Synthesis of (*E*,*E*)-Germacrane Sesquiterpene Alcohols via Enolate-Assisted 1,4-Fragmentation

Adriaan J. Minnaard, Joannes B. P. A. Wijnberg,* and Aede de Groot*

Laboratory of Organic Chemistry, Agricultural University, Dreijenplein 8, 6703 HB Wageningen, The Netherlands

Received May 20, 1997[⊗]

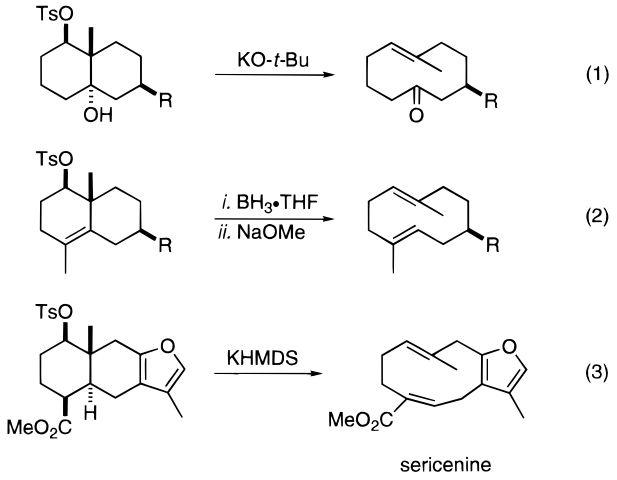
An efficient method has been developed for the synthesis of (*E*,*E*)-germacrane sesquiterpene alcohols. The key step in these syntheses involves the enolate-assisted 1,4-fragmentation of properly functionalized perhydro-1-naphthalenecarboxaldehydes with 1 equiv of sodium *tert*-amylate as base, to give the corresponding (*E*,*E*)-germacrane aldehydes. These aldehydes are not very stable, and in situ reduction of the aldehyde function with Red-Al is required to obtain high yields of the desired germacrane alcohols. This procedure has led to the successful synthesis of 15-hydroxygermacrene B (**4**) and 15-hydroxyhedycaryol (**35**) from the mesylates **6** and **33**, respectively. When KHMDS is used instead of sodium *tert*-amylate in the fragmentation reaction of **6**, isomerization of the initially formed C(4)−C(5) *E* double bond cannot be avoided and results, after in situ reduction with Red-Al, in the formation of the (*E*,*Z*)-germacrane alcohol **24**. The 15-hydroxy-(*E*,*E*)-germacranes are excellent starting materials for the selective synthesis of the corresponding 4,5-epoxides, which in turn can perfectly well be used in studies on the biomimetic formation of guaiane sesquiterpenes.

Introduction

Because of their unique structural and conformational features, their general occurrence in nature,[1] and their central role in the biosynthesis of other sesquiterpenes,[2] germacranes have received much attention in modern organic chemistry.[3] The main synthetic approaches toward the cyclodeca-1(10),4-diene ring system of germacranes can be classified as intramolecular C−C bond formation, ring expansion reactions, and cleavage of the central bond in decalin systems. In the latter approach, three closely related Grob-type fragmentation reactions can be distinguished. First, the Wharton fragmentation[4] in which 5-cyclodecenone systems are formed upon treatment of perhydronaphthalene-1,3-diol monosulfonate esters with strong bases (Scheme 1, eq 1). This method has been used several times in sesquiterpene synthesis[5] but suffers from the fact that only one double bond is formed regio- and stereospecifically. Its application in germacrane synthesis is therefore limited.

The boronate fragmentation reaction introduced by Marshall circumvents this problem because both double bonds are formed regio- and stereospecifically (Scheme 1, eq 2).[6] The method has been applied in the synthesis of hedycaryol[7] and its C(5)−C(6) and C(9)−C(10) double bond isomers allohedycaryol[8] and neohedycaryol,[9] respectively. The usually moderate regio- and stereoselectivity of the BH_3 addition to tetrasubstituted double bonds[10] and the fact that several functional groups are not compatible with the use of BH_3[11] limit the application of the boronate fragmentation reaction in germacrane synthesis.

Scheme 1



The third reaction, developed by Mander *et al.*,[12] involves an enolate-assisted 1,4-fragmentation via α-deprotonation of an ester function.[13] The synthesis of the heliangolide sericenine is the only known example of this approach in germacrane synthesis (Scheme 1, eq 3).[14] Under the basic conditions, isomerization of the C(4)−

[⊗] Abstract published in *Advance ACS Abstracts,* September 15, 1997.

(1) Connolly, J. D.; Hill, R. A. *Dictionary of Terpenoids*; Chapman & Hall: London, 1991; Vol. 1, Mono- and Sesquiterpenoids.

(2) Banthorpe, D. V. In *Natural Products: Their Chemistry and Biological Significance*; Longman Scientific & Technical: Harlow, 1994; Chapter 5.

(3) Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*; VCH: Weinheim, 1996; Chapter 13 and 21.

(4) For a review of the Wharton fragmentation, see: Caine, D. *Org. Prep. Proced. Int.* **1988**, *20*, 1.

(5) (a) González, A. G.; Galindo, A.; Mansilla, H.; Gutiérrez, A.; Palenzuela, J. A. *J. Org. Chem.* **1985**, *50*, 5856. (b) Cauwberghs, S.; De Clercq, P. J. *Tetrahedron Lett.* **1988**, *29*, 6501.

(6) Marshall, J. A.; Bundy, G. L. *J. Am. Chem. Soc.* **1966**, *88*, 4291.

(7) (a) Wharton, P. S.; Sundin, C. E.; Johnson, D. W.; Kluender, H. C. *J. Org. Chem.* **1972**, *37*, 34. (b) Minnaard, A. J.; Wijnberg, J. B. P. A.; de Groot, A. *Tetrahedron* **1994**, *50*, 4755.

(8) Zhabinskii, V. A.; Minnaard, A. J.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1996**, *61*, 4022.

(9) Minnaard, A. J.; Stork, G. A.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1997**, *62*, 2344.

(10) Marshall J. A. *Synthesis* **1971**, 229.

(11) For an example, see ref 9.

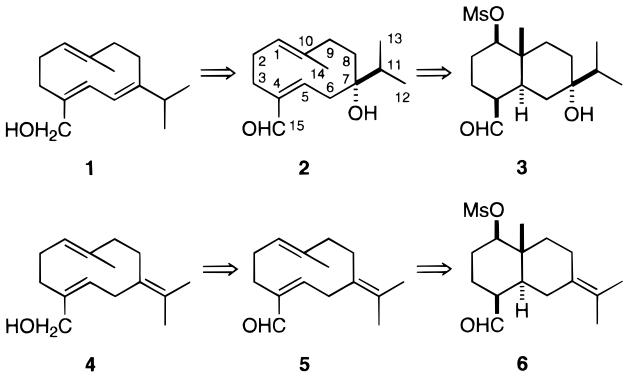
(12) Brown, J. M.; Cresp, T. M.; Mander, L. N. *J. Org. Chem.* **1977**, *42*, 3984.

(13) The fragmentation reaction induced by α-deprotonation of a ketone in a bicyclo[5.4.0]undecane derivative has been used to construct an 11-membered ring system: (a) Clark, D. A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3567. Wender *et al.* reported the ester enolate-assisted fragmentation of a cis-fused decalin system resulting in the formation of a cyclodecadiene with a double bond stereochemistry that cannot be explained by the stereochemical rules valid for this reaction. (b) Wender, P. A.; Manly, C. J. *J. Am. Chem. Soc.* **1990**, *112*, 8579.

(14) Honan, M. C.; Balasuryia, A.; Cresp, T. M. *J. Org. Chem.* **1985**, *50*, 4326.

S0022-3263(97)00901-8 CCC: $14.00

Scheme 2

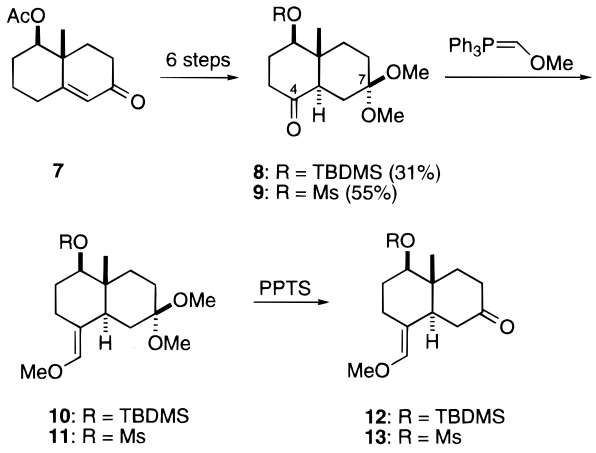


C(5) double bond in the initially formed (*E*,*E*)-germacrane led to the (*E*,*Z*)-germacrane ring system present in sericenine. We realized that, if the isomerization of the C(4)−C(5) double bond could be prevented, the enolate-assisted 1,4-fragmentation would offer an efficient method for the synthesis of (*E*,*E*)-germacranes in which the Me group at C(4) is oxidized.[15] To establish whether this is indeed the case, we decided to synthesize the aldehydes **3** and **6** (Scheme 2). In contrast to the fragmentation reaction leading to sericenine (Scheme 1, eq 3), it was expected that the fragmentation of **3** would lead to selective formation of the (*E*,*E*)-germacrane derivative **2**[16] without isomerization (*E* → *Z*) of the C(4)−C(5) double bond because the carbon atom at the 7-position in **2** possesses sp^3 hybridization which makes H-6 less acidic. Reduction of the aldehyde function in **2** and subsequent elimination of water would then complete the synthesis of 15-hydroxygermacrene C (**1**). In a similar way, fragmentation of **6** followed by reduction of the resulting aldehyde **5** would lead to 15-hydroxygermacrene B (**4**). We realized that sp^2 hybridization at C(7) in **5** could lead to isomerization of the C(4)−C(5) double bond, but it was hoped that the use of only 1 equiv of strong base would suppress this isomerization. The presence of a hydroxyl group at C(15) in **1** and **4** allows the regioselective epoxidation of the C(4)−C(5) double bond. This is an important aspect because easy access to germacrane 4,5-epoxides will facilitate investigations on the biomimetic formation of guaiane sesquiterpenes. In addition, asymmetric Sharpless epoxidation creates the possibility to develop a synthetic route toward enantiomerically enriched guaianes in which chirality is introduced at a very late stage of the reaction sequence.[17]

Results and Discussion

For the synthesis of the aldehyde **3**, two slightly different reaction pathways were followed starting from the easily accessible racemic acetate **7**[18] (Scheme 3). By modest adaptions of existing procedures,[19] **7** was converted into the known TBDMS ether **8**[20] and also into the mesylate **9**, both in a six-step reaction sequence without the need of interim purification. In this way, **8** and **9** were obtained in 31% and 55% overall yield, respectively, from acetate **7**.

Scheme 3



Because the introduction of the isopropyl side chain at C(7) via an organometal addition is not compatible with the presence of an aldehyde group, the presence of a masked aldehyde function at C(4) is required and for that purpose **8** was converted into the methyl enol ether **10** in 89% yield with (methoxymethyl)triphenylphosphonium chloride[21] and (dimethylsulfinyl)sodium in dry DMSO. In contrast to **8**, application of these reaction conditions on mesylate **9** completely failed due to a competitive γ-elimination of the mesylate group via abstraction of H-5.[22] Only the use of KHMDS in THF in this reaction gave a moderate yield (48%) of the desired product **11**. The hydrolysis of the dimethyl acetal function in **10** and **11** with PPTS in aqueous acetone[18] proceeded smoothly and afforded **12** and **13**, respectively, in almost quantitative yield.

At this stage of the reaction sequence, the isopropyl group at C(7) was introduced. Because addition of iPrMgCl to the keto group of **12** failed, probably as a result of enolization and reduction, iPrMgCl was transmetalated with $CeCl_3$.[23] With this cerium analogue, **12** gave an easily separable 5:1 mixture of **14** and **15**, respectively, in excellent yield (Scheme 4). In order to obtain reproducible high yields in this reaction, ultrasonic treatment of the $CeCl_3$ suspension turned out to be essential.[24] After removal of the TBDMS protecting group in **14** with TBAF in hot DMSO,[25] treatment of the resulting alcohol **16** with MsCl in pyridine afforded the mesylate **17**.[26] In contrast to **12**, the organocerium reaction mentioned above applied on **13** proceeded selectively and gave **17** as the sole product in 93% yield. Hydrolysis of the masked aldehyde function in **17** with

(15) This kind of (*E*,*E*)-germacranes, especially those with a carbinol group at C(4), are regularly found in nature; see ref 1.

(16) The numbering system as given in structure **2** will be followed throughout the text of this paper.

(17) See following paper.

(18) Wijnberg, J. B. P. A.; Vader, J.; de Groot, A. *J. Org. Chem.* **1983**, *48*, 4380 and references cited therein.

(19) Kim, M.; Kawada, K.; Watt, D. S. *Synth. Commun.* **1989**, *19*, 2017.

