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Total Synthesis of Solandelactones A, B, E, and F Exploiting a Tandem Petasis−Claisen Lactonization Strategy

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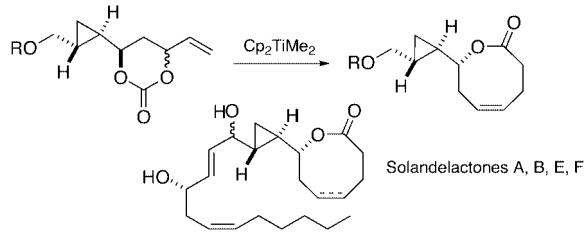

Solandelactones A, B, E, and F were synthesized using Nozaki−Hiyama−Kishi coupling of iododiene **13** with aldehydes **14** and **99** obtained by oxidation of alcohols **92** and **94**. Key steps in the synthesis of **92** and **94** were (i) a Nagao asymmetric acetate aldol reaction of aldehyde **77** with thionothiazolidine **78** to set in place an alcohol that becomes the (7*S*) lactone center of solandelactones, (ii) a Simmons−Smith cyclopropanation of **80** directed by this alcohol, and (iii) Petasis methylenation of cyclic carbonate **90** in tandem with a Claisen rearrangement that generates the octenalactone portion of solandelactones. Synthesis of solandelactones A, B, E, and F confirmed their gross structure and absolute configuration at C7, 8, 10, and 14 but showed that alcohol configuration at C11 must be reversed in pairs, A/B and E/F, from the previous assignment made to these hydroid metabolites. Thus, solandelactones A and B are correctly represented by **2** and **1**, respectively, whereas solandelactones E and F are **6** and **5**. A biogenesis of solandelactones is proposed for these C_{22} oxylipins that parallels a hypothesis put forward previously to explain the origin of C_{20} cyclopropane-containing algal products.

Introduction

The growing interest attached to substances present in marine invertebrates and algae has led to discovery of a large number of new compounds and even to several unique structural classes from the marine environment.[1] However, the chemistry of hydroids (class Hydrazoa) remains largely unexplored, and aside from a few common steroids, phospholipids, aromatic polypeptides, and β-carbolines, little is known of the chemical constituents of this family of organisms.[2] In 1996, Shin and coworkers reported the isolation of eight new substances, which he named solandelactones A−H, from the hydroid *Solanderia secunda* found near the island of Jaeju in Korea.[3] Structures **1**−**8** (Figure 1) were assigned to these metabolites primarily on the basis of detailed NMR analysis.

Solandelactones belong to the family of marine metabolites known as oxylipins, a group that includes constanolactones A (**9**) and B (**10**),[4] halicholactone (**11**)[5] and neohalicholactone (**12**) (Figure 2).[5] The eicosanoid oxylipins are believed to have their origin in the C_{20} progenitor arachidonic acid; biosynthetic pathways have been put forward that account for structural variations within the class.[4b,6] Solandelactones, as C_{22} metabolites, present an immediate anomaly, however. There is also a curious configurational divergence within the solandelactone, constanolactone and halicholactone families that remains unexplained. Thus, the disubstituted cyclopropane of solandelactones has the same absolute configuration as that of halicholactone (**11**) and neohalicholactone (**12**)[7] but reversed configuration when compared with the corresponding cyclopropane carbons in constanolactones A (**9**) and B (**10**). On the other hand, the

(1) Wessjohann, L. A.; Brandt, W. *Chem. Rev.* **2003**, *103*, 1625.
(2) (a) Fahy, E.; Andersen, R. J.; He, C.-H.; Clardy, J. *J. Org. Chem.* **1985**, *50*, 1149. (b) Aiello, A.; Fattorusso, E.; Magno, S.; Mayol, L. *Tetrahedron* **1987**, *43*, 5929. (c) Faulkner, D. J. *Nat. Prod. Rep.* **1995**, *12*, 223. and references cited therein.
(3) Seo, Y.; Cho, K. W.; Rho, J.-R.; Shin, J.; Kwon, B.-M.; Bok, S,-H.; Song, J.-I. *Tetrahedron* **1996**, *52*, 10583.
(4) (a) Nagle, D. G.; Gerwick, W. H. *Tetrahedron Lett.* **1990**, *31*, 2995. (b) Nagle, D. G.; Gerwick, W. H. *J. Org. Chem.* **1994**, *59*, 7227.
(5) Niwa, H.; Wakamatsu, K.; Yamada, K. *Tetrahedron Lett.* **1989**, *30*, 4543.
(6) Brash, A. R. *J. Am. Chem. Soc.* **1989**, *111*, 1891.
(7) Kigoshi, H.; Niwa, H.; Yamada, K.; Stout, T. J.; Clardy, J. *Tetrahedron Lett.* 199132, 2427.

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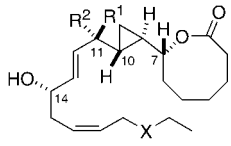
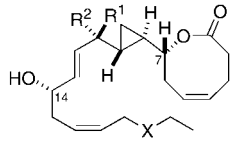


Solandelactones A-D

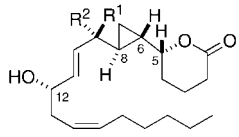
1, **A**, R^1 = OH, R^2 = H, X = CH_2CH_2
2, **B**, R^1 = H, R^2 = OH, X = CH_2CH_2
3, **C**, R^1 = OH, R^2 = H, X = *cis* CH=CH
4, **D**, R^1 = H, R^2 = OH, X = *cis* CH=CH



Solandelactones E-H

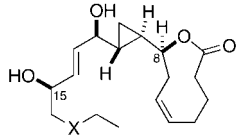
5, **E**, R^1 = OH, R^2 = H, X = CH_2CH_2
6, **F**, R^1 = H, R^2 = OH, X = CH_2CH_2
7, **G**, R^1 = OH, R^2 = H, X = *cis* CH=CH
8, **H**, R^1 = H, R^2 = OH, X = *cis* CH=CH

FIGURE 1. Shin's structural assignments to solandelactones A−H.



Constanolactones A and B

9, **A**, R^1 = H, R^2 = OH
10, **B**, R^1 = OH, R^2 = H



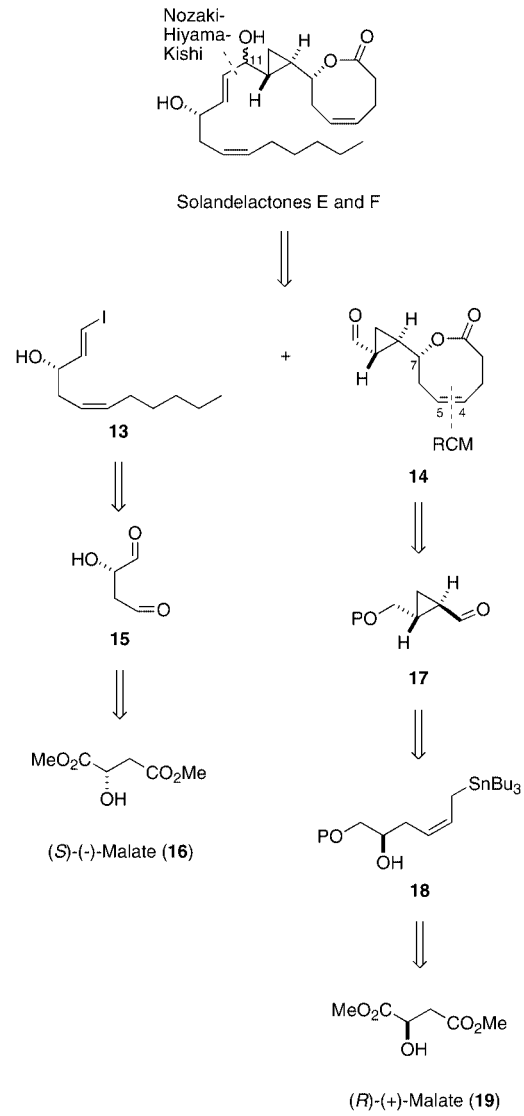
11, **Halicholactone**, X = CH_2CH_2
12, **Neohalicholactone**, X = *cis* CH=CH

FIGURE 2. Cyclopropane-containing C_{20} oxylipins.

lactonized C7 oxygen and the C14 alcohol of solandelactones correspond stereochemically to C5 and C12 in constanolactones but are reversed in configuration from the analogous centers, C8 and C15, in **11** and **12**.

The absolute configuration of constanolactones A and B was assigned unambiguously as (5*R*,6*S*,8*S*,12*S*) through total synthesis, epimers A and B being given (9*S*) and (9*R*) designation, respectively.[8] Likewise, the absolute configuration of halicholactone and neohalicholactone has been confirmed by synthesis.[9] The structural assignments made to solandelactones by Shin and shown in Figure 1 placed heavy reliance on data that included NOE correlation between protons at C10 and C11.[3] A conformation about the C10−C11 bond was assumed on the basis of NMR analysis that predicted (11*R*) configuration for the series A, C, E, and G and reversed (11*S*) configuration for solandelactones B, D, F, and H. These assignments, when taken with the absence of stereochemical congruence among the structural families represented in Figures 1 and 2, lent impetus to a synthetic plan for solandelactones that would unambiguously establish their stereochemistry. While our work was in progress, a publication by Davoren and Martin appeared describing asymmetric synthesis of **6**,[10] that is, the structure assigned by Shin to solandelactone F. However, NMR data for Martin's synthetic compound matched those of the epimer solandelactone E, implying that C11 configuration of the E/F pair should be reversed.

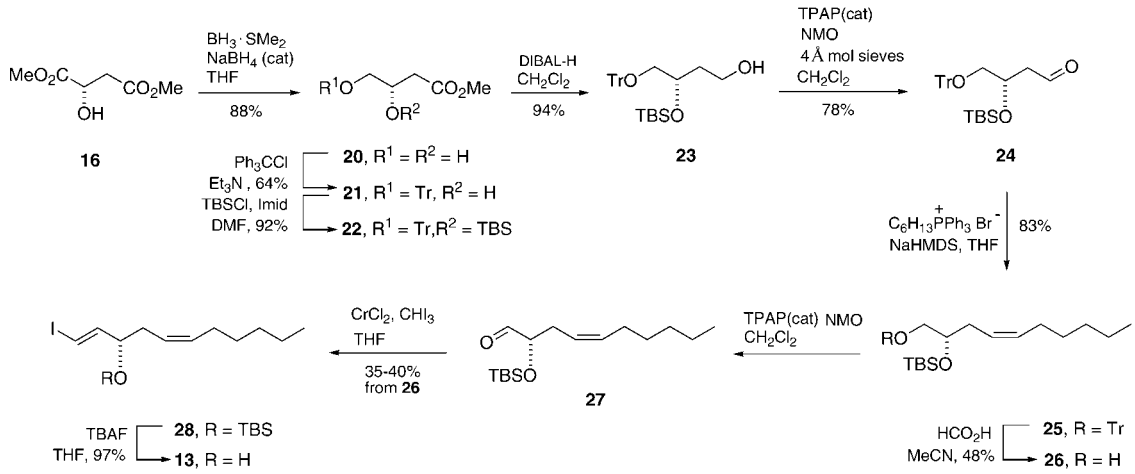
SCHEME 1



Our initial goal was synthesis of solandelactone E and F having unsaturation in the eight-membered lactone, anticipating that the saturated lactones A and B would become accessible through reduction. This led to a strategy for synthesis of solandelactones E and F shown in Scheme 1.[11] The final step in this plan is a Nozaki−Hiyama−Kishi coupling of iodoalkene **13** with aldehyde **14**, for which the anticipated stereochemical outcome with respect to the C11 center in solandelactones was addressed in our synthesis of constanolactones A and B.[8] Based on that analogy, the Felkin product having (11*S*) configuration corresponding to **5**, the structure assigned by Shin to solandelactone E, was expected to be the major stereoisomer.

