Synthesis of Optically Active Olivil Type of Lignan from L-Arginose Using threeo-Selective Aldol Condensation as a Key Reaction

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Received April 10, 2000; Accepted June 20, 2000

The threeo-selective aldol condensation of (3R, 4S)-3-hydroxy-5-trityloxy-4-pentanolido, which was prepared from l-arabinose, with piperonal was applied to the stereoselective synthesis of the olivil type of lignan, (2R, 3R, 4R)-4-benzyl-4-hydroxy-3-hydroxymethyl-2-(3,4-methylenedioxyphenyl)tetrahydrofuran.

Key words: lignan; tetrahydrofuran lignan; olivil; threeo selective aldol condensation

Olivil (I) (Fig.), which is a 4-oxidized 2-aryl-4-benzyl-3-hydroxymethyltetrahydrofuran type of lignan, was isolated from the bark of Fraxinus mandschurica Rupr. var japonica Maxim (oleaceae), which was used as a diuretic, an antipyretic, analgesic, and an antirheumau agent and expected to provide new classes of chemotherapeutic agents.1) As for the stereoselective synthesis of optically active 4-oxidized 2-aryl-4-benzyl-3-hydroxymethyltetrahydrofuran, synthesis of 2,3-trans-olivil type of lignan from D-xylene was done recently.2) As a next experiment, synthesis of the 2,3-cis olivil type of lignan 2 was tried.

The discovery of erythro or threeo selective aldol condensation of γ-butyrolactone with methoxybenzaldehydes3) has provided us the stimulus for search further erythro or threeo selective aldol condensation. In our effort, it was found that the aldol condensation of 4-pentanolido 3, which was prepared from l-arabinose, with piperonal gave predominantly threeo aldol product 4 (erythro:threeo = 1:9, Scheme 1). This result could be applied to synthesis of the 2,3-cis olivil type of lignan 2.

The stereoselective synthetic plan, in which the configuration at the benzylic position of aldol product 4 could be kept through all the steps, is shown in Scheme 2. The benzylic position of aldol product 4 would be transformed to the C2 carbon of 2,3-cis-olivil type of lignan 5. The 2,3-cis-olivil type of lignan 5 might be obtained from ketone 6 through stereoselective benzylation. This ketone 6 could be obtained from tetrahydrofuran derivative 7 by halogenation followed by radical elimination while retaining intact the benzyllic stereochemistry. This hemiacetal 8 would be obtained from threeo aldol product 4.

This report describes the stereoselective synthesis of (2R, 3R, 4R)-4-benzyl-4-hydroxy-3-hydroxymethyl-2-(3,4-methylenedioxyphenyl)tetrahydrofuran 2 using threeo selective aldol condensation as a key reaction. This is a first report of a stereoselective synthesis of an optically active 2,3-cis olivil type of lignan.

Results and Discussion

The 4-pentanolido 3 was prepared from l-arabinose through 4 steps in 46% overall yield by a modification of Sharma and Marquez's method.4)
Synthesis of Olivil Type of Lignan

Scheme 2. Retrosynthetic Analysis of Olivil Type of Lignan 5.

Scheme 3. Synthesis of Olivil Type of Lignan 2 (1). (a) LDA, piperonal, THF, −75°C, 1 h (56% yield). (b) MOMCl, (iso-Pr)2EtN, CH2Cl2, r.t., 3 h (84% yield). (c) LiAlH4, THF, r.t., 30 min; (2) PivCl, pyridine, r.t., 1 h (88% yield, 2 steps). (d) PPTS, MeOH, reflux, 3 h (76% yield). (e) NaOEt, MeOH, r.t., 3 h (85% yield). (f) PPTS, tert-butyl alcohol, reflux, 2 h (82% yield).

