Stereoselective Synthesis of Cytotoxic Marine Metabolite Harzialactone A by Three Different Routes¹

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Abstract: The cytotoxic marine metabolite harzialactone A has been synthesized stereoselectively starting from phenylacetaldehyde through three different routes. The key steps were: in the first approach Sharpless asymmetric dihydroxylation, in the second approach diastereoselective iodo carbonate preparation, and in the third approach Jacobsen's hydrolytic kinetic resolution. In all these three schemes the triol was successfully converted into the lactone by using highly chemoselective oxidation with TEMPO and (diacetoxyiodo)benzene.

Key words: harzialactone A, stereoselective synthesis, Maruoka allylation, Sharpless asymmetric dihydroxylation, stereoselective iodo carbonate preparation, Jacobsen's hydrolytic kinetic resolution

Bioactive compounds from marine organisms have attracted much attention in recent years due to their interesting structural features and important biological properties.² Harzialactone A (1), a marine metabolite, was isolated from the culture broth of a strain of *Trichoderma harianium* OUPS-N115;³ it showed cytotoxicity against cultured P388 cells.³ The absolute configuration (3R,5R) of harzialactone A (1) was established by its synthesis from D-glucose and D-xylose.⁴ A few other syntheses of compound 1 have also been reported⁵ but in some cases the long synthetic steps and the low overall yields are the problem. The synthesis of compounds related to harzialactone A have also currently attracted the attention of organic chemists.⁶

In continuation of our recent work⁷ on the stereoselective synthesis of bioactive compounds, we have developed an efficient short synthesis of harzialactone A (1) starting from readily available phenylacetaldehyde (2). The synthesis was achieved by three different routes. The retrosynthetic analysis (Scheme 1) indicates that 1 can be prepared from the triol 3 by selective oxidation and this triol 3 can be obtained from the homoallylic alcohol 4, generated from phenylacetaldehyde (2).

In the first approach (Scheme 2), phenylacetaldehyde (2) was subjected to an enantioselective Maruoka allylation⁸ using titanium complex (S,S)-I (Figure 1) and allyltributyltin to form the homoallylic alcohol **4**.^{7c} The hydroxyl group of 4 was protected as its TBS ether by treatment with tert-butyldimethylsilyl chloride in the presence of imidazole to afford 5. Compound 5 underwent Sharpless asymmetric dihydroxylation⁹ using β-admix at room temperature to give the diol 6 along with its diastereomer in the ratio 62:38 (favoring **6**) (total yield 86%). These two products (6 and its diastereomer) were separated by repeated column chromatography (silica gel, hexane-EtOAc, 1:1) to furnish pure 6 (yield 50%). Deprotection of the TBS group of 6 using 4-toluenesulfonic acid in methanol produced the desired triol. When the hydroxy group of 4 was not protected and the compound was directly subjected to Sharpless asymmetric dihydroxylation, compound 3 and its diastereomers were formed in almost equal amount and their separation was also difficult. However, from the TBS ether 5 it was convenient to obtain 3 in pure form. Finally, the chemoselective oxidation of this triol **3** with 2,2,6,6-tetramethylpiperidin-1-oxyl and excess (diacetoxyiodo)benzene afforded the target compound, harzialactone A (1). Monitoring of the reaction showed the initial formation of the intermediate lactol species, which then underwent further oxidation to the lactone.10

In the second approach (Scheme 3) the homoallylic alcohol **4** was treated with di*-tert*-butyl dicarbonate in the presence of 4-(dimethylamino)pyridine and triethylamine in acetonitrile to form the homoallylic *tert*-butyl carbonate **7** in high yield. The treatment of **7** with *N*-iodosuccinimide in acetonitrile at 0 °C afforded the diastereoselective iodo carbonate **8** (with required stereogenic center) as the sole product.¹⁰ The iodo carbonate **8** was subsequently reacted with potassium carbonate in methanol to produce the *syn*-epoxy alcohol **9**,¹¹ which on treatment



