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STUDIES ON THE SYNTEHSIS OF KIJANOLIDE: SYNTHESIS OF AN ADVANCED SECO-ACID INTERMEDIATE[#]

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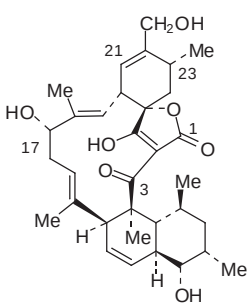
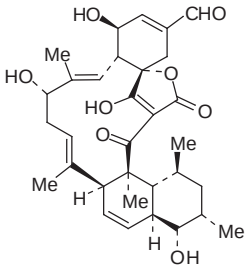
Abstract — A synthesis of an advanced seco acid intermediate (**7**) in a projected total synthesis of kijanolide is described. Key steps in the synthesis of **7** include the highly diastereoselective allylation reaction of **15**, the Suzuki cross coupling of dienyl iodide (**11**) and vinylboronic acid (**12**), and the IMDA reaction of **9**. Elaboration of the spirotetronic acid unit of **7** was accomplished by a Dieckmann cyclization of the α-acetoxy ester intermediate derived from the IMDA cycloadduct (**39**).

Introduction

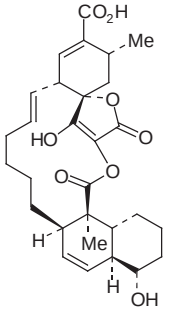
Kijanolide (**1**) is the aglycon of an antibiotic, kijanimicin, that is active against an unusual range of microorganisms, including *Plasmodium berghei* and *P. chabaudin*, two malarial parasites.[2,3] Kijanolide is structurally related to tetronolide (**2**) and chlorothricolide (**3**), the aglycones of the tetrocarcins[4] and chlorothricin,[5] which also display a range of interesting biological properties.[6-9] Total syntheses of tetronolide[10] and 24-*O*-methyl chlorothricolide[11] have been accomplished by Yoshii and coworkers. We have reported a total synthesis of (-)-chlorothricolide[12,13] as well as a formal synthesis of tetronolide.[14] Extensive studies on the



kijanolide (**1**)



tetronolide (**2**)

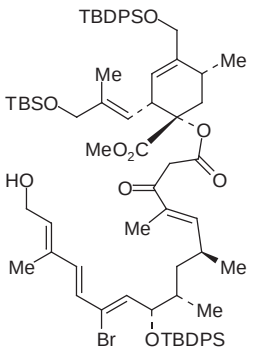


chlorothricolide (**3**)

[#]Dedicated to Prof. Albert I. Meyers on the occasion of his 70th birthday.

synthesis of these molecules have also been reported from the laboratories of Marshall and Boeckman;[15-19] a complete list of citations to this body of work is provided in our earlier publications.[13,14,20]

In earlier papers we reported highly enantio- and diastereoselective syntheses of the top and bottom half fragments of kijanolide,[21,22] along with efforts to complete a total synthesis of **1** *via* intermediates (**4**) and (**5**).[23] The strategy that we pursued at that time involved the coupling of precursors to the two major fragments *via* a C(1) ester linkage in **4**, or *via* the 2-acyl tetronate substructure in **5**, prior to closure of the octahydronaphthalene nucleus by an intramolecular Diels-Alder (IMDA) reaction. We envisaged that the C(16)-C(17) bond would be formed at a very late stage in the synthesis, by analogy to the work of Yoshii in the tetronolide series.[10] Unfortunately, intermediate (**4**) undergoes thermal deacylation at *ca.* 115 °C *via* an acyl ketene intermediate faster than the IMDA reaction required to establish the octahydronaphthalene unit.[23] Attempts to accomplish a Lewis acid catalyzed IMDA reaction of **4** were also unsuccessful. The thermal instability of **4** was successfully addressed by synthesis of the 2-acyl spirotetronate (**5**), however this intermediate also failed to undergo an IMDA reaction, owing to steric problems in the IMDA transition state.[23]



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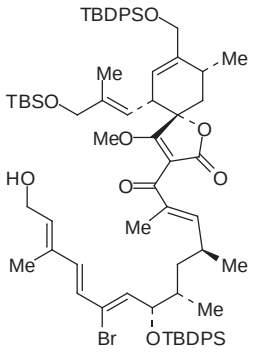

