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Synthetic Studies on Macrolactin A: Construction of C4−C24 Fragment

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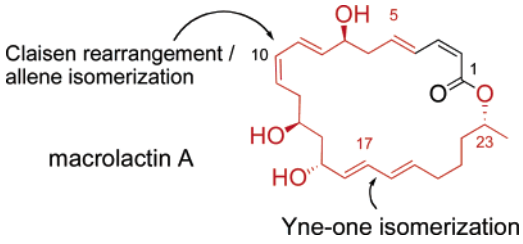

The preparation of the C4−C24 fragment of the macrolactin A is described. The adopted synthetic strategy involves two isomerizations to selectively construct the (8*E*,10*Z*) and (16*E*,*18E*) dienes, using a sequential Claisen rearrangement/allene isomerization and a Ph_3P-catalyzed isomerization of an yne-one, respectively.

Introduction

The macrolactin family was discovered in 1989 by Fenical et al. from a taxonomically undefined deep sea marine bacterium.[1a] More recently, macrolactins have been re-isolated from other biological sources.[1b−h] The parent aglycone, macrolactin A **1**, is a 24-membered polyene macrolide possessing three stereodefined (*Z*,*E*-, *E*,*Z*-, and *E*,*E*-) 1,3-dienes systems and four chiral hydroxy groups. Macrolactin A displays a broad spectrum of biological activity: a strong cytotoxicity on B16-F10 murine melanoma cell (IC_{50} = 3.5 μg/mL) and antiviral activity against *Herpes simplex* types I and II and HIV virus replication.[1] Owing to its original macrocyclic structure, potent biological activities, and some unreliability in the cell culture, macrolactin A appeared to be an attractive target for total synthesis. Indeed, starting from the seminal work initiated by Rychnovsky establishing the relative and absolute stereochemistry of the chiral centers,[2] considerable synthetic efforts have been undertaken culminating in three total syntheses by Smith, Carreira, and Marino,[3−5] a great number of different synthetic approaches,[6−13] and the synthesis of a simplified analogue.[14] In these works, palladium-catalyzed Stille cross-coupling and

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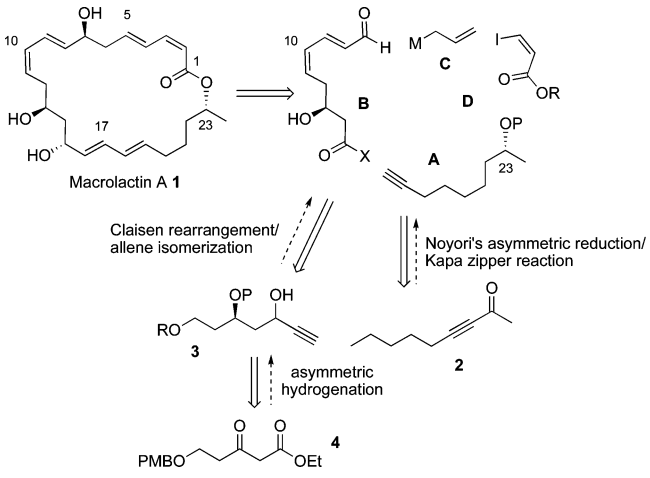
SCHEME 1. Retrosynthetic Analysis of Macrolactin A

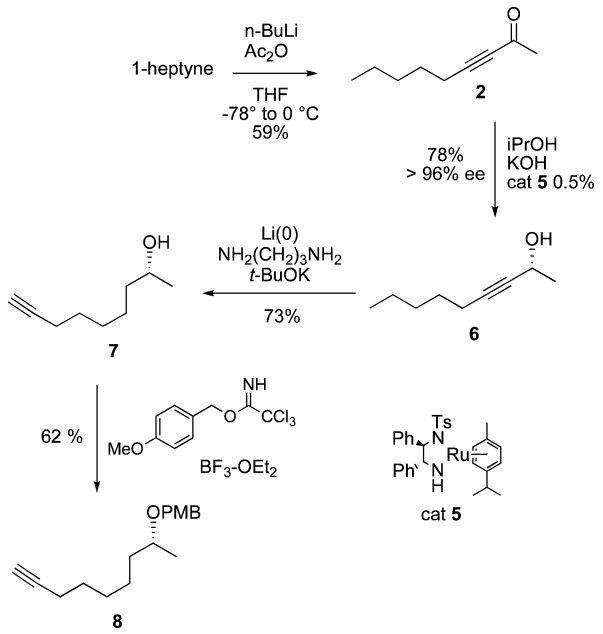


Wittig-type reactions have been mainly used to stereoselectively construct the 1,3 diene subunits. In our retrosynthetic approach, we planned to construct these 1,3 dienes using different strategies: (i) a sequential Claisen rearrangement/allene isomerization to construct the C8−C11 (*E*,*Z*) diene,[15−17] (ii) a Ph_3P-catalyzed isomerization of an ynone precursor for building the C16−C19 (*E*,*E*) diene,[18−20] and (iii) an intramolecular Heck reaction to obtain C2−C5 (*Z*,*E*) conjugated diene. In this paper, we would like to disclose our route to the C4−C24 fragment of macrolactin A.

Results and Discussion

Our convergent synthetic strategy is outlined in Scheme 1. In the light of constructing the 1,3 dienes subunits (vide supra), macrolactin A was ultimately divided in four distinct fragments denoted **A**, **B**, **C**, and **D**. Fragment **A** could be obtained by an asymmetric Noyori's hydrogen transfer[21] on alkynone **2** followed by an alkyne zipper reaction.[22] The chiral alcohol in fragment **B** could be synthesized by the asymmetric Noyori's hydrogenation of β-keto ester **4**, and the (*E*,*Z*) 1,3 diene could be then obtained by a sequential Claisen rearrangement/allene isomerization starting from propargylic alcohol **3**.[15] Fragment **D** has been previously described,[23] and **C** is a precursor for an asymmetric allylation.[24] In a second step, these molecular fragments could then be joined by (i) an asymmetric allylation (**B** + **C**), (ii) the alkynylation of an aldehyde (**B** + **A**), (iii) an esterification or a macrolactonisation (**A** + **D**), and (iv) an (inter- or intramolecular) Heck reaction (**D** + **C**).