The aldol condensation of this 4-pentanolide 3 with piperonal using lithium diisopropylamide gave selectively three aldol product 4 in 56% yield. The erythro isomer was produced in only 6% yield. The coupling constant between benzylic proton and 2-H of three isomer was 8.7 Hz. On the other hand, that of erythro isomer was 4.4 Hz.5 The stereosemistry at the 2 position of aldol product 4 was identified by a different NOE experiment. The fact that the NOE was observed between 2-H and 4-H confirmed that the configuration at 2 position was R.

Methoxymethyl ether was selected for the protection of two hydroxy groups of aldol product 4. The bis(methoxymethyl) ether 9 was obtained by treatment of 4 with chloromethyl methyl ether and N-ethyl diisopropylamine in 84% yield. When the aldol product 4 was converted to bis(tert-butyldimethylsilyl) ether, the desilylation occurred in the next reduction process. After lithium aluminum hydride reduction of 9, the primary hydroxy group of the resulting diol was protected as a pivaloyl chloride in pyridine in 88% yield. The detritylation of 10 was done by treatment with pyridinium p-toluenesulfonate in refluxing methanol to give glycol 11 in 76% yield. The sodium periodate oxidation of 11 (85%) followed by selective deprotection of methoxymethyl ether at the benzylic position using pyridinium p-toluenesulfonate in refluxing tert-butyl alcohol afforded hemiacetal 13 as a single isomer in 82% yield. The existence of NOE between 3-H and two methylene protons of pivaloyloxyethyl group at 4 position clarified the epimerization at 3 position to S. Because of no NOE between 2-H and 4-H, the configuration of 2 position was assumed to be R (Scheme 3).

Next stage was reduction of hemiacetal 13 to
tetrahydrofuran derivative 14. The conversion of hemiacetal 13 to phenylthiocetacetal was low yield (9% yield), however, the transformation to chloride using oxalyl chloride proceeded well. Without purification, the chloride was treated with tri-n-butyltin hydride and 2,2'-azobisisobutyronitrile to give 2,3-cis-tetrahydrofuran derivative 14 in 71% yield from hemiacetal 13. After deprotection of pivaloyl ester 14 by diisobutylaluminum hydride reduction (86%), the resulting methoxymethyl ether was treated with HCl to give a crude diol. Without purification, the crude diol was converted to tert-butylidiphenylsilyl ether 16 by using tert-butyldiphenylsilyl chloride and imidazole in 67% yield. In the process of demethoxymethyl ether by HCl, partial epimerization at the benzylic 2 position occurred, giving (2S)-16 in 6% yield. The chemical shift of 3- $H$ of (2S)-16 resonated at higher field (2.10 ppm) than that of (2R)-16 (2.60-2.68 ppm), because of the shielding effect of the aromatic ring of 2 position.

After Swern oxidation of (2R)-16 (86% yield), the resulting ketone 17 was stereoselectively benzylated using benzyllmagnesium chloride to give benzyltetrahydrofuran 18 as a single isomer in 58% yield. The existence of NOE between two benzylic protons at 4 position and 3- $H$ showed that the configuration at 4 position was $R$. Finally, desilylation of 18 by treatment with tetra-$n$-butylammonium fluoride gave the olivyl type of lignan 2 in 67% yield (Scheme 4).

(2R, 3R, 4R)-4-Benzyl-4-hydroxy-3-hydroxymethyl-2-(3,4-methylenedioxyphenyl)tetrahydrofuran 2, which was an olivyl type of lignan, was stereoselectively synthesized from L-arabinose through 19 steps in 1.4% overall yield. This result showed a stereoselective model synthesis of optically active stereoisomer of oliv using stereorecognizing aldol condensation as a key reaction.

**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 values were evaluated with a HORIBA SEPA-200. The silica gel used was Wako gel C-300 (Wako, 200–300 mesh), and preparative TLC was done with Merck silica gel 60 F$_{254}$ (0.5 mm thickness, 20 × 20 cm).

