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Efficient total synthesis of *iso*-cladospolide B and cladospolide B

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Abstract—An efficient synthesis of *iso*-cladospolide B and cladospolide B has been achieved using Jacobsen's hydrolytic kinetic resolution (HKR), Sharpless asymmetric dihydroxylation and Yamaguchi macrolactonization as the key steps.

The novel hexaketide compounds *iso*-cladospolide B **1** and cladospolide B **2** were isolated from the fungal isolate I96S215.[1] Cladospolide A **3**, cladospolide B **2** along with cladospolide C **4** were also isolated from the soil fungi *Cladosporium tenuissimum*, whose culture filtrate showed plant growth retardant activity towards rice seedlings. Cladospolide B **2** is inhibitory to shoot elongation of rice seedlings (*Oryza sativa* L.) without damaging the cells.[2] Recently, cladospolide D **5** isolated from *Cladosporium* sp. FT-0012 whose configuration remains to be fully determined, was shown to exhibit antimicrobial activity against *Mucor racemosus* and *Pyricularia oryzae* with IC_{50} values of 0.15 and 29 μg ml^{-1}, respectively[3] (Fig. 1). The absolute configuration of the three stereogenic centres (4*S*,5*S* and 11*R*) of *iso*-cladospolide B **1** was determined by Figadere and co-workers who also accomplished its synthesis for the first time.[4] Very recently, Banwell and co-workers reported the first total synthesis of cladospolide B using a chemoenzymatic 16-step synthesis via a ring-closing metathesis and photorearrangement of an *E* isomer.[5]

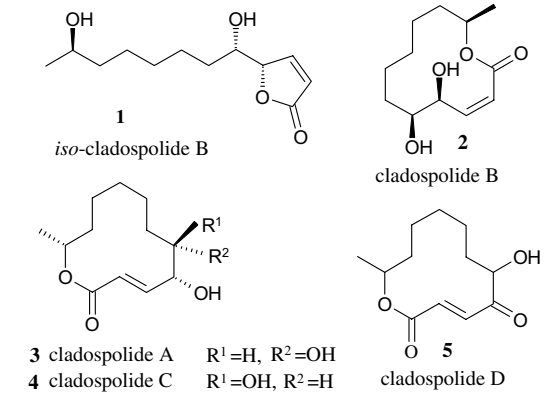

Figure 1.

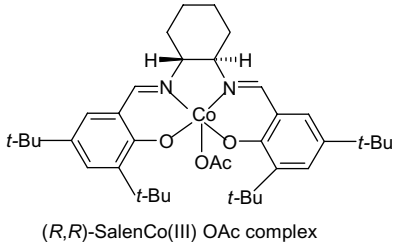

Figure 2.

As part of our research programme aimed at developing enantioselective syntheses of naturally occurring lactones[6] and amino alcohols,[7] we have accomplished the total synthesis of *iso*-cladospolide B **1** and cladospolide B **2** from commercially available propylene oxide employing Jacobsen's HKR, a Sharpless asymmetric dihydroxylation and Yamaguchi macrolactonization as the key steps.

Propylene oxide **6** was subjected to Jacobsen's HKR using (*R*,*R*)-Salen-Co-(OAc) catalyst (Fig. 2) to give *R*-propylene oxide **6a** as a single isomer $[\alpha]_D^{25}$ +11.7 (neat) {lit.[8] for (*S*)-propylene oxide $[\alpha]_D^{25}$ −11.6 (neat)},

Keywords: Cladospolide B; *iso*-Cladospolide B; Sharpless asymmetric dihydroxylation; Hydrolytic kinetic resolution; Yamaguchi macrolactonization.
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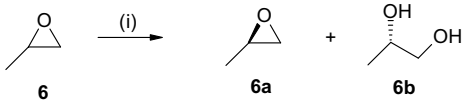


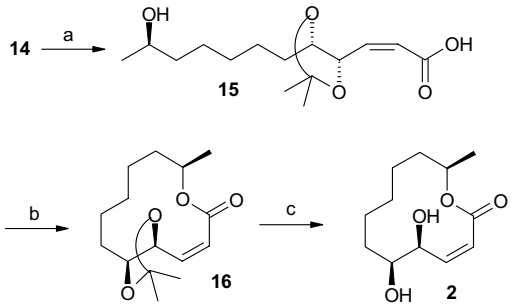
Scheme 1. Reagents and conditions: (i) *R,R*-Salen-Co-(OAc) (0.5 mol %), distd H_2O (0.55 equiv), 0 °C, 14 h, (46% for **6a**, 45% for **6b**).

which was easily isolated from the more polar diol **6b** by distillation (Scheme 1).

