Monatsh Chem
DOI 10.1007/s00706-015-1464-1

ORIGINAL PAPER

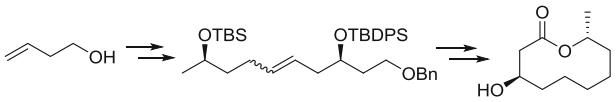
A concise stereoselective total synthesis of diplodialide C

Bommareddy Pratapareddy[1] · Reddymasu Sreenivasulu[2] · Islavathu Hatti[2] · Mandava Venkata Basaveswara Rao[1] · Rudraraju Ramesh Raju[2]

Received: 1 October 2014 / Accepted: 22 March 2015

Abstract An asymmetric total synthesis of diplodialide C has been achieved starting from commercially available homoallylic alcohol. Regioselective opening of the chiral epoxide, cross-metathesis reaction, and Yamaguchi macrolactonization were used as the key steps in this synthesis.

Graphical Abstract



Keywords Homoallylic alcohol · Cross-metathesis reaction · Yamaguchi macrolactonization · Diplodialide C

Introduction

The first 10-membered lactone pentaketides are diplodialide structures A(**1**), B(**2**), C(**3**), and D(**4**) (Fig. 1), which were isolated from the plant pathogenic fungus Diplodiapinea (IFO 6472) by Wada and Ishida [1, 2]. Diplodialides exhibit various biological activities, in particular, diplodialide A(**1**) displays significant inhibitory activity against progesterone 11α-hydroxylase in vegetable cell cultures of *Rhizopus stolonifer* at 125 ppm. The absolute stereochemistry of diplodialides were (9*R*)-**1**, (3*S*,9*R*)-**2**, and (3*R*,9*R*)-**3** and determined by Wada and Ishida [3].

The interesting biological activity combined with simple stereochemistry of diplodialides attracted scientists and researchers worldwide. The first total synthesis of (±)-diplodialide C was reported by Wakamatsu and co-workers [4] in 1977. Further, the total synthesis of diplodialide C was reported by Takeshi and co-workers [5] in 1979 using Barbier-Grignard and Sharpless asymmetric dihydroxylation reactions as key steps. Sharma and Reddy [6] reported the stereoselective synthesis of diplodialides including diplodialide C, by the combination of Jacobsen's hydrolytic kinetic resolution and sharpless epoxidation followed by ring-closing metathesis strategy. The stereoselective total syntheses of natural products (−)-curvularin, curvulin, and (−)-diplodialide C were reported by Tadross and co-workers [7] using Grubbs' second-generation catalyst, Grubbs-Hoveyda third-generation catalyst and utilizing an aryne acyl-alkylation reaction followed by ring-closing metathesis.

The reported synthetic routes to diplodialide C mainly associated with hard reaction conditions and low yields. To overcome these disadvantages with the earlier approaches, herein we reported an alternative route for the synthesis of diplodialide C. In this context, we would like to report an efficient and high yielding enantioselective synthesis of diplodialide C employing an entirely different approach. This strategy involves a concise divergent synthesis of the target molecule **3** from inexpensive starting material, i.e., homoallylic alcohol, and subsequent cross-metathesis reaction followed by Yamaguchi macrolactonization to form the cyclic ring.

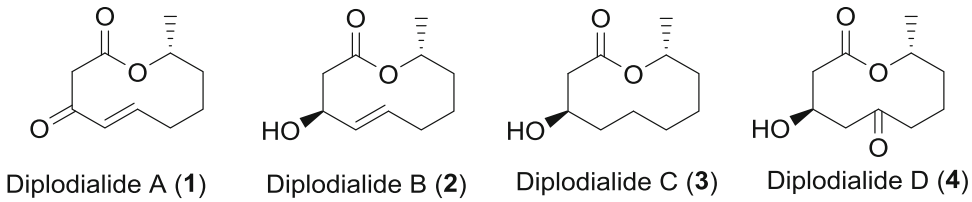
✉ Mandava Venkata Basaveswara Rao
professormandava@gmail.com

