Synthesis R. Karnekanti et al. Paper

Stereoselective Total Synthesis of (+)-Anamarine and 8-*epi*-(–)-Anamarine from D-Mannitol

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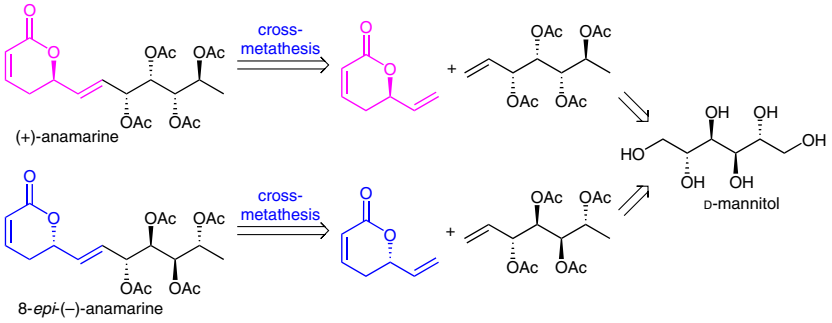

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Abstract Stereoselective total synthesis of (+)-anamarine and the first synthesis of 8-*epi*-(–)-anamarine, its nonnatural diastereomer, were achieved from readily available D-mannitol. The key reactions involved were asymmetric dihydroxylation, cross-metathesis and ring-closing metathesis reactions. The approach is adoptable advantageously for the diversity-oriented synthesis of several related classes of natural products.

Key words (+)-anamarine, 8-*epi*-(–)-anamarine, D-mannitol, asymmetric dihydroxylation, cross-metathesis and ring-closing metathesis

The δ-lactone moiety is an important structural unit found in various bioactive natural products, which show a wide range of biological activities.[1–4] The 5,6-dihydro-2*H*-pyran-2-one-containing natural product (+)-anamarine (**1**) was isolated from the flowers and leaves of a *Peruvian hyptis* species.[5] Lactone **1** contains five stereocenters (5*R*,8*R*,9*S*,10*S*,11*S*), a *trans* double bond and an α,β-unsaturated lactone moiety (Figure 1). Due to its biological importance, several syntheses[6–10] have been reported for **1**. In continuation of our interest in the synthesis of biologically active lactones,[11] herein, we report a flexible route for the synthesis of (+)-anamarine (**1**) and its nonnatural diastereomer, 8-*epi*-(–)-anamarine (**3**), from D-mannitol as common starting material.

The retrosynthetic analysis of (+)-anamarine (**1**) revealed that it could be obtained by an olefin cross-metathesis reaction of the vinyl lactone **4** and tetraacetate **5**, wherein both, in turn, could be realized from D-mannitol through **6** and **7**, respectively (Scheme 1).

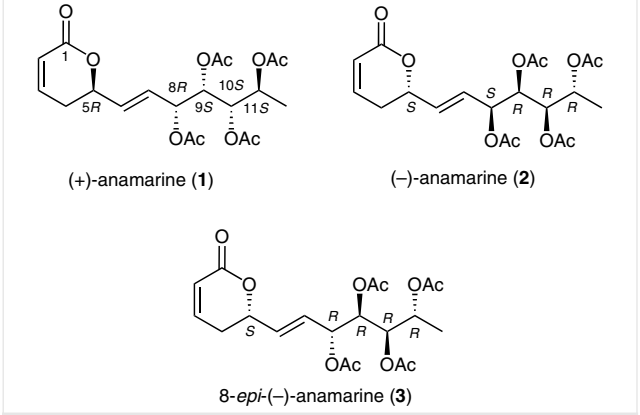
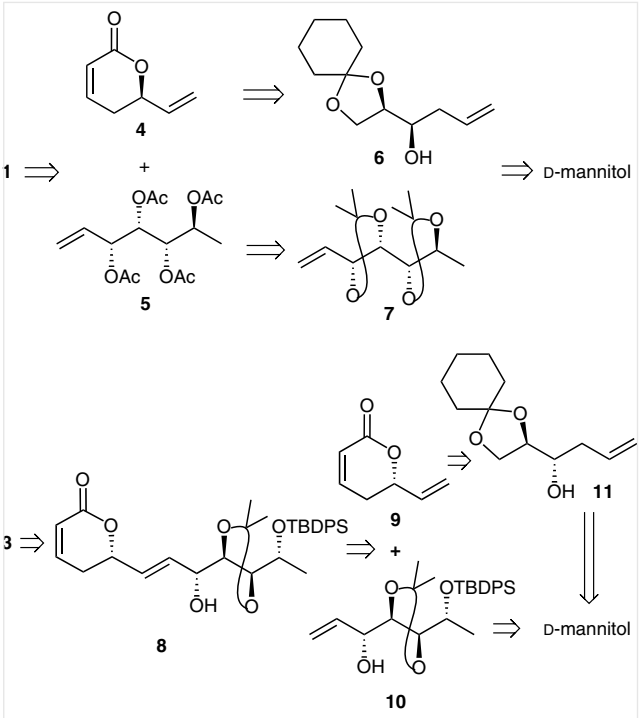


Figure 1 Structures of anamarines **1**, **2** and **3**

Similarly, the retrosynthetic analysis of 8-*epi*-(–)-anamarine (**3**) revealed that **8** (Scheme 1) is the late-stage intermediate. Olefin **8** could be realized from lactone **9** and olefin **10** by a cross-metathesis reaction. The requisite lactone **9** and olefin **10** could be prepared from D-mannitol as common starting material.

Vinyl lactones **4** and **9** were prepared from alcohol **11** (Scheme 2). Accordingly, alcohol **11**,[12] obtained from D-mannitol, was subjected to Mitsunobu inversion[13] upon treatment with *p*-nitrobenzoic acid, triphenylphosphane and diisopropyl azodicarboxylate (DIAD) in tetrahydrofuran to give **12** (74%), which on subsequent base hydrolysis (K_2CO_3, MeOH) afforded **6** in 86% yield (Scheme 2). Reaction of alcohol **6** with acryloyl chloride and triethylamine in dichloromethane furnished the acrylate **13** (82%), which on a ring-closing metathesis (RCM) reaction with Grubbs I[14] catalyst gave α,β-unsaturated lactone **14** in 89% yield. Treatment of **14** with copper(II) chloride dihydrate ($CuCl_2 \cdot 2H_2O$) in acetonitrile[15] afforded the corresponding diol, which on

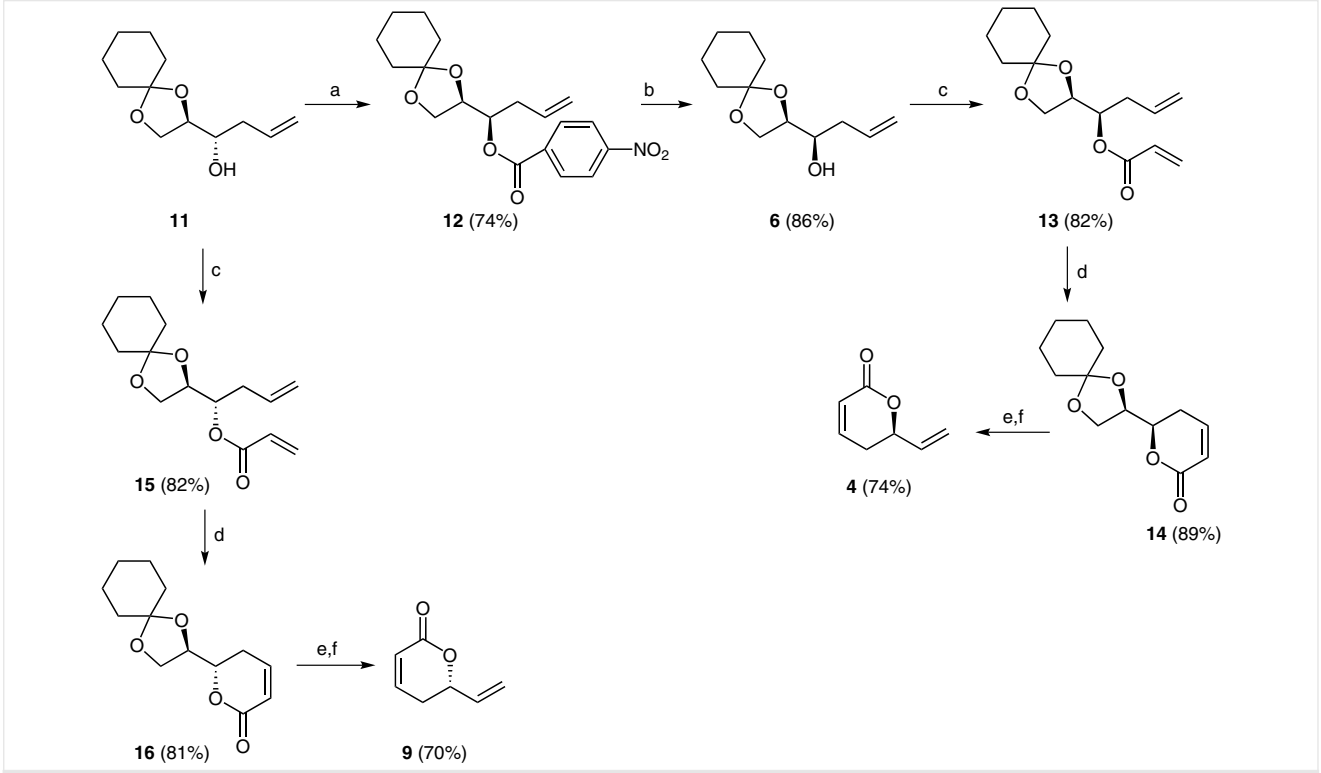


Scheme 1 Retrosynthetic analysis of **1** and **3**

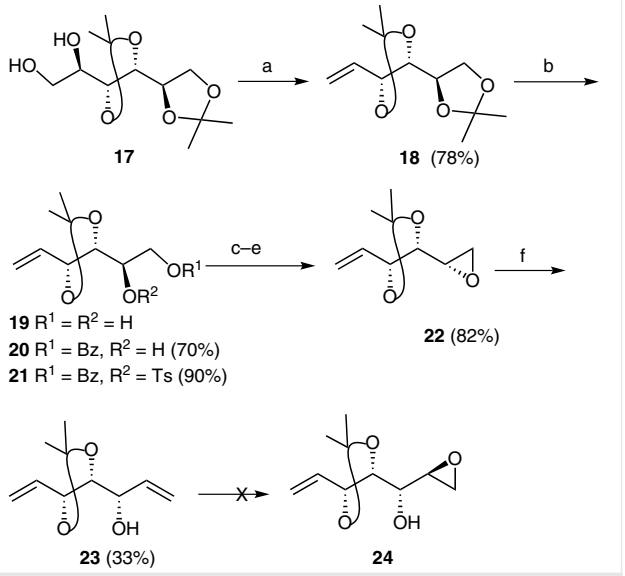
subsequent treatment with triphenylphosphane,[16] iodine and imidazole in dichloromethane furnished olefin **4** in 74% yield {$[\alpha]_D^{25}$ +93.8 (*c* 0.10, $CHCl_3$); Lit.[10] $[\alpha]_D^{20}$ +90.4 (*c* 0.7, $CHCl_3$)}.