SCHEME 2. Fragment A Synthesis of Macrolactin A



Synthesis of C16−C24 Fragment A. Our route to C16−C24 fragment **A** starts from 1-heptyne (Scheme 2). After treatment of the lithium salt of heptyne with acetic anhydride, the corresponding ketone **2** was then asymmetrically reduced to the propargylic alcohol **6** under Noyori's hydrogen transfer conditions.[21]

At this stage, the enantiopurity of **6** was checked using proton-decoupled carbon-13 (^{13}C-{^1H}) NMR spectroscopy in polypeptide chiral liquid crystals (CLCs).[25a] This original analytical strategy proved to be very efficient for analyzing a large range of chiral compounds, including alkyne compounds.[25b−d] As illustration, the ^{13}C-{^1H} signals of C-3 and C-4 atoms for (±)-**6** and (*R*)-**6** dissolved in the PBLG/chloroform system are shown in Figure 1a and b. For this compound, the ^{13}C chemical shift anisotropy (CSA) of sp-hybridized carbons causes a sufficiently large ^{13}C chemical shift difference (at 100.6 MHz) to discriminate the NMR signals of each enantiomer (Ds ≈ 0.14 ppm (≈ 14 Hz).[25a] This enables a direct and easy determination of the ee value of enantioenriched **6** by peak integration or deconvo-

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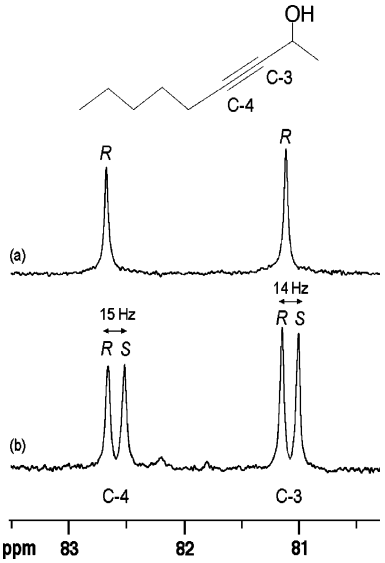


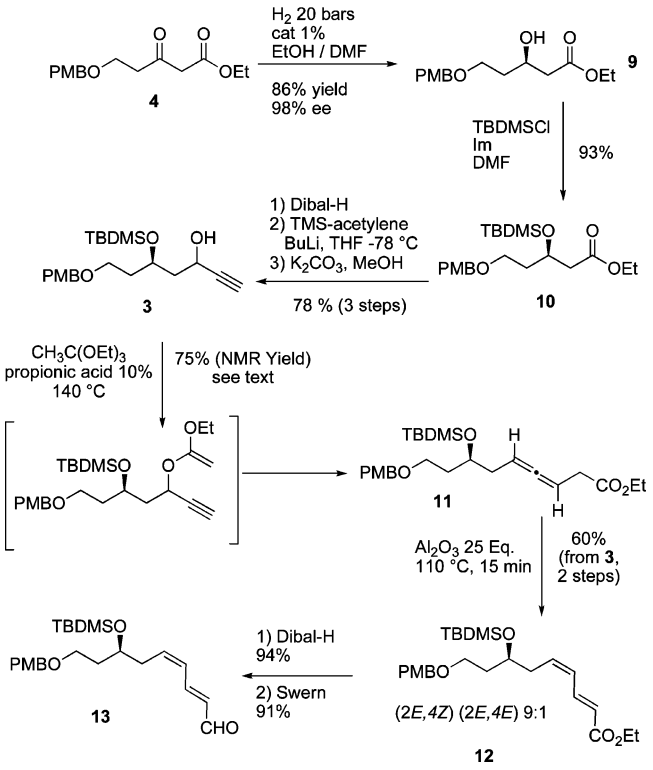
FIGURE 1. ^{13}C-{^{1}H} NMR signals (100.6 MHz) for the acetylenic carbons (C-3 and C-4) of (±)-**6** and (*R*)-**6** both dissolved in the chiral liquid-crystalline phase (PBLG/chloroform) at 310 K; 1700 scans were recorded and added prior to Fourier transformation.

lution ^{13}C-{^{1}H} resonances. The ee experimentally measured is over 95 ± 3% (averaged value on a series of measurements). The (*R*) absolute configuration was confirmed by comparison of the rotation with the same compound previously obtained in 68% ee.[26]

Propargylic alcohol **6** was then submitted to an alkyne zipper reaction[22b] to give alcohol **7** in 73% yield. Note here that the alkyne zipper reaction does not modify the enantiomeric purity of chiral propargyl alcohols.[25c] Construction of fragment **A** was finally achieved by the protection of the alcohol as a PMB ether, in the presence of *p*-methoxybenzyltrichloroacetimidate, in 62% yield. Fragment **A** (C16−C24) **8** was thus obtained in only four steps, in 25% overall yield and an ee >95%.

Synthesis of C7−C15 Fragment B. As described in Scheme 3, our synthesis starts from known β-keto ester **4**,[27] which was first subjected to an asymmetric Noyori hydrogenation[28] to give alcohol **9** in 86% yield and 98% ee (HPLC). The alcohol was next protected as TMBDS ether **10** in 93% yield. Reduction of the ester to the aldehyde, followed by the alkynylation with TMS-acetylene and further deprotection of the TMS group led to compound **3** (in a 4:3 dr) in 78% overall yield. The key Johnson-Claisen/allene isomerization was next investigated.[15] After some experimentation, we conclude that, in our hands, the best conditions to obtain allene **11** are the following: 140 °C in the presence of 10% of propionic acid during 8 h. Note that every 2 h, ethanol is removed in vacuo and ethyl orthoacetate/propionic acid is re-added. Allene **11** was found to be quite unstable under purification and/or storage. Consequently, after evaporation of the reaction mixture, allene **11** was found to be pure enough to be engaged in the next step without any further purification (a 75% yield could be estimated by NMR). The allene isomerization also required some optimization: the source (Brockmann I, 150 mesh from Aldrich) and

SCHEME 3. Fragment B Synthesis of Macrolactin A



the amount (25 equiv) of alumina (dried 2 h at 200 °C under vacuum) proved to be essential in this reaction. Indeed after 15 min, at 110 °C, the conjugated diene **12** could be isolated in 80% yield and as a 9:1 (2*E*,4*Z*)/(2*E*,4*E*) mixture.[29] The two-step conversion of the ester to the corresponding aldehyde ultimately led to the C7−C15 fragment B **13** (9 steps, 32% overall yield from **4**).

At this stage, due to tactics reasons, the introduction of fragment **C** (an asymmetric allylation on the C7 aldehyde) was first examined.

Introduction of Fragment C: Asymmetric Allylation on a Conjugated Diene. The catalytic enantioselective addition of allyl-metal reagents to aldehydes has emerged as a key transformation in the total synthesis of numerous natural products.[24] However, such asymmetric allylations on unsaturated aldehydes have been scarcely reported so far. Consequently, the asymmetric allylation was first investigated on a model reaction in the presence of sorbaldehyde (Table 1). The original Keck's conditions[30] were rather deceptive because they lead to the allylated product **14** in low conversion and relatively poor ee (Table 1, entry 1).

By increasing the amount of catalyst to 30%, the enantioselectivity could be raised up to 68% but the conversion was still very low (Table 1, entry 2). The use of additives in this procedure has been reported by Yu[31] but was unsuccessful when applied in our case (Table 1, entry 3). We next moved to the procedure described by Yamamoto[32] in the presence of silver salts and binap. Under these conditions, the conversion is still low, but the enantioselectivity is 83% ee (Table 1, entry 4).

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(29) At this stage the (2 *E*,4*E*) minor isomer could not be separated from the (2 *E*,4*Z*) isomer. This separation was only possible at the aldehyde **13** stage.

