Formal Total Synthesis of Hemibrevetoxin B by an Oxiranyl Anion Strategy

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The synthesis of the tetracyclic structure of hemibrevetoxin B (**1**) was achieved through a linear approach involving sequential coupling of three kinds of sulfonyl-stabilized oxiranyl anions, **5b**, **6b**, and **7b**, to the monocyclic tetrahydropyran **4** containing the requisite substituents. Two iterations of alkylation of an oxiranyl anion and 6-*endo* cyclization provided the 6,6,6-tricyclic ring system **34**, which was efficiently transformed into the 6,6,7-ring system **35** by ring expansion using trimethylsilyldiazomethane. Installation of the final oxepane ring into **38** was carried out using a combination of the oxiranyl anion methodology and ring enlargement just described. Stereoselective introduction of a tertiary methyl group into **41** provided the tetracyclic compound **42a**, which contains all the asymmetric centers of **1**. Elaboration of **42a** to the known compound **2**, which was already transformed into hemibrevetoxin B, completed the formal total synthesis of the natural product.

Introduction

One of the most characteristic and interesting classes of marine toxins produced by dinoflagellates is the polycyclic ethers. The linear cyclic structure was first demonstrated in brevetoxin B, the major toxin in the Florida red tide organism *Gymnodinium breve*, and its unprecedented structure was elucidated by X-ray crystallography in 1980.[1] Subsequently, the structure of the most toxic component, brevetoxin A, was also determined by X-ray crystallography.[2] Although several other brevetoxin-type metabolites have been reported,[3] a new type of toxin, hemibrevetoxin B (**1**), which has about half the skeleton of brevetoxins, has been recently discovered in the cultured cells of the same organism.[4]

Hemibrevetoxin B is the smallest member of the marine polycyclic ethers. This unique 6,6,7,7-tetracyclic structure containing 10 stereocenters, an α-vinyl aldehyde moiety, and a *Z*-diene system has attracted the attention of synthetic chemists, and a variety of approaches to its synthesis have been explored.[5] Recently, three total syntheses of hemibrevetoxin B have been accomplished by using new synthetic methods: 6-*endo* cyclization and dioxepane ring formation by the hydroboration of an enol ether derived from thionolactone by Nicolaou,[6] the Lewis acid-mediated intramolecular allylstannane−aldehyde condensation by Yamamoto,[7] and a double rearrangement-ring expansion of a 6,6-bicyclic ether to a dioxepane ring by the Nakata group.[8] Herein we report in detail the formal total synthesis of hemibrevetoxin B using unique nucleophilic oxiranyl anions as building blocks.[9]

Retrosynthetic Analysis. The retrosynthetic analysis of hemibrevetoxin B (**1**) based on a linear approach is shown in Scheme 1. The two side chains in the target structure were partially disconnected to provide the key intermediate **2**. We envisioned that the two oxepane rings of **2** are constructed by the ring expansion of tetrahydropyrans, so we tentatively regarded the tetracyclic tetrahydropyran **3** as an imaginary precursor. The indicated C−O and C−C bonds of **3** were disconnected to unravel the monocyclic diol **4** and three oxiranyl anions **5b**, **6b**, and **7b**, which could be generated from the corresponding epoxy sulfones **5a**, **6a**, and **7a**, respectively.

The sulfonyl-stabilized oxiranyl anions are unique nucleophilic epoxides and serve as a new type of functionalized acyl anion equivalent.[10,11] Based on our strategy, the use of the sulfonyl-stabilized *cis*-oxiranyl anions was expected to induce an efficient C−C bond formation on an epoxide ring, a stereocontrolled 6-*endo* mode of cyclization, and a facile generation of a carbonyl group

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(11) For reviews of oxiranyl anions, see: (a) Satoh, T. *Chem. Rev.* **1996**, *96*, 3303−3325; (b) Mori, Y. *J. Synth. Org. Chem. Jpn.* **1997**, *55*, 26−35; (c) Mori, Y. *Reviews on Heteroatom Chemistry*; Oae, S., Ed.; MYU: Tokyo, 1997; Vol. 17, pp 183−211.

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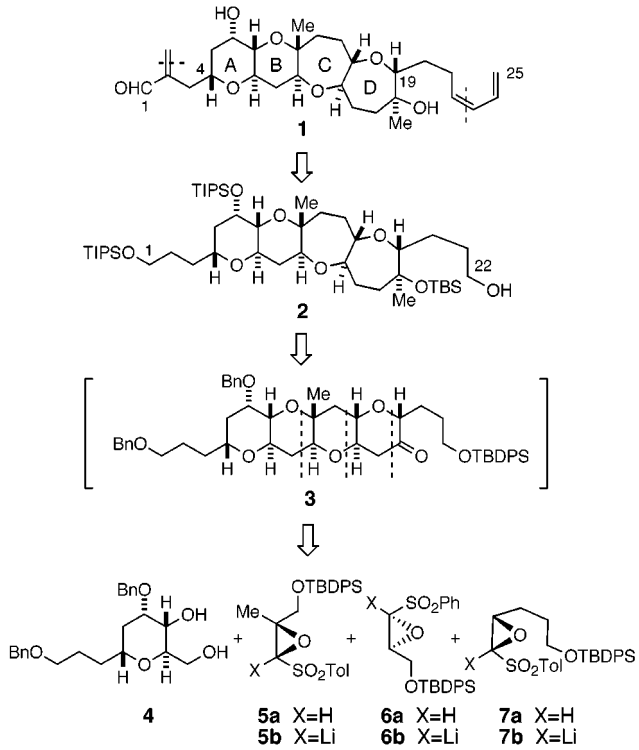
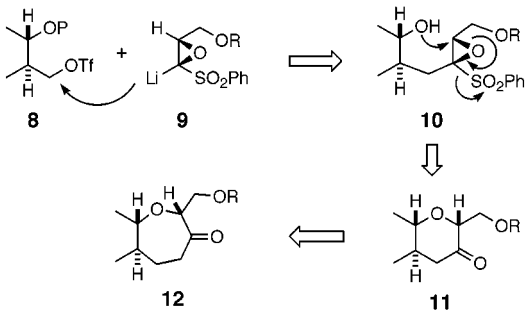
Scheme 1



Scheme 2

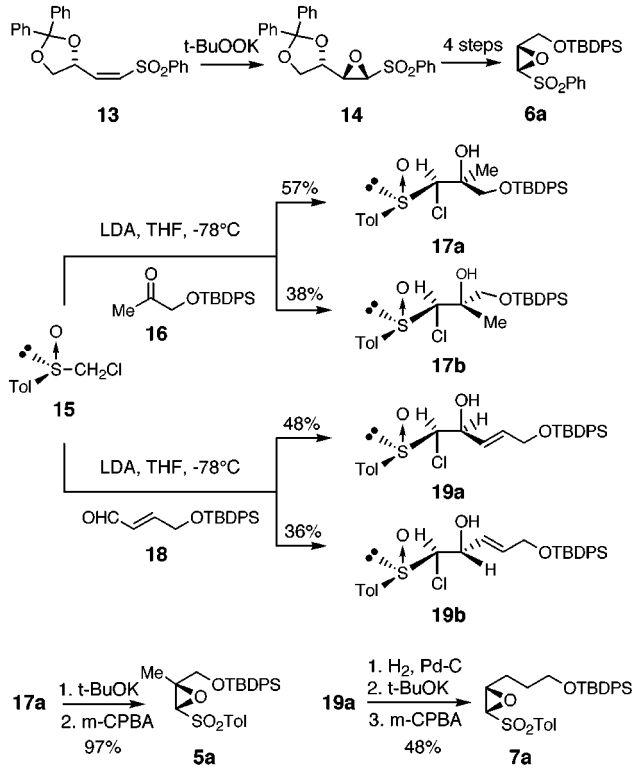


as shown in Scheme 2. Theoretically, the coupling product **10** could suffer ring closure through the 5-*exo* and 6-*endo* mode of cyclization, leading to a tetrahydrofuran or a tetrahydropyran system, respectively. However, the strong electron-withdrawing ability of the sulfonyl group works against the adjacent C−O bond-breaking in an acid-catalyzed epoxide ring-opening process and, consequently, favors the *endo*-mode pathway, which yields tetrahydropyranone **11** after elimination of benzenesulfinic acid.[12] Moreover, the resulting ketone **11** can be directly converted to oxepane **12** by a ring expansion reaction.[13] A combination of the stepwise couplings of three oxiranyl anions **5b**, **6b**, and **7b** to diol **4** and the ring expansion at suitable stages would give the key intermediate **2**. Yamamoto has already described the conversion of **2** into hemibrevetoxin B,[7] so the synthesis of **2** constitutes the formal total synthesis of the natural product.

Results and Discussion

Synthesis of Epoxy Sulfones. Optically active epoxy sulfone **6a** was synthesized from *cis*-vinyl sulfone **13** by

Scheme 3



epoxidation and the subsequent four-step manipulation.[13] The synthesis of two other chiral epoxy sulfones **5a** and **7a** was carried out according to the procedure developed by Satoh et al.,[14] as shown in Scheme 3. Reactions of the carbanion generated from optically active (*R*)-(−)-chloromethyl *p*-tolyl sulfoxide **15** (98% ee) with ketone **16** and the unsaturated aldehyde **18** gave a mixture of two diastereoisomers **17a**,**b** and **19a**,**b**, respectively.[15] After chromatographic separation, the major chlorohydrins **17a** and **19a** were converted into epoxy sulfones **5a** and **7a**, respectively, via oxirane formation followed by oxidation. It is noteworthy that the reaction of **15** with a saturated aldehyde of **18** caused serious epimerization at the stereogenic center containing a chlorine atom to give an unseparable mixture of four diastereoisomers, whereas only two isomers were obtained when the unsaturated aldehyde **18** was employed. Presently, no reasonable explanation can be offered for this result.

Synthesis of Hemibrevetoxin B. Tri-*O*-acetyl-D-glucal (**20**) was utilized as the starting material for the construction of the tetracyclic system of hemibrevetoxin B (Scheme 4). Treatment of **20** with allyltrimethylsilane under the reported conditions[16] followed by methanolysis of the resulting diacetate gave diol **21** in 94% overall yield. Regio- and stereoselective epoxidation of the ring double bond in **21** was accomplished with *m*-chloroperoxybenzoic acid (*m*-CPBA) in toluene at 0 °C for 2 h, leading to an α-epoxy diol that was protected with benzylidene acetal to give **22** in 46% overall yield.[17] Selective reduction of epoxide **22** with $LiAlH_4$ and ben-

(12) (a) Mori, Y.; Yaegashi, K.; Furukawa, H. *J. Am. Chem. Soc.* **1996**, *118*, 8158−8159; (b) Mori, Y. *Chem. Eur. J.* **1997**, *3*, 849−852.

