Total Synthesis of (+)-Fostriecin and (+)-Phoslactomycin B

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Abstract: (+)-Fostriecin and (+)-phoslactomycin B, which are potent and selective inhibitors of protein phosphatase, were synthesized by a highly enantio- and stereoselective approach that enabled us to prepare all possible isomers at both the C11 secondary alcohol position and the Δ^{12}-double bond.

Key words: antibiotics, fostriecin, phoslactomycin, total synthesis

The soil bacteria species *Streptomyces* produce a series of structurally novel antifungal and antitumor antibiotics that include fostriecin,[1] PD113,271,[1] the phoslactomycins A–F and I,[2] the phosphazomycins C_1 and C_2,[3] and the leustroducsins A–C and H.[2e,4] These compounds are highly potent and selective inhibitors of protein serine/threonine phosphatase 2A, which may account for their antitumor activity.[5,6] Because of their intriguing molecular architectures and their potential as a lead compounds for anticancer drugs, as well as their importance as biological tools, this class of compounds has attracted much attention in the chemical and biological communities.[7] As a result, there have been a number of formal and total syntheses of fostriecin,[5a,8,9] PD113,271,[10] leustroducsin B,[11,12] and phoslactomycin A and B,[13] including ours. Here, we describe details of our total syntheses of (+)-fostriecin (**1**)[9f] and (+)-phoslactomycin B (**2**);[13c] the methods used also enabled us to prepare various analogues of these compounds.

The close structural similarity between (+)-fostriecin (**1**) and (+)-phoslactomycin B (**2**) allowed us to devise a common synthetic plan, which is illustrated in Scheme 1. We envisaged ynone **7** as a precursor to make our approach flexible. We expected that the advanced intermediate **3**, as well as its stereoisomers **4**, **5**, and **6**, would each be available from **7** by a combination of stereoselective formation of the (*E*)- or (*Z*)-iodoenone[14] and C9-OH directed *anti*- or *syn*-selective reduction.[15] To access **7**, we envisaged an approach from alcohol **8** involving ring-closing metathesis[16] and Sharpless asymmetric dihydroxylation,[17] both of which were thought to be challenging in terms of selectivity because of the possibility of reaction occurring at several sites. In addition, the key issues to be addressed for the synthesis of **2** were stereoselective construction of the C4 asymmetric center and the installation of the C8 asymmetric quaternary center along with its aminoethyl substituent.

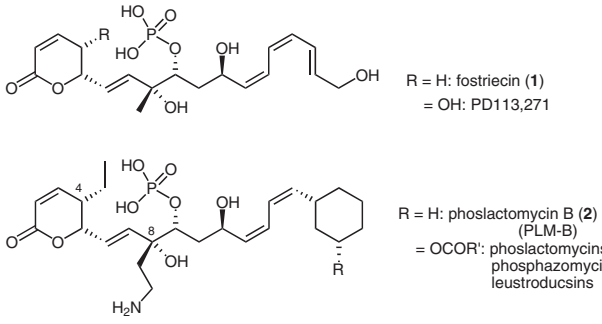
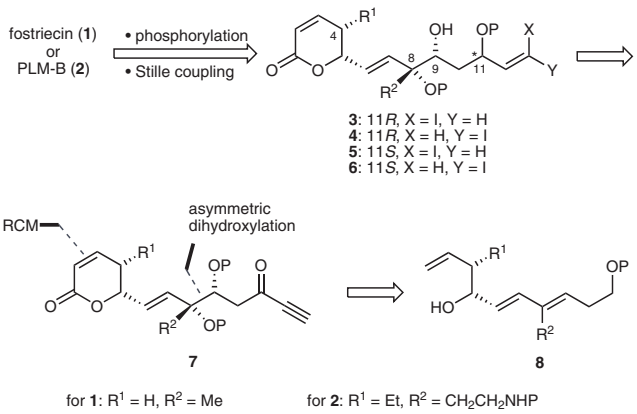


Figure 1 Related phosphate esters produced by *Streptomyces* species



Scheme 1 Retrosynthetic analysis of fostriecin and phoslactomycin B

The synthesis of fostriecin (**1**) began with the stereoselective preparation of trienol **12** (Scheme 2). 2,3-Dihydrofuran was first converted into the (3*E*)-4-(tributylstannyl)pent-3-en-1-ol with complete *E*-selectivity by means of Aldisson's procedure.[18] (3*E*)-4-(Tributylstannyl)pent-3-en-1-ol was subjected to *p*-methoxybenzylation to give the ether **9**, which was iodinated to give alkenyl iodide **10**. Heck reaction[19] of the iodide **10** with acrolein, gave the aldehyde **11**. Brown's asymmetric allylation[20] of **11** gave alcohol **12** in good yield. The optical purity of **12** was not determined at this stage because of its instability both under the conditions for HPLC analysis on a chiral column and for formation of the corresponding 2-methoxy-2-(trifluoromethyl)(phenyl)acetate (MTPA) esters.

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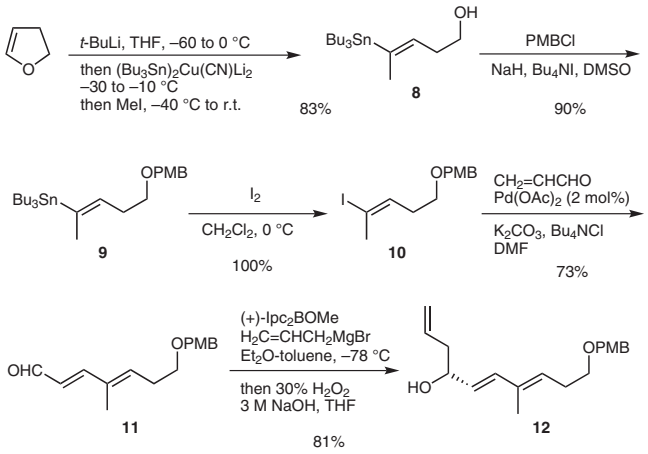
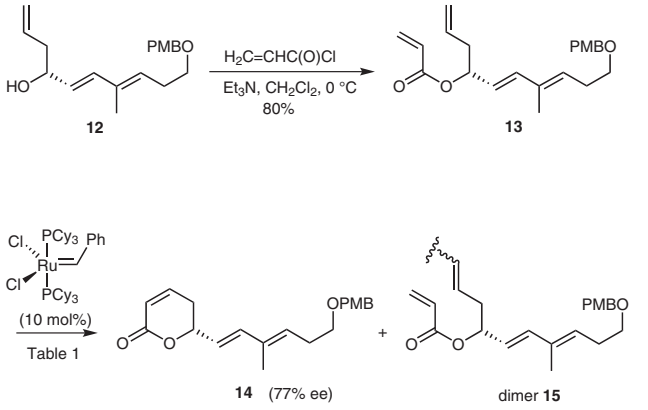


Scheme 2 Preparation of alcohol **12**

After acryloylation of alcohol **12**, the key ring-closing metathesis of acrylate **13** in the presence of the first-generation Grubbs catalyst was examined under various conditions (Scheme 3 and Table 1). Dichloromethane was identified as the solvent of choice, and the cyclization took place selectively between the two terminal olefinic double bonds. When the reaction was conducted under the conditions shown in entry 3, the desired dihydropyranone **14** was obtained in 75% yield, along with the dimer **15** (4% yield). Dimer **15** was the only byproduct that was isolated in all the reactions, and the conjugated diene moiety did not react at all. Addition of titanium tetraisopropoxide[21] did not improve the yield of **14** (entry 2). The optical purity of **14** was determined to be 77% ee by HPLC using a chiral column, confirming the enantioselectivity of the asymmetric allylation leading to **12**.



Scheme 3 Preparation of lactone **3**

To introduce the (8*R*,9*R*)-diol functionality, **14** was exposed to Sharpless asymmetric dihydroxylation conditions using AD-mix-β (Scheme 4). As a result, dihydroxylation took place at the most electron-rich and the sterically least-hindered olefin with complete regio- and diastereoselectivity to give diol **16** in good yield.[22] Interestingly, enantiomerically pure **16** was obtained from **14** with 77% ee, suggesting that the dihydroxylation reaction was accompanied by kinetic resolution. To elaborate the C11–C13 moiety, diol **16** was converted into ynone **21** in 84% overall yield by a five-step sequence involving silylation, oxidative removal of the *p*-methoxybenzyl group, Dess–Martin oxidation, addition of acetylene, and a second Dess–Martin oxidation.

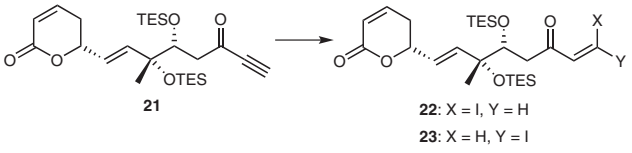
Table 1 Ring-Closing Metathesis of Acrylate **13**

				Yield (%)[b]	
Entry	Solvent[a]	Temp (°C)	Time (h)	**14**	**15**
1	CH_2Cl_2	r.t.	24	60	7
2	CH_2Cl_2	r.t.	24	53	8
3	CH_2Cl_2[c]	40	20	75	4
4	EtOAc	80	23	25	13
5	THF	r.t.	24	17	10
6	toluene	r.t.	24	31	19

[a] All reactions were carried out in 10 mM soln.
[b] Isolated yields.
[c] Ti(O-*i*-Pr)$_4$ (0.3 equiv) was added.

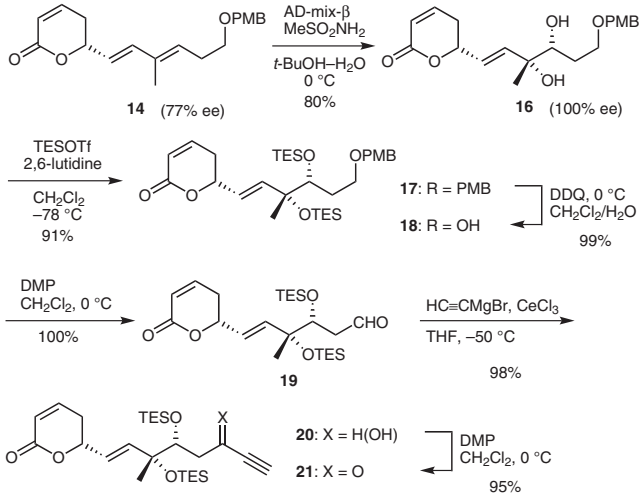
To apply Kishi's methodology,[14] the addition of hydrogen iodide to ynone **21** was then examined under various conditions (Table 2). When **21** was exposed to 1.1 equivalents of sodium iodide and 4.4 equivalents of acetic acid in the absence of an added solvent at room temperature, the kinetically formed (*Z*)-isomer **22** isomerized into the thermodynamically more stable (*E*)-isomer **23** to an appreciable extent (*Z*/*E* = 76:24; entry 1) even after only 30 min; after 3 h, pure (*E*)-**23** was obtained in 81% yield (entry 2). After we had experimented with various conditions in which a solvent was used to retard the isomerization, we eventually found that acetone was the solvent of choice for the predominant production of the (*Z*)-isomer **22**. Thus, on treatment of **21** with 2 equivalents of sodium

Table 2 Addition of Hydrogen Iodide to Ynone **21**



	Reagent (equiv)[a]				Yield (%)[b]		
Entry	NaI	AcOH	Solvent	Time (h)	**22**	**23**	**21**
1	1.1	4.4	none	0.5	31	10	25
2	1.1	4.4	none	3	0	81	0
3	1.1	4.4	acetone	14	53	17	11
4	2	1.1	acetone	48	62	1	23
5	2	1.1	acetone	72	63	6	0

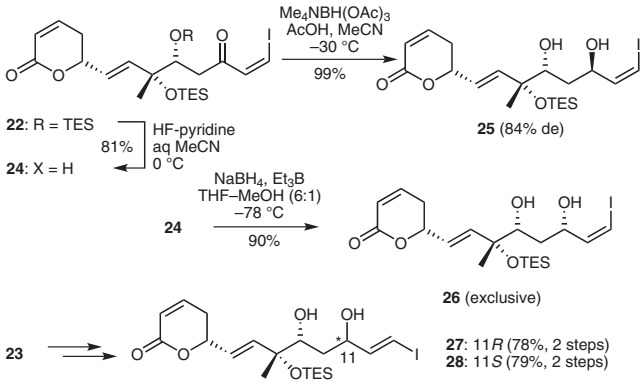
[a] All reactions were carried out at r.t.
[b] Isolated yield.



Scheme 4 Preparation of ynone **21**

iodide and 1.1 equivalents of acetic acid in acetone at room temperature for 2 days, **22** and **23** were obtained in 62% and 1% yields, respectively, together with unreacted **21** (23% yield; entry 4); the yield of the (*Z*)-isomer **22** corresponds to 81% based on recovered **21**.

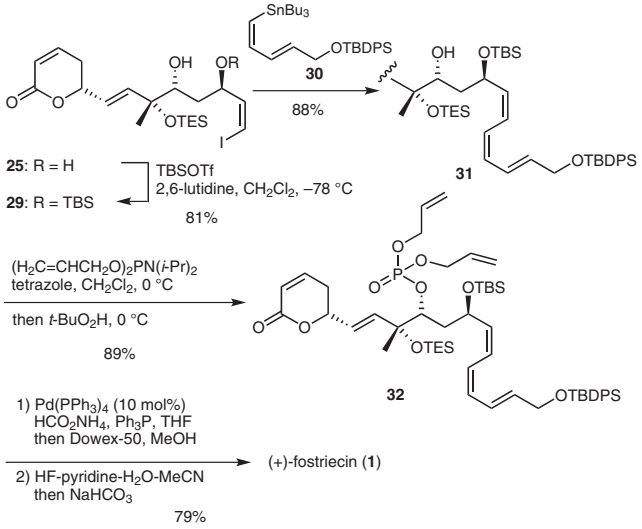
From (*Z*)-isomer **22,** either an (11*R*)- or an (11*S*)-stereocenter was established selectively by two methods via the deprotected alcohol **24** (Scheme 5).



Scheme 5 Preparation of pivotal intermediates

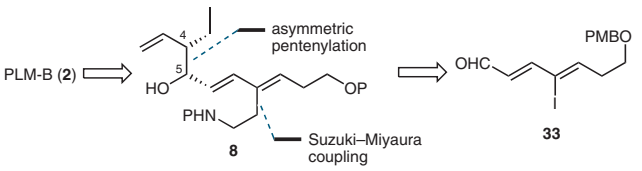
After selective desilylation of **22**, Evans's *anti*-selective reduction[23] of **24** by sodium triacetoxyborohydride resulted in the formation of the (11*R*)-diol **25** with 84% de in excellent yield. On the other hand, sodium borohydride reduction using triethylborane[24] converted **24** into the (11*S*)-diol **26** with complete selectivity in good yield. Similarly, from the (*E*)-isomer **23**, the corresponding (11*R*)-diol **27** and (11*S*)-diol **28** were obtained, again with excellent selectivity.

Having developed a methodology for preparing diol **25** and all its isomers at the C11 stereocenter and the Δ^{12}-double bond, we then investigated the conversion of **25** into fostriecin (**1**). Selective silylation of **25** afforded Jacobsen's intermediate **29**,[9c] which was then subjected to palladium-catalyzed Stille coupling[25] with stannane **30**[26] to produce the (*Z*)-triene **31** as the sole product in a satisfactory yield. As we reported previously,[9f] we successfully improved the final phosphorylation–deprotection step by the use of a diallyl phosphate group. Thus, reaction of **31** with diallyl diisopropylaminophosphine[27] followed by treatment of the resulting phosphite with *tert*-butyl hydroperoxide gave phosphate **32**. Finally, palladium-catalyzed reductive deallylation[28] followed by desilylation using hydrogen fluoride/pyridine gave (+)-fostriecin (**1**) cleanly. The synthetic substance was identical in every respect to natural fostriecin. Note that possible side reactions, such as cleavage of the lactone via a π-allyl palladium complex or isomerization of the triene system, did not occur under palladium-catalyzed deallylation conditions.



Scheme 6 Completion of the total synthesis of fostriecin

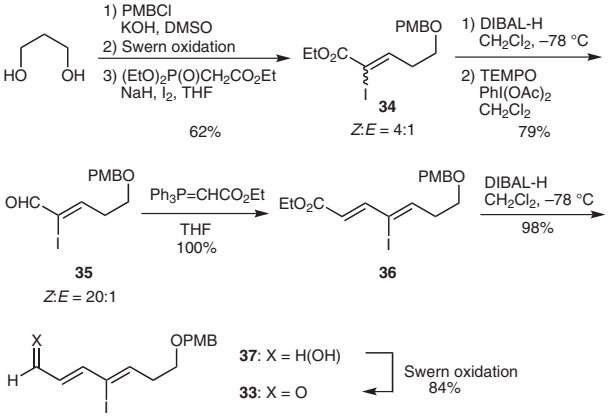
For the preparation of alcohol **8**, a key precursor of phoslactomycin B, as shown in Scheme 1, we envisaged an approach from alcohol **33** involving Suzuki–Miyaura coupling[29] and asymmetric pentenylation. We expected that the reaction of **33** with a chiral (2*Z*)-pent-2-en-1-ylborane or -boronate would proceed in the same fashion as Brown's or Roush's asymmetric crotylation,[30,31] allowing us to assemble the C4 and C5 stereogenic centers with the desired diastereo- and enantioselectivity, although such asymmetric pentenylation was unprecedented.[32]



Scheme 7 Synthetic plan for the preparation of key intermediate **8**

The required aldehyde **33** was prepared stereoselectively from propane-1,3-diol, as shown in Scheme 8. Thus, propane-1,3-diol was first converted into iodoalkene **34** as a 4:1 *Z*/*E* mixture by *p*-methoxybenzylation, Swern oxidation, and Horner–Emmons reaction with ethyl (diethoxy-

phosphoryl)iodoacetate generated in situ.[33] Reduction of **34** with diisobutylaluminum hydride (DIBAL-H), followed by oxidation with 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) gave the (*Z*)-aldehyde **35** with a high geometric purity (20:1), so that the moderate *Z*/*E*-selectivity of the iodoalkenylation step did not become a serious problem. Interestingly, Dess–Martin and Swern oxidation conditions did not promote this isomerization effectively. Wittig reaction of **35** with ethyl (triphenylphosphoranylidene)acetate gave the ester **36** stereoselectively; this was then subjected to DIBAL-H reduction and Swern oxidation to give aldehyde **33** in good yield.

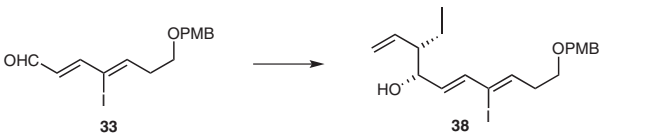


Scheme 8 Preparation of aldehyde **33**

We first examined the key asymmetric pentenylation of **33** by following the procedures for asymmetric crotylation developed by Brown et al.[30] (Table 3). When the reaction was conducted by using a pentenylborane reagent prepared from (2*Z*)-pent-2-en-1-ylmagnesium bromide and *B*-methoxydi(isopinocampheyl)borane [(+)-(Ipc)$_2$BOMe], a 1:3 *syn*/*anti* mixture was unexpectedly obtained, although the yield was almost quantitative (entry 1). This result suggests that a partial isomerization may have taken place during the preparation of the Grignard reagent from (2*Z*)-1-bromopent-2-ene. However, to our delight, the use of the reagent prepared from pent-2-en-1-ylpotassium and (+)-(Ipc)$_2$BOMe allowed highly diastereo- and enantioselective pentenylation to give the (*S*)-*syn*-isomer **38** in 100% de and 93% ee in 81% yield (entry 2). In the reaction with a (2*Z*)-pent-2-en-1-ylboronate following Roush's protocol,[31] the enantioselectivity was unsatisfactorily low, although the diastereoselectivity was perfect (entry 3).

The aminoethyl group was introduced at the C8 position by means of the Suzuki–Miyaura coupling conditions developed by Overman et al.[34] Thus, **38** was treated with 9-{[*N*-(*tert*-butoxycarbonyl)amino]ethyl}-9-borabicyclononane, prepared in situ from *tert*-butyl vinylcarbamate in the presence of [1,1′-bis(diphenylphosphino)ferrocene](dichloro)palladium [PdCl$_2$(dppf)] to give amino alcohol **39** stereoselectively. After acryloylation of **39**, acrylate **40** was subjected to ring-closing metathesis using the second-generation Grubbs catalyst in boiling dichloromethane to give unsaturated lactone **41** cleanly. In this particular case, the first-generation Grubbs catalyst did not induce efficient cyclization.

