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Formal Total Synthesis of Neocarzinostatin Chromophore

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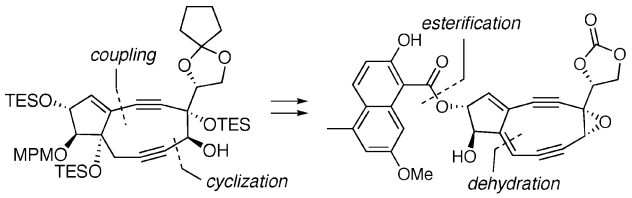
Received September 28, 2005



Neocarzinostatin chromophore aglycon

An efficient route to the neocarzinostatin chromophore aglycon has been developed. The present strategy involves a stereoselective intramolecular acetylide−aldehyde cyclization to form the C5−C6 bond, followed by efficient installation of α-epoxide, naphthoate, and carbonate functionalities. The C8−C9-olefin was introduced by using the Martin sulfurane dehydration reaction to furnish the highly reactive aglycon.

Introduction

Neocarzinostatin (NCS), the first enediyne antibiotic,[1] was isolated from a culture of *Streptomyces carzinostaticus* var. F-41 in 1965.[2] Its potent antibacterial and antitumor activities derive from the inhibition of DNA synthesis and DNA degradation in cells.[3] The poly(styrene−maleic acid)−NCS conjugate, namely, SMANCS, shows promising clinical activity against primary hepatocellular carcinoma.[3c,4] NCS is composed of a very unstable chromophore[5] and a carrier apoprotein.[6] The bioactive small molecular chromophore (NCS-chr, **1**) consists of a naphthoate intercalator, a 2′-methylamino sugar, and an epoxy bicyclo[7,3,0]dodecadienediyne core (Figure 1).[7] The naked chromophore is highly sensitive to light,[8] heat,[9] base,[10] and nucleophiles[11] and readily undergoes cycloaromatization to generate bioactive diradical species.[1c,12] This chemical instability, complex structure, and fascinating mode of action make **1** a challenging target for total synthesis.

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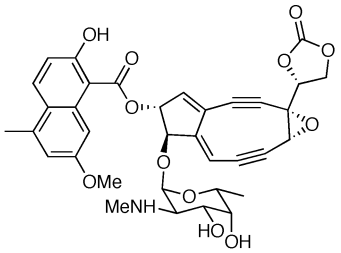
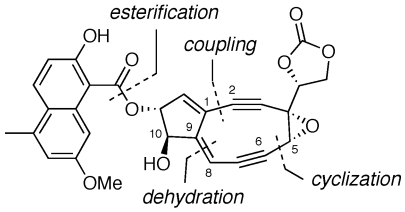
10.1021/jo052031o CCC: $33.50
Published on Web 12/20/2005



1: Neocarzinostatin chromophore



2: Aglycon

FIGURE 1. Structure of the neocarzinostatin chromophore and the strategy for the synthesis of the aglycon.

Although many notable synthetic approaches in this area have been reported,[13] total synthesis of the nine-membered enediyne natural product has been elusive.[14,15] With respect to the NCS-chr (**1**), only one successful total synthesis has been achieved by Myers and co-workers.[16] Their synthesis involves the stereocontrolled glycosidic coupling between the 2′-methylamino sugar and the labile aglycon **2** in unprotected form.[16b,c] This highly practical methodology avoids the need for protecting the 2′-methylamino group and minimizes synthetic manipulations after installation of the labile enediyne functionality. Furthermore, aglycon **2** serves as a viable substrate for glycosylation; the fucosyl analogue and the radiolabeled NCS-chr can both be prepared by introducing the suitable glycoside into **2**.[16c,17]

We therefore considered aglycon **2** a valuable synthetic target for further developing NCS-chr (**1**). Herein we report a synthesis of **2**, featuring convergent assembly of the functionalized cyclopentenone with the acetylenic fragment, followed by stereoselective intramolecular acetylide−aldehyde cyclization[18,19] between the C5 and C6 positions[14b,20] (Figure 1). The crucial C8−C9-olefin was efficiently installed in the final stage by dehydration of the C9-tertiary alcohol.

Results and Discussion

Nine-Membered Ring Closure. The synthesis began with the optically active (1*R*,4*S*,5*S*)-4,5-bis(methoxymethoxy)-2-cyclopenten-1-ol (**3**), which was readily prepared on a large scale from commercially available methyl D-glucopyranoside by recently developed RCM technology[21,22] (Scheme 1). Before further details of the synthesis are presented, it should be emphasized that the highly oxygenated nature of several intermediates required an elaborate protecting group strategy. Thus, the hydroxyl group of **3** was protected as the acid-stable TBDPS ether, and the MOM ethers were cleaved selectively in the presence of a catalytic amount of $ZrCl_4$.[23] Other deprotection conditions, including the use of alkylboron bromide or PPTS in *t*-BuOH, gave disappointing results. Selective oxidation of the allylic alcohol with MnO_2 afforded the α-hydroxy enone **4**. Despite its moderate sensitivity under oxidative conditions, the MPM ether was determined to be the most appropriate protecting group of the C10-alcohol moiety due to its robustness to basic, nucleophilic, and mildly acidic conditions. However, because of the chemical instability of enone **4** under both acidic and basic conditions, it was necessary to employ 4-methoxybenzyl 2,2,2-trichloroacetimidate[24] at low temperature to install the MPM group. Subsequent α-iodination[25] afforded the Sonogashira coupling precursor **5**.

Parallel synthetic studies had suggested that slightly harsh conditions were required to remove the acetonide group of the

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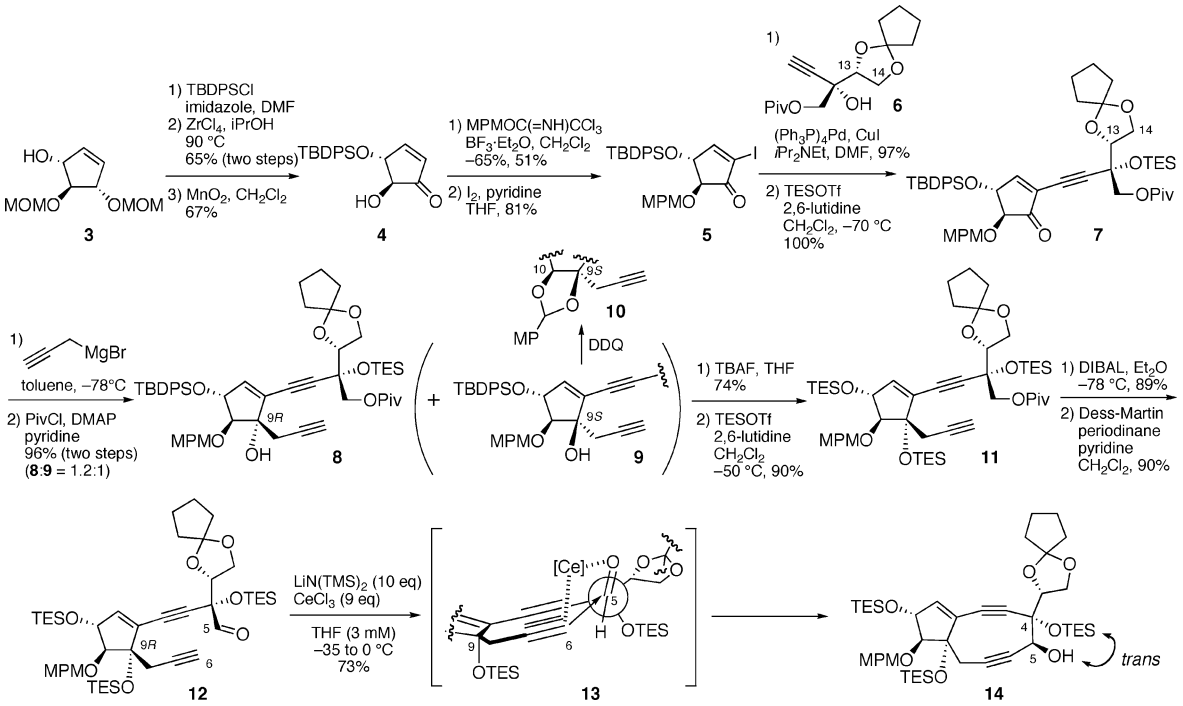
SCHEME 1. Construction of the Nine-Membered Ring



C13,C14-diol in the right half of the molecule.[14a,b] Heeswijk et al. showed that cyclopentylidene ketals of 1,2-diols tend to be 3 times more susceptible to acid-catalyzed hydrolysis than their corresponding acetonides.[26] Therefore, the C13,C14-diol moiety of the acetylenic fragment **6**[27] was protected as its cyclopentylidene ketal prior to coupling. Palladium-catalyzed coupling[28] between **5** and **6**, followed by TES protection, afforded the expected enyne **7** in high yield. Addition of propargylmagnesium bromide to **7** proceeded quantitatively, but in a nonstereoselective manner. During this transformation, partial loss of pivaloyl ester was observed. Therefore, the crude products were treated with PivCl without purification to yield a separable mixture of 9*R*- and 9*S*-isomers (**8** and **9**) in a 1.2:1 ratio. Interestingly, the proportion of the 9*R*-isomer (**8**) in the present case was less than that reported previously,[20a] and there was no significant change in product ratio upon addition of $ZnCl_2$.[29] It was thought that the protecting groups on the cyclopentenone moiety played an important role in defining the selectivity of the Grignard addition. Since NOE data were inconclusive, the stereochemistry of the C9-tertiary alcohol of **9** was determined by derivatization to its MP-acetal **10** upon anhydrous DDQ treatment.