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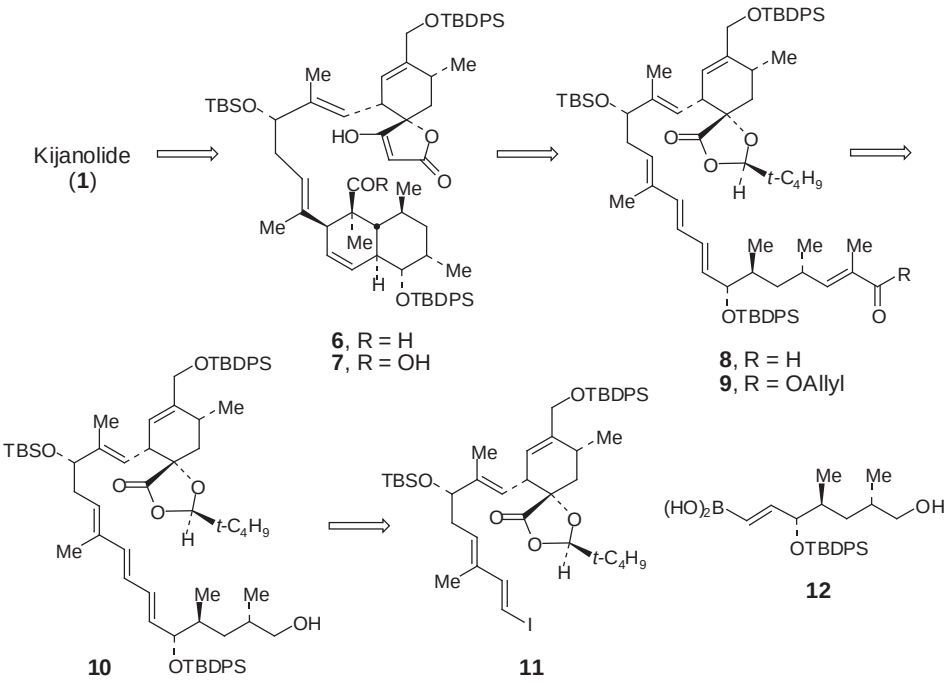
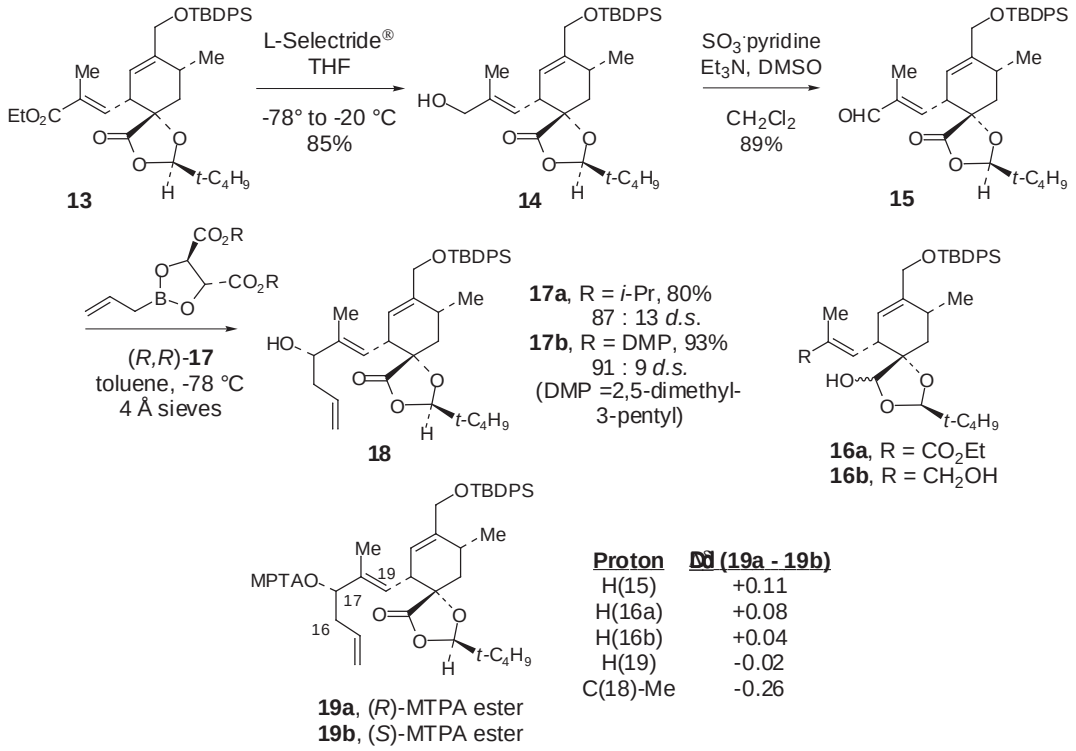
In view of these problems, we elected to pursue a revised strategy in which the kijanolide macrocycle is closed at the end of the synthesis, after construction of the C(16)-C(17) linkage connecting the two major halves of the molecule. Thus, we identified seco aldehyde (**6**) and seco acid (**7**) as plausible penultimate synthetic intermediates. In turn, we envisaged that these intermediates would be accessible by the IMDA reactions of **8** and **9**, respectively. Finally, we decided to synthesize the Diels-Alder substrates *via* the Suzuki coupling of the top half dienyl iodide (**11**) and the vinylboronic acid (**12**).

