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Supporting Information

Asymmetric Iodocyclization Catalyzed by Salen–Cr (?)Cl : its Synthetic Application to Swainsonine

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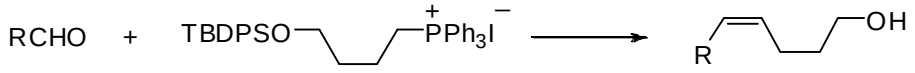
General Experimental

NMR spectra were obtained on Bruker AVANCE 400 spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) and measured in $CDCl_3$. Chemical shifts were recorded in ppm relative to internal standard $CDCl_3$, and coupling constants were reported in Hz. The high resolution mass spectra were recorded on VG Autospec Ultima spectrometer. The enantioselectivities were determined by HPLC or GC analysis. HPLC measurements were done on a RAININ model equipped with SD-200 pump, DVW-100 detector (D-Star Instruments) measured at 254 nm, and chiral column such as DAICEL OD-H and DAICEL AD-H. Eluting solvent was a mixture of 2-propanol and hexane. GC was measured on Donam DS-6200 GC with CHIRALDEX B-DM. All reactions were carried out in oven-dried glassware under a N_2 atmosphere. While toluene employed in the iodo-cyclization was used directly from the stock bottle (Junsei, EP grade) without purification, all other solvents were distilled from the indicated drying reagents right before use: Et_2O and THF (Na, benzophenone), CH_2Cl_2 (P_2O_5) and MeCN (CaH_2). The normal work-up included extraction, drying over Na_2SO_4 and evaporation of volatile materials *in vacuo*. Purifications by column chromatography were performed using Merck silica gel 60 (230 ~ 400 mesh).

I. Synthesis of γ-Hydroxy-*cis*-alkenes 9 and 11-19

- Alkenes **9, 11** and **13-17**



43

9 : R = $(CH_2)_2Ph$ **15** : R = *n*-Pr
11 : R = CH_2Ph **16** : R = *i*-Pr
13 : R = Me **17** : R = *i*-Bu
14 : R = Et

To the known phosphonium salt **43** (2.74 g, 3.91 mmol) in a mixture of THF (16 mL) and HMPA (4 mL) was added *n*-BuLi (2.5 M in hexane, 1.64 mL, 4.11 mmol) at 0 ^{o}C, and the mixture was stirred at room temperature for 20 minutes. After injecting cinnamaldehyde (500 mg, 3.73 mmol) in THF (3 mL) to the generated ylid at 0 ^{o}C, the reaction mixture was reacted at room temperature for 2 hours, and then quenched with saturated aqueous NH_4Cl (10 mL). Work-up with Et_2O (10 mL × 3) gave the crude olefin. The crude olefin in THF (5 mL) was desilylated with TBAF (2.73 M in THF, 2 mL, 5.46 mmol) at room temperature for 8 hours, and subsequently the reaction was quenched with saturated aqueous NH_4Cl (10

mL). Work-up with Et_2O (10 mL × 3) and chromatographic purification (EtOAc/hexane = 1/5) furnished the desired alkene **9** (570 mg, 80 % from cinnamaldehyde).

For **9**: ^{1}H NMR (400 MHz, $CDCl_3$) d 7.28 – 7.14 (2H, m), 7.18 – 7.14 (3H, m), 5.46 – 5.34 (2H, m), 3.55 (2H, t, *J* = 6.5 Hz), 2.65 (2H, t, *J* = 7.6 Hz), 2.39 – 2.33 (2H, m), 2.07 – 2.01 (2H. m), 1.56 – 1.49 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 142.0, 129.7, 129.5, 128.5, 128.2, 125.8, 62.5, 35.9, 32.4, 29.1, 23.5; HRMS (EI) calcd for $C_{13}H_{18}O$: 190.1358, found: 190.1356.

Alkenes **11** and **13-17** were prepared similarly in 57%, 48 %, 46 %, 64 %, 77 %, and 48 % yields, respectively, from the corresponding aldehydes. In the case of **13** and **14**, somewhat lower yields were obtained due to their lower boiling points.

