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Synthesis of Luminacin D

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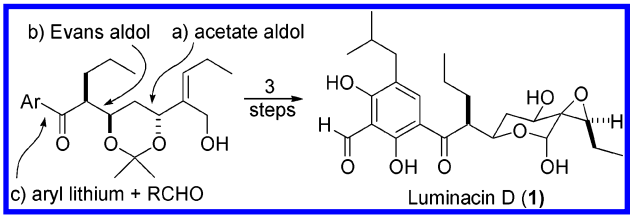

The total synthesis of luminacin D (**1**) is reported on the basis of two aldol reactions to form the carbohydrate sector, aldehyde **30**. Reaction of aldehyde **30** with the aryllithium intermediate derived from aryl iodide **38**, cleavage of the silyl ether, and oxidation led to keto aldehyde **41**. This advanced intermediate could be converted to luminacin **1** and its 6′,8′-epimer.

Introduction

Anticancer compounds generally work by interfering with the process of cell division. Another strategy for the treatment of cancer targets the blood supply chain of a tumor. Thus, angiogenesis inhibitors block the formation of new blood capillaries from an existing vessel.[1] Among these compounds, the luminacins, isolated from the fermentation broth of a soil bacterium, represent promising structural leads.[2] Several of the luminacins showed activity with IC_{50} values of less than 0.1 mg mL^{-1} in a rat aorta matrix culture model.[3] Some very active members include luminacin D (**1**), C1 (**2**), and C2 (**3**) (Figure 1). The luminacins feature a highly functionalized aromatic ring which is connected to a carbohydrate like subunit. So far total syntheses of luminacins were described by Crews et al.[4] and a group at the Eisai company.[5] Prior to these publications the group of Tatsuta et al. reported on the synthesis of *ent*-luminacins C1 and C2 from D-glucal.[6] While this route was rather lengthy, it clarified the relative and absolute configurations of these and related luminacins.

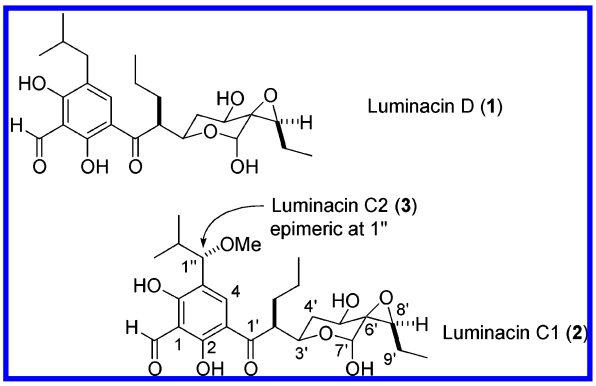

FIGURE 1. Structures of important luminacins.

A recent study described the synthesis of luminacin D analogues with a simplified carbohydrate sector.[7] From this work it was concluded that the epoxide is not essential for biological activity.[8] Our goal in this field differed in that we intended to develop a concise synthesis of the carbohydrate sector that would

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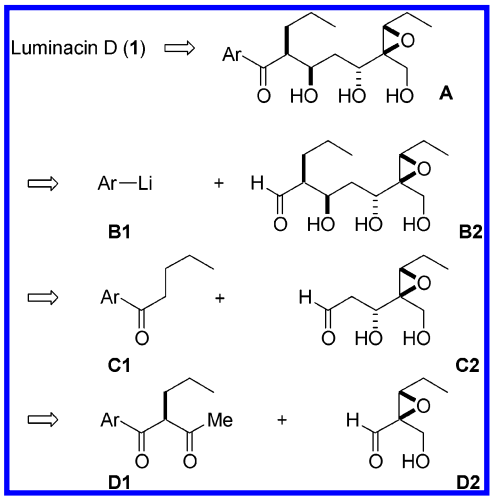


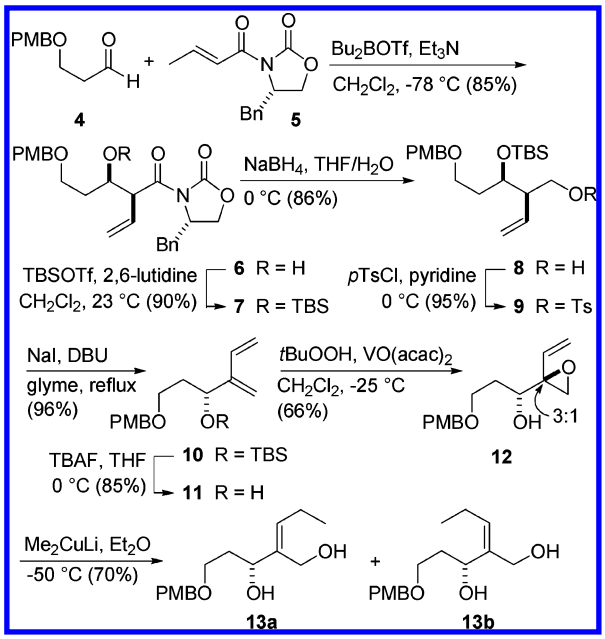
FIGURE 2. Possible retrosynthetic cuts for luminacins.

allow for simple variation of the aromatic ring at a late stage of the synthesis. Thus, retrosynthetic cuts as shown in Figure 2 were considered (protecting groups omitted). Accordingly, the open-chain luminacin precursor **A** might originate from an aryllithium reagent **B1** and the carbohydrate fragment **B2**. Alternatively, an aldol reaction of an aryl ketone **C1** with aldehyde **C2** could be used.[7] In a variation thereof, an asymmetric aldol reaction using a pentanoyl derivative might be considered. Finally, an aldol reaction of a 2-acetylpentanoate derivative, such as **D1** with an aldehyde of type **D2** might be employed. Since it is not clear whether the epoxide function would survive the conditions for the aldol reactions, the corresponding unsaturated aldehydes might be more appropriate substrates.

Results and Discussion

The initial goal was to prepare an epoxide containing aldehyde of type **C2** and to extend this aldehyde via an Evans aldol reaction. To establish the trisubstituted double bond, the precursor functional group for the epoxide, we opted for the use of a nucleophilic S_N2' opening of allylic epoxide **12** with dimethyl cuprate (Scheme 1).[9−11] In the event, aldol reaction[12] of the crotonyl oxazolidinone[13] **5** with aldehyde[14] **4** provided compound **6**. Three routine steps (OH protection, reductive removal of the auxiliary, tosylation) gave alkene **9**. Via an elimination reaction and deprotection the allylic alcohol, **11** was obtained.[15] A directed epoxidation[16] furnished the allylic epoxide **12** (as an inseparable 3:1 diastereomeric mixture). Subsequent treatment of the epoxide **12** with dimethylcuprate did indeed

SCHEME 1. Attempted Synthesis of the Part with the Trisubstituted Double Bond



generate the desired trisubstituted double bond. However, there was no selectivity and a 1:1 mixture of the two double bond isomers **13a** and **13b** was obtained.

Therefore, another strategy was followed. This route began with the known Baylis−Hillman adduct **14** which was transformed via an allylic substitution reaction to the benzoate **15** (Scheme 2).[17] This ester could be converted to aldehyde **19** as shown in Scheme 2. The choice of the PMB-protecting group was crucial. With a TBS protecting group we encountered severe problems in removing the chiral auxiliary in the second aldol step.[18] The next step called for a stereoselective acetate aldol reaction with aldehyde **19**. Eventually, a practical solution was found with the $TiCl_4$-mediated aldol reaction using thiazolidinethione **20**.[19,20] This produced the aldol product **21** (non-Evans product)[21] essentially as a single diastereomer in 70% yield. In continuation with the synthesis, the hydroxyl group was protected as silyl ether, the auxiliary was removed, and the resulting alcohol **23** was oxidized to aldehyde **24**. Two further stereocenters were established by an Evans aldol reaction[12,22] using the pentanoyloxazolidinone[23] **25**. Conversion of **26** to the Weinreb amide **27** could be achieved under standard condi-

