Allyltitanates in Stereospecific Additions to Chiral δ-Lactol: Efficient Enantioselective Route to a Potential Precursor of the C1−C9 Portion of Tylonolide

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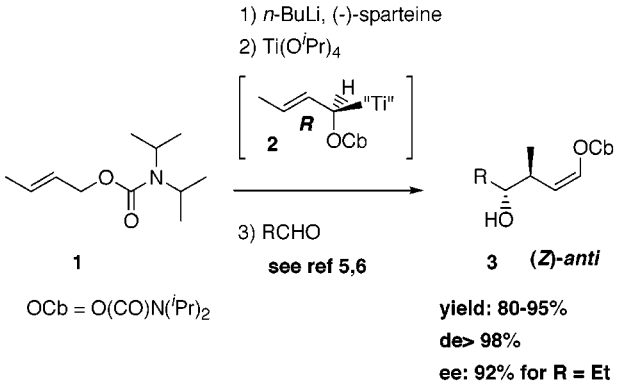
The Hoppe reaction, which is an allylation reaction of aldehydes using an optically active titanated crotyl carbamate intermediate generated from the corresponding *N*,*N*-diisopropyl crotyl carbamate with *n*-BuLi/(−)-sparteine, was in most cases applied to achiral aldehydes. In this work an extension of this reaction is reported using a racemic γ-alkoxy allyltitanate (**17**) and an optically active aldehyde (**16**) to deliver in good yield the anti adduct **18** as the major isomer. When the corresponding δ-lactol **24** was used in place of aldehyde **16**, the anti adduct **25** was obtained in 94% yield as the only product. Structural modifications effected on **25** delivered aldehyde **28** which was in turn submitted to a second allylation reaction in the presence of the optically active titanated crotyl carbamate **2**, prepared as described by Hoppe from crotyl carbamate **1**, to conduct to compound **29** in 80% yield. This derivative corresponds to a potential precursor of the C1−C9 portion of Tylonolide, aglycon of Tylosin (**4**).

Allylation of aldehydes have been largely described in the literature for many years.[1] In most cases the diastereoselectivities obtained were fair to excellent, in an S_E' Lewis-acid-catalyzed reaction[2,3] via an open transition state or via a Zimmerman−Traxler transition state in others cases.[4] The enantioselectivity in these reactions arise either from the allylmetal or the aldehyde, or from both enantiopure partners.

The Hoppe reaction,[5] which was reported as an allylation of an achiral aldehyde with an optically active (*E*)-crotyltitanate **2**, proceeds with a high diastereo- and enantioselectivities via a cyclic Zimmerman−Traxler transition state to deliver the anti isomer **3** (Scheme 1).

Scheme 1



Reaction of (*E*)-crotylcarbamate **1** with *n*-BuLi/(−)-sparteine gave both diastereomers of the (*E*)-crotyllithium−(−)-sparteine complex; crystallization led to the corresponding (*S*) complex[6] in a second-order asymmetric induction. After transmetalation with $Ti(O^iPr)_4$, the (*R*)-(*E*)-allyltitanate **2** was formed and gave, by reaction with aldehydes, the (*Z*)-anti homoallylic alcohol **3** with good enantiomeric excess (92% ee for R = Et).

In an approach to the C10−C15 western part of Tylonolide, aglycon of the 16-membered Tylosin antibiotic **4**,[7] we employed the Hoppe reaction for a stereocontrolled construction of C14 and C15 centers.[8] In the present work

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(2) Pereyre, M.; Quintard, J. P. *Pure Appl. Chem.* **1981**, *53*, 2401. Quintard, J. P.; Elisondo, B.; Pereyre, M. *J. Org. Chem.* **1983**, *48*, 1559. Quintard, J.-P.; Dumartin, G.; Elisondo, B.; Rahm, A.; Pereyre, M. *Tetrahedron* **1989**, *45*, 1017.

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(4) (a) For allylation via boronates, see: Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.* **1987**, *52*, 316. Roush, W. R.; Adam, M. A.; Walts, A. E.; Harris, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 3422. Roush, W. R.; Banfi, L. *J. Am. Chem. Soc.* **1988**, *110*, 3979. Roush, W. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1986**, *108*, 294. Coe, J. W. Roush, W. R. *J. Org. Chem.* **1989**, *54*, 915. (b) For allylation via boranes, see: Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 5919. Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Am. Chem. Soc.* **1989**, *54*, 1570. Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1988**, *110*, 1535.

(5) For a recent review, see: Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl* **1997**, *36*, 2282.

(6) Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 932. Hoppe, D.; Zschage, O. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 69. Paulsen, H.; Hoppe, D. *Tetrahedron* **1992**, *48*, 5667. Zschage, O.; Hoppe, D. *Tetrahedron* **1992**, *48*, 5657.

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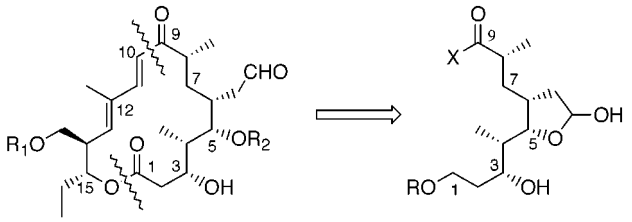
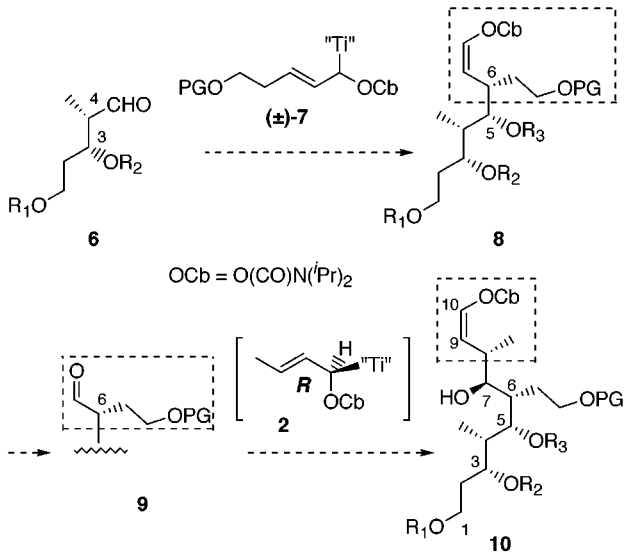
Scheme 2



Scheme 3

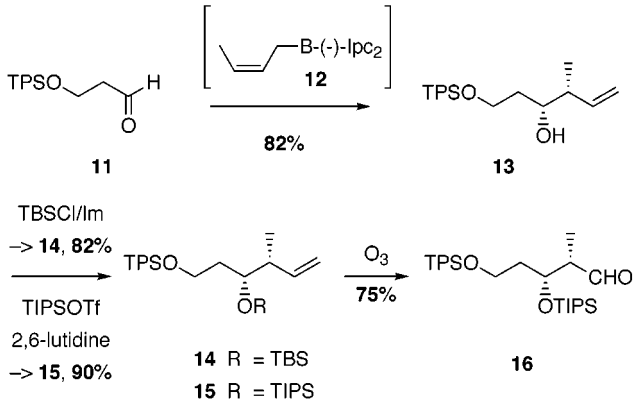


we describe the results obtained in an application and extension of the Hoppe reaction to a synthetic approach to the C1−C9 eastern part **5** of Tylonolide (Scheme 2).

In our synthesis of the eastern part of Tylonolide, we planned to prepare compound **10** (Scheme 3); for this purpose, two allylations were designed as the key steps. We envisaged a reaction of allyltitanate **7** with optically active aldehyde **6** in order to prepare homoallylic alcohol **8**. After oxidative cleavage of the vinylic function into aldehyde **9**, the later could be reacted with (*R*)-(*E*)-crotyltitanate **2** to furnish the expected key intermediate **10**.[9] Allylation with this intermediate **2** was well described, but at this time only a few cases of double asymmetric induction were reported for this reaction.[10]

The first allylation we wanted to develop, between enantiopure aldehyde **6** and **(±)**-(*E*)-allyltitanate **7** must be considered as an extension of the Hoppe reaction; to our knowledge the Hoppe reaction has always been performed with (*R*)-(*E*)-crotyltitanate **2**. Using a different

Scheme 4



allylcarbamate in this reaction resulted in the lack of crystallization of corresponding (*R*)- or (*S*)-allyllithium and neither second-order asymmetric induction or enantioselective deprotonation could be induced.[11] Therefore, reaction of aldehyde **6** was envisioned to be governed by kinetic resolution using the intermediate allyltitanate (±)-**7**.[12]

Preparation of alcohol **13** was performed by reaction of aldehyde **11**[13] with (*Z*)-(−)-$(Ipc)_2$B-crotyl **12**[4b] [$(Ipc)_2$ = diisopinocampheyl] (82% yield, Scheme 4). The secondary alcohol at C3 was protected as a triisopropylsilyl ether (**15**, R = TIPS, 90%), and ozonolysis of the double bond led to aldehyde **16**. Alcohol **13** was protected as the *tert*-butyldimethylsilyl ether **14** (R = TBS, 82%) which appeared to be identical to the product described by Boeckman [$[\alpha]_D$ + 20.9 (*c* 1.0, $CHCl_3$)].[14]

For allylation of aldehyde **16**, several carbamates **7** were synthesized, starting with commercial 3-propyn-1-ol, and after some experiments the tetrahydropyranyloxy derivative **17** was retained for this approach.

In a first model study of reaction of **17** with propanal, formation of the intermediate allyltitanate was not observed when 1 equiv of *n*-BuLi/TMEDA was used. However, deprotonation of **17** was effected in good yield when 1.5−2 equiv of *n*-BuLi/TMEDA was employed. Transmetalation with $Ti(O^iPr)_4$ then occurred at −78 °C, and reaction with propanal was carried out at −78 °C for 2 h to deliver the expected anti allylic alcohol in 90% yield.[15]

The allylation reaction of aldehyde **16** with allylcarbamate **17** was then carried out at −78 °C for 5 h using

Macrolides Antibiotics; Academic Press: 1984. Kirst, H. A. *J. Antimicrob. Chemother.* **1991**, *28*, 787. Kirst, H. A. In *Recent Progress in the Chemical Synthesis of Antibiotics*; Lukacs, G., Ohno, M., Eds.; Springer-Verlag: Berlin, 1990; p 39.

(8) Le Ménez, P.; Fargeas, V.; Berque, I.; Poisson, J.; Ardisson, J.; Lallemand, J.-Y.; Pancrazi, A. *J. Org. Chem.* **1995**, *60*, 3592.

(9) Our approch is slightly different from the synthesis of tylonolide developed by Marshall et al. (Marshall, J. A.; Yashunsky, D. V. *J. Org. Chem.* **1991**, *56*, 5493) which also involved a crucial step based on an allylation reaction.