Scheme 1 Retrosynthetic analysis of harzialactone A (1)

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Scheme 2 Synthesis of harzialactone A (1). *Reagents and conditions*: (a) (*S*,*S*)-**I** (10 mol%), Bu₃SnCH₂CH₂CH₂-CH₂Cl₂, -15 to 0 °C, 15 h, 84.5%; (b) TBSCl, imidazole, CH₂Cl₂, 0 °C to r.t., 2 h, 92%; (c) β-admix, *t*-BuOH–H₂O, 12 h, 86% (total), 50% (**6**); (d) PTSA, MeOH, 0 °C to r.t., 1 h, 95%; (e) TEMPO, PhI(OAc)₂, CH₂Cl₂, 0 °C to r.t., 5 h, 74%.



(S,S)-Salen-Co(III)-OAc complex

Figure 1

with *tert*-butyldiphenylsilyl chloride using imidazole and 4-(dimethylamino)pyridine furnished the TBDPS-protected epoxide **10**. The hydroxy group of **9** could also be protected as TBS ether but the yields in the subsequent

steps were found to be somewhat lower. The acid-catalyzed opening of the epoxide ring of **10** afforded the major product **11**, which was separated from its minor diastereomer by column chromatography (as discussed earlier). Deprotection of the TBDPS group of **11** using 4-toluenesulfonic acid in methanol furnished the triol **3** which was subsequently converted into harzialactone A (**1**) as outlined above in Scheme 2.

In the third approach (Scheme 4) the homoallylic alcohol **4** was treated with *tert*-butyldiphenylsilyl chloride in the presence of imidazole and 4-(dimethylamino)pyridine to produce the olefin **12**. The epoxidation of this compound **12** was carried out with 3-chloroperoxybenzoic acid to form the racemic epoxide **13**. This epoxide **13** underwent Jacobsen's hydrolytic kinetic resolution¹² by treatment with (*S*,*S*)-Salen–Co(III)–OAc complex and water to afford the diol **11** along with the less polar corresponding α -epoxide, which was separated by column chromatography. Deprotection of the TBDPS group of **11** using 4-toluenesulfonic acid in methanol yielded the triol **3** which was then converted into the desired molecule, harzialactone A (**1**) as discussed above.



Scheme 3 Synthesis of harzialactone A (1). *Reagents and conditions*: (a) Boc_2O , Et_3N , DMAP, CH_2Cl_2 , 0 °C to r.t., 2 h, 91%; (b) NIS, MeCN, -40 to 0 °C, 1.5 h, 89%; (c) K_2CO_3 , MeOH, r.t., 0.5 h, 91%; (d) TBDPSCl, imidazole, DMAP, CH_2Cl_2 , r.t., 3.5 h, 93%; (e) 5% HClO₄, H₂O-MeCN (1:3), r.t., 2 h, 71%; (f) TBAF, THF, 0 °C to r.t., 3.5 h, 89%; (g) TEMPO, PhI(OAc)₂, CH₂Cl₂, 0 °C to r.t., 5 h, 74%.



Scheme 4 Synthesis of harzialactone A (1). *Reagents and conditions*: (a) TBDPSCl, imidazole, DMAP, CH_2Cl_2 , r.t., 2 h, 94%; (b) MCPBA, CH_2Cl_2 , 0 °C to r.t., 6 h, 94%; (c) (*S*,*S*)-Salen–Co(III)–OAc (0.5 mol%), distilled H_2O (0.45 equiv), THF, 0 °C to r.t., 49%; (d) TBAF, THF, 0 °C to r.t., 3.5 h, 89%; (e) TEMPO, PhI(OAc)₂, CH₂Cl₂, 0 °C to r.t., 5 h, 74%.

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In conclusion we have developed the stereoselective synthesis of harzialactone A starting from phenylacetaldehyde through three different simple and efficient approaches.

