sup>+1).

**Acetylation of ( $\pm$ )-**7**** The primary hydroxyl group of ( $\pm$ )-**7** (45 mg, 0.14 mmol) was acetylated with Ac<sub>2</sub>O (45 mg, 0.44 mmol) in pyridine (2 mL) in the usual manner to give ( $\pm$ )-**9** (49 mg, 96%) as colorless plates (from n-hexane). ( $\pm$ )-**9**: mp 83-83.5 °C; IR (KBr): 1738 cm<sup>-1</sup> (OAc); <sup>1</sup>H NMR :  $\delta$  0.82 (3H, s), 0.86 (3H, s), 0.88 (3H, s), 0.90~1.77 (11H, m), 1.95 (3H, s), 2.32~2.37 (1H, m), 3.42~3.50

(1H, m), 4.26 (1H, dd,  $J=4$ , 11 Hz), 4.30 (1H, dd,  $J=3$ , 11 Hz), 4.38 (1H, d,  $J=12$  Hz), 4.63 (1H, d,  $J=12$  Hz), 7.22~7.35 (5H, m). FAB MS  $m/z$ : 359 ( $M^++1$ ).

**Acetylation of ( $\pm$ )-8** The secondary hydroxyl group of ( $\pm$ )-8 (95 mg, 0.3 mmol) was acetylated with  $\text{Ac}_2\text{O}$  (45 mg, 0.44 mmol), DMAP (12 mg, 0.1 mmol) in pyridine (2 mL) in the usual manner to give ( $\pm$ )-10 (106 mg, 99%) as a colorless oil. ( $\pm$ )-10: IR (neat):  $1736\text{ cm}^{-1}$  (OAc);  $^1\text{H NMR}$ :  $\delta$  0.81 (3H, s), 0.87 (3H, s), 0.91 (3H, s), 0.92~1.83 (11H, m), 1.91 (3H, s), 2.09~2.15 (1H, m), 3.39 (1H, dd,  $J=3.5$ , 10 Hz), 3.52 (1H, dd,  $J=4$ , 10 Hz), 4.38 (1H, d,  $J=11$  Hz), 4.42 (1H, d,  $J=11$  Hz), 4.95 (1H, dt,  $J=5.5$ , 11 Hz), 7.23~7.34 (5H, m). *Anal.* Calcd for  $\text{C}_{23}\text{H}_{34}\text{O}_3$ : C, 77.05; H, 9.56. Found: C, 77.32; H, 9.09. FAB MS  $m/z$ : 359 ( $M^++1$ ).

**[(3S\*,4aR\*,6aS\*,10aS\*,10bS\*)-Decahydro-7,7,10a-trimethyl-1H-naphtho[2,1d][1,3]-dioxin-3-yl]benzene (( $\pm$ )-11)** To a solution of ( $\pm$ )-6 (1.509 g, 6.67 mmol), and benzaldehyde (1.06 g, 10 mmol) in DMSO (25 mL) was added conc.  $\text{H}_2\text{SO}_4$  (5 mL) at  $0\text{ }^\circ\text{C}$  and the whole mixture was stirred at rt for 30 min, and then diluted with saturated aqueous  $\text{NaHSO}_3$  and extracted with ether. The organic layer was washed with saturated brine and dried over  $\text{MgSO}_4$ . The organic layer was evaporated to give a residue. To a solution of the residue in a mixed solvent ( $\text{H}_2\text{O}$  (10 mL)-DMSO (10 mL)) was added  $\text{NaHSO}_3$  (200 mg) at rt and the whole mixture was stirred at rt for 12 h. The reaction mixture was diluted with  $\text{H}_2\text{O}$  and extracted with ether. The organic layer was dried over  $\text{MgSO}_4$  and evaporated. The residue was chromatographed on silica gel (25 g, n-hexane-AcOEt=20:1) to afford ( $\pm$ )-11 (1.967 g, 94%) as crystals. Recrystallization from n-hexane-AcOEt gave ( $\pm$ )-11 as colorless plates. ( $\pm$ )-11: mp  $90\text{ }^\circ\text{C}$ ; IR (KBr):  $1041\text{ cm}^{-1}$ ;  $^1\text{H NMR}$ :  $\delta$  0.85 (3H, s), 0.89 (3H, s), 0.94 (3H, s), 1.01~1.62 (10H, m), 1.73~1.79 (1H, m), 2.09~2.14 (1H, m), 3.78 (1H, t,  $J=11$  Hz), 3.85 (1H, dt,  $J=5$ , 11 Hz), 4.21 (1H, dd,  $J=4$ , 11 Hz), 5.46 (1H, s), 7.28~7.34 (3H, m), 7.46~7.49 (2H, m). *Anal.* Calcd for  $\text{C}_{21}\text{H}_{30}\text{O}_2$ : C, 80.21; H, 9.62. found: C, 80.58; H, 9.39. FAB MS  $m/z$ : 315 ( $M^++1$ ).

