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Total Synthesis of Dysidiolide

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Abstract: The cdc25A protein phosphatase inhibitor dysidiolide (**1**) has been synthesized enantioselectively, starting from the enantiomerically pure ketal enone **2** and using a cationic rearrangement as the key step to produce the fully substituted bicyclic core of the natural product. Once the central portion of **1** was established, elaboration of the side chains was accomplished expediently via steps that included (1) vinyl cuprate displacement of an iodide to complete the C-1 side chain, (2) a highly diastereoselective oxazaborolidine-catalyzed (CBS) reduction to form carbinol **11**, and (3) photochemical oxidation of **11** to generate the γ-hydroxybutenolide functionality of **1**. Additionally, this synthesis proves the absolute stereochemistry of dysidiolide (**1**).

Described herein (Scheme 1) is the first enantioselective total synthesis of the marine sponge metabolite dysidiolide (**1**), the structure of which was reported by Gunasekera, Clardy, and colleagues in 1996.[1] Isolated from the Caribbean sponge *Dysidea etheria* de Laubenfels, dysidiolide is the first naturally derived inhibitor of the cdc25A protein phosphatase, one of three homologues (cdc25A, -B, -C) of a signaling enzyme shown to activate the G_2/M transition of the cell cycle.[2] Dysidiolide exhibits micromolar activity against A-549 human lung carcinoma and P388 murine leukemia cancer cell lines. This *in vitro* antitumor activity, which is probably due to inhibition of cdc25A by dysidiolide, may be a good lead in the search for improved agents in the treatment of cancer and other proliferative disorders. Dysidiolide is a γ-hydroxybutenolide of the rearranged sesterterpene class whose [4.4.0] bicyclic nucleus and appendant side chains define a type of structure not previously encountered in a natural product. A key step of our synthesis of **1** is a controlled, biomimetic carbocation rearrangement which simultaneously creates the unusual quaternary center at C-1 and the endocyclic double bond within the highly substituted bicyclic core. The synthesis also proves the absolute stereochemistry of dysidiolide, which was not determined in the original[1] X-ray crystallographic analysis.

The synthesis of **1** commenced from the enantiomerically pure bicyclic ketal enone **2**, which is readily available in three steps starting from 2-methyl-1,3-cyclohexanedione and ethyl vinyl ketone.[3] Reduction of **2** with 4 equiv of lithium and 1 equiv of H_2O in liquid ammonia−tetrahydrofuran (THF) at −40 °C for 10 min, followed by reaction of the excess lithium with 4 equiv of isoprene (−78 °C, 15 min) and enolate alkylation with excess allyl bromide (gradual warming and −35 °C for 30 min), provided allyl ketone **3** (82% yield) as a single diastereomer.[4] Conversion of **3** to the corresponding α,β-enone (69% yield and 21% recovered **3**) was accomplished by a three-step sequence:[5] (1) deprotonation of **3** with 2 equiv of lithium diisopropylamide in hexamethylphosphoramide (HMPA)−THF (23 °C, 20 min), followed by phenylsulfenation with 3 equiv of diphenyl disulfide (23 °C, 20 min); (2) oxidation of the resulting α-phenylthio ketone with excess *m*-chloroperbenzoic acid in dichloromethane (CH_2Cl_2, −78 °C, 2 h); and (3) elimination of the resulting α-phenylsulfinyl ketone by heating at reflux in benzene (13 h) in the presence of excess trimethyl phosphite to form the α,β-unsaturated analogue of **3**. Slow

⊗ Abstract published in *Advance ACS Abstracts,* December 15, 1997.

(1) Gunasekera, G. P.; McCarthy, P. J.; Kelly-Borges, M.; Lobkovsky, E.; Clardy, J. *J. Am. Chem. Soc.* **1996**, *118*, 8759−8760.

(2) Millar, J. B. A.; Russell, P. *Cell* **1992**, *68*, 407.

(3) Hagiwara, H.; Uda, H. *J. Org. Chem.* **1988**, *53*, 2308.

(4) Allyl ketone **3** has been described previously: Hagiwara, H.; Inome, K.; Uda, H. *J. Chem. Soc. Perkin Trans. I* **1995**, 757.

(5) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.

(6) Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063. A more reliable procedure to prepare trimethylsilyl lithium has been detailed: Hudrlik, P. F.; Waugh, M. A.; Hudrlik, A. M. *J. Organomet. Chem.* **1984**, *271*, 69.

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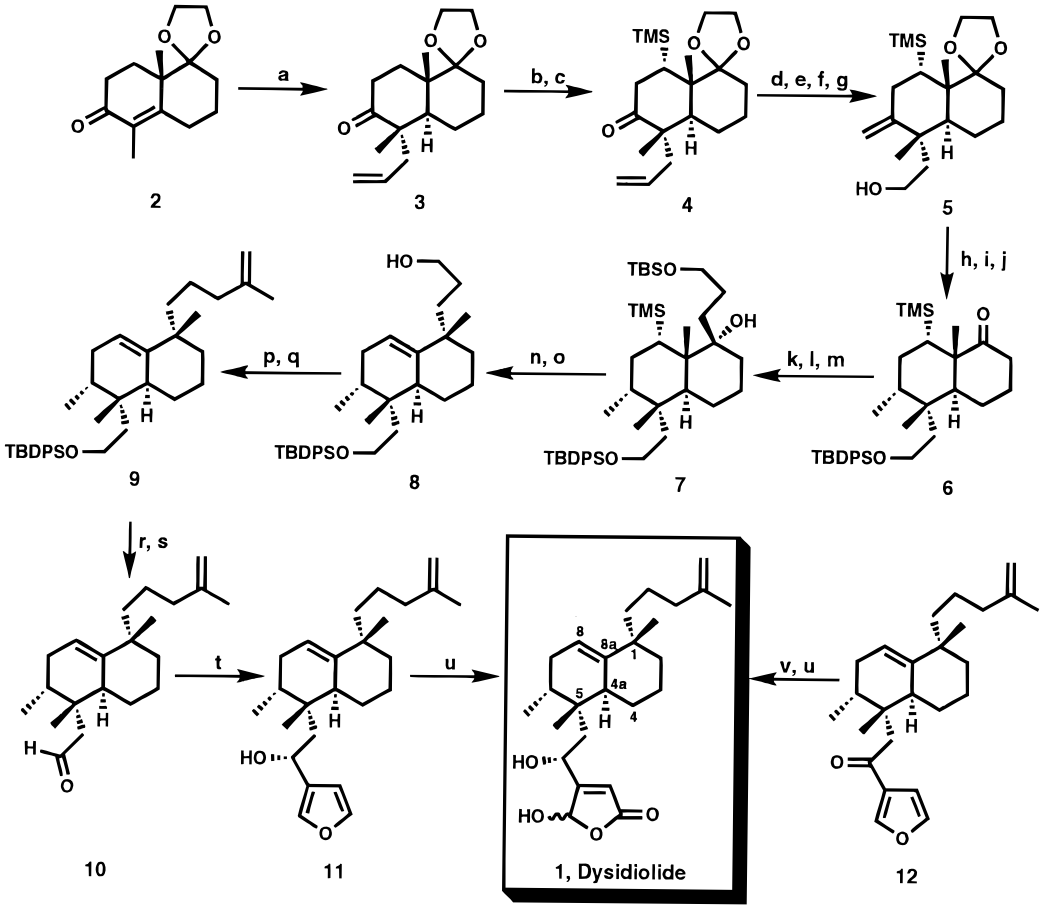
Scheme 1[a]



[a] Reagents (a) Li−NH_3, THF, −40 °C, 10 min, then isoprene, −78 °C, 15 min; allyl bromide, −78 to −35 °C, then −35 °C for 30 min (82% yield). (b) LDA, PhSSPh, HMPA−THF, 23 °C, 20 min; *m*-CPBA, CH_2Cl_2, −78 °C, 2 h; $(MeO)_3P$, C_6H_6, 80 °C, 13 h (69% yield and 21% recovered **3**). (c) TMSLi, HMPA−Et_2O, −78 °C, 3 h (64% yield). (d) KH, DMSO, Ph_3PCH_3Br, 23 °C, 2 h (97% yield). (e) $(DHQD)_2PYDZ$, $K_2OsO_4 \cdot 2H_2O$, K_2CO_3, $K_3Fe(CN)_6$, $MeSO_2NH_2$, 1:1 *t*-BuOH−H_2O, 0 °C, 4 h (97% yield). (f) $NaIO_4$, 4:1 THF−H_2O, 23 °C, 30 min. (g) $NaBH_4$, 6:1 THF−EtOH, 0 °C, 20 min (94% yield for two steps). (h) PPTS, 4:1 acetone−H_2O, 65 °C; 2 h (100% yield). (i) TBDPSCl, DMAP, 2,6-lutidine, CH_2Cl_2, 23 °C, 1.5 h (96% yield). (j) $(Ph_3P)_3RhCl$, H_2 (1000 psi), C_6H_6, 65 °C, 23 h (76% yield). (k) allylMgBr, Et_2O, −78 to 23 °C, 10 min (99% yield). (l) BH_3−DMS, Et_2O, 23 °C, 2.5 h; EtOH, NaOH, H_2O_2, 23 °C, 3.5 h (95% yield). (m) TBSCl, DMAP, 2,6-lutidine, CH_2Cl_2, 23 °C, 12 h (97% yield). (n) BF_3 (g), CH_2Cl_2, −78 °C, 3 h. (o) PPTS, EtOH, 55 °C, 2.5 h (70% yield for two steps). (p) I_2, Ph_3P, imidazole, CH_2Cl_2, 23 °C, 10 min (97% yield). (q) 2-bromopropene, *t*-BuLi, CuI, Et_2O, −30 to 0 °C, 30 min (97% yield). (r) TBAF, THF, 23 °C, 8.5 h (96% yield). (s) Dess-Martin periodinane, pyridine, CH_2Cl_2, 23 °C, 1 h (94% yield). (t) 3-bromofuran, *n*-BuLi, THF, −78 °C, 30 min (98% yield, 1:1 **11**−*epi*-**11**). (u) O_2, *hν*, Rose Bengal, *i*-Pr_2EtN, CH_2Cl_2, −78 °C, 2 h (98% yield). (v) CBS catalyst **13**, BH_3−DMS, toluene, −30 °C, 15 h (91% yield).