We describe herein highly stereoselective syntheses of the advanced kijanolide precursors (**6**) and (**7**), along with attempts to close the kijanolide macrocycle from these intermediates.

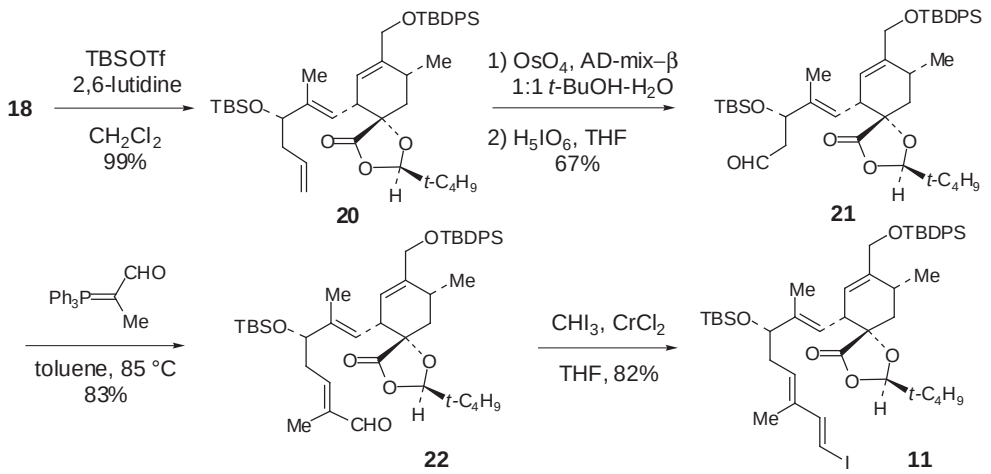


Results and Discussion

Synthesis of Vinyl Iodide (11). The synthesis of the vinyl iodide fragment (**11**) originates from the kijanolide top half exo-Diels-Alder adduct (**13**).[21] Direct reduction of **13** to the corresponding allylic alcohol (**14**) was successful in small experiments by using L-Selectride®, as we had successfully demonstrated in our synthesis of the top half of tetronolide.[14] Small amounts of hemi-acetal (**16a**) were also obtained. Oxidation of **14** to the targeted aldehyde (**15**) was then accomplished by using the Parikh-Doering protocol (SO_3-pyridine, DMSO, Et_3N, ambient temperature) in good yield.[24] However, for larger scale experiments it proved more convenient to reduce **13** to the known[21] diol (**16b**) with DIBAL (CH_2Cl_2, -78 °C), and then to oxidize **16b** to aldehyde lactone (**15**) by using the standard Swern protocol (75% overall).[25] The C(17) stereocenter was then set by an asymmetric allylboration reaction. Best results were obtained when **15** was treated with allylboronate (**17b**) containing the bulky bis(2,5-dimethyl-3-pentyl) tartrate auxiliary,[26,27] which provided **18** in 91% yield and with 10 : 1 diastereoselectivity. In contrast, homoallylic alcohol (**18**) was obtained with 7 : 1 d.s. when the conventional DIPT reagent ((*R,R*)-**17a**) was employed. Attempts to use Keck's asymmetric allylstannation protocol for this reaction (e.g., $Bu_3SnCH_2CH{=}CH_2$, (*S*)-(Binol)Ti(OiPr)$_2$, CH_2Cl_2, -20 °C)[28] gave **18** in only 12% yield after an 80 h reaction period, with recovery of 65% of **15**. The stereochemistry of the new C(17) stereocenter of **18** was assigned initially based on the known stereochemical course of allylboration reactions of the tartrate allylboronates.[29,30] This assignment was subsequently confirmed by application of the Mosher method (see data for the MTPA esters (**19a**) and (**19b**)).[31,32]