✉ Rudraraju Ramesh Raju
rrraju1@gmail.com

[1] Department of Chemistry, Krishna University, Machilipatnam 521 001, Andhra Pradesh, India

[2] Department of Chemistry, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur 522510, Andhra Pradesh, India

Fig. 1 Structures of diplodialides



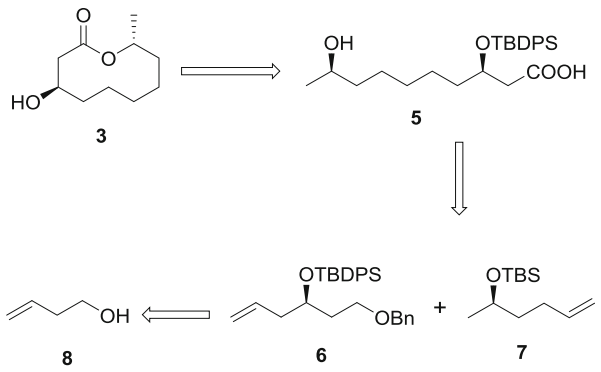
Results and discussion

The retrosynthesis route for the synthesis of diplodialide C is outlined in Scheme 1. The target molecule **3** could be synthesized through Yamaguchi's macrolactonization of a hydroxyl acid **5** which in turn could be obtained from olefins **6** and **7** [14]. The olefin **6** could be prepared from commercially available homoallylic alcohol (**8**) by simple chemical transformations.

The total synthesis of **3** was initiated with commercially available homoallylic alcohol (**8**) as illustrated in Scheme 2. Accordingly, homoallylic alcohol (**8**) protected as benzyl ether by treating with benzyl bromide and sodium hydride in tetrahydrofuranat, 0–25 °C for 8 h yielded **9** in 94 % yield. Epoxidation of terminal olefin **9** was accomplished with *m*-CPBA in $CHCl_3$ in 91 % yield as a racemic mixture. The racemic epoxide **9a**, on hydrolytic kinetic resolution using Jacobsen's (*S,S*)-catalyst [8] in the presence of AcOH and H_2O for 16 h stirring at 0–25 °C afforded enantiopure (*S*)-epoxide **10** (>99 % ee) in 44 % yield and *R*-diol **10a** in 39 % yield. Regioselective opening of the chiral epoxide **10,** upon reaction with vinylmagnesium bromide in dry ether in the presence of CuI [9, 10] gave alcohol **11** (88 %), which upon subsequent treatment with TBDPSCl and imidazole in CH_2Cl_2 gave silyl ether **6** in 90 % yield. Further, silyl ether **6** was subjected to cross-metathesis [11–13] with known olefin **7** [14] in the presence of 10 mol% Grubbs second-generation catalyst in CH_2Cl_2, at reflux afforded cross-metathesis product **12** (*E*/*Z* 90:10) in 57 % yield, along with **12a** in 21 % yield, a homodimer of **7**. The simultaneous reduction of olefin and deprotection of the benzyl group with Pd/C in EtOAc yielded saturated alcohol **13** in 91 % yield. Oxidation of alcohol **13** with TEMPO and BIAB [15, 16] in aq. CH_2Cl_2 afforded acid **14** in 76 % yield, which on desilylation with TBAF in dry THF gave hydroxyacid **5** in 88 % yield. The resulting hydroxy acid **5** was subjected to macrolactonization under the Yamaguchi [17, 18] protocol by using 2,4,6-trichlorobenzoyl chloride, followed by cyclization in the presence of DMAP under high dilution conditions in toluene afforded the lactone **15** in 63 % yield.

Finally, desilylation of lactone **15** with TBAF in dry THF, afforded the diplodialide C in 84 % yield. The spectral and analytical data of synthetic diplodialide C (**3**) were in good agreement with the reported values in the literature [6].