(10) Smith, N. D.; Kocienski, P. J.; Street, S. D. A. *Synthesis* **1996**, 652. Férézou, J.-P.; Julia, M.; Li, Y.; Liu, L. W.; Pancrazi, A. *Bull. Soc. Chim. Fr.* **1995**, *132*, 428. Férézou, J.-P.; Julia, M.; Khourzom, R.; Li, Y.; Liu, L. W.; Pancrazi, A.; Robert, P. *Synlett* **1991**, 611.

(11) Second-order asymmetric induction was also described with the 1-(*N*,*N*-diisopropylcarbamoyloxy)-3-trimethylsilylallyl: Marsch, M.; Harms, K.; Zschage, O.; Hoppe, D.; Boche, G. *Angew. Chem., Int. Ed. Engl* **1991**, *30*, 321. When we tried to check this reaction with the 1-(*N*,*N*-diisopropylcarbamoyloxy)-4-dimethylphenylsilyl-2-butene (ref 8), no crystallization occurred and no enantioselective deprotonation could be obtained.

(12) Hoffmann, R. W.; Lanz, J.; Metternich, R.; Tarara, G.; Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1145. Hoppe, D.; Tarara, G.; Wilckens, M. *Synthesis* **1989**, 83.

(13) Pirrung, M. C.; Webster, N. J. G.; Nicholas, J. G. *J. Org. Chem* **1987**, *52*, 3603.

(14) Boeckman, R. K.; Charette, A. B.; Asberom, T.; Johnston, B. H. *J. Am. Chem. Soc.* **1991**, *113*, 5337.

(15) Allylation of propanal with allylcarbamate **17** was performed at −78 °C for 2 h using 2 equiv of BuLi/TMEDA for 1 equivalent of **17**.

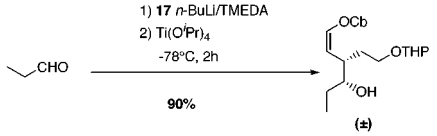


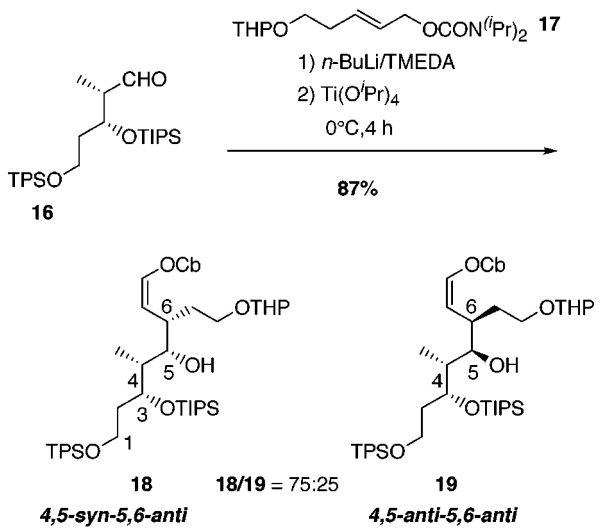
Table 1. Allylation of Aldehyde 16 and Lactol 24

entry	ratio **17**/**16**	temp (°C)	reaction time (h)	syn-anti **18** yield (%)[a]	anti-anti **19** yield (%)	overall yield (%)	selectivity
1	2:1	−78	5	55	36	91	60:40
2	2:1	0	4	58	19	77	75:25
3	3:1	0	4	65	22	87	75:25
4	3:1	20	5	66	9	75	88:12

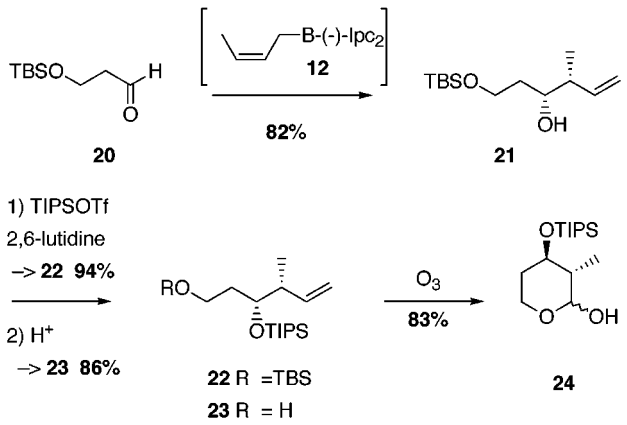
entry	ratio **17**/**24**	temp (°C)	reaction time (h)	solvent	anti-anti **25** yield (%)	selectivity
5	3:1	0	6	Et_2O	38	100:0
6	3:1	0	15	Et_2O	45	100:0
7	3:1	20	6	Et_2O	45	100:0
8	2:1	20	6	Et_2O	46	100:0
9	3:1	20	6	THF[b]	65	100:0
10	3:1	20	6	THF[c]	94	100:0

[a] Isolated yields. [b] Carbamate and BuLi/TMEDA were dissolved in diethyl ether and lactol in THF. [c] Lactol, carbamate, and BuLi/TMEDA were dissolved in THF.

Scheme 5



Scheme 6



2 equiv of **17** (Scheme 5). Deprotonation was effected at −78 °C with 4 equiv of *n*-BuLi/TMEDA for 30 min, a transmetalation occurred by addition of 6 equiv of Ti(O^{i}Pr)$_4$ at −78 °C for 30 min, and aldehyde was then added at −78 °C. This attempt resulted in formation of syn-anti **18** (55% isolated yield) and anti-anti **19** (36% isolated yield) isomers in 91% overall yield and a 60:40 ratio (Table 1, entry 1). When this reaction was performed at higher temperature (−78 → 0 °C) for 4 h compounds, **18** and **19** were obtained in 77% yield and a 75:25 ratio (Table 1, entry 2). This increasing diastereoselectivity (60:40 → 75:25) was in fact due to the lower yield obtained for the anti-anti isomer **9** (19% instead of 36% yield), while **18** was yielded as before (58% in place of 55% yield). This loss of the minor isomer **19** was assigned and tentatively proved to occur during the increase of temperature from −78 to 0 °C; treatment of a 60:40 mixture of **18** and **19** under the conditions led to 70:30 ratio after 2 h at 0 °C while allylic alcohols **18** and **19** were recovered in 70% yield.

With three equivalents of carbamate **17**, at 0 °C for 4 h, reaction led to isomers **18** and **19** in respectively 65% and 22% yield (**18/19** = 75:25, 87% overall yield). When this reaction was carried out at 20 °C for 5 h, the yield decreased to 75% but the isomer ratio **18/19** increased to 88:12.

During this study we decided to prepare δ-lactol **24** which could be considered as a masked aldehyde, and to turn to the reaction of the allyltitanate **17** with lactol **24** in place of aldehyde **16**.[16] Starting from aldehyde **20**, allylic alcohol **21** was prepared in 82% yield using allylborane **12** (Scheme 6).[17] The secondary alcohol of **21** was protected as a TIPS ether (94% yield) and the primary alcohol was revealed by acidic treatment with Amberlyst 15 to furnish compound **23** in 86% yield. Ozonolysis of the double bond then delivered δ-lactol **24** in 83% yield.

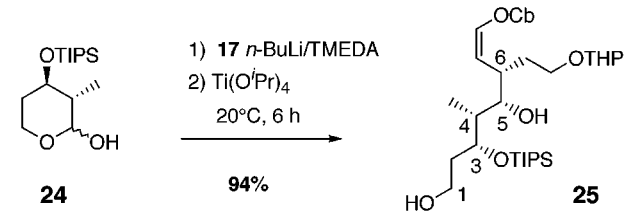
Treatment of **17** (3 equiv) with *n*-BuLi/TMEDA (6 equiv) at −78 °C followed by transmetalation with Ti(O^{i}Pr)$_4$ (9 equiv, −78 °C) led to the corresponding racemic allyltitanate which did not react with δ-lactol **24** at −78 °C for 6 h. When the temperature increased to 0 °C, reaction took place to furnish only syn-anti isomer **25** (Scheme 7, Table 1, entries 5 and 6).

We then found that allylation of δ-lactol **24** took place in 45% yield under the same conditions but when temperature was maintained at 20 °C for 6 h (Table 1, entry 7) to deliver the only 4,5-syn-5,6-anti adduct **25**; despite a high reaction temperature, this allylation reaction was carried out without epimerization of lactol **24**, and no 5,6-syn adduct was observed (Scheme 7). Attempt to use only 2 equiv of the carbamate **17** in the allylation reaction of lactol **24** (0 °C for 6 h) resulted in formation of allylic alcohol **25** in the same yield (46%, Table 1, entry 8).

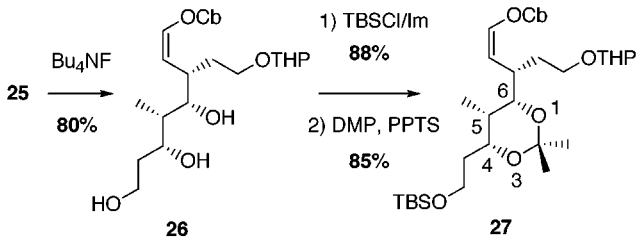
(16) For examples using lactols in such a reaction, see: Smith, A. L.; Pitsinos, E. N.; Hwang, C. K.; Mizuno, Y.; Saimoto, H.; Scarlato, G. R.; Suzuki, T.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1993**, *115*, 7612. Hoffmann, R. W.; Rolle, U. *Tetrahedron Lett.* **1994**, *35*, 4751.

(17) For structural proof, compound **21** was converted into the bis-silylated derivative **14**.

Scheme 7



Scheme 8



As an interesting assay, when the δ-lactol **24** was dissolved in THF in place of Et_2O, the carbamate **7** and the *n*-BuLi/TMEDA base added in diethyl ether, the allylation reaction led to the syn-anti adduct **25** in 65% isolated yield (Table 1, entry 9). The beneficial effect of THF was clearly shown when lactol, carbamate and BuLi/TMEDA were dissolved in THF: the syn-anti adduct **25** was obtained as a pure isomer in high yield (Table 1, entry 10, 94% isolated yield).

Realization of the strategy depicted in Scheme 3 involved at this stage to generate the aldehyde function from vinylic carbamate **25** and to perform a second allylation reaction using crotylcarbamate **1**.

Homoallylic alcohol **25** was deprotected to triol **26** (Bu_4NF, 80%), which was transformed into acetonide **27** after selective protection of the primary alcohol (Scheme 8, 75% overall yield).

