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Studies toward the Enantioselective Syntheses of Oxylipins: Total Synthesis and Structure Revision of Solandelactone E

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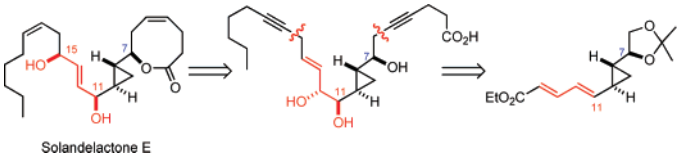
Received August 10, 2007



An efficient and general entry to unsaturated cyclopropane- and lactone-containing oxylipins of marine origin has been designed and applied to the first enantioselective total synthesis of solandelactone E. The synthesis, which proceeds in a total of 23 steps from commercially available materials, features a diastereoselective acetal-directed cyclopropanation of an electron-deficient diene, a regioselective Sharpless enantioselective dihydroxylation, and a stereoselective [2,3]-sigmatropic rearrangement of a selenoxide to effect a 1,3-transposition of an allylic alcohol. Comparison of spectral data for the synthetic solandelactone, thus prepared, with data in the literature led to a revision of the original structural assignments of the C(11)-epimeric solandelactones.

1. Introduction

The solandelactones A−H **(1**−**8)** comprise a family of novel oxygenated fatty acids that were first isolated from the marine invertebrate *Solanderia secunda* off the Korean coast in 1996.[1] There are two primary subfamilies of solandelactones that vary with respect to the absolute stereochemistry of the hydroxyl-bearing carbon atom at C(11). Namely, compounds **1**−**4** have the *S*-configuration at C(11), whereas **5**−**8** possess the *R*-configuration (Figure 1). The solandelactones also vary in the degree of unsaturation in their lactone rings and their pendant side chains. There are a number of marine oxylipins that are related to the solandelactones, including halicholactone **(9)** and neohalicholactone **(10)**[2] and constanolactones A and B **(11** and **12)**.[3] These oxylipins differ from the solandelactones in that they have two fewer carbon atoms, opposite absolute configurations at various stereocenters, and either larger or smaller lactone rings.

Members of the oxylipin family exhibit an array of useful biological activities. For example, halicholactone (**9**) displays

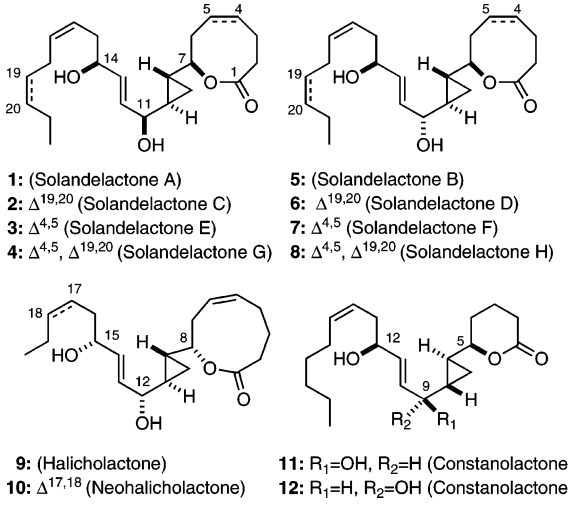


FIGURE 1. Cyclopropane containing marine oxylipins.

weak inhibitory activity against 5-lipoxygenase. Although the solandelactones are not known to share this property, solandelactones C, D, and G do show biological activity as inhibitors of farnesyl transferase,[1] an enzyme responsible for the expression of ras proteins that are found in many types of cancer cells.[4]

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(3) (a) Nagle, D. G.; Gerwick, W. H. *Tetrahedron Lett.* **1990**, *31*, 2995−2998. (b) Nagle, D. G.; Gerwick, W. H. *J. Org. Chem.* **1994**, *59*, 7227−7237.

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10.1021/jo701739v CCC: $40.75
Published on Web 12/19/2007

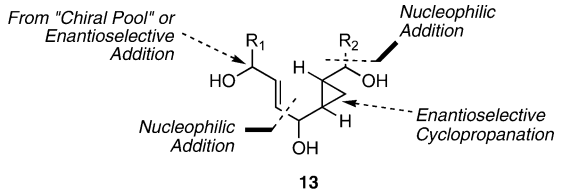


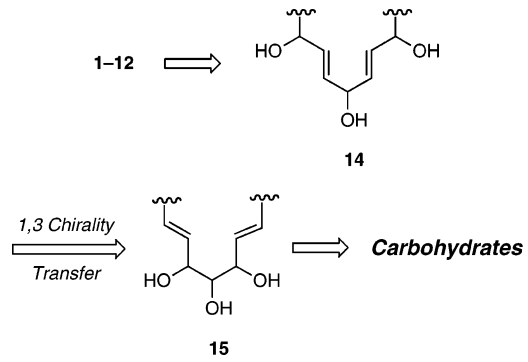
FIGURE 2. Controlling the five stereocenters in the oxylipins.

Unfortunately, because the availability of solandelactones from natural sources is limited, their biological properties have not been adequately explored.

The challenging structural features of the oxylipins coupled with the biological activities of some members of this family have stimulated significant interest in their preparation by total synthesis. Although the total syntheses of oxylipins **9**−**12** and some of their analogues had been reported,[5,6] none of the solandelactones had been synthesized prior to our work in this area.[7,8] Subsequently, White and co-workers completed the syntheses of solandelactones E and F.[9] At the time we initiated our work, none of the approaches to the oxylipins enabled complete stereochemical control at all five of the stereogenic centers resident in these natural products. The various tactics that had been employed in the prior art to control the stereochemistry at these five centers are summarized in Figure 2. Protocols for the enantioselective cyclopropanation of an olefin and for establishing the correct stereochemistry of an allylic alcohol function distal to the cyclopropane ring were well established. On the other hand, the most commonly employed tactic for forming the cyclopropyl carbinyl centers in **13** had involved nucleophilic additions of organometallic reagents to a substituted cyclopropane carboxaldehyde, and there was typically little stereochemical control in these reactions. We therefore queried how we might develop a general entry to the oxylipin natural products that would be both stereochemically and chemically efficient.

There is an underlying symmetry common to natural products **1**−**12** that is revealed in the diene triol **14** (Scheme 1). Surprisingly, none of the previous syntheses of any oxylipin exploited this structural feature. A compound of general form **14** might be accessible by two stereoselective 1,3-transpositions of the allylic alcohol functions of the isomeric triol **15**, which might be conveniently derived from a suitable carbohydrate starting material. We now report the details of our investigations

SCHEME 1

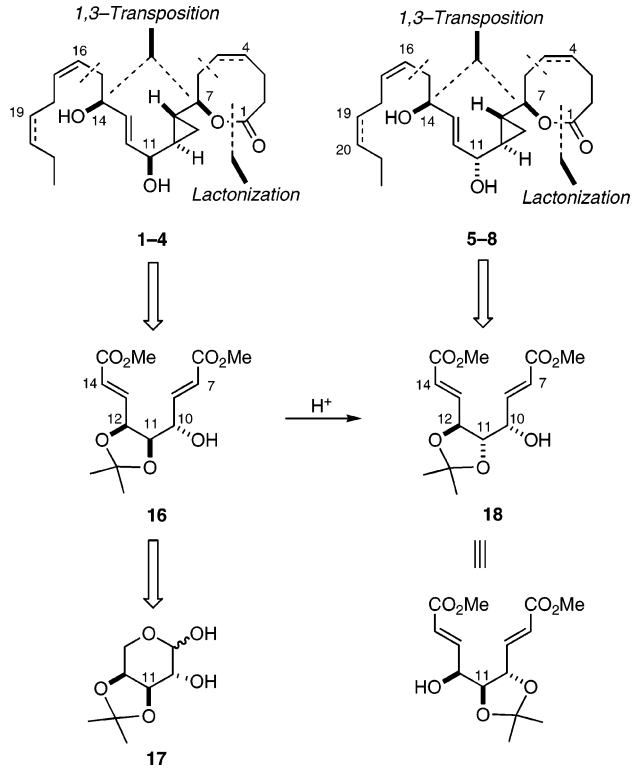


that resulted in the first total synthesis of solandelactone E (**3**) and a structural revision of members of the solandelactone family of oxylipins.[8]

2. Results and Discussion

2.1. First-Generation Approach. In light of the preliminary analysis depicted in Scheme 1, we envisioned that solandelactones A, C, E, and G (**1**−**4**) and solandelactones B, D, F, and H (**5**−**8**) might be synthesized from the common intermediate **16** according to the retrosynthetic format outlined in Scheme 2. The stereochemistry at C(7) and C(14) would be controlled by stereoselective 1,3-transpositions of the corresponding C(10) and C(12) alcohols in **16**. Formation of the correct stereochemistry at C(7) would require prior inversion at C(10), whereas introducing the stereocenter at C(14) would not. Following these two sequential transpositions, the carbon atoms in the eight-membered lactone ring and the olefinic side chain would be introduced. We envisioned that **16** would be available via two *E*-selective Wittig olefinations of the known acetonide **17**, which may be readily prepared from commercially available L-

SCHEME 2



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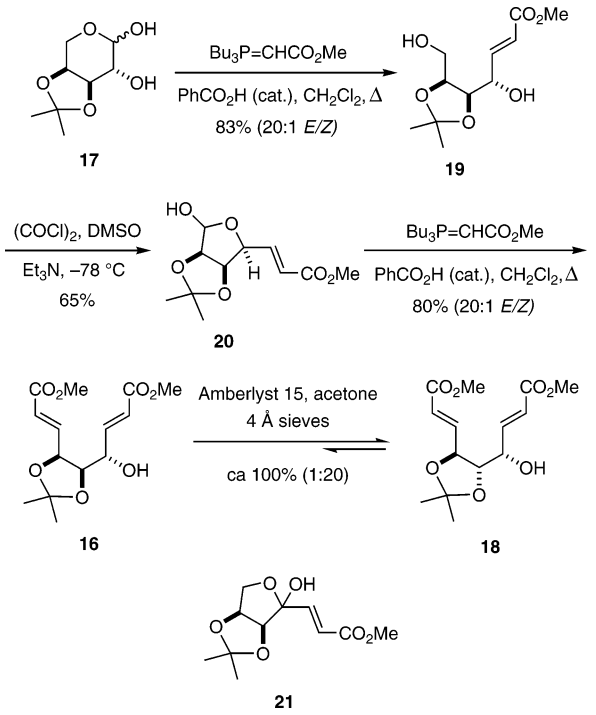
(9) White, J. D.; Martin, W. H. C.; Lincoln, C.; Yang, J. *Org. Lett*, **2007**, *9*, 3481−3483.

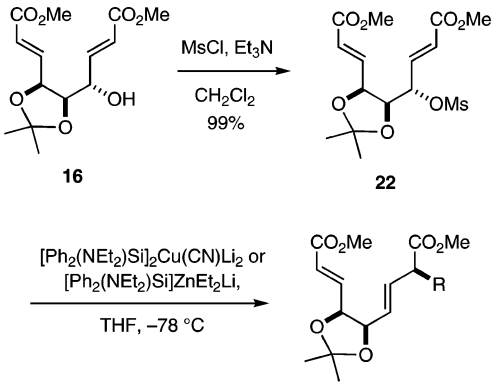
SCHEME 3



arabinose. In order to prepare solandelactones B, D, F, and H (**5**−**8**) from **16**, it would be necessary to effect a transketalization to provide the diastereomeric diester **18**, which was predicted to be thermodynamically more stable owing to the *trans* relationship of the two side chains on the dioxolane ring.