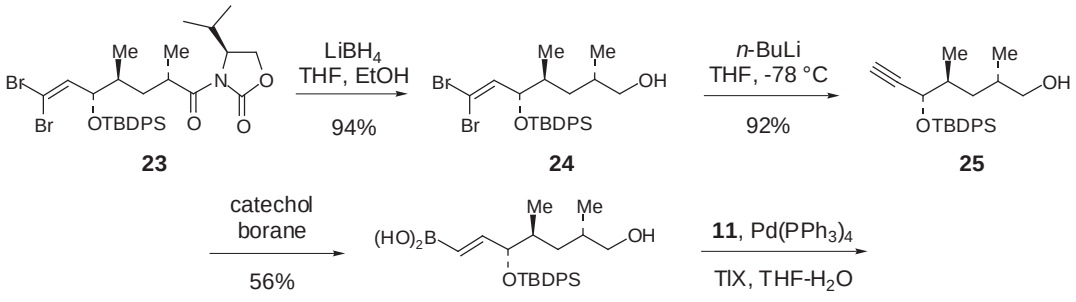


Protection of the new C(17)-hydroxyl group in **18** as a TBS ether provided **20** in near quantitative yield. Because the two trisubstituted olefins in **20** are quite hindered,[33,34] we anticipated that it would be possible to selectively cleave the vinyl group by using a dihydroxylation-periodate sequence.[35] However, treatment of **20** with stoichiometric OsO_4 and pyridine in 5 : 1 THF-H_2O, or with catalytic OsO_4 and *N*-methylmorpholine *N*-oxide in acetone, *t*-BuOH, and water gave the desired diol in only *ca.* 30-50% yield.[36] Substantial dihydroxylation of the trisubstituted olefins also occurred under these conditions. However, application of the Sharpless asymmetric dihydroxylation protocol provided the desired diol in 71% yield.[35,37] Oxidative cleavage of the diol intermediate by using periodic acid in THF then provided aldehyde (**21**) in 67% overall yield. Treatment of **21** with α-(triphenylphosphoranylidene)propionaldehyde in toluene at 85 °C provided enal (**22**) in 83% yield. Finally, the targeted vinyl iodide unit was installed by using the Takai protocol (CHI_3,

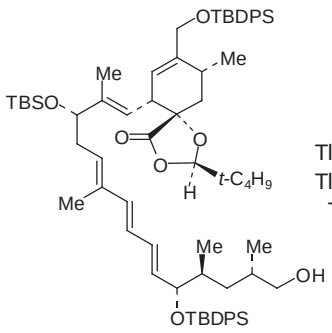


$CrCl_2$, THF),[38] thereby completing the synthesis of fragment (**11**).

Synthesis of Vinylboronic Acid (12) and Initial Fragment Coupling. The synthesis of the vinylboronic acid fragment (**12**) begins with the $LiBH_4$ reduction[39] of the known[23] acyl oxazolidinone (**23**). Treatment of the resulting alcohol (**24**) with *n*-BuLi in THF at –78 °C provided alkynol (**25**),[40] which was then converted to the vinylboronic acid (**12**) by hydroboration with catecholborane.[41,42]



23 **24** **25** **12**



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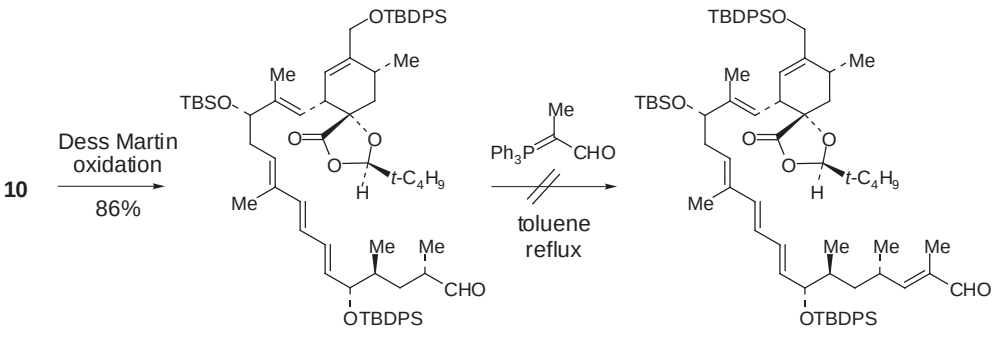
TlX source	Reagent Age	Yield
TlOH (10% stock solution)	1 month old	71%
TlOH (10% stock solution)	5 months old	50%
TlOH (fresh, from solid)	12 months old	52%
TlOEt	--	83%

We anticipated at the outset that the coupling of **11** and **12** would be accomplished by using the Suzuki cross coupling protocol.[43,44] We have found that Kishi's modification of the Suzuki protocol,[45] involving use of TlOH as the base, is an excellent procedure for coupling of highly functionalized synthetic intermediates.[22,23,46,47] Indeed, treatment of a mixture of **11** and **12** with aqueous TlOH and catalytic $Pd(PPh_3)_4$ provided conjugated triene (**10**) in up to 71% yield. However, the efficiency of this reaction is dependent on the age of the TlOH solution, with yields decreasing substantially with older batches of reagent. Thus, for example, when a 5 month old stock solution of TlOH was used in the coupling of **11** and **12**, the yield of **10** dropped to 50%. It is known that aqueous solutions of TlOH are air and light sensitive and have an inferior shelf life.[48] We therefore turned to use of solid TlOH as a reagent for this reaction. However, generation of a 10% solution of TlOH in water (0.5 M) gives an initially clear solution from which a brown-black precipitate separates even when stored carefully to exclude exposure to atmospheric oxygen.[49] Moreover, use of a freshly prepared solution of TlOH (from a one-year old commercial sample of solid reagent) in the Suzuki cross coupling of **11** and **12** also gave only a 52% yield of **10**. These results also suggest that TlOH may be somewhat unstable in the solid state.