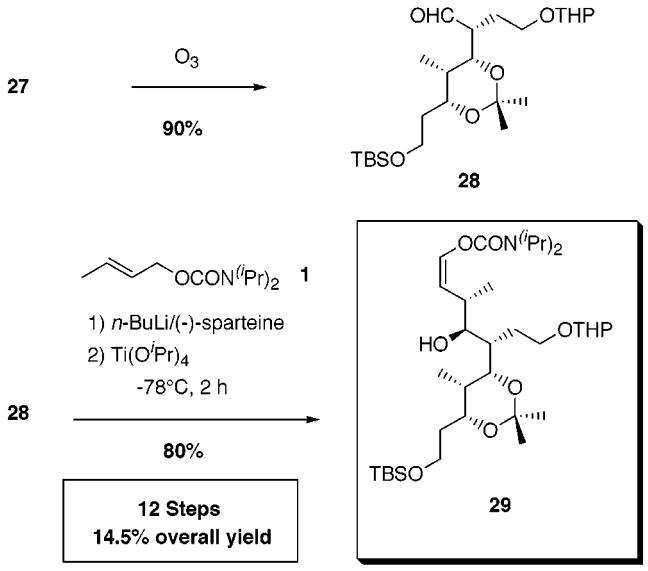
After ozonolysis of the vinylic ether of **27** to give aldehyde **28** in 90% yield, the allylation reaction using a double asymmetric induction was tested. Treatment of crotylcarbamate **1** under Hoppe conditions [(1) *n*-BuLi/(−)-sparteine, (2) $Ti(O^iPr)_4$, −78 °C] and reaction with aldehyde **28** resulted in formation of compound **29** in 80% yield (Scheme 9).

For structural elucidations of compound **18**, **19**, and **25**, some chemical transformations were needed and compound **25** was first transformed into **18** by silylation with TPSCl/Im in 80% yield.

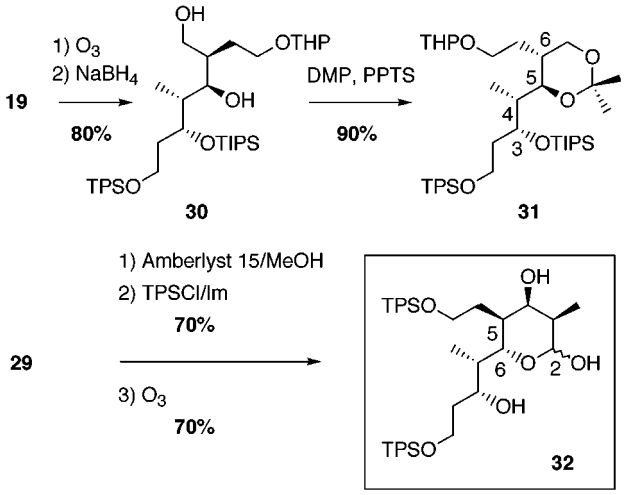
A ^{13}C analysis of acetonide **27** (obtained from **25** or **18**) allowed us to determine the syn relationship between the two oxygen atoms at C3 and C5 of the ketal by observation of the chemical shifts of the acetonide methyl groups at 19.7 and 29.8 ppm.[18] The methyl function at C4 was observed at 4.8 ppm which corresponds to an axial orientation; this configuration at C4 demonstrated that no epimerization of lactol **24** occurred at 20 °C during the allylation reaction.

For the minor anti-anti **19** derivative, ozonolysis followed by reduction of the intermediate aldehyde produced diol **30** in 80% overall yield (Scheme 10). Formation of the acetonide **31** was then carried out in 90% yield. ^1H NMR analysis of **31** clearly shown a trans relationship

Scheme 9



Scheme 10



between the two side chains at C5 and C6 ($J_{H_5-H_6} = 11.5$ Hz).

The stereochemisty at C5 and C6 centers for compound **29** was proven by transformation into δ-lactol **32**. Removal of the acetonide and the THP group from **29** was realized using Amberlyst 15/ MeOH, both primary alcohols of the resulting pentol were then selectively protected as *tert*-butyldiphenylsilyl ethers (TPS). Ozonolysis of the vinyl carbamate then led to δ-lactol **32** as a mixture of two epimeric derivatives (Scheme 10). ^1H NMR study and 2D experiments on the epimeric mixture determined all configurations at the C5, C6, C7, and C8 centers.

Although the reason for the excellent selectivity of the allylation of lactol **24** is not clearly established, this reaction runs in good yield; the strategy used here provided an efficient access to the C1−C9 fragment **29** in 12 steps and 14.5% overall yield. The final steps envisioned for the synthesis of Tylonolide, aglycon of Tylosin **4**, from **29** are now under study through a Barton−Mc-Combie deoxygenation reaction[19] at C7 after oxidation of the vinylcarbamate function.

(18) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945.

(19) Barton, D. H. R.; Mc-Combie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

Experimental Section

Mass spectra were obtained via direct introduction by chemical ionization with ammonia (CIMS, NH_3). ^1H NMR spectra were recorded at 200 and 400 MHz, and ^{13}C NMR were at 50.3 and 100.6 MHz. The chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane (TMS, $\delta = 0$) and referenced to residual chloroform ($\delta = 7.27$ ppm). Assignments were obtained using *J*-mod experiments and, when necessary, COSY, HMBC, HMQC, and NOESY experiments. Thin-layer chromatography (TLC) was performed on precoated plate of silica gel 60F 254 or aluminum oxide 60F 254. Flash chromatography was performed on silica gel 60, 230−400 mesh.

3-{[*(tert*-Butyldiphenyl)silyl]oxy}propionaldehyde (11). To a solution of 3-butenol (2.36 g, 32.8 mmol) in dried DMF (40 mL) was added a solution of imidazole (5 g, 73.5 mmol) and *tert*-butyldiphenylsilyl chloride (9.9 g, 36 mmol) in dried DMF (10 mL). After 12 h of stirring at 20 °C, the reaction mixture was partitioned between diethyl ether and an aqueous hydrochloric acid solution (2 N) and extracted with diethyl ether. The organic layer was then washed with brine, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 98:02) to give 4-{[(*tert*-butyldiphenyl)silyl]oxy}-1-butene as a colorless oil (10.1 g, 99% yield): ^1H NMR (200 MHz) δ 1.02 (s, 9H), 2.29 (q, $J = 7.0$ Hz, 2H), 3.68 (t, $J = 7.0$ Hz, 2H), 4.98 (dq, $J = 19.0$, 1.5 Hz, 1H), 5.05 (dq, $J = 10.0$, 1.5 Hz, 1H), 5.88 (ddt, $J = 19.0$, 10.0, 7.0 Hz, 1H), 7.37 (m, 6H), 7.65 (m, 4H); IR (CCl_4) ν 3080 cm^{-1}; CIMS (NH_3) *m/z* 311 (MH^+). Anal. Calcd for $C_{20}H_{26}OSi$: C, 77.37; H, 8.44. Found: C, 77.41; H, 8.46.

Ozone was bubbled into a solution of 4-{[(*tert*-butyldiphenyl)silyl]oxy}-1-butene (514 mg, 1.7 mmol) in CH_2Cl_2 (7 mL) and methanol (3 mL) at −78 °C until the solution turned light blue. Dimethyl sulfide (5 mL) was added at −78 °C, and the mixture was allowed to warm to room temperature and stirred for 8 h. The mixture was washed with water and a saturated aqueous sodium chloride solution, dried over sodium sulfate, and evaporated under reduced pressure to afford aldehyde **11** as a colorless liquid (0.513 mg, quantitative yield), pure enough to be used in the next step.

For **11:** ^1H NMR (200 MHz) δ 1.02 (s, 9H), 2.58 (dt, $J = 6.0$, 2.0 Hz, 2H), 4.00 (t, $J = 6.0$ Hz, 2H), 7.39 (m, 6H), 7.64 (m, 4H), 9.10 (t, $J = 2.0$ Hz, 1H); IR (CCl_4) ν 3060, 1720 cm^{-1}; CIMS (NH_3) *m/z* 313 (MH^+). Anal. Calcd for $C_{19}H_{24}O_2Si$: C, 73.01; H, 7.74. Found: C, 73.15; H, 7.83.

(3*R*,4*R*)-6-{[*(tert*-Butyldiphenyl)silyl]oxy}-4-hydroxy-3-methylhex-1-ene (13). To a solution of freshly sublimed potassium *tert*-butoxide (3 g, 26.7 mmol) in THF (40 mL) at −78 °C was cannulated a solution of *cis*-2-butene (6 mL) in THF (6 mL). *n*-BuLi (9.5 M in hexane, 3.3 mL, 31.3 mmol) was then added dropwise, and the yellow mixture was stirred at −78 °C for 5 min and at −45 °C for 40 min. The resulting orange solution was cooled to −78 °C, and a solution of (−)-*B*-diisopinocamphenylmethoxyborane (12 g, 38 mmol) in 30 mL of diethyl ether was added dropwise over ca. 15 min. The resulting white solution was stirred at −78 °C for 45 min. Boron trifluoride etherate (5 mL, 39.2 mmol) was added dropwise followed after 5 min by addition of a solution of aldehyde **11** (3.61 g, 11.5 mmol) in THF (5 mL). The resulting solution was stirred at −78 °C for 4 h. The reaction was then quenched by addition of aqueous NaOH (24 mL, 2.5 N) followed by aqueous H_2O_2 (8 mL, 30%). The mixture was heated at 45 °C for 45 min. The cloudy solution was cooled to room temperature, diluted with diethyl ether (50 mL), washed with brine, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure to give, after flash chromatography on silica gel (hexane/ethyl acetate, 90:10), the title compound **13** as a colorless liquid (3.47 g, 82% yield): ^1H NMR (200 MHz) δ 1.03−1.05 (m, 12H), 1.66 (m, 2H), 2.26 (m, 1H), 3.18 (d, $J = 2.8$ Hz, 1H, OH), 3.72 (m, 1H), 4.85 (m, 2H), 5.02 (m, 2H), 5.76 (m, 1H), 7.39 (m, 6H), 7.65 (m, 4H); IR (CCl_4) ν 3500, 3060 cm^{-1}; CIMS (NH_3) *m/z* 369 (MH^+); $[\alpha]_D$ + 3.4 (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75. Found: C, 74.99; H, 8.79.