For **11**: ^{1}H NMR (400 MHz, $CDCl_3$) d 7.28 – 7.24 (2H, m), 7.18 –7.15(3H, m), 5.61 – 5.58 (1H, m), 5.57 – 5.50 (1H, m), 3.66 (2H, t, *J* = 6.4 Hz), 3.40 (2H, d, *J* = 7.1 Hz), 2.26 – 2.21 (2H, q, *J* = 7.27 Hz), 1.70 – 1.63 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 140.9, 129.9, 128.8, 128.4, 128.2, 125.8, 62.4, 33.4, 32.5, 23.5; HRMS (EI) calcd for $C_{12}H_{16}O$: 176.1201, found: 176.1238.

For **13**: ^{1}H NMR (400 MHz, $CDCl_3$) d 5.46 – 5.36 (2H, m), 3.63 (2H, t, *J* = 6.5 Hz), 2.14 – 2.08 (2H, m), 1.65 – 1.59 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 129.8, 124.5, 62.6, 32.4, 23.2, 12.7; HRMS (EI) calcd for $C_6H_{12}O$: 100.0888, found: 100.0899.

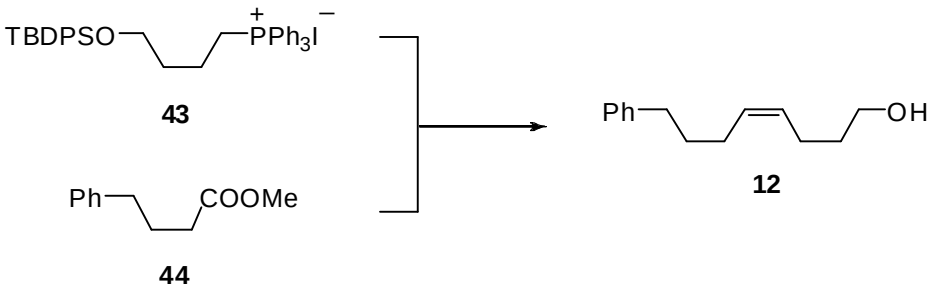
For **14**: ^{1}H NMR (400 MHz, $CDCl_3$) d 5.41 – 5.28 (2H, m), 3.62 (2H, t, *J* = 6.5 Hz), 2.11 – 2.01 (4H, m), 1.64 – 1.57 (2H, m), 0.93 (3H, t, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) d 132.4, 128.2, 62.6, 32.6, 23.4, 20.4, 14.3; HRMS (EI) calcd for $C_7H_{14}O$: 114.1045, found: 114.1042.

For **15**: ^{1}H NMR (400 MHz, $CDCl_3$) d 5.40 – 5.31 (2H, m), 3.61 (2H, t, *J* = 6.6 Hz), 2.11 – 2.08 (2H, m), 2.01 – 1.96 (2H, m), 1.63 – 1.56 (2H, m), 1.38 – 1.29 (2H, m), 0.87 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) d 130.5, 129.0, 62.5, 32.6, 29.2, 23.5, 22.8, 13.7; HRMS (EI) calcd for $C_8H_{16}O$: 128.1201, found: 128.1204.

For **16**: ^{1}H NMR (400 MHz, $CDCl_3$) d 5.23 – 5.20 (2H, m), 3.64 (2H, t, *J* = 6.5 Hz), 2.63 – 2.57 (1H, m), 2.11 (2H, td, *J* = 7.4, 5.9 Hz), 1.64 – 1.57 (2H, m), 0.92 (6H, d, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) d 138.3, 126.4, 62.7, 32.8, 26.4, 23.7, 23.2; HRMS (EI) calcd for $C_9H_{18}O$: 142.1358, found: 142.1361.

For **17**: ^{1}H NMR (400 MHz, $CDCl_3$) d 5.39 – 5.37 (2H, m), 3.64 – 3.60 (2H, t, *J* = 6.5 Hz), 2.11 – 2.06 (2H, q, *J* = 7.2 Hz), 1.91 – 1.88 (2H, t, *J* = 6.6 Hz), 1.63 – 1.54 (3H, m), 0.87 (6H, d, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) d 129.5, 129.4, 62.6, 36.3, 32.6, 28.6, 23.6, 22.3; HRMS (EI) calcd for $C_9H_{18}O$: 142.1358, found: 142.1321.

