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# Stereoselective Synthesis of (2*S*,3*S*)-2-Benzyl-2-hydroxy-3-(3,4-methylenedioxybenzyl)-$\gamma$-butyrolactone from L-(+)-Arabinose *via* a Carissanol-type of Lignan

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**As a model experiment for the synthesis of optically active $\alpha,\beta$-dibenzyl-$\alpha$-hydroxy-$\gamma$-butyrolactone (1), (2*S*,3*S*)-2-benzyl-2-hydroxy-3-(3,4-methylenedioxybenzyl)-$\gamma$-butyrolactone (3) was stereoselectively synthesized from L-(+)-arabinose *via* the carissanol-type of lignan, (2*R*/*S*,3*S*,4*S*)-3-benzyl-2,3-dihydroxy-4-(3,4-methylenedioxybenzyl)tetrahydrofuran (4).**

**Key words:** lignan; $\alpha,\beta$-dibenzyl-$\gamma$-butyrolactone; carissanol-type lignan

It has been reported that $\alpha,\beta$-dibenzyl-$\alpha$-hydroxy-$\gamma$-butyrolactones (**1**), which are one of the $\alpha,\beta$-dibenzyl-$\gamma$-butyrolactone type of lignans, had interesting biological activity, antitumor activity[1] and Ca$^{2+}$ antagonist activity.[2] While many types of lignans have been synthesized from $\alpha,\beta$-dibenzyl-$\gamma$-butyrolactones,[3] the synthesis of $\alpha,\beta$-dibenzyl-$\alpha$-hydroxy-$\gamma$-butyrolactones (**1**) is important, since they have interesting biological activity and can also be expected as key precursors for the synthesis of many other lignans. The only reported stereoselective synthesis of this type of lignan involved $\alpha$-hydroxylation to lactones by potassium hexamethyldisilazane and oxidodiperoxy(pyridine)(hexamethylphosphoric triamide)molybdenum.[4] Carissanol (**2**)[5] also has potential as a medicinal agent. This report describes the stereoselective synthesis of optically active (2*S*,3*S*)-2-benzyl-2-hydroxy-3-(3,4-methylenedioxybenzyl)-$\gamma$-butyrolactone (**3**) *via* the carissanol-type of lignan, (2*R*/*S*,3*S*,4*S*)-3-benzyl-2,3-dihydroxy-4-(3,4-methylenedioxybenzyl)tetrahydrofuran (**4**) (Fig.).

We decided to use (2*S*,4*S*)-ketone **5**[6] as the starting compound to synthesize $\gamma$-butyrolactone **3** (Scheme). It was assumed that the benzyl group could be stereoselectively introduced to the 3 position of this ketone **5**. We had two strategies for converting 2-hydroxymethyltetrahydrofuran to $\gamma$-butyrolactone after stereoselectively introducing the benzyl group and desilylation: one was direct conversion by pyridinium dichromate in refluxing acetic anhydride, *N*,*N*-dimethylformamide, and dichloromethane;[7] the other was conversion in several steps *via* a hemiacetal. With this latter strategy, transformation to 2-iodomethyltetrahydrofuran, reductive ring opening and oxidative cleavage of the resulting olefin would give a hemiacetal, and oxidation of this hemiacetal might give $\gamma$-butyrolactone.

We have reported that ketone **5** could be obtained from L-(+)-arabinose through 10 steps in a 5% overall yield.[6] The stereoselective benzylation to ketone **5** was achieved by a reaction with benzylmagnesium chloride in tetrahydrofuran at 5°C to give *trans*-dibenzyltetrahydrofuran **6** as a single isomer in a 99% conversion yield. A differential NOE experiment revealed the effect between 4-H and two benzylic protons at the 3 position. This fact indicated that the absolute configuration of the 3 position was *S*.

Desilylation of **6** by tetra-*n*-butylammonium fluoride[8] gave diol **7** in an 88% yield. Since direct conversion of this diol **7** to lactone **3** with pyridinium dichromate in refluxing acetic acid, *N*,*N*-dimethylformamide, and dichloromethane[7] was unsuccessful to recover diol **7**, we chose a conversion in several steps to lactone **3** *via* hemiacetal **4**. The selective iodination of diol **7** by treating with triphenylphosphine, imidazole, and iodine[9] in refluxing toluene was successful to give iodide **8** in a 74% yield. Reductive ring opening with zinc[10] in refluxing ethanol then transformed iodide **8** to olefin **9** in a 95% yield.

We first tried to prepare olefin **12** as a substrate for osmium and sodium periodate oxidation to give hemiacetal **4**. Selective protection of the primary hydroxy group of **9** by the benzoyl group was achieved by using benzoyl chloride and triethylamine to give benzoate **10b** in a 91% yield. Selective protection was also successful by treating with acetic anhydride in the presence of 4-dimethylaminopyridine to give acetate **10a** in an 89% yield. After triethylsilylation of the tertiary hydroxy groups of **10a** and **10b** with triethylsilyl trifluoromethanesulfonate[11] and 2,6-lutidine (**11a**, 71%; **11b**, 76%), deprotection of the primary hydroxy groups was attempted with potassium carbonate and diisobutylaluminum hydride, respectively, to convert to **12**. However, hydroxy silyl ether **12** was decomposed to diol **9** after purification. This result forced us to try the next step, oxidative cleavage of the olefin, without deprotecting the primary hydroxy group.