(8) (a) White, J. D.; Jensen, M. S. *J. Am. Chem. Soc.* **1993**, *115*, 2970. (b) White, J. D.; Jensen, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 6224.
(9) (a) Critcher, D. J.; Connolly, S.; Wills, M. *Tetrahedron Lett.* **1995**, *36*, 3763. (b) Critcher, D. J.; Connolly, S.; Wills, M. *J. Org. Chem.* **1997**, *62*, 6638.
(10) (a) Davoren, J. E.; Martin, S. F. *J. Am. Chem. Soc.* **2007**, *129*, 510. (b) Davoren, J. E.; Harcken, C.; Martin, S. F. *J. Org. Chem.* **2008**, *73*, 391.
(11) White, J. D.; Martin, W. H. C.; Lincoln, C. M.; Yang, J. *Org. Lett.* **2007**, *9*, 3481.

SCHEME 2



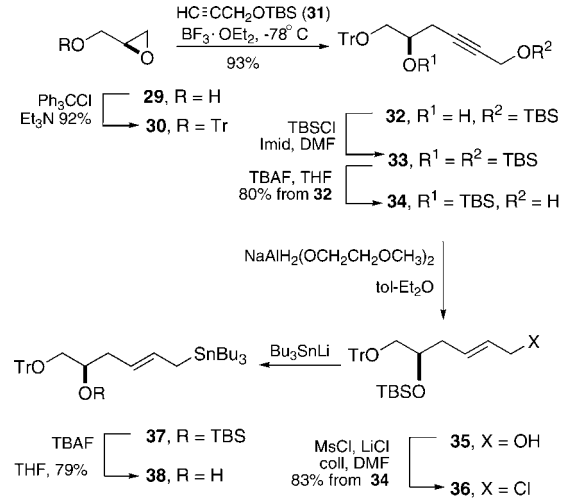
Construction of (*E,Z*)-iododiene **13** was foreseen from a 1,4-dicarbonyl synthon **15** whose single stereogenic center originates in (*S*)-(−)-malate ester **16**. The first option considered for assembling the $\Delta^{4,5}$-octenalactone portion **14**[12] recognized the possibility of a ring-closing metathesis, but this strategy was subsequently abandoned in favor of an approach based upon Claisen rearrangement. Installation of the key C7 stereogenic center in **14** would take place by a stereocontrolled addition to aldehyde **17**. The cyclopropane moiety **17** was initially envisioned as the product of a previously disclosed tin-assisted elimination of the triflate from alcohol **18**.[13] The latter is available from (*R*)-(−)-malate **19**, a design feature that enables construction of the two halves of solandelactones from antipodal starting materials.

Results and Discussion

Synthesis of Iododiene 13. Our previous synthesis of **13** employed an eleven-step sequence commencing from D-arabinose, expunging two of the three stereogenic centers of the pentose en route.[8] This was clearly unsatisfactory as a multigram preparation of **13**. We therefore implemented a new route to **13** and selected dimethyl (*S*)-malate (**16**) as the point of departure. Our intention was to preserve the configuration of **16** as surrogate for the C14 alcohol of the solandelactones while building outward from the pair of methyl esters toward the hexyl and (*E*)-iodoalkene termini, respectively (Scheme 2).

Diester **16** was first reduced, as previously described,[14] to diol **20**. Selective tritylation of the primary alcohol furnished **21** which was further protected as its TBS ether **22**. Reduction of this ester to an aldehyde with diisobutylaluminum hydride was inefficient, and it was found more practical to take **22** to alcohol **23** and then oxidize this substance with catalytic Ley's reagent[15] to aldehyde **24**. The latter proved to be unstable and was promptly subjected to Wittig olefination with the ylide from *n*-hexytriphenylphosphonium bromide. The resulting (*Z*)-alkene **25** was deprotected under conditions which removed only the trityl residue,[16] and alcohol **26** was then oxidized to aldehyde **27**. This aldehyde was also unstable and was immediately treated with chromous chloride and iodoform under Takai-Utimoto conditions.[17] Yields of **28** from this reaction were found to depend on the scale as well as the provenance of reactants, but a reliable 35−40% could be obtained from the two-step sequence from alcohol **26**.[18] The need for TBS protection of **28** in the projected Nozaki−Hiyama−Kishi union with **14** was uncertain at this point, and as a cautionary move we unmasked only a portion of **28** to afford **13**.

SCHEME 3



Synthesis of Lactone 14. First Generation Approach. A strategic issue to be considered in an approach to **14** was the sequence in which the cyclopropane and lactone rings should be assembled. A plan in which the $\Delta^{4,5}$-octenalactone portion of **14** would be fabricated using a late-stage ring-closing metathesis, taken with the assumption that C7 configuration could be installed through a stereocontrolled aldol-type reaction of cyclopropanecarboxaldehyde **17**, persuaded us that the cyclopropane should be elaborated before the lactone.

Two routes to cyclopropane **17** were explored, the first of which employed (*S*)-(−)-glycidol (**29**) as the source of chirality

(12) For an earlier approach to the synthesis of this portion of solandelactones, see: (a) Varadarajan, S.; Mohapatra, D. K.; Datta, A. *Tetrahedron Lett.* **1998**, *39*, 1075. (b) Mohapatra, D. K.; Yelleo, G. S. *ARKIVOC* **2003**, 21.

(13) Lincoln, C. M.; White, J. D.; Yokochi, A. F. T. *Chem. Commun.* **2004**, 2846.

(14) Saito, S.; Hasegawa, T.; Inaba, M.; Nishida, R.; Fujii, T.; Nomizu, S.; Moriwake, T. *Chem. Lett.* **1984**, 1389.

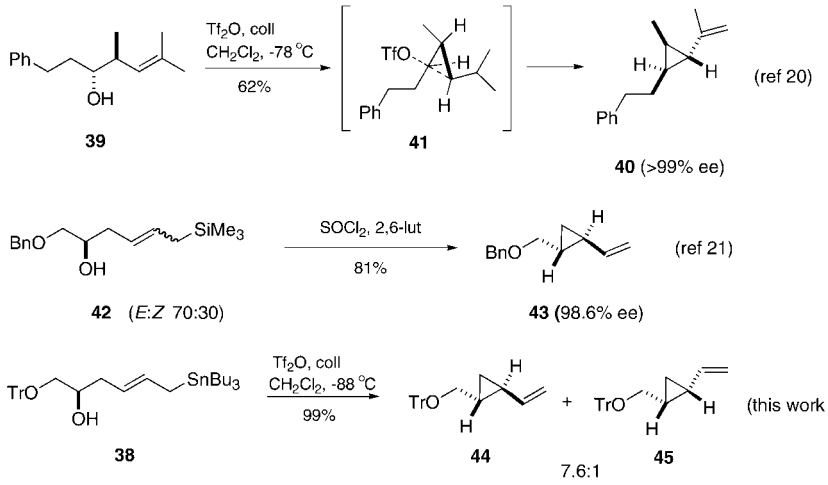
(15) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.

(16) Bessodes, M.; Komiotis, D.; Antonakis, K. *Tetrahedron Lett.* **1986**, *27*, 579.

(17) Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.

(18) For other routes to **13**, see: (a) Da Silva, C. B.; Pale, P *Tetrahedron: Asymmetry* **1998**, *9*, 3951. (b) Pietruszka, J.; Wilhelm, T. *Synlett* **2003**, 1698.

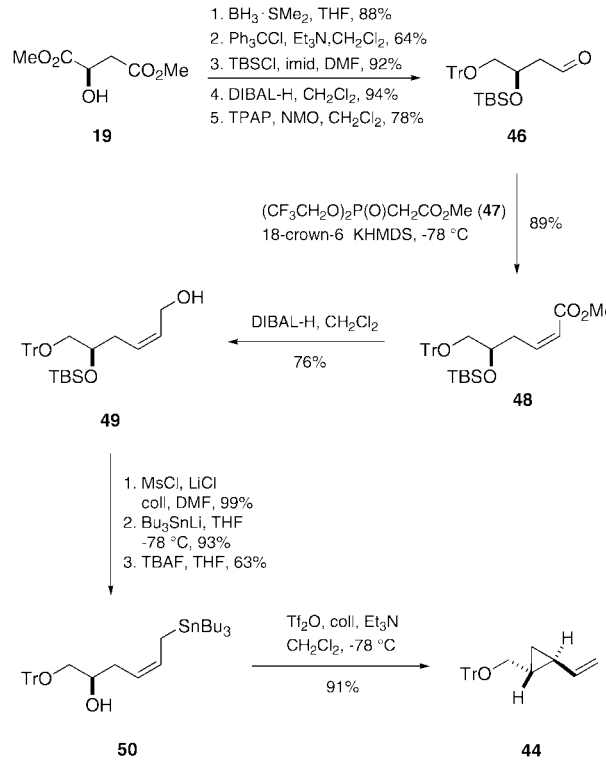
SCHEME 4



(Scheme 3). After protection of **29** as its trityl ether **30**, the epoxide was opened with the lithio alkyne prepared from propargyl ether **31**. Hexynol **32** was converted to bis TBS ether **33,** from which the primary silyl ether was selectively cleaved to yield **34**. Reduction of alkynol **34** with Red-Al cleanly afforded (*E*)-allylic alcohol **35** which was advanced to chloride **36**. Exposure of **36** to lithio tri-*n*-butylstannane[19] led to **37** from which the silyl ether was cleaved to furnish enantiopure homoallylic alcohol **38**.

Suzuki showed that the triflate of homoallylic alcohol **39**, when exposed to a base, underwent elimination to give cyclopropane **40** in very high enantiomeric excess (Scheme 4).[20] A mechanism was proposed in which displacement of triflate occurs with inversion via transition state **41** that orients phenethyl and propenyl substituents in a 1,3-anti relationship. Taylor later extended Suzuki's observation by attaching a silylmethylene unit at the alkene terminus.[21] He found that an *E*,*Z* mixture of **42** gave trans disubstituted cyclopropane **43** with excellent stereoselectivity. Our belief that a carbocation stabilized through stannyl participation in the elimination of the triflate from **38** would also lead efficiently to a cyclopropane was upheld when we subjected **38** to conditions essentially identical to those employed by Suzuki on **39**. The result was a quantitative yield of trans and cis cyclopropanes **44** and **45** in the ratio 7.6:1, respectively. Both **44** and **45** were enantiomerically pure as determined by chiral HPLC. The major cyclopropane **44** is believed to result from elimination of triflate in a 1,3-anti conformation analogous to the transition state **41** proposed by Suzuki.[20] Formation of the minor cis disubstituted cyclopropane **45** from **38** presumably occurs through a transition state that places the alkene and trityl ether in a 1,3-syn orientation, and although this should be less favorable for steric reasons than the 1,3-anti conformation analogous to **41,** the spacial interaction of substituents is not sufficiently large to guide **38** uniquely toward **44**. This suggested that a modified version of **38**, in which the trans double bond was replaced by a cis alkene, would create a larger steric impediment to the pathway proceeding via a 1,3-syn transition state because stannyl and trityl groups would now be in closer proximity. Formation of **44** relative to **45** should therefore be enhanced.

SCHEME 5



An attractive feature of the new route shown in Scheme 5 was that it could begin from the enantiomer of the starting material used to prepare **13**, namely dimethyl (*R*)-(+)-malate (**19**). The latter was taken forward to aldehyde **46**, which was subjected to Gennari−Still condensation[22] with phosphonate **47** to give (*Z*) unsaturated ester **48**. The latter was reduced to allylic alcohol **49** and the alcohol was converted to the corresponding chloride. Displacement of this chloride with lithium tri-*n*-butylstannane[19] produced the (*Z*) allylstannane from which the TBS group was removed to yield (*R*) alcohol **50**. Exposure of **50** to triflic anhydride under the identical conditions used with **38** furnished **44** in excellent yield as the sole detectable product

(19) Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237.
(20) (a) Nagasawa, T.; Handa, Y.; Onoguchi, Y.; Ohba, S.; Suzuki, K. *Synlett* **1995**, 739. (b) Nagasawa, T.; Handa, Y.; Onoguchi, Y.; Suzuki, K. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 31.
(21) Taylor, R. E.; Engelhardt, F. C.; Schmitt, M. J.; Yuan, H. *J. Am. Chem. Soc.* **2001**, *123*, 2964.
(22) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.