Table 3 Asymmetric Pentenylation of **33**



Entry	Method[a]	Yield (%)[b]	*syn*/*anti*[c,d]	ee (%) (config.)[e]
1	A	98	25:75	not determined
2	B	82	100:0	93 (*S*)
3	C	79	100:0	46 (*S*)

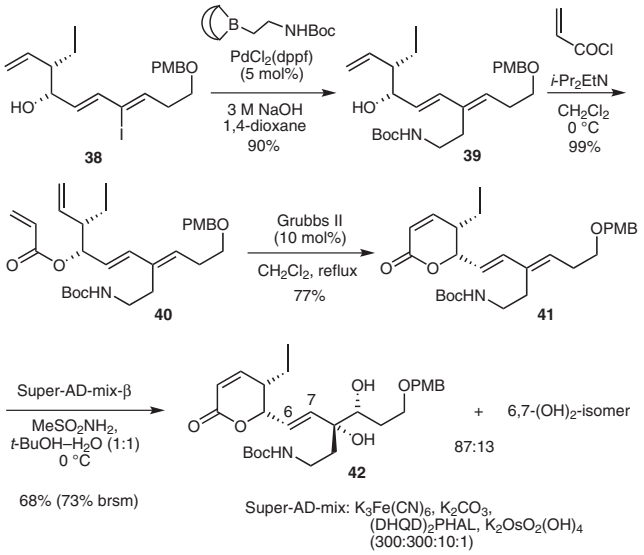
[a] Method A: (2*Z*)-1-bromopent-2-ene, Mg, Et$_2$O, –20 °C, then (+)-(Ipc)$_2$BOMe, –78 °C to r.t., then **33**, toluene, –78 °C; Method B: (2*Z*)-pent-2-ene, *t*-BuOK, BuLi, THF, –78 °C, then (+)-(Ipc)$_2$BOMe, BF$_3$·Et$_2$O, **33**, THF, –78 to –50 °C; Method C: (2*Z*)-pent-2-ene, *t*-BuOK, BuLi, THF, –78 °C, then B(O-*i*-Pr)$_3$, then 1 M HCl, diisopropyl D-tartrate, then **33**, toluene, –78 °C.
[b] Isolated yield.
[c] Determined by ^{1}H NMR analysis of the product.
[d] Determined by NOE analysis of **38** and its C4-epimer.
[e] Determined by ^{1}H NMR analysis of the corresponding (*R*)- and (*S*)-MTPA esters, as well as by HPLC analysis of **38** using a chiral column.

To introduce the (8*R*,9*R*)-diol functionality, lactone **41** was subjected to dihydroxylation conditions using AD-mix-β, as established in the synthesis of fostriecin (**1**); however, these conditions turned out to be unsatisfactory in terms of reproducibility. After exploring various conditions, we eventually found that reaction of **41** with Super-AD-mix,[35] using the ligand for Sharpless asymmetric dihydroxylation [(DHQD)$_2$PHAL] as a chiral ligand, resulted in highly diastereoselective dihydroxylation preferentially at the Δ^8-double bond to give diol **42** together with its 6,7-dihydroxy isomer in a ratio of 87:13; however, very high regioselectivity was not observed in this case, unlike the dihydroxylation of **14** discussed above.

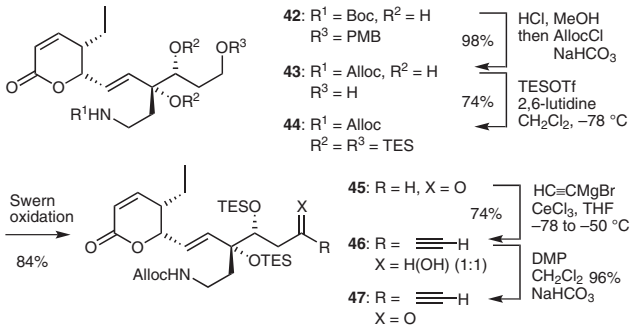
The diol **42** thus obtained was subjected to successive acidic hydrolysis and allyloxycarbonylation in the same flask to afford triol **43**. After silylation of **43**, exposure of **44** to Swern oxidation conditions[36] allowed the direct production of aldehyde **45** through selective cleavage of the primary triethylsilyl ether group. Aldehyde **45** was then converted into ynone **47** via **46** by ethynylation followed by Dess–Martin oxidation.

By adopting the methodology employed for the synthesis of fostriecin (**1**), we successfully converted ynone **47** into the advanced intermediate **51** and three other isomers **52**, **53**, and **54** by *Z*- or *E*-selective addition of hydrogen iodide and 9-OH-directed *anti*- or *syn*-selective reduction, as shown in Scheme 11.

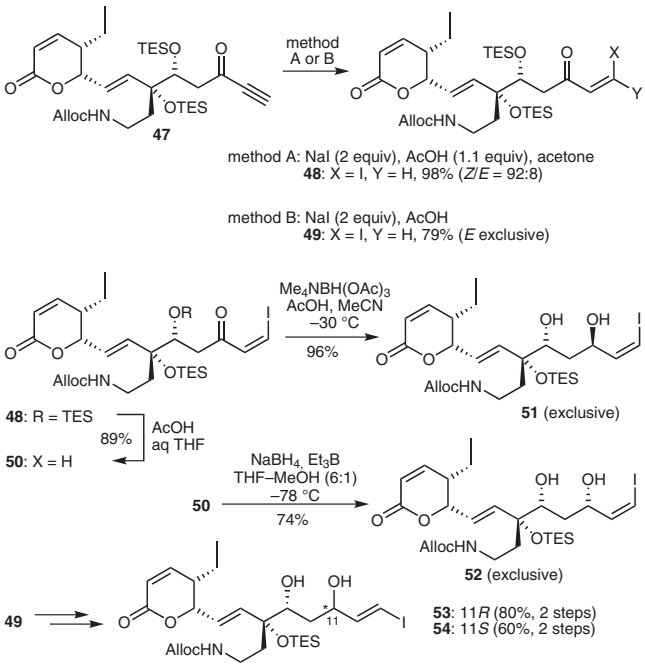
Having secured reliable routes to **51** and all of its isomers at the C11 stereocenter and the Δ^{12}-double bond, we then moved on to the final stage of the total synthesis of phos-



Scheme 9 Preparation of diol **42**



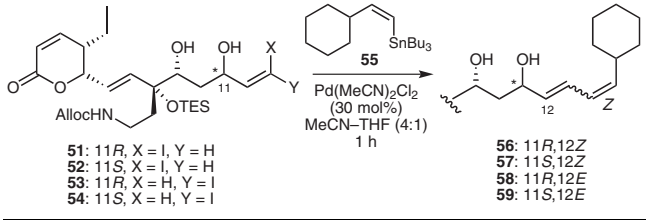
Scheme 10 Preparation of ynone **47**



Scheme 11 Preparation of advanced intermediate **51** and its isomers

lactomycin B (**2**). In this particular case, Stille coupling of **51** with stannane **55** was low yielding under a variety of conditions. However, we eventually found a reliable method that gave **56** with good reproducibility (Table 4). When **51** was treated with **55** in the presence of 0.3 equivalents of bis(acetonitrile)di(chloro)palladium [$Pd(MeCN)_2Cl_2$] in acetonitrile–tetrahydrofuran (4:1) at room temperature for 1 hour, **56** was obtained in 46% yield, along with clean recovery of **51** (43%). After separation, the recovered **51** was again subjected to these coupling conditions to give **56** in >60% total yield. Similarly, the other stereoisomers **57**, **58**, and **59** were also obtained from **52**, **53**, and **54**, respectively, in moderate yields (entries 2–4).

Table 4 Stille Coupling of Diols **51**–**54** with Stannane **55**



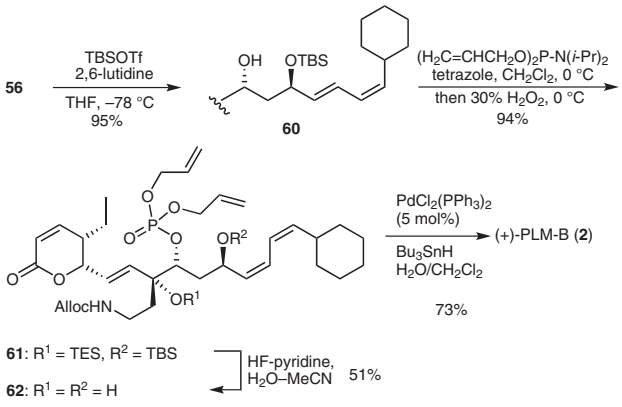
Entry[a]	Iodide	Product	Yield (%)[b]	Recovered SM[c]
1	**51**	**56**	46 (81[d])	43
2	**52**	**57**	56	0
3	**53**	**58**	42 (57[d])	26
4	**54**	**59**	52	0

[a] All reactions were carried out at r.t. for 1 h.
[b] Isolated yield.
[c] Starting material.
[d] Based on recovered starting material.

Finally, according to the procedure described in Scheme 6, the total synthesis of (+)-phoslactomycin B (**2**) was accomplished from **56** via **60**, **61**, and **62** by a four-step sequence involving selective silylation of the C11 hydroxy group, phosphorylation of the C9 hydroxy group, desilylation, and palladium-catalyzed deallylation.[13a] Note that in the final deallylation, the reaction conditions employed for the synthesis of fostriecin (**1**) were less effective, leading to a complex mixture. The spectral data for the synthesized **2** showed good agreement with those reported for the natural specimen.[2c]

In conclusion, we have accomplished total syntheses of (+)-fostriecin (**1**) and (+)-phoslactomycin B (**2**) in 4.5% (21 steps) and 1.3% (26 steps) overall yields, respectively. The synthetic method that we developed is flexible and of potential value for the preparation of various analogues. The synthesis of stereoisomers of **1** and **2** from **26**, **27**, **28**, **57**, **58**, and **59** is currently under investigation.

Where appropriate, reactions were performed under an argon atmosphere. All extracts were dried over $MgSO_4$ and concentrated by ro-



Scheme 12 Completion of the total synthesis of phoslactomycin B

tary evaporation below 30 °C at 25 Torr, unless otherwise noted. TLC was performed on glass-packed silica gel plates. Column chromatography was performed on silica gel. Optical rotations were recorded on a digital polarimeter at r.t. IR spectra were measured on a Fourier-transform IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were measured by using $CDCl_3$, C_6D_6, or CD_3OD as the solvent, and chemical shifts are reported as δ values in ppm based on internal $CHCl_3$ (7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C), benzene (7.15 ppm, ^{1}H; 128.0 ppm, ^{13}C), H_2O (4.65 ppm, ^{1}H), or MeOH (49.9 ppm, ^{13}C). HRMS spectra were recorded in EI or FAB mode.

(3*E*)-4-(Tributylstannyl)pent-3-en-1-ol

A THF soln of $(Bu_3Sn)_2CuCNLi_2$ was prepared as follows. A 1.56 M soln of BuLi in hexane (6.4 mL, 10 mmol) was slowly added to a stirred soln of $(Bu_3Sn)_2$ (5.1 mL, 10 mmol) in THF (6 mL) at –40 °C. After 15 min, the resulting soln was added to a suspension of CuCN (447.6 mg, 5 mmol) in Et_2O (10 mL) at –40 °C, and the mixture was stirred at –25 °C for 1 h.

A THF soln of 2,3-dihydrofuran-2-yllithium was prepared as follows. A 1.47 M soln of *t*-BuLi in pentane (4.1 mL, 6 mmol) was added to a stirred soln of 2,3-dihydrofuran (0.38 mL, 5 mmol) in THF (5 mL) at –60 °C. After 10 min, the mixture was allowed to warm to 0 °C and stirred for 50 min.

The THF soln of 2,3-dihydrofuran-2-yllithium was cooled to –30 °C and added to the THF soln of $(Bu_3Sn)_2CuCNLi_2$ at –30 °C. The mixture was stirred at 0 °C for 1.5 h, allowed to warm to r.t. over 1 h, and stirred at r.t. for 3 h. The reaction was quenched by the addition of sat. aq NH_4Cl (24 mL) and concd aq NH_4OH (6 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min then diluted with Et_2O. The extracts were washed with H_2O and brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel pretreated with 8% Et_3N in hexane (100 g), 1% Et_3N–hexane] gave (3*E*)-4-(tributylstannyl)pent-3-en-1-ol as a colorless oil; yield: 1.55 g (63%). The spectral data (^{1}H and ^{13}C NMR) were identical with those reported.[18]

(2*E*)-2-(Tributylstannanyl)-5-[(4-methoxybenzyl)oxy]pent-2-ene (9)

NaH (60% in oil; 1.75 g, 43.8 mmol) was added to a soln of (3*E*)-4-(tributylstannyl)pent-3-en-1-ol (10.9 g, 29.1 mmol) in DMSO (100 mL) at 0 °C, and the mixture was stirred at r.t. for 1.5 h. Bu_4NI (328.7 mg, 0.890 mmol) and PMBCl (5.5 mL, 40.6 mmol) were added, and the mixture was stirred overnight. The mixture was then diluted with ice-water (200 mL) and extracted with Et_2O. The extracts were washed with brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel pretreated with 8% Et_3N–hexane (100 g), 4% Et_3N–hexane] gave **9** as a pale yellow oil; yield: 13.0 g (90%).

FTIR (film): 1514, 1456, 1247, 1097, 1039 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 8.4 Hz, 2 H), 6.88 (d, *J* = 8.4 Hz, 2 H), 5.53 (qt, *J* = 0.9, 6.6 Hz, J^{119}Sn-H–J^{117}Sn-H = 69.6 Hz, 1 H), 4.46 (s, 2 H), 3.80 (s, 3 H), 3.47 (t, *J* = 6.6 Hz, 2 H), 2.45 (q, *J* = 6.6 Hz, 2 H), 1.84 (d, *J* = 0.9 Hz, J^{119}Sn-H–J^{117}Sn-H = 49.2 Hz, 3 H), 1.48 (m, 6 H), 1.29 (m, 6 H), 0.89 (m, 15 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2, 140.4, 136.4 (J^{119}Sn-C–J^{117}Sn-C = 29.6 Hz), 129.3, 113.8, 29.2 (J^{119}Sn-C–J^{117}Sn-C = 19.3 Hz), 28.9, 27.5 (J^{119}Sn-C–J^{117}Sn-C = 54.7 Hz), 19.3 (J^{119}Sn-C–J^{117}Sn-C = 42.8 Hz), 13.8, 9.16 (J^{119}Sn-C = 342.8 Hz, J^{117}Sn-C = 311.9 Hz).

MS (FAB, NBA): *m/z* = 439 [M – Bu$^+$] for major ^{120}Sn isotope.

(2*E*)-2-Iodo-5-[(4-methoxybenzyl)oxy]pent-2-ene (10)

I_2 (9.52 g, 37.5 mmol) was added to an ice-cooled soln of stannane **9** (17.5 g, 35.6 mmol) in CH_2Cl_2 (170 mL), and the mixture was stirred for 10 min at 0 °C. The reaction was quenched with sat. aq $NaHCO_3$ (50 mL) and 10% $Na_2S_2O_3$ (50 mL). The mixture was extracted with Et_2O, and the extracts were dried and concentrated. Purification of the residue by column chromatography [silica gel pretreated with 8% Et_3N–hexane (100 g), 4% Et_3N–hexane] gave **10** as a pale yellow oil; yield: 11.82 g (quant).

FTIR (film): 1610, 1510, 1450, 1360, 1242, 1085 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 6.18 (tq, *J* = 7.4, 0.6 Hz, 1 H), 4.43 (s, 2 H), 3.80 (s, 3 H), 3.43 (t, *J* = 6.6 Hz, 2 H), 2.37 (d, *J* = 0.6 Hz, 3 H), 2.32 (dt, *J* = 7.4, 6.6 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 137.5, 130.4, 129.3, 113.9, 95.4, 72.7, 68.4, 55.4, 34.3, 27.7.

HRMS (EI): *m/z* calcd for $C_{13}H_{17}IO_2$: 205.1224; found: 205.1242.

(2*E*,4*E*)-7-[(4-Methoxybenzyl)oxy]-4-methylhepta-2,4-dien-1-al (11)

A soln of iodo derivative **10** (10.0 g, 30.1 mmol), acrolein (0.41 mL, 60.34 mmol), Bu_4NCl (5.05 g, 18.20 mmol), K_2CO_3 (10.51 g, 76.14 mmol), and $Pd(OAc)_2$ (119 mg, 0.593 mmol) in DMF (300 mL) was stirred at r.t. for 4 h. The mixture was diluted with Et_2O, washed with H_2O and brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel (300 g), hexane–EtOAc, 5:1] gave **11** (5.71 g, 73%) as a colorless oil.

FTIR (film): 1678, 1618, 1512, 1248, 1132, 1097 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.54 (d, *J* = 7.8 Hz, 1 H), 7.25 (d, *J* = 8.7 Hz, 2 H), 7.10 (d, *J* = 15.6 Hz, 1 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 6.09 (dd, *J* = 7.8, 15.6 Hz, 1 H), 6.05 (t, *J* = 6.6 Hz, 1 H), 4.45 (s, 2 H), 3.77 (s, 3 H), 3.54 (t, *J* = 6.6 Hz, 2 H), 2.53 (q, *J* = 6.6 Hz, 2 H), 1.80 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.9, 159.0, 157.3, 140.5, 134.6, 130.1, 129.1, 126.8, 113.6, 72.5, 68.3, 55.0, 29.6, 12.2.

HRMS (EI): *m/z* calcd for $C_{16}H_{20}O_3$: 260.1412; found: 260.1424.

(4*R*,5*E*,7*E*)-10-[(4-Methoxybenzyl)oxy]-7-methyldeca-1,5,7-trien-4-ol (12)

A 1.0 M soln of allylmagnesium bromide in Et_2O (22 mL, 22 mmol) was added to a stirred soln of (+)-*B*-methoxy(diisopinocampheyl)borane (6.80 g, 21.6 mmol) in Et_2O (25 mL) at –78 °C. After 15 min, the mixture was allowed to warm to r.t. and stirred for 11 h. The resulting soln was added through a cannula to a mixture of aldehyde **11** (3.47 g, 13.7 mmol) and 4-Å molecular sieves (2.00 g) in toluene (40 mL) at –78 °C, and the mixture was stirred for 6 h at –78 °C. 3 M aq NaOH (40 mL) and THF (40 mL) were then added, and the mixture was allowed to warm to 0 °C and treated with 30% H_2O_2 (20 mL). After being stirred at r.t. overnight, the mixture was diluted with 3 M NaOH (100 mL) and extracted with Et_2O. The ex-

tracts were washed with H_2O and brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel (200 g), hexane–EtOAc, 8:1 to 4:1] gave **12** as a pale yellow oil; yield: 3.26 g (81%); $[\alpha]_D^{23}$ +5.3 (*c* 1.05, $CHCl_3$).

FTIR (film): 3404, 1612, 1512, 1244, 1088, 1033 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.4 Hz, 2 H), 6.88 (d, *J* = 8.4 Hz, 2 H), 6.25 (d, *J* = 15.9 Hz, 1 H), 5.82 (m, 1 H), 5.60 (dd, *J* = 6.6, 15.6 Hz, 1 H), 5.50 (t, *J* = 7.2 Hz, 1 H), 5.16 (br d, *J* = 7.5 Hz, 1 H), 5.12 (s, 1 H), 4.45 (s, 2 H), 4.22 (q, *J* = 6.6 Hz, 1 H), 3.80 (s, 3 H), 3.47 (t, *J* = 6.9 Hz, 2 H), 2.45 (q, *J* = 6.9 Hz, 2 H), 2.33 (m, 2 H), 1.75 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2, 135.5, 134.6, 134.4, 130.6, 129.3, 129.1, 128.9, 118.2, 113.8, 72.7, 72.0, 69.3, 55.3, 42.2, 29.1, 12.6.

HRMS (EI): *m/z* calcd for $C_{19}H_{26}O_3$: 302.1882; found: 302.1873.

(4*R*,5*E*,7*E*)-10-[(4-Methoxybenzyl)oxy]-7-methyldeca-1,5,7-trien-4-yl Acrylate (13)

Acryloyl chloride (0.69 mL, 8.67 mmol) was added to an ice-cooled soln of trienol **12** (2.28 g, 7.54 mmol) and Et_3N (1.27 mL, 9.05 mmol) in CH_2Cl_2 (22 mL), and the mixture was stirred for 40 min at 0 °C. The mixture was then poured into sat. aq $NaHCO_3$ (350 mL) and extracted with CH_2Cl_2. The extracts were dried, and concentrated, and the residue was purified by column chromatography [silica gel (60 g) hexane–EtOAc, 3:1] to give **13** as a colorless oil; yield: 2.14 g (80%); $[\alpha]_D^{21}$ +2.9 (*c* 1.03, $CHCl_3$).

FTIR (film): 1722, 1512, 1250, 1190, 1095, 1037, 966, 815 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.4 Hz, 2 H), 6.88 (d, *J* = 8.4 Hz, 2 H), 6.40 (dd, *J* = 1.5, 17.4 Hz, 1 H), 6.30 (d, *J* = 15.6 Hz, 1 H), 6.11 (dd, *J* = 10.5, 17.4 Hz, 1 H), 5.81 (dd, *J* = 1.5, 10.5 Hz, 1 H), 5.74 (m, 1 H), 5.53 (dd, *J* = 6.9, 15.6 Hz, 1 H), 5.53 (t, *J* = 6.9 Hz, 1 H), 5.43 (q, *J* = 6.9 Hz, 1 H), 5.10 (br d, *J* = 15.9 Hz, 1 H), 5.07 (br d, *J* = 9.6 Hz, 1 H), 4.44 (s, 2 H), 3.80 (s, 3 H), 3.46 (t, *J* = 6.9 Hz, 2 H), 2.44 (q, *J* = 6.9 Hz, 4 H), 1.73 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.5, 159.2, 137.7, 134.4, 133.4, 130.7, 130.5, 130.2, 129.4, 128.9, 124.2, 118.0, 113.8, 74.3, 72.7, 69.3, 55.3, 39.3, 29.1, 12.5.

MS (FAB, NBA): *m/z* = 379 [M + Na^+].

(6*R*)-6-{(1*E*,3*E*)-6-[(4-Methoxybenzyloxy)]-3-methylhexa-1,3-dien-1-yl}-5,6-dihydro-2*H*-pyran-2-one (14)

[$(Cy_3P)_2Cl_2Ru$=CHPh] (103 mg, 0.125 mmol) was added to a degassed soln of acrylate **13** (444 mg, 1.25 mmol) in CH_2Cl_2 (125 mL), and the mixture was refluxed for 20 h. The mixture was then concentrated and subjected to chromatography [silica gel (25 g), hexane–EtOAc, 3:1] to give dienone **14** as a pale yellow oil [yield: 306 mg (75%)], together with dimer **15** (34 mg, 4%). The optical purity of **14** was determined to be 77% ee by HPLC (Chiralcel OD, Daicel, *i*-PrOH–hexane, 1:4); $[\alpha]_D^{22}$ +22.8 (*c* 1.09, $CHCl_3$).