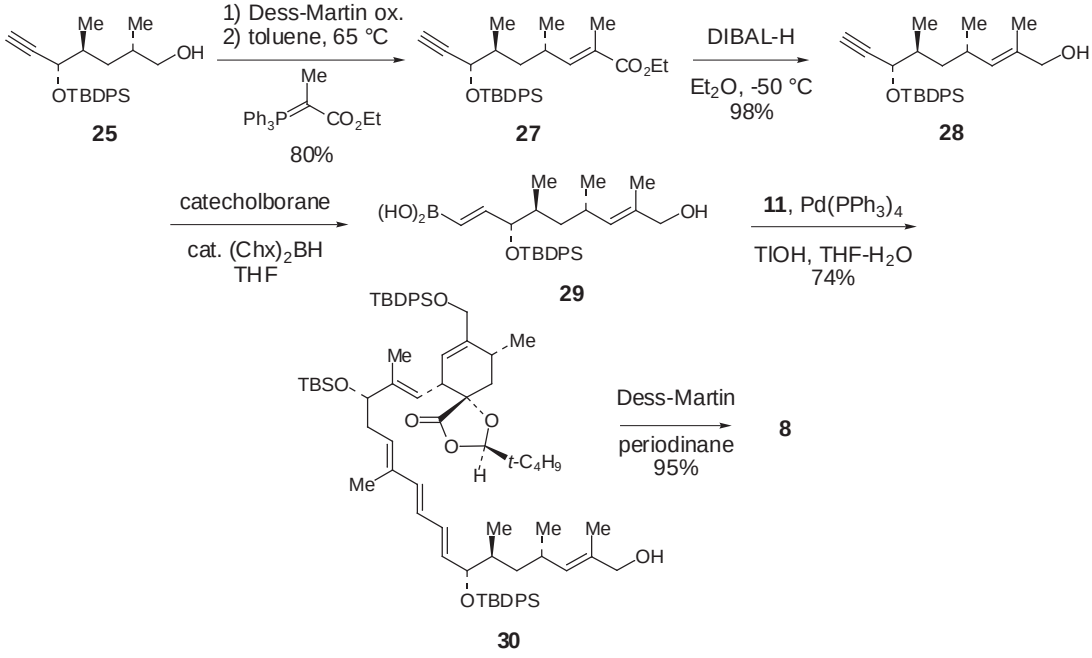
Searching for a stable alternative to TlOH for use in these reactions led us to consider use of TlOEt, which is commercially available from multiple sources and is an easily handled liquid. Prior to our work, there were relatively few application of TlOEt in Suzuki cross coupling reactions,[45,50] and Kishi had reported that TlOEt did not give the same level of rate acceleration as TlOH.[45] Several other examples had been reported where TlOEt failed to give acceptable results.[51,52] However, we found that use of TlOEt in the cross coupling of **11** and **12** , using an aqueous THF solvent system, provided **10** in 83% yield. We have obtained excellent results using TlOEt in Suzuki reactions of other substrates. We also have observed that, at least qualitatively, the rates of reactions promoted by TlOEt are comparable to those performed by using TlOH, when the reaction is performed in an aqueous co-solvent system.[53] Since our communication on this topic appeared in 2000, other investigators have adopted the TlOEt modification of the Suzuki reaction.[54,55]

Synthesis of Seco Aldehyde (**6**). All that remained to reach the targeted IMDA substrate (**8**) was to oxidize alcohol (**10**) to the aldehyde and to introduce the dienophilic unit *via* a Wittig reaction. Oxidation of **10** to aldehyde (**26**) was accomplished in 86% yield by using the Dess-Martin periodinane reagent.[56] However, attempted Wittig homologation of **26** by using α-(triphenylphosphoranylidene)propionaldehyde in refluxing toluene for extended periods of time led only to epimerization of the aldehyde and ultimately decomposition of the substrate. None of the desired enal (**8**) was obtained by this sequence. Although we recognized that **8** probably could be prepared by Horner-Wadsworth-Emmons olefination of **26** with a more reactive phosphonoacetate reagent followed by reduction of the enoate to the enal, we decided to pursue a more convergent approach in which the dienophilic double bond was introduced before the Suzuki fragment coupling step.

