the paucity of data. Refinement: anisotropic thermal coefficients for non-hydrogen atoms, isotropic group thermal parameter for hydrogen atoms (SHELX-76). Final: no significant features in the difference Fourier map (range $-0.20 < e/Å^3 < 0.18$); agreement factors, $R = 0.049$ and $R_w = 0.052$.

Acknowledgment. We are grateful to the Research Board of the University of Illinois, Research Corporation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their support of this work.

Registry No. 1, 66873-39-0; 2, 116726-51-3; 3, 764-32-9; 4, 116808-55-0; 4 (alcohol), 116726-35-3; (±)-5, 116726-37-5; (±)-5 (*t*-BuSiMe$_2$ ether), 116747-43-4; (±)-6, 116784-19-1; (±)-8, 116726-39-7; (±)-8 (ketone), 116726-40-0; (±)-8 (benzoate), 116726-70-6; (±)-8 (*t*-BuSiMe$_2$ ether), 116726-41-1; (±)-8 (aldehyde, *t*-BuSiMe$_2$ ether), 116733-73-4; (±)-9, 116726-38-6; (±)-10, 116726-43-3; (±)-10 (*t*-BuSiMe$_2$ ether), 116726-42-2; (±)-11, 116839-32-8; (±)-11 (bromide), 116726-44-4; (±)-14, 116726-45-5; (±)-14 (sulfoxide, isomer 1), 116726-46-6; (±)-14 (sulfoxide, isomer 2), 116836-81-8; (±)-15 (isomer 1), 116726-47-7; (±)-15 (isomer 2), 116836-82-9; (±)-16, 116726-49-9; (±)-16 (alcohol, isomer 1), 116726-48-8; (±)-16 (alcohol, isomer 2), 116836-83-0; (±)-17, 116836-84-1; (±)-18, 116726-50-2; (±)-19 (isomer 1), 116726-52-4; (±)-19 (isomer 2), 116836-85-2; (±)-20, 116836-86-3; (±)-24, 116726-69-3; 24 (formate aldehyde), 116726-67-1; 24 (diol), 116726-68-2; 25, 35784-67-9; 25 (*t*-BuSiPh$_2$ ether), 116726-53-5; 26, 116726-54-6; 27, 116726-56-8; 27 (dihydro deriv), 116726-57-9; 27 (dihydro aldehyde), 116726-58-0; 28 (isomer 1), 116726-59-1; 28 (isomer 2), 116726-60-4; 29 (isomer 1), 116784-20-4; 29 (isomer 2), 116784-21-5; α-30, 116726-66-0; β-30, 116836-87-4; α-30 (acetonide, *t*-BuSiPh$_2$ ether), 116726-63-7; α-30 (acetonide), 116726-65-9; 31, 116726-64-8; 36, 116726-61-5; 36 (mesylate), 116726-62-6; (±)-$(CH_3)_2C{=}CH(CH_2)_2CH(OH)CH(CH_3)_2$, 116726-32-0; (±)-$(CH_3)_2C{=}CH(CH_2)_2CH(OSiMe_2Bu\text{-}t)CH(CH_3)_2$, 116726-33-1; (±)-(*Z*)-$HO(CH_2)_2C(CH_3){=}CH(CH_2)_2CH(OSiMe_2Bu\text{-}t)CH(CH_3)_2$, 116726-36-4; (±)-(*Z*)-$MSO(CH_2)_2C(CH_3){=}CH(CH_2)_2CH(OSiMe_2Bu\text{-}t)CH(CH_3)_2$, 116747-01-4; $Ph_3P{=}CH_2$, 3487-44-3; $(CH_3)_2C{=}CH(CH_2)_2Br$, 2270-59-9; $Ph_3P{=}CHCO_2Me$, 2605-67-6; $CH_2{=}CBrCH_3$, 557-93-7; 3-(dimethyl-*tert*-butylsiloxy)-2,7-dimethyl-6,7-epoxyoctane, 116726-34-2; 3-*O*-(*tert*-butyldiphenylsilyl)-1,2-isopropylidene-3-*C*-methyl-α-D-ribofuranodialdose, 116726-55-7.

Synthesis of (±)-4-De(3′-hydroxypropionyl)betaenone B, an Advanced Model for the Betaenones and Stemphyloxin I

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Received February 3, 1988

A stereocontrolled synthesis of (±)-3, a model for the stereochemically complex naturally occurring phytotoxins 1, 2, and 6, is reported. The synthesis relies upon the steric bias of a cis decalone skeleton for the establishment of appendage stereochemistry. The tricyclic bromo enone 9 prepared in five steps from methoxybenzoquinone was converted in nine steps to the dione 37. Ten additional steps were required to transform 37 to cis decalone 48. As predicted by molecular mechanics calculations, the cis decalone 48 was equilibrated essentially quantitatively to trans decalone 49 on exposure to base. Deprotection of 49 afforded (±)-3, the structure of which was proven by single-crystal X-ray analysis.

In 1983, Ichihara and co-workers reported the isolation and characterization by single-crystal X-ray analysis of the phytotoxin betaenone A (6).[2] Obtained from the same fungal source was the closely related compound betaenone B (1), whose spectroscopic properties were consistent with formulation as shown.[2] In the same year, Clardy and co-workers reported the structure of a closely related phytotoxin of fungal origin, stemphyloxin I (2), whose structure was proven by single-crystal X-ray analysis.[3] The stereochemical density and complexity of these substances renders them challenging targets for total synthesis. A synthesis of a structurally related mycotoxin, diplodiatoxin, has recently been reported by Ichihara et al.[4] We describe herein a conceptually distinct synthetic approach to the phytotoxins 1, 2, and 6.[5] These studies have culminated in the synthesis of (±)-4-de(3′-hydroxypropionyl)betaenone B (3) by an approach that resolves the stereochemical issues surrounding the synthesis of this family.[6]

It has previously been shown that oxidation of betaenone B (1) with PCC followed by exposure to base affords betaenone A (6).[2] As such, we focused our attention at the outset on betaenone B (1) as a synthetic target. The trans decalone skeleton of 1 appeared not particularly attractive as a synthetic cornerstone, since its essentially planar structure lacked the steric bias that would be useful for the stereocontrolled delivery of appendages. In contrast, the corresponding cis decalone (1, H-10α) was of interest, because this skeleton possesses a relatively less sterically encumbered α-face, the face upon which alkyl substituents are required at carbons 2–4, 6, and 8. The synthetic plan, therefore, was to utilize a cis decalone nucleus as a key structural feature, in anticipation of epimerization of C-10

(1) Alfred P. Sloan Research Fellow, 1988–1990; Searle Scholar 1984–1988; ICI Award Recipient, 1988.

(2) Ichihara, A.; Oikawa, H.; Hayashi, K.; Sakamura, S.; Furusaki, A.; Matsumoto, T. *J. Am. Chem. Soc.* **1983**, *105*, 2907.

(3) (a) Barash, I.; Manulis, S.; Kashman, Y.; Springer, J. P.; Chen, M. H. M.; Clardy, J.; Strobel, G. A. *Science (Washington, D.C.)* **1983**, *220*, 1065; (b) Steyn, P. S.; Wessels, P. L.; Holzapfel, C. W.; Potgieter, D. J. J.; Louw, W. K. A. *Tetrahedron* **1972**, 4775.

(4) Ichihara, A.; Kawagishi, H.; Tokugawa, N.; Sakamura, S. *Tetrahedron Lett.* **1986**, *27*, 1347.

(5) Taken in part from the Ph.D. Thesis of Daniel V. Pratt, University of Washington, 1988.

(6) For preliminary communications regarding this work, see: (a) Pratt, D. V.; Hopkins, P. B. *Tetrahedron Lett.* **1987**, *28*, 3065. (b) Pratt, D. V.; Hopkins, P. B. *J. Am. Chem. Soc.* **1987**, *109*, 5553. (c) Pratt, D. V.; Ruan, F.; Hopkins, P. B. *J. Org. Chem.* **1987**, *52*, 5053.

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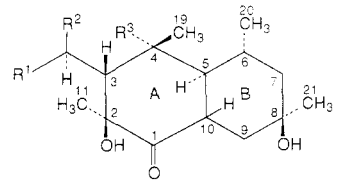
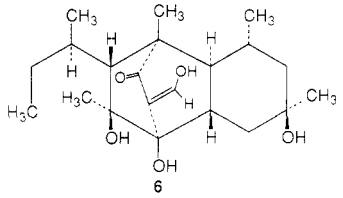


	R^1	R^2	R^3	H^{10}
1	C_2H_5	CH_3	$C(O)CH_2CH_2OH$	β
2	C_2H_5	CH_2OH	$C(O)CH{=}CHOH$	β
3	C_2H_5	CH_3	H	β
4	CH_3	CH_3	CH_3	α
5	CH_3	CH_3	CH_3	β



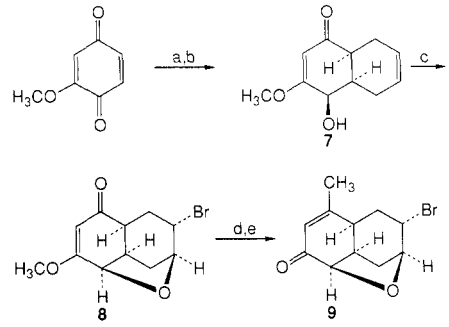
6

late in the synthesis, converting the unnatural, cis decalone to the naturally occurring trans decalone skeleta of **1**, **2**, and **6**.

The viability of the latter transformation, isomerization of a highly substituted cis- to a trans-fused decalone is worthy of further comment. Comfort taken from the known thermodynamic preference in the parent 1-decalone for the trans- over the cis-fused form (9:1 at 250 °C) is unjustified, because this preference is readily overcome. For example, in 9-methyl-1-decalone there exists a thermodynamic preference for the cis fusion over trans of 6:4 at 250 °C![7] The epimerization in the much more highly substituted betaenone series was thus far from assured. Inspection of molecular models of **1** and its C-10 epimer in all possible chair–chair conformations revealed significant unfavorable 1,3-diaxial interactions and suggested that twist boat forms of both the cis- and trans-fused isomers might be important. Further guidance was sought through molecular mechanics energy minimizations (MM2),[8] using the somewhat simplified models **4** and **5**. Fifteen starting conformations of cis-fused decalone **4** were energy minimized; the lowest eight minima were all within 1.0 kcal/mol of one another, and included not only the $chair_A$–$chair_B$ conformations, but also $chair_A$–$twist\ boat_B$ and $twist\ boat_A$–$twist\ boat_B$ conformers. Minimization of the $chair_A$–$chair_B$ and $twist\ boat_A$–$chair_B$ (as seen in the X-ray crystal structure of stemphyloxin I[2]) conformers of **5** suggested that the former would be preferred by 2 kcal/mol, but more importantly, led to the prediction that the trans-fused isomer **5** would be preferred over cis- fused **4** by almost 6 kcal/mol. The fact that this calculation did not account for hydrogen-bonding interactions was not of concern, since such interactions are in principle preventable in the laboratory by suitable protection of the hydroxyl functions.

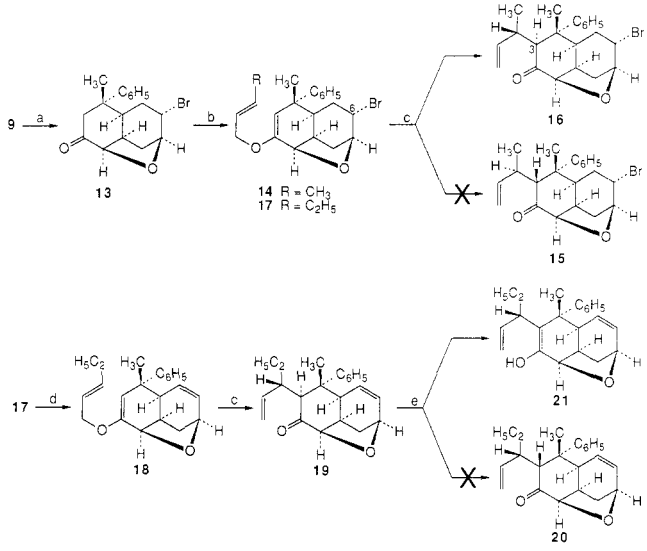
Bolstered by the theoretical prediction that an appropriately functionalized cis-fused decalone should be convertible under thermodynamic control to the trans-fusion present in the nature products, the synthesis commenced as shown in Scheme I. Methoxy-1,4-benzoquinone, prepared from vanillin by a modification of the literature

Scheme I[a]



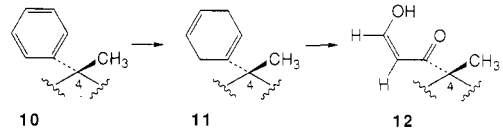
[a] (a) 1,3-Butadiene, 67%; (b) $NaBH_4$, 60%; (c) NBS; (d) MeLi; (e) H^+, 62% (three steps).

