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A Flexible Common Approach to α-Substituted Serines and Alanines: Diastereoconvergent Syntheses of Sphingofungins E and F

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Dedicated to Professor Guo-Bin Rong on the occasion of his retirement

Keywords: Amino acids / Asymmetric synthesis / Epoxides / Natural products / Quaternary stereocenters

A flexible common approach for the asymmetric syntheses of sphingofungins E and F is reported, with efficient use of both diastereomers of the Baylis–Hillman adduct in a stereoconvergent manner. Pronounced steric effects of the 2-substituents in diastereoselective dihydroxylations of (*E*)-2-hydroxymethyl-2,3-alkenoates were observed. This strategy also allowed full control over the absolute configurations of the quaternary stereocenters in α-substituted amino acids through tunable site-specific adjustment of oxidation states.

Introduction

There has been enduring interest in asymmetric synthesis of nonproteinogenic amino acids, due to their versatile roles in biological studies and drug discovery.[1] Among these unnatural amino acids, the α,α-disubstituted type occupies a conspicuous position, because α-quaternary amino acids possess improved metabolic stability as well as rich structural features and functions.[2] α-Substituted serines and alanines are important representatives of this category; despite their formal similarity, however, they have seldom shared a common synthetic strategy, due to the limitations of the "enolate of serine".[3]

Sphingofungins E (**1**) and F (**2**),[4] two highly oxygenated α-quaternary amino acids, were isolated from the fermentation broth of *Paecilomyces variotii* in 1992. Like other members of the sphingofungin family, each compound possesses a polar head bearing four contiguous stereocenters and a lipophilic tail connected by a *trans*-olefin (Figure 1). The two compounds are distinct from congeners **4**–**7** primarily in their respective α-substituted serine and alanine structural motifs. Instead, they bear close resemblance to myriocin (**3**), an immunosuppressant 10–100 times more potent than cyclosporine A.[5] As sphingosine[6] analogues, they are potent serine palmitoyltransferase (SPT) inhibitors (IC_{50} = 7.2 and 57 nM, respectively) with antifungal activities against several human pathogenic fungi.[4]

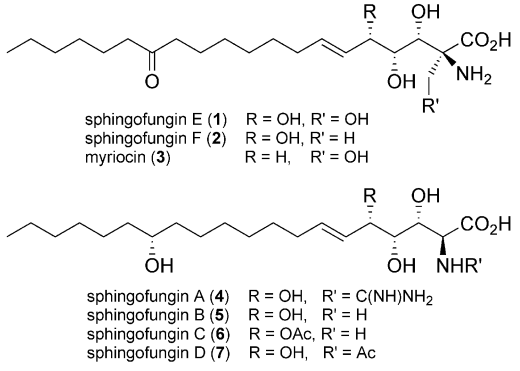

Figure 1. Sphingofungin E and F and related natural products.

The unique structural features and the biological importance of **1** and **2** have stimulated considerable synthetic efforts. To date, four groups have accomplished the synthesis of **1**,[7] whereas five independent syntheses of **2** have been reported.[8] The Trost group, for example, developed the asymmetric allylic alkylation (AAA) of azlactones with *gem*-diacetates as electrophiles to construct the requisite quaternary stereocenters of **1** and **2**.[7d] The groups of Chida[7b,7c] and Shiozaki[7a,7e] both started from D-glucose (chiral pool approach) and applied key rearrangement transformations to establish the α-quaternary amino acid unit of **1**. Kobayashi utilized the Sn^{II}-catalyzed asymmetric aldol reaction of Schöllkopf's bislactam for the synthesis of **2**,[8e,8g,8h] whereas Li employed a substrate-directed aza-Michael addition to introduce the tertiary carbinamine of

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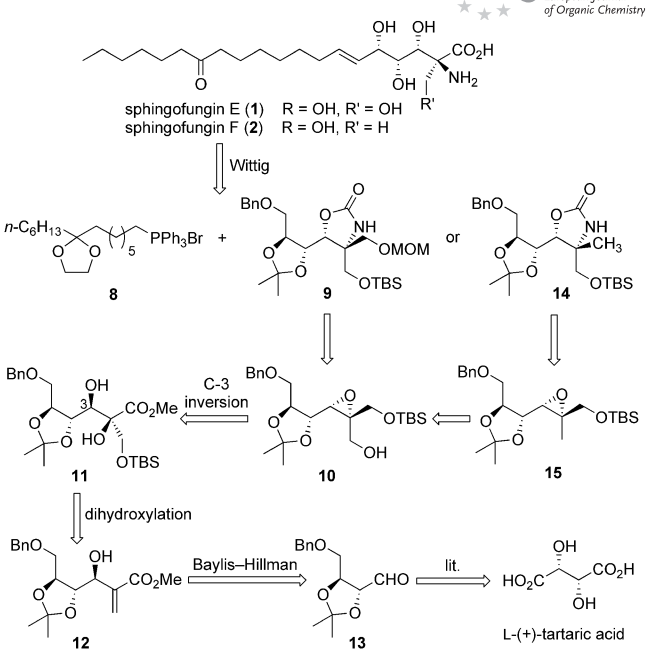
2.[8a] Ham's approach to **2** depended on a diastereoselective Pd-catalyzed oxazoline formation and Lewis-acid-promoted allylation.[8b] Of these, only the route described by Trost, which used a silyl group as a masked hydroxy function, was applicable to both **1** and **2**.

Our previous individual approaches to **1** and **2** had both focused on the ring-opening of epoxides, using Lewis-acid-promoted rearrangement of trichloroacetimidates[9] for the formation of quaternary stereocenters. In our preliminary report, the synthesis of **1** involved a Baylis–Hillman reaction[10] of an α,β-chiral aldehyde, which produced a pair of diastereomers in a 7:3 ratio.[7f] Utilization of the minor adduct was proposed but was yet to be validated. On the other hand, the key asymmetric epoxidation step in our synthesis of **2** also yielded a moderate *dr* (3:1), and the minor product could not be transformed into desired intermediates.[8d] With these factors in mind, and in continuation of our interests in the synthesis of chiral amino alcohols,[11] we set out to develop a common and flexible synthetic strategy applicable to both α-substituted serine and alanine. Here we report the full details of this study.