(3R, 4S)-3-Hydroxy-3-trityloxy-4-pentanolide (3). After a reaction mixture of L-arabinose (40.0 g, 0.27 mol), 4-dimethylaminopyridine (0.20 g, 0.0016 mol), and trityl chloride (75.3 g, 0.27 mol) in pyridine (50 mL) was stirred at 60°C for 1 h, H$_2$O and ethyl acetate were added. The organic solution was separated, washed with sat. aq. CuSO$_4$ soln., sat. aq. NaHCO$_3$ soln., and brine, and dried (Na$_2$SO$_4$). Concentration followed by silica gel column chromatography (ethyl acetate/hexane = 1/1) gave trityloxyethyl hemiacetal (70.6 g, 0.18 mol, 67%) as a colorless oil. To a mixture of the trityloxyethyl hemiacetal (57.2 g, 0.15 mol) and NaHCO$_3$ (480 g, 5.71 mol) in 10% H$_2$O/ethanol (500 mL) was added 2 m bromine solu-
tion in 10% H₂O/ethanol (550 ml). The resulting reaction mixture was stirred at room temperature for 16 h before addition of Na₂S₂O₅. After the mixture was filtered, the filtrate was concentrated, and then the residue was dissolved in ethyl acetate and H₂O. The organic solution was separated, washed with brine, and dried (Na₂SO₄). Concentration followed by silica gel column chromatography (ethyl acetate/hexane = 1/1) gave (2R, 3R, 4S)-2,3-dihydroxy-5-trityloxy-4-pentanolide (49.1 g, 0.13 mol, 87%) as a colorless oil. [α]D²⁰ = −20.0 (c 0.95, CHCl₃). NMR δ₀ (CDCl₃): 3.32 (1H, dd, J = 10.9, 4.4 Hz), 3.32–3.35 (1H, m), 3.49 (1H, dd, J = 10.9, 3.2 Hz, 4.05 (1H, br, s), 4.23 (1H, ddd, J = 8.3, 4.4, 3.2 Hz), 4.31 (1H, ddd, J = 8.3, 8.3, 3.4 Hz), 4.43 (1H, br, d, J = 8.3 Hz), 7.19–7.30 (11H, m), 7.40–7.42 (4H, m). To a solution of (2R, 3R, 4S)-2,3-dihydroxy-5-trityloxy-4-pentanolide (39.4 g, 0.10 mol), pyridine (12.5 ml, 0.15 mol), and 4-dimethylaminopyridine (2.5 g, 0.020 mol) in acetonitrile (200 ml) was added phenyl chloroformate (19.9 ml, 0.14 mol) in acetonitrile (50 ml) at 0°C. After stirring at 0°C for 1 h, ethyl acetate and H₂O were added. The organic solution was separated, washed with sat. aq. Na₂CO₃ soln., sat. aq. NaHCO₃ soln. and brine, and dried (Na₂SO₄). Concentration followed by silica gel column chromatography (ethyl acetate/hexane = 1/4) gave (2R, 3S, 4S)-3-hydroxy-2-(phenoxycarbonyloxy)trityloxy-4-pentanolide (45.2 g, 0.086 mol, 86%) as a colorless oil. [α]D²⁰ = −25.2 (c 0.95, CHCl₃). NMR δ₀ (CDCl₃): 2.99 (1H, s), 3.35 (1H, d, J = 10.3 Hz), 3.62 (1H, d, J = 10.3 Hz), 4.43 (1H, m), 4.76 (1H, m), 6.08 (1H, d, J = 6.8 Hz), 7.15 (2H, d, J = 7.8 Hz), 7.25–7.34 (10H, m), 7.46–7.51 (8H, m). A reaction solution of (2R, 3S, 4S)-3-hydroxy-2-(phenoxycarbonyloxy)trityloxy-4-pentanolide (45.2 g, 0.086 mol), tri-n-butylhydride (28.5 ml, 0.11 mol), and 2,2’-azobisisobutyronitrile (1.76 g, 0.011 mol) in benzene (300 ml) was heated under reflux for 1 h. Concentration of the solvent followed by silica gel column chromatography (ethyl acetate/hexane = 1/4) gave 4-pentanolide (3 (29.6 g, 0.079 mol, 92%) as colorless crystals, mp 132–133°C (diisopropyl ether/methanol = 9/1). [α]D²⁰ = −30.8 (c 1.72, CHCl₃). NMR δ₀ (CDCl₃): 2.30 (1H, d, J = 4.4 Hz), 2.49 (1H, dd, J = 18.1, 2.4 Hz), 3.04 (1H, dd, J = 18.1, 6.8 Hz), 3.20 (1H, dd, J = 10.7, 2.9 Hz), 3.52 (1H, dd, J = 10.7, 3.9 Hz), 4.00–4.42 (2H, m), 7.22–7.32 (11H, m), 7.37–7.39 (4H, m). NMR δ₀ (CDCl₃): 38.5, 63.2, 69.9, 86.4, 87.4, 127.3, 128.0, 128.5, 143.2, 175.7. IR νmax (CHCl₃): 3609, 3088–2876, 1779, 1491, 1449, 1227, 1186, 1154, 1102, 1092 cm⁻¹. EIMS m/z (20 eV): 374 (M⁺), 243 (100), 183 (91), 105 (83). Anal. Found: C, 76.91; H, 6.02. Calcd. for C₅₉H₄₂O₄: C, 76.99; H, 5.92%.

