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Synthesis of the C8–C16 fragment of amphidinolide R

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ABSTRACT

An asymmetric synthesis of the C8–C16 fragment with several stereogenic centers of amphidinolide R, is described. The key reaction, Sharpless asymmetric epoxidation has provided the basis for generation of the required stereocenters. The target fragment was accomplished in a convergent manner in nine steps (longest linear synthesis of the sequence) and 32% overall yield was obtained starting from 2-butene-1,4-diol.

1. Introduction

Amphidinolides represent one of the largest groups of marine originated macrolides with diverse and biologically significant secondary metabolite structures isolated from symbiotic dinoflagellates *Amphidinium* sp., which were separated from cells of Okinawan marine flatworms.[1] Amphidinolides share a common feature with one or more *exo*-methylene units, and a highly oxygenated ring ranging in size from 12 to 29 atoms. Due to their scarcity, studies of structure determination and the assignment of stereochemistry are serious challenges and subsequent biological studies have also been very limited. Several members of this family exhibit cytotoxicity against a variety of National Cancer Institute (NCI) tumor cell lines as well as human epidermoid carcinoma KB cells. Consequently, the amphidinolides have become synthetic targets.[2]

Amphidinolide R **1a** is a cytotoxic macrolide that is isolated from the cultured marine dinoflagellate *Amphidinium* sp., along with amphidinolide S **1b** (Fig. 1).[3] The structure of **1a** including its absolute configuration was elucidated on the basis of spectroscopic data and chemical experiments. It contains four double bonds including one exomethylene unit, three chiral hydroxyl groups including one in the lactone linkage, three asymmetric methyl groups and a total of six stereogenic centers. The structure of **1a** was found to be a 14-membered macrolactone ring with the lactone linkage at a different location compared to amphidinolide J **1c**.[4] The evidence for the absolute stereochemistry of **1a** was provided based on the known stereochemistry of amphidinolide J. Amphidinolide R showed potent cytotoxicity, compared to its congeners J and S, against murine lymphoma L1210 (IC_{50} = 1.4 μg/mL for **1a**, 4.0 μg/mL for **1b**, 2.7 μg/mL for **1c**) and human epidermoid carcinoma KB cells (IC_{50} = 0.67 μg/mL for **1a**, 6.5 μg/mL for **1b**, 3.9 μg/mL for **1c**). Although, there are two total synthesis of amphidinolide J,[5] there are no reports in literature for the synthesis of amphidinolide R. During the synthesis of **1c**, Cossy et al. have observed the formation of amphidinolide R as a mixture along with amphidinolide J.[5b] In continuation of our interests in the synthesis of macrolides,[6] we herein report a convergent approach for the synthesis of C8–C16 fragment, a highly functionalized central unit of amphidinolide R.

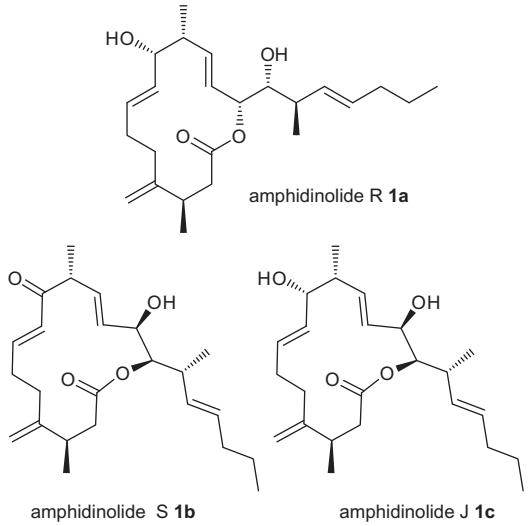

Figure 1. Structures of amphidinolide R, S and J.