Scheme II[a]



[a] (a) $(C_6H_5)_2CuLi$, 98%; (b) $RCH{=}CHCH_2OH$, H^+, 50% (**17**); (c) 210 °C, 86% (**19**); (d) DBU, 86%; (e) $NaOCH_3$, 99%.

Scheme III



procedure,[6c] was converted to the known decalone **7**.[9] Bromoetherification provided the relatively unstable tricyclic ether **8**, which was treated with methyllithium and hydrolyzed to the tricyclic bromo enone **9**, a key intermediate.

The tricyclic bromo ether **9** was an attractive intermediate for several reasons: the sequence of reactions leading to **9** could be conducted on a large scale, the starting materials were all relatively inexpensive, and no chromatography of intermediates was necessary. Furthermore, this intermediate possesses the convex α-face desired for stereocontrolled appendage attachment. Finally, **9** is highly functionalized with independently manipulable functional groups.

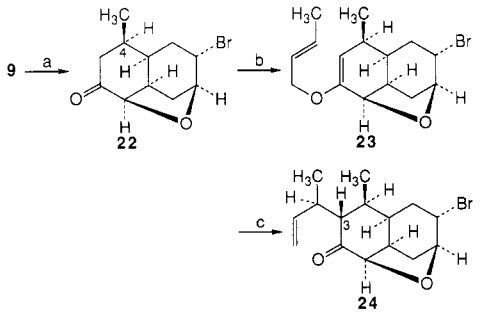
As shown in Scheme II, attention was turned to appendage attachment at C(3) and C(4). The phenyl group was selected as a protected form of the α-face oxidized propyl side chain of the natural products. Such a

(7) *Conformational Analysis*; Eliel, E. L., Allinger, N. L., Angyal, S. J., Morrison, G. S., Eds.; American Chemical Society: Washington, DC, 1981; pp 231–2.

(8) (a) *Molecular Mechanics*; Burket, U., Allinger, N. L., Eds.; American Chemical Society: Washington, DC, 1982. (b) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (c) Allinger, N. L.; Chang, S. H. M.; Glaser, D. H.; Honig, H. *Isr. J. Chem.* **1980**, *20*, 51.

(9) Birnbaum, G. I. *J. Org. Chem.* **1960**, *25*, 1660.

Scheme IV[a]



[a] (a) H_2, Pt/C; (b) $H_3CCH{=}CHCH_2OH$, H^+; (c) 130 °C, 64% (three steps).

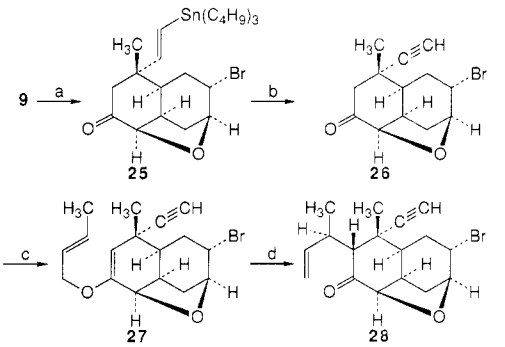
"protecting group" would be unmasked as shown in Scheme III by Birch reduction followed by oxidative cleavage of the resulting 1,4-diene (**11**).[10] Treatment of bromo enone **9** with lithium diphenylcuprate afforded ketone **13**, whose stereochemistry was proven at a subsequent stage. As a prelude to appendage attachment at C(3), ketone **13** was converted to the enol ether **14** as shown. Claisen rearrangement of **14** occurred at 185 °C in 1,4-dichlorobenzene to afford predominantly a single stereoisomer as indicated by 500-MHz ^{1}H NMR analysis. Nuclear Overhauser enhancement studies suggested that the product, however, was not the anticipated product of α-face appendage attachment, **15**. Instead, β-face attachment was indicated. Assuming that the pericyclic transition state was a chair, the major product apparently was **16**.

That appendage attachment proceeded on the crowded concave face of **14** is best explained by the steric requirements of the phenyl group, blocking convex face attachment. Two solutions to this problem are apparent: either the phenyl group must be replaced with some smaller substituent or the stereochemistry of **16** must be modified to that found in the phytotoxins. The latter was explored first. It appeared possible that the C(3) stereocenter of **16** might be "corrected" by a thermodynamically driven epimerization; likewise, attachment of a five-carbon, rather than four-carbon appendage (as in **17**) would enable the conversion of the side chain to that found in either stemphyloxin I or the betaenones.

Accordingly, ketone **13** was converted to enol ether **17**. In anticipation of eventual functionalization of C(6), it was expedient at this juncture to remove the elements of HBr from **17**, affording **18**. Claisen rearrangement of **18** proceeded smoothly at 210 °C in 4% *N,N*-dimethylaniline in *n*-dodecane. On cooling, the major product crystallized directly from the reaction medium in 86% yield and complete stereochemical purity (500-MHz ^{1}H NMR). The structure of the product was **19**, proven by single-crystal X-ray analysis.[6b]

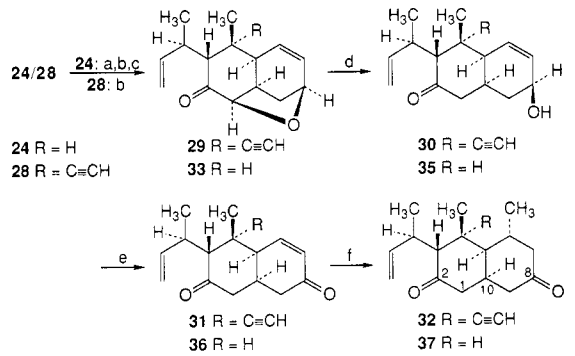
Attempts to epimerize **19** did not produce the anticipated ketone **20**, but instead the enol **21**. This phenomenon has been discussed in detail elsewhere.[6b] In the present context, the X-ray structure of enol **21** is of interest because it reveals that one ortho hydrogen of the phenyl group obscures the α-face of C(3), providing further support for the contention that the phenyl group plays a critical role in determining the stereochemical outcome of the Claisen rearrangement, directing appendage attachment to the concave face.

Scheme V[a]



[a] (a) $(n\text{-}C_4H_9)_3SnCH{=}CHCuC{\equiv}C\text{-}n\text{-}C_3H_7Li$; (b) $Pb(OAc)_4$, 94% (two steps); (c) $H_3CCH{=}CHCH_2OH$, H^+, 50%; (d) 160 °C, 62%.

Scheme VI[a]



[a] (a) $NaBH_4$; (b) DBU, Δ; (c) PCC, 28% (three steps, **33**); (d) SmI_2; (e) PCC; (f) $n\text{-}C_5H_{11}C{\equiv}CCuCH_3Li$, $(C_6H_5)_3P$.

The problems associated with the bulk of the phenyl substituent outweighed its advantages as a protecting group, and the second option, diminishing the size of this substituent, was explored. To ensure that the steric blockage hypothesis was in fact correct. Scheme IV was implemented. Hydrogenation of **9** afforded **22**, the stereochemistry of which at C(4) was at this time assumed, but eventually proven by single-crystal X-ray analysis of **3** (vide infra). Enol ether **23** was prepared as before, and on thermolysis at 130 °C in 1,4-dichlorobenzene provided essentially exclusively the product of convex-face appendage attachment, **24**. The stereochemistry at C(3) was clear from NOE studies; the stereochemistry of the side chain stereocenter is, again, proven by the X-ray structure of **3**. Both the lower temperature at which **23** is converted to **24** (130 °C versus ca. 200 °C for **14** to **16** and **18** to **19**) and the stereochemistry of **24** indicate that the phenyl substituent was in fact responsible for the stereochemical results in the Claisen rearrangements of **14** and **18**.

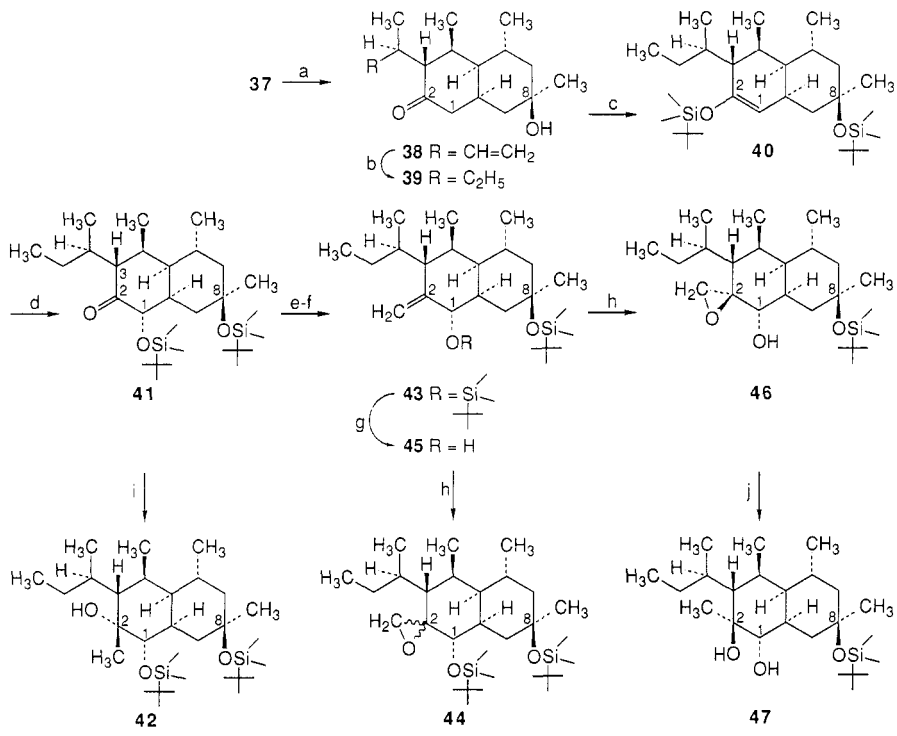
Based upon the above results, the smallest possible C(4) α-substituent that could be expected to eventually provide the required side chain was selected. As shown in Scheme V, an acetylene group was installed by the method of Corey and Wollenberg.[11] Enol ether **27** was prepared as before, and on thermolysis in 4% *N,N*-dimethylaniline in *n*-dodecane at 160 °C for 6 h afforded the ketone **28**, whose structure was proven by single-crystal X-ray analysis[6a] to be appropriate for the target natural products.

Bromo ketone **28** was advanced several stages as shown in Scheme VI. Elimination of HBr gave **29**. Reductive cleavage[12] of the α-keto ether was accomplished to provide

(10) (a) Birch, A. J. *J. Chem. Soc. (London)* **1944**, 430. (b) Kirchemo, C. L.; White, J. D. *J. Org. Chem.* **1985**, *50*, 1316. (c) Evans, D. A.; Sjogren, E. B. *Tetrahedron Lett.* **1985**, *26*, 3787.

(11) Corey, E. J.; Wollenberg, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 5581.
(12) Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 1135.

Scheme VII[a]

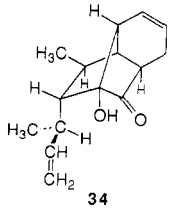


[a] (a) $(CH_3)_2CuLi$, CH_3Li, 59% (four steps from **33**); (b) H_2, Pd/C, 92%; (c) t-$C_4H_9(CH_3)_2SiOSO_2CF_3$, 2,6-$(CH_3)_2C_5H_3N$; (d) m-$ClC_6H_4CO_3H$, Na_2CO_3, 83% (two steps); (e) $(CH_3)_3SiCH_2Li$; (f) KH; (g) $(n$-$C_4H_9)_4NF$, 35% (three steps); (h) m-$ClC_6H_4CO_3H$, $NaHCO_3$; (i) CH_3Li; (j) $LiBH(C_2H_5)_3$, 61% (two steps).