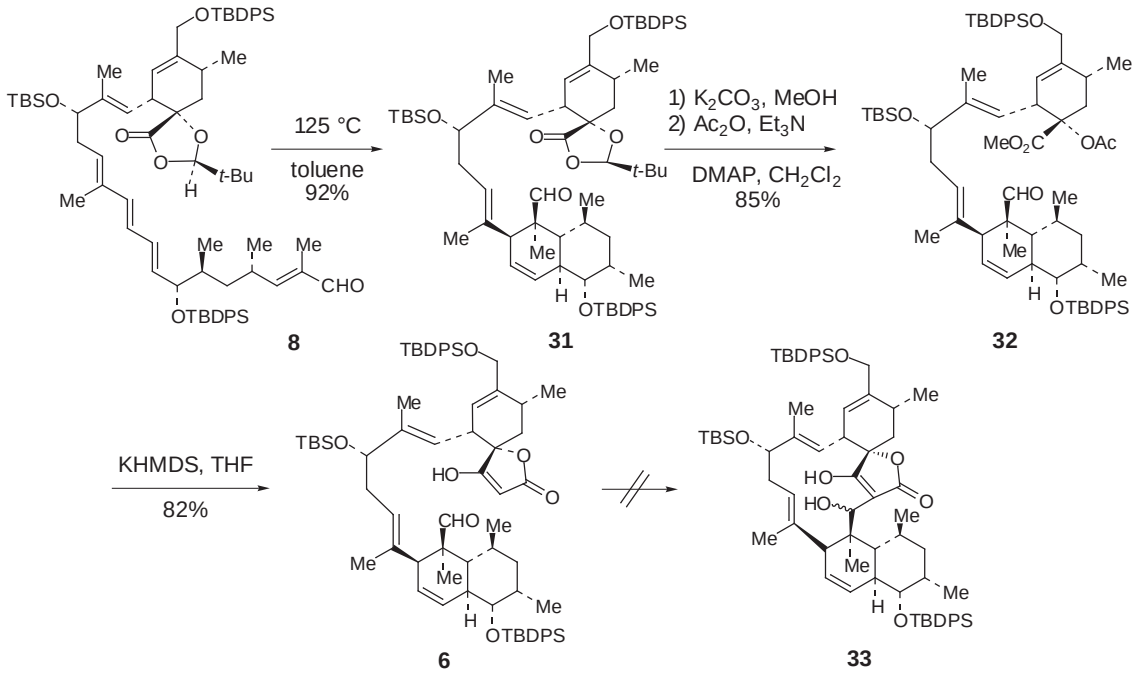


Oxidation of primary alcohol (**25**) with the Dess-Martin periodinane[56] gave the corresponding aldehyde that was treated with ethyl α-(triphenylphosphoranylidene)-propionate in toluene at 65 °C to give enoate (**27**) in 80% yield for the two steps. Reduction of **27** to the allylic alcohol (**28**) then set the stage for synthesis of the vinylboronic acid (**29**). However, poor results were obtained when **28** was heated with catecholborane.[41,42] Ultimately, best results were obtained when the catecholboration of **28** was performed at ambient temperature in the

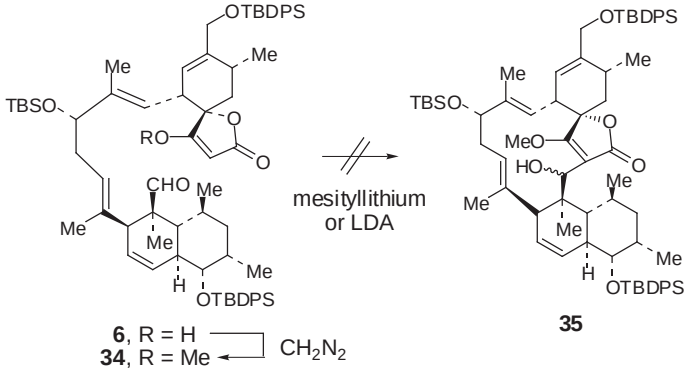
presence of catalytic amounts of dicyclohexylborane.[57,58] However, vinylboronic acid (**29**) proved to be unstable to chromatographic purification, and therefore was used directly in the Suzuki cross coupling with **11** without purification. Treatment of a mixture of **11** (1 equiv), **29** (1.4 equiv) and $Pd(PPh_3)_4$ (0.3 equiv) with aqueous TlOH in THF provided **30** in 74% yield (based on **11**).[45,59] Finally, oxidation of allylic alcohol (**30**) with the Dess-Martin periodinane reagent provided the IMDA substrate (**8**) in 95% yield.