(3*R*,4*R*)-4-{[*(tert*-Butyldimethyl)silyl]oxy}-6-{[*(tert*-butyldiphenyl)silyl]oxy}-3-methylhex-1-ene (14). To a solution of alcohol **13** (250 mg, 0.7 mmol) in dried CH_2Cl_2 (15 mL) at 0 °C was added triethylamine (0.2 mL, 1.4 mmol) and *tert*-butyldimethylsilyltriflate (0.2 mL, 0.85 mmol). After 2 h of stirring at 20 °C, the reaction mixture was partitioned between diethyl ether and a saturated aqueous ammonium chloride solution and extracted with diethyl ether. The organic layer was then dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 97:3) to give the title compound **14** as a colorless oil (272 mg, 82% yield): ^1H NMR (200 MHz) δ 0.05 (s, 6H), 0.96 (d, $J = 7.0$ Hz, 3H), 1.08 (m, 30H), 1.71 (qd, $J = 6.0$, 2.0 Hz, 2H), 2.38 (m 1H), 3.72 (t, $J = 6.0$ Hz, 2H), 4.05 (q, $J = 6.0$ Hz, 1H), 4.97 (dd, $J = 11.5$, 1.2 Hz, 1H), 5.05 (dd, $J = 18.0$, 1.2 Hz, 1H), 6.05 (ddd, $J = 18.0$, 11.5, 6.5 Hz, 1H), 7.39 (m, 6H), 7.65 (m, 4H); IR (CCl_4) ν 3060 cm^{-1}; CIMS (NH_3) *m/z* 483 (MH^+); $[\alpha]_D$ + 20.9 (*c* 1.01, $CHCl_3$) [lit.[14] +21 (*c* 1.0, $CHCl_3$)]. Anal. Calcd for $C_{29}H_{46}O_2Si_2$: C, 74.14; H, 9.60. Found: C, 72.20; H, 9.65.

(3*R*,4*R*)-6-{[*(tert*-Butyldiphenyl)silyl]oxy}-3-methyl-4-{[(triisopropyl)silyl]oxy}hex-1-ene (15). To a solution of alcohol **13** (1.74 g, 4.74 mmol) in dried CH_2Cl_2 (12 mL) at 0 °C were added 2,6-lutidine (0.86 mL, 7.6 mmol) and TIPSOTf (1.4 mL, 5.2 mmol). After 2.5 h of stirring at 20 °C, the reaction mixture was partitioned between diethyl ether and an aqueous hydrochloric acid solution (1.5 N) and extracted with diethyl ether. The organic layer was washed with brine, dried over sulfate sodium, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 98:02) to give compound **15** (2.24 g, 90% yield): ^1H NMR (200 MHz) δ 0.96 (d, $J = 7.0$ Hz, 3H), 1.08 (s, 30H), 1.71 (qd, $J = 6.0$, 2.0 Hz, 2H), 2.38 (m, 1H), 3.72 (t, $J = 6.0$ Hz, 2H), 4.05 (q, $J = 6.0$ Hz, 1H), 4.97, 5.05 (2dd, $J = 18.0$, 11.5, 1.5 Hz, 2H), 6.05 (ddd, $J = 18.0$, 11.5, 6.5 Hz, 1H), 7.4 (m, 6H), 7.7 (m, 4H); ^{13}C NMR (50.3 MHz) δ 12.9 (3C), 14.0, 18.0 (6C), 18.1, 26.8 (3C), 36.7, 42.4, 61.0, 73.3, 113.7, 127.6 (4C), 129.5 (4C), 133.4 (2C), 135.6 (2C), 141.3; IR (CCl_4) ν 3060 cm^{-1}; CIMS (NH_3) *m/z* 525 (MH^+); $[\alpha]_D$ + 15.4 (*c* 1.37, hexane). Anal. Calcd for $C_{32}H_{52}O_2Si_2$: C, 73.22; H, 9.98. Found: C, 73.28; H, 10.01.

(2*S*,3*R*)-5-{[*(tert*-Butyldiphenyl)silyl]oxy}-2-methyl-3-{[(triisopropyl)silyl]oxy}pentanal (16). Ozone was bubbled into a solution of compound **15** (1.5 g, 2.86 mmol) in CH_2Cl_2 (63 mL) and methanol (3 mL) at −78 °C until the solution turned light blue. Dimethyl sulfide (15 mL) was added at −78 °C, and the mixture was allowed to warm to room temperature and stirred for 8 h. The solvents were then removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 90:10) to give aldehyde **16** as a colorless oil (1.13 g, 75% yield): ^1H NMR (200 MHz) δ 1.03 (d, $J = 7.0$ Hz, 3H), 1.01 (s wide, 30H), 1.83 (m, 2H), 2.47 (qd, $J = 7.0$, 3.0 Hz, 1H), 3.70 (m, 2H), 4.6 (td, $J = 6.0$, 3.0 Hz, 1H), 7.4 (m, 6H), 7.7 (m, 4H), 9.83 (s, 1H); ^{13}C NMR (50.3 MHz) δ 7.1, 12.8 (3C), 18.2 (6C), 19.1, 26.8 (3C), 37.1, 50.9, 60.6, 69.7, 127.7 (4C), 129.7 (4C), 133.5 (2C), 135.5 (2C), 205.2; IR (CCl_4) ν 3060, 1750 cm^{-1}; CIMS (NH_3) *m/z* 527 (MH^+); $[\alpha]_D$ + 18.5 (*c* 1.2, MeOH). Anal. Calcd for $C_{31}H_{50}O_3Si_2$: C, 70.67; H, 9.57. Found: C, 70.72; H, 9.61.

1-[(*N*,*N*-Diisopropyl)carbamate]-5-[(2-tetrahydropyranyl)oxy]pent-2-ene (17). To a solution of 3,4-dihydro-2*H*-pyran (14 mL, 154 mmol) in aqueous concentrated hydrochloric acid solution (10 N, 0.05 mL), was added 3-butyn-1-ol (11 mL, 145 mmol), and the reaction was regulated to keep the temperature at 50 °C. After the addition was complete, the solution was stirred for 2.5 h at 20 °C. At room temperature, the mixture was diluted with diethyl ether and washed 2 times with a saturated aqueous sodium bicarbonate solution. The etheral phase was then dried over sodium sulfate and filtered, and the solvent was removed under reduced pressure. The crude oil was purified by flash chromatography on silica gel (hexane/ethyl acetate, 90:10) to furnish 4-[(2-tetrahydropyranyl)oxy]butyne (22 g, 98% yield): bp: 70 °C/2 mmHg; ^1H NMR (200 MHz) δ 1.42−1.88 (m, 6H), 1.94 (t, $J = 2.5$ Hz, 1H), 2.45 (td, $J = 7.0$, 2.5 Hz, 2H), 3.45, 3,77 (2m, 2H), 3.45−3.77 (m,

1H), 3.77−3.94 (m, 1H), 4.6 (t, J = 3.5 Hz, 1H); ^{13}C NMR (50.3 MHz) δ 19.3, 25.3, 30.4, 19.9, 62.1, 65.4, 69.1, 81.3, 98.7; IR (CCl_4) ν 2110 cm^{-1}; CIMS (NH_3) m/z 172 (MH^+ + 17), 155 (MH^+). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.13; H, 9.13.

To a solution of 4-[(2-tetrahydropyranyl)oxy]butyne (22 g, 143 mmol) in dried THF (150 mL) at −78 °C was slowly added *n*-BuLi (1.6M in hexane, 96.5 mL, 154.5 mmol). After 15 min of stirring, the temperature was then warmed to 0 °C and a stream of formaldehyde, obtained by depolymerization of dried paraformaldehyde (14.6 g, 157 mmol) at 180 °C, was blown on the surface of the anion solution. After 12 h of stirring at 20 °C, the solution was poured into a cold saturated aqueous ammonium chloride solution. After extraction with diethyl ether, drying over sodium sulfate and filtration, the solvents were removed under reduced pressure. The crude oil was purified by flash chromatography on silica gel (hexane/ethyl acetate, 70:30) to give the 5-[(2-tetrahydropyranyl)oxy]pent-2-yn-1-ol as a colorless oil (23,6 g, 90% yield): ^{1}H NMR (200 MHz) δ 1.40−1.89 (m, 6H), 2.48 (m 2H), 2.49 (s wide, 1H), 3.45, 3.74 (2 m, 2H), 3.57−3.74 (m, 1H), 3.75−3.90 (m, 1H), 4.17 (m, 2H), 4.57 (t, J = 3.5 Hz, 1H); ^{13}C NMR (50.3 MHz) δ 19.3, 20.1, 25.3, 30.4, 51.0, 62.2, 65.6, 79.5, 82.9, 98.7; IR (CCl_4) ν 3610, 3420, 2210 cm^{-1}; CIMS (NH_3) m/z 185 (MH^+). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.22; H, 8.77.

To a solution of 5-[(2-tetrahydropyranyl)oxy]pent-2-yn-1-ol (10.95 g, 59.5 mmol) in dried diethyl ether (70 mL) at 0 °C was slowly added lithium aluminum hydride (LAH, 1 M in THF, 65.5 mL, 65.5 mmol). The reaction mixture was placed in a preheated bath and refluxed for 2.5 h. The solution was then cooled to 0 °C and carefully and successively treated with water (20 mL), an aqueous solution of sodium hydroxide (10 N, 5.2 mL), and water (10 mL). The precipitate was filtered on Celite and washed with diethyl ether. The filtrate was dried over sodium sulfate, filtered, concentrated in vacuo, and purified by flash chromatography on silica gel (hexane/ethyl acetate, 50:50) to give (2*E*)-5-[(2-tetrahydropyranyl)oxy]pent-2-en-1-ol (9.7 g, 88% yield): ^{1}H NMR (200 MHz) δ 1.40−1.97 (m, 7H), 2.35 (m, 2H), 3.40, 3.71 (2 m, 2H), 3.41−3.54 (m, 1H), 3.72−3.90 (m, 1H), 4.07 (m, 2H), 4.54 (t, J = 3.5 Hz, 1H), 5.55−5.76 (m, 2H); ^{13}C NMR (50.3 MHz) δ 19.6, 25.4, 30.6, 32.5, 62.3, 63.5, 66.8, 98.8, 129.1, 131.0; IR (CCl_4) ν 3600, 3440 cm^{-1}; CIMS (NH_3) m/z 187 (MH^+). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.48; H, 9.74. Found: C, 64.51; H, 9.72.

To a suspension of NaH (60% in oil, 768 mg, 19.2 mmol) in dried diethyl ether (10 mL) at 0 °C, was slowly added a solution of (2*E*)-5-[(2-tetrahydropyranyl)oxy]pent-2-en-1-ol (3 g, 16 mmol) in dried diethyl ether (10 mL). The resulting solution was stirred for 20 min at 20 °C, and a solution of diisopropylcarbamyl chloride (5.22 g, 32 mmol) in dried diethyl ether (10 mL) was added. After 12 h of stirring at 20 °C, the mixture was diluted at 0 °C with diethyl ether, treated with an aqueous hydrochloric acid solution (1 N, 10 mL), and extracted with diethyl ether. The combined organic phases were then washed with brine, dried over sodium sulfate, filtered and concentrated in vacuo. The oily residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give the title compound **17** as a colorless oil (4.55 g, 90% yield).

