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Enantioselective Total Synthesis of (−)-Candelalides A, B and C: Potential Kv1.3 Blocking Immunosuppressive Agents

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Abstract: Novel Kv1.3 blocking immunosuppressants, (−)-candelalides A, B and C, were efficiently synthesized for the first time in a convergent and unified manner starting from (+)-5-methyl-Wieland–Miescher ketone. The synthetic method involved the following key steps: i) a strategic [2,3]-Wittig rearrangement of a stannylmethyl ether to install the stereogenic center at C9 and the *exo*-methylene function at C8 present in the decalin portion; ii) a straightforward coupling of a *trans*-decalin portion (BC ring) and a γ-pyrone moiety through the C16–C3′ bond to assemble the requisite carbon framework; and iii) a construction of a characteristic di or tetrahydropyran ring (A ring) by internal nucleophilic ring closure of a hydroxy aldehyde or a hydroxy epoxide. The present total synthesis has fully established the absolute configuration of these natural products.

Keywords: candelalides · immunosuppressive agents · natural products · total synthesis

Introduction

In 2001, the Merck research group reported the isolation and structural elucidation of candelalides A (**1**), B (**2**) and C (**3**) (Figure 1) from the culture broth of *Sesquicillium candelabrum*.[1] These substances were found to be novel blockers of the voltage-gated potassium channel Kv1.3 (IC_{50} = 3.7 μM for **1**, 1.2 μM for **2** and 2.5 μM for **3**).[1] In human T cells, Kv1.3 channels exist as tetramers of four identical subunits that control the resting membrane potential of the cells.[2] Membrane depolarization that results from blockage of Kv1.3 channels causes a reduction in Ca^{2+} entry into T cell, thereby decreasing the intracellular Ca^{2+} levels required for T-cell activation and proliferation.[3] Consequently, these natural products show promise as new agents for potential treatments of T cell-mediated autoimmune diseases such as multiple sclerosis, rheumatoid arthritis and insulin-dependent diabetes.[1–3]

The gross structure and relative stereochemistry of **1–3** have been determined by extensive spectroscopic studies, in-

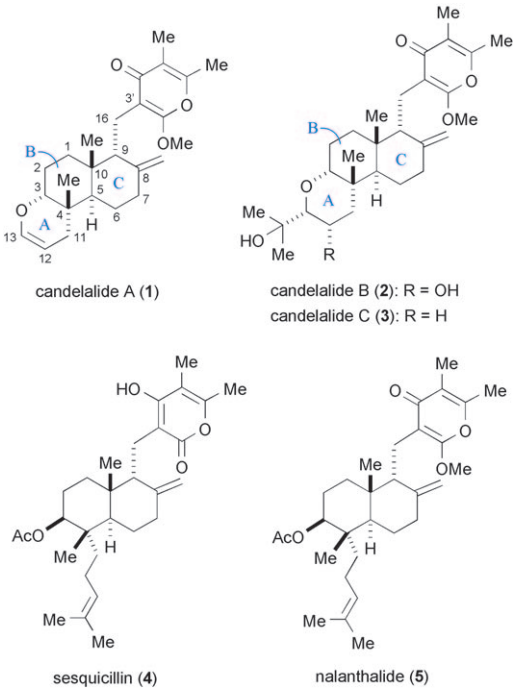

Figure 1. Candelalides A (**1**), B (**2**), C (**3**), sesquicillin (**4**) and nalanthalide (**5**).

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cluding 2D NMR experiments (COSY, HMBC, NOESY and HETCOR spectra), whereas their absolute configurations have not yet been confirmed.[1] These natural products possess a novel tricyclic decahydro- or dodecahydro-1*H*-benzo[*f*]chromene skeleton (ABC ring system) connected to a fully substituted γ-pyrone ring via a methylene linkage involving five to seven asymmetric carbon centers.[1] Interestingly, the structurally most complex candelalide B exhibits the most potent Kv1.3 blocking activity.[1]

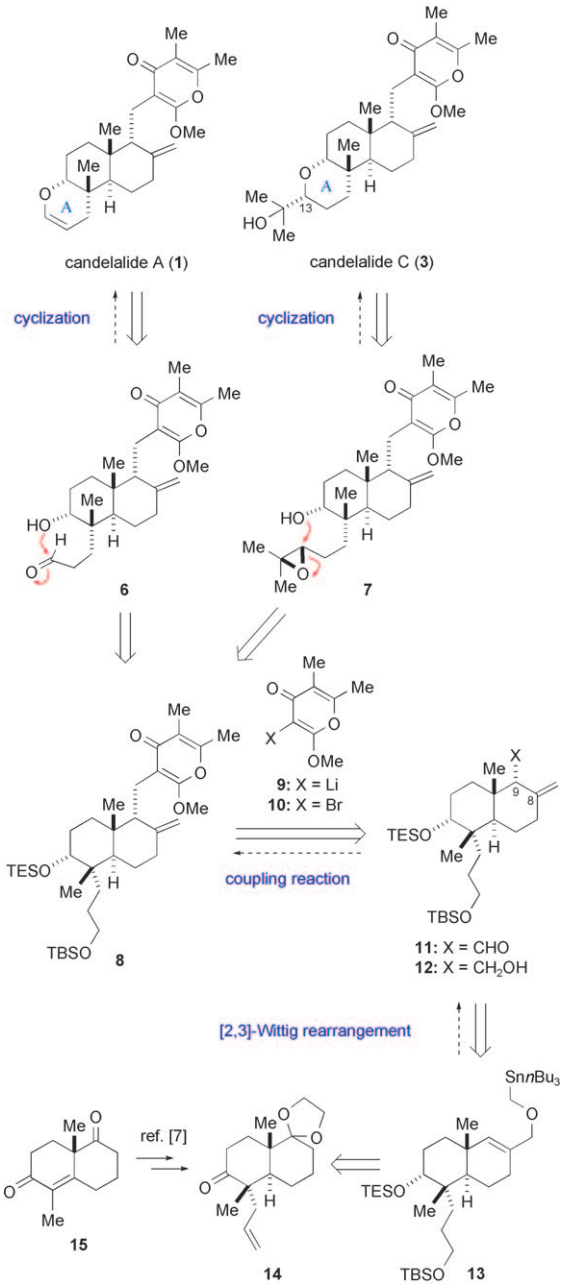
Structurally related and biologically attractive diterpenoid pyrones have been studied: In 2002, Danishefsky and Zhang reported an elegant total synthesis of (±)-sesquicillin (**4**) containing an α-pyrone ring, a glucocorticoid antagonist from *Acremonium* sp.[4] The desirable biological properties, unique structural features and the necessity of confirming the absolute configurations prompted us to undertake a project directed towards the total synthesis of optically active **1**–**3**. We have previously reported our preliminary results on the enantioselective total syntheses of (−)-**1**[5] and (−)-nalanthalide (**5**),[6] potential Kv1.3 blocking immunosuppressants, which led to the establishment of their absolute configurations. In this paper, we describe in full detail our first unified total synthesis of (−)-**1**–**3** using a convergent and enantioselective scheme.

Results and Discussion

Synthesis of (−)-candelalides A (1) and C (3): Our initial synthetic efforts were targeted towards candelalides A (**1**) and C (**3**), because the structures of these compounds are less complex than that of candelalide B (**2**).

Synthetic plan: In our synthetic plan for candelalides A (**1**) and C (**3**), we envisioned that the first target molecule **1** would be derived from hydroxy aldehyde **6** (accessible from disilyl ether **8**) by construction of the characteristic dihydropyran ring (A ring) via intramolecular hemiacetal formation followed by dehydration (Scheme 1). Intermediate **8** would be produced through a coupling reaction between the appropriately functionalized decalin segment **11**, available from alcohol **12**, and the fully substituted 3-lithio-γ-pyrone **9**, accessible from bromide **10**. From the synthetic point of view, this coupling reaction poses a considerable challenge because the C9 formyl group in decalin **11** lies in a sterically congested axial orientation. Intermediate **12**, having both a hydroxylmethyl group at C9 and an *exo*-methylene moiety at C8, would be formed through the strategic [2,3]-Wittig rearrangement of stannylmethyl ether **13**. We expected that the C9 stereogenic center and the C8 *exo*-methylene function in product **12** would be simultaneously established. Intermediate **13** would, in turn, be derived from the known *trans*-decalone **14**,[7] which is readily prepared from the enantiomerically pure (+)-5-methyl-Wieland–Miescher ketone (**15**)[8] (> 99% *ee*).

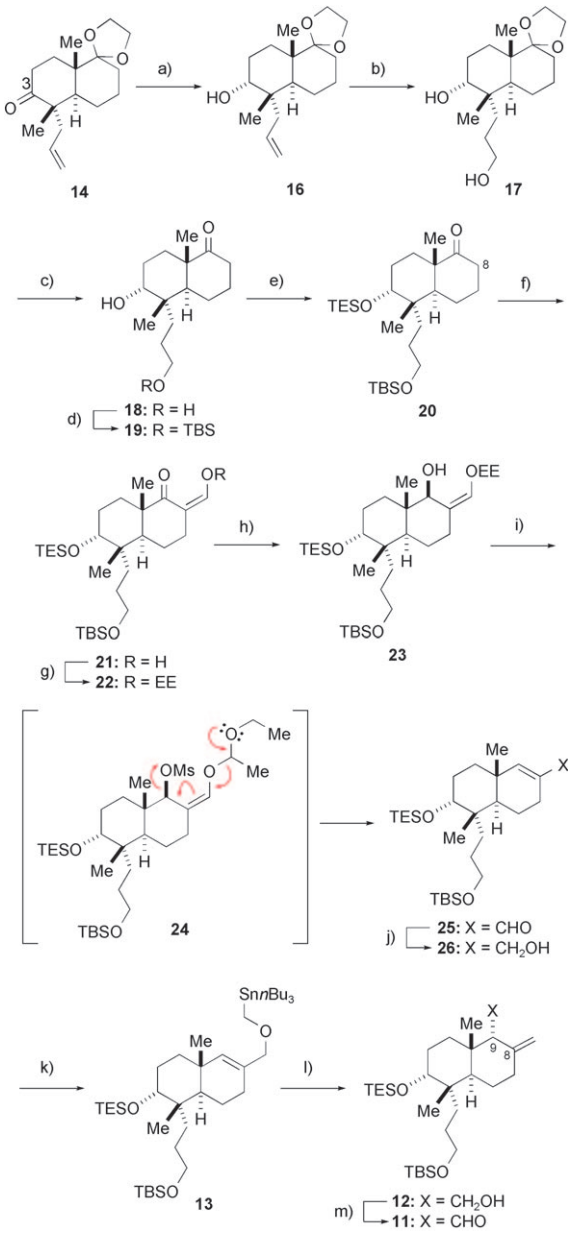
In a parallel synthesis, the second target molecule **3** would be produced by the construction of the tetrahydropyran ring



Scheme 1. Synthetic plan for candelalides A (**1**) and C (**3**). TES = triethylsilyl, TBS = *tert*-butyldimethylsilyl.

(A ring) through a 6-*exo* cyclization of hydroxy epoxide **7**, where the requisite stereogenic center at C13 in **3** is created. Intermediate **7** would be derived from the common intermediate **8** by sequential functional group manipulation and deprotection or vice versa.

Synthesis of decalin segment 11: We first pursued the synthesis of decalin segment **11** starting from the known enatiomerically pure *trans*-decalone **14**[7] (> 99% *ee*), wherein the route to allyl alcohol **26** was based on Danishefsky's synthesis of (±)-sesquicillin (**4**) (Scheme 2).[4] Thus, stereoselective reduction of the C3 carbonyl group in **14** with L-selectride



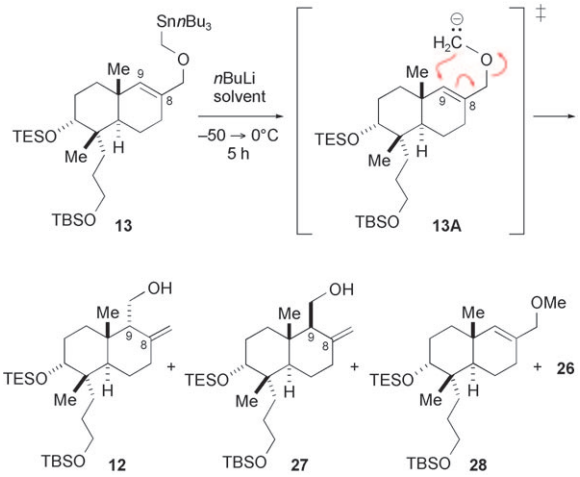
Scheme 2. Synthesis of decalin segment **11**. a) L-Selectride, THF, −10 °C, 3 h, 91 %; b) BH_3·THF, THF, 0 °C, 1 h; 30 % aq. H_2O_2, 3 M NaOH, THF, 0 °C, 1 h, 96 %; c) 5 % aq. HCl, THF, RT, 4 h, 91 %; d) TBSCl, imidazole, DMF, RT, 14 h, 93 %; e) TESOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 30 min, 82 %; f) ethyl formate, NaH, THF, 0 °C → RT, 1 h, 97 %; g) ethyl vinyl ether, PPTS, THF, RT, 1.5 h, 96 %; h) $NaBH_4$, THF/H_2O 10:1, 0 °C → RT, 2 h, 98 %; i) MsCl, Et_3N, CH_2Cl_2, 0 °C, 30 min, 90 %; j) $NaBH_4$, THF/H_2O 10:1, 0 °C → RT, 30 min, 98 %; k) nBu_3SnCH_2I, KH, [18]crown-6, THF, 0 °C → RT, 3 h, 86 %; l) *n*BuLi, hexane, −50 → 0 °C, 5 h, 78 % (see entry 1 in Table 1); m) Dess–Martin periodinane, CH_2Cl_2, RT, 1 h, 98 %. DMF = *N*,*N*-dimethylformamide, Tf = trifluoromethanesulfonyl, PPTS = pyridinium *p*-toluenesulfonate, Ms = methanesulfonyl, EE = 1-ethoxyethyl.

produced the desired α-alcohol **16** in 91 % yield as a single stereoisomer. Subsequent hydroboration of **16**, followed by oxidative treatment with 30 % aqueous hydrogen peroxide, produced the requisite diol **17** in 96 % yield. After deprotection of the ethylene acetal moiety in **17** by acid hydrolysis (91 %), the two hydroxy groups in the resulting ketone **18** were differentially protected as the *tert*-butyldimethylsilyl (TBS) and triethylsilyl (TES) ethers, providing the corresponding disilyl ether **20** in 76 % yield in two steps via the monosilyl ether **19**. To introduce a formyl group at the C8 position, compound **20** was treated with ethyl formate in the presence of sodium hydride to yield enol **21** (97 %).

The hydroxy group on enol **21** was then protected as ethoxyethyl (EE) ether to furnish enol ether **22** in 96 % yield. Subsequent sodium borohydride reduction of **22** produced alcohol **23** in 98 % yield as a single stereoisomer, which was then subjected to dehydration employing methanesulfonyl chloride (MsCl) and triethylamine to produce the desired α,β-unsaturated aldehyde **25** in 90 % yield via the intermediary methanesulfonate **24**. Compound **25** was further converted to the requisite stannylmethyl ether **13**, the substrate for the critical [2,3]-Wittig rearrangement, in 84 % overall yield via a two-step sequence involving sodium borohydride reduction of the formyl group in **25** followed by stannylmethylation[9] of the resulting alcohol **26** with iodomethyltributyltin in the presence of potassium hydride and [18]crown-6.

Having obtained intermediate **13**, we next examined the critical [2,3]-Wittig rearrangement[10,11] to construct the requisite decalin system **12** having both a hydroxymethyl group at C9 with the correct stereochemistry and an *exo*-methylene functionality at C8. After screening several reaction conditions (Table 1), we found that the proposed [2,3]-Wittig rearrangement of **13** proceeded smoothly and cleanly in a stereoselective manner by treatment with *n*-butyllithium in hexane at −50 to 0 °C for 5 h (entry 1), yielding the desired product **12** (78 %) with a small amount of its C9

Table 1. [2,3]-Wittig rearrangement of stannylmethyl ether **13**.



Entry	Solvent	Yield[a] [%]			
		12	**27**	**28**	**26**
1	hexane	78	9	0	3
2	THF	29	6	32	11
3	Et_2O	50	16	5	2

[a] Isolated yield.

epimer **27** (9%) and the hydroxy compound **26** (3%); these products were readily separated by silica gel column chromatography. The structure and stereochemistry of the rearrangement products **12** and **27** were unambiguously confirmed by extensive spectroscopic analysis, including 600 MHz ^{1}H NMR NOESY spectra (selected NOESY correlation, Figure 2).

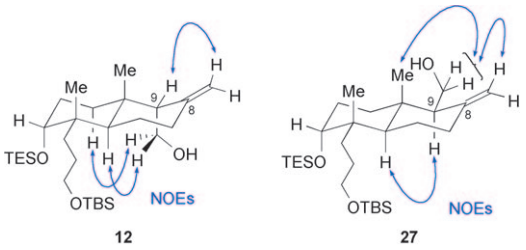
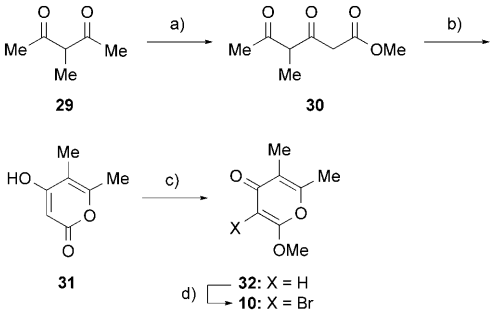


Figure 2. Selected NOESY correlation of **12** and **27**.

The stereoselectivity for this [2,3]-Wittig rearrangement can be rationalized by assuming that the attack of the intermediate carboanion **13A** (cf. Table 1), generated in situ by tin/lithium exchange of stannane **13**, on the C9 olefinic carbon occurs preferentially from the less hindered α-face on the molecule under the influence of the β-oriented axial methyl group at the decalin junction, yielding **12** as the major product. It should be noted that the use of hexane as the solvent was crucial in this reaction. When THF or Et_2O was used instead of hexane, the yield of the desired rearrangement product **12** was reduced (29–50%); moreover, the undesired methyl ether **28** was produced (5–32%) as a by-product (entries 2 and 3). By-product **28** was probably formed by protonation of carboanion **13A**; this reactive species might have caused proton abstraction from the ethereal solvents such as THF and Et_2O, because the methylene position adjacent to the oxygen atom in those solvents is slightly activated. To continue the synthesis (cf. Scheme 2), the rearrangement product **12** was then subjected to Dess–Martin oxidation[12] to provide the desired decalin segment **11** in 98% yield.

Synthesis of γ-pyrone segment 10: With decalin segment **11** synthesized, we next performed the synthesis of γ-pyrone segment **10**, the coupling partner of **11** (Scheme 3). α-Pyrone **31** has been previously prepared by Hagiwara et al.[13] starting from methyl 3-oxopentanoate and acetaldehyde in three steps with 19% overall yield. Recently, Shishido et al.[14] reported an improved synthesis of **31** starting from 3-methylpentane-2,4-dione (**29**) in two steps with 57% overall yield. Therefore, we decided to apply the improved method to our synthesis. Thus, methoxycarbonylation of **29** with dimethyl carbonate in the presence of sodium bis(trimethylsilyl)amide [$NaN(SiMe_3)_2$] afforded β,δ-diketoester **30** in 85% yield. Subsequent cyclization of **30** by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing benzene produced the desired α-pyrone **31** in 86% yield.

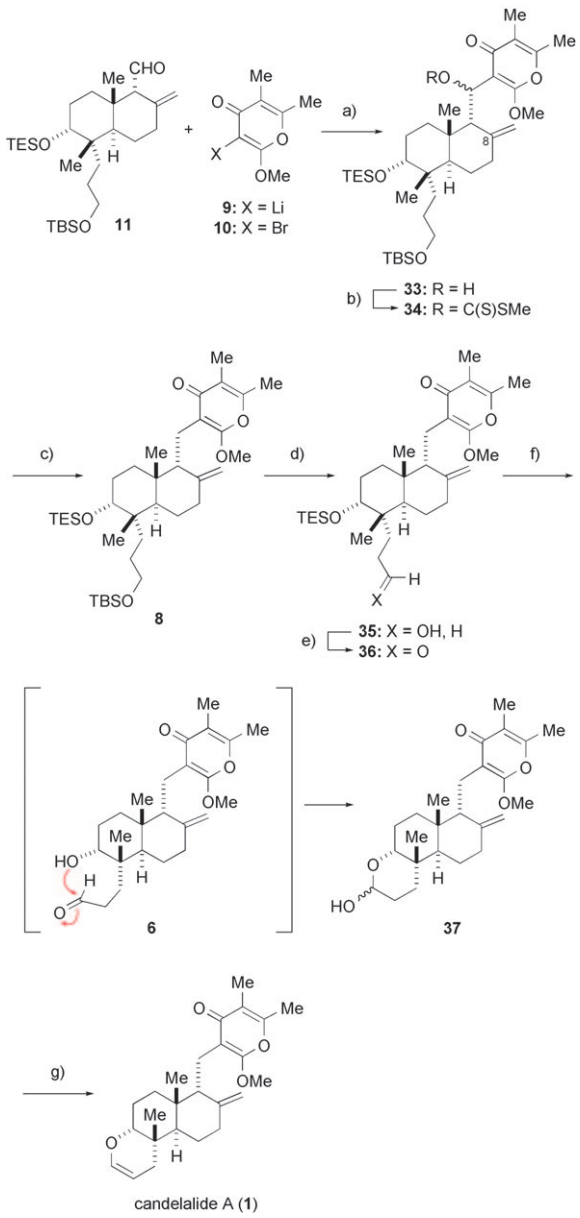


Scheme 3. Synthesis of γ-pyrone segment **10**. a) $(MeO)_2CO$, $NaN(SiMe_3)_2$, THF, −78°C → RT, 24 h, 85%; b) DBU, benzene, reflux, 2 h, 86%; c) $MeOSO_2F$, CH_2Cl_2, RT, 24 h, 89%; d) NBS, THF, 0°C, 2 h, 71%. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, NBS = *N*-bromosuccinimide.

