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A modified approach to the phomoidrides: synthesis of a late-stage intermediate containing a key carbon quaternary stereocenter

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Abstract—A previously developed approach to the synthesis of the phomoidrides has been modified to incorporate all necessary carbon atoms prior to the key tandem carbonylation/Cope rearrangement reaction. This modification necessitated the synthesis of a challenging all-carbon quaternary stereocenter, which in turn rendered ineffective several reactions from the original synthesis. An oxidative radical cleavage of a spirocyclopropane ring system was developed that accomplishes the synthesis of the quaternary center, and a regioselective double hydroboration reaction was devised that provides an alternate approach to a key sequence of functional group interconversions, where the originally developed route was found to be ineffective.

1. Introduction

In the context of a screening program, Kaneko and coworkers identified two new natural products, phomoidrides A (CP-225917) and B (CP-263114), which displayed moderate activity against both RAS farnesyl transferase and squalene synthase (Fig. 1).[1] The discovery was followed a few years later by the identification of two new secondary metabolites in the fermentation broth, phomoidrides C and D, both thought to derive from the same primary biosynthetic product, phomoidride B.[2] The intriguing and novel structures of these natural products inspired intensive synthetic effort that has thus far culminated in four total syntheses from the Nicolaou,[3] Shair,[4] Fukuyama,[5] and Danishefsky[6] groups as well as numerous synthetic approaches.[7]

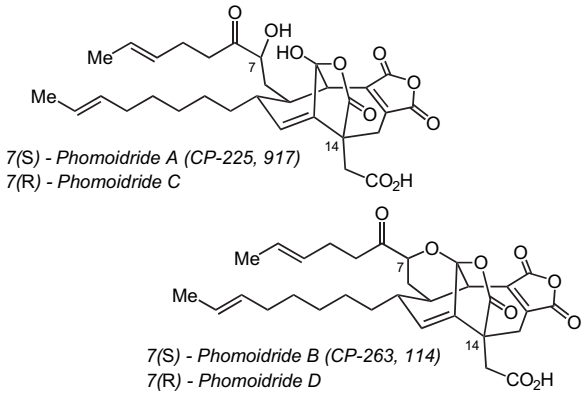

Figure 1. Phomoidrides A–D.

We have previously described an approach to the synthesis of phomoidride D based on a tandem carbonylation/silyloxy-Cope rearrangement sequence exemplified by the conversion of **1** to **2** (Scheme 1).[8] Although there is precedent for the conversion of the silyl enol ether into the requisite maleic anhydride moiety, we became intrigued by the notion of building the two missing carbon atoms of the anhydride into the carbonylation/Cope precursor so as to produce **3** from **4**. A straightforward and precedented oxidation sequence[9] would then be all that remained to carry out following the tandem reaction, minimizing the number of transformations that would have to be carried out in the presence of the sensitive pseudoester. While this looked like an attractive possibility on paper, it also necessitated a significantly redesigned synthesis of the densely functionalized [2.2.1]-bicycloheptane precursor to the tandem carbonylation/Cope rearrangement reaction. Specifically, whereas the vinyl group of **1** was installed by a simple vinyl lithium addition to the corresponding ketone, the modified synthetic plan necessitated the design of a synthesis that would allow the efficient construction of a carbon quaternary stereocenter (marked * in structure **4**, Scheme 1). In the retrosynthesis of **4** to **5**, it was assumed that what had worked in the previous route to convert the endocyclic olefin into the β-trifloxy enone would work in this series as well (as will be described, this assumption proved unwarranted). Compound **5** was identified as an initial target due to its straightforward, at least in principle, disconnection into two simpler fragments by way of a Diels–Alder (DA) cycloaddition. In this case, however, the

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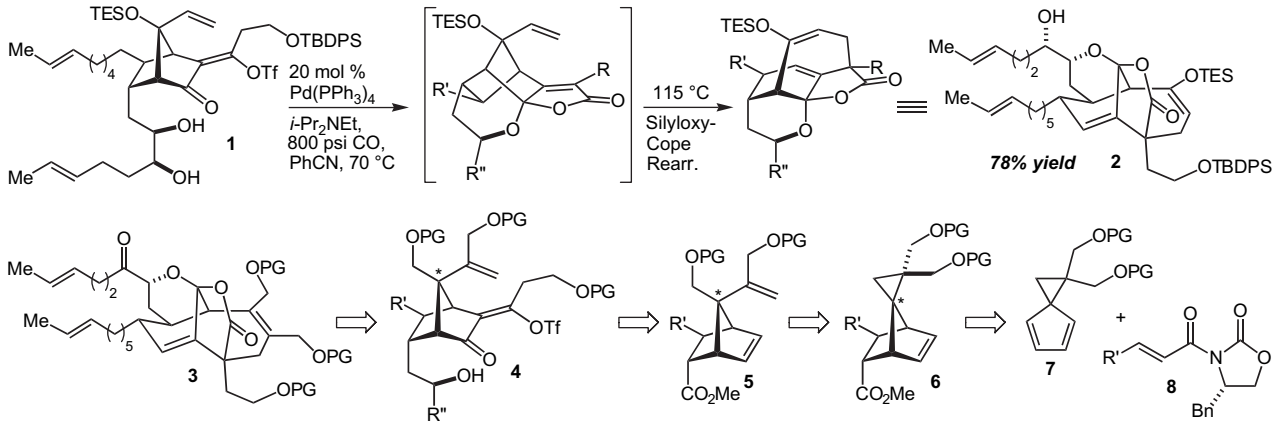


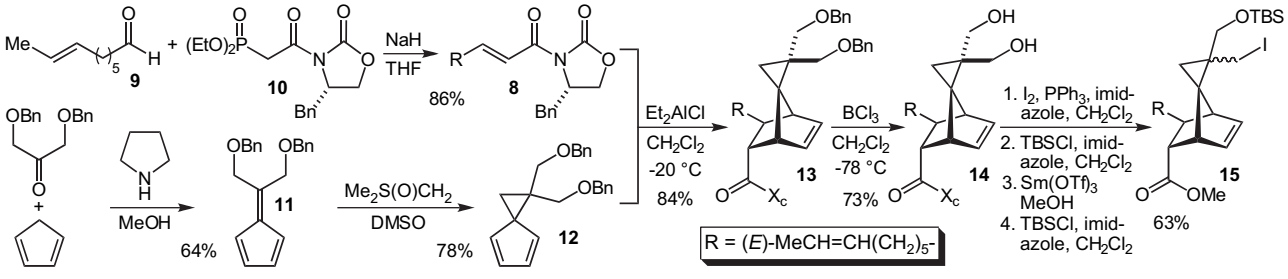
Scheme 1. Modified retrosynthesis with all necessary carbon atoms built into the Cope rearrangement precursor.

disconnection leads back to a 5,5-disubstituted cyclopentadiene, and a DA reaction that would very likely be highly problematic, at best. Thus, it was envisioned that the carbon atoms of the target quaternary center would be 'packaged' as a spirocyclopropane as in structure **6**, which leads to diene **7** and dienophile **8** upon DA disconnection. This notion was inspired by a demonstration by Corey that if constrained in a cyclopropane ring along these lines, 5,5-dialkyl substituted cyclopentadienes are competent partners in DA cycloadditions,[10] and by a demonstration by Carreira that a cyclopropane similar to **6** could be subjected to radical fragmentation under oxidative conditions to install the requisite hydroxymethyl group on the carbon quaternary center.[11] An additional benefit of this new retrosynthesis was that, in contrast to our earlier route, it would lend itself well to an enantioselective version by employing the Evans Diels–Alder protocol.[12] Herein, we describe the successful realization of this strategy in the form of a synthesis of a version of compound **4** (wherein R″=H and PG=TBS) that efficiently incorporates the requisite carbon quaternary stereocenter.

