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Total Synthesis of Reported Structure of Baulamycin A and Its Congeners

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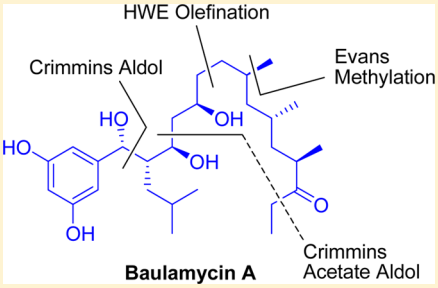
Supporting Information

ABSTRACT: A convergent and flexible strategy for the stereoselective total synthesis of the reported structure of baulamycin A and its congeners has been developed for the first time. Synthetic highlights include a Crimmins aldol reaction to construct the C-1′ and C-14 centers, a Crimmins acetate aldol reaction to generate the hydroxy group at the C-13 position, Horner−Wadsworth−Emmons olefination to form the C_9-C_{10} bond, and Evans methylation to install the C-8 center. This synthetic study disclosed that the reported structure of baulamycin A needs to be revised, as its spectroscopic data are not identical with those of the synthetic baulamycin A.



INTRODUCTION

Multidrug-resistant pathogens are a serious threat to human health.[1] Pathogens usually survive in host cells by scavenging iron with the help of siderophores.[2,3] Thus, inhibition of the biosynthesis of siderophores is believed to be a potential approach to fight against pathogens which have developed immunity against antibiotics. Therefore, the discovery of new chemical inhibitors of siderophore biosynthesis is crucial for the development of anti-infective agents.[4] Sherman et al., in 2014, first discovered a new structural class of antibiotic baulamycins A (**1**) and B (**2**) (Figure 1) from marine microbial-derived

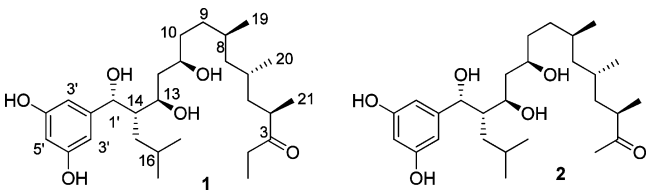


Figure 1. Chemical structures of baulamycin A (**1**) and baulamycin B (**2**).

natural product extracts collected in Costa Rica, Panama, and Papua New Guinea.[5] Baulamycins A (**1**) and B (**2**) exhibited in vitro activity against nonribosomal peptide synthetase independent siderophore (NIS) synthetase, SbnE and AsbA, which are involved in the biosynthesis of siderophores staphyloferrin B in *S. aureus* and petrobactin in *B. anthracis*, respectively. The IC_{50} values of both compounds **1** and **2** against SbnE were 4.8 and 19 μM, respectively, whereas the values against AsbA were 180 and 200 μM, respectively.[5a] Cultures of several bacterial pathogens containing baulamycins A (**1**) and B (**2**) revealed that these natural products can inhibit the growth of both Gram-positive and Gram-negative bacteria.[5a] The basic skeleton of this family of marine natural products was determined by the extensive use of NMR (^{1}H, ^{13}C, HSQCAD, gCOSY, HMBCAD, ROESY) and mass spectroscopic methods, which revealed that architecturally baulamycins A (**1**) and B (**2**) possess linear backbones terminated on one side with ethyl and methyl ketones, respectively, whereas the other ends have a common resorcinol moiety. There are seven asymmetric centers in the molecules, among which three are hydroxylated, three are methylated, and one is isobutylated. *J*-based configuration analysis (JBCA) was employed to determine the relative configuration of those chiral centers by calculation of the $^3J_{H-H}$ and $^2J_{C-H}$ values of the respective centers using homonuclear 2D*J* spectroscopy (HOMO2D*J*) and heteronuclear 2D*J* (HET2D*J*) spectral analysis techniques.[5] The interesting antibiotic activities of baulamycins A and B, their limited natural abundance, their structural complexity, and our continual interest[6] in the synthesis of bioactive natural products prompted us to envisage the total synthesis of baulamycin A, one of the most active members of baulamycin family of natural products. In this report, we describe a highly convergent and flexible stereoselective total synthesis of the proposed structure of baulamycin A (**1**) along with two of its congeners for the first time.

RESULTS AND DISCUSSION

First Approach. The initial retrosynthetic analysis of the proposed structure of baulamycin A is depicted in Scheme 1. In order to have a shorter synthetic route, we first relied on a cross-metathesis (CM) approach[7] which would disconnect the target molecule (**1**) into the suitably protected coupling partners **3** and **4**. The requisite partner **3** could be synthesized

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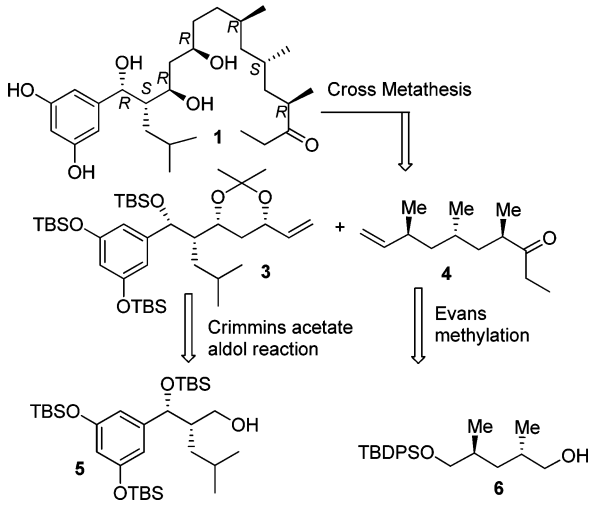
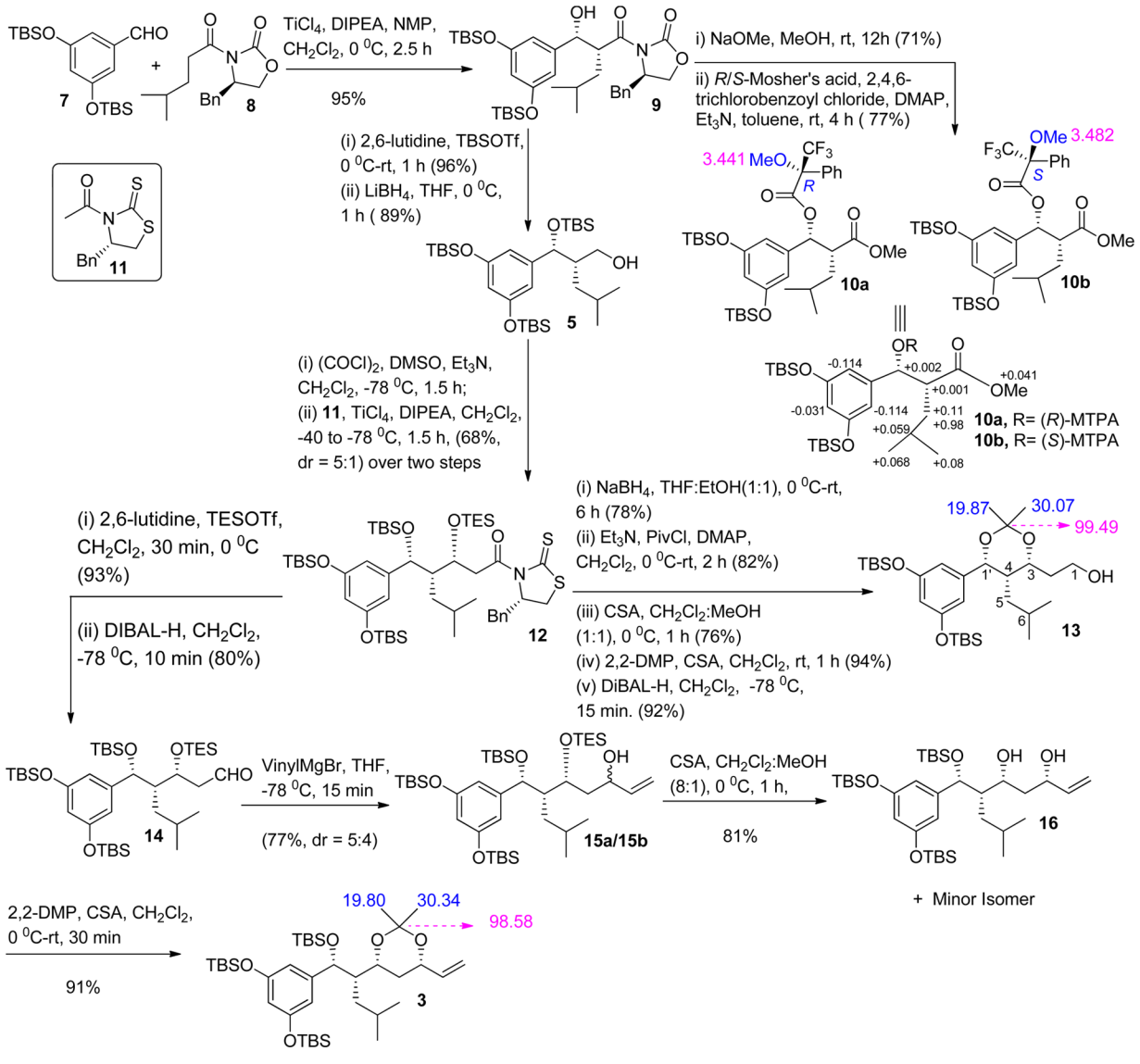
Scheme 1. Initial Retrosynthetic Analysis of Baulamycin A (1)



from compound **5**, adopting a Crimmins acetate aldol reaction[8] as one of the key steps, whereas the other coupling partner **4** could be accessed from compound **6**, employing an Evans asymmetric methylation reaction[9] as one of the pivotal steps.

The synthesis of one of the key coupling partners, **3**, is shown in Scheme 2. Our synthetic endeavor began from the known aldehyde **7**,[10] which was subjected to a Crimmins aldol reaction[11] using the known chiral auxiliary **8**[12] in the presence of $TiCl_4$, Hunig's base, and NMP to give compound **9** as a single isomer in 95% yield. In order to confirm the stereochemistry of the newly generated hydroxy center of compound **9**, it was transformed to the corresponding Mosher's esters **10a,b** in two steps.[13,6c] All of the protons of Mosher's esters **10a,b** were assigned by ^{1}H NMR (Scheme 2). The positive $\Delta\delta$ values ($\Delta\delta = \delta^S - \delta^R$) obtained for all the nonaromatic protons from the set of esters **10a,b** revealed that the C-1′ center is in the *R* configuration. Moreover, the positive $\Delta\delta^{SR}$ value observed from the Mosher's ester −OMe group resonating at δ 3.482 and 3.441 ppm unambiguously confirmed the *R* stereochemistry of this newly generated hydroxy center.[14] The free hydroxy of compound **9** was then protected as a TBS

Scheme 2. Synthesis of Intermediate 3



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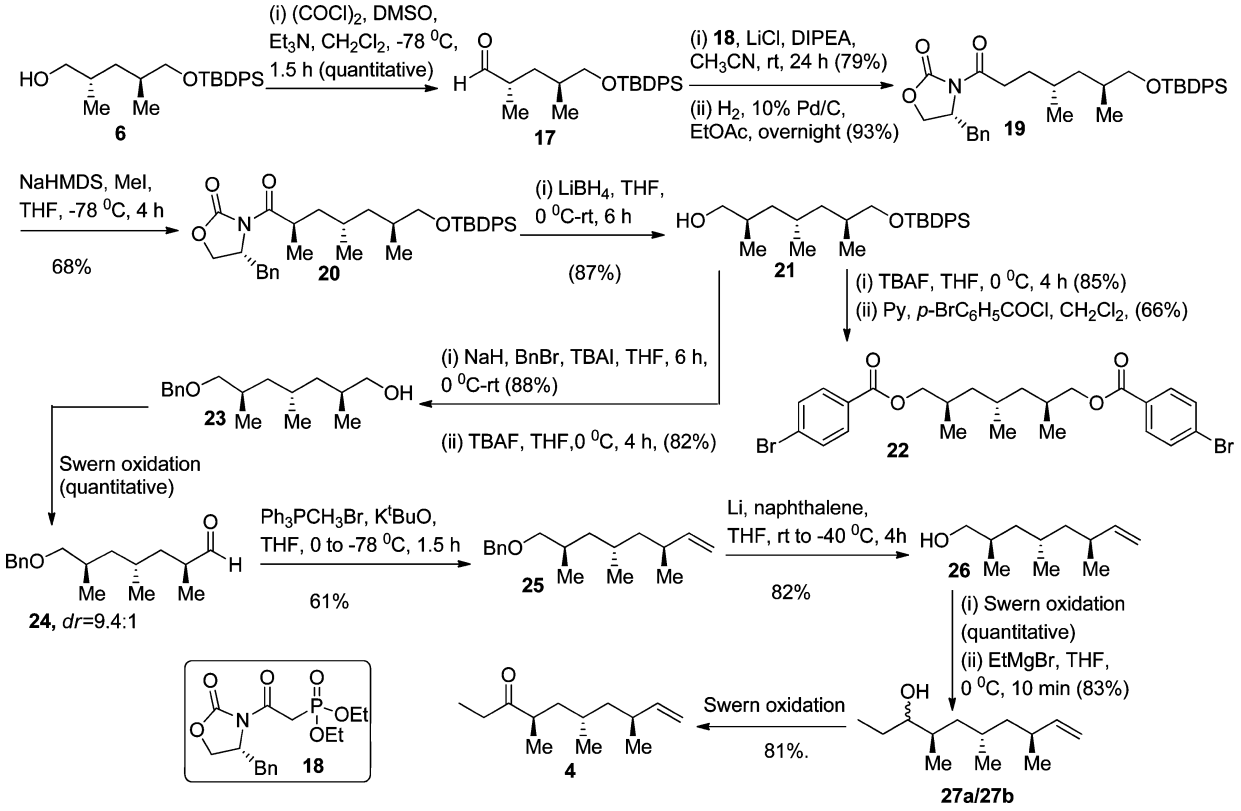
Scheme 3. Synthesis of Intermediate 4



ether using TBSOTf/2,6-lutidine and subsequently treated with $LiBH_4$ to give alcohol **5**. Next, alcohol **5** was oxidized to the corresponding aldehyde using Swern conditions and subsequently subjected to a Crimmins acetate aldol reaction[8] using (*S*)-phenylalanine-derived *N*-acetylthiazolidinethione **11**[15] to give compound **12** as the major isomer (dr = 5:1). To verify the relative configurations of all the chiral centers in compound **12**, it was converted to the acetonide derivative **13** in five steps through functional group manipulations (Scheme 2). Compound **13** was studied extensively, employing two-dimensional NMR experiments: i.e., COSY, NOESY, and $^1H-^{13}C$ HSQC. $^1H-^1H$ vicinal coupling constants, $^3J_{C1'H-C4H} \approx 1.3$ Hz and $^3J_{C3H-C4H} \approx 2.0$ Hz, suggested their gauche orientations in the constrained six-membered ring. Further, strong NOEs for C1′H↔C3H, C1′H↔acetonide Me (at δ 1.52 ppm), and C3H↔acetonide Me (at δ 1.52 ppm) (please see Table S4 for assignment of protons and carbons and Figure S19a,b for NOE correlations in the Supporting Information) strongly supported the axial disposition of C1′H and C3H and equatorial disposition of C4H. Moreover, the ^{13}C NMR chemical shifts of the ketal carbon resonating at 99.49 ppm and acetonide methyls resonating at 30.07 and 19.87 ppm unambiguously confirmed that C1′H and C3H are in a syn relatioship.[16] The free hydroxy of compound **12** was then protected as a TES ether using TESOTf/2,6-lutidine and further subjected to selective reduction of the thiazolidinethione moiety using DIBAL-H to produce aldehyde **14**, which was subsequently reacted with vinylmagnesium bromide to yield an inseparable mixture of isomers **15a,b** (dr = 5:4) in good overall yield (57% in three steps). The TES ethers of the mixture of compounds **15a,b** were then deprotected using CSA, and the resultant compounds were separated easily by silica gel column chromatography to give the pure compound **16** as a major isomer along with its minor counterpart. The major isomer **16** was finally reacted with 2,2-DMP/CSA to give compound **3**, and it is evident from ^{13}C NMR data (δ 98.58 (ketal), 30.34 and 19.80 (acetonide methyl) ppm)[16] that the newly formed hydroxy centers are in a syn orientation with respect to the existing β-hydroxy center.

The synthesis of the other coupling partner, **4**, is delineated in Scheme 3. We have started our synthesis from the known alcohol **6**[17] (please see Table S1 in the Supporting Information for a comparison of NMR for the synthetic compound with that of the reported compound). Initially, we planned to test a number of oxidizing agents for the conversion of alcohol **6** to aldehyde **17** to see whether epimerization of the α-methyl center to the carbonyl moiety took place, which is often the case in similar systems.[18] The alcohol **6** was thus oxidized separately to access aldehyde **17** using Swern oxidation, DMP oxidation, and TEMPO-BAIB-mediated[18,19] Piancatelli oxidation. The ^1H NMR data of these aldehydes were compared (please see Figure S24 in the Supporting Information), but no diastereomeric peak(s) due to the epimerization of the α-methyl center was detected. It might also be the case that epimeric peaks were not distinguishable on the NMR time scale or the rate of epimerization was too slow to observe. Next, aldehyde **17** obtained from the Swern oxidation was then subjected to Horner−Wadsworth−Emmons (HWE) olefination[20] with the known phosphonate **18**,[21] derived from D-phenylalanine, in the presence of LiCl/DIPEA to give the corresponding coupled product exclusively. This was hydrogenated further to give compound **19** as a colorless liquid. Comparison of the spectroscopic data of compound **19** with those of its known C-4 epimeric compound[22] revealed that there are considerable mismatches (please see Table S2 in the Supporting Information). This clearly indicated that the α-

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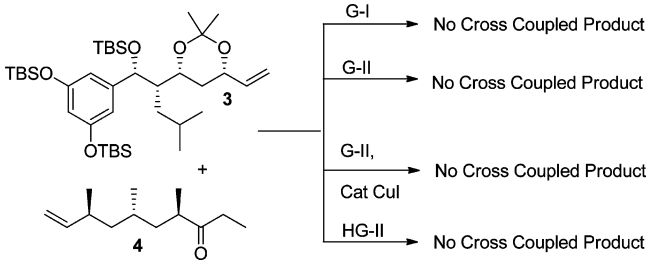
J. Org. Chem. 2017, 82, 2414−2435

chiral methyl center of aldehyde **17** did not epimerize during the Swern oxidation or in the subsequent base-catalyzed HWE reaction.

Next, compound **19** was treated with NaHMDS in the presence of MeI following the Evans alkylation protocols[9] to obtain compound **20** as a single isomer in good yield. Considerable efforts were carried out at this stage to make some suitable crystalline derivatives of it for X-ray analysis. Initially, the *p*-nitro or *p*-bromo benzoate derivatives of the corresponding alcohol obtained from the desilylation of compound **20** were made, but none of them produced any solid residue. Compound **20** was then subjected to $LiBH_4$ reduction to obtain compound **21**. This was then treated with TBAF to access the corresponding diol, which was converted to the *p*-bromo benzoate derivative **22** as a yellow crystalline solid. Single-crystal X-ray analysis supported its structure unequivocally (please see Figure S5 in the Supporting Information). Compound **21** was then reacted with BnBr/NaH/TBAI to yield the corresponding benzylated compound, which was subjected further to desilylation using TBAF to produce alcohol **23** in 72% overall yield. A range of oxidizing agents such as Swern, DMP, TPAP-NMO,[23] and TEMPO-BAIB[18,19] were tested at this stage for the conversion of alcohol **23** to aldehyde **24** separately. Careful observation of the ^{1}H NMR of these aldehydes disclosed that there are some new peaks of similar nature (please see Figure S31 in the Supporting Information). This prompted us to attempt deliberate epimerization of the α-methyl center of aldehyde **24** to confirm whether these new signals were associated with its epimerization. Thus, aldehyde **24**, obtained from the Swern oxidation, was treated with $Ba(OH)_2{\cdot}8H_2O$ at room temperature. The ^{1}H NMR spectra of the resultant aldehyde at different time spans were recorded and compared with the data of aldehyde **24** obtained from the Swern oxidation (please see Figure S32 in the Supporting Information). It was clear that the rate of epimerization of the α-methyl center of aldehyde was slow (~50% in 48 h). It was also evident that the extent of epimerization of the α-methyl center of the aldehyde varied with the nature of the oxidizing agents used. The extent of epimerization was considerable for the TPAP-NMO (dr = 3.4:1.0) and TEMPO-BAIB (dr = 4.3:1.0) oxidations, whereas the DMP conditions were better (dr = 6.7:1.0), but the Swern condition was the best[24] (dr = 9.4:1.0) in our system. It is noteworthy that these epimerized aldehydes were inseparable by silica gel column chromatography. We proceeded further with Swern oxidation, as it yielded the best results in our system. Aldehyde **24** was further subjected to Wittig olefination using Ph_3PCH_3Br/K^tBuO to give olefin **25**, which was subsequently treated with Li/naphthalene[25] to access alcohol **26** in good overall yield. The minor counterpart generated from the partially epimerized aldehyde **24** (dr = 9.4:1.0) was separated during the purification process. Next, alcohol **26** was oxidized to the corresponding aldehyde following the Swern conditions and subsequently treated with EtMgBr to give an inseparable mixture of diastereomers **27a,b**. This mixture of compounds finally was oxidized under the Swern conditions to construct the requisite intermediate **4** in very good overall yield (67% in three steps).

Our initial synthetic efforts to complete the total synthesis of proposed structure of baulamycin A (**1**) are described in Scheme 4. With the two key coupling partners **3** and **4** in hand, our attention was turned to couple them by a cross-metathesis reaction.[7] A number of olefin metathesis catalysts (G-I, G-II, HG-II) with or without CuI additive under different reaction conditions were screened at this stage. However, it was quite unfortunate that under none of these conditions could a cross-coupled product be obtained. In most of the cases the reaction did not proceed well. This outcome might be due to either steric hindrance between the reacting olefins or coordination between ruthenium and the carbonyl functionality of olefin **4** leading to the inactivation of catalytically active species. In order to have a suitable synthetic route for the proposed structure of baulamycin A (**1**), we therefore decided to move to an alternative approach.

Scheme 4. First Attempt to Synthesized Baulamycin A (1) using Cross Olefin Metathesis



Second Approach. The second retrosynthetic strategy for reported structure of baulamycin A (**1**) is shown in Scheme 5, where we planned to use HWE olefination[20] to construct the C_9-C_{10} bond. Baulamycin A (**1**) could be prepared from compound **30** via the intermediate compounds **29** and **28** by functional group manipulations. Compound **30** eventually would disconnect into the two key coupling partners **24** and **31** following HWE olefination as a pivotal step.

The final synthetic endeavor for preparing the proposed structure of baulamycin A (**1**) is depicted in Scheme 6. Compound **12** (Scheme 2) was first treated with imidazole/MeOH to give the corresponding methyl ester, which subsequently converted to TES ether **32** using TESOTf/2,6-lutidine in good overall yield (83% in two steps). Next compound **32** was transmuted to phosphonate **31** using $(MeO)_2P(O)Me/^nBuLi$[20c] and further subjected to HWE olefination[20] with aldehyde **24** obtained by Swern oxidation (Scheme 3) in the presence of $Ba(OH)_2{\cdot}8H_2O$ to give compound **30** as an isolable isomer. Finally this was hydrogenated to give compound **29** with good overall yield (68% in three steps). The selective deprotection of the TES ether of compound **29** using CSA followed by treatment with DIBAL-H produced compound **33** as a major product (dr = 3:1). Our efforts to obtain suitable derivatives from compounds **29** and **33** for X-ray crystallographic analysis by making their corresponding *p*-bromo benzoate derivatives were not successful, as the mono- and tribenzoate derivatives of compounds **29** and **33**, respectively, were liquid at room temperature. We thus planned to perform an HWE reaction between the epimeric mixture (~50%) of aldehyde **24** obtained earlier from $Ba(OH)_2{\cdot}8H_2O$ treatment and the phosphonate **31** to contrast with the NMR spectrum of pure compound **30** with this epimeric (C-6 position) mixture. A comparison of the ^{1}H and ^{13}C NMR of this mixture of epimeric products with those of pure compound **30** (please see Figures S39 and S40 in the Supporting Information) clearly indicates that no such epimerization occurred during the preparation of compound **30**.