(20) The TBDMS ether **8** has been used a number of times in synthesis, see: (a) Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; Brunekreef, G. A.; de Groot, A. *J. Org. Chem.* **1990**, *55*, 941. (b) Jenniskens, L. H. D.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 6585. (c) Magee, T. V.; Bornmann, W. G.; Isaacs, R. C. A.; Danishefsky, S. J. *J. Org. Chem.* **1992**, *57*, 3274. (d) Masters, J. J.; Link, J. T.; Snyder, L. B.; Young, W. B.; Danishefsky, S. J. *Angew. Chem.* **1995**, *107*, 2017.

(21) For an overview of the use of this reagent, see: Anderson, C. L.; Soderquist, J. A.; Kabalka, G. W. *Tetrahedron Lett.* **1992**, *33*, 6915.

(22) Heathcock, C. H.; Ratcliffe, R. *J. Am. Chem. Soc.* **1971**, *93*, 1746.

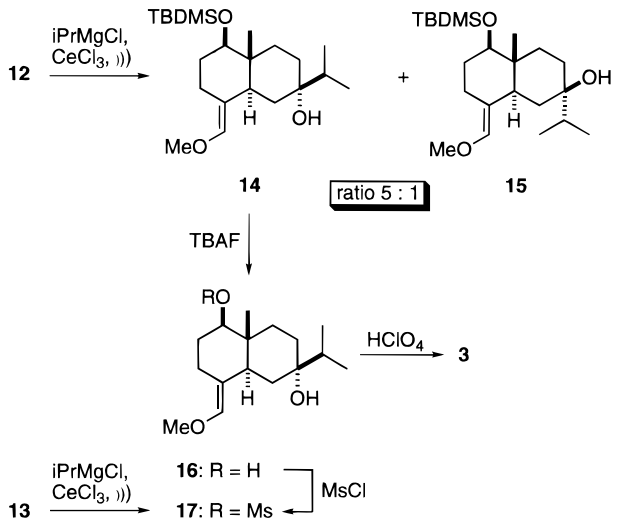
(23) (a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392. (b) Denmark, S. E.; Edwards, J. P.; Nicaise, O. *J. Org. Chem.* **1993**, *58*, 569.

(24) Greeves, N.; Lyford, L. *Tetrahedron Lett.* **1992**, *33*, 4759.

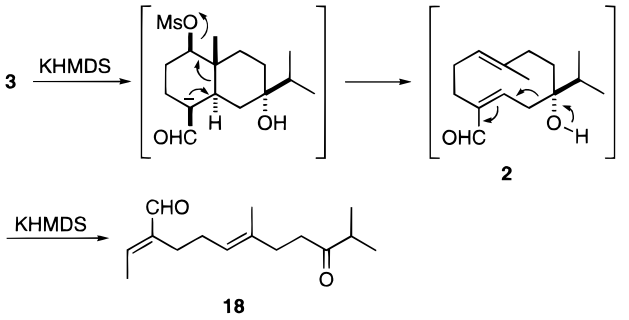
(25) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Bouwman, C. T.; de Groot, A. *J. Org. Chem.* **1994**, *59*, 374.

(26) The stereochemistry at C(7) in **17** could be ascertained with NMR experiments. With the use of the shift reagent Eu(fod)$_3$ in ^{1}H NMR measurements, the close proximity of H-5 and the hydroxyl group at C(7) was demonstrated. NOE-difference studies showed a clear NOE between H-1 and H-5. A NOE between H-5 and the isopropyl group at C(7) was not observed.

Scheme 4



Scheme 5

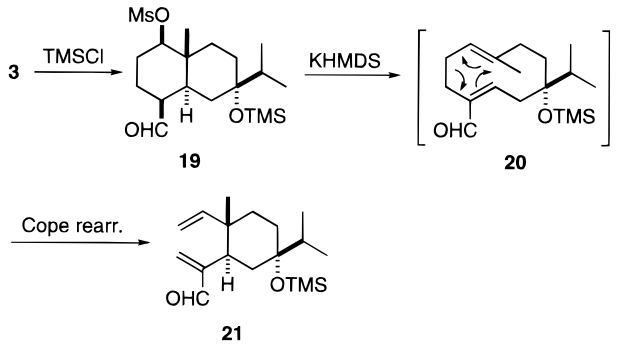


35% aqueous $HClO_4$ in ether[27] completed the synthesis of **3** in which the aldehyde group most likely possesses the axial orientation.[28] The route **7** ⟹ **13** ⟹ **3** was slightly shorter (10 steps) than the one via **12** (12 steps), but both routes gave about the same overall yield of **3** (ca 20%).

With aldehyde **3** in hand, the enolate-assisted 1,4-fragmentation reaction could now be investigated. Upon treatment of **3** with KHMDS in THF,[14] a fast reaction took place resulting in a product which partly decomposed during flash chromatography. Instead of the expected 10-membered ring system **2**, the isolated product (20% yield) turned out to be the linear compound **18** (Scheme 5). The stereochemistry of the enal function in **18** follows from its ^{1}H NMR spectrum.[29] Its formation can easily be explained by a vinologous retro-aldol reaction of the initially formed fragmentation product **2** under the basic reaction conditions used.[30]

In order to avoid the undesired retro-aldol reaction, the hydroxyl group in **3** was protected as its TMS ether **19**.[31] When **19** was treated with KHMDS in THF, again a fast reaction took place to give the rather unstable elemane-like compound **21** as the sole product that could be isolated (Scheme 6). It is obvious that the formation of **21** proceeds via a Cope rearrangement of the initially formed intermediate **20**.[32] This [3,3]-sigmatropic rearrangement is a characteristic feature of (*E*,*E*)-cyclodeca-1(10),4-diene systems[33] and makes the isolation of (*E*,*E*)-germacranes from natural sources and reaction mixtures rather complicated.[34]

Scheme 6



Because the Cope rearrangement can only take place via the chairlike transition state, the fast and selective formation of **21** may be an indication that intermediate **20** easily adopts such a chair-like conformation. Since the nature of the C(7) side chain has a profound impact on the conformational behavior of these compounds,[32] it is obvious that the rate of the Cope rearrangement (**20** → **21**) strongly depends on the stereochemistry and structural features of the C(7) substituents. Another structural characteristic of **20** that might favor the Cope rearrangement is the aldehyde function at C(15). This has been concluded from the observation that natural germacrane aldehydes undergo Cope rearrangement at a much lower temperature than their corresponding alcohols or C(15) unfunctionalized derivatives.[35]

Confronted with the easy Cope rearrangement of **20** to **21**, we stopped trying to synthesize 15-hydroxygermacrene C (**1**) and focused our attention on the synthesis of 15-hydroxygermacrene B (**4**). We opted for an isopropylidene group at C(7) because an additional *sp*^{2} center in the 10-membered ring will partly relieve the strain,[36] thereby diminishing the tendency toward Cope rearrangement. Introduction of the isopropylidene side chain was easily achieved by treatment of **12** with isopropyltriphenylphosphonium iodide and (dimethylsulfinyl)sodium in DMSO to give **22** in high yield (Scheme 7). Further conversion of **22** into the crystalline aldehyde **6** was accomplished with standard procedures.

Initially, the fragmentation reaction of **6** was studied in THF with ca. 1 equiv of KHMDS (Scheme 8). These reaction conditions led to the formation of a complex

(27) Levine, S. G. *J. Am. Chem. Soc.* **1958**, *80*, 6150.

(28) (a) Nagata, W.; Sugasawa, T.; Narisada, M.; Wakabayashi, T.; Hayase, Y. *J. Am. Chem. Soc.* **1967**, *89*, 1483. ^{1}H NMR studies on a system similar to **3** revealed that an axially oriented aldehyde gives rise to a singlet whereas an equatorially oriented aldehyde appears as a doublet (J = 3.9 Hz): (b) García, B.; Skaltsa, H.; Navarro, F. I.; Pedro, J. R.; Lazari, D. *Phytochemistry* **1996**, *41*, 1113.

(29) Herz, W.; Kalyanaraman, P. S. *J. Org. Chem.* **1975**, *40*, 3486.

(30) For a related example of this reaction, see: Walborsky, H. M.; Reddy, S. M. *J. Org. Chem.* **1988**, *53*, 4851.

(31) The stereochemistry at C(4) in aldehyde **19** could be established unambiguously by reduction with $NaBH_4$ to the corresponding alcohol: ^{1}H NMR δ 0.10 (s, 9 H), 0.78 (s, 3 H), 0.88 (d, J = 6.8 Hz, 6 H), 1.40−1.97 (m, 14 H), 2.98 (s, 3 H), 3.56 (br d, J = 6.8 Hz, 2 H), 4.31 (dd, J = 7.1, 9.2 Hz, 1 H); ^{13}C NMR δ 2.67 (3 q), 13.53 (q), 17.45 (q), 17.58 (q), 24.69 (t), 25.93 (t), 28.43 (t), 33.56 (t), 35.30 (t), 38.42 (q), 38.61 (d), 38.61 (s), 39.91 (d), 41.70 (d), 60.87 (t), 78.68 (s), 91.44 (d); MS m/z (relative intensity) 363 (M^+ − 43, 100), 181 (11), 131 (11), 119 (11), 73 (11), 69 (22); HRMS calcd for $C_{16}H_{31}O_5SSi$ (M^+ − 43) 363.1662, found 363.1655. NOE-difference experiments showed a strong NOE between the angular Me group and the carbinol group at C(4), thereby establishing the axial orientation of the C(4) substituent.

(32) Cleavage of the C(2)−C(3) bond via a 1,4-fragmentation reaction would result in the same product, but it has been shown that this process is very unlikely: Marshall, J. A.; Babler, J. H. *J. Org. Chem.* **1969**, *34*, 4186.

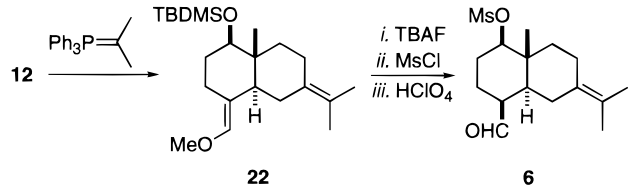
(33) Takeda, K. *Tetrahedron* **1974**, *30*, 1525.

(34) Reichardt, P. B.; Anderson, B. J.; Clausen, T. P.; Hoskins, L. C. *Can. J. Chem.* **1989**, *67*, 1174.

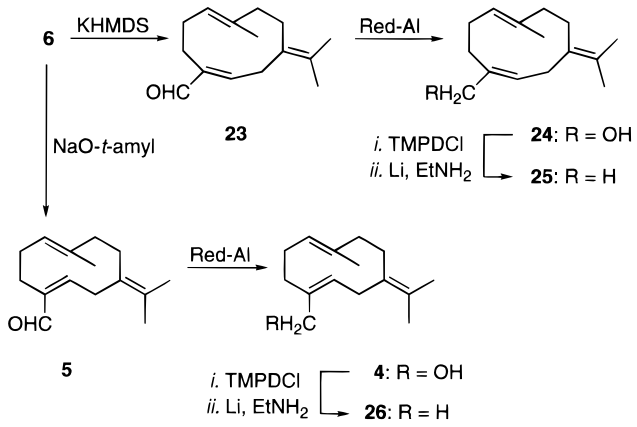
(35) (a) Bohlmann, F.; Zdero, C. *Phytochemistry* **1979**, *18*, 95. (b) Appendino, G.; Özen, H. C. *Gazz. Chim. Ital.* **1993**, *123*, 93.

(36) (a) Allen, F. H.; Rogers, D. *J. Chem. Soc., Chem. Commun.* **1967**, 588. (b) Allen, F. H.; Rogers, D. *J. Chem. Soc.* B **1971**, 257.

Scheme 7



Scheme 8



product mixture from which only the unstable aldehyde **23** with a C(4)−C(5) *Z* double bond could be isolated in rather poor yield (27%). From this experiment it was concluded that, despite the fact that only 1 equiv of KHMDS was used, isomerization of the initially formed C(4)−C(5) *E* double bond immediately followed the fragmentation of **6**. Support for the presence of an aldehyde group connected to a *Z* double bond in **23** was obtained from its ^{1}H NMR spectrum in which a one-proton signal appears at δ 9.28.[29] A much better product yield was achieved when the fragmentation reaction of **6** was performed with KHMDS under oxygen-free conditions[37] and the reaction mixture quenched with Red-Al at −78 °C. In this way, the (*E*,*Z*)-germacrane alcohol **24** was obtained as the sole product in 77% yield. The presence of the C(4)−C(5) *Z* double bond in **24** was demonstrated by its conversion into the known (*E*,*Z*)-germacrane **25**.[38] Whereas treatment of **24** with SO_3·pyridine and in situ reduction of the resulting sulfate[39] led to complex product mixtures,[40] reduction of the phosphordiamidate of **24** with Li in $EtNH_2$[41] was more successful and provided **25** in 42% yield.[42] The ^{1}H NMR data of **25** were identical with those reported in the literature,[38] thereby confirming the *Z* geometry of the C(4)−C(5) double bond in **24**.

