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Total synthesis of the proposed structure of iriomoteolide-1a

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ABSTRACT

Full details of the total synthesis of the proposed structure of iriomoteolide-1a (**1**) are described. The key steps include (i) a Sakurai reaction between allylsilane **11** and aldehyde **10** that bears both a tertiary chiral center and vinyl iodide moiety (ii) an *anti*-aldol reaction to construct the C18/C19 chiral centers (iii) a *B*-alkyl Suzuki–Miyaura coupling reaction to assemble the C7–C23 fragment, and (iv) a macrocyclic ring-closing metathesis to complete the construction of the target molecule. Two different approaches to access penultimate precursor **2** are delineated. The NMR spectra of the synthetic iriomoteolide-1a (**1**) were found not to match those reported for the natural product bringing into question its true structural identity.

1. Introduction

Iriomoteolide-1a (**1**) was isolated from the *Amphidinium* sp. strain HYA024 by Tsuda's group and its structure was elucidated through 2D NMR and mass spectral analysis.[1] Iriomoteolide-1a possesses potent cytotoxicity with IC_{50} values against human B lymphocyte DG-75 cells and Epstein–Barr virus-infected human B lymphocytes of 2 and 3 ng/mL, respectively. Iriomoteolide-1a (**a**) is a synthetically challenging target characterized by a hemiketal ring that consists of a tertiary chiral center and an exocyclic methylene group, three pairs of chiral vicinal methyl/hydroxyl groups, and a trisubstituted *Z*-unsaturated ester. Because of its important biological activity and unique structure, iriomoteolide-1a (**1**) has become a target of significant interest for synthetic chemists.[2] Herein, we report the full account of the total synthesis of the proposed structure of iriomoteolide-1a (**1**) for which synthetic iriomoteolide-1a (**1**) was found not to match that of the natural material isolated from nature.[3]

2. Results and discussion

2.1. First generation synthesis of key intermediate 2

2.1.1. Retrosynthetic analysis. The retrosynthetic strategy for iriomoteolide-1a (**1**) is shown in Fig. 1. The final assembly of **1** by this route was approached via ring-closing metathesis.[4] Key intermediate **2** could be obtained from esterification between C7–C23 fragment **3** and C1–C6 acid fragment **4**. The C7–C23 fragment **3** can be further dissected into smaller subunits, that is, comprised of vinyl iodide **5** or **6** and alkyl iodide **7**, derived from a *B*-alkyl Suzuki–Miyaura cross-coupling reaction.[5] Vinyl iodides **5** or **6** could be prepared from allylsilane **11** and aldehydes **9** or **10**, respectively using Sakurai methodology.[6] Alkyl iodide **7** is approached via an *anti*-aldol reaction whereas C1–C6 fragment **4** can be generated from known diol **8** that also harbors the two requisite chiral centers.

*2.1.2. Synthesis of **5** with PMB group on tertiary center.* The preparation of allylsilane **11** commenced with ring opening of epoxide **13**[7] with commercially available **12** in the presence of *t*-BuLi and CuI to provide allyltrimethylsilane **14** in excellent yield.[8] The resulting alcohol was protected with TES to generate **11** (Scheme 1).

The synthesis of aldehyde **9** began with primary alcohol **15**[2c] which contains the requisite chiral tertiary center. Oxidation of **15** followed by homologation with Bestmann–Ohira reagent[9] produced alkyne **16**. Hydrohalogenation[10] of **16** was accomplished in two steps to afford *E*-vinyl iodide **17**. When *E*-vinyl iodide **17** was treated with DIBAL-H, the anticipated primary alcohol, **18**, was formed only as the minor product. The ratio of **18** to **19** is approximately 1:4 in 72% overall yield (Scheme 2).

Because of the disappointing yield of forming primary alcohol **18**, an alternative method was pursued (Scheme 3). Acetal substrate **21** was prepared from known diol **20**.[11] Although DIBAL-H reduction of a similar substrate has been reported in the literature[12] (ethyl group instead of methyl at the tertiary center) to provide the desired primary alcohol corresponding to **23**, reduction of substrate

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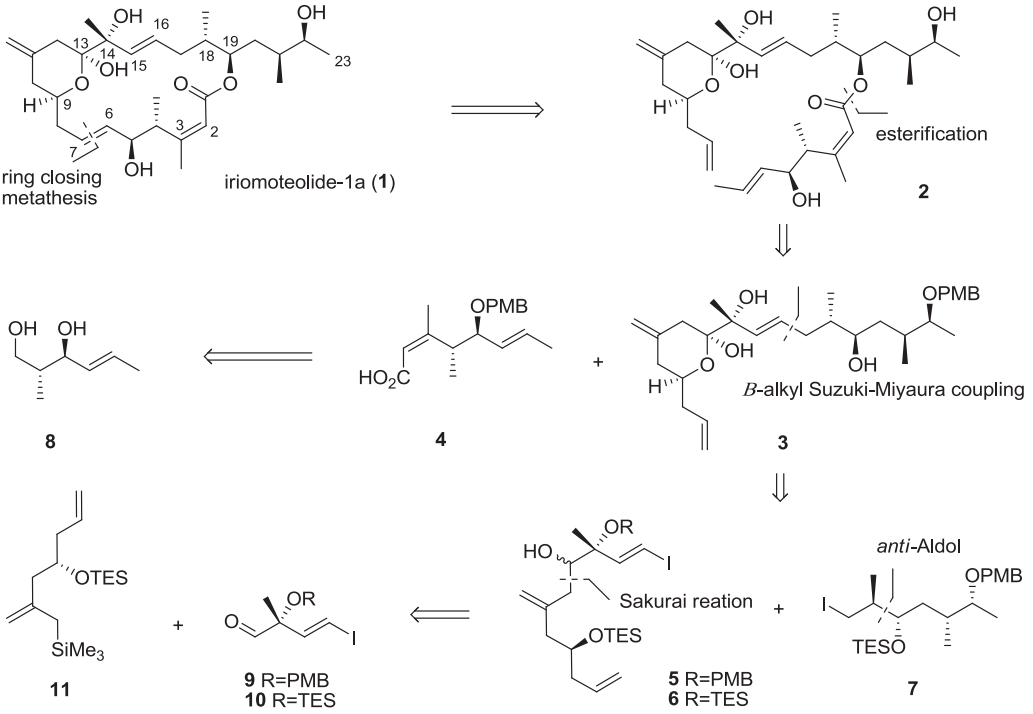
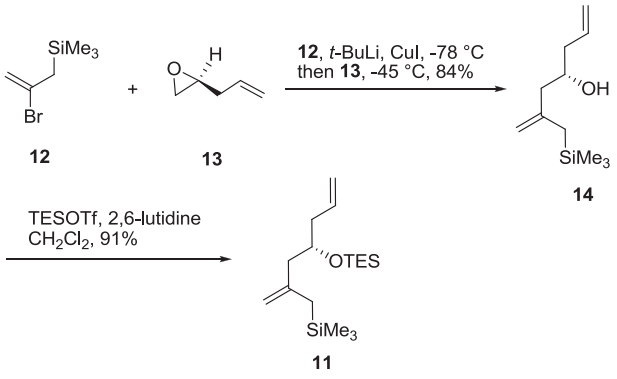
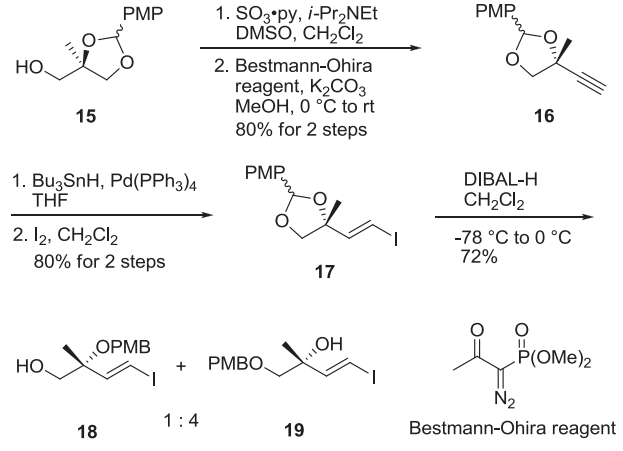


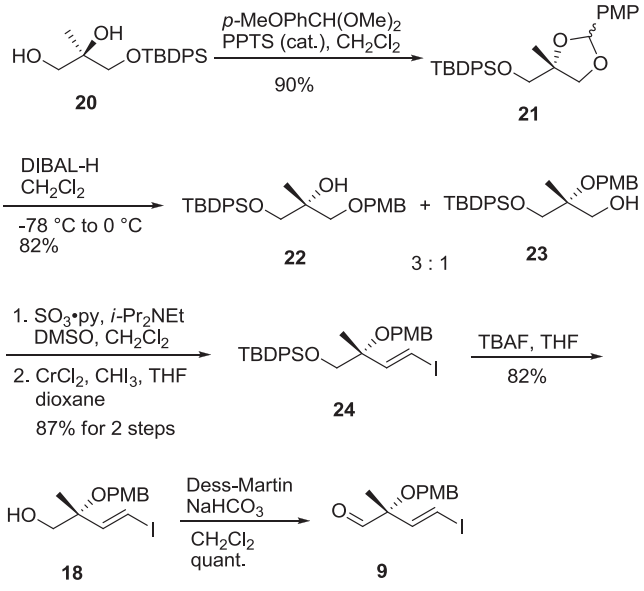
Fig. 1. Retrosynthetic analysis of iriomoteolide-1a (**1**).



Scheme 1. Synthesis of **11**.



Scheme 2. Synthesis of **18**.

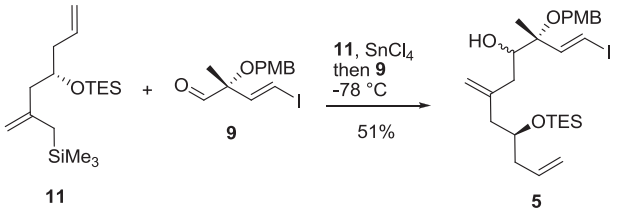


Scheme 3. Synthesis of **9**.

21 with DIBAL-H under the same conditions resulted in product **23** as the minor product (ratio of **22** to **23** is approximately 3:1) in 82% overall yield. Oxidation of the primary alcohol **23** followed by reaction with $CrCl_2$ and CHI_3 yielded vinyl iodide **24**.[13] The desired aldehyde, **9**, is obtained via deprotection of TBDPS followed by oxidation of the resulting alcohol with Dess–Martin reagent.[14]

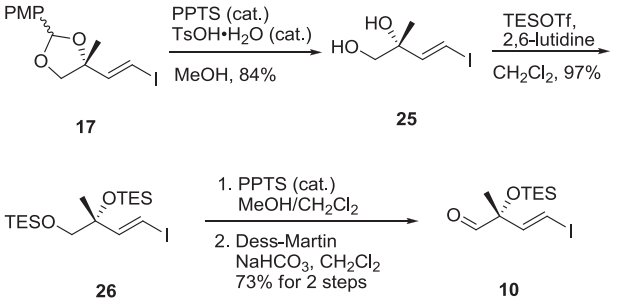
Sakurai reaction[6] between aldehyde **9** and allylsilane **11** was initially attempted with $BF_3{\cdot}OEt_2$. While these conditions were successfully adopted in our previous model system, only trace amounts of desired product **5** was observed. Fortunately, when $SnCl_4$ was used, product **5** was obtained in 51% yield and 2:1 dr (Scheme 4). To consistently obtain decent yields, this reaction should be quenched with Et_3N before adding satd $NaHCO_3$.

*2.1.3. Synthesis of **6** with TES group on tertiary center.* Although the Sakurai reaction worked well for aldehyde **9**, the yield to prepare **9** was



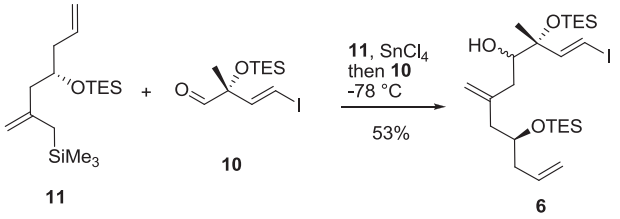
Scheme 4. Synthesis of **5**.

too low for scale up. To circumvent this problem, aldehyde **10** bearing a TES group on the tertiary alcohol instead of PMB group was pursued (Scheme 5). Conversion of acetal **17** into its bisTES ether **26** was accomplished in two steps. Selective deprotection of the primary TES group and subsequent oxidation yielded aldehyde **10**. This versatile intermediate represents a key structural component to which the remainder of the fragment can be linked in a bidirectional manner.



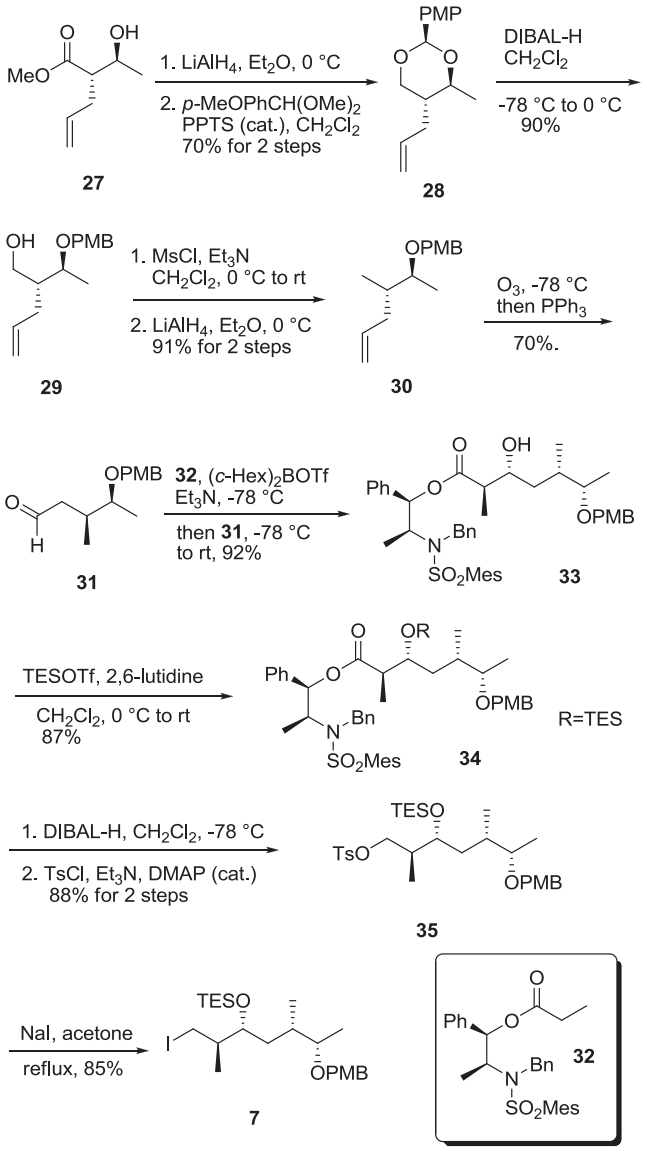
Scheme 5. Synthesis of **10**.

When $SnCl_4$ was used in the reaction with allylsilane **11** and aldehyde **10**, product **6** was obtained in satisfactory yield and 4:1 dr (Scheme 6). The configuration of the newly formed chiral center was not determined at this time; however, a chelation controlled addition product is presumed. Note that chirality at this center is removed in subsequent steps via oxidation to the corresponding ketone functionality. At this point, vinyl iodide **6**, which will be used in Suzuki–Miyaura coupling reaction, has been obtained.



Scheme 6. Synthesis of **6**.

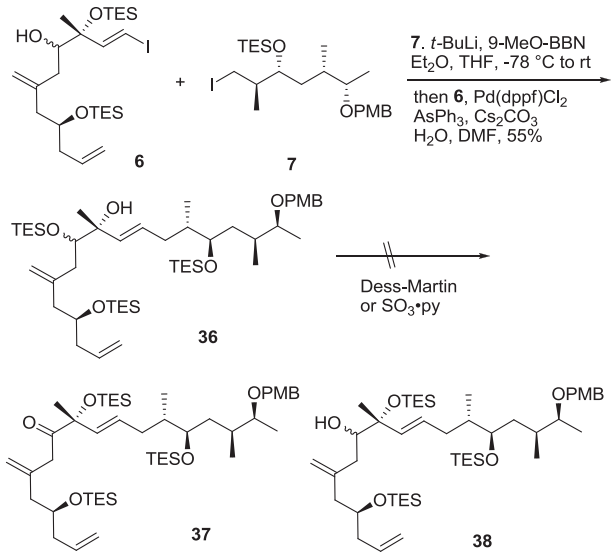
2.1.4. Synthesis of alkyl iodide **7**. Starting from (3*S*)-methyl hydroxybutyrate, allylation provided **27** in good yield with high dr.[15] Reduction of **27** with $LiAlH_4$ followed by treatment with 4-methoxybenzaldehyde dimethyl acetal afforded acetal **28**. Selective reduction with DIBAL-H generated primary alcohol **29**, which was converted to **30** via mesylation and reduction. Ozonolysis of the terminal alkene provided aldehyde **31**. In the presence of **32** and $(c\text{-Hex})_2$BOTf, *anti*-aldol product, **33**, was obtained in excellent yield and good dr.[16] The newly formed secondary alcohol was protected as its TES ether. DIBAL-H reduction of **34** yielded the corresponding primary alcohol but due to difficulties in separation of the desired product from the chiral auxiliary, the crude mixture was treated with excess TsCl. This afforded tosylate **35** in pure form and excellent yield as well as recovery of the chiral auxiliary after chromatography. Displacement of tosylate **35** with iodide under Finkelstein conditions afforded Suzuki–Miyaura coupling partner, alkyl iodide **7** (Scheme 7).



Scheme 7. Synthesis of **7**.

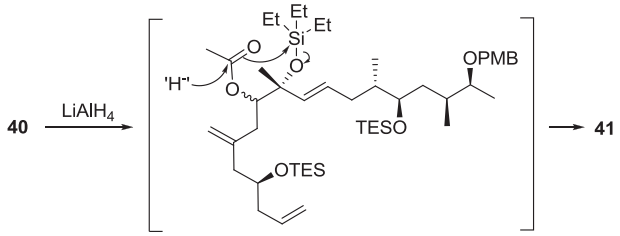
2.1.5. Synthesis of complete C7–C23 fragment **3**. With alkyl iodide **7** and vinyl iodide **6** in hand, the *B*-alkyl Suzuki–Miyaura coupling[17] reaction was performed (Scheme 8). Treatment of alkyl iodide **7** with *t*-BuLi and 9-BBN followed by subsequent coupling with vinyl iodide **6** in the presence of $Pd(dppf)Cl_2$ catalyst afforded coupled products. Initially, we thought the desired product, **38**, was produced but upon oxidation of this product with Dess–Martin reagent or $SO_3\cdot py$ only trace amounts of product **37** could be obtained. Based on this result, we reconsidered that the main product of the Suzuki–Miyaura coupling reaction was in fact, **36** not **38**. The tertiary TES group undergoes migration to the vicinal secondary alcohol under the Suzuki–Miyaura coupling conditions.

To prevent migration of the TES group in **6** during the Suzuki–Miyaura coupling reaction, the alcohol moiety was protected as



Scheme 8. Attempted synthesis of **37**.

