TOTAL SYNTHESIS OF (+)-GALANOLACTONE

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Abstract - Regioselective monobenzylation of the chemoenzymatically prepared chiral decalin-type diol ((8aS)-6) via the benzylidene acetal ((8aS)-11) afforded the primary alcohol ((8aS)-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) effect² 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 1⁵ and 2⁶ as racemic form⁵,⁶ in multiple steps and conversion of natural sclareol into (+)-1,⁷ (+)-3⁷ and (+)-4⁸ are reported. In connection with our synthetic study of decalin-type chiral synthon ((8aS)-6) based on enzymatic function and its application to terpenoid synthesis, the synthesis of labdane-type diterpenoids possessing biological activities has aroused our interest. (8aS)-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 ((8aS)-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 ((8aS)-6).

In the synthesis of (8aS)-5 from (8aS)-6, the regioselective protection of two hydroxyl groups of (8aS)-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. H₂SO₄ afforded the benzylidene acetal ((±)-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 (±)-11 was treated with various kinds of reducing agent in the presence of Lewis acid, the results are...
shown in Table. In case of using LiAlH₄ (1 eq)-AlCl₃ (4 eq) system as shown in entry 4, chemical yield (99%) and regioselectivity \((±)-7: (±)-8 = 17:1\) 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. H₂SO₄ afforded the acetal \((±)-11\) exclusively in 98% yield, which was
reduced with a mixed reducing reagent \( \text{LiAlH}_4 \) (1 eq)-\( \text{AlCl}_3 \) (4 eq)) to provide selectively primary alcohol ((8a\text{S})-7) (93% yield) along with a small amount of secondary alcohol ((8a\text{S})-8) (5% yield). Conversion of (8a\text{S})-7 into the keto nitrile ((8a\text{S})-15) via bromination ((8a\text{S})-12; 98% yield), reduction ((8a\text{S})-13; 99% yield), CN substitution ((8a\text{S})-14; 97% yield) and oxidation ((8a\text{S})-15; 96% yield) was reported by us.\(^{11}\) The Wittig olefination of (8a\text{S})-15 with \( \text{Ph}_3\text{P}=\text{CH}_2 \) provided the \( \text{exo} \) olefin ((8a\text{S})-16) in 96% yield, which was reduced with diisobutylaluminum hydride (Dibal-H) to give the desired ((8a\text{S})-5) in 92% yield. Coupling of the aldehyde ((8a\text{S})-5) with the anion of diethylphosphono-2-butyrolactone afforded the isomeric lactones ((10\text{S})-17) (\( Z \)-form, 26% yield) and ((10\text{S})-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 (10\text{S})-17 was indicated, no nOe enhancement between 12-H (\( \delta \) 6.72) and 14-H (\( \delta \) 2.85) of (10\text{S})-18 was observed.

Isomerization of (10\text{S})-17 to (10\text{S})-18 was effected by irradiation in the presence of diphenyl disulfide\(^{12}\) and 91% conversion yield of 18 was obtained. By applying the reported procedure,\(^2\) epoxidation of exomethylene at \( \text{C}(8) \) of (10\text{S})-18 with an excess of \( m \)-chloroperbenzoic acid (\( m \text{CPBA} \)) at \( 0^\circ\text{C} \) gave (+)-galanolactone (1) (19% yield, mp 126°C, \([\alpha]_D^{27}+30.0^\circ \) (c=0.75, CHCl\(_3\))) whose spectral data were identical with those (mp 125.5-126°C, \([\alpha]_D^{28}+28.0^\circ \) (c=0.26, CHCl\(_3\)), and \( 1^\text{H}-\text{NMR} \)) of natural (+)-1.
Conversion of \((10S)-18\) into \((+)-(E)-8\beta(17),12\text{-labddiene}-15,16\text{-dial}\ ((+)-3) via\ reduction followed by Swern oxidation was already achieved.\(^7\) The above-mentioned aldehyde \((8aS)-5\) was also led to \((+)-\text{coronarin E}\ (4) via\ treatment with 3-furyllithium followed by dehydration.\(^8\)

In conclusion, regioselective monobenzylation of the chemoenzymatically prepared diol \((8aS)-6\) via the benzylidene acetal \((8aS)-11\) afforded the primary alcohol \((8aS)-7\), from which total synthesis of \((+)-\text{galanolactone}\ (1)\ was achieved and formal syntheses of \((+)-(E)-8\beta(17),12\text{-labddiene}-15,16\text{-dial}\ ((+)-3)\ and \((+)-\text{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: \textit{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.