The fragmentation reactions of **6** with KHMDS as base also showed that, regardless of the amount of KHMDS employed in these reactions, the *E* → *Z* isomerization of the C(4)−C(5) conjugated double bond could not be avoided. A possible explanation could be that hexamethyldisilazane formed during these reactions would act as a basic catalyst for the isomerization and, therefore, we decided to use sodium *tert*-amylate (NaO-*t*-amyl) instead of KHMDS. NaO-*t*-amyl in benzene or toluene is the most effective base−solvent combination in the fragmentation reactions of 1,4-diol monosulfonate esters,[43] and in contrast to hexamethyldisilazane, *tert*-amyl alcohol should not interfere with the reaction. When **6** was treated with 1 equiv of NaO-*t*-amyl in toluene[44] under oxygen-free conditions, a fast reaction took place resulting in the formation of the unstable (*E*,*E*)-germacrane aldehyde **5** and trace amounts of **23** (Scheme 8). The Cope rearrangement was not observed in this reaction.[45] The same reaction combined with in situ reduction with Red-Al afforded 15-hydroxygermacrene B (**4**) together with a small amount of **24**. Purification was easily achieved with aqueous $AgNO_3$ extraction[46] and gave **4** in 72% yield. The byproduct **24** was not extracted with aqueous $AgNO_3$.[47] Conversion of the phosphordiamidate of **4**, via a short treatment (5 min) with Li in $EtNH_2$,[48] into germacrene B (**26**)[49] confirmed the *E* geometry of the C(4)−C(5) double bond in **4**.

Significant differences between the aldehydes **5** and **23** and between the alcohols **4** and **24** were observed in the ^{1}H NMR spectra of these compounds. The ^{1}H NMR spectrum of **5** shows the aldehyde singlet at δ 9.93, while the corresponding signal in the ^{1}H NMR spectrum of **23** appears at δ 9.28. These observations obey the empirical NMR rules formulated by Lange *et al.*[42a] Distinction between **4** and **24** can be made by comparing the multiplicities of the C(15) carbinol protons in their ^{1}H NMR spectra; an AB system was found for **4**, a broad singlet for **24**. Marshall and Flynn observed similar differences in the ^{1}H NMR spectra of the related betweenanenes.[50]

Although the results described above clearly show that both **5** and **23** (or **4** and **24**, after reduction with Red-Al) can be synthesized selectively and in good yield from **6** by changing the base (KHMDS vs NaO-*t*-amyl), the reason for this difference in reaction outcome remains unclear. Our initial idea that hexamethyldisilazane might act as a basic catalyst for the isomerization of **5** to **23** proved to be incorrect. This was concluded from an experiment in which **5** was exposed to hexamethyldisilazane in toluene[51] at room temperature for 1 h. Although **5** partly decomposed, isomerization to **23** was not observed.

(37) Autoxidation of the trienol form of **23** might be responsible for the low yield (27%) of **23** in the fragmentation reaction of **6**. For example, see: Wydra, R.; Paryzek, Z. *Pol. J. Chem.* **1984**, *58*, 705.

(38) Itoh, A.; Nozaki, H.; Yamamoto, H. *Tetrahedron Lett.* **1978**, 2903.

(39) Corey, E. J.; Achiwa, K. *J. Org. Chem.* **1969**, *34*, 3667.

(40) The formation of a complex product mixture was partly caused by shifting of the C(4)−C(5) double bond. This complication has been noted before in germacrane synthesis: Matsuo, A.; Nozaki, H.; Kubota, N.; Uto, S.; Nakayama, M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 203.

(41) (a) Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098. (b) Trost, B. M.; Renaut, P. *J. Am. Chem. Soc.* **1982**, *104*, 6668.

(42) Another product similar to **25** but with the *E* C(1)−C(10) double bond assumably being reduced was also formed in this reaction. This assumption was based on the empirical NMR rules developed for the structure elucidation of germacrane sesquiterpenes: (a) Lange, G. L.; Lee, M. *Magn. Reson. Chem.* **1984**, *106*, 723. The hydrogenation of the C(1)−C(10) double bond with Li in $EtNH_2$ was rather unexpected, all the more so because reduction of 8-acetoxygermacrene B with Li in NH_3 only gave germacrene B: (b) Brown, E. D.; Sam, T. W.; Sutherland, J. K.; Torre, A. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2326.

(43) (a) Reference 20a. (b) Bastiaansen, P. M. F. M.; Wijnberg, J. P. B. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 4240.

(44) The use of more than one equiv of NaO-*t*-amyl also led to *E* → *Z* isomerization of the conjugated C(4)−C(5) double bond.

(45) After completion of this research, we noticed that in a recent synthesis of a nine-membered 3-ene-1,5-diyne system the same tactic has been employed. Thus, an exocyclic double bond was introduced to avoid rapid Cope rearrangement: Iida, K.; Hirama, M. *J. Am. Chem. Soc.* **1994**, *116*, 10310.

(46) Southwell, I. A. *Phytochemistry* **1970**, *9*, 2243.

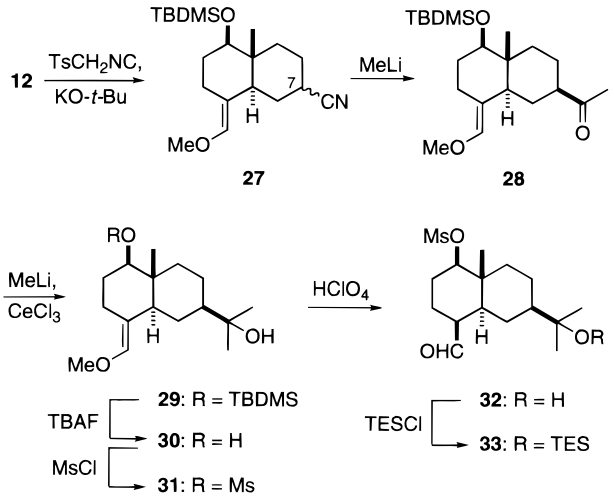
(47) Cyclic (*E*)-olefins complexate stronger with silver than cyclic (*Z*)-olefins: van Beek, T. A.; Subrtova, D. *Phytochem. Anal.* **1995**, *6*, 1.

(48) Longer reaction times led to a mixture of **27** and hydrogenated products with the latter compounds in excess.

(49) Germacrene B, a widespread naturally occurring hydrocarbon, has been synthesized before from natural germacrone, see ref 42b and references cited therein.

(50) Marshall, J. A.; Flynn, K. E. *J. Am. Chem. Soc.* **1984**, *106*, 723.

Scheme 9

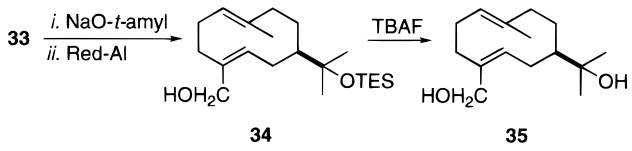


As has been demonstrated here, the enolate-assisted 1,4-fragmentation reaction with NaO-*t*-amyl as base offers an useful method for the synthesis of (*E*,*E*)-germacranes with sp^2 hybridization at C(7). The question raised, however, whether this method could also be employed for the synthesis of (*E*,*E*)-germacranes with sp^3 hybridization at C(7). We had already demonstrated that the fragmentation product of aldehyde **19** with two subsituents at C(7) easily underwent Cope rearrangement. On the other hand, an (*E*,*E*)-germacrane like hedycaryol, with only one substituent at C(7), is stable at room temperature and undergoes Cope rearrangement only at (slightly) elevated temperatures.[7a,52] These two facts combined led to the assumption that it might be possible to employ the enolate-assisted 1,4-fragmention for the synthesis of (*E*,*E*)-germacranes with only one C(7) substituent.[53] To test this hypothesis, we decided to investigate the fragmentation of the aldehyde **33** with a protected 2-hydroxyisopropyl side chain at C(7).

The synthesis of aldehyde **33** with the TBDMS ether **12** as the starting material required the conversion of a carbonyl function into a 2-hydroxyisopropyl group. For this purpose, the approach of Marshall *et al.*[54] was followed, except that the three-step reaction sequence to convert a ketone into a nitrile was replaced by a one-step procedure using tosylmethyl isocyanide (TosMIC).[55]

Treatment of **12** with TosMIC gave **27** as an epimeric mixture of two nitriles (Scheme 9). Addition of MeLi to **27** afforded, after basic hydrolysis, selectively compound **28** possessing an equatorial acyl group.[54] The introduction of the second Me group was performed with the cerium analogue of MeLi to avoid enolization of the acyl group and afforded **29** in excellent yield. Via standard procedures **29** was converted into the aldehyde **32**, i.e., **29** → **30** → **31** → **32**. Treatment of **32** with chlorotriethylsilane (TESCl) gave the corresponding TES ether **33** in 56% yield.[56] The protection of the C(11) hydroxyl group was needed to avoid the use of more than 1 equiv of base in the fragmentation step.

Scheme 10



The fragmentation reaction of **33** was performed with 1 equiv of NaO-*t*-amyl in toluene and afforded, after reduction and workup, almost pure **34** in high yield (Scheme 10). No Cope rearrangement products were found. Removal of the TES protecting group in **34** was achieved by treatment with TBAF in THF, and the following purification by aqueous $AgNO_3$ extraction afforded pure 15-hydroxyhedycaryol (**35**) in good yield. Just as found for hedycaryol,[57] the ^1H NMR spectrum of **35** indicates the presence of at least three distinct conformers at room temperature.

Concluding Remarks

In the first instance, our study on the use of the enolate-assisted 1,4-fragmentation in (*E*,*E*)-gemacrane synthesis was frustrated by reactions (vinologous retro-aldol reaction, Cope rearrangement, isomerization) immediately following the fragmentation step. Nevertheless, by the characterization of the isolated products, it was clear that the fragmentation reaction itself proceeds rapidly and unambiguously. After the discovery that the *E* → *Z* isomerization of the C(4)−C(5) double bond in the initially formed (*E*,*E*)-germacrane can be suppressed by the use of 1 equiv of sodium *tert*-amylate as base, the desired breakthrough was realized and resulted in the synthesis of 15-hydroxygermacrene B and germacrene B itself. The synthesis of 15-hydroxyhedycaryol proved that this approach was not limited to germacranes with sp^2 hybridization at C(7).

Finally, as stated in the Introduction, the asymmetric Sharpless epoxidation of 15-hydroxygermacranes lacking a chiral carbon atom like 15-hydroxygermacrene B creates the possibility to synthesize enantiomerically enriched guaiane sesquiterpenes.[17]

Experimental Section[58]

Materials. All reagents were purchased from Aldrich or Janssen except for *N*,*N*,*N*′,*N*′-tetramethylphosphorodiamidic chloride (TMPDCl) which was purchased from Fluka. (Methoxymethyl)triphenylphosphonium chloride and isopropyltriphenylphosphonium iodide were dried in a vacuum desiccator over P_2O_5 before use. The compounds **7**,[18] **8**,[20b] **25**,[38] and **26**[42b] have been characterized before.

(4aα,5α)-(±)-5-Acetoxy-4,4a,5,6,7,8-hexahydro-4a-methyl-2(3*H*)-naphthalenone (7). To a stirred solution of crude (4aα,5α)-(±)-4,4a,5,6,7,8-hexahydro-5-hydroxy-4a-methyl-2(3*H*)-naphthalenone (prepared from 2-methylcyclohexane-1,3-dione (100 g, 0.79 mol) and freshly distilled methyl vinyl ketone (MVK) (129 mL, 1.58 mol) following known procedures)[59] in 500 mL of dry pyridine was added dropwise 252 mL of Ac_2O at 10−15 °C. When the addition was complete, the reaction mixture was stirred at room temperature (rt) for 3 days. Standard workup gave an oil which was taken up in 500 mL of diisopropyl ether and left overnight to crystallize. The crystals were filtered off to give 60.9 g of pure **7**. The mother

(51) The outcome of the fragmentation reaction did not depend on the solvent used. Fragmentation of **6** with KHMDS in toluene or THF both afforded **23**.

(52) Kodama, M.; Yokoo, S.; Matsuki, Y.; Itô, S. *Tetrahedron Lett.* **1979**, 1687.

(53) The majority of (*E*,*E*)-germacranes found in nature possesses only one substituent at C(7), see ref 1.

(54) Marshall, J. A.; Pike, M. T.; Carroll, R. D. *J. Org. Chem.* **1966**, *31*, 2933.

(55) Oldenziel, O. H.; van Leusen, D.; van Leusen, A. M. *J. Org. Chem.* **1977**, *42*, 3114.

(56) This reaction also gave a byproduct with a silyl enol ether function at C(4).

(57) (a) Wharton, P. S.; Poon, Y. C.; Kluender, H. C. *J. Org. Chem.* **1973**, *38*, 735. (b) Minnaard, A. J. unpublished results.