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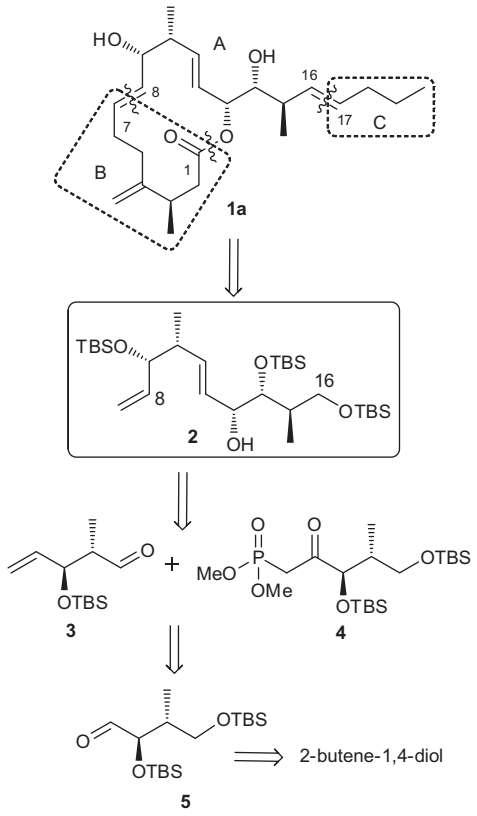
2. Results and discussion

In our retrosynthetic plan (Scheme 1) we envisaged a disconnection into three fragments, **A**–**C**, which can then be combined using esterification (C1—O bond) followed by a ring-closing metathesis reaction (C7—C8 bond) between **A** (C8–C16 fragment) and **B** (C1–C7 unit) and a late stage installation of the four-carbon side chain **C** (C17–C20) through a Julia–Kocienski olefination to enable the generation of analogs. The synthesis of fragment **A** was planned in its protected form **2**. Further analysis of **2** revealed two subunits, aldehyde **3** and β-ketophosphonate **4**, which could be coupled by Horner–Wadsworth–Emmons olefination. Both of these fragments, **3** and **4**, were envisioned from a common aldehyde intermediate **5**, which in turn could be obtained from 2-butene-1,4-diol using a Sharpless asymmetric reaction as one of the key steps.



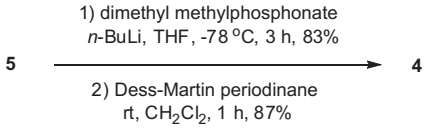
Scheme 1. Retrosynthetic analysis of **1a**.

The synthesis of the aldehyde intermediate **3**, (Scheme 2) began from the epoxy alcohol **6** (readily prepared from 2-butene-1,4-diol in three steps using a literature protocol).[7] By means of regio- and stereoselective epoxide opening of **6** in the presence of Me_3Al/n-BuLi, diol **7** was obtained in 89% yield.[8]

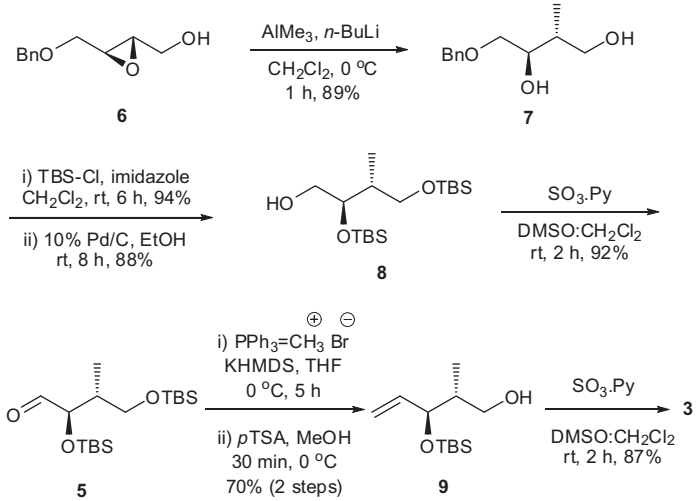
Protection of the diol using TBS-Cl/imidazole in CH_2Cl_2 conditions gave the corresponding bis-TBS ether (94%), which upon debenzylation using hydrogenolysis (10% Pd/C) provided alcohol **8** in 88% yield. Oxidation of alcohol **8** using Parikh–Doering oxidation (SO_3·Py, DMSO)[9] gave the corresponding aldehyde **5** (a common intermediate for synthesis of both fragments **3** and **4**) in 92% yield. A one-carbon Wittig methylenation of **5** ($Ph_3PCH_3^+Br^-$/KHMDS/THF/0 °C), followed by selective desilylation (*p*TSA/MeOH/0 °C) gave alcohol **9** (70%), which was subjected to Parikh–Doering oxidation to give the desired aldehyde fragment **3** in 87% yield.

