Supporting Information

Cobalt(diamine)-catalyzed Cross-coupling Reaction of Alkyl Halides with Arylmagnesium Reagents: Stereoselective Constructions of Arylated Asymmetric Carbons and Application to Total Synthesis of AH13205

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Table of Contents

Instrumentation and Chemicals	S2
Experimental Procedure	S3–S8
Characterization Data of New Compounds	S9–S21
¹ H NMR and ¹³ C NMR Spectra of 18–AH13205	S22–S33
Assignment of Absolute Stereochemistry of 8 and 9	S34–S37

Instrumentation and Chemicals

^1H NMR (500 MHz) and ^{13}C NMR (125.7 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl_3 . Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.2 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra (EI unless otherwise noted) were determined on a JEOL Mstation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Anhydrous CoCl_2 was purchased from Wako Pure Chemicals and was used after removal of water. Specifically, in each experiment, CoCl_2 was dried in a reaction flask carefully under reduced pressure (0.5 torr) by heating with a hair dryer for 2 min immediately before use. Diamine (*R,R*)-**1** was prepared according to the literature.¹ Arylmagnesium bromide was prepared from magnesium metal and the corresponding bromoarene in THF. THF was purchased from Kanto Chemical Co., stored under nitrogen, and used as it is. Dichloromethane was dried over molecular sieves 3A. All reactions were carried out under argon atmosphere.

¹ Benson, S. C.; Cai, P.; Colon, M.; Haiza, M. A.; Tokles, M.; Snyder, J. K. *J. Org. Chem.* **1998**, *53*, 5335–5341.

Experimental Procedure

Synthesis of optically pure bromo acetal **8:** A suspension of *N*-bromosuccinimide (7.12 g, 40 mmol) in CH₂Cl₂ (20 mL) was placed in a 50-mL flask. 2,3-Dihydrofuran (2.45 g, 35 mmol) and (+)-isomenthol (6.9 g, 44 mmol) were successively added to the reaction mixture at 0 °C. The mixture was stirred for 12 h at room temperature. After the mixture was diluted with hexane, the mixture was passed through a pad of Florisil. The filtrate was concentrated in vacuo. Silica gel column purification under 1 atm of air (hexane/ether = 20:1) of the crude product allowed us to obtain (2*R*,3*S*)-**8** (faster moving band, *R_f* = 0.34) and (2*S*,3*R*)-**8** (slower moving band, *R_f* = 0.31) separately. Combined yields were 30–40%. The diastereomer ratio was 1:1.

Reduction of arylated acetal **9:** A solution of (2*R*,3*R*)-**9b** (140 mg, 0.40 mmol) in CH₂Cl₂ (3 mL) was placed in a 30-mL flask. Triethylsilane (0.08 mL, 0.5 mmol) and boron trifluoride diethyl etherate (0.04 mL, 0.4 mmol) were sequentially added dropwise to the reaction mixture at 0 °C. After being stirred for 1 h at room temperature, the reaction mixture was poured into water. The products were extracted with ethyl acetate (10 mL × 2). The combined organic layer was dried over Na₂SO₄ and concentrated. Silica gel column purification (hexane/ethyl acetate = 10:1) of the crude oil afforded **10** (63 mg, 0.32 mmol) in 80% isolated yield. HPLC analysis of **10** (CHIRALCEL[®]-OJ column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 99:1, 1.0 mL/min, 40 °C, 254

nm UV detector) showed that the enantiomeric ratio was 2.5 : 97.5 (retention time = 11.9 min for the minor isomer and 12.6 min for the major isomer).

Jones oxidation of 9 to produce lactone 11: A solution of (2*R*,3*R*)-**9a** (92 mg, 0.30 mmol) in acetone (5 mL) was placed in a 30-mL flask. An excess of Jones reagent was added to the reaction mixture at 0 °C. After being stirred for 1 h at room temperature, the reaction mixture was quenched with 2-propanol. The products were extracted with ethyl acetate (10 mL × 2). The combined organic layer was dried over Na₂SO₄ and concentrated. Silica gel column purification (hexane/ethyl acetate = 2:1) furnished **11** (34 mg, 0.21 mmol) in 71% isolated yield. HPLC analysis of **11** (CHIRALCEL[®] AD column, 4.6 mm × 250 mm, Daisel Chemical Industries, hexane/2-propanol = 96:4, 0.8 mL/min, 40 °C, 254 nm UV detector) revealed that the enantiomeric excess of **11** was 97% (retention time = 21.0 min for the major isomer and 23.1 min for the minor isomer).

BF₃-mediated reaction of acetal 9 with silyl enolate 13: A solution of (2*R*,3*R*)-**9a** (124 mg, 0.40 mmol) in CH₂Cl₂ (3 mL) was placed in a 30-mL flask. (2-Methyl-1-phenyl-1-propenyloxy)trimethylsilane (**13**, 108 mg, 0.49 mmol) and boron trifluoride diethyl etherate (0.11 mL, 1.2 mmol) were sequentially added dropwise to the reaction mixture at –78 °C. The mixture was allowed to warm up to room temperature. After being stirred for 12 h, the reaction mixture was poured into water. The products were extracted with ethyl acetate (10 mL × 2). The combined organic layer was dried over Na₂SO₄ and concentrated. Silica gel column purification (hexane/ethyl acetate = 10:1) of the crude

product afforded **12** (90.4 mg, 0.31 mmol) in 77% isolated yield. The product **12** consisted of (2*S*,3*R*)-**12** and (2*R*,3*S*)-**12** in a ratio of 98.5:1.5 by HPLC analysis (CHIRALCEL[®]-OJ column, 4.6 mm × 250 mm, Daicel Chemical Industries, hexane/2-propanol = 90:10, 1.0 mL/min, 40 °C, 254 nm UV detector, retention time = 10.1 min for the minor isomer and 13.6 min for the major isomer).

Iodoetherification to provide 15: A suspension of *N*-iodosuccinimide (629 mg, 2.8 mmol) in CH₂Cl₂ (5 mL) was placed in a 50-mL flask. Commercially available alcohol **14** (355 mg, 2.5 mmol) and *n*-butyl vinyl ether (0.36 mL, 2.8 mmol) were successively added to the reaction mixture at 0 °C. The mixture was stirred for 20 h at room temperature. After the mixture was diluted with hexane, the mixture was passed through a pad of Florisil. The filtrate was concentrated in vacuo. Purification of the crude oil by silica gel column chromatography (hexane/ethyl acetate = 5:1) provided iodo acetal **15** (853 mg, 2.3 mmol) in 93% yield.

Sequential cyclization/coupling reaction of 15 to yield 18: Anhydrous cobalt (II) chloride (24.5 mg, 0.19 mmol) was placed in a 50-mL reaction flask and was heated with a hair dryer in vacuo for 2 min. After the color of the cobalt salt became blue, anhydrous THF (6 mL) and (*R,R*)-**1** (116 mg, 0.68 mmol) were sequentially added under argon. The mixture was stirred for 3 min at 25 °C. Iodo acetal **15** (700 mg, 1.9 mmol) and the Grignard reagent **17** (0.8 M THF solution, 4.8 mL, 3.8 mmol) were then added over 3 s to the reaction mixture at 0 °C. While the reagent was being added, the mixture turned

brown. After being stirred for 15 min at 25 °C, the reaction mixture was poured into a saturated ammonium chloride solution. The products were extracted with ethyl acetate (20 mL × 2). The combined organic layer was dried over Na₂SO₄ and concentrated. Silica gel column purification (hexane/ethyl acetate = 5:1) of the crude product afforded the corresponding bicyclic acetal. Jones oxidation of the acetal in acetone (5 mL) at room temperature followed by usual workup and purification (hexane/ethyl acetate = 2:1) provided **18** (465 mg, 1.03 mmol) in 54% yield.