In order to explore the feasibility of the plan in Scheme 2, L-arabinose was converted into the known acetonide **17**, which was isolated as an anomeric, presumably thermodynamic, mixture (ca. 4:1) (Scheme 3).[10] The installation of the *E*-α,*β*-unsaturated ester moiety found in **19** proved to be somewhat problematic. Wittig reactions of stabilized ylides, such as (alkoxycarbonylmethylene)triphenylphosphoranes, with sugar lactols and α-alkoxy aldehydes were known to proceed with low *E*-selectivity.[11] Not surprisingly, the reaction of **17** with methyl(triphenylphosphoranylidene)acetate under standard Wittig conditions gave the α,*β*-unsaturated ester **19** and its *Z*-isomer as a mixture (1:1) in 55% yield. The reaction was also conducted in the presence of benzoic acid, which was known to enhance trans selectivity,[12] but there was no significant improvement in the diastereomeric ratio. After some experimentation, it was found that reaction of **17** with freshly prepared methyl-(tributylphosphoranylidene)acetate[13] and a catalytic amount of benzoic acid gave **19** in 83% yield (*E*/*Z* = 20:1). This method for effecting trans selective olefination of **17** was developed into a general method and extended to include a variety of other α-alkoxy aldehydes and sugar lactols.[14]

SCHEME 4



The diol **19** was selectively oxidized using a single equivalent of Swern reagent at −78 °C to provide the lactol **20** in 65% yield. The undesired regioisomeric lactol **21**, which arose from oxidation of the secondary allylic alcohol, was also isolated in approximately 18% yield. When **20** was treated with methyl-(tributylphosphoranylidene)acetate under the same conditions employed for the *E*-selective olefination of **17**, the diester **16** was isolated in 80% yield as a mixture (20:1) of *E*/*Z*-isomers. We had thus prepared the key intermediate **16** in four steps and 37% overall yield from L-arabinose. In accordance with our expectations, treatment of **16** with Amberlyst 15 in acetone afforded a separable mixture (20:1) of the isomeric acetonides **18** and **16**. When **18** was resubjected to the reaction conditions, the same mixture of **16** and **18** was obtained, thus confirming that this ratio is thermodynamically controlled.

The next stage of the synthetic plan required that the first of two 1,3-chirality transfer reactions be performed. Toward this goal, **16** was converted into its mesylate **22** (Scheme 4). We had originally envisioned that **22** would undergo highly stereoselective S_N2' displacement with a (diethylamino)diphenylsilyl organometallic derivative to give **23**,[15,16] oxidation of which would then lead to the desired alcohol **24**.[17] However, all attempts to convert **22** into **23** were unsuccessful, and the deconjugated ester **25** was obtained in 50−85% yields. We were unable to suppress this deleterious side reaction.

We then adopted an alternative strategy for converting **16** into **24** that would involve the [2,3]-sigmatropic rearrangement of an intermediate allylic selenoxide (Scheme 5).[18] Although we were unable to convert the mesylate **22** into the selenide **26** directly, we found that reaction of phenyl selenocyanate with **16** in the presence of tri-*n*-butylphosphine gave the phenylselenide **26** in 55−64% yield together with variable amounts of the deconjugated ester **25**.[19] When the selenide **26** was treated

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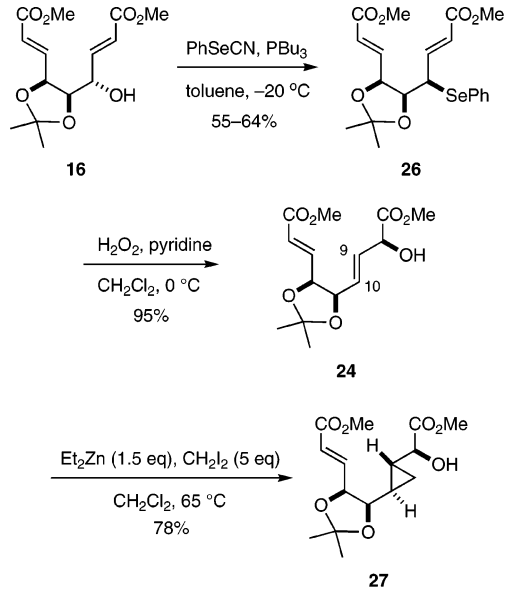
SCHEME 5

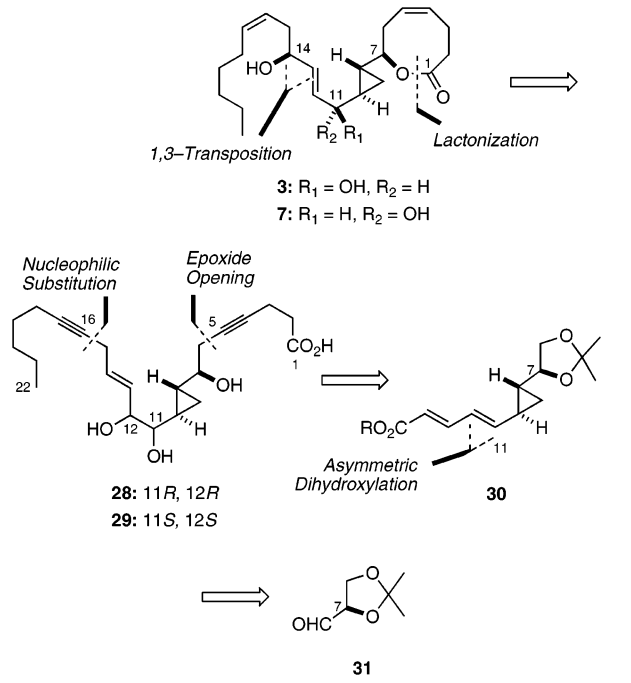


with hydrogen peroxide and pyridine, the *trans* α-hydroxyester **24** was obtained as a single isomer in 95% yield. The assignment of the *trans*-geometry of the newly formed olefin was based upon the observed vicinal coupling constant of 15.5 Hz for the olefinic protons on C(9) and C(10), whereas the stereochemistry of the hydroxyl group was assigned assuming that the reaction proceeded via the more stable envelope transition state that is usually observed for such rearrangements.[20]

Having successfully effected the key chirality transfer step, we turned toward the diastereoselective installation of the cyclopropane ring. Charette had showed that good to excellent (6:1 to >200:1) facial selectivity in the cyclopropanations of *E*-allylic alcohols could be achieved utilizing Et_2Zn/CH_2I_2,[21] a reagent first described by Furukawa.[22] Accordingly, we discovered that heating **24** in CH_2Cl_2 with 2 equiv of $Zn(CH_2I)_2$ in a sealed tube at 65 °C resulted in complete consumption of starting material and a 78% isolated yield of **27**, the structure of which was assigned based upon Charette's results. Although the synthesis of **27** in eight steps from L-arabinose did validate the underlying feasibility of the original unified approach to the solandelactones that is outlined in Scheme 2, the selenation step leading to **26** proved to be problematic upon scale-up, and yields dropped to 10−15%. Consequently, we turned to developing an alternate plan.

2.2. Second-Generation Approach. Our second-generation approach to the solandelactones was also designed to provide access to all known members of the solandelactone family, and the essential elements of the plan are exemplified for the syntheses of the C(11)-epimeric solandelactones E (**3**) and F (**7**) (Scheme 6). The allylic alcohol array at C(12)−C(14) would be introduced by a stereoselective 1,3-transposition. The preparation of **3** would thus entail an allylic 1,3-transposition of a compound derived from **28** that proceeded with overall inversion of the stereochemistry of the C(12) alcohol, whereas the allylic transposition of **29** en route to **7** would require net

SCHEME 6



retention of stereochemistry. Inasmuch as the 1,3-transposition had previously been problematic, this new entry to the solandelactones was attractive because only one such transposition was required and the reorganization could potentially be postponed until late in the synthesis. The requisite C(1)−C(5) and C(16)−C(22) subunits would be introduced by carbon-carbon bond-forming reactions involving an epoxide opening and a S_N2 reaction, respectively, to provide the advanced intermediates **28** and **29**. The absolute stereochemistry of the vicinal diol at C(11)−C(12) of **28** and **29** would be introduced via a Sharpless enantioselective dihydroxylation of a diene related to **30**, which we envisioned would be accessible from commercially available D-glyceraldehyde acetonide (**31**).

2.2.1. Assembly of the Central Core of C(6)−C(15). The known dienoate **32** was first prepared in 72% yield as a mixture (10:1) of *E*/*Z* isomers in a single step via the HWE olefination of **31** with *trans*-triethyl phosphonocrotonate (Scheme 7).[23] Heating **32** with an excess of Simmons-Smith reagent in a sealed tube provided the cyclopropane **33** (72%), the stereochemistry of which was tentatively assigned based upon analogy with the literature.[24] The diastereoisomeric cyclopropane was not isolated. Use of dichloromethane as solvent consistently gave somewhat higher yields (5−10% higher) of **33** than did dichloroethane, although the latter solvent was more convenient for preparative purposes as the reaction did not have to be performed in a sealed tube. The chain extension of the unsaturated ester in **33** was then initiated by reduction with DIBAL to provide the allylic alcohol **34**. The stereochemistry of the cyclopropanation step was then unequivocally established by converting **34** in two steps into the carbamate **36**; X-ray analysis of a single crystal of **36** confirmed the relative stereochemical relationship between the two stereocenters at C(8)−C(10) and C(7). Having established three of the requisite

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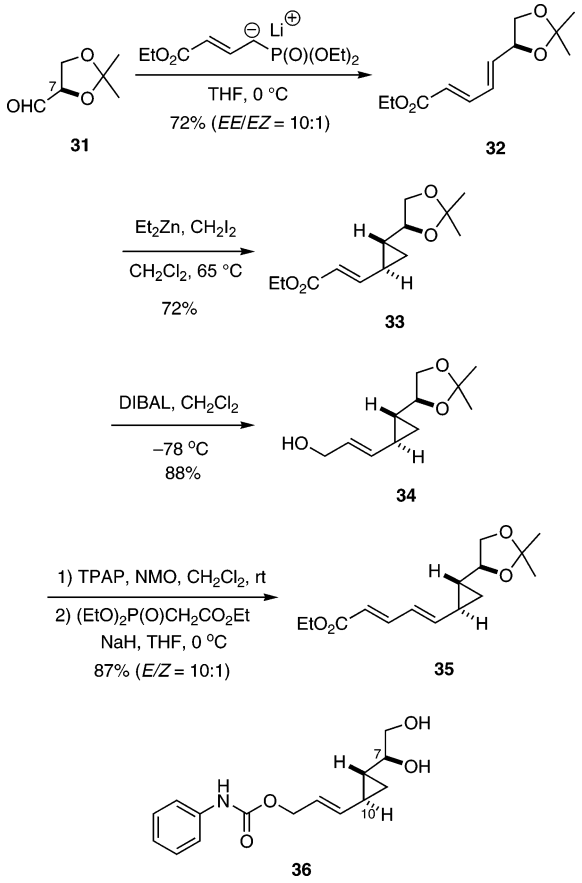
(23) Li, S.-K.; Xu, R.; Xiao, X.-S.; Bai, D.-L. *Chinese J. Chem.* **2000**, *18*, 910−923.

(24) Morikawa, T.; Sasaki, H.; Hanai, R.; Shibuya, A.; Taguchi, T. *J. Org. Chem.* **1994**, *59*, 97−103.

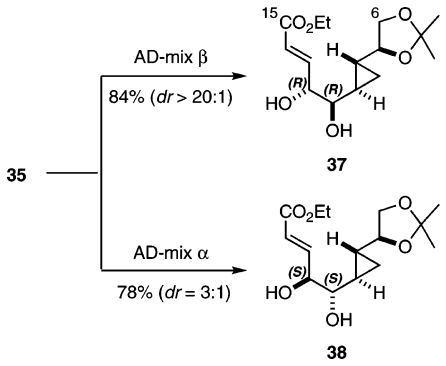
SCHEME 7



stereocenters, **34** was oxidized with catalytic tetrapropylammonium perruthenate (TPAP)[25] in the presence of *N*-methylmorpholine *N*-oxide (NMO) to give an intermediate α,*β*-unsaturated aldehyde that was allowed to react with the anion of triethyl phosphonoacetate to furnish **35** and small amounts of the *Z*-isomer (*E*/*Z* = 10:1) in 87% overall yield.