Compound **31** was successfully converted to γ-pyrone segment **10** in 63% overall yield via a two-step operation involving regioselective methyl etherification of the ambidentate hydroxy group under the conditions of Beak et al.[15] ($MeOSO_2F$, CH_2Cl_2, RT), followed by bromination of the resulting methyl ether **32** with *N*-bromosuccinimide (NBS).

Synthesis of (−)-candelalide A (1): Having obtained both decalin segment **11** and γ-pyrone segment **10** in an efficient way, we next investigated the synthesis of the first target candelalide A (**1**) (Scheme 4). The sequence involved the challenging coupling of the two segments and the crucial construction of the dihydropyran ring (A ring). To this end, the coupling reaction of **11** with 3-lithio-γ-pyrone **9** was successfully achieved by an initial bromine/lithium exchange on **10** and subsequent reaction with **11** at −78 to −30°C for 2 h. The expected coupling product **33** was obtained in 95% yield as a mixture of epimeric alcohols (ca. 8:1 by 400 MHz ^{1}H NMR) that was very difficult to separate. It is noteworthy that the regiochemical integrity of the sensitive C8 *exo*-methylene functionality was maintained during the coupling reaction. Removal of the sterically hindered hydroxy group in **33** was achieved by applying the Barton–McCombie procedure[16] with some improvements in the reaction conditions. Thus, treatment of a mixture of **33** and carbon disulfide with $NaN(SiMe_3)_2$ at −78°C, followed by addition of iodomethane at the same temperature, provided the corresponding methyl xanthate **34** in 93% yield. This was further treated with tri-*n*-butyltin hydride in the presence of 2,2′-azobis(isobutyronitrile) (AIBN) in refluxing toluene to produce the desired deoxygenated product **8** in 77% yield.

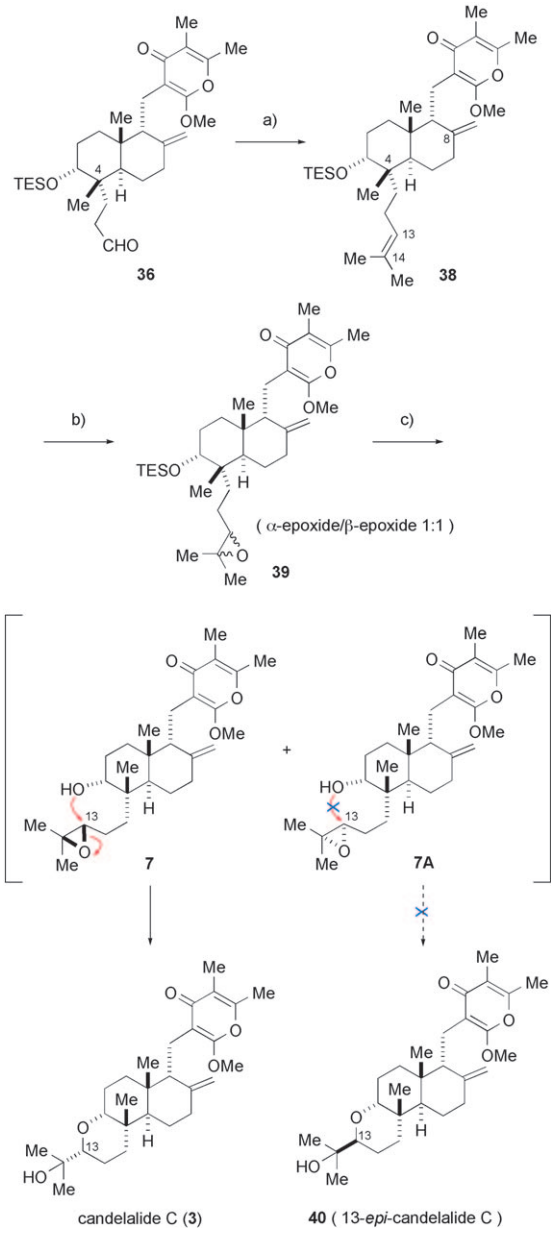
Having successfully obtained, the advanced key intermediate **8**, which has the whole carbon framework with the requisite substituents and asymmetric carbons, we next undertook the crucial construction of the dihydropyran ring to complete the total synthesis of **1**. Thus, selective deprotection of the TBS group in **8** by exposure to aqueous acetic acid in THF, followed by Dess–Martin oxidation of the resulting alcohol **35**, provided the corresponding aldehyde **36** in 81% yield in two steps. Subsequent deprotection of the



Scheme 4. Synthesis of candelalide A (**1**). a) 3-Bromo-2-methoxy-5,6-dimethyl-4*H*-pyran-4-one (**10**), *n*BuLi, THF, −78 °C; at −78 °C, add **11**, −78 → −30 °C, 2 h, 95 %; b) $NaN(SiMe_3)_2$, THF, −78 °C, 1 h; CS_2, THF, −78 °C, 1 h; MeI, −78 °C, 1 h, 93 %; c) nBu_3SnH, AIBN, toluene, reflux, 1 h, 77 %; d) AcOH/THF/H_2O 3:2:2, RT, 2 h, 84 %; e) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, RT, 1 h, 96 %; f) TBAF, THF, 0 °C → RT, 40 min, 99 %; g) MsCl, Et_3N, THF, 0 °C → RT, 1 h, 87 %. AIBN = 2,2′-azobis(isobutyronitrile), TBAF = tetrabutylammonium fluoride.

TES group in **36** with tetrabutylammonium fluoride (TBAF) resulted in the expected cyclized hemiacetal **37** in 99 % yield via the intermediary hydroxy aldehyde **6**. Finally, dehydration of **37** was efficiently achieved by treatment with MsCl in THF containing triethylamine at 0 °C warming to room temperature over 1 h, leading to the first target candelalide A (**1**) in 87 % yield. The spectroscopic properties (IR, ^1H and ^{13}C NMR, HRMS) of the synthetic sample **1** were identical to those of natural **1**.[1] The optical rotation of synthetic **1** {$[\alpha]_D^{22} = -25.1$ ($c = 0.35$ in CH_3OH)} showed good agreement with that of natural **1** {lit.[1] $[\alpha]_D^{22} = -23.1$ ($c = 0.26$ in CH_3OH)}; we therefore assigned the absolute configuration of natural **1** (Scheme 4).

Synthesis of (−)-candelalide C (3): Having synthesized the first target candelalide A (**1**), we next examined the synthesis of the second target candelalide C (**3**) starting from the common intermediate **36** (Scheme 5). The sequence involved the stereocontrolled formation of the isopropanol-substituted tetrahydropyran ring (A ring) present in **3** as the crucial step. Thus, to set up the requisite homoprenyl side



Scheme 5. Synthesis of candelalide C (**3**). a) Ph_3PCHMe_2I, *n*BuLi, THF, −20 → −5 °C, 1 h, 82 %; b) *m*CPBA, $NaHCO_3$, CH_2Cl_2, 0 °C, 2 h, 98 %; c) TBAF, THF, RT, 1 h, 43 % for **3**. *m*CPBA = 3-chloroperoxybenzoic acid.

chain at C4, compound **36** was initially subjected to a Wittig reaction using isopropylidene(triphenyl)phosphorane, which provided the product **38** in 82% yield. Subsequent chemoselective epoxidation of the C13–C14 olefinic double bond in **38** was efficiently achieved by treatment with 3-chloroperoxybenzoic acid (*m*CPBA) in the presence of $NaHCO_3$ at 0°C for 2 h, producing the desired epoxide **39** in 98% yield as a mixture of diastereomers, which was difficult to separate (α-epoxide/β-epoxide = ca. 1:1 by 400 MHz ^{1}H NMR). It is noteworthy that the C8 sensitive *exo*-olefin moiety remained intact during the epoxidation reaction. Finally, removal of the TES protecting group in **39** by exposure to TBAF at room temperature triggered the expected 6-*exo* cyclization of the liberated alcohol **7** to produce the target candelalide C (**3**) as the sole product in 43% yield. The spectroscopic properties (IR, ^{1}H and ^{13}C NMR, HRMS) of the synthetic sample **3** were identical to those of natural **3**. The optical rotation of synthetic **3** {$[\alpha]_D^{22} = -68.8$ ($c = 0.98$ in CH_3OH)] was essentially identical to that of natural **3** {lit.[1] $[\alpha]_D^{22} = -67.0$ ($c = 1.03$ in CH_3OH)}, confirming the absolute configuration of natural **3** (Scheme 5). In this reaction, another possible cyclization product such as **40** (13-*epi*-candelalide C) via the diastereomeric epoxide **7A** was not obtained from the reaction mixture. It is well known that this type of epoxide-mediated cyclization is accompanied by inversion of the stereochemistry at the carbon undergoing nucleophilic attack (S_N2-type cyclization mode);[17] therefore, we believed that the desired cyclized product **3** (candelalide C) should be obtained from intermediate **7**.

From these results, it is evident that the stereochemistry at the epoxide moiety in substrate **39** plays an important role in the cyclization event. The difference in reactivity between hydroxy epoxides **7** and **7A** can be rationalized by a plausible mechanism (Figure 3). Thus, in the case of **7**, the internal nucleophilic attack of the C3 hydroxy group at the C13 position would occur from the backside of the epoxide ring, leading to desired **3** with inversion of the stereochemistry at C13. On the other hand, in the case of **7A**, the internal nucleophilic attack at the C13-epoxide carbon would be precluded by a severe steric interaction between the C14 methyl groups and the cyclohexane ring; this phenomenon would prohibit the formation of **40** (13-*epi*-candelalide C).

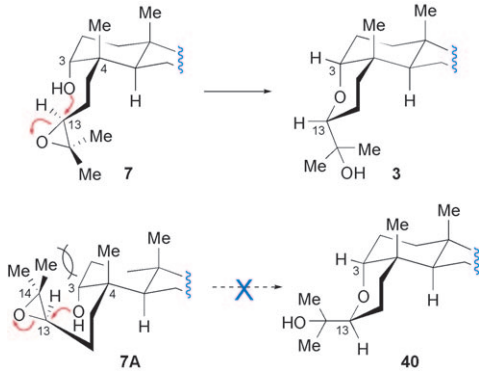
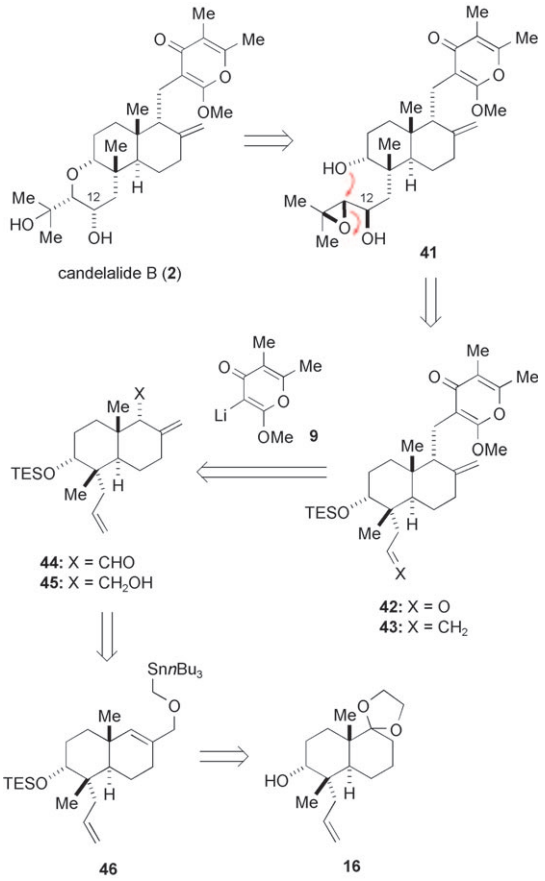


Figure 3. Possible mechanisms for the difference in reactivity between **7** and **7A** in the ether cyclization reaction.

Synthesis of (−)-candelalide B (2)

Synthetic plan: Our synthetic plan for the final target candelalide B (**2**), representing the most complex structure among candelalides A–C, is based on the synthesis of candelalides A (**1**) and C (**3**) mentioned above (Scheme 6). We envisaged

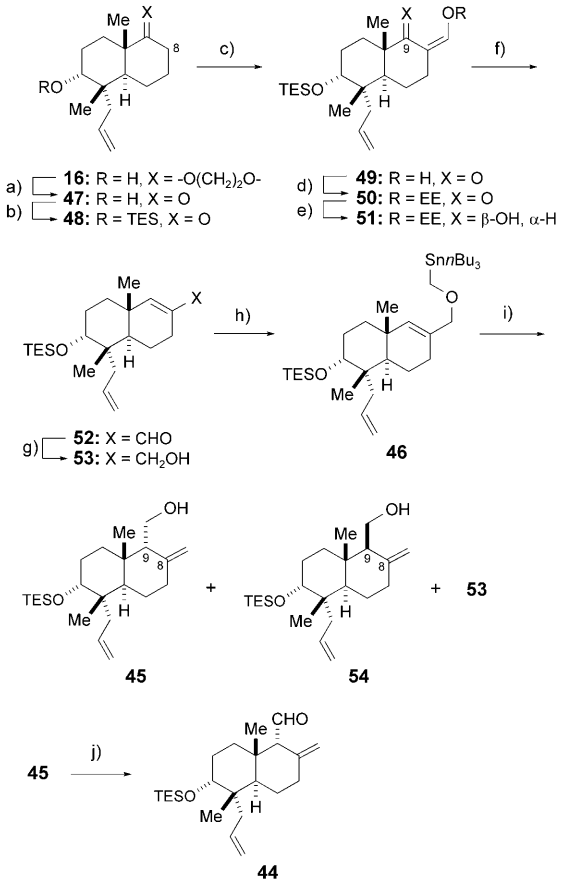


Scheme 6. Synthetic plan for candelalide B (**2**).

that the target molecule **2** would be produced through the 6-*exo* cyclization of epoxy alcohol **41**, followed by inversion of configuration at the C12 hydroxy group. The advanced key intermediate **41** would be derived from aldehyde **42**, accessible from diene **43** by functional group manipulation and deprotection or vice versa. Intermediate **43** would be formed through a coupling reaction of decalin segment **44**, accessible from alcohol **45**, and the common γ-pyrone segment **9**. Intermediate **45** would be synthesized through the [2,3]-Wittig rearrangement of stannylmethyl ether **46**, available from decalin alcohol **16**, in the same manner as described above.

Synthesis of decalin segment 44: First, the synthesis of decalin segment **44** was investigated starting from the common

intermediate **16** (Scheme 7) by employing a reaction sequence similar to that described in the section on the synthesis of decalin segment **11** (cf. Scheme 2). Thus, compound



Scheme 7. Synthesis of decalin segment **44**. a) PPTS, acetone/H_2O 5:1, reflux, 4 h; b) TESOTf, *i*Pr_2NEt, CH_2Cl_2, 0 °C, 30 min, 97 % (2 steps); c) ethyl formate, NaH, THF, 0 °C → RT, 1 h, 92 %; d) ethyl vinyl ether, PPTS, THF, RT, 1.5 h, 96 %; e) $NaBH_4$, THF/H_2O 10:1, 0 °C → RT, 3 h, 98 %; f) MsCl, Et_3N, CH_2Cl_2, 0 °C, 30 min, 96 %; g) $NaBH_4$, THF/H_2O 10:1, 0 °C → RT, 30 min, 98 %; h) *n*Bu_3SnCH_2I, KH, [18]crown-6, THF, 0 °C → RT, 3 h, 83 %; i) *n*BuLi, hexane, −50 → 0 °C, 9 h, 76 % for **45**, 17 % for **54**, 5 % for **53**; j) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, RT, 1 h, 91 %.

16 was converted to decalone **48** in 97 % overall yield via a two-step operation involving acid hydrolysis of the ethylene acetal moiety in **16** and TES protection of the resulting alcohol **47**. Subsequent formylation at C8 in **48** and EE protection of the resulting enol **49** yielded enol ether **50** in 88 % yield in two steps. After sodium borohydride reduction of the C9 carbonyl group in **50** (98 %), the resulting alcohol **51** was subjected to dehydration, providing the desired α,β-unsaturated aldehyde **52** in 96 % yield. Compound **52** was then successfully converted to stannylmethyl ether **46** in 81 % overall yield via a two-step sequence involving sodium borohydride reduction and stannylmethylation[9] of the resulting alcohol **53**. The crucial [2,3]-Wittig rearrangement of **46** proceeded smoothly and cleanly under the optimized conditions employed in the section on the synthesis of decalin segment **11** (cf. **13** → **12**, Scheme 2 and Table 1). The desired product **45** was obtained in 76 % yield, along with the C9 epimer **54** (17 %) and the hydroxy compound **53** (5 %). The stereostructure of the rearrangement products **45** and **54** was confirmed by NOESY experiments (Figure 4), in a manner similar to that described above (cf. Figure 2). Finally, Dess–Martin oxidation[12] of **45** provided decalin segment **44** in 91 % yield.

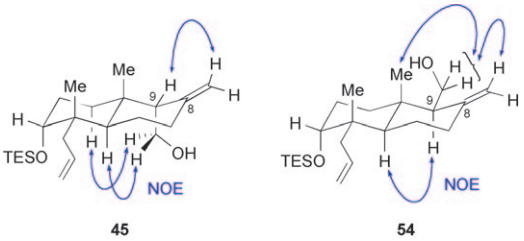
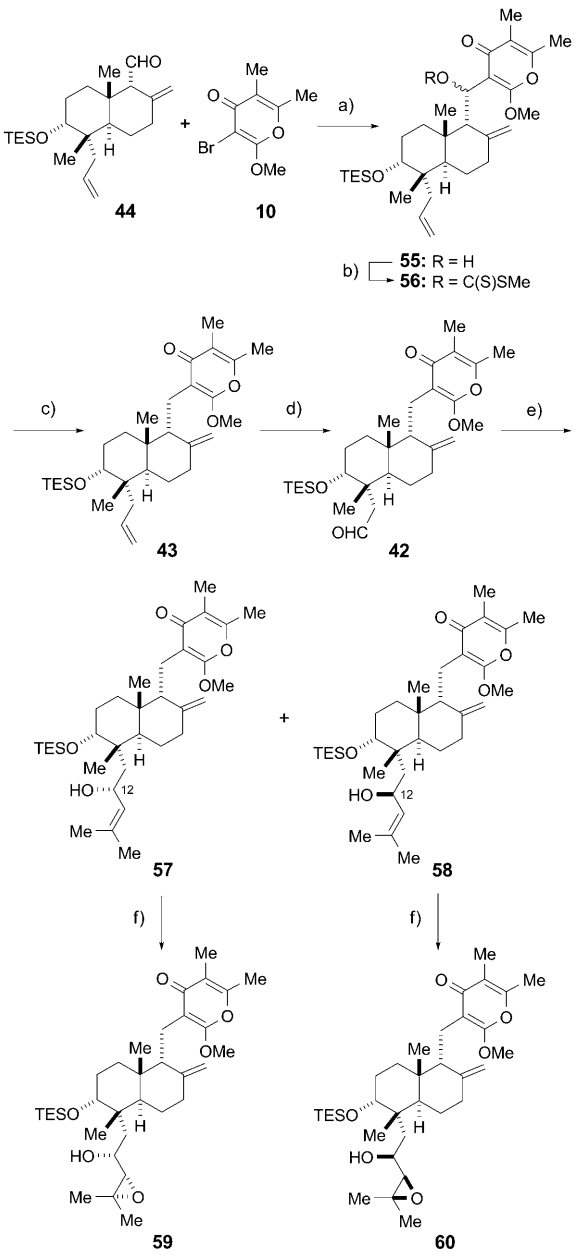


Figure 4. Selected NOESY correlation of **45** and **54**.

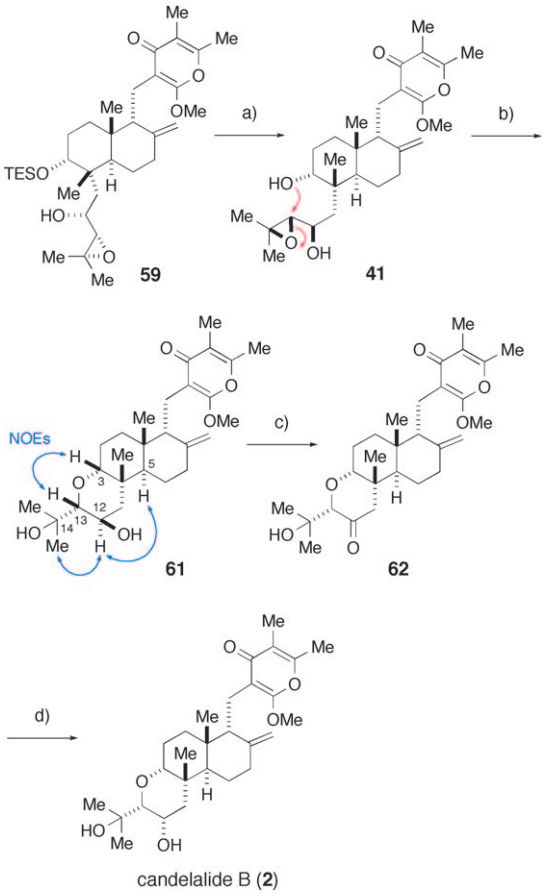
Synthesis of (−)-candelalide B (2): After obtaining the requisite decalin segment **44**, we next performed the synthesis of epoxy alcohol **59**, which has the appropriate stereochemistry at the epoxide ring (Scheme 8). Compound **59** represents an *O*-TES protecting variant of the advanced key intermediate **41**, designed as a substrate for the critical ether cyclization (cf. Scheme 6 and the section on our synthetic plan). To this end, the coupling reaction of **44** and γ-pyrone pyrone **10** was achieved under the same conditions described in the section on the synthesis of (−)-candelalide A (**1**) [cf. **11** + **9** (**10**) → **33**, Scheme 4]. The desired coupling product **55** was obtained in 86 % yield as an inseparable mixture of epimeric alcohol (ca. 8:1 by 400 MHz ^{1}H NMR). Removal of the hydroxy group in **55** was similarly carried out by the method described above (cf. **33** → **34** → **8**, Scheme 4), which provided the desired deoxygenated product **43** in 68 % overall yield via methyl xanthate **56**. After Lemieux–Johnson oxidation[18] (OsO_4, $NaIO_4$, 2,6-lutidine, dioxane/H_2O, RT, 85 %) of **43**, the resulting aldehyde **42** was reacted with a Grignard reagent (2-methyl-1-propenyl magnesium bromide) to furnish the desired products **57** (42 %) and **58** (40 %) as mixture of epimeric alcohols that can be separated by silica gel column chromatography. The stereochemistry newly formed at C12 in both products **57** and **58** could not be assigned at this stage; therefore, the assignment was made at a later stage by NOESY studies of the transformed cyclic compounds **61** and **64**, respectively (see below, cf. Schemes 9 and 10 and Figure 6). Hydroxy-directed epoxidation[19] [$VO(acac)_2$, TBHP, benzene, 0 °C → RT] of **57** and **58** delivered the corresponding epoxides **59** (84 %) and **60** (80 %) as a single diastereomer, respectively.