Sequential protecting group manipulation and oxidation[30] of **8** provided the key cyclization precursor **12**. The 9*R*-configured aldehyde **12** underwent ring closure smoothly using the $CeCl_3$/$LiN(TMS)_2$-mediated cyclization protocol[31] to afford the C4,C5-*trans*-alcohol **14** as a single stereoisomer in 73% yield. The remarkable *trans*-selectivity observed in **14** was consistent with a number of previous results[14b,18a−d,20a−c] and presumably arose via the energetically favored transition state **13**, in which the cerium-chelated carbonyl oxygen is sterically remote from the neighboring TES group. Furthermore, it should be pointed out that the corresponding 9*S*-isomer derived from **9** was inactive to the nine-membered ring closure, another strong indication that the relative stereochemistry of the precursors is responsible for efficient cyclization.[14a,b,18a,b]

Synthesis of the Neocarzinostatin Chromophore Aglycon. On the basis of previous research, the C4,C5-epoxide was strategically constructed by taking advantage of the different reactivities of the three TES groups in **14** under fluoride-mediated deprotection conditions (Scheme 2).[14b] Treatment of **14** with MsCl provided the corresponding mesylate, which was exposed to 2 equiv of TBAF at −35 °C to afford the desired epoxide **16** as a major product. The minor diol intermediate **15** was readily converted into **16** by potassium carbonate in EtOH. Importantly, the C9-O(TES) group was left untouched during these selective deprotection and tandem epoxidation steps, thereby allowing the manipulations which followed. Alcohol **16** thus obtained was condensed with naphthoic acid (**17**)[32] without concern for bisnaphthoate formation.[14b] Further investigation revealed that the C9-hydroxyl group must be protected during the next carbonate formation step; otherwise the desired carbonate was formed in less than 35% yield. To overcome this inefficiency, selective conditions to cleave the cyclopentylidene ketal in the presence of the acid-labile TES and epoxide functionalities were investigated. It was found that the cyclopentylidene group could be removed selectively upon treatment with dilute aqueous hydrofluoric acid in CH_3CN to give the desired triol **18** in 69% yield. Facile carbonate formation could

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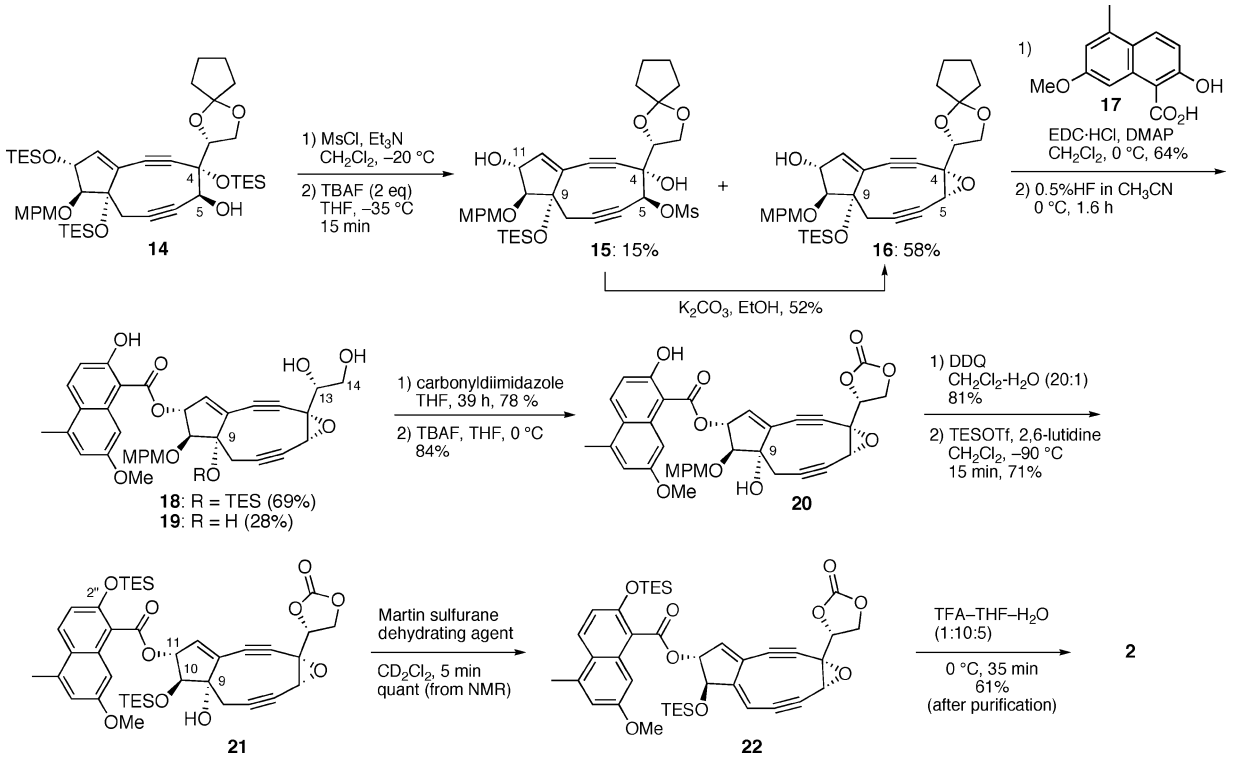
SCHEME 2. Completion of the NCS-chr Aglycon



then be realized, forming **20** after removal of the C9-O(TES) group (66% yield in two steps). In view of the instability of aglycon **2**, it was advisable at this stage to cleave the MPM ether.[14a,b] The MPM group in **20** was replaced by a TES group via DDQ oxidation and selective protection. In contrast to the behavior of the C10-deoxy substrate, which underwent dehydration at 0 °C,[14b] alcohol **21** remained unaltered upon treatment with a large excess of Ms_2O, Et_3N, and DMAP; only incomplete formation of the C9-mesylate resulted. Addition of DBU to the resulting mesylate led to rapid decomposition, while other dehydration conditions including Tf_2O and 2,6-lutidine[14a] were not effective. The steric hindrance due to the C10-O(TES) and the C11-naphthoate groups is likely to inhibit such dehydrations. After numerous trials, the desired enediyne **22** was finally obtained by using the Martin sulfurane dehydrating reagent.[33] Remarkably, the reaction proceeded quantitatively as determined by NMR within 5 min at room temperature. The protected aglycon **22** was found to be stable to silica gel but rapidly decomposed in neat form. The final deprotection was carefully achieved with a system of TFA−THF−H_2O (1:10:5) to furnish the highly unstable aglycon **2**. TLC monitoring of the reaction indicated that clean deprotection occurred, but the purified aglycon **2** was extremely sensitive to concentration and degraded much more rapidly than the protected aglycon **22**, both in solution and, especially, in neat form. It seems likely that the bulkiness of the protecting groups again contributed to the stability of the chromophore core.[34] All spectroscopic data of synthetic **2** were identical to those reported in the literature.[16a] In addition, the high-resolution mass spectrum (ESI-FT-ICR-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{28}H_{20}NaO_9$ 523.1000, found 523.1002) was obtained. An efficient conversion of aglycon **2** to NCS-chr (**1**) has previously been accomplished by Myers' group.[16b,c]

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Conclusion

An efficient route to the neocarzinostatin chromophore aglycon was developed. The present synthesis involves convergent assembly of the functionalized cyclopentenone with the acetylenic fragment, followed by stereocontrolled nine-membered ring closure. After introduction of epoxide, naphthoate, and carbonate functionalities, a central dienediyne system was elaborated by using sulfurane-mediated dehydration reaction. A highly efficient protecting group strategy was also developed to access the sensitive substrate.

Experimental Section

Enone 4. To a solution of allyl alcohol **3** (11.0 g, 54.1 mmol) in DMF (54 mL) were added imidazole (9.21 g, 135 mmol) and (TBDPS)Cl (15.2 mL, 59.5 mmol). The mixture was stirred for 6 h at room temperature and poured into water. The resulting mixture was extracted with hexane (2×), and the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. Concentration of the solution gave the corresponding TBDPS ether (19.9 g), which was subjected to the next reaction without purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (s, 9H), 3.39 (s, 3H), 3.42 (s, 3H), 4.30 (t, 1H, J = 4.3 Hz), 4.37 (br s, 1H), 4.69 (br s, 1H), 4.73 (d, 1H, J = 7.0 Hz), 4.75 (d, 1H, J = 7.0 Hz), 4.75 (d, 1H, J = 7.0 Hz), 4.81 (d, 1H, J = 7.0 Hz), 5.58 (d, 1H, J = 6.5 Hz), 5.76 (d, 1H, J = 6.5 Hz), 7.38−7.45 (m, 6H), 7.71−7.77 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.5, 27.2, 55.7, 56.0, 81.0, 85.1, 91.9, 96.5 (2C), 127.9, 128.0, 130.0, 130.1, 131.9, 133.8, 134.5, 135.1, 136.2, 136.2; FT-IR (neat) ν 3017, 2932, 2891, 2858, 2823, 1962, 1894, 1827, 1589, 1471, 1428, 1369, 1307, 1261, 1212 cm^{-1}.

To a solution of the above TBDPS ether (19.9 g) in *i*PrOH (98 mL) was added $ZrCl_4$ (1.14 g, 4.89 mmol) at 90 °C. The mixture

was stirred for 4.5 h at 90 °C and cooled to 0 °C. The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated. The residue was purified by column chromatography (Florisil, hexane−hexane/AcOEt = 1) to give the corresponding diol (12.5 g, 35.2 mmol, 65% in two steps) as a colorless oil: $[\alpha]_D^{30.0}$ −9.0° (*c* 0.442, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (s, 9H), 4.05 (br s, 1H), 4.35 (br s, 1H), 4.52 (br s, 1H), 5.70 (br d, 1H, *J* = 6.5 Hz), 5.73 (br d, 1H, *J* = 6.5 Hz), 7.39−7.45 (m, 6H), 7.67−7.75 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3, 27.0, 80.2, 82.0, 89.8, 128.0, 128.1, 130.1, 130.2, 133.0, 133.7, 134.1, 134.5, 135.9; FT-IR (neat) ν 3362, 3071, 2931, 2858, 1471, 1427, 1362 cm^{-1}; MALDI-TOF-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{21}H_{26}NaO_3Si$ 377.1549, found 377.1529.