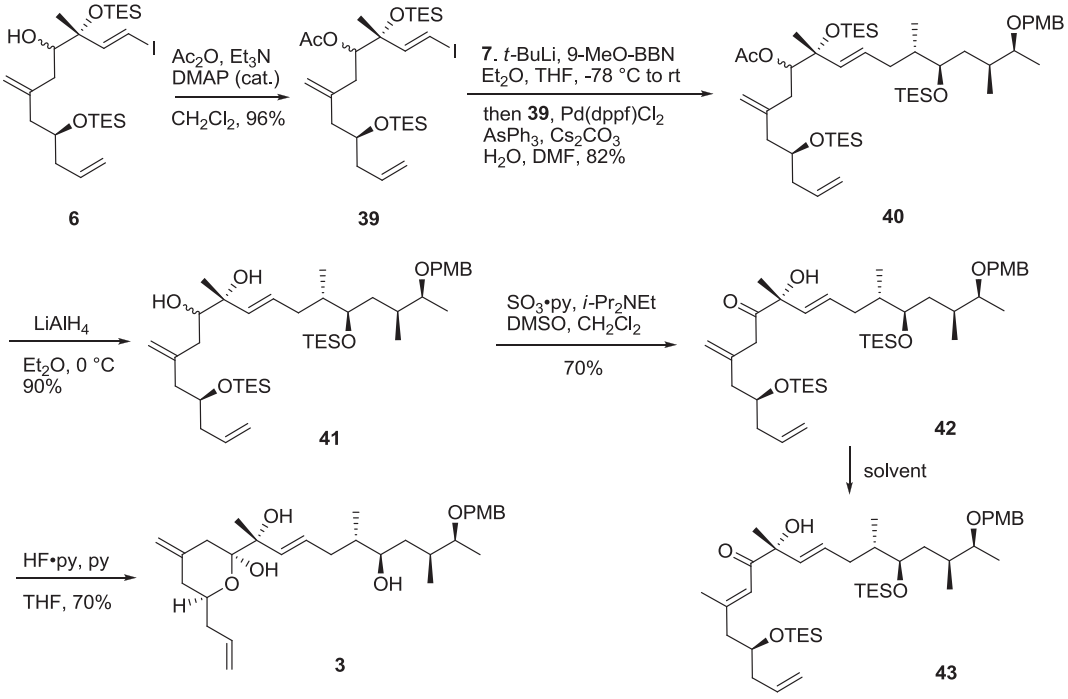
the corresponding acetate to furnish **39** in high overall efficiency (Scheme 9). The new vinyl iodide, **39**, and alkyl iodide **7** underwent smooth coupling in excellent yield to afford the linear C7–C23 fragment **40** of iriomoteolide-1a. Upon $LiAlH_4$ cleavage of the acetate functionality of **40**, concomitant deprotection of the vicinal tertiary TES group was observed producing diol, **41**, in excellent yield. The secondary TES group was untouched during this process. The likely mechanism is shown in Scheme 10. Interestingly, this sequence may have general implications for selectively removing TES groups over others that are not vicinal to acetates. Oxidation of diol **41** produced β,γ-unsaturated ketone **42**. It is worth noting that β,γ-unsaturated ketone **42** is relatively unstable and the double bond slowly migrates to afford α,β-unsaturated ketone **43** in solution. Ketone **42** should be used immediately in the next step. Following conditions previously developed in our model study[2c] treatment of **42** with HF·py produced **3**. Under these conditions, double bond migration of the β,γ-unsaturated ketone to α,β-unsaturated system was not observed.



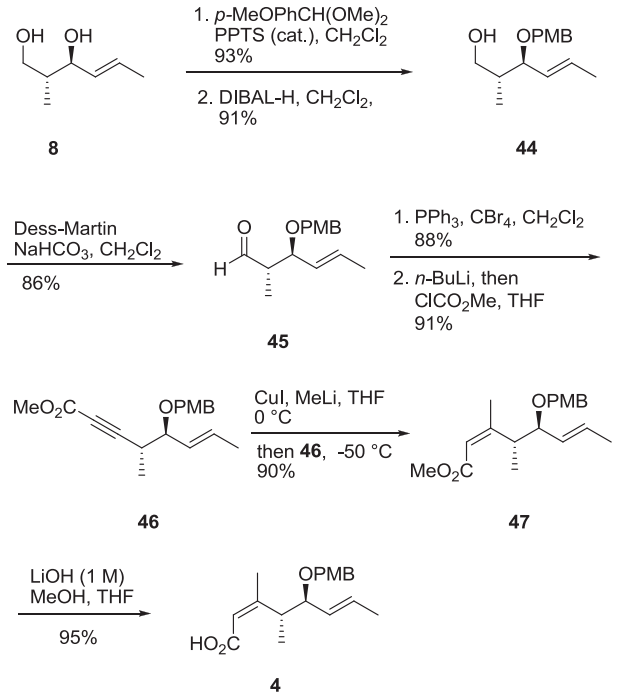
Scheme 10. Mechanism vicinal TES group cleavage.

*2.1.6. Synthesis of C1–C6 fragment **4**.* With the C7–C23 fragment in hand, our attention turned to the preparation of the acid fragment containing C1–C6. The synthesis of acid fragment **4** starts from known diol **8**[16] (Scheme 11). Treatment of diol **8** with 4-methoxybenzaldehyde dimethyl acetal followed by selective reduction with DIBAL-H afforded primary alcohol **44**, which was oxidized to aldehyde **45** with Dess–Martin periodinane. Conversion of **45** to propionate **46** was achieved via two steps. Addition of propionate **46** with methyllithium in the presence of copper(I) iodide[18] generated *Z*-alkenoic ester **47**. Ester saponification using 1 M LiOH in MeOH/THF gave acid fragment **4** in high yield upon acidic work-up.

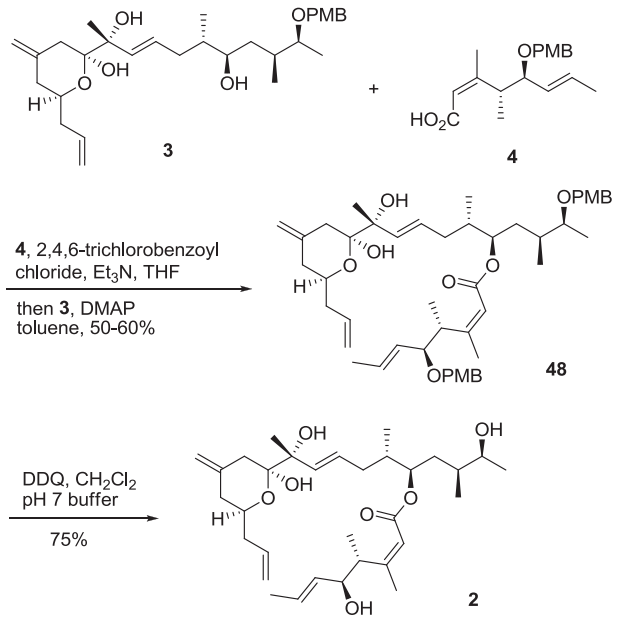
*2.1.7. Synthesis of key intermediate **2**.* With secondary alcohol **3** and acid **4** in hand, esterification was accomplished under Yamaguchi conditions[19] (Scheme 12). Treatment of **4** with 2,4,6-trichlorobenzoyl chloride and Et_3N followed by addition of DMAP and alcohol **3** generated desired product **48** in 50–60% yield with some decomposed material due to instability of the exocyclic methylene-bearing ketal unit. Application of other conditions such



Scheme 9. Synthesis of **3**.



Scheme 11. Synthesis of **4**.



Scheme 12. Synthesis of **2**.

as EDCI, MNBA(2-methyl-6-nitrobenzoic anhydride)[20] only provided trace amounts of product. Deprotection of the PMB group afforded precursor **2**, which is primed for ring-closing metathesis.

2.2. Second generation synthesis of key intermediate *2*

2.2.1. Retrosynthetic analysis. Since esterification between **3** and **4** proceeded in relatively low yield coupled to the difficulty in chromatographic separation of by-products, an alternative strategy for preparing penultimate intermediate **2** was pursued. The retrosynthetic analysis is shown in Fig. 2. Key intermediate **2** could be formed from **49** through global deprotection of PMB groups and concominant cyclization. In turn, **49** would be obtained from vinyl iodide **50**, which would be derived from allylsilane **51** and aldehyde **10**. This approach involves performing the esterification prior to hemiketal ring formation for which a possible improvement in the efficiency of esterification may be realized.

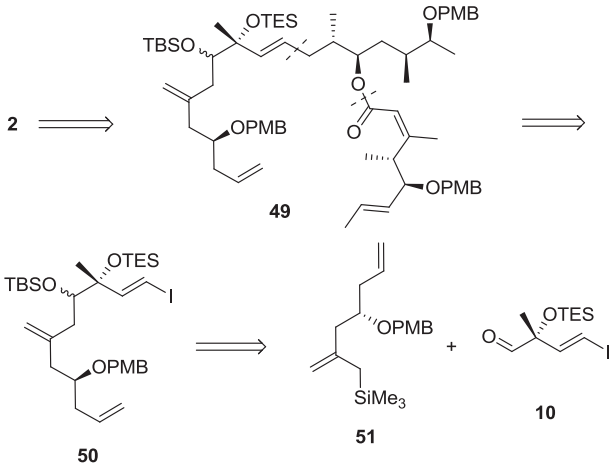
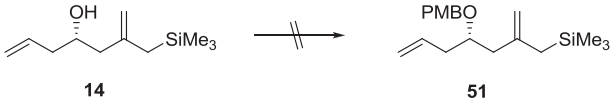


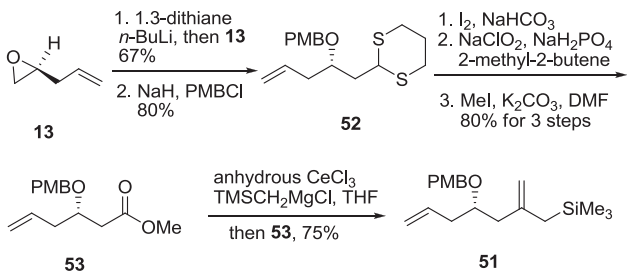
Fig. 2. Retrosynthetic analysis.

*2.2.2. Synthesis of **51**.* At first, the preparation of allylsilane **51** directly from its corresponded alcohol **14** through protection with PMB (Scheme 13) was attempted. Efforts, however, to obtain **51** failed under both basic and acidic conditions (basic conditions: NaH, PMBCl or KHMDS, PMBCl; acidic conditions: $Sc(OTf)_3$ or PPTS or TsOH, and $PMBO(C{=}NH)CCl_3$).



Scheme 13. Attempted Synthesis of **51**.

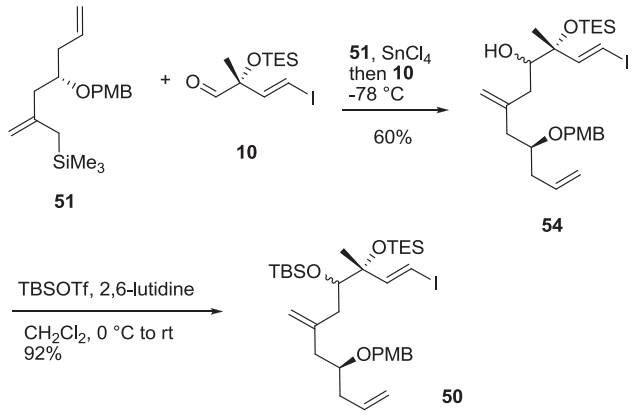
Since the allylsilane group in **14** is sensitive to acidic and basic conditions, PMB installation on the chiral hydroxyl moiety needs to occur prior to formation of the allylsilane (Scheme 14). Epoxide ring opening of **13** with 1,3-dithiane followed by protection with PMB provided **52** in good yield.[21] The dithiane group was converted into ester **53** in three steps (i) hydrolysis to the aldehyde, (ii) Pinnick oxidation[22] to the corresponding carboxylic acid, and (iii) methylation in 80% yield. Treatment of ester **53** with anhydrous $CeCl_3$ and $TMSCH_2MgCl$ generated desired allylsilane **51**.[23]



Scheme 14. Synthesis of **51**.

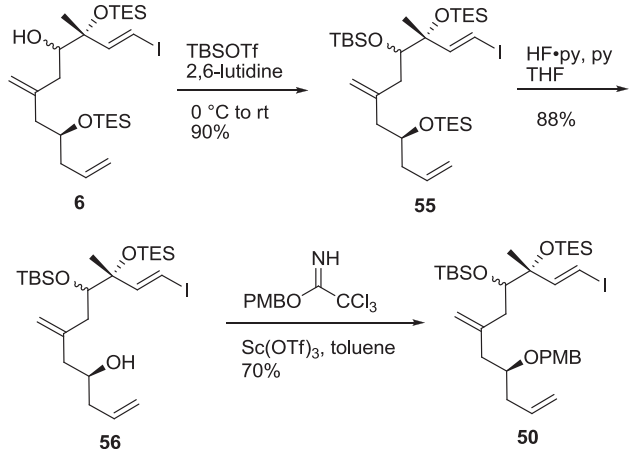
*2.2.3. Synthesis of **50**.* With allylsilane **51** in hand, Sakurai reaction with aldehyde **10** gave **54** in satisfactory yield (Scheme 15).

Protection of the newly formed hydroxyl group gave vinyl iodide **50**, the key substrate in the *B*-alkyl Suzuki–Miyaura coupling reaction.



Scheme 15. Synthesis of **50**.

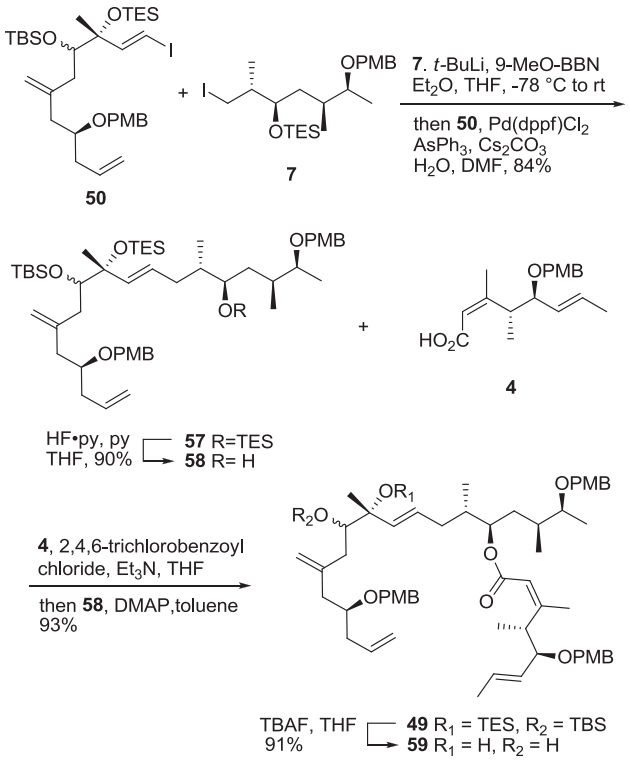
Alternatively, vinyl iodide, **50**, also can be obtained from previously synthesized fragment **6** through exchange of protecting groups (Scheme 16). Protection of **6** with TBS group and selective deprotection of secondary TES group produced **56**. The hydroxyl group of **56** was protected with PMB in the presence of catalytic amount of $Sc(OTf)_3$ to provide **50**.



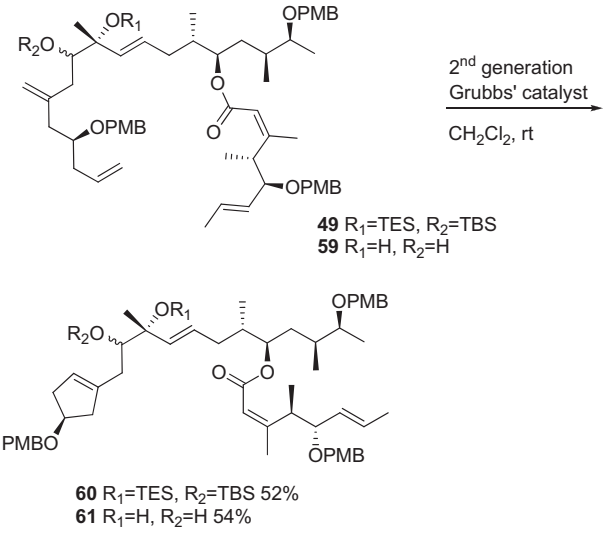
Scheme 16. Alternative synthesis of **50**.

2.2.4. Yamaguchi reaction for new substrates. *B*-Alkyl Suzuki–Miyaura coupling reaction between **50** and **7** produced desired fragment **57** in good yield. Selective deprotection of the TES group afforded substrate **58** for Yamaguchi esterification.[19] Since decomposition of the sensitive hemiketal functionality was averted (which was prevalent in the conversion of **3**–**48**), esterification between **58** and acid **4** provided **49** in 93% yield. With this gratifying result, removal of the two Si protecting groups with TBAF produced olefin metathesis precursor **59** (Scheme 17).

2.2.5. Attempted synthesis of macrocyclic ring. As noted, ring-closing metathesis of **49** and **59** was attempted as a means to access the macrocyclic ring products; however, when **49** or **59** were treated with second generation Grubbs' catalyst,[24] only five-member ring products **60** or **61** were formed (Scheme 18). In order to obtain the desired macrocyclic ring product, it was evident that the hemiketal unit must be formed prior to olefin metathesis.



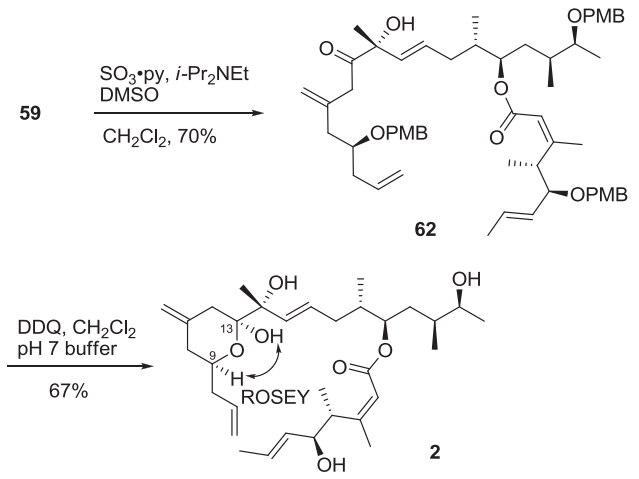
Scheme 17. Synthesis of **59**.



Scheme 18. Attempted synthesis of macrocyclic ring.

2.2.6. Alternative synthesis of key intermediate ***2****.* At this stage, only two steps remained to key intermediate **2** from diol **59** (Scheme 19). Diol **59** was oxidized to β,γ-unsaturated ketone **62** with $SO_3 \cdot$py. Global deprotection along with concomitant hemiketal cyclization was observed after treatment of **62** with DDQ to afford key intermediate **2** in 67% yield. The C13 stereochemistry of hemiketal **2**

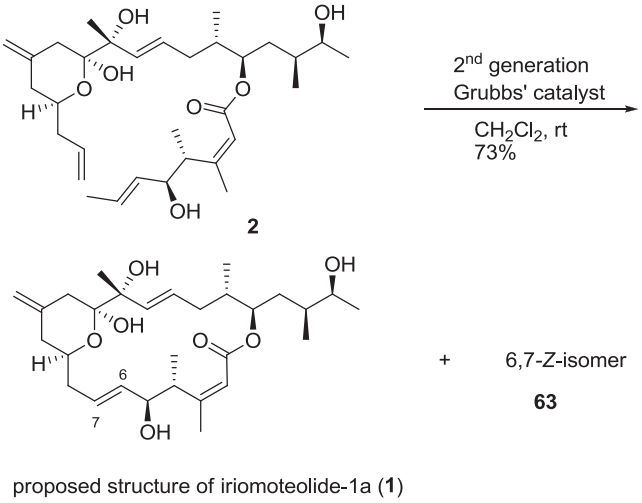
was confirmed through an observed ROSEY interaction between H9 and C13–OH.



Scheme 19. Alternative synthesis of key intermediate **2**.