The stage was now set to install the chiral centers at C(11) and C(12) via enantioselective dihydroxylation of the more electron-rich, *γ*,*δ*-double bond of the dienoate **35.**[26] When **35** was treated with commercially available AD-mix α and AD-mix *β*, significant amounts of starting material remained, even after prolonged reaction times (48 h) at room temperature. After some experimentation with standard conditions, we found that use of modified AD mixtures, which were prepared by combining increased amounts of $(DHQ)_2PHAL$ or $(DHDQ)_2PHAL$ (8 mol %) and $K_2OsO_2(OH)_4$ (5 mol %) with the usual quantities of noncatalytic ingredients, led to more rapid and complete conversions. When diene **35** was treated with modified AD-mix *β*, the diol **37** was isolated as a single diastereomer (dr > 20:1) in 84% yield (Scheme 8). The same reaction of **35** with modified AD-mix α provided an inseparable mixture (dr = 3:1) of diols **38** and **37**, suggesting a mismatch of ligand and olefin. The stereochemistry of **37** and **38** were assigned to be 11*R*,12*R* and 11*S*,12*S*, respectively, by applying the Sharpless model.[27] In accordance with our synthetic plan, diol **37** would be a key

SCHEME 8

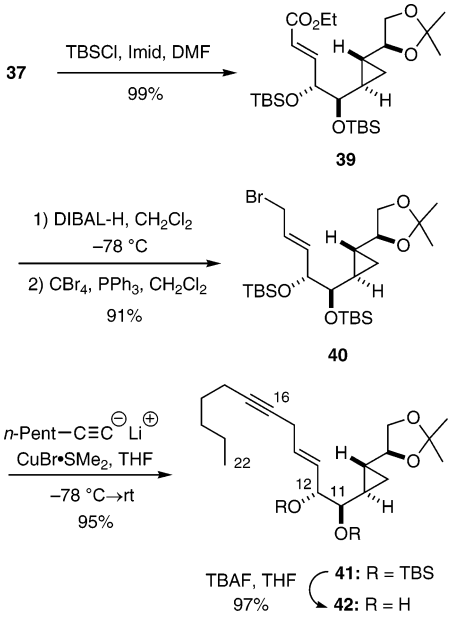


intermediate in the synthesis of solandelactone E (**3**), whereas **38** could be a precursor of solandelactone F (**7**).

2.2.2. Elaborating the C(12)−C(22) Segment. Having developed an efficient entry to the C(6)−C(15) central core of the solandelactones, we began to explore various tactics for introducing the side chains at C(6) and C(15) that would be required for solandelactones E (**3**) and F (**7**) and for effecting the 1,3-transposition. We decided to append the C(16)−C(22) subunit first because compared to an unsaturated lactone ring the double bonds were expected to be more tolerant of a number of projected synthetic operations. Toward that end, the diol **37** was first converted into the bis-TBS ether **39**, a reaction that was sluggish and required prolonged reaction times or mild heating to induce complete conversion (Scheme 9). The ester of **39** was then reduced with DIBAL, and the intermediate allylic alcohol was converted to its bromide **40** in 91% overall yield. When **40** was allowed to react with 1-heptynyllithium in the presence of $CuBr\cdot SMe_2$, the desired enyne **41** was isolated in 95% yield. To examine the feasibility of the key allylic transposition, the silyl protecting groups were selectively removed by treating **41** with excess tetrabutylammonium fluoride (TBAF) to afford the diol **42** in near quantitative yield.

With the diol **42** in hand, it was time to examine the 1,3-chirality transfer. Both of the hydroxyl groups required protection prior to appending the C(1)−C(5) fragment, so a strategy

SCHEME 9



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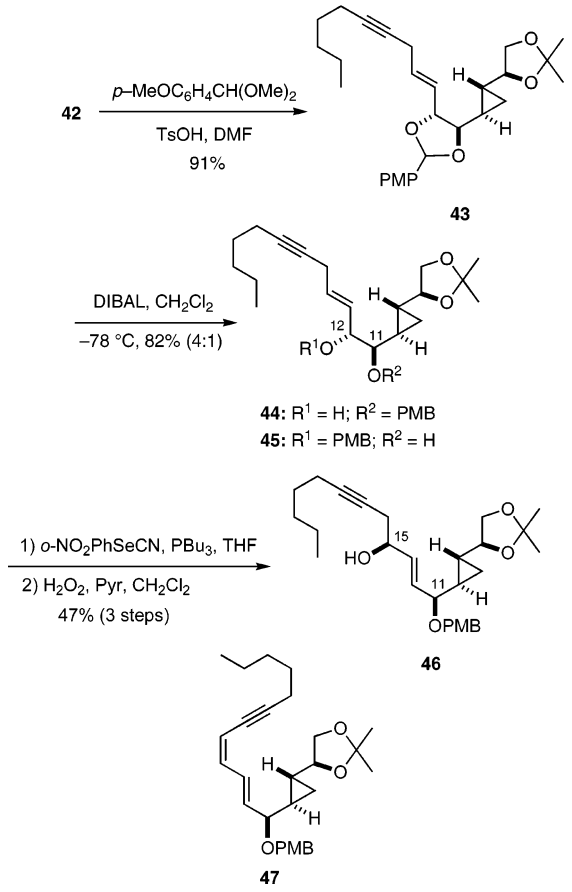
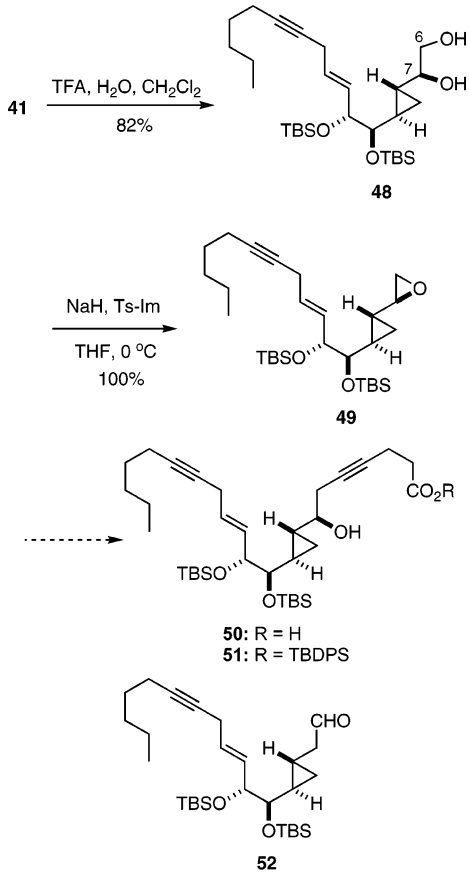
SCHEME 10



SCHEME 11



was adopted that would first involve the selective protection of the more hindered C(11) hydroxyl group. Anisylidine acetals are known to undergo selective cleavage at the least hindered carbon-oxygen bond using hydride reagents, and DIBAL is commonly employed for this process because it usually provides excellent regiocontrol.[28] In the event, diol **42** was treated with anisaldehyde dimethyl acetal in the presence of a catalytic amount of TsOH to furnish the anisylidine acetal **43** as a mixture (1:1) of diastereomers in 91% yield (Scheme 10). When **43** was treated with DIBAL (3 equiv) in CH_2Cl_2 at −78 °C, an inseparable mixture (4:1) of **44** and **45** was obtained in 82% yield. In ancillary model studies, we discovered that use of a combination of $(i\text{-Bu})_3Al$ as a Lewis acid and $NaCNBH_3$ as a reducing agent in CH_2Cl_2 cleaved acetals having substitution patterns similar to **43** with higher regioselectivity than DIBAL. Unfortunately, reduction of **43** under these conditions was less selective than DIBAL. In analogy with the conversion of **16** into **26** (Scheme 5), the mixture of **44** and **45** was allowed to react with PhSeCN and Bu_3P, and the intermediate selenide was oxidized with H_2O_2 in the presence of pyridine to provide a separable mixture (1:1) of **46** (ca. 23% yield) together with an elimination product that was tentatively assigned the structure of **47**. The structure of **46** was assigned based upon the observed coupling constant of 15.6 Hz for the vicinal protons on C(12) and C(13) that is consistent with the *E*-olefin geometry, and the preferred five-membered transition state that would lead to the desired configuration at C(14). In a modified procedure, we discovered that when the mixture (4:1) of **44** and **45** was treated with *o*-NO_2PhSeCN and Bu_3P followed by reaction of the intermediate nitrophenylselenide with H_2O_2 and pyridine, the transposed alcohol **46** was obtained in 47% overall yield from **43**; none of the dienyne **47** was isolated.

2.2.3. Constructing the C(1)−C(7) Lactone. Owing to the modest overall yield in converting **42** into **46**, we elected to postpone the allylic transposition sequence until later stage in the synthesis. We thus turned to the task of appending a C(1)−C(5) side chain that was suitably functionalized to elaborate the unsaturated eight-membered lactone ring in solandelactones E and F. We envisioned that these carbon atoms could be introduced by the opening of a C(6)−C(7) epoxide. Toward this end, the acetonide moiety in **41** was selectively hydrolyzed in a biphasic system of CH_2Cl_2 and aqueous trifluoroacetic acid (TFA) to provide the diol **48** in 82% yield (Scheme 11).[29] A modification of a Fraser-Reid protocol was then employed to prepare **49** in nearly quantitative yield via sequential treatment of **48** with NaH and *N*-tosylimidazole.[30] Although the epoxide **49** was rather unstable and rearranged readily to the aldehyde **52**, the crude epoxide was >95% pure and could be used directly in subsequent reactions.

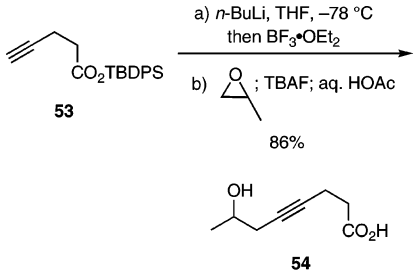
Our strategy for introducing the unsaturated, eight-membered lactone onto **49** entailed opening of the epoxide ring with a functionalized acetylide anion. However, treating **49** with the dianion of 4-pentynoic acid under a variety of conditions led only to recovered starting material or complex mixtures, and

(28) For an example used in the total synthesis of constanolactones A and B, see: Da Silva, C. B.; Pale, P. *Tetrahedron: Asymmetry* **1998**, *9*, 3951−3954.

(29) Smith, A. B., III; Doughty, V. A.; Sfouggatakis, C.; Bennett, C. S.; Koyanagi, J.; Takeuchi, M. *Org. Lett.* **2002**, *4*, 783−786.

(30) Hicks, D. R.; Fraser-Reid, B. *Synthesis* **1974**, 203.