Likewise, alcohol **11** on treatment with acryloyl chloride and triethylamine in dichloromethane furnished ester **15** in 82% yield (Scheme 2). The RCM reaction of **15** with Grubbs I catalyst in dichloromethane gave the lactone **16** (81%). Hydrolysis of the acetonide in **16** ($CuCl_2{\cdot}2H_2O$, MeCN) gave the corresponding diol, which on further reaction with triphenylphosphane, iodine and imidazole in dichloromethane afforded the olefin **9** in 70% yield {$[\alpha]_D^{25}$ –87.5 (*c* 0.10, $CHCl_3$); Lit.[17] $[\alpha]_D^{25}$ –93.4 (*c* 0.10, $CHCl_3$)}.

The diol **17** prepared from tri-*O*-isopropylidene-D-(+)-mannitol,[18] on treatment with triphenylphosphane, iodine and imidazole in dichloromethane, gave olefin **18** in 78% yield (Scheme 3). Selective deprotection of the 1,2-*O*-isopropylidene group in **18** using $CuCl_2{\cdot}2H_2O$ in acetonitrile gave the diol **19** in 98% yield (with the recovery of starting material). Reaction of **19** with benzoyl chloride in the presence of triethylamine and dibutyltin(IV) oxide[19] in dichloromethane furnished the monobenzoate **20** selectively in 70% yield. Alcohol **20** on further reaction with *p*-tosyl chloride in the presence of triethylamine and catalytic 4-(dimethylamino)pyridine in dichloromethane gave **21**



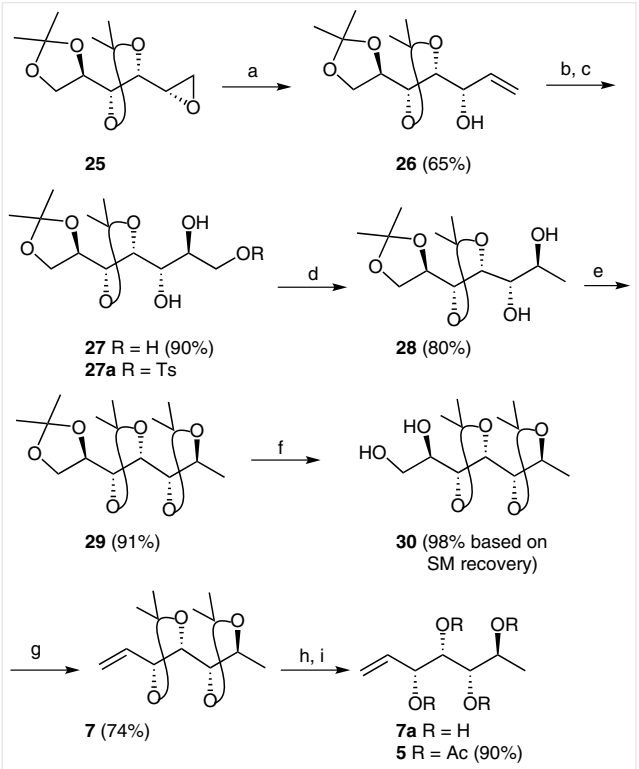
Scheme 2 *Reagents and conditions*: a) *p*-nitrobenzoic acid, Ph_3P, DIAD, THF, r.t., 5 h; b) K_2CO_3, MeOH, r.t., 1 h; c) acryloyl chloride, Et_3N, DMAP (cat.), CH_2Cl_2, 0 °C to r.t., 2 h; d) Grubbs I catalyst, CH_2Cl_2, reflux, 6 h; e) $CuCl_2{\cdot}2H_2O$, MeCN, 0 °C, 30 min; f) I_2, Ph_3P, imidazole, CH_2Cl_2, 0 °C to r.t., 4 h.



Scheme 3 *Reagents and conditions*: a) I_2, Ph_3P, imidazole, CH_2Cl_2, 0 °C to r.t., 4 h; b) $CuCl_2{\cdot}2H_2O$, MeCN, 0 °C, 15 min; c) BzCl, Et_3N, *n*-Bu_2SnO, CH_2Cl_2, 0 °C to r.t., 1 h; d) *p*-TsCl, Et_3N, DMAP (cat.), CH_2Cl_2, r.t., 5 h; e) K_2CO_3, MeOH, 0 °C to r.t., 1 h; f) TMSI, *n*-BuLi, THF, –20 °C, 30 min.

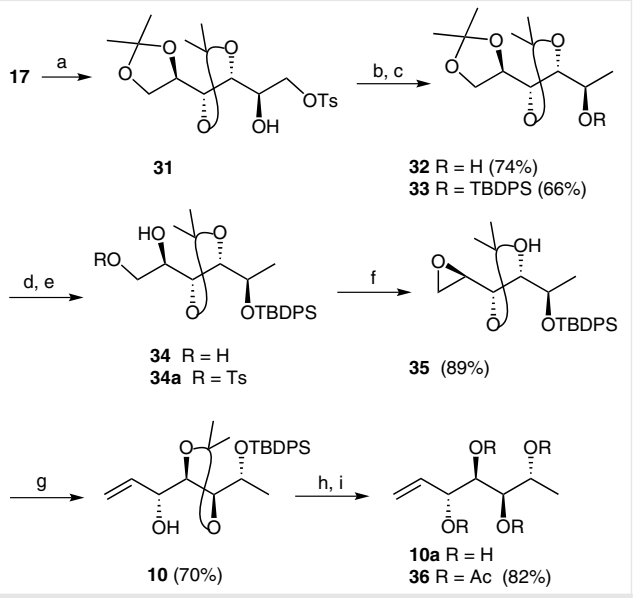
(90%), which on treatment with methanolic potassium carbonate at room temperature afforded the epoxide **22** in 82% yield. Regioselective opening of the epoxide **22** with trimethylsilyl iodide and *n*-butyllithium[20] in tetrahydrofuran at –20 °C furnished the allylic alcohol **23** (33%), which on Sharpless asymmetric epoxidation under different reaction conditions met with failure to give the expected epoxide **24**, to introduce the C11 stereocenter of target **1**.

Alternatively, olefin **5** was prepared as shown in Scheme 4, from the known epoxide **25**.[21] Accordingly, regioselective opening of epoxide **25** with trimethylsilyl iodide and *n*-butyllithium in tetrahydrofuran at –20 °C gave the allylic alcohol **26** in 65% yield. The olefin **26** was subjected to asymmetric dihydroxylation[22] using AD-mix-β and methanesulfonamide in aqueous *tert*-butyl alcohol (1:1) at 0 °C to afford the triol **27** in 90% yield (dr 9:1). Reaction of triol **27** with *p*-tosyl chloride, triethylamine and dibutyltin(IV) oxide in dichloromethane furnished **27a**, which on reduction with lithium aluminum hydride in tetrahydrofuran gave diol **28** in 80% yield. Treatment of **28** with 2,2-dimethoxypropane in acetone in the presence of catalytic *p*-toluenesulfonic acid furnished **29** (91%), which on selective deprotection ($CuCl_2{\cdot}2H_2O$, MeCN) afforded the diol **30** (98% based on starting material recovery). Reaction of **30** with triphenylphosphane, iodine and imidazole in dichloromethane gave olefin **7** in 74% yield. Reaction of **7** with trifluoroacetic acid in dichloromethane furnished the tetrol **7a**, which on subsequent treatment with acetic anhydride and pyridine in dichloromethane gave the tetraacetate **5**[10] in 90% yield (Scheme 4).



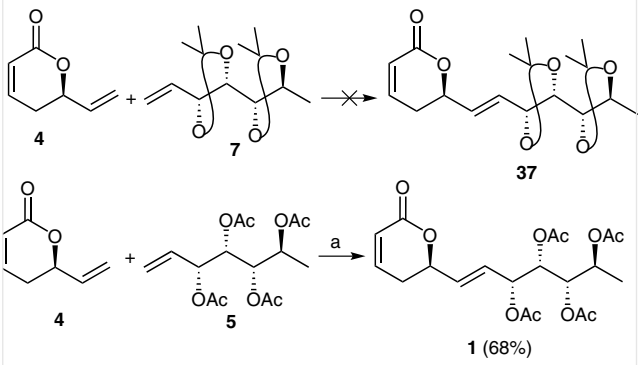
Scheme 4 *Reagents and conditions*: a) TMSI, *n*-BuLi, THF, –20 °C, 30 min; b) AD-mix-β, $MsNH_2$, *t*-BuOH–H_2O (1:1), 0 °C, 24 h; c) *p*-TsCl, Et_3N, *n*-Bu_2SnO, CH_2Cl_2, 0 °C to r.t., 1 h; d) LAH, THF, 0 °C to r.t., 3 h; e) 2,2-dimethoxypropane, PTSA (cat.), acetone, 0 °C to r.t., 1 h; f) $CuCl_2{\cdot}2H_2O$, MeCN, 0 °C, 15 min; g) I_2, Ph_3P, imidazole, CH_2Cl_2, 0 °C to r.t., 4 h; h) TFA, CH_2Cl_2, 0 °C to r.t., 15 min; i) Ac_2O, pyridine, DMAP (cat.), CH_2Cl_2, r.t., 20 h.

For the synthesis of fragment **10**, diol **17** was treated with *p*-tosyl chloride, triethylamine and dibutyltin(IV) oxide in dichloromethane to give tosylate **31**, which on further deoxygenation with lithium aluminum hydride in tetrahydrofuran furnished **32** in 74% yield (Scheme 5). Alcohol **32** on reaction with *tert*-butyldiphenylsilyl chloride and imidazole in dichloromethane afforded **33** in 66% yield. Selective deprotection of **33** ($CuCl_2{\cdot}2H_2O$, MeCN) and subsequent tosylation (*p*-TsCl, Et_3N, *n*-Bu_2SnO) of diol **34** in dichloromethane gave **34a**. Reaction of **34a** with methanolic potassium carbonate afforded the epoxide **35** (89%), which on ring opening with trimethylsilyl iodide and *n*-butyllithium in tetrahydrofuran at –20 °C furnished the allylic alcohol **10** in 70% yield. Exposure of **10** to trifluoroacetic acid in dichloromethane and subsequent acetylation (Ac_2O, pyridine) of tetrol **10a** in dichloromethane afforded the tetraacetate **36** in 82% yield.



Scheme 5 *Reagents and conditions*: a) *p*-TsCl, Et_3N, *n*-Bu_2SnO, CH_2Cl_2, 0 °C to r.t., 1 h; b) LAH, THF, 0 °C to r.t., 3 h; c) TBDPSCl, imidazole, CH_2Cl_2, 0 °C to r.t., 1 h; d) $CuCl_2{\cdot}2H_2O$, MeCN, 0 °C, 30 min; e) *p*-TsCl, Et_3N, *n*-Bu_2SnO, CH_2Cl_2, r.t., 30 min; f) K_2CO_3, MeOH, r.t., 1 h; g) TMSI, *n*-BuLi, THF, –20 °C, 30 min; h) TFA, CH_2Cl_2, 0 °C to r.t., 15 min; i) Ac_2O, pyridine, DMAP (cat.), CH_2Cl_2, r.t., 20 h.

For the synthesis of (+)-anamarine (**1**), attempted cross-metathesis of olefins **4** and **7** with the Grubbs II[23] catalyst met with failure to give the expected product **37** (Scheme 6). This may be attributed to the presence of the bulky acetonide protection next to the olefin. Hence, vinyl lactone **4** was subjected to a cross-metathesis reaction with tetraacetate **5** using Grubbs II[23] catalyst to give the target **1** in 68% yield.