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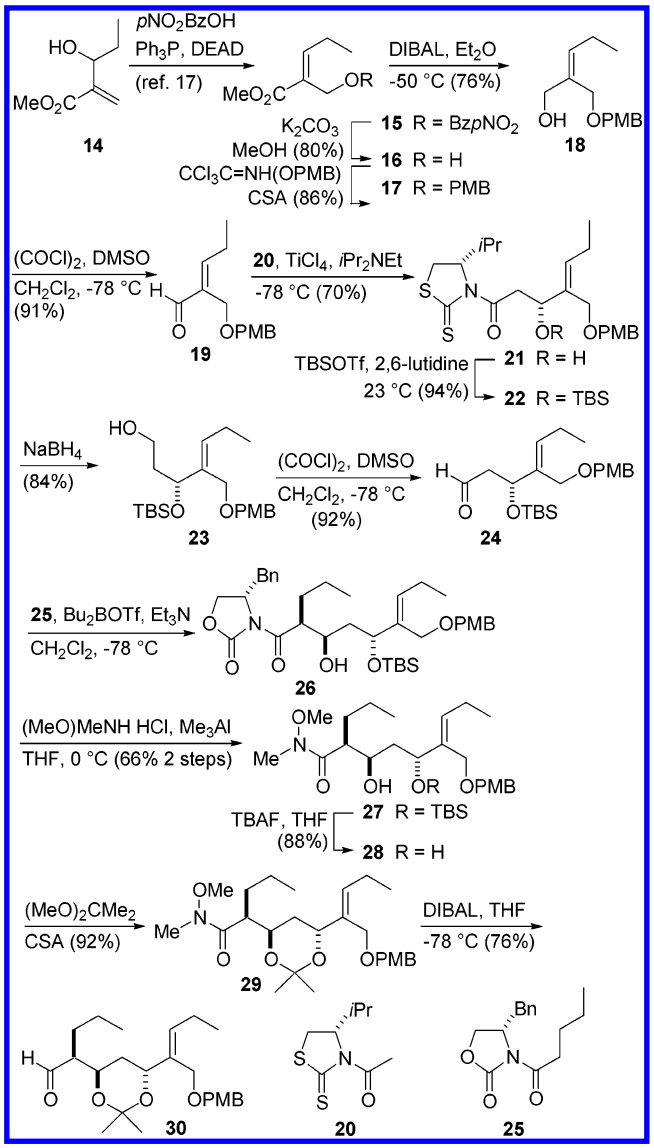
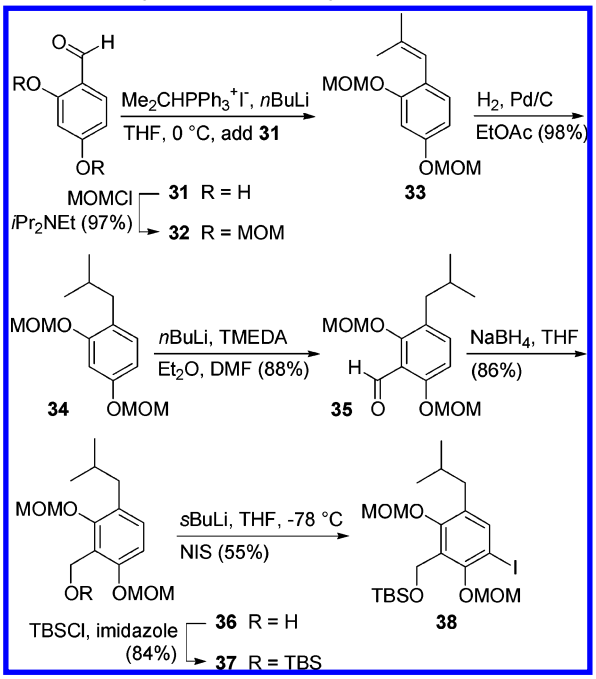
SCHEME 2. Synthesis of Aldehyde 30 by Successive Aldol Reactions



SCHEME 3. Synthesis of the Aryl Iodide 38



tions.[24] After cleavage of the silyl ether, the 1,3-diol was protected as an acetal, leading to amide **29**. The *anti*-stereochemistry of **29** is clearly evident from the chemical shift of the acetal C (δ = 100.8 ppm).[25] In addition, the acetal methyl groups appear at similar chemical shifts (δ = 24.4 and 24.8 ppm) which is typical for the twist-boat conformation of *anti*-1,3-diol acetonides.[26] Reduction of the amide **29** with DIBAL in THF provided the key aldehyde **30**.

The synthesis of the aryl building block required for luminacin D is shown in Scheme 3. Thus, MOM protection of 2,4-dihydroxybenzaldehyde (**31**) provided aldehyde **32** (97% yield). Via Wittig reaction with (2-methylpropyl)(triphenyl)phosphonium iodide/*n*BuLi followed by hydrogenation of the styrene **33**, the resorcinol derivative **34** was secured. Formylation could be achieved by metalation and trapping of the aryllithium intermediate with DMF.[27,28] Reduction of the aldehyde **35** to the primary alcohol **36** and silylation furnished compound **37**. Iodination of **37** via metalation gave rise to the key building block, aryl iodide **38**.

The combination of the two fragments **30** and **38** was initiated by lithiation of aryl iodide **38** followed by addition of aldehyde **30** (Scheme 4). Thereafter, the silyl ether was cleaved. Treatment of the diol **40** with the Dess−Martin reagent (3 equiv) gave the keto aldehyde **41**. At this stage, the PMB-protecting group was removed using DDQ resulting in allylic alcohol **42**. The epoxidation of the allylic double bond was initially tried under Sharpless conditions using D-(−)-diisopropyl tartrate, *t*BuOOH, and Ti(O*i*Pr)$_4$.[29] This reagent combination was expected to give the desired epoxide. However, even after one week at −10 °C only a trace of product could be detected by LCMS.

Epoxidation of **42** with *t*BuOOH in the presence of VO(acac)$_2$ led to a mixture of two epoxides[4] **43a**,**b**. This mixture was converted to the luminacins 6′,8′-*epi*-**1** and luminacin D (**1**) by oxidation to **44**, acid induced deprotection and cyclization. At this stage a chromatographic separation of the epoxide diastereomers was easily possible on diol-modified silica gel. The spectral data for synthetic **1** nicely matched the reported data.[2] Very characteristic for luminacin D (**1**) are the values for C-8′ (59.2), C-6′ (64.3), C-3′ (69.8), C-7′ (92.5), and C-1′ (206.5 ppm) in the ^{13}C NMR spectrum. The epimer 6′,8′-*epi*-**1** seems to be a mixture of two anomers (around 1:1). This is evident from the fact that several peaks appear as pairs. Thus, the following chemical shifts were observed in the ^{13}C NMR spectrum of 6′,8′-*epi*-**1**: C-8′ (69.2, 69.5), C-6′ (74.3, 74.5), C-3′ (72.0, 72.5), C-7′ (94.6, 95.8), and C-1′ (206.7, 207.0 ppm).

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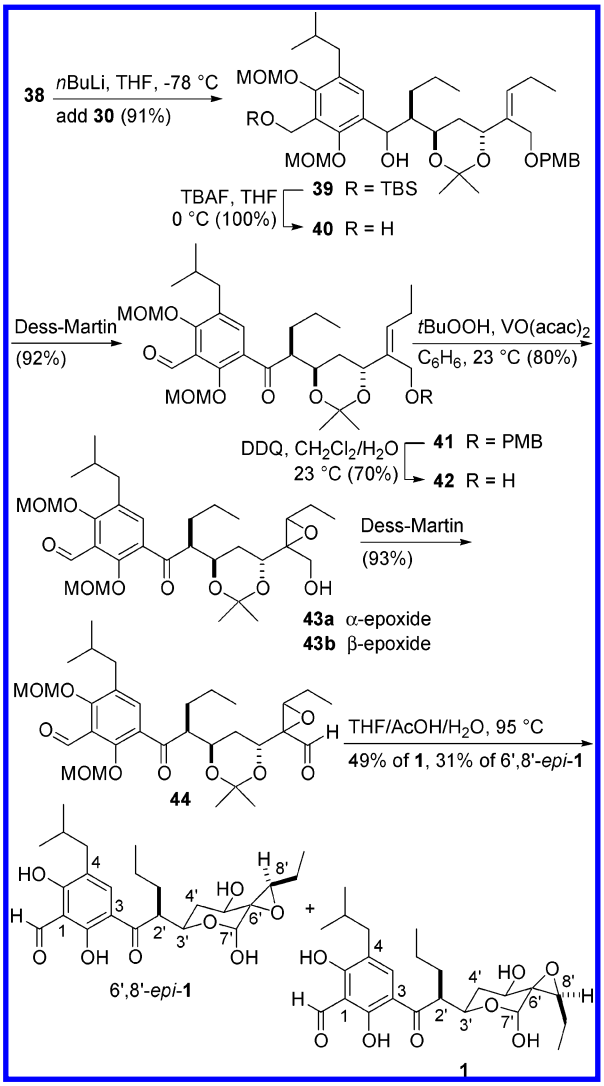
SCHEME 4. Synthesis of Luminacin D (1) and Its Epimer



Conclusion

To summarize, we developed a novel route to luminacin D (**1**). The starting aldehyde **19** was obtained by a simple Baylis−Hillman reaction followed by allylic OH transposition. This should allow for easy variations at this terminus. This aldehyde was then extended by two highly stereoselective asymmetric aldol reactions. The combination of aldehyde **30** with the aryllithium derivative of **38** led to keto aldehyde **41** after cleavage of the silyl ether and oxidation of the primary and secondary alcohol functions. Four further steps provided luminacin D (**1**) together with its epoxide epimer. The overall strategy is concise and convergent which should allow for the synthesis of aryl modified luminacin analogues. Future work will focus on a stereoselective introduction of the epoxide function, either by direct epoxidation[30] or creation of the epoxide from a diol precursor.

Experimental Section

(2*Z*)-2-{[(4-Methoxybenzyl)oxy]methyl}pent-2-en-1-ol (18). To a cooled (−50 °C) solution of ester **17** (4.0 g, 15.0 mmol) in anhydrous Et_2O (58 mL) was added DIBALH (37.4 mL, 1 M in hexane, 37.4 mmol) dropwise over 20 min. After 1 h anhydrous methanol (2.2 mL) was added slowly at −50 °C, and the resulting mixture was allowed to warm to room temperature over 4 h. Then the mixture was poured into a 1:1 mixture of Et_2O and 50% aqueous Rochelle's salt (130 mL of each), and the reaction mixture was stirred for 1 h followed by separation of the layers. The aqueous layer was extracted with ether (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (25% EtOAc/petroleum ether) to yield alcohol **18** (2.7 g, 76%) as a colorless oil. R_f = 0.23 (25% EtOAc/petroleum ether). IR (film): ν_{max} = 3401, 2954, 2930, 1612, 1511, 1457, 1245, 1176, 1033, 821 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.6 Hz, 3H, CH_3CH_2), 2.04 (q$_n$, J = 7.6 Hz, 2H, CH_2CH_3), 3.32 (s, 1H, OH), 3.71 (s, 3H, OCH_3), 4.06 (s, 4H, CH_2OPMB and CH_2OH), 4.37 (s, 2H, OCH_2Ph), 5.59 (t, J = 7.6 Hz, 1H, HC=C), 6.83 (d, J = 8.6 Hz, 2H, CH_{arom}), 7.21 (d, J = 8.6 Hz, 2H, CH_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8 (CH_3CH_2), 20.3 (CH_2CH_3), 54.6 (OCH_3), 64.3 (CH_2OH), 65.4 (CH_2OPMB), 71.4 (OCH_2Ph), 113.3 (CH_{arom}), 128.9 (CH_{arom}), 129.8 ($C_{quat}Ph$), 132.4 (HC=C), 134.2 (=CCH_2), 158.7 ($C_{quat}Ph$) ppm. HRMS (ESI): calcd for $C_{14}H_{20}O_3Na$ [M + Na]$^+$, 259.1305; found, 259.1306.