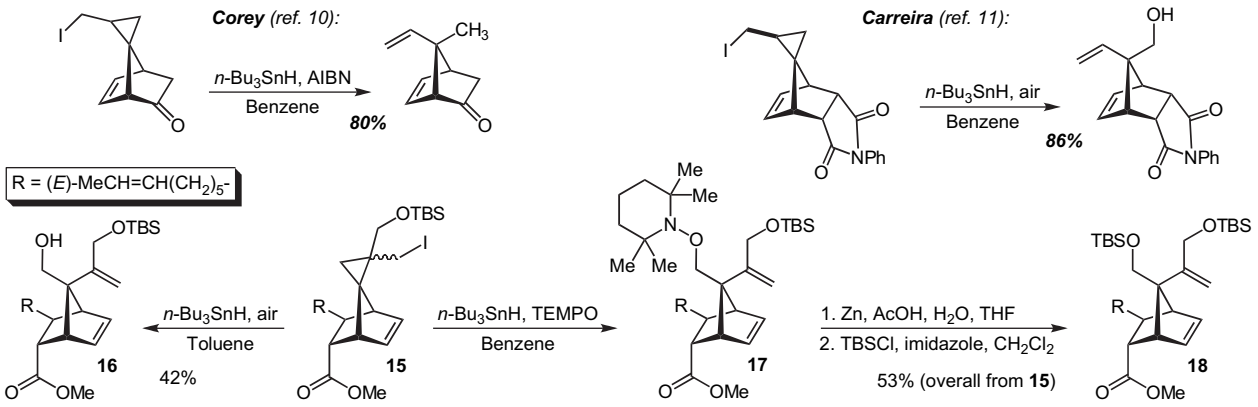
2. Results and discussion

Our studies began with syntheses of the requisite diene **7** and dienophile **8** for the asymmetric Diels–Alder process. Thus, Horner–Wadsworth–Emmons reaction between aldehyde **9** and phosphonate **10**[13] proceeded smoothly to provide dienophile **8** in 86% yield (Scheme 2). The synthesis of diene **7** was initiated with a condensation reaction of cyclopentadiene with dialkoxyacetones employing the conditions reported by Little.[14] We ultimately chose benzyl protecting groups and the condensation reaction in this case gave the fully substituted fulvene **11** in 64% yield. Cyclopropanations of fulvenes using dimethylsulfoxonium methylide[15] had previously been demonstrated,[16] and we were delighted to discover that the method worked well in the case of fulvene **11**, delivering the requisite spirocyclopropyl cyclopentadiene **12** in 78% yield. Diels–Alder cycloaddition of **8** and **12** using the proscribed conditions of Evans[12] proceeded smoothly and delivered **13** in 84% yield, with excellent (>97:3) diastereoselectivity. Removal of both benzyl groups could be accomplished with BCl_3, and gave diol **14** in 73% yield. In anticipation of the radical cleavage of the cyclopropane ring to reveal the fully elaborated carbon quaternary center, it was necessary to convert one of the alcohols into an iodide, to protect the other alcohol, and in addition it proved expedient to remove the oxazolidinone auxiliary at this stage. After some experimentation, a reliable four-step sequence was worked out that led to **15** as a 1:1 mixture of diastereomers. Thus, diol **14** could be smoothly mono-iodinated and the remaining alcohol was protected as its *tert*-butyldimethylsilyl (TBS) ether. $Sm(OTf)_3$-catalyzed methanolysis of the auxiliary followed, but was accompanied by a significant amount of TBS ether deprotection. Simple reprotection of the alcohol as its TBS ether completed the four-step sequence and delivered **15** in 63% overall yield from **14**.

With iodide **15** in hand, we turned our attention to the key radical fragmentation process. Originally developed in a similar context as a reductive process by Corey,[10] this reaction was adapted by Carreira[11] such that the initially produced primary homoallylic radical could be oxidatively trapped to give the illustrated hydroxymethyl product using a Nakamura protocol[17] (Scheme 3). It seemed a straightforward matter to apply this procedure to our system, and indeed,



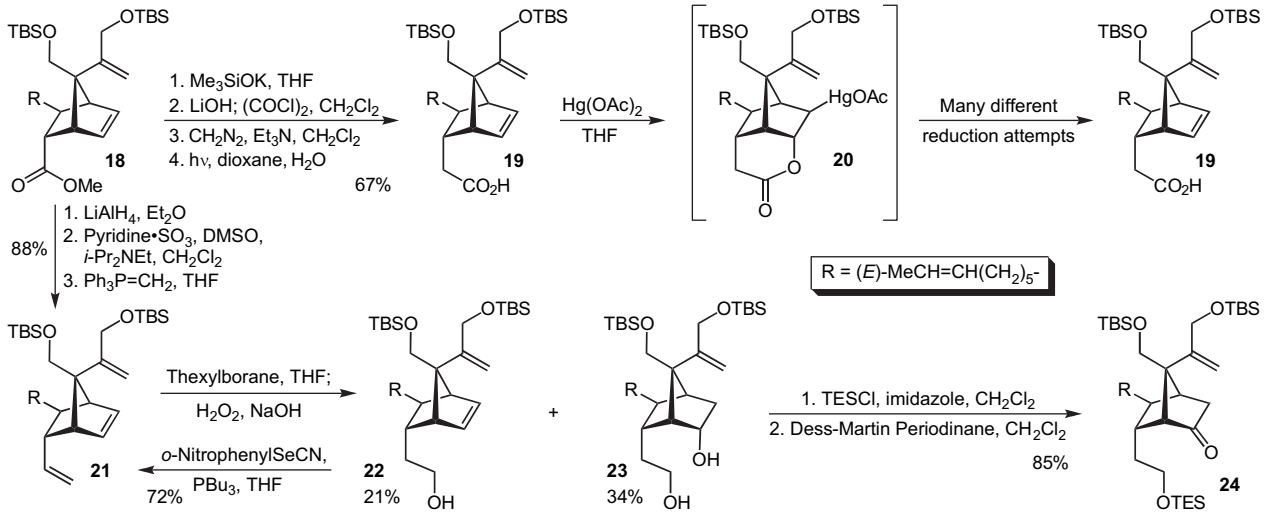
Scheme 2. The key enantioselective Diels–Alder cycloaddition with a 5,5-disubstituted cyclopentadiene.