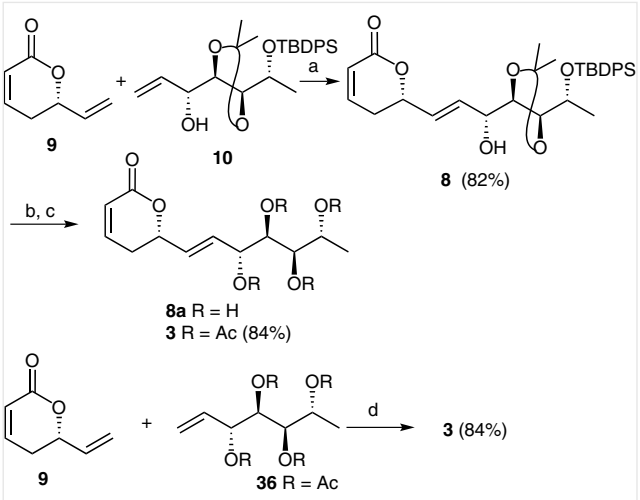


Scheme 6 *Reagents and conditions*: a) Grubbs II catalyst, CH_2Cl_2, reflux, 5 h.

The spectroscopic data of the synthetic **1** match the reported[5] values (see Supporting Information, Tables 1 and 2) {$[\alpha]_D^{25}$ +16.8 (*c* 0.3, $CHCl_3$); Lit.[7–9] $[\alpha]_D^{25}$ +17.8 (*c* 0.3, $CHCl_3$)}.

For the synthesis of 8-*epi*-(–)-anamarine (**3**), vinyl lactone **9** was reacted with olefin **10** in the presence of Grubbs II catalyst in toluene at reflux to give **8** in 82% yield (Scheme 7). Lactone **8** was treated with trifluoroacetic acid in dichloromethane to give tetrol **8a**, by the simultaneous deprotection of the silyl and acetonide groups. Finally, reaction of **8a** with acetic anhydride and pyridine in dichloromethane furnished 8-*epi*-(–)-anamarine (**3**) in 84% yield, paving the way for its first synthesis {$[\alpha]_D^{25}$ –9.0 (*c* 1.12, $CHCl_3$)}.

Alternatively, cross-metathesis of olefins **9** and **36** using Grubbs II catalyst afforded 8-*epi*-(–)-anamarine (**3**) in 84% yield (Scheme 7). Though **3** could be obtained from this alternative coupling, the yield was albeit less than the earlier experiment. From these studies, it is evident that, in the absence of an acetyl group at the allylic position, the cross-metathesis reaction is more facile and the yields are high.



Scheme 7 *Reagents and conditions*: a) Grubbs II catalyst, toluene, reflux, 8 h; b) TFA, CH_2Cl_2, 0 °C to r.t., 15 min; c) Ac_2O, pyridine, DMAP (cat.), CH_2Cl_2, r.t., 20 h; d) Grubbs II catalyst, CH_2Cl_2, reflux, 5 h.

In conclusion, a general and efficient convergent synthetic strategy has been developed for the synthesis of (+)-anamarine and the first synthesis of its nonnatural diastereomer 8-*epi*-(–)-anamarine from D-mannitol. Two enantiomeric vinyl lactones and two olefinic acyclic fragments, encompassing five stereocenters, were synthesized and coupled to give this anamarine class of δ-lactones. This approach is adoptable for the diversity-oriented efficient synthesis of related lactone classes of compounds.

Solvents were dried over standard drying agents and were freshly distilled prior to use. Chemicals were purchased and used without further purification. All column chromatographic separations were performed using silica gel (Acme, 60–120 mesh). Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40 °C under reduced pressure. ^1H NMR (300 MHz and 500 MHz) and ^{13}C NMR (75

MHz and 125 MHz) spectra were measured with Bruker Avance 300 and Varian Unity Inova-500 instruments with tetramethylsilane as an internal standard for solutions in $CDCl_3$; *J* values are given in hertz. IR spectra were recorded on Perkin-Elmer IR-683 and JASCO FT/IR-5300 spectrophotometers with NaCl and KBr optics. Optical rotations were measured with a JASCO DIP 300 digital polarimeter. Mass spectra were recorded on Bruker maXis, CEC-21-11013 or Finnigan Mat 1210 double-focusing mass spectrometers operating with a direct inlet system or LC/MSD Trap SL (Agilent Technologies).

(*R*)-1-{(*R*)-1,4-Dioxaspiro[4.5]decan-2-yl}but-3-enyl 4-Nitrobenzoate (12)

To a stirred solution of **11** (1.2 g, 5.66 mmol) in THF (10 mL), Ph_3P (2.22 g, 8.49 mmol) and *p*-nitrobenzoic acid (1.42 g, 8.49 mmol) were added, and the mixture was stirred for 20 min. DIAD (1.71 g, 8.49 mmol) was added at 0 °C and the reaction mixture was stirred at r.t. for 5 h. Then, it was quenched with sat. aq $NaHCO_3$ solution (10 mL) and extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 1:9) to afford **12** (1.52 g, 74%) as a pale yellow syrup.

$[\alpha]_D^{25}$ +12.0 (*c* 0.62, $CHCl_3$).

IR (neat): 3019, 2934, 2857, 2315, 1726, 1645, 1608, 1529, 1449, 1347, 1272, 1216, 1164, 1101, 1045, 1015, 925, 873, 846, 771, 721, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 9.1 Hz, 2 H, Ar-H), 8.23 (d, *J* = 9.1 Hz, 2 H, Ar-H), 5.82 (ddd, *J* = 7.4, 10.2, 14.4 Hz, 1 H, olefinic), 5.26 (td, *J* = 5.3, 10.6 Hz, 1 H, OCH), 5.13 (dd, *J* = 1.5, 17.0 Hz, 1 H, olefinic), 5.07 (d, *J* = 10.2 Hz, 1 H, olefinic), 4.34 (q, *J* = 6.0 Hz, 1 H, OCH), 4.08 (dd, *J* = 6.6, 8.5 Hz, 1 H, OCH), 3.80 (dd, *J* = 6.0, 8.7 Hz, 1 H, OCH), 2.63–2.44 (m, 2 H, allylic), 1.74–1.48 (m, 8 H, cyclohexyl), 1.47–1.29 (m, 2 H, cyclohexyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2, 150.5, 135.6, 132.6, 123.5, 118.6, 110.3, 75.6, 74.5, 65.2, 35.9, 35.4, 34.7, 25.0, 23.9, 23.8.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{23}NO_6$: 384.13935; found: 384.13366.

(*R*)-1-{(*R*)-1,4-Dioxaspiro[4.5]decan-2-yl}but-3-en-1-ol (6)

To a stirred solution of **12** (1.50 g, 4.16 mmol) in MeOH (10 mL) at 0 °C, K_2CO_3 (1.72 g, 12.47 mmol) was added, and the mixture was stirred at r.t. for 1 h. Then, it was filtered through a pad of Celite® which was then washed with EtOAc (3 × 15 mL). The combined organic layers were dried (Na_2SO_4) and concentrated, and the residue was purified by silica gel column chromatography (EtOAc–PE, 8:92) to afford **6** (0.76 g, 86%) as a colorless syrup.

$[\alpha]_D^{25}$ +6.5 (*c* 0.20, $CHCl_3$).

IR (neat): 3396, 3018, 2936, 2860, 2314, 1644, 1551, 1433, 1367, 1334, 1281, 1216, 1164, 1101, 1045, 926, 848, 771, 668, 626 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.87 (ddd, *J* = 7.2, 10.4, 14.2 Hz, 1 H, olefinic), 5.21–5.07 (m, 2 H, olefinic), 4.08–3.97 (m, 2 H, OCH_2), 3.80–3.70 (m, 1 H, OCH), 3.59 (m, 1 H, OCH), 2.35 (br s, 1 H, OH), 2.25 (t, *J* = 6.4 Hz, 2 H, allylic), 1.70–1.51 (m, 8 H, cyclohexyl), 1.50–1.31 (m, 2 H, cyclohexyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.0, 117.7, 109.9, 78.0, 71.6, 65.7, 38.2, 36.2, 34.8, 25.1, 24.0, 23.7.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{20}O_3$: 235.13047; found: 235.13033.

(*R*)-1-{(*R*)-1,4-Dioxaspiro[4.5]decan-2-yl}but-3-enyl Acrylate (13)

To a stirred solution of **6** (0.74 g, 3.49 mmol) in CH_2Cl_2 (7.5 mL) at 0 °C, Et_3N (1.46 mL, 10.46 mmol) and DMAP (cat.) followed by acryloyl chloride (0.31 mL, 3.84 mmol) were added, and the mixture was stirred at r.t. for 2 h. Then, it was diluted with $CHCl_3$ (10 mL), washed with water (10 mL) and brine (10 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 5:95) to afford **13** (0.76 g, 82%) as a pale yellow syrup.

$[\alpha]_D^{25}$ +5.6 (*c* 0.30, $CHCl_3$).

IR (neat): 3746, 3668, 3625, 3020, 2938, 2861, 2314, 1725, 1644, 1610, 1551, 1531, 1482, 1467, 1449, 1407, 1350, 1277, 1216, 1190, 1164, 1101, 1049, 1018, 984, 925, 874, 844, 771, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.43 (dd, *J* = 1.5, 17.4 Hz, 1 H, olefinic), 6.14 (dd, *J* = 10.2, 17.4 Hz, 1 H, olefinic), 5.85 (dd, *J* = 1.5, 10.4 Hz, 1 H, olefinic), 5.80–5.69 (m, 1 H, olefinic), 5.16–5.04 (m, 2 H, olefinic), 4.44 (q, *J* = 7.2 Hz, 1 H, OCH), 4.27–4.16 (m, 1 H, OCH), 4.06–3.97 (m, 1 H, OCH), 3.73 (m, 1 H, OCH), 2.52–2.31 (m, 2 H, allylic), 1.71–1.49 (m, 8 H, cyclohexyl), 1.48–1.30 (m, 2 H, cyclohexyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7, 133.0, 131.0, 128.3, 118.2, 110.1, 75.6, 72.7, 65.2, 35.7, 35.3, 34.9, 25.1, 23.9, 23.8.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{22}O_4$: 289.14103; found: 289.14129.

(*R*)-6-{(*R*)-1,4-Dioxaspiro[4.5]decan-2-yl}-5,6-dihydro-2*H*-pyran-2-one (14)

To a stirred solution of **13** (0.05 g, 0.19 mmol) in CH_2Cl_2 (50 mL), Grubbs I catalyst (10 mol%) was added, and the mixture was stirred at reflux for 6 h. Most of the solvent was then distilled off and the concentrated solution was left to stir at r.t. for 2 h under a flow of air to decompose the catalyst. The mixture was concentrated and the residue was purified by silica gel column chromatography (EtOAc–PE, 3:7) to afford **14** (0.04 g, 89%) as a colorless syrup.

$[\alpha]_D^{25}$ +61.0 (*c* 0.37, $CHCl_3$).

IR (neat): 3010, 2933, 2856, 2314, 1727, 1645, 1551, 1500, 1466, 1449, 1383, 1216, 1162, 1095, 1047, 928, 847, 816, 748, 667, 627 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.93 (ddd, *J* = 2.5, 6.0, 8.7 Hz, 1 H, olefinic), 6.03 (dd, *J* = 2.3, 9.8 Hz, 1 H, olefinic), 4.55 (td, *J* = 4.2, 12.1 Hz, 1 H, OCH), 4.33 (dt, *J* = 4.2, 6.2 Hz, 1 H, OCH), 4.13–4.00 (m, 2 H, OCH_2), 2.63–2.47 (m, 1 H, allylic), 2.43–2.31 (m, 1 H, allylic), 1.75–1.52 (m, 8 H, cyclohexyl), 1.50–1.30 (m, 2 H, cyclohexyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.0, 132.7, 117.8, 109.8, 75.5, 72.6, 65.4, 35.8, 35.1, 34.6, 24.8, 23.6, 23.5.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{18}O_4$: 261.10973; found: 261.10974.