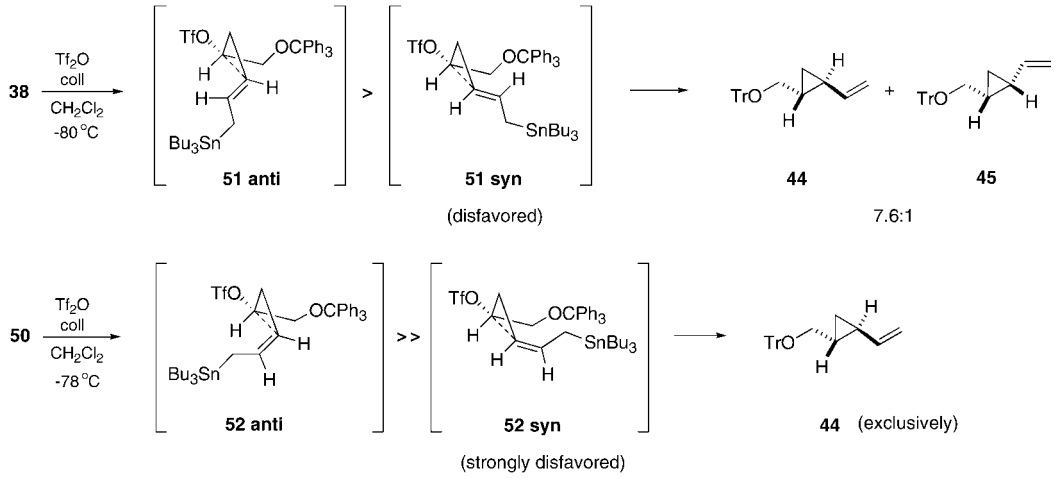
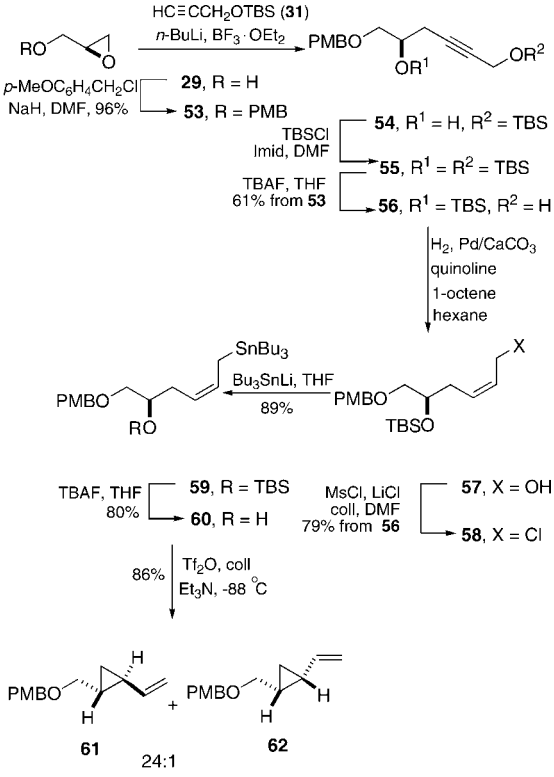
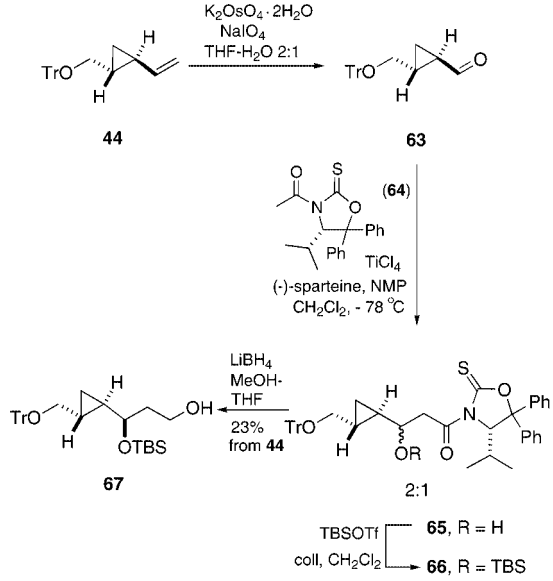


FIGURE 3. Transition states for elimination of triflates from **38** and **50**.

SCHEME 6



SCHEME 7



using an assay in which the detection limit was 36:1. Characterization of **44** by chiral stationary phase HPLC demonstrated that this substance was enantiopure. Thus, results obtained with **38** and **50** are consistent with a prediction based on steric effects operative in the transition states involved in triflate elimination (Figure 3). Transition states **51 anti** and **52 anti**, analogous to Suzuki's **41**, are clearly more favorable than their 1,3-syn counterparts, and **52 syn** is more highly strained than **51 syn** as a result of cis alkene geometry in the former.

The preference for a 1,3-anti conformation over its 1,3-syn counterpart in steering elimination of triflate toward a trans disubstituted cyclopropane was further supported by a sequence shown in Scheme 6 in which the trityl ether of **50** was replaced by a *p*-methoxybenzyl ether. Ether **53**, prepared from (*S*)-(−)-glycidol (**29**), was advanced as in Scheme 3 to alkyne **54** and then, via triether **55**, to alcohol **56**. Semihydrogenation of **56** afforded cis allylic alcohol **57** which was converted to chloride **58**. Displacement with lithio tri-*n*-butylstannane gave allylstannane **59** from which the TBS ether was cleaved to yield **60**. Exposure of alcohol **60** to triflic anhydride in collidine-triethylamine under the conditions used with **50** produced trans and cis cyclopropanes **61** and **62** in the ratio 24:1. Here again, a 1,3-anti transition state is highly favored over its syn counterpart but a slightly diminished steric demand by the *p*-methoxybenzyl group relative to trityl leads to a less decisive outcome in favor of trans disubstituted cyclopropane **61**.

The efficient preparation of enantiopure cyclopropane **44** allowed us to advance this substance along lines programmed in Scheme 1 toward lactone **14** via aldehyde **17**. Oxidative cleavage of the vinyl substituent of **44** was accomplished in good yield with potassium osmate and sodium periodate (Scheme 7), but the resulting aldehyde **63** was unstable and resisted full characterization. For that reason, **63** was immediately subjected to an acetate aldol reaction with Phillips' *N*-acetyloxazolidinethione **64**[23] under conditions specified by Crimmins,[24] our intention being to acquire (*R*) alcohol **65**. In the event, a stereoisomeric mixture of hydroxy amides was

(23) Guz, N. R.; Phillips, A. J. *Org. Lett.* **2002**, *4*, 2253.

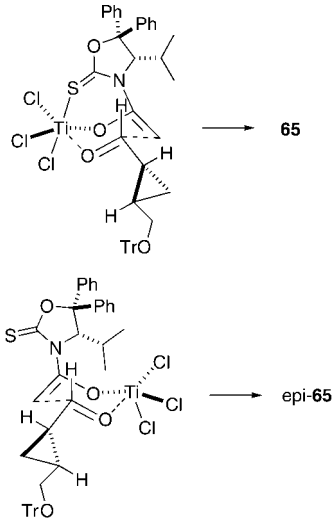


FIGURE 4. Coordinated and noncoordinated dipole-minimized transition states for the reaction of **63** with **64** leading to **65** and its epimer.

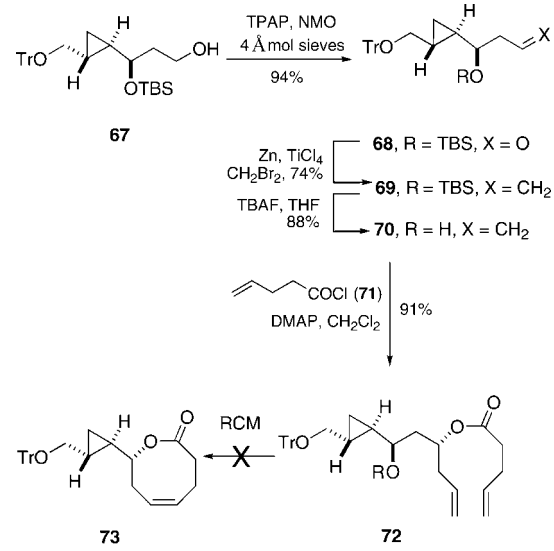
obtained from this reaction in which the desired (*R*) isomer **65** predominated over its epimer by only a ratio of 2:1. The isomers could not be separated but, after silylation to afford **66**, reductive cleavage of the chiral auxiliary produced **67** which could be obtained in pure form by chromatography.

The relatively poor stereoselectivity observed in the reaction of aldehyde **63** with the enolate of **64** is surprising in light of results reported by Phillips.[23] Our supposition that **63** would react in a bisected conformation via the chair transition state shown in Figure 4 appears to be only partially correct. Thus, although titanium−sulfur coordination would lead to *si* face attack at the aldehyde by the enolate of **64** and to a transition state that produces **65**, one or more competing pathways such as a noncoordinated dipole-minimized chair assemblage must intervene. The latter would result in *re* face attack at aldehyde **63** and leads to epi-**65**.

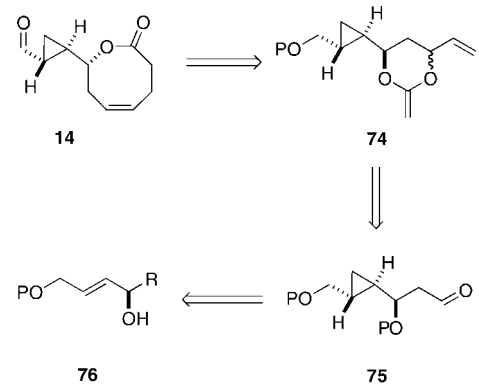
The way forward from **67** to $\Delta^{4,5}$-octenalactone **14** was predicated upon elaborating both the primary alcohol and the secondary silyl ether while retaining the primary trityl ether. To this end, **67** was oxidized to aldehyde **68** which was treated with Lombardo's reagent to give alkene **69** (Scheme 8). Removal of silyl protection from **69** and acylation of the resulting homoallylic alcohol **70** with 4-pentenoyl chloride (**71**) furnished ester **72**, our prospective substrate for ring-closing metathesis. Unfortunately, no hint of lactone formation could be discerned from more than a dozen experiments that exposed **72** to metathesis catalysts under a variety of conditions.[25] In most instances, oligomers were produced from intermolecular reactions at each of the terminal alkenes.

Our failure to close diene **72** to eight-membered lactone **73**, together with poor stereoselectivity in the acetate aldol reaction of **63** with **64**, caused us to revise our strategy for obtaining **14**. It was decided that a revised plan should install a hydroxyl group corresponding to (7*R*) configuration of the solandelactones as early as possible, ideally before construction of the cyclopropane moiety. Foregoing results also persuaded us to devise

SCHEME 8



SCHEME 9



a route to the octenalactone that did not hinge upon ring-closing metathesis. These two paradigms were our guides in planning a new pathway to **14**.

Synthesis of Lactone 14. Second Generation Approach. The key features of the new route to **14** are expressed in Scheme 9. The $\Delta^{4,5}$-octenalactone segment of **14** is projected as the rearrangement product of cyclic ketene acetal **74**, while cyclopropane **75** is the result of a directed Simmons-Smith reaction on allylic alcohol **76**. Petrzilka was the first to demonstrate, in his elegant synthesis of phoracantholide J, that thermal rearrangement of a vinyl substituted cyclic ketene acetal can lead to an unsaturated medium ring lactone, [26] and Holmes subsequently extended this variant of the Claisen rearrangement to a $\Delta^{4,5}$-octenalactone in his synthesis of laurencin.[27] More recently, the same tactic has appeared in a synthesis of discodermolide by Paterson.[28] A noteworthy difference between the plan shown in Scheme 9 and our first generation approach to **14** is early introduction of the (7*R*) oxygen function of solandelactones via an acetate aldol reaction on an *achiral* substrate, thus removing the possibility of a mismatched coupling.

(24) (a) Crimmins, M. T.; King, B. W.; Tabet, E. A. *J. Am. Chem. Soc.* **1997**, *119*, 7883. (b) Crimmins, M. T.; King, B. W.; Tabet, E. A.; Chaudhary, K. *J. Org. Chem.* **2001**, *66*, 894.