Deacetoxylation of 18: A solution of **18** (450 mg, 1.0 mmol) in methanol (5 mL) was placed in a 30-mL flask. Potassium carbonate (165 mg, 1.2 mmol) was added to the reaction mixture. The resulting suspension was stirred for 30 min at room temperature and was then poured into water. The aqueous layer was extracted with ethyl acetate (20 mL × 2). The organic layer was dried and concentrated. The oil was chromatographed on silica gel (hexane/ethyl acetate = 1:1) to yield the deacetylated product (347 mg, 0.85 mmol) in 85% yield. A solution of the deacetylated product (347 mg, 0.85 mmol) in CH₂Cl₂ (4 mL) was placed in a 30-mL flask. Pyridine (0.27 mL, 3.4 mmol), phenyl chlorothionoformate (0.34 mL, 2.55 mmol) and *N,N*-dimethyl-4-aminopyridine (trace) were successively added to the reaction mixture. After being stirred for 12 h at room temperature, the mixture was quenched with water. The products were extracted with ethyl acetate (20 mL × 2), and the combined organic layer was dried and concentrated to give a yellow oil (374 mg). The crude product was dissolved in anhydrous toluene (5 mL).

AIBN (23 mg, 0.14 mL) and tris(trimethylsilyl)silane (0.32 mL, 1.04 mmol) were then added. After being heated at reflux for 1 h, the mixture was cooled to room temperature. The products were extracted with ethyl acetate (20 mL $\times$ 2). The combined organic layer was dried and concentrated in vacuo. Chromatographic purification on silica gel afforded **19** (235 mg, 0.60 mmol) in 70% yield, and in 60% overall yield.

Installation of the α chain: DIBAL-H (1.0 M hexane solution, 0.7 mL, 0.7 mmol) was added to a solution of **19** (137 mg, 0.35 mmol) in anhydrous toluene (5 mL) at $-60\text{ }^{\circ}\text{C}$. After the mixture was stirred for 30 min at $-60\text{ }^{\circ}\text{C}$, the reaction mixture was poured into a saturated ammonium chloride solution. The products were extracted with ethyl acetate (10 mL $\times$ 2). The combined organic layer was dried over Na_2SO_4 and concentrated. The crude residue was purified on silica gel (hexane/ethyl acetate = 1:1) to yield the corresponding lactol (116 mg, 0.29 mmol) in 84% yield. A suspension of (4-carboxybutyl)triphenylphosphonium bromide (476 mg, 1.07 mmol) in THF (3.5 mL) was placed in a 50-mL reaction flask. Sodium hexamethyldisilazide (1.9 M THF solution, 1.13 mL, 2.15 mmol) was added dropwise to the mixture at $0\text{ }^{\circ}\text{C}$. During the addition, the mixture turned orange. The reaction mixture was stirred for 20 min at room temperature. A solution of lactol (106 mg, 0.27 mmol) in THF (3.5 mL) was added to the orange mixture at $0\text{ }^{\circ}\text{C}$. The mixture was stirred for 1 h at room temperature and was then quenched with a saturated ammonium chloride solution. The aqueous layer was extracted with ethyl acetate (20 mL $\times$ 4), dried over Na_2SO_4 and concentrated in vacuo. The residue was

chromatographed on silica gel (hexane/ethyl acetate = 1:1) to produce **20** (111 mg, 0.23 mmol) in 87% yield.

The final step to AH13205: Carboxylic acid **20** (36 mg, 0.075 mmol) was placed in a 20-mL flask. CH₂Cl₂ (1 mL) and Pyridinium chlorochromate (48 mg, 0.22 mmol) were sequentially added to the reaction flask. After the reaction mixture was stirred for 1 h at room temperature, the solvent was evaporated under a reduced pressure to give a black oil. Silica gel column purification (hexane/ethyl acetate = 1:1) of the crude residue provided the corresponding keto carboxylic acid (18 mg, 0.038 mmol) in 50 % yield. A suspension of 10% palladium on charcoal (2 mg) in water (1 mL) was placed in a 20-mL flask under hydrogen. The keto carboxylic acid (11 mg, 0.023 mmol) in ethanol (0.5 mL) was added to the reaction mixture. After being heated at reflux for 24 h, the mixture was cooled to room temperature. The aqueous layer was extracted with ethyl acetate (10 mL × 4). The combined organic layer was dried and concentrated in vacuo. Chromatographic purification on silica gel (hexane/ethyl acetate = 1:1) afforded AH13205 (3.5 mg, 0.0090 mmol) and benzylated AH13205 (3.8 mg, 0.0088 mmol) in 39% and 38% yields, respectively.

Characterization Data

The compounds shown in Table 1 are well known compounds, except for entry 15.

Compounds **3**², **4**³, and **5**³ are found in the literature.

Diethyl 2-Allyl-2-[(E)-4-bromo-2-butenyl]-1,3-propanedioate (Table 1, entry 15, starting material): oil. IR (neat) 1206, 1444, 1732, 2981 cm⁻¹; ¹H NMR (CDCl₃) δ 1.25 (t, *J* = 7.0 Hz, 6H), 2.61–2.63 (m, 4H), 3.89 (d, *J* = 7.5 Hz, 2H), 4.18 (q, *J* = 7.0 Hz, 4H), 5.10–5.14 (m, 2H), 5.58–5.66 (m, 2H), 5.76 (m, 1H); ¹³C NMR (CDCl₃) δ 14.32, 32.57, 35.27, 37.17, 57.38, 61.58, 119.67, 129.82, 130.84, 132.20, 170.72.

Diethyl 2-Allyl-2-[(E)-4-phenyl-2-butenyl]-1,3-propanedioate (Table 1, entry 15, product): oil. IR (neat) 1029, 1214, 1445, 1733, 2981 cm⁻¹; ¹H NMR (CDCl₃) δ 1.21 (t, *J* = 7.0 Hz, 6H), 2.61 (d, *J* = 8.0 Hz, 2H), 2.64 (d, *J* = 7.5 Hz, 2H), 3.32 (d, *J* = 6.5 Hz, 2H), 4.11–4.17 (m, 4H), 5.05–5.08 (m, 2H), 5.37 (m, 1H), 5.60–5.68 (m, 2H), 7.14–7.19 (m, 3H), 7.26–7.29 (m, 2H); ¹³C NMR (CDCl₃) δ 14.29, 35.61, 36.93, 39.29, 57.66, 61.37, 119.29, 125.17, 126.20, 128.55, 128.64, 132.56, 134.01, 140.45, 171.03.

6-Iodo-1-undecene (eq. 1, starting material): oil. IR (neat) 912, 1457, 2928 cm⁻¹; ¹H NMR (CDCl₃) δ 0.89 (t, *J* = 7.5 Hz, 3H), 1.22–1.43 (m, 5H), 1.45–1.56 (m, 2H), 1.60–1.73 (m, 3H), 1.81–1.90 (m, 2H), 2.01–2.13 (m, 2H), 4.11 (m, 1H), 4.95–5.04 (m, 2H), 5.79 (ddd, *J* = 17.0, 10.5, 7.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.23, 22.70, 28.90, 29.37, 31.20, 33.08, 40.14, 40.46, 40.80, 115.10, 138.48.

² Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 1340–1341.

³ Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 5374–5375.

6-Bromo-1-undecene (eq. 1, starting material): oil. IR (neat) 911, 1435, 2928 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.89 (t, $J = 7.0$ Hz, 3H), 1.22–1.45 (m, 5H), 1.47–1.56 (m, 2H), 1.66 (m, 1H), 1.75–1.86 (m, 4H), 2.03–2.12 (m, 2H), 4.03 (m, 1H), 4.95–5.04 (m, 2H), 5.79 (ddd, $J = 17.0, 10.5, 7.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 14.22, 22.71, 26.95, 27.43, 31.41, 33.28, 38.66, 39.33, 58.87, 115.08, 138.50.

1-benzyl-2-pentylcyclopentane (eq. 1, product, 75:25 mixture of diastereomers): oil. IR (neat) 698, 1453, 2925 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.88 (t, $J = 6.5$ Hz, $0.25 \times 1\text{H}$), 0.90 (t, $J = 7.0$ Hz, $0.75 \times 3\text{H}$), 1.09–1.74 (m, 14H), 1.81–1.88 (m, 1H), 2.11–2.18 (m, 1H), 2.25 (dd, $J = 13.0, 11.0$ Hz, $0.75 \times 1\text{H}$), 2.35 (dd, $J = 13.5, 9.5$ Hz, $0.25 \times 1\text{H}$), 2.73 (dd, $J = 13.5, 4.5$ Hz, $0.75 \times 1\text{H}$), 2.83 (dd, $J = 14.0, 4.0$ Hz, $0.25 \times 1\text{H}$), 7.15–7.18 (m, 3H), 7.25–7.28 (m, 2H); ^{13}C NMR (CDCl_3) δ 14.33 (2C overlapping), 22.34, 22.87, 22.91, 23.75, 28.28, 28.49, 29.86, 30.03, 30.25, 32.29, 32.35, 32.38, 32.47, 35.29, 35.41, 41.49, 43.18, 44.35, 45.66, 47.91, 125.60, 125.67, 128.26, 128.30, 129.10 (2C overlapping), 142.47, 142.79.

6-Bromo-1,4-dioxaspiro[4.4]nonane (6): oil, IR (neat) 833, 1109, 1473, 2360, 2887 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.71 (m, 1H), 1.83 (m, 1H), 1.93 (m, 1H), 2.02–2.14 (m, 2H), 2.30 (m, 1H), 3.92–4.07 (m, 4H), 4.12 (t, $J = 6.5$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.82, 32.31, 34.01, 55.20, 65.33, 65.68, 116.49; Found: C, 40.63; H, 5.23%. Calcd for $\text{C}_7\text{H}_{11}\text{BrO}_2$: C, 40.60; H, 5.35%.

6-Phenyl-1,4-dioxaspiro[4.4]nonane (7): oil, IR (neat) 700, 758, 1060, 1496, 2956 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.75 (m, 1H), 1.86 (m, 1H), 1.94 (m, 1H), 2.00–2.09 (m, 3H),

3.10–3.14 (m, 2H), 3.60 (m, 1H), 3.68–3.75 (m, 2H), 7.20–7.34 (m, 5H); ^{13}C NMR (CDCl_3) δ 20.97, 30.37, 36.95, 53.41, 64.86, 65.04, 118.17, 126.56, 127.96, 129.31, 139.85; Found: C, 76.59; H, 7.85%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$: C, 76.44; H, 7.90%; retention time (major) = 7.1 min, retention time (minor) = 7.5 min (CHIRALCEL[®]-OJ, 4.6 mm $\times$ 250 mm, hexane/2-propanol = 99/1, 0.80 mL/min, 40 $^\circ\text{C}$, 254 nm UV detector).

***trans*-3-Iodo-2-methoxy-1-oxacyclohexane** (Table 2, entry 1, starting material): oil, IR (neat) 945, 1037, 1380, 2947 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.56 (m, 1H), 1.73 (m, 1H), 2.02 (m, 1H), 2.36 (m, 1H), 3.44 (s, 3H), 3.59 (ddd, J = 11.0, 7.5, 3.5 Hz, 1H), 3.98 (m, 1H), 4.06 (m, 1H), 4.53 (d, J = 5.5 Hz, 1H); ^{13}C NMR (CDCl_3) δ 25.89, 29.22, 33.08, 56.10, 63.81, 103.90; Found: C, 29.83; H, 4.42%. Calcd for $\text{C}_6\text{H}_{11}\text{IO}_2$: C, 29.77; H, 4.58%.

2-Methoxy-3-phenyl-1-oxacyclohexane (Table 2, entry 1, product, 1:1 mixture of diastereomers): oil, IR (neat) 700, 756, 1134, 1402, 2941 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.63–1.86 (m, 3H), 2.05 (m, 0.5 $\times$ 1H, *trans*), 2.18 (m, 0.5 $\times$ 1H, *cis*), 2.71 (ddd, J = 11.0, 7.0, 4.0 Hz, 0.5 $\times$ 1H, *trans*), 2.95 (dt, J = 12.5, 3.0 Hz, 0.5 $\times$ 1H, *cis*), 3.24 (s, 0.5 $\times$ 3H, *cis*), 3.37 (s, 0.5 $\times$ 3H, *trans*), 3.60 (ddt, J = 11.5, 5.0, 2.0 Hz, 0.5 $\times$ 1H, *cis*), 3.62 (m, 0.5 $\times$ 1H, *trans*), 3.80 (m, 0.5 $\times$ 1H, *cis*), 4.07 (dtd, J = 11.0, 4.5, 1.5 Hz, 0.5 $\times$ 1H, *trans*), 4.47 (d, J = 7.0 Hz, 0.5 $\times$ 1H, *trans*), 4.66 (d, J = 3.0 Hz, 0.5 $\times$ 1H, *cis*), 7.17–7.33 (m, 5H); ^{13}C NMR (CDCl_3) δ 23.85, 24.77, 26.20, 30.24, 46.93, 47.25, 55.11, 56.24, 59.11, 65.25, 101.16, 105.28, 126.59, 126.60, 128.06, 128.26, 128.45, 128.50, 142.00, 142.35; Found: C, 74.87; H, 8.33%. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$: C, 74.97; H, 8.39%.

***trans*-3-Iodo-2-isopropoxy-1-oxacyclohexane** (Table 2, entry 2, starting material): oil, IR (neat) 696, 1020, 1380, 2970 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.19 (d, $J = 6.0$ Hz, 3H), 1.22 (d, $J = 6.0$ Hz, 3H), 1.57–1.69 (m, 2H), 2.04 (m, 1H), 2.41 (m, 1H), 3.56 (ddd, $J = 11.5, 8.5, 3.5$ Hz, 1H), 3.93 (quintet, $J = 6.0$ Hz, 1H), 3.99–4.04 (m, 2H), 4.64 (d, $J = 6.5$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 21.78, 23.58, 26.59, 30.75, 34.10, 64.41, 71.00, 101.56; Found: C, 35.66; H, 5.41%. Calcd for $\text{C}_8\text{H}_{15}\text{IO}_2$: C, 35.57; H, 5.60%.

