ENANTIOSELECTIVE SYNTHESIS OF STRUCTURALLY INTRICATE AND COMPLEMENTARY POLYOXYGENATED BUILDING BLOCKS OF SPONGISTATIN 1 (ALTOHYRTIN A)

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Dedicated to Dr. Alfred Bader on the occasion of his 85th birthday in recognition of his outstanding contributions to the science of chemistry.

Enantioselective approaches to the construction of four complex building blocks of the structurally intricate marine macrolide known as spongistatin 1 are presented. The first phase of the synthetic effort relies on a practical approach to a desymmetrized, enantiomerically pure spiroketal ring system incorporating rings A and B. Concurrently, the C17–C28 subunit, which houses one-fifth of the stereogenic centers of the target in the form of rings C and D, was assembled via a composite of stereocontrolled aldol condensations. Once arrival at the entire C1–C28 sector had been realized, routes were devised to provide two additional highly functionalized sectors consisting of C29–C44 and C38–C51. A series of subsequent transformations including cyclization of the E ring and hydroboration to afford the *B*-alkyl intermediate for the key Suzuki coupling to append the side chain took advantage of efficient stereocontrol. Ultimately, complete assembly and functionalization of the western EF sector of spongistatin was thwarted by an inoperative Suzuki coupling step intended to join the side chain to the C29–C44 sector, and later because of complications due to protecting groups, which precluded the complete elaboration of the late stage C29–C51 intermediate.

Keywords: Total synthesis; Cytotoxic agents; Marine macrolides; Spiroketals; Coupling reactions.

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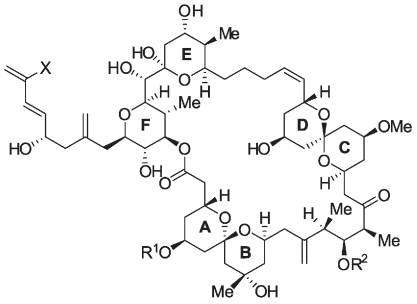
The anticipation that marine organisms would constitute important sources of promising anticancer agents of unusual structural type has been justified on many occasions. In recent years, powerful cell growth inhibitory macrolides such as bryostatin **1**[1,2] and halichondrin B[3,4] have been discovered. These complex large-ring lactones, which contain interlocked tetrahydropyran subunits, bear some resemblance to the equally cytotoxic antitumor agents swinholide A[5,6] and misakinolide A[7,8]. The latter two fascinating compounds, although obtained from marine sponges, may ultimately be derived from symbiotic blue-green algae[7c].

In 1993, Pettit succeeded in isolating from an Eastern Indian sponge of the genus *Spongia* the extremely potent antineoplastic macrocyclic lactone spongistatin 1 (**1a**) and congeners thereof[9]. In the same year, bioassay-guided isolation led Fusetani and co-workers to the discovery of cinachyrolide A, subsequently recognized to be identical to spongistatin 4 (**1b**)[10]. Kitagawa also identified additional examples of this important new compound class, which he termed the altohyrtins (**1a**, **1d**–**1e**)[11]. Although several macrolide antibiotics featuring one spiro ketal as a vital structural component (e.g., the avermectins[12,13], oligomycins A–C[14,15], cytovaricin[16,17], and rutamycins A and B[18,19]), have previously been discovered as fermentation products of actinomycetes, none of these share the distinctive bisspiro ketal pattern present in **1a**–**1e**.

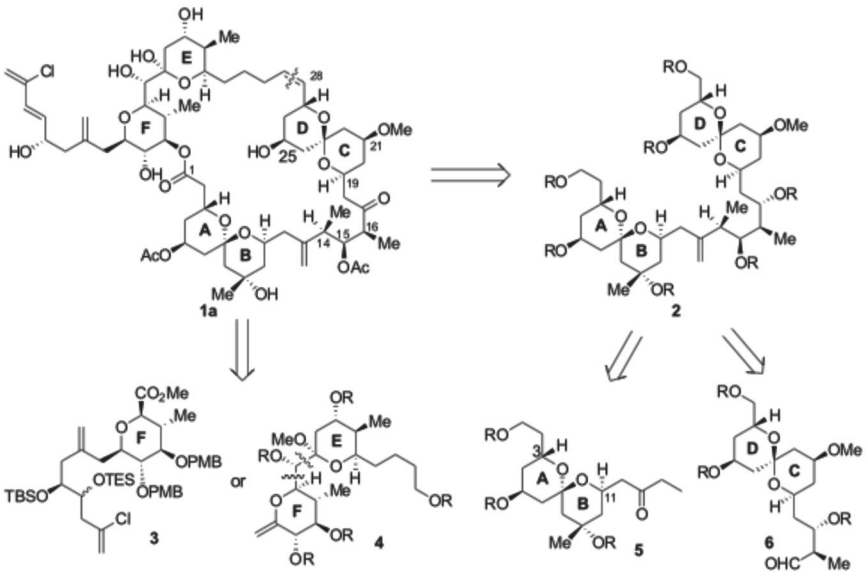


1a: Spongistatin 1 (Altohyrtin A); X = Cl, $R^1 = R^2$ = Ac
1b: Spongistatin 4 (Cinachyrolide A); X = Cl, R^1 = Ac, R^2 = H
1c: Altohyrtin B; X = Br, $R^1 = R^2$ = Ac
1d: Spongistatin 2 (Altohyrtin C); X = H, $R^1 = R^2$ = Ac
1e: Spongistatin 3 (5-Desacetylaltohyrtin A); X = Cl, R^1 = H, R^2 = Ac

Spongistatin 1 inhibits the glutamate-induced polymerization of tubulin with an incredibly low IC_{50} (3.6 nmol dm^{-3})[9c]. This inhibition of mitosis is accomplished not by occupation of the domain utilized by colchicine in its binding to tubulin, but by alternative positioning near the Vinca alkaloid

domain. Spongistatin 4 inhibits L12120 murine leukemia cells with an IC_{50} of <0.6 ng/ml[10]. As a consequence, **1a** and **1b** have given evidence of being among the most potent cancer cell growth inhibitory antimitotic substances uncovered to the present time!

The challenge presented by the total synthesis of the architecturally complex spongipyran macrolides has attracted wide interest, and routes aimed at the stereocontrolled assembly of the AB[20] and CD spiroketal sectors[21], as well as the E and F rings[22] have been defined[23]. However, the masterful total syntheses of (+)-spongistatin 2 by the Evans group[24] and of (+)-spongistatin 1 by Kishi and co-workers[25] established convincingly that the spongistatins and altohyrtins were indeed configurationally identical. Five additional more recent syntheses, of **1d** by Smith[26a–26d], Heathcock[26e,26f], and (formally) Nakata[22v,26g], of **1a** by Paterson[27a] and by Ley[27b], and of both targets by Crimmins[27c] constitute key benchmarks of strategy level design. Our own approach to spongistatin 1 envisioned macrocyclization subsequent to the conjoining of the two bisspiroketal subunits and linkup of suitably functionalized E and F pyran rings. The tactics are expressed retrosynthetically in Scheme 1 where the eastern A–D sector was projected to arise from enantiocontrolled aldol coupling of the proper enolate of ketone **5** with aldehyde **6**. This mode of assembly was selected so as to capi-



SCHEME 1

talize on the thermodynamically advantaged double anomeric arrangement resident in **5**, which was expected to guarantee the equatorial disposition of the side chains positioned at C3 and C11. Beyond this, the logistical demands of appropriately setting the stereocenters in building block **6** were anticipated to be solved by the proper combination of aldol condensations in acyclic precursors. Elaboration of the western sector was envisioned to involve either possible Suzuki–Miyaura cross-coupling to afford **3** or carbonyl addition chemistry to eventually yield enol ether **4**.

Herein we detail the implementation of a plan for the synthesis of subunits **4** to **6** based on the above strategy elements and variants thereof as dictated by the experimental results.

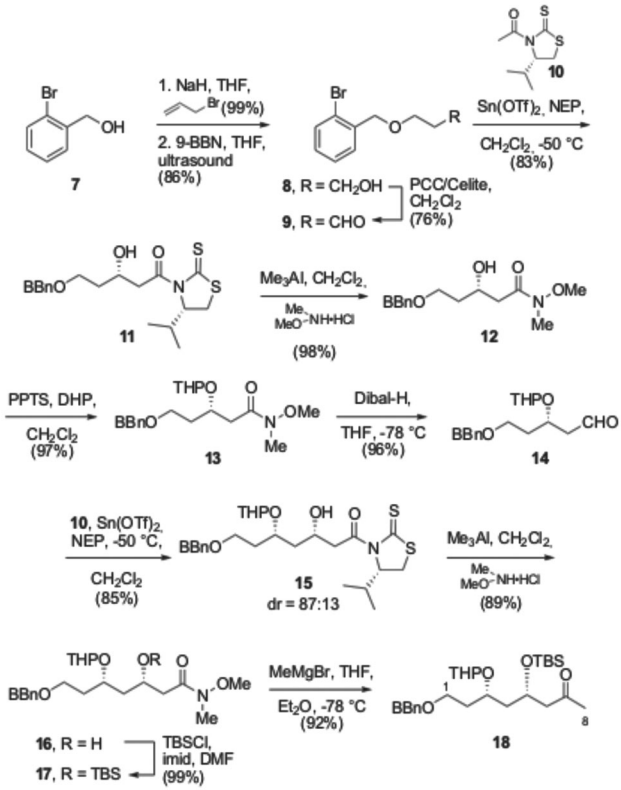
RESULTS AND DISCUSSION

Assembly of the AB Spiroketal. This fragment of the cytotoxic target incorporates C1–C14 and features a [5.5] spirocyclic framework whose stereochemistry at C7 is presumably governed by a thermodynamically favored double anomeric arrangement. If so, those substituents residing at C3 and C11 are equatorially disposed. Beyond this, we envisioned the assembly of **5** to be most gainfully realized by means of an approach that skirts C_2-symmetrical intermediates and passes through properly desymmetrized, enantiomerically pure precursors. Amalgamation of the two acyclic precursors **18** and **27** was considered to be consistent with this synthetic plan.

The first generation route to **14**, detailed in Scheme 2, began with the two-step conversion of commercial 2-bromobenzyl alcohol (**7**) to aldehyde **9** via the carbinol **8**. Alternate attempts to generate **9** by the Michael addition of **7** to acrolein proved unsuccessful. The condensation of **9** with the levorotatory (*S*)-thiazolidinethione **10**[28] under Nagao conditions with tin(II) triflate in the presence of *N*-ethylpiperidine furnished exclusively the aldol product **11** in 83% yield. After significant experimentation, it was made clear that the optimal way to secure aldehyde **14** from this direction was through generation of the Weinreb amide[29], protection of the hydroxyl substituent as its tetrahydropyranyl (THP) ether, and reduction with Dibal-H at –78 °C.

From this point, enantiocontrolled chain extension was realized by repeat application of the Nagao protocol, which generated **15** as an 87:13 ratio of diastereomers. Successful transformation into the corresponding Weinreb amide **16** was followed by protection of the hydroxyl group in the form of its *tert*-butyldimethylsilyl (TBS) ether as in **17**. The need to introduce a methyl group in order to secure **18** was met with methylmagnesium

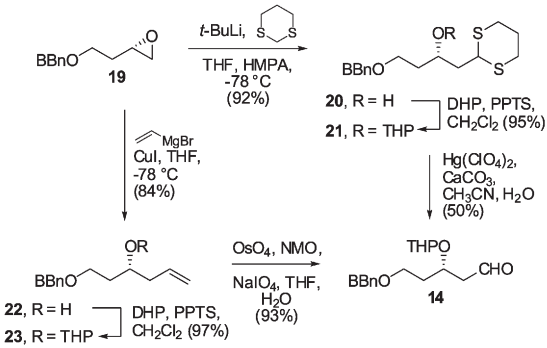
bromide. The two chromatographic purifications that followed the generation of **15** as an 87:13 diastereomeric mixture proved sufficient to deliver pure **18**, the structural features of which were assigned through spectroscopic means and on the basis of well precedented transition state analysis[30].



SCHEME 2

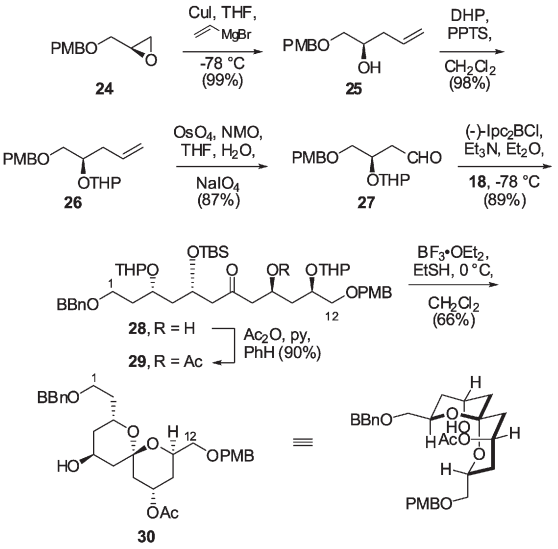
Although the pathway to **14** defined above is characterized by very reasonable efficiency at each step, the sequence is rather long. Consideration was therefore given to the possibility that increased brevity could be achieved. Two alternate, somewhat shorter routes to this aldehyde are outlined in Scheme 3. Both rely on the ready availability of enantiopure oxirane **19** from (*R*)-aspartic acid by the Rapoport protocol[31]. Controlled nucleophilic attack of the dithianyl anion on epoxide **19**[32], followed by exposure to 3,4-dihydropyran in the presence of pyridinium *p*-toluenesulfonate, and treatment with mercuric perchlorate in 9:1 acetonitrile–water buffered with calcium carbonate[20a] furnished **14** in modest yield. An

improved sequence involved initial exposure of epoxide **19** to the vinyl cuprate reagent and arrival at **14** by periodate cleavage of the 1,2-glycol[33].



SCHEME 3

The C9–C12 segment was next elaborated by conversion of the *p*-methoxybenzyl (PMB) ether of (*S*)-glycidol (**24**, 96% ee) to carboxaldehyde **27** in a manner paralleling the **19** → **14** sequence. With two necessary building blocks in hand, their aldol coupling was next entertained (Scheme 4). Although the stereogenicity of the chiral center would appear to carry little import because of pending oxidation to the ketone level, recourse was nevertheless made to a highly (*S*)-diastereoselective reaction[34] for the purpose of simplifying analysis and facilitating spirocyclization

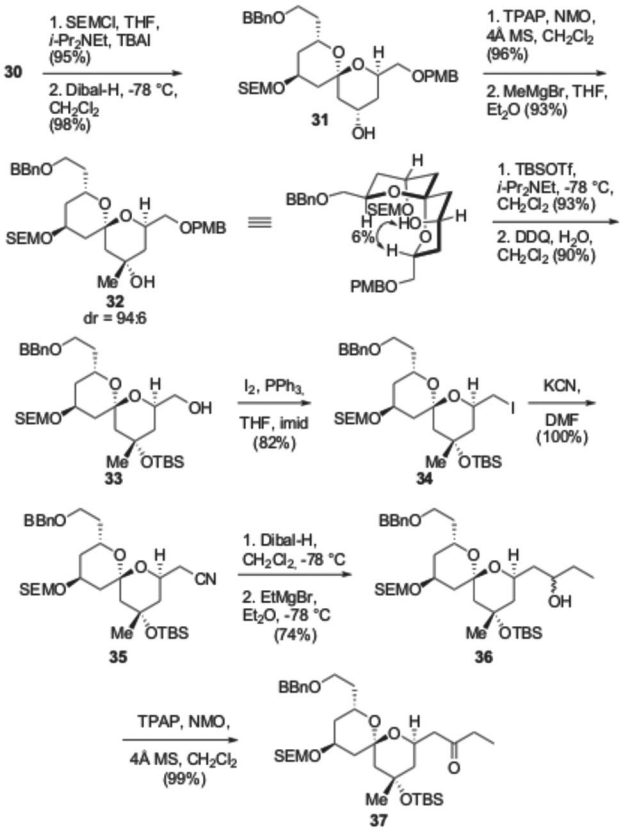


SCHEME 4

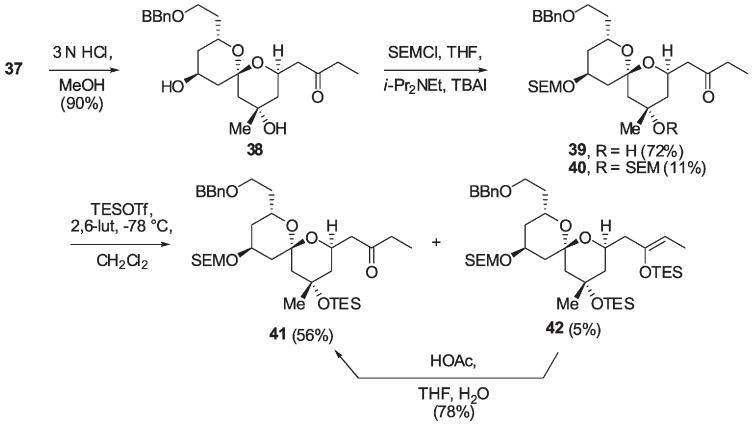
through hydrogen bonding. When a number of accepted methods for the deprotection of THP groups in **28**[35] were unexpectedly found not to result in ring closure, we made recourse to the reagent combination consisting of boron trifluoride etherate and ethanethiol in CH_2Cl_2[36]. Under these conditions, the desired transformation did occur, but with concomitant cleavage of the TBS protecting group[37]. Further studies involving the resulting diol (viz. deacetoxy **30**) were not pursued because of an anticipated inability to distinguish chemically between the two secondary hydroxyl groups. An experimentally valid alternative materialized in the form of acetylation prior to cyclization. This tactic resulted in the conversion of **29** to **30** in 66% yield and provided an advanced intermediate amenable to X-ray crystallographic analysis[20g]. The absolute configuration of **30** was thereby confirmed to be fully as expected.

Next, the structural modification of **30** so as to generate **37** in an unambiguous fashion was undertaken. The remaining OH functionality was masked as its SEM ether[38] prior to reduction with Dibal-H to furnish **31** (Scheme 5). Ensuing perruthenate oxidation[39] provided the corresponding ketone, which responded to the action of methylmagnesium bromide in a very diastereoselective fashion (94:6) by way of equatorial attack to make **32** available in 93% yield. The diastereoselectivity of the 1,2-addition process was readily confirmed by COSY and nOe analysis. The tertiary nature and axial disposition of the newly generated hydroxyl substituent required recourse to a silyl triflate[40] for protection purposes. Following introduction of a TBS group in this manner, the primary carbinol **33** was acquired by DDQ oxidation. Both steps proceeded in a highly efficient manner. At this point, it proved possible to prepare the primary iodide **34** and to bring about homologation of the side chain by SN2 displacement with cyanide ion. Our concern for potential complications arising from β-elimination within **35** prompted its direct transformation into the ethyl ketone **37** by a three-step sequence comprised of Dibal-H reduction to the aldehyde, 1,2-addition of ethylmagnesium bromide without delay, and perruthenate oxidation[39].

Our intent was to carry the TBS group present in **37** through to the end of the synthesis. We subsequently became aware of the fact that this deprotection could not be successfully implemented in the late stages when most of the spongistatin structure had been established[41]. Therefore, the substitution of a triethylsilyl (TES) group at this site was undertaken. Attention was turned initially to the acidic hydrolysis of **37** with 3 M HCl in methanol. As expected, no selectivity was observed and diol **38** was isolated in 90% yield (Scheme 6). Treatment of **38** with a slight excess of SEM chlo-



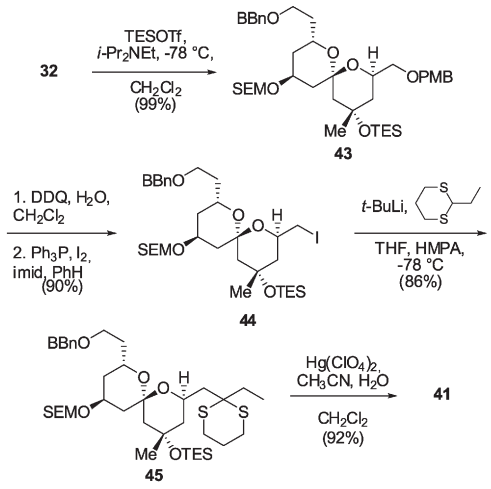
SCHEME 5



SCHEME 6

ride in the presence of tetra-*n*-butylammonium iodide gave predominantly **39** along with significantly lesser quantities of the two-fold *O*-alkylated product **40**. Reaction of **39** with TES triflate in the presence of Hünig's base afforded **41** in 56% yield along with 5% of silyl enol ether **42**. The latter could readily be converted into **41** by selective hydrolysis in dilute aqueous acetic acid.

Although the studies defined in Scheme 6 demonstrate that the critical exchange of protecting groups is clearly feasible, the tactics implemented for this purpose are hardly economical of steps. A more efficient route to **41**, defined in Scheme 7, begins with the efficient low-temperature conversion of **32** to the TES derivative **43** in advance of conversion to primary iodide **44** (90% over two steps). Coupling of **44** to lithiated 2-ethyl-1,3-dithiane[42] at –78 °C in THF containing HMPA proved well suited to the generation of **45** without concurrent E_2 elimination[22v,26]. Hydrolysis of **45** with hydrated mercury(II) perchlorate according to a predescribed protocol[43] made **41** readily available.

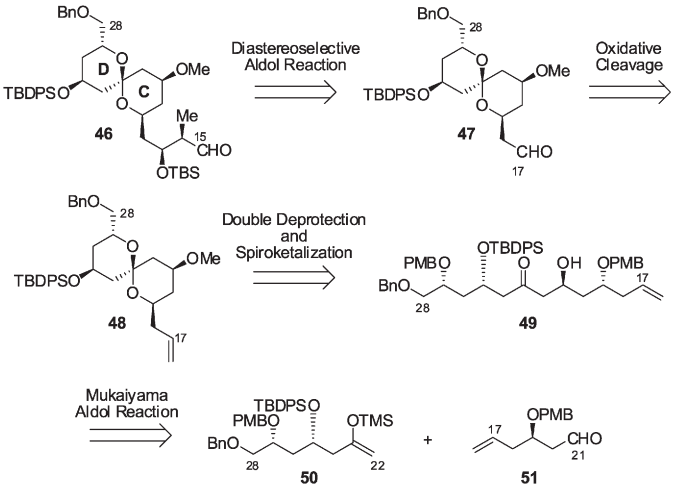


SCHEME 7

Enantioselective Synthesis of the CD Spiroketal Component

From the outset, the successful elaboration of the AB sector was to be complemented by a concise, convergent and highly stereocontrolled route to the CD subunit consisting of C17–C28. The retrosynthetic analysis presented in Scheme 8 indicates that reliance was to be placed on a diastereoselective *syn*-aldol condensation to set the two side chain stereocenters in target compound **46**. Aldehyde **47** was to be obtained in turn by oxidative

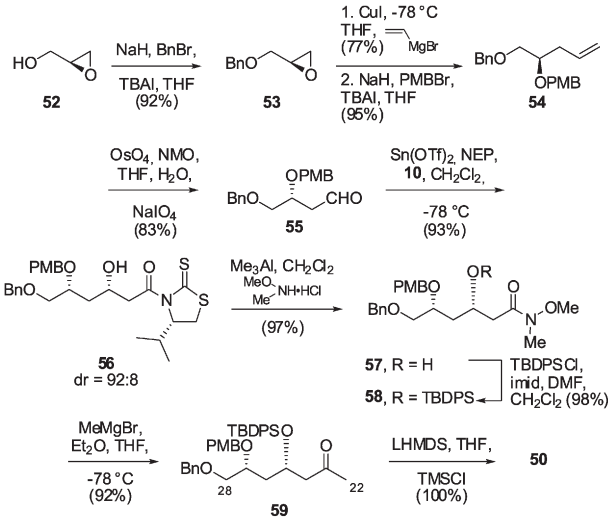
cleavage of the double bond in spiroacetal **48**. The key step was considered to be the two-fold PMB-group deprotection within hydroxy ketone **49** that would hopefully trigger a spontaneous, thermodynamically controlled spirocyclization. This open-chain intermediate was to be prepared stereoselectively by a Mukaiyama reaction[44] between silyl enol ether **50** and aldehyde **51**.



SCHEME 8

The acquisition of **50** began with commercially available (*S*)-(–)-glycidol **52**, which was transformed into its benzyl ether **53** under conventional conditions[45]. Regioselective opening of the oxirane ring[46] with vinylmagnesium bromide in the presence of CuI was followed directly by conversion[47,48] to the PMB ether **54** (Scheme 9). Following the exposure of **54** to catalytic levels of OsO_4 in the presence of NMO as co-oxidant[49], the resulting diastereomeric diols were cleaved with sodium periodate[50] to afford the desired aldehyde **55**.

Introduction of a second chiral center was undertaken with the tin enolate of the Nagao auxiliary **10** derived from L-valine[51]. Under these conditions, **56** was formed smoothly with high diastereoselectivity (92:8). The success of this transformation was matched by that involving conversion to the corresponding Weinreb amide **57** (97% yield)[52]. Protection of the secondary hydroxyl group in this product as its TBDPS ether[53] proceeded very slowly at room temperature even in the presence of DMAP. Appreciable acceleration was noted in a dichloromethane/DMF solvent mixture at reflux (98% yield of **58**). Following the addition of methylmagnesium bro-

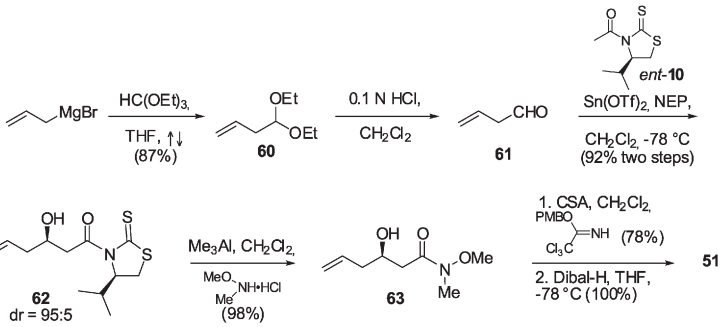


SCHEME 9

mide[29,52] to **58** in order to generate methyl ketone **59**, regioselective enolization and in situ *O*-silylation was accomplished with the bulky lithium hexamethyldisilazide base in the presence of chlorotrimethylsilane[54]. The very high purity of **50** so formed enabled it to be used without any recourse to chromatography. The ten-step conversion of **52** to **50** is notable in that it proceeds with an average yield of 93% for each step.

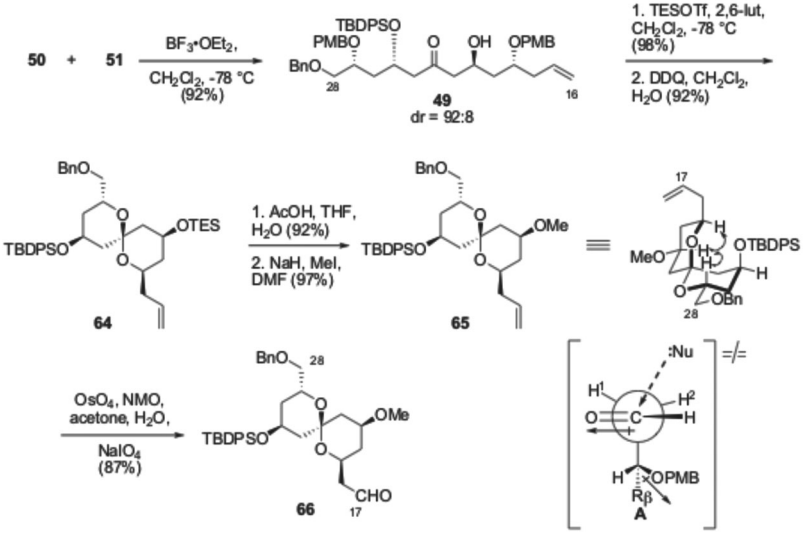
The complementary right half of **49** was crafted from the previously described 3-butenal **61**[55]. For our purposes, the isolation of this low-boiling β,γ-unsaturated aldehyde was skirted by simple extraction of the acid hydrolysis mixture and drying of the combined organic phases prior to use. Since no solvent evaporation was involved, mechanical losses of this starting material were minimized (Scheme 10). In light of the convenience and reliability of the Nagao aldol reaction[30], this protocol was selected for generation of the third resident chiral center. Consonant with earlier examples, the condensation of *ent*-**10** with **61** led to thiazolidinethione **62** as the major product with excellent diastereoselection (95:5). It is noteworthy that the very mild conditions of this aldol reaction do not induce double bond migration within the sensitive aldehyde **61**. As before, the transamidation leading to **63** once again proceeded smoothly. In contrast, subsequent introduction of the PMB protecting group proved to be uncharacteristically difficult. Not unexpectedly, the sodium hydride/DMF conditions proved too basic. However, the trichloroacetimidate alternative, as catalyzed by camphorsulfonic acid in dichloromethane[56], gave a 78% yield of the pro-

tected alcohol alongside unreacted **63** (22%). Finally, low-temperature reduction with Dibal-H in tetrahydrofuran[57] gave aldehyde **51** of high purity (^{1}H NMR analysis). Thus, the sequence from allylmagnesium bromide to **51** traverses six transformations at an average yield per step of 92%.



SCHEME 10

With the cross-coupling partners **50** and **51** in hand, their proper amalgamation was effected by way of catalysis with boron trifluoride etherate[58]. Advantage was taken of the ability of the β-OPMB substituent present in the aldehyde to guide 1,3-stereoinduction heavily in the *anti* direction (Scheme 11)[59–63]. In agreement with precedent[64], this effect proved to be operative, and **49** was produced with a facial bias in excess of 92:8. As



SCHEME 11

a consequence of the interplay of those dipole moments depicted in **A**, only one side of the carbonyl group is available for attack by the incoming nucleophile.

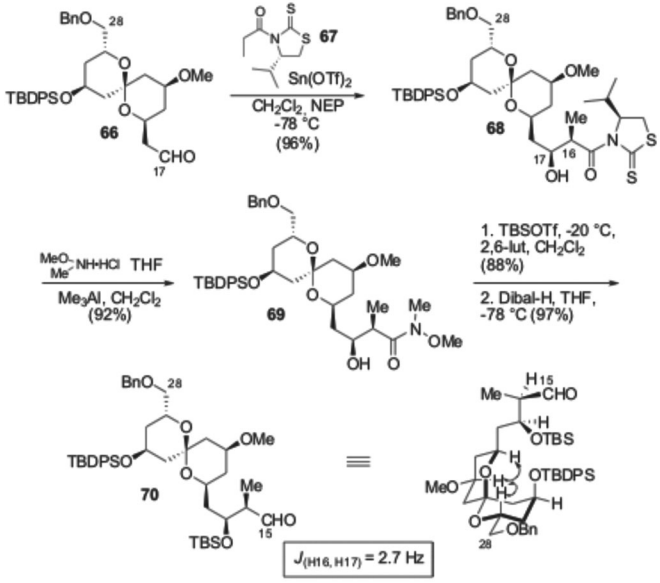
The time had now arrived to effect the spirocyclization. Rather unexpectedly, the treatment of **49** with DDQ in a dichloromethane–water solvent system[65] did not afford the desired product. TLC analysis of the reaction mixture indicated formation of very polar material, presumably the triol. We considered a possible reason for kinetic retardation of the ring closure to be the presence of a free hydroxyl at C21, which by way of intramolecular hydrogen bonding, could hamper proper functional group interaction. Indeed once the OH group was masked as its TES derivative[66], the conversion to **64** proceeded very efficiently (92%). Chemoselective cleavage of the TES ether was readily accomplished with aqueous acetic acid in THF[67], thereby making possible conventional *O*-methylation[68] only at C21 to yield **65** (98%). Alternatively, aldol **49** can be directly *O*-methylated at C21 (Me_3OBF_4, proton sponge, CH_2Cl_2) and treated with DDQ to give rise to spiroacetal **65** efficiently. In contrast to the complications experienced by several research groups involved in the synthesis of spongistatin 1[20j,k;21a,b,d,e;22s;24b,d], the present route avoided the problem of non-selective spiroketal formation. In our view, this success stems from the presence of a sterically demanding TBDPS protecting group at C25, which apparently serves as an effective control element during ketal formation.

At this stage, proof of the absolute configuration of **65** was secured with the help of nOe experiments as shown. The diagnostic 300 MHz ^{1}H NMR spectrum in C_6D_6 solution nicely corroborates each of the stereochemical expectations. Thus H19 (δ 3.85) exhibits a significant (6%) nOe interaction with H21 (δ 3.60), and neither of these protons resides in close proximity to H25 (δ 4.18). These data require that H19 and H21 be axially disposed. Furthermore, H27 (δ 4.24) interacts with H21 (6%), thereby mandating axial residency for H27 as well. Finally, selective irradiation of H27 gave rise to a nOe interaction (2%) with the phenyl protons of the TBDPS group. These features and the equatorial nature of H25 appear to mimic the conformation of the CD sector present in **1**[11a].

Cleavage of the double bond in **65** to arrive at aldehyde **66** was best realized by OsO_4-promoted dihydroxylation followed by periodate cleavage of the diastereomeric diol mixture.

Side Chain Elaboration on the CD Spiroketal Ring System

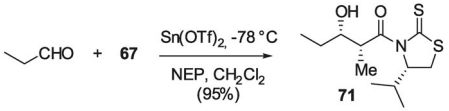
With the ready availability of aldehyde **66** in quantity, the next order of business was to properly establish the stereogenic centers positioned at C16 and C17. To this end, the $Sn(OTf)_2$-promoted aldol reaction of **67** with **66** was carried out (Scheme 12). The only isolated product, expected to be **68**, was isolated in 97% yield. Elucidation of the *syn* arrangement of the methyl and hydroxyl substituents was approached by way of detailed NMR analyses (300 MHz, C_6D_6). The small coupling constant of 2.7 Hz between H16 and H17 suggested the presence of a *syn* relationship[69]. However, the question of absolute configuration persisted. To address this question, the



SCHEME 12

model reaction between **67** and propionaldehyde was implemented in the expectation that the *Z*-enolate of the thiazolidinethione would again be formed and enter into the aldol reaction via a chelated chair-like transition state[70]. Excellent kinetic control was operative and only **71** was produced in 96% yield (Scheme 13). Particularly useful to us was the high crystallinity of this yellow solid, which permitted unequivocal definition of the absolute stereochemical relationships by X-ray methods[20h].

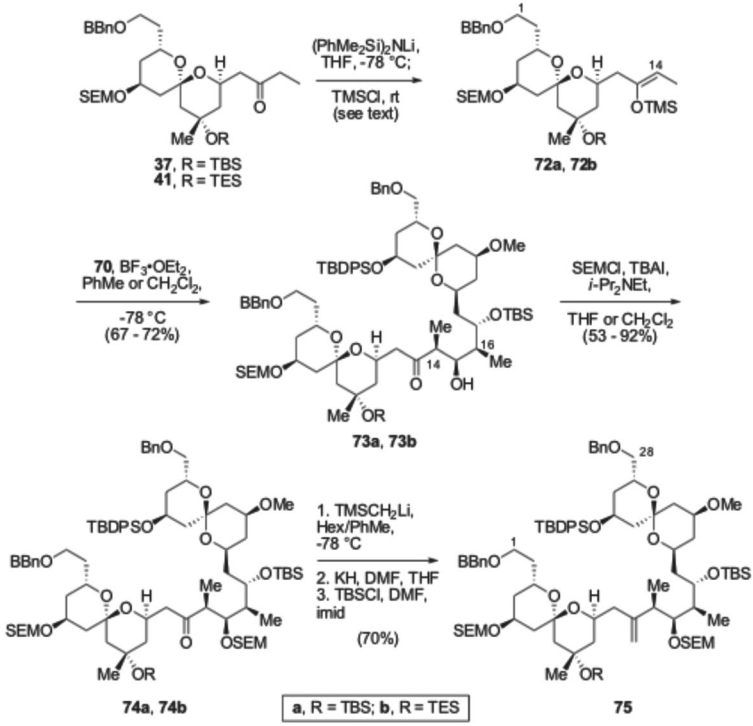
To set the stage for covalent bonding to the AB subunit, **68** was subjected to clean transamidation for the purpose of arriving at Weinreb amide **69**. Subsequent masking of the hydroxyl as a TBS ether allowed for reductive conversion to the targeted aldehyde **70**. We note here that **70** was generated from (*S*)-glycidol in 23% yield over 21 steps (93% average yield).



SCHEME 13

Construction of the Complete C1–C28 Sector

Although several synthetic strategies for amalgamation of the AB and CD building blocks were initially pursued[37], recourse was ultimately made to the conjoining of ketones **37** and **41** to aldehyde **70** via a Mukaiyama aldol reaction[44]. Scheme 14 depicts the route developed to arrive at **75**. Initially,



SCHEME 14

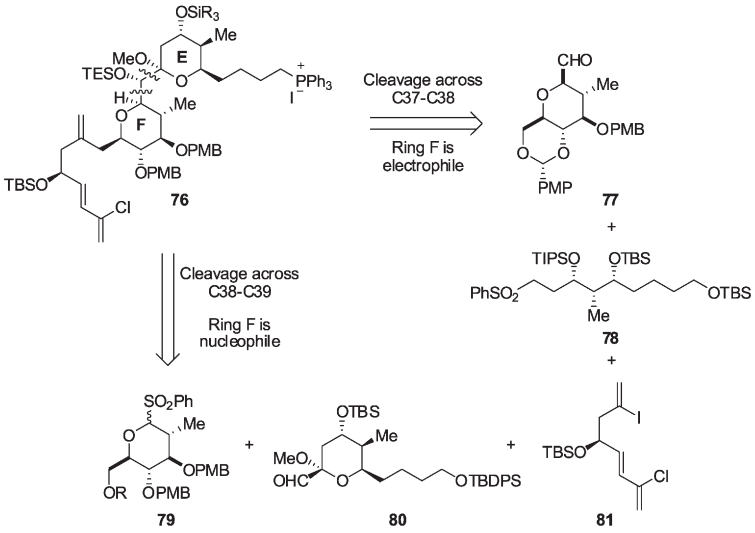
the **a** (R = TBS) and **b** (R = TES) series were advanced simultaneously. However, when it was made known that insurmountable difficulties had been encountered elsewhere[22v,26] in the attempted removal of a similarly positioned TBS protecting group, our focus was restricted exclusively to the TES derivatives.

The two-step procedure for arrival at **73** involved initial conversion of **37** and **41** to their *Z*-enolsilanes according to the Masamune protocol[71]. Very high levels of regio- and stereocontrol (>99:1) were realized through the agency of the bulky bis(phenyldimethylsilyl)amide base. When **72a** and **72b** were purified chromatographically, severe material losses were incurred. When exposure to an adsorbent was skirted and the unpurified enol ethers were treated directly with **70** in the presence of boron trifluoride etherate, the yields of **73** (67–72%) proved to be quite satisfactory. When this aldol reaction was performed at –78 °C, *syn* selectivity was observed as expected, leading to proper installation of absolute configuration at C15 and C16. The assignment of stereochemistry was addressed by ^{1}H NMR analysis of the acetate of **73a** in C_6D_6 solution at 500 MHz. The *syn* relationship between H14 (δ 2.88) and H15 (δ 4.22) was readily deduced on the basis of the low magnitude (2.8 Hz) of the corresponding coupling constant. Similarly, the significant spin–spin interaction between H15 and H16 (9.2 Hz) unequivocally defined their *anti* relationship. No added confirmation was secured and the assignment should therefore be regarded as tentative. Following selection of the SEM protecting group[38], it became necessary to effect methylenation of the ketone carbonyl at C13. Although this transformation proved to be problematic when a variety of direct methods (Tebbe[72,73], Lombardo[74], Wittig[75], Nysted[76], Cp_2ZrCl_2[77], etc.) were applied, the Peterson olefination[78] proved itself to be reliable and reproducible under the proper circumstances. However, initial recourse to Me_3SiCH_2Li in THF gave rise to no reaction as a consequence of wholesale enolization, as recognized by the formation of a deep red color. Alternate use of the nonpolar solvent system 1:1 toluene/hexanes at –78 °C resulted instead in efficient formation of the adduct. Treatment of the resulting α-hydroxysilane with KH in 10:1 THF/DMF led to clean elimination, but with some concurrent removal of the TBS protecting group. Consequently, reprotection was routinely practiced in advance of the isolation of **75** (70% overall).

Retrosynthetic Analysis of the Western Region

Two imperatives directed our earliest thinking in this phase of the investigation. Certainly, our planned routes should be as distinctive as possible

and differ intrinsically from earlier precedent. As well, we looked forward to the implementation of two complementary pathways (Scheme 15). Cleavage across C37–C38 would mandate the evaluation of ring F as the electrophilic reaction partner **77**. Hopefully in this way we could assess the feasibility of engaging sulfone **78** in 1,2-addition to this aldehyde. Also to be focused on was alternative dissection of the C38–C39 bond in **76**, such that sulfone **79** might be coupled to the highly functionalized tetrahydropyranyl aldehyde **80**. In both cases, we remained mindful of the fact that the chlorodiene side chain had to be assimilated at a more advanced point in the total synthesis. At this juncture, vinyl iodide **81** was regarded to be a potentially useful prospect.

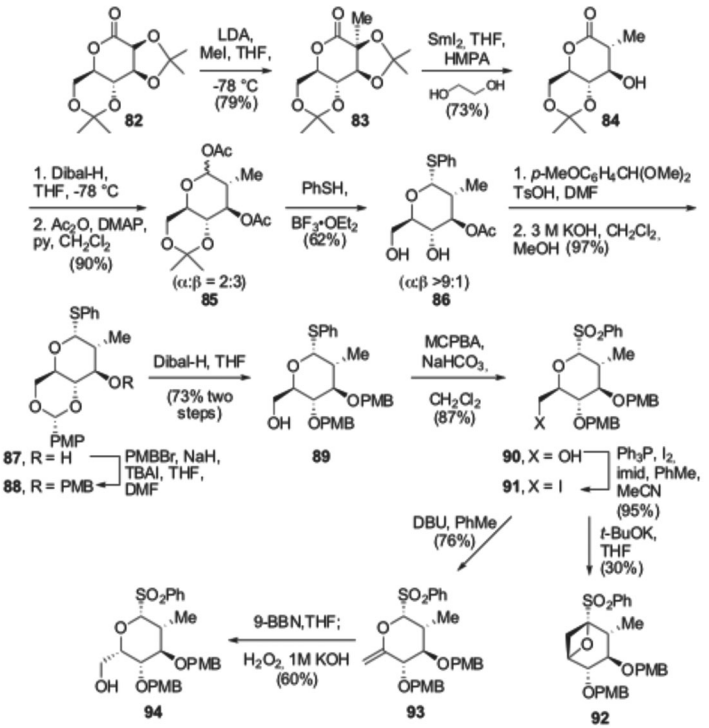


SCHEME 15

Synthesis and Chemistry of 2-(Phenylsulfonyl) Pyrans

Pursuit of the second retrosynthetic option outlined in Scheme 15 required that attention be paid to the preparation of oxidized derivatives of thioglycoside **89** (Scheme 16). To this end, we made recourse to the readily available lactone **84**. Sequential acid-catalyzed two-fold ketalization and Swern oxidation of D-mannose gave **82**[79]. As a consequence of the α-oxygenated nature[80] of the lactone carbonyl in **82** and the possibility that the derived enolate anion could undergo β-elimination, serious reservations existed with regard to the base-promoted α-methylation of **82**. We were therefore delighted to uncover that the desired conversion to **83** was partic-

ularly facile[81]. Reduction of **83** with samarium iodide as the electron-transfer reagent[82] accomplished concurrent α-deoxygenation and loss of acetone to liberate the C3 hydroxyl as in **84**. Its hydroxyl function need not be masked during Dibal-H reduction to the lactol level, thereby providing the opportunity for dual acetylation. Diacetate **85** was obtained as an inseparable 2:3 mixture of α- and β-anomers (^{1}H NMR analysis). Treatment of **85** with boron trifluoride etherate in the presence of thiophenol resulted in the formation of **86** with enhancement of the diastereotopic modality to >9:1 in favor of the α-sulfide. Since cleavage of the ketal in **85** is competitive with thiol capture, routine use was made of an excess of boron trifluoride etherate in order to unmask the pair of hydroxyl groups to the maximally elevated level. This reactivity pattern allowed for direct formation of *p*-methoxybenzylidine acetal **87**, whose transformation into the bis-PMB alcohol **89** was accomplished in a two-step sequence capped by a regiodirected Dibal-H reduction of the *m*-dioxane ring. In contrast to other alternatives, this sequence of steps proved uneventful and allowed for the



SCHEME 16

subsequent implementation of peracid oxidation to generate the hydroxymethyl sulfone **90**. The axial nature of the $PhSO_2$ group rests securely on the small magnitude of the coupling constant registered for the interaction of H2 and H3 ($J_{ax\text{-}eq}$ = 5.3 Hz).

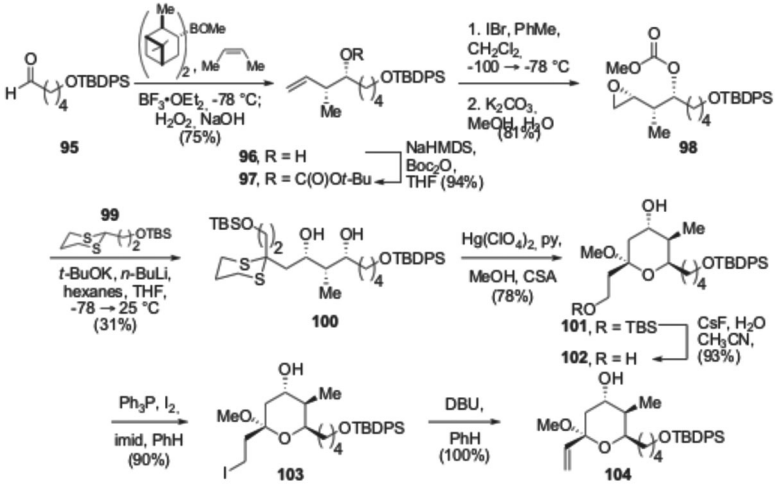
We were now positioned to introduce an exocyclic double bond at C6 in order to allow for possible Suzuki–Miyaura coupling between the F-ring fragment and a trienyl side chain. Although iodide **91** was secured by exposure of **90** to the action of triphenylphosphine and elemental iodine in the presence of imidazole, attempts to accomplish E_2 elimination within **91** proved more problematic than anticipated. For example, the addition of **90** to a solution of potassium *tert*-butoxide in THF gave rise to oxetane **92** in 30% yield alongside a myriad of other products that were left unidentified. On the positive side, the desired conversion to **93** could be accomplished with moderate efficiency by heating with DBU in toluene.

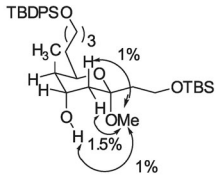
Submission of **93** to conventional hydroboration with 9-BBN afforded uniquely **94** rather than the desired diastereomer **90**. Experiments conducted at 100 °C for prolonged reaction periods did not alter the stereochemical outcome. Operating on the belief that this eventuality may arise as a result of the axial orientation of the $PhSO_2$ substituent, we undertook efforts to equilibrate the anomeric carbon in **93** to no avail, in line with precedent[83]. The manner in which this complication was bypassed is discussed later.

Route Selection for Ring E Construction

To continue the projected route to **1a**, we had need for a heavily functionalized E-ring subtarget akin to **80**. Generation of aldehyde **95** from pentane-1,5-diol initiated the effort. The stereocontrolled four-carbon chain extension to deliver alcohol **96** (Scheme 17) took advantage of the reliability provided by (–)-*B*-methoxydiisopinocampheylborane, boron trifluoride etherate and *cis*-2-butene under strongly basic conditions to provide the *syn* homoallylic alcohol **96**[84]. Following generation of the mixed BOC carbonate **97**[85], iodocyclization by way of IBr[86] set the stage for arrival at epoxy ester **98** upon treatment with K_2CO_3 in aqueous MeOH[87]. The union of **98** with the lithiated anion of dithiane **99** proved to be a somewhat erratic process, advancing to **100** with modest efficiency (31%) under the conditions specified in the scheme. This assembly step was followed by conversion to the functionalized tetrahydropyran **101**, a maneuver best accomplished through the use of mercuric perchlorate in aqueous pyridine containing a catalytic quantity of camphorsulfonic acid[43b]. The stereo-

chemistry of **101**, readily deduced to be as in **B** on the basis of nOe experiments, conforms to expectations based on the anomeric effect.

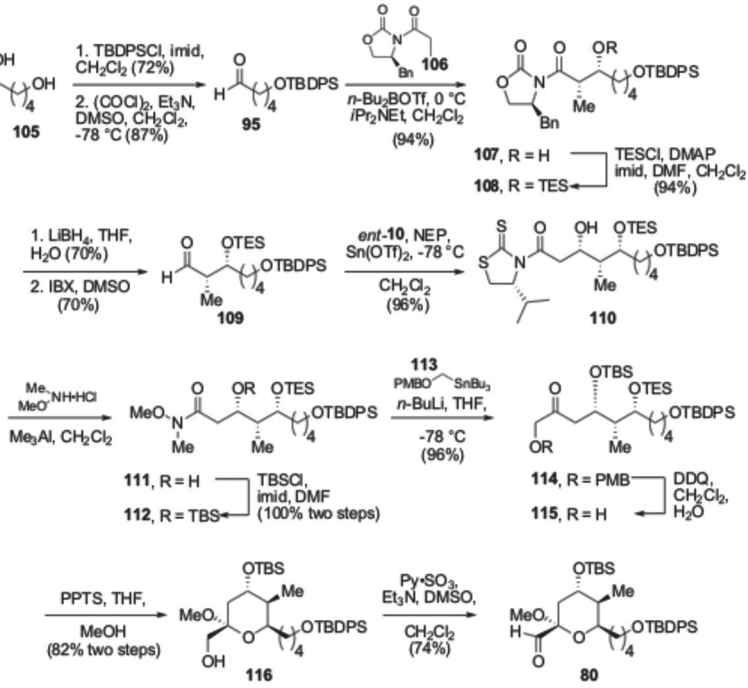




SCHEME 17

Heating **101** with cesium fluoride in 9:1 acetonitrile–water for 4 days made available diol **102**, the primary hydroxyl functionality in which could be selectively transformed into iodide **103** in advance of E_2 elimination promoted by DBU in benzene at reflux. The conversion to **104** proceeded quantitatively. Quite unexpected, however, was our inability to protect the hydroxyl at C4 in **104**. When **101** proved to be equally recalcitrant to various masking protocols, we recognized that the axial orientation of this OH group (see **B**) was bringing into play sufficient steric congestion so as to make this step kinetically unrewarding. Consequently, the alternative thrust depicted in Scheme 18 was pursued. We first implemented the monosilylation of pentane-1,5-diol (**105**) with *tert*-butyldiphenylchlorosilane[88] (TBDPSCl) and followed with a Swern oxidation[89]. Pentanal **95** was then brought into reaction with the dibutylboron enolate of **106**[90,91],

thereby giving rise to the enantiopure *syn* aldol **107** as a single diastereomer in 94% yield (Scheme 18). The newly formed hydroxyl group in **107** was also transformed into a TES ether to conform with our projected stratagem for the simultaneous unmasking of hydroxyl functionalities at a later stage. The subsequent lithium borohydride reduction and *o*-iodoxybenzoic acid (IBX)[92] oxidation of **108** resulted in conversion to the homologated aldehyde **109**, thus setting the stage for a second iteration of the aldol process using the Nagao protocol[28]. In the event, the tin(II) enolate of *ent*-**10** functioned very efficiently to furnish **110** as the single diastereomer shown (96%). Once **110** was in hand, its two-step conversion to **112** was brought about by transamidation to Weinreb amide **111** and generation of the TBS ether.

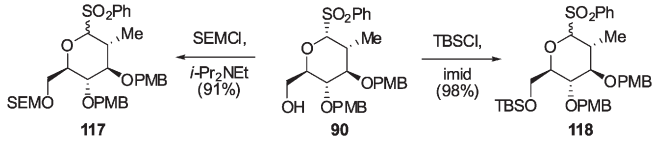


SCHEME 18

Treatment of **112** with the lithium reagent produced by transmetalation of **113**[93,94] with *n*-BuLi gave rise to **114**. This reaction is very temperature dependent and considerable attention to detail is necessary to achieve a 96% yield of the ketone product. Removal of the PMB group in **114** to give **115** was expected to allow for subsequent acid-catalyzed cyclization. In-

deed, conversion to the anomerically homogeneous methyl acetal **116** was smoothly accomplished in 82% overall yield. Oxidation to aldehyde **80** was subsequently brought about with the Parikh–Doering reagent[95].

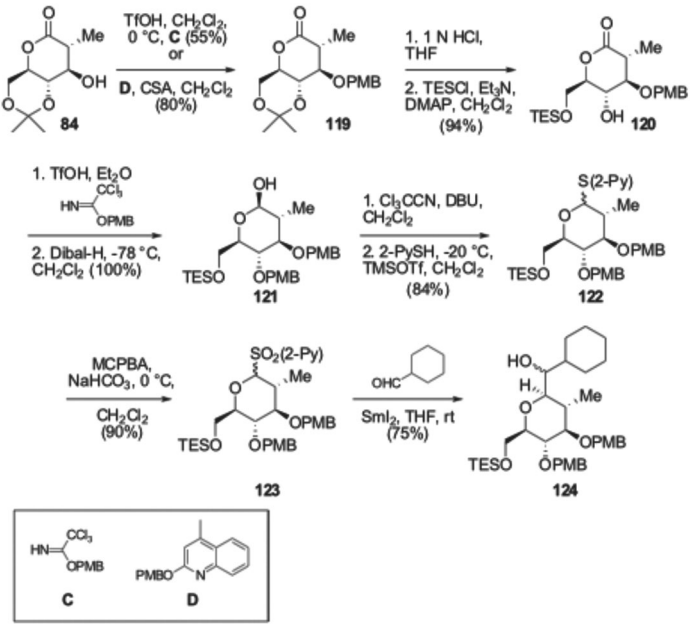
At this point, it was our intention to couple **80** with a protected form of sulfone **90** via the corresponding carbanion. The feasibility studies involved both **117** and **118** (Scheme 19). Following the deprotonation of both intermediates with a variety of bases (LDA, *n*-BuLi, *t*-BuLi, MeMgBr, PhLi, mesityllithium) and admixture with **80** under a variety of conditions, no evidence was obtained that the targeted C–C bond formation had taken place. The failure of these reactions proved contrary to results defined in similar sterically congested substrates[22m] and led us to screen simpler aldehydes such as CH_2O, PhCHO, and *t*-BuCHO. The possibility that these failures stem from the low reactivity of the sulfone prompted companion investigation of the 2-pyridyl congener **123**. This modification would allow the fusion of rings E and F to be effected instead via a samarium iodide-induced Barbier reaction[96].



SCHEME 19

The route to **123** that was developed (Scheme 20) capitalized on the ability of unstable trichloroacetimidates[97] to give 2-pyridyl sulfides when treated with 2-mercaptopyridine and a catalytic amount of trimethylsilyl triflate[98]. Readily available **84** can be protected as its PMB ether **119**. Due to the potential β-elimination, acidic or neutral conditions were exploited. While use of PMB-trichloroacetimidate was effective, removal of the amide byproducts was far from trivial and led to complications in subsequent chemistry. Exploitation of the lepidine derivative allowed for facile access of **119**[99]. Hydrolysis of the acetonide and subsequent silyl protection of the primary alcohol yielded **120**, which could undergo another PMB protection, followed by hemiacetal formation. Following the oxidation of **122**, we were in a position to exploit the interesting coupling involving samarium iodide. When this reaction was applied to cyclohexane carboxaldehyde, carbinol **124** was obtained in 75% yield as a 3:1:1 mixture of diastereomers. However, the adaptation of this chemistry to aldehyde **80** proved singularly unconstructive. The magnitude of this effort was extensive and included demonstration of the fact that nickel(II) iodide was also ineffective as a pro-

moter[96d]. These experiments have seemingly demonstrated the heightened steric screening in **80** to be a serious deterrent to attack at its carbonyl group. The development of a different route was therefore mandated.



SCHEME 20

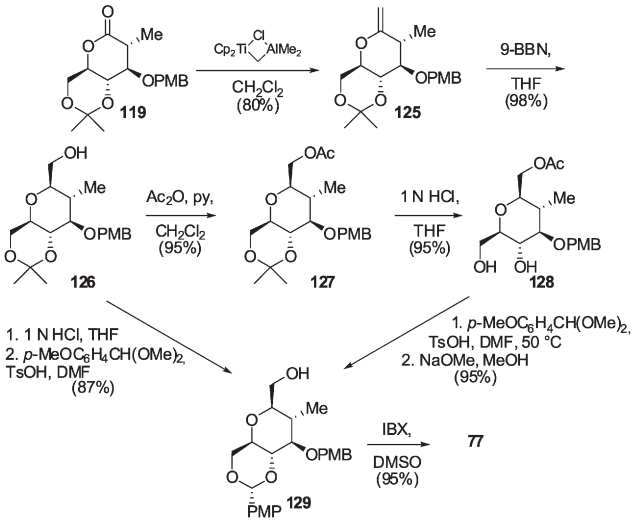
*Synthesis of Aldehyde **77***

One of the more interesting alternative possibilities for constructing the western sector of spongistatin 1 involves application of the Suzuki–Miyaura cross-coupling of an alkylborane to a vinyl iodide[100]. More specifically, the palladium-catalyzed conjoining of a borane derived from a suitable 2-methylenepyran (see **4**) and **81** held the prospect of a convenient approach to installation of the C44–C45 bond that links the chloro-diene side chain to the E/F segment. In the nearly twenty years since its discovery[101], this reaction has seen ever-increasing application in total synthesis[102], although it had not previously been utilized in pursuit of spongipyran marine macrolides.

It was further conjectured that this approach could develop along two avenues. The Suzuki–Miyaura step could be performed after proper amalgamation of hydropyrans E and F (see **4**). The second option would entail

incorporation of the side chain into an extensively functionalized F-ring building block with subsequent union to ring E (see **3**). A description of both approaches follows in this section.

Operationally, the route to **77** began with the readily available PMB-protected lactone **119**. The carbonyl was converted to the olefin with the Tebbe reagent[72,73] to effect conversion to **125** (Scheme 21), which was hydroborated immediately so as to avoid adventitious rearrangement with internalization of the double bond. With arrival at **126**, all five stereogenic centers about the hydropyran ring had been set in their proper absolute configuration.



SCHEME 21

The remaining issues to be addressed included a change in the nature of the acetal protecting group. While the acetonide moiety was quite amenable to acidic hydrolysis, concern over other possible side reactions during subsequent exposure to *p*-methoxybenzaldehyde dimethylacetal prompted initial advancement by way of acetate **127**. The conservative three-step sequence interconnecting **127** with **129** was subsequently improved upon by a more direct routing from **126** as shown. IBX[92] was exploited for the oxidative conversion of **129** to **77**.

*Formation of the Sulfone Fragment **78***

To generate the desired sulfone, we first implemented the monosilylation of pentane-1,5-diol (**105**) with TBSCl[88] and followed with a Swern oxidation[89]. The conversion of **105** to **136** closely parallels the pathway from **105** to **110** developed earlier, with proper proviso for a different array of protecting groups. The subsequent lithium borohydride reduction and Swern oxidation[89] of **132** resulted in conversion to the homologated aldehyde **133**, thus setting the stage for a second aldol process in the sequence. Adaptation of the Evans protocol involving the (*S*)-configured *N*-acetyloxazolidinone proceeded sluggishly and was maximized at 50% of **135**. As a direct consequence of this limitation, we turned to the Nagao alternative[28]. Since the first of these aldols proceeds through a non-chelated transition state such as **E** and the second is highly chelated (see **F**), the thiazolidinethione must be constituted of the opposite configuration to the oxazolidinone (Fig. 1). The tin(II) enolate of *ent*-**10** thus functioned very efficiently to furnish **136** as the single diastereomer shown (91%).

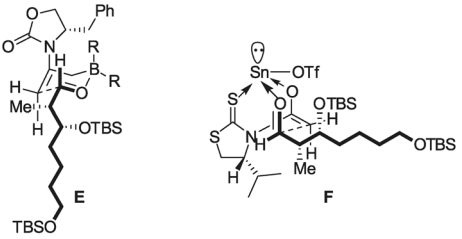
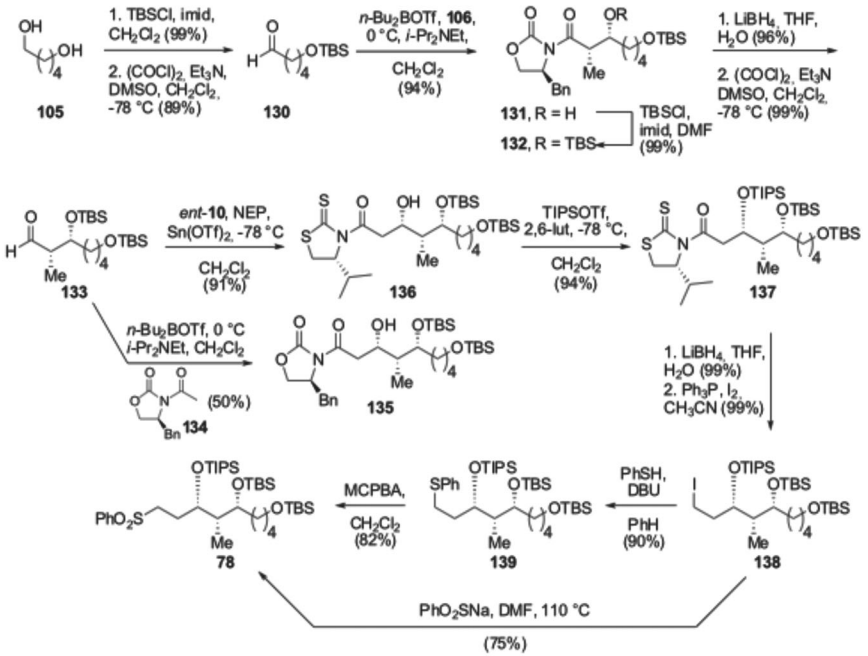


FIG. 1

The availability of **136** translated into a relatively direct route to the targeted sulfone. Protection of the free hydroxyl as the triisopropylsilyl (TIPS) ether as planned was followed by efficient reductive cleavage of the thiazolidinethione. The subsequent generation of iodide **138** provided the opportunity to compare a two-step sequence to generate **78** relative to a one-step alternative (Scheme 22).

*The Status of **E**/**F** Assembly Involving Sulfone **78** and Aldehyde **77***

As a specific version of an operational route to **76** (Scheme 15), we next studied the usefulness of combining the readily available sulfone **78** to the heavily functionalized pyranyl aldehyde **77**. After considerable experimentation, it was recognized that the presence of HMPA as an additive was es-

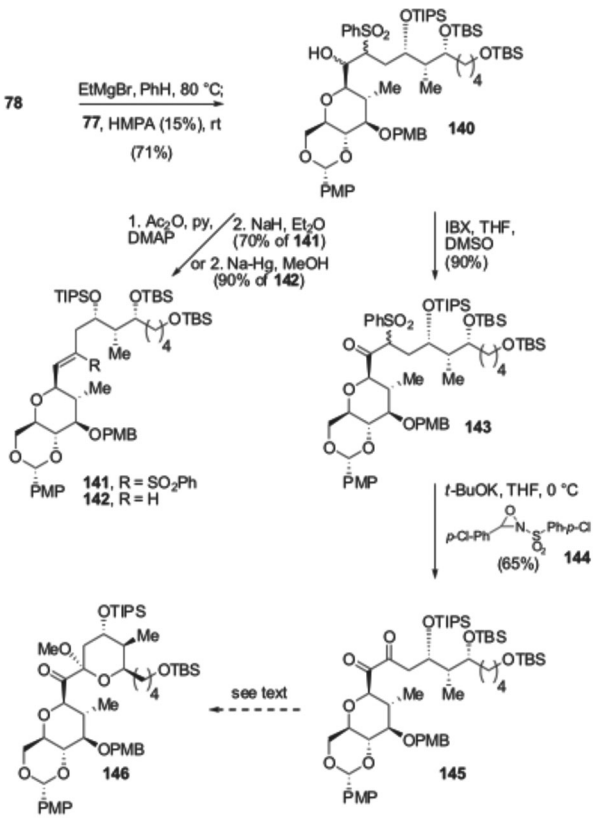


SCHEME 22

sential to the production of carbinol **140** (Scheme 23). Under optimized conditions, this coupling step was best implemented by heating **78** initially with ethylmagnesium bromide in benzene at 95 °C for 3 h. This step was followed by cooling to room temperature, addition of 15% HMPA in advance of the carboxaldehyde, and continued stirring for 1 h. In the event, **140** was isolated in 71% yield as a mixture of diastereomers.