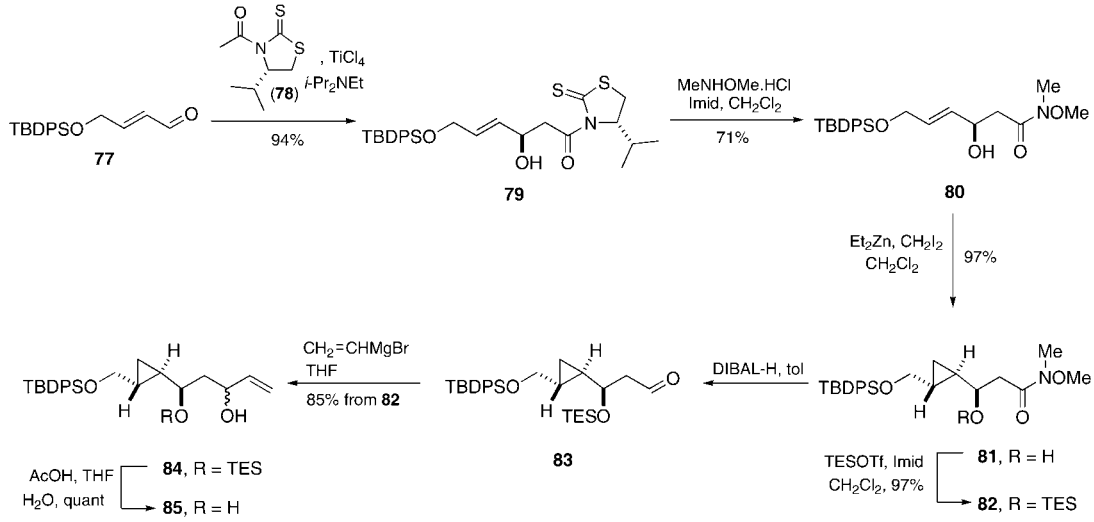
(25) A possible explanation for this failure lies in the barrier, estimated to be 7.9 kcal/mol by a Hartree−Fock/6-31G** calculation, for conversion of the more stables trans ester conformation to *s*-cis conformation **72** required for RCM.

(26) (a) Petrzilka, M. *Helv. Chim. Acta* **1978**, *61*, 3075. (b) Baudat, R.; Petrzilka, M. *Helv. Chim. Acta* **1979**, *62*, 1406.

(27) (a) Robinson, R. A.; Clark, J. S.; Holmes, A. B. *J. Am. Chem. Soc.* **1993**, *115*, 10400. (b) Burton, J. W.; Clark, J. S.; Derrer, S.; Stork, T. C.; Bendall, J. G.; Holmes, A. B. *J. Am. Chem. Soc.* **1997**, *119*, 7483.

(28) Paterson, I.; Florence, G. J.; Gerlach, K.; Scott, J. P.; Sereinig, N. *J. Am. Chem. Soc.* **2001**, *123*, 9535.

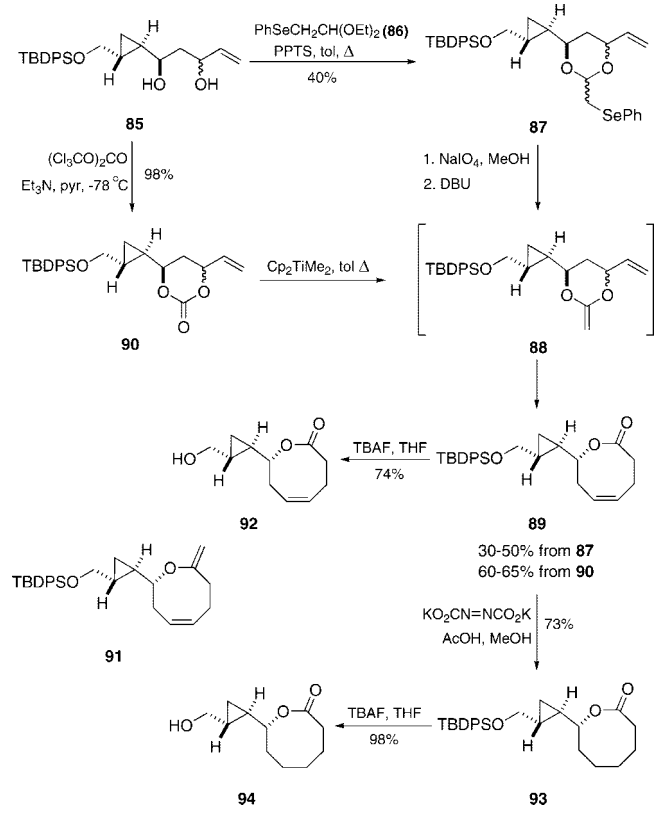
SCHEME 10



Trans-α,*β*-unsaturated aldehyde **77**, obtained from *cis*-2-butene-1,4-diol, [29] was reacted with the titanium enolate of Nagao's (4*S*)-3-acetyl-4-isopropyl-2-thionothiazolidine (**78**)[30] to give (*R*) hydroxy amide **79** as a single diastereomer in excellent yield (Scheme 10). The thiazolidine auxiliary was cleaved from **79** with *N*,*O*-dimethylhydroxylamine and the resulting Weinreb amide **80** was treated with diiodomethane and diethylzinc. This variant of the directed Simmons-Smith reaction due to Charette[31] afforded cyclopropane **81** as the sole detectable isomer. To prevent retro aldol fission of **81**, the alcohol was masked as its TES ether **82** before reduction of the amide function. The unstable aldehyde **83** from reduction of **82** was reacted promptly with vinylmagnesium bromide to give allylic alcohol **84** as an inseparable 1:1 mixture of diastereomers, and removal of TES protection from **84** produced stereoisomeric diols **85**. Because the configuration of the allylic hydroxyl group in **85** was likely to be inconsequential to the lactone construction envisioned in Scheme 9, the mixture of stereoisomers was carried forward without separation.

Our initial approach to ketene acetal **74** from diol **85** took its cue from Holmes' work[27] and employed acid-catalyzed condensation of the diol with α-phenylselenoacetaldehyde diethyl acetal (**86**)[32] (Scheme 11). Subsequent elimination of the selenoxide from oxidation of **87** and in situ exposure of ketene acetal **88** to hot xylene produced lactone **89**. In practical terms, however, access to **89** by this pathway was problematic due to the sensitivity of cyclopropylcarbinol **85** as well as acetal **87** to PPTS. A more reliable synthesis of lactone **89** was achieved via cyclic carbonate **90** along lines described by Holmes.[33] Treatment of **90**, prepared from **85** with triphosgene, with a toluene solution of Petasis reagent[34] at 110 °C resulted in methylenation of the carbonate followed by in situ rearrangement of **88** to give **89** in a reproducible yield of 60−65%. The only significant byproduct (ca. 10%) from this sequence was

SCHEME 11

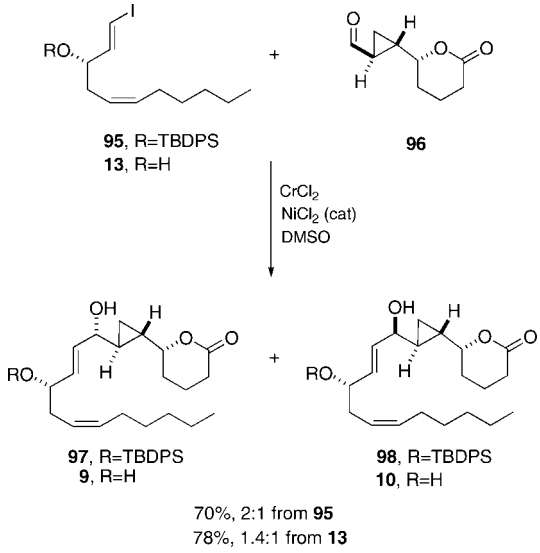


enol ether **91** resulting from methylenation of lactone **89** with residual Petasis reagent. Removal of silyl protection from **89** gave alcohol **92** but aldehyde **14** from oxidation of **92** proved to be a sensitive compound that could not be fully characterized without decomposition. It was therefore prepared as needed and used in situ for subsequent coupling with iododiene **13**.

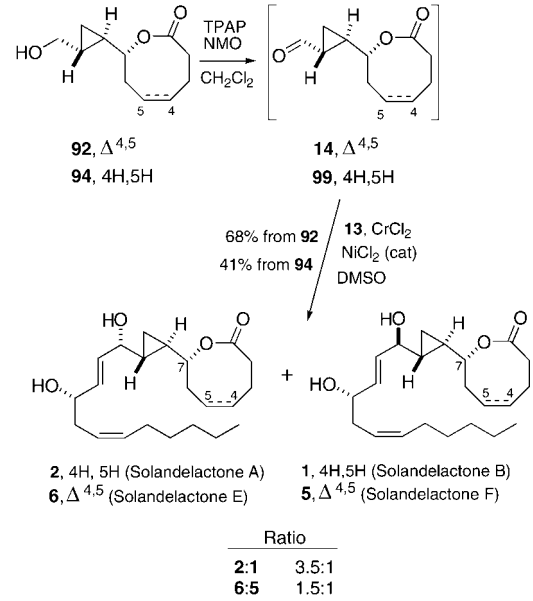
Octenalactone **89** is nominally an entrance point to saturated lactone **93** needed for the synthesis of solandelactones A and B, but neither hydrogenation of **89** over Wilkinson's catalyst nor catalyzed transfer hydrogenation produced any trace of **93**. In most cases, the cyclopropane of **89** was destroyed in these reactions. By contrast, reduction of **89** with diimide led smoothly to saturated lactone **93**, and removal of silyl protection gave

(29) Vlieghe, P.; Clerc, T.; Pannecouque, C.; Witvrouw, M.; De Clercq, E.; Salles, J. P.; Kraus, J. L. *J. Med. Chem.* **2001**, *44*, 3014.
(30) Nagao, Y.; Hagiwara, Y.; Kumagai, T.; Ochiai, M.; Inoue, T.; Hashimoto, K.; Fujita, E. *J. Org. Chem.* **1986**, *51*, 2391.
(31) Charette, A. B.; Lebel, H. *J. Org. Chem.* **1995**, *60*, 2966.
(32) Carling, R. W.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1986**, 325.
(33) Anderson, E. A.; Davidson, J. E. P.; Harrison, J. R.; O'Sullivan, P. T.; Burton, J. W.; Collins, I.; Holmes, A. B. *Tetrahedron* **2002**, *58*, 1943.
(34) Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392.

SCHEME 12



SCHEME 13



alcohol **94** in virtually quantitative yield. As was the case with **92**, oxidation of **94** yielded an unstable aldehyde that was best used in situ for coupling with **13**.

Our initial approach to constanolactones A (**9**) and B (**10**) coupled **95**, the TBDPS protected version of **13** with aldehyde **96** in a Nozaki-Hiyama-Kishi reaction that gave **97** and **98** in the ratio 2:1, respectively (Scheme 12). The major product **97** was shown by NMR to correspond in configuration to constanolactone A and is the result of Felkin addition to **96** by the organochromium species from **95**. However, a problem emerged in the final deprotection of **97** and **98**; the TBDPS ether could not be cleaved without destruction of the cyclopropane. The problem was solved by removing the silyl protection from **95**and using **13** for NHK coupling with **96**. In that case, constanolactones A and B were obtained directly in the proportion 1.4:1. This showed that protonation by the free alcohol of the organochromium species from **13** is not a competing reaction and convinced us that **13**, rather than its TBS ether **28**, should be employed for NHK coupling with aldehyde **14** and its saturated counterpart from **93**.

Therefore, aldehyde **14**, obtained by oxidation of **92** was reacted with iododiene **13** under conditions that had been used in the direct preparation of constanolactones A and B (scheme 13). Two stereoisomeric alcohols were produced in the ratio 3.5:1, the major alcohol corresponding precisely in the chemical shift and coupling constants of its C11 proton to the C9 hydrogen of constanolactone A (**9**). Thus, the major alcohol from **14** has (11*S*) configuration and is again the result of Felkin addition. As found previously by Martin, the NMR spectra for this alcohol did not match the data reported by Shin for solandelactone F[3] but instead were identical to the data for natural solandelactone E. Likewise, the C11 proton signal in the NMR spectrum of the minor alcohol from aldehyde **14** matched the C9 proton of constanolactone B and confirmed that this isomer was solandelactone F. Thus, the assignment of C11 configuration made to solandelactones E and F by Shin must be reversed, a conclusion that was reached independently by Davoren and Martin in their synthesis of solandelactone E.[10]

An analogous NHK coupling to that conducted on **14** was carried out on aldehyde **99** obtained from **94** and led to major and minor alcohols in the ratio 1.5:1, respectively. The C11 proton signal in the NMR spectrum of the major isomer matched constanolactone A (**9**) as well as solandelactone E, and on that basis it is again assigned 11(*S)* configuration. This configuration was previously assigned to solandelactone B[3] but is now shown to belong to solandelactone A. Conversely, the minor alcohol from **99** represents solandelactone B. In light of these results, it is likely that C11 configuration of stereochemical pairs C/D and G/H must be reversed from the assignment made by Shin.