2-Isopropoxy-3-phenyl-1-oxacyclohexane (Table 2, entry 2, product): oil, IR (neat) 700, 1076, 1379, 2970 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.77 (d, $J = 6.0$ Hz, $0.4 \times 3\text{H}$, *cis*), 0.79 (d, $J = 6.0$ Hz, $0.6 \times 3\text{H}$, *trans*), 1.14 (d, $J = 6.0$ Hz, $0.6 \times 3\text{H}$, *trans*), 1.18 (d, $J = 6.0$ Hz, $0.4 \times 3\text{H}$, *cis*), 1.60–2.22 (m, 4H), 2.68 (ddd, $J = 11.0, 7.5, 4.5$ Hz, $0.6 \times 1\text{H}$, *trans*), 2.94 (dt, $J = 13.0, 3.0$ Hz, $0.4 \times 1\text{H}$, *cis*), 3.59 (m, $0.6 \times 1\text{H}$, *trans*), 3.60 (ddt, $J = 11.0, 5.0, 1.5$ Hz, $0.4 \times 1\text{H}$, *cis*), 3.71 (quintet, $J = 6.0$ Hz, $0.4 \times 1\text{H}$, *cis*), 3.78 (quintet, $J = 6.0$ Hz, $0.6 \times 1\text{H}$, *trans*), 3.95 (ddd, $J = 13.0, 11.0, 3.0$ Hz, $0.4 \times 1\text{H}$, *cis*), 4.06 (dtd, $J = 11.0, 4.5, 1.5$ Hz, $0.6 \times 1\text{H}$, *trans*), 4.53 (d, $J = 7.5$ Hz, $0.6 \times 1\text{H}$, *trans*), 4.82 (d, $J = 3.0$ Hz, $0.4 \times 1\text{H}$, *cis*), 7.18–7.30 (m, 5H); ^{13}C NMR (CDCl_3) δ 21.43, 21.54, 23.56, 23.63, 23.89, 24.95, 26.41, 30.09, 47.45, 47.66, 59.32, 65.85, 69.65, 70.65, 98.43, 102.99, 126.42 ($\times 2$), 127.97, 128.21, 128.31, 128.73, 142.31, 142.44; Found: C, 76.56; H, 8.99%. Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C, 76.33; H, 9.15%.

***trans*-2-Methoxy-3-phenyl-1-oxacyclopentane** (Table 2, entry 3, product): oil, IR (neat) 702, 1043, 1456, 2893 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.96 (dtd, $J = 12.5, 8.0, 5.5$ Hz, 1H),

2.46 (m, 1H), 3.32 (ddd, $J = 8.0, 5.5, 1.5$ Hz, 1H), 3.36 (s, 3H), 4.04 (dt, $J = 8.0, 7.5$ Hz, 1H), 4.13 (m, 1H), 4.93 (d, $J = 1.5$ Hz, 1H), 7.21–7.24 (m, 3H), 7.30–7.33 (m, 2H); ^{13}C NMR (CDCl_3) δ 33.40, 51.63, 55.11, 67.43, 110.82, 126.78, 127.44, 128.80, 142.56. Found: C, 74.11; H, 7.86%. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$: C, 74.13; H, 7.92%.

***trans*-3-Bromo-2-isopropoxy-1-oxacyclopentane** (Table 2, entry 4, starting material): oil, IR (neat) 918, 1024, 1380, 2974 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.14 (d, $J = 6.0$ Hz, 3H), 1.16 (d, $J = 6.0$ Hz, 3H), 2.20 (m, 1H), 2.64 (m, 1H), 3.89 (quintet, $J = 6.0$ Hz, 1H), 4.04 (td, $J = 8.0, 3.0$ Hz, 1H), 4.12 (td, $J = 8.0, 7.0$ Hz, 1H), 4.17 (dd, $J = 6.0, 2.0$ Hz, 1H), 5.30 (s, 1H); ^{13}C NMR (CDCl_3) δ 22.00, 23.55, 34.11, 50.96, 66.56, 69.52, 107.13; Found: C, 40.15; H, 6.01%. Calcd for $\text{C}_7\text{H}_{13}\text{BrO}_2$: C, 40.21; H, 6.27%.

***trans*-2-Isopropoxy-3-phenyl-1-oxacyclopentane** (Table 2, entry 4, product): oil, IR (neat) 700, 1022, 1379, 2972 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.11 (d, $J = 6.0$ Hz, 3H), 1.22 (d, $J = 6.0$ Hz, 3H), 1.95 (dtd, $J = 12.5, 8.0, 6.0$ Hz, 1H), 2.47 (m, 1H), 3.30 (ddd, $J = 8.0, 6.0, 2.0$ Hz, 1H), 3.89 (quintet, $J = 6.0$ Hz, 1H), 4.06 (q, $J = 8.0$ Hz, 1H), 4.10 (dt, $J = 8.0, 4.5$ Hz, 1H), 5.13 (d, $J = 2.0$ Hz, 1H), 7.21–7.26 (m, 3H), 7.30–7.34 (m, 2H); ^{13}C NMR (CDCl_3) δ 22.01, 23.84, 33.27, 51.74, 67.11, 69.22, 107.85, 126.66, 127.43, 128.73, 142.86; Found: C, 75.77; H, 8.91%. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2$: C, 75.69; H, 8.80%.

***(2R,3S)*-3-Bromo-2-*{(+)-isomenthoxy}*-1-oxacyclopentane** (*(2R,3S)*-**8**, faster moving band, $R_f = 0.34$, ether/hexane = 20:1): oil, IR (neat) 910, 1024, 1384, 2931 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.83 (d, $J = 7.0$ Hz, 3H), 0.88 (d, $J = 7.0$ Hz, 3H), 0.90 (d, $J = 7.0$ Hz, 3H),

1.18–1.29 (m, 2H), 1.31–1.45 (m, 3H), 1.50 (m, 1H), 1.58 (m, 1H), 1.82–1.93 (m, 2H), 2.21 (m, 1H), 2.64 (m, 1H), 3.76 (td, $J = 7.5, 3.5$ Hz, 1H), 4.01 (td, $J = 8.5, 3.5$ Hz, 1H), 4.13 (td, $J = 8.5, 7.5$ Hz, 1H), 4.14 (dm, $J = 5.5$ Hz, 1H), 5.30 (s, 1H); ^{13}C NMR (CDCl_3) δ 18.02, 19.94, 20.18, 21.20, 25.96, 27.69, 30.55, 34.18, 35.90, 47.68, 51.13, 66.54, 72.39, 105.90; Found: C, 55.08; H, 8.03%. Calcd for $\text{C}_{14}\text{H}_{25}\text{BrO}_2$: C, 55.09; H, 8.26%.

((2*S*,3*R*)-3-Bromo-2- $\{(+)$ -isomenthoxy}-1-oxacyclopentane ((2*S*,3*R*)-8, slower moving band, $R_f = 0.31$, ether/hexane = 20:1): oil, IR (neat) 912, 1024, 1436, 2852 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.85 (d, $J = 7.0$ Hz, 3H), 0.88 (d, $J = 7.0$ Hz, 3H), 0.89 (d, $J = 7.0$ Hz, 3H), 1.11–1.22 (m, 2H), 1.26 (m, 1H), 1.29–1.56 (m, 4H), 1.76–1.85 (m, 2H), 2.19 (m, 1H), 2.64 (m, 1H), 3.73 (td, $J = 6.0, 3.5$ Hz, 1H), 4.03 (td, $J = 8.5, 3.5$ Hz, 1H), 4.11 (td, $J = 8.5, 7.5$ Hz, 1H), 4.19 (dm, $J = 6.0$ Hz, 1H), 5.27 (s, 1H); ^{13}C NMR (CDCl_3) δ 19.40, 20.78, 21.02, 21.32, 26.00, 27.52, 30.14, 34.18, 37.59, 46.24, 50.94, 66.40, 75.08, 108.43; Found: C, 55.07; H, 8.39%. Calcd for $\text{C}_{14}\text{H}_{25}\text{BrO}_2$: C, 55.09; H, 8.26%.