(2R, 3R, 4S)-3-Hydroxy-2-[(1R)-1-hydroxy-1-(3,4-methylenedioxyphenyl)methyl]-5-trityloxy-4-pentanolide (9). A reaction mixture of three-diol 4 (26.3 g, 0.050 mol), N-ethylisopropylamine (280 ml, 1.61 mol), and chloromethyl methyl ether (63.6 ml, 0.84 mol) in dichloromethane (50 ml) was stirred at room temperature for 3 h. After additions of dichloromethane and H₂O, the organic solution was separated, washed with 1 M aq. HCl soln., sat. aq. NaHCO₃ soln., and brine, and dried
(Na₂SO₄). Concentration followed by silica gel column chromatography (ethyl acetate/hexane = 1/3) gave bis(methoxymethyl) ether 9 (25.5 g, 0.042 mol, 84%) as a colorless oil. [α]D = +14.5 (c 3.04, CHCl₃). NMR δH (CDCl₃): 2.91 (1H, dd, J = 10.7, 5.4 Hz), 3.10–3.15 (2H, m), 3.13 (3H, s), 3.34 (3H, s), 4.24 (1H, m), 4.29 (1H, m), 4.42 (2H, s), 4.57 (2H, s), 5.10 (1H, d, J = 4.4 Hz), 5.85 (2H, s), 6.64 (1H, d, J = 8.1 Hz), 6.74 (1H, d, J = 8.1 Hz), 6.85 (1H, s), 7.21–7.30 (11H, m), 7.36–7.38 (4H, m). NMR δC (CDCl₃): 54.2, 55.5, 56.0, 62.7, 74.6, 74.9, 82.7, 94.1, 95.7, 101.0, 107.9, 108.2, 121.1, 127.1, 127.3, 127.9, 128.0, 128.5, 128.6, 131.1, 143.2, 143.4, 147.5, 147.8, 173.4. IR νmax (CHCl₃): 2934, 2896, 1775, 1505, 1489, 1449, 1254, 1242, 1221, 1154, 1103, 1042 cm⁻¹. EIMS m/z (20 eV): 612 (M⁺, 2), 243 (100), 195 (47). Anal. Found: C, 70.15; H, 5.91. Calcd. for C₃₅H₃₆O₇C, C, 70.57; H, 5.92%.