With the absolute configuration of solandelactones A, B, E, and F firmly established, a biogenesis of these substances can be offered along lines put forward to explain the origin of C_{20} eicosanoids derived from arachidonic acid. A proposal initially made by Corey to account for the biogenesis of prostanoids[35] was subsequently extended by Brash to include oxylipins that would be precursors of cyclopropane containing metabolites such as the constanolactones.[36] A key intermediate in the Corey−Brash postulate is an allene oxide formed from arachidonic acid via oxidation to a (8*R*) hydroperoxide with lipoxygenase. Supporting evidence for an allene oxide intermediate was obtained by Brash who isolated and characterized the compound from an incubation of (8*R*)-*cis*,*trans*,*cis*,*cis*-8-hydroperoxyeicosa-5,9,11,14-tetraenoic acid with an acetone powder prepared from the marine coral *Plexaura homomalla.*[37]

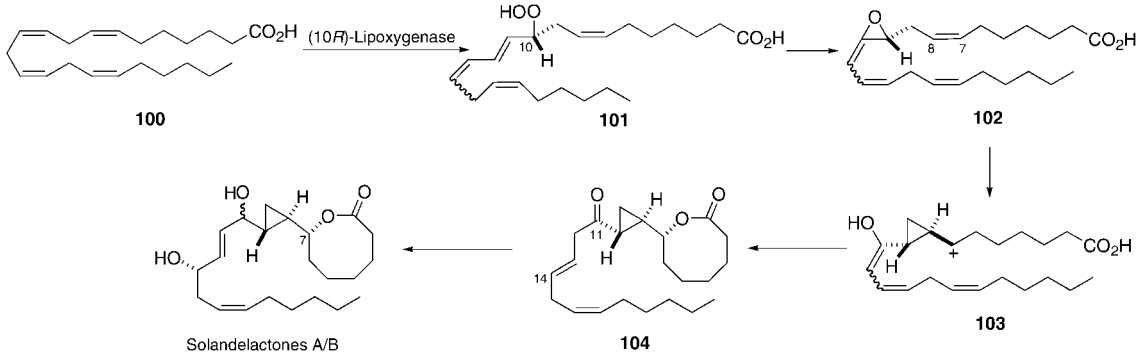
By analogy with the Corey−Brash proposal, biogenesis of solandelactones **1**−**8** would take place from all *cis*-docosa-7,10,13,16-tetraenoic acid (**100**) and would invoke (10*R*) hydroperoxide **101** (Scheme 14). The derived allene oxide **102** is positioned for attack (with inversion) by the cis $\Delta^{7,8}$ double bond, which would lead to cyclopropylcarbinyl cation **103**. This intermediate has the cyclopropane absolute configuration of the solandelactones. Lactone formation from **103**, followed by enzymatic oxidation at C14 and reduction of the C11 ketone of **104**, would produce solandelactones A and B. Solandelactones C−H presumably arise from a C_{22} carboxylic acid analogous to **100** but which contains additional cis alkenes at C4,5 or C19,20 or at both sites. The fact that all known solandelactones possess (7*R*) configuration would be consistent with a pathway

(35) (a) Corey, E. J.; Matsuda, S. P. T. *Tetrahedron Lett.* **1987**, *28*, 4247. (b) Corey, E. J.; d'Alarcao, M.; Matsuda, S. P. T.; Lansbury, P. T.; Yamada, Y. *J. Am. Chem. Soc.* **1987**, *109*, 289.

(36) Baertschi, S. W.; Brash, A. R.; Harris, T. M. *J. Am. Chem. Soc.* **1989**, *111*, 5003.

(37) Gerwick, W. H *Chem. Rev.* **1993**, *93*, 1807.

SCHEME 14



in which lactone formation to give **104** takes place in concert with epoxide opening of allene oxide **102** by the *cis*-7,8-alkene. However, in the case of constanolactone biosynthesis, a δ-hydroxy acid has been implicated prior to lactonization.[36] An alternative biogenesis of solandelactones to that shown in Scheme 14 has been suggested by Shin[3] based on a previous proposal by Gerwick.[37]

In summary, total syntheses of solandelactones A, B, E, and F have been completed. Their previously assigned absolute configuration at C7, 8, 10, and 14 has been confirmed but configuration at C11 in pairs A/B and E/F must be reversed from the attribution made by Shin[3] in the course of his structural elucidation of the solandelactones.

Experimental Section

***tert*-Butyl[(S,1E,5Z)-1-iodoundeca-1,5-dien-3-yloxy]dimethylsilane (28).**[18b] To a solution of **26** (23 mg, 80.3 μmol) and 4-methylmorpholine-*N*-oxide (14.0 mg, 120 μmol) in CH_2Cl_2 (3.5 mL) was added 4 Å molecular sieves (93 mg, powdered). After 10 min, TPAP (5.6 mg, 16.1 μmol) was added to the mixture and stirring was continued for 1 h. The mixture was diluted with pentane (7 mL), filtered through a short column of silica gel (20% EtOAc in pentane), and concentrated under reduced pressure to give **27** (19.6 mg), which was used for the next step without further purification.

$CrCl_2$ was added to a flask that contained **27** obtained above and CHI_3 (63.2 mg, 0.161 mmol). THF (1 mL) was added to the flask under Ar at 0 °C and the mixture was stirred for 16 h at 0 °C. The reaction was quenched with saturated NaCl solution and the mixture was extracted with Et_2O (3 × 6 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography (petroleum ether) gave **28** (12.1 mg, 37%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.89 (s, 9H), 0.89 (t, J = 7.0 Hz, 3H), 1.25−1.36 (m, 6H), 2.00 (q, J = 7.1 Hz, 2H), 2.23 (m, 1H), 4.09 (q, J = 6.0 Hz, 1H), 5.29−5.50 (m, 2H), 6.21 (dd, J = 0.9, 14.4 Hz, 1H), 6.53 (dd, J = 5.7, 14.4 Hz, 1H), ; ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.6, −4.4, 14.3, 18.4, 22.8, 26.0, 27.7, 29.5, 31.8, 35.9, 75.3, 75.9, 124.3, 132.9, 149.0.

(3S,1E,5Z)-3-Hydroxy-1-iodoundeca-1,5-diene (13). To a solution of **28** (11.5 mg, 28 μmol) in THF (0.2 mL) at room temperature was added TBAF (56 μL, 1 M THF, 56 μmol). After 30 min, the reaction was quenched with saturated NH_4Cl solution and the mixture was extracted with CH_2Cl_2 (5 × 6 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Column chromatography (12% ethyl acetate/pentane) gave **13** (8.0 mg, 97%) as a colorless oil whose NMR data were in agreement with those previously reported.[8b]

Methyl (2Z,5R)-5-(*tert*-Butyldimethylsilanyloxy)-6-trityloxyhex-2-enoate (48). A solution of **47** (1.30 g, 4.08 mmol) and 18-crown-6 (5.40 g, 20.4 mmol) in THF (60 mL) was cooled to −78 °C under argon. KHMDS (6.81 mL, 0.60 M in toluene) was added slowly, and after 30 min a solution of **46** (1.88 g, 4.08 mmol) in THF (5 mL) was added. The mixture was stirred for 1 h, then the reaction was quenched with saturated aqueous NH_4Cl (10 mL) and the mixture was extracted with Et_2O (2 × 25 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (2−10% EtOAc in hexane) to yield **48** (1.88 g, 89%) as a colorless oil:[α^{23}_D]-5.8 (c 1.0, $CHCl_3$); IR (neat) 3.86, 3059, 3033, 2953, 2928, 2884, 2856, 1724, 1647, 1597, 1491, 1471, 1448, 1407, 1361, 1323, 1255, 1174 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.01 (s, 3H), 0.03 (s, 3H), 0.80−0.95 (m, 9H), 2.96−3.05 (m, 1H), 3.06−3.13 (m, 1H), 3.69 (s, 3H), 3.83−3.99 (m, 1H), 5.78−5.83 (m, 1H), 5.78−5.83 (m, 1H), 7.19−7.34 (m, 9H), 7.42−7.49 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.9, −4.6, 18.0, 25.8, 34.5, 51.0, 67.1, 70.8, 86.5, 120.6, 126.9, 127.7, 128.3, 128.6, 128.7, 144.1, 146.4, 166.7; MS (CI) m/z 485 (M − [OCH_3])$^+$, 473, 439, 407, 333, 327, 291, 277, 271, 257; HRMS (CI) m/z 485.2503 (calcd for $C_{31}H_{37}O_3Si$ (M − [OCH_3])$^+$: 485.2512).

(2R,4Z)-2-(*tert*-Butyldimethylsilanyloxy)-1-trityloxyhex-4-en-6-ol (49). A solution of **48** (1.85 g, 3.58 mmol) in CH_2Cl_2 (20 mL) was cooled to 0 °C under argon and DIBAl-H (1.40 mL, 7.88 mmol) was added slowly. The mixture was stirred for 45 min, then the reaction was quenched with saturated aqueous Na^+/K^+ tartrate (20 mL). After 1 h of vigorous stirring, the aqueous phase was extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was purified by column chromatography (5−40% EtOAc in hexane) to yield **49** (1.33 g, 76%) as a colorless oil: α^{22}_D + 2.8 (c 1.0, $CHCl_3$); IR (neat) 3348, 3086, 3059, 3023, 2958, 2928, 2883, 2856, 1597, 1491, 1471, 1448, 1388, 1361, 1322, 1255, 1220, 1184, 1154 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.03 (s, 3H), 0.02 (s, 3H), 0.85 (s, 9H), 1.56 (brs, 1H), 2.32−2.54 (m, 2H), 2.98 (dd, J = 6.6, 9.1 Hz, 1H), 3.10 (dd, J = 4.9, 9.1 Hz, 1H), 3.79−3.89 (m, 1H), 4.04−4.17 (m, 2H), 5.64−5.74 (m, 1H), 5.47−5.58 (m, 1H), 7.20−7.34 (m, 9H), 7.42−7.49 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.7, −4.6, 18.1, 25.8, 33.0, 58.5, 67.0, 71.1, 86.6, 127.0, 127.7, 128.7, 128.8, 130.6, 144.0; MS (CI) m/z 488 (M − H)$^+$, 484, 471, 411, 333, 297, 271, 257; HRMS (CI) m/z 411.2360 (calcd for $C_{25}H_{35}O_3Si$ (M − [C_6H_5])$^+$: 411.2356).

(2R,4Z)-6-(Tri-*n*-butylstannyl)-1-trityloxyhex-4-en-2-ol (50). TBAF (2.43 mL, 1.0 M in THF) was added dropwise *via* syringe to a stirred solution of (2*R*,4*Z*)-2-(*tert*-butyldimethylsilanyloxy)-6-(tri-*n*-butylstannyl)-1-trityloxyhex-4-ene (906 mg, 1.18 mmol) and collidine (227 μL) in THF (18 mL) at 0 °C under argon, and the mixture was stirred at ambient temperature for 21 h. The mixture was placed in a separatory funnel containing CH_2Cl_2 (50 mL) and saturated aqueous NH_4Cl (20 mL), and the separated aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure, and the residue was purified by column chromatography (2−10% EtOAc in hexane) to give **50** (516 mg, 63%) as a colorless oil: α^{22}_D −2.4 (c 1.0, $CHCl_3$); IR (neat) 3460, 3086,

3059, 3022, 2955, 2924, 2870, 2853, 1637, 1597, 1491, 1448, 1418, 1376, 1220, 1183, 1153 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.82−0.92 (m, 15H), 1.22−1.36 (m, 6H), 1.42−1.54 (m, 6H), 1.69 (d, J = 9.2 Hz, 2H), 2.18−2.27 (m, 2H), 2.30 (d, J = 3.8 Hz, 1H), 3.11 (dd, J = 6.9, 9.3 Hz, 1H), 3.22 (dd, J = 3.8, 9.3 Hz, 1H), 3.77−3.88 (m, 1H), 4.97−5.07 (m, 1H), 5.59−5.72 (m, 1H), 7.22−7.35 (m, 9H), 7.43−7.49 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.3, 10.7, 13.7, 27.3, 29.1, 31.2, 67.3, 71.0, 86.6, 118.6, 127.0, 127.8, 128.7, 131.4, 143.9; MS (CI) m/z 648 $(M)^+$, 603, 523, 467, 405, 349, 291, 257; HRMS (CI) m/z 648.2973 (calcd for $C_{37}H_{52}O_2{}^{120}Sn$: 648.2989).