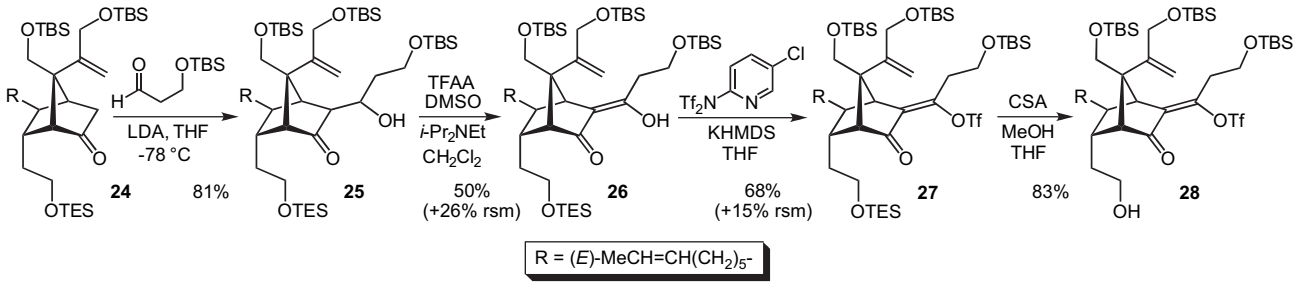
Scheme 3. A radical cleavage of the cyclopropane with an oxidative trap establishes the quaternary stereocenter.

subjection of **15** to these conditions did allow the isolation of alcohol **16** in 42% yield. While the 42% yield in the transformation of **15** to **16** was disappointing, far more problematic was the fact that this reaction was not entirely reliable, and required constant attention for the more than 40 h it took to perform. As it stood, the procedure was simply not amenable to shepherding multi-gram quantities through the sequence, and we were forced to stop and optimize the procedure. The source of the problem seemed to be inefficient trapping of the primary radical by O_2, as the concentration of the reaction and rate of bubbling of air through the solution had to be very carefully controlled. We considered other oxygen atom sources and TEMPO seemed a promising candidate especially in light of Boger's demonstration of the trapping of a primary radical with TEMPO in a high-yielding reaction.[18] Gratifyingly, when **15** was subjected to the action of tributyltin hydride in the presence of TEMPO, smooth and reproducible conversion to **17** ensued. N–O bond reduction was effected with Zn/AcOH, and TBS protection of the resulting alcohol furnished **18** in 53% overall yield from **15**. This three-step sequence proceeded in higher overall yield than the original procedure, and, more importantly, allowed us to access multi-gram quantities of **18**, wherein the all-important carbon quaternary center has been successfully incorporated.

The next task was the one-carbon homologation of the ester and the regioselective functionalization of the endocyclic olefin. Our previously reported route made use of an Arndt–Eistert homologation followed by a mercuriolactonization-reduction sequence,[8a] and we first attempted to apply this sequence to ester **18**. While the Arndt–Eistert sequence proceeded smoothly and gave homologated acid **19** in 67% overall yield, all attempts to induce mercurio or halolactonization reactions followed by reduction of the organomercury or halide species were met with complete failure (Scheme 4). In some cases evidence for successful mercuriolactonization (**20**) could be secured, but attempts at reduction invariably caused reversion to carboxylic acid **19**. As an alternative strategy, hydroboration reactions were considered but it was not clear how the regioselectivity would be controlled. Using the ester group, or a related functional group, as a directing group seemed worth considering and that ultimately inspired the idea that we might orchestrate a double hydroboration on diene **21** (prepared in three simple steps and 88% overall yield from **18**) with a primary borane (RBH_2).[19] Thus, the vinyl group would react first and the resulting dialkylborane would undergo an intramolecular, and thereby regiocontrolled, hydroboration of the endocyclic olefin. In practice, treatment of diene **21** with thexylborane (prepared in situ[20]), followed by an oxidative workup afforded



Scheme 4. Regioselective functionalization of the endocyclic olefin by a double hydroboration reaction.



Scheme 5. Stereoselective installation of the tetrasubstituted β-trifloxy enone.

mono-hydroboration product **22** (which could be recycled back to **21**) in 20% yield, and the desired diol **23** in 34% yield. Attempts to push the reaction to completion or to screen other boranes did not lead to better results. Despite the low yield of **23**, we were delighted that, compared to our original route, we had developed a significantly *more* step-efficient process, and one that proceeded in comparable overall yield relative to the Arndt–Eistert/mercuriolactonization/reduction sequence employed in the original route. Selective protection of the primary alcohol as its triethylsilyl (TES) ether, and oxidation of the secondary alcohol using the Dess–Martin periodinane[21] furnished ketone **24** in 85% yield (over two steps).

Completion of the synthesis of the target late-stage intermediate proved to be straightforward and followed from the originally developed route. Thus, enolization of ketone **24** with LDA and subsequent aldol addition to 3-(*tert*-butyldimethylsilyloxy)-propionaldehyde gave **25** as a 2:1 mixture of diastereomers in 81% yield (Scheme 5). Swern oxidation[22] to give enol **26** proceeded in 50% yield, along with 26% recovered starting material. *Z*-Selective triflation of the enol was accomplished by deprotonation with KHMDS and treatment of the resulting enolate with 2-[*N*,*N*-bis(trifluoromethylsulfonyl)amino]-5-chloropyridine (Comins' reagent[23]) to give triflate **26** in 68% yield, along with 15% recovered starting material. In each of these last two reactions, attempts to force full conversion led to significantly lower yields. Nevertheless, significant quantities of material could be brought through this sequence, and selective methanolysis of the TES ether provided alcohol **27** in 83% yield. This compound is poised for addition of an appropriately configured side chain (R″ in structure **4**, Scheme 1), and the tandem carbonylation/Cope rearrangement reaction.

3. Conclusion

We have developed a modified route to a late-stage intermediate in a projected phomoidride synthesis. This modified route required the synthesis of a challenging all-carbon quaternary stereocenter, which in turn necessitated non-trivial modifications to other parts of the established synthesis. An efficient modification to the oxidative radical cleavage of a tetrasubstituted cyclopropane was developed, and a regioselective double hydroboration was developed as well that gracefully provides a new path through some key functional group interconversions. In all the synthesis of **28** required 19 steps from diene **12** and dienophile **8**, and proceeds efficiently enough that we have been able to prepare gram quantities of **28**. With access to **28** secured, we are now in a position to investigate the installation of the remaining side chain, and the tandem carbonylation/Cope rearrangement in this new more densely functionalized context.