FTIR (film): 1714, 1512, 1381, 1240 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.4 Hz, 2 H), 6.89 (m, 1 H), 6.87 (d, *J* = 8.4 Hz, 2 H), 6.34 (d, *J* = 15.9 Hz, 1 H), 6.04 (dt, *J* = 1.8, 9.6 Hz, 1 H), 5.64 (dd, *J* = 6.9, 15.9 Hz, 1 H), 5.57 (t, *J* = 7.5 Hz, 1 H), 4.96 (q, *J* = 6.9 Hz, 1 H), 4.44 (s, 2 H), 3.79 (s, 3 H), 3.47 (t, *J* = 6.9 Hz, 2 H), 2.44 (m, 4 H), 1.74 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.1, 159.2, 144.8, 138.2, 134.1, 131.2, 130.5, 129.3, 123.0, 121.7, 113.8, 78.5, 72.7, 69.2, 55.3, 30.0, 29.1, 12.5.

MS (FAB, NBA): *m/z* = 351 [M + Na^+].

(6*R*)-6-[(1*E*,3*R*,4*R*)-3,4-Dihydroxy-6-[(4-methoxybenzyl)oxy]-3-methyl-hex-1-en-1-yl]-5,6-dihydro-2*H*-pyran-2-one (16)

AD-mix-β (6.68 g) was added to an ice-cooled soln of **14** (1.09 g, 3.34 mmol) and $MeSO_2NH_2$ (321 mg, 3.37 mmol) in 1:1 *t*-BuOH–H_2O (40 mL), and the mixture was stirred at 0 °C for 6 h. The mixture was then diluted with sat. aq $Na_2S_2O_3$ (15 mL) and extracted with EtOAc. The extracts were washed with brine (10 mL), dried, and concentrated. The residue was purified by column chromatography [silica gel (50 g), Et_2O] gave **16** as a pale yellow oil; yield: 965 mg (80%); $[\alpha]_D^{20}$ +34.7 (*c* 0.99, $CHCl_3$). This compound was shown to be enantiomerically pure by ^1H NMR (500 MHz) analysis of the corresponding (*R*)- and (*S*)-MTPA esters.

FTIR (film): 3496, 1707, 1248 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 6.86 (m, 1 H), 6.02 (dt, *J* = 9.9, 1.2 Hz, 1 H), 5.95 (d, *J* = 15.6 Hz, 1 H), 5.87 (dd, *J* = 5.1, 15.6 Hz, 1 H), 4.93 (dt, *J* = 9.9, 5.1 Hz, 1 H), 4.44 (s, 2 H), 3.79 (s, 3 H), 3.67 (m, 3 H), 3.48 (br s, 1 H), 2.78 (br s, 1 H), 2.43 (m, 2 H), 1.75 (m, 2 H), 1.23 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.1, 159.4, 144.9, 138.5, 129.7, 129.5, 126.1, 121.5, 113.9, 76.9, 74.3, 73.1, 69.0, 55.3, 29.9, 28.7, 26.9, 22.8.

MS (FAB, NBA): *m/z* = 363 [M + H^+].

(6*R*)-6-[(1*E*,3*R*,4*R*)-6-[(4-Methoxybenzyl)oxy]-3-methyl-3,4-bis[(triethylsilyl)oxy]hex-1-en-1-yl]-5,6-dihydro-2*H*-pyran-2-one (17)

TESOTf (1.3 mL, 5.75 mmol) was added to a soln of **16** (851 mg, 2.35 mmol) and 2,6-lutidine (0.82 mL, 7.04 mmol) in CH_2Cl_2 (17 mL) at –78 °C, and the mixture was stirred at –78 °C for 30 min. The reaction was then quenched with sat. aq $NaHCO_3$ (100 mL), and the mixture was extracted with CH_2Cl_2. The extracts were dried and concentrated to give a residue that was purified by column chromatography [silica gel (30 g), hexane–EtOAc, 5:1] to give **17** as a colorless oil; yield: 1.26 g (91%); $[\alpha]_D^{18}$ +36.5 (*c* 1.04, $CHCl_3$).

FTIR (film): 1730, 1514, 1246, 1105, 1007 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.4 Hz, 2 H), 6.87 (d, *J* = 8.4 Hz, 2 H), 6.86 (m, 1 H), 6.04 (dt, *J* = 9.6, 1.7 Hz, 1 H), 5.92 (d, *J* = 15.9 Hz, 1 H), 5.76 (dd, *J* = 6.6, 15.9 Hz, 1 H), 4.92 (q, *J* = 7.2 Hz, 1 H), 4.40 (s, 2 H), 3.80 (s, 3 H), 3.58 (dd, *J* = 3.6, 7.8 Hz, 1 H), 3.45 (dd, *J* = 6.3, 7.8 Hz, 2 H), 2.40 (m, 2 H), 1.94 (ddt, *J* = 3.6, 14.1, 7.8 Hz, 1 H), 1.41 (ddt, *J* = 7.8, 14.1 Hz, 1 H), 6.3, 1.33 (s, 3 H), 0.942 (t, *J* = 7.8 Hz, 9 H), 0.937 (t, *J* = 7.8 Hz, 9 H), 0.59 (q, *J* = 7.8 Hz, 6 H), 0.58 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.3, 159.1, 144.8, 138.3, 129.3, 125.6, 121.7, 113.7, 78.1, 77.8, 76.9, 72.5, 67.5, 55.3, 33.4, 29.9, 25.6, 7.2, 7.1, 6.9, 5.4.

MS (FAB, NBA): *m/z* = 363 [M + H^+].

(6*R*)-6-[(1*E*,3*R*,4*R*)-6-Hydroxy-3-methyl-3,4-bis[(triethylsilyl)oxy]hex-1-en-1-yl]-5,6-dihydro-2*H*-pyran-2-one (18)

DDQ (344 mg, 0.731 mmol) was added to an ice-cooled soln of **17** (356 mg, 0.603 mmol) in 20:1 CH_2Cl_2/H_2O (27 mL), and the mixture was stirred for 1 h, The mixture was then diluted with sat. aq $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2. The extracts were washed with H_2O and brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel (10 g), hexane–EtOAc, 4:1 to 3:1] gave **18** as a colorless oil; yield: 282 mg (99%); $[\alpha]_D^{23}$ +42.8 (*c* 1.01, $CHCl_3$).

FTIR (film): 3448, 1724, 1459, 1381, 1244, 1105, 1012 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.88 (dt, *J* = 3.9, 9.6 Hz, 1 H), 6.05 (dt, *J* = 1.5, 9.9 Hz, 1 H), 5.93 (dd, *J* = 0.9, 15.9 Hz, 1 H), 5.77 (dd, *J* = 6.3, 15.9 Hz, 1 H), 4.96 (q, *J* = 6.3 Hz, 1 H), 3.671 (br quint,

J = 5.1 Hz, 2 H), 2.45 (m, 2 H), 1.95 (br t, J = 5.1 Hz, 1 H), 1.86 (m, 1 H), 1.58 (d, J = 2.4 Hz, 3 H), 1.53 (m, 1 H), 0.97 (t, J = 8.1 Hz, 9 H), 0.96 (t, J = 8.1 Hz, 9 H), 0.63 (q, J = 8.1 Hz, 6 H), 0.62 (q, J = 8.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.1, 144.7, 138.0, 125.8, 121.59, 78.0, 77.9, 77.7, 60.2, 36.4, 29.8, 25.4, 7.1, 7.0, 6.8, 5.2.

MS (FAB, NBA): m/z = 493 [M + Na^+].

(3*R*,4*R*,5*E*)-4-Methyl-6-[(2*R*)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]-3,4-bis[(triethylsilyl)oxy]hex-5-enal (19)

Dess–Martin periodinane (2.70 g, 6.38 mmol) was added to an ice-cooled soln of **18** (997 mg, 2.12 mmol) in CH_2Cl_2 (20 mL) was added, and the mixture was stirred at 0 °C for 1 h. The reaction was then quenched with sat. aq $NaHCO_3$ (50 mL) and 10% aq $Na_2S_2O_3$ (50 mL), and the mixture was extracted with EtOAc. The extracts were washed with sat. aq $NaHCO_3$ and brine then dried and concentrated. Purification of the residue by column chromatography [silica gel (10 g), hexane–EtOAc, 3:1] gave **19** as a colorless oil: yield: 996 mg (quant); $[\alpha]_D^{24}$ +42.5 (c 1.00, $CHCl_3$).

FTIR (film): 1728, 1240, 1107, 1011 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.70 (t, J = 2.1 Hz, 1 H), 6.89 (ddd, J = 4.5, 5.1, 9.6 Hz, 1 H), 6.05 (dt, J = 2.1, 9.9 Hz, 1 H), 5.93 (d, J = 15.6 Hz, 1 H), 5.78 (dd, J = 6.3, 15.6 Hz, 1 H), 4.97 (dt, J = 6.3, 8.7 Hz, 1 H), 4.03 (dd, J = 5.1, 6.0 Hz, 1 H), 2.62 (ddd, J = 2.1, 6.0, 16.5 Hz, 1 H), 2.45 (m, 2 H), 2.36 (ddd, J = 2.1, 5.1, 16.5 Hz, 1 H), 1.40 (s, 3 H), 0.95 (t, J = 7.8 Hz, 9 H), 0.94 (t, J = 7.8 Hz, 9 H), 0.62 (q, J = 7.8 Hz, 6 H), 0.59 (q, J = 7.8 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.5, 164.1, 144.7, 137.0, 128.3, 126.8, 121.1, 77.6, 75.2, 47.9, 29.8, 25.6, 6.9, 4.99.

MS (FAB, NBA): m/z = 491 [M + Na^+].

3-{(1*E*,3*R*,4*S*,6*R*)- and 3-{(1*E*,3*R*,4*S*,6*S*)-6-Hydroxy-3-methyl-3,4-bis[(triethylsilyl)oxy]oct-1-en-7-yn-1-yl]-5,6-dihydro-2*H*-pyran-2-one (20)

Commercial anhyd $CeCl_3$ (609 mg, 2.47 mmol) was heated under vacuum at 140 °C for 2 h. THF (6 mL) was added, and the resulting suspension was stirred at r.t. for 18 h. A 0.5 M soln of ethynylmagnesium bromide in THF (4.9 mL, 2.45 mmol) was added to the suspension over 5 min at –78 °C, and the mixture was stirred at –78 °C for 1 h. A soln of enal **19** (366 mg, 0.781 mmol) in THF (5 mL) was added over 7 min at –78 °C. After 10 min, the mixture was allowed to warm to –50 °C then stirred for 50 min. The reaction was quenched with H_2O (15 mL) and the mixture was filtered through Celite. The filtrate was extracted with Et_2O, and the extracts were washed with H_2O, dried, and concentrated. Purification of the residue by column chromatography [silica gel (15 g), hexane–EtOAc, 4:1 to 3:1] gave **20** as a colorless oil; yield: 379 mg (98%; epimeric mixture 6*R*/6*S* = 1:1.8). The following data were collected after separation of the epimers by flash column chromatography.

(*R*)-Isomer: $[\alpha]_D^{24}$ +46.0 (c 1.03, $CHCl_3$).

FTIR (film): 3440, 3309, 1722, 1382, 1242, 1103, 1009 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.89 (ddd, J = 4.2, 5.1, 9.9 Hz, 1 H), 6.05 (dt, J = 9.9, 1.5 Hz, 1 H), 5.93 (dd, J = 0.6, 15.6 Hz, 1 H), 5.78 (dd, J = 6.3, 15.6 Hz, 1 H), 4.97 (ddt, J = 0.6, 6.0, 8.1 Hz, 1 H), 4.48 (br d, J = 9.6 Hz, 1 H), 3.75 (dd, J = 4.8, 6.9 Hz, 1 H), 2.46 (m, 2 H), 2.40 (br s, 1 H), 2.02 (ddd, J = 4.8, 9.6, 14.1 Hz, 1 H), 1.62 (ddd, J = 3.6, 6.9, 14.1 Hz, 1 H), 1.38 (s, 3 H), 1.25 (s, 1 H), 0.97 (t, J = 8.1 Hz, 9 H), 0.96 (t, J = 8.1 Hz, 9 H), 0.65 (q, J = 8.1 Hz, 6 H), 0.63 (q, J = 8.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2, 144.7, 137.7, 126.3, 121.8, 85.4, 77.9, 72.6, 59.6, 41.7, 29.9, 25.5, 7.2, 7.1, 6.9, 5.4.

MS (FAB, NBA): m/z = 517 [M + Na^+].

(*S*)-Isomer: $[\alpha]_D^{17}$ +25.8 (c 1.00, $CHCl_3$).

FTIR (film): 3429, 3309, 1724, 1382, 1242, 1105 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.88 (dt, J = 3.6, 9.9 Hz, 1 H), 6.05 (dt, J = 9.9, 1.5 Hz, 1 H), 5.94 (dd, J = 0.6, 15.9 Hz, 1 H), 5.77 (dd, J = 6.3, 15.9 Hz, 1 H), 4.96 (ddt, J = 0.6, 7.8, 6.3 Hz, 1 H), 4.45 (br q, J = 4.2 Hz, 1 H), 3.79 (dd, J = 5.1, 6.3 Hz, 1 H), 2.46 (m, 3 H), 2.02 (ddd, J = 5.1, 6.9, 14.1 Hz, 1 H), 1.70 (dt, J = 14.1, 6.3 Hz, 1 H), 1.40 (s, 3 H), 1.25 (s, 1 H), 0.97 (t, J = 8.1 Hz, 18 H), 0.65 (q, J = 8.1 Hz, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.1, 144.7, 137.6, 126.3, 121.7, 84.9, 78.1, 77.8, 76.8, 73.5, 60.3, 41.6, 30.0, 25.5, 7.2, 7.1, 6.9, 5.4.

MS (FAB, NBA): m/z = 517 [M + Na^+].

(6*R*)-6-{(1*E*,3*R*)-3-Methyl-6-oxo-3,4-bis[(triethylsilyl)oxy]oct-1-en-7-yn-1-yl}-5,6-dihydro-2*H*-pyran-2-one (21)

Dess–Martin periodinane (3.78 g, 8.90 mmol) was added to an ice-cooled soln of alkynol **20** (887 mg, 1.80 mmol) in CH_2Cl_2 (40 mL), and the mixture was stirred at 0 °C for 4 h. The reaction was quenched with sat. aq $NaHCO_3$ (120 mL) and 10% $Na_2S_2O_3$ (60 mL), and then the mixture was extracted with EtOAc. The extracts were washed with sat. aq $NaHCO_3$ and brine, then dried and concentrated. Purification of the residue by column chromatography [silica gel (20 g), 20% EtOAc–hexane] gave **21** as a colorless oil; yield: 841 mg (95%); $[\alpha]_D^{24}$ +56.2 (c 1.05, $CHCl_3$).

IR (film): 1730, 1682, 1460, 1383, 1244, 1111, 1007 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.88 (ddd, J = 3.6, 4.8, 9.6 Hz, 1 H), 6.03 (ddd, J = 1.5, 2.1, 9.6 Hz, 1 H), 5.88 (d, J = 15.6 Hz, 1 H), 5.78 (dd, J = 5.7, 15.6 Hz, 1 H), 4.96 (dt, J = 5.7, 9.3 Hz, 1 H), 4.17 (dd, J = 4.8, 6.6 Hz, 1 H), 3.22 (s, 1 H), 2.89 (dd, J = 4.8, 16.5 Hz, 1 H), 2.45 (m, 2 H), 2.40 (dd, J = 6.6, 16.5 Hz, 1 H), 1.38 (s, 3 H), 0.92 (t, J = 8.1 Hz, 9 H), 0.93 (t, J = 8.1 Hz, 9 H), 0.59 (q, J = 8.1 Hz, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.3, 164.2, 144.7, 136.9, 126.6, 121.7, 81.9, 78.6, 77.6, 77.3, 75.2, 50.0, 29.9, 25.6, 7.2, 7.0, 6.8, 5.1.

HRMS (EI): m/z calcd for $C_{26}H_{44}O_5Si_2$: 492.2727; found: 492.2776.

(6*R*)-6-{(1*E*,3*R*,4*R*,7*Z*)-8-Iodo-3-methyl-6-oxo-3,4-bis[(triethylsilyl)oxy]octa-1,7-dien-1-yl]-5,6-dihydro-2*H*-pyran-2-one (22)

NaI (115 mg, 0.770 mmol) was added to a soln of ynone **21** (190 mg, 0.385 mmol) and AcOH (23 µl, 0.400 mmol) in acetone (0.4 mL) at r.t., and the mixture was stirred for 3 days. The mixture was basified with sat. aq $NaHCO_3$ (10 mL) and extracted with EtOAc. The extracts were dried and concentrated to give a residue that was purified flash column chromatography [silica gel (20 g), benzene] to give (*Z*)-isomer **22** [yield: 150 mg (63%)] and (*E*)-isomer **23** [yield: 15 mg (6%)], each as a yellow oil.

(7*Z*)-Isomer 22: $[\alpha]_D^{23}$ +54.6 (c 0.97, $CHCl_3$).

FTIR (film): 1726, 1240, 1091, 1008 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, J = 8.7 Hz, 1 H), 7.17 (d, J = 8.7 Hz, 1 H), 6.89 (ddd, J = 3.6, 5.1, 9.6 Hz, 1 H), 6.05 (dt, J = 9.6, 1.8 Hz, 1 H), 5.93 (dd, J = 0.6, 15.9 Hz, 1 H), 5.79 (dd, J = 5.7, 15.9 Hz, 1 H), 4.97 (dt, J = 5.7, 8.7 Hz, 1 H), 4.18 (dd, J = 3.6, 6.9 Hz, 1 H), 2.86 (dd, J = 3.6, 17.4 Hz, 1 H), 2.46 (m, 2 H), 2.38 (dd, J = 6.9, 17.4 Hz, 1 H), 1.38 (s, 3 H), 0.91 (t, J = 7.8 Hz, 18 H), 0.59 (q, J = 7.8 Hz, 6 H), 0.57 (q, J = 7.8 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.1, 164.2, 144.7, 137.4, 126.0, 121.7, 90.5, 77.6, 77.3, 75.0, 48.5, 29.8, 25.6, 7.2, 7.1, 6.8, 5.1.

MS (FAB, NBA): m/z = 643 [M + Na^+].

(6*R*)-6-[(1*E*,3*R*,4*R*,7*E*)-8-Iodo-3-methyl-6-oxo-3,4-bis[(triethylsilyl)oxy]octa-1,7-dienyl]-5,6-dihydro-2*H*-pyran-2-one (23)

NaI (196 mg, 1.31 mmol) was added to a soln of ynone **21** (158 mg, 0.321 mmol) in AcOH (0.4 mL) at r.t. The mixture was stirred for 3 h then poured into a mixture of sat. aq $NaHCO_3$ (50 mL) and 10%

aq $Na_2S_2O_3$ (20 mL) at 0 °C. The mixture was extracted with EtOAc, and the extracts were washed with sat. aq $NaHCO_3$ and brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel (6 g), hexane–EtOAc (5:1) containing 1% Et_3N to hexane–EtOAc (4:1) containing 1% Et_3N] gave **23** as a yellow oil; yield: 162 mg (81%); $[\alpha]_D^{23}$ +53.1 (*c* 1.01, $CHCl_3$).

FTIR (film): 1728, 1690, 1567, 1379, 1242, 1097, 1010 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 15.0 Hz, 1 H), 7.08 (d, *J* = 15.0 Hz, 1 H), 6.87 (ddd, *J* = 3.3, 5.1, 9.6 Hz, 1 H), 6.02 (dt, *J* = 9.6, 1.2 Hz, 1 H), 5.90 (d, *J* = 16.5 Hz, 1 H), 5.76 (dd, *J* = 5.7, 16.5 Hz, 1 H), 4.95 (dt, *J* = 5.7, 9.3 Hz, 1 H), 4.09 (dd, *J* = 3.6, 6.9 Hz, 1 H), 2.78 (dd, *J* = 3.6, 16.5 Hz, 1 H), 2.45 (m, 2 H), 2.31 (dd, *J* = 6.9, 16.5 Hz, 1 H), 1.34 (s, 3 H), 0.89 (t, *J* = 7.5 Hz, 18 H), 0.54 (q, *J* = 7.5 Hz, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.7, 164.1, 145.3, 144.6, 137.2, 126.1, 121.6, 98.8, 77.4, 77.3, 75.2, 44.4, 29.8, 25.6, 7.1, 6.9, 6.7, 5.0.

MS (FAB, NBA): *m/z* = 643 [M + Na^+].

(6*R*)-6-{(1*E*,3*R*,4*S*,7*E*)-4-Hydroxy-8-iodo-3-methyl-6-oxo-3-[(triethylsilyl)oxy]octa-1,7-dien-1-yl}-5,6-dihydro-2*H*-pyran-2-one (24)

A soln of (*Z*)-isomer **22** (221 mg, 0.356 mmol) in 47% HF–pyridine–H_2O–MeCN (1:4:2:20; 77 mL) was stirred with cooling in an ice bath for 8 h. The mixture was then basified with sat. aq $NaHCO_3$ (50 mL) and extracted with EtOAc. The extracts were dried and concentrated to give a residue that was purified by column chromatography [silica gel (5 g), hexane–EtOAc, 2:1 containing 1% Et_3N] to give **24** as a yellow oil; yield: 146 mg (81%); $[\alpha]_D^{24}$ +39.4 (*c* 1.00, $CHCl_3$).