(1*R*,2*S*)-1-(Trityloxymethyl)-2-vinylcyclopropane (44). Triflic anhydride (246 μL, 1.46 mmol) was added dropwise *via* syringe to a stirred solution of **50** (630 mg, 0.973 mmol) and collidine (192 μL, 1.46 mmol) in CH_2Cl_2 (10 mL) at −78 °C under argon, and the mixture was stirred for 1 h. Et_3N (443 μL, 3.42 mmol) was added dropwise *via* syringe, and the mixture was stirred for an additional 19 h at −78 °C. The mixture was allowed to warm to ambient temperature and concentrated under reduced pressure. The residue was purified by column chromatography (2−4% EtOAc in hexane, containing 1% Et_3N) to yield **44** (302 mg, 91%) (Chiral OD, 0.85 mL/min, 100% hexanes): $[\alpha^{23}{}_D]$ −45.3 (c 1.0, $CHCl_3$); IR (neat) 3083, 3059, 3021, 2993, 2955, 2915, 2868, 1635, 1597, 1491, 1448, 1402, 1317, 1218, 1182, 1153 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.66 (t, J = 6.9 Hz, 2H), 1.07−1.23 (m, 1H), 1.24−1.34 (m, 1H), 2.94 (dd, J = 6.5, 9.6 Hz, 1H), 3.07 (dd, J = 6.1, 9.6 Hz, 1H), 4.88 (dd, J = 1.7, 10.3 Hz, 1H), 5.06 (ddd, J = 0.5, 1.7, 17.1 Hz, 1H), 5.45 (ddt, J = 8.5, 10.2, 17.1 Hz, 2H), 7.20−7.34 (m, 9H), 7.44−7.49 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 20.4, 20.6, 66.7, 86.2, 111.9, 126.9, 127.7, 128.7, 141.2, 144.3; MS (CI) m/z 340 $(M)^+$, 263, 243, 228, 183, 165, 143, 105, 91; HRMS (CI) m/z 340.1828 (calcd for $C_{25}H_{24}O$: 340.1827).

(3*R*)-6-(*tert*-Butyldiphenylsilanyloxy)-3-hydroxy-1-(4*S*-isopropyl-2-thionothiazolidin-3-yl)hex-4-en-1-one (79). To a solution of **78**, (0.645 g, 3.42 mmol) in CH_2Cl_2 (25 mL) at 0 °C was added titanium tetrachloride (416 μL, 3.80 mmol). After 5 min, the solution was cooled to −78 °C and diisopropylethylamine (662 μL, 3.80 mmol) was added dropwise over 5 min. The solution was stirred at −78 °C for 2 h and **77** (740 mg, 2.28 mmol) in CH_2Cl_2 (7 mL) was added *via* cannula over 5 min. The dark solution was stirred at −78 °C for a further 6 h, then the reaction was quenched with a saturated solution of NH_4Cl (10 mL), and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was dried over Na_2SO_4 and the solvent was removed. Column chromatography (10% to 25% EtOAc in pentane) gave **79** (1.154 g, 94%) as a yellow oil: $[\alpha]^{23}{}_D$ +172.5 (*c* 1.8; $CHCl_3$); IR (neat) 3462 (br), 3067, 2959, 2852, 1695, 1471, 1247, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (3H, d, J = 6.7 Hz), 1.13−1.08 (12H, m), 2.41 (1H, oct, J = 6.4 Hz), 2.83 (1H, brs), 3.06 (1H, dd, J = 11.4, 0.9 Hz), 3.36 (1H, ddd, J = 17.7, 8.8, 0.8 Hz), 3.54 (1H, dd, J = 11.4, 7.9 Hz), 3.66 (1H, dd, J = 17.7, 3.0 Hz), 4.27 (2H, s), 4.73 (1H, m), 5.18 (1H, ddd, J = 7.9, 6.4, 0.9 Hz), 5.85 (1H, dd, J = 15.7, 3.9 Hz), 5.90 (1H, dd, J = 15.7, 3.2 Hz), 7.49−7.40 (6H, m), 7.73−7.69 (4H, m); ^{13}C NMR ($CDCl_3$) δ 17.9, 19.1, 19.3, 26.9 (x3), 30.7, 30.9, 36.4, 45.3, 63.8, 68.3, 71.4, 127.7 (x4), 129.7, 130.2, 130.3, 133.6, 135.6 (×4), 172.5, 203.0; MS (CI) m/z 550 $(M^+ + Na)$, 510 $(M^+ - OH)$; HRMS m/z 550.1849 (calcd for $C_{28}H_{37}NO_3NaSiS_2$ 550.1882).

(3*R*)-6-(*tert*-Butyldiphenylsilanyloxy)-3-hydroxyhex-4-enoic Acid Methoxymethylamide (80). To a solution of **79** (220 mg, 0.41 mmol) in CH_2Cl_2 (5 mL) at room temperature were added imidazole (300 mg, 4.40 mmol) and $HN(OCH_3)CH_3$•HCl (215 mg, 2.21 mmol, azeotroped from benzene three times). The heterogeneous solution was stirred at room temperature for 16 h, the reaction was quenched with a saturated solution of NH_4Cl (10 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic extract was dried over Na_2SO_4 and the solvent was removed. Column chromatography (25% EtOAc in pentane) gave **80** (0.126 g, 71%) as a pale-yellow oil: $[\alpha]^{23}{}_D$ +19.1 (*c* 2.2 $CHCl_3$); IR (neat) 3437 (br), 2925, 2856, 1652, 1475, 1424, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (9H, s), 2.60 (1H, dd, J = 16.7, 9.1 Hz), 2.70 (1H, dd, J = 16.7, 2.2 Hz), 3.20 (3H, s), 3.69 (3H, s), 3.89 (1H, s), 4.24 (2H, m), 4.61 (1H, m), 5.82 (1H, m), 5.89 (1H, ddd, J = 15.5, 3.3, 0.9 Hz), 7.43−7.36 (6H, m), 7.70−7.67 (4H, m); ^{13}C NMR ($CDCl_3$) δ 19.3, 26.9 (x3), 31.9, 38.4, 61.3, 63.8, 68.3, 127.7 (×4), 129.6, 129.7 (×2), 130.6, 133.7, 135.6 (×4), 173.3; MS (CI) m/z 450 $(M^+ + Na)$, 410 $(M^+$-OH); HRMS m/z 450.2057 (calcd for $C_{24}H_{33}NO_4NaSi$ 450.2077).

(3*R*)-3-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-3-hydroxy-*N*-methoxy-*N*-methylpropionamide (81). To a solution of **80** (0.427 g, 1.16 mmol) in CH_2Cl_2 (12 mL) at −15 °C was added diethylzinc (5.8 mL, 5.8 mmol, 1 M in hexanes) followed by diiodomethane (0.467 mL, 5.80 mmol). The solution was allowed to warm to room temperature over 1 h and was stirred for a further 2 h. The reaction was quenched with a saturated solution of NH_4Cl (10 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic extract was dried over Na_2SO_4, and the solvent was removed to give pure **81** (0.427 g, 97%) as a colorless oil: $[\alpha]^{23}{}_D$ +13.4 (*c* 0.65 $CHCl_3$); IR (neat) 3458 (br), 2933, 2851, 1647, 1428, 1114 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.52 (1H, ddd, J = 8.3, 8.3, 5.1 Hz), 0.68 (1H, ddd, J = 8.3, 8.3, 5.1 Hz), 1.07−0.87 (2H, m), 1.08 (9H, s), 2.75 (1H, dd, J = 16.6, 9.8 Hz), 2.97 (1H, brd, J = 16.6 Hz), 3.23 (3H, s), 3.32 (1H, dd, J = 10.6, 7.3 Hz), 3.46 (1H, dt, J = 9.2, 2.2 Hz), 3.67 (3H, s), 3.82 (1H, dd, J = 10.6, 5.2 Hz), 4.33 (1H, brs), 7.47−7.37 (6H, m), 7.73−7.66 (4H, m); ^{13}C NMR ($CDCl_3$) δ 8.7, 18.7, 19.3, 22.7, 26.9 (×3), 32.1, 38.1, 61.4, 66.6, 72.3, 127.7 (×4), 129.7 (×3), 133.8, 135.6 (×4), 173.9; MS (CI) m/z 441 (M^+), 408, 398, 384; HRMS m/z 441.2335 (calcd for $C_{25}H_{35}NO_4Si$ 441.2077).

(3*R*)-3-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-*N*-methoxy-*N*-methyl-3-triethylsilanyloxypropionamide (82). To a solution of **81** (0.408 g, 0.91 mmol) in CH_2Cl_2 (6 mL) at 0 °C were added 2,6-lutidine (0.20 mL, 1.82 mmol) and TESOTf (0.308 mL, 1.37 mmol). The solution was stirred at 0 °C for 45 min, the reaction was quenched with a saturated solution of $NaHCO_3$ (10 mL), and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic extract was washed with brine, dried over Na_2SO_4, and the solvent was removed. Column chromatography (10% EtOAc in pentane) gave **82** (0.500 g, 98%) as a pale-yellow oil: $[\alpha]^{23}{}_D$ −2.3 (*c* 2.0 $CHCl_3$); IR (neat) 2958, 2879, 1671, 1472, 1429, 1111, 1075 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.49 (1H, ddd, J = 9.4, 4.5, 4.4 Hz), 0.62 (1H, m), 0.64 (6H, q, J = 8.1 Hz), 0.99 (9H, t, J = 8.1 Hz), 1.00−0.93 (2H, m), 1.09 (9H, s), 2.60 (1H, dd, J = 14.4, 4.4 Hz), 3.48 (1H, dd, J = 14.4, 8.3 Hz), 3.69 (3H, s), 3.70 (1H, dd, J = 10.6, 5.6 Hz), 3.81 (1H, ddd, J = 8.1, 8.1, 4.5 Hz), 7.45−7.37 (6H, m), 7.73−7.67 (4H, m); ^{13}C NMR ($CDCl_3$) δ 6.5 (x3), 6.9 (x3), 9.0, 18.4, 19.2, 23.7, 26.9 (x3), 32.0, 40.7, 61.2, 66.5, 72.2, 127.7 (×4), 129.6 (×3), 133.9, 135.6 (×4), 173.3; MS (CI) m/z 578 $(M^+ + Na)$, 346 $(M^+ - OTES)$; HRMS m/z 578.3074 (calcd for $C_{31}H_{49}NO_4NaSi_2$ 578.3098).