To a solution of the above diol (7.60 g, 21.4 mmol) in CH_2Cl_2 (428 mL) was added MnO_2 (27.9 g, 321 mol). The mixture was stirred for 7 h at room temperature and filtered. The filter cake was washed with hexanes−EtOAc, and the filtrate was concentrated. The residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 3.4) to give enone **4** (5.07 g, 14.4 mmol, 67%) as a pale yellow oil: $[\alpha]_D^{30.0}$ +6.6° (*c* 2.36, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (s, 9H), 2.46 (br s, 1H), 4.29 (br s, 1H), 4.76 (br d, 1H, *J* = 1.5 Hz), 6.15 (dd, 1H, *J* = 6.5, 1.0 Hz), 7.16 (dd, 1H, *J* = 6.5, 1.8 Hz), 7.36−7.49 (m, 6H), 7.71−7.76 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3, 26.9, 27.0, 78.1, 81.7, 127.7, 127.8, 127.9, 127.9, 128.0, 130.3, 130.3, 131.5, 132.8, 133.4, 135.8, 135.9, 136.0, 161.0, 203.9; FT-IR (neat) ν 3436, 3071, 2932, 2892, 2858, 1729, 1472, 1427, 1363 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{21}H_{24}NaO_3Si$ 375.1387, found 375.1387.

Iodide 5. To a solution of enone **4** (4.09 g, 11.6 mmol) in CH_2Cl_2 (116 mL) were added 4-methoxybenzyl 2,2,2-trichloroacetimidate (4.92 g, 17.4 mmol) and BF_3·Et_2O (147 μL, 1.16 μmol) at −65 °C. The mixture was stirred for 1.5 h at −65 °C and quenched with saturated $NaHCO_3$ solution. The resulting mixture was extracted with AcOEt (2×), and the combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 12 to 10 to 8 to 5 to 3 to 2) to give the corresponding MPM ether (2.81 g, 5.95 mmol, 51%) as a yellow oil: $[\alpha]_D^{29.0}$ −7.9° (c 1.07, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (s, 9H), 3.81 (s, 3H), 4.16 (d, 1H, *J* = 3.0 Hz), 4.58 (d, 1H, *J* = 11 Hz), 4.89 (br s, 1H), 4.90 (d, 1H, *J* = 11 Hz), 6.06 (br d, 1H, *J* = 6.5 Hz), 6.86 (d, 2H, *J* = 6.0 Hz), 7.05 (dd, 1H, *J* = 6.0, 2.0 Hz), 7.24 (dd, 2H, *J* = 6.5 Hz), 7.36−7.46 (m, 6H), 7.66−7.73 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3, 27.0, 55.4, 71.6, 72.7, 77.0, 86.0, 113.9, 113.9, 128.0, 129.6, 129.8, 129.9, 130.2, 132.7, 132.8, 133.5, 135.9, 136.0, 159.5, 160.0, 203.5; FT-IR (neat) ν 3071, 2999, 2932, 2858, 1963, 1888, 1727, 1613, 1587, 1514, 1463, 1428, 1391, 1361, 1327, 1302, 1248 cm^{-1}; MALDI-TOF-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{29}H_{32}NaO_4Si$ 495.1968, found 495.1990.

To a solution of the above MPM ether (3.02 g, 6.36 mmol) in THF (64 mL) were added pyridine (1.54 mL, 19.1 mmol) and I_2 (3.23 g, 12.7 mmol). The mixture was stirred for 30 min at room temperature, diluted with Et_2O, and quenched with saturated $Na_2S_2O_3$ solution. The resulting mixture was extracted with AcOEt (2×), and the combined organic phase was washed with brine and dried over anhydrous $MgSO_4$. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 20) to give iodide **5** (3.09 g, 5.17 mmol, 81%) as a colorless oil: $[\alpha]_D^{29.0}$ −61.0° (*c* 0.602, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (s, 9H), 3.81 (s, 3H), 4.17 (d, 1H, *J* = 2.5 Hz), 4.58 (d, 1H, *J* = 11 Hz), 4.84 (t, 1H, *J* = 2.5 Hz), 4.92 (d, 1H, *J* = 11 Hz), 6.86 (d, 2H, *J* = 8.0 Hz), 7.23 (d, 2H, *J* = 9.0 Hz), 7.37−7.40 (m, 4H), 7.45 (d, 1H, *J* = 2.5 Hz), 7.45−7.48 (m, 2H), 7.65−7.70 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3, 26.9, 55.4, 72.7, 78.4, 83.4, 102.3, 113.9, 128.1, 128.1, 129.4, 130.1, 130.4, 130.4, 132.5, 133.0, 135.9, 135.9, 159.6, 165.7, 198.4; FT-IR (neat) ν 3071, 2932, 2858, 1730, 1613, 1587, 1514, 1470, 1427, 1392, 1352, 1302, 1248 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{29}H_{31}NaIO_4Si$ 621.0929, found 621.0930.

Cyclopentylidene Ketal 6. To a solution of (2*S*)-2-hydroxy-2-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-butyn-1-yl 2,2-dimethylpropanoate[27] (0.219 g, 0.810 mmol) in MeOH (8.1 mL) was added TsOH·H_2O (15.4 mg, 81.0 μmol). The mixture was stirred for 4 h at room temperature and concentrated. The residue was dissolved in MeOH (8.1 mL) and stirred for another 5 h at room temperature. After concentration, 1,1-dimethoxycyclopentane (213 μL, 1.62 mmol) and cyclopentanone (3.5 mL) were added, and the mixture was stirred for 30 min at room temperature. The reaction mixture was quenched with Et_3N (500 μL) followed by saturated $NaHCO_3$ solution and extracted with AcOEt (2×). The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After concentration, the remaining cyclopentanone was distilled out azeotropically with toluene. The residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 8 to 6 to 5) to give cyclopentylidene ketal **6**, which was further purified by recrystallization from hexane to afford **6** (0.138 g, 0.510 mmol, 63%) as colorless needles: mp 102−103 °C (hexane); $[\alpha]_D^{28.0}$ +21.7° (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (s, 9H), 1.67−1.70 (m, 4H), 1.74−1.77 (m, 2H), 1.87−1.95 (m, 2H), 2.49 (s, 1H), 3.03 (s, 1H), 4.05 (dd, 1H, *J* = 7.3, 5.8 Hz), 4.12 (t, 1H, *J* = 5.3 Hz), 4.14 (dd, 1H, *J* = 7.3, 5.3 Hz), 4.19 (d, 1H, *J* = 12 Hz), 4.40 (d, 1H, *J* = 12 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.4, 23.9, 27.3, 36.1, 36.4, 39.1, 65.9, 68.0, 71.7, 74.9, 77.6, 81.4, 120.5, 179.1; FT-IR (KBr) ν 3443, 3270, 2945, 1708, 1669, 1541, 1475 cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.83; H, 8.28.

Enone 7. A mixture of iodide **5** (3.09 g, 5.17 mmol), acetylenic fragment **6** (1.84 g, 6.20 mmol), and CuI (0.394 g, 2.07 mmol) was dissolved in DMF (50 mL). To the solution were added *i*Pr_2NEt (2.70 mL, 15.5 mmol) and $(Ph_3P)_4Pd$ (0.598 g, 0.517 mmol), and the mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with hexane−AcOEt and quenched with saturated NH_4Cl solution. The resulting mixture was extracted with AcOEt (2×), and the combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 5 to 4 to 3 to 2 to 1) to give the coupling product (3.86 g, 5.03 mmol, 97%) as a yellow oil: $[\alpha]_D^{27.0}$ −21.0° (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9H), 1.21 (s, 9H) 1.61−1.70 (m, 4H), 1.72−1.77 (m, 2H), 1.78−1.90 (m, 2H), 3.39 (s, 1H), 3.81 (s, 3H), 4.04 (dd, 1H, *J* = 11, 9.0 Hz), 4.09−4.13 (m, 2H), 4.16 (d, 1H, *J* = 2.5 Hz), 4.18 (d, 1H, *J* = 11 Hz), 4.40 (d, 1H, *J* = 11 Hz), 4.56 (d, 1H, *J* = 11 Hz), 4.84 (t, 1H, *J* = 2.5 Hz), 4.89 (d, 1H, *J* = 11 Hz), 6.85 (d, 2H, *J* = 8.5 Hz), 7.04 (d, 1H, *J* = 2.5 Hz), 7.22 (d, 2H, *J* = 8.5 Hz), 7.35−7.39 (m, 4H), 7.43−7.46 (m, 2H), 7.64−7.69 (m, 4H); FT-IR (neat) ν 3437, 3072, 2960, 1731, 1613, 1588, 1514, 1471, 1428, 1395, 1337, 1283, 1249 cm^{-1}; MALDI-TOF-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{45}H_{54}NaO_9Si$ 789.3435, found 789.3447.