((2*R*,3*R*)-2- $\{(+)$ -isomenthoxy}-3-phenyl-1-oxacyclopentane ((2*R*,3*R*)-9a): oil, IR (neat) 700, 1024, 1080, 1456, 2931 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.86 (d, $J = 7.0$ Hz, 3H), 0.87 (d, $J = 7.0$ Hz, 3H), 0.92 (d, $J = 7.0$ Hz, 3H), 1.24–1.45 (m, 5H), 1.52–1.58 (m, 2H), 1.87–2.02 (m, 3H), 2.48 (m, 1H), 3.30 (ddd, $J = 7.5, 5.5, 1.5$ Hz, 1H), 3.75 (dm, $J = 8.0$ Hz, 1H), 4.03 (dt, $J = 8.0, 7.5$ Hz, 1H), 4.09 (td, $J = 8.0, 5.5$ Hz, 1H), 5.14 (d, $J = 1.5$ Hz, 1H), 7.21–7.32 (m, 5H); ^{13}C NMR (CDCl_3) δ 17.91, 19.86, 20.08, 21.28, 25.92, 27.72, 30.70, 33.17,

35.97, 47.91, 51.66, 67.13, 71.95, 106.42, 126.62, 127.42, 128.73, 143.00; Found: C, 79.37; H, 9.78%. Calcd for C₂₀H₃₀O₂: C, 79.42; H, 10.00%.

(2*S*,3*S*)-2- $\{(+)$ -isomenthoxy}-3-phenyl-1-oxacyclopentane ((2*S*,3*S*)-9a): oil, IR (neat) 700, 1026, 1082, 1456, 2927 cm⁻¹; ¹H NMR (CDCl₃) δ 0.74 (d, J = 7.0 Hz, 3H), 0.85 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H), 1.14–1.20 (m, 2H), 1.31–1.43 (m, 2H), 1.50–1.61 (m, 3H), 1.80 (m, 1H), 1.88–1.99 (m, 2H), 2.46 (m, 1H), 3.32 (ddd, J = 8.0, 4.0, 2.5 Hz, 1H), 3.68 (dm, J = 4.0 Hz, 1H), 4.04–4.11 (m, 2H), 5.07 (d, J = 2.5 Hz, 1H), 7.19–7.34 (m, 5H); ¹³C NMR (CDCl₃) δ 19.07, 20.60, 20.89, 21.29, 25.93, 27.69, 30.32, 33.23, 38.12, 46.47, 51.91, 67.10, 75.02, 109.6, 126.64, 127.47, 128.72, 142.77; Found: C, 79.44; H, 10.29%. Calcd for C₂₀H₃₀O₂: C, 79.42; H, 10.00%.

(2*R*,3*R*)-2- $\{(+)$ -isomenthoxy}-3-(1-naphthyl)-1-oxacyclopentane ((2*R*,3*R*)-9b): oil, IR (neat) 777, 1008, 1456, 2852 cm⁻¹; ¹H NMR (CDCl₃) δ 0.86 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H), 0.94 (d, J = 7.0 Hz, 3H), 1.27–1.35 (m, 2H), 1.37–1.47 (m, 3H), 1.58 (m, 1H), 1.93 (m, 1H), 2.04 (m, 1H), 2.12–2.18 (m, 2H), 2.64 (m, 1H), 3.79 (td, J = 8.0, 4.0 Hz, 1H), 4.10 (dd, J = 8.5, 3.5 Hz, 1H), 4.13 (t, J = 7.0 Hz, 2H), 5.32 (d, J = 1.0 Hz, 1H), 7.39–7.43 (m, 2H), 7.45–7.55 (m, 2H), 7.74 (d, J = 8.0 Hz, 1H), 7.87 (m, 1H), 8.17 (d, J = 8.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 17.83, 19.84, 20.03, 21.32, 25.96, 27.80, 30.77, 31.43, 35.99, 47.13, 48.08, 67.31, 71.74, 105.71, 123.24, 123.90, 125.71 (x2), 126.17, 127.30, 129.05, 131.82, 134.08, 138.17; Found: C, 81.48; H, 9.02%. Calcd for C₂₄H₃₂O₂: C, 81.77; H, 9.15%.

(2*S*,3*S*)-2-(+)-isomenthoxy-3-(1-naphthyl)-1-oxacyclopentane ((2*S*,3*S*)-9b): oil, IR (neat) 777, 1028, 1456, 2869 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.73 (d, $J = 7.0$ Hz, 3H), 0.84 (d, $J = 7.0$ Hz, 3H), 0.92 (d, $J = 7.0$ Hz, 3H), 1.16-1.24 (m, 2H), 1.34-1.45 (m, 2H), 1.55-1.66 (m, 3H), 1.84 (m, 1H), 1.96 (m, 1H), 2.14 (m, 1H), 2.63 (m, 1H), 3.73 (td, $J = 6.5, 4.0$ Hz, 1H), 4.12-4.20 (m, 3H), 5.27 (d, $J = 1.5$ Hz, 1H), 7.39-7.45 (m, 2H), 7.48-7.55 (m, 2H), 7.74 (d, $J = 8.0$ Hz, 1H), 7.87 (m, 1H), 8.19 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.08, 20.60, 20.93, 21.34, 25.93, 27.74, 30.36, 31.70, 38.18, 46.40, 47.27, 67.23, 74.67, 108.81, 123.33, 123.83, 125.72 (x2), 126.15, 127.29, 129.05, 131.84, 134.08, 138.24; Found: C, 81.72; H, 9.22%. Calcd for $\text{C}_{24}\text{H}_{32}\text{O}_2$: C, 81.77; H, 9.15%.

(2*S*,3*S*)-2-[(+)-isomenthoxy]-3-(2-naphthyl)-1-oxacyclopentane ((2*S*,3*S*)-9c): white solid, IR (nujol) 738, 1028, 1265, 2927 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.73 (d, $J = 7.0$ Hz, 3H), 0.85 (d, $J = 7.0$ Hz, 3H), 0.91 (d, $J = 7.0$ Hz, 3H), 1.13-1.44 (m, 4H), 1.52-1.63 (m, 3H), 1.82 (m, 1H), 1.99 (m, 1H), 2.05 (m, 1H), 2.53 (m, 1H), 3.49 (ddd, $J = 14.0, 10.5, 3.5$ Hz, 1H), 3.71 (td, $J = 10.5, 7.0$ Hz, 1H), 4.07-4.19 (m, 2H), 5.17 (d, $J = 3.5$ Hz, 1H), 7.37-7.49 (m, 3H), 7.68 (s, 1H), 7.79-7.81 (m, 3H); ^{13}C NMR (CDCl_3) δ 19.09, 20.63, 20.91, 21.29, 25.95, 27.70, 30.33, 33.34, 38.15, 46.47, 52.05, 67.15, 75.06, 109.56, 125.67, 125.71, 126.09, 126.26, 127.75, 127.84, 128.45, 132.42, 133.65, 140.22; Found: C, 81.80; H, 9.29%. Calcd for $\text{C}_{24}\text{H}_{32}\text{O}_2$: C, 81.77; H, 9.15%. m.p. 59-62 $^{\circ}\text{C}$.