(58) For a general description of the experimental procedures employed in this research, see ref 7b.

liquor was concentrated and dissolved in a mixture of 150 mL of diisopropyl ether and 50 mL of petroleum ether (bp 40−60 °C). After standing overnight at 0 °C, a second crop (9.7 g) of pure **7** was obtained. The remaining mother liquor was concentrated and afforded, after flash chromatography (4:1 petroleum ether (bp 40−60 °C)/EtOAc) and crystallization from diisopropyl ether, a third portion (17.0 g) of pure **7**. The total yield of pure **7** amounted to 87.6 g (50% overall from 2-methylcyclohexane-1,3-dione). The spectroscopic data of **7** were identical with those reported in the literature.[18]

(4α,4aα,8a*β*)-(±)-Octahydro-7,7-dimethoxy-4a-methyl-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1(2*H*)-naphthalenone (8). To a stirred solution of 87.6 g (398 mmol) of **7** and 250 g NaI in 600 mL of Ac_2O was added dropwise 200 mL of TMSCl over a period of 30 min at 0 °C. After being stirred at 0 °C for 1 h, the reaction mixture was filtered and concentrated under reduced pressure. The concentrate was carefully mixed with 500 mL of saturated aqueous $NaHCO_3$ and, after addition of 120 g of $Na_2S_2O_3$, stirred at 0 °C for 1 h. The aqueous layer was then extracted with three 500-mL portions of EtOAc. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried, and evaporated to leave 103 g of a brown oil. To a solution of this oil in 850 mL of MeOH was added 250 g of $NaHCO_3$. The mixture was stirred vigorously, and then 1.3 L of 1 M oxone in water was added dropwise at 0 °C. After stirring at 0 °C for 2.5 h, an additional 130 mL of 1 M oxone in water was added dropwise. The reaction mixture was stirred 0 °C for another 1 h and then filtered. After removal of MeOH under reduced pressure, the remaining aqueous phase was extracted with four 500 mL portions of CH_2Cl_2. The combined organic layers were washed with brine, dried, and evaporated to leave 71 g of a yellow solid. To a stirred solution of this solid in a mixture of 280 mL of CH_2Cl_2 and 800 mL of ether was added 5 mL of 47% aqueous HBr. After being stirred at rt for 45 min, the reaction mixture was cooled to 0 °C and mixed with 250 mL of saturated aqueous $NaHCO_3$. The two-phase mixture was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with brine, dried, and evaporated to leave 67 g of a brown solid. To a stirred solution of this solid in 1.4 L of CH_2Cl_2 was added 105 mL of trimethyl orthoformate and 1.4 g of TsOH. After being stirred at rt for 2.5 h, the reaction mixture was quenched with 15 mL of Et_3N, washed with brine, dried, and evaporated to leave 82 g of a brown oil. To a stirred solution of this oil in 1 L of dry MeOH was added dropwise 200 mL of 0.076 M NaOMe in dry MeOH. The reaction mixture was stirred at rt overnight and concentrated under reduced pressure to a volume of ca. 250 mL. After addition of 2 L of CH_2Cl_2, the organic layer was washed with 200 mL of water and 400 mL of brine, dried, and evaporated to leave 55 g of a dark brown oil. This oil was taken up in 400 mL of diisopropyl ether and filtered. Evaporation of the filtrate afforded 50 g of crude octahydro-4-hydroxy-7,7-dimethoxy-4a-methyl-1(2*H*)-naphthalenone as a light brown oil.[60] This oil was dissolved in 270 mL of dry DMF, and then 35.0 g (515 mmol) of imidazole and 37.4 g (248 mmol) of TBDMSCl were added. The reaction mixture was stirred at rt overnight and then poured into 600 mL of ice−water. The aqueous layer was extracted with five 250-mL portions of petroleum ether (bp 40−60 °C). The combined organic layers were washed with brine, dried, and evaporated to leave ca. 70 g of crude **8**. Flash chromatography (20:1 to 3:1 petroleum ether (bp 40−60 °C)/EtOAc) and recrystallization from dry EtOH afforded 44.4 g (31% overall from **7**) of pure **8**. The spectroscopic data of **8** were identical with those reported in the literature.[20b]

(4α,4aα,8a*β*)-(±)-Octahydro-7,7-dimethoxy-4a-methyl-4-[(methylsulfonyl)oxy]-1(2*H*)-naphthalenone (9). The procedures described above for the synthesis of **8** were employed with the exception of the silylation step which was replaced by the following mesylation procedure. To a stirred solution of 14.9 g of crude octahydro-4-hydroxy-7,7-dimethoxy-4a-methyl-1(2*H*)-naphthalenone in 100 mL of pyridine was added 11 mL (143 mmol) of MsCl at 0 °C. The reaction mixture was allowed to come to rt, stirred for 4 h, and concentrated under reduced pressure. The concentrate was taken up in EtOAc, mixed with saturated aqueous $NaHCO_3$, and stirred for 10 min. After addition of water and separation of the two-phase mixture, the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (3:1 to 1:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 16.13 g (55% overall from **7**) of **9** as an oil: ^{1}H NMR δ 0.82 (s, 3 H), 0.90−2.51 (m, 11 H), 3.02 (s, 3 H), 3.06 (s, 3 H), 3.16 (s, 3 H), 4.81 (dd, J = 4.5, 11.5 Hz, 1 H); ^{13}C NMR δ 11.29 (q), 26.79 (t), 27.39 (t), 27.90 (t), 33.25 (t), 38.10 (t), 38.79 (q), 41.37 (s), 47.43 (q), 47.74 (q), 51.07 (d), 85.68 (d), 99.56 (s), 208.04 (s); MS m/z (relative intensity) 320 (M^+, 23), 289 (54), 224 (25), 193 (46), 114 (41), 101 (100), 88 (28), 84 (40); HRMS calcd for $C_{14}H_{24}O_6S$ (M^+) 320.1294, found 320.1290.

(4aα,5α,8a*β*)-(±)-Decahydro-2,2-dimethoxy-8-(1-methoxymethylene)-4a-methyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]naphthalene (10). To 210 mL of 0.40 M (dimethylsulfinyl)sodium in DMSO was added with stirring 100 mL of THF at rt. The solution was cooled to 0 °C and, after addition of a slurry of 30.0 g (85 mmol) of (methoxymethyl)-triphenylphosphonium chloride in 50 mL of DMSO, stirred at 0 °C for 1 h. To the dark red reaction mixture was then added, via syringe, a solution of 14.81 g (41.6 mmol) of **8** in 40 mL of THF. Stirring was continued at 0 °C for 0.5 h and at rt for 1 h. The reaction mixture was poured into ice−water and extracted with ether. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (100:1 to 12:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 14.25 g (89%) of **10** as a clear oil: ^{1}H NMR δ 0.00 (s, 6 H), 0.66 (s, 3 H), 0.84 (s, 9 H), 1.05−1.94 (m, 10 H), 2.76 (ddd, J = 2.0, 4.5, 11.0 Hz, 1 H), 3.11 (s, 3 H), 3.19 (s, 3 H), 3.30 (dd, J = 4.3, 10.9 Hz, 1 H), 3.51 (s, 3 H), 5.47 (br s, 1 H); ^{13}C NMR δ −4.75 (q), −3.93 (q), 9.57 (q), 18.03 (s), 23.75 (t), 25.85 (3 q), 28.34 (t), 29.67 (t), 31.07 (t), 33.59 (t), 40.44 (s), 41.15 (d), 47.45 (q), 47.49 (q), 59.45 (q), 79.54 (d), 100.57 (s), 117.54 (s), 139.58 (d); MS m/z (relative intensity) 352 (M^+ − 32, 100), 295 (47), 263 (28), 221 (27), 220 (67), 189 (80), 157 (35), 75 (30), 73 (23); HRMS calcd for $C_{21}H_{40}O_4Si$ (M^+) 384.2696, found 384.2699.

(1α,4a*β*,8aα)-(±)-Decahydro-6,6-dimethoxy-4-(1-methoxymethylene)-8a-methyl-1-naphthalenol Methanesulfonate (11). To a stirred suspension of 6.08 g (17.2 mmol) of (methoxymethyl)triphenylphosphonium chloride in 45 mL of THF was added dropwise 35.4 mL of KHMDS (15% in toluene) at −40 °C. When the addition was complete, the reaction mixture was stirred at 0 °C for 20 min. To the resulting deep red solution was added, via syringe, a solution of 1.891 g (5.91 mmol) of **9** in 10 mL of THF. After being stirred at 0 °C for 15 min, the reaction mixture was allowed to come to rt and then stirred for an additional 4 h. The brown reaction mixture was poured into water and extracted with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (2:1 petroleum ether (bp 40−60 °C)/EtOAc) afforded 0.977 g (2.81 mmol, 48%) of **11**: mp 118 °C (from diisopropyl ether); ^{1}H NMR δ 0.75 (s, 3 H), 1.07−2.08 (m, 10 H), 2.85 (dd, J = 2.2, 9.0 Hz, 1 H), 2.97 (s, 3 H), 3.09 (s, 3 H), 3.18 (s, 3 H), 3.52 (s, 3 H), 4.42 (dd, J = 4.9, 11.2 Hz, 1 H), 5.51 (br s, 1 H); ^{13}C NMR δ 10.17 (q), 23.33 (t), 27.70 (t), 28.44 (t), 29.49 (t), 32.91 (t), 38.77 (q), 39.43 (s), 41.31 (d), 47.46 (q), 47.59 (q), 59.57 (q), 89.99 (d), 99.94 (s), 115.08 (s), 140.61 (d); MS m/z (relative intensity) 316 (M^+ − 32, 100), 285 (37), 271 (14), 221 (21), 220 (15), 205 (17), 189 (23), 173 (11), 101 (12), 85 (20), 83 (26), 79 (12); HRMS calcd for $C_{15}H_{24}O_5S$ (M^+ − 32) 316.1344, found 316.1340. Anal. Calcd for $C_{16}H_{28}O_6S$: C, 55.15; H, 8.10. Found: C, 54.96; H, 8.13.

(59) The reaction sequence employed for the synthesis of crude (4aα,5α)-(±)-4,4a,5,6,7,8-hexahydro-5-hydroxy-4a-methyl-2(3*H*)-naphthalenone from 2-methylcyclohexane-1,3-dione and MVK involved (a) Michael addition (1 mol % of hydroquinone, water, 50 °C, 2 days), (b) cyclization (0.15 equiv of pyrrolidine, toluene, 100 °C), and (c) reduction ($NaBH_4$, EtOH, 0 °C). In all cases, the crude product of each individual step was used for the next reaction. See: (a) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1612. (b) Marshall, J. A.; Seitz, D. E.; Snyder, W. R.; Goldberg, B. *Synth. Commun.* **1974**, *4*, 79. (c) Boyce, C. B. C.; Whitehurst, J. S. *J. Chem. Soc.* **1960**, 2680.

(60) The ^{1}H NMR spectrum of crude octahydro-4-hydroxy-7,7-dimethoxy-4a-methyl-1(2*H*)-naphthalenone was identical with that reported in ref 20a.

(4aα,5α,8a*β*)-(±)-Octahydro-8-(1-methoxymethylene)-4a-methyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2(3*H*)-naphthalenone (12). To a solution of 16.2 g (42.2 mmol) of **10** in 250 mL of acetone and 25 mL of water was added 5 g of PPTS. After being stirred at rt for 1 h, the reaction mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, and dried. Evaporation and flash chromatography (10:1 petroleum ether (bp 40−60 °C)/EtOAc) afforded 13.98 g (98%) of **12** as a white solid: mp 101 °C (from diisopropyl ether); ^{1}H NMR δ 0.01 (s, 3 H), 0.03 (s, 3 H), 0.86 (s, 9 H), 0.88 (s, 3 H), 1.10−1.69 (m, 6 H), 2.03−2.50 (m, 4 H), 2.82 (dd, J = 3.9, 10.5 Hz, 1 H), 3.31 (dd, J = 4.7, 10.7 Hz, 1 H), 3.54 (s, 3 H), 5.44 (br, s 1 H); ^{13}C NMR δ −4.87 (q), −3.92 (q), 9.41 (q), 17.99 (s), 23.62 (t), 25.79 (3 q), 30.71 (t), 36.80 (t), 37.64 (t), 39.69 (t), 40.27 (s), 45.26 (d), 59.59 (q), 79.31 (d), 116.41 (s), 140.33 (d), 211.64 (s); MS m/z (relative intensity) 338 (M^+, 21), 282 (24), 281 (100), 206 (48), 189 (21), 171 (30), 75 (33), 73 (16); HRMS calcd for $C_{19}H_{34}O_3Si$ (M^+) 338.2277, found 338.2274. Anal. Calcd for $C_{19}H_{34}O_3Si$: C, 67.42; H, 10.13. Found: C, 67.53; H, 10.38.