2.3. Completion of the total synthesis and NMR spectra comparison

*2.3.1. Completion of the total synthesis of **1**.* After the successful preparation of **2** by two different strategies, treatment with second generation Grubbs' catalyst yielded *E*- and *Z*-products iriomoteolide-1a (**1**) and **63** in 2.5:1 ratio, respectively (Scheme 20).[24]



Scheme 20. Completion of the total synthesis of **1**.

2.3.2. Comparison of NMR spectra. ^{1}H and ^{13}C NMR spectral comparison of synthetic iriomoteolide-1a (**1**) did not match those reported for the natural material.[1] While minor inconsistencies are noted throughout the spectra, the main discrepancies reside with proton and carbon chemicals shifts at C4 (see Table in Supplementary data). For synthetic iriomoteolide-1a (**1**), the H4 hydrogen resonates at 3.95 ppm and the carbon-13 shift occurs at 41.0 ppm compared to 2.46 ppm and 47.9 ppm for natural product, respectively. Attempts to prepare crystalline derivatives of **1** have not been successful; however, the significant difference in NMR spectral data brings into question the original structural assignment of the natural product. Based on chemical shift of H4 in natural product, it is likely that the C2–C3 double bond configuration of natural product is *E* instead of *Z*. Recently, Yang's group[2j] reported the synthesis of this iriomoteolide-1a diastereomer, however, this diastereomer still does not match that of the natural product. Finally, anti-cancer activity for synthetic **1** was examined in two different cell lines (Raji and A431) and unfortunately no significant cytotoxicity was observed at 10 μM concentration.

3. Conclusion

Our group was the first to complete the total synthesis of the proposed structure of iriomoteolide-1a (**1**) by applying a late stage Yamaguchi esterification and ring closing metathesis reaction. The advanced ring closing metathesis precursor, **2**, was obtained from two different routes, the latter of which proved to be more efficient. *B*-Alkyl Suzuki–Miyaura cross-coupling reaction was efficiently utilized in constructing the C7–C23 fragment of iriomoteolide-1a. The versatile aldehyde intermediate **10**, which bears the requisite tertiary chiral center and vinyl iodide group, possesses bidirectional functionality, that is, suitable for Sakurai and *B*-alkyl Suzuki–Miyaura coupling reactions. Comparison of the NMR spectra of synthetic iriomoteolide-1a (**1**) with those of the natural product suggests that the original structure of iriomoteolide-1a (**1**) was misassigned.[25] The actual structure of **1** remains a mystery. The extremely potent anti-cancer activity displayed by iriomoteolide-1a warrants further investigation of this active principle and work in this area is currently in progress.

4. Experimental section

4.1. General information

All reagents and solvents were commercial grade and purified prior to use when necessary. TLC was performed on Silica Gel 60 F_{254} from EMD. Visualization was performed by ultraviolet light and/or by staining with potassium permanganate. Flash Chromatography was performed using Silica Gel 60 (particle size 40–63 μm). All ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz (Varian), respectively, at rt. Optical rotations were measured on JASCO p-2000 polarimeter. High-resolution mass spectrometry (HRMS) data were obtained from Thermo Electron LTQ-FT hybrid linear ion trap and Fourier transform ion cyclotron resonance mass spectrometer. IR spectra were recorded as thin films on Thermo Nicolet IR200 and are reported at 23 °C in wavenumbers (cm^{-1}).

4.2. Experimental procedure

*4.2.1. Allylsilane **14**.* To a stirred solution of **12** (900 mg, 4.68 mmol, 2 equiv) in Et_2O (1.5 mL) was added *t*-BuLi (1.5 M in pentane, 9.83 mmol, 4.2 equiv) at −78 °C. After 2 h at −78 °C, the solution was transferred to suspension of CuI (492 mg, 2.57 mmol, 1.1 equiv) in Et_2O (7 mL) at −78 °C. After 2 h, the mixture was treated with **13** (197 mg, 2.34 mmol, 1 equiv). After 1 h at −78 °C, the reaction was warmed up to at −40 °C and stirred overnight. The reaction was quenched with satd NH_4Cl and extracted with Et_2O. The combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (1.5–2% EtOAc/hexane) to afford **14** (389 mg, 84%) as a colorless oil. $[\alpha]_D^{20}$ −13.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.91–5.81 (m, 1H), 5.16–5.11 (m, 2H), 4.70 (d, 1H, *J*=1.0 Hz), 4.68 (d, 1H, *J*=1.0 Hz), 3.81–3.74 (m, 1H), 2.30–2.20 (m, 2H), 2.17 (ddd, 1H, *J*=1.0, 3.9, 13.8 Hz), 2.05 (dd, 1H, *J*=9.0 Hz, 13.8 Hz), 1.92 (d, 1H, *J*=2.3 Hz), 1.60–1.50 (m, 2H), 0.03 (s, 9H); ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm):

144.8, 135.1, 117.9, 110.7, 68.2, 46.1, 41.6, 26.8, −1.1; HRMS calcd for $C_{11}H_{22}OSi$ $[M+Na]^+$ 221.1332, found 221.1332; IR ν_{max} (film) 3395, 3074, 2954,1632, 1423, 1250, 1157, 1041, 854 cm^{-1}.

*4.2.2. Allylsilane **11**.* To a stirred solution of **14** (80 mg, 0.4 mmol) in CH_2Cl_2 (2 mL) were added 2,6-lutidine (103 mg, 0.96 mmol, 2.4 equiv) and TESOTf (127 mg, 0.48 mmol, 1.2 equiv) at 0 °C, after 30 min at 0 °C, the reaction was quenched with satd $NaHCO_3$ and extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (1% EtOAc/hexane) to afford **11** (115 mg, 91%) as a colorless oil. $[\alpha]_D^{20}$ 0.56 (*c* 0.57, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.90–5.79 (m, 1H), 5.07–5.02 (m, 2H), 4.61 (s, 1H), 4.57 (s, 1H), 3.87–3.81 (m, 1H), 2.32–2.13 (m, 2H), 2.10 (d, 2H, *J*=6.5 Hz), 1.52 (s, 2H), 0.96 (t, 9H, *J*=7.8 Hz), 0.60 (q, 6H, *J*=7.8 Hz), 0.02 (s, 9H); ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm): 144.5, 135.7, 117.1, 110.2, 71.2, 46.3, 41.9, 27.3, 7.2, 5.3, −1.1; HRMS calcd for $C_{17}H_{36}OSi_2$ $[M+Na]^+$ 335.2197, found 335.2201; IR ν_{max} (film) 3394, 3074, 2954, 2918, 1632, 1423, 1249, 1040, 853 cm^{-1}.

*4.2.3. Alkyn **16**.* To a stirred solution of **15** (448 mg, 2 mmol) in CH_2Cl_2 (20 mL) were added $(i\text{-}Pr)_2NEt$ (2.1 g, 16 mmol, 8 equiv), DMSO (2.4 mL), and $SO_3\cdot py$ (950 mg, 6.0 mmol, 3 equiv) at 0 °C. The reaction was stirred for 30 min and quenched with satd $NaHCO_3$ and the mixture was diluted with Et_2O. The organic layer was washed successively with H_2O, brine, and dried over $MgSO_4$. The resulting residue was used in the next step without further purification. To a stirred solution of crude product and Bestmann–Ohira reagent (518 mg, 2.7 mmol, 1.35 equiv) in MeOH (10 mL) was added K_2CO_3 (497 mg, 3.6 mmol, 1.8 equiv) at 0 °C. After 10 min, the mixture was warmed to rt. The reaction was stirred for 1 h and quenched with satd NH_4Cl. MeOH was removed under reduced pressure and the residue was extracted with Et_2O. The organic layer was washed with H_2O, brine, dried over $MgSO_4$, and concentrated. The resulting residue was purified by flash chromatography (3–5% EtOAc/hexane) to afford **16** (344 mg, 80%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) (data as a 1:1 diastereomeric mixture) δ (ppm): 7.49 (d, 1H, *J*=8.6 Hz), 7.42 (d, 1H, *J*=8.6 Hz), 6.90 (d, 2H, *J*=8.6 Hz), 5.97 (s, 0.5H), 5.90 (s, 0.5H), 4.37 (d, 0.5H, *J*=8.2 Hz), 4.18 (d, 0.5H, *J*=7.6 Hz), 3.94 (d, 0.5H *J*=7.6 Hz), 3.81 (s, 3H), 3.80 (d, 0.5H, *J*=8.2 Hz), 2.57 (s, 0.5H), 2.53 (s, 0.5H), 1.68 (s, 1.5H), 1.66 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) (data as a 1:1 diastereomeric mixture) δ (ppm): 160.8, 160.7, 129.7, 129.0, 128.7, 128.4, 114.0, 113.9, 105.2, 104.3, 85.7, 84.9, 77.1, 74.2, 74.1, 73.2, 72.2, 55.5, 26.6, 25.7; HRMS calcd for $C_{13}H_{14}IO_3$ $[M+Na]^+$ 241.0835, found 241.0838; IR ν_{max} (film) 3282, 2937, 2844, 1679, 1600, 1511, 1263, 1161, 1028, 833 cm^{-1}.

*4.2.4. Vinyl iodide **17**.* To a stirred solution of **16** (790 mg, 3.6 mmol) and $Pd(PPh_3)_4$ (208 mg, 0.18 mmol, 0.05 equiv) in THF (18 mL) was added *n*-Bu_3SnH (1.26 g, 4.3 mmol, 1.2 equiv). After 20 min, THF was removed under reduced pressure. The resulting residue was purified by flash chromatography (2–3% EtOAc/hexane) to afford vinyl tributyltin as a colorless oil, which was used directly in the next step. To a stirred solution of vinyl tributyltin in CH_2Cl_2 (30 mL) was added 1 M I_2 in CH_2Cl_2 solution until the color persisted. The reaction was quenched with satd Na_2SO_3 and 1 M KF and extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (3% EtOAc/hexane) to afford **17** (997 mg, 80% for two steps) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) (data as a 1:1 diastereomeric mixture) δ (ppm): 7.41 (d, 1H, *J*=8.8 Hz), 7.40 (d, 1H, *J*=8.8 Hz), 6.92 (d, 1H, *J*=8.8 Hz), 6.91 (d, 1H, *J*=8.8 Hz), 6.69 (d, 0.5H, *J*=14.4 Hz), 6.68 (d, 0.5H, *J*=14.4 Hz), 6.54 (d, 0.5H, *J*=14.4 Hz), 6.43 (d, 0.5H, *J*=14.4 Hz), 5.88 (s, 0.5H), 5.84 (s, 0.5H), 4.05 (d, 0.5H, *J*=8.4 Hz), 3.91 (d, 0.5H, *J*=8.4 Hz), 3.87 (d, 0.5H, *J*=8.4 Hz), 3.82 (s, 1.5H), 3.81 (s, 1.5H), 3.75 (d, 0.5H, *J*=8.4 Hz), 1.48 (s, 1.5H), 1.46 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) (data as a 1:1 diastereomeric mixture) δ (ppm): 160.8, 160.7, 148.6, 147.8, 129.7, 129.5, 128.3, 128.2, 114.0, 113.9, 104.3, 104.1, 83.3, 82.9, 77.5, 77.3, 75.8, 75.0, 55.5, 25.2, 23.4; HRMS calcd for $C_{13}H_{15}IO_3$ $[M+Na]^+$ 368.9958, found 368.9966; IR ν_{max} (film) 3069, 2972, 2866, 1714, 1613, 1515, 1249, 1170, 1068, 1033, 833 cm^{-1}.

*4.2.5. Alcohol **18** and **19**.* To a stirred solution of **17** (35 mg, 0.1 mmol) in CH_2Cl_2 (1 mL) was added DIBAL-H (1.2 M in toluene, 0.25 mL, 0.3 mmol, 3 equiv) at −78 °C. After 1.5 h at −78 °C, the reaction was quenched with a solution of Rochelle's salt and extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (10–15% EtOAc/hexane) to afford **18** (5 mg, 14%) and **19** (20 mg, 58%) as a colorless oil.

Compound **18**: $[\alpha]_D^{20}$ −1.1 (*c* 0.86, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.21 (d, 2H, *J*=8.8 Hz), 6.86 (d, 2H, *J*=8.8 Hz), 6.65 (d, 1H, *J*=14.8 Hz), 6.42 (d, 1H, *J*=14.8 Hz), 4.36–4.29 (m, 2H), 3.79 (s, 3H), 3.51–3.44 (m, 2H), 2.00 (t, 1H, *J*=6.6 Hz), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.4, 147.8, 130.7, 129.4, 114.1, 80.7, 79.4, 69.2, 65.2, 55.5, 18.8; HRMS calcd for $C_{13}H_{17}IO_3$ $[M+Na]^+$ 371.0115, found 371.0113; IR ν_{max} (film) 3439, 3069, 2932, 2860, 1615, 1512, 1463, 1383, 1249, 1174, 1107, 1036, 956, 827, 702 cm^{-1}.

Compound **19**: $[\alpha]_D^{20}$ 10.4 (*c* 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24 (d, 2H, *J*=8.8 Hz), 6.89 (d, 2H, *J*=8.8 Hz), 6.57 (d, 1H, *J*=14.4 Hz), 6.39 (d, 1H, *J*=14.4 Hz), 4.49 (s, 2H), 3.82 (s, 3H), 3.33 (d, 1H, *J*=9.0 Hz), 3.28 (d, 1H, *J*=9.0 Hz), 2.58 (s, 1H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.6, 149.8, 129.9, 129.7, 114.1, 77.5, 76.2, 75.5, 73.4, 55.5, 24.4; HRMS calcd for $C_{13}H_{17}IO_3$ $[M+Na]^+$ 371.0115, found 371.0113; IR ν_{max} (film) 3439, 3069, 2927, 2852, 1610, 1508, 1463, 1383, 1249, 1174, 1089, 1036, 947, 818, 702 cm^{-1}.

*4.2.6. Acetal **21**.* To a stirred solution of **20** (395 mg, 1.15 mmol) in CH_2Cl_2 (10 mL) was added PPTS (14 mg, 0.06 mmol, 0.05 equiv) and acetal (250 mg, 1.38 mmol, 1.2 equiv). The reaction was stirred overnight and quenched with Et_3N. The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (5.5–6.5% EtOAc/hexane) to afford **21** (435 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.70–7.64 (m, 4H), 7.43–7.32 (m, 8H), 6.89 (d, 1H, *J*=8.8 Hz), 6.82 (d, 1H, *J*=8.8 Hz), 5.87 (s, 0.5H), 5.81 (s, 0.5H), 4.27 (d, 0.5H, *J*=8.4 Hz), 4.15 (d, 0.5H, *J*=8.2 Hz), 3.83–3.52 (m, 3H), 3.80 (s, 1.5H), 3.77 (s, 1.5H), 1.41 (s, 1.5H), 1.38 (s, 1.5H), 1.07 (s, 4.5H), 1.06 (s, 4.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):160.59, 160.57, 135.89, 135.86, 135.8, 133.5, 133.4, 131.9, 130.4, 130.0, 129.96, 129.94, 129.87, 128.33, 128.28, 128.1, 127.97, 127.95, 127.92, 114.0, 113.9, 113.7, 104.7, 103.5, 81.6, 81.3, 73.6, 73.1, 68.6, 68.2, 55.53, 55.50, 27.05, 26.97, 23.1, 21.5, 19.5; HRMS calcd for $C_{28}H_{34}O_4Si$ $[M+Na]^+$ 485.2119, found 485.2114; IR ν_{max} (film) 2976, 2932, 2869, 1614, 1516, 1472, 1387, 1249, 1156, 1076, 831, 738 cm^{-1}.

*4.2.7. Alcohol **22** and **23**.* To a stirred solution of **21** (837 mg, 1.8 mmol) in CH_2Cl_2 (10 mL) was added DIBAL-H (1.2 M in toluene, 4.5 mL, 5.4 mmol, 3 equiv) at −78 °C. After 1.5 h at −78 °C, the reaction was quenched with a solution of Rochelle's salt and extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5–9% EtOAc/hexane) to afford **22** (510 mg, 61%) and **23** (173 mg, 21%) as a colorless oil.

Compound **22**: $[\alpha]_D^{20}$ 0.2 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.65 (d, 4H, *J*=8.8 Hz), 7.44–7.33 (m, 6H), 7.21 (d, 2H, *J*=8.6 Hz), 6.86 (d, 2H, *J*=8.6 Hz), 4.47 (s, 2H), 3.81 (s, 3H), 3.54–3.57 (m, 2H), 3.47 (d, 1H, *J*=8.8 Hz), 3.40 (d, 1H, *J*=8.8 Hz), 2.58 (s, 1H),

1.18 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):159.4, 135.83, 135.82, 133.5, 133.4, 130.6, 130.0, 129.4, 127.9, 114.0, 74.0, 73.3, 72.7, 68.0, 55.5, 27.1, 21.6, 19.5; HRMS calcd for $C_{28}H_{36}O_4Si$ $[M+Na]^+$ 487.2275, found 487.2270; IR ν_{max} (film) 3448, 2927, 2852, 1615, 1512, 1472, 1249, 1112, 827, 702 cm^{-1}.

Compound **23**: $[\alpha]_D^{20}$ 1.2 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.65 (d, 4H, *J*=8.8 Hz), 7.42–7.32 (m, 6H), 7.21 (d, 2H, *J*=8.2 Hz), 6.83 (d, 2H, *J*=8.2 Hz), 4.44–4.41 (m, 2H), 3.77 (s, 3H), 3.76–3.58 (m, 4H), 2.14 (m, 1H), 1.24 (s, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm):159.2, 135.90, 135.86, 133.3, 133.1, 131.3, 130.0, 129.3, 128.0, 127.9, 114.0, 78.0, 67.3, 66.1, 64.4, 55.5, 27.0, 19.5, 17.8; HRMS calcd for $C_{28}H_{36}O_4Si$ $[M+Na]^+$ 487.2275, found 487.2272; IR ν_{max} (film) 3461, 2958, 2860, 1615, 1512, 1428, 1249, 1112, 1036, 827, 702 cm^{-1}.

4.2.8. Vinyl iodide ***24***. To a stirred solution of **23** (170 mg, 0.37 mmol) in CH_2Cl_2 (4 mL) were added (*i*-Pr)$_2$NEt (239 mg, 1.85 mmol, 5 equiv), DMSO (0.26 mL), and $SO_3\cdot$py (159 mg, 1.11 mmol, 3 equiv) at 0 °C. The reaction was stirred for 30 min and quenched with satd $NaHCO_3$ and the mixture was diluted with Et_2O. The organic layer was washed successively with H_2O, brine, and dried over $MgSO_4$. After concentration under reduced pressure, the resulting residue was used for next step without purification. To a stirred solution of slurry of anhydrous chromium chloride (455 mg, 3.7 mmol, 10 equiv) in THF (0.8 mL) was added a solution of crude aldehyde and iodoform (437 mg, 1.1 mmol, 3 equiv) in dioxane (6 mL) at rt. The reaction was stirred overnight and quenched with H_2O, the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (4% EtOAc/hexane) to afford **24** (188 mg, 88%) as a colorless oil. $[\alpha]_D^{20}$ 1.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.65–7.62 (m, 4H), 7.41–7.33 (m, 6H), 7.20 (d, 2H, *J*=8.8 Hz), 6.83 (d, 2H, *J*=8.8 Hz), 6.60 (d, 1H, *J*=14.8 Hz), 6.36 (d, 1H, *J*=14.8 Hz), 4.39–4.34 (m, 2H), 3.78 (s, 3H), 3.57 (s, 2H), 1.39 (s, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.2, 149.3, 136.0, 135.9, 133.5, 133.4, 131.2, 129.92, 129.90, 129.1, 127.92, 127.90, 114.0, 81.1, 78.7, 70.0, 65.1, 55.5, 27.0, 19.8, 19.5; HRMS calcd for $C_{29}H_{35}IO_3Si$ $[M+Na]^+$ 609.1292, found 609.1285; IR ν_{max} (film) 3069, 2958, 2932, 2860, 1615, 1512, 1428, 1249, 1112, 827, 702 cm^{-1}.