(2*E*)-2-{[(4-Methoxybenzyl)oxy]methyl}pent-2-enal (19). To a solution of oxalyl chloride (2.2 mL, 24.9 mmol) in CH_2Cl_2 (49 mL) was added DMSO (3.1 mL, 40.7 mmol) in CH_2Cl_2 (10 mL) at −78 °C. The mixture was stirred for 30 min before a solution of alcohol **18** (3.90 g, 16.6 mmol) in CH_2Cl_2 (13 mL) was slowly added at −78 °C. After being stirred for 30 min, Et_3N (9.2 mL, 66.4 mmol) was added slowly at −78 °C, and the mixture allowed to warm to room temperature over 3 h. The mixture was diluted with H_2O (20 mL) and CH_2Cl_2 (20 mL). The organic layer was washed with 1 N HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was filtered through a short pad of silica to afford aldehyde **19** (3.55 g, 91%) as a pale yellow oil. R_f = 0.39 (25% EtOAc/petroleum ether). IR (film): ν_{max} = 2962, 2865, 2719, 1685, 1612, 1511, 1457, 1249, 1079, 1033, 848 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.14 (t, J = 7.6 Hz, 3H, CH_3CH_2), 2.48 (q$_n$, J = 7.6 Hz, 2H, CH_2CH_3), 3.81 (s, 3H, OCH_3), 4.21 (s, 2H, CH_2OPMB), 4.45 (s, 2H, OCH_2Ph), 6.71 (t, J = 7.6 Hz, 1H, HC=C), 6.89 (d, J = 8.6 Hz, 2H, CH_{arom}), 7.27 (d, J = 8.6 Hz, 2H, CH_{arom}), 9.45 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.0 (CH_3CH_2), 22.6 (CH_2CH_3), 55.2 (OCH_3), 60.6 (CH_2OPMB), 72.4 (OCH_2Ph), 113.7 (CH_{arom}), 129.4 (CH_{arom}), 130.1 ($C_{quat}Ph$), 139.0 (=CCH_2), 159.2 ($C_{quat}Ph$), 161.0 (HC=C), 193.9 (CHO) ppm. HRMS (ESI): calcd for $C_{14}H_{18}O_3Na$ [M + Na]$^+$, 257.1148; found, 257.1149.

(4*S*)-3-((3*R*,4*E*)-3-Hydroxy-4-{[(4-methoxybenzyl)oxy]methyl}-hept-4-enoyl)-4-isopropyl-1,3-thiazolidine-2-thione (21). To a stirred solution of the Nagao acetate[31] **20** (4.66 g, 23.0 mmol) in CH_2Cl_2 (184 mL) at 0 °C was added $TiCl_4$ (2.76 mL, 25.2 mmol). The reaction mixture was stirred for 5 min at 0 °C, cooled to −78 °C, then treated dropwise with iPr$_2$NEt (4.29 mL, 25.1 mmol) and stirred for 2 h at −78 °C. Then aldehyde **19** (3.16 g, 13.48 mmol) in CH_2Cl_2 (15 mL) was added dropwise, and the mixture was stirred for 30 min at −78 °C. The reaction was quenched with saturated aqueous NH_4Cl solution (50 mL), and the mixture was diluted with CH_2Cl_2 (100 mL). After separation of the layers, the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (5% EtOAc/CH_2Cl_2) to provide the aldol product **21** (4.12 g, 70%) as a yellow oil. R_f = 0.21 (5% EtOAc/CH_2Cl_2);

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$[\alpha]^{20}_D = +238.0$ (*c* 1.10 in CH_2Cl_2). IR (film): $\nu_{max} = 3482, 2962, 2950, 1693, 1612, 1511, 1461, 1361, 1249, 1164, 1037$ cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.97$ (d, $J = 6.8$ Hz, 3H, $(CH_3)_2$CH), 0.98 (t, $J = 7.6$ Hz, 3H, CH_3CH_2), 1.05 (d, $J = 6.8$ Hz, 3H, $(CH_3)_2$CH), 2.08 (q$_n$, $J = 7.6$ Hz, 2H, CH_2CH_3), 2.36 (app oct, $J = 6.8$ Hz, 1H, $CH(CH_3)_2$), 2.99 (d, $J = 11.6$ Hz, 1H, SCH_2CHN), 3.24 (d, $J = 5.3$ Hz, 1H, OH), 3.47 (dd, $J = 11.5, 8.0$ Hz, 1H, SCH_2CHN), 3.57 (d, $J = 6.1$ Hz, 2H, CH_2CHOH), 3.80 (s, 3H, OCH_3), 4.07 (d, $J = 11.1$ Hz, 1H, CH_2OPMB), 4.14 (d, $J = 11.1$ Hz, 1H, CH_2OPMB), 4.44 (s, 2H, OCH_2Ph), 4.71 (q, $J = 5.9$ Hz, 1H, CHOH), 5.12 (t, $J = 6.8$ Hz, 1H, CHNCS), 5.73 (t, $J = 7.3$ Hz, 1H, C=CH), 6.87 (d, $J = 8.6$ Hz, 2H, CH_{arom}), 7.26 (d, $J = 8.6$ Hz, 2H, CH_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.0$ (CH_3CH_2), 17.6 ($(CH_3)_2$CH), 18.9 ($(CH_3)_2$CH), 20.8 (CH_2CH_3), 30.5 (SCH_2CHN), 30.7 ($CH(CH_3)_2$), 44.4 ($NCOCH_2$), 55.1 (OCH_3), 65.3 (CH_2OPMB), 71.4 (CHNCS), 71.5 (CHOH), 72.1 (OCH_2Ph), 113.7 (CH_{arom}), 129.3 (CH_{arom}), 129.9 (C_{quat}Ph), 133.5 (=CH), 134.9 (C=CH), 159.1 (C_{quat}Ph), 172.4 (C=O), 202.8 (C=S) ppm. HRMS (ESI): calcd for $C_{22}H_{31}NO_4S_2Na$ $[M + Na]^+$, 460.1587; found, 460.1589.

(3*R*,4*E*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-4-{[(4-methoxybenzyl)oxy]methyl}hept-4-en-1-ol (23). A stirred solution of **22** (2.13 g, 3.86 mmol) in THF (140 mL) was treated dropwise with a solution of $NaBH_4$ (0.729 g, 19.30 mmol) in H_2O (27.7 mL) at 0 °C. The mixture was stirred at 0 °C overnight. The reaction was quenched by the addition of saturated aqueous NH_4Cl (50 mL), and the mixture was stirred for 1.5 h. After separation of the layers, the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (50 mL), H_2O (50 mL), and brine (50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (5% EtOAc/CH_2Cl_2) to afford alcohol **23** (1.28 g, 84%) as a colorless oil. $R_f = 0.29$ (5% EtOAc/CH_2Cl_2); $[\alpha]^{20}_D = +12.63$ (*c* 1.05 in CH_2Cl_2). IR (film): $\nu_{max} = 3432, 2946, 2930, 1612, 1511, 1461, 1249, 1176, 1037, 782$ cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = -0.07$ (s, 3H, $Si(CH_3)_2$), 0.00 (s, 3H, $Si(CH_3)_2$), 0.82 (s, 9H, $SiC(CH_3)_3$), 0.91 (t, $J = 7.5$ Hz, 3H, CH_3CH_2), 1.74−1.79 (m, 2H, CH_2CHOTBS), 2.04 (q$_n$, $J = 7.5$ Hz, 2H, CH_2CH_3), 2.68 (br s, 1H, OH), 3.56−3.66 (m, 2H, CH_2CH_2CHOTBS), 3.72 (s, 3H, OCH_3), 3.87 (d, $J = 10.9$ Hz, 1H, CH_2OPMB), 3.91 (d, $J = 10.9$ Hz, 1H, CH_2OPMB), 4.31 (t, $J = 5.7$ Hz, 1H, CHOTBS), 4.33 (d, $J = 11.6$ Hz, 1H, OCH_2Ph), 4.37 (d, $J = 11.6$ Hz, 1H, OCH_2Ph), 5.64 (t, $J = 7.6$ Hz, 1H, C=CH), 6.80 (d, $J = 8.6$ Hz, CH_{arom}), 7.17 (d, $J = 8.6$ Hz, CH_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = -5.3$ ($Si(CH_3)_2$), −4.6 ($Si(CH_3)_2$), 14.1 (CH_3CH_2), 18.0 ($C(CH_3)_3$), 20.8 (CH_2CH_3), 25.7 ($SiC(CH_3)_3$), 38.4 (CH_2CHOTBS), 55.1 (OCH_3), 60.1 (CH_2CH_2CHOTBS), 64.5 (CH_2OPMB), 72.0 (OCH_2Ph), 74.7 (CHOTBS), 113.6 (CH_{arom}), 129.1 (CH_{arom}), 130.3 (C_{quat}Ph), 133.2 (=CH), 136.3 (C=CH), 159.1 (C_{quat}Ph) ppm. HRMS (ESI): calcd for $C_{22}H_{38}O_4SiNa$ $[M + Na]^+$, 417.2432; found, 417.2434.