(4aα,5α,8a*β*)-(±)-Octahydro-8-(1-methoxymethylene)-4a-methyl-5-[(methylsulfonyl)oxy]-2(3*H*)-naphthalenone (13). The mesylate **11** (1.396 g, 4.01 mmol) was treated with PPTS for 1.5 h as described for **10**. Workup and flash chromatography (2:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 1.123 g (93%) of **13** as a white solid: mp 107 °C (from diisopropyl ether/acetone); ^{1}H NMR δ 0.98 (s, 3 H), 1.52−1.90 (m, 3 H), 2.02−2.42 (m, 7 H), 2.93 (ddd, J = 2.3, 2.3, 10.5 Hz, 1 H), 3.00 (s, 3 H), 3.56 (s, 3 H), 4.44 (dd, J = 4.9, 11.4 Hz, 1 H), 5.51 (br s, 1 H); ^{13}C NMR δ 10.02 (q), 23.23 (t), 28.18 (t), 35.87 (t), 37.03 (t), 39.01 (q), 39.20 (t), 39.24 (s), 45.13 (d), 59.80 (q), 88.84 (d), 114.01 (s), 141.50 (d), 209.80 (s); MS m/z (relative intensity) 302 (M^+, 94), 207 (40), 206 (100), 191 (24), 174 (23), 159 (17), 135 (20), 132 (17), 131 (18), 119 (23), 105 (18), 79 (17); HRMS calcd for $C_{14}H_{22}O_5S$ (M^+) 302.1188, found 302.1189. Anal. Calcd for $C_{14}H_{22}O_5S$: C, 55.61; H, 7.33. Found: C, 55.38; H, 7.34.

(2α,4a*β*,5*β*,8aα)- and (2α,4aα,5α,8a*β*)-(±)-Decahydro-8-(1-methoxymethylene)-4a-methyl-2-(1-methylethyl)-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-naphthalenol (14 and 15). Anhydrous $CeCl_3$ (prepared from 3.15 g (8.45 mmol) of $CeCl_3 \cdot 7H_2O$ according to the procedure of Imamoto *et al.*)[23a] and 20 mL of THF were mixed at 0 °C and stirred at rt overnight under Ar. The flask was then placed in an ultrasonic bath for 1.5 h. To the resulting fine dispersion was added, via syringe, 8.3 mL of *i*-PrMgCl (ca. 1 M in ether) at 0 °C. The mixture was stirred at 0 °C for 2.5 h and then, via syringe, a solution of 0.940 g (2.78 mmol) of **12** in 10 mL of THF was added. After being stirred at 0 °C for another 0.5 h, the reaction mixture was treated with concentrated aqueous KF and extracted with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (20:1 to 12:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.859 g (81%) of **14** and 0.170 g (16%) of **15**, both as white solids. The physical and spectroscopic data of **14** and **15** are shown below.

14: mp 77−78 °C (from pentane); ^{1}H NMR δ 0.03 (s, 6 H), 0.63 (s, 3 H), 0.86 (s, 9 H), 0.93 (d, J = 6.9 Hz, 3 H), 0.94 (d, J = 6.9 Hz, 3 H), 0.97 (s, OH), 1.34−1.70 (m, 10 H), 2.10 (dd, J = 4.15, 13.5 Hz, 1 H), 2.79 (ddd, J = 1.6, 1.6, 13.4 Hz, 1 H), 3.36 (dd, J = 4.4, 11.4 Hz, 1 H), 3.54 (s, 3 H), 5.48 (s, 1 H); ^{13}C NMR δ −4.78 (q), −3.96 (q), 9.11 (q), 16.78 (q), 16.84 (q), 18.02 (s), 23.77 (t), 25.83 (3 q), 28.98 (t), 31.09 (t), 31.27 (t), 32.31 (t), 39.00 (d), 39.65 (d), 40.37 (s), 59.38 (q), 73.30 (s), 79.61 (d), 118.35 (s), 139.33 (d); MS m/z (relative intensity) 382 (M^+, 3), 364 (58), 322 (29), 321 (100), 232 (34), 189 (50), 163 (21), 132 (28), 123 (20), 75 (30), 73 (24); HRMS calcd for $C_{22}H_{42}O_3Si$ (M^+) 382.2903, found 382.2900. Anal. Calcd for $C_{22}H_{42}O_3Si$: C, 69.07; H, 11.07. Found: C, 69.03; H, 11.31.

15: mp 131−133 °C (from pentane); ^{1}H NMR δ 0.02 (s, 6 H), 0.72 (s, 3 H), 0.85 (s, 9 H), 0.85 (d, J = 6.8 Hz, 3 H), 0.91 (d, J = 6.8 Hz, 3 H), 0.95−1.86 (m, 11 H), 2.01 (septet, J = 6.8 Hz, 1 H), 2.77 (dd, J = 2.2, 9.8 Hz, 1 H), 3.27 (dd, J = 4.2, 10.9 Hz, 1 H), 3.53 (s, 3 H), 5.52 (br s, 1 H); ^{13}C NMR δ −4.77 (q), −3.93 (q), 10.33 (q), 15.93 (q), 16.07 (q), 18.00 (s), 23.79 (t), 25.81 (3 q), 28.84 (d), 31.12 (t), 31.97 (t), 33.45 (t), 34.17 (t), 40.43 (s), 41.61 (d), 59.43 (q), 74.11 (s), 79.99 (d), 117.38 (s), 139.82 (d); MS m/z (relative intensity) 382 (M^+, 41), 339 (31), 325 (31), 308 (27), 307 (100), 275 (54), 250 (84), 232 (31), 75 (56), 73 (34), 71 (30), 43 (39); HRMS calcd for $C_{22}H_{42}O_3Si$ (M^+) 382.2903, found 382.2900. Anal. Calcd for $C_{22}H_{42}O_3Si$: C, 69.07; H, 11.07. Found: C, 69.21; H, 11.34.

(1α,4a*β*,6*β*)-(±)-Decahydro-4-(1-methoxymethylene)-8a-methyl-6-(1-methylethyl)-1,6-naphthalenediol (16). To a solution of 0.865 g (2.26 mmol) of **14** in 15 mL of dry DMSO was added at once 5.13 mL of TBAF (1.1 M in THF) at 100 °C. The resulting brown reaction mixture was stirred at 100 °C for 80 min, poured into water, and extracted with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (2:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.522 g (87%) of **16**: mp 99 °C (from pentane/diisopropyl ether); ^{1}H NMR δ 0.63 (s, 3 H), 0.93 (d, J = 6.8 Hz, 6 H), 1.10 (br s, OH), 1.32−1.80 (m, 11 H), 2.12 (dd, J = 5.0, 10.8 Hz, 1 H), 2.82 (ddd, J = 2.1, 2.1, 13.6 Hz, 1 H), 3.39 (dd, J = 4.3, 11.0 Hz, 1 H), 3.54 (s, 3 H), 5.48 (br s, 1 H); ^{13}C NMR δ 8.93 (q), 16.80 (2 q), 23.76 (t), 28.84 (t), 30.38 (t), 30.97 (t), 31.66 (t), 38.98 (d), 39.43 (d), 39.76 (s), 59.41 (q), 73.21 (s), 79.18 (d), 117.87 (s), 139.58 (d); MS m/z (relative intensity) 268 (M^+, 2), 250 (15), 208 (14), 207 (100), 175 (17), 131 (14), 69 (5); HRMS calcd for $C_{16}H_{28}O_3$ (M^+) 268.2038, found 268.2036. Anal. Calcd for $C_{16}H_{28}O_3$: C, 71.60; H, 10.52. Found: C, 71.85; H, 10.73.

(2α,4a*β*,5*β*,8aα)-(±)-Decahydro-8-(1-methoxymethylene)-4a-methyl-2-(1-methylethyl)-5-[(methylsulfonyl)oxy]-2-naphthalenol (17). a. To a stirred solution of 0.194 g (0.72 mmol) of **16** in 3 mL of pyridine was added 0.084 mL (1.09 mmol) of MsCl at rt. The reaction mixture was stirred at rt for 1.5 h and, after addition of water, extracted with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (3:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.247 g (99%) of **17**: mp 101 °C (from diisopropyl ether); ^{1}H NMR δ 0.66 (s, 3 H), 0.86 (d, J = 6.8 Hz, 6 H), 1.20−2.01 (m, 11 H), 2.18 (br d, J = 9.8 Hz, 1 H), 2.81 (dd, J = 2.1, 9.1 Hz, 1 H), 2.93 (s, 3 H), 3.49 (s, 3 H), 4.41 (dd, J = 4.8, 11.2 Hz, 1 H), 5.47 (br s, 1 H); ^{13}C NMR δ 9.74 (q), 16.76 (2 q), 23.38 (t), 28.48 (t), 28.64 (t), 30.65 (t), 31.72 (t), 38.57 (q), 38.82 (d), 39.41 (d), 39.63 (s), 59.45 (q), 72.79 (s), 90.49 (d), 115.84 (s), 140.37 (d); MS m/z (relative intensity) 328 (M^+ − 18, 12), 287 (7), 286 (19), 285 (100), 207 (7), 189 (11), 157 (10), 83 (8); HRMS calcd for $C_{17}H_{28}O_4S$ (M^+ − 18) 328.1708, found 328.1708. Anal. Calcd for $C_{17}H_{30}O_5S$: C, 58.93; H, 8.73. Found: C, 59.14; H, 8.93.

b. The procedure described above for the organocerium addition to **12** was employed, except that the reaction mixture was stirred at 0 °C for 2.5 h. Starting from 1.126 g of mesylate **13** (3.73 mmol), workup and flash chromatography (2:1 petroleum ether (bp 40−60 °C)/EtOAc) afforded 1.197 g (93%) of pure **17** as the sole product.

(1α,4α,4aα,7*β*,8a*β*)-(±)-Decahydro-7-hydroxy-4a-methyl-7-(1-methylethyl)-4-[(methylsulfonyl)oxy]-1-naphthalenecarboxaldehyde (3). To a stirred solution of 0.500 g (1.44 mmol) of **17** in 20 mL of ether was added dropwise 4 mL of 35% aqueous $HClO_4$ at 0 °C. The solution was allowed to come to rt and stirred for 1 h. After addition of water, the reaction mixture was extracted with EtOAc. The combined organic layers were washed with saturated aqueous $NaHCO_3$ (twice) and brine, dried over Na_2SO_4, and evaporated. Flash chromatography (1:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.463 g (97%) of **3** as an oil:[61] ^{1}H NMR δ 0.68 (s, 3 H), 0.86 (d, J = 6.8 Hz, 6 H), 1.30−2.32 (m, 14 H), 2.92 (s, 3 H), 4.30 (dd, J = 6.0, 10.4 Hz, 1 H), 9.82 (br s, 1 H); ^{13}C NMR δ 11.39 (q), 16.63 (q), 16.72 (q), 23.03 (t), 25.49 (t), 29.51 (t), 32.91 (t), 33.60 (t), 38.65 (d), 38.76 (q), 39.07 (s), 40.31 (d), 49.86 (d), 73.29 (s), 89.64 (d), 203.74 (d); MS m/z (relative intensity) 289 (M^+ − 43, 100), 261 (37), 193 (98), 163 (31), 147 (52), 105 (30), 83 (30), 81 (44), 57 (37), 55 (38), 43 (52); HRMS calcd for $C_{13}H_{21}O_5S$ (M^+ − 43) 289.11097, found 289.11095.

(*E*,*E*)-2-Ethylidene-6,10-dimethyl-9-oxo-5-undecenal (18). To a stirred solution of 1.46 mL of KHMDS (0.5 M in toluene) in 4 mL of dry THF was added dropwise, via syringe, a solution of 0.097 g (0.29 mmol) of **3** in 2 mL of THF at rt.

(61) Aldehyde **3** was susceptible to air oxidation and had to be stored under N_2 in the refrigerator.

The reaction mixture was stirred at rt for 10 min and, after addition of saturated aqueous NH_4Cl, extracted with EtOAc. The combined organic layers were washed with brine and dried over Na_2SO_4. After evaporation at rt, the remaining residue (0.057 g) was taken up in a 4:1 mixture of petroleum ether (bp 40−60 °C) and ether and filtered over a short neutral alumina column to give 0.014 g (20%) of **18**: ^{1}H NMR δ 1.07 (d, J = 6.9 Hz, 6 H), 1.56 (br s, 3 H), 1.97 (d, J = 7.1 Hz, 3 H), 2.00−2.51 (m, 8 H), 2.56 (septet, J = 6.9 Hz, 1 H), 5.10 (dd, J = 5.8, 6.5 Hz, 1 H), 6.56 (dd, J = 7.1, 14.1 Hz, 1 H), 9.34 (s, 1 H); ^{13}C NMR δ 14.87 (q), 16.02 (q), 18.22 (2 q), 23.61 (t), 26.61 (t), 33.39 (t), 38.92 (t), 40.84 (d), 123.75 (d), 134.85 (s), 144.25 (s), 150.10 (d), 194.97 (d), 214.81 (s); MS m/z (relative intensity) 236 (M^+, 46), 193 (33), 150 (76), 138 (45), 135 (100), 133 (50), 121 (47), 109 (41), 107 (59), 81 (63), 71 (88), 43 (60); HRMS calcd for $C_{15}H_{24}O_2$ (M^+) 236.1776, found 236.1772.