\((1S*, 2R*, 4aS*, 8aS*)-2\text{-Benzyloxydecahydro-5,5,8a-trimethyl-1-naphthylmethanol}\ ((\pm)-7)\ and \((1R*, 2R*, 4aS*, 8aS*)-1\text{-Benzyloxymethyl-2-hydroxy-decahydro-5,5,8a-trimethylNaphthalene}\ ((\pm)-8)\)

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\(_4\) 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; \textit{IR} (KBr): 3479 cm\(^{-1}\) (OH); \(^1\)H NMR: \(\delta\ 0.75\ (3\ H, \ s), 0.79\ (3\ H, \ s), 0.88\ (3\ H, \ s), 0.90\sim1.58\ (9\ H, \ m), 1.71\sim1.85\ (2\ H, \ m), 2.30\sim2.36\ (1\ H, \ m), 3.39\ (1\ H, \ d, \ J=11\ Hz, \ OH), 3.59\ (1\ H, \ dd, \ J= 8, 11\ Hz), 3.64\ (1\ H, \ dt, \ J=5, 11\ Hz), 3.78\ (1\ H, \ t, \ J=11\ Hz), 4.44\ (1\ H, \ d, \ J=11.5\ Hz), 4.70\ (1\ H, \ d, \ J=11.5\ Hz), 7.26\sim7.37\ (5\ H, \ m). \textit{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\(^{+}\)). \((\pm)-8\): \textit{IR} (neat): 3480 cm\(^{-1}\) (OH); \(^1\)H NMR: \(\delta\ 0.81\ (3\ H, \ s), 0.81\ (3\ H, \ s), 0.88\ (3\ H, \ s), 0.91\sim1.75\ (11\ H, \ m), 2.05\sim2.12\ (1\ H, \ m), 3.61\ (1\ H, \ t, \ J=9\ Hz), 3.82\ (1\ H, \ dt, \ J=5, 10.5\ Hz), 3.85\ (1\ H, \ dd, \ J=3, 9\ Hz), 4.05\ (1\ H, \ br\ s), 4.51\ (2\ H, \ s), 7.26\sim7.36\ (5\ H, \ m). \textit{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\(^{+}\)).

**Acetylation of \((\pm)-7\)**

The primary hydroxyl group of \((\pm)-7\) (45 mg, 0.14 mmol) was acetylated with Ac\(_2\)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; \textit{IR} (KBr): 1738 cm\(^{-1}\) (OAc); \(^1\)H NMR: \(\delta\ 0.82\ (3\ H, \ s), 0.86\ (3\ H, \ s), 0.88\ (3\ H, \ s), 0.90\sim1.77\ (11\ H, \ m), 1.95\ (3\ H, \ s), 2.32\sim2.37\ (1\ H, \ m), 3.42\sim3.50
Acetylation of (±)-8  The secondary hydroxyl group of (±)-8 (95 mg, 0.3 mmol) was acetylated with Ac₂O (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).

[(3S*,4aR*,6aS*,10aS*,10bS*)-Decahydro-7,7,10a-trimethyl-1H-naphtho[2,1d][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. H₂SO₄ (5 mL) at 0 °C and the whole mixture was stirred at rt for 30 min, and then diluted with saturated aqueous NaHSO₃ and extracted with ether. The organic layer was washed with saturated brine and dried over MgSO₄. The organic layer was evaporated to give a residue. To a solution of the residue in a mixed solvent (H₂O (10 mL)-DMSO (10 mL)) was added NaHSO₃ (200 mg) at rt and the whole mixture was stirred at rt for 12 h. The reaction mixture was diluted with H₂O and extracted with ether. The organic layer was dried over MgSO₄ 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 °C; 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), 5.46 (1H, s), 7.28~7.34 (3H, m), 7.46~7.49 (2H, m). Anal. Calcd for C₂₁H₃₀O₂: 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 °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 °C. 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 CH₃CN (1 mL) at −20 °C were added NaBH₃CN (32 mg, 0.52 mmol) and TiCl₄ (0.2 mL, 1.82 mmol), and the whole mixture was stirred for 30 min at −20 °C. 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 Et₂O (1 mL) at −20 °C were added LiAlH₄ (14 mg, 0.36 mmol) and BF₃·Et₂O (0.15 mL, 1.22 mmol), and the whole mixture was stirred for 30 min at −20 °C. 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 Et₂O (1 mL) at −20 °C were added LiAlH₄ (20 mg, 0.53 mmol) and AlCl₃ (212 mg, 1.59 mmol), and the whole mixture was stirred for 30 min at −20 °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.

\[
\left[\left(3S,4aR,6aS,10aS,10bS\right)-\text{Decahydro-}7,7,10a\text{-trimethyl-1H-naphtho[2,1d][1,3]-dioxin-3-yl}\right]\text{benzene }\left(\text{(-)-11}\right)
\]
A small amount of conc. H\(_2\)SO\(_4\) (15 drops) was added to a solution of \((-)-(8aS)-6\) (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\(_2\)O 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\(_2\)O (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\(_2\)O 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 \((-)-(8aS)-11\) as crystals. Recrystallization from n-hexane gave \((-)-(8aS)-11\) (463 mg, 98%) as colorless needles. \((-)-(8aS)-9\): mp 98.5~99 °C; \([\alpha]_D^{23} -9.5°\) (c=1.12, CHCl\(_3\)). Spectral data (IR and \(^1\)H NMR) of \((-)-(8aS)-11\) were identical with those of \((\pm)-11\). FAB MS m/z: 315 (M\(^++\)+1).