4.2.9. Alcohol ***18***. To a stirred solution of **24** (185 mg, 0.32 mmol) in THF (3 mL) was added TBAF (1 M in THF, 1.28 mL, 1.28 mmol, 4 equiv). The reaction was stirred overnight and quenched with satd $NaHCO_3$ and extracted with Et_2O. The combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5–15% EtOAc/hexane) to afford **18** (97 mg, 87%) as a colorless oil.

4.2.10. Alcohol ***5***. To a stirred solution of **18** (94 mg, 0.27 mmol) in CH_2Cl_2 (8 mL) were added $NaHCO_3$ (227 mg, 2.7 mmol, 10 equiv) and the Dess–Martin reagent (117 mg, 0.41 mmol, 1.5 equiv). After 1.5 h, the reaction was quenched with satd Na_2SO_3 and satd $NaHCO_3$, extracted with CH_2Cl_2, The organic layer was washed with H_2O, brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was used in the next step without further purification. To a stirred solution of **11** in CH_2Cl_2 (0.6 mL) was added $SnCl_4$ (22.4 mg, 0.086 mmol, 1.3 equiv) at −78 °C. After 45 min, crude aldehyde **9** (23 mg, 0.066 mmol) in CH_2Cl_2 (0.2 mL) was added and stirred for an additional 3 h at −78 °C. The reaction was quenched with Et_3N (10 equiv) and satd $NaHCO_3$, warmed to rt, extracted with CH_2Cl_2, and dried over $MgSO_4$. The combined organic extracts were concentrated under reduced pressure. The resulting residue was purified by flash chromatography (3.2–3.6% EtOAc/hexane) to afford **5** (20 mg, 51%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.20 (d, 2H, *J*=8.6 Hz), 6.86 (d, 2H, *J*=8.6 Hz), 6.54 (d, 1H, *J*=14.8 Hz), 6.39 (d, 1H, *J*=14.8 Hz), 5.83–5.76 (m, 1H), 5.05–5.00 (m, 2H), 4.92 (s, 1H), 4.88 (s, 1H), 4.37–4.31 (m, 2H), 3.84–3.79 (m, 1H), 3.79 (s, 3H), 3.68–3.62 (m, 1H), 2.53 (d, 1H, *J*=1.9 Hz), 2.28–2.14 (m, 5H), 2.03–1.95 (m, 1H), 1.34 (s, 3H), 0.93 (t, 9H, *J*=7.8 Hz), 0.57 (q, 6H, *J*=7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 159.3, 148.0, 143.7, 135.2, 130.9, 129.1, 117.5, 115.3, 114.0, 83.1, 79.6, 75.2, 71.2, 64.9, 55.5, 43.4, 42.0, 38.4, 16.2, 7.2, 5.2; HRMS calcd for $C_{27}H_{43}IO_4Si$ $[M+Na]^+$ 609.1868, found 609.1869; IR ν_{max} (film); 3563, 2954, 2909, 2874, 1641, 1614, 1512, 1459, 1249, 1081, 911, 747 cm^{-1}.

4.2.11. Diol ***25***. To a stirred solution of **17** (197 mg, 0.57 mmol) in MeOH (5 mL) were added PPTS (14 mg, 0.057 mmol, 0.1 equiv) and $TsOH\cdot H_2O$ (11 mg, 0.057 mmol, 0.1 equiv). After 2 h, the reaction was quenched with Et_3N and the solvent was removed under reduced pressure. The resulting residue was purified by flash chromatography (20–40% EtOAc/hexane) to afford **25** (113 mg, 88%) as a colorless oil. $[\alpha]_D^{20}$ −11.8 (*c* 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.59 (d, 1H, *J*=14.4 Hz), 6.48 (d, 1H, *J*=14.4 Hz), 3.53 (dd, 1H, *J*=5.2, 11.0 Hz), 3.43 (dd, 1H, *J*=7.2, 11.0 Hz), 2.29 (s, 1H), 1.80 (br, 1H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 149.3, 77.7, 76.4, 69.4, 24.0. HRMS calcd for $C_5H_9IO_2$ $[M+Na]^+$ 250.9539, found 250.9543; IR ν_{max} (film) 3368, 2972, 2866, 1607, 1462, 1376, 1198, 1048, 950 cm^{-1}.

4.2.12. Vinyl iodide ***26***. To a stirred solution of **25** (284 mg, 1.26 mmol) in CH_2Cl_2 (12 mL) was added 2,6-lutidine (607 mg, 5.67 mmol, 4.5 equiv) and TESOTf (995 mg, 3.77 mmol, 3 equiv) at −78 °C. After 30 min, the reaction was warmed to rt and allowed to stir an additional hour. The reaction was quenched with satd $NaHCO_3$, extracted with CH_2Cl_2 (3×40 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (hexane) to afford **26** (553 mg, 97%) as a colorless oil. $[\alpha]_D^{20}$ −6.0 (*c* 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.62 (d, 1H, *J*=14.4 Hz), 6.26 (d, 1H, *J*=14.4 Hz), 3.39 (d, 1H, *J*=9.4 Hz), 3.35 (d, 1H, *J*=9.4 Hz), 1.28 (s, 3H), 0.97–0.91 (m, 18H), 0.61–0.54 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 151.3, 78.8, 76.3, 70.8, 24.3, 7.2, 7.0, 6.8, 4.6; HRMS calcd for $C_{17}H_{37}IO_2Si_2$ $[M+Na]^+$ 479.1269, found 479.1276; IR ν_{max} (film) 2950, 2870, 1607, 1462, 1236, 1103, 1010, 736 cm^{-1}.

4.2.13. Aldehyde ***10***. To a stirred solution of **26** (210 mg, 0.46 mmol) in 3:1 MeOH/CH_2Cl_2 (4.6 mL) was added PPTS (12 mg, 0.046 mmol, 0.1 equiv). After 15 min, the reaction was quenched with satd $NaHCO_3$ and diluted with Et_2O. The organic layer was washed with H_2O, brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was used in the next step without further purification. To a stirred solution of alcohol in CH_2Cl_2 (14 mL) was added $NaHCO_3$ (384 mg, 4.6 mmol, 10 equiv) and the Dess–Martin reagent (292 mg, 0.69 mmol, 1.5 equiv). After 1 h, the reaction was quenched with satd Na_2SO_3 and satd $NaHCO_3$, extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5% EtOAc/hexane) to afford **10** (114 mg, 73% for two steps) as a colorless oil. $[\alpha]_D^{20}$ 139.2 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.36 (s, 1H), 6.58 (d, 1H, *J*=14.4 Hz), 6.42 (d, 1H, *J*=14.4 Hz), 1.40 (s, 3H), 0.96 (t, 9H, *J*=8.0 Hz), 0.63 (q, 6H, *J*=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 199.5, 145.1, 83.4, 80.1, 22.7, 7.1, 6.6; HRMS calcd for $C_{11}H_{21}IO_2Si$ $[M+Na]^+$ 363.0248, found 363.0247; IR ν_{max} (film) 2959, 2874, 1735, 1601, 1460, 1201, 1125, 1010, 938, 738 cm^{-1}.

4.2.14. Alcohol ***6***. To a stirred solution of **11** (177 mg, 0.56 mmol, 1.2 equiv) in CH_2Cl_2 (4 mL) was added $SnCl_4$ (146 mg, 0.56 mmol,

1.2 equiv) at −78 °C. After 45 min, **10** (161 mg, 0.47 mmol) in CH_2Cl_2 (1.5 mL) was added and stirred for an additional 3 h at −78 °C. The reaction was quenched with Et_3N (10 equiv) and satd $NaHCO_3$, warmed to rt, extracted with CH_2Cl_2, and dried over $MgSO_4$. The combined organic extracts were concentrated under reduced pressure. The resulting residue was purified by flash chromatography (1–1.2% EtOAc/hexane) to afford **6** (146 mg, 53%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 6.61 (d, 1H, J=14.6 Hz), 6.32 (d, 1H, J=14.6 Hz), 5.87–5.77 (m, 1H), 5.08–5.04 (m, 2H), 4.93 (s, 1H), 4.91 (s, 1H), 3.86–3.80 (m, 1H), 3.50–3.43 (m, 1H), 2.55–2.45 (m, 1H), 2.33–2.14 (m, 5H), 1.90 (dd, 1H, J=10.6, 14.4 Hz), 1.34 (s, 3H), 0.98–0.93 (m, 18H), 0.64–0.57 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 149.8, 144.1, 135.2, 117.5, 115.4, 80.5, 77.5, 76.5, 71.4, 43.5, 42.1, 38.4, 22.2, 7.3, 7.2, 6.8, 5.2; HRMS calcd for $C_{25}H_{49}IO_3Si_2$ $[M+Na]^+$ 603.2157, found 603.2156; IR ν_{max} (film) 3565, 3074, 2954, 2875, 1644, 1604, 1413, 1192, 1086, 1002, 741 cm^{-1}.

*4.2.15. Acetal **28**.* To a stirred solution of **27** (238 mg, 1.5 mmol) in THF (15 mL) was added $LiAlH_4$ (2 M in THF, 1.5 mL, 2 equiv) at 0 °C. After 1.5 h at 0 °C, the reaction was quenched with solution of Rochelle's salt and the aqueous layer was extracted with EtOAc, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was used for the next step without purification. To a stirred solution of crude diol in CH_2Cl_2 (15 mL) were added PPTS (19 mg, 0.075 mmol, 0.05 equiv) and acetal (328 mg, 1.8 mmol, 1.2 equiv). The reaction was stirred overnight and quenched with Et_3N. The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (5% EtOAc/hexane) to afford **28** (262 mg, 70% for two steps) as a colorless oil. $[\alpha]_D^{20}$ 0.45 (*c* 0.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.42 (d, 2H, J=8.8 Hz), 6.88 (d, 2H, J=8.8 Hz), 5.80–5.69 (m, 1H), 5.43 (s, 1H) 5.09–5.04 (m, 2H), 4.17 (dd, 1H, J=4.0, 11.6 Hz), 3.79 (s, 3H), 3.69–3.61 (m, 1H), 3.56–3.51 (m, 1H), 2.22–2.16 (m, 1H), 1.86–1.77 (m, 2H), 1.33 (d, 3H, J=6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 160.1, 135.1, 131.4, 127.6, 117.2, 113.9, 101.3, 78.1, 71.5, 55.5, 40.4, 32.9, 19.5; HRMS calcd for $C_{15}H_{20}O_3$ $[M+Na]^+$ 271.1305, found 271.1309; IR ν_{max} (film) 3074, 2977, 2835, 1618, 1516, 1378, 1249, 1170, 1033, 917, 825 cm^{-1}.

*4.2.16. Alcohol **29**.* To a stirred solution of **28** (112 mg, 0.45 mmol) in CH_2Cl_2 (4.5 mL) was added DIBAL-H (1.2 M in toluene, 1.1 mL, 1.35 mmol, 3 equiv) at −78 °C. After the addition, the reaction was warmed to 0 °C. After 30 min at 0 °C, the reaction was quenched with MeOH and stirred for 30 min at rt. The solid was removed through filtration and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash chromatography (8–12% EtOAc/hexane) to afford **29** (101 mg, 90%) as a colorless oil. $[\alpha]_D^{20}$ 53.5 (*c* 0.58, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.25 (d, 2H, J=8.4 Hz), 6.88 (d, 2H, J=8.4 Hz), 5.82–5.71 (m, 1H), 5.05–5.00 (m, 2H), 4.59 (d, 1H, J=11.2 Hz), 4.31 (d, 1H, J=11.2 Hz), 3.85 (ddd, 1H, J=2.8, 5.6, 11.2 Hz), 3.80 (s, 3H), 3.67–3.55 (m, 2H), 2.89 (t, 1H, J=5.6 Hz), 2.26–2.10 (m, 2H), 1.63–1.57 (m, 1H), 1.27 (d, 3H, J=6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.5, 136.9, 130.5, 129.6, 116.8, 114.1, 78.2, 70.9, 63.7, 55.5, 45.9, 33.6, 17.8; HRMS calcd for $C_{15}H_{22}O_3$ $[M+Na]^+$ 273.1461, found 273.1464; IR ν_{max} (film) 3439, 3074, 2977, 2835, 1614, 1512, 1378, 1249, 1033, 917, 825 cm^{-1}.

*4.2.17. Alkene **30**.* To a stirred solution of **29** (243 mg, 0.97 mmol) in CH_2Cl_2 (5 mL) were added Et_3N (294 mg, 2.91 mmol, 3 equiv), DMAP (cat.), and MsCl (223 mg, 1.94 mmol, 2 equiv) at 0 °C. The reaction was stirred overnight and quenched with satd $NaHCO_3$ and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O, brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was used for the next step without purification. To a stirred solution of crude product in Et_2O (10 mL) was added $LiAlH_4$ (2 M in THF, 1 mL, 2 equiv) at 0 °C, the reaction was stirred at 23 °C for 3 h and quenched with EtOAc, H_2O and 1 M HCl. The aqueous layer was extracted with Et_2O and the combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (3% EtOAc/hexane) to afford **30** (208 mg, 91% for two steps) as a colorless oil. $[\alpha]_D^{20}$ 31.2 (*c* 0.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24 (d, 2H, J=7.4 Hz), 6.85 (d, 2H, J=7.4 Hz), 5.80–5.69 (m, 1H), 5.00–4.94 (m, 2H), 4.48 (d, 1H J=11.2 Hz), 4.35 (d, 1H, J=11.2 Hz), 3.78 (s, 3H), 3.41–3.36 (m, 1H), 2.29–2.23 (m, 1H), 1.89–1.82 (m, 1H), 1.69–1.63 (m, 1H), 1.11 (d, 3H, J=6.4 Hz), 0.88 (d, 3H, J=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.2, 138.1, 131.5, 129.3, 115.8, 113.9, 77.7, 70.4, 55.5, 38.3, 37.1, 16.4, 15.1; HRMS calcd for $C_{15}H_{22}O_2$ $[M+Na]^+$ 257.1512, found 257.1515; IR ν_{max} (film) 3074, 2977, 2835, 1614, 1512, 1378, 1249, 1033, 917, 825 cm^{-1}.

*4.2.18. Aldehyde **31**.* To a stirred solution of **30** (47 mg, 0.2 mmol) in CH_2Cl_2 (5 mL) was bubbled with O_2 for 2 min at −78 °C after which O_3 was bubbled through the solution until the reaction maintained a blue color. At this point, O_2 was bubbled through the solution until blue color disappeared. PPh_3 (262 mg, 1 mmol, 5 equiv) was added, the reaction was warmed to rt and stirred overnight. The solvent was removed under reduced pressure. The resulting residue was purified by silica gel column chromatography (5%–7.5% EtOAc/hexane) to afford **31** (33 mg, 70%) as a colorless oil. $[\alpha]_D^{20}$ 25.4 (*c* 0.63, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.74 (t, 1H, J=2.0 Hz), 7.24 (d, 2H, J=8.6 Hz), 6.87 (d, 2H, J=8.6 Hz), 4.48 (d, 1H J=11.2 Hz), 4.35 (d, 1H, J=11.2 Hz), 3.80 (s, 3H), 3.62–3.44 (m, 1H), 2.59 (ddd, 1H, J=2.0, 5.6, 16.0 Hz), 2.41–2.32 (m, 1H), 2.59 (ddd, 1H, J=2.4, 8.0, 16.0 Hz), 1.12 (d, 3H, J=6.4 Hz), 0.95 (d, 3H, J=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 203.0, 159.3, 131.1, 129.4, 114.0, 77.1, 70.4, 55.5, 46.8, 33.0, 15.8, 15.5; HRMS calcd for $C_{14}H_{20}O_3$ $[M+Na]^+$ 259.1305, found 259.1308; IR ν_{max} (film) 2968, 2835, 2725, 1723, 1614, 1512, 1378, 1249, 1033, 825 cm^{-1}.

*4.2.19. Alcohol **33**.* To a stirred solution of **32** (225 mg, 0.47 mmol, 1.1 equiv) in CH_2Cl_2 (2.4 mL) at −78 °C were added Et_3N (119 mg, 1.17 mmol, 2.75 equiv) and (*c*-Hex)$_2$BOTf (1 M in hexane, 1 mL, 2.4 equiv). After 3 h at −78 °C, **31** (100 mg, 0.43 mmol) in CH_2Cl_2 (0.4 mL) was added and stirred for additional 2 h. The reaction was warmed to rt over 1 h and quenched with H_2O, MeOH, and 30% H_2O_2. The aqueous layer was extracted with CH_2Cl_2 (3×40 mL) and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (8–12% EtOAc/hexane) to afford **33** (295 mg, 92%). $[\alpha]_D^{20}$ 33.0 (*c* 0.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.33 (d, 2H, J=7.0 Hz), 7.25–7.12(m, 8H), 6.88 (s, 2H), 6.83–6.77 (m, 4H), 5.77 (d, 1H, J=3.9 Hz), 4.78 (d, 1H, J=16.6 Hz), 4.58 (d, 1H, J=16.6 Hz), 4.52 (d, 1H, J=11.2 Hz), 4.29 (d, 1H, J=11.2 Hz), 4.05–4.02 (m, 1H), 3.79–3,77 (m, 1H), 3.76 (s, 3H), 3.54–3.49 (m, 1H), 3.25 (d, 1H, J=5.6 Hz), 2.51–2.41 (m, 1H), 2.47 (s, 6H), 2.28 (s, 3H), 2.05–2.00 (m, 1H), 1.67–1.61 (m, 1H), 1.29–1.22 (m, 1H), 1.12 (m, 6H), 1.06 (d, 3H, J=7.2 Hz), 0.89 (d, 3H, J=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.9, 159.3, 142.8, 140.6, 139.1, 138.6, 133.7, 132.4, 130.8, 129.4, 128.6, 128.5, 128.0, 127.9, 127.3, 126.1, 114.0, 78.2, 77.3, 71.3, 70.4, 57.0, 55.5, 48.5, 46.4, 37.5, 34.4, 23.1, 21.1, 17.1, 14.8, 14.3, 13.7; HRMS calcd for $C_{42}H_{53}NO_7S$ $[M+Na]^+$ 738.3435, found 738.3442; IR ν_{max} (film) 3477, 2968, 2932, 1737, 1614, 1515, 1453, 1249, 1153, 1033, 860, 758, 701 cm^{-1}.