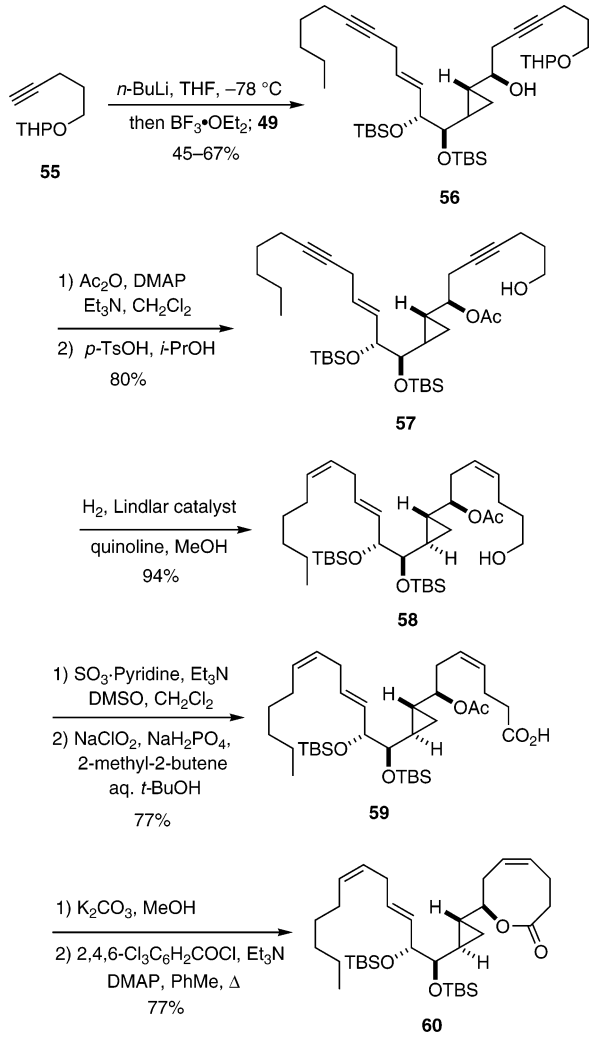
none of the desired acid **50** was isolated. Wipf reported that TBDPS-protected esters may be used as starting materials in a variety of metal-catalyzed transformations,[31] and it occurred to us that the anion of the TBDPS ester of 4-pentynoic acid might be employed as a nucleophile for opening epoxides, including **49**. We conducted a simple model study and found that when propylene oxide was treated with an alkynyl borane derived from the TBDPS-protected pentynoic acid **53**, the known hydroxy acid **54** was isolated in unoptimized yield of 86% (eq 1).[32] To our knowledge, this is the first example of a nucleophilic ring opening of an epoxide with an alkynyl borane containing a silyl ester. Although this reaction may be of general use in synthesis, we were disappointed to find that, when **49** was used as the reactant, a complex mixture of compounds was again produced, from which only 5% of **51** could be isolated.



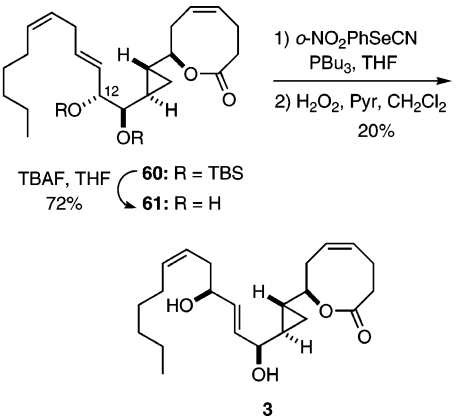
(1)

Eventually we discovered that reaction of the epoxide **49** with the acetylide anion generated from tetrahydropyranyl-protected 4-pentyn-1-ol using a procedure reported by Yamaguchi gave the desired alcohol **56**, although the yields, which ranged from 45−67%, in this reaction were somewhat irreproducible (Scheme 12).[33] Acylation of the free hydroxyl group in **56**, followed by acid-catalyzed acetal exchange with *i*-PrOH provided **57** in 80% yield. Use of more conventional solvents, such as MeOH or the previously described biphasic aqueous TFA/CH_2Cl_2 conditions, for removing the tetrahydropyranyl protecting group resulted in a significant loss of the silyl protecting groups. Hydrogenation of both of the triple bonds in **57** using Lindlar's catalyst poisoned with excess quinoline provided the triene **58** as the only isolable stereoisomer in 94% yield. A two-stage oxidation of the primary alcohol in **58** furnished the carboxylic acid **59**. Subsequent saponification of the acetate moiety in **59** then gave a hydroxy acid intermediate that underwent facile lactonization using the Yamaguchi protocol to give lactone **60** in 77% overall yield from **59**.[34]

SCHEME 12



2.2.4. Completion of Synthesis and Revision of Structure. It now remained to effect the 1,3-transposition of the allylic alcohol at C(12) of **60**. The sequence was initiated by treating **60** with TBAF to give the diol **61** (eq 2). In our previous experiments such transpositions were performed on a protected diol. However, owing to the different steric environments of the two hydroxyl groups, we postulated that it might be possible to effect this transformation on an unprotected diol. Such a tactic would obviously eliminate the problems associated with selective protection of the more hindered hydroxyl group at C(11). Although treatment of **61** with *o*-NO_2PhSeCN in the presence of (*n*-Bu)$_3$P followed by oxidation of the intermediate selenide with H_2O_2 provided the transposed diol **3**, the transformation proceeded in only 20% yield. Approximately 15% of starting **61** remained even under the best conditions, and none of the other products of the reaction could be identified.

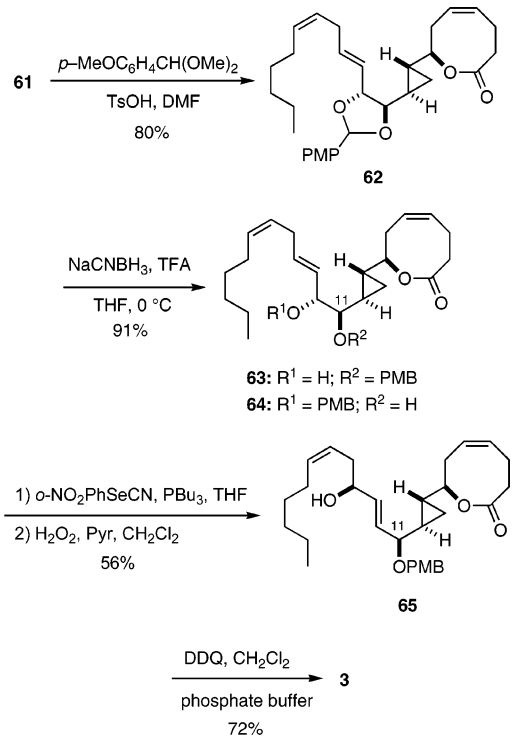


(2)

On the basis of the original report of Shin,[1] we believed we had thus completed the first total synthesis of solandelactone F (**7**). However, when we compared our ^{1}H and ^{13}C NMR spectral data with those published for the respective solandelactones, we found that our data were actually more consistent with those

(31) For a recent example, see: Wipf, P.; Pierce, J. G.; Zhuang, N. *Org. Lett.* **2005**, *7*, 483−485.
(32) Seidel, W.; Seebach, D. *Tetrahedron Lett.* **1982**, *23*, 159−62.
(33) Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 391−394.
(34) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989−1993.

SCHEME 13



reported for the C(11) epimeric natural product solandelactone E (**3**). Our structural assignment of synthetic **3** seemed firmly based upon the X-ray analysis of **34**, the known stereochemical preference for enantioselective dihydroxylations,[27] and the preferred stereoselectivity of [2,3]-sigmatropic rearrangements.[35] Although these data were highly supportive of our assignment, unambiguous proof of our structure was lacking. In subsequent correspondence with Professor Shin, it became apparent that a mistake had been made in correlating the names of the C(11)-epimeric solandelactones with their respective structures in the original paper,[1] and he agreed that those assignments should be revised in accord with our findings. Namely, the C(11) stereochemistry depicted in that paper should be corrected to C(11)*S* for solandelactones A, C, E, and G and C(11)*R* for solandelactones B, D, F and H. In this context, it is noteworthy that White has confirmed this revised assignment in a recent report detailing the syntheses of solandelactones E and F.[9]

Before White had verified our proposal for revising the absolute stereochemistry at C(11) of the solandelactones, we considered the possibility that the 1,3-allylic transformation of **61** might have occurred via epoxide intermediates to furnish diastereoisomeric allylic selenides that could have delivered solandelactone F (**7**) or the C(14) epimer of **3** upon oxidation and [2,3]-sigmatropic rearrangement. That this was not the case was established by an independent synthesis of **3** from **61** by a five-step reaction sequence. Thus, diol **61** was treated with anisaldehyde dimethyl acetal in the presence of a catalytic amount of TsOH to furnish **62** (Scheme 13). Reductive cleavage of the acetal moiety in **62** with $NaCNBH_3$ and TFA gave alcohols **63** and **64** as a separable mixture (1.2:1) of regioisomers. When **64** was treated with DDQ in the presence of a pH 7 phosphate buffer, the starting acetal **62** was isolated in 65% yield,[36] thereby allowing the recycling of the undesired regioisomer **64** to increase the overall efficiency. Reaction of **63** with *o*-NO_2PhSeCN and (*n*-Bu)$_3$P followed by oxidation of the intermediate allylic selenide with H_2O_2 and [2,3]-sigmatropic rearrangement of the allylic selenoxide thus delivered alcohol **65** as the sole product. The *p*-methoxybenzyl ether protecting group on **65** was then cleaved using DDQ to give a diol that was identical to the compound that was obtained directly from the allylic transposition of **61** (cf eq 2). Because no epoxide intermediates could be formed in this sequence, our structural assignment of **3** and its identification as solandelactone E was secured.

3. Summary

We designed a convergent approach to the oxylipins that provides an effective solution to the numerous stereochemical challenges posed by this important family of natural products. The efficacy of the approach was validated in the first enantioselective total synthesis of solandelactone E (**3**) in 23 steps from commercially available D-glyceraldehyde acetonide. Comparison of spectral data for our synthetic solandelactone with data in the literature led to a revision of the original structural assignments of the C(11)-epimeric solandelactones, a finding that was subsequently confirmed by White and co-workers.[9] Highlights of the synthesis include a diastereoselective, acetal-directed cyclopropanation of an electron-deficient olefin, a diastereoselective and enantioselective dihydroxylation that can lead to both C(11) epimeric series of the solandelactones, and a stereoselective 1,3-chirality transfer process featuring the [2,3]-sigmatropic rearrangement of an allylic selenoxide. During the course of these investigations, we also discovered and developed an efficient procedure for the highly *E*-stereoselective Wittig olefination of α-alkoxy aldehydes and sugar lactols, for the regioselective reductive cleavage of anisylidine acetals, and a potential method for opening substituted epoxides with alkynyl silyl esters. The utility of these latter methods is being explored in separate studies, the results of which will be reported in due course.

4. Experimental Section

(*E*)-Ethyl 3-((1*S*,2*R*)-2-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-cyclopropyl)acrylate (33). Diiodomethane (5.4 mL, 67.2 mmol) was added dropwise over 1 min to a stirred solution of Et_2Zn (1.0 M solution in hexane, 20.2 mL, 20.2 mmol) and diene **32** (3.8 g, 16.8 mmol) in anhydrous CH_2Cl_2 (200 mL) in a sealed tube at room temperature. Once the addition was complete, the tube was sealed, and the bottom third of the sealed tube was immersed in a 65 °C oil bath and stirred for 4 h whereupon the tube was removed from the bath and cooled in a refrigerator at 5 °C for 12 h. Once cooled, the tube was opened, and the contents were poured into a separatory funnel containing aqueous 1 M HCl (100 mL). The remaining salts in the sealed tube were dissolved with aqueous 1 M HCl (2 × 20 mL) and CH_2Cl_2 (2 × 20 mL) and then poured into the funnel. The biphasic mixture was shaken until both layers were transparent, and additional aqueous 1 M HCl was added as necessary until both layers were transparent. The layers were separated, and the organic layer was washed with saturated aqueous $NaHCO_3$ (50 mL) and saturated aqueous $Na_2S_3O_5$ (30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (9:1 to 5:1) to give 2.90 g (72%) of **33** as a clear oil; $[\alpha]^{22}_D$ + 28.4

(35) Nishibayashi, Y.; Uemura, S. *Top. Curr. Chem.* **2000**, *208*, 2015.

(36) Oikawa, Y.; Nishi, T.; Yonemitsu, O. *Tetrahedron Lett.* **1983**, *24*, 4037−4040.