(2*S*,3*S*)-2-[(+)-isomenthoxy]-3-(1-pyrenyl)-1-oxacyclopentane ((2*S*,3*S*)-9d): oil, IR (neat) 1026, 1384, 2868, 2925 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.69 (d, $J = 7.0$ Hz, 3H), 0.83

(d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 7.0$ Hz, 3H), 1.13-1.49 (m, 5H), 1.54-1.73 (m, 3H), 1.84 (m, 1H), 1.98 (m, 1H), 2.28 (m, 1H), 2.75 (m, 1H), 3.78 (m, 1H), 4.26 (t, $J = 12.0$ Hz, 2H), 4.45 (m, 1H), 5.39 (d, $J = 3.0$ Hz, 1H), 7.95-8.04 (m, 4H), 8.12-8.20 (m, 4H), 8.46 (d, $J = 15.5$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.06, 20.63, 20.95, 21.30, 25.95, 27.76, 30.36, 33.04, 38.22, 46.47, 47.82, 67.45, 74.92, 109.58, 123.29, 124.06, 125.02, 125.09, 125.19, 125.25, 125.27, 126.08, 127.15, 127.61, 127.67, 128.81, 130.16, 130.96, 131.62, 136.39.

3-(1-naphthyl)-1-oxacyclopentane (10): oil, IR (neat) 779, 1056, 1398, 1512, 1596, 2866 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.19 (m, 1H), 2.48 (m, 1H), 3.96-4.23 (m, 4H), 4.29 (m, 1H), 7.42-7.57 (m, 4H), 7.75 (m, 1H), 7.88 (m, 1H), 8.14 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 33.71, 40.52, 68.35, 73.85, 122.93, 123.51, 125.71, 125.75, 126.19, 127.24, 129.13, 132.02, 134.09, 138.61; HRMS (EI) Found: 198.1045 [M^+]; $\text{C}_{14}\text{H}_{14}\text{O}$ Calcd: 198.1046; CHIRALCEL[®]-OJ, hexane/2-propanol = 99/1, 1.0 mL/min, retention time (–) = 11 min, retention time (+) = 13 min. (*R*); $[\alpha]_{\text{D}}^{25} = +20$ ($c = 2$, CHCl_3) (*S*); $[\alpha]_{\text{D}}^{25} = -20$ ($c = 1.8$, CHCl_3).

α -Phenyl- γ -butyrolactone (11)⁴: oil, CHIRALCEL[®]-AD, hexane/2-propanol = 96/4, 0.80 mL/min, retention time (+) = 21 min, retention time (–) = 23 min. (*R*); $[\alpha]_{\text{D}}^{25} = +4.5$ ($c = 1$, CHCl_3).

***trans*-2-Methyl-1-phenyl-2-(2-phenyl-5-oxacyclopentyl)propan-1-one ((2*S*,3*R*)-12):** oil, IR (neat) 702, 1068, 1674, 2360, 2937 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.12 (s, 3H), 1.28

⁴ Chen, Y.; Deng, L. *J. Am. Chem. Soc.* **2001**, *123*, 11302–11303.

(s, 3H), 2.02 (dtd, $J = 12.5, 8.0, 7.5$ Hz, 1H), 2.34 (m, 1H), 3.30 (dt, $J = 8.5, 8.0$ Hz, 1H), 3.96 (1H, m), 4.05 (dt, $J = 5.5, 5.0$ Hz, 1H), 4.44 (d, $J = 8.0$ Hz, 1H), 7.18 (m, 1H), 7.22–7.28 (m, 4H), 7.31–7.34 (m, 2H), 7.39 (m, 1H), 7.54–7.56 (m, 2H); ^{13}C NMR (CDCl_3) δ 21.66, 23.62, 37.85, 46.69, 52.09, 68.67, 90.27, 126.69, 127.66, 127.93, 128.02, 128.86, 130.47, 139.94, 143.60, 209.20; Found: C, 81.65; H, 7.77%. Calcd for $\text{C}_{20}\text{H}_{22}\text{O}_2$: C, 81.60; H, 7.53%; CHIRALCEL[®]-OJ, hexane/2-propanol = 90/10, 1.0 mL/min, retention time = 10 min for the minor enantiomer, retention time = 14 min for the major enantiomer. (2*S*,3*R*); $[\alpha]_{\text{D}}^{25} = +2$ ($c = 2$, CHCl_3).

Compound 15 (mixture of diastereomers): oil, IR (neat) 1020, 1240, 1363, 1735, 2958 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.93 (t, $J = 7.5$ Hz, 3H), 1.36–1.44 (m, 2H), 1.55–1.61 (m, 2H), 1.74–1.80 (m, 1H), 2.05 (s, 3H), 2.75–2.82 (m, 1H), 3.18–3.25 (m, 2H), 3.45–3.53 (m, 1H), 3.55–3.63 (m, 1H), 4.63–4.68 (m, 1H), 4.72 (t, $J = 5.5$ Hz, $0.5 \times 1\text{H}$), 4.74 (t, $J = 5.5$ Hz, $0.5 \times 1\text{H}$), 5.47–5.50 (m, 1H), 5.99–6.00 (m, 1H), 6.07–6.10 (m, 1H); ^{13}C NMR (CDCl_3) δ 5.69, 5.75, 14.05 ($\times 2\text{C}$), 19.51 ($\times 2\text{C}$), 21.36 ($\times 2\text{C}$), 31.86, 31.92, 38.02, 38.79, 65.81, 66.37, 76.75, 76.90, 78.77, 78.87, 101.62, 101.95, 133.21, 133.27, 136.15, 136.64, 171.07 ($\times 2\text{C}$); Found: C, 42.37; H, 5.94%. Calcd for $\text{C}_{13}\text{H}_{21}\text{IO}_4$: C, 42.41; H, 5.75%.

(1*S*,5*R*,6*S*,7*R*)-7-acetoxy-2-oxa-3-oxo-6-phenylbicyclo[3.3.0]octane (16): oil, IR (neat) 1029, 1172, 1240, 1732, 2945 cm^{-1} ; ^1H NMR (CDCl_3) δ 2.00 (s, 3H), 2.11 (ddd, $J = 15.0, 5.0, 2.0$ Hz, 1H), 2.52 (dd, $J = 18.5, 2.0$ Hz, 1H), 2.64 (dt, $J = 15.0, 7.0$ Hz, 1H), 2.83 (dd, $J = 18.5, 10.0$ Hz, 1H), 3.09 (m, 1H), 3.16 (t, $J = 7.0$ Hz, 1H), 5.11–5.18 (m, 2H),

7.17–7.19 (m, 2H), 7.26–7.29 (m, 1H), 7.33–7.36 (m, 2H); ^{13}C NMR (CDCl_3) δ 21.18, 35.37, 37.59, 43.86, 56.75, 80.26, 83.49, 127.52, 127.69, 129.13, 139.05, 170.67, 176.54; $[\alpha]_{\text{D}}^{25} = -60$ ($c = 4$, CHCl_3). Found: C, 69.01; H, 6.28%. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4$: C, 69.22; H, 6.20%.