*4.2.20. Ester **34**.* To a stirred solution of **33** (295 mg, 0.41 mmol) in CH_2Cl_2 (3 mL) were added 2,6-lutidine (133 mg, 1.24 mmol, 3 equiv) and TESOTf (219 mg, 0.83 mmol, 2 equiv) at 0 °C and stirred overnight at rt. The mixture was quenched with satd $NaHCO_3$, the

aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5–8% EtOAc/hexane) to afford **34** (290 mg, 87%). $[\alpha]_D^{20}$ 17.9 (*c* 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.33 (d, 2H, *J*=7.2 Hz), 7.24–7.08 (m, 8H), 6.89–6.79 (m, 6H), 5.77 (d, 1H, *J*=4.7 Hz), 4.77 (d, 1H, *J*=16.6 Hz), 4.53 (d, 1H, *J*=16.6 Hz), 4.33 (d, 1H, *J*=11.4 Hz), 4.18 (d, 1H, *J*=11.4 Hz), 4.09–4.06 (m, 1H), 3.96–3.92 (m, 1H), 3.79 (s, 3H), 3.23–3.21 (m, 1H), 2.48–2.46 (m, 1H), 2.44 (s, 6H), 2.27 (s, 3H), 1.54–1.47 (m, 2H), 1.26–1.19 (m, 1H), 1.16 (d, 3H, *J*=6.8 Hz), 1.11 (d, 3H, *J*=7.0 Hz), 0.97 (d, 3H, *J*=6.4 Hz), 0.93 (t, 9H, *J*=8.0 Hz), 0.80 (d, 3H, *J*=6.4 Hz), 0.57 (q, 6H, *J*=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 172.2, 159.1, 142.7, 140.5, 138.7, 138.6, 133.5, 132.3, 131.6, 129.3, 128.6, 128.4, 128.0, 127.9, 127.4, 126.6, 113.8, 78.3, 77.5, 72.7, 70.5, 57.0, 55.5, 48.3, 45.6, 37.5, 35.3, 23.2, 21.1, 16.6, 15.5, 14.0, 12.2, 7.2, 5.3; HRMS calcd for $C_{48}H_{67}NO_7SSi$ $[M+Na]^+$ 852.4300, found 852.4309; IR ν_{max} (film) 2954, 2875, 1732, 1608, 1515, 1453, 1249, 1153, 1033, 860, 758, 701 cm^{-1}.

4.2.21. Sulfonate ester ***35***. To a stirred solution of **34** (290 mg, 0.35 mmol) in CH_2Cl_2 (3.5 mL) was added DIBAL-H (1.2 M in toluene, 0.9 mL, 1.05 mmol, 3 equiv) at −78 °C. After 2.5 h at −78 °C, the reaction was quenched with a solution of Rochelle's salt and extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was used in the next step without further purification. To a stirred solution of crude product in CH_2Cl_2 (3.5 mL) were added DMAP (cat.), Et_3N (350 mg, 3.5 mmol, 10 equiv), and TsCl (334 mg, 1.75 mmol, 5 equiv). After 20 h at rt, the reaction was quenched with satd $NaHCO_3$ and extracted with Et_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (4–5% EtOAc/hexane) to afford **35** (174 mg, 88% for two steps) as a colorless oil. $[\alpha]_D^{20}$ −27.4 (*c* 0.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.75 (d, 2H, *J*=8.4 Hz), 7.29 (d, 2H, *J*=8.4 Hz), 7.23 (d, 2H, *J*=8.4 Hz), 6.87 (d, 2H, *J*=8.4 Hz), 4.48 (d, 1H *J*=11.2 Hz), 4.31 (d, 1H *J*=11.2 Hz), 4.09 (dd, 1H, *J*=5.6, 9.6 Hz), 3.81 (s, 3H), 3.83–3.78 (m, 1H), 3.68–3.63 (m, 1H), 3.35–3.32 (m, 1H), 2.42 (s, 3H), 1.98–1.88 (m, 1H), 1.60–1.51 (m, 2H), 1.25–1.18 (m, 1H), 1.08 (d, 3H, *J*=6.4 Hz), 0.89 (d, 3H, *J*=6.8 Hz), 0.88 (t, 9H, *J*=8.0 Hz), 0.86 (d, 3H, *J*=6.8 Hz), 0.60 (q, 6H, *J*=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.2, 144.8, 133.3, 131.4, 130.0, 129.4, 128.2, 114.0, 77.1, 72.6, 72.4, 70.4, 55.5, 37.5, 37.3, 35.0, 21.8, 16.4, 15.3, 14.4, 7.2, 5.3; HRMS calcd for $C_{30}H_{48}O_6SSi$ $[M+Na]^+$ 587.2833, found 587.2838; IR ν_{max} (film) 2959, 2875, 1613, 1515, 1453, 1360, 1249, 1179, 1095, 971, 820, 740, 701 cm^{-1}.

4.2.22. Alkyl iodide ***7***. To a stirred solution of **35** (174 mg, 0.31 mmol) in acetone (6 mL) was added NaI (465 mg, 3.1 mmol, 10 equiv). The mixture was refluxed for 24 h and diluted with Et_2O. The organic layer was washed with H_2O, brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (2% EtOAc/hexane) to afford **7** (136 mg, 85%) as a colorless oil. $[\alpha]_D^{20}$ 13.4 (*c* 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.27 (d, 2H, *J*=8.4 Hz), 6.87 (d, 2H, *J*=8.4 Hz), 4.51 (d, 1H, *J*=11.6 Hz), 4.37 (d, 1H, *J*=11.6 Hz), 3.81 (s, 3H), 3.78–3.74 (m, 1H), 3.47–3.40 (m, 1H), 3.19 (dd, 1H, *J*=5.3, 9.8 Hz), 2.97 (dd, 1H, *J*=8.6, 9.8 Hz), 1.89–1.82 (m, 1H), 1.68–1.59 (m, 2H), 1.22–1.17 (m, 1H), 1.14 (d, 3H, *J*=6.4 Hz), 1.04 (d, 3H, *J*=6.8 Hz), 0.95 (t, 9H, *J*=8.0 Hz), 0.91 (d, 3H, *J*=6.8 Hz), 0.58 (q, 6H, *J*=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.2, 131.5, 129.4, 114.0, 77.5, 73.7, 70.5, 55.5, 41.7, 35.9, 35.0, 17.1, 16.4, 15.8, 11.2, 7.2, 5.5; HRMS calcd for $C_{23}H_{41}IO_3Si$ $[M+Na]^+$ 543.1762, found 543.1768; IR ν_{max} (film) 2959, 2870, 1613, 1520, 1453, 1369, 1245, 1081, 820, 736 cm^{-1}.

4.2.23. Vinyl iodide ***39***. To a stirred solution of **6** (146 mg, 0.25 mmol) in CH_2Cl_2 (2.5 mL) was added Et_3N (253 mg, 2.5 mmol, 10 equiv), DMAP (cat.), and Ac_2O (128 mg, 1.25 mmol, 5 equiv). The reaction was stirred for 4 h and quenched with satd $NaHCO_3$. The aqueous layer was extracted with Et_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (1% EtOAc/hexane) to afford **39** (150 mg, 96%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 6.57 (d, 1H, *J*=14.4 Hz), 6.32 (d, 1H, *J*=14.4 Hz), 5.88–5.77 (m, 1H), 5.07–5.01 (m, 2H), 4.92–4.90 (m, 1H), 4.79 (s, 2H), 3.81–3.74 (m, 1H), 2.38 (d, 1H, *J*=14.4 Hz), 2.31–2.03 (m, 5H), 2.01 (s, 3H), 1.28 (s, 3H), 0.98–0.93 (m, 18H), 0.64–0.54 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 170.5, 148.9, 142.6, 135.3, 117.4, 115.4, 79.4, 77.3, 76.7, 70.8, 43.9, 42.3, 36.3, 24.3, 21.3, 7.3, 7.2, 6.9, 5.3; HRMS calcd for $C_{27}H_{51}IO_4Si_2$ $[M+Na]^+$ 645.2263, found 645.2258; IR ν_{max} (film) 3074, 2954, 2875, 1746, 1644, 1604, 1413, 1232, 1086, 1002, 741 cm^{-1}.

4.2.24. Acetate ***40***. To a stirred solution of **7** (57 mg, 0.11 mmol, 1.1 equiv) in Et_2O (1 mL) was added 9-MeO/9-BBN (1 M in hexane, 0.28 mL, 0.28 mmol, 2.8 equiv). The mixture was cooled to −78 °C and treated with *t*-BuLi (1.6 M in pentane, 144 μL, 0.23 mmol, 2.3 equiv). After 5 min, THF (1 mL) was added dropwise. The reaction was warmed to rt and stirred for 1 h. In another flask (dppf) $PdCl_2$ (5 mg, 0.0061 mmol, 0.05 equiv), $AsPh_3$ (5.5 mg, 0.018 mmol, 0.15 equiv), $CsCO_3$ (130 mg, 0.4 mmol, 4 equiv), and H_2O (44 mg, 2.4 mmol, 24 equiv) were added to a solution of **39** (62 mg, 0.1 mmol) in DMF (1.6 mL), the alkyl boronate solution was transferred to the DMF solution. The reaction was stirred overnight and quenched with pH 7 buffer and 30% H_2O_2. After 30 min, the mixture was diluted with Et_2O. The organic layer was washed with H_2O, brine, and dried over $MgSO_4$. After concentration under reduced pressure, the resulting residue was purified by flash chromatography (1.5–2% EtOAc/hexane) to afford **40** (73 mg, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25 (d, 2H, *J*=8.4 Hz), 6.86 (d, 2H, *J*=8.4 Hz), 5.87–5.77 (m, 1H), 5.63–5.54 (m, 1H), 5.46 (d, 1H, *J*=15.4 Hz), 5.05–5.00 (m, 2H), 4.91 (d, 1H, *J*=9.6 Hz), 4.78 (s, 1H), 4.77 (s, 1H), 4.51 (d, 1H *J*=11.4 Hz), 4.35 (d, 1H, *J*=11.4 Hz), 3.79 (s, 3H), 3.79–3.74 (m, 1H), 3.69–3.65 (m, 1H), 3.42–3.36 (m, 1H), 2.37 (d, 1H, *J*=14.4 Hz), 2.28–2.05 (m, 6H), 2.03–2.00 (m, 1H), 1.98 (s, 3H), 1.86–1.78 (m, 1H), 1.67–1.60 (m, 2H), 1.26 (s, 3H), 1.25–1.18 (m, 1H), 1.14 (d, 3H, *J*=6.4 Hz), 0.97–0.91 (m, 33H), 0.62–0.54 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 170.6, 159.2, 143.1, 135.4, 134.2, 131.4, 130.1, 129.3, 117.3, 115.2, 113.9, 77.4, 77.0, 76.4, 74.8, 70.8, 70.5, 55.5, 43.9, 42.4, 38.6, 36.5, 36.1, 35.4, 34.6, 24.5, 21.3, 16.6, 15.9, 15.6, 7.3, 7.2, 7.0, 5.5, 5.3, 5.2; HRMS calcd for $C_{50}H_{92}O_7Si_3$ $[M+Na]^+$ 911.6043, found 911.6045; IR ν_{max} (film) 2954, 2871, 1746, 1609, 1516, 1456, 1374, 1245, 1086, 1006, 741 cm^{-1}.

4.2.25. Diol ***41***. To a stirred solution of **40** (169 mg, 0.19 mmol) in THF (2 mL) was added $LiAlH_4$ (2 M in THF, 0.66 mL, 7 equiv) at 0 °C. After 2 h at 0 °C, the reaction was quenched with MeOH, H_2O, and a solution of Rochelle's salt. The aqueous layer was extracted with Et_2O and the combined organic extracts were dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (10–15% EtOAc/hexane) to afford **41** (125 mg, 90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25 (d, 2H, *J*=8.4 Hz), 6.86 (d, 2H, *J*=8.4 Hz), 5.85–5.77 (m, 1H), 5.75–5.65 (m, 1H), 5.46 (d, 1H, *J*=15.6 Hz), 5.06–5.03 (m, 2H), 4.95 (s, 1H), 4.93 (s, 1H), 4.51 (d, 1H, *J*=11.4 Hz), 4.34 (d, 1H, *J*=11.4 Hz), 3.88–3.82 (m, 1H), 3.79 (s, 3H), 3.68–3.64 (m, 1H), 3.52–3.49 (m, 1H), 3.41–3.36 (m, 1H), 2.46–1.98 (m, 10H), 1.85–1.77 (m, 1H), 1.68–1.63 (m, 2H), 1.22 (s, 3H), 1.25–1.16 (m, 1H), 1.13 (d, 3H, *J*=6.4 Hz), 0.97–0.91 (m, 21H), 0.87 (d, 3H, *J*=6.8 Hz), 0.62–0.54 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 159.2, 144.0, 135.4, 135.1, 131.5, 129.9, 129.3, 117.5, 115.7, 113.9, 77.4, 75.3, 74.8, 74.6, 71.3, 70.4,

55.5, 43.1, 42.0, 38.7, 38.3, 36.0, 35.3, 34.6, 22.6, 16.5, 15.9, 15.7, 7.3, 7.2, 5.5, 5.2; HRMS calcd for $C_{42}H_{76}O_6Si_2$ $[M+Na]^+$ 755.5073, found 755.5074; IR ν_{max} (film) 3457, 2954, 2871, 1641, 1614, 1512, 1459, 1374, 1245, 1076, 1009, 742 cm^{-1}.

4.2.26. Ketone ***42***. To a stirred solution of **41** (124 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) were added $(i\text{-}Pr)_2NEt$ (175 mg, 1.36 mmol, 8 equiv), DMSO (0.2 mL) and $SO_3\cdot Py$ (108 mg, 0.68 mmol, 4 equiv) at 0 °C. The reaction was stirred for 30 min and quenched with satd $NaHCO_3$ and the mixture was diluted with Et_2O. The organic layer was washed successively with H_2O, brine, and dried over $MgSO_4$. After concentration under reduced pressure, the resulting residue was purified by flash chromatography (4–5% EtOAc/hexane) to afford **42** (89 mg, 70%) as a colorless oil. $[\alpha]_D^{20}$ −20.3 (*c* 0.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.25 (d, 2H, *J*=8.4 Hz), 6.86 (d, 2H, *J*=8.4 Hz), 5.84–5.76 (m, 2H), 5.48 (d, 1H, *J*=15.2 Hz), 5.06–5.02 (m, 2H), 4.99 (s, 1H), 4.87 (s, 1H), 4.51 (d, 1H, *J*=11.4 Hz), 4.34 (d, 1H, *J*=11.4 Hz), 3.91 (s, 1H), 3.84–3.78 (m, 1H), 3.79 (s, 3H), 3.67–3.63 (m, 1H), 3.39–3.37 (m, 1H), 3.37–3.25 (m, 2H), 2.27–2.10 (m, 6H), 1.82–1.76 (m, 1H), 1.66–1.60 (m, 2H), 1.43 (s, 3H), 1.22–1.19 (m, 1H), 1.13 (d, 3H, *J*=6.4 Hz), 0.96–0.90 (m, 21H), 0.84 (d, 3H, *J*=6.8 Hz), 0.61–0.53 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 210.0, 159.2, 140.0, 135.0, 132.5, 131.8, 131.5, 129.3, 117.5, 117.3, 113.9, 79.2, 77.4, 74.6, 71.4, 70.4, 55.5, 43.9, 43.5, 42.0, 38.1, 36.2, 35.3, 34.3, 25.1, 16.5, 15.9, 15.8, 7.3, 7.2, 5.5, 5.2; HRMS calcd for $C_{42}H_{74}O_6Si_2$ $[M+Na]^+$ 753.4916, found 753.4912; IR ν_{max} (film) 3475, 2954, 2871, 1712, 1614, 1512, 1463, 1374, 1245, 1076, 1009, 742 cm^{-1}.

4.2.27. Ketone ***43***. Compound **42** was completely converted into **43** in 5% EtOAc/hexane after 5 days. $[\alpha]_D^{20}$ −25.2 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24 (d, 2H, *J*=8.4 Hz), 6.86 (d, 2H, *J*=8.4 Hz), 6.19 (s, 1H), 5.84–5.76 (m, 2H), 5.48 (d, 1H, *J*=15.4 Hz), 5.09–5.03 (m, 2H), 4.50 (d, 1H, *J*=11.4 Hz), 4.38 (s, 1H), 4.34 (d, 1H, *J*=11.4 Hz), 3.95–3.92 (m, 1H), 3.80 (s, 3H), 3.67–3.60 (m, 1H), 3.39–3.35 (m, 1H), 2.40–2.10 (m, 6H), 2.20 (s, 3H), 1.83–1.75 (m, 1H), 1.66–1.60 (m, 2H), 1.39 (s, 3H), 1.22–1.19 (m, 1H), 1.13 (d, 3H, *J*=6.4 Hz), 0.96–0.90 (m, 21H), 0.83 (d, 3H, *J*=6.8 Hz), 0.61–0.53 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 200.7, 160.9, 159.2, 134.6, 132.3, 132.0, 131.5, 129.3, 120.3, 117.9, 113.9, 77.9, 77.4, 74.6, 70.6, 70.4, 55.5, 49.5, 42.3, 38.3, 36.2, 35.3, 34.4, 25.2, 21.0, 16.6, 15.8, 15.6, 7.3, 7.1, 5.5, 5.2; HRMS calcd for $C_{42}H_{74}O_6Si_2$ $[M+Na]^+$ 753.4916, found 753.4910; IR ν_{max} (film) 3475, 2954, 2871, 1700, 1614, 1512, 1463, 1374, 1245, 1076, 1009, 742 cm^{-1}.

4.2.28. Ketal ***3***. To a stirred solution of **42** (30 mg, 0.041 mmol) in THF (2 mL) was added 0.3 mL of an HF·py solution consisting of 1.7 mL 70% HF·py: 4 mL THF: 1.7 mL pyridine. After 15 min, the reaction was quenched with satd $NaHCO_3$ and extracted with Et_2O. The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (20–27% EtOAc/hexane) to afford **3** (14 mg, 68%) as a colorless oil. $[\alpha]_D^{20}$ 0.3 (*c* 0.73, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.23 (d, 2H, *J*=8.4 Hz), 6.86 (d, 2H, *J*=8.4 Hz), 5.83–5.67 (m, 3H), 5.09–5.03 (m, 2H), 4.85 (d, 1H, *J*=1.2 Hz), 4.82 (d, 1H, *J*=1.2 Hz), 4.54 (d, 1H, *J*=11.6 Hz), 4.35 (d, 1H, *J*=11.6 Hz), 3.93–3.86 (m, 1H), 3.79 (s, 3H), 3.54–3.47 (m, 2H), 3.14 (s, 1H), 2.73 (br, 1H), 2.42 (s, 1H), 2.33–2.22 (m, 6H), 2.03–1.85 (m, 3H), 1.66–1.55 (m, 2H), 1.35–1.25 (m, 1H), 1.28 (s, 3H), 1.13 (d, 3H, *J*=6.4 Hz), 0.91 (d, 3H, *J*=6.8 Hz), 0.87 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.3, 141.8, 134.7, 133.8, 130.8, 129.6, 129.3, 117.3, 114.0, 111.3, 99.4, 78.0, 77.4, 73.2, 70.7, 70.4, 55.5, 40.4, 39.6, 39.0, 38.0, 37.0, 35.6, 34.4, 21.3, 17.6, 15.9, 14.6; HRMS calcd for $C_{30}H_{46}O_6$ $[M+Na]^+$ 525.3187, found 525.3186; IR ν_{max} (film) 3441, 2963, 2928, 1614, 1515, 1463, 1374, 1245, 1033, 1009, 913, 816 cm^{-1}.