Although the yield from osmium oxidation[12] of acetate **11a** was low (50%, based on conversion), aldehyde **13** was obtained by subsequent sodium periodate oxidative cleavage in a 59% yield. Deprotection of both the primary and tertiary hydroxy groups could be achieved at the same time by treating with potassium carbonate in methanol to give (2*R*/*S*,3*S*,4*S*)-3-benzyl-2,3-dihydroxy-4-(3,4-methylenedioxybenzyl)tetrahydro-

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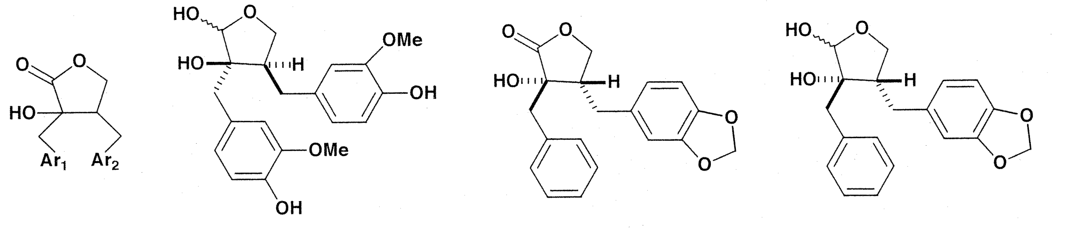

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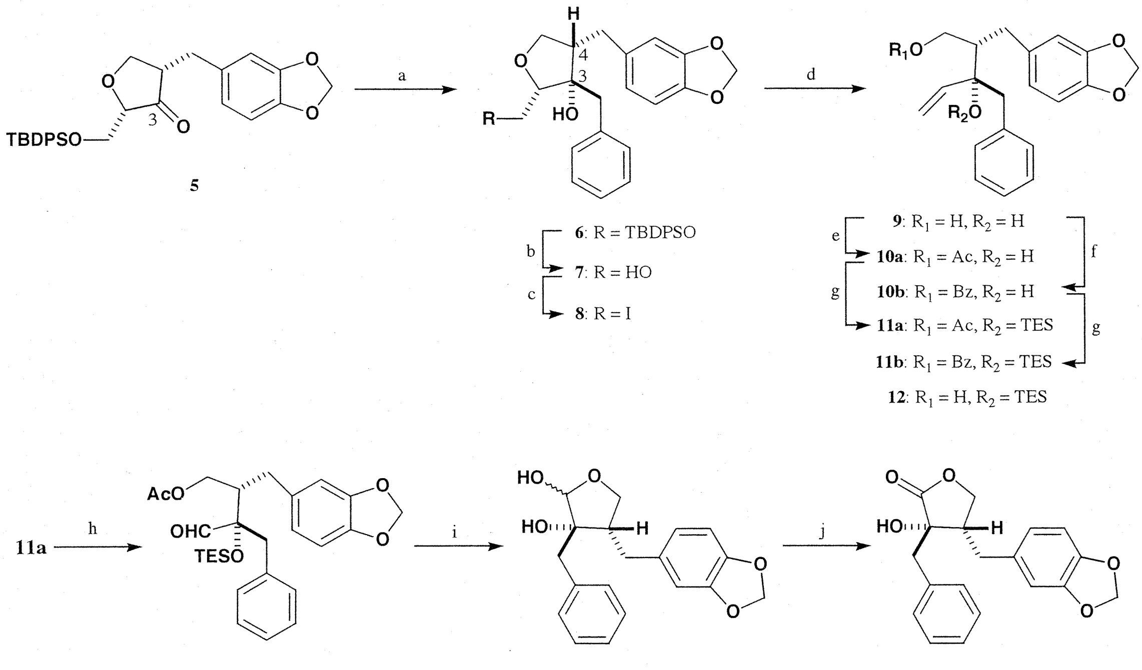
**Fig.** $\alpha,\beta$-Dibenzyl-$\alpha$-hydroxy-$\gamma$-butyrolactones and Carissanol-type of Lignans



13 4 3

**Scheme.** Synthesis of $\alpha,\beta$-Dibenzyl-$\alpha$-hydroxy-$\gamma$-butyrolactone **3** *via* Carissanol-type of Lignan **4** from Ketone **5**.

(a) $PhCH_2MgCl$, THF, 5°C; (b) *n*-$Bu_4NF$, THF, 0°C; (c) $I_2$, imidazole, $Ph_3P$, toluene, reflux; (d) Zn, EtOH, reflux; (e) $Ac_2O$, DMAP, r.t.; (f) BzCl, $Et_3N$, $CH_2Cl_2$, r.t.; (g) TESOTf, 2,6-lutidine, $CH_2Cl_2$, r.t.; (h) (1) $OsO_4$, NMO, acetone, *tert*-BuOH, $H_2O$, r.t.; (2) $NaIO_4$, EtOAc, $H_2O$, r.t.; (i) $K_2CO_3$, MeOH, r.t.; (j) $Ag_2CO_3$-celite, toluene, reflux

furan (**4**) as a diastereomeric mixture with a 3:2 ratio in an 88% yield. Finally, oxidation of hemiacetal **4** with silver carbonate-celite[13] in refluxing toluene gave (2*S*,3*S*)-2-benzyl-2-hydroxy-3-(3,4-methylenedioxybenzyl)-$\gamma$-butyrolactone (**3**) in a 51% yield.