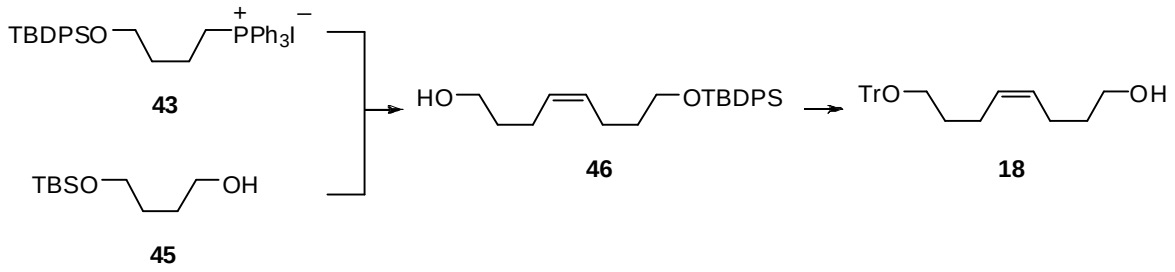
o Alkenes **12**



At –78 ^{o}C, DIBAL (1.5 M in PhMe, 4.3 mL, 6.45 mmol) was injected to ester **44** (1.05 g, 5.89 mmol) in CH_2Cl_2 (10 mL), and stirred for 2 hours. After quenching the reaction with MeOH (3 mL) at –78 ^{o}C, saturated potassium sodium tartrate (5 mL) was added. Work-up with Et_2O (10 mL × 3) yielded the crude aldehyde. The ylid was generated by treating **43** (4.33 g, 6.18 mmol) in a mixture of THF (10 mL) and HMPA (7 mL) with *n*-BuLi (2.5 M in hexane, 2.72 mL, 6.80 mmol) at 0 ^{o}C for 20 minutes, and reacted with the prepared aldehyde in THF (3 mL) at 0 ^{o}C for 1 hour. Quenching the reaction with saturated aqueous NH_4Cl (10 mL) and the subsequent work-up with Et_2O (10 mL × 3) gave rise to the crude alkene. It was dissolved in THF (5 mL) and desilylated with TBAF (2.73 M in THF, 2.71 mL, 7.40 mmol) at room temperature for 8 hours. Aqueous work-up with Et_2O (10 mL × 3) and chromatographic separation (EtOAc /hexane = 1/5) afforded alkene **12** (1.03 g, 86 % from **44**).

For **12**: ^{1}H NMR (400 MHz, $CDCl_3$) d 7.28 – 7.24 (2H, m), 7.18 – 7.15 (3H, m), 5.46 – 5.36 (2H, m), 3.62 (2H, t, *J* = 6.5 Hz), 2.61 (2H, t, *J* = 7.8 Hz), 2.11 – 2.01 (4H, m), 1.71 – 1.57 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 142.4, 130.1, 129.4, 128.4, 128.2, 125.6, 62.6, 35.4, 32.6, 31.3, 26.7, 23.6; HRMS (EI) calcd for $C_{14}H_{20}O$: 204.1514, found: 204.1511.