4.2.29. Alcohol ***44***. To a stirred solution of diol **8** (159 mg, 1.22 mmol) in CH_2Cl_2 (12 mL) were added PPTS (15 mg, 0.06 mmol, 0.05 equiv) and 4-methoxybenzaldehyde dimethyl acetal (267 mg, 1.47 mmol, 1.2 equiv). The reaction was stirred overnight and quenched with Et_3N. The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (4.5% EtOAc/hexane) to afford acetal (283 mg, 93%). $[\alpha]_D^{20}$ −44.5 (*c* 0.80, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.42 (d, 2H, *J*=8.7 Hz), 6.87 (d, 2H, *J*=8.7 Hz), 5.80 (qd, 1H, *J*=6.6, 15.3 Hz), 5.52 (m, 1H), 5.48 (s, 1H), 4.14 (dd, 1H, *J*=4.6, 11.4 Hz), 3.82 (m, 1H), 3.79 (s, 3H), 3.51 (t, 1H, *J*=11.2 Hz), 1.92–1.83 (m, 1H), 1.73 (dd, 3H, *J*=1.5, 6.4 Hz), 0.75 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 160.1, 131.4, 130.5, 129.7, 127.8, 113.8, 101.4, 84.9, 73.3, 55.5, 34.3, 18.1, 12.7; HRMS calcd for $C_{15}H_{20}O_3$ $[M+Na]^+$ 271.1305, found 271.1304; IR ν_{max} (film) 3074, 2977, 2835, 1641, 1516, 1378, 1249, 1170, 1033, 917, 825 cm^{-1}. To a stirred solution of acetal (46 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) was added DIBAL-H (1.2 M in toluene, 0.47 mL, 0.56 mmol, 3 equiv) at −78 °C. After the addition, the reaction was warmed to 0 °C. After 30 min at 0 °C, the reaction was quenched with MeOH and stirred for 30 min at rt. The solid was removed through filtration and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash chromatography (10–12% EtOAc/hexane) to afford **5** (43 mg, 92%) as a colorless oil. $[\alpha]_D^{20}$ 72.0 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.23 (d, 2H, *J*=8.6 Hz), 6.87 (d, 2H, *J*=8.6 Hz), 5.65 (qd, 1H, *J*=6.4, 15.3 Hz), 5.35 (ddd, 1H, *J*=1.6, 8.6, 15.3 Hz), 4.53 (d, 1H, *J*=11.4 Hz), 4.24 (d, 1H, *J*=11.4 Hz), 3.80 (s, 3H), 3.64–3.52 (m, 3H), 3.15 (dd, 1H, *J*=3.5, 8.2 Hz), 1.86–1.80 (m, 1H), 1.77 (dd, 3H, *J*=1.6, 6.4 Hz), 0.77 (d, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.4, 130.9, 130.6, 130.5, 129.7, 114.1, 86.3, 69.7, 68.0, 55.5, 40.1, 18.0, 14.1; HRMS calcd for $C_{15}H_{22}O_3$ $[M+Na]^+$ 273.1461, found 273.1459; IR ν_{max} (film) 3439, 3074, 2977, 2835, 1614, 1512, 1378, 1249, 1033, 917, 825 cm^{-1}.

4.2.30. Aldehyde ***45***. To a stirred solution of **44** (40 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) were added $NaHCO_3$ (134 mg, 1.6 mmol, 10 equiv) and the Dess–Martin reagent (103 mg, 0.24 mmol, 1.5 equiv). After 1 h, the reaction was quenched with satd Na_2SO_3 and satd $NaHCO_3$, extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (4% EtOAc/hexane) to afford **45** (114 mg, 86%) as a colorless oil. $[\alpha]_D^{20}$ 80.7 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.68 (d, 1H, *J*=2.7 Hz), 7.20 (d, 2H, *J*=8.6 Hz), 6.87 (d, 2H, *J*=8.6 Hz), 5.73 (qd, 1H, *J*=6.4, 15.3 Hz), 5.36 (ddd, 1H, *J*=1.6, 8.6, 15.3 Hz), 4.52 (d, 1H, *J*=11.4 Hz), 4.26 (d, 1H, *J*=11.4 Hz), 3.86 (t, 1H, *J*=8.6 Hz), 3.80 (s, 3H), 2.55–2.51 (m, 1H), 1.78 (d, 3H, *J*=6.4 Hz), 0.97 (d, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 204.7, 159.4, 131.8, 130.5, 129.6, 129.1, 114.0, 80.8, 69.7, 55.5, 51.0, 18.0, 11.0; HRMS calcd for $C_{15}H_{20}O_3$ $[M+Na]^+$ 271.1305, found 271.1308; IR ν_{max} (film) 2923, 2856, 1726, 1605, 1512, 1454, 1249, 1036, 969, 822 cm^{-1}.

4.2.31. Propionate ***46***. To a stirred solution of CBr_4 (93 mg, 0.28 mmol, 2 equiv) in CH_2Cl_2 (0.3 mL) was added Ph_3P (147 mg, 0.56 mmol, 4 equiv) in CH_2Cl_2 (0.3 mL) solution at 0 °C. The mixture was stirred 10 min at rt and recooled to 0 °C. Aldehyde **45** (35 mg, 0.14 mmol) in CH_2Cl_2 (0.3 mL) was added. After 2 h, the reaction was quenched with satd $NaHCO_3$ and extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (1–2% EtOAc/hexane) to afford dibromoalkene (50 mg, 88%) as a colorless oil. $[\alpha]_D^{20}$ 5.6 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.23 (d, 2H, *J*=8.6 Hz), 6.87 (d, 2H, *J*=8.6 Hz), 6.30 (d, 1H, *J*=9.4 Hz), 5.64 (qd, 1H, *J*=6.4, 15.3 Hz), 5.33 (ddd, 1H, *J*=1.4, 8.4, 15.3 Hz), 4.52 (d, 1H, *J*=11.6 Hz), 4.22 (d, 1H, *J*=11.6 Hz), 3.81 (s, 3H), 3.53 (dd, 1H, *J*=5.7, 8.4 Hz), 2.63–2.58 (m, 1H), 1.76 (dd, 3H, *J*=1.4, 6.4 Hz), 0.98 (d, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.2, 141.4, 131.0, 130.7, 129.7, 129.5, 113.9, 88.5, 82.0, 69.5, 55.5, 43.5, 18.1, 15.5;

HRMS calcd for $C_{16}H_{20}Br_2O_2$ $[M+Na]^+$ 424.9722, found 424.9722; IR ν_{max} (film) 2923, 2856, 1587, 1512, 1454, 1249, 1036, 980, 822 cm^{-1}. To a stirred solution of dibromoalkene (48 mg, 0.12 mmol) in THF (1 mL) was added *n*-BuLi (2.4 M in hexane, 0.11 mL, 0.26 mmol, 2.2 equiv) at −78 °C. After 30 min, the reaction was treated with methyl chloroformate (22 mg, 0.24 mmol, 2 equiv) and warmed to rt over 2.5 h. The reaction was quenched with satd NH_4Cl and extracted with Et_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (3–5% EtOAc/hexane) to afford **46** (33 mg, 91%) as a colorless oil. $[\alpha]_D^{20}$ 38.7 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.27 (d, 2H, *J*=8.6 Hz), 6.86 (d, 2H, *J*=8.6 Hz), 5.70 (qd, 1H, *J*=6.4, 15.3 Hz), 5.38 (ddd, 1H, *J*=1.6, 8.4, 15.3 Hz), 4.56 (d, 1H, *J*=11.6 Hz), 4.31 (d, 1H, *J*=11.6 Hz), 3.80 (s, 3H), 3.77 (s, 3H), 3.66 (dd, 1H, *J*=6.6, 8.2 Hz), 2.77–2.70 (m, 1H), 1.77 (dd, 3H, *J*=1.6, 6.4 Hz), 1.16 (d, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.3, 154.5, 131.7, 130.6, 129.6, 128.7, 113.9, 91.7, 81.2, 73.9, 69.8, 55.5, 52.8, 32.0, 18.1, 16.0; HRMS calcd for $C_{18}H_{22}O_4$ $[M+Na]^+$ 325.1410, found 325.1408; IR ν_{max} (film) 2940, 2840, 2238, 1717, 1610, 1512, 1436, 1254, 1169, 1036, 970, 828 cm^{-1}.

*4.2.32. Z-Alkenoic ester **47**.* To a stirred suspension of CuI (57 mg, 0.3 mmol, 3 equiv) in THF (1 mL) was added MeLi (2.2 M in hexane, 0.27 mL, 0.6 mmol, 6 equiv) at 0 °C. After 15 min, the reaction was cooled to −50 °C and treated with **46** (32 mg, 0.1 mmol) in THF (1 mL) solution. After 1.5 h, the reaction was quenched with AcOH (33 μL) and satd NH_4Cl, extracted with Et_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (3% EtOAc/hexane) to afford **47** (30 mg, 90%). $[\alpha]_D^{20}$ −25.2 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.19 (d, 2H, *J*=8.6 Hz), 6.84 (d, 2H, *J*=8.6 Hz), 5.67 (s, 1H), 5.69–5.64 (m, 1H), 5.33 (ddd, 1H, *J*=1.6, 8.6, 15.3 Hz), 4.48 (d, 1H, *J*=11.6 Hz), 4.21 (d, 1H, *J*=11.6 Hz), 4.06–4.02 (m, 1H), 3.79 (s, 3H), 3.65 (s, 3H), 3.59 (t, 1H, *J*=9.0 Hz), 1.77 (dd, 3H, *J*=1.6, 6.4 Hz), 1.72 (d, 3H, *J*=1.2 Hz), 0.93 (d, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.9, 163.1, 159.1, 131.1, 130.9, 130.8, 129.6, 117.1, 113.8, 82.0, 69.2, 55.5, 51.0, 39.3, 20.3, 18.0, 15.8; HRMS calcd for $C_{19}H_{26}O_4$ $[M+Na]^+$ 341.1723, found. 341.1719; IR ν_{max} (film) 2949, 2856, 1717, 1641, 1512, 1454, 1245, 1036, 970, 822 cm^{-1}.

*4.2.33. Acid **4**.* To a stirred solution of **47** (64 mg, 0.2 mmol) in MeOH (1 mL) and THF (1 mL) was added LiOH (1 M, 2 mL, 2 mmol, 10 equiv), after 60 h at rt, the pH value was adjusted to 2–3 with 1 M HCl and the mixture was extracted with Et_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (25% EtOAc/hexane) to afford acid **4** (58 mg, 95%). $[\alpha]_D^{20}$ −5.2 (*c* 0.38, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.16 (d, 2H, *J*=8.6 Hz), 6.86 (d, 2H, *J*=8.6 Hz), 5.79 (s, 1H), 5.70 (qd, 1H, *J*=6.4, 15.3 Hz), 5.32 (ddd, 1H, *J*=1.6, 8.6, 15.3 Hz), 4.58 (d, 1H, *J*=11.6 Hz), 4.26 (d, 1H, *J*=11.6 Hz), 3.80 (s, 3H), 3.54 (t, 1H, *J*=9.6 Hz), 3.42–3.32 (m, 1H), 1.80 (dd, 3H, *J*=1.5, 6.4 Hz), 1.64 (d, 3H, *J*=1.6 Hz), 0.89 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 169.4, 159.5, 157.9, 132.2, 129.9, 129.7, 129.6, 119.7, 114.0, 81.4, 69.5, 55.5, 40.8, 19.3, 18.1, 15.4; HRMS calcd for $C_{18}H_{24}O_4$ $[M+Na]^+$ 327.1567, found 327.1565; IR ν_{max} (film) 2940, 2870, 1686, 1632, 1512, 1454, 1249, 1036, 970, 822 cm^{-1}.

*4.2.34. Ester **48**.* To a stirred solution of Acid **4** (18 mg, 0.06 mmol, 1.5 equiv) in THF (0.8 mL) were added Et_3N (16 mg, 0.16 mmol, 4 equiv) and 2,4,6-trichlorobenzoyl chloride (24 mg, 0.1 mmol, 2.5 equiv) at rt. After 4 h at rt, the solid was removed and the filtrate was transferred to a solution of **3** (20 mg, 0.04 mmol) and DMAP (8 mg, 0.064 mmol, 1.6 equiv) in toluene (3 mL). After 18 h at rt, the mixture was quenched with satd $NaHCO_3$ and diluted with Et_2O, the organic layer was washed with H_2O, brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (14.5–15% EtOAc/hexane) to afford **48** (16 mg, 53%). $[\alpha]_D^{20}$ −4.2 (*c* 1.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.25 (d, 2H, *J*=8.4 Hz), 7.19 (d, 2H, *J*=8.4 Hz), 7.86 (t, 4H, *J*=9.0 Hz), 5.82–5.61 (m, 5H), 5.32 (dd, 1H, *J*=8.4, 15.3 Hz), 5.09–5.03 (m, 2H), 4.93–4.89 (m, 1H), 4.85 (s, 1H), 4.81 (s, 1H), 4.48 (d, 1H, *J*=11.6 Hz), 4.47 (d, 1H, *J*=11.6 Hz), 4.34 (d, 1H, *J*=11.6 Hz), 4.19 (d, 1H, *J*=11.6 Hz), 4.08–4.02 (m, 1H), 3.94–3.86 (m, 1H), 3.79 (s, 6H), 3.59 (t, 1H, *J*=8.8 Hz), 3.54–3.47 (m, 1H), 3.13 (s, 1H), 2.42 (s, 1H), 2.31–2.17 (m, 6H), 1.91–1.79 (m, 4H), 1.76 (d, 3H, *J*=6.4 Hz), 1.73 (s, 3H), 1.30–1.42 (m, 2H), 1.27 (s, 3H), 1.09 (d, 3H, *J*=6.2 Hz), 0.93 (d, 3H, *J*=7.0 Hz), 0.90 (d, 3H, *J*=6.8 Hz), 0.84 (d, 3H, *J*=6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.3, 162.4, 159.2, 159.0, 141.9, 134.7, 134.1, 131.5, 131.2, 130.9, 130.7, 129.4, 129.3, 129.1, 117.9, 117.3, 114.0, 113.8, 111.3, 99.4, 82.1, 77.4, 76.6, 75.3, 70.7, 70.5, 69.1, 55.5, 40.4, 39.6, 39.3, 38.0, 37.1, 35.3, 35.1. 33.6, 21.4, 20.4, 18.0, 16.6, 15.9, 15.8, 15.4; HRMS calcd for $C_{48}H_{68}O_9$ $[M+Na]^+$ 811.4756, found 811.8744; IR ν_{max} (film) 3506, 3074, 2967, 2932, 1708, 1641, 1614, 1512, 1454, 1378, 1245, 1160, 1040, 974, 822 cm^{-1}.

*4.2.35. Alcohol **2**.* To a stirred solution of **48** (26 mg, 0.033 mmol) in CH_2Cl_2 (1 mL)+pH 7 buffer (0.5 mL) was added DDQ (30 mg, 0.13 mmol, 4 equiv) at rt. After 30 min, the reaction was quenched with satd $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (30–33% EtOAc/hexane) to afford **2** (13.5 mg, 75%) as a colorless oil. $[\alpha]_D^{20}$ −38.3 (*c* 0.85, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.80–5.64 (m, 5H), 5.32 (dd, 1H, *J*=7.6, 15.3 Hz), 5.11–5.03 (m, 2H), 5.01–4.97 (m, 1H), 4.85 (s, 1H), 4.82 (s, 1H), 3.93–3.88 (m, 1H), 3.84–3.78 (m, 2H), 3.74–3.68 (m, 1H), 3.19 (s, 1H), 2.69 (br, 1H), 2.60 (s, 1H), 2.34–2.17 (m, 6H), 1.99–1.74 (m, 4H), 1.88 (s, 3H), 1.71 (d, 3H, *J*=6.4 Hz), 1.61–1.33 (m, 2H), 1.29 (s, 3H), 1.12 (d, 3H, *J*=6.2 Hz), 0.93 (d, 3H, *J*=6.8 Hz), 0.90 (d, 3H, *J*=6.8 Hz), 0.87 (d, 3H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.6, 161.6, 141.9, 134.8, 134.4, 133.2, 128.7, 128.6, 119.0, 117.3, 111.4, 99.4, 77.3, 75.9, 75.8, 70.7, 69.8, 41.4, 40.4, 39.5, 38.0, 36.9, 36.2, 35.5, 33.5, 21.5, 20.3, 20.1, 18.0, 15.8, 15.5, 15.1; HRMS calcd for $C_{32}H_{52}O_7$ $[M+Na]^+$ 571.3605, found 571.3597; IR ν_{max} (film) 3439, 2967, 2923, 1694, 1637, 1450, 1374, 1245, 1160, 1009, 969 cm^{-1}.

*4.2.36. Alkene **52**.* To a stirred solution of dithiane (216 mg, 1.8 mmol, 1.5 equiv) in dry THF (4 mL) was added *n*-BuLi at −40 °C. After 1 h at −40 °C, the epoxide **13** (105 mg, 1.25 mmol, 1 equiv) in THF (3 mL) was added. After 1 h at −40 °C, the reaction was warmed to rt and quenched with satd NH_4Cl. the aqueous layer was extracted with Et_2O and the combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (8–12% EtOAc/hexane) to afford (*S*)-1-(1,3-dithian-2-yl)pent-4-en-2-ol (170 mg, 67%). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.87–5.76 (m, 1H), 5.17–5.13 (m, 2H), 4.27 (t, 1H, *J*=7.0 Hz), 4.01–3.96 (m, 1H), 2.96–2.81 (m, 4H), 2.33–2.18 (m, 2H), 2.16–2.09 (m, 1H), 1.96 (d, 1H, *J*=4.0 Hz), 1.95–1.84 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 134.3, 118.8, 67.7, 44.4, 42.3, 42.2, 30.6, 30.3, 26.2; HRMS calcd for $C_9H_{16}OS_2$ $[M+Na]^+$ 227.0535, found 227.0535. To a stirred suspension of NaH (160 mg, 4 mmol, 2 equiv) in DMF (2.5 mL) was added (*S*)-1-(1,3-dithian-2-yl)pent-4-en-2-ol (400 mg, 2 mmol, 1 equiv) in DMF (1.5 mL) at 0 °C. After 1 h at 0 °C, PMBCl (470 mg, 3 mmol, 1.5 equiv) was added. The reaction was stirred overnight at rt and quenched with satd NH_4Cl. the aqueous layer was extracted with Et_2O and the combined organic layer was washed with H_2O and brine, dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (3–4.5% EtOAc/hexane) to afford **52** (518 mg, 80%). $[\alpha]_D^{20}$ 34.1 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.28 (d, 2H, *J*=8.6 Hz), 6.88 (d, 2H, *J*=8.6 Hz), 5.87–5.76 (m, 1H), 5.13–5.08 (m, 2H), 4.56 (d, 1H, *J*=11.0 Hz), 4.43 (d,

1H, *J*=11.0 Hz), 4.16 (dd, 1H, *J*=4.9, 9.6 Hz), 3.81 (s, 3H), 3.80–3.75 (m, 1H), 2.90–2.74 (m, 4H), 2.40–2.28 (m, 2H), 2.13–2.08 (m, 1H), 1.99–1.81 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.4, 134.4, 131.0, 129.7, 117.9, 114.0, 75.0, 71.5, 55.5, 44.2, 40.3, 38.7, 30.6, 30.2, 26.3; HRMS calcd for $C_{17}H_{24}O_2S_2$ $[M+Na]^+$ 347.1110, found 347.1111; IR ν_{max} (film) 2936, 2900, 1614, 1512, 1245, 1076, 911, 818 cm^{-1}.

4.2.37. Ester ***53****.* To a stirred solution of **52** (106 mg, 0.33 mmol, 1 equiv) in CH_3CN (2.5 mL) and H_2O (0.7 mL) were added $NaHCO_3$ (277 mg, 3.3 mmol, 10 equiv) and MeI (465 mg, 3.3 mmol, 10 equiv) at rt. After 20 h, the reaction was quenched with satd $NaHCO_3$ and extracted with Et_2O, the combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was used for next step without purification. To a stirred solution of crude product in *t*-BuOH (4 mL) and 2-methyl-2-butene (1.2 mL) was added a solution of $NaClO_2$ (362 mg, 3.96 mmol, 12 equiv) and NaH_2PO_4 (552 mg, 3.96 mmol, 12 equiv) in H_2O (1 mL) at 0 °C. After 30 min at rt, the reaction was diluted with H_2O and extracted with EtOAc, the combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was used for next step without purification. To a stirred solution of crude product in DMF (3.3 mL) were added K_2CO_3 (88 mg, 0.66 mmol, 2 equiv) and MeI (90 mg, 0.66 mmol, 2 equiv) at rt. The reaction was stirred overnight and quenched with satd NH_4Cl, the aqueous layer was extracted with Et_2O and the combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (10% EtOAc/hexane) to afford **53** (68 mg, 80% for three steps). $[\alpha]_D^{20}$ 22.8 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24 (d, 2H, *J*=8.6 Hz), 6.86 (d, 2H, *J*=8.6 Hz), 5.85–5.78 (m, 1H), 5.13–5.08 (m, 2H), 4.53 (d, 1H, *J*=11.0 Hz), 4.47 (d, 1H, *J*=11.0 Hz), 3.98–3.93 (m, 1H), 3.80 (s, 3H), 3.67 (s, 3H), 2.57 (dd, 1H, *J*=7.8, 15.4 Hz), 2.50 (dd, 1H, *J*=5.2, 15.4 Hz), 2.41–2.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 172.4, 159.4, 134.2, 130.7, 129.6, 118.1, 114.0, 75.3, 71.5, 55.5, 51.9, 39.6, 38.7; HRMS calcd for $C_{15}H_{20}O_4$ $[M+Na]^+$ 287.1254, found 287.1252; IR ν_{max} (film) 2949, 2838, 1734, 1610, 1512, 1245, 1076, 911, 818 cm^{-1}.