30, which was oxidized to **31** and functionalized at C(6) with lithium dimethyl cuprate to yield **32**.

The preparation of **32** completed the elaboration of the stereochemistry of the northern periphery of the target substances. Modification of carbons 1, 2, 8, and 10 was required at this stage. It was decided that these issues were best addressed in a model not possessing the acetylene side chain. This had the advantage of postponing problems arising from the reactivity of the acetylene group, but the disadvantage that the product of this model study would not be convertible to any of the natural products for lack of an α-face C(4) substituent.

The sequence of reactions that had converted **28** to **32** required subtle modification when **24** was used a starting material. Specifically, DBU-promoted elimination of HBr from **24** afforded **33** as a transient intermediate, which was further transformed by an unexpected rearrangement to a substance believed to be the tricyclic ketone **34**.[13] The



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latter reaction, formally the Claisen rearrangement of an enol tautomer of **33**, was more thoroughly studied in a less substituted system and is discussed in detail elsewhere.[13] This reaction could be avoided by reduction of the carbonyl group of **24**, elimination of HBr, and reoxidation of the alcohol to yield **33**, which was processed essentially as before to diketone **37**.

Summarized in Scheme VII are transformations which led to the introduction of an oxygen atom at C(1) and methyl groups with the requisite stereochemistry at C(2) and C(8). Diketone **37** could be regio- and stereospecifically methylated with the 1:1 complex of methyllithium and lithium dimethyl cuprate, the method of Still and MacDonald.[14] This reagent combination is known to deliver an equatorial methyl group to cyclohexanones. Inspection of models of ketone **37** suggested that this would be appropriate. A trace (<5%) of diadduct could also be detected. The vinyl side chain of **38** was hydrogenated, and the resulting ketone **39** was converted to enol ether **40** with a silyl triflate reagent. The desirable regiochemistry of enol ether formation is presumably of kinetic origin, but this was not further investigated. The enol ether was oxidized to the α-silyloxy ketone **41** with MCPBA.[15] The new stereocenter at C(1) is important only insofar as it influences subsequent transformations, because it will be oxidized to a ketone in the final product. This stereocenter, however, is believed to possess the relative configuration shown, as indicated by an NOE between the C(1) and C(3) hydrogens of **41**.

Although treatment of ketone **41** with methyllithium afforded a single product, the stereostructure of this substance could not be assigned with certainty by available spectroscopic techniques. Inspection of models of **41** suggested that the desired α-face attachment of a methyl group was unlikely, this face of the molecule being shielded by the neighboring secondary butyl appendage. Based upon this, the methyllithium adduct was assigned stereostructure **42**, the unnatural isomer at C(2), and an alternative approach was sought. Peterson olefination[16] of **41**

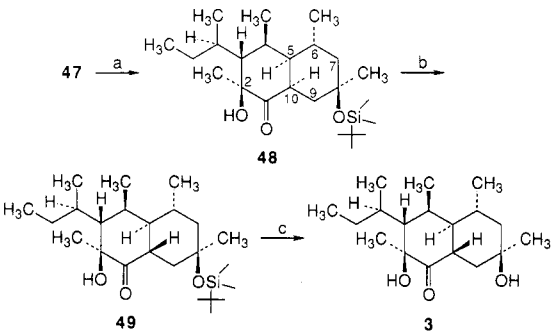
(13) Kirchner, J. J.; Pratt, D. V.; Hopkins, P. B. *Tetrahedron Lett.* **1988**, *29*, 4229.

(14) (a) Macdonald, T. L.; Still, W. C. *J. Am. Chem. Soc.* **1975**, *97*, 5280. (b) Still, W. C.; Macdonald, T. L. *Tetrahedron Lett.* **1976**, *31*, 2659.

(15) Rubottom, G. M.; Marrero, R. *Synth. Commun.* **1981**, *11*, 505.

(16) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780.

Scheme VIII[a]



[a] (a) ClCOCOCl, $(C_2H_5)_3N$, DMSO, 94%; (b) $NaOCH_3$, $HOCH_3$, 89%; (c) HF, H_2O, CH_3CN, 60%.

afforded the alkene **43** in modest yield. Epoxidation of this substance was nonselective, giving a 1:1 mixture of two isomeric epoxides, **44**. Finally, monodesilylation of **43** provided **45**, which was epoxidized to yield a single epoxide stereoisomer, which on reduction with lithium triethylborohydride[17] was isomeric with the diol obtained by monodesilylation of the methyllithium adduct **42**. That is, independent routes to both stereoisomers at C(2) had been achieved, but uncertainty surrounded the structure assignments.

Scheme VIII summarizes, the resolution of this problem. Oxidation[18] of **47** afforded a keto alcohol (**48**), which yielded to ^1H NMR stereochemical assignment by NOE. Specifically, irradiation of the C(2) methyl group resulted in enhancement of hydrogens at C(5) and C(10), consistent with the illustrated stereostructure. Thus, the olefination/desilylation/epoxidation/reduction sequence (**41** → **47**) afforded the desired stereochemistry.

The conversion of **45** to **46** is worthy of comment. The stereochemistry of this epoxidation is opposite that normally seen in hydroxyl-directed epoxidations.[19] The trivial possibility that the stereochemistry at C(1) has been misassigned seems unlikely in light of the NOE results on **41**. An alternate explanation is that the stereochemistry of the epoxidation of **45**, which yields **46**, is a consequence of the relative steric environments of the β- and α-faces, the α-face being somewhat occluded by the secondary butyl appendage. This requires, then, that the stereorandom epoxidation of **43** reflects a balanced steric environment on the two faces. Inspection of space-filling models reveals that the *tert*-butyldimethylsilyl moiety at C(1) of **43** can in fact reside in the vicinity of the β-face of the exocyclic double bond. There is no obvious structural feature, however, to mandate such a conformation. Interestingly, a peracid epoxidation with a stereochemical outcome opposite that expected based upon direction by allylic hydroxyl has recently been reported in a structurally related steroidal system.[20] A steric-crowding explanation was invoked by these workers, as well.

The availability of ketone **48** at last enabled the exploration of the key cis to trans decalone conversion. As predicted by the molecular mechanics method, treatment of ketone **48** with excess sodium methoxide in methanol at 25 °C for 1.5 h resulted in complete consumption of **48** as indicated by TLC and ^1H NMR analysis. From the reaction mixture, **49** could be isolated in 89% yield. Finally, desilylation of **49** gave **3**, the structure of which was proven by X-ray analysis, and shown in Figure 1.

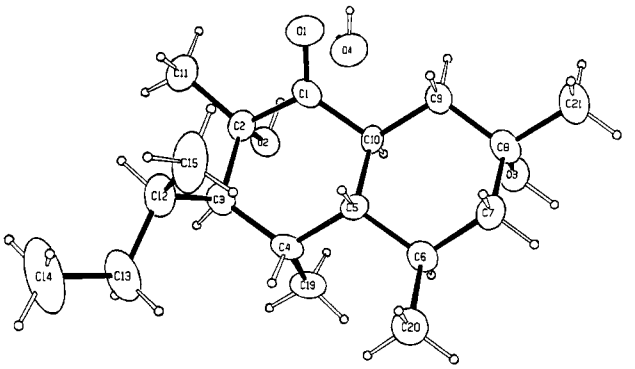


Figure 1. X-ray structure of **3**.

The computations described above indicated that the cis-fused decalone **4**, the computer model for **48**, should be sufficiently strained to have access to twist boat conformations. The availability of **48** provided the opportunity to investigate this experimentally. Remarkably, the ^1H NMR coupling constants for the B ring of **48** measured in $CDCl_3$ are strongly supportive of a twist boat conformation. Specifically, the following proton–proton vicinal coupling constants were assigned:

$$J_{5,6} = 12 \text{ Hz}, J_{6,7\alpha} = 12 \text{ Hz}, J_{6,7\beta} = 3 \text{ Hz}, J_{9\alpha,10} = 4 \text{ Hz}, J_{9\beta,10} = 13 \text{ Hz}, J_{5,10} = 11 \text{ Hz}$$

These data suggest that the molecular mechanics prediction rests on a sound structural basis.

The synthesis of (±)-**3** recorded herein suggests that the cis-fused decalin approach to betaenones and stemphyloxin I is fundamentally sound and provides a unified solution to most of the stereochemical issues posed by these molecules. To apply this synthetic sequence to the synthesis of the parent compounds, it would be necessary to surmount two remaining synthetic obstacles. The reactivity of the acetylene moiety which permits the Claisen rearrangement to proceed with the required stereochemical outcome (i.e. compounds **26–32**) is possibly incompatible with a few of the specific oxidation and reduction reagents selected here, and some modification, either of the acetylene or the reagents, would be required. Furthermore, a sequence which converts an acetylenic substituent to the required β-hydroxy ketone of betaenone B or the β-keto aldehyde of betaenone A and stemphyloxin I would be required. The latter obstacles seem not insurmountable.

Experimental Section[21]

(4a*R,8a*S**)-5,8-Dihydro-2-methoxy-1,4(4a*H*,8a*H*)-naphthalenedione.** A 3-L stainless steel, high-pressure vessel was charged with 600 g (4.34 mol) of 2-methoxy-1,4-benzoquinone, 12 g (6.08 mol) of 2-methoxy-1,4-hydroquinone, and 1.2 L of benzene. The vessel was sealed, and the lower half cooled to −78 °C. The inlet valve was opened, and a total of 413 mL (257 g, 4.77 mol) of 1,3-butadiene was distilled into the vessel, after which the inlet valve was closed. The vessel was heated to 95 °C for 1.7 h and then cooled to 25 °C. The excess 1,3-butadiene was vented, and the vessel was opened. The brown slurry was removed from the vessel, collected on a glass frit, and washed with ether to yield 555 g (67%) of **6** as a brown solid: ^1H NMR (80 MHz, $CDCl_3$) δ 2.3 [4 H, m, H(5, 5, 8, 8)], 3.2 [2 H, m, H(4a, 8a)], 3.75 (3 H, s, OMe), 5.65 [2 H, m, H(6,7)], 5.9 [1 H, s, H(2)]; IR (neat)

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(21) General procedures are described in detail elsewhere: Shea, R. G.; et al. *J. Org. Chem.* **1986**, *51*, 5243. The purity of all compounds for which yields and spectroscopic data are reported exceeds 95% as judged by ^1H NMR (300 or 500 MHz) and analytical thin-layer chromatography.

3040, 2960, 1735 (C=O), 1680 (C=O), 1610, 1220, 1100 cm^{-1}; LRMS (EI), *m/e* 192 (M^+), 177.

(4*R,4a*R**,8a*S**)-4-Hydroxy-3-methoxy-4,4a,5,8-tetrahydro-1(8a*H*)-naphthalenone (7).** To a solution of 5 g (26 mmol) of **6** in 14 mL of ethanol at 25 °C was added 5.9 mL (5.4 g, 52 mmol) of trimethyl borate, and the mixture was cooled to 0 °C. Sodium borohydride, 0.25 g (6.5 mmol), was then added in one portion. After 1 h, 7 mL of saturated aqueous sodium chloride was added, and the reaction mixture was extracted with two 25-mL portions of ethyl acetate. The combined extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude brown solid was dissolved in acetone and concentrated in vacuo to yield 3 g (60%) of **7** as a light brown solid: ^1H NMR (80 MHz, $CDCl_3$) δ 1.9 [4 H, m, H(5, 5, 8, 8)], 2.4 [2 H, m, H(4a, 8a)], 3.5 [3 H, s, OMe], 4.6 [1 H, m, H(4)], 5.1 [1 H, br s, H(2)], 5.4 [2 H, br s, H(6, 7)]; IR (neat) 3600 (OH), 1670 (C=O), 1620 (C=C), 1210 cm^{-1}; LRMS (EI), *m/e* 194 (M^+), 163 ($M^+ - CH_3O$), 140 ($M^+ - C_4H_6$).