To a solution of the above coupling product (1.98 g, 2.58 mmol) in CH_2Cl_2 (26 mL) were added 2,6-lutidine (1.80 mL, 15.5 mmol) and (TES)OTf (1.16 mL, 5.16 mmol) at −70 °C. The mixture was stirred for 40 min at −70 °C and quenched with saturated $NaHCO_3$ solution. The resulting mixture was extracted with hexane (2×), and the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by flash column chromatography (silica gel, hexane−hexane/AcOEt = 25 to 20) to give TES ether **7** (2.27 g, 2.58 mmol, 100%) as a colorless oil: $[\alpha]_D^{27.0}$ −31.9° (*c* 0.66, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67 (q, 6H, *J* = 8.0 Hz), 0.92 (t, 9H, *J* = 8.0 Hz), 1.08 (s, 9H), 1.21 (s, 9H) 1.60−1.68 (m, 4H), 1.71−1.74 (m, 2H), 1.76−1.79 (m, 1H), 1.81−1.87 (m, 1H), 3.81 (s, 3H), 4.01 (dd, 1H, *J* = 8.3, 6.8 Hz), 4.05 (dd, 1H, *J* = 8.3, 5.8 Hz), 4.10 (d, 1H, *J* = 11 Hz), 4.14 (t, 1H, *J* = 6.3 Hz), 4.18 (d, 1H, *J* = 3.0 Hz), 4.31 (d, 1H, *J* = 11 Hz), 4.59 (d, 1H, *J* = 11 Hz), 4.86 (t, 1H, *J* = 2.5 Hz), 4.92 (d, 1H, *J* = 11 Hz), 6.86 (d, 2H, *J*

= 8.5 Hz), 7.00 (d, 1H, *J* = 2.5 Hz), 7.23 (d, 2H, *J* = 8.5 Hz), 7.36−7.39 (m, 4H), 7.44−7.47 (m, 2H), 7.65−7.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.0, 7.1, 15.4, 19.3, 23.5, 23.8, 26.9, 27.3, 36.5, 36.6, 39.0, 53.6, 55.5, 66.0, 66.5, 67.6, 72.8, 73.0, 75.6, 77.6, 77.9, 85.7, 95.1, 113.9, 120.4, 127.7, 128.0, 128.1, 129.6, 130.0, 130.3, 130.4, 132.6, 133.2, 135.9, 136.0, 159.6, 160.2, 198.5; FT-IR (neat) ν 3072. 2957, 2876, 1732, 1613, 1588, 1514, 1463, 1428, 1395, 1336, 1283, 1249 cm^{-1}; MALDI-TOF-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{51}H_{68}NaO_9Si_2$ 903.4300, found 903.4302.

Alcohols 8 and 9. To a suspension of magnesium turnings (1.46 g, 60.0 mmol) and mercury(II) chloride (5 mg) in Et_2O (30 mL) was slowly added a solution of propargyl bromide (3.56 mL, 40.0 mmol) in Et_2O (10 mL) over 20 min at room temperature. The mixture was refluxed for 1.5 h to give a 1.0 M solution of propargylmagnesium bromide. To a solution of enone **7** (2.27 g, 2.58 mmol) in toluene (86 mL) was added the above propargylmagnesium bromide solution (5.16 mL, 5.16 mmol) at −78 °C. The mixture was stirred for 15 min at −78 °C and quenched with saturated NH_4Cl solution. The resulting mixture was extracted with hexanes−EtOAc (2×), and the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After concentration, the residue was dissolved in pyridine (10 mL) and treated with PivCl (396 μL, 3.22 mmol) and DMAP (∼5 mg). The mixture was stirred for 17 h and concentrated. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 20 to 10) to give a less polar (9*R*)-alcohol, **8** (1.24 g, 1.34 mmol, 52%), and a polar (9*S*)-alcohol, **9** (1.05 g, 1.14 mmol, 44%), as pale yellow oils. Data for **8**: $[\alpha]_D^{26.0}$ −28.9° (*c* 2.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (q, 6H, *J* = 7.8 Hz), 0.91 (t, 9H, *J* = 7.8 Hz), 1.06 (s, 9H), 1.23 (s, 9H) 1.65−1.71 (m, 6H), 1.76 (t, 1H, *J* = 2.3 Hz), 1.90 (m, 2H), 2.47 (dd, 1H, *J* = 16, 2.8 Hz), 2.59 (dd, 1H, *J* = 16, 2.8 Hz), 3.34 (s, 1H), 3.81 (s, 3H), 4.00 (t, 1H, *J* = 6.5 Hz), 4.11−4.17 (m, 2H), 4.13 (d, 1H, *J* = 11 Hz), 4.14 (d, 1H, *J* = 5.5 Hz), 4.32 (d, 1H, *J* = 11 Hz), 4.56 (d, 1H, *J* = 11 Hz), 4.78 (d, 1H, *J* = 11 Hz), 4.82 (dd, 1H, *J* = 5.5, 1.5 Hz), 5.76 (d, 1H, *J* = 2.0 Hz), 6.85 (d, 2H, *J* = 8.5 Hz), 7.24 (d, 2H, *J* = 8.5 Hz), 7.30−7.43 (m, 6H), 7.65−7.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.0, 7.0, 19.3, 23.3, 23.8, 26.4, 27.1, 27.3, 35.9, 36.0, 39.1, 55.4, 66.3, 67.4, 70.8, 72.9, 73.2, 77.4, 78.5, 79.6, 80.7, 83.2, 92.2, 93.9, 113.7, 114.0, 120.4, 127.7, 127.8, 127.9, 128.0, 128.1, 129.4, 129.7, 129.8, 129.9, 130.7, 133.4, 134.0, 135.9, 136.0, 136.0, 139.3, 159.2, 178.0; FT-IR (neat) ν 3443, 3311, 2958, 1732, 1613, 1588, 1514, 1463, 1428, 1336, 1248, 1112 cm^{-1}; MALDI-TOF-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{54}H_{72}NaO_9Si_2$ 943.4613, found 943.4591. Data for **9**: $[\alpha]_D^{26.0}$ −11.4° (*c* 1.77, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.68 (q, 6H, *J* = 7.7 Hz), 0.93 (t, 9H, *J* = 7.8 Hz), 1.09 (s, 9H), 1.23 (s, 9H) 1.58−1.69 (m, 4H), 1.72−1.77 (m, 2H), 1.79−1.91 (m, 2H), 2.07 (t, 1H, *J* = 2.5 Hz), 2.66 (dd, 1H, *J* = 17, 2.8 Hz), 2.76 (dd, 1H, *J* = 17, 2.5 Hz), 3.21 (s, 1H), 3.80 (s, 3H), 4.02 (dd, 1H, *J* = 8.0, 7.0 Hz), 4.07 (dd, 1H, *J* = 8.5, 6.5 Hz), 4.12 (d, 1H, *J* = 2.5 Hz), 4.14 (d, 1H, *J* = 11 Hz), 4.16 (t, 1H, *J* = 6.5 Hz), 4.34 (d, 1H, *J* = 12 Hz), 4.43 (d, 1H, *J* = 11 Hz), 4.52 (d, 1H, *J* = 11 Hz), 4.81 (t, 1H, *J* = 2.5 Hz), 5.82 (d, 1H, *J* = 2.0 Hz), 6.85 (d, 2H, *J* = 8.0 Hz), 7.16 (d, 2H, *J* = 8.5 Hz), 7.38−7.41 (m, 4H), 7.44−7.47 (m, 2H), 7.65−7.72 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.0, 7.0, 19.3, 23.5, 23.8, 27.0, 27.3, 29.0, 36.3, 36.5, 39.0, 55.4, 66.5, 67.7, 70.9, 73.0, 73.1, 77.7, 80.2, 80.3, 81.4, 81.7, 86.6, 92.2, 113.9, 120.2, 127.9, 128.0, 129.7, 129.7, 130.1, 130.1, 130.7, 133.3, 133.6, 135.9, 136.0, 139.6, 159.6, 178.0; FT-IR (neat) ν 3522, 3311, 2957, 1732, 1613, 1588, 1514, 1462, 1428, 1337, 1249, 1111 cm^{-1}; MALDI-TOF-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{54}H_{72}NaO_9Si_2$ 943.4613, found 943.4599.

Identification of the C9 Stereochemistry. To a solution of alcohol **9** (30.0 mg, 0.0326 mmol) in CH_2Cl_2 (8 mL) was added DDQ (29.6 mg, 0.130 mmol). The mixture was stirred for 19 h at room temperature and concentrated. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 12 to 11 to 10 to 6 to 4) to give MP-acetal **10** (1.1:1 diastereomeric mixture, 12.9 mg, 0.0140 mmol, 43%) as a colorless syrup: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (q, 6H, *J* = 8.0 Hz), 0.65 (q, 6H, *J* = 8.0 Hz), 0.87 (t, 9H, *J* = 8.0 Hz), 0.88 (t, 9H, *J* = 8.0 Hz), 1.06 (s, 9H), 1.07 (s, 9H), 1.20 (s, 9H), 1.21 (s, 9H), 1.53−1.66 (m, 8H), 1.68−1.73 (m, 4H), 1.75−1.88 (m, 4H), 2.10 (t, 1H, *J* = 2.5 Hz), 2.10 (t, 1H, *J* = 2.5 Hz), 2.74 (dd, 1H, *J* = 17, 3.0 Hz), 2.87 (dd, 1H, *J* = 17, 2.5 Hz), 3.05 (dd, 1H, *J* = 17, 3.0 Hz), 3.10 (dd, 1H, *J* = 17, 2.5 Hz), 3.76 (s, 3H), 3.80 (s, 3H), 3.99 (t, 1H, *J* = 6.5 Hz), 4.01 (t, 1H, *J* = 6.5 Hz), 4.06 (t, 1H, *J* = 6.5 Hz), 4.07 (t, 1H, *J* = 6.5 Hz), 4.12 (d, 1H, *J* = 11 Hz), 4.13 (t, 1H, *J* = 6.5 Hz), 4.14 (d, 1H, *J* = 11 Hz), 4.14 (t, 1H, *J* = 6.5 Hz), 4.32 (d, 1H, *J* = 11 Hz), 4.33 (d, 1H, *J* = 11 Hz), 4.66 (br s, 1H), 4.75 (br d, 1H, *J* = 2.5 Hz), 4.75 (br s, 1H), 4.77 (d, 1H, *J* = 2.5 Hz), 5.42 (s, 1H), 5.71 (dd, 1H, *J* = 2.5, 1.0 Hz), 6.00 (dd, 1H, *J* = 2.5, 1.0 Hz), 6.07 (s, 1H), 6.79 (d, 2H, *J* = 9.0 Hz), 6.86 (d, 2H, *J* = 8.0 Hz), 7.25 (d, 2H, *J* = 9.0 Hz), 7.35−7.47 (m, 14H), 7.62−7.69 (m, 8H); ESI-TOF-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{54}H_{70}NaO_9Si_2$ 941.4456, found 941.4456.