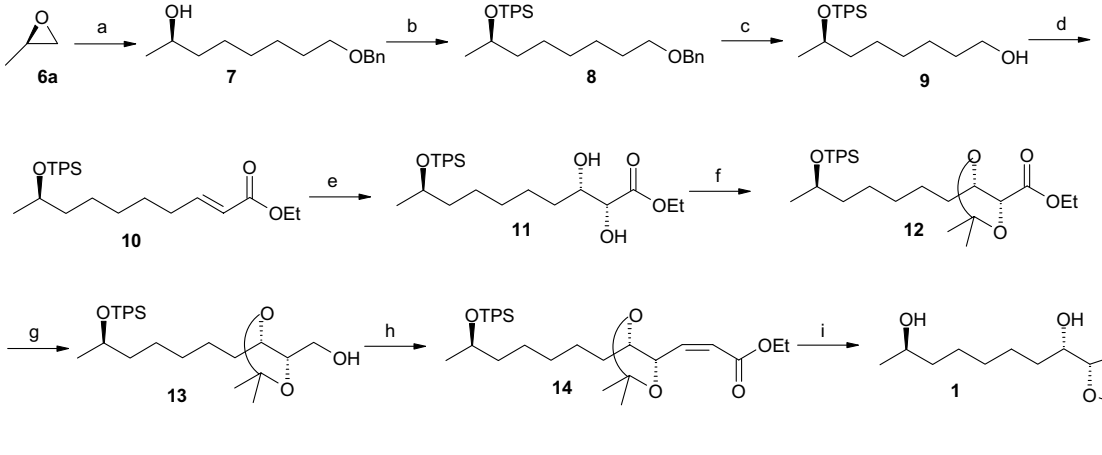
With enantiomerically pure propylene oxide **6a** in hand, we then subjected it to copper-catalyzed (CuI) regioselective opening with the Grignard reagent, derived from benzyl protected bromopentanol to furnish alcohol **7** in 77% yield (Scheme 2). Hydroxyl protection of **7** with *tert*-butyldiphenylsilyl chloride and imidazole in the presence of a catalytic amount of DMAP afforded the silyl ether **8** in 95% yield which on debenzylation using H_2–Pd/C furnished the alcohol **9** in 91% yield. Compound **9** was then oxidized to the corresponding aldehyde by Swern oxidation[9] and subsequently treated with (ethoxycarbonylmethylene)triphenylphosphorane in dry THF to furnish the Wittig product **10** in 92% yield. The olefin **10** was treated with osmium tetroxide and potassium ferricyanide as co-oxidant in the presence of $(DHQ)_2PHAL$ under Sharpless asymmetric conditions[10] to give the diol **11** in 94% yield with 96% de.[11] Treatment of diol **11** with 2,2-dimethoxypropane in the presence of a catalytic amount of *p*-TSA gave compound **12**, which on subsequent reduction using $LiAlH_4$ provided the alcohol **13** in excellent yield. The alcohol was oxidized to the aldehyde under Swern conditions and subsequently treated with (ethoxycarbonylmethylene)triphenylphosphorane in dry methanol at −78 °C for 24 h to give the Wittig product **14**[12] in 82% yield with a *Z*:*E* ratio of 85:15,[12] the isomers of which could easily be separated by silica gel column chromatography. Finally, deprotection of the acetonide and TPS groups and concomitant cyclization of the olefin **14** was achieved in one-pot using 3% methanolic HCl to furnish the target molecule, *iso*-cladospolide B **1** in 77% yield; $[\alpha]_D^{25}$ −105.3 (*c* 0.23, MeOH) {lit.[4] $[\alpha]_D^{25}$ −105.0 (*c* 0.23, MeOH)}. The physical and spectroscopic data were in full agreement with the literature.[1]

The synthesis of cladospolide B **2** started from the olefin **14** as illustrated in Scheme 3. Ester hydrolysis of **14** with LiOH followed by TPS deprotection using TBAF led to the *seco*-acid **15** in 88% yield. Macrolactonization of **15** under Yamaguchi conditions[13] provided lactone **16** in excellent yield, which on subsequent cleavage of the acetonide afforded the target molecule **2** in 88% yield; $[\alpha]_D^{25}$ −164.3 (*c* 0.10, MeOH), {lit.[5] $[\alpha]_D^{25}$ −162.0 (*c* 0.10, MeOH)}. The physical and spectroscopic data were in full agreement with the literature.[5]