(4*R,4a*R**,6*S**,7*S**,8a*S**)-7-Bromo-4,6-epoxy-4,4a,5,6,7,8-hexahydro-3-methoxy-1(8a*H*)-naphthalenone (8).** To 100 mL of freshly distilled tetrahydrofuran under argon was added 20 g (0.10 mol) of **7**. *N*-Bromosuccinimide, 20 g (0.11 mol), was added in one portion at 25 °C and the solution was stirred vigorously. After 1 h the reaction mixture was added to 100 mL of water. The organic layer was separated, and the aqueous layer was extracted with 200 mL of ether. The combined extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to afford **8** as an amorphous solid, which was used without purification in the next step. [*Caution*: Do not exceed 30 °C at any time during isolation of this product. Temperatures above 25 °C and exposure to air led to accelerated decomposition]: ^1H NMR (300 MHz, $CDCl_3$) δ 1.3 [1 H, m, H(8)], 1.95 [1 H, m, H(8)], 2.1 [1 H, m, H(5)], 2.15 [1 H, d, *J* = 12 Hz, H(5)], 2.35 [1 H, m, H(4a)], 2.6 [1 H, m H(8a)], 3.0 [3 H, s, OMe], 3.9 [2 H, m, H(6,7)], 4.25 [1 H, m, H(4)], 5.1 [1 H, s, H(2)]; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 30.93, 33.15, 38.37, 42.37, 48.88, 55.64, 76.36, 79.99, 100.48, 170.57, 199.76; LRMS (EI), *m/e* 274/272 (M^+), 243 ($M^+ - CH_3O$), 193 (M^+ - Br).

(1*R,4a*S**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4a,5,6,7,8,8a-hexahydro-4-methyl-2(1*H*)-naphthalenone (9).** To a solution of **8** (27.5 g, 0.1 mol) in 200 mL of tetrahydrofuran at 0 °C was added 120 mL [(0.12 mol) 1 M in diethyl ether] of methyllithium. The reaction mixture was stirred an additional 0.5 h and then added to 175 mL of pH 7 aqueous phosphate buffer. The reaction mixture was extracted with four 12-mL portions of ether. The extracts were combined, dried ($MgSO_4$), filtered, and concentrated to 200 mL. A total of 200 mL of methylene chloride was added, followed by 1.9 g (0.01 mol) of *p*-toluenesulfonic acid monohydrate. The mixture was stirred 0.5 h at 25 °C and then concentrated to 200 mL. Ether (250 mL) was added, and the solution was washed with 50 mL of 2 N aqueous sodium hydroxide and then 50 mL of saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to yield 16 g (62%, three steps) of **9** as a light brown solid: ^1H NMR (300 MHz, $CDCl_3$) δ 2.0 [1 H, m, H(8a)], 2.1 [3 H, s, CH_3(4)], 2.2 [2 H, m, H(5,5)], 2.6 [1 H, d, *J* = 11 Hz, H(8)], 2.75 [1 H, m, H(4a)], 2.85 [1 H, m, H(8a)], 4.0 [1 H, d, *J* = 4 Hz, H(1)], 4.15 [1 H, t, *J* = 8 Hz, H(6)], 4.7 [1 H, d, *J* = 7 Hz, H(7)], 6.0 [1 H, s, H(3)]; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 23.21, 30.36, 34.07, 36.56, 38.05, 49.81, 78.07, 80.92, 125.02, 164.33, 192.78; IR (neat) 2960, 1690 (C=O), 1040 cm^{-1}; LRMS (EI), *m/e* 258/256 (M^+), 177 (M^+ - Br).

(1*R,4*S**,4a*S**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-methyl-3,4,4a,5,6,7,8,8a-octahydro-4-phenyl-2(1*H*)-naphthalenone (13).** To a white slurry of 0.963 g (5.07 mmol) of copper iodide in 10 mL of ether was added 5.5 mL (9.4 mmol, 1.7 M in cyclohexane/diethyl ether, 70:30) of phenyllithium at 0 °C. After the mixture was stirred for 10 min and cooled to −35 °C, the enone **9**, 1.0 g (3.9 mmol), in 11 mL of ether and 4 mL of tetrahydrofuran was added via cannula, and the resulting mixture was stirred an additional 0.5 h at −40 °C and then quenched with 33 mL of saturated aqueous ammonium chloride. The reaction mixture was extracted with 20 mL of ether and then 20 mL of ethyl acetate. The extracts were combined, dried ($MgSO_4$), and concentrated in vacuo. The crude product was taken up in ethyl acetate, and the solid was removed by filtration through a pad of silica gel on Celite. The filtrate was concentrated in vacuo to yield 1.28 g (98%) of **13** as a crude yellow oil, which was used in the next step without purification: ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 [3 H, s, CH_3], 1.85 [1 H, br s, H(8)], 2.25 [1 H, br s, H(4a)], 2.3 [1 H, m, H(5)], 2.4 [1 H, m, H(5)], 2.45 [1 H, d, *J* = 13 Hz, H(8)], 2.5 [1 H, m, H(8a)], 2.75 [1 H, d, *J* = 16 Hz, H(3)], 3.1 [1 H, d, *J* = 16 Hz, H(3)], 3.75 (1 H, d, *J* = 4 Hz, H(1)], 4.0 [1 H, br s, H(6)], 4.3 [1 H, t, *J* = 4 Hz, H(7)], 7.25 (3 H, m, C_6H_5), 7.35 (2 H, m, C_6H_5); IR (neat) 2960, 1720 (C=O), 1600, 1500, 1450, 1030 cm^{-1}; LRMS (EI), *m/e* 336/334 (M^+), 321/319 ($M^+ - CH_3$), 255 (M^+ - Br), 237 ($M^+ - H_2BrO$).

(1*R,4*R**,4a*S**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-methyl-1,4,4a,5,6,7,8,8a-octahydro-2-(1-oxahex-3(*E*)-enyl)-4-phenylnaphthalene (17).** A solution of 2.38 g (7.1 mmol) of **13**, *trans*-2-penten-1-ol, 6.1 g (0.71 mmol), and 0.134 g (0.71 mmol) of *p*-toluenesulfonic acid monohydrate in 35 mL of benzene was heated under reflux with continuous removal of the water by the use of Dean–Stark trap. After 4 h the solution was cooled to 25 °C and added to 75 mL of ether. The organic layer was washed with two 20-mL portions of saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and concentrated in vacuo. The crude product was chromatographed on 30 g of silica gel (10% ethyl acetate/hexanes) to yield 1.45 g (50%) of **17** as a light yellow oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.0 [3 H, t, *J* = 8 Hz, CH_3(6′)], 1.3 [3 H, s, CH_3(4)], 1.8 [1 H, m, H(8a)], 2.0 [1 H, m, H(4a)], 2.1 [3 H, m, H(5, 5′, 5′)], 2.35 [1 H, m, H(8a)], 2.45 [1 H, d, *J* = 12 Hz, H(8)], 2.55 [1 H, ddd, *J* = 16, 9, and 5 Hz, H(5)], 4.2 [1 H, d, *J* = 5 Hz, H(1)], 4.4 [4 H, m, H(6, 7, 2′, 2′)], 4.6 [1 H, s, H(3)], 5.7 [1 H, dt, *J* = 16 and 7 Hz, H(4′)], 5.9 [1 H, dt, *J* = 16 and 7 Hz, H(3′)], 7.5 [5 H, m, C_6H_5]; IR (neat) 2985, 1650, 1200, 1040, 1030, 970 cm^{-1}; LRMS (EI), *m/e* 404/402 (M^+), 336/334 ($M^+ - C_5H_8$), 255 (M^+ - Br).

(1*R,4*R**,4a*S**,7*S**,8a*R**)-1,7-Epoxy-1,4,4a,7,8,8a-hexahydro-4-methyl-2-(1-oxahex-3(*E*)-enyl)-4-phenylnaphthalene (18).** A flask containing a solution of **17**, 1.45 g (3.6 mmol), in 3.2 mL (3.28 g, 22 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene was evacuated, flushed with argon three times, and then heated to 115 °C for 3 h. The reaction mixture was cooled to 25 °C and added to 35 mL of 3% aqueous hydrochloric acid. The acidic mixture was extracted with three 10-mL portions of methylene chloride. The extracts were combined, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude product was chromatographed on 10 g of silica gel (10% ethyl acetate/hexanes) to yield 997 mg (86%) of **18** as a light brown oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.0 [3 H, t, *J* = 8 Hz, CH_3(6′)], 1.5 [3 H, s, CH_3(4)], 1.8 [1 H, d, *J* = 10 Hz, H(8)], 1.95 [1 H, dd, *J* = 5 Hz, H(8)], 2.1 [2 H, m, H(5′, 5′)], 2.3 [1 H, br s, H(10)], 2.85 [1 H, s, H(4a)], 4.2 [1 H, d, *J* = 5 Hz, H(1)], 4.3 [1 H, t, *J* = 5 Hz, H(7)], 4.4 [2 H, m, H(2′, 2′)], 4.5 [1 H, s, H(3)], 5.7 [1 H, m, H(6)], 5.8 [2 H, m, H(3′, 4′)], 6.1 [1 H, br s, H(5)], 7.35 [5 H, m, C_6H_5]; ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.47, 25.53, 28.48, 36.28, 36.78, 44.37, 49.27, 68.11, 71.20, 74.79, 101.95, 115.84, 119.74, 132.55, 136.18, 154.92; IR ($CDCl_3$) 2990, 1660, 1210, 1050 cm^{-1}; LRMS (EI), *m/e* 322 (M^+), 294 ($M^+ - C_2H_4$), 254 ($M^+ - C_5H_8$).

(1*R,1′*S**,3*S**,4*R**,4a*S**,7*S**,8a*R**)-1,7-Epoxy-3-(1′-ethylprop-2′-enyl)-3,4,4a,7,8,8a-hexahydro-4-methyl-4-phenyl-2(1*H*)-naphthalenone (19).** To a flask (previously silylated with 10% trimethylsilyl chloride in ether) were added 50 mg (0.15 mmol) of **18**, 0.1 mL (0.76 mmol) of *N*,*N*-dimethylaniline, and 2.5 mL of dodecane. The flask was evacuated and flushed with argon three times then heated under reflux for 4 h. The reaction mixture was cooled to 25 °C, and crystals that formed upon cooling were collected on a glass frit. The crystals were rinsed with hexane then dried in vacuo. The dodecane and hexane rinses were concentrated in vacuo, and the residue was chromatographed on 0.5 g of silica gel (25% ethyl acetate/hexanes). The crystals and product obtained from chromatography afforded a combined yield of 43 mg (86%) of **19**. A sample was recrystallized from diethyl ether/methylene chloride for use in single-crystal X-ray analysis: ^1H NMR (500 MHz, C_6D_6) δ 0.65 [3 H, t, *J* = 7 Hz, CH_3(2″)], 0.75 [1 H, m, H(1″)], 1.0 [1 H, m, H(1″)], 1.25 [1 H, d, *J* = 10 Hz, H(8)], 1.3 [3 H, s, CH_3(4)], 1.55 [1 H, m, H(1′)], 2.2 [1 H, br s, H(4a)], 2.45 [1 H, dd, *J* = 4 Hz, H(8)], 3.0 [1 H, s, H(8a)], 3.1 [1 H, d, *J* = 10 Hz, H(3)], 4.1 [1 H, dd, *J* = 6 Hz, H(7)], 4.2 [1 H, d, *J* = 6 Hz, H(1)], 5.0 [2 H, dd, *J* = 16 and 10 Hz, H(3′, 3′)], 5.4 [1 H, d, *J* = 10 Hz, H(6)], 5.75 [1 H, br s, H(5)], 5.8 [1 H, ddd, *J* = 16, 10 and 8 Hz, H(2′)],

7.2 (5 H, m, C_6H_5); IR (neat) 2985, 1740 (C=O) cm^{-1}; LRMS (EI), *m/e* 322 (M^+), 253 ($M^+ - C_5H_9$), 244 ($M^+ - C_6H_6$), 175 ($M^+ - C_{11}H_{15}$).