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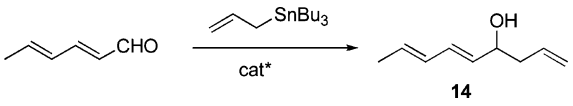
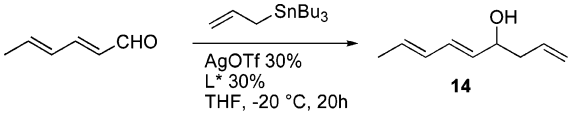
TABLE 1. Asymmetric Allylation of Sorbaldehyde



	catalyst	additive	*T* (°C)	time (h)	yield % (conv %)	ee %
1	Ti(O*i*Pr)$_4$ 10% (*S*)-Binol 10%	4 Å MS (17)	−20	70	-	46 (*S*)
2	Ti(O*i*Pr)$_4$ 30% (*S*)-Binol 30%	4 Å MS (25)	−20	73	16	68 (*S*)
3	Ti(O*i*Pr)$_4$ 10% (*S*)-Binol 10%	4 Å MS B(OMe)$_3$ 50%	0 (20)	20	-	28 (*S*)
4	AgOTf 5% (*R*)-Binap 5%	−20 (50)	23	19	83 (*R*)	
5	**AgOTf 30% (*S*)-Binap 30%**		**−20**	**4**	**72**	**87 (*S*)**
6	AgF 20% (*S*)-Tol-Binap 5%		−20	3	43	63 (*S*)
7	$InCl_3$ 20% (*S*)-Binol 22%	4 Å MS	−78	16	69	44 (*S*)

TABLE 2. Optimization of the Asymmetric Allylation of Sorbaldehyde



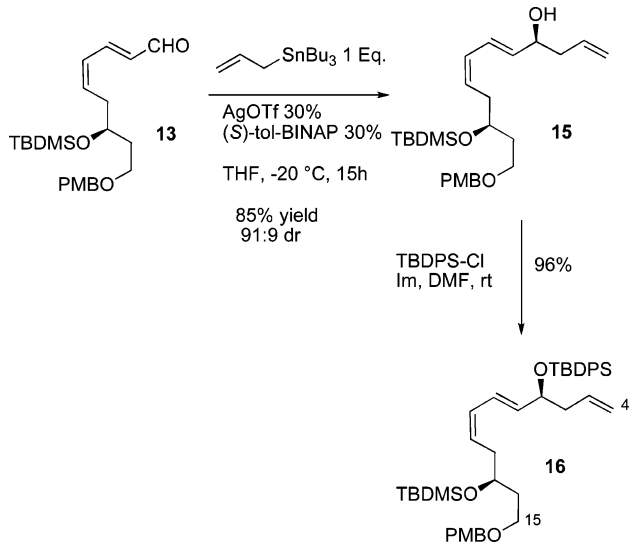
	ligand	yield	ee %
1	(*S*)-binap	72	87 (*S*)
2	(*R*)-difluorphos	(17)	63 (*R*)
3	(*R*)-SEGPHOS	64	67 (*R*)
4	**(*S*)-Tol-binap**	**76**	**89 (*S*)**

Increasing the amount of catalyst to 30%, compound **14** was isolated in an interesting 72% yield and 87% ee (Table 1, entry 5). Other procedures in the presence of silver or indium salts led to rather disappointing results (Table 1, entries 6 and 7).[33−34] Finally, we tried to further improve the enantioselectivity by screening other phosphorus ligands in this reaction (Table 2). As a consequence, among the several ligands tested, (*S*)-Tol-binap was the most efficient, leading to **14** in slightly better yield (76%) and higher enantioselectivity (89% ee).

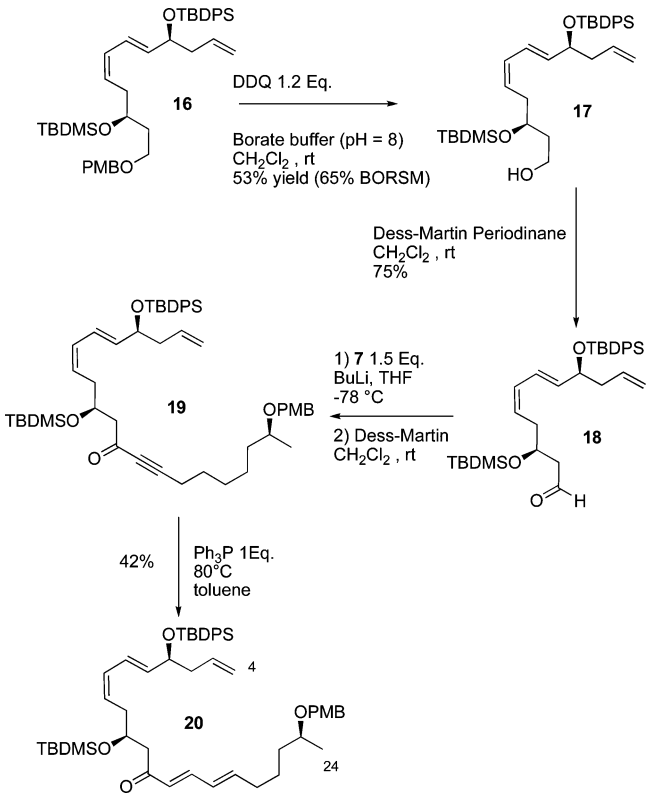
Starting from this model reaction study, the asymmetric allylation on aldehyde **13** was next tested (Scheme 4). Gratifyingly, under optimized reaction conditions (1 g scale, 15 h, −20 °C), the homoallylic compound **15** was obtained in 85% yield and a 91:9 dr.[35] The homoallylic alcohol was then transformed into the TBDPS ether **16** in 96% yield.

Synthesis of C4−C24 Fragment (A-B-C). Having secured the C4−C15 (**B-C** fragment) skeleton of macrolactin A, the introduction of fragment **A** was next undertaken. The PMB ether was first removed in the presence of DDQ in buffered dichloromethane in 53% yield (65% based on recovered starting material). A Dess−Martin periodinane-mediated oxidation of the primary alcohol **17** was then carried out in 75% yield. Introduction of the lithium acetylide of compound **7** (fragment **A**) led to the propargylic alcohol, which was further oxidized to the corresponding propargylic ketone **19** in 94% yield (over 2 steps). The yne-one isomerization of compound **19** was finally carried out in the presence of triphenylphosphine at 80 °C[18] to give the expected C4−C24 fragment **20** of macrolactin A in a nonoptimized 42% yield and as a single (16*E*,18*E*) isomer (Scheme 5).

SCHEME 4. C4−C15 Fragment of Macrolactin A



SCHEME 5. C4−C24 Fragment of Macrolactin A



Conclusion

In summary, a convergent and efficient synthesis of the C4−C24 fragment of macrolactin A is described. The synthesis was

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(35) At this stage of the synthesis, the minor isomer could not be separated from major isomer **15**.

completed in 16 steps from β-keto ester **4**. This synthesis approach was highlighted by the stereoselective syntheses of the C9−C11 (*E*,*Z*) and C16−C19 (*E*,*E*) dienes using the isomerizations of an allene and an yne-one, respectively. C7, C13, and C23 chiral centers have been obtained using a Yamamoto asymmetric allylation, a Noyori aymmetric hydrogenation, and a Noyori asymmetric hydrogen transfer respectively.