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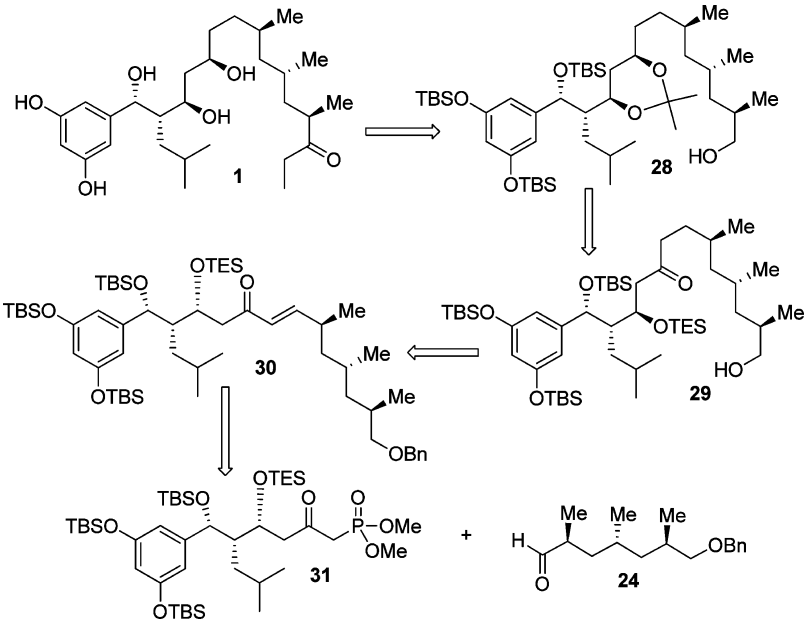
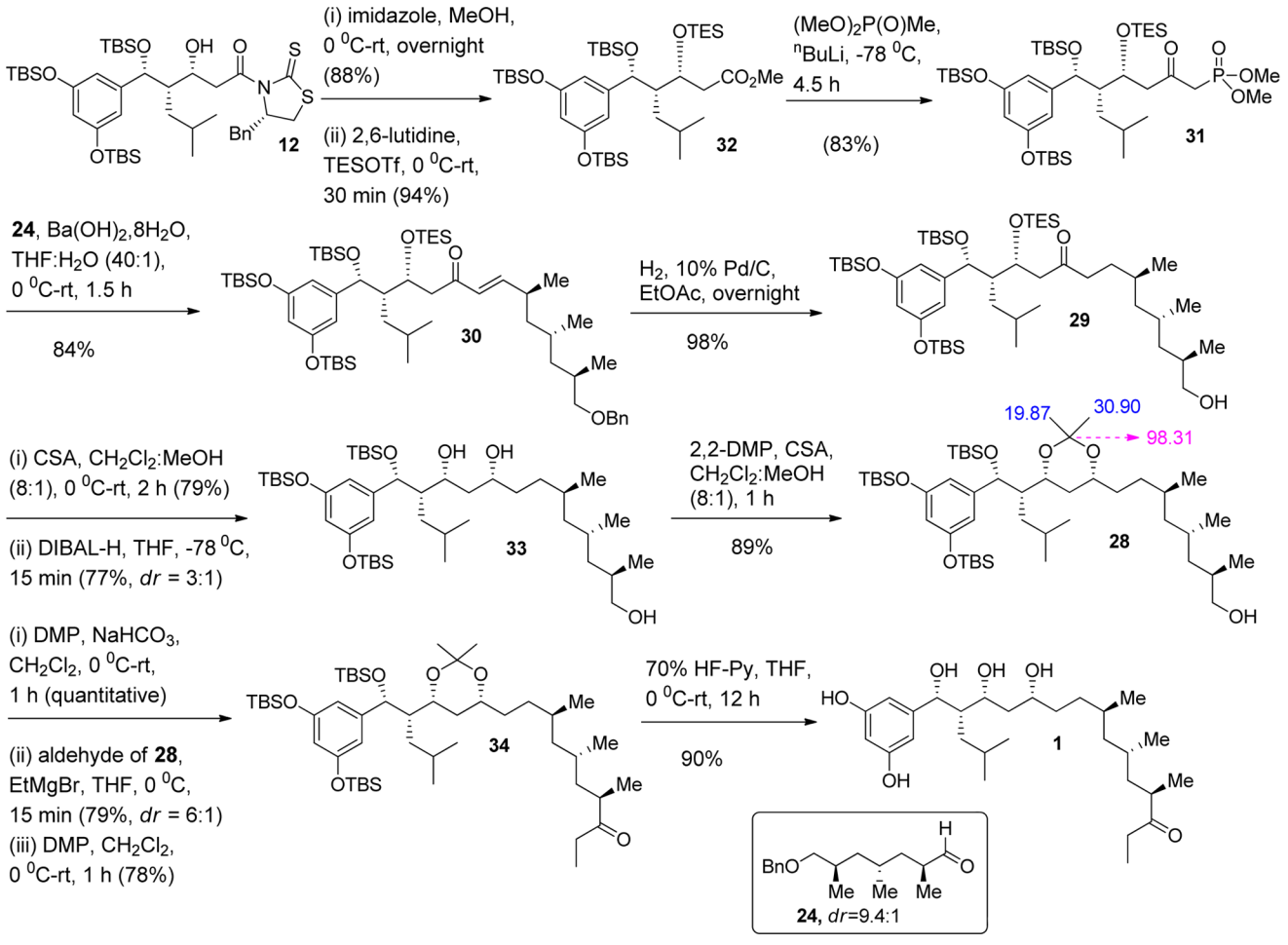
J. Org. Chem. 2017, 82, 2414−2435

Scheme 5. Second Retrosynthetic Strategy for Proposed Structure of Baulamycin A (1)



Scheme 6. Completion of Total Synthesis of Reported Structure of Baulamycin A (1)



The relative stereochemistry of the newly generated hydroxy center of compound **33** using DIBAL-H was confirmed in the next step, where compound **33** was treated with 2,2-DMP/CSA to give 1,3-acetonide compound **28**. It is evident from ^{13}C NMR analysis data[16] (δ 98.87 (ketal), 30.90 and 19.87 (acetonide methyl) ppm) that both of the acetonide-protected hydroxy centers are in a syn configuration. Compound **28** was then subjected to DMP oxidation to give the corresponding

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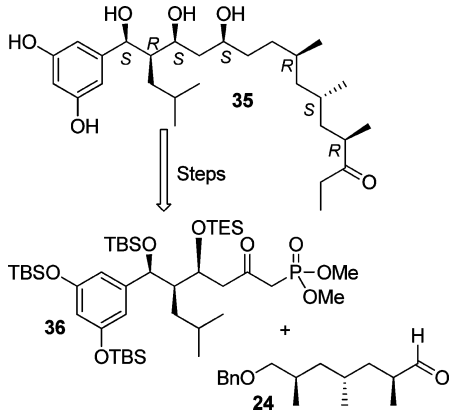
aldehyde, which further was treated with EtMgBr followed by DMP to synthesize compound **34** with 62% overall yield over three steps. Several conditions were screened at this stage to obtain the optimal conditions for deprotection of all the protecting groups. It was observed that treatment of compound **34** with either $TiCl_4/CH_2Cl_2$ or CSA/MeOH yielded some unidentified products, whereas a CSA/CH_2Cl_2−MeOH (1/1) combination deprotected all the protecting groups except for the two aromatic TBS ethers. An $AcOH/H_2O$ (4/1) combination even under reflux conditions was also found to be unsuitable, cleaving the protecting groups except for the aliphatic TBS ether. Interestingly, the reaction of compound **34** with TBAF produced only the aromatic TBS deprotected compound and the aliphatic TBS ether remained intact. This compound further was converted to the required product **1** using CSA/CH_2Cl_2−MeOH (1/1), but the overall yield was not satisfactory. Finally, we were indeed happy to see that HF-Py functioned efficiently for the global deprotection of all the protecting groups of compound **34**, which eventually produced the target molecule **1** in good yield (90%). Both the ^1H and ^{13}C NMR spectra of pure compound **1** were recorded, initially in CD_3OD, and compared with those obtained for the isolated natural product. Unfortunately, significant mismatches in both the ^1H and ^{13}C NMR spectra (please see a comparison in Table S5 in the Supporting Information) were observed. The major mismatches in the ^1H NMR signals of synthesized compound **1** in comparison to the isolated compound were seen for the H-1′, H-14, and H_3-17 protons. The chemical shifts of H-1′, H-14, and H_3-17 protons, for the synthesized compound **1**, appeared at δ 4.82, 1.67, and 0.64 ppm, respectively, whereas these protons in the isolated baulamycin A were observed at δ 4.47, 1.88, and 0.83 ppm, respectively. Apart from minor variations, discrepancies in the ^{13}C NMR were also noted. The ^{13}C NMR signals of C-12, C-13, C-15, and C-16 carbons of the synthesized compound **1** were recorded at δ 42.4, 75.1, 33.4, and 28.3 ppm, respectively, while these resonances were reported to be at δ 40.6, 73.3, 37.3, and 26.6 ppm for the isolated compound. Mismatches were also observed when ^1H and ^{13}C NMR spectra of compound **1** were recorded in d_6-DMSO. A downfield shift of the H-1′ proton of synthesized compound **1** in comparison to the corresponding proton in naturally occurring baulamycin A was observed when ^1H NMR was recorded in CD_3OD. To determine whether the existence of any intramolecular hydrogen bonding between the 1,3-diol moiety of synthesized compound **1** was responsible for these deviations in the data, the ^1H NMR data were collected at variable temperature and varying dilution (please see Figure S59a,b in the Supporting Information). Unfortunately, none of the data obtained on the synthesized structure were in accordance with the data reported[5a] on the isolated baulamycin A. Moreover, the specific rotation of synthesized compound **1** ($[\alpha]^{30}_D$ +2.0 (*c* 0.6, MeOH)) deviated significantly from the reported value[5a] ($[\alpha]^{20}_D$ −10.3 (*c* 0.2, MeOH)). Our attempts to produce a solid *p*-bromobenzoate derivative of synthesized compound **1** for crystallization were unsuccessful, as a complex inseparable mixture of products was obtained irrespective of the conditions used. However, the relative stereochemistry of the asymmetric centers at C1′, C14, C13, and C11 were established unequivocally as *R*, *S*, *R*, and *R* using an extensive NMR analysis utilizing the vicinal coupling constants ($^3J_{H,H}$) from ^1H and HOMO2DJ experiments in combination with the spatial correlations derived from the 2D-ROESY spectrum.[26] Determination of the detailed relative configurations of the methyl sterocenters embedded in the right half of molecule **1** was not possible by NMR, as the diastereotopic protons were resonating at similar chemical shift positions. However, we believe that the configurations of these stereocenters are indeed correct, as was evident from the X-ray crystallographic data as mentioned above. These results strongly suggest that the structure proposed (**1**) for isolated baulamycin A may not be entirely accurate.

Next, we thought about the possibility that the isolated baulamycin A is a diastereomer of the proposed structure **1**. To search for the suitable structure, we first concentrated on those ^1H NMR signals which deviated significantly from the reported values. We observed that chemical shifts of H-1′, H-14, and H_3-17 protons differed substantially from the literature data. The relative configurations of C-1′, C-14, C-13, and C-11 centers were determined to be in a syn relationship using ROESY correlation and *J*-based configuration analysis (JBCA).[5a] As the absolute stereochemistry of these centers were not established, one may need to consider their opposite relative configurations, which are expected to have similar types of dihedral angle spin-coupling constants as described by the isolation group. As the major mismatches were recorded around the C-1′ and C-14 asymmetric centers, we planned to make compound **35** (Scheme 7), where the C-1′ and C-14 centers are in an opposite configuration in comparison to the reported structure. The C-13 and C-11 chiral centers were also inverted accordingly to get all the centers in a syn configuration. However, the chiral centers embedded in the C_1−C_9 segment remained unaltered, as they are remote from the centers (C-1′, C-14) showing deviations in the ^1H NMR data. Thus, compound **35** was taken as our new synthetic target, which could be synthesized from the key intermediates **36** and **24** (Scheme 7) following a chemistry similar to that described earlier.

Scheme 7. Synthetic Strategy for Compound 35, an Analogue of the Reported Structure of Baulamycin A



The synthetic endeavor for the total synthesis of compound **35** is shown in Scheme 8. We started our synthesis from the known oxazolidinone **37**,[27] derived from L-phenylalanine. The reaction between aldehyde **7** and auxiliary **37** following a Crimmins aldol protocol[11] produced compound **38** as a single isomer, which was finally transformed to phosphonate **36** through the intermediates **39**, **40**, **42**, and **43** following the chemistry developed previously (Schemes 2 and 6). It is noteworthy that intermediate **40** was converted to intermediate **42** using a Crimmins acetate aldol protocol[8] as one of the key

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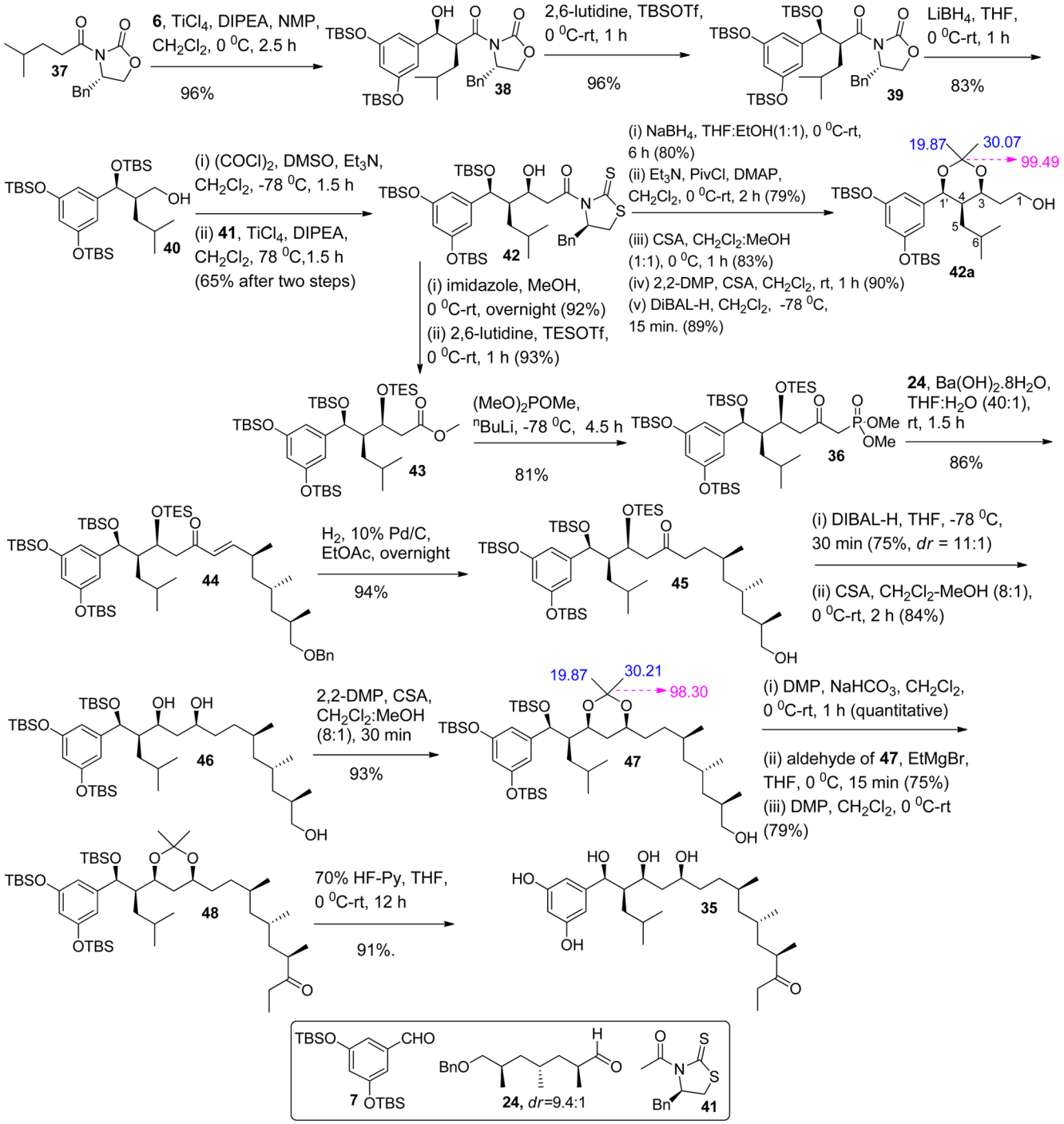
Scheme 8. Completion of Synthesis of Compound 35



steps in the presence of *N*-acetylthiazolidinethione **41**,[15] derived from D-phenylalanine. To confirm the relative stereochemistry of compound **42**, the acetonide derivative **42a** was synthesized in five steps (Scheme 8). All of the stereogenic centers of compound **42a** are in a syn orientation, which was confirmed by the NMR experiments (please see Table S6 for the assignment of protons and carbons and Figure S68a,b for NOE correlations in the Supporting Information) similar to those performed for compound **13**. The phosphonate **36** and aldehyde **24** (dr = 9.4:1.0) were coupled together by HWE olefination[20] to give compound **44**, which further was hydrogenated to access pure compound **45** in good overall yield (81% in two steps). The keto functionality of compound **45** was reduced selectively using DIBAL-H to give a mixture of the corresponding products (dr = 11:1), which were separated by column chromatography. The major isomer was then treated with CSA to produce compound **46**. This stereoselective carbonyl reduction had also been tested using the TES ether deprotected counterpart of compound **45** in the presence of DIBAL-H, but the diastereoselectivity was superior in the earlier case.

The free 1,3-diol of compound **46** was protected as an acetonide to access compound **47**, and the syn stereochemistry was confirmed further by ^{13}C NMR data (δ 98.30 (ketal), 30.21

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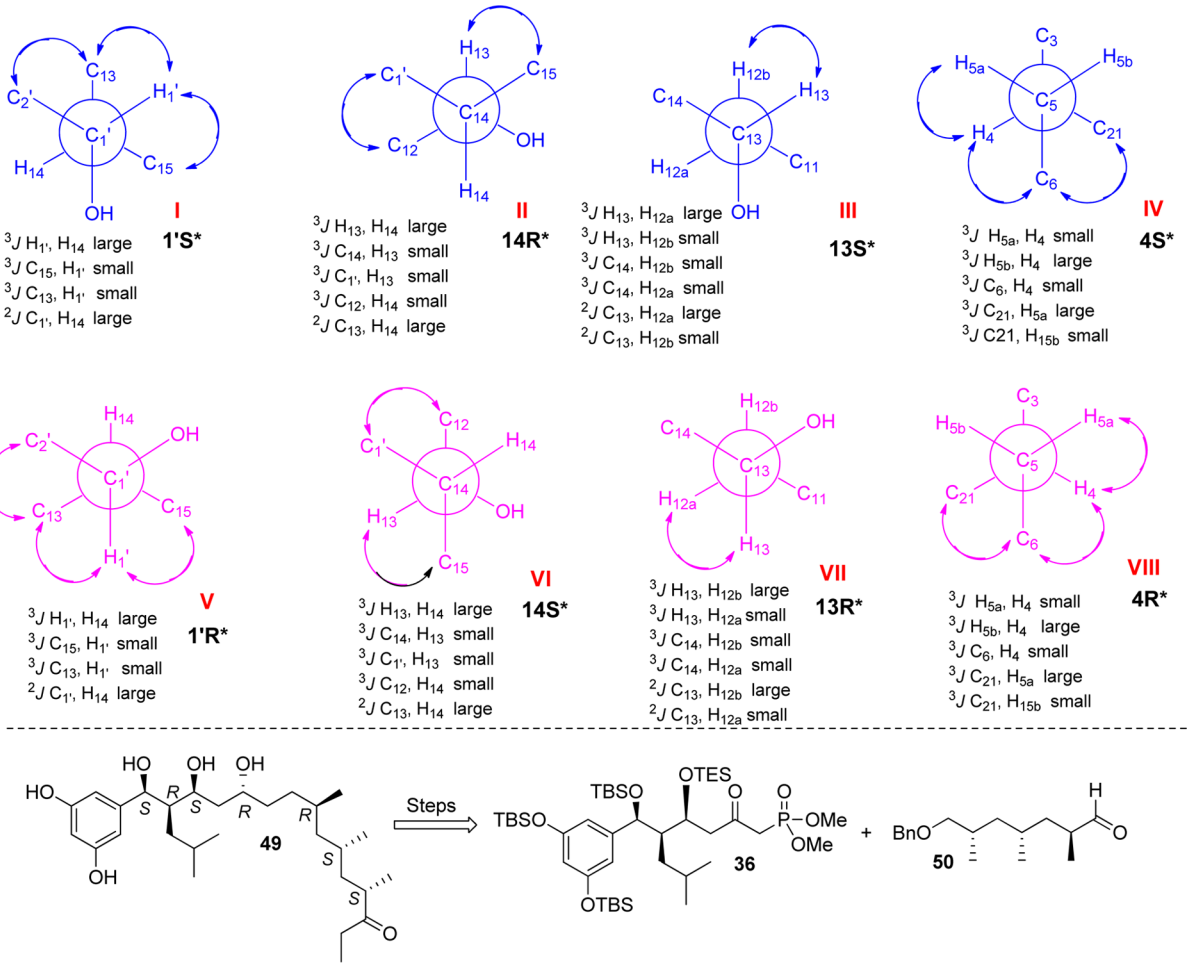
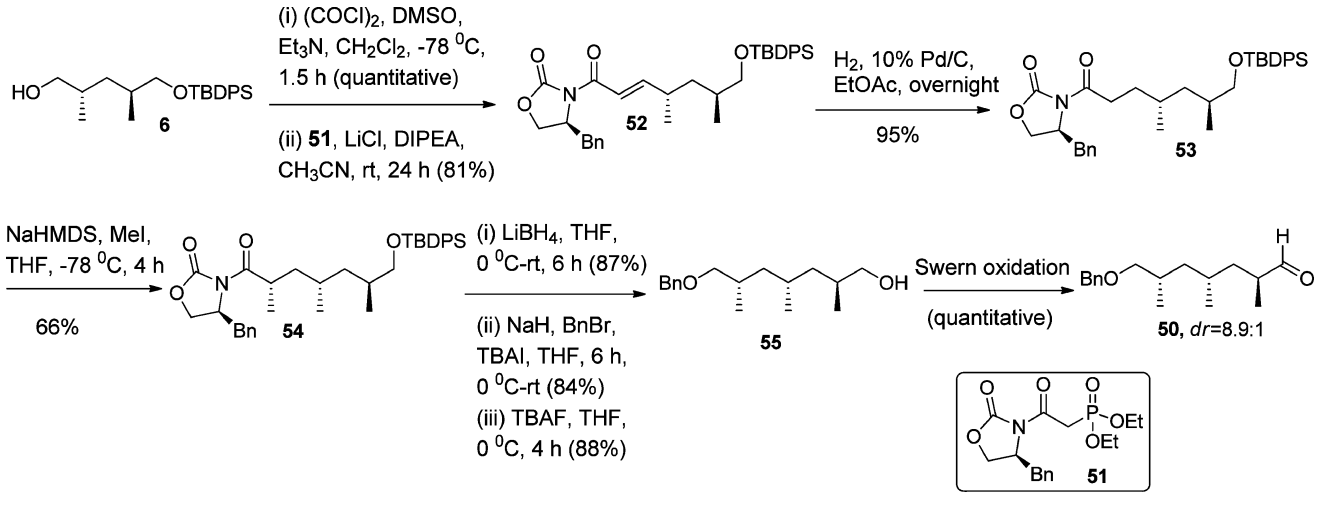


Figure 2. Chemical structure of possible diastereomer **49** and its synthetic strategy: Newman projections of some common centers of compound **49** and the proposed structure of baulamycin A (**1**) with expected ROESY correlations and coupling constants.

Scheme 9. Synthesis of Requisite Aldehyde (50) for Target Compound 49



and 19.87 (acetonide methyl) ppm) analysis.[16] Finally, compound **47** was converted to the target compound **35** via intermediate **48** by following the chemistry developed earlier. The ^{1}H and ^{13}C NMR spectra were recorded in CD_3OD and compared to the data reported for isolated baulamycin A. It was quite puzzling to see that the NMR data of synthesized compound **35** were not in accordance with the values reported[5a] for the isolated natural product (please see a comparison in Table S7 in the Supporting Information), although consistency in the specific rotation (observed $[\alpha]^{29}_D$ −13.3 (*c* 0.6, MeOH); reported $[\alpha]^{20}_D$ −10.3 (*c* 0.2, MeOH)) was observed. This led us to consider an alternate possibility.

