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TOTAL SYNTHESIS OF (+)-GALANOLACTONE

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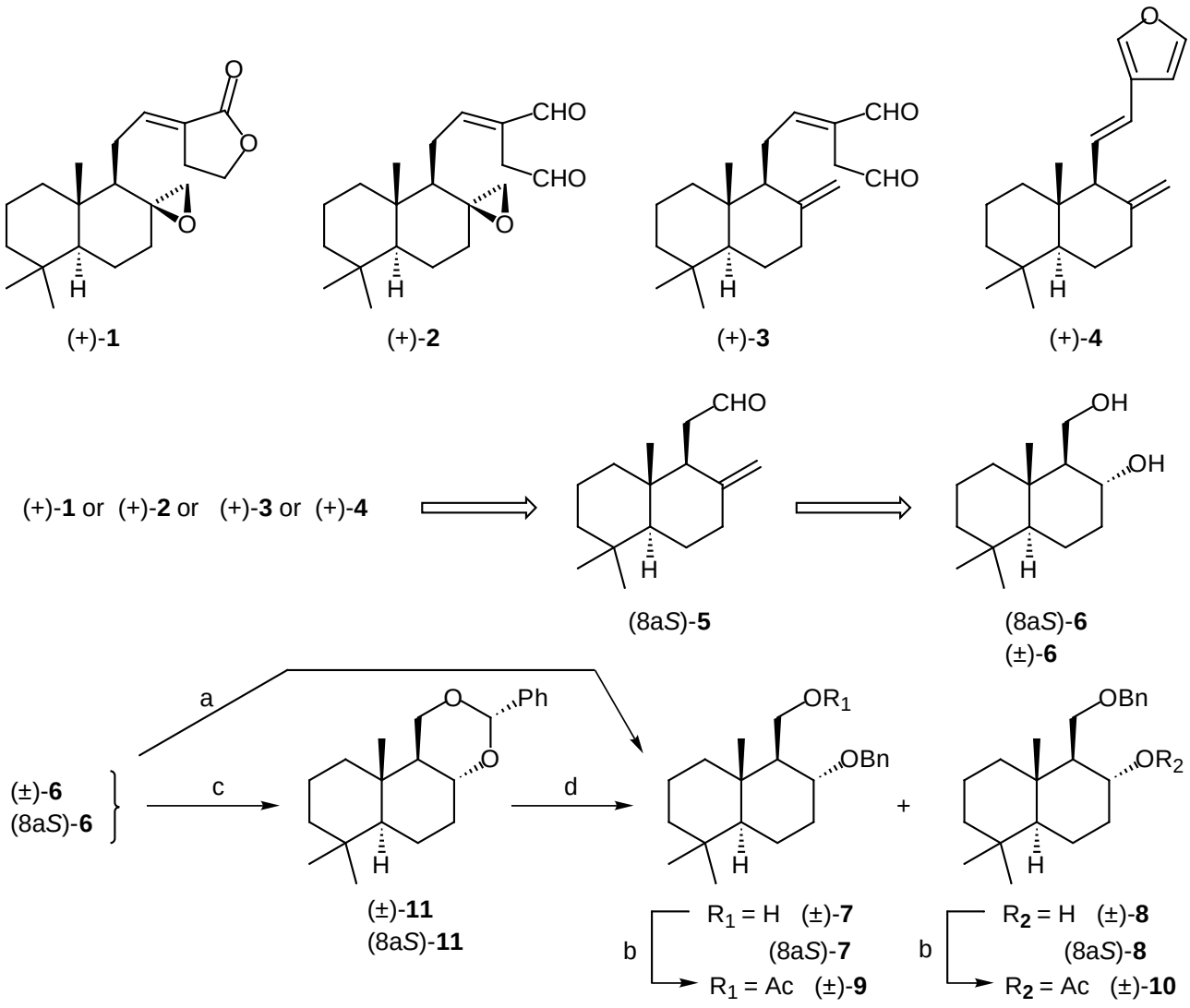
Abstract - Regioselective monobenzylation of the chemoenzymatically prepared chiral decalin-type diol ((8a*S*)-**6**) *via* the benzylidene acetal ((8a*S*)-**11**) afforded the primary alcohol ((8a*S*)-**7**), from which total synthesis of (+)-galanolactone (**1**) was achieved and formal syntheses of (+)-(*E*)-8β(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*)-8β(17),12-labddiene-15,16-dial ((+)-**3**) were isolated from *Alpinia galanga* (Zingiberaceae) together with (*E*)-8(17) - epoxylabd-12-ene-15,16-dial ((+)-**2**) and these compounds exhibited the cytotoxic and antifungal activities.[1] Recently, ((+)-**1**) is reported to exhibit anti-5HT (serotonin) effect[2] and the inhibitory effect of (+)-**2** against cholesterol biosynthesis is also reported.[3] Coronarin E ((+)-**4**) has been isolated from the rhizomes of the Brazilian medical plant *Hedychium coronarium* (Zingiberaceae).[4] Total syntheses of **1**[5] and **2**[6] as racemic form[5,6] in multiple steps and conversion of natural sclareol into (+)-**1**,[7] (+)-**3**[7] and (+)-**4**[8] 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.[9] 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 (±)-**6** using one equivalent of benzyl bromide gave the monobenzyl ethers ((±)-**7**) (7% yield) and ((±)-**8**) (37% yield). The structure of both monobenzyl ethers ((±)-**7**) and ((±)-**8**) was confirmed by derivation to the corresponding acetates ((±)-**9**) and ((±)-**10**), respectively. This drawback could be overcome by the regioselective and reductive cleavage of acetal bond of benzylideneacetal (**11**). Treatment of (±)-**6** with benzaldehyde in the presence of a catalytic amount of conc. H_2SO_4 afforded the benzylidene acetal ((±)-**11**) exclusively in 94% yield. Benzylidene-acetals 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 (±)-**11** was treated with various kinds of reducing agent in the presence of Lewis acid, the results are