(*c* 3.50, $CHCl_3$); ^1H NMR (500 MHz) δ 6.42 (dd, J = 15.1, 9.4 Hz, 1 H), 5.83 (dd, J = 15.1, 0.5 Hz, 1 H), 4.14 (q, J = 7.2 Hz, 2 H), 4.06 (dd, J = 8.0, 5.5 Hz, 1 H), 3.71 (dd, J = 7.0, 5.5 Hz, 1 H), 3.65 (dd, J = 8.0, 7.0 Hz, 1 H), 1.51 (app dt, J = 9.4, 4.6 Hz, 1 H), 1.39 (s, 3 H), 1.31 (s, 3 H), 1.24 (t, J = 7.2 Hz, 3 H), 1.20 (ddd, J = 8.5, 4.6, 2.5, 1.5 Hz, 1 H), 1.05 (app dt, J = 8.5, 5.5 Hz, 1 H), 0.89 (dt, J = 8.5, 5.0 Hz, 1 H); ^{13}C NMR (125 MHz) δ 166.5, 151.3, 119.0, 109.1, 77.7, 69.0, 60.1, 26.6, 25.6, 24.5, 18.3, 14.3, 12.8; IR (neat) 2984, 2860, 1715, 1645, 1370, 1254, 1146, 1064 cm^{-1}; mass spectrum (CI) *m*/*z* 241 (base) 183, 165. HRMS $C_{13}H_{21}O_4$ (M + 1) calcd 241.1440, found 241.1432.

(4*R*,5*R*,*E*)-Ethyl 5-((1*R*,2*R*)-2-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)cyclopropyl)-4,5-dihydroxypent-2-enoate (37). A dry mixture of "super" AD-Mix β was prepared by combining K_3FeCN_6 (7.3 g, 22.5 mmol), K_2CO_3 (3.11 g, 22.5 mmol), $K_2OsO_2(OH)_4$ (183 mg, 0.53 mmol), $(DHQD)_2PHAL$ (550 mg, 0.60 mmol), and methanesulfonamide (1.43 g, 15.0 mmol). H_2O (40 mL) and *t*-BuOH (40 mL) were added to the mixture, and the resultant mixture was stirred at room temperature until all of the solids were dissolved (ca. 0.5 h). This solution of AD-Mix β was then transferred into a second flask containing diene **35** (2.0 g, 7.51 mmol), and the solution was stirred for 8 h at room temperature. Solid Na_2SO_3 (4.73 g, 37.5 mmol) was added, and stirring continued for an additional 12 h. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography, eluting with hexanes/EtOAc (2:1 to 1:3) to give a pale-yellow solid contaminated with excess methanesulfonamide. The mixture was triturated with $CHCl_3$, and the crystalline impurity was removed to give 1.76 g (78%) of diol **37** as a pale-yellow wax: mp 41−43 °C; $[\alpha]^{22}_D$ + 8.4 (*c* 2.53, $CHCl_3$); ^1H NMR (500 MHz) δ 6.97 (ddd, J = 15.7, 5.0, 1.7 Hz, 1 H), 6.11 (dt, J = 15.7, 1.6 Hz, 1 H), 4.23 (td, J = 5.0, 1.5 Hz, 1 H), 4.17 (dq, J = 7.2, 1.7 Hz, 2 H), 4.03 (dd, J = 7.4, 4.8 Hz, 1 H), 3.69 (dd, J = 7.8, 4.8 Hz, 1 H), 3.65 (app t, J = 7.4 Hz, 1 H), 2.99 (dd, J = 8.5, 5.0 Hz, 1 H), 1.40 (s, 3 H), 1.31 (s, 3 H), 1.26 (dt, J = 7.2, 1.7 Hz, 3 H), 1.05 (app ddt, J = 8.5, 7.8, 5.0 Hz, 1 H), 0.93 (app tt, J = 8.5, 5.0 Hz, 1 H), 0.68 (app dt, J = 8.5, 5.0 Hz, 1 H), 0.58 (dt, J = 8.5, 5.0 Hz, 1 H); ^{13}C NMR (100 MHz) δ 166.3, 146.4, 122.0, 109.1, 78.3, 74.6, 76.7, 68.7, 60.6, 26.7, 25.5, 18.5, 18.1, 14.2, 7.9; IR (neat) 3413, 2978, 2884, 2332, 1718, 1261, 1059, 668 cm^{-1}; mass spectrum (CI) *m*/*z* 301, 283, 265, 243 (base), 225, 207. HRMS $C_{15}H_{25}O_6$ (M+1) calcd 301.1651, found 301.1654.

(5*R*,6*R*)-5-((*E*)-dec-1-en-4-ynyl)-6-((1*R*,2*R*)-2-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)cyclopropyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecane (41). 1-Heptyne (0.90 mL, 6.87 mmol) and *n*-butyllithium (2.5 M solution in hexanes, 2.23 mL, 5.58 mmol) was added to a solution of $CuBr{\cdot}SMe_2$ (132 mg, 0.64 mmol) in THF (42 mL) at −78 °C. Stirring was continued for 1.5 h at −78 °C, whereupon a solution of allylic bromide **40** (2.36 g, 4.29 mmol) in THF (5 mL) was added dropwise. The −78 °C bath was removed, and stirring continued for 8 h at room temperature. Et_2O (10 mL) and saturated aqueous NH_4Cl (20 mL) were added, and stirring was continued for an additional 12 h at room temperature. The layers were separated, and the organic layer was dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (20:1) to provide 2.29 g (95%) of **41** as a pale-yellow oil; $[\alpha]^{22}_D$ + 9.8 (*c* 0.85, $CHCl_3$); ^1H NMR (500 MHz) d 5.86 (ddt, J = 15.5, 4.5, 2.0 Hz, 1 H), 5.59 (dtd, J = 15.5, 5.0, 1.5, 1 H), 4.13 (app dt, J = 4.5, 1.5 Hz, 1 H), 3.95 (dd, J = 8.0, 6.0 Hz, 1 H), 3.64 (app t, J = 8.0, 1 H), 3.42 (app t, J = 4.5 Hz, 1 H), 3.36 (dt, J = 8.0, 6.0 Hz, 1 H), 2.92 (dt, J = 5.0, 2.0 Hz, 2 H), 2.14 (tt, J = 7.2, 2.0 Hz, 2 H), 1.47 (p, J = 7.6 Hz, 2 H), 1.39 (s, 3 H), 1.30 (s, 3 H), 1.36−1.26 (comp, 4 H), 0.92−0.84 (comp, 23 H), 0.58 (dt, J = 9.4, 4.7 Hz, 1H), 0.47 (dt, J = 9.4, 4.7 Hz, 1 H), 0.02 (s, 3 H), 0.02 (s, 3 H), 0.02 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (125 MHz) δ 130.1, 125.4, 108.4, 82.8, 80.8, 76.9, 75.4, 75.1, 69.4, 31.1, 28.8, 26.8, 25.9, 25.9, 25.8, 22.2, 21.9, 18.7, 18.1, 17.9, 16.3, 16.3, 14.0, 6.4, −4.4, −4.6, −4.6, −4.8; IR (neat) 2930, 2858, 2360, 1472, 1368, 1252, 1125, 1065, 913, 836, 743, 668 cm^{-1}; mass spectrum (CI) *m*/*z* 565, 549, 507, 433, 285 (base), 227. HRMS $C_{32}H_{61}O_4Si_2$ (M + 1) calcd 565.4108, found 565.4090.

(*S*)-1-((1*R*,2*R*)-2-((5*R*,6*R*)-6-((*E*)-Dec-1-en-4-ynyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)cyclopropyl)ethane-1,2-diol (48). A solution of trifluoroacetic acid (0.35 mL, 4.74 mmol) in H_2O (1.8 mL) was added to a solution of acetonide **41** (1.34 g, 2.37 mmol) in CH_2Cl_2 (25 mL) at room temperature. Stirring was continued for 6 h at room temperature, whereupon saturated aqueous $NaHCO_3$ (10 mL) was added. After 15 min the layers were separated, and the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (6:1) to provide 1.02 g (82%) of **48** as a clear oil; ^1H NMR (500 MHz) d 5.92 (ddt, J = 15.5, 4.5, 2.0 Hz, 1 H), 5.64 (dtd, J = 15.5, 4.5, 2.0 Hz, 1 H), 4.18 (dt, J = 4.5, 2.0 Hz, 1 H), 3.66 (br, 1 H), 3.53 (dd, J = 10.7, 6.7 Hz, 1 H), 3.44 (app t, J = 4.5 Hz, 1 H), 3.04−3.01 (m, 1 H), 2.92 (dt, J = 4.5, 2.0 Hz), 2.14 (tt, J = 7.2, 2.0 Hz, 2 H), 1.90 (br, 2 H), 1.48 (p, 7.2 Hz, 2H), 1.36−1.27 (comp, 4 H), 1.00 (dtd, J = 9.7, 5.2, 5.2 Hz, 1H), 0.98 (s, 9 H), 0.87 (s, 9 H), 0.86−0.81 (m, 1 H), 0.53 (app dt, J = 8.7, 4.7 Hz, 1 H), 0.42 (app dt, J = 8.7, 4.7 Hz, 1 H), 0.03 (s, 3 H), 0.03 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (125 MHz) d 130.0, 125.6, 82.9, 76.9, 76.2, 75.1, 75.0, 66.4, 31.1, 28.8, 25.9, 25.8, 22.2, 21.9, 18.7, 18.2, 18.0, 17.6, 16.4, 14.0, 6.0, −4.4, −4.6, −4.7, −4.8; IR (neat) 3382, 2929, 2857, 1471, 1253, 1079, 835, 774 cm^{-1}; mass spectrum (CI) *m*/*z* 523, 507, 468, 393, 375, 279 (base), 245, 185. HRMS $C_{29}H_{55}O_4Si_2$ (M − 1) calcd 523.3639, found 523.3639.

(5*R*,6*R*)-5-((*E*)-Dec-1-en-4-ynyl)-2,2,3,3,8,8,9,9-octamethyl-6-((1*R*,2*R*)-2-((*S*)-oxiran-2-yl)cyclopropyl)-4,7-dioxa-3,8-disiladecane (49). Sodium hydride (60% suspension in mineral oil, 223 mg, 5.58 mmol) was added to a solution of diol **48** (997 mg, 1.86 mmol) in anhydrous THF (19 mL) at 0 °C. After 15 min at 0 °C, 1-(*p*-toluenesulfonyl)imidazole (413 mg, 1.86 mmol) was added. Stirring was continued for an additional 3 h at 0 °C, whereupon the ice bath was removed and stirring continued for 12 h at room temperature. Et_2O (20 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added to the reaction mixture, and the layers were separated. The organic layer was further washed with saturated aqueous NH_4Cl (10 mL) and brine (10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to provide 975 mg (99%) of **49** as a pale-yellow oil which was used without further purification; ^1H NMR (400 MHz) δ 5.86 (ddt, J = 15.4, 4.5, 2.0 Hz, 1 H), 5.59 (dtd, J = 15.4, 5.2, 1.6 Hz, 1 H), 4.13 (app dt, J = 4.5, 1.6 Hz, 1 H), 3.55 (app t, J = 4.2, 1 H), 2.90 (ddd, J = 6.8, 4.4, 2.0 Hz, 2 H), 2.71 (dd, J = 5.0, 4.0 Hz, 1 H), 2.60 (ddd, J = 6.8, 4.0, 2.6 Hz, 1 H), 2.55 (dd, J = 5.0, 2.6 Hz, 1 H), 2.13 (tt, J = 7.2, 2.4 Hz, 2 H), 1.47 (p, J = 7.2 Hz, 2 H), 1.37−1.24 (comp, 4 H), 1.09−1.03 (m, 1 H), 0.89 (s, 9 H), 0.84 (s, 9 H), 0.88−0.75 (comp, 4 H), 0.45−0.39 (comp, 2 H), 0.03 (s, 3 H), 0.02 (s, 3 H), 0.02 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (75 MHz) δ 130.3, 125.0, 82.7, 77.0, 75.6, 74.3, 54.2, 47.3, 31.1, 28.8, 25.9, 25.7, 22.2, 21.8, 18.7, 18.2, 18.0, 16.3, 15.1, 14.0, 4.5, −4.3, −4.6, −4.7, −4.8; IR (neat) 2928, 2857, 2363, 1471, 1253, 1124, 1076, 836 cm^{-1}; mass spectrum (CI) *m*/*z* 507.3687, 491, 449, 375, 279 (base), 227. HRMS $C_{29}H_{55}O_3Si_2$ (M + 1) calcd 507.3690, found 507.3687.