The IMDA reaction was accomplished by heating a toluene solution of **8** at 125 °C in a sealed tube overnight. This provided **31** as the major component of an inseparable 7 : 1 mixture of two cycloadducts in 92% yield. The stereochemistry of the minor component of the reaction mixture was not assigned. Treatment of the mixture with K_2CO_3 in MeOH at ambient temperature provided the corresponding a-hydroxy methyl ester, which was converted to α-acetoxy ester (**32**) in 85% yield after treatment with Ac_2O, DMAP and Et_3N. The spirotetronate unit of the seco aldehyde (**6**) was then established in 82% yield by treatment of **32** with KHMDS in THF at -78 ° to 0 °C.[14,21,60,61] We had hoped that this intermediate would spontaneously cyclize *via* an intramolecular aldol process, however seco aldehyde (**6b**) proved to be unreactive under a range of conditions. The potassium salt of **6**, an intermediate in the Dieckmann cyclization of **32**, failed to cyclize. Treatment of **6** with a variety of amine bases, including an excess of DBU, failed to effect any reaction. Intermediate (**6**) also proved to be stable to a number of acidic conditions, including exposure to silica gel.

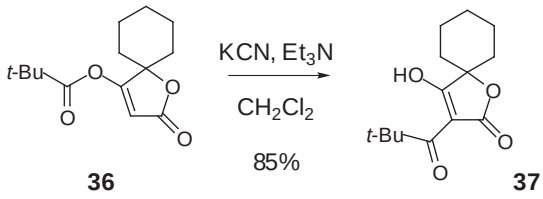


The lack of aldol reactivity of **6** promoted us to explore cyclization strategies involving more nucleophilic reaction conditions. Yoshii used an α-lithiotetronate nucleophile to form the C(2)-C(3) bond in a bimolecular coupling of the top and bottom half fragments of tetronolide,[10,62,63] so we anticipated that it might be possible to apply this reaction to the cyclization reaction of methyl ether (**34**) prepared by esterification of the tetronic acid **6** with diazomethane. However, treatment of **34** with mesityllithium (THF, -78 °C, 1 h, with warming to 23 °C) gave no reaction under conditions analogous to those that Yoshii had successfully employed in the tetronolide total synthesis. Alternatively, treatment of **34** with LDA (THF, -78 °C, 3 h) to effect α-metallation of the tetronate unit led to extensive decomposition, and none of the desired ring closed product (**35**) was obtained.



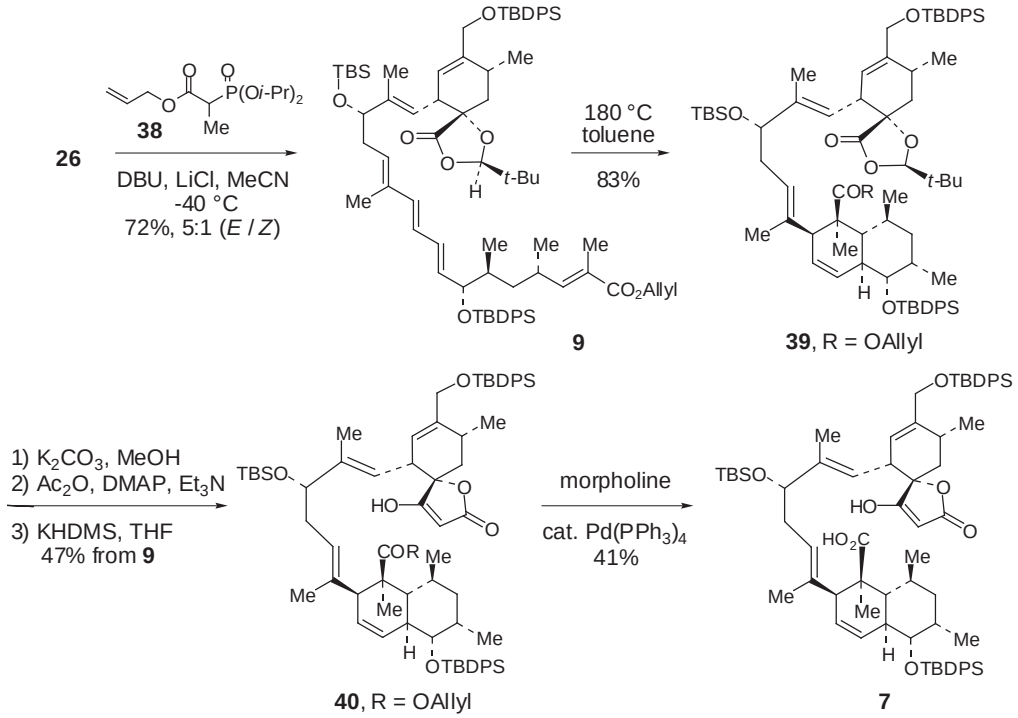
Synthesis of Seco Acid (**7**). The lack of success realized in attempts to effect the cyclizations of seco aldehyde intermediates (**6**) and (**34**) prompted us to consider alternative strategies for effecting this ring closure. Yoshii has demonstrated that 2-acyltetronates can be synthesized by treatment of tetronic acids with active esters in the presence of DMAP. This reaction appears to proceed by way of initial O-acylation followed by O → C acyl migration catalyzed

by DMAP.[64,65] The acyl migration reaction works well in all cases except when the acyl group is aromatic or very hindered (e.g., pivaloyl). However, a coworker in our laboratory has demonstrated that KCN is an effective acyl transfer catalyst in such cases, as illustrated below by the isomerization of **36** to **37**.[66,67]