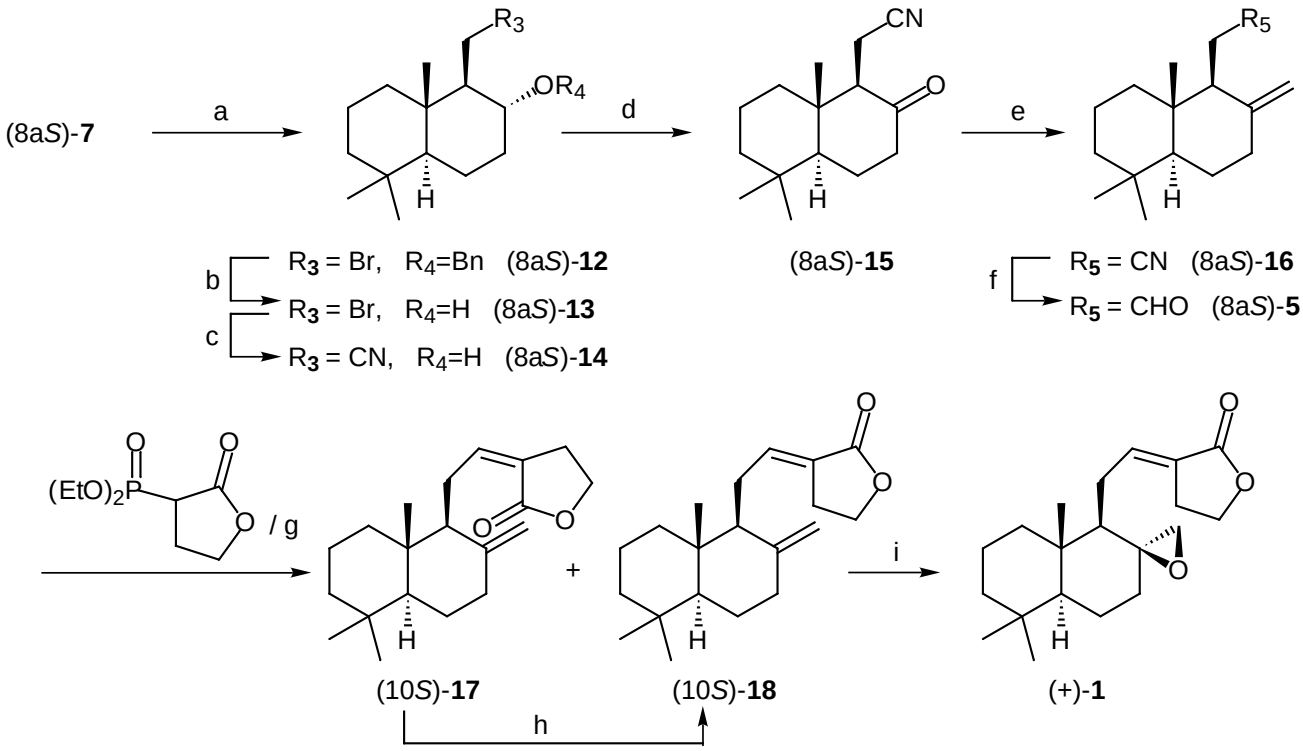
Scheme 1

Table

(±)-**11** —reducing reagents→ (±)-**11** + (±)-**7** + (±)-**8** + (±)-**6**

entry	conditions	products (%)
1	HAl(*i*-Bu)$_2$) / THF	(±)-**11**(96%)
2	$NaBH_3CN$ / $TiCl_4$ / MeCN	(±)-**7**+ (±)-**8** (33%, (±)-**7** : (±)-**8** = 1: 5.5) (±)-**6** (43%)
3	$LiAlH_4$ / $BF_3{\cdot}Et_2O$ / Et_2O	(±)-**11**(62%) (±)-**7**+ (±)-**8** (8%, (±)-**7** : (±)-**8** = 1: 1.2) (±)-**6** (29%)
4	$LiAlH_4$ / $AlCl_3$ / Et_2O	(±)-**7**+ (±)-**8** (99%, (±)-**7** : (±)-**8** = 17:1)

shown in Table. In case of using $LiAlH_4$ (1 eq)-$AlCl_3$ (4 eq) system[10] 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 (8a*S*)-**6** with benzaldehyde in the presence of a catalytic amount of conc. H_2SO_4 afforded the acetal ((8a*S*)-**11**) exclusively in 98% yield, which was



Scheme 2

reduced with a mixed reducing reagent ($LiAlH_4$ (1 eq)-$AlCl_3$ (4 eq)) to provide selectively primary alcohol ((8a*S*)-**7**) (93% yield) along with a small amount of secondary alcohol ((8a*S*)-**8**) (5% yield). Conversion of (8a*S*)-**7** into the keto nitrile ((8a*S*)-**15**) *via* bromination ((8a*S*)-**12**; 98% yield), reduction ((8a*S*)-**13**; 99% yield), CN substitution ((8a*S*)-**14**; 97% yield) and oxidation ((8a*S*)-**15**; 96% yield) was reported by us.