(1*R*)-1-((1*R*,2*R*)-2-((5*R*,6*R*)-6-((*E*)-Dec-1-en-4-ynyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)cyclopropyl)-7-(tetrahydro-2*H*-pyran-2-yloxy)hept-3-yn-1-ol (56). *n*-Butyllithium (2.45 M in hexane, 2.35 mL, 5.89 mmol) was added to a solution of 2-(4-pentynyloxy)tetrahydro-2H-pyran (1.23 g, 7.36 mmol) in anhydrous THF (30 mL) at −78 °C. Stirring was continued for 1 h at −78 °C, whereupon $BF_3{\cdot}OEt_2$ (0.56 mL, 4.41 mmol) was added and the mixture was stirred at −78 °C for an additional 45 min. The reaction was cooled to −100 °C for 15 min, and epoxide **49** dissolved in THF (10 mL) was added dropwise.

Stirring was continued for 2 h at −100 °C, and AcOH (1 mL) was added. After 5 min at −100 °C, the ice bath was removed, and saturated aqueous NH_4Cl (30 mL) was added. When the reaction reached room temperature (ca. 30 min), the layers were separated, and the aqueous layer was extracted with ether (2 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (100:3) to give 549 mg (55%) of **56** as a clear oil; ^{1}H NMR (400 MHz) δ 5.87 (ddt, J = 15.4, 4.4, 1.6 Hz, 1 H), 5.60 (dtd, J = 15.6, 4.6, 1.6 Hz, 1 H), 4.56 (dd, J = 4.4, 2.8 Hz, 1 H), 4.12 (dt, J = 4.4, 1.6 Hz, 1 H), 3.87−3.76 (comp, 2 H), 3.50−3.42 (comp, 2 H), 3.33 (app dt, J = 4.4, 1.6 Hz, 1 H), 3.06 (tdd, J = 7.4, 3.6, 1.6 Hz, 1 H), 2.91 (app dt, J = 4.6, 1.6 Hz, 2 H), 2.51−2.45 (m, 1 H), 2.32 (ddt, J = 16.4, 7.4, 2.4 Hz, 1 H), 2.27 (tt, J = 7.2, 1.4 Hz, 2 H), 2.14 (tt, J = 7.2, 2.4 Hz, 2 H), 2.00 (br, 1 H), 1.83−1.65 (comp, 4 H), 1.59−1.45 (comp, 6 H), 1.37−1.26 (comp, 4 H), 0.96−0.81 (comp, 23 H), 0.52−0.45 (comp, 2 H), 0.02 (s, 3 H), 0.02 (s, 3 H), 0.02 (s, 3 H), 0.01 (s, 3 H); ^{13}C (100 MHz) δ 130.3, 125.6, 98.8, 82.5, 82.1, 77.2, 77.2, 75.8, 75.4, 73.7, 65.9, 62.2, 31.1, 30.7, 29.1, 28.8, 27.6, 25.9, 25.8, 25.4, 22.2, 21.9, 20.1, 19.5, 18.7, 18.1, 17.9, 16.8, 15.7, 14.0, 6.7, −4.4, −4.5, −4.5, −4.8; IR (neat) 3467, 2929, 2856, 1471, 1360, 1252, 1121, 835 cm^{-1}; mass spectrum (CI) *m*/*z* 673, 657, 573, 543, 327, 279 (base) 179. HRMS $C_{39}H_{69}O_5Si_2$ (M − 1) calcd 673.4684, found 673.4694.

(1*R*)-1-((1*R*,2*R*)-2-((5*R*,6*R*)-6-((*E*)-Dec-1-en-4-ynyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)cyclopropyl)-7-(tetrahydro-2*H*-pyran-2-yloxy)hept-3-ynyl Acetate. Acetic anhydride (0.28 mL, 2.98 mmol) and Et_3N (1.26 mL, 8.93 mmol) were added to a solution of alcohol **56** (402 mg, 0.60 mmol) and 4-dimethylaminopyridine (7 mg, 0.06 mmol) in anhydrous CH_2Cl_2 (12 mL) at room temperature. Stirring was continued for 3.5 h at room temperature, whereupon a 1 M solution of aqueous HCl (10 mL) was added. The layers were separated, and the organic layer was washed with saturated aqueous $NaHCO_3$ (5 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography eluting with hexanes/EtOAc (20:1) to provide 391 mg (92%) of the acetate as a pale-yellow oil; $[\alpha]^{22}_D$ + 3.7 (*c* 0.37, $CHCl_3$); ^{1}H NMR (400 MHz) δ 5.86 (J = 15.2, 4.6, 2.0 Hz, 1 H), 5.60 (dtd, J = 15.2, 5.0, 1.6 Hz, 1 H), 4.56 (br, 1 H), 4.37 (app dt, J = 7.5, 4.8 Hz, 1 H), 4.12 (dt, J = 4.6, 1.6 Hz, 1 H), 3.85−3.81 (m, 1 H), 3.76 (dt, J = 9.2, 6.6 Hz, 1 H), 3.49−3.45 (m, 1 H), 3.42 (dtd, J = 9.0, 6.0, 3.0 Hz, 1 H), 3.33 (app t, J = 4.6 Hz, 1 H), 2.92 (app dt, J = 5.0, 2.0 Hz, 2 H), 2.52 (ddt, J = 16.8, 4.8, 2.2 Hz, 1 H), 2.43 (ddt, J = 16.8, 7.5, 2.2 Hz, 1 H), 2.24−2.20 (m, 2 H), 2.15 (tt, J = 7.2, 2.4 Hz, 2 H), 2.04 (s, 3 H), 1.83−1.65 (comp, 4 H), 1.57−1.44 (comp, 6 H), 1.38−1.25 (comp, 4 H), 1.07 (dtd, J = 9.6, 4.8, 4.8 Hz, 1 H), 0.95 (dtd, J = 9.4, 4.8, 4.8 Hz, 1 H), 0.88 (s, 3 H), 0.87 (s, 3H), 0.86−0.81 (m, 3 H), 0.51 (dt, J = 9.0, 4.8 Hz, 1 H), 0.46 (dt, J = 9.0, 4.8 Hz, 1 H), 0.02 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), 0.01 (s, 3H); ^{13}C (100 MHz) δ 170.5, 130.1, 125.8, 98.7, 82.5, 81.1, 77.3, 76.2, 75.6, 75.5, 75.3, 66.1, 62.1, 31.1, 30.7, 29.2, 28.8, 25.9, 25.8, 25.5, 24.8, 22.2, 21.9, 21.1, 19.5, 18.7, 18.1, 17.9, 17.6, 15.7, 14.0, 7.0, −4.4, −4.6, −4.6, −4.8; IR (neat) 2929, 2857, 1743, 1471, 1237, 1033, 836 cm^{-1}; mass spectrum (CI) *m*/*z* 717, 658, 617, 525, 437, 279 (base) 161. HRMS $C_{41}H_{73}O_6Si_2$ (M + 1) calcd 717.4946, found 717.4919.

(*R*)-1-((1*R*,2*R*)-2-((5*R*,6*R*)-6-((*E*)-Dec-1-en-4-ynyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)cyclopropyl)-7-hydroxyhept-3-ynyl Acetate (57). *p*-Toluenesulfonic acid (318 mg, 1.67 mmol) was added to a solution of the product of the previous experiment (776 mg, 1.08 mmol) in anhydrous *i*-PrOH (11.0 mL) at room temperature. Stirring was continued for 6 h at room temperature, whereupon saturated aqueous $NaHCO_3$ (5 mL) and Et_2O (20 mL) were added. Stirring was continued for an additional 5 min at room temperature, the layers were separated, and the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (6:1 to 3:1) to provide 596 mg (87%) of alcohol **57** as a pale-yellow oil; ^{1}H NMR (500 MHz) δ 5.85 (ddt, J = 15.5, 4.6, 2.0 Hz, 1 H), 5.59 (dtd, J = 15.5, 5.5, 1.5 Hz, 1 H), 4.39 (dt, J = 7.5, 4.3 Hz, 1 H), 4.11 (app dt, J = 4.6, 1.5 Hz, 1 H), 3.69 (dt, J = 6.2, 1.5 Hz, 2 H), 3.35 (app t, J = 4.6 Hz, 1 H), 2.91 (dt, J = 5.5, 2.0 Hz, 2 H), 2.50 (ddt, J = 17.0, 4.3, 2.5 Hz, 1 H), 2.41 (ddt, J = 17.0, 7.5, 2.5 Hz, 1 H), 2.21 (tt, J = 6.5, 2.5 Hz, 2 H), 2.15 (tt, J = 7.2, 2.0 Hz, 2 H), 2.02 (s, 3 H), 1.85 (br, 1 H), 1.67 (p, J = 6.2 Hz, 2 H), 1.46 (p, J = 7.2 Hz, 2 H), 1.38−1.24 (comp, 4 H), 1.05 (app dt, J = 8.5, 4.6 Hz, 1 H), 0.99−0.92 (m, 1 H), 0.92−0.83 (comp, 21 H), 0.48 (app dt, J = 8.5, 4.9 Hz, 1 H), 0.45 (app dt, 8.4, 4.9 Hz, 1 H), 0.01 (s, 3 H), 0.00 (s, 3 H), 0.00 (s, 3 H), 0.00 (s, 3 H); ^{13}C (125 MHz) δ 170.6, 130.1, 125.9, 82.56, 81.0, 77.0, 76.9, 75.6, 75.4, 75.3, 61.7, 31.3, 31.1, 28.8, 25.8, 25.8, 24.8, 22.2, 21.9, 21.1, 18.7, 18.1, 17.9, 17.9, 15.4, 14.0, 7.0, −4.4, −4.6, −4.7, −4.9; IR (neat) 3435, 2929, 2557, 1743, 1471, 1369, 1251, 1075, 836 cm^{-1}; mass spectrum (CI) *m*/*z* 633, 615, 573, 501, 441, 353 (base) 309, 279. HRMS $C_{36}H_{65}O_5Si_2$ (M + 1) calcd 633.4371, found 633.4357.