4.2.38. Allylsilane ***51****.* The powered $CeCl_3 \cdot 7H_2O$ (430 mg, 1.15 mmol, 5 equiv) was heated to 155 °C over 3 h with stirring and continued to be heated at 155 °C overnight in the high vacuum. The solid was cooled to rt and filled with N_2. THF (2 mL) was added and the suspension was stirred for 5 h. The mixture was cooled to −78 °C and treated with $TMSCH_2MgCl$ (1.3 M in THF, 1.1 mL, 6 equiv). After 1 h at −78 °C, **53** (61 mg, 0.23 mmol, 1 equiv) in 0.3 mL THF was added and the reaction was slowly warmed to rt. The reaction was stirred overnight and quenched with 1 M HCl at −78 °C. The mixture was warmed to rt and diluted with Et_2O. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (4 mL) and silica gel (1 g) was added. The suspension was stirred overnight. The silica was removed and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash chromatography (2% EtOAc/hexane) to afford **51** (55 mg, 75%). $[\alpha]_D^{20}$ 5.2 (*c* 0.88, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.24 (d, 2H, *J*=8.6 Hz), 6.86 (d, 2H, *J*=8.6 Hz), 5.92–5.82 (m, 1H), 5.11–5.05 (m, 2H), 4.66 (s, 1H), 4.60 (s, 1H), 4.49 (s, 2H), 3.80 (s, 3H), 3.62–3.56 (m, 1H), 2.24 (m, 3H), 2.12 (dd, 1H, *J*=6.2, 14.0 Hz), 1.53 (s, 2H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 159.3, 144.7, 135.4, 131.2, 129.5, 117.1, 113.9, 110.0, 77.3, 71.0, 55.5, 43.1, 38.6, 27.2, −1.1; HRMS calcd for $C_{19}H_{30}O_2Si$ $[M+Na]^+$ 241.1907, found 341.1910; IR ν_{max} (film) 2949, 2905, 1734, 1611, 1512, 1245, 1076, 841 cm^{-1}.

4.2.39. Alcohol ***54****.* To a stirred solution of **51** in CH_2Cl_2 (0.8 mL) was added $SnCl_4$ (34 mg, 0.13 mmol, 1.3 equiv) at −78 °C. After 45 min, **10** (35 mg, 0.1 mmol) in CH_2Cl_2 (0.3 mL) was added and stirred for an additional 3 h at −78 °C. The reaction was quenched with Et_3N (10 equiv) and satd $NaHCO_3$, warmed to rt, extracted with CH_2Cl_2, and dried over $MgSO_4$. The combined organic extracts were concentrated under reduced pressure. The resulting residue was purified by flash chromatography (3–4.5% EtOAc/hexane) to afford **54** (36 mg, 60%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25 (d, 2H, *J*=8.6 Hz), 6.87 (d, 2H, *J*=8.6 Hz), 6.57 (d, 1H, *J*=14.8 Hz), 6.27 (d, 1H, *J*=14.8 Hz), 5.89–5.78 (m, 1H), 5.11–5.07 (m, 2H), 4.93 (s, 1H), 4.92 (s, 1H), 4.51 (d, 1H, *J*=11.2 Hz), 4.43 (d, 1H, *J*=11.2 Hz), 3.80 (s, 3H), 3.62–3.54 (m, 1H), 3.44–3.39 (m, 1H), 2.55 (d, 1H, *J*=2.0 Hz), 2.38–2.16 (m, 5H), 1.88 (dd, 1H, *J*=10.6, 14.4 Hz), 1.29 (s, 3H), 0.94 (q, 9H, *J*=7.8 Hz), 0.60 (t, 6H, *J*=7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm):159.4, 149.8, 144.3, 134.9, 130.8, 129.7, 117.6, 115.0, 114.0, 80.5, 77.1, 76.5, 76.2, 70.9, 55.5, 40.5, 38.5, 38.4, 22.1, 7.3, 6.8; HRMS calcd for $C_{27}H_{43}IO_4Si$ $[M+Na]^+$ 609.1868, found 609.1862; IR ν_{max} (film) 3452, 2954, 2874, 1641, 1610, 1512, 1249, 1085, 1000, 747 cm^{-1}.

4.2.40. Vinyl iodide ***50****.* To a stirred solution of **54** (29 mg, 0.05 mmol) in CH_2Cl_2 (0.5 mL) were added 2,6-lutidine (16 mg, 0.15 mmol, 3 equiv) and TBSOTf (26 mg, 0.1 mmol, 2 equiv) at 0 °C. The reaction was stirred overnight at rt and quenched with satd $NaHCO_3$, the aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (1.5% EtOAc/hexane) to afford **50** (32 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25 (d, 2H, *J*=8.6 Hz), 6.86 (d, 2H, *J*=8.6 Hz), 6.59 (d, 1H, *J*=14.4 Hz), 6.18 (d, 1H, *J*=14.4 Hz), 5.91–5.81 (m, 1H), 5.11–5.06 (m, 2H), 4.88 (s, 2H), 4.50–4.43 (m, 2H), 3.80 (s, 3H), 3.56–3.50 (m, 2H), 2.45 (d, 1H, *J*=14.4 Hz), 2.38–2.27 (m, 3H), 2.12 (dd, 1H, *J*=5.6, 14.4 Hz), 1.87 (dd, 1H, *J*=8.4, 14.4 Hz), 1.31 (s, 3H), 0.97–0.85 (m, 18H), 0.59 (q, 6H, *J*=8.0 Hz), 0.03 (s, 3H), −0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm):159.3, 150.0, 143.5, 135.3, 133.9, 129.5, 117.3, 115.3, 114.1, 81.3, 78.1, 77.9, 76.0, 71.2, 55.5, 41.8, 40.3, 39.0, 26.4, 25.0, 18.4, 7.4, 7.0, −3.1, −3.8; HRMS calcd for $C_{33}H_{57}IO_4Si_2$ $[M+Na]^+$ 723.2732, found 723.2746; IR ν_{max} (film) 3070, 2954, 2878, 1641, 1601, 1463, 1249, 1192, 1098, 1005, 836, 738 cm^{-1}.

4.2.41. Vinyl iodide ***55****.* To a stirred solution of **6** (304 mg, 0.52 mmol) in CH_2Cl_2 (2.6 mL) were added 2,6-lutidine (139 mg, 1.3 mmol, 2.5 equiv) and TBSOTf (206 mg, 0.78 mmol, 1.5 equiv) at 0 °C and stirred 1.5 h at rt. The mixture was quenched with satd $NaHCO_3$, the aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (0.4% EtOAc/hexane) to afford **55** (319 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 6.59 (d, 1H, *J*=14.6 Hz), 6.19 (d, 1H, *J*=14.6 Hz), 5.88–5.77 (m, 1H), 5.06–5.03 (m, 2H), 4.84 (s, 1H), 4.83 (s, 1H), 3.82–3.77 (m, 1H), 3.57–3.49 (m, 1H), 2.42 (d, 1H, *J*=14.4 Hz), 2.27–2.11 (m, 4H), 1.84 (dd, 1H, *J*=8.4, 14.4 Hz), 1.31 (s, 3H), 0.97–0.84 (m, 27H), 0.63–0.55 (m, 12H), 0.03 (s, 3H), −0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 150.0, 143.5, 135.5, 117.2, 115.4, 81.3, 78.4, 75.9, 70.8, 44.9, 42.2, 40.3, 26.4, 25.0, 18.4, 7.4, 7.2, 7.0, 5.3, −3.1, −3.8; HRMS calcd for $C_{31}H_{63}IO_3Si_3$ $[M+Na]^+$ 717.3022, found 717.3045; IR ν_{max} (film) 3074, 2954, 2875, 1641, 1605, 1413, 1254, 1192, 1098, 1000, 836, 741 cm^{-1}.

4.2.42. Alcohol ***56****.* To a stirred solution of **55** (319 mg, 0.46 mmol) in THF (4.6 mL) was added 1.4 mL of an HF·py solution consisting of 1.7 mL 70% HF·py: 4 mL THF: 1.7 mL pyridine. After 30 min, the reaction was quenched with satd $NaHCO_3$ and extracted with Et_2O.

The combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (1.5% EtOAc/hexane) to afford **56** (234 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 6.59 (d, 1H, J=14.6 Hz), 6.19 (d, 1H, J=14.6 Hz), 5.89–5.77 (m, 1H), 5.16–5.11 (m, 2H), 4.96 (s, 1H), 4.91 (s, 1H), 3.73–3.68 (m, 1H), 3.50–3.47 (m, 1H), 2.50 (d, 1H, J=14.4 Hz), 2.27–2.17 (m, 3H), 2.07–2.01 (m, 1H), 1.89 (dd, 1H, J=8.8, 14.4 Hz), 1.84 (d, 1H, J=2.2 Hz), 1.33 (s, 3H), 0.97–0.85 (m, 18H), 0.59 (q, 6H, J=8.0 Hz), 0.04 (s, 3H), −0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 149.7, 143.5, 135.0, 118.0, 116.9, 81.2, 77.7, 75.9, 67.8, 43.7, 41.8, 39.8, 26.3, 25.4, 18.4, 7.4, 7.0, −2.9, −3.7; HRMS calcd for $C_{25}H_{49}IO_3Si_2$ $[M+Na]^+$ 603.2157, found 603.2168; IR ν_{max} (film) 3457, 3074, 2954, 2878, 1641, 1601, 1463, 1254, 1192, 1098, 1000, 836, 738 cm^{-1}.

*4.2.43. Vinyl iodide **50**.* To a stirred solution of **56** (234 mg, 0.4 mmol) and PMBO(C=NH)CCl_3 (226 mg, 0.8 mmol, 2 equiv) in toluene (4 mL) was added $Sc(OTf)_3$ (16 mg, 0.032 mmol, 0.08 equiv). After 3 h, the solvent was removed. The resulting residue was purified by flash chromatography (1% EtOAc/hexane) to afford **50** (206 mg, 73%).

*4.2.44. Alkene **57**.* To a stirred solution of alkyl iodide **7** (41 mg, 0.078 mmol, 1.1 equiv) in Et_2O (0.8 mL) was added 9-MeO/9-BBN (1 M in hexane, 0.2 mL, 0.2 mmol, 2.8 equiv). The mixture was cooled to −78 °C and treated with *t*-BuLi (1.6 M in pentane, 0.1 mL, 0.16 mmol, 2.3 equiv). After 5 min, THF (0.8 mL) was added dropwise. The reaction was warmed to rt and stirred for 1 h. In another flask (dppf)$PdCl_2$ (2.9 mg, 0.0036 mmol, 0.05 equiv), $AsPh_3$ (3.1 mg, 0.01 mmol, 0.15 equiv), $CsCO_3$ (92 mg, 0.28 mmol, 4 equiv), and H_2O (31 mg, 1.7 mmol, 24 equiv) were added to a solution of **50** (50 mg, 0.071 mmol) in DMF (1.3 mL), the alkyl boronate solution was transferred to the DMF solution. The reaction was stirred overnight and quenched with pH 7 buffer and 30% H_2O_2. After 30 min, the mixture was diluted with Et_2O. The organic layer was washed with H_2O, brine, and dried over $MgSO_4$. After concentration under reduced pressure, the resulting residue was purified by flash chromatography (1–1.8% EtOAc/hexane) to afford **57** (57 mg, 84%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25–7.23 (m, 4H), 6.86–6.83 (m, 4H), 5.91–5.81 (m, 1H), 5.56–5.44 (m, 2H), 5.10–5.05 (m, 2H), 4.85 (s, 2H), 4.50 (d, 1H J=11.6 Hz), 4.44 (s, 2H), 4.35 (d, 1H, J=11.6 Hz), 3.78 (s, 6H), 3.67–3.62 (m, 1H), 3.60–3.51 (m, 2H), 3.42–3.35 (m, 1H), 2.52 (d, 1H, J=14.4 Hz), 2.37–2.21 (m, 3H), 2.19–2.11 (m, 2H), 1.86 (dd, 1H, J=8.6, 14.4 Hz), 1.83–1.76 (m, 1H), 1.65–1.58 (m, 3H), 1.30 (s, 3H), 1.25–1.18 (m, 1H), 1.13 (d, 3H, J=6.2 Hz), 0.97–0.82 (m, 33H), 0.61–0.544 (m, 12H), 0.03 (s, 3H), −0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 159.3, 159.2, 144.1, 135.4, 134.8, 131.5, 131.2, 129.4, 129.3, 128.9, 117.1, 114.9, 113.9, 78.7, 78.1, 77.3, 77.1, 74.9, 71.2, 70.5, 55.48, 55.46, 41.5, 40.6, 39.1, 38.9, 36.2, 35.4, 34.9, 26.4, 25.6, 18.5, 16.7, 15.9, 15.5, 7.5, 7.3, 7.1, 5.5, −3.1, −3.7; HRMS calcd for $C_{56}H_{98}O_7Si_3$ $[M+Na]^+$ 989.6513, found 989.6536; IR ν_{max} (film): 2963, 2932, 2878, 1614, 1512, 1463, 1249, 1098, 1005, 836, 742 cm^{-1}.

*4.2.45. Alcohol **58**.* To a stirred solution of **57** (202 mg, 0.21 mmol) in THF (3 mL) was added 1 mL of an HF·py solution consisting of 1.7 mL 70% HF·py: 4 mL THF: 1.7 mL pyridine. After 45 min, the reaction was quenched with satd $NaHCO_3$ and extracted with Et_2O. The combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (8–10% EtOAc/hexane) to afford **58** (154 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25–7.23 (m, 4H), 6.86–6.83 (m, 4H), 5.91–5.81 (m, 1H), 5.57–5.46 (m, 2H), 5.10–5.04 (m, 2H), 4.85 (s, 2H), 4.54 (d, 1H, J=11.6 Hz), 4.45 (s, 2H), 4.36 (d, 1H, J=11.6 Hz), 3.79 (s, 6H), 3.60–3.47 (m, 4H), 2.66 (d, 1H, J=4.8 Hz), 2.52 (d, 1H, J=14.6 Hz), 2.37–2.28 (m, 4H), 2.16–2.11 (dd, 1H, J=5.4, 14.2 Hz), 2.05–1.95 (m, 1H), 1.90–1.80 (m, 2H), 1.67–1.56 (m, 2H), 1.30 (s, 3H), 1.25–1.18 (m, 1H), 1.13 (d, 3H, J=6.2 Hz), 0.95–0.82 (m, 24H), 0.56 (q, 6H, J=7.8 Hz), 0.03 (s, 3H), −0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 159.3, 159.2, 144.1, 135.4, 135.1, 131.2, 130.9, 129.5, 129.3, 128.5, 117.2, 114.9, 114.0, 113.9, 78.7, 78.2, 78.1, 77.0, 73.2, 71.2, 70.5, 55.49, 55.46, 41.5, 40.6, 39.5, 39.0, 36.8, 35.8, 34.5, 26.4, 25.6, 18.5, 17.6, 15.8, 14.7, 7.5, 7.1, −3.1, −3.7; HRMS calcd for $C_{50}H_{84}O_7Si_2$ $[M+Na]^+$ 875.5648, found 875.5663; IR ν_{max} (film): 3460, 2963, 2932, 2878, 1614, 1512, 1463, 1249, 1098, 1005, 836, 742 cm^{-1}.

*4.2.46. Ester **49**.* To a stirred solution of acid **4** (82 mg, 0.27 mmol, 1.5 equiv) in THF (2 mL) were added Et_3N (73 mg, 0.72 mmol, 4 equiv) and 2,4,6-trichlorobenzoylchloride (110 mg, 0.45 mmol, 2.5 equiv) at rt. After 4 h at rt, the solid was removed and the filtrate was transferred to a solution of **58** (154 mg, 0.18 mmol) and DMAP (35 mg, 0.29 mmol, 1.6 equiv) in toluene (6 mL). After 12 h at rt, the mixture was quenched with satd $NaHCO_3$ and diluted with Et_2O, the organic layer was washed with H_2O, brine, dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (4–4.5% EtOAc/hexane) to afford **49** (191 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25–7.15 (m, 6H), 6.85–6.82 (m, 6H), 5.90–5.80 (m, 1H), 5.66–5.60 (m, 2H), 5.53–5.43 (m, 2H), 5.32 (dd, 1H, J=8.4, 15.4 Hz), 5.09–5.04 (m, 2H), 4.97–4.92 (m, 1H), 4.85 (s, 2H), 4.48–4.44 (m, 4H), 4.35 (d, 1H, J=11.6 Hz), 4.20 (d, 1H, J=11.6 Hz), 4.10–4.03 (m, 1H), 3.78 (s, 9H), 3.61–3.45 (m, 4H), 2.51 (d, 1H, J=14.2 Hz), 2.34–2.17 (m, 4H), 2.12 (dd, 1H, J=5.4, 14.2 Hz), 1.85 (dd, 1H, J=8.6, 14.6 Hz), 1.77–1.72 (m, 3H), 1.74 (d, 3H, J=6.4 Hz), 1.72 (s, 3H), 1.63–1.58 (m, 1H), 1.40–1.33 (m, 1H), 1.30 (s, 3H), 1.09 (d, 3H, J=6.2 Hz), 0.95–0.81 (m, 27H), 0.57 (q, 6H, J=7.8 Hz), 0.02 (s, 3H), −0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 166.3, 162.3, 159.3, 159.2, 159.1, 144.1, 135.4, 135.3, 131.6, 131.22, 131.18, 130.9, 130.6, 129.5, 129.4, 129.3, 128.1, 117.9, 117.2, 114.9, 113.9, 113.7, 82.0, 78.6, 78.1, 77.0, 76.7, 75.7, 71.2, 70.5, 69.2, 55.49, 55.45, 41.5, 40.6, 39.3, 39.1, 37.3, 35.3, 35.2, 33.6, 26.4, 25.8, 20.5, 18.5, 18.0, 16.6, 16.0, 15.8, 15.5, 7.5, 7.1, −3.0, −3.7; HRMS calcd for $C_{68}H_{106}O_{10}Si_2$ $[M+Na]^+$ 1161.7217, found 1161.7261; IR ν_{max} (film) 2958, 2932, 2874, 1708, 1641, 1614, 1512, 1459, 1249, 1089, 1036, 831, 742 cm^{-1}.