We next investigated the final route that led to completion of the total synthesis of **2** (Scheme 9). Critical to the sequence was the construction of the highly substituted tetrahydropyran ring present in **2**. To this end, the TES-protect-



Scheme 8. Synthesis of intermediate **59**. a) **10**, *n*BuLi, THF, −78 °C; at −78 °C, add **44**, −78 → −30 °C, 2 h, 86 %; b) CS_2, THF, −78 °C; NaN($SiMe_3$)$_2$, −78 °C; MeI, −78 °C, 1 h; c) nBu_3SnH, AIBN, toluene, reflux, 1 h, 68 % (2 steps); d) OsO_4, $NaIO_4$, 2,6-lutidine, dioxane/H_2O 3:1, RT, 1 h, 85 %; e) $Me_2C{=}CHMgBr$, THF, RT, 1 h, 42 % for **57**, 40 % for **58**; f) VO(acac)$_2$, TBHP, benzene, 0 °C → RT, 1 h, 84 % for **59**, 80 % for **60**. acac = acetylacetonyl, TBHP = *tert*-butylhydroperoxide.

ing group in **59**, having favorable stereochemistries at the epoxide ring for the subsequent ether cyclization, was removed by treatment with TBAF at room temperature for 1 h, producing the liberated epoxy alcohol **41** in quantitative yield. In contrast to the case of candelalide C (**3**) (cf. **39** → **7** → **3**, Scheme 5), no ether cyclization products were produced during the deprotection step. Several attempts to obtain the desired cyclized product **61** by treatment of **41**



Scheme 9. Synthesis of candelalide B (**2**). a) TBAF, THF, 0 °C → RT, 1 h, 100 %; b) PPTS, CH_2Cl_2, 0 °C → RT, 4 h, 79 %; c) TPAP, NMO, 4 Å MS, CH_2Cl_2, RT, 30 min, 82 %; d) $NaBH_4$, THF/H_2O 10:1, −30 °C, 1 h, 88 %. TPAP = tetra-*n*-propylammonium perruthenate, NMO = *N*-methylmorpholine *N*-oxide, MS = molecular sieves.

under basic conditions (cf. K_2CO_3, NaOMe, in MeOH; DBU in THF; LiN($SiMe_3$)$_2$, NaN($SiMe_3$)$_2$ in THF, 0 °C → reflux) were unsuccessful; the starting material **41** was recovered at temperatures between 0 °C to room temperature, and unidentified decomposition products were detected at higher temperatures. After several experiments, the desired 6-*exo* ether cyclization was successfully realized under mildly acidic conditions. Thus, exposure of **41** to PPTS at 0 °C warming to room temperature for 4 h resulted in the formation of the requisite cyclization product **61** in 79 % yield. The structure of this product and its stereochemistry were confirmed by NOESY experiments, which showed clear NOE interactions between C3-H and C13-H, and between C12-H and C5-H, C14-Me. The elucidation of this structure also verified the stereochemistry at C12 of the Grignard reaction product **57** (cf. Scheme 8).

The reason for the distinctly different reactivity of **41** under basic (or neutral) and acidic conditions is unclear, but a plausible explanation is the conformational change in the substrate (Figure 5). Under basic (or neutral) conditions, the substrate would mainly occupy conformation **41A**, wherein the epoxide ring takes an *anti* position to the C12 hydroxy

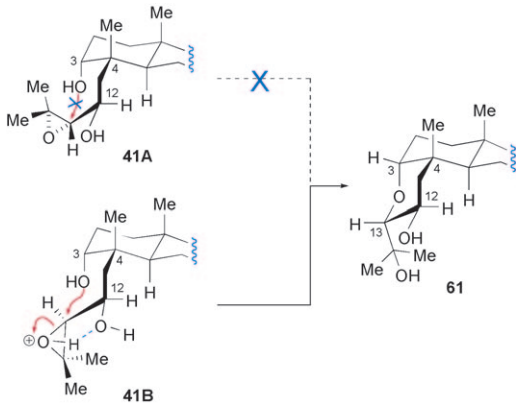
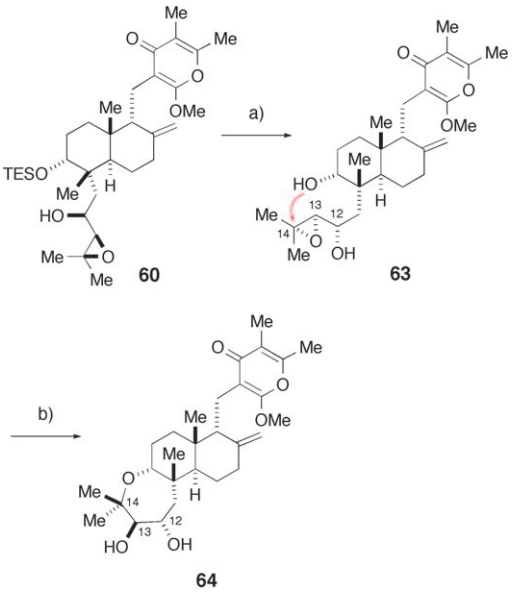


Figure 5. Possible mechanism for the difference in reactivity for the favored conformations **41A** and **41B** in the ether cyclization reaction.

group resulting from the C–O/C–O dipole–dipole repulsion. That conformation would preclude any possibility of epoxide ring opening by an S_N2-type nucleophilic attack of the C3 hydroxy group. However, under acidic conditions, the substrate, upon protonation of the epoxide ring, would predominantly take conformation **41B**, wherein the epoxide ring is in a *syn* orientation to the C12-hydroxy group due to an internal hydrogen bond between the C12-hydroxy group and the epoxonium hydrogen. That conformation may facilitate the nucleophilic ether cyclization to yield the desired product **61**.

To complete the synthesis (cf. Scheme 9), inversion of the configuration at the C12-hydroxy group in **61** was next achieved by oxidation with tetra-*n*-propyl ammonium perruthenate (TPAP)[20] (82%) followed by sodium borohydride reduction of the resulting ketone **62** with complete stereoselectivity, resulting in the production (88%) of the final target candelalide B (**2**). The spectroscopic properties (IR, ^{1}H and ^{13}C NMR, HRMS) of the synthetic sample **2** were identical to those of the natural product **2**. The optical rotation of synthetic **2** {$[\alpha]_D^{22} = -56.3$ ($c = 0.75$ in CH_3OH)} was in good agreement with that of natural **2** {lit.[1] $[\alpha]_D^{22} = -50.9$ ($c = 0.49$ in CH_3OH)}, which confirmed its absolute configuration (**2**, Figure 1).

Interestingly, as shown in Scheme 10, the same acid treatment of the diastereomeric hydroxy epoxide **63**, derived from **60** by *O*-TES deprotection (quantitative yield) as described for the cyclization of **41** to **61**, provided the unexpected seven-membered cyclized product **64** in 86% yield. The structure and stereochemistry of **64** was unambiguously confirmed by extensive spectroscopic analysis, including high-resolution MS and 2D NMR experiments. The selected NOESY correlation of **64** (Figure 6), wherein clear NOE interactions between C12-H and C3-H, C14-β-Me, between C3-H and C14-β-Me, and between C13-H and C14-α-Me are observed, permitting also determination of the stereochemistry at C12 of the Grignard reaction product **58** (cf. Scheme 8). It should be noted that this reaction proceeded through a 7-*endo* cyclization process without producing the alternative 6-*exo* ring-closure product.



Scheme 10. Conversion of **60** to candelalide B analogue **64**. a) TBAF, THF, 0°C → RT, 1 h, 100%; b) PPTS, CH_2Cl_2, 0°C → RT, 3 h, 86%.

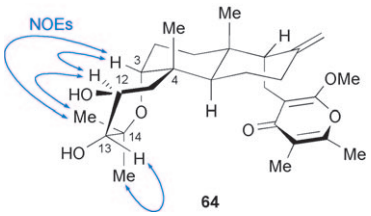


Figure 6. Selected NOESY correlation of **64**.

The unique acid-induced cyclization reaction of **63** leading to **64** must be attributed to the stereostructural nature inherent in substrate **63**. Thus, conformation **63A** might be preferentially formed through an internal hydrogen bond between the C12-hydroxy group and the epoxonium hydrogen (Figure 7). That conformation is obviously unfavorable for 6-*exo* ring closure by nucleophilic attack of the C3-hydroxy group at the C13-epoxide carbon, as a result of well-known stereoelectronic factors. Consequently, intermediate **63A** can undergo epoxide ring opening to produce the putative intermediate **63B**, wherein the C14-carbocation center must be trapped by the C3-hydroxy group, forming the seven-membered cyclized product **64**.

Conclusion

We have accomplished the first total synthesis of (−)-candelalides A (**1**), B (**2**) and C (**3**), which are novel Kv1.3 blocking immunosuppressive agents, in a convergent and unified manner starting from (+)-5-methyl-Wieland–Miescher ketone (**15**). The method explored features: i) strategic [2,3]-Wittig rearrangement of stannylmethyl ethers **13** and

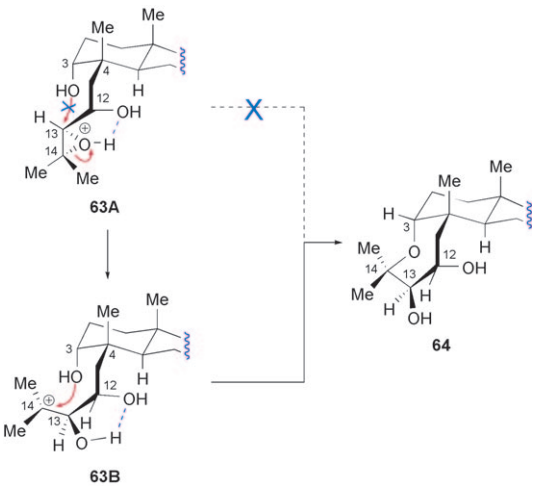


Figure 7. Possible mechanism for the ether cyclization reaction of **63** leading to **64** via **63A** and **63B**.

46 to deliver to the requisite decalin portions **11** and **44**, having both a hydroxy group at C9 with the correct stereochemistry and an *exo*-methylene function at C8 (**13** → **12**, Scheme 2, Table 1; **46** → **45**, Scheme 7), ii) coupling reaction of decalin portions **11** and **44** with a common γ-pyrone portion **9** (**10**) to build up the desired carbon frameworks **33** and **55** [**11** + **9** (**10**) → **33**, Scheme 4; **44** + **9** (**10**) → **55**, Scheme 8] and iii) formation of the characteristic di- or tetrahydropyran rings by cyclization of hydroxy aldehyde **6** and hydroxy epoxides **7** and **41** to produce the target molecules **1**–**3** (**36** → [**6**] → **37** → **1**, Scheme 4; **39** → [**7**] → **3**, Scheme 5; **41** → **61**, Scheme 9). The synthesis fully confirmed the absolute configurations of these natural products. On the basis of the present research, synthesis of candelalide analogues with the aim of exploring the structure-activity relationships is currently under investigation in our laboratory.

Experimental Section

General techniques: All reactions involving air- and moisture-sensitive reagents were carried out using oven dried glassware and standard syringe–septum cap techniques. Routine monitoring of reaction were carried out using glass-supported Merck silica gel 60 F_{254} TLC plates. Flash column chromatography was performed on Kanto Chemical Silica Gel 60N (spherical, neutral 40–50 μm) with the solvents indicated.

All solvents and reagents were used as supplied with following exceptions. Tetrahydrofuran (THF) and Et_2O were freshly distilled from Na/benzophenone under argon. Toluene was distilled from Na metal under argon. *N*,*N*-Dimethylformamide (DMF), CH_2Cl_2, pyridine, and hexane were distilled from CaH under argon.

Measurements of optical rotations were performed with a JASCO DIP-370 automatic digital polarimeter. Melting points were taken on a Yanaco MP-3 micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured with a JEOL AL-400 or a JEOL JNM-LA600 spectrometer. Chemical shifts were expressed in ppm using Me_4Si ($\delta=0$) as an internal standard. The following abbreviations are used: singlet (s), triplet (t), quartet (q), multiplet (m), and broad (br). Copies of ^{1}H and ^{13}C NMR spectra for all new compounds are shown in the Supporting Information. Infrared (IR) spectra measurements were carried out with a JASCO FT/IR-4100 spectrometer. Low- and High-resolution mass (MS and HRMS) spectra were measured on a JEOL JMS-DX 303/JMA-DA 5000 SYSTEM high resolution mass spectrometer. Elemental analyses were performed with a Perkin Elmer 2400II apparatus.

(4a*S*,5*S*,6*R*,8a*S*)-5-Allyl-5,8a-dimethyl-6-(hydroxy)decahydronaphthalen-1-one 1-ethyleneacetal (16): L-Selectride in THF (1.0 M solution, 34.0 mL, 34 mmol) was added dropwise to a stirred solution of **14**[7] (5.90 g, 21 mmol) in dry THF (220 mL) at −10 °C under argon. After 3 h, 3 M NaOH (50 mL) and 30% aqueous H_2O_2 (12 mL) was added to the mixture at 0 °C, and stirring was continued for 30 min at the same temperature. The reaction was diluted with water (150 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×200 mL). The combined extracts were washed with brine (2×50 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 5:1→4:1) to give **16** (5.41 g, 91%) as a white solid. Recrystallization from hexane afforded colorless prisms. M.p. 77–78 °C; $[\alpha]_D^{20} = -23.6$ ($c=1.00$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.87$ (s, 3H), 1.09 (s, 3H), 1.14–1.19 (m, 1H), 1.29 (dq, $J=13.0$, 3.4 Hz, 1H), 1.43–1.55 (m, 3H), 1.58–1.72 (m, 3H), 1.80–1.97 (m, 4H), 2.07–2.18 (m, 2H), 3.49–3.51 (m, 1H), 3.81–3.86 (m, 1H), 3.90–4.02 (m, 2H), 5.08–5.15 (m, 2H), 5.94–6.05 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=16.7$, 18.9, 20.0, 23.0, 23.1, 24.6, 30.4, 40.4, 42.6, 43.2, 44.8, 64.8, 65.3, 72.3, 113.2, 117.3, 136.2 ppm; IR (KBr): $\tilde{\nu}=3491$, 3448, 3073, 2956, 2936, 2882, 2366, 1637, 1475, 1398, 1383, 1184, 1138, 1084, 910, 733, 509 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{17}H_{28}O_3$: 280.2038, found 280.2040 $[M]^+$.

(4a*S*,5*S*,6*R*,8a*S*)-5,8a-Dimethyl-6-hydroxy-5-(3-hydroxypropyl)decahydronaphthalen-1-one 1-ethyleneacetal (17): A solution of BH_3·THF in THF (0.93 M solution, 7.80 mL, 7.3 mmol) was added dropwise to a stirred solution of **16** (744 mg, 2.6 mmol) in dry THF (20 mL) at 0 °C under argon. After 1 h, 3 M NaOH (4.0 mL) and 30% aqueous H_2O_2 (4.0 mL) was added to the reaction mixture at 0 °C, and stirring was continued for 1 h at the same temperature. The reaction was quenched with water (10 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×60 mL). The combined extracts were washed with brine (2×50 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 2:1→1:2) to give **17** (760 mg, 96%) as a white amorphous solid. $[\alpha]_D^{20}=-24.6$ ($c=1.10$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.83$ (s, 3H), 1.10 (s, 3H), 1.16–1.20 (m, 1H), 1.24–1.32 (m, 1H), 1.35–1.55 (m, 6H), 1.55–1.71 (m, 6H), 1.79 (dd, $J=12.6$, 2.4 Hz, 1H), 1.88 (d, $J=9.8$ Hz, 2H), 3.56–3.63 (m, 2H), 3.64–3.70 (m, 1H), 3.80–3.86 (m, 1H), 3.90–4.01 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=16.7$, 18.6, 19.9, 22.8, 22.9, 24.6, 25.4, 30.2, 35.0, 39.1, 42.7, 43.1, 63.1, 64.6, 65.0, 71.3, 113.3 ppm; IR (KBr): $\tilde{\nu}=3385$, 2949, 2878, 1657, 1447, 1383, 1337, 1283, 1211, 1184, 1136, 1111, 1076, 993, 951, 909, 862, 797, 756, 666, 581, 513, 471 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{17}H_{30}O_4$: 298.2144, found 298.2144 $[M]^+$.

(4a*S*,5*S*,6*R*,8a*S*)-5,8a-Dimethyl-6-hydroxy-5-(3-hydroxypropyl)decahydronapthalen-1-one (18): 5% Aqueous HCl (14 mL) was added dropwise to a stirred solution of **17** (480 mg, 1.6 mmol) in THF (12 mL) at room temperature. After 4 h, 3 M NaOH (5 mL) and saturated aqueous $NaHCO_3$ (5 mL) were added slowly to the mixture at 0 °C. The resulting mixture was extracted with EtOAc (4×50 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2×50 mL) and brine (2×50 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 1:1→1:2) to give **18** (372 mg, 91%) as a white solid. Recrystallization from THF afforded colorless needles. M.p. 169–170 °C; $[\alpha]_D^{20}=-47.8$ ($c=1.00$ in CH_3OH); ^{1}H NMR (400 MHz, CD_3OD): $\delta=0.94$ (s, 3H), 1.20 (s, 3H), 1.24–1.28 (m, 1H), 1.32–1.40 (m, 2H), 1.42–1.56 (m, 2H), 1.58–1.67 (m, 3H), 1.68–1.76 (m, 2H), 1.86–1.95 (m, 1H), 2.00 (dd, $J=13.9$, 3.4 Hz, 1H), 2.06–2.15 (m, 2H), 2.66 (td, $J=13.9$, 7.3 Hz, 1H), 3.46–3.56 ppm (m, 3H); ^{13}C NMR (100 MHz, CD_3OD): $\delta=19.55$, 19.64, 21.1, 25.9, 26.90, 26.94, 27.3, 31.7, 38.5, 41.2, 48.5, 50.2, 63.9, 72.1, 218.1 ppm; IR (KBr): $\tilde{\nu}=3387$, 2959, 2934, 2880, 1696, 1451, 1433, 1385, 1306, 1242, 1117, 1055, 1015, 976, 961, 920, 822, 748, 556 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{15}H_{26}O_3$: 254.1882, found 254.1887 $[M]^+$; el-

emental analysis calcd (%) for $C_{15}H_{26}O_3$: C 70.83, H 10.30; found C 70.85, H 9.89.

(4a*S*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-6-(hydroxy)decahydronaphthalen-1-one (19): *tert*-Butyldimethylsilyl chloride (TBSCl) (426 mg, 3.8 mmol) was added to a stirred solution of **18** (360 mg, 1.4 mmol) in dry DMF (8 mL) containing imidazole (240 mg, 3.6 mmol) at room temperature. After 14 h, the reaction was quenched with saturated aqueous NH_4Cl (5 mL) at 0 °C, and the resulting mixture was extracted with Et_2O (3×60 mL). The combined extracts were washed successively with 3% aqueous HCl (2×50 mL), saturated aqueous $NaHCO_3$ (2×50 mL) and brine (2×50 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1) to give **19** (485 mg, 93%) as a white solid. Recrystallization from hexane/Et_2O 10:1 afforded colorless needles. M.p. 75–77 °C; $[\alpha]_D^{20}=-27.8$ ($c=1.31$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.06$ (s, 6H), 0.90 (s, 9H), 0.91 (s, 3H), 1.17 (s, 3H), 1.29–1.39 (m, 2H), 1.42–1.49 (m, 1H), 1.50–1.54 (m, 2H), 1.59–1.65 (m, 2H), 1.65–1.74 (m, 3H), 1.81–1.90 (m, 1H), 1.93 (d, $J=3.4$ Hz, 1H), 1.97–2.09 (m, 2H), 2.18–2.26 (m, 1H), 2.57 (dt, $J=13.7$, 6.9 Hz, 1H), 3.52–3.66 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=-5.2$, −5.3, 18.4, 18.9, 19.1, 20.2, 24.7, 25.7, 25.8, 26.0 (3C), 34.9, 37.5, 40.3, 46.8, 48.8, 63.8, 71.0, 77.2, 215.2 ppm; IR (KBr): $\tilde{\nu}=3474$, 2953, 2930, 2859, 1698, 1472, 1385, 1256, 1209, 1167, 1063, 1019, 966, 891, 837, 775, 735, 662, 559, 498, 421 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{21}H_{40}O_3Si$: 368.2747, found 368.2748 $[M]^+$; elemental analysis calcd (%) for $C_{21}H_{40}O_3Si$: C 68.42, H 10.94; found C 68.42, H 10.94.