(*R*,*Z*)-1-((1*R*,2*R*)-2-((5*R*,6*R*)-6-((1*E*,4*Z*)-Deca-1,4-dienyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)cyclopropyl)-7-hydroxyhept-3-enyl acetate (58). A vacuum (0.5 mm Hg), using a 20-gauge needle plunged through a standard rubber septum, was pulled on a solution of dialkyne **57** (54 mg, 0.085 mmol), quinoline (11 μL), and Lindlar's catalyst (11 mg) in anhydrous MeOH (1.7 mL) at room temperature. Stirring was continued under vacuum for 5 sec, or until the reaction began to gently reflux, whereupon the reaction vessel was backfilled with H_2 gas. This procedure was repeated six times. Stirring was continued for 15 min at room temperature, whereupon the reaction was diluted with CH_2Cl_2 (3 mL) and filtered through a pad of Celite. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography eluting with hexanes/EtOAc (10:1) to give 51 mg (94%) of triene **58** as a colorless oil; ^{1}H NMR (400 MHz) δ 5.61−5.50 (comp, 2 H), 5.46−5.31 (comp, 4 H), 4.34 (dt, J = 7.6, 5.6 Hz, 1 H), 4.06 (dd, J = 4.6, 2.8 Hz, 1 H), 3.61 (t, J = 6.6 Hz, 2 H), 3.26 (dd, J = 5.5, 4.6 Hz, 1 H), 2.78−2.75 (m, 2 H), 2.42−2.38 (comp, 2 H), 2.10 (app sex, J = 7.6 Hz, 2 H), 2.03−1.98 (m, 2 H), 1.60 (dp, J = 6.8, 2.6 Hz, 2 H), 1.53 (br, 1 H), 1.36−1.21 (comp, 6 H) 1.02−0.90 (comp, 2 H), 0.88−0.84 (comp, 21 H), 0.51 (dt, J = 8.6, 5.2 Hz, 1 H), 0.46 (dt, J = 8.6, 5.2 Hz, 1 H), 0.01 (s, 3 H), 0.01 (s, 3 H), 0.00 (s, 3 H), −0.01 (s, 3 H); ^{13}C (100 MHz) δ 170.7, 131.3, 130.8, 129.9, 129.2, 127.0, 125.7, 77.2, 76.3, 75.9, 62.1, 32.6, 32.3, 31.5, 30.2, 29.3, 27.1, 25.8, 25.8, 23.5, 22.5, 21.2, 18.9, 18.1, 17.9, 17.7, 14.0, 7.3, −4.3, −4.5, −4.5, −4.9; IR (neat) 3446, 2929, 2857, 1740, 1471, 1370, 1250, 1076, 836 cm^{-1}; mass spectrum (CI) 637, 621, 577, 505, 489, 445, 373, 355, 313, 281 (base). HRMS $C_{36}H_{69}O_5Si_2$ (M + 1) calcd 637.4684, found 637.4674.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((5*R*,6*R*)-6-((1*E*,4*Z*)-Deca-1,4-dienyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)cyclopropyl)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (60). 2,4,6-Trichlorobenzoyl chloride (1.06 mL, 1.03 mmol) was added to a solution of hydroxy acid (210 mg, 0.34 mmol) and Et_3N (0.24 mL, 1.72 mmol) in anhydrous THF (3.5 mL) at room temperature. Stirring was continued for 1 h at room temperature, whereupon the formed triethylamine hydrochloride salt was removed by filtration through a short plug of Celite. The filtrate was diluted with anhydrous toluene (300 mL) and added dropwise over 3 h via an addition funnel into a refluxing solution of 4-dimethylaminopyridine (842 mg, 6.90 mmol) in anhydrous toluene (40 mL). After the addition was complete, the reaction was refluxed for an additional 4 h and concentrated under reduced pressure. The solid was dissolved in CH_2Cl_2 (30 mL) and washed with 1 M aqueous HCl (2 × 30 mL) and aqueous saturated $NaHCO_3$ (10 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (30:1) to provide 165 mg (81%) of lactone **60** as a pale-yellow oil; ^{1}H NMR (400 MHz) δ 5.76 (dd, J = 11.2, 6.4 Hz, 1 H), 5.70 (dd, J = 11.2, 7.6

Hz, 1 H), 5.62−5.53 (comp, 2 H), 5.44−5.31 (comp, 2 H), 4.08−4.07 (m, 1 H), 3.88 (ddd, J = 10.4, 8.6, 1.8 Hz, 1 H), 3.33 (app t, J = 4.6 Hz, 1 H), 3.85 (dtd, J = 12.4, 8.6, 5.9 Hz, 1 H), 2.78−2.75 (m, 2 H), 2.71 (ddd, J = 13.2, 5.9, 2.9 Hz, 1 H), 2.55 (ddd, J = 16.0, 10.4, 5.6 Hz, 1 H), 2.30−2.22 (comp, 2 H), 2.10−2.05 (m, 1 H), 2.01 (q, J = 7.2 Hz, 2 H), 1.36−1.25 (comp, 6 H), 1.03−0.98 (comp, 2 H), 0.92−0.85 (comp, 21 H), 0.59−0.52 (comp, 2 H), 0.02 (s, 6 H), 0.01 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (100 MHz) δ 177.2, 132.7, 131.1, 130.2, 129.4, 128.8, 127.2, 82.8, 76.1, 76.0, 37.9, 34.6, 31.7, 30.5, 29.6, 27.4, 26.1, 24.7, 22.8, 18.7, 18.3, 18.2, 14.3, 7.9, −4.1, −4.2; IR (neat) 2929, 2857, 1751, 1472, 1253, 1083, 836 cm^{-1}; mass spectrum (CI) *m*/*z* 591, 574, 539, 533, 460, 441, 327, 309 (base), 282. HRMS $C_{34}H_{63}O_4Si_2$ (M + 1) calcd 591.4265, found 591.4260.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((1*R*,2*R*,3*E*,6*Z*)-1,2-Dihydroxydodeca-3,6-dienyl)cyclopropyl)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (61). A solution of tetrabutylammonium fluoride (264 mg, 0.84 mmol) in THF (1 mL) was added to a solution of bis-silyl ether **60** (165 mg, 0.28 mmol) at 0 °C. The solution was stirred at 0 °C for 20 min, whereupon the bath was removed and stirring continued for an additional 3 h at room temperature. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography eluting with hexanes/EtOAc (2:1) to give 72 mg (72%) of diol **61** as a clear oil; $[\alpha]^{22}_D$ + 5.6 (*c* 0.55, $CHCl_3$); ^{1}H NMR (500 MHz) δ 5.78−5.68 (comp, 3 H), 5.50 (ddt, J = 15.5, 7.0, 1.5 Hz, 1 H), 5.45−5.40 (m, 1 H), 5.43−5.29 (m, 1 H), 4.00 (ddd, J = 10.0, 8.0, 1.5 Hz, 1 H), 3.98 (appt, J = 7.0 Hz, 1 H), 2.93 (app t, J = 7.0 Hz, 1 H), 2.82 (app ddt, J = 15.0, 9.0, 6.0 Hz, 1 H), 2.77 (app dt, J = 7.5, 1.5 Hz, 2 H), 2.70 (ddd, J = 13.5, 6.0, 3.0 Hz, 1 H), 2.59 (ddd, J = 17.0, 10.0, 6.0 Hz, 1 H), 2.50 (br, 1 H), 2.4 (br, 1 H), 2.29−2.21 (comp, 2 H), 2.11−2.06 (m, 1 H), 1.99 (dq, J = 7.2, 1.2 Hz, 2 H), 1.37 (p, J = 7.2 Hz, 2 H), 1.30−1.21 (comp, 4 H), 1.12 (app dtd, J = 9.0, 5.0, 5.0 Hz, 1 H), 0.92−0.84 (comp, 4 H), 0.67 (app dt, J = 9.0, 5.0 Hz, 1 H), 0.55 (app dt, J = 9.0, 5.0 Hz, 1 H); ^{13}C NMR (100 MHz) δ 177.0, 132.7, 132.6, 131.4, 129.1, 128.2, 126.2, 81.0, 77.0, 76.4, 37.7, 34.1, 31.4, 30.1, 29.2, 27.1, 24.4, 22.5, 19.8, 19.6, 14.0, 8.7; IR (neat) 3406, 2928, 2856, 1747, 1458, 1213, 1054, 967 cm^{-1}; mass spectrum (CI) *m*/*z* 363, 345, 327, 195 179 (base) 149. HRMS $C_{22}H_{33}O_3$ (M + 1 − H_2O) calcd 345.2429, found 345.2420.