(1*R,1′*S**,4*S**,4a*S**,7*S**,8a*R**)-1,7-Epoxy-3-(1′-ethylprop-3′-enyl)-1,4,4a,7,8,8a-hexahydro-2-hydroxy-4-methyl-4-phenylnaphthalene (21).** Argon was bubbled through a solution of **19** (40 mg, 0.12 mmol) in 2 mL of 1:1 methanol/tetrahydrofuran. Sodium methoxide, 64.8 mg (1.2 mmol), was added, and the reaction mixture was stirred vigorously under an atmosphere of argon for 1 h. Water was added, and the reaction mixture was extracted with dichloromethane under an atmosphere of argon. The extracts were combined, dried ($MgSO_4$), filtered, and concentrated in vacuo to yield 39 mg (99%) of enol **21** as a white solid. A sample was recrystallized from ether/methylene chloride for single-crystal X-ray analysis: ^1H NMR (500 MHz, $CDCl_3$) δ 0.85 [3 H, t, *J* = 5 Hz, $CH_3(2'')$], 1.65 [3 H, s, $CH_3(4)$], 1.65 [1 H, m, H(1″)], 1.8 [1 H, d, *J* = 10 Hz, H(8)], 1.95 [1 H, m, H(8)], 2.05 [1 H, m, H(1″)], 2.3 [1 H, br s, H(4a)], 2.45 [1 H, br s, H(1′)], 2.55 [1 H, s, H(8a)], 4.3 [2 H, m, H(1,7)], 4.7 [1 H, s, OH], 5.0 [2 H, dd, *J* = 16 and 10 Hz, H(3′, 3′)], 5.8 [1 H, d, *J* = 10 Hz, H(5)], 6.1 [2 H, m, H(6, 2′)], 7.35 [5 H, s, C_6H_5); IR(CH_2Cl_2) 3580 (OH), 2980, 1020 cm^{-1}; LRMS (EI), *m/e* 322 (M^+), 307 ($M^+ - CH_3$), 293 ($M^+ - C_2H_5$), 275 ($M^+ - C_2H_7O$), 244 ($M^+ - C_6H_6$).

(1*R,4*R**,4a*R**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-methyl-3,4,4a,5,6,7,8,8a-octahydro-2(1*H*)-naphthalenone (22).** A solution of the enone **9** (32.7 g, 127 mmol) in 400 mL of ethanol at 25 °C was flushed with argon; 1.4 g of 5% platinum on carbon was added. The flask was flushed with hydrogen, a balloon with hydrogen was attached, and the black slurry was vigorously stirred with an overhead stirrer. After completion of the reaction, as determined by TLC analysis, the slurry was filtered through a pad of Celite. The Celite was rinsed with ether, and the filtrate was concentrated in vacuo to yield 26.5 g of the ketone **22** as a white solid, which was used without purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (25% ethyl acetate/hexanes): ^1H NMR (500 MHz, $CDCl_3$) δ 1.0 (3 H, d, *J* = 5 Hz, CH_3), 2.6 [1 H, dd, *J* = 12.5, 5 Hz, H(8)], 2.68 [1 H, dd, *J* = 5 and 2.5 Hz, H(8a)], 2.85 [1 H, d, *J* = 8.75 Hz, H(3)], 4.0 [1 H, s, H(1)], 4.25 [1 H, d, *J* = 3.75 Hz, H(6)], 4.5 [1 H, m, H(7)]; IR (CH_2Cl_2) 2960, 1740 (C=O), 1020 cm^{-1}; LRMS (EI), *m/e* 260/258 (M^+), 232/230, 179 (M^+ - Br).

(1*R,4*S**,4a*R**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-methyl-1,4,4a,5,6,7,8,8a-octahydro-2-(1-oxapent-3(*E*)-enyl)-naphthalene (23).** A solution of 20 g of the crude product **22** from the previous step, crotyl alcohol (16.6 g, 0.231 mol), and *p*-toluenesulfonic acid monohydrate (0.66 g, 3.5 mmol) in 300 mL of benzene was heated under reflux, and the water produced was removed with a Dean–Stark trap. After 6 h, the reaction mixture was cooled to 25 °C and washed sequentially with 60 mL of water and 60 mL of saturated aqueous sodium chloride. The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to yield 24 g of the enol ether **23** as a yellow oil, which was used without purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (25% ethyl acetate/hexanes): ^1H NMR (300 MHz, $CDCl_3$) δ 1.0 [3 H, d, *J* = 7 Hz, $CH_3(4)$], 1.75 [3 H, d, *J* = 7 Hz, $CH_3(5')$], 1.85 [1 H, dd, *J* = 14, 14 Hz, H(8)], 2.0 [1 H, m, H(5)], 2.15 [1 H, m, H(4)], 2.25 [1 H, m, H(8a)], 2.4 [1 H, m, H(5)], 2.55 [1 H, m, H(4a)], 2.65 [1 H, d, *J* = 14 Hz, H(8)], 4.2 [3 H, m, H(2′, 2′)], 4.3 [1 H, t, *J* = 6 Hz, H(6)], 4.45 [1 H, s, H(3)], 4.5 [1 H, d, *J* = 4 Hz, H(7)], 5.8 (2 H, m, H(3′, 4′)]; IR (neat) 2960, 1650 (C=C), 1450, 1200 cm^{-1}; LRMS (EI), *m/e* 314/312 (M^+), 260/258 ($M^+ - C_4H_6$), 233 (M^+ - Br).

(1*R,1′*R**,3*R**,4*S**,4a*R**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-methyl-3-(1′-methylprop-2′-enyl)-3,4,4a,5,6,7,8,8a-octahydro-2(1*H*)-naphthalenone (24).** Argon was bubbled through a solution of the entire product **23** of the previous step in 127 mL of *o*-xylene. The solution was heated to 130 °C for 5 h then cooled to 24 °C. After concentration in vacuo, the crude product was column chromatographed on silica gel (25% ethyl acetate/hexanes) to yield 12.4 g (64%, three steps, based on recovered enol ether) of the ketone **24** as a white solid. The enol ether (5 g, 20%) was recovered. **24**: ^1H NMR (500 MHz, $CDCl_3$) δ 0.95 [3 H, d, *J* = 9 Hz, $CH_3(4)$], 1.1 [3 H, d, *J* = 9 Hz, $CH_3(1'')$], 1.7 [1 H, m, H(5)], 1.95–2.05 (3 H, m), 2.1 [1 H, m, H(4)], 2.2 [1 H, m, H(4a)], 2.4 [1 H, m, H(1′)], 2.65 [1 H, br s, H(8a)], 2.65 [1 H, d, *J* = 10 Hz, H(8)], 3.95 [1 H, d, *J* = 5 Hz, H(1)], 4.2 [1 H, br s, H(6)], 4.4 [1 H, t, *J* = 5 Hz, H(7)], 5.05 [2 H, dd, *J* = 15, 10 Hz, H(3′, 3′)], 5.6 [1 H, ddd, *J* = 15, 10, 10 Hz, H(2′)]; IR (neat) 2970, 1710 (C=O), 1450, 1210 cm^{-1}; LRMS (EI), *m/e* 314/312 (M^+), 260/258, 233 (M^+ - Br).

(1*R,4*S**,4a*S**,6*S**,7*S*,8a*R**)-6-Bromo-1,7-epoxy-4-methyl-3,4,4a,5,6,7,8,8a-octahydro-4-[2-(tributylstannyl)-1-(*E*)-ethenyl]-2(1*H*)-naphthalenone (25).** To a solution of 3.2 g (5.28 mmol) of *trans*-1,2-bis(tri-*n*-butylstannyl)ethylene in 17 mL of tetrahydrofuran at −78 °C was added 3.12 mL (5.61 mmol, 1.8 M in hexanes) of *n*-butyllithium. The light yellow solution was warmed to −40 °C over 30 min and then added via cannula to a suspension of 0.86 g (5.43 mmol) of 1-heptynyl copper and 3.77 g (14.4 mmol) of triphenylphosphine in 11 mL of tetrahydrofuran at −40 °C over 30 min. The solution was cooled to −78 °C and stirred for an additional 0.75 h. The enone **9**, 0.727 g (2.82 mmol), in 5 mL of tetrahydrofuran was added over 12 min via cannula to the mixed cuprate. The reaction mixture was warmed to −40 °C over 0.25 h and then reacted with 25 mL of saturated aqueous ammonium sulfate. The reaction mixture was extracted with two 25-mL portions of ether. The extracts were combined, dried ($MgSO_4$), filtered through a pad of Celite, and concentrated in vacuo. The crude product was chromatographed on 60 g of silica gel [(1) hexanes; (2) 5% ethyl acetate/hexanes] to remove the triphenylphosphine. The crude **25** was used in the next step without purification: ^1H NMR (500 MHz, $CDCl_3$) δ 0.9 (15 H, m, $SnBu_3$), 1.0 [3 H, s, $CH_3(4)$], 1.5 (6 H, m), 1.95 [1 H, m, H(8)], 2.12 [2 H, m, H(5, 5)], 2.15 [1 H, m, H(4a)], 2.25 [1 H, d, *J* = 16 Hz, H(3)], 2.6 [1 H, d, *J* = 16 Hz, H(8)], 2.65 [1 H, d, *J* = 16 Hz, H(3)], 2.75 [1 H, s, H(8a)], 4.0 [1 H, d, *J* = 4 Hz, H(1)], 4.3 [1 H, br s, H(6)], 4.45 [1 H, t, *J* = 4 Hz, H(7)], 5.95 [2 H, d, *J* = 6 Hz, HC=CHSn]; IR (neat) 2980, 1720 (C=O), 1590 (C=O), 1460 cm^{-1}; LRMS (EI), *m/e* 446 ($M^+ - C_4H_9Br$), 313 ($C_{14}H_{29}Sn$), 259 ($M^+ - C_{14}H_{29}Sn$), 177 ($M^+ - C_{14}H_{30}BrSn$).

(1*R,4*S**,4a*S**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-ethynyl-3,4,4a,5,6,7,8,8a-octahydro-2(1*H*)-naphthalenone (26).** A solution of the entire crude product (**25**) of the previous step in 25 mL of acetonitrile was treated with 5 g (11.28 mmol) of lead tetraacetate in one portion and stirred vigorously for 0.25 h; 20 mL of pentane was added, and the solution was filtered through a pad of alumina. The pad of alumina was rinsed with additional pentane and then methylene chloride. The organic rinses were combined, concentrated in vacuo, and chromatographed on 6 g of silica gel (5% ethyl acetate/hexanes) to yield 757.5 mg (94%, two steps) of **26** as a light yellow oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.3 [3 H, s, $CH_3(4)$], 2.0 [4 H, m, H(4a, 5, 5, 8)], 2.2 [1 H, s, C≡CH], 2.5 [1 H, d, *J* = 12 Hz, H(3)], 2.65 [1 H, d, *J* = 15 Hz, H(8)], 2.7 [1 H, d, *J* = 12 Hz, H(3)], 3.3 [1 H, br s, H(8a)], 4.0 [1 H, d, *J* = 4 Hz, H(1)], 4.3 [1 H, br s, H(6)], 4.5 [1 H, dd, *J* = 4 and 4 Hz, H(7)]; IR (neat) 3300 (≡CH), 2980, 1720 (C=O), 1570, 1410 cm^{-1}; LRMS (EI), *m/e* 284/282 (M^+), 269/267 ($M^+ - CH_3$), 259/257 ($M^+ - C_2H$), 203 (M^+ - Br).

(1*R,4*R**,4a*S**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-ethynyl-4-methyl-1,4,4a,5,6,7,8,8a-octahydro-2-(1-oxapent-3-(*E*)-enyl)naphthalene (27).** A solution of **26**, 62 mg (0.22 mmol), crotyl alcohol, 172.8 mg (2.4 mmol), and 4.5 mg (0.024 mmol) of *p*-toluenesulfonic acid monohydrate in 1.2 mL of benzene was heated under reflux with continuous removal of the water by the use of a Dean–Stark trap. After 4 h the reaction mixture was cooled to 25 °C and concentrated in vacuo. The crude product was purified by column chromatography on 3 g of silica gel (10% ethyl acetate/hexanes) to yield 37 mg (50%) of **27** as a yellow (≡CH), ^1H NMR (500 MHz, $CDCl_3$) δ 1.25 [3 H, s, $CH_3(4)$], 1.7 [3 H, d, *J* = 6 Hz, $CH_3(5')$], 1.9 [1 H, dd, *J* = 16 and 6 Hz, H(5)], 2.0 [1 H, m, H(5)], 2.2 [2 H, m, H(4a, 8)], 2.65 [1 H, d, *J* = 15 Hz, H(8)], 2.95 [1 H, m, H(8a)], 4.2 [3 H, m, H(1, 2′, 2′)], 4.3 [1 H, br s, H(6)], 4.4 [1 H, dd, *J* = 4 and 4 Hz, H(7)], 4.45 [1 H, s, H(3)], 5.64 [1 H, m, H(3′)], 5.75 [1 H, m, H(2′)]; IR (neat) 3300 (≡CH), 2980, 2250, 2100, 1650 (C=C), 1200, 1050 cm^{-1}; LRMS (EI), *m/e* 338/336 (M^+), 284/282 ($M^+ - C_4H_6$), 257 (M^+ - Br), 203 ($M^+ - C_4H_6Br$).