Scheme 1



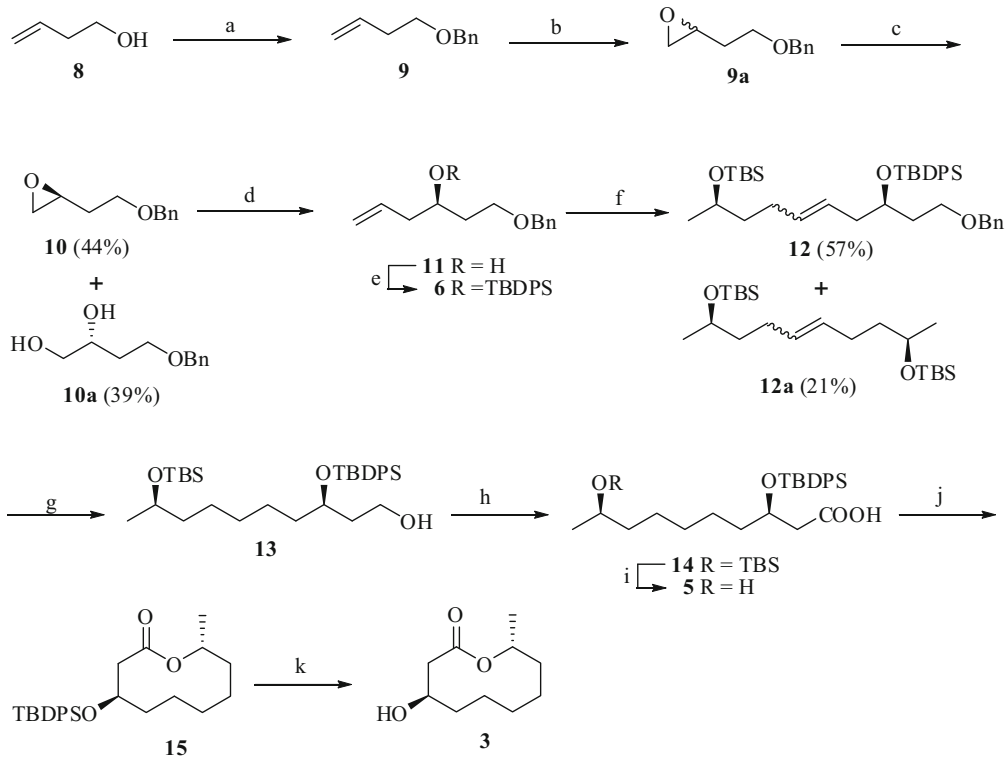
Conclusion

In conclusion, a concise stereoselective total synthesis of diplodialide C (**3**) was accomplished. A combination of regioselective opening of the chiral epoxide, cross-metathesis reaction, and Yamaguchi macrolactonization were used as key steps.

Experimental

All chemicals and solvents were purchased from Sigma Aldrich and Merck, and used without further purification. All reactions were monitored by thin layer chromatography (TLC) on silica Merck 60 F254 percolated aluminum plates. ^1H and ^{13}C NMR spectra were recorded in 500, 300, 150, and 75 MHz Bruker spectrometer. Chemical shifts are reported in δ units (ppm) with tetramethylsilane (TMS) as a reference. All coupling constants (*J*) are reported in Hertz. Multiplicity is indicated as s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), m (multiplet). FT-IR spectra were taken on IR spectrophotometer by using NaCl optics. Mass spectra were performed on direct inlet system or LC by MSD trap SL. Optical rotation values are recorded on digital polarimeter at 25 °C.

Scheme 2



Reagents and conditions: *(a)* BnBr, NaH, THF, 0 °C to 25 °C, 8 h; *(b)* *m*-CPBA, $CHCl_3$, 25 °C, 8 h; *(c)* (S,S)-Jacobsen's catalyst, H_2O, THF, 0 °C to 25°C; *(d)* vinylMgBr, THF, −40 °C, 4 h; *(e)* TBDPSCl, imidazole, CH_2Cl_2, 0 °C to 25 °C; *(f)* **7**, Grubbs II catalyst (10 mol %), CH_2Cl_2, reflux, 2 h; *(g)* Pd/C, MeOH, 25 °C, 6 h; (h) TEMPO, BIAB, H_2O:CH_2Cl_2, (1:1), 0 °C, 1 h; *(i)* PPTS, MeOH, 0 °C to 25 °C, 3 h; *(j)* (i) 2,4,6-trichlorobenzoyl chloride, Et_3N, dry THF, 0 °C to 25 °C, 2 h; (ii) DMAP, dry toluene, 70 °C, 5 h; *(k)* TBAF, dry THF, 25°C, 1 h