(4a*S*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-6-(triethylsiloxy)decahydronaphthalen-1-one (20): Triethylsilyl trifluoromethanesulfonate (TESOTf) (0.88 mL, 3.8 mmol) was added dropwise to a stirred solution of **19** (460 mg, 1.3 mmol) in dry CH_2Cl_2 (12 mL) containing 2,6-lutidine (0.47 mL, 4.2 mmol) at 0 °C under argon. After 30 min, the reaction was quenched with saturated aqueous NH_4Cl (5 mL) at 0 °C, and the resulting mixture was extracted with Et_2O (3×50 mL). The combined extracts were washed successively with 3% aqueous HCl (2×40 mL), saturated aqueous $NaHCO_3$ (2×40 mL) and brine (2×40 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 50:1) to give **20** (494 mg, 82%) as a colorless viscous liquid. $[\alpha]_D^{20}=-19.4$ ($c=1.34$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.04$ (s, 6H), 0.61 (dq, $J=7.9$, 5.3 Hz, 6H), 0.88 (s, 3H), 0.89 (s, 9H), 0.95 (t, $J=7.9$ Hz, 9H), 1.16 (s, 3H), 1.23–1.33 (m, 4H), 1.44–1.53 (m, 2H), 1.58–1.66 (m, 4H), 1.79 (ddt, $J=14.4$, 3.4, 2.1 Hz, 1H), 1.97–2.07 (m, 2H), 2.17–2.24 (m, 1H), 2.50–2.61 (m, 1H), 3.46–3.54 (m, 1H), 3.55–3.62 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=-5.2$, −5.3, 5.4 (3C), 7.1 (3C), 18.3, 19.2, 19.3, 20.1, 25.3, 25.8, 25.9, 26.0 (3C), 26.7, 35.4, 37.5, 40.8, 46.4, 48.8, 64.1, 72.9, 215.6 ppm; IR (neat): $\tilde{\nu}=2955$, 2878, 1711, 1462, 1385, 1362, 1306, 1252, 1096, 1007, 963, 941, 909, 837, 775, 739, 687, 559 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{27}H_{54}O_3Si_2$: 482.3611, found 482.3608 $[M]^+$.

(*Z*)-(4a*S*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-2-hydroxymethylene-6-(triethylsilyloxy)decahydronaphthalen-1-one (21): A solution of **20** (460 mg, 0.48 mmol) in dry THF (12 mL) containing ethyl formate (0.92 mL, 11 mmol) was added to a stirred suspension of NaH (60% dispersion in mineral oil, 576 mg, 14 mmol) in dry THF (12 mL) at 0 °C under argon, and stirring was continued for 1 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (5 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×50 mL). The combined extracts were washed with brine (2×40 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1) to give **21** (472 mg, 97%) as a pale yellow viscous liquid. $[\alpha]_D^{20}=+6.9$ ($c=1.01$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.05$ (s, 6H), 0.61 (dq, $J=7.9$, 2.3 Hz, 6H), 0.83 (s, 3H), 0.89 (s, 9H), 0.95 (t, $J=7.9$ Hz, 9H), 1.21 (s, 3H), 1.27–1.34 (m, 3H), 1.41–1.53 (m, 3H), 1.57–1.67 (m, 2H), 1.68–1.74 (m, 1H), 1.80–1.88 (m, 2H), 2.32 (ddd, $J=15.2$, 11.5, 7.0 Hz, 1H), 2.44 (ddd, $J=15.2$, 6.6, 1.8 Hz, 1H), 3.49–3.56 (m, 1H), 3.56–3.64 (m, 2H), 8.40 (d, $J=4.5$ Hz, 1H), 14.65 ppm (d, $J=4.5$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=-5.2$, −5.3, 5.4 (3C), 7.2 (3C), 17.8, 18.4, 19.0, 20.6, 23.1, 25.6, 26.0 (3C), 26.6, 35.0, 40.2, 42.0, 42.1, 48.7, 64.1, 72.9, 106.0, 184.5, 195.5 ppm; IR (neat): $\tilde{\nu}=2955$, 2879, 1705, 1640, 1584, 1462, 1412, 1385, 1362, 1334, 1254, 1100, 1057, 1009, 966, 936, 907, 837, 797, 775, 739, 687, 556 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{28}H_{54}O_4Si_2$: 510.3561, found 510.3563 $[M]^+$.

(*Z*)-(4a*S*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-2-(ethoxyethan-1-yl)oxymethylene-5,8a-dimethyl-6-(triethylsiloxy)decahydronaphthalen-1-one (22): Pyridinium *p*-toluenesulfonate (PPTS) (22.0 mg, 88 μmol) was added to a stirred solution of **21** (448 mg, 0.88 mmol) in dry THF (12 mL) containing ethyl vinyl ether (1.44 mL, 18 mmol) at room temperature. After 1.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (8 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×50 mL). The combined extracts were washed with brine (3×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 20:1→10:1) to give **22** (1:1 diastereomeric mixture caused by the EE group) (490 mg, 96%) as a pale yellow viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.05$ (s, 6H), 0.56–0.64 (m, 6H), 0.85 (s, 3H), 0.90 (s, 9H), 0.94 (t, $J=7.9$ Hz, 9H), 1.12 (s, 3H), 1.21 (t, $J=7.1$ Hz, 3H), 1.30–1.36 (m, 2H), 1.42 (d, $J=5.2$ Hz, $^3/_2$H), 1.43 (d, $J=5.2$ Hz, $^3/_2$H), 1.46–1.53 (m, 2H), 1.55–1.65 (m, 3H), 1.70–1.90 (m, 4H), 2.20–2.30 (m, 1H), 2.64–2.72 (m, 1H), 3.45–3.55 (m, 2H), 3.56–3.63 (m, 2H), 3.68–3.75 (m, 1H), 5.07 (quint, $J=5.2$ Hz, 1H), 7.40–7.44 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=-5.2$, −5.3, 5.4 (3C), 7.2 (3C), 14.9 ($^1/_2$C), 15.0 ($^1/_2$C), 18.0, 18.4, 19.4, 19.6 ($^1/_2$C), 19.7 ($^1/_2$C), 21.1, 22.2 ($^1/_2$C), 22.3 ($^1/_2$C), 25.6, 26.0 (3C), 26.7, 26.8, 35.0, 40.6, 42.1 ($^1/_2$C), 42.2 ($^1/_2$C), 46.4, 63.6 ($^1/_2$C), 63.7 ($^1/_2$C), 64.2, 73.0, 103.5 ($^1/_2$C), 103.7 ($^1/_2$C), 114.0 ($^1/_2$C), 114.1 ($^1/_2$C), 151.3 ($^1/_2$C), 151.4 ($^1/_2$C), 206.5 ($^1/_2$C), 206.6 ppm ($^1/_2$C); IR (neat): $\tilde{\nu}=2955$, 2880, 1680, 1599, 1462, 1385, 1345, 1254, 1209, 1101, 1046, 1005, 972, 882, 837, 775, 739, 689 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{32}H_{62}O_5Si_2$: 582.4136, found 582.4138 $[M]^+$.

(*Z*)-(1*R*,4a*R*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-2-(ethoxyethan-1-yl)oxymethylene-5,8a-dimethyl-6-(triethylsiloxy)decahydronaphthalen-1-ol (23): $NaBH_4$ (1.10 g, 29 mmol) was added in small portions to a stirred solution of **22** (3.40 g, 5.8 mmol) in THF (60 mL) containing water (6 mL) at 0 °C, and stirring was continued for 2 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (20 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×80 mL). The combined extracts were washed with brine (2×60 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 8:1) to give **23** (1:1 diastereomeric mixture caused by EE group) (3.34 g, 98%) as a colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.04$ (s, 6H), 0.58–0.65 (m, 6H), 0.77 (s, 3H), 0.78 (s, 3H), 0.89 (s, 9H), 0.97 (t, $J=7.9$ Hz, 9H), 1.20 (t, $J=7.1$ Hz, $^3/_2$H), 1.21 (t, $J=7.1$ Hz, $^3/_2$H), 1.17–1.32 (m, 4H), 1.36 (d, $J=5.3$ Hz, 3H), 1.40 (dd, $J=5.2$, 1.0 Hz, 1H), 1.43–1.52 (m, 5H), 1.57–1.68 (m, 2H), 1.75–1.85 (m, 1H), 2.90 (dd, $J=14.0$, 2.9 Hz, 1H), 3.45–3.54 (m, 2H), 3.55–3.62 (m, 2H), 3.70–3.77 (m, 2H), 4.86–4.94 (m, 1H), 6.21–6.27 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=-5.2$, −5.3, 5.4 (3C), 7.2 (3C), 13.0 ($^1/_2$C), 13.1 ($^1/_2$C), 15.1 ($^1/_2$C), 15.2 ($^1/_2$C), 18.4, 19.0, 20.5 ($^1/_2$C), 20.6 ($^1/_2$C), 21.0 ($^1/_2$C), 21.1 ($^1/_2$C), 24.3, 25.9, 26.0 (3C), 26.8, 30.1 ($^1/_2$C), 30.2 ($^1/_2$C), 35.3, 39.7, 40.5 ($^1/_2$C), 40.6 ($^1/_2$C), 45.6, 62.3 ($^1/_2$C), 62.4 ($^1/_2$C), 64.3, 73.4, 80.8, 100.8 ($^1/_2$C), 100.9 ($^1/_2$C), 119.0 ($^1/_2$C), 119.1 ($^1/_2$C), 133.4 ($^1/_2$C), 133.7 ppm ($^1/_2$C); IR (neat): $\tilde{\nu}=2955$, 2878, 1686, 1462, 1383, 1341, 1254, 1086, 1007, 965, 936, 837, 808, 775, 739 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{32}H_{64}O_5Si_2$: 584.4292, found 584.4291 $[M]^+$.

(4a*R*,5*S*,6*R*,8a*R*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-6-triethylsiloxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carbaldehyde (25): Methanesulfonyl chloride (MsCl) (0.59 mL, 7.5 mmol) was added dropwise to a stirred solution of **23** (436 mg, 0.75 mmol) in dry CH_2Cl_2 (10 mL) containing Et_3N (1.25 mL, 8.9 mmol) at 0 °C under argon. After 30 min, the reaction was quenched with saturated aqueous NH_4Cl (5 mL) at 0 °C, and the resulting mixture was extracted with $CHCl_3$ (3×40 mL). The combined extracts were washed with brine (2×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 20:1) to give **25** (332 mg, 90%) as a colorless viscous liquid. $[\alpha]_D^{20}=+2.1$ ($c=1.36$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.05$ (s, 6H), 0.61 (q, $J=$

7.9 Hz, 6H), 0.82 (s, 3H), 0.90 (s, 9H), 0.95, (t, J=7.9 Hz, 9H), 1.06 (s, 3H), 1.24–1.33 (m, 3H), 1.33–1.44 (m, 1H), 1.45–1.55 (m, 2H), 1.56–1.62 (m, 1H), 1.64 (dd, J=12.8, 1.7 Hz, 1H), 1.72–1.86 (m, 2H), 1.90–1.99 (m, 1H), 2.06–2.16 (m, 1H), 2.39 (dd, J=18.2, 6.2 Hz, 1H), 3.48–3.56 (m, 1H), 3.56–3.66 (m, 2H), 6.39 (s, 1H), 9.39 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=−5.2, −5.3, 5.4 (3C), 7.2 (3C), 17.0, 18.4, 18.5, 20.9, 23.1, 25.9, 26.0 (3C), 26.7, 31.5, 35.0, 36.6, 40.0, 43.9, 64.2, 73.4, 137.6, 162.8, 195.1 ppm; IR (neat): $\tilde{\nu}$=2955, 2880, 2712, 1690, 1644, 1462, 1385, 1304, 1254, 1182, 1101, 1043, 1007, 965, 936, 837, 799, 775, 739, 567, 426 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{54}O_3Si_2$: 494.3611, found 494.3611 $[M]^+$.

(4a*R*,5*S*,6*R*,8a*R*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-6-triethylsiloxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-methanol (26): $NaBH_4$ (254 mg, 6.7 mmol) was added in small portions to a stirred solution of **25** (2.20 g, 4.5 mmol) in THF (50 mL) containing water (5 mL) at 0°C, and stirring was continued for 30 min at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (15 mL) at 0°C, and the resulting mixture was extracted with EtOAc (3×80 mL). The combined extracts were washed with brine (2×50 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1→8:1) to give **26** (2.16 g, 98%) as a colorless viscous liquid. $[\alpha]_D^{20}$=−5.3 (c=1.19 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.05 (s, 6H), 0.59–0.64 (m, 6H), 0.79 (s, 3H), 0.90 (s, 9H), 0.93–0.98 (m, 9H), 0.95 (s, 3H), 1.14 (dt, J=12.5, 3.2 Hz, 1H), 1.22 (t, J=6.0 Hz, 1H), 1.25–1.30 (m, 2H), 1.34–1.45 (m, 1H), 1.46–1.54 (m, 3H), 1.61 (dd, J=12.7, 1.5 Hz, 1H,), 1.64–1.72 (m, 2H), 1.82–1.92 (m, 1H), 1.99–2.14 (m, 2H), 3.48–3.55 (m, 1H), 3.56–3.63 (m, 2H), 3.96 (br d, J=6.0 Hz, 2H), 5.34 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=−5.2, −5.3, 5.4 (3C), 7.2 (3C), 17.9, 18.4, 18.5, 21.9, 26.0 (3C), 26.3, 26.8, 27.4, 32.6, 34.9, 35.0, 39.7, 44.3, 64.4, 67.3, 73.8, 133.3, 136.9 ppm; IR (neat): $\tilde{\nu}$=3328, 2955, 2280, 1462, 1414, 1385, 1360, 1254, 1186, 1101, 1041, 1007, 965, 837, 775, 739, 681 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{56}O_3Si_2$: 496.3768, found 496.3763 $[M]^+$.

(4a*R*,5*S*,6*R*,8a*R*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-2-(tri-*n*-butylstannylmethoxymethyl)-5,8a-dimethyl-6-triethylsiloxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene (13): KH (30% dispersion in mineral oil) (68.2 mg, 1.7 mmol), [18]crown-6 (450 mg, 1.7 mmol), and iodomethyl tri-*n*-butyltin (0.49 mL, 1.1 mmol) were added successively to a stirred solution of **26** (282 mg, 0.57 mmol) in dry THF (10 mL) at 0°C under argon, and stirring was continued for 3 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (4 mL) at 0°C, and resulting mixture was extracted with EtOAc (3×50 mL). The combined extracts were washed with brine (2×40 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography [hexane/EtOAc 100:1→50:1 (containing 0.2% Et_3N)] to give **13** (391 mg, 86%) as a colorless viscous liquid. $[\alpha]_D^{20}$=−3.6 (c=1.31 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.04 (s, 6H), 0.56–0.64 (m, 6H), 0.78 (s, 3H), 0.86–0.91 (m, 21H), 0.93–0.99 (m, 13H), 1.13 (dt, J=12.5, 3.2 Hz, 1H), 1.24–1.35 (m, 9H), 1.45–1.56 (m, 11H), 1.59–1.74 (m, 3H), 1.81–1.90 (m, 1H), 1.91–2.01 (m, 1H), 2.02–2.11 (m, 1H), 3.48–3.55 (m, 1H), 3.55–3.62 (m, 2H), 3.62–3.70 (m, 4H), 5.30 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=−5.2, −5.3, 5.4 (3C), 7.2 (3C), 9.0 (3C), 13.7 (3C), 17.9, 18.4, 18.5, 22.0, 26.0 (3C), 26.3, 26.7, 27.3 (3C), 27.6, 29.2 (3C), 32.7, 34.9, 35.0, 39.7, 44.3, 60.4, 64.4, 73.8, 79.3, 130.7, 138.7 ppm; IR (neat): $\tilde{\nu}$=2955, 1462, 1416, 1383, 1254, 1101, 1007, 961, 837, 775, 739, 683, 596, 511 cm^{-1}; HRMS (EI): m/z: calcd for $C_{41}H_{84}O_3Si_2Sn$: 800.4981, found 800.4984 $[M]^+$.

(1*R*,4a*R*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decahydronaphthalen-1-methanol (12), its (1*S*,4a*R*,5*S*,6*R*,8a*S*)-isomer (27), and (4a*R*,5*S*,6*R*,8a*R*)-5-(3-*tert*-butyldimethylsiloxypropyl)-2-methoxymethyl-5,8a-dimethyl-6-triethylsiloxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene (28): *n*BuLi in hexane (1.58 M solution, 0.91 mL, 1.4 mmol) was added dropwise to a stirred solution of **13** (116 mg, 0.14 mmol) in dry hexane (3 mL) at −50°C under argon, and the mixture was gradually warmed up to 0°C over 4 h, and stirring was continued for 1 h at 0°C. The reaction was quenched with saturated aqueous NH_4Cl (3 mL) at 0°C, and the resulting mixture was extracted with EtOAc (3×30 mL). The combined extracts were washed with brine (2×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 20:1) to give **12** (57.7 mg, 78%), **27** (6.6 mg, 9%), and **26** (2.2 mg, 3%).

When THF was used as a solvent instead of hexane, **12**, **27**, **28**, and **26** were obtained in 29, 6, 32, and 11% yields, respectively. In the case of using Et_2O as a solvent instead of hexane, **12**, **27**, **28**, and **26** were obtained in 50, 16, 5, and 2% yields, respectively.

Compound 12: white prisms (recrystallization from hexane); m.p. 49–51°C; $[\alpha]_D^{20}$=−19.3 (c=1.20 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.04 (s, 6H), 0.58–0.65 (m, 6H), 0.76 (s, 3H), 0.89 (s, 9H), 0.97 (t, J=7.9 Hz, 9H), 0.98 (s, 3H), 1.21–1.27 (m, 3H), 1.27–1.39 (m, 1H), 1.44–1.54 (m, 4H), 1.56–1.64 (m, 1H), 1.71 (dd, J=12.9, 2.8 Hz, 1H), 1.81–1.91 (m, 2H), 1.95–2.04 (m, 1H), 2.10–2.20 (m, 1H), 2.29 (br d, J=13.9, 1H), 3.47–3.53 (m, 1H), 3.55–3.61 (m, 2H), 3.62–3.69 (m, 1H), 3.81 (dt, J=10.0, 4.9 Hz, 1H), 4.74 (t, J=2.1 Hz, 1H), 4.91 ppm (t, J=2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=−5.2, −5.3, 5.4 (3C), 7.2 (3C), 18.4, 19.1, 22.4, 23.2, 26.0 (3C), 26.1, 26.8, 29.0, 31.6, 35.4, 37.4, 40.0, 40.5, 59.0, 60.9, 64.3, 73.6, 112.7, 147.3 ppm; IR (KBr): $\tilde{\nu}$=3341, 2957, 2880, 2361, 1653, 1462, 1414, 1358, 1360, 1256, 1101, 1034, 1011, 970, 936, 889, 837, 814, 777, 737, 666 cm^{-1}; HRMS (EI): m/z: calcd for $C_{29}H_{58}O_3Si_2$: 510.3925, found 510.3905 $[M]^+$.

Compound 27: colorless viscous liquid; $[\alpha]_D^{20}$=−17.3 (c=0.83 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.04 (s, 6H), 0.58–0.61 (m, 6H), 0.74 (s, 3H), 0.75 (s, 3H), 0.89 (s, 9H), 0.98 (t, J=7.9 Hz, 9H), 1.21–1.35 (m, 4H), 1.36–1.41 (m, 1H), 1.45–1.55 (m, 4H), 1.60–1.71 (m, 2H), 1.73–1.83 (m, 1H), 2.01–2.10 (m, 2H), 2.38–2.46 (m, 1H), 3.47–3.54 (m, 1H), 3.55–3.61 (m, 2H), 3.73–3.80 (m, 1H), 3.81–3.88 (m, 1H), 4.64 (d, J=1.0 Hz, 1H), 4.93 ppm (d, J=1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=−5.2, −5.3, 5.4 (3C), 7.2 (3C), 16.0, 18.4, 19.0, 23.5, 26.0 (3C), 26.3, 26.8, 31.5, 35.6, 37.8, 38.8, 40.1, 48.2, 58.8, 59.2, 64.3, 73.3, 106.1, 148.0 ppm; IR (neat): $\tilde{\nu}$=3404, 2953, 2878, 1644, 1462, 1385, 1362, 1254, 1100, 1053, 1009, 965, 937, 891, 837, 814, 775, 739 cm^{-1}; HRMS (EI): m/z: calcd for $C_{29}H_{58}O_3Si_2$: 510.3925, found 510.3938 $[M]^+$.

Compound 28: colorless viscous liquid; $[\alpha]_D^{20}$ = −4.8 (c=1.04 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.05 (s, 6H), 0.60 (q, J=8.2 Hz, 6H), 0.78 (s, 3H), 0.90 (s, 9H), 0.93–0.97 (m, 12H), 1.13 (dt, J=12.1, 2.9 Hz, 1H), 1.24–1.29 (m, 2H), 1.34–1.45 (m, 1H), 1.47–1.55 (m, 3H), 1.61–1.72 (m, 3H), 1.83–1.90 (m, 1H), 1.95–2.13 (m, 2H), 3.28 (s, 3H), 3.48–3.62 (m, 3H), 3.74 (s, 2H), 5.34 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=−5.29, −5.28, 5.4 (3C), 7.2 (3C), 17.9, 18.35, 18.40, 21.9, 26.0 (3C), 26.3, 26.7, 27.7, 32.6, 34.9, 35.0, 39.7, 44.2, 57.4, 64.4, 73.8, 77.1, 130.4, 139.0 ppm; IR (neat): $\tilde{\nu}$=2953, 2877, 2817, 1470, 1415, 1384, 1254, 1187, 1103, 1043, 1005, 960, 836, 775, 665 cm^{-1}; HRMS (EI): m/z: calcd for $C_{29}H_{58}O_3Si_2$: 510.3924, found 510.3931 $[M]^+$.