Experimental Section

(*R*)-1-Methoxy-4-((non-8-yn-2-yloxy)methyl)benzene (*R*)-8. To a solution of the alcohol **7** (130 mg, 0.91 mmol) and *p*-methoxybenzyltrichloroacetimidate (450 mg, 1.6 mmol) in cyclohexane (3 mL) and dichloromethane (1.5 mL) at 0 °C, was added $BF_3{\cdot}Et_2O$ (1 μL, 1 mol %). A white precipitate was formed. The suspension was warmed up to room temperature and stirred for 2 h until the reaction was complete (TLC). The white solid was filtrated on a pad of celite and washed with a 2:1 mixture of cyclohexane and dichloromethane. The filtrate was concentrated in vacuo, and the crude product was purified by flash chromatography to afford the desired protected alcohol **8** (148 mg, 62%). $[\alpha]_D = -13$ ($CHCl_3$, *c* 2, 28 °C); ee 96%. $R_f = 0.63$ (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 3292, 2933, 2858, 2118. NMR ^1H ($CDCl_3$, 300 MHz) δ ppm: 1.18 (d, $J = 6.1$ Hz, 3H),1.29−1.47 (m, 6H), 1.51 − 1.62 (m, 2H), 1.95 (t, $J = 2.6$ Hz, 1H), 2.19 (dd, $J = 2.6$ Hz, $J = 7$ Hz, 2H), 3.46−3.52 (m, 1H), 3.81 (s, 3H), 4.39 (d, $J = 11.4$ Hz, 2H), 4.51 (d, $J = 11.4$ Hz, 2H), 6.88 (d, $J = 8.7$ Hz, 2H), 7.28 (d, $J = 8.7$ Hz, 2H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: 18.5, 19.8, 25.2, 28.6, 29.0, 36.7, 55.4, 68.3, 70.1, 74.6, 84.9, 113.9, 129.3, 131.4, 159.2. MS (ESI) (*m*/*z*): 283.2 (100, $[MNa]^+$); 284.2 (3, $[MHNa]^+$). Anal. Calcd for $C_{15}H_{24}O_2$: C, 78.42, H, 9.29. Found: C, 78.21, H, 9.45.

(5*R*)-5-(*tert*-Butyldimethylsilyloxy)-7-(4-methoxybenzyloxy)-hept-1-yn-3-ol (3). (a) Ester Reduction. To a solution of ester **10**[27] (11.3 g, 28.5 mmol) in dry dichloromethane (200 mL), at −78 °C, was added dropwise diisobutylaluminium hydride (1 M in hexanes, 31.3 mL, 31.3 mmol). The solution was stirred at −78 °C for 1 h and warmed up to room temperature. It was then treated with saturated potassium and sodium tartrate (Rochelle salt) and stirred for 14 h. The aqueous layer was extracted with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude aldehyde was used without further purification. $[\alpha]_D = +7$ (CH_2Cl_2, *c* 1.04, 25 °C). $R_f = 0.64$ (heptane/AcOEt 6:4). IR-FT (neat) cm^{-1}: 2954, 2929, 2895, 2856, 2725, 1725 (C═O). NMR ^1H ($CDCl_3$, 500 MHz) δ ppm: 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.79−1.90 (m, 2H), 2.53 (ddd, $J = 2.9$ Hz, $J = 5.9$ Hz, $J = 15.7$ Hz, 1H), 2.59 (ddd, $J = 2$ Hz, $J = 5.2$ Hz, $J = 15.7$ Hz, 1H), 3.52 (t, $J = 5.9$ Hz, 2H), 3.81 (s, 3H), 4.34−4.40 (m, 1H), 4.39 (d, $J = 11.7$ Hz, 1H), 4.44 (d, $J = 11.7$ Hz, 1H), 6.89 (d, $J = 8.5$ Hz, 2H), 7.26 (d, $J = 8.5$ Hz, 2H), 9.80 (t, $J = 2.6$ Hz, 1H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.5, 18.1, 25.8, 37.8, 51.2, 55.4, 65.8, 66.2, 72.8, 113.9, 129.4, 130.5, 159.3, 202.3. Data in accordance with previously reported results.[27]

(b) TMS-Acetylene Addition. To a solution of trimethylsilylacetylene (5 mL, 34 mmol) in THF (200 mL), at −78 °C, was added dropwise *n*-butyllithium (1.6 M in hexanes, 27.2 mL, 34 mmol). After 1 h of stirring, a solution of the previously obtained aldehyde (9.9 g, 28 mmol) in THF was added via cannula. The resulting mixture was slowly warmed up to room temperature and stirred for another 16 h. It was then quenched with saturated NH_4Cl. The aqueous layer was extracted with Et_2O (600 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting oil was used without further purification (12.3 g). The desired product came as a 3:4 mixture of two diastereoisomers. In order to carry out the analyses, part of the crude product was purified by flash chromatography: $R_f = 0.65$ and 0.70 (heptane/AcOEt 6:4). IR-FT (neat) cm^{-1}: 3412, 2954, 2928, 2896, 2855, 2170 (C≡C). NMR ^1H ($CDCl_3$, 300 MHz) δ ppm: first diastereoisomer 0.10 (s, 3H), 0.14 (s, 3H), 0.18 (s, 9H), 0.89 (s, 9H), 1.80−1.98 (m, 4H), 3.18 (d, $J = 5.1$ Hz, 1H), 3.50 (t, $J = 6.3$ Hz, 2H), 3.81 (s, 3H), 4.21−4.29 (m, 1H), 4.40 (d, $J = 11.5$ Hz, 1H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.56−4.62 (m, 1H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H); second diastereosiomer 0.08 (s, 3H), 0.09 (s, 3H), 0.17 (s, 9H), 0.88 (s, 9H), 1.80−1.96 (m, 4H), 2.66 (d, $J = 4$ Hz, 1H), 3.51 (t, $J = 6.3$ Hz, 2H), 3.81 (s, 3H), 4.06−4.14 (m, 1H), 4.40 (d, $J = 11.5$ Hz, 1H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.50−4.56 (m, 1H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: first diastereisomer −4.4, 0.04, 18.1, 26.0, 37.0, 43.4, 55.4, 60.5, 66.3, 68.3, 72.8, 89.1, 106.8, 113.9, 129.4, 130.6, 159.3; second diastereosiomer −4.5, −4.3, 0.02, 18.1, 26.0, 37.7, 44.3, 55.4, 61.4, 66.3, 68.7, 72.8, 89.7, 106.7, 113.9, 129.4, 130.6, 159.3. MS (ESI) (*m*/*z*) 473.1 (100, $[MNa]^+$); 474.2 (80, $[MHNa]^+$). Anal. Calcd for $C_{24}H_{42}O_4Si_2$: C, 63.95, H, 9.39; found: C, 63.95, H 9.43.