**Reduction of ( $\pm$ )-11** i) entry 1; To a solution of ( $\pm$ )-11 (96 mg, 0.31 mmol) in THF (1 mL) at  $-78\text{ }^\circ\text{C}$  was added 1 M Dibal in toluene (0.4 mL, 0.4 mmol) and the whole mixture was stirred for 1 h at  $-20\text{ }^\circ\text{C}$ . The reaction mixture was worked up in the usual manner to give ( $\pm$ )-11 (92 mg, 96% recovery). ii) entry 2; To a solution of ( $\pm$ )-11 (100 mg, 0.32 mmol) in  $\text{CH}_3\text{CN}$  (1 mL) at  $-20\text{ }^\circ\text{C}$  were added  $\text{NaBH}_3\text{CN}$  (32 mg, 0.52 mmol) and  $\text{TiCl}_4$  (0.2 mL, 1.82 mmol), and the whole mixture was stirred for 30 min at  $-20\text{ }^\circ\text{C}$ . The reaction mixture was worked up in the usual manner to give a mixture (33 mg, 33%; ( $\pm$ )-7 : ( $\pm$ )-8 = 1 : 5.5) of ( $\pm$ )-7 and ( $\pm$ )-8, and ( $\pm$ )-6 (31 mg, 43%). The ratio of ( $\pm$ )-7 and ( $\pm$ )-8 was determined by NMR analysis. iii) entry 3; To a solution of ( $\pm$ )-11 (95 mg, 0.3 mmol) in  $\text{Et}_2\text{O}$  (1 mL) at  $-20\text{ }^\circ\text{C}$  were added  $\text{LiAlH}_4$  (14 mg, 0.36 mmol) and  $\text{BF}_3\cdot\text{Et}_2\text{O}$  (0.15 mL, 1.22 mmol), and the whole mixture was stirred for 30 min at  $-20\text{ }^\circ\text{C}$ . The reaction mixture was worked up in the usual manner to give ( $\pm$ )-11 (59 mg, 62% recovery), a mixture (8 mg, 8%; ( $\pm$ )-7 : ( $\pm$ )-8 = 1 : 1.2) of ( $\pm$ )-7 and ( $\pm$ )-8, and ( $\pm$ )-6 (20 mg, 29%). iv) entry 4; To a solution of ( $\pm$ )-11 (106 mg, 0.34 mmol) in  $\text{Et}_2\text{O}$  (1 mL) at  $-20\text{ }^\circ\text{C}$  were added  $\text{LiAlH}_4$  (20 mg, 0.53 mmol) and  $\text{AlCl}_3$  (212 mg, 1.59 mmol), and the whole mixture was stirred for 30 min at  $-20\text{ }^\circ\text{C}$ . The

reaction mixture was worked up in the usual manner to give a mixture (105 mg, 99%; ( $\pm$ )-**7** : ( $\pm$ )-**8** =17 : 1) of ( $\pm$ )-**7** and ( $\pm$ )-**8**. The ratio of ( $\pm$ )-**7** and ( $\pm$ )-**8** was determined by NMR analysis.