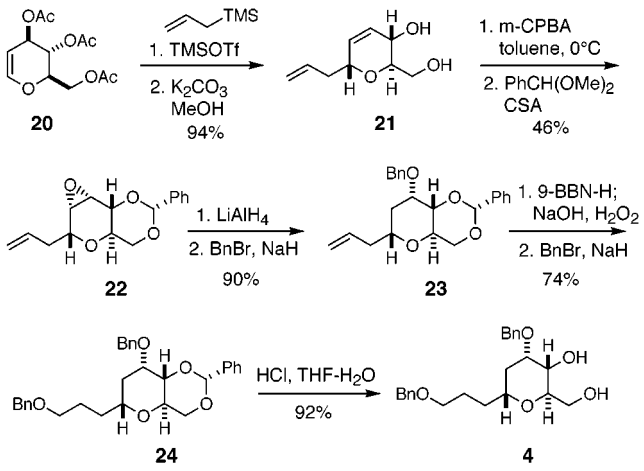
(13) Mori, Y.; Yaegashi, K.; Furukawa, H. *Tetrahedron* **1997**, *35*, 12917−12932.

(14) Satoh, T.; Oohara, T.; Ueda, Y.; Yamakawa, K. *J. Org. Chem.* **1989**, *54*, 3130−3136.

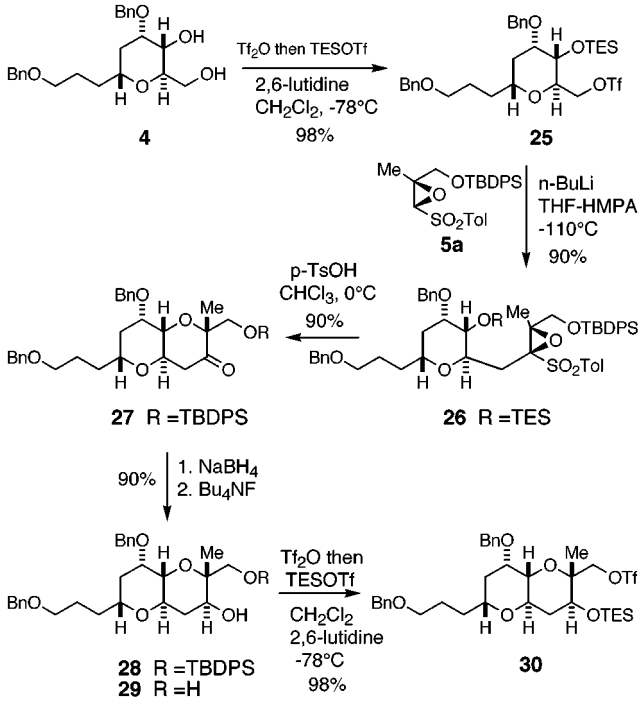
(15) The stereochemistry of chlorohydrins **17a**,**b** and **19a**,**b** were deduced from the ^{1}H NMR analysis of the corresponding epoxy sulfones obtained by treatment of the chlorohydrins with *tert*-BuOK: see Experimental Section and ref 14.

(16) Toshima, K.; Ishizuka, T.; Matsuo, G.; Nakata, M. *Tetrahedron Lett.* **1994**, *35*, 5673−5676.

Scheme 4



Scheme 5



zylation of the resulting α-axial alcohol gave the benzyl ether **23** in 90% yield. Hydroboration of the terminal olefin in **23** with 9-borabicyclo[3.3.1]nonane (9-BBN-H) in tetrahydrofuran (THF) followed by oxidative workup furnished an alcohol, which was benzylated to **24** in 74% overall yield. The monocyclic diol **4** was obtained from **24** in 92% yield by acid hydrolysis of the benzylidene acetal.

Regioselective activation and protection of the diol **4** as a triflate **25** were carried out using a one-pot process (Scheme 5). Thus, the treatment of a solution of **4** and 2,6-lutidine in CH_2Cl_2 with one equivalent of triflic anhydride at −78 °C for 30 min followed by the addition of a slight excess of triethylsilyl triflate gave the triflate **25** in 98% yield. The crucial coupling of **25** with the oxiranyl anion **5b** was accomplished by the addition of *n*-BuLi to a mixture of **5a** and **25** in THF−hexamethylphosphoramide (HMPA) at −110 °C,[18] providing the

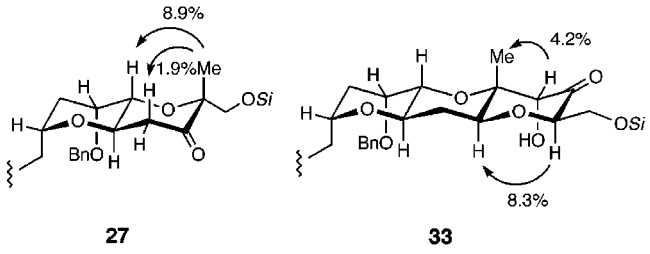


Figure 1. Important NOE interactions in **27** and **33**.

epoxy sulfone **26** in 90% yield. Compound **26** was appropriately designed to undergo an epoxide opening−ring closure type reaction.[12] Treatment with *p*-TsOH in $CHCl_3$ at 0 °C led to the desilylation at the secondary hydroxyl group and the subsequent stereospecific 6-*endo* cyclization to afford the bicyclic ketone **27** in 90% yield. The cyclization was accompanied with inversion of stereochemistry at the carbon undergoing nucleophilic attack as expected and as supported by the nuclear Overhauser effect (NOE) experiments depicted in Figure 1. Stereoselective reduction of **27** with $NaBH_4$ (>99% de) followed by desilylation gave the bicyclic diol **29**.

Installation of the third ring involved the challenging preparation of an oxepane ring. Unfortunately, several attempts to couple the triflate **30** derived from **29** with the oxiranyl anion **6b** were unsuccessful due to the considerable steric hindrance of the methyl group adjacent to the reaction site. This unexpected difficulty was circumvented by inducing the reaction between an oxiranyl anion and an aldehyde. The transformation of **29** to an aldehyde **31** was accomplished by bis(triethylsilylation), followed by regioselective desilylation of the primary hydroxyl group with pyridinium *p*-toluenesulfonate (PPTS) in CH_2Cl_2−methanol at −20 °C and SO_3·pyridine oxidation in 87% overall yield (Scheme 6).

The addition of the aldehyde **31** to a solution of the oxiranyl anion **6b** generated from the epoxy sulfone **6a** with *n*-BuLi in THF at −100 °C resulted in a low yield of the coupling product because of the serious decomposition of the unstable *cis*-oxiranyl anion.[10a] To prevent the decomposition of the oxiranyl anion, an in situ trapping method was attempted. Thus, a mixture of **6a** and **31** in THF−HMPA at −110 °C was treated with *n*-BuLi. To our surprise, a very good yield of the coupled product was obtained as a 3:1 mixture of epimers, from which **32a** and **32b** were isolated in 63 and 25% yield, respectively. It is noteworthy that the deprotonation of **6a** by *n*-BuLi is much faster than the butyl addition to the aldehyde **31**. Exposure of the major isomer **32a** to BF_3·OEt_2 led to its clean cyclization to the tricyclic hydroxy ketone **33** in 76% yield, whereas the minor isomer **32b** did not cyclize under the same conditions. In a presumed 6-*endo* cyclization transition state for the minor isomer **32b**, the methyl, hydroxyl, and sulfonyl substituents should be arrayed on the same side of a forming ring, which causes the serious steric interactions and prevents the cyclization. The configuration of the hydroxyl group of **33** was determined on the basis of the NOE interactions as indicated in Figure 1. The removal of the hydroxy group of **33** proved to be more problematic, although reduction

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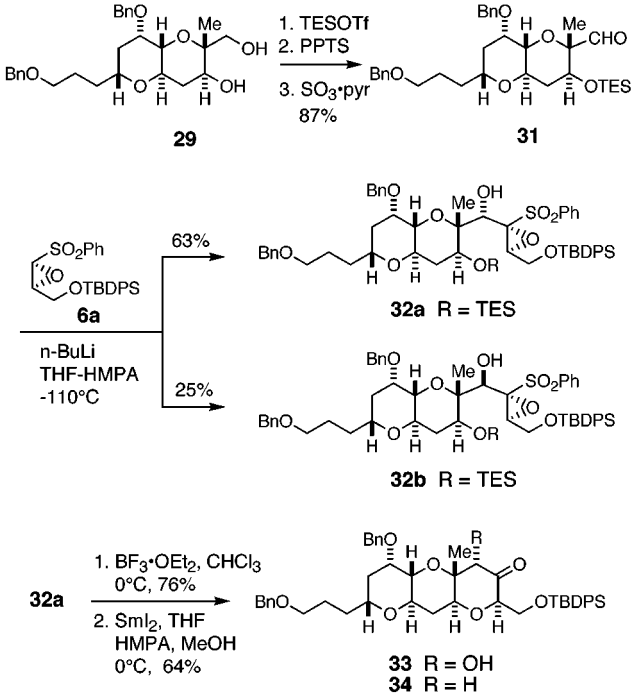
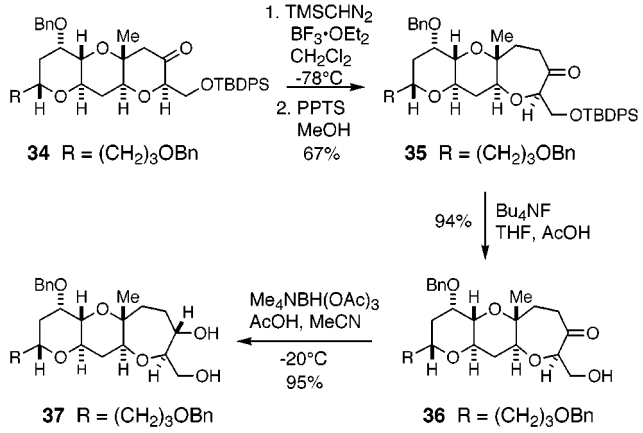
Scheme 6



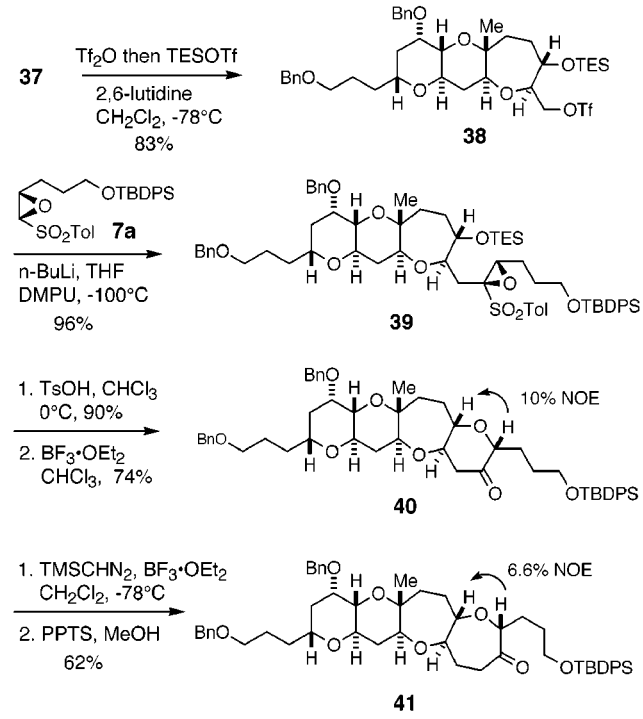
of the α-oxygenated ketones to the corresponding unsubstituted ketone has seen substantial use as a routine synthetic transformation. Because the introduction of leaving groups, such as acetyl, methanesulfonyl, and trifluoromethanesulfonyl groups, to the hydroxyl group under standard conditions resulted in low product yields, the direct dehydroxylation was undertaken. After several attempts with different reagents and different conditions, it was found that the best yields were obtained using four equivalents of SmI_2[19] in THF−HMPA−methanol at 0 °C leading to the tricyclic ketone **34** in 64% yield.