For **17:** bp 160 °C/ 2 mmHg; ^{1}H NMR (200 MHz) δ 1.20 (d, J = 7.0 Hz, 12H), 1.44−1.95 (m, 6H), 2.43 (q, J = 7.0 Hz, 2H), 3.42−3.6 (m, 2H), 3.69−4.05 (m, 4H), 4.56 (d, J = 5.0 Hz, 2H), 4.62 (m, 1H), 5.65 (dt, J = 16.0, 5.0 Hz, 1H), 5.79 (dt, J = 16.0, 7.0 Hz, 1H); ^{13}C NMR (50.3 MHz) δ 19.3, 20.8 (4C), 25.3, 30.5, 32.5, 45.6 (2C), 62.0, 64.9, 66.5, 98.5, 126.8, 130.7, 155.3; IR (CCl_4) ν 1670 cm^{-1}; CIMS (NH_3) m/z 331 (MH^+ + 17), 314 (MH^+). Anal. Calcd for $C_{17}H_{31}O_4N$: C, 65.14; H, 9.97; N, 4.57. Found: C, 65.17; H, 9.95; N, 4.48.

{3*R*,4*S*,5*S*,6*S*[2*R*/*S*-(2-tetrahydropyranyl)oxy]}-[1-{[(*tert*-Butyldiphenyl)silyl]oxy}-8-[(*N*,*N*-diisopropyl)carbamate]-5-hydroxy-4-methyl-6-{(2-[(2-tetrahydropyranyl)oxy]ethyl}-3-{[(triisopropyl)silyl]oxy}oct-7-ene (18) and {3*R*,4*S*,5*R*,-6*R*-[2*R*/*S*-(2-tetrahydropyranyl)oxy]}-1-{[(*tert*-Butyldiphenyl)-silyl]oxy}-8-[(*N*,*N*-diisopropyl)carbamate]-5-hydroxy-4-methyl-6-{(2-[(2-tetrahydropyranyl)oxy]ethyl-}-3-{[(triisopropyl)silyl]oxy}oct-7-ene (19). To a solution of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA, 0.7 mL, 4.5 mmol) in dried diethyl ether (3 mL) at −78 °C, under argon atmosphere, was added *n*-BuLi (1.6M in hexane, 2.8 mL, 4.5 mmol). After 30 min of stirring at −78 °C, a solution of the allylcarbamate **17** (704 mg, 2.25 mmol), in dried diethyl ether (2.5 mL), was slowly added. After 30 min of stirring at −78 °C, titanium tetraisopropoxide [$Ti(O^iPr)_4$, 2 mL, 6.75 mmol] was slowly added, and the mixture became limpid and turned orange. After 30 min at −78 °C, aldehyde **16** (395 mg, 0.75 mmol) in dried diethyl ether (2 mL) was slowly added, the reaction mixture was stirred for 4 h at 0 °C, and the reaction was quenched by addition of methanol (5 mL). The solution was then poured into a mixture of diethyl ether/aqueous hydrochloric acid solution (2 N). After extraction with diethyl ether, the organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give the title compound **18** (409 mg, 65% yield) and its stereoisomer **19** (138 mg, 22% yield).

For **18:** ^{1}H NMR (400 MHz) {*two diastereomers*} δ 0.89, 0.91 (2d, J = 6.5 Hz, 3H), 1.15 (m, 30H), 1.22 (m, 12H), 1.37−1.83 (m, 8H), 1.75 (m, 1H), 1.87 (m, 2H), 2.87 (m, 1H), 3.31 (m, 1H), 3.46 (m, 1H), 3.67 (m, 3H), 3.75 (m, 2H), 3.82 (m, 2H), 4.07 (m, 1H), 4.2 (m, 1H), 4.51, 4.53 (2t, J = 3.5 Hz, 1H), 4.65, 4.67 (2dd, J = 10.0, 6.5 Hz, 1H), 7.18 (d, J = 6.5 Hz, 1H), 7.37, 7.40 (m, 6H), 7.64 (m, 4H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ 6.5, 13.2 (3C), 18.0, 18.2 (3C), 18.3 (3C), 19.1 and 19.6 (1C), 20.1 (2C), 21.1 (2C), 25.4, 26.8 (3C), 30.7, 30.9, 37.2, 37.7, 38.6, 45.6, 46.3, 60.8, 62.2 and 62.3 (1C), 65.8, 75.3, 76.3, 98.6 and 99.0 (1C), 111.2 and 111.3 (1C), 127.4 (4C), 129.4 (4C), 133.6 (2C), 135.4 (2C), 137.3, 152.4; IR (CCl_4) ν 3570, 3500, 3060, 1700 cm^{-1}; CIMS (NH_3) m/z 840 (MH^+); $[\alpha]_D$ + 10.3 (*c* 1.27, MeOH). Anal. Calcd for $C_{48}H_{81}O_7NSi_2$: C, 68.60; H, 9.72; N, 1.70. Found: C, 68.65; H, 9.77; N, 1.72.

For **19:** ^{1}H NMR (400 MHz) {*two diastereomers*} δ 0.71, 0.73 (2d, J = 6.5 Hz, 3H), 1.03 (s wide, 30H), 1.26 (m, 12H), 1.45−1.95 (m, 9H), 1.81 (m, 2H), 1.92 (m, 1H), 2.81 (m, 1H), 3.40 (m, 1H), 3.48 (m, 1H), 3.73 (m, 1H), 3.75 (t, J = 6.0 Hz, 2H), 3.82 (m, 1H), 3.86 (m, 1H), 3.94 (m, 2H), 4.17 (m, 1H), 4.55, 4.57 (2t, J = 3.5 Hz, 1H), 4.87, 4.89 (2dd, J = 10.0, 6.5 Hz, 1H), 7.10, 7.18 (2d, J = 6.5 Hz, 1H), 7.37 (m, 6H), 7.64 (m, 4H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ 12.4, 13.2 (3C), 17.9 (6C), 18.1, 19.3, 20.1 (2C), 21.1 (2C), 25.3, 26.6 (3C), 30.6, 32.1, 34.9, 35.2 and 35.3 (1C), 40.8, 45.2, 46.0, 60.7, 61.9 and 62.1 (1C), 65.3, 74.7, 75.0, 98.5, 109.3 and 109.5 (1C), 127.4 (4C), 129.4 (4C), 133.6 (2C), 135.4 (2C), 137.0, 152.4; CIMS (NH_3) m/z 840 (MH^+); $[\alpha]_D$ − 11 (*c* 3.8, MeOH). Anal. Calcd for $C_{48}H_{81}O_7NSi_2$: C, 68.60; H, 9.72; N, 1.70. Found: C, 68.67; H, 9.79; N, 1.73.

Preparation of 18 from 25. To a solution of compound **25** (390 mg, 0.65 mmol) in dried DMF (3 mL), was added a solution of imidazole (66 mg, 0.85 mmol) and *tert*-butyldiphenylsilyl chloride (0.2 mL, 0.71 mmol). After 12 h of stirring at 20 °C, the reaction mixture was partitioned between diethyl ether and an aqueous hydrochloric acid solution (2 N) and extracted with diethyl ether. The organic layer was then washed with brine, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give compound **18** as a colorless oil (436 mg, 80% yield).

3-{[(*tert*-Butyldimethyl)silyl]oxy}propionaldehyde (20). To a solution of 1,3-propanediol (50 mL, 0.69 mol) in dried CH_2Cl_2 (400 mL) was added a solution of imidazole (17 g, 0.25 mol) and *tert*-butyldimethylsilyl chloride (30 g, 0.2 mol) in dried CH_2Cl_2 (100 mL). After 12 h of stirring at 20 °C, the reaction mixture was partitioned between CH_2Cl_2 and an aqueous hydrochloric acid solution (2 N) and extracted with CH_2Cl_2. The diol excess was removed into the aqueous layer. The organic layer was then washed with brine, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give 3-{[(*tert*-butyldimethyl)silyl]oxy}propanol as a colorless oil (31.16 g, 82% yield): ^{1}H NMR (200 MHz) δ 0.09 (s, 6H), 0.90 (s, 9H),

1.78 (quint, J = 6.0 Hz, 2H), 3.67 (t, J = 5.0 Hz, 1H, OH), 3.76 and 3.80 (2m, 4H); ^{13}C NMR (50.3 MHz) δ −5.6 (2C), 18.0, 25.7 (3C), 34.2, 61.7, 62.4; IR (CCl_4) ν 3560 cm^{-1}; CIMS (NH_3) m/z 191 (MH^+). Anal. Calcd for $C_9H_{22}O_2Si$: C, 56.86; H, 11.65. Found: C, 56.91; H, 11.67.

To a solution of the 3-{[(*tert*-butyldimethyl)silyl]oxy}-propanol (7.85 g, 41 mmol) and dried triethylamine (38 mL) in dried DMSO was added, at room temperature, a solution of pyridine·sulfur trioxide complex (19.65 g, 124 mmol) in dried DMSO (55 mL). After 10 min of stirring, the mixture was dropped in ice and diluted hydrochloric acid was added to adjust the pH to about 7. The solution was extracted with diethyl ether, and the organic layer was washed with brine, dried over sodium sulfate, and filtered. The solvent was then removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 90:10) to give compound **20** as a colorless oil (5.95 g, 77% yield).

For **20:** ^{1}H NMR (200 MHz) δ 0.06 (s, 6H), 0.85 (s, 9H), 2.55 (td, J = 6.0, 2.0 Hz, 2H), 4.95 (t, J = 6.0 Hz, 2H), 9.78 (t, J = 2.0 Hz, 1H); ^{13}C NMR (50.3 MHz) δ −5.5 (2C), 18.1, 25.7 (3C), 46.5, 57.3, 176.4; IR (CCl_4) ν 1730 cm^{-1}; CIMS (NH_3) m/z 189 (MH^+). Anal. Calcd for $C_9H_{20}O_2Si$: C, 57.40; H, 10.70. Found: C, 57.72; H, 10.73.

(3*R*,4*R*)-6-{[(*tert*-Butyldimethyl)silyl]oxy}-4-hydroxy-3-methylhex-1-ene (21). To a solution of freshly sublimed potassium *tert*-butoxide (8 g, 71.3 mmol) in THF (110 mL) at −78 °C was cannulated a solution of *cis*-2-butene (13.5 mL) in THF (13 mL); *n*-BuLi (1.5 M in hexane, 49 mL, 73.5 mmol) was then added dropwise, and the yellow mixture was stirred at −78 °C for 5 min and at −45 °C for 20 min. The resulting orange solution was cooled to −78 °C, and a solution of (−)-*B*-diisopinocamphenylmethoxyborane (27 g, 85 mmol) in 50 mL of diethyl ether was added dropwise over ca. 15 min. The resulting white solution was stirred at −78 °C for 40 min. Boron trifluoride etherate (13 mL, 102 mmol) was added dropwise followed after 5 min by addition of a solution of the aldehyde **20** (11.2 g, 59.5 mmol) in THF (26 mL). The resulting solution was stirred at −78 °C for 4 h. The reaction was then quenched by addition of aqueous NaOH (70 mL, 2.5 N) followed by aqueous H_2O_2 (21 mL, 30%). The acetone−dry ice bath was then removed, and the mixture was heated at 45 °C for 45 min. The cloudy solution was cooled to room temperature, diluted with diethyl ether (150 mL), washed with brine, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure to give, after a flash chromatography on silica gel (hexane/ethyl acetate, 90:10), compound **21** as a colorless liquid (11.9 g, 82% yield): ^{1}H NMR (200 MHz) δ 0.07 (s, 6H), 0.88 (s, 9H), 1.03 (d, J = 7.0 Hz, 3H), 1.63 (m, 2H), 2.23 (sext, J = 7.0 Hz, 1H), 3.36 (d, J = 2.5 Hz, 1H, OH), 3.63 (dtd, J = 7.0, 6.0, 2.5 Hz, 1H), 4.12 (m, 2H), 4.99, 5.00 (2d, J = 17.5, 10.5 Hz, 2H), 5.75 (ddd, J = 17.5, 10.5, 7.0 Hz, 1H); ^{13}C NMR (50.3 MHz) δ −5.6 (2C), 15.2, 18.1, 25.8 (3C), 35.5, 43.9, 62.9, 75.2, 114.6, 141.1; IR (CCl_4) ν 3510, 3050 cm^{-1}; CIMS (NH_3) m/z 245 (MH^+). Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.55. Found: C, 63.92; H, 11.58.