(2S, 3R, 4R, 5R)-3,5-Bis(methoxymethoxy)-5-(3,4-methylenedioxyphenyl)-4-pivaloyloxymethyl-1-trityloxy-2-pentanol (10). To an ice-cooled suspension of lithium aluminum hydride (1.05 g, 0.028 mol) in tetrahydrofuran (20 ml) was added a solution of lactone 9 (15.0 g, 0.024 mol) in tetrahydrofuran (50 ml). The reaction mixture was stirred at room temperature for 30 min, and then sat. aq. MgSO₄ soln. and K₂CO₃ were added. After this was stirred at room temperature for 1 h, the mixture was filtered. The filtrate was concentrated to give the crude diol. To a solution of the crude diol in pyridine (50 ml) was added pivaloyl chloride (3.66 ml, 0.030 mol). After this was stirred at room temperature for 1 h, ethyl acetate and H₂O were added. The organic solution was separated, washed with sat. aq. CuSO₄ soln., sat. aq. NaHCO₃ soln. and brine, and dried (Na₂SO₄). Concentration followed by silica gel column chromatography (ethyl acetate/hexane = 1/4) gave pivaloyl ester 10 (14.7 g, 0.021 mol, 88%) as a colorless oil. [α]D = +56.2 (c 1.30, CHCl₃). NMR δH (CDCl₃): 1.19 (9H, s), 2.47 (1H, m), 2.68 (1H, br. s), 3.13 (1H, dd, J = 10.0, 5.4 Hz), 3.15 (3H, s), 3.30 (3H, s), 3.33 (1H, dd, J = 10.0, 3.7 Hz), 3.61 (1H, dd, J = 7.3, 4.4 Hz), 3.74 (1H, m), 4.28 (1H, d, J = 6.6 Hz), 4.33 (1H, d, J = 6.6 Hz), 4.41–4.43 (2H, m), 4.45 (2H, s), 4.92 (1H, d, J = 6.8 Hz), 5.92 (1H, d, J = 1.5 Hz), 5.95 (1H, d, J = 1.5 Hz), 6.76 (1H, d, J = 7.8 Hz), 6.80 (1H, dd, J = 7.8, 1.5 Hz), 6.85 (1H, d, J = 1.5 Hz), 7.20–7.29 (11H, m), 7.35–7.37 (4H, m). NMR δC (CDCl₃): 27.2, 38.8, 46.8, 55.9, 61.5, 61.5, 64.4, 70.8, 76.1, 79.2, 86.7, 94.4, 98.0, 101.0, 107.9, 108.0, 121.3, 127.1, 127.8, 128.7, 134.6, 143.7, 147.0, 147.8, 178.3. IR νmax (CHCl₃): 3715, 3088–2778, 1721, 1505, 1489, 1449, 1287, 1240, 1211, 1156, 1096, 1034 cm⁻¹. EIMS m/z (20 eV): 700 (M⁺, 1), 243 (100), 195 (68). Anal. Found: C, 69.77; H, 6.97. Calcd. for C₃₅H₃₆O₇C, C, 70.27; H, 6.90%.