(1α,4α,4aα,7*β*,8a*β*)-(±)-Decahydro-4a-methyl-7-(1-methylethyl)-7-[(trimethylsilyl)oxy]-4-[(methylsulfonyl)oxy]-1-naphthalenecarboxaldehyde (19). To a stirred solution of 0.525 g (1.58 mmol) of **3** in 15 mL of pyridine was added 0.34 mL (1.6 mmol) of hexamethyldisilazane and 0.63 mL (4.8 mmol) of TMSCl at 0 °C. After being stirred at 0 °C for 3 h, the reaction mixture was poured into ice−water and extracted with EtOAc. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried, and evaporated. Flash chromatography (3:2 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.510 g (80%) of **19** as an oil: ^{1}H NMR δ 0.12 (s, 9 H), 0.74 (s, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 0.91 (d, J = 6.8 Hz, 3 H), 1.42−1.60 (m, 6 H), 1.72 (septet, J = 6.8 Hz, 1 H), 1.81−2.38 (m, 6 H), 2.97 (s, 3 H), 4.31 (dd, J = 6.0, 10.6 Hz, 1 H), 9.86 (d, J = 0.7 Hz, 1 H); ^{13}C NMR δ 2.66 (3 q), 11.75 (q), 17.48 (q), 17.56 (q), 23.12 (t), 25.51 (t), 28.61 (t), 32.52 (t), 33.91 (t), 38.37 (q), 38.79 (d), 39.09 (s), 40.49 (d), 49.94 (d), 78.58 (s), 89.94 (d), 203.69 (d); MS m/z (relative intensity) 361 (M^+ − 43, 100), 347 (15), 333 (40), 171 (15); HRMS calcd for $C_{16}H_{29}O_5SSi$ (M^+ − 43) 361.1505, found 361.1506.

(±)-2-[2-Ethenyl-2-methyl-5-(1-methylethyl)-5-[(trimethylsilyl)oxy]-1-cyclohexyl]-2-propenal (21). The TMS ether **19** (0.157 g, 0.39 mmol) was treated with KHMDS for 15 min as described for **3**. After workup, the remaining residue (0.120 g) was flash chromatographed (10:1 petroleum ether (bp 40−60 °C)/EtOAc) to give 0.043 g (36%) of **21**:[62] ^{1}H NMR δ 0.13 (s, 9 H), 0.85 (s, 3 H), 0.91 (d, J = 6.8 Hz, 6 H), 1.03−2.0 (m, 7 H), 3.21 (dd, J = 3.2, 13.4 Hz, 1 H), 4.71 (dd, J = 1.4, 17.3 Hz, 1 H), 4.77 (dd, J = 1.4, 10.9 Hz, 1 H), 5.68 (dd, J = 10.9, 17.3 Hz, 1 H), 6.01 (br s, 1 H), 6.06 (br s, 1 H), 9.38 (s, 1 H); ^{13}C NMR δ 2.56 (3 q), 14.20 (q), 17.44 (q), 17.54 (q), 28.72 (t), 34.42 (t), 34.68 (t), 36.38 (d), 38.72 (d), 39.46 (s), 78.42 (s), 110.26 (t), 134.88 (t), 149.19 (d), 151.95 (s), 194.22 (d); MS m/z (relative intensity) 265 (M^+ − 43, 19), 86 (51), 84 (100), 51 (27), 50 (92); HRMS calcd for $C_{15}H_{25}O_2Si$ (M^+ − 43) 265.1624, found 265.1623.

(1α,4a*β*,8aα)-(±)-Decahydro-4-(1-methoxymethylene)-8a-methyl-6-(1-methylethylidene)-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]naphthalene (22). To a stirred solution of 150 mL of 0.50 M (dimethylsulfinyl)sodium in DMSO was added a slurry of 32.5 g (75.2 mmol) of isopropyltriphenylphosphonium iodide in 30 mL of DMSO at rt. The reaction mixture was stirred at rt for 1.5 h.[63] To the resulting deep red solution was added, via syringe, a solution of 9.90 g (29.3 mmol) of **12** in 60 mL of THF. After being stirred at rt overnight, the reaction mixture was poured into ice−water and extracted with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. Repeated flash chromatography (50:1 petroleum ether (bp 40−60 °C)/*tert*-butyl methyl ether) gave 8.897 g (83%) of **22**: ^{1}H NMR δ 0.00 (s, 6 H), 0.75 (s, 3 H), 0.85 (s, 9 H), 1.57 (br s, 6 H), 0.93−1.96 (m, 8 H), 2.41−2.58 (m, 2 H), 2.77 (dd, J = 4.2, 9.7 Hz, 1 H), 3.23 (dd, J = 5.0, 10.9 Hz, 1 H), 3.55 (s, 3 H), 5.55 (s, 1 H); ^{13}C NMR δ −4.76 (q), −3.90 (q), 9.86 (q), 18.08 (s), 19.99 (q), 20.09 (q), 23.77 (t), 25.36 (t), 25.91 (3 q), 27.10 (t), 31.15 (t), 38.26 (t), 40.88 (s), 46.29 (d), 59.55 (q), 79.92 (d), 118.50 (s), 120.70 (s), 131.25 (s), 139.64 (d); MS m/z (relative intensity) 364 (M^+, 50), 307 (70), 232 (100), 231 (61), 145 (30), 84 (31), 75 (54), 73 (36); HRMS calcd for $C_{22}H_{40}O_2Si$ (M^+) 364.2798, found 364.2793.

(1α,4α,4aα,8a*β*)-(±)-Decahydro-4a-methyl-7-(1-methylethylidene)-4-[(methylsulfonyl)oxy]-1-naphthalenecarboxaldehyde (6). The TBDMS ether **22** (8.897 g, 24.4 mmol) was desilylated with TBAF for 45 min as described for **14**. Workup and flash chromatography (10:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 5.429 g (89%) of the corresponding alcohol: mp 131 °C (from diisopropyl ether); ^{1}H NMR δ 0.76 (s, 3 H), 1.65 (br s, 6 H), 1.00−1.18 (m, 2 H), 1.35−1.98 (m, 7 H), 2.43−2.58 (m, 2 H), 2.82 (ddd, J = 2.2, 4.6, 11.2 Hz, 1 H), 3.28 (dd, J = 4.1, 11.0 Hz, 1 H), 3.57 (s, 3 H), 5.58 (br s, 1 H); ^{13}C NMR δ 9.59 (q), 19.97 (q), 20.07 (q), 23.67 (t), 25.06 (t), 26.87 (t), 30.36 (t), 37.42 (t), 40.23 (s), 45.97 (d), 59.50 (q), 79.53 (d), 117.87 (s), 121.20 (s), 130.63 (s), 139.91 (d); MS m/z (relative intensity) 250 (M^+, 100), 232 (8), 218 (11), 207 (16), 168 (54), 153 (71), 135 (40), 93 (20); HRMS calcd for $C_{16}H_{26}O_2$ (M^+) 250.1933, found 250.1929. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.36; H, 10.66. A solution of this alcohol (7.114 g, 28.5 mmol) in pyridine was treated with MsCl as described for **16**. Workup and flash chromatography (10:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 9.24 g (99%) of the corresponding mesylate: mp 103 °C (from pentane/diisopropyl ether); ^{1}H NMR δ 0.81 (s, 3 H), 1.14 (ddd, J = 4.1, 9.3, 9.3 Hz, 1 H), 1.60 (br s, 6 H), 1.60−2.00 (m, 7 H), 2.40−2.56 (m, 2 H), 2.83 (ddd, J = 2.3, 2.3, 9.1 Hz, 1 H), 2.93 (s, 3 H), 3.30 (s, 3 H), 4.30 (dd, J = 4.9, 11.2 Hz, 1 H), 5.53 (br s, 1 H); ^{13}C NMR δ 10.42 (q), 19.99 (q), 20.07 (q), 23.33 (t), 24.83 (t), 26.65 (t), 28.49 (t), 37.52 (t), 38.67 (q), 39.88 (s), 46.26 (d), 59.54 (q), 90.42 (d), 115.86 (s), 121.81 (s), 129.66 (s), 140.74 (d); MS m/z (relative intensity) 328 (M^+, 41), 285 (22), 246 (16), 232 (33), 217 (14), 189 (20), 135 (43), 73 (100); HRMS calcd for $C_{17}H_{28}O_4S$ (M^+) 328.1708, found 328.1705. Anal. Calcd for $C_{17}H_{28}O_4S$: C, 62.16; H, 8.59. Found: C, 61.86; H, 8.79. A solution of this mesylate (2.38 g, 7.26 mmol) in ether was treated with 35% $HClO_4$ for 3.5 h as described for **17**. Workup and recrystallization from diisopropyl ether/acetone afforded 2.228 g (98%) of **6**: mp 126 °C; ^{1}H NMR δ 0.89 (s, 3 H), 1.14 (ddd, J = 4.2, 9.4, 9.4 Hz, 1 H), 1.38 (m, 1 H), 1.65 (s, 3 H), 1.68 (s, 3 H), 1.60−1.99 (m, 5 H), 2.24−2.46 (m, 3 H), 2.55−2.76 (m, 2 H), 2.98 (s, 3 H), 4.29 (dd, J = 6.9, 9.3 Hz, 1 H), 9.96 (d, J = 1.0 Hz, 1 H); ^{13}C NMR δ 11.83 (q), 20.03 (q), 20.07 (q), 22.92 (t), 24.98 (t), 25.51 (t), 29.22 (t), 38.83 (q), 39.21 (t), 39.51 (s), 46.96 (d), 50.42 (d), 89.61 (d), 122.42 (s), 129.49 (s), 203.40 (d); MS m/z (relative intensity) 314 (M^+, 10), 218 (11), 189 (9), 147 (8), 136 (9), 135 (100), 107 (8); HRMS calcd for $C_{16}H_{26}O_4S$ (M^+) 314.1552, found 314.1547. Anal. Calcd for $C_{16}H_{26}O_4S$: C, 61.11; H, 8.33. Found: C, 61.24; H, 8.61.

(*E*,*E*)-7-Methyl-4-(1-methylethylidene)-1,7-cyclodecadienecarboxaldehyde (23). To a stirred solution of 0.053 g (0.17 mmol) of **6** in 2 mL of THF was added 0.37 mL of KHMDS (0.5 M in toluene) at −78 °C. The reaction mixture was stirred at −78 °C for 10 min and, after removal of the dry-ice bath, for an additional 25 min. After addition of ether, the reaction mixture was washed with water and brine, dried, and evaporated. Column chromatography on neutral alumina (5:1 petroleum ether (bp 40−60 °C)/*tert*-butyl methyl ether) afforded 0.010 g (27%) of **23**: ^{1}H NMR δ 1.34 (s, 3 H), 1.65 (s, 3 H), 1.73 (s, 3 H), 1.95−2.36 (m, 8 H), 2.98 (m, 2 H), 5.13 (dd, J = 7.8, 7.8 Hz, 1 H), 6.49 (dd, J = 8.5, 8.5 Hz, 1 H), 9.28 (s, 1 H); ^{13}C NMR δ 18.96 (q), 20.48 (q), 21.19 (q), 23.10 (t), 25.99 (t), 33.51 (t), 36.40 (t), 37.20 (t), 123.61 (d), 128.50 (s), 128.99 (s), 135.70 (s), 140.36 (s), 155.09 (d), 195.94 (d); MS m/z (relative intensity) 218 (M^+, 100), 190 (9), 175 (68), 162 (57), 136 (71), 135 (52), 122 (54), 121 (82), 107 (91), 105 (48), 93 (68), 91 (65), 79 (59), 67 (46); calcd for $C_{15}H_{22}O$ (M^+) 218.1671, found 218.1678.

(*E*,*E*)-7-Methyl-4-(1-methylethylidene)-1,7-cyclodecadienemethanol (24). To a degassed solution of 0.111 g (0.35 mmol) of **6** in 3 mL of toluene was added with stirring 0.74 mL of KHMDS (0.5 M in toluene) at −40 °C under an Ar atmosphere. After being stirred at −40 °C for 30 min, the reaction mixture was gradually warmed to 0 °C over a period of 20 min. The yellowish reaction mixture was cooled to −78 °C, and then excess Red-Al (65% in toluene) was added dropwise. After being stirred at −78 °C for 10 min, the reaction mixture was allowed to come to rt and carefully

(62) The NMR spectra of **21** revealed the presence of a trace amount of an isomer.

(63) Shorter reaction times led to lower yields.

quenched with 1 mL of water. The reaction mixture was then diluted with EtOAc, dried, and evaporated. The remaining residue (0.091 g) was flash chromatographed (5:1 hexane/*tert*-butyl methyl ether) to afford 0.059 g (77%) of **24**: ^{1}H NMR (C_6D_6) δ 1.51 (d, J = 1.2 Hz, 3 H), 1.65 (s, 3 H), 1.71 (s, 3 H), 1.95−2.3 (m, 9 H), 2.79 (m, 2 H), 3.93 (s, 2 H), 5.25 (br m, 1 H), 5.65 (dd, J = 8.2, 8.2 Hz, 1H); ^{13}C NMR (C_6D_6) δ 18.47 (q), 20.32 (q), 20.96 (q), 25.94 (t), 26.91 (t), 33.53 (t), 34.76 (t), 37.92 (t), 67.40 (t), 123.84 (d), 126.29 (d), 126.67 (s), 131.54 (s), 135.17 (s), 135.73 (s); MS *m*/*z* (relative intensity) 220 (M^+, 26), 205 (12), 202 (26), 189 (48), 136 (38), 133 (37), 121 (66), 107 (36), 93 (44), 91 (49), 31 (100); HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827, found 220.1827.