Next, we focused on the synthesis of keto-phosphonate **4**, which was prepared from the aldehyde intermediate **5** in two steps (Scheme 3). In the first step, aldehyde **5** was treated with dimethyl methylphosphonate using *n*BuLi as the base in THF at −78 °C to obtain a β-hydroxy phosphonate (83%), which was subsequently oxidized under Dess–Martin periodinane conditions to afford the desired β-keto phosphonate fragment **4** in 87% yield.

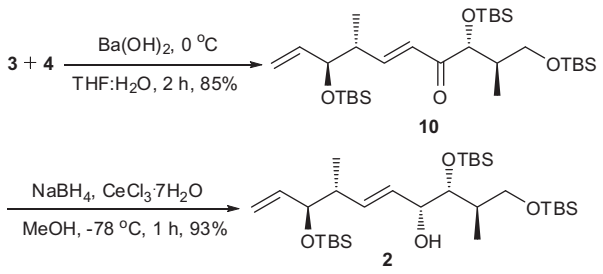
With both fragments in hand, we concentrated on the coupling of **3** and **4** to complete the synthesis of C8–C16 fragment (Scheme 4). Aldehyde **3** was subjected to a Horner–Wadsworth–Emmons reaction with β-keto phosphonate **4** in the presence of $Ba(OH)_2{\cdot}8H_2O$, which gave α,β-unsaturated enone **10** in 85% yield. Finally, Luche reduction[10] of keto functionality in enone **10** using $NaBH_4/CeCl_3{\cdot}7H_2O$ in MeOH at −78 °C furnished *syn*-product **2** in good yield (93%) with excellent diastereoselectivity, which com-



Scheme 3. Synthesis of keto-phosphonate **4**.



Scheme 2. Synthesis of aldehyde fragment **3**.



Scheme 4. Synthesis of C8–C16 fragment of amphidinolide R.

pletes the synthesis of the C8–C16 fragment of amphidinolide R in good overall yield.

3. Conclusion

In conclusion, we have reported on the synthesis of the C8–C16 fragment of amphidinolide R in nine steps with 32% overall yield. The key features of the approach are the successful exploitation of Sharpless asymmetric epoxidation, regioselective methylation of an epoxide, Horner–Wadsworth–Emmons olefination, and Luche reduction. The present approach is amicable for scale up and also facilitates the synthesis of a similar framework present in amphidinolide J and S.

4. Experimental

4.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and acetone-d_6 with 300, 500, or 75 and 125 MHz spectrometers at ambient temperature. Chemical shifts are reported in ppm relative to TMS as the internal standard. FTIR spectra were recorded on a Perkin–Elmer 683 infrared spectrophotometer, neat or as thin films in KBr. Optical rotations were measured on an Anton Paar MLP 200 modular circular digital polarimeter by using a 2-mL cell with a path length of 1 dm. Low-resolution MS were recorded on an Agilent Technologies LC-MSD trap SL spectrometer. All of the reagents and solvents were of reagent grade and used without further purification unless otherwise stated. Technical-grade EtOAc and hexanes used for column chromatography were distilled before use. THF, when used as solvent for the reactions, was freshly distilled from sodium benzophenone ketyl. Column chromatography was carried out on silica gel (60–120 mesh) packed in glass columns. All reactions were performed under N_2 in flame or oven dried glassware with magnetic stirring.