4. Experimental

4.1. General

All reactions were conducted under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring unless otherwise indicated. Degassed solvents were purified by passage through an activated alumina column. ^{1}H NMR spectra were recorded on a Bruker DPX-300 (300 MHz) or a DRX-400 (400 MHz) spectrometer and are reported in parts per million from $CDCl_3$ internal standard (7.26 ppm). Data are reported as follows: (s=singlet, d=doublet, t=triplet, q=quartet, dd=doublet of doublets; coupling constant(s) in hertz; integration; assignment). Proton decoupled ^{13}C NMR spectra were recorded on a Bruker DPX-300 (75 MHz) or a DRX-400 (100 MHz) spectrometer and are reported in parts per million from $CDCl_3$ internal standard (77.0 ppm). Infrared spectra were recorded on a Perkin–Elmer Paragon 1000 FTIR spectrometer. Optical rotations were recorded on a JASCO DIP-1000 digital polarimeter. Low resolution mass spectra were obtained on a JEOL HX110 mass spectrometer in the Columbia University Mass Spectrometry Laboratory.

4.1.1. Dienophile 8. NaH (60% in mineral oil, 4.04 g, 101 mmol) was washed three times with hexanes and suspended in THF (600 mL). Phosphonate **10**[12] (35.9 g, 101 mmol) was dissolved in 50 mL THF and added *slowly* over 30 min to the NaH suspension (*caution*!! H_2 evolution!). The mixture was stirred for an additional 5 h. The clear solution was cooled to 0 °C and aldehyde **9** was added via cannula. The mixture was warmed to room temperature and stirred overnight. The resulting solution was diluted with Et_2O and washed with satd aq NH_4Cl, followed by brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (10% EtOAc/hexanes) to give 24.7 g of **8** (86%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.21 (m, 7H), 5.42–5.40 (m, 2H), 4.72–4.70 (m, 1H), 4.20–4.15 (m, 2H), 3.33 (dd, J=3.1, 13.4 Hz, 1H), 2.79 (dd, J=9.6, 13.4 Hz, 1H), 2.30 (q, J=7.1 Hz, 2H), 1.98 (br s, 2H), 1.64 (d, J=3.3 Hz, 3H), 1.51 (quint, J=7.0 Hz, 2H), 1.36–1.34 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 153.9,

152.5, 135.8, 131.8, 129.9, 129.4, 127.7, 125.3, 120.7, 66.5, 55.8, 38.2, 33.2, 32.9, 29.8, 29.1, 28.4, 18.4; IR ($CHCl_3$ soln) 3009, 2927–2844, 1779, 1768, 1679, 1628 cm^{-1}; $[\alpha]_D$ +54.0 (*c* 1.19, $CHCl_3$); LRMS (FAB^+, M+H) calcd for $C_{21}H_{28}NO_3$ 342.21, found 342.21.

4.1.2. Cyclopentadiene 12. Dibenzyloxyacetone (47.6 g, 176 mmol) and freshly distilled cyclopentadiene (36.3 mL, 440 mmol) were dissolved in MeOH (175 mL). Freshly distilled pyrrolidine (22.3 mL, 264 mmol) was added, and the mixture was stirred for 2 h, after which it was diluted with Et_2O (1.5 L), washed with 1 N HCl (300 mL), and then washed with brine (100 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated. The resulting oil was purified by flash chromatography on silica (10% EtOAc/hexanes) to give 35.6 g of fulvene **11** (64%) as a bright orange oil. *Note*: fulvene **11** is unstable, and the workup and purification must be carried out quickly, and the product was taken on to the next step without delay.

NaH (60% suspension in mineral oil, 12.8 g, 320 mmol) was washed twice with dry pentane, dried under a stream of dry nitrogen, agitated into a free flowing powder, and suspended in DMSO (100 mL). Trimethyl sulfoxonium iodide (73.2 g, 332.8 mmol) was added in portions over the course of 3 h (*caution*!! H_2 evolution!). Another portion of DMSO (250 mL) was added after the addition, and then a solution of fulvene **11** (40.6 g, 128 mmol) in DMSO (100 mL) was added by way of an addition funnel over 20 min. After 14 h, the mixture was poured in an addition funnel containing CH_2Cl_2 (1.2 L) and the mixture was washed with water (2×400 mL). The organic layer was dried with $MgSO_4$, filtered through a short silica pad, and concentrated. The residue was purified by flash chromatography on silica (10% Et_2O/hexanes) to give 33.4 g of **12** (78%) as a slightly yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.34 (m, 10H), 6.62–6.60 (m, 2H), 6.30–6.28 (m, 2H), 4.62 (d, *J*=12 Hz, 2H), 4.56 (d, *J*=12 Hz, 2H), 3.91 (d, *J*=10 Hz, 2H), 3.76 (d, *J*=10 Hz, 2H), 1.91 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 136.0, 130.5, 128.7, 128.1, 128.0, 73.4, 72.3, 46.1, 38.5, 22.3; IR (thin film) 3065, 3030, 2862, 1952 (w), 1871 (w), 1812 (w), 1496, 1482, 1454, 1365, 1146, 1094, 1076 cm^{-1}; LRMS (FAB^+, M+H) calcd for $C_{23}H_{24}O_2$ 333.19, found 333.31.

4.1.3. Diels–Alder product 13. To a cooled (−78 °C) solution of **8** (818 mg, 2.40 mmol) and **12** (1.12 g, 3.35 mmol) in CH_2Cl_2 was added Et_2AlCl (2.67 mL, 1.8 M in toluene, 4.8 mmol) and the mixture was left in a −20 °C freezer overnight. The mixture was added slowly to 1 N HCl (60 mL), and the resulting bi-phasic mixture was extracted with CH_2Cl_2. The organic layer was washed with satd aq $NaHCO_3$ (30 mL), dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (5–10% EtOAc/hexanes) to afford 1.36 g of **13** (84%) as a single (>95:5) diastereomer. ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.24 (m, 15H), 6.57–6.54 (m, 1H), 5.96–5.94 (m, 1H), 5.52–5.38 (m, 2H), 4.74–4.64 (m, 1H), 4.60–4.47 (m, 4H), 4.21–4.16 (m, 2H), 3.82 (dd, *J*=3.4, 4.8 Hz, 1H), 3.61–3.41 (m, 4H), 3.28 (dd, *J*=3.1, 13.2 Hz, 1H), 3.01 (br s, 1H), 2.69 (dd, *J*=10.0, 13.1 Hz, 1H), 2.36 (br s, 1H), 2.23–2.16 (m, 1H), 2.03–1.95 (m, 2H), 1.70–1.68 (m, 3H), 1.65–1.52 (m, 2H), 1.41–1.22 (m, 6H), 0.92 (d, *J*=5.8 Hz, 1H), 0.84 (d, *J*=5.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 153.9, 140.4, 139.33, 139.27, 135.9, 132.1, 130.9, 129.9, 129.5, 128.8, 128.2, 128.1, 127.9, 125.2, 73.4, 72.2, 71.9, 66.8, 55.9, 53.3, 51.3, 50.4, 49.7, 44.7, 38.8, 34.5, 33.1, 30.1, 29.8, 29.5, 24.9, 18.6, 18.3; IR (thin film) 3064–2856, 1778, 1697, 1497, 1454, 1383, 1352, 1216, 1097, 1074 cm^{-1}; $[\alpha]_D$ +53.8 (*c* 1.15, CH_2Cl_2); LRMS (FAB^+, M+H) calcd for $C_{44}H_{51}NO_5$ 673.38, found 674.3.