Lactone 18: oil, IR (neat) 734, 1070, 1236, 1737, 1770, 2931 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.84 (t, $J = 7.0$ Hz, 3H), 1.21–1.29 (m, 5H), 1.42 (m, 1H), 1.60 (m, 1H), 1.82 (m, 1H), 2.02 (d, $J = 2.0$ Hz, 3H), 2.14 (dd, $J = 15.5, 4.5$ Hz, 1H), 2.55 (dd, $J = 18.5, 2.5$ Hz, 1H), 2.62 (m, 1H), 2.86 (dd, $J = 18.5, 10.0$ Hz, 1H), 3.13 (m, 1H), 3.20 (m, 1H), 4.24 (d, $J = 12.0$ Hz, 1H), 4.27 (m, 1H), 4.43 (d, $J = 12.0$ Hz, 1H), 5.15–5.18 (m, 2H), 7.14–7.16 (m, 2H), 7.27–7.35 (m, 7H); ^{13}C NMR (CDCl_3) δ 14.23, 21.28, 22.74, 25.71, 31.85, 35.65, 37.65, 38.47, 43.83, 56.75, 70.66, 80.58, 81.27, 83.74, 83.77, 127.52, 127.70, 127.89, 127.91, 128.52, 138.33, 138.73, 142.45, 170.74, 176.62; Found: C, 74.61; H, 7.55%. Calcd for $\text{C}_{28}\text{H}_{34}\text{O}_5$: C, 74.64; H, 7.61%. $[\alpha]_{\text{D}}^{25} = -27$ ($c = 1$, CHCl_3).

Deacetylated derivative of 18: oil, IR (neat) 1087, 1766, 2929, 3425 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.84 (t, $J = 7.5$ Hz, 3H), 1.20–1.30 (m, 5H), 1.43 (m, 1H), 1.60 (m, 1H), 1.78 (brs, 1H), 1.82 (m, 1H), 2.07 (ddd, $J = 15.0, 8.0, 3.5$ Hz, 1H), 2.52 (m, 1H), 2.66 (dt, $J = 14.5, 7.0$ Hz, 1H), 2.75 (dd, $J = 18.5, 9.5$ Hz, 1H), 2.87 (t, $J = 8.0$ Hz, 1H), 2.98 (m, 1H), 4.25 (d, $J = 12.0$ Hz, 1H), 4.26–4.30 (m, 2H), 4.44 (d, $J = 12.0$ Hz, 1H), 5.04 (dt, $J = 7.0, 3.0$ Hz, 1H), 7.18–7.20 (m, 2H), 7.26–7.34 (m, 7H); ^{13}C NMR (CDCl_3) δ 14.23, 22.73, 25.74, 31.85, 34.73, 38.50, 38.52, 40.16, 44.07, 44.10, 58.97, 70.67, 70.68, 78.55, 78.58,

81.31, 81.32, 82.32, 82.53, 127.60, 127.67, 127.74, 127.87, 128.50, 138.32, 138.74, 142.49, 176.88.

Thiocarbonate derivative of 18: oil, ^1H NMR (CDCl_3) δ 0.85 (t, J = 6.5 Hz, 3H), 1.20–1.31 (m, 5H), 1.45 (m, 1H), 1.62 (m, 1H), 1.84 (m, 1H), 2.37 (dd, J = 15.5, 4.0 Hz, 1H), 2.59 (dd, J = 18.5, 2.5 Hz, 1H), 2.86 (dd, J = 18.0, 10.0 Hz, 1H), 2.89 (m, 1H), 3.16 (m, 1H), 3.41 (td, J = 7.0, 3.0 Hz, 1H), 4.26 (d, J = 12.0 Hz, 1H), 4.30 (m, 1H), 4.46 (d, J = 12.0 Hz, 1H), 5.18 (m, 1H), 5.65 (q, J = 7.0 Hz, 1H), 7.02–7.05 (m, 2H), 7.22–7.40 (m, 12H); ^{13}C NMR (CDCl_3) δ 14.22, 22.72, 25.69, 31.74, 31.84, 35.12, 37.05, 38.44, 38.47, 43.91, 56.06, 56.09, 70.67, 70.69, 81.25, 83.03, 83.07, 89.23, 89.26, 121.94, 121.95, 126.82, 127.62, 127.69, 127.87, 127.89, 128.50, 129.69, 137.45, 137.47, 138.69, 142.72, 153.37, 176.19, 194.42.

Lactone 19: oil, IR (neat) 756, 1163, 1770, 2931 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.85 (t, J = 7.0 Hz, 3H), 1.20–1.30 (m, 5H), 1.44 (m, 1H), 1.62 (m, 1H), 1.79–1.98 (m, 2H), 2.01 (m, 1H), 2.24 (m, 1H), 2.39 (m, 1H), 2.46 (d, J = 18.0 Hz, 1H), 2.73–2.89 (m, 3H), 4.24 (d, J = 12.0 Hz, 1H), 4.27 (dd, J = 7.5, 5.5 Hz, 1H), 4.44 (d, J = 12.0 Hz, 1H), 5.09 (td, J = 7.0, 3.5 Hz, 1H), 7.17–7.19 (m, 2H), 7.26–7.35 (m, 7H); ^{13}C NMR (CDCl_3) δ 14.23, 22.73, 25.75, 31.85, 32.45, 33.80, 34.67, 38.51, 38.52, 47.18, 47.20, 51.42, 70.57, 81.34, 86.00, 127.28, 127.33, 127.63, 127.87, 128.48, 138.82, 141.22, 141.72, 141.74, 177.12; HRMS (FAB) Found: 393.2430. Calcd for $\text{C}_{26}\text{H}_{33}\text{O}_3$, $[\text{M}+\text{H}]^+ = 393.2430$; $[\alpha]_{\text{D}}^{25} = +33$ ($c = 2.7$, CHCl_3).

Carboxylic acid 20: oil, IR (neat) 733, 1454, 1708, 3425 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.84 (t, $J = 7.0$ Hz, 3H), 1.21–1.28 (m, 5H), 1.43 (m, 1H), 1.59–1.89 (m, 7H), 1.93 (m, 1H), 2.01 (m, 1H), 2.07–2.18 (m, 2H), 2.20–2.32 (m, 4H), 2.92 (dt, $J = 11.5, 9.0$ Hz, 1H), 4.25 (dd, $J = 12.0, 2.5$ Hz, 1H), 4.26 (m, 1H), 4.35 (t, $J = 4.0$ Hz, 1H), 4.45 (dd, $J = 12.0, 2.5$ Hz, 1H), 5.29–5.43 (m, 2H), 7.18–7.19 (m, 2H), 7.24–7.25 (m, 2H), 7.30–7.34 (m, 5H); ^{13}C NMR (CDCl_3) δ 14.25, 22.75, 24.68, 25.23, 25.80, 26.59, 31.88, 32.55, 33.31, 34.02, 38.33, 38.41, 48.32, 54.12, 54.14, 70.46, 74.27, 74.31, 81.50, 127.06, 127.08, 127.58, 127.71, 127.95, 128.46, 129.43, 129.79, 138.90, 140.58, 140.64, 144.21, 178.51, 178.57; HRMS (FAB) Found: 477.3008. Calcd for $\text{C}_{31}\text{H}_{41}\text{O}_4$, $[\text{M}-\text{H}]^- = 477.3005$; $[\alpha]_{\text{D}}^{25} = +69$ ($c = 1$, CHCl_3).