4.1.1. (2*R*,3*R*)-4-(Benzyloxy)-2-methylbutane-1,3-diol 7

To a solution of hydroxy epoxide **6** (1.04 g, 5.3 mmol in CH_2Cl_2 (20 mL) cooled to 0 °C was added *n*-BuLi (1.6 M solution in hexane, 3.7 mL, 5.9 mmol), and the resultant mixture was stirred at 0 °C for 30 min. To this solution was added trimethyl aluminum (1.0 M solution in hexane, 16.2 mL, 16.2 mmol) over a period of 5 min, and the resultant mixture was stirred at 0 °C for 1 h. The reaction mixture was carefully treated with MeOH and diluted with saturated aqueous potassium sodium tartrate (20 mL) and EtOAc (50 mL). After being stirred at room temperature for several hours, the organic layer was separated and washed with brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (30% EtOAc/hexane) gave diol **7** (1.00 g, 89%) as a colorless oil. $[\alpha]_D^{27}$ = −14.4 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} 3281, 3073, 2971, 2859, 1525, 1059, 911 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37–7.31 (m, 5H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 3.72 (m, 1H), 3.65–3.56 (m, 3H), 3.43 (dd, *J* = 9.6, 7.6 Hz, 1H), 3.10–3.39 (br s, 2H), 1.80 (m, 1H), 0.85 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.7, 128.3, 127.7, 75.3, 73.4, 72.7, 67.4, 37.6, 13.6; HRMS (EI) *m*/*z* calcd for $C_{12}H_{19}O_3$ $(M+H)^+$ 211.1334, found 211.1338. The spectroscopic data were consistent with those reported.[3]

4.1.2. (2*R*,3*R*)-2,4-Bis(*tert*-butyldimethylsilyloxy)-3-methylbutan-1-ol 8

To a stirred solution of alcohol **7** (600 mg, 2.85 mmol) in DMF (5 mL) was added imidazole (1.16 g, 17.1 mmol) followed by *tert*-butyl dimethylsilyl chloride (1.71 g, 11.4 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 12 h. After completion of the reaction, the mixture was diluted by the addition of saturated aqueous $NaHCO_3$ (20 mL) and the aqueous phase was extracted with ether (2 × 20 mL). The combined organic layer was washed with brine (20 mL), dried over Na_2SO_4, and the organic solvent evaporated under reduced pressure. The crude residue was purified by flash column chromatography (hexanes/EtOAc = 95:5) to give TBS-protected compound (1.17 g, 94%) as a colorless oil.

Palladium on carbon (26.5 mg, 10% w/w) was added to a solution of the above compound (1.1 g, 2.51 mmol) in EtOH (5 mL) and the heterogeneous mixture was stirred overnight under a hydrogen atmosphere. After completion of the reaction, the mixture was filtered through a small pad of Celite and the resulting filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexanes/EtOAc = 80:20) to give compound **8** (769 mg, 88%) as a colorless liquid. $[\alpha]_D^{27}$ = +3.1 (*c* 1.1, $CHCl_3$); IR (KBr): ν_{max} 3435, 2923, 2853, 1437, 1280, 1109, 1059, 968, 770 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.73 (dd, *J* = 4.9, 10.0 Hz, 1H), 3.63 (dd, *J* = 6.6, 10.0 Hz, 1H), 3.55–3.50 (m, 2H), 3.47 (dd, *J* = 4.3, 10.0 Hz, 1H), 2.41–2.31 (m, 1H), 1.96–1.88 (m, 1H), 0.90 (s, 18 H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.12–0.01 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 74.1, 64.4, 64.0, 38.9, 25.8, 18.2, 18.0, 13.0, −4.4, −4.8, −5.4, −5.5; HRMS (EI) *m*/*z* calcd for $C_{17}H_{41}O_3Si_2$ $(M+H)^+$ 349.2589, found 349.2592.