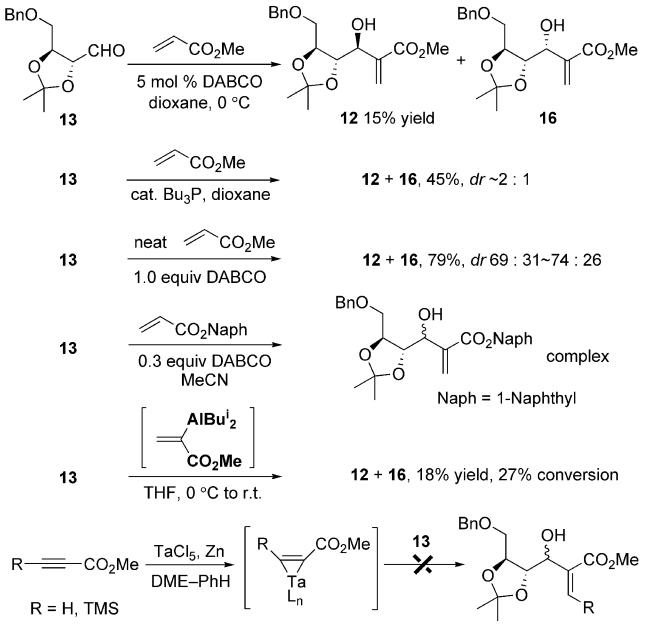
Scheme 1. Retrosynthetic analysis of sphingofungins E (**1**) and F (**2**).

Results and Discussion

The general retrosynthetic plan of our improved route is outlined in Scheme 1. For sphingofungin E (**1**), disconnection of the *trans*-double bond (Wittig olefination) led to the known phosphonium salt **8**[12] and the chiral polar "head" **9**, which possessed all four requisite stereogenic centers. The chiral tertiary carbinamine was expected to be installed by Lewis-acid-promoted rearrangement of trichloroacetimidates derived from the 2,3-epoxy-alcohol **10**. However, the 3,4-*syn* stereochemistry in **10** was a challenge, because it was the product of an apparent mismatched epoxidation. We reasoned that, to overcome this unfavorable influence, the trisubstituted oxirane moiety could be established in a more stereoselective manner through regioselective ring-closure of diol **11** with inversion at C-3.[11b,11e] Compound **11** was in turn the dihydroxylation product of **12**, which was clearly a Baylis–Hillman adduct. The known aldehyde **13** was conveniently prepared from L-(+)-tartaric acid.[13]

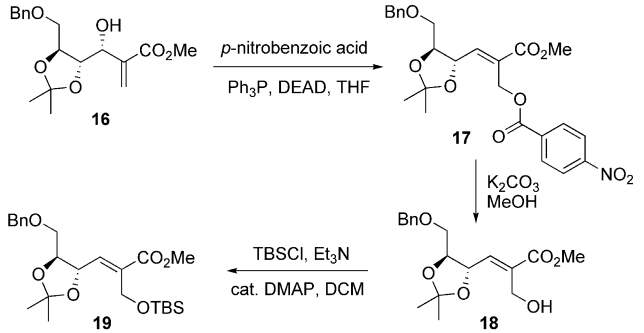
The synthesis of the α-substituted alanine **2** diverged from the above in that deoxygenation at C-1′ would be required, and we envisaged that this key transformation could be achieved en route to **15** from the pivotal compound **10**. Sphingofungins E and F could thus be synthesized by a common approach converging at the intermediate **10**. Moreover, the mismatched epoxidation with unsatisfactory *dr* encountered in our previous approach could be avoided, because the new route hinged on diol **11**, the preparation of which was highly stereocontrolled in this second-generation synthesis.

We first attempted to improve the efficiency or the *dr* of the Baylis–Hillman reaction (Scheme 2). Initially, the reaction was carried out with DABCO as the catalyst in dioxane at 0 °C.[14a] This proved very slow, and only a trace yield of **12** was obtained. Use either of an alternative Lewis base catalyst (Bu_3P[14b]) or of a different reaction partner (1-naphthyl acrylate[15]) did accelerate the reaction, but the yields were compromised by significant side reactions and the impurities were difficult to separate from the desired product. A double asymmetric induction protocol had recently been reported to give a high *dr* for a substrate similar to **13**, but two additional steps of auxiliary removal (74%) and esterification (60%) were required and lowered the overall efficiency.[16] On the other hand, reactions involving functionalized organoaluminum[17] and tantalum[18] rea-



Scheme 2. Attempted optimization of the Baylis–Hillman reaction of **13**.

gents to yield formal Baylis–Hillman adducts were also attempted without success. It thus became clear that the α-oxygenation of the chiral aldehyde **13** posed considerable problems, in terms either of reactivity or of stereoselectivity. Consequently, we adhered to our optimized conditions [neat methyl acrylate, DABCO (0.5–1.0 equiv.), room temp., 2–7 days], which provided up to 79% yield and 74:26 *dr*. Our focus then shifted to utilization of the minor Baylis–Hillman adduct **16** (Scheme 3).



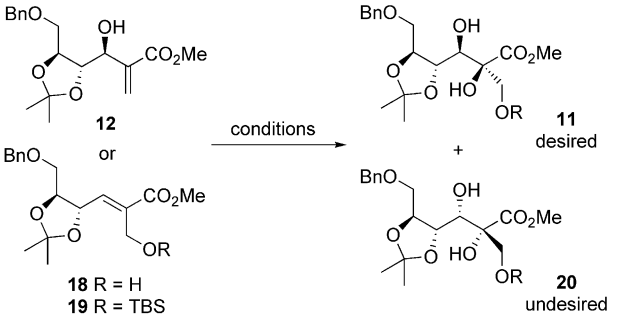
Scheme 3. Transformations of minor Baylis–Hillman adduct **16**.

Through the allylic transposition of their hydroxy groups under Mitsunobu conditions,[19] both **16** and its epimer **12** could be converted into the *p*-nitrobenzoate **17** in 85–91% yields (Scheme 3). The configuration of the trisubstituted olefin was exclusively *E*, as confirmed by NOE experimentation. Removal of the *p*-nitrobenzoyl (PNB) group in high yield was achieved under mild conditions, and the resulting alcohol **18** was protected with TBS to prevent possible intervention of the free hydroxy group in the subsequent dihydroxylation reaction.[20] From a practical point of view, using the crude Baylis–Hillman adducts without the need for meticulous separation of diastereomers was a notable advantage.

With intermediate **19** to hand, its stereoselective dihydroxylation was investigated, with the aim of achieving high 3,4-*anti* selectivity (Table 1). Consistent with Scolastico's excellent study,[21] the dihydroxylation of **12** under Upjohn conditions was diastereospecific, producing the desired **11** as a single diastereomer after TBS protection of the terminal hydroxy group. The substrate stereoinduction for **19** under the same conditions was not effective, however, resulting in a poor 3,4-*anti*/*syn* ratio of 1.8:1. Because the asymmetric dihydroxylation of 2-hydroxymethyl crotonates has not been studied, we then tested AD-mix-β in order to obtain a satisfactory *dr* by double diastereoselection. The AD reaction was found to be very sluggish under the standard conditions (0 °C), whereas running the reaction at 20 °C for 48 h afforded **11** and the undesired **20** in a moderate ratio of 4.2:1 (Entry 3).