[11] The Wittig olefination of (8a*S*)-**15** with $Ph_3P=CH_2$ provided the *exo* olefin ((8a*S*)-**16**) in 96% yield, which was reduced with diisobutylaluminum hydride (Dibal-H) to give the desired ((8a*S*)-**5**) in 92% yield. Coupling of the aldehyde ((8a*S*)-**5**) with the anion of diethylphosphono-2-butyrolactone afforded the isomeric lactones ((10*S*)-**17**) (*Z*-form, 26% yield) and ((10*S*)-**18**) (*E*-form, 59% yield). While the nOe enhancement (2.6%) between 12-H (δ 6.17) and one of 14-methylene (δ 1.78) protons of (10*S*)-**17** was indicated, no nOe enhancement between 12-H (δ 6.72) and 14-H (δ 2.85) of (10*S*)-**18** was observed. Isomerization of (10*S*)-**17** to (10*S*)-**18** was effected by irradiation in the presence of diphenyl disufide[12] and 91% conversion yield of **18** was obtained. By applying the reported procedure,[7] epoxidation of exomethylene at C(8) of (10*S*)-**18** with an excess of *m*-chloroperbenzoic acid (*m*CPBA) at 0℃ gave (+)-galanolactone (**1**) (19% yield, mp 126°C, $[\alpha]_D^{27}$+30.0° (c=0.75, $CHCl_3$)) whose spectral data were identical with those (mp 125.5-126°C, $[\alpha]_D$+28.0° (c=0.26, $CHCl_3$), and ^{1}H-NMR) of natural (+)-**1**.