TES Ether 11. To a solution of alcohol **8** (944 mg, 1.03 mmol) in THF (10 mL) was added TBAF (1.0 M solution in THF, 2.56 mL, 2.56 mmol). The mixture was stirred for 1.5 h at room temperature and concentrated. The residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 2 to 1) to give the corresponding triol (429 mg, 0.755 mmol, 74%) as a colorless amorphous solid: $[\alpha]_D^{27.0}$ −6.9° (*c* 2.35, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (s, 9H), 1.63−1.76 (m, 6H), 1.92−1.96 (m, 2H), 2.04 (s, 1H), 2.64 (t, 2H, *J* = 2.8 Hz), 3.18 (s, 1H), 3.58 (s, 1H), 3.80 (s, 3H), 3.89 (d, 1H, *J* = 5.0 Hz), 4.04 (dd, 1H, *J* = 9.0, 7.0 Hz), 4.09 (dd, 1H, *J* = 7.0, 3.3 Hz), 4.16 (d, 1H, *J* = 12 Hz), 4.31 (dd, 1H, *J* = 8.5, 3.3 Hz), 4.52 (d, 1H, *J* = 11 Hz), 4.64 (d, 1H, *J* = 12 Hz), 4.68 (dd, 1H, *J* = 5.0, 1.5 Hz), 4.83 (d, 1H, *J* = 11 Hz), 6.04 (d, 1H, *J* = 2.0 Hz), 6.89 (d, 2H, *J* = 9.0 Hz), 7.34 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.3, 23 8, 26.1, 27.3, 36.0, 36.0, 39.1, 55.4, 66.1, 67.7, 71.4, 72.2, 72.9, 77.1, 77.4, 79.5, 79.9, 83.5, 92.5, 93.9, 114.0, 120.7, 129.0, 129.5, 130.4, 138.2, 159.3, 179.2; FT-IR (film) ν 3417, 3307, 2961, 2875, 1730, 1613, 1514, 1480, 1398, 1337, 1285, 1248, 1172, 1107 cm^{-1}; MALDI-TOF-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{32}H_{40}NaO_9$ 591.2570, found 591.2592.

To a solution of the above triol (429 mg, 0.755 mmol) in CH_2Cl_2 (10 mL) were added 2,6-lutidine (703 μL, 6.04 mmol) and (TES)OTf (680 μL, 3.02 mmol) at −50 °C. The mixture was stirred for 1 h at −50 °C and quenched with saturated $NaHCO_3$ solution. The resulting mixture was extracted with hexanes−EtOAc (2×), and the combined organic layer was dried over anhydrous Na_2SO_4. After concentration, the residue was purified by flash column chromatography (silica gel, hexane−hexane/AcOEt = 10) to give tris(TES ether) **11** (619 mg, 0.680 mmol, 90%) as a pale yellow syrup: $[\alpha]_D^{22.0}$ −23.9° (*c* 2.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.61 (q, 6H, *J* = 8.0 Hz), 0.63 (q, 6H, *J* = 8.0 Hz), 0.71 (q, 6H, *J* = 8.0 Hz), 0.93 (t, 9H, *J* = 8.0 Hz), 0.95 (t, 9H, *J* = 8.0 Hz), 0.97 (t, 9H, *J* = 8.0 Hz), 1.23 (s, 9H), 1.60−1.69 (m, 4H), 1.72−1.75 (m, 2H), 1.83−1.94 (m, 2H), 1.87 (t, 1H, *J* = 2.5 Hz), 2.50 (dd, 1H, *J* = 16, 2.8 Hz), 2.73 (dd, 1H, *J* = 16, 2.3 Hz), 3.81 (s, 3H), 4.01 (d, 1H, *J* = 4.5 Hz), 4.02 (dd, 1H, *J* = 8.5, 7.0 Hz), 4.07 (dd, 1H, *J* = 8.5, 7.0 Hz), 4.12 (d, 1H, *J* = 12 Hz), 4.17 (t, 1H, *J* = 6.8 Hz), 4.35 (d, 1H, *J* = 11 Hz), 4.63 (d, 1H, *J* = 12 Hz), 4.77 (d, 1H, *J* = 11 Hz), 4.83 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.04 (d, 1H, *J* = 2.0 Hz), 6.88 (dd, 2H, *J* = 7.0, 2.0 Hz), 7.32 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.2, 6.0, 6.1, 6.5, 6.6, 6.9, 7.1, 7.2, 23.5, 23.8, 27.0, 27.3, 36.4, 36.6, 39.0, 55.4, 66.5, 67.7, 69.9, 72.2, 73.0, 77.6, 78.7, 80.6, 82.6, 86.2, 90.9, 95.0, 113.7, 113.7, 120.1, 129.0, 129.4, 129.7, 130.9, 139.8, 159.1, 177.9; FT-IR (neat) ν 3313, 2955, 1732, 1614, 1587, 1515, 1463, 1416, 1397, 1336, 1282, 1247 cm^{-1}; MALDI-TOF-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{50}H_{82}NaO_9Si_3$ 933.5164, found 933.5162.

Aldehyde 12. To a solution of pivalate **11** (688 mg, 0.755 mmol) in Et_2O (10 mL) was added DIBAL (0.94 M solution in hexane, 3.21 mL, 3.02 mmol) at −78 °C. The mixture was stirred for 30 min at −78 °C and quenched with saturated Rochelle salt solution.

The resulting mixture was stirred at room temperature until the two phases were clearly separated. The organic phase was separated, and the aqueous phase was extracted with hexane. The combined organic layer was dried over anhydrous Na_2SO_4. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 7) to give the corresponding alcohol (553 mg, 0.672 mmol, 89%) as a colorless oil: $[\alpha]_D^{20.0}$ −28.9° (*c* 0.59, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.61 (q, 6H, *J* = 7.5 Hz), 0.63 (q, 6H, *J* = 7.5 Hz), 0.74 (q, 6H, *J* = 7.5 Hz), 0.93 (t, 9H, *J* = 7.5 Hz), 0.97 (t, 18H, *J* = 7.5 Hz), 1.60−1.69 (m, 4H), 1.70−1.81 (m, 2H), 1.85−1.95 (m, 2H), 1.88 (t, 1H, *J* = 2.5 Hz), 2.18 (dd, 1H, *J* = 10, 3.8 Hz), 2.51 (dd, 1H, *J* = 16, 2.5 Hz), 2.71 (dd, 1H, *J* = 16, 2.5 Hz), 3.68 (dd, 1H, *J* = 11, 3.3 Hz), 3.77 (t, 1H, *J* = 10 Hz), 3.81 (s, 3H), 4.00 (d, 1H, *J* = 5.0 Hz), 4.03 (dd, 1H, *J* = 8.5, 7.0 Hz), 4.07 (dd, 1H, *J* = 8.5, 6.0 Hz), 4.17 (t, 1H, *J* = 6.5 Hz), 4.62 (d, 1H, *J* = 12 Hz), 4.77 (d, 1H, *J* = 11 Hz), 4.83 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.02 (d, 1H, *J* = 2.0 Hz), 6.89 (d, 2H, *J* = 9.0 Hz), 7.32 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.2, 6.1, 6.4, 6.9, 7.1, 7.2, 23.5, 23.7, 27.0, 36.3, 36.7, 55.4, 55.4, 66.6, 68.1, 70.0, 72.2, 74.4, 77.9, 78.7, 78.8, 80.6, 83.0, 86.1, 91.4, 95.0, 113.8, 120.2, 129.0, 129.5, 130.9, 139.5, 159.2; FT-IR (neat) ν 3499, 3312, 2955, 1614, 1514, 1462, 1415, 1336, 1247, 1110 cm^{-1}; MALDI-TOF-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{45}H_{74}NaO_8Si_3$ 849.4589, found 849.4596.