(1*R*,4a*R*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decahydronaphthalene-1-carbaldehyde (11): Dess–Martin periodinane (366 mg, 0.86 mmol) was added in small portions to a stirred solution of **12** (147 mg, 0.29 mmol) containing $NaHCO_3$ (244 mg, 2.90 mmol) in dry CH_2Cl_2 (12 mL) at room temperature. After 1 h, the reaction was quenched with 10% aqueous $Na_2S_2O_3$ (10 mL) at 0°C, and the resulting mixture was extracted with $CHCl_3$ (3×50 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2×20 mL) and brine (2×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 50:1) to give **11** (143 mg, 98%) as a colorless viscous liquid. $[\alpha]_D^{20}$=−3.1 (c=1.22 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.05 (s, 6H), 0.57–0.64 (m, 6H), 0.80 (s, 3H), 0.90 (s, 9H), 0.96 (t, J=7.9 Hz, 9H), 0.98 (s, 3H), 1.09 (dt, J=12.9, 3.1 Hz, 1H), 1.24–1.35 (m, 2H), 1.37–1.54 (m, 4H), 1.69–1.77 (m, 1H), 1.83–1.93 (m, 1H), 1.99–2.11 (m, 2H), 2.26–2.36 (m, 1H), 2.41–2.47 (m, 1H), 2.49 (d, J=3.9 Hz, 1H), 3.48–3.55 (m, 1H), 3.56–3.66 (m, 2H), 4.73 (s, 1H), 4.89 (s, 1H), 10.03 ppm (d, J=3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=−5.2, −5.3, 5.4 (3C), 7.1 (3C), 18.4, 18.9, 22.2, 22.3, 25.8, 26.0 (3C), 26.7, 30.1, 33.7, 35.3, 38.9, 40.1, 42.2, 64.2, 71.4, 73.3, 113.1, 143.1, 203.4 ppm; IR (neat): $\tilde{\nu}$=2955, 2880, 2730, 1719, 1647, 1462, 1414, 1385, 1362, 1258, 1100, 1013, 966, 895, 837, 810, 777, 739 cm^{-1}; HRMS (EI): m/z: calcd for $C_{29}H_{56}O_3Si_2$: 508.3768, found 508.3750 $[M]^+$.

Methyl 4-methyl-3,5-dioxohexanoate (30): A solution of 3-methyl-2,4-pentanedione (**29**; 7.40 mL, 63 mmol) in dry THF (50 mL) was added dropwise to a stirred solution of $NaN(SiMe_3)_2$ in THF (1.9 M solution, 100 mL, 190 mmol) in dry THF (100 mL) at −78 °C under argon, and the reaction mixture was stirred for 4 h at room temperature. Dimethylcarbonate (5.4 mL, 64.0 mmol) was added dropwise to the mixture at −78 °C, and the resulting solution was further stirred for 24 h at room temperature. The reaction mixture was acidified with 2 M HCl (150 mL) at 0 °C. The resulting mixture was extracted with EtOAc (3×200 mL). The combined extracts were washed with brine (2×100 mL), and dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1→5:1) to give **30** (ca. 1:1 tautomeric mixture) (9.21 g, 85 %) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (d, J = 7.3 Hz, $^3/_2$H), 1.85 (s, $^3/_2$H), 2.15 (s, $^3/_2$H), 2.23 (s, $^3/_2$H), 3.48 (s, 1H), 3.55 (s, 1H), 3.74 (s, $^3/_2$H), 3.75 (s, $^3/_2$H), 3.87 ppm (q, J = 7.3 Hz, $^1/_2$H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.4 ($^1/_2$C), 12.6 ($^1/_2$C), 23.5 ($^1/_2$C), 28.5 ($^1/_2$C), 42.5 ($^1/_2$C), 47.5 ($^1/_2$C), 52.3 ($^1/_2$C), 60.7 ($^1/_2$C), 90.2 ($^1/_2$C), 105.4 ($^1/_2$C), 167.3 ($^1/_2$C), 168.1 ($^1/_2$C), 184.1 ($^1/_2$C), 191.8 ($^1/_2$C), 199.5 ppm; IR (neat): $\tilde{\nu}$ = 3628, 3566, 3461, 3421, 2992, 2955, 1744, 1704, 1615, 1437, 1406, 1327, 1263, 1160, 1056, 1003, 887, 846, 816 cm^{-1}; HRMS (EI): m/z: calcd for $C_8H_{12}O_4$: 172.0736, found 172.0743 $[M]^+$.

4-Hydroxy-5,6-dimethyl-2*H*-pyran-2-one (31): 1,8-Diazabicyclo-[5.4.0]undec-7-ene (DBU) (2.18 mL, 14 mmol) was added dropwise to a stirred solution of **30** (5.00 g, 29 mmol) in benzene (250 mL) at room temperature under argon, and the mixture was heated at reflux for 1 h. After cooling, the reaction was quenched with 1 M HCl (60 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×300 mL). The combined extracts were washed with brine (2×200 mL), and dried over Na_2SO_4. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (EtOAc) to give **31** (3.46 g, 86 %) as a yellow solid. Recrystallization from acetone afforded a pale yellow solid. M.p. 209–210 °C; ^{1}H NMR (400 MHz, CD_3OD): δ = 1.91 (s, 3H), 2.23 (s, 3H), 5.39 ppm (s, 1H); ^{13}C NMR (100 MHz, CD_3OD): δ = 9.4, 17.4, 89.5, 109.3, 160.5, 168.1, 173.3 ppm; IR (KBr): $\tilde{\nu}$ = 3313, 2938, 2797, 2616, 1672, 1570, 1508, 1366, 1308, 1267, 1120, 916, 821, 758, 629, 461 cm^{-1}; HRMS (EI): m/z: calcd for $C_7H_8O_3$: 140.0473, found 140.0475 $[M]^+$.

3-Bromo-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (10): Methyl fluorosulfonate (3.40 mL, 42 mmol) was added dropwise to a stirred solution of **31** (1.00 g, 7.1 mmol) in CH_2Cl_2 (60 mL) at room temperature. After 24 h, the reaction mixture was concentrated in vacuo taking great care to avoid exposure to the volatile and highly toxic methyl fluorosulfonate. In order to remove an excess of methyl fluorosulfonate, the residue was diluted with CH_2Cl_2 (40 mL), and the resulting mixture was concentrated in vacuo. This operation was repeated three times, affording crude methoxy-γ-pyrone (**32**; 978 mg, 89 %) as a pale yellow solid, which was used for the next reaction without purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.91 (s, 3H), 2.26 (s, 3H), 3.83 (s, 3H), 5.49 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.6, 16.9, 55.8, 88.3, 118.7, 156.8, 167.1, 181.3 ppm; IR (KBr): $\tilde{\nu}$ = 3448, 2962, 2854, 1671, 1599, 1420, 1376, 1254, 1123, 1064, 938, 841 cm^{-1}; HRMS (EI): m/z: calcd for $C_8H_{10}O_3$: 154.0630, found 154.0627 $[M]^+$.

N-Bromosuccinimide (NBS) (1.95 g, 11 mmol) was added in small portions to a stirred solution of **32** (978 mg, 6.4 mmol) in THF (70 mL) at 0 °C. After 2 h, the reaction mixture was quenched with 1 M NaOH (40 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×120 mL). The combined extracts were washed with brine (2×80 mL), and dried over $MgSO_4$. Concentration of the solvent in vacuo to afforded a residue, which was purified by column chromatography (hexane/EtOAc 2:1→1:1) to give **10** (1.04 g, 71 %) as a white solid. Recrystallization from acetone afforded white needles. M.p. 110–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.99 (s, 3H), 2.31 (s, 3H), 4.06 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.7, 16.8, 56.3, 89.2, 118.8, 155.1, 161.8, 175.3 ppm; IR (KBr): $\tilde{\nu}$ = 2961, 2930, 2866, 1665, 1626, 1584, 1460, 1393, 1368, 1327, 1217, 1013, 1179, 1138, 1065, 990, 955, 924, 804, 752, 664, 608, 586, 469 cm^{-1}; HRMS (EI): m/z: calcd for $C_8H_9BrO_3$: 231.9735, found 231.9724 $[M]^+$; elemental analysis calcd (%) for $C_8H_9BrO_3$: C 41.23, H 3.89; found C 41.32, H 3.95.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*S*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decahydronaphthalen-1-yl]hydroxymethyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (33): *n*BuLi in hexane (1.58 M solution, 0.66 mL, 1.0 mmol) was added dropwise to a stirred solution of **10** (254 mg, 1.1 mmol) in dry THF (8 mL) at −78 °C under argon. After 30 min, a solution of **11** (139 mg, 0.27 mmol) in dry THF (8 mL) was added dropwise to the above mixture at −78 °C, and stirring was continued for 2 h at −30 °C. The reaction was quenched with saturated aqueous NH_4Cl (8 mL) at −30 °C, and the resulting mixture was extracted with EtOAc (3×60 mL). The combined extracts were washed with brine (2×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 5:1) to give **33** (ca. 8:1 diastereomeric mixture) (172 mg, 95 %) as a colorless viscous liquid. $[\alpha]_D^{20}$ = −17.7 (c = 1.13 in $CHCl_3$). The ^{1}H and ^{13}C NMR spectra described below represent the major isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 6H), 0.58–0.69 (m, 6H), 0.77 (s, 3H), 0.80–0.87 (m, 1H), 0.90 (s, 9H), 0.94 (s, 3H), 0.99 (t, J = 7.9 Hz, 9H), 1.25–1.41 (m, 3H), 1.48–1.55 (m, 3H), 1.58–1.66 (m, 1H), 1.82–1.92 (m, 2H), 1.87 (s, 3H), 2.25 (s, 3H), 2.30–2.37 (m, 2H), 2.44 (dd, J = 12.8, 2.9 Hz, 1H), 2.50–2.60 (m, 1H), 3.48–3.54 (m, 1H), 3.55–3.65 (m, 2H), 3.95 (s, 3H), 4.32 (s, 1H), 4.72 (s, 1H), 4.84 (d, J = 9.9 Hz, 1H), 5.22 ppm (dd, J = 9.9, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.2, −5.3, 5.4 (3C), 7.2 (3C), 9.7, 16.9, 18.4, 19.6, 23.0, 23.2, 26.0 (3C), 26.5, 27.1, 28.9, 35.0, 35.6, 38.5, 40.2, 40.3, 55.7, 62.0, 64.5, 67.7, 74.2, 105.7, 111.6, 119.5, 148.7, 155.3, 161.0, 181.6 ppm; IR (neat): $\tilde{\nu}$ = 3301, 2955, 2878, 1671, 1588, 1464, 1424, 1379, 1319, 1296, 1254, 1152, 1096, 1009, 937, 835, 802, 779, 741, 669 cm^{-1}; HRMS (EI): m/z: calcd for $C_{37}H_{66}O_6Si_2$: 662.4398, found 662.4383 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5-(3-*tert*-Butyldimethylsiloxypropyl)-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decahydronaphthalen-1-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (8): $NaN(SiMe_3)_2$ in THF (1.0 M solution, 0.31 mL, 0.31 mmol) was added dropwise to a stirred solution of **33** (172 mg, 0.26 mmol) in dry THF (5 mL) containing CS_2 (0.31 mL, 5.2 mmol) at −78 °C under argon. After 1 h, MeI (0.20 mL, 2.6 mmol) was added dropwise to the mixture at −78 °C, and the resulting solution was further stirred for 1 h at same temperature. The reaction was quenched with saturated aqueous NH_4Cl (4 mL), and resulting mixture was extracted with EtOAc (3×40 mL). The combined extracts were washed with brine (2×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded crude methyl xanthate **34** (182 mg, 93 %), which was used for the next reaction without purification.

nBu$_3$SnH (0.13 mL, 0.48 mmol) and 2,2′-azobisisobutyronitrile (AIBN) (7.9 mg, 48 μmol) were added to a stirred solution of **34** (182 mg, 0.24 mmol) in dry toluene (8 mL) at room temperature. For the deaeration of the reaction mixture, it was frozen using liquid nitrogen, and the reaction vessel was evacuated in vacuo for 30 min followed by filled with dry argon. The mixture was then heated at reflux for 1 h under argon. After cooling, the reaction mixture was concentrated in vacuo to afforded a residue, which was purified by column chromatography (benzene/EtOAc 30:1) to give **8** (129 mg, 77 %) as a colorless viscous liquid. $[\alpha]_D^{20}$ = −43.7 (c = 0.41 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.05 (s, 6H), 0.58–0.66 (m, 6H), 0.77 (s, 3H), 0.90 (s, 9H), 0.94–1.00 (m, 1H), 0.95 (s, 3H), 0.97 (t, J = 7.9 Hz, 9H), 1.24–1.38 (m, 3H), 1.45–1.55 (m, 4H), 1.84–1.95 (m, 3H), 1.90 (s, 3H), 2.07–2.18 (m, 1H), 2.23 (s, 3H), 2.28–2.43 (m, 2H), 2.48 (t, J = 12.8 Hz, 1H), 2.75 (dd, J = 12.8, 3.4 Hz, 1H), 3.45–3.55 (m, 1H), 3.56–3.63 (m, 2H), 3.84 (s, 3H), 4.14 (t, J = 2.4 Hz, 1H), 4.47 ppm (t, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.2, −5.3, 5.5 (3C), 7.2 (3C), 10.0, 17.0, 18.4, 19.1, 19.8, 22.9, 23.1, 26.0 (3C), 26.2, 26.9, 28.6, 31.5, 35.4, 37.8, 39.2, 39.9, 55.3, 56.3, 64.5, 74.0, 103.8, 108.8, 118.6, 124.9, 149.6, 154.8, 180.4 ppm; IR (neat): $\tilde{\nu}$ = 2955, 2282, 1736, 1672, 1605, 1460, 1414, 1375, 1318, 1256, 1163, 1100, 1009, 835, 810, 779, 725 cm^{-1}; HRMS (EI): m/z: calcd for $C_{37}H_{66}O_5Si_2$: 646.4449, found 646.4454 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5,8a-Dimethyl-5-(3-hydroxypropyl)-2-methylene-6-(triethylsiloxy)decahydronaphthalen-1-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (35): A solution of **8** (120 mg, 0.19 mmol) in

AcOH/THF/H_2O 3:2:2 (20 mL) was stirred for 2 h at room temperature. The reaction mixture was basified with 1 M NaOH (7 mL) and saturated aqueous $NaHCO_3$ (10 mL) at 0 °C. The resulting mixture was extracted with EtOAc (3×50 mL). The combined extracts were washed with saturated aqueous NH_4Cl (2×30 mL) and brine (30 mL), and dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 2:1) to give **35** (82.9 mg, 84 %) as a colorless viscous liquid. $[\alpha]_D^{20} = -45.6$ ($c = 0.80$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.59$–0.67 (m, 6H), 0.78 (s, 3H), 0.94–1.01 (m, 1H), 0.95 (s, 3H), 0.98 (t, $J = 7.9$ Hz, 9H), 1.15–1.22 (m, 1H), 1.24–1.36 (m, 3H), 1.40–1.48 (m, 1H), 1.54–1.62 (m, 3H), 1.83–1.94 (m, 1H), 1.90 (s, 3H), 2.07–2.14 (m, 1H), 2.23 (s, 3H), 2.29–2.44 (m, 2H), 2.48 (t, $J = 12.8$ Hz, 1H), 2.75 (dd, $J = 12.8$, 3.5 Hz, 1H), 3.55–3.68 (m, 3H), 3.85 (s, 3H), 4.14 (t, $J = 2.4$ Hz, 1H), 4.48 ppm (t, $J = 2.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.5$ (3C), 7.2 (3C), 10.0, 17.0, 19.2, 19.7, 22.9, 23.1, 26.2, 26.8, 28.6, 31.5, 35.4, 37.8, 39.2, 39.9, 55.3, 56.2, 64.3, 74.0, 103.7, 108.9, 118.6, 149.4, 154.8, 163.0, 180.4 ppm; IR (neat): $\tilde{\nu} =$ 3409, 3065, 2955, 2878, 1726, 1671, 1589, 1462, 1420, 1377, 1319, 1258, 1182, 1148, 1078, 1011, 885, 810, 750, 478 cm^{-1}; HRMS (EI): m/z: calcd for $C_{31}H_{52}O_5Si$: 532.3584, found 532.3555 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5,8a-Dimethyl-2-methylene-5-(3-oxopropyl)-6-(triethylsiloxy)decahydronaphthalen-1-yl]-methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (36): Dess–Martin periodinane (191 mg, 0.42 mmol) was added in small portions to a stirred solution of **35** (80.0 mg, 0.14 mmol) in dry CH_2Cl_2 (8 mL) containing $NaHCO_3$ (120 mg, 1.4 mmol) at room temperature. After 30 min, the reaction was quenched with 20 % aqueous $Na_2S_2O_3$ (8 mL) at 0 °C, and the resulting mixture was extracted with Et_2O (3×50 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2×30 mL) and brine (2×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 4:1) to give **36** (76.7 mg, 96 %) as a colorless viscous liquid. $[\alpha]_D^{20} = -46.7$ ($c = 0.65$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.58$–0.67 (m, 6H), 0.78 (s, 3H), 0.94–0.99 (m, 12H), 0.99–1.05 (m, 1H), 1.20–1.39 (m, 2H), 1.55–1.66 (m, 2H), 1.69–1.78 (m, 1H), 1.84–1.98 (m, 3H), 1.91 (s, 3H), 2.08–2.15 (m, 1H), 2.24 (s, 3H), 2.28–2.37 (m, 1H), 2.38–2.51 (m, 4H), 2.76 (dd, $J = 12.9$, 3.5 Hz, 1H), 3.58 (br s, 1H), 3.85 (s, 3H), 4.15 (t, $J = 2.3$ Hz, 1H), 4.49 (t, $J = 2.3$ Hz, 1H), 9.80 ppm (d, $J = 1.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.4$ (3C), 7.2 (3C), 10.0, 17.0, 19.4, 19.8, 23.0, 26.1, 28.5, 29.7, 31.4, 31.5, 37.7, 38.8, 39.1, 39.7, 55.3, 56.0, 74.3, 103.5, 109.2, 118.6, 149.1, 154.8, 163.0, 180.4, 203.6 ppm; IR (neat): $\tilde{\nu} =$2953, 1726, 1672, 1603, 1460, 1414, 1383, 1318, 1256, 1090, 802, 741, 567, 476, 403 cm^{-1}; HRMS (EI): m/z: calcd for $C_{31}H_{50}O_5Si$: 530.3428, found 530.3447 $[M]^+$.

3-[(4a*R*,6a*R*,7*R*,10a*R*,10b*R*)-6a,10b-Dimethyl-3-hydroxy-8-(methylene)-perhydro-1*H*-benzo[*f*]chromen-7-yl]-methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (37): Tetrabutylammonium fluoride (TBAF) in THF (1.0 M solution, 0.45 mL, 0.45 mmol) was added dropwise to a stirred solution of **36** (23.7 mg, 45 μmol) in THF (3 mL) at 0 °C under argon, and stirring was continued for 40 min at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (2 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×30 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (3×20 mL) and brine (2×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 2:1→1:1) to give **37** (1:1 diastereomeric mixture) (18.8 mg, 99 %) as a colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.80$ (s, $^3/_2$H), 0.84 (s, $^3/_2$H), 0.97 (s, 3H), 0.98–1.03 (m, $^1/_2$H), 1.28–1.36 (m, 3H), 1.41–1.52 (m, 2H), 1.59–1.72 (m, $^5/_2$H), 1.88–2.04 (m, 3H), 1.90 (s, 3H), 2.08–2.14 (m, $^1/_2$H), 2.15–2.20 (m, $^1/_2$H), 2.24 (s, 3H), 2.26–2.38 (m, 2H), 2.39–2.46 (m, $^1/_2$H), 2.54–2.63 (m, 1H), 2.68–2.74 (m, $^1/_2$H), 2.81 (dd, $J = 13.2$, 4.7 Hz, $^1/_2$H), 3.05–3.12 (m, $^1/_2$H), 3.35 (t, $J = 2.7$ Hz, $^1/_2$H), 3.80–3.84 (m, $^1/_2$H), 3.86 (s, $^3/_2$H), 3.87 (s, $^3/_2$H), 4.17–4.20 (m, $^1/_2$H), 4.22–4.25 (m, $^1/_2$H), 4.44–4.56 (m, 1H), 4.71 (br s, $^1/_2$H), 5.33 ppm (br s, $^1/_2$H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 10.1$, 14.1, 16.9, 19.8, 22.6, 22.9, 23.3, 24.4, 29.1, 31.4, 33.8, 34.5, 35.1, 37.5, 55.3, 56.0, 80.3, 96.9, 103.5, 109.0, 120.1, 149.3, 154.7, 162.7, 180.4 ppm; IR (neat): $\tilde{\nu} =$3403, 2930, 2292, 1726, 1671, 1589, 1462, 1422, 1377, 1321, 1260, 1019, 951, 885, 802, 754 cm^{-1}; HRMS (EI): m/z: calcd for $C_{25}H_{34}O_4$: 398.2457, found 398.2447 $[M\text{-}H_2O]^+$.