(*E*,*Z*)-1,5-Dimethyl-8-(1-methylethylidene)-1,5-cyclodecadiene (25). To a stirred solution of 0.078 g (0.35 mmol) of **24** and 0.7 mL of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine in 3 mL of THF was added dropwise 0.26 mL of BuLi (1.6 M in hexane) at −78 °C. The reaction mixture was stirred at −78 °C for 15 min, and then 0.075 mL (0.52 mmol) of TMPDCl was added. After being stirred at −78 °C for 5 min, the reaction mixture was allowed to come to rt and stirred for an additional 1 h. The reaction mixture was then added, via syringe, to a solution of 0.09 g (12.9 mmol) of Li in 25 mL of $EtNH_2$ at 0 °C. Stirring was continued at 0 °C for 25 min, and excess aqueous NH_4Cl was added. The reaction mixture was stirred for another 40 min and extracted with pentane. The combined organic layers were washed with brine, dried, and carefully evaporated. Repeated flash chromatography (pentane) gave 0.017 g (23%) of (*Z*)-1,7-dimethyl-4-(1-methylethenyl)cyclodecene[64] and 0.030 g (42%) of **25**: ^{1}H NMR δ 1.54 (d, J = 1.2 Hz, 3 H), 1.66 (s, 3 H), 1.70 (s, 6 H), 2.02−2.25 (m, 8 H), 2.67 (m, 2 H), 5.18 (dd, J = 7.8, 7.8 Hz, 1 H), 5.31 (ddd, J = 1.2, 8.2, 8.2 Hz, 1 H); ^{13}C NMR δ 18.44 (q), 20.48 (q), 21.06 (q), 24.41 (q), 25.11 (t), 30.96 (t), 33.39 (t), 34.84 (t), 37.91 (t), 123.69 (d), 125.24 (d), 126.70 (s), 131.49 (s), 131.65 (s), 135.71 (s); MS *m*/*z* (relative intensity) 204 (M^+, 55), 189 (35), 161 (35), 147 (20), 136 (21), 133 (35), 121 (100), 107 (50), 105 (47), 93 (54), 41 (35); HRMS calcd for $C_{15}H_{24}$ (M^+) 204.1878, found 204.1876. The ^{1}H NMR spectrum of **25** corresponded with that reported in the literature.[38]

(*Z*,*E*)-7-Methyl-4-(1-methylethylidene)-1,7-cyclodecadienecarboxaldehyde (5). To a degassed solution of 0.122 g (0.39 mmol) of **6** in 4 mL of toluene was added with stirring 0.25 mL of NaO-*t*-amyl (1.55 M in benzene)[65] at −78 °C under an Ar atmosphere. The reaction mixture was stirred at −78 °C for 10 min and then allowed to come to 0 °C. After being stirred at 0 °C for an additional 35 min, the reaction mixture was poured into water and extracted with *tert*-butyl methyl ether. The combined organic layers were washed with brine and dried. Evaporation afforded 0.082 g (97%) of almost pure **5**:[66] ^{1}H NMR (C_6D_6) δ 1.23 (s, 3 H), 1.52 (s, 3 H), 1.57 (s, 3 H), 1.9−2.45 (m, 7 H), 2.7−3.0 (m, 2 H), 3.12 (ddd, J = 1.6, 5.3, 12.3 Hz, 1 H), 4.70 (dd, J = 4.9, 11.7 Hz, 1 H), 5.58 (dd, J = 5.7, 9.9 Hz, 1 H), 9.93 (s, 1 H); ^{13}C NMR (C_6D_6)[67] δ 16.96 (q)*, 20.09 (q), 20.36 (q), 26.81 (t), 30.08 (t), 31.21 (t), 31.99 (t)*, 40.70 (t)*, 125.72 (d), 130.65 (s), 136.28 (s), 138.07 (s), 150.89 (d), 188.53 (d); MS *m*/*z* (relative intensity) 218 (M^+, 66), 203 (28), 189 (25), 175 (44), 136 (100), 135 (75), 123 (55), 122 (51), 121 (63), 107 (83), 105 (52), 96 (57), 93 (53), 91 (61), 79 (54); HRMS calcd for $C_{15}H_{22}O$ (M^+) 218.1671, found 218.1677.

(*Z*,*E*)-7-Methyl-4-(1-methylethylidene)-1,7-cyclodecadienemethanol (15-Hydroxygermacrene B) (4). To a degassed solution of 0.285 g (0.91 mmol) of **6** in 5 mL of dry toluene was added with stirring 0.59 mL of NaO-*t*-amyl (1.55 M in benzene) at −78 °C under an Ar atmosphere. After being stirred at −78 °C for 15 min, the reaction mixture was allowed to come to rt, stirred at that temperature for 15 min, and then cooled to 0 °C. Stirring was continued at 0 °C for an additional 20 min, after which the reaction mixture was cooled again to −78 °C. After dropwise addition of 1 mL of Red-Al (65% in toluene) followed by stirring at −78 °C for 15 min, excess Red-Al was destroyed by careful addition of saturated aqueous NH_4Cl. The reaction mixture was allowed to come to rt and, after addition of Na_2SO_4, stirred for 20 min. The resulting suspension was diluted with EtOAc and filtered over a short silica column. After thorough evaporation, the remaining residue was dissolved in 15 mL of *tert*-butyl methyl ether and extracted with five portions of 20% aqueous $AgNO_3$. The combined aqueous layers were washed with *tert*-butyl methyl ether and then cooled to 0 °C. After addition of 15 mL of 25% aqueous NH_3, the aqueous layer was extracted with *tert*-butyl methyl ether. The combined organic layers were washed with brine, dried, and evaporated to afford 0.143 g (72%) of **4**: ^{1}H NMR (C_6D_6)[68] δ 1.37 (br s, 3 H), 1.64 (s, 3 H), 1.67 (s, 3 H), 1.7−2.7 (m, 10 H), 3.00 (m, 1 H), 3.81 (d, AB system, J = 11.8 Hz, 1 H), 4.13 (d, AB system, J = 11.8 Hz, 1 H), 4.78 (m, 2 H); ^{13}C NMR (C_6D_6)[67] δ 16.86 (q)*, 20.15 (q), 20.48 (q), 26.39 (t), 32.13 (t), 32.78 (t)*, 34.57 (t), 40.42 (t)*, 59.71 (t), 126.18 (d), 131.39 (d), 132.80 (s)*, 135.13 (s), 136.81 (s)*; MS *m*/*z* (relative intensity) 220 (M^+, 31), 205 (18), 202 (46), 189 (82), 137 (91), 133 (63), 122 (72), 121 (100), 119 (79), 107 (96), 105 (81), 93 (87), 91 (87), 81 (93), 79 (70); HRMS calcd for $C_{15}H_{24}O$ (M^+) 220.1827, found 220.1825.

Germacrene B (26). The germacrane alcohol **4** (0.047 g, 0.21 mmol) was treated with TMPDCl and then with Li in $EtNH_2$ for 5 min as described for **24**. Workup and flash chromatography (pentane) gave, in order of elution, 0.013 g of a mixture of hydrogenated products and 0.023 g (53%) of pure germacrene B (**26**). The NMR and mass spectral data for **26** corresponded with those reported in the literature.[42b]

(2α,4aα,5α,8a*β*)- and (2*β*,4aα,5α,8a*β*)-(±)-Decahydro-8-(1-methoxymethylene)-4a-methyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-naphthalenecarbonitrile (27). To a stirred solution of 1.158 g (3.42 mmol) of **12**, 0.870 g (4.46 mmol) of TosMIC, and 0.34 mL (5.82 mmol) of dry EtOH in 20 mL of dry DME was added 0.667 g (8.6 mmol) of KO*t*-Bu at 0 °C. After being stirred at 0 °C for 5 min, the reaction mixture was warmed to 35 °C and stirred at this temperature overnight. After addition of water, the reaction mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (20:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.883 g (74%) of **27** as a 1:1 mixture of two diastereomers: ^{1}H NMR (major peaks) δ 0.00, 0.01, 0.02, 0.04 (s, s, s, s, 1:1:1:1 ratio, 6 H), 0.66, 0.69 (s, s, 1:1 ratio, 3 H), 0.84, 0.85 (s, s, 1:1 ratio, 9 H), 3.52, 3.53 (s, s, 1:1 ratio, 3 H), 5.42, 5.47 (s, s, 1:1 ratio, 1 H); ^{13}C NMR δ −4.85 (q), −3.94 (q), 10.01 (q), 17.98 (s), 23.38 (t), 25.19 (t), 25.78 (3 q), 26.75 (t), 28.51 (d), 30.75 (t), 35.72 (t), 40.09 (s), 44.42 (d), 59.56 (q), 79.27 (d), 116.23 (s), 122.66 (s), 140.03 (d); HRMS calcd for $C_{20}H_{35}NO_2Si$ (M^+) 349.2437, found 349.2438.

(2α,4aα,5α,8a*β*)-(±)-1-[Decahydro-8-(1-methoxymethylene)-4a-methyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-naphthalenyl]ethanone (28). To a stirred solution of 1.526 g (4.37 mmol) of **27** in 50 mL of ether was added dropwise 8.2 mL of MeLi (1.6 M in ether) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and, after addition of water, extracted with ether. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (30:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 1.311 g (82%) of **28** as an oil: ^{1}H NMR δ 0.02 (s, 6 H), 0.66 (s, 3 H), 0.85 (s, 9 H), 1.09 (ddd, J = 3.9, 13.2, 13.2 Hz, 1 H); 1.2−1.85 (m, 8 H), 1.96 (ddd, J = 3.3, 3.3, 12.9 Hz, 1 H), 2.14 (s, 3 H), 2.34 (dddd, J = 3.3, 3.3, 12.9, 12.9 Hz, 1 H), 2.78 (dd, J = 4.6, 9.8 Hz, 1 H), 3.26 (dd, J = 4.6, 9.8 Hz, 1 H), 3.53 (s, 3 H), 5.54 (br s, 1 H); ^{13}C NMR δ −4.84 (q), −3.97 (q), 10.11 (q), 17.96

(64) This compound has been characterized by NMR and MS: ^{1}H NMR δ 0.81 (d, J = 6.6 Hz, 3 H), 1.67 (br s, 9 H), 0.9−2.3 (m, 10 H), 2.45 (ddd, J = 4.0, 4.0, 11.9 Hz, 1 H), 2.89 (m, 2 H), 5.20 (dd, J = 8.7, 8.7 Hz, 1 H); ^{13}C NMR δ 20.40 (2 q), 21.58 (t), 22.15 (q), 22.70 (q), 26.88 (t), 28.10 (d), 28.61 (t), 29.46 (t), 30.89 (t), 36.77 (t), 124.79 (d), 125.31 (s), 131.65 (s), 134.95 (s); MS *m*/*z* (relative intensity) 206 (M^+, 72), 191 (18), 163 (43), 135 (33), 121 (50), 109 (52), 107 (70), 95 (73), 93 (59), 81 (100), 41 (65); HRMS calcd for $C_{15}H_{26}$ (M^+) 206.2035, found 206.2034.

(65) A stock solution of NaO-*t*-amyl (1.55 M in benzene) was prepared as described: Conia, M. J.-M. *Bull. Soc. Chim. Fr.* **1950**, *17*, 537.

(66) The NMR spectra of **5** revealed the presence of trace amounts of **23**.

(67) Coalescence was observed for the marked signals. One singlet in the ^{13}C NMR spectrum was obscured.

(68) In the ^{1}H NMR spectrum of **4** the peaks are slightly coalescenced.

(s), 23.51 (t), 23.90 (t), 24.63 (t), 25.78 (3 q), 28.06 (q), 30.94 (t), 37.57 (t), 40.48 (s), 44.64 (d), 51.61 (d), 59.37 (q), 79.69 (d), 117.15 (s), 139.91 (d), 211.80 (s); MS *m*/*z* (relative intensity) 366 (M^+, 35), 310 (20), 309 (100), 234 (73), 185 (35), 159 (23), 135 (16), 119 (19), 75 (46); HRMS calcd for $C_{21}H_{38}O_3Si$ (M^+) 366.2590, found 366.2584.