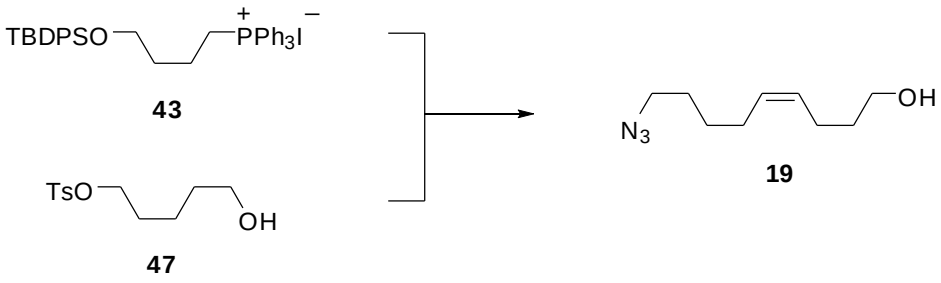
o Alkenes **18**



At –78 °C, DMSO (1.04 mL, 14.66 mmol) was added dropwise to oxalyl chloride (0.64 mL, 7.34 mmol) in CH_2Cl_2 (8 mL), stirred for 20 minutes, and alcohol **45** (500 mL, 2.45 mmol) in CH_2Cl_2 (3 mL) was injected. After stirring the mixture at –78 °C for 20 minutes, Et_3N (3.41 mL, 24.47 mmol) was added. The reaction proceeded at –78 °C for 10 minutes and 0 °C for 10 minutes, and was quenched with saturated aqueous NH_4Cl (10 mL). Work-up with Et_2O (10 mL × 3) afforded the crude aldehyde. The ylid from **43** (1.93 g, 2.75 mmol) was generated in a mixture of THF (7 mL) and HMPA (3 mL) by treatment with *n*-BuLi (2.5 M in hexane, 1.1 mL, 2.75 mmol) at 0 °C for 20 minutes, and room temperature for 1 hour. After quenching the reaction with saturated aqueous NH_4Cl (10 mL), normal work-up with Et_2O (10 mL × 3) yielded the crude disilyl ether. Its desilylation was performed with PPTS (10 mg) in EtOH (5 mL) at room temperature for 20 hours, and quenched with K_2CO_3 (20 mg). Work-up with EtOAc (5 mL × 3) and chromatographic separation (EtOAc/hexane = 1/4) provided alcohol **46** (482 mg, 52 % from **45**). **46** (482 mg, 1.26 mmol) was reacted with trityl chloride (629 mg, 2.26 mmol) in the presence of 4-dimethylaminopyridine (7 mg) in a mixture of Et_3N (1 mL) and CH_2Cl_2 (3 mL) at room temperature for 8 hours. After work-up with Et_2O (10 mL × 3) and chromatographic purification (Et_2O/hexane = 1/2) produced alcohol **18** (414 mg, 85 % from **46**).

For **18**: ^{1}H NMR (400 MHz, $CDCl_3$) d 7.44 – 7.42 (6H, m), 7.30 – 7.19 (9H, m), 5.38 – 5.29 (2H, m), 3.59 (2H, t, *J* = 6.5 Hz), 3.05 (2H, t, *J* = 6.5 Hz), 2.15 – 2.10 (2H, m), 2.09 – 2.07 (2H, m), 1.70 – 1.63 (2H, m), 1.60 – 1.53 (2H, m), 0.99 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) d 144.4, 130.0, 129.3, 128.7, 127.7, 126.8, 86.3, 63.1, 62.6, 32.5, 30.1, 24.0, 23.5; HRMS (EI) calcd for $C_{27}H_{30}O$: 386.2246, found: 386.2245.

- Alkene **19**



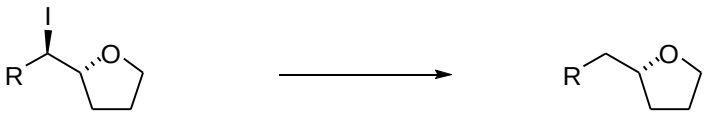
To **47** (240 mg, 0.93 mmol) dissolved in CH_2Cl_2 (2 mL) were added celite (0.5 g) and PCC (307 mg, 1.39 mmol) at room temperature. After stirring the mixture at room temperature for 1 hour, it was filtered through a short column of silica gel (2 g) with a 1 : 1 mixture of EtOAc and hexane. Evaporation of the volatile materials in vacuo rendered the crude aldehyde. The phosphonium salt **43** (712 mg, 1.02 mmol) in a 4 : 1 mixture of THF and HMPA (2.5 mL) was deprotonated with *n*-BuLi (2.5 M in hexane, 0.4 mL, 1.0 mmol) at 0 ^oC for 20 minutes. The crude aldehyde in THF (1mL) was injected to the generated ylid at 0 ^oC and the mixture was stirred at room temperature for 30 minutes. After quenching the reaction with saturated aqueous NH_4Cl (3 mL), normal work-up with Et_2O (3 mL × 3) followed by column chromatography (EtOAc/hexane = 1/1) afforded the *cis*-alkene (333 mg, 65 % yield). NaN_3 (117 mg, 1.8 mmol) was added to the alkene in DMF (2 mL) at room temperature and the mixture was heated at 50 ^oC for 6 hours. After cooling down the mixture to room temperature, water (4 mL) was added. Normal work-up with Et_2O (3 mL × 3) and the subsequent chromatographic separation (Et_2O/hexane = 1/20) furnished the azide (233 mg, 92 % yield). The azide was desilylated with TBAF (75 wt % in H_2O, 0.4 mL, 1.1 mmol) in THF (2 mL) at room temperature for 3 hours. Normal work-up with Et_2O (3 mL × 3) and the following chromatographic purification (Et_2O/hexane = 1/2) gave the alcohol **19** (86 mg, 85 % yield).