(1*R,1′*R**,3*R**,4*R**,4a*S**,6*S**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-4-ethynyl-3-(1′-methylprop-2′-enyl)-4-methyl-3,4,4a,5,6,7,8,8a-octahydro-2(1*H*)-naphthalenone (28).** A flask containing a solution of 200 mg (0.59 mmol) of **27** and 357 mg

(2.95 mmol) of *N,N*-dimethylaniline in 9.4 mL of dodecane was evacuated, flushed with argon three times, and heated to 160 °C for 6 h. The reaction mixture was then cooled to 25 °C, and the crystals that formed upon cooling were collected on a glass frit and then rinsed with hexane. The crystals were dried in vacuo to yield 124 mg (62%) of **28**. A sample was recrystallized from hexanes for single-crystal X-ray analysis: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 [3 H, d, J = 6 Hz, CH_3(1″)], 1.3 [3 H, s, CH_3(4)], 2.0 [3 H, m, H(5, 5, 8)], 2.3 [1 H, d, J = 6 Hz, H(3)], 2.35 [1 H, m, H(4a)], 2.35 [1 H, s, C≡CH], 2.6 [1 H, d, J = 10 Hz, H(8)], 2.8 [1 H, m, H(1′)], 3.3 [1 H, br s, H(8a)], 4.0 [1 H, d, J = 4 Hz, H(1)], 4.25 [1 H, br s, H(6)], 4.45 [1 H, br s, H(7)], 4.95 [1 H, d, J = 12 Hz, H(3′)], 5.05 [1 H, d, J = 16 Hz, H(3′)], 6.0 [1 H, ddd, J = 16, 12, and 4 Hz, H(2′)]; IR (neat) 3250 (C≡CH), 2980, 1700 (C=O) cm^{-1}; LRMS (EI), m/e 338/336 (M^+), 323/321 ($M^+ - CH_3$), 283/281 ($M^+ - C_4H_7$).

(1*R,1′*R**,3*R**,4*S**,4a*R**,6*S**,7*S**,8a*R**)-6-Bromodecahydro-1,7-epoxy-2-hydroxy-4-methyl-3-(1′-methylprop-2′-enyl)naphthalene.** To a well-stirred solution of the ketone **24** (12.4 g, 39.5 mmol) in 165 mL of ethanol at 5 °C was added 1.5 g (39.5 mmol) of sodium borohydride. After 0.75 h, 110 mL of water was added, and the mixture was extracted with two 200-mL portions of ether. The ether extracts were combined and concentrated in vacuo to yield 13 g of the title alcohol as a yellow oil. The crude product was used without purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (25% ethyl acetate/hexanes): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 [3 H, d, J = 8 Hz, CH_3(4)], 1.2 [3 H, d, J = 8 Hz, CH_3(1″)], 1.5 (1 H, t, J = 12 Hz), 1.55 (1 H, m), 1.75 (1 H, m), 1.95 (1 H, m), 2.0 (1 H, m), 2.1 (1 H, m), 2.15 (1 H, br s), 2.3 (1 H, m), 2.4 [1 H, d, J = 12 Hz, H(8)], 2.85 [1 H, br s, H(1′)], 3.6 [1 H, br s, H(2)], 4.1 [1 H, dd, J = 4 and 4 Hz, H(1)], 4.25 [1 H, m, H(6)], 4.5 [1 H, m, H(7)], 5.05 [1 H, d, J = 4 Hz, H(3′)], 5.1 [1 H, d, J = 12 Hz, H(3′)], 6.0 [1 H, ddd, J = 12, 4, 4 Hz, H(2′)]; IR (neat) 3440, 2960, 1450, 1000 cm^{-1}; LRMS (EI), m/e 316/314 (M^+), 301/299 ($M^+ - CH_3$), 298/296 ($M^+ - H_2O$), 260/258, 243/241, 217 ($M^+ - H_2BrO$).

(1*R,1′*R**,3*R**,4*S**,4a*R**,7*S**,8a*R**)-6-Bromo-1,7-epoxy-2-hydroxy-4-methyl-3-(1′-methylprop-2′-enyl)-1,2,3,4,4a,7,8,8a-octahydronaphthalene.** A solution of the entire crude product of the previous step in 25 mL of 1,8-diazabicyclo[5.4.0]undec-7-ene (24.6 g, 162 mmol) was evacuated and flushed with argon three times then heated to 100 °C. After 4 h, the solution was cooled to 25 °C and taken up in 300 mL of methylene chloride. The organic layer was washed with two 100-mL portions of 3% aqueous hydrochloric acid, dried ($MgSO_4$), filtered, and concentrated in vacuo to afford 9 g of the crude title alkene as an oil, which was used without purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (25% ethyl acetate/hexanes): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.1 [3 H, d, J = 7.5 Hz, CH_3(4)], 1.2 [3 H, d, J = 7.5 Hz, CH_3(1″)], 1.9 [1 H, d, J = 11 Hz, H(8)], 2.1 [1 H, m, H(8)], 2.4 [1 H, m, H(4a)], 2.5 [1 H, br s, H(8a)], 2.9 [1 H, m, H(1′)], 3.55 [1 H, m, H(2)], 4.25 [1 H, br s, H(1)], 4.4 [1 H, dd, J = 6 and 6 Hz, H(7)], 5.05 [2 H, m, H(3′, 3′)], 5.7 [1 H, m, H(6)], 6.0 [1 H, ddd, J = 16, 11, 7 Hz, H(2′)], 6.3 [1 H, m, H(5)]; LRMS (EI), m/e 234 (M^+), 219 ($M^+ - CH_3$), 179 ($M^+ - C_4H_7$); IR (neat) 3430, 2960, 1630, 1450 cm^{-1}.

(1*R,1′*R**,3*R**,4*S**,4a*R**,7*S**,8a*R**)-1,7-Epoxy-3,4,4a,7,8,8a-hexahydro-4-methyl-3-(1′-methylprop-2′-enyl)-2(1*H*)-naphthalenone (33).** To a solution of the entire crude product of the previous step in 300 mL of methylene chloride at 25 °C was added pyridinium chlorochromate (30 g, 130 mmol), and the mixture was stirred vigorously. After 1.5 h, 200 mL of ether was added, and the mixture was filtered through a pad of silica gel (5 g). The flask was rinsed with an additional 500 mL of ether. The ether rise was also filtered through a pad of silica gel. The ether rinses were combined and concentrated in vacuo. Chromatography on 300 g of silica gel (25% ethyl acetate/hexanes) yielded 2.5 g (28%, three steps) of the keto diene **33** as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 [6 H, d, CH_3 H(1″, 4)], 2.0 (3 H, m), 2.3 [1 H, dd, J = 7, 5 Hz, H(8)], 2.5 [1 H, m, H(1′)], 2.6 [1 H, m, H(4a)], 2.8 [1 H, m, H(8a)], 4.0 [1 H, d, J = 4 Hz, H(1)], 4.4 [1 H, dd, J = 4 and 4 Hz, H(7)], 4.97 [1 H, d, J = 7 Hz, H(3′)], 5.05 [1 H, d, J = 11 Hz, H(3′)], 5.75 [1 H, d, J = 7 Hz, H(6)], 5.85 [1 H, ddd, J = 11, 7, 7 Hz, H(2′)], 6.1 [1 H, m, H(5)]; IR (neat) 3010, 2960, 1710 (C=O), 1450, 1380 cm^{-1}; LRMS (EI), m/e 232 (M^+), 217 ($M^+ - CH_3$), 177 ($M^+ - C_4H_7$).

(1′*R,3*R**,4*S**,4a*R**,7*S**,8a*S**)-3,4,4a,7,8,8a-Hexahydro-7-hydroxy-4-methyl-3-(1′-methylprop-2′-enyl)-2(1*H*)-naphthalenone (35).** To a slurry of samarium powder (2.6 g, 17.2 mmol) in 18 mL of tetrahydrofuran at 25 °C was added diiodoethane (4.34 g, 17.21 mmol) in 18 mL of tetrahydrofuran via cannula over 0.25 h. The transfer was completed with 5 mL of tetrahydrofuran. A dark blue-green color developed. After being stirred at 25 °C for 1 h the solution was cooled to −78 °C and the keto ether **33** (1.7 g, 7.3 mmol) in 24 mL of tetrahydrofuran was added over 10 min via cannula. The transfer was completed with 5 mL of tetrahydrofuran. The reaction mixture was stirred for 0.5 h, followed by addition of 30 mL of saturated, aqueous potassium carbonate. The reaction mixture was warmed to 25 °C, the organic layer was separated, and the aqueous layer was extracted with four 100-mL portions of ether. The organic extracts were combined, washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to yield 1.71 g of crude ketol **35** as a yellow oil, which was used without purification in the following experiment. A sample for spectral analysis was purified by preparative thin-layer chromatography (25% ethyl acetate/hexanes): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.2 [6 H, d, J = 8 Hz, CH_3(1″, 4)], 1.6 (2 H, m), 1.75 (1 H, m), 1.95 (1 H, m), 2.05 (1 H, s), 2.3 (2 H, m), 2.55 (1 H, m), 4.3 [1 H, br s, H(7)], 4.95 [1 H, d, J = 7 Hz, H(3′)], 5.0 [1 H, d, J = 14 Hz, H(3′)], 5.9 [3 H, m, H(5, 6, 2′)]; IR (neat) 3420, 2960, 1700 (C=O) cm^{-1}; LRMS (EI), m/e 234 (M^+), 216 ($M^+ - H_2O$), 201 ($M^+ - CH_5O$), 166.

(1′*R,3*R**,4*S**,4a*R**,8a*S**)-4-Methyl-3-(1′-methylprop-2′-enyl)-3,4,4a,8a-tetrahydro-2,7(1*H*,8*H*)-naphthalenedione (36).** To a solution of the entire crude product **35** of the previous step in 31 mL of dichloromethane were added sodium acetate (0.239 g, 2.92 mmol) and pyridinium chlorochromate (3.14 g, 14.6 mmol), and the mixture was vigorously stirred for 1 h. Ether (100 mL) was added, and the ether was decanted from the black residue. The black residue was washed with three additional 100-mL portions of ether. The ether washings were combined and stirred over 4 g of silica gel for 10 min and the filtered through 8 g of silica gel. The pad of silica gel was rinsed with ether, the ether rinses were combined and concentrated in vacuo to yield 1.7 g of crude enone **36**, as an oil. The crude product was used without purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (50% ethyl acetate/hexanes): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.15 [3 H, d, J = 7 Hz, CH_3(4)], 1.3 [3 H, d, J = 7 Hz, H(1″)], 1.6 (1 H, m), 2.15 (2 H, m), 2.3 (1 H, dd), 2.45 (2 H, m), 2.7 (2 H, m), 2.9 (1 H, br s), 5.1 [2 H, dd, J = 15, 13 Hz, H(3′, 3′)], 6.1 [1 H, ddd, J = 15, 13, 13 Hz, H(2′)], 6.3 [1 H, d, J = 13 Hz, H(6)], 7.1 [1 H, d, J = 13 Hz, H(7)]; IR (neat) 3080, 2960, 1700 (C=O), 1380 cm^{-1}.