TLC used silica gel F_{254} plates with the spots were examined under UV light and then developed by an I_2 vapor. Column chromatography was performed with silica gel (BDH 100–200 mesh). Solvents were purified according to standard procedures. The spectra were recorded with the following instruments; IR: Perkin-Elmer RX FT-IR spectrophotometer; NMR: Varian Gemini 200 MHz (¹H) and 50 MHz (¹³C) spectrometer; ESIMS: VG-Autospec micromass. Organic extracts were dried over anhyd Na₂SO₄. Optical rotations were measured with Jasco DIP 300 digital polarimeter at 25 °C.

(S)-1-Phenylpent-4-en-2-ol (4)

To a stirred soln of TiCl₄ (0.380 g, 2 mmol) in CH₂Cl₂ (30 mL) was added dried Ti(O*i*-Pr)₄ (1.716 g, 6 mmol) at 0 °C under a N₂ atmosphere and the mixture was allowed to warm to r.t.. After 1.5 h, Ag₂O (0.496 g, 4 mmol) was added and the reaction was continued for 6 h under exclusion of direct light. The mixture was diluted with CH₂Cl₂ (80 mL), treated with (*S*)-BINOL (2.184 g, 8 mmol) at r.t. for 2.5 h to furnish the chiral bis-Ti(IV) oxide (*S*,*S*)-**I**. This complex was cooled to -15 °C and treated sequentially with aldehyde **2** (2.40 g, 20 mmol) and allyltributyltin (17.21 g, 52 mmol) at the same temperature. The mixture was quenched with sat. aq NaHCO₃ (50 mL) and extracted with Et₂O (3 × 100 mL). The combined organic extracts were dried (anhyd Na₂SO₄). Evaporation of the solvents and purification of the residue by column chromatography (EtOAc–hexane, 1:9) gave pure **4** (2.74 g, 84.5%) as a colorless liquid.

 $[\alpha]_D^{32}$ +12.6 (*c* 1.2, CHCl₃).

IR (KBr): 3418, 1640, 1495, 1448 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.33–7.10 (m, 5 H), 5.83 (m, 1 H), 5.18–5.05 (m, 2 H), 3.78 (m, 1 H), 2.84–2.61 (m, 2 H), 2.38–2.10 (m, 2 H).

¹³C NMR (50 MHz, CDCl₃): δ = 138.4, 134.7, 129.4, 128.4, 126.4, 117.8, 71.7, 43.3, 41.1.

MS (ESI): $m/z = 163 [M + H]^+$.

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.17. Found: C, 81.38; H, 8.12.

(S)-4-(tert-Butyldimethylsiloxy)-5-phenylpent-1-ene (5)

Imidazole (0.680 g, 10 mmol) was added to a stirred soln of alcohol **4** (0.81 g, 5.0 mmol) in CH₂Cl₂ (10 mL). TBDCl (1.00 g, 6.5 mmol) was then added to this soln at 0 °C, and the mixture was stirred at r.t. for 2 h. The reaction was quenched with sat. aq NH₄Cl (5 mL) and extracted with CH₂Cl₂ (3 × 10 mL). The organic extracts were washed with brine, dried (Na₂SO₄), and then concentrated. Column chromatography of the crude product (silica gel, EtOAc–hexane, 20:1) provided **5** (1.27 g, 92%) as a colorless liquid.

 $[\alpha]_D^{32}$ +13.4 (*c* 1.4, CHCl₃).

IR (KBr): 3445, 1643, 1458, 1242 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.60–7.31 (m, 5 H), 6.11 (m, 1 H), 5.38–5.22 (m, 2 H), 4.05 (m, 1 H), 3.07–2.83 (m, 2 H), 2.54–2.40 (m, 2 H), 1.09 (s, 9 H), 0.20 (s, 6 H).