The stereoselective synthesis of optically active *trans*-$\alpha,\beta$-dibenzyl-$\alpha$-hydroxy-$\gamma$-butyrolactone **3** *via* carissanol-type of lignan **4** was accomplished from L-(+)-arabinose through 20 steps in a 0.3% overall yield. This result also shows that ketone **5** was a useful intermediate for synthesizing lignans.

## Experimental

All melting point (mp) data are uncorrected. NMR data were measured by a JNM-EX400 spectrometer. EIMS and FABMS data were measured with Hitachi M-80B and JEOL HX-110 spectrometers, respectively, and optical rotation was evaluated with HORIBA SEPA-200 equipment. The silica gel used was Wakogel C-300 (Wako, 200–300 mesh), and preparative TLC was conducted with Merck silica gel 60 $F_{254}$ (0.5 mm thickness, 20 × 20 cm).

*(2S,3S,4S)-3-Benzyl-2-[(tert-butyldiphenylsilyl)oxy]methyl-3-hydroxy-4-(3,4-methylenedioxybenzyl)tetrahydrofuran* (**6**). To a solution of ketone **5** (0.96 g, 1.96 mmol) in tetrahydrofuran (5 ml) was added benzylmagnesium chloride (4 ml, 1 M in ether, 4 mmol) at 5°C in an $N_2$ gas. The reaction solution was stirred at 5°C for 30 min before addition of saturated aqueous $NH_4Cl$ solution. The organic solution was separated, washed with brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane = 1/9) gave alcohol **6** (0.88 g, 1.52 mmol, 78%) as colorless crystals, mp 104–105°C (diisopropyl ether). Ketone **5** (0.20 g, 0.41 mmol, 21%) was recovered. When based on a 79% conversion, the yield was 99%. $[\alpha]_D^{25} = -55.76$ (*c*0.52, $CHCl_3$). $^1$H-NMR $\delta_H(CDCl_3)$: 1.04 (9H, s, $(CH_3)_3CSi$), 2.35 (1H, m, 4-*H*), 2.64 (1H, dd, $J$ = 12.2, 12.2 Hz, 4-Ar$CH_2$), 2.82–2.85 (2H, m, 3-

Ar$CH_2$ and 4-Ar$CH_2$), 3.12 (1H, d, $J$=13.2 Hz, 3-Ar$CH_2$), 3.47 (1H, d, $J$=11.2 Hz, TBDPSO$CH_2$), 3.78–3.80 (3H, m, TBDPSO$CH_2$ and 5-*H*), 3.83 (1H, m, 2-*H*), 4.68 (1H, s, O*H*), 5.92 (2H, s, O$CH_2$O), 6.62 (1H, d, $J$=9.3 Hz, Ar*H*), 6.65 (1H, s, Ar*H*), 6.72 (1H, d, $J$=7.8 Hz, Ar*H*), 7.37–7.44 (3H, m, Ar*H*), 7.54 (1H, d, $J$=6.4 Hz, Ar*H*), 7.71 (1H, d, $J$=6.4 Hz, Ar*H*). $^{13}$C-NMR $\delta_C$($CDCl_3$): 19.03, 26.64, 31.77, 43.94, 50.61, 63.99, 71.89, 81.30, 82.98, 100.77, 108.20, 109.00, 121.34, 126.65, 127.77, 128.21, 129.86, 129.89, 130.35, 131.95, 132.40, 134.52, 135.49, 135.72, 137.23, 145.74, 147.60. EIMS (m/z): 580 ($M^+$, 1), 289 (28), 199 (38), 135 (100). *Anal.* Found: C, 74.50; H, 6.92. Calcd. for $C_{36}H_{40}O_5Si$: C, 74.45; H, 6.94%.