**[(3*S*,4*aR*,6*aS*,10*aS*,10*bS*)-Decahydro-7,7,10*a*-trimethyl-1*H*-naphtho[2,1*d*][1,3]-dioxin-3-yl]benzene ((-)-**11**)** A small amount of conc. H<sub>2</sub>SO<sub>4</sub> (15 drops) was added to a solution of (-)-(8*aS*)-**6** (338 mg, 1.5 mmol) and benzaldehyde (462 mg, 4.36 mmol) in DMSO (3 mL) at 0 °C and the whole mixture was stirred at rt for 30 min, and then diluted with H<sub>2</sub>O and extracted with ether. The organic layer was washed with saturated brine and dried over MgSO<sub>4</sub>. The organic layer was evaporated to give a residue. To a solution of the residue in a mixed solvent (H<sub>2</sub>O (1 mL)-DMSO (1 mL)) was added NaHSO<sub>3</sub> (548 mg, 5.27 mmol) at rt and the whole mixture was stirred at rt for 12 h. The reaction mixture was diluted with H<sub>2</sub>O and extracted with ether. The organic layer was dried over MgSO<sub>4</sub> and evaporated. The residue was chromatographed on silica gel (15 g, n-hexane-AcOEt=20:1) to afford (-)-(8*aS*)-**11** as crystals. Recrystallization from n-hexane gave (-)-(8*aS*)-**11** (463 mg, 98%) as colorless needles. (-)-(8*aS*)-**9**: mp 98.5~99 °C; [ $\alpha$ ]<sub>D</sub><sup>23</sup> -9.5° (c=1.12, CHCl<sub>3</sub>). Spectral data (IR and <sup>1</sup>H NMR) of (-)-(8*aS*)-**11** were identical with those of ( $\pm$ )-**11**. FAB MS m/z: 315 (M<sup>+</sup>+1).

**(-)-(1*S*,2*R*,4*aS*,8*aS*)-2-Benzyloxydecahydro-5,5,8*a*-trimethyl-1-naphthylmethanol ((-)-(8*aS*)-**7**) and (+)-(1*R*,2*R*,4*aS*,8*aS*)-1-Benzyloxy-2-hydroxydecahydro-5,5,8*a*-trimethyl-naphthalene ((+)-(8*aS*)-**8**)** To a solution of (-)-(8*aS*)-**11** (359 mg, 1.14 mmol) in Et<sub>2</sub>O (10 mL) at -20°C was added LiAlH<sub>4</sub> (51 mg, 1.35 mmol) and the whole mixture was stirred for 10 min. Then AlCl<sub>3</sub> (734 mg, 5.52 mmol) was added to the above mixture and the whole mixture was stirred at -20 °C for 30 min. The reaction mixture was diluted with H<sub>2</sub>O, acidified with 2M aqueous HCl and extracted with ether. The organic layer was washed with saturated brine and dried over MgSO<sub>4</sub>. Evaporation of the organic solvent gave a residue which was chromatographed on silica gel (15 g, n-hexane-AcOEt=20:1) to give (-)-(8*aS*)-**7** (336 mg, 93%) as crystals and (+)-(8*aS*)-**8** (18 mg, 5%) as a colorless oil, respectively. Recrystallization of the former from n-hexane gave (-)-(8*aS*)-**7** as colorless plates. (-)-(8*aS*)-**7**: mp 110.5~111 °C; [ $\alpha$ ]<sub>D</sub><sup>23</sup> -67.0° (c=1.08, CHCl). Spectral data (IR and <sup>1</sup>H NMR) of (-)-(8*aS*)-**7** were identical with those of ( $\pm$ )-**7**. FAB MS m/z: 317 (M<sup>+</sup>+1). (+)-(8*aS*)-**8**: [ $\alpha$ ]<sub>D</sub><sup>22</sup> +32.5° (c=1.36, CHCl<sub>3</sub>). Spectral data (IR and <sup>1</sup>H NMR) of (-)-(8*aS*)-**8** were identical with those of ( $\pm$ )-**8**. FAB MS m/z: 317 (M<sup>+</sup>+1).