To search for a possible diastereomer, we next planned to reinvestigate the JBCA calculations from which the Newman

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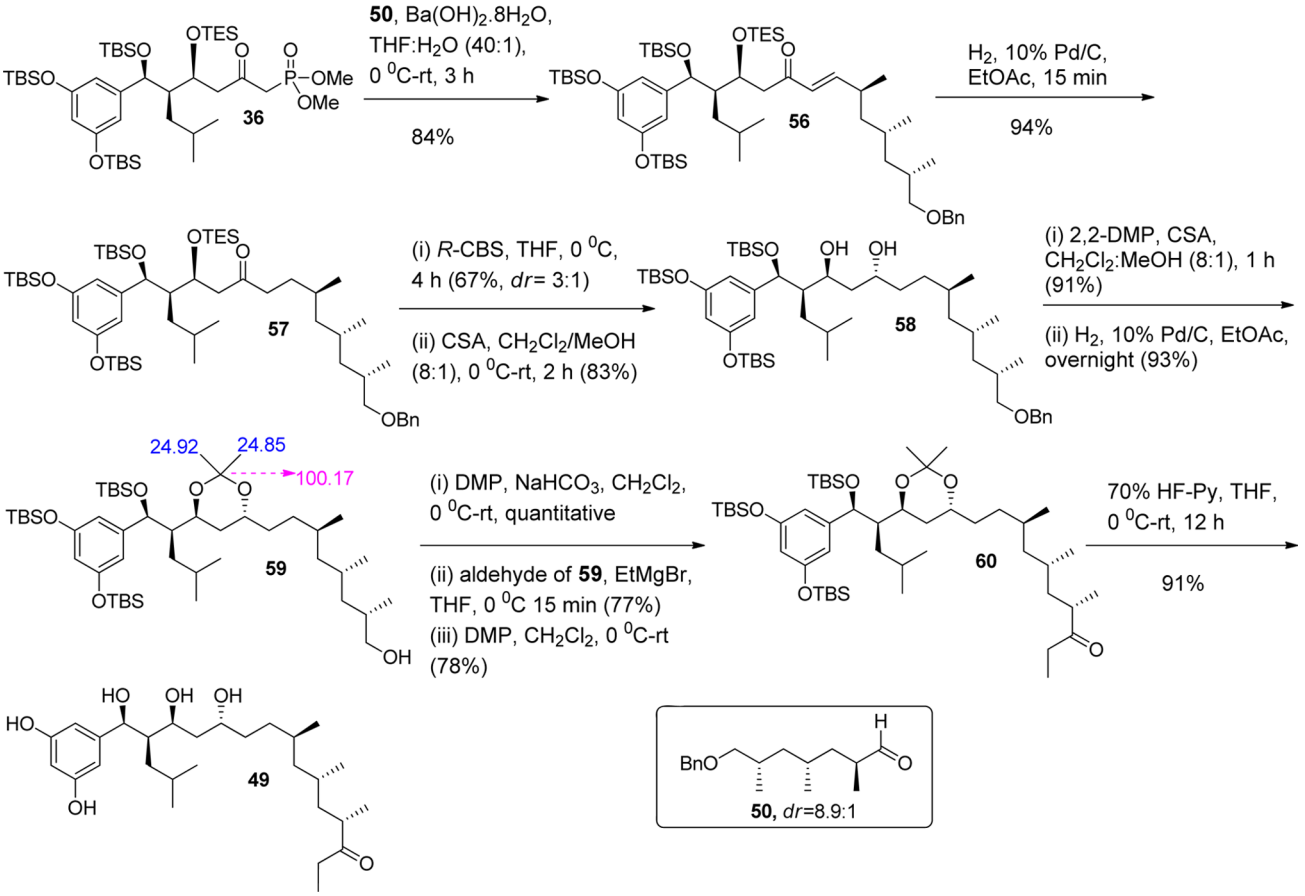
Scheme 10. Completion of Synthesis of Compound 49



projections of the different stereogenic centers of proposed structure of baulamycin A (**1**) have been constructed. Careful analysis of those Newman projections[5a] sketched by the isolation group revealed that the C-1′, C-14, C-13, and C-4 centers are not in accordance with the stereochemistry as documented. The reported Newman projections for C-1′, C-14, C-13, and C-4 centers are denoted I–IV (Figure 2), respectively, which indicate 1′*S*, 14*R*, 13*S*, and 4*S* configurations of those centers, respectively. The Newman projections (Figure 2) for the aforementioned chiral centers in the proposed structure of baulamycin A (**1**) might be changed accordingly: i.e. V (1′*R*), VI (14*S*), VII (13*R*), and VIII (4*R*). Although the orientations of the substituents around those chiral centers (C-1′, C-14, C-13, C-4) are different, the ROESY correlations and coupling constants ($^3J_{H,H}$, $^3J_{C,H}$, $^2J_{C,H}$) can be expected to be comparable to the reported Newman projections (I–IV), as the dihedral angles between the substituents are not likely to vary substantially. Thus, we portrayed compound **49** as our new synthetic target, which could be accessed from the key intermediates **36** and **50** by following the chemistry developed previously.

The synthetic endeavor of aldehyde **50** is depicted in Scheme 9. By a chemistry similar to that described earlier, the known compound **6** was oxidized using Swern conditions to give the corresponding aldehyde, which was subsequently subjected to HWE olefination[20] in the presence of the known phosphonate **51**,[21] derived from L-phenylalanine, to give compound **52**, which was converted finally to the partially epimerized aldehyde **50** (dr = 8.9:1, inseparable) in five steps via the intermediates **53**–**55**.

The completion of the total synthesis of compound **49** is shown in Scheme 10. Phosphonate **36** (Scheme 8) and aldehyde **50** (Scheme 9) were coupled together to produce compound **56**. Modification of our prior strategy for the conversion of compound **29** to compound **33** (Scheme 6) or the transformation of compound **45** to compound **46** (Scheme 8) was done at this stage to make the purification of the resulting intermediates easier. The olefin moiety of compound **56** was reduced regioselectively[28] to give compound **57** using 10% Pd/C; **57** was subsequently treated with (*R*)-Me-CBS[29] to yield an inseparable mixture of the corresponding products (dr = 3:1). The mixture of compounds was then subjected to TES deprotection to yield compound **58** as the major isomer along with its corresponding minor isomer, which were separated easily by column chromatography. The 1,3-diol compound **58** was then protected with 2,2-DMP and subsequently hydrogenated to give compound **59**. The ^{13}C NMR data (δ 100.17 (ketal), 24.92 and 24.85 (acetonide methyl) ppm)[16] clearly confirmed the represented structure. Finally, compound **59** was transformed to the targeted compound **49** through the intermediate **60** in good overall yield (55% in four steps) following a chemistry similar to that developed earlier. Both the ^{1}H and ^{13}C NMR data of compound **49** were recorded in CD_3OD. The specific rotation of synthesized **49** was in agreement (observed $[\alpha]^{29}_D$ −9.7 (*c* 0.9, MeOH)) with the literature value (reported $[\alpha]^{20}_D$ −10.3 (*c* 0.2, MeOH)). However, it was quite unfortunate that the spectroscopic data differ significantly (please see a comparison in Table S8 in the Supporting Information) from the reported values.[5a]

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CONCLUSION

In summary, a flexible and convergent synthetic route for the proposed structure of baulamycin A along with its congeners has been developed for the first time. The proposed structure of baulamycin A (**1**) was synthesized from the known compounds **7** and **8** in 17 linear longest steps with an overall yield of 6%. This synthetic study disclosed that the proposed structure of baulamycin A needs to be revised. We also have synthesized two other possible diastereomers to determine the original structure of baulamycin A. Unfortunately, none of the diastereomers were found to reproduce the spectral data recorded for the isolated compound. It is likely that the actual structure of the isolated molecule is a different diastereomer of the proposed structure. A conspicuously aberrant C1′H resonance at around δ 4.82 ppm in the synthesized molecule did not match the reported value (δ 4.47 ppm). It was observed that variation in relative stereochemistry of some of the methyl centers in the deoxypropionate chain of these molecules did not resolve this anomaly. We believe that the mismatch may result from uncertainty in the stereochemistry proposed for the polyhydroxy segment (left part) of the molecule. With the establishment of a synthetically viable route, further study is in progress in our laboratory to determine the actual chemical structure of isolated baulamycin A, which will be reported in due course.

EXPERIMENTAL SECTION

(*R*)-4-Benzyl-3-((*R*)-2-((*R*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)(hydroxy)methyl)-4-methylpentanoyl)oxazolidin-2-one (9). To an ice-cold solution of compound **8** (6.45 g, 23.43 mmol, 1 equiv) in anhydrous CH_2Cl_2 (60 mL) under argon was added dropwise freshly distilled $TiCl_4$ (2.84 mL, 25.77 mmol, 1.1 equiv) over 3 min. The yellow mixture was stirred for 5 min, and DIPEA (4.49 mL, 28.12 mmol, 1.2 equiv) was added over 3 min. The dark brownish solution was kept for 1 h at the same temperature before addition of NMP (2.26 mL, 23.43 mmol, 1.0 equiv), and the reaction mixture was stirred further for 15 min prior to cannulation of aldehyde **7** (8.64 g, 23.43 mmol, 1.1 equiv). The reaction was continued further for 45 min before quenching it with a saturated aqueous NH_4Cl solution (10 mL). The resultant mixture was extracted with CH_2Cl_2 (2 × 100 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by flash column chromatography (SiO_2, 100−200 mesh, 10% EtOAc in hexane as eluent) to afford compound **9** (14.28 g, 95%) as a yellowish liquid: R_f = 0.3 (20% EtOAc in hexane); $[\alpha]^{27}_D$ = −38.6 (*c* 3.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.19 (m, 5H), 6.53 (d, *J* = 2.1 Hz, 2H), 6.24 (t, *J* = 2.1 Hz, 1H), 4.83 (d, *J* = 3.0 Hz, 1H), 4.59−4.53 (m, 1H), 4.41−4.35 (m, 1H), 4.08 (dd, *J* = 2.3, 9.2 Hz, 1H), 4.01−3.95 (m, 1H), 3.30 (dd, *J* = 3.2, 13.4 Hz, 1H), 2.69 (dd, *J* = 9.9, 13.2 Hz, 1H), 2.47 (s, 1H), 1.97−1.89 (m, 1H), 1.49−1.35 (m, 2H), 0.97 (s, 18H), 0.87 (d, *J* = 6.0 Hz, 3H), 0.83 (d, *J* = 6.3 Hz, 3H), 0.19 (s, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.5, 156.6, 153.2, 143.7, 135.4, 129.5, 129.1, 127.5, 111.5, 111.2, 74.7, 66.0, 55.8, 48.3, 38.1, 35.7, 26.6, 25.9, 23.8, 22.0, 18.4, −4.3, −4.3 ppm; IR (neat) ν_{max} 3471, 2957, 1782, 1693, 1591, 1452, 1385, 1165 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{35}H_{55}O_6NSi_2Na$ [M + Na]$^+$ 664.3466, found 664.3469.

(*R*)-Methyl 2-((*R*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)(((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)oxy)methyl)-4-methylpentanoate (10a). To a solution of compound **9** (200 mg, 0.31 mmol, 1.0 equiv) in MeOH (3 mL) under argon was added NaOMe (0.29 mL, 1.56 mmol, 5.4 M in MeOH, 5.0 equiv), and the mixture was stirred overnight prior to quenching with pH 7 phosphate buffer solution (3 mL). The resultant mixture was extracted with EtOAc (2 × 15 mL), washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude reaction mixture was purified by flash column chromatography (silica gel, 60−120 mesh, 5% EtOAc in hexane as eluent) to give the corresponding ester (109 mg, 71%) as a colorless oil: R_f = 0.3 (5% EtOAc in hexane); $[\alpha]^{27}_D$ = +8.0 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.45 (d, *J* = 2.1 Hz, 2H), 6.24 (t, *J* = 2.1 Hz, 1H), 4.85−4.83 (m, 1H), 3.63 (s, 3H), 2.79 (d, *J* = 2.4 Hz, 1H), 2.75−2.69 (m, 1H), 1.75−1.66 (1H), 1.45−1.25 (m, 3H), 0.97 (s, 18H), 0.84 (d, *J* = 6.3 Hz, 3H), 0.77 (d, *J* = 6.3 Hz, 3H), 0.18 (s, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.0, 156.6, 143.8, 111.6, 111.5, 74.1, 51.8, 50.9, 35.6, 26.4, 25.9, 23.6, 21.6, 18.4, −4.2 ppm; IR (neat) ν_{max} 3501, 2958, 2931, 2860, 1739, 1592, 1455, 1333, 1260, 1164 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{48}O_5Si_2Na$ [M + Na]$^+$ 519.2937, found 519.2938.

To a solution of (*R*)-Mosher's acid (25 mg, 0.09 mmol, 3.0 equiv) in anhydrous toluene (0.5 mL) at room temperature under argon were added sequentially DMAP (12.8 mg, 0.11 mmol, 3.5 equiv), Et_3N (0.015 mL, 0.11 mmol, 3.5 equiv), and 2,4,6-trichlorobenzoyl chloride (0.014 mL, 0.09 mmol, 3.0 equiv). The white turbid mixture was stirred for 30 min prior to cannulation of the above ester (15 mg, 0.03 mmol, dissolved in 0.5 mL of anhydrous toluene, 1.0 equiv). The reaction mixture was stirred further for 3.5 h at same temperature and subsequently quenched with saturated aqueous NH_4Cl (0.5 mL). The resultant mixture was extracted with EtOAc (2 × 10 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (silica gel, 60−120 mesh, 5% EtOAc in hexane as eluent) gave (*R*)-MTPA ester **10a** (16.5 mg, 77%) as a yellowish oil: R_f = 0.5 (5% EtOAc in hexane); $[\alpha]^{29}_D$ = +27.8 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.44−7.29 (m, 5H), 6.46 (d, *J* = 2.1 Hz, 2H), 6.29 (t, *J* = 2.3 Hz, 1H), 5.95 (d, *J* = 8.7 Hz, 1H), 3.46 (s, 3H), 3.44 (s, 3H), 2.97−2.89 (m, 1H), 1.66−1.60 (m, 1H), 1.39−1.36 (m, 1H), 1.17−1.08 (m, 1H), 0.96 (s, 18H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.72 (d, *J* = 6.3 Hz, 3H), 0.16 (s, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7, 165.8, 156.7, 138.9, 132.5, 129.7, 128.5, 127.7, 127.5, 125.4, 112.9, 112.5, 78.4, 51.8, 49.9, 37.8, 26.2, 25.8, 23.6, 21.3, 18.4, −4.3, −4.3 ppm; IR (neat) ν_{max} 2956, 2931, 2859, 1752, 1593, 1456, 1254, 1168, cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{36}H_{55}O_7NF_3Si_2Na$ [M + Na]$^+$ 735.3336, found 735.3338.

(*R*)-Methyl 2-((*R*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)-phenyl)(((*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)-oxy)methyl)-4-methylpentanoate (10b). Following the same experimental procedure as described in the preparation of compound **10a**, the above ester (15 mg) was converted to the (*S*)-MTPA ester **10b** (16.7 mg, 78%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) as a yellowish oil. R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{29}_D$ = +10.0 (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43−7.31 (m, 5H), 6.35 (d, *J* = 2.1 Hz, 2H), 6.26 (t, *J* = 2.1 Hz, 1H), 5.95 (d, *J* = 7.8 Hz, 1H), 3.50 (s, 3H), 3.48 (s, 3H), 2.97−2.89 (m, 1H), 1.78−1.69 (m, 1H), 1.52−1.43 (m, 1H), 1.33−1.26 (m, 1H), 0.95 (s, 18H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.79 (d, *J* = 6.3 Hz, 3H), 0.15 (s, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.8, 165.6, 156.6, 139.0, 132.0, 129.7, 128.5, 127.7, 125.4, 112.7, 112.5, 78.8, 55.6, 51.8, 50.0, 37.5, 26.3, 25.8, 23.6, 21.4, 18.4, −4.3, −4.4 ppm; IR (neat) ν_{max} 2956, 2931, 2859, 1751, 1594, 1455, 1254, 1168 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{36}H_{55}O_7NF_3Si_2Na$ [M + Na]$^+$ 735.3336, found 735.3337.

(*S*)-2-((*R*)-(3,5-bis((*tert*-Butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-4-methylpentan-1-ol (5). To an ice-cold solution of compound **9** (12.13 g, 18.91 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (40 mL) under argon was added 2,6-lutidine (4.13 mL, 37.83 mmol, 2.0 equiv). The reaction mixture was stirred for 10 min, and TBSOTf (5.21 mL, 22.68 mmol, 1.2 equiv) was then added. The reaction was continued at the same temperature for 45 min and subsequently quenched by a saturated aqueous solution of $NaHCO_3$ (15 mL). The resultant mixture was extracted with EtOAc (2 × 200 mL), washed with aqueous $CuSO_4$, water, and brine, dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 1.0−1.5% EtOAc in hexane as eluent) furnished the corresponding TBS-protected compound (13.73 g, 96%) as a yellowish liquid: R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{30}_D$ = −38.1 (*c* 8.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz); δ 7.33−7.22 (m, 3H), 7.19−7.16 (m, 2H), 6.47 (d, *J* = 2.1

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J. Org. Chem. 2017, 82, 2414−2435

Hz, 2H), 6.19 (t, J = 2.3 Hz, 1H), 4.63 (d, J = 6.6 Hz, 1H), 4.33−4.20 (m, 2H), 3.97 (dd, J = 1.8, 9 Hz, 1H), 3.75−3.70 (m, 1H), 3.22 (dd, J = 3.2, 13.4 Hz, 1H), 2.68 (dd, J = 9.8, 13.4 Hz, 1H), 2.01−1.88 (m, 1H), 1.55−1.47 (m, 2H), 0.95 (s, 18H), 0.91−0.87 (m, 15H), 0.17 (s, 12H), 0.01 (s, 3H), −0.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.4, 156.3, 152.9, 144.9, 135.6, 129.5, 129.0, 127.3, 111.8, 111.4, 76.9, 65.9, 56.1, 50.3, 38.0, 37.3, 26.7, 25.9, 25.8, 23.9, 22.1, 18.3, 18.2, −4.3, −4.3, −4.5, −5.2 ppm; IR (neat) ν_{max} 2956, 2928, 1781, 1593, 1453, 1257, 1165 cm^{-1}; 2926, 1709, 1454, 1217 cm^{-1}; HRMS (ESI) m/z calcd for $C_{41}H_{69}O_6NSi_3Na$ $[M + Na]^+$ 778.4330, found 778.4331.

To an ice-cold solution of the above TBS-protected compound (13.23 g, 17.19 mmol, 1.1 equiv) in anhydrous THF (30 mL) moistened with a catalytic amount of water was added $LiBH_4$ (750 mg, 34.38 mmol, 2.0 equiv) portionwise over 5 min under argon. After 1 h of stirring at the same temperature, the reaction mixture was quenched cautiously with saturated NH_4Cl solution (10 mL), extracted with EtOAc (2 × 150 mL), washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 6% EtOAc in hexane as eluent) provided pure compound **5** (9.08 g, 89%) as a colorless liquid: R_f = 0.3 (5% EtOAc in hexane); $[\alpha]^{28}_D$ = +9.3 (c 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (d, J = 2.4 Hz, 2H), 6.25 (t, J = 2.3 Hz, 1H), 4.74 (d, J = 4.2 Hz, 1H), 3.61−3.45 (m, 2H), 2.75 (s, 1H), 2.04−1.95 (m, 1H), 1.65−1.49 (m, 2H), 1.12−1.02 (m, 1H), 0.97 (s, 18H), 0.91 (s, 9H), 0.86 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H), 0.18 (s, 6H), 0.17 (s, 6H), 0.06 (s, 3H), −0.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.3, 144.2, 112.4, 111.5, 77.8, 63.8, 45.3, 36.2, 26.0, 25.9, 25.7, 23.6, 22.3, 18.4, 18.2, −4.2, −4.2, −4.5, −5.2 ppm; IR (neat) ν_{max} 3462, 2957, 2930, 1591, 1472, 124, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{31}H_{62}O_4Si_3Na$ $[M + Na]^+$ 605.3854, found 605.3856.

(3*R*,4*S*)-1-((*S*)-4-Benzyl-2-thioxothiazolidin-3-yl)-4-((*R*)-(3,5-bis((*tert*-butyldimethylsilyl) oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-3-hydroxy-6-methylheptan-1-one (12). To a stirred solution of $(COCl)_2$ (0.3 mL, 3.37 mmol, 1.5 equiv) in anhydrous CH_2Cl_2 (12 mL) under argon at −78 °C was added DMSO (0.48 mL, 6.75 mmol, 3.0 equiv) dropwise over 2 min. After 15 min, a solution of compound **5** (1.31 g, 2.25 mmol, dissolved in 5 mL of anhydrous CH_2Cl_2, 1.0 equiv) was cannulated into the reaction mixture and stirred further for 30 min at the same temperature. Et_3N (1.56 mL, 11.25 mmol, 5.0 equiv) was then added and stirred further for 15 min at the same temperature. The reaction mixture was then warmed to 0 °C and quenched with a saturated aqueous solution of NH_4Cl (5 mL). The resultant mixture was extracted with CH_2Cl_2 (2 × 50 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Flash chromatography of the crude residue using a short pad of silica gave the corresponding aldehyde (1.3 g, quantitative) as a colorless liquid, which was taken for the next step without further characterization.

To a solution of thiazolidinethione **11** (673 mg, 2.68 mmol, 1.2 equiv) in anhydrous CH_2Cl_2 (10 mL) at −40 °C under argon, freshly distilled $TiCl_4$ (0.31 mL, 2.79 mmol, 1.25 equiv) was added dropwise over 1 min. The yellowish slurry was stirred for 5 min at the same temperature, and DIPEA (0.49 mL, 2.79 mmol, 1.25 equiv) was added over 1 min. The resultant deep reddish solution was stirred further for another 1 h at the same temperature and then cooled to −78 °C. The aldehyde (1.3 g, 2.23 mmol, dissolved in 6 mL of anhydrous CH_2Cl_2, 1.0 equiv) from the previous step was cannulated into the reaction mixture and stirred further for 30 min at the same temperature before quenching with saturated aqueous NH_4Cl (5 mL). The resultant mixture was extracted with EtOAc (2 × 50 mL), washed with water and brine, dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 230−400 mesh, 5−8% EtOAc in hexane as eluent) yielded the major diastereomer **12** (1.07 g, 57%, dr = 5:1) as a yellow oil: R_f = 0.3 (5% EtOAc in hexane); $[\alpha]^{27}_D$ = +5.8 (c 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36−7.28 (m, 5H), 6.46 (d, J = 2.4 Hz, 2H), 6.24 (t, J = 2.1 Hz, 1H), 5.39−5.34 (m, 1H), 4.70 (d, J = 6.0 Hz, 1H), 4.22−4.17 (m, 1H), 3.40−3.34 (m, 3H), 3.16 (dd, J = 3.6, 13.2 Hz, 1H), 3.01 (dd, J = 10.5, 12.9 Hz, 1H), 2.86 (d, J = 11.4 Hz, 1H), 1.66−1.64 (m, 1H), 1.48−1.31 (m, 3H), 0.98 (s, 18H), 0.90 (s, 9H), 0.85 (d, J = 6.0 Hz, 3H), 0.79 (d, J = 6.0 Hz, 3H), 0.18 (s, 12H), 0.08 (s, 3H), −0.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.3, 172.9, 156.4, 146.3, 136.7, 129.6, 129.0, 127.4, 112.2, 111.5, 78.2, 69.1, 68.5, 48.9, 44.8, 36.9, 33.7, 32.0, 27.7, 26.1, 25.9, 23.1, 23.0, 18.4, 18.2, −4.2, −4.2, −4.8 ppm; IR (neat) ν_{max} 3545, 2956, 2931, 2857, 1699, 1591, 1455, 1341, 1258, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{43}H_{73}NO_5Si_3S_2Na$ $[M + Na]^+$ 854.4136, found 854.4134.

2-((4*R*,5*S*,6*R*)-6-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-5-isobutyl-2,2-dimethyl-1,3-dioxan-4-yl)ethyl Pivalate (13). To an ice-cold solution of compound **12** (300 mg, 0.36 mmol, 1.0 equiv) in anhydrous THF/MeOH (1/1, 3 mL) under argon was added $NaBH_4$ (28 mg, 0.72 mmol, 2.0 equiv). The reaction mixture was warmed slowly to room temperature and stirred further for 6 h at the same temperature. The reaction mixture was cooled to 0 °C prior to quenching with a saturated NH_4Cl solution (1 mL). The resultant mixture was extracted with EtOAc (2 × 30 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 20% EtOAc in hexane as eluent) provided the corresponding diol (180 mg, 78%) as a colorless liquid: R_f = 0.3 (30% EtOAc in hexane); $[\alpha]^{29}_D$ = +18.0 (c 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.44 (d, J = 2.4 Hz, 2H), 6.23 (t, J = 2.3 Hz, 1H), 4.74 (d, J = 4.2 Hz, 1H), 4.12 (d, J = 9.3 Hz, 1H), 3.81−3.77 (m, 2H), 2.42 (s, 1H), 1.93−1.80 (m, 1H), 1.58−1.56 (m, 1H), 1.50−1.34 (m, 2H), 1.32−1.24 (m, 2H), 0.97 (s, 18 H), 0.92 (s, 9H), 0.80 (d, J = 5.7 Hz, 3H), 0.74 (d, J = 5.7 Hz, 3H), 0.17 (s, 12H), 0.07 (s, 3H), −0.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.6, 145.7, 111.7, 111.5, 77.8, 74.2, 62.6, 49.4, 37.0, 32.5, 27.0, 26.1, 25.8, 23.3, 22.5, 18.4, 18.2, −4.2, −4.3, −5.0 ppm; IR (neat) ν_{max} 3401, 2956, 2931, 2859, 1591, 1451, 1254, 1162 cm^{-1}; HRMS (ESI) m/z calcd for $C_{33}H_{66}O_5Si_3Na$ $[M + Na]^+$ 649.4116, found 649.4118.