(3*R*)-3-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-3-triethylsilanyloxypropionaldehyde (83). To a solution of **82** (0.120 g, 0.220 mmol) in THF (2 mL) at −78 °C was added DIBAL-H (0.26 mL, 1 M solution in THF) over a period of 5 min. After 10 min, the reaction was quenched with a saturated solution of Rochelle's salt (8 mL), and the mixture was allowed to warm to room temperature and extracted with CH_2Cl_2 (3 × 20 mL). The organic extract was dried over Na_2SO_4, and the solvent was removed to give **83** as a colorless oil: $[\alpha]^{23}{}_D$ −7.8 (*c* 1.2 $CHCl_3$); IR (neat): 2950, 2872, 1722, 1469, 1112 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.50 (1H, ddd, J = 9.4, 4.5, 4.4 Hz), 0.66−0.56 (7H, m), 1.00−0.89 (11H, m), 1.07 (9H, s), 2.64 (1H, ddd, J = 15.5, 5.2, 2.5 Hz), 2.70 (1H, ddd, J = 15.5, 6.5, 2.5 Hz), 3.40 (1H, dd, J = 10.4, 6.3 Hz), 3.74−3.64 (2H, m), 7.46−7.39 (6H, m), 7.71−7.67 (4H, m), 9.87 (1H, t, J = 2.5 Hz); ^{13}C NMR ($CDCl_3$) δ 5.3 (×3), 6.9 (×3), 9.2, 18.5, 19.2, 23.6, 26.9 (×3), 52.1, 66.3, 71.3, 127.7 (×4), 129.7 (×3), 133.8, 135.6 (×4), 201.9; MS (CI) m/z 519 $(M^+ + Na)$; HRMS m/z 519.2761 (calcd for $C_{29}H_{44}O_3NaSi_2$ 519.2727). This

material was unstable and was used promptly in the next step without further purification.

(5*R*)-5-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-5-triethylsilanyloxypent-1-en-3-ol (84). To a solution of **83** (0.116 g, 0.220 mmol) in THF (3 mL) at −78 °C was added vinylmagnesium bromide (0.44 mL, 1 M solution in THF). After 40 min, some starting material was still apparent by tlc analysis and an additional quantity of vinylmagnesium bromide (0.22 mL) was added. After a further 10 min, the reaction was quenched with a saturated solution of NH_4Cl, and the mixture was allowed to warm to room temperature and extracted with CH_2Cl_2 (3 × 20 mL). The organic extract was dried over Na_2SO_4 and the solvent was removed. Column chromatography (10% EtOAc in pentane) gave **84** (0.074 g, 85%, 1:1 mixture of diastereomers) as a pale-yellow oil: IR (neat) 3459 (br s), 2960, 2870, 1652, 1424, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.63−0.50 (4H, m), 0.68 (12H, q, J = 8.1 Hz), 1.00 (18H, t, J = 8.1 Hz), 1.00−0.88 (4H, m), 1.09 (18H, s), 1.91−1.79 (4H, m), 3.50−3.28 (6H, m), 3.74 (2H, m), 4.38 (1H, m), 4.56 (1H, m), 5.11 (2H, m), 5.30 (2H, m), 5.89 (2H, ddd, J = 17.2, 10.9, 5.2 Hz), 7.49−7.39 (12H, m), 7.73−7.67 (8H, m); ^{13}C NMR ($CDCl_3$) δ 5.3, 6.9, 10.0, 10.4, 18.5, 19.0, 19.2, 22.9, 23.9, 26.9, 43.5, 44.4, 66.4, 66.5, 69.9, 72.0, 74.9, 113.8, 127.7, 129.7, 133.8, 135.6, 140.9, 141.22; MS (CI) m/z 547 (M^+ + Na); HRMS m/z 547.3014 (calcd for $C_{31}H_{48}O_3NaSi_2$ 547.3040).

(5*R*)-5-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-5-hydroxypent-1-en-3-ol (85). To **84** (18 mg, 0.034 mmol) was added a mixture of AcOH, THF and H_2O (6:2:1, 2.0 mL). The solution was stirred for 1 h at room temperature and the reaction was quenched with $NaHCO_3$. The mixture was extracted with CH_2Cl_2 (3 × 20 mL), and the organic extract was dried over Na_2SO_4 to give **85** as a colorless oil that was carried forward to the next reaction without further purification: IR (neat) 3367 (br s), 2927, 2853, 1733, 1472, 1428, 1263, 1115, 1076, 823 cm^{-1}: ^1H NMR ($CDCl_3$) δ 0.48 (2H, m), 0.56 (2H, ddd, J = 9.6, 4.6, 4.6 Hz), 1.03−0.86 (4H, m), 1.08 (18H, s), 1.97−1.76 (4H, m), 3.27 (2H, dq, J = 8.6, 3.6 Hz), 3.40 (2H, dd, J = 10.9, 7.3 Hz), 3.76 (2H, m), 4.40 (1H, m), 4.53 (1H, m), 5.14 (1H, d, J = 10.6 Hz), 5.17 (1H, d, J = 10.6 Hz), 5.29 (1H, d, J = 17.2 Hz), 5.33 (1H, d, J = 17.2 Hz), 5.92 (2H, m), 7.49−7.39 (12H, m), 7.72−7.67 (8H, m); ^{13}C NMR ($CDCl_3$) δ 1.1, 8.0, 8.1, 18.7, 18.7, 19.2, 23.6, 24.0, 26.9, 29.7, 42.2, 43.1, 66.4, 70.4, 73.2, 73.4, 76.3, 114.3, 127.7, 129.7, 133.8, 135.6, 140.7; MS (CI) m/z 433 (M^+ + Na); HRMS m/z 433.2166 (calcd for $C_{25}H_{34}O_3NaSi$ 433.2175).

(4*R*)-4-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-6-vinyl-[1,3]-dioxan-2-one (90). To **85** (0.105 g, 0.26 mmol) in CH_2Cl_2 (2 mL) at −78 °C were added 4 Å molecular sieves, Et_3N (0.154 mL, 1.52 mmol), pyridine (0.120 g, 1.52 mmol), and triphosgene (0.386 g, 1.30 mmol). The solution was stirred for 30 min, the reaction was quenched with an aqueous solution of NH_4Cl (2 mL), and the separated organic phase was washed with an aqueous solution of $CuSO_4$, water, and brine. The organic phase was dried over Na_2SO_4, and the solvent was removed to give **90** (113 mg, 98%) as a colorless oil: IR (neat) 2963, 2912, 2843, 1742, 1424, 1260, 1105 cm^{-1}: ^1H NMR ($CDCl_3$) δ 0.74−0.58 (4H, m), 1.12−0.90 (22H, m), 1.89−1.76 (2H, m), 2.24−2.13 (2H, m), 3.42−3.29 (2H, m), 3.87−3.76 (4H, m), 4.81 (1H, m), 5.07 (1H, m), 5.44−5.30 (4H, m), 5.92−5.78 (2H, m), 7.45−7.35 (12H, m), 7.67−7.61 (8H, m); ^{13}C NMR ($CDCl_3$) δ 8.2, 8.6, 18.3, 18.5, 19.3, 20.4, 20.6, 26.6, 26.9, 31.5, 33.5, 65.6, 65.7, 76.2, 76.8, 77.1, 77.4, 78.6, 79.7, 82.1, 118.2, 118.3, 127.8, 129.8, 133.5, 133.6, 134.3, 134.4, 135.6, 148.8, 149.0; MS (CI) m/z 459 (M^+ + Na); HRMS m/z 459.1978 (calcd for $C_{26}H_{32}O_4NaSi$ 459.1968). This material was carried forward to the next reaction without further purification.

(8*R*)-8-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-3,4,7,8-tetrahydrooxocin-2-one (89). To **90** (0.025 g, 0.06 mmol) in toluene (2 mL) was added dicyclopentadienyldimethyltitanium (0.044 g of a 33% by wt solution in toluene). The solution was stirred in the dark at 100 °C for 2 h. The reaction vessel was cooled to room temperature and the solvent was removed. Column chromatography (10% EtOAc in pentane) gave **89** (0.011 g, 43%, 63% brsm) as a colorless oil: $[\alpha]^{23}_D$ −173.3 (*c* 0.45 $CHCl_3$); IR (neat): 2958, 2929, 2855, 1746, 1478, 1425, 1110, 1074 cm^{-1}: ^1H NMR ($CDCl_3$) δ 0.50 (1H, ddd, J = 8.8, 5.2, 5.2 Hz), 0.64 (1H, ddd, J = 8.8, 4.9, 4.9 Hz), 0.88 (1H, m), 0.97 (1H, m), 1.05 (9H, s), 2.34−2.23 (2H, m), 2.12 (1H, m), 2.60 (1H, ddd, J = 13.5, 10.6, 5.7 Hz), 2.73 (1H, ddd, J = 13.5, 6.1, 3.4 Hz), 2.86 91H, m), 3.40 (1H, dd, J = 10.6, 6.9 Hz), 3.75 (1H, dd, J = 10.6, 4.9 Hz), 3.94 (1H, dt, J = 10.4, 1.3 Hz), 5.83−5.72 (2H, m), 7.45−7.36 (6H, m), 7.68−7.64 (4H, m); ^{13}C NMR ($CDCl_3$) δ 8.6, 19.2, 19.6, 20.4, 24.5, 26.9 (×3), 37.8, 66.1, 81.8, 127.7 (×4), 128.4, 129.7 (×2), 132.7, 133.8 (×2), 135.6 (×4), 177.0; MS (CI) m/z 457 (M^+ + Na); HRMS m/z 452.2604 (calcd for $C_{27}H_{38}NO_3Si$ 452.2621).

(8*R*)-8-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]-3,4,7,8-tetrahydrooxocin-2-one (92). To **89** (0.012 g, 0.027 mmol) in THF (1.5 mL) was added TBAF (0.068 mL, 1 M in THF) at room temperature. After 1 h, the reaction was quenched with an aqueous solution of NH_4Cl (0.5 mL) and was extracted with CH_2Cl_2 (4 × 10 mL). The combined organic extracts were dried over Na_2SO_4, and the solvent was removed. Column chromatography (50% EtOAc in pentane) gave **92** (0.004 g, 74%) as a colorless oil: $[\alpha]^{23}_D$ +5.8 (*c* 0.4 $CHCl_3$); IR (neat) 3435, 2923, 2850, 1742, 1433, 1330, 1212, 1013 cm^{-1}: ^1H NMR ($CDCl_3$) δ 0.55 (1H, dt, J = 10.5, 5.2 Hz), 0.75 (1H, dt, J = 10.5, 5.2 Hz), 1.00 (1H, ddd, J = 13.0, 8.6, 4.7 Hz), 1.11 (1H, m), 2.11 (1H, m), 2.31 (1H, ddd, J = 13.2, 7.6, 1.6 Hz), 2.62 (1H, ddd, J = 13.5, 10.3, 6.5 Hz), 2.73 (1H, ddd, J = 13.5, 6.0, 2.9 Hz), 2.85 (1H, m), 3.46 (1H, dd, J = 11.2, 7.3 Hz), 3.55 (1H, dd, J = 11.2, 6.7 Hz), 4.04 (1H, dt, J = 8.5, 1.9 Hz), 5.73 (1H, m), 5.79 (1H, m); ^{13}C NMR ($CDCl_3$) δ 8.7, 19.7, 20.7, 24.5, 34.3, 37.7, 66.0, 80.9, 128.1, 132.8, 177.0; HRMS (CI) m/z 197.1179 (calcd for $C_{11}H_{17}O_3$ 197.1178).

(8*R*)-8-[1*S*,2*R*-(*tert*-Butyldiphenylsilanyloxymethyl)cyclopropyl]octahydrooxocin-2-one (93). To a solution of **89** (42 mg, 0.10 mmol) in pyridine (4 mL) was added potassium azodicarboxylate (378 mg, 1.94 mmol). AcOH (0.23 mL) in MeOH was added to this solution over 1 h at rt. The mixture was stirred at rt for 13 h diluted with Et_2O (10 mL) and was washed with saturated aqueous $NaHCO_3$, aqueous $CuSO_4$ and brine. The separated organic phase was dried over Na_2SO_4 and the solvent was removed under reduced pressure. Column chromatography (10:1 pentane:EtOAc) gave **93** (30.8 mg, 73%) as a colorless oil: $[\alpha]^{23}_D$ +2.6 (*c* 1.5, $CHCl_3$): IR (neat) 3071, 2930, 2858, 1731, 1428, 1232, 1112 cm_{-1}; ^1H NMR ($CDCl_3$) δ 0.50 (1H, dt, J = 5.0, 7.4 Hz), 0.57 (1H, dt, J = 8.2, 5.0 Hz), 1.05 (9H, s), 1.08−0.9 (2H, m), 1.58−1.47 (3H, m), 1.92−1.78 (4H, m), 2.47−2.37 (2H, m), 3.42 (1H, dd, J = 10.6, 6.5 Hz), 3.73 (1H, dd, J = 10.6, 5.3 Hz), 3.95 (1H, dt, J = 7.6, 6.5 Hz), 7.46−7.35 (6H, m), 7.70−7.62 (4H, m); ^{13}C NMR ($CDCl_3$) δ 8.4, 19.2, 21.2, 24.2, 26.9, 29.0, 26. 5, 32.6, 37.2, 66.1, 82.5, 127.7, 129.7, 133.8, 135.6, 176.6; MS (CI) m/z 437 (M + H), 379 (M^+ − *t*-Bu); HRMS m/z 437.2504 (calcd for $C_{27}H_{37}O_3Si$ 437.2511).