The crucial oxepane formation was accomplished by one-carbon homologation of the C-ring. Thus, reaction of **34** with trimethylsilyldiazomethane[20] in the presence of BF_3•OEt_2 in CH_2Cl_2 at −78 °C gave the seven-membered ketone **35** in 67% yield along with 17% of its isomeric ketone after acid hydrolysis of the intermediary trimethylsilyl enol ether (Scheme 7). The electron-inductive effect of the C-ring oxygen might control the direction of this ring expansion to a less crowded α-trimethylsilyl ketone, and the immediate rearrangement to the corresponding trimethylsily enol ether under the reaction conditions prevents the undesirable multiple homologation of the initially formed ketone.[13] Reduction of **35** under a variety of conditions led to the predominant formation of the undesired cis alcohol.[21] To reverse the stereoselectivity, **35** was desilylated with Bu_4NF in the presence of acetic acid, and the resulting hydroxy ketone (**36**) was subjected to the hydroxy-directed reduction with $Me_4NBH(OAc)_3$[22] to provide the expected *trans*-diol **37** as a single diastereoismer.

Scheme 7



Scheme 8



The third coupling of triflate **38** with epoxy sulfone **7a** with a three-carbon side chain was performed by an in situ trapping method; the coupling proceeded uneventfully to afford **39** in 96% yield (Scheme 8). When this epoxy sulfone was subjected to cyclization conditions using *p*-TsOH,[12] only desilylation of the triethylsilyl (TES) group was observed. Boron trifluoride etherate was then used to induce the 6-*endo* cyclization to give the tetracyclic ketone **40** in 67% yield. Once again, the ring expansion reaction was applied using trimethylsilyldiazomethane to afford a new tetracyclic ketone **41** in 62% yield and its isomeric ketone in 3% yield. The NOE experiments of the tetracyclic ketones **40** and **41** revealed that both ketones have the correct stereochemistry, as shown in Scheme 8.

The addition of MeMgBr to **41** in toluene[5d] led to a 4:1 epimeric mixture of products from which the desired **42a** was isolated in 77% yield by chromatography (Scheme

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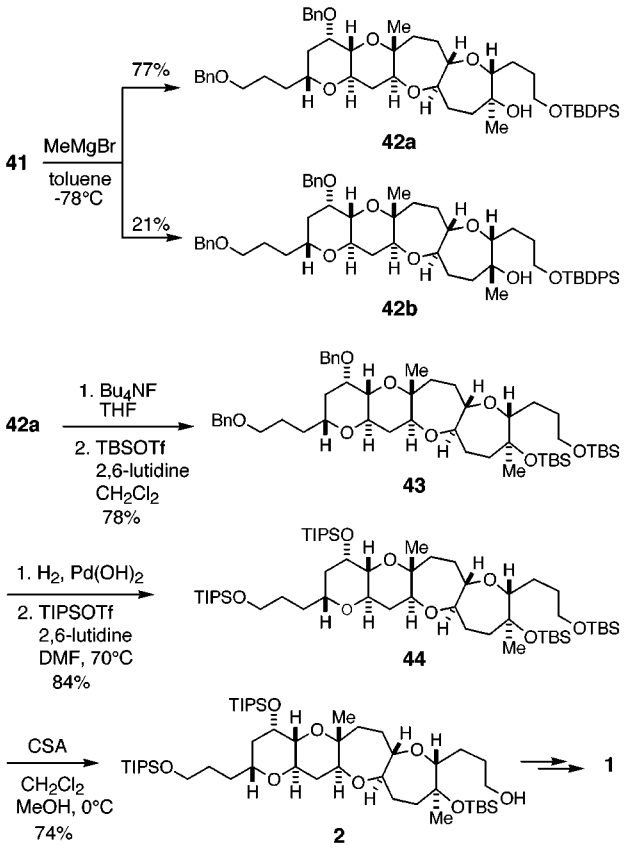
(22) (a) Evans, D. A.; Chapman, K. T. *Tetrahedron Lett.* **1986**, *27*, 5939−4942; (b) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560−3578.

Scheme 9



9). The minor isomer (**42b**), isolated in 21% yield, showed a 3.2% NOE enhancement between the newly introduced methyl and the adjacent methine protons, whereas no NOE was observed in the major isomer **42a**. Desilylation of **42a** with Bu_4NF followed by disilylation with *tert*-butyldimethylsilyl triflate gave **43** in 78% yield, which was debenzylated and then disilylated with triisopropylsilyl triflate to give the tetrasilylated derivative **44** in 84% yield. Finally, selective removal of the TBS group at the primary position by CSA in CH_2Cl_2−methanol at 0 °C provided the alcohol **2** [$[\alpha]_D^{25}$ +24.8° (*c* 0.21, $CHCl_3$)] in 74% yield. The ^{1}H NMR spectrum of **2** was in complete agreement with that of an authentic sample kindly provided by Professor Y. Yamamoto, and further elaboration of the side chains of **2** to hemibrevetoxin B (**1**) has been already accomplished by Yamamoto and co-workers,[7] thereby completing the formal total synthesis of hemibrevetoxin B.

Conclusion

The present synthesis of hemibrevetoxin B using oxiranyl anions demonstrated a conceptually new approach to marine polycyclic ethers containing six- and seven-membered rings. Although epoxides are widely recognized to be extremely versatile synthetic intermediates as electrophiles, because of a high degree of ring strain, the reactions of epoxides as nucleophiles are less common. Oxiranyl anions are unique reactive nucleophiles and their usefulness in organic synthesis lies in the direct C−C bond formation on the epoxide ring. Therefore, oxiranyl anions can be employed as building blocks for the synthesis of complex natural products. Eliminating the conventional manipulations of double-bond formation and epoxidation of a substrate allows one to construct a given target in fewer linear steps. Further applications of this methodology to the synthesis of other marine natural products are now in progress.

Experimental Section

(1*R*,2*S*)-1-(*tert*-Butyldiphenylsilyl)oxy-3-chloro-2-hydoxy-2-methyl-3-(*p*-tolylsulfinyl)propanone (17a) and Its (2*R*,3*R*)-Isomer (17b). To a solution of lithium diisopropylamide (LDA) (3.45 mmol) in THF (5 mL) at −78 °C was added a solution of (*R*)-1-chloromethyl *p*-tolyl sulfoxide (**15**; 565 mg, 3.00 mmol) in THF (2 mL), and the resulting solution was stirred at −78 °C for 30 min. To this solution was added a solution of ketone **16** (1.12 g, 3.60 mmol) in THF (2 mL), and the mixture was stirred for 30 min at −78 °C. The reaction was quenched with saturated NH_4Cl (2 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography gave (50% ether in hexane) gave chlorohydrins **17a** (861 mg, 57%) and **17b** (566 mg, 38%). **17a**: colorless oil; $[\alpha]_D^{20}$ −89.2° (*c* 0.64, $CHCl_3$); IR ($CHCl_3$) 3545, 1471 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (9H, s), 1.57 (3H, s), 2.43 (3H, s), 3.16 (1H, s, OH), 3.80 (1H, d, J = 10.6 Hz), 3.92 (1H, d, J = 10.6 Hz), 4.68 (1H, s), 7.26−7.48 (10H), 7.65−7.70 (4H); FABMS *m*/*z* 501 (MH − ^{35}Cl), 503 (MH − ^{37}Cl). **17b**: colorless oil; $[\alpha]_D^{20}$ −106.4° (*c* 0.73, $CHCl_3$); IR ($CHCl_3$) 3545, 1471, 1427, 1113 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (9H, s), 1.42 (3H, s), 2.44 (3H, s), 3.32 (1H, s, OH), 3.70 (1H, d, J = 10.6 Hz), 3.86 (1H, d, J = 10.6 Hz), 4.60 (1H, s), 7.26−7.50 (10H), 7.59−7.65 (4H); fast-atom bombardment mass spectrometry (FABMS) *m*/*z* 501 (MH − ^{35}Cl), 503 (MH − ^{37}Cl).

(2*R*,3*R*)-2,3-Epoxy-1-(*tert*-butyldiphenylsilyl)oxy-2-methyl-3-(*p*-tolylsulfonyl)propane (5a). To a solution of chlorohydrin **17a** (853 mg, 1.70 mmol) in CH_2Cl_2 (5 mL) and *t*-BuOH (5 mL) was added *t*-BuOK (210 mg, 1.87 mmol), and the mixture was stirred at room temperature for 30 min. The reaction mixture was diluted with EtOAc and washed with water and brine. The organic layer was dried and concentrated. Flash chromatography (20% EtOAc in hexane) gave 788 mg (100%) of (2*R*,3*R*)-2,3-epoxy-1-(*tert*-butyldiphenylsilyl)-oxy-2-methyl-3-(*p*-tolylsulfinyl)propane: $[\alpha]_D^{20}$ +32.2° (*c* 1.67, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.11 (9H, s), 1.53 (3H, s), 2.42 (3H, s), 3.70 (1H, s), 3.99 (1H, d, J = 11.7 Hz), 4.15 (1H, d, J = 11.7 Hz), 7.32−7.48 (10H), 7.72−7.73 (4H); FABMS *m*/*z* 465 (MH). The (2*S*,3*R*)-isomer prepared from **17b** in the same way showed the following data: $[\alpha]_D^{20}$ −27.7° (*c* 1.37, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (9H, s), 1.72 (3H, s), 2.44 (3H, s), 3.64 (1H, d, J = 12.1 Hz), 3.77 (1H, d, J = 12.1 Hz), 3.90 (1H, s), 7.34−7.44 (8H), 7.60−7.63 (6H); FABMS *m*/*z* 465 (MH).

To a solution of the (2*R*,3*R*)-epoxy sulfoxide (782 mg, 1.69 mmol) in CH_2Cl_2 (8.0 mL) was added *m*-CPBA (80% purity, 436 mg, 2.02 mmol), and the reaction mixture was stirred at room temperature for 4 h. The mixture was extracted with EtOAc and the extract was washed with aqueous $Na_2S_2O_3$, $NaHCO_3$, and brine. The organic layer was dried and concentrated under reduced pressure. Flash chromatography (15% EtOAc in hexane) gave epoxy sulfone **5a** (788 mg, 97%) as a colorless oil: $[\alpha]_D^{20}$ −79.8° (*c* 1.05, $CHCl_3$); IR ($CHCl_3$) 1597, 1427, 1330, 1155 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.10 (9H, s), 1.50 (3H, s), 2.44 (3H, s), 3.84 (1H, s), 4.24 (1H, d, J = 11.8 Hz), 4.31 (1H, d, J = 11.8 Hz), 7.32−7.45 (10H), 7.68−7.77 (4H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 19.37, 19.75, 21.68, 26.86 (3 × C), 63.67, 67.75, 74.46, 127.70, 127.73, 128.43, 129.76, 129.78, 129.99, 133.05, 133.15, 135.52, 135.66, 135.69, 145.39; high-resolution (HR)FABMS *m*/*z* calcd for $C_{27}H_{33}O_4SSi$ (MH) 481.1867, found 481.1874.