¹³C NMR (50 MHz, CDCl₃): δ = 138.2, 132.2, 128.1, 128.0, 127.8, 127.4, 126.2, 115.7, 72.4, 45.7, 42.8, 25.4, 18.2, -5.7.

MS (ESI): $m/z = 277 [M + H]^+$.

Anal. Calcd for C₁₇H₂₈O: C, 73.85; H, 10.21. Found: C, 73.78; H, 10.23.

(2*R*,4*R*)-4-(*tert*-Butyldimethylsiloxy)-5-phenylpentane-1,2-diol (6)

To a 100-mL round-bottomed flask were added *t*-BuOH (15 mL), H_2O (15 mL), and ADmix- β (0.934 g, 1.2 mmol) and MsNH₂ (0.38 g, 4.0 mmol). The mixture was stirred at r.t. for about 5 min, and cooled to 0 °C. To this cooled soln was added **5** (1.104 g, 4.0 mmol) and the mixture was stirred for 12 h at r.t. The reaction was quenched with solid Na₂SO₃ (4 g). The mixture was diluted with EtOAc (30 mL) and after separation of the layers, the aqueous layer was further extracted with EtOAc (30 mL). The combined organic layers were washed with brine (30 mL) and dried (anhyd Na₂SO₄). After evaporation of the solvent, the residue was purified by repeated column chromatography (silica gel, hexane–EtOAc, 1:1) to give diol **6** (0.654 g, 50%).

 $[\alpha]_{D}^{32}$ +18.2 (*c* 0.9, CHCl₃).

IR (KBr): 1744, 1637, 1389, 1215 cm⁻¹.

¹H NMR (200 MHz, $CDCl_3$): $\delta = 7.41-7.21$ (m, 5 H), 4.19 (m, 1 H), 3.93 (m, 1 H), 3.62 (m, 1 H), 3.46 (m, 1 H), 3.08-2.82 (m, 2 H), 1.82-1.34 (m, 2 H), 1.01 (s, 9 H), 0.20 (s, 6 H).

¹³C NMR (50 MHz, CDCl₃): δ = 138.8, 128.4, 127.8, 127.7, 127.6, 126.3, 70.0, 69.0, 66.2, 45.3, 40.2, 25.8, 18.8, -5.6.

MS (ESI): $m/z = 311 [M + H]^+$.

Anal. Calcd for $C_{17}H_{30}O_3$: C, 65.76; H, 9.74. Found C, 65.78; H, 9.75.

(2*R*,4*R*)-5-Phenylpentane-1,2,4-triol (3)

To a stirred soln of **6** (0.640 g, 2 mmol) in MeOH (10 mL), PTSA (cat.) was added at 0 °C and the mixture was stirred at r.t. for 1 h. After completion of the reaction, the mixture was quenched with sat. aq NaHCO₃ (8 mL) and extracted with CH₂Cl₂ (3×50 mL). The organic extracts were dried (anhyd Na₂SO₄). Evaporation of the solvents and purification of the residue by column chromatography (EtOAc–hexane, 7:3) gave pure **3** (0.374 g, 95%) as a colorless liquid.

 $[\alpha]_D^{32}$ +16.5 (*c* 1.0, CHCl₃).

IR (KBr): 3419, 1642, 1492, 1445 cm⁻¹.

¹H NMR (200 MHz, $CDCl_3$): $\delta = 7.40-7.20$ (m, 5 H), 4.25 (m, 1 H), 3.98 (m, 1 H), 3.70 (m, 1 H), 3.50 (m, 1 H), 3.10-2.82 (m, 2 H), 1.82-1.53 (m, 2 H).

¹³C NMR (50 MHz, CDCl₃): δ = 139.1, 128.8, 128.0, 127.2, 71.1, 69.2, 66.4, 44.9, 40.0.

MS (ESI): $m/z = 197 [M + H]^+$.

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.33; H, 8.25.