3-[(4a*R*,6a*R*,7*R*,10a*R*,10b*R*)-6a,10b-Dimethyl-8-methylene-4a,5,6,6a,7,8,9,10,10a,10b-perhydro-1*H*-benzo[*f*]chromen-7-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (candelalide A) (1): MsCl (70.0 μL, 90 μmol) was added to a stirred solution of **37** (15.0 mg, 35 μmol) in dry THF (3 mL) containing Et_3N (40 μL, 0.29 mmol) at 0 °C under argon, and stirring was continued at room temperature for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (1.0 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (3×15 mL) and brine (2×15 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 1:1) to give **1** (12.2 mg, 87 %) as a colorless amorphous powder. $[\alpha]_D^{22} = -25.1$ ($c = 0.35$ in CH_3OH) {lit.[1] $[\alpha]_D^{22} = -23.1$ ($c = 0.26$ in CH_3OH)}. The ^{1}H and ^{13}C NMR, IR, and MS spectra (see below) are identical to those of natural (−)-candelalide A. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 0.90$ (s, 3H), 0.99 (s, 3H), 1.04 (dt, $J = 13.2$, 3.2 Hz, 1H), 1.36 (dq, $J = 13.2$, 4.8 Hz, 1H), 1.54–1.55 (m, 1H), 1.59 (dt, $J = 17.9$, 2.5 Hz, 1H), 1.73–1.77 (m, 1H), 1.86 (dd, $J = 11.6$, 3.3 Hz, 1H), 1.89 (s, 3H), 1.95–1.96 (m, 1H), 1.98 (dd, $J = 12.8$, 9.9 Hz, 1H), 2.08–2.14 (m, 2H), 2.23 (s, 3H), 2.37 (dd, $J = 13.2$, 4.1 Hz, 1H), 2.40–2.49 (m, 2H), 2.70 (dd, $J = 13.2$, 3.3 Hz, 1H), 3.71 (s, 1H), 3.84 (s, 3H), 4.17 (t, $J = 2.6$ Hz, 1H), 4.49 (t, $J = 2.6$ Hz, 1H), 4.54 (dt, $J = 6.0$, 2.2 Hz, 1H), 6.38 ppm (dd, $J = 6.1$, 2.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 10.1$, 16.9, 19.7, 22.8, 23.4, 23.5, 23.9, 28.7, 31.3, 32.5, 33.6, 34.4, 37.4, 55.3, 56.6, 78.9, 97.6, 103.5, 108.9, 118.5, 142.6, 149.2, 154.7, 162.8, 180.3 ppm; IR (KBr): $\tilde{\nu} =$ 2935, 2361, 1783, 1670, 1591, 1462, 1255, 1145, 1060, 985, 952, 754 cm^{-1}; HRMS (EI): m/z: calcd for $C_{25}H_{34}O_4$: 398.2457, found 398.2447 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5,8a-Dimethyl-2-methylene-5-(4-methylpent-3-enyl)-6-(triethylsiloxy)decahydronaphthalen-1-yl]methyl-2-methoxy-5,6-dimethyl-4*H*-pyran-4-one (38): *n*BuLi in hexane (1.56 M, 0.17 mL, 0.26 mmol) was added dropwise to a stirred suspension of isopropyltriphenylphosphonium iodide (127 mg, 0.30 mmol) in dry THF (10 mL) at −20 °C under argon, and stirring was continued for 30 min at the same temperature. A solution of **36** (52.0 mg, 98 μmol) in dry THF (3 mL) was added dropwise to the above mixture at −20 °C, and the mixture was warmed up to −5 °C over 1 h. The reaction was quenched with saturated aqueous NH_4Cl (8 mL), and the resulting mixture was extracted with EtOAc (3×50 mL). The combined extracts were washed with brine (2×40 mL), and dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1→5:1) to give **38** (44.8 mg, 82 %) as a colorless amorphous powder. $[\alpha]_D^{20} = -43.4$ ($c = 0.93$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.60$–0.66 (m, 6H), 0.80 (s, 3H), 0.94–1.00 (m, 12H), 1.18–1.35 (m, 2H), 1.44–1.59 (m, 4H), 1.62 (s, 3H), 1.69 (s, 3H), 1.85–1.98 (m, 5H), 1.92 (s, 3H), 2.09 (dd, $J = 13.2$, 3.4 Hz, 1H), 2.23 (s, 3H), 2.32–2.38 (m, 2H), 2.45–2.50 (m, 1H), 2.76 (dd, $J = 12.7$, 3.4 Hz, 1H), 3.64 (s, 1H), 3.84 (s, 3H), 4.14 (s, 1H), 4.47 (s, 1H), 5.08 ppm (t, $J = 6.8$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.4$ (3C), 7.2 (3C), 10.0, 16.9, 17.7, 19.0, 19.7, 21.8, 22.9, 23.1, 25.7, 26.2, 28.5, 31.5, 37.7, 39.2, 39.6, 40.1, 55.3, 56.1, 73.7, 103.7, 108.8, 118.6, 125.8, 130.5, 149.5, 154.8, 162.9, 180.4 ppm; IR (KBr): $\tilde{\nu} =$2952, 2932, 2876, 1729, 1672, 1604, 1460, 1415, 1374, 1316, 1254, 1084, 1005, 885, 812, 782, 723 cm^{-1}; HRMS (EI): m/z: calcd for $C_{34}H_{56}O_4Si$: 556.3948, found 556.3937 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5,8a-Dimethyl-2-methylene-5-(3,3-dimethyloxiran-2-yl)ethyl-6-(triethylsiloxy)decahydronaphthalen-1-yl]methyl-2-methoxy-5,6-dimethyl-4*H*-pyran-4-one (39): 3-Chloroperoxybenzoic acid (*m*CPBA) (17.1 mg, 64 μmol) was added in small portions to a stirred solution of **38** (36.0 mg, 63 μmol) in CH_2Cl_2 (4 mL) containing $NaHCO_3$ (10.8 mg, 0.13 mmol) at 0 °C, and stirring was continued for 2 h at the same temperature. The reaction was quenched with 20 % aqueous $Na_2S_2O_3$ (2 mL) at 0 °C, and the resulting mixture was extracted with $CHCl_3$ (3×30 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2×20 mL) and brine (2×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 5:1) to give **39** (ca. 1:1 diastereomeric mixture) (36.3 mg, 98 %) as a colorless amorphous

powder. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.60–0.67 (m, 6H), 0.77 (s, $^3/_2$H), 0.78 (s, $^3/_2$H), 0.95–1.00 (m, 12H), 1.19–1.36 (m, 2H), 1.27 (s, $^3/_2$H), 1.29 (s, $^3/_2$H), 1.31 (s, $^3/_2$H), 1.32 (s, $^3/_2$H), 1.43–1.71 (m, 6H), 1.85–1.95 (m, 3H), 1.91 (s, 3H), 2.08–2.13 (m, 1H), 2.24 (s, 3H), 2.30–2.40 (m, 2H), 2.44–2.52 (m, 1H), 2.64–2.69 (m, 1H), 2.73–2.78 (m, 1H), 3.59–3.61 (m, 1H), 3.85 (s, 3H), 4.14–4.56 (m, 1H), 4.48–4.49 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.4 (3C), 7.2 (3C), 10.0, 17.0, 18.6, 18.9 ($^1/_2$C), 19.0 ($^1/_2$C), 19.4 ($^1/_2$C), 19.7 ($^1/_2$C), 22.88 ($^1/_2$C), 22.94 ($^1/_2$C), 22.98 ($^1/_2$C), 23.07 ($^1/_2$C), 23.09 ($^1/_2$C), 23.11 ($^1/_2$C), 24.9 ($^1/_2$C), 25.0 ($^1/_2$C), 26.1 ($^1/_2$C), 26.2 ($^1/_2$C), 28.48 ($^1/_2$C), 28.53 ($^1/_2$C), 31.4 ($^1/_2$C), 31.5 ($^1/_2$C), 35.6 ($^1/_2$C), 36.5 ($^1/_2$C), 37.6, 39.0 ($^1/_2$C), 39.3 ($^1/_2$C), 39.98 ($^1/_2$C), 40.0 ($^1/_2$C), 55.3, 56.09 ($^1/_2$C), 56.13 ($^1/_2$C), 58.1 ($^1/_2$C), 58.4 ($^1/_2$C), 65.3 ($^1/_2$C), 65.5 ($^1/_2$C), 73.6 ($^1/_2$C), 74.3 ($^1/_2$C), 103.6 ($^1/_2$C), 103.7 ($^1/_2$C), 109.0, 118.6, 149.3 ($^1/_2$C), 149.4, ($^1/_2$C), 154.8, 162.9 ($^1/_2$C), 163.0 ($^1/_2$C), 180.4 ppm; IR (KBr): $\tilde{\nu}$ = 2954, 2876, 1672, 1603, 1460, 1415, 1375, 1317, 1254, 1075, 1004, 928, 887, 812, 783, 732, 673 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{34}H_{56}O_5Si$: 572.3897, found 572.3887 $[M]^+$.

3-[(3*R*,4a*R*,6a*R*,7*R*,10a*R*,10b*R*)-6a,10b-Dimethyl-3-(1-hydroxy-1-methylethyl)-(8-methylene)perhydor-1*H*-benzo[*f*]chromen-7-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-4-one (candelalide C) (3): TBAF in THF (1.0 M solution, 0.24 mL, 0.24 mmol) was added dropwise to a stirred solution of **39** (ca. 1:1 diastereomeric mixture) (13.8 mg, 24 μmol) in THF (3 mL) at 0 °C under argon, and stirring was continued for 1 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (2 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×40 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2×20 mL) and brine (2×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 2:1→1:1) to give **3** (4.8 mg, 43%) as a colorless amorphous powder. $[\alpha]_D^{22}$ = −68.8 (*c* = 0.98 in CH_3OH) {lit. [1] $[\alpha]_D^{22}$ = −67.0 (*c* = 1.03 in CH_3OH)}. The ^{1}H and ^{13}C NMR, IR, and MS spectra (see below) are identical to those of natural (−)-candelalide C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (s, 3H), 0.96 (s, 3H), 0.99–1.07 (m, 2H), 1.17 (s, 3H), 1.20 (s, 3H), 1.30–1.36 (m, 2H), 1.49–1.54 (m, 1H), 1.63–1.69 (m, 2H), 1.86 (dd, *J* = 11.7, 2.9 Hz, 1H), 1.90 (s, 3H), 1.92–2.00 (m, 2H), 2.11–2.16 (m, 1H), 2.19 (dd, 1H, *J* = 13.2, 2.9 Hz), 2.24 (s, 3H), 2.34–2.49 (m, 3H), 2.77 (dd, *J* = 13.2, 3.4 Hz, 1H), 3.16 (dd, *J* = 11.7, 2.4 Hz, 1H), 3.24 (t, *J* = 2.9 Hz, 1H), 3.85 (s, 3H), 4.19–4.20 (m, 1H), 4.49–4.51 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.0, 17.0, 19.8, 22.0, 22.4, 22.9, 23.3, 23.8, 24.6, 25.7, 29.2, 31.3, 33.7, 34.7, 36.1, 37.5, 55.3, 56.7, 72.0, 81.7, 83.9, 103.7, 108.9, 118.6, 149.4, 154.8, 162.9, 180.3 ppm; IR (KBr): $\tilde{\nu}$ = 3419, 2937, 2857, 1725, 1670, 1591, 1461, 1418, 1376, 1318, 1255, 1149, 1097, 1071, 986, 887, 753 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{28}H_{42}O_5$: 458.3032, found 458.3026 $[M]^+$.

(4a*S*,5*S*,6*R*,8a*S*)-5-Allyl-5,8a-dimethyl-6-(triethylsiloxy)decahydronaphthalen-1-one (48): PPTS (1.11 g, 4.4 mmol) was added to a stirred solution of **16** (6.16 g, 22 mmol) in acetone (200 mL) containing water (40 mL) at room temperature. The mixture was heated at reflux for 4 h. After cooling, the reaction was diluted with saturated aqueous $NaHCO_3$ (100 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (2×300 mL). The combined extracts were washed with brine (2×100 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded crude keto alcohol **47** (5.38 g), which was used for the next reaction without purification.

TESOTf (10.3 mL, 46 mmol) was added dropwise to a stirred solution of **47** (5.38 g, 23 mmol) in dry CH_2Cl_2 (200 mL) containing *i*Pr_2NEt (19.4 mL, 0.11 mol) at 0 °C under argon. After 30 min, the reaction was quenched with saturated aqueous NH_4Cl (50 mL) at 0 °C, and the resulting mixture was extracted with Et_2O (3×300 mL). The combined extracts were washed with brine (2×200 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1) to give **48** (7.71 g, 97%, 2 steps) as a colorless viscous liquid; $[\alpha]_D^{20}$ = −48.5 (*c* = 1.01 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.59–0.65 (m, 6H), 0.87 (s, 3H), 0.96 (t, *J* = 8.0 Hz, 9H), 1.15 (s, 3H), 1.29 (dt, *J* = 13.7, 3.4 Hz, 1H), 1.54–1.63 (m, 3H), 1.65–1.71 (m, 2H), 1.76–1.84 (m, 1H), 1.94–2.07 (m, 3H), 2.16–2.23 (m, 2H), 2.56 (td, *J* = 13.7, 7.3 Hz, 1H), 3.54 (t, *J* = 2.9 Hz, 1H), 4.97–5.04 (m, 2H), 5.83–5.93 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.3 (3C), 7.1 (3C), 19.1, 19.2, 20.1, 25.2, 25.8, 25.9, 37.5, 41.6, 44.2, 45.8, 48.7, 73.3, 117.1, 135.9, 215.5 ppm; IR (neat): $\tilde{\nu}$ = 3399, 3073, 2954, 2876, 1712, 1636, 1455, 1382, 1239, 1084, 999, 909, 823, 789, 724 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{21}H_{38}O_2Si$: 350.2641, found 350.2643 $[M]^+$.

(*Z*)-(4a*S*,5*S*,6*R*,8a*S*)-5-Allyl-5,8a-dimethyl-2-hydroxymethylene-6-(triethylsiloxy)decahydronaphthalen-1-one (49): A solution of **48** (7.71 g, 22 mmol) in dry THF (50 mL) containing ethyl formate (26.7 mL, 0.33 mol) was added to a stirred suspension of NaH (60% dispersion in mineral oil) (13.2 g, 0.33 mol) in dry THF (300 mL) at 0 °C under argon, and stirring was continued for 1 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (50 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×300 mL). The combined extracts were washed with brine (2×200 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 30:1) to give **49** (7.66 g, 92%) as a pale yellow viscous liquid. $[\alpha]_D^{20}$ = +4.3 (*c* = 1.02 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.62 (q, *J* = 7.8 Hz, 6H), 0.82 (s, 3H), 0.96 (t, *J* = 7.8 Hz, 9H), 1.21 (s, 3H), 1.47 (ddd, *J* = 24.4, 13.2, 6.8 Hz, 1H), 1.57–1.63 (m, 2H), 1.71–1.79 (m, 3H), 1.83–1.91 (m, 1H), 2.01 (dd, *J* = 13.2, 8.3 Hz, 1H), 2.20 (dd, *J* = 13.2, 5.9 Hz, 1H), 2.28–2.36 (m, 1H), 2.41–2.46 (m, 1H), 3.57 (brs, 1H), 4.99–5.05 (m, 2H), 5.86–5.97 (m, 1H), 8.42 (d, *J* = 4.4 Hz, 1H), 14.67 ppm (d, *J* = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.3 (3C), 7.1 (3C), 17.7, 19.1, 20.6, 23.0, 25.5, 26.6, 41.0, 41.4, 42.0, 44.0, 73.3, 106.0, 117.2, 136.0, 184.8, 195.1 ppm; IR (neat): $\tilde{\nu}$ = 3073, 2953, 2876, 1704, 1635, 1584, 1455, 1414, 1383, 1361, 1283, 1079, 1009, 969, 910, 823, 795, 723 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{22}H_{38}O_3Si$: 378.2590, found 378.2589 $[M]^+$.

(*Z*)-(4a*S*,5*S*,6*R*,8a*S*)-5-Allyl-2-(ethoxyethan-1-yl)oxymethylene-5,8a-dimethyl-6-(triethylsiloxy)decahydronaphthalen-1-one (50): PPTS (485 mg, 1.9 mmol) was added to a stirred solution of **49** (7.31 g, 19 mmol) in dry THF (200 mL) containing ethyl vinyl ether (37.0 mL, 39 mmol) at room temperature. After 1.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$, 80 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (2×300 mL). The combined extracts were washed with brine (2×200 mL), then dried over $MgSO_4$. Concentration of solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1) to give **50** (1:1 diastereomeric mixture caused by the EE group) (8.35 g, 96%) as a pale yellow viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.58–0.64 (m, 6H), 0.84 (s, 3H), 0.95 (t, *J* = 7.8 Hz, 9H), 1.12 (s, 3H), 1.211 (t, *J* = 6.8 Hz, $^3/_2$H), 1.213 (t, *J* = 6.8 Hz, $^3/_2$H), 1.42–1.44 (m, 3H), 1.53–1.65 (m, 3H), 1.71–1.91 (m, 4H), 2.00–2.06 (m, 1H), 2.21–2.29 (m, 2H), 2.64–2.70 (m, 1H), 3.45–3.53 (m, 1H), 3.55 (s, 1H), 3.68–3.76 (m, 1H), 4.98–5.09 (m, 3H), 5.86–5.97 (m, 1H), 7.43 ppm (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.3 (3C), 7.1 (3C), 14.9 ($^1/_2$C), 15.0 ($^1/_2$C), 17.7, 19.48, 19.52 ($^1/_2$C), 19.54 ($^1/_2$C), 21.1, 22.16 ($^1/_2$C), 22.19 ($^1/_2$C), 25.5, 26.8, 41.4, 41.60 ($^1/_2$C), 41.63 ($^1/_2$C), 44.0, 46.3, 63.6 ($^1/_2$C), 63.7 ($^1/_2$C), 73.4, 103.5 ($^1/_2$C), 103.7 ($^1/_2$C), 117.0, 136.1, 151.4, 206.39 ($^1/_2$C), 206.41 ppm ($^1/_2$C); IR (neat): $\tilde{\nu}$ = 3073, 2953, 2914, 2877, 1681, 1600, 1455, 1383, 1344, 1284, 1211, 1001, 821, 725 cm^{-1}; HRMS (EI): *m*/*z*: calcd for $C_{26}H_{46}O_4Si$: 450.3165, found 450.3177 $[M]^+$.

(*Z*)-(4a*R*,5*S*,6*R*,8a*S*)-5-Allyl-2-(ethoxyethan-1-yl)oxymethylene-5,8a-dimethyl-6-(triethylsiloxy)decahydronaphthalen-1-ol (51): $NaBH_4$ (2.24 g, 59 mmol) was added in small portions to a stirred solution of **50** (5.33 g, 12 mmol) in THF (120 mL) containing water (12 mL) at 0 °C, and stirring was continued for 4 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (60 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×200 mL). The combined extracts were washed with brine (2×100 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1) to give **51** (1:1 diastereomeric mixture caused by the EE group) (5.25 g, 98%) as a colorless viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.63 (q, *J* = 7.8 Hz, 6H), 0.77 (s, 3H), 0.78 (s, 3H), 0.98 (t, *J* = 7.8 Hz, 9H), 1.16–1.18 (m, 1H), 1.20 (t, *J* = 6.8 Hz, $^3/_2$H), 1.21 (t, *J* = 6.8 Hz, $^3/_2$H), 1.37 (d, *J* = 5.4 Hz, 3H), 1.41–1.54 (m, 5H), 1.60–1.66 (m, 2H), 1.78–1.85 (m, 1H), 1.96 (dd, *J* = 13.2, 8.8 Hz, 1H), 2.19 (dd, *J* = 13.2, 5.9 Hz, 1H), 2.90 (dd, *J* = 13.9, 2.9 Hz, 1H), 3.44–3.54 (m, 1H), 3.57 (brs, 1H), 3.69–3.78 (m, 2H), 4.87–4.93 (m, 1H), 4.96–5.02 (m, 2H), 5.84–5.95 (m, 1H), 6.24–6.25 ppm (m, 1H); ^{13}C NMR

(100 MHz, $CDCl_3$): $\delta = 5.4$ (3C), 7.2 (3C), 12.9, 15.1 ($^1/_2$C), 15.2 ($^1/_2$C), 19.0, 20.47 ($^1/_2$C), 20.55 ($^1/_2$C), 20.90 ($^1/_2$C), 20.93 ($^1/_2$C), 24.2, 25.8, 30.11 ($^1/_2$C), 30.14 ($^1/_2$C), 40.5, 40.57 ($^1/_2$C), 40.60 ($^1/_2$C), 44.2, 45.0, 62.2 ($^1/_2$C), 62.4 ($^1/_2$C), 73.6, 80.7, 100.8, 116.9, 119.0 ($^1/_2$C), 119.1 ($^1/_2$C), 133.4 ($^1/_2$C), 133.7 ($^1/_2$C), 136.3 ppm; IR (neat): $\tilde{\nu} = 3478$, 3073, 2952, 2912, 2876, 1683, 1636, 1455, 1381, 1340, 1239, 1149, 1081, 1008, 933, 910, 806, 726 cm^{-1}; HRMS (EI): m/z: calcd for $C_{26}H_{48}O_4Si$: 452.3322, found 452.3333 $[M]^+$.