(2S, 3R, 4R, 5R)-3,5-Bis(methoxymethoxy)-5-(3,4-methylenedioxyphenyl)-4-pivaloyloxymethyl-tetrahydrofuran (13). A reaction solution of trityl ether 12 (1.53 g, 3.59 mmol) and pyridinium p-toluenesulfonate (10 mg, 0.040 mmol) in tert-butyl alcohol (40 ml) was heated under refluxing for 2 h before addition of a few drops of triethylamine. Concentration of the solvent followed
by silica gel column chromatography (20% ethyl acetate/benzene) gave hemiacetal 13 (1.13 g, 2.92 mmol, 82%) as a colorless oil. \([\text{C}_9\text{H}_{16}\text{O}_2]^+ = 28.0 (0.4, \text{CHCl}_3)\). NMR \(\delta_1 (\text{CDCl}_3): 1.14 (9H, s), 2.71 (1H, d, \(J = 2.4 \text{ Hz}\)), 3.13 (1H, m), 3.42 (3H, s), 3.79 (1H, dd, \(J = 11.2, 6.4 \text{ Hz}\)), 3.83 (1H, dd, \(J = 11.2, 8.3 \text{ Hz}\)), 4.15 (1H, d, \(J = 5.4 \text{ Hz}\)), 4.70 (1H, d, \(J = 6.8 \text{ Hz}\)), 4.75 (1H, d, \(J = 6.8 \text{ Hz}\)), 5.30 (1H, d, \(J = 9.8 \text{ Hz}\)), 5.64 (1H, d, \(J = 2.4 \text{ Hz}\)), 5.94 (2H, s), 6.72 (1H, d, \(J = 7.8 \text{ Hz}\)), 6.79 (1H, dd, \(J = 7.8, 1.5 \text{ Hz}\)), 6.97 (1H, d, \(J = 1.5 \text{ Hz}\)). NMR \(\delta_{\text{C}} (\text{CDCl}_3): 27.1, 38.6, 42.8, 55.9, 60.5, 81.5, 81.9, 96.9, 100.7, 101.0, 107.6, 108.2, 121.2, 132.0, 147.2, 147.5, 178.1. IR \(\nu_{\text{max}} (\text{CHCl}_3): 3602, 2975-2780, 1725, 1505, 1489, 1482, 1447, 1285, 1256, 1242, 1156, 1042, 939 \text{ cm}^{-1}. \text{EIMS } m/z (20 \text{ eV}): 382 (M\(^+\), 53), 195 (57), 189 (65), 149 (100). \text{Anal. Found: C}, 59.76; \text{H}, 6.90. \text{Calcd. for C}_{10}\text{H}_{14}\text{O}_2: C, 59.68; H, 6.85\%.

(2R, 3R, 4S)-4-Methoxymethoxy-2-(3, 4-methylenedioxyphenyl)-4-pivaloyloxyoxymethyloxetrahydrofuran (14). To an ice-cooled solution of hemiacetal 13 (1.31 g, 3.43 mmol) in dichloromethane (20 ml) and N,N-dimethylformamide (0.82 ml) was added oxalyl chloride (1.05 ml, 12.0 mmol). The reaction mixture was stirred in an ice-bath for 30 min and poured into an ice-cooled sat. aq. NaHCO\(_3\) soln. The organic solution was separated, washed with brine, and dried (Na\(_2\)SO\(_4\)). After concentration, the residue was dissolved in toluene (40 ml). To the solution was added tri-n-butyltin hydride (1.10 ml, 4.09 mmol) and 2,2'-azobisis(isobutyronitrile) (40 mg, 0.24 mmol). The reaction solution was heated under refluxing for 1 h under N\(_2\) atmosphere. Concentration of the solvent followed by silica gel column chromatography (10% ethyl acetate/benzene) gave tetrahydrofuran derivative 14 (0.89 g, 2.43 mmol, 71%) as a colorless oil. \([\text{C}_9\text{H}_{16}\text{O}_2]^+ = -9.7 (0.72, \text{CHCl}_3)\). NMR \(\delta_1 (\text{CDCl}_3): 1.14 (9H, s), 2.80 (1H, m), 3.40 (3H, s), 3.82-3.86 (2H, m), 3.92 (1H, dd, \(J = 11.2, 7.8 \text{ Hz}\)), 4.23 (1H, dd, \(J = 10.3, 1.0 \text{ Hz}\)), 4.34 (1H, m), 4.67 (1H, d, \(J = 6.8 \text{ Hz}\)), 4.73 (1H, d, \(J = 6.8 \text{ Hz}\)), 5.03 (1H, d, \(J = 9.3 \text{ Hz}\)), 5.91 (1H, d, \(J = 1.5 \text{ Hz}\)), 5.92 (1H, d, \(J = 1.5 \text{ Hz}\)), 6.71 (1H, d, \(J = 7.8 \text{ Hz}\)), 6.79 (1H, dd, \(J = 7.8, 1.5 \text{ Hz}\)), 6.97 (1H, d, \(J = 1.5 \text{ Hz}\)). NMR \(\delta_{\text{C}} (\text{CDCl}_3): 27.2, 38.6, 46.3, 55.7, 61.0, 73.1, 78.0, 81.6, 96.3, 100.9, 107.6, 108.2, 120.9, 133.1, 147.2, 147.6, 178.1. IR \(\nu_{\text{max}} (\text{CHCl}_3): 3011-2780, 1723, 1505, 1489, 1482, 1445, 1285, 1250, 1244, 1161, 1154, 1042, 939 \text{ cm}^{-1}. \text{EIMS } m/z (20 \text{ eV}): 366 (M\(^+\), 53), 219 (53), 202 (92), 189 (76), 176 (58), 149 (100). \text{Anal. Found: C}, 62.39; H, 6.90. \text{Calcd. for C}_{10}\text{H}_{16}\text{O}_2: C, 62.28; H, 7.21\%.