To an ice-cold solution of the above diol (280 mg, 0.45 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (3 mL) under argon were added Et_3N (0.07 mL, 0.50 mmol, 1.1 equiv), PivCl (0.07 mL, 0.5 mmol, 1.1 equiv), and DMAP (4 mg, 0.02 mmol, 0.05 equiv) sequentially. The reaction mixture was warmed slowly to room temperature and stirred further for 2 h before quenching it with a saturated aqueous solution of NH_4Cl (1 mL). The resultant mixture was extracted with CH_2Cl_2 (2 × 15 mL), washed with water and brine, dried over Na_2SO_4, and evaporated under reduced pressure. Flash column chromatographic purification (SiO_2, 100−200 mesh, 15% EtOAc in hexane as eluent) of the crude residue gave the corresponding pivolyl-protected compound (260 mg, 82%) as a colorless oil: R_f = 0.4 (20% EtOAc in hexane); $[\alpha]^{29}_D$ = +20.9 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.43 (d, J = 1.5 Hz, 2H), 6.21 (t, J = 1.7 Hz, 1H), 4.69 (d, J = 3.6 Hz, 1H), 4.25−4.18 (m, 1H), 4.13−4.08 m, 1H), 3.88 (d, J = 7.2 Hz, 1H), 2.11 (d, J = 1.8 Hz, 1H), 1.82−1.74 (m, 1H), 1.60−1.58 (m, 2H), 1.43−1.32 (m, 2H), 1.26−1.22 (m, 1H), 1.17 (s, 9H), 0.97 (s, 18H), 0.90 (s, 9H), 0.81 (d, J = 4.5 Hz, 3H), 0.78 (d, J = 4.5 Hz, 3H), 0.17 (s, 12H), 0.05 (s, 3H), −0.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.9, 156.6, 146.0, 111.9, 111.4, 77.6, 69.1, 61.9, 49.3, 38.9, 34.7, 33.1, 27.4, 27.1, 26.1, 25.8, 23.3, 22.6, 18.4, 18.2, −4.2, −4.2, −4.3, −4.9 ppm; IR (neat) ν_{max} 3427, 2957, 2930, 1732, 1916, 1452, 1254, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{38}H_{74}Si_3O_6Na$ $[M + Na]^+$ 733.4691, found 733.4692.

To an ice-cold solution of the above pivolyl-protected compound (105 mg, 0.15 mmol, 1.0 equiv) in CH_2Cl_2/MeOH (1/1, 2 mL) was added CSA (4 mg, 0.002 mmol, 0.01 equiv). The reaction mixture was slowly warmed to room temperature and stirred further for 1 h prior to quenching with Et_3N (2.5 μL, 0.11 equiv). The resultant mixture was concentrated in vacuo and purified by flash column chromatography (SiO_2, 100−200 mesh, 15−25% EtOAc in hexane as eluent) to obtain the corresponding diol compound (67 mg, 76%) as a colorless liquid: R_f = 0.4 (30% EtOAc in hexane); $[\alpha]^{29}_D$ = +11.5 (c 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.46 (d, J = 2.1 Hz, 2H), 6.21 (t, J = 2.1 Hz, 1H), 4.93 (s, 1H), 4.42−4.34 (m, 1H), 4.18−4.11 (m, 1H), 4.01 (d, J = 9.6 Hz, 1H), 3.06 (d, J = 3 Hz, 1H), 2.90 (d, J = 1.8 Hz, 1H), 1.92−1.72 (m, 2H), 1.63−1.62 (m, 1H), 1.44−1.36 (m, 1H), 1.29−1.24 (m, 1H), 1.22 (s, 9H), 1.11−1.04 (m, 1H), 0.97 (s, 18H), 0.74 (d,

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J = 6.3 Hz, 3H), 0.56 (d, J = 6.6 Hz, 3H), 0.18 (s, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.4, 156.6, 145.9, 111.1, 111.0, 77.8, 72.9, 62.0, 47.7, 39.0, 34.7, 30.6, 27.4, 27.4, 25.9, 22.8, 22.7, 18.4, −4.2 ppm; IR (neat) ν_{max} 3460, 2957, 2932,2860, 1730, 1591, 1448, 1254, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{32}H_{60}O_6Si_2Na$ [M + Na]$^+$ 619.3826, found 619.3828.

To an ice-cold solution of the above diol compound (30 mg, 0.05 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (1 mL) under argon were added 2,2-DMP (0.02 mL, 0.08 mmol, 1.6 equiv) and CSA (1 mg, 0.01 mmol, 0.1 equiv) sequentially. The reaction mixture was warmed slowly to room temperature and stirred further for 1 h before quenching by Et_3N (0.8 μL, 0.11 equiv). The mixture was concentrated in vacuo and purified by flash column chromatography (SiO_2, 60−120 mesh, 2% EtOAc in hexane as eluent) to provide the corresponding acetonide compound (30 mg, 94%) as a colorless oil: R_f = 0.4 (2% EtOAc in hexane); $[\alpha]^{27}_D$ = +11.2 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.43 (d, J = 2.0 Hz, 2H), 6.20 (t, J = 2.3 Hz, 1H), 4.93 (d, J = 2.0 Hz, 1H), 4.19−4.16 (m, 3H), 1.88−1.82 (m, 1H), 1.74−1.68 (m, 1H), 1.46 (s, 3H), 1.45 (s, 3H), 1.42 (m, 1H), 1.23 (s, 9H), 1.21−1.17 (m, 2H), 0.97 (s, 18H), 0.89−0.84 (m, 1H), 0.69 (d, J = 6.5 Hz, 3H), 0.45 (d, J = 6.5 Hz, 3H), 0.18 (s, 6H) 0.17 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 178.7, 156.5, 143.3, 111.1, 110.7, 99.4, 75.1, 70.6, 61.4, 41.7, 38.9, 32.6, 30.4, 30.0, 27.6, 27.4, 25.9, 22.9, 22.6, 19.6, 18.4, −4.2, −4.2 ppm; IR (neat) ν_{max} 2957, 2932, 1732, 1591, 1452, 1256, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{35}H_{64}O_6Si_2Na$ [M + Na]$^+$ 659.4139, found 659.4137.

To a solution of the above acetonide-protected compound (20 mg, 0.031 mmol, 1.2 equiv) in anhydrous CH_2Cl_2 (2 mL) at −78 °C under argon was added DIBAL-H (0.1 mL, 0.1 mmol, 1.0 M in toluene, 3.0 equiv) dropwise over 3 min. The reaction was continued for 15 min and then quenched by MeOH (0.2 mL) at the same temperature. A saturated solution of sodium−potassium tartrate (2 mL) was added to it and stirred further until the two layers (organic and aqueous) separated well at room temperature. The resultant mixture was extracted with EtOAc (2 × 5 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 8% EtOAc in hexane as eluent) yielded compound **13** (15 mg, 85%) as a colorless oil: R_f = 0.2 (10% EtOAc in hexane); $[\alpha]^{27}_D$ = +8.6 (c 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.42 (d, J = 2.1 Hz, 2H), 6.20 (t, J = 2.1 Hz, 1H), 4.97 (d, J = 1.3 Hz, 1H), 4.31 (dt, J = 2.0, 10.1 Hz, 1H), 3.80 (m, 2H), 2.39 (m, 1H), 1.93 (dddd, J = 4.3, 8.2, 10.5, 14.1 Hz, 1H), 1.58 (m, 1H), 1.52 (s, 3H), 1.48 (s, 3H), 1.44 (m, 1H), 1.24 (m, 1H), 1.15 (ddd, J = 4.3, 7.2, 14.2 Hz, 1H), 0.97(s, 18H), 0.88 (m, 1H), 0.70 (d, J = 6.3 Hz, 3H), 0.45 (d, J = 6.3 Hz, 3H), 0.18 (s, 6H) 0.17 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.5, 143.1, 111.0, 110.7, 99.5, 75.0, 74.6, 62.0, 41.9, 35.6, 30.5, 30.1, 27.7, 25.9, 22.9, 22.6, 19.9, 18.4−4.2, −4.2 ppm; IR (neat) ν_{max} 3375, 2958, 2927, 1478, 1233, 1142 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{56}O_5Si_2Na$ [M + Na]$^+$ 575.3564, found 575.3562.

(5*R*,6*S*)-6-((*R*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-((*tert*-butyldimethylsilyl)oxy)methyl)-8-methyl-5-((triethylsilyl)oxy)non-1-en-3-ol (15a,b). To an ice-cold solution of compound **12** (3.2 g, 3.84 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (10 mL) under argon were added 2,6-lutidine (0.84 mL, 7.69 mmol, 2.0 equiv) and TESOTf (1.74 mL, 7.68 mmol, 1.1 equiv) sequentially. The reaction was continued for 30 min at the same temperature prior to quenching with a saturated solution of $NaHCO_3$ (4 mL). The resultant mixture was extracted with CH_2Cl_2 (2 × 50 mL), washed with aqueous $CuSO_4$, water, and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 1−2% EtOAc in hexane as eluent) afforded the corresponding TES-protected compound (3.38 g, 93%) as a light yellow oil: R_f = 0.6 (3% EtOAc in hexane); $[\alpha]^{28}_D$ = +46.5 (c 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38−7.28 (m, 5H), 6.40 (d, J = 2.4 Hz, 2H), 6.20 (t, J = 2.1 Hz, 1H), 5.24−5.18 (m, 1H), 4.85 (d, J = 4.5 Hz, 1H), 4.39−4.33 (m, 1H), 3.56−3.22 (m, 4H), 3.07−2.99 (m, 1H), 2.87 (d, J = 11.7 Hz, 1H), 1.84−1.77 (m,1H), 1.59−1.50 (m, 1H), 1.34−1.29 (m, 2H), 0.99−0.93 (m, 27H), 0.90 (s, 9H), 0.84 (d, J = 6.6 Hz, 3H), 0.74 (d, J = 6.3 Hz, 3H), 0.62 (q, J = 7.9 Hz, 6H), 0.17 (s, 12H), 0.05 (s, 3H), −0.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.6, 173.0, 156.1, 147.9, 136.9, 129.6, 129.1, 127.3, 112.6, 111.0, 74.2, 69.5, 69.0, 49.9, 44.0, 36.5, 34.4, 32.3, 29.9, 26.4, 26.4, 25.9, 23.6, 22.9, 22.4, 18.4, 7.3, 5.5, −4.1, −4.2, −4.3 ppm; IR (neat) ν_{max} 2955, 2858, 1697, 1591, 1454, 1258, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{49}H_{87}O_5Si_4S_2NNa$ [M + Na]$^+$ 968.5000, found 968.5004.

To a solution of the above TES-protected compound (3.07 g, 3.24 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (9 mL) at −78 °C under argon was added DIBAL-H (6.49 mL, 6.49 mmol, 1.0 M in toluene, 2.0 equiv) dropwise over 10 min. The reaction was then quenched by MeOH (2 mL). A saturated solution of sodium−potassium tartrate (6 mL) was added to it and stirred further until the two layers (organic and aqueous) separated well. The resultant mixture was extracted with EtOAc (2 × 50 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Flash column chromatography (SiO_2, 60−120, 5−6% EtOAc in hexane as eluent) of the crude residue provided aldehyde **14** (1.92 g, 80%) as a yellow liquid, which was taken for the next step without further characterization.

To a solution of aldehyde **14** (1.91 g, 2.58 mmol, 1.0 equiv) in anhydrous THF (10 mL) at −78 °C under argon was added vinylmagnesium bromide (3.87 mL, 3.87 mmol, 1.0 M in THF, 1.5 equiv) slowly over 5 min. The reaction mixture was stirred for 15 min at the same temperature and subsequently quenched by a saturated aqueous solution of NH_4Cl (2 mL). The resultant mixture was extracted with EtOAc (2 × 50 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 230−400 mesh, 2% EtOAc in hexane as eluent) provided an inseparable mixture of compounds **15a,b** (1.52 g, 77%) as a colorless liquid with dr = 5:4: R_f = 0.5 (5% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 300 MHz, major peaks are mentioned) δ 6.42−6.40 (d, 2H), 6.19−6.17(m, 1H), 5.93−5.77 (m, 1H), 5.29−5.19 (m, 1H), 4.09−4.99 (m, 1H), 4.34−4.31 (m, 1H), 4.22−4.16 (m, 1H), 4.05−3.96 (m, 1H), 2.97 (s, 1H), 2.09−1.86 (m, 1H), 1.77−1.63 (m, 2H), 1.42−1.18 (m, 3H), 1.05−0.97 (m, 27H), 0.91 (m, 9H), 0.81−0.78 (m, 3H), 0.75−0.61 (m, 9H), 0.17 (s, 6H), 0.16 (s, 6H), 0.10 (s, 3H), −0.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, diastereomer peaks are given in parentheses) δ 156.1(156.1), 148.1(147.9), 142.0, 141.1(141.1), 114.1(113.8), 112.3(112.2), 110.9(110.8), 74.0, 72.8(72.5), 70.8(70.1), 49.9(49.4), 40.1(39.6), 33.5(33.5), 26.3(26.3), 25.8, 23.9(23.8), 22.1, 18.4(18.2), 7.2(7.2), 5.6(5.5), −3.8(−3.8), −4.2(−4.3), −4.5(4.6) ppm; IR (neat) ν_{max} 2955, 2931, 2858, 1591, 1466, 1448, 1256, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{41}H_{82}O_5Si_4Na$ [M + Na]$^+$ 789.5137, found 789.5135.

(5*R*,6*S*)-6-((*R*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-((*tert*-butyldimethylsilyl)oxy)methyl)-8-methylnon-1-ene-3,5-diol (16). To an ice-cold solution of compounds **15a,b** (120 mg, 0.17 mmol, 1.0 equiv) in CH_2Cl_2/MeOH (8/1, 1 mL) was added CSA (1 mg, 0.003 mmol, 0.02 equiv). The reaction was continued for 1 h at room temperature and subsequently quenched with Et_3N (2.6 μL, 0.11 equiv). The resultant mixture was concentrated in vacuo and subjected to purification by flash column chromatography (SiO_2, 230−400 mesh, 5−6% EtOAc in hexane as eluent) to obtain compound **16** (83 mg, 81%) as a colorless oil: R_f = 0.2 (10% EtOAc in hexane); $[\alpha]^{29}_D$ = +13.3 (c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.44 (d, J = 2.1 Hz, 2H), 6.23 (t, J = 2.1 Hz, 1H), 5.91−5.80 (m, 1H), 5.28−5.22 (m, 1H), 5.10−5.05 (m, 1H), 4.73 (d, J = 1.5 Hz, 1H), 4.34−4.30 (m, 1H), 4.13 (d, J = 10.8 Hz, 1H), 3.46 (s, 1H), 2.65 (s, 1H), 1.81−1.69 (m, 1H), 1.46−1.23 (m, 5H), 0.97 (s, 18H), 0.91 (s, 9H), 0.80 (d, J = 5.7 Hz, 3H), 0.75 (d, J = 5.7 Hz, 3H), 0.17 (s, 12H), 0.07 (s, 3H), −0.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.6, 145.8, 140.9, 114.3, 111.8, 111.5, 77.6, 74.1, 73.8, 49.6, 41.8, 32.7, 27.1, 26.1, 25.8, 23.2, 22.6, 18.4, 18.2, −4.2, −4.3, −5.0 ppm; IR (neat) ν_{max} 2955, 2932, 2858, 1591, 1448, 1256, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{35}H_{68}O_5Si_3Na$ [M + Na]$^+$ 675.4272, found 675.4274.

((5-((1*R*,2*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-((4*R*,6*S*)-2,2-dimethyl-6-vinyl-1,3-dioxan-4-yl)-4-methylpentyl)-1,3-phenylene)bis(oxy))bis(*tert*-butyldimethylsilane) (3). Following the same synthetic procedure as for compound **13**, compound **16** (70 mg) was converted to compound **3** (68 mg, 91%, purification by flash

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column chromatography, SiO_2, 60−120 mesh, 2−3% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.7 (4% EtOAc in hexane); $[\alpha]^{27}_D$ = +17.4 (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 6.40 (d, *J* = 2.1 Hz, 2H), 6.21 (t, *J* = 2.3 Hz, 1H), 5.85−5.74 (m, 1H), 5.23−5.07 (m, 2H), 4.57 (d, *J* = 6.3 Hz, 1H), 4.20−4.13 (m, 1H), 3.66−3.61 (m, 1H), 1.64−1.60 (m, 1H), 1.55−1.40 (m, 3H), 1.38 (s, 3H), 1.35−1.34 (m, 2H), 1.30 (s, 3H), 0.97 (s, 18H), 0.87 (s, 9H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.17 (s, 12H), 0.04 (s, 3H), −0.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.1, 147.0, 139.2, 115.3, 112.6, 110.9, 98.6, 75.9, 70.7, 69.0, 49.6, 34.9, 34.7, 30.3, 27.8, 26.1, 25.9, 23.1, 22.9, 19.8, 18.4, 18.3, −4.1, −4.1, −4.2, −4.6 ppm; IR (neat) ν_{max} 2955, 2932, 2858, 1591, 1448, 1256, 1161 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{38}H_{72}O_5Si_3Na$ $[M + Na]^+$ 715.4586, found 715.4589.

(*R*)-4-Benzyl-3-((4*S*,6*S*,*E*)-7-((*tert*-butyldiphenylsilyl)oxy)-4,6-dimethylhept-2-enoyl)oxazolidin-2-one (17). Following the same Swern oxidation conditions as described in the preparation of compound **12**, alcohol **6** (4.26 g) was transformed to the corresponding aldehyde **17** (4.23 g, quantitative, purified by flash column chromatography using a short pad of 60−120 silica, 5−6% EtOAc in hexane as eluent) as a yellowish liquid which was taken for the next step: R_f = 0.7 (5% EtOAc in hexane); $[\alpha]^{29}_D$ = 0.3 (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.60 (d, *J* = 1.8 Hz, 1H), 7.66 (dd, *J* = 1.7, 7.7, Hz, 4H), 7.46−7.36 (m, 6H), 3.51 (d, *J* = 5.7 Hz, 2H), 2.43−2.36 (m, 1H), 1.82−1.69 (m, 1H), 1.58−1.38 (m, 2H), 1.07−1.05 (m, 12H), 0.92 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 205.4, 135.8, 134.0, 129.8, 127.8, 69.0, 44.3, 34.1, 33.4, 27.0, 19.5, 16.7, 13.6 ppm; IR (neat) ν_{max} 2927, 2852, 1731, 1458, 1110 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{32}O_2SiNa$ $[M + Na]^+$ 391.2069, found 391.2067.

(*R*)-4-Benzyl-3-((4*R*,6*S*)-7-((*tert*-butyldiphenylsilyl)oxy)-4,6-dimethylheptanoyl)oxazolidin-2-one (19). To a stirred suspension of activated LiCl (1.94 g, 45.80 mmol, 4.0 equiv) in anhydrous CH_3CN (40 mL) under argon at room temperature were added phosphonate **18** (4.48 g, 12.60 mmol, 1.1 equiv) and DIPEA (1.92 mL, 11.48 mmol, 1.0 equiv) sequentially, and the mixture was stirred for 30 min prior to cannulation of the above aldehyde **17** (4.23 g, 11.48 mmol, dissolved in 15 mL of anhydrous CH_3CN, 1.0 equiv). The reaction was continued further for 24 h at the same temperature and the mixture diluted with water (10 mL). The resultant mixture was extracted with EtOAc (2 × 100 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Flash column chromatography (SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) purification of the crude residue provided the coupled product (5.2 g, 79%) as a colorless liquid: R_f = 0.5 (5% EtOAc in hexane); $[\alpha]^{29}_D$ = −13.0 (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.68−7.65 (m, 4H), 7.43−7.07 (m, 13H), 4.75−4.70 (m, 1H), 4.23−4.14 (m, 2H), 3.56−3.44 (m, 2H), 3.35 (dd, *J* = 3.2, 13.4 Hz, 1H), 2.79 (dd, *J* = 9.6, 13.5 Hz, 1H), 2.50−2.41 (m, 1H), 1.79−1.69 (m, 1H), 1.55−1.48 (m, 1H), 1.23−1.18 (m, 1H), 1.06−1.03 (m, 12H), 0.94 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.5, 157.7, 153.6, 135.8, 135.6, 134.1, 129.7, 129.6, 129.1, 127.8, 127.5, 118.5, 68.8, 66.3, 55.5, 39.6, 38.1, 38.1, 34.7, 33.5, 27.1, 19.5, 17.2 ppm; IR (neat) ν_{max} 2962, 2930, 1778, 1677, 1353, 1215 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{35}H_{43}O_4SiNNa$ $[M + Na]^+$ 592.2859 found 592.2858.

To a stirred solution of the above coupled product (3.52 g, 6.18 mmol, 1.0 equiv) in EtOAc (10 mL) was added 10% Pd/C (360 mg) under a hydrogen atmosphere (balloon) at room temperature and stirred overnight. The reaction mixture was then filtered using a short bed of Celite and washed with EtOAc (3 × 15 mL). The combined organic layers were concentrated under reduced pressure and purified by flash column chromatography (SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) to provide compound **19** (3.28 g, 93%) as a colorless oil: R_f = 0.5 (5% EtOAc in hexane); $[\alpha]^{29}_D$ = −18.6 (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.69−7.66 (m, 4H), 7.42−7.20 (m, 11H), 4.71−4.61 (m, 1H), 4.22−4.13 (m, 2H), 3.55−3.40 (m, 2H), 3.30 (dd, *J* = 3.3, 13.5 Hz, 1H), 2.97−2.90 (m, 2H), 2.76 (dd, *J* = 9.6, 13.2, 1H), 1.82−1.62 (m, 2H), 1.55−1.40 (m, 2H), 1.34−1.22 (m, 2H), 1.06 (s, 9H), 0.91−0.88 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.8, 153.6, 135.8, 135.5, 134.3, 129.6, 129.6, 129.1, 127.7, 127.5, 69.6, 66.3, 55.3, 40.6, 38.1, 33.5, 33.4, 32.3, 29.9, 27.0, 19.5, 19.3, 16.8 ppm; IR (neat) ν_{max} 2957, 2930, 1784, 1699, 1387, 1211 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{35}H_{45}O_4SiNNa$ $[M + Na]^+$ 594.3016 found 594.3018.

(*R*)-4-Benzyl-3-((2*R*,4*S*,6*S*)-7-((*tert*-butyldiphenylsilyl)oxy)-2,4,6-trimethylheptanoyl)oxazolidin-2-one (20). To a stirred solution of compound **19** (3.1 g, 5.43 mmol, 1.0 equiv) in anhydrous THF (15 mL) at −78 °C under argon was added NaHMDS (8.12 mL, 8.12 mmol 1.0 M solution in THF, 1.5 equiv) dropwise over 10 min. After 30 min freshly distilled MeI (1.1 mL, 16.29 mmol, 3.0 equiv) was added and the reaction mixture was stirred further for 3.5 h at the same temperature. The reaction was quenched with saturated NH_4Cl solution (5 mL) and warmed to room temperature before extracting with EtOAc (2 × 50 mL). The combined organic extracts were washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) provided compound **20** (2.15 g, 68%) as a colorless oil: R_f = 0.4 (10% EtOAc in hexane); $[\alpha]^{29}_D$ = −30.8 (*c* 5.6, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.70−7.67 (m, 4H), 7.44−7.22 (m, 11H), 4.71−4.63 (m, 1H), 4.16 (d, *J* = 4.8 Hz, 2H), 3.91−3.80 (m, 1H), 3.54−3.42 (m, 2H), 3.29 (dd, *J* = 3.3, 13.2 Hz, 1H), 2.79 (dd, *J* = 9.6, 13.5 Hz, 1H), 1.81−1.65 (m, 1H), 1.60−1.52 (m, 2H), 1.46−1.23 (m, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.08 (s, 9H), 0.91−0.86 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.8, 153.1, 135.7, 135.5, 134.2, 129.6, 129.6, 129.1, 127.7, 127.4, 69.4, 66.1, 55.5, 41.4, 41.3, 38.0, 35.5, 33.4, 28.0, 27.0, 19.4, 19.3, 17.3, 16.8 ppm; IR (neat) ν_{max} 2930, 2858, 1784, 1699, 1541, 1521, 1456, 1388, 1211 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{36}H_{47}O_4SiNNa$ $[M + Na]^+$ 608.3172 found 608.3171.

(2*R*,4*R*,6*S*)-7-((*tert*-Butyldiphenylsilyl)oxy)-2,4,6-trimethylheptan-1-ol (21). Following the same $LiBH_4$ reduction experimental procedure as described in the preparation of compound **5**, compound **20** (150 mg) was converted to the corresponding primary alcohol **21** (92 mg, 87%, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.3 (10% EtOAc in hexane); $[\alpha]^{29}_D$ = +3.0 (*c* 2.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.69−7.66 (m, 4H), 7.45−7.35 (m, 6H), 3.54−3.36 (m, 4H), 1.81−1.65 (m, 2H), 1.58−1.50 (m, 1H), 1.25−1.11 (m, 4H), 1.06 (s, 9H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.81 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.8, 134.3, 129.6, 127.7, 69.5, 69.2, 41.8, 41.5, 33.3, 33.3, 27.3, 27.0, 19.5, 19.4, 17.0, 16.5 ppm; IR (neat) ν_{max} 3362, 2927, 1458, 1110 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{40}O_2SiNa$ $[M + Na]^+$ 435.2695 found 435.2697.