In conclusion, a practical and enantioselective synthesis of *iso*-cladospolide B and cladospolide B has been achieved employing Jacobsen's HKR, a Sharpless asymmetric dihydroxylation and Yamaguchi macrolactonization as the key steps. The merits of this synthesis are



Scheme 3. Reagents and conditions: (a) (i) LiOH, $MeOH/H_2O$ (3:2), 0 °C to rt; (ii) TBAF, CH_2Cl_2, 0 °C to rt, 88%, two steps; (b) 2,4,6-trichlorobenzoyl chloride, Et_3N, THF, then DMAP, benzene, 86%; (c) CF_3COOH, THF/H_2O, 0 °C, 1 h, 88%.



Scheme 2. Reagents and conditions: (a) $C_6H_5CH_2O(CH_2)_5MgBr$, CuI, THF, −78 °C, 12 h, 77%; (b) TBDPSCl, imidazole, DMAP, DMF, 0 °C, 2 h, 95%; (c) H_2–Pd/C, EtOAc, rt, 91%; (d) (i) $(COCl)_2$, DMSO, CH_2Cl_2, −78 °C, Et_3N, −65 °C, 1 h; (ii) $Ph_3P{=}CHCO_2Et$, THF, reflux, 6 h, 92%; (e) $(DHQ)_2PHAL$ (1 mol %), 0.1 M OsO_4 (0.4 mol %), K_2CO_3, $K_3Fe(CN)_6$, $MeSO_2NH_2$, *t*-BuOH/H_2O 1:1, 0 °C, 24 h, 94%; (f) 2,2-DMP, *p*-TSA (cat.) CH_2Cl_2, 2 h, 89%; (g) $LiAlH_4$, THF, 0 °C to rt, 3 h, 85%; (h) (i) $(COCl)_2$, DMSO, CH_2Cl_2, −78 °C, Et_3N, −65 °C, 1 h; (ii) $Ph_3P{=}CHCO_2Et$, MeOH, −78 °C, 24 h, 82%; (i) 3% MeOH/HCl, 0 °C to rt, 5 h, 77%.

high enantio- and diastereoselectivity with high yielding reaction steps. The synthetic strategy described has significant potential for further extension to other stereoisomers and analogues of *iso*-cladospolide B and cladospolide B.