addition of this α,β-enone to excess trimethylsilyl (TMS) lithium[6] in HMPA−diethyl ether (Et_2O) at −78 °C effected conjugate addition to form exclusively the axial β-TMS ketone **4** (64% yield).[7] Wittig methylenation of ketone **4** with excess methylenetriphenylphosphorane in dimethyl sulfoxide (Ph_3PCH_3Br, KCH_2SOCH_3, 23 °C, 2 h, 97% yield)[8] was followed by conversion of the allyl appendage to a 2-hydroxyethyl group to produce **5** by the following three-step sequence: (1) position-selective dihydroxylation of the vinyl group by the Sharpless reagent system (0.05 equiv of $DHQD_2$-PYDZ, 0.01 equiv of $K_2OsO_4 \cdot 2H_2O$, 3.5 equiv of K_2CO_3, 3.5 equiv of $K_3Fe(CN)_6$, 1 equiv of $MeSO_2NH_2$, 1:1 *t*-butanol−H_2O, 0 °C, 4 h)[9] to form the corresponding 1,2-diol; (2) glycol cleavage with 5 equiv of $NaIO_4$ in 4:1 THF−H_2O (23 °C, 30 min); and (3) reduction of the aldehyde with 3 equiv of $NaBH_4$ in 6:1 THF−EtOH (0 °C, 20 min) to provide alcohol **5** in 91% overall yield. Deketalization of **5** using 1 equiv of pyridinium *p*-toluenesulfonate (PPTS) in 4:1 acetone−H_2O (65 °C, 2 h, 100% yield), protection of the hydroxyl functionality as the *t*-butyldiphenylsilyl (TBDPS) ether [3 equiv of TBDPSCl, 1 equiv of 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, 23 °C, 1.5 h, 96% yield], and hydrogenation using Wilkinson's catalyst[10] [0.15 equiv of $(Ph_3P)_3RhCl$, 1000 psi H_2, benzene, 65 °C, 23 h, 76% yield], followed by silica gel radial chromatography, gave diastereomerically pure **6**.[11,12]

Although attempted nucleophilic addition of the 4-methyl-

(7) Slow addition of the α,β-enone to the TMSLi was necessary in order to minimize the formation of dimeric side products.

(8) Sampath, V.; Lund, E. C.; Knudsen, M. J.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1987**, *52*, 3595.

(9) For reviews of the Sharpless catalytic asymmetric dihydroxylation, see (a) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483; (b) Corey, E. J.; Noe, M. C. *J. Am. Chem. Soc.* **1996**, *118*, 11038. The cinchona alkaloid ligand ($DHQD_2$-PYDZ), with its well-defined structural characteristics, afforded enhanced selectivity for dihydroxylation of the monosubstituted double bond relative to the 1,1-disubstituted exocyclic double bond. This strategy has been used previously: Corey, E. J.; Roberts, B. E.; Dixon, B. R. *J. Am. Chem. Soc.* **1995**, *117*, 193. The diastereoselection of the attack on the monosubstituted double bond was only moderate, as expected[9b] (2.6:1).

(10) (a) Jardine, F. H.; Wilkinson, G. *J. Chem. Soc. C*, **1960**, 270. (b) Piers, E.; Waal, W.; Britton, R. W. *J. Am. Chem. Soc.* **1971**, *93*, 5113.

(11) The crude reaction mixture also contained the 6*S* diastereomer of **6** (21%), which was removed during silica gel radial chromatography.

(12) Efforts to improve the diastereoselectivity of the hydrogenation were unproductive. It appears that the cyclohexyl ring containing the exocyclic olefin is distorted out of the usual chair conformation as a result of steric interactions between the 1,3-diaxial methyl groups. As a result, the two faces of the olefin are nearly equally accessible to hydrogenation.

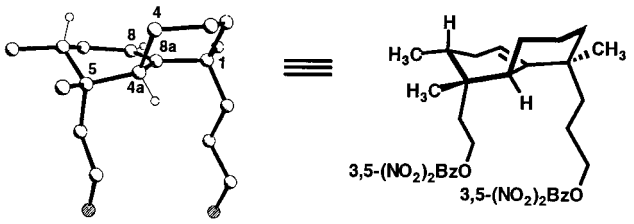


Figure 1. X-ray crystal structure of the bis(3,5-dinitrobenzoate) derivative of **8**. The two 3,5-dinitrobenzoate functional groups have been removed for improved clarity.

4-pentenyl lithium, magnesium, and cerium reagents to the carbonyl group of **6** simply returned starting material, addition of allylmagnesium bromide in Et_2O (4 equiv, −78 to 23 °C, 10 min) to this substrate occurred smoothly and stereospecifically to afford the axial tertiary alcohol in 99% yield. Hydroboration of the vinyl group with excess BH_3·DMS in Et_2O (23 °C, 2.5 h) and subsequent treatment with excess EtOH, NaOH, and H_2O_2 (23 °C, 3.5 h) gave a primary−tertiary diol (95% yield), which was then selectively protected at the primary hydroxyl by reaction with 3 equiv of *t*-butyldimethylsilyl (TBS) chloride (1 equiv of DMAP, CH_2Cl_2, 23 °C, 12 h) to provide **7** in 97% yield. Treatment of **7** with 6 equiv of BF_3(g) (CH_2Cl_2, −78 °C, 3 h) and subsequent selective cleavage of the TBS ether[13] (1 equiv of PPTS, EtOH, 55 °C, 2.5 h) furnished alcohol **8** (70% yield over two steps), which contains the fully substituted bicyclic core of dysidiolide (**1**).[14] The relative stereochemistry of **8** was confirmed by single-crystal X-ray diffraction analysis of its bis(3,5-dinitrobenzoate) derivative (Figure 1).[15] In the rearrangement of **7** to form **8**, the trimethylsilyl (TMS) group facilitates the migration of methyl to the cationic carbon generated by C−O heterolysis of **7** (by β-hyperconjugation of TMS in TMSC−C^+). In addition, the very facile elimination of that TMS group guarantees the location of the double bond.

The next stage of the synthesis involved the elaboration of the two ring appendages of **8** to generate the complete dysidiolide structure **1**. The C-1 side chain was emplaced via a two-step sequence: (1) iodination[16] of alcohol **8** (I_2, Ph_3P, imidazole, CH_2Cl_2, 23 °C, 10 min) and (2) iodide displacement with the vinyl cuprate derived from 2-lithiopropene (10 equiv of 2-bromopropene, 21 equiv of *t*-BuLi, 5 equiv of CuI, Et_2O, −30 to 0 °C, then 0 °C for 30 min) to afford **9** in 94% overall yield. Cleavage of the TBDPS ether in **9** with excess tetrabutylammonium fluoride (THF, 23 °C, 8.5 h, 96% yield) and subsequent oxidation (Dess Martin periodinane,[17] pyridine, CH_2Cl_2, 23 °C, 1 h, 94% yield) provided aldehyde **10**. Treatment of **10** with excess 3-lithiofuran[18] (3-bromofuran, *n*-BuLi, THF, −78 °C, 30 min) afforded a 1:1 mixture (98% yield) of the diastereomeric carbinols **11** and *epi*-**11**, which were readily separated by silica gel chromatography. Undesired *epi*-**11** was efficiently converted to **11** by a two-step sequence: (1) oxidation of *epi*-**11** to ketone **12** (1.5 equiv of Dess−Martin periodinane, 3.8 equiv of pyridine, CH_2Cl_2, 23 °C, 10 min, 100% yield) and (2) oxazaborolidine-catalyzed (CBS) reduction[19] using CBS catalyst **13** (Figure 2) (2 equiv of **13**, 2 equiv of BH_3·DMS, toluene, −30 °C, 15 h) to give **11** in 91% yield.[20] The recycling of *epi*-**11** allows for an overall 95% yield for the transformation of **10** to **11**. Photochemical oxidation[21] of **11** (O_2, Rose Bengal, 10 equiv of *i*-Pr_2EtN, CH_2Cl_2, −78 °C, 2 h) furnished dysidiolide (**1**, 98% yield), $[\alpha]_D^{23}$ −10.8 (*c* 0.60, 1:1 CH_2Cl_2−MeOH),[22] as a white solid. The infrared, ^1H and ^{13}C NMR, and MS/HRMS spectra were identical to those recorded previously, and comparison of synthetic **1** with an authentic sample of **1** by thin-layer chromatography showed them to be identical.[23]

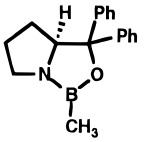


Figure 2. (*S*)-*B*-methyl CBS catalyst (**13**).