FTIR (film): 3471, 1718, 1697, 1568, 1458, 1381, 1244, 1076 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 8.7 Hz, 1 H), 7.26 (d, *J* = 8.7 Hz, 1 H), 6.89 (ddd, *J* = 3.6, 4.8, 9.9 Hz, 1 H), 6.05 (dt, *J* = 1.5, 9.9 Hz, 1 H), 5.91 (d, *J* = 15.9 Hz, 1 H), 5.82 (dd, *J* = 5.0, 15.9 Hz, 1 H), 4.96 (dt, *J* = 5.4, 9.3 Hz, 1 H), 3.96 (ddd, *J* = 2.1, 3.1, 9.6 Hz, 1 H), 2.92 (d, *J* = 3.6 Hz, 1 H), 2.79 (dd, *J* = 2.1, 17.4 Hz, 1 H), 2.51 (dd, *J* = 9.6, 17.4 Hz, 1 H), 2.43–2.48 (m, 2 H), 1.39 (s, 3 H), 0.94 (t, *J* = 8.1 Hz, 9 H), 0.59 (q, *J* = 8.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.0, 164.0, 144.6, 137.1, 135.4, 127.3, 121.7, 91.8, 77.4, 76.7, 74.6, 45.7, 29.5, 23.1, 7.2, 6.7.

MS (FAB, NBA): *m/z* = 529 [M + Na^+].

(6*R*)-6-{(1*E*,3*R*,4*R*,6*R*,7*Z*)-4,6-Dihydroxy-8-iodo-3-methyl-3-[(triethylsilyl)oxy]octa-1,7-dien-1-yl}-5,6-dihydro-2*H*-pyran-2-one (25)

A soln of $Me_4NBH(OAc)_3$ (180 mg, 0.685 mmol) and AcOH (0.14 mL) in MeCN (0.1 mL) was stirred for 30 min. To the mixture was added a soln of enone **24** (43 mg, 0.084 mmol) in MeCN (1.1 mL) at –40 °C, and the resulting mixture was allowed to warm to –30 °C and stirred at –30 °C for 1 week. 20% aq Rochelle's salt (5 mL) and sat. aq $NaHCO_3$ (5 mL) were added and the mixture was stirred at r.t. for 30 min. The mixture was then extracted with EtOAc, and the extracts were dried, and concentrated to give a residue that was purified by preparative TLC (hexane–EtOAc, 1:1) to give **25** as a colorless oil; yield: 43 mg (99%; epimeric mixture 11*R*/11*S* = 92:8); $[\alpha]_D^{25}$ +58.8 (*c* 1.05, $CHCl_3$).

FTIR (film): 3437, 1714, 1382, 1243, 1056 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.89 (ddd, *J* = 3.5, 5.3, 9.9 Hz, 1 H), 6.42 (t, *J* = 7.5 Hz, 1 H), 6.29–6.32 (m, 1 H), 6.06 (dt, *J* = 2.1, 9.9 Hz, 1 H), 5.88 (d, *J* = 15.9 Hz, 1 H), 5.78 (dd, *J* = 5.1, 15.8 Hz, 1 H), 4.96 (dt, *J* = 5.1, 9.6 Hz, 1 H), 4.53–4.66 (br m, 1 H), 3.67 (dt, *J* = 2.9, 10.5 Hz, 1 H), 2.90 (br s, 1 H), 2.79 (s, 1 H), 2.47–2.41 (m, 2 H), 1.72 (dd, *J* = 7.8, 13.5 Hz, 1 H), 1.57 (ddd, *J* = 6.5, 7.8, 10.8 Hz, 1 H), 1.33 (s, 3 H), 0.94 (t, *J* = 7.8 Hz, 9 H), 0.59 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.8, 144.5, 143.5, 137.8, 127.6, 121.8, 81.4, 77.4, 77.3, 75.2, 72.7, 35.4, 29.6, 20.8, 7.1, 6.7.

MS (FAB, NBA): *m/z* 531 [M + Na^+].

(6*R*)-6-[(1*E*,3*R*,4*R*,6*S*,7*Z*)-4,6-Dihydroxy-8-iodo-3-methyl-3-[(triethylsilyl)oxy]octa-1,7-dien-1-yl}-5,6-dihydro-2*H*-pyran-2-one (26)

A 0.11 M soln of Et_3B in 4:1 MeOH–THF (0.7 mL, 0.077 mmol) and $NaBH_4$ (3.0 mg, 0.079 mmol) were added to a soln of enone **24** (32 mg, 0.063 mmol) in THF (0.25 mL) at –78 °C, and the mixture was stirred at –78 °C for 14 h. 30% H_2O_2 (0.32 mL) was added, followed by MeOH (1 mL), EtOAc (1 mL), and sat. aq $NaHCO_3$ (1 mL) at r.t. The mixture was stirred for 10 min then extracted with EtOAc. The extracts were dried and concentrated to give a residue that was purified by preparative TLC (hexane–EtOAc, 1:1) to give **26** as a colorless oil; yield: 29 mg (90%); $[\alpha]_D^{27}$ –88.0 (*c* 0.30, $CHCl_3$).

FTIR (film): 3435, 1712, 1382, 1247, 1084 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.89 (ddd, *J* = 3.6, 5.1, 9.9 Hz, 1 H), 6.30 (m, 2 H), 6.07 (td, *J* = 2.0, 10.0 Hz, 1 H), 5.90 (d, *J* = 16.8 Hz, 1 H), 5.81 (dd, *J* = 5.4, 16.8 Hz, 1 H), 4.97 (td, *J* = 5.4, 9.9 Hz, 1 H), 4.56 (br d, *J* = 9.3 Hz, 1 H), 3.69 (td, *J* = 2.1, 10.8 Hz, 1 H), 3.53 (d, *J* = 1.2 Hz, 1 H), 3.03 (br dd, *J* = 1.2, 2.4 Hz, 1 H), 2.46 (m, 2 H), 1.68 (br d, *J* = 14.1 Hz, 1 H), 1.40–1.55 (m, 1 H), 1.33 (s, 3 H), 0.95 (t, *J* = 8.1 Hz, 9 H), 0.61 (q, *J* = 8.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.8, 144.4, 143.4, 137.4, 127.9, 81.7, 77.4, 76.9, 75.5, 35.8, 29.7, 20.8, 7.2, 6.7.

MS (FAB, NBA): *m/z* = 531 [M + Na^+].

(6*R*)-6-{(1*E*,3*R*,4*R*,6*R*,7*E*)-4,6-Dihydroxy-8-iodo-3-methyl-3-[(triethylsilyl)oxy]octa-1,7-dien-1-yl}-5,6-dihydro-2*H*-pyran-2-one (27)

Compound **23** was desilylated in the same manner as described for the preparation of **24** from **22** to give the corresponding hydroxy ketone in 80% yield: $[\alpha]_D^{19}$ +49.8 (*c* 1.00, $CHCl_3$).

IR (film): 3446, 1718, 1568, 1381, 1244, 1078 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 15.0 Hz, 1 H), 7.18 (d, *J* = 15.0 Hz, 1 H), 6.90 (ddd, *J* = 3.9, 5.1, 9.6 Hz, 1 H), 6.06 (dt, *J* = 1.5, 9.6 Hz, 1 H), 5.91 (d, *J* = 15.9 Hz, 1 H), 5.82 (dd, *J* = 5.4, 15.9 Hz, 1 H), 4.96 (dt, *J* = 5.4, 9.3 Hz, 1 H), 3.90 (dq, *J* = 2.1, 9.6 Hz, 1 H), 2.86 (d, *J* = 3.3 Hz, 1 H), 2.72 (dd, *J* = 2.1, 16.5 Hz, 1 H), 2.48 (dd, *J* = 9.6, 17.4 Hz, 1 H), 2.43–2.47 (m, 2 H), 1.39 (s, 3 H), 0.94 (t, *J* = 8.1 Hz, 9 H), 0.59 (q, *J* = 8.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.3, 163.9, 144.8, 144.6, 137.1, 127.4, 121.8, 100.3, 77.4, 76.8, 74.6, 41.9, 29.6, 23.1, 7.2, 6.7.

MS (FAB, NBA): *m/z* = 529 [M + Na^+].

Reduction of the hydroxy ketone with $Me_4NBH(OAc)_3$ in the same manner as described for the preparation of **25** from **24** gave compound **27** as a colorless oil; yield: 98%; $[\alpha]_D^{27}$ +28.8 (*c* 0.68, $CHCl_3$).

IR (film): 3423, 1712, 1245 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.90 (ddd, *J* = 3.5, 5.1, 9.6 Hz, 1 H), 6.57 (dd, *J* = 3.6, 5.1, 9.6 Hz, 1 H), 6.40 (dd, *J* = 1.2, 14.1 Hz, 1 H), 6.07 (dt, *J* = 1.8, 11.1 Hz, 1 H), 5.86 (d, *J* = 15.9 Hz, 1 H), 5.78 (dd, *J* = 5.1, 15.9 Hz, 1 H), 4.95 (dt, *J* = 5.1, 9.6 Hz, 1 H), 4.40 (quint, *J* = 6.0 Hz, 1 H), 3.65 (m, 1 H), 2.88 (d, *J* = 6.6 Hz, 1 H), 2.73 (*J* = 2.4 Hz, 1 H), 2.44 (m, 2 H), 1.31 (s, 3 H), 0.95 (t, *J* = 7.8 Hz, 9 H), 0.59 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.8, 148.1, 144.5, 143.5, 137.8, 127.9, 121.8, 77.3, 75.1, 77.3, 72.3, 36.0, 29.6, 20.5, 7.1, 6.7.

MS (FAB, NBA): *m/z* = 531 [M + Na^+].

(6*R*)-6-[(1*E*,3*R*,4*R*,6*S*,7*E*)-4,6-Dihydroxy-8-iodo-3-methyl-3-[(triethylsilyl)oxy]octa-1,7-dien-1-yl}-5,6-dihydro-2*H*-pyran-2-one (28)

Compound **28**, a colorless oil, was obtained by reduction of the hydroxy ketone with $NaBH_4/Et_3B$ in the same manner as described for the preparation of **26** from **24**; yield: 99%; $[\alpha]_D^{26}$ +75.6 (*c* 0.36, $CHCl_3$).

FTIR (film): 3438, 1711, 1250 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.90 (ddd, *J* = 3.3, 5.1, 9.6 Hz, 1 H), 6.53 (dd, *J* = 5.4, 14.1 Hz, 1 H), 6.40 (dd, *J* = 1.2, 14.1 Hz, 1 H), 6.07 (ddd, *J* = 1.2, 2.4, 9.9 Hz, 1 H), 5.86 (d, *J* = 15.9 Hz, 1 H), 5.57 (dd, *J* = 5.1, 15.9 Hz, 1 H), 4.96 (dt, *J* = 5.1, 9.6 Hz, 1 H), 4.56 (br s, 1 H), 3.71 (s, 1 H), 3.59 (d, *J* = 11.1 Hz, 1 H), 3.01 (br s, 1 H), 2.45 (m, 2 H), 1.62 (br s, 1 H), 1.25–1.47 (m, 1 H), 1.31 (s, 3 H), 0.94 (t, *J* = 7.5 Hz, 9 H), 0.59 (q, *J* = 7.5 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.7, 147.6, 144.4, 137.4, 128.1, 121.8, 78.7, 77.4, 77.2, 74.7, 37.0, 29.6, 20.48, 7.1, 6.7.

MS (FAB, NBA): *m/z* = 531 [(M + $Na)^+$].

(6*R*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*)-6-{[*tert*-Butyl(dimethyl)silyl]oxy}-4-hydroxy-8-iodo-3-methyl-3-[(triethylsilyl)oxy]octa-1,7-dien-1-yl]-5,6-dihydro-2*H*-pyran-2-one (29)

TBDMSOTf (20 μL, 0.087 mmol) was added to a soln of dienediol **25** (38 mg, 0.074 mmol, 84% de) and 2,6-lutidine (12 μL, 0.103 mmol) in CH_2Cl_2 (0.7 mL) at –78 °C, and the mixture was stirred at –78 °C for 10 min. The reaction was then quenched with sat. aq $NaHCO_3$ (5 mL), and the mixture was extracted with CH_2Cl_2. The extracts were dried and concentrated to give a residue that was purified by preparative TLC (EtOAc–benzene, 1:9) to gave **29** [yield: 37 mg (81%)] and its (6*S*)-isomer [yield: 3 mg (7%)] both as yellow oils.

Compound 29: $[\alpha]_D^{24}$ +35.9 (*c* 1.13, $CHCl_3$).

FTIR (film): 3500, 1726, 1462, 1382, 1249, 1081 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.89 (dt, *J* = 9.9, 4.2 Hz, 1 H), 6.33 (t, *J* = 7.5 Hz, 1 H), 6.21 (dd, *J* = 1.2, 7.5 Hz, 1 H), 6.05 (dt, *J* = 1.5, 9.9 Hz, 1 H), 5.90 (dd, *J* = 0.9, 15.9 Hz, 1 H), 5.79 (dd, *J* = 5.7, 15.9 Hz, 1 H), 4.95 (ddt, *J* = 0.9, 9.0, 5.7 Hz, 1 H), 4.65 (dt, *J* = 1.2, 6.6 Hz, 1 H), 3.62 (ddd, *J* = 1.5, 2.7, 10.8 Hz, 1 H), 3.03 (d, *J* = 2.7 Hz, 1 H), 2.46–2.43 (m, 2 H), 1.70 (ddd, *J* = 1.5, 7.5, 14.1 Hz, 1 H), 1.38 (ddd, *J* = 3.3, 10.8, 14.1 Hz, 1 H), 1.33 (s, 3 H), 0.93 (t, *J* = 8.1 Hz, 9 H), 0.87 (s, 9 H), 0.57 (q, *J* = 8.1 Hz, 6 H), 0.10 (s, 3 H), 0.05 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.0, 144.6, 144.1, 137.9, 126.8, 121.8, 84.9, 80.0, 77.7, 74.9, 74.2, 37.0, 29.7, 25.8, 22.5, 18.1, 7.2, 6.8, –4.3, –5.0.

MS (FAB, NBA): *m/z* = 645 [M + Na^+].

(6*S*)-Isomer: $[\alpha]_D^{25}$ –8.0 (*c* 0.25, $CHCl_3$); $[\alpha]_D^{26}$ 0.80 (*c* 0.25, EtOH).

IR (film): 3523, 1726, 1248, 1078 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.89 (dt, *J* = 9.9, 3.9 Hz, 1 H), 6.24 (d, *J* = 7.8 Hz, 1 H), 6.19 (t, *J* = 7.8 Hz, 1 H), 6.05 (dt, *J* = 1.8, 9.9 Hz, 1 H), 5.91 (dd, *J* = 1.3, 16.2 Hz, 1 H), 5.80 (dd, *J* = 6.0, 16.2 Hz, 1 H), 4.95 (br q, *J* = 6.9 Hz, 1 H), 4.58 (dt, *J* = 4.8, 7.8 Hz, 1 H), 3.55 (br d, *J* = 10.2 Hz, 1 H), 3.17 (d, *J* = 1.5 Hz, 1 H), 2.45 (m, 2 H), 1.80 (dd, *J* = 5.4, 14.4 Hz, 1 H), 1.38 (s, 3 H), 1.25–1.43 (m, 1 H), 0.96 (t, *J* = 7.8 Hz, 9 H), 0.89 (s, 9 H), 0.61 (q, *J* = 7.8 Hz, 6 H), 0.14 (s, 3 H), 0.08 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2, 144.6, 144.0, 137.7, 126.4, 121.8, 80.5, 77.7, 77.3, 73.2, 37.4, 29.8, 25.9, 23.7, 18.0, 7.3, 6.9, –4.0, –4.7.

MS (FAB, NBA): *m/z* = 645 [M + Na^+].

(6*R*)-6-{(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*,11*E*)-6-{[*tert*-Butyl(dimethyl)silyl]oxy}-13-{[*tert*-butyl(diphenyl)silyl]oxy}-4-hydroxy-3-methyl-3-[(triethylsilyl)oxy]trideca-1,7,9,11-tetraen-1-yl}-5,6-dihydro-2*H*-pyran-2-one (31)

To an-ice-cooled soln of **29** (37 mg, 0.060 mmol) and stannane **30**[26] (135 mg, 0.238 mmol) in DMF (0.3 mL) was added $[Pd(MeCN)_2Cl_2]$ (0.8 mg, 0.003 mmol), and the mixture was stirred at 0 °C for 24 h. Sat. aq $NaHCO_3$ (5 mL) was added and the mixture was extracted with Et_2O. The extracts were dried and concentrated to give a residue that was purified by preparative TLC (10% EtOAc–benzene) to give **31** as a pale yellow oil; yield: 43 mg (88%); $[\alpha]_D^{24}$ –0.38 (*c* 1.04, $CDCl_3$).

FTIR (film): 3484, 2949, 1726, 1379, 1248, 1072 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.71 (dd, *J* = 2.1, 8.1 Hz, 4 H), 7.38–7.41 (m, 6 H), 6.88 (dt, *J* = 4.5, 9.6 Hz, 1 H), 6.77 (dd, *J* = 11.7, 14.7 Hz, 1 H), 6.34 (d, *J* = 11.1 Hz, 1 H), 6.15 (d, *J* = 11.1 Hz, 1 H), 6.06 (dt, *J* = 1.5, 9.6 Hz, 1 H), 5.94 (dd, *J* = 10.2, 15.9 Hz, 1 H) 5.89 (d, *J* = 15.9 Hz, 1 H), 5.79 (dd, *J* = 5.7, 15.9 Hz, 1 H), 5.76–5.84 (m, 1 H), 5.53 (dd, *J* = 9.9, 10.8 Hz, 1 H), 5.01–4.90 (m, 1 H), 4.96 (dt, *J* = 6.0, 8.4 Hz, 1 H), 4.29 (d, *J* = 3.9 Hz, 2 H), 3.69 (d, *J* = 10.8 Hz, 1 H), 3.04 (d, *J* = 2.1 Hz, 1 H), 2.43–2.47 (m, 2 H), 1.64 (dt, *J* = 6.9, 14.1 Hz, 1 H), 1.32 (s, 3 H), 1.26–1.37 (m, 1 H), 1.07 (s, 9 H), 0.92 (t, *J* = 8.1 Hz, 9 H), 0.88 (s, 9 H), 0.57 (q, *J* = 8.1 Hz, 6 H), 0.07 (s, 3 H), 0.04 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.0, 144.5, 138.0, 135.6, 134.4, 133.6, 130.1, 127.8, 126.8, 124.5, 123.2, 122.3, 121.8, 77.6, 77.2, 75.0, 67.1, 64.2, 39.9, 29.7, 26.9, 25.9, 22.3 19.3, 18.1, 7.1, 6.8, –4.3, –5.0.

MS (FAB, NBA): *m/z* = 839 [M + Na^+].

Diallyl (1*R*,3*R*,4*Z*,6*Z*,8*E*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-10-{[*tert*-butyl(diphenyl)silyl]oxy}-1-{(1*R*)-1-methyl-3-[(2*R*)-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]-1-[(triethylsilyl)oxy]allyl}deca-4,6,8-trien-1-yl Phosphate (32)

$(CH_2{=}CHCH_2O)_2PN(i\text{-}Pr)_2$ (105 mg, 0.428 mmol) was added to an ice-cooled soln of enol **31** (43 mg, 0.052 mmol) and tetrazole (58 mg, 0.830 mmol) in CH_2Cl_2 (0.8 mL), and the mixture was stirred stirring for 1.5 h at 0 °C. A 3.04 M soln of *t*-BuOOH in CH_2Cl_2 (140 μL, 0.426 mmol) was added, and the mixture was stirred at 0 °C for 1.5 h. The reaction was then quenched with 10% aq $Na_2S_2O_3$ (1 mL). The mixture was stirred at r.t. for 30 min., diluted with sat. aq $NaHCO_3$ (5 mL), and extracted with CH_2Cl_2. The extracts were dried and concentrated, and the residue was purified by preparative TLC (hexane–EtOAc, 2:1) to give **32** as a pale yellow oil; yield: 46 mg (89%); $[\alpha]_D^{24}$ +18.8 (*c* 1.00, $CHCl_3$).

FTIR (film): 1729, 1504, 1248, 1016 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 7.8 Hz, 4 H), 7.39 (q, *J* = 7.3 Hz, 6 H), 6.87 (dq, *J* = 4.5, 9.3 Hz, 1 H), 6.75 (dd, *J* = 10.8, 14.7 Hz, 1 H), 6.31 (t, *J* = 10.2 Hz, 1 H), 6.23 (d, *J* = 10.2 Hz, 1 H), 6.04 (dd, *J* = 2.2, 9.9 Hz, 1 H), 5.87 (d, *J* = 15.6 Hz, 1 H), 5.98–5.78 (m, 5 H), 5.79 (dd, *J* = 5.1, 15.6 Hz, 1 H), 5.41 (dd, *J* = 1.5, 3.6 Hz, 1 H), 5.35 (dd, *J* = 1.5, 3.6 Hz, 2 H), 5.26 (ddd, *J* = 1.5, 4.5, 10.8 Hz, 1 H), 4.91–4.98 (m, 1 H), 4.94 (dt, *J* = 5.7, 9.3 Hz, 1 H), 4.52–4.58 (m, 4 H), 4.44 (t, *J* = 8.2 Hz, 1 H), 4.28 (d, *J* = 4.5 Hz, 2 H), 2.42–2.48 (m, 2 H), 1.96 (t, *J* = 14.4 Hz, 1 H), 1.43 (s, 3 H), 1.19–1.33 (m, 1 H), 1.07 (s, 9 H), 0.95 (t, *J* = 7.8 Hz, 9 H), 0.88 (s, 9 H), 0.61 (q, *J* = 7.8 Hz, 6 H), 0.11 (s, 3 H), 0.03 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.1, 144.7, 136.8, 136.3, 135.6, 134.2, 133.6, 132.7 ($J_{C\text{-}P}$ = 5.9 Hz), 129.9, 129.8, 127.8, 127.0, 124.6, 123.7, 122.4, 123.4, 122.4, 121.7, 118.4, 118.2, 82.6 ($J_{C\text{-}P}$ = 6.8 MHz), 77.6, 77.3, 76.1 ($J_{C\text{-}P}$ = 4.5 MHz), 68.16 ($J_{C\text{-}P}$ = 2.5 MHz), 68.23 ($J_{C\text{-}P}$ = 2.6 MHz), 65.1, 64.6, 40.4, 29.7, 26.9, 26.4, 26.0, 24.9, 19.3, 18.1, 7.2, 6.8, –3.9, –4.4.