(4a*R*,5*S*,6*R*,8a*R*)-5-Allyl-5,8a-dimethyl-6-triethylsiloxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carbaldehyde (52): MsCl (11.0 mL, 0.14 mol) was added dropwise to a stirred solution of **51** (6.44 g, 14 mmol) in dry CH_2Cl_2 (140 mL) containing Et_3N (23.8 mL, 0.17 mmol) at 0 °C under argon. After 30 min, the reaction was quenched with saturated aqueous NH_4Cl (60 mL) at 0 °C, and the resulting mixture was extracted with $CHCl_3$ (3×250 mL). The combined extracts were washed with brine (2× 200 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc, 100:1→50:1) to give **52** (4.94 g, 96%) as a colorless viscous liquid. $[\alpha]_D^{20} = +3.7$ ($c = 1.01$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.62$ (q, $J = 7.8$ Hz, 6H), 0.82 (s, 3H), 0.96 (t, $J = 7.1$ Hz, 9H), 1.06 (s, 3H), 1.31 (dt, $J = 12.7$, 2.9 Hz, 1H), 1.35–1.42 (m, 1H), 1.61 (q, $J =$ 3.4 Hz, 1H), 1.70 (dd, $J = 12.7$, 2.0 Hz, 1H), 1.74–1.79 (m, 1H), 1.83–1.87 (m, 1H), 1.91–1.96 (m, 1H), 1.98–2.03 (m, 1H), 2.06–2.15 (m, 1H), 2.19 (dd, $J = 13.4$, 6.3 Hz, 1H), 2.38 (dd, $J = 18.5$, 6.3 Hz, 1H), 3.60–3.61 (m, 1H), 5.00–5.05 (m, 2H), 5.85–5.95 (m, 1H), 6.40 (s, 1H), 9.40 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.3$ (3C), 7.1 (3C), 16.9, 18.5, 20.7, 22.9, 25.9, 31.4, 36.5, 40.8, 43.3, 43.8, 73.7, 117.1, 135.9, 137.5, 162.4, 194.9 ppm; IR (neat): $\tilde{\nu} = 3354$, 3073, 2953, 2913, 2876, 2804, 2711, 1690, 1642, 1456, 1382, 1237, 1185, 1079, 1005, 909, 823, 796, 723 cm^{-1}; HRMS (EI): m/z: calcd for $C_{22}H_{38}O_2Si$: 362.2641, found 362.2639 $[M]^+$.

(4a*R*,5*S*,6*R*,8a*R*)-5-Allyl-5,8a-dimethyl-6-triethylsiloxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-methanol (53): $NaBH_4$ (773 mg, 20 mmol) was added in small portions to a stirred solution of **52** (4.94 g, 14 mmol) in THF (140 mL) containing water (14 mL) at 0 °C, and stirring was continued for 30 min at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (80 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×200 mL). The combined extracts were washed with brine (2×80 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 10:1→8:1) to give **53** (4.85 g, 98%) as a colorless viscous liquid. $[\alpha]_D^{20} = -15.9$ ($c = 1.01$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.59$–0.65 (m, 6H), 0.78 (s, 3H), 0.94–0.98 (m, 12H), 1.15 (dt, $J = 12.2$, 3.4 Hz, 1H), 1.36–1.45 (m, 2H), 1.52 (dq, $J = 14.1$, 3.4 Hz, 1H), 1.64–1.73 (m, 3H), 1.83–1.92 (m, 1H), 1.96–2.09 (m, 3H), 2.19 (dd, $J =$ 13.2, 5.9 Hz, 1H), 3.57–3.58 (m, 1H), 3.95 (s, 2H), 4.97–5.03 (m, 2H), 5.34 (s, 1H), 5.87–5.97 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 5.4 (3C), 7.1 (3C), 17.9, 18.5, 21.8, 26.2, 27.3, 32.6, 34.9, 40.6, 43.8, 43.9, 67.2, 74.1, 116.8, 133.4, 136.6, 136.7 ppm; IR (neat): $\tilde{\nu} = 3303$, 3072, 2953, 2876, 1823, 1636, 1457, 1382, 1238, 1184, 1078, 1004, 909, 859, 796, 724 cm^{-1}; HRMS (EI): m/z: calcd for $C_{22}H_{40}O_2Si$: 364.2798, found 364.2806 $[M]^+$.

(4a*R*,5*S*,6*R*,8a*R*)-5-Allyl-5,8a-dimethyl-2-(tri-*n*-butylstannylmethoxymethyl)-6-triethylsiloxy-3,4,4a,5,6,7,8,8a-octahydronaphthalene (46): KH (30% dispersion in mineral oil) (5.34 g, 13 mmol), [18]crown-6 (10.6 g, 40 mmol), and iodomethyl tri-*n*-butyltin (8.0 mL, 26 mmol) were added successively to a stirred solution of **53** (4.85 g, 13 mmol) in dry THF (260 mL) at 0 °C under argon, and stirring was continued for 3 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (80 mL) at 0 °C, and resulting mixture was extracted with EtOAc (3× 150 mL). The combined extracts were washed with brine (2×100 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography [hexane/EtOAc 100:1 (containing 0.2% Et_3N)] to give **46** (7.39 g, 83%) as a colorless viscous liquid. $[\alpha]_D^{20} = -8.5$ ($c = 1.01$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.58$–0.62 (m, 6H), 0.77 (s, 3H), 0.87–0.92 (m, 16H), 0.94–0.98 (m, 12H), 1.12–1.17 (m, 1H), 1.26–1.35 (m, 6H), 1.36–1.45 (m, 1H), 1.47–1.55 (m, 6H), 1.63–1.74 (m, 3H), 1.83–1.86 (m, 1H), 1.87–2.08 (m, 3H), 2.19 (dd, $J = 13.2$, 5.9 Hz, 1H), 3.56–3.58 (m, 1H), 3.63–3.69 (m, 4H), 4.97–5.02 (m, 2H), 5.31 (br s, 1H), 5.86–5.97 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.4$ (3C), 7.1 (3C), 9.0 (3C), 13.7 (3C), 18.0, 18.4, 21.9, 26.2, 27.3 (3C), 27.5, 29.2 (3C), 32.7, 35.1, 40.6, 43.8, 43.9, 60.5, 74.1, 79.3, 116.7, 130.8, 136.6, 138.5 ppm; IR (neat): $\tilde{\nu} = 3073$, 2955, 2921, 2874, 1636, 1463, 1380, 1237, 1128, 1076, 1004, 960, 909, 799, 775, 726 cm^{-1}; HRMS (EI): m/z: calcd for $C_{35}H_{68}O_2SiSn$: 668.4011, found 668.3988 $[M]^+$.

(1*R*,4a*S*,5*S*,6*R*,8a*S*)-5-Allyl-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)-decahydronaphthalene-1-methanol (45) and its (1*S*,4a*R*,5*S*,6*R*,8a*S*)-isomer (54): *n*BuLi in hexane (1.55 M solution, 33.8 mL, 52 mmol) was added dropwise to a stirred solution **46** (7.00 g, 10 mmol) in dry hexane (500 mL) at −50 °C under argon, and the mixture was gradually warmed up to 0 °C over 4 h, and stirring was continued for 5 h at 0 °C. The reaction was quenched with saturated aqueous NH_4Cl (100 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3×250 mL). The combined extracts were washed with brine (2×200 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 20:1→10:1) to give **45** (3.01 g, 76%), **54** (673 mg, 17%), and **53** (198 mg, 5%).

Compound 45: white crystals (recrystallization from Et_2O); M.p. 102–103 °C; $[\alpha]_D^{20} = -39.0$ ($c = 1.03$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.62$ (q, $J = 7.8$ Hz, 6H), 0.76 (s, 3H), 0.90 (dt, $J = 12.2$, 2.9 Hz, 1H), 0.96–1.00 (m, 12H), 1.25–1.39 (m, 2H), 1.51 (dq, $J = 13.9$, 3.4 Hz, 1H), 1.58–1.61 (m, 1H), 1.77 (dd, $J = 13.2$, 2.9 Hz, 1H), 1.84–1.92 (m, 2H), 1.95–2.04 (m, 2H), 2.10–2.20 (m, 2H), 2.27–2.29 (m, 1H), 3.56 (d, $J =$ 2.0 Hz, 1H), 3.66 (dd, $J = 10.7$, 10.2 Hz, 1H), 3.79–3.85 (m, 1H), 4.74 (t, $J = 2.0$ Hz, 1H), 4.92 (t, $J = 2.0$ Hz, 1H), 4.95–5.02 (m, 2H), 5.84–5.94 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.4$ (3C), 7.1 (3C), 19.2, 22.4, 23.1, 25.8, 29.0, 31.4, 37.4, 39.9, 40.8, 44.4, 59.0, 60.7, 74.0, 112.7, 116.9, 136.2, 147.2 ppm; IR (KBr): $\tilde{\nu} = 3323$, 3067, 2962, 2913, 2879, 1653, 1459, 1382, 1234, 1084, 1003, 911, 815, 737 cm^{-1}; HRMS (EI): m/z: calcd for $C_{23}H_{42}O_2Si$: 378.2954, found 378.2964 $[M]^+$.

Compound 54: white crystals (recrystallization from Et_2O); M.p. 96–97 °C; $[\alpha]_D^{20} = -41.6$ ($c = 1.00$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 0.60–0.67 (m, 6H), 0.74 (s, 3H), 0.75 (s, 3H), 0.99 (t, $J = 7.8$ Hz, 9H), 1.29–1.33 (m, 2H), 1.41 (dd, $J = 8.8$, 2.9 Hz, 1H), 1.53–1.56 (m, 1H), 1.65–1.69 (m, 2H), 1.77–1.81 (m, 1H), 1.94 (dd, $J = 13.7$, 8.3 Hz, 1H), 2.00–2.07 (m, 2H), 2.17 (dd, $J = 13.2$, 5.9 Hz, 1H), 2.41 (dq, $J = 12.7$, 2.0 Hz, 1H), 3.74–3.88 (m, 2H), 4.64 (s, 1H), 4.93–5.03 (m, 3H), 5.85–5.96 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.4$ (3C), 7.1 (3C), 15.8, 18.9, 23.4, 26.1, 31.5, 37.6, 38.8, 40.9, 44.4, 47.7, 58.7, 59.0, 73.5, 106.2, 116.9, 136.3, 147.8 ppm; IR (KBr): $\tilde{\nu} = 3323$, 3254, 3078, 2953, 2876, 1638, 1459, 1438, 1383, 1238, 1088, 1005, 909, 884, 737 cm^{-1}; HRMS (EI): m/z: calcd for $C_{23}H_{42}O_2Si$: 378.2954, found 378.2964 $[M]^+$.

(1*R*,4a*R*,5*S*,6*R*,8a*S*)-5-Allyl-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)-decahydronaphthalene-1-carbaldehyde (44): Dess–Martin periodinane (1.74 g, 4.1 mmol) was added in small portions to a stirred solution of **45** (1.04 g, 2.7 mmol) containing $NaHCO_3$ (2.30 g, 27 mmol) in dry CH_2Cl_2 (280 mL) at room temperature. After 1 h, the reaction was quenched with 10% aqueous $Na_2S_2O_3$ (50 mL) at 0 °C, and the resulting mixture was extracted with $CHCl_3$ (3×100 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 50:1) to give **44** (941 mg, 91%) as a colorless viscous liquid. $[\alpha]_D^{20} = -29.1$ ($c = 1.01$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.61$ (q, $J = 7.7$ Hz, 6H), 0.79 (s, 3H), 0.94–0.99 (m, 12H), 1.10 (dt, $J = 13.0$, 3.4 Hz, 1H), 1.42 (dq, $J = 13.0$, 4.8 Hz, 1H), 1.51–1.55 (m, 1H), 1.70–1.75 (m, 1H), 1.84–1.93 (m, 1H), 1.97–2.08 (m, 2H), 2.12 (dd, $J = 12.6$, 2.9 Hz, 1H), 2.23 (dd, $J = 13.5$, 6.3 Hz, 1H), 2.26–2.34 (m, 1H), 2.41–2.46 (m, 1H), 2.50 (d, $J =$ 3.9 Hz, 1H), 3.59–3.60 (m, 1H), 4.74 (t, $J = 1.9$ Hz, 1H), 4.89 (t, $J =$ 1.9 Hz, 1H), 4.98–5.05 (m, 2H), 5.85–5.95 (m, 1H), 10.0 ppm (d, $J =$ 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 5.3$ (3C), 7.1 (3C), 19.0, 22.0, 22.2, 25.7, 30.0, 33.5, 38.8, 40.9, 41.5, 44.2, 71.3, 73.7, 113.2, 117.2, 135.9, 143.0, 203.3 ppm; IR (neat): $\tilde{\nu} = 3073$, 2952, 2877, 2725, 1717, 1645, 1457, 1385, 1239, 1082, 1004, 967, 909, 811, 725 cm^{-1}; HRMS (EI): m/z: calcd for $C_{23}H_{40}O_2Si$: 376.2798, found 376.2789 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*S*)-5-Allyl-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decahydronaphthalen-1-yl]hydroxymethyl-5,6-dimethyl-2-methoxy-

4*H*-pyran-4-one (55): *n*BuLi in hexane (1.55 M solution, 3.48 mL, 5.4 mmol) was added dropwise to a stirred solution of **10** (1.26 g, 5.4 mmol) in dry THF (120 mL) at −78 °C under argon. After 20 min, a solution of **44** (507 mg, 1.4 mmol) in dry THF (20 mL) was added to the above mixture at −78 °C, and stirring was continued for 1 h at −40 °C. The reaction was quenched with saturated aqueous NH_4Cl (50 mL) at −40 °C, and the resulting mixture was extracted with EtOAc (3× 100 mL). The combined extracts were washed brine (2×50 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 4:1) to give **55** (ca. 8:1 diastereomeric mixture) (615 mg, 86%) as a white solid. Recrystallization from hexane/Et_2O 10:1 afforded single major isomer of **55** as colorless needles. M.p. 167–168 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.62–0.68 (m, 6H), 0.76 (s, 3H), 0.85 (dt, J = 12.2, 3.4 Hz, 1H), 0.90 (s, 3H), 0.97–1.02 (m, 9H), 1.30 (qd, J = 12.9, 4.9 Hz, 1H), 1.53 (dq, J = 14.1, 3.4 Hz, 1H), 1.63–1.67 (m, 1H), 1.84–1.92 (m, 2H), 1.87 (s, 3H), 2.00 (dd, J = 13.2, 8.3 Hz, 1H), 2.23–2.28 (m, 1H), 2.26 (s, 3H), 2.33–2.40 (m, 2H), 2.48–2.58 (m, 2H), 3.56 (br s, 1H), 3.95 (s, 3H), 4.32 (t, J = 2.4 Hz, 1H), 4.72 (t, J = 2.4 Hz, 1H), 4.94–5.01 (m, 2H), 5.21 (br s, 1H), 5.91–6.04 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.4 (3C), 7.1 (3C), 9.7, 16.9, 19.6, 22.9, 23.0, 26.4, 28.9, 34.9, 38.5, 39.8, 41.0, 44.6, 55.7, 61.8, 67.8, 74.5, 105.6, 111.6, 116.3, 119.4, 137.1, 148.6, 155.3, 161.0, 181.6 ppm; IR (KBr): $\tilde{\nu}$ = 3448, 3244, 2939, 2876, 1663, 1597, 1573, 1458, 1421, 1376, 1321, 1241, 1153, 1077, 1007, 913, 883, 802, 780, 739, 474 cm^{-1}; HRMS (EI): m/z: calcd for $C_{31}H_{50}O_5Si$: 530.3428, found 530.3416 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5-Allyl-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decanaphthalen-1-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (43): $NaN(SiMe_3)_2$ in THF (1.0 M solution, 1.62 mL, 1.6 mmol) was added dropwise to a stirred solution of **55** (431 mg, 0.81 mmol) in dry THF (30 mL) containing CS_2 (0.24 mL, 4.1 mmol) at −78 °C under argon. After 1 h, MeI (0.51 mL, 8.1 mmol) was added dropwise to the mixture at −78 °C, and the resulting solution was further stirred for 1 h at the same temperature. The reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the resulting mixture was extracted with EtOAc (3× 50 mL). The combined extracts were washed with brine (2×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded crude methyl xanthate **56** (350 mg), which was used for the next reaction without purification.

nBu$_3$SnH (0.46 mL, 1.7 mmol) and 2,2′-azobisisobutyronitrile (AIBN) (18.6 mg, 0.11 mmol) were added successively to a stirred solution of **56** (351 mg, 0.57 mmol) in dry toluene (15 mL) at room temperature. For the deaeration of the reaction mixture, it was frozen using liquid nitrogen, and the reaction vessel was evacuated in vacuo for 30 min followed by filled with dry argon. The mixture was heated at reflux for 1 h under argon. After cooling, the reaction mixture was concentrated in vacuo to afford a residue, which was purified by column chromatography (benzene/EtOAc 30:1→20:1) to give **43** (284 mg, 68%, 2 steps) as a pale yellow amorphous powder. $[\alpha]_D^{20}$ = −63.3 (c = 1.03 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.60–0.67 (m, 6H), 0.76 (s, 3H), 0.94 (s, 3H), 0.98 (t, J = 7.8 Hz, 9H), 1.24–1.41 (m, 2H), 1.53–1.65 (m, 2H), 1.85–1.96 (m, 3H), 1.91 (s, 3H), 1.98–2.01 (m, 1H), 2.07–2.11 (m, 1H), 2.21–2.28 (m, 1H), 2.24 (s, 3H), 2.32–2.44 (m, 2H), 2.49 (t, J = 12.7 Hz, 1H), 2.76 (dd, J = 12.7, 3.4 Hz, 1H), 3.58 (d, J = 2.0 Hz, 1H), 3.85 (s, 3H), 4.14 (t, J = 2.4 Hz, 1H), 4.48 (t, J = 2.4 Hz, 1H), 4.96–5.03 (m, 2H), 5.88–5.98 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.4 (3C), 7.2, (3C), 10.0, 16.9, 19.1, 19.7, 22.8, 22.9, 26.1, 28.6, 31.4, 37.8, 38.8, 40.8, 44.3, 55.3, 56.1, 74.3, 103.7, 108.9, 116.5, 118.5, 136.7, 149.4, 154.7, 162.9, 180.4 ppm; IR (KBr): $\tilde{\nu}$ = 3069, 2952, 2876, 1672, 1604, 1461, 1415, 1375, 1316, 1254, 1148, 1079, 1004, 885, 813, 782, 741 cm^{-1}; HRMS (EI): m/z: calcd for $C_{31}H_{50}O_4Si$: 514.3478, found 514.3465 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5,8a-Dimethyl-2-methylene-5-(2-oxoethyl)-6-(triethylsiloxy)decahydronaphthalen-1-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (42): 4% Aqueous OsO_4 (0.32 mL, 50 μmol) and $NaIO_4$ (438.4 mg, 2.1 mmol) was added slowly to a stirred solution of **43** (264 mg, 0.51 mmol) in dioxane/water 3:1 (8 mL) containing 2,6-lutidine (0.12 mL, 1.0 mmol) at room temperature. After 1 h, the reaction mixture was diluted with water (10 mL), and the resulting mixture was extracted with EtOAc (3×50 mL). The combined extracts were washed with brine (3×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 5:1) to give **42** (226 mg, 85%) as a white amorphous powder. $[\alpha]_D^{20}$ = −72.7 (c = 1.07 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.63 (q, J = 7.8 Hz, 6H), 0.94–0.99 (m, 15H), 1.06 (dt, J = 13.2, 3.4 Hz, 1H), 1.40 (qd, J = 12.9, 4.9 Hz, 1H), 1.48–1.52 (m, 1H), 1.62–1.66 (m, 1H), 1.91 (s, 3H), 1.93–1.99 (m, 2H), 2.10–2.21 (m, 3H), 2.24 (s, 3H), 2.33–2.46 (m, 4H), 2.77 (dd, J = 12.7, 3.4 Hz, 1H), 3.77 (br s, 1H), 3.85 (s, 3H), 4.17 (t, J = 2.4 Hz, 1H), 4.51 (t, J = 2.4 Hz, 1H), 9.94–9.95 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.1 (3C), 7.0 (3C), 9.9, 16.9, 19.7, 21.3, 22.8, 23.0, 25.8, 28.3, 31.1, 37.5, 37.8, 42.8, 53.7, 55.3, 55.8, 75.8, 103.3, 109.5, 118.5, 148.7, 154.8, 162.9, 180.3, 204.0 ppm; IR (KBr): $\tilde{\nu}$ = 2952, 2876, 1714, 1671, 1602, 1462, 1415, 1375, 1317, 1254, 1163, 1146, 1085, 1004, 886, 812, 742 cm^{-1}; HRMS (EI): m/z: calcd for $C_{30}H_{48}O_5Si$: 516.3271, found 516.3254 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5,8a-Dimethyl-2-methylene-5-[(*R*)-2-hydroxy-4-methylpent-3-enyl]-6-(triethylsiloxy)decahydronaphthalen-1-yl]methyl-2-methoxy-5,6-dimethyl-4*H*-pyran-4-one (57) and its 5-[(*S*)]-isomer (58): 2-Methyl-1-propenyl magnesium bromide in THF (0.5 M solution, 2.40 mL, 1.2 mmol) was added dropwise to a stirred solution of **42** (209 mg, 0.40 mmol) in dry THF (20 mL) at room temperature under argon. After 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (3× 60 mL). The combined extracts were washed with brine (2×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 4:1) to give **57** (97.3 mg, 42%) and **58** (92.7 mg, 40%).

Compound 57: white amorphous powder. $[\alpha]_D^{20}$ = −43.6 (c = 1.01 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.70 (q, J = 7.8 Hz, 6H), 0.87 (s, 3H), 0.95 (s, 3H), 1.01 (t, J = 7.8 Hz, 9H), 1.30 (qd, J = 13.2, 4.4 Hz, 1H), 1.51–1.63 (m, 2H), 1.66–1.74 (m, 1H), 1.69 (s, 3H), 1.71 (s, 3H), 1.79–1.84 (m, 2H), 1.87–1.94 (m, 2H), 1.90 (s, 3H), 2.07–2.12 (m, 1H), 2.20–2.24 (m, 4H), 2.27–2.43 (m, 2H), 2.47 (t, J = 12.7 Hz, 1H), 2.74 (dd, J = 12.7, 3.4 Hz, 1H), 3.85 (s, 3H), 3.89–3.90 (m, 1H), 4.15 (s, 1H), 4.47–4.53 (m, 2H), 5.22 ppm (td, J = 8.8, 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.4 (3C), 7.1 (3C), 9.9, 16.9, 18.1, 19.1, 19.8, 23.1, 23.4, 25.7, 25.9, 28.7, 31.4, 37.8, 40.0, 40.7, 46.6, 55.3, 56.1, 65.0, 75.0, 103.5, 109.0, 118.5, 130.4, 132.5, 149.1, 154.8, 162.9, 180.3 ppm; IR (KBr): $\tilde{\nu}$ = 3434, 2952, 2876, 1671, 1593, 1463, 1417, 1376, 1318, 1255, 1086, 1005, 886, 813, 751 cm^{-1}; HRMS (EI): m/z: calcd for $C_{34}H_{56}O_5Si$: 572.3897, found 572.3889 $[M]^+$.