\((-)-(1S,2R,4aS,8aS)-2\text{-Benzxyloxydecahydro-}5,5,8a\text{-trimethyl-1-naphthylmethanol }\left((-)-(8aS)-7\right)\) and \((+)-(1R,2R,4aS,8aS)-1\text{-Benzxyloxy-2-hydroxydecahydro-}5,5,8a\text{-trimethyl-naphthalene }\left((+)-(8aS)-8\right)\) To a solution of \((-)-(8aS)-11\) (359 mg, 1.14 mmol) in Et\(_2\)O (10 mL) at -20°C 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 °C for 30 min. The reaction mixture was diluted with H\(_2\)O, 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 crude residue, which was chromatographed on silica gel (15 g, n-hexane-AcOEt=20:1) to afford \((-)-(8aS)-7\) (336 mg, 93%) as crystals and \((+)-(8aS)-8\) (18 mg, 5%) as a colorless oil, respectively. Recrystallization of the former from n-hexane gave \((-)-(8aS)-7\) as colorless plates. \((-)-(8aS)-7\): mp 110.5~111 °C; \([\alpha]_D^{23} -67.0°\) (c=1.08, CHCl\(_3\)). Spectral data (IR and \(^1\)H NMR) of \((-)-(8aS)-7\) were identical with those of \((\pm)-7\). FAB MS m/z: 317 (M\(^++\)+1). \((+)-(8aS)-8\): \([\alpha]_D^{22} +32.5°\) (c=1.36, CHCl\(_3\)). Spectral data (IR and \(^1\)H NMR) of \((-)-(8aS)-8\) were identical with those of \((\pm)-8\). FAB MS m/z: 317 (M\(^++\)+1).

\((+)-(1R,4aS,8aS)-\text{Decahydro-}5,5,8a\text{-trimethyl-2-methylene-1-naphthaleneacetonitrile }\left((8aS)-16\right)\) A suspension of Ph\(_3\)P+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\(_3\)P=CH\(_2\)) was poured into \((8aS)-15\) (190 mg, 0.81 mmol) at 0 °C. The whole was stirred for 15 min at rt. The reaction mixture was diluted with H\(_2\)O 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 \((8aS)-16\) (180 mg, 95%), which was recrystallized from n-hexane to give colorless plates. \((8aS)-16\): mp 91 °C; \([\alpha]_D^{24} + 42.2°\) (c=1.02, CHCl\(_3\)); IR (KBr): 2240 cm\(^{-1}\) (CN); \(^1\)H-NMR: \(\delta\) 0.69 (3H, s), 0.82 (3H, s),

\[\text{Ph}_3\text{P+MeBr} + \text{NaNH}_2 \rightarrow \text{Ph}_3\text{P}=\text{CH}_2 + \text{NaBH}_3\]
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). 13C-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 (q), 53.2 (d), 55.0 (d), 107.8 (s), 120.3 (s), 146.3 (t). Anal. Calcd for C16H25N: 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).

(+)-(1R,4aS,8aS)-Decahydro-5,5,8a-trimethyl-2-methylene-1-naphthaleneacetaldehyde ((8aS)-5) To a solution of (8aS)-1 (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° 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 MgSO4. Evaporation of the organic solvent gave a residue, which was chromatographed on silica gel to afford a colorless oil ((8aS)-5) (373 mg, 92%). (8aS)-5: IR (neat): 1725 cm⁻¹ (CHO); [α]D²¹ -25.5° (c=1.07, CHCl₃); 1H-NMR: 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, d, t, 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). 13C-NMR: 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 C16H26O: C, 81.98; H, 11.18. Found: C, 82.32; H, 11.28. FAB MS m/z: 235 (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 MgSO4. The organic layer was evaporated to give a crude residue, which was chromatographed on silica gel (20 g, n-hexane:AcOEt=100:1) to afford a colorless oil. Recrystallization of (10aS)-17 from n-hexane afforded colorless powder. (10aS)-17: mp 64 °C; [α]D²² + 25.2° (c=1.37, CHCl₃); IR (KBr): 1741 cm⁻¹; 1H-NMR: 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). 13C-NMR: 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 C20H30O2: C, 79.42; H, 11.85. Found: C, 79.42; H, 11.85. FAB MS m/z: 303 (M⁺+1). (10aS)-18: [α]D²⁰ +16.7° (c=1.12, CHCl₃); IR (neat): 1757 cm⁻¹; 1H-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 C20H30O2: C, 79.42; H, 10.00. Found: C, 79.67; H, 9.97. FAB MS m/z: 303 (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 (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 CHCl3 (10 mL) was added 85% of mCPBA (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 Na2SO3 and extracted with Et2O. The organic layer was washed with 7% aqueous NaHCO3, saturated brine and dried over MgSO4. 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 cm⁻¹; [α]D²⁷ +30.0° (c=0.75, CHCl₃); 1H-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 C₂₀H₃₁O₃ (M++1) 319.2273; found 319.2249.

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