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References and notes

1. Cameron, J. S.; Abbanat, D.; Bernan, V. S.; Maiese, W. M.; Greenstein, M.; Jompa, J.; Ireland, C. M. *J. Nat. Prod.* **2000**, *63*, 142–145.
2. (a) Hirota, H.; Hirota, A.; Sakai, H.; Isogai, A.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2147–2148; (b) Hirota, A.; Sakai, H.; Isogai, A. *Agric. Biol. Chem.* **1985**, *49*, 731–735; (c) Fujii, Y.; Fukuda, A.; Hamasaki, T.; Ichimoto, I.; Nakajima, H. *Phytochemistry* **1995**, *40*, 1443–1446.
3. Zhang, H.; Tomoda, H.; Tabata, N.; Miura, H.; Namikoshi, M.; Yamaguchi, Y.; Masuma, R.; Omura, S. *J. Antibiot.* **2001**, *54*, 635–641.
4. Franck, X.; Araujo, M. E.; Jullian, J.-C.; Hocquemiller, R.; Figadere, B. *Tetrahedron Lett.* **2001**, *42*, 2801–2803.
5. Austin, K. A. B.; Banwell, M. G.; Loong, D. T. J.; Rae, D.; Willis, A. C. *Org. Biomol. Chem.* **2005**, *3*, 1081–1088.
6. (a) Fernandes, R. A.; Kumar, P. *Eur. J. Org. Chem.* **2002**, 2921–2923; (b) Kandula, S. V.; Kumar, P. *Tetrahedron Lett.* **2003**, *44*, 6149–6151; (c) Gupta, P.; Naidu, S. V.; Kumar, P. *Tetrahedron Lett.* **2004**, *45*, 849–851; (d) Naidu, S. V.; Gupta, P.; Kumar, P. *Tetrahedron Lett.* **2005**, *46*, 2129–2131; (e) Kumar, P.; Naidu, S. V.; Gupta, P. *J. Org. Chem.* **2005**, *70*, 2843–2846; (f) Kumar, P.; Naidu, S. V. *J. Org. Chem.* **2005**, *70*, 4207–4210.
7. (a) Fernandes, R. A.; Kumar, P. *Eur. J. Org. Chem.* **2000**, 3447–3449; (b) Pandey, R. K.; Fernandes, R. A.; Kumar, P. *Tetrahedron Lett.* **2002**, *43*, 4425–4426; (c) Fernandes, R. A.; Kumar, P. *Tetrahedron Lett.* **2000**, *41*, 10309–10312; (d) Naidu, S. V.; Kumar, P. *Tetrahedron Lett.* **2003**, *44*, 1035–1037; (e) Gupta, P.; Fernandes, R. A.; Kumar, P. *Tetrahedron Lett.* **2003**, *44*, 4231–4232; (f) Kondekar, N. B.; Kandula, S. V.; Kumar, P. *Tetrahedron Lett.* **2004**, *45*, 5477–5479; (g) Pandey, S. K.; Kandula, S. V.; Kumar, P. *Tetrahedron Lett.* **2004**, *45*, 5877–5879; (h) Pandey, S. K.; Kumar, P. *Tetrahedron Lett.* **2005**, *46*, 4091–4093; (i) Kumar, P.; Bodas, M. S. *J. Org. Chem.* **2005**, *70*, 360–363.
8. Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307–1315.
9. For reviews on the Swern oxidation, see: (a) Tidwell, T. T. *Synthesis* **1990**, 857–870; (b) Tidwell, T. T. *Org. React.* **1990**, *39*, 297–572.
10. (a) Becker, H.; Sharpless, K. B. *Angew Chem., Int. Ed. Engl.* **1996**, *35*, 448–451; (b) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547; (c) Torri, S.; Liu, P.; Bhuvaneswari, N.; Amatore, C.; Jutand, A. *J. Org. Chem.* **1996**, *61*, 3055–3060.
11. The diastereoselectivity was determined from ^{13}C NMR spectral data. Spectral data of compound **11**: colorless oil, $[\alpha]_D^{25}$ +6.68 (*c* 1.0, $CHCl_3$); IR (neat): ν_{max} 3410, 2932, 1713, 1653, 1609, 1590, 1216 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.06 (s, 9H), 1.07 (t, $J = 5.9$ Hz, 3H), 1.18–1.58 (m, 13H), 2.10 (br s, 2H), 3.76–3.90 (m, 2H), 4.06 (d, $J = 2.0$ Hz, 1H), 4.30 (q, $J = 7.2$ Hz, 2H), 7.32–7.47 (m, 6H), 7.66–7.71 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.1, 19.2, 23.2, 25.1, 25.6, 27.0, 29.4, 33.6, 39.2, 61.9, 69.4, 72.5, 73.1, 127.3, 129.3, 134.5, 134.8, 135.8, 173.7. Anal. Calcd for $C_{28}H_{42}O_5Si$ (486.72): C, 69.10; H, 8.70. Found: C, 69.04; H, 8.73.
12. The *Z*:*E* ratio of compound **14** was determined from the ^1H NMR spectrum. Spectral data of compound **14**: $[\alpha]_D^{25}$ +29.22 (*c* 1.0, $CHCl_3$); IR (neat): ν_{max} 3071, 2932, 1723, 1655, 1589, 1462, 1378, 1191; ^1H NMR (200 MHz, $CDCl_3$): δ 1.05 (s, 9H), 1.14–1.37 (m, 12H), 1.44 (s, 6H), 1.51–1.65 (m, 4H), 3.64–3.90 (m, 2H), 4.18 (q, $J = 7.1$ Hz, 2H), 5.27 (t, $J = 8.6$ Hz, 1H), 5.93 (d, $J = 11.8$ Hz, 1H), 6.13 (dd, $J = 11.7$, 8.7 Hz, 1H), 7.32–7.46 (m, 6H), 7.66–7.70 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.1, 19.2, 23.1, 25.0, 26.0, 27.0, 29.6, 31.9, 39.3, 60.3, 69.4, 76.0, 80.9, 109.1, 122.9, 127.3, 129.3, 134.5, 134.8, 135.8, 145.5, 165.3. Anal. Calcd for $C_{33}H_{48}O_5Si$ (552.82): C, 71.70; H, 8.75. Found: C, 71.66; H, 8.74.
13. Inanaga, J.; Hirata, K.; Sacki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989–1993.