*(2S,3S,4S)-3-Benzyl-3-hydroxy-2-hydroxymethyl-4-(3,4-methylenedioxybenzyl)tetrahydrofuran* (**7**). To an ice-cooled solution of silyl ether **6** (0.88 g, 1.52 mmol) in tetrahydrofuran (20 ml) was added tetra-*n*-butylammonium fluoride (1.68 ml, 1 M in tetrahydrofuran, 1.68 mmol). The reaction solution was stirred in an ice bath for 30 min before addition of saturated aqueous $NN_4Cl$ solution and ethyl acetate. The organic solution was separated, washed with brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane=1/3 and 3/1) gave diol **7** (0.46 g, 1.34 mmol, 88%) as colorless crystals, mp 94–95°C (ethyl acetate/diisopropyl ether=1/9). $[\alpha]_D^{25}$ =−12.49 ($c$0.40, $CHCl_3$). $^1$H-NMR $\delta_H$($CDCl_3$): 2.36 (1H, m, 4-*H*), 2.55 (1H, dd, $J$=13.9, 10.5 Hz, 4-Ar$CH_2$), 2.65 (1H, m, $CH_2$O*H*), 2.77 (1H, dd, $J$=13.9, 4.2 Hz, 4-Ar$CH_2$), 2.83 (1H, d, $J$=13.7 Hz, 3-Ar$CH_2$), 3.04 (1H, d, $J$=13.7 Hz, 3-Ar$CH_2$), 3.39–3.45 (1H, m, $CH_2$OH), 3.68–3.80 (4H, m, $CH_2$OH, 2-*H*, 5-*H*), 3.94 (1H, s, 3-O*H*), 5.91 (2H, s, O$CH_2$O), 6.59 (1H, d, $J$=7.8 Hz, Ar*H*), 6.62 (1H, s, Ar*H*), 6.71 (1H, d, $J$=7.8 Hz, Ar*H*), 7.24–7.34 (5H, m, Ar*H*). $^{13}$C-NMR $\delta_C$($CDCl_3$): 31.83, 43.49, 50.06, 61.48, 72.00, 81.03, 83.37, 100.80, 108.24, 108.89, 121.28, 126.92, 128.40, 130.15, 134.06, 136.69, 145.83, 147.65. EIMS (m/z): 342 ($M^+$, 34), 233 (25), 189 (20), 161 (16), 135 (100). *Anal.* Found: C, 70.01; H, 6.45. Calcd. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48%.

*(2R,3S,4S)-3-Benzyl-3-hydroxy-2-iodomethyl-4-(3,4-methylenedioxybenzyl)tetrahydrofuran* (**8**). A reaction mixture of diol **7** (0.46 g, 1.34 mmol), triphenylphosphine (1.06 g, 4.04 mmol), imidazole (0.27 g, 3.97 mmol), and iodine (0.70 g, 2.76 mmol) in toluene (30 ml) was heated at reflux for 1 h. After cooling to room temperature, $H_2O$ was added. The organic solution was separated, washed with brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane=1/9 and 1/3) gave iodide **8** (0.45 g, 0.99 mmol, 74%) as a colorless oil. $[\alpha]_D^{25}$=−27.50 ($c$0.40, $CHCl_3$). $^1$H-NMR $\delta_H$($CDCl_3$): 2.44–2.50 (1H, m, 4-*H*), 2.44 (1H, d, $J$=9.3 Hz, 3-Ar$CH_2$), 2.62 (1H, d, $J$=9.3 Hz, 3-Ar$CH_2$), 2.92 (2H, d, $J$=4.9 Hz, I$CH_2$), 2.99 (1H, dd, $J$=10.5, 3.7 Hz, 4-Ar$CH_2$), 3.09 (1H, dd, $J$=10.5, 10.5 Hz, 4-Ar$CH_2$), 3.67 (1H, dd, $J$=8.8, 8.8 Hz, 5-*H*), 3.76 (1H, dd, $J$=8.8, 8.8 Hz, 5-*H*), 4.04 (1H, dd, $J$=9.3, 3.4 Hz, 2-*H*), 5.92 (2H, s, O$CH_2$O), 6.55 (1H, d, $J$=7.8 Hz, Ar*H*), 6.57 (1H, s, Ar*H*), 6.70 (1H, d, $J$=7.8 Hz, Ar*H*), 7.23–7.39 (5H, m, Ar*H*). $^{13}$C-NMR $\delta_C$($CDCl_3$): 3.03, 32.68, 43.45, 49.78, 70.85, 80.56, 86.18, 100.88, 108.31, 108.82, 121.28, 127.40, 128.80, 129.93, 133.38, 135.80, 145.98, 147.74. EIMS m/z (20 eV): 452 ($M^+$, 11), 135 (100), 91 (46). *Anal.* Found: C, 52.83; H, 4.89. Calcd. for $C_{20}H_{21}O_4I$: C, 53.11; H, 4.68%.