(c) TMS Deprotection. To a solution of the TMS-protected alkyne (12.3 g, 27.2 mmol) in methanol (200 mL) at 0 °C was added K_2CO_3 (8.2 g, 59 mmol). The resulting suspension was warmed up to room temperature and stirred for 19 h. After quenching with saturated NH_4Cl, the aqueous layer was extracted with Et_2O. The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford the terminal alkyne as a 3:4 mixture of two diastereoisomers. (8.4 g, 78% over 3 steps). $R_f = 0.52$ and 0.54 (heptane/AcOEt 6:4). IR-FT (neat) cm^{-1}: 3406, 3307, 2952, 2928, 2884, 2855. NMR ^1H ($CDCl_3$, 300 MHz) δ ppm: first diastereoisomer 0.10 (s, 3H), 0.14 (s, 3H), 0.89 (s, 9H), 1.78−1.93 (m, 4H), 2.47 (d, $J = 2.4$ Hz, 1H), 3.35 (d, $J = 5.2$ Hz, 1H), 3.50 (t, $J = 6.4$ Hz, 2H), 3.82 (s, 3H), 4.21−4.29 (m, 1H), 4.40 (d, $J = 11.6$ Hz, 1H), 4.44 (d, $J = 11.6$ Hz, 1H), 4.57−4.62 (m, 1H), 6.89 (d, $J = 8.6$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H); second diastereoisomer 0.08 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 1.80−1.96 (m, 4H), 2.48 (d, $J = 2.2$ Hz, 1H); 2.82 (d, $J = 3.4$ Hz, 1H), 3.51 (t, $J = 6.4$ Hz, 2H), 3.81 (s, 3H), 4.06−4.14 (m, 1H), 4.40 (d, $J = 11.6$ Hz, 1H), 4.44 (d, $J = 11.6$ Hz, 1H), 4.50−4.56 (m, 1H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: first diastereoisomer −4.5, −4.4, 18.1, 26.0, 38.8, 43.0, 55.4, 59.8, 66.2, 68.3, 72.6, 72.8, 85.1, 113.9, 129.4, 130.5, 159.3; second diastereoisomer −4.6, −4.3, 18.1, 26.0, 37.6, 44.3, 55.4, 60.7, 66.2, 68.8, 72.8, 73.1, 85.0, 113.9, 129.4, 130.5, 159.3. MS (ESI) = (*m*/*z*) 401.2 (100, $[MNa]^+$); 402.2 (30, $[MHNa]^+$). HRMS (ESI) *m*/*z* $[MNa]^+$ calcd for $C_{21}H_{34}O_4SiNa$ 401.2124, found 401.2129.

(7*S*)-Ethyl 7-(*tert*-Butyldimethylsilyloxy)-9-(4-methoxybenzyloxy)nona-3,4-dienoate (11). To a solution of propargylic alcohol **3** (170 mg, 0.45 mmol) in triethyl orthoacetate (580 μL, 3 mmol) was added one drop of propionic acid. The solution was stirred at 110 °C for 7 h. Every 2 h the ethanol produced by the reaction was evaporated, and fresh triethyl orthoacetate (200 μL, 1 mmol) and propionic acid (one drop) were added. When the reaction was complete (TLC), the mixture was cooled down to room temperature and concentrated in vacuo. The desired allene (125 mg) was used without further purification. In order to carry out the analyses, part of the crude product was purified by flash chromatography on neutral alumina (heptane/AcOEt 95:5). $[\alpha]_D = +7$ (CH_2Cl_2, *c* 1.03, 23 °C). $R_f = 0.68$ (heptane/AcOEt 6:4). IR-FT (neat) cm^{-1}: 2952, 2928, 2854, 1969 (C═C═C), 1736 (C═O). NMR ^1H ($CDCl_3$, 300 MHz) δ ppm: 0.05 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.27 (t, $J = 7.1$ Hz, 3H), 1.69−1.86 (m, 2H), 2.11−2.27 (m, 2H), 2.99−3.03 (m, 2H), 3.51 (t, $J = 6.4$ Hz, 2H), 3.81 (s, 3H), 3.87−3.96 (m, 1H), 4.16 (q, $J = 7.2$ Hz, 2H), 4.39 (d, $J = 11.4$ Hz, 1H), 4.44 (d, $J = 11.4$ Hz, 1H), 5.14−5.25 (m, 2H), 6.89 (d, $J = 8.6$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.3, −4.6, 14.3, 18.2, 25.8, 35.0, 37.3, 37.3, 55.4, 60.9, 66.8, 69.1, 72.8, 83.7, 88.2, 113.9, 129.4, 130.8, 131.7, 159.3, 171.7.

MS (ESI) (*m*/*z*) 471.2 (100, $[MNa]^+$), 472.2 (30, $[MHNa]^+$). HRMS (ESI) *m*/*z* $[MNa]^+$ calcd for $C_{25}H_{40}O_5SiNa$ 471.2543, found 471.2527.

(*S*,2*E*,4*Z*)-Ethyl 7-(*tert*-Butyldimethylsilyloxy)-9-(4-methoxybenzyloxy)nona-2,4-dienoate (12). The weakly basic alumina (Brockmann I type, Aldrich, 710 mg, 7 mmol) was placed in a round-bottom flask connected to a vacuum pump and heated at 200 °C for 2 h to remove the water. It was then placed under argon atmosphere and a solution of the allene (125 mg, 0.28 mmol) in dry toluene (1.5 mL) was added. The resulting suspension was vigorously stirred at 100 °C until the reaction was complete. This was followed by FT-IR as the two products have different C═O vibration wavelengths (1737 vs 1713 cm^{-1}). The alumina was then filtered and washed with dichloromethane. The filtrate was concentrated in vacuo, and the crude product was purified by flash chromatography to afford the desired diene as a 9:1 mixture of the 2*E*,4*Z* and 2*E*,4*E* isomers (99 mg, 60% over 2 steps). $[\alpha]_D = +7$ (CH_2Cl_2, *c* 1.03, 23 °C). $R_f = 0.68$ (heptane/AcOEt 6:4). IR-FT (neat) cm^{-1}: 2952, 2928, 2855, 2358, 1714 (C═O). NMR ^1H (C_6D_6, 500 MHz) δ ppm: 0.04 (s, 3H), 0.05 (s, 3H), 0.95 (s, 9H), 0.99 (t, $J = 7.1$ Hz, 3H), 1.6 (t, $J = 6.1$ Hz, 1H), 2.28 (dd, $J = 6.1$ Hz, $J = 7$ Hz, 2H), 3.31 (s, 3H), 3.34 (dt, $J = 5.7$ Hz, $J = 9.2$ Hz, 1H), 3.43 (dt, $J = 6.5$ Hz, $J = 9.2$ Hz, 1H),; 3.88 (quint, $J = 5.8$ Hz, 1H), 4.05 (q, $J = 7.1$ Hz, 2H), 4.28 (d, $J = 11.5$ Hz, 1H), 4.34 (d, $J = 11.5$ Hz, 1H), 5.75 (dt, $J = 7.8$ Hz, $J = 10.7$ Hz, 1H), 5.94 (d, $J = 15.3$ Hz, 1H), 5.98 (t, $J = 11.3$ Hz, 1H), 6.82 (d, $J = 8.7$ Hz, 2H), 7.24 (d, $J = 8.7$ Hz, 2H), 7.87 (dd, $J = 11.6$ Hz, $J = 15.6$ Hz, 1H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm; −4.3, −4.5, 14.5, 18.2, 26.0, 36.5, 37.2, 55.4, 60.4, 66.7, 68.9, 72.8, 113.9, 121.9, 128.5, 129.5, 130.7, 137.2, 139.5, 159.3, 167.3. MS (ESI) (*m*/*z*) 471.2 (100, $[MNa]^+$), 472.2 (30, $[MHNa]^+$). Anal. Calcd for $C_{25}H_{40}O_5Si$: C, 66.92, H, 8.99. Found: C, 66.96, H, 8.88.