*[(But-3-enyloxy)methyl]benzene (**9**) [19]*

To a suspension of 8.0 g NaH (333.32 mmol, 60 % w/v dispersion in mineral oil, 4.0 eq) in 100 cm^3, anhydrous THF was added drop wise to a solution of 6.0 g 3-buten-1-ol **8** (83.33 mmol, 1.0 eq) at 0 °C. To this mixture, 0.150 g TBAI and 11.9 cm^3 benzyl bromide (99.99 mmol, 1.2 eq) were added, and stirring was continued for 2 h at the same temperature and overnight at 25 °C. The reaction mixture was quenched by small crushed ice flakes until a clear solution (biphasic) had formed. The reaction mixture was extracted with ether and the extract was washed with water (1 × 100 cm^3), brine (1 × 100 cm^3) and dried over anhydrous Na_2SO_4. Evaporation of the solvents followed by column chromatography (silica gel, 60–120 mesh, 5 % EtOAc in pet. ether) afforded the pure product **9** (12.2 g, 91 % yield) as a colorless liquid.

*(S)-2-[2-(Benzyloxy)ethyl]oxirane (**10**) [19]*

Crude benzyl ether **9** (12.0 g, 74.07 mmol, 1.0 eq) was dissolved in 100 cm^3 dichloromethane and the solution was cooled to 0 °C. $NaHCO_3$ (15.2 g) was added, followed by 25.5 g *m*-CPBA (148.14 mmol, 70 % w/w, 4.0 eq). The solution was stirred for 16 h before being filtered through a pad of Celite and concentrated under reduced pressure. The residue was then dissolved in 100 cm^3 water and extracted with Et_2O (3 × 50 cm^3). The combined organic extracts were then washed with 3 M NaOH (3 × 50 cm^3), followed by brine (50 cm^3), dried over Na_2SO_4, and evaporated. Chromatography (silica gel, 60-120 mesh, 8 % EtOAc in pet. ether) gave **9a**, as a colorless oil (11.3 g, 89 %). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.32–7.23 (m, 5H), 4.50 (s, 2H), 3.62–3.56 (m, 2H), 3.14–2.99 (m, 1H), 2.74 (dd, J = 5.84, 4.61 Hz, 1H), 2.47 (dd, J = 5.84, 2.92 Hz, 1H),

1.91–1.85 (m, 1H), 1.77–1.71 (m, 1H) ppm; ESI–MS: *m/z* = 201 ($[M + Na]^+$).

A mixture of 0.21 g (*S,S*)-(−)-*N,N*$_1$-bis(3,5-di-*tert*-butylsalicyclidene)-1,2-cyclohexanediaminocobalt(II) (0.31 mmol, 0.005 eq), toluene, and 0.04 cm^3 AcOH (0.63 mmol, 0.01 eq) was stirred while open to the air for 1 h at 25 °C. The solvent was removed under reduced pressure and the brown residue was dried over high vacuum. The oxirane **9a** (11 g, 63.95 mmol, 1.0 eq) was added in one portion, the stirred mixture was cooled in an ice water bath. Water (0.63 cm^3, 35.17 mmol, 0.55 eq) was slowly added and the temperature of the reaction mixture was maintained in such a way that it never rises more than 20 °C. After completion of reaction within one hour, removed the ice bath. Now the reaction mixture was stirred for 22 h at room temperature and finally the residue was purified by column chromatography to afford the epoxide 10 (4.9 g, 44 %) as colorless oil $[\alpha]_D^{25} = -18.8$ ($c = 0.8$, $CHCl_3$).