(*R*)-6-Vinyl-5,6-dihydro-2*H*-pyran-2-one (4)

To a stirred solution of **14** (0.3 g, 1.27 mmol) in MeCN (5 mL) at 0 °C, $CuCl_2{\cdot}2H_2O$ (0.23 g, 1.38 mmol) was added, and the reaction mixture was stirred at r.t. for 30 min. Then, it was quenched with sat. aq $NaHCO_3$ solution (1 mL), filtered through a pad of Celite® and the pad was washed with EtOAc (10 mL). The organic layer was dried (Na_2SO_4), concentrated and used as such for the next reaction.

To a solution of the above diol (0.2 g, 1.27 mmol), Ph_3P (1.33 g, 5.08 mmol) and imidazole (0.35 g, 5.08 mmol) in CH_2Cl_2 (5 mL) at 0 °C, I_2 (0.97 g, 3.81 mmol) was added, and the mixture was stirred at r.t. for 4 h. Then, the reaction mixture was quenched with sat. aq NaOH solution (1 mL) and extracted with $CHCl_3$ (3 × 5 mL). The organic layers

were washed with sat. aq $Na_2S_2O_3$ (4 mL) and brine (4 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 2:8) to give olefin **4** (0.12 g, 74%) as a colorless liquid.

$[\alpha]_D^{25}$ +93.8 (*c* 0.10, $CHCl_3$) {Lit.[10] $[\alpha]_D^{20}$ +90.4 (*c* 0.7, $CHCl_3$)}.

IR (neat): 3020, 2945, 2881, 2777, 1728, 1421, 1273, 1214, 1118, 1071, 1027, 928, 748, 667, 626 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.87 (ddd, *J* = 3.4, 5.3, 8.7 Hz, 1 H, olefinic), 6.04 (td, *J* = 1.9, 9.6 Hz, 1 H, olefinic), 5.94 (m, 1 H, olefinic), 5.39 (d, *J* = 17.4 Hz, 1 H, olefinic), 5.28 (d, *J* = 10.6 Hz, 1 H, olefinic), 4.92 (m, 1 H, OCH), 2.45 (m, 2 H, allylic).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.7, 144.3, 134.8, 121.6, 117.8, 77.7, 29.3.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_7H_8O_2$: 147.0422; found: 147.0425.

(*S*)-1-{(*R*)-1,4-Dioxaspiro[4.5]decan-2-yl}but-3-enyl Acrylate (15)

To a stirred solution of **11** (0.74 g, 3.49 mmol) in CH_2Cl_2 (7.5 mL) at 0 °C, Et_3N (1.46 mL, 10.46 mmol), DMAP (cat.) and acryloyl chloride (0.31 mL, 3.84 mmol) were added sequentially, and the mixture was stirred at r.t. for 2 h. Workup as described for **13** and purification of the residue by silica gel column chromatography (EtOAc–PE, 5:95) afforded **15** (0.76 g, 82%) as a pale yellow syrup.

$[\alpha]_D^{25}$ +17.5 (*c* 0.30, $CHCl_3$).

IR (neat): 2935, 2858, 2313, 1727, 1644, 1568, 1551, 1516, 1466, 1449, 1406, 1367, 1264, 1047, 925, 846, 807, 772, 669 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.41 (d, *J* = 17.4 Hz, 1 H, olefinic), 6.11 (dd, *J* = 10.2, 17.0 Hz, 1 H, olefinic), 5.88–5.69 (m, 2 H, olefinic), 5.15–5.03 (m, 2 H, olefinic), 4.22–3.98 (m, 3 H, 3 × OCH), 3.82 (dd, *J* = 6.4, 7.9 Hz, 1 H, OCH), 2.55–2.33 (m, 2 H, allylic), 1.67–1.50 (m, 8 H, cyclohexyl), 1.40–1.32 (m, 2 H, cyclohexyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.4, 133.0, 131.1, 128.3, 118.1, 110.1, 75.8, 72.9, 65.7, 36.0, 35.3, 34.8, 25.1, 23.9, 23.8.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{22}O_4$: 289.14103; found: 289.14077.

(*S*)-6-{(*R*)-1,4-Dioxaspiro[4.5]decan-2-yl}-5,6-dihydro-2*H*-pyran-2-one (16)

To a stirred solution of **15** (0.07 g, 0.27 mmol) in CH_2Cl_2 (50 mL), Grubbs I catalyst (10 mol%) was added, and the mixture was stirred at reflux for 6 h. Workup as described for **14** and purification of the residue by silica gel column chromatography (EtOAc–PE, 3:7) afforded **16** (0.05 g, 81%) as a colorless syrup.

$[\alpha]_D^{25}$ –59.0 (*c* 0.70, $CHCl_3$).

IR (neat): 3020, 2314, 1727, 1711, 1663, 1569, 1551, 1533, 1483, 1467, 1215, 928, 742, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.91 (m, 1 H, olefinic), 6.02 (dd, *J* = 2.0, 10.1 Hz, 1 H, olefinic), 4.30–4.24 (m, 1 H, OCH), 4.18–4.12 (m, 2 H, OCH), 4.06–4.00 (m, 1 H, OCH), 2.61 (td, *J* = 5.0, 18.1 Hz, 1 H, allylic), 2.48 (td, *J* = 3.0, 10.1 Hz, 1 H, allylic), 1.65–1.53 (m, 8 H, cyclohexyl), 1.48–1.32 (m, 2 H, cyclohexyl).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 144.9, 121.3, 110.6, 78.1, 75.8, 66.7, 36.6, 34.5, 26.4, 25.0, 23.7.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{18}O_4$: 261.1097; found: 261.1097.

(*S*)-6-Vinyl-5,6-dihydro-2*H*-pyran-2-one (9)

To a stirred solution of **16** (0.3 g, 1.27 mmol) in MeCN (5 mL) at 0 °C, $CuCl_2·2H_2O$ (0.23 g, 1.38 mmol) was added, and the reaction mixture was stirred at r.t. for 30 min. Then, it was quenched with sat. aq $NaHCO_3$ solution (1 mL), filtered through a pad of Celite® and the pad was washed with EtOAc (10 mL). The organic layer was dried (Na_2SO_4), concentrated and used as such for the next reaction.

To a stirred solution of the above diol (0.2 g, 1.27 mmol), Ph_3P (1.33 g, 5.08 mmol) and imidazole (0.35 g, 5.08 mmol) in CH_2Cl_2 (10 mL) at 0 °C, I_2 (0.97 g, 3.81 mmol) was added, and the mixture was stirred at r.t. for 4 h. Workup as described for **4** and purification of the residue by silica gel column chromatography (EtOAc–PE, 2:8) gave olefin **9** (0.11 g, 70%) as a colorless liquid.

$[\alpha]_D^{25}$ –87.5 (*c* 0.10, $CHCl_3$) {Lit.[17] $[\alpha]_D^{25}$ –93.4 (*c* 0.10, $CHCl_3$)}.

IR (neat): 3016, 2943, 2882, 1726, 1426, 1382, 1215, 1160, 1108, 971, 819, 748, 703, 667, 609 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.89 (ddd, *J* = 3.8, 5.3, 9.8 Hz, 1 H, olefinic), 6.10–5.90 (m, 2 H, olefinic), 5.42 (d, *J* = 17.4 Hz, 1 H, olefinic), 5.31 (d, *J* = 10.6 Hz, 1 H, olefinic), 4.94 (m, 1 H, OCH), 2.52–2.41 (m, 2 H, allylic).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.7, 144.4, 134.8, 121.6, 117.8, 77.7, 29.3.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_7H_8O_2$: 147.0422; found: 147.0429.

(4*S*,4′*R*,5*R*)-2,2,2′,2′-Tetramethyl-5-vinyl-4,4′-bi(1,3-dioxolane) (18)

To a solution of diol **17** (6.48 g, 24.73 mmol), Ph_3P (25.92 g, 98.93 mmol) and imidazole (6.73 g, 98.93 mmol) in CH_2Cl_2 (60 mL) at 0 °C, I_2 (18.84 g, 74.20 mmol) was added, and the mixture was stirred at r.t. for 4 h. Workup as described for **4** and purification of the residue by silica gel column chromatography (EtOAc–PE, 5:95) gave olefin **18** (4.39 g, 78%) as a pale yellow syrup.

$[\alpha]_D^{25}$ –36.3 (*c* 0.16, $CHCl_3$).

IR (neat): 2924, 2853, 1744, 1659, 1458, 1371, 1254, 1067, 1022, 793 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.88 (m, 1 H, olefinic), 5.37 (d, *J* = 17.2 Hz, 1 H, olefinic), 5.16 (d, *J* = 10.6 Hz, 1 H, olefinic), 4.31 (t, *J* = 6.2 Hz, 1 H, OCH), 4.09–4.00 (m, 2 H, OCH), 3.89 (m, 1 H, OCH), 3.60 (t, *J* = 7.6 Hz, 1 H, OCH), 1.38 (s, 6 H, 2 × Me), 1.37 (s, 3 H, Me), 1.31 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.8, 109.4, 109.2, 81.1, 80.3, 76.5, 66.9, 26.7, 26.5, 26.1.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{20}O_4$: 251.1259; found: 251.1251.

(*R*)-1-[(4*R*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]ethane-1,2-diol (19)

To a stirred solution of **18** (2.8 g, 12.28 mmol) in MeCN (56 mL) at 0 °C, $CuCl_2·2H_2O$ (1.88 g, 11.05 mmol) was added, and the reaction mixture was stirred for 15 min. Then, it was quenched with sat. aq $NaHCO_3$ solution (4 mL), filtered through a pad of Celite® and the pad was washed with EtOAc (40 mL). The organic layer was dried (Na_2SO_4) and concentrated, and the residue was purified by silica gel column chromatography (EtOAc–PE, 3:7) to afford **19** (1.40 g, 98% based on starting material recovery) as a colorless syrup.

$[\alpha]_D^{25}$ +11.9 (*c* 0.12, $CHCl_3$).

IR (neat): 3433, 2990, 2934, 2110, 1725, 1645, 1454, 1429, 1377, 1246, 1219, 1167, 1053, 926, 874 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.87 (m, 1 H, olefinic), 5.39 (d, *J* = 17.2 Hz, 1 H, olefinic), 5.20 (d, *J* = 10.4 Hz, 1 H, olefinic), 4.38 (t, *J* = 7.2 Hz, 1 H, OCH), 3.77 (m, 1 H, OCH), 3.70–3.54 (m, 3 H, OCH), 3.49 (br s, 1 H, OH), 3.26 (br s, 1 H, OH), 1.41 (s, 3 H, Me), 1.39 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.8, 118.4, 109.3, 80.8, 79.3, 72.2, 63.4, 26.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_9H_{16}O_4$: 211.0940; found: 211.0946.

(*R*)-2-[(4*R*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]-2-hydroxyethyl Benzoate (20)

To a stirred and cooled (0 °C) solution of **19** (0.71 g, 3.77 mmol) in CH_2Cl_2 (5 mL), Et_3N (0.53 mL, 3.18 mmol), *n*-Bu_2SnO (0.018 g, 0.075 mmol) and BzCl (0.18 mL, 1.56 mmol) were sequentially added, and the mixture was stirred at r.t. for 1 h. Then, it was diluted with CH_2Cl_2 (8 mL), washed with water (2 × 5 mL) and brine (2 × 5 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 1:9) to furnish **20** (0.78 g, 70%) as a light yellow syrup.