(3*R*,4*R*)-6-{[(*tert*-Butyldimethyl)silyl]oxy}-3-methyl-4-{[(triisopropyl)silyl]oxy}hex-1-ene (22). To a solution of alcohol **21** (10.5 g, 43 mmol) in dried CH_2Cl_2 (86 mL) at 0 °C were added 2,6-lutidine (8.2 mL, 70 mmol) and TIPSOTf (12.8 mL, 47.6 mmol). After 1.5 h of stirring at 20 °C, the reaction mixture was partitioned between diethyl ether and an aqueous hydrochloric acid solution (1.5 N) and extracted with diethyl ether. The organic layer was washed with brine, dried over sulfate sodium, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 98:02) to give the title compound **22** (16.2 g, 94% yield): ^{1}H NMR (200 MHz) δ 0.04 (s, 6H), 0.88 (s, 9H), 0.94 (d, J = 6.0 Hz, 3H), 1.1 (s, 21H), 1.63 (q, J = 6.0 Hz, 2H), 2.41 (m, 1H), 3.70 (t, J = 6.0 Hz, 2H), 3.95 (q, J = 6.0 Hz, 1H), 4.96, 5.04 (2dd, J = 17.0, 10.0, 1.0 Hz, 2H), 6.15 (ddd, J = 17.0, 10.0, 6.0 Hz, 1H); ^{13}C NMR (50.3 MHz) δ −5.3 (2C), 8.0, 12.9 (3C), 18.0, 18.3 (6C), 25.9 (3C), 36.8, 42.5, 60.1, 73.3, 113.7, 141.2; IR (CCl_4) ν 3050 cm^{-1}; CIMS (NH_3) m/z 401 (MH^+); $[\alpha]_D$ + 29 (*c* 2.83, hexane). Anal. Calcd for $C_{22}H_{48}O_2Si_2$: C, 65.93; H, 12.07. Found: C, 65.95; H, 12.11.

(3*R*,4*R*)-3-Methyl-4-{[(triisopropyl)silyl]oxy}hex-1-en-6-ol (23). To a solution of compound **21** (696 mg, 1.75 mmol) in methanol (5 mL) and CH_2Cl_2 (1 mL) was added Amberlyst H^+ 15 (500 mg). After 4 h of stirring at room temperature, the reaction mixture was filtered through Celite, and the solvent was removed under reduced pressure. The crude oily residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 90:10) to give alcohol **23** as a colorless oil (430 mg, 86% yield): ^{1}H NMR (200 MHz) δ 1.01 (d, J = 6.0 Hz, 3H), 1.1 (s, 22H), 1.75 (m, 2H), 2.50 (sext, J = 6.0 Hz, 1H), 3.72 (t, J = 6.0 Hz, 2H), 4.05 (q, J = 6.0 Hz, 1H), 5.03 (dq, J = 19.0, 1.5 Hz, 1H), 5.05 (dq, J = 10.0, 1.5 Hz, 1H), 6.05 (ddd, J = 19.0, 10.0, 6.0 Hz, 1H); ^{13}C NMR (50.3 MHz) δ 12.9 (3C), 15.0, 18.2 (6C), 35.3, 42.6, 60.2, 74.9, 114.3, 140.2; IR (CCl_4) ν 3620, 3530, 3060 cm^{-1}; CIMS (NH_3) m/z 287 (MH^+); $[\alpha]_D$ + 44.2 (*c* 0.97, hexane). Anal. Calcd for $C_{16}H_{34}O_2Si$: C, 67.07; H, 11.96. Found: C, 67.10; H, 11.99.

(2*RS*,3*S*,4*R*)-2-Hydroxy-3-methyl-4-{[(triisopropyl)silyl]oxy}tetrahydropyrane (24). Ozone was bubbled into a solution of compound **23** (1.85 g, 6.50 mmol) in CH_2Cl_2 (145 mL) and methanol (5 mL) at −78 °C until the solution turned light blue. Dimethyl sulfide (30 mL) was added at −78 °C, and the mixture was allowed to warm to room temperature and stirred for 6 h. The solvents were then removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give lactol **24** as a colorless oil (1.55 g, 83% yield): ^{1}H NMR (400 MHz) {*two epimers at C-2*} δ 1.10 (m, 24H), 1.55 (m, 1H), 1.98 (m, 1H), 2.05 (m, 1H), 3.56 (m, 1H), 3.99 (m, 1H), 4.23 (td, J = 12.0, 4.0 Hz, 1H), 4.76 (s wide, 1H), 5.29 (s wide, 1H, OH); {*epimer*} δ 1.79 (m, 1H), 1.89 (m, 1H), 3.70 (m, 1H), 3.90 (m, 1H), 5.13 (m, J = 3.0 Hz, 1H); ^{13}C NMR (100.6 MHz) {*two epimers at C-2*} δ 12.1 (3C), 14.5, 17.9 (3C), 18.0 (3C), 29.3, 40.7, 55.3, 71.7, 96.9; {*epimer*} δ 33.0, 42.7, 59.7, 70.2, 95.6; IR (CCl_4) ν 3600, 3360, 3460 cm^{-1}; CIMS (NH_3) m/z 289 (MH^+); $[\alpha]_D$ − 38.1 (*c* 2.07, MeOH). Anal. Calcd for $C_{15}H_{32}O_3Si$: C, 62.45; H, 11.18. Found: C, 62.49; H, 11.21.

{3*R*,4*S*,5*S*,6*S*[2*R*/*S*-(2-Tetrahydropyranyl)oxy]}-1,5-dihydroxy-8-[(*N*,*N*-diisopropyl)carbamate]-4-methyl-6-{(2-[(2-tetrahydropyranyl)oxy]ethyl}-3-{[(triisopropyl)silyl]oxy}oct-7-ene (25). To a solution of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA, 0.9 mL, 6.0 mmol) in dried THF (4 mL) at −78 °C, under argon atmosphere, was added *n*-BuLi (1.6M in hexane, 3.7 mL, 6.0 mmol). After 30 min of stirring at −78 °C, a solution of the allylcarbamate **17** (940 mg, 3.0 mmol), in dried THF (3 mL), was slowly added. After 45 min of stirring at −78 °C, titanium tetraisopropoxide ($Ti(O^iPr)_4$, 2.7 mL, 9.0 mmol) was slowly added, and the mixture became limpid and turned orange. After 35 min at −78 °C, lactol **24** (288 mg, 1.0 mmol) in dried THF (3 mL), was slowly added. The cooled bath was removed after 5 min, and the reaction mixture was cooled at −5°-0 °C for 5−10 min before it was stirred for 6 h at 20 °C. The solution was then poured into a cooled mixture (0 °C) of diethyl ether/aqueous hydrochloric acid solution (2 N). After extraction with diethyl ether, the organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give compound **25** (565 mg, 94% yield): ^{1}H NMR (400 MHz) {*correlations COSY, HMBC, HMQC, two diastereomers*}-δ 0.97, 0.98 (2d, J = 6.5 Hz, 3H), 1.06 (m, 21H), 1.5−1.8 (m, 12H), 1.20 (m, 12H), 1.80 (m, 1H), 2.95 (m, 1H), 3.30 (m, 1H), 3.50 (m, 1H), 3.70 (m, 1H), 3.70 (m, 2H), 3.80 (m, 1H), 3.80 (m, 1H), 3.84 (m, 1H), 4.10 (m, 1H), 4.12 (m, 1H), 4.55 (2t, J = 3.5 Hz, 1H), 4.75, 4.76 (2dd, J = 10.5, 6.5 Hz, 1H), 7.10, 7.12 (2d, J = 6.5 Hz, 1H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ 8.1, 13.2 (3C), 18.2 (3C), 18.3 (3C), 19.6, 20.1 (2C), 21.3 (2C), 25.4, 30.7, 32.0 and 32.1 (1C), 36.8, 37.6, 39.6, 46.3, 46.5, 59.7, 62.4 and 62.5 (1C), 65.6 and 65.7 (1C), 74.2, 74.4, 98.2 and 98.8 (1C), 111.1 and 111.4 (1C), 134.5, 152.6; IR (CCl_4) ν 3630, 3400−3500, 1690 cm^{-1}; CIMS (NH_3) m/z 602 (MH^+); $[\alpha]_D$ + 11.4 (*c* 0.97, MeOH). Anal. Calcd for $C_{32}H_{63}O_7NSi$: C, 63.85; H, 10.55; N, 2.33. Found: C, 63.88; H, 10.59; N, 2.35.