*(2S,3R)-3-Benzyl-2-(3,4-methylenedioxybenzyl)-4-penten-1,3-diol* (**9**). A reaction mixture of iodide **8** (0.25 g, 0.55 mmol) and zinc dust (0.14 g, 2.14 mmol) in ethanol (20 ml) was heated at reflux for 30 min. After filtration, the filtrate was concentrated. The residue was applied to silica gel column chromatography (ethyl acetate/hexane=1/3) to give diol **9** (0.17 g, 0.52 mmol, 95%) as a colorless oil. $[\alpha]_D^{25}$=+7.50 ($c$0.40, $CHCl_3$). $^1$H-NMR $\delta_H$($CDCl_3$): 1.81 (1H, m, 4-*H*), 2.34 (1H, br. s, O*H*), 2.62 (1H, s, O*H*), 2.78 (1H, dd, $J$=13.9, 11.5 Hz, 4-Ar$CH_2$), 2.94 (1H, d, $J$=13.2 Hz, 3-Ar$CH_2$), 3.06 (1H, d, $J$=13.2 Hz, 3-Ar$CH_2$), 3.08 (1H, dd, $J$=13.9, 3.7 Hz, 4-Ar$CH_2$), 3.55 (1H, dd, $J$=10.7, 3.8 Hz, $CH_2$OH), 3.75 (1H, br. d, $J$=10.7 Hz, $CH_2$OH), 5.15 (1H, d, $J$=10.7 Hz, $CH_2$=CH), 5.18 (1H, d, $J$=17.1 Hz, $CH_2$=CH), 5.92 (2H, s, O$CH_2$O), 5.99 (1H, dd, $J$=17.1, 10.7 Hz, $CH_2$=C*H*), 6.69–6.75 (3H, m, Ar*H*), 7.21–7.32 (5H, m, Ar*H*). $^{13}$C-NMR $\delta_C$($CDCl_3$): 31.04, 44.46, 48.57, 61.57, 78.62, 100.79, 108.21, 109.46, 113.70, 121.97, 126.73, 128.12, 130.77, 134.44, 136.13, 143.03, 145.80, 147.67. EIMS m/z (20 eV): 326 ($M^+$, 5), 217 (33), 135 (100). HRMS (EI) m/z ($M^+$): calcd. for $C_{20}H_{22}O_4$, 326.1516; found, 326.1516.

*(3R,4R)-5-Acetoxy-3-benzyl-4-(3,4-methylenedioxybenzyl)-1-penten-3-ol* (**10a**). A reaction solution of diol **9** (0.29 g, 0.89 mmol) and 4-dimethylaminopyridine (10 mg, 0.082 mmol) in acetic anhydride (10 ml) was allowed to stand at room temperature for 1 h before addition of ice. After 2 h at room temperature, ethyl acetate was added. The organic solution was separated, washed with a saturated aqueous $NaHCO_3$ solution and brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane=1/3) gave acetate **10a** (0.29 g, 0.79 mmol, 89%) as a colorless oil. $[\alpha]_D^{25}$=+13.33 ($c$0.30, $CHCl_3$). $^1$H-NMR $\delta_H$($CDCl_3$): 2.02 (3H, s, $CH_3$C=O), 2.10 (1H, m, 4-*H*), 2.51 (1H, dd, $J$=14.2, 10.7 Hz, 4-Ar$CH_2$), 2.97 (2H, s, 3-Ar$CH_2$), 3.11 (1H, dd, $J$=14.2, 3.9 Hz, 4-Ar$CH_2$), 4.11 (2H, d, $J$=4.4 Hz, AcO$CH_2$), 5.09 (1H, dd, $J$=17.2, 1.5 Hz, $CH_2$=CH), 5.13 (1H, dd, $J$=10.7, 1.5 Hz, $CH_2$=CH), 5.92 (2H, s, O$CH_2$O), 5.97 (1H, dd, $J$=17.2, 10.7 Hz, $CH_2$=C*H*), 6.62 (1H, dd, $J$=7.8, 1.5 Hz, Ar*H*), 6.68 (1H, d, $J$=1.5 Hz, Ar*H*), 6.72 (1H, d, $J$=7.8 Hz, Ar*H*), 7.18–7.20 (2H, m, Ar*H*), 7.22–7.31 (3H, m, Ar*H*). $^{13}$C-NMR $\delta_C$($CDCl_3$): 20.94, 32.34, 45.42, 48.08, 63.69, 76.92, 100.80, 108.20, 109.33, 114.23, 121.88, 126.79, 128.11, 130.82, 134.33, 135.95, 141.60, 145.81, 147.67, 170.64. EIMS m/z (20 eV): 368 ($M^+$, 5), 217 (28), 135 (100). HRMS (EI) m/z ($M^+$): calcd. for $C_{22}H_{24}O_5$, 368.1622; found, 368.1629.

*(3R,4R)-5-Benzoyloxy-3-benzyl-4-(3,4-methylenedioxybenzyl)-1-penten-3-ol* (**10b**). To an ice-cooled solution of diol **9** (0.15 g, 0.46 mmol) and triethylamine (71 $\mu$l, 0.51 mmol) in dichloromethane (10 ml) was added benzoyl chloride (59 $\mu$l, 0.51 mmol). The reaction solution was stirred at room temperature for 2 h before addition of a saturated aqueous $NaHCO_3$ solution. The organic solution was separated, washed with brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane=1/9 and 1/5) gave benzoate **10b** (0.18 g, 0.42 mmol, 91%) as a colorless oil. $[\alpha]^{25}_{D}=+40.00$ (c0.40, $CHCl_3$). $^1$H-NMR $\delta_H(CDCl_3)$: 2.25 (1H, m, 4-*H*), 2.65 (1H, dd, $J=14.1$, 11.0 Hz, 4-Ar$CH_2$), 3.05 (2H, s, 3-Ar$CH_2$), 3.20 (1H, dd, $J=14.1$, 3.4 Hz, 4-Ar$CH_2$), 4.34 (1H, dd, $J=11.7$, 4.4 Hz, $CH_2$OBz), 4.40 (1H, dd, $J=11.7$, 3.9 Hz, $CH_2$OBz), 5.11 (1H, d, $J=17.6$ Hz, $CH_2$=CH), 5.16 (1H, d, $J=10.8$ Hz, $CH_2$=CH), 5.87 (2H, s, O$CH_2$O), 6.06 (1H, dd, $J=17.6$, 10.8 Hz, $CH_2$=C*H*), 6.63–6.74 (3H, m, Ar*H*), 7.18–7.31 (5H, m, Ar*H*), 7.42–7.46 (2H, m, Ar*H*), 7.55–7.58 (1H, m, Ar*H*), 7.95–7.97 (2H, m, Ar*H*). $^{13}$C-NMR $\delta_C(CDCl_3)$: 32.58, 45.59, 48.75, 64.01, 76.88, 100.76, 108.24, 109.33, 114.47, 121.92, 126.84, 128.15, 128.44, 129.47, 129.86, 130.04, 130.84, 133.01, 134.27, 135.87, 141.64, 145.81, 147.69, 166.28. EIMS m/z (20 eV): 430 ($M^+$, 2), 324 (20), 233 (20), 217 (19), 189 (14), 161 (25), 135 (100), 105 (41), 91 (49). HRMS (EI) m/z ($M^+$): calcd. for $C_{27}H_{26}O_5$, 430.1778; found, 430.1772.