$[\alpha]_D^{25}$ +19.8 (*c* 0.38, $CHCl_3$).

IR (neat): 3478, 3069, 2988, 2936, 1719, 1713, 1603, 1452, 1375, 1273, 1069, 932, 874, 810, 712 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 7.4 Hz, 2 H, Ar-H), 7.53 (t, *J* = 7.4 Hz, 1 H, Ar-H), 7.41 (t, *J* = 7.4 Hz, 2 H, Ar-H), 5.89 (m, 1 H, olefinic), 5.41 (d, *J* = 17.4 Hz, 1 H, olefinic), 5.20 (d, *J* = 10.4 Hz, 1 H, olefinic), 4.47 (m, 2 H, OCH), 4.34 (dd, *J* = 6.9, 11.9 Hz, 1 H, OCH), 4.06 (m, 1 H, OCH), 3.76 (t, *J* = 6.9 Hz, 1 H, OCH), 2.61 (d, *J* = 4.0 Hz, 1 H, OH), 1.42 (s, 3 H, Me), 1.41 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7, 135.8, 133.2, 129.6, 128.4, 118.4, 109.4, 80.5, 79.2, 70.6, 66.1, 26.9.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{20}O_5$: 315.1208; found: 315.1203.

(*R*)-2-[(4*S*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]-2-(tosyloxy)ethyl Benzoate (21)

To a stirred and cooled (0 °C) solution of **20** (0.75 g, 2.55 mmol) in CH_2Cl_2 (5 mL), Et_3N (0.24 mL, 1.72 mmol) followed by DMAP (cat.) and *p*-TsCl (0.26 g, 1.37 mmol) were added, and the mixture was stirred at r.t. for 5 h. Workup as described for **20** and purification of the residue by silica gel column chromatography (EtOAc–PE, 7:93) afforded **21** (1.03 g, 90%) as a colorless syrup.

$[\alpha]_D^{25}$ +53.3 (*c* 1.60, $CHCl_3$).

IR (neat): 3745, 3701, 3609, 3020, 2926, 2854, 2313, 1726, 1645, 1629, 1586, 1551, 1532, 1499, 1451, 1371, 1272, 1216, 1177, 1115, 1096, 1070, 988, 924, 874, 772, 668, 627 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 7.2 Hz, 2 H, Ar-H), 7.74 (d, *J* = 8.3 Hz, 2 H, Ar-H), 7.57 (t, *J* = 7.4 Hz, 1 H, Ar-H), 7.42 (m, 2 H, Ar-H), 7.18 (d, *J* = 8.1 Hz, 2 H, Ar-H), 5.84 (m, 1 H, olefinic), 5.47 (d, *J* = 17.0 Hz, 1 H, olefinic), 5.30 (d, *J* = 10.4 Hz, 1 H, olefinic), 4.99 (m, 1 H, OCH), 4.58–4.35 (m, 3 H, 3 × OCH), 4.01 (dd, *J* = 5.1, 7.9 Hz, 1 H, OCH), 2.31 (s, 3 H, Me), 1.40 (s, 3 H, Me), 1.36 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.9, 142.9, 132.6, 131.6, 131.2, 127.7, 127.2, 126.3, 125.7, 117.7, 108.2, 75.4, 75.0, 74.5, 60.9, 24.8, 24.6, 19.6.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{26}O_7S$: 469.12914; found: 469.12911.

(4*S*,5*R*)-2,2-Dimethyl-4-[(*S*)-oxiran-2-yl]-5-vinyl-1,3-dioxolane (22)

To a stirred solution of **21** (1.00 g, 2.23 mmol) in MeOH (5 mL) at 0 °C, K_2CO_3 (0.92 g, 6.69 mmol) was added, and the mixture was stirred at r.t. for 1 h. Then, it was treated with aq NH_4Cl solution (3 mL), the MeOH was evaporated below 40 °C under reduced pressure and the residue was extracted with Et_2O (3 × 10 mL). The organic layer was washed with water (10 mL) and brine (10 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 9:91) to afford **22** (0.32 g, 82%) as a colorless syrup.

$[\alpha]_D^{25}$ –15.9 (*c* 0.29, $CHCl_3$).

IR (neat): 2928, 2852, 1722, 1611, 1513, 1462, 1370, 1301, 1240, 1214, 1175, 1089, 1031, 924, 878, 817, 750 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.82 (m, 1 H, olefinic), 5.39 (d, *J* = 17.0 Hz, 1 H, olefinic), 5.25 (d, *J* = 11.0 Hz, 1 H, olefinic), 4.31 (t, *J* = 8.0 Hz, 1 H, OCH), 3.52 (dd, *J* = 4.0, 8.0 Hz, 1 H, OCH), 2.95 (m, 1 H, epoxide), 2.73 (t, *J* = 5.0 Hz, 1 H, epoxide), 2.65 (dd, *J* = 3.0, 6.0 Hz, 1 H, epoxide), 1.39 (s, 3 H, Me), 1.38 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.8, 118.4, 109.3, 80.8, 79.3, 72.2, 63.4, 26.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_9H_{14}O_3$: 193.0847; found: 193.1001.

(*S*)-1-[(4*R*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]prop-2-en-1-ol (23)

To a stirred solution of TMSI (0.30 g, 1.48 mmol) in THF (5 mL) at –20 °C, 2.5 M *n*-BuLi in hexane (0.86 mL, 2.15 mmol) was added, and the mixture was stirred at –20 °C for 30 min. A solution of **22** (0.50 g, 2.90 mmol) in THF (5 mL) was added and stirring was continued at –20 °C for an additional 30 min. The reaction mixture was quenched with aq NH_4Cl solution (2 mL) and extracted with EtOAc (2 × 10 mL). The organic layers were washed with water (10 mL) and brine (10 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 12:88) to afford **23** (0.18 g, 33%) as a pale yellow syrup.

$[\alpha]_D^{25}$ –13.1 (*c* 0.13, $CHCl_3$).

IR (neat): 3453, 3086, 2986, 2926, 2859, 1728, 1647, 1453, 1429, 1373, 1246, 1217, 1167, 1113, 1057, 928, 877 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.87 (m, 3 H, olefinic), 5.44 (dd, *J* = 10.1, 17.0 Hz, 1 H, olefinic), 5.21 (dd, *J* = 10.0, 17.0 Hz, 2 H, olefinic), 4.41–4.31 (m, 2 H, OCH), 4.03 (br s, 1 H, OH), 3.64 (dd, *J* = 4.0, 8.0 Hz, 1 H, OCH), 1.42 (s, 3 H, Me), 1.41 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1, 135.2, 119.3, 116.8, 109.5, 83.0, 78.8, 71.3, 27.1, 26.9.

HRMS: *m*/*z* [M + Na]$^+$ calcd $C_{10}H_{16}O_3$: 207.0997; found: 207.1091.

(*S*)-1-[(4*R*,4′*R*,5*R*)-2,2,2′,2′-Tetramethyl-4,4′-bi(1,3-dioxolan)-5-yl]prop-2-en-1-ol (26)

To a stirred solution of TMSI (1.85 g, 8.13 mmol) in THF (25 mL) at –20 °C, 2.5 M *n*-BuLi in hexane (4.71 mL, 11.78 mmol) was added, and the mixture was stirred at –20 °C for 30 min. A solution of **25** (0.34 g, 2.03 mmol) in THF (15 mL) was added and stirring was continued for an additional 30 min. Workup as described for **23** and purification of the residue by silica gel column chromatography (EtOAc–PE, 8:92) afforded **26** (0.23 g, 65%) as a pale yellow syrup.

$[\alpha]_D^{25}$ +1.6 (*c* 1.60, $CHCl_3$).

IR (neat): 3451, 2988, 2833, 2801, 1476, 1371, 1251, 1215, 1155, 1127, 1069, 1000, 932, 836, 773, 669 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.06–5.93 (m, 1 H, olefinic), 5.44–5.37 (td, *J* = 1.5, 17.4 Hz, 1 H, olefinic), 5.28–5.23 (td, *J* = 1.5, 10.6 Hz, 1 H, olefinic), 4.33 (br s, 1 H, OH), 4.22–4.12 (m, 2 H, OCH_2), 4.11–4.00 (m, 3 H, OCH), 3.91–3.84 (m, 1 H, OCH), 1.43 (s, 3 H, Me), 1.41 (s, 3 H, Me), 1.38 (s, 3 H, Me), 1.35 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.4, 116.0, 110.0, 109.6, 82.4, 77.3, 76.9, 70.8, 67.7, 27.1, 27.0, 26.5, 25.2.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{22}O_5$: 281.13649; found: 281.13646.

(1*S*,2*S*)-1-[(4*R*,4′*R*,5*R*)-2,2,2′,2′-Tetramethyl-4,4′-bi(1,3-dioxolan)-5-yl]propane-1,2,3-triol (27)

A stirred solution of AD-mix-β (7.78 g, 10.0 mmol) in *t*-BuOH–H_2O (1:1, 5 mL) was treated with $MsNH_2$ (0.47 g, 5.0 mmol) at r.t. After 30 min, the clear yellow solution was cooled to 0 °C and **26** (1.3 g, 5.0 mmol) was added. The reaction mixture was stirred vigorously at 0 °C for 24 h, then quenched with solid Na_2SO_3 (1.5 g) and warmed to r.t. After 1 h, it was extracted with EtOAc (3 × 10 mL), and the combined organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography (EtOAc–PE, 8:2) to afford **27** (1.32 g, 90%) as a pale yellow syrup; dr 9:1.

$[\alpha]_D^{25}$ +9.4 (*c* 0.70, $CHCl_3$).

IR (neat): 3760, 3642, 3561, 3432, 2924, 2854, 2311, 1727, 1694, 1645, 1586, 1568, 1551, 1533, 1500, 1380, 1219, 1155, 1068, 846, 772, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.94–4.78 (br s, 2 H, 2 × OH), 4.26–4.13 (m, 2 H, OCH_2), 4.12–3.94 (m, 5 H, 5 × OCH), 3.86–3.70 (m, 2 H, CH_2OH), 2.34 (br s, 1 H, OH), 1.43 (s, 6 H, 2 × Me), 1.40 (s, 3 H, Me), 1.35 (s, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 110.0, 109.5, 82.0, 79.8, 76.4, 72.7, 70.2, 67.7, 63.8, 43.2, 26.9, 26.7, 26.4, 25.1.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{24}O_7$: 315.14197; found: 315.14140.

(1*S*,2*S*)-1-[(4*R*,4′*R*,5*R*)-2,2,2′,2′-Tetramethyl-4,4′-bi(1,3-dioxolan)-5-yl]propane-1,2-diol (28)

To a stirred solution of **27** (1.2 g, 4.11 mmol) in CH_2Cl_2 (10 mL) at 0 °C, Et_3N (0.72 mL, 5.14 mmol), *n*-Bu_2SnO (0.03 g, 0.10 mmol) and then *p*-TsCl (0.78 g, 4.11 mmol) were added, and the mixture was stirred at r.t. for 1 h. Workup as described for **20** gave the tosylate **27a**, which was used in the next step without any further purification.