4.1.4. Diol 14. To a cooled (−78 °C) solution of compound **13** (15.6 g, 23 mmol) in CH_2Cl_2 (180 mL) was added BCl_3 (1.0 M in CH_2Cl_2, 69 mL, 69 mmol) over 2 min via addition funnel (added by letting the solution slide on the cold flask-side to cool it down before it is in contact with the solution). The reaction mixture was allowed to stir for 15 min after which MeOH (70 mL) was added in the same fashion. The mixture was poured into cold (ca. −40 °C) MeOH (300 mL) containing solid $NaHCO_3$. The mixture was allowed to warm to room temperature with vigorous stirring and then concentrated. The residue was dissolved in Et_2O, and satd Rochelle's salt was added. The bi-phasic mixture was stirred overnight and then extracted three times with EtOAc. The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (30–50% EtOAc/hexanes) to give 8.33 g of diol **14** (73% yield) as a thick foamy oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (m, 5H), 6.63–6.60 (m, 1H), 6.03–6.01 (m, 1H), 5.47–5.35 (m, 2H), 4.70–4.65 (m, 1H), 4.23–4.14 (m, 2H), 3.88–3.76 (m, 3H), 3.52 (t, *J*=10.6 Hz, 2H), 3.25 (dd, *J*=3.1, 13.2 Hz, 1H), 3.11 (br s, 1H), 2.65 (dd, *J*=10.2, 13.1 Hz, 1H), 2.46 (br s, 1H), 2.27 (s, 2H), 2.24–2.17 (m, 1H), 1.98–1.94 (m, 2H), 1.64 (d, *J*=4 Hz, 3H), 1.63–1.58 (m, 2H), 1.35–1.21 (m, 6H), 0.88 (d, *J*=5.8, 1H), 0.78 (d, *J*=5.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 154.0, 141.4, 135.9, 132.1, 131.9, 129.9, 129.6, 128.0, 125.3, 67.9, 67.7, 66.9, 56.0, 53.9, 51.2, 50.3, 49.9, 44.5, 38.8, 34.6, 33.1, 30.1, 29.8, 29.5, 27.6, 18.6, 18.3; LRMS (FAB^+, M+H) calcd for $C_{30}H_{40}NO_5$ 494.29, found 494.23.

4.1.5. Compound 15. To a solution of diol **14** (8.33 g, 16.9 mmol) in CH_2Cl_2 (200 mL) were added imidazole (1.15 g, 16.9 mmol) and PPh_3 (4.43 g, 16.9 mmol). The mixture was cooled to −40 °C and I_2 (4.29 g, 16.9 mmol) was added. The mixture was stirred at −40 °C for 30 min during which time most of the I_2 dissolved. The mixture was then warmed to room temperature over 1 h and then diluted with Et_2O. The mixture was washed with 1 N HCl, followed by satd Na_2SO_3, and then brine. The organic layer was dried with $MgSO_4$, filtered through a small pad of silica, and concentrated. The residue was purified by flash chromatography on silica (10–20% EtOAc/hexanes) to give a 1:1 diastereomeric mixture of mono-iodinated compounds (8.36 g, 13.8 mmol, 82% yield), which was used immediately in the next step.

To a solution of the mixture of iodides (8.36 g, 13.8 mmol) in CH_2Cl_2 (100 mL) were added imidazole (3.80 g, 55.9 mmol) and TBSCl (4.16 g, 27.6 mmol). The mixture was stirred overnight, diluted with Et_2O, and washed with 1 N HCl followed by satd $NaHCO_3$ and then brine. The organic layer was dried over $MgSO_4$, filtered, and

concentrated. The residue was purified by flash chromatography on silica (5–10% Et_2O/hexanes) to give a 1:1 diastereomeric mixture of mono-iodinated TBS ethers (9.25 g, 12.9 mmol, 93%) as a slightly yellow oil, which was used immediately in the next step.

To a solution of the mixture of mono-iodinated TBS ethers (9.25 g, 12.9 mmol) in MeOH (100 mL) was added $Sm(OTf)_3$ (770 mg, 1.29 mmol) and the mixture was stirred for 3 days at room temperature. The solution was then concentrated and the residue was purified by flash chromatography on silica (5–30% Et_2O/hexanes) to give a 1:1 diastereomeric mixture of methyl esters **15** (910 mg, 12%) and 5.28 g of material wherein the TBS ether had been hydrolyzed. To a solution of this desilylated material in CH_2Cl_2 (100 mL) were added imidazole (2.35 g, 34.5 mmol) and TBSCl (2.60 g, 17.2 mmol). The mixture was stirred overnight, diluted with Et_2O, and washed with 1 N HCl followed by satd $NaHCO_3$ and then brine. The organic layer was dried with $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (5–10% Et_2O/hexanes) to give 5.21 g of **15** (70% yield) for a total of 82% yield. Epimer A: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35–6.33 (m, 1H), 6.04–6.02 (m, 1H), 5.45–5.43 (m, 2H), 3.69–3.66 (m, 4H), 3.42–3.39 (m, 3H), 2.83 (br s, 1H), 2.66 (t, J=4.6 Hz, 1H), 2.39 (br s, 1H), 2.03–1.97 (m, 2H), 1.90–1.82 (m, 1H), 1.68–1.66 (m, 3H), 1.65–1.50 (m, 2H), 1.41–1.30 (m, 6H), 0.92–0.88 (m, 10H), 0.60 (d, J=5.8 Hz, 1H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 174.8, 139.1, 132.8, 131.4, 125.0, 65.6, 57.7, 52.1, 51.5, 49.5, 49.1, 48.9, 46.2, 35.3, 33.2, 30.2, 29.9, 29.2, 28.0, 26.6, 26.5, 22.2, 18.9, 18.6, 16.2, −4.5; IR (solution in $CHCl_3$) 2921, 2855, 1732, 1602, 1463, 1362, 1322, 1098 cm^{-1}. Epimer B: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27–6.25 (m, 1H), 5.94–5.91 (m, 1H), 5.40–5.32 (m, 2H), 3.62–3.57 (m, 4H), 3.37–3.26 (m, 3H), 2.76 (br s, 1H), 2.56–2.54 (m, 1H), 2.25 (br s, 1H), 1.94–1.86 (m, 2H), 1.83–1.77 (m, 1H), 1.58–1.45 (m, 5H), 1.31–1.20 (m, 6H), 0.83 (s, 9H), 0.73 (d, J=5.8 Hz, 1H), 0.59 (d, J=5.8 Hz, 1H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 138.9, 132.9, 131.8, 125.0, 65.8, 57.4, 52.1, 51.7, 49.6, 48.9, 45.7, 35.1, 33.2, 30.2, 29.9, 29.2, 27.8, 26.5, 22.2, 18.9, 18.6, 16.0, −4.6; IR (thin film) 3062, 2928–2856, 1737, 1463, 1435, 1252, 1178, 1091 cm^{-1}; LRMS (FAB$^+$, M+H) calcd for $C_{27}H_{46}ISi_1O_3$ 573.23, found 573.4.