Interestingly, **11** was also the major product when AD-mix-α was used, albeit in a lower *dr* of 1.5:1 (Entry 4). This suggested that the sterically demanding CH_2OTBS substituent rendered **19** too bulky to enter the binding pocket of the catalytic system, and that the rigid five-membered acetonide ring at the γ,δ-position could only afford moderate

Table 1. Diastereoselective dihydroxylation of 2-substituted acrylates.

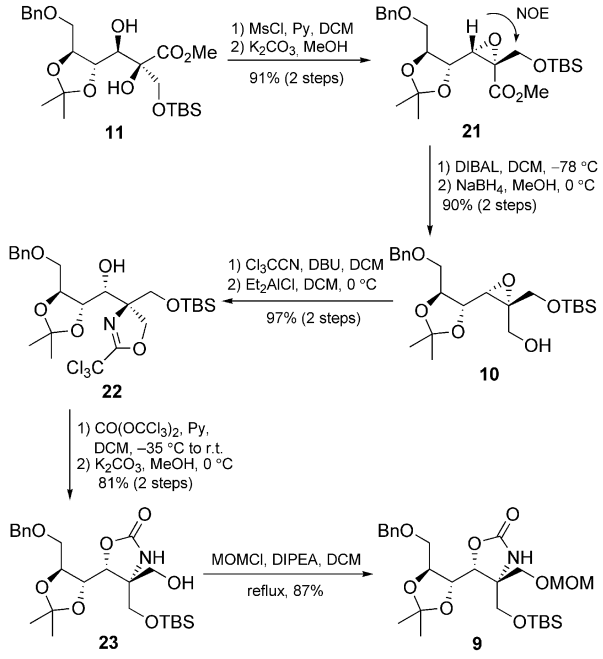


Entry	Substrate	Dihydroxylation conditions	Product, yield (%)[a]	*dr* (**11**/**20**)
1[b]	**12**	cat. OsO_4, NMO, acetone/H_2O (8:1), 20 °C	**11**, 89	100:0[c]
2	**19**	cat. OsO_4, NMO, acetone/H_2O (8:1), 20 °C	**11** + **20**, 92	1.8:1[d]
3	**19**	AD-mix-β, $MsNH_2$, *t*BuOH/H_2O (1:1), 20 °C	**11** + **20**, 82	4.2:1[c]
4	**19**	AD-mix-α, $MsNH_2$, *t*BuOH/H_2O (1:1), 20 °C	**11** + **20**, 80	1.6:1[d]
5[b]	**18**	AD-mix-β, $MsNH_2$, *t*BuOH/H_2O (1:1), 0 °C	**11** + **20**, 85	16.8:1[c]

[a] Combined yields of both diastereomers (separable). [b] Dihydroxylation followed by selective TBS protection of primary alcohol. [c] Determined by HPLC. [d] Determined from the yield of each isomer.

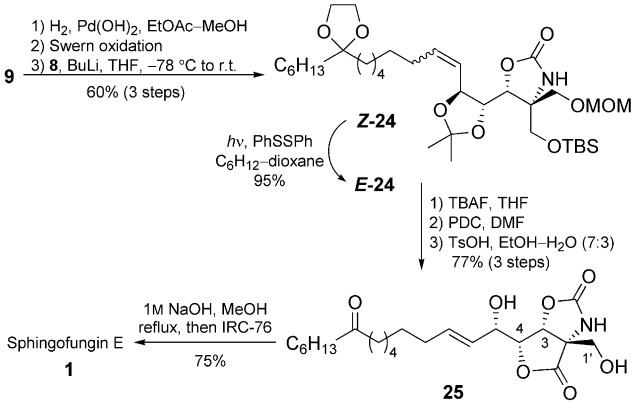
stereocontrol favoring the 3,4-*anti* product. The unprotected compound **18** was hence subjected to the standard AD protocol, and excellent *dr* (16.8:1) and yield were obtained (Entry 5).[22] In this manner, the minor Baylis–Hillman adduct **16** was efficiently transformed into **11** in a short sequence (56% yield over four steps). The combined yield of pure **11** from **12** and **16** was 80%, and overall diastereoconvergence was achieved.

Then the C-2 and C-3 stereochemistry had to be elaborated (Scheme 4). The conversion of the diol **11** into the epoxide **21** was achieved by regioselective mesylation of the secondary hydroxy group and base-induced ring-closure, which was reminiscent of our total synthesis of allopumiliotoxins.[11b,11e] The structure of **21** was confirmed by a NOE between 3-H and 1′-H, which corresponded to the correct 3,4-*syn* stereochemistry in **1** and **2**. The ester group was then subjected to a two-stage reduction, firstly with DIBAL at –78 °C to afford the aldehyde, and then with $NaBH_4$ to afford **10**. Notably, use of excess DIBAL or raising the temperature resulted in complex mixtures, probably due to the stability of the hemiacetal aluminate intermediate[23] together with the competing reductive ring-opening of epoxide. Trichloroacetimidate formation and a Hatakeyama reaction[9a] with Et_2AlCl as the Lewis acid afforded the oxazoline **22** in almost quantitative yield. Treatment with triphosgene and removal of trichloroacetyl under mild conditions delivered the cyclic carbamate **23**, the hydroxy group of which was subsequently protected with MOM in 87% yield.



Scheme 4. Elaboration of the polar "head" segment.

As shown in Scheme 5, debenzylation of compound **9** and Swern oxidation gave a crude aldehyde, which was condensed with the ylide derived from **8** to afford **24** as a geometric mixture ($Z/E \approx 9:1$, separable by silica gel column chromatography) in 60% yield over three steps. Photoisomerization[24] of the *Z* isomer in the presence of PhSSPh converted it smoothly into the desired (*E*)-**24** in excellent yield. After routine desilylation and PDC oxidation to carboxylic acid,[25] the crude product was heated at reflux in aq. ethanol under acid catalysis conditions to effect lactonization and concomitant removal of the MOM, acetonide, and ketal protecting groups. The NOE between 1′-H, 3-H, and 4-H in the bicyclic product **25** corroborated its stereochemistry. Finally, saponification of **25** followed by neutralization with IRC-76 resin completed the total synthesis of sphingofungin E (**1**), the spectroscopic data of which were consistent with the literature values.

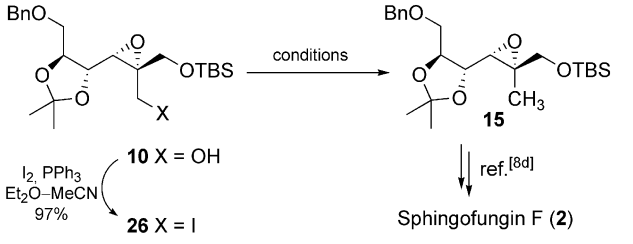


Scheme 5. Synthesis of sphingofungin E (**1**).