**(+)-(1*R*,4*aS*,8*aS*)-Decahydro-5,5,8*a*-trimethyl-2-methylene-1-naphthaleneacetonitrile ((8*aS*)-**16**)** A suspension of Ph<sub>3</sub>P<sup>+</sup>MeBr<sup>-</sup> (3.137 g, 8.78 mmol) and NaNH<sub>2</sub> (332 mg, 8.51 mmol) in toluene (30 mL) was heated under reflux for 4.5 h under argon. After the suspension had settled, the decanted yellow solution (Ph<sub>3</sub>P=CH<sub>2</sub>) was poured into (8*aS*)-**15** (190 mg, 0.81 mmol) at 0 °C. The whole was stirred for 15 min at rt. The reaction mixture was diluted with H<sub>2</sub>O and extracted with ether. The ether layer was washed with brine and dried over MgSO<sub>4</sub>. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (20 g, n-hexane:AcOEt=100:1) to give (8*aS*)-**16** (180 mg, 95%), which was recrystallized from n-hexane to give colorless plates. (8*aS*)-**16**: mp 91 °C; [ $\alpha$ ]<sub>D</sub><sup>24</sup> + 42.2° (c=1.02, CHCl<sub>3</sub>); IR (KBr): 2240 cm<sup>-1</sup> (CN); <sup>1</sup>H-NMR:  $\delta$  0.69 (3H, s), 0.82 (3H, s),

0.90 (3H, s), 1.13 (1H, dd,  $J=2.5, 12.5$  Hz), 1.14-1.25 (2H, m), 1.33 (1H, dq,  $J=4, 12$  Hz), 1.40-1.45 (1H, m), 1.50-1.62 (3H, m), 1.76 (1H,  $J=2, 13$  Hz), 2.08 (1H, dt,  $J=5, 13$  Hz), 2.17 (1H, dd,  $J=4, 11$  Hz), 2.33 (1H, dd,  $J=11, 17$  Hz), 2.45 (1H, ddd,  $J=2, 4, 13$  Hz), 2.54 (1H, dd,  $J=4, 17$  Hz), 4.62 (1H, br s), 4.96 (1H, br s).  $^{13}\text{C-NMR}$ : 13.7 (q), 13.9 (t), 19.1 (t), 21.7 (q), 23.7 (t), 33.5 (q and s), 37.2 (t), 39.1 (t), 39.3 (s), 41.7 (t), 53.2 (d), 55.0 (d), 107.8 (s), 120.3 (s), 146.3 (t). *Anal.* Calcd for  $\text{C}_{16}\text{H}_{25}\text{N}$ : C, 83.06; H, 10.89; N, 6.05. Found: C, 83.38; H, 10.85; N, 5.95. FAB MS  $m/z$ : 232 ( $\text{M}^++1$ ).

**(+)-(1R,4aS,8aS)-Decahydro-5,5,8a-trimethyl-2-methylene-1-naphthaleneacetaldehyde ((8aS)-5)** To a solution of (8aS)-**16** (402 mg, 1.74 mmol) in toluene (10 mL) was added 1 M Dibal-H in toluene (2.6 mL, 2.6 mmol) at  $-78^\circ\text{C}$ , the whole was stirred for 30 min at the same temperature. After addition of MeOH (1 mL), the reaction mixture was diluted with 2 M aqueous HCl and extracted with ether. The organic layer was washed with saturated brine and dried over  $\text{MgSO}_4$ . Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel (20 g, n-hexane:AcOEt=100:1) to afford a colorless oil ((8aS)-**5**) (373 mg, 92%). (8aS)-**5**: IR (neat):  $1725\text{ cm}^{-1}$  (CHO);  $[\alpha]_{\text{D}}^{21} -25.5^\circ$  ( $c=1.07$ ,  $\text{CHCl}_3$ );  $^1\text{H-NMR}$ :  $\delta$  0.71 (3H, s), 0.82 (3H, s), 0.90 (3H, s), 1.09 (1H, dt,  $J=4.5, 13$  Hz), 1.22 (1H, dd,  $J=2.5, 12.5$  Hz), 1.17-1.24 (1H, m), 1.35 (1H, dq,  $J=4, 12.5$  Hz), 1.40-1.45 (1H, m), 1.47-1.53 (3H, m), 1.74 (1H, dq,  $J=2.5, 13$  Hz), 2.10 (1H, dt,  $J=5, 12$  Hz), 2.34-2.37 (1H, m), 2.42 (1H, ddd,  $J=2.5, 4, 13$  Hz), 2.43 (1H, ddd,  $J=1.5, 4.5, 16$  Hz), 2.49 (1H, ddd,  $J=3, 10, 16$  Hz), 9.64 (1H, dd,  $J=1.5, 3$  Hz).  $^{13}\text{C-NMR}$ :  $\delta$  14.6 (q), 19.2 (t), 21.7 (q), 23.9 (t), 33.5 (q and s), 37.5 (t), 38.9 (s), 39.4 (t), 39.8 (t), 42.0 (t), 51.0 (d), 55.3 (d), 108.0 (t), 148.5 (s), 203.5 (d). *Anal.* Calcd for  $\text{C}_{16}\text{H}_{26}\text{O}$ : C, 81.98; H, 11.18. Found: C, 82.32; H, 11.28. FAB MS  $m/z$ : 235 ( $\text{M}^++1$ ).