4.1.6. Compound 18. To a solution of compound **15** (692 mg, 1.21 mmol) and 10 mL benzene was added TEMPO (0.567 g, 3.63 mmol), followed by tributyltin hydride (320 μL, 1.21 mmol). The mixture was heated to reflux and additional TEMPO (0.567 g, 3.63 mmol) and tributyltin hydride (1.28 mL, 4.84 mmol) were added simultaneously over 1 h in four portions. The mixture was stirred an additional 20 min, cooled to room temperature, and concentrated. The residue was purified by flash chromatography on silica (0–5% Et_2O/hexanes) to give **17**, which was used immediately in the next step.

To a solution of compound **17** in THF (2 mL) and H_2O (2 mL) were added acetic acid (6 mL) and zinc powder (820 mg). The mixture was heated to 70 °C with vigorous stirring for 2 h and then cooled to room temperature. The mixture was diluted with 200 mL CH_2Cl_2 and a solution of NaOH (3.8 g) in H_2O (150 mL) was added to neutralize the solution. The mixture was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (30–50% EtOAc/hexanes) and the material thus obtained was used immediately in the next step.

To a solution of this material in CH_2Cl_2 were added imidazole (6 equiv) and TBSCl (3 equiv). Upon completion of the reaction (as monitored by TLC) the mixture was diluted with ether, washed with 1 N HCl, followed by $NaHCO_3$ and brine, dried with $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (10% EtOAc/hexanes) to give 370 mg of **18** (53% overall yield from **15**) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.25–6.22 (m, 1H), 5.80, 5.77 (m, 1H), 5.48–5.36 (m, 2H), 5.15 (d, J=1.8 Hz, 1H), 4.86 (d, J=1.8 Hz, 1H), 3.96 (s, 2H), 3.67–3.23 (m, 5H), 3.13 (br s, 1H), 2.85 (dd, J=3.5, 5.3 Hz, 1H), 2.79 (br s, 1H), 2.00–1.94 (m, 2H), 1.84–1.77 (m, 1H), 1.66–1.62 (m, 5H), 1.39–1.28 (m, 6H), 0.91 (s, 9H), 0.90 (s, 9H), 0.05 (s, 6H), 0.004 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 151.2, 140.1, 132.3, 130.6, 125.3, 110.7, 69.9, 66.9, 66.0, 52.3, 50.8, 49.6, 49.2, 45.1, 34.3, 33.2, 30.2, 30.0, 26.6, 19.0, 18.6, −4.7, −4.8; IR (thin film) 3061, 2926–2833, 1737, 1644, 1463, 1435, 1361, 1256, 1197, 1131, 1073 cm^{-1}; $[\alpha]_D$ +7.4 (c 1.24, $CHCl_3$); LRMS (FAB$^+$, M+H) calcd for $C_{33}H_{61}O_4Si_2$ 577.4, found 577.0.

4.1.7. Compound 21. To a cooled (0 °C) solution of compound **18** (1.36 g, 2.35 mmol) in 25 mL of Et_2O was added $LiAlH_4$ (1.0 M in Et_2O, 2.47 mL, 2.47 mmol). After 30 min the mixture was warmed to room temperature and stirred for an additional 30 min. The reaction was quenched by the addition of 94 μL of water followed by 190 μL of 15% NaOH and then an additional 282 μL of water was added. The mixture was stirred for 3 h, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (10% Et_2O/CH_2Cl_2) to give 1.29 g of the primary alcohol product (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.17–6.14 (m, 1H), 5.87–5.84 (m, 1H), 5.42–5.39 (m, 2H), 5.15 (d, J=1.8 Hz, 1H), 4.86 (d, J=1.8 Hz, 1H), 3.97 (s, 2H), 3.74 (d, J=10.0 Hz, 1H), 3.65 (d, J=10.0 Hz, 1H), 3.56–3.44 (m, 1H), 3.29 (t, J=9.6 Hz, 1H), 2.91 (br s, 1H), 2.73 (br s, 1H), 2.23–2.19 (m, 1H), 2.00, 1.94 (m, 2H), 1.66–1.56 (m, 5H), 1.40–1.25 (m, 7H), 0.91 (s, 9H), 0.89 (s, 9H), 0.05 (s, 6H), −0.003 (s, 3H), −0.008 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 138.9, 131.9, 130.2, 125.0, 109.8, 69.7, 66.8, 66.7, 65.6, 50.6, 47.7, 47.2, 44.7, 34.3, 33.2, 30.6, 30.3, 30.0, 26.63, 26.60, 19.02, 18.97, 18.6, −4.6, −4.7, −4.8; IR (thin film) 3326 (br), 2928–2856, 1643, 1463, 1255, 1106, 1074 cm^{-1}; $[\alpha]_D$ −10.1 (c 1.76, $CHCl_3$); LRMS (FAB$^+$, M+H) calcd for $C_{32}H_{61}Si_2O_3$ 549.42, found 549.05.

To a solution of the alcohol (1.35 g, 2.45 mmol) in CH_2Cl_2 (30 mL) were added DMSO (1.04 mL, 14.7 mmol), diisopropylethylamine (1.71 mL, 9.8 mmol), and $Pyr\cdot SO_3$ (1.15 g, 7.35 mmol). The mixture was stirred for 30 min, diluted with Et_2O, and washed with 1 N HCl followed by satd $NaHCO_3$ and then brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified

by flash chromatography on silica (10% Et_2O/hexanes) and the aldehyde thus obtained was used immediately in the next step.