4.1.3. (2*R*,3*R*)-2,4-Bis((*tert*-butyldimethylsilyl)oxy)-3-methylbutanal 5

A solution of **8** (1.5 g, 2.43 mmol) and *i*-Pr_2NEt (2.9 mL, 16.9 mmol) in 20 mL of 3:1 DMSO at 0 °C was treated with SO_3·Pyridine (1.5 g, 9.6 mmol) and stirred for 2 h at 25 °C. The reaction was diluted with ether (30 mL), washed sequentially with H_2O (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and saturated aqueous NaCl (20 mL) and dried (Na_2SO_4). The crude product was purified by flash column chromatography (hexanes/EtOAc = 9:1) to give compound **5** (1.37 g, 92%) as a colorless liquid. $[\alpha]_D^{27}$ = +2.2 (*c* 1.09, $CHCl_3$); IR (KBr): ν_{max} 2956, 2887, 1736, 1470, 1253, 1092, 955, 836, 773, 668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.60 (s, 1H), 3.86 (m, 1H), 3.60 (t, *J* = 9.4 Hz, 1H), 3.41 (dd, *J* = 4.9, 9.6 Hz, 1H), 2.31–2.19 (m, 1H), 0.93 (s, 9H), 0.87 (d, *J* = 6.2 Hz, 3H), 0.86 (s, 9H), 0.01–0.06 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.2, 79.6, 63.0, 40.9, 25.7, 18.2, 13.5, −4.4, −5.1, −5.6; HRMS (EI) *m*/*z* calcd for $C_{17}H_{38}O_3Si_2Na$ $(M+Na)^+$ 369.2254 found 369.2257.

4.1.4. (2*R*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-2-methylpent-4-en-1-ol 9

Methyl triphenylphosphonium bromide (2.64 g, 3.16 mmol) and a stirrer bar were added to a flask. Anhydrous THF (30 mL) was added under nitrogen and the resulting suspension was cooled to −78 °C prior to the addition of KHMDS (7.32 mL, 3.16 mmol, 0.5 M in toluene) in a dropwise fashion. The resulting suspension was warmed to 25 °C for 1 h and then recooled to −78 °C prior to the addition of aldehyde **5** (320 mg, 0.92 mmol) in anhydrous THF (5.0 mL). The reaction was completed within 2 h and then

quenched by the addition of saturated aqueous NH_4Cl (20 mL). The mixture was then extracted with Et_2O (2 × 50 mL), washed sequentially with H_2O (20 mL) and saturated aqueous NaCl (20 mL), and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave a crude olefin, which was used in next step without further purification.

A solution of the above olefin in MeOH (5 mL) was cooled to 0 °C and *p*TSA (cat.) was added. The resulting solution was stirred at 0 °C for 30 min, then diluted with ether (20 mL) after which saturated aqueous $NaHCO_3$ (10 mL) was added. The resulting layers were separated and washed with brine (10 mL), dried over Na_2SO_4, and the solvents were evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 10→20% EtOAc in hexanes) to yield alcohol **9** (148 mg, 70%, two steps) as a colorless oil. $[\alpha]_D^{27}$ = +26.8 (*c* 1.34, $CHCl_3$); IR (KBr): ν_{max} 3310, 2924, 2854, 1465, 1369, 1110, 1057, 765, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.87 (m, 1H), 5.64–5.37 (m, 2H), 4.10 (m, 1H), 3.62 (dd, *J* = 8.6, 10.5 Hz, 1H), 3.46 (dd, *J* = 4.3, 10.5 Hz, 1H), 2.02–1.90 (m, 1H), 0.91 (s, 9H), 0.81 (d, *J* = 7.1 Hz, 3H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.5, 128.3, 72.8, 64.2, 44.3, 26.1, 18.3, 14.2, −4.3, −4.9; HRMS (EI) *m*/*z* calcd for $C_{12}H_{27}O_2Si$ $(M+H)^+$ 231.1775 found 231.1772.