*4.2.47. Diol **59**.* To a stirred solution of **49** (191 mg, 0.17 mmol) in THF (1.2 mL) was added TBAF (1 M in THF, 0.5 mmol, 3 equiv) at rt. After 8 h, the reaction was quenched with satd $NaHCO_3$ and extracted with Et_2O. The combined organic layer was washed with H_2O and brine, dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (12–25% EtOAc/hexane) to afford **59** (144 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.25–715 (m, 6H), 6.86–6.82 (m, 6H), 5.90–5.78 (m, 1H), 5.70–5.60 (m, 3H), 5.44 (d, 1H, J=15.6 Hz), 5.32 (dd, 1H, J=8.6, 15.4 Hz), 5.10–5.06 (m, 2H), 4.95 (s, 1H), 4.93 (s, 1H), 4.90–4.86 (m, 1H), 4.52–4.40 (m, 4H), 4.33 (d, 1H, J=11.6 Hz), 4.18 (d, 1H, J=11.6 Hz), 4.10–4.02 (m, 1H), 3.78 (s, 9H), 3.62–3.56 (m, 2H), 3.53–3.45 (m, 2H), 2.70 (br, 1H), 2.39–2.23 (m, 6H), 2.16–2.11 (m, 1H), 2.07–2.00 (m, 1H), 1.88–1.81 (m, 1H), 1.80–1.74 (m, 1H), 1.75 (d, 3H, J=6.2 Hz), 1.73 (s, 3H), 1.66–1.57 (m, 1H), 1.34–1.28 (m, 1H), 1.13 (s, 3H), 1.07 (d, 3H, J=5.2 Hz), 0.92 (d, 3H, J=7.6 Hz), 0.89 (d, 3H, J=6.6 Hz), 0.83 (d, 3H, J=6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 166.3, 162.6, 159.4, 159.2, 144.3, 136.5, 135.0, 131.6, 131.2, 130.9, 130.8, 130.7, 129.7, 129.4, 129.3, 128.2, 117.9, 117.5, 115.0, 114.0, 113.9, 113.8, 82.1, 77.1, 76.6, 75.13, 75.11, 74.9, 70.8, 70.4, 69.2, 55.5, 40.4, 39.3, 38.4, 38.3, 37.1, 35.2, 35.1, 33.7, 22.6, 20.3, 18.0, 16.5, 16.0,

15.9, 15.5; HRMS calcd for $C_{56}H_{78}O_{10}$ $[M+Na]^+$ 933.5487, found 933.5501; IR ν_{max} (film) 3497, 2967, 2927, 2869, 1708, 1641, 1610, 1512, 1459, 1245, 1169, 1031, 822 cm^{-1}.

*4.2.48. Cyclopentene **60**.* To a stirred solution of **49** (9 mg, 7.9 μmol) in CH_2Cl_2 (8 mL) was added second generation Grubbs catalyst (0.7 mg, 0.8 μmol) at rt. After 3 h, the solvent was removed. The resulting residue was purified by flash chromatography (6% EtOAc/hexane) to afford **60** (5 mg, 57%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.27–7.18 (m, 6H), 6.87–6.82 (m, 6H), 5.67–5.60 (m, 2H), 5.50–5.43 (m, 2H), 5.36–5.27 (m, 2H), 4.93–4.91 (m, 1H), 4.47 (d, 2H, *J*=11.4 Hz), 4.41 (s, 2H), 4.36 (d, 1H *J*=11.4 Hz), 4.27–4.25 (m, 1H), 4.20 (d, 1H, *J*=11.6 Hz), 4.09–4.05 (m, 1H), 3.79 (s, 3H), 3.78 (s, 6H), 3.60 (t, 1H *J*=8.6 Hz), 3.52–3.47 (m, 2H), 2.62–2.52 (m, 2H), 2.50–2.35 (m, 2H), 2.30–2.17 (m, 2H), 2.04–1.99 (m, 1H), 1.80–1.72 (m, 8H), 1.66–1.58 (m, 1H), 1.40–1.33 (m, 2H), 1.29 (s, 3H), 1.09 (d, 3H, *J*=6.2 Hz), 0.95–0.81 (m, 27H), 0.57 (q, 6H, *J*=7.8 Hz), 0.02 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 166.3, 162.2, 159.3, 159.2, 159.1, 140.5, 135.2, 131.6, 131.2, 131.1, 130.9, 130.6, 129.52, 129.46, 129.3, 128.0, 123.8, 118.0, 114.0, 113.9, 113.7, 82.0, 78.6, 78.1, 77.0, 76.7, 75.7, 71.2, 70.5, 69.2, 55.49, 55.45, 41.5, 39.6, 39.3, 39.1, 37.2, 35.3, 35.1, 33.6, 26.3, 25.7, 20.5, 18.4, 18.0, 16.6, 15.9, 15.8, 15.5, 7.5, 7.1, −3.6, −3.8; HRMS calcd for $C_{66}H_{102}O_{10}Si_2$ $[M+Na]^+$ 1133.6904, found 1133.6941; IR ν_{max} (film): 2958, 2932, 2874, 1708, 1641, 1614, 1512, 1459, 1249, 1089, 1036, 831, 742 cm^{-1}.

*4.2.49. Cyclopentene **61**.* To a stirred solution of **59** (7 mg, 7.7 μmol) in CH_2Cl_2 (8 mL) was added second generation Grubbs catalyst (0.7 mg, 0.8 μmol) at rt. After 3 h, the solvent was removed. The resulting residue was purified by flash chromatography (25–30% EtOAc/hexane) to afford **61** (4.1 mg, 61%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 7.27–7.17 (m, 6H), 6.87–6.82 (m, 6H), 5.70–5.60 (m, 3H), 5.50–5.41 (m, 2H), 5.32 (dd, 1H, *J*=8.6, 15.4 Hz), 4.88–4.83 (m, 1H), 4.47 (d, 1H, *J*=11.4 Hz), 4.46 (d, 1H, *J*=11.4 Hz), 4.41 (s, 2H), 4.34 (d, 1H *J*=11.4 Hz), 4.29–4.22 (m, 1H), 4.19 (d, 1H, *J*=11.6 Hz), 4.08–4.03 (m, 1H), 3.79 (s, 3H), 3.78 (s, 6H), 3.60–3.42 (m, 3H), 2.64–2.57 (m, 2H), 2.46–2.01 (m, 8H), 1.95–1.82 (m, 1H), 1.80–1.76 (m, 1H), 1.75 (d, 1H, *J*=6.4 Hz), 1.73 (s, 3H), 1.66–1.58 (m, 1H), 1.37–1.33 (m, 2H), 1.17 (s, 3H), 1.08 (d, 3H, *J*=6.2 Hz), 0.92 (d, 3H, *J*=7.0 Hz), 0.89 (d, 3H, *J*=6.8 Hz), 0.85 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (data for major diastereomer) δ (ppm): 166.3, 162.6, 159.3, 159.2, 159.0, 139.7, 136.7, 131.6, 131.2, 131.0, 130.9, 130.8, 129.5, 129.4, 129.3, 128.0, 124.1, 117.9, 114.0, 113.9, 113.8, 82.1, 78.9, 76.6, 75.01, 74.98, 74.93, 70.6, 70.4, 69.2, 55.5, 41.8, 39.5, 39.2, 37.1, 35.1, 33.8, 33.1, 22.6, 20.3, 18.0, 16.5, 15.92, 15.90, 15.5; HRMS calcd for $C_{54}H_{74}O_{10}$ $[M+Na]^+$ 905.5174, found 905.5173; IR ν_{max} (film): 3490, 2958, 2932, 2874, 1708, 1641, 1614, 1512, 1459, 1249, 1089, 1036, 831, 742 cm^{-1}.

*4.2.50. Ketone **62**.* To a stirred solution of **59** (144 mg, 0.16 mmol) in CH_2Cl_2 (1.6 mL) was added $(i\text{-}Pr)_2NEt$ (165 mg, 1.28 mmol, 8 equiv), DMSO (0.18 mL), and $SO_3\cdot py$ (102 mg, 0.64 mmol, 4 equiv) at 0 °C. After 30 min at rt, the reaction was quenched with satd $NaHCO_3$ and diluted with Et_2O. The organic layer was washed successively with H_2O, brine, and dried over $MgSO_4$. After concentration under reduced pressure, the resulting residue was purified by flash chromatography (24–30% Et_2O/hexane) to afford **62** (110 mg, 70%) as a colorless oil. $[\alpha]_D^{20}$ −11.8 (*c* 1.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.25–7.15 (m, 6H), 6.86–6.82 (m, 6H), 5.85–5.61 (m, 4H), 5.42 (d, 1H, *J*=15.2 Hz), 5.32 (dd, 1H, *J*=8.6, 15.4 Hz), 5.10–5.05 (m, 2H), 5.01 (s, 1H), 4.87 (s, 1H), 4.92–4.84 (m, 1H), 4.51–4.45 (m, 3H), 4.39 (d, 1H, *J*=11.2 Hz), 4.32 (d, 1H *J*=11.6 Hz), 4.19 (d, 1H, *J*=11.6 Hz), 4.09–4.01 (m, 1H), 3.86 (s, 1H), 3.78 (s, 9H), 3.61–3.47 (m, 3H), 3.32–3.22 (m, 2H), 2.33–2.23 (m, 4H), 2.20–2.12 (m, 1H), 1.80–1.60 (m, 3H), 1.75 (d, 3H, *J*=6.6 Hz), 1.73 (s, 3H), 1.62–1.56 (m, 1H), 1.34 (s, 3H), 1.34–1.28 (m, 1H), 1.08 (d, 3H, *J*=6.2 Hz), 0.93 (d, 3H, *J*=7.0 Hz), 0.89 (d, 3H, *J*=6.4 Hz), 0.79 (d, 3H, *J*=6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 210.1, 166.2, 162.6, 159.4, 159.2, 159.0, 140.0, 134.8, 132.5, 131.5, 131.4, 131.2, 130.90, 130.86, 130.75, 129.6, 129.4, 129.29, 128.26, 117.8, 117.5, 117.2, 114.0, 113.9, 113.8, 82.1, 79.2, 77.1, 76.6, 75.2, 70.7, 70.4, 69.2, 55.50, 55.48, 43.7, 40.5, 39.3, 38.4, 36.9, 35.2, 34.9, 33.6, 25.0, 20.4, 18.0, 16.5, 15.9, 15.8, 15.5; HRMS calcd for $C_{56}H_{76}O_{10}$ $[M+Na]^+$ 931.5331, found: 931.5323; IR ν_{max} (film) 3470, 2954, 2927, 2869, 1715, 1708, 1641, 1610, 1512, 1459, 1245, 1169, 1031, 822 cm^{-1}.

*4.2.51. Ketal **2**.* To a stirred solution of **62** (110 mg, 0.12 mmol) in CH_2Cl_2 (6 mL)+pH 7 buffer (3 mL) was added DDQ (158 mg, 0.72 mmol, 6 equiv) at rt. After 20 min, the reaction was quenched with satd $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (30–33% EtOAc/hexane) to afford **2** (44 mg, 67%) as a colorless oil.

*4.2.52. Iriomoteolide-1a **1**.* To a stirred solution of **2** (18.8 mg, 0.034 mmol) in CH_2Cl_2 (34 mL) was added second generation Grubbs catalyst (3 mg, 0.0034 mmol, 0.1 equiv) at rt. After 3 h, the solvent was removed under reduced pressure. The resulting residue was purified by flash chromatography (35–45% EtOAc/hexane) to afford (*E*)-isomer **1** (9 mg, 52%) and (*Z*)-isomer **63** (3.6 mg, 21%).

(*E*)-*Isomer iriomoteolide*-1a **1**: $[\alpha]_D^{20}$ −27.8 (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.89–5.79 (m, 3H), 5.77 (s, 1H), 5.67 (dd, 1H, *J*=6.8 Hz, 15.5 Hz), 5.01–4.95 (m, 1H), 4.85 (s, 1H), 4.83 (s, 1H), 4.06–3.92 (m, 3H), 3.86–3.80 (m, 1H), 3.25 (s, 1H), 2.63 (s, 1H), 2.34–2.09 (m, 7H), 2.02–1.82 (m, 2H), 1.93 (s, 3H), 1.78 (ddd, 1H, *J*=3.4, 7.8, 14.2 Hz), 1.55–1.42 (m, 1H), 1.35–1.25 (m, 1H), 1.31 (s, 3H), 1.09 (d, 3H, *J*=6.6 Hz), 1.07 (d, 3H, *J*=7.8 Hz), 0.98 (d, 3H, *J*=7.0 Hz), 0.87 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.6 (C), 160.3 (C), 142.0 (C), 135.2 (CH), 133.0 (CH), 129.9 (CH), 127.5 (CH), 119.2 (CH), 111.1 (CH_2), 99.4 (C), 77.4 (C), 75.3 (CH), 74.7 (CH), 70.6 (CH), 69.6 (CH), 41.0 (CH), 40.0 (CH_2), 38.1 (CH_2), 37.7 (CH_2), 37.0 (CH), 35.9 (CH), 34.54 (CH_2), 34.50 (CH_2), 21.1 (CH_3), 20.9 (CH_3), 20.3 (CH_3), 16.2 (CH_3), 16.0 (CH_3), 15.2 (CH_3); HRMS calcd for $C_{29}H_{46}O_7$ $[M+Na]^+$ 529.3136, found 529.3129; IR ν_{max} (film) 3452, 2963, 2923, 2869, 1694, 1632, 1450, 1383, 1218, 1156, 965 cm^{-1}.

(*Z*)-*Isomer* **63**: $[\alpha]_D^{20}$ −29.1 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.87–5.81 (m, 2H), 5.77 (s, 1H), 5.67–5.55 (m, 2H), 4.91–4.85 (m, 1H), 4.86 (s, 1H), 4.84 (s, 1H), 4.38–4.27 (m, 1H), 4.25–4.18 (m, 1H), 3.99–3.90 (m, 1H), 3.82–3.77 (m, 1H), 3.73 (s, 1H), 2.46–2.18 (m, 6H), 2.00–1.87 (m, 3H), 1.95 (s, 3H), 1.78 (dd, 1H, *J*=8.2, 12.4 Hz), 1.50–1.42 (m, 1H), 1.35–1.25 (m, 1H), 1.26 (s, 3H), 1.09 (d, 3H, *J*=5.5 Hz), 1.08 (d, 3H, *J*=6.2 Hz), 0.95 (d, 3H, *J*=6.8 Hz), 0.83 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.3 (C), 162.8 (C), 142.0 (C), 135.5 (CH), 132.7 (CH), 129.8 (CH), 125.7 (CH), 118.4 (CH), 111.2 (CH_2), 100.0 (C), 77.7 (C), 73.3 (CH), 71.7 (CH), 70.8 (CH), 69.5 (CH), 40.4 (CH_2), 39.7 (CH), 37.7 (CH), 37.0 (CH_2), 35.9 (CH), 34.7 (CH_2), 34.6 (CH_2), 34.2 (CH_2), 22.8 (CH_3), 22.0 (CH_3), 20.3 (CH_3), 15.51 (CH_3), 15.46 (CH_3), 15.42 (CH_3); HRMS calcd for $C_{29}H_{46}O_7$ $[M+Na]^+$ 529.3136, found 529.3135; IR ν_{max} (film) 3439, 2967, 2923, 2869, 1694, 1632, 1450, 1383, 1205, 1160, 965 cm^{-1}.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.07.066.

References and notes

1. Tsuda, M.; Oguchi, K.; Iwamoto, R.; Okamoto, Y.; Kobayashi, J.; Fukushi, E.; Kawabata, J.; Ozawa, T.; Masuda, A.; Kitay, Y.; Omasa, K. *J. Org. Chem.* **2007**, *72*, 4469.
2. (a) Fang, L.; Xue, H.; Yang, J. *Org. Lett.* **2008**, *10*, 4645; (b) Ghosh, A. K.; Yuan, H. *Tetrahedron Lett.* **2009**, *50*, 1416; (c) Xie, J.; Horne, D. A. *Tetrahedron Lett.* **2009**, *50*, 4485; (d) Chin, Y. J.; Wang, S. Y.; Loh, T. P. *Org. Lett.* **2009**, *11*, 3674; (e) Ye, Z.; Deng, L.; Qian, S.; Zhao, G. *Synlett* **2009**, 2469; (f) Wang, S. Y.; Chin, Y. J.; Loh, T. P. *Synthesis* **2009**, 3557; (g) Paterson, I.; Rubenbauer, P. *Synlett* **2010**, 571; (h) Li, S.; Chen, Z.; Xu, Z.; Ye, T. *Chem. Commun.* **2010**, 4773; (i) Ghosh, A. K.; Yuan, H. *Org. Lett.* **2010**, *12*, 3120; (j) Fang, L.; Yang, J.; Yang, F. *Org. Lett.* **2010**, *12*, 3124; (k) Liu, Y.; Wang, J.; Li, H.; Wu, J.; Feng, G.; Dai, W.-M. *Synlett* **2010**, 2184.
3. For previous communications (a) Xie, J.; Ma, Y.; Horne, D. A. *Org. Lett.* **2009**, *11*, 5082; (b) Xie, J.; Ma, Y.; Horne, D. A. *Chem. Commun.* **2010**, 4770.
4. (a) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012; (b) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4490; (c) Gradillas, A.; Pěrez-Castells, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 6086.
5. (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457; (b) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544.
6. Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, *17*, 1295.
7. Burova, S. A.; McDonald, F. E. *J. Am. Chem. Soc.* **2004**, *126*, 2495.
8. (a) Williams, D. R.; Kiryanov, A. A.; Emde, U.; Clark, M. P.; Berliner, M. A.; Reeves, J. T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 12058; (b) Munoz-Torrero, D.; Bruckner, R. *Eur. J. Org. Chem.* **1998**, 1031.
9. (a) Ohira, S. *Synth. Commun.* **1989**, *19*, 561; (b) Muller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521.
10. Olpp, T.; Brückner, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 1553.
11. Hale, K. J.; Manaviazar, S.; Peak, S. A. *Tetrahedron Lett.* **1994**, *35*, 425.
12. Hale, K. J.; Cai, J. *Tetrahedron Lett.* **1996**, *37*, 4233.
13. Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408.
14. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.
15. (a) Zuger, M.; Weller, T.; Seebach, D. *Helv. Chim. Acta* **1980**, *63*, 2005; (b) Fráter, G.; Müller, U.; Günther, W. *Tetrahedron* **1984**, *40*, 1269; (c) Kraft, P.; Tochtermann, W. *Tetrahedron* **1995**, *51*, 10875.
16. (a) Abiko, A.; Liu, J. F.; Masamune, S. *J. Am. Chem. Soc.* **1997**, *119*, 2586; (b) Inoue, T.; Liu, J. F.; Buske, D. C.; Abiko, A. *J. Org. Chem.* **2002**, *67*, 5250.
17. (a) Marshall, J. A.; Johns, B. A. *J. Org. Chem.* **1998**, *63*, 7885; (b) Marshall, J. A.; Bourbeau, M. P. *J. Org. Chem.* **2002**, *67*, 2751.
18. Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851.
19. Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.
20. Shiina, I.; Kubota, M.; Oshiumi, H.; Hashizume, M. *J. Org. Chem.* **2004**, *69*, 1822.
21. (a) Yokokawa, F.; Asano, T.; Shioiri, T. *Tetrahedron* **2001**, *57*, 6311; (b) Yokokawa, F.; Asano, T.; Shioiri, T. *Org. Lett.* **2000**, *2*, 4169.
22. Bal, B. S.; Childers, W. E.; Pinnick, H. W. *Tetrahedron* **1981**, *37*, 2091.
23. (a) Narayanan, B. A.; Bunnelle, W. H. *Tetrahedron Lett.* **1987**, *28*, 6261; (b) Narayanan, B. A.; Bunnelle, W. H. *Org. Synth.* **1990**, *69*, 89.
24. (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953; (b) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18.
25. (a) Nicolaou, K. C.; Snyder, S. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1012; (b) Maier, M. E. *Nat. Prod. Rep.* **2009**, *26*, 1105; (c) Usami, Y. *Mar. Drugs* **2009**, *7*, 314.