To a cooled (−78 °C) solution of triphenylmethylphosphonium bromide (1.05 g, 2.94 mmol) in THF (20 mL) was added potassium *tert*-butoxide (1.0 M in THF, 2.70 mL, 2.70 mmol) and the resulting mixture was warmed to room temperature, stirred for 10 min, and then recooled to −78 °C. A solution of the aldehyde in 5 mL THF was added and the mixture was warmed to 0 °C and stirred for 1.5 h. The mixture was diluted with Et_2O and washed with satd NH_4Cl and with brine. The organic layer was dried over $MgSO_4$, filtered through a small pad of silica, and concentrated. The residue was purified by flash chromatography on silica (2% Et_2O/hexanes) to give 1.19 g of **21** (89% overall yield from the primary alcohol). ^1H NMR (400 MHz, $CDCl_3$) δ 6.22–6.20 (m, 1H), 5.88–5.86 (m, 1H), 5.60–5.51 (m, 1H), 5.45–5.42 (m, 2H), 5.17 (d, J=2 Hz, 1H), 5.03 (dd, J=1.3, 17.0 Hz, 1H), 4.90–4.86 (m, 2H), 4.04–3.94 (m, 2H), 3.74 (s, 2H), 2.79 (s, 1H), 2.74 (s, 1H), 2.61–2.57 (m, 1H), 2.01–1.96 (m, 2H), 1.67 (m, 3H), 1.60–1.57 (m, 2H), 1.39–1.29 (m, 6H), 1.20–1.15 (m, 1H), 0.93–0.90 (m, 18H), 0.05 (s, 6H), 0.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 143.0, 138.2, 131.4, 130.2, 124.4, 113.4, 109.2, 69.2, 66.3, 65.3, 51.3, 50.4, 48.6, 47.8, 33.5, 32.7, 29.80, 29.76, 29.5, 26.1, 18.54, 18.48, 18.1, −5.13, −5.19; IR (thin film) 3062, 2928–2856, 1638, 1463, 1255, 1090, 1073, 1006 cm^{-1}; $[\alpha]_D$ +1.6 (*c* 1.32, $CHCl_3$); LRMS (FAB^+, M+H) calcd for $C_{33}H_{61}Si_2O_2$ 545.42, found 545.09.

4.1.8. Compound 23. To a cooled (−20 °C) solution of compound **21** (574 mg, 1.05 mmol) in THF (40 mL) was added thexylborane (1.0 M in THF, 1.05 mL, 1.05 mmol) dropwise. After 45 min the mixture was warmed to 0 °C for 1 h and then to room temperature for 30 min. The reaction was quenched by the addition of 1 mL of 3 N NaOH followed by H_2O_2 (30% aq, 500 μL). The resulting mixture was stirred for 1 h. Satd Rochelle's salt was added and the mixture was stirred for 1 h, and then extracted three times with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (10–30% EtOAc/hexanes) to give 206 mg of **23** (34%) and 124 mg of **22** (21% yield). Compound **22** was dehydrated as described in Scheme 4, and **21** was used immediately in the next step.

To a cooled (−20 °C) solution of diol **23** (116 mg, 0.20 mmol) in CH_2Cl_2 (5 mL) was added imidazole (40.8 mg, 0.60 mmol) and TESCl (33.6 μL, 0.20 mmol). The mixture was allowed to warm to room temperature slowly and monitored by TLC. The mixture was recooled to −20 °C, and an additional portion of TESCl (13.4 μL, 0.080 mmol) was added and the mixture was warmed to room temperature. TLC analysis showed complete consumption of the starting material, and the mixture was then diluted with Et_2O and washed with satd NH_4Cl followed by satd $NaHCO_3$ and then brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (5% Et_2O/hexanes) to give 124 mg of the mono-TES ether, which was used immediately in the next step.

To a solution of the mono-TES ether (123.8 mg, 0.178 mmol) in CH_2Cl_2 (5 mL) was added Dess–Martin periodinane (113.2 mg, 0.267 mmol). After 30 min the mixture was treated with satd $NaHCO_3$ and after 5 min the mixture was extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (5% Et_2O/hexanes) to give 123 mg of **24** (85% overall yield from **23**). ^1H NMR (300 MHz, $CDCl_3$) δ 5.47–5.35 (m, 2H), 5.29 (s, 1H), 4.89 (s, 1H), 4.12–4.32 (m, 1H), 4.05 (d, J=14 Hz, 1H), 3.80–3.73 (m, 2H), 3.70–3.55 (m, 2H), 2.68 (br s, 1H), 2.47–2.22 (m, 3H), 2.00–1.92 (m, 2H), 1.68–1.12 (m, 16H), 0.95 (t, J=8 Hz, 9H), 0.89–0.87 (m, 18H), 0.58 (q, J=8 Hz), 0.04 (s, 6H), 0.00 (s, 3H), −0.003 (s, 3H); IR (thin film) 2955, 2929, 2879, 2857, 1749, 1462, 1255, 1097, 1007 cm^{-1}; $[\alpha]_D$ +39.9 (*c* 1.0, $CHCl_3$); LRMS (FAB^+, M+H) calcd for $C_{39}H_{77}Si_3O_4$ 693.5, found 693.3.

4.1.9. Compound 27. To a cooled (−78 °C) solution of *i*-Pr_2NH (510 μL, 3.64 mmol) in THF (1 mL) was added *n*-BuLi (2.5 M in hexanes, 1.46 mL, 3.64 mmol). The solution was warmed to 0 °C for 30 min and then recooled to −78 °C. To this solution was added a solution of compound **24** (1.94 g, 2.80 mmol) in 15 mL of THF by cannula. After 30 min a solution of 3-(*tert*-butyldimethylsilyloxy)-propionaldehyde (1.37 g, 7.28 mmol) in THF (2 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 40 min. The mixture was then diluted with Et_2O and washed with satd NH_4Cl followed by brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (2–8% Et_2O/hexanes with 0.2% Et_3N) to give 2.00 g of **25** (81%) as an unassigned 2:1 mixture of diastereomers, which was used immediately in the next step.

To a cooled (−60 °C) solution of DMSO (0.065 mL, 0.917 mmol) in 4 mL CH_2Cl_2 was added trifluoroacetic anhydride (0.0556 mL, 0.394 mmol). After 1 h a solution of **25** (116 mg, 0.131 mmol) in CH_2Cl_2 (4 mL) over 4 Å molecular sieves was added. After 35 min Hunig's base (0.183 mL, 1.05 mmol) was added and the resulting solution was allowed to warm to room temperature and stirred for 40 min. The solution was then diluted with Et_2O and washed with water. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (2–4% Et_2O/hexanes) to give 57.6 mg of **26** (50%) and 30 mg (26%) of recovered **25**. Compound **26** was used immediately in the next step.

To a cooled (−78 °C) solution of **26** (74.7 mg, 0.085 mmol) in Et_2O (2 mL) was added KHMDS (0.256 mL, 0.128 mmol, 0.50 M in Et_2O). After 30 min a solution of 2-[*N*,*N*-bis(trifluoromethylsulfonyl)amino]-5-chloropyridine (Comins' reagent[22]) (50 mg, 0.127 mmol) in Et_2O (1 mL) was added by cannula. The mixture was warmed to room temperature and stirred for 5 h. The mixture was diluted with Et_2O and washed with aq NH_4Cl and then brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (2% Et_2O/hexanes) to give 58.5 mg (68%) of **27** and 11.5 mg (15%) of recovered **26**. Data for **27**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.43–5.40 (m, 2H), 5.32 (s, 1H), 4.89 (s, 1H), 4.16 (d, J=14 Hz, 1H), 3.98 (d, J=14 Hz, 1H), 4.01–3.78

(m, 4H), 3.70–3.60 (m, 2H), 3.13 (br s, 1H), 2.86 (br s, 1H), 2.64–2.55 (m, 2H), 2.46–2.38 (m, 1H), 2.01–1.95 (m, 2H), 1.68–1.28 (m, 14H), 0.97 (t, J=8 Hz, 9H), 0.9 (m, 27H), 0.60 (q, J=8 Hz, 6H), 0.05–0.00 (m, 18H); IR (thin film) 2955, 2930, 2883, 2858, 1745, 1672, 1472, 1463, 1421, 1413, 1254, 1205, 1103, 1007 cm^{-1}; $[\alpha]_D$ +29.2 (c 2.0, $CHCl_3$); LRMS (FAB$^+$, M+H) calcd for $C_{49}H_{93}F_3SSi_4O_8$ 1011.6, found 1011.4.