A number of peripheral findings from our studies should be mentioned. First, the presence of the trimethylsilyl group in **7** was essential for successful rearrangement to form **8**. The analogues of **7** with H or $C_6H_5(CH_3)_2Si$ instead of $(CH_3)_3Si$ afforded little, if any, of the desired rearrangement under a variety of conditions. In the case of the latter substrate, the major reaction pathway was that in which the axial tertiary hydroxyl attacked silicon to give after workup the analogue of **7** with $HO(CH_3)_2Si$ replacing $(CH_3)_3Si$. Second, the 4-methyl-4-pentenyl appendage could not be introduced directly since its presence interferes with the cationic rearrangement step (step n), which is disfavored relative to direct cation−olefin cyclization (without rearrangement) to form a new spiro ring. Finally, attempted Mitsunobu reaction to convert *epi*-**11** to **11** proceeded with only partial (ca. 3:1) inversion at carbon. Oxidation of *epi*-**11** to ketone **12** followed by reduction with L-Selectride, $NaBH_4$, or $LiBH_4$ also provided diastereomeric mixtures of alcohols with *epi*-**11** predominating. On the other hand, CBS reduction of ketone **12** was highly diastereoselective and afforded **11** in excellent yield, as described above.

In conclusion, the research described above demonstrates the first synthesis of dysidiolide (**1**), a C_{25} isoprenoid antimitotic agent possessing exceptional bioactivity and an unusual rearranged structure.[24]

Experimental Section

Chemical shifts for NMR spectra are reported as δ in units of parts per million (ppm) downfield from tetramethylsilane (δ 0.0) using the residual solvent signal as an internal standard: chloroform-*d* (^1H NMR δ 7.26, singlet; ^{13}C NMR δ 77.0, triplet) or DMSO-d_6 (^1H NMR δ

(13) Prakash, C.; Saleh, S.; Blair, I. A. *Tetrahedron Lett.* **1989**, *30*, 19.

(14) Approximately 7% of a minor (nonrearranged) product derived from elimination of the initially formed carbocation of **7** was isolated from this reaction. After TBS ether cleavage, this product was separated from **8** by silica gel radial chromatography.

(15) We are indebted to Dr. Marcus Semones for carrying out the X-ray crystallographic analysis. Detailed X-ray crystallographic data are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(16) Garegg, P. J.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. I* **1980**, 2866.

(17) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. An improved procedure for the preparation of the Dess Martin periodinane has been reported: Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.

(18) Ihara, M.; Suzuki, S.; Taniguchi, N.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2251.

(19) (a) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551. (b) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C. P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925. (c) Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *31*, 611. (d) Corey, E. J. *Pure Appl. Chem.* **1990**, *62*, 1209.

(20) For other examples of diastereoselective CBS reductions, see (a) Corey, E. J.; Helal, C. J. *Tetrahedron Lett.*, in press (Cicaprost ω-side chain); (b) Rao, M. N.; McGuigan, M. A.; Zhang, X.; Shaked, Z.; Kinney, W. A.; Bulliard, M.; Laboue, B.; Lee, N. E. *J. Org. Chem.* **1997**, *62*, 4541 (steroidal side chains); (c) Tschaen, D. M.; Abramson, L.; Cai, D.; Desmond, R.; Dolling, U.-H.; Frey, L.; Karady, S.; Shi, Y.-J.; Verhoeven, T. R. *J. Org. Chem.* **1995**, *60*, 4324 (MK-0499).

(21) Kernan, M. R.; Faulkner, D. J. *J. Org. Chem.* **1988**, *53*, 2773.

(22) Reported rotation of dysidiolide $[\alpha]_D^{23}$ −11.1 (*c* 0.60, 1:1 CH_2Cl_2−MeOH).[1]

(23) Obtained from Dr. Sarath P. Gunasekera, Harbor Branch Oceanographic Institute, Fort Pierce, FL.

(24) This research was assisted financially by a grant from the National Institutes of Health.

2.49, quintet; ^{13}C NMR δ 39.5, septet). Analytical thin-layer chromatography was performed using Merck 60 F_{254} precoated silica gel plates (0.25 mm thickness). Subsequent to elution, ultraviolet illumination at 254 nm allowed for visualization of UV active material. Staining with Verghn's reagent followed by warming of the silica gel plate allowed for further visualization. Verghn's reagent was prepared by dissolving ammonium molybdate (40 g) and ceric sulfate (1.6 g) in 10% aqueous H_2SO_4 (800 mL). Radial chromatography was performed on a Harrison Research Chromatotron 7924 and silica gel plates (no. 7749, Kieselgel 60 PF_{254}, Merck).

(4a*S*,5*S*,8a*S*)-(+)-3,4,4a,7,8,8a-Hexahydro-5,8a-dimethyl-5-(2-propenyl)naphthalene-1,6(2*H*,5*H*)-dione 1-(Ethylene Acetal) (3). To a solution of lithium (519 mg, 74.8 mmol, 4.3 equiv) in liquid ammonia (100 mL) at −40 °C was added a solution of **2**[3] (4.09 g, 17.32 mmol, 1.0 equiv, azeotropically dried with benzene) and water (337 μL, 0.867 mmol, 1.08 equiv) in dry THF (70 mL).[25] After the mixture was stirred for 10 min at −40 °C, isoprene (7.5 mL, 74.8 mmol, 4.3 equiv) was added, and the dark suspension was cooled to −78 °C and treated with allyl bromide (16.2 mL, 187 mmol, 10.8 equiv). The suspension was slowly warmed to −35 °C over 1 h, and after 0.5 h at −35 °C it was cooled to −78 °C and treated with water (5 mL, dropwise). The mixture was warmed to 23 °C over 2 h, diluted with water (200 mL), and extracted with Et_2O (3 × 200 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (200 g of SiO_2; eluent, 5% Et_2O−hexanes; product, fractions 12−18; 125 mL/fraction) afforded **3**[4] (3.96 g, 14.2 mmol, 82% yield) as a clear oil: R_f starting material, 0.24; product, 0.48 (3:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ +19.4 (*c* 1.00, MeOH); FTIR (film) 2947, 2880, 1703, 1439, 1184, 1047, 910 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60−5.71 (m, 1 H), 4.95−5.04 (m, 2 H), 3.84−3.96 (m, 4 H), 2.48−2.57 (m, 2 H), 2.32 (ddd, 1 H, J = 3.5, 5.8, and 16.0 Hz), 2.12 (dd, 1 H, J = 3.5 and 12.7 Hz), 1.88−2.01 (m, 2H), 1.60−1.70 (m, 3 H), 1.50−1.58 (m, 1 H), 1.35−1.45 (m, 3 H), 1.19 (s, 3 H), 1.02 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.8, 135.2, 117.4, 112.9, 65.3, 64.9, 50.9, 44.3, 42.6, 42.4, 35.0, 30.3, 28.9, 22.7, 21.8, 21.4, 16.4; HRMS (EI, Pos) *m*/*z* calcd for $[C_{17}H_{26}O_3]^+$, 278.1882; found, 278.1877.

Conversion of 3 to the Corresponding α,*β*-Enone. A solution of **3**[4] (1.1 g, 3.95 mmol, 1.0 equiv, azeotropically dried with benzene) in dry THF (10 mL) was added to a solution of lithium diisopropylamide (2.35 equiv of *n*-BuLi, 2.40 equiv of diisopropylamine) in THF (4 mL) at −78 °C.[25] HMPA (6 mL) was added, and the yellow solution was warmed to 0 °C. After 20 min, the red solution was warmed to 23 °C for 20 min, cooled to 0 °C, and treated with a solution of diphenyl disulfide (2.58 g, 11.8 mmol, 3.0 equiv, azeotropically dried with benzene) in THF (6 mL). The purple solution was warmed to 23 °C and, after 20 min, was poured into saturated aqueous $NaHCO_3$ (250 mL) and Et_2O (250 mL). The organic fraction was washed sequentially with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), diluted with CH_2Cl_2 (300 mL), and then dried (Na_2SO_4) and concentrated *in vacuo*. The crude α-phenylthio ketone was azeotropically dried with benzene and used immediately in the next reaction.

A solution of *m*-chloroperbenzoic acid (4.0 g, 19.8 mmol, 5.0 equiv) in dry CH_2Cl_2 (200 mL) was added dropwise via cannula over 30 min to a suspension of the crude α-phenylthio ketone and NaH_2PO_4 (3.9 g, 27.7 mmol, 7.0 equiv) in CH_2Cl_2 (100 mL) at −78 °C over 30 min.[25] After 1.5 h, trimethyl phosphite (3.26 mL, 27.7 mmol, 7.0 equiv) was added, and after 5 min, the suspension was poured into saturated aqueous $NaHCO_3$ (250 mL). The organic fraction was washed sequentially with saturated aqueous $NaHCO_3$ (100 mL), brine (100 mL), and water (100 mL) and then dried (Na_2SO_4) and concentrated *in vacuo*. The crude sulfoxide was used immediately in the next reaction.