*(R)-1-(Benzyloxy)hex-5-en-3-ol (**11**) [20, 21]*

Copper iodide (0.53 g, 2.79 mmol, 0.1 eq)was gently heated under vacuum and slowly cooled under nitrogen atmosphere, then 10 cm^3 THF was added and the resulting suspension was cooled to −20 °C and 55 cm^3 vinyl magnesium bromide (29.04 mmol, 1.1 eq) was added at the same temperature while stirring. A solution of 4.8 g epoxide **5** (27.90 mmol, 1.0 eq) in 20 cm^3 dry THF was added to the above reagent and the mixture was stirred at −20 °C for 1 h. After completion of the reaction, the reaction was quenched with saturated aqueous NH_4Cl, extracted into EtOAc (3 × 30 cm^3), the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated, to give the crude product which was purified by column chromatography (silica gel, 60–120 mesh, 15 % EtOAc in pet. ether) to afford **11** (5.1 g, 88 %) as a colorless liquid $[\alpha]_D^{25} = +3.3$ ($c = 1$, $CHCl_3$).

(R)-[1-(Benzyloxy)hex-5-en-3-yloxy](tert-butyl)diphenylsilane (**6**, $C_{29}H_{36}O_2Si$)

To a cooled (0 °C) solution of 3.0 g compound **11** (14.56 mmol, 1.0 eq) and 1.98 g imidazole (29.12 mmol, 2.0 eq) in 30 cm^3 dry dichloromethane was added 4.8 g *tert*-butyldiphenylsilylchloride (17.47 mmol, 1.2 eq) drop wise and stirred for 4 h. After the completion of reaction, the reaction mixture was diluted with 20 cm^3 water and extracted into dichloromethane (3 × 30 cm^3). The combined organic layer was washed with 10 cm^3 brine solution, dried over anhydrous Na_2SO_4, and concentrated under vacuum to furnish the crude residue, which was purified by column chromatography (silica gel, 60–120 mesh, 5 % EtOAc in pet. ether) to afford the pure compound **7** (5.8, 90 %). $[\alpha]_D^{25} = -8.2$ ($c = 0.9$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.71–7.65$ (m, 5H, Ar–H), 7.42–7.18 (m, 10H, Ar–H), 5.81–5.64 (m, 1H, olefinic), 4.94–4.88 (m, 2H, olefinic), 4.33 (s, 2H, benzylic CH_2), 3.96 (m, 1H, –OCH), 3.48 (t, $J = 4.3$ Hz, 2H, –OCH_2), 2.28 (m, 2H, allylic CH_2), 1.86–1.78 (m, 2H, –CH_2), 1.05 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.1$, 136.8, 135.1, 132.8, 128.9, 128.1, 127.9, 127.2, 126.9, 117.3, 82.2, 75.8, 69.2, 42.1, 38.3, 27.2, 18.9 ppm; ESI–MS: *m/z* = 467 ($[M + Na]^+$).

(5S,11R)-5-[2-(4-Methoxybenzyloxy)ethyl]-2,2,11,13,13,14,14-heptamethyl-3,3-diphenyl-4,12-dioxa-3,13-disilapentadec-6-ene (**12**, $C_{39}H_{58}O_3Si_2$)

1.92 g olefin **7** (9.0 mmol, 2.0 eq) and 2nd Grubbs' generation catalyst (10 mol %) were added to a solution of 2.0 g olefin **6** (4.50 mmol, 1.0 eq) in 100 cm^3 CH_2Cl_2 under N_2 atmosphere at room temperature. The temperature was raised to reflux and the reaction allowed stirring for 48 h. The reaction mixture was directly adsorbed on silica to perform the column chromatography (silica gel, 60–120 mesh, 4 % EtOAc in pet. ether), to give **12** in 57 % yield as a colorless syrup. $[\alpha]_D^{25} = +32.99$ ($c = 1.2$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.63–7.54$ (m, 4H, Ar–H), 7.40–7.28 (m, 6H, Ar–H), 7.24–7.16 (m, 5H, Ar–H), 5.15–5.02 (m, 2H, olefinic), 4.57 (d, 1H, $J = 11.7$ Hz, benzylic), 4.53 (d, 1H, $J = 11.7$ Hz, benzylic), 3.69–3.57 (m, 2H, 2 –OCH), 3.42(t, 1H, $J = 6.8$ Hz, CH), 2.42–2.29 (m, 2H, allylic), 2.08–1.98 (m, 2H, allylic), 1.72–1.54 (m, 4H, 2 –CH_2), 1.16 (d, 3H, $J = 6.8$ Hz, –CH_3), 1.02 (s, 9H, *t*-Bu), 0.87 (s, 9H, *t*-Bu), 0.22 (s, 6H, 2 –CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 136.8$, 133.8, 132.9, 129.8, 128.3, 128.1, 127.8, 127.6, 76.1, 71.1, 68.2, 38.8, 36.6, 35.8, 30.9, 27.2, 26.1, 23.8, 19.6, 18.3, −4.2 ppm; IR (neat): $\bar{\nu} = 3010$, 2940, 1610, 1190, 1100 cm^{-1}; ESI–MS: *m/z* = 653 ($[M + Na]^+$).