(*3R*,5*R*)-5-Benzyl-3-hydroxydihydrofuran-2(*3H*)-one (Harzialactone A, 1)

To a stirred r.t. soln of triol **3** (0.372 g, 1.8 mmol) in CH₂Cl₂ (20 mL) was added sequentially PhI(OAc)₂ (0.044 g, 6.4 mmol) and TEMPO (30 mg, 12 mmol%). After stirring at r.t. for 5 h, sat. aq Na₂S₂O₃ and Et₂O (35 mL) were added. The separated organic phase was washed with sat. aq NaHCO₃ then H₂O. The combined aqueous washes were extracted with Et₂O (3×25 mL) and the combined organic fractions were washed with brine, dried (Na₂SO₄), filtered, and concentrated by rotary evaporation. The residue was purified by flash column chromatography (hexanes–EtOAc, 5:5) to provide lactone **1** (0.269 g, 74%) as a white solid.

 $[\alpha]_{D}^{32}$ +36.4 (*c* 0.9, CHCl₃).

IR (KBr): 1742, 1638, 1388, 1217 cm⁻¹.

¹H NMR (200 MHz, $CDCl_3$): $\delta = 7.36-7.16$ (m, 5 H), 4.91 (m, 1 H), 4.04 (*t*, *J* = 7.5 Hz, 1 H), 3.28 (b, 1 Hrs), 2.97 (d, *J* = 6.0 Hz, 2 H), 2.40-2.16 (m, 2 H).

¹³C NMR (50 MHz, CDCl₃): δ = 177.6, 135.2, 129.5, 128.8, 127.1, 78.3, 67.0, 41.07, 34.4.

MS (ESI): $m/z = 215 [M + Na]^+$.

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.67; H, 6.33. Found C, 68.74; H, 6.29.

(S)-4-(tert-Butoxycarbonyloxy)-5-phenylpent-1-ene (7)

Alcohol 4 (0.810 g, 5 mmol) was dissolved in anhyd CH_2Cl_2 (20 mL) and stirred at 0 °C and then warmed to r.t. Boc_2O (3.44 mL, 7.5 mmol) was added followed Et_3N (1.39 mL, 2 mmol) and DMAP (0.066 g, 0.1 mmol). The mixture was stirred for 2 h and then extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried (anhyd Na_2SO_4) and concentrated in vacuo. The residue on purification by column chromatography (EtOAc–hexane, 1:9) afforded pure 7 (1.274 g, 91%) as a colorless liquid.

 $[\alpha]_{D}^{32}$ +92 (*c* 1, CHCl₃).

IR (KBr): 1739, 1642, 1454, 1368, 1277 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.28–7.10 (m, 5 H), 5.67 (m, 1 H), 5.12–4.99 (m, 2 H), 4.82 (m, 1 H), 2.97–2.75 (m, 2 H), 2.38–2.21 (m, 2 H), 1.43 (s, 9 H).

¹³C NMR (50 MHz, CDCl₃): δ = 153.0, 137.5, 133.7, 129.2, 128.4, 126.9, 118.2, 80.8, 76.8, 40.0, 38.1, 27.9.

MS (ESI): $m/z = 285 [M + Na]^+$.

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.28, H, 8.40. Found: C, 73.34, H, 8.37.

(4R,6R)-4-Benzyl-6-(iodomethyl)-1,3-dioxan-2-one (8)

To a stirred soln of **7** (1.179 g, 4.5 mmol) in anhyd MeCN (15 mL) under N₂ at -40 °C was added NIS (3.426 g, 13.5 mmol) and the temperature was raised to 0 °C. The mixture was stirred for 1.5 h. After completion of the reaction, the mixture was quenched with a sat. Na₂S₂O₃ soln (15 mL) and workup with EtOAc (3×20 mL) and H₂O (15 mL). The combined organic layers were dried (anhyd Na₂SO₄) and concentrated in vacuo. Purification of the residue by column chromatography (EtOAc–hexane, 4:6) afforded pure **8** (1.32 g, 89%) as light-yellow color liquid.