To a solution of the above alcohol (482 mg, 0.583 mmol) in CH_2Cl_2 (12 mL) were added pyridine (236 μL, 2.92 mmol) and Dess−Martin periodinane (494 mg, 1.17 mmol). The mixture was stirred for 2 h at room temperature, diluted with hexane, and quenched with saturated $Na_2S_2O_3$ solution and then saturated $NaHCO_3$ solution. The resulting mixture was extracted with hexane (2×), and the combined organic layer was dried over anhydrous $MgSO_4$. After concentration, the residue was purified by column chromatography (Florisil, hexane/AcOEt = 10) to give aldehyde **12** (433 mg, 0.525 mmol, 90%) as a colorless syrup: $[\alpha]_D^{24.0}$ +2.1° (*c* 0.570, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.60 (q, 6H, *J* = 7.8 Hz), 0.63 (q, 6H, *J* = 7.8 Hz), 0.71 (q, 6H, *J* = 7.8 Hz), 0.92 (t, 9H, *J* = 7.8 Hz), 0.97 (t, 9H, *J* = 7.8 Hz), 0.97 (t, 9H, *J* = 7.8 Hz), 1.63−1.69 (m, 4H), 1.71−1.76 (m, 2H), 1.84−1.95 (m, 2H), 1.88 (brs, 1H), 2.52 (dd, 1H, *J* = 16, 1.8 Hz), 2.73 (dd, 1H, *J* = 16, 1.5 Hz), 3.81 (s, 3H), 4.01 (d, 1H, *J* = 5.0 Hz), 4.04 (dd, 1H, *J* = 8.5, 7.0 Hz), 4.12 (dd, 1H, *J* = 8.5, 6.0 Hz), 4.16 (t, 1H, *J* = 6.5 Hz), 4.62 (d, 1H, *J* = 12 Hz), 4.77 (d, 1H, *J* = 11 Hz), 4.83 (d, 1H, *J* = 5.0 Hz), 6.08 (s, 1H), 6.89 (d, 2H, *J* = 8.0 Hz), 7.32 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.2, 6.1, 6.4, 6.9, 7.0, 7.2, 23.5, 23.8, 27.0, 36.2, 36.4, 55.4, 55.4, 66.3, 70.0, 70.1, 72.3, 78.1, 78.7, 78.7, 79.7, 80.5, 85.1, 86.1, 87.9, 95.0, 113.8, 120.9, 129.0, 129.1, 130.8, 140.5, 159.2, 195.5, 195.6; FT-IR (neat) ν 3312, 2956, 2877, 1745, 1614, 1515, 1462, 1415, 1337, 1248, 1172, 1120 cm^{-1}; MALDI-TOF-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{45}H_{72}NaO_8Si_3$ 847.4433, found 847.4418.

Alcohol 14. To well-ground anhydrous $CeCl_3$ (1.00 g, 4.06 mmol) was slowly added THF (50 mL) with vigorous stirring at 0 °C. The suspension was stirred for 36 h at room temperature. A cooled (0 °C) solution of $LiN(TMS)_2$ in THF, which was freshly prepared from 1,1,1,3,3,3-hexamethyldisilazane (1.04 mL, 4.91 mmol) and *n*BuLi (1.56 M solution in hexane, 2.85 mL, 4.45 mmol) in THF (50 mL), was added to the above suspension at −40 °C. The mixture was gradually warmed to −20 °C over 1 h, and a solution of aldehyde **12** (386 mg, 0.468 mmol) in THF (50 mL) was added in one portion. The resulting mixture was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was quenched with phosphate buffer (pH 7.0) and filtered through a pad of Celite. The precipitate was washed with Et_2O, and the combined filtrate was concentrated. The residue was again extracted with hexane, and the organic extracts were washed with saturated NH_4Cl solution and brine and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/EtOAc = 10 to 8) to give the nine-membered alcohol **14** (282 mg, 0.342 mmol, 73%) as a yellow syrup: $[\alpha]_D^{24.0}$ −46.4° (*c* 0.450, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (q, 6H, *J* = 7.5 Hz), 0.67 (q, 6H, *J* = 8.3 Hz), 0.73 (q, 6H, *J* = 7.8 Hz), 0.96 (t, 9H, *J* = 7.5 Hz), 0.97 (t, 9H, *J* = 8.0 Hz), 0.98 (t, 9H, *J* = 7.5 Hz), 1.57−1.67 (m, 4H), 1.70−1.77 (m, 2H), 1.79−1.85 (m, 2H), 2.25 (dd, 1H, *J* = 17, 3.8 Hz), 2.36 (br s, 1H), 2.67 (dd, 1H, *J* = 17, 1.8 Hz), 3.81 (s, 3H), 4.01 (d, 1H, *J* = 4.5 Hz), 4.06 (dd, 1H, *J* = 8.0, 7.0 Hz), 4.09 (dd, 1H, *J* = 8.5, 6.0 Hz), 4.35 (t, 1H, *J* = 6.5 Hz), 4.54 (dd, 1H, *J* = 4.8, 2.3 Hz), 4.58 (d, 1H, *J* = 11 Hz), 4.67 (br s, 1H), 4.70 (d, 1H, *J* = 11 Hz), 5.87 (d, 1H, *J* = 2.0 Hz), 6.89 (d, 2H, *J* = 9.0 Hz), 7.26 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.2, 5.9, 6.5, 7.0, 23.4, 23.8, 29.5, 29.9, 36.3, 36.6, 55.5, 67.0, 72.7, 75.3, 75.4, 78.7, 78.8, 78.9, 82.8, 84.5, 85.3, 91.0, 91.8, 95.3, 97.2, 113.9, 119.6, 129.3, 130.3, 131.4, 135.8, 135.9, 159.4; FT-IR (neat) ν 3469, 2955, 2877, 1614, 1515, 1457, 1415, 1337, 1302, 1247, 1108 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{45}H_{72}NaO_8Si_3$ 847.4427, found 847.4425.

Epoxide 16. To a solution of the nine-membered ring alcohol **14** (983 mg, 1.19 mmol) in CH_2Cl_2 (24 mL) were added Et_3N (1.66 mL, 11.9 mmol) and MsCl (138 μL, 1.79 mmol) at −20 °C. The mixture was stirred for 15 min at −20 °C and quenched with saturated $NaHCO_3$ solution. The resulting mixture was extracted with hexane (2×), and the combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. Concentration of the solution gave the corresponding mesylate (1.06 g), which was subjected to the next reaction without purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (q, 6H, *J* = 8.0 Hz), 0.67 (q, 6H, *J* = 8.0 Hz), 0.77 (q, 6H, *J* = 8.0 Hz), 0.98 (t, 9H, *J* = 8.0 Hz), 0.98 (t, 18H, *J* = 8.0 Hz), 1.59−1.70 (m, 4H), 1.71−1.77 (m, 2H), 1.79−1.85 (m, 2H), 2.29 (dd, 1H, *J* = 17, 4.0 Hz), 2.72 (dd, 1H, *J* = 17, 1.8 Hz), 3.12 (s, 3H), 3.81 (s, 3H), 3.40 (dd, 1H, *J* = 9.0, 7.0 Hz), 4.03 (d, 1H, *J* = 4.5 Hz), 4.04 (dd, 1H, *J* = 9.0, 6.0 Hz), 4.32 (dd, 1H, *J* = 7.0, 6.0 Hz), 4.55 (dd, 1H, *J* = 4.5, 2.0 Hz), 4.57 (d, 1H, *J* = 11 Hz), 4.70 (d, 1H, *J* = 11 Hz), 5.35 (dd, 1H, *J* = 4.0, 1.8 Hz), 5.93 (d, 1H, *J* = 2.0 Hz), 6.89 (d, 2H, *J* = 8.5 Hz), 7.26 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.2, 5.8, 6.5, 6.9, 7.0, 7.2, 23.4, 23.9, 29.7, 29.9, 36.1, 36.4, 38.9, 55.5, 66.6, 72.7, 78.4, 78.8, 80.1, 80.8, 81.3, 84.4, 91.6, 95.0, 95.9, 97.3, 114.0, 119.6, 128.5, 129.4, 130.1, 130.8, 136.6, 159.5; FT-IR (neat) ν 2956, 2877, 1614, 1515, 1462, 1415, 1370, 1336, 1248, 1180, 1109 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{46}H_{74}NaO_{10}SSi_3$ 925.4203, found 925.4207.

To a solution of the above mesylate (1.06 g) in THF (23 mL) was added TBAF (1.0 M solution in THF, 2.57 mL, 2.57 mmol) at −40 °C. The mixture was stirred for 15 min at −40 to −35 °C and quenched with saturated NH_4Cl solution. The resulting mixture was extracted with AcOEt (3×), and the combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 8 to 3 to 2 to 1) to give epoxide **16** (393 mg, 0.679 mmol, 58% in two steps) and diol **15** (121 mg, 0.180 mmol, 15% in two steps) as yellow syrups. To a solution of diol **15** (121 mg, 0.180 mmol) in EtOH (3.6 mL) was added K_2CO_3 (24.9 mg, 0.180 mmol). The mixture was stirred for 17 h at room temperature and concentrated. The residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 3) to give epoxide **16** (54.2 mg, 0.0936 mmol, 52% from **15**): $[\alpha]_D^{23.0}$ +7.6° (*c* 0.810, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (q, 6H, *J* = 8.0 Hz), 0.95 (t, 9H, *J* = 8.0 Hz), 1.66−1.73 (m, 4H), 1.74−1.81 (m, 2H), 1.88−1.97 (m, 2H), 2.35 (d, 1H, *J* = 18 Hz), 2.74 (d, 1H, *J* = 18 Hz), 3.52 (s, 1H), 3.81 (s, 3H), 3.94 (d, 1H, *J* = 5.0 Hz), 4.01 (dd, 1H, *J* = 5.5, 8.0 Hz), 4.05 (t, 1H, *J* = 5.8 Hz), 4.13 (dd, 1H, *J* = 6.0, 8.0 Hz), 4.53−4.56 (m, 1H),4.65 (d, 1H, *J* = 11.5 Hz), 4.69 (d, 1H, *J* = 11.5 Hz), 5.91 (d, 1H, *J* = 2.0 Hz), 6.90 (d, 2H, *J* = 8.0 Hz), 7.29 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.4, 7.2, 23.5, 23.8, 29.3, 36.2, 36.3, 54.3, 55.5, 64.3, 67.5, 72.9, 74.4, 78.1, 83.2, 85.1, 88.1, 88.6, 95.1, 96.3, 114.1, 120.8, 129.4, 130.2, 131.7, 134.3, 159.6; FT-IR (neat) ν 3480, 2954, 2875, 1613, 1514, 1455, 1337, 1302, 1247, 1108 cm^{-1}; HR-

ESI-FT-ICR-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{33}H_{42}NaO_7Si$ 601.2592, found 601.2592.