(4*S*,5*R*)-1-(*tert*-Butyldiphenylsilyl)oxy-5-chloro-4-hydroxy-5-(*p*-tolylsulfinyl)-2-pentene (19a) and Its (4*R*,5*R*)-Isomer (19b). The experimental procedure as described for compounds **17a** and **b** was followed by employing sulfoxide **15** (415 mg, 2.20 mmol) and the unsaturated aldehyde **18** (660

mg, 2.00 mmol) to give chlorohydrins **19a** (494 mg, 48%) and **19b** (375 mg, 36%). **19a**: colorless oil; $[\alpha]_D^{20}$ −81.1° (*c* 0.17, $CHCl_3$); IR ($CHCl_3$) 3545, 1471 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (9H, s), 2.44 (3H, s), 2.69 (1H, d, J = 4.6 Hz, OH), 4.26 (2H, br s), 4.39 (1H, d, J = 4.2 Hz), 4.77 (1H, ddd, J = 9.0, 4.6, 4.2 Hz), 5.89−6.01 (2H, m), 7.34−7.67 (14H); FABMS *m*/*z* 519 (MH − ^{35}Cl), 521 (MH − ^{37}Cl). **19b**: colorless oil; IR ($CHCl_3$) 3545, 1471 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (9H, s), 2.44 (3H, s), 3.39 (1H, d, J = 4.1 Hz, OH), 4.25 (2H, t, J = 2.2 Hz), 4.40 (1H, d, J = 8.3 Hz), 4.57 (1H, ddd, J = 8.3, 4.1, 4.1 Hz), 6.47 (2H, m), 7.34−7.68 (14H); FABMS *m*/*z* 515 (MH − ^{35}Cl), 517 (MH − ^{37}Cl).

(4*S*,5*R*)-4,5-Epoxy-1-(*tert*-butyldiphenylsilyl)oxy-5-(*p*-tolylsulfonyl)pentane (7a). To a solution of the unsaturated chlorohydrin **19a** (400 mg, 0.78 mmol) in EtOAc (20 mL) was added 5% Pd-C (150 mg), and the resulting mixture was stirred for 2 h under a hydrogen atmosphere. The catalyst was filtered through Celite, and the filtrate was concentrated. Flash chromatography (30% EtOAc in hexane) gave 358 mg (90%) of a saturated chlorohydrin. This chlorohydrin (358 mg, 0.69 mmol) was transformed to epoxy sulfone **7a** (184 mg, 53% in two steps) according to the procedure described for compound **5a**: $[\alpha]_D^{20}$ −62.5° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1597, 1427, 1321, 1155, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06 (9H, s), 1.83 (2H, m), 2.27 (2H, m), 2.43 (3H, s), 3.30 (1H, m), 3.76 (2H, t, J = 5.9 Hz), 3.92 (1H, d, J = 3.9 Hz), 7.37−7.85 (14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.20, 21.70, 23.62, 26.85 (3 × C), 29.68, 61.09, 63.15, 68.86, 127.66, 128.32, 129.59, 130.05, 133.77, 135.56, 135.94, 145.40; HRFABMS *m*/*z* calcd for $C_{28}H_{35}O_4SSi$ (MH) 495.2023, found 495.2035.

3-(2,3-Anhydro-4,6-*O*-benzylidene-α-D-allopyranosyl)-1-propene (22). To a solution of diol **21** (1.90 g, 11.2 mmol) in toluene (45 mL) at 0 °C were added Na_2HPO_4 (6.36 g, 44.8 mmol) and *m*-CPBA (80% purity, 7.25 g, 33.6 mmol), and the resulting mixture was stirred at 0 °C for 2 h. The mixture was filtered though a short pad of Celite, and the filtrate was concentrated. The residue was purified by flash chromatography (80% EtOAc in hexane) to give 1.46 g of an epoxy diol. A solution of this epoxy diol (1.46 g), benzaldehyde dimethyl acetal (1.77 mL, 11.78 mmol), and CSA (90.6 mg, 0.39 mmol) in CH_2Cl_2 (16 mL) was stirred at room temperature for 48 h. After addition of Et_3N (0.5 mL), the reaction mixture was concentrated. Flash chromatography (15% EtOAc in hexane) gave epoxide **22** (1.13 g, 46% in two steps) as a colorless needles: mp 101−103 °C; $[\alpha]_D^{20}$ +50.8° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1384, 1117, 1076 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.54 (2H, m), 3.41 (1H, dd, J = 4.8, 3.3 Hz), 3.58 (1H, br d, J = 4.8 Hz), 3.64 (1H, dd, J = 10.3, 10.3 Hz), 3.86 (1H, ddd, J = 10.3, 9.2, 5.1 Hz), 3.99 (1H, dd, J = 9.2, 0.9 Hz), 4.10 (1H, ddd, J = 7.2, 7.2, 3.3 Hz), 4.18 (1H, dd, J = 10.3, 5.1 Hz), 5.13 (1H, dd, J = 10.3, 1.4 Hz), 5.20 (1H, dd, J = 17.0, 1.4 Hz), 5.58 (1H, s), 5.86 (1H, dddd, J = 17.0, 10.3, 7.0, 7.0 Hz), 7.25−7.51 (5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 34.67, 51.81, 55.27, 61.07, 69.21, 70.87, 78.17, 102.62, 118.13 (C═C), 126.26, 128.30, 129.17, 133.46 (C═C), 137.19; FABMS *m*/*z* 275 (MH). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.04; H, 6.62. Found: C, 70.05; H, 6.65.

3-(3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-allopyranosyl)-1-propene (23). To a solution of epoxide **22** (2.0 g, 7.30 mmol) in ether (80 mL) was added $LiAlH_4$ (561 mg, 14.76 mmol), and the suspension was stirred at room temperature for 1.5 h. The reaction mixture was quenched with 1 M NaOH (1.0 mL), and stirring was continued until precipitates formed. The organic layer was separated by decantation and the precipitates were washed with ether. The combined organic layer was dried and concentrated. Flash chromatography (25% EtOAc in hexane) gave 1.94 g (95%) of an alcohol as colorless prisms: mp 68−69 °C; $[\alpha]_D^{20}$ +73.9° (*c* 1.0, $CHCl_3$). To a stirred solution of this alcohol (1.93 g, 6.99 mmol) in dimethylformamide (DMF, 13 mL) was added NaH (60% suspension in mineral oil, 0.56 g, 14.1 mmol) at 0 °C. After stirring at room temperature for 30 min, benzyl bromide (1.0 mL, 8.46 mmol) was added and stirring was continued for 3 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL) and extracted with ether. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (10% EtOAc in hexane) gave benzyl ether **23** (2.44 g, 95%) as a colorless oil: $[\alpha]_D^{20}$ +54.6° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1454, 1381, 1102, 1069 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.00 (2H, m), 2.58 (1H, ddd, J = 14.0, 7.3, 7.3 Hz), 2.93 (1H, ddd, J = 14.0, 8.1, 7.3 Hz), 3.68 (2H, m), 3.94 (1H, m), 4.02 (1H, q, J = 2.9 Hz), 4.25 (2H, m), 4.65 and 4.90 (each 1H, d, J = 12.5 Hz), 5.06 (1H, dd, J = 10.2, 1.0 Hz), 5.10 (1H, dd, J = 17.2, 1.0 Hz), 5.56 (1H, s), 5.79 (1H, dddd, J = 17.2, 10.2, 7.3, 7.3 Hz), 7.25−7.52 (10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 32.31, 37.51, 59.79, 67.00, 72.45, 72.56, 72.76, 81.14, 102.09, 116.93, 126.19, 127.19, 127.24, 128.20, 128.25, 128.97, 135.73, 137.83, 139.15; HRFABMS *m*/*z* calcd for $C_{23}H_{27}O_4$ (MH) 367.1908, found 367.19096.

Benzyl 3-(3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-allopyranosyl)propyl Ether (24). A solution of olefin **23** (1.90 g, 5.19 mmol) in THF (20 mL) was treated with 9-BBN-H (18.7 mL of a 0.5 M solution in THF, 9.35 mmol) at 0 °C, and the resulting solution was stirred at room temperature for 4 h. To this solution were added 3 M NaOH (4.3 mL, 12.9 mmol) and 30% H_2O_2 (1.2 mL, 11.75 mmol) at 0 °C, and stirring was continued for 1 h at room temperature. The reaction mixture was extracted with ether, washed with water and brine, dried, and concentrated. Flash chromatography (40% EtOAc in hexane) gave 1.60 g (80%) of an alcohol. This alcohol was benzylated according to the procedure described for **23**, and the product was purified by flash chromatography (25% EtOAc in hexane) to give benzyl ether **24** (1.82 g, 92%) as a colorless oil: $[\alpha]_D^{20}$ +36.2° (*c* 0.75, $CHCl_3$); IR ($CHCl_3$) 1454, 1363, 1211, 1105, 1027 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.63 (1H, m), 1.73 (2H, m), 1.96 (1H, br dd, J = 14.2, 2.9 Hz), 2.02 (1H, ddd, J = 14.2, 6.6, 2.9 Hz), 2.37 (1H, m), 3.45−3.53 (2H, m), 3.66 (1H, dd, J = 10.3, 2.9 Hz), 3.67 (1H, dd, J = 10.3, 10.3 Hz), 3.88 (1H, m), 4.00 (1H, q, J = 2.9 Hz), 4.20 (1H, ddd, J = 10.3, 10.3, 5.1 Hz), 4.25 (1H, dd, J = 10.3, 5.1 Hz), 4.50 (2H, s), 4.64 and 4.87 (each 1H, d, J = 12.5 Hz), 5.55 (1H, s), 7.24−7.51 (15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.96, 29.21, 33.25, 59.54, 70.06, 70.10, 72.58, 72.63, 72.74, 72.89, 81.26, 102.14, 126.24, 127.16, 127.19, 127.47, 127.62, 128.20, 128.26, 128.34, 128.97, 137.88, 138.62, 139.23; HRFABMS *m*/*z* calcd for $C_{30}H_{35}O_5$ (MH) 475.2482, found 475.2449.