{3*R*,4*S*,5*S*,6*S*[2*R*/*S*-(2-Tetrahydropyranyl)oxy]}-8-[(*N*,*N*-diisopropyl)carbamate]-4-methyl-6-{(2-[(2-tetrahydropyranyl) oxy]ethyl}-1,3,5-trihydroxyoct-7-ene (26). To a solution of compound **25** (2 g, 2.4 mmol) in dried THF (8 mL) at 20 °C was added tetrabutylammonium fluoride (Bu_4NF, 1.1M in THF, 4.4 mL, 4.8 mmol). After 4 h of stirring, the mixture was poured into a saturated aqueous ammonium chloride solution (5 mL) and extracted with ethyl acetate (six times). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. A flash chromatography on silica gel of the crude oil (ethyl acetate, 80:20) gave the triol **26** (855 mg, 80% yield): ^{1}H NMR (400 MHz) {*two diastereomers*} δ 0.97, 0.98 (2d, J = 6.5 Hz, 3H), 1.20 (m, 12H), 1.5−1.8 (m, 13H), 1.90 (m, 1H), 2.90 (m, 1H), 3.40 (m, 1H), 3.55 (m, 1H), 3.60 (dd, J = 10.0, 2.0 Hz, 1H), 3.70 (m, 2H), 3.85 (m, 1H), 3.90 (m, 1H), 3.91 (m, 1H), 4.10 (m, 1H), 4.12 (m, 1H), 4.51, 4.55 (2t, J = 3.5 Hz, 1H), 4.58, 4.61 (2dd, J = 10.5, 6.5 Hz, 1H), 7.24 (2d, J = 6.5 Hz, 1H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ 4.9, 19.7, 20.3 (2C), 21.4 (2C), 24.0, 25.3, 30.6, 36.5, 37.0 and 37.2 (1C), 38.8, 45.7, 47.0, 61.8, 62.3 and 62.5 (1C), 65.4, 78.3, 78.5, 98.6 and 99.3 (1C), 111.1 and 111.2 (1C), 138.9, 152.7; IR (CCl_4) ν 3400−3500, 1690 cm^{-1}; CIMS (NH_3) m/z 446 (MH^+); $[\alpha]_D$ + 19.3 (c 0.47, MeOH). Anal. Calcd for $C_{23}H_{43}O_7N$: C, 62.00; H, 9.73; N, 3.14. Found: C, 62.05; H, 9.79; N, 3.16.

{4*R*,5*S*,6*S*(3*S*)[2*R*/*S*-(2-Tetrahydropyranyl)oxy]}-4-({2-[(*tert*-butyldimethyl)silyl]oxy}ethyl)-6-[(5-[(*N*,*N*-diisopropyl)carbamate]-1-{[(2-tetrahydropyranyl)oxy]}-pent-4-en)-3-yl]-2,2,5-trimethyl[1,3]dioxolan (27). To a solution of triol **26** (805 mg, 1.8 mmol) in dried CH_2Cl_2 (3.5 mL) and dried DMF (0.7 mL) were added imidazole (157 mg, 2.3 mmol) and *tert*-butyldimethylsilyl chloride (301 mg, 2 mmol) in solution of dried CH_2Cl_2 (1.5 mL). After 12 h of stirring at 20 °C, the reaction mixture was partitioned between CH_2Cl_2 and a saturated aqueous ammonium chloride solution and extracted with CH_2Cl_2. The organic layer was then dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 70:30) to give [3*R*,4*S*,5*S*,6*S*]-3,5-dihydroxy-8-[(*N*,*N*-diisopropyl)carbamate]-4-methyl-6-{(2-[(2-tetrahydropyranyl)oxy]ethyl}-1-{[(*tert*-butyldimethyl)silyl]-oxy}oct-7-ene as a colorless oil (885 mg, 88% yield): ^{1}H NMR (400 MHz) {*two diastereomers*} δ 0.05 (s, 6H), 0.86 (s, 9H), 0.97, 0.98 (2d, J = 6.5 Hz, 3H), 1.5−1.8 (m, 12H), 1.22 (m, 12H), 1.70 (m, 1H), 2.90 (m, 1H), 3.30 (m, 1H), 3.50 (m, 1H), 3.50 (m, 1H), 3.62 (m, 1H), 3.80 (m, 1H), 3.80 (m, 1H), 3.80 (m, 1H), 3.84 (m, 1H), 3.99 (m, 1H), 4.12 (m, 1H), 4.52, 4.54 (2t, J = 3.5 Hz, 1H), 4.50, 4.60 (2dd, J = 10.0, 6.5 Hz, 1H), 7.2 (2d, J = 6.5 Hz, 1H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ −5.0 (2C), 5.5, 18.1, 19.7, 20.1 (2C), 21.3 (2C), 25.4, 25.6 (3C), 30.7, 31.4, 37.1, 37.2, 39.3, 45.9, 46.3, 62.2, 62.3 and 62.5 (1C), 65.5 and 65.6 (1C), 75.0 and 75.1 (1C), 77.8 and 77.9 (1C), 98.7, 111.3, 128.8, 152.8; IR (CCl_4) ν 3570, 3500, 1700 cm^{-1}; CIMS (NH_3) m/z 560 (MH^+); $[\alpha]_D$ + 10.1 (c 1.48, MeOH). Anal. Calcd for $C_{29}H_{57}O_7NSi$: C, 62.23; H, 10.26; N, 2.50. Found: C, 62.27; H, 10.31; N, 2.53.

To a solution of {3*R*,4*S*,5*S*,6*S*[2*R*/*S*-(2-tetrahydropyranyl)-oxy]}-3,5-dihydroxy-8-[(*N*,*N*-diisopropyl)carbamate]-4-methyl-6-{(2-[(2-tetrahydropyranyl)oxy]ethyl}-1-{[(*tert*-butyldimethyl)-silyl]oxy}oct-7-ene (870 mg, 1.55 mmol) in CH_2Cl_2 (4 mL) were added 2,2-dimethoxypropane (4 mL, 42 mmol) and *p*-toluenesulfonic pyridinium (10%). The reaction mixture was stirred for 2 h at 20 °C. Triethylamine (2 mL) was then added, and the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 85:15) to give acetonide **27** as a colorless oil (836 mg, 90% yield).

For **27:** ^{1}H NMR (400 MHz) {*correlations, COSY, HMBC, HMQC, two diastereomers*} δ 0.03, 0.04 (s, 6H), 0.87 (m, 12H), 1.14−1.81 (m, 25H), 1.33 (m, 3H), 1.70 (m, 1H), 2.88 (m, 1H), 3.31 (m, 1H), 3.44 (m, 1H), 3.57 (m, 1H), 3.62 (m, 2H), 3.71 (m, 1H), 3.81 (m, 2H), 4.02 (m, 1H), 4.15 (m, 1H), 4.43 (2dd, J = 10.0, 6.5 Hz, 1H), 4.49, 4.53 (2t, J = 3.5 Hz, 1H), 7.09 (d, J = 6.5 Hz, 1H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ −5.4 (2C), 4.8, 18.2, 19.7, 20.3 and 20.5 (1C), 20.3 (2C), 21.6 (2C), 25.4, 25.9 (3C), 29.5 and 29.8 (1C), 29.8, 30.7, 33.4, 34.8, 36.2, 45.5, 46.7, 59.3, 62.2 and 62.4 (1C), 65.4 and 65.5 (1C), 69.6, 75.7 and 75.8 (1C), 98.6 and 99.2 (1C), 98.8, 111.7 and 111.8 (1C), 136.6 and 136.7 (1C), 152.1; IR (CCl_4) ν 1700 cm^{-1}; CIMS (NH_3) m/z 600 (MH^+); $[\alpha]_D$ + 63.4 (c 1.47, MeOH). Anal. Calcd for $C_{32}H_{61}O_7NSi$: C, 64.06; H, 10.25; N, 2.33. Found: C, 64.11; H, 10.30; N, 2.35.

{2*R*(4*R*,5*S*,6*R*)[2*R*/*S*-(2-Tetrahydropyranyl)oxy]}-2-{4-[2-{[(*tert*-butyldimethyl)silyl]oxy}ehyl]]-2,2,5-trimethyl-[1,3]dioxolan-6-yl}-4-{[(2-tetrahydropyranyl)-oxy]}-butyraldehyde (28). Ozone was bubbled into a solution of compound **27** (1.2 g, 2 mmol) in CH_2Cl_2 (37 mL) and methanol (3 mL) at −78 °C until the solution turned light blue. Dimethyl sulfide (6 mL) was added at −78 °C, and the mixture was allowed to warm to room temperature and stirred for 12 h. The mixture was washed with water and saturated aqueous sodium chloride solution, dried over sodium sulfate, and evaporated under reduce pressure to afford, after flash chromatography on silica gel (hexane/ethyl acetate 90:10), the desired aldehyde **28** as a colorless liquid (825 g, 90% yield): ^{1}H NMR (400 MHz) {*correlations COSY, HMBC, HMQC, two diastereomers*} δ 0.03, 0.04 (s, 6H), 0.83 (s, 9H), 0.9 (d, J = 7.0 Hz, 3H), 1.14−1.81 (m, 8H), 1.30 (m, 3H), 1.35 (m, 3H), 1.70 (m, 1H), 2.70 (m, 1H), 3.35 (m, 1H), 3.50 (m, 1H), 3.70 (m, 2H), 3.70 (m, 3H), 3.80 (m, 1H), 4.10 (2m, 1H), 4.20 (2dd, J = 10.5, 2.0 Hz, 1H), 4.52, 4.53 (2t, J = 3.5 Hz, 1H), 9.65 (2d, J = 2.5 Hz, 1H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ −5.4 (2C), 4.9, 18.2, 19.3, 19.5, 25.3, 25.5, 25.9 (3C), 29.7, 30.5, 32.7, 36.1, 50.5 and 50.6 (1C), 59.1, 62.2, 65.4 and 65.5(1C), 69.5, 73.4 and 73.5 (1C), 98.8 and 99.0 (1C), 98.6 and 99.2 (1C), 204.4 and 204.5 (1C); IR (CCl_4) ν 1710 cm^{-1}; CIMS (NH_3) m/z 459 (MH^+); $[\alpha]_D$ − 7.5 (c 0.8, hexane). Anal. Calcd for $C_{24}H_{46}O_6$-Si: C, 62.84; H, 10.11. Found: C, 62.89; H, 10.16.