Triol 18. To a suspension of epoxide **16** (86.8 mg, 0.150 mmol) and naphthoic acid **17** (105 mg, 0.450 mmol) in CH_2Cl_2 (3.0 mL) were added EDC·HCl (115 mg, 0.600 mmol) and DMAP (1.8 mg, 0.015 mmol) at 0 °C. The mixture was stirred for 10 min at 0 °C, and naphthoic acid **17** (21.5 mg, 0.0926 mmol), EDC·HCl (17.8 mg, 0.0926 mmol), and DMAP (1.1 mg, 0.0093 mmol) were further added. The resulting mixture was stirred for 10 min at 0 °C and quenched with water. The mixture was extracted with EtOAc (3×), and the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 8 to 6) to give the corresponding ester (74.3 mg, 0.0937 mmol, 64%) as a colorless syrup: $[\alpha]_D^{24.0}$ −14.5° (*c* 0.510, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (q, 6H, *J* = 7.8 Hz), 0.93 (t, 9H, *J* = 7.8 Hz), 1.66−1.73 (m, 4H), 1.74−1.80 (m, 2H), 1.88−1.98 (m, 2H), 2.52 (d, 1H, *J* = 18 Hz), 2.65 (s, 3H), 2.82 (d, 1H, *J* = 18 Hz), 3.56 (s, 1H), 3.72 (s, 3H), 3.83 (s, 3H), 4.03 (dd, 1H, *J* = 7.5, 5.0 Hz), 4.06 (t, 1H, *J* = 5.3 Hz), 4.14 (dd, 1H, *J* = 7.5, 5.8 Hz), 4.40 (d, 1H, *J* = 5.0 Hz), 4.61 (d, 1H, *J* = 11 Hz), 4.65 (d, 1H, *J* = 11 Hz), 5.93 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.12 (d, 1H, *J* = 2.0 Hz), 6.72 (d, 2H, *J* = 8.5 Hz), 6.92 (br s, 1H), 7.05 (d, 1H, *J* = 9.5 Hz), 7.16 (d, 2H, *J* = 8.5 Hz), 8.07 (br s, 1H), 8.07 (d, 1H, *J* = 9.5 Hz), 12.12 (s, 1H); FT-IR (neat) ν 2954, 2876, 1644, 1614, 1514, 1455, 1414, 1376, 1337, 1306, 1248, 1203 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{46}H_{52}NaO_{10}Si$ 815.3222, found 815.3226.

To a solution of the above ester (147 mg, 0.186 mmol) in CH_3CN (6.2 mL) was added 46% aqueous hydrofluoric acid (67.4 μL) at 0 °C. The mixture was stirred for 1.6 h at 0 °C and quenched with saturated $NaHCO_3$ solution. The resulting mixture was diluted with Et_2O and stirred for 30 min at 0 °C. The mixture was extracted with AcOEt (3×), and the combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 2 to 1 to 0.33, containing 2.5% MeOH) to give triol **18** (93.0 mg, 0.128 mmol, 69%) as a colorless syrup and tetrol **19** (31.8 mg, 0.0520 mmol, 28%) as colorless solid. Data for **18**: $[\alpha]_D^{22.0}$ −55.1° (*c* 0.482, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.93 (br s, 1H), 2.38 (br s, 1H), 2.63 (s, 3H), 2.68 (d, 1H, *J* = 18 Hz), 2.86 (d, 1H, *J* = 18 Hz), 3.65 (s, 3H), 3.72 (s, 3H), 3.76 (s, 1H), 3.80 (br dd, 1H, *J* = 12, 5.7 Hz), 3.96 (br dd, 1H, *J* = 12, 2.5 Hz), 4.02 (br dd, 1H, *J* = 4.5, 3.5 Hz), 4.42 (d, 1H, *J* = 5.0 Hz), 4.63 (d, 1H, *J* = 12 Hz), 4.71 (d, 1H, *J* = 12 Hz), 6.00 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.12 (d, 1H, *J* = 2.0 Hz), 6.66 (d, 2H, *J* = 8.5 Hz), 6.88 (d, 1H, *J* = 2.0 Hz), 7.04 (d, 1H, *J* = 9.5 Hz), 7.16 (d, 2H, *J* = 8.5 Hz), 7.91 (d, 1H, *J* = 2.0 Hz), 8.06 (d, 1H, *J* = 9.5 Hz), 12.02 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.4, 7.2, 20.3, 29.5, 53.0, 55.3, 55.3, 63.5, 64.0, 69.6, 73.0, 80.8, 83.4, 85.0, 87.9, 88.5, 91.1, 97.3, 104.2, 105.0, 114.0, 115.8, 116.3, 123. 2, 129.3, 129.4, 130.6, 133.2, 134.2, 134.3, 137.3, 159.5, 159.6, 165.2, 172.0; FT-IR (film) ν 3417, 2954, 2876, 1644, 1615, 1514, 1463, 1412, 1377, 1345, 1306, 1248, 1204 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) [M + Na]$^+$ calcd for $C_{41}H_{46}NaO_{10}Si$ 749.2752, found 749.2755. Data for **19**: $[\alpha]_D^{22.0}$ −110° (*c* 0.610, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (q, 6H, *J* = 8.0 Hz), 0.94 (t, 9H, *J* = 8.0 Hz), 1.98 (br s, 1H), 2.36 (br s, 1H), 2.54 (d, 1H, *J* = 18 Hz), 2.65 (s, 3H), 2.82 (d, 1H, *J* = 18 Hz), 3.70 (s, 1H), 3.72 (s, 3H), 3.79 (br dd, 1H, *J* = 12, 5.5 Hz), 3.83 (s, 3H), 3.96 (br dd, 1H, *J* = 12, 2.5 Hz), 4.04−4.08 (m, 1H), 4.40 (d, 1H, *J* = 5.0 Hz), 4.61 (d, 1H, *J* = 12 Hz), 4.65 (d, 1H, *J* = 12 Hz), 5.93 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.13 (d, 1H, *J* = 2.0 Hz), 6.73 (d, 2H, *J* = 8.5 Hz), 6.92 (d, 1H, *J* = 2.0 Hz), 7.05 (d, 1H, *J* = 9.0 Hz), 7.16 (d, 2H, *J* = 8.5 Hz), 8.06 (d, 1H, *J* = 2.0 Hz), 8.07 (d, 1H, *J* = 9.0 Hz), 12.11 (s, 1H); FT-IR (film) ν 3391, 2932, 1644, 1614, 1514, 1454, 1414, 1378, 1307, 1248, 1204 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{35}H_{32}NaO_{10}$ 635.1888, found 635.1892.

Diol 20. To a solution of triol **18** (24.1 mg, 0.0332 mmol) in THF (1 mL) was added 1,1′-carbonyldiimidazole (10.8 mg, 0.066 mmol). The mixture was stirred for 15 h at room temperature, and 1,1′-carbonyldiimidazole (5.4 mg, 0.033 mmol) was further added. The resulting mixture was stirred for 24 h and concentrated. The residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 3 to 2) to give the corresponding carbonate (19.4 mg, 0.0258 mmol, 78%) as a colorless syrup: $[\alpha]_D^{22.0}$ −57.7° (*c* 0.388, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.63 (q, 6H, *J* = 7.5 Hz), 0.93 (t, 9H, *J* = 7.5 Hz), 2.55 (d, 1H, *J* = 18 Hz), 2.66 (s, 3H), 2.84 (d, 1H, *J* = 18 Hz), 3.63 (s, 1H), 3.73 (s, 3H), 3.84 (s, 3H), 4.41 (d, 1H, *J* = 5.0 Hz), 4.55 (dd, 1H, *J* = 7.5, 5.5 Hz), 4.57−4.66 (m, 4H, H14), 5.96 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.21 (d, 1H, *J* = 2.0 Hz), 6.73 (d, 2H, *J* = 8.5 Hz), 6.92 (d, 1H, *J* = 1.5 Hz), 7.05 (d, 1H, *J* = 9.5 Hz), 7.16 (d, 2H, *J* = 8.5 Hz), 8.05 (d, 1H, *J* = 1.5 Hz), 8.08 (d, 1H, *J* = 9.5 Hz), 12.08 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.4, 7.2, 20.4, 29.6, 55.2, 55.4, 55.4, 63.6, 67.3, 73.1, 74.8, 80.8, 82.4, 85.1, 89.7, 90.4, 91.0, 94.2, 104.2, 105.2, 114.1, 115.9, 116.4, 123.3, 129.3, 129.5, 131.8, 133.3, 133.6, 134.2, 137.4, 153.9, 159.7, 159.7, 165.4, 172.0; FT-IR (film) ν 2955, 2876, 1821, 1644, 1615, 1514, 1464, 1412, 1377, 1344, 1306, 1248, 1205 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) [M+Na]$^+$, calcd for $C_{42}H_{44}NaO_{11}Si$ 775.2545, found 775.2546.