(2*S*,3*R*,5*R*,6*E*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-3-hydroxy-*N*-methoxy-6-{[(4-methoxybenzyl)oxy]methyl}-*N*-methyl-2-propylnon-6-enamide (27). A solution of (4*S*)-4-benzyl-3-pentanoyl-1,3-oxazolidin-2-one (**25**) (1.15 g, 4.42 mmol) in CH_2Cl_2 (7.6 mmol) at 0 °C was treated with Bu_2BOTf (4.36 mL, 1 M in CH_2Cl_2, 4.36 mmol) followed by Et_3N (0.83 mL, 5.96 mmol). After stirring for 15 min, the mixture was cooled to −78 °C, and a solution of aldehyde **24** (1.16 g, 2.95 mmol) in CH_2Cl_2 (7.6 mL) was added. After stirring for 2 h at −78 °C, the mixture was allowed to warm to room temperature over a period of 2 h and stirred at room temperature for 1.5 h. The reaction was quenched by addition of a pH = 7 aqueous phosphate buffer solution (11 mL) followed by a 2:1 mixture of MeOH and 30 wt % aqueous H_2O_2 (33 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with H_2O (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The next step on aldol product **26** was carried out without any further purification.

To a stirred solution of N,O-dimethyl hydroxylamine hydrochloride (0.834 g, 8.55 mmol) in THF (4.3 mL) at 0 °C was added $AlMe_3$ (4.34 mL, 2 M in toluene, 8.69 mmol). The flask was allowed to warm to room temperature, and the mixture was stirred for 1 h. After recooling the flask to 0 °C, a solution of the crude aldol product **26** (1.87 g, 2.87 mmol) in THF (4.3 mL) was added, and the reaction mixture was allowed to stir in an ice bath for 14 h before it was warmed to room temperature and stirred for an additional 2 h. The reaction mixture was transferred via a cannula to a cooled, vigorously stirred solution of 0.5 N HCl (40 mL) and CH_2Cl_2 (20 mL). Stirring was continued for 1 h, and then the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (5% EtOAc/CH_2Cl_2) to yield the amide **27** (860 mg, 66%) as a colorless oil. $R_f = 0.23$ (5% EtOAc/CH_2Cl_2); $[\alpha]^{20}_D = +6.12$ (*c* 1.77 in CH_2Cl_2). IR (film): $\nu_{max} = 3475, 2958, 2930, 2857, 1657, 1614, 1514, 1464, 1386, 1249, 1174, 1080, 1037, 1004$ cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = -0.06$ (s, 3H, $Si(CH_3)_2$), 0.00 (s, 3H, $Si(CH_3)_2$), 0.81 (s, 9H, $SiC(CH_3)_3$), 0.82 (t, $J = 7.3$ Hz, 3H, $CH_3CH_2CH_2$), 0.91 (t, $J = 7.6$ Hz, 3H, CH_3CH_2), 1.13−1.23 (m, 2H, CH_2CH_2CH), 1.55−1.72 (m, 4H, CH_2CHC=O and CH_2CHOTBS), 1.98−2.09 (m, 2H, CH_2CH_3), 2.85−2.93 (m, 1H, CHCON(OMe)Me), 3.10 (s, 3H, CH_3N), 3.60 (s, 3H, CH_3ON), 3.74 (s, 3H, OCH_3), 3.81−3.86 (m, 1H, CHCON), 3.84 (d, $J = 10.9$ Hz, CH_2OPMB), 3.98 (d, $J = 10.9$ Hz, CH_2OPMB), 4.29 (d, $J = 11.6$ Hz, 1H, OCH_2Ph), 4.36 (d, $J = 11.6$ Hz, 1H, OCH_2Ph), 4.44 (t, $J = 4.8$ Hz, 1H, CHOTBS), 5.66 (t, $J = 7.3$ Hz, 1H, C=CH), 6.80 (d, $J = 8.3$ Hz, 2H, CH_{arom}), 7.18 (d, $J = 8.6$ Hz, 2H, CH_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = -5.2$ ($Si(CH_3)_2$), −4.7 ($Si(CH_3)_2$), 14.3 (CH_3CH_2), 14.3 ($CH_3CH_2CH_2$), 18.3 ($C(CH_3)_3$), 20.8 (CH_2CH_2CH), 21.0 (CH_2CH_3), 25.8 ($SiC(CH_3)_3$), 30.1 (CH_2CHC=O), 31.9 (CH_3N), 40.2 (CH_2CHOTBS), 46.2 (CHCON(OMe)Me), 55.2 (OCH_3), 61.4 (CH_3ON), 64.6 (CH_2OPMB), 69.5 (CHOH), 71.8 (OCH_2Ph), 73.4 (CHOTBS), 113.7 (CH_{arom}), 129.2 (CH_{arom}), 130.5 (C_{quat}Ph), 132.8 (=CH), 135.9 (C=CH), 159.1 (C_{quat}Ph) 176.7 (C=O) ppm. HRMS (ESI): calcd for $C_{29}H_{51}NO_6SiNa$ $[M + Na]^+$, 560.3378; found, 560.3379.

(2*S*)-*N*-Methoxy-2-[(4*R*,6*R*)-6-((1*E*)-1-{[(4-methoxybenzyl)oxy]methyl}but-1-enyl)-2,2-dimethyl-1,3-dioxan-4-yl]-*N*-methylpentanamide (29). To a solution of the diol **28** (450 mg, 1.06 mmol) in THF (20 mL) was added 2,2-dimethoxypropane (1.32 mL, 10.6 mmol) followed by CSA (25 mg, 0.11 mmol) at room temperature. The mixture was stirred for 4 h at room temperature, and then the reaction was quenched with a few drops of Et_3N. The solvent was evaporated in vacuo. The crude product was purified by flash chromatography (30% EtOAc/petroleum ether) to yield acetal **29** (452 mg, 92%) as a colorless oil. $R_f = 0.44$ (50% EtOAc/petroleum ether); $[\alpha]^{20}_D = 6.78$ (*c* 0.68 in CH_2Cl_2). IR (film): $\nu_{max} = 2960, 2932, 2871, 1654, 1511, 1454, 1384, 1245, 1174, 1073, 1035$ cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.86$ (t, $J = 7.3$ Hz, 3H, $CH_3CH_2CH_2$), 0.94 (t, $J = 7.6$ Hz, 3H, CH_3CH_2), 1.20−1.29 (m, 2H, CH_2CH_2CH), 1.32 (s, 3H, $C(CH_3)_2$), 1.33 (s, 3H, $C(CH_3)_2$), 1.54−1.63 (m, 1H, CH_2CHC=ON), 1.65−1.74 (m, 2H, CH_2CHCON and CH_2CHOC=CH), 1.86−1.93 (m, 1H, CH_2CHOC=CH), 2.07 (q$_n$, $J = 7.5$ Hz, 2H, CH_2CH_3), 3.02 (m, 1H, CHCON(OMe)Me), 3.13 (s, 3H, CH_3N), 3.63 (s, 3H, CH_3ON), 3.76 (s, 3H, OCH_3), 3.89−3.95 (m, 1H, CHCON), 3.98 (s, 2H, CH_2OPMB), 4.32 (dd, $J = 9.7, 6.2$ Hz, 1H, CHC=CH), 4.36 (s, 2H, OCH_2Ph), 5.63 (t, $J = 7.3$ Hz, 1H, C=CH), 6.82 (d, $J = 8.6$ Hz, 2H, CH_{arom}), 7.21 (d, $J = 8.6$ Hz, 2H, CH_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.1$ (CH_3CH_2), 14.3 ($CH_3CH_2CH_2$), 20.5 (CH_2CH_2CH), 21.0 (CH_2CH_3), 24.5 ($(CH_3)_2C$), 24.8 ($(CH_3)_2C$), 32.0 (CH_3N), 32.1 (CH_2CHCON), 34.4 (CH_2CHOC=CH), 46.0 (CHCON(OMe)Me), 55.2 (OCH_3), 61.4 (CH_3ON), 64.9 (CH_2OPMB), 68.2 (CHOC=CH), 68.6 (CHCHCON), 71.9 (OCH_2Ph), 100.8 ($C(CH_3)_2$),

113.7 (CH_{arom}), 129.4 (CH_{arom}), 130.6 (C_{quat}Ph), 133.6 (=CH), 134.8 (*C*=CH), 159.1 (C_{quat}Ph) 175.2 (C=O) ppm. HRMS (ESI): calcd for $C_{26}H_{41}NO_6Na$ $[M + Na]^+$, 486.2826; found, 486.2829.