(2R, 3R, 4S)-3-Hydroxymethyl-4-methoxymethoxy-2-(3, 4-methylenedioxyphenyl)tetrahydrofuran (15). To a solution of pivaloyl ester 14 (0.89 g, 2.43 mmol) in dichloromethane (10 ml) was added disobutyrlu-
(100). Anal. Found: C, 71.04; H, 6.83. Calcd. for C₂₅H₃₃O₇Si: C, 70.56; H, 6.77%. (2S, 3S, 4S)-16. [α]₂⁰° = +36.4 (c 0.88, CHCl₃). NMR δH (CDCl₃): 1.07 (9H, s), 2.10 (1H, m, 3-H), 3.13 (1H, br. s), 3.83–3.94 (3H, m), 4.29 (1H, dd, J = 9.8, 3.9 Hz), 4.64 (1H, br. s), 4.73 (1H, d, J = 9.8 Hz), 5.91 (2H, s), 6.52 (1H, d, J = 6.8 Hz), 6.63–6.65 (2H, m), 7.35–7.45 (6H, m), 7.60–7.67 (4H, m). NMR δC (CDCl₃): 19.1, 26.9, 53.8, 60.6, 74.1, 75.7, 80.4, 100.9, 106.5, 108.0, 119.8, 127.9, 130.0, 130.1, 132.5, 135.0, 135.5, 135.6, 147.1, 147.8. IR νmax (CHCl₃): 3500, 2975–2861, 1505, 1489, 1472, 1447, 1429, 1252, 1113, 1082, 1042, 938 cm⁻¹. FABMS m/z: 476 (M⁺ + 5), 191 (48), 161 (100), 135 (76). HRMS (FAB) m/z [M + Na⁺]: Calcd. for C₂₅H₃₃O₇SiNa, 499.1916; found, 499.1914.

(4R, 5R)-4-(tert-Butyldiphenylsilyl) oxyethyl-5-(3,4-methylenedioxyphenyl)dihydro-3(2H)-furanone (17). To a solution of dimethylsulfoxide (0.051 ml, 0.72 mmol) in dichloromethane (10 ml) was added oxalyl chloride (0.031 ml, 0.36 mmol). After 10 min at −75°C, alcohol (2R)-16 (0.14 g, 0.29 mmol) in dichloromethane (5 ml) was added. The reaction solution was stirred at −75°C for 1 h before addition of triethylamine (0.14 ml, 1.00 mmol). After the mixture was warmed to 0°C, sat. aq. NH₄Cl soln. and dichloromethane were added, and then the organic solution was separated, washed with brine, and dried (Na₂SO₄). Concentration followed by silica gel column chromatography (ethyl acetate/hexane = 1/3) gave ketone 17 (0.12 g, 0.25 mmol, 86%) as a colorless oil. [α]₂⁰° = +31.3 (c 0.51, CHCl₃). NMR δH (CDCl₃): 1.04 (9H, s), 2.35 (1H, m), 3.66 (1H, dd, J = 10.3, 2.9 Hz), 3.99 (1H, d, J = 16.8 Hz), 4.16 (1H, dd, J = 10.3, 3.4 Hz), 4.34 (1H, d, J = 16.8 Hz), 5.27 (1H, d, J = 9.8 Hz), 5.95 (2H, s), 6.74 (2H, s), 6.84 (1H, s), 7.37–7.44 (6H, m), 7.63–7.65 (4H, m). NMR δC (CDCl₃): 19.3, 26.8, 57.2, 58.9, 72.4, 81.2, 101.1, 106.6, 108.2, 120.1, 127.7, 128.7, 129.9, 132.6, 132.9, 133.6, 135.6, 137.7, 148.1, 213.9. IR νmax (CHCl₃): 3013–2861, 1763, 1507, 1489, 1472, 1449, 1429, 1254, 1113, 1042, 974, 938 cm⁻¹. FABMS m/z: 497 ((M + Na⁺), 100), 267 (66), 173 (60), 135 (93). HRMS (FAB) m/z [M + Na⁺]: Calcd. for C₂₅H₃₃O₇SiNa, 497.1750; found, 497.1759.