(*S*,2*E*,4*Z*)-7-(*tert*-Butyldimethylsilyloxy)-9-(4-methoxybenzyloxy)nona-2,4-dienal (13). (a) Reduction to the Alcohol. To a solution of ester **12** (50 mg, 0.11 mmol) in dry dichloromethane (1 mL), at −78 °C, was added dropwise DIBALH (1 M in hexanes, 210 mL, 0.21 mmol). The reaction was followed by TLC and was complete after 5 min. The mixture was quenched with saturated potassium and sodium tartrate and stirred for 30 min. The aqueous layer was extracted with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford the desired alcohol (42 mg, 95%). $[\alpha]_D = +20.5$ (CH_2Cl_2, *c* 1.51, 27 °C). $R_f = 0.33$ (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 3401 (OH), 2951, 2926, 2854. NMR ^1H ($CDCl_3$, 300 MHz) δ ppm: 0.06 (s, 3H), 0.07 (2 s, 3H), 0.89 (s, 9H), 1.44 (bs, 1H), 1.64−1.83 (m, 2H), 2.37 (ddd, $J = 1.2$ Hz, $J = 6.1$ Hz, $J = 7$ Hz, 2H), 3.52 (dd, $J = 6.2$ Hz, $J = 6.7$ Hz, 2H), 3.82 (s, 3H), 3.88−3.96 (m, 1H), 4.19 (d, $J = 5.6$ Hz, 2H), 4.39 (d, $J = 11.5$ Hz, 1H), 4.46 (d, $J = 11.5$ Hz, 1H), 5.51 (dt, $J = 7.8$ Hz, $J = 10.8$ Hz, 1H), 5.82 (dt, $J = 5.9$ Hz, $J = 15.1$ Hz, 1H), 6.09 (t, $J = 11$ Hz, 1H), 6.49 (ddd, $J = 1.2$ Hz, $J = 8.7$ Hz, $J = 15$. Hz, 2H), 6.89 (d, $J = 8.7$ Hz, 2H), 7.27 (d, $J = 8.7$ Hz, 2H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.3, −4.5, 18.2, 26.0, 36.1, 37.0, 55.4, 63.7, 66.9, 69.2, 72.7, 113.9, 127.0, 128.5, 129.4, 129.5, 130.7, 132.3, 159.2. MS (ESI) (*m*/*z*) 429.2 (100, $[MNa]^+$), 430.2 (30, $[MHNa]^+$). Anal. Calcd for $C_{23}H_{38}O_4Si$: C, 67.94, H, 9.42. Found: C, 67.57, H, 9.64.

(b) Alcohol Oxidation. To a solution of DMSO (23 μL, 0.3 mmol) in dichloromethane (1 mL), at −78 °C, was added dropwise oxalyl chloride (13 μL, 0.15 mmol). After 30 min of stirring, a solution of the alcohol (38 mg, 0,09 mmol) in dichloromethane (0.4 mL) was added via cannula. The resulting mixture was stirred for 1 h, and triethylamine (41 μL, 0.3 mmol) was added. The reaction was complete after 15 min (TLC). The mixture was quenched with saturated NH_4Cl. The aqueous layer was extracted with dichloromethane. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford the desired aldehyde (34 mg, 91%). $[\alpha]_D = +12$ (CH_2Cl_2, *c* 1.03, 25 °C). $R_f = 0.47$ (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 2928, 2854, 1681 (C═O). NMR ^1H ($CDCl_3$, 300 MHz) δ ppm: 0.06 (s, 3H), 0.07 (s, 3H), 0.88 (s, 9H), 1.75 (q, $J = 6.2$ Hz, 2H), 2.51 (t, $J = 7$ Hz, 2H), 3.52 (t, $J = 6.2$ Hz, 2H), 3.81 (s, 3H), 4.01 (quint., $J = 5.9$ Hz, 1H), 4.38 (d, $J = 11.4$ Hz, 1H), 4.46 (d, $J = 11.4$ Hz, 1H), 6.07 (dt, $J = 7.9$ Hz, $J = 10.9$ Hz, 1H), 6.14 (dd, $J = 7.9$ Hz, $J = 15.2$ Hz, 1H), 6.35 (t, $J = 11$ Hz, 1H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H), 7.38 (dd, $J = 11.5$ Hz, $J = 15.2$ Hz, 2H), 9.55 (d, $J = 8$ Hz, 1H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.6, −4.3, 18.2, 25.9, 36.7, 37.3, 55.4, 66.5, 68.9, 72.8, 113.9, 128.5, 129.4, 130.5, 132.2, 139.9, 147.0, 159.2, 194,1. MS (ESI) (*m*/*z*) 427.2 (100, $[MNa]^+$), 428.2 (30, $[MHNa]^+$). HRMS (ESI) (*m*/*z*) $[MNa]^+$ calcd for $C_{23}H_{36}O_4NaSi$ 427.2281, found 427.2264.