4.1.5. Dimethyl (3*R*,4*R*)-3,5-bis(*tert*-butyldimethylsilyloxy)-4-methyl-2-oxopentylphosphonate 4

To dimethyl methylphosphonate (114 mg, 0.92 mmol), anhydrous THF (3 mL) was added under nitrogen. The resulting suspension was cooled to −78 °C prior to the addition of *n*-BuLi (0.37 mL, 2.5 M in THF, 0.92 mmol) in a dropwise fashion. The resulting suspension was stirred for 1 h and aldehyde **5** (160 mg, 0.46 mmol) in anhydrous THF (2.0 mL) was added. After 2 h the reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL). The mixture was extracted with Et_2O (2 × 10 mL), washed with H_2O (10 mL) and saturated aqueous NaCl (10 mL), and dried (Na_2SO_4). Removal of the solvent under reduced pressure followed by flash chromatographic purification provided hydroxy phosphonate (180 mg, 83%) as a colorless oil.

To a solution of the above hydroxy phosphonate (180 mg, 0.38 mmol) in 5 mL of CH_2Cl_2 was added Dess–Martin periodinane (193 mg, 0.45 mmol). After stirring at room temperature for 1 h, the reaction was quenched by the addition of a 5:1 solution of saturated aqueous $Na_2S_2O_3$/$NaHCO_3$. The layers were separated and the aqueous layer was washed twice with CH_2Cl_2 (10 mL). The combined organic extracts were then dried over Na_2SO_4 and concentrated in vacuo. Purification by flash column chromatography (25% EtOAc in hexanes) provided 154 mg (87%) of ketone **4** as a colorless oil. $[\alpha]_D^{27}$ = +23.4 (*c* 1.20, $CHCl_3$); IR (KBr): ν_{max} 3024, 2926, 2853, 1696, 1471, 1297, 1166, 1056, 824, 770 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.13 (d, *J* = 4.2 Hz, 1H), 3.79 (d, *J* = 4.2 Hz, 3H), 3.77 (d, *J* = 3.4 Hz, 3H), 3.63–3.56 (m, 1H), 3.40 (dd, *J* = 4.2, 9.3 Hz, 1H), 3.33 (dd, *J* = 15.3, 20.4 Hz, 1H), 2.99 (dd, *J* = 15.3, 22.1 Hz, 1H), 2.26–2.17 (m, 1H), 0.94–0.85 (m, 21H), 0.10–0.01 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.5, 79.8, 63.3, 52.8, 52.7, 40.0, 37.1, 35.3, 25.8, 25.7, 18.3, 18.1, 13.5, −4.8, −5.4, −5.7; HRMS (EI) *m*/*z* calcd for $C_{20}H_{48}O_6PSi_2$ $(M+H)^+$ 469.2565, found 469.2568.

4.1.6. ((6*R*,7*R*,11*R*,12*S*,*E*)-7-(*tert*-Butyldimethylsilyloxy)-2,2,3,3,6,11,14,14,15,15-decamethyl-12-vinyl-4,13-dioxa-3,14-disilahexadec-9-en-8-one) 10

To a solution of alcohol **9** (32 mg, 0.14 mmol) in 2 mL of CH_2Cl_2 was added Dess–Martin periodinane (70 mg, 0.16 mmol). After stirring at room temperature for 1 h, the reaction was quenched by the addition of a 5:1 solution of saturated aqueous $Na_2S_2O_3$/$NaHCO_3$. The layers were separated and the aqueous layer was washed twice with CH_2Cl_2 (10 mL). The combined organic extracts were then dried over Na_2SO_4 and concentrated in vacuo to give crude aldehyde **3**, which was used directly in the next step.