Benzyl 3-(3-*O*-Benzyl-2-deoxy-α-D-allopyranosyl)propyl Ether (4). To a solution of **24** (6.38 g, 13.46 mmol) in THF (60 mL) and water (9 mL) was added concentrated HCl (2.2 mL), and the solution was heated at 40 °C for 5 h. The reaction mixture was neutralized with 25% NH_4OH and extracted with ether. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (90% EtOAc in hexane) gave diol **4** (4.76 g, 92%) as colorless prisms: mp 49−50 °C; $[\alpha]_D^{20}$ +35.3° (*c* 0.73, $CHCl_3$); IR ($CHCl_3$) 3556, 3442, 1454, 1363, 1068 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.59 (1H, m), 1.70 (2H, m), 1.80 (1H, ddd, J = 13.9, 4.4, 4.4 Hz), 1.90 (1H, ddd, J = 13.9, 7.3, 7.3 Hz), 1.98 (1H, m), 2.25 (1H, dd, J = 7.3, 4.4 Hz, OH), 2.50 (1H, d, J = 6.6 Hz, OH), 3.44 (1H, m), 3.52 (1H, m), 3.64 (1H, ddd, J = 11.7, 7.3, 4.4 Hz), 3.67 (1H, ddd, J = 6.6, 6.6, 3.7 Hz), 3.72 (1H, ddd, J = 11.7, 7.3, 4.4 Hz), 3.75 (2H, m), 3.92 (1H, ddd, J = 7.3, 6.6, 4.4 Hz), 4.48 and 4.50 (each 1 H, d, J = 12.5 Hz), 4.49 and 4.66 (each 1H, d, J = 11.0 Hz), 7.26−7.37 (10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.13, 31.08, 31.20, 61.38, 66.77, 69.98, 70.14, 70.64, 72.93, 73.55, 74.30, 127.56, 127.72, 127.75, 127.98, 128.34, 128.57, 137.60, 138.37. Anal. Calcd for $C_{23}H_{30}O_5$: C, 71.46; H, 7.83. Found: C, 71.22; H, 8.07.

Benzyl 3-(3-*O*-Benzyl-2-deoxy-4-*O*-triethylsilyl-6-*O*-trifluoromethanesulfonyl-α-D-allopyranosyl)propyl Ether (25). To a stirred solution of diol **4** (750 mg, 1.94 mmol) in CH_2Cl_2 (19 mL) at −78 °C were added 2,6-lutidine (1.12 mL, 9.72 mmol) and Tf_2O (343 μL, 2.04 mmol). After stirring at −78 °C for 30 min, triethylsilyl trifluoromethanesulfonate (TESOTf) (646 μL, 2.92 mmol) was added and stirring was continued for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (4 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and

concentrated. Flash chromatography (10% EtOAc in hexane) gave triflate **25** (1.21 g, 98%) as a pale yellow oil: $[\alpha]_D^{20}$ +48.3° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1454, 1413, 1246, 1146, 958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.61 (6H, q, J = 7.8 Hz), 0.95 (9H, t, J = 7.8 Hz), 1.57−1.76 (3H, m), 1.81 (1H, ddd, J = 14.1, 5.7, 3.9 Hz), 1.99 (1H, ddd, J = 14.1, 4.4, 3.4 Hz), 2.12 (1H, m), 3.43 (1H, ddd, J = 9.8, 5.9, 5.9 Hz), 3.48 (1H, ddd, J = 9.8, 5.9, 5.9 Hz), 3.72 (2H, m), 3.81 (1H, m), 4.13 (1H, ddd, J = 8.3, 5.9, 2.9 Hz), 4.48 (2H, s), 4.56 and 4.63 (each 1H, d, J = 11.7 Hz), 4.57 (1H, dd, J = 11.7, 5.9 Hz), 4.62 (1H, dd, J = 11.7, 2.9 Hz), 7.24−7.35 (10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.88 (3 × C), 6.79 (3 × C), 26.52, 29.66, 31.27, 68.94, 69.00, 69.89, 71.59, 71.93, 72.80, 75.31, 76.06, 127.47, 127.61, 127.68 (4 × C), 128.32 (4 × C), 138.19, 138.61; FABMS *m*/*z* 519 (M − Et_3Si + 2H).

Epoxy Sulfone 26. A solution of triflate **25** (1.20 g, 1.90 mmol), epoxy sulfone **5a** (1.35 g, 2.81 mmol), and HMPA (1.32 mL, 7.59 mmol) in THF (28 mL) was cooled to −110 °C and treated with *n*-BuLi (1.76 mL of a 1.6 M solution in hexane, 2.81 mmol). After stirring at −100 °C for 10 min and then −80 °C for 10 min, the reaction was quenched with saturated aqueous NH_4Cl (2 mL). The reaction mixture was extracted with EtOAc, washed with water and brine, dried, and concentrated. The residue was subjected to flash chromatography (30% ether in hexane) to give epoxy sulfone **26** (1.64 g, 90%) as a colorless oil: $[\alpha]_D^{20}$ +15.4° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1597, 1427, 1421, 1321, 1153, 1113, 815 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.60 (6H, q, J = 7.8 Hz), 0.94 (9H, t, J = 7.8 Hz), 1.07 (9H, s), 1.46 (3H, s), 1.50−1.74 (5H, m), 1.81 (1H, q, J = 10.7 Hz), 2.01 (1H, dd, J = 15.6, 4.4 Hz), 2.29 (3H, s), 2.44 (1H, dd, J = 15.6, 7.8 Hz), 3.37−3.45 (3H, m), 3.52 (1H, ddd, J = 10.7, 4.4, 2.9 Hz), 3.64 (1H, br s), 3.91 (1H, m), 4.12 and 4.24 (each 1H, d, J = 11.7 Hz), 4.45 and 4.48 (each 1H, d, J = 11.7 Hz), 4.51 and 4.55 (each 1H, d, J = 12.2 Hz), 7.12−7.66 (24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.95 (3 × C), 6.94 (3 × C), 16.43, 19.33, 21.60, 25.91, 26.85 (3 × C), 27.85, 31.69, 32.20, 64.54, 68.87, 69.10, 69.91, 70.20, 70.58, 72.82, 73.71, 74.42, 74.98, 127.32, 127.48, 127.63, 127.66, 127.71, 128.22, 128.34, 128.42, 128.77, 129.72, 129.79, 129.82, 129.98, 132.94, 134.77, 135.59, 135.64, 135.69, 138.92, 145.01; HRFABMS *m*/*z* calcd for $C_{56}H_{75}O_8SSi_2$ (MH) 963.4717, found 963.4758.

Bicyclic Ketone 27. A solution of **26** (1.63 g, 1.69 mmol) and *p*-TsOH·H_2O (483 mg, 2.54 mmol) in $CHCl_3$ (17 mL) was stirred at 0 °C for 30 min and then at room temperature for 3 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (2 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (20 → 30% EtOAc in hexane) gave bicyclic ketone **27** (1.05 g, 90%) as a colorless oil: $[\alpha]_D^{20}$ +8.82° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1718, 1454, 1427, 1361, 1113, 775, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.99 (9H, s), 1.23 (3H, s), 1.60−1.82 (3H, m), 1.98 (2H, t, J = 2.9 Hz), 2.34 (1H, m), 2.41 (1H, dd, J = 17.6, 10.2 Hz), 2.90 (1H, dd, J = 17.6, 6.3 Hz), 3.48 (2H, m), 3.53 (1H, dd, J = 9.8, 2.9 Hz), 3.68 (1H, d, J = 9.8 Hz), 3.87 (1H, m), 3.90 (1H, d, J = 9.8 Hz), 4.01 (1H, q, J = 2.9 Hz), 4.36 (1H, ddd, J = 10.2, 9.8, 6.3 Hz), 4.50 (2H, s), 4.66 and 4.92 (each 1H, d, J = 12.7 Hz), 7.20−7.41 (16H), 7.63−7.68 (4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.47, 19.23, 26.63 (3 × C), 27.08, 29.15, 33.15, 43.80, 62.22, 69.28, 70.17, 72.18, 72.89, 73.05, 73.20, 74.20, 85.03, 126.97, 127.04, 127.47, 127.61, 128.14, 128.34, 129.59, 133.09, 133.18, 135.64, 138.61, 139.36, 210.08; HRFABMS *m*/*z* calcd for $C_{43}H_{53}O_6Si$ (MH) 693.3608, found 693.3581.

Bicyclic Diol 29. To a stirred solution of ketone **27** (1.05 g, 1.52 mmol) in MeOH (8 mL) and CH_2Cl_2 (8 mL) at −78 °C was added $NaBH_4$ (115 mg, 3.03 mmol), and the mixture was stirred at −78 °C for 2 h. The reaction mixture was diluted with EtOAc, washed with water and brine, dried, and concentrated. Flash chromatography (30% EtOAc in hexane) gave alcohol **28** (964 mg, 92%) as a colorless oil. To a solution of **28** (963 mg, 1.39 mmol) in THF (14 mL) was added Bu_4NF (2.08 mL of a 1.0 M solution in THF, 2.08 mmol). After stirring at room temperature for 2 h, the reaction mixture was concentrated under reduced pressure and subjected to flash chromatography (EtOAc) to give diol **29** (621 mg, 98%) as a colorless oil: $[\alpha]_D^{20}$ +23.9° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3597, 3444, 1454, 1363, 1234, 1101, 1041 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.15 (3H, s), 1.56−1.80 (4H, m), 1.88 (1H, br, OH), 1.90 (1H, ddd, J = 14.6, 6.3, 2.9 Hz), 1.96 (1H, ddd, J = 14.6, 3.4, 1.5 Hz), 2.09 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 2.28 (1H, m), 2.36 (1H, br, OH), 3.33 (1H, dd, J = 9.8, 2.9 Hz), 3.49 (2H, m), 3.50 and 3.59 (each 1H, d, J = 11.2 Hz), 3.78 (1H, ddd, J = 11.7, 9.8, 4.4 Hz), 3.84 (2H, m), 3.93 (1H, dd, J = 11.7, 4.4 Hz), 4.50 (2H, s), 4.59 and 4.65 (each 1H, d, J = 12.0 Hz), 7.24−7.33 (10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.91, 27.03, 29.09, 32.48, 34.24, 62.72, 66.95, 68.12, 70.09, 72.31, 72.89, 73.30, 73.91, 76.69, 77.61, 127.04, 127.42, 127.48, 127.61, 128.34, 138.59, 138.88; HRFABMS *m*/*z*: calcd for $C_{27}H_{37}O_6$ (MH) 457.2588, found 457.2557.