(2*R*,4*s*,6*S*)-2,4,6-Trimethylheptane-1,7-diyl Bis(4-bromobenzoate) (22). To an ice-cold solution of the above primary alcohol **21** (90 mg, 0.218 mmol, 1.0 equiv) in anhydrous THF (3 mL) under argon was added TBAF (0.33 mL, 0.33 mmol, 1 M solution in THF, 1.5 equiv) over 2 min. The reaction mixture was stirred for 4 h at room temperature prior to quenching with a saturated NH_4Cl solution (1 mL). The mixture was extracted with EtOAc (2 × 10 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) afforded the TBDPS deprotected corresponding diol (33 mg, 85%) as a colorless oil: R_f = 0.4 (40% EtOAc in hexane); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.46 (dd, *J* = 5.7, 10.5 Hz, 2H), 3.38 (dd, *J* = 6.5, 10.4 Hz, 2H), 1.91 (s, 2H), 1.771.55 (m, 3H), 1.23−1.14 (m, 2H), 1.09−1.00 (m, 2H), 0.8 (d, *J* = 6.6 Hz, 6H), 0.83 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 69.0, 41.6, 33.3, 27.2, 19.2, 16.6 ppm; IR (neat) ν_{max} 3374, 2927, 2857, 1463, 1123 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{10}H_{22}O_2Na$ $[M + Na]^+$ 197.1517, found 197.1516.

To an ice-cold solution of the above diol compound (30 mg, 0.17 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (3 mL) under argon was added pyridine (0.03 mL, 0.26 mmol, 1.5 equiv. The mixture was stirred for 10 min, and then *p*-bromobenzoyl chloride (82 mg, 0.37 mmol, 2.2 equiv) and DMAP (2 mg, 0.009 mmol, 0.05 equiv) were added sequentially. The reaction mixture was warmed slowly to room temperature and stirred further overnight and quenched with a saturated aqueous solution of NH_4Cl (2 mL). The resultant mixture was extracted with CH_2Cl_2 (2 × 10 mL), washed with water and brine,

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J. Org. Chem. 2017, 82, 2414−2435

dried over Na_2SO_4, and evaporated under reduced pressure. Flash column chromatographic purification (SiO_2, 60−120 mesh, 1% EtOAc in hexane as eluent) of the crude residue gave corresponding compound **22** (61 mg, 66%) as a yellowish solid (mp 68−70 °C): R_f = 0.6 (3% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.87−7.86 (m, 4H), 7.58 (d, J = 8.4 Hz, 4H), 4.19 (dd, J = 5.7, 10.8 Hz, 2H), 4.08 (dd, J = 6.8, 10.7 Hz, 2H), 2.10 (m, 2H), 1.74−1.66 (m, 1H), 1.33−1.27 (m, 2H), 1.23−1.15 (m, 2H), 1.00 (d, J = 6.6 Hz, 6H), 0.88 (d, J = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.1, 131.9, 131.2, 129.5, 128.1, 70.6, 41.7, 30.3, 27.9, 19.2, 17. ppm; IR (neat) ν_{max} 2960, 2925, 1722, 1591, 1398, 1270, 1102 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{28}O_4Br_2Na$ $[M + Na]^+$ 561.0252, found 561.0250.

((((2*R*,4*S*,6*S*)-2,4,6-Trimethyloct-7-en-1-yl)oxy)methyl)-benzene (23). To an ice-cold solution of primary alcohol **21** (1.82 g, 4.41 mmol, 1.0 equiv) in anhydrous THF (10 mL) under argon was added NaH (194 mg, 8.0 mmol, 60% dispersion in mineral oil, 1.8 equiv) cautiously over 5 min. The mixture was stirred for 15 min, and then BnBr (0.58 mL, 4.85 mmol, 1.1 equiv) and TBAI (82 mg, 0.22 mmol, 0.05 equiv) were added sequentially. The resultant suspension was stirred at room temperature for 6 h. The mixture was then cooled to 0 °C and subsequently quenched with a saturated NH_4Cl solution (2 mL). The resultant mixture was extracted with EtOAc (2 × 50 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 3−4% EtOAc in hexane as eluent) furnished the benzyl-protected compound (1.95 g, 88%) as a yellow oil: R_f = 0.7 (4% EtOAc in hexane); $[\alpha]^{27}_D$ = −1.5 (c 2.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70−7.67 (m, 4H), 7.43−7.28 (m, 11H), 4.51 (s, 2H), 3.53−3.39 (m, 2H), 3.33−3.19 (m, 2H), 1.92−1.70 (m, 2H), 1.53−1.50 (m, 1H), 1.29−1.15 (m, 2H), 1.07−0.97 (s, 11H), 0.94−0.87 (m, 6H), 0.81 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.0, 135.8, 134.3, 129.6, 128.4, 127.7, 127.7, 127.5, 76.7, 73.1, 69.5, 42.0, 41.7, 33.3, 31.0, 27.3, 27.1, 19.5, 19.4, 17.1, 17.0 ppm; IR (neat) ν_{max} 2928, 2858, 1585, 1109 cm^{-1}; HRMS (ESI) m/z calcd for $C_{33}H_{46}O_2SiNa$ $[M + Na]^+$ 525.3165 found 525.3167.

Following the same TBAF experimental procedure as described in the preparation of compound **22**, the above benzyl-protected compound (1.0 g) was converted to the corresponding benzyl-protected primary alcohol **23** (430 mg, 82%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.1 (10% EtOAc in hexane); $[\alpha]^{28}_D$ = −3.9 (c 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.27 (m, 5H), 4.50 (s, 2H), 3.51−3.37 (m, 2H), 3.34−3.20 (m, 2H), 1.94−1.82 (m, 1H), 1.78−1.60 (m, 2H), 1.25−1.13 (m, 2H), 1.10−1.00 (m, 2H), 0.92 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.83 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.0, 128.5, 127.7, 127.6, 76.6, 73.1, 69.1, 42.1, 41.6, 33.3, 31.0, 27.2, 19.2, 17.2, 16.6 ppm; IR (neat) ν_{max} 3371, 2921, 1099 cm^{-1}; HRMS (ESI) m/z calcd $C_{17}H_{28}O_2Na$ $[M + Na]^+$ 287.1987 found 287.1985.

(2*S*,4*R*,6*R*)-7-(Benzyloxy)-2,4,6-trimethylheptanal (24). Following the same Swern oxidation conditions described in the preparation of compound **12**, the above TBDPS-deprotected compound (600 mg) was transformed to the corresponding inseparable mixture (dr = 9.4:1.0) of aldehyde **24** (595 mg, quantitative, purification by flash column chromatography, SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) as a yellowish liquid which was taken for the next step: R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{29}_D$ = +6.6 (c 2.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.59 (d, J = 1.5 Hz, 1H), 7.36−7.28 (m, 5H), 4.53−4.44 (m, 2H), 3.34−3.20 (m, 2H), 2.43−2.37 (m, 1H), 1.91−1.80 (m, 1H), 1.66−1.55 (m, 1H), 1.51−1.29 (m, 4H), 1.05 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 205.4, 138.9, 128.4, 127.6, 127.6, 76.0, 73.2, 44.3, 42.1, 37.4, 31.0, 27.8, 20.1, 18.0, 13.4 ppm; IR (neat) ν_{max} 2933, 2851, 1728, 1531, 1426, 1233 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{26}O_2Na$ $[M + Na]^+$ 285.1830, found 285.1828.

((((2*R*,4*S*,6*S*)-2,4,6-Trimethyloct-7-en-1-yl)oxy)methyl)-benzene (25). To a suspension of Ph_3PCH_3Br (1.88 g, 4.98 mmol, 2.2 equiv) in anhydrous THF (15 mL) at 0 °C under argon was added K^{t}BuO (500 mg, 4.52 mmol, 2.0 equiv), and the mixture was stirred for 30 min at the same temperature. The reaction mixture was cooled to −78 °C, and aldehyde **24** (595 mg, 2.27 mmol, dissolved in 5 mL of anhydrous THF, 1.0 equiv) was cannulated into it. The reaction mixture was stirred for another 1 h at −78 °C and then warmed to room temperature before it was quenched with a saturated aqueous NH_4Cl solution (5 mL). The resultant mixture was extracted with EtOAc (2 × 30 mL), washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. Flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) of the crude residue gave compound **25** (360 mg, 61%) as a colorless oil: R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{27}_D$ = +11.2 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42−7.27, (m, 5H), 5.74−5.62 (m, 1H), 4.98−4.87 (m, 2H), 4.58−4.44 (m, 2H), 3.33−3.20 (m, 2H), 2.27−2.18 (m, 1H), 1.90−1.81 (m, 1H), 1.63−1.52 (m, 1H), 1.19−1.10 (m, 4H), 0.95 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.4, 139.0, 128.5, 127.7 127.6, 112.2, 76.9, 73.1, 45.3, 41.0, 35.3, 31.1, 27.5, 20.4, 19.9, 17.0 ppm; IR (neat) ν_{max} 2928, 2856, 1649, 1454, 1376, 1101 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{28}ONa$ $[M + Na]^+$ 283.2038, found 283.2036.

(2*R*,4*S*,6*S*)-2,4,6-Trimethyloct-7-en-1-ol (26). To a solution of naphthalene (690 mg, 6.75 mmol, 5 equiv) in anhydrous THF (15 mL) under argon was added Li (47 mg, 6.75 mmol, 1.1 equiv) as small pieces. After it was stirred for 3 h at room temperature, the reaction mixture was cooled to −40 °C and subsequently a solution of compound **25** (350 mg, 1.35 mmol, dissolved in 4 mL of anhydrous THF, 1.0 equiv) was cannulated into it. The reaction was continued further for 1 h at the same temperature and then quenched with a saturated aqueous solution of NH_4Cl (5 mL). The resultant mixture was extracted with EtOAc (2 × 30 mL), washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) to give compound **26** (188 mg, 82%) as a yellowish oil: R_f = 0.3 (5% EtOAc in hexane); $[\alpha]^{28}_D$ = +12.8 (c 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.73−5.61 (m, 1H), 4.98−4.87 (m, 2H), 3.53−3.34 (m, 2H), 2.30−2.16 (m, 1H), 1.79−1.52 (m, 2H), 1.19−1.08 (m, 4H), 0.95 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.3, 112.3, 69.3 45.3, 40.5, 35.4, 33.4, 27.5, 20.4, 19.9, 16.4 ppm; IR (neat) ν_{max} 3257, 2927, 1582, 1220 cm^{-1}; HRMS (ESI) m/z calcd for $C_{11}H_{22}ONa$ $[M + Na]^+$ 193.1568, found 193.1570.

(4*R*,6*S*,8*S*)-4,6,8-Trimethyldec-9-en-3-ol (27a,b). Following the same Swern oxidation conditions described in the preparation of compound **12**, compound **26** (150 mg) was transformed to the corresponding aldehyde (148 mg, quantitative, purified by flash column chromatography using a short pad of 60−120 silica and EtOAc as eluent) as a yellowish oil, which was taken for the next step without further characterization.

To a stirred solution of the above aldehyde (148 mg, 0.88 mmol, 1.0 equiv) in anhydrous THF (2 mL) at 0 °C under argon was added EtMgBr (1.3 mL, 1.3 mmol, 1.0 M in THF, 1.5 equiv), and the reaction was continued for 10 min at the same temperature. The reaction was then quenched by a saturated aqueous solution of NH_4Cl (1 mL). The resultant mixture was then extracted with EtOAc (2 × 20 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane) yielded an inseparable mixture of compounds **27a,b** (145 mg, 83%) as a colorless oil which was taken for the next reaction without further characterization.

(4*R*,6*S*,8*S*)-4,6,8-Trimethyldec-9-en-3-one (4). Following the same Swern oxidation conditions described in the preparation of compound **12**, the mixture of compounds **27a,b** (100 mg) was converted to compound **4** (80 mg, 81%, purification by flash column chromatography, SiO_2, 60−120 mesh, 2% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.5 (3% EtOAc in hexane); $[\alpha]^{25}_D$ = −3.9 (c 1.1 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.72−5.60 (m, 1H), 4.98−4.87 (m, 2H), 2.63−2.56 (m, 1H), 2.50−2.42 (m, 2H), 2.26−2.19 (m, 1H), 1.55−1.44 (m, 1H), 1.38−1.30 (m, 2H), 1.19−1.14 (t, J = 7.1 Hz, 2H), 1.04−1.01 (m, 6H), 0.94 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.3

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J. Org. Chem. 2017, 82, 2414−2435

Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 215.7, 145.1, 112.5, 44.7, 43.9, 40.1, 35.3, 34.2, 28.1, 20.3, 19.9, 16.3, 8.0 ppm; IR (neat) ν_{max} 2962, 2928, 1715, 1456, 1377 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{24}ONa$ $[M + Na]^+$ 219.1725, found 219.1723.

(3*R*,4*S*)-Methyl 4-((*R*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)-phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-6-methyl-3-((triethylsilyl)oxy)heptanoate (32). To an ice-cold solution of compound **12** (4.84 g, 5.80 mmol, 1.1 equiv) in anhydrous methanol (15 mL) at 0 °C under argon was added imidazole (1.98 g, 29.07 mmol, 5.0 equiv), and the mixture was stirred overnight at room temperature. The reaction mixture was then quenched with a saturated solution of NH_4Cl (3 mL). Methanol was removed under vacuum and the residue extracted with EtOAc (2 × 100 mL), washed with water and brine, dried over Na_2SO_4, and concentrated. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) afforded the corresponding ester (3.35 g, 88%) as a colorless oil: R_f = 0.5 (10% EtOAc in hexane); $[\alpha]^{30}_D$ = +20.6 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.44 (d, *J* = 2.1 Hz, 2H), 6.22 (t, *J* = 2.1 Hz, 1H), 4.73 (d, *J* = 5.1 Hz, 1H), 4.08−4.05 (m, 1H), 3.67 (s, 3H), 2.75 (d, *J* = 2.7 Hz, 1H), 2.58 (dd, *J* = 9.6, 15.9 Hz, 1H), 2.34 (dd, *J* = 3.9, 15.9 Hz, 1H), 1.61−1.60 (m, 1H), 1.45−1.29 (m, 3H), 0.97 (s, 18H), 0.90 (s, 9H), 0.81 (d, *J* = 6 Hz, 3H), 0.76 (d, *J* = 6 Hz, 3H), 0.18 (s, 6H), 0.17 (s, 6H), 0.06 (s, 3H), −0.211 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.4, 156.5, 146.2, 112.1, 111.4, 77.3, 69.3, 51.8, 48.8, 39.7, 33.3, 27.3, 26.1, 25.9, 23.0, 22.8, 18.4, 18.2, −4.2, −4.8 ppm; IR (neat) ν_{max} 3430, 2932, 1747,1651, 1541, 1456, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{34}H_{66}O_6Si_3Na$ $[M + Na]^+$ 677.4065, found 677.4067.

To an ice-cold solution of the above ester (2.56 g, 3.91 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (12 mL) was added 2,6-lutidine (2.13 mL, 7.82 mmol, 2.0 equiv), and the mixture was stirred for 5 min prior to addition of TESOTf (1.74 mL, 7.82 mmol, 2.0 equiv). The reaction was continued at the same temperature for 30 min and subsequently quenched with a saturated solution of $NaHCO_3$ (4 mL). The resultant mixture was extracted with CH_2Cl_2 (2 × 50 mL), washed with aqueous $CuSO_4$, water, and brine, dried with Na_2SO_4, and concentrated in vacuo. Purification of the crude residue by flash column chromatography (SiO_2, 60−120 mesh, 1.0−1.5% EtOAc in hexane as eluent) provided compound **32** (2.83 g, 94%) as a light yellow oil: R_f = 0.5 (2% EtOAc in hexane); $[\alpha]^{23}_D$ = +34.9 (*c* 2.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.40 (d, *J* = 2.4 Hz, 2H), 6.18 (t, *J* = 2.1 Hz, 1H), 5.11 (d, *J* = 2.1 Hz, 1H), 4.30−4.24 (m, 1H), 3.66 (s, 3H), 2.71−2.51 (m, 2H), 1.72−1.66 (m, 1H), 1.40−1.33 (m, 1H), 1.26−1.08 (m, 2H), 1.01−0.94 (m, 36H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.67−0.59 (m, 9H), 0.16 (s, 6H), 0.16 (s, 6H), 0.11(s, 3H), −0.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.7, 156.1, 148.0, 112.2, 110.9, 72.1, 70.3, 51.5, 50.1, 39.0, 33.2, 26.3, 25.9, 25.5, 23.9, 21.8, 18.4, 18.2, 7.1, 5.3, −3.8, −4.2, −4.3, −4.6 ppm; IR (neat) ν_{max} 2955, 1745, 1541, 1456, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{40}H_{80}O_6Si_4Na$ $[M + Na]^+$ 791.4930, found 791.4932.

Dimethyl ((4*R*,5*S*)-5-((*R*)-(3,5-Bis((*tert*-butyldimethylsilyl)-oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-7-methyl-2-oxo-4-((triethylsilyl)oxy)octyl)phosphonate (31). To a stirred solution of $(MeO)_2P(O)Me$ (1.40 mL, 11.28 mmol, 4.0 equiv) in anhydrous THF (25 mL) at −78 °C under argon was added ^{n}BuLi (6.12 mL, 9.87 mmol, 1.6 M in hexane, 3.5 equiv) slowly over 10 min and the resultant solution stirred for 30 min. A solution of compound **32** (2.17 g, 2.82 mmol, dissolved in 8 mL of anhydrous THF, 1.1 equiv) was added dropwise to the reaction mixture and stirred further for 4 h. The reaction was quenched with a saturated solution of NH_4Cl (3 mL), and the resultant mixture was extracted with EtOAc (2 × 50 mL), washed with water and brine, dried over Na_2SO_4, and evaporated in vacuo. The crude residue was purified by flash column chromatography (SiO_2, 60% EtOAc in hexane as eluent) to access phosphonate **31** (1.95 g, 83%) as a yellowish viscous liquid: R_f = 0.3 (60% EtOAc in hexane); $[\alpha]^{28}_D$ = +42.3 (*c* 3.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, *J* = 2.1 Hz, 2H), 6.18 (t, *J* = 2.3 Hz, 1H), 5.12 (d, *J* = 1.8 Hz, 1H), 4.36−3.31 (m, 1H), 3.80 (d, *J* = 3.6 Hz, 3H), 3.76 (d, *J* = 3.6 Hz, 3H), 3.17−2.95 (m, 2H), 2.91−2.79 (m, 2H), 1.65 (m, 1H), 1.23−1.17 (m, 3H), 1.00−0.95 (m, 36H), 0.75 (d, *J* = 5.7 Hz, 3H), 0.67−0.57 (m, 9H), 0.16 (s, 6H), 0.15 (s, 6H), 0.12 (s, 3H), −0.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.4, 156.1, 147.9, 112.1, 110.9, 71.9, 68.6, 53.2, 53.1, 53.0, 52.9, 50.0, 48.6, 41.3, 33.1, 26.3, 25.8, 25.4, 23.8, 21.8, 18.4, 18.2, 7.2, 5.3, −3.8, −4.2, −4.3, −4.5 ppm; IR (neat) ν_{max} 2955, 2880, 1717, 1701, 1541, 1458, 1258, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{42}H_{85}O_8Si_4PNa$ $[M + Na]^+$ 883.4957, found 883.4955.

(4*S*,5*R*,10*S*,12*S*,14*R*,*E*)-15-(Benzyloxy)-4-((*R*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)-methyl)-2,10,12,14-tetramethyl-5-((triethylsilyl)oxy)pentadec-8-en-7-one (30). Into a solution of compound **31** (500 mg, 0.58 mmol, 1.0 equiv) in anhydrous THF (3 mL) under argon at room temperature was poured freshly activated $Ba(OH)_2{\cdot}8H_2O$ (150 mg, 0.45 mmol, 0.8 equiv). After being stirred for 30 min, the reaction mixture was cooled to 0 °C and subsequently a solution of aldehyde **24** (dr = 9.4:1.0, 152 mg, 0.58 mmol, 1.0 equiv) dissolved in THF/H_2O 40/1 (3 mL) was cannulated into it. The reaction mixture was stirred further for 1 h before quenching it with a saturated NH_4Cl solution (1 mL). The resultant mixture was extracted with EtOAc (2 × 30 mL), washed with water and brine, dried over Na_2SO_4, and concentrated under vacuum. Purification of the crude residue by flash chromatography (SiO_2, 60−120 mesh, 4−5% EtOAc in hexane as eluent) gave compound **30** (490 mg, 84%) as a colorless oil: R_f = 0.6 (2% EtOAc in hexane); $[\alpha]^{29}_D$ = +40.1 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.27 (m, 5H), 6.69 (q, *J* = 8.0 Hz, 1H), 6.41 (d, *J* = 2.1 Hz, 2H), 6.18 (t, *J* = 2.3 Hz, 1H), 6.05 (dd, *J* = 0.5 Hz, 1H), 5.18 (s, 1H), 4.50 (s, 2H), 4.45−4.39 (m, 1H), 3.31−3.21 (m, 2H), 2.97 (dd, *J* = 8.7, 16.5 Hz, 1H), 2.61 (dd, *J* = 1.8, 16.5 Hz, 1H), 2.45−2.36 (m, 1H), 1.91−1.80 (m, 1H), 1.72−1.66 (m, 1H), 1.55−1.49 (m, 1H), 1.33−1.08 (m, 7H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.97−0.92 (m, 36H), 0.86 (dd, *J* = 6.5, 9.2 Hz, 6H), 0.76 (d, *J* = 6.3 Hz, 3H), 0.64−0.56 (m, 9H), 0.17−0.14 (m, 15H), −0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.4, 156.0, 153.0, 148.3, 139.9, 129.7, 128.5, 127.7, 127.6, 112.2, 110.8, 77.4, 73.1, 72.0, 69.2, 50.4, 44.7, 44.0, 41.0, 34.5, 33.1, 31.0, 27.8, 26.4, 25.8, 25.3, 23.9, 21.8, 19.8, 19.7, 18.4, 18.2, 17.0, 7.2, 5.3, −3.7, −4.2, −4.3, −4.3 ppm; IR (neat) ν_{max} 2954, 2929, 1591, 1454, 1257, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{57}H_{104}O_6Si_4Na$ $[M + Na]^+$ 1019.6808, found 1019.6808.

(4*S*,5*R*,10*R*,12*S*,14*R*)-4-((*R*)-(3,5-Bis((*tert*-butyldimethylsilyl)-oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-15-hydroxy-2,10,12,14-tetramethyl-5-((triethylsilyl)oxy)pentadecan-7-one (29). Following the same experimental procedure as for compound **20**, compound **30** (400 mg) was converted to compound **29** (365 mg, 98%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.4 (2% EtOAc in hexane); $[\alpha]^{27}_D$ = +30.9 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.40 (d, *J* = 2.1 Hz, 2H), 6.18 (t, *J* = 2.3 Hz, 1H), 5.15 (d, *J* = 1.2 Hz, 1H), 4.38−4.33 (m, 1H), 3.51−3.38 (m, 2H), 2.84 (dd, *J* = 8.7, 16.5 Hz, 1H), 2.53 (dd, *J* = 2.4, 16.5 Hz, 1H), 2.38 (t, *J* = 7.8 Hz, 2H), 1.78−1.61 (m, 3H), 1.51−1.29 (m, 5H), 1.22−1.02 (m, 5H), 0.99−0.94 (m, 36H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.83 (t, *J* = 6.8 Hz, 6H), 0.75 (d, *J* = 6.3 Hz, 3H), 0.61 (dd, *J* = 7.7, 15.8 Hz, 9H), 0.16−0.13 (m, 15H), −0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 211.0, 156.1, 148.1, 112.1, 110.8, 71.9, 69.2, 69.2, 50.2, 46.6, 45.7, 42.5, 41.6, 33.4, 33.1, 31.4, 29.9, 27.4, 26.3, 25.8, 25.3, 23.9, 21.8, 19.4, 19.3, 18.4, 18.2, 16.6, 7.2, 5.3, −3.7, −4.2, −4.3, −4.4 ppm; IR (neat) ν_{max} 3407, 2957, 2930, 1713, 1591, 1454, 1257, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{50}H_{100}O_6Si_4Na$ $[M + Na]^+$ 931.6495, found 931.6497.