(2*S*)-2-[(4*R*,6*S*)-6-((1*E*)-1-{[(4-Methoxybenzyl)oxy]methyl}-but-1-enyl)-2,2-dimethyl-1,3-dioxan-4-yl]pentanal (30). To a solution of the amide **29** (270 mg, 0.58 mmol) in THF (2.7 mL) was added DIBALH (1.75 mL, 1.75 mmol) dropwise at −78 °C. The mixture was stirred for 3 h at −78 °C and then treated with saturated aqueous Na K tartrate (2.7 mL) at −78 °C. After being stirred for 1 h at room temperature, the layers were separated. The aqueous layer was extracted with ether (3 × 1 mL). The combined organic layers were washed with water (2 mL) and brine (2 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to yield aldehyde **30** (180 mg, 76%) as a colorless oil. $R_f = 0.40$ (25% EtOAc/petroleum ether); $[\alpha]^{20}_D = +1.24$ (*c* 0.97 in CH_2Cl_2). IR (film): $\nu_{max} = 2984, 2959, 2934, 2872, 1724, 1613, 1586, 1513, 1463, 1378, 1301, 1248, 1225, 1172, 1080, 1037$ cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.84$ (t, $J = 7.2$ Hz, 3H, C*H*$_3$CH$_2$CH$_2$), 0.91 (t, $J = 7.6$ Hz, 3H, C*H*$_3$CH$_2$), 1.16−1.23 (m, 2H, C*H*$_2$CH$_2$CH), 1.26 (s, 3H, C(CH$_3$)$_2$), 1.27 (s, 3H, C(CH$_3$)$_2$), 1.41−1.49 (m, 1H, C*H*$_2$CHCHO), 1.58−1.72 (m, 2H, C*H*$_2$CHCHO and C*H*$_2$CHOC=CH), 1.84 (ddd, $J = 12.9, 10.0, 6.4$ Hz, 1H, C*H*$_2$-CHOC=CH), 2.04 (q_n, $J = 7.3$ Hz, 2H, C*H*$_2$CH$_3$), 2.31−2.37 (m, 1H, C*H*CHO), 3.72 (s, 3H, OCH$_3$), 3.94 (s, 2H, CH$_2$OPMB), 4.01−4.06 (m, 1H, C*H*CHCHO), 4.26 (dd, $J = 9.9, 6.1$ Hz, 1H, C*H*C=CH), 4.32 (d, $J = 11.6$ Hz, 1H, OCH$_2$Ph), 4.35 (d, $J = 11.4$ Hz, 1H, OCH$_2$Ph), 5.59 (t, $J = 7.3$ Hz, 1H, C=CH), 6.80 (d, $J = 8.6$ Hz, 2H, CH_{arom}), 7.18 (d, $J = 8.6$ Hz, 2H, CH_{arom}), 9.63 (d, $J = 2.5$ Hz, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.1$ (*C*H$_3$CH$_2$), 14.3 (*C*H$_3$CH$_2$CH$_2$), 20.5 (*C*H$_2$CH$_2$CH), 20.9 (*C*H$_2$CH$_3$), 24.3 ((*C*H$_3$)$_2$C), 24.6 ((*C*H$_3$)$_2$C), 26.7 (*C*H$_2$CHCHO), 34.2 (*C*H$_2$-CHOC=CH), 55.2 (OCH$_3$), 56.2 (*C*HCHO), 64.6 (CH$_2$OPMB), 66.1 (*C*HCHCHO), 68.1 (*C*HC=CH), 71.9 (OCH$_2$Ph), 100.8 (*C*(CH$_3$)$_2$), 113.6 (CH_{arom}), 129.4 (CH_{arom}), 130.4 (C_{quat}Ph), 133.4 (=CH), 134.6 (C=CH), 159.1 (C_{quat}Ph) 204.2 (CHO) ppm. HRMS (ESI): calcd for $C_{24}H_{36}O_5Na$ $[M + Na]^+$, 427.2455; found, 427.2457.

2,4-Bis(methoxymethoxy)benzaldehyde (32). To a stirred solution of 2,4-dihydroxybenzaldehyde (**31**) (2.0 g, 14.5 mmol) in DMF (43 mL), *i*Pt$_2$NEt (10.0 mL, 57.92 mmol) followed by MOMCl (4.4 mL, 57.92 mmol) were added dropwise at room temperature. The reaction mixture was allowed to stir for 5 h before it was poured into water (40 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with 5% NaOH solution (2 × 10 mL) followed by brine (2 × 10 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude product was filtered through a short column of flash silica gel to provide aldehyde **32** (3.20 g, 98%) as a colorless oil. $R_f = 0.48$ (25% EtOAc/petroleum ether). IR (film): $\nu_{max} = 3613, 2946, 2356, 1681, 1600, 1492, 1257, 1157, 1079, 998$ cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.42$ (s, 3H, OCH$_3$), 3.46 (s, 3H, OCH$_3$), 5.15 (s, 2H, OC*H*$_2$OCH$_3$), 5.22 (s, 2H, OC*H*$_2$OCH$_3$), 6.68 (d, $J = 8.6$ Hz, 1H, CH_{meta}), 6.78 (s, 1H, CH_{meta}), 7.73 (d, $J = 8.6$ Hz, 1H, CH_{ortho}), 10.28 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 56.2$ (OCH$_3$), 56.3 (OCH$_3$), 94.0 (OCH$_2$OCH$_3$), 94.5 (OCH$_2$-OCH$_3$), 102.4 (CH_{meta}), 109.2 (CH_{meta}), 120.0 (C_{quat}CHO), 129.9 (CH_{ortho}), 161.1 (C_{quat}OMOM), 163.4 (C_{quat}OMOM), 188.1 (CHO) ppm. HRMS (ESI): calcd for $C_{11}H_{14}O_5Na$ $[M+Na]^+$, 249.0733; found, 249.0734.

2,4-Bis(methoxymethoxy)-1-(2-methylprop-1-enyl)benzene (33). To a stirred solution of $(CH_3)_2CHP(Ph)_3I$ (6.87 g, 15.91 mmol) in THF (50 mL) was added *n*-BuLi (6.4 mL, 2.5 M in hexane, 15.9 mmol) at 0 °C. The mixture was stirred for 30 min, before a solution of aldehyde **32** (2.0 g, 8.84 mmol) in THF (25 mL) was added dropwise. The reaction was stirred at room temperature for 4 h and then quenched by the addition of water (40 mL). After separation of the layers, the aqueous layer was extracted with Et_2O (3 × 40 mL). The combined organic layers were washed with H_2O (2 × 40 mL) and brine (40 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to provide styrene **33** (2.10 g, 94%) as a colorless liquid. $R_f = 0.56$ (25% EtOAc/petroleum ether). IR (film): $\nu_{max} = 2950, 2911, 1604, 1496, 1265, 1211, 1157, 1076, 1006, 782$ cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.67$ (s, 3H, C=C(CH$_3$)$_2$), 1.78 (s, 3H, C=C(CH$_3$)$_2$), 3.35 (s, 3H, OCH$_3$), 3.40 (s, 3H, OCH$_3$), 5.02 (s, 2H, OC*H*$_2$OCH$_3$), 5.03 (s, 2H, OC*H*$_2$OCH$_3$), 6.12 (s, 1H, C*H*=C(CH$_3$)$_2$), 6.55 (dd, $J = 8.3, 2.28$ Hz, 1H, CH_{meta}), 6.57 (d, $J = 2.3$ Hz, 1H, CH_{meta}), 6.69 (d, $J = 8.3$ Hz, 1H, CH_{ortho}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 19.3$ (C=C(*C*H$_3$)$_2$), 26.4 (C=C(*C*H$_3$)$_2$), 55.8 (OCH$_3$), 55.9 (OCH$_3$), 94.4 (OCH$_2$OCH$_3$), 94.5 (OCH$_2$OCH$_3$), 103.7 (CH_{meta}), 108.4 (CH_{meta}), 120.0 (*C*H=C(CH$_3$)$_2$), 122.2 (C_{quat}CH=C), 130.7 (CH_{ortho}), 134.4 (=*C*(CH$_3$)$_2$), 155.4 (C_{quat}OMOM), 156.6 (C_{quat}-OMOM) ppm. HRMS (ESI): calcd for $C_{14}H_{20}O_4Na$ $[M+Na]^+$, 275.1254; found, 275.1256.

3-Isobutyl-2,6-bis(methoxymethoxy)benzaldehyde (35). To a stirred solution of resorcinol derivative **34** (2.90 g, 11.40 mmol) and TMEDA (1.9 mL, 12.65 mmol) in Et_2O (36 mL) was added *n*-BuLi (5.0 mL, 12.5 mmol, 2.5 M in hexane) dropwise at 0 °C followed by stirring of the mixture for 2 h at the same temperature. The mixture was warmed to room temperature, then DMF (1.96 mL, 25.1 mmol) was added and stirring continued for 3 h. The reaction mixture was poured into a separating funnel containing water (20 mL) and ether (20 mL). The layers were separated and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with water (20 mL), saturated aqueous NH_4Cl (10 mL), and brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (15% EtOAc/petroleum ether) to provide aldehyde **35** (2.74 g, 86%) as a colorless liquid. $R_f = 0.46$ (25% EtOAc/petroleum ether). IR (film): $\nu_{max} = 2956, 2891, 2811, 1691, 1592, 1477, 1386, 1157, 1079, 1033, 738$ cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.8$ Hz, 6H, CH(C*H*$_3$)$_2$), 1.86 (nonet, $J = 6.8$ Hz, 1H, C*H*(CH$_3$)$_2$), 2.43 (d, $J = 7.3$ Hz, 2H, C*H*$_2$-CH(CH$_3$)$_2$), 3.43 (s, 3H, OCH$_3$), 3.51 (s, 3H, OCH$_3$), 4.96 (s, 2H, OC*H*$_2$OCH$_3$), 5.17 (s, 2H, OC*H*$_2$OCH$_3$), 6.85 (d, $J = 8.6$ Hz, 1H, CH_{meta}), 7.21 (d, $J = 8.6$ Hz, 1H, CH_{meta}), 10.39 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 22.3$ (CH(*C*H$_3$)$_2$), 28.9 (*C*H(CH$_3$)$_2$), 38.9 (*C*H$_2$CH(CH$_3$)$_2$), 56.4 (OCH$_3$), 57.4 (OCH$_3$), 94.9 (OCH$_2$OCH$_3$), 101.9 (OCH$_2$OCH$_3$), 110.5 (CH_{meta}), 119.1 (C_{quat}-CHO), 129.1 (C_{quat}CH$_2$CH), 137.0 (CH_{ortho}), 157.2 (C_{quat}OMOM), 158.6 (C_{quat}OMOM), 189.6 (CHO) ppm. HRMS (ESI): calcd for $C_{15}H_{22}O_5Na$ $[M + Na]^+$, 305.1359; found, 305.1360.