A solution of the crude sulfoxide and trimethyl phosphite (1.86 mL, 15.8 mmol, 4.0 equiv) in dry benzene (130 mL) was heated to reflux (oil bath, 90 °C).[25] After 13 h, the reaction solution was cooled to 23 °C and concentrated *in vacuo*. Flash chromatography (200 g of SiO_2; eluent, 10% Et_2O−hexanes for fractions 1−20, 15% Et_2O−hexanes for fractions 21−40, 20% Et_2O−hexanes for fractions 41−60 and 25% Et_2O− hexanes thereafter; product, fractions 54−78; 25 mL/fraction) afforded pure α,*β*-enone (747 mg, 2.70 mmol, 69% yield) and recovered **3** (232 mg, 0.83 mmol, 21% yield) as clear oils: R_f starting material, 0.45; product, 0.38 (3:1 hexanes−EtOAc, Verghn's). Spectroscopic data for the α,*β*-enone: $[\alpha]_D^{23}$ +28.0 (*c* 1.00, MeOH); FTIR (film) 2979, 1668, 1446, 1186, 1066, 914 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, 1 H, J = 10.3 Hz), 5.93 (d, 1 H, J = 10.3 Hz), 5.55−5.65 (m, 1 H), 4.99−5.04 (m, 2 H), 3.93−4.04 (m, 4 H), 2.65 (dd, 1H, J = 5.6 and 13.9 Hz), 2.45−2.48 (m, 1 H), 2.12 (dd, 1 H, J = 9.1 and 13.9 Hz), 1.42−1.74 (m, 6 H), 1.27 (s, 3 H), 1.07 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.8, 155.3, 134.6, 127.3, 117.6, 111.8, 65.0, 64.8, 47.8, 45.2, 43.3, 41.6, 29.5, 22.5, 21.9, 20.3, 19.2; HRMS (EI, Pos) *m*/*z* calcd for $[C_{17}H_{24}O_3]^+$, 276.1725; found, 276.1728.

(4a*S*,5*S*,8*S*,8a*S*)-(+)-3,4,4a,7,8,8a-Hexahydro-5,8a-dimethyl-5-(2-propenyl)-8-trimethylsilylnaphthalene-1,6(2*H*,5*H*)-dione 1-(Ethylene Acetal) (4). Methyllithium (10.2 mL, 14.3 mmol, 1.4 M in Et_2O, 9.0 equiv) and Et_2O (20 mL) were sequentially added to frozen hexamethyldisilane (3.26 mL, 15.9 mmol, 10.0 equiv) in HMPA (5 mL) at −78 °C.[25] The mixture was warmed to 0 °C and stirred vigorously for several minutes. The resulting red solution was cooled to −78 °C, and a solution of α,*β*-enone (440 mg, 1.59 mmol, 1.0 equiv) in Et_2O (150 mL) was added dropwise via cannula at −78 °C over 2.5 h. After 30 min, methanol (5 mL) and water (5 mL) were added to the yellow solution, and the mixture was warmed to 23 °C and diluted with 1:1 Et_2O−hexanes (300 mL). The combined organic fractions were washed with water (2 × 100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Flash chromatography (50 g of SiO_2; eluent, 7% Et_2O−hexanes for fractions 1−20 and 15% Et_2O−hexanes thereafter; product, fractions 20−34; 10 mL/fraction) afforded **4** (357 mg, 1.02 mmol, 64% yield) as a clear oil: R_f starting material, 0.38; product, 0.60 (3:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ +55.9 (*c* 1.00, MeOH); FTIR (film) 2952, 1710, 1451, 1380, 1250, 1119, 857 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.60−4.70 (m, 1 H), 4.94−5.04 (m, 2 H), 3.90−4.01 (m, 4 H), 2.77 (dd, 1 H, J = 11.1 and 13.4 Hz), 2.26−2.33 (m, 2 H), 2.10 (dd, 1 H, J = 7.6 and 13.8 Hz), 1.84 (dd, 1 H, J = 4.0 and 11.0 Hz), 1.43−1.55 (m, 6 H), 1.25 (s, 1 H), 1.17 (s, 3 H), 1.00 (s, 3 H), 0.06 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 217.4, 134.1, 117.7, 113.4, 64.4, 63.7, 47.4, 45.4, 44.9, 37.4, 29.7, 28.7, 28.3, 22.3, 22.1, 18.7, 18.2, 0.9; HRMS (CI, NH_3) *m*/*z* calcd for $[C_{20}H_{34}O_3Si]^+NH_4$ 368.2621; found, 368.2621.

Wittig Methylenation of 4. Dimethyl sulfoxide (20 mL) was slowly added to potassium hydride (628 mg, 15.66 mmol, 6.1 equiv, washed thoroughly with hexanes) at 23 °C, and the resulting mixture was stirred until gas evolution ceased.[25] After 20 min, Ph_3PCH_3Br (6.43 g, 18.0 mmol, 7.0 equiv, azeotropically dried with toluene) was added, and the yellow suspension was stirred for 15 min, after which it was added via cannula into neat **4** (900 mg, 2.57 mmol, 1.0 equiv) at 23 °C. After 2 h, the red solution was cooled to 0 °C and diluted with water (10 mL), and the mixture was extracted with Et_2O (3 × 100 mL). The combined organic fractions were diluted with CH_2Cl_2 (200 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography (50 g of SiO_2; eluent, 3% Et_2O−hexanes; product, fractions 7−21; 10 mL/fraction) afforded the diene (869 mg, 2.50 mmol, 97% yield) as a clear oil: R_f starting material, 0.54; product, 0.68 (5:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ +61.4 (*c* 1.00, $CHCl_3$); FTIR (film) 2951, 2869, 1380, 857, 833 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70−5.79 (m, 1 H), 4.90−5.00 (m, 2 H), 4.85 (s, 1 H), 4.70 (s, 1 H), 3.86−3.98 (m, 4 H), 2.48 (ddd, 1 H, J = 1.0, 9.7, and 13.7 Hz), 2.25 (dd, 1 H, J = 3.2 and 13.7 Hz), 2.10 (s, 1 H), 2.08 (s, 1 H), 1.86 (dd, 1 H, J = 3.2 and 11.8 Hz), 1.37−1.64 (m, 6 H), 1.26 (s, 1 H), 1.16 (s, 3 H), 0.95 (s, 3 H), 0.06 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 135.5, 116.5, 113.7, 108.1, 64.3, 63.5, 46.6, 46.3, 46.0, 41.7, 31.6, 29.0, 28.1, 22.5, 22.4, 21.3, 19.1, 1.7; HRMS (CI, NH_3) *m*/*z* calcd for $[C_{21}H_{36}O_2Si]^+H$, 349.2563; found, 349.2561.

(4a*S*,5*S*,8*S*,8a*S*)-(+)-3,4,4a,5,6,7,8,8a-Octahydro-5-(2-hydroxyethyl)-6-methenyl-5,8a-dimethyl-8-trimethylsilylnaphthalen-1(2*H*)-one 1-(Ethylene Acetal) (5). A solution of $DHQD_2$-PYDZ[9b] (91 mg, 0.13 mmol, 0.05 equiv), potassium ferricyanide (2.96 g, 9.0 mmol, 3.5 equiv), potassium carbonate (1.24 g, 9.0 mmol, 3.5 equiv) and methanesulfonamide (238 mg, 2.5 mmol, 1.0 equiv) in *t*-butyl alcohol−water (1:1, 30 mL) at 23 °C was added to the diene (860 mg, 2.5 mmol, 1.0 equiv). The resulting solution was cooled to 0 °C with vigorous stirring. After 15 min, potassium osmate (VI) dihydrate (9 mg, 0.03 mmol, 0.01 equiv) was added to the biphasic mixture, which was stirred for 4 h. The suspension was treated with excess Na_2SO_3 and water (20 mL), and the mixture was extracted with EtOAc (3 × 100 mL). The combined

(25) This reaction was conducted under an atmosphere of dry nitrogen.

organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (60 g of SiO_2; eluent, 40% EtOAc−hexanes for 1−10 and 60% EtOAc−hexanes thereafter; product, fractions 13−34; 10 mL/fraction) afforded the 1,2-diol (925 mg, 2.42 mmol, 97% yield) as a 2.6:1 mixture of diastereomers and a clear oil: R_f starting material, 0.80; product, 0.26 (1:1 hexanes−EtOAc, Verghn's); FTIR (film) 3405, 2948, 1443, 1247, 1067, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.98 (s, 1 H, major), 4.97 (s, 1 H, major), 4.93 (s, 1 H, minor), 4.90 (s, 1 H, minor), 3.84−3.98 (m, 5 H), 3.30−3.44 (m, 2 H), 2.67 (br s, 1 H), 2.57−2.63 (m, 1 H, major), 2.47−2.53 (m, 1 H, minor), 2.34 (d, 1 H, J = 13.4 Hz, major), 2.27 (d, 1 H, J = 13.4 Hz, minor), 2.15 (br s, 1 H), 1.87−1.90 (m, 1 H), 1.38−1.65 (m, 9 H), 1.16 (s, 3 H, minor), 1.13 (s, 3 H, major), 1.09 (s, 3 H, minor), 1.07 (s, 3 H, major), 0.06 (s, 9 H); HRMS (CI, NH_3) m/z calcd for $[C_{21}H_{38}O_4Si]NH_4^+$, 400.2883; found, 400.2874.