(2*R*,4*S*,6*R*,9*R*,11*R*,12*S*)-12-((*R*)-(3,5-Bis((*tert*-butyldimethyl-silyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-2,4,6,14-tetramethylpentadecane-1,9,11-triol (33). Following the same experimental procedure as for compound **16**, compound **29** (280 mg) was converted to the corresponding TES-deprotected compound (220 mg, 79%, purification by flash column chromatography, SiO_2, 60−120 mesh, 10% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.2 (10% EtOAc in hexane); $[\alpha]^{25}_D$ = +29.2 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.44 (d, *J* = 2.4, 2H), 6.21 (t, *J* = 2.3 Hz, 1H), 4.31 (d, *J* = 5.4 Hz, 1H), 4.06 (d, *J* = 6.6 Hz, 1H), 3.50−3.37 (m, 2H), 2.90 (d, *J* = 2.4 Hz,1H), 2.66 (dd, *J* = 6.3, 17.1 Hz, 1H), 2.45−2.30 (m, 3H), 1.77−1.66 (m, 1H), 1.55−1.25 (m, 9H), 1.21−1.00 (m, 5H), 0.97 (s, 18H), 0.90−0.88 (m, 12H), 0.84−0.76(m, 12H), 0.17 (s, 12H), 0.06

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(s, 3H), −0.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 212.0, 156.4, 146.4, 112.9, 111.4, 77.3, 69.1, 68.8, 73.3, 69.1, 68.8, 48.8, 47.6, 45.5, 41.6, 41.4, 33.5, 33.3, 31.3, 29.9, 27.4, 27.4, 26.1, 25.9, 23.1, 22.9, 19.4, 19.3, 18.4, 18.2, 16.6, −4.2, −4.8 ppm; IR (neat) ν_{max} 3407, 2930, 1593, 1720, 1447, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{44}H_{86}O_6Si_3Na$ $[M + Na]^+$ 817.5630, found 817.5632.

To a solution of the above TES-deprotected compound (200 mg, 0.23 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (2 mL) at −78 °C under argon was added DIBAL-H (0.7 mL, 0.7 mmol, 1.0 M in toluene, 3.0 equiv) dropwise over 5 min, and the mixture was stirred for 15 min. The reaction mixture was then quenched with MeOH (0.2 mL), and a saturated solution of sodium−potassium tartrate (2 mL) was added. The resulting mixture was stirred further until the two layers (organic and aqueous) were separated. The mixture was finally extracted with EtOAc (2 × 30 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Flash column chromatography (SiO_2, 60−120 mesh, 20% EtOAc in hexane as eluent) of the crude residue afforded the major compound **33** (116 mg, 58%, dr = 3:1) as a colorless oil: R_f = 0.2 (20% EtOAc in hexane); $[\alpha]^{28}_D$ = +9.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (d, *J* = 2.1, 2H), 6.22 (t, *J* = 2.1 Hz, 1H), 4.73 (d, *J* = 4.2 Hz, 1H), 4.10 (d, *J* = 10.2 Hz, 1H), 3.79−3.71 (m, 1H), 3.51−3.36 (m, 2H), 2.66 (s, 1H), 1.78−1.61 (m, 2H), 1.60−1.39 (m, 5H), 1.35−1.39 (m, 5H), 1.35−1.23 (m, 6H), 1.18−1.02 (m,4H), 0.97 (s, 18H), 0.93−0.88 (m, 12H), 0.85−0.79 (m, 9H), 0.75 (d, *J* = 6.0 Hz, 3H), 0.17 (s, 12H), 0.06 (s, 3H), −0.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.6, 145.8, 111.8, 111.5, 74.7, 73.3, 69.1, 69.1, 49.7, 45.8, 41.6, 36.8, 35.4, 33.4, 33.4, 32.7, 30.3, 27.4, 27.0, 26.1, 25.8, 23.3, 22.6, 19.7, 19.4, 18.4, 18.2, 16.6, −4.2, −4.3, −5 ppm; IR (neat) ν_{max} 3368, 2955, 2859, 1591, 1451, 1254, 1162 cm^{-1}; HRMS (ESI) m/z calcd for $C_{44}H_{88}O_6Si_3Na$ $[M + Na]^+$ 819.5787, found 819.5786.

(2*R*,4*S*,6*R*)-8-((4*R*,6*R*)-6-((1*R*,2*S*)-1-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-1-((*tert*-butyldimethylsilyl)-oxy)-4-methylpentan-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)-2,4,6-trimethyloctan-1-ol (28). Following the same experimental procedure as described in the synthesis of compound **3**, compound **33** (110 mg) was converted to compound **28** (102 mg, 89%, purification by flash column chromatography, SiO_2, 60−120 mesh, 2% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (4% EtOAc in hexane); $[\alpha]^{25}_D$ = +15.0 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, *J* = 2.1, 2H), 6.20 (t, *J* = 2.1 Hz, 1H), 4.57 (d, *J* = 6.0 Hz, 1H), 3.60−3.36 (m, 4H), 1.77−1.61 (m, 2H), 1.50−1.37 (m, 5H), 1.33 (s, 3H), 1.30−1.28 (m, 3H), 1.25 (s, 3H), 1.21−1.02 (m, 7H), 0.97 (s, 18H), 0.90−0.88 (m, 12H), 0.84−0.78 (m, 12H), 0.17 (s, 12H), 0.04 (s, 3H), −0.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.1, 147.2, 112.7, 110.9, 98.3, 75.9, 69.7, 69.4, 69.2, 49.7, 45.6, 41.6, 35.0, 34.1, 33.3, 32.9, 30.4, 30.1, 27.8, 27.4, 26.1, 25.9, 23.1, 22.9, 19.9, 19.7, 19.4, 18.4, 18.4, 18.3, 16.6, −4.1, −4.1, −4.2, −4.6 ppm; IR (neat) ν_{max} 3355, 2955, 2930, 1591, 1454, 1258, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{47}H_{92}O_6Si_3Na$ $[M + Na]^+$ 859.6099, found 859.6097.

(4*R*,6*S*,8*R*)-10-((4*R*,6*R*)-6-((1*R*,2*S*)-1-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-1-((*tert*-butyldimethylsilyl)-oxy)-4-methylpentan-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)-4,6,8-trimethyldecan-3-one (34). To an ice-cold solution of compound **28** (100 mg, 0.12 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (2 mL) were added $NaHCO_3$ (50 mg, 0.60 mol, 5.0 equiv) and DMP (101 mg, 0.24 mmol, 2.0 equiv) sequentially. The reaction mixture was warmed gradually to room temperature and stirred further for 1 h. The reaction was then quenched with a saturated aqueous solution of $Na_2S_2O_3$ (1 mL) and $NaHCO_3$ (1 mL) and then diluted with CH_2Cl_2 (5 mL) and stirred until the two phases were separated. The resultant mixture was extracted with CH_2Cl_2 (2 × 15 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude residue was subjected to flash column chromatography (using a short pad of 60−120 silica and EtOAc as eluent) to give the pure aldehyde (100 mg, quantitative) as a colorless liquid, which was taken for the next reaction without further characterization.

To an ice-cold solution of above aldehyde (100 mg, 0.12 mmol, 1.0 equiv) in anhydrous THF (2 mL) under argon was added EtMgBr (0.2 mL, 0.2 mL, 1 M in THF, 1.7 equiv), and the mixture was stirred for 10 min at the same temperature. The reaction was then quenched by a saturated aqueous solution of NH_4Cl (1 mL) and extracted with EtOAc (2 × 15 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. Flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) of the crude residue provided the corresponding mixture of alcohols (82 mg, 79%, dr = 6:1) as a colorless oil: R_f = 0.6 (3% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, *J* = 2.1, 2H), 6.21−6.18 (m, 1H), 4.57 (d, *J* = 6.0 Hz, 1H), 3.66−3.53 (m, 2H), 3.37−3.32 (m, 1H), 1.53−1.38 (m, 7H), 1.33 (s, 3H), 1.29−1.1.27 (m, 5H), 1.25 (s, 3H), 1.23−1.1.00 (m, 7H), 0.97 (s, 18H), 0.96−0.93 (m, 3H), 0.89−0.87 (m, 9H), 0.86−0.76 (m, 15H), 0.17 (s, 12H), 0.04 (s, 3H), −0.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz, with observed rotamer peaks in parentheses) δ 156.1, 147.2, 117.9, 112.7(112.4), 110.87, 98.3, 77.5, 75.9, 69.7, 69.4, 49.7, 45.7, 41.8, 35.2, 34.9(35.0), 34.2, 33.0(32.8), 30.4, 30.1, 27.8, 27.5, 27.4, 26.1, 25.9, 23.1, 22.9, 19.9, 19.8(19.7), 19.3, 18.4, 18.3, 13.6, 10.7(10.6), −4.1, −4.2, −4.2, −4.6 ; IR (neat) ν_{max} 2956, 2859, 1716, 1591, 1455, 1254, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{49}H_{96}O_6Si_3Na$ $[M + Na]^+$ 887.6412, found 887.6414.

To an ice-cold solution of the above alcohols (82 mg, 0.10 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (4 mL) under argon was added DMP (80 mg, 0.20 mmol, 2.0 equiv). The reaction mixture was warmed slowly to room temperature and stirred for 1 h. Then the reaction mixture was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (1 mL) and $NaHCO_3$ (1 mL) and then diluted with CH_2Cl_2 (4 mL) and stirred until the two phases were separated well. The mixture was extracted with CH_2Cl_2 (2 × 15 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude residue was subjected to flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) to afford pure compound **34** (64 mg, 78%) as a colorless liquid: R_f = 0.6 (3% EtOAc in hexane); $[\alpha]^{28}_D$ = +13.4 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, *J* = 2.1, 2H), 6.21 (t, *J* = 2.1 Hz, 1H), 4.57 (d, *J* = 6.0 Hz, 1H), 3.62−3.53 (m, 2H), 2.67−2.56 (m, 1H), 2.49−2.38 (m, 2H), 1.63−1.57 (m, 1H), 1.51−1.37 (m, 7H), 1.33 (s, 4H), 1.30−1.27 (m, 4H), 1.25 (s, 3H), 1.18−1.13 (m, 3H), 1.07−1.02 (m, 6H), 0.97 (s, 18H), 0.88 (s, 9H), 0.84−0.78 (m, 12H), 0.17 (s, 12H), 0.04 (s, 3H), −0.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 215.7, 156.1, 147.2, 112.7, 110.9, 98.3, 75.9, 69.6, 69.4, 49.7, 45.0, 43.9, 41.3, 35.0, 34.9, 34.3, 34.1, 33.0, 30.4, 30.1, 28.1, 27.8, 26.1, 25.9, 23.1, 22.9, 19.9, 19.6, 19.5, 18.4, 18.3, 16.6, 8.0, −4.1, −4.1, −4.2, −4.6; IR (neat) ν_{max} 2956, 2859, 1716, 1591, 1455, 1254, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{49}H_{94}O_6Si_3Na$ $[M + Na]^+$ 885.6256, found 885.6254.

(4*R*,6*S*,8*R*,11*R*,13*R*,14*S*)-14-((*R*)-(3,5-Dihydroxyphenyl)-(hydroxy)methyl)-11,13-dihydroxy-4,6,8,16-tetramethylheptadecan-3-one (1). A solution of compound **34** (30 mg, 0.062 mmol, 1.0 equiv) in anhydrous THF (1 mL) was placed in a plastic vial and cooled to 0 °C. HF-pyridine (70%, 0.1 mL, 2.54 mol, 41.0 equiv) was added and the mixture stirred for 12 h at room temperature. The reaction mixture was again cooled to 0 °C and quenched cautiously with a saturated aqueous solution of $NaHCO_3$ (2 mL). The resultant mixture was extracted with EtOAc (2 × 15 mL), washed with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash column chromatography (SiO_2, 60−120 mesh, 5−6% MeOH in CH_2Cl_2 as eluent) to furnish the title compound **1** (15 mg, 90%) as a yellowish liquid: R_f = 0.2 (6% MeOH in CH_2Cl_2); $[\alpha]^{30}_D$ = +2.0 (*c* 0.6, MeOH); ^{1}H NMR (CD_3OD, 700 MHz) δ 6.32 (d, *J* = 2.0, 2H), 6.12 (t, *J* = 2.0 Hz, 1H), 4.82 (d, *J* = 3.7 Hz, 1H), 3.96 (dt, *J* = 8.2, 4.2 Hz, 1H), 3.69 (dt, *J* = 8.1, 4.2 Hz, 1H), 2.70 (dq, *J* = 7.1, 13.8 Hz, 1H), 2.52 (m, 2H), 1.67 (m, 1H), 1.667 (ddd, *J* = 3.8, 8.2, 13.8 Hz, 1H), 1.627 (ddd, *J* = 4.2, 9.4, 13.8, 1H), 1.50 (m, 1H), 1.48 (m, 1H), 1.46 (m, 1H), 1.44 (m, 2H), 1.38 (m, 1H), 1.28 (m, 2H), 1.23 (m, 2H), 1.20 (m, 1H), 1.09 (m, 2H), 1.03 (d, J 6.9 Hz, 3H), 1.00 (t, *J* = 7.1 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.78 (d, *J* = 6.1 Hz, 3H), 0.64 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (CD_3OD, 125 MHz) δ 218.4, 159.3, 148.6, 105.7, 102.0, 76.8, 75.1, 72.3, 49.3, 46.2, 45.0, 42.4, 42.4, 35.9, 35.1, 34.4, 33.4, 31.4, 29.2, 28.3, 23.4, 22.9, 19.8, 19.8, 17.0, 8.1 ppm; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 6.33 (d, *J* = 1.8, 2H), 5.99 (t, *J* = 2.1 Hz, 1H), 4.88 (d, *J* = 3.6 Hz, 1H), 4.66 (m, 1H), 4.57 (d, J = 3 Hz,

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J. Org. Chem. 2017, 82, 2414−2435

1H), 3.78−3.72 (m, 1H), 3.56−3.51 (m, 1H), 2.64−2.56 (m, 1H), 2.47−2.40 (m, 2H), 1.58−1.54 (m, 1H), 1.42−1.30 (m, 3H), 1.39−1.30 (m, 3H), 1.23−1.10 (m, 10H), 1.05−1.00 (m, 2H), 0.99−0.89 (m, 6H), 0.79−0.75 (m, 6H), 0.70 (d, J = 6 Hz, 3H), 0.57 (d, J = 5.7 Hz, 3H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 214.5, 157.7, 148.3, 104.1, 100.4, 73.3, 72.1, 69.6, 48.6, 48.1, 44.6, 42.8, 41.0, 34.5, 33.3, 32.8, 32.5, 29.6, 27.5, 26.5, 23.1, 22.4, 19.3, 19.3, 16.3, 7.8 ppm; IR (neat) ν_{max} 3361, 2930, 2800, 1701, 1605, 1458, 1157 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{48}O_6Na$ [M + Na]$^+$ 503.3349, found 503.3347.

(*S*)-4-Benzyl-3-((*S*)-2-((*S*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)(hydroxy)methyl)-4-methylpentanoyl)oxazolidin-2-one (38). Following the same experimental procedure as for compound **9**, compound **37** (6.45 g) was reacted with compound **7** (8.64 g) to produce compound **38** (14.42 g, 96%, purification by flash column chromatography, SiO_2, 60−120 mesh, 10% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.3 (20% EtOAc in hexane); $[\alpha]^{27}_D$ = +16.0 (c 1.9, $CHCl_3$) ; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.19 (m, 5H), 6.53 (d, J = 2.4 Hz, 2H), 6.23 (t, J = 2.1 Hz, 1H), 4.84−4.82 (m, 1H), 4.60−4.52 (m, 1H), 4.41−4.35 (m, 1H), 4.08 (dd, J = 2.4, 9.0 Hz, 1H), 4.01−3.95 (m, 1H), 3.30 (dd, J = 3.3, 13.2 Hz, 1H), 2.69 (dd, J = 9.9, 13.5 Hz, 1H), 2.44 (d, J = 3 Hz, 1H), 1.98−1.89 (m, 1H), 1.48−1.34 (m, 2H), 0.96 (s, 18H), 0.87 (d, J = 6.3, Hz, 3H), 0.83 (d, J = 6.3, Hz, 3H), 0.19 (s, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.5, 156.6, 153.2, 143.7, 135.4, 129.5, 129.1, 127.5, 111.5, 111.2, 74.7, 66.0, 55.8, 48.3, 38.1, 35.8, 26.7, 25.9, 23.8, 22.0, 18.4, −4.3, −4.3 ppm; IR (neat) ν_{max} 3475, 2925, 1772, 1698, 1595, 1398, 1157 cm^{-1}; HRMS (ESI) m/z calcd for $C_{35}H_{55}O_6NSi_2Na$ [M + Na]$^+$ 664.3466, found 664.3469.

(*S*)-4-Benzyl-3-((*S*)-2-((*S*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethyl silyl)oxy)methyl)-4-methylpentanoyl)oxazolidin-2-one (39). Following the same experimental procedure as described in the synthesis of compound **5**, compound **38** (11.65 g) was converted to compound **39** (13.19 g, 96%, purification by flash column chromatography, SiO_2, 60−120 mesh, 1−2% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{27}_D$ = +16.6 (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33−7.16 (m, 5H), 6.46 (d, J = 2.1 Hz, 2H), 6.18 (t, J = 2.3 Hz, 1H), 4.63 (d, J = 6.6 Hz, 1H), 4.33−4.19 (m, 2H), 3.97 (dd, J = 1.8, 8.7 Hz, 1H), 3.72 (t, J = 8.3 Hz, 1H), 3.22 (dd, J = 3.2, 13.2 Hz, 1H), 2.67 (dd, J = 9.9, 13.2 Hz, 1H), 2.00−1.88 (m, 1H), 1.53−1.45 (m, 2H), 0.95 (s, 18H), 0.91−0.86 (m, 15H), 0.16 (s, 12H), 0.00 (s, 3H), −0.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.4, 156.3, 152.9, 145.0, 135.7, 129.5, 129.0, 127.4, 111.8, 111.4, 76.9, 65.9, 56.1, 50.3, 38.0, 37.3, 26.8, 26.0, 25.8, 23.9, 22.1, 18.4, 18.3, −4.3, −4.3, −4.5, −5.1 ppm; IR (neat) ν_{max} 2956, 2930, 1782, 1593, 1454, 1385, 1255, 1165 cm^{-1}; HRMS (ESI) m/z calcd for $C_{41}H_{69}O_6NSi_3Na$ [M + Na]$^+$ 778.4330, found 778.4331.

(*R*)-2-((*S*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-4-methylpentan-1-ol (40). Following the same LiBH$_4$ reduction procedure described in the synthesis of compound **5**, compound **39** (13.0 g) was converted to compound **40** (8.32 g, 83%, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.3 (5% EtOAc in hexane); $[\alpha]^{28}_D$ = −15.2 (c 2.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (d, J = 2.1 Hz, 2H), 6.25 (t, J = 2.1 Hz, 1H), 4.75 (d, J = 3.9 Hz, 1H), 3.61−3.46 (m, 2H), 2.79 (s, 1H), 2.04−1.94 (m, 1H), 1.62−1.51 (m, 2H), 1.08−1.01 (m, 1H), 0.97 (s, 18 H), 0.91 (s, 9H), 0.86 (d, J = 6.3 Hz, 3H), 0.81 (d, J = 6.3 Hz, 3H), 0.18 (s, 12H), 0.06 (s, 3H), −0.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.3, 144.2, 112.4, 111.5, 77.8, 63.8, 45.3, 36.2, 26.0, 25.9, 25.7, 23.6, 22.3, 18.4, 18.2, −4.2, −4.2, −4.6, −5.2 ppm; IR (neat) ν_{max} 3456, 2955, 1594, 1465, 1252, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{31}H_{62}O_4Si_3Na$ [M + Na]$^+$ 605.3854, found 605.3856.

(3*S*,4*R*)-Methyl 4-((*S*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)-phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-3-hydroxy-6-methylheptanoate (42). Following the same experimental procedure described in the synthesis of compound **12**, compound **40** (1.02 g) was converted to the corresponding aldehyde (1.02 g, quantitative) as a colorless oil which was directly used for the next step without further characterization.

Following the same experimental procedure described in the synthesis of compound **12**, the above aldehyde (1.02 g) in the presence of thiazolidinethione **41** (552 mg) was converted to compound **42** (1.17 g, 80%). The removal of thaizolidinethione impurities from compound **42** was not possible at this stage, even after substantial efforts, and we used the impure compound **42** in the next step without further characterization.

2-((4*R*,5*R*,6*S*)-6-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-5-isobutyl-2,2-dimethyl-1,3-dioxan-4-yl)ethanol (42a). Following the same experimental procedure as for compound **13**, the above compound **42** (200 mg) was converted to the corresponding alcohol compound (120 mg, 80%, purification by flash column chromatography, SiO_2, 60−120 mesh, 20% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.3 (30% EtOAc in hexane); $[\alpha]^{24}_D$ = −14.4 (c 4.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (d, J = 2.1 Hz, 2H), 6.22 (t, J = 2.3 Hz, 1H), 4.74 (d, J = 4.2 Hz, 1H), 4.10 (d, J = 9.9 Hz, 1H), 3.81−3.77 (m, 2H), 2.51 (s, 1H), 1.92−1.80 (m, 1H), 1.60−1.55 (m, 1H), 1.48−1.25 (m, 4H), 0.97 (s, 18 H), 0.91 (s, 9H), 0.79 (d, J = 5.7 Hz, 3H), 0.73 (d, J = 6.3 Hz, 3H), 0.17 (s, 12H), 0.07 (s, 3H), −0.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.6, 145.7, 111.8, 111.5, 77.8, 74.2, 62.5, 49.4, 37.0, 32.5, 27.1, 26.0, 25.8, 23.3, 22.5, 18.4, 18.2, −4.2, −4.3, −5.0 ppm; IR (neat) ν_{max} 3405, 2952, 2855, 1578, 1453, 1162 cm^{-1}; HRMS (ESI) m/z calcd for $C_{33}H_{66}O_5Si_3Na$ [M + Na]$^+$ 649.4116, found 649.4117.

Following the same experimental procedure as for compound **13**, the above diol compound (105 mg) was converted to the corresponding primary pivolyl-protected compound (94 mg, 79%, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.4 (20% EtOAc in hexane); $[\alpha]^{24}_D$ = −9.6 (c 7.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (d, J = 2.1 Hz, 2H), 6.21 (t, J = 2.1 Hz, 1H), 4.68 (d, J = 4.5 Hz, 1H), 4.26−4.08 (m, 2H), 3.89 (dd, J = 1.9, 9.6 Hz, 1H), 1.84−1.72 (m, 1H), 1.66−1.55 (m, 2H), 1.42−1.17 (m, 2H), 1.17 (s, 9H), 0.96 (s, 18H), 0.90 (s, 9H), 0.81 (d, J = 6.3 Hz, 3H), 0.77 (d, J = 6.0 Hz, 3H), 0.16 (s, 12H), 0.05 (s, 3H), −0.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.9, 156.6, 146.0, 111.8, 111.4, 77.6, 69.0, 61.9, 49.2, 38.8, 34.6, 33.0, 27.3, 27.0, 26.0, 25.8, 23.3, 22.6, 18.3, 18.2, −4.2, −4.3, −4.4, −5.0 ppm; IR (neat) ν_{max} 3423, 2952, 2928, 1729, 1451, 1249, 1162 cm^{-1}; HRMS (ESI) m/z calcd for $C_{38}H_{74}Si_3O_6Na$ [M + Na]$^+$ 733.4691, found 733.4690.

Following the same experimental procedure as for compound **13**, the above pivolyl-protected compound (80 mg) was converted to the corresponding secondary diol compound (56 mg, 83%, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.4 (20% EtOAc in hexane); $[\alpha]^{26}_D$ = +2.8 (c 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.45 (d, J = 2.1 Hz, 2H), 6.21 (t, J = 2.0 Hz, 1H), 4.92 (s, 1H), 4.41−4.32 (m, 1H), 4.18−4.10 (m, 1H), 4.01 (d, J = 9.3 Hz, 1H), 3.13 (s, 1H), 3.00 (s, 1H), 1.91−1.71 (m,), 1.63−1.62 (m, 1H), 1.44−1.35 (m, 1H), 1.29−1.23 (m, 1H), 1.21 (s, 9H), 1.12−1.03 (m, 1H), 0.97 (s, 18H), 0.73 (d, J = 6.6 Hz, 3H), 0.55 (d, J = 6.3 Hz, 3H), 0.17 (s, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.4, 156.6, 145.9, 111.0, 111.0, 77.8, 72.9, 62.0, 47.6, 39.0, 34.7, 30.6, 27.4, 27.4, 25.9, 22.8, 22.7, 18.4, −4.2 ppm; IR (neat) ν_{max} 3454, 2958, 2928, 1731, 1589, 1452, 1254 cm^{-1}; HRMS (ESI) m/z calcd for $C_{32}H_{60}O_6Si_2Na$ [M + Na]$^+$ 619.3826, found 619.3829.

Following the same experimental procedure as for compound **13**, the above diol compound (40 mg) was converted to the corresponding acetonide-protected compound (38 mg, 90%, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.4 (2% EtOAc in hexane); $[\alpha]^{26}_D$ = −17.1 (c 2.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (d, J = 2.1 Hz, 2H), 6.20 (t, J = 2.1 Hz, 1H), 4.94 (d, J = 1.5 Hz, 1H), 4.20−4.16 (m, 3H), 1.92−1.80 (m, 1H), 1.77−1.66 (m, 1H), 1.47 (s, 3H), 1.45 (s, 3H), 1.43−1.40 (m, 1H), 1.23 (s, 9H), 1.22−1.16 (m, 2H), 0.97 (s, 18H), 0.89−0.83 (m, 1H), 0.69 (d, J = 6.3 Hz, 3H), 0.46 (d, J = 6.3 Hz, 3H), 0.18 (s, 6H) 0.18 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.7, 156.4, 143.3, 111.1, 110.7, 99.4, 75.1, 70.5, 61.4, 41.7, 38.9, 32.6, 30.4, 30.0, 27.6, 27.4, 25.9, 22.9, 22.6, 19.6, 18.4, −4.2, −4.2 ppm; IR (neat) ν_{max} 2956, 2927, 1728, 1593, 1255, 1163 cm^{-1}; HRMS

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(ESI) m/z calcd for $C_{35}H_{64}O_6Si_2Na$ $[M + Na]^+$ 659.4139, found 659.4137.