A diastereoconvergent synthesis of **1** from the readily available aldehyde **13** in 22 steps and 11.6% overall yield, and making use of both diastereomers of the Baylis–Hillman product, has thus been achieved. Alternatively, conversion of the free hydroxymethyl group in **23** into an ester could eventually afford 2-*epi*-**1**, providing structural diversity in this route. This also means that the absolute configurations of the quaternary stereocenters in α-substituted amino acids could be controlled through tunable site-specific adjustment of oxidation states of the "prochiral" hydroxymethyls.

Because this strategy is more stereoselective than our previous one involving epoxidation,[8d] we further pursued the synthesis of sphingofungin F from the alcohol **10**. Replacement of the free hydroxy group in **10** with hydrogen would afford **15** (Table 2), the key intermediate for the synthesis of **2**, so we carried out the required deoxygenation in a two-step approach.[26] The alcohol was first converted into the iodide in excellent yield by Garegg's protocol,[27] and appropriate reductive dehalogenation conditions were then screened. Hydrogenolysis in the presence either of Pearlman's catalyst or of Raney nickel[28] was first tested, but no conversion was observed. The mild reductant $NaBH_3CN$[29] in THF/HMPA (4:1) was also ineffective. Ni-mediated reduction[30] resulted in a complex mixture, presumably due to reductive opening of the adjacent epoxide. $NaBH_4$ in DMSO[31] offered a moderate yield of **15**, but side reactions were still significant. Fortunately, when we shifted to Super-Hydride reduction,[32] a satisfactory yield (80%) was obtained. The spectroscopic data for **15** were identical with those for the product previously obtained by epoxidation.[8d] A formal synthesis of sphingofungin F (**2**) had thus been achieved, and a higher overall yield of **2** than in our previous synthesis could be obtained.

Table 2. De-iodination study.



Entry	Conditions	Yield (%)[a]
1	H_2 (1 atm), $Pd(OH)_2/C$, K_2CO_3, MeOH	NR
2	H_2 (1 atm), Raney Ni, MeOH	NR
3	$NaBH_3CN$, THF/HMPA	NR
4	$NaBH_4$, $NiCl_2 \cdot 6H_2O$, EtOH	complex
5	$NaBH_4$, DMSO	56
6	$LiBHEt_3$, THF, 25 °C, 15 min	80

[a] Isolated yields.

Conclusions

In summary, we have developed a flexible common approach for the asymmetric syntheses of both sphingofung-

ins E and F, representatives of highly oxygenated α-substituted amino acid natural products. The minor Baylis–Hillman adduct **16** has been efficiently utilized in the development of a diastereoconvergent route. The dihydroxylation of (*E*)-2-hydroxymethyl-2,3-alkenoates was examined and a pronounced steric effect of the 2-substituent was observed. Excellent *dr* and *er* values could be obtained for 2-(hydroxymethyl)crotonates under the standard Sharpless asymmetric dihydroxylation conditions. In addition, our strategy could provide full control over the absolute configurations of the quaternary stereocenters in the α-substituted amino acids through tunable site-specific adjustment of oxidation states.

Experimental Section

General Information: All reactions were performed under argon in oven-dried glassware. All ^1H and ^{13}C NMR spectra were recorded at ambient temperature in $CDCl_3$ unless noted otherwise. Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity, coupling constant, and integration. Optical rotations were measured at ambient temperature, and concentrations are reported in g per 100 mL. HR-MS were recorded on a Kratos Concept 1H apparatus. HR-ESI-MS were recorded on a Shimadzu LCMS-IT-TOF apparatus. Melting points were not corrected. THF was distilled from sodium/benzophenone ketyl, dichloromethane and DMF were distilled from CaH_2, and all other solvents and chemical reagents were used as received.

Baylis–Hillman Reaction: DABCO (850 mg, 7.6 mmol) was added under Ar to the crude aldehyde **13** (1.908 g, 7.6 mmol) in methyl acrylate (5 mL), the solution was stirred for 2 days at room temp., and the volatile components were removed under reduced pressure. The residue was purified by silica gel flash column chromatography (EtOAc/hexanes, 1:7 to 1:3) to yield **12** (1.403 g, 55%) and **16** (0.631 g, 25%) as colorless oils.

Compound 12: $[\alpha]_D^{20} = -10.1$ ($c = 1.36$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.20 (m, 5 H), 6.31 (s, 1 H), 5.97 (s, 1 H), 4.62 (t, J = 4.2 Hz, 1 H), 4.56 (s, 2 H), 4.15–4.05 (m, 2 H), 3.72 (s, 3 H), 3.53 (d, J = 4.5 Hz, 2 H), 3.28 (d, J = 4.3 Hz, 1 H), 1.42 (s, 3 H), 1.40 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 138.3, 137.7, 128.3 (2 C), 128.0, 127.6 (2 C), 127.1, 109.6, 78.9, 77.1, 73.4, 71.0, 70.9, 51.9, 27.0, 26.9 ppm. $C_{18}H_{24}O_6$ (336.38): calcd. C 64.27, H 7.19; found C 64.38, H 7.30.

Compound 16: $[\alpha]_D^{20} = -9.4$ ($c = 1.32$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.20 (m, 5 H), 6.34 (s, 1 H), 5.95 (s, 1 H), 4.59 (s, 2 H), 4.55 (d, J = 2.6 Hz, 1 H), 4.23 (dt, J = 8.2, 5.0 Hz, 1 H), 4.03 (dd, J = 8.2, 3.1 Hz, 1 H), 3.73 (s, 3 H), 3.61 (d, J = 1.2 Hz, 1 H), 3.60 (s, 1 H), 2.96 (d, J = 8.8 Hz, 1 H), 1.44 (s, 3 H), 1.41 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 139.8, 137.8, 128.4 (2 C), 128.0, 127.7 (2 C), 126.6, 109.9, 79.8, 76.6, 73.5, 70.3, 69.1, 51.9, 27.1, 26.9 ppm. $C_{18}H_{24}O_6$ (336.38): calcd. C 64.27, H 7.19; found C 64.02, H 7.29.

***p*-Nitrobenzoate 17:** DEAD (2.2 mL, 40% in toluene, 4.84 mmol) was added dropwise to a cooled (0 °C) solution of compound **16** (628 mg, 1.87 mmol), Ph_3P (740 mg, 2.82 mmol), and *p*-nitrobenzoic acid (470 mg, 2.81 mmol) in THF (18 mL), and the solution was allowed to warm to room temp. and stirred for 3 h. The solvent was removed, and the residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:12 to 1:6) to afford **17** (828 mg, 91%) as a yellow oil. $[\alpha]_D^{18} = -11.3$ ($c = 1.33$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, J = 8.9 Hz, 2 H), 8.13 (d, J = 8.9 Hz, 2 H), 7.34–7.15 (m, 5 H), 7.02 (d, J = 8.4 Hz, 1 H), 5.20–5.10 (AB, J_{AB} = 12.0 Hz, 2 H), 4.91 (t, J = 8.2 Hz, 1 H), 4.57–4.48 (AB, J_{AB} = 12.0 Hz, 2 H), 4.04 (dt, J = 8.0, 4.6 Hz, 1 H), 3.81 (s, 3 H), 3.64 (d, J = 4.6 Hz, 2 H), 1.45 (s, 2 × 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.0, 164.2, 150.6, 144.2, 137.6, 135.3, 130.8 (2 C), 129.8, 128.4 (2 C), 127.8, 127.6 (2 C), 123.5 (2 C), 110.6, 79.7, 74.5, 73.7, 69.0, 59.3, 52.4, 26.9 (2 C) ppm. $C_{25}H_{27}NO_9$ (485.48): calcd. C 61.85, H 5.60, N 2.88; found C 61.87, H 5.75, N 2.62.