(2R, 3R, 4R)-4-Benzyl-3-(tert-butyldiphenylsilyl) oxyethyl-4-hydroxy-2-(3,4-methylenedioxyphenyl) tetrahydrofuran (18). To an ice-cooled solution of ketone 17 (88 mg, 0.19 mmol) in tetrahydrofuran (5 ml) was added benzylmagnesium chloride (0.57 mmol, 1 ml in diethyl ether, 0.57 mmol). After the reaction solution was stirred in an ice-bath for 30 min, sat. aq. NH₄Cl soln. and ethyl acetate were added. The organic solution was separated, washed with brine, and dried (Na₂SO₄). Concentration followed by silica gel TLC (ethyl acetate/hexane = 1/3) gave benzyltetrahydrofuran 18 (62 mg, 0.11 mmol, 58%) as a colorless oil. [α]₂⁰° = +23.4 (c 0.56, CHCl₃). NMR δH (CDCl₃): 0.95 (9H, s), 2.46 (1H, ddd, J = 8.3, 7.8, 5.9 Hz), 2.92 (1H, d, J = 13.7 Hz), 3.09 (1H, d, J = 13.7 Hz), 3.25 (1H, s), 3.29 (1H, ddd, J = 10.7, 5.9 Hz), 3.70 (1H, dd, J = 10.7, 7.8 Hz), 3.89 (2H, s), 5.04 (1H, d, J = 8.3 Hz), 5.86 (1H, d, J = 1.5 Hz), 5.87 (1H, d, J = 1.5 Hz), 6.61 (2H, s), 6.76 (1H, s), 7.23–7.25 (3H, m), 7.27–7.36 (7H, m), 7.39–7.45 (3H, m), 7.49–7.51 (2H, m). NMR δC (CDCl₃): 18.9, 26.8, 45.2, 51.4, 61.7, 78.4, 81.9, 82.3, 100.8, 107.2, 107.7, 119.6, 126.6, 127.6, 127.7, 128.4, 129.7, 129.8, 130.2, 132.6, 132.7, 133.0, 135.5, 137.1, 146.6, 147.4. IR νmax (CHCl₃): 3380, 3056–2778, 1505, 1489, 1445, 1429, 1254, 1240, 1113, 1105, 1042, 939 cm⁻¹. FABMS m/z: 589 ([M + Na⁺], 86), 199 (65), 161 (94), 135 (100), 91 (55). HRMS (FAB) m/z [M + Na⁺]: Calcd. for C₂₅H₃₃O₇SiNa, 589.2387; found, 589.2388.

Acknowledgments

We measured 400 MHz NMR data at Advanced Instrumentation Center for Chemical Analysis Ehime University. We thank the staff of Advanced Instrumentation Center for Chemical Analysis Ehime University for EIMS measurement, and the staff of NMR and MS Operation Center in Faculty of Pharmaceutical Science at Fukuoka University for FABMS measurements.
References