Sodium periodate (2.6 g, 12.05 mmol, 5 equiv) was added to a solution of the 1,2-diol (920 mg, 2.41 mmol, 1.0 equiv) in THF−water (4:1; 40 mL) at 23 °C. After 30 min, the white suspension was diluted with brine (40 mL), and the resulting mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. The crude aldehyde was immediately subjected to the next reaction.

Sodium borohydride (274 mg, 7.23 mmol, 3 equiv) was added to a solution of the crude aldehyde in THF−ethanol (6:1; 30 mL) at 0 °C.[25] After 20 min, the clear solution was diluted with water (50 mL), and the resulting mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (60 g of SiO_2; eluent, 40% Et_2O−hexanes for fractions 1−5, 70% Et_2O−hexanes thereafter; product, fractions 16−32; 30 mL/fraction) afforded **5** (795 mg, 2.25 mmol, 94% yield) as a clear foam: R_f starting material, 0.26; aldehyde, 0.77; product, 0.58 (1:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ +37.9 (*c* 1.00, $CHCl_3$); FTIR (film) 3352, 2929, 1467, 1452, 1246, 1112, 1068, 1027, 855 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.87 (s, 1 H), 4.83 (s, 1 H), 3.95−3.98 (m, 1 H), 3.86−3.92 (m, 3 H), 3.58−3.66 (m, 2 H), 2.53 (dd, 1 H, J = 10.0 and 13.5 Hz), 2.28 (dd, 1 H, J = 2.9 and 13.5 Hz), 1.83 (dd, 1 H, J = 3.2 and 11.8 Hz), 1.40−1.70 (m, 10 H), 1.14 (s, 3 H), 1.03 (s, 3 H), 0.06 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 113.6, 108.2, 64.3, 63.5, 59.6, 47.9, 46.3, 43.9, 40.9, 31.4, 29.0, 28.1, 22.6, 22.5, 21.0, 19.0, 1.7; HRMS (EI, Pos) m/z calcd for $[C_{20}H_{36}O_3Si]^+$, 352.2434; found, 352.2434.

Deketalization and Silylation of 5. Pyridinium *p*-toluenesulfonate (564 mg, 2.24 mmol, 1.0 equiv) was added to a solution of **5** (790 mg, 2.24 mmol, 1.0 equiv) in acetone−water (4:1, 35 mL) at 23 °C. The solution was heated to 65 °C for 2 h, cooled to 23 °C, and diluted with brine (40 mL), and the mixture was extracted with CH_2Cl_2 (3 × 75 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (50 g of SiO_2; eluent, 60% Et_2O− hexanes; product, fractions 6−24; 30 mL/fraction) afforded the ketone (690 mg, 2.24 mmol, 100% yield) as a clear syrup: R_f starting material, 0.58; product, 0.50 (1:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −24.3 (*c* 0.82, $CHCl_3$); FTIR (film) 3400, 2950, 1708, 1439, 1247, 1025, 862 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.78 (s, 1 H), 4.68 (s, 1 H), 3.65−3.71 (m, 1 H), 3.46−3.53 (m, 1 H), 2.63−2.73 (m, 1 H), 2.30−2.36 (m, 1 H), 2.05−2.24 (m, 3 H), 1.74−1.84 (m, 4 H), 1.35−1.53 (m, 2 H), 1.22−1.30 (m, 2 H), 1.29 (s, 3 H), 1.08 (s, 3 H), −0.03 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.6, 153.6, 106.4, 58.8, 53.9, 52.6, 42.7, 41.3, 37.8, 31.6, 31.1, 27.2, 24.2, 21.8, 17.0, −0.2; HRMS (CI, NH_3) m/z calcd for $[C_{18}H_{32}O_2Si]^+NH_4$, 326.2515; found, 326.2514.

2,6-Lutidine (1.05 mL, 8.95 mmol, 4.0 equiv), *t*-butyldiphenylsilyl chloride (1.74 mL, 6.71 mmol, 3.0 equiv), and DMAP (273 mg, 2.24 mmol, 1.0 equiv) were added sequentially to a solution of the ketone (690 mg, 2.24 mmol, 1.0 equiv) in dry CH_2Cl_2 (25 mL) at 23 °C.[25] After the mixture was stirred at 23 °C for 1.5 h, brine (20 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (80 g of SiO_2; eluent, 2% Et_2O−hexanes for fractions 1−10, 4% Et_2O−hexanes thereafter; product, fractions 7−37; 30 mL/fraction) afforded the TBDPS ether (1.18 g, 2.16 mmol, 96% yield) as a clear syrup: R_f starting material, 0.19; product, 0.72 (3:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −2.4 (*c* 1.00, $CHCl_3$); FTIR (film) 2942, 1710, 1472, 1428, 1247, 1112, 863 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63−7.66 (m, 4 H), 7.35−7.42 (m, 6 H), 4.63 (s, 1 H), 4.50 (s, 1 H), 3.72 (ddd, 1 H, J = 4.7, 10.2, and 10.2 Hz), 3.41 (ddd, 1 H, J = 5.9, 10.2, and 10.2 Hz), 2.55−2.63 (m, 1 H), 2.26 (dd, 1 H, J = 14.1 Hz), 2.08 (dd, 2 H, J = 4.7 and 14.1 Hz), 1.83−1.93 (m, 2 H), 1.57−1.74 (m, 2 H), 1.38−1.42 (m, 1 H), 1.20−1.30 (m, 3 H), 1.23 (s, 3 H), 1.03 (s, 9 H), 1.00 (s, 3 H), −0.05 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 214.6, 153.1, 135.6, 134.0, 133.9, 129.5, 127.7, 127.6, 106.3, 59.7, 53.7, 52.5, 42.5, 41.3, 37.7, 31.6, 31.2, 31.1, 27.2, 26.9, 24.5, 21.4, 16.9, −0.2; HRMS (FAB, NaI) m/z calcd for $[C_{34}H_{50}O_2Si_2]^+Na$, 569.3247; found, 569.3264.

(4a*S*,5*R*,6*R*,8*S*,8a*S*)-(−)-3,4,4a,5,6,7,8,8a-Octahydro-5-(2-*t*-butyldiphenylsiloxyethyl)-5,6,8a-trimethyl-8-trimethylsilylnaphthalen-1(2*H*)-one (6). Tris(triphenylphosphonium)rhodium chloride (137 mg, 0.148 mmol, 0.15 equiv) was added to a solution of the TBDPS ether (540 mg, 0.987 mmol, 1.0 equiv, azeotropically dried with benzene) in dry benzene (18 mL) at 23 °C. The red suspension was placed in a Parr high-pressure vessel which was purged and then filled with hydrogen (1000 psi). After stirring for 23 h at 65 °C, the solution was filtered through SiO_2 (15 g, 300 mL of 10% Et_2O−hexanes) and then concentrated *in vacuo* to afford a 3.67:1 mixture of **6** and a minor diastereomer (6*S* configuration). Radial chromatography (2 × 4 mm SiO_2 plate; eluent, 250 mL of hexanes followed by 1% Et_2O−hexanes; product, fractions 88−110; 10 mL/fraction) afforded **6** (411 mg, 0.749 mmol, 76% yield) as a clear syrup: R_f starting material, 0.25; product **6**, 0.23; 6*S* diastereomer, 0.28 (10:1 hexanes−Et_2O, Verghn's); $[\alpha]_D^{23}$ −31.9 (*c* 1.00, $CHCl_3$); FTIR (film) 2956, 2858, 1707, 1428, 1247, 1112, 1085, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65−7.68 (m, 4 H), 7.35−7.43 (m, 6 H), 3.66−3.70 (m, 2 H), 2.60−2.69 (m, 1 H), 2.04−2.14 (m, 2 H), 1.49−1.64 (m, 5 H), 1.20 (s, 3 H), 1.14−1.37 (m, 5 H), 1.03 (s, 9 H), 0.92 (s, 3 H), 0.71 (d, 3 H, J = 7.0 Hz), −0.10 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.0, 135.6, 134.1, 134.0, 129.6, 129.5, 127.6, 60.1, 52.8, 51.2, 42.6, 38.4, 37.7, 35.9, 31.6, 27.7, 27.2, 26.9, 22.7, 22.3, 21.5, 20.4, 19.1, 17.5, 14.5, 14.1, −0.4; HRMS (FAB, NaI) m/z calcd for $[C_{34}H_{52}O_2Si_2]^+Na$, 571.3404; found, 571.3403.