(1′*R,3*R**,4*S**,4a*S**,5*R**,8a*S**)-4,5-Dimethyl-3,4,4a,5,6,8a-hexahydro-3-(1′-methylprop-2′-enyl)-2,7(1*H*,8*H*)-naphthalenedione (37).** To a slurry of $CH_3(CH_2)_4C{\equiv}CCu$ (4.6 g, 29.3 mmol) and triphenylphosphine (16.8 g, 64.2 mmol) in 250 mL of ether at −30 °C was added 25 mL (29.3 mmol, 1.14 M in ether) of a solution of methyllithium. After 0.5 h, the entire crude product **36** of the previous step in 125 mL of ether was added via cannula over 10 min. The transfer was completed with an additional 13 mL of ether. After an additional 0.5 h at −30 °C, the reaction mixture was added to 1 L of saturated aqueous ammonium sulfate at 25 °C. The organic layer was separated and washed with an additional 500 mL of saturated aqueous ammonium sulfate. The aqueous washings were back extracted with three 500-mL portions of ether. The ether extracts were combined, dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was dissolved in absolute ethanol, and the insoluble white solid was removed by filtration through a pad of Celite. After concentration in vacuo the crude product was chromatographed on 45 g of silica gel [(1) hexanes; (2) 10% ethyl acetate/hexanes; (3) 25% ethyl acetate/hexanes] to yield 1.4 g of ketone **37** as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 [3 H, d, J = 8 Hz, CH_3(5)], 1.2 [3 H, d, J = 7 Hz, CH_3(4)], 1.3 [3 H, d, J = 8 Hz, CH_3(1″)], 2.0 (1 H, m), 2.3 (6 H, m), 2.5 (3 H, m), 2.7 (2 H, m), 5.05 [2 H, dd, J = 12, 7 Hz, H(3′, 3′)], 5.9 [1 H, ddd, J = 12, 7, 7 Hz, H(2′)]; IR (neat) 2960, 1700 (C=O), 1440, 1120

cm^{-1}; LRMS (EI), m/e 248 (M^+), 233 ($M^+ - CH_3$), 178 ($M^+ - C_5H_{10}$).

(1′*R,3*R**,4*S**,4a*S**,5*R**,7*R**,8a*S**)-7-Hydroxy-3-(1′-methylprop-2′-enyl)-3,4,4a,5,6,7,8,8a-octahydro-4,5,7-trimethyl-2(1*H*)-naphthalenone (38).** To a slurry of copper iodide (3.2 g, 16.8 mmol) in 186 mL of ether at −30 °C was added 39 mL (44.5 mmol, 1.14 M in ether) of methyllithium. After 0.25 h, the solution was cooled to −78 °C, and the entire crude product **37** of the previous step in 186 mL of ether was added via cannula over 0.33 h. The transfer was completed with an additional 12 mL of ether. After 0.5 h at −78 °C, 200 mL of saturated aqueous ammonium chloride was added. The reaction mixture was warmed to 25 °C, the ether layer was separated, and the aqueous layer was extracted with 200 mL of ether. The ether extracts were combined and washed with two 100-mL portions of saturated aqueous ammonium chloride, dried (Na_2SO_4), filtered, and concentrated in vacuo to yield after column chromatography on 40 g of silica gel (25% ethyl acetate/hexanes) 710 mg (59%, 4 steps) of the ketone **38** as a pale yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.1 [3 H, d, J = 8 Hz, $CH_3(5)$], 1.15 [3 H, d, J = 8 Hz, $CH_3(4)$], 1.19 [3 H, d, J = 8 Hz, $CH_3(1'')$], 1.2 [3 H, s, $CH_3(7)$], 1.5 (5 H, m), 2.0 (1 H, m), 2.3 (4 H, m), 2.6 (4 H, m), 3.1 [1 H, dd, J = 12, 12 Hz, H(1)], 4.9 [2 H, dd, J = 16, 8 Hz, H(3′, 3′)], 5.9 [1 H, ddd, J = 16, 10, 8 Hz, H(2′)]; IR (neat) 3400 (OH), 2960, 1700 (C=O), 1450, 1370 cm^{-1}; LRMS (EI), m/e 264 (M^+), 246 ($M^+ - H_2O$), 231 ($M^+ - CH_5O$), 191 ($M^+ - C_4H_9O$).

(1′*R,3*R**,4*S**,4a*S**,5*R**,7*R**,8a*S**)-7-Hydroxy-3-(1′-methylpropyl)-3,4,4a,5,6,7,8,8a-octahydro-4,5,7-trimethyl-2-(1*H*)-naphthalenone (39).** To a solution of ketone **38** (710 mg, 2.67 mmol) in 106 mL of absolute ethanol at 25 °C was added 40 mg of 5% palladium on carbon. The black slurry was vigorously stirred under an atmosphere of hydrogen (balloon) with use of an overhead stirrer. After 10 min the reaction mixture was filtered through a pad of Celite, which was rinsed with additional ethanol. The rinses were combined and concentrated in vacuo to yield 656 mg (92%) of ketone **39** as a white solid, which was used without purification in the following step. The crude product was sufficiently pure for spectroscopic analysis: ^1H NMR (500 MHz, $CDCl_3$) δ 0.8 [3 H, t, J = 8 Hz, $CH_3(3')$], 0.9 (3 H, d, J = 8 Hz, CH_3), 1.0 (3 H, d, J = 6 Hz, CH_3), 1.1 (3 H, d, J = 8 Hz, CH_3), 1.2 [3 H, s, $CH_3(7)$], 3.0 [1 H, dd, J = 12, 12 Hz, H(1)]; IR (neat) 3460 (OH), 2960, 1700 (C=O), 1460, 1360 cm^{-1}; LRMS (EI), m/e 266 (M^+), 248 ($M^+ - H_2O$), 233 ($M^+ - CH_5O$).

(1′*R,3*R**,4*S**,4a*R**,5*R**,7*R**,8a*R**)-2,7-Bis[(*tert*-butyldimethylsilyl)oxy]-3-(1′-methylpropyl)-3,4,4a,5,6,7,8,8a-octahydro-4,5,7-trimethylnaphthalene (40).** To a solution of ketone **39** (656 mg, 2.5 mmol) in 26 mL of dichloromethane at 0 °C was added 1.89 mL (1.71 g, 16.02 mmol) of 2,6-lutidine followed by 3.06 mL (3.52 g, 13.35 mmol) of (*tert*-butyldimethylsilyl)trifluoromethane sulfonate. The mixture was stirred 0.5 h at 0 °C and warmed to 25 °C, and water was added. The organic layer was separated and sequentially washed with two 10-mL portions of 3% aqueous hydrochloric acid, 5 mL of 5% aqueous sodium carbonate, and 10 mL of saturated aqueous solution chloride. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo to yield 2 g of the crude silyl enol ether **40** as an oil. The enol ether was used without purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (5% ethyl acetate/hexanes): ^1H NMR (300 MHz, $CDCl_3$) δ 0.12 (3 H, s, $SiCH_3$), 0.13 (3 H, s, $SiCH_3$), 0.20 (3 H, s, $SiCH_3$), 0.21 (3 H, s, $SiCH_3$), 0.9 [9 H, s, $SiC(CH_3)_3$], 0.95 (3 H, d, J = 7 Hz, CH_3), 1.0 [9 H, s, $SiC(CH_3)_3$], 1.05 (3 H, d, J = 8 Hz, CH_3), 1.3 [3 H, s, CH_3], 4.6 [1 H, d, J = 4 Hz, H(1)]; IR (neat) 2960, 1660, 1460, 1250 cm^{-1}; LRMS (EI), m/e 494 (M^+), 479 ($M^+ - CH_3$), 437 ($M^+ - C_4H_9$), 362 ($M^+ - C_6H_{16}OSi$), 347 ($M^+ - C_7H_{19}OSi$).

(1*R,1′*S**,3*S**,4*R**,4a*S**,5*S**,7*S**,8a*S**)-1,7-Bis[(*tert*-butyldimethylsilyl)oxy]-3-(1′-methylpropyl)-3,4,4a,5,6,7,8,8a-octahydro-2(1*H*)-naphthalenone (41).** A solution of the entire crude product **40** of the previous step in 55 mL of dichloromethane at 0 °C was treated sequentially with 2.1 g (25 mmol) sodium bicarbonate and *m*-chloroperoxybenzoic acid (400 mg, 2.32 mmol) portionwise over 1 h. After an additional 0.5 h at 0 °C, the reaction mixture was sequentially washed with two 10-mL portions of 10% aqueous sodium sulfite, 10 mL of aqueous 5% sodium carbonate, and 10 mL of saturated aqueous sodium chloride. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography on 30 g of silica gel (5% ethyl acetate/hexanes) yielded 1.06 g (83%, 2 steps) of α-silyloxy ketone **41** as an oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (3 H, s, $SiCH_3$), 0.13 (3 H, s, $SiCH_3$), 0.13 (3 H, s, $SiCH_3$), 0.18 (3 H, s, $SiCH_3$), 0.95 [9 H, s, $SiC(CH_3)_3$], 1.0 [9 H, s, $SiC(CH_3)_3$], 1.25 [3 H, s, CH_3], 1.35 (3 H, d, CH_3), 2.1 (1 H, br s), 2.25 (1 H, m), 4.35 [1 H, d, J = 8 Hz, H(1)]; IR (neat) 2960, 1740 (C=O), 1460, 1250 cm^{-1}; LRMS (EI), m/e 510 (M^+), 495 ($M^+ - CH_3$), 453 ($M^+ - C_4H_7$), 451 ($M^+ - C_4H_9$), 363 ($M^+ - C_7H_{19}OSi$), 362 ($M^+ - C_7H_{20}OSi$).

(1*R,1′*S**,3*S**,4*R**,4a*S**,5*S**,7*S**,8a*S**)-1,7-Bis[(*tert*-butyldimethylsilyl)oxy]decahydro-2-hydroxy-3-(1′-methylpropyl)-4,5,7-trimethyl-2-[(trimethylsilyl)methyl]naphthalene.** To a solution of [(trimethylsilyl)methyl]tri-*n*-butyltin (360 mg, 0.98 mmol) in 2 mL of tetrahydrofuran at 0 °C was added 0.68 mL (0.93 mmol, 1.27 M in hexanes) of *n*-butyllithium, and the mixture was stirred for 0.5 h at 0 °C. The resulting solution was added to ketone **41** (168 mg, 0.33 mmol) in 7 mL of tetrahydrofuran at 0 °C via cannula. The reaction mixture was stirred for 0.5 h at 0 °C and then warmed to 25 °C and stirred an additional 10 min. Water was added to the reaction mixture, and the organic layer was washed with saturated aqueous sodium chloride, dried (Na_2SO_4), filtered, and concentrated in vacuo to yield the title alcohol as an oil. The product was used in the next step without further purification. A sample for spectral analysis was purified by preparative thin-layer chromatography (5% ethyl acetate/hexanes): ^1H NMR (300 MHz, $CDCl_3$) δ 0.095 [6 H, s, $Si(CH_3)_2$], 0.1 [9 H, s, $Si(CH_3)_3$], 0.195 [3 H, s, $Si(CH_3)$], 0.20 [3 H, s, $Si(CH_3)$], 0.9 [9 H, s, $SiC(CH_3)_3$], 0.95 [9 H, s, $SiC(CH_3)_3$], 3.62 [1 H, d, J = 8 Hz, H(1)]; IR (neat) 3570 (OH), 2960, 1460, 1250 cm^{-1}; LRMS (EI), m/e 598 (M^+), 583 ($M^+ - CH_3$), 466, 451.

(1*R,1′*S**,3*S**,4*R**,4a*S**,5*S**,7*S**,8a*S**)-1,7-Bis[(*tert*-butyldimethylsilyl)oxy]decahydro-2-methylidene-3-(1′-methylpropyl)-4,5,7-trimethylnaphthalene (43).** The product of the previous step in 10 mL of tetrahydrofuran was treated with excess potassium hydride, and the mixture was heated under reflux for 1 h under argon. The solution was cooled to 25 °C, and water was added. The aqueous layer was separated and extracted with two 35-mL portions of ether. The organic extracts were combined and washed with two 20-mL portions of saturated aqueous sodium chloride, dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product **43** was used without further purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (5% ethyl acetate/hexanes): ^1H NMR (500 MHz, $CDCl_3$) δ 0.00 [9 H, s, $Si(CH_3)_3$], 0.1 (3 H, s, $SiCH_3$), 0.85 [9 H, s, $SiC(CH_3)_3$], 0.95 [9 H, s, $SiC(CH_3)_3$], 1.1 (3 H, d, J = 8 Hz), 1.25 [3 H, s, $CH_3(7)$], 4.0 [1 H, d, J = 8 Hz, H(1)], 4.76 (1 H, br s), 5.1 (1 H, br s); IR (neat) 2960, 2920, 1460 cm^{-1}; LRMS (EI), m/e 451 ($M^+ - C_4H_9$), 376 [$M^+ - HOSi(CH_3)_2C(CH_3)_3$], 361 [$M^+ - HOSi(CH_3)_2C(CH_3)_3$, CH_3].