*(3R,4S)-5-Acetoxy-3-benzyl-4-(3,4-methylenedioxybenzyl)-3-[(triethylsilyl)oxy]-1-pentene* (**11a**). To a solution of alcohol **10a** (0.15 g, 0.41 mmol) and 2,6-lutidine (0.3 ml, 2.58 mmol) in dichloromethane (6 ml) was added triethylsilyl trifluoromethanesulfonate (0.3 ml, 1.33 mmol). The reaction solution was stirred at room temperature for 2 h before addition of saturated aqueous $NaHCO_3$ solution and dichloromethane. The organic solution was separated, washed with a 5% aqueous $Cu(NO_3)_2$ solution and brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane=1/9) gave silyl ether **11a** (0.14 g, 0.29 mmol, 71%) as a colorless oil. $[\alpha]^{25}_{D}=+18.75$ (c0.64, $CHCl_3$). $^1$H-NMR $\delta_H(CDCl_3)$: 0.67 (6H, q, $J=7.8$ Hz, $(CH_3CH_2)_3$Si), 0.97 (9H, t, $J=7.8$ Hz, $(CH_3CH_2)_3$Si), 1.80 (3H, s, $CH_3$C=O), 2.05–2.14 (1H, m, 4-*H*), 2.50 (1H, dd, $J=11.2$, 11.2 Hz, 4-Ar$CH_2$), 2.99 (1H, d, $J=13.7$ Hz, 3-Ar$CH_2$), 3.12–3.22 (2H, m, 3-Ar$CH_2$ and 4-Ar$CH_2$), 3.99 (2H, d, $J=4.4$ Hz, $CH_2$OAc), 5.19 (1H, d, $J=10.7$ Hz, $CH_2$=CH), 5.30 (1H, d, $J=17.6$ Hz, $CH_2$=CH), 5.90 (2H, s, O$CH_2$O), 5.96 (1H, dd, $J=17.6$, 10.7 Hz, $CH_2$=C*H*), 6.58 (1H, d, $J=7.8$ Hz, Ar*H*), 6.61 (1H, s, Ar*H*), 6.69 (1H, d, $J=7.8$ Hz, Ar*H*), 7.21–7.39 (5H, m, Ar*H*). $^{13}$C-NMR $\delta_C(CDCl_3)$: 7.15, 7.30, 20.76, 33.39, 44.00, 46.02, 63.85, 79.50, 100.73, 108.08, 109.21, 113.69, 121.78, 126.51, 128.00, 130.94, 134.64, 137.02, 141.69, 145.64, 147.54, 170.75. FABMS m/z: 505 (M+$Na^+$, 100), 331 (19), 261 (18), 135 (75), 87 (25). HRMS (FAB) m/z (M+$Na^+$): calcd. for $C_{28}H_{38}O_5$SiNa, 505.2386; found, 505.2391.