 $[\alpha]_D^{32}$ +20.3 (*c* 0.5, CHCl₃).

IR (KBr): 1744, 1637, 1389, 1215 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.08–6.77 (m, 5 H), 4.35 (m, 1 H), 4.08 (m, 1 H), 3.04 (dd, *J* = 12.0, 5.0 Hz, 1 H), 2.91 (dd, *J* = 12.0, 9.0 Hz, 1 H), 2.85 (dd, *J* = 14.0, 6.0 Hz, 1 H), 2.62 (dd, *J* = 14.0, 8.0 Hz, 1 H), 1.99 (m, 1 H), 1.32 (m, 1 H).

¹³C NMR (50 MHz, CDCl₃): δ = 148.2, 135.0, 129.7, 128.9, 127.2, 78.8, 77.0, 41.21, 32.5.

MS (ESI): m/z = 333 [M + H], 355 [M + Na]⁺.

Anal. Calcd for $C_{12}H_{13}IO_3$: C, 43.37; H, 3.92. Found: C, 43.42; H, 3.89.

(R)-1-[(R)-Oxiran-2-yl]-3-phenylpropan-2-ol (9)

 K_2CO_3 (1.44 g, 10.5 mmol) was added to a soln of cyclic carbonate **8** (1.16 g, 3.5 mmol) in anhyd MeOH (10 mL) at r.t. and the resulting mixture was stirred for 0.5 h. The mixture was diluted with Et_2O (10 mL) and quenched with a mixture of sat. aq $Na_2S_2O_3$ -sat. aq $NaHCO_3$ (1:1). The aqueous phase was extracted with Et_2O (3 × 30 mL) and the organic extracts were washed with brine, dried (Na_2SO_4), and then concentrated. Purification of the crude product by column chromatography (silica gel, EtOAc–hexane, 4:6) afforded pure epoxide **9** (0.566 g, 91%) as a colorless liquid.

 $[\alpha]_{D}^{32}$ –9.9 (*c* 0.5, CHCl₃).

IR (KBr): 3422, 1637, 1492, 1458 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.33–7.12 (m, 5 H), 4.03 (m, 1 H), 3.07 (m, 1 H), 2.69 (d, *J* = 7.0 Hz, 2 H), 2.71 (m, 1 H), 2.48 (m, 1 H), 1.98 (br s, 1 H), 1.88 (m, 1 H), 1.52 (m, 1 H).

¹³C NMR (50 MHz, CDCl₃): δ = 138.0, 129.6, 128.8, 126.9, 71.1, 50.2, 46.9, 44.0, 38.9.

MS (ESI): $m/z = 179 [M + H]^+$.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.16; H, 7.89. Found: C, 74.32; H, 7.81.

(*R*)-2-(*tert*-Butyldiphenylsiloxy)-1-[(*R*)-oxiran-2-yl]-3-phenyl-propane (10)

To a stirred soln of **9** (0.534 g, 3.0 mmol) in anhyd CH_2Cl_2 (20 mL) were added imidazole (0.306 g, 4.5 mmol) and TBDPSCl (0.921 mL, 4.5 mmol) at r.t. and the mixture was stirred at this temperature for 3.5 h. The solvent was removed and the residue was taken up in EtOAc (20 mL) and washed with H_2O and brine. The organic layer was separated, dried (anhyd Na_2SO_4), and evaporated. Purification by column chromatography (silica gel, hexane–EtOAc, 8:2) gave **10** (1.151 g, 93%) as a colorless liquid.

 $[\alpha]_D^{32}$ –21.1 (*c* 0.5, CHCl₃).