***tert*-Butyl{[3-iodo-5-isobutyl-2,6-bis(methoxymethoxy)benzyl]-oxy}dimethylsilane (38).** To a solution of resorcinol derivative **37** (1.0 g, 2.50 mmol) in THF (7.5 mL) was added *sec*-BuLi (2.3 mL, 1.3 M in cyclohexane/hexane, 3.01 mmol) dropwise at −78 °C followed by stirring of the mixture at this temperature for 2 h. Then, iodosuccinimide (0.79 g, 3.51 mmol) in THF (5 mL) was added dropwise, and the mixture was stirred for additional 3 h. The mixture was treated with saturated aqueous NH_4Cl (4 mL) and then warmed to room temperature. The layers were separated, and the aqueous layer was extracted with ether (3 × 2 mL). The combined organic layers were washed with saturated aqueous $Na_2S_2O_3$ (5 mL), saturated aqueous $NaHCO_3$ (5 mL), and brine (5 mL). The organic layer was dried over $MgSO_4$, filtered, and evaporated in vacuo. The crude product was purified by flash chromatography (5% diethyl ether/petroleum ether) to give aryl iodide **38** (0.72 g, 55%) as a colorless oil. $R_f = 0.31$ (5% diethyl ether/petroleum ether). IR (film): $\nu_{max} = 2954, 2911, 2857, 1581, 1461, 1382, 1255, 1193, 1162, 1049, 798$ cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = -0.13$ (s, 6H, Si(CH$_3$)$_2$), 0.88 (s, 9H, C(CH$_3$)$_3$), 0.89 (d, $J = 6.8$ Hz, 6H, CH(C*H*$_3$)$_2$), 1.90 (nonet, $J = 6.8$ Hz, 6H, C*H*(CH$_3$)$_2$), 2.48 (d, $J = 7.1$ Hz, 2H, C*H*$_2$CH(CH$_3$)$_2$), 3.57 (s, 3H, OCH$_3$), 3.67 (s, 3H, OCH$_3$), 4.70 (s, 2H, CH$_2$OTBS), 5.05 (s, 2H, OC*H*$_2$OCH$_3$), 5.12 (s, 2H, OC*H*$_2$OCH$_3$), 7.55 (s, 1H, CH_{ortho}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = -5.5$ (Si(CH$_3$)$_2$), 18.1 (*C*(CH$_3$)$_3$), 22.4 (CH-

(CH_3)$_2$), 25.9 (C(CH_3)$_3$), 29.1 (CH(CH_3)$_2$), 39.2 (CH_2CH(CH_3)$_2$), 56.3 (CH_2OTBS), 57.5 (OCH_3), 58.4 (OCH_3), 86.7 (C_{quat}I), 100.9 (OCH_2OCH_3), 101.4 (OCH_2OCH_3), 128.9 ($C_{quat}CH_2CH$), 134.0 ($C_{quat}CH_2$OTBS), 140.2 (CH_{ortho}), 154.9 (C_{quat}OMOM), 157.0 (C_{quat}-OMOM) ppm. HRMS (ESI): calcd for $C_{21}H_{37}IO_5SiNa$ $[M + Na]^+$, 547.1347; found, 547.1350.

3-Isobutyl-5-{(2*S*)-2-[(4*R*,6*R*)-6-((1*E*)-1-{[(4-methoxybenzyl)-oxy]methyl}but-1-enyl)-2,2-dimethyl-1,3-dioxan-4-yl]pentanoyl}-2,6-bis(methoxymethoxy)benzaldehyde (41). To a stirred solution of aryl iodide **38** (215 mg, 0.409 mmol) in THF (2.4 mL) was added *n*-BuLi (0.16 mL, 2.5 M in hexane, 0.40 mmol) at −78 °C. After 2 h, aldehyde **30** (55 mg, 0.136 mmol) in THF (1.8 mL) was added dropwise followed by stirring of the mixture for 2 h at −78 °C. Then the mixture was allowed to warm to room temperature slowly over a period of 10 h and then treated with saturated aqueous NH_4Cl (2 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (2 × 1 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (2 mL) and brine (2 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to give the alcohol **39** (98 mg, 90%) as a colorless oil. R_f = 0.22 (10% EtOAc/petroleum ether). This compound (1:1 diastereomeric mixture) was used directly for the next step (cleavage of the *tert*-butyldimethylsilyl ether).

To a stirred solution of alcohol **39** (98 mg, 0.122 mmol) in THF (1.5 mL) was added TBAF (0.25 mL, 0.244 mL) at 0 °C and followed by stirring of the mixture for 12 h in the ice bath. The mixture was diluted with ether and concentrated in vacuo. The crude product was purified by flash chromatography (50% EtOAc/petroleum ether) to obtain the diol **40** (84 mg, 100%) as a colorless oil. R_f = 0.20 (25% EtOAc/petroleum ether). This compound (1:1 diastereomeric mixture) was used directly for the next step (oxidation to keto aldehyde).

To a stirred solution of diol **40** (95 mg, 0.137 mmol) in CH_2Cl_2 (4.5 mL) was added Dess−Martin periodinane (175.4 mg, 0.413 mmol), and the mixture was allowed to stir for 1 h. Then it was treated with 10% $Na_2S_2O_3$ solution (2 mL). The mixture was diluted with ether (2 mL), the layers were separated, and the aqueous layer was extracted with ether (2 × 1 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (2 mL) and brine (2 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (25% EtOAc/petroleum ether) to give keto aldehyde **41** (86 mg, 92%) as a pale yellow oil. R_f = 0.48 (25% EtOAc/petroleum ether). $[\alpha]^{20}_D$ = +2.8 (*c* 1.1 in CH_2Cl_2). IR (film): ν_{max} = 2958, 2933, 2871, 1612, 1565, 1513, 1461, 1382, 1249, 1160, 1072, 769 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.3 Hz, 3H, CH_3CH$_2$CH$_2$), 0.88 (d, *J* = 2.5 Hz, 3H, (CH_3)$_2$CH), 0.89 (d, *J* = 2.5 Hz, 3H, (CH_3)$_2$CH), 0.95 (t, *J* = 7.3 Hz, 3H, CH_3CH$_2$), 1.16−1.33 (m, 2H, CH_2CH$_2$CH), 1.25 (s, 3H, (CH_3)$_2$C), 1.26 (s, 3H, (CH_3)$_2$C), 1.48−1.58 (m, 1H, CH_2CHCOPh), 1.75−1.86 (m, 2H, (1H) CH_2CHCOPh and (1H) CH_2CHC═CH), 1.90−2.01 (m, 2H, (1H) CH_2CHC═CH and (1H) CH(CH_3)$_2$), 2.08 (q$_n$, *J* = 7.6 Hz, 2H, CH_2CH$_3$), 2.53 (d, *J* = 7.3 Hz, 2H, CH_2CH(CH_3)$_2$), 3.44 (s, 3H, OCH$_2$OCH_3), 3.50−3.54 (m, 1H, CHCOPh), 3.58 (s, 3H, OCH$_2$OCH_3), 3.76 (s, 3H, OCH_3), 3.99 (s, 2H, CH_2OPMB), 4.04−4.14 (m, 1H, CHCHCOPh), 4.29 (dd, *J* = 9.9, 5.8 Hz, 1H, CHC═CH), 4.37 (s, 2H, OCH_2PhOMe), 5.04 (d, *J* = 1.8 Hz, 2H, OCH_2OCH$_3$), 5.06 (s, 2H, OCH_2OCH$_3$), 5.63 (t, *J* = 7.3 Hz, 1H, C═CH), 6.83 (d, *J* = 8.8 Hz, 2H, CH_{arom}), 7.22 (d, *J* = 8.6 Hz, 2H, CH_{arom}), 7.59 (s, 1H, CH_{ortho}), 10.30 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (*C*H$_3$CH$_2$), 14.4 (*C*H$_3$CH$_2$-CH$_2$), 20.2 (*C*H$_2$CH$_2$CH), 20.9 (*C*H$_2$CH$_3$), 22.3, 22.4 ((*C*H$_3$)$_2$CH), 24.3, 24.7 ((*C*H$_3$)$_2$C), 28.8 (*C*H(CH$_3$)$_2$), 30.0 (*C*H$_2$CHCOPh), 34.0 (*C*H$_2$CHC═CH), 39.0 (*C*H$_2$CH(CH$_3$)$_2$), 54.5 (*C*HCOPh), 55.1 (OCH$_3$), 57.6, 58.0 (OCH$_2$OCH$_3$), 64.7 (CH$_2$OPMB), 67.4 (*C*HCH-COPh), 68.0 (*C*HC═CH), 71.8 (OCH$_2$PhOMe), 100.6 (C(CH$_3$)$_2$), 102.2, 102.9 (OCH$_2$OCH$_3$), 113.6 (CH_{arom}), 124.0 (C_{quat}), 129.3 (CH_{arom}), 130.4, 130.7 (C_{quat}), 132.2 (C_{quat}), 133.3 (C═*C*H), 134.7 (*C*═CH), 136.8 (CH_{ortho}), 157.2 (C_{quat}), 159.0, 159.5 (C_{quat}), 189.8 (CHO), 203.3 (C═O) ppm. HRMS (ESI): calcd for $C_{39}H_{56}O_{10}Na$ $[M + Na]^+$, 707.3766; found, 707.3762.