For **19**: ^1H NMR (400 MHz, $CDCl_3$) d 5.37 – 5.33 (2H, m), 3.61 – 3.58 (2H, t, *J* = 6.5 Hz), 3.24 – 3.21 (2H, t, *J* = 6.9 Hz), 2.10 – 2.01 (2H, m), 1.62 – 1.53 (2H, m), 1.43 – 1.38 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 129.6, 129.65, 62.4, 51.3, 32.5, 28.3, 26.6, 26.5, 23.5; HRMS (EI) calcd for $C_9H_{17}N_3O$: 183.1372, found: 183.1367.

II. Determination of Absolute Configuration

After reductive deiodination of (*R*)-**10**, **21** and **24**–**26** from asymmetric iodocyclization, the absolute configuration was determined by comparing GC or HPLC chromatograms of the prepared tetrahydrofurans with those from the following synthetic routes. In the case of **27**, it was converted into benzoate **53**, and then reductively deiodinated. The resulting tetrahydrofuran was compared with the authentic sample in the same way as the above to corroborate the absolute configuration of **27**.

o Reductive deiodination of (*R*)-**10**, **21** and **24**–**26**



(*R*)-**10** : R = $(CH_2)_2Ph$ **25** : R = *i*-Pr
21 : R = $(CH_2)_3Ph$ **26** : R = *i*-Bu
24 : R = *n*-Pr

48 : R = $(CH_2)_2Ph$ **51** : R = *i*-Pr
49 : R = $(CH_2)_3Ph$ **52** : R = *i*-Bu
50 : R = *n*-Pr

Since the same procedure was applied to all the substrates, reductive deiodination of (*R*)-**10** is described as a representative. To (*R*)-**10** (260 mg, 0.82 mmol) in THF (2 mL) was added *n*-Bu_3SnH (0.41 mL, 1.52 mmol) and Et_3B (1.0 M in THF, 0.82 mL, 0.82 mmol) at –78 °C, in sequence, and stirred at –78 °C for 2 hours. After quenching the reaction with saturated aqueous KF (5 mL), work-up with Et_2O (5 mL × 3) and chromatographic separation (Et_2O/hexane = 1/20) provided **48** (140 mg, 90 %). Similarly, **49** was obtained in 96 % yield, while **50**–**52** were produced in 20~30 % yields due to the lower boiling points.

For **48**: ^{1}NMR (400 MHz, $CDCl_3$) d 7.28 – 7.24 (2H, m), 7.18 – 7.14 (3H, m), 3.86 – 3.75 (2H, m), 3.69 (1H, td, *J* = 7.9, 6.4 Hz), 2.65 – 2.61 (2H, m), 1.98 – 1.56 (6H, m), 1.53 – 1.36 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 142.5, 128.4, 128.2, 125.6, 79.2, 67.6, 35.9, 35.3, 31.3, 28.1, 25.7; HRMS (EI) calcd for $C_{13}H_{18}O$: 190.1358, found: 190.1361.

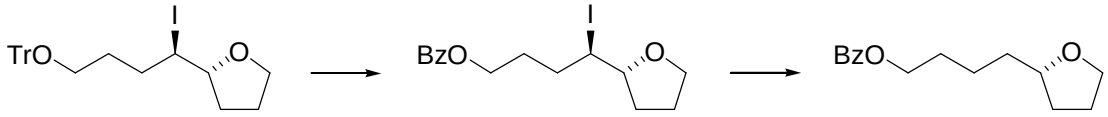
For **49**: ^{1}NMR (400 MHz, $CDCl_3$) d 7.29 – 7.24 (2H, m), 7.18 – 7.15 (3H, m), 3.84 (1H, td, *J* = 7.7, 6.3 Hz), 3.79 – 3.73 (1H, m), 3.69 (1H, td, *J* = 7.9, 6.4 Hz), 2.62 (2H, t, *J* = 7.8 Hz), 1.97 – 1.79 (3H, m), 1.67 – 1.56 (3H, m), 1.51 – 1.33 (4H, m); ^{13}C(100 MHz, $CDCl_3$) d 142.7, 128.4, 128.2, 125.6, 79.3, 67.6, 35.9, 35.6, 31.6, 31.4, 26.1, 25.7; HRMS (EI) calcd for $C_{14}H_{20}O$: 204.1514, found: 204.1505.