Conversion of (10*S*)-**18** into (+)-(*E*)-8β(17),12-labddiene-15,16-dial ((+)-**3**) *via* reduction followed by Swern oxidation was already achieved.[7] The above-mentioned aldehyde ((8a*S*)-**5**) was also led to (+)-coronarin E (**4**) *via* treatment with 3-furyllithium followed by dehydration.[8]

In conclusion, regioselective monobenzylation of the chemoenzymatically prepared 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*)-8β(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. ^{1}H- and ^{13}C-NMR spectra were recorded on JEOL EX 400 spectrometer in $CDCl_3$. 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**,4a*S**,8a*S**)-2-Benzyloxydecahydro-5,5,8a-trimethyl-1-naphthylmethanol ((±)-7) and (1*R**,2*R**,4a*S**,8a*S**)-1-Benzyloxymethyl-2-hydroxy-decahydro-5,5,8a-trimethylnaphthalene ((±)-8)** A mixture of (±)-**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 $MgSO_4$ and evaporated to give a residue which was chromatographed on silica gel (20 g, n-hexane-AcOEt=10:1) to give (±)-**7** (45 mg, 7%) as crystals and (±)-**8** (215 mg, 37%) as a colorless oil, respectively. Recrystallization of the former from n-hexane gave (±)-**7** as colorless plates. (±)-**7**: mp 67 ℃; IR (KBr): 3479 cm^{-1} (OH); ^{1}H NMR : δ 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 $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.98; H, 10.04. FAB MS m/z: 317 (M^++1). (±)-**8**: IR (neat): 3480 cm^{-1} (OH); ^{1}H NMR : δ 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 $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.73; H, 10.08. FAB MS m/z: 317 (M^++1).

Acetylation of (±)-7 The primary hydroxyl group of (±)-**7** (45 mg, 0.14 mmol) was acetylated with Ac_2O (45 mg, 0.44 mmol) in pyridine (2 mL) in the usual manner to give (±)-**9** (49 mg, 96%) as colorless plates (from n-hexane). (±)-**9**: mp 83-83.5 ℃; IR (KBr): 1738 cm^{-1} (OAc); ^{1}H NMR : δ 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 (±)-8 The secondary hydroxyl group of (±)-**8** (95 mg, 0.3 mmol) was acetylated with Ac_2O (45 mg, 0.44 mmol), DMAP (12 mg, 0.1 mmol) in pyridine (2 mL) in the usual manner to give (±)-**10** (106 mg, 99%) as a colorless oil. (±)-**10**: IR (neat): 1736 cm^{-1} (OAc); ^1H NMR : δ 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 $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.32; H, 9.09. FAB MS m/z: 359 (M^++1).

[(3*S,4a*R**,6a*S**,10a*S**,10b*S**)-Decahydro-7,7,10a-trimethyl-1*H*-naphtho[2,1*d*][1,3]-dioxin-3-yl]benzene ((±)-11)** To a solution of (±)-**6** (1.509 g, 6.67 mmol), and benzaldehyde (1.06 g, 10 mmol) in DMSO (25 mL) was added conc. H_2SO_4 (5 mL) at 0 ℃ and the whole mixture was stirred at rt for 30 min, and then diluted with saturated aqueous $NaHSO_3$ and extracted with ether. The organic layer was washed with saturated brine and dried over $MgSO_4$. The organic layer was evaporated to give a residue. To a solution of the residue in a mixed solvent (H_2O (10 mL)-DMSO (10mL)) was added $NaHSO_3$ (200 mg) at rt and the whole mixture was stirred at rt for 12 h. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (25 g, n-hexane-AcOEt=20:1) to afford (±)-**11** (1.967 g, 94%) as crystals. Recrystallization from n-hexane-AcOEt gave (±)-**11** as colorless plates. (±)-**11**: mp 90 ℃; IR (KBr): 1041 cm^{-1} ; ^1H NMR : δ 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 $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. found: C, 80.58; H, 9.39. FAB MS m/z: 315 (M^++1).