(3R,9R)-9-(tert-Butyldimethylsilyloxy)-3-(tert-butyldiphenylsilyloxy)decan-1-ol (**13**, $C_{32}H_{54}O_3Si_2$)

To a stirred solution of 1.5 g **12** (2.37 mmol, 1.0 eq) in 10 cm^3 EtOAc, 10 % palladium adsorbed on carbon (Pd/C) was added and stirred under H_2 atmosphere for 12 h at room temperature. The reaction mixture was filtered through Celite and the filtrate was concentrated under reduced pressure and purified by column chromatography (silica gel, 60–120 mesh, 20 % EtOAc in pet. ether) to furnish **13** (1.1 g, 91 %) as colorless syrup. $[\alpha]_D^{25} = +9.9$ ($c = 0.8$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.68–7.56$ (m, 4H, Ar–H), 7.35–7.27 (m, 6H, Ar–H), 3.67–3.56 (m, 2H, 2 –OCH), 3.53 (t, 2H, $J = 6.8$ Hz, –OCH_2), 2.04 (br.s, 1H, –OH), 1.78–1.52 (m, 2H, –CH_2), 1.46–1.17 (m, 10H, 5 –CH_2), 1.17 (d, 3H, $J = 6.6$ Hz, –CH_3), 0.98 (s, 9H, *t*-Bu), 0.83 (s, 9H, *t*-Bu), 0.19 (s, 6H, 2 –CH_3) ppm;

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.1$, 133.6, 129.8, 128.1, 78.3, 68.1, 61.3, 38.7, 32.3, 29.8, 27.2, 26.7, 26.1, 25.9, 24.1, 19.5, 18.2, −4.1 ppm; IR (neat): $\bar{\nu} = 3368$, 2934, 2859, 1428, 1108, 1055 cm^{-1}; ESI–MS: $m/z = 543$ ($[M + H]^+$).

(3R,9R)-9-(tert-Butyldimethylsilyloxy)-3-(tert-butyldiphenylsilyloxy)decanoicacid (**14**, $C_{32}H_{52}O_4Si_2$)
To a stirred solution of 1.1 g **13** (2.02 mmol, 1.0 eq) in CH_2Cl_2:H_2O (1:1, 1 cm^3), 94 mg TEMPO (0.61 mmol, 0.3 eq), and 0.19 g BIAB (0.61 mmol, 0.3 eq) were added at 0 °C and stirred for 1 h. The reaction mixture was diluted with 5 cm^3 water and extracted with CH_2Cl_2 (2 × 20 cm^3). The organic layers were washed with 10 cm^3 brine, dried (Na_2SO_4), evaporated, and the residue purified by column chromatography (silica gel, 60–120 mesh, 30 % EtOAc in pet. ether) to give acid **14** (0.85 g, 76 %) as a colorless gummy oil. $[\alpha]_D^{25} = -105.3$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.67$–7.54 (m, 4H, Ar–H), 7.39–7.28 (m, 6H, Ar–H), 3.71–3.63 (m, 1H, –OCH), 3.61–3.53 (m, 1H, –OCH), 2.73 (dd, 1H, $J = 8.6$, 15.1 Hz, –C*H*–COOH), 2.64 (dd, 1H, $J = 5.8$, 15.1 Hz, –C*H*–COOH), 1.69–1.52 (m, 2H, $–CH_2$), 1.42–1.27 (m, 8H, 4 $–CH_2$), 1.16 (d, 3H, $J = 6.4$ Hz, $–CH_3$), 0.99 (s, 9H, *t*-Bu), 0.81 (s, 9H, *t*-Bu), 0.21 (s, 6H, 2 $–CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.8$, 136.9, 133.8, 129.9, 128.2, 81.3, 67.8, 44.2, 39.3, 33.2, 30.4, 27.1, 26.3, 25.8, 24.2, 20.3, 18.6, −4.6 ppm; IR (neat): $\bar{\nu} = 3450$, 2928, 2855, 1737, 1639, 1438, 1363, 1277, 1075, 1040, 921, 699 cm^{-1}; ESI–MS: $m/z = 557$ ($[M + H]^+$).