Following the same experimental procedure as for compound **13**, the above acetonide-protected compound (15 mg) was converted to the corresponding alcohol compound **42a** (12 mg, 89%, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.2 (10% EtOAc in hexane); $[\alpha]^{27}_D$ = −15.5 (c 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.42 (d, J = 2.1 Hz, 2H), 6.20 (t, J = 2.1 Hz, 1H), 4.97 (d, J = 1.5 Hz, 1H), 4.32 (dt, J = 2.0, 10.1 Hz, 1H), 3.79 (m, 2H), 2.41 (m, 1H), 1.93 (dddd, J = 4.3, 8.2, 10.5, 14.1 Hz, 1H), 1.58 (m, 1H), 1.52 (s, 3H), 1.48 (s, 3H), 1.44 (m, 1H), 1.24 (m, 1H), 1.15 (ddd, J = 4.3, 7.2, 14.2 Hz, 1H), 0.97(s, 18H), 0.89 (m, 1H), 0.69 (d, J = 6.6 Hz, 3H), 0.45 (d, J = 6.6 Hz, 3H), 0.18 (s, 6H) 0.17 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.5, 143.1, 111.0, 110.7, 99.5, 75.0, 74.6, 61.9, 41.9, 35.6, 30.5, 30.1, 27.7, 25.9, 22.9, 22.6, 19.9, 18.4, −4.2, −4.2 ppm; IR (neat) ν_{max} 3372, 2956, 2928, 1481, 1233 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{56}O_5Si_2Na$ $[M + Na]^+$ 575.3564, found 575.3563.

(3*S*,4*R*)-Methyl 4-((*S*)-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)-phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-6-methyl-3-((triethylsilyl)oxy)heptanoate (43). Following the same experimental procedure described in the synthesis of compound **32**, compound **42** (4.82 g) was converted to the corresponding ester (3.49 g, 92%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) as a yellowish oil: R_f = 0.4 (10% EtOAc in hexane); $[\alpha]^{24}_D$ = −16.7 (c 2.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.44 (d, J = 2.1 Hz, 2H), 6.22 (t, J = 2.1 Hz, 1H), 4.73 (d, J = 5.1 Hz, 1H), 4.08−4.05 (m, 1H), 3.67 (s, 3H), 2.77 (d, J = 2.4 Hz, 1H), 2.58 (dd, J = 9.6, 15.9 Hz, 1H), 2.34 (d, J = 3.8 Hz, 15.9 Hz, 1H), 1.62−1.60 (m, 1H), 1.45−1.28 (m, 3H), 0.97 (s, 18H), 0.90 (s, 9H), 0.81 (d, J = 6 Hz, 3H), 0.76 (d, J = 6 Hz, 3H), 0.17 (s, 12H), 0.06 (s, 3H), −0.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.4, 156.4, 146.2, 112.1, 111.4, 77.3, 69.3, 51.8, 48.7, 39.7, 33.2, 27.3, 26.1, 25.8, 23.0, 22.8, 18.4, 18.2, −4.2, −4.9 ppm; IR (neat) ν_{max} 3438, 2929, 1746, 1650, 1549, 1456, 1160 cm^{-1}; HRMS (ESI) m/z calcd for $C_{34}H_{66}O_6Si_3Na$ $[M + Na]^+$ 677.4065, found 677.4067.

Following the same experimental procedure described in the synthesis of compound **32**, the above ester compound (1.33 g) was converted to compound **43** (1.45 mg, 93%, purification by flash column chromatography, SiO_2, 60−120 mesh, 3−4% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.7 (3% EtOAc in hexane); $[\alpha]^{24}_D$ = −33.4 (c 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.40 (d, J = 2.1 Hz, 2H), 6.18 (t, J = 2.3 Hz, 1H), 5.12 (d, J = 2.1 Hz, 1H), 4.30−4.24 (m, 1H), 3.66 (s, 3H), 2.67 (dd, J = 9, 15.6, Hz, 1H), 2.53 (dd, J = 3, 15.6, Hz, 1H), 1.72−1.65 (m, 1H), 1.38−1.08 (m, 3H), 1.01−0.94 (m, 36H), 0.78 (d, J = 6.3 Hz, 3H), 0.66−0.58 (m, 9H), 0.16 (s, 6H), 0.16 (s, 6H), 0.11 (s, 3H), −0.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.7, 156.1, 148.0, 112.2, 110.8, 72.0, 70.3, 51.5, 50.1, 39.0, 33.2, 26.3, 25.8, 25.4, 23.9, 21.8, 18.4, 18.2, 7.1, 5.3, −3.8, −4.2, −4.3, −4.6 ppm; IR (neat) ν_{max} 2956, 1743, 1542, 1454, 1162 cm^{-1}; HRMS (ESI) m/z calcd for $C_{40}H_{80}O_6Si_4Na$ $[M + Na]^+$ 791.4930, found 791.4932.

Dimethyl ((4*S*,5*R*)-5-((*S*)-(3,5-bis((*tert*-butyldimethylsilyl)-oxy)phenyl)((*tert*-butyldimethyl silyl)oxy)methyl)-7-methyl-2-oxo-4-((triethylsilyl)oxy)octyl)phosphonate (36). Following the same experimental procedure as for compound **31**, compound **43** (1.31 g) was converted to compound **36** (1.17 g, 81%, purification by flash column chromatography, SiO_2, 100−200 mesh, 60% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.2 (60% EtOAc in hexane); $[\alpha]^{25}_D$ = −27.5 (c 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, J = 2.1 Hz, 2H), 6.18 (t, J = 2.3 Hz, 1H), 5.12 (d, J = 1.5 Hz, 1H), 4.36−4.31 (m, 1H), 3.81 (d, J = 3.6 Hz, 3H), 3.77 (d, J = 3.6 Hz, 3H), 3.17−2.80 (m, 4H), 1.67−1.64 (m, 1H), 1.25−1.17 (m, 3H), 1.00−0.95 (m, 36H), 0.75 (d, J = 5.7 Hz, 3H), 0.67−0.58 (m, 9H), 0.16 (s, 6H), 0.16 (s, 6H), 0.13 (m, 3H), −0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.5, 156.1, 147.9, 112.1, 110.9, 71.9, 68.6, 53.2, 53.1, 53.0, 52.9, 50.0, 48.6, 43.1, 33.1, 26.3, 25.8, 25.5, 23.8, 21.8, 18.4, 18.2, 7.2, 5.3, −3.8, −4.2, −4.3, −4.5 ppm; IR (neat) ν_{max} 2957, 2880, 1717, 1543, 1459, 1260, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{42}H_{85}O_8Si_4PNa$ $[M + Na]^+$ 883.4957, found 883.4955.

(4*R*,5*S*,10*S*,12*S*,14*R*,*E*)-15-(Benzyloxy)-4-((*S*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)-methyl)-2,10,12,14-tetramethyl-5-((triethylsilyl)oxy)pentadec-8-en-7-one (44). Following the same experimental procedure as for compound **30**, compound **36** (490 mg) and aldehyde **24** (dr = 9.4:1.0, 136 mg) were converted to product **44** (486 mg, 86%, purification by flash column chromatography, SiO_2, 60−120 mesh, 4−5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (2% EtOAc in hexane); $[\alpha]^{29}_D$ = −33.9 (c 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.27 (m, 5H), 6.70 (q, J = 8.0 Hz, 1H), 6.41 (d, J = 2.1 Hz, 2H), 6.18 (t, J = 2.3 Hz, 1H), 6.05 (d, J = 15.9 Hz, 1H), 5.19 (d, J = 1.2 Hz, 1H), 4.50 (s, 2H), 4.44−4.39 (m, 1H), 3.31−3.20 (m, 2H), 2.98 (dd, J = 8.6, 16.4 Hz, 1H), 2.59 (dd, J = 1.8, 16.2 Hz, 1H), 2.45−2.36 (m, 1H), 1.91−1.80 (m, 1H), 1.73−1.66 (m, 1H), 1.55−1.48 (m, 1H), 1.34−1.05 (m, 7H), 1.03−0.92 (m, 39H), 0.86 (dd, J = 6.6, 8.4, 6H), 0.76 (d, J = 6.3 Hz, 3H), 0.64−0.56 (q, J = 7.8 Hz, 9H), 0.17−0.14 (m, 15H), −0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.6, 156.1, 153.1, 148.3, 138.9, 129.7, 128.5, 127.7, 127.6, 112.2, 110.8, 76.7 (merged with $CDCl_3$), 73.1, 72.0, 69.3, 50.4, 44.7, 44.1, 41.0, 34.5, 33.2, 31.1, 27.8, 26.4, 25.9, 25.3, 23.9, 21.8, 19.9, 19.8, 18.4, 18.2, 17.0, 7.2, 5.3, −3.7, −4.2, −4.3, −4.3 ppm; IR (neat) ν_{max} 2955, 2930, 1593, 1453, 1258, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{57}H_{104}O_6Si_4Na$ $[M + Na]^+$ 1019.6808, found 1019.6808.

(4*R*,5*S*,10*R*,12*S*,14*R*)-4-((*S*)-(3,5-Bis((*tert*-butyldimethylsilyl)-oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-15-hydroxy-2,10,12,14-tetramethyl-5-((triethylsilyl)oxy)pentadecan-7-one (45). Following the same experimental procedure as for compound **29**, compound **44** (450 mg) was converted to compound **45** (422 mg, 94%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.3 (2% EtOAc in hexane); $[\alpha]^{29}_D$ = −30.1 (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.40 (d, J = 2.1 Hz, 2H), 6.18 (t, J = 2.1 Hz, 1H), 5.16 (s, 1H), 4.39−4.34 (m, 1H), 3.51−3.38 (m, 2H), 2.85 (dd, J = 8.7, 16.8 Hz, 1H), 2.53 (dd, J = 2.1, 16.8 Hz, 1H), 2.47−2.28 (m, 2H), 1.78−1.60 (m, 3H), 1.54−1.34 (m, 4H), 1.28−1.02 (m, 6H), 0.99−0.90 (m, 39H), 0.83 (dd, J = 6.5, 8.0 Hz, 6H), 0.75 (d, J = 6.3 Hz, 3H), 0.65−0.57 (m, 9H), 0.16−0.13 (m, 15H), −0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 210.9, 156.1, 148.1, 112.1, 110.8, 71.9, 69.1, 69.1, 50.2, 46.6, 45.7, 42.5, 41.6, 33.3, 33.1, 31.4, 30.0, 27.4, 26.3, 25.8, 25.3, 23.9, 21.8, 19.5, 19.3, 18.4, 18.2, 16.6, 7.2, 5.3, −3.7, −4.2, −4.3, −4.4 ppm; IR (neat) ν_{max} 3410, 2955, 1720, 1592, 1451, 1260, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{50}H_{100}O_6Si_4Na$ $[M + Na]^+$ 931.6495, found 931.6497.

(2*R*,4*S*,6*R*,9*S*,11*S*,12*R*)-12-((*S*)-(3,5-Bis((*tert*-butyldimethylsil-yl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)methyl)-2,4,6,14-tetramethylpentadecane-1,9,11-triol (46). Following the same experimental procedure as described in the preparation of compound **33**, compound **45** (401 mg) was converted to the corresponding mixture of alcohols (dr = 11:1) by DIBAL-H, which were separated to obtain the major alcohol isomer (283 mg, 70%) by column chromatography (SiO_2, 230−400 mesh, 5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.4 (10% EtOAc in hexane); $[\alpha]^{30}_D$ = −16.7 (c 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.42 (d, J = 2.4, 2H), 6.18 (t, J = 2.1 Hz, 1H), 5.01 (d, J = 2.1 Hz, 1H), 4.01−3.95 (m, 1H), 3.63−3.56 (m, 1H), 3.49 (dd, J = 5.7, 10.5 Hz, 1H), 3.39 (dd, J = 6.6, 10.5 Hz, 1H), 3.07 (s, 1H), 1.92−1.67 (m, 2H), 1.60−1.53 (m, 1H), 1.52−1.05 (m, 13H), 1.04−0.97 (m, 27H), 0.93−0.89 (m, 12H), 0.86−0.79 (m, 9H), 0.74−0.64 (m, 9H), 0.17 (s, 6H), 0.16 (s, 6H), 0.11 (s, 3H), −0.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.1, 148.1, 112.3, 110.9, 75.1, 75.0, 72.7, 72.5, 69.1, 49.9, 45.7, 41.7, 39.3, 35.5, 33.7, 33.6, 33.4, 30.4, 27.4, 26.3, 25.8, 23.9, 22.1, 19.7, 19.4, 18.4, 18.2, 16.7, 7.2, 5.6, −3.8, −4.2, −4.3, −4.4 ppm; IR (neat) ν_{max} 2958, 2928, 1592, 1454, 1253, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{50}H_{102}O_6Si_4Na$ $[M + Na]^+$ 933.6651, found 933.6653.

Following the same experimental procedure as described in the preparation of compound **16**, the above alcohol (270 mg) was converted to compound **46** (198 mg, 84%, purification by flash column chromatography, SiO_2, 60−120 mesh, 20% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.2 (20% EtOAc in hexane); $[\alpha]^{28}_D$ = −7.3 (c 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (d, J = 2.1, 2H), 6.20 (t, J = 2.1 Hz, 1H), 4.72 (d, J = 4.2 Hz, 1H), 4.09 (d, J =

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J. Org. Chem. 2017, 82, 2414−2435

10.2 Hz, 1H), 3.76−3.71 (m, 1H), 3.58 (s, 1H), 3.47 (dd, J = 5.7, 10.2 Hz, 1H), 3.37 (dd, J = 6.6, 10.5 Hz, 1H), 2.71 (s, 1H), 1.77−1.63 (m, 3H), 1.56−1.55 (m, 2H), 1.45−1.25 (m, 7H), 1.19−1.00 (m, 5H), 0.97 (s, 18H), 0.91−0.88 (m, 10H), 0.85−0.79 (m, 11H), 0.74 (d, J = 5.7 Hz, 3H), 0.17 (s, 12H), 0.06 (s, 3H), −0.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.6, 145.8, 111.8, 111.4, 77.6, 74.7, 73.4, 69.0, 49.6, 45.6, 41.6, 41.5, 35.5, 33.5, 33.3, 32.7, 30.4, 27.4, 27.0, 26.1, 25.8, 23.2, 22.6, 19.7, 19.4, 18.4, 18.2, 16.7, −4.2, −4.3, −5 ppm; IR (neat) ν_{max} 3364, 2956, 2859, 1593, 1451, 1253, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{44}H_{88}O_6Si_3Na$ $[M + Na]^+$ 819.5787, found 819.5786.

(2*R*,4*S*,6*R*)-8-((4*S*,6*S*)-6-((1*S*,2*R*)-1-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-1-((*tert*-butyldimethylsilyl)-oxy)-4-methylpentan-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)-2,4,6-trimethyloctan-1-ol (47). Following the same experimental procedure as described in the preparation of compound **28**, compound **46** (230 mg) was converted to compound **47** (203 mg, 93%, purification by flash column chromatography, SiO_2, 60−120 mesh, 4% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{29}_D$ = −13.5 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, J = 2.1, 2H), 6.20 (t, J = 2.1 Hz, 1H), 4.56 (d, J = 6.3 Hz, 1H), 3.59−3.53 (m, 2H), 3.47 (dd, J = 5.7, 10.2 Hz, 1H), 3.38 (dd, J = 6.6, 10.2 Hz, 1H), 1.77−1.37 (m, 9H), 1.33 (s, 3H), 1.30−1.28 (m, 3H), 1.25 (m, 3H), 1.18−1.01 (m, 5H), 0.97 (s, 18H), 0.90−0.87 (m, 12H), 0.84−0.79 (m, 12H), 0.17 (s, 12H), 0.04 (s, 3H), −0.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.1, 147.2, 112.7, 110.9, 98.3, 75.9, 69.9, 69.3, 69.1, 49.7, 45.7, 41.5, 34.9, 34.2, 33.3, 32.9, 30.4, 30.2, 27.8, 27.3, 26.1, 25.9, 23.1, 22.9, 19.9, 19.7, 19.4, 18.4, 18.4, 18.3, 16.6, −4.1, −4.1, −4.2, −4.6 ppm; IR (neat) ν_{max} 3353, 2955, 2930, 1594, 1455, 1256, 1161 cm^{-1}; HRMS (ESI) m/z calcd for $C_{47}H_{92}O_6Si_3Na$ $[M + Na]^+$ 859.6099, found 859.6097.

(4*R*,6*S*,8*R*)-10-((4*S*,6*S*)-6-((1*S*,2*R*)-1-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-1-((*tert*-butyldimethylsilyl)-oxy)-4-methylpentan-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)-4,6,8-trimethyldecan-3-one (48). Following the same DMP oxidation procedure as for compound **34**, compound **47** (100 mg) was converted to the corresponding aldehyde (99 mg, quantitative, purification by flash column chromatography, SiO_2, 60−120 mesh, EtOAc as eluent) as a colorless oil, which was directly used for the next step without further characterization.

Following the same experimental procedure as described in the preparation of compound **34**, the above aldehyde (99 mg) was converted to the corresponding alcohols by treatment with EtMgBr. Purification of the crude mixture using flash column chromatography (SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) afforded an inseparable mixture of the corresponding alcohols (77 mg, 75%) as a colorless oil, which was used for the next reaction without further characterization.

Following the same DMP oxidation procedure as described in the preparation of compound **34**, the above mixture of alcohols (77 mg) was converted to compound **48** (61 mg, 79%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.7 (3% EtOAc in hexane); $[\alpha]^{27}_D$ = −22.5 (c 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, J = 2.4, 2H), 6.20 (t, J = 2.1 Hz, 1H), 4.56 (d, J = 6.0 Hz, 1H), 3.59−3.53 (m, 2H), 2.67−2.55 (m, 1H), 2.45 (q, J = 7.5 Hz, 2H), 1.60−1.54 (m, 1H), 1.50−1.37 (m, 7H), 1.33 (s, 3H), 1.29−1.27 (m, 4H), 1.25 (s, 3H), 1.21−1.16 (m, 2H), 1.06−1.01 (m, 8H), 0.97 (s, 18H), 0.87 (s, 9H), 0.84−0.77 (m, 12H), 0.17 (s, 12H), 0.03 (s, 3H), −0.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 215.7, 156.1, 147.1, 112.6, 110.9, 98.3, 75.8, 69.8, 69.3, 49.6, 45.0, 43.9, 41.3, 34.9, 34.9, 34.3, 34.2, 33.1, 30.4, 30.3, 28.1, 27.8, 26.1, 25.9, 23.1, 22.9, 19.9, 19.5, 19.4, 18.4, 18.2, 16.6, 8.0, −4.1, −4.2, −4.2, −4.6 ppm; IR (neat) ν_{max} 2956, 1716, 1591, 1455, 1254, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{49}H_{94}O_6Si_3Na$ $[M + Na]^+$ 885.6256, found 885.6254.

(4*R*,6*S*,8*R*,11*S*,13*S*,14*R*)-14-((*S*)-(3,5-Dihydroxyphenyl)-(hydroxy)methyl)-11,13-dihydroxy-4,6,8,16-tetramethylheptadecan-3-one (35). Following the same experimental procedure as for compound **1**, compound **48** (25 mg) was converted to compound **35** (13 mg, 91%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% MeOH in CH_2Cl_2 as eluent) as a yellowish oil: R_f = 0.2 (6% MeOH in CH_2Cl_2); $[\alpha]^{29}_D$ = −13.3 (c 0.6, MeOH); ^{1}H NMR (CD_3OD, 300 MHz) δ 6.33 (d, J = 2.1, 2H), 6.12 (t, J = 2.1 Hz, 1H), 4.83 (1H), 3.98 (ddd, 8.3, 4.4, 2.9 Hz, 1H), 3.69 (m, 1H), 2.69 (m, 1H), 2.52 (m, 2H), 1.68 (m, 1H), 1.65 (m, 2H), 1.49 (m, 2H), 1.48 (m, 1H), 1.46 (m, 1H), 1.40 (m, 2H), 1.39 (m, 1H), 1.23 (m, 2H), 1.20 (m, 1H), 1.16 (m, 1H), 1.09 (m, 2H), 1.04 (m, 3H), 1.03 (m, 3H), 0.84 (d, J = 6.0 Hz, 3H), 0.83 (d, J = 6.0 Hz, 3H), 0.77 (d, J = 6.0 Hz, 3H), 0.63 (d, J = 6.0 Hz, 3H); ^{13}C NMR (CD_3OD, 75 MHz) δ 218.4, 159.3, 148.6, 105.7, 102.0, 76.8, 75.1, 72.4, 49.3, 46.0, 44.9, 42.4, 42.3, 36.0, 35.1, 34.5, 33.4, 31.4, 29.3, 28.3, 23.4, 23.0, 20.0, 19.8, 17.0, 8.1 ppm; IR (neat) ν_{max} 3360, 2928, 2803, 1701, 1602, 1455, 1156 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{48}O_6Na$ $[M + Na]^+$ 503.3349, found 503.3347.

(*S*)-4-Benzyl-3-((4*S*,6*S*,*E*)-7-((*tert*-butyldiphenylsilyl)oxy)-4,6-dimethylhept-2-enoyl)oxazolidin-2-one (52). Following the same Swern oxidation experimental procedure as described in the preparation of compound **17**, compound **6** (1.93 g) was converted to the corresponding aldehyde (1.92 g, quantitative, flash column chromatography, SiO_2, 60−120 mesh, 20% EtOAc in hexane as eluent) as a colorless oil, which was used for the next step without further characterization.

Following the same experimental procedure as for compound **19**, the above aldehyde compound (1.92 g) and phosphonate **51** (2.04 g) were converted to compound **52** (2.39 g, 81%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.5 (5% EtOAc in hexane); $[\alpha]^{25}_D$ = +32.0 (c 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.68−7.64 (m, 4H), 7.41−7.06 (m, 13H), 4.74−4.69 (m, 1H), 4.20−4.15 (m, 2H), 3.50−3.46 (m, 2H), 3.35 (dd, J = 3.0, 13.2 Hz, 1H), 2.78 (dd, J = 9.9, 13.5 Hz, 1H), 2.50−2.40 (m, 1H), 1.78−1.67 (m, 1H), 1.55−1.48 (m, 1H), 1.22−1.18 (m, 1H), 1.06−1.04 (m, 12H), 0.93 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.4, 157.6, 153.5, 135.8, 135.6, 134.1, 129.7, 129.6, 129.1, 127.8, 127.4, 118.5, 68.7, 66.2, 55.6, 39.6, 38.1, 38.1, 34.7, 33.5, 27.0, 19.5, 17.3 ppm; IR (neat) ν_{max} 1778, 1677, 1353, 1215 cm^{-1}; HRMS (ESI) m/z calcd for $C_{35}H_{43}O_4SiNNa$ $[M + Na]^+$ 592.2859 found 592.2858.

(*S*)-4-Benzyl-3-((4*R*,6*S*)-7-((*tert*-butyldiphenylsilyl)oxy)-4,6-dimethylheptanoyl)oxazolidin-2-one (53). Following the same experimental procedure as for compound **19**, compound **52** (1.97 g) was converted to compound **53** (1.91 g, 95%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) as a colorless oil. R_f = 0.4 (5% EtOAc in hexane); $[\alpha]^{25}_D$ = +12.0 (c 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69−7.66 (m, 4H), 7.45−7.20 (m, 11H), 4.69−4.64 (m, 1H), 4.22−4.15 (m, 2H), 3.52−3.42 (m, 2H), 3.30 (dd, J = 3.3, 13.5 Hz, 1H), 3.05−2.83 (m, 2H), 2.76 (dd, J = 9.6, 13.2, 1H), 1.82−1.60 (m, 2H), 1.55−1.47 (m, 1H), 1.34−1.19 (m, 2H), 1.14−1.09 (m, 1H), 1.06 (s, 9H), 0.91−0.88 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.8, 153.6, 135.8, 135.5, 134.3, 129.6, 129.6, 129.1, 127.7, 127.5, 69.6, 66.3, 55.3, 40.6, 38.1, 33.5, 33.4, 32.3, 29.9, 27.0, 19.5, 19.3, 16.8 ppm; IR (neat) ν_{max} 2928, 1784, 1697, 1387, 1211, 1110 cm^{-1}; HRMS (ESI) m/z calcd for $C_{35}H_{45}O_4SiNNa$ $[M + Na]^+$ 594.3016 found 594.3018.