When subsequent attempts to effect direct oxidation of the anion of **140** with reagents such as MoOPh[103], O_2, or the Davis oxaziridine[104] failed, subsequent effort was focused on the dihydroxylation of unsaturated intermediates **141** and **142** as a means of introducing an oxygen atom at C37. Unfortunately, these easily accessible intermediates proved totally unreactive to OsO_4 and NMO, even at stoichiometric levels of OsO_4. Therefore **140** was oxidized with IBX[92] to provide the α-sulfonyl ketone **143**. Although a comparable recalcitrance to oxidation was exhibited by **143**, recourse to the more reactive Williams oxaziridine **144**[105] proved to be an effective ploy. In this way, α-diketone **145** was reached in 65% yield.

With **145** in hand, we entered one of the most frustrating phases of this undertaking. From the beginning, we expected that the projected removal



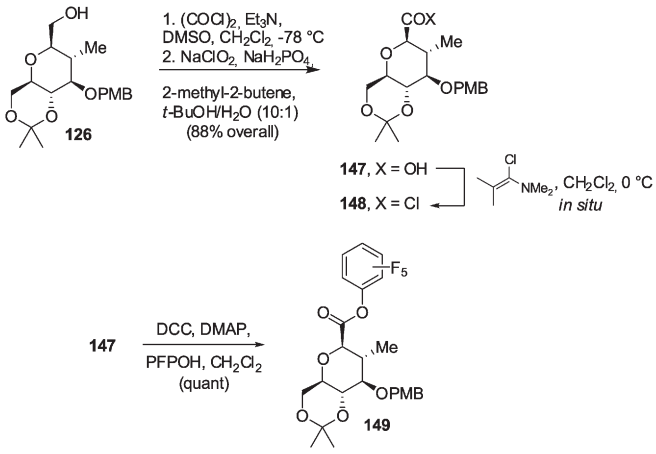
SCHEME 23

of the two TBS groups would be readily achieved, this deprotection maneuver lending itself in turn to conventional intramolecular cyclization with generation of the E-ring. However, the prospect of dual deblocking under conditions involving acidic reagents such as the HF·pyridine complex was thwarted by competing cleavage of the acetal. Under basic conditions, the primary OTBS group could be selectively removed, but regiocontrol during cleavage of a second Si–O bond was not realized.

Advance Toward Assembly of the Western EF Sector

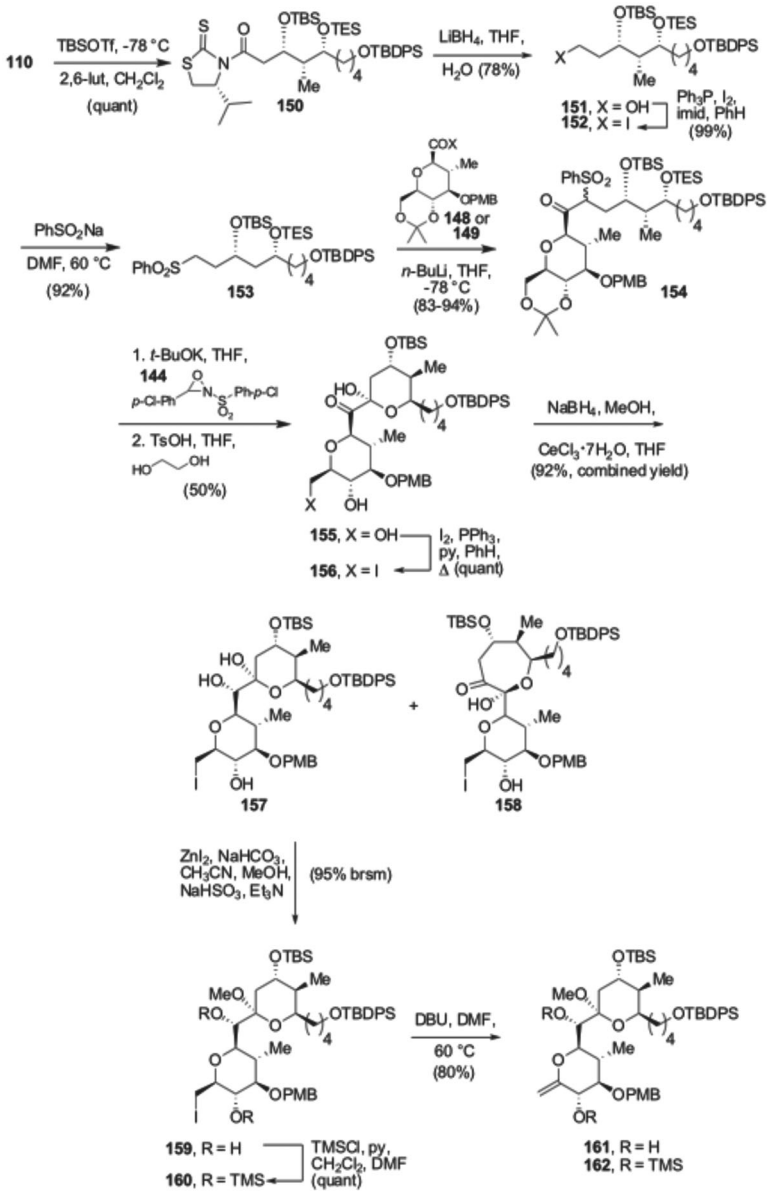
The elaboration of an alternate ring F candidate was next addressed. Thus carbinol **126** was oxidized to carboxylic acid **147** via sequential application of the Swern protocol[89] and the Lindgren–Kraus oxidation[106] (Scheme 24).

Conversion to the coupling partners **148** and **149** was accomplished via either in situ formation of acid chloride **148** or carbodiimide-mediated coupling to arrive at pentafluorophenyl ester **149**.



SCHEME 24

Concomitant with development of the new F-ring intermediates **148** and **149**, investigation of the likelihood that thiazolidinethione intermediate **110** could be used to our advantage for the synthesis of the E-ring sulfone **153** began. Silylation of the remaining free hydroxyl group was made distinctive through formation of the TBS derivative (Scheme 25). Reduction with lithium borohydride in THF served to convert **150** to **151** and enable subsequent formation of primary iodide **152**. Treatment of this substance with sodium benzenesulfinate in warm DMF afforded the targeted sulfone **153** in good yield. With reasonable amounts of **153** in hand, we proceeded to examine the acylation of its lithium salt with **148**, which was independently generated by exposing the carboxylic acid to the action of 1-chloro-*N*,*N*-trimethylpropenylamine[107]. Although effective, use of the acid chloride was undermined by instability issues. In the interest of working with a more stable intermediate, alternative use of the pentafluorophenyl ester was also developed[108]. Following discovery of the sluggishness exhibited by the anion of keto sulfone **154** toward, for example, MoOPH[103] and *trans*-2-(phenylsulfonyl)-3-phenyloxaziridine[104], recourse was again made to the purportedly more reactive reagent **144**[105]. Formation of the α-diketone was reproducibly achieved in this manner. Direct chemoselective removal of the TES group and hydrolysis of the acetonide were simultaneously accomplished with *p*-toluenesulfonic acid in a solvent system consisting of THF


110
TBSOTf, -78 °C
2,6-lut, CH2Cl2
(quant)
150
LiBH4, THF,
H2O (78%)
151, X = OH
152, X = I
Ph3P, I2,
imid, PhH
(99%)
PhSO2Na
DMF, 60 °C
(92%)
153
148 or
149
n-BuLi, THF,
-78 °C
(83-94%)
154
1. t-BuOK, THF,
144
2. TsOH, THF,
(50%)
NaBH4, MeOH,
CeCl3·7H2O, THF
(92%, combined yield)
155, X = OH
156, X = I
I2, PPh3,
py, PhH,
Δ (quant)
157
158
ZnI2, NaHCO3,
CH3CN, MeOH,
NaHSO3, Et3N
(95% brsm)
DBU, DMF,
60 °C
(80%)
159, R = H
160, R = TMS
TMSCl, py,
CH2Cl2, DMF
(quant)
161, R = H
162, R = TMS

SCHEME 25

and ethylene glycol. Under these conditions, the TBS substituent is not affected, and cyclization to give lactol **155** occurs in a fully stereocontrolled manner.

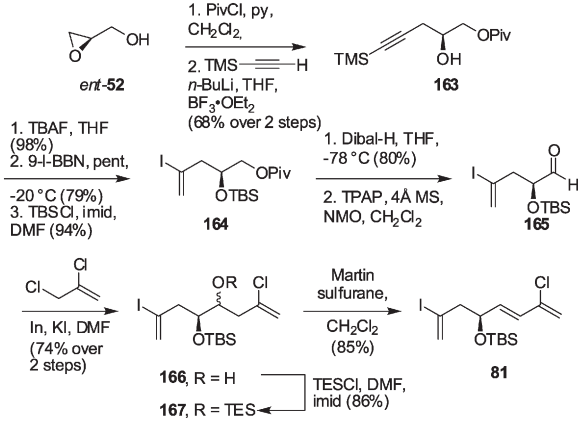
The next step was originally programmed to involve formation of the *O*-methyl glycoside. However, our efforts to reach this goal directly from **154** were seemingly thwarted by the presence of the neighboring carbonyl in **155**. This step was therefore deferred. Conversion to iodide **156** was followed by reduction under Luche conditions[109]. The latter step led to the formation of two products (**157** and **158**). When the time interval between the introduction of $CeCl_3$ and $NaBH_4$ was on the order of 5 min, the desired triol **157** was found to be the more dominant isomer, but only by a factor of 6:1. Matters are improved significantly by shortening of the time gap to only 5 s. This simple operational modification led to an increase in the product distribution to 20:1.

At this point, the methanolysis of **157** to generate **159** proceeded normally; conversion of the diol to the bis-silyl ether **160** was realized without event. In line with expectations, both methyl ethers featured exclusively an axial methoxy group. Both **159** and **160** underwent facile elimination in the presence of DBU to deliver the pair of exocyclic olefins **161** and **162**. A major effort was next invested in probing the workability of the Suzuki–Miyaura coupling of these advanced intermediates to a suitable trienyl side chain. No palladium catalyst, solvent system, temperature, or choice of base gave evidence of C–C bond formation within reasonable time limits. Enhancements in the stoichiometric levels of reagents were likewise unable to override this serious limitation. The very appreciable kinetic retardation observed here appears to exceed that noted by Kishi[110] during his application of the related Pd(0)-mediated Suzuki diene process to the assembly of palytoxin. The extreme rate deceleration that accompanies an appreciable increase in the molecular weight of the reactants may be a general phenomenon. In our case, it proved to be an insurmountable roadblock requiring reliance on an alternative means of structural assembly.

Investigation of Initial Suzuki–Miyaura Cross-Coupling

This phase of the undertaking started with generation of the chlorinated C45–C51 side chain derivative **81**. (*R*)-(+)-Glycidol (*ent*-**52**) was first converted into alkynol **163** according to precedent[111] (Scheme 26). Removal of the TMS group and treatment of the terminal alkyne with *B*-iodo-9-BBN[112] led uneventfully to the 2-iodo-1-alkene, which was subsequently protected as the TBS derivative **164**. From this point, the pivalate ester was reduct-

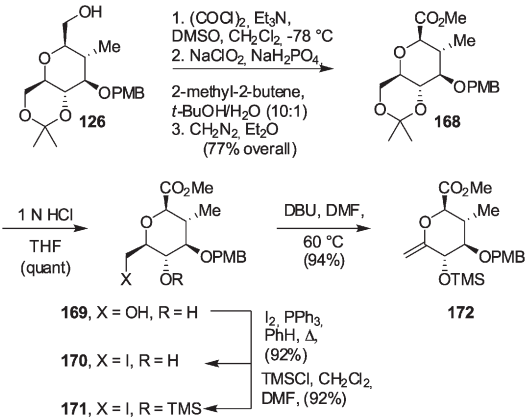
ively cleaved, thereby enabling oxidation to aldehyde **165**. The candidate reaction selected for three-carbon chain extension was the indium-mediated allylation with 2,3-dichloropropene in DMF[113]. Once the mixture of homoallylic alcohols had been formed, it proved an easy matter to dehydrate **166** regioselectively with the Martin sulfurane reagent[114] to generate **81**. Given the likely instability of the chlorodiene side chain **81**, protection of the diastereomeric mixture of alcohols as their respective TES ethers provided **167** as an alternate coupling partner.



SCHEME 26

The elaboration of a ring F candidate was next addressed in order to assess its suitability as a co-reactant in the intermolecular palladium-catalyzed C–C bond formation. Thus carbinol **126** was oxidized to the carboxylic acid via sequential application of the Swern protocol[89] and the Lindgren–Kraus oxidation[106]. Direct treatment with diazomethane furnished ester **168** (Scheme 27). Controlled hydrolysis of the acetonide functionality in **168** provided dihydroxy ester **169**, the primary OH group of which could be chemoselectively replaced by iodine. Once this was accomplished, the secondary hydroxyl was protected as a silyl ether, as in **160**, in advance of dehydroiodination with DBU in DMF at 60 °C[115]. This critical step delivered **172** as a colorless oil, thereby allowing us to take advantage of the propensity of exocyclic enol ethers of this class to undergo smooth hydroboration with 9-BBN[116].

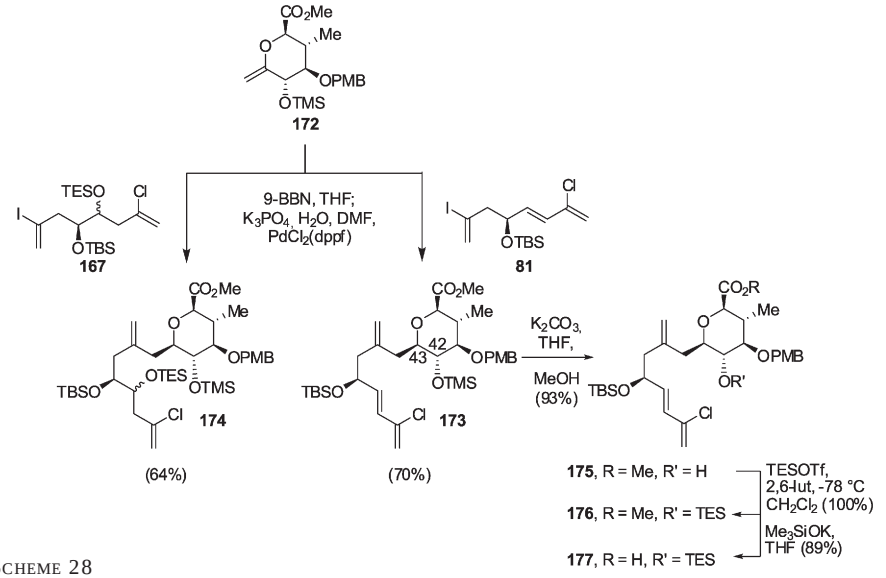
These two steps were of particular concern to us from the outset. The role of steric screening on the rate of E_2 elimination was expected to be significant and indeed it was. In fact, the conversion to **172** could best be accomplished when the neighboring protecting group was Me_3Si. Although



SCHEME 27

deceleration was noted in all other examples screened, desired enol ethers could be isolated, albeit in varying yields. We were mindful as well of the capricious nature of the hydroboration of disubstituted double bonds in the 4-position of carbohydrates[117–119]. This phenomenon was not apparent when transforming either **172** or analogs thereof into an alkylborane.

The next important hurdle involved transmetalation of the type R-B to R-Pd en route to coupled product **173** (Scheme 28). This was accomplished cleanly and efficiently through the combined action of $PdCl_2$(dppf) and



SCHEME 28

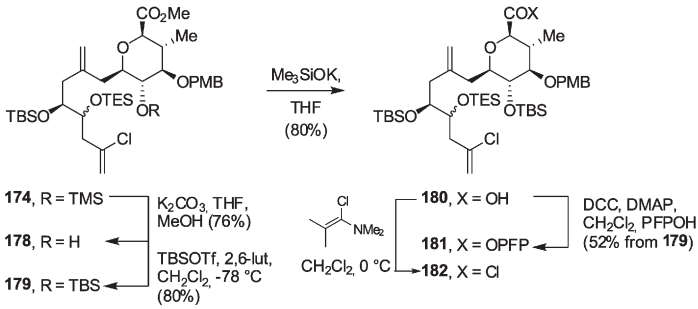
K_3PO_4. When this reaction was performed in aqueous DMF, proper side chain attachment was achieved in 60–70% yield. That the desired stereochemistry had been defined at C43 was made evident on the basis of the 9.3 Hz coupling constant between H42 and H43, this level of spin interaction being diagnostic of their *trans*-diaxial nature.

It was at this stage that we investigated the possibility of conjoining **173** to a fully functionalized E-ring fragment. In the event, desilylation to give **175** and reprotection as in **176** was found to be possible and necessary given the lability of the TMS ether. We soon recognized that the three intermediates **175**–**177** and, more particularly the derived acid chloride, were rather unstable to numerous reaction conditions. Hydrolysis of the methyl ester was successfully accomplished only by making use of potassium trimethylsilanolate under non-aqueous conditions[120]. Initial attempts involving activated esters such as the imidazolide led only to degradation as attempts to append the E-ring were carried out. These negative exploratory studies encouraged us to adopt a route in which the triene could be assembled at a later stage.

One potential way to circumvent the problems encountered by the instability associated with **173** and variants, as well as the lack of reactivity observed with **162**, led us to consider employing **167** as a protected triene in the Suzuki–Miyaura coupling. Use of **167** in place of **81** in the coupling reaction proceeded without event and the coupled product **174** could be isolated in good yield.

Revisiting Activated Esters

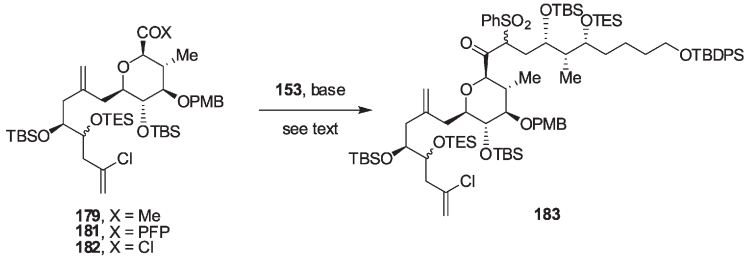
We were pleased to find that unlike **173**, Suzuki coupled **174** was easily amenable to further functional group manipulation (Scheme 29). Conversion of the TMS ether to the more robust TBS ether provided **179**. In the in-



SCHEME 29

terest of considering the penultimate coupling of the E-ring fragment, we investigated several potential substrates. Deprotection of the methyl ester was accomplished with potassium trimethylsilanoate (80%). While the acid chloride could be generated in situ in similar fashion to **148**, another option for coupling with the sulfonyl anion would be the more stable pentafluorophenyl (PFP) ester produced via DCC coupling between acid **180** and pentafluorophenol.

With facile access to both the acid chloride and the PFP ester, investigation of the key coupling with the E-ring fragment to generate the full C29–C51 fragment ensued. Initial generation of the sulfonyl anion derived from **153** was accomplished with KHMDS. However the anion failed to react with pentafluorophenyl ester **181** at low temperature, even in the presence of additives (Scheme 30). Analogous conditions with acid chloride **182** (generated in situ with 1-chloro-*N*,*N*,2-trimethylpropenylamine[107]) also failed to yield any product. Use of *n*-BuLi did allow for product formation with **181**, albeit in very low yields (<15%). Addition of HMPA or raising the temperature led to deleterious results. The acid chloride proved to be unstable under the reaction conditions and the pentafluorophenyl ester appeared to be too nonreactive, presumably due to steric effects.



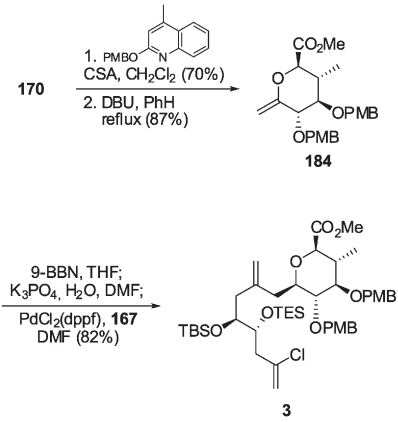
179, X = Me
181, X = PFP
182, X = Cl

SCHEME 30

While results with **181** and **182** could not be optimized further, reaction with methyl ester **179** also produced coupled product **183**[121]. Both the size of the methyl ester, as well as its inherent stability, were found to be advantageous as a series of conditions was probed. When methyl ester **179** and sulfone **153** (2 equiv.) were treated with LHMDS (2 equiv.) at –78 °C and allowed to warm to –30 °C over 5 h, conversion to the coupled product was observed in 80% yield. Excess sulfone could be recovered from the reaction mixture.

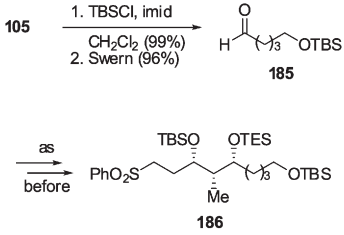
Further Elaboration of the C29–C51 Fragment

With the complete C29–C51 skeleton obtainable, we decided to again change the protecting group scheme to better fit our endgame. First, instead of the previously utilized TMS ether (**172**) that was then converted to the TBS ether (**179**) after the Suzuki coupling, we opted to utilize our PMBO-lepidine conditions to install a second PMB ether at C42 (Scheme 31). Although iodo alcohol **170** had previously shown itself to be unstable, the protection step afforded **184** in good yield, even over the 2 days reaction time. The synthesis then proceeded as before to afford the Suzuki cross-coupled product **3** in an improved 82% yield.



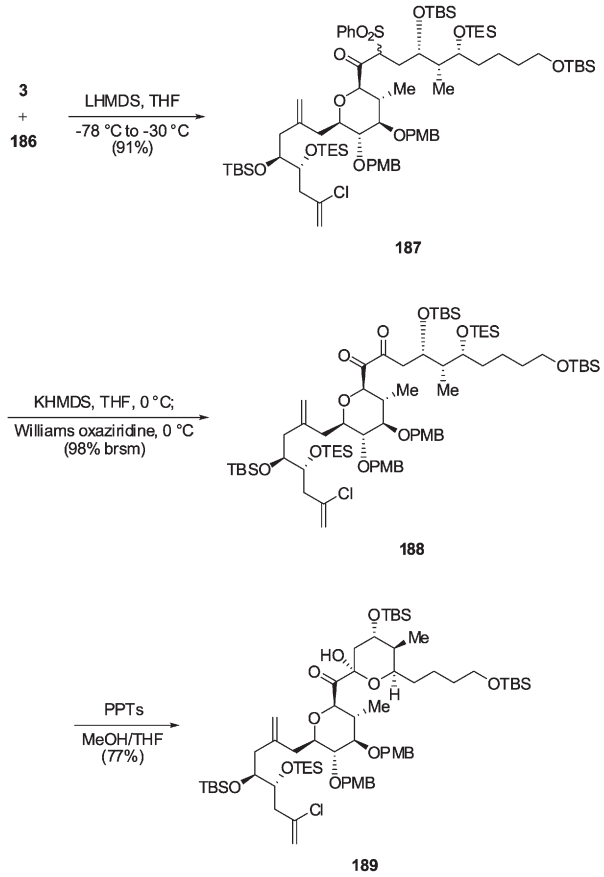
SCHEME 31

In the meantime, we had determined that the terminal TBDPS ether at C29 of our E segment sulfone **153** could prove difficult to remove in the presence of secondary TBS ethers later in the synthesis. To ease concern, Scheme 21 was altered by initiating the sequence with a mono-TBS protection (**185**), which in the end afforded **186** with an easier to cleave terminal protecting group (Scheme 32).



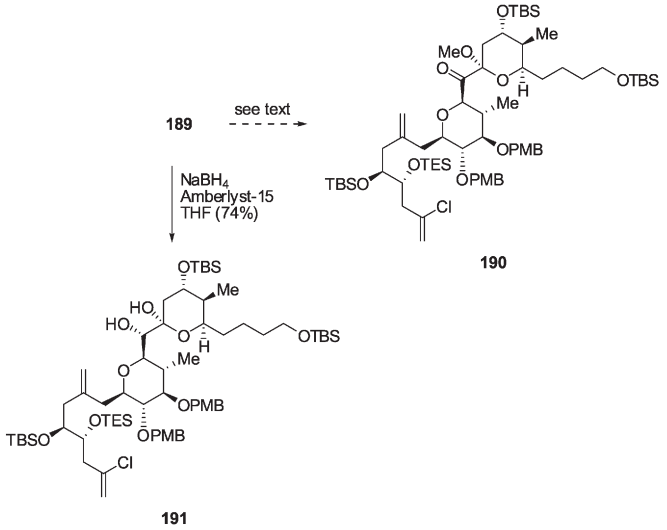
SCHEME 32

The modified E segment was then carried forward into the sulfonyl anion addition to the predescribed C38–C51 segment **3**, affording **187** in a good and reproducible yield (Scheme 33). At this point, we began to explore oxidation of the β-keto sulfone to α-diketone **188**. Application of previous conditions (*t*-BuOK followed by Williams oxaziridine at –78 °C) afforded no product. Further efforts at low temperatures using various oxidants, such as O_2 and $(BnOCOO)_2$, resulted in decomposition or recovered starting material. However, deprotonation and treatment with Williams oxaziridine at 0 °C allowed us to obtain **188** in 98% yield based on recovered starting material. Exploration was then focused on finding conditions to effect selective removal of the TES group at C33 and subsequent cyclization to afford the α-keto hemiketal adduct **189**. Optimal results were obtained using PPTs in MeOH/THF.



SCHEME 33

At this juncture we were hoping to avoid the hemiketal migration seen in our previous route (conversion of **156** to **158**) under reductive conditions, so we proceeded to attempt methylation of the hemiketal to give **190** prior to reduction of the C38 ketone (Scheme 34). Unfortunately, a wide variety of conditions (acidic, Lewis acidic, and basic) were applied, all to no avail, and we were forced to resort to the reduction being performed first. Initially we applied conditions that were most prevalent in the literature, such as Dibal-H, and the Luche[109] reduction that we successfully used in the earlier route. We obtained mostly no reaction with the conditions employed. However, utilizing the combination of $NaBH_4$ and Amberlyst-15[121] afforded the desired α-hydroxy hemiketal **191** in good yield, with no migration product observed.



SCHEME 34

Again focus was turned to methylating the hemiketal and it was found that the most widely acidic conditions regularly resulted in the loss of silyl groups. Although we wanted to remove the primary TBS and side chain TES in a subsequent step, we were unable to tune the conditions to favor both methylation and consistant removal of any silyl groups.

CONCLUSIONS

In conclusion, we have developed stereoselective routes to the major structural segments of spongistatin 1. Assembly of the core components in the

manner indicated herein is expected to allow the advancement of these highly functionalized intermediates toward completion of a total synthesis of **1a**. Integration of the protocols developed herein has required the implementation of robust procedures and the judicious selection of protecting groups. The applicability of these findings to other targets is an ongoing objective in our laboratory.

EXPERIMENTAL

Melting points are uncorrected. The column chromatographic separations were performed with silica gel. Solvents were reagent grade and in most cases dried and/or distilled prior to use. The purity of all compounds was shown to be >95% by TLC and high field ^{1}H and ^{13}C NMR spectroscopy (δ, ppm; *J*, Hz). The high-resolution mass spectra were obtained at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at Atlantic Microlab, Inc., Norcross, GA. Optical rotations were taken at 22 °C unless otherwise noted.

Allyl *o*-Bromobenzyl Ether

To a stirred solution of *o*-bromobenzyl alcohol **7** (30.00 g, 160 mmol) in THF (350 ml) precooled to 0 °C was added NaH (7.68 g, 320 mmol) portionwise. The cooling bath was removed and the reaction mixture was stirred at r.t. for 1 h. Allyl bromide (38.71 g, 320 mmol) was added dropwise over a 15 min period. The reaction mixture was further stirred for 4 h, cooled to 0 °C and diluted with H_2O (150 ml) and Et_2O (50 ml). The separated aqueous layer was extracted with Et_2O. The combined organic extracts were washed with H_2O and brine prior to drying, and the solvent was removed under reduced pressure to give the allyl ether (36.07 g, 99%). Distillation of this material furnished a colorless liquid (34.74 g, 95%), b.p. 78–80 °C (0.5 Torr); IR (neat, cm^{-1}) 1647, 1569, 1468; ^{1}H NMR (300 MHz, $CDCl_3$): 7.43 (dd, *J* = 8.0, 1.2, 1 H), 7.41 (dd, *J* = 8.0, 1.2, 1 H), 7.21 (td, *J* = 7.5, 1.2, 1 H), 7.04 (td, *J* = 7.7, 1.8, 1 H), 5.96–5.80 (m, 1 H), 5.26 (dq, *J* = 17.2, 1.6, 1 H), 5.13 (dq, *J* = 10.4, 1.3, 1 H), 4.49 (s, 2 H), 4.01 (dt, *J* = 5.6, 1.4, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 137.6, 134.5, 132.4, 128.9, 128.8, 127.3, 122.5, 117.2, 71.6, 71.3; EI HRMS *m/z* calculated for $C_{10}H_{11}BrO$ (M^+) 226.0193, observed 225.9989. Calculated for $C_{10}H_{11}BrO$: C, 52.89; H, 4.88. Found: C, 52.81; H, 4.82.

Alcohol **8**

To a stirred solution of allyl *o*-bromobenzyl ether (24.34 g, 107 mmol) in THF (20 ml) precooled to 0 °C was added a 0.5 M solution of 9-BBN in THF (220 ml, 107 mmol) via cannula. The reaction mixture was allowed to warm to r.t., at which point it was subjected to ultrasonication over a 1.5 h period (60 working cycles per min), cooled again to 0 °C, treated with 0.5 M aqueous solution of NaOH (220 ml) followed carefully by 30% H_2O_2 (107 ml), heated at reflux for 1 h, cooled to r.t. and poured into cold H_2O (100 ml). The separated aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine prior to drying and solvent evaporation. Purification of the residue by column chromatography on silica gel (pet ether/EtOAc 6:1 to 2:1) gave **8** as a colorless oil (22.50 g, 86%); IR (neat, cm^{-1}) 3375, 1569, 1469; ^{1}H NMR (300 MHz, $CDCl_3$): 7.55 (dd, *J* = 8.0, 1.2, 1 H),

7.42 (dd, *J* = 7.7, 1.2, 1 H), 7.30 (td, *J* = 7.5, 1.2, 1 H), 7.15 (td, *J* = 7.5, 1.2, 1 H), 4.55 (s, 2 H), 3.82 (t, *J* = 5.7, 2 H), 3.75 (t, *J* = 5.8, 2 H), 2.06 (br s, 1 H), 1.92 (quintet, *J* = 5.8, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 137.3, 132.5, 129.1, 129.0, 127.4, 122.8, 72.5, 69.5, 61.4, 32.1; EI HRMS *m/z* calculated for $C_{10}H_{13}BrO_2$ (M^+) 244.0299, observed 244.0277. Calculated for $C_{10}H_{13}BrO_2$: C, 49.00; H, 5.25. Found: C, 49.06; H, 5.35.

Aldehyde **9**

To a stirred suspension of PCC (4.40 g, 20.4 mmol) and Celite (4.40 g) in CH_2Cl_2 (25 ml) was added a solution of **8** (2.00 g, 8.16 mmol) in CH_2Cl_2 (7 ml). The dark reaction mixture was stirred at r.t. for 2.5 h, diluted with Et_2O (30 ml) and filtered through a short pad of Florisil. The flask was washed with Et_2O (8 × 30 ml) and the combined organics were concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1) to give **9** as a colorless oil (1.51 g, 76%); IR (neat, cm^{-1}) 1728, 1592, 1470; ^{1}H NMR (300 MHz, $CDCl_3$): 9.83 (t, *J* = 1.8, 1 H), 7.54 (dd, *J* = 7.9, 1.2, 1 H), 7.43 (dd, *J* = 7.7, 1.2, 1 H), 7.31 (td, *J* = 7.5, 1.2, 1 H), 7.15 (td, *J* = 7.9, 1.2, 1 H), 4.60 (s, 2 H), 3.88 (t, *J* = 6.0, 2 H), 2.75 (td, *J* = 5.8, 1.8, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 201.0, 137.2, 132.5, 132.4, 129.1, 127.4, 122.7, 72.5, 64.4, 43.8; EI HRMS *m/z* calculated for $C_{10}H_{11}BrO_2$ (M^+) 242.0142, observed 241.9952. Calculated for $C_{10}H_{11}BrO_2$: C, 49.41; H, 4.56. Found: C, 49.51; H, 4.57.

Thiazolidinethione **11**

To a suspension of $Sn(OTf)_2$ (1.845 g, 4.45 mmol) in CH_2Cl_2 (9.5 ml) cooled to –50 °C was added *N*-ethylpiperidine (0.61 ml, 4.45 mmol) and **10** (0.753 g, 3.71 mmol) in CH_2Cl_2 (4.5 ml) via cannula. The solution was stirred at –40 °C for 4 h and cooled to –78 °C. Aldehyde **9** (0.851 g, 3.50 mmol) in CH_2Cl_2 (4.0 ml) was added via cannula. The reaction mixture was stirred at that temperature for 3 h, quenched with pH 7 phosphate buffer (20 ml) and allowed to warm to r.t. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and solvent was evaporated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1 to 2:1) to give **11** as a yellow oil (1.187 g, 76%); IR (neat, cm^{-1}) 3510, 1692, 1568; ^{1}H NMR (300 MHz, $CDCl_3$): 7.52 (dd, *J* = 8.0, 1.2, 1 H), 7.45 (dd, *J* = 8.0, 1.2, 1 H), 7.30 (td, *J* = 7.5, 1.2, 1 H), 7.13 (td, *J* = 7.7, 1.8, 1 H), 5.15 (t, *J* = 7.9, 1 H), 4.56 (s, 2 H), 4.44–4.33 (m, 1 H), 3.83–3.67 (m, 2 H), 3.60 (dd, *J* = 15.0, 2.2, 1 H), 3.51 (dd, *J* = 10.2, 7.0, 1 H), 3.27 (dd, *J* = 15.0, 7.5, 1 H), 3.02 (dd, *J* = 10.2, 0.8, 1 H), 2.73 (br s, 1 H), 2.35 (sextet, *J* = 5.8, 1 H), 1.87 (q, *J* = 5.8, 2 H), 1.12 (d, *J* = 7.0, 3 H), 0.97 (d, *J* = 7.0, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.9, 172.7, 137.4, 132.5, 129.1, 129.0, 127.4, 122.8, 72.5, 71.4, 68.2, 66.5, 45.4, 35.9, 30.8, 30.6, 19.1, 17.8; EI HRMS *m/z* calculated for $C_{18}H_{24}BrNO_3S_2$ (M^+) 445.0581, observed 445.0396; $[\alpha]_D$ +234 (*c* 3.10, $CHCl_3$). Calculated for $C_{18}H_{24}BrNO_3S_2$: C, 48.43; H, 5.42. Found: C, 48.42; H, 5.44.

Amide **12**

To a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (0.528 g, 5.42 mmol) in CH_2Cl_2 (11 ml) cooled to 0 °C was added a 2.0 M solution of Me_3Al in hexanes (2.71 ml, 5.42 mmol). The clear solution was stirred at that temperature for 10 min and at r.t. for 30 min prior to cooling to –15 °C. A solution of **11** (1.160 g, 2.71 mmol) in CH_2Cl_2 (3.0 ml) was added via cannula and the reaction mixture was stirred at –10 °C for 30 min and at r.t.

overnight, quenched with 1.0 M tartaric acid (40 ml), warmed to r.t., and stirred vigorously for 1 h. The separated aqueous layer was extracted with CH_2Cl_2, the combined organic extracts were dried, and the solvent was evaporated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:4) to give **12** as a colorless oil (0.881 g, 98%); IR (neat, cm^{-1}) 3451, 1650, 1569; ^1H NMR (300 MHz, $CDCl_3$): 7.46 (d, *J* = 7.9, 1 H), 7.39 (d, *J* = 7.6, 1 H), 7.24 (t, *J* = 7.4, 1 H), 7.07 (t, *J* = 7.8, 1 H), 4.51 (s, 2 H), 4.26–4.18 (m, 1 H), 3.83–3.62 (m, 2 H), 3.59 (s, 3 H), 3.12 (s, 3 H), 2.65–2.48 (m, 3 H), 1.81 (q, *J* = 6.3, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 173.5, 137.6, 132.5, 129.0, 128.9, 127.3, 122.7, 72.4, 68.0, 66.1, 61.2, 38.4, 36.3, 31.8; FAB MS *m/z* calculated for $C_{14}H_{21}BrNO_4$ (M^+ + H) 346.09, observed 346.07; $[\alpha]_D$ +18.2 (*c* 1.31, $CHCl_3$). Calculated for $C_{14}H_{20}BrNO_4$: C, 48.57; H, 5.82. Found: C, 48.53; H, 5.81.

THP-Protected Amide **13**

To a solution of PPTS (79 mg, 0.31 mmol) in CH_2Cl_2 (5.0 ml) was added a solution of **12** (0.657 g, 3.67 mmol) and DHP (369 mg, 4.38 mmol) in CH_2Cl_2 (13.0 ml) at r.t. The reaction mixture was stirred for 22 h. Half-saturated brine (40 ml) was added and the layers were shaken extensively. The separated aqueous layer was extracted with CH_2Cl_2 (3 × 20 ml). The combined organic extracts were dried, and the solvent was evaporated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 1:1) to give **13** as a colorless oil (790 mg, 97%); IR (neat, cm^{-1}) 1662, 1468, 1440; ^1H NMR (300 MHz, $CDCl_3$): 7.52 (d, *J* = 8.1, 1 H), 7.51 (d, *J* = 7.9, 1 H), 7.49 (d, *J* = 8.6, 1 H), 7.48 (d, *J* = 7.7, 1 H), 7.30 (t, *J* = 7.7, 2 H), 7.12 (t, *J* = 7.9, 2 H), 4.72–4.68 (m, 1 H), 4.66–4.60 (m, 1 H), 4.56 (s, 4 H), 4.37–4.31 (m, 2 H), 3.91–3.83 (m, 2 H), 3.74 (t, *J* = 6.5, 2 H), 3.67 (s, 3 H), 3.66 (s, 3 H), 3.50–3.41 (m, 2 H), 3.17 (s, 6 H), 2.99–2.97 (m, 2 H), 2.84–2.81 (m, 2 H), 2.64–2.49 (m, 2 H), 2.05–1.62 (m, 8 H), 1.58–1.48 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$): 172.3, 172.2, 138.0, 137.9, 132.4, 132.3, 129.0, 128.9, 128.8, 128.7, 128.6, 127.3, 122.5, 122.4, 99.6 (2C), 72.5 (2C), 72.4 (2C), 72.1 (2C), 67.6, 67.2, 63.3, 63.2, 61.2, 61.1, 35.9, 34.7, 32.0, 31.2, 31.1 (2C), 25.3, 25.2, 20.3 (2C); FAB MS *m/z* calculated for $C_{19}H_{28}BrNO_5$ (M^+ + H) 430.14, observed 430.14. Calculated for $C_{19}H_{29}BrNO_5$: C, 53.03; H, 6.56. Found: C, 52.91; H, 6.55.

Aldehyde **14**

To a stirred solution of **13** (742 mg, 1.72 mmol) in THF (15 ml) cooled to –78 °C was added a 1.0 M solution of Dibal-H in hexanes (3.44 ml, 3.44 mmol) dropwise. The reaction mixture was stirred at –78 °C for 2 h, quenched by the addition of acetone (0.8 ml) and stirred at –78 °C for an additional 5 min. After transfer into a rapidly stirred mixture of CH_2Cl_2 and aqueous Rochelle's salt solution at r.t., the resulting two-phase mixture was stirred at r.t. for 30 min. The separated aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried and concentrated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 4:1) to give **14** as a colorless oil (0.615 g, 96%); IR (neat, cm^{-1}) 1724, 1691, 1569; ^1H NMR (300 MHz, $CDCl_3$): 9.65 (dd, *J* = 3.0, 1.5, 1 H), 9.46 (dd, *J* = 2.2, 1.8, 1 H), 7.47 (d, *J* = 7.7, 1 H), 7.41 (d, *J* = 7.7, 1 H), 7.34 (d, *J* = 7.9, 2 H), 7.00 (d, *J* = 7.5, 1 H), 6.99 (d, *J* = 7.5, 1 H), 6.72 (t, *J* = 8.0, 2 H), 4.60 (dd, *J* = 4.5, 3.1, 1 H), 4.55 (dd, *J* = 4.9, 3.4, 1 H), 4.46 (s, 2 H), 4.41 (d, *J* = 2.5, 1 H), 4.33–4.25 (m, 2 H), 3.78–3.23 (m, 8 H), 2.58–2.45 (m, 4 H), 2.35–1.35 (m, 8 H), 1.35–1.10 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$): 201.6, 201.1, 137.8, 137.6, 132.6, 132.5, 129.2, 129.0 (2C), 128.8, 127.4, 127.3, 122.8, 122.6, 99.6, 98.3, 72.3, 72.2, 70.9, 70.2, 67.3, 66.8, 63.2, 63.1, 49.7, 48.6, 35.8, 35.1, 31.0 (2C),

25.4, 25.3, 20.1, 19.9; FAB MS *m/z* calculated for $C_{17}H_{24}BrO_4$ (M^+ + H) 371.11, observed 371.09. Calculated for $C_{17}H_{23}BrO_4$: C, 55.00; H, 6.24. Found: C, 55.10; H, 6.17.

Thiazolidinethione **15**

To a suspension of $Sn(OTf)_2$ (900 mg, 2.16 mmol) in CH_2Cl_2 (4.0 ml) cooled to –50 °C was added *N*-ethylpiperidine (0.30 ml, 2.15 mmol) and **10** (363 mg, 1.79 mmol) dissolved in CH_2Cl_2 (3.0 ml) via cannula. The solution was stirred at –40 °C for 4 h and cooled to –78 °C. Aldehyde **14** (583 mg, 1.57 mmol) in CH_2Cl_2 (3.0 ml) was added via cannula. The reaction mixture was stirred at that temperature for 3 h, quenched with pH 7 phosphate buffer (28 ml) and warmed to r.t. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried. The solvent was evaporated and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1 to 2:1) to give **15** as a yellow oil (767 mg, 85%); IR (neat, cm^{-1}) 3474, 1695, 1478; ^{1}H NMR (300 MHz, C_6D_6): 7.57 (d, *J* = 7.6, 1 H), 7.49 (d, *J* = 7.7, 1 H), 7.34 (d, *J* = 8.0, 2 H), 7.03 (t, *J* = 7.5, 2 H), 6.73 (t, *J* = 8.0, 2 H), 4.73 (q, *J* = 7.0, 2 H), 4.70–4.66 (m, 2 H), 4.53 (s, 2 H), 4.50 (m, 1 H), 4.45 (s, 2 H), 4.24–4.17 (m, 2 H), 3.90 (d, *J* = 3.0, 1 H), 3.84–3.73 (m, 2 H), 3.73–3.52 (m, 5 H), 3.51–3.18 (m, 6 H), 3.16 (d, *J* = 3.4, 1 H), 2.47 (t, *J* = 7.8, 1 H), 2.44 (t, *J* = 7.6, 1 H), 2.25–2.00 (m, 4 H), 2.00–1.82 (m, 4 H), 1.75 (q, *J* = 6.1, 2 H), 1.72–1.33 (m, 8 H), 1.28–1.00 (m, 6 H), 0.71 (d, *J* = 7.0, 3 H), 0.69 (d, *J* = 6.5, 6 H), 0.67 (d, *J* = 6.6, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 203.3 (2C), 173.2 (2C), 139.3, 139.0, 133.0, 132.9, 129.6, 129.4, 129.2, 128.0, 127.6, 127.3, 123.2, 123.0, 100.1, 98.8, 74.7, 74.1, 72.7 (2C), 72.0, 71.8, 68.4, 67.6 (2C), 66.9, 64.7, 63.4, 47.0, 46.7, 42.8, 41.5, 36.2, 35.8, 32.1 (2C), 31.4 (2C), 30.4, 30.3, 26.1, 25.8, 21.6, 20.8, 19.3 (2C), 17.9 (2C); FAB MS *m/z* calculated for $C_{25}H_{37}BrNO_5S_2$ (M^+ + H) 574.15, observed 574.24. Calculated for $C_{25}H_{36}BrNO_5S_2$: C, 52.26; H, 6.31. Found: C, 52.01; H, 6.35.

Amide **16**

To a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (328 mg, 3.359 mmol) in CH_2Cl_2 (5.0 ml) cooled to 0 °C was added a 2.0 M solution of Me_3Al in hexanes (1.70 ml, 3.359 mmol). The clear solution was stirred at that temperature for 10 min and at r.t. for 1 h prior to being cooled to –15 °C. A solution of **15** (386 mg, 0.672 mmol) in CH_2Cl_2 (3.0 ml) was added via cannula and the reaction mixture was stirred at –20 °C for 2 h, quenched with 1.0 M tartaric acid (10 ml), warmed to r.t. and stirred vigorously for 30 min. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried, and the solvent was evaporated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:8) to give **16** as a colorless oil (284 mg, 89%); IR (neat, cm^{-1}) 3463, 1654, 1569; ^{1}H NMR (300 MHz, C_6D_6): 7.61 (d, *J* = 7.7, 1 H), 7.51 (d, *J* = 7.7, 1 H), 7.34 (d, *J* = 8.0, 2 H), 7.00 (t, *J* = 7.6, 2 H), 6.71 (t, *J* = 7.9, 2 H), 4.83–4.62 (m, 2 H), 4.58 (dd, *J* = 6.0, 2.4, 1 H), 4.55 (s, 2 H), 4.47 (s, 2 H), 4.42–4.36 (m, 1 H), 4.36–4.28 (m, 2 H), 4.17 (d, *J* = 2.5, 1 H), 3.81–3.77 (m, 2 H), 3.73 (t, *J* = 6.5, 2 H), 3.50–3.40 (m, 2 H), 3.32–3.21 (m, 2 H), 3.03 (s, 3 H), 2.93 (s, 3 H), 2.81 (s, 3 H), 2.77 (s, 3 H), 2.74–2.65 (m, 1 H), 2.56–2.42 (m, 1 H), 2.17–2.07 (m, 3 H), 2.02–1.77 (m, 5 H), 1.77–1.42 (m, 8 H), 1.30–1.15 (m, 7 H); ^{13}C NMR (75 MHz, C_6D_6): 173.9 (2C), 139.3, 138.9, 132.9, 132.8, 129.6 (2C), 129.2, 129.1, 127.9, 127.6, 123.1, 122.9, 99.8, 98.4, 74.2, 73.1, 72.7 (2C), 68.6, 67.8, 67.2, 66.2, 64.0, 63.3, 61.0 (2C), 43.2, 41.9, 39.8, 39.6, 36.1, 35.4, 32.1, 32.0, 31.9 (2C), 26.2, 26.0, 21.2, 20.8; FAB MS *m/z* calculated for $C_{21}H_{33}BrNO_6$ (M^+ + H) 474.17, observed 474.25. Calculated for $C_{21}H_{32}BrNO_6$: C, 53.17; H, 6.80. Found: C, 53.23; H, 6.68.

Silylated Amide **17**

To a solution of **16** (109 mg, 0.23 mmol) in DMF (0.8 ml) were added imidazole (78 mg, 1.15 mmol) and TBSCl (173 mg, 1.15 mmol). The reaction mixture was stirred at r.t. for 6 h and treated with H_2O (40 ml) and CH_2Cl_2 (30 ml). The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:4) to give **17** as a colorless oil (133 mg, 99%); IR (neat, cm^{-1}) 1740, 1664, 1570; ^1H NMR (300 MHz, C_6D_6): 7.59 (d, *J* = 7.6, 1 H), 7.50 (d, *J* = 7.7, 1 H), 7.33 (d, *J* = 7.9, 2 H), 7.03 (td, *J* = 7.5, 1.1, 1 H), 7.02 (dd, *J* = 7.6, 1.2, 1 H), 6.73 (td, *J* = 7.8, 1.6, 2 H), 4.85–4.73 (m, 2 H), 4.70 (t, *J* = 3.8, 1 H), 4.65 (t, *J* = 5.1, 1 H), 4.55 (s, 2 H), 4.46 (d, *J* = 1.2, 2 H), 4.18–4.12 (m, 2 H), 3.98–3.92 (m, 1 H), 3.88–3.71 (m, 2 H), 3.70–3.65 (m, 1 H), 3.53–3.29 (m, 4 H), 3.16 (s, 3 H), 3.12 (s, 3 H), 2.90 (s, 3 H), 2.89 (s, 3 H), 2.69 (dd, *J* = 15.0, 4.1, 1 H), 2.54 (dd, *J* = 15.3, 4.9, 1 H), 2.26–2.14 (m, 1 H), 2.13–2.03 (m, 1 H), 2.02–1.76 (m, 4 H), 1.76–1.47 (m, 4 H), 1.31–1.21 (m, 12 H), 1.02 (s, 9 H), 1.01 (s, 9 H), 0.25 (s, 3 H), 0.23 (s, 3 H), 0.22 (s, 3 H), 0.18 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 172.8, 172.6, 139.3, 138.9, 132.9, 132.8, 129.6 (2C), 129.2, 129.1, 127.9, 127.8, 123.1, 122.9, 98.8, 98.6, 72.7 (2C), 71.9 (2C), 68.4, 67.9 (2C), 67.8, 63.4, 63.3, 61.2, 61.1, 45.0, 43.9, 40.8, 40.3, 36.7, 35.2, 32.2 (2C), 32.1, 31.9, 26.6 (3C), 26.5 (3C), 26.3 (2C), 20.9, 20.7, 18.7, 18.6, –3.7, –3.8, –4.1 (2C); FAB MS *m/z* calculated for $C_{27}H_{47}BrNO_6Si$ (M^+ + H) 588.26, observed 588.10. Calculated for $C_{27}H_{46}BrNO_6Si$: C, 55.09; H, 7.88. Found: C, 54.90; H, 7.82.

Methyl Ketone **18**

To a solution of **17** (133 mg, 0.226 mmol) in THF (0.8 ml) precooled to –78 °C was added a 3.0 M solution of MeMgBr in Et_2O (0.20 ml, 0.570 mmol). The solution was immediately warmed to 0 °C and stirred for 1.5 h. The reaction mixture was quenched with NH_4Cl solution (2 ml), followed by H_2O (30 ml) and CH_2Cl_2 (30 ml). The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried. The solvent was evaporated and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 8:1 to 2:1) to give **18** as a colorless oil (113 mg, 92%); IR (neat, cm^{-1}) 1717, 1570, 1471; ^1H NMR (300 MHz, C_6D_6): 7.59 (d, *J* = 7.7, 1 H), 7.50 (d, *J* = 7.7, 1 H), 7.34 (d, *J* = 8.0, 2 H), 7.03 (t, *J* = 7.4, 1 H), 7.02 (t, *J* = 7.5, 1 H), 6.72 (t, *J* = 7.8, 2 H), 4.70 (m, 2 H), 4.60 (dd, *J* = 5.5, 2.9, 1 H), 4.56 (s, 2 H), 4.48 (d, *J* = 0.4, 2 H), 4.46–4.42 (m, 1 H), 4.05 (t, *J* = 6.0, 1 H), 4.02–4.00 (m, 1 H), 3.88–3.78 (m, 2 H), 3.78–3.70 (m, 1 H), 3.70–3.60 (m, 1 H), 3.50–3.30 (m, 4 H), 2.61–2.27 (m, 4 H), 2.10–1.98 (m, 3 H), 1.92–1.51 (m, 11 H), 1.85 (s, 3 H), 1.76 (s, 3 H), 1.30–1.19 (m, 6 H), 0.99 (s, 9 H), 0.98 (s, 9 H), 0.20 (s, 3 H), 0.17 (s, 3 H), 0.16 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 206.2, 205.9, 140.0, 138.8, 133.0, 132.9, 129.7, 129.6, 129.3, 129.1, 127.9, 127.8, 123.2, 123.0, 99.0, 98.8, 72.8, 72.7, 72.3, 71.9, 68.3, 67.7, 67.5, 67.1, 63.8, 63.4, 51.5, 50.9, 44.6, 43.5, 36.6, 35.6, 32.1, 32.0, 31.5 (2C), 26.5 (6C), 26.2, 26.1, 21.1, 20.9, 18.6 (2C), –3.9 (2C), –4.0 (2C); FAB MS *m/z* calculated for $C_{26}H_{44}BrO_5Si$ (M^+ + H) 543.23, observed 543.45. Calculated for $C_{26}H_{43}BrO_5Si$: C, 57.45; H, 7.97. Found: C, 57.53; H, 8.03.

Epoxide **19**

To a cold (0 °C) stirred solution of (*R*)-2-bromo-1,4-butanediol (1.0 g, 5.9 mmol) in THF (100 ml) was added NaH (426 mg, 17.8 mmol). The resulting mixture was stirred at 0 °C for 30 min,

at which point TBAI (100 mg, 0.27 mmol) and *o*-bromobenzyl bromide (1.8 g, 7.2 mmol) were introduced. The reaction mixture was heated at reflux overnight, cooled to r.t. and treated with saturated NH_4Cl solution (20 ml). The separated aqueous layer was extracted with EtOAc. The combined organic extracts were dried, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 100:0 to 97:3) to give **19** (413 mg, 54%) as a pale orange oil; IR (neat, cm^{-1}) 1568, 1470, 1440; ^1H NMR (300 MHz, $CDCl_3$): 7.56 (m, 1 H), 7.49 (m, 1 H), 7.34 (m, 1 H), 7.18 (m, 1 H), 4.62 (s, 2 H), 3.73 (m, 2 H), 3.13 (m, 1 H), 2.82 (dd, *J* = 5.0, 4.8, 1 H), 2.56 (dd, *J* = 5.0, 2.7, 1 H), 2.04–1.91 (m, 1 H), 1.91–1.76 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): 137.5, 132.4, 128.9, 128.8, 127.3, 122.6, 72.2, 67.5, 49.9, 47.0, 32.9; $[\alpha]_D$ –10.7 (*c* 1.64, $CHCl_3$); ES HRMS *m/z* calculated for $C_{11}H_{13}BrO_2Na$ (M^+ + Na) 278.9991, observed 279.0005.

Dithiane Alcohol **20**

To a –78 °C stirred solution of 1,3-dithiane (480 mg, 4.00 mmol) in a 10:1 mixture of THF/HMPA (30 ml) was added dropwise a 1.4 M solution of *t*-BuLi (2.8 ml, 4.0 mmol). The reaction mixture was warmed to –30 °C, stirred at this temperature for 1 h, returned to –78 °C and treated with a solution of **19** (340 mg, 1.32 mmol) in THF (10 ml). The mixture was stirred for 30 min at this temperature, treated with a saturated solution of NH_4Cl (10 ml) and warmed to r.t. The separated aqueous layer was extracted with EtOAc. The combined organic extracts were dried, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc 95:5 to 90:10) to give **20** (458 mg, 92%) as a pale yellow oil; IR (neat, cm^{-1}) 3442, 1422, 1358; ^1H NMR (300 MHz, $CDCl_3$): 7.53 (d, *J* = 7.9, 1 H), 7.42 (d, *J* = 7.6, 1 H), 7.30 (t, *J* = 7.4, 1 H), 7.14 (dt, *J* = 7.6, 1.5, 1 H), 4.57 (s, 2 H), 4.28 (dd, *J* = 9.3, 5.1, 1 H), 4.15 (m, 1 H), 3.76 (m, 2 H), 3.00–2.77 (m, 4 H), 2.65 (d, *J* = 9.3, 1 H), 2.18–2.03 (m, 1 H), 2.03–1.75 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$): 136.9, 132.4, 128.9 (2C), 127.3, 122.6, 72.4, 68.9, 67.2, 43.8, 42.5, 36.4, 30.2, 29.8, 25.7; ES HRMS *m/z* calculated for $C_{15}H_{21}BrO_2S_2Na$ (M^+ + Na) 399.0058, observed 399.0027; $[\alpha]_D$ +14.9 (*c* 1.7, $CHCl_3$).

Dithianyl Ether **21**

To a stirred solution of **20** (458 mg, 1.21 mmol) in CH_2Cl_2 (20 ml) was added PPTS (30 mg, 0.12 mmol) followed by DHP (221 µl, 2.42 mmol). The reaction mixture was stirred at r.t. for 5 h. A saturated solution of $NaHCO_3$ (5 ml) was introduced. The separated aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 90:10) to give **21** (532 mg, 95%) as pale yellow oil; IR (neat, cm^{-1}) 1440, 1353, 1200; ^1H NMR (300 MHz, $CDCl_3$): 7.48 (m, 2 H), 7.29 (m, 1 H), 7.11 (m, 1 H), 4.67 (m, 0.5 H), 4.59 (m, 0.5 H), 4.52 (s, 2 H), 4.48 (dd, *J* = 8.8, 5.7, 0.5 H), 4.07 (m, 1.5 H), 3.87 (m, 1 H), 3.66 (t, *J* = 6.5, 1 H), 3.58 (t, *J* = 6.3, 1 H), 3.46 (m, 1 H), 2.79 (m, 4 H), 2.14–1.58 (m, 8 H), 1.58–1.37 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$): 136.9, 136.7, 131.4, 131.3, 128.0 (2C), 127.9 (2C), 127.8 (2C), 127.6 (2C), 126.3, 122.8, 122.6, 98.3, 97.7, 71.4, 71.1(2C), 71.0, 66.4, 66.0, 62.1, 42.8, 42.6, 40.5, 39.4, 34.6, 33.4, 30.2, 30.1, 29.3, 29.0, 28.7, 25.0 (2C), 24.4, 19.2, 19.1; ES HRMS *m/z* calculated for $C_{20}H_{29}BrO_3S_2Na$ (M^+ + Na) 683.0634, observed 683.0677.

Alcohol **22**

To a cold (0 °C) stirred suspension of CuI (2.0 g, 10.5 mmol) in THF (10 ml) was added a 1 M solution of vinylmagnesium bromide (70.0 ml, 70.0 mmol). The mixture was stirred at this temperature for 30 min before being cooled to –78 °C. A solution of **19** (9.0 g, 35.0 mmol) in THF (45 ml) was introduced and the mixture was stirred for 30 min at –78 °C before being warmed to 0 °C, stirred for 30 min at this temperature and treated with a saturated solution of NH_4Cl (100 ml). After 30 min of vigorous stirring, the separated aqueous layer was extracted with EtOAc. The combined organic extracts were dried, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 10:1 to 5:1) to give **22** (8.4 g, 84%) as a pale yellow oil; IR (neat, cm^{-1}) 3429, 1640, 1569; ^1H NMR (300 MHz, $CDCl_3$): 7.53 (dd, *J* = 7.8, 1.5, 1 H), 7.43 (dd, *J* = 7.6, 1.4, 1 H), 7.32 (dt, *J* = 7.4, 1.5, 1 H), 7.17 (dt, *J* = 7.6, 1.4, 1 H), 5.94–5.77 (m, 1 H), 5.15 (br d, *J* = 8.2, 1 H), 5.10 (s, 1 H), 4.57 (s, 2 H), 3.92 (m, 1 H), 3.89–3.65 (m, 2 H), 2.81 (br s, 1 H), 2.26 (m, 2 H), 1.81 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 137.2, 134.7, 132.5, 129.1, 129.0, 127.4, 122.8, 117.6, 72.5, 70.0, 69.2, 41.8, 35.7; ES HRMS *m/z* calculated for $C_{13}H_{17}BrO_2Na$ (M^+ + Na) 307.0304, observed 307.0300; $[\alpha]_D$ –28.9 (*c* 1.35, $CHCl_3$).

Diether **23**

To a stirred solution of **22** (8.4 g, 29.0 mmol) in CH_2Cl_2 (170 ml) was added PPTS (0.76 g, 3.0 mmol) followed by DHP (5.4 ml, 59.0 mmol). The mixture was stirred at r.t. for 3 h. A saturated solution of $NaHCO_3$ (100 ml) was introduced and the separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine (50 ml), dried, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 8:1 to 6:1) to give **23** (10.4 g, 97%) as a pale yellow oil and 1:1 mixture of dieasteroisomers; IR (neat, cm^{-1}) 1440, 1354, 1200; ^1H NMR (300 MHz, $CDCl_3$): 7.59 (m, 2 H), 7.31 (m, 1 H), 7.18 (m, 1 H), 5.92–5.75 (m, 1 H), 5.08 (br d, *J* = 10, 1, 1 H), 5.04 (s, 1 H), 4.71 (m, 0.5 H), 4.65 (m, 0.5 H), 4.54 (m, 2 H), 4.00–3.79 (m, 2 H), 3.71 (m, 1 H), 3.60 (m, 1 H), 3.47 (m, 1 H), 2.40 (m, 1 H), 2.30 (m, 1 H), 1.95–1.62 (m, 4 H), 1.62–1.44 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$): 138.0, 137.6, 134.9, 134.3, 132.2, 128.9, 128.8, 128.7, 128.5, 127.2, 122.6, 122.3, 117.2, 116.9, 99.6, 99.0, 96.8 (2C), 74.4, 72.3, 72.0 (2C), 67.6, 67.1, 62.6 (2C), 40.3 (2C), 38.2 (2C), 34.8, 33.8, 31.0, 30.8, 25.4, 19.8; ES HRMS *m/z* calculated for $C_{18}H_{25}BrO_3Na$ (M^+ + Na) 391.0879, observed 391.0888.

Alternate Routes to Aldehyde **14**

A. From dithiane **21**. To a stirred solution of **21** (104 mg, 0.23 mmol) in a 9:1 mixture of CH_3CN and H_2O was added $CaCO_3$ (217 mg, 2.2 mmol) followed by $HgClO_4 \cdot 3\ H_2O$ (153 mg, 0.34 mmol) in three portions over a 2 h period. The resulting mixture was filtered through a pad of Celite and the cake was washed several times with CH_2Cl_2. The filtrate was dried and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 95:5 to 90:10) to give **14** (42 mg, 50%) as a colorless oil identical to that described earlier.

B. From diether **23**. To a stirred solution of **23** (100 mg, 0.27 mmol) in a 10:1 mixture of THF/H_2O (5 ml) was added a small crystal of OsO_4 followed by NMO (38 mg, 0.32 mmol). The resulting solution was stirred at r.t. for 2 h prior to dilution with H_2O (1 ml), followed

by the addition of $NaIO_4$ (174 mg, 0.81 mmol) and an additional 1 h of stirring. H_2O was added to dissolve the precipitate followed by EtOAc. The separated aqueous layer was extracted with EtOAc. The combined organic extracts were dried, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 95:5 to 90:10) to give **14** (94 mg, 93%) as a colorless oil identical to the other samples produced in this study.