For **50**: ^{1}NMR (400 MHz, $CDCl_3$) d 3.84 (1H, td, *J* = 7.7, 6.3 Hz), 3.79 – 3.73 (1H, m), 3.69 (1H, td, *J* = 7.9, 6.4 Hz), 1.97 – 1.81 (3H, m), 1.59 – 1.27 (7H, m), 0.88 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) d 79.4, 67.6, 35.4, 31.4, 28.6, 25.7, 22.8, 14.0; HRMS (EI) calcd for $C_8H_{16}O$: 128.1201, found: 128.1214.

For **51**: ^{1}NMR (400 MHz, $CDCl_3$) d 3.86 – 3.80 (2H, m), 3.67 (1H, td, *J* = 7.9, 6.3 Hz), 1.96 – 1.89 (1H, m), 1.87 – 1.79 (2H, m), 1.73 – 1.65 (1H, m), 1.52 – 1.45 (1H, m), 1.42 – 1.33 (1H, m), 1.29 – 1.22 (1H, m), 0.89 (6H, dd, *J* = 6.6, 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) d 77.6, 67.5, 44.9, 31.8, 25.7, 25.6, 23.2, 22.5; HRMS (EI) calcd for $C_8H_{16}O$: 128.1201, found: 128.1205.

For **52**: ^{1}NMR (400 MHz, $CDCl_3$) d 3.85 – 3.81 (1H, m), 3.74 – 3.65 (2H, m), 1.99 – 1.90 (1H, m), 1.90 – 1.76 (2H, m), 1.60 – 1.45 (2H, m), 1.45 – 1.37 (2H, m), 1.35 – 1.22 (1H, m), 1.21 – 1.18 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 79.7, 67.6, 33.5, 31.3, 28.1, 25.7, 22.6 (2peaks). HRMS (EI) calcd for $C_9H_{18}O$: 142.2386, found: 142.2402.

o Reductive deiodination of **27** via **53**



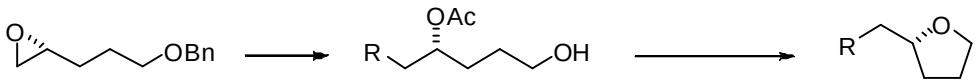
27 **53** **54**

27 (38 mg, 0.074 mmol) was hydrolyzed in MeOH (2 mL) in the presence of 1 M HCl (0.1 mL) at room temperature for 1 hour. After work-up with EtOAc (5 mL × 3), the crude alcohol was treated with benzoyl chloride (0.01 mL, 0.086 mmol) in a mixture of Et_3N (0.1 mL) and CH_2Cl_2 (1 mL) in the presence of DMAP (3 mg) at room temperature for 30 minutes. The reaction was quenched with saturated aqueous NH_4Cl (3 mL). Work-up with EtOAc (5 mL × 3) followed by chromatographic purification afforded **53** (22 mg, 79 %). **53** was reductively deiodinated under the same conditions as described for (*R*)-**10** to furnish **54** (11 mg, 75 %).

For **53**: ^{1}NMR (400 MHz, $CDCl_3$) d 8.02 – 8.00 (2H, m), 7.56 – 7.52 (1H, m), 7.44 – 7.40 (2H, m), 4.35 – 4.31 (2H, m), 4.15 – 4.10 (1H, m), 3.94 (1H, td, *J* = 8.2, 6.8 Hz), 3.81 (1H, td, *J* = 7.8, 5.8 Hz), 3.71 (1H, td, *J* = 7.2, 4.6 Hz), 2.14 – 1.84 (7H, m), 1.74 – (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 166.5, 132.9, 130.2, 129.5, 128.3, 82.3, 69.0, 64.0, 41.3, 33.2, 30.9, 29.1, 26.1; HRMS (EI) calcd for $C_{15}H_{19}IO_3$: 374.0379, found: 374.0376.