IR (KBr): 1692, 1460, 1371, 1243, 1163 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.72 (d, *J* = 8.0 Hz, 2 H), 7.61 (d, *J* = 8.0 Hz, 2 H), 7.48–7.3 (m, 6 H), 7.18–7.09 (m, 3 H), 6.81 (d, *J* = 8.0 Hz, 2 H), 4.10 (m, 1 H), 2.89 (m, 1 H), 2.82–2.60 (m, 3 H), 2.25 (m, 1 H), 1.53–1.46 (m, 2 H), 1.04 (s, 9 H).

¹³C NMR (50 MHz, CDCl₃): δ =138.2, 136.1, 134.1, 134.0, 130.0, 129.9, 129.8, 128.1, 127.6, 127.5, 126.1, 72.9, 49.8, 47.3, 44.4, 39.0, 27.0, 19.2.

MS (ESI): $m/z = 439 [M + Na]^+$.

Anal. Calcd for $C_{27}H_{32}O_2Si:$ C, 77.84; H, 7.74. Found: C, 77.86, 7.76.

(2R,4R)-4-(*tert*-Butyldiphenylsiloxy)-5-phenylpentane-1,2-diol (11)

To a cold soln of **10** (0.868 g, 2.0 mmol) in MeCN (1 mL), H₂O (350 μ L) and 65% HClO₄ were added. The mixture was stirred at 0 °C for 2 h. After completion of the reaction the mixture was neutralized with aq NaHCO₃. The aqueous layer was extracted with EtOAc (2 × 20 mL) and washed with sat. aq NaHCO₃ (3 mL) and brine (3 mL). The combined organic layer was dried (anhyd Na₂SO₄) and concentrated. The residue was purified by column chromatography (hexane–EtOAc, 6:4) to give **11** (0.616 g, 71%) as a colorless liquid.

 $[\alpha]_{D}^{32}$ –8.1 (*c* 0.5, CHCl₃).

IR (KBr): 1695, 1462, 1373, 1242, 1161 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.75 (d, *J* = 8.0 Hz, 2 H), 7.68 (d, *J* = 8.0 Hz, 2 H), 7.50–7.32. (m, 6 H), 7.11–7.01 (m, 3 H), 6.65 (d, *J* = 8.0 Hz, 2 H), 4.10 (m, 1 H), 3.82 (m, 1 H), 3.41 (m, 1 H), 3.22 (m, 1 H), 2.71 (m, 1 H), 2.60 (m, 1 H), 1.58 (m, 1 H), 1.41 (m, 1 H), 1.04 (s, 9 H).

¹³C NMR (50 MHz, CDCl₃): δ = 138.2, 136.1, 133.9, 133.1, 130.0, 129.9, 129.1, 129.0, 128.0, 127.9, 127.2, 126.1, 75.2, 73.8, 70.9, 44.4, 38.5, 27.0, 19.2.

MS (ESI): $m/z = 457 [M + Na]^+$.

Anal. Calcd for $C_{27}H_{34}O_3Si: C, 74.65; H, 7.83$. Found: C, 74.52; H, 7.87.

(2R,4R)-5-Phenylpentane-1,2,4-triol (3)

To an ice-cooled soln of **11** (0.616 g, 1.3 mmol) in anhyd THF (5 mL) was added 1 M TBAF in THF (0.75 mL, 1.95 mmol) and the mixture was stirred at r.t. for 3.5 h. After completion of the reaction, H_2O (2 mL) was added to the mixture and THF was removed under vacuum. The aqueous layer was extracted with EtOAc (2 × 15 mL)

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and washed with sat. aq NaHCO₃ (4 mL) and brine (4 mL). The combined organic layers were dried (anhyd Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane–EtOAc, 2:8) to give **3** (0.229 g, 89%) as a viscous liquid.

$[\alpha]_{D}^{32}$ +25.6 (*c* 0.5, CHCl₃).

IR (KBr): 1690, 1462, 1372, 1245, 1161 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.40–7.20 (m, 5 H), 4.25 (m, 1 H), 3.98 (m, 1 H), 3.70 (m, 1 H), 3.50 (m, 1 H), 3.10–2.82 (m, 2 H), 1.82–1.53 (m, 2 H).