(3R,9R)-3-(tert-Butyldiphenylsilyloxy)-9-hydroxydecanoic acid (**5**, $C_{26}H_{38}O_4Si$)
To a cooled (0 °C) solution of 0.8 g **14** (1.43 mmol, 1.0 eq) in 5 cm^3 methanol, 36 mg PPTS (0.14 mmol, 0.1 eq) was added and stirred for 6 h. After completion of the reaction, methanol was removed and extracted with EtOAc (2 × 20 cm^3). The combined organic layers were washed with water (2 × 20 cm^3), brine (10 cm^3), dried (Na_2SO_4), evaporated, and purified the residue by column chromatography (silica gel, 60–120 mesh, 35 % EtOAc in pet. ether) to afford **5** (0.63 g, 88 %) as a colorless liquid. $[\alpha]_D^{25} = -89.81$ ($c = 0.55$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.66$–7.57 (m, 4H, Ar–H), 7.42–7.31 (m, 6H, Ar–H), 3.81–3.73 (m, 2H, 2 –OCH), 2.78 (dd, 1H, $J = 8.8$, 15.3 Hz, –C*H*–COOH), 2.63 (dd, 1H, $J = 6.1$, 15.3 Hz, –C*H*–COOH), 1.73–1.32 (m, 10H, 5 $–CH_2$), 1.19 (d, 3H, $J = 6.2$ Hz, $–CH_3$), 0.94 (s, 9H, *t*-Bu) ppm; ^{13}CNMR (75 MHz, $CDCl_3$): $\delta = 173.6$, 136.8, 134.1, 130.1, 128.2, 81.3, 68.1, 43.3, 40.4, 32.2, 30.4, 27.1, 26.2, 25.3, 23.8, 19.1 ppm; IR (neat): $\bar{\nu} = 3425$, 2927, 2856, 1653, 1512, 1456, 1378, 1249, 1025, 699 cm^{-1}; ESI–MS: $m/z = 465$ ($[M + Na]^+$).

(4R,10R)-4-(tert-Butyldiphenylsilyloxy)-10-methyloxecan-2-one (**15**, $C_{16}H_{36}O_3Si$)
A solution of 0.2 g hydroxy acid **5** (0.45 mmol, 1.0 eq) in 2 cm^3 dry THF at 0 °C under an N_2 atmosphere was treated with 0.25 cm^3 Et_3N (1.80 mmol, 4.0 eq) and 0.21 mg 2,4,6-trichlorobenzoyl chloride (1.35 mmol, 3.0 eq) sequentially. After stirring at room temperature for 2 h, it was diluted with 20 cm^3 toluene. Next, this mixture was added dropwise over 5 h, to a solution of 55 mg DMAP (0.45 mmol) in 250 cm^3 dry toluene preheated at 60 °C. After completion of addition, the reaction mixture was allowed for stirring at 60 °C for 1 h. It was then cooled to room temperature and concentrated under reduced pressure. Purification of the residue by column chromatography (silica gel, 60–120 mesh, 8 % EtOAc inpet. ether) furnished lactone **15** (0.12 g, 63 %) as a colorless oil. $[\alpha]_D^{25} = -19.7$ ($c = 0.6$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.65$–7.54 (m, 4H, Ar–H), 7.44–7.33 (m, 6H, Ar–H), 4.94 (m, 1H, –CH), 4.16 (m, 1H, –CH), 2.71 (dd, 1H, $J = 5.4$, 15.4 Hz, –CH), 2.45 (dd, 1H, $J = 8.3$, 15.4 Hz, –CH), 1.79–1.33 (m, 10H, 5 $–CH_2$), 1.23 (d, 3H, $J = 6.5$ Hz, $–CH_3$) ppm; ^{13}CNMR (75 MHz, $CDCl_3$): $\delta = 172.4$, 133.8, 133.6, 129.8, 128.0, 81.1, 67.8, 43.1, 34.3, 32.0, 29.8, 27.2, 26.1, 23.9, 22.1, 19.0 ppm; IR (neat): $\bar{\nu} = 2938$, 1730,1646, 1377, 1207, 1096, 1044, 869 cm^{-1}; ESI–MS: $m/z = 425$ ($[M + H]^+$).