For **54**: ^{1}H NMR (400 MHz, $CDCl_3$) d 8.03 – 8.00 (2H, m), 7.54 – 7.39 (3H, m), 4.30 (2H, t, *J* = 6.6 Hz), 3.86 – 3.75 (2H, m), 3.69 (1H, td, *J* = 7.9, 6.5 Hz), 2.01 – 1.90 (1H, m), 1.89 – 1.75 (4H, m), 1.65 – 1.38 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) d 166.6, 132.7, 130.4, 129.5, 128.3, 79.1, 67.6, 64.9, 35.3, 31.4, 28.8, 25.6, 22.9; HRMS (EI) calcd for $C_{15}H_{20}O_3$: 248.1413, found: 248.1415.

o Synthesis of the authentic tetrahydrofurans (*S*)-**48** – (*S*)-**52**.



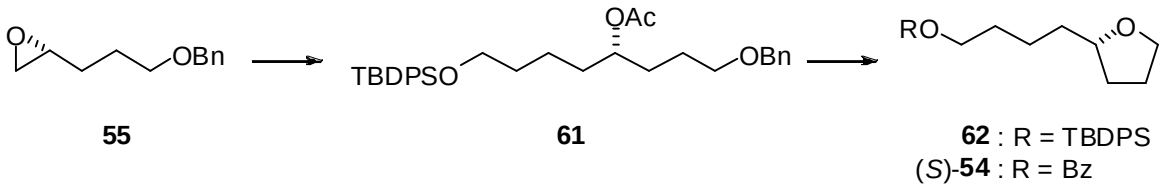
55

56 : R = $(CH_2)_2Ph$ **59** : R = *i*-Pr (*S*)-**48** : R = $(CH_2)_2Ph$ (*S*)-**51** : R = *i*-Pr
57: R = $(CH_2)_3Ph$ **60** : R = *i*-Bu (*S*)-**49** : R = $(CH_2)_3Ph$ (*S*)-**52** : R = *i*-Bu
58 : R = *n*-Pr (*S*)-**50** : R = *n*-Pr

Since the authentic compounds (*S*)-**48** – (*S*)-**52** were prepared from the known epoxide **55** using the corresponding Grignard reagents by the identical procedure, synthesis of (*S*)-**48** is described as a representative. **55** (77 mg, 0.40 mmol) was dissolved in Et_2O (2 mL) in the presence of $CuBr{\cdot}SMe_2$ (34 mg, 0.17 mmol). To the resulting solution was added $PhCH_2CH_2MgBr$ (0.73 M in THF, 2.0 mL, 1.46 mmol) at –40 ^oC. The reaction mixture was stirred at –40 ^oC to –30 ^oC for 1 hour, and quenched with saturated aqueous NH_4Cl (5 mL). Work-up with Et_2O (5 mL × 3) followed by chromatographic purification (EtOAc/hexane = 1/5) gave the desired alcohol (114 mg, 95 %). The alcohol (114 mg, 0.38 mmol) reacted with Ac_2O (0.11 mL, 1.17 mmol) in CH_2Cl_2 (3 mL) in the presence of Et_3N (0.5 mL) at room temperature for 4 hours. The reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL). After work-up with Et_2O (5 mL × 3), the crude product was purified to afford the expected acetate (120 mg, 92 %). Debenzylation of the acetate (120 mg, 0.35 mmol) was carried out under H_2 atmosphere (1 atm) using 10 % Pd/C (20 mg) in EtOH (2 mL) at room temperature for 8 hours. The reaction mixture was filtered though celite, the volatile materials were evaporated under reduced pressure, and the residue was separated by column chromatography (EtOAc/hexane = 1/1) to furnish alcohol **56** (72 mg, 82 %). **56** (72 mg, 0.29 mmol) was tosylated with TsCl (80 mg, 0.42 mmol) in CH_2Cl_2 (2 mL) and Et_3N (0.5 mL) in the presence of DMAP (5 mg) at room temperature for 4 hours. The reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL). After work-up with Et_2O (5 mL × 3), the residue was purified by column chromatography (EtOAc/hexane = 1/3) to provide tosylate (110 mg, 95 %). The tosylate (110 mg, 0.27 mmol) was cyclized with K_2CO_3 (56 mg, 0.41 mmol) in MeOH (2 mL) and H_2O (0.1 mL) at room temperature for 8 hours. Work-up with saturated aqueous NH_4Cl (5 mL) and Et_2O (5 mL × 3) and the following chromatographic separation (EtOAc/hexane = 1/30) produced tetrahydrofuran (*S*)-**48** (39 mg, 75 %).