MS (FAB, NBA): *m/z* = 999 [M + Na^+].

(+)-Fostriecin (1)

$Pd(PPh_3)_4$ (1.6 mg, 0.0014 mmol), $HCONH_2$ (3 mg, 0.044 mmol), and PPh_3 (1 mg, 0.004 mmol) in THF (1 mL) were added to a degassed soln of diallyl phosphate **32** (14 mg, 0.014 mmol), and the mixture was stirred at r.t. for 4 h. MeOH (0.5 mL) and ion-exchange resin (Dowex 50WX8-200, 85.4 mg prewashed with THF and MeOH) were added and the mixture was stirred at r.t. for 20 min. The mixture was then filtered through Celite and concentrated. The crude product was dissolved in pyridine (25 mL), and a 1:2:20 mixture of 47% HF, H_2O, and MeCN (0.5 mL) was added with cooling in an ice bath. The mixture was stirred at r.t. for 2 h then aq $NaHCO_3$ (0.5 mL) was added with cooling in an ice-bath. The mixture was washed with Et_2O (1 mL × 3), and the aqueous layer was concentrated by lyophilization. Purification of the residue by reversed-phase column chromatography [Cosmosil 140C_{18}-PREP (Nacalai Tesque Co. Inc.; 0.5 g), H_2O to MeCN–H_2O, 1:9] gave (+)-fostriecin (**1**) as a white powder; yield: 5 mg (79%); $[\alpha]_D^{26}$ +27.6 (*c* 0.50, 0.1 M sodium phosphate buffer).

^{1}H NMR (500 MHz, D_2O): δ = 7.10 (ddd, *J* = 3.0, 5.5, 10.0 Hz, 1 H), 6.76 (ddd, *J* = 0.5, 11.0, 15.0 Hz, 1 H), 6.56 (t, *J* = 11.5 Hz, 1 H), 6.35 (t, *J* = 11.5 Hz, 1 H), 6.15 (t, *J* = 11.0 Hz, 1 H), 6.01 (ddd, *J* = 1.5, 2.5, 10.0 Hz, 1 H), 5.90–5.96 (m, 3 H), 5.54 (t, *J* = 9.5 Hz, 1 H), 5.10 (m, 1 H), 4.92 (t, *J* = 10.0 Hz, 1 H), 4.16 (d, *J* = 6.0 Hz, 2 H), 4.14 (dt, *J* = 2.0, 10.0 Hz, 1 H), 2.60 (dddd, *J* = 1.0, 4.5, 5.5, 18.5 Hz, 1 H), 2.51 (ddt, *J* = 10.5, 18.5, 3.0 Hz, 1 H), 1.68 (t, *J* = 13.0 Hz, 1 H), 1.54 (ddd, *J* = 2.5, 11.0, 14.0 Hz, 1 H), 1.29 (s, 3 H).

^{13}C NMR (125 MHz, D_2O): δ = 170.8, 152.0, 140.6, 136.8, 136.3, 133.4, 129.8, 129.1, 127.1, 127.0, 122.3, 81.8, 79.9, 78.2, 66.6, 65.0, 41.7, 31.9, 24.1.

HRMS (FAB, NBA): *m/z* = 453 [M + Na^+], 476 [M + 2Na^+].

UV/Vis (MeOH): λ_{max} 268 nm, with inflections at 259 and 278 nm.

The spectral data were identical to those for natural fostriecin obtained from a sample (supplied by Dr. Schultz) by purification using the exactly same procedure as described for the synthetic fostriecin; $[\alpha]_D^{26}$ +28.3 (*c* 0.60, 0.1 M sodium phosphate buffer) {Lit.[1c] $[\alpha]_D^{26}$ +33 (*c* 1.0, 0.1 M sodium phosphate buffer)}.

3-[(4-Methoxybenzyl)oxy]propan-1-ol

Powdered KOH (34 g, 0.60 mol) and 4-methoxybenzyl chloride (41 mL, 0.30 mol) were added to a stirred soln of propane-1,3-diol (44 mL) in DMSO (200 mL) at r.t. After 2.5 h, 5 M HCl (120 mL) was carefully added with cooling in an ice bath, and the mixture was extracted with Et_2O. The extracts were washed with H_2O and brine, dried, concentrated, and purified by chromatography [silica gel, (800 g), hexane–EtOAc, 5:2 to 3:2) to a pale yellow oil; yield: 54 g (92%).

FTIR (film): 3400, 1612, 1514, 1463, 1248, 1176, 1089 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.2 Hz, 2 H), 6.88 (d, *J* = 8.2 Hz, 2 H), 4.45 (s, 2 H), 3.80 (s, 3 H), 3.77 (t, *J* = 5.8 Hz, 2 H), 3.63 (t, *J* = 5.8 Hz, 2 H), 2.35 (br s, 1 H), 1.85 (quint, *J* = 5.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 130.1, 129.2, 113.8, 72.8, 69.0, 61.8, 55.2, 32.0.

HRMS (EI): *m/z* calcd for $C_{11}H_{18}O_3$: 196.1170; found: 196.1182.

Ethyl 2-Iodo-5-[(4-methoxybenzyl)oxy]pent-2-enoate (34)

A soln of DMSO (51 mL, 0.72 mmol) in CH_2Cl_2 (150 mL) was added to a stirred soln of oxalyl chloride (31 mL, 0.36 mol) in CH_2Cl_2 (300 mL) at –78 °C, and the mixture was stirred at –78 °C for 40 min. A soln of 3-[(4-methoxybenzyl)oxy]propan-1-ol (36 g, 0.18 mol) in CH_2Cl_2 (150 mL) was then added and the mixture was stirred at –78 °C for a further 40 min. Et_3N (200 mL, 1.4 mol) was added and the mixture was stirred at 0 °C for 20 min. The mixture was neutralized with 5 M HCl (110 mL) and extracted with Et_2O. The extracts were washed with H_2O and brine, dried, and concentrated to give the corresponding aldehyde as a yellow oil that was used without purification in the next reaction; yield 35 g.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (t, *J* = 1.8 Hz, 1 H), 7.25 (d, *J* = 8.8 Hz, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 4.46 (s, 2 H), 3.81 (s, 3 H), 3.79 (t, *J* = 6.3 Hz, 2 H), 2.68 (td, *J* = 6.3 Hz, 1.8 Hz, 2 H).

$(EtO)_2P(O)CO_2Et$ (72 mL, 0.36 mol) was added to a stirred soln of NaH (60% oil dispersion, 29 g, 0.72 mol) in THF (450 mL) at 0 °C, and the mixture was stirred at r.t. for 1 h. The mixture was cooled to 0 °C, I_2 (119 g, 0.47 mol) was added, and the mixture stirred in darkness at r.t. for 1 h. This mixture was again cooled to 0 °C and a soln of the aldehyde (35 g) in THF (150 mL) was added. The mixture was stirred in darkness at r.t. for 1.5 h and then the reaction was quenched with sat. aq NH_4Cl (120 mL). The mixture was extracted with Et_2O and the extracts were washed with sat. aq $Na_2S_2O_3$ and brine then dried, concentrated, and purified by chromatography [silica gel (700 g), hexane–EtOAc, 20:1 to 10:1) to give iodopentenoate **34** as a yellow oil; yield: 47 g [67% (two steps); 4:1 *Z*/*E* mixture]

FTIR (film): 1723, 1613, 1514, 1463, 1363, 1264, 1116, 1042 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (t, *J* = 6.6 Hz, 4/5 H), 7.26 (d, *J* = 8.5 Hz, 2 H), 7.00 (t, *J* = 7.0 Hz, 1/5 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 4.47 (s, 2 × 4/5 H), 4.44 (s, 2 × 1/5 H), 4.26 (q, *J* = 7.0 Hz, 2 × 4/5 H), 4.23 (q, *J* = 7.0 Hz, 2 × 1/5 H), 3.60 (t, *J* = 6.6 Hz, 2 × 4/5 H), 3.52 (t, *J* = 7.0 Hz, 2 × 1/5 H), 2.77 (q, *J* = 7.0 Hz, 2 × 1/5 H), 2.59 (q, *J* = 6.6 Hz, 2 × 4/5 H), 1.33 (t, *J* = 7.0 Hz, 3 × 4/5 H), 1.31 (t, *J* = 7.0 Hz, 3 × 1/5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.7, 159.2, 153.0, 150.0, 130.0, 129.3, 113.8, 96.7, 72.7, 72.6, 67.9, 67.1, 62.6, 62.2, 55.3, 37.7, 33.8, 14.2, 14.1.

HRMS (EI): *m/z* calcd for $C_{15}H_{19}IO_4$: 390.0338; found: 390.0322.

(2*Z*)-2-Iodo-5-[(4-methoxybenzyl)oxy]pent-2-enal (35)

A 1.02 M soln of DIBAL-H in hexane (285 mL, 0.29 mol) was added to a soln of enoate **34** (47 g, 0.12 mol) in CH_2Cl_2 (400 mL) at –78 °C, and the mixture was stirred at –78 °C for 1 h. The reaction was quenched with sat. aq Rochelle's salt (200 mL), and the mixture was diluted with Et_2O and filtered through Celite. The filtrate was washed with H_2O and brine, dried, and concentrated to give the corresponding alcohol (42 g) as a pale yellow oil (4:1 *Z*/*E* mixture) that was used without purification in the next reaction.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.8 Hz, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 6.34 (t, *J* = 5.7 Hz, 1/5 H), 6.00 (t, *J* = 6.6Hz, 4/5 H), 4.45 (s, 2 H), 4.24 (d, *J* = 5.5 Hz, 2 H), 3.81 (s, 3 H), 3.53 (t, *J* = 6.6 Hz, 2 × 4/5 H), 3.45 (t, *J* = 5.7 Hz, 2 × 1/5 H), 2.19–2.50 (m, 2 H), 2.05 (t, *J* = 5.5 Hz, 1 H).

$PhI(OAc)_2$ (77 g, 0.24 mol) and TEMPO (1.9 g, 0.012 mol) were added to a stirred soln of the crude alcohol (42 g) in CH_2Cl_2 (130 mL) at 0 °C, and the mixture was stirred in darkness at r.t. for 3 h. The mixture was then diluted with Et_2O, washed with sat. aq $Na_2S_2O_3$, H_2O, and brine then concentrated. Purification of the residue by column chromatography [silica gel (800 g), hexane–EtOAc, 10:1 to 5:1] gave **35** as an yellow oil; yield: 33 g (79% for two steps; 20:1 *Z*/*E* mixture)

FTIR (film): 1693, 1609, 1513, 1361, 1249, 1176, 1096, 1034, cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.08 (s, 1/20 H), 8.66 (s, 19/20 H), 7.55 (t, *J* = 8.3 Hz, 1/20 H), 7.22–7.33 (m, 59/20 H), 6.89 (d, *J* = 7.3 Hz, 2 H), 4.48 (s, 2 × 19/20 H), 4.46 (s, 2 × 1/20 H), 3.81 (s, 3 H), 3.67 (t, *J* = 6.1 Hz, 2 × 19/20 H), 3.58 (t, *J* = 5.9 Hz, 2 × 1/20 H), 2.92–2.97 (m, 2 × 1/20 H), 2.80 (q, *J* = 6.1 Hz, 2 × 19/20 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.8, 184.5, 159.6, 159.4, 159.3, 157.9, 129.8, 129.7, 129.4, 129.3, 113.9, 112.8, 76.7, 72.8, 67.3, 66.8, 55.3, 53.4, 37.2, 32.4.

HRMS (EI): calcd for $C_{13}H_{15}IO_3$: 346.0092; found: 346.0052.

Ethyl (2*E*,4*Z*)-4-Iodo-7-[(4-methoxybenzyl)oxy]hepta-2,4-dienoate (36)

$Ph_3P{=}CHCO_2Et$ (60 g, 171 mmol) was added to a soln of **35** (33 g, 95 mmol) in THF (480 mL) at 0 °C, and the mixture was stirred in darkness at r.t. for 2 h. Half the THF was evaporated and the mixture was diluted with hexane, filtered through Celite, and concentrated. The residue was purified by chromatography [silica gel (800 g), hexane–EtOAc, 10:1 to 5:1] to give **36** as a pale reddish oil; yield: 40 g (quant).

FTIR (film): 1719, 1627, 1514, 1463, 1364, 1303, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.8 Hz, 2 H), 7.00 (d, *J* = 14.2 Hz, 1 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 6.41 (t, *J* = 6.8 Hz, 1 H), 6.12 (d, *J* = 14.2 Hz, 1 H), 4.46 (s, 2 H), 4.22 (q, *J* = 7.3 Hz, 2 H), 3.81 (s, 3 H), 3.58 (t, *J* = 6.8 Hz, 2 H), 2.64 (q, *J* = 6.8 Hz, 2 H), 1.31 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 159.3, 146.4, 146.1, 130.1, 129.3, 125.3, 113.8, 104.5, 72.7, 67.5, 60.6, 55.3, 37.6, 14.3.

HRMS (FAB): *m/z* [M^+] calcd for $C_{17}H_{21}IO_4$: 416.0485; found: 416.0506.

(2*E*,4*Z*)-4-Iodo-7-[(4-methoxybenzyl)oxy]hepta-2,4-dien-1-ol (37)

A 1.02 M soln of DIBAL-H in hexane (216 mL, 220 mmol) was added to a soln of dienoate **36** (34 g, 82 mmol) in CH_2Cl_2 (460 mL) at –78 °C, and the mixture was stirred in darkness at –78 °C for 1 h. The reaction was quenched with sat. aq Rochelle's salt (200 mL), and the mixture was diluted with Et_2O and filtered through Celite. The filtrate was washed with H_2O and brine, dried, and concentrated to give a residue that was purified by chromatography [silica gel (600 g), hexane–EtOAc, 5:1 to 3:1] to give **37** as a pale yellow oil; yield: 30 g (98%).

FTIR (film): 3417, 1614, 1516, 1254, 1174, 1103 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.6 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 6.09 (dt, *J* = 14.4, 5.5 Hz, 1 H), 5.99 (t, *J* = 6.3 Hz, 1 H), 5.97 (d, *J* = 14.4 Hz, 1 H), 4.45 (s, 2 H), 4.29 (t, *J* = 5.5 Hz, 2 H), 3.81 (s, 3 H), 3.54 (t, *J* = 6.3 Hz, 2 H), 2.60 (q, *J* = 6.3 Hz, 2 H), 1.50 (t, *J* = 5.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 137.3, 135.8, 132.3, 130.1, 129.3, 128.1, 113.8, 107.3, 72.5, 68.0, 62.1, 55.3, 37.1.

HRMS (EI): *m/z* calcd for $C_{15}H_{19}IO_3$: 374.0379; found: 374.0364.

(2*E*,4*Z*)-4-Iodo-7-[(4-Methoxybenzyl)oxy]hepta-2,4-dienal (33)

A soln of DMSO (2.87 mL, 40.4 mmol) in CH_2Cl_2 (10 mL) was added to stirred soln of oxalyl chloride (1.76 mL, 20.2 mmol) in CH_2Cl_2 (71 mL) at –78 °C, and the mixture was stirred at –78 °C for 40 min. A soln of **37** (3.78 g, 10.1 mmol) in CH_2Cl_2 (30 mL) was then added, and the mixture was stirred in darkness at –78 °C for 70 min. Et_3N (11.3 mL, 80.8 mmol) was added, and the mixture was stirred in darkness at 0 °C for 20 min, then neutralized with 1 M HCl (100 mL) and extracted with Et_2O. The extracts were washed with H_2O and brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel (38 g), hexane–EtOAc, 4:1] gave **33** as a pale yellow oil; yield: 3.14 g (84%).

FTIR (film): 1678, 1610, 1512, 1456, 1244, 1092, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.71 (d, *J* = 7.6 Hz, 1 H), 7.26 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 6.83 (d, *J* = 14.6 Hz, 1 H), 6.55 (t, *J* = 6.6 Hz, 1 H), 6.41 (dd, *J* = 14.6, 7.6 Hz, 1 H), 4.47 (s, 2 H), 3.81 (s, 3 H), 3.61 (t, *J* = 6.3 Hz, 2 H), 2.68 (dt, *J* = 6.6, 6.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 192.2, 159.3, 153.5, 148.7, 134.9, 130.0, 129.3, 113.8, 104.0, 72.7, 67.3, 55.3, 37.8.

HRMS (EI): *m/z* calcd [M^+] for $C_{15}H_{17}IO_3$: 372.0222; found: 372.0231.

(3*S*,4*S*,5*E*,7*Z*)-3-Ethyl-7-iodo-10-[(4-methoxybenzyl)oxy]deca-1,5,7-trien-4-ol (38)

(2*Z*)-Pent-2-ene (17 mL, 153 mmol) and a 2.77 M soln of BuLi in hexane (37 mL, 102 mmol) were added to a stirred suspension of *t*-BuOK (11 g, 102 mmol) in THF (100 mL) at –78 °C, and the mixture was stirred at –50 °C for 10 min. The mixture was then cooled to –78 °C and a soln of (+)-*B*-methoxy(diisopinocampheyl)borane (40 g, 128 mmol) in Et_2O (80 mL), $BF_3{\cdot}Et_2O$ (32 mL, 255 mmol), and dienal **33** (19 g, 51 mmol) were added sequentially. The mixture was stirred in darkness at –78 °C for 9 h then 3 M aq NaOH (160 mL) and 30% H_2O_2 (160 mL) were added, and the mixture was stirred in darkness at 0 °C for 6 h. The mixture was then filtered through Celite and extracted with Et_2O. The extracts were washed with H_2O and brine, dried, and concentrated. Purification of the residue by flash column chromatography [silica gel (800 g), hexane–EtOAc, 30:1 to 6:1] gave **38** as a pale yellow oil; yield: 18 g (82%); $[\alpha]_D^{25}$ +26.9 (*c* 1.00, $CHCl_3$).

FTIR (film): 3446, 1606, 1512, 1456, 1246, 1092, 1034 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.8 Hz, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 6.01–5.90 (m, 3 H), 5.57 (dt, *J* = 17.0, 9.8 Hz, 1 H), 5.19 (dd, *J* = 10.2, 2.0 Hz, 1 H), 5.14 (dd, *J* = 17.1, 2.0 Hz, 1 H), 4.45 (s, 2 H), 4.24 (br s, 1 H), 3.80 (s, 3 H), 3.54 (t, *J* = 6.3 Hz, 2 H), 2.59 (dt, *J* = 6.3, 6.9 Hz, 2 H), 2.19–2.14 (m, 1 H), 1.58–1.52 (m, 1 H), 1.34–1.26 (m, 1 H), 0.90 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 137.9, 137.1, 132.6, 130.2, 129.2, 118.4, 113.7, 107.5, 73.6, 72.5, 67.9, 55.2, 52.6, 37.1, 23.1, 11.8.

HRMS (EI): *m/z* calcd for $C_{20}H_{27}IO_3$: 442.1005; found: 442.0965.

***tert*-Butyl [(3*E*,4*E*,6*S*,7*S*)-7-Ethyl-6-hydroxy-3-{3-[(4-methoxybenzyl)oxy]propylidene}nona-4,8-dien-1-yl]carbamate (39)**

A 0.5 M soln of 9-BBN in THF (7.9 mL, 3.94 mmol) was added to a soln of *tert*-butyl vinylcarbamate[34] (845 mg, 5.91 mmol) in 1,4-dioxane (20 mL) at 10 °C, and the mixture was stirred at r.t. for 9 h. The mixture was then cooled to 10 °C, and 3 M aq NaOH (7.9 mL) was added. The resulting mixture was added to a mixture of trienol **38** (870 mg, 1.97 mmol) and [$PdCl_2$(dppf)] (73 mg, 0.10 mmol) in 1,4-dioxane (20 mL) at 10 °C, and the mixture was stirred in darkness at r.t. for 7 h. Most of the 1,4-dioxane was evaporated and the residue was extracted with Et_2O. The extracts were washed with brine, dried, and concentrated. The residue was purified by chromatography [silica gel (30 g), hexane–EtOAc, 6:1 to 3:1] to give **39** as a pale yellow oil; yield: 816 mg (90%); $[\alpha]_D^{25}$ +4.9 (*c* 0.98, $CHCl_3$).

FTIR (film): 3371, 1699, 1516, 1458, 1363, 1250, 1173, 1093 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 8.3 Hz, 2 H), 6.87 (d, *J* = 8.3 Hz, 2 H), 6.13 (d, *J* = 15.6 Hz, 1 H), 5.65–5.50 (m, 3 H), 5.15 (d, *J* = 10.3 Hz, 1 H), 5.10 (d, *J* = 17.6 Hz, 1 H), 4.90–4.80 (br s, 1 H), 4.46 (s, 2 H), 4.10–4.00 (br s, 1 H), 3.80 (s, 3 H), 3.47 (t, *J* = 6.4 Hz, 2 H), 3.21–3.10 (br s, 2 H), 2.50–2.30 (m, 4 H), 2.15–2.00 (m, 1 H), 2.00–1.88 (br s, 1 H), 1.87–1.78 (br s, 1 H), 1.60–1.45 (m, 1 H), 1.42 (s, 9 H), 1.30–1.15 (m, 1 H), 0.88 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 155.9, 138.3, 135.7, 134.2, 131.2, 130.3, 129.2, 127.5, 117.9, 113.7, 75.0, 72.5, 68.9, 55.2, 52.7, 39.2, 29.0, 28.4, 28.2, 27.0, 23.3, 11.8.