To a solution of keto phosphonate **4** (100 mg, 0.20 mmol) in THF (5 mL) was added $Ba(OH)_2{\cdot}8H_2O$ (79 mg, 0.41 mmol) under N_2 and stirred for 45 min at rt. The reaction mixture was cooled to 0 °C, after which was slowly added aldehyde **3** in 2 mL of THF/H_2O (40:1) and the mixture was allowed to warm to rt and stirring continued for 1 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL), the organic layer was washed with aqueous saturated $NaHCO_3$ (5 mL), brine (5 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, hexanes/EtOAc 1:1) to afford enone **10** (68 mg, 85%) as a colorless oil. R_f = 0.50 (10% EtOAc in hexanes). $[\alpha]_D^{27}$ = +10.1 (*c* 1.0, $CHCl_3$); IR (KBr): ν_{max} 2932, 2859, 1675, 1428, 1260, 996, 822, 772, 613 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.87 (m, 1H), 6.47 (dd, *J* = 8.7, 16.2 Hz, 1H), 5.75–5.66 (m, 1H), 5.14–5.09 (m, 1H), 4.08–4.01 (m, 1H), 3.95 (t, *J* = 6.5 Hz, 1H), 3.62 (dd, *J* = 5.4, 9.8 Hz, 1H), 3.51 (dd, *J* = 5.4, 9.8 Hz, 1H), 2.46–2.38 (m, 1H), 1.95–1.87 (m, 1H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.92–0.86 (m, 30H), 0.02–0.05 (m, 18H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.9, 149.3, 139.0, 125.1, 115.6, 79.4, 77.3, 63.7, 43.7, 40.6, 25.9, 25.7, 18.1, 14.8, 14.6, 13.1, 13.0, −4.7, −4.9, −5.1, −5.4; HRMS (EI) *m*/*z* calcd for $C_{30}H_{63}O_4Si_3$ $(M+H)^+$ 571.4029, found 571.4026.

4.1.7. (6*R*,7*R*,8*R*,11*R*,12*S*,*E*)-7-((*tert*-Butyldimethylsilyl)oxy)-2,2,3,3,6,11,14,14,15,15-decamethyl-12-vinyl-4,13-dioxa-3,14-disilahexadec-9-en-8-ol 2

A solution of ketone **13** (53 mg, 0.13 mmol) and $CeCl_3{\cdot}7H_2O$ (31 mg, 0.13 mmol) in MeOH (1.3 mL) was stirred and cooled to −78 °C, after which $NaBH_4$ (5 mg, 0.13 mmol) was added slowly. The solution was stirred for 30 min, after which it was warmed to 0 °C and stirred for another 30 min. The reaction mixture was quenched with water (2 mL) and EtOAc (5 mL) was added. The aqueous layer was extracted with EtOAc (2 × 5 mL). The organic layers were combined, washed with water (5 mL), brine (5 mL), and dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography to afford alcohol **2** (49 mg, 93%) as a clear colorless oil. $[\alpha]_D^{27}$ = +19.6 (*c* 0.65, $CHCl_3$); IR (KBr): ν_{max} 3310, 3066, 2993, 2873, 1455, 1383, 1238, 1025, 944, 755, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.79–5.70 (m, 1H), 5.65 (dd, *J* = 15.5, 7.7 Hz, 1H), 5.46 (dd, *J* = 15.5, 7.7 Hz, 1H), 5.13 (d, *J* = 17.1 Hz, 1H), 5.05 (d, *J* = 10.2 Hz, 1H), 4.10–4.05 (m, 1H), 4.01–3.96 (m, 1H), 3.69 (t, *J* = 3.8 Hz, 1H), 3.61 (dd, *J* = 10.2, 7.4 Hz, 1H), 3.46 (dd, *J* = 10.2, 7.4 Hz, 1H), 2.64 (d, *J* = 6.7 Hz, 1H), 2.33–2.23 (m, 1H), 1.97–1.88 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 7.1 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 18H), 0.09–0.01 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.6, 134.2, 132.0, 115.1, 77.7, 77.3, 72.4, 65.0, 43.6, 40.7, 26.3, 26.2, 18.5, 15.5, 13.5, −3.8, −3.9, −4.0; HRMS (EI) *m*/*z* calcd for $C_{30}H_{64}O_4Si_3Na$ $(M+Na)^+$ 595.4005, found 595.4001.

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