4.1.10. Compound 28. To a cooled (0 °C) solution of compound **27** (46.7 mg, 0.046 mmol) in THF (1 mL) was added CSA (0.1 M in MeOH, 0.092 mL, 0.0092 mmol). After 1.5 h the reaction was quenched by the addition of satd $NaHCO_3$ and after 5 min the mixture was extracted with Et_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica (30% Et_2O/hexanes) to give 34.1 mg (83%) of **28**. ^1H NMR (400 MHz, $CDCl_3$) δ 5.44–5.40 (m, 2H), 5.32 (s, 1H), 4.90 (s, 1H), 4.15 (d, 1H), 4.00–3.78 (m, 5H), 3.69 (m, 2H), 3.14 (br s, 1H), 2.97 (br s, 1H), 2.64–2.52 (m, 2H), 2.37–2.3 (m, 1H), 2.00–1.94 (m, 2H), 1.72–1.63 (m, 5H), 1.58–1.25 (m, 1H), 0.89 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.05–0.01 (m, 18H); IR (thin film) 3425 (br), 2955, 2927, 2850, 1742, 1672, 1462, 1427, 1251, 1202, 1104 cm^{-1}; $[\alpha]_D$ +28.9 (c 1.83, $CHCl_3$); LRMS (FAB$^+$, M+H) calcd for $C_{43}H_{80}F_3SSi_3O_8$ 897.5, found 897.3.

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References and notes

1. (a) Dabrah, T. T.; Harwood, H. J.; Huang, L. H.; Jankovich, N. D.; Kaneko, T.; Li, J. C.; Lindsey, S.; Moshier, P. M.; Subashi, T. A.; Therrien, M.; Watts, P. C. *J. Antibiot.* **1997**, *50*, 1–7; (b) Dabrah, T. T.; Kaneko, T.; Massefski, W.; Whipple, E. B. *J. Am. Chem. Soc.* **1997**, *119*, 1594–1598.
2. Spencer, P.; Agnelli, F.; Sulikowski, G. A. *Org. Lett.* **2001**, *3*, 1443–1445.
3. (a) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Choi, H. S.; Yoon, W. H.; He, Y.; Fong, K. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 1669–1675; (b) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Fong, K. C.; He, Y.; Yoon, W. H.; Choi, H. S. *Angew. Chem., Int. Ed.* **1999**, *38*, 1676–1678; (c) Nicolaou, K. C.; Jung, J.-K.; Yoon, W. H.; He, Y.; Zhong, Y.-L.; Baran, P. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 1829–1832; (d) Nicolaou, K. C.; Jung, J.; Yoon, W. H.; Fong, K. C.; Choi, H. S.; He, Y.; Zhong, Y.-L.; Baran, P. S. *J. Am. Chem. Soc.* **2002**, *124*, 2183–2189; (e) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Fong, K. C.; Choi, H. S. *J. Am. Chem. Soc.* **2002**, *124*, 2190–2201; (f) Nicolaou, K. C.; Zhong, Y.-L.; Baran, P. S.; Jung, J.; Choi, H. S.; Yoon, W. H. *J. Am. Chem. Soc.* **2002**, *124*, 2202–2211.
4. (a) Chen, C.; Layton, M. E.; Shair, M. D. *J. Am. Chem. Soc.* **1998**, *120*, 10784–10785; (b) Chen, C.; Layton, M. E.; Sheehan, S. M.; Shair, M. D. *J. Am. Chem. Soc.* **2000**, *122*, 7424–7425.
5. (a) Waizumi, N.; Itoh, T.; Fukuyama, T. *Tetrahedron Lett.* **1998**, *39*, 6015–6018; (b) Waizumi, N.; Itoh, T.; Fukuyama, T. *J. Am. Chem. Soc.* **2000**, *122*, 7825–7826; (c) Hayashi, Y.; Itoh, T.; Fukuyama, T. *Org. Lett.* **2003**, *5*, 2235–2238.
6. (a) Meng, D.; Tan, Q.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 3197–3201; (b) Tan, Q.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 4509–4511.
7. For a comprehensive review of all approaches to the synthesis of the phomoidrides, see: Spiegel, D. A.; Njardarson, J. T.; McDonald, I. M.; Wood, J. L. *Chem. Rev.* **2003**, *103*, 2691–2727.
8. (a) Bio, M. M.; Leighton, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 890–891; (b) Bio, M. M.; Leighton, J. L. *Org. Lett.* **2000**, *2*, 2905–2907; (c) Bio, M. M.; Leighton, J. L. *J. Org. Chem.* **2003**, *68*, 1693–1700.
9. Clive, D. L. J.; Ou, L. *Tetrahedron Lett.* **2002**, *43*, 4559–4563.
10. Corey, E. J.; Shiner, C. S.; Volante, R. P.; Cyr, C. R. *Tetrahedron Lett.* **1975**, 1161–1164.
11. Starr, J. T.; Koch, G.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 8793–8794.
12. Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238–1256.
13. Shapiro, G.; Chengzhi, C. *Tetrahedron Lett.* **1992**, *33*, 2447–2450.
14. Stone, K. J.; Little, R. D. *J. Org. Chem.* **1984**, *49*, 1849–1853.
15. Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353–1364.
16. Schröer, W.-D.; Friedrichsen, W. *Liebigs Ann. Chem.* **1978**, 1648–1654.
17. Nakamura, E.; Inubushi, T.; Aoki, S.; Machii, D. *J. Am. Chem. Soc.* **1991**, *113*, 8980–8982.
18. Boger, D. L.; Mckie, J. A. *J. Org. Chem.* **1995**, *60*, 1271–1275.
19. Brown, H. C.; Pfaffenberger, C. D. *J. Am. Chem. Soc.* **1967**, *89*, 5475–5477.
20. Kanth, K. V. B.; Brown, H. C. *Inorg. Chem.* **2000**, *39*, 1795–1802.
21. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156; (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.
22. Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165–185.
23. Comins, D. L.; Dehghani, A. *Tetrahedron Lett.* **1992**, *33*, 6299–6302.