Epoxide **24**

To a solution of PMBBr (5.43 g, 0.027 mmol) in THF (16 ml) and DMF (8 ml) precooled to 0 °C were added NaH (0.624 g, 0.026 mmol) and (*S*)-glycidol (1.000 g, 0.013 mmol). The resulting suspension was stirred at 0 °C for 25 min and at r.t. for 7 h, followed by quenching with H_2O at 0°C. The separated aqueous layer was extracted with Et_2O. The combined organic extracts were dried, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1 to 4:1) to give **24** as a colorless oil (2.50 g, 95%); IR (neat, cm^{-1}) 1612, 1514, 1249; ^1H NMR (300 MHz, $CDCl_3$): 7.27 (d, *J* = 8.8, 2 H), 6.88 (d, *J* = 8.8, 2 H), 4.54 (d, *J* = 11.5, 1 H), 4.48 (d, *J* = 11.5, 1 H), 3.80 (s, 3 H), 3.72 (dd, *J* = 11.4, 3.1, 1 H), 3.41 (dd, *J* = 11.4, 5.8, 1 H), 3.19–3.13 (m, 1 H), 2.78 (dd, *J* = 5.1, 4.2, 1 H), 2.60 (dd, *J* = 5.0, 2.7, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.2, 129.8, 129.3 (2C), 113.7 (2C), 72.8, 70.4, 55.1, 50.8, 44.2; HRMS *m/z* calculated for $C_{11}H_{14}O_3$ (M^+) 194.0943, observed 194.0945; $[\alpha]_D$ +2.7 (*c* 3.6, $CHCl_3$). Calculated for $C_{11}H_{14}O_3$: C, 68.02, H, 7.27. Found: C, 67.91; H, 7.16.

Alcohol **25**

Anhydrous CuI powder (347 mg, 1.81 mmol) was cooled to 0 °C and treated with a 1 M solution of vinylmagnesium bromide in THF (11.6 ml, 11.6 mmol). After the addition was complete, the dark-brown slurry was stirred at that temperature for 30 min and cooled to –78 °C. A solution of **24** (1.13 g, 5.81 mmol) in THF (4.0 ml) was added. The resulting slurry was stirred at –78 °C for 45 min and at 0 °C for 2 h. A solution of NH_4Cl (40 ml) (buffered with NH_4OH to pH 8) was added. The mixture was warmed to r.t. and vigorously stirred for 30 min. The separated aqueous layer was extracted with Et_2O, the combined organic layers were dried. After evaporation of the solvent, the final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 4:1 to 2:1) to afford **25** as a yellowish oil (1.28 g, 99%); IR (neat, cm^{-1}) 3445, 1613, 1514; ^1H NMR (300 MHz, $CDCl_3$): 7.26 (d, *J* = 8.8, 2 H), 6.89 (d, *J* = 8.8, 2 H), 5.89–5.76 (m, 1 H), 5.15–5.06 (m, 2 H), 4.49 (s, 2 H), 3.90–3.81 (m, 1 H), 3.81 (s, 3 H), 3.49 (dd, *J* = 9.5, 3.4, 1 H), 3.34 (dd, *J* = 9.5, 7.4, 1 H), 2.30 (br s, 1 H), 2.26 (t, *J* = 5.5, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.2, 134.2, 130.0, 129.3 (2C), 117.5, 113.8 (2C), 73.5, 72.9, 69.6, 55.2, 37.8; HRMS *m/z* calculated for $C_{13}H_{18}O_3$ (M^+) 222.1256, observed 222.1256; $[\alpha]_D$ –2.2 (*c* 1.1, $CHCl_3$).

Diether **26**

To a solution of PPTS (33 mg, 0.130 mmol) in CH_2Cl_2 (3.0 ml) was added a solution of **25** (291 mg, 1.310 mmol) and DHP (184 mg, 2.19 mmol) in CH_2Cl_2 (6.0 ml). The reaction mixture was stirred for 5 h. Half-saturated brine (50 ml) was added and the layers were shaken extensively. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried, the solvent was removed under reduced

pressure, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1) to give **26** as a colorless oil with a pleasant odor (392 mg, 98%); IR (neat, cm^{-1}) 1613, 1514, 1248; ^1H NMR (300 MHz, $CDCl_3$): 7.26 (d, *J* = 8.8, 2 H), 7.23 (d, *J* = 8.8, 2 H), 6.86 (d, *J* = 8.8, 2 H), 6.85 (d, *J* = 8.8, 2 H), 5.93–5.72 (m, 2 H), 5.12–5.00 (m, 4 H), 4.83 (t, *J* = 3.0, 1 H), 4.71 (t, *J* = 2.9, 1 H), 4.48 (s, 2 H), 4.44 (s, 2 H), 3.97–3.79 (m, 4 H), 3.78 (s, 6 H), 3.57 (dd, *J* = 10.0, 5.1, 1 H), 3.51–3.39 (m, 5 H), 2.44–2.23 (m, 4 H), 1.87–1.46 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.0 (2C), 134.8, 134.5, 130.5, 130.4, 129.2 (2C), 129.0 (2C), 117.1, 116.8, 113.6 (4C), 97.8 (2C), 75.0, 74.4, 72.8 (2C), 71.8, 71.5, 62.3, 62.2, 55.1 (2C), 37.2, 35.9, 30.9, 30.7, 25.4 (2C), 19.5 (2C); HRMS *m/z* calculated for $C_{18}H_{26}O_4$ (M^+) 306.1831, observed 306.1828.

Aldehyde **27**

To a solution of **26** (297 mg, 0.969 mmol) in THF (3.0 ml) were added H_2O (0.5 ml), OsO_4 (one tiny crystal) and NMO monohydrate (138 mg, 1.176 mmol). The reaction mixture was stirred at r.t. for 1.75 h. H_2O (1.0 ml) and $NaIO_4$ (628 mg, 2.937 mmol) were added and the resulting mixture was further stirred at r.t. for 1 h. H_2O was added to dissolve the precipitate formed, followed by Et_2O. The separated aqueous layer was extracted with Et_2O. The combined organic layers were dried and evaporated, and the final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 6:1) to afford **27** as a light tan oil (259 mg, 87%); IR (neat, cm^{-1}) 1725, 1612, 1514; ^1H NMR (300 MHz, $CDCl_3$): 9.77 (t, *J* = 2.3, 1 H), 9.76 (t, *J* = 2.3, 1 H), 7.22 (d, *J* = 8.7, 2 H), 7.21 (d, *J* = 8.7, 2 H), 6.85 (d, *J* = 8.6, 2 H), 6.84 (d, *J* = 8.6, 2 H), 4.74 (m, 1 H), 4.71 (m, 1 H), 4.46 (s, 2 H), 4.45 (s, 2 H), 4.36 (m, 1 H), 4.28 (m, 1 H), 3.89–3.76 (m, 2 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.66 (dd, *J* = 9.7, 4.4, 1 H), 3.53–3.43 (m, 5 H), 2.74–2.57 (m, 4 H), 1.83–1.61 (m, 4 H), 1.58–1.45 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$): 201.2, 200.8, 159.1 (2C), 130.0, 129.9, 129.2 (2C), 129.1 (2C), 113.7 (2C), 113.6 (2C), 98.9, 98.3, 72.9 (2C), 71.8, 71.7, 70.9, 70.8, 62.7 (2C), 55.1 (2C), 46.7, 46.4, 30.7 (2C), 25.2 (2C), 19.6 (2C); HRMS *m/z* calculated for $C_{17}H_{24}O_5$ (M^+) 308.1624, observed 308.1628. Calculated for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 65.93; H, 7.89.

Spiroacetal **30**

To a solution of (–)-diisopinocampheylchloroborane (260 mg, 0.811 mmol) in Et_2O (1.5 ml) precooled to 0 °C was added Et_3N (0.13 ml, 0.92 mmol) and the resulting solution was stirred at that temperature for 30 min. A solution of **18** (294 mg, 0.541 mmol) in Et_2O (6.5 ml) was added and the reaction mixture was stirred at 0 °C for 2 h, then cooled to –78 °C. A solution of **27** (203 mg, 0.658 mmol) in Et_2O (3.0 ml) was added at –78 °C and the resulting mixture was stirred at that temperature for 4 h and at –20 °C for 16 h, quenched with pH 7 buffer (5 ml) and treated with 30% H_2O_2 (10 ml) and MeOH (6 ml) prior to warming to r.t. After 2.5 h of stirring, pH 7 buffer (80 ml) and Et_2O (60 ml) were introduced, the separated aqueous layer was extracted with Et_2O. The combined organic extracts were dried. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 4:1 to 1:4) to give **28** as a colorless oil (409 mg, 89%); IR (neat, cm^{-1}) 3462, 1738, 1712; due to the complexity of both the ^1H and ^{13}C NMR spectra of **28**, they are not reported here; FAB MS *m/z* calculated for $C_{43}H_{68}BrO_{10}Si$ (M^+ + H) 851.40, observed 851.00. Calculated for $C_{43}H_{67}BrO_{10}Si$: C, 60.62; H, 7.93. Found: C, 60.57; H, 7.98.

To a solution of **28** (85 mg, 0.10 mmol) in PhH (3.0 ml) precooled to 0 °C were added pyridine (90 μl, 1.08 mmol) and AcCl (80 μl, 1.11 mmol). The reaction mixture was warmed to r.t., stirred for 4 h, and diluted with saturated $NaHCO_3$ solution and H_2O. The separated aqueous layer was extracted with CH_2Cl_2, the combined organic extracts were dried, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:2) to give **29** as a colorless oil (80 mg, 90%); IR (neat, cm^{-1}) 1739, 1613, 1570; due to the complexity of both the ^1H and ^{13}C NMR spectra of **29** they are not reported here; FAB MS *m/z* calculated for $C_{45}H_{70}BrO_{11}Si$ (M^+ + H) 893.40, observed 893.20. Calculated for $C_{45}H_{69}BrO_{11}Si$: C, 60.46; H, 7.78. Found: C, 60.62; H, 7.81.

To a solution of **29** (569 mg, 0.636 mmol) in CH_2Cl_2 (2.8 ml) precooled to –20 °C was added ethanethiol (0.7 ml, 1.26 mmol) and the solution was stirred for 15 min. $BF_3{\cdot}OEt_2$ (70 μl, 0.13 mmol) was introduced dropwise. The reaction mixture was allowed to warm to 0 °C with stirring for 2 h, at which point saturated $NaHCO_3$ solution and H_2O were added. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 4:1 to 1:8) to give **30** as a white crystalline solid (247 mg, 66%), m.p. 98–99 °C; IR (neat, cm^{-1}) 3504, 1730, 1612; ^1H NMR (300 MHz, C_6D_6): 7.58 (d, *J* = 7.3, 1 H), 7.33 (d, *J* = 8.0, 1 H), 7.21 (d, *J* = 8.6, 2 H), 7.00 (d, *J* = 7.5, 1 H), 6.82 (d, *J* = 8.6, 2 H), 6.75 (t, *J* = 7.5, 1 H), 4.95 (m, 1 H), 4.56 (d, *J* = 13.4, 1 H), 4.50 (d, *J* = 13.4, 1 H), 4.47–4.41 (m, 2 H), 4.28 (d, *J* = 11.9, 1 H), 4.24 (m, 1 H), 4.18 (d, *J* = 11.9, 1 H), 4.01 (br s, 1 H), 3.87–3.79 (m, 1 H), 3.63–3.54 (m, 1 H), 3.30 (s, 3 H), 3.12 (dd, *J* = 9.8, 7.7, 1 H), 3.02 (dd, *J* = 9.8, 3.4, 1 H), 1.92–1.59 (m, 5 H), 1.84 (s, 3 H), 1.44 (d, *J* = 13.8, 1 H), 1.27–1.11 (m, 4 H); ^{13}C NMR (75 MHz, C_6D_6): 169.8, 159.7, 138.6, 132.4, 130.7, 129.3 (2C), 129.0, 128.8, 127.6, 122.3, 114.1 (2C), 98.2, 72.9, 72.4, 72.2, 67.4, 66.5, 65.0, 64.2, 61.1, 54.7, 40.3, 38.6, 37.4, 36.3, 30.7, 21.2; FAB MS *m/z* calculated for $C_{29}H_{38}BrO_8$ (M^+ + H) 593.20, observed 593.50; $[\alpha]_D$ –61 (*c* 0.50, $CHCl_3$).

Hydroxy Acetal **31**

To a solution of **30** (195 mg, 0.329 mmol) in THF (0.6 ml) were added *i*-Pr_2NEt (0.16 ml, 0.91 mmol), SEMCl (0.10 ml, 0.58 mmol) and TBAI (15 mg, 0.04 mmol). The reaction mixture was stirred at r.t. for 24 h, quenched with $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layers were dried, and after solvent evaporation, the residue was purified by column chromatography on silica gel (hexanes/EtOAc 2:1) to give the fully protected acetate as a colorless oil (227 mg, 95%); IR (neat, cm^{-1}) 1737, 1613, 1586; ^1H NMR (300 MHz, C_6D_6): 7.58 (d, *J* = 7.6, 1 H), 7.31 (d, *J* = 8.0, 1 H), 7.26 (d, *J* = 8.6, 2 H), 6.99 (t, *J* = 7.5, 1 H), 6.81 (d, *J* = 8.6, 2 H), 6.72 (t, *J* = 7.8, 1 H), 5.06 (m, 1 H), 4.77 (d, *J* = 7.0, 1 H), 4.67 (d, *J* = 7.0, 1 H), 4.60 (d, *J* = 13.4, 1 H), 4.54 (d, *J* = 13.4, 1 H), 4.53 (d, *J* = 11.8, 1 H), 4.53–4.46 (m, 1 H), 4.41 (d, *J* = 11.8, 1 H), 4.39–4.28 (m, 1 H), 3.92–3.84 (m, 2 H), 3.75–3.61 (m, 3 H), 3.47–3.35 (m, 2 H), 3.33 (s, 3 H), 1.98 (d, *J* = 14.8, 1 H), 1.90–1.63 (m, 5 H), 1.84 (s, 3 H), 1.45–1.16 (m, 4 H), 0.94 (t, *J* = 7.9, 2 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 169.8, 159.6, 138.7, 132.4, 131.5, 129.3 (2C), 129.1, 128.7, 127.5, 122.4, 114.0 (2C), 96.4, 93.1, 73.1 (2C), 72.3, 68.7, 67.6, 67.3, 65.0, 64.8, 61.3, 54.7, 38.2, 37.9, 36.5, 36.1, 31.5, 21.2, 18.3, –1.2 (3C); TOF MS ES^+ *m/z* calculated for $C_{35}H_{52}BrO_9Si$ (M^+ + H) 723.2764, observed 723.2272; $[\alpha]_D$ –57 (*c* 0.50, $CHCl_3$). Calculated for $C_{35}H_{51}BrO_9Si$: C, 58.08; H, 7.10. Found: C, 57.83; H, 7.05.

To a stirred solution of the above acetate (227 mg, 0.314 mmol) in CH_2Cl_2 (3.5 ml) cooled to –78 °C was added a 1.0 M solution of Dibal-H in hexanes (0.63 ml, 0.63 mmol) dropwise. The solution was stirred at –78 °C for 45 min, at which point it was quenched by the addition of acetone (0.8 ml). The solution was stirred at –78 °C for 5 min and transferred into a rapidly stirred mixture of CH_2Cl_2 and aqueous Rochelle's salt solution at r.t. The resulting two-phase mixture was stirred for 30 min. The separated aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried and concentrated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:2) to give **31** as a colorless oil (205 mg, 98%); IR (neat, cm^{-1}) 3517, 1714, 1612; ^1H NMR (300 MHz, C_6D_6): 7.55 (d, *J* = 7.6, 1 H), 7.32 (d, *J* = 7.8, 1 H), 7.30 (d, *J* = 8.6, 2 H), 6.99 (t, *J* = 7.5, 1 H), 6.82 (d, *J* = 8.6, 2 H), 6.72 (t, *J* = 7.8, 1 H), 4.77 (d, *J* = 7.1, 1 H), 4.66 (d, *J* = 7.1, 1 H), 4.60 (d, *J* = 11.8, 1 H), 4.52 (s, 2 H), 4.52–4.38 (m, 2 H), 4.50 (d, *J* = 11.8, 1 H), 4.23 (d, *J* = 10.2, 1 H), 4.09–4.03 (m, 1 H), 3.87 (m, 1 H), 3.74–3.64 (m, 2 H), 3.61–3.35 (m, 4 H), 3.34 (s, 3 H), 1.96–1.73 (m, 4 H), 1.69–1.52 (m, 2 H), 1.45–1.21 (m, 4 H), 1.93 (t, *J* = 8.0, 2 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 159.5, 138.5, 132.5, 131.7, 129.5, 129.3 (2C), 128.8, 127.5, 122.7, 114.0 (2C), 98.5, 93.1, 73.4, 73.1, 72.4, 68.2, 67.9, 65.1, 65.0, 64.9, 63.2, 54.7, 41.0, 37.7, 36.2 (2C), 35.0, 18.3, –1.2 (3C); FAB MS *m/z* calculated for $C_{33}H_{50}BrO_8Si$ (M^+ + H) 681.27, observed 681.20; $[\alpha]_D$ –33.1 (*c* 1.34, $CHCl_3$). Calculated for $C_{33}H_{49}BrO_8Si$: C, 58.14; H, 7.24. Found: C, 57.91; H, 7.34.

Hydroxy Spiroacetal **32**

To a solution of **31** (205 mg, 0.308 mmol) in CH_2Cl_2 (1 ml) were added NMO (54 mg, 0.462 mmol) and 4Å MS (154 mg). After the reaction mixture was cooled to 0 °C, TPAP (10 mg, 0.028 mmol) was added and the mixture was stirred at r.t. for 1 h. After the evaporation of CH_2Cl_2, the residue was diluted with Et_2O and filtered through a short plug of silica gel. Evaporation of the filtrate gave the ketone (195 mg, 96%), pure enough to be used in the next step; IR (neat, cm^{-1}) 1725, 1612, 1586; ^1H NMR (300 MHz, C_6D_6): 7.47 (d, *J* = 7.7, 1 H), 7.30 (d, *J* = 8.0, 1 H), 7.20 (d, *J* = 8.7, 2 H), 6.98 (t, *J* = 7.5, 1 H), 6.80 (d, *J* = 8.7, 2 H), 6.71 (t, *J* = 7.6, 1 H), 4.75 (d, *J* = 7.1, 1 H), 4.64 (d, *J* = 7.1, 1 H), 4.46 (d, *J* = 11.8, 1 H), 4.45–4.34 (m, 1 H), 4.40 (d, *J* = 2.9, 2 H), 4.36 (d, *J* = 11.8, 1 H), 4.25–4.20 (m, 1 H), 3.85 (m, 1 H), 3.71–3.55 (m, 3 H), 3.41–3.30 (m, 3 H), 3.33 (s, 3 H), 2.38–2.31 (m, 2 H), 2.18 (dd, *J* = 14.5, 11.5, 1 H), 2.04–1.97 (m, 2 H), 1.73–1.56 (m, 3 H), 1.25–1.16 (m, 1 H), 1.11 (dd, *J* = 14.7, 4.2, 1 H), 0.93 (t, *J* = 8.0, 2 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 203.4, 159.7, 138.6, 132.4, 131.2, 129.4 (2C), 129.1, 128.7, 127.5, 122.5, 114.0 (2C), 99.4, 93.1, 73.1, 72.3, 72.2 69.3, 68.2, 66.9, 65.1, 62.0, 54.8, 52.2, 43.4, 37.2, 36.1, 35.7, 18.3, –1.2 (3C); FAB MS *m/z* calculated for $C_{33}H_{48}BrO_8Si$ (M^+ + H) 679.25, observed 679.30; $[\alpha]_D$ –58 (*c* 0.79, $CHCl_3$). Calculated for $C_{33}H_{47}BrO_8Si$: C, 58.31; H, 6.97. Found: C, 58.17; H, 6.88.

To a solution of the above ketone (195 mg, 0.294 mmol) in THF (4.5 ml), precooled to –78 °C was added a 3.0 M solution of MeMgBr in Et_2O (0.20 ml, 0.59 mmol). The solution was immediately warmed to 0 °C and stirred at that temperature for 2.5 h prior to quenching with NH_4Cl solution (2 ml), H_2O and CH_2Cl_2. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and evaporated, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:8) to give **32** as a colorless oil (186 mg, 93%); IR (neat, cm^{-1}) 3511, 1613, 1586; ^1H NMR (300 MHz, C_6D_6): 7.39 (t, *J* = 7.8, 2 H), 7.16 (d, *J* = 8.6, 2 H), 7.12 (d, *J* = 7.5, 1 H), 7.00 (t, *J* = 7.5, 1 H), 6.75 (d, *J* = 8.6, 2 H), 4.65 (d, *J* = 7.2, 1 H), 4.55 (d, *J* = 7.2, 1 H), 4.52 (d, *J* = 15.2, 1 H), 4.46 (s,

2 H), 4.38 (d, *J* = 15.2, 1 H), 4.28–4.18 (m, 1 H), 4.08–3.97 (m, 1 H), 3.97–3.90 (m, 1 H), 3.69 (s, 3 H), 3.60–3.33 (m, 4 H), 1.91 (d, *J* = 14.8, 1 H), 1.80–1.69 (m, 4 H), 1.66 (d, *J* = 14.0, 1 H), 1.54 (d, *J* = 14.9, 1 H), 1.51–1.42 (m, 4 H), 1.36 (d, *J* = 11.4, 1 H), 1.28 (d, *J* = 12.8, 1 H), 1.10 (s, 3 H), 0.80 (t, *J* = 8.1, 2 H), –0.09 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 159.6, 138.5, 132.4, 131.6, 129.4, 129.3 (2C), 128.7, 127.5, 122.7, 114.0 (2C), 98.5, 93.1, 73.3, 73.1, 72.4, 68.2, 67.8 (2C), 66.8, 65.1, 63.1, 54.7, 46.7, 40.7, 37.8, 36.2, 36.1, 30.7, 18.3, –1.2 (3C); TOF MS ES$^+$ *m/z* calculated for $C_{34}H_{51}BrO_8SiNa$ (M^+ + Na) 717.2635, observed 717.2571; $[\alpha]_D$ –38 (*c* 2.1, $CHCl_3$).

Alcohol **33**

To a solution of **32** (184 mg, 0.264 mmol) in CH_2Cl_2 (3.2 ml), cooled to –40 °C were added *i*-Pr_2NEt (0.23 ml, 1.32 mmol) and TBSOTf (0.18 ml, 0.79 mmol). The reaction mixture was allowed to warm to 0 °C over 1 h and maintained at that temperature for 1 h prior to the addition of saturated $NaHCO_3$ solution (10 ml). The separated aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried and evaporated, and purification was achieved by column chromatography on silica gel (pet ether/EtOAc 8:1 to 4:1) to afford the silyl ether as a colorless oil (200 mg, 93%); IR (neat, cm^{-1}) 1612, 1586, 1570; ^{1}H NMR (300 MHz, C_6D_6): 7.61 (d, *J* = 7.7, 1 H), 7.32 (d, *J* = 8.7, 3 H), 7.00 (t, *J* = 7.6, 1 H), 6.82 (d, *J* = 8.6, 2 H), 6.71 (t, *J* = 7.7, 1 H), 4.84 (d, *J* = 7.0, 1 H), 4.72 (d, *J* = 7.0, 1 H), 4.63 (t, *J* = 11.8, 1 H), 4.62–4.32 (m, 4 H), 4.49 (d, *J* = 11.8, 1 H), 3.98 (m, 1 H), 3.77–3.44 (m, 6 H), 3.33 (s, 3 H), 2.10–1.78 (m, 5 H), 1.72 (d, *J* = 13.4, 1 H), 1.48–1.25 (m, 3 H), 1.20 (d, *J* = 14.2, 1 H), 1.09 (s, 3 H), 1.05 (s, 9 H), 0.95 (t, *J* = 7.6, 2 H), 0.17 (s, 3 H), 0.16 (s, 3 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 159.6, 149.2, 132.4, 131.7, 129.3 (2C), 129.0, 128.6, 127.5, 122.4, 114.0 (2C), 97.2, 93.2, 73.3, 73.1, 72.3, 71.1, 69.1, 68.2, 65.8, 65.0, 62.6, 54.7, 48.8, 41.9, 39.2, 36.4, 36.0, 32.8, 26.4 (3C), 18.5, 18.3, –1.2 (3C), –1.4, –1.5; TOF MS ES$^+$ *m/z* calculated for $C_{40}H_{65}BrO_8Si_2Na$ (M^+ + Na) 831.3499, observed 831.3336; $[\alpha]_D$ –41 (*c* 0.52, $CHCl_3$).

A solution of the above product (49 mg, 0.060 mmol) in CH_2Cl_2 (3.2 ml) and H_2O (0.2 ml) was treated with DDQ (21 mg, 0.092 mmol), and the resulting mixture was allowed to stir at r.t. for 1 h. The reaction mixture was diluted with saturated $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic extracts were dried and evaporated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 3:1 to 2:1) to give **33** as a colorless oil (38 mg, 90%); IR (neat, cm^{-1}) 3489, 1472, 1440; ^{1}H NMR (300 MHz, C_6D_6): 7.66 (d, *J* = 7.5, 1 H), 7.33 (d, *J* = 8.0, 1 H), 7.07 (t, *J* = 7.5, 1 H) 6.72 (t, *J* = 7.8, 1 H), 4.69 (d, *J* = 7.0, 1 H), 4.62 (d, *J* = 7.0, 1 H), 4.55 (s, 2 H), 4.52–4.39 (m, 1 H), 4.30–4.22 (m, 1 H), 3.90 (m, 1 H), 3.70–3.61 (m, 4 H), 3.67 (t, *J* = 7.9, 2 H), 3.51 (dd, *J* = 10.7, 8.6, 1 H), 2.03 (dq, *J* = 13.9, 6.3, 2 H), 1.86–1.74 (m, 4 H), 1.39–1.28 (m, 3 H), 1.15 (d, *J* = 14.1, 1 H), 1.07 (d, *J* = 11.6, 1 H), 1.04 (s, 3 H), 1.03 (s, 9 H), 0.94 (t, *J* = 8.2, 2 H), 0.15 (s, 3 H), 0.11 (s, 3 H), 0.02 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 138.8, 132.4, 129.2, 128.7. 127.6, 122.4, 96.9, 93.6, 72.3, 70.9, 69.7, 68.0, 66.1, 65.9, 65.2, 62.6, 48.5, 41.0, 39.1, 36.2, 35.6, 32.8, 26.3 (3C), 18.5, 18.3, –1.2, –1.4, –1.6 (3C); TOF MS ES$^+$ *m/z* calculated for $C_{32}H_{57}BrO_7Si_2Na$ (M^+ + Na) 711.2724, observed 711.2736; $[\alpha]_D$ –56 (*c* 0.34, $CHCl_3$).

Iodide **34**

To a solution of **33** (27 mg, 0.039 mmol) in PhH (1 ml) at r.t. were added imidazole (22 mg, 0.322 mmol), PPh_3 (84 mg, 0.322 mmol) and I_2 (66 mg, 0.258 mmol). The reaction mixture was stirred for 1.5 h. Saturated $Na_2S_2O_3$ solution was added and the two-phase system was stirred for 20 min (until the organic layer became clear). The separated aqueous layer was extracted with PhH. The combined organic extracts were dried and evaporated, and the residue was purified by column chromatography on silica gel (PhH/EtOAc 20:1) to give **34** as a colorless oil (27 mg, 82%); IR (neat, cm^{-1}) 1471, 1440, 1370; ^1H NMR (300 MHz, C_6D_6): 7.62 (d, *J* = 7.6, 1 H), 7.34 (d, *J* = 7.9, 1 H), 7.03 (t, *J* = 7.7, 1 H), 6.72 (t, *J* = 7.8, 1 H), 4.94 (d, *J* = 7.1, 1 H), 4.81 (d, *J* = 7.1, 1 H), 4.63–4.54 (m, 1 H), 4.62 (d, *J* = 13.6, 1 H), 4.56 (d, *J* = 13.6, 1 H), 4.07–3.97 (m, 2 H), 3.85–3.62 (m, 4 H), 2.98 (d, *J* = 5.7, 2 H), 2.07–1.95 (m, 2 H), 1.89–1.80 (m, 2 H), 1.68 (dd, *J* = 14.3, 1.6, 1 H), 1.59 (d, *J* = 13.1, 1 H), 1.45–1.28 (m, 3 H), 1.08 (d, *J* = 14.3, 1 H), 1.03 (s, 9 H), 1.00 (s, 3 H), 0.99 (t, *J* = 7.9, 2 H), 0.15 (s, 3 H), 0.13 (s, 3 H), 0.02 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 138.8, 132.5, 129.0, 128.7, 127.2, 122.4, 97.8, 93.1, 72.3, 71.2, 68.5, 68.1, 65.7, 65.1, 62.9, 48.2, 45.0, 38.5, 36.2, 36.1, 32.4, 26.3 (3C), 18.5, 18.3, 10.4, –1.2 (3C), –1.4, –1.6; TOF MS ES$^+$ *m/z* calculated for $C_{32}H_{56}BrIO_6Si_2Na$ (M^+ + Na) 821.1741, observed 821.1736; $[\alpha]_D$ –66 (*c* 0.16, $CHCl_3$).

Nitrile **35**

To a solution of **34** (690 mg, 0.863 mmol) in DMF (5 ml) was added KCN (1.13 g, 17.26 mmol). The reaction mixture was warmed to 65 °C for 36 h, returned to r.t., quenched with aqueous $NaHCO_3$ solution and extracted with a 1:1 pet ether/Et_2O mixture. The combined organic extracts were dried and evaporated, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 10:1 to 1:1) to give **35** as a colorless oil (603 mg, 100%); IR (neat, cm^{-1}) 2280, 1472, 1439; ^1H NMR (300 MHz, C_6D_6): 7.54 (d, *J* = 7.7, 1 H), 7.32 (d, *J* = 8.0, 1 H), 7.03 (t, *J* = 7.5, 1 H), 6.75 (t, *J* = 7.7, 1 H), 4.81 (d, *J* = 7.1, 1 H), 4.70 (d, *J* = 7.1, 1 H), 4.50 (s, 2 H), 4.46–4.35 (m, 1 H), 4.14–4.08 (m, 1 H), 3.88 (m, 1 H), 3.77–3.50 (m, 4 H), 1.97 (dd, *J* = 16.7, 5.4, 1 H), 1.96–1.68 (m, 6 H), 1.62 (dd, *J* = 14.4, 1.2, 1 H), 1.33 (d, *J* = 13.3, 1 H), 1.24 (dd, *J* = 14.6, 4.0, 1 H), 1.08 (d, *J* = 13.1, 1 H), 0.98 (d, *J* = 13.1, 1 H), 0.96 (s, 9 H), 0.95 (s, 3 H), 0.94 (t, *J* = 8.2, 2 H), 0.09 (s, 3 H), 0.06 (s, 3 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 138.6, 132.5, 129.0, 128.8, 127.6, 122.4, 117.1, 97.6, 93.1, 72.2, 70.8, 68.6, 67.8, 65.1, 62.6, 61.7, 47.8, 43.8, 38.5, 36.0, 35.8, 32.4, 26.3 (3C), 23.8, 18.5, 18.3, –1.1 (3C), –1.4, –1.6; TOF MS ES$^+$ *m/z* calculated for $C_{34}H_{57}BrNO_6Si_2Na$ (M^+ + Na) 720.2727, observed 720.2703; $[\alpha]_D$ –48.1 (*c* 2.23, $CHCl_3$).

Alcohol **36**

To a solution of **35** (179 mg, 0.256 mmol) in CH_2Cl_2 (2.8 ml) and cooled to –78 °C was added Dibal-H (0.28 ml, 0.28 mmol) dropwise. The reaction mixture was stirred at that temperature for 10 min. Acetone (1 ml) was added, followed 5 min later with Rochelle's salt solution (7 ml), phosphate pH 7 buffer (8 ml) and CH_2Cl_2 (15 ml). The mixture was warmed to r.t. and stirred for 30 min. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried and evaporated in vacuo. The residue (180 mg, 100%) was dried azeotropically with PhH and used without further purification in the next reaction; IR (neat, cm^{-1}) 1728, 1472, 1439; ^1H NMR (300 MHz, C_6D_6): 9.78 (dd, *J* = 3.5, 1.3, 1 H), 7.57 (d, *J* = 7.7, 1 H), 7.33 (d, *J* = 8.0, 1 H), 7.06 (t, *J* = 7.6, 1 H), 6.72 (t, *J* = 7.5, 1 H),

4.77(d, *J* = 7.1, 1 H), 4.65 (d, *J* = 7.1, 1 H), 4.56 (d, *J* = 13.5, 1 H), 4.52–4.37 (m, 1 H), 4.49 (d, *J* = 13.5, 1 H), 4.35–4.28 (m, 1 H), 4.15–4.05 (m, 1 H), 3.91–3.54 (m, 4 H), 2.25–1.63 (m, 8 H), 1.39 (d, *J* = 11.3, 1 H), 1.24 (dd, *J* = 14.4, 3.9, 1 H), 1.15–1.10 (m, 2 H), 1.07 (s, 3 H), 1.02 (s, 9 H), 0.94 (t, *J* = 8.0, 2 H), 0.14 (s, 3 H), 0.12 (s, 3 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 200.1, 138.9, 132.5, 128.9, 128.7, 127.7, 122.3, 97.2, 93.0, 72.2, 68.6, 67.9, 65.0, 62.2, 61.4, 49.3, 48.1, 44.8, 38.5, 36.1, 35.9, 32.6, 26.4 (3C), 18.6, 18.3, 15.6, –1.0, –1.2 (3C), –1.5; TOF MS ES$^+$ *m/z* calculated for $C_{33}H_{57}BrO_7Si_2Na$ (M^+ + Na) 723.2724, observed 723.2722; $[\alpha]_D$ –48 (*c* 0.33, $CHCl_3$).

To a solution of the above aldehyde (180 mg, 0.256 mol) in Et_2O (5.0 ml) and cooled to –78 °C was added a 2.0 M solution of EtMgBr in Et_2O (0.64 ml, 1.28 mmol). The reaction mixture was stirred at that temperature for 1 h, warmed to 0 °C and stirred for 2 h prior to quenching with NH_4Cl solution (5 ml) and CH_2Cl_2 (10 ml) and warming to r.t. The separated aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried and evaporated to give **36** as a colorless oil (139 mg, 74%) which was pure enough by ^{1}H NMR analysis to be used directly in the next step; IR (neat, cm^{-1}) 3499, 1472, 1440; ^{1}H NMR (300 MHz, C_6D_6): 7.65 (d, *J* = 7.7, 1 H), 7.59 (d, *J* = 7.7, 1 H), 7.34 (d, *J* = 7.9, 2 H), 7.10 (t, *J* = 7.7, 1 H), 7.07 (t, *J* = 7.7, 1 H), 6.74 (t, *J* = 7.7, 2 H), 4.94 (br s, 1 H), 4.78 (d, *J* = 7.0, 2 H), 4.72 (d, *J* = 7.0, 2 H), 4.67–4.52 (m, 5 H), 4.51–4.38 (m, 2 H), 4.32–4.27 (m, 1 H), 4.30–4.20 (m, 1 H), 4.00–3.85 (m, 4 H), 3.82–3.70 (m, 6 H), 3.68–3.58 (m, 2 H), 2.12–1.95 (m, 2 H), 1.85–1.70 (m, 5 H), 1.68–0.90 (m, 21 H), 1.05 (s, 6 H), 1.03 (s, 18 H), 0.97 (t, *J* = 7.0, 6 H), 0.94 (t, *J* = 8.0, 4 H), 0.20 (s, 3 H), 0.19 (s, 3 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.02 (s, 9 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 139.1, 139.0, 132.9, 132.8, 129.5, 129.3, 129.2, 129.1, 128.2, 128.1, 122.9, 122.6, 97.5, 97.3, 93.8, 93.7, 73.4, 72.7, 71.4, 71.1, 70.7, 69.9, 69.7, 68.3, 68.2, 68.0, 65.6, 63.5, 63.2, 62.7, 48.8, 48.6, 46.3, 45.5, 43.5 (2C), 41.5, 40.4 (2C), 36.7, 36.5, 35.3, 33.2, 33.0, 31.7 (2C), 30.8, 26.7 (6C), 18.9 (2C), 18.7, 11.3, 10.5 (2C), –0.8 (6C), –0.9, –1.0, –1.1, –1.2; TOF MS ES$^+$ *m/z* calculated for $C_{35}H_{63}BrO_7Si_2Na$ (M^+ + Na) 753.3193, observed 753.3178.

Ketone **37**

To a solution of **36** (13.8 mg, 0.019 mmol) in CH_2Cl_2 (1.0 ml) were added NMO (10.2 mg, 0.087 mmol) and 4Å MS (30 mg), and the reaction mixture was cooled to 0 °C. TPAP (on the tip of a spatula) was added, and the mixture was warmed to r.t. and stirred for 8 h. After the evaporation of CH_2Cl_2, the residue was diluted with Et_2O, filtered through a short plug of silica gel and evaporated to give **37** as a colorless oil (13.7 mg, 99%), pure enough by ^{1}H NMR to be used in the next step; IR (neat, cm^{-1}) 1714, 1462, 1441; ^{1}H NMR (300 MHz, C_6D_6) 7.66 (d, *J* = 7.5, 1 H), 7.33 (d, *J* = 7.5, 1 H), 7.05 (t, *J* = 7.5, 1 H), 6.73 (t, *J* = 7.5, 1 H), 4.73 (d, *J* = 7.0, 1 H), 4.64 (d, *J* = 7.0, 1 H), 4.62 (d, *J* = 5.6, 2 H), 4.65–4.50 (m, 1 H), 4.27–4.24 (m, 1 H), 3.90 (m, 1 H), 3.78 (q, *J* = 6.6, 2 H), 3.69 (t, *J* = 7.9, 2 H), 2.55–2.35 (m, 2 H), 2.30–2.00 (m, 3 H), 1.62–1.52 (m, 1 H), 1.42–1.23 (m, 4 H), 1.05 (s, 9 H), 1.04 (s, 3 H), 1.15–0.85 (m, 9 H), 0.18 (s, 3 H), 0.17 (s, 3 H), 0.02 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 208.3, 139.0, 132.4, 129.0, 128.6, 127.4, 122.4, 97.1, 93.1, 72.2, 71.0, 68.9, 68.4, 65.0, 63.8, 62.7, 48.4, 48.2, 45.0, 39.2, 37.5, 36.3, 35.7, 32.7, 26.3 (3C), 18.5, 18.3, 7.8, –1.2 (3C), –1.4, –1.5; TOF MS ES$^+$ *m/z* calculated for $C_{35}H_{61}BrO_7Si_2Na$ (M^+ + Na) 751.3037, observed 751.3008; $[\alpha]_D$ –52 (*c* 0.37, $CHCl_3$).

Diol **38**

To a solution of **37** (100 mg, 0.137 mmol) in MeOH (15 ml) was added aqueous 3 M HCl (4 ml) at r.t. After 12 h of stirring, 1 M $NaHCO_3$ solution (12 ml) was added. The mixture was extracted with CH_2Cl_2. The combined organic layers were dried and evaporated and the residue was purified by column chromatography on silica gel (40–70% EtOAc/hexanes) to give **38** as a colorless oil (60 mg, 90%); IR (neat, cm^{-1}) 3510, 1715, 1408; ^1H NMR (300 MHz, $CDCl_3$): 7.53 (m, 2 H), 7.29 (dt, *J* = 7.5, 1.2, 1 H), 7.14 (dt, *J* = 7.8, 1.7, 1 H), 4.60 (s, 2 H), 4.59–4.40 (m, 2 H), 4.02 (t, *J* = 2.8, 1 H), 3.75 (t, *J* = 6.3, 2 H), 2.64 (dd, *J* = 16.8, 9.5, 1 H), 2.46 (dd, *J* = 16.7, 3.6, 1 H), 2.38 (m, 4 H), 1.95–1.72 (m, 5 H), 1.70–1.44 (m, 4 H), 1.33 (dd, *J* = 13.2, 11.9, 1 H), 1.19 (s, 3 H), 1.02 (t, *J* = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 208.8, 137.7, 132.2, 129.1, 128.6, 127.2, 122.5, 99.9, 72.1, 67.9, 67.4, 64.4, 63.3, 62.6, 47.4, 45.2, 43.2, 39.8, 38.0, 36.6, 35.6, 29.9, 7.5; ES HRMS *m/z* calculated for $C_{23}H_{33}BrO_6Na$ (M^+ + Na) 507.1358, observed 507.1346; $[\alpha]_D$ –60 (*c* 1.1, $CHCl_3$).

SEM Protection of **38**

To a solution of **38** (640 mg, 1.32 mmol) in THF (5 ml) was added *i*-Pr_2NEt (1.15 ml, 6.6 mmol), SEMCl (0.26 ml, 1.45 mmol) and TBAI (500 mg, 1.36 mmol) at r.t. After 18 h of stirring, more SEMCl (0.13 ml, 0.73 mmol) was introduced. After 10 h, the reaction mixture was quenched with aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried and evaporated. The residue was purified by column chromatography on silica gel (5–30% EtOAc/hexanes) to give **39** (580 mg, 72%) and **40** (100 mg, 11%), both as colorless oils.

For **39**: IR (neat, cm^{-1}) 3508, 1714, 1407; ^1H NMR (300 MHz, $CDCl_3$): 7.53 (t, *J* = 7.1, 2 H), 7.30 (t, *J* = 7.1, 1 H), 7.12 (dt, *J* = 7.8, 1.5, 1 H), 4.68 (d, *J* = 7.1, 1 H), 4.63–4.55 (m, 4 H), 4.40 (m, 1 H), 4.15 (m, 1 H), 3.95 (m, 1 H), 3.71 (t, *J* = 6.4, 2 H), 3.60 (m, 2 H), 2.65 (dd, *J* = 13.2, 9.3, 1 H), 2.58–2.40 (m, 2 H), 2.35 (dd, *J* = 14.2, 3.6, 1 H), 1.95–1.77 (m, 3 H), 1.77–1.70 (m, 3 H), 1.57–1.40 (m, 3 H), 1.30 (dd, *J* = 12.3, 12.3, 1 H), 1.11 (s, 3 H), 1.00 (t, *J* = 7.2, 3 H), 0.90 (t, *J* = 6.4, 2 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 209.8, 137.9, 132.3 129.2, 128.7, 127.3, 122.7, 98.2, 92.6, 72.2, 68.2, 68.0, 67.6, 64.9, 64.0, 63.6, 48.0, 46.0, 43.4, 37.6, 37.3, 35.8, 35.5, 30.0, 18.1, 7.5, –1.4 (3C); ES HRMS *m/z* calculated for $C_{29}H_{47}BrO_7SiNa$ (M^+ + Na) 637.2167, observed 637.2192; $[\alpha]_D$ –62.7 (*c* 1.26, $CHCl_3$).

For **40**: IR (neat, cm^{-1}) 1715, 1373, 1248; ^1H NMR (300 MHz, $CDCl_3$): 7.52 (m, 2 H), 7.30 (dt, *J* = 7.6, 1.0, 1 H), 7.12 (dt, *J* = 7.8, 1.6, 1 H), 4.95 (d, *J* = 7.8, 1 H), 4.73–4.52 (m, 5 H), 4.35 (m, 1 H), 3.99 (m, 2 H), 3.82–3.65 (m, 3 H), 3.64–3.44 (m, 3 H), 2.68–2.40 (m, 3 H), 2.34 (dd, *J* = 13.8, 4.2, 1 H), 2.04 (dd, *J* = 14.9, 2.0, 1 H), 1.89–1.69 (m, 5 H), 1.47 (m, 2 H), 1.30–1.17 (m, 2 H), 1.23 (s, 3 H), 0.99 (t, *J* = 7.2, 3 H), 0.90 (m, 4 H), 0.02 (s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$): 210.3, 138.2, 132.3, 128.9, 128.5, 127.2, 122.4, 96.4, 92.6, 90.3, 72.8, 72.1, 68.3, 68.1, 65.0, 64.8, 63.7, 61.7, 47.9, 42.6, 42.3, 38.3, 37.4, 36.0, 35.4, 29.0, 18.2, 18.1, 7.5, –1.4 (6C); ES HRMS *m/z* calculated for $C_{35}H_{61}BrO_8Si_2Na$ (M^+ + Na) 767.2981, observed 767.3026; $[\alpha]_D$ –78 (*c* 1.2, $CHCl_3$).

TES Protection of 39

To a solution of **39** (200 mg, 0.33 mmol) in CH_2Cl_2 (3 ml) was added 2,6-lutidine (0.12 ml, 0.97 mmol) and TESOTf (0.11 ml, 0.49 mmol) at –78 °C. After 3 h of stirring at –78 °C, the reaction mixture was quenched with aqueous $NaHCO_3$ solution and the aqueous layer was

extracted with CH_2Cl_2. The combined organic layers were dried and evaporated, and the residue was purified by column chromatography on silica gel (5–10% EtOAc/hexanes) to give **41** (130 mg, 56%) and **42** (15 mg, 5%), both as colorless oils.

For **41**: IR (neat, cm^{-1}) 1715, 1370; ^1H NMR (300 MHz, $CDCl_3$): 7.54 (m, 2 H), 7.32 (dt, *J* = 7.5, 1.3, 1 H), 7.12 (dt, *J* = 7.8, 1.7, 1 H), 4.69 (d, *J* = 7.1, 1 H), 4.63 (d, *J* = 7.1, 1 H), 4.59 (s, 2 H), 4.43 (m, 1 H), 3.97 (m, 2 H), 3.75 (m, 2 H), 3.60 (m, 2 H), 2.40–2.12 (m, 3 H), 2.34 (dd, *J* = 13.5, 4.5, 1 H), 1.90–1.70 (m, 5 H), 1.65–1.40 (m, 3 H), 1.29 (m, 2 H), 1.22 (s, 3 H), 1.10–0.85 (m, 5 H), 0.96 (t, *J* = 7.7, 9 H), 0.61 (q, *J* = 7.7, 6 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 210.6, 138.3, 132.3, 128.8, 128.5, 127.3, 122.3, 96.9, 92.7, 72.0, 70.4, 68.6, 68.2, 64.8, 63.8, 62.0, 48.2, 47.7, 45.0, 38.9, 37.5, 35.9, 35.2, 32.3, 18.1, 7.6, 7.2 (3C), 6.8 (3C), –1.4 (3C); ES HRMS *m/z* calculated for $C_{35}H_{61}BrO_7Si_2Na$ (M^+ + Na) 751.3031, observed 751.2959; $[\alpha]_D$ –71.2 (*c* 1.0, $CHCl_3$).

For **42**: ^1H NMR (300 MHz, $CDCl_3$): 7.52 (dd, *J* = 0.8, 7.8, 2 H), 7.30 (dt, *J* = 1.0, 7.5, 1 H), 7.12 (dt, *J* = 2.6, 7.8, 1 H), 4.74 (d, *J* = 7.2, 1 H), 4.68 (d, *J* = 7.1, 1 H), 4.56 (s, 2 H), 4.55 (m, 1 H), 4.16 (m, 2 H), 3.94 (m, 1 H), 3.76 (m, 1 H), 3.70–3.55 (m, 3 H), 2.30 (dd, *J* = 6.6, 4.0, 1 H), 2.06–1.72 (m, 5 H), 1.70 (d, *J* = 13.3, 1 H), 1.58–1.42 (m, 5 H), 1.30 (d, *J* = 13.8, 1 H), 1.21 (s, 3 H), 1.15 (dd, *J* = 13.1, 11.4, 1 H), 1.03–0.90 (m, 21 H), 0.68 (t, *J* = 7.9, 6 H), 0.60 (t, *J* = 7.6, 6 H), 0.20 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 148.1, 138.3, 132.2, 128.6, 128.5, 127.3, 121.2, 103.8, 96.9, 92.8, 72.0, 70.6, 68.9, 68.4, 64.8, 63.8, 62.1, 48.1, 44.6, 43.1, 39.0, 35.8, 35.3, 32.3, 18.1, 10.7, 7.2 (3C), 6.9 (3C), 6.8 (3C), 5.6 (3C), –1.4 (3C).

Controlled Hydrolysis of **42**

A solution of **42** (10 mg, 0.012 mmol) in a mixture of AcOH (0.1 ml), THF (0.5 ml) and H_2O (0.1 ml) was stirred at r.t. for 3 h, diluted with Et_2O (20 ml) and washed with saturated $NaHCO_3$ solution. The separated organic phase was dried and evaporated to leave a residue that was purified by column chromatography (20% EtOAc/hexanes) on silica gel to give **41** as a colorless oil (6.9 mg, 78%).

TES Protection of **32**

A cold (–78 °C), stirred solution of **32** (1.0 g, 1.4 mmol) in CH_2Cl_2 was treated sequentially with *i*-Pr_2NEt (1.2 ml, 7.2 mmol) and TESOTf (952 μl, 4.3 mmol). The mixture was stirred at –78 °C for 30 min, slowly warmed to –40 °C, and stirred at this temperature for 5 h. After the addition of saturated $NaHCO_3$ solution (10 ml), the mixture was warmed to r.t. and the separated aqueous layer extracted with CH_2Cl_2 (3 × 30 ml). The combined organic phases were dried and evaporated. The residue was purified by column chromatography on silica gel (10% EtOAc/hexanes) to give **43** as a yellowish oil (1.15 g, 99%); IR (neat, cm^{-1}) 1614, 1514, 1248; ^1H NMR (300 MHz, $CDCl_3$): 7.52 (dd, *J* = 7.8, 0.9, 2 H), 7.27 (m, 3 H), 7.12 (dt, *J* = 7.8, 1.7, 1 H), 6.86 (d, *J* = 8.7, 2 H), 4.73 (dd, *J* = 23.4, 7.1, 2 H), 4.66 (d, *J* = 11.7, 1 H), 4.58 (d, *J* = 11.7, 1 H), 4.56 (s, 2 H), 4.27 (m, 2 H), 4.02 (m, 1 H), 3.80 (s, 3 H), 3.74 (br t, *J* = 7.0, 2 H), 3.63 (m, 2 H), 3.49 (m, 2 H), 1.96–1.76 (m, 5 H), 1.67–1.50 (m, 3 H), 1.63 (s, 1 H), 1.57 (s, 1 H), 1.51 (s, 3 H), 1.03–0.86 (series of m, 11 H), 0.61 (q, *J* = 7.6, 6 H), 0.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 158.9, 138.2, 132.2, 131.4, 129.0 (2C), 128.7, 128.5, 127.2, 122.2 (2C), 113.6, 96.9, 92.7, 72.9 (2C), 72.0, 70.4, 68.7, 68.0, 65.7, 64.8, 61.8, 55.2, 48.0, 41.5, 38.7, 35.9, 35.5, 32.3, 18.1, 7.2 (3C), 6.9 (3C), –1.4 (3C); ES HRMS *m/z* calculated for $C_{40}H_{65}BrO_8Si_2Na$ (M^+ + Na) 831.3294, observed 831.3304; $[\alpha]_D$ –44.3 (*c* 1.01, $CHCl_3$). Calculated for $C_{40}H_{65}BrO_8Si_2$: C, 59.31; H, 8.09. Found: C, 59.27; H, 8.08.

Iodide **44**

To a cold (0 °C), stirred solution of **43** (1.15 g, 1.42 mmol) in a 9:1 mixture of CH_2Cl_2 and H_2O (30 ml) was added DDQ (483 mg, 2.13 mmol). The resulting mixture was stirred at 0 °C for 1 h and treated with saturated $NaHCO_3$ solution (10 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 30 ml). The combined organic phases were dried and evaporated under reduced pressure, and the residue was filtered through a pad of silica gel (20% EtOAc/hexanes) prior to direct use in the next step.

The preceding material was dissolved in PhH (40 ml) and treated sequentially with PPh_3 (557 mg, 2.13 mmol), imidazole (289 mg, 4.25 mmol) and I_2 (540 mg, 2.13 mmol). The resulting mixture was stirred at r.t. for 2 h, freed of solvent, taken up in Et_2O and filtered. The filter cake was rinsed several times with Et_2O, and the filtrate was evaporated under reduced pressure to leave a residue that was purified chromatographically (1% EtOAc/hexanes) to give **44** as a yellowish oil (1.02 g, 90% over 2 steps); IR (neat, cm^{-1}) 1454, 1415, 1370, 1248; ^1H NMR (300 MHz, $CDCl_3$): 7.54 (d, *J* = 7.8, 2 H), 7.32 (t, *J* = 7.4, 1 H), 7.13 (t, *J* = 7.4, 1 H), 4.80 (dd, *J* = 23.8, 7.3, 2 H), 4.60 (s, 2 H), 4.38 (m, 1 H), 4.01 (m, 2 H), 3.74 (m, 2 H), 3.62 (m, 1 H), 3.17 (m, 2 H), 1.98–1.65 (series of m, 6 H), 1.54 (m, 2 H), 1.37–1.16 (m, 6 H), 1.02–0.87 (m, 11 H), 0.60 (q, *J* = 7.7, 6 H), 0.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 138.1, 132.3, 128.8, 128.5, 127.3, 122.3, 97.5, 93.0, 72.0, 70.6, 68.8, 68.0, 65.8, 65.0, 62.1, 47.6, 45.0, 38.2, 35.8, 35.5, 32.0, 18.1, 10.2, 7.2 (3C), 6.8 (3C), –1.4 (3C); ES HRMS *m/z* calculated for $C_{32}H_{56}BrIO_6Si_2$ (M^+ + Na) 821.1736, observed 821.1749; $[\alpha]_D$ –55.9 (*c* 1.13, $CHCl_3$). Calculated for $C_{32}H_{56}BrIO_6Si_2$: C, 48.06; H, 7.06. Found: C, 48.45; H, 6.93.

Conversion of **44** to **41** via Dithiane **45**

1.4 M *t*-BuLi (4.55 ml, 6.38 mmol, cooled to –78 °C) was added dropwise to a cold (–78 °C) solution of 2-ethyl-1,3-dithiane (943 mg, 6.38 mmol) in THF/HMPA 10:1 (10 ml), stirred at this temperature for 1 h, slowly warmed to –35 °C over 1 h and recooled to –78 °C prior to the dropwise addition of a solution of iodide **44** (1.02 g, 1.28 mmol) in THF (20 ml). The resulting mixture was stirred at –78 °C for 1 h, quenched with saturated NH_4Cl solution (20 ml) and warmed to r.t. The separated aqueous layer was extracted with EtOAc (3 × 40 ml). The combined organic phases were dried and evaporated, and the residue was purified by column chromatography on silica gel (1–5% EtOAc/hexanes) to provide **45** (899 mg, 86%) as a yellowish oil; IR (KBr, cm^{-1}) 1151, 1102, 1055; ^1H NMR (400 MHz, $CDCl_3$): 7.53 (m, 2 H), 7.32 (dt, *J* = 7.5, 1.0, 1 H), 7.14 (dt, *J* = 7.9, 1.6, 1 H), 4.70 (d_{AB}, *J* = 7.1, 1 H), 4.65 (d_{AB}, *J* = 7.1, 1 H), 4.51 (s, 2 H), 4.39 (m, 1 H), 4.27 (m, 1 H), 3.94 (m, 1 H), 3.82–3.68 (m, 2 H), 3.60 (m, 2 H), 2.91 (m, 1 H), 2.81–2.62 (m, 4 H), 2.22–1.92 (m, 5 H), 1.90–1.73 (m, 4 H), 1.61 (m, 1 H), 1.57–1.46 (m, 2 H), 1.36–1.23 (m, 3 H), 1.21 (s, 3 H), 1.04 (t, *J* = 7.3, 3 H), 0.97 (t, *J* = 8.0, 9 H), 0.92 (m, 2 H), 0.61 (dq, *J* = 7.2, 2.8, 6 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 138.2, 132.3, 128.7, 128.5, 127.3, 122.3, 92.7, 72.0, 70.4, 68.6, 68.4, 64.8, 63.7, 62.6, 53.6, 48.0 (2C), 46.7, 43.1, 39.4, 35.8, 35.2, 32.2, 31.8, 26.1, 25.9, 25.4, 18.1, 9.01, 7.3 (3C), 6.9 (3C), –1.4 (3C); ES HRMS *m/z* calculated for $C_{38}H_{67}BrO_6S_2Si_2Na$ (M^+ + Na) 841.2993, observed 841.3049; $[\alpha]_D$ –43 (*c* 0.98, $CHCl_3$).

The above material was taken up in a mixture of $CH_3CN/CH_2Cl_2/H_2O$ 8:1:1 (30 ml), cooled to 0 °C and stirred vigorously while being treated in turn with $CaCO_3$ (1.1 g, 11.0 mmol), pyridine (443 µl, 5.48 mmol), and $HgClO_4 \cdot 3\ H_2O$ (745 mg, 1.64 mmol). After the mixture had been stirred at 0 °C for 30 min, pH 7 buffer solution (10 ml) and CH_2Cl_2 (10 ml) were introduced and the separated aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml). The

combined extracts were dried and purified by column chromatography on silica gel (10–20% EtOAc/hexanes) to furnish **41** (736 mg, 92%) identical in all respects to the material described above.

Benzyl Ether **53**

To a stirred, cold (0 °C) solution of (*S*)-glycidol (10.00 g, 135 mmol) in THF (100 ml) was added NaH (8.10 g of an 80% suspension in mineral oil, 270 mmol). After hydrogen evolution was complete, BnBr (32 ml, 270 mmol) and TBAI (4.96 g, 14 mmol) were added. The cooling bath was removed and the reaction mixture was stirred at r.t. for 48 h, cooled to 0 °C and carefully quenched with aqueous NH_4Cl solution (200 ml). The separated aqueous layer was extracted with Et_2O. The combined organic layers were dried and solvent was removed under reduced pressure. The final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 4:1) to afford **53** as a colorless liquid (20.39 g, 92%); IR (neat, cm^{-1}) 1496, 1454, 1097; ^1H NMR (300 MHz, $CDCl_3$): 7.37–7.26 (m, 5 H), 4.63 (d, *J* = 11.9, 1 H), 4.57 (d, *J* = 11.9, 1 H), 3.77 (dd, *J* = 11.4, 3.0, 1 H), 3.45 (dd, *J* = 11.4, 5.8, 1 H), 3.20 (m, 1 H), 2.80 (dd, *J* = 4.9, 4.3, 1 H), 2.62 (dd, *J* = 5.0, 2.7, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): 137.8, 128.3 (2C), 127.6 (3C), 73.2, 70.7, 50.7, 44.1; EI HRMS *m/z* calculated for $C_{10}H_{12}O_2$ (M^+) 164.0834, observed 164.0839; $[\alpha]_D$ +2.2 (*c* 1.53, $CHCl_3$). Calculated for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.01; H, 7.31.

PMB Ether **54**

Anhydrous CuI powder (362 mg, 1.90 mmol) was cooled to 0 °C and treated with a 1.0 M solution of vinylmagnesium bromide in THF (18.3 ml, 18.27 mmol). After the addition was complete, the dark-brown slurry was stirred at 0 °C for 30 min, cooled to –78 °C and treated with a solution of **53** (1.00 g, 6.09 mmol) in THF (3.5 ml). The resulting slurry was stirred at –78 °C for 45 min and at 0 °C for 2 h. A solution of NH_4Cl (30 ml), buffered with NH_4OH to pH 8, was added. The mixture was warmed to r.t. and vigorously stirred for 30 min. The separated aqueous layer was extracted with Et_2O. The combined organic layers were dried, the solvent was evaporated and the final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 6:1 to 2:1) to afford the alcohol as a yellowish liquid (902 mg, 77%); IR (neat, cm^{-1}) 3448, 1641, 1496; ^1H NMR (300 MHz, $CDCl_3$): 7.38–7.25 (m, 5 H), 5.91–5.76 (m, 1 H), 5.15–5.07 (m, 2 H), 4.56 (s, 2 H), 3.89 (m, 1 H), 3.52 (dd, *J* = 9.5, 3.4, 1 H), 3.37 (dd, *J* = 9.5, 7.4, 1 H), 2.41 (br s, 1 H), 2.27 (t, *J* = 6.7, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 138.0, 134.2, 128.4 (2C), 127.8, 127.7 (2C), 117.6, 73.9, 73.3, 69.7, 37.9; EI HRMS *m/z* calculated for $C_{20}H_{24}O_3$ (M^+) 192.1146, observed 192.1163; $[\alpha]_D$ –3.2 (*c* 1.5, $CHCl_3$).

To a stirred, cold (0 °C) solution of the above alcohol (302 mg, 1.57 mmol) in THF (3.0 ml) was added NaH (142 mg of an 80% suspension in mineral oil, 4.75 mmol). After completion of hydrogen evolution, PMBBr (1.02 g, 5.05 mmol) and TBAI (59 mg, 0.160 mmol) were added. The cooling bath was removed and the reaction mixture was stirred at r.t. for 5 h, cooled to 0 °C and was carefully quenched with aqueous NH_4Cl solution (10 ml). The separated aqueous layer was extracted with Et_2O and the combined organic layers were dried and evaporated. Final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 9:1) to afford **54** as a colorless liquid (466 mg, 95%); IR (neat, cm^{-1}) 1641, 1613, 1586; ^1H NMR (300 MHz, $CDCl_3$): 7.45–7.35 (m, 5 H), 7.34 (d, *J* = 8.6, 2 H), 6.92 (d, *J* = 8.6, 1 H), 5.96–5.83 (m, 2 H), 5.18–5.09 (m, 2 H), 4.66 (d, *J* = 11.4, 1 H), 4.60 (d, *J* = 11.4, 1 H), 4.59 (s, 2 H), 3.83 (s, 3 H), 3.72 (m, 1 H), 3.60 (dd, *J* = 5.1, 1.4, 2 H), 2.42 (t, *J* =

6.3, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.0, 138.3, 134.6, 130.8, 129.2 (2C), 128.2 (2C), 127.5 (2C), 127.4, 116.9, 113.5 (2C), 77.2, 73.2, 72.2, 71.4, 55.1, 36.2; EI HRMS *m/z* calculated for $C_{20}H_{24}O_3$ (M^+) 312.1719, observed 312.1728; $[\alpha]_D$ +4.5 (*c* 1.6, $CHCl_3$). Calculated for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.78; H, 7.89.

Aldehyde **55**

To a solution of **54** (23.31 g, 75 mmol) in THF (235 ml) were added H_2O (118 ml), OsO_4 (254 mg, 1 mmol) and NMO monohydrate (12.16 g, 90 mmol). The reaction mixture was stirred at r.t. for 2.5 h. H_2O (235 ml), THF (100 ml) and $NaIO_4$ (48.13 g, 225 mmol) were added and the resulting mixture was stirred for an additional 3 h. H_2O (200 ml) was added to dissolve the precipitate formed, followed by the addition of Et_2O (200 ml). The separated aqueous layer was extracted with Et_2O, the combined organic layers were dried, and the solvent was evaporated. Final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 4:1) to afford **55** as a tan oil (19.57 g, 83%); IR (neat, cm^{-1}) 1724, 1613, 1586; ^{1}H NMR (300 MHz, $CDCl_3$): 9.75 (t, *J* = 1.9, 1 H), 7.39–7.28 (m, 5 H), 7.25 (d, *J* = 11.2, 2 H), 6.87 (d, *J* = 8.6, 2 H), 4.61 (d, *J* = 11.2, 1 H), 4.55 (s, 2 H), 4.52 (d, *J* = 11.2, 1 H), 4.13 (m, 1 H), 3.80 (s, 3 H), 3.58 (dq, *J* = 11.0, 5.2, 2 H), 2.70–2.66 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 200.8, 159.3, 137.9, 130.1, 129.4 (2C), 128.4 (2C), 127.7, 127.6 (2C), 113.8 (2C), 73.4, 72.8, 71.7, 71.5, 55.2, 46.4; EI HRMS *m/z* calculated for $C_{19}H_{22}O_4$ (M^+) 314.1513, observed 314.1536; $[\alpha]_D$ +14.6 (*c* 2.20, $CHCl_3$). Calculated for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.36; H, 6.99.