AH13205: oil, IR (neat) 1708, 1735, 3386 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.85–0.88 (m, 3H), 1.07–1.94 (m, 19H), 2.22–2.34 (m, 5H), 2.51 (dd, $J = 15.5, 10.0$ Hz, 1H), 2.95 (m, 1H), 4.67 (t, $J = 7.0$ Hz, 1H), 7.23–7.25 (m, 2H), 7.30–7.32 (m, 2H); ^{13}C NMR (CDCl_3) δ 14.23, 22.76, 24.60, 24.67, 26.43, 26.46, 28.19, 28.73, 28.85, 28.90, 30.50, 31.87, 33.75, 38.50, 39.09, 48.91, 49.02, 55.68, 55.90, 74.74, 126.58, 127.39, 127.41, 142.58, 143.29, 143.37, 177.23, 219.95; HRMS (FAB) Found: 387.2536. Calcd for $\text{C}_{24}\text{H}_{35}\text{O}_4$, $[\text{M}-\text{H}]^- = 387.2535$; $[\alpha]_{\text{D}}^{25} = -30$ ($c = 0.1$, CHCl_3).

Figure S1. ^1H NMR spectrum of **18**

Figure S2. ^{13}C NMR spectrum of **18**

Figure S3. ^1H NMR spectrum of the deacetylated derivative of **18**

Figure S4. ^{13}C NMR spectrum of the deacetylated derivative of **18**

Figure S5. ^1H NMR spectrum of the thiocarbonate derivative of **18**:

174

Figure S6. ^{13}C NMR spectrum of the thiocarbonate derivative of **18**:

Figure S7. ^1H NMR spectrum of **19**

Figure S8. ^{13}C NMR spectrum of **19**

7

Figure S10. ^{13}C NMR spectrum of **20**

Figure S11. ^1H NMR spectrum of AH13205

Figure S12. ^{13}C NMR spectrum of **18**

Assignment of Absolute Stereochemistry of **8** and **9**

The isomer of **8** that moves faster on silica gel was subjected to the arylation reaction as shown in Scheme S1. At that time, the absolute configurations of the 2 and 3 positions were not known. Anhydrous cobalt(II) chloride (6.5 mg, 0.05 mmol) was placed in a 20-mL reaction flask and was dried in vacuo with heating. Anhydrous THF (2 mL) and (*R,R*)-**1** (20 mg, 0.12 mmol) were sequentially added under argon. The mixture was stirred for 3 min at room temperature. The faster moving isomer of **8** (305 mg, 1.0 mmol in 1.0 mL of THF) was added. 4-(*tert*-Butyldimethylsilyloxy)phenylmagnesium bromide (0.81 M THF solution, 1.5 mL, 1.2 mmol) was then added to the reaction mixture at 0 °C. After being stirred for 15 min at 25 °C, the reaction mixture was poured into saturated ammonium chloride solution. The products were extracted with ethyl acetate (20 mL × 2). The combined organic layer was dried over Na₂SO₄ and concentrated. Silica gel column purification (5% ether in hexane) of the crude product provided the corresponding arylated product (**9e**, 228 mg, 0.53 mmol) in 53% isolated yield. The product consisted of two isomers in a ratio of 95:5. The mixture of the two isomers was purified again on silica gel to isolate the major isomer of **9e**. At this stage, we had no stereochemical information.

A solution of the major isomer of **9e** (173 mg, 0.40 mmol) in THF (2 mL) was placed in a 20-mL flask. Tetrabutylammonium fluoride (1.0 M in THF, 0.48 mL, 0.48 mmol) was added dropwise to the reaction mixture at 0 °C. After being stirred for 1 h at the room temperature, the mixture was poured into water. The products were extracted

with ethyl acetate (10 mL $\times$ 2). The organic layer was dried and concentrated. The oil was chromatographed on silica gel (hexane / ethyl acetate = 5:1) to yield **9f** (120 mg, 0.38 mmol, 95% yield). X-ray quality crystals were grown from CH₂Cl₂/hexane. The absolute configuration of **9f**, (2*R*,3*R*), was unambiguously determined by X-ray crystallographic analysis (Figure S13). Crystallographic data for the structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 279680). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: 44-1223-3360033 or E-mail: deposit@ccdc.cam.ac.uk

The absolute stereochemistry of the major isomer of **9e** was found to be (2*R*,3*R*). Bromoetherification always proceeds in an *anti* manner. Thus we could inversely determined that the faster moving **8** has (2*R*,3*S*) configuration. The arylation reaction proved to proceed, avoiding the alkoxy group on the tetrahydrofuran ring.

Scheme S1. Determination of the absolute stereochemistry of acetals **8** and **9**

Figure S13. ORTEP Diagram of **(2R,3R)-9f**. Most hydrogen atoms are omitted for clarity.

(2*R*,3*R*)-**9e**: oil, IR (neat) 918, 1026, 1510, 2929 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.18 (6H, s), 0.86 (d, $J = 7.0$ Hz, 3H), 0.86 (d, $J = 7.0$ Hz, 3H), 0.91 (d, $J = 7.0$ Hz, 3H), 0.97 (s, 9H), 1.23-1.44 (m, 4H), 1.52-1.57 (m, 2H), 1.87-1.91 (m, 3H), 1.97 (m, 1H), 2.44 (m, 1H), 3.23 (ddd, $J = 8.0, 5.5, 1.5$ Hz, 1H), 3.73 (td, $J = 8.0, 3.5$ Hz, 1H), 4.00 (q, $J = 8.0$ Hz, 1H), 4.06 (td, $J = 8.0, 5.5$ Hz, 1H), 5.08 (d, $J = 1.5$ Hz, 1H), 6.75-6.78 (m, 2H), 7.06-7.09 (m, 2H); ^{13}C NMR (CDCl_3) δ -4.24, 17.92, 18.36, 19.86, 20.10, 21.28, 25.86, 25.91, 27.72, 30.71, 33.13, 35.99, 47.91, 50.87, 61.10, 71.92, 106.59, 120.17, 128.28, 135.56, 154.30; Found: C, 72.42; H, 10.00%. Calcd for $\text{C}_{26}\text{H}_{44}\text{O}_3\text{Si}$: C, 72.17; H, 10.25%.

(2*R*,3*R*)-**9f**: crystal, IR (nujol) 740, 1022, 1265, 1515, 2929, 3346 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.86 (d, $J = 7.0$ Hz, 3H), 0.86 (d, $J = 7.0$ Hz, 3H), 0.90 (d, $J = 7.0$ Hz, 3H), 1.23-1.43 (m, 5H), 1.52-1.57 (m, 2H), 1.87-1.95 (m, 2H), 1.97 (m, 1H), 2.45 (m, 1H), 3.24 (ddd, $J = 8.0, 5.0, 2.0$ Hz, 1H), 3.74 (td, $J = 8.0, 5.5$ Hz, 1H), 4.02 (q, $J = 8.0$ Hz, 1H), 4.08 (td, $J = 8.0, 5.0$ Hz, 1H), 5.09 (d, $J = 2.0$ Hz, 1H), 5.12 (brs, 1H), 6.76 (m, 2H), 7.09 (m, 2H); ^{13}C NMR (CDCl_3) δ 17.89, 19.84, 20.05, 21.26, 25.91, 27.70, 30.68, 33.13, 35.96, 47.88, 50.76, 67.11, 72.03, 106.57, 115.51, 128.55, 134.98, 154.37; Found: C, 75.15; H, 9.69%. Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_3$: C, 75.43; H, 9.50%. m.p. 90–93 $^\circ\text{C}$.