HRMS (EI): *m/z* calcd for $C_{27}H_{41}NO_5$: 459.2984; found: 459.2973.

(3*S*,4*S*,5*E*,7*E*)-7-{2-[(*tert*-Butoxycarbonyl)amino]ethyl}-3-ethyl-10-[(4-methoxybenzyl)oxy]deca-1,5,7-trien-4-yl Acrylate (40)

Acryloyl chloride (2.2 mL, 26 mmol) was added to an ice-cooled soln of **39** (6.0 g, 13 mmol) and DIPEA (4.9 mL, 29 mmol) in CH_2Cl_2 (130 mL), and the mixture was stirred stirring at 0 °C for 1 h. The mixture was then poured into sat. aq $NaHCO_3$ (100 mL), extracted with CH_2Cl_2, dried, and concentrated. Purification of the residue by column chromatography [Florisil (180 g), hexane–EtOAc, 20:1 to 10:1] gave **40** as a yellow oil; yield 6.6 g (99%); $[\alpha]_D^{24}$ +17.5 (*c* 0.53, $CHCl_3$).

FTIR (film): 3359, 1712, 1616, 1512, 1400, 1252, 1180, 1093 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 6.40 (dd, *J* = 17.3, 1.5 Hz, 1 H), 6.17 (d, *J* = 15.1 Hz, 1 H), 6.15 (dd, *J* = 17.3, 10.3 Hz, 1 H), 5.81 (dd, *J* = 10.3, 1.5 Hz, 1 H), 5.63–5.53 (m, 3 H), 5.33 (t, *J* = 7.3 Hz, 1 H), 5.12 (dd, *J* = 10.4, 1.8 Hz, 1 H), 5.05 (dd, *J* = 17.3, 1.8 Hz, 1 H), 4.92–4.84 (br s, 1 H), 4.46 (s, 2 H), 3.80 (s, 3 H), 3.46 (t, *J* = 6.3 Hz, 2 H), 3.21–3.02 (br s, 2 H), 2.45–2.40 (m, 4 H), 2.31–2.20 (m, 1 H), 1.57–1.49 (m, 1 H), 1.42 (s, 9 H), 1.31–1.23 (m, 1 H), 0.88 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2, 159.0, 155.7, 137.4, 137.3, 136.4, 132.4, 130.5, 130.3, 129.2, 128.7, 123.1, 117.4, 113.7, 78.9, 77.2, 72.5, 68.8, 55.2, 50.0, 39.2, 29.1, 28.5, 28.4, 23.2, 11.6.

HRMS (EI): *m/z* calcd for $C_{30}H_{43}NO_6$: 513.3091; found: 513.3079.

***tert*-Butyl {(3*E*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-6-[(4-methoxybenzyl)oxy]hex-3-en-1-yl}carbamate (41)**

Grubbs second-generation catalyst (1.01 g, 1.19 mmol) was added to a degassed soln of acrylate **40** (6.09, 11.9 mmol) in CH_2Cl_2 (1187 mL), and the mixture was refluxed for 11 h. The mixture was then washed with sat. aq $NaHCO_3$, dried, and concentrated. The residue was purified by chromatography [silica gel (200 g), hexane–EtOAc 4:1–2:1] to give **41** as a pale yellow oil; yield: 4.41 g (77%); $[\alpha]_D^{24}$ +68.7 (*c* 0.69, $CHCl_3$). The optical purity was determined to be 93% ee by HPLC (Chiralcel AD, Daicel, hexane–*i*-PrOH, 8:1).

FTIR (film): 3361, 1716, 1614, 1512, 1373, 1248, 1171, 1097 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.3 Hz, 2 H), 6.97 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.88 (d, *J* = 8.3 Hz, 2 H), 6.32 (d, *J* = 16.1 Hz, 1 H), 6.05 (dd, *J* = 10.2, 1.4 Hz, 1 H), 5.73–5.65 (m, 2 H), 5.02 (t, *J* = 4.4 Hz, 1 H), 4.93–4.84 (br s, 1 H), 4.47 (s, 2 H), 3.81 (s, 3 H), 3.48 (t, *J* = 6.3 Hz, 2 H), 3.22–3.06 (br m, 2 H), 2.52–2.35 (m, 5 H), 1.68–1.55 (m, 1 H), 1.52–1.44 (m, 1 H), 1.42 (s, 9 H), 0.96 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.9, 159.0, 155.7, 150.0, 139.9, 136.3, 135.1, 133.1, 130.2, 129.1, 120.8, 120.6, 113.6, 80.1, 72.4, 68.7, 55.1, 39.5, 39.1, 28.9, 28.2, 26.9, 21.4, 10.9.

HRMS (EI): *m/z* calcd for $C_{28}H_{39}NO_6$: 485.2778; found: 485.2769.

Dihydroxylation of Carbamate 41

Super AD-mix^2 prepared by mixing $K_3Fe(CN)_6$ (4.0 g, 12.3 mmol), K_2CO_3 (1.7 g, 12.3 mmol), $(DHQD)_2PHAL$ (320 mg, 0.41 mmol), $K_2OsO_2(OH)_4$ (15 mg, 0.041 mmol), and $MeSO_2NH_2$ (800 mg, 8.2 mmol), was added to an ice-cooled soln of **41** (2.0 g, 4.1 mmol) in 1:1 *t*-BuOH–H_2O (40 mL). The mixture was stirred at 0 °C for 10 h, sat. aq $Na_2S_2O_3$ (40 mL) was added, and the mixture was stirred for another 40 min at r.t. The mixture was then extracted with EtOAc, and the extracts were washed with brine, dried, and concentrated. Purification of the residue by column chromatography [silica gel (60 g), hexane–EtOAc 2:1–1:4] gave diol **42** [yield: 1.26 g (59%, 63% based on recovered starting material)] as a colorless amorphous solid, the 6,7-$(OH)_2$-isomer [yield: 180 mg (9%, 10% based on recovered starting material)] as a colorless viscous oil, and recovered **17** (130 mg, 7%) as a pale yellow oil. The enantiomeric purities of **42** and the recovered **41** were determined to be 100% ee and 59% ee, respectively, by means of ^1H NMR (500 MHz) analysis of the corresponding (*R*)- and (*S*)-MTPA esters.

Compound 42

$[\alpha]_D^{26}$ +83.2 (*c* 1.00, $CHCl_3$).

FTIR (film): 3417, 1730, 1612, 1520, 1260, 1180 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 8.5 Hz, 2 H), 6.95 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 6.04 (d, *J* = 9.8 Hz, 1 H), 5.91–5.89 (m, 2 H), 5.10–4.95 (m, 2 H), 4.44 (s, 2 H), 3.80 (s, 3 H), 3.70–3.60 (m, 3 H), 3.48–3.40 (m, 1 H), 3.30–3.09 (m, 2 H), 3.09 (s, 1 H), 2.44–2.40 (m, 1 H), 1.86–1.65 (m, 4 H), 1.65–1.54 (m, 1 H), 1.43 (s, 9 H), 1.59–1.39 (m, 1 H), 0.94 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.0, 159.2, 156.1, 150.1, 135.7, 129.6, 129.2, 125.0, 120.6, 113.7, 100.5, 79.9, 79.0, 76.5, 72.8, 68.8, 55.1, 39.1, 36.0, 35.3, 30.5, 28.3, 21.4, 10.9.

HRMS (EI): *m/z* calcd for $C_{28}H_{41}NO_8$: 519.2833; found: 519.2841.

6,7-$(OH)_2$-Isomer

$[\alpha]_D^{20}$ +76.0 (*c* 0.80, $CHCl_3$).

FTIR (film): 3367, 1707, 1514, 1456, 1375, 1248, 1169, 1066 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.5 Hz, 2 H), 7.12 (dd, *J* = 9.6 Hz, 6.6 Hz, 1 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 6.04 (d, *J* = 9.6 Hz, 1 H), 5.70 (t, *J* = 7.4 Hz, 1 H), 4.89–4.75 (m, 1 H), 4.52 (d, *J* = 3.3 Hz, 1 H), 4.49 (d, *J* = 3.3 Hz, 1 H), 4.45 (s, 2 H), 4.41 (d, *J* = 4.1 Hz, 1 H), 3.81 (s, 3 H), 3.75 (t, *J* = 7.4 Hz, 1 H), 3.66–3.57 (m, 1 H), 3.47 (t, *J* = 7.1 Hz, 2 H), 3.41–3.19 (m, 2 H), 2.62–2.53 (m, 1 H), 2.48–2.36 (m, 3 H), 2.32–2.18 (m, 1 H), 1.90–1.74 (m, 1 H), 1.40 (s, 9 H), 1.59–1.38 (m, 1 H), 0.97 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.3, 159.1, 157.0, 151.7, 137.8, 130.2, 129.3, 126.6, 120.6, 113.7, 79.6, 78.3, 72.6, 72.3, 69.9, 62.2, 55.2, 39.6, 35.7, 29.0, 28.6, 28.3, 20.4, 10.9.

HRMS (EI): *m/z* calcd for $C_{28}H_{41}NO_8$: 519.2832; found: 519.2822.

Allyl [(3*R*,4*R*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-3,4,6-trihydroxyhexyl]carbamate (43)

To an ice-cooled soln of diol **42** (720 mg, 1.39 mmol) in THF (9.8 mL) was treated with 5 M HCl (4.2 mL), and the mixture was stirred at r.t. for 2.5 days. The mixture was then cooled to 0 °C and $NaHCO_3$ (2.0 g, 28.8 mmol) and allyl chloroformate (0.3 mL, 2.78 mmol) were added. The mixture was stirred at r.t. for 3 h, then diluted with sat. aq $NaHCO_3$ (10 mL) and extracted with EtOAc. The extracts were dried and concentrated, and the residue was purified by column chromatography [silica gel (22 g), EtOAc] to give **43** as an amorphous solid; yield: 520 mg (98%); $[\alpha]_D^{24}$ +90.6 (*c* 0.53, $CHCl_3$).

FTIR (film): 3390, 1714, 1533, 1385, 1257, 1061 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (dd, *J* = 9.8 Hz, 5.4 Hz, 1 H), 6.05 (d, *J* = 9.8 Hz, 1 H), 5.97–5.89 (m, 3 H), 5.30 (d, *J* = 17.1 Hz, 1 H), 5.20 (d, *J* = 10.5 Hz, 1 H), 5.28–5.19 (br s, 1 H), 5.08–5.01 (m, 1 H), 4.56 (d, *J* = 5.6 Hz, 2 H), 3.95–3.80 (m, 2 H), 3.75–3.65 (m, 1 H), 3.58–3.43 (m, 1 H), 3.38–3.28 (m, 2 H), 3.28–3.14 (m, 2 H), 2.49–2.41 (m, 1 H), 2.45–2.27 (m, 1 H), 1.97–1.84 (m, 1 H), 1.80–1.63 (m, 3 H), 1.55–1.40 (m, 1 H), 0.96 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.3, 156.5, 150.4, 135.3, 132.7, 125.0, 120.3, 117.4, 80.1, 75.8, 74.6, 65.4, 60.5, 39.1, 36.6, 35.3, 32.7, 21.5, 11.0.

HRMS (EI): *m/z* calcd for $C_{19}H_{29}NO_7$: 383.1944; found: 383.1930.

Allyl {(3*R*,4*R*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-3,4,6-tris[(triethylsilyl)oxy]hexyl}carbamate (44)

TESOTf (2.1 mL, 9.1 mmol) was added to a soln of triol **43** (500 mg, 1.3 mmol) and 2,6-lutidine (1.5 mL, 13 mmol) in CH_2Cl_2 (13 mL) at –78 °C, and the mixture was stirred at –78 °C for 3 h. The reaction was quenched with brine (15 mL), and the mixture was stirred at r.t. for a further 10 h. The mixture was then extracted with Et_2O and the extracts were washed with brine then dried and concentrated. Purification of the residue by column chromatography [silica gel (25 g), hexane–EtOAc, 10:1 to 5:1] gave **44** as a colorless oil; yield: 700 mg (74%); $[\alpha]_D^{23}$ +52.2 (*c* 0.65, $CHCl_3$).

FTIR (film): 3350, 1727, 1520, 1461, 1382, 1244, 1104, 1011 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.93 (dd, *J* = 9.8, 5.1 Hz, 1 H), 6.05 (d, *J* = 9.8 Hz, 1 H), 5.97–5.74 (m, 3 H), 5.29 (d, *J* = 17.3 Hz, 1 H), 5.19 (d, *J* = 10.2 Hz, 1 H), 5.03–5.00 (m, 1 H), 4.96–4.82 (br s, 1 H), 4.55 (d, *J* = 4.9 Hz, 2 H), 3.77–3.52 (m, 3 H), 3.38–3.06 (m, 2 H), 2.46–2.38 (m, 1 H), 2.08–1.99 (m, 1 H), 1.92–1.70 (m, 2 H), 1.70–1.48 (m, 2 H), 1.38–1.24 (m, 1 H), 1.00–0.87 (m, 30 H), 0.72–0.50 (m, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6, 155.8, 149.5, 136.5, 132.8, 124.4, 120.7, 117.0, 80.3, 79.8, 75.0, 65.1, 59.4, 39.5, 37.6, 36.5, 35.6, 21.5, 10.9, 7.1, 7.0, 6.8, 6.7, 5.4, 4.3.

HRMS (FAB): *m/z* [M + Na^+] calcd for $C_{37}H_{71}NO_7Si_3Na$: 748.4439; found: 748.4422.

Allyl {(3*R*,4*R*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-6-oxo-3,4-bis[(triethylsilyl)oxy]hexyl}carbamate (45)

DMSO (1.11 mL, 15.6 mmol) and a soln of carbamate **44** (1.29 g, 1.78 mmol) in CH_2Cl_2 (8 mL) were added to a stirred soln of oxalyl chloride (0.68 mL, 7.82 mmol) in CH_2Cl_2 (4.9 mL) at –78 °C, and the mixture was stirred at –78 °C for 20 min and then at –40 °C for 20 min. The mixture was cooled to –78 °C, Et_3N (3.72 mL, 26.7 mmol) was added, and the mixture was stirred at 0 °C for 20 min. The mixture was then diluted with Et_2O, washed with 1 M HCl, H_2O, and sat. aq $NaHCO_3$, then dried and concentrated. Purification of the residue by column chromatography [Florisil (20 g), hexane–EtOAc, 5:1] gave **45** as a pale yellow oil; yield: 909 mg (84%); $[\alpha]_D^{25}$ +24.8 (*c* 0.75, $CHCl_3$).

FTIR (film): 3346, 1718, 1525, 1460, 1242, 1107, 1005 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.77 (s, 1 H), 6.95 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.06 (d, *J* = 9.8 Hz, 1 H), 5.98–5.89 (m, 2 H), 5.83 (dd, *J* = 15.6, 5.2 Hz, 1 H), 5.30 (d, *J* = 17.1 Hz, 1 H), 5.20 (d, *J* = 10.2 Hz, 1 H), 5.03 (t, *J* = 5.2 Hz, 1 H), 4.88–4.75 (br s, 1 H), 4.65–4.55 (m, 2 H), 4.15 (t, *J* = 3.9 Hz, 1 H), 3.41–3.07 (m, 2 H), 2.64 (dd, *J* = 18.0, 3.9 Hz, 1 H), 2.49–2.37 (m, 2 H), 2.15–2.05 (m, 1 H), 1.85–1.71 (m, 1 H), 1.65–1.45 (m, 2 H), 1.10–0.80 (m, 21 H), 0.64 (q, *J* = 7.5 Hz, 6 H), 0.62 (q, *J* = 7.5 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.7, 163.8, 156.0, 149.7, 135.3, 133.0, 125.9, 121.0, 117.5, 80.1, 79.8, 73.0, 65.5, 47.7, 39.5, 37.8, 36.8, 21.8, 11.2, 7.3, 7.1, 6.9, 5.2.

HRMS (EI): *m/z* calcd for $C_{31}H_{55}NO_7Si_2$: 609.3517; found: 609.3515.

Ethynylation of Aldehyde 45

Aldehyde **45** (909 mg, 1.49 mmol) was subjected to ethynylation by using anhyd $CeCl_3$ (1.07 g, 4.33 mmol) and a 1.07 M soln of ethynylmagnesium bromide in THF (4.0 mL, 4.33 mmol), in the same manner as described for the preparation of **20** from **19**. Purification by column chromatography [silica gel (50 g), hexane–EtOAc, 5:1 to 2:1] gave **46**, a colorless oil, as an epimeric mixture; yield: 698 mg (74%; 11*R*/11*S* = 1:1).

Less-Polar Epimer of 46

$[\alpha]_D^{26}$ +46.9 (*c* 0.75, $CHCl_3$).

FTIR (film): 3408, 1714, 1520, 1456, 1244, 1103, 1007 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (dd, *J* = 9.8, 4.9 Hz, 1 H), 6.06 (d, *J* = 9.8 Hz, 1 H), 5.96–5.85 (m, 2 H), 5.83 (dd, *J* = 15.6, 5.6 Hz, 1 H), 5.29 (d, *J* = 17.5 Hz, 1 H), 5.19 (d, *J* = 10.2 Hz, 1 H), 5.04 (t, *J* = 5.6 Hz, 1 H), 5.00–4.91 (br s, 1 H), 4.64–4.50 (m, 2 H), 4.49–4.39 (br, 1 H), 3.85 (d, *J* = 7.8 Hz, 1 H), 3.31–3.11 (m, 2 H), 2.48–2.39 (m, 2 H), 2.18–2.10 (br, 1 H), 2.08–1.96 (m, 2 H), 1.92–1.70 (m, 1 H), 1.70–1.44 (m, 3 H), 0.99–0.84 (m, 21 H), 0.72–0.58 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 155.9, 149.5, 136.3, 132.9, 125.1, 120.8, 117.3, 85.2, 80.2, 79.6, 74.6, 72.4, 65.3, 58.6, 41.0, 39.5, 37.4, 36.5, 21.6, 11.1, 7.2, 7.0, 6.9, 5.4.

HRMS (EI): *m/z* calcd for $C_{33}H_{57}NO_7Si_2$: 635.3673; found: 635.3672.

More-Polar Epimer of 46

$[\alpha]_D^{26}$ +27.3 (*c* 0.81, $CHCl_3$).

FTIR (film): 3305, 1712, 1522, 1456, 1242, 1107, 1009 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.94 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.06 (d, *J* = 9.8 Hz, 1 H), 5.98–5.85 (m, 2 H), 5.82 (dd, *J* = 15.6, 5.6 Hz, 1 H), 5.30 (d, *J* = 17.0 Hz, 1 H), 5.20 (d, *J* = 10.7 Hz, 1 H), 5.03 (t, *J* = 5.6 Hz, 1 H), 5.03–4.94 (br s, 1 H), 4.62–4.50 (m, 2 H), 4.49–4.40 (m, 1 H), 3.79 (d, *J* = 6.4 Hz, 1 H), 3.36–3.10 (m, 2 H), 2.53 (s, 1 H), 2.50–2.40 (m, 1 H), 2.08–1.90 (m, 2 H), 1.90–1.74 (m, 2 H), 1.74–1.58 (m, 2 H), 1.55–1.44 (m, 1 H), 1.00–0.88 (m, 21 H), 0.72–0.64 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 156.0, 149.5, 136.2, 132.9, 125.2, 120.8, 117.3, 84.6, 80.2, 79.7, 75.6, 74.1, 65.4, 60.5, 41.0, 39.4, 37.4, 36.6, 21.7, 11.1, 7.2, 7.1, 6.9, 5.5.

HRMS (EI): *m/z* calcd for $C_{33}H_{57}NO_7Si_2$: 635.3673; found: 635.3669.

Allyl {(3*R*,4*R*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-6-oxo-3,4-bis[(triethylsilyl)oxy]oct-7-yn-1-yl}carbamate (47)

Alcohol **46** (698 mg, 1.10 mmol) was oxidized by using Dess–Martin periodinane (1.42 g, 3.29 mmol) and $NaHCO_3$ (924 mg, 11.0 mmol) in the same manner as described for the preparation of **21** from **20**. Purification by column chromatography [silica gel (24 g), hexane–EtOAc, 5:1] gave **47** as a colorless oil; yield: 666 mg (96%); $[\alpha]_D^{26}$ +38.6 (*c* 1.00, $CHCl_3$).

FTIR (film): 3350, 1720, 1523, 1460, 1242, 1105, 1009 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.07 (d, *J* = 9.8 Hz, 1 H), 5.97–5.85 (m, 2 H), 5.82 (dd, *J* = 15.6, 5.9 Hz, 1 H), 5.30 (d, *J* = 17.3 Hz, 1 H), 5.20 (d, *J* = 10.2 Hz, 1 H), 5.06 (t, *J* = 5.9 Hz, 1 H), 4.84–4.75 (br s, 1 H), 4.62–4.45 (m, 2 H), 4.25 (d, *J* = 5.8 Hz, 1 H), 3.26 (s, 1 H), 3.35–3.11 (m, 2 H), 2.88 (dd, *J* = 17.6, 2.5 Hz, 1 H), 2.54 (dd, *J* = 17.6, 5.8 Hz, 1 H), 2.49–2.40 (m, 1 H), 2.13–2.05 (m, 1 H), 1.82–1.70 (m, 1 H), 1.70–1.45 (m, 2 H), 1.01–0.92 (m, 21 H), 0.71–0.56 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.1, 163.7, 156.0, 149.5, 135.3, 133.0, 125.5, 120.9, 117.5, 81.7, 80.1, 79.5, 79.1, 73.0, 65.5, 49.9, 39.6, 37.6, 36.7, 21.8, 11.2, 7.3, 7.1, 6.9, 5.2.