36 **37**

Horner-Wadsworth-Emmons olefination of aldehyde (**26**) with the α-phosphonopropionate reagent (**38**)[68] provided the IMDA substrate (**9**) as a 5 : 1 mixture of olefin isomers in 72% yield.[69] The selectivity of this reaction was only 1 : 1 to 1.5 : 1 when bases such as KHDMS or LiHDMS (both in THF at –78 °C) were employed. When the diethyl phosphonate ester corresponding to **38** was used, the (Z)-olefin isomer predominated with selectivity of *ca.* 3 : 1.[70] The IMDA reaction of **9** was performed at 180 °C, and impure cycloadduct (**39**) was isolated in 83% yield. Treatment of **39** with K_2CO_3 in MeOH provided the expected α-hydroxy ester in 70% yield. ^{1}H NOSEY experiments performed on the latter intermediate confirmed the expected stereochemical assignments in the bottom-half octahydronaphthalene ring system. Acylation of the α-hydroxy ester with Ac_2O and DMAP, followed by Dieckmann closure of the spirotetronate provided tetronic acid intermediate (**40**) in 47% overall yield from **9**. Finally, in an initial small-scale deprotection experiment, we demonstrated that the allyl ester protecting group could be removed by treatment of **40** with morpholine and $Pd(PPh_3)_4$.[71] It

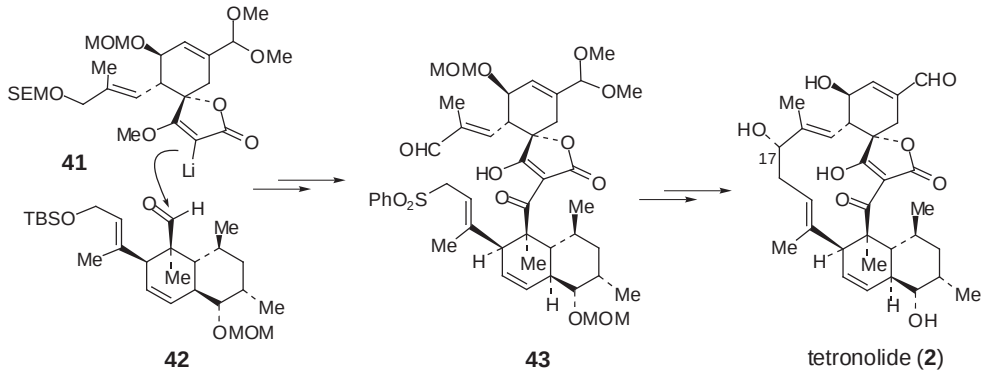


9 **39**, R = OAllyl

40, R = OAllyl **7**

remains for the synthesis of **40** to be scaled up to provide sufficient quantities of the seco acid (**7**) for a systematic study of the final macrocyclization and deprotection sequence, en route to completion of a total synthesis of kijanolide.

Summary. Establishment of the 13-membered carbocyclic ring of kijanolide remains a challenging problem. To date, the only successful strategy for synthesis of this macrocyclic ring system, which appears in both kijanolide and tetronolide, remains the method demonstrated by Yoshii in his tetronolide total synthesis.[10] This procedure entails the addition of an α-lithiotetronate (**41**) to the bottom half aldehyde (**42**) followed by macrocyclization at the stage of **43** by the addition of the α-sulfonyl carbanion to the α,β-unsaturated aldehyde. However, this strategy requires 15 transformations for completion of the total synthesis from intermediates (**41)**and (**42**).



One of our goals in pursuing the total synthesis of kijanolide has been to develop a simple method for synthesis of the 13-membered carbocyclic ring. We have developed a relatively efficient, stereocontrolled synthesis of an advanced seco-ester intermediate (**40**) in which the top and bottom half fragments are connected *via* flexible the C(14)-C(19) chain. Key steps in this synthesis are the Suzuki cross coupling of the top half vinyl iodide (**11b**) and vinylboronic acid (**12**), and then the IMDA reaction of derived trienoate (**9**) which establishes the bottom half octahydronaphthalene nucleus in intermediate (**39**). Seco acid intermediate (**7**) is then prepared in four additional steps from **39**. In order to complete a total synthesis of kijanolide, it will be necessary to devise a method to accomplish the intramolecular C-acylation of the spirotetronic acid unit with an active ester generated from the bottom half carboxylic acid fragment of seco acid **7**. Further progress towards this