Allylation of 6. Allylmagnesium bromide (2.89 mL, 1.0 M in Et_2O, 2.89 mmol, 4.0 equiv) was added to a solution of **6** (395 mg, 0.720 mmol, 1.0 equiv, azeotropically dried with benzene) in dry Et_2O (40 mL) at −78 °C.[25] The gray solution was stirred for 10 min and then warmed to 23 °C. After 10 min, the reaction solution was cooled to −78 °C and treated with saturated aqueous NH_4Cl (5 mL, dropwise), and the mixture was warmed to 23 °C. The mixture was partitioned between brine (40 mL) and CH_2Cl_2 (40 mL), and the aqueous portion was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (40 g of SiO_2; eluent, hexanes for fractions 1−10, 4% Et_2O−hexanes thereafter; product, fractions 12−17; 30 mL/fraction) afforded the tertiary alcohol (420 g, 0.711 mmol, 99% yield) as a clear syrup: R_f starting material, 0.55; product, 0.65 (5:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −20.2 (*c* 0.79, $CHCl_3$); FTIR (film) 3573, 2998, 2891, 1472, 1428, 1243, 1112, 1076, 1036, 859 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.69 (m, 4 H), 7.36−7.44 (m, 6 H), 5.84−5.91 (m, 1 H), 5.14−5.19 (m, 2 H), 3.68−3.72 (m, 2 H), 2.63 (dd, 1 H, J = 7.1 and 13.7 Hz), 2.41 (dd, 1 H, J = 7.7 and 13.7 Hz), 1.65−1.83 (m, 2 H), 1.15−1.56 (m, 11 H), 1.04 (s, 12 H), 0.83 (s, 3 H), 0.76 (d, 3 H, J = 6.8 Hz), 0.02 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 135.0, 134.1, 129.5, 127.6, 118.7, 76.9, 60.4, 47.9, 44.0, 42.9, 37.4, 36.7, 35.9, 33.0, 28.4, 26.9, 22.8, 22.4, 21.8, 20.7, 19.1, 15.3, 15.0, 2.3; HRMS (FAB, NaI) m/z calcd for $[C_{37}H_{58}O_2Si_2]^+Na$, 613.3873; found, 613.3868.

(1*S*,4a*S*,5*R*,6*R*,8*S*,8a*S*)-(−)-Decahydro-1-[3-(*t*-butyldimethylsiloxy)propyl]-5-[2-(*t*-butyldiphenylsiloxy)ethyl]-1-hydroxy-5,6,8a-trimethyl-8-trimethylsilylnaphthalene (7). Borane−dimethyl sulfide complex (360 μL, 10.0 M, 3.60 mmol, 5.4 equiv) was added to a solution of the tertiary alcohol (397 mg, 0.672 mmol, 1.0 equiv) in dry Et_2O (50 mL) at −78 °C.[25] The clear solution was warmed to 23 °C. After 2.5 h, the solution was cooled to 0 °C, and ethanol (9 mL), NaOH (9 mL, 3 M aqueous solution) and H_2O_2 (9 mL, 30% aqueous solution) were added sequentially and dropwise (to control gas evolution). The white mixture was warmed to 23 °C, stirred for 3.5 h, and partitioned between brine (100 mL) and Et_2O (50 mL). The aqueous portion was

extracted with Et_2O (2 × 100 mL) and the combined organic fractions were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (60 g of SiO_2; eluent, 25% Et_2O−hexanes for fractions 1−10, 40% Et_2O− hexanes thereafter; product, fractions 20−33; 30 mL/fraction) afforded the primary−tertiary diol (390 mg, 0.640 mmol, 95% yield) as a clear foam: R_f starting material, 0.65; product, 0.12 (5:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −21.4 (*c* 1.00, $CHCl_3$); FTIR (film) 3322, 2950, 2867, 1462, 1381, 1238, 1119, 1075, 856 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66−7.68 (m, 4 H), 7.36−7.42 (m, 6 H), 3.67−3.71 (m, 4 H), 1.92−1.98 (m, 1 H), 1.49−1.82 (m, 8 H), 1.11−1.43 (m, 8 H), 1.04 (s, 9 H), 1.02 (s, 3 H), 0.83 (s, 3 H), 0.77 (d, 3 H, J = 6.8 Hz), 0.01 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 134.1, 129.5, 127.6, 77.1, 63.6, 60.4, 48.4, 44.2, 42.9, 37.5, 36.7, 32.5, 31.6, 28.4, 27.7, 26.9, 26.8, 22.7, 22.5, 21.3, 20.7, 19.1, 15.2, 15.1, 2.2; HRMS (FAB, NaI) *m*/*z* calcd for $[C_{37}H_{60}O_3Si_2]^+Na$, 631.3979; found, 631.3973.

2,6-Lutidine (614 μL, 5.27 mmol, 4.0 equiv), *t*-butyldimethylsilyl chloride (595 mg, 3.95 mmol, 3.0 equiv), and DMAP (161 mg, 1.32 mmol, 1.0 equiv) were added sequentially to a solution of the primary−tertiary diol (802 mg, 1.32 mmol, 1.0 equiv) in dry CH_2Cl_2 (30 mL) at 23 °C.[25] After 12 h, brine (50 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (60 g of SiO_2; eluent, 3% Et_2O−hexanes; product, fractions 6−40; 30 mL/fraction) afforded **7** (914 mg, 1.27 mmol, 97% yield) as a clear foam: R_f starting material, 0.12; product, 0.59 (5:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −20.9 (*c* 1.00, $CHCl_3$); FTIR (film) 3406, 2930, 2867, 1453, 1254, 1106, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66−7.68 (m, 4 H), 7.37−7.41 (m, 6 H), 3.66−3.71 (m, 4 H), 1.91−1.97 (m, 1 H), 1.76−1.82 (m, 1 H), 1.12−1.73 (m, 16 H), 1.04 (s, 9 H), 1.03 (s, 3 H), 0.92 (s, 9 H), 0.83 (s, 3 H), 0.76 (d, 3 H, J = 6.9 Hz), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.00 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 134.1, 129.4, 127.5, 77.1, 63.9, 60.4, 48.2, 44.0, 42.8, 37.4, 36.6, 32.3, 28.3, 28.1, 26.8, 26.7, 25.9, 22.6, 22.5, 21.2, 20.7, 19.0, 18.3, 15.2, 14.9, 14.0, 2.2, −5.3, −5.4; HRMS (FAB, NaI) *m*/*z* calcd for $[C_{43}H_{74}O_3Si_3]^+Na$, 745.4844; found, 745.4842.

Cationic Rearrangement of 7. Anhydrous boron trifluoride gas (55 mL, 2.28 mmol, 6.0 equiv) was added portionwise (11 × 5 mL) via gastight syringe to a sealed solution of **7** (275 mg, 0.38 mmol, 1.0 equiv, azeotropically dried with benzene) in dry CH_2Cl_2 (75 mL) at −78 °C.[25] After 3 h, triethylamine (5 mL) and THF−water (1:1, 15 mL) were added at −78 °C, and the mixture was warmed to 23 °C. Brine (50 mL) was added, and the aqueous portion was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (20 g of SiO_2; eluent, hexanes for fractions 1−10, 3% Et_2O−hexanes thereafter; product, fractions 4−12; 10 mL/fraction) afforded an inseparable 9:1 mixture of the rearranged bicycle and an elimination product (244 mg) as a clear syrup: R_f starting material, 0.41; product, 0.59 (10:1 hexanes−EtOAc, Verghn's). The mixture was immediately subjected to the next reaction.

(1*S*,4a*S*,5*R*,6*R*)-(−)-1,2,3,4,4a,5,6,7-Octahydro-5-[2-(*t*-butyldiphenylsiloxy)ethyl]-1-(3-hydroxypropyl)-1,5,6-trimethylnaphthalene (8). Pyridinium *p*-toluenesulfonate (96 mg, 0.38 mmol, 1.0 equiv) was added to a solution of the above mixture of rearrangement and elimination products (244 mg) in ethanol (15 mL) at 23 °C, and the clear solution was heated to 55 °C. After 2.5 h, the solution was cooled to 23 °C and treated with saturated aqueous $NaHCO_3$ (50 mL), and the mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. Radial chromatography (4 mm SiO_2 plate; eluent, 10% Et_2O−hexanes; product, fractions 30−48; 10 mL/fraction) afforded **8** (136.2 mg, 0.263 mmol, 70% yield) as a clear syrup: R_f starting material, 0.74; product, 0.27 (5:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −31.7 (*c* 1.00, $CHCl_3$); FTIR (film) 3407, 3071, 3050, 2955, 2859, 1471, 1428, 1112, 1028, 908 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66−7.70 (m, 4 H), 7.36−7.44 (m, 6 H), 5.28 (dd, 1 H, J = 3.4 Hz), 3.41−3.79 (m, 4 H), 1.85−2.00 (m, 3 H), 1.43−1.70 (m, 9 H), 1.03−1.33 (m, 5 H), 1.05 (s, 9 H), 0.97 (s, 3 H), 0.62−0.65 (m, 6 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.6 (br), 135.6, 135.5, 133.9, 133.8, 129.6, 129.5, 127.6, 127.5, 117.1 (br), 63.4, 61.2, 42.1 (br), 41.0 (br), 39.7 (br), 35.3, 33.2, 32.8, 31.5, 29.4 (br), 28.0, 26.8, 25.9, 22.6, 22.3, 22.0, 19.0, 14.6, 14.0; HRMS (FAB, NaI) *m*/*z* calcd for $[C_{34}H_{50}O_2Si]^+Na$, 541.3478; found, 541.3471.