Aldehyde 31. To a stirred solution of **29** (120 mg, 0.263 mmol) in CH_2Cl_2 (2.6 mL) at 0 °C were added 2,6-lutidine (152 μL, 1.316 mmol) and TESOTf (146 μL, 0.658 mmol), and the reaction mixture was stirred at 0 °C for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (0.5 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (10% EtOAc in hexane) gave a disilyl ether (176 mg, 98%) as a colorless oil. To a solution of this disilyl ether (154 mg, 0.225 mmol) in CH_2Cl_2 (2.2 mL) and MeOH (0.22 mL) at −20 °C was added PPTS (170 mg, 0.675 mmol), and the resulting mixture was stirred at −20 °C for 2 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (1.0 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (20% EtOAc in hexane) gave an alcohol (118 mg, 92%) as a colorless oil. To a solution of the resulting alcohol (130 mg, 0.228 mmol) in CH_2Cl_2 (0.7 mL) and DMSO (1.5 mL) were added Et_3N (0.7 mL) and SO_3·pyridine (290 mg, 1.825 mmol), and the resulting mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with EtOAc, and the organic layer was washed with water and brine, dried, and concentrated. Flash chromatography (20% EtOAc in hexane) gave aldehyde **31** (125 mg, 96%) as a pale yellow oil: $[\alpha]_D^{20}$ −5.64° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1743, 1454, 1363, 1114, 1018, 827 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.33 (6H, q, J = 8.3 Hz), 0.91 (9H, t, J = 8.3 Hz), 1.31 (3H, s), 1.61−1.74 (4H, m), 1.94 (2H, m), 2.10 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 2.28 (1H, m), 3.36 (1H, dd, J = 9.8, 2.9 Hz), 3.50 (2H, m), 3.81−3.89 (3H, m), 3.90 (1H, dd, J = 11.2, 4.4 Hz), 4.51 (2H, s), 4.63 and 4.78 (each 1H, d, J = 12.7 Hz), 7.24−7.36 (10H), 9.41 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 4.88 (3 × C), 6.69 (3 × C), 10.51, 27.06, 29.22, 35.01, 35.10, 62.03, 66.50, 70.12, 72.46, 72.80, 72.90, 73.46, 73.55, 81.92, 127.04, 127.22, 127.50, 127.58, 128.22, 128.34, 139.23, 199.81; HRFABMS *m*/*z*: calcd for $C_{32}H_{49}O_6Si$ (MH) 569.3296, found 569.3271.

Hydroxy Epoxy Sulfones 32a and 32b. The procedure for **26** was employed with aldehyde **31** (120 mg, 0.211 mmol) and epoxy sulfone **6a** (162 mg, 0.359 mmol), and purification by flash chromatography (20 → 30% EtOAc in hexane) gave **32a** (135 mg, 63%) and **32b** (52.8 mg, 25%). **32a**: colorless oil; $[\alpha]_D^{20}$ +27.7° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3552, 3446, 1456, 1427, 1323, 1113 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.64 (6H, m), 0.93 (9H, t, J = 8.3 Hz), 1.04 (9H, s), 1.20 (3H, s), 1.57−1.82 (6H, m), 2.13−2.22 (2H, m), 2.38 (1H, d, J = 9.8 Hz, OH), 3.20 (1H, dd, J = 9.8, 2.9 Hz), 3.34 (2H, m), 3.65 (1H, q, J = 2.9 Hz), 3.81 (1H, m), 3.90 (1H, ddd, J = 11.7, 9.8, 4.9 Hz), 4.10 (1H, dd, J = 11.7, 4.9 Hz), 4.30 (1H, dd, J = 12.7, 5.4 Hz), 4.38 (1H, d, J = 9.8 Hz), 4.41 (2H, s), 4.44 and 4.77 (each 1H, d, J = 13.1 Hz), 4.45 (1H, dd, J = 12.7, 3.4 Hz), 4.76 (1H, dd, J = 5.4, 3.4 Hz), 7.15−7.89 (25H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.44 (3 × C), 6.94 (3 × C), 13.42, 19.20, 26.83 (3 × C), 27.11, 29.05, 32.62, 35.27, 61.20, 61.81, 67.69, 69.55, 69.91, 71.44, 72.46, 72.64, 72.72, 72.92, 73.33, 77.51, 80.72, 127.37, 127.52, 127.61, 127.73, 127.76, 128.24, 128.34, 128.73, 129.34, 129.74, 130.08, 132.86, 133.92, 135.17, 135.45, 135.51, 138.16; HRFABMS *m*/*z* calcd for $C_{58}H_{77}O_{10}Si_2$ (MH) 1021.4771, found 1021.4814. **32b**: colorless oil; $[\alpha]_D^{20}$ +41.5° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3525, 3456, 1456, 1323, 1113 cm^{-1}; ^1H NMR (400 MHz,

$CDCl_3$) δ 0.55 (6H, m), 0.84 (3H, s), 0.92 (9H, t, J = 8.3 Hz), 1.04 (9H, s), 1.51 (1H, q, J = 11.7 Hz), 1.55−1.72 (3H, m), 1.86 (2H, m), 1.94 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 2.20 (1H, m), 3.03 (1H, d, J = 9.8 Hz, OH), 3.23 (1H, dd, J = 10.2, 2.9 Hz), 3.45 (2H, m), 3.67 (1H, ddd, J = 11.7, 10.2, 4.4 Hz), 3.80 (2H, m), 3.94 (1H, dd, J = 6.3, 2.0 Hz), 4.01 (1H, dd, J = 11.7, 4.4 Hz), 4.10 (1H, d, J = 9.8 Hz), 4.29 (1H, dd, J = 12.7, 2.0 Hz), 4.36 (1H, dd, J = 12.7, 6.3 Hz), 4.47 (2H, s), 4.55 and 4.60 (each 1H, d, J = 11.2 Hz), 7.18−7.82 (25 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.03 (3 × C), 6.84 (3 × C), 11.78, 19.23, 26.85 (3 × C), 27.06, 29.15, 32.33, 34.25, 61.47, 61.83, 66.09, 67.00, 70.06, 71.41, 72.39, 72.72, 72.90, 73.15, 74.86, 79.06, 80.49, 127.40, 127.50, 127.58, 127.71, 128.34, 128.91, 129.28, 129.72, 134.05, 135.51, 135.58, 138.56; FABMS m/z 1021 (MH).

Tricyclic Hydroxy Ketone 33. To a solution of **32a** (89.7 mg, 0.088 mmol) in $CHCl_3$ (0.8 mL) at 0 °C was added BF_3·OEt_2 (16.2 μL, 0.132 mmol), and the solution was stirred at 0 °C for 1 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (0.2 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (25% EtOAc in hexane) gave hydroxy ketone **33** (51.2 mg, 76%) as a colorless oil: $[\alpha]_D^{20}$ +9.39° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3525, 1736, 1454, 1427, 1113, 823 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (9H, s), 1.19 (3H, s), 1.64−1.78 (4H, m), 1.93 (1H, ddd, J = 14.6, 6.3, 2.9 Hz), 2.01 (1H, dd, J = 14.6, 2.9 Hz), 2.19 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 2.32 (1H, m), 2.96 (1H, br, OH), 3.48 (1H, dd, J = 9.8, 2.4 Hz), 3.52 (2H, m), 3.86 (1H, s), 3.88−3.93 (3H, m), 3.96 (2H, d, J = 4.4 Hz), 4.07 (1H, dd, J = 11.7, 4.4 Hz), 4.30 (1H, t, J = 4.4 Hz), 4.52 (2H, s), 4.55 and 4.68 (each 1H, d, J = 12.2 Hz), 7.23−7.71 (20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.85, 19.23, 26.67 (3 × C), 27.01, 29.04, 30.48, 32.36, 62.22, 62.87, 69.61, 70.01, 72.36, 72.52, 72.90, 73.50, 73.97, 76.21, 78.43, 80.62, 127.12, 127.52, 127.56, 127.63, 128.35, 128.49, 129.59, 133.29, 133.41, 135.51, 135.56, 135.68, 135.73, 138.51, 202.37; HRFABMS m/z calcd for $C_{46}H_{57}O_8Si$ (MH) 765.3846, found 765.3822.

Tricyclic Ketone 34. To a stirred mixture of hydroxy ketone **33** (48.3 mg, 0.063 mmol) and 0.1 M SmI_2 in THF (3.16 mL, 0.316 mmol) at 0 °C were added HMPA (0.6 mL) and MeOH (25.6 μL, 0.632 mmol), and the resulting mixture was stirred at 0 °C for 2 h. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (20% EtOAc in hexane) gave ketone **34** (30.2 mg, 64%) as a colorless oil: $[\alpha]_D^{20}$ +15.3° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 1724, 1454, 1427, 1113, 823 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 1.01 (9H, s), 1.29 (3H, S), 1.57−1.75 (4H, m), 1.98 (2H, t, J = 3.4 Hz), 2.11 (1H, ddd, J = 11.2, 4.4, 4.4 Hz), 2.36 (1H, m), 2.60 and 2.64 (each 1H, d, J = 16.1 Hz), 3.48 (1H, dd, J = 9.8, 2.9 Hz), 3.50 (2H, t, J = 6.3 Hz), 3.74 (1H, dd, J = 11.2, 4.4 Hz), 3.82 (1H, m), 3.91 (2H, m), 3.98 (1H, ddd, J = 11.2, 9.8, 4.4 Hz), 4.06 (1H, dd, J = 11.2, 3.9 Hz), 4.13 (1H, dd, J = 3.9, 2.9 Hz), 4.49 (2H, s), 4.63 and 4.76 (each 1H, d, J = 12.7 Hz), 7.21−7.47 (16H), 7.74−7.77 (4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.30, 19.21, 26.67 (3 × C), 27.01, 29.14, 31.11, 33.17, 54.10, 62.70, 62.72, 63.10, 70.11, 72.59, 72.85, 73.53, 73.61, 73.84, 76.64, 84.22, 126.96, 127.19, 127.47, 127.58, 128.21, 128.34, 129.57, 129.62, 133.18, 135.66, 135.76, 138.64, 139.31, 205.57; HRFABMS m/z calcd for $C_{46}H_{57}O_7Si$ (MH) 749.3870, found 749.3903.

Tricyclic Ketone 35. To a stirred solution of ketone **34** (175 mg, 0.235 mmol) in CH_2Cl_2 (2.4 mL) at −78 °C were added BF_3·OEt_2 (34.7 μL, 0.282 mmol) and $TMSCHN_2$ (124 μL of a 2.0 M solution in hexane, 0.247 mmol), and the resulting solution was stirred at −78 °C for 3 h and then allowed to warm to −20 °C over 1 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (0.4 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. The oily residue was dissolved in CH_2Cl_2 (1.2 mL) and MeOH (1.2 mL) and the solution was treated with PPTS (88.7 mg, 0.353 mmol). After stirring at room temperature for 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (30% ether in hexane) gave ketone **35** (120 mg, 67%) and its isomeric ketone (30.8 mg, 17%). **35**: colorless oil; $[\alpha]_D^{20}$ +46.8° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 1712, 1454, 1429, 1209, 1090, 823 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 1.02 (9H, s), 1.46 (3H, s), 1.55−1.67 (4H, m), 1.68 (1H, q, J = 11.7 Hz), 1.91−1.97 (3H, m), 2.03 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 2.30 (1H, m), 2.38 (1H, ddd, J = 12.7, 6.3, 2.0 Hz), 3.02 (1H, ddd, J = 15.1, 12.7, 2.9 Hz), 3.24 (1H, dd, J = 11.7, 4.4 Hz), 3.46 (3H, m), 3.77−3.81 (2H, m), 3.83−3.89 (2H, m), 3.92 (1H, dd, J = 10.7, 3.9 Hz), 3.99 (1H, dd, J = 3.9, 2.4 Hz), 4.45 (2H, s), 4.60 and 4.78 (each 1H, d, J = 12.2 Hz), 7.22−7.47 (16H), 7.67−7.79 (4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.69, 19.13, 26.65 (3 × C), 27.03, 29.15, 33.12, 33.28, 38.40, 39.29, 63.03, 66.03, 70.12, 72.49, 72.59, 72.84, 73.53, 73.71, 76.69, 81.66, 87.88, 126.96, 127.14, 127.47, 127.56, 127.61, 127.68, 128.17, 128.32, 129.69, 129.75, 132.83, 132.91, 135.61, 135.69, 138.62, 215.79; HRFABMS m/z calcd for $C_{47}H_{59}O_7Si$ (MH) 763.4027, found 763.4041.