Thiazolidinethione **56**

To a suspension of $Sn(OTf)_2$ (8.34 g, 20 mmol) in CH_2Cl_2 (42 ml) cooled to –40 °C was added *N*-ethylpiperidine (2.75 ml, 20 mmol) and **10** (3.456 g, 17 mmol) in CH_2Cl_2 (24 ml) via cannula. The solution was stirred at –40 °C for 4 h and cooled to –78 °C. Aldehyde **55** (4.392 g, 14 mmol) in CH_2Cl_2 (23 ml) was added via cannula. The reaction mixture was stirred at that temperature for 2 h and quenched with pH 7 phosphate buffer (100 ml). After being warmed to r.t., the organic phase was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and evaporated, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1 to 1:1) to give **56** as a yellow oil (6.74 g, 93%); IR (neat, cm^{-1}) 3482, 1697, 1612, 1586; ^{1}H NMR (300 MHz, $CDCl_3$): 7.38–7.26 (m, 5 H), 7.24 (d, *J* = 8.7, 2 H), 6.85 (d, *J* = 8.7, 2 H), 5.12 (t, *J* = 6.7, 1 H), 4.66 (d, *J* = 11.2, 1 H), 4.55 (s, 2 H), 4.50 (d, *J* = 11.2, 1 H), 4.34 (m, 1 H), 3.88–3.79 (m, 1 H), 3.79 (s, 3 H), 3.63–3.39 (m, 5 H), 3.27 (dd, *J* = 17.4, 8.5, 1 H), 2.99 (dd, *J* = 11.5, 0.8, 1 H), 2.36 (sextet, *J* = 6.6, 1 H), 1.87–1.76 (m, 2 H), 1.05 (d, *J* = 6.9, 3 H), 0.97 (d, *J* = 6.9, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.8, 172.3, 159.2, 138.0, 130.3, 129.5 (2C), 128.4 (2C), 127.6 (3C), 113.8 (2C), 76.8, 73.4, 72.3, 71.5 (2C), 66.6, 55.2, 45.6, 38.4, 30.8, 30.6, 19.1, 17.7; FAB MS *m/z* calculated for $C_{27}H_{36}NO_5S_2$ (M^+ + H) 518.20, observed 518.19; $[\alpha]_D$ +11.5 (*c* 1.47, $CHCl_3$). Calculated for $C_{27}H_{35}NO_5S_2$: C, 62.64; H, 6.81. Found: C, 62.38; H, 6.78.

Weinreb Amide **58**

To a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (2.15 g, 22 mmol) in CH_2Cl_2 (45 ml) cooled to 0 °C was added a 2.0 M solution of Me_3Al in hexanes (11 ml, 22 mmol). The clear solution was stirred at 0 °C for 10 min, at r.t. for 30 min and cooled to –15 °C.

A solution of **56** (5.93 g, 11 mmol) in CH_2Cl_2 (20 ml) was added via cannula and the stirred reaction mixture was allowed to warm to –10 °C over 7 h, quenched with Rochelle's salt solution (150 ml), warmed to r.t., and stirred for an additional 30 min. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic phases were dried. The solvent was removed in vacuo and the residue purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:4) to give the hydroxy amide **57** as a colorless oil (4.45 g, 97%); IR (neat, cm^{-1}) 3456, 1651, 1613; ^1H NMR (300 MHz, $CDCl_3$): 7.35–7.28 (m, 5 H), 7.26 (d, *J* = 8.6, 2 H), 6.85 (d, *J* = 8.6, 2 H), 4.66 (d, *J* = 11.2, 1 H), 4.56 (s, 2 H), 4.50 (d, *J* = 11.2, 1 H), 4.22 (m, 1 H), 3.87 (m, 1 H), 3.79 (s, 3 H), 3.63 (s, 3 H), 3.60 (d, *J* = 4.7, 2 H), 3.17 (s, 3 H), 2.56–2.48 (m, 2 H), 1.89–1.75 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 173.2, 159.1, 138.2, 130.4, 129.5 (2C), 128.3 (2C), 127.6, 127.5 (2C), 113.7 (2C), 76.2, 73.3, 72.4, 71.4, 66.2, 61.1, 55.2, 38.5, 38.4, 31.8; FAB MS *m/z* calculated for $C_{23}H_{32}NO_6$ (M^+ + H) 418.22, observed 418.20; $[\alpha]_D$ +9.0 (*c* 2.4, $CHCl_3$). Calculated for $C_{23}H_{31}NO_6$: C, 66.17; H, 7.48. Found: C, 65.89; H, 7.36.

To a solution of **57** (3.88 g, 9 mmol) in CH_2Cl_2 (54 ml) and DMF (5 ml) were added imidazole (1.91 g, 28 mmol), TBDPSCl (3.6 ml, 14 mmol) and DMAP (733 mg, 6 mmol). The reaction mixture was stirred under reflux overnight, cooled to r.t. and quenched with aqueous $NaHCO_3$ solution (100 ml). The separated aqueous layer was extracted with CH_2Cl_2. The combined organic phases were dried and evaporated, and the final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 4:1) to afford **58** as a colorless oil (5.79 g, 98%); IR (neat, cm^{-1}) 1658, 1616, 1558; ^1H NMR (300 MHz, $CDCl_3$): 7.73–7.68 (m, 4 H), 7.44–7.24 (m, 11 H), 7.21 (d, *J* = 8.6, 2 H), 6.83 (d, *J* = 8.6, 2 H), 4.53 (d, *J* = 11.3, 1 H), 4.52 (m, 1 H), 4.44 (s, 2 H), 4.42 (d, *J* = 11.3, 1 H), 3.80 (s, 3 H), 3.77 (m, 1 H), 3.46 (s, 3 H), 3.33 (d, *J* = 4.8, 2 H), 3.06 (s, 3 H), 2.72 (dd, *J* = 14.4, 5.8, 1 H), 2.61 (dd, *J* = 15.4, 6.2, 1 H), 1.88–1.73 (m, 2 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.8, 158.9, 138.5, 135.9 (4C), 134.1, 134.0, 131.1, 129.5 (2C), 129.1 (2C), 128.2 (2C), 127.5 (5C), 127.3 (2C), 113.6 (2C), 74.6, 73.1, 72.8, 71.0, 68.0, 61.0, 55.2, 39.5, 39.2, 31.9, 27.0 (3C), 19.3; FAB MS *m/z* calculated for $C_{39}H_{50}NO_6Si$ (M^+ + H) 656.34, observed 655.33; $[\alpha]_D$ +9.4 (*c* 1.7, $CHCl_3$). Calculated for $C_{39}H_{49}NO_6Si$: C, 71.42; H, 7.53. Found: C, 71.15; H, 7.58.

Methyl Ketone **59**

To a solution of **58** (5.90 g, 9 mmol) in THF (35 ml) cooled to –78 °C was added a 3.0 M solution of MeMgBr in Et_2O (9.0 ml, 27 mmol). The reaction mixture was allowed to warm to 0 °C and stirred for 3 h. Aqueous NH_4Cl solution (50 ml) was added and the mixture was warmed to r.t. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic phases were dried and evaporated, and final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 6:1 to 4:1) to afford **59** as a colorless oil (5.06 g, 92%); IR (neat, cm^{-1}) 1715, 1612, 1513; ^1H NMR (300 MHz, $CDCl_3$): 7.67 (d, *J* = 6.4, 4 H), 7.46–7.22 (m, 11 H), 7.18 (d, *J* = 8.7, 2 H), 6.84 (d, *J* = 8.7, 2 H), 4.55 (d, *J* = 11.4, 1 H), 4.47 (s, 2 H), 4.41 (d, *J* = 11.4, 1 H), 4.40 (m, 1 H), 3.80 (s, 3 H), 3.77 (m, 1 H), 3.37 (d, *J* = 4.8, 2 H), 2.61 (dd, *J* = 15.8, 6.2, 1 H), 2.48 (dd, *J* = 15.8, 6.2, 1 H), 1.87 (s, 3 H), 1.87–1.66 (m, 2 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 207.1, 159.0, 138.4, 135.9 (4C), 133.9, 133.8, 130.8, 129.6 (2C), 129.3 (2C), 128.3 (2C), 127.5 (5C), 127.4 (2C), 113.6 (2C), 74.2, 73.2, 72.7, 71.0, 67.4, 55.2, 50.4, 38.9, 30.7, 27.0 (3C), 19.2; FAB MS *m/z* calculated for $C_{38}H_{47}O_5Si$ (M^+ + H) 611.32, observed 611.30; [α] +15 (*c* 0.79, $CHCl_3$). Calculated for $C_{38}H_{46}O_5Si$: C, 74.72; H, 7.59. Found: C, 74.48; H, 7.68.

Thiazolidinethione **62**

To a suspension of $Sn(OTf)_2$ (34.18 g, 82 mmol) in CH_2Cl_2 (173 ml) cooled to –40 °C was added *N*-ethylpiperidine (11.3 ml, 82 mmol) and *ent*-**10** (13.81 g, 68 mmol) in CH_2Cl_2 (83 ml) via cannula. The solution was stirred at –40 °C for 4 h and cooled to –78 °C. 3-Butenal (10.51 g, 150 mmol) in CH_2Cl_2 (300 ml) was introduced via cannula. The reaction mixture was stirred at –78 °C for 4 h, quenched with pH 7 phosphate buffer (200 ml), and warmed to r.t. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic solutions were dried and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 8:1 to 1:1) to give **62** as a yellow oil (12.77 g, 69%); IR (neat, cm^{-1}) 3680, 1602, 1469; ^1H NMR (300 MHz, $CDCl_3$): 5.89–5.75 (m, 1 H), 5.16–5.09 (m, 2 H), 4.19 (m, 1 H), 3.59 (dd, *J* = 19.2, 2.6, 1 H), 3.49 (dd, *J* = 11.5, 8.0, 1 H), 3.15 (dd, *J* = 17.7, 9.2, 1 H), 3.00 (dd, *J* = 11.5, 1.0, 1 H), 2.82 (d, *J* = 3.1, 1 H), 2.40–2.27 (m, 4 H), 1.04 (d, *J* = 6.7, 3 H), 0.96 (d, *J* = 7.0, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.9, 172.8, 134.0, 118.0, 71.3, 67.3, 44.8, 40.7, 30.8, 30.6, 19.0, 17.7; EI HRMS *m/z* calculated for $C_{12}H_{19}NO_2S_2$ (M^+) 273.0857, observed 273.0856; $[\alpha]_D$ –418 (*c* 1.00, $CHCl_3$). Calculated for $C_{12}H_{19}NO_2S_2$: C, 52.73; H, 7.01. Found: C, 52.68; H, 6.98.

When no attempt was made to purify **61**, the two-step conversion to **62** proceeded in 92% yield.

Weinreb Amide **63**

To a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (2.15 g, 22 mmol) in CH_2Cl_2 (45 ml) cooled to 0 °C was added a 2.0 M solution of Me_3Al in hexanes (11 ml, 22 mmol). The clear solution was stirred at that temperature for 10 min and r.t. for 30 min prior to cooling to –15 °C. A solution of **62** (3.0 g, 11 mmol) in CH_2Cl_2 (20 ml) was introduced via cannula and the reaction mixture was allowed to warm to –10 °C with stirring for 7 h. The reaction mixture was quenched with Rochelle's salt solution (150 ml), warmed to r.t. and stirred for 30 min. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried, and the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1:4) to give **63** as a colorless oil (1.86 g, 98%); IR (neat, cm^{-1}) 3482, 1642, 1462; ^1H NMR (300 MHz, $CDCl_3$): 5.90–5.76 (m, 1 H), 5.12–5.05 (m, 2 H), 4.05 (m, 1 H), 3.76 (d, *J* = 2.2, 1 H), 3.65 (s, 3 H), 3.15 (s, 3 H), 2.63 (m, 1 H), 2.44 (dd, *J* = 16.7, 9.3, 1 H), 2.36–2.18 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 173.6, 134.4, 117.5, 67.3, 61.1, 40.9, 37.4, 31.8; EI HRMS *m/z* calculated for $C_8H_{15}NO_3$ (M^+) 173.1052, observed 173.1049; $[\alpha]_D$ –55.0 (*c* 1.00, $CHCl_3$).

Aldehyde **51**

To a solution of **63** (300 mg, 1.73 mmol) in CH_2Cl_2 were added *p*-methoxybenzyl trichloroacetimidate (734 mg, 2.60 mmol) in CH_2Cl_2 and CSA (40 mg, 0.17 mmol). The reaction mixture was stirred at r.t. for 12 h. The precipitate that formed was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 4:1 to 1:2) to give the PMB ether as a colorless oil (386 mg, 78%); IR (neat, cm^{-1}) 1657, 1613, 1514; ^1H NMR (300 MHz, $CDCl_3$): 7.27–7.21 (m, 2 H), 6.89–6.77 (m, 2 H), 5.91–5.77 (m, 1 H), 5.14–5.05 (m, 2 H), 4.49 (dd, *J* = 16.5, 11.0, 2 H), 4.09–4.01 (m, 1 H), 3.77 (s, 3 H), 3.63 (s, 3 H), 3.17 (s, 3 H), 2.83–2.76 (m, 1 H), 2.48 (dd, *J* = 15.4, 5.1, 1 H), 2.39–2.33 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 172.5,

159.1, 134.4, 130.8, 129.3 (2C), 128.6, 117.5, 113.7 (2C), 75.3, 71.5, 61.3, 55.2, 38.8, 36.9; EI HRMS *m/z* calculated for $C_{16}H_{23}NO_4$ (M^+) 293.1626, observed 293.1637; $[\alpha]_D$ –12.8 (*c* 1.00, $CHCl_3$). Calculated for $C_{16}H_{23}NO_4$: C, 65.49; H, 7.91. Found: C, 65.55; H, 7.89.

To a stirred solution of the above product (6.26 g, 21 mmol) in THF (60 ml) cooled to –78 °C was added a 1.0 M solution of Dibal-H in hexanes (63 ml, 63 mmol) dropwise. The solution was stirred at –78 °C for 2 h, quenched by the addition of acetone (5 ml), stirred at –78 °C for 5 min and transferred into a rapidly stirred mixture of CH_2Cl_2 and aqueous Rochelle's salt solution. The resulting two-phase system was stirred at r.t. for 30 min. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic solutions were dried and concentrated. The residual oil was purified by column chromatography on silica gel (pet ether/EtOAc 8:1) to give **51** as a colorless oil (4.92 g, 100%); IR (neat, cm^{-1}) 1723, 1612, 1513; ^{1}H NMR (300 MHz, $CDCl_3$): 9.76 (t, *J* = 2.0, 1 H), 7.24 (d, *J* = 8.6, 2 H), 6.89–6.86 (m, 2 H), 5.87–5.74 (m, 1 H), 5.15–5.10 (m, 2 H), 4.56 (d, *J* = 11.0, 1 H), 4.46 (d, *J* = 11.0, 1 H), 4.05–3.97 (m, 2 H), 3.80 (s, 3 H), 2.68–2.62 (m, 1 H), 2.59–2.51 (m, 1 H), 2.48–2.31 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): 201.4, 159.5, 133.6, 130.1, 129.4 (2C), 118.2, 113.8 (2C), 73.3, 70.9, 55.2, 48.0, 38.3; EI HRMS *m/z* calculated for $C_{14}H_{18}O_3$ (M^+) 234.1258, observed 234.1255; $[\alpha]_D$ –37.0 (*c* 1.00, $CHCl_3$).

Hydroxy Ketone **49**

To a solution of **59** (4.82 g, 7.89 mmol) in THF (205 ml) cooled at –78 °C was added TMSCl (11.0 ml, 86.8 mmol) and LHMDS (48.5 ml, 63.1 mmol). The reaction mixture was warmed to r.t. and stirred for 1 h. Et_3N (10 ml) and pentane (100 ml) were added. After evaporation of solvent, the residue was diluted with pentane and the mixture was filtered through a plug of Celite and the residue was washed thoroughly with pentane. The solvent was evaporated under reduced pressure. The crude product **50** was dried azeotropically with PhH and used directly in the next step.

To a solution of **50**, prepared above, and aldehyde **51** (4.20 g, 17.9 mmol) in CH_2Cl_2 (100 ml) cooled to –78 °C was added freshly distilled $BF_3{\cdot}OEt_2$ (1.09 ml, 8.68 mmol). The reaction mixture was stirred at –78 °C for 30 min, quenched with saturated aqueous $NaHCO_3$ solution and warmed to r.t. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1 to 1:2) to give **49** as a colorless oil (6.13 g, 92%); IR (neat, cm^{-1}) 3490, 1707, 1612; ^{1}H NMR (300 MHz, $CDCl_3$): 7.64 (d, *J* = 6.5, 4 H), 7.45–7.22 (m, 11 H), 7.25 (d, *J* = 8.6, 2 H), 7.15 (d, *J* = 8.6, 2 H), 6.86 (d, *J* = 8.6, 2 H), 6.81 (d, *J* = 8.6, 2 H), 5.91–5.73 (m, 1 H), 5.13–5.06 (m, 2 H), 4.62 (br s, 1 H), 4.55 (d, *J* = 11.4, 1 H), 4.53 (d, *J* = 11.4, 1 H), 4.45 (s, 2 H), 4.42 (d, *J* = 11.4, 1 H), 4.37 (d, *J* = 11.4, 1 H), 4.13 (m, 1 H), 3.79 (s, 3 H), 3.78 (s, 3 H), 3.84–3.67 (m, 2 H), 3.34 (d, *J* = 5.0, 2 H), 3.10 (d, *J* = 3.0, 1 H), 2.58 (dd, *J* = 16.1, 6.1, 1 H), 2.46 (dd, *J* = 16.1, 6.1, 1 H), 2.38–2.22 (m, 4 H), 1.85–1.65 (m, 2 H), 1.45 (qd, *J* = 9.4, 3.0, 1 H), 1.37 (qd, *J* = 9.4, 3.0, 1 H), 1.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 209.9, 159.3, 159.1, 138.4, 135.9 (5C), 134.6, 133.9, 130.8, 130.7, 129.7 (2C), 129.4 (2C), 128.6, 128.3 (2C), 127.6 (3C), 127.5 (5C), 117.3, 113.8 (2C), 113.7 (2C), 75.1, 74.2, 73.2, 72.7, 71.3, 71.1, 67.2, 64.2, 55.3 (2C), 50.4, 50.3, 40.6, 38.9, 38.5, 27.0 (3C), 19.2; FAB MS *m/z* calculated for $C_{52}H_{65}O_8Si$ (M^+ + H) 845.44, observed 845.32; $[\alpha]_D$ –3.3 (*c* 1.1, $CHCl_3$). Calculated for $C_{52}H_{64}O_8Si$: C, 73.90; H, 7.63. Found C, 73.87; H, 7.59.

Spiroacetal **64**

To a solution of **49** (7.04 g, 8.33 mmol) in CH_2Cl_2 (75 ml) cooled to –20 °C were added 2,6-lutidine (1.46 ml, 12.50 mmol) and TESOTf (2.16 ml, 9.99 mmol). The reaction mixture was stirred at –20 °C for 1.5 h, saturated $NaHCO_3$ solution was added and the separated aqueous layer was extracted with CH_2Cl_2. The combined organic phases were dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 8:1 to 2:1) to give the TES ether as a colorless oil (7.86 g, 98%); IR (neat, cm^{-1}) 1716, 1613, 1514; ^1H NMR (300 MHz, $CDCl_3$): 7.65 (d, *J* = 7.9, 4 H), 7.42–7.20 (m, 11 H), 7.26 (d, *J* = 8.7, 2 H), 7.16 (d, *J* = 8.7, 2 H), 6.86 (d, *J* = 8.7, 2 H), 6.82 (d, *J* = 8.7, 2 H), 5.91–5.73 (m, 1 H), 5.11–5.05 (m, 1 H), 4.52 (d, *J* = 11.2, 1 H), 4.49 (d, *J* = 11.2, 1 H), 4.44 (s, 2 H), 4.39 (m, 1 H), 4.39 (d, *J* = 14.2, 1 H), 4.35 (d, *J* = 14.2, 1 H), 4.23 (m, 1 H), 3.79 (s, 3 H), 3.78 (s, 3 H), 3.80–3.72 (m, 1 H), 3.53 (m, 1 H), 3.33 (d, *J* = 4.8, 2 H), 2.61 (dd, *J* = 16.3, 6.4, 1 H), 2.50 (dd, *J* = 16.3, 6.4, 1 H), 2.39 (dd, *J* = 16.3, 6.4, 1 H), 2.29 (dd, *J* = 16.3, 6.4, 1 H), 2.34–2.25 (m, 2 H), 1.81–1.68 (m, 2 H), 1.64–1.44 (m, 2 H), 1.02 (s, 9 H), 0.89 (t, *J* = 7.7, 9 H), 0.52 (q, *J* = 7.7, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 207.0, 159.0 (2C), 138.5, 135.9 (4C), 134.6, 133.9 (2C), 131.0 (2C), 129.6 (2C), 129.2 (2C), 129.1 (2C), 128.3 (2C), 127.6 (4C), 127.5 (2C), 127.4, 117.1, 113.7 (2C), 113.6 (2C), 75.1, 74.5, 73.1, 72.9, 71.1, 69.7, 67.2, 66.0, 55.2 (3C), 51.1, 42.5, 39.0, 38.3, 27.0 (3C), 19.3, 6.9 (3C), 5.1 (3C); FAB MS *m/z* calculated for $C_{58}H_{79}O_8Si_2$ (M^+ + H) 959.53, observed 959.36; $[\alpha]_D$ –7.7 (*c* 1.98, $CHCl_3$).

A solution of the above product (7.76 g, 8.09 mmol) in CH_2Cl_2 (750 ml) and H_2O (30 ml) was treated with DDQ (4.77 g, 21.03 mmol) and the resulting mixture was allowed to stir at r.t. for 1.25 h, prior to partitioning between saturated $NaHCO_3$ solution and CH_2Cl_2. The organic extracts were combined, dried, and evaporated. The resultant oil was purified by column chromatography on silica gel (pet ether/EtOAc 8:1 to 4:1) to give **64** as a colorless oil (5.22 g, 92%); IR (neat, cm^{-1}) 1642, 1590, 1455; ^1H NMR (300 MHz, $CDCl_3$): 7.66 (d, *J* = 6.3, 4 H), 7.45–7.24 (m, 11 H), 5.92–5.62 (m, 1 H), 5.04–4.95 (m, 2 H), 4.46 (s, 2 H), 4.20 (m, 2 H), 4.03 (m, 1 H), 3.86 (m, 1 H), 3.46 (dd, *J* = 9.8, 6.3, 1 H), 3.32 (dd, *J* = 9.8, 6.3, 1 H), 2.53 (ddd, *J* =14.6, 4.2, 1.5, 1 H), 2.22–2.08 (m, 2 H), 1.84–1.76 (m, 1 H), 1.76–1.73 (m, 2 H), 1.57 (m, 2 H), 1.28 (dd, *J* = 10.7, 2.1, 1 H), 1.17 (q, *J* = 11.5, 1 H), 1.08 (s, 9 H), 0.95 (t, *J* = 8.0, 9 H), 0.60 (q, *J* = 8.0, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 138.5, 135.8 (5C), 134.6, 134.1, 133.9, 129.7, 129.6, 128.3 (2C), 127.6 (2C), 127.5 (2C), 127.4 (2C), 116.9, 99.7, 73.1, 72.8, 70.2, 68.4, 64.7, 64.6, 44.1, 43.8, 40.7, 40.4, 34.9, 27.0 (3C), 19.1, 6.8 (3C), 4.9 (3C); FAB MS *m/z* calculated for $C_{42}H_{61}O_5Si_2$ (M^+ + H) 701.41, observed 701.22; $[\alpha]_D$ +21.5 (*c* 0.84, $CHCl_3$).

Methyl Ether **65**

A solution of **64** (4.53 g, 6.46 mmol) in AcOH (45 ml), THF (45 ml), and H_2O (9 ml) was stirred at r.t. for 1 h. $NaHCO_3$ powder and H_2O were added until the evolution of CO_2(g) was complete. The mixture was extracted with Et_2O. The combined organic layers were dried and evaporated, and the final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 8:1 to 1:1) to afford the secondary alcohol as a colorless oil (3.49 g, 92%); IR (neat, cm^{-1}) 3404, 1642, 1589; ^1H NMR (300 MHz, $CDCl_3$): 7.68 (d, *J* = 6.3, 4 H), 7.47–7.26 (m, 11 H), 5.92–5.60 (m, 1 H), 5.04–4.97 (m, 2 H), 4.44 (s, 2 H), 4.28–4.12 (m, 2 H), 4.06 (m, 1 H), 3.86 (m, 1 H), 3.46 (dd, *J* = 9.7, 6.2, 1 H), 3.29 (dd, *J* = 9.7, 6.2, 1 H), 2.49 (ddd, *J* = 14.4, 2.8, 1.6, 1 H), 2.25–2.08 (m, 2 H), 1.96–1.90 (m, 1 H), 1.86 (dd, *J* = 13.2, 4.1, 1 H), 1.75–1.54 (m, 3 H), 1.21 (q, *J* = 11.5, 1 H), 1.10 (s, 9 H), 1.08 (m, 1 H);

^{13}C NMR (75 MHz, $CDCl_3$): 138.3, 135.7 (5C), 134.5, 134.1, 133.9, 129.6 (2C), 128.3 (2C), 127.6 (2C), 127.5 (4C), 117.0, 99.7, 73.1, 72.6, 70.6, 68.3, 64.4, 64.2, 44.3, 43.9, 40.3, 40.0, 34.9, 27.0 (3C), 19.1; FAB MS *m/z* calculated for $C_{36}H_{47}O_5Si$ (M^+ + H) 587.32, observed 587.28; $[\alpha]_D$ +20 (*c* 0.79, $CHCl_3$). Calculated for $C_{36}H_{46}O_5Si$: C, 73.68; H, 7.90. Found: C, 73.67; H, 7.86.

To a suspension of NaH (33 mg of an 80% suspension in mineral oil, 1.08 mol) in DMF (1.0 ml) cooled to 0 °C were added the above alcohol (127 mg, 0.216 mmol) and MeI (0.13 ml, 2.16 mmol). After the completion of H_2(g) evolution, the reaction mixture was warmed to r.t., stirred overnight, returned to 0 °C, quenched with aqueous NH_4Cl solution (5 ml) and warmed to r.t. CH_2Cl_2 (5 ml) was added and the separated aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried and evaporated. The final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 6:1) to afford **65** as a colorless oil (126 mg, 97%); IR (neat, cm^{-1}) 1642, 1589, 1471; ^{1}H NMR (300 MHz, $CDCl_3$): 7.67 (d, *J* = 7.8, 4 H), 7.46–7.26 (m, 11 H), 5.92–5.66 (m, 1 H), 5.04–4.96 (m, 2 H), 4.47 (d, *J* = 12.2, 1 H), 4.42 (d, *J* = 12.2, 1 H), 4.24 (m, 1 H), 4.18 (m, 1 H), 3.90–3.81 (m, 1 H), 3.60 (m, 1 H), 3.47 (dd, *J* = 9.7, 6.4, 1 H), 3.34 (s, 3 H), 3.29 (dd, *J* = 9.7, 6.1, 1 H), 2.65–2.58 (m, 1 H), 2.25–2.07 (m, 2 H), 2.04–1.97 (m, 1 H), 1.85 (dd, *J* = 13.1, 4.0, 1 H), 1.72 (dd, *J* = 13.2, 7.2, 1 H), 1.67–1.54 (m, 2 H), 1.17 (dd, *J* = 12.7, 11.4, 1 H), 1.09 (s, 9 H), 1.06 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): 138.4, 135.7 (5C), 134.5, 134.1, 133.9, 129.6 (2C), 128.3 (2C), 127.6 (3C), 127.5 (3C), 117.0, 99.7, 73.1, 72.9, 72.6, 70.6, 68.4, 64.2, 55.4, 44.4, 40.5, 40.4, 36.8, 35.0, 27.0 (3C), 19.1; FAB MS *m/z* calculated for $C_{37}H_{49}O_5Si$ (M^+ + H) 601.33, observed 601.30; $[\alpha]_D$ +20 (*c* 1.6, $CHCl_3$). Calculated for $C_{37}H_{48}O_5Si$: C, 73.96; H, 8.05. Found: C, 74.09; H, 8.01.

Aldehyde **66**

To a solution of **65** (1.39 g, 2.31 mmol) in acetone (20 ml) were added H_2O (4 ml), OsO_4 (25 mg, 0.100 mmol) and NMO monohydrate (325 mg, 2.78 mmol). The reaction mixture was stirred at r.t. for 3 h at which point aqueous Na_2SO_3 solution (20 ml) was added and the reaction mixture was extracted with EtOAc. The combined organic solutions were evaporated in vacuo and the residue was dissolved in a H_2O (15 ml)/acetone (25 ml) mixture. $NaIO_4$ (1.48 g, 6.94 mmol) was added and the resulting mixture was further stirred at r.t. for 2.5 h. H_2O (20 ml) was added to dissolve the precipitate formed, followed by Et_2O (20 ml). The separated aqueous layer was extracted with Et_2O. The combined organic layers were dried and evaporated, and the final purification was achieved by column chromatography on silica gel (pet ether/EtOAc 10:1 to 2:1) to afford **66** as a tan oil (1.21 g, 87%); IR (neat, cm^{-1}) 1726, 1589, 1472; ^{1}H NMR (300 MHz, $CDCl_3$): 9.62 (t, *J* = 2.3, 1 H), 7.66 (d, *J* = 7.7, 4 H), 7.47–7.28 (m, 11 H), 4.49 (s, 2 H), 4.38 (m, 1 H), 4.25–4.18 (m, 2 H), 3.66 (m, 1 H), 3.47 (dd, *J* = 9.9, 5.6, 1 H), 3.35 (s, 3 H), 3.29 (dd, *J* = 9.9, 5.6, 1 H), 2.73–2.67 (m, 1 H), 2.46–2.41 (m, 2 H), 2.08–2.02 (m, 1 H), 1.82–1.66 (m, 2 H), 1.63–1.58 (m, 2 H), 1.09 (m, 2 H), 1.27–1.06 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 200.9, 138.3, 135.7 (5C), 133.9, 133.8, 129.7 (2C), 128.3 (2C), 127.6 (4C), 127.5 (2C), 99.7, 73.1, 72.7, 72.5, 70.2, 64.7, 64.3, 55.4, 49.4, 43.8, 39.9, 37.2, 34.7, 27.0 (3C), 19.1; FAB MS *m/z* calculated for $C_{36}H_{47}O_6Si$ (M^+ + H) 603.31, observed 603.31; $[\alpha]_D$ +1.9 (*c* 0.56, $CHCl_3$).

Thiazolidinethione **67**

To a solution of (4*S*)-isopropyl-1,3-thiazolidine-2-thione (534 mg, 3.311 mmol) in PhH (18 ml) at 0 °C were added pyridine (0.32 ml, 4.0 mmol) and propionyl chloride (0.35 ml, 4.0 mmol). The reaction mixture was warmed to r.t. and allowed to stir overnight. The precipitate that formed was filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 6:1) to afford **67** as a yellow oil (712 mg, 99%); IR (neat, cm^{-1}) 1698, 1462, 1351; ^1H NMR (300 MHz, $CDCl_3$): 5.14 (t, *J* = 6.8, 1 H), 3.48 (dd, *J* = 11.5, 8.1, 1 H), 3.34 (dq, *J* = 21.5, 7.1, 1 H), 3.12 (dq, *J* = 21.5, 7.1, 1 H), 3.00 (d, *J* = 11.5, 1 H), 2.35 (t, *J* = 6.8, 1 H), 1.15 (t, *J* = 7.2, 3 H), 1.03 (d, *J* = 6.8, 3 H), 0.94 (d, *J* = 6.8, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.6, 174.8, 71.5, 31.9, 30.7, 30.3, 18.9, 17.6, 8.9; EI HRMS *m/z* calculated for $C_9H_{15}NOS_2$ (M^+) 217.0591, observed 217.0602; $[\alpha]_D$ +435 (*c* 1.62, $CHCl_3$). Calculated for $C_9H_{15}NOS_2$: C, 49.74; H, 6.96. Found: C, 50.01; H, 6.86.

Thiazolidinethione **71**

To a suspension of $Sn(OTf)_2$ (17.27 g, 41.44 mmol) in CH_2Cl_2 (40 ml) cooled to –78 °C were added *N*-ethylpiperidine (6.7 ml, 48.9 mmol) and **67** (3.00 g, 14.8 mmol) in CH_2Cl_2 (30 ml) via cannula. The solution was stirred at –78 °C for 2 h. Propionaldehyde (3.0 ml, 41.4 mmol) was introduced via syringe. The reaction mixture was stirred at –78 °C for 3 h, quenched with pH 7 phosphate buffer (20 ml) and allowed to warm to r.t. The separated aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and evaporated, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 3:1) to give **71** as a yellow solid (3.87 g, 95%), m.p. 81–83 °C; IR (neat, cm^{-1}) 3460, 1684, 1461; ^1H NMR (300 MHz, C_6D_6): 4.93 (qd, *J* = 7.0, 2.9, 1 H), 4.75–4.69 (m, 1 H), 4.05–3.99 (m, 1 H), 2.62 (br s, 1 H), 2.40 (dd, *J* = 11.6, 8.1, 1 H), 2.07 (t, *J* = 6.2, 1 H), 1.93 (dd, *J* = 11.5, 1.3, 1 H), 1.64–1.51 (m, 1 H), 1.49–1.33 (m, 1 H), 1.16 (d, *J* = 7.0, 3 H), 0.97 (t, *J* = 7.4, 3 H), 0.68 (d, *J* = 6.8, 3 H), 0.65 (d, *J* = 7.0, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 203.3, 178.0, 73.3, 71.9, 42.8, 30.9, 29.4, 27.3, 18.8, 17.4, 10.8, 10.6; EI HRMS *m/z* calculated for $C_{12}H_{21}NO_2S_2$ (M^+) 275.1008, observed 275.0999; $[\alpha]_D$ +363 (*c* 0.59, $CHCl_3$). Calculated for $C_{12}H_{21}NO_2S_2$: C, 52.33; H, 7.69. Found: C, 52.22; H, 7.62.

Thiazolidinethione **68**

To a suspension of $Sn(OTf)_2$ (2.86 g, 6.86 mmol) in CH_2Cl_2 (7.0 ml) cooled to –78 °C was added *N*-ethylpiperidine (1.11 ml, 8.10 mmol) and **67** (533 mg, 2.45 mmol) in CH_2Cl_2 (4.0 ml) via cannula. The solution was stirred at –78 °C for 2 h, **66** (700 mg, 1.161 mmol) dissolved in CH_2Cl_2 (4.0 ml) was introduced via cannula, and the reaction mixture was quenched with pH 7 phosphate buffer (20 ml) after 3 h. The separated aqueous layer was extracted with CH_2Cl_2, the combined organic phases were dried and evaporated, and the residue was purified by column chromatography on silica gel (pet ether/EtOAc 10:1 to 1:1) to give **68** as a yellow oil (914 mg, 96%); IR (neat, cm^{-1}) 3524, 1696, 1454; ^1H NMR (300 MHz, $CDCl_3$): 7.66 (d, *J* = 7.7, 4 H), 7.45–7.27 (m, 11 H), 5.20 (t, *J* = 6.2, 1 H), 4.72–4.68 (m, 1 H), 4.53 (d, *J* = 2.7, 2 H), 4.25–4.17 (m, 4 H), 3.63–3.58 (m, 1 H), 3.55–3.42 (m, 2 H), 3.34 (s, 3 H), 3.38–3.33 (m, 1 H), 3.23 (d, *J* = 1.6, 1 H), 2.98 (dd, *J* = 11.5, 1.3, 1 H), 2.89–1.84 (m, 1 H), 2.31 (t, *J* = 6.3, 1 H), 2.06–2.01 (m, 1 H), 1.79 (dd, *J* = 13.5, 5.4, 1 H), 1.70 (dd, *J* = 13.5, 5.4, 1 H), 1.73–1.67 (m, 1 H), 1.60–1.49 (m, 3 H), 1.16 (d, *J* = 6.9, 3 H), 1.09 (s, 9 H), 1.24–1.05

(m, 2 H), 1.01 (d, *J* = 6.8, 3 H), 0.95 (d, *J* = 6.9, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.7, 176.7, 138.5, 135.7 (5C), 133.9, 133.6, 129.8, 129.7, 128.3 (2C), 127.7 (2C), 127.6 (2C), 127.5 (2C), 99.4, 73.2, 72.9, 72.7, 72.0, 70.8, 69.0, 65.0, 55.4, 43.5, 43.4, 39.9, 39.2, 37.4 (2C), 34.7, 30.8, 29.8, 27.0 (3C), 19.1 (2C), 17.4, 11.0; FAB MS *m/z* calculated for $C_{45}H_{62}NO_7S_2Si$ (M^+ + H) 820.37, observed 820.29; $[\alpha]_D^{21}$ +137 (*c* 1.71, $CHCl_3$). Calculated for $C_{45}H_{61}NO_7S_2Si$: C, 65.90; H, 7.50. Found: C, 65.57; H, 7.53.

Weinreb Amide **69**

To a suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (514 mg, 5.27 mmol) in THF (6.0 ml) cooled to 0 °C was added a 2.0 M solution of Me_3Al in hexanes (2.53 ml, 5.06 mmol). The cloudy solution was stirred at 0 °C for 10 min and at r.t. for 30 min prior to cooling to –15 °C. A solution of **68** (865 mg, 1.055 mmol) in CH_2Cl_2 (6.0 ml) and THF (8.0 ml) was introduced via cannula. The reaction mixture was allowed to warm to –5 °C for 1.75 h, quenched with Rochelle's salt solution (150 ml) and stirred at r.t. for 30 min. The separated aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried and evaporated. The residue was purified by column chromatography on silica gel (pet ether/EtOAc 2:1 to 1.8) to give **69** as a colorless oil (697 mg, 92%); IR (neat, cm^{-1}) 3491, 1738, 1660, 1634; ^{1}H NMR (300 MHz, $CDCl_3$): 7.65 (d, *J* = 6.4, 4 H), 7.43–7.26 (m, 11 H), 4.52 (d, *J* = 3.7, 2 H), 4.25–4.15 (m, 2 H), 4.14 (t, *J* = 7.2, 1 H), 3.97 (m, 1 H), 3.78 (br s, 1 H), 3.66 (s, 3 H), 3.60 (m, 1 H), 3.51 (dd, *J* = 10.0, 5.3, 1 H), 3.36 (dd, *J* = 10.0, 5.3, 1 H), 3.34 (s, 3 H), 3.18 (s, 3 H), 2.92–2.87 (m, 2 H), 2.07–2.01 (m, 1 H), 1.78 (dd, *J* = 13.8, 5.4, 1 H), 1.69–1.64 (m, 2 H), 1.61–1.47 (m, 3 H), 1.17 (d, *J* = 7.0, 3 H), 1.08 (s, 9 H), 1.28–1.04 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 177.1, 138.4, 135.7 (5C), 133.8, 133.6, 129.7 (2C), 128.3 (2C), 127.6 (4C), 127.5 (2C), 99.3, 73.2, 72.8, 72.7, 70.8, 69.4, 68.7, 65.1, 61.4, 55.3, 43.5, 39.9, 39.8, 39.1, 37.3, 34.7, 31.9, 26.9 (3C), 19.0, 12.1; FAB MS *m/z* calculated for $C_{41}H_{58}NO_8Si$ (M^+ + H) 720.39, observed 719.33; $[\alpha]_D$ +15.5 (*c* 2.00, $CHCl_3$).

Aldehyde **70**

To a solution of **69** (243 mg, 0.34 mmol) in CH_2Cl_2 (2.6 ml) cooled to –20 °C were added 2,6-lutidine (0.16 ml, 1.35 mmol) and TBSOTf (0.23 ml, 1.01 mmol). The reaction mixture was stirred at –20 °C for 1.25 h, quenched with aqueous $NaHCO_3$ solution (10 ml) and warmed to r.t. The separated aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried and evaporated. Purification was achieved by column chromatography on silica gel (pet ether/EtOAc 8:1 to 1:1) to afford the TBS ether as a colorless oil (247 mg, 88%); IR (neat, cm^{-1}) 1666, 1592, 1580; ^{1}H NMR (300 MHz, C_6D_6): 7.79–7.74 (m, 4 H), 7.36–7.13 (m, 11 H), 4.49 (d, *J* = 12.2, 1 H), 4.43 (d, *J* = 12.2, 1 H), 4.42–4.38 (m, 1 H), 4.37–4.25 (m, 1 H), 3.86–3.79 (m, 1 H), 3.57 (dd, *J* = 9.7, 5.6, 1 H), 3.43 (dd, *J* = 9.7, 5.6, 1 H), 3.29 (s, 3 H), 3.23 (s, 3 H), 3.23–3.09 (m, 2 H), 2.96 (s, 3 H), 2.22 (dd, *J* = 10.4, 1.8, 1 H), 2.06–1.83 (m, 4 H), 1.71–1.52 (m, 2 H), 1.48–1.10 (m, 4 H), 1.35 (d, *J* = 6.8, 3 H), 1.21 (s, 9 H), 1.07 (s, 9 H), 0.18 (s, 3 H), 0.16 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 175.7, 139.1, 136.1 (4C), 134.1, 130.1, 130.0, 128.5 (2C), 128.3 (2C), 127.9 (5C), 99.5, 73.5, 73.4, 73.3, 70.5, 69.5, 66.6, 65.8, 61.0, 55.1, 44.0, 42.9, 41.6, 40.1, 38.1, 35.3, 32.2, 27.2 (3C), 26.3 (3C), 19.3, 18.4, 12.6, –4.0, –4.3; TOF MS ES$^+$ *m/z* calculated for $C_{47}H_{71}NO_8Si_2Na$ (M^+ + Na) 856.4616, observed 856.4568; $[\alpha]_D$ +14 (*c* 0.24, $CHCl_3$).

To a solution of the above product (61.5 mg, 0.074 mmol) in THF (2.6 ml) cooled to –78 °C was added Dibal-H (0.29 ml, 0.30 mmol) dropwise. The reaction mixture was stirred

for 10 min, acetone (0.5 ml) was added, and the solution was stirred for 5 min prior to the addition of Rochelle's salt solution (7 ml), phosphate pH 7 buffer (8 ml), and CH_2Cl_2 (15 ml). The mixture was warmed to r.t. and stirred for 30 min. The separated aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried and evaporated in vacuo. The residue (55.4 mg, 97%) was dried azeotropically with PhH and used directly in the next reaction; IR (neat, cm^{-1}) 1728, 1589, 1472; ^1H NMR (300 MHz, $CDCl_3$): 9.64 (s, 1 H), 7.80–7.74 (m, 4 H), 7.32–7.13 (m, 11 H), 4.51–4.43 (m, 1 H), 4.39 (d, *J* = 3.2, 2 H), 4.39–4.29 (m, 2 H), 4.09–4.03 (m, 1 H), 3.82–3.75 (m, 1 H), 3.46 (dd, *J* = 9.8, 5.8, 1 H), 3.30 (dd, *J* = 9.8, 5.8, 1 H), 3.26 (s, 3 H), 2.93 (dd, *J* = 13.1, 3.2, 1 H), 2.47 (qd, *J* = 7.0, 2.7, 1 H), 2.00–1.72 (m, 3 H), 1.68–1.59 (m, 3 H), 1.38 (t, *J* = 11.5, 1 H), 1.30–1.15 (m, 2 H), 1.22 (s, 9 H), 1.06 (d, *J* = 6.9, 3 H), 0.95 (s, 9 H), 0.08 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 203.3, 140.0, 136.1 (5C), 134.3, 134.1, 130.1 (2C), 128.5 (4C), 128.0 (2C), 127.6 (2C), 99.6, 73.2 (2C), 73.1, 69.7, 68.2, 65.9, 65.2, 55.1, 50.4, 43.8, 41.3, 40.6, 38.0, 35.2, 27.2 (3C), 26.0 (3C), 19.3, 18.2, 7.1, –4.1, –4.6; TOF MS ES^+ *m/z* calculated for $C_{45}H_{66}O_7Si_2Na$ (M^+ + Na) 797.4245, observed 797.4219; $[\alpha]_D$ –0.81 (*c* 0.37, $CHCl_3$).

Silyl Enol Ether **72a**

To a solution of bis(dimethylphenylsilyl)amine (0.30 ml, 1.06 mmol) in THF (0.2 ml) at 0 °C was added a 1.60 M solution of *n*-BuLi in hexanes (0.67 ml, 1.06 mmol). The resulting solution was stirred at 0 °C for 10 min, cooled to –78 °C, treated slowly via cannula with a solution of **37** (25.9 mg, 0.035 mmol) in THF (0.8 ml) and stirred for 1 h. TMSCl (0.05 ml, 0.30 mmol) was added dropwise and the mixture was allowed to warm to r.t., at which point a white precipitate had formed. After 6 h of stirring at r.t., the excess TMSCl was quenched with Et_3N, followed by the addition of $NaHCO_3$ solution. The separated aqueous layer was extracted with pentane and the combined organic layers were dried and evaporated. The residue was purified by column chromatography on silica gel (3% Et_3N/hexanes) to give **72a** as a colorless oil (8.5 mg, 15%); ^1H NMR (300 MHz, C_6D_6): 7.64 (d, *J* = 7.1, 1 H), 7.34 (d, *J* = 7.9, 1 H), 7.04 (t, *J* = 7.5, 1 H), 6.73 (t, *J* = 7.5, 1 H), 4.90 (d, *J* = 7.0, 1 H), 4.74 (d, *J* = 7.0, 1 H), 4.73 (q, *J* = 6.6, 1 H), 4.62 (s, 2 H), 4.48–4.40 (m, 2 H), 3.99 (m, 1 H), 3.80–3.66 (m, 4 H), 2.53 (dd, *J* = 13.6, 6.2, 1 H), 2.23–2.09 (m, 2 H), 2.02–1.77 (m, 2 H), 1.63 (d, *J* = 6.6, 2 H), 1.55–1.13 (m, 8 H), 1.10 (s, 3 H), 1.09 (s, 9 H), 0.99 (t, *J* = 8.0, 2 H), 0.22 (s, 9 H), 0.19 (s, 3 H), 0.18 (s, 3 H), 0.03 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6): 148.5, 138.9, 132.5, 129.0, 128.7, 127.3, 122.4, 104.9, 97.3, 93.1, 72.4, 71.2, 69.0, 68.5, 65.0, 63.6, 63.0, 48.8, 44.6, 43.9, 39.1, 36.3, 35.9, 32.9, 26.5 (3C), 18.6, 11.1, 0.8 (4C), –1.2 (3C), –1.5.

Hydroxy Ketone **73a**

To a solution of **72a** (4.1 mg, 0.005 mmol) and aldehyde **70** (8.5 mg, 0.011 mmol) in PhMe (0.3 ml) at –78 °C was added a 0.42 M solution of $BF_3{\cdot}OEt_2$ in PhMe (12 µl, 0.005 mmol). The reaction mixture was stirred at –78 °C for 1.5 h and quenched with $NaHCO_3$ solution. After arrival at r.t., the separated aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried and evaporated, and the residue was purified by column chromatography on silica gel (hexanes/EtOAc 12:1 to 1:1) to give **73a** as a colorless oil (5.7 mg, 67%). IR (neat, cm^{-1}) 3519, 1708, 1462, 1429; ^1H NMR (300 MHz, $CDCl_3$): 7.80–7.65 (m, 4 H), 7.34 (t, *J* = 7.5, 1 H), 7.30 (t, *J* = 7.5, 1 H), 7.27 (t, *J* = 7.5, 1 H), 7.25–7.15 (m, 10 H), 7.04 (t, *J* = 7.5, 1 H), 6.72 (t, *J* = 7.5, 1 H), 4.90 (t, *J* = 8.8, 1 H), 4.82 (d, *J* = 7.1, 1 H), 4.76 (d, *J* = 7.1, 1 H), 4.72 (d, *J* = 10.3, 2 H), 4.53 (d, *J* = 6.7, 1 H), 4.50 (d, *J* = 6.7, 1 H), 4.48–4.40

(m, 1 H), 4.40–4.32 (m, 1 H), 4.32–4.23 (m, 2 H), 4.22 (m, 1 H), 4.22 (dd, *J* = 9.2, 2.8, 1 H), 4.18 (t, *J* = 10.1, 1 H), 4.03–3.96 (m, 2 H), 3.84–3.73 (m, 3 H), 3.53 (dd, *J* = 10.0, 6.0, 1 H), 3.43–3.30 (m, 2 H), 3.27 (s, 3 H), 3.26–3.13 (m, 1 H), 3.07 (dd, *J* = 16.5, 9.4, 1 H), 2.88 (dq, *J* = 6.9, 2.8, 1 H), 2.28–2.12 (m, 1 H), 2.07–1.88 (m, 5 H), 1.88–1.70 (m, 6 H), 1.68–1.62 (m, 1 H), 1.60–1.52 (m, 3 H), 1.50–0.80 (m, 11 H), 1.30 (d, *J* = 6.9, 3 H), 1.26 (d, *J* = 6.7, 3 H), 1.17 (s, 9 H), 1.10 (s, 9 H), 1.03 (s, 9 H), 0.24 (s, 3 H), 0.23 (s, 3 H), 0.22 (s, 3 H), 0.15 (s, 3 H), 0.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 212.9, 139.3, 139.0, 136.2 (2C), 134.0, 133.5, 132.4, 130.1, 129.0 (2C), 128.3 (6C), 128.2 (3C), 127.6 (3C), 127.5, 122.4, 99.1, 97.1, 92.8, 74.1, 73.7, 73.6, 73.5, 72.3, 71.0, 70.0, 68.8, 68.7, 68.6, 66.7, 66.2, 65.1, 62.7, 62.5, 55.2, 50.0, 47.0, 45.0, 44.8, 43.5, 41.8, 38.4, 38.2, 36.4, 35.3, 35.0, 32.8, 30.2, 27.2 (3C), 26.4 (3C), 26.3 (3C), 19.3, 18.6, 18.4 (2C), 9.4, 9.1, 1.4, –1.2 (3C), –1.4, –1.5, –3.4, –4.2; TOF MS ES$^+$ *m/z* calculated for $C_{80}H_{127}BrO_{14}Si_4Na$ (M^+ + Na) 1528.1127, observed 1527.7305; $[\alpha]_D$ –0.83 (*c* 0.12, CH_2Cl_2).

Hydroxy Ketone **73b**

A 0 °C solution of bis(dimethylphenylsilyl)amine (890 µl, 3.4 mmol) in THF (20 ml) was treated with a 2.5 M solution of *n*-BuLi in pentane (1.37 ml, 3.4 mmol). The resulting solution was stirred for 15 min at 0 °C before being cooled to –78 °C. A solution of **41** (500 mg, 0.68 mmol) in THF (10 ml) was added dropwise and the resulting mixture was warmed to –35 °C and stirred at this temperature for 2 h before being returned to –78 °C. To this solution was added TMSCl (259 µl, 2.05 mmol) and the resulting mixture was warmed to r.t. for 30 min, recooled to –78 °C and treated with additional TMSCl (432 µl, 3.4 mmol). After 30 min at this temperature, the mixture was treated with Et_3N (1.9 ml, 13.7 mmol), warmed to r.t., and stirred for 30 min prior to solvent removal under vacuum. The resulting solid was filtered and washed with PhH containing 1% Et_3N. The filtrate was evaporated under vacuum, and the residue was treated with a solution of **70** (584 mg, 0.72 mmol) in PhH, evaporated to dryness and dried under high vacuum. The residue was dissolved in 0.03 M CH_2Cl_2 (25 ml), cooled to –95 °C and treated slowly and uniformly (0.5 ml/min) with $BF_3{\cdot}OEt_2$ (868 µl, 6.8 mmol) with the cannula in the middle of the solution. The mixture was slowly warmed over 30 min to –78 °C, stirred 90 min at this temperature, treated with Et_3N (1.9 ml, 13.7 mmol), and warmed to r.t. before adding H_2O (20 ml). The separated aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 95:5 to 90:10) to give **73b** (742 mg, 72%) as a pale yellow oil; IR (neat, cm^{-1}) 3516, 1741, 1706, 1462; ^{1}H NMR (400 MHz, $CDCl_3$): 7.66 (m, 4 H), 7.53 (d, *J* = 7.7, 1 H), 7.49 (d, *J* = 8.0, 1 H), 7.47–7.26 (m, 12 H), 7.10 (t, *J* = 7.6, 1 H), 4.67–4.51 (m, 6 H), 4.24 (m, 2 H), 4.07–3.93 (m, 3 H), 3.93–3.78 (m, 4 H), 3.56 (m, 3 H), 3.48 (m, 1 H), 3.41 (d, *J* = 4.9, 1 H), 3.37 (s, 3 H), 3.16 (br d, *J* = 12.6, 1 H), 3.04 (br s, 1 H), 2.87 (dd, *J* = 16.4, 9.3, 1 H), 2.67 (m, 1 H), 2.18 (dd, *J* = 13.0, 9.3, 1 H), 1.98–1.40 (m, 18 H), 1.25 (m, 2 H), 1.20 (s, 3 H), 1.15 (m, 1 H), 1.09 (apparent s, 12 H), 0.96 (m, 12 H), 0.86 (apparent s, 11 H), 0.60 (q, *J* = 7.6, 6 H), 0.05 (s, 6 H), –0.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 213.3, 138.4, 135.6, 135.8 (4C), 133.9 (2C), 133.5, 132.2 (2C), 129.8 (2C), 128.8 (2C), 128.5, 128.3, 127.7 (2C), 127.4 (2C), 127.2, 122.3, 98.7, 96.8, 92.2, 73.7, 73.5, 73.3, 72.0 (2C), 70.3, 69.6, 68.4, 68.3, 68.0 (2C), 66.1, 65.8, 64.7, 62.3, 61.9, 55.3, 49.2, 47.8, 46.9, 44.7, 42.9, 41.0, 39.3, 38.1, 37.9, 37.4, 35.9, 34.8, 34.6, 32.2, 27.2 (3C), 25.8 (3C),

19.1, 18.1, 9.2, 8.8, 7.2 (3C), 6.7 (3C), –1.4 (3C), –3.6, –4.5; ES HRMS *m/z* calculated for $C_{80}H_{127}BrO_{14}Si_4Na$ (M^+ + Na) 1525.7379, observed 1525.7462; $[\alpha]_D$ –4.7 (*c* 0.86, $CHCl_3$).

SEM Protection of **73a**

To a solution of **73a** (5.7 mg, 0.003 mmol) in THF (0.3 ml) were added *i*-Pr_2NEt (0.12 ml, 0.681 mmol), SEMCl (0.10 ml, 0.584 mmol) and TBAI (15.0 mg, 0.040 mmol). The reaction mixture was stirred at r.t. for 2 days and quenched with $NaHCO_3$ solution. The separated aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried and evaporated. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 12:1 to 8:1) to give **74a** as a colorless oil (3.3 mg, 53%). IR (neat, cm^{-1}) 1714, 1475, 1462, 1428; ^1H NMR (300 MHz, $CDCl_3$): 7.74–7.71 (m, 4 H), 7.45–7.10 (m, 13 H), 7.05 (t, *J* = 7.5, 1 H), 6.70 (t, *J* = 7.5, 1 H), 4.86 (d, *J* = 6.9 HZ, 1 H), 4.82 (m, 1 H), 4.76–4.73 (m, 2 H), 4.71 (d, *J* = 13.5, 1 H), 4.65 (d, *J* = 13.5, 1 H), 4.50 (d, *J* = 12.2, 1 H), 4.45 (d, *J* = 12.2, 1 H), 4.45 (m, 1 H), 4.33–4.27 (m, 4 H), 4.02 (m, 1 H), 3.91 (t, *J* = 6.8, 2 H), 3.80–3.73 (m, 3 H), 3.57–3.47 (m, 3 H), 3.34 (dd, *J* = 10.0, 5.0, 1 H), 3.29 (s, 3 H), 3.12–3.06 (m, 2 H), 2.70 (dd, *J* = 15.0, 4.0, 1 H), 2.25 (m, 1 H), 2.04 (t, *J* = 12.8, 1 H), 2.10–2.05 (m, 2 H), 2.10–1.90 (m, 2 H), 1.90–1.77 (m, 6 H), 1.55 (d, *J* = 13.5, 1 H), 1.49 (m, 1 H), 1.40 (d, *J* = 7.0, 3 H), 1.45–1.20 (m, 9 H), 1.19 (d, *J* = 7.0, 3 H), 1.18 (s, 9 H), 1.12 (s, 3 H), 1.10 (s, 9 H), 1.09 (s, 9 H), 1.02 (q, *J* = 5.5, 4 H), 0.30 (s, 3 H), 0.26 (s, 3 H), 0.22 (s, 6 H), 0.09 (s, 9 H), 0.08 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 210.3, 139.8, 139.5, 136.5 (2C), 134.0, 133.5, 132.8, 130.5, 129.5 (2C), 128.6 (3C), 128.5 (3C), 128.4 (3C), 128.0 (3C), 127.8, 122.8, 99.6, 97.5, 97.0, 92.9, 81.1, 74.3, 74.0, 73.9, 71.5, 70.3, 69.2, 69.1, 68.2, 67.2, 66.7, 66.6, 65.5, 64.5, 63.4, 55.6, 51.7, 48.0, 47.6, 45.6, 43.7, 42.5, 40.0, 39.7, 39.3, 39.0, 36.8, 35.6, 33.2, 30.5, 27.6 (3C), 26.9 (3C), 26.8 (3C), 19.7, 19.0, 18.9, 18.8, 18.6, 10.4, 10.1, 1.8, –0.7 (3C), –0.8 (3C), –1.0, –1.1, –2.5, –3.2; TOF MS ES^+ *m/z* calculated for $C_{86}H_{141}BrO_{15}Si_5Na$ (M^+ + Na) 1658.1941, observed 1657.8236; $[\alpha]_D$ –23 (*c* 0.08, CH_2Cl_2).

SEM Protection of **73b**

To a solution of **73b** (300 mg, 0.20 mmol) in CH_2Cl_2 (5 ml) was added *i*-Pr_2NEt (693 µl, 4.0 mmol), TBAI (7.6 mg, 0.02 mmol) and SEMCl (177 µl, 1.0 mmol). The resulting mixture was stirred for 2 days before the introduction of a saturated NaHCO3 solution (5 ml). The separated aqueous layer was extracted with CH_2Cl_2, and the organic extracts were dried. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 95:5 to 90:10) to give **74b** (300 mg, 0.18 mmol, 92%) as yellow oil; IR (neat, cm^{-1}) 1714, 1461, 1372; ^1H NMR (400 MHz, $CDCl_3$): 7.65 (d, *J* = 7.1, 4 H), 7.54 (d, *J* = 6.4, 1 H), 7.47 (dd, *J* = 7.9, 1.6, 1 H), 7.44–7.24 (m, 12 H), 7.07 (dt, *J* = 7.9, 1.6, 1 H), 4.63–4.48 (m, 7 H), 4.47 (m, 1 H), 4.24 (m, 2 H), 4.04 (m, 1 H), 3.96 (m, 1 H), 3.89 (m, 3 H), 3.82 (m, 1 H), 3.75 (m, 1 H), 3.61–3.44 (m, 6 H), 3.37 (dd, *J* = 10.5, 4.8, 1 H), 3.35 (s, 3 H), 3.17 (br dd, *J* = 12.8, 2.8, 1 H), 2.82 (m, 2 H), 2.41 (dd, *J* = 14.9, 3.9, 1 H), 2.05 (m, 2 H), 1.93–1.80 (m, 3 H), 1.80–1.52 (m, 10 H), 1.52–1.38 (m, 4 H), 1.37–1.23 (m, 3 H), 1.21 (m, 1 H), 1.20 (s, 3 H), 1.13 (d, *J* = 9.6, 2 H), 1.09 (s, 9 H), 1.02 (d, *J* = 6.7, 3 H), 0.96 (t, *J* = 8.0, 9 H), 0.91–0.81 (m, 12 H), 0.60 (q, *J* = 7.9, 6 H), 0.09 (s, 3 H), 0.07 (s, 3 H), 0.02 (s, 9 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 210.5, 138.6, 138.5, 135.8 (4C), 133.8, 133.5 (3C), 132.2 (3C), 129.7 (3C), 128.9, 128.4, 127.7 (4C), 127.4 (2C), 127.2, 122.3, 96.7, 95.8, 92.1, 79.5, 73.7, 73.5, 73.3, 71.9, 70.3, 69.7, 68.4, 67.6, 66.1, 66.0, 65.9, 64.7, 63.6, 62.1, 55.4, 50.6, 47.9, 47.0, 44.9, 42.9, 40.8, 38.9, 38.0, 37.9, 35.9, 34.9, 34.7, 32.3, 29.7, 27.0

(3C), 26.1 (3C), 25.7, 20.7, 19.1, 18.4, 17.9, 10.0, 9.6, 7.2 (3C), 6.8 (3C), –1.3 (3C), –1.4 (3C), –3.4, –4.0; ES HRMS *m/z* calculated for $C_{86}H_{141}BrO_{15}Si_5Na$ (M^+ + Na) 1657.8207, observed 1657.8253.

Olefination of **74b**

To a cold (–78 °C), stirred solution of **74b** (100 mg, 0.061 mmol) in a 1:1 mixture of PhMe and hexanes (50 ml) was slowly added a 1 M solution of $TMSCH_2Li$ in pentane (612 µl, 0.61 mmol). The resulting solution was stirred at –78 °C for 15 h before the introduction of saturated $NaHCO_3$ solution (10 ml). The separated aqueous layer was extracted with EtOAc. The organic extracts were dried and the solvent was evaporated under reduced pressure. The residue was dissolved in a 10:1 mixture of THF/DMF (20 ml) before introduction of KH (24 mg, 0.61 mmol). The resulting mixture was stirred at r.t. for 1 h prior to the careful addition of H_2O (5 ml). The separated aqueous layer was extracted with EtOAc. The organic extracts were dried and the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 ml). Imidazole (21 mg, 0.31 mmol), DMAP (1 crystal) and TBSCl (16 ml, 0.061 mmol) were added, and the resulting mixture was stirred for 10 h before the addition of saturated $NaHCO_3$ solution (5 ml). The separated aqueous layer was extracted with CH_2Cl_2 and the organic extracts were dried. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexanes/EtOAc 95:5) to give **75** (70 mg, 70%) as a yellow oil; IR (neat, cm^{-1}) 1462, 1428, 1371, 1249; ^1H NMR (400 MHz, $CDCl_3$): 7.73 (dd, *J* = 7.7, 1.8, 1 H), 7.65 (d, *J* = 6.7, 4 H), 7.49 (m, 2 H), 7.44–7.37 (m, 12 H), 7.09 (dt, *J* = 7.4, 1.1, 1 H), 4.97 (br s, 1 H), 4.72 (d, *J* = 7.1, 1 H), 4.63 (m, 2 H), 4.57 (m, 2 H), 4.52 (m, 2 H), 4.23 (m, 3 H), 4.15 (m, 1 H), 4.06 (m, 2 H), 3.94 (m, 1 H), 3.81 (m, 1 H), 3.73 (m, 1 H), 3.68–3.47 (m, 9 H), 3.40 (dd, *J* = 10.2, 5.3, 1 H), 3.36 (s, 3 H), 3.14 (br d, *J* = 13.3, 1 H), 2.40 (m, 1 H), 2.21 (dd, *J* = 14.8, 7.1, 1 H), 2.14 (m, 1 H), 2.14–1.97 (m, 2 H), 1.90–1.59 (m, 9 H), 1.59–1.46 (m, 4 H), 1.30–1.23 (m, 3 H), 1.19 (s, 3 H), 1.08 (s, 9 H), 1.00 (d, *J* = 6.8, 3 H), 0.95 (m, 12 H), 0.88 m, 13 H), 0.70 (q, *J* = 7.9, 6 H), 0.05 (q, *J* = 7.9, 6 H), 0.02 (s, 9 H), –0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 149.8, 138.6, 138.1, 135.8 (4C), 133.9, 133.5 (2C), 132.3 (2C), 129.6, 128.7 (2C), 128.3, 127.7 (2C), 127.6, 127.4, 127.3 (2C), 122.3, 111.6, 96.9, 96.6, 92.3, 81.8, 77.2, 73.6, 73.4, 73.3, 72.0, 70.5, 70.4, 68.3, 68.0, 66.2, 65.9, 65.8, 64.8, 62.1, 55.4, 47.9, 45.0, 43.0, 42.7, 41.6, 40.9, 39.8, 38.8, 38.2, 37.8, 35.8, 35.4, 34.8, 32.3, 27.0 (3C), 26.5, 26.2 (3C), 25.8, 19.1, 18.2, 18.1, 14.9, 10.5, 7.3 (3C), 6.9 (3C), 4.71, –1.3 (3C), –1.4 (3C), –3.5, –3.9; ES HRMS *m/z* calculated for $C_{87}H_{143}BrO_{14}Si_5Na$ (M^+ + Na) 1655.8414, observed 1655.8334.