Allylic Alcohol 18: K_2CO_3 (848 mg, 6.14 mmol) was added to a cooled (0 °C) solution of compound **17** (1.494 g, 3.07 mmol) in MeOH (30 mL), and the mixture was stirred for 1 h, poured into brine, and extracted with Et_2O (3 × 30 mL). The combined organic phase was washed twice with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:6 to 1:3) to afford **18** (873 mg, 84%) as a colorless oil. $[\alpha]_D^{20} = -31.3$ ($c = 1.18$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.26 (m, 5 H), 6.80 (d, J = 8.7 Hz, 1 H), 4.83 (t, J = 8.4 Hz, 1 H), 4.63–4.54 (AB, J_{AB} = 11.7 Hz, 2 H), 4.41–4.26 (AB, J_{AB} = 12.6 Hz, 2 H), 3.97 (dt, J = 8.4, 4.5 Hz, 1 H), 3.80 (s, 3 H), 3.66 (dd, J = 4.5, 0.9 Hz, 1 H), 2.66 (br. s, 1 H), 1.46 (s, 3 H), 1.45 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1, 140.4, 137.5, 134.6, 128.4 (2 C), 127.9 (3 C), 110.3, 79.5, 74.4, 73.8, 68.9, 57.2, 52.2, 26.9 (2 C) ppm. $C_{18}H_{24}O_6$ (336.38): calcd. C 64.27, H 7.19; found C 64.11, H 7.16.

TBS Ether 19: TBSCl (1.130 g, 7.51 mmol) was added at room temp. to a solution of compound **18** (1.217 g, 3.62 mmol), Et_3N (1.28 mL, 9.2 mmol), and DMAP (19 mg) in CH_2Cl_2 (18 mL), and stirring was continued overnight. The mixture was diluted with EtOAc, washed successively with HCl (1 M), water, and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:10) to afford **19** (1.591 g, 98%) as a colorless oil. $[\alpha]_D^{20} = -25.8$ ($c = 1.69$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 5 H), 6.72 (d, J = 8.9 Hz, 1 H), 4.85 (t, J = 8.6 Hz, 1 H), 4.58 (s, 2 H), 4.46–4.32 (AB, J_{AB} = 11.9 Hz, 2 H), 4.00 (ddd, J = 8.3, 5.5, 3.2 Hz, 1 H), 3.76 (s, 3 H), 3.67 (dd, J = 10.8, 3.3 Hz, 1 H), 3.61 (dd, J = 10.8, 5.5 Hz, 1 H), 1.46 (s, 2 × 3 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 140.1, 138.0, 135.2, 128.4 (2 C), 127.6 (3 C), 110.3, 80.2, 73.7, 73.6, 69.2, 57.6, 52.0, 27.0 (2 C), 25.9 (3 C), 18.3, –5.4 (2 C) ppm. $C_{24}H_{38}O_6Si$ (450.64): calcd. C 63.96, H 8.50; found C 64.29, H 8.70.

Diol 11: OsO_4/*t*BuOH (0.1 M, 0.7 mL, 0.07 mmol) was added at room temp. to a solution of compound **12** (202 mg, 0.60 mmol) and NMO·H_2O (270 mg, 2.00 mmol) in acetone/H_2O (8:1, 18 mL), and stirring was continued for 3 h. The mixture was quenched with Na_2SO_3 (0.90 g), stirred vigorously for 1 h, and filtered. The filtrate was concentrated under reduced pressure and the residue was passed through a short silica gel column (eluted with EtOAc). The crude triol (245 mg) was dissolved in CH_2Cl_2 (6 mL) and treated at room temp. overnight with Et_3N (0.10 mL, 0.72 mmol), DMAP (10 mg), and TBSCl (108 mg, 0.72 mmol). The mixture was diluted with EtOAc, washed successively with HCl (1 M), water, and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:3) to afford **11** (260 mg, 89%) as a colorless oil. $[\alpha]_D^{20} = +1.1$ ($c = 1.08$, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.24 (m, 5 H), 4.64–4.54 (AB, J_{AB} = 12.2 Hz, 2 H), 4.22 (dt, J = 7.5, 5.2 Hz, 1 H), 3.92–3.84 (AB, J_{AB} = 10.6 Hz, 2 H), 3.86–3.82 (m, 1 H), 3.80 (s, 3 H), 3.68 (dd, J = 9.8, 5.1 Hz, 1 H), 3.66

(br. s, 1 H), 3.60 (dd, J = 9.8, 5.2 Hz, 1 H), 3.04 (br. d, J = 8.1 Hz, 1 H), 1.38 (s, 2 × 3 H), 0.95 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.8, 137.5, 128.4 (2 C), 127.8 (3 C), 109.6, 81.9, 78.6, 77.2, 74.1, 73.5, 70.6, 66.0, 52.7, 26.9, 26.8, 25.7 (3 C), 18.1, –5.5, –5.7 ppm. $C_{24}H_{40}O_8Si$ (484.66): calcd. C 59.48, H 8.32; found C 59.27, H 8.31.

Epoxide 21: MsCl (0.15 mL, 1.94 mmol) was added dropwise to a cooled (0 °C) solution of compound **11** (470 mg, 0.97 mmol) and Py (1.2 mL, 14.9 mmol) in CH_2Cl_2 (10 mL), and stirring was continued for 48 h at room temp. The solvent was removed under reduced pressure, and the residue was diluted with MeOH (6 mL), treated with K_2CO_3 (1.45 g, 10.5 mmol) at room temp. for 1 h, and diluted with Et_2O. The organic layer was washed successively with satd. aq. $CuSO_4$ and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:10) to afford **21** (411 mg, 91%) as a colorless oil. $[\alpha]_D^{20}$ = –22.2 (c = 2.34, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.26 (m, 5 H), 4.56 (s, 2 H), 4.21–3.76 (AB, J_{AB} = 11.8 Hz, 2 H), 4.12 (dt, J = 8.0, 4.7 Hz, 1 H), 3.96 (dd, J = 7.8, 6.7 Hz, 1 H), 3.62 (s, 3 H), 3.55 (dd, J = 10.6, 4.9 Hz, 1 H), 3.52 (dd, J = 10.6, 4.5 Hz, 1 H), 3.24 (d, J = 6.6 Hz, 1 H), 1.43 (s, 3 H), 1.40 (s, 3 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 137.9, 128.5 (2 C), 127.8, 127.7 (2 C), 110.6, 77.4, 75.8, 73.7, 69.5, 62.6, 59.0, 52.3, 27.1, 26.8, 25.8, 18.3, –5.4 (2 C) ppm. $C_{24}H_{38}O_7Si$ (466.64): calcd. C 61.77, H 8.21; found C 62.08, H 8.29.