To a stirred suspension of LAH (0.16 g, 4.11 mmol) in THF (5 mL) at 0 °C, a solution of **27a** (1.90 g, 4.24 mmol) in THF (5 mL) was added dropwise under nitrogen atmosphere. The reaction mixture was stirred at r.t. for 3 h, cooled to 0 °C, treated with sat. aq Na_2SO_4 solution (10 mL) and filtered. The aqueous layer was extracted EtOAc (50 mL) and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 3:7) to furnish **28** (0.91 g, 80%) as a colorless oil.

$[\alpha]_D^{25}$ +14.7 (*c* 2.40, $CHCl_3$).

IR (neat): 3745, 3460, 2987, 2925, 2854, 2313, 1727, 1678, 1629, 1551, 1455, 1374, 1216, 1155, 1066, 887, 846, 772, 663 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.18–4.12 (m, 2 H, 2 × OCH), 4.07 (m, 1 H, OCH), 4.00–3.94 (m, 1 H, OCH), 3.87 (m, 1 H, OCH), 3.60–3.54 (dd, *J* = 5.3, 6.0 Hz, 2 H, OCH), 1.43 (s, 3 H, Me), 1.42 (s, 3 H, Me), 1.39 (s, 3 H, Me), 1.35 (s, 3 H, Me), 1.31 (d, *J* = 6.8 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.8, 109.6, 79.9, 77.3, 77.2, 72.3, 70.1, 67.9, 27.1, 26.8, 26.6, 25.2, 19.7.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{24}O_6$: 299.14651; found: 299.14634.

(4*S*,4′*R*,4″*R*,5*S*,5′*R*)-2,2,2′,2′,2″,2″,5-heptamethyl-4,4′,5′,4″-ter(1′,3′-dioxolane) (29)

To a stirred and cooled (0 °C) solution of **28** (0.85 g, 3.08 mmol) in acetone (4 mL), 2,2-dimethoxypropane (0.83 mL, 6.78 mmol) and PTSA (cat.) were added. After the reaction mixture was stirred at r.t. for 1 h, it was quenched with Et_3N (3 mL) and extracted with CH_2Cl_2 (15 mL). The extract was washed with water (10 mL) and brine (10 mL), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 6:94) to furnish **29** (0.89 g, 91%) as a light yellow syrup.

$[\alpha]_D^{25}$ –7.0 (*c* 0.50, $CHCl_3$).

IR (neat): 2988, 2925, 2854, 2312, 1711, 1678, 1663, 1610, 1568, 1551, 1533, 1379, 1219, 1071, 847, 772, 670 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.39 (dd, *J* = 6.0, 13.0 Hz, 1 H, OCH), 4.19 (d, *J* = 6.0 Hz, 1 H, OCH), 4.13 (dd, *J* = 3.0, 6.0 Hz, 1 H, OCH), 4.07–4.00 (m, 1 H, OCH), 3.96 (dd, *J* = 3.0, 5.0 Hz, 1 H, OCH), 3.90 (t, *J* = 8.0 Hz, 1 H, OCH), 3.84 (d, *J* = 8.0 Hz, 1 H, OCH), 1.42–1.38 (m, 12 H, 4 × Me), 1.35 (s, 6 H, 2 × Me), 1.33 (d, *J* = 6.0 Hz, 3 H, Me).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 109.7, 109.6, 108.0, 79.1, 77.5, 77.4, 76.1, 72.9, 68.0, 27.2, 27.0, 26.8, 26.6, 25.5, 25.3, 15.2.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{28}O_6$: 339.17781; found: 339.17835.

(*R*)-1-[(4*S*,4′*S*,5*R*,5′*S*)-2,2,2′,2′,5′-Pentamethyl-4,4′-bi(1,3-dioxolan)-5-yl]ethane-1,2-diol (30)

To a stirred solution of **29** (0.85 g, 2.69 mmol) in MeCN (10 mL) at 0 °C, $CuCl_2·2H_2O$ (0.41 g, 2.68 mmol) was added, and the mixture was stirred at 0 °C for 15 min. Workup as described for **19** and purification of the residue by silica gel column chromatography (EtOAc–PE, 3:7) afforded **30** (0.65 g, 98% based on starting material recovery) as a colorless syrup.

$[\alpha]_D^{25}$ +16.8 (*c* 1.30, $CHCl_3$).

IR (neat): 3745, 3702, 3642, 3561, 2987, 2924, 2854, 2312, 1765, 1727, 1710, 1693, 1663, 1610, 1551, 1533, 1500, 1381, 1219, 1168, 1064, 991, 931, 873, 772, 672 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.21–4.16 (dd, *J* = 6.5, 12.5 Hz, 1 H, OCH), 4.10 (d, *J* = 5.5 Hz, 2 H, OCH_2), 3.82 (d, *J* = 8.0 Hz, 1 H, OCH), 3.74–3.72 (m, 3 H, OCH), 2.77 (br s, 1 H, OH), 2.02 (br s, 1 H, OH), 1.43–1.41 (m, 12 H, 4 × Me), 1.32 (d, *J* = 6.5 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.6, 108.6, 81.0, 77.3, 77.2, 73.2, 72.8, 63.8, 27.4, 27.2, 26.7, 26.5, 17.8.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{24}O_6$: 299.14651; found: 299.14674.

(4*S*,4′*S*,5*S*,5′*R*)-2,2,2′,2′,5-Pentamethyl-5′-vinyl-4,4′-bi(1,3-dioxolane) (7)

To a stirred solution of **30** (0.62 g, 2.25 mmol), Ph_3P (2.35 g, 8.99 mmol) and imidazole (0.60 g, 8.85 mmol) in CH_2Cl_2 (10 mL) at 0 °C, I_2 (1.71 g, 6.74 mmol) was added, and the mixture was stirred at r.t. for 4 h. Workup as described for **4** and purification of the residue by silica gel column chromatography (EtOAc–PE, 6:94) gave olefin **7** (0.40 g, 74%) as a pale yellow syrup.

$[\alpha]_D^{25}$ –20.0 (*c* 0.30, $CHCl_3$).

IR (neat): 3020, 2925, 2854, 2314, 1728, 1678, 1646, 1610, 1568, 1551, 1450, 1216, 929, 722, 668, 626 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.84 (m, 1 H, olefinic), 5.44 (d, *J* = 16.6 Hz, 1 H, olefinic), 5.30 (d, *J* = 9.8 Hz, 1 H, olefinic), 4.45 (t, *J* = 8.3 Hz, 1 H, OCH), 4.34–4.05 (m, 3 H, 3 × OCH), 1.49–1.38 (m, 12 H, 4 × Me), 1.30 (d, *J* = 6.2 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.5, 120.0, 109.9, 108.8, 81.3, 77.5, 77.4, 73.4, 27.6, 27.4, 26.9, 26.7, 18.0.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{22}O_4$: 265.15182; found: 265.15209.

(2*S*,3*S*,4*S*,5*R*)-Hept-6-ene-2,3,4,5-tetrayl Tetraacetate (5)

A solution of **7** (0.10 g, 0.41 mmol) in CH_2Cl_2 (1 mL) at 0 °C was treated with TFA (0.5 mL), and the mixture was stirred at r.t. for 15 min. The solvent was evaporated and the crude tetrol **7a** was used as such for the next reaction.

A solution of the above tetrol **7a** dissolved in pyridine (3 mL) was cooled (0 °C) and treated with Ac_2O (1 mL) and DMAP (cat.); the reaction mixture was stirred at r.t. for 20 h. Then, it was quenched with solid $NaHCO_3$ (0.2 g), diluted with EtOAc (3 mL) and filtered through a pad of Celite®. The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 1:9) to give tetraacetate **5** (0.13 g, 90%) as a light yellow oil.

$[\alpha]_D^{25}$ +10.9 (*c* 0.16, $CHCl_3$).

IR (neat): 2993, 2881, 2780, 1747, 1426, 1370, 1217, 1059, 1034, 949, 851, 771, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.80–5.69 (m, 1 H, olefinic), 5.34 (d, *J* = 2.3 Hz, 1 H, olefinic), 5.33 (d, *J* = 3.0 Hz, 1 H, olefinic), 5.28 (d, *J* = 2.3 Hz, 1 H, OCH), 5.16 (d, *J* = 6.0 Hz, 1 H, OCH), 5.09 (t, *J* = 5.3 Hz, 1 H, OCH), 5.00 (t, *J* = 6.0 Hz, 1 H, OCH), 2.10 (s, 3 H, OAc), 2.09 (s, 3 H, OAc), 2.08 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 1.20 (d, *J* = 6.0 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.0, 169.8, 169.5, 131.3, 119.8, 72.5, 72.03, 71.6, 71.0, 20.9, 20.8, 20.6, 16.3.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{22}O_8$: 353.12069; found: 353.12072.

(*R*)-1-[(4*R*,4′*R*,5*R*)-2,2,2′,2′-Tetramethyl-4,4′-bi(1,3-dioxolan)-5-yl]ethanol (32)

To a stirred solution of **17** (21.0 g, 80.15 mmol) in CH_2Cl_2 (210 mL) at 0 °C, Et_3N (13.94 mL, 100.19 mmol), then *n*-Bu_2SnO (0.50 g, 2.00 mmol) and *p*-TsCl (15.28 g, 80.15 mmol) were added. The reaction mixture was stirred at r.t. for 1 h. Workup as described for **20** afforded **31**, which was used as such for the next step.

To a stirred suspension of LAH (2.92 g, 76.92 mmol) in THF (50 mL) at 0 °C, a solution of **31** (32.0 g, 76.92 mmol) in THF (100 mL) was added dropwise under nitrogen atmosphere, and the mixture was stirred at r.t. for 3 h. Workup as described for **28** and purification of the residue by silica gel column chromatography (EtOAc–PE, 2:8) furnished **32** (13.9 g, 74%) as a light yellow syrup.

$[\alpha]_D^{25}$ +6.4 (*c* 0.20, $CHCl_3$).

IR (neat): 3470, 3434, 2990, 2936, 2890, 1597, 1460, 1373, 1306, 1252, 1217, 1179, 1069, 938, 841, 710, 667, 554, 513, 490 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.15 (q, *J* = 5.7 Hz, 1 H, OCH), 4.05–4.00 (m, 2 H, OCH), 3.71 (m, 1 H, OCH), 3.67–3.57 (m, 2 H, OCH), 2.47 (br s, 1 H, OH), 1.44 (s, 3 H, Me), 1.35 (s, 6 H, 2 × Me), 1.34 (s, 3 H, Me), 1.24 (d, *J* = 6.0 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 110.1, 109.1, 84.4, 80.8, 76.4, 68.5, 26.8, 26.7, 26.5, 25.1, 19.5.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{22}O_5$: 269.1364; found: 269.1353.

tert-Butyldiphenyl{(1*R*)-1-[(4*R*,4′*R*,5*S*)-2,2,2′,2′-tetramethyl-4,4′-bi(1,3-dioxolan)-5-yl]ethoxy}silane (33)

To a stirred solution of alcohol **32** (13.80 g, 56.09 mmol) in CH_2Cl_2 (68 mL), imidazole (11.44 g, 168.29 mmol), TBDPSCl (17.61 mL, 67.31 mmol) and DMAP (cat.) were added sequentially, and the mixture was stirred at r.t. for 1 h. Then, it was treated with water (25 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine (65 mL) and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by silica gel column chromatography (EtOAc–PE, 5:95) to afford **33** (18.20 g, 66%) as a colorless syrup.

$[\alpha]_D^{25}$ +4.4 (*c* 0.10, $CHCl_3$).