(4*S*,5*E*,7*Z*,10*S*)-10-(*tert*-Butyldimethylsilyloxy)-12-(4-methoxybenzyloxy)dodeca-1,5,7-trien-4-ol (15). (*S*)-Tol-BINAP (126 mg, 0.2 mmol) and AgOTf (51 mg, 0.2 mmol) were sheltered from light and stirred in dry THF (8 mL) for 20 min. A solution of aldehyde **13** (410 mg, 1.01 mmol) in dry THF (0.5 mL) was then added. The resulting mixture was cooled down to −20 °C, and allyltributyltin (0.32 mL, 1.03 mmol) was added. The solution was stirred at −20 °C for 20 h and then quenched with saturated $NaHCO_3$ and Et_2O. The mixture was filtered on a pad of celite and washed with Et_2O (50 mL). The filtrate was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford 381 mg of the desired alcohol (85%). $R_f = 0.41$ (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 3424 (OH), 2928, 2854. NMR ^1H ($CDCl_3$, 500 MHz) δ ppm: 0.05 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.63 − 1.83 (m, 2H), 1.68 (bs, 1H), 2.22 − 2.41 (m, 4H), 3.51 (t, $J = 6.5$ Hz, 2H), 3.81 (s, 3H), 3.87 − 3.95 (m, 1H), 4.17−4.25 (m, 1H), 4.39 (d, $J = 11,5$ Hz, 1H), 4.45 (d, $J = 11.5$ Hz, 1H), 5.15 (d, $J = 10.8$ Hz, 1H), 5.16 (d, $J = 16.5$ Hz, 1H), 5.50 (dt, $J = 7.7$ Hz, $J = 10.8$ Hz, 1H), 5.70 (dd, $J = 6.4$ Hz, $J = 15.1$ Hz, 1H), 5.82 (ddt, $J = 7.4$ Hz, $J = 10.4$ Hz, $J = 16.9$ Hz, 1H), 6.06 (t, $J = 11$ Hz, 1H), 6.48 (dd, $J = 11$ Hz, $J = 15.2$ Hz, 1H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.16 (d, $J = 8.6$ Hz, 2H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.6, −4.2, 18.2, 26.0, 36.2, 37.0, 42.1, 55.4, 66.9, 69.3, 71.6, 72.8, 113.9, 118.4, 126.1, 128.6, 129.4, 129.5, 130.8, 134.,3, 135.4, 159.2. MS (ESI) = (*m*/*z*) 469.2 (100, $[MNa]^+$), 470.3 (10, $[MHNa]^+$). Anal. Calcd for $C_{26}H_{42}O_4Si$: C, 69.91, H, 9.48. Found: C, 69.89, H, 9.55.

(5*S*,6*E*,8*Z*,11*S*)-5-Allyl-11-(2-(4-methoxybenzyloxy)ethyl)-2,2,-13,13,14,14-hexamethyl-3,3-diphenyl-4,12-dioxa-3,13-disilapentadeca-6,8-diene (16). To a solution of alcohol **15** (313 mg, 0.67 mmol) and imidazole (57 mg, 0.83 mmol) in dry DMF (3 mL) was added TBDPSCl (390 μL, 1.5 mmol). The resulting mixture was stirred at room temperature for 16 h and then quenched with saturated NH_4Cl. The aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford the desired protected alcohol **16** (440 mg, 96%). $R_f = 0.77$ (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 2957, 2928, 2896, 2855. NMR ^1H ($CDCl_3$, 500 MHz) δ ppm: 0.03 (s, 6H), 0.88 (s, 9H), 1.08 (s, 9H), 1.58 − 1.78 (m, 2H), 2.20 − 2.28 (m, 4H), 3.46 − 3.53 (m, 2H1), 3.81 (s, 3H), 3.83 − 3.90 (m, 1H), 4.25 (q, $J = 6$ Hz, 1H), 4.37 (d, $J = 11.7$ Hz, 1H), 4.43 (d, $J = 11.4$ Hz, 1H), 4.93 (d, $J = 14.1$ Hz, 1H), 4.97 (d, $J = 9.4$ Hz, 1H), 5.39 (dt, $J = 7.8$ Hz, $J = 10.8$ Hz, 1H), 5.61 (dd, $J = 6.9$ Hz, $J = 15.3$ Hz, 1H), 5.71 (ddt, $J = 7.2$ Hz, $J = 9.9$ Hz, $J = 16.8$ Hz, 1H), 5.94 (t, $J = 11.1$ Hz, 1H), 6.15 (dd, $J = 11.1$ Hz, $J = 14.7$ Hz, 1H), 6.87 (d, $J = 8.7$ Hz, 2H), 7.25 (d, $J = 8.7$ Hz, 2H), 7.33 − 7.42 (m, 6H), 7.63 − 7.75 (m, 4H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.6, −4.2, 18.2, 19.5, 26.0, 27.2, 36.2, 37.1, 42.8, 55.4, 66.9, 69.2, 72.7, 74.7, 113.9, 117.2, 125.8, 127.5, 127.6, 127.9, 129.4, 129.6, 129.7, 129.8, 130.9, 134.3, 134.5,-135.0, 135.7, 136.1, 159.3. MS (ESI) *m*/*z* 707.4 (100, $[MNa]^+$), 708.4 (30, $[MHNa]^+$). Anal. Calcd for $C_{42}H_{60}O_4Si_2$: C, 73.63, H, 8.83. Found: C, 73.84, H, 9.01.

(3*S*,5*Z*,7*E*,9*S*)-3-(*tert*-Butyldimethylsilyloxy)-9-(*tert*-butyldiphenylsilyloxy)dodeca-5,7,11-trienal (18). To a solution of protected alcohol (613 mg, 0.895 mmol) in dichloromethane (10 mL) and borate buffer (pH = 8, 10 mL) was added DDQ (305 mg, 1.34 mmol). The black suspension was stirred at room temperature for 1.5 h and became white. The precipitate was filtered on a pad of celite and washed with dichloromethane. The filtrate was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford a 1:1 unseparable mixture of the desired unprotected alcohol (53% yield, NMR estimation) and anisaldehyde, along with 122 mg of recovered starting material.

To a solution of the previous mixture of unprotected alcohol and anisaldehyde in dichloromethane (1 mL) was added Dess−Martin periodinane (15 wt % solution in dichloromethane, 1.2 mL, 0.57 mmol). A white precipitate formed, and the suspension was stirred at room temperature for 20 min. The solid was filtered on a pad of celite and washed with dichloromethane. The filtrate was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford 160 mg of the desired aldehyde (60%). Yield over 2 steps: 32%. R_f = 0.72 (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 3069, 2928, 2856, 2718, 1726 (C═O). NMR ^1H ($CDCl_3$, 500 MHz) δ ppm: 0.06 (s, 3H), 0.07 (s, 3H), 0.88 (s, 9H), 1.09 (s, 9H), 2.25 − 2.31 (m, 4H), 2.30 (ddd, *J* = 2 Hz, *J* = 4.6 Hz, *J* = 15.7 Hz, 1H), 2.48 (ddd, *J* = 2.7 Hz, *J* = 7.3 Hz, *J* = 15.7 Hz, 1H), 4.18 − 4.30 (m, 2H), 4.95 (d, *J* = 15.9 Hz, 1H), 4.99 (d, *J* = 10.8 Hz, 1H), 5.35 (dt, *J* = 7.8 Hz, *J* = 10.5 Hz, 1H), 5.66 (dd, *J* = 6.6 Hz, *J* = 14.7 Hz, 1H), 5.72 (ddt, *J* = 7.2 Hz, *J* = 10.2 Hz, *J* = 17.4 Hz, 1H), 6.00 (t, *J* = 10.8 Hz, 1H), 6.14 (dd, *J* = 11 Hz, *J* = 14;7 Hz, 1H), 7.35 − 7.44 (m, 6H), 7.64 − 7.75 (m, 4H), 9.75 (t, *J* = 2,3 Hz, 1H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.7, −4.3, 18.1, 19.5, 26.0, 26.7, 36.1, 42.7, 50.6, 68.0, 73.9, 117.3, 125.2, 126.2,127.5, 127.6, 129.7, 129.8, 130.8, 134.4, 134.4, 136.1, 136.7, 202.0. MS (ESI) *m*/*z* 585.3 (5, $[MNa]^+$), 617.4 (100, $[M + MeOH + Na]^+$). HRMS (ESI) *m*/*z* $[M + MeOH + Na]^+$ calcd for $C_{34}H_{50}O_3NaSi_2$ 585.3196, found 585.3226.