(8*R*,*Z*)-8-((1*R*,2*R*)-2-((4*R*,5*R*)-5-((1*E*,4*Z*)-Deca-1,4-dienyl)-2-(4-methoxyphenyl)-1,3-dioxolan-4-yl)cyclopropyl)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (62). *p*-Toluenesulfonic acid (4 mg, 0.02 mmol) was added to a solution of *p*-anisaldehyde dimethyl acetal (25 μL, 0.14 mmol) and diol **61** (38 mg, 1.08 mmol) in anhydrous DMF (0.5 mL) at room temperature. Stirring was continued for 20 min at room temperature, whereupon saturated aqueous $NaHCO_3$ (2 mL) and Et_2O (5 mL) were added. The layers were separated, and the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (5:1) to give 40 mg (80%) of anisylidine acetal **62,** an inconsequential mixture of C(23) diastereomers, as a clear oil; ^{1}H NMR (400 MHz) δ 7.38 (dd, J = 8.4, 2.4 Hz, 2 H), 6.88 (dd, J = 8.4, 2.4 Hz, 2 H), 5.92−5.68 (comp, 4 H), 5.55−5.42 (comp, 2 H), 5.37−5.31 (comp, 1 H), 4.28 (app t, J = 7.6 Hz, 0.5 H), 4.25 (app t, J = 7.6 Hz, 0.5 H), 4.01 (dt, J = 7.6, 1.5 Hz, 0.5 H), 3.97 (dt, J = 7.6, 1.5 Hz, 0.5 H), 3.80 (s, 1.5 H), 3.79 (s, 1.5 H), 3.33 (app t, J = 7.6 Hz, 0.5 H), 3.30 (app t, J = 7.6 Hz, 0.5 H), 2.88−2.78 (comp, 3 H), 2.74−2.67 (comp, 1 H), 2.67−2.58 (comp, 1 H), 2.32−2.23 (comp, 2 H), 2.12−2.07 (comp, 1 H), 2.00 (app q, J = 7.1 Hz, 2 H), 1.36−1.23 (comp, 6 H), 1.17 (dt, J = 8.8, 4.8 Hz, 0.5 H), 1.16 (dt, J = 8.8, 4.8 Hz, 0.5 H), 1.04−0.95 (comp, 1 H), 0.87 (t, J = 6.8 Hz, 1.5 H), 0.86 (t, J = 6.8 Hz, 1.5 H), 0.74 (app dt, J = 8.6, 4.8 Hz, 1 H), 0.63 (app dt, J = 8.6, 4.8 Hz, 0.5 H), 0.58 (app dt, J = 8.6, 4.8 Hz, 0.5 H); ^{13}C (100 MHz) δ 176.8, 176.8, 160.3, 160.2, 134.8, 134.1, 132.6, 131.6, 131.6, 130.3, 130.3, 128.1, 127.9, 127.8, 126.8, 126.3, 125.9, 125.8, 113.7, 113.6, 103.3, 102.9, 84.6, 84.0, 83.3, 80.9, 80.9, 55.2, 37.7, 34.3, 34.2, 31.4, 30.0, 29.2, 27.1, 24.4, 22.5, 19.9, 18.3, 18.0, 14.0, 7.6, 7.4; IR (neat) 3009, 2929, 2855, 1746, 1614, 1516, 1248, 1213, 1077, 966 cm^{-1}; mass spectrum (CI) *m*/*z* 481, 436, 373, 345 (base), 327, 315, 315, 287. HRMS $C_{30}H_{41}O_5$ (M + 1) calcd 481.2954. found 481.2956.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((1*R*,2*R*,3*E*,6*Z*)-2-Hydroxy-1-(4-methoxybenzyloxy)dodeca-3,6-dienyl)cyclopropyl)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (63) and (*R*,*Z*)-8-((1*R*,2*R*)-2-((1*R*,2*R*,3*E*,6*Z*)-1-Hydroxy-2-(4-methoxybenzyloxy)dodeca-3,6-dienyl)cyclopropyl)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (64). Trifluoroacetic acid (14 μL, 0.19 mmol) was added to a solution of anisylidine acetal **62** (30 mg, 0.06 mmol) and $NaCNBH_3$ (39 mg, 0.62 mmol) in anhydrous THF (1 mL) at 0 °C. Stirring was continued for 15 min at 0 °C, whereupon the ice bath was removed and the reaction was warmed to room temperature. Stirring was continued for an additional 1 h at room temperature, and an aqueous solution of 1 M HCl (0.5 mL) was added. The layers were separated, and the aqueous layer extracted with Et_2O (2 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (1 mL) and brine (1 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (10:1) to give 11 mg (34%) of cyclopropyl alcohol **64** (less polar) as a pale-yellow oil and 14 mg (47%) of allylic alcohol **63** (more polar) as a pale-yellow oil and an additional 3 mg (10%) of a mixture of **63** and **64**. **For 63:** ^{1}H NMR (400 MHz) δ 7.22 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 5.81−5.69 (comp, 3 H), 5.50 (ddt, J = 15.4, 7.0, 1.5 Hz, 1 H), 5.45−5.31 (comp, 2 H), 4.68 (d, J = 11.0 Hz, 1 H), 4.45 (d, 11.0 Hz, 1 H), 4.08−4.03 (comp, 2 H), 3.78 (s, 3 H), 2.88−2.76 (comp, 4 H), 2.71 (ddd, J = 13.2, 5.6, 2.8 Hz, 1 H), 2.61 (ddd, J = 14.0, 10.0, 6.0 Hz, 1 H), 2.53 (br, 1 H), 2.31−2.23 (comp, 2 H), 2.15−2.07 (m, 1 H), 2.00 (app q, J = 7.2 Hz, 2 H), 1.33 (p, J = 7.2 Hz, 2 H), 1.29−1.23 (comp, 4 H), 1.14 (app tt, J = 8.8, 4.4 Hz, 1 H), 0.94 (app tt, J = 8.8, 4.4 Hz, 1 H), 0.86 (t, J = 7.2 Hz, 3 H), 0.67 (dt, J = 8.6, 5.2 Hz, 1 H), 0.48 (dt, J = 8.6, 5.2 Hz, 1 H); ^{13}C NMR (75 MHz) δ 176.7, 159.4, 132.8, 132.0, 131.3, 130.1, 129.4, 129.2, 128.1, 126.4, 113.9, 84.3, 80.8, 75.4, 72.3, 55.3, 37.6, 34.0, 31.5, 30.1, 29.3, 27.1, 24.4, 22.5, 20.6, 18.0, 14.0, 7.9; IR (neat) 3469, 3009, 2929, 2856, 1746, 1612, 1514, 1454, 1248, 1212, 1172, 1052, 967 cm^{-1}; mass spectrum (CI) *m*/*z* 483, 466, 448, 436, 345, 317, 299 (base), 257, 195. HRMS $C_{30}H_{43}O_5$ (M + 1) calcd 483.3110, found 483.3102. **For 64:** ^{1}H NMR (500 MHz) δ 7.21 (d, J = 8.5 Hz, 2 H), 6.86 (dt, J = 8.6,. 2.4 Hz, 2 H), 5.79−5.67 (comp, 3 H), 5.49−5.43 (m, 1 H), 5.39−5.33 (comp, 2 H), 4.54 (app d, J = 11.0 Hz, 1 H), 4.25 (app d, J = 11.0 Hz, 1 H), 3.92 (app dt, J = 9.0, 1.5 Hz, 1 H), 3.79 (s, 3 H), 3.63 (dd, J = 8.0, 7.0 Hz, 1 H), 3.00 (app t, J = 7.0 Hz, 1 H), 2.88−2.77 (comp, 3 H), 2.71 (ddd, J = 13.6, 6.0, 3.0 Hz, 1 H), 2.61 (ddd, J = 16.0, 9.0, 6.0 Hz, 1 H), 2.30−2.23 (comp, 2 H), 2.11−2.07 (m, 1 H), 2.01 (app q, J = 7.0 Hz, 2 H), 1.35 (p, J = 7.0 Hz, 2 H), 1.30−1.25 (comp, 4 H), 1.12 (app tt, J = 9.0, 5.0 Hz, 1 H), 0.82 (t, J = 7.1 Hz, 3 H), 0.82 (app tt, J = 9.0, 5.0 Hz, 1 H), 0.61 (app dt, J = 8.5, 5.0 Hz, 1 H), 0.54 (app dt, J = 8.5, 5.0 Hz, 1 H); ^{13}C NMR (125 MHz) δ 177.0, 159.3, 135.1, 132.6, 131.5, 130.2, 129.5, 128.4, 127.0, 126.2, 113.9, 83.8, 81.6, 75.9, 69.6, 55.3, 37.7, 34.3, 31.5, 30.3, 29.2, 27.1, 24.4, 22.5, 19.8, 19.5, 14.0, 8.8; IR (neat) 3540, 3010, 2927, 2856, 1745, 1612, 1513, 1454, 1248, 1212, 1052 cm^{-1}; mass spectrum (CI) *m*/*z* 483, 466, 447, 345, 299, 121 (base). HRMS $C_{30}H_{43}O_5$ (M + 1) calcd 483.3110, found 483.3102.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((1*S*,2*E*,4*S*,6*Z*)-4-Hydroxy-1-(4-methoxybenzyloxy)dodeca-2,6-dienyl)cyclopropyl)-3,4,7,8-tetrahydro-2*H*-oxocin-2-one (65). Tributylphosphine (28 μL, 0.11 mmol) was added dropwise to a solution of **63** (9 mg, 0.02 mmol) and *o*-NO_2-PhSeCN (13 mg, 0.06 mmol) at room temperature. The reaction turned from a pale yellow to dark brown. Stirring was continued for 1 h at room temperature, whereupon the reaction was concentrated under reduced pressure and filtered through a short plug of silica gel eluting with hexanes/EtOAc (5:1). The eluted material was concentrated under reduced pressure. Pyridine (50 μL) and 30% H_2O_2 (0.5 mL) were added to a solution of the crude mixture

in CH_2Cl_2 (1 mL) at room temperature, and the solution was stirred for 3 h whereupon 1 M HCl (0.5 mL) was added. The layers were separated, and the organic layer was washed with saturated aqueous $NaHCO_3$ (0.5 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (5:1) to give 5 mg (56%) of allylic alcohol **65** as a pale-yellow oil. ^{1}H NMR (400 MHz) δ 7.20 (d, J = 8.8 Hz, 2 H), 6.85 (d, J = 8.8 Hz, 2 H), 5.80−5.40 (comp, 5 H), 5.40−5.33 (m, 1 H), 4.49 (d, J = 11.8 Hz, 1 H), 4.28 (d, J = 11.8 Hz, 1 H), 4.20 (app q, J = 6.4 Hz, 1 H), 3.94 (ddd, J = 10.0, 8.4, 1.6 Hz, 1 H), 3.79 (s, 3 H), 3.28 (app t, J = 6.4 Hz, 1 H), 2.84 (dtd, J = 12.0, 8.8, 6.0 Hz, 1 H), 2.70 (ddd, J = 13.2, 5.6, 3.2 Hz, 1 H), 2.63 (ddd, J = 13.6, 10.0, 5.4 Hz, 1 H), 2.39−2.24 (comp, 4 H), 2.15−2.08 (m, 1 H), 2.04 (app q, J = 7.1 Hz, 2 H), 1.66 (br, 1 H), 1.34 (p, J = 7.1 Hz, 2 H), 1.31−1.23 (comp, 4 H), 1.07−0.95 (comp, 2 H), 0.86 (t, J = 7.1 Hz, 3 H), 0.66 (dt, J = 8.6, 5.2 Hz, 1 H), 0.54 (dt, J = 8.6, 5.2 Hz, 1 H); ^{13}C NMR (75 MHz) δ 177.0, 159.1, 135.1, 133.9, 132.7, 130.6, 130.0, 129.1, 128.3, 124.1, 113.7, 81.4, 80.5, 71.6, 69.6, 55.3, 37.7, 35.4, 34.3, 31.5, 29.3, 27.4, 24.4, 22.5, 22.1, 21.0, 14.0, 8.0; IR (neat) 3447, 3011, 2928, 2856, 1745, 1612, 1513, 1247, 1051 cm^{-1}; mass spectrum (CI) m/z 483, 465, 436, 365, 345 (base), 327, 283, 219. HRMS $C_{30}H_{43}O_5$ (M + 1) calcd 483.3110, found 483.3112.

Solandelactone E (3). Procedure A. Tributylphosphine (35 μL, 0.138 mmol) was added dropwise over 0.5 min to a solution of diol **61** (10 mg, 0.028 mmol) and 2-nitrophenyl selenocyanate (31 mg, 0.138 mmol) in anhydrous THF (0.28 mL) at room temperature. The mixture was stirred for 1 h at room temperature, whereupon the mixture was concentrated under reduced pressure and filtered through a short plug of silica gel eluting with hexanes/EtOAc (5:1). The filtrate was concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 (1 mL) at 0 °C, whereupon pyridine (0.05 mL) and a 30% aqueous solution of H_2O_2 (1 mL) were added. The solution was stirred for 5 h at 0 °C, whereupon 1 M aqueous HCl (0.5 mL) was added. The layers were separated, and the organic layer was washed with saturated aqueous $NaHCO_3$ (0.5 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (2:1) to give 2 mg (20% over 2 steps from **61**) of solandelactone E (**1**) as a clear oil. **Procedure B.** 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (12 mg, 0.05 mmol) was added to a solution of **65** (5 mg, 0.01 mmol) in CH_2Cl_2 (0.5 mL) and a pH 7 phosphate buffer (0.1 mL) at room temperature. Stirring was continued for 1 h at room temperature, whereupon the reaction was washed with H_2O (0.2 mL) and saturated aqueous $NaHCO_3$ (0.2 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with pentanes/Et_2O (1:1) to provide 2.5 mg (71%) of solandelactone E (**3**) as a clear oil; ^{1}H NMR (500 MHz) δ 5.84−5.70 (comp, 4 H), 5.57 (dtt, J = 11.0, 7.4, 1.5, 1 H), 5.36 (dtt, J = 11.0, 7.0, 1.8 Hz, 1 H), 4.17 (br ddd, J = 7.0, 5.5, 0.0 Hz, 1 H), 4.02 (ddd, J = 10.0, 8.0, 1.5 Hz, 1 H), 3.65 (dd, J = 7.5, 4.5 Hz, 1 H), 2.88−2.80 (m, 1 H), 2.71 (ddd, 13.5, 6.0, 3.0 Hz, 1 H), 2.61 (ddd, J = 14.0, 10.4, 5.6 Hz, 1 H), 2.32−2.25 (comp, 3 H), 2.24 (ddd, J = 14.0, 7.5, 1.5 Hz, 1 H), 2.13−2.08 (m, 2 H), 2.03 (app q, J = 7.1 Hz, 2 H), 1.52 (br, 1 H), 1.37−1.24 (comp, 6 H), 1.12 (tt, J = 8.5, 5.5 Hz, 1 H), 0.99 (dtd, J = 8.5, 8.5, 5.0 Hz, 1 H), 0.87 (t, J = 7.1 Hz, 3 H), 0.72 (dt, J = 9.0, 5.0 Hz, 1 H), 0.59 (dt, J = 8.5, 5.0 Hz, 1 H); ^{13}C NMR (125 MHz) δ 176.9, 134.0, 133.2, 132.8, 131.7, 128.1, 124.0, 80.9, 74.4, 71.4, 37.7, 35.3, 34.2, 31.5, 29.3, 27.4, 24.4, 23.4, 22.5, 20.6, 14.0, 8.0.

Acknowledgment. We thank the National Institutes of Health (GM 31077), the Robert A. Welch Foundation, Pfizer, Inc., and Merck Research Laboratories for generous support of this research. We are also grateful to Prof. Jongheon Shin (College of Pharmacy, Seoul National University) for providing spectral data for solandelactones E and F and for helping to clarify the origin of the structural misassignment for the C(11) epimeric solandelactones. We also thank Justin Leong for his help in synthesizing various key intermediates.

Supporting Information Available: Summary of general experimental practices, experimental procedures, and spectral characterization for compounds **16**, **18**, **19**−**22**, **24**−**27**, **34**−**36**, **39**, **40**, **42**−**46**, **52**, **54**, and **59**, copies of ^{1}H NMR spectra for all new compounds, a tabular comparison of ^{1}H and ^{13}C NMR data for synthetic and natural **1**, and crystallographic data CIF file for **36**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO701739V