(1*R,1′*S*,3*S**,4*R**,4a*S**,5*S**,7*S**,8a*S**)-7-[(*tert*-Butyldimethylsilyl)oxy]decahydro-1-hydroxy-2-methylidene-3-(1′-methylpropyl)-4,5,7-trimethylnaphthalene (45).** The crude product **43** of the previous step in 5 mL of tetrahydrofuran at 25 °C was treated with 4 mL (4 mmol, 1 M in THF) of tetra-*n*-butylammonium fluoride then warmed to 45 °C. After 2 h, the reaction mixture was cooled to 25 °C, water was added, and the mixture was extracted with two 50-mL portions of ether. The organic extracts were washed with saturated aqueous sodium bicarbonate, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude allylic alcohol **45** was purified by column chromatography on 1 g of silica gel (10% ethyl acetate/hexanes) to produce 23 mg (35%, 3 steps) of pure allylic alcohol **45**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.13 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 4.2 [1 H, br s, H(1)], 4.9 (1 H, br s), 5.2 (1 H, br s); IR (neat) 3400 (OH), 2960, 1460 cm^{-1}; LRMS (EI), m/e 394 (M^+), 379 ($M^+ - CH_3$), 337 ($M^+ - C_4H_9$), 319 ($M^+ - C_4H_{11}O$).

(1*R,1″*S**,2*S**,3*S**,4*R**,4a*S**,5*S**,7*S**,8a*S**)-7-[(*tert*-Butyldimethylsilyl)oxy]decahydro-1-hydroxy-3-(1″-methylpropyl)-4,5,7-trimethylnaphthalene-2-spiro-2′-oxirane. (46).** To a solution of allylic alcohol **45** (27 mg, 0.07 mmol) in 3 mL of chloroform at 25 °C were sequentially added sodium bicarbonate (29 mg, 0.35 mmol) and *m*-chloroperoxybenzoic acid

(35.6 mg, 0.21 mmol), and the mixture was vigorously stirred. After 0.66 h, 10% aqueous sodium sulfite was added. The organic layer was separated and washed sequentially with 5% aqueous sodium carbonate and saturated aqueous sodium chloride. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to yield the crude epoxy alcohol **46** as an oil, which was used without further purification in the following step. A sample for spectral analysis was purified by preparative thin-layer chromatography (25% ethyl acetate/hexanes): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.1 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.0 (3 H, d, J = 7 Hz, CH_3), 1.2 (3 H, d, J = 7 Hz, CH_3), 1.3 (3 H, s, CH_3), 2.8 (1 H, d, J = 5 Hz), 3.03 (1 H, d, J = 5 Hz), 4.0 [1 H, d, J = 10 Hz, H(1)]; IR (neat) 3460 (OH), 2960, 1460, 1250 cm^{-1}; LRMS (EI), m/e 395 ($M^+ - CH_3$), 353 ($M^+ - C_4H_9$), 335 ($M^+ - C_4H_{11}O$), 279 [$M^+ - OSi(CH_3)_2C(CH_3)_3$], 261 [$M^+ - OSi(CH_3)_2C(CH_3)_3$, H_2O].

(1*R,1′*S**,2*R**,3*S**,4*R**,4a*S**,5*S**,7*S**,8a*S**)-1,2-Dihydroxy-7-[(*tert*-butyldimethylsilyl)oxy]decahydro-3-(1′-methylpropyl)-2,4,5,7-tetramethylnaphthalene (47).** Lithium triethylborohydride (0.279 ml, 0.279 mmol, 1 M in THF) was added to the crude epoxy alcohol **46** in 1 mL of tetrahydrofuran at 25 °C. After 0.75 h at 25 °C, 4 mL of water was added followed by 4 mL of 2 N aqueous sodium hydroxide and 3 mL of 30% aqueous hydrogen peroxide. The aqueous layer was separated from the organic layer and extracted with 2 mL of ether. The organic extracts were combined, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. Purification by column chromatography on 0.9 g of silica gel [(1) hexanes; (2) 25% ethyl acetate/hexanes] yielded 17 mg (61%, two steps) of diol **47** as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.2 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 0.95 (3 H, d, J = 8 Hz, CH_3), 1.2 (3 H, s, CH_3), 1.3 (3 H, s, CH_3); IR (neat) 3400 (OH), 2960, 1460, 1255 cm^{-1}.

(1′*R,2*S**,3*R**,4*S**,4a*R**,5*R**,7*R**,8a*R**)-7-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxy-3-(1′-methylpropyl)-3,4,4a,5,6,7,8,8a-octahydro-2,4,5,7-tetramethyl-1(2*H*)-naphthalenone (48).** To a solution of oxalyl chloride (54.6 mg, 0.43 mmol) in 8 mL of CH_2Cl_2 at −78 °C was added a solution of dimethyl sulfoxide (67 mg, 0.86 mmol) in 2 mL of CH_2Cl_2 via cannula. After 5 min the diol **46** (35.6 mg, 0.086 mmol) in 2 mL of CH_2Cl_2 was added via cannula. After 5 min at −78 °C, 0.3 mL (217.6 mg, 2.15 mmol) of triethylamine was added. The reaction mixture was stirred for 5 min at −78 °C and then warmed to 25 °C over 5 min. Water was added followed by sequential washings with 3% aqueous hydrochloric acid, 5% aqueous sodium carbonate, and saturated aqueous sodium chloride. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by chromatography on 0.9 g of silica gel (25% ethyl acetate/hexanes) afforded 33 mg (94%) of ketone **48** as an oil: ^{1}H NMR (300 MHz, CD_3OD) δ 0.18 [6 H, s, $Si(CH_3)_2$], 0.89 [3 H, d, J = 7 Hz, $CH_3(4)$], 0.93 [9 H, s, $SiC(CH_3)_3$], 1.0 [3 H, t, J = 7 Hz, $CH_3(3')$], 1.03 [3 H, d, J = 7 Hz, $CH_3(5)$], 1.1 [3 H, d, J = 7 Hz, $CH_3(1')$], 1.3 [3 H, s, $CH_3(7)$], 1.35 [2 H, m, H(2′), H(6)], 1.5 [3 H, s, $CH_3(2)$], 1.5 [1 H, m, H(2′)], 1.62 [1 H, dd, J = 15, 3 Hz, H(6)], 1.64 [1 H, dd, J = ~3, 3 Hz, H(3)], 1.66 [1 H, dd, J = 14, 13 Hz, H(8)], 1.92 [1 H, m, H(1′)], 1.95 [1 H, dddq, J = 12, 12, 3, 7 Hz, H(5)], 2.14 [1 H, m, H(4)], 2.18 [1 H, dd, J = 14, 4 Hz, H(8)], 2.25 [1 H, ddd, J = 12, 11, 4 Hz, H(4a)], 2.55 [1 H, ddd, J = 13, 11, 4 Hz, H(8a)]; IR (neat) 3460 (OH), 2960, 1700 (C=O), 1460, 1250 cm^{-1}; LRMS (EI), m/e 410 (M^+), 395 ($M^+ - CH_3$), 357, 335 ($M^+ - C_4H_{11}O$), 295 [$M^+ - Si(CH_3)_2C(CH_3)_3$], 279 [$M^+ - OSi(CH_3)_2C(CH_3)_3$], 261 [$M^+ - HOSi(CH_3)_2C(CH_3)_3$, H_2O].

(1′*R,2*S**,3*R**,4*S**,4a*R**,5*R**,7*R**,8a*S**)-7-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxy-3-(1′-methylpropyl)-3,4,4a,5,6,7,8,8a-octahydro-2,4,5,7-tetramethyl-1(2*H*)-naphthalenone (49).** A solution of the ketone **48** (30 mg, 0.073 mmol) in 1 mL of methanol was treated with excess sodium methoxide at 25 °C. After 1.5 h, saturated aqueous sodium chloride was added, and the reaction mixture was extracted with ether. The ether extracts were combined, washed with 3% aqueous hydrochloric acid and then saturated aqueous sodium chloride, dried over sodium sulfate, filtered, and concentrated in vacuo. Chromatography on 1 g of silica gel (10% ethyl acetate/hexanes) afforded 26.8 mg (89%) of ketone **49** as an oil: ^{1}H NMR (300 MHz, C_6D_6) δ 0.15 (3 H, s, $SiCH_3$), 0.25 (3 H, s, $SiCH_3$), 0.77 [1 H, dd, J = 12, 12 Hz, H(6)], 0.86 [3 H, d, J = 7 Hz, $CH_3(5)$], 0.94 [3 H, d, J = 7 Hz, $CH_3(1')$], 0.95 [3 H, t, J = 7 Hz, $CH_3(3')$], 1.08 [9 H, s, $SiC(CH_3)_3$], 1.11 [3 H, d, J = 7 Hz, $CH_3(4)$], 1.16 [3 H, s, $CH_3(7)$], 1.22 [1 H, m, H(8)], 1.26 [3 H, s, $CH_3(2)$], 1.4 [3 H, m, H(4a, 2′, 2′)], 1.6 [1 H, ddd, J = 13, 4, 3 Hz, H(6)], 1.74 [1 H, dd, J = 3,3 Hz, H(3)], 1.90 [1 H, m, H(1′)], 2.04 [1 H, m, H(5)], 2.16 [1 H, m, H(4)], 2.24 [1 H, ddd, J = 13, 4, 3 Hz, H(8)], 3.21 [1 H, ddd, J = 13, 13, 4 Hz, H(8a)]; IR (neat) 3460 (OH), 2960, 1700 (C=O), 1450, 1260 cm^{-1}; LRMS (EI), m/e 410 (M^+), 395 ($M^+ - CH_3$), 377 ($M^+ - CH_5O$), 353 ($M^+ - C_4H_9$), 335 ($M^+ - C_4H_{11}O$), 261 [$M^+ - OSi(CH_3)_2C(CH_3)_3$, H_2O].

(1′*R,2*S**,3*R**,4*S**,4a*R**,5*R**,7*R**,8a*S**)-2,7-Dihydroxy-3-(1′-methylpropyl)-3,4,4a,5,6,7,8,8a-octahydro-2,4,5,7-tetramethyl-1(2*H*)-naphthalenone (3).** To ketone **49** (26.8 mg, 0.065 mmol) was added 0.3 mL of CH_3CN/concentrated aqueous HF/H_2O (19:1:1), and the mixture was heated to 60 °C for 2 h. The mixture was cooled to 25 °C, water was added, and the product was extracted with dichloromethane. The organic extracts were washed with saturated aqueous sodium bicarbonate, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. Purification by chromatography on 1 g of silica gel (50% ethyl acetate/hexanes) produced 11 mg (60%) of keto diol **3** as a solid. A sample recrystallized from ethanol/water was subjected to single-crystal X-ray analysis: ^{1}H NMR [300 MHz, $C_6D_6/CDCl_3$ (1:1)] δ 0.78 [3 H, d, J = 7 Hz, $CH_3(5)$], 0.8 [1 H, m, H(6)], 0.85 [3 H, d, J = 7 Hz, $CH_3(1'')$], 0.88 [3 H, t, J = 7 Hz, $CH_3(3')$], 0.9 [3 H, d, J = 7 Hz, $CH_3(4)$], 1.0 [3 H, s, $CH_3(7)$], 1.15 [1 H, m, H(8)], 1.2 [3 H, s, $CH_3(2)$], 1.2–1.38 [3 H, m, H(4a, 2′, 2′)], 1.42 [1 H, ddd, J = 14, 4, 3 Hz, H(6)], 1.54 [1 H, dd, J = 3,3 Hz, H(3)], 1.74 [1 H, m, H(5)], 1.76 [1 H, m, H(1′)], 1.84 [1 H, ddd, J = 13, 4, 3 Hz, H(8)], 2.05 [1 H, m, H(4)], 2.84 [1 H, ddd, J = 15, 12, 4 Hz, H(8a)]; IR (neat) 3400 (OH), 2960, 1720 (C=O), 1450, 1260 cm^{-1}; LRMS (EI), m/e 296 (M^+), 279 ($M^+ - OH$), 278 ($M^+ - H_2O$), 263 ($M^+ - CH_5O$).

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Supplementary Material Available: Crystal and refinement data, tables of atomic coordinates, temperature factors, and bond distances and angles (7 pages); observed and calculated structure factors from the X-ray structure determination of **3** (7 pages). Ordering information is given on any current masthead page.