*(3R,4S)-5-Benzoyloxy-3-benzyl-4-(3,4-methylenedioxybenzyl)-3-[(triethylsilyl)oxy]-1-pentene* (**11b**). To a solution of alcohol **10b** (0.16 g, 0.37 mmol) and 2,6-lutidine (0.12 ml, 1.03 mmol) in dichloromethane (10 ml) was added triethylsilyl trifluoromethanesulfonate (0.17 ml, 0.75 mmol). The reaction solution was stirred at room temperature for 2 h before addition of a saturated aqueous $NaHCO_3$ solution and dichloromethane. The organic solution was separated, washed with a 5% aqueous $Cu(NO_3)_2$ solution and brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane=1/9) gave silyl ether **11b** (0.15 g, 0.28 mmol, 76%) as a colorless oil. $[\alpha]^{25}_{D}=+15.00$ (c0.40, $CHCl_3$). $^1$H-NMR $\delta_H(CDCl_3)$: 0.68 (6H, q, $J=7.8$ Hz, $(CH_3CH_2)_3$Si), 0.98 (9H, t, $J=7.8$ Hz, $(CH_3CH_2)_3$Si), 2.24 (1H, m, 4-*H*), 2.62 (1H, dd, $J=13.7$, 11.2 Hz, 4-Ar$CH_2$), 3.07 (1H, d, $J=13.4$ Hz, 3-Ar$CH_2$), 3.21 (1H, d, $J=13.4$ Hz, 3-Ar$CH_2$), 3.26 (1H, dd, $J=13.7$, 2.8 Hz, 4-Ar$CH_2$), 4.25 (1H, dd, $J=11.6$, 5.0 Hz, $CH_2$OBz), 4.30 (1H, dd, $J=11.6$, 4.2 Hz, $CH_2$OBz), 5.21 (1H, d, $J=10.7$ Hz, $CH_2$=CH), 5.33 (1H, d, $J=17.6$ Hz, $CH_2$=CH), 5.79 (2H, s, O$CH_2$O), 6.03 (1H, dd, $J=17.6$, 10.7 Hz, $CH_2$=C*H*), 6.58–6.68 (3H, m, Ar*H*), 7.25–7.36 (7H, m, Ar*H*), 7.47–7.50 (1H, m, Ar*H*), 7.72–7.74 (2H, m, Ar*H*). $^{13}$C-NMR $\delta_C(CDCl_3)$: 7.15, 7.31, 33.92, 43.94, 46.55, 64.77, 79.52, 100.65, 108.15, 109.15, 114.10, 121.71, 126.56, 128.04, 129.42, 130.24, 130.99, 132.55, 134.61, 136.96, 141.66, 145.64, 147.58, 166.25. FABMS m/z: 567 (M+$Na^+$, 8), 543 (10), 331 (39), 291 (16), 261 (26), 207 (20), 173 (11), 135 (100), 105 (39), 87 (35). HRMS (FAB) m/z (M+$Na^+$): calcd. for $C_{33}H_{40}O_5$SiNa, 567.2543; found, 567.2544.

*(2S,3S)-4-Acetoxy-2-benzyl-3-(3,4-methylenedioxybenzyl)-2-[(triethylsilyl)oxy]butanal* (**13**). A reaction mixture of olefin **11a** (0.14 g, 0.29 mmol), 4-methylmorpholine *N*-oxide (45 mg, 0.38 mmol) and osmium tetroxide (2% $H_2O$ solution, 5 ml) in acetone, *tert*-butyl alcohol and $H_2O$ (4/1/1, 10 ml) was stirred at room temperature for 24 h in an $N_2$ gas in the dark. After addition of $NaHSO_3$ (5 g) in $H_2O$ (20 ml), the mixture was filtered, and the filtrate was concentrated. The residue was dissolved in ethyl acetate and $H_2O$. The organic solution was separated, washed with brine, and dried ($Na_2SO_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane=1/3) gave a diol (36 mg, 0.070 mmol, 24%) as a colorless oil. Olefin **11a** (0.07 g, 0.15 mmol, 52%) was recovered. When based on a 48% conversion, the yield was 50%.

The reaction mixture of the diol (15 mg, 0.029 mmol) and sodium periodate (40 g, 0.19 mmol) in ethyl acetate (10 ml) and $H_2O$ (160 ml) was stirred at room temperature for 2 h. The organic solution was separated, washed with brine, and dried ($Na_2SO_4$). Concentration followed by silica gel TLC (ethyl acetate/hexane=1/3) gave aldehyde **13** (8 mg, 0.017 mmol, 59%) as a colorless oil. $[\alpha]^{25}_{D}=+60.86$ (c0.46, $CHCl_3$). $^1$H-NMR $\delta_H(CDCl_3)$: 0.59 (6H, m, $(CH_3CH_2)_3$Si), 0.93 (9H, t, $J=7.8$ Hz, $(CH_3CH_2)_3$Si), 1.90 (3H, s, $CH_3$C=O), 2.40–2.44 (1H, m, 3-*H*), 2.46 (1H, dd, $J=11.2$, 11.2

Hz, 3-ArC$H_2$), 3.07 (1H, d, $J$=14.3 Hz, 2-ArC$H_2$), 3.18 (1H, br. d, $J$=11.2 Hz, 3-ArC$H_2$), 3.20 (1H, d, $J$=14.3 Hz, 2-ArC$H_2$), 3.94 (2H, d, $J$=5.4 Hz, C$H_2$OAc), 5.92 (2H, s, OC$H_2$O), 6.57–6.59 (2H, m, Ar$H$), 6.72 (1H, d, $J$=7.8 Hz, Ar$H$), 7.21–7.33 (5H, m, Ar$H$), 9.64 (1H, s, C$H$O). $^{13}$C-NMR $\delta_C$(CDCl$_3$): 6.90, 7.29, 20.66, 31.88, 42.21, 44.48, 62.81, 83.90, 100.90, 108.33, 109.01, 121.82, 127.01, 127.10, 128.39, 128.50, 130.58, 130.69, 133.00, 135.06, 146.12, 147.82, 171.14, 202.47. FABMS m/z: 507 (M+Na$^+$, 16), 483 (11), 395 (42), 135 (100), 87 (26). HRMS (FAB) m/z (M+Na$^+$): calcd. for $C_{27}H_{36}O_6SiNa$, 507.2179; found, 507.2178.