Compound 58: white amorphous powder. $[\alpha]_D^{20}$ = −29.6 (c = 1.00 in $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.67–0.73 (m, 6H), 0.87 (s, 3H), 0.96–1.01 (m, 12H), 1.08 (dt, J = 13.2, 3.4 Hz, 1H), 1.41–1.51 (m, 2H), 1.54–1.57 (m, 1H), 1.707 (s, 3H), 1.711 (s, 3H), 1.91 (s, 3H), 1.96–1.99 (m, 2H), 2.13–2.16 (m, 2H), 2.24 (s, 3H), 2.27–2.36 (m, 1H), 2.42–2.50 (m, 2H), 2.80 (dd, J = 12.9, 3.4 Hz, 1H), 3.60 (br s, 1H), 3.83 (s, 3H), 4.17 (s, 1H), 4.26 (br s, 1H), 4.49–4.55 (m, 2H), 5.20 ppm (d, J = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 4.9 (3C), 7.0 (3C), 9.9, 16.9, 18.1, 19.9, 23.2, 24.1, 24.4, 25.8, 26.5, 28.7, 31.3, 36.4, 37.6, 41.6, 48.9, 55.3, 55.8, 64.4, 77.4, 103.6, 109.6, 118.6, 130.2, 132.2, 149.2, 154.8, 163.1, 180.4 ppm; IR (neat): $\tilde{\nu}$ = 3329, 2952, 2876, 1669, 1586, 1463, 1422, 1376, 1320, 1257, 1147, 1080, 1005, 986, 885, 783, 753 cm^{-1}; HRMS (EI): m/z: calcd for $C_{34}H_{56}O_5Si$: 572.3897, found 572. 572.3897 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5-[(*R*)-2[(*S*)-3,3-Dimethyloxiran-2-yl]-2-hydroxyethyl]-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decanaphthlen-1-yl]-methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (59): *tert*-Butylhydroperoxide (TBHP) in decane (5.0–6.0 M solution, 33.0 μL, 0.18 mmol) was added dropwise to a stirred solution of **57** (69.1 mg, 0.12 mmol) in benzene (7 mL) containing vanadyl acetylacetonate $[VO(acac)_2]$ (6.40 mg, 24 μmol) at 0 °C, and stirring was continued for 1 h at room temperature. The reaction was quenched with 10% aqueous $Na_2S_2O_3$ (5 mL), and the resulting mixture was extracted with EtOAc (3×40 mL). The combined extracts were washed with brine (3×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 3:1) to give **59** (59.6 mg, 84%) as a white amorphous powder. $[\alpha]_D^{20}$ = −35.9 (c = 1.02 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.68 (q, J = 7.8 Hz, 6H), 0.87 (s, 3H), 0.97–1.01 (m, 12H), 1.26–1.39 (m, 1H), 1.32 (s, 3H), 1.33 (s, 3H), 1.47–

1.57 (m, 2H), 1.61–1.66 (m, 1H), 1.84–1.98 (m, 4H), 1.91 (s, 3H), 2.12 (dd, J=13.7, 3.4 Hz, 1H), 2.24 (s, 3H), 2.32 (dd, J=12.9, 3.4 Hz, 1H), 2.36–2.43 (m, 1H), 2.47–2.55 (m, 2H), 2.70–2.74 (m, 2H), 3.58–3.63 (m, 1H), 3.86 (s, 3H), 3.88–3.89 (m, 1H), 4.16 (s, 1H), 4.49 ppm (t, J= 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=5.3 (3C), 7.1 (3C), 10.0, 16.9, 18.9, 19.5, 19.7, 23.2, 23.4, 24.8, 25.9, 28.5, 31.4, 37.8, 39.6, 40.6, 42.0, 55.3, 56.2, 59.4, 67.5, 69.1, 74.9, 103.5, 109.1, 118.5, 149.0, 154.8, 162.8, 180.3 ppm; IR (KBr): $\tilde{\nu}$=3435, 2952, 2875, 1671, 1595, 1462, 1417, 1376, 1317, 1254, 1096, 1079, 1006, 888, 815, 751 cm^{-1}; HRMS (EI): m/z: calcd for $C_{34}H_{56}O_6Si$: 588.3846, found 588.3829 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5-[(*S*)-2[(*R*)-3,3-Dimethyloxiran-2-yl]-2-hydroxyethyl]-5,8a-dimethyl-2-methylene-6-(triethylsiloxy)decanaphthlen-1-yl]-methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (60): *tert*-Butylhydroperoxide (TBHP) in decane (5.0–6.0 M solution, 30.0 μL, 0.17 mmol) was added dropwise to a stirred solution of **58** (62.5 mg, 0.11 mmol) in benzene (5 mL) containing [VO(acac)$_2$] (5.80 mg, 21 μmol) at 0°C, and stirring was continued for 1 h at room temperature. The reaction was quenched with 10% aqueous $Na_2S_2O_3$ (5 mL), and the resulting mixture was extracted with EtOAc (3×40 mL). The combined extracts were washed with brine (3×30 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 3:1) to give **60** (51.4 mg, 80%) as a white amorphous powder. $[\alpha]_D^{20}$=−26.2 (c=0.81 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.69–0.77 (m, 6H), 0.93 (s, 3H), 0.97–1.02 (m, 12H), 1.11 (dt, J=13.5, 3.4 Hz, 1H), 1.33 (s, 3H), 1.34 (s, 3H), 1.45 (dd, J=12.6, 3.9 Hz, 1H), 1.52 (dd, J=14.9, 2.0 Hz, 1H), 1.63–1.70 (m, 2H), 1.81–2.01 (m, 3H), 1.90 (s, 3H), 2.08–2.12 (m, 2H), 2.24 (s, 3H), 2.28–2.32 (m, 1H), 2.36–2.46 (m, 2H), 2.67 (d, J=7.2 Hz, 1H), 2.78 (dd, J= 12.6, 3.0 Hz, 1H), 3.55–3.63 (m, 2H), 3.83 (s, 3H), 4.16 (s, 1H), 4.51 (s, 1H), 4.88 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=4.9 (3C), 7.0 (3C), 9.9, 16.9, 19.4, 19.7, 23.1, 24.37, 24.4, 24.9, 26.5, 28.7, 31.1, 36.5, 37.5, 41.5, 45.3, 55.2, 55.8, 58.1, 66.4, 68.9, 77.4, 103.3, 109.6, 118.5, 148.9, 154.9, 163.2, 180.4 ppm; IR (KBr): $\tilde{\nu}$=3376, 2954, 2877, 1671, 1595, 1460, 1417, 1376, 1318, 1255, 1146, 1082, 1005, 887, 783, 747 cm^{-1}; HRMS (EI): m/z: calcd for $C_{34}H_{56}O_6Si$: 588.3846, found 588.3829 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5-[(*R*)-2[(*S*)-3,3-Dimethyloxiran-2-yl]-2-hydroxyethyl]-5,8a-dimethyl-2-methylene-(6-hydroxy)decanaphthlen-1-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (41): TBAF in THF (1.0 M solution, 0.18 mL, 0.18 mmol) was added dropwise to a stirred solution of **59** (52.5 mg, 89 μmol) in THF (5 mL) at 0°C under argon, and stirring was continued for 1.5 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (3 mL) at 0°C, and the resulting mixture was extracted with EtOAc (3×30 mL). The combined extracts were washed with brine (2×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 1:4) to give **41** (42.3 mg, 100%) as a white amorphous powder. $[\alpha]_D^{20}$=−27.2 (c=1.05 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.84 (s, 3H), 0.97 (s, 3H), 1.04 (dt, J=13.2, 3.4 Hz, 1H), 1.26–1.39 (m, 2H), 1.31 (s, 3H), 1.34 (s, 3H), 1.49–1.55 (m, 1H), 1.71–1.83 (m, 2H), 1.90 (s, 3H), 1.94–2.01 (m, 3H), 2.13 (dd, J= 14.1, 3.4 Hz, 1H), 2.24 (s, 3H), 2.35 (dd, J=13.7, 3.4 Hz, 1H), 2.40–2.49 (m, 1H), 2.56 (dd, J=12.7, 11.7 Hz, 1H), 2.76–2.80 (m, 2H), 3.67 (t, J= 8.8 Hz, 1H), 3.73 (s, 1H), 3.85 (s, 3H), 4.20 (s, 1H), 4.50–4.51 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=10.0, 16.9, 19.2, 19.5, 20.1, 22.6, 22.9, 24.8, 25.0, 28.5, 31.4, 37.9, 40.18, 40.23, 43.6, 55.3, 55.9, 59.3, 67.1, 68.4, 71.8, 103.6, 108.9, 118.5, 149.1, 154.8, 162.8, 180.4 ppm; IR (KBr): $\tilde{\nu}$=3330, 2929, 1668, 1584, 1462, 1422, 1377, 1320, 1257, 1147, 1058, 1030, 984, 886, 753 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{42}O_6$: 474.2981, found 474.2963 $[M]^+$.

3-[(2*R*,3*R*,4a*R*,6a*R*,7*R*,10a*R*,10b*R*)-6a,10b-Dimethyl-2-hydroxy-3-(1-hydroxy-1-methylethyl)-(8-methylene)perhydro-1*H*-benzo[*f*]chromen-7-yl]-methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (61): PPTS (12.4 mg, 50 μmol) was added to a stirred solution of **41** (46.8 mg, 98 μmol) in CH_2Cl_2 (10 mL) at 0°C, and stirring was continued for 4 h at room temperature. The reaction was quenched with Et_3N (30 μL) at 0°C, and the resulting mixture was concentrated in vacuo to afford a residue, which was purified by column chromatography (hexane/EtOAc 3:1) to give **61** (37.2 mg, 79%) as a white amorphous powder. $[\alpha]_D^{20}$=−37.6 (c=1.00 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.84 (s, 3H), 0.91 (s, 3H), 0.94–1.03 (m, 2H), 1.29–1.38 (m, 1H), 1.32 (s, 3H), 1.33 (s, 3H), 1.62–1.71 (m, 2H), 1.85–1.93 (m, 2H), 1.90 (s, 3H), 2.05 (dd, J=12.7, 2.9 Hz, 1H), 2.15 (dd, J=14.4, 4.4 Hz, 1H), 2.22–2.29 (m, 1H), 2.24 (s, 3H), 2.30 (dd, J= 13.7, 3.4 Hz, 1H), 2.35–2.42 (m, 2H), 2.73 (dd, J=12.7, 2.9 Hz, 1H), 2.96 (d, J=3.0 Hz, 1H), 3.23 (s, 1H), 3.85 (s, 3H), 4.00 (ddd, J=11.2, 9.3, 4.4 Hz, 1H), 4.17 (s, 1H), 4.50 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=10.0, 16.9, 19.6, 22.58, 22.62, 23.1, 24.0, 24.1, 28.3, 29.1, 31.2, 35.6, 37.5, 38.1, 45.0, 55.3, 56.3, 64.7, 74.1, 81.5, 85.8, 103.5, 109.1, 118.5, 149.0, 154.9, 163.0, 180.4 ppm; IR (neat): $\tilde{\nu}$=3346, 2970, 2933, 2860, 1668, 1584, 1463, 1422, 1376, 1321, 1257, 1164, 1097, 1051, 984, 888, 754 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{42}O_6$: 474.2981, found 474. 2998 $[M]^+$.

(3*S*,4a*R*,6a*R*,7*R*,10a*R*,1b*R*)-6a,1b-Dimethyl-3-(1-hydroxy-1-methylethyl)-7-[(4-oxo-5,6-dimethyl-2-methoxy-4*H*-pyran-3-yl)methyl]-(8-methylene)-perhydro-1*H*-benzo[*f*]chromen-2(3*H*)-one (62): Tetra-*n*-propylammonium perruthenate (TPAP) (1.34 mg, 3.7 μmol) was added to a stirred solution of **61** (17.6 mg, 37 μmol) in CH_2Cl_2 (3 mL) containing *N*-methylmorpholine *N*-oxide (6.72 mg, 56 μmol) and 4 Å molecular sieves (20 mg, 0.5 g mmol^{-1}) at room temperature. After 30 min, the reaction was quenched with 10% aqueous $Na_2S_2O_3$ (3 mL), and the resulting mixture was extracted with EtOAc (3×20 mL). The combined extracts were washed with brine (3×20 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified column chromatography (hexane/EtOAc 2:1) to give **62** (14.4 mg, 82%) as a colorless viscous liquid. $[\alpha]_D^{20}$=−71.2 (c=0.96 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.94 (s, 3H), 0.95 (s, 3H), 1.12 (dt, J=13.2, 3.4 Hz, 1H), 1.26 (s, 3H), 1.32 (s, 3H), 1.35–1.42 (m, 1H), 1.52–1.57 (m, 1H), 1.84–1.93 (m, 3H), 1.90 (s, 3H), 1.94 −2.02 (m, 1H), 2.05 (d, J=15.1 Hz, 1H), 2.15 (dd, J=13.7, 2.9 Hz, 1H), 2.24 (s, 3H), 2.30 (dd, J=12.7, 11.7 Hz, 1H), 2.34–2.46 (m, 2H), 2.66 (d, J=15.1 Hz, 1H), 2.77 (dd, J=12.7, 2.9 Hz, 1H), 3.47 (br s, 1H), 3.60–3.61 (m, 1H), 3.66 (s, 1H), 3.83 (s, 3H), 4.20 (t, J= 2.0 Hz, 1H), 4.52 ppm (t, J=2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=9.9, 16.9, 19.8, 22.4, 22.5, 22.7, 23.8, 24.9, 26.1, 28.9, 30.9, 37.7, 38.8, 42.5, 53.2, 55.3, 56.0, 71.8, 80.8, 86.7, 103.2, 109.5, 118.6, 148.4, 154.9, 163.0, 180.3, 211.5 ppm; IR (neat): $\tilde{\nu}$=3442, 2972, 2934, 2877, 1715, 1670, 1593, 1462, 1418, 1376, 1318, 1255, 1167, 1093, 986, 889, 753 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{40}O_6$: 472.2825, found 472.2824 $[M]^+$.

3-[(2*S*,3*R*,4a*R*,6a*R*,7*R*,10a*R*,10b*R*)-6a,10b-Dimethyl-2-hydroxy-3-(1-hydroxy-1-methylethyl)-(8-methylene)perhydro-1*H*-benzo[*f*]chromen-7-yl]-methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (candelalide B) (2): $NaBH_4$ (1.51 mg, 40 μmol) in water (0.2 mL) was added dropwise to a stirred solution of **62** (9.4 mg, 20 μmol) in THF (2 mL) at −30°C. After 1 h, the reaction was quenched with saturated aqueous NH_4Cl (1 mL), and the resulting mixture was extracted with EtOAc (3×15 mL). The combined extracts were washed with brine (2×10 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo to afforded a residue, which was purified by column chromatography (hexane/EtOAc 2:1) to give **2** (8.3 mg, 88%) as a white amorphous powder. $[\alpha]_D^{20}$=−56.3 (c= 0.75 in CH_3OH) {lit.[1] $[\alpha]_D^{22}$=−50.9 (c=0.49 in CH_3OH)}. The ^{1}H and ^{13}C NMR, IR, and MS spectra (see below) are identical to those of natural (−)-candelalide B. ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.76 (s, 3H), 0.85–0.89 (m, 1H), 0.92 (s, 3H), 0.95–0.96 (m, 1H), 1.23–1.31 (m, 2H), 1.33 (s, 3H), 1.38 (s, 3H), 1.65–1.75 (m, 2H), 1.83–1.93 (m, 2H), 1.90 (s, 3H), 2.10–2.16 (m, 2H), 2.24 (s, 3H), 2.26–2.40 (m, 3H), 2.96–3.05 (m, 3H), 3.26–3.27 (m, 1H), 3.85 (s, 3H), 4.06 (s, 1H), 4.31 (s, 1H), 4.52 ppm (t, J=2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=10.1, 16.9, 21.3, 22.7, 23.1 (2C), 24.0, 24.5, 28.1, 29.2, 31.5, 34.7, 35.0, 37.6, 42.0, 55.2, 57.4, 67.2, 73.7, 81.8, 83.0, 104.5, 107.6, 118.6, 151.2, 154.7, 163.1, 179.9 ppm; IR (neat): $\tilde{\nu}$=3357, 2971, 2931, 2860, 1668, 1586, 1463, 1420, 1376, 1320, 1260, 1171, 1146, 1102, 1077, 985, 884, 554 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{42}O_6$: 474.2981, found 474.2975 $[M]^+$.

3-[(1*R*,4a*R*,5*S*,6*R*,8a*R*)-5-[(*S*)-2[(*R*)-3,3-Dimethyloxiran-2-yl]-2-hydroxyethyl]-5,8a-dimethyl-2-methylene-(6-hydroxy)decanaphthlen-1-yl]methyl-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (63): TBAF in THF (1.0 M solution, 0.17 mL, 0.17 mmol) was added dropwise to a stirred solution of **60** (49.1 mg, 84 μmol) in THF (4 mL) at 0°C under argon, and stirring was continued for 1 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (3 mL) at 0°C, and the resulting mixture was

extracted with EtOAc (3×20 mL). The combined extracts were washed with brine (2×15 mL), then dried over $MgSO_4$. Concentration of the solvent in vacuo afforded a residue, which was purified by column chromatography (hexane/EtOAc 1:4) to give **63** (39.5 mg, 100%) as a white amorphous powder. $[\alpha]_D^{20}=-37.0$ ($c=0.99$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.91$ (s, 3H), 0.96 (s, 3H), 1.03 (dt, $J=13.2$, 2.9 Hz, 1H), 1.24–1.28 (m, 1H), 1.34 (s, 3H), 1.36 (s, 3H), 1.39–1.41 (m, 2H), 1.58–1.65 (m, 1H), 1.69–1.74 (m, 1H), 1.90 (s, 3H), 1.92–1.97 (m, 2H), 2.04–2.11 (m, 2H), 2.24 (s, 3H), 2.32–2.41 (m, 2H), 2.49 (dd, $J=$ 12.7, 11.7 Hz, 1H), 2.74–2.79 (m, 2H), 3.55 (s, 1H), 3.71 (t, $J=8.8$ Hz, 1H), 3.84 (s, 3H), 4.20 (s, 1H), 4.50 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=10.0$, 16.9, 19.6, 20.1, 23.1, 23.2, 23.3, 25.0, 26.2, 28.3, 31.1, 36.0, 37.8, 40.7, 45.5, 55.3, 56.2, 59.5, 66.5, 68.6, 74.4, 103.5, 109.3, 118.6, 149.0, 155.0, 163.0, 180.5 ppm; IR (KBr): $\tilde{\nu}=3278$, 2927, 1668, 1584, 1464, 1320, 1257, 1147, 1067, 985, 885, 819, 753 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{42}O_6$: 474.2981, found 474.2972 $[M]^+$.

3-{(2*S*,3*R*,5a*R*,7a*S*,8*R*,11a*S*,11b*S*)-2,3-Dihydroxy-9-methylene-4,4,7a-(trimethyl)perhydro[*b*]oxepin-8-yl}methyl}-5,6-dimethyl-2-methoxy-4*H*-pyran-4-one (64): PPTS (1.90 mg, 7.7 μmol) was added to a stirred solution of **63** (18.3 mg, 39 μmol) in CH_2Cl_2 (3 mL) at 0°C, and stirring was continued for 3 h at room temperature. The reaction was quenched with Et_3N (20 μL) at 0°C, and the resulting mixture was concentrated in vacuo to afford a residue, which was purified by column chromatography (hexane/EtOAc 3:1) to give **64** (15.8 mg, 86%) as a white amorphous powder. $[\alpha]_D^{20}=-26.5$ ($c=1.02$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.90$ (s, 3H), 0.91 (s, 3H), 1.00 (dt, $J=12.7$, 2.9 Hz, 1H), 1.20 (s, 3H), 1.24–1.28 (m, 2H), 1.30 (s, 3H), 1.32–1.40 (m, 1H), 1.42–1.51 (m, 2H), 1.55–1.61 (m, 1H), 1.68–1.71 (m, 1H), 1.78 (dd, $J=12.7$, 2.9 Hz, 1H), 1.83–1.88 (m, 2H), 1.90 (s, 3H), 2.01–2.13 (m, 1H), 2.24 (s, 3H), 2.27–2.36 (m, 1H), 2.39–2.44 (m, 1H), 2.47–2.53 (m, 1H), 2.73 (dd, $J=13.2$, 3.4 Hz, 1H), 3.16 (d, $J=9.3$ Hz, 1H), 3.31 (dd, $J=2.9$, 2.4 Hz, 1H), 3.67 (dd, $J=9.8$, 9.3 Hz, 1H), 3.85 (s, 3H), 4.16 (t, $J=2.4$ Hz, 1H), 4.50 ppm (t, $J=2.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=10.1$, 16.9, 18.7, 19.8, 21.2, 21.5, 23.1, 26.4, 28.9, 30.9, 31.5, 37.5, 37.9, 42.9, 49.3, 55.3, 55.9, 68.4, 73.3, 75.3, 84.7, 103.7, 109.1, 118.6, 149.4, 154.8, 162.9, 180.5 ppm; IR (KBr): $\tilde{\nu}=3376$, 2932, 2873, 1728, 1669, 1583, 1464, 1422, 1377, 1320, 1258, 1207, 1186, 1149, 1077, 1037, 986, 885, 754 cm^{-1}; HRMS (EI): m/z: calcd for $C_{28}H_{42}O_6$: 474.2981, found 474.2985 $[M]^+$.

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