IR (neat): 2930, 2859, 1659, 1462, 1428, 1379, 1240, 1152, 1111, 1057, 845, 739, 702 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (m, 4 H, Ar-H), 7.36 (m, 6 H, Ar-H), 4.06–3.92 (m, 3 H, 3 × OCH), 3.88–3.75 (m, 3 H, 3 × OCH), 1.32 (s, 6 H, 2 × Me), 1.24 (s, 6 H, 2 × Me), 1.06 (d, *J* = 6.04 Hz, 3 H, Me), 1.06 (s, 9 H, 3 × Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.9, 134.4, 133.9, 129.6, 129.5, 127.5, 127.4, 109.5, 109.3, 84.4, 78.3, 76.9, 69.8, 66.8, 27.3, 27.2, 27.0, 26.4, 25.3, 19.3, 18.6.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{40}O_5Si$: 507.2542; found: 507.2533.

(*R*)-1-{(4*R*,5*R*)-5-[(*R*)-1-(*tert*-Butyldiphenylsilyloxy)ethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}ethane-1,2-diol (34)

To a stirred solution of **33** (18.0 g, 37.11 mmol) in MeCN (360 mL) at 0 °C, $CuCl_2{\cdot}2H_2O$ (5.69 g, 33.40 mmol) was added, and the mixture was stirred at 0 °C for 30 min. Workup as described for **19** and purification of the residue by silica gel column chromatography (EtOAc–PE, 3:7) afforded **34** (9.0 g, 98% based on starting material recovery) as a colorless syrup.

$[\alpha]_D^{25}$ –14.6 (*c* 1.0, $CHCl_3$).

IR (neat): 3335, 3073, 2934, 2859, 1721, 1590, 1474, 1429, 1381, 1319, 1252, 1159, 1113, 1082, 1024, 949, 912, 872, 822, 743, 702, 612, 500 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.74–7.67 (m, 4 H, Ar-H), 7.43–7.35 (m, 6 H, Ar-H), 3.90–3.78 (m, 3 H, 3 × OCH), 3.71–3.43 (m, 3 H, 3 × OCH), 2.69 (d, *J* = 4.5 Hz, 1 H, OH), 1.95 (t, *J* = 5.3 Hz, 1 H, OH), 1.34 (s, 3 H, Me), 1.28 (s, 3 H, Me), 1.08 (d, *J* = 5.3 Hz, 3 H, Me), 1.05 (s, 9 H, 3 × Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.9, 135.8, 133.7, 133.1, 129.9, 129.8, 127.7, 127.7, 109.6, 83.9, 79.5, 73.0, 71.6, 63.8, 27.1, 26.9, 19.9, 19.2.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{36}O_5Si$: 467.2229; found: 467.2233.

tert-Butyl{(1*R*)-1-[(4*S*,5*R*)-2,2-dimethyl-5-{(*R*)-oxiran-2-yl}-1,3-dioxolan-4-yl]ethoxy}diphenylsilane (35)

To a stirred solution of **34** (1.10 g, 2.46 mmol) in CH_2Cl_2 (10 mL) at 0 °C, Et_3N (0.39 mL, 2.81 mmol), then *n*-Bu_2SnO (cat.) and *p*-TsCl (0.43 g, 2.25 mmol) were added, and the mixture was stirred at r.t. for 30 min. Workup as described for **20** afforded **34a**, which was used as such for the next reaction.

To a stirred solution of **34a** (1.35 g, 2.24 mmol) in MeOH (4 mL) at 0 °C, K_2CO_3 (0.93 g, 6.74 mmol) was added, and the mixture was stirred at r.t. for 1 h. Workup as described for **22** and purification of the residue by silica gel column chromatography (EtOAc–PE, 15:85) afforded **35** (0.86 g, 89%) as a colorless syrup.

$[\alpha]_D^{25}$ +18.0 (*c* 0.20, $CHCl_3$).

IR (neat): 3073, 3052, 2984, 2934, 2894, 2859, 1809, 1760, 1588, 1474, 1428, 1374, 1308, 1256, 1213, 1159, 1113, 1069, 868, 822, 741, 704 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (m, 4 H, Ar-H), 7.44–7.31 (m, 6 H, Ar-H), 3.98–3.87 (m, 2 H, 2 × OCH), 3.76 (m, 1 H, OCH), 2.97 (m, 1 H, epoxide), 2.75 (t, *J* = 5.3 Hz, 1 H, epoxide), 2.68 (dd, *J* = 2.6, 5.3 Hz, 1 H, epoxide), 1.36 (s, 3 H, Me), 1.33 (s, 3 H, Me), 1.05 (s, 9 H, 3 × Me), 1.04 (d, *J* = 5.3 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.9, 129.7, 129.6, 127.6, 127.5, 109.6, 85.1, 82.7, 69.9, 52.3, 44.8, 27.4, 27.0, 19.9, 19.3.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{34}O_4Si$: 449.2124; found: 449.2107.

(*R*)-1-{(4*R*,5*S*)-5-[(*R*)-1-(*tert*-Butyldiphenylsilyloxy)ethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}prop-2-en-1-ol (10)

To a stirred solution of TMSI (0.48 g, 2.34 mmol) in THF (5 mL) at –20 °C, 2.5 M *n*-BuLi in hexane (1.36 mL, 3.39 mmol) was added, and the mixture was stirred for 30 min. A solution of **35** (0.25 g, 0.58 mmol) in THF (3 mL) was added and stirring was continued for 30 min at –20 °C. Workup as described for **23** and purification of the residue by silica gel column chromatography (EtOAc–PE, 1:9) afforded **10** (0.18 g, 70%) as a colorless syrup.

$[\alpha]_D^{25}$ +27.0 (*c* 0.10, $CHCl_3$).

IR (neat): 3464, 3075, 2932, 2859, 1468, 1428, 1379, 1242, 1165, 1108, 822, 741, 704, 436 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.65 (m, 4 H, Ar-H), 7.45–7.33 (m, 6 H, Ar-H), 5.81 (m, 1 H, olefinic), 5.26 (d, *J* = 17.0 Hz, 1 H, olefinic), 5.14 (d, *J* = 10.6 Hz, 1 H, olefinic), 4.07 (q, *J* = 4.5 Hz, 1 H, OCH), 3.90–3.78 (m, 3 H, 3 × OCH), 1.35 (s, 3 H, Me), 1.29 (s, 3 H, Me), 1.07 (d, *J* = 5.3 Hz, 3 H, Me), 1.06 (s, 9 H, 3 × Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.5, 135.9, 134.1, 133.4, 129.9, 129.7, 127.7, 127.6, 117.4, 109.5, 82.6, 81.4, 73.9, 71.3, 27.2, 27.1, 27.0, 19.8, 19.3.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{26}H_{36}O_4Si$: 463.2280; found: 463.2273.

(2*R*,3*R*,4*R*,5*R*)-Hept-6-ene-2,3,4,5-tetrayl Tetraacetate (36)

A solution of **10** (0.10 g, 0.22 mmol) in CH_2Cl_2 (1 mL) at 0 °C was treated with TFA (0.5 mL), and the mixture was stirred at r.t. for 15 min. Workup as described for **7a** gave tetrol **10a**, which was used as such for the next reaction.

The above tetrol **10a** dissolved in pyridine (3 mL) was cooled to 0 °C and treated with Ac_2O (1 mL) and DMAP (cat.); the mixture was stirred at r.t. for 20 h. Workup as described for **5** and purification of the residue by silica gel column chromatography (EtOAc–PE, 1:9) gave tetraacetate **36** (0.61 g, 82%) as a light yellow oil.

$[\alpha]_D^{25}$ +22.0 (*c* 1.70, $CHCl_3$).

IR (neat): 2924, 2853, 2813, 2314, 1747, 1646, 1586, 1551, 1512, 1483, 1450, 1371, 1218, 1059, 1034, 989, 948, 772, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.71 (m, 1 H, olefinic), 5.40–5.17 (m, 5 H, 2 × olefinic, 3 × OCH), 4.94 (m, 1 H, OCH), 2.09 (s, 3 H, OAc), 2.04 (s, 6 H, 2 × OAc), 2.01 (s, 3 H, OAc), 1.18 (d, *J* = 6.0 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.0, 169.8, 169.6, 132.3, 120.8, 71.7, 71.1, 69.8, 67.0, 29.7, 21.0, 20.7, 16.3.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{22}O_8$: 353.12069; found: 353.12072.

(2*S*,3*S*,4*S*,5*R*,*E*)-7-[(*R*)-6-Oxo-3,6-dihydro-2*H*-pyran-2-yl]hept-6-ene-2,3,4,5-tetrayl Tetraacetate [(+)-Anamarine, 1]

To a solution of **4** (0.04 g, 0.36 mmol) and **5** (0.03 g, 0.09 mmol) in CH_2Cl_2 (2 mL) under nitrogen atmosphere, Grubbs II catalyst (0.01 g, 0.01 mmol) was added, and the mixture was stirred at reflux for 5 h. Workup as described for **14** and purification of the residue by silica gel column chromatography (EtOAc–PE, 1:3) afforded **1** (0.03 g, 68%) as a white solid; mp 109–111 °C (Lit.[9] 109–111 °C).

$[\alpha]_D^{25}$ +16.8 (*c* 0.3, $CHCl_3$) {Lit.[9] $[a]_D^{25}$ +17.8 (*c* 0.3, $CHCl_3$)}.

IR (neat): 3870, 3761, 3642, 3610, 3023, 2923, 2853, 2314, 1743, 1711, 1694, 1663, 1645, 1551, 1533, 1483, 1451, 1415, 1373, 1218, 1028, 929, 772, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.88 (ddd, *J* = 3.5, 5.2, 9.9 Hz, 1 H, olefinic), 6.06 (ddd, *J* = 1.7, 1.7, 9.9 Hz, 1 H, olefinic), 5.88–5.74 (m, 2 H, olefinic), 5.36 (dd, *J* = 5.2, 7.2 Hz, 1 H, OCH), 5.30 (dd, *J* = 3.5, 7.2 Hz, 1 H, OCH), 5.17 (dd, *J* = 3.5, 7.0 Hz, 1 H, OCH), 4.96 (m, 1 H, OCH), 4.90 (dq, *J* = 6.4, 6.4 Hz, 1 H, OCH), 2.45 (m, 2 H, allylic), 2.11 (s, 3 H, OAc), 2.07 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 1.17 (d, *J* = 6.4 Hz, 3 H, Me).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.0, 169.9, 169.7, 169.5, 163.4, 144.5, 133.0, 125.6, 121.5, 75.9, 71.9, 71.5, 70.4, 67.5, 29.5, 21.0, 20.9, 20.8, 20.7, 15.9.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{26}O_{10}$: 449.14198; found: 449.14240.

(*S*)-6-[(*R*,*E*)-3-{(4*R*,5*S*)-5-[(*R*)-1-(*tert*-Butyldiphenylsilyloxy)ethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-3-hydroxyprop-1-enyl]-5,6-dihydro-2*H*-pyran-2-one (8)

To a mixture of olefins **9** (0.08 g, 0.64 mmol) and **10** (0.14 g, 0.32 mmol) in toluene (1 mL) under nitrogen atmosphere, Grubbs II catalyst (0.01 g, 0.01 mmol) was added, and the mixture was stirred at reflux for 8 h. Workup as described for **14** and purification of the residue by silica gel column chromatography (EtOAc–PE, 35:65) afforded **8** (0.14 g, 82%) as a light yellow syrup.

$[\alpha]_D^{25}$ –68.0 (*c* 0.20, $CHCl_3$).