Lactone **82**

To a cold (–78 °C) solution of $(COCl)_2$ (18.0 ml, 208 mmol in dry CH_2Cl_2 (400 ml) was added DMSO (29.4 ml, 415 mmol) dropwise by syringe. After 15 min at –78 °C, the known lactol (18.0 g, 69.2 mmol) was added as a solution in dry CH_2Cl_2 (150 ml) via syringe. The resulting mixture was stirred at –78 °C for 1 h, treated with Et_3N (87.0 ml, 623 mmol), warmed to r.t. for 1 h and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 (2 × 50 ml). The combined organic layers were dried and concentrated, and the residue was triturated (EtOAc/H_2O) to afford **82** (17.0 g, 95%) as a white solid, m.p. 199–201 °C; IR (neat, cm^{-1}) 1775, 1386, 1266; ^1H NMR (300 MHz, $CDCl_3$): 4.75 (d, *J* = 8.5, 1 H), 4.58 (dd, *J* = 8.5, 6.4, 1 H), 4.10–4.03 (m, 2 H), 3.88–3.80 (m, 2 H), 1.54 (s, 3 H), 1.51 (s, 3 H),

1.44 (s, 3 H), 1.40 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 168.6, 112.8, 100.2, 76.7, 72.6, 72.1, 67.2, 61.4, 28.6, 26.6, 25.0, 18.7; EI HRMS *m/z* calculated for $C_{12}H_{19}O_6$ $(M + H)^+$ 259.1182, observed 259.1198; $[\alpha]_D$ +46.7 (*c* 1.58, $CHCl_3$). Calculated for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.69; H, 7.02.

Lactone **83**

To a solution of **82** (16.6 g, 64.4 mmol) in THF (400 ml) was added 1.68 M LDA in THF (50 ml, 84.0 mmol) dropwise at –78 °C. After 15 min, the reaction mixture was warmed to –40 °C, stirred for 45 min, returned to –78 °C and treated with MeI (14.0 ml, 225 mmol) dropwise. The mixture was stirred at –78 °C for 15 min and at –40 °C for 2 h, quenched by the slow addition of pH 7 phosphate buffer (100 ml) and saturated NH_4Cl solution (50 ml) at –78 °C, warmed to r.t., diluted with EtOAc (800 ml), washed with brine (2 × 500 ml), dried and concentrated. The residue was recrystallized (EtOAc/H_2O) to afford **83** (14.58 g, 79%) as a white solid, m.p. 212 °C; IR (neat, cm^{-1}) 1771, 1381, 1266; ^{1}H NMR (300 MHz, $CDCl_3$): 4.15 (d, *J* = 6.3, 1 H), 4.10–4.03 (m, 2 H), 3.87–3.79 (m, 2 H), 1.66 (s, 3 H), 1.53 (s, 3 H), 1.43 (s, 6 H), 1.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.4, 112.0, 100.1, 82.7, 79.4, 73.5, 67.0, 61.5, 28.6, 27.2, 26.7, 26.0, 18.8; EI HRMS *m/z* calculated for $C_{13}H_{20}O_6$ (M^+) 272.1260, observed 272.1286; $[\alpha]_D$ +24.9 (*c* 1.71, $CHCl_3$). Calculated for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.25; H, 7.34.

Hydroxy Lactone **84**

A mixture of lactone **83** (7.4 g, 27.2 mmol) in ethylene glycol (15 ml, 26.9 mmol) and HMPA (30 ml, 17.2 mmol) was dissolved in deoxygenated (Ar, 15 min) THF (50 ml). A 0.1 M solution of SmI_2 in THF (800 ml, 80 mmol) was added via cannula, first giving a nearly clear yellow solution, then an opaque white mixture by the end of the addition. The reaction mixture was immediately poured into hexanes (600 ml). The slurry was passed through a pad of Celite and silica gel. The solid was washed with hexanes/EtOAc 1:1. The organics were concentrated in vacuo to give a total of 13.3 g of crude product as a yellow oil with some solids. Purification by column chromatography (EtOAc/hexanes 1:1) gave pure **84** as a white crystalline solid (4.3 g, 73%), m.p. 100 °C; IR (neat, cm^{-1}) 3415, 1755, 1380, 1291; ^{1}H NMR (400 MHz, $CDCl_3$): 4.01 (dd, *J* = 10.4, 5.2, 1 H), 3.96–3.89 (m, 1 H), 3.82 (t, *J* = 10.4, 1 H), 3.76 (t, *J* = 9.2, 1 H), 3.68 (t, *J* = 9.2, 1 H), 2.65–2.57 (m, 2 H), 1.55 (s, 3 H), 1.48 (d, *J* = 7.6, 2 H), 1.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 171.4, 100.3, 73.2, 72.5, 69.0, 61.5, 43.6, 28.9, 19.0, 14.9; EI HRMS *m/z* calculated for $C_{10}H_{17}O_5$ $(M + H)^+$ 217.1076, observed 217.1095; $[\alpha]_D$ +52.2 (*c* 1.59, $CHCl_3$). Calculated for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.63; H, 7.52.

Diacetate **85**

To a solution of **84** (2.3 g, 10.7 mmol) in PhMe (35 ml) was added 1 M Dibal-H (23.4 ml, 23.4 mmol) at –78 °C. After 0.5 h of stirring, the reaction mixture was quenched with Rochelle's salt solution, stirred for 1 h and extracted wtih EtOAc (3 ×). The combined organic layers were dried and the solvent evaporated. The crude diol (2.4 g, 100%, α:β = 2:3) was used in the next step without further purification.

A solution of the above diol (2.50 g, 10.7 mmol) in CH_2Cl_2 (100 ml) was treated with Ac_2O (4.0 ml, 42.6 mmol), pyridine (5.2 ml, 64 mmol), and DMAP (130 mg, 1.0 mmol),

stirred at r.t. for 1 h, diluted with CH_2Cl_2 and washed sequentially with 0.1 M HCl (2 ×) and saturated $NaHCO_3$ solution. The separated aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were dried and evaporated to leave **85** (2.9 g, 90%, α:β = 2:3) as a white solid, which was used without further purification; IR (neat, cm^{-1}) 1748, 1462, 1374; ^1H NMR (300 MHz, $CDCl_3$): 6.03 (d, *J* = 3.6, 0.4 H), 5.49 (d, *J* = 9.2, 0.6 H), 5.09 (dd, *J* = 10.8, 9.3, 0.4 H), 4.89 (dd, *J* = 10.6, 9.3, 0.6 H), 3.90 (dd, *J* = 10.7, 5.4, 0.6 H), 3.82 (ddd, *J* = 8.5, 8.5, 3.7, 0.4 H), 3.66 (m, 1.4 H), 3.62 (dd, *J* = 9.4, 9.4, 1 H), 3.40 (ddd, *J* = 9.9, 9.9, 5.4, 0.6 H), 2.11 (s, 1.2 H), 2.10 (s, 1.8 H), 2.08 (s, 1.8 H), 2.07 (s, 1.2 H), 2.06 (m, 0.4 H), 1.90 (m, 0.6 H), 1.44 (s, 1.2 H), 1.43 (s, 1.8 H), 1.35 (s, 1.2 H), 1.34 (s, 1.8 H), 0.90 (d, *J* = 6.5, 1.8 H), 0.88 (d, *J* = 6.5, 1.2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 170.3, 170.2, 169.5, 169.0, 99.9, 99.7, 95.6, 93.8, 77.2, 73.7, 72.9, 72.3, 72.3, 71.8, 68.2, 66.2, 62.2, 61.9, 40.8, 39.2, 29.0, 28.9, 20.8, 20.7, 19.0, 18.9, 12.0, 11.9; ES HRMS *m/z* calculated for $C_{14}H_{27}O_7Na$ (M^+ + Na) 325.1258, observed 325.1278; $[\alpha]_D$ +13 (*c* 1.8, $CHCl_3$).

Dihydroxy Sulfide **86**

To a solution of **85** (2.88 g, 9.73 mmol) and 1 M PhSH in CH_2Cl_2 (7.0 ml, 68.1 mmol) in CH_2Cl_2 (60 ml) was slowly added $BF_3{\cdot}OEt_2$ (7.4 ml, 58.4 mmol) at 0 °C. The reaction mixture was stirred for 10 min, slowly quenched with saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2 (3 ×). The combined organic layers were dried and evaporated, and the residue was purified by way of chromatography on silica gel (50–80% EtOAc/hexanes) to provide **86** (1.88 g, 62%, α:β > 9:1) as a white solid; IR (neat, cm^{-1}) 3417, 1722, 1373, 1246; ^1H NMR (300 MHz, $CDCl_3$): 7.50 (m, 2 H), 7.30 (m, 3 H), 5.45 (d, *J* = 6.0, 1 H), 4.98 (dd, *J* = 11.3, 9.1, 1 H), 4.25 (ddd, *J* = 9.8, 3.8, 3.8, 1 H), 3.85 (m, 2 H), 3.65 (ddd, *J* = 9.5, 9.5, 5.6, 1 H), 3.05 (br s, 1 H), 2.35 (m, 1 H), 2.15 (s, 3 H), 2.10 (br s, 1 H), 1.09 (d, *J* = 6.8, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 172.4, 134.2, 131.9 (2C), 129.0 (2C), 124.4, 89.8, 77.0, 72.9, 70.9, 62.3, 40.2, 21.0, 14.2; ES HRMS *m/z* calculated for $C_{15}H_{20}O_5SNa$ (M^+ + Na) 335.0924, observed 335.0907; $[\alpha]_D$ +257 (*c* 1.15, $CHCl_3$).

Hydroxy Acetal **87**

To a solution of **86** (1.0 g, 3.2 mmol) in DMF (5 ml) was added *p*-methoxybenzaldehyde dimethylacetal (1.75 g, 9.6 mmol) and TsOH (0.02 g, 0.1 mmol). After being stirred at r.t. for 6 h, the reaction mixture was diluted with Et_2O and washed with saturated $NaHCO_3$ solution and H_2O (2 ×). The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried and concentrated. The residue was dried at 60 °C and 0.5 Torr for 5 h to leave 1.4 g (100%) of the protected acetate, which was used directly in the next step.

The above material (1.4 g, 3.2 mmol) was dissolved in MeOH (30 ml) and CH_2Cl_2 (30 ml), treated with 3 M KOH (10 ml), and stirred at r.t. for 3 h prior to dilution with CH_2Cl_2 and washing with H_2O. The dried organic phase was concentrated to leave a residue that was taken up in hot CH_2Cl_2 and filtered. The filtrate was dried at 70 °C and 0.5 Torr for 12 h to give 1.2 g (97%) of a mixture of α- and β- anomers.

For **87**: m.p. 121–124 °C; IR (neat, cm^{-1}) 3386, 1615, 1519, 1455; ^1H NMR (300 MHz, $CDCl_3$): 7.48 (m, 3 H), 7.30 (m, 4 H), 6.92 (m, 2 H), 5.54 (s, 1 H), 5.45 (d, *J* = 5.2, 1 H), 4.40 (dt, *J* = 5.0, 9.9, 1 H), 4.20 (dd, *J* = 5.0, 10.3, 1 H), 3.84 (s, 3 H), 3.79 (m, 2 H), 3.51 (dd, *J* = 9.2, 9.2, 1 H), 2.46 (d, *J* = 2.3, 1 H), 2.35 (m, 1 H), 1.25 (d, *J* = 6.8, 3 H); ^{13}C NMR (75 MHz,

$CDCl_3$): 160.3, 134.4, 131.8 (2C), 129.7, 129.0 (2C), 127.6 (2C), 127.3, 113.7 (2C), 102.1, 90.7, 83.6, 71.3, 68.8, 63.7, 55.3, 42.1, 14.1; ES HRMS *m/z* calculated for $C_{21}H_{24}O_5SNa$ (M^+ + Na) 411.1237, observed 411.1210; $[\alpha]_D$ +311 (*c* 1.00, $CHCl_3$).

Protection/Reduction of Alcohol **87**

To a solution of **87** (140 mg, 0.40 mmol) in THF (2 ml) and DMF (0.4 ml) was added NaH (40 mg, 60% in oil, 1.0 mmol). After 30 min of stirring, PMBBr (90 mg, 0.43 mmol) and TBAI (0.015 g, 0.04 mmol) were introduced and reaction was allowed to proceed at r.t. for 1 h prior to dilution with Et_2O (30 ml) and washing with H_2O (3 ×). The organic phase was dried and evaporated at 0 °C to leave a residue of **88** that was diluted with CH_2Cl_2 (5 ml), cooled to 0 °C and treated with 1 M Dibal-H (3.9 ml, 3.9 mmol). This mixture was stirred for 1 h, quenched with Rochelle's salt solution over 60 min and extracted with CH_2Cl_2 (3 ×). The combined organic layers were dried and evaporated and the residue was purified by chromatography on silica gel (25% EtOAc/hexanes) to furnish **89** as a colorless oil (135 mg, 73%).

For **88**: ^{1}H NMR (300 MHz, $CDCl_3$): 7.45 (m, 3 H), 7.30 (m, 6 H), 6.90 (m, 4 H), 5.59 (s, 1 H), 5.44 (d, *J* = 5.2, 1 H), 4.89 (d, *J* = 10.8, 1 H), 4.62 (d, *J* = 10.8, 1 H), 4.44 (dt, *J* = 5.0, 9.8, 1 H), 4.19 (dd, *J* = 4.9, 10.2, 1 H), 3.83 (s, 3 H), 3.81 (s, 3 H), 3.80–3.55 (m, 3 H), 2.34 (m, 1 H), 1.17 (d, *J* = 6.8, 3 H).

For **89**: IR (neat, cm^{-1}) 3461, 1612, 1513, 1462; ^{1}H NMR (300 MHz, $CDCl_3$): 7.45 (m, 2 H), 7.30 (m, 7 H), 6.90 (m, 4 H), 5.44 (d, *J* = 6.0, 1 H), 4.86 (d, *J* = 10.5, 1 H), 4.85 (d, *J* = 10.7, 1 H), 4.66 (d, *J* = 10.5, 1 H), 4.60 (d, *J* = 10.7, 1 H), 4.25 (dt, *J* = 3.4, 9.4, 1 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.75 (m, 2 H), 3.55 (m, 2 H), 2.25 (m, 1 H), 1.63 (br s, 1 H), 1.15 (d, *J* = 6.8, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.4, 159.3, 134.4, 131.9 (2C), 130.5, 130.3, 129.6 (2C), 129.5 (2C), 128.9 (2C), 127.2, 113.8 (2C), 113.8 (2C), 90.4, 82.5, 79.2, 75.2, 74.7, 72.6, 62.0, 55.3 (2C), 42.2, 14.5; ES HRMS *m/z* calculated for $C_{29}H_{34}O_6SNa$ (M^+ + Na) 533.1968, observed 533.1947; $[\alpha]_D$ +214 (*c* 1.1, $CHCl_3$).

Hydroxy Sulfone **90**

A cold (0 °C) solution of **118** (200 mg, 0.38 mmol) in CH_2Cl_2 (4 ml) was treated with MCPBA (330 mg of 70% purity, 1.34 mmol) and $NaHCO_3$ (140 mg, 0.17 mmol), stirred for 3 h and quenched with aqueous $NaHSO_3$ solution. The product was extracted into CH_2Cl_2 (3 ×), dried and evaporated. Chromatography of the residue on silica gel (50% EtOAc/hexanes) gave **90** (180 mg, 87%) as a white solid, m.p. 95–98 °C; IR (neat, cm^{-1}) 3502, 1612, 1514, 1302; ^{1}H NMR (300 MHz, $CDCl_3$): 7.90 (m, 2 H), 7.75–7.50 (m, 3 H), 7.30 (m, 4 H), 6.90 (m, 4 H), 4.86 (d, *J* = 10.5, 1 H), 4.82 (d, *J* = 10.3, 1 H), 4.81 (d, *J* = 5.3, 1 H), 4.72 (d, *J* = 10.5, 1 H), 4.59 (d, *J* = 10.9, 1 H), 4.25 (m, 2 H), 3.83 (s, 3 H), 3.82 (s, 3 H), 3.50 (m, 3 H), 2.39 (m, 1 H), 1.53 (d, *J* = 7.2, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$): 159.3 (2C); 138.3, 133.9, 130.4, 130.1, 129.7 (2C), 129.6 (2C), 129.1 (2C), 128.5 (2C), 113.9 (4C), 92.7, 80.5, 78.1, 76.0, 75.3, 74.5, 61.7, 55.3 (2C), 39.6, 12.3; ES HRMS *m/z* calculated for $C_{29}H_{34}O_8SNa$ (M^+ + Na) 565.1867, observed 565.1810; $[\alpha]_D$ +131 (*c* 1.00, $CHCl_3$).

Iodo Sulfone **91**

A solution of **90** (180 mg, 0.32 mmol) in PhMe (4 ml) and CH_3CN (1 ml) was treated with I_2 (163 mg, 0.65 mmol), PPh_3 (220 mg, 0.81 mmol), and imidazole (80 mg, 1.23 mmol) and

heated at reflux for 2 h. The cooled reaction mixture was washed with aqueous $NaHCO_3$ solution, and the combined organic layers were dried and evaporated. The residue was purified by chromatography on silica gel (20% EtOAc/hexanes). Product **91** (200 mg, 95%) was isolated as a white solid, m.p. 111–114 °C; IR (neat, cm^{-1}) 1513, 1302, 1248, 1116; ^1H NMR (300 MHz, $CDCl_3$): 7.88 (m, 2 H), 7.62 (m, 3 H), 7.30 (m, 4 H), 6.90 (m, 4 H), 4.90 (d, *J* = 10.7, 1 H), 4.86 (d, *J* = 5.8, 1 H), 4.83 (d, *J* = 10.5, 1 H), 4.71 (d, *J* = 10.5, 1 H), 4.69 (d, *J* = 10.7, 1 H), 4.32 (dd, *J* = 4.6, 10.7, 1 H), 3.87 (dt, *J* = 3.6, 8.9, 1 H), 3.83 (s, 6 H), 3.40 (dd, *J* = 8.7, 8.7, 1 H), 3.35 (dd, *J* = 4.1, 11.0, 1 H), 3.03 (dd, *J* = 3.1, 11.0, 1 H), 2.45 (m, 1 H), 1.54 (d, *J* = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.4 (2C), 138.3, 134.0, 130.1 (2C), 129.7 (2C), 129.4 (2C), 129.2 (2C), 128.5 (2C), 114.0 (4C), 92.5, 81.8, 80.1, 75.2, 74.8, 73.4, 55.3 (2C), 39.4, 12.4, 8.2; ES HRMS *m/z* calculated for $C_{29}H_{33}IO_7SNa$ (M^+ + Na) 675.0884, observed 675.0884; $[\alpha]_D$ +113 (*c* 1.2, $CHCl_3$).

Oxetane Sulfone **92**

A solution of **91** (5 mg, 0.008 mmol) in THF (1 ml) at –78 °C was treated with *t*-BuOK (4 mg, 0.038 mmol) in one portion, stirred for 1 h and allowed to warm to r.t. After an additional hour of stirring, the reaction mixture was quenched with H_2O (1 ml), diluted with Et_2O and extracted with Et_2O. The combined organic layers were dried and evaporated to leave a residue that was purified by chromatography on silica gel (15% EtOAc/hexanes) to give **92** (1.5 mg, 30%) as a colorless oil; IR (neat, cm^{-1}) 1613, 1513, 1446, 1305; ^1H NMR (300 MHz, $CDCl_3$): 7.92 (m, 2 H), 7.62 (m, 3 H), 7.25 (m, 4 H), 6.87 (m, 4 H), 4.51 (d, *J* = 11.4, 1 H), 4.47 (m, 3 H), 4.41 (d, *J* = 11.4, 1 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.60 (d, *J* = 1.3, 1 H), 3.52 (br s, 1 H), 2.99 (dd, *J* = 7.9, 9.7, 1 H), 2.70 (dt, *J* = 7.1, 7.1, 1 H), 2.40 (dd, *J* = 1.1, 9.7, 1 H), 1.29 (d, *J* = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.3 (2C), 135.8, 134.0, 130.0 (2C), 129.7, 129.6, 129.5 (2C), 129.4 (2C), 128.9 (2C), 113.8 (4C), 84.6, 79.1, 77.4, 77.0, 71.1, 70.6, 55.3 (2C), 38.6, 33.8, 15.1.

Dehydroiodination of **91**

To a solution of **91** (130 mg, 0.20 mmol) in PhMe (20 ml) was added DBU (120 mg, 0.80 mmol). The reaction mixture was heated at reflux for 12 h, cooled, diluted with Et_2O, filtered and evaporated. The residue was purified by chromatography on silica gel (20% EtOAc/hexanes) to give **93** (80 mg, 76%) as a white solid; IR (neat, cm^{-1}) 1613, 1514, 1447, 1307; ^1H NMR (500 MHz, $CDCl_3$): 7.99 (m, 2 H), 7.64 (m, 3 H), 7.25 (m, 4 H), 6.89 (m, 4 H), 4.90 (d, *J* = 6.1, 1 H), 4.64 (d, *J* = 11.4, 1 H), 4.62 (d, *J* = 11.1, 1 H), 4.60 (s, 1 H), 4.57 (d, *J* = 11.1, 1 H), 4.48 (s, 1 H), 4.44 (d, *J* = 11.4, 1 H), 3.86 (dd, *J* = 5.9, 5.9, 1 H), 3.83 (m, 1 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 2.65 (m, 1 H), 1.49 (d, *J* = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.3, 159.2, 154.7, 138.5, 133.9, 129.9, 129.8, 129.6 (2C), 129.3 (2C), 129.0 (2C), 128.9 (2C), 113.9 (2C), 113.8 (2C), 97.3, 91.4, 79.8, 77.6, 73.0, 72.0, 55.3 (2C), 35.9, 12.6; ES HRMS *m/z* calculated for $C_{29}H_{32}O_7SNa$ (M^+ + Na) 547.1761, observed 547.1797; $[\alpha]_D$ +15 (*c* 1.0, $CHCl_3$).

Hydroboration/Oxidation of **93**

A solution of **93** (10 mg, 0.02 mmol) in THF (1 ml) was treated with 9-BBN (12 mg, 0.10 mmol), stirred at r.t. for 6 h prior to quenching with H_2O_2 (0.1 ml) and 1 M KOH (0.3 ml), and stirred for an additional 10 min. The product was extracted into CH_2Cl_2 and the combined organic phases were dried and evaporated. Chromatography of the resi-

due on silica gel (20% EtOAc/hexanes) resulted in the isolation of pure **94** (7 mg, 60%) as a colorless oil; IR (neat, cm^{-1}) 3519, 1612, 1513, 1321; ^1H NMR (500 MHz, C_6D_6): 8.0 (m, 2 H), 7.03 (m, 2 H), 6.94 (m, 2 H), 6.80 (m, 3 H), 6.70 (m, 2 H), 6.62 (m, 2 H), 4.93 (d, *J* = 2.5, 1 H), 4.23 (d, *J* = 11.6, 1 H), 4.21 (d, *J* = 10.1, 1 H), 4.10 (d, *J* = 11.8, 1 H), 3.98 (d, *J* = 11.2, 1 H), 3.81 (ddd, *J* = 3.6, 7.1, 10.8, 1 H), 3.62 (ddd, *J* = 2.1, 4.8, 6.9, 1 H), 3.52 (m, 1 H), 3.47 (m, 1 H), 3.29 (s, 3 H), 3.28 (s, 3 H), 3.18 (m, 1 H), 2.97 (m, 1 H), 2.97 (m, 1 H), 1.74 (d, *J* = 7.3, 3 H) (OH not observed); ^{13}C NMR (125 MHz, C_6D_6): 160.0, 159.9, 139.9, 133.3, 130.2, 130.0, 129.5 (2C), 129.8 (2C), 129.1 (2C), 128.8 (2C), 114.2 (2C), 114.2 (2C), 91.2, 79.6, 76.4, 73.3, 71.8, 71.2, 62.3, 54.8 (2C), 33.0, 12.3.

Alcohol **96**

A mixture of pentane-1,5-diol (59.5 g, 571 mmol), imidazole (32.4 g, 476 mmol), TBDPSCl (32.0 g, 116 mmol) and DMAP (cat) in CH_2Cl_2 (100 ml) was stirred at r.t. for 12 h, poured into 500 ml of EtOAc, washed with brine (3 ×), dried and concentrated. Chromatography of the residue on silica gel (EtOAc/hexanes 1:6) provided the monoprotected alcohol (28.6 g, 72%) as a colorless oil.

Into a cold (–78 °C) solution of $(COCl)_2$ (9.20 ml, 105.5 mmol) in dry CH_2Cl_2 (350 ml) was introduced DMSO (14.92 ml, 210.2 mmol) via syringe. After 15 min of stirring at –78 °C, the above alcohol (12.0 g, 35 mmol) dissolved in CH_2Cl_2 (200 ml) was added via cannula. The resulting mixture was stirred at –78 °C for 3 h before Et_3N (44 ml, 315 mmol) was introduced. Once warmed to r.t., the reaction mixture was washed with brine (3 ×), dried and concentrated. Chromatography of the residue on silica gel (EtOAc/hexanes 1:8) gave **95** (10.4 g, 87%) as a pale yellow liquid.

To a stirred mixture of *t*-BuOK (6.24 g, 55.6 mmol) and *cis*-2-butene (11.0 ml) in dry THF at –78 °C was added 2.5 M *n*-BuLi in hexanes (22.3 ml, 55.8 mmol). After 10 min at –45 °C, the mixture was returned to –78 °C and (–)-*B*-methoxydiisopinocampheylborane (21.0 g, 66.4 mmol) dissolved in dry THF (100 ml) was introduced via cannula. Stirring was maintained at –78 °C for 30 min prior to the addition of $BF_3{\cdot}OEt_2$ (9.0 ml), followed by another 200 ml of dry THF to give a clear solution. After 30 min, a solution of **95** (12.63 g, 37.09 mmol) in dry THF (50 ml) was introduced via cannula. The mixture was stirred at –78 °C for 4 h, treated with 3 M NaOH (41 ml) and 30% H_2O_2 (17.0 ml), stirred at –78 °C overnight, diluted with 200 ml of Et_2O, warmed to r.t. over 1 h, washed with brine, dried and evaporated. Chromatography of the residue on silica gel (EtOAc/hexanes 1:8) gave **96** (11.5 g, 75%) as a colorless oil; IR (neat, cm^{-1}) 3393, 1640, 1590, 1462, 1427; ^1H NMR (300 MHz, $CDCl_3$): 7.70–7.66 (m, 4 H), 7.46–7.35 (m, 6 H), 5.85–5.73 (m, 1 H), 5.12–5.09 (m, 1 H), 5.07–5.05 (m, 1 H), 3.68 (t, *J* = 6.0, 2 H), 3.49–3.46 (m, 1 H), 2.27–2.25 (m, 1 H), 1.62–1.34 (m, 6 H), 1.06 (s, 9 H), 1.02 (d, *J* = 7.0, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$): 141.1, 135.6 (4C), 134.1 (2C), 129.5 (2C), 127.6 (4C), 115.2, 74.6, 63.8, 43.4, 33.7, 32.5, 26.9 (3C), 22.3, 19.2, 14.0; ES HRMS *m/z* calculated for $C_{25}H_{36}O_2SiNa$ (M^+ + Na) 419.2382, observed 419.2392; $[\alpha]_D$ +14.5 (*c* 2.13, $CHCl_3$).

t-Butyl Carbonate **97**

A solution of **96** (4.81 g, 12.14 mmol) in dry THF (150 ml) was treated with 1 M NaHMDS in THF (18.0 ml, 18.0 mmol) at –78 °C. After 15 min, 1 M Boc_2O in THF (18.0 ml, 18 mmol) was added and stirring was maintained with slow warming to r.t. overnight. After dilution

with Et_2O (100 ml), washing with 2 M NaOH (2 ×) and brine (3 ×), the combined organics were dried and concentrated in vacuo. Chromatography of the residue on silica gel (EtOAc/hexanes 1:8) afforded **97** (5.66 g, 94%) as a thick colorless oil; IR (neat, cm^{-1}) 1732, 1472, 1462; ^1H NMR (300 MHz, $CDCl_3$): 7.67–7.64 (m, 4 H), 7.42–7.34 (m, 6 H), 5.80–5.68 (m, 1 H), 5.69 (d, *J* = 9, 1 H), 5.01 (s, 1 H), 4.56–4.54 (m, 1 H), 3.63 (t, *J* = 6, 2 H), 2.42–2.39 (m, 1 H), 1.58–1.49 (m, 6 H), 1.47 (s, 9 H), 1.03 (s, 9 H), 1.00 (d, *J* = 7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 153.8, 139.7, 135.5 (4C), 134.0 (2C), 129.5 (2C), 127.6 (4C), 115.3, 81.5, 80.1, 63.7, 41.7, 32.4, 31.4, 27.8 (3C), 26.8 (3C), 21.9, 19.2, 15.3; ES HRMS *m/z* calculated for $C_{30}H_{44}O_4SiNa$ (M^+ + Na) 519.2907, observed 519.2890; $[\alpha]_D$ +11.4 (*c* 2.15, $CHCl_3$).

Epoxy Ester **98**

To **97** (7.60 g, 14.82 mmol) in dry PhMe (150 ml) cooled to –95 °C was added 1.0 M IBr in CH_2Cl_2 (32.0 ml, 32.0 mmol). The reaction mixture was stirred overnight at –78 °C, and treated sequentially with 20% $Na_2S_2O_3$ solution (75 ml), 5% $NaHCO_3$ solution (20 ml) and Et_2O (300 ml). The separated organic phase was washed with brine (3 ×), dried and concentrated to leave 10.55 g of unpurified iodocarbonate that was used directly. Chromatography of a small portion on silica allowed for spectral characterization of this intermediate: ^1H NMR (300 MHz, $CDCl_3$): 7.68–7.65 (m, 4 H), 7.46–7.36 (m, 6 H), 4.67–4.60 (m, 1 H), 4.41–4.37 (m, 1 H), 3.69 (t, *J* = 6.0, 2 H), 3.88 (dd, *J* = 6.0, 10.3, 1 H), 3.12 (t, *J* = 10.3, 1 H), 2.37–2.34 (m, 1 H), 1.78–1.45 (m, 6 H), 1.06 (s, 9 H), 0.89 (d, *J* = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 148.1, 135.5 (4C), 133.9, 133.8, 129.6 (2C), 127.6 (4C), 82.6, 81.7, 63.3, 31.9, 31.6, 31.1, 26.9 (3C), 21.3, 19.2, 3.1, 0.9.

To a mixture of the crude iodocarbonate (10.50 g, 14.82 mmol) in MeOH (50 ml), H_2O (20 ml) and Et_2O (55 ml) was added K_2CO_3 (3.0 g, 21.7 mmol). After 30 min of stirring, 20% $Na_2S_2O_3$ solution (40 ml) and Et_2O (350 ml) were introduced, and the organic layer was washed with brine (3 ×), dried and concentrated. Chromatography of the residue on silica gel (EtOAc/hexanes 1:4) gave **98** (5.82 g, 81%) as a thick, colorless oil; IR (neat, cm^{-1}) 3546, 1747, 1589, 1567; ^1H NMR (300 MHz, $CDCl_3$): 7.68–7.65 (m, 4 H), 7.46–7.35 (m, 6 H), 4.80–4.75 (m, 1 H), 3.78 (s, 3 H), 3.63 (t, *J* = 6, 2 H), 2.85–2.81 (m, 1 H), 2.77 (t, *J* = 4.8, 1 H), 2.55 (dd, *J* = 3.1, 4.8, 1 H), 1.70–1.51 (m, 5 H), 1.50–1.37 (m, 2 H), 1.06 (d, *J* = 7.0, 3 H), 1.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 155.7, 135.5 (4C), 133.9 (2C), 129.5 (2C), 127.6 (4C), 80.1, 63.5, 54.7, 53.8, 46.5, 39.9, 32.2, 31.1, 26.8 (3C), 21.9, 19.2, 11.6; ES HRMS *m/z* calculated for $C_{30}H_{44}O_5SiNa$ (M^+ + Na) 493.2386, observed 493.2396; $[\alpha]_D$ +6.5 (*c* 1.75, $CHCl_3$).

Dithiane **100**

A solution of 1,3-dithiane (7.22 g, 60.2 mmol) in dry THF (200 ml) cooled to –78 °C was treated dropwise with 1.3 M *n*-BuLi in hexanes (46.5 ml, 60.5 mmol), stirred at 0 °C for 45 min and returned to –78 °C, at which point ethylene oxide (6.6 ml, 132 mmol) was added. The resulting mixture was allowed to warm to r.t. overnight and diluted with saturated NH_4Cl solution and Et_2O (150 ml). The separated organic phase was washed with saturated NH_4Cl solution (2 ×) and brine (2 ×), dried and concentrated. The resulting dithiane alcohol (9.50 g) was used directly without purification.

The material from above (5.43 g, 33.1 mmol), imidazole (9.02 g, 132 mmol), TBSCl (8.26 g, 54.8 mmol) and DMAP (cat) in CH_2Cl_2 (50 ml) was stirred at r.t. for 12 h, poured

into Et_2O (300 ml), washed with H_2O and brine (3 ×), dried and concentrated. Vacuum distillation gave **99** (6.73 g, 73%) as a colorless oil.

To *t*-BuOK (1.06 g, 9.45 mmol) in dry hexanes (6.0 ml) at 0 °C was added 1.3 M *n*-BuLi in hexanes (7.30 ml, 9.49 mmol). The reaction mixture was stirred at 0 °C for 2 h, cooled to –78 °C and treated slowly with dry THF (15 ml). After 15 min, the dithiane from above (2.63 g, 9.46 mmol) dissolved in dry THF (5.0 ml) was added. Stirring was maintained at –78 °C for 1 h 40 min prior to the introduction of **98** (520 mg, 1.11 mmol) and stirring was continued at –25 °C for 14 h. Saturated NH_4Cl solution and Et_2O (150 ml) were added, and the separated organic phase was washed with saturated NH_4Cl solution (2 ×) and brine, dried and concentrated. Chromatography of the residue on silica gel (EtOAc/hexanes 1:4) afforded **100** (239 mg, 31%) as a colorless gum; IR (neat, cm^{-1}) 3390, 1589, 1471, 1462; ^1H NMR (300 MHz, $CDCl_3$): 7.68–7.65 (m, 4 H), 7.44–7.34 (m, 6 H), 4.28 (d, *J* = 6.9, 2 H), 4.02–3.94 (m, 1 H), 3.90–3.78 (m, 2 H), 3.70–3.64 (m, 3 H), 2.87–2.75 (m, 4 H), 2.45–2.19 (m, 3 H), 2.00–1.93 (m, 2 H), 1.64–1.53 (m, 4 H), 1.52–1.26 (m, 4 H), 1.04 (s, 9 H), 0.91–0.89 (m, 12 H), 0.10 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 135.6 (4C), 134.1 (2C), 129.5 (2C), 127.6 (4C), 76.2, 73.2, 63.9, 60.1, 51.3, 44.5 (2C), 42.7, 40.2, 34.6, 32.6, 26.9 (3C), 26.2, 26.1 (3C), 25.1, 22.4, 19.2, 18.4, 4.7, –5.36, –5.41; ES HRMS *m/z* calculated for $C_{37}H_{62}O_4S_2Si_2Na$ (M^+ + Na) 713.3526, observed 713.3543; $[\alpha]_D$ –4.0 (*c* 5.1, $CHCl_3$).

Pyranyl Alcohol **101**

To a cold (0 °C), magnetically stirred solution of diol **100** (1.00 g, 1.45 mmol) in CH_2Cl_2/MeOH 1:1 (30 ml) was added pyridine (1.3 ml, 14.5 mmol), CSA (5.1 mg, 0.02 mmol) and $HgClO_4 \cdot 3H_2O$ (1.4 g, 2.9 mmol). The reaction mixture was allowed to warm to r.t., and stirred for 5 h prior to filtration through a pad of Celite, which was rinsed with CH_2Cl_2, and the combined filtrates were evaporated to 25% of the original volume and treated with a saturated solution of $NaHCO_3$ (15 ml). The separated aqueous phase was extracted with CH_2Cl_2 (3 × 40 ml), and the combined extracts were dried and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (5–10% EtOAc/hexanes) to provide **101** (692 mg, 78%) as a faint yellow oil; IR (neat, cm^{-1}) 3520, 1471, 1428; ^1H NMR (300 MHz, $CDCl_3$): 7.71 (d, *J* = 6.7, 4 H), 7.48–7.41 (m, 6 H), 4.20 (d, *J* = 9.3, 1 H), 3.96 (m, 1 H), 3.73–3.68 (m, 5 H), 3.21 (s, 3 H), 1.96 (m, 1 H), 1.86 (m, 2 H), 1.85–1.77 (m, 1 H), 1.73 (m, 1 H), 1.70–1.56 (m, 3 H), 1.47 (m, 1 H), 1.41–1.29 (m, 2 H), 1.09 (s, 9 H), 0.93 (s, 9 H), 0.87 (d, *J* = 7.1, 3 H), 0.10 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 135.5 (4C), 134.0 (2C), 129.5 (2C), 127.5 (4C), 70.6, 66.5, 63.7, 58.5, 47.3, 39.1, 37.6, 33.7, 32.6, 32.3, 26.8 (3C), 25.9 (3C), 22.5, 19.2, 18.2, 14.2, 10.6, –5.4 (2C); ES HRMS *m/z* calculated for $C_{35}H_{58}O_5Si_2Na$ (M^+ + Na) 637.3715, observed 637.3736; $[\alpha]_D$ +30 (*c* 0.86, $CHCl_3$).

Diol **102**

A magnetically stirred solution of **101** (692 mg, 1.12 mmol) in a 10:1 mixture of CH_3CN and H_2O (20 ml) was treated with CsF (3.2 g, 21 mmol), heated at reflux for 4 days, cooled to r.t., diluted with CH_2Cl_2 (20 ml) and H_2O (20 ml) and mixed with saturated $NaHCO_3$ solution (10 ml). The separated aqueous phase was extracted with CH_2Cl_2 (3 × 20 ml), and the combined organic extracts were dried and evaporated. The residue was purified by chromatography on silica gel (EtOAc/hexanes 1:1) to give **102** as a pale yellow oil (587 mg, 93%); IR (neat, cm^{-1}) 3451, 1471, 1428; ^1H NMR (400 MHz, C_6D_6): 7.79 (m, 4 H), 7.25 (m, 6 H), 4.11 (br d, *J* = 9.4, 1 H), 3.94 (m, 1 H), 3.75 (m, 1 H), 3.66 (t, *J* = 6.2, 2 H), 3.47 (m, 2 H),

2.86 (s, 3 H), 1.86 (m, 1 H), 1.77–1.66 (m, 3 H), 1.66–1.58 (m, 2 H), 1.58–1.40 (m, 6 H), 1.19 (s, 9 H), 0.67 (d, *J* = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 135.9 (4C), 134.3 (2C), 129.9 (2C), 128.0 (4C), 101.9, 70.6, 67.1, 64.0, 58.3, 47.0, 38.2, 37.9, 33.2, 32.9, 32.5, 27.0 (3C), 22.8, 19.4, 10.7; ES HRMS *m/z* calculated for $C_{29}H_{44}O_5SiNa$ (M^+ + Na) 523.2850, observed 523.2857; $[\alpha]_D$ +37 (*c* 0.75, CH_3OH).

Iodo Alcohol **103**

A solution of **102** (587 mg, 1.05 mmol) in PhH (20 ml) was treated with imidazole (356 mg, 5.23 mmol), PPh_3 (411 mg, 1.57 mmol), and I_2 (292 mg, 1.05 mmol), stirred at r.t. for 2 h, diluted with saturated NaHCO3 solution (10 ml) and extracted with EtOAc (3 × 30 ml). The combined organic layers were dried and concentrated to leave an oil that was purified chromatographically on silica gel (1–10% EtOAc/hexanes). Product **103** (575 mg, 90%) was isolated as an unstable, pale yellow oil; ^{1}H NMR (400 MHz, C_6D_6): 7.80 (m, 4 H), 7.27 (m, 6 H), 3.90 (br d, *J* = 9.4, 1 H), 3.83 (m, 1 H), 3.68 (t, *J* = 6.1, 2 H), 3.64 (m, 1 H), 2.74 (m, 1 H), 2.70 (s, 3 H), 2.65 (m, 1 H), 2.06 (m, 1 H), 1.93 (m, 1 H), 1.64 (m, 1 H), 1.54 (m, 4 H), 1.46 (m, 1 H), 1.39 (m, 1 H), 1.26 (m, 1 H), 1.20 (s, 9 H), 1.09 (m, 1 H), 0.59 (d, *J* = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 136.0 (4C), 134.4 (2C), 130.0 (2C), 127.9 (4C), 101.5, 70.3, 67.2, 64.1, 47.0, 42.0, 38.1, 33.0, 32.6 (2C), 32.5, 27.1 (3C), 22.8, 19.5, 10.8.

Vinyltetrahydropyranyl Alcohol **104**

A magnetically stirred solution of **103** (575 mg, 0.92 mmol) in PhH (10 ml) containing DBU (702 µl, 4.7 mmol) was heated at reflux for 3 days, cooled to r.t. and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexanes/EtOAc 9:1) to give **104** (455 mg, 100%) as a pale yellow oil; IR (neat, cm^{-1}) 3504, 1472, 1428; ^{1}H NMR (400 MHz, C_6D_6): 7.81 (m, 4 H), 7.25 (m, 6 H), 5.53 (dd, *J* = 17.4, 10.5, 1 H), 5.41 (dd, *J* = 17.4, 2.1, 1 H), 5.03 (dd, *J* = 10.5, 2.1, 1 H), 4.26 (br d, *J* = 9.6, 1 H), 4.03 (m, 1 H), 3.76 (m, 1 H), 3.67 (t, *J* = 6.3, 2 H), 2.94 (s, 3 H), 1.82 (m, 1 H), 1.74 (m, 1 H), 1.67–1.52 (m, 4 H), 1.44–1.26 (m, 3 H), 1.18 (s, 9 H), 0.71 (d, *J* = 7.2, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) rearranged during overnight run; ES HRMS *m/z* calculated for $C_{29}H_{42}O_4SiNa$ (M^+ + Na) 523.2850, observed 523.2857.

Oxazolidinone **107**

To a cold (–78 °C) solution of **106** (7.25 g, 31.1 mmol) in CH_2Cl_2 (400 ml) was added 1 M *n*-Bu_2BOTf in CH_2Cl_2 (40 ml, 40 mmol). The reaction mixture was stirred at 0 °C for 30 min, recooled to –78 °C prior to the introduction of *i*-Pr_2NEt (8.7 ml, 49.8 mmol), and stirred for 10 min. The reaction mixture was stirred at 0 °C for 30 min, recooled to –78 °C, and aldehyde **95** (12.7 g, 37.3 mmol) dissolved in CH_2Cl_2 (200 ml) was added dropwise. After stirring at –78 °C for 1 h and at 0 °C for 3 h, the mixture was treated slowly with pH 7 buffer (200 ml) and stirred at r.t. for 30 min. The separated aqueous layer was extracted with CH_2Cl_2 (3 × 200 ml), and the combined organic solutions were dried and evaporated. Chromatography of the crude product on silica gel (5–20% EtOAc/hexanes) gave **107** (16.8 g, 94%) as a 70:30 mixture of diastereomers; IR (neat, cm^{-1}) 3462, 1782, 1694; ^{1}H NMR (400 MHz, $CDCl_3$): 7.66 (m, 4 H), 7.46–7.24 (m, 9 H), 7.21 (m, 2 H), 4.69 (m, 1 H), 4.23 (m, 2 H), 4.12 (m, 1 H), 3.94 (m, 1 H), 3.77 (m, 1 H), 3.69 (t, *J* = 6.2, 1.4 H), 3.60 (d, *J* = 6.2, 0.6 H), 3.33 (dd, *J* = 13.3, 3.2, 0.3 H), 3.26 (dd, *J* = 8.9, 3.3, 0.7 H), 2.79 (dd, *J* = 9.4, 3.9,

1 H), 1.66–1.48 (m, 4 H), 1.48–1.30 (m, 2 H), 1.27 (d, *J* = 7.1, 2.1 H), 1.21 (d, *J* = 7.4, 0.9 H), 1.04 (s, 7 H), 1.02 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 177.5, 175.1, 153.1, 152.9, 135.3 (4C), 135.4 (2C), 135.0 (2C), 134.0 (2C), 129.5 (4C), 129.4 (4C), 128.9 (4C), 128.8 (4C), 127.5 (2C), 127.4 (2C), 127.3 (2C), 127.2 (2C), 72.2, 71.4, 66.2, 66.1, 63.8, 63.7, 55.7, 55.1, 42.8, 42.1, 37.9, 33.8, 33.6, 32.4, 32.3, 26.8 (6C), 25.4, 22.2 (2C), 19.2, 10.4 (2C); ES HRMS *m/z* calculated for $C_{34}H_{44}NO_5SiNa$ (M^+ + Na) 596.2803, observed 596.2757.

Protected Oxazolidinone **108**

To a stirred solution of **107** (as a 70:30 mixture of diastereomers; 16.8 g, 30.5 mmol) in a 2:1 mixture of CH_2Cl_2 and DMF (200 ml) were introduced imidazole (10.2 g, 150 mmol), DMAP (100 mg) and TESCl (5.3 ml, 31.4 mmol). The reaction mixture was stirred at r.t. for 3 h before being quenched with saturated $NaHCO_3$ solution. The aqueous phase was extracted with CH_2Cl_2 (3 × 200 ml), and the combined organic solutions were washed with brine (200 ml), dried and evaporated. Chromatography of the residue on silica gel (hexanes/EtOAc 9:1) provided pure **108** (15.8 g, 94% based on the isomer ratio) as a faint yellow oil; IR (neat, cm^{-1}) 1788, 1704, 1456, 1428; ^{1}H NMR (400 MHz, $CDCl_3$): 7.68 (m, 4 H), 7.46–7.27 (m, 9 H), 7.24 (m, 2 H), 4.62 (m, 1 H), 4.18 (dd, *J* = 9.0, 3.2, 1 H), 4.12 (d, *J* = 7.3, 1 H), 4.05 (dd, *J* = 12.1, 6.8, 1 H), 3.88 (m, 1 H), 3.69 (br t, *J* = 6.3, 2 H), 3.33 (d, *J* = 13.3, 3.1, 1 H), 2.78 (dd, *J* = 13.3, 9.7, 1 H), 1.65–1.27 (m, 6 H), 1.23 (d, *J* = 6.9, 3 H), 1.06 (s, 9 H), 0.98 (t, *J* = 8.1, 9 H), 0.63 (q, *J* = 8.1, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 175.3, 153.0, 135.5 (4C), 135.4, 134.1, 129.5 (4C), 128.9 (3C), 127.6 (4C), 127.3, 73.2, 65.9, 63.8, 55.7, 43.1, 37.7, 35.6, 32.9, 26.8 (3C), 21.7, 19.2, 11.9, 6.9 (3C), –5.7 (3C); ES HRMS *m/z* calculated for $C_{40}H_{57}NO_5Si_2Na$ (M^+ + Na) 710.3667, observed 710.3701; $[\alpha]_D$ +29 (*c* 0.92, $CHCl_3$).

Aldehyde **109**

A cold (0 °C), magnetically stirred solution of **108** (15.8 g, 23.4 mmol) in THF (400 ml) was treated with H_2O (2.1 ml, 117 mmol) and $LiBH_4$ (2.54 g, 117 mmol), stirred for 2 days and slowly quenched with pH 7 buffer (200 ml). After 30 min, the aqueous layer was separated and extracted with EtOAc (3 × 200 ml). The combined organic solutions were dried and evaporated to leave a residue that was purified by chromatography on silica gel (hexanes/EtOAc 9:1). The alcohol (8.32 g, 70%) was isolated as a yellowish oil; IR (neat, cm^{-1}) 3448, 1461, 1428; ^{1}H NMR (400 MHz, $CDCl_3$): 7.68 (m, 4 H), 7.47–7.35 (m, 6 H), 3.78 (m, 1 H), 3.71 (m, 1 H), 3.67 (br t, *J* = 6.1, 2 H), 3.55 (m, 1 H), 2.72 (br s, 1 H), 1.96 (m, 1 H), 1.64–1.53 (m, 4 H), 1.53–1.44 (m, 2 H), 1.06 (s, 9 H), 0.97 (t, *J* = 7.8, 9 H), 0.82 (d, *J* = 7.1, 3 H), 0.63 (q, *J* = 7.8, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 135.5 (4C), 134.1 (2C), 129.5 (2C), 127.6 (4C), 76.2, 66.2, 63.8, 39.4, 32.9, 32.3, 26.8 (3C), 22.7, 19.2, 11.9, 6.9 (3C), 5.3 (3C); ES HRMS *m/z* calculated for $C_{30}H_{50}O_3Si_2Na$ (M^+ + Na) 537.3191, observed 537.3163; $[\alpha]_D$ +3.0 (*c* 1.5, $CHCl_3$).

To a stirred solution of the alcohol (8.32 g, 16.2 mmol) in a 3:1 mixture of CH_2Cl_2 and DMSO (200 ml) was added IBX (9.0 g, 32.1 mmol), and stirring was maintained for 2 h prior to the addition of saturated $NaHCO_3$ solution (200 ml) and filtration (CH_2Cl_2 rinse). The separated aqueous phase was extracted with CH_2Cl_2 (3 × 200 ml), and the combined organic solutions were washed with brine, dried and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexanes/EtOAc 98:2) to deliver **109** (5.8 g, 70%) as a yellowish oil; IR (neat, cm^{-1}) 1727, 1461, 1428; ^{1}H NMR (400 MHz, $CDCl_3$): 9.79 (s, 1 H), 7.68 (m, 4 H), 7.42 (m, 6 H), 4.12 (m, 1 H), 3.68 (br t, *J* = 6.2, 2 H), 2.44 (m, 1 H),

1.63–1.53 (m, 3 H), 1.54–1.41 (m, 3 H), 1.08 (m, 12 H), 0.96 (t, *J* = 8.0, 9 H), 0.58 (q, *J* = 7.8, 6 H); ES HRMS *m/z* calculated for $C_{30}H_{48}O_3Si_2Na$ (M^+ + Na) 535.3034, observed 535.3051; $[\alpha]_D$ +27 (*c* 0.95, $CHCl_3$).

Thiazolidinethione **110**

A cold (–50 °C) stirred suspension of $Sn(OTf)_2$ (7.1 g, 17.0 mmol) in CH_2Cl_2 (100 ml) was treated with *N*-ethylpiperidine (2.3 ml, 17.0 mmol) followed by a solution of *ent*-**10** (2.8 g, 13.6 mmol) in CH_2Cl_2 (100 ml). The resulting mixture was stirred at –40 °C for 4 h before cooling to –78 °C and treatment with a solution of **109** (5.8 g, 10.1 mmol) in CH_2Cl_2 (150 ml). After 1 h at this temperature, pH 7 buffer (100 ml) was introduced and the contents were allowed to warm to r.t. The separated aqueous layer was extracted with CH_2Cl_2 (3 × 200 ml). The combined organic phases were dried and evaporated, and the residue was purified by chromatography on silica gel (hexanes/EtOAc 9:1). Product **110** (7.79 g, 96%) was isolated as a bright yellow oil; IR (neat, cm^{-1}) 3513, 1704, 1692, 1679; ^1H NMR (400 MHz, $CDCl_3$): 7.67 (m, 4 H), 7.41 (m, 6 H), 5.29 (t, *J* = 6.7, 1 H), 4.37 (m, 1 H), 3.89 (m, 1 H), 3.68 (t, *J* = 6.3, 2 H), 3.53 (dd, *J* = 11.4, 8.0, 1 H), 3.43 (m, 2 H), 3.03 (dd, *J* = 11.4, 0.9, 1 H), 2.48 (m, 1 H), 1.66–1.43 (m, 5 H), 1.37–1.25 (m, 3 H), 1.08 (m, 12 H), 1.02–0.90 (m, 15 H), 0.62 (q, *J* = 7.7, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.9, 172.6, 135.5 (4C), 134.0 (2C), 129.5 (2C), 127.6 (4C), 76.8, 71.5, 70.9, 63.7, 60.3, 44.1, 40.4, 34.3, 32.7, 30.8, 30.6, 26.8 (3C), 21.9, 19.2, 19.0, 17.7, 6.9 (3C), 5.4 (3C); ES HRMS *m/z* calculated for $C_{38}H_{61}NO_4S_2Si_2Na$ (M^+ + Na) 738.3473, observed 738.3462; $[\alpha]_D$ –153 (*c* 0.97, $CHCl_3$).

Weinreb Amide **112**

A cold (0 °C), stirred suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (5.3 g, 54.4 mmol) in CH_2Cl_2 (150 ml) was slowly treated with a solution of 2 M Me_3Al in hexanes (27.1 ml, 54.4 mmol). After 15 min, the reaction mixture was warmed to 0 °C for 1 h, returned to –40 °C, and **110** (7.79 g, 10.9 mmol) was introduced in CH_2Cl_2 (200 ml). After 2 h at –40 °C, a 1 M solution of tartaric acid in H_2O (150 ml) was added, followed by 30 min of stirring at r.t. The separated aqueous phase was extracted with CH_2Cl_2 (3 × 150 ml), and the combined organic layers were dried and evaporated. Unpurified **111** was used directly in the next step.

The above material was dissolved in CH_2Cl_2 (150 ml), cooled to –78 °C, treated wtih 2,6-lutidine (6.3 ml, 54.4 mmol) and TBSOTf (2.53 ml, 21.8 mmol), and stirred for 3 h prior to the addition of pH 7 buffer (50 ml) and warming to r.t. The separated aqueous phase was extracted with CH_2Cl_2 (3 × 50 ml), and the combined organic layers were dried and evaporated to leave a residue that was purified by chromatography on silica gel (hexanes/EtOAc 95:5). Product **112** (7.94 g, 100%) was isolated as a colorless oil; IR (neat, cm^{-1}) 1668, 1463, 1428; ^1H NMR (400 MHz, $CDCl_3$): 7.68 (m, 4 H), 7.40 (m, 6 H), 4.31 (m, 1 H), 3.90 (m, 1 H), 3.69 (s, 3 H), 3.67 (t, *J* = 6.7, 2 H), 3.17 (s, 3 H), 2.74 (br dd, *J* = 15.4, 7.9, 1 H), 2.51 (dd, *J* = 15.3, 4.1, 1 H), 1.67 (m, 1 H), 1.62–1.45 (m, 4 H), 1.42–1.31 (m, 2 H), 1.06 (m, 9 H), 0.97 (t, *J* = 8.0, 9 H), 0.92 (d, *J* = 6.9, 3 H), 0.87 (s, 9 H), 0.62 (q, *J* = 8.0, 6 H), 0.05 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 173.5, 135.5 (4C), 134.1 (2C), 129.4 (2C), 127.5 (4C), 72.1, 70.8, 63.9, 61.2, 60.3, 42.5, 37.3, 35.1, 33.1, 26.8 (3C), 25.9 (3C), 21.6, 19.2, 18.0, 10.1, 7.0 (3C), 5.5 (3C), –4.4, –4.7; ES HRMS *m/z* calculated for $C_{40}H_{71}NO_5Si_3Na$ (M^+ + Na) 752.4532, observed 752.4489.

Ketone **114**

To a cold (–78 °C), magnetically stirred solution of **113** (2.4 g, 5.44 mmol) in dry THF (40 ml) was added 2.5 M *n*-BuLi in hexanes (2.2 ml, 5.44 mmol). After 30 min of stirring, a solution of **113** (1.0 g, 1.37 mmol) in THF (30 ml) was added dropwise at –78 °C. After 30 min of agitation, pH 7 buffer (10 ml) was added, the mixture was warmed to r.t., the aqueous phase was extracted with EtOAc (3 × 30 ml) and the combined organic solutions were dried and concentrated. The residue was purified by chromatography on silica gel (1–2% EtOAc/hexanes) to provide **114** (790 mg, 96%) as a pale yellow oil; IR (neat, cm^{-1}) 1721, 1613, 1514; ^{1}H NMR (400 MHz, $CDCl_3$): 7.68 (m, 4 H), 7.41 (m, 6 H), 7.29 (d, *J* = 8.6, 2 H), 6.90 (d, *J* = 8.7, 2 H), 4.52 (d, *J* = 2.6, 2 H), 4.23 (m, 1 H), 4.02 (s, 2 H), 3.90 (m, 1 H), 3.81 (s, 3 H), 3.66 (t, *J* = 6.4, 2 H), 2.69 (dd, *J* = 16.0, 7.4, 1 H), 2.55 (dd, *J* = 16.0, 4.1, 1 H), 1.68–1.41 (m, 5 H), 1.39–1.30 (m, 2 H), 1.06 (s, 9 H), 0.95 (t, *J* = 8.0, 9 H), 0.84 (m, 12 H), 0.58 (q, *J* = 7.8, 6 H), 0.03 (s, 3 H), –0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 207.5, 159.4, 135.5 (4C), 134.0 (2C), 129.6 (2C), 129.5 (2C), 129.2, 127.5 (4C), 113.8 (2C), 75.5, 72.8, 71.6, 70.2, 63.8, 55.2, 43.8, 42.0, 35.2, 33.0, 26.8 (3C), 25.9 (3C), 21.7, 19.2, 18.0, 9.8, 7.0 (3C), 5.5 (3C), –4.5, –4.6; ES HRMS *m/z* calculated for $C_{47}H_{76}O_6Si_3Na$ (M^+ + Na) 843.4842, observed 843.4842; $[\alpha]_D$ –23 (*c* 0.81, $CHCl_3$).

Pyranyl Carbinol **116**

To a stirred solution of **114** (100 mg, 0.12 mmol) in a 10:1 mixture of CH_2Cl_2 and H_2O was added DDQ (83 mg, 0.37 mmol). After 1 h of stirring, saturated $NaHCO_3$ solution (10 ml) was introduced. After 10 min, the organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 ml). The combined organic solutions were dried and evaporated under reduced pressure to leave a residue that was purified by chromatography on silica gel (hexanes/EtOAc 99:1 to 97:3) to give **115** admixed with anisaldehyde.

Without further purification, this material was dissolved in THF/MeOH 10:1 (5 ml), treated with PPTS (39 mg, 0.17 mmol), stirred for 2 h and diluted with saturated $NaHCO_3$ solution (3 ml) and CH_2Cl_2 (3 × 5 ml). The combined extracts were dried and evaporated. The residue was purified by chromatography on silica gel (1–5% EtOAc/hexanes) to give **116** as a faint yellow oil (70 mg, 82% over 2 steps); IR (neat, cm^{-1}) 3470, 1472, 1428; ^{1}H NMR (400 MHz, C_6D_6): 7.80 (m, 4 H), 7.26 (m, 6 H), 4.29 (m, 1 H), 3.73 (m, 1 H), 3.67 (t, *J* = 6.1, 2 H), 3.43 (m, 2 H), 3.10 (s, 3 H), 1.92 (dd, *J* = 14.6, 3.8, 1 H), 1.73 (dd, *J* = 14.6, 2.8, 1 H), 1.65–1.47 (m, 5 H), 1.37 (m, 2 H), 1.24 (m, 1 H), 1.18 (s, 9 H), 1.04 (s, 9 H), 0.77 (d, *J* = 7.2, 3 H), 0.11 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 136.8 (4C), 135.2 (2C), 130.8 (2C), 128.9 (4C), 99.6, 71.8, 68.0, 65.9, 64.9, 48.5, 39.8, 33.8 (2C), 33.4, 27.9 (3C), 26.8 (3C), 23.7, 20.3, 19.1, 11.3, –3.6, –4.0; ES HRMS *m/z* calculated for $C_{34}H_{56}O_5Si_2Na$ (M^+ + Na) 623.3558, observed 623.3522; $[\alpha]_D$ +41 (*c* 0.71, CH_3OH).

Pyranyl Carboxaldehyde **80**

To a stirred solution of **116** (33 mg, 0.056 mmol) in CH_2Cl_2 (5 ml) was added a solution of the pyridine·SO_3 complex (88 mg, 0.55 mmol) and Et_3N (153 µl, 1.1 mmol) in DMSO (1 ml). The reaction mixture was stirred for 2 h, quenched with pH 7 buffer (5 ml) and extracted with CH_2Cl_2 (2 × 5 ml). The combined organic layers were washed with brine, dried and evaporated. The residue was purified by chromatography on silica gel pretreated with Et_3N (1–5% EtOAc/hexanes) to give **80** (24 mg, 74%) as a pale yellow oil. This compound was un-

stable and used directly; IR (neat, cm^{-1}) 1769, 1672, 1428; ^1H NMR (500 MHz, C_6D_6): 9.30 (s, 1 H), 7.78 (m, 4 H), 7.24 (m, 6 H), 4.32 (m, 1 H), 3.66 (t, *J* = 6.2, 2 H), 3.63 (m, 1 H), 3.18 (s, 3 H), 1.69–1.47 (m, 5 H), 1.46 (m, 2 H), 1.38 (m, 2 H), 1.17 (s, 9 H), 1.01 (s, 9 H), 0.73 (d, *J* = 7.2, 3 H), 0.07 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 197.4, 135.9 (4C), 134.4 (2C), 129.9 (2C), 128.1 (4C), 99.1, 70.2, 67.5, 64.0, 50.1, 38.6, 32.9, 32.3, 30.1, 27.1 (3C), 25.9 (3C), 22.8, 19.5, 18.2, 10.3, –4.6, –4.9; $[\alpha]_D$ +50 (*c* 0.44, CH_2Cl_2).