*(2R/S,3S,4S)-3-Benzyl-2,3-dihydroxy-4-(3,4-methylenedioxybenzyl)tetrahydrofuran* (**4**). A reaction mixture of acetate **13** (8 mg, 0.017 mmol) and potassium carbonate (20 mg, 0.14 mmol) in methanol (4 ml) was stirred at room temperature for 30 min. After addition of a saturated aqueous $NH_4Cl$ solution, the mixture was concentrated. The residue was dissolved in ethyl acetate and $H_2O$. The organic solution was separated, washed with brine, and dried ($Na_2SO_4$). Concentration followed by silica gel TLC (ethyl acetate/hexane=1/2) gave hemiacetal **4** (5 mg, 0.015 mmol, 88%). $[\alpha]_D^{25}=-36.36$ ($c$0.39, CHCl$_3$). $^1$H-NMR $\delta_H$(CDCl$_3$): 2.32 (1H, m, 4-$H$), 2.51 (0.4H, dd, $J$=13.7, 10.7 Hz, 4-ArC$H_2$), 2.65 (1H, s, O$H$), 2.66 (0.4H, dd, $J$=13.7, 4.4 Hz, 4-ArC$H_2$), 2.72 (0.6H, dd, $J$=13.7, 4.4 Hz, 4-ArC$H_2$), 2.81 (0.6H, dd, $J$=13.7, 10.7 Hz, 4-ArC$H_2$), 2.89 (1.2H, d, $J$=8.3 Hz, 3-ArC$H_2$), 2.91 (0.4H, d, $J$=13.7 Hz, 3-ArC$H_2$), 3.14 (0.4H, d, $J$=13.7 Hz, 3-Ar$H$), 3.72–3.80 (1.6H, m, 5-$H$), 4.07 (0.4H, dd, $J$=8.3, 8.3 Hz, 5-$H$), 4.86 (0.4H, s, 2-$H$), 5.22 (0.6H, s, 2-$H$), 5.92 (1.2H, s, OC$H_2$O), 5.93 (0.8H, s, OC$H_2$O), 6.55–6.59 (1H, m, Ar$H$), 6.65–6.74 (2H, m, Ar$H$), 7.26–7.36 (5H, m, Ar$H$). $^{13}$C-NMR $\delta_C$(CDCl$_3$): 31.98, 32.48, 38.96, 43.55, 45.61, 48.02, 70.90, 72.85, 78.79, 81.99, 100.84, 100.96, 103.08, 108.26, 108.93, 109.01, 121.37, 121.43, 126.95, 127.06, 128.52, 128.60, 130.26, 130.44, 133.75, 135.92, 145.90, 147.68, 147.72. EIMS m/z (20 eV): 328 (M$^+$, 14), 298 (16), 161 (24), 148 (34), 135 (100), 91 (28). HRMS (EI) m/z (M$^+$): calcd. for $C_{19}H_{20}O_5$, 328.1309; found, 328.1306.

*(2S,3S)-2-Benzyl-2-hydroxy-3-(3,4-methylenedioxybenzyl)*-γ-butyrolactone (**3**). A reaction mixture of hemiacetal **4** (4 mg, 0.012 mmol) and $Ag_2CO_3$-celite (20 mg, containing 0.02 mmol of silver salt) in toluene (10 ml) was heated at reflux for 1 h. After filtration, the filtrate was concentrated. The residue was applied to silica gel TLC (ethyl acetate/benzene=1/9) to give γ-butyrolactone **3** (2 mg, 0.0061 mmol, 51%) as a colorless oil. $[\alpha]_D^{25}=-32.46$ ($c$0.15, CHCl$_3$). $^1$H-NMR $\delta_H$(CDCl$_3$): 2.65 (1H, dd, $J$=14.0, 6.8 Hz, 3-ArC$H_2$), 2.77 (1H, dd, $J$=14.0, 8.3 Hz, 3-ArC$H_2$), 3.25 (1H, m, 3-$H$), 3.56 (2H, s, 2-ArC$H_2$), 4.23–4.28 (2H, m, 4-$H$), 5.94 (2H, s, OC$H_2$O), 6.52–6.54 (2H, m, Ar$H$), 6.71 (1H, d, $J$=7.3 Hz, Ar$H$), 7.04–7.06 (2H, m, Ar$H$), 7.25–7.31 (3H, m, Ar$H$), 7.89 (1H, s, O$H$). $^{13}$C-NMR $\delta_C$(CDCl$_3$): 29.69, 34.78, 51.26, 51.28, 63.71, 100.99, 108.42, 109.11, 121.91, 127.16, 128.67, 129.60, 129.65, 131.33, 132.89, 160.37. EIMS m/z (20 eV): 326 (M$^+$, 32), 189 (69), 135 (100). HRMS (EI) m/z (M$^+$): calcd. for $C_{19}H_{18}O_5$, 326.1153; found, 326.1161.

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