3-((2*S*)-2-{(4*R*,6*R*)-6-[(1*E*)-1-(Hydroxymethyl)but-1-enyl]-2,2-dimethyl-1,3-dioxan-4-yl}pentanoyl)-5-isobutyl-2,6-bis-(methoxymethoxy)benzaldehyde (42). To a stirred solution of keto aldehyde **41** (86 mg, 0.125 mmol) in CH_2Cl_2 (0.94 mL) was added H_2O (94 μL) followed by DDQ (43.3 mg). The whole mixture was stirred vigorously at room temperature for 1 h. After dilution with diethyl ether (1 mL), the reaction mixture was stirred with saturated aqueous $NaHCO_3$ solution (1 mL) for 5 min. The layers were separated, and the aqueous layer was extracted with ether (2 × 1 mL). The combined organic layers were washed with H_2O (1 mL) and brine (1 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (30% EtOAc/petroleum ether) to provide alcohol **42** (50 mg 71%) as a pale yellow oil. R_f = 0.29 (25% EtOAc/petroleum ether). $[\alpha]^{20}_D$ = +1.8 (*c* 1.0 in CH_2Cl_2). IR (film): ν_{max} = 3509, 2958, 2931, 2871, 1691, 1565, 1461, 1382, 1255, 1201, 1160, 1074, 740 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.3 Hz, 3H, CH_3-CH$_2$CH$_2$), 0.88 (d, *J* = 2.8 Hz, 3H, (CH_3)$_2$CH), 0.89 (d, *J* = 2.8 Hz, 3H, (CH_3)$_2$CH), 0.95 (t, *J* = 7.5 Hz, 3H, CH_3CH$_2$), 1.16−1.24 (m, 2H, CH_2CH$_2$CH), 1.28 (s, 6H, (CH_3)$_2$C), 1.47−1.56 (m, 1H, CH_2CHCOPh), 1.74−1.86 (m, 2H, (1H) CH_2CHCOPh and (1H) CH_2CHC═CH), 1.90−2.01 (m, 2H, (1H) CH_2CHC═CH and (1H) CH(CH$_3$)$_2$), 2.06−2.17 (m, 2H, CH_2CH$_3$), 2.42 (br s, 1H, OH), 2.53 (d, *J* = 7.3 Hz, 2H, CH_2CH(CH$_3$)$_2$), 3.42−3.53 (m, 1H, CHCOPh), 3.46 (s, 3H, OCH$_2$OCH_3), 3.56 (s, 3H, OCH$_2$OCH_3), 4.10−4.15 (m, 2H, (1H) CH_2OH and (1H) CHCHCOPh), 4.20−4.25 (m, 1H, CH_2OH), 4.34 (dd, *J* = 9.6, 6.0 Hz, 1H, CHC═CH), 5.06 (s, 4H, OCH_2OCH$_3$), 5.48 (t, *J* = 7.2 Hz, 1H, C═CH), 7.58 (s, 1H, CH_{ortho}), 10.30 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (*C*H$_3$CH$_2$), 14.4 (*C*H$_3$CH$_2$CH$_2$), 20.2 (*C*H$_2$CH$_2$CH), 20.7 (*C*H$_2$CH$_3$), 22.3, 22.4 ((*C*H$_3$)$_2$CH), 24.4, 24.8 ((*C*H$_3$)$_2$C), 28.8 (*C*H(CH$_3$)$_2$), 30.1 (*C*H$_2$CHCOPh), 34.0 (*C*H$_2$CHC═CH), 39.1 (*C*H$_2$CH(CH$_3$)$_2$), 54.4 (*C*HCOPh), 57.6, 58.1 (OCH$_2$O*C*H$_3$), 58.5 (CH$_2$OH), 67.5 (*C*HCH-COPh), 71.53 (*C*HC═CH), 100.8 (C(CH$_3$)$_2$), 102.2, 102.9 (O*C*H$_2$-OCH$_3$), 124.1 (C_{quat}), 130.7, 132.3 (C_{quat}), 132.5 (C═*C*H), 136.3 (*C*═CH), 136.7 (CH_{ortho}), 157.1, 159.7 (C_{quat}), 189.8 (CHO), 203.3 (C═O) ppm. HRMS (ESI): calcd for $C_{31}H_{48}O_9Na$ $[M + Na]^+$, 587.3191; found, 587.3191.

3-((2*S*)-2-{(4*R*,6*R*)-6-[3-Ethyl-2-(hydroxymethyl)oxiran-2-yl]-2,2-dimethyl-1,3-dioxan-4-yl}pentanoyl)-5-isobutyl-2,6-bis-(methoxymethoxy)benzaldehyde (43). To a stirred solution of allylic alcohol **42** (44 mg, 0.078 mmol), in benzene (2 mL) were added VO(acac)$_2$ (4.3 mg, 0.016 mmol) and TBHP (29.5 μL, 0.163 mmol) at room temperature. The mixture was stirred vigorously for 3 h at room temperature. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ solution (1 mL), and the layers were separated. The aqueous layer was extracted with diethyl ether (2 × 1 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (50% EtOAc/petroleum ether) to give the epoxides **43a** and **43b** as an inseparable mixture (32 mg, 71%, pale yellow oil). R_f = 0.15 (25% EtOAc/petroleum ether). IR (film): ν_{max} = 3502, 2958, 2930, 2870, 1693, 1565, 1459, 1382, 1255, 1201, 1160, 1074, 773 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.2 Hz, 3H, CH_3CH$_2$CH$_2$), 0.83 (d, *J* = 3.8 Hz, 3H, (CH_3)$_2$CH), 0.84 (d, *J* = 3.8 Hz, 3H, (CH_3)$_2$CH), 0.95 (t, *J* = 7.6 Hz, 1.5H, CH_3CH$_2$), 0.98 (t, *J* = 7.6 Hz, 1.5H, CH_3CH$_2$),1.10−1.19 (m, 2H, CH_2CH$_2$CH), 1.22 (s, 3H, (CH$_3$)$_2$C), 1.24 (s, 3H, (CH$_3$)$_2$C), 1.40−1.50 (m, 1H, CH_2CHCOPh), 1.52−1.60 (m, 2H, CH_2CH$_3$), 1.68−1.77 (m, 2H, (1H) CH_2CHCOPh and (1H) CH_2-CHC$_{quat}$ epoxide), 1.81−1.92 (m, 2H, (1H) CH_2CHC$_{quat}$ epoxide, (1H) CH(CH$_3$)$_2$), 2.25 (t, *J* = 6.1 Hz, 0.5H, OH), 2.40−2.44 (m, 0.5H, OH), 2.48 (d, *J* = 7.1 Hz, 1H, CH_2CH(CH$_3$)$_2$), 2.49 (d, *J* = 7.1 Hz, 1H, CH_2CH(CH$_3$)$_2$), 2.80 (t, *J* = 6.3 Hz, 0.5H, CH epoxide), 2.86 (t, *J* = 6.3 Hz, 0.5H, CH epoxide), 3.42 (s, 3H, OCH$_2$OCH_3),

3.47−3.51 (m, 1H, CHCOPh), 3.52 (s, 3H, OCH_2OCH_3), 3.60 (ddd, J = 11.8, 10.0, 6.7 Hz, 1H, CH_2OH), 3.76 (dd, J = 9.9, 6.3 Hz, 0.5H, CHC_{quat}epoxide), 3.82 (dd, J = 11.9, 5.1 Hz, 0.5H, CH_2-OH), 3.91−3.98 (m, 1H, (0.5H) CH_2OH and (0.5H) CHC_{quat}-epoxide), 4.02−4.09 (m, 1H, CHCHCOPh), 5.01 (s, 4H, OCH_2-OCH_3), 7.52 (s, 1H, CH_{ortho}), 10.25, 10.26 (s, 1H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.6, 10.7 (CH_3CH_2), 14.4 (CH_3-CH_2CH_2), 20.1, 20.2 (CH_2CH_2CH), 21.2 (CH_2CH_3), 22.3, 22.4 (($CH_3)_2$CH), 24.3, 24.4 (($CH_3)_2$C), 24.4, 24.6 (($CH_3)_2$C), 28.8 (CH-$(CH_3)_2$), 29.9, 30.1 (CH_2CHCOPh), 30.3, 30.8 (CH_2CHC_{quat}-epoxide), 39.1 ($CH_2CH(CH_3)_2$), 54.3 (CHCOPh), 57.7, 58.2 (OCH_2OCH_3), 60.7, 60.8 (CH_2OH), 61.5, 61.9 (CH epoxide), 62.3, 62.9 (C_{quat}epoxide), 67.2, 67.3 (CHCHCOPh), 68.4, 70.6 (CHC_{quat}-epoxide), 101.0, 101.1 ($C(CH_3)_2$), 102.2, 103.1 (OCH_2OCH_3), 124.1 (C_{quat}), 130.7, 130.8 (C_{quat}), 132.3, 132.4 (C_{quat}), 136.7 (CH_{ortho}), 157.0, 157.1 (C_{quat}), 159.7, 159.8 (C_{quat}), 189.8, 189.9 (CHO), 203.3, 203.4 (C=O) ppm. HRMS (ESI): calcd for $C_{31}H_{48}O_{10}Na$ [M + Na]$^+$, 603.3140; found, 603.3142.