Pyranyl Sulfone **117**

A solution of **90** (23 mg, 0.042 mmol) in CH_2Cl_2 was treated with SEMCl (0.011 ml, 0.064 mmol), *i*-Pr_2NEt (0.015 ml, 0.085 mmol) and TBAI (2 mg, 0.004 mmol) at r.t., stirred for 50 min, diluted with Et_2O (30 ml) and washed with H_2O (3 ×). The organic layer was dried and evaporated to leave a residue that was purified by chromatography on silica gel (20% EtOAc/hexanes) furnished **117** (25 mg, 91%) as a colorless oil; IR (neat, cm^{-1}) 1613, 1586, 1514; ^1H NMR (300 MHz, $CDCl_3$): 7.90 (m, 2 H), 7.62 (m, 1 H), 7.57 (m, 2 H), 7.25 (m, 4 H), 6.89 (m, 4 H), 4.92–4.78 (m, 3 H), 4.70 (d, *J* = 10.5, 1 H), 4.57 (d, *J* = 10.5, 1 H), 4.46 (m, 2 H), 4.36 (m, 1 H), 4.25 (dd, *J* = 11.3, 8.3, 1 H), 3.82 (s, 6 H), 3.65 (dd, *J* = 11.3, 3.9, 1 H), 3.54–3.42 (m, 3 H), 3.35 (dd, *J* = 11.2, 2.0, 1 H), 2.40 (m, 1 H), 1.54 (d, *J* = 8.2, 3 H), 0.80 (m, 2 H), –0.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.3 (2C), 138.6, 133.7, 130.6, 130.4, 129.5 (2C), 129.3 (2C), 128.9 (2C), 128.8 (2C), 113.9 (4C), 95.0, 92.9, 80.7, 78.5, 75.3, 75.2, 74.4, 66.0, 65.2, 55.2 (2C), 39.5, 18.0, 12.4, –1.4 (3C); ES HRMS *m/z* calculated for $C_{35}H_{48}O_9SSiNa$ (M^+ + Na) 695.2681, observed 695.2639; $[\alpha]_D$ +110 (*c* 1.5, $CHCl_3$).

Pyranyl Sulfone **118**

To a solution of **90** (100 mg, 0.18 mmol) in CH_2Cl_2 (4 ml) was added TBSCl (54 mg, 0.36 mmol) and imidazole (33 mg, 0.48 mmol) at 20 °C. After 1 h of stirring, the mixture was diluted with Et_2O (50 ml), washed with H_2O (2 ×), dried and evaporated. Purification by chromatography on silica gel (20% EtOAc/hexanes) gave rise to **118** (120 mg, 98%) as a colorless oil; IR (neat, cm^{-1}) 1613, 1514; ^1H NMR (300 MHz, $CDCl_3$): 7.88 (m, 2 H), 7.65 (m, 1 H), 7.59 (m, 2 H), 7.25 (m, 4 H), 6.90 (m, 4 H), 4.89 (d, *J* = 10.4, 1 H), 4.81 (d, *J* = 7.8, 1 H), 4.80 (d, *J* = 9.0, 1 H), 4.69 (d, *J* = 10.5, 1 H), 4.63 (d, *J* = 10.6, 1 H), 4.22 (dd, *J* = 11.2, 2.1, 1 H), 4.14 (m, 1 H), 3.83 (s, 6 H), 3.77 (dd, *J* = 11.7, 2.7, 1 H), 3.59 (dd, *J* = 9.5, 9.5, 1 H), 3.30 (dd, *J* = 11.7, 1.8, 1 H), 2.35 (m, 1 H), 1.54 (d, *J* = 7.5, 3 H), 0.80 (s, 9 H), –0.17 (s, 6 H); ES HRMS *m/z* calculated for $C_{35}H_{48}O_8SSiNa$ (M^+ + Na) 679.2731, observed 679.2732; $[\alpha]_D$ +87 (*c* 1.5, $CHCl_3$).

Lactone **119**

A. With the PMB-acetimidate. To *p*-methoxybenzyl trichloroacetimidate (11.3 g, 40 mmol) dissolved in Et_2O (200 ml) was added **84** (4.32 g, 20 mmol) and a 1.0 M solution of TfOH in Et_2O (0.1 ml, 0.3 mole %) at r.t. The mixture was stirred for 20 min, diluted with Et_2O (500 ml), washed with saturated $NaHCO_3$ solution (500 ml) and dried. Chromatography of the residue on silica gel (EtOAc/pet ether 1:7) gave **85** (5.84 g, 55%) as a white solid, m.p. 78–79 °C; IR (neat, cm^{-1}) 1747, 1613, 1514, 1248; ^1H NMR (300 MHz, $CDCl_3$): 7.28–7.24 (m, 2 H), 6.91–6.86 (m, 2 H), 4.80 (d, *J* = 11.2, 1 H), 4.59 (d, *J* = 11.2, 1 H), 4.04–3.77 (m, 4 H), 3.81 (s, 3 H), 3.48 (t, *J* = 8.2, 1 H), 2.63 (pent, *J* = 7.5, 1 H), 1.56 (s, 3 H), 1.47 (s, 3 H), 1.37 (d, *J* = 7.3, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.9, 159.4, 130.1, 129.7 (2C), 113.8 (2C),

99.8, 79.1, 73.7, 73.6, 68.7, 61.6, 55.3, 42.9, 29.0, 19.0, 15.7; EI HRMS *m/z* calculated for $C_{18}H_{24}O_6$ (M^+) 336.1573, observed 336.1553; $[\alpha]_D$ +68.0 (*c* 2.64, $CHCl_3$). Calculated for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.14; H, 7.02.

B. With the PMB-lepidine[99a]. A mixture of alcohol **84** (2.00 g, 9.25 mmol) and PMBO-lepidine (5.14 g, 18.5 mmol) was taken up in a minimal amount of PhH, concentrated in vacuo and the flask flushed with Ar. The mixture was taken up in CH_2Cl_2 (18.5 ml) and treated with CSA (215 mg, 0.925 mmol) at 27 °C. The reaction mixture was stirred for 50 h, concentrated under reduced pressure and purified by column chromatography (hexanes/EtOAc 100:0 to 5:1) to give **119** as a white crystalline solid (2.50 g, 80%).

Lactone **120**

A solution of **119**81 (1.0 g, 3.0 mmol) in a 2:1 mixture of THF and 1 M HCl (30 ml) was stirred for 1 h, taken to pH 9 with saturated $NaHCO_3$ solution and extracted with EtOAc (3 × 50 ml). The combined organic extracts were dried and evaporated to leave a residue that was purified by chromatography on silica gel (hexanes/EtOAc 7:3 to 0:100) afforded the dihydroxy lactone as a pale yellow oil (881 mg, 100%); IR (neat, cm^{-1}) 3429, 1777, 1613, 1514; ^1H NMR (400 MHz, $CDCl_3$): 7.27 (d, *J* = 8.6, 2 H), 6.90 (d, *J* = 8.6, 2 H), 4.65 (d, *J* = 11.3, 1 H), 4.52 (dd, *J* = 8.8, 5.4, 1 H), 4.44 (d, *J* = 11.3, 1 H), 4.13–4.04 (m, 2 H), 3.88 (dd, *J* = 11.6, 3.1, 1 H), 3.83 (s, 3 H), 3.74 (dd, *J* = 11.6, 5.0, 1 H), 2.83 (m, 1 H), 1.97 (br s, 2 H), 1.32 (d, *J* = 7.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 177.7, 159.6, 129.5 (2C), 128.6, 114.1 (2C), 80.7, 78.4, 71.7, 69.0, 63.4, 55.2, 41.1; ES HRMS *m/z* calculated for $C_{15}H_{20}O_6Na$ (M^+ + Na) 319.1152, observed 319.1144.

The above compound (881 mg, 2.98 mmol) was dissolved in cold (0 °C) CH_2Cl_2 (50 ml), treated sequentially with Et_3N (2.07 ml, 14.9 mmol), DMAP (18 mg, 0.15 mmol) and TESCl (527 µl, 3.13 mmol), stirred at this temperature for 1 h and quenched with saturated $NaHCO_3$ solution (10 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 20 ml), and the combined organic extracts were dried and evaporated. Chromatography on silica gel (hexanes/EtOAc 95:5 to 70:30) furnished **120** (1.15 g, 94%) as a faint yellow oil; IR (neat, cm^{-1}) 3519, 1781, 1613; ^1H NMR (400 MHz, $CDCl_3$): 7.27 (d, *J* = 8.6, 2 H), 6.89 (d, *J* = 8.6, 2 H), 4.60 (d, *J* = 11.4, 1 H), 4.53 (d, *J* = 11.4, 1 H), 4.46 (dd, *J* = 8.6, 4.6, 1 H), 4.10 (m, 1 H), 4.04 (dd, *J* = 4.5, 1.9, 1 H), 3.87 (dd, *J* = 10.4, 3.5, 1 H), 3.82 (s, 3 H), 3.78 (dd, *J* = 10.4, 4.8, 1 H), 2.77 (m, 1 H), 1.57 (br s, 1 H), 1.27 (d, *J* = 7.8, 3 H), 0.97 (t, *J* = 8.0, 9 H), 0.63 (q, *J* = 7.7, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 177.9, 159.5, 129.4 (2C), 129.1, 113.9 (2C), 80.6, 79.1, 71.7, 68.3, 63.5, 55.2, 41.7, 13.6, 6.6 (3C), 4.2 (3C); ES HRMS *m/z* calculated for $C_{21}H_{34}O_6SiNa$ (M^+ + Na) 433.2017, observed 433.2026; $[\alpha]_D$ +26.0 (*c* 1.23, $CHCl_3$).

Lactol **121**

An Et_2O solution (50 ml) containing **120** (1.15 g, 2.80 mmol) and *p*-methoxybenzyl trichloroacetimidate (1.13 g, 4.2 mmol) was treated with a 1 M solution of TfOH in Et_2O (28 µl, 0.028 mmol), stirred for 1 h and quenched with saturated $NaHCO_3$ solution (10 ml). The separated aqueous layer was extracted with EtOAc (3 × 20 ml), and the combined organic layers were dried and freed of solvent. Chromatographic purification (hexanes/EtOAc 95:5 to 90:10) gave the pure PMB ether (1.49 g, 100%) as a white foam; IR (neat, cm^{-1}) 1778, 1690, 1614; ^1H NMR (400 MHz, $CDCl_3$): 7.20 (d, *J* = 6.3, 4 H), 6.85 (d, *J* = 8.6, 4 H), 4.93 (d, *J* = 6.5, 1 H), 4.93 (d, *J* = 6.5, 1 H), 4.72 (d, *J* = 10.8, 1 H), 4.59 (m, 1 H), 4.52–4.39 (m, 3 H), 3.97 (m, 3 H), 3.80 (s, 6 H), 2.79 (m, 1 H), 1.22 (d, *J* = 7.8, 3 H), 0.96 (t, *J* = 8.0,

9 H), 0.62 (q, *J* = 7.7, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 178.3, 159.2 (2C), 129.4 (2C), 129.3 (2C), 113.9 (2C), 113.7 (2C), 99.7 (2C), 80.6, 78.7, 76.3, 72.4, 71.3, 62.4, 55.2 (2C), 41.6, 13.4, 6.7 (3C), 4.3 (3C); ES HRMS *m/z* calculated for $C_{29}H_{42}O_7SiNa$ (M^+ + Na) 553.2592, observed 553.2562.

The preceding material (1.49 g, 2.80 mmol) in PhMe (50 ml) was cooled to –78 °C, treated with 1 M Dibal-H in PhMe (8.4 ml, 8.4 mmol) and stirred for 2 h. A saturated Rochelle's salt solution (30 ml) was introduced, and the mixture was warmed to r.t. for 1 h. The separated aqueous layer was extracted with EtOAc (3 × 30 ml). The combined organic phases were dried and concentrated to leave a residue that was purified by chromatography on silica gel (hexanes/EtOAc 9:1) to give **121** (1.50 g, 100%) as a white solid, m.p. 104–105 °C; IR (neat, cm^{-1}) 1694, 1414, 1268; ^{1}H NMR (300 MHz, $CDCl_3$): 7.25 (m, 4 H), 6.86 (m, 4 H), 4.98 (s, 1 H), 4.80 (d, *J* = 10.8, 1 H), 4.61 (d, *J* = 13.0, 1 H), 4.56–4.38 (m, 2 H), 4.14 (dd, *J* = 9.2, 3.6, 1 H), 4.07 (d, *J* = 10.9, 1 H), 3.96–3.84 (m, 4 H), 3.80 (s, 6 H), 2.46 (m, 1 H), 1.03–0.89 (series of m, 12 H), 0.64 (q, *J* = 7.8, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.3 (2C), 129.6 (2C), 129.2 (2C), 114.0 (2C), 113.7 (2C), 104.5 (2C), 98.5, 83.6, 79.7, 78.1, 72.3, 71.5, 63.6, 55.2, 45.1, 14.1, 6.8 (3C), 6.3 (3C).

Sulfide **122**

A magnetically stirred solution of **121** (200 mg, 0.38 mmol) in CH_2Cl_2 (10 ml) was treated with Cl_3CCN (376 μl, 3.76 mmol) followed by DBU (56 μl, 0.38 mmol) and stirred at r.t. for 3 h before Et_3N was introduced and the solvent evaporated under reduced pressure to approximately 25% of the original volume. The reaction mixture was diluted with hexanes/EtOAc 70:30 containing 1% Et_3N and placed directly on Et_3N-pretreated silica gel. Elution with the indicated solvent system afforded an oil that was evacuated to 1 Torr for 1 h, flushed with N_2 and dissolved in dry CH_2Cl_2 (10 ml). To this solution was added a dry stirring bar, 4Å MS (1 g) and 2-pyridinethiol (83 mg, 0.75 mmol). This mixture was cooled to –30 °C, treated with TMSOTf (3.4 μl, 3.76 mmol), stirred at –20 °C for 1 h and treated with Et_3N (523 μl, 3.76 mmol). After warming to r.t., the mixture was poured into a separatory funnel containing saturated $NaHCO_3$ solution (10 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml), dried and freed of solvent to leave a residue that was purified by chromatography on silica gel (hexanes/EtOAc 95:5 to 90:10). Product **122** (198 mg, 84%) was isolated as an inseparable 2:3 mixture of α- and β-anomers as a yellow foam; IR (neat, cm^{-1}) 1614, 1514, 1249; ^{1}H NMR (500 MHz, $CDCl_3$): 8.48 (m, 1 H), 7.64 (t, *J* = 7.9, 0.3 H), 7.59 (m, 0.7 H), 7.48 (br d, *J* = 7.7, 0.7 H), 7.42 (d, *J* = 8.0, 0.3 H), 7.30 (d, *J* = 8.5, 0.7 H), 7.23–7.19 (m, 3.3 H), 7.09 (m, 1 H), 6.85 (m, 4 H), 6.22 (d, *J* = 5.9, 0.7 H), 5.78 (d, *J* = 2.8, 0.3 H), 4.79 (d, *J* = 10.9, 0.7 H), 4.74 (dt, *J* = 10.8, 3.6, 0.3 H), 4.61 (d, *J* = 11.2, 0.3 H), 4.55 (d, *J* = 11.2, 0.7 H), 4.51–4.42 (m, 2 H), 4.24 (dd, *J* = 8.9, 3.9, 0.7 H), 4.21 (dd, *J* = 9.2, 4.4, 0.3 H), 3.98 (m, 1 H), 3.97 (m, 1 H), 3.91 (m, 0.7 H), 3.83 (m, 0.3 H), 3.80 (s, 6 H), 3.76 (m, 1 H), 2.82 (m, 0.7 H), 2.67 (m, 0.3 H), 1.16 (d, *J* = 7.9, 0.9 H), 1.15 (d, *J* = 7.9, 2.1 H), 0.97 (m, 2.7 H), 0.93 (m, 6.3 H), 0.63 (m, 1.2 H), 0.58 (m, 4.2 H); ^{13}C NMR (75 MHz, $CDCl_3$) (major isomer): 159.2, 159.0 (2C), 137.4, 131.3, 130.1, 129.3 (2C), 129.3 (2C), 120.4, 117.8, 113.8 (2C), 113.4 (2C), 113.6, 84.4, 79.1, 71.5, 71.4, 71.3, 55.3 (2C), 43.2, 29.7, 14.1, 6.8 (3C), 4.4 (3C); ES HRMS *m/z* calculated for $C_{34}H_{47}NO_6SSiNa$ (M^+ + Na) 648.2786, observed 648.2744.

Sulfone **123**

A cold (0 °C) solution of **122** (198 mg, 0.32 mol) in CH_2Cl_2 (10 ml) was treated with $NaHCO_3$ (186 mg, 2.2 mmol) and MCPBA (273 mg, 1.26 mmol), stirred at this temperature for 6 h, quenched with half-saturated $Na_2S_2O_3$ solution (10 ml) and agitated an additional 30 min before being diluted with CH_2Cl_2 (10 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml), and the combined organic layers were dried and freed of solvent. Chromatography of the residue on silica gel (hexanes/EtOAc 95:5 to 80:20) gave **123** (187 mg, 90%) as a pale yellow oil consisting of an inseparable 2:3 mixture of α- and β-anomers; IR (neat, cm^{-1}) 1613, 1514, 1249; ^1H NMR (500 MHz, $CDCl_3$): 8.77 (d, *J* = 4.0, 0.7 H), 8.73 (d, *J* = 1.2, 0.3 H), 8.11 (d, *J* = 7.8, 0.3 H), 8.06 (d, *J* = 7.8, 0.7 H), 7.91 (m, 1 H), 7.53 (m, 0.7 H), 7.49 (m, 0.3 H), 7.25 (d, *J* = 8.6, 1 H), 7.19 (t, *J* = 8.4, 2 H), 7.15 (d, *J* = 8.7, 1 H), 6.85–6.80 (m, 4 H), 5.52 (d, *J* = 7.0, 0.7 H), 5.00 (d, *J* = 4.6, 0.3 H), 4.70 (d, *J* = 11.0, 0.7 H), 4.64 (d, *J* = 10.9, 0.3 H), 4.55 (t, *J* = 11.7, 0.7 H), 4.49 (d, *J* = 11.4, 1 H), 4.44–4.39 (m, 2.3 H), 4.09 (m, 0.3 H), 4.07 (t, *J* = 3.9, 0.7 H), 4.02 (m, 0.7 H), 3.88 (m, 0.3 H), 3.80 (s, 0.9 H), 3.80 (s, 2.1 H), 3.79 (s, 1 H), 3.79 (s, 0.3 H), 3.72 (m, 1 H), 3.57 (dd, *J* = 11.1, 6.0, 0.7 H), 3.54 (dd, *J* = 11.1, 4.9, 0.3 H), 3.23 (m, 0.3 H), 3.05 (m, 0.7 H), 1.48 (d, *J* = 5.8, 2.1 H), 1.27 (d, *J* = 7.5, 0.9 H), 0.91–0.85 (m, 9 H), 0.53 (q, *J* = 7.8, 4.2 H), 0.48 (q, *J* = 7.8, 7.8 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.4, 159.2, 159.1, 157.1, 156.0, 150.3, 150.2, 137.6, 131.0, 129.8 (2C), 129.4 (2C), 129.3, 129.2, 127.2, 127.1, 124.4, 123.7, 113.9 (2C), 113.8, 113.7 (2C), 113.6, 96.0, 91.3, 84.8, 83.1, 81.6, 80.6, 76.5, 72.4, 72.2, 71.9, 70.9, 68.8, 62.8, 55.7 (2C), 41.6, 38.6, 29.7, 21.0, 18.1, 14.2, 14.1, 13.0, 6.7 (3C), 4.4 (3C).

Merged Carbinol **124**

A stirred, deoxygenated (N_2, 10 min) solution of **123** (30 mg, 46 mmol) and cyclohexane carboxaldehyde (6.9 µl, 59 mmol) in dry THF (1 ml) was treated rapidly with 0.1 M SmI_2 in THF until a blue color persisted (approx. 1.4 ml, 1.3 equiv.). The resulting mixture was quenched with saturated NH_4Cl solution (2 ml) and EtOAc (2 ml). The separated aqueous phase was extracted with EtOAc (3 × 2 ml), and the combined organic solutions were washed with brine, dried and evaporated. Chromatography of the residue on silica gel (1–10% EtOAc/hexanes) afforded **124** (21 mg, 75%) as an inseparable 3:1:1 mixture of diastereomers; ^1H NMR (300 MHz, $CDCl_3$): 7.22 (m, 4 H), 6.83 (m, 4 H), 4.73 (d, *J* = 8.9, 0.6 H), 4.61–4.49 (m, 1.2 H), 4.49–4.42 (m, 1.6 H), 4.37 (m, 0.6 H), 4.32 (m, 0.2 H), 4.15 (t, *J* = 5.3, 0.6 H), 4.10 (dd, *J* = 6.3, 2.4, 0.6 H), 4.05 (m, 0.2 H), 4.01 (t, *J* = 7.2, 1 H), 3.90 (d, *J* = 3.2, 0.6 H), 3.85 (m, 1 H), 3.80 (m, 6 H), 3.74 (m, 1.6 H), 3.65 (m, 0.4 H), 3.51 (m, 0.6 H), 3.38 (m, 0.6 H), 3.16 (m, 0.2 H), 2.84 (br s, 0.2 H), 2.76 (br s, 0.2 H), 2.54 (m, 0.2 H), 2.46 (m, 0.2 H), 2.33 (m, 0.6 H), 2.25 (m, 0.2 H), 2.02 (m, 0.2 H), 1.77 (m, 0.2 H), 1.66 (m, 2 H), 1.58 (m, 0.8 H), 1.37–1.11 (m, 6 H), 1.06 (t, *J* = 7.8, 3 H), 0.97 (m, 5.4 H), 0.90 (m, 3.6), 0.73 (q, *J* = 7.6, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.0, 158.9, 131.2, 130.6, 130.0, 129.4, 129.3, 128.0 (2C), 113.7 (2C), 113.6 (2C), 85.8, 85.7, 79.9, 78.4, 6.4, 72.8, 72.2, 71.2, 71.1, 55.2 (2C), 41.6, 41.4, 40.7, 39.9, 30.0, 29.7, 26.7, 26.6, 26.4, 18.4, 17.8, 12.8, 7.0, 6.8 (3C), 5.2, 4.4 (3C).

2-Methylenepyran **125**

A solution of **119** (279 mg, 1:1 mixture with trichloroacetamide) in THF/pyridine 3:1 (7.1 ml/2.4 ml) was cooled to –78 °C and treated dropwise with a 0.67 M solution of the

Tebbe reagent in PhMe (6.7 ml, 4.48 mmol). The red solution was stirred at –78 °C for 30 min, warmed to –10 °C and stirred for 30 min. The cold bath was removed and the red-brown solution was stirred at 26 °C for 1 h, cooled to –10 °C and quenched by the slow addition of 20% aqueous NaOH (3 ml). After gas evolution ceased, the mixture was diluted with Et_2O (30 ml) and the aqueous layer extracted with Et_2O (1 × 20 ml). The combined organic layers were filtered through Celite, dried and concentrated in vacuo to give an orange oil. Rapid chromatography on silica gel pretreated with 1% Et_3N/hexanes (hexanes/EtOAc 3:1) gave **125** as a slightly yellow oil (150 mg, 80%); IR (neat, cm^{-1}) 1651, 1514, 1248; ^1H NMR (300 MHz, $CDCl_3$): 7.31–7.26 (m, 2 H), 6.90–6.86 (m, 2 H), 4.81 (d, *J* = 10.9, 1 H), 4.57 (dd, *J* = 1.9, 1.2, 1 H), 4.56 (d, *J* = 10.9, 1 H), 4.34 (dd, *J* = 1.9, 1.2, 1 H), 3.96 (dd, *J* = 10.7, 5.4, 1 H), 3.86 (dd, *J* = 9.7, 8.7, 1 H), 3.81 (s, 3 H), 3.80 (t, *J* = 10.6, 1 H), 3.31 (dt, *J* = 10.0, 5.3, 1 H), 3.16 (dd, *J* = 10.1, 8.6, 1 H), 2.38–2.31 (m, 1 H), 1.55 (s, 3 H), 1.44 (s, 3 H), 1.17 (d, *J* = 6.6, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 161.7, 159.2, 130.8, 129.7 (2C), 113.7 (2C), 94.2, 80.9, 76.6, 76.1, 74.0, 71.8, 62.5, 55.3, 39.6, 29.2, 19.3, 13.9; EI HRMS *m/z* calculated for $C_{19}H_{26}O_5$ (M^+) 334.1780, observed 334.1787; $[\alpha]_D$ +110 (*c* 1.82, $CHCl_3$). Calculated for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 68.15; H, 7.84.

Pyranyl Alcohol **126**

To a solution of **125** (494 mg, 1.48 mmol) in THF (20 ml) was added 0.5 M 9-BBN in THF (8.86 ml, 4.46 mmol) at 0 °C. Stirring was maintained at r.t. for 12 h. Additional 0.5 M 9-BBN in THF (8.86 ml, 4.46 mmol) was added and stirring was continued at r.t. for 6 h. Water (5 ml), 20% NaOH solution (5 ml) and 30% H_2O_2 (5 ml) were added at 0 °C, diluted with EtOAc (50 ml), washed with brine (30 ml), dried and concentrated. Chromatography of the residue on silica gel (EtOAc/pet ether 1:3 to 1:1) gave **126** (527 mg, 98%) as a white solid, m.p. 66–68 °C; IR (neat, cm^{-1}) 3478, 1613, 1514, 1379; ^1H NMR (300 MHz, $CDCl_3$): 7.30–7.25 (m, 2 H), 6.90–6.85 (m, 2 H), 4.82 (d, *J* = 10.9, 1 H), 4.55 (d, *J* = 10.9, 1 H), 3.90 (dd, *J* = 11.3, 5.4, 1 H), 3.80 (s, 3 H), 3.79–3.67 (m, 3 H), 3.53 (dd, *J* = 11.5, 6.5, 1 H), 3.33–3.22 (m, 2 H), 3.16 (dd, *J* = 9.9, 8.7, 1 H), 1.74–1.62 (m, 2 H), 1.52 (s, 3 H), 1.44 (s, 3 H), 0.95 (d, *J* = 6.5, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.2, 131.0, 129.7 (2C), 113.7 (2C), 99.2, 82.2, 81.2, 76.5, 74.1, 71.4, 63.5, 62.4, 55.2, 37.9, 29.3, 19.3, 13.1; EI HRMS *m/z* calculated for $C_{19}H_{28}O_6$ (M^+) 352.1886, observed 352.1838; $[\alpha]_D$ +23.0 (*c* 1.36, $CHCl_3$). Calculated for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01. Found: C, 64.71; H, 7.95.

Pyranyl Acetate **127**

To a solution of alcohol **126** (382 mg, 1.08 mmol) in dry CH_2Cl_2 (10 ml) was added Ac_2O (222 mg, 2.17 mmol), Et_3N (329 mg, 3.25 mmol) and DMAP (cat). The reaction mixture was stirred at r.t. for 0.5 h, diluted with EtOAc (50 ml), washed with brine (30 ml), dried and concentrated. Chromatography of the residue on silica gel (EtOAc/pet ether 1:3) gave **127** (406 mg, 95%) as a colorless oil; IR (neat, cm^{-1}) 1741, 1514, 1378, 1245; ^1H NMR (300 MHz, $CDCl_3$): 7.29–7.26 (m, 2 H), 6.91–6.86 (m, 2 H), 4.83 (d, *J* = 10.8, 1 H), 4.55 (d, *J* = 10.8, 1 H), 4.22 (dd, *J* = 12.1, 2.1, 1 H), 4.11 (dd, *J* = 12.1, 5.4, 1 H), 3.90 (dd, *J* = 10.7, 5.4, 1 H), 3.80 (s, 3 H), 3.83–3.68 (m, 2 H), 3.36 (dq, *J* = 5.5, 2.1, 1 H), 3.25 (dt, *J* = 9.7, 5.4, 1 H), 3.15 (dd, *J* = 9.8, 9.7, 1 H), 2.06 (s, 3 H), 1.78–1.72 (m, 1 H), 1.53 (s, 3 H), 1.44 (s, 3 H), 0.98 (d, *J* = 6.5, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 170.9, 159.2, 130.8, 129.7 (2C), 113.7 (3C), 99.2, 81.2, 79.8, 76.3, 74.2, 71.5, 64.5, 62.4, 55.2, 37.9, 29.3, 20.8, 19.3, 13.3; EI HRMS *m/z* calcu-

lated for $C_{21}H_{30}O_7$ (M^+) 394.1992, observed 394.1943; $[\alpha]_D$ +20 (*c* 0.68, $CHCl_3$). Calculated for $C_{21}H_{30}O_7$: C, 63.94; H, 7.67. Found: C, 63.85; H, 7.66.

Acetoxy Diol **128**

A solution of **127** (2.60 g, 6.58 mmol) in 1 M HCl/THF (1:1, 120 ml) was stirred at r.t. for 1 h, quenched with aqueous $NaHCO_3$ solution (12 ml), washed with brine (30 ml), dried and concentrated. Chromatography of the residue on silica gel (EtOAc/pet ether 1:1 to 1:0) gave **128** (2.2 g, 95%) as a colorless oil; IR (neat, cm^{-1}) 3430, 1738, 1514, 1248; ^1H NMR (300 MHz, $CDCl_3$): 7.30–7.26 (m, 2 H), 6.91–6.88 (m, 2 H), 4.71 (d, *J* = 11.2, 1 H), 4.67 (d, *J* = 11.2, 1 H), 4.27 (dd, *J* = 12.1, 2.1, 1 H), 4.12 (dd, *J* = 12.1, 5.6, 1 H), 3.86 (dd, *J* = 11.6, 3.5, 1 H), 3.80 (s, 3 H), 3.75 (dd, *J* = 11.6, 4.9, 1 H), 3.56 (t, *J* = 9.0, 1 H), 3.37–3.27 (m, 2 H), 3.11 (t, *J* = 9.0, 1 H), 2.31–2.11 (br s, 2 H), 2.07 (s, 3 H), 1.78–1.69 (m, 1 H), 0.97 (d, *J* = 5.6, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 171.0, 159.4, 130.5, 129.5 (2C), 114.1 (2C), 86.3, 79.1, 79.0, 74.5, 71.8, 64.6, 62.9, 55.3, 38.0, 20.9, 13.0; EI HRMS *m/z* calculated for $C_{18}H_{26}O_7$ (M^+) 354.1679, observed 354.1696; $[\alpha]_D$ –4.4 (*c* 0.45, $CHCl_3$).

Pyranyl Carbinol **129**

A. From **128**. A solution of **128** (623 mg, 1.76 mmol), 4-methoxybenzaldehyde dimethylacetal (736 mg, 4.04 mmol) and TsOH (one crystal) in DMF was rotated under aspirator pressure at 50 °C for 5 h. The temperature was then raised to 70 °C, at which point the volatiles were removed. The reaction mixture was added to saturated $NaHCO_3$ solution (20 ml) and Et_2O (100 ml). The separated organic layer was washed with brine (3 × 50 ml), dried and concentrated to furnish the acetal (830 mg, 100%), which was used directly without further purification.

A solution of unpurified acetal (800 mg, 1.69 mmol) in MeOH (20 ml) was treated with NaOMe (93.0 mg, 1.69 mmol) in several portions at r.t. and stirred for 1 h. The reaction mixture was filtered through silica gel, washed with EtOAc and concentrated. Chromatography of the residue on silica gel (EtOAc/pet ether 1:2 to 1:1) gave **129** (691 mg, 95%) as a white solid, m.p. 103–105 °C; IR (neat, cm^{-1}) 3440, 1614, 1514, 1464; ^1H NMR (300 MHz, $CDCl_3$): 7.46 (d, *J* = 8.7, 2 H), 7.29 (d, *J* = 8.7, 2 H), 6.93 (d, *J* = 8.7, 2 H), 6.87 (d, *J* = 8.7, 2 H), 5.59 (s, 1 H), 4.91 (d, *J* = 10.9, 1 H), 4.61 (d, *J* = 10.9, 1 H), 4.32 (dd, *J* = 10.3, 4.9, 1 H), 3.83 (s, 3 H), 3.81 (s, 3 H), 3.80–3.75 (m, 1 H), 3.72 (d, *J* = 10.2, 1 H), 3.66 (d, *J* = 9.1, 1 H), 3.58 (dd, *J* = 11.9, 6.5, 1 H), 3.48 (td, *J* = 9.8, 4.9, 1 H), 3.38–3.25 (m, 2 H), 2.30–1.90 (br s, 1 H), 1.82–1.70 (m, 1 H), 0.99 (d, *J* = 6.6, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.9, 159.2, 130.6, 130.1, 129.8 (2C), 127.2 (2C), 113.7 (2C), 113.5 (2C), 101.1, 83.9, 82.2, 80.9, 74.4, 70.5, 68.8, 63.4, 55.3, 55.2, 37.9, 13.0; EI HRMS *m/z* calculated for $C_{24}H_{30}O_7$ (M^+) 430.1992, observed 430.1982; $[\alpha]_D$ +17 (*c* 0.60, $CHCl_3$).

B. Directly from **126**. A solution of acetonide **126** (2.9 g, 8.3 mmol) in 1 M HCl/THF (1:5) was stirred at r.t. for 3 h. The reaction mixture was quenched with aqueous $NaHCO_3$ solution and extracted with EtOAc (3 × 100 ml). After solvent evaporation, the crude product was used directly in the next step; white solid, m.p. 113–134 °C; IR (neat, cm^{-1}) 3315, 1513, 1095; ^1H NMR (300 MHz, $CDCl_3$): 7.32 (m, 2 H), 6.88 (m, 2 H), 4.78 (d, *J* = 11.0, 1 H), 4.65 (d, *J* = 11.0, 1 H), 4.00–3.81 (m, 2 H), 3.81 (s, 3 H), 3.80–3.60 (m, 3 H), 3.62–3.47 (m, 2 H), 3.30 (m, 2 H), 3.18 (m, 1 H), 3.10 (dd, *J* = 9.0, 10.2, 1 H), 1.70 (m, 1 H), 0.92 (d, *J* = 6.5, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.4, 130.7, 129.6 (2C), 113.9 (2C), 86.1, 81.3, 79.5, 74.3,

71.3, 63.1, 62.3, 55.2, 37.4, 12.9; ES HRMS *m/z* calculated for $C_{16}H_{24}O_6Na$ (M^+ + Na) 335.1465, observed 335.1455; $[\alpha]_D$ +14 (*c* 1.0, $CHCl_3$).

A sample of unpurified triol (2.6 g, 8.3 mmol) was dissolved in DMF (10 ml) and treated sequentially with *p*-methoxybenzaldehyde dimethylacetal (1.82 g, 10 mmol) and TsOH (0.15 g, 0.8 mmol). After 3 h of stirring, more acetal (1.5 g, 8.3 mmol) was introduced and the reaction mixture was quenched with saturated $NaHCO_3$ solution (10 ml) and H_2O (20 ml) 30 min later. The product was extracted into EtOAc, and the combined organic phases were dried and concentrated to leave a residue that was purified by chromatography on silica gel (10–50% EtOAc/hexanes) to give **129** (3.1 g, 87%), identical in all respects to the material prepared in Part *A*.

Aldehyde **77**

A mixture of IBX (45 mg, 0.16 mmol) and **129** (20 mg, 0.046 mmol) in DMSO (0.3 ml) was stirred at r.t. for 4 h, filtered through a pad of silica gel (EtOAc rinse) concentrated in vacuo and purified by chromatography on silica gel (EtOAc/hexanes 1:1) to provide **77** (19 mg, 95%) as a colorless oil; IR (neat, cm^{-1}) 1739, 1613, 1463, 1380; ^1H NMR (500 MHz, $CDCl_3$) 9.59 (d, *J* = 2.1, 1 H), 7.48 (m, 2 H), 7.29 (m, 2 H), 7.00–6.67 (m, 4 H), 5.64 (s, 1 H), 4.92 (d, *J* = 10.9, 1 H), 4.68 (d, *J* = 10.9, 1 H), 4.40 (dd, *J* = 4.9, 10.3, 1 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.87 (m, 1 H), 3.79 (dd, *J* = 9.1, 9.2, 1 H), 3.68 (dd, *J* = 11.2, 2.1, 1 H), 3.57 (ddd, *J* = 5.1, 9.8, 9.8, 1 H), 3.41 (dd, *J* = 9.2, 9.7, 1 H), 1.94 (ddd, *J* = 11.1, 9.9, 6.5, 1 H), 1.12 (d, *J* = 6.5, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 198.4, 160.0, 159.3, 130.3, 129.9 (2C), 129.8, 127.3 (2C), 113.8 (2C), 113.6 (2C), 101.3, 84.8, 83.2, 80.7, 74.7, 70.4, 68.6, 55.32, 55.31, 37.3, 12.4; ES HRMS *m/z* calculated for $C_{24}H_{28}O_7Na$ (M^+ + Na) 451.1727, observed 451.1729; $[\alpha]_D$ +14 (*c* 1.3, $CHCl_3$).

Silyloxy Aldehyde **130**

Pentane-1,5-diol (27.8 ml, 265.2 mmol) was dissolved in dry CH_2Cl_2 (100 ml) in a round bottom flask under N_2 and cooled to 0 °C. Imidazole (6.8 g, 99.5 mmol) was added. TBSCl (10 g, 66.3 mmol) was dissolved in CH_2Cl_2 (100 ml) and added to the reaction mixture dropwise over 90 min via an addition funnel, followed by warming to r.t. over 12 h. The reaction mixture was transferred to a separatory funnel containing saturated NH_4Cl (100 ml) solution and CH_2Cl_2 (100 ml). The aqueous layer was extracted with CH_2Cl_2 (3 × 80 ml). The combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo. Aldehyde **130** (14.39 g, 99%) was isolated as a pale yellow oil. IR (neat, cm^{-1}) 3640, 3480, 1390, 1360; ^1H NMR ($CDCl_3$, 400 MHz): 3.63 (m, 4 H), 1.55 (m, 4 H), 1.42 (m, 2 H), 0.89 (s, 9 H), 0.042 (s, 3 H), 0.039 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 63.16, 62.96, 32.51, 26.01, 22.04, 18.41, –5.24.

To a cooled (–78 °C) solution of $(COCl)_2$ (2.40 ml, 27.5 mmol) in dry CH_2Cl_2 (60 ml) was added DMSO (3.9 ml, 54.9 mmol) dropwise by syringe. After 15 min at –78 °C, the above alcohol (4.0 g, 18.3 mmol) was introduced as a solution in dry CH_2Cl_2 (25 ml) via syringe. The resulting mixture was stirred at –78 °C for 1 h, treated with Et_3N (15.3 ml, 110 mmol), warmed to r.t. for 1 h and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 (2 × 50 ml) and the combined organic solutions were dried and concentrated. Chromatography of the residue on silica gel (EtOAc/pet ether 1:13) gave **130** (3.53 g, 89%) as a pale yellowish liquid; IR (neat, cm^{-1}) 1730, 1470, 1270; ^1H NMR (80 MHz, $CDCl_3$): 9.78 (s, 1 H), 3.62 (t, *J* = 6.0, 2 H), 2.48 (t, *J* = 6.0, 2 H), 1.95–1.30 (m, 4 H), 0.94 (s, 9 H), 0.07 (s, 6 H).

Acylated Oxazolinedione **131**

To a cold (–78 °C) solution of **106** (2.15 g, 9.23 mmol) in CH_2Cl_2 (25 ml) was added 1.0 M *n*-Bu_2BOTf in CH_2Cl_2 (12.0 ml, 12.0 mmol) at such a rate as to maintain an internal temperature below +5 °C. The introduction of *i*-Pr_2NEt (2.6 ml, 14.8 mmol) followed. After 10 min, the reaction mixture was cooled to –78 °C and a solution of **130** (2.6 g, 12.0 mmol) in CH_2Cl_2 (25 ml) was added. Stirring was continued at –78 °C for 1 h, and at 0 °C for 1 h. Quenching with pH 7.0 phosphate buffer (10 ml) was followed by MeOH (25 ml). After 10 min at 0 °C, 30% H_2O_2 (12.5 ml) was added, stirring was maintained at 0 °C for 1 h, and the mixture was concentrated. The residue was extracted with Et_2O, washed with saturated $NaHCO_3$ solution and brine, dried and concentrated to leave an oil that was purified chromatographically on silica gel (EtOAc/hexanes 1:2) to provide **131** (3.89 g, 94%) as a colorless oil; IR (neat, cm^{-1}) 3524, 1783, 1698, 1455; ^1H NMR (300 MHz, $CDCl_3$) 7.37–7.19 (m, 5 H), 4.74–4.66 (m, 1 H), 4.26–4.16 (m, 2 H), 3.95 (dd, *J* = 8.2, 2.5, 1 H), 3.76 (dd, *J* = 7.0, 2.6, 1 H), 3.61 (t, *J* = 5.9, 2 H), 3.26 (dd, *J* = 13.3, 3.6, 1 H), 2.79 (dd, *J* = 13.3, 9.4, 1 H), 1.70–1.34 (series of m, 7 H), 1.25 (d, *J* = 7.0, 3 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 177.5, 153.0, 135.0, 129.4, 129.0 (2C), 127.4 (2C), 71.4, 66.2, 63.1, 55.1, 42.1, 37.8, 33.6, 32.7, 26.0, 22.3, 18.4 (3C), 10.4, –5.3 (2C); EI HRMS *m/z* calculated for $C_{24}H_{39}NO_5Si$ (M^+) 449.2598, observed 449.2585; $[\alpha]_D$ +38.7 (*c* 1.26, $CHCl_3$). Calculated for $C_{24}H_{39}NO_5Si$: C, 64.11; H, 8.74. Found: C, 64.12; H, 8.84.

Silyl Protection of **131**

To a warm (50 °C) solution of **131** (3.89 g, 8.65 mmol) and TBSCl (3.3 g, 26 mmol) in dry DMF (15 ml) was added imidazole (2.45 g, 34.5 mmol) and DMAP (100 mg). The reaction mixture was stirred at 50 °C for 3 h, diluted with Et_2O (150 ml), and washed sequentially with 5% HCl (50 ml), saturated $NaHCO_3$ solution (50 ml) and brine (50 ml). The organic phase was dried, filtered and concentrated in vacuo. Chromatography of the residue on silica gel (EtOAc/hexanes 1:5) gave **132** (4.82 g, 99%) as a white powder, m.p. 90–92 °C; IR (film, cm^{-1}) 1784, 1699, 1472, 1254; ^1H NMR (300 MHz, $CDCl_3$): 7.36–7.21 (m, 5 H), 4.63–4.56 (m, 1 H), 4.19–4.11 (m, 2 H), 4.00 (dd, *J* = 10.6, 5.5, 1 H), 3.87–3.83 (m, 1 H), 3.60 (t, *J* = 6.3, 2 H), 3.30 (dd, *J* = 13.3, 3.0, 1 H), 2.76 (dd, *J* = 13.3, 9.8, 1 H), 1.59–1.42 (m, 4 H), 1.41–1.32 (m, 2 H), 1.21 (d, *J* = 6.8, 3 H), 0.88 (s, 18 H), 0.04 (s, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): 175.2, 153.0, 135.4, 129.4 (2C), 128.9, 127.3 (2C), 72.8, 65.9, 63.1, 55.8, 42.8, 37.6, 35.4, 33.1, 26.0, 25.8, 21.4, 18.5, 18.0 (3C), 11.5 (3C), –4.1, –4.9, –5.3 (2C); EI HRMS *m/z* calculated for $C_{26}H_{44}NO_5Si_2$ ($M^+ - C_4H_9$) 506.2758, observed 506.2734; $[\alpha]_D$ +43.8 (*c* 1.19, $CHCl_3$). Calculated for $C_{30}H_{53}NO_5Si_2$: C, 63.90; H, 9.47. Found: C, 63.84; H, 9.27.

Aldehyde **133**

To a cooled (0 °C), stirred solution of $LiBH_4$ (1.32 g, 57.6 mmol) and H_2O (1.03 g, 57.6 mmol) in THF (20 ml) was added **132** (6.5 g, 11.5 mmol). The reaction mixture was stirred at 0 °C for 1 h, at r.t. for 2 h, and quenched with 2 M NaOH (15.0 ml). The resulting mixture was stirred for 10 min, washed with brine (100 ml), dried, concentrated and purified over silica gel (EtOAc/hexanes 1:5) to provide the primary alcohol (4.3 g, 96%) as a colorless oil; IR (neat, cm^{-1}) 3404, 1472, 1463; ^1H NMR (300 MHz, $CDCl_3$): 3.80–3.72 (m, 1 H), 3.68 (dd, *J* = 10.6, 8.7, 1 H), 3.60 (t, *J* = 6.2, 2 H), 3.50 (dd, *J* = 10.6, 5.1, 1 H), 2.75–2.55 (br s, 1 H), 2.06–1.85 (m, 1 H), 1.62–1.37 (m, 5 H), 1.36–1.16 (m, 1 H), 0.88 (s, 18 H), 0.79 (d, *J* = 7.1,

3 H), 0.08 (s, 3 H), 0.06 (s, 3 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 74.9, 65.4, 62.8, 39.5, 32.8, 32.5, 25.8, 25.5, 22.4, 18.1 (3C), 17.8 (3C), 11.5, –4.5, –4.7, –5.5 (2C); EI HRMS *m/z* calculated for $C_{17}H_{39}O_2Si_2$ (M^+ – $CH(CH_3)CH_2OH$) 331.2489, observed 331.2482; $[\alpha]_D$ +3.0 (*c* 1.43, $CHCl_3$). Calculated for $C_{20}H_{46}O_3Si_2$: C, 61.48; H, 11.87. Found: C, 61.50; H, 11.37.

To a cold (–78 °C) solution of $(COCl)_2$ (780 mg, 6.14 mmol) in dry CH_2Cl_2 (10 ml) was added DMSO (960 µl, 12.3 mmol) dropwise by syringe. After 15 min at –78 °C, the alcohol (1.2 g, 3.07 mmol) was added as a solution in dry CH_2Cl_2 (1 ml) via syringe. The resulting mixture was stirred at –78 °C for 1 h and treated with Et_3N (1.87 g, 18.4 mmol). After a further 10 min, the reaction mixture was allowed to warm, washed with 5% aqueous HCl (30 ml), saturated $NaHCO_3$ solution (30 ml), and brine (30 ml) then dried. The filtrate was concentrated and purified on silica gel (EtOAc/hexanes 1:5) to provide **133** (1.19 g, 99%) as a colorless oil; IR (neat, cm^{-1}) 2954, 2930, 1728, 1472; ^{1}H NMR (300 MHz, $CDCl_3$): 9.77 (s, 1 H), 4.12–4.07 (m, 1 H), 3.60 (t, *J* = 6.2, 2 H), 2.49–2.41 (m, 1 H), 1.57–1.22 (series of m, 6 H), 1.04 (d, *J* = 6.9, 3 H), 0.88 (s, 9 H), 0.85 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 6 H), 0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 205.4, 72.1, 62.8, 51.2, 34.3, 32.8, 25.9, 25.7, 22.1, 18.3 (3C), 18.0 (3C), 7.6, –4.2, –4.7, –5.3 (2C); $[\alpha]_D$ +36.9 (*c* 1.34, $CHCl_3$).

Acylated Oxazolidinone **135**

To a cold (–78 °C) solution of (*S*)-*N*-acetyl benzyloxazolidinone **134** (2.2 g, 10.1 mmol) in CH_2Cl_2 (10 ml) was added 1.0 M *n*-Bu_2BOTf in CH_2Cl_2 (12.0 ml, 12.0 mmol) at such a rate as to maintain the internal temperature below +5 °C. The introduction of *i*-Pr_2NEt (1.82 g, 14.1 mmol) followed. After 1 h at 0 °C, the reaction mixture was cooled to –78 °C, a solution of **133** (2.6 g, 6.7 mmol) in CH_2Cl_2 (15 ml) was added, stirring was continued at –78 °C for 2 h and at 0 °C for 2 h prior to quenching by the addition of pH 7.0 phosphate buffer (10.0 ml) and MeOH (20 ml). Stirring was maintained for 10 min at 0 °C. 30% H_2O_2 (12.0 ml) was added and agitation was continued at 0 °C for 1 h. The mixture was concentrated and the residue extracted with Et_2O. The combined organic phases were washed with saturated $NaHCO_3$ solution and brine, dried and concentrated to leave a residue that was purified on silica gel (EtOAc/pet ether 1:2) to provide **135** (2.07 g, 50%) as a colorless oil; IR (neat, cm^{-1}) 3530, 1789, 1698, 1387; ^{1}H NMR (300 MHz, $CDCl_3$): 7.36–7.20 (m, 5 H), 4.74–4.66 (m, 1 H), 4.31–4.26 (m, 1 H), 4.23–4.14 (m, 2 H), 3.85–3.80 (m, 1 H), 3.60 (t, *J* = 6.4, 2 H), 3.31 (dd, *J* = 13.5, 3.4, 1 H), 3.23 (dd, *J* = 16.8, 9.2, 1 H), 3.31 (dd, *J* = 13.5, 3.4, 1 H), 3.23 (dd, *J* = 16.8, 9.2, 1 H), 3.04 (dd, *J* = 16.8, 3.4, 1 H), 2.77 (dd, *J* = 13.5, 9.5, 1 H), 1.70–1.63 (m, 1 H), 1.62–1.46 (m, 3 H), 1.34–1.24 (m, 2 H), 0.97 (d, *J* = 7.0, 3 H), 0.89 (s, 18 H), 0.08 (s, 6 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 172.5, 153.5, 135.2, 129.4 (2C), 129.0 (2C), 127.3, 75.9, 70.0, 66.2, 63.0, 55.1, 41.3, 41.2, 37.8, 34.1, 33.0, 26.0, 25.9, 21.9, 18.3 (3C), 18.1 (3C), 7.9, –3.9, –4.5, –5.3 (2C); EI HRMS *m/z* calculated for $C_{28}H_{68}NO_6Si_2$ (M^+ – C_4H_9) 550.3020, observed 550.3039; $[\alpha]_D$ +12.1 (*c* 1.48, $CHCl_3$). Calculated for $C_{32}H_{57}NO_6Si_2$: C, 63.22; H, 9.45. Found: C, 62.95; H, 9.59.

Acylated Thiazolidinethione **136**

$Sn(OTf)_2$ (7.09 g, 17.0 mmol) was placed in a flask that was evacuated and filled with N_2. CH_2Cl_2 (70 ml) was introduced prior to cooling to –50 °C, at which point *N*-ethylpiperidine (1.92 g, 17.0 mmol) was added followed by a CH_2Cl_2 (30 ml) solution of *ent*-**10** (3.46 g, 17.0 mmol). The mixture was stirred at –50 °C to –40 °C for 4 h. After the addition of **133**

(3.50 g, 8.99 mmol) at –78 °C, agitation was continued at the same temperature for 1 h prior to quenching with pH 7.0 phosphate buffer (100 ml) and filtration through Celite (CH_2Cl_2 wash). The combined filtrates were dried and evaporated, and the residue was purified by silica gel chromatography (EtOAc/pet ether 1:7) to afford **136** (4.83 g, 91%) alongside recovered *ent*-**10** (1.53 g).

For **136**: IR (neat, cm^{-1}) 1783, 1694, 1471, 1362; ^1H NMR (300 MHz, $CDCl_3$): 5.18 (t, *J* = 6.9, 1 H), 4.31–4.28 (m, 1 H), 3.84–3.80 (m, 1 H), 3.60 (t, *J* = 6.4, 2 H), 3.54–3.48 (m, 2 H), 3.32 (dd, *J* = 17.4, 9.3, 1 H), 3.00 (d, *J* = 11.6, 2 H), 2.40–2.33 (m, 1 H), 1.66–1.58 (m, 1 H), 1.55–1.32 (m, 4 H), 1.29–1.23 (m, 2 H), 1.06 (d, *J* = 6.8, 3 H), 0.97 (d, *J* = 7.0, 3 H), 0.94 (d, *J* = 7.0, 3 H), 0.88 (s, 18 H), 0.08 (s, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.9, 172.8, 76.0, 71.5, 70.4, 62.9, 44.1, 40.6, 34.3, 32.9, 30.8, 30.6, 26.0, 25.9, 21.7, 19.0, 18.3, 18.0 (3C), 17.8 (3C), 7.5, –3.7, –4.5, –5.3 (2C); EI HRMS *m/z* calculated for $C_{24}H_{48}NO_4S_2Si_2$ ($M^+ - C_4H_9$) 534.2563, observed 534.2558; $[\alpha]_D$ –199 (*c* 0.61, $CHCl_3$). Calculated for $C_{28}H_{57}NO_4S_2Si_2$: C, 56.80; H, 9.70. Found: C, 56.99; H, 9.61.

Silylation of **136**

TIPSOTf (8.8 ml, 32.7 mmol) was added to an ice-cooled, stirred solution of **136** (8.9 g, 15.03 mmol) and 2,6-lutidine (10.51 ml, 90.18 mmol) in CH_2Cl_2 (150 ml). Upon completion of the addition, the ice-bath was removed and stirring was continued for 15 h. The mixture was concentrated in vacuo, taken up in Et_2O (200 ml), washed with brine (100 ml), dried and concentrated. The residue was purified by chromatography on silica gel (EtOAc/pet ether 1:100 to 1:7) to afford of **137** (10.57 g, 94%) as a yellow oil; IR (neat, cm^{-1}) 1699, 1463, 1256; ^1H NMR (300 MHz, $CDCl_3$): 5.12 (t, *J* = 7.0, 1 H), 4.54–4.45 (m, 1 H), 3.74 (t, *J* = 6.0, 1 H), 3.67–3.32 (series of m, 5 H), 3.00 (d, *J* = 11.4, 1 H), 2.40–2.27 (m, 1 H), 1.78–1.63 (m, 1 H), 1.63–1.22 (series of m, 8 H), 1.15–0.65 (series of m, 7 H), 1.05 (s, 18 H), 0.95 (d, *J* = 7.6, 3 H), 0.89 (s, 18 H), 0.04 (s, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.4, 171.8, 73.2, 71.5, 69.7, 63.3, 44.4, 42.5, 34.5, 33.5, 30.7, 30.4, 26.0, 25.98, 20.7 (2C), 19.1 (2C), 18.3 (2C), 18.2 (3C), 18.0 (3C), 17.7 (3C), 13.1 (2C), 10.3, –4.1, –4.3 (2C), –5.3 (2C); EI HRMS *m/z* calculated for $C_{35}H_{75}NO_3S_2Si_3$ ($M^+ - C_2H_2O$) 705.4496, observed 705.4496; $[\alpha]_D$ –128 (*c* 2.00, $CHCl_3$). Calculated for $C_{37}H_{77}NO_4S_2Si_3$: C, 59.38; H, 10.37. Found: C, 59.64; H, 10.43.

Iodide **138**

To a cooled (0 °C), stirred solution of $LiBH_4$ (1.62 g, 70.2 mmol) and H_2O (1.27 g, 70.2 mmol) in THF (136 ml) was added **137** (10.5 g, 14.0 mmol). The reaction mixture was stirred at 0 °C for 1 h and at r.t. for 2 h, quenched with 2 M NaOH (15 ml), stirred at 0 °C for 10 min, washed with brine (100 ml), dried, concentrated and purified by chromatography on silica gel (Et_2O/pet ether 1:9) to provide the primary alcohol (1.293 g, 99%) as a colorless oil; IR (neat, cm^{-1}) 3362, 1463, 1388, 1255; ^1H NMR (300 MHz, $CDCl_3$): 4.15–4.03 (m, 1 H), 3.92–3.74 (m, 2 H), 3.73–3.55 (m, 1 H), 3.60 (t, *J* = 6.4, 2 H), 2.30–1.85 (br s, 1 H), 2.05–1.77 (m, 2 H), 1.75–1.66 (m, 1 H), 1.65–1.38 (m, 4 H), 1.37–1.22 (m, 2 H), 1.09 (s, 21 H), 0.93 (d, *J* = 6.9, 3 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.04 (s, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): 73.0, 72.1, 63.1, 59.6, 48.8, 40.7, 36.6, 34.8, 33.3, 26.0, 25.9, 21.2 (3C), 18.3 (3C), 18.1 (3C), 17.9 (3C), 13.2, 13.1, 9.6, –3.9, –4.4 (2C), –5.3 (2C); EI HRMS *m/z* calculated for $C_{38}H_{65}O_3Si_3$ ($M^+ - C_3H_7 - H_2O$) 529.3928, observed 529.3947; $[\alpha]_D$ –1.1 (*c* 1.3, $CHCl_3$).

A solution of the primary alcohol (1.29 g, 2.19 mmol) in PhMe (40 ml) and acetonitrile (10 ml) was treated with PPh_3 (1.5 g, 5.7 mmol) and imidazole (490 mg, 8.10 mmol), heated nearly to the reflux temperature and admixed with I_2 (313 mg, 4.82 mmol) in several portions. After 30 min of heating, the mixture was cooled to r.t., diluted with Et_2O (100 ml), washed with brine (3 × 30 ml), dried and evaporated. Chromatography of the residue on silica gel (Et_2O/pet ether 1:120 to 1:100) gave **138** (1.53 g, 99%) as a colorless liquid; IR (neat, cm^{-1}) 1463, 1255; ^1H NMR (300 MHz, $CDCl_3$): 3.97–3.78 (m, 1 H), 3.76–3.70 (m, 1 H), 3.61 (t, *J* = 6.5, 2 H), 3.28–3.15 (m, 1 H), 3.12–2.93 (m, 1 H), 2.22–2.05 (m, 2 H), 1.70–1.46 (series of m, 5 H), 1.45–1.25 (m, 2 H), 1.07 (s, 21 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.87 (m, 3 H), 0.05 (s, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): 99.9, 73.9, 72.7, 63.1, 40.3, 39.3, 34.7, 33.6, 29.7, 25.9, 21.0, 18.1 (6C), 15.0 (3C), 13.2 (2C), 9.7, 1.0, –3.9, –4.3 (2C), –5.3 (2C); EI HRMS *m/z* calculated for $C_{38}H_{66}O_3Si_3$ ($M^+ - C_3H_7I$) 530.4007, observed 530.4031; $[\alpha]_D$ +6.4 (*c* 0.70, $CHCl_3$).

Sulfide **139**

To a solution of PhSH (70 μl, 0.65 mmol) in PhH (2 ml) was added DBU (110 μl, 0.72 mmol). After 1 h of stirring at 4 °C, a solution of **138** (152 mg, 0.22 mmol) in PhH (2 ml) was added over 5 min period. The resulting slurry was stirred at r.t. for 12 h, filtered, rinsed with Et_2O and concentrated in vacuo. Chromatography of the residue on silica gel (EtOAc/pet ether 1:60) provided **139** (133 mg, 90%) as a viscous oil; IR (neat, cm^{-1}) 1586, 1463, 1255; ^1H NMR (300 MHz, $CDCl_3$): 7.40–7.24 (m, 4 H), 7.23–7.14 (m, 1 H), 4.02 (dd, *J* = 10.6, 5.2, 1 H), 3.70 (dd, *J* = 10.6, 5.3, 1 H), 3.61 (t, *J* = 6.5, 2 H), 3.00–2.77 (m, 2 H), 2.00–1.82 (m, 2 H), 1.75–1.60 (m, 1 H), 1.60–1.43 (m, 4 H), 1.40–1.24 (m, 2 H), 1.05 (s, 21 H), 0.90 (m, 3 H), 0.91 (s, 9 H), 0.88 (s, 9 H), 0.06 (s, 6 H), 0.03 (s, 3 H), –0.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 129.6 (2C), 128.8 (2C), 126.0 (2C), 73.0, 72.3, 63.2, 45.1, 40.6, 34.6, 34.4, 33.4, 29.5, 21.2, 18.3 (3C), 18.1 (3C), 13.2 (2C), 9.5 (2C), –3.9, –4.4 (2C), –5.3 (2C); EI HRMS *m/z* calculated for $C_{47}H_{78}O_3SSi_3$ (M^+) 682.4667, observed 682.4706.

Sulfone **78**

A. Oxidation of **139**. To a slurry of $NaHCO_3$ (106 mg, 1.26 mmol) in CH_2Cl_2 (2 ml) was added **139** (123 mg, 0.18 mmol) dissolved in CH_2Cl_2 (2 ml). After 5 min, a solution of MCPBA (89 mg, 0.36 mmol) in CH_2Cl_2 (2 ml) was added at 0 °C. The resulting slurry was stirred at 0 °C for 1 h and at r.t. for 2 h prior to being quenched with saturated $NaHSO_3$ solution (2 ml). The mixture was diluted with Et_2O (30 ml), washed with saturated $NaHCO_3$ solution (30 ml) and brine, dried and concentrated. Chromatography of the residue on silica gel (Et_2O/pet ether 1:11 to 1:7) gave **78** (105 mg, 82%) as a colorless oil; IR (neat, cm^{-1}) 1453, 1320, 1255, 1150; ^1H NMR (300 MHz, $CDCl_3$): 7.88 (d, *J* = 7.3, 2 H), 7.65 (d, *J* = 7.3, 1 H), 7.55 (d, *J* = 7.3, 2 H), 4.00–3.82 (m, 1 H), 3.58 (t, *J* = 6.5, 2 H), 3.60–3.45 (m, 1 H), 3.28–3.13 (m, 1 H), 3.07–2.89 (m, 1 H), 2.03–1.81 (m, 2 H), 1.55–1.36 (m, 4 H), 1.35–1.10 (m, 3 H), 1.05–0.91 (m, 18 H), 0.90–0.85 (m, 6 H), 0.88 (s, 9 H), 0.83 (s, 9 H), 0.04 (s, 6 H), 0.01 (s, 3 H), –0.07 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 139.1 (2C), 133.6, 129.2, 128.2 (2C), 72.4, 71.7, 62.9, 51.8, 45.1, 30.6, 34.7, 33.2, 29.7, 27.6, 26.0, 25.9, 21.6, 18.2 (6C), 15.3, 13.0 (2C), 9.3 (2C), –3.8, –4.5 (2C), –5.3 (2C); EI HRMS *m/z* calculated for $C_{47}H_{78}O_5SSi_3$ (M^+) 714.4541, observed 714.4565; $[\alpha]_D$ +9.4 (*c* 0.98, $CHCl_3$).

B. Direct substitution of **138**. To a solution of **138** (71 mg, 0.10 mmol) in DMF (4 ml) was added $PhSO_2Na$ (172 mg, 1.01 mmol). The reaction mixture was stirred at 110 °C for 1 h, cooled to r.t., diluted with Et_2O (10 ml), washed with brine (4 × 10 ml), dried and concentrated in vacuo. Chromatography of the residue on silica gel (Et_2O/pet ether 1:14 to 1:9) gave **78** (54 mg, 75%), identical in all respects with the material generated in Part *A*.

Hydroxy Sulfone **140**

A solution of **78** (78 mg, 1.01 mmol) in dry PhH (3 ml) was treated with 3 M EtMgBr in Et_2O (0.44 ml, 1.31 mmol), and the mixture was heated at 95 °C for 3 h and allowed to cool to r.t. HMPA (0.5 ml) was introduced, followed by a solution of **77** (156 mg, 0.364 mmol) in dry PhH (2 ml) via cannula. After 1 h, saturated NH_4Cl solution was added and the product was extracted into Et_2O (3 × 20 ml). The combined extracts were dried and concentrated to leave a residue that was purified by chromatography over silica gel (2–10% EtOAc/hexanes). After the recovery of unreacted **78** (400 mg), product **140** was isolated as a mixture of diastereomers (0.295 g, 71%), which was used directly in the next step.