**Wittig-Horner Reaction of (8aS)-5 and Diethylphosphono-2-butyrolactone** A solution of diethylphosphono-2-butyrolactone (4.678 g, 21 mmol) and NaOMe (1.039 g, 19.2 mmol) in MeOH (20 mL) was stirred for 4.5 h at rt. A solution of (8aS)-**5** (448 mg, 1.91 mmol) in MeOH (10 mL) was added dropwise to the above reaction mixture and the whole mixture was stirred for 3 h at reflux. The reaction mixture was diluted with saturated brine and extracted with ether. The ether layer was washed with brine and dried over  $\text{MgSO}_4$ . The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (20 g, n-hexane:AcOEt=20:1) to give (10aS)-**17** (150 mg, 26%) and (10aS)-**18** (341 mg, 59%) as a colorless oil. Recrystallization of (10aS)-**17** from n-hexane afforded colorless powder. (10aS)-**17**: mp  $64^\circ\text{C}$ ;  $[\alpha]_{\text{D}}^{22} +25.2^\circ$  ( $c=1.37$ ,  $\text{CHCl}_3$ ); IR (KBr):  $1741\text{ cm}^{-1}$ ;  $^1\text{H-NMR}$ :  $\delta$  0.73 (3H, s), 0.81 (3H, s), 0.87 (3H, s), 1.05-1.22 (4H, m), 1.34 (1H, dq,  $J=4.5, 13$  Hz), 1.37-1.42 (1H, m), 1.45-1.63 (3H, m), 1.70-1.82 (3H, m), 1.99 (1H, dt,  $J=5, 13$  Hz), 2.39 (1H, ddd,  $J=3, 6, 13$  Hz), 2.73-2.97 (4H, m), 4.30 (2H, t,  $J=7$  Hz), 4.50 (1H, d,  $J=1.5$  Hz), 4.82 (1H, d,  $J=1.5$  Hz), 6.15-6.19 (1H, m).  $^{13}\text{C-NMR}$ :  $\delta$  14.4 (q), 19.3 (t), 21.7 (q), 23.1 (t), 24.3 (t), 29.1 (t), 33.6 (s), 33.7 (q), 38.1 (t), 39.1 (t), 39.7 (s), 42.2 (t), 55.5 (d), 57.3 (d), 65.3 (t), 107.6 (t), 122.9 (s), 145.4 (d), 148.5 (s), 170.3 (s). *Anal.* Calcd for  $\text{C}_{20}\text{H}_{30}\text{O}_2$ : C, 79.42; H, 10.00. Found: C, 79.42; H, 9.93. FAB MS  $m/z$ : 303 ( $\text{M}^++1$ ). (10aS)-**18**:  $[\alpha]_{\text{D}}^{20} +16.7^\circ$  ( $c=1.12$ ,  $\text{CHCl}_3$ ); IR (neat):  $1757\text{ cm}^{-1}$ ;  $^1\text{H-NMR}$ :  $\delta$