Alcohol 10: DIBAL/hexane (1.0 M, 6.8 mL, 6.8 mmol) was added dropwise to a cooled (–78 °C) solution of **21** (749 mg, 1.61 mmol) in CH_2Cl_2 (7 mL), and stirring was continued for 2 h. The reaction mixture was quenched with satd. aq. NH_4Cl, allowed to warm to room temp., and stirred for another 30 min. The mixture was filtered through celite, the filter cake was washed with CH_2Cl_2, and the combined filtrate was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was taken up in MeOH (7 mL) and cooled to 0 °C, $NaBH_4$ (67 mg, 1.81 mmol) was added, and the mixture was stirred for 30 min at room temp., diluted with water, and extracted with Et_2O. The combined organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:3) to afford **10** (616 mg, 90%) as a colorless oil. $[\alpha]_D^{20}$ = –18.2 (c = 2.04, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 5 H), 4.62–4.55 (AB, J_{AB} = 12.0 Hz, 2 H), 4.12–4.08 (m, 1 H), 4.01 (t, J = 7.5 Hz, 1 H), 3.86 (dd, J = 12.0, 7.5 Hz, 1 H), 3.83–3.72 (AB, J_{AB} = 12.0 Hz, 2 H), 3.69 (dd, J = 9.5, 4.5 Hz, 1 H), 3.63 (dd, J = 11.0, 6.0 Hz, 1 H), 3.58 (dd, J = 12.0, 4.5 Hz, 1 H), 3.09 (d, J = 8.5 Hz, 1 H), 2.76 (br. t, J = 6.0 Hz, 1 H), 1.46 (s, 3 H), 1.40 (s, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8, 128.3 (2 C), 127.9, 127.8 (2 C), 110.0, 77.1, 77.0, 73.7, 69.5, 63.9, 63.3, 60.6, 60.1, 26.9, 26.8, 25.6 (3 C), 18.0, –5.7 (2 C) ppm. $C_{23}H_{38}O_6Si$ (438.63): calcd. C 62.98, H 8.73; found C 63.32, H 8.80.

Carbamate 23: Cl_3CCN (0.18 mL, 1.8 mmol) was added to a cooled (0 °C) solution of compound **10** (603 mg, 1.38 mmol) in CH_2Cl_2 (12 mL), followed by DBU (0.038 mL, 0.25 mmol). The mixture was stirred for 30 min, diluted with EtOAc, washed with water and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was passed through a short silica gel column (eluted with EtOAc/hexanes, 1:6) to afford the crude trichloroacetimidate (823 mg) as a colorless oil.

The above intermediate was dissolved in CH_2Cl_2 (12 mL) and cooled (0 °C), and Et_2AlCl (1.0 M in hexane, 0.69 mL, 0.69 mmol) was added dropwise. The solution was allowed to warm to room temp., stirring was continued for 30 min, and the reaction mixture was quenched with aq. $NaHCO_3$, followed by extraction with Et_2O. The combined organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:6) to afford **22** (780 mg, 97%) as a colorless oil.

A solution of triphosgene in CH_2Cl_2 (0.67 M, 0.85 mL, 0.57 mmol) was added to a cooled (–35 °C) solution of **22** (780 mg, 1.34 mmol) and pyridine (0.14 mL, 1.73 mmol) in CH_2Cl_2 (10 mL), the mixture was stirred at room temp. for 4 h, and water (0.072 mL, 4.0 mmol) was added. After having been stirred for an additional 1 h, the mixture was diluted with EtOAc, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was taken up in MeOH (24 mL) and treated with K_2CO_3 (146 mg, 1.06 mmol) for 30 min at room temp., filtered through celite, concentrated under reduced pressure, and purified by silica gel column chromatography (EtOAc/hexanes, 1:1) to afford **23** (520 mg, 81%) as a pale yellow oil. $[\alpha]_D^{20}$ = –48.4 (c = 1.64, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.24 (m, 5 H), 6.34 (br. s, 1 H), 4.55 (s, 2 H), 4.38 (s, 1 H), 4.31–4.23 (m, 1 H), 4.20 (d, J = 8.5 Hz, 1 H), 4.06–3.77 (AB, J_{AB} = 9.8 Hz, 2 H), 3.74–3.60 (m, 3 H), 3.60–3.44 (m, 2 H), 1.42 (s, 2 × 3 H), 0.86 (s, 9 H), 0.05 (s, 2 × 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 137.8, 128.4 (2 C), 127.7, 127.6 (2 C), 110.3, 77.9, 76.9, 75.4, 73.6, 70.0, 65.5, 63.5, 62.2, 27.4, 26.2, 25.7 (3 C), 18.0, –5.7, –5.8 ppm. $C_{24}H_{39}NO_7Si$ (481.65): calcd. C 59.85, H 8.16, N 2.91; found C 59.55, H 8.44, N 2.64.

MOM Ether 9: A solution of compound **23** (224 mg, 0.46 mmol), DIPEA (0.72 mL, 4.36 mmol), and MOMCl (0.17 mL, 2.1 mmol) in CH_2Cl_2 (10 mL) was heated at reflux for 4 h, cooled, poured into water, and extracted with EtOAc (2 × 20 mL). The combined organic layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:6) to afford **9** (213 mg, 87%) as a colorless oil. $[\alpha]_D^{18}$ = –40.4 (c = 1.77, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 5 H), 5.39 (br. s, 1 H), 4.59 (s, 2 H), 4.55 (s, 2 H), 4.33 (s, 1 H), 4.31 (dt, J = 6.2, 4.5 Hz, 1 H), 4.06 (d, J = 8.4 Hz, 1 H), 3.99–3.87 (AB, J_{AB} = 9.6 Hz, 2 H), 3.72 (part of AB-d, J_{AB} = 9.9, J = 4.7 Hz, 1 H), 3.63–3.54 (AB, J_{AB} = 9.5 Hz, 2 H), 3.53 (part of AB-d, J_{AB} = 9.9, J = 6.1 Hz, 1 H), 3.30 (s, 3 H), 1.44 (s, 3 H), 1.42 (s, 3 H), 0.87 (s, 9 H), 0.06 (s, 2 × 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 137.8, 128.4 (2 C), 127.8, 127.6 (2 C), 110.5, 96.9, 77.9, 77.4, 75.1, 73.7, 70.2, 69.4, 62.4, 61.2, 55.5, 27.4, 26.1, 25.7 (3 C), 18.1, –5.7, –5.8 ppm. $C_{26}H_{43}NO_8Si$ (525.71): calcd. C 59.40, H 8.24, N 2.66; found C 59.43, H 8.34, N 2.81.