*Diplodialide C (**3**)*
To a cooled (0 °C) solution of 0.11 g **15** (0.25 mmol, 1.0 eq) in 1 cm^3 dry THF under nitrogen atmosphere, 0.4 cm^3 of a solution of TBAF in THF (1.0 M, 0.38 mmol, 1.5 eq) was added and stirred for 1 h. The reaction was diluted with 5 cm^3 water and extracted with EtOAc (2 × 20 cm^3). The combined organic layers were washed with water (2 × 10 cm^3), brine (10 cm^3), dried (Na_2SO_4), evaporated, and purified the residue by column chromatography (silica gel, 60–120 mesh, 20 % EtOAc in pet. ether) to afford **3** (40 mg, 84 %) as a colorless liquid. $[\alpha]_D^{25} = -38.9$ ($c = 0.7$, $CHCl_3$) (Ref. [6] $[\alpha]_D^{25} = -41.0$ ($c = 0.61$, $CHCl_3$)); spectral data were in good agreement with the reported values in the literature [6].

Acknowledgments We are grateful to CSIR-IICT, Hyderabad for providing analytical facilities.

References

1. Wada K, Ishida T (1975) J Chem Soc Chem Commun 209
2. Wada K, Ishida T (1976) J Chem Soc Chem Commun 340
3. Wada K, Ishida T (1979) J Chem Soc Perkin Trans 1:1154
4. Wakamatsu T, Akasaka K, Ban Y (1977) Tetrahedron Lett 32:2755
5. Wakamatsu T, Akasaka K, Ban Y (1979) J Org Chem 44:2008

6. Sharma GVM, Reddy KL (2006) Tetrahedron Asymmetry 17:3197
7. Tadross PM, Virgil SC, Stoltz BM (2010) Org Lett 12:1612
8. Tokunaga M, Larrow JF, Kakiuchi F, Jacobsen EN (1997) Science 277:936
9. Felpin FX, Lebreton J (2002) J Org Chem 67:9192
10. Shyla G, Arumugam S (2007) Tetrahedron Lett 48:8544
11. Grubbs RH (2004) Tetrahedron 60:7117
12. Nolen EG, Kurish AJ, Wong KA, Orlando MD (2003) Tetrahedron Lett 44:2449
13. Chatterjee AK, Choi TL, Sanders DP, Grubbs RH (2003) J Am Chem Soc 125:11360
14. Sharma GVM, Mallesham S, Chandramouli C (2009) Tetrahedron Asymmetry 20:2513
15. Huang L, Teumelsan N, Huang X (2006) Chem Eur J 12:5246
16. Epp JB, Widlanski TS (1999) J Org Chem 64:293
17. Inanaga J, Hirata K, Saeki H, Katsuki T, Yamaguchi M (1979) Bull Chem Soc Jpn 52:1989
18. Parenty A, Moreau X, Campagne JM (2006) Chem Rev 106:911
19. Xu Y-C, Kohlman DT, Liang SX, Erikkson C (1999) Org Lett 1:1599
20. Sawant P, Maier ME (2010) Tetrahedron 66:9738
21. Sabitha G, Rao AS, Yadav JS (2010) Synthesis 3:505