Tricyclic Diol 37. To a solution of **35** (110 mg, 0.144 mmol) in THF (1.5 mL) at 0 °C were added AcOH (16.6 μL, 0.288 mmol) and Bu_4NF (217 μL of a 1.0 M solution in THF, 0.217 mmol). After stirring at room temperature for 5 h, the reaction mixture was concentrated and subjected to flash chromatography (80% EtOAc in hexane) to give hydroxy ketone **36** (71.1 mg, 94%) as a colorless oil. A solution of **36** (71.1 mg, 0.136 mmol) in MeCN (0.2 mL) was added to a stirred solution of $Me_4NBH(OAc)_3$ (250 mg, 0.950 mmol) in AcOH (1.0 mL) and MeCN (1.0 mL) at −20 °C. After stirring at −20 °C for 3 h, saturated aqueous NH_4Cl (0.3 mL) was added and the reaction mixture was warmed to room temperature. Saturated aqueous potassium sodium tartrate (0.3 mL) was added to the mixture and stirring continued for 20 min. After addition of $MgSO_4$ (100 mg), the mixture was diluted with EtOAc and passed through a short pad of silica gel. The filtrate was concentrated and subjected to flash chromatography (80% EtOAc in hexane) to give diol **37** (67.8 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ +7.91° (c 0.54, $CHCl_3$); IR ($CHCl_3$) 3600, 3438, 1454, 1363, 1113 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 1.19 (3H, s), 1.46 (1H, q, J = 11.7 Hz), 1.47−1.83 (6H, m), 1.91−1.96 (3H, m), 2.11 (1H, ddd, J = 13.2, 13.2, 3.4 Hz), 2.29 (1H, m), 3.32 (1H, dd, J = 9.8, 2.4 Hz), 3.36−3.52 (5H, m), 3.63 (1H, ddd, J = 6.3, 6.3, 3.9 Hz), 3.64 (1H, dd, J = 11.7, 4.4 Hz), 3.72−3.80 (2H, m), 3.83 (1H, q, J = 2.9 Hz), 3.90 (1H, d, J = 3.9 Hz), 3.97 (1H, dddd, J = 3.9, 3.9, 3.9, 2.4 Hz), 4.46 (2H, s), 4.60 and 4.82 (each 1H, d, J = 12.7 Hz), 7.19−7.39 (10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.58, 27.03, 28.30, 29.17, 33.03, 33.38, 35.12, 63.15, 64.58, 70.17, 71.90, 72.41, 72.64, 72.85, 73.48, 73.91, 77.20, 79.45, 85.92, 126.99, 127.02, 127.45, 127.60, 128.14, 128.34, 139.61; HRFABMS m/z calcd for $C_{31}H_{43}O_7$ (MH) 527.3006, found 527.3047.

Tricyclic Triflate 38. The procedure for **25** was employed with diol **37** (69.3 mg, 0.132 mmol) and purification by flash chromatography (20% EtOAc in hexane) gave triflate **38** (84.9 mg, 83%) as a colorless oil: $[\alpha]_D^{20}$ +9.78° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 1454, 1415, 1211, 1146, 1093, 960 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.59 (6H, q, J = 7.8 Hz), 0.95 (9H, t, J = 7.8 Hz), 1.12 (3H, s), 1.57 (1H, q, J = 11.7 Hz), 1.58−1.84 (6H, m), 1.91 (2H, br s), 2.01 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 2.05 (1H, ddd, J = 13.3, 13.3, 2.0 Hz), 2.25 (1H, m), 3.34 (1H, dd, J = 9.8, 2.4 Hz), 3.48 (2H, m), 3.57 (1H, dd, J = 12.2, 4.4 Hz), 3.76−3.85 (4H, m), 3.90 (1H, ddd, J = 5.4, 2.9, 2.9 Hz), 4.37 (1H, dd, J = 10.3, 5.9 Hz), 4.41 (1H, dd, J = 10.3, 4.4 Hz), 4.49 (2H, s), 4.58 and 4.81 (each 1H, d, J = 12.2 Hz), 7.22−7.35 (10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.75 (3 × C), 6.77 (3 × C), 15.46, 27.06, 28.11, 29.25, 32.79, 33.43, 34.93, 63.13, 70.17, 71.26, 72.41, 72.64, 72.84, 73.56, 73.96, 76.44, 76.95, 78.96, 83.01, 126.92, 126.99, 127.45, 127.60, 128.09, 128.32, 138.67, 139.67; FABMS m/z 773 (MH).

Epoxy Sulfone 39. The procedure for **26** was employed with triflate **38** (81.8 mg, 0.106 mmol), epoxy sulfone **7a** (105 mg, 0.212 mmol), and *N,N′*-dimethylpropyleneurea (DMPU) (38.4 μL), and purification by flash chromatography (45% ether in hexane) gave epoxy sulfone **39** (114 mg, 96%) as a colorless oil: $[\alpha]_D^{20}$ +22.8° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 1599, 1454, 1321,

1111, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.43 (6H, q, J = 8.3 Hz), 0.83 (9H, t, J = 8.3 Hz), 1.06 (9H, s), 1.11 (3H, s), 1.46 (1H, q, J = 11.7 Hz), 1.48 (1H, m), 1.54−1.63 (2H, m), 1.64−1.82 (3H, m), 1.87 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 1.88−1.91 (3H, m), 1.97 (1H, m), 2.15−2.24 (3H, m), 2.34 (3H, s), 3.29 (2H, m), 3.41−3.51 (4H, m), 3.53 (1H, dd, J = 11.7, 4.4 Hz), 3.69−3.76 (3H, m), 3.81 (2H, m), 4.46 (2H, s), 4.45 and 4.80 (each 1H, d, J = 12.2 Hz), 7.20−7.43 (20H), 7.65−7.80 (4H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.72 (3 × C), 6.79 (3 × C), 15.71, 19.20, 21.63, 23.87, 26.86 (3 × C), 27.08, 29.28, 30.27, 33.02, 33.40, 34.29, 34.60, 63.06, 63.38, 64.89, 70.16, 72.36, 72.61, 72.82, 73.51, 73.94, 75.11, 75.54, 76.67, 76.87, 80.29, 126.86, 126.91, 127.42, 127.56, 127.63, 128.24, 128.30, 128.93, 129.51, 129.74, 133.87, 134.92, 135.59, 139.71, 144.97; HRFABMS *m/z* calcd for $C_{65}H_{89}O_{10}SSi_2$ (MH) 1117.5710, found 1117.5753.

Tetracyclic Ketone 40. A solution of epoxy sulfone **39** (111 mg, 0.099 mmol) and *p*-TsOH·H_2O (28.4 mg, 0.149 mmol) in $CHCl_3$ (1.0 mL) was stirred at 0 °C for 3 h. After addition of saturated aqueous $NaHCO_3$ (0.1 mL), the reaction mixture was extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (40% EtOAc in hexane) gave an alcohol (90.1 mg, 90%). A solution of the alcohol (77.2 mg, 0.077 mmol) in $CHCl_3$ (1.0 mL) at 0 °C was treated with BF_3·OEt_2 (14.2 μL, 0.116 mmol), and the resulting reaction mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (0.2 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (25% EtOAc in hexane) gave tetracyclic ketone **40** (48.5 mg, 74%) as a colorless oil: $[\alpha]_D^{20}$ +9.62° (c 0.85, $CHCl_3$); IR ($CHCl_3$) 1726, 1454, 1427, 1097, 1025 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.04 (9H, s), 1.23 (3H, s), 1.52−1.74 (7H, m), 1.80−2.06 (7H, m), 2.10 (1H, m), 2.29 (1H, m), 2.37 (1H, dd, J = 15.6, 10.3 Hz), 2.86 (1H, dd, J = 15.6, 5.9 Hz), 3.31 (1H, dd, J = 9.8, 2.4 Hz), 3.39 (1H, m), 3.42 (1H, dd, J = 12.2, 3.9 Hz), 3.49 (2H, m), 3.58 (1H, ddd, J = 10.3, 10.3, 5.9 Hz), 3.62 (1H, dd, J = 7.8, 3.9 Hz), 3.67 (2H, t, J = 6.4 Hz), 3.78−3.85 (3H, m), 4.49 (2H, s), 4.61 and 4.77 (each 1H, d, J = 12.7 Hz), 7.23−7.44 (16H), 7.64−7.67 (4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.09, 19.18, 25.68, 26.86 (3 × C), 27.03, 28.16, 28.39, 29.15, 32.85, 33.33, 38.12, 46.17, 63.23, 63.67, 70.14, 72.43, 72.62, 72.82, 73.61, 73.84, 77.51, 80.06, 80.52, 80.83, 82.11, 126.97, 127.10, 127.45, 127.58, 128.17, 128.32, 129.52, 133.93, 133.97, 135.58, 138.65, 139.53, 205.89; HRFABMS *m/z* calcd for $C_{52}H_{67}O_8Si$ (MH) 847.4601, found 847.4637.

Tetracyclic Ketone 41. The procedure for **35** was employed with ketone **40** (37.4 mg, 0.044 mmol), BF_3·OEt_2 (6.5 μL, 0.053 mmol), and $TMSCHN_2$ (24.3 μL, 0.048 mmol). Purification by flash chromatography (50% ether in hexane) gave tetracyclic ketone **41** (23.6 mg, 62%) and its isomeric ketone (1.2 mg, 3%). **41**: colorless oil; $[\alpha]_D^{20}$ +48.0° (*c* 0.69, $CHCl_3$); IR ($CHCl_3$) 1712, 1454, 1429, 1109, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.04 (9H, s), 1.18 (3H, s), 1.51−1.78 (10H, m), 1.86−2.04 (6H, m), 2.17 (1H, m), 2.56−2.33 (2H, m), 2.82 (1H, ddd, J = 12.2, 12.2, 2.0 Hz), 2.98 (1H, ddd, J = 8.3, 8.3, 5.4 Hz), 3.33 (1H, dd, J = 9.8, 2.4 Hz), 3.46 (1H, dd, J = 10.3, 3.9 Hz), 3.47−3.52 (3H, m), 3.65 (2H, t, J = 5.9 Hz), 3.73 (1H, dd, J = 8.8, 3.9 Hz), 3.80−3.86 (3H, m), 4.50 (2H, s), 4.61 and 4.79 (each 1H, d, J = 12.7 Hz), 7.23−7.43 (16H), 7.64−7.66 (4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.44, 19.18, 26.85 (3 × C), 27.01, 28.44, 29.04, 29.17, 30.35, 31.36, 32.76, 33.43, 36.65, 38.04, 63.36, 63.52, 70.16, 72.46, 72.69, 72.82, 73.92, 74.06, 77.23, 80.44, 84.44, 86.53, 86.66, 126.96, 127.09, 127.45, 127.56, 127.60, 128.16, 128.32, 129.56, 133.85, 133.87, 135.56, 138.65, 139.58, 216.37; HRFABMS *m/z* calcd for $C_{53}H_{69}O_8Si$ (MH) 861.4758, found 861.4794.