X-ray Analysis Summary for the Bis(3,5-Dinitrobenzoate) Derivative of 8.[15] Data was collected using a Siemens SMART CCD-(charge-coupled device-) based diffractometer equipped with an LT-2 low-temperature apparatus at 213 K. A suitable crystal (crystallized from ether at 4 °C as small colorless plates) was chosen and mounted on a glass fiber using grease. Data was measured using Ω scans of 0.3 °/frame for 30 s, such that a hemisphere was collected. A total of 1271 frames were collected with a final resolution of 0.75 Å. Cell parameters were retrieved using SMART software and refined using SAINT on all observed reflections. Data reduction was performed using SAINT software, which corrects for Lp and decay. The structure was solved by the direct method using the SHELXS-90 program and refined by the least-squares method on F^2, SHELXL-93, incorporated in SHELXTL-IRIX V 5.03. Summary of crystal parameters: formula, $C_{32}H_{36}N_4O_{12}$; MW = 668.65; a = 9.7272 (18); b = 11.997 (4); c = 15.216 (5); α = 75.93 (3)°; β = 72.45 (2)°; γ = 74.952 (19)°; vol = 1608.5 (7) Å^3; triclinic; *P*-1; Z = 2; crystal size = 0.11 × 0.05 × 0.12 mm; GOF = 1.010; final R indices [$I > 2\sigma(I)$], R_1 = 6.25%, wR_2 = 16.65%; R indices (all data), R_1 = 7.46%, wR_2 = 17.93%.

Iodination of 8. Iodine (255 mg, 1.00 mmol, 4 equiv) was added to a solution of triphenyl phosphine (329 mg, 1.25 mmol, 5 equiv) and imidazole (128 mg, 1.88 mmol, 7.5 equiv) in dry CH_2Cl_2 (10 mL) at 0 °C.[25] After 10 min at 23 °C, the yellow suspension was treated with 2-methyl-2-butene (0.5 mL), stirred for 10 min, and added to a solution of **8** (130 mg, 0.251 mmol, 1.0 equiv) in dry CH_2Cl_2 (2 mL) at 23 °C. After 10 min, water (20 mL) and Et_2O (50 mL) were added, and the organic portion was washed with $Na_2S_2O_3$ (20 mL, 0.1 N aqueous solution), dilute H_2O_2 (20 mL, to remove excess triphenyl phosphine), and water (30 mL). The organic fraction was diluted with hexanes (50 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography (20 g of SiO_2; eluent, 4% Et_2O−hexanes; product, fractions 3−13; 10 mL/fraction) afforded the iodide (153 mg, 0.243 mmol, 97% yield) as a clear oil that was immediately subjected to the next reaction: R_f starting material, 0.27; product, 0.68 (5:1 hexanes−EtOAc, Verghn's).

(1*S*,4a*S*,5*R*,6*R*)-(−)-1,2,3,4,4a,5,6,7-Octahydro-5-[2-(*t*-butyldiphenylsiloxy)ethyl]-1-(4-methyl-4-pentenyl)-1,5,6-trimethylnaphthalene (9). *t*-Butyllithium (3.1 mL, 5.27 mmol, 1.7 M in pentanes, 21.7 equiv) was added to a solution of 2-bromopropene (223 μL, 2.51 mmol, 10.3 equiv) in dry Et_2O (5 mL) at −78 °C.[25] After 30 min, the pale yellow solution was warmed to 23 °C for 1 h, recooled to −78 °C, and added to a gray suspension of copper (I) iodide (239 mg, 1.25 mmol, 5.15 equiv) in Et_2O (5 mL) at −78 °C. The resulting white suspension was stirred for 1 h at −40 to −50 °C, during which time it became a gray, then black, suspension and then a dark green-yellow solution. A solution of the iodide (153 mg, 0.243 mmol, 1.0 equiv) in Et_2O (3 mL) at −78 °C was added, and the black-green solution was warmed to 0 °C. After 30 min, 1:1 saturated aqueous NH_4Cl−10% NH_4OH (8 mL) was added, and the mixture was warmed to 23 °C with vigorous stirring. After 20 min, water (50 mL) and Et_2O (50 mL) were added, the aqueous portion was extracted with Et_2O (2 × 50 mL), and the combined organic fractions were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (20 g of SiO_2; eluent, 1% Et_2O−hexanes; product, fractions 3−9; 10 mL/ fraction) afforded **9** (128 mg, 0.236 mmol, 97% yield) as a clear oil: R_f starting material, 0.68; product, 0.75 (5:1 hexanes− EtOAc, Verghn's); $[\alpha]_D^{23}$ −17.6 (*c* 1.00, $CHCl_3$); FTIR (film) 3071, 2930, 2858, 1725, 1462, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66−7.69 (m, 4 H), 7.36−7.42 (m, 6 H), 5.27 (dd, 1H, J = 3.5 Hz), 4.64 (s, 1 H), 4.61 (s, 1 H), 3.69−3.73 (m, 2H), 1.44−1.88 (m, 12 H), 1.65 (s, 3 H), 1.06−1.30 (m, 6 H), 1.04 (s, 9 H), 0.95 (s, 3 H), 0.73 (s, 3 H), 0.70 (d, 3 H, J = 6.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.1, 135.5, 134.1, 129.4, 127.5, 116.6 (br), 109.6, 60.8, 41.2 (br), 40.1 (br), 38.6, 37.2, 35.6, 33.1, 32.2, 31.5, 29.8, 26.8, 26.0, 25.3, 22.3, 22.2, 19.0, 17.2, 14.7, 14.0; HRMS (FAB, NaI) *m*/*z* calcd for $[C_{37}H_{54}OSi]^+Na$, 565.3842; found, 565.3837.

TBDPS Ether Cleavage of 9. Tetrabutylammonium fluoride (1.65 mL, 1.65 mmol, 1.0 M in THF, 9.0 equiv) was added to a solution of **9** (100 mg, 0.184 mmol, 1.0 equiv) in THF (6 mL) at 23 °C. After 8.5 h, water (40 mL) and EtOAc (40 mL) were added, the aqueous portion was extracted with EtOAc (2 × 40 mL), and the combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. The yellow oil was filtered through SiO_2 (20 g; eluent, 150 mL of 15% EtOAc−

hexanes) to afford a mixture of the alcohol (54 mg, 0.177 mmol, 96% yield) and TBDPSF as a clear oil. This mixture was generally subjected to the next reaction without further purification; however, radial chromatography (4 mm SiO_2 plate; eluent, 5% EtOAc−hexanes; product, fractions 31−43; 10 mL/fraction) affords an analytically pure sample of the alcohol. Analytical data for the alcohol: R_f starting material, 0.76; product, 0.38 (5:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −54.2 (*c* 1.00, $CHCl_3$); FTIR (film) 3374, 2955, 1428, 1113, 884, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.29 (dd, 1 H, $J = 3.4$ Hz), 4.67 (s, 1 H), 4.66 (s, 1 H), 3.64−3.68 (m, 2 H), 1.94−1.98 (m, 2 H), 1.89 (d, 1 H, $J = 12.3$ Hz), 1.49−1.74 (m, 8 H), 1.70 (s, 3 H), 1.06−1.37 (m, 7 H), 0.97 (s, 3 H), 0.85 (s, 3 H), 0.81 (d, 3 H, $J = 6.8$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.8, 145.2 (br), 116.9 (br), 109.3, 59.7, 41.8 (br), 41.2 (br), 39.8 (br), 38.7, 37.2, 35.5, 32.9, 31.5 (br), 29.3, 29.0 (br), 26.0, 22.5, 22.4, 22.3, 14.8, 14.7; HRMS (CI, Pos) *m*/*z* calcd for $[C_{21}H_{36}O]^+NH_4$, 322.3110; found, 322.3120.

(1*S*,4a*S*,5*R*,6*R*)-1,2,3,4,4a,5,6,7-Octahydro-5-(formylmethyl)-1-(4-methyl-4-pentenyl)-1,5,6-trimethylnaphthalene (10). A solution of Dess−Martin periodinane (306 mg, 0.722 mmol, 5.0 equiv) and pyridine (117 μL, 1.44 mmol, 10.0 equiv) in dry CH_2Cl_2 (5 mL) at 0 °C was added to a solution of the alcohol (44 mg, 0.144 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL).[25] After 1 h at 23 °C, hexanes (30 mL) were added, the resulting white suspension was filtered through Celite, and the filtrate was concentrated *in vacuo*. Flash chromatography (10 g of SiO_2; eluent, 3% Et_2O−hexanes; product, fractions 3−9; 10 mL/ fraction) afforded **10** (41 mg, 0.135 mmol, 94% yield) as a clear oil that was immediately subjected to the next reaction: R_f starting material, 0.38; product, 0.61 (5:1 hexanes−EtOAc, Verghn's); ^1H NMR (500 MHz, $CDCl_3$) δ 9.90 (dd, 1 H, $J = 3.1$ Hz), 5.33 (m, 1 H), 4.67 (s, 1 H), 4.64 (s, 1 H), 2.33 (dd, 1 H, $J = 1.9$ and 14.2 Hz), 2.24 (dd, 1 H, $J = 3.4$ and 14.2 Hz), 1.90−2.08 (m, 4 H), 1.77−1.82 (m, 1 H), 1.68 (s, 3 H), 1.51−1.74 (m, 6 H), 1.09−1.35 (m, 5 H), 1.07 (s, 3 H), 0.99 (s, 3 H), 0.84 (d, 3 H, $J = 6.5$ Hz).