¹³C NMR (50 MHz, CDCl₃): δ = 139.1, 128.8, 128.0, 127.2, 71.1, 69.2, 66.4, 44.9, 40.0.

MS (ESI): $m/z = 197 [M + H]^+$.

Anal. Calcd for $C_{11}H_{16}O$: C, 67.32; H, 8.22. Found: C, 67.33; H, 8.25.

(S)-4-(tert-Butyldiphenylsiloxy)-5-phenylpent-1-ene (12)

To a stirred soln of **4** (0.810 g, 5.0 mmol) in anhyd CH_2Cl_2 (25 mL) were added imidazole (0.510 g, 7.5 mmol) and TBDPSCl (1.56 mL, 6.0 mmol) at r.t. and the mixture was stirred at this temperature for 2 h. The solvent was removed and the residue was taken up in EtOAc (30 mL) and washed with H_2O (10 mL) and brine (10 mL). The organic layer was separated, dried (anhyd Na_2SO_4), and evaporated. Purification by column chromatography (silica gel, hexane–EtOAc, 8:2) gave **12** (1.88 g, 94%) as a colorless liquid.

 $[\alpha]_D^{32}$ +11.5 (*c* 0.5, CHCl₃).

IR (KBr): 1691, 1465, 1374, 1240, 1161 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.66 (d, *J* = 8.0 Hz, 2 H), 7.52 (d, *J* = 8.0 Hz, 2 H), 7.41–7.24 (m, 6 H), 7.19–7.08 (m, 3 H), 6.91 (d, *J* = 8.0 Hz, 2 H), 5.80 (m, 1 H), 5.04–4.85 (m, 2 H), 3.93 (m, 1 H), 2.78–2.41 (m, 2 H), 2.19–1.94 (m, 2 H), 1.04 (s, 9 H).

¹³C NMR (50 MHz, CDCl₃): δ = 139.0, 136.1, 135.0, 134.2, 134.1, 129.9, 129.8, 129.7, 128.1, 128.0, 127.4, 127.3, 126.1, 117.2, 74.1, 42.9, 40.1, 27.0, 19.1.

MS (ESI): $m/z = 423 [M + Na]^+$.

Anal. Calcd for $C_{27}H_{32}OSi: C$, 81.00; H, 8.00. Found: C, 81.19; H, 8.07.

(*R*)-2-(*tert*-Butyldiphenylsiloxy)-1-(oxiran-2-yl)-3-phenylpropane (13)

To a stirred soln of olefin **12** (1.60 g, 4 mmol) in CH₂Cl₂ (50 mL) at 0 °C was added MCPBA (50%, 0.816 g, 4.8 mmol). The mixture was stirred at r.t. for 6 h and then quenched with sat. NaHCO₃ (5 mL) soln. The resulting mixture was extracted with CH₂Cl₂ (3×30 mL), washed with sat. NaHCO₃ (6 mL) and brine (6 mL), dried (Na₂SO₄), concentrated, and then purified by column chromatography (silica gel, hexane–EtOAc, 7:3) to yield the epoxide **13** (1.564 g, 94%) as a colorless liquid; diastereometic mixture.

(2R,4R)-4-(*tert*-Butyldiphenylsiloxy)-5-phenylpentane-1,2-diol (11)

A soln of epoxide **13** (1.456 g, 3.5 mmol) and (*S*,*S*)-Salen–Co(III)– OAc (0.010 g, 1.75 mmol) in THF (0.3 mL) was stirred at 0 $^{\circ}$ C for 5 min and then distilled H_2O (24 mL, 1.45 mmol) was added. After stirring for 10 h, this mixture was concentrated and purified by column chromatography (silica gel, hexane–EtOAc 2:8) to afford **11** (0.744 g, 49%) as a colorless liquid.

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