(2*R*,12*S*,14*Z*,16*E*,18*S*)-12-(*tert*-Butyldimethylsilyloxy)-18-(*tert*-butyldiphenylsilyloxy)-2-(4-methoxybenzyloxy)henicosa-14,16,-20-trien-8-yn-10-one (19). To a solution of alkyne **7** (13 mg, 0.05 mmol) in dry THF (0.4 mL) at −78 °C was added dropwise *n*-butyllithium (1.6 M in hexanes, 30 μL, 0.048 mmol). The reaction mixture was stirred at −78 °C for 20 min. A solution of aldehyde **18** (15 mg, 0.034 mmol) in dry THF (0.3 mL) was added via cannula, and the resulting mixture was stirred at −78 °C for 1.5 h. The reaction was quenched with saturated NH_4Cl (1 mL). The aqeous layer was extracted with Et_2O (5 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude mixture (35 mg) was dissolved in dry dichloromethane (1 mL), and Dess−Martin periodinane (15 wt % in dichloromethane, 0.11 mL, 0.05 mmol) was added. After 10 min, a white precipitate was formed and the reaction was complete (TLC). The solvent was evaporated and the crude mixture was purified by flash chromatography to afford the desired ketone (26 mg, 94% over 2 steps). R_f = 0.63 (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 2929, 2855, 2211 (C≡C), 1673 (C═O). NMR ^1H ($CDCl_3$, 500 MHz) δ ppm: 0.05 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.08 (s, 9H), 1.18 (d, *J* = 6 Hz, 3H), 1.30−1.46 (m, 6H), 1.55 − 1.61 (m, 2H), 2.24 − 2.28 (m, 4H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.49 (dd, *J* = 4 Hz, *J* = 15 Hz, 1H), 2.65 (dd, *J* = 4 Hz, *J* = 15 Hz, 1H), 3.49 (sext, *J* = 6 Hz, 1H), 3.81 (s, 3H), 4.24 − 4.27 (m, 1H), 4.27 − 4.31 (m, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 4.50 (d, *J* = 11.5 Hz), 4.94 (d, *J* = 17 Hz, 1H), 4.98 (d, *J* = 10.5 Hz, 1H), 5.36 (dt, *J* = 7.5 Hz, *J* = 11 Hz, 1H), 5,64 (dd, *J* = 7 Hz, *J* = 15 Hz, 1H), 5.72 (ddt, *J* = 7 Hz, *J* = 10.5 Hz, *J* = 17.5 Hz, 1H), 5.97 (t, *J* = 11 Hz, 1H), 6.12 (dd, *J* = 11 Hz, *J* = 15 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.33 − 7.44 (m, 6H), 7.65 (d, *J* = 6.5 Hz, 2H), 7.69 (d, *J* = 6.5 Hz, 2H). MS (ESI) *m*/*z* 843.4 (100, $[MNa]^+$), 844.5 (45, $[MHNa]^+$). HRMS (ESI) $[MNa]^+$ calcd for $C_{51}H_{72}O_5NaSi_2$ 843.4816, found 843.4809.

(2*R*,6*E*,8*E*,12*S*,14*Z*,16*E*,18*S*)-12-(*tert*-Butyldimethylsilyloxy)-18-(*tert*-butyldiphenylsilyloxy)-2-(4-methoxybenzyloxy)henicosa-6,8,14,16,20-pentaen-10-one (20). To a solution of propargylic ketone **19** (100 mg, 0.12 mmol) in dry toluene (0.5 mL) at 80 °C was added triphenylphosphine (36 mg, 0.15 mmol). The mixture was stirred at 80 °C for 48 h and then quenched with water. The aqeous layer was extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography to afford 42 mg of the desired dienone (42%). R_f = 0.63 (heptane/AcOEt 7:3). IR-FT (neat) cm^{-1}: 2928, 2855, 1687 (C═O). NMR ^1H ($CDCl_3$, 500 MHz) δ ppm: 0.02 (s, 3H), 0.04 (s, 3H), 0.84 (s, 9H), 1.07 (s, 9H), 1.19 (d, *J* = 6.2 Hz, 3H), 1.42−1.50 (m, 2H), 1.53 − 1.62 (m, 2H), 2.15 − 2.19 (m, 2H), 2.25 − 2.33 (m, 4H), 2.43 (dd, *J* = 4.4 Hz, *J* = 14.9 Hz, 1H), 2.72 (dd, *J* = 7.6 Hz, *J* = 15 Hz, 1H), 3.50 (sext, *J* = 5.7 Hz, 1H), 3.81 (s, 3H), 4.21 − 4.28 (m, 2H), 4.38 (d, *J* = 11.4 Hz), 4.51 (d, *J* = 11.4 Hz), 4.94 (d, *J* = 17.4 Hz, 1H), 4.97 (d, *J* = 11.2 Hz, 1H), 5.40 (dt, *J* = 7.9 Hz, *J* = 10.7 Hz, 1H), 5.63 (dd, *J* = 6.9 Hz, *J* = 15.2 Hz, 1H), 5.71 (ddt, *J* = 7.3 Hz, *J* = 10.3 Hz, *J* = 17 Hz, 1H), 5.98 (t, *J* = 11 Hz, 1H), 6.06 (d, *J* = 15.6 Hz, 1H), 6.13 (dd, *J* = 11 Hz, *J* = 14.6 Hz, 1H), 6.17 − 6.16 (m, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 7.05 (m, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.32 − 7.44 (m, 6H), 7.64 (d, *J* = 6.4 Hz, 2H), 7.69 (d, *J* = 6.4 Hz, 2H). NMR ^{13}C ($CDCl_3$, 75 MHz) δ ppm: −4.8, −4.6, 18.0, 19.4, 19.6, 25.9, 27.0, 33.2, 36.1, 36.3, 42.6, 47.3, 55.3, 69.3, 70.0, 73.9, 74.1, 113.8, 117.1, 125.4, 126.9, 127.4, 127.5, 129.1, 129.2, 129.5, 129.6, 130.2, 131.1, 134.1, 134.3, 136.0, 136.0, 143.5, 145.5, 159.1, 199.7. MS (ESI) *m*/*z* 843.5 (100, $[MNa]^+$), 844.6 (35, $[MHNa]^+$). HRMS (ESI) $[MNa]^+$ calcd for $C_{51}H_{72}O_5NaSi_2$ 843.4816, found 843.4832.

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Supporting Information Available: Expiremental procedures and characterizations for known compounds **2**, **6**, **7**, **9**, **10**, and **14** and copies of the ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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