HRMS (EI): *m/z* calcd for $C_{33}H_{55}NO_7Si_2$: 633.3517; found: 633.3509.

Allyl {(3*R*,4*R*,7*Z*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-8-iodo-6-oxo-3,4-bis[(triethylsilyl)oxy]oct-7-en-1-yl}carbamate (48)

Ynone **47** (339 mg, 0.521 mmol) was subjected to *Z*-selective hydroiodination by using AcOH (31 μL, 0.546 mmol) and NaI (156

mg, 1.04 mmol) in acetone (0.52 mL) in darkness at r.t. for 7 days, in the same manner as described for the preparation of **22** from **21**. Purification by flash column chromatography [silica gel (15 g), hexane–*t*-BuOMe, 3:1] gave **48** [yield: 360 mg (90%)] and **49** [yield: 30 mg (8%)], each as a yellow oil.

Compound 48

$[\alpha]_D^{24}$ +68.2 (*c* 1.05, $CHCl_3$).

FTIR (film): 3349, 1722, 1569, 1460, 1243, 1103, 1009 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 8.8 Hz, 1 H), 7.17 (d, *J* = 8.8 Hz, 1 H), 6.95 (dd, *J* = 9.8, 5.3 Hz, 1 H), 6.07 (d, *J* = 9.8 Hz, 1 H), 5.98–5.87 (m, 2 H), 5.81 (dd, *J* = 15.6, 5.4 Hz, 1 H), 5.29 (d, *J* = 17.1 Hz, 1 H), 5.20 (d, *J* = 10.3 Hz, 1 H), 5.06 (t, *J* = 5.4 Hz, 1 H), 4.89–4.76 (br s, 1 H), 4.62–4.49 (m, 2 H), 4.30 (d, *J* = 6.3 Hz, 1 H), 3.35–3.08 (m, 2 H), 2.82 (dd, *J* = 18.0, 1.5 Hz, 1 H), 2.49 (dd, *J* = 18.0, 7.8 Hz, 1 H), 2.52–2.40 (m, 1 H), 2.14–2.04 (m, 1 H), 1.81–1.71 (m, 1 H), 1.71–1.58 (m, 1 H), 1.58–1.45 (m, 1 H), 1.00–0.90 (m, 21 H), 0.68–0.53 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 163.6, 155.9, 149.4, 135.6, 135.3, 132.9, 125.0, 120.9, 117.3, 90.8, 80.0, 79.5, 73.0, 65.3, 48.4, 39.4, 37.5, 36.7, 21.7, 11.1, 7.2, 7.0, 6.8, 5.1.

HRMS (EI): *m/z* calcd for $C_{33}H_{56}INO_7Si_2$: 761.2640; found: 761.2624.

Allyl {(3*R*,4*R*,7*E*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-8-iodo-6-oxo-3,4-bis[(triethylsilyl)oxy]oct-7-en-1-yl}carbamate (49)

Ynone **47** (10 mg, 0.015 mmol) was subjected to *E*-selective hydroiodination by using AcOH (0.1 mL) and NaI (5.2 mg, 0.035 mmol) in acetone (0.15 mL) in darkness at r.t. for 3 h, in the same manner as described for the preparation of **23** from **21**. Purification by preparative TLC (hexane–*t*-BuOMe, 1:1) gave **49** as a yellow oil; yield: 9.5 mg (79%); $[\alpha]_D^{24}$ +68.2 (*c* 1.05, $CHCl_3$).

FTIR (film): 3359, 1716, 1566, 1244, 1101, 1001 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 14.9 Hz, 1 H), 7.13 (d, *J* = 14.9 Hz, 1 H), 6.96 (dd, *J* = 9.8, 4.8 Hz, 1 H), 6.08 (d, *J* = 9.8 Hz, 1 H), 5.97–5.87 (m, 2 H), 5.82 (dd, *J* = 15.6, 5.2 Hz, 1 H), 5.30 (d, *J* = 17.1 Hz, 1 H), 5.20 (d, *J* = 10.2 Hz, 1 H), 5.08 (t, *J* = 5.2 Hz, 1 H), 4.84–4.77 (br s, 1 H), 4.62–4.50 (m, 2 H), 4.23 (d, *J* = 7.3 Hz, 1 H), 3.35–3.08 (m, 2 H), 2.70 (d, *J* = 16.5 Hz, 1 H), 2.52–2.40 (m, 2 H), 2.20–2.00 (m, 1 H), 1.80–1.70 (m, 1 H), 1.70–1.45 (m, 2 H), 1.00–0.88 (m, 21 H), 0.68–0.52 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 163.6, 155.9, 149.4, 145.0, 135.4, 132.9, 125.1, 120.9, 117.4, 99.0, 79.9, 79.5, 73.2, 65.4, 44.3, 39.5, 37.6, 36.7, 21.8, 11.2, 7.2, 7.0, 6.8, 5.1.

HRMS (EI): *m/z* calcd $C_{33}H_{56}INO_7Si_2$: 761.2640; found: 761.2631.

Allyl {(3*R*,4*R*,7*Z*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4-hydroxy-8-iodo-6-oxo-3-[(triethylsilyl)oxy]oct-7-en-1-yl}carbamate (50)

H_2O (0.7 mL) and AcOH (2.1 mL) were added to an ice-cooled soln of **48** (188 mg, 0.247 mmol) in THF (2.1 mL), and the mixture was stirred in darkness at r.t. for 2.5 days. The mixture was then diluted with EtOAc, washed with sat. aq $NaHCO_3$, dried, and concentrated. The residue was purified by chromatography [silica gel (6 g), hexane–EtOAc, 10:1 to 2:1] to give **50** as a colorless oil; yield: 142 mg (89%); $[\alpha]_D^{24}$ +43.8 (*c* 0.73, $CHCl_3$).

FTIR (film): 3388, 2951, 2877, 1707, 1522, 1458, 1381, 1238, 1078, 735 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 8.7 Hz, 1 H), 7.26 (d, *J* = 8.7 Hz, 1 H), 6.96 (dd, *J* = 9.7, 5.3 Hz, 1 H), 6.06 (d, *J* = 9.7 Hz, 1 H), 5.98–5.88 (m, 2 H), 5.84 (dd, *J* = 15.6, 5.3 Hz, 1 H), 5.30 (d, *J* = 18.5 Hz, 1 H), 5.20 (d, *J* = 10.2 Hz, 1 H), 5.03 (t, *J* = 5.3 Hz, 1 H), 5.12–4.96 (br s, 1 H), 4.70–4.45 (m, 2 H), 4.08 (d, *J* = 7.8 Hz, 1 H), 3.20–3.04 (m, 2 H), 2.82 (d, *J* = 17.1 Hz, 1 H), 2.56 (dd, *J* = 17.1, 9.8 Hz, 1 H), 2.50–2.35 (m, 1 H), 2.07–1.88 (m, 2 H), 1.70 (d, *J* = 9.3 Hz, 1 H), 1.70–1.40 (m, 2 H), 0.96 (t, *J* = 7.8 Hz, 12 H), 0.65 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.8, 163.5, 156.1, 149.6, 135.3, 135.0, 132.9, 126.1, 120.8, 117.4, 92.1, 79.9, 78.6, 72.8, 65.4, 45.8, 39.4, 36.5, 36.5, 21.7, 11.1, 7.3, 6.9.

HRMS (EI): *m/z* calcd for $C_{27}H_{42}INO_7Si$: 647.1775; found: 647.1783.

Allyl {(3*R*,4*R*,6*R*,7*Z*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-8-iodo-3-[(triethylsilyl)oxy]oct-7-en-1-yl}carbamate (51)

Hydroxy ketone **50** (64 mg, 0.099 mmol) was subjected to *anti*-selective reduction using $Me_4NBH(OAc)_3$ (313 mg, 1.19 mmol) and AcOH (0.37 mL) in MeCN (5.0 mL) at –10 °C for 3 h, in the same manner as described for the preparation of **25** from **24**. Purification by column chromatography [silica gel (2 g), CH_2Cl_2–MeOH, 40:1 to 30:1] gave **51** as a colorless oil; yield: 62 mg (96%); $[\alpha]_D^{21}$ +43.7 (*c* 0.90, $CHCl_3$).

FTIR (film): 3373, 1711, 1527, 1412, 1248, 1090 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (dd, *J* = 9.7, 5.3 Hz, 1 H), 6.41 (t, *J* = 7.5 Hz, 1 H), 6.31 (d, *J* = 7.5 Hz, 1 H), 6.05 (d, *J* = 9.7 Hz, 1 H), 5.97–5.88 (m, 2 H), 5.82 (dd, *J* = 15.6, 5.2 Hz, 1 H), 5.29 (d, *J* = 18.5 Hz, 1 H), 5.20 (d, *J* = 10.3 Hz, 1 H), 5.33–5.15 (br s, 1 H), 5.02 (t, *J* = 5.2 Hz, 1 H), 4.75–4.48 (m, 3 H), 3.92–3.75 (m, 1 H), 3.50–3.12 (m, 4 H), 2.53–2.38 (m, 1 H), 2.05–1.82 (m, 2 H), 1.82–1.70 (m, 1 H), 1.70–1.40 (m, 3 H), 1.05–0.94 (m, 12 H), 0.64 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6, 156.3, 149.6, 143.0, 135.9, 132.8, 126.0, 120.8, 117.4, 81.4, 80.1, 79.9, 73.5, 72.6, 65.4, 39.4, 36.6, 36.0, 35.7, 21.7, 11.1, 7.2, 6.9.

HRMS (EI): *m/z* calcd for $C_{27}H_{44}INO_7Si$: 649.1932; found: 649.1944.

Allyl {(3*R*,4*R*,6*S*,7*Z*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-8-iodo-3-[(triethylsilyl)oxy]oct-7-en-1-yl}carbamate (52)

Hydroxy ketone **50** (20 mg, 0.030 mmol) was subjected to *syn*-selective reduction by using $NaBH_4$ (2 mg, 0.045 mmol) and Et_3B (1.0 M in THF, 45 μL, 0.045 mmol) in THF (0.6 mL) and MeOH (0.1 mL) at –78 °C for 14 h, in the same manner as described for the preparation of **26** from **24**. Purification by preparative TLC (hexane–EtOAc, 1:1) gave **52** as a colorless oil; yield: 14 mg (74%); $[\alpha]_D^{21}$ +44.2 (*c* 0.6, $CHCl_3$).

FTIR (film): 3346, 1718, 1519, 1460, 1383, 1252, 1090, 1012 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (dd, *J* = 9.3, 5.2 Hz, 1 H), 6.44–6.26 (m, 2 H), 6.06 (d, *J* = 9.3 Hz, 1 H), 6.00–5.81 (m, 3 H), 5.30 (d, *J* = 17.0 Hz, 1 H), 5.20 (d, *J* = 10.2 Hz, 1 H), 5.28–5.15 (br s, 1 H), 5.06 (t, *J* = 3.9 Hz, 1 H), 4.63–4.48 (m, 3 H), 4.30–4.10 (br s, 1 H), 3.80 (t, *J* = 5.8 Hz, 1 H), 3.65–3.48 (br s, 1 H), 3.40–3.08 (m, 2 H), 2.52–2.40 (m, 1 H), 1.96–1.74 (m, 4 H), 1.71–1.58 (m, 1 H), 1.58–1.42 (m, 1 H), 0.96 (t, *J* = 7.8 Hz, 12 H), 0.64 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6, 149.6, 148.5, 142.7, 135.5, 132.6, 125.2, 120.6, 117.3, 81.7, 79.6, 77.2, 75.2, 71.5, 65.4, 39.0, 38.8, 36.3, 21.3, 10.7, 6.7, 4.8.

HRMS (FAB): *m/z* [M^+] calcd for $C_{27}H_{44}NO_7SiI$: 649.1932; found: 649.1940.

Allyl {(3*R*,4*R*,6*R*,7*E*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-8-iodo-3-[(triethylsilyl)oxy]oct-7-en-1-yl}carbamate (53)

Compound **49** (100 mg, 0.13 mmol) was subjected to desilylation using AcOH (1.2 mL) and H_2O (0.4 mL) in THF (1.2 mL) at r.t. for 1.5 days, in the same manner as described for the preparation of **50** from **48**. Purification by preparative TLC (hexane–EtOAc, 1:1) gave recovered **49** (41 mg, 41%) and the corresponding hydroxy ketone as a yellow oil; yield: 40 mg (48%, 81% based on recovered starting material); $[\alpha]_D^{21}$ +88.5 (*c* 2.0, $CHCl_3$).

FTIR (film): 3380, 2956, 2877, 1718, 1567, 1460, 1382, 1248, 1083 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 4.8 Hz, 1 H), 7.17 (d, *J* = 4.8 Hz, 1 H), 6.97 (dd, *J* = 9.7, 4.4 Hz, 1 H), 6.07 (d, *J* = 9.7 Hz, 1 H), 5.98–5.89 (m, 2 H), 5.83 (dd, *J* = 15.6, 5.4 Hz, 1 H), 5.30 (d, *J* = 11.5 Hz, 1 H), 5.21 (d, *J* = 10.3 Hz, 1 H), 5.16–5.07 (br s, 1 H), 5.03 (t, *J* = 5.4 Hz, 1 H), 4.66–4.50 (m, 2 H), 4.03 (d, *J* = 8.8 Hz, 1 H), 3.38–3.20 (m, 2 H), 3.21 (s, 1 H), 2.75 (d, *J* = 17.1 Hz, 1 H), 2.60–2.40 (m, 3 H), 2.02–1.88 (m, 2 H), 1.64–1.46 (m, 2 H), 1.03–0.92 (m, 12 H), 0.65 (q, 7.3 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.2, 163.7, 156.2, 149.7, 144.6, 135.3, 132.9, 126.2, 120.9, 117.6, 100.5, 85.0, 79.8, 78.5, 72.8, 65.4, 41.7, 39.3, 36.5, 21.6, 11.0, 7.1, 6.7

MS (FAB): *m/z* (%): 136 (85), 154 (100), 648 [M^+].

HRMS (FAB): *m/z* [(M + 1)$^+$] calcd for $C_{27}H_{43}NO_7SiI$: 648.1854; found: 648.1835.

The hydroxy ketone (20 mg, 0.031 mmol) thus obtained was subjected to *anti*-selective reduction in the same manner as described for the preparation of **26** from **24**. Purification by preparative TLC (hexane–EtOAc, 1:2) gave **53** as a colorless oil; yield: 17 mg (85%); $[\alpha]_D^{21}$ +69.5 (*c* 0.85, $CHCl_3$).

FTIR (film): 3408, 1709, 1526, 1459, 1383, 1249, 1084 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.58 (dd, *J* = 14.6, 5.3, Hz, 1 H), 6.40 (d, *J* = 14.6 Hz, 1 H), 6.07 (d, *J* = 9.8 Hz, 1 H), 6.05–5.78 (m, 3 H), 5.30 (d, *J* = 17.1 Hz, 1 H), 5.17 (d, *J* = 10.2 Hz, 1 H), 5.25–5.10 (br s, 1 H), 5.02 (t, *J* = 4.8 Hz, 1 H), 4.70–4.51 (br, 2 H), 4.60–4.38 (br, 1 H), 3.92–3.70 (br, 1 H), 3.42–3.22 (br, 2 H), 3.22–3.10 (br s, 1 H), 3.05–2.83 (br s, 1 H), 2.55–2.40 (m, 1 H), 2.11–1.80 (m, 2 H), 1.80–1.40 (m, 4 H), 1.18–0.85 (m, 12 H), 0.64 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 156.4, 149.7, 148.1, 136.0, 132.8, 126.4, 120.9, 117.7, 117.6, 80.0, 78.8, 73.5, 72.2, 65.5, 39.3, 36.5, 36.2, 35.7, 21.6, 11.0, 7.1, 6.8.

HRMS (FAB): *m/z* [M^+] calcd for $C_{27}H_{44}NO_7SiI$: 649.1932; found: 649.1939.

Allyl {(3*R*,4*R*,6*S*,7*E*)-3-{(*E*)-2-[(2*S*,3*S*)-3-Ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-8-iodo-3-[(triethylsilyl)oxy]oct-7-en-1-yl}carbamate (54)

Syn-selective reduction of the hydroxy ketone prepared from **49** followed by purification by preparative TLC (hexane–EtOAc, 1:2) gave **54** in the same manner as described for the preparation of **26** from **24**; yield: 74%; $[\alpha]_D^{21}$ +79.0 (*c* 0.5, $CHCl_3$).

FTIR (film): 3369, 1715, 1521, 1383, 1247, 1097, 1011 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.54 (dd, *J* = 14.2, 5.4 Hz, 1 H), 6.38 (d, *J* = 14.2 Hz, 1 H), 6.06 (d, *J* = 9.8 Hz, 1 H), 5.96–5.81 (m, 3 H), 5.30 (dd, *J* = 17.1, 1.5 Hz, 1 H), 5.21 (dd, *J* = 10.3, 1.5 Hz, 1 H), 5.25–5.10 (br s, 1 H), 5.04 (t, *J* = 4.0 Hz, 1 H), 4.56 (d, *J* = 5.8 Hz, 2 H), 4.38–4.30 (br s, 1 H), 4.13–3.95 (br s, 1 H), 3.92–3.80 (br s, 1 H), 3.77 (dd, *J* = 3.7, 6.3 Hz, 1 H), 3.38–3.12 (m, 2 H), 2.47–2.42 (m, 1 H), 1.93–1.70 (m, 3 H), 1.70–1.58 (m, 2 H), 1.58–1.45 (m, 1 H), 1.00–0.88 (m, 12 H), 0.66–0.58 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.8, 149.9, 149.8, 147.8, 136.0, 132.8, 125.5, 120.9, 117.7, 79.8, 77.2, 76.7, 75.2, 65.8, 39.9, 39.3, 36.5, 36.2, 21.6, 11.0, 6.9, 5.1.

HRMS (FAB): *m/z* [M^+] calcd for $C_{27}H_{44}NO_7SiI$: 649.1932; found: 649.1959.

Allyl {(3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-3-{(*E*)-2-[(2*S*,3*S*)-3-ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-3-[(triethylsilyl)oxy]deca-7,9-dien-1-yl}carbamate (56)

A soln of stannane **55** (479 mg, 1.17 mmol) in THF (4 mL) and $[Pd(MeCN)_2Cl_2]$ (31 mg, 0.117 mmol) were added to a degassed soln of **51** (250 mg, 0.39 mmol) in MeCN (16 mL) at 0 °C, and the mixture was stirred at r.t. for 1 h. The mixture was then concentrated and the residue was purified by chromatography [silica gel (15 g), hexane–EtOAc, 2:1 to 1:1] to give unreacted **51** (108 mg, 43%) and **56** as a colorless oil; yield: 113 mg (46%, 81% based on residual starting material); $[\alpha]_D^{21}$ +78.4 (*c* 1.0, $CHCl_3$).

FTIR (film): 3385, 1712, 1523, 1451, 1382, 1248, 1083 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.94 (dd, *J* = 9.7, 5.4 Hz, 1 H), 6.33 (t, *J* = 11.5 Hz, 1 H), 6.12 (t, *J* = 11.5 Hz, 1 H), 6.06 (d, *J* = 9.7 Hz, 1 H), 5.95–5.79 (m, 3 H), 5.45 (t, *J* = 10.2 Hz, 1 H), 5.39 (t, *J* = 10.2 Hz, 1 H), 5.29 (d, *J* = 17.3 Hz, 1 H), 5.20 (d, *J* = 10.8 Hz, 1 H), 5.30–5.20 (m, 1 H), 5.01 (t, *J* = 4.4 Hz, 1 H), 5.00–4.90 (br s, 1 H), 4.55 (m, 2 H), 3.86 (d, *J* = 9.2 Hz, 1 H), 3.32 (m, 2 H), 3.01 (s, 1 H), 2.45–2.40 (m, 2 H), 2.15–2.10 (br s, 1 H), 1.99–1.83 (m, 2 H), 1.72–1.03 (m, 14 H), 0.97–0.91 (m, 12 H), 0.63 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 166.5, 152.6, 140.3, 137.7, 135.4, 134.6, 129.3, 126.6, 124.5, 122.7, 121.1, 117.4, 82.2, 81.0, 74.3, 66.2, 65.4, 40.7, 40.3, 37.8, 37.7, 34.3, 29.2, 27.9, 27.1, 22.8, 14.0, 11.4, 7.8.

HRMS (FAB): *m/z* [M^+] calcd for $C_{35}H_{57}NO_7Si$: 631.3905; found: 631.3895.

Allyl {(3*R*,4*R*,6*S*,7*Z*,9*Z*)-10-Cyclohexyl-3-{(*E*)-2-[(2*S*,3*S*)-3-ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-3-[(triethylsilyl)oxy]deca-7,9-dien-1-yl}carbamate (57)

Coupling of **52** (12 mg, 0.018 mmol) with **55** (21 mg, 0.054 mmol) was carried out by using $Pd(MeCN)_2Cl_2$ (1.4 mg, 0.0054 mmol) in 4:1 MeCN–THF (2 mL), in the same manner as described for the preparation of **56** from **51**. Purification by preparative TLC (hexane–EtOAc, 1:1) gave **57** as a yellow oil; yield: 6.5 mg (56%); $[\alpha]_D^{21}$ +115.5 (*c* 0.40, $CHCl_3$).