Reduction of (±)-11 i) entry 1; To a solution of (±)-**11** (96 mg, 0.31 mmol) in THF (1 mL) at –78 ℃ was added 1 M Dibal in toluene (0.4 mL, 0.4 mmol) and the whole mixture was stirred for 1 h at –20 ℃. The reaction mixture was worked up in the usual manner to give (±)-**11** (92 mg, 96% recovery). ii) entry 2; To a solution of (±)-**11** (100 mg, 0.32 mmol) in CH_3CN (1 mL) at –20 ℃ were added $NaBH_3CN$ (32 mg, 0.52 mmol) and $TiCl_4$ (0.2 mL, 1.82 mmol), and the whole mixture was stirred for 30 min at –20 ℃. The reaction mixture was worked up in the usual manner to give a mixture (33 mg, 33%; (±)-**7** : (±)-**8** =1 : 5.5) of (±)-**7** and (±)-**8**, and (±)-**6** (31 mg, 43%). The ratio of (±)-**7** and (±)-**8** was determined by NMR analysis. iii) entry 3; To a solution of (±)-**11** (95 mg, 0.3 mmol) in Et_2O (1 mL) at –20 ℃ were added $LiAlH_4$ (14 mg, 0.36 mmol) and $BF_3 \cdot Et_2O$ (0.15 mL, 1.22 mmol), and the whole mixture was stirred for 30 min at –20 ℃. The reaction mixture was worked up in the usual manner to give (±)-**11** (59 mg, 62% recovery), a mixture (8 mg, 8%; (±)-**7** : (±)-**8** =1 : 1.2) of (±)-**7** and (±)-**8**, and (±)-**6** (20 mg, 29%). iv) entry 4; To a solution of (±)-**11** (106 mg, 0.34 mmol) in Et_2O (1 mL) at –20 ℃ were added $LiAlH_4$ (20 mg, 0.53 mmol) and $AlCl_3$ (212 mg, 1.59 mmol), and the whole mixture was stirred for 30 min at –20 ℃. The

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

[(3*S*,4a*R*,6a*S*,10a*S*,10b*S*)-Decahydro-7,7,10a-trimethyl-1*H*-naphtho[2,1*d*][1,3]-dioxin-3-yl]benzene ((-)-11) A small amount of conc. H_2SO_4 (15 drops) was added to a solution of (-)-(8a*S*)-**6** (338 mg, 1.5 mmol) and benzaldehyde (462 mg, 4.36 mmol) in DMSO (3 mL) at 0 ℃ and the whole mixture was stirred at rt for 30 min, and then diluted with H_2O and extracted with ether. The organic layer was washed with saturated brine and dried over $MgSO_4$. The organic layer was evaporated to give a residue. To a solution of the residue in a mixed solvent (H_2O (1 mL)-DMSO (1 mL)) was added $NaHSO_3$ (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_2O and extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (15 g, n-hexane-AcOEt=20:1) to afford (-)-(8a*S*)-**11** as crystals. Recrystallization from n-hexane gave (-)-(8a*S*)-**11** (463 mg, 98%) as colorless needles. (-)-(8a*S*)-**9**: mp 98.5~99 ℃; $[\alpha]_D^{23}$ -9.5° (c=1.12, $CHCl_3$). Spectral data (IR and ^{1}H NMR) of (-)-(8a*S*)-**11** were identical with those of (±)-**11**. FAB MS m/z: 315 (M^++1).

(-)-(1*S*,2*R*,4a*S*,8a*S*)-2-Benzyloxydecahydro-5,5,8a-trimethyl-1-naphthylmethanol ((-)-(8a*S*)-7) and (+)-(1*R*,2*R*,4a*S*,8a*S*)-1-Benzyloxy-2-hydroxydecahydro-5,5,8a-trimethyl-naphthalene ((+)-(8a*S*)-8) To a solution of (-)-(8a*S*)-**11** (359 mg, 1.14 mmol) in Et_2O (10 mL) at -20℃ was added $LiAlH_4$ (51 mg, 1.35 mmol) and the whole mixture was stirred for 10 min. Then $AlCl_3$ (734 mg, 5.52 mmol) was added to the above mixture and the whole mixture was stirred at -20 ℃ for 30 min. The reaction mixture was diluted with H_2O, acidified with 2M aqueous HCl and extracted with ether. The organic layer was washed with saturated brine and dried over $MgSO_4$. Evaporation of the organic solvent gave a residue which was chromatographed on silica gel (15 g, n-hexane-AcOEt=20:1) to give (-)-(8a*S*)-**7** (336 mg, 93%) as crystals and (+)-(8a*S*)-**8** (18 mg, 5%) as a colorless oil, respectively. Recrystallization of the former from n-hexane gave (-)-(8a*S*)-**7** as colorless plates. (-)-(8a*S*)-**7**: mp 110.5~111 ℃; $[\alpha]_D^{23}$ -67.0° (c=1.08, CHCl). Spectral data (IR and ^{1}H NMR) of (-)-(8a*S*)-**7** were identical with those of (±)-**7**. FAB MS m/z: 317 (M^++1). (+)-(8a*S*)-**8**: $[\alpha]_D^{22}$ +32.5° (c=1.36, $CHCl_3$). Spectral data (IR and ^{1}H NMR) of (-)-(8a*S*)-**8** were identical with those of (±)-**8**. FAB MS m/z: 317 (M^++1).