Unsaturated Sulfone **141**

A solution of **140** (10 mg, 0.0087 mmol) in pyridine (0.4 ml) was treated with Ac_2O (0.2 ml) and DMAP (cat), stirred for 4 h, diluted with Et_2O (10 ml), washed with H_2O, and dried. After solvent evaporation, the unpurified acetate was taken up in Et_2O (2 ml) and treated with NaH (2 mg, 0.042 mmol). After 1 h, the reaction mixture was quenched with saturated NH_4Cl solution (0.5 ml) and extracted with Et_2O (2 × 10 ml). The dried combined extracts were concentrated and purified by chromatography on silica gel (5–10% EtOAc/hexanes) to give **141** (6.5 mg, 70%) as a pale yellow gum; IR (neat, cm^{-1}) 1613, 1514, 1462, 1384; ^1H NMR (300 MHz, $CDCl_3$): 7.83 (m, 2 H), 7.55 (m, 3 H), 7.46 (m, 2 H), 7.26 (m, 2 H), 6.90 (m, 4 H), 6.76 (d, *J* = 8.5, 1 H), 5.60 (s, 1 H), 4.70 (d, *J* = 10.9, 1 H), 4.60 (d, *J* = 10.9, 1 H), 4.49 (m, 1 H), 4.23 (dd, *J* = 4.9, 10.4, 1 H), 3.98 (dd, *J* = 8.8, 10.2, 1 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.70 (m, 3 H), 3.60 (m, 2 H), 3.45 (ddd, *J* = 4.8, 9.8, 9.8, 1 H), 3.32 (dd, *J* = 9.1, 9.1, 1 H), 2.60 (dd, *J* = 7.5, 14.7, 1 H), 2.24 (dd, *J* = 5.8, 14.6, 1 H), 1.65–1.60 (m, 2 H), 1.60–1.40 (m, 3 H), 1.40–1.15 (m, 3 H), 1.05 (m, 21 H), 0.95–0.75 (m, 6 H), 0.91 (s, 9 H), 0.83 (s, 9 H), 0.06 (s, 6 H), 0.01 (s, 3 H), –0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 160.0, 159.3, 143.6, 140.7, 139.4, 133.3, 130.4, 130.0, 129.8 (2C), 129.1 (2C), 128.1 (2C), 127.2 (2C), 113.8 (2C), 113.6 (2C), 101.2, 83.5, 80.7, 77.0, 74.6, 72.4, 71.9, 71.0, 68.7, 63.3, 55.3, 55.2, 42.4, 41.1, 35.1, 33.5, 33.0, 26.0 (6C), 20.2, 18.4 (3C), 18.3 (3C), 18.1 (2C), 13.1 (4C), 10.9, –3.7 (2C), –4.3, –5.3; ES HRMS *m/z* calculated for $C_{61}H_{100}O_{11}SSi_3Na$ (M^+ + Na) 1147.6186, observed 1147.6165; $[\alpha]_D$ –1.8 (*c* 1.0, $CHCl_3$).

Alkene **142**

To a solution of **140** (20 mg, 0.017 mmol) in pyridine (0.5 ml) was added Ac_2O (0.2 ml) and DMAP (cat). After 4 h of stirring, the reaction mixture was diluted with Et_2O (10 ml), washed with H_2O and dried. After solvent evaporation, the unpurified acetate was dissolved in MeOH (1 ml) and treated with 6% Na amalgam (50 mg) for 30 min prior to dilution with Et_2O (30 ml), washing with H_2O, drying and solvent evaporation. The residue was purified by chromatography on silica gel (2–5% EtOAc/hexanes) to furnish **142** (13 mg, 90%) as a pale yellow gum; IR (neat, cm^{-1}) 1514, 1462, 1453; ^1H NMR (300 MHz, $CDCl_3$): 7.45 (m,

2 H), 7.26 (m, 2 H), 6.90 (m, 4 H), 5.70 (m, 1 H), 5.60 (s, 1 H), 5.40 (dd, *J* = 7.5, 15.2, 1 H), 4.90 (d, *J* = 10.9, 1 H), 4.61 (d, *J* = 10.9, 1 H), 4.30 (dd, *J* = 4.9, 10.4, 1 H), 4.03 (m, 1 H), 3.83 (m, 3 H), 3.81 (m, 3 H), 3.70 (m, 3 H), 3.59 (m, 3 H), 3.43 (m, 1 H), 3.30 (dd, *J* = 9.3, 9.5, 1 H), 2.35 (m, 2 H), 1.63 (m, 2 H), 1.50 (m, 3 H), 1.29 (m, 3 H), 1.09 (s, 18 H), 1.15–0.80 (m, 9 H), 0.91 (s, 9 H), 0.89 (s, 9 H), 0.06 (s, 6 H), 0.03 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 159.9, 159.2, 131.9, 130.8, 130.4, 130.3, 129.8 (2C), 127.2 (2C), 113.7 (2C), 113.6 (2C), 101.1, 84.0, 83.4, 81.2, 74.4, 73.6, 72.1, 70.5, 69.0, 63.2, 55.3, 55.2, 41.9, 41.0, 38.6, 34.2, 33.4, 26.0 (6C), 21.4, 18.32 (3C), 18.29 (3C), 18.1 (2C), 13.8, 13.2 (3C), 9.3, –4.0, –4.3, –5.3 (2C); ES HRMS *m/z* calculated for $C_{55}H_{96}O_9Si_3Na$ (M^+ + Na) 1007.6254, observed 1007.6285; $[\alpha]_D$ +14 (*c* 1.6, $CHCl_3$).

α-Keto Sulfone **143**

A solution of **140** (100 mg, 0.088 mmol) in DMSO (2 ml) and THF (2 ml) was treated with IBX (250 mg, 0.88 mmol), stirred at r.t. for 36 h, diluted with Et_2O (50 ml) and washed with H_2O. After drying and solvent evaporation, the residue was purified by chromatography on silica gel (5–10% EtOAc/hexanes) to give **143** (89 mg, 90%) as a pale yellow gum; IR (neat, cm^{-1}) 1722, 1613, 1515, 1462; ^{1}H NMR (300 MHz, $CDCl_3$): 7.70 (m, 3 H), 7.56 (m, 2 H), 7.48 (m, 2 H), 7.26 (m, 2 H), 6.90 (m, 4 H), 5.62 (s, 0.5 H), 5.43 (s, 0.5 H), 5.02 (dd, *J* = 5.0, 9.0, 0.5 H), 4.89 (d, *J* = 10.5, 0.5 H), 4.87 (d, *J* = 11.0, 0.5 H), 4.71 (dd, *J* = 5.2, 5.2, 0.5 H), 4.61 (d, *J* = 10.8, 0.5 H), 4.60 (d, *J* = 11.0, 0.5 H), 4.35 (dd, *J* = 4.9, 10.4, 0.5 H), 4.25 (dd, *J* = 4.9, 10.4, 0.5 H), 4.00 (d, *J* = 10.6, 0.5 H), 3.90 (m, 0.5 H), 3.83 (s, 3 H), 3.80 (s, 3 H), 3.80–3.50 (m, 6 H), 3.45 (dd, *J* = 4.6, 9.6, 0.5 H), 3.40 (dd, *J* = 4.8, 9.8, 0.5 H), 3.30 (ddd, *J* = 3.8, 9.5, 9.5, 1 H), 2.45 (m, 1 H), 2.15–1.90 (m, 2 H), 1.60–1.30 (m, 7 H), 1.10–0.91 (m, 21 H), 0.91–0.80 (m, 22.5 H), 0.66 (d, *J* = 6.7, 1.5 H), 0.07 (s, 3 H), 0.05 (s, 6 H), –0.02 (s, 1.5 H), –0.05 (s, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$): 200.6, 190.4, 160.0, 159.2, 136.6, 134.3, 134.1, 130.6, 130.5, 130.0, 129.9, 129.83, 129.76, 129.5, 129.0, 128.8, 127.33, 127.26, 113.7, 113.60, 113.57, 101.3, 101.2, 86.6, 84.3, 83.0, 82.8, 81.2, 80.6, 74.5, 72.9, 72.8, 72.0, 71.2, 70.7, 69.7, 68.5, 68.0, 65.2, 63.23, 63.20, 55.3, 55.2, 40.8, 40.3, 38.1, 37.5, 34.8, 34.4, 34.2, 33.6, 32.1, 26.02, 25.99, 25.95, 20.6, 20.0, 18.32, 18.25, 18.2, 18.1, 13.09, 13.06, 12.9, 9.3, 8.2, –3.89, –3.92, –4.2, –4.5, –5.19, –5.22, –5.3; ES HRMS *m/z* calculated for $C_{61}H_{100}O_{12}SSi_3Na$ (M^+ + Na) 1163.6135, observed 1163.6198.

α-Diketone **145**

To a solution of **143** (30 mg, 0.026 mmol) in dry THF (1.5 ml) was added 0.7 M *t*-BuOK in THF (0.049 ml, 0.034 mmol) at 0 °C. After 40 min of stirring, **144** (43 mg, 0.13 mmol) was added, and stirring in the cold was maintained for an additional 5 h prior to quenching with saturated NH_4Cl solution (1 ml) and extraction with Et_2O (3 × 20 ml). Solvent evaporation left a residue that was purified by chromatography on silica gel (1–5% EtOAc/hexanes) to provide **145** (16 mg, 65%) as a yellow gum; IR (neat, cm^{-1}) 1719, 1612, 1514, 1461; ^{1}H NMR (300 MHz, $CDCl_3$): 7.47 (m, 2 H), 7.25 (m, 2 H), 6.90 (m, 4 H), 5.55 (s, 1 H), 4.90 (d, *J* = 11.0, 1 H), 4.62 (d, *J* = 11.0, 1 H), 4.48 (m, 1 H), 4.39 (d, *J* = 10.8, 1 H), 4.25 (dd, *J* = 5.0, 10.5, 1 H), 3.90 (m, 1 H), 3.76 (s, 3 H), 3.74 (s, 3 H), 3.70 (m, 2 H), 3.63 (m, 2 H), 3.50 (m, 1 H), 3.37 (dd, *J* = 9.7, 9.7, 1 H), 3.25 (dd, *J* = 6.5, 18.2, 1 H), 2.90 (dd, *J* = 4.9, 18.5, 1 H), 2.25 (m, 1 H), 1.70 (m, 1 H), 1.50 (m, 4 H), 1.25 (m, 2 H), 1.10–0.95 (m, 21 H), 0.90 (m, 12 H), 0.89 (s, 9 H), 0.84 (d, *J* = 6.9, 3 H), 0.05 (s, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): 199.2, 195.0, 160.0, 159.3, 130.5, 130.0, 129.8 (2C), 127.3 (2C), 113.7 (2C), 113.6 (2C),

101.2, 83.3, 80.6, 79.6, 74.5, 71.9, 71.6, 68.8, 68.5, 63.1, 55.27, 55.25, 42.9, 41.9, 38.0, 34.9, 33.4, 26.03 (3C), 25.97 (3C), 21.1, 18.3, 18.2 (6C), 18.1, 12.9 (4C), 9.5, –3.9, –4.2, –5.3 (2C); ES HRMS *m/z* calculated for $C_{55}H_{94}O_{11}Si_3Na$ (M^+ + Na) 1037.5996, observed 1037.6040; $[\alpha]_D$ –13.0 (*c* 1.60, $CHCl_3$).

Acid **147**

A. Hydrolysis of the methyl ester. A solution of ester **168** (4.16 g, 0.01 mmol) in a 5:1 mixture of THF and H_2O (100 ml) was treated with LiOH (1.3 g, 0.055 mmol), stirred at r.t. for 3 h and acidified with 0.1 M HCl (50 ml). The separated aqueous layer was extracted with EtOAc (3 × 50 ml), and the combined organic phases were dried and evaporated to leave the carboxylic acid **147** as a white solid (4.0 g, 100%) that was used directly; IR (neat, cm^{-1}) 3700–3200, 1745, 1613, 1514; ^1H NMR (400 MHz, $CDCl_3$): 10.5 (br s, 1 H), 7.27 (d, *J* = 8.6, 2 H), 6.87 (d, *J* = 8.6, 2 H), 4.82 (d, *J* = 11.0, 1 H), 4.58 (d, *J* = 11.0, 1 H), 3.93 (m, 1 H), 3.84 (m, 1 H), 3.81 (s, 3, H), 3.78 (m, 2 H), 3.34 (m, 1 H), 3.19 (t, *J* = 9.4, 1 H), 1.94 (m, 1 H), 1.54 (s, 3 H), 1.45 (s, 3 H), 1.07 (d, *J* = 6.6, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): 173.5, 159.3, 130.6, 129.7 (2C), 113.7 (2C), 99.5, 81.0, 80.7, 75.5, 74.2, 71.8, 62.1, 55.2, 39.3, 29.2, 19.3, 12.9; ES HRMS *m/z* calculated for $C_{19}H_{26}O_7Na$ (M^+ + Na) 389.1571, observed 389.1573; $[\alpha]_D$ +49 (*c* 0.9, $CHCl_3$).

B. Oxidation. A cold (–78 °C) solution of $(COCl)_2$ (0.36 ml, 4.1 mmol) in CH_2Cl_2 (14 ml) was treated dropwise with DMSO (0.44 ml, 6.3 mmol) and stirred for 30 min prior to the introduction of **126** (146 mg, 0.41 mmol) dissolved in CH_2Cl_2 (3 ml). After an additional hour at –78 °C and 1 h at –50 °C, the reaction mixture was returned to –78 °C, treated with Et_3N (1.7 ml, 12.2 mmol), and agitated for another 2 h at –78 °C before being quenched with H_2O (10 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml). The combined organic layers were dried and evaporated, and the residue was taken up in *t*-BuOH/H_2O 10:1 (11 ml) and treated with 2-methyl-2-butene (1 ml). This solution was treated sequentially with NaH_2PO_4 (86 mg, 0.62 mmol) and $NaOCl_2$ (113 mg, 1.2 mmol), stirred at r.t. for 2 h and evaporated under reduced pressure. The residue was further diluted with H_2O and extracted with CH_2Cl_2 (3 × 10 ml). The combined organic phases were washed with brine (10 ml), dried and freed of solvent. Column chromatography (CH_2Cl_2/MeOH 100:0 to 97:3) gave **147** (133 mg, 88% over 2 steps).

Pentafluorophenyl Ester **149**

The acid **147** (110 mg, 0.30 mmol) dissolved in EtOAc (10 ml) was stirred at 0 °C and treated sequentially with pentafluorophenol (60.7 mg, 0.33 mmol), DCC (80 mg, 0.45 mmol) and DMAP (5 mg, 0.004 mmol). After being stirred for 30 min at 0 °C, the mixture was warmed to r.t. for 2 h, diluted with EtOAc (15 ml) and filtered. The solution was concentrated in vacuo to yield a residue which was purified by chromatography (10% EtOAc/hexanes) to yield **149** (174 mg, 100%) as a white solid; IR (neat, cm^{-1}) 2919, 1796, 1520, 1248, 1098, 996; ^1H NMR (400 MHz, $CDCl_3$): 7.29 (d, *J* = 8.8, 2 H), 6.92 (d, *J* = 8.8, 2 H), 4.87 (d, *J* = 11.2, 1 H), 4.63 (d, *J* = 11.2, 1 H), 4.08 (d, *J* = 8.8, 1 H), 3.97 (dd, *J* = 10.8, 5.2, 1 H), 3.97–3.86 (m, 2 H), 3.83 (s, 3 H), 3.41 (ddd, *J* = 9.6, 9.6, 5.2, 1 H), 3.28 (d, *J* = 10.0, 1 H), 2.21–2.07 (m, 1 H), 1.58 (s, 3 H), 1.48 (s, 3 H), 1.21 (d, *J* = 6.4, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): 165.4, 159.4, 142.0, 140.0, 139.0, 137.0, 130.5, 129.9, 124.5, 113.8, 99.6, 81.1, 80.4, 75.7, 74.3, 72.3, 62.1, 55.9, 55.3, 39.5, 34.9, 29.4, 19.3, 12.6; $[\alpha]_D$ +11.7 (*c* 0.35, CH_2Cl_2).

Silylation of **110**

To a cold (–78 °C) solution of **110** (5.0 g, 7.0 mmol) in CH_2Cl_2 (200 ml) was added 2,6-lutidine (2.4 ml, 20.9 mmol) followed by TBSOTf (2.4 ml, 10.5 mmol). The reaction mixture was stirred at this temperature for 6 h, quenched with H_2O (50 ml) and warmed to r.t. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 ml), and the combined organic layers were dried and evaporated. Chromatography of the residue on silica gel (hexanes/EtOAc 98:2) gave **150** (5.8 g, 100%) as a pale yellow oil; IR (neat, cm^{-1}) 1694; ^1H NMR (400 MHz, $CDCl_3$): 7.68 (m, 4 H), 7.41 (m, 6 H), 5.07 (t, *J* = 6.7, 1 H), 4.37 (m, 1 H), 3.73 (m, 1 H), 3.67 (m, 2 H), 3.63 (m, 1 H), 3.42 (dd, *J* = 9.2, 5.6, 1 H), 3.31 (dd, *J* = 17.5, 4.4, 1 H), 2.97 (dd, *J* = 11.4, 0.8, 1 H), 2.36 (m, 1 H), 1.64 (m, 1 H), 1.64–1.50 (m, 4 H), 1.40 (m, 2 H), 1.06 (m, 12 H), 0.96 (m, 12 H), 0.90 (d, *J* = 11.9, 3 H), 0.87 (s, 9 H), 0.59 (q, *J* = 7.7, 6 H), 0.08 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 202.5, 172.0, 135.6 (4C), 134.1 (2C), 129.2 (2C), 127.5 (4C), 73.2, 71.6, 69.7, 64.0, 44.4, 42.9, 34.6, 33.2, 30.7 (2C), 26.9 (3C), 26.0 (3C), 21.1, 19.2, 19.1, 18.2, 17.8, 10.6, 7.0 (3C), 5.4 (3C), –4.2 (2C); ES HRMS *m/z* calculated for $C_{44}H_{75}NO_4S_2Si_3Na$ (M^+ + Na) 852.4337, observed 852.4323; $[\alpha]_D$ –129 (*c* 1.3, $CHCl_3$).

Alcohol **151**

A cold (0 °C), stirred solution of **150** (5.8 g, 7.0 mmol) in THF (200 ml) was treated with H_2O (629 μl, 35 mmol) followed by $LiBH_4$ (769 mg, 35 mmol), stirred at this temperature for 10 h and slowly quenched with pH 7 buffer solution (100 ml). The separated aqueous phase was extracted with EtOAc (3 × 100 ml). The combined organic layers were dried and evaporated, and the residue was purified by chromatography on silica gel (hexanes/EtOAc 98:2) to provide **151** (3.74 g, 78%) as a colorless oil; IR (neat, cm^{-1}) 3410, 1462; ^1H NMR (400 MHz, $CDCl_3$): 7.68 (m, 4 H), 7.41 (m, 6 H), 3.87 (m, 1 H), 3.77 (m, 2 H), 3.69 (m, 1 H), 3.66 (t, *J* = 6.4, 2 H), 2.15 (br s, 1 H), 1.85 (m, 2 H), 1.72 (m, 1 H), 1.60–1.41 (m, 4 H), 1.34 (m, 2 H), 1.06 (s, 9 H), 0.97 (t, *J* = 8.0, 9 H), 0.93 (s, 9 H), 0.88 (d, *J* = 6.9, 3 H), 0.59 (q, *J* = 7.8, 6 H), 0.13 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 135.6 (4C), 134.1 (2C), 129.5 (2C), 127.6 (4C), 72.7, 72.3, 63.8, 60.0, 40.9, 35.8, 35.2, 33.0, 26.9 (3C), 25.9 (3C), 21.8, 18.0 (2C), 9.9, 7.0 (3C), 5.5 (3C), –4.2, –4.4; ES HRMS *m/z* calculated for $C_{38}H_{68}O_4Si_3Na$ (M^+ + Na) 695.4318, observed 695.4352; $[\alpha]_D$ –5.1 (*c* 1.1, $CHCl_3$).

Iodide **152**

To a stirred solution of **151** (3.74 g, 5.45 mmol) in PhH (100 ml) was added imidazole (1.85 g, 27 mmol), PPh_3 (2.85 g, 10.9 mmol) and I_2 (2.77 g, 10.9 mmol). After 1 h of stirring at r.t., additional I_2 (140 mg, 0.54 mmol) was introduced. After a further 10 min, saturated $Na_2S_2O_3$ solution (20 ml), H_2O (20 ml) and EtOAc were added. Following extraction of the aqueous phase with EtOAc (2 × 50 ml), the combined organic layers were dried and evaporated. Purification of the crude product by chromatography on silica gel (hexanes/EtOAc 99:1) afforded **152** (4.3 g, 99%) as a colorless oil; IR (neat, cm^{-1}) 1471, 1462; ^1H NMR (400 MHz, $CDCl_3$): 7.67 (m, 4 H), 7.41 (m, 6 H), 3.80 (m, 1 H), 3.69 (m, 1 H), 3.66 (t, *J* = 6.4, 2 H), 3.15 (t, *J* = 7.4, 2 H), 2.08 (m, 2 H), 1.65–1.46 (m, 5 H), 1.09 (s, 9 H), 0.97 (t, *J* = 7.8, 9 H), 0.92 (d, *J* = 6.9, 3 H), 0.89 (s, 9 H), 0.60 (q, *J* = 8.0, 6 H), 0.09 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 135.6 (4C), 134.1 (2C), 129.5 (2C), 127.6 (4C), 74.0, 72.2, 63.9, 41.0, 38.8, 35.0, 33.1, 26.9 (3C), 25.9 (3C), 21.5, 19.2 (2C), 9.8, 7.0 (3C), 5.5 (3C), 2.8,

–4.0, –4.2; ES HRMS *m/z* calculated for $C_{38}H_{67}IO_3Si_3Na$ (M^+ + Na) 805.3334, observed 805.3329; $[\alpha]_D$ –9.5 (*c* 1.8, $CHCl_3$).

Sulfone **153**

A solution of **152** (4.3 g, 5.5 mmol) in DMF (100 ml) was treated with $PhSO_2Na$ (8.8 g, 54 mmol), heated at 60 °C for 3 h and cooled prior to dilution with Et_2O (200 ml) and H_2O (100 ml). The organic phase was washed with brine (50 ml) and the aqueous layer was extracted with Et_2O (3 × 100 ml). The combined organic solutions were dried and evaporated, and the residue was subjected to chromatography on silica gel (hexanes/EtOAc 99:1 to 95:5) to furnish of **153** (3.96 g, 92%) as a colorless gum; IR (neat, cm^{-1}) 1471, 1428, 1389; ^1H NMR (500 MHz, $CDCl_3$): 7.89 (d, *J* = 7.2, 2 H), 7.68 (m, 4 H), 7.63 (d, *J* = 7.5, 1 H), 7.54 (t, *J* = 7.9, 2 H), 7.39 (m, 6 H), 3.72 (m, 1 H), 3.65 (t, *J* = 6.4, 2 H), 3.61 (m, 1 H), 3.16 (m, 1 H), 3.07 (m, 1 H), 2.10–1.83 (m, 2 H), 1.53 (m, 2 H), 1.43–1.34 (m, 3 H), 1.17 (m, 2 H), 1.06 (s, 9 H), 0.91 (t, *J* = 7.8, 9 H), 0.85 (s, 9 H), 0.82 (d, *J* = 6.8, 3 H), 0.52 (q, *J* = 7.9, 6 H), 0.01 (s, 3 H), –0.05 (s, 3 H);^{13}C NMR (75 MHz, $CDCl_3$): 139.2, 135.5 (4C), 134.0 (2C), 133.5, 129.5 (2C), 129.2 (2C), 128.0 (2C), 127.6 (4C), 72.1, 71.7, 63.7, 52.1, 41.0, 34.9, 32.9, 27.2, 26.9 (3C), 25.8 (3C), 22.0, 19.2, 18.0, 9.8, 7.0 (3C), 5.4 (3C), –4.4, –4.6; ES HRMS *m/z* calculated for $C_{44}H_{72}O_5SSi_3Na$ (M^+ + Na) 819.4300, observed 819.4252; $[\alpha]_D$ +3.4 (*c* 1.72, $CHCl_3$).

Keto Sulfone **154**

A. From the acid chloride. Acid **147** (3.0 g, 8.2 mmol) dissolved in CH_2Cl_2 (50 ml) was treated with 1-chloro-*N*,*N*-2-trimethylpropenylamine (2.2 ml, 16.4 mmol), stirred at r.t. for 10 h, evaporated and dried under high vacuum for 3 h. The resulting solid was dissolved in dry THF (50 ml), and added to a cold (–78 °C) solution prepared from sulfone **153** and 2.5 M *n*-BuLi in hexanes (3.3 ml, 8.2 mmol). Immediately after this addition, a saturated solution of NH_4Cl (50 ml) was introduced and the reaction mixture was allowed to warm to r.t. prior to extraction of the aqueous phase with EtOAc (3 × 50 ml). The combined organic phases were dried and evaporated in advance of chromatographic purification of the residue on silica gel (hexanes/EtOAc 99:1 to 90:10). Product **154** (8.8 g, 94%) was isolated as a yellowish viscous oil; IR (neat, cm^{-1}) 1732, 1463, 1428; ^1H NMR (500 MHz, $CDCl_3$): 7.75 (d, *J* = 7.4, 2 H), 7.71–7.63 (m, 5 H), 7.53 (m, 2 H), 7.45–7.35 (m, 6 H), 7.28 (d, *J* = 8.6, 2 H), 6.88 (d, *J* = 8.6, 2 H), 4.81 (d, *J* = 11.0, 1 H), 4.76 (dd, *J* = 9.5, 3.1, 1 H), 4.57 (d, *J* = 11.0, 1 H), 4.01 (d, *J* = 10.6, 1 H), 3.85 (dd, *J* = 10.5, 5.2, 1 H), 3.82 (s, 3 H), 3.78 (dd, *J* = 8.8, 2.4, 1 H), 3.72–3.57 (m, 4 H), 3.50 (m, 1 H), 3.38 (m, 1 H), 3.18 (t, *J* = 5.6, 1 H), 2.20 (m, 1 H), 1.99 (m, 1 H), 1.94 (m, 1 H), 1.60–1.52 (m, 5 H), 1.48 (s, 3 H), 1.44 (s, 3 H), 1.43 (m, 1 H), 1.37 (m, 1 H), 1.07 (s, 9 H), 1.05 (d, *J* = 6.3, 3 H), 0.95 (t, *J* = 8.0, 9 H), 0.81 (s, 9 H), 0.76 (d, *J* = 6.7, 3 H), 0.58 (q, *J* = 7.8, 6 H), –0.04 (s, 3 H), –0.12 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): 196.3, 159.1, 137.2, 136.9, 135.4 (4C), 134.1, 133.9 130.7 (2C), 129.6 (2C), 129.5 (2C), 129.4 (2C), 129.1, 128.6, 127.5 (4C), 113.6, 99.2, 84.2, 80.8, 75.5, 74.0, 72.1, 71.8, 71.7, 71.5, 68.1, 63.7, 62.0, 55.5, 41.1, 37.2, 35.1, 33.0, 31.7, 29.1, 26.8 (3C), 25.8 (3C), 21.3, 19.1, 17.8, 13.7, 9.3, 6.9 (3C), 5.3 (3C), –4.3, –4.9; ES HRMS *m/z* calculated for $C_{63}H_{96}O_{11}SSi_3Na$ (M^+ + Na) 1167.5873, observed 1167.5853.

B. From the pentafluorophenyl ester. To a cold (–78 °C) solution of sulfone **153** (425 mg, 0.55 mmol) in dry THF (2 ml) was added 1.38 M *n*-BuLi in hexanes (0.40 ml, 0.55 mmol) dropwise. The resulting yellow solution was stirred at –78 °C for 2 h before pentafluorophenyl ester **149** (146 mg, 0.275 mmol) was added via cannula as a solution in THF (2 ml).

After 30 min, the reaction mixture was quenched with saturated NH_4Cl, warmed to r.t., transferred to a separatory funnel, and extracted with CH_2Cl_2 (3 × 10 ml). The combined organic phases were dried, filtered and concentrated in vacuo to yield a residue which could be purified by chromatography (10% EtOAc/hexanes) to provide **154** (260 mg, 83%) as a yellowish, viscous oil, whose spectral features are consistent with those reported above.

Triol **155**

A cold (0 °C) stirred solution of **154** (4.0 g, 3.5 mmol) in dry THF (50 ml) was treated with *t*-BuOK (430 mg, 3.83 mmol) and stirred at this temperature for 1 h prior to the introduction of a solution of oxaziridine **144** (1.68 g, 5.24 mmol) in dry THF (30 ml). After 1 h at 0 °C, the reaction mixture was quenched with saturated NH_4Cl solution (50 ml), and the separated aqueous phase was extracted with EtOAc (3 × 50 ml). The combined organic solutions were dried and concentrated to leave a residue that was dissolved in THF/ethylene glycol 10:1 (100 ml), treated with TsOH (729 mg, 3.8 mmol) and stirred for 2 h before being quenched with saturated $NaHCO_3$ solution (100 ml). The separated aqueous phase was extracted with EtOAc (3 × 100 ml), and the combined organic layers were dried and evaporated. Purification of the residue by chromatography on silica gel (hexanes/EtOAc 90:10 to 60:40) afforded **155** (1.51 g, 50% over 2 steps) as a white amorphous solid, m.p. 45–46 °C; IR (neat, cm^{-1}) 3437, 1745, 1613, 1514; ^1H NMR (500 MHz, C_6D_6): 7.80 (m, 4 H), 7.28 (m, 8 H), 6.82 (d, *J* = 8.6, 2 H), 6.10 (s, 1 H), 4.62 (d, *J* = 10.4, 2 H), 4.58 (d, *J* = 11.3, 1 H), 4.57 (m, 1 H), 3.86 (dd, *J* = 10.9, 7.7, 1 H), 3.83–3.73 (m, 3 H), 3.70 (t, *J* = 6.1, 2 H), 3.44 (m, 1 H), 3.32 (s, 3 H), 3.17 (t, *J* = 9.5, 1 H), 2.57–2.43 (m, 2 H), 2.22 (dd, *J* = 14.6, 2.5, 1 H), 1.75 (dd, *J* = 14.6, 2.8, 1 H), 1.69–1.55 (m, 4 H), 1.55–1.41 (m, 2 H), 1.41–1.26 (m, 2 H), 1.18 (s, 9 H), 1.13 (d, *J* = 6.6, 3 H), 0.84 (s, 9 H), 0.69 (d, *J* = 7.1, 3 H), –0.10 (s, 6 H); ^{13}C NMR (125 MHz, C_6D_6): 200.1, 159.7, 136.0 (4C), 134.4, 131.8 (2C), 130.0 (2C), 129.6 (4C), 128.1 (2C), 114.1 (2C), 97.3, 86.6, 81.1, 78.6, 74.0, 73.1, 72.3, 66.7, 64.1, 63.1, 54.8, 38.8, 37.8, 32.8, 32.0, 31.5, 27.1 (3C), 25.7 (3C), 22.5, 19.5, 17.9, 13.4, 10.3, –5.2, –5.3; ES HRMS *m/z* calculated for $C_{48}H_{72}O_{10}Si_2Na$ (M^+ + Na) 887.4556, observed 887.4543; $[\alpha]_D$ +11 (*c* 0.8, CH_2Cl_2).

Dihydroxy Iodide **156**

A stirred solution of **155** (1.51 g, 1.75 mmol) in PhH (50 ml) was treated with pyridine (705 μl, 8.73 mmol), PPh_3 (2.28 g, 1.75 mmol) and I_2 (887 mg, 3.49 mmol), heated at reflux for 1 h, cooled to r.t. and diluted with EtOAc (50 ml) and H_2O (50 ml). The separated aqueous layer was extracted with EtOAc (3 × 50 ml), and the combined organic solutions were dried and evaporated. The product was purified by chromatography on silica gel (hexanes/EtOAc 95:5 to 90:10) to give **156** as a colorless oil (1.70 g, 100%); IR (neat, cm^{-1}) 3462, 1746, 1612, 1514; ^1H NMR (500 MHz, C_6D_6): 7.79 (m, 4 H), 7.26 (m, 6 H), 7.16 (d, *J* = 8.6, 2 H), 6.80 (d, *J* = 8.6, 2 H), 6.03 (s, 1 H), 4.64 (d, *J* = 10.5, 1 H), 4.55 (m, 1 H), 4.46 (d, *J* = 11.4, 1 H), 4.40 (d, *J* = 11.4, 1 H), 3.80 (br d, *J* = 2.8, 1 H), 3.79 (t, *J* = 5.7, 2 H), 3.39 (d, *J* = 8.3, 1 H), 3.31 (s, 3 H), 3.14–3.02 (m, 2 H), 2.98 (t, *J* = 10.3, 1 H), 2.54 (m, 1 H), 2.30 (dd, *J* = 14.5, 2.6, 1 H), 1.87 (dd, *J* = 14.5, 2.8, 1 H), 1.72–1.58 (m, 4 H), 1.56 (br d, *J* = 3.8, 1 H), 1.55–1.50 (m, 1 H), 1.50–1.39 (m, 1 H), 1.39–1.30 (m, 2 H), 1.18 (s, 9 H), 1.07 (d, *J* = 6.5, 3 H), 0.87 (s, 9 H), 0.74 (d, *J* = 7.1, 3 H), –0.04 (s, 3 H), –0.08 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6): 199.4, 159.7, 135.9 (4C), 134.3 (2C), 131.2, 129.9 (2C), 129.5 (2C), 128.0 (4C), 114.2 (2C), 97.5, 86.3, 80.1, 78.8, 74.9, 73.7, 73.0, 66.6, 64.0 (2C), 54.9, 38.2, 37.8,

32.8, 32.0, 27.1 (3C), 26.0, 25.8 (3C), 22.5, 19.4, 17.9, 13.3, 10.4, 7.3, –5.1(2C); ES HRMS *m/z* calculated for $C_{48}H_{71}IO_9Si_2Na$ (M^+ + Na) 997.3573, observed 997.3513; $[\alpha]_D$ +9.7 (*c* 1.17, $CHCl_3$).

Reduction of **156**

To a cold (0 °C), stirred solution of **156** (1.0 g, 1.0 mmol) in THF/MeOH 3:1 (40 ml) was added $CeCl_3 \cdot 7H_2O$ (1.9 g, 5.1 mmol) followed immediately by $NaBH_4$ (78 mg, 2.05 mmol). After 15 min, saturated NH_4Cl solution (10 ml) was introduced and the separated aqueous layer was extracted with EtOAc (3 × 20 ml). The combined organic solutions were dried and concentrated. The residue was purified by chromatography on silica gel (hexanes/EtOAc 99:5 to 90:10) to afford **157** (877 mg, 87%) and **158** (50 mg, 5%).

For **157**: amorphous white solid, m.p. 53–55 °C; IR (neat, cm^{-1}) 3473, 1513, 1471; ^1H NMR (500 MHz, C_6D_6): 7.81 (m, 4 H), 7.25 (m, 6 H), 7.16 (d, *J* = 8.6, 2 H), 6.80 (d, *J* = 8.6, 2 H), 5.52 (s, 1 H), 4.61 (m, 1 H), 4.44 (d, *J* = 11.3, 1 H), 4.37 (d, *J* = 11.3, 1 H), 4.01 (br d, *J* = 3.0, 1 H), 3.81 (d, *J* = 10.5, 1 H), 3.77 (d, *J* = 7.3, 1 H), 3.69 (t, *J* = 6.1, 2 H), 3.47 (dd, *J* = 10.5, 1.7, 1 H), 3.31 (s, 3 H), 3.16–3.05 (m, 2 H), 2.95 (dd, *J* = 10.5, 7.8, 1 H), 2.82 (dd, *J* = 10.5, 8.3, 1 H), 2.52 (d, *J* = 7.2, 1 H), 2.51 (dd, *J* = 15.0, 2.8, 1 H), 2.30 (m, 1 H), 2.23 (dd, *J* = 14.8, 3.0, 1 H), 1.73–1.57 (m, 4 H), 1.52 (d, *J* = 3.5, 1 H), 1.49 (m, 1 H), 1.35 (m, 1 H), 1.20 (s, 9 H), 1.02–0.95 (m, 12 H), 0.82 (d, *J* = 7.1, 3 H), 0.13 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6): 159.8, 136.0 (4C), 134.5 (2C), 131.4, 129.9 (2C), 129.4 (2C), 128.5 (4C), 114.2 (2C), 99.1, 86.5, 79.8, 79.6, 75.0, 74.5, 73.7, 73.3, 66.5, 64.1, 54.8, 38.2, 38.1, 33.1, 33.0, 32.5, 27.2 (3C), 25.9 (3C), 22.7, 19.5, 18.1, 13.1, 10.5, 7.2, –4.7, –4.8; ES HRMS *m/z* calculated for $C_{48}H_{73}IO_9Si_2Na$ (M^+ + Na) 999.3730, observed 999.3774; $[\alpha]_D$ +0.6 (*c* 0.9, CH_2Cl_2).

For **158**: colorless gum; IR (neat, cm^{-1}) 3484, 1715, 1613, 1514; ^1H NMR (500 MHz, C_6D_6): 7.77 (m, 4 H), 7.24 (m, 6 H), 7.16 (d, *J* = 8.6, 2 H), 6.78 (d, *J* = 8.6, 2 H), 4.51 (d, *J* = 11.3, 1 H), 4.41 (d, *J* = 11.3, 1 H), 4.27 (m, 1 H), 4.19 (s, 1 H), 3.77 (d, *J* = 11.5, 1 H), 3.73 (m, 1 H), 3.68 (t, *J* = 5.7, 2 H), 3.32–3.25 (m, 4 H), 3.14–3.06 (m, 2 H), 2.97 (d, *J* = 10.0, 1 H), 2.82–2.74 (m, 2 H), 2.42 (m, 1 H), 2.33 (m, 1 H), 1.78 (m, 1 H), 1.74–1.61 (m, 3 H), 1.61–1.51 (m, 3 H), 1.33 (d, *J* = 6.5, 3 H), 1.28 (m, 1 H), 1.17 (s, 9 H), 1.09 (d, *J* = 7.1, 3 H), 0.96 (s, 9 H), 0.12 (s, 3 H), –0.03 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6): 211.9, 159.8, 136.0 (4C), 134.5, 131.3, 129.8 (2C), 129.4 (2C) 128.3 (4C), 114.2 (2C), 99.1, 86.5, 86.4, 77.7, 74.5, 74.4, 73.2, 70.9, 64.2, 54.8, 46.4, 44.5, 37.7, 34.5, 32.7, 27.1 (3C), 26.0 (3C), 22.9, 19.5 (2C), 18.3, 13.5, 10.4, 8.1, –4.6, –4.9; ES HRMS *m/z* calculated for $C_{48}H_{71}IO_9Si_2Na$ (M^+ + Na) 997.3574, observed 997.3638; $[\alpha]_D$ –7.9 (*c* 0.76, CH_2Cl_2).

Methyl Pyranoside **159**

To a stirred solution of lactol **157** (877 mg, 0.90 mmol) in CH3CN (20 ml) was added $NaHCO_3$ (1.5 g, 18 mmol) followed by a 1 M solution of ZnI_2 in MeOH (4.5 ml, 4.5 mmol). The reaction mixture was stirred at r.t. for 3 h prior to the addition of $NaHSO_3$ (1.5 g) and Et_3N (20 ml). The separated aqueous layer was extracted with EtOAc (3 × 20 ml), and the combined organic solutions were dried and evaporated to leave a residue that was purified by chromatography on silica gel (1–5% CH_2Cl_2/acetone) to furnish **159** (755 mg, 85%; 95% brsm) and unreacted **157** (125 mg, 13%).

For **159**: amorphous white solid, m.p. 54–55 °C; IR (neat, cm^{-1}) 3483, 1614, 1514; ^1H NMR (400 MHz, C_6D_6): 7.81 (m, 4 H), 7.26 (m, 6 H), 7.20 (d, *J* = 8.6, 2 H), 6.83 (d, *J* = 8.6, 2 H), 4.47 (d, *J* = 11.4, 1 H), 4.43 (d, *J* = 11.4, 1 H), 4.36 (m, 1 H), 4.01 (br d, *J* = 2.8, 1 H), 3.85 (d, *J* = 6.6, 1 H), 3.72 (t, *J* = 6.3, 2 H), 3.44 (dd, *J* = 10.6, 2.0, 1 H), 3.36 (d, *J* = 10.4, 1 H), 3.32 (s, 3 H), 3.24 (s, 3 H), 3.08 (m, 1 H), 2.98 (dd, *J* = 10.5, 7.4, 1 H), 2.91 (dt, *J* = 9.2, 1.9, 1 H), 2.74 (dd, *J* = 10.4, 8.9, 1 H), 2.39 (dd, *J* = 15.3, 3.9, 1 H), 2.27 (d, *J* = 6.6, 1 H), 2.19–2.12 (m, 2 H), 1.82–1.77 (m, 1 H), 1.77–1.54 (m, 4 H), 1.50 (m, 1 H), 1.47 (d, *J* = 4.0, 1 H), 1.33 (m, 1 H), 1.21 (s, 9 H), 1.09 (s, 9 H), 0.91 (m, 6 H), 0.27 (s, 3 H), 0.15 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 159.9, 136.0 (4C), 134.5 (2C), 131.4, 130.0 (2C), 129.5 (2C), 128.2 (4C), 114.3 (2C), 101.3, 86.2, 79.1, 78.5, 75.0, 73.8, 71.0, 70.8, 67.4, 64.1, 54.9, 47.5, 38.9, 38.4, 33.1, 32.9, 31.9, 27.2 (3C), 26.2 (3C), 23.0, 19.6, 18.4, 13.4, 10.4, 7.2, –3.9, –4.5; ES HRMS *m/z* calculated for $C_{49}H_{75}IO_9Si_2Na$ (M^+ + Na) 1013.3887, observed 1013.3962; $[\alpha]_D$ +5.7 (*c* 1.2, CH_2Cl_2).

Methylenepyran **161**

A solution of **159** (100 mg, 0.10 mmol) and DBU (124 µl, 1.01 mmol) in DMF (2 ml) was stirred at 60 °C for 24 h, cooled to r.t. and diluted with Et_2O (10 ml) and H_2O (5 ml). The resulting organic phase was washed with brine (2 × 5 ml) and the aqueous phase was extracted with Et_2O (3 × 10 ml). The combined organic solutions were dried and evaporated to leave a residue that was purified by chromatography on silica gel (1–10% EtOAc/hexanes) to afford **161** (70 mg, 80%) as a colorless oil; ^1H NMR (500 MHz, C_6D_6): 7.78 (m, 4 H), 7.26–7.22 (m, 8 H), 6.80 (d, *J* = 8.6, 2 H), 4.96 (d, *J* = 1.7, 1 H), 4.90 (d, *J* = 1.7, 1 H), 4.75 (d, *J* = 11.3, 1 H), 4.54 (d, *J* = 11.3, 1 H), 4.30 (m, 1 H), 4.09 (br d, *J* = 8.6, 1 H), 3.82 (m, 2 H), 3.68 (t, *J* = 6.0, 2 H), 3.56 (d, *J* = 10.6, 1 H), 3.30 (s, 3 H), 3.14 (s, 3 H), 2.99 (t, *J* = 10.1, 1 H), 2.36 (m, 1 H), 2.28 (dd, *J* = 15.8, 3.8, 1 H), 2.23 (br s, 1 H), 2.11 (br d, *J* = 5.8, 1 H), 2.04 (d, *J* = 15.3, 1 H), 1.70 (m, 1 H), 1.62–1.55 (m, 2 H), 1.53 (m, 1 H), 1.40 (m, 1 H), 1.33 (m, 1 H), 1.27 (m, 1 H), 1.17 (s, 9 H), 1.06 (m, 9 H), 0.90 (d, *J* = 6.5, 3 H), 0.84 (d, *J* = 7.11, 3 H), 0.20 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6): 161.5, 159.8, 136.0 (4C),134.5, 131.6, 130.0 (2C), 129.7 (2C), 128.4, 128.3 (4C), 114.2 (2C), 101.4, 92.7, 85.9, 80.7, 74.3, 73.6, 71.1, 70.7, 67.4, 64.1, 54.8, 47.4, 38.8, 38.5, 38.3, 33.1, 32.9, 31.0, 27.2, 26.2 (3C), 23.0, 19.6, 18.4, 13.4, 10.4, –4.2, –4.7; ES HRMS *m/z* calculated for $C_{49}H_{74}O_9Si_2Na$ (M^+ + Na) 885.4764, observed 885.4822; $[\alpha]_D$ +11 (*c* 2.2, CH_2Cl_2).

Methylenepyran **162**

A cold (0 °C) solution of **159** (50 mg, 0.051 mmol) in a 10:1 mixture of CH_2Cl_2 and DMF (1 ml) was added pyridine (203 µl, 2.5 mmol), DMAP (31 mg, 0.25 mmol) and TMSCl (129 µl, 1.01 mmol). The resulting mixture was warmed to r.t., stirred for 24 h and quenched with H_2O (1 ml). The separated aqueous layer was washed with brine (2 × 5 ml). The combined organic solutions were dried and concentrated. The unpurified **160** so obtained was used directly; ^1H NMR (500 MHz, C_6D_6): 7.80 (m, 4 H), 7.34 (d, *J* = 8.5, 2 H), 7.25 (m, 6 H), 6.83 (d, *J* = 8.5, 2 H), 4.87 (d, *J* = 11.3, 1 H), 4.50 (d, *J* = 11.3, 1 H), 4.31 (m, 1 H), 4.04 (br s, 1 H), 3.90 (s, 1 H), 3.72 (t, *J* = 5.9, 2 H), 3.59 (d, *J* = 7.8, 1 H), 3.49 (t, *J* = 8.2, 1 H), 3.41 (d, *J* = 10.5, 1 H), 3.31 (s, 3 H), 3.18 (s, 3 H), 3.12 (d, *J* = 7.7, 2 H), 2.90 (t, *J* = 10.0, 1 H), 2.53 (dd, *J* = 15.4, 3.7, 1 H), 2.29 (br d, *J* = 15.1, 1 H), 2.05 (m, 1 H), 1.80–1.63 (m, 4 H), 1.63–1.55 (m, 1 H), 1.51–1.43 (m, 1 H), 1.36–1.28 (m, 1 H), 1.20 (s, 9 H), 1.11 (s,

9 H), 0.96 (d, *J* = 6.6, 3 H), 0.95 (d, *J* = 6.2, 3 H), 0.30 (s, 3 H), 0.26 (s, 9 H), 0.17 (s, 3 H), 0.14 (s, 9 H).

The iodide produced above was heated with DBU (62 μl, 0.51 mmol) in DMF (1 ml) at 60 °C for 24 h. The prior workup was applied and gave **162** (41 mg, 80% over 2 steps) as a colorless oil; IR (neat, cm^{-1}) 1514, 1463, 1428; ^1H NMR (500 MHz, C_6D_6): 7.78 (m, 4 H), 7.32 (d, *J* = 8.6, 2 H), 7.25 (m, 6 H), 6.81 (d, *J* = 8.6, 2 H), 5.02 (d, *J* = 11.3, 1 H), 5.00 (d, *J* = 1.7, 1 H), 4.93 (d, *J* = 1.7, 1 H), 4.59 (d, *J* = 11.3, 1 H), 4.27 (d, *J* = 5.8, 2 H), 3.91 (s, 1 H), 3.87 (d, *J* = 2.6, 1 H), 3.70 (m, 2 H), 3.65 (d, *J* = 10.7, 1 H), 3.30 (s, 3 H), 3.16 (m, 1 H), 3.10 (s, 3 H), 2.49 (dd, *J* = 15.3, 3.8, 1 H), 2.24–2.18 (m, 2 H), 1.72–1.61 (m, 4 H), 1.61–1.53 (m, 1 H), 1.43 (m, 1 H), 1.31 (m, 1 H), 1.19 (s, 9 H), 1.10 (s, 9 H), 0.93 (m, 6 H), 0.25 (s, 12 H), 0.18 (s, 9 H), 0.13 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6): 162.5, 159.8, 136.0 (4C), 134.5, 131.6, 130.0 (2C), 129.7 (2C), 128.4, 128.3 (4C), 114.1 (2C), 107.7, 93.3, 85.9, 81.6, 75.4, 75.3, 71.7, 71.3, 67.4, 64.3, 54.5, 47.0, 39.0, 38.8, 33.2, 33.0, 31.1, 27.2 (3C), 26.2 (3C), 23.1, 19.5, 18.5, 13.8, 10.8, 1.4 (3C), 0.30 (3C), –4.2, –4.7; ES HRMS *m/z* calculated for $C_{55}H_{90}O_9Si_4Na$ (M^+ + Na) 1029.5554, observed 1029.5549; $[\alpha]_D$ +12 (*c* 0.65, CH_2Cl_2).

Acetylenic Alcohol **163**

To a solution of (*R*)-glycidol (*ent*-**52**, 140 mg, 2.0 mmol) in CH_2Cl_2 (2 ml) was added pyridine (0.81 ml, 10 mmol) and PivCl (0.32 ml, 2.6 mmol) at 0 °C. After being stirred at r.t. for 5 h, the mixture was diluted with Et_2O (20 ml) and washed with 1 M HCl, 1 M $NaHCO_3$ solution and brine. After drying and solvent evaporation, the epoxy pivalate (320 mg, 99%) was used directly in the next step; IR (neat, cm^{-1}) 3501, 1731, 1481, 1397; ^1H NMR (300 MHz, $CDCl_3$): 4.30 (dd, *J* = 3.0, 12.4, 1 H), 3.84 (dd, *J* = 6.0, 12.4, 1 H), 3.10 (m, 1 H), 2.74 (dd, *J* = 4.2, 4.2, 1 H), 2.55 (dd, *J* = 2.6, 4.9, 1 H), 1.15 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 178.2, 64.5, 49.3, 44.3, 38.7, 27.0 (3C); $[\alpha]_D$ +20.7 (*c* 1.81, $CHCl_3$).

A cold (–78 °C) solution of trimethylsilylacetylene (0.42 ml, 3.0 mmol) in THF (15 ml) was treated with 1.38 M *n*-BuLi in hexanes (2.2 ml, 3.0 mmol) and stirred for 20 min prior to the addition of $BF_3{\cdot}OEt_2$ (0.63 ml, 5.0 mmol). After 10 min, the epoxide from above (310 mg, 2.0 mmol) was added at –78 °C, and the solution was stirred for 30 min, diluted with NH_4Cl solution and extracted with CH_2Cl_2. The combined organic layers were dried and freed of solvent to leave a residue that was purified chromatographically on silica gel (100% hexanes) to give **163** (350 mg, 68% over 2 steps) as a colorless oil; IR (neat, cm^{-1}) 3474, 1731, 1712, 1481; ^1H NMR (300 MHz, $CDCl_3$): 4.15 (ddd, *J* = 1.5, 4.6, 11.5, 1 H), 4.09 (ddd, *J* = 1.3, 5.6, 11.4, 1 H), 3.96 (m, 1 H), 2.53 (br s, 1 H), 2.45 (dd, *J* = 1.3, 6.2, 2 H), 1.20 (s, 9 H), 0.10 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 178.6, 101.7, 88.1, 68.2, 66.9, 38.8, 27.1 (3C), 25.2, –0.7 (3C); $[\alpha]_D$ +10 (*c* 1.2, $CHCl_3$).

Iodopivalate **164**

A solution of **163** (500 mg, 1.95 mmol) in THF (10 ml) was treated with, 1 M TBAF in THF (2.9 ml, 2.9 mmol), stirred for 1 h and diluted with saturated $NaHCO_3$ solution. The separated aqueous layer was extracted with CH_2Cl_2, and the combined organic phases were dried and evaporated to leave a residue that was purified by chromatography on silica gel (10% EtOAc/hexanes) to yield the free alcohol (350 mg, 98%) as a colorless oil; IR (neat, cm^{-1}) 3460, 1730, 1481, 1285; ^1H NMR (300 MHz, $CDCl_3$): 4.23 (dd, *J* = 5.9, 11.5, 1 H), 4.17 (dd, *J* = 4.4, 11.5, 1 H), 4.05 (m, 1 H), 2.48 (dd, *J* = 2.7, 6.4, 2 H), 2.37 (d, *J* = 5.2, 1 H), 2.09 (dd,

J = 2.7, 2.7, 1 H), 1.24 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 178.6, 79.6, 71.0, 68.2, 66.8, 38.8, 27.1 (3C), 23.7; ES HRMS *m/z* calculated for $C_{10}H_{16}O_3Na$ (M^+ + Na) 207.0992, observed 207.1010; $[\alpha]_D$ +8.8 (*c* 0.8, $CHCl_3$).

To a solution of 1 M *B*-iodo-9-BBN in THF (4.27 ml, 4.27 mmol) in pentane (7 ml) was added the above product (314 mg, 1.71 mmol) dissolved in pentane (3 ml) at –25 °C. The reaction mixture was stirred for 2 h, quenched with AcOH (1 ml) and kept at 0 °C for 1 h. At this point, 3 M NaOH (24 ml) and 30% H_2O_2 (4 ml) were introduced and stirring was maintained for 30 min at r.t. The separated aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried and evaporated. Purification was achieved by chromatography on silica gel (7% EtOAc/hexanes) to give the vinyl iodide (420 mg, 79%) as a colorless oil; IR (neat, cm^{-1}) 3448, 1734, 1618, 1480; ^{1}H NMR (300 MHz, $CDCl_3$): 6.19 (s, 1 H), 5.85 (s, 1 H), 4.12 (m, 3 H), 2.60 (m, 2 H), 2.30 (br s, 1 H), 1.25 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 178.6, 129.0, 105.6, 68.5, 60.8, 49.1, 38.9, 27.2 (3C); ES HRMS *m/z* calculated for $C_{10}H_{17}IO_3Na$ (M^+ + Na) 335.0115, observed 335.0089; $[\alpha]_D$ +3.7 (*c* 2.5, $CHCl_3$).

To a solution of the above vinyl iodide (87 mg, 0.278 mmol) in DMF (2 ml) was added imidazole (95 mg, 1.4 mmol) and TBSCl (85 mg, 0.56 mmol) at r.t. The reaction mixture was stirred for 4 h, diluted with Et_2O, and washed in turn with aqueous 1 M HCl and aqueous $NaHCO_3$ solution. The organic layers were dried and concentrated to leave a residue, which was purified by column chromatography on silica gel (1% EtOAc/hexanes) to give **164** (110 mg, 94%) as a colorless oil; IR (neat, cm^{-1}) 1732, 1281, 1157; ^{1}H NMR (75 MHz, $CDCl_3$): 6.06 (dd, *J* = 1.1, 1 H), 5.73 (d, *J* = 1.2, 1 H), 4.05 (m, 1 H), 3.99 (m, 2 H), 2.59 (ddd, *J* = 0.9, 4.7, 14.1, 1 H), 2.50 (ddd, *J* = 0.7, 7.0, 14.1, 1 H), 1.18 (s, 9 H), 0.59 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 177.9, 128.6, 106.9, 68.8, 66.6, 50.6, 38.7, 27.2 (3C), 25.7 (3C), 17.9, –4.4, –4.6; ES HRMS *m/z* calculated for $C_{16}H_{31}IO_3Si_3Na$ (M^+ + Na) 449.0979, observed 449.0959; $[\alpha]_D$ –0.76 (*c* 2.1, $CHCl_3$).

Iodo Aldehyde **165**

A solution of **164** (300 mg, 0.70 mmol) in THF (5 ml) was cooled to –78 °C, treated with 1 M Dibal-H in THF (3.18 ml, 3.18 mmol), stirred for 4 h and quenched with Rochelle's salt solution. After 1 h, the product was extracted into CH_2Cl_2. The combined organic layers were dried and evaporated, and the residue was purified by chromatography on silica gel (7% EtOAc/hexanes). The alcohol was isolated as a colorless oil (190 mg, 80%); IR (neat, cm^{-1}) 3426, 1471, 1255; ^{1}H NMR (300 MHz, $CDCl_3$): 6.12 (d, *J* = 1.2, 1 H), 5.76 (d, *J* = 1.3, 1 H), 4.00 (m, 1 H), 3.60 (dd, *J* = 4.1, 11.2, 1 H), 3.48 (dd, *J* = 4.1, 11.2, 1 H), 2.65 (ddd, *J* = 1.0, 6.4, 14.1, 1 H), 2.55 (ddd, *J* = 1.0, 6.4, 14.1, 1 H), 2.00 (br s, 1 H), 0.90 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 128.5, 106.8, 71.2, 65.1, 49.5, 25.8 (3C), 18.0, –4.3, –4.5; ES HRMS *m/z* calculated for $C_{11}H_{23}IO_2SiNa$ (M^+ + Na) 365.0404, observed 365.0403; $[\alpha]_D$ –4.8 (*c* 2.1, $CHCl_3$).

A mixture of the above alcohol (350 mg, 1.02 mmol) and 4Å MS (800 mg) in CH_2Cl_2 (10 ml) was treated with NMO (240 mg, 2.05 mmol) and TPAP (35 mg, 0.1 mmol), stirred for 1 h, filtered through a pad of silica gel and rinsed with CH_2Cl_2. After solvent evaporation, unpurified **165** was used directly in the next step; ^{1}H NMR (300 MHz, $CDCl_3$): 9.70 (d, *J* = 1.1, 1 H), 6.15 (d, *J* = 1.2, 1 H), 5.83 (d, *J* = 1.4, 1 H), 4.24 (ddd, *J* = 1.1, 3.8, 8.7, 1 H), 2.82 (ddd, *J* = 1.0, 3.9, 14.4, 1 H), 2.59 (ddd, *J* = 0.9, 8.7, 14.4, 1 H), 0.96 (s, 9 H), 0.15 (s, 6 H).

Iodo Alcohol **166**

A solution of 2,3-dichloropropene (0.24 ml, 2.55 mmol) and KI (496 mg 2.98 mmol) in DMF (8 ml) was stirred at r.t. for 30 min in the dark. Indium powder (176 mg, 1.53 mmol) was introduced, followed 30 min later with **165** from above as a solution in DMF (7 ml). After 5 h of rapid stirring, the reaction mixture was diluted with Et_2O and H_2O, and the separated aqueous phase was extracted with Et_2O. The combined organic layers were dried and evaporated, and the residue was purified by chromatography on silica gel (1–5% EtOAc/hexanes). Product **166** (270 mg, 74% over 2 steps) was isolated as a mixture of isomers 3:1, colorless oil; IR (neat, cm^{-1}) 3450, 1636, 1471; ^1H NMR (300 MHz, $CDCl_3$): 6.18 (s, 1 H), 5.80 (s, 1 H), 5.26 (s, 1 H), 5.21 (s, 1 H), 4.05–3.80 (m, 2 H), 2.83 (dd, *J* = 7.2, 13.9, 1 H), 2.60–2.35 (m, 3 H), 2.15 (br s, 1 H), 0.85 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): 139.4, 129.0, 114.5, 106.5, 72.3, 68.8, 48.8, 43.8, 25.9 (3C), 18.0, –3.8, –4.5; ES HRMS *m/z* calculated for $C_{14}H_{26}ClIO_2SiNa$ (M^+ + Na) 439.0328, observed 439.0360.

Protection of **166**

Alcohol **166** (40 mg, 0.096 mmol) in DMF (40 µl) was treated with imidazole (24 mg, 0.36 mmol) and cooled to 0 °C. TESCl (40 µl, 0.19 mmol) was added and the reaction mixture stirred 30 min. The cold bath was removed and the white precipitate dissolved. The reaction mixture was stirred at r.t. overnight, diluted with Et_2O (3 ml) and saturated NH_4Cl (0.5 ml). The layers were separated and the aqueous phase was extracted with Et_2O (3 × 3 ml). The combined organics were washed with brine (1 × 3 ml), dried and concentrated in vacuo to give a yellow/orange oil. Column chromatography on silica gel (1% EtOAc/hexanes) afforded **167** as a clear, colorless oil (44 mg, 86%, 2:1 *anti/syn*). Major isomer (*anti*): ^1H NMR (400 MHz, $CDCl_3$): 6.07 (s, 1 H), 5.76 (s, 1 H), 5.20 (s, 1 H), 5.18 (s, 1 H), 4.06–4.02 (m, 1 H), 3.92–3.87 (m, 1 H), 2.78 (d, *J* = 14, 1 H), 2.67 (d, *J* = 14, 1 H), 2.28–2.17 (m, 2 H), 1.00–0.96 (m, 9 H), 0.88 (s, 9 H), 0.67–0.61 (m, 6 H), 0.14–0.11 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.5, 128.5, 114.9, 110.0, 72.6, 71.1, 46.5, 41.3, 26.0 (3C), 18.0, 7.0 (3C), 5.0 (3C), –4.0, –4.1.

Iodo Chloro Triene **81**

A solution of **155** (180 mg, 0.43 mmol) in CH_2Cl_2 (5 ml) was treated with Martin sulfurane (434 mg, 0.646 mmol) at r.t., stirred for 3 h and quenched with saturated $NaHCO_3$ solution. The mixture was extracted with 2% EtOAc/hexanes. The combined organic layers were dried and evaporated, and the residue was purified by chromatography on silica gel (pet ether) to give **81** as a colorless oil (154 mg, 85%); ^1H NMR (300 MHz, $CDCl_3$): 6.35 (dd, *J* = 0.9, 14.9, 1 H), 6.16 (dd, *J* = 5.6, 14.9, 1 H), 6.10 (d, *J* = 1.2, 1 H), 5.79 (d, *J* = 1.4, 1 H), 5.39 (d, *J* = 4.4, 2 H), 4.51 (m, 1 H), 2.65 (ddd, *J* = 0.9, 7.2, 14.0, 1 H), 2.55 (ddd, *J* = 1.0, 5.4, 14.0, 1 H), 0.93 (s, 9 H), 0.17 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 138.1, 136.6, 128.7, 126.8, 115.4, 106.5, 70.7, 53.9, 25.8 (3C), 18.2, –4.3, –4.6.

Acetonide Methyl Ester **168**

A cold (–78 °C) solution of $(COCl)_2$ (7.4 ml, 85 mmol) in CH_2Cl_2 (300 ml) was treated dropwise with DMSO (9.0 ml, 130 mmol) and stirred for 30 min prior to the introduction of **126** (3.0 g, 8.5 mmol) dissolved in CH_2Cl_2 (60 ml). After an additional hour at –78 °C and

1 h at –50 °C, the reaction mixture was returned to –78 °C, treated with Et_3N (36 ml, 260 mmol) and agitated for another 2 h at –78 °C before being quenched with H_2O (100 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 60 ml). The combined organic layers were dried and evaporated, and the residue was taken up in *t*-BuOH/H_2O 10:1 (130 ml) and treated with 2-methyl-2-butene (1.0 ml). This solution was treated sequentially with NaH_2PO_4 (3.5 g, 25 mmol) and $NaClO_2$ (4.6 g, 51 mmol), stirred at r.t. for 2 h and evaporated under reduced pressure. The residue was further diluted with H_2O and extracted with dichloromethane (3 × 30 ml). The combined organic phases were washed with brine (20 ml), dried and freed of solvent. The crude acid was dissolved in dry Et_2O (100 ml) and treated portionwise with ethereal CH_2N_2 until a yellow color persisted. After solvent evaporation, purification by chromatography on silica gel (hexanes/EtOAc 95:5) afforded **168** (2.5 g, 77%) as a white solid, m.p. 90–91 °C; IR (neat, cm^{-1}) 1747, 1613, 1514; ^1H NMR (400 MHz, $CDCl_3$): 7.28 (d, *J* = 8.6, 2 H), 6.90 (d, *J* = 8.6, 2 H), 4.82 (d, *J* = 11.0, 1 H), 4.57 (d, *J* = 11.0, 1 H), 3.90 (m, 1 H), 3.87 (m, 1 H), 3.82 (m, 1 H), 3.81 (s, 3 H), 3.77 (s, 3 H), 3.75 (m, 1 H), 3.31 (m, 1 H), 3.19 (dd, *J* = 8.8, 1.2, 1 H), 1.97 (m, 1 H), 1.58 (s, 3 H), 1.44 (s, 3 H), 0.96 (d, *J* = 6.6, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 169.7, 159.2, 130.8, 129.6 (2C), 113.7 (2C), 99.4, 81.8, 80.8, 75.8, 74.0, 72.1, 62.2, 55.2, 52.2, 39.3, 29.2, 19.3, 12.8; ES HRMS *m/z* calculated for $C_{20}H_{28}O_7Na$ (M^+ + Na) 403.1727, observed 403.1719; $[\alpha]_D$ +41 (*c* 1.3, $CHCl_3$).