FTIR (film): 3353, 2927, 1716, 1517, 1453, 1247, 1092, 1012 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (dd, *J* = 9.7, 5.4 Hz, 1 H), 6.33 (t, *J* = 11.2 Hz, 1 H), 6.10 (t, *J* = 11.2 Hz, 1 H), 6.06 (d, *J* = 9.7 Hz, 1 H), 5.96–5.90 (m, 2 H), 5.86 (dd, *J* = 6.6, 4.9 Hz, 1 H), 5.45 (t, *J* = 9.8 Hz, 1 H), 5.40 (t, *J* = 11.2 Hz, 1 H), 5.30 (dd, *J* = 17.1, 1.5 Hz, 1 H), 5.40–5.30 (br s, 1 H), 5.20 (dd, *J* = 10.8, 1.5 Hz, 1 H), 5.05 (t, *J* = 4.9Hz, 1 H), 4.91–4.82 (br, 1 H), 4.55 (d, *J* = 5.8 Hz, 2 H), 4.18–4.05 (br 1 H), 3.78 (t, *J* = 4.4 Hz, 1 H), 3.42–3.10 (m, 2 H), 2.99–2.80 (br s, 1 H), 2.51–2.39 (m, 2 H), 1.94–1.56 (m, 9 H), 1.56–1.41 (m, 1 H), 1.35–1.01 (m, 6 H), 0.93 (t, *J* = 7.8 Hz, 12 H), 0.61 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 166.5, 158.7, 152.6, 140.8, 137.4, 134.6, 126.3, 126.3, 126.0, 122.9, 121.1, 117.3, 82.3, 77.9, 77.0, 66.3, 65.9, 43.0, 40.7, 38.6, 37.7, 37.5, 34.4, 34.2, 27.1, 22.8, 11.3, 7.5, 6.3.

HRMS (FAB): *m/z* [M^+] calcd for $C_{35}H_{57}NO_7Si$: 631.3905; found: 631.3879.

Allyl {(3*R*,4*R*,6*R*,7*E*,9*Z*)-10-Cyclohexyl-3-{(*E*)-2-[(2*S*,3*S*)-3-ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-3-[(triethylsilyl)oxy]deca-7,9-dien-1-yl}carbamate (58)

Coupling of **53** (17 mg, 0.026 mmol) with **55** (31 mg, 0.078 mmol) was carried out by using $[Pd(MeCN)_2Cl_2]$ (2.0 mg, 0.0078 mmol) in 4:1 MeCN–THF (2.5 mL), in the same manner as described for the preparation of **56** from **51**. Purification by preparative TLC (hexane–EtOAc, 1:1) gave recovered **53** (4.4 mg, 26%) and **58** as a yellow oil: yield: 7.1 mg (42%); $[\alpha]_D^{21}$ 75.0 (*c* 0.40, $CHCl_3$).

FTIR (film): 3421, 2925, 1717, 1522, 1454, 1246, 1083 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (dd, *J* = 9.6, 5.4 Hz, 1 H), 6.55 (dd, *J* = 11.0, 14.8 Hz, 1 H), 6.06 (d, *J* = 9.6 Hz, 1 H), 5.95–5.78 (m, 4 H), 5.67 (dd, *J* = 14.8, 5.8 Hz, 1 H), 5.32–5.25 (m, 2 H), 5.20 (d, *J* = 10.3 Hz, 1 H), 5.18–5.07 (br s, 1 H), 5.01 (t, *J* = 4.8 Hz, 1 H), 4.55 (d, *J* = 4.9 Hz, 2 H), 4.52–4.45 (m, 1 H), 3.91–3.75 (br s, 1 H), 3.40–3.22 (m, 2 H), 3.04–2.95 (br s, 1 H), 2.52–2.40 (m, 2 H), 2.38–2.20 (br s, 1 H), 2.03–1.80 (m, 2 H), 1.74–1.44 (m, 8 H), 1.35–1.00 (m, 6 H), 0.97 (t, *J* = 7.3 Hz, 3 H), 0.96 (t, *J* = 7.8 Hz, 9 H), 0.64 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 158.7, 152.6, 138.8, 137.8, 137.7, 134.6, 127.5, 126.6, 126.0, 121.1, 117.3, 82.2, 80.9, 79.5, 74.4, 69.9, 66.2, 40.7, 40.1, 38.1, 37.7, 34.4, 27.1, 27.0, 22.8, 11.4, 7.9, 7.7.

HRMS (FAB): *m/z* [(M + 1)$^+$] calcd for $C_{35}H_{57}NO_7Si$: 632.3983; found: 632.4003.

Allyl {(3*R*,4*R*,6*S*,7*E*,9*Z*)-10-Cyclohexyl-3-{(*E*)-2-[(2*S*,3*S*)-3-ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-4,6-dihydroxy-3-[(triethylsilyl)oxy]deca-7,9-dien-1-yl}carbamate (59)

Coupling of **54** (10 mg, 0.015 mmol) with **55** (18 mg, 0.045 mmol) was carried out by using $[Pd(MeCN)_2Cl_2]$ (1.2 mg, 0.0045 mmol) in 4:1 MeCN–THF (1.5 mL) in the same manner as described for the preparation of **56** from **51**. Purification by preparative TLC (hexane–EtOAc, 1:1) gave recovered **53** (4.4 mg, 26%) and **59** as a yellow oil; yield: 4.9 mg (52%); $[\alpha]_D^{21}$ +111.0 (*c* 0.20, $CHCl_3$).

FTIR (film): 3370, 2926, 1715, 1519, 1454, 1248, 1101 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (dd, *J* = 9.7, 5.4 Hz, 1 H), 6.52 (dd, *J* = 11.0, 15.1 Hz, 1 H), 6.06 (d, *J* = 9.7 Hz, 1 H), 5.95–5.80 (m, 4 H), 5.63 (dd, *J* = 15.1, 6.4 Hz, 1 H), 5.35–5.20 (m, 3 H), 5.20 (d, *J* = 10.3 Hz, 1 H), 5.07–5.02 (br, 1 H), 4.55 (d, *J* = 4.8 Hz, 2 H), 4.49–4.40 (br s, 1 H), 3.95–3.80 (br s, 1 H), 3.78–3.70 (br, 1 H), 3.38–3.00 (m, 3 H), 2.50–2.38 (m, 2 H), 1.92–1.40 (m, 12 H), 1.33–1.00 (m, 4 H), 0.95 (t, *J* = 7.4 Hz, 12 H), 0.61 (q, *J* = 7.4 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 158.7, 152.6, 139.5, 137.5, 136.5, 134.6, 128.2, 127.2, 126.3, 121.1, 117.3, 82.3, 77.7, 77.5, 71.1, 66.3, 42.2, 40.7, 38.3, 38.1, 37.5, 34.4, 34.1, 27.0, 22.8, 11.3, 7.5, 6.5.

HRMS (FAB): *m/z* [M$^+$] calcd for $C_{35}H_{57}NO_7Si$: 631.3904; found: 631.3876.

Allyl {(3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-3-{(*E*)-2-[(2*S*,3*S*)-3-ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-6-{[*tert*-butyl(dimethyl)silyl]oxy}-4-hydroxy-3-[(triethylsilyl)oxy]deca-7,9-dien-1-yl}carbamate (60)

TBDMSOTf (54 μL, 0.24 mmol) was added to a soln of **56** (100 mg, 0.16 mmol) and 2,6-lutidine (37 μL, 0.32 mmol) in CH_2Cl_2 (8.0 mL) at –78 °C, and the mixture was stirred at –78 °C for 40 min. The reaction was then quenched with sat. aq $NaHCO_3$ (10 mL), and the mixture was extracted with EtOAc. The extracts were washed with brine, dried, and concentrated. Purification of the residue by preparative TLC (CH_2Cl_2–EtOAc, 15:1) gave **60** as a yellow oil; yield: 113 mg (95%); $[\alpha]_D^{21}$ +57.1 (*c* 0.35, $CHCl_3$).

FTIR (film): 3450 1725, 1520, 1463, 1382, 1251, 1079 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.93 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.22 (t, *J* = 11.7 Hz, 1 H), 6.05 (d, *J* = 9.8 Hz, 1 H), 6.02 (t, *J* = 11.7 Hz, 1 H), 5.95–5.87 (m, 2 H), 5.78 (dd, *J* = 15.8, 5.0 Hz, 1 H), 5.44 (t, *J* = 9.8 Hz, 1 H), 5.36 (t, *J* = 9.8 Hz, 1 H), 5.28 (d, *J* = 17.1 Hz, 1 H), 5.18 (d, *J* = 10.3 Hz, 1 H), 5.20–5.17 (m, 1 H), 5.01 (t, *J* = 5.0 Hz, 1 H), 4.97–4.88 (br, 1 H), 4.62–4.49 (br, 2 H), 3.83 (d, *J* = 10.7 Hz, 1 H), 3.38 (s, 1 H), 3.31–3.29 (m, 2 H), 2.43–2.38(m, 2 H), 1.95–1.85 (m, 2 H), 1.72–1.62 (m, 7 H), 1.60–1.41 (m, 2 H), 1.31–1.02 (m, 5 H), 0.97–0.89 (m, 12 H), 0.87 (s, 9 H), 0.61 (q, *J* = 7.7 Hz, 6 H), 0.06 (s, 3 H), 0.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 156.2, 149.6, 140.1, 136.1, 133.4, 133.1, 125.5, 123.1, 120.9, 120.8, 117.2, 80.1, 79.0, 73.4, 67.5, 65.3, 39.4, 38.5, 36.5, 36.4, 36.0, 33.1, 33.0, 25.9, 25.8, 25.7, 21.6, 17.9, 11.0, 7.1, 6.8, –4.4, –5.2.

HRMS (FAB): *m/z* [(M +Na)$^+$] calcd for $C_{41}H_{71}NO_7Si_2Na$: 768.4667; found: 768.4669.

Allyl {(3*R*,4*R*,6*R*,7*Z*,9*Z*)-4-{[Bis(allyloxy)phosphoryl]oxy}-6-{[*tert*-butyl(dimethyl)silyl]oxy}-10-cyclohexyl-3-{(*E*)-2-[(2*R*,3*R*)-3-ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-3-[(triethylsilyl)oxy]deca-7,9-dien-1-yl}carbamate (61)

$(CH_2{=}CHO)_2PN(i\text{-}Pr)$ (0.26 mL, 1.04 mmol) was added to an ice-cooled soln of **60** (100 mg, 0.13 mmol) and tetrazole (140 mg, 2.08 mmol) in CH_2Cl_2 (6.5 mL), and the mixture was stirred at r.t. for 1 h. 30% H_2O_2 (0.21 mL) was added at 0 °C, and the mixture was stirred at 0 °C for 2 h. The reaction was quenched with sat. aq $Na_2S_2O_3$ (10 mL), and the mixture was extracted with EtOAc. The extracts were washed with brine, dried, concentrated, and purified by preparative TLC (hexane–EtOAc, 1:1) to give **61** (111 mg, 94%) as a colorless oil: $[\alpha]_D^{21}$ +58.3 (*C* 0.40, $CHCl_3$).

FTIR (film): 3336, 1724, 1525, 1457, 1252, 1084, 1018 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.93 (dd, *J* = 9.8, 5.4 Hz, 1 H), 6.18 (t, *J* = 11.2 Hz, 1 H), 6.09 (t, *J* = 11.2 Hz, 1 H), 6.04 (d, *J* = 9.8 Hz, 1 H), 5.98–5.89 (m, 5 H), 5.76 (dd, *J* = 15.9, 5.6 Hz, 1 H), 5.39–5.17 (m, 8 H), 5.02–4.95 (br s, 1 H), 4.91 (t, *J* = 9.5 Hz, 1 H), 4.62 (t, *J* = 7.3 Hz, 1 H), 4.53 (m, 6 H), 3.45–3.24 (br, 2 H), 2.39–2.27 (m, 2 H), 2.12–1.80 (m, 2 H), 1.69–1.46 (m, 10 H), 1.38–1.08 (m, 4 H), 0.99–0.90 (m, 12 H), 0.87 (s, 9 H), 0.68 (q, *J* = 7.4 Hz, 6 H), 0.10 (s, 3 H), 0.03 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 162.5, 158.8, 148.5, 141.8, 135.4, 135.0, 133.8, 133.1, 127.2, 123.5, 123.0, 122.2, 121.2, 118.0, 117.7, 116.8, 80.1, 79.6, 78.3, 77.6, 68.3, 65.8, 65.3, 40.8, 39.4, 37.1, 36.8, 36.7, 33.4, 30.0, 26.5, 26.4, 26.2, 21.8, 18.4, 11.0, 7.7, 7.2, –3.7, –4.0.

HRMS (FAB): *m/z* [(M +Na)$^+$] calcd for $C_{47}H_{80}NO_{10}PSi_2Na$: 928.4956; found: 928.4957.

Desilylation of 61

H_2O (0.8 mL), 47% HF (1.6 mL), and pyridine (0.4 mL) were added to an ice-cooled soln of phosphate **61** (101 mg, 0.11 mmol) in MeCN (8.0 mL), and the mixture was stirred at r.t. for 2 h. The mixture was then cooled to 0 °C, basified with sat. aq $NaHCO_3$ (10 mL), and extracted with EtOAc. The extracts were washed with sat. aq $NaHCO_3$ and brine, dried, concentrated, and purified by preparative TLC (EtOAc) to give diol **62** (22 mg) and the partially desilylated 11-hydroxy derivative (50 mg). The latter was dissolved in MeCN (4.9 mL) and desilylated again by treatment with H_2O (0.49 mL), 47% HF (0.98 mL), and pyridine (0.25 mL) at r.t. for 2 h. After work-up, preparative TLC (EtOAc) gave diol **62** (16 mg) and the 11-monohydroxy derivative (10 mg). As a result, diol **62** was obtained as a colorless oil; total yield: 38 mg (51%). Note that exposure of **61** to the desilylation conditions for 3 hours caused appreciable decomposition of **62**. The optimal procedure for obtaining **62** involves a 2-hour reaction of **61**, and a further 2-hour reaction of the 11-mono hydroxy deriviative.

11-Mono Hydroxy Derivative
Colorless oil; $[\alpha]_D^{21}$ +45.5 (*C* 1.5, MeOH).

FTIR (film): 3415, 1725, 1525, 1455, 1248, 1019 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.92 (dd, *J* = 9.7, 5.3 Hz, 1 H), 6.26 (t, *J* = 11.2 Hz, 1 H), 6.14–5.75 (m, 7 H), 5.52–5.25 (m, 7 H), 5.19 (d, *J* = 10.3 Hz, 1 H), 5.02 (t, *J* = 4.4 Hz, 1 H), 4.94–4.82 (br s, 1 H), 4.82–4.70 (br s, 1 H), 4.70–4.50 (m, 7 H), 3.95–3.78 (br s, 1 H), 3.40–3.11 (m, 2 H), 2.51–2.35 (m, 2 H), 2.18–2.00 (m, 1 H), 2.00–1.38 (m, 10 H), 1.38–0.85 (m, 17 H), 0.68 (q, *J* = 7.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 156.0, 149.6, 139.9, 134.2, 132.8, 132.1, 132.1, 132.0, 126.2, 123.9, 121.2, 121.0, 118.9, 118.8, 117.4, 80.0, 79.9, 79.8, 68.8, 68.7, 65.3, 62.6, 39.4, 38.2, 37.5, 36.4, 33.1, 33.0, 25.9, 21.6, 11.0, 7.1, 6.7.

HRMS (FAB): *m/z* [M^+] calcd for $C_{41}H_{66}NO_{10}PSi$: 791.4194; found: 791.4182.

Allyl {(3*R*,4*R*,6*R*,7*Z*,9*Z*)-4-{[Bis(allyloxy)phosphoryl]oxy}-10-cyclohexyl-3-{(*E*)-2-[(2*S*,3*S*)-3-ethyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl]vinyl}-3,6-dihydroxydeca-7,9-dien-1-yl}carbamate (62)
Colorless oil; $[\alpha]_D^{21}$ +30.1 (*C* 0.25, MeOH).

FTIR (film): 3372, 1725, 1522, 1449, 1254, 1022 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.91 (dd, *J* = 9.8, 5.9 Hz, 1 H), 6.30 (t, *J* = 11.7 Hz, 1 H), 6.10–5.83 (m, 8 H), 5.44–5.28 (m, 8 H), 5.23 (dd, *J* = 14.4, 1.4 Hz, 1 H), 5.12–5.00 (br s, 1 H), 4.79 (t, *J* = 8.8 Hz, 1 H), 4.62–4.50 (m, 6 H), 4.48 (t, *J* = 9.8 Hz, 1 H), 4.12–3.90 (br s, 1 H), 3.42–3.08 (m, 2 H), 2.51–2.38 (m, 2 H), 1.94–1.42 (m, 10 H), 1.34–1.03 (m, 6 H), 0.94 (t, *J* = 7.8 Hz, 3 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 166.6, 158.9, 152.9, 141.0, 135.6, 135.0, 134.8, 134.1, 134.1, 134.0, 127.8, 122.8, 121.2, 119.1, 117.6, 83.8, 83.7, 82.1, 76.6, 70.1, 66.5, 64.7, 40.7, 40.2, 38.2, 37.9, 37.4, 34.5, 27.4, 27.1, 23.0, 11.5.

HRMS (FAB): *m/z*: [(M + Na)$^+$] calcd for $C_{35}H_{52}NO_{10}PNa$: 700.3227; found: 700.3220.

(+)-Phoslactomycin B (2)
To an ice-cooled soln of **62** (10 mg, 0.015 mmol) in CH_2Cl_2 (1.5 mL) were added H_2O (13 μL), [$PdCl_2(PPh_3)_2$] (0.5 mg, 0.75 mmol), and Bu_3SnH (15 μL, 0.057 mmol), and the mixture was stirred at 0 °C for 1.5 h. The mixture was concentrated and the residue was subjected to preparative TLC (MeCN–H_2O, 5:2) followed by reverse-phase HPLC (J'sphere ODSM-80, MeCN–H_2O, 1:2) to give **2** as a colorless powder; yield: 5.6 mg (73%); $[\alpha]_D^{22}$ +82.0 (*c* 0.2, MeOH) [Lit.[2c] $[\alpha]_D^{21}$ +81 (*c* 1.0, MeOH)].

FTIR (film): 3209, 1724, 1642, 1450, 1384, 1246, 1105 cm^{-1}.

^1H NMR (500 MHz, CD_3OD): δ = 7.08 (dd, *J* = 9.6, 5.0, 1 H), 6.14–6.05 (m, 1 H), 6.23 (d, *J* = 8.0 Hz, 2 H), 6.01 (dd, *J* = 9.6, 1.2 Hz, 1 H), 5.91 (d, *J* = 16.0 Hz, 1 H), 5.41 (t, *J* = 8.0 Hz, 1 H), 5.31 (t, *J* = 8.0 Hz, 1 H), 5.09 (t, *J* = 4.8 Hz, 1 H), 4.98 (t, *J* = 9.1 Hz, 1 H), 4.32–4.20 (br, 1 H), 3.15–2.98 (br, 2 H), 2.60–2.40 (m, 2 H), 2.35–2.18(m, 1 H), 1.78–1.00 (m, 17 H), 0.95 (t, J = 7.5 Hz, 3 H).

^{13}C NMR (100 Hz, CD_3OD): δ = 166.4, 152.7, 140.2, 137.4, 134.6, 127.5, 124.5, 123.0, 121.0, 82.3, 78.2, 77.9, 64.6, 40.6, 37.6, 37.1, 34.4, 34.3, 27.1, 26.9, 22.7, 11.4.

HRMS (FAB): *m/z* [(M + Na)$^+$] calcd for $C_{25}H_{40}NO_8PNa$: 536.2389; found: 536.2380.

These spectral data exhibited good agreement with those reported for the natural specimen.[2c]

Tributyl[(*Z*)-2-cyclohexylvinyl]stannane (55)
A 1.58 M soln of BuLi in hexane (5.9 mL, 9.25 mmol) was added to a stirred soln of ethynylcyclohexane (1.0 g, 9.25 mmol) in THF (46 mL) at –78 °C, and stirring was maintained at –78 °C for 30 min. Bu_3SnCl (2.26 mL, 8.33 mmol) was added, and the mixture was stirred at –78 °C for 5 h. The mixture was then diluted with hexane, washed with H_2O, dried, and concentrated to give tributyl(2-cyclohexylethynyl)stannane (3.90 g) as a colorless oil that was used for the next reaction without purification.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.48–2.39 (m, 1 H), 1.82–1.39 (m, 13 H), 1.39–1.22 (m, 9 H), 0.98–0.84 (m, 15 H).

A soln of crude tributyl(2-cyclohexylethynyl)stannane (1.42 g) in THF (7.0 mL) was added to a soln of [Cp_2ZrHCl] (1.38 g, 5.35 mmol) in THF (10.9 mL), and the mixture was stirred at r.t. for 7 h. The mixture was then diluted with hexane and stirred at r.t. for 20 min. The resulting precipitates were filtered off and the filtrate was concentrated. Purification of the residue by column chromatography [silica gel (30 g), hexane] gave **55** as a colorless oil; yield: 977 mg (69% for two steps)

FTIR (film): 1595, 1452 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.32 (dd, *J* = 12.2, 9.3 Hz, 1 H), 5.66 (d, *J* = 12.2, 7.3 Hz, 1 H), 1.80–1.39 (m, 11 H), 1.39–1.08 (m, 12 H), 1.00–0.97 (m, 15 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9, 125.3, 46.9, 33.3, 29.2, 27.4, 25.9, 13.7, 10.4.

HRMS (EI): *m/z* calcd for $C_{20}H_{40}Sn$: 400.2152; found: 400.2166.

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