0.73 (3H, s), 0.82 (3H, s), 0.88 (3H, s), 1.02-1.25 (4H, m), 1.33 (1H, dq,  $J=4$ , 13.5 Hz), 1.39-1.44 (1H, m), 1.46-1.64 (2H, m), 1.68-1.73 (2H, m), 2.00 (1H, dt,  $J=4$ , 13 Hz), 2.16-2.26 (1H, m), 2.33-2.42 (2H, m), 2.84-2.90 (2H, m), 4.37 (2H, t,  $J=7.5$  Hz), 4.38 (1H, d,  $J=1$  Hz), 4.82 (1H, d,  $J=1$  Hz), 6.69-6.74 (1H, m).  $^{13}\text{C-NMR}$ :  $\delta$  14.4 (q), 19.3 (t), 21.7 (q), 24.1 (t), 25.3 (t), 25.5 (t), 33.6 (q and s), 37.8 (t), 39.3 (t), 39.4 (s), 42.0 (t), 55.4 (d), 56.2 (d), 65.3 (t), 107.4 (t), 124.5 (s), 142.4 (d), 148.1 (s), 171.3 (s). *Anal.* Calcd for  $\text{C}_{20}\text{H}_{30}\text{O}_2$ : C, 79.42; H, 10.00. Found: C, 79.67; H, 9.97. FAB MS  $m/z$ : 303 ( $\text{M}^++1$ ).

**Conversion of 12(Z)-(10aS)-17 to 12(E)-(10aS)-18** A solution of 12(Z)-(10aS)-**17** (181 mg, 0.6 mmol) and  $(\text{PhS})_2$  (65 mg, 0.3 mmol) in benzene (5 mL) was irradiated for 3 h by means of high pressure Hg lamp equipped with UVL-100P at rt. The reaction mixture was evaporated to afford a residue which was chromatographed on silica gel (15 g, n-hexane:AcOEt=20:1) to give (10aS)-**17** (18 mg, 8%), and 12(E)-(10aS)-**18** (164 mg, 91%). Spectral data of the present 12(E)-(10aS)-**18** were identical with those of the above-mentioned 12(E)-(10aS)-**18**.

**Galanolactone ((+)-1)** To a solution of 12(E)-(10aS)-**18** (340 mg, 1.13 mmol) in  $\text{CHCl}_3$  (10 mL) was added 85% of *m*CPBA (968 mg, 5.63 mmol) at 0 °C and the whole mixture was stood for 12 h in a refrigerator. The reaction mixture was diluted with 10% aqueous  $\text{Na}_2\text{SO}_3$  and extracted with  $\text{Et}_2\text{O}$ . The organic layer was washed with 7% aqueous  $\text{NaHCO}_3$ , saturated brine and dried over  $\text{MgSO}_4$ . Evaporation of organic solvent gave a residue which was chromatographed on silica gel (20 g, n-hexane:AcOEt=5:1) to give (+)-**1** as solid. Recrystallization of crude (+)-**1** from MeOH afforded colorless needles (+)-**1** (70 mg, 19%). (+)-**1**: mp 126 °C; IR(KBr):  $1701\text{ cm}^{-1}$ ;  $[\alpha]_{\text{D}}^{27} +30.0^\circ$  ( $c=0.75$ ,  $\text{CHCl}_3$ );  $^1\text{H-NMR}$ :  $\delta$  0.88 (3H, s), 0.92 (3H, s), 0.93 (3H, s), 1.01-1.21 (2H, m), 1.34-1.94 (12H, m), 2.31 (1H, d,  $J=4$  Hz), 2.44 (1H, d,  $J=4$  Hz), 2.75-2.93 (2H, m), 4.38 (2H, t,  $J=7$  Hz), 6.61-6.66 (1H, m). FAB MS  $m/z$ : 319 ( $\text{M}^++1$ ). HRMS (FAB-MS, matrix: NBA): calcd for  $\text{C}_{20}\text{H}_{31}\text{O}_3$  ( $\text{M}^++1$ ) 319.2273; found 319.2249.

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