Dihydroxy Methyl Ester **169**

A solution of **168** (5.0 g, 13.1 mmol) in a mixture of THF and 1 M HCl 1:1 (100 ml) was stirred for 2 h and diluted with EtOAc (100 ml). The separated aqueous phase was extracted with EtOAc (3 × 50 ml), and the combined organic layers were washed with brine, dried and evaporated. Flash chromatography of the residue on silica gel (hexanes/EtOAc 7:3) provided **169** (4.47 g, 100%) as a colorless oil; IR (neat, cm^{-1}) 3445, 1738, 1607, 1514; ^1H NMR (400 MHz, $CDCl_3$): 7.28 (d, *J* = 8.7, 2 H), 6.91 (d, *J* = 8.7, 2 H), 4.73 (d, *J* = 11.2, 1 H), 4.65 (d, *J* = 11.2, 1 H), 3.87–3.71 (m, 2 H), 3.82 (s, 3 H), 3.78 (s, 3 H), 3.74 (d, *J* = 10.6, 1 H), 3.64 (br t, *J* = 8.7, 1 H), 3.36 (m, 1 H), 3.13 (dd, *J* = 10.3, 8.9, 1 H), 2.38 (br s, 1 H), 2.23 (br m, 1 H), 1.96 (m, 1 H), 1.01 (d, *J* = 6.6, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 1.70.4, 159.2, 130.5, 129.5 (2C), 113.8 (2C), 85.2, 80.8, 80.2, 74.2, 71.1, 62.2, 55.1, 52.0, 39.2, 12.6; ES HRMS *m/z* calculated for $C_{17}H_{24}O_7Na$ (M^+ + Na) 363.1414, observed 363.1391; $[\alpha]_D$ +25 (*c* 2.0, $CHCl_3$).

Iodo Ester **171**

To a stirred solution of **169** (2.0 g, 5.9 mmol) in PhH (100 ml) was added pyridine (2.38 ml, 29.4 mmol), PPh_3 (7.7 g, 29.4 mmol) and I_2 (4.48 g, 17.6 mmol). This mixture was heated at reflux for 2 h, cooled to r.t. and diluted with H_2O (50 ml) and EtOAc (50 ml). The separated aqueous phase was extracted with EtOAc (3 × 50 ml), and the combined organic layers were dried and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexanes/EtOAc 95:5 to 70:30) to provide **170** (2.43 g, 92%) as a colorless oil that was used directly.

A cold (0 °C) stirred solution of **170** (500 mg, 1.11 mmol) in CH_2Cl_2/DMF 10:1 (10 ml) was treated with pyridine (890 µl, 11.1 mmol), DMAP (136 mg, 1.11 mmol) and TMSCl (709 µl, 5.57 mmol), warmed to r.t., stirred for 1 h and quenched with H_2O (5 ml) and CH_2Cl_2 (5 ml). The separated aqueous phase was extracted with CH_2Cl_2 (2 × 5 ml), and the combined organic solutions were washed with brine, dried and evaporated. The crude prod-

uct was purified by chromatography on silica gel (hexanes/EtOAc 95:1 to 90:10) to afford **171** as a colorless oil (551 mg, 92%); IR (neat, cm^{-1}) 1748, 1614, 1514; ^1H NMR (400 MHz, $CDCl_3$): 7.28 (d, *J* = 8.6, 2 H), 6.87 (d, *J* = 8.6, 2 H), 4.81 (d, *J* = 11.0, 1 H), 4.52 (d, *J* = 11.0, 1 H), 3.82 (s, 3 H), 3.78 (s, 3 H), 3.74 (d, *J* = 10.6, 1 H), 3.54 (dd, *J* = 13.2, 2.3, 1 H), 3.52 (s, 1 H), 3.27 (dd, *J* = 10.6, 6.8, 1 H), 3.16–3.06 (m, 2 H), 1.97 (m, 1 H), 0.89 (d, *J* = 6.6, 3 H), 0.21 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 169.6, 159.1, 130.3, 129.0 (2C), 113.7 (2C), 85.5, 81.1, 79.6, 75.9, 75.0, 55.2, 52.2, 40.0, 12.6, 7.0, 0.9 (3C); ES HRMS *m/z* calculated for $C_{20}H_{31}IO_6SiNa$ (M^+ + Na) 545.0827, observed 545.0819; $[\alpha]_D$ +60 (*c* 1.3, $CHCl_3$).

Methylene Pyranyl Ester **172**

A solution of **171** (551 mg, 1.06 mmol) and DBU (1.30 ml, 10.6 mmol) in DMF (10 ml) was stirred at 60 °C for 2 h, cooled to r.t. and quenched with H_2O (10 ml) and Et_2O (30 ml). The separated organic layer was washed with brine (2 × 20 ml) and the aqueous layer was extracted with Et_2O (3 × 30 ml). The combined organic solutions were dried and evaporated to leave a residue that was purified by chromatography on silica gel (1–10% EtOAc/hexanes) to afford **172** as a colorless oil (391 mg, 94%); IR (neat, cm^{-1}) 1756, 1661, 1614, 1514; ^1H NMR (400 MHz, C_6D_6): 7.24 (d, *J* = 8.8, 2 H), 6.81 (d, *J* = 8.8, 2 H), 4.87 (d, *J* = 2.0, 1 H), 4.83 (d, *J* = 2.0, 1 H), 4.82 (d, *J* = 11.2, 1 H), 4.44 (d, *J* = 11.3, 1 H), 4.23 (dt, *J* = 8.2, 1.8, 1 H), 3.90 (d, *J* = 10.4, 1 H), 3.31 (s, 3 H), 3.29 (s, 3 H), 3.12 (dd, *J* = 9.4, 8.3, 1 H), 2.35 (m, 1 H), 0.87 (d, *J* = 6.7, 3 H), 0.14 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): 169.6, 160.7, 159.7, 129.5 (2C), 114.0 (2C), 94.4, 84.8, 82.1, 74.8, 74.4 (2C), 54.7, 51.6, 39.8, 13.3, 0.1 (3C); ES HRMS *m/z* calculated for $C_{20}H_{30}O_6SiNa$ (M^+ + Na) 417.1704, observed 417.1719; $[\alpha]_D$ +0.54 (*c* 1.3, $CHCl_3$).

Suzuki–Miyaura Coupling to Generate **173**

A solution of **172** (100 mg, 0.25 mmol) in THF (0.5 ml) was cooled to 0 °C, treated with a solution of 0.5 M 9-BBN (1.5 ml, 0.75 mmol), warmed to r.t., and stirred for 1 h. 3 M K_3PO_4 in H_2O (0.25 ml, 0.75 mmol) and DMF (0.2 ml) were introduced and stirring was maintained for 15 min before a premixed solution of **81** (152 mg, 0.38 mmol) and $PdCl_2$(dppf) (19 mg, 0.026 mmol) in DMF (1.2 ml) was added. The reaction mixture was stirred for 5 h before being diluted with Et_2O (10 ml) and H_2O (5 ml). The organic layer was washed with brine (2 × 3 ml) and the aqueous layer was extracted with Et_2O (3 × 5 ml). The combined organic solutions were dried and concentrated. The residue was purified by chromatography on silica gel (hexanes/EtOAc 97:3) to furnish **173** as a colorless oil (119 mg, 70%); IR (neat, cm^{-1}) 1752, 1613, 1514; ^1H NMR (400 MHz, C_6D_6): 7.28 (d, *J* = 8.4, 2 H), 6.83 (d, *J* = 8.6, 2 H), 6.47–6.38 (m, 2 H), 5.17 (s, 1 H), 5.11 (s, 1 H), 5.07 (s, 1 H), 5.01 (s, 1 H), 4.79 (d, *J* = 11.2, 1 H), 4.56 (m, 1 H), 4.45 (d, *J* = 11.2, 1 H), 3.59 (d, *J* = 10.6, 1 H), 3.53 (t, *J* = 9.0, 1 H), 3.42 (t, *J* = 9.3, 1 H), 3.33 (s, 3 H), 3.32 (s, 3 H), 2.94 (dd, *J* = 10.4, 8.6, 1 H), 2.76 (d, *J* = 14.5, 1 H), 2.53 (dd, *J* = 13.7, 5.6, 1 H), 2.46 (dd, *J* = 13.6, 7.4, 1 H), 2.29 (dd, *J* = 14.4, 10.2, 1 H), 2.21 (m, 2 H), 1.02 (s, 9 H), 0.88 (d, *J* = 6.6, 3 H), 0.20 (s, 9 H), 0.14 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): 169.8, 159.7, 143.6, 139.1, 139.0, 131.2, 128.9 (2C), 126.4, 115.2, 115.1, 114.1 (2C), 86.3, 81.8, 81.5, 76.7, 75.0, 71.3, 54.8, 51.5, 46.3, 40.5, 38.8, 26.7 (3C), 18.5, 13.0, 1.11 (3C), –4.1, –4.5; ES HRMS *m/z* calculated for $C_{34}H_{55}ClO_7Si_2Na$ (M^+ + Na) 689.3067, observed 689.3068; $[\alpha]_D$ +39 (*c* 1.6, $CHCl_3$).

Desilylation of **173**

A solution of **173** (100 mg, 0.150 mmol) in THF/MeOH 3:1 (4 ml) was treated with K_2CO_3 (41 mg, 0.30 mmol), stirred at r.t. for 5 h, and diluted with EtOAc (5 ml) and saturated $NaHCO_3$ solution (5 ml). The separated aqueous layer was extracted with EtOAc (3 × 5 ml), and the combined organic layers were dried and concentrated. Chromatographic purification of the residue on silica gel (hexanes/EtOAc 95:5 to 80:20) gave **175** as a colorless oil (83 mg, 93%); IR (neat, cm^{-1}) 3504, 1613, 1588, 1514; ^1H NMR (400 MHz, C_6D_6): 7.22 (d, *J* = 8.6, 2 H), 6.82 (d, *J* = 8.6, 2 H), 6.38 (m, 2 H), 5.17 (s, 1 H), 5.06 (s, 2 H), 4.96 (s, 1 H), 4.53 (s, 2 H), 4.49 (dd, *J* = 11.5, 6.0, 1 H), 3.56 (d, *J* = 10.5, 1 H), 3.37 (d, *J* = 9.1, 3.5, 1 H), 3.34 (s, 3 H), 3.32 (s, 3 H), 3.29 (m, 1 H), 2.87 (dd, *J* = 10.4, 8.5, 1 H), 2.71 (dd, *J* = 14.8, 1.9, 1 H), 2.48–2.41 (m, 2 H), 2.34 (dd, *J* = 14.8, 8.2, 1 H), 2.18 (m, 1 H), 1.74 (d, *J* = 3.5, 1 H), 1.02 (s, 9 H), 0.95 (d, *J* = 6.4, 3 H), 0.13 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 169.6, 159.9, 143.3, 139.0, 138.9, 131.3, 129.5 (2C), 126.3 (2C), 115.5, 115.0, 114.2 (2C), 86.1, 81.4, 80.3, 74.8, 74.0, 71.2, 54.8, 51.4, 46.0, 39.6, 38.8, 26.1 (3C), 18.4, 13.0, –4.3, –4.6; ES HRMS *m/z* calculated for $C_{31}H_{47}ClO_7SiNa$ (M^+ + Na) 617.2672, observed 617.2696; $[\alpha]_D$ +14 (*c* 0.84, $CHCl_3$).

Silyl Protection of **175**

A cold (–78 °C) solution of **175** (83 mg, 0.139 mmol) in CH_2Cl_2 (3 ml) was treated with 2,6-lutidine (162 µl, 1.40 mmol) and TESOTf (155 µl, 0.770 mmol), stirred for 30 min, and quenched with H_2O (2 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 3 ml), and the combined organic phases were dried and evaporated. The product was purified by chromatography on silica gel (hexanes/EtOAc 97:3) and **176** was obtained as a colorless oil (99 mg, 100%); IR (neat, cm^{-1}) 1755, 1614, 1589, 1514; ^1H NMR (400 MHz, C_6D_6): 7.31 (d, *J* = 8.6, 2 H), 6.84 (d, *J* = 8.6, 2 H), 6.48–6.39 (m, 2 H), 5.17 (s, 1 H), 5.13 (s, 1 H), 5.08 (s, 1 H), 5.02 (s, 1 H), 4.78 (d, *J* = 11.3, 1 H), 4.59 (m, 1 H), 4.45 (d, *J* = 11.3, 1 H), 3.58 (m, 2 H), 3.39 (dt, *J* = 10.4, 1.6, 1 H), 3.34 (s, 3 H), 3.32 (s, 3 H), 2.94 (dd, *J* = 10.4, 8.6, 1 H), 2.81 (br d, *J* = 14.3, 1 H), 2.57 (dd, *J* = 13.7, 5.6, 1 H), 2.48 (dd, *J* = 13.7, 7.4, 1 H), 2.34 (dd, *J* = 14.4, 10.3, 1 H), 2.23 (m, 1 H), 1.08–0.97 (series of m, 18 H), 0.90 (d, *J* = 6.7, 3 H), 0.73 (q, *J* = 7.8, 6 H), 0.16 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 169.7, 159.6, 143.8, 139.0, 138.9, 131.2, 128.6 (2C), 126.4 (2C), 115.1, 115.0, 114.0, 86.4, 82.2, 81.4, 76.4, 74.0, 71.1, 54.7, 51.4, 46.3, 40.4, 38.7, 26.1 (3C), 18.5, 13.0, 7.3 (3C), 5.9 (3C), –4.3, –4.6; ES HRMS *m/z* calculated for $C_{37}H_{61}ClO_7Si_2Na$ (M^+ + Na) 731.3537, observed 731.3523; $[\alpha]_D$ +37 (*c* 0.74, $CHCl_3$).

Carboxylic Acid **177**

A stirred solution of **176** (99 mg, 1.4 mmol) in dry THF (5 ml) was treated with Me_3SiOK (36 mg, 280 mmol), stirred at r.t. for 1 h and diluted with EtOAc (5 ml) and 0.1 M HCl (5 ml). The resulting organic phase was washed with brine, and the aqueous phase was extracted with EtOAc (3 × 5 ml). The combined organic solutions were dried and evaporated, and the residue was purified by chromatography on silica gel (hexanes/EtOAc 90:10 to 70:30) to yield **177** (86 mg, 89%) as a colorless oil; IR (neat, cm^{-1}) 3500, 1725, 1514; ^1H NMR (400 MHz, C_6D_6): 7.31 (d, *J* = 8.5, 2 H), 6.86 (d, *J* = 8.5, 2 H), 6.46–6.33 (m, 2 H), 5.19 (s, 1 H), 5.07 (s, 1 H), 5.01 (s, 1 H), 4.97 (s, 1 H), 4.52 (d, *J* = 11.2, 1 H), 4.51 (m, 1 H), 4.42 (d, *J* = 11.2, 1 H), 3.42 (m, 2 H), 3.32 (m, 1 H), 3.31 (s, 3 H), 2.84 (t, *J* = 9.8, 1 H), 2.72 (d, *J* =

14.6, 1 H), 2.42 (m, 2 H), 2.18 (dd, *J* = 14.4, 10.3, 1 H), 1.93 (m, 1 H), 1.13 (d, *J* = 6.6, 1 H), 1.06–0.99 (series of m, 18 H), 0.70 (q, *J* = 8.1, 6 H), 0.15 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6): 190.2, 159.6, 143.4, 138.8, 132.0, 131.1, 128.5 (2C), 126.5, 115.2, 114.4, 114.0 (2C), 86.4, 80.6, 76.3, 74.5, 71.4, 67.8, 54.9, 46.0, 40.5, 39.0, 30.2 (3C), 18.2, 13.2, 7.3 (3C), 6.1 (3C), –4.2, –4.6; ES HRMS *m/z* calculated for $C_{36}H_{59}ClO_7Si_2Na$ (M^+ + Na) 717.3380, observed 717.3403; $[\alpha]_D$ +27 (*c* 1.3, $CHCl_3$).

Suzuki–Miyaura Coupling to Generate **174**

Enol ether **172** (41 mg, 0.104 mmol) was taken up in dry THF (0.21 ml), cooled to 0 °C, treated with a 0.5 M solution of 9-BBN in THF (0.62 ml, 0.31 mmol) and stirred for 10 min. The cold bath was removed and the mixture was stirred at r.t. for 2 h. A mixture of DMF 1:1 (0.10 ml) and 3 M K_3PO_4 (0.1 ml, 0.31 mmol) was added and the mixture was stirred for 30 min. A slurry of **167** (83 mg, 0.16 mmol) and $PdCl_2$(dppf) (8.5 mg, 0.010 mmol) in DMF (0.52 ml) was added to the reaction mixture. After stirring for an additional 2 h, the reaction mixture was diluted with Et_2O (10 ml) and H_2O (1.5 ml). The separated aqueous layer was extracted with Et_2O (3 × 5 ml). The combined organics were dried and concentrated in vacuo. Column chromatography on silica gel (1–5% EtOAc/pet ether) afforded **174** contaminated with some borane residues (53 mg, 64%); ^{1}H NMR (300 MHz, $CDCl_3$): 7.27 (d, *J* = 8.6, 2 H), 6.87 (d, *J* = 8.6, 2 H), 5.24 (s, 1 H), 5.19 (s, 1 H), 4.90 (s, 1 H), 4.88 (s, 1 H), 4.81 (d, *J* = 11.0, 1 H), 4.52 (d, *J* = 11.0, 1 H), 4.00–3.96 (m, 1 H), 3.80 (s, 3 H), 3.80–3.78 (m, 1 H), 3.72 (s, 3 H), 3.43–3.38 (m, 1 H), 3.33–3.27 (m, 1 H), 3.04 (dd, *J* = 10.2, 8.4, 1 H), 2.53–2.38 (m, 3 H), 2.31–2.24 (m, 1 H), 2.15–2.01 (m, 2 H), 1.96–1.84 (m, 1 H), 0.97–0.83 (m, 21 H), 0.67–0.56 (m, 6 H), 0.17 (s, 9 H), 0.08 (s, 3 H), 0.02 (s, 3 H).

Deprotection/Reprotection of **174**

The Suzuki adduct **174** (76.9 mg, 0.0962 mmol) was stirred in a solution of THF (1.9 ml) and MeOH (0.6 ml). K_2CO_3 (27 mg, 0.192 mmol) was added in one portion and the reaction mixture was stirred at r.t. for 4 h, diluted with EtOAc (3 ml), and quenched with saturated $NaHCO_3$ solution (5 ml). The mixture was transferred to a separatory funnel and extracted with EtOAc (3 × 5 ml). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo to yield the free hydroxyl compound which was purified by flash column chromatography (10–25% EtOAc/hexanes) to provide the free alcohol **178** (53.3 mg, 76%); IR (thin film, cm^{-1}) 3500, 2955, 2920, 1747, 1639, 1613, 1514, 1463, 1250, 1097; ^{1}H NMR ($CDCl_3$, 400 MHz) (major diastereomer): 7.28 (d, *J* = 8.4, 2 H), 6.88 (d, *J* = 8.6, 2 H), 5.19 (s, 1 H), 5.18 (s, 1 H), 4.98 (br s, 1 H), 4.89 (br s, 1 H), 4.69 (AB, J_{AB} = 11.0, 2 H), 3.97 (m, 1 H), 3.80 (s, 3 H), 3.77 (m, 1 H), 3.75 (s, 3 H), 3.64 (d, *J* = 10.5, 1 H), 3.48 (d, *J* = 8.7, 1 H), 3.40 (d, *J* = 8.4, 1 H), 3.09 (t, *J* = 10.3, 1 H), 2.65 (d, *J* = 13.8, 1 H), 2.57 (dd, *J* = 14.6, 4.1, 1 H), 2.49 (d, *J* = 14.2, 1 H), 2.16–2.40 (m, 3 H), 1.90–2.06 (m, 2 H), 0.91–1.05 (m, 9 H), 0.87 (s, 9 H), 0.87 (m, 3 H), 0.60 (q, *J* = 8.1, 6 H), 0.07 (s, 3 H), –0.01 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) (major diastereomer): 169.95, 159.40, 144.17, 140.80, 130.55, 129.54, 114.75, 114.09, 113.98, 85.74, 81.16, 78.48, 75.54, 74.42, 73.65, 71.87, 55.28, 52.04, 40.84, 39.26, 37.05, 29.70, 25.90, 17.98, 12.81, 6.96, 5.07, –4.24, –4.53; ES HRMS *m/z* calculated for $C_{37}H_{63}ClO_8Si_2Na$ $(M + Na)^+$ 749.3648, observed 749.3650; $[\alpha]_D$ + 9.3 (*c* 3.45, $CHCl_3$).

The free alcohol was dissolved in dry CH_2Cl_2 (1.6 ml) in a flame-dried round bottom flask under N_2 and cooled to –78 °C. 2,6-Lutidine (10 µl, 0.088 mmol) was added followed by dropwise addition of TBSOTf (18 µl, 0.077 mmol). The reaction mixture was transferred to

a separatory funnel containing saturated NH_4Cl solution (10 ml) and CH_2Cl_2 (10 ml). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 ml). The combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo. Flash column chromatography (10% Et_2O/hexanes) provided **179** (44.9 mg, 80%); ^{1}H NMR ($CDCl_3$, 400 MHz) (major diastereomer): 7.27 (d, *J* = 8.8, 2 H), 6.87 (d, *J* = 8.4, 2 H), 5.19 (br s, 1 H), 5.18 (br s, 1 H), 4.89 (s, 1 H), 4.85 (s, 1 H), 4.78 (d, *J* = 11.2, 1 H), 4.50 (d, *J* = 11.2, 1 H), 3.98 (dd, *J* = 8.0, 4.4, 1 H), 3.80 (s, 3 H), 3.76 (dd, *J* = 8.0, 4.4, 1 H), 3.72 (s, 3 H), 3.62 (d, *J* = 10.8, 1 H), 3.41 (t, *J* = 8.8, 1 H), 3.31 (t, *J* = 8.8, 1 H), 3.06 (dd, *J* = 10.4, 8.4, 1 H), 2.64 (d, *J* = 13.6, 1 H), 2.53 (d, *J* = 14.4, 1 H), 2.44 (d, *J* = 14.0, 1 H), 2.29 (dd, *J* = 13.6, 9.6, 1 H), 2.05 (dd, *J* = 14.4, 10.8, 1 H), 1.94 (td, *J* = 10.4, 6.4, 1 H), 1.87 (dd, *J* = 14.0, 10.4, 1 H), 0.95 (m, 12 H), 0.87 (s, 18 H), 0.61 (q, *J* = 7.6, 6 H), 0.09 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H), –0.01 (s, 3 H); ES HRMS *m/z* calculated for $C_{43}H_{77}ClO_8Si_3Na$ $(M + Na)^+$ 863.4513, observed 863.4485; $[\alpha]_D$ +43 (*c* 0.18, $CHCl_3$).

Carboxylic Acid **180**

Ester **179** (36 mg, 0.043 mmol) was stirred in dry THF (1 ml) in a flame-dried round bottom flask under N_2. Me_3SiOK (11 mg, 0.086 mmol) was added in one portion and the reaction mixture was stirred for 12 h, poured into a separatory funnel containing saturated NH_4Cl solution (5 ml) and Et_2O (5 ml), and extracted with Et_2O (3 × 5 ml) and CH_2Cl_2 (2 × 5 ml). The combined organic layers were washed with saturated NaCl solution, dried over $MgSO_4$, filtered and concentrated in vacuo. Flash column chromatography (5% MeOH/CH_2Cl_2) yielded carboxylic acid **180** (28 mg, 78%); IR (thin film, cm^{-1}) 3394, 1734, 1507, 1458, 1270; ^{1}H NMR ($CDCl_3$, 400 MHz) (diastereomeric mixture): 7.27 (d, *J* = 8.4, 2 H), 6.87 (d, *J* = 8.0, 2 H), 5.21 (m, 2 H), 4.92 (m, 2 H), 4.78 (d, *J* = 11.2, 1 H), 4.52 (d, *J* = 11.2, 1 H), 3.99 (dd, *J* = 7.6, 4.4, 1 H), 3.82 (m, 1 H), 3.80 (s, 3 H), 3.65 (m, 1 H), 3.39 (m, 2 H), 3.08 (m, 1 H), 2.63 (m, 2 H), 2.47 (m, 2 H), 2.25 (m, 1 H), 2.09 (m, 2 H), 1.91 (m, 1 H), 1.04 (d, *J* = 6.4, 3 H), 0.85–1.00 (m, 27 H), 0.60 (m, 6 H), 0.00–0.15 (m, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz) (diastereomeric mixture): 159.11, 142.82, 140.30, 130.32, 128.91, 114.95, 114.85, 113.72, 85.99, 80.33, 75.46, 75.36, 75.05, 74.89, 72.93, 55.25, 43.60, 42.90, 40.54, 40.32, 39.16, 29.70, 26.04, 25.98, 25.90, 25.85, 18.21, 18.05, 17.99, 17.96, 13.24, 6.98, 5.08, 5.04, –3.55, –3.77, –4.12, –4.30, –4.57, –4.63; ES HRMS *m/z* calculated for $C_{42}H_{75}ClO_8Si_3$ $(M + Na)^+$ 849.4358, observed 849.4364; $[\alpha]_D$ +2.8 (*c* 10.4, $CHCl_3$).

Pentafluorophenyl ester **181**

Carboxylic acid **180** (28 mg, 0.034 mmol) in dry CH_2Cl_2 (0.8 ml) was treated with DMAP (0.3 mg, 0.0021 mmol), DCC (8.6 mg, 0.0418 mmol) and pentafluorophenol (7.7 mg, 0.0418 mmol). The reaction mixture was stirred at r.t. for 1.5 h, evaporated under reduced pressure, and purified by column chromatography (10% EtOAc/hexanes) to afford ester **181** (10.8 mg, 52% from **179**); ^{1}H NMR (300 MHz, $CDCl_3$): 7.30–7.26 (m, 2 H), 6.90–6.87 (m, 2 H), 5.20–5.17 (m, 2 H), 4.91–4.89 (m, 2 H), 4.83 (d, *J* = 8.4, 1 H), 4.54 (d, *J* = 8.4, 1 H), 3.98–3.81 (series of m, 3 H), 3.81 (s, 3 H), 3.46–3.34 (series of m, 2 H), 3.15–3.10 (m, 1 H), 2.67–2.00 (series of m, 7 H), 1.00–0.81 (series of m, 30 H), 0.62–0.52 (m, 6 H), 0.11 (s, 6 H), 0.07 (s, 3 H), 0.01 (s, 3 H).

Ketosulfone **183**

A neat mixture of methyl ester **179** (16.6 mg, 0.020 mmol) and sulfone **153** (31.4 mg, 0.039 mmol) was taken up in anhydrous THF (0.20 ml), cooled to –78 °C, and treated with a 0.85 M solution of LHMDS in THF (50 µl, 0.039 mmol). The reaction mixture was allowed to warm with stirring to –30 °C over 5 h, then the reaction mixture maintained at –30 °C for 30 min. The reaction mixture was quenched with saturated NH_4Cl solution (1 ml), diluted with Et_2O (2 ml) and allowed to warm to r.t. The separated aqueous layer was extracted with Et_2O (3 × 2 ml) and the combined organics were dried over Na_2SO_4 and concentrated in vacuo to give a clear, colorless oil. Column chromatography (5–10% Et_2O/hexanes) afforded the desired ketosulfone **183** (43 mg, >100%) contaminated with excess sulfone **153**; TOF MS ES$^+$ *m/z* calculated for (M^+ + Na) 1627.8659, observed 1627.8636.

Enol Ether **184**

A mixture of iodo alcohol **170** (0.95 g, 2.11 mmol), PMBO-lepidine (1.77 g, 6.33 mmol), and CSA (49.0 mg, 0.211 mmol) in CH_2Cl_2 (10 ml) was stirred at r.t. for 43.5 h. The resulting slurry was diluted with a small amount of CH_2Cl_2 and loaded directly onto the column (hexanes/EtOAc 5:1 to 4.5:1), which afforded the bis-PMB protected intermediate as a slightly off-white semi-solid (0.85 g, 70%); IR (neat, cm^{-1}) 1745, 1612, 1514, 1249; ^{1}H NMR (500 MHz, $CDCl_3$): 7.28–7.24 (m, 4 H), 6.89–6.88 (m, 4 H), 4.86 (d, *J* = 10.7, 1 H), 4.84 (d, *J* = 10.7, 1 H), 4.68 (d, *J* = 10.7, 1 H), 4.60 (d, *J* = 10.7, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.78 (s, 3 H), 3.72 (d, *J* = 10.7, 1 H), 3.49 (dd, *J* = 2.6, 10.8, 1 H), 3.28–3.24 (m, 1 H), 3.17–3.13 (m, 1 H), 2.05–1.97 (m, 1 H), 0.95 (d, *J* = 6.6, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 169.7, 159.6, 159.5, 130.4, 130.1, 129.7 (2C), 129.6 (2C), 114.1 (2C), 114.0 (2C), 85.3, 82.3, 81.2, 78.9, 75.2, 75.1, 55.42, 55.40, 52.3, 40.2, 12.6, 6.5; ES HRMS *m/z* calculated for (M^+ + Na) 593.1012, observed 593.0999; $[\alpha]_D^{25}$ +30.0 (*c* 0.09, $CHCl_3$).

A solution of the above iodide (93 mg, 0.16 mmol) in PhH (1.6 ml) was treated with DBU (0.24 ml, 1.6 mmol) and the mixture was heated at 60 °C for 4 h. The solvent was removed under reduced pressure to give a pale yellow mixture, which was purified by column chromatography on silica gel treated with 2% Et_3N/hexanes (hexanes/EtOAc 100:0 to 4:1) to afford **184** as a semi-opaque, colorless oil (62 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$): 7.31–7.20 (m, 4 H), 6.90–6.85 (m, 4 H), 4.79–4.65 (m, 4 H), 4.54 (d, *J* = 11.2, 1 H), 4.50 (d, *J* = 11.2, 1 H), 3.99–3.96 (m, 2 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.77 (s, 3 H), 3.25–3.21 (m, 1 H), 2.12–2.04 (m, 1 H), 0.96 (d, *J* = 6.8, 3 H).

Suzuki Adduct **3**

A solution of enol ether **184** (62 mg, 0.14 mmol) in THF (0.28 ml) was cooled to 0 °C (ice/NaCl) and treated with a 0.5 M solution of 9-BBN in THF (0.84 ml, 0.42 mmol). The reaction mixture was stirred at 0 °C for 15 min and at 26 °C for 2.5 h. Gas evolution occurred upon addition of 9-BBN. A neat mixture of side chain **167** (110 mg, 0.21 mmol) and $PdCl_2$(dppf) (17 mg, 0.021 mmol) was allowed to stand at 26 °C for 30 min before dilution with DMF (0.74 ml) and another 30 min of standing. To the hydroboration flask was added a 1:1 mixture of 3 M aqueous K_3PO_4 solution (0.14 ml, 0.42 mmol) and DMF (0.14 ml). The resulting mixture was stirred for 30 min and treated with the side chain/$PdCl_2$(dppf) mixture to give a dark brown reaction mixture, which was stirred at 26 °C for 2 h and gradually lightened to a red-orange color. The reaction mixture was diluted with H_2O (3 ml) and Et_2O

(20 ml). The separated aqueous layer was extracted with Et_2O (3 × 10 ml) and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to give a red oil. After purification twice by column chromatography (1, 2, 5, 10% EtOAc/pet ether) the desired coupled product **3** was obtained as a clear, nearly colorless oil (98 mg, 82%); IR (neat, cm^{-1}) 1748, 1638, 1613, 1586, 1514, 1250; ^1H NMR (400 MHz, $CDCl_3$): 7.26–7.23 (m, 4 H), 6.88–6.85 (m, 4 H), 5.19 (s, 1 H), 5.18 (s, 1 H), 4.91 (s, 1 H), 4.86 (s, 1 H), 4.82 (d, *J* = 10.8, 2 H), 4.60 (d, *J* = 7.2, 1 H), 4.57 (d, *J* = 7.6, 1 H), 3.98–3.95 (m, 1 H), 3.801 (s, 3 H), 3.797 (s, 3 H), 3.80–3.73 (m, 1 H), 3.73 (s, 3 H), 3.61 (d, *J* = 10.8, 1 H), 3.47–3.42 (m, 1 H), 3.30–3.20 (m, 2 H), 2.65 (d, *J* = 14, 1 H), 2.95 (d, *J* = 15.2, 1 H), 2.43 (d, *J* = 13.6, 1 H), 2.28 (dd, *J* = 9.6, 14, 1 H), 2.25–2.19 (m, 1 H), 2.00–1.93 (m, 1 H), 1.92–1.86 (m, 1 H), 0.96–0.86 (m, 21 H), 0.61–0.55 (m, 6 H), 0.53 (s, 3 H), –0.02 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 170.2, 159.5, 159.4, 143.5, 141.0, 130.7, 130.6, 129.6 (2C), 129.4 (2C), 114.8, 114.02 (2C), 113.99 (2C), 113.6, 86.1, 82.8, 81.3, 79.2, 75.2, 74.9, 74.4, 72.1, 55.5, 55.4, 52.1, 41.0, 40.4, 39.2, 37.3, 26.1 (3C), 22.2, 18.2, 7.12 (3C), 5.26 (3C), –4.13, –4.30; ES HRMS *m/z* calculated for (M^+ + Na) 869.4223, observed 869.4185; $[\alpha]_D^{25}$ –10.2 (*c* 0.85, $CHCl_3$).

Pentanal **185**

Pentane-1,5-diol (27.8 ml, 265.2 mmol) was dissolved in dry CH_2Cl_2 (100 ml) in a round bottom flask under N_2 and cooled to 0 °C. Imidazole (6.8 g, 99.5 mmol) was added. TBSCl (10 g, 66.3 mmol) was dissolved in 100 ml CH_2Cl_2 and added to the reaction mixture dropwise over 90 min via an addition funnel. The reaction mixture was warmed to r.t. over 12 h and transferred to a separatory funnel containing saturated aqueous NH_4Cl (100 ml) and CH_2Cl_2 (100 ml). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 80 ml). The combined organic layers were washed with saturated aqueous NaCl solution, dried over $MgSO_4$, filtered, and concentrated in vacuo. 5-(*tert*-Butyldimethylsilyloxy)pentan-1-ol (14.39 g, 99%) was isolated as a pale yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): 3.63 (m, 4 H), 1.55 (m, 4 H), 1.42 (m, 2 H), 0.89 (s, 9 H), 0.042 (s, 3 H), 0.039 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 63.16, 62.96, 32.51, 26.01, 22.04, 18.41, –5.24.

A solution of $(COCl)_2$ (5.2 ml, 59.5 mmol) in CH_2Cl_2 (100 ml) was cooled to –78 °C and treated dropwise with a solution of DMSO (6.5 ml, 73.3 mmol) in CH_2Cl_2 (50 ml). The above alcohol (10 g, 45.8 mmol) was taken up in CH_2Cl_2 (50 ml) and added to the above solution. The reaction mixture was stirred at –78 °C for 15 min. Et_3N (16 ml, 114.5 mmol) was added slowly and the resulting mixture was stirred for 90 min at –78 °C and for 20 min after the cold bath was removed. The reaction mixture was poured into a separatory funnel containing a 1:1 mixture of saturated aqueous NH_4Cl solution and CH_2Cl_2. The separated aqueous layer was extracted with CH_2Cl_2 and the combined organics were washed with brine, dried ($MgSO_4$), and filtered through a plug of silica gel to afford **185** (9.5 g, 96%) as an oil; ^1H NMR ($CDCl_3$, 400 MHz): 9.75 (t, *J* = 1.6, 1 H), 3.61 (t, *J* = 6.0, 2 H), 2.44 (td, *J* = 7.2, 1.6, 2 H), 1.67 (quintet, *J* = 7.6, 2 H), 1.53 (m, 2 H), 0.88 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 202.58, 62.55, 43.58, 32.08, 25.94, 18.61, 18.28, –5.37.

Terminal TBS-Protected Sulfone **186**

(*S*)-4-Benzyl-3-propionyloxazolidin-2-one (4.49 g, 19.3 mmol) was stirred in dry CH_2Cl_2 (75 ml) in a flame-dried round bottom flask under N_2 and cooled to –78 °C. Neat Bu_2BOTf (5.8 ml, 23.1 mmol) was added in one portion. After 5 min, the bath was replaced with a

0 °C bath for 30 min. The solution was recooled to –78 °C and *i*-Pr_2NEt (5.4 ml, 30.8 mmol) was added. After being stirred at –78 °C for 10 min, the solution was warmed to 0 °C for 60 min, followed by recooling to –78 °C. Aldehyde **185** (5.0 g, 23.1 mmol) was dissolved in dry CH_2Cl_2 (75 ml) and added to the reaction mixture dropwise over 20 min via an addition funnel. The reaction mixture was stirred at –78 °C for 2 h and quenched at low temperature with pH 7 buffer. Over 30 min, the reaction mixture was allowed to warm to r.t. and was extracted with CH_2Cl_2 (3 × 50 ml). The combined organic layers were washed with saturated NaCl solution, dried over $MgSO_4$, and concentrated in vacuo. Purification via flash column chromatography (20% EtOAc/hexanes) provided the Evans aldol product (7.25 g, 84%) as an inseparable mixture of diastereomers; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.15–7.40 (m, 5 H), 4.70 (m, 1 H), 4.20 (m, 2 H), 3.94 (m, 1 H), 3.76 (qd, *J* = 6.8, 2.4, 1 H), 3.61 (t, *J* = 6.4, 2 H), 3.25 (dd, *J* = 13.2, 2.8, 1 H), 2.87 (d, *J* = 2.8, 1 H), 2.78 (dd, *J* = 13.2, 9.6, 1 H), 1.35–1.60 (m, 6 H), 1.25 (d, *J* = 7.2, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 177.51, 171.20, 135.01, 129.93, 128.95, 127.41, 71.41, 66.14, 63.08, 60.36, 55.09, 42.12, 37.79, 33.59, 25.96, 21.01, 18.87, –5.30.

The above intermediate (8.3 g, 18.5 mmol) was dissolved in dry DMF (25 ml). Imidazole (3.1 g, 46.1 mmol) was added and TESCl (3.9 ml, 22.2 mmol) was added dropwise over 10 min. The reaction mixture was stirred at r.t. for 12 h and quenched by the addition of saturated NH_4Cl solution (50 ml) and Et_2O (50 ml). The aqueous layer was extracted with Et_2O (3 × 50 ml) and the combined organic layers were washed with H_2O (2 × 50 ml) and saturated NaCl solution (50 ml), dried over $MgSO_4$, and concentrated in vacuo. Flash column chromatography (5–10% EtOAc/hexanes) provided the desired major diastereomer (8.85 g, 85%) as an oil; IR (thin film, cm^{-1}) 1785, 1703, 1461, 1382; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.29 (m, 5 H), 4.62 (m, 1 H), 4.16 (m, 2 H), 4.01 (q, *J* = 5.2, 1 H), 3.86 (m, 1 H), 3.60 (td, *J* = 6.4, 2.4, 2 H), 3.29 (dd, *J* = 13.2, 3.2, 1 H), 2.76 (dd, *J* = 13.2, 9.6, 1 H), 1.50 (m, 4 H), 1.36 (m, 2 H), 1.25 (d, *J* = 6.8, 3 H), 0.95 (t, *J* = 8.0, 9 H), 0.89 (s, 9 H), 0.60 (q, *J* = 8.0, 6 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 175.31, 153.02, 135.41, 129.50, 128.93, 127.31, 73.19, 65.98, 63.11, 62.67, 55.78, 43.07, 37.67, 35.54, 35.06, 33.14, 25.96, 21.67, 6.93, 5.14, –5.30, –5.32; ES HRMS *m/z* calculated for $C_{30}H_{53}NO_5Si_2Na$ (M^+ + Na) 586.3360, observed 586.3359; $[\alpha]_D^{20}$ +29.7 (*c* 1.0, $CHCl_3$).

The above protected aldol adduct (15.3 g, 27.1 mmol) was stirred in THF (300 ml). H_2O (1.2 ml, 67.5 mmol) was added and the reaction mixture was cooled to 0 °C. $LiBH_4$ (1.5 g, 67.7 mmol) was cautiously added in one portion. The reaction mixture was stirred at 0 °C for 5 h and allowed to warm to r.t. over 12 h, quenched with 1 M NaOH (60 ml), diluted with EtOAc (90 ml), and stirred for 15 min. The separated aqueous layer was extracted with EtOAc (2 × 80 ml). The combined organic layers were washed with saturated NaCl solution (80 ml), dried over $MgSO_4$, filtered and concentrated in vacuo. Flash column chromatography (15% EtOAc/hexanes) provided the corresponding alcohol (8.26 g, 78%) as a clear oil; IR (thin film, cm^{-1}) 3362, 1462, 1414, 1384, 1360; ^{1}H NMR ($CDCl_3$, 400 MHz): 3.77 (m, 1 H), 3.68 (m, 1 H), 3.61 (t, *J* = 5.9, 2 H), 3.52 (m, 1 H), 2.81 (dd, *J* = 5.6, 3.7, 1 H), 1.95 (m, 1 H), 1.4–1.6 (m, 6 H), 0.96 (t, *J* = 7.8, 9 H), 0.89 (s, 9 H), 0.81 (d, *J* = 7.0, 3 H), 0.62 (q, *J* = 7.8, 6 H), 0.05 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 76.33, 66.20, 63.04, 39.57, 33.02, 32.23, 25.95, 22.69, 18.35, 11.93, 6.88, 5.12, –5.32; ES HRMS *m/z* calculated for $C_{20}H_{46}O_3Si_2Na$ (M^+ + Na) 413.2883, observed 413.2882; $[\alpha]_D^{20}$ +1.8 (*c* 3.0, $CHCl_3$).

The above alcohol (232 mg, 0.593 mmol) in CH_2Cl_2 (5 ml) was treated with Dess–Martin periodinane (288 mg, 0.889 mmol) in one portion. After being stirred at r.t. for 45 min, the reaction mixture was quenched by the addition of sodium thiosulfate doped $NaHCO_3$

(10 ml). CH_2Cl_2 (10 ml) was added and the biphasic solution stirred vigorously until two clear layers were present. The separated aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml) and the combined organic layers were washed with saturated NaCl solution (20 ml), dried over $MgSO_4$, filtered and concentrated in vacuo to yield the resultant aldehyde (205 mg, 89%), which could be used without any further purification; IR (thin film, cm^{-1}) 1728, 1462, 1414, 1255, 1101; ^{1}H NMR ($CDCl_3$, 400 MHz): 9.78 (d, 1 H, *J* = 0.9), 4.11 (td, 1 H, *J* = 6.5, 3.6), 3.60 (t, 2 H, *J* = 6.3), 2.44 (qdd, 1 H, *J* = 6.9, 3.7, 0.7), 1.52 (m, 4 H), 1.41 (m, 1 H), 1.29 (m, 1 H), 1.05 (d, 3 H, *J* = 7.0), 0.94 (t, 9 H, *J* = 8.0), 0.89 (s, 9 H), 0.58 (q, 6 H, *J* = 8.1), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 205.37, 72.26, 62.88, 51.39, 34.51, 32.82, 25.95, 22.19, 18.34, 7.71, 6.86, 5.13, –5.31, –5.32; ES HRMS *m/z* calculated for $C_{20}H_{44}O_3Si_2Na$ (M^+ + Na) 411.2727, observed 411.2724; $[\alpha]_D^{20}$ +17.2 (*c* 0.65, $CHCl_3$).

In a drybox, a flame-dried round bottom flask was charged with $Sn(OTf)_2$ (3.86 g, 9.26 mmol). Dry CH_2Cl_2 (35 ml) was added and the mixture cooled to –50 °C. *N*-Ethylpiperidine (1.27 ml, 9.26 mmol) was added followed by the addition of (*R*)-1-(4-isopropyl-2-thioxothiazolidin-3-yl)ethanone (1.49 g, 9.26 mmol) in CH_2Cl_2 (4 ml). The solution was stirred at –50 °C for 3 h and cooled to –78 °C. The above aldehyde (1.28 g, 3.29 mmol) was added in CH_2Cl_2 (4 ml). After being stirred at –78 °C for 2.5 h, the reaction mixture was quenched by the addition of pH 7 buffer and warmed to r.t. The separated aqueous layer was extracted with CH_2Cl_2 (3 × 25 ml). The combined organic layers were washed with saturated NaCl solution (30 ml), dried over $MgSO_4$, and concentrated in vacuo. Purification of the crude oil by flash column chromatography (10–25% EtOAc/hexanes) provided the Nagao adduct (1.2 g, 62%) as a yellow oil and a mixture of product and (*R*)-1-(4-isopropyl-2-thioxothiazolidin-3-yl)ethanone; IR (thin film, cm^{-1}) 3514, 1698, 1463, 1372, 1255, 1165, 1094; ^{1}H NMR ($CDCl_3$, 400 MHz): 5.16 (t, *J* = 6.8, 1 H), 4.33 (dt, *J* = 8.9, 3.2, 1 H), 3.87 (m, 1 H), 3.59 (t, *J* = 6.4, 2 H), 3.50 (dd, *J* = 11.4, 8.0, 1 H), 3.44 (A of ABX, J_{AB} = 7.5, J_{AX} = 3.3, 1 H), 3.35 (B of ABX, J_{AB} = 7.4, J_{BX} = 8.9, 1 H), 3.30 (br s, 1 H), 3.00 (d, *J* = 11.5, 1 H), 2.36 (sextet, *J* = 6.8, 1 H), 1.44–1.65 (m, 5 H), 1.26 (m, 2 H), 1.05 (d, *J* = 6.8, 3 H), 0.96 (d, *J* = 6.9, 3 H), 0.94 (t, *J* = 8.0, 9 H), 0.92 (d, *J* = 6.9, 3 H), 0.88 (s, 9 H), 0.60 (q, *J* = 8.0, 6 H), 0.03 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 202.94, 172.66, 76.79, 71.53, 70.92, 62.90, 44.14, 40.34, 34.31, 32.92, 32.23, 30.85, 30.62, 25.95, 21.89, 19.05, 18.33, 17.78, 6.90, 5.38, –5.29; ES HRMS *m/z* calculated for $C_{28}H_{57}NO_4S_2Si_2Na$ (M^+ + Na) 614.3165, observed 614.3146; $[\alpha]_D^{20}$ –170 (*c* 0.22, $CHCl_3$).

The above Nagao product (1.2 g, 2.03 mmol) was dissolved in dry CH_2Cl_2 (15 ml) in a flame-dried round bottom flask under N_2 and cooled to –78 °C. 2,6-Lutidine (0.47 ml, 4.06 mmol) was added, followed by the dropwise addition of TBSOTf (0.65 ml, 2.84 mmol). After being stirred at –78 °C for 4.5 h, the reaction mixture was quenched by addition to a separatory funnel containing saturated NH_4Cl solution and CH_2Cl_2. The separated aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml) and the combined organic layers were washed with saturated NaCl solution, dried over $MgSO_4$ and concentrated in vacuo. Purification of the crude material by flash column chromatography (5–25% EtOAc/hexanes) provided the TBS protected Nagao adduct (740 mg, 52%) as an oil, and the separable C34 diastereomer; IR (thin film, cm^{-1}) 1698, 1478, 1462, 1372; ^{1}H NMR ($CDCl_3$, 400 MHz): 5.08 (t, *J* = 7.0, 1 H), 4.37 (dt, *J* = 7.4, 4.1, 1 H), 3.71 (q, *J* = 5.3, 1 H), 3.59 (m, 3 H), 3.44 (dd, *J* = 11.4, 7.8, 1 H), 3.08 (dd, *J* = 17.6, 4.2, 1 H), 3.01 (d, *J* = 11.4, 1 H), 2.37 (sextet, *J* = 6.7, 1 H), 1.63 (m, 1 H), 1.52 (m, 4 H), 1.45 (m, 2 H), 1.05 (d, *J* = 6.8, 3 H), 0.95 (m, 15 H), 0.89 (s, 9 H), 0.85 (s, 9 H), 0.60 (q, *J* = 6.9, 6 H), 0.06 (s, 3 H), 0.05 (s, 6 H), 0.01 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 202.52, 172.04, 73.22, 71.63, 69.70, 63.25, 44.37, 42.95, 34.62, 33.42, 30.75,

30.72, 25.98, 25.92, 21.05, 19.11, 18.35, 18.17, 17.87, 10.67, 7.06, 5.38, –4.21, –4.47, –5.27; ES HRMS *m/z* calculated for $C_{28}H_{57}NO_4S_2Si_2Na$ (M^+ + Na) 728.4030, observed 728.4010; $[\alpha]_D^{20}$ –88 (*c* 0.19, $CHCl_3$).

A solution of the above intermediate (75 mg, 0.106 mmol) in THF (1 ml) was stirred and cooled to 0 °C. H_2O (5 µl, 0.265 mmol) was added, followed by the cautious addition of $LiBH_4$ (6 mg, 0.265 mmol) in one portion. The reaction mixture was stirred at 0 °C for 4 h, warmed slowly to r.t. over 12 h, and cautiously quenched with 1 M NaOH (2 ml). EtOAc (5 ml) was added and the reaction mixture stirred for 15 min. The separated aqueous layer was extracted with EtOAc (2 × 10 ml) and the combined organic layers were washed with saturated NaCl solution (10 ml), dried over $MgSO_4$, and concentrated in vacuo. Flash column chromatography (5–25% EtOAc/hexanes) provided the resulting alcohol (44.3 mg, 76%) as an oil; IR (thin film, cm^{-1}) 3451, 1472, 1462, 1255, 1102; ^1H NMR ($CDCl_3$, 400 MHz): 3.87 (q, *J* = 6.3, 1 H), 3.77 (m, 2 H), 3.68 (m, 1 H), 3.60 (t, *J* = 5.5, 2 H), 2.23 (br s, 1 H), 1.84 (m, 2 H), 1.72 (m, 1 H), 1.50 (m, 5 H), 1.28 (m, 1 H), 0.95 (t, *J* = 7.9, 9 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.58 (q, *J* = 8.0, 6 H), 0.10 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): 72.77, 72.46, 63.04, 60.06, 40.85, 35.74, 33.21, 25.96, 25.92, 22.69, 21.71, 18.35, 18.01, 9.93, 7.01, 5.47, –4.22, –4.45, –5.29; ES HRMS *m/z* calculated for $C_{28}H_{64}O_4Si_3Na$ (M^+ + Na) 571.4010, observed 571.3998; $[\alpha]_D^{20}$ +3.8 (*c* 0.16, $CHCl_3$).

The above alcohol (2.66 g, 4.84 mmol) was dissolved in dry PhH (30 ml) in a flame-dried round bottom flask under N_2. Imidazole (1.6 g, 24.2 mmol) was added, followed by the addition of PPh_3 (1.5 g, 5.81 mmol). Lastly, I_2 (1.5 g, 5.81 mmol) was added in 3 portions over 5 min. The reaction mixture was stirred at r.t. for 1 h, quenched by the addition of $Na_2S_2O_3$ doped $NaHCO_3$, and stirred until two clear layers were observed. The mixture was extracted with CH_2Cl_2 (3 × 20 ml) and the combined organic layers were washed with saturated aqueous NaCl solution (30 ml), dried over $MgSO_4$, and concentrated in vacuo. Hexanes (15 ml) were added and the mixture was frozen for 15 min. The triphenylphosphine oxide was removed by filtration and the organic layer was concentrated in vacuo to yield the desired primary iodide (2.88 g, 90%) as an oil; IR (thin film, cm^{-1}) 1462, 1384, 1254; ^1H NMR ($CDCl_3$, 400 MHz): 3.80 (m, 1 H), 3.69 (m, 1 H), 3.61 (t, *J* = 6.8, 2 H), 3.16 (t, *J* = 7.2, 2 H), 2.08 (m, 2 H), 1.61 (m, 1 H), 1.49 (m, 4 H), 1.31 (m, 2 H), 0.96 (t, *J* = 8.0, 9 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.89 (m, 3 H), 0.60 (q, *J* = 8.0, 6 H), 0.08 (s, 3 H), 0.05 (s, 6 H), 0.02 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 74.05, 72.21, 63.12, 41.01, 38.81, 35.06, 33.33, 29.72, 29.68, 26.00, 25.92, 25.72, 22.71, 21.54, 7.07, 5.49, –2.93, –4.03, –4.23, –5.26; ES HRMS *m/z* calculated for $C_{28}H_{63}IO_3Si_3Na$ (M^+ + Na) 681.3028, observed 681.3024; $[\alpha]_D^{20}$ –0.56 (*c* 5.0, $CHCl_3$).

The above iodide (2.86 g, 4.34 mmol) was dissolved in dry DMF (40 ml) in a flame-dried round bottom flask under N_2. Sodium phenylsulfinate (7.1 g, 43.4 mmol) was added in one portion. The reaction mixture was warmed at 60 °C for 2 h, cooled to r.t., and transferred to a separatory funnel containing 1:1 half saturated NH_4Cl solution and Et_2O (60 ml). The mixture was extracted with Et_2O (3 × 30 ml) and the combined organic layers were washed with H_2O (2 × 25 ml) and saturated NaCl solution (25 ml), dried over $MgSO_4$, and concentrated in vacuo. The crude oil was purified by flash column chromatography (5–10% EtOAc/hexanes) to yield sulfone **186** (2.1 g, 72%) as a clear oil; IR (thin film, cm^{-1}) 1471, 1462, 1447, 1389; ^1H NMR ($CDCl_3$, 400 MHz): 7.90 (d, *J* = 5.6, 2 H), 7.65 (t, *J* = 6.0, 1 H), 7.56 (t, *J* = 6.4, 2 H), 3.71 (m, 1 H), 3.62 (m, 1 H), 3.59 (t, *J* = 5.2, 2 H), 3.16 (td, *J* = 9.2, 3.6, 1 H), 3.08 (td, *J* = 10.0, 4.4, 1 H), 1.90 (m, 2 H), 1.48 (m, 4 H), 1.40 (m, 1 H), 1.21 (m, 2 H), 0.91 (t, *J* = 6.0, 9 H), 0.89 (s, 9 H), 0.84 (s, 9 H), 0.81 (d, *J* = 5.2, 3 H), 0.51 (q, *J* = 6.0, 6 H), 0.05 (s, 6 H), –0.01 (s, 3 H), –0.07 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): 139.23, 133.54, 129.24,

128.09, 72.13, 71.72, 62.95, 52.11, 40.97, 31.95, 29.72, 29.68, 29.38, 25.99, 25.86, 22.71, 21.97, 18.37, 7.02, 5.45, –4.37, –4.52, –5.26; ES HRMS *m/z* calculated for $C_{34}H_{68}O_5SSi_3Na$ (M^+ + Na) 695.3993, observed 695.3990; $[\alpha]_D^{20}$ +0.51 (*c* 5.5, $CHCl_3$).

β-Ketosulfone **187**

A mixture of **3** (104 mg, 0.12 mmol) and **186** (162 mg, 0.24 mmol) in THF (1.2 ml) was cooled to –78 °C (CO_2/acetone) and treated with a 1.0 M solution of LiHMDS in THF (0.25 ml, 0.25 mmol) to afford a yellow solution, which was stirred at –78 to –70 °C for 2 h. The bath was allowed to warm to –40 °C over 1 h and then to –28 °C over 20 min. The reaction mixture was stirred at –35 °C to –20 °C for 1 h 15 min, quenched by the addition of saturated aqueous NH_4Cl solution (1 ml), diluted with Et_2O (2 ml), and allowed to warm to r.t. The separated aqueous layer was extracted with Et_2O (4 × 4 ml) and the combined organics were dried (Na_2SO_4) and concentrated in vacuo to give a yellow oil. Column chromatography (1, 2, 5% EtOAc/pet ether) gave **187** as a clear colorless oil (120 mg, 67%), recovered **186** (86 mg, 53%), and recovered **3** (25 mg, 24%); IR (neat, cm^{-1}) 1731, 1639, 1614, 1586, 1514; ^1H NMR/^{13}C NMR: indistinguishable mixture of diastereomers; ES HRMS *m/z* calculated for (M^+ + Na) 1510.8081, observed 1510.8102.

α-Diketone **188**

A solution of sulfone **187** (13 mg, 0.0085 mg) in THF (0.14 ml) was cooled to 0 °C (ice/NaCl), and treated with an 0.5 M solution of KHMDS in toluene (22 μl, 0.011 mmol) to give an intensely yellow solution that was stirred for 28 min at 0 °C. A solution of Williams' oxaziridine (14 mg, 0.043 mmol) in THF (0.10 ml, 0.10 ml rinse) was added dropwise and the yellow color faded quickly to a very pale yellow. The reaction mixture was stirred at 0 °C for 2 h, quenched with saturated aqueous NH_4Cl solution (0.5 ml), diluted with Et_2O (2 ml), and allowed to warm to r.t. The separated aqueous layer was extracted with Et_2O (3 × 2 ml) and the combined organics were dried ($MgSO_4$) and concentrated in vacuo to afford a yellow semi-solid. Purification twice by column chromatography (2, 5% EtOAc/pet ether) gave starting material **187** (7.5 mg, 58%) as a nearly colorless oil and **188** as a semi-opaque, nearly colorless oil (4.6 mg, 40%); IR (neat, cm^{-1}) 1731, 1613, 1514, 1463, 1250; ^1H NMR (400 MHz, $CDCl_3$): 7.26–7.22 (m, 4 H), 6.88–6.84 (m, 4 H), 5.19 (s, 1 H), 5.17 (s, 1 H), 4.82 (d, *J* = 10.4, 4 H), 4.58 (d, *J* = 10.4, 2 H), 4.28–4.22 (m, 2 H), 4.13–3.94 (m, 2 H), 3.91 (s, 3 H), 3.90 (s, 3 H), 3.80–3.74 (m, 1 H), 3.72–3.48 (m, 3 H), 3.29–3.18 (m, 2 H), 3.02–2.97 (m, 1 H), 2.89–2.83 (m, 1 H), 2.65–2.57 (m, 2 H), 2.36 (d, *J* = 13.2, 1 H), 2.29–2.32 (m, 1 H), 2.13–2.07 (m, 1 H), 1.84–1.78 (m, 1 H), 1.65–1.21 (series of m, 7 H), 0.98–0.79 (m, 51 H), 0.62–0.47 (m, 12 H), 0.05 (s, 6 H), 0.06 (s, 6 H), –0.01 (s, 3 H), –0.05 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 200.0, 195.8, 159.5, 159.4, 143.0, 141.0, 130.7, 130.6, 129.6 (2C), 129.3 (2C), 114.9, 114.1 (2C), 114.03 (2C), 113.98, 86.2, 83.1, 79.2, 79.0, 75.3, 74.9, 74.6, 72.0, 71.8, 69.1, 63.3, 55.5, 55.4, 42.6, 42.2, 41.0, 39.11, 39.06, 37.5, 35.4, 33.5, 29.9, 26.14 (3C), 26.07 (3C), 26.03 (3C), 21.7, 18.5, 18.1 (2C), 7.21 (3C), 7.13 (3C), 5.63 (3C), 5.26 (3C), –4.16, –4.25, –4.28 (2C), –5.12, –5.14; ES HRMS *m/z* calculated for (M^+ + Na) 1384.7942, observed 1384.8062; $[\alpha]_D^{25}$ –5.6 (*c* 0.16, $CHCl_3$).

α-Ketohemiketal **189**

To a solution of diketone **188** (5.7 mg, 0.0042 mmol) in MeOH/THF (0.42 ml/0.28 ml) was added PPTs (1.5 mg, 0.0084 mmol) and the reaction mixture was stirred at r.t. for 2.5 h, quenched by the addition of pyridine (0.1 ml), and diluted with brine (1 ml) and Et_2O (2 ml). The separated aqueous layer was extracted with Et_2O (3 × 2 ml) and the combined organics were dried (Na_2SO_4) and concentrated in vacuo to give a pale yellow residue. Column chromatography (hexanes/EtOAc 100:0 to 4:1) afforded **189** as a nearly colorless residue (4.0 mg, 77%); ^{1}H NMR (400 MHz, $CDCl_3$): 7.26–7.23 (m, 4 H), 6.87–6.84 (m, 4 H), 5.82 (s, 1 H), 5.82 (s, 1 H), 5.18 (br s, 1 H), 5.16 (br s, 1 H), 4.98 (br s, 1 H), 4.84 (d, *J* = 10.4, 1 H), 4.82 (br s, 1 H), 4.80 (d, *J* = 10.4, 1 H), 4.58 (d, *J* = 10.4, 2 H), 4.33–4.26 (m, 1 H), 4.25 (d, *J* = 10.8, 1 H), 4.05–4.01 (m, 1 H), 3.96–3.93 (m, 1 H), 3.80 (s, 6 H), 3.74–3.71 (m, 1 H), 3.62 (t, *J* = 6.4, 2 H), 3.57–3.55 (m, 1 H), 3.31–3.22 (m, 2 H), 2.64 (br d, *J* = 14, 1 H), 2.57 (br d, *J* = 15.6, 1 H), 2.38 (br d, *J* = 13.6, 1 H), 2.25 (dd, *J* = 14, 10, 1 H), 2.17–2.08 (m, 3 H), 1.85 (dd, *J* = 13.6, 10.4, 1 H), 1.66–1.58 (m, 2 H), 1.44–1.35 (m, 2 H), 0.96–0.79 (series of m, 42 H), 0.59–0.52 (m, 6 H), 0.12 to –0.08 (series of m, 18 H); TOF MS ES *m/z* calculated for (M^+ + Na) 1269.7052, observed 1269.7072.

α-Hydroxyhemiketal **191**

A solution of **189** (6.1 mg, 0.0049 mmol) in THF (0.25 ml) was treated with Amberlyst-15 (7 beads) followed immediately by $NaBH_4$ (1.8 mg, 0.048 mmol) at r.t. The reaction mixture was stirred for 40 min, filtered through a pad of Celite (EtOAc), and concentrated in vacuo to give an off-white residue. Column chromatography (hexanes/EtOAc 100:1 to 4:1) gave **191** as a colorless residue (4.5 mg, 74%); IR (neat, cm^{-1}) 3456, 1514, 1463, 1250, 1098; ^{1}H NMR (400 MHz, $CDCl_3$): 7.27–7.24 (m, 4 H), 6.87–6.84 (m, 4 H), 5.34 (s, 1 H), 5.18 (s, 1 H), 5.15 (s, 1 H), 4.93 (s, 1 H), 4.84 (d, *J* = 10.4, 1 H), 4.81 (d, *J* = 10.4, 1 H), 4.57 (d, *J* = 10.4, 2 H), 4.26–4.19 (m, 1 H), 3.97–3.92 (series of m, 2 H), 3.797 (s, 3 H), 3. 795 (s, 3 H), 3.73–3.71 (m, 1 H), 3.62–3.59 (m, 2 H), 3.50–3.44 (m, 2 H), 3.39 (d, *J* = 6.8, 1 H), 3.25–3.16 (m, 2 H), 2.65 (d, *J* = 14, 2 H), 2.44 (d, *J* = 6.8, 1 H), 2.40 (d, *J* = 12.8, 1 H), 2.25 (dd, *J* = 14, 9.6, 1 H), 2.11–1.96 (m, 2 H), 1.92–1.85 (m, 2 H), 1.78–1.72 (m, 1 H), 1.70–1.10 (series of m, 7 H), 1.01–0.79 (series of m, 42 H), 0.63–0.54 (m, 6 H), 0.10 to –0.04 (m, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$): 159.4, 159.3, 144.3, 140.9, 131.0, 130.8, 129.6 (2C), 129.2 (2C), 114.9, 114.1, 114.0 (2C), 113.9 (2C), 98.6, 86.7, 83.1, 78.9, 78.6, 75.0, 74.9, 74.7, 73.9, 73.0, 72.0, 66.3, 63.2, 55.44, 55.39, 41.2, 39.0, 38.8, 38.4, 37.2, 33.0, 32.1, 31.4, 29.5, 26.13 (3C), 26.05 (3C), 25.9 (3C), 22.8, 22.1, 18.5, 18.2, 18.0, 7.16 (3C), 5.25 (3C), –4.25 (2C), –4.74, –4.85, –5.10 (2C); TOF MS ES *m/z* calculated for (M^+ + Na) 1271.7208, observed 1271.7111; $[\alpha]_D^{24}$ –7.8 (*c* 0.23, $CHCl_3$).

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