(+)-(1*R*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-2-methylene-1-naphthaleneacetonitrile ((8a*S*)-16) A suspension of $Ph_3P^+MeBr^-$ (3.137 g, 8.78 mmol) and $NaNH_2$ (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 ($Ph_3P=CH_2$) was poured into (8a*S*)-**15** (190 mg, 0.81 mmol) at 0 ℃. The whole was stirred for 15 min at rt. The reaction mixture was diluted with H_2O and extracted with ether. The ether layer was washed with brine and dried over $MgSO_4$. 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 (8a*S*)-**16** (180 mg, 95%), which was recrystallized from n-hexane to give colorless plates. (8a*S*)-**16**: mp 91 ℃; $[\alpha]_D^{24}$ + 42.2° (c=1.02, $CHCl_3$); IR (KBr): 2240 cm^{-1} (CN); ^{1}H-NMR: δ 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}C-NMR: δ 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 $C_{16}H_{25}N$: C, 83.06; H, 10.89; N, 6.05. Found: C, 83.38; H, 10.85; N, 5.95. FAB MS m/z: 232 (M^++1).

(+)-(1*R*,4a*S*,8a*S*)-Decahydro-5,5,8a-trimethyl-2-methylene-1-naphthaleneacetaldehyde ((8a*S*)-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℃, 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 $MgSO_4$. 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 ((8a*S*)-**5**) (373 mg, 92%). (8a*S*)-**5**: IR (neat): 1725 cm^{-1} (CHO); $[\alpha]_D^{21}$ -25.5° (c=1.07, $CHCl_3$); ^{1}H-NMR:δ 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}C-NMR : δ 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 $C_{16}H_{26}O$: C, 81.98; H, 11.18. Found: C, 82.32; H, 11.28. FAB MS m/z: 235 (M^++1).

Wittig-Horner Reaction of (8a*S*)-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 (8a*S*)-**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 $MgSO_4$. 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 (10a*S*)-**17** (150 mg, 26%) and (10a*S*)-**18** (341 mg, 59%) as a colorless oil. Recrystallization of (10a*S*)-**17** from n-hexane afforded colorless powder. (10a*S*)-**17**: mp 64 ℃; $[\alpha]_D^{22}$ + 25.2° (c=1.37, $CHCl_3$); IR (KBr): 1741 cm^{-1}; ^{1}H-NMR: δ 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}C-NMR: δ 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 $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.42; H, 9.93. FAB MS m/z: 303 (M^++1). (10a*S*)-**18**: $[\alpha]_D^{20}$ +16.7° (c=1.12, $CHCl_3$); IR (neat): 1757 cm^{-1}; ^{1}H-NMR: δ

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}C-NMR: δ 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 $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.67; H, 9.97. FAB MS m/z: 303 (M^++1).

Conversion of 12(*Z*)-(10a*S*)-17 to 12(*E*)-(10a*S*)-18 A solution of 12(*Z*)-(10a*S*)-**17** (181 mg, 0.6 mmol) and $(PhS)_2$ (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 (10a*S*)-**17** (18 mg, 8%), and 12(*E*)-(10a*S*)-**18** (164 mg, 91%). Spectral data of the present 12(*E*)-(10a*S*)-**18** were identical with those of the above-mentioned 12(*E*)-(10a*S*)-**18**.

Galanolactone ((+)-1) To a solution of 12(*E*)-(10a*S*)-**18** (340 mg, 1.13 mmol) in $CHCl_3$ (10 mL) was added 85% of *m*CPBA (968 mg, 5.63 mmol) at 0 ℃ and the whole mixture was stood for 12 h in a refrigerator. The reaction mixture was diluted with 10% aqueous Na_2SO_3 and extracted with Et_2O. The organic layer was washed with 7% aqueous $NaHCO_3$, saturated brine and dried over $MgSO_4$. 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 ℃; IR(KBr): 1701 cm^{-1}; $[\alpha]_D^{27}$ +30.0° (c=0.75, $CHCl_3$); ^{1}H-NMR: δ 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 (M^++1). HRMS (FAB-MS, matrix: NBA): calcd for $C_{20}H_{31}O_3$ (M^++1) 319.2273; found 319.2249.

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