Synthesis of 24: A suspension of compound **9** (114 mg, 0.22 mmol) and $Pd(OH)_2$/C (20%, 18 mg) in EtOAc/MeOH (4:1, 2.4 mL) was stirred under hydrogen at room temp. for 2 h, filtered through celite, and concentrated to afford the crude alcohol (95 mg) as a colorless oil. DMSO (0.046 mL, 0.65 mmol) was added to a cooled (–78 °C) solution of $(COCl)_2$ (0.039 mL, 0.45 mmol) in CH_2Cl_2 (2.5 mL), the mixture was stirred for 5 min, and a solution of the above alcohol in CH_2Cl_2 (2.0 mL) was added. After the system had been stirred for 30 min, Et_3N (0.31 mL, 2.2 mmol) was added, and the mixture was stirred at –78 °C for an additional 30 min, allowed to warm gradually to 0 °C, poured into water, and extracted with CH_2Cl_2. The combined organic layer was washed with water and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford the crude aldehyde (98 mg) as a pale yellow oil.

A cooled (0 °C) solution of phosphonium salt **8** (450 mg, 0.75 mmol) in THF (4 mL) was treated with BuLi (1.6 M in hexane,

0.41 mL, 0.66 mmol), stirred at room temp. for 10 min, and cooled to –78 °C, and a solution of the above aldehyde in THF (1.6 mL) was added dropwise. The mixture was stirred at this temperature for 1 h, allowed to warm to room temp., and quenched with satd. aq. NH_4Cl. The aq. phase was extracted with Et_2O, and the combined organic layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:6 to 1:3) to afford (*Z*)-**24** (77 mg, 53%) and (*E*)-**24** (9 mg, 6%) as colorless oils.

Compound (*Z*)-24: $[\alpha]_D^{18}$ = –25.6 (*c* = 0.92, $CHCl_3$). NMR peaks were broadened, due to the presence of rotamers. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.74 (dt, *J* = 10.7, 7.1 Hz, 1 H), 5.40 (br. s, 1 H), 5.31 (dd, *J* = 10.7, 9.1 Hz, 1 H), 4.88 (t, *J* = 9.1 Hz, 1 H), 4.62 (s, 2 H), 4.09 (s, 1 H), 3.98–3.86 (AB, J_{AB} = 9.6 Hz, 2 H), 3.92 (s, 4 H), 3.76 (d, *J* = 8.8 Hz, 1 H), 3.64–3.56 (AB, J_{AB} = 9.6 Hz, 2 H), 3.34 (s, 3 H), 2.26–1.97 (m, 2 H), 1.63–1.50 (m, 4 H), 1.44 (s, 3 H), 1.43 (s, 3 H), 1.42–1.16 (m, 16 H), 0.89 (s, 9 H), 0.87 (t, *J* = 6.9 Hz, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0, 137.8, 124.7, 111.8, 110.0, 96.8, 78.6, 76.4, 72.7, 69.4, 64.8 (2 C), 62.4, 61.1, 55.5, 37.1, 37.0, 31.8, 29.7, 29.5 (2 C), 29.1, 27.8, 27.5, 26.1, 25.7 (3 C), 23.7 (2 C), 22.5, 18.0, 14.0, –5.7, –5.8 ppm. HR-MS: calcd. for $C_{34}H_{62}NO_9Si$ $[M - CH_3]^+$ 656.4220; found 656.4247.

Compound (*E*)-24: A solution of (*Z*)-**24** (33 mg, 0.049 mmol) and PhSSPh (21 mg, 0.096 mmol) in cyclohexane/dioxane (19:1, 8 mL) was irradiated with a high-pressure mercury lamp for 9 h at room temp. The mixture was poured into satd. aq. $NaHCO_3$ (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:3) to afford (*E*)-**24** [21 mg, 95% based on reacted (*Z*)-**24**] as a colorless oil, together with unreacted (*Z*)-**24** (12 mg). $[\alpha]_D^{18}$ = –38.2 (*c* = 1.01, $CHCl_3$). NMR peaks were broadened, due to the presence of rotamers. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.90 (dt, *J* = 15.4, 6.9 Hz, 1 H), 5.38 (dd, *J* = 15.4, 8.0 Hz, 1 H), 5.24 (br. s, 1 H), 4.64 (s, 2 H), 4.47 (t, *J* = 8.5 Hz, 1 H), 4.14 (s, 1 H), 3.97–3.87 (AB, J_{AB} = 9.6 Hz, 2 H), 3.93 (s, 4 H), 3.80 (d, *J* = 8.8 Hz, 1 H), 3.67–3.58 (AB, J_{AB} = 9.3 Hz, 2 H), 3.35 (s, 3 H), 2.10–1.95 (m, 2 H), 1.75–1.45 (m, 4 H), 1.44 (s, 3 H), 1.43 (s, 3 H), 1.42–1.10 (m, 16 H), 0.90 (s, 9 H), 0.88 (t, *J* = 6.9 Hz, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.8, 138.5, 125.4, 111.8, 109.9, 96.9, 78.5, 78.4, 76.4, 69.4, 64.9 (2 C), 62.3, 61.1, 55.5, 37.1 (2 C), 32.3, 31.8, 29.8, 29.6, 29.2, 28.8, 27.5, 26.1, 25.7 (3 C), 23.8, 23.7, 22.6, 18.1, 14.1, –5.7 (2 C) ppm. HR-MS: calcd. for $C_{31}H_{56}NO_9Si$ $[M - C_4H_9]^+$ 614.3698; found 614.3672.