3-Ethyl-2-((4*R*,6*R*)-6-{(1*S*)-1-[3-formyl-5-isobutyl-2,4-bis-(methoxymethoxy)benzoyl]butyl}-2,2-dimethyl-1,3-dioxan-4-yl)-oxirane-2-carbaldehyde (44). To a stirred solution of the foregoing epoxy alcohols **43** (24 mg, 0.041 mmol) in CH_2Cl_2 (1.5 mL) was added Dess−Martin periodinane (26.3 mg, 0.062 mmol) in CH_2-Cl_2 (0.4 mL) dropwise at room temperature. After stirring at room temperature for 45 min, the reaction was quenched with 10% aqueous $Na_2S_2O_3$ solution (1 mL) and diluted with ether (2 mL). The layers were separated and the aqueous layer was extracted with ether (3 × 1 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (2 mL) and brine (2 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was filtered through a short pad of silica gel to obtain the dialdehydes **44** (22 mg, 93%) as a slightly yellow oil. R_f = 0.31 (25% EtOAc/petroleum ether). IR (film): ν_{max} = 2958, 2938, 2873, 1693, 1569, 1461, 1384, 1253, 1199, 1172, 1133, 763 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, J = 7.3 Hz, 3H, $CH_3CH_2CH_2$), 0.82−0.91 (m, 6H, $(CH_3)_2$CH), 1.01 (t, J = 7.5 Hz, 1.5H, CH_3CH_2), 1.04 (t, J = 7.5 Hz, 1.5H, CH_3CH_2), 1.24 (s, 6H, $(CH_3)_2$C), 1.28−2.00 (m, 9H, (2H) CH_2CH_2CH, (2H) CH_2CH_3, (1H) $CH(CH_3)_2$, (2H) CH_2CHC_{quat}epoxide and (2H) CH_2CHCOPh), 2.53 (d, J = 7.1 Hz, 1H, $CH_2CH(CH_3)_2$), 2.54 (d, J = 7.1 Hz, 1H, $CH_2CH(CH_3)_2$), 2.98 (dd, J = 7.1, 5.8 Hz, 0.5H, CHepoxide), 3.36 (dd, J = 7.5, 5.8 Hz, 0.5H, CHepoxide), 3.46 (s, 3H, OCH_2OCH_3), 3.51−3.55 (m, 1H, CHCOPh), 3.57 (s, 3H, OCH_2OCH_3), 4.02−4.07 (m, 1H, CHC_{quat}-epoxide), 4.28 (dd, J = 9.8, 6.3 Hz, 0.5H, CHCHCOPh), 4.52 (dd, J = 9.8, 6.6 Hz, 0.5H, CHCHCOPh), 5.05, 5.06 (s, 2H, OCH_2-OCH_3), 7.56 (d, J = 5.6 Hz, 1H, CH_{ortho}), 9.42 (s, 0.5H, CHO), 9.51 (s, 0.5H, CHO), 10.30, 10.31 (CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.5, 10.7 (CH_3CH_2), 14.3 ($CH_3CH_2CH_2$), 20.2, 20.3 (CH_2CH_3), 21.2, 21.3 (CH_2CH_2CH), 22.3, 22.4 (($CH_3)_2$CH), 23.8, 24.1 (($CH_3)_2$C), 24.3, 24.5 (($CH_3)_2$C), 28.8 ($CH(CH_3)_2$), 29.0 (CH_2CHCOPh), 30.0, 30.2 (CH_2CHC_{quat}epoxide), 39.1 (CH_2CH-$(CH_3)_2$), 54.1, 54.2 (CHCOPh), 57.6, 57.7 (OCH_2OCH_3), 58.1, 58.2 (OCH_2OCH_3), 62.8 (CHepoxide), 63.8, 64.2 (CHCHCOPh), 66.2, 67.0 (C_{quat}epoxide), 67.1, 67.2 (CHC_{quat}epoxide), 100.9, 101.1 (($C(CH_3)_2$), 102.2, 103.1 (OCH_2OCH_3), 124.0 (C_{quat}), 130.7, 130.8 (C_{quat}), 132.3 (C_{quat}), 136.7, 136.8 (CH_{ortho}), 157.1, 157.2 (C_{quat}), 159.6, 159.7 (C_{quat}), 189.8, 189.9 (CHO), 199.3, 199.4 (CHO), 203.2, 203.4 (C=O) ppm. HRMS (ESI): calcd for $C_{31}H_{46}O_{10}Na$ [M + Na]$^+$, 601.2983; found, 601.2990.

Luminacin D (1) and 6′,8′-*epi*-Luminacin (6′,8′-*epi*-1). A mixture of acetal **44** (21 mg, 0.036 mmol), THF (0.38 mL), AcOH (0.38 mL) and water (0.2 mL) was stirred for 3 h at 95 °C. After cooling, the mixture was concentrated in vacuo. The residue was diluted with toluene, and the solvent removed in vacuo. This was repeated several times to remove the acetic acid. The crude product was purified by flash chromatography (50% EtOAc/petroleum ether) to furnish pure luminacin D (**1**) (8 mg, 49%) and the epoxide diastereomer 6′,8′-*epi*-**1** (5 mg, 31%) as colorless oils: R_f = 0.30 (50% EtOAc/petroleum ether). To avoid decomposition, further purification and separation should be done on diol-modified silica gel (Merck 40−63 μm, 2% MeOH/CH_2Cl_2). The NMR spectra (^{1}H, ^{13}C) data matched the reported ones. The epi-compound turned out to be a mixture (1:1) of anomers.

Luminacin D (1): First Spot. R_f = 0.27 (silica gel, 30% acetone/hexane); 0.2 (diol-modified silica gel, 2% MeOH/DCM); $[\alpha]^{20}_D$ = −12.2 (*c* 0.2 in $CHCl_3$). IR (film): ν_{max} = 3446, 2958, 2930, 2853, 1735, 1693, 1461, 1384, 1253, 1199, 1133, 1075, 1039, 763 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.5 Hz, 3H, 11′-CH_2CH_3), 0.89 (d, J = 6.6 Hz, 3H, $(CH_3)_2$CH), 0.90 (d, J = 6.4 Hz, 3H, $(CH_3)_2$CH), 0.92 (t, J = 7.6 Hz, 3H, 10′-H), 1.19−1.30 (m, 1H, 11′-CH_2CH_3), 1.37−1.47 (m, 2H, 11′-CH_2CH_3, 9-H′), 1.50 (q, J = 12.1 Hz, 1H, 4′-H), 1.63−1.71 (m, 2H, 9′-H, 11′-H), 1.83−1.91 (m, 2H, 11′-H, $(CH_3)_2CH$), 2.12 (ddd, J = 12.7, 4.5, 1.9 Hz, 1H, 4′-H), 2.41 (dd, J = 13.9, 7.6 Hz, 1H, CH_2iPr), 2.45 (dd, J = 13.9, 7.6 Hz, 1H, CH_2iPr), 2.81 (br s, 1H, OH), 3.27 (t, J = 6.7 Hz, 1H, 8′-H), 3.54−3.58 (m, 1H, 2′-H), 4.38 (dd, J = 11.4, 5.1 Hz, 1H, 5′-H), 4.45 (ddd, J = 11, 7.6, 1.5 Hz, 1H, 3′-H), 4.96 (s, 1H, 7′-H), 7.73 (s, 1H, 4-H), 10.39 (s, 1H, CHO), 12.97 (s, 1H, 6-OH), 14.15 (s, 1H, 2-OH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 10.0 (C-10′), 14.2 (11′-CH_2CH_3), 20.7 (11′-CH_2CH_3), 21.2 (C-9′), 22.2 (($CH_3)_2$CH), 28.2 (($CH_3)_2$CH), 31.7 (C-11′), 36.5 (C-4′), 37.9 (CH_2iPr), 49.0 (C-2′), 59.2 (C-8′), 62.8 (C-5′), 64.3 (C-6′), 69.8 (C-3′), 92.5 (C-7′), 109.2 (C-1), 112.5 (C-3), 120.8 (C-5), 139.7 (C-4), 167.4 (2), 167.9 (C-6), 194.3 (CHO), 206.5 (C-1′) ppm. HRMS (ESI): calcd for $C_{24}H_{34}O_8Na$ [M + Na]$^+$, 473.2146; found, 473.2143.

6′,8′-*epi*-Luminacin (6′,8′-*epi*-1): Second Spot. R_f = 0.20 (silica gel, 30% acetone/hexane); 0.31 (diol-modified silica gel, 4% MeOH/CH_2Cl_2); $[\alpha]^{20}_D$ = +6.3 (c 0.3 in $CHCl_3$). IR (film): ν_{max} = 3450, 2958, 2873, 1633, 1461, 1384, 1253, 1199, 1133, 1075, 1039, 763 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.85 (t, J = 7.6 Hz, 3H, 11′-CH_2CH_3), 0.88 (d, J = 6.7 Hz, 1.5H, $(CH_3)_2$CH), 0.89 (d, J = 6.7 Hz, 1.5H, $(CH_3)_2$CH), 0.90 (d, J = 7.0 Hz, 3H, $(CH_3)_2$CH), 1.05 (t, J = 7.3 Hz, 1.5H, 10′-H), 1.09 (t, J = 7.3 Hz, 1.5H, 10′-H), 1.16−1.27 (m, 2H, 11′-CH_2CH_3), 1.35−1.64 (m, 2H, 9′-H), 1.67 (dd, J = 12.1, 4.5 Hz, 1H, 4′-H), 1.75−1.82 (m, 2H, 4′-H, 11′-H), 1.86−1.96 (m, 2H, 11′-H, $(CH_3)_2CH$), 2.33−2.38 (m, 1H, CH_2iPr), 2.43−2.50 (m, 1H, CH_2iPr), 3.56−3.59 (m, 2H, 3′-H, 2′-H), 3.60−3.64 (m, 0.5H, 8′-H), 3.98 (dd, J = 11.4, 5 Hz, 0.5H, 5′-H), 4.23−4.27 (m, 0.5H, 8′-H), 4.35 (dd, J = 11.4, 5 Hz, 0.5H, 5′-H), 4.53 (s, 0.5H, 7′-H), 5.13 (s, 0.5H, 7′-H), 7.73 (s, 0.5H, 4-H), 7.74 (s, 0.5H, 4-H), 10.39 (s, 1H, CHO), 12.97 (s, 0.5H, 6-OH), 12.98 (s, 0.5H, 6-OH), 14.09 (s, 0.5H, 2-OH), 14.15 (s, 0.5H, 2-OH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 11.1, 11.3 (C-10′), 14.2 (11′-CH_2CH_3), 20.4, 20.5 (11′-CH_2CH_3), 22.2, 22.4 (($CH_3)_2$CH), 23.6, 25.1 (C-9′), 28.2 (($CH_3)_2$CH), 32.2, 32.5 (C-11′), 32.9, 33.3 (C-4′), 37.9 (CH_2iPr), 49.3, 49.6 (C-2′), 64.6 (C-5′), 69.2, 69.5 (C-8′), 72.0, 72.5 (C-3′), 74.3, 74.5 (C-6′), 94.6, 95.8 (C-7′), 109.3 (C-1), 112.4, 112.5 (C-3), 121.1, 121.3 (C-5), 139.3, 139.4 (C-4), 167.4 (C-2), 168.0, 168.1 (C-6), 194.2, 194.3 (CHO), 206.7, 207.0 (C-1′) ppm. HRMS (ESI): calcd for $C_{24}H_{34}O_8$-$Na + H_2O$ [M + Na]$^+$, 491.2251; found, 491.2254.

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Supporting Information Available: Experimental procedures and characterization for all other new compounds reported and copies of NMR spectra for important intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

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