IR (neat): 3020, 2314, 1765, 1728, 1694, 1645, 1569, 1551, 1516, 1500, 1467, 1449, 1430, 1216, 929, 743, 668, 626 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.73 (dd, *J* = 7.3, 20.1 Hz, 4 H, Ar-H), 7.49–7.37 (m, 6 H, Ar-H), 6.87 (m, 1 H, olefinic), 6.05 (d, *J* = 9.8 Hz, 1 H, olefinic), 5.99 (dd, *J* = 4.9, 15.6 Hz, 1 H, olefinic), 5.91 (dd, *J* = 5.4, 15.6 Hz, 1 H, olefinic), 4.94 (q, *J* = 5.9 Hz, 1 H, OCH), 4.15 (m, 1 H, OCH), 3.94–3.80 (m, 3 H, OCH), 2.5 (br s, 1 H, OH), 2.4 (m, 2 H, allylic), 1.37 (s, 3 H, Me), 1.30 (s, 3 H, Me), 1.09 (d, *J* = 5.8 Hz, 3 H, Me), 1.07 (s, 9 H, 3 × Me).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.8, 144.5, 135.9, 133.9, 133.2, 132.6, 130.0, 129.8, 128.8, 127.8, 127.6, 121.6, 109.7, 83.1, 81.5, 77.2, 72.5, 71.6, 29.7, 29.6, 27.1, 27.0, 20.1, 19.2.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{31}H_{40}O_6Si$: 559.2486; found: 559.2487.

(2*R*,3*R*,4*R*,5*R*,*E*)-7-[(*S*)-6-Oxo-3,6-dihydro-2*H*-pyran-2-yl]hept-6-ene-2,3,4,5-tetrayl Tetraacetate [8-*epi*-(–)-Anamarine, 3]

A solution of **8** (0.05 g, 0.09 mmol) in CH_2Cl_2 (1 mL) at 0 °C was treated with TFA (0.3 mL), and the mixture was stirred at r.t. for 15 min. Evaporation of the solvent gave tetrol **8a**, which was used as such for the next reaction.

To a solution of the above tetrol **8a** in pyridine (2 mL) at 0 °C, Ac_2O (0.5 mL) and DMAP (cat.) were added, and the mixture was stirred at r.t. for 20 h. Workup as described for **5** and purification of the residue by silica gel column chromatography (EtOAc–PE, 3:7) gave tetraacetate **3** (0.03 g, 84%) as a gummy liquid.

$[\alpha]_D^{25}$ –9.0 (*c* 1.12, $CHCl_3$).

IR (neat): 2924, 2853, 2313, 1744, 1679, 1646, 1630, 1552, 1500, 1450, 1372, 1220, 1031, 772, 686 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 6.90 (ddd, *J* = 3.1, 5.1, 9.4 Hz, 1 H, olefinic), 6.06 (td, *J* = 1.9, 9.8 Hz, 1 H, olefinic), 5.95 (dd, *J* = 5.2, 15.7 Hz, 1 H, olefinic), 5.75 (dd, *J* = 8.4, 15.9 Hz, 1 H, olefinic), 5.33 (m, 1 H, OCH), 5.30–5.23 (m, 2 H, 2 × OCH), 4.99–4.91 (m, 2 H, 2 × OCH), 2.49–2.35 (m, 2 H, allylic), 2.12 (s, 3 H, OAc), 2.07 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 1.21 (d, *J* = 6.5 Hz, 3 H, Me).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 170.1, 169.9, 169.6, 163.6, 144.5, 133.0, 127.1, 121.5, 76.2, 70.7, 70.4, 69.6, 66.8, 29.4, 22.7, 21.1, 21.0, 20.8, 16.2.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{26}O_{10}$: 449.14182; found: 449.14196.

(2*R*,3*R*,4*R*,5*R*,*E*)-7-[(*S*)-6-Oxo-3,6-dihydro-2*H*-pyran-2-yl]hept-6-ene-2,3,4,5-tetrayl Tetraacetate [8-*epi*-(–)-Anamarine, 3]

To a stirred solution of olefins **36** (0.15 g, 0.48 mmol) and **9** (0.12 g, 0.96 mmol) in CH_2Cl_2 (2 mL) under nitrogen atmosphere, Grubbs II catalyst (0.01 g, 0.01 mmol) was added, and the mixture was heated at reflux for 5 h. Workup as described for **14** and purification of the residue by silica gel column chromatography (EtOAc–PE, 1:3) afforded **3** (0.16 g, 84%), whose spectroscopic data were comparable with **3** synthesized from **8**.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1380864.

References

(1) Marco, J. A.; Carda, M.; Murga, J.; Falomir, E. *Tetrahedron* **2007**, *63*, 2929.
(2) Kikuchi, H.; Sasaki, K.; Sekiya, J.; Maeda, Y.; Amagai, A.; Kubohara, Y.; Ohsima, Y. *Bioorg. Med. Chem.* **2004**, *12*, 3203.
(3) (a) Agrawal, V. K.; Singh, J.; Mishra, K. C.; Khadikar, P. V.; Jaliwala, Y. A. *ARKIVOC* **2006**, *(ii)*, 162. (b) Hagen, S. E.; Domagala, J. M.; Gajda, C.; Lovdahl, M.; Tait, B. D.; Wise, E.; Holler, T.; Hupe, D.; Nouhan, C.; Urumov, A.; Zeikus, G.; Zeikus, E.; Lunney, E. A.; Pavlovsky, A.; Gracheck, S. J.; Saunders, J. M.; VanderRoest, S.; Brodfuehrer, J. *J. Med. Chem.* **2001**, *44*, 2319. (c) Hagen, S. E.; Vara-Prasad, J. V. N.; Tait, B. D. *Adv. Med. Chem.* **2000**, *5*, 159. (d) Aristoff, P. A. *Drugs Future* **1998**, *23*, 995. (e) Romines, K. R.; Chrusciel, R. A. *Curr. Med. Chem.* **1995**, *2*, 825. (f) Chan, K. M.; Rajab, N. F.; Ishak, M. H. A.; Ali, A. M.; Yusoff, K.; Din, L. B.; Inayat-Hussain, S. H. *Chem.-Biol. Interact.* **2006**, *159*, 129. (g) Inayat-Hussain, S. H.; Annuar, B. O.; Din, L. B.; Ali, A. M.; Ross, D. *Toxicol. in Vitro* **2003**, *17*, 433. (h) Inayat-Hussain, S. H.; Annuar, B. O.; Din, L. B.; Taniguchi, N. *Toxicol. Lett.* **2002**, *131*, 153. (i) Veena, B.; Sharma, G. V. M. *Synlett* **2014**, *25*, 1283.
(4) Marco, J. A.; Carda, M. *Recent Advances in the Field of Naturally Occurring 5,6-Dihydropyran-2-ones*, In *Natural Lactones and Lactams, Synthesis, Occurrence and Biological Activity*; Janecki, T., Ed.; Wiley-VCH: Weinheim, **2013**, 51–100.
(5) Alemany, A.; Márquez, C.; Pascual, C.; Valverde, S.; Martínez-Ripoll, M.; Fayos, J.; Perales, A. *Tetrahedron Lett.* **1979**, 3583.
(6) (a) Lorenz, K.; Lichtenthaler, F. W. *Tetrahedron Lett.* **1987**, *28*, 6437. (b) Diaz-Oltra, S.; Murga, J.; Falomir, E.; Carda, M.; Marco, J. A. *Tetrahedron* **2004**, *60*, 2979.
(7) Gao, D.; Doherty, G. A. O. *J. Org. Chem.* **2005**, *70*, 9932.
(8) Sabitha, G.; Reddy, C. N.; Gopal, P.; Yadav, J. S. *Tetrahedron Lett.* **2010**, *51*, 5736.
(9) Kumar, K. S.; Reddy, C. S. *Org. Biomol. Chem.* **2012**, *10*, 2647.
(10) (a) Prasad, K. R.; Kumar, S. M. *Tetrahedron* **2014**, *70*, 4552. (b) Reddy, B. V. S.; Reddy, V. V.; Praneeth, K. *Tetrahedron Lett.* **2014**, *55*, 1398.
(11) (a) Sharma, G. V. M.; Mallesham, S.; Chandramouli, C. *Tetrahedron: Asymmetry* **2009**, *20*, 2513. (b) Mallesham, S.; Sharma, G. V. M. *Tetrahedron: Asymmetry* **2010**, *21*, 2646. (c) Sharma, G. V. M.; Chary, D. H.; Chandramouli, N.; Achrainer, F.; Patrudu, S.; Zipse, H. *Org. Biomol. Chem.* **2011**, *9*, 4079. (d) Sharma, G. V. M.; Sai Reddy, P. *Eur. J. Org. Chem.* **2012**, 2414. (e) Sharma, G. V. M.; Reddy, S. V.; Ramakrishna, K. V. S. *Org. Biomol. Chem.* **2012**, *10*, 3689. (f) Rajesh, A.; Sharma, G. V. M.; Damera, K. *Tetrahedron Lett.* **2014**, *55*, 4067. (g) Rajesh, A.; Sharma, G. V. M.; Damera, K. *Tetrahedron Lett.* **2014**, *55*, 6474. (h) Veena, B.; Sharma, G. V. M. *Synlett* **2014**, *25*, 2039. (i) Sharma, G. V. M.; Doddi, V. R. *Macrolactones*, In *Natural Lactones and Lactams: Synthesis, Occurrence and Biological Activity*; Janecki, T., Ed.; Wiley-VCH: Weinheim, **2013**, 229–272.
(12) (a) Chattopadhyay, A.; Mamdapur, V. R. *J. Org. Chem.* **1995**, *60*, 585. (b) Chattopadhyay, A. *J. Org. Chem.* **1996**, *61*, 6104.
(13) (a) Mitsunobu, O. *Synthesis* **1981**, 1. (b) Ahn, C.; Correia, R.; Deshong, P. *J. Org. Chem.* **2002**, *67*, 1751. (c) Swamy, K. C. K.; Kumar, N. N. B.; Balaraman, E.; Kumar, K. V. P. P. *Chem. Rev.* **2009**, *109*, 2551.
(14) (a) Furstner, A.; Langemann, K. *J. Org. Chem.* **1996**, *61*, 3942. (b) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199. (c) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746.
(15) Saravanan, P.; Chandrasekhar, M.; Anand, R. V.; Singh, V. K. *Tetrahedron Lett.* **1998**, *39*, 3091.
(16) (a) Garegg, P. J.; Samuelsson, B. *Synthesis* **1979**, 813. (b) Garegg, P. J. *Pure Appl. Chem.* **1984**, *56*, 845.
(17) Ramesh, P.; Meshram, H. M. *Tetrahedron Lett.* **2012**, *53*, 4008.
(18) Yadav, V. K.; Agrawal, D. *Chem. Commun.* **2007**, 5232.
(19) Martinelli, M. J.; Nayyar, N. K.; Moher, E. D.; Dhokte, U. P.; Pawlak, J. M.; Vaidyanathan, P. *Org. Lett.* **1999**, *1*, 447.
(20) Alcaraz, L.; Harnett, J. J.; Mioskowski, C.; Martel, J. P.; Le Gall, T.; Shin, D.-S.; Falck, J. R. *Tetrahedron Lett.* **1994**, *35*, 5449.
(21) Regeling, H.; Chitenden, G. J. F. *Carbohydr. Res.* **1989**, *190*, 313.
(22) Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568.

(23) (a) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036. (b) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371. (c) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (d) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (e) Nolen, E. G.; Kurish, A. J.; Wong, K. A.; Orlando, M. D. *Tetrahedron Lett.* **2003**, *44*, 2449. (f) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117.