{4*R*,5*S*,6*R*(3*S*,4*S*,5*S*)[2*R*/*S*-(2-Tetrahydropyranyl)oxy]}-4-({2-[(*tert*-butyldimethyl)silyl]oxy}ethyl)-6-[(7-[(*N*,*N*-diisopropyl)carbamate]-4-hydroxy-5-methyl-1-{[(2-tetrahydropyranyl)oxy]}-hept-6-en)-3-yl]-2,2,5-trimethyl[1,3]-dioxolan (29). To a rapidly stirred solution of crotylcarbamate **1** (900 mg, 4.5 mmol) and (−)-sparteine (1.1 g, 4.63 mmol) in pentane (6 mL) and cyclohexane (0.9 mL) at −78 °C, was added a solution of *n*-BuLi (1.6 M in hexane, 3 mL, 4.8 mmol), and after 10 min white crystals appeared. After 3 h of crystallization at − 78 °C, a precooled (−50 °C, 30 min) solution of titanium tetraisopropoxide ($Ti(O^iPr)_4$ (4 mL, 13.5 mmol) in pentane (10 mL) was quickly added via cannula to the reaction mixture of lithio carbamate which became limpid and turned orange. After 1 h at −78 °C, aldehyde **28** (1.03 g, 2.25 mmol) in pentane (3 mL) was slowly added to the orange solution. The reaction mixture was stirred for 2 h at − 78 °C, and the reaction was quenched by addition of an aqueous hydochloric acid solution (2 N). After extraction with diethyl ether, the organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give compound **29** as a colorless oil (1.18 g, 80% yield): ^{1}H NMR (400 MHz) {*correlations COSY, HMBC, HMQC, two diastereomers*} δ 0.2 (s, 6H), 0.87 (s, 9H), 0.9 (d, J = 6.5 Hz, 3H), 1.12 (d, J = 6.5 Hz, 3H), 1.14−1.81 (m, 24H), 1.39 (m, 3H), 1.47 (m, 3H), 2.95 (m, 1H), 3.27 (m, 1H), 3.50 (m, 1H), 3.65 (m, 2H), 3.74 (m, 1H), 3.76 (m, 1H), 3.81 (m, 1H), 3.83 (m, 1H), 4.09 (m, 1H), 4.15 (m, 1H), 4.25 (dd, J = 10.0, 1.5 Hz, 1H), 4.4 (d, J = 11.0 Hz, 1H, OH), 5.02 (2dd, J = 10.0, 6.5 Hz, 1H), 4.53 (2t, J = 3.5 Hz, 1H), 7.10 (d, J = 6.5 Hz, 1H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ −5.0 (2C), 5.1, 18.2, 18.6, 19.8, 19.3 and 19.5 (1C), 20.3 (2C), 21.4 (2C), 25.4 and 25.5 (1C), 25.9 (3C), 29.9, 30.6, 30.7, 33.2 and 33.3 (1C), 36.1 and 36.2 (1C), 40.0, 40.2, 46.4 and 46.5 (1C), 59.1 and 59.2 (1C), 62.1 and 62.2 (1C), 64.2 and 64.3 (1C), 69.8 and 70.1 (1C), 77.2, 77.5, 98.8 and 99.0 (1C), 99.1, 111.5 and 111.6 (1C), 138.5, 152.9; IR (CCl_4) ν 3590, 1710 cm^{-1}; CIMS (NH_3) m/z 658 (MH^+); $[\alpha]_D$ + 16.4 (c 3.36, MeOH). Anal. Calcd for $C_{34}H_{67}O_8NSi$: C, 63.87; H, 10.26; N, 2.13. Found: C, 63.91; H, 10.29; N, 2.15.

{3*R*,4*S*,5*R*,6*R*[2*R*/*S*-(2-Tetrahydropyranyl)oxy]}-1-[(*tert*-butyldiphenylsilyl)oxy]-5,7-dihydroxy-4-methyl-6-[2-{(2-tetrahydropyranyl) oxy]ethyl}-1-yl]-3-{[(triisopropyl)-silyl]oxy}octane (30). Ozone was bubbled into a solution of compound **19** (50 mg, 0.06 mmol) in CH_2Cl_2 (5 mL) and methanol (2.5 mL) at −78 °C until the solution turned light blue. Sodium borohydride (14 mg, 0.36 mmol) was added at −78 °C, and the mixture was allowed to warm to room temperature and stirred for 5 h. The reaction mixture was then cooled, treated with an aqueous hydrochloric acid solution (0.5 N, 2 mL), and extracted with diethyl ether. The organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give diol **30** as a colorless oil (34 mg, 80% yield): ^{1}H NMR (400 MHz) {*two diastereomers*} δ 0.78 (2d, J = 7.0 Hz, 3H), 0.87 (s wide, 9H), 1.10 (s wide, 21H), 1.37−1.83 (m, 10H), 1.71 (m, 1H), 2.17 (m, 1H), 3.52 (m, 1H), 3.84 (m, 1H), 3.90 (m, 1H), 3.41 (m, 1H), 3.53 (m, 1H), 3.75 (m, 2H), 3.87 (m, 1H), 3.92 (m, 1H), 4.25 (m, 1H), 4.60 (2t, J = 3.5 Hz, 1H), 3.52 (m, 1H), 3.90 (m, 1H), 7.38 (m, 6H), 7.64 (t, J = 7.8 Hz, 4H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ 12.7 (3C), 13.3, 18.1, 18.2 (6C), 19.7, 25.4, 26.8 (3C), 29.4, 30.7, 30.7, 35.5, 38.4, 60.8, 62.0, 62.3 and 63.4, (1C), 65.7, 74.7, 78.0, 99.0, 127.6 (4C), 129.7 (4C), 133.6 (2C), 135.6 (2C); CIMS (NH_3) m/z 701 (MH^+).

{5*R*,6*R*(2*S*,3*R*)[2*R*/*S*-(2-Tetrahydropyranyl)oxy]}-6-(5-[(*tert*-butyldiphenylsilyl)oxy]-3-{[(triisopropyl)silyl]oxy}-pentane-4-ol-2-yl)-2,2-trimethyl-5-[2-{(2-tetrahydropyranyl)oxy]ethyl}-1-yl][1,3] dioxane (31). To a solution of compound **30** (27 mg, 0.04 mmol) in CH_2Cl_2 (1 mL) were added 2,2-dimethoxypropane (1 mL, 8.2 mmol) and *p*-toluenesulfonic pyridinium (10%). The reaction mixture was stirred for 1.5 h. Triethylamine (0.5 mL) was then added, and the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 90:10) to give acetonide **31** as a colorless oil (26 mg, 90% yield): ^{1}H NMR (400 MHz) {*correlations COSY, HETCOR, HMQC two diastereomers*} δ 0.87 (2d, J = 7.0 Hz, 3H), 0.89 (m, 9H), 1.06 (m, 21H), 1.29 (s, 3H), 1.35 (s, 3H), 1.5−1.8 (m, 8H), 1.52 (m, 1H), 1.66, 1.84 (m, 2H), 1.74 (m, 1H), 3.35 (m, 1H), 3.47 (dd, J = 11.5, 3.0 Hz, 1H), 3.47 (m, 1H), 3.52 (m, 1H), 3.63 (m, 2H), 3.77 (m, 1H), 3.77 (m, 1H), 3.88 (dd, J = 11.5, 3.9 Hz, 1H), 4.46 (m, 1H), 4.55 (2t, J = 3.5 Hz, 1H), 7.4 (m, 4H), 7.65 (m, 6H); ^{13}C NMR (100.6 MHz) {*two diastereomers*} δ 8.8 and 8.9 (1C), 13.1 (3C), 18.1, 18.5 (6C), 19.4, 19.5, 25.5, 26.7 (3C), 28.2, 29.5, 30.6, 37.1 and 37.3 (1C), 38.1, 42.5, 60.8, 61.5 and 61.7 (1C), 62.0 and 62.1 (1C), 65.1 and 65.3 (1C), 68.7, 73.5, 98.0, 99.0, 127.6 (4C), 129.5 (4C), 135.6 (2C), 135.7 (2C); CIMS (NH_3) m/z 741 (MH^+); $[\alpha]_D$ − 11.4 (*c* 0.7, MeOH). Anal. Calcd for $C_{43}H_{72}O_6Si_2$: C: 69.68, H: 9.79. Found: C: 69.73, H: 9.82.

[2*R*/*S*,3*R*,4*R*,5*R*,6*R*(1*S*,2*R*)]-5-{2-[(*tert*-Butyldiphenylsilyl)oxy]ethyl}-6-{5-[(*tert*-butyldiphenylsilyl)oxy]-3-hydroxypent-2-yl}-3-methyl-tetrahydropyran-2,4-diol (32). To a solution of compound **29** (360 mg, 0.53 mmol) in methanol (3 mL) was added Amberlyst H^+ 15. After 48 h of stirring at room temperature, the reaction mixture was filtered through Celite, and the solvent was removed under reduced pressure.

To a solution of the crude oily residue obtained above in dried DMF (0.7 mL) was added a solution of imidazole (94 mg, 1.38 mmol) and *tert*-butyldiphenylsilyl chloride (0.3 mL, 1.16 mmol) in dried DMF (0.7 mL). After 24 h of stirring at 20 °C, the reaction mixture was partitioned between diethyl ether and an aqueous hydrochloric acid solution (2 N) and extracted with diethyl ether. The organic layer was then washed with brine, dried over sodium sulfate, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give [3*R*,4*S*,5*R*,6*S*,7*S*,8*S*]-1-{[(*tert*-butyldiphenyl)-silyl]oxy}-6-{(2-{[(*tert*-butyldiphenyl)silyl]oxy}-ethyl}-10-[(*N*,*N*-diisopropyl)carbamate]-4,8-dimethyl-3,5,7-trihydroxydeca-9-ene as a colorless oil (332 mg, 70% yield).

Ozone was bubbled into a solution of [3*R*,4*S*,5*R*,6*S*,7*S*,8*S*]-1-{[(*tert*-butyldiphenyl)silyl]oxy}-6-{(2-{[(*tert*-butyldiphenyl)-silyl]oxy}-ethyl}-10-[(*N*,*N*-diisopropyl)carbamate]-4,8-dimethyl-3,5,7-trihydroxydeca-9-ene (302 mg, 0.33 mmol) in CH_2Cl_2 (7 mL) and methanol (1 mL) at −78 °C until the solution turned light blue. Dimethyl sulfide (2 mL) was added at −78 °C, and the mixture was allowed to warm to room temperature and stirred for 12 h. The mixture was washed with water and a saturated aqueous sodium chloride solution, dried over sodium sulfate, and evaporated under reduce pressure to afford, after flash chromatography on silica gel (hexane/ethyl acetate 80: 20), the desired lactol **32** as a colorless liquid (174 mg, 70% yield).

For **32:** ^{1}H NMR (400 MHz) {*correlations COSY, HMBC, HMQC, two epimers, the minor is in italics*} δ 0.89, *0.91* (2d, J = 6.9 Hz, 3H), 1.06 (s wide, 18H), 1.10.(d, J = 6.0 Hz, 3H), 1.55 (m, 2H), 1.65 (m, 1H), 1.78, 1.82 (m, 2H), 1.79 (m, 2H), 3.67 (dd, J = 10.0, 5.0 Hz, 1H), 3.72 (dd, J = 10.0, 5.0 Hz, 1H), 3.81 (t, J = 6.2 Hz, 2H), 3.95 (m, 1H), 3.98, *4.01* (2dd, J = 4.7, 2.8 Hz, 1H), 4.15 (dd, J = 10.7, 1.8 Hz, 1H), *4.81* (d, J = 9.0 Hz, 0.5H), 4.96 (d, J = 6.2 Hz, 0.5H), 7.40 (m, 12H), 7.65 (t, J = 7.8 Hz, 8H); ^{13}C NMR (100.6 MHz) {*two epimers*} δ 5.7, 13.7, 18.1 (2C), 26.8 (3C), 26.9 (3C), 29.4, 36.7, 37.0, 37.9, 40.6, 61.5, 62.3, 70.2, 70.9, 74.0, 96.0, 127.6 (4C), 127.8 (4C), 129.6 (4C), 129.8 (4C), 132.8 (2C), 133.7 (2C), 135.6 (4C); CIMS (NH_3) m/z 755 (MH^+).

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