To a solution of the above carbonate (19.4 mg, 0.0258 mmol) in THF (1 mL) was added TBAF (1.0 M solution in THF, 38.7 μL, 0.0387 mmol) at 0 °C. The mixture was stirred for 40 min at 0 °C and concentrated. The residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 1.5 to 0.5 followed by AcOEt/MeOH = 20) to give diol **20** (13.9 mg, 0.0218 mmol, 84%) as a colorless solid: $[\alpha]_D^{22.0}$ −119° (*c* 0.560, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.64 (s, 3H), 2.71 (d, 1H, *J* = 18 Hz), 2.78 (br s, 1H), 2.87 (d, 1H, *J* = 18 Hz), 3.65 (s, 3H), 3.71 (s, 1H), 3.72 (s, 3H), 4.41 (d, 1H, *J* = 5.0 Hz), 4.55−4.59 (m, 2H), 4.64 (d, 1H, *J* = 12 Hz), 4.66 (t, 1H, *J* = 11 Hz), 4.70 (d, 1H, *J* = 12 Hz), 6.02 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.21 (d, 1H, *J* = 2.0 Hz), 6.67 (d, 2H, *J* = 9.0 Hz), 6.89 (br s, 1H), 7.05 (d, 1H, *J* = 9.5 Hz), 7.16 (d, 2H, *J* = 9.0 Hz), 7.90 (br s, 1H), 8.07 (d, 1H, *J* = 9.5 Hz), 11.99 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.2, 28.4, 55.1, 55.2, 55.2, 63.3, 67.2, 73.2, 74.3, 80.2, 82.8, 83.6, 88.2, 88.3, 88.8, 94.6, 104.2, 104.2, 114.0, 116.1, 116.6, 123.2, 128.9, 129.6, 131.8, 132.3, 133.2, 134.2, 137.1, 153.6, 159.6, 159.6, 165.1, 171.8; FT-IR (film) ν 3387, 2932, 1820, 1644, 1614, 1514, 1465, 1412, 1378, 1307, 1249, 1204 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{36}H_{30}NaO_{11}$ 661.1680, found 661.1677.

TES Ether 21. To a solution of diol **20** (35.9 mg, 0.0562 mmol) in CH_2Cl_2 (2 mL) were added H_2O (100 μL) and DDQ (38.3 mg, 0.169 mmol). The mixture was stirred for 10 h at room temperature and quenched with saturated $NaHCO_3$ solution and then saturated $Na_2S_2O_3$ solution. The resulting mixture was extracted with EtOAc (3×), and the combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After concentration, the residue was purified by flash column chromatography (silica gel, hexane/AcOEt = 2 to 0.5) to give the corresponding triol (23.5 mg, 0.0453 mmol, 81%) as a colorless solid: $[\alpha]_D^{23.0}$ −39.0° (*c* 0.384, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.63 (s, 3H), 2.65 (d, 1H, *J* = 18 Hz), 2.83 (br s, 1H), 2.97 (d, 1H, *J* = 18 Hz), 3.63 (br s, 1H), 3.71 (s, 1H), 3.90 (s, 3H), 4.51 (d, 1H, *J* = 4.5 Hz), 4.53 (dd, 1H, *J* = 8.0, 5.5 Hz), 4.61 (dd, 1H, *J* = 9.0, 5.5 Hz), 4.68 (t, 1H, *J* = 8.5 Hz), 5.73 (dd, 1H, *J* = 4.5, 2.0 Hz), 6.22 (d, 1H, *J* = 2.0 Hz), 6.91 (d, 1H, *J* = 2.0 Hz), 7.04 (d, 1H, *J* = 9.0 Hz), 7.98 (d, 1H, *J* = 2.0 Hz), 8.08 (d, 1H, *J* = 9.0 Hz), 11.83 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.2, 28.2, 55.3, 55.4, 63.4, 67.3, 74.5, 83.4, 83.5, 84.0, 84.3, 88.3, 88.9, 94.7, 103.7, 104.1, 116.1, 116.6, 123.2, 130.9, 132.5, 133.7, 134.1, 137.4, 153.7, 159.8, 165.4, 173.4; FT-IR (film) ν 3461, 2930, 1818, 1790, 1644, 1615, 1454, 1413, 1379, 1310, 1265, 1206 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) [M + Na]$^+$, calcd for $C_{28}H_{22}NaO_{10}$ 541.1105, found 541.1107.

To a solution of the above triol (19.2 mg, 0.0370 mmol) in CH_2Cl_2 (2 mL) were added 2,6-lutidine (129 μL, 1.11 mmol) and (TES)-

OTf (66.9 μL, 0.296 mmol) at −90 °C. The mixture was stirred for 15 min at −90 °C and quenched with saturated $NaHCO_3$ solution. The resulting mixture was extracted with AcOEt (2×), and the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by flash column chromatography (silica gel, hexane−hexane/AcOEt = 4 to 3 to 2) to give bis(TES ether) **21** (19.5 mg, 0.0261 mmol, 71%) as a pale yellow syrup: $[\alpha]_D^{21.5}$ −17.7° (*c* 0.390, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.56 (q, 6H, *J* = 8.0 Hz), 0.81 (q, 6H, *J* = 8.0 Hz), 0.85 (t, 9H, *J* = 8.0 Hz), 1.00 (t, 9H, *J* = 8.0 Hz), 2.58 (d, 1H, *J* = 18 Hz), 2.61 (s, 3H), 2.76 (d, 1H, *J* = 18 Hz), 3.69 (s, 1H), 3.84 (s, 3H), 4.45 (d, 1H, *J* = 5.0 Hz), 4.57 (dd, 1H, *J* = 7.3, 5.0 Hz), 4.60 (dd, 1H, *J* = 7.3, 5.0 Hz), 4.67 (t, 1H, *J* = 7.5 Hz), 5.57 (dd, 1H, *J* = 5.0, 2.0 Hz), 6.36 (d, 1H, *J* = 2.0 Hz), 6.88 (d, 1H, *J* = 2.0 Hz), 6.90 (d, 1H, *J* = 2.0 Hz), 6.94 (d, 1H, *J* = 9.0 Hz), 7.85 (d, 1H, *J* = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.8, 5.5, 6.7, 6.8, 19.7, 28.1, 55.0, 55.2, 63.3, 67.1, 74.3, 82.6, 82.7, 83.3, 88.7, 89.4, 94.1, 100.8, 116.9, 117.8, 118.5, 123.6, 127.7, 131.2, 132.9, 133.3, 136.5, 152.0, 153.7, 158.7, 168.6; FT-IR (film) ν 2956, 2877, 1822, 1730, 1621, 1512, 1465, 1410, 1338, 1267, 1205 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{40}H_{50}NaO_{10}Si_2$ 769.2835, found 769.2839.

Neocarzinostatin Chromophore Aglycon (2). To a solution of alcohol **21** (3.9 mg, 0.0052 mmol) in CH_2Cl_2 (1.2 mL) was added Martin sulfurane dehydrating reagent (23.0 mg, 0.0340 mmol). The mixture was stirred for 10 min at room temperature and concentrated to 0.1 mL. A solution of trifluoroacetic acid−THF−water (1:10:5) was added, and the mixture was stirred for 35 min at 0 °C. Et_2O (10 mL) and saturated $NaHCO_3$ solution (5 mL) were added, and the resulting mixture was stirred for 1 h at 0 °C. The aqueous phase was extracted with Et_2O−AcOEt (2×), and the combined organic layer was dried over anhydrous $MgSO_4$. After filtration, the solution was concentrated to 0.3 mL and exposed to flash column chromatography (silica gel, hexane/AcOEt = 1.5 at 0 °C). The fractions containing aglycon were pooled, concentrated to 0.2 mL, and then subjected to HPLC (Mightysil Si 60, 250-10 (5 μm), flow rate 4 mL/min, eluent hexane/AcOEt = 1, UV detection 254 nm). The fractions including pure aglycon **2** (retention time 10 min 15 s) were concentrated to 0.2 mL, diluted with MeOH (3 mL), and concentrated to 0.2 mL. This process was repeated, and the concentrate was taken up in MeOH (5 mL). A 0.5 mL solution was diluted to 10 mL with MeOH. UV absorbance was determined to quantitate **2** (A_{302} = 0.51, ϵ_{302} = 7040 M^{-1} cm^{-1},[16c] 2.3 mg, 0.0032 mmol, 61% in two steps from **21**): ^{1}H NMR (400 MHz, CD_3CN) δ 2.60 (s, 3H), 3.83 (s, 3H), 4.06 (d, 1H, *J* = 1.6 Hz), 4.24 (brd, 1H, *J* = 5.2 Hz), 4.39 (dd, 1H, *J* = 9.2, 5.2 Hz), 4.62 (t, 1H, *J* = 8.8 Hz), 4.91 (dd, 1H, *J* = 8.4, 5.6 Hz), 4.89−4.93 (m, 1H), 5.66 (br s, 1H), 6.01 (t, 1H, *J* = 3.0 Hz), 6.67 (br s, 1H), 6.92 (br s, 1H), 7.04 (d, 1H, *J* = 9.2 Hz), 7.95 (br s, 1H), 8.13 (d, 1H, *J* = 9.2 Hz), 11.59 (s, 1H); FT-IR (film) ν 3677, 3068, 2926, 1820, 1739, 1613, 1465, 1380 cm^{-1}; HR-ESI-FT-ICR-MS (*m*/*z*) $[M + Na]^+$, calcd for $C_{28}H_{20}NaO_9$ 523.1000, found 523.1002; CD (MeOH) λ_{ext} 330.4 nm ($\Delta\epsilon$ +1.06), 314.7 (0.0), 294.1 (−1.92), 289.8 (−1.86), 264.1 (−5.84), 243.9 (0.0).

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research (Wakate B) from the Japan Society for the Promotion of Science (JSPS). We are grateful to Mr. Hiroyuki Monma, Research and Analytical Center for Giant Molecules, Tohoku University, for measurement of ESI-FT-ICR mass spectrometry, and to Prof. Masahiro Toyota, Osaka Prefecture University, for his generous support.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **4**−**22**, and ^{1}H NMR, UV, CD, and mass spectra of aglycon **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO052031O