Tetracyclic Alcohols 42a and 42b. A 0.92 M solution of MeMgBr in THF (282 μL, 0.259 mmol) was charged in a flask flushed with argon. After removal of the solvent under reduced pressure, the flask was flushed with argon and charged with toluene (0.2 mL). To this stirred and cold solution at −78 °C a solution of ketone **41** (22.3 mg, 0.026 mmol) in toluene (0.3 mL) was added. After stirring at −78 °C for 2 h, the reaction was quenched with saturated aqueous NH_4Cl (0.2 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (36% EtOAc in hexane) gave **42a** (17.4 mg, 77%) and **42b** (4.8 mg, 21%). **42a**: colorless oil; $[\alpha]_D^{20}$ +18.6° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3597, 3456, 1454, 1429, 1090, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (9H, s), 1.09 (3H, s), 1.18 (3H, s), 1.30 (1H, m), 1.53−1.91 (17H, m), 2.00 (1H, ddd, J = 11.7, 3.9, 3.9 Hz), 2.09 (1H, m), 2.28 (1H, m), 3.19 (1H, br d, J = 10.3 Hz), 3.26 (1H, dd, J = 12.2, 3.9 Hz), 3.29 (1H, dd, J = 10.3, 2.4 Hz), 3.32 (2H, br s), 3.48 (2H, m), 3.70 (2H, m), 3.81 (3H, br s), 4.49 (2H, s), 4.60 and 4.78 (each 1H, d, J = 12.7 Hz), 7.23−7.44 (16H), 7.66−7.68 (4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.10, 19.21, 23.38, 26.90 (4 × C), 27.01, 28.94, 29.14, 29.43, 29.92, 33.07, 33.38, 37.67, 38.14, 63.48, 64.10, 70.17, 72.38, 72.57, 72.80, 73.53, 73.86, 74.61, 77.40, 82.13, 84.65, 86.15, 88.16, 126.96, 127.04, 127.43, 127.58, 128.14, 128.32, 129.52, 134.03, 134.05, 135.58, 138.67, 139.61; HRFABMS *m/z* calcd for $C_{54}H_{73}O_8Si$ (MH) 877.5707, found 877.5673. **42b**: colorless oil; $[\alpha]_D^{20}$ +24.9° (*c* 0.49, $CHCl_3$); IR ($CHCl_3$) 3587, 3465, 1454, 1429, 1211, 1088 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (9H, s), 1.11 (3H, s), 1.16 (3H, s), 1.48 (1H, m), 1.50−1.86 (14H, m), 1.89 (2H, m), 1.97−2.14 (3H, m), 2.28 (1H, m), 3.13 (1H, br d, J = 10.2 Hz), 3.23 (1H, dd, J = 12.2 Hz, 3.4 Hz), 3.28 (1H, br dd, J = 8.8, 8.8 Hz), 3.29 (1H, dd, J = 9.8, 2.4 Hz), 3.43 (1H, m), 3.48 (2H, m), 3.69 (2H, m), 3.78−3.84 (3H, m), 4.49 (2H, s), 4.59 and 4.78 (each 1H, d, J = 12.7 Hz), 7.23−7.44 (16H), 7.66−7.68 (4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.72, 19.20, 25.66, 25.93, 26.88 (4 × C), 27.01, 29.05, 29.14, 29.58, 33.02, 33.40, 36.97, 37.43, 63.46, 63.85, 70.17, 72.39, 72.57, 72.80, 73.50, 73.81, 74.70, 77.38, 82.50, 83.80, 85.70, 89.31, 126.96, 127.04, 127.43, 127.60, 128.14, 128.30, 129.54, 133.97, 134.03, 135.58, 139.59; FABMS *m/z* 877 (MH).

Disilyl Ether 43. A solution of **42a** (8.6 mg, 9.8 μmol) in THF (0.1 mL) was treated with Bu_4NF (20 μL of a 1.0 M solution in THF, 20 μmol) and the solution was stirred at room temperature for 15 h. After evaporation of the solvent, the residue was purified by flash chromatography (10% acetone in EtOAc) to give a diol (6.1 mg, 97%). To a solution of this diol (5.7 mg, 8.9 μmol) in CH_2Cl_2 (0.1 mL) at 0 °C were added 2,6-lutidine (7.2 μL, 63 μmol) and TBSOTf (6.2 μL, 27 μmol). After stirring at room temperature for 3 h, the reaction mixture was treated with saturated aqueous $NaHCO_3$ (0.1 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (14% EtOAc in hexane) gave disilyl ether **43** (6.2 mg, 80%) as a colorless oil: $[\alpha]_D^{20}$ +21.7° (*c* 0.48, $CHCl_3$); IR ($CHCl_3$) 1462, 1375, 1255, 1087 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.06 (6H, s), 0.83 (9H, s), 0.90 (9H, s), 1.09 (3H, s), 1.21 (3H, s), 1.25 (2H, m), 1.46−1.96 (15H, m), 2.00 (1H, ddd, J = 11.7, 4.4, 4.4 Hz), 2.16 (1H, m), 2.28 (1H, m), 3.19 (1H, br d, J = 10.3 Hz), 3.24−3.39 (4H, m), 3.48 (2H, m), 3.57−3.70 (2H, m), 3.81 (3H, m), 4.49 (2H, s), 4.59 and 4.78 (each 1H, d, J = 12.7 Hz), 7.23−7.35 (10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.24, −5.22, −2.20, −2.16, 16.12 (2 × C), 23.84, 25.75 (3 × C), 26.03 (3 × C), 26.93, 27.03, 28.81, 29.15, 29.55, 29.71, 30.50, 33.13, 33.41, 37.51, 37.77, 63.49, 63.66, 70.20, 73.39, 72.62, 72.82, 73.55, 73.87, 77.13, 77.41, 82.17, 85.01, 86.17, 88.53, 126.97, 127.04, 127.43, 127.58, 128.14, 128.32, 137.93; HRFABMS *m/z* calcd for $C_{50}H_{83}O_8Si_2$ (MH) 867.5622, found 867.5635.

Tetrasilyl Ether 44. A mixture of **43** (5.5 mg, 6.5 μmol) and $Pd(OH)_2$−C (20 mg) in MeOH (0.2 mL) was stirred under a hydrogen atmosphere for 1 h. The mixture was filtered through Celite and the filtrate was concentrated. Flash chromatography (EtOAc) gave an diol (4.0 mg, 92%). To a stirred solution of this diol (3.7 mg, 5.4 μmol) in DMF (0.1 mL) at 0 °C were added 2,6-lutidine (6.2 μL, 54 μmol) and TIPSOTf (7.2 μL, 27 μmol), and the resulting solution was heated at 70 °C for 4 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (0.1 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash

chromatography (14% EtOAc in hexane) gave tetrasilyl ether **44** (4.9 mg, 91%) as a colorless oil: $[\alpha]_D^{20}$ +22.8° (*c* 0.38, $CHCl_3$); IR ($CHCl_3$) 1462, 1383, 1255, 1090 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.06 (6H, s), 0.83 (9H, s), 0.90 (9H, s), 1.06 (42H, m), 1.09 (3H, s), 1.19 (3H, s), 1.23 (2H, m), 1.46−2.03 (16H, m), 2.13 (1H, m), 2.29 (1H, m), 3.17 (1H, dd, J = 10.3, 2.4 Hz), 3.20 (1H, br d, J = 10.3 Hz), 3.22 (1H, dd, J = 12.2, 4.4 Hz), 3.27−3.37 (2H, m), 3.57−3.71 (4H, m), 3.73−3.83 (2H, m), 4.19 (1H, br d, J = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.24 (2 × C), −2.29 (2 × C), 12.01 (3 × C), 12.38 (3 × C), 16.30 (3 × C), 18.03 (3 × C), 18.24 (6 × C), 23.92, 25.73 (4 × C), 26.01 (3 × C), 26.95, 28.84, 29.43, 29.58, 30.50, 30.55, 33.07, 36.44, 37.58, 37.61, 62.62, 63.23, 63.64, 67.65, 72.66, 72.95, 77.17, 82.33, 82.58, 85.08, 86.64, 88.49; HRFABMS *m*/*z* calcd for $C_{54}H_{111}O_8Si_4$ (MH) 999.7350, found 999.7369.

Compound 2. A soution of tetrasilyl ether **44** (4.6 mg, 4.6 μmol) and CSA (0.3 mg, 1.4 μmol) in MeOH (0.05 mL) and CH_2Cl_2 (0.05 mL) was stirred at 0 °C for 1 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (0.1 mL) and extracted with EtOAc. The extract was washed with water and brine, dried, and concentrated. Flash chromatography (18% EtOAc in hexane) gave **2** (3.0 mg, 74%) as a colorless oil: $[\alpha]_D^{20}$ +24.8° (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) 3473, 1462, 1377, 1255, 1103, 1014, 883 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (3H, s), 0.07 (3H, s), 0.83 (9H, s), 0.83−1.06 (42H, m), 1.10 (3H, s), 1.19 (3H, s), 1.32 (2H, m), 1.50−2.03 (17H, m), 2.16 (1H, m), 2.30 (1H, m), 3.18 (1H, dd, J = 9.8, 2.4 Hz), 3.20 (1H, br d, J = 8.8 Hz), 3.21 (1H, dd, J = 12.2, 4.4 Hz), 3.29−3.41 (2H, m), 3.67 (2H, t, J = 6.3 Hz), 3.69 (2H, t, J = 6.3 Hz), 3.73−3.83 (2H, m), 4.19 (br d, J = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −2.29, −2.16, 12.01 (3 × C), 12.38 (3 × C), 16.19, 18.03 (6 × C), 18.24 (6 × C), 23.84, 25.71 (4 × C), 26.37, 28.79, 29.43, 29.51, 30.25, 30.55, 33.05, 36.44, 37.46 (2 × C), 62.62, 62.92, 63.23, 67.64, 72.66, 72.95, 77.13, 77.20, 82.48, 84.80, 86.54, 88.42; HRFABMS *m*/*z* calcd for $C_{48}H_{97}O_8Si_3$ (MH) 885.6486, found 885.6449.

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Supporting Information Available: ^1H NMR spectra for compounds **2**, **4**, **25**−**29**, and **31**−**44** (25 pages). This material is contained in libraries on microfiche, immediately follows this article in microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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