By the similar synthetic route, (*S*)-**49** was produced in 51 % overall yield, while (*S*)-**50**, (*S*)-**51** and (*S*)-**52** were obtained in about 20 % overall yields due to their low boiling points.

o Synthesis of the authentic tetrahydrofuran (*S*)-**54**.



55 **61** **62** : R = TBDPS
(*S*)-**54** : R = Bz

After mixing 3-butenylmagnesium bromide (0.5 M, 3.7 mL, 1.85 mmol) with CuCN (85 mg, 0.95 mmol) at –40 ^{o}C for 30 minutes, epoxide **55** (90 mg, 0.47 mmol) in THF (1.5 mL) was added to the mixture and warmed up to 0 ^{o}C for 2 hours. The reaction mixture was quenched with saturated aqueous NH_4Cl (5 mL) and 10 % NH_4OH (5 mL). Work-up with Et_2O (5 mL × 3) and the subsequent chromatographic purification (EtOAc/hexane = 1/4) generated alcohol (99 mg, 85 %). The alcohol (99 mg, 0.4 mmol) was acetylated by the same procedure as described in the synthesis of (*S*)-**48** to afford acetate (109 mg, 94 %). The acetate (109 mg, 38 mmol) in MeOH (3 mL) was exposed to ozone at –78 ^{o}C for a few minutes and reduced by $NaBH_4$ (29 mg, 0.77 mmol) at –78 ^{o}C to 0 ^{o}C for 30 minutes. Work-up with saturated aqueous NH_4Cl and EtOAc (5 mL × 3) followed by chromatographic separation (EtOAc/hexane = 1/2) furnished alcohol (90 mg, 81 %). The alcohol (90 mg, 0.31 mmol) reacted with TBDPSCl (0.12 mL, 0.46 mmol) in CH_2Cl_2 (1 mL) and Et_3N (0.2 mL) at room temperature for 2 hours. Work-up with saturated aqueous NH_4Cl (5 mL) and Et_2O (5 mL × 3), and the following chromatographic purification (EtOAc/hexane = 1/15) gave acetate **61** (152 mg, 93 %). **61** (152 mg, 0.29 mmol) was debenzylated under H_2 atmosphere (1 atm) in MeOH (2 mL) in the presence of 20 % $Pd(OH)_2/C$ (15 mg) at room temperature 8 hours. The reaction mixture was filtered through celite, and evaporated *in vacuo*. The crude primary alcohol was treated with MsCl (0.04 mL, 0.52 mmol) in CH_2Cl_2 (1 mL) and Et_3N (0.3 mL) at 0 ^{o}C to room temperature for 1 hour. Work-up with saturated aqueous NH_4Cl (5 mL) and Et_2O (5 mL × 3), and the subsequent chromatographic purification (EtOAc/hexane = 1/5) provided mesylate (132 mg, 89 % from **61**). The mesylate (132 mg, 0.25 mmol) was cyclized with K_2CO_3 (53 mg, 0.38 mmol) in MeOH (2 mL) at room temperature for 8 hours. After work-up with saturated aqueous NH_4Cl (5 mL) and Et_2O (5 mL × 3), the crude product was purified by column chromatography (EtOAc/hexane = 1/20) to give rise to **62** (88 mg, 91 %). **62** (88 mg, 0.23 mmol) was desilylated with TBAF (2.73 M in THF, 0.16 mL, 0.44 mmol) in THF (2 mL) at room temperature for 8 hours. Work-up with saturated aqueous NH_4Cl (3 mL) and Et_2O (5 mL × 3) afforded the crude alcohol. The crude alcohol was benzoylated with Bz_2O (90 %, 80 mg, 0.32 mmol) in a mixture of Et_3N (0.5 mL) and CH_2Cl_2 (3 mL) in the presence of DMAP (5 mg) at room temperature for 4 hours. After quenching the reaction with saturated aqueous NH_4Cl (3 mL), work-up with Et_2O (5 mL × 3) followed by chromatographic separation (EtOAc/hexane = 1/5) furnished (*S*)-**54** (49 mg, 86 %).