(8*R*)-8-[1*S*,2*R*-(Hydroxymethyl)cyclopropyl]octahydrooxocin-2-one (94). To a solution of **93** (30 mg, 0.069 mmol) in THF (5 mL) was added TBAF (170 μL, 1 M in THF). After 30 min, the solution was diluted with Et_2O and washed with brine. The separated organic phase was dried over Na_2SO_4 and the solvent was removed. Column chromatography (10:1 pentane:EtOAc) gave **94** (13.6 mg, 99%) as a colorless oil: $[\alpha]^{22}_D$ +4.5 (*c* 1.5, $CHCl_3$); IR (neat) 3049 (br), 2922, 2851, 1713, 1456, 1238, 1056, 731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.55 (1H, dt, J = 8.3, 5.1 Hz), 0.67 (1H, dt, J = 8.6, 5.1 Hz), 0.85 (1H, m), 1.01 (1H, ddd, J = 9.1, 8.4, 4.7 Hz), 1.57−1.49 (3H, m), 1.70 (1H, m), 1.89−1.79 (4H, m), 2.43 (1H, dd, J = 6.4, 5.9 Hz), 3.43 (1H, dd, J = 11.7, 7.0 Hz), 3.57 (1H, dd, J = 11.7, 6.4 Hz), 4.07 (1H, q, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 8.5, 19.3, 21.5, 24.2, 26.5, 29.1, 32.7, 37.1, 66.0, 81.7, 176.7; MS (EI) m/z 198 (M^+), 181 (M^+ − OH); HRMS m/z 198.1247 (calcd for $C_{11}H_{18}O_3$ 198.1256).

Solandelactones E (6) and F (5). To **92** (0.004 g, 0.020 mmol) in CH_2Cl_2 (1 mL) were added 4 Å molecular sieves (0.024 g) and 4-methylmorpholine *N*-oxide (0.0036 g, 0.030 mmol). Tetrapro-

pylammonium perruthenate (0.0016 g, 0.0046 mmol) was added and, after 20 min at room temperature, the solution was passed through a short plug of silica gel. Removal of the solvent gave **14** (0.004 g, quant) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (1H, m), 1.33 (1H, dt, J = 9.5, 4.7 Hz), 1.79 (1H, dddd, J = 10.6, 6.6, 6.6, 4.0 Hz), 1.94 (1H, ddd, J = 8.8, 8.8, 4.0 Hz), 2.13 (1H, dddd, J = 12.3, 6.6, 5.0 3.0 Hz), 2.32, 1H, ddd, J = 14.1, 8.1, 1.3 Hz), 2.60 (1H, dddd, J = 14.1, 10.3, 7.2, 1.4 Hz), 2.74 (1H, ddd, J = 13.4, 5.9, 3.0 Hz), 2.84 (1H, m), 4.28 (1H, ddd, J = 10.6, 6.7, 1.9 Hz), 5.74 (1H, m), 5.81 (1H, dddd, J = 11.0, 9.6, 6.9, 1.6 Hz), 9.21 (1H, d, J = 4.6 Hz); ^{13}C NMR ($CDCl_3$) δ 12.5, 24.4, 25.0, 27.5, 34.0, 37.7, 77.8, 127.6, 133.2, 176.5, 199.9. This compound was unstable and was carried forward without further purification.

A mixture of **14** prepared above and **13** was thoroughly dried by azeotropic removal of benzene (twice). To the mixture was added degassed DMSO (0.5 mL), chromium(II) chloride (6.6 mg, 0.054 mmol) and nickel(II) chloride (0.05 mg), and the green solution was stirred at room temperature for 18 h. The reaction was quenched by addition of saturated aqueous NaCl and the mixture was extracted with EtOAc (3 × 5 mL). The combined organic extracts were dried over Na_2SO_4, after which column chromatography (50% EtOAc in pentane) gave solandelactone E (**6**, 3.7 mg, 53%) and solandelactone F (**5**, 1.0 mg, 15%) as colorless oils. **6**; $[\alpha]^{23}_D$ +2.7 (*c* 0.03 MeOH); IR (neat): 3401, 2921, 2848, 1746, 1455, 1214, 1099, 1057 cm^{-1}: ^{1}H NMR ($CDCl_3$) δ 0.61 (1H, dt, J = 10.0, 5.0 Hz), 0.75 (1H, dt, J = 10.0, 5.0 Hz), 0.89 (3H, t, J = 6.7 Hz), 1.01 (1H, m), 1.14 (1H, ddd, J = 12.6, 8.5, 4.7 Hz), 1.38−1.30 (6H, m), 2.05 (2H, m), 2.12 (2H, m), 2.35−2.22 (4H, m), 2.63 (1H, ddd, J = 14.1, 10.6, 6.0 Hz), 2.73 (1H, ddd, J = 13.0, 5.3, 3.2 Hz), 2.86 (1H, m), 3.67 (1H, dd, J = 7.4, 3.5 Hz), 4.04 (1H, ddd, J = 10.5, 8.1, 2.1 Hz), 4.19 (1H, m), 5.38 (1H, dt, J = 12.0, 6.7 Hz), 5.59 (1H, dt, J = 12.0, 6.7 Hz), 5.84−5.72 (4H, m); ^{13}C NMR ($CDCl_3$) δ 8.1, 14.1, 20.7, 22.6, 23.4, 24.5, 27.5, 29.3, 31.5, 34.3, 35.3, 37.8, 71.5, 74.5, 80.9, 124.1, 128.1, 131.7, 132.8, 133.2, 134.1, 177.0; MS (CI) *m*/*z* 385 (M^+ + Na), 345 (M^+-OH; HRMS *m*/*z* 385.2371 (calcd for $C_{22}H_{34}O_4Na$ 385.2355). **5**: $[\alpha]^{23}_D$ +2.0 (*c* 0.01 MeOH); IR (neat) 3449, 2922, 2844, 1739, 1450, 1378, 1325, 1009 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71 (1H, dt, J = 7.6, 5.6 Hz), 0.78 (1H, dt, J = 7.3, 5.3 Hz), 0.89 (3H, t, J = 6.7 Hz), 1.06−1.00 (2H, m), 1.37−1.22 (6H, m), 2.07−2.02 (2H, m), 2.12 (1H, m), 2.18 (1H, ddd, J = 13.9, 8.0, 1.2 Hz), 2.38−2.26 (4H, m), 2.58 (1H, ddd, J = 14.0, 10.1, 6.2 Hz), 2.73 (1H, ddd, J = 13.0, 5.9, 3.0 Hz), 2.85 (1H, m), 3.67 (1H, dd, J = 6.0, 4.3 Hz), 4.01 (1H, dt, J = 10.6, 1.7 Hz), 4.18 (1H, m), 5.38 (1H, dt, J = 10.6, 7.7 Hz), 5.59 (1H, dt, J = 10.6, 7.2 Hz), 5.82−5.72 (2H, m); ^{13}C NMR ($CDCl_3$) δ 9.0, 14.0, 19.8, 22.6, 23.6, 24.4, 27.4, 29.3, 31.5, 34.3, 35.3, 37.7, 71.5, 74.8, 80.7, 124.0, 128.0, 131.7, 132.8, 133.6, 134.0; MS (CI) *m*/*z* 385 (M^+ + Na); HRMS *m*/*z* 385.2364 (calcd for $C_{22}H_{34}O_4Na$ 385.2355). Solandelactones E and F undergo mutarotation in MeOH due to methanolysis of the lactone.

Solandelactone A (2) and B (1). To a solution of **94** (0.008 g, 0.040 mmol) in CH_2Cl_2 (2 mL) were added 4 Å molecular sieves (0.040 g) and 4-methylmorpholine oxide (0.0072 g, 0.060 mmol). After 10 min, tetra-*n*-propylammonium perruthenate (0.0032 g, 0.0092 mmol) was added, and after 20 min at room temperature, the solution was passed through a short plug of silica gel. Removal of the solvent gave **99** (0.008 g, quant) as a colorless oil. This aldehyde was unstable and was carried forward to the next reaction without further purification.

A mixture of **99** prepared above and **13** was thoroughly dried by azeotropic removal of benzene (twice). To the mixture was added degassed DMSO (1 mL), chromium(II) chloride (13 mg, 0.11 mmol) and nickel(II) chloride (2.0 mg). The green solution was stirred at room temperature for 12 h and the reaction was quenched by addition of saturated aqueous NH_4Cl. The mixture was extracted with EtOAc (3 × 5 mL), and the combined organic extracts were dried over Na_2SO_4. Column chromatography (50% EtOAc in pentane) gave solandelactone A (**2**, 4.7 mg, 32%) and solandelactone B (**1**, 1.3 mg, 9%) as colorless oils. **2**: $[\alpha]^{23}_D$ +0.8 (*c* 0.13 MeOH); IR (neat) 3416, 2935, 2851, 1721, 1457, 1141, 1097, 1064 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.60 (1H, ddd, J = 8.6, 5.5 Hz), 0.68 (1H, ddd, J = 8.6, 5.2 Hz), 0.89 (1H, t, J = 6.2 Hz), 0.99 (1H, ddd, J = 8.9, 8.9, 4.6 Hz), 1.16 (1H, ddd, J = 8.6, 8.6, 4.9 Hz), 1.39−1.22 (6H, m), 1.60−1.50 (4H, m), 1.69 (1H, m), 1.90−1.82 (3H, m), 2.09−2.00 (2H, m), 2.35−2.29 (2H, m), 2.44 (2H, dd, J = 6.8, 6.2 Hz), 3.65 (1H, dd, J = 7.4, 4.0 Hz), 4.10 (1H, dt, J = 6.5, 7.9 Hz), 4.18 (1H, m), 5.38 (1H, dt, J = 11.0, 7.6 Hz), 5.59 (1H, dt, J = 11.0, 7.4 Hz), 5.76 (1H, dd J = 15.4, 7.2 Hz), 5.81 (1H, dd, J = 15.4, 4.2 Hz); ^{13}C NMR ($CDCl_3$) δ 7.9, 14.1, 21.5, 22.6, 23.1, 24.2, 26.5, 27.5, 29.1, 29.3, 31.5, 32.7, 35.3, 37.1, 71.5, 74.6, 81.5, 124.1, 131.7, 133.2, 134.1, 176.6; HRMS (CI) *m*/*z* 365.2701 (calcd for $C_{22}H_{37}O_4$: 365.2691). **1**: $[\alpha]^{23}_D$ +2.5 (c 0.08 MeOH); IR (neat) 3387, 2928, 1718, 1565, 1461, 1098 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.73−0.68 (2H, m), 0.88 (1H, t J = 6.6 Hz), 0.98 (1H, m), 1.06 (1H, m), 1.38−1.23 (6H, m), 1.72−1.49 (6H, m) 1.79 (1H, m), 1.86 (1H, m), 2.09−2.00 (2H, m), 2.36−2.27 (2H, m), 2.46−2.39 (2H, m), 3.67 (1H, dd J = 7.46, 4.8 Hz), 4.06 (1H, m), 4.17 (1H, m), 5.37 (1H, ddt, J = 10.7, 7.3, 1.3 Hz), 5.59 (1H, dtt, J = 10.9, 6.9, 0.8 Hz), 5.80−5.74 (2H, m); ^{13}C NMR ($CDCl_3$) δ 9.0, 14.1, 20.5, 22.6, 23.3, 24.2, 26.5, 27.5, 29.1, 29.3, 31.5, 32.8, 35.4, 37.2, 71.6, 74.8, 81.6, 124.0, 131.6, 133.6, 134.0, 176.6; HRMS *m*/*z* 365.2682 (calcd for $C_{22}H_{37}O_4$: 365.2691).

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Supporting Information Available: Experimental procedures and characterization data of compounds not described in the Experimental Section; ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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