(*S*)-4-Benzyl-3-((2*S*,4*S*,6*S*)-7-((*tert*-butyldiphenylsilyl)oxy)-2,4,6-trimethylheptanoyl)oxazolidin-2-one (54). Following the same experimental procedure as for compound **20**, compound **53** (1.71 g) was converted to compound **54** (1.16 g, 66%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.4 (10% EtOAc in hexane); $[\alpha]^{25}_D$ = +10.4 (c 2.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69−7.65 (m, 4H), 7.42−7.19 (m, 11H), 4.66−4.59 (m, 1H), 4.14 (d, J = 5.1 Hz, 2H), 3.92−3.81 (m, 1H), 3.53−3.41 (m, 2H), 3.25 (dd, J = 3.2, 13.5 Hz, 1H), 2.76 (dd, J = 9.6, 13.5 Hz, 1H), 1.85−1.71 (m, 2H), 1.54−1.41 (m, 1H), 1.27−1.15 (m, 5H), 1.12−1.08 (m, 1H), 1.06 (s, 9H), 0.90 (d, J = 6.6 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.5, 153.1, 135.8, 135.5, 134.3, 129.6, 129.1, 127.7, 127.7, 127.5, 69.6, 66.1, 55.4, 41.6, 40.6, 38.0, 35.5, 33.3, 28.2, 27.0, 19.9, 19.5, 18.4, 16.8 ppm; IR (neat) ν_{max} 2929, 1784, 1695, 1540, 1521, 1390, 1236 cm^{-1}; HRMS (ESI) m/z calcd for $C_{36}H_{47}O_4SiNNa$ $[M + Na]^+$ 608.3172 found 608.3171.

(2*S*,4*S*,6*S*)-7-(Benzyloxy)-2,4,6-trimethylheptan-1-ol (55). Following the same experimental procedure described in the synthesis

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of compound **21**, compound **54** (1.73 g) was converted to the corresponding alcohol (1.06 g, 87%, purification by flash column chromatography, SiO_2, 60−120 mesh, 4−5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.3 (10% EtOAc in hexane); $[\alpha]^{25}_D$ = −11.4 (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69−7.66 (m, 4H), 7.45−7.35 (m, 6H), 3.51−3.31 (m, 4H), 1.81−1.50 (m, 3H), 1.29−1.20 (m, 2H), 1.14−1.08 (m, 1H), 1.06 (s, 9H), 1.01−0.94 (m, 1H), 0.91 (d, *J* = 4.8 Hz, 3H), 0.89 (d, *J* = 4.8 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.8, 134.3, 129.6, 127.7, 69.8, 68.6, 41.9, 40.4, 33.3, 33.2, 27.4, 27.0, 20.4, 19.5, 17.3, 16.7 ppm; IR (neat) ν_{max} 3365, 2927, 2857, 1454, 1117 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{40}O_2SiNa$ $[M + Na]^+$ 435.2695 found 435.2697.

Following the same experimental procedure described in the synthesis of compound **23**, the above alcohol (1.13 g) was converted to the corresponding benzylated compound (1.16 g, 84%, purification by flash column chromatography, SiO_2, 60−120 mesh, 3−4% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.5 (3% EtOAc in hexane); $[\alpha]^{25}_D$ = −4.0 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.68−7.65 (m, 4H), 7.44−7.24 (m, 11H), 4.48 (d, *J* = 3 Hz, 2H), 3.50−3.38 (m, 2H), 3.32 (dd, *J* = 5.1, 9 Hz, 1H), 3.17 (dd, *J* = 6.9, 9 Hz, 1H), (m, 2H), 1.88−1.66 (m, 2H) 1.53−1.50 (m, 1H), 1.31−1.20 (m, 1H), 1.17−0.97 (m, 12H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.0, 135.8, 134.3, 129.6, 128.4, 127.7, 127.6, 127.5, 76.3, 73.1, 69.9, 42.5, 40.5, 33.4, 31.0, 27.4, 27.1, 20.4, 19.5, 18.0, 16.6 ppm; IR (neat) ν_{max} 2928, 2856, 1108 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{33}H_{46}O_2SiNa$ $[M + Na]^+$ 525.3165 found 525.3167.

Following the same synthetic procedure described in the synthesis of compound **23**, the above benzylated compound (1.04 g) was converted to compound **55** (481 mg, 88%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.3 (20% EtOAc in hexane); $[\alpha]^{26}_D$ = −1.4 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38−7.24 (m, 5H), 4.50 (d, *J* = 2.7 Hz, 2H), 3.48−3.39 (m, 2H), 3.33 (dd, *J* = 5.4, 9 Hz, 1H), 3.22 (dd, *J* = 6.9, 9 Hz, 1H), 1.93−1.82 (m, 1H), 1.77−1.60 (m, 2H) 1.37−1.26 (m, 2H), 1.11−0.97 (m, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 4.5 Hz, 3H), 0.86 (d, *J* = 4.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.0, 128.5, 127.7, 127.6, 76.3, 73.2, 69.3, 42.5, 40.4, 33.3, 31.0, 27.4, 20.3, 18.0, 16.4 ppm; IR (neat) ν_{max} 3368, 2920, 1107 cm$^{-1;}$ HRMS (ESI) *m*/*z* calcd for $C_{17}H_{28}O_2Na$ $[M + Na]^+$ 287.1987 found 287.1985.

(2*S*,4*R*,6*S*)-7-(Benzyloxy)-2,4,6-trimethylheptanal (50). Following the same Swern oxidation conditions described in the synthesis of compound **12**, compound **55** (170 mg) was converted to an inseparable mixture (dr = 8.9:1.0) of aldehyde **50** (169 mg, quantitative, flash column chromatography, SiO_2, 60−120 mesh, 20% EtOAc in hexane as eluent) as a colorless oil, which was used for the next reaction: R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{26}_D$ = +0.9 (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.60 (s, 1H), 7.41−7.28 (m, 5H), 4.53−4.46 (m, 2H), 3.34−3.21 (m, 2H), 2.44−2.39 (m, 1H), 1.90−1.81 (m, 1H), 1.66−1.63 (m, 1H), 1.50−1.26 (m, 4H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 205.4, 138.9, 128.5, 127.9, 127.6, 76.0, 73.2, 44.3, 42.1, 37.4, 31.0, 27.8, 20.1, 18.0, 13.4 ppm; IR (neat) ν_{max} 2928, 2856, 1722, 1432, 1228 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{26}O_2Na$ $[M + Na]^+$ 285.1830, found 285.1829.

(4*R*,5*S*,10*S*,12*S*,14*S*,*E*)-15-(Benzyloxy)-4-((*S*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)-methyl)-2,10,12,14-tetramethyl-5-((triethylsilyl)oxy)pentadec-8-en-7-one (56). Following the same experimental procedure as for compound **30**, compound **36** (550 mg) and aldehyde **50** (169 mg) were converted to compound **56** (535 mg, 84%, purification by flash column chromatography, SiO_2, 60−120 mesh, 4−5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (2% EtOAc in hexane); $[\alpha]^{26}_D$ = −16.1 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34−7.25 (m, 5H), 6.73 (q, *J* = 7.7 Hz, 1H), 6.41 (d, *J* = 2.1 Hz, 2H), 6.18 (t, *J* = 2.3 Hz, 1H), 6.05 (dd, *J* = 0.9, 15.9 Hz, 1H), 5.18 (d, *J* = 1.2 Hz, 1H), 4.49 (s, 2H), 4.45−4.38 (m, 1H), 3.33 (dd, *J* = 5.1, 9 Hz, 1H), 3.19 (dd, *J* = 6.9, 9 Hz, 1H), 2.98 (dd, *J* = 8.6, 16.4 Hz, 1H), 2.58 (dd, *J* = 2.0, 15.3 Hz, 1H), 2.44−2.35 (m, 1H), 1.91−1.80 (m, 1H), 1.72−1.66 (m, 1H), 1.53−1.51 (m, 1H), 1.39−1.06 (m, 7H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.97−0.92 (m, 39H), 0.88 (d, *J* = 6.6, 3H), 0.76 (d, *J* = 6.0 Hz, 3H), 0.64−0.56 (m, 9H), 0.17−0.14 (m, 15H), −0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.5, 156.1, 153.2, 148.2, 139.0, 129.5, 128.5, 127.6, 127.5, 112.2, 110.8 76.1, 73.2, 72.1, 69.4, 50.5, 44.1, 43.7, 42.0, 34.4, 33.2, 31.1, 28.0, 26.4, 25.9, 25.4, 23.9, 21.8, 20.5, 19.2, 18.4, 18.2, 18.2, 7.2, 5.3, −3.7, −4.2, −4.3 ppm; IR (neat) ν_{max} 2953, 2927, 1595,1453, 1256, 1162 cm^{-1}; HRMS (ESI) *m*/*z* calcd for HRMS (ESI) *m*/*z* calcd for $C_{57}H_{104}O_6Si_4Na$ $[M + Na]^+$ 1019.6808, found 1019.6808.

(4*R*,5*S*,10*R*,12*S*,14*S*)-15-(Benzyloxy)-4-((*S*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)-methyl)-2,10,12,14-tetramethyl-5-((triethylsilyl)oxy)-pentadecan-7-one (57). Following the same experimental procedure as for compound **20**, compound **56** (510 mg) was converted to compound **57** (480 mg, 94%, purification by flash column chromatography, SiO_2, 60−120 mesh, 4−5% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (2% EtOAc in hexane); $[\alpha]^{28}_D$ = −27.2 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.28 (m, 5H), 6.40 (d, *J* = 2.1 Hz, 2H), 6.18 (t, *J* = 2.3 Hz, 1H), 5.16 (d, *J* = 0.9 Hz, 1H), 4.50 (d, *J* = 3 Hz, 2H), 4.39−4.34 (m, 1H), 3.34 (dd, *J* = 5.3, 9 Hz, 1H), 3.21 (dd, *J* = 7.21, 9 Hz, 1H), 2.85 (dd, *J* = 8.7, 16.5 Hz, 1H), 2.53 (dd, *J* = 2.1, 16.8 Hz, 1H), 2.42−2.34 (m, 2H), 1.92−1.81 (m, 1H), 1.68−1.59 (m, 2H), 1.54−1.38 (m, 3H), 1.33-(m, 2H), 1.23−1.02 (m, 7H), 0.99−0.92 (m, 39H), 0.84−0.82 (m, 6H), 0.75 (d, *J* = 6.0 Hz, 3H), 0.66−0.57 (m, 9H), 0.16−0.13 (m, 15H), −0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.9, 156.1, 148.2, 139.1, 128.5, 127.6, 127.5, 112.1, 110.8, 76.4, 73.2, 72.0, 69.1, 50.2, 46.7, 44.4, 42.7, 42.5, 33.1, 31.8, 31.0, 30.1, 27.6, 26.3, 25.9, 25.4, 23.9, 21.8, 20.3, 19.2, 18.4, 18.2, 18.0, 7.2, 5.3, −3.7, −4.2, −4.3, −4.4 ppm; IR (neat) ν_{max} 2956, 2930, 1719, 1591, 1451, 1254, 1162 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{57}H_{106}O_6Si_4Na$ $[M + Na]^+$ 1021.6964, found 1021.6963.

(4*R*,5*S*,7*R*,10*R*,12*S*,14*S*)-15-(Benzyloxy)-4-((*S*)-(3,5-bis((*tert*-butyldimethylsilyl)oxy)phenyl)((*tert*-butyldimethylsilyl)oxy)-methyl)-2,10,12,14-tetramethylpentadecane-5,7-diol (58). To a stirred solution of (*R*)-Me-CBS (63 mg, 0.22 mmol, 0.5 equiv) in anhydrous THF (2 mL) at 0 °C under argon was added BH_3·THF (0.7 mL, 0.14 mmol, 2.0 M in THF, 0.3 equiv) over 2 min, and the mixture was stirred for 10 min at the same temperature. A solution of compound **57** (460 mg, 0.46 mmol, 1.0 equiv) in anhydrous THF (2 mL) was added to the reaction mixture, and the reaction was continued for 5 h at the same temperature prior to quenching with MeOH (1 mL). The resultant mixture was extracted with EtOAc (2 × 15 mL), washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (SiO_2, 60−120 mesh, 8−10% EtOAc in hexane as eluent) to give an inseparable mixture of the corresponding alcohols (308 mg, 67%, dr = 3:1) as a colorless liquid: R_f = 0.4 (10% EtOAc in hexane); $[\alpha]^{23}_D$ = −24.8 (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.35−7.28 (m, 5H), 6.43−6.40 (m, 2H), 6.18 (t, *J* = 2.1 Hz, 1H), 4.93 (d, *J* = 1.2 Hz, 1H), 4.50 (d, *J* = 2.7 Hz, 2H), 4.11−4.00 (m, 1H), 3.90−3.82 (m, 1H), 3.43 (dd, *J* = 5.4, 9 Hz, 1H), 3.21 (dd, *J* = 6.9, 9 Hz, 1H), 2.34 (s, 1H), 1.94−1.76 (m, 3H), 1.59−1.51 (m, 4H), 1.51−1.29 (m, 6H), 1.23−1.05 (m, 4H), 1.04−1.0 (m, 10H), 0.98 (s, 18H), 0.95−0.93 (m, 9H), 0.86−0.82 (m, 6H), 0.77 (d, *J* = 2.1 Hz, 3H), 0.79−0.56 (m, 10H), 0.17 (s, 6H), 0.17 (s, 6H), 0.04 (s, 3H), −0.3 (s, 3H); ^{13}C NMR (CD_3OD, 75 MHz, diastereomer peaks are given in parentheses) δ 156.1, 148.2(147.8), 139.4(139.0), 128.4, 127.6, 127.5, 112.3(112.1), 110.8(110.8), 76.4, 73.1, 72.9, 71.7, 69.2, 49.9(49.2), 44.6, 42.7, 40.3, 36.2, 34.2, 33.9, 32.1, 30.9, 30.4, 27.7, 26.3(26.3), 25.8, 23.7, 22.8, 22.1, 20.3, 19.3, 18.4(18.3), 17.9, 7.2, 5.6(5.4), −3.8(−3.8), −4.2, −4.3(−4.3), −4.6 ppm; IR (neat) ν_{max} 2955, 2930, 1590, 1452, 1253, 1161 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{57}H_{108}O_6Si_4Na$ $[M + Na]^+$ 1023.7121, found 1023.7124.

Following the same experimental procedure as described in the preparation of compound **16**, the TES ether of the above alcohols (300 mg) was deprotected and the resultant mixture was purified (flash column chromatography, SiO_2, 100−200 mesh, 15% EtOAc in hexane as eluent) to give the major compound **58** (165 mg, 62%) as a colorless liquid: R_f = 0.3 (20% EtOAc in hexane); $[\alpha]^{28}_D$ = −15.4 (*c*

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J. Org. Chem. 2017, 82, 2414−2435

1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.34−7.28 (m, 5H), 6.43 (d, J = 2.1, 2H), 6.22 (t, J = 2.1 Hz, 1H), 4.78 (d, J = 3.6 Hz, 1H), 4.50 (d, J = 2.4 Hz, 2H), 4.28 (d, J = 10.2, 1H), 3.79 (s, 1H), 3.34 (dd, J = 5.1, 9 Hz, 1H), 3.21 (dd, J = ,7.2, 9 Hz, 1H), 2.41 (s, 2H), 1.93−1.75 (m, 2H), 1.57−1.41 (m, 5H), 1.39−1.28 (m, 4H), 1.26−1.01 (m, 7H), 0.97 (s, 18H), 0.93 (s, 12H), 0.84−0.82 (m, 6H), 0.78 (d, J = 6.3 Hz, 3H), 0.71 (d, J = 6.3 Hz, 3H), 0.17 (s, 12H), 0.08 (s, 3H), −0.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.6, 145.7, 139.0, 128.4, 127.6, 127.5, 111.6, 111.4, 77.9, 76.3, 73.1, 70.5, 69.9, 49.2, 44.4, 42.6, 41.3, 34.8, 34.4, 32.2, 30.9, 30.3, 27.5, 27.0, 26.1, 25.8, 23.3, 22.5, 20.4, 19.4, 18.3, 18.2, 18.0, −4.2, −4.3, −5.0 ppm; IR (neat) ν_{max} 3370, 2926, 2855, 1462, 1219 cm^{-1}; HRMS (ESI) m/z calcd for $C_{51}H_{94}O_6Si_3Na$ $[M + Na]^+$ 909.6256, found 909.6258.

(2*S*,4*S*,6*R*)-8-((4*R*,6*S*)-6-((1*S*,2*R*)-1-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-1-((*tert*-butyldimethylsilyl)oxy)-4-methylpentan-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)-2,4,6-trimethyloctan-1-ol (59). Following the same experimental procedure as for compound **28**, compound **58** (210 mg) was converted to the corresponding acetonide-protected compound (200 mg, 91%, purification by flash column chromatography, SiO_2, 60−120 mesh, 3% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.7 (5% EtOAc in hexane); $[\alpha]^{28}_D$ = −29.1 (c 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.34−7.28 (m, 5H), 6.39 (d, J = 2.1, 2H), 6.19 (t, J = 2.1 Hz, 1H), 4.64 (d, J = 4.8 Hz, 1H), 4.54−4.45 (m, 2H), 3.68−3.61 (m, 2H), 3.363.33 (dd, J = 5.4, 9 Hz, 1H), 3.20 (dd, J = 7.2, 9 Hz, 1H), 1.93−1.79 (m, 2H), 1.65−1.31 (m, 10H), 1.29 (s, 3H), 1.25−1.18 (m, 6H), 1.10−1.02 (m, 2H), 0.97 (s, 18H), 0.94−0.90 (m, 12H), 0.84−0.80 (m, 9H), 0.69 (d, J = 6.6 Hz, 3H), 0.17 (s, 12H), 0.04 (s, 3H), −0.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.1, 147.2, 139.0, 128.4, 127.6, 127.5, 112.4, 110.9, 100.2, 76.4, 74.9, 73.1, 67.3, 67.3, 49.4, 44.3, 42.7, 37.1, 35.2, 33.9, 33.7, 30.9, 30.2, 27.5, 27.3, 26.1, 25.9, 24.9, 24.9, 23.1, 22.9, 20.3, 19.4, 18.4, 18.3, 17.9, −4.0, −4.2, −4.2, −4.6 ppm; IR (neat) ν_{max} 2955, 2929, 1591, 1454, 1362, 1257, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{54}H_{98}O_6Si_3Na$ $[M + Na]^+$ 949.6569, found 949.6567.

Following the same experimental procedure as for compound **20**, the above acetonide-protected compound (190 mg) was converted to compound **59** (160 mg, 93%, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (5% EtOAc in hexane); $[\alpha]^{30}_D$ = −18.6 (c 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, J = 2.1, 2H), 6.19 (t, J = 2.1 Hz, 1H), 4.64 (d, J = 4.5 Hz, 1H), 3.74−3.59 (m, 2H), 3.54- 3.35 (m, 2H), 1.89−1.67 (m, 2H), 1.55−1.33 (m, 8H), 1.29−1.25 (m, 8H), 1.23−1.17 (m, 3H), 1.10−1.00 (m, 2H), 0.97 (s, 18H), 0.92−0.89 (m, 12H), 0.85−0.79 (s, 9H), 0.69 (d, J = 6.6 Hz, 3H), 0.17 (s, 12H), 0.04 (s, 3H), −0.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.1, 147.2, 112.4, 110.9, 100.2, 74.9, 68.6, 67.3, 67.3, 49.4, 44.3, 42.0, 37.0, 35.2, 33.7, 33.6, 33.2, 30.1, 27.5, 27.3, 26.1, 25.9, 24.9, 24.9, 23.1, 22.9, 20.4, 19.4, 18.4, 18.3, 17.3, −4.0, −4.2, −4.2, −4.6 ppm; IR (neat) ν_{max} 3365, 2929, 2858, 1592, 1454, 1220, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{47}H_{92}O_6Si_3Na$ $[M + Na]^+$ 859.6099, found 859.6098.

(4*S*,6*S*,8*R*)-10-((4*R*,6*S*)-6-((1*S*,2*R*)-1-(3,5-Bis((*tert*-butyldimethylsilyl)oxy)phenyl)-1-((*tert*-butyldimethylsilyl)oxy)-4-methylpentan-2-yl)-2,2-dimethyl-1,3-dioxan-4-yl)-4,6,8-trimethyldecan-3-one (60). Following the same experimental procedure described in the synthesis of compound **34**, compound **59** (101 mg) was converted to the corresponding aldehyde (100 mg, quantitative, purification by flash column chromatography, SiO_2, 60−120 mesh, 6% EtOAc in hexane as eluent) as a colorless oil, which was used directly for the next step without further characterization.

Following the same experimental procedure as described in the preparation of compound **34**, the above aldehyde (100 mg) was converted to the corresponding inseparable alcohols (80 mg, 77%, purification by SiO_2, 60−120 mesh, 5% EtOAc in hexane as eluent) as a colorless oil, which was used for the next step without further characterization.

Following the same experimental procedure as described in the preparation of compound **34**, the above alcohols (80 mg) were converted to compound **60** (49 mg, 78%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% EtOAc in hexane as eluent) as a colorless oil: R_f = 0.6 (3% EtOAc in hexane); $[\alpha]^{29}_D$ = −30.0 (c 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 6.39 (d, J = 0.1.8, 2H), 6.19 (t, J = 2.1 Hz, 1H), 4.64 (d, J = 4.5 Hz, 1H), 3.71−3.59 (m, 2H), 2.68−2.61 (m, 1H), 2.49- 2.40 (m, 2H), 1.89−1.80 (m, 1H), 1.64−1.59 (m, 1H), 1.55−1.33 (m, 9H), 1.29 (s, 3H), 1.25 (s, 3H), 1.20−1.08 (m, 3H), 1.06−1.02 (m, 8H), 0.97 (s, 18H), 0.89 (s, 9H), 0.84−0.79 (m, 9H), 0.69 (d, J = 6.6 Hz, 3H), 0.16 (s, 12H), 0.04 (s, 3H), −0.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 215.6, 156.1, 147.2, 112.4, 110.9, 100.2, 74.9, 67.3, 67.3, 49.4, 44.5, 43.9, 41.7, 37.1, 35.2, 34.2, 33.7, 30.1, 28.2, 27.3, 26.1, 25.9, 24.9, 24.9, 23.1, 22.9, 19.9, 19.4, 18.4, 18.3, 17.2, 8.0, −4.0, −4.2, −4.2, −4.6 ppm; IR (neat) ν_{max} 2954, 1711, 1594, 1453, 1251, 1163 cm^{-1}; HRMS (ESI) m/z calcd for $C_{49}H_{94}O_6Si_3Na$ $[M + Na]^+$ 885.6256, found 885.6254.

(4*S*,6*S*,8*R*,11*R*,13*S*,14*R*)-14-((*S*)-(3,5-Dihydroxyphenyl)(hydroxy)methyl)-11,13-dihydroxy-4,6,8,16-tetramethylheptadecan-3-one (49). Following the same experimental procedure as described in the preparation of compound **1**, compound **60** (30 mg) was converted to compound **49** (15 mg, 91%, purification by flash column chromatography, SiO_2, 60−120 mesh, 5−6% MeOH in CH_2Cl_2 as eluent) as a yellowish oil: R_f = 0.2 (6% MeOH in CH_2Cl_2); $[\alpha]^{29}_D$ = −9.7 (c 0.9, MeOH); ^1H NMR (CD_3OD, 500 MHz) δ 6.32 (d, J = 2.0 Hz, 2H), 6.11 (t, J = 1.8 Hz, 1H), 4.83 (d, J = 3.5 Hz, 1H), 4.07 (dt, J = 10.1, 2.6 Hz, 1H), 3.6 (m, 1H), 2.73 (m, 1H), 2.59, 2.45 (m, 2H), 1.70 (m, 1H), 1.66 (m, 2H), 1.55 (m, 1H), 1.50 (m, 1H), 1.45 (m, 3H), 1.38 (m, 1H), 1.28 (m, 2H), 1.25 (m, 1H), 1.24 (m, 1H), 1.07 (m, 3H), 1.01 (m, 3H), 1.00 (d, J = 6.9 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.0 Hz, 3H), 0.63 (d, J = 6.0 Hz, 3H); ^{13}C NMR (CD_3OD, 125 MHz) δ 218.5, 159.3, 148.7, 105.7, 101.9, 76.7, 72.4, 69.7, 49.9, 46.1, 45.0, 43.2, 42.7, 36.6, 35.3, 34.8, 33.5, 31.3, 29.4, 28.3, 23.4, 22.9, 20.2, 19.9, 17.7, 8.1 ppm; IR (neat) ν_{max} 3363, 2930, 2802, 1703, 1605, 1458, 1156 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{48}O_6Na$ $[M + Na]^+$ 503.3349, found 503.3348.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02838. Crystallographic data for compound **22** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (CCDC deposition number 1488063). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax, + 44-(0)1223-336033; e-mail, deposit@ccdc.cam.ac.uk).

General experimental procedure, assignment and comparison tables, NMR (^1H and ^{13}C) and HRMS of representative compounds, single-crystal X-ray crystallographic data and final refinement parameters for compound **22**, 2D NMR of some representative compounds, variable-temperature and concentration-dependent ^1H NMR of compound **1** and its average structure from molecular dynamics calculations (PDF)

Crystallographic data for compound **22** (CIF)

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Notes

The authors declare no competing financial interest.

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J. Org. Chem. 2017, 82, 2414−2435

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