(1*S*,4a*S*,5*R*,6*R*)-(−)-1,2,3,4,4a,5,6,7-Octahydro-5-[2*R*-2-hydroxy-2-(3-furyl)ethyl]-1-(4-methyl-4-pentenyl)-1,5,6-trimethylnaphthalene (11). *n*-Butyllithium (727 μL, 1.64 M in hexanes, 1.19 mmol, 10.0 equiv) was added to a solution of 3-bromofuran (107 μL, 1.19 mmol, 10.0 equiv) in dry THF (2 mL) at −78 °C, and after 30 min, the yellow solution was treated with a solution of **10** (36 mg, 0.119 mmol, 1.0 equiv) in THF (3 mL).[25] After 30 min, saturated aqueous NH_4Cl (1 mL) and water (5 mL) were added, the mixture was warmed to 23 °C, and water (20 mL) and Et_2O (50 mL) were added. The aqueous portion was extracted with Et_2O (2 × 50 mL), and the combined organic fractions were diluted with CH_2Cl_2 (100 mL), dried (Na_2SO_4), and concentrated *in vacuo* to give a 1:1 mixture of the two alcohol diastereomers, **11** (desired) and *epi*-**11**. Flash chromatography (20 g of SiO_2; eluent, 5% Et_2O−hexanes for fractions 1−20 and 8% Et_2O−hexanes thereafter; product *epi*-**11**, fractions 14−23, product **11**, fractions 29−40; 10 mL/ fraction) afforded the desired diastereomer **11** (22 mg, 0.059 mmol, 50% yield) and the undesired diastereomer *epi*-**11** (21 mg, 0.057 mmol, 48% yield) as clear oils: R_f starting material, 0.75; product (**11**), 0.32; undesired diastereomer (*epi*-**11**), 0.46 (5:1 hexanes−EtOAc, Verghn's). Spectroscopic data for **11**: $[\alpha]_D^{23}$ −36.9 (*c* 1.00, $CHCl_3$); FTIR (film) 3397, 2930, 2863, 1444, 1024, 875 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 2 H), 6.38 (s, 1 H), 5.31 (s, 1 H), 4.84 (s, 1 H), 4.65 (s, 1 H), 4.58 (s, 1 H), 1.01−1.88 (m, 21 H), 1.64 (s, 3 H), 0.95 (s, 3 H), 0.87 (d, 3 H, $J = 6.5$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9 (br), 143.2, 138.4, 131.1, 117.1 (br), 109.7, 108.7, 64.0, 41.4 (br), 39.9 (br), 38.4, 37.0 (br), 36.3 (br), 33.4 (br), 31.6, 29.7 (br), 26.0, 23.4 (br), 22.3, 21.9, 14.9; HRMS (CI, NH_3) *m*/*z* calcd for $[C_{25}H_{38}O_2]^+NH_4$, 388.3216; found, 388.3224.

(1*S*,4a*S*,5*R*,6*R*)-1,2,3,4,4a,5,6,7-Octahydro-5-[2-keto-2-(3-furyl)ethyl]-1-(4-methyl-4-pentenyl)-1,5,6-trimethylnaphthalene (12). A solution of Dess−Martin periodinane (10 mg, 0.024 mmol, 1.5 equiv) and pyridine (5 μL, 0.062 mmol, 3.8 equiv) in dry CH_2Cl_2 (0.5 mL) at 0 °C was added to a solution of *epi*-**11** (6 mg, 0.016 mmol, 1.0 equiv) in CH_2Cl_2 (0.5 mL).[25] The solution was warmed to 23 °C for 10 min, hexanes (5 mL) were added, the resulting white suspension was filtered through Celite, and the filtrate was concentrated *in vacuo*. Flash chromatography (3 g of SiO_2; eluent, 7% Et_2O−hexanes; product, fractions 2−6; 10 mL/fraction) afforded **12** (6 mg, 0.016 mmol, 100% yield) as a clear oil that was subjected to the next reaction: R_f starting material, 0.46; product, 0.60 (5:1 hexanes−EtOAc, Verghn's); ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1 H), 7.39 (s, 1 H), 6.72 (s, 1 H), 5.33 (d, 1 H, $J = 3.7$ Hz), 4.57 (s, 1 H), 4.55 (s, 1 H), 2.55−2.72 (m, 2 H), 1.59−1.94 (m, 10 H), 1.59 (s, 3 H), 1.05−1.43 (m, 6 H), 0.99 (s, 3 H), 0.97 (s, 3 H), 0.87 (d, 3 H, $J = 6.5$ Hz).

(1*S*,4a*S*,5*R*,6*R*)-(−)-1,2,3,4,4a,5,6,7-Octahydro-5-[2*R*-2-hydroxy-2-(3-furyl)ethyl]-1-(4-methyl-4-pentenyl)-1,5,6-trimethylnaphthalene (11). A freshly prepared solution of borane−dimethyl sulfide (48 μL, 0.024 mmol, 0.5 M in toluene, 2.0 equiv) was added to a solution of **12** (4.5 mg, 0.012 mmol, 1.0 equiv, azeotropically dried with benzene) and (*S*)-B-methyl CBS catalyst **13** (470 μL, 0.024 mmol, 0.05 M in toluene, 2.0 equiv) at −78 °C.[25] After the mixture was stirred for 15 h at −30 °C, methanol (100 μL) was added, followed by water (0.5 mL) and Et_2O (2 mL), and the mixture was warmed to 23 °C. Water (10 mL) and Et_2O (10 mL) were added, and the aqueous portion was extracted with Et_2O (2 × 20 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (3 g of SiO_2; eluent, 8% Et_2O−hexanes; product, fractions 12−22; 10 mL/ fraction) afforded **11** (4.1 mg, 0.011 mmol, 91% yield) as a clear oil.

Dysidiolide (1). Rose Bengal (2 mg) was added to a solution of **11** (20 mg, 0.054 mmol, 1.0 equiv, azeotropically dried with benzene) and diisopropylethylamine (94 μL, 0.541 mmol, 10.0 equiv) in dry CH_2Cl_2 (30 mL) at 23 °C. The suspension was cooled to −78 °C and anhydrous oxygen was bubbled in for 20 min, after which the suspension was placed under an oxygen atmosphere and irradiated with a 250-W tungsten filament lamp. After 2 h, irradiation was stopped, the pink solution was warmed to 23 °C, and saturated aqueous oxalic acid (2 mL) was added. After 30 min of vigorous stirring, water (10 mL) and CH_2Cl_2−methanol (3:1, 50 mL) were added to the colorless mixture, and the aqueous portion was extracted with CH_2Cl_2−methanol (3:1, 2 × 50 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (30 g of SiO_2; eluent, 2% MeOH−CH_2Cl_2; product, fractions 9−20; 10 mL/fraction) afforded **1** (21.4 mg, 0.053 mmol, 98% yield) as a white solid: R_f product, 0.40 (1:1 hexanes−EtOAc, Verghn's); $[\alpha]_D^{23}$ −10.8 (*c* 0.60, 1:1 CH_2Cl_2−MeOH; $[\alpha]_{D\,lit.}^{23}$ −11.1); melting point: 179−181 °C; FTIR (film) 3387, 2925, 1744, 1643, 1581, 1444, 1375, 1131 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, 1 H, $J = 6.4$ Hz), 6.09 (d, 1 H, $J = 6.4$ Hz), 5.91 (br s, 1 H), 5.27, 5.18 (br s, 1 H), 4.64 (s, 1 H), 4.60 (s, 1 H), 4.50 (s, 1 H), 4.37 (dd, 1 H, $J = 8.4$ Hz), 1.61 (s, 3 H), 1.51 (br s, 3 H), 0.93 (s, 3 H), 0.81 (d, 3 H, $J = 6.5$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0 (br), 170.4, 145.3, 142.2 (br), 118.3 (br), 116.2 (br), 110.0, 98.1 97.6, 63.8 (br), 41.2 (br), 37.9, 36.4 (br), 33.0, 31.2 (br), 29.7 (br), 26.6 (br), 25.9, 23.5 (br), 22.1, 21.7, 21.5 (br), 14.9; HRMS (FAB, NaI) *m*/*z* calcd for $[C_{25}H_{38}O_4]^+Na$, 425.2668; found, 425.2663.

Supporting Information Available: Structure of dysidiolide and five tables, showing crystallographic data, atom coordinates, temperature factors, and bond lengths and angles (11 pages). See any current masthead page for ordering and Internet access instructions.

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