(2α,4aα,5α,8a*β*)-(±)-Decahydro-8-(1-methoxymethylene)-α,α,4a-trimethyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-naphthalenemethanol (29). The same procedure as described above for the organocerium addition to **12** was employed, except that MeLi was used instead of iPrMgCl, and the reaction mixture stirred at −78 °C for 15 min. Starting from 1.19 g of **28** (3.25 mmol), workup and crystallization from heptane afforded 1.222 g (98%) of **29**: mp 121 °C; ^{1}H NMR δ 0.00 (s, 6 H), 0.63 (s, 3 H), 0.84 (s, 9 H), 1.16 (s, 3 H), 1.18 (s, 3 H), 0.9−1.7 (m, 11 H), 1.91 (ddd, *J* = 3.2, 3.2, 13.0 Hz, 1 H), 2.75 (m, 1 H), 3.24 (dd, *J* = 4.2, 11.1 Hz, 1 H), 3.52 (s, 3 H), 5.51 (s, 1 H); ^{13}C NMR δ −4.81 (q), −3.96 (q), 10.32 (q), 18.00 (s), 22.44 (t), 23.70 (t), 23.70 (t), 25.83 (3 q), 26.57 (q), 27.60 (q), 31.08 (t), 37.25 (t), 40.52 (s), 45.47 (d), 49.25 (d), 59.36 (q), 72.73 (s), 79.94 (d), 118.14 (s), 139.64 (d); MS *m*/*z* (relative intensity) 382 (M^+, 32), 325 (100), 307 (31), 250 (97), 232 (36), 123 (38), 85 (35), 83 (54), 75 (46); HRMS calcd for $C_{22}H_{42}O_3Si$ (M^+) 382.2903, found 382.2904. Anal. Calcd for $C_{22}H_{42}O_3Si$: C, 69.07; H, 11.07. Found: C, 68.84; H, 11.32.

(2α,4aα,5α,8a*β*)-(±)-Decahydro-5-hydroxy-8-(1-methoxymethylene)-α,α,4a-trimethyl-2-naphthalenemethanol (30). The TBDMS ether **29** (0.734 g, 1.92 mmol) was treated with TBAF as described for **14**. Workup and flash chromatography (3:2 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.432 g (84%) of **30** as white crystals: mp 174 °C (from acetone); ^{1}H NMR δ 0.67 (s, 3 H), 1.19 (s, 3 H), 1.20 (s, 3 H), 1.0−1.82 (m, 12 H), 1.96 (ddd, *J* = 2.8, 2.8, 11.1 Hz, 1 H), 2.83 (ddd, *J* = 2.5, 2.5, 11.9 Hz, 1 H), 3.32 (dd, *J* = 4.2, 15.0 Hz, 1 H), 3.55 (s, 3 H), 5.55 (br s, 1 H); ^{13}C NMR δ 10.10 (q), 22.20 (t), 23.60 (t), 23.60 (t), 26.75 (q), 27.54 (q), 30.42 (t), 36.52 (t), 39.98 (s), 45.25 (d), 49.09 (d), 59.11 (q), 73.02 (s), 79.61 (d), 118.05 (s), 140.00 (d); MS *m*/*z* (relative intensity) 268 (M^+, 100), 250 (45), 178 (18), 160 (59), 145 (41), 59 (54); HRMS calcd for $C_{16}H_{28}O_3$ (M^+) 268.2038, found 268.2037. Anal. Calcd for $C_{16}H_{28}O_3$: C, 71.60; H, 10.52. Found: C, 71.53; H, 10.71.

(2α,4aα,5α,8a*β*)-(±)-Decahydro-8-(1-methoxymethylene)-α,α,4a-trimethyl-5-[(methylsulfonyl)oxy]-2-naphthalenemethanol (31). The alcohol **30** (0.571 g, 2.13 mmol) was treated with MsCl for 2 h as described for **16**. Workup and flash chromatography (3:2 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.716 g (97%) of **31**: ^{1}H NMR δ 0.70 (s, 3 H), 1.13 (s, 3 H), 1.14 (s, 3 H), 1.0−2.1 (m, 12 H), 2.82 (ddd, *J* = 2.8, 2.8, 11.3 Hz, 1 H), 2.94 (s, 3 H), 3.50 (s, 3 H), 4.35 (dd, *J* = 4.9, 11.1 Hz, 1 H), 5.53 (br s, 1 H); ^{13}C NMR δ 10.86 (q), 21.95 (t), 23.32 (t), 23.32 (t), 26.60 (q), 27.66 (q), 28.45 (t), 36.59 (t), 38.77 (q), 39.55 (s), 45.52 (d), 48.76 (d), 59.50 (q), 72.48 (s), 90.54 (d), 115.59 (s), 140.78 (d); MS *m*/*z* (relative intensity) 346 (M^+, 3), 293 (15), 250 (6), 229 (27), 203 (58), 161 (41), 86 (63), 84 (100), 49 (82); HRMS calcd for $C_{17}H_{30}O_5S$ (M^+) 346.1814, found 346.1813.

(1α,4α,4aα,7*β*,8a*β*)-(±)-Decahydro-7-(1-hydroxy-1-methylethyl)-4a-methyl-4-[(methylsulfonyl)oxy]-1-naphthalenecarboxaldehyde (32). The mesylate **31** (0.131 g, 0.38 mmol) was treated with 35% aqueous $HClO_4$ as described for **17**. Workup and flash chromatography (2:3 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.110 g (87%) of **32**: ^{1}H NMR δ 0.76 (s, 3 H), 1.18 (s, 3 H), 1.19 (s, 3 H), 1.1−1.45 (m, 4 H), 1.6−1.95 (m, 8 H), 2.21 (dd, *J* = 3.4, 4.9 Hz, 1 H), 2.37 (ddd, *J* = 1.7, 1.7, 13.6 Hz, 1 H), 2.98 (s, 3 H), 4.29 (dd, *J* = 6.1, 10.4 Hz, 1 H), 9.89 (d, *J* = 1.0 Hz, 1 H); ^{13}C NMR δ 12.23 (q), 22.18 (t), 22.87 (t), 25.45 (t), 26.06 (t), 26.66 (q), 27.67 (q), 38.34 (t), 38.83 (q), 39.18 (s), 46.20 (d), 49.83 (d), 50.46 (d), 72.29 (s), 89.66 (d), 203.56 (d); MS *m*/*z* (relative intensity) 332 (M^+, 2), 314 (8), 218 (15), 178 (100), 149 (63), 135 (39), 107 (35), 59 (58); HRMS calcd for $C_{15}H_{22}O$ (M^+ − 114) 218.1671, found 218.1667.

(1α,4α,4aα,7*β*,8a*β*)-(±)-Decahydro-7-[1-[(triethylsilyl)oxy]-1-methylethyl]-4a-methyl-4-[(methylsulfonyl)oxy]-1-naphthalenecarboxaldehyde (33). To a stirred solution of 0.430 g (1.29 mmol) of **32** in 3 mL of DMF was added 0.175 g (2.57 mmol) of imidazole and 0.32 mL (1.94 mmol) of TESCl at rt. After being stirred at rt for 90 min, the reaction mixture was diluted with water and extracted with petroleum ether (bp 40−60 °C). The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography (7:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 0.137 g (19%) of (1α,4a*β*,6α,8aα)-(±) decahydro-4-[1-[(triethylsilyl)oxy]methylene]-6-[1-[(triethylsilyl)oxy]-1-methylethyl]-1-naphthalenol methanesulfonate: ^{1}H NMR δ 0.58 (q, *J* = 7.4 Hz, 6 H),) 0.60 (q, *J* = 7.4 Hz, 6 H), 0.65 (s, 3 H), 0.92 (t, *J* = 7.4 Hz, 9 H), 0.97 (t, *J* = 7.4 Hz, 9 H), 1.18 (s, 3 H), 1.22 (s, 3 H), 1.1−2.15 (m, 11 H), 2.95 (m, 1 H), 2.99 (s, 3 H), 4.42 (dd, *J* = 4.7, 11.2 Hz, 1 H), 5.89 (br s, 1 H); ^{13}C NMR δ 4.43 (t), 5.79 (t), 6.41 (t), 6.55 (t), 6.59 (t), 6.80 (t), 6.88 (3 q), 7.17 (3 q), 10.84 (q), 21.88 (t), 23.23 (t), 23.23 (t), 27.16 (q), 28.43 (q), 28.64 (t), 36.82 (t), 38.81 (q), 39.68 (s), 45.62 (d), 49.62 (d), 74.92 (s), 91.05 (d), 119.49 (s), 132.82 (d); MS *m*/*z* (relative intensity) 560 (M^+, 4), 464 (2), 435 (3), 291 (7), 217 (73), 189 (49), 173 (65), 103 (100), 75 (82); HRMS calcd for $C_{28}H_{56}O_5SSi_2$ (M^+) 560.3387, found 560.3389. Further elution afforded 0.322 g (56%) of **33**: mp 105 °C (from diisopropyl ether); ^{1}H NMR δ 0.54 (q, *J* = 7.5 Hz, 6 H), 0.77 (s, 3 H), 0.93 (t, *J* = 7.5 Hz, 9 H), 1.18 (s, 3 H), 1.19 (s, 3 H), 1.1−1.5 (m, 3 H), 1.63−1.95 (m, 8 H), 2.19 (ddd, *J* = 0.8, 4.8, 4.8 Hz, 1 H), 2.37 (ddd, *J* = 1.5, 1.5, 13.5 Hz, 1 H), 2.98 (s, 3 H), 4.31 (dd, *J* = 7.4, 9.1 Hz, 1 H), 9.91 (d, *J* = 1.0 Hz, 1 H); ^{13}C NMR δ 6.80 (3 t), 7.13 (3 q), 12.05 (q), 21.87 (t), 22.88 (t), 25.50 (t), 26.03 (t), 27.57 (q), 28.05 (q), 38.40 (t), 38.82 (q), 39.21 (s), 46.18 (d), 50.72 (d), 50.72 (d), 74.60 (s), 89.83 (d), 203.53 (d); MS *m*/*z* (relative intensity) 431 (M^+ − 15, 1), 417 (5), 403 (1), 321 (3), 173 (100), 115 (20); HRMS calcd for $C_{21}H_{39}O_5SSi$ (M^+ − 15) 431.2288, found 431.2291. Anal. Calcd for $C_{22}H_{42}O_5SSi$: C, 59.16; H, 9.48. Found: C, 59.06; H, 9.54.

(*Z*,*E*)-(±)-4-[1-[(Triethylsilyl)oxy]-1-methylethyl]-7-methyl-1,7-cyclodecadienemethanol (34). The mesylate **33** (0.112 g, 0.25 mmol) was treated with NaO-*t*-amyl and Red-Al under oxygen-free conditions as described for **6**. Workup afforded 0.086 g (97%) of almost pure **34**: ^{1}H NMR (C_6D_6, major peaks)[69] δ 0.67 (q, *J* = 7.9 Hz, 6 H), 1.09 (t, *J* = 7.9 Hz, 9 H), 1.13 (s, 6 H); MS *m*/*z* (relative intensity) 305 (M^+ − 47, 1), 220 (8), 202 (3), 173 (100), 115 (26), 87 (9), 75 (10); HRMS calcd for $C_{19}H_{33}OSi$ (M^+ − 47) 305.2301, found 305.2293.

(*Z*,*E*)-(±)-4-Hydroxymethyl-α,α,8-trimethyl-3,7-cyclodecadienemethanol (15-Hydroxyhedycaryol) (35). To a stirred solution of 0.027 g (0.077 mmol) of **34** in 1 mL of THF was added 0.1 mL of TBAF (1 M in THF) at rt. After stirring at rt for 4 h, another 0.05 mL of TBAF was added, and stirring was continued at rt overnight. After addition of *tert*-butyl methyl ether, the reaction mixture was washed with water and brine, dried on Na_2SO_4, and evaporated. The remaining residue was dissolved in 3 mL of *tert*-butyl methyl ether and extracted with four 1-mL portions of 20% aqueous $AgNO_3$. The combined aqueous layers were washed with *tert*-butyl methyl ether and cooled to 0 °C. After addition of 10 mL of 25% aqueous NH_3, the aqueous layer was extracted with *tert*-butyl methyl ether. The combined organic layers were washed with brine, dried on Na_2SO_4, and evaporated to afford 0.017 g (94%) of **35**: ^{1}H NMR (C_6D_6, major peaks)[69] δ 1.08 (s, 3 H), 1.12 (s, 3 H); MS *m*/*z* (relative intensity) 220 (M^+ − 18, 45), 205 (7), 202 (24), 189 (84), 177 (66), 162 (44), 159 (79), 147 (56), 133 (98), 119 (56), 107 (67), 105 (84), 93 (89), 91 (60), 81 (60), 79 (57), 59 (100); HRMS calcd for $C_{15}H_{24}O$ (M^+ − 18) 220.1827, found 220.1823.

Acknowledgment. We thank A. van Veldhuizen for recording ^{1}H and ^{13}C NMR spectra and H. Jongejan for mass spectral data and elemental analyses.

Supporting Information Available: ^{1}H NMR spectra of those new compounds lacking combustion data (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO970901Z

(69) In the NMR spectra of this compound strong coalescence was observed. The ^{1}H NMR spectrum pointed to the presence of at least three different conformers.