Lactone 25: A solution of (*E*)-**24** (140 mg, 0.21 mmol) in THF (2.6 mL) was treated with TBAF/THF (1 M, 0.31 mL, 0.31 mmol) for 15 min at room temp., diluted with EtOAc, washed with water and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was passed through a short silica gel column (eluted with EtOAc) to afford a colorless oil (108 mg, 93%). The above crude alcohol (87 mg, 0.17 mmol) was dissolved in DMF (1.0 mL), PDC (535 mg, 1.42 mmol) was added in one portion, and stirring was continued for 24 h. The mixture was diluted with water and extracted with Et_2O (6 × 10 mL), and the combined organic layer was washed with water and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude acid (85 mg, 0.16 mmol) was dissolved in EtOH/H_2O (7:3, 4.5 mL), TsOH·H_2O (134 mg, 0.70 mmol) was added, and the system was heated at reflux for 8 h, allowed to cool, diluted with Et_2O, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 2:1) to afford **25** (53 mg, 77%) as a colorless oil. $[\alpha]_D^{18}$ = –11.9 (*c* = 0.50, $CHCl_3$). NMR peaks were broadened, due to the presence of rotamers. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.44 (br. s, 1 H), 5.95 (dt, *J* = 15.4, 6.9 Hz, 1 H), 5.54 (dd, *J* = 15.4, 6.0 Hz, 1 H), 5.16 (d, *J* = 4.1 Hz, 1 H), 4.65–4.40 (m, 3 H), 4.15–3.80 (br. m, 1 H), 4.02–3.87 (AB, J_{AB} = 11.3 Hz, 2 H), 2.38 (t-like, *J* = 7.1 Hz, 2 × 2 H), 2.14–1.93 (m, 2 H), 1.62–1.45 (m, 4 H), 1.45–1.10 (m, 12 H), 0.87 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 212.5, 174.8, 157.6, 136.2, 125.7, 84.4, 78.9, 69.9, 66.8, 61.3, 42.8, 42.7, 32.2, 31.5, 28.9 (3 C), 28.5, 23.8, 23.7, 22.4, 14.0 ppm. HR-MS: calcd. for $C_{21}H_{39}NO_7$ $[M]^+$ 425.2387; found 425.2361.

Sphingofungin E (1): Aq. NaOH (1 M, 1.0 mL) was added to a solution of **25** (34 mg, 0.08 mmol) in MeOH (1.0 mL) and the mixture was heated at reflux for 2 h, allowed to cool, and neutralized with IRC-76 resin. The resin was filtered off and washed with MeOH, and the combined filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($CHCl_3$/MeOH/H_2O 10:3:1) to afford **1** (25 mg, 75%) as a white solid. M.p. 147–149 °C. $[\alpha]_D^{18}$ = –13.0 (*c* = 0.30, MeOH). ^1H NMR (500 MHz, CD_3OD): δ = 5.76 (dt, *J* = 15.4, 6.6 Hz, 1 H), 5.45 (dd, *J* = 15.4, 7.7 Hz, 1 H), 4.10 (t, *J* = 7.3 Hz, 1 H), 3.98–3.83 (AB, J_{AB} = 10.9 Hz, 2 H), 3.95 (s, 1 H), 3.63 (d, *J* = 6.8 Hz, 1 H), 2.44 (t, *J* = 7.2 Hz, 4 H), 2.05 (q-like, 2 H), 1.60–1.47 (m, 4 H), 1.46–1.21 (m, 12 H), 0.89 (t, *J* = 7.3 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 214.4, 173.0, 135.7, 130.2, 76.2, 75.6, 71.2, 70.2, 64.9, 43.5 (2 C), 33.4, 32.8, 30.2, 30.1, 30.0 (2 C), 24.9, 24.7, 23.6, 14.3 ppm. HR-ESI-MS: calcd. for $C_{21}H_{40}NO_7$ $[M + H]^+$ 418.2799; found 418.2799.

Iodide 26: I_2 (240 mg, 0.94 mmol) was added at room temp. to a solution of compound **10** (236 mg, 0.54 mmol), Ph_3P (212 mg, 0.82 mmol), and imidazole (55 mg, 0.81 mmol) in Et_2O/MeCN (3:1, 6 mL), and stirring was continued for 3 h. The mixture was quenched with satd. aq. $Na_2S_2O_3$ and extracted with CH_2Cl_2 (2 × 15 mL), and the combined organic layer was washed with water and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:15) to afford **26** (288 mg, 97%) as a colorless oil. $[\alpha]_D^{23}$ = –12.2 (*c* = 1.55, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 5 H), 4.62–4.54 (AB, J_{AB} = 12.0 Hz, 2 H), 4.16 (dt, *J* = 8.5, 2.7 Hz, 1 H), 4.01 (dd, *J* = 8.0, 5.0 Hz, 1 H), 3.83–3.70 (AB, J_{AB} = 11.0 Hz, 2 H), 3.67 (part of AB-d, J_{AB} = 10.5, *J* = 4.5 Hz, 1 H), 3.64 (part of AB-d, J_{AB} = 10.5, *J* = 5.5 Hz, 1 H), 3.46–3.32 (AB, J_{AB} = 10.5 Hz, 2 H), 3.20 (d, *J* = 7.0 Hz, 1 H), 1.44 (s, 3 H), 1.43 (s, 3 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.6, 128.5 (2 C), 127.9 (3 C), 110.4, 77.8, 75.7, 73.7, 69.4, 65.0, 63.6, 63.0, 27.0, 26.8, 25.8 (3 C), 18.2, 3.3, –5.4 (2 C) ppm. HR-ESI-MS: calcd. for $C_{23}H_{37}IO_5SiNa$ $[M + Na]^+$ 571.1353; found 571.1370.

Epoxide 15: $LiBHEt_3$/THF (1.0 M, 0.26 mL, 0.26 mmol) was added dropwise at room temp. to a solution of compound **26** (69 mg, 0.13 mmol) in THF (1.2 mL), stirring was continued for 15–20 min, and the solution was then cooled to 0 °C and quenched with aq. H_2O_2 (30%). After the system had been stirred for 5 min, satd. aq. $Na_2S_2O_3$ was added and the mixture was extracted with Et_2O (3 × 15 mL). The combined organic phase was washed with aq. $FeSO_4$ and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexanes, 1:15) to afford **15** (42 mg, 80%)

as a colorless oil. $[\alpha]_D^{24}$ = –22.7 (*c* = 0.42, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H), 4.61–4.54 (AB, J_{AB} = 12.1 Hz, 2 H), 4.07 (dt, *J* = 8.1, 4.2 Hz, 1 H), 3.86 (t, *J* = 8.0 Hz, 1 H), 3.63 (part of AB-d, J_{AB} = 10.5, *J* = 4.0 Hz, 1 H), 3.58 (part of AB-d, J_{AB} = 10.5, *J* = 4.8 Hz, 1 H), 3.56–3.48 (AB, J_{AB} = 11.2 Hz, 2 H), 2.95 (d, *J* = 8.0 Hz, 1 H), 1.47 (s, 3 H), 1.43 (s, 3 H), 1.24 (s, 3 H), 0.88 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.7, 128.4 (2 C), 127.7 (3 C), 110.1, 77.7, 73.67, 69.2, 67.3, 60.7, 60.5, 27.1, 26.9, 25.8 (3 C), 18.3, 14.8, –5.4 (2 C) ppm. HR-ESI-MS: calcd. for $C_{23}H_{39}O_5Si$ $[M + Na]^+$ 445.2386; found 445.2380.

Supporting Information (see also the footnote on the first page of this article): ^1H and ^{13}C NMR spectra for the new compounds **9**–**12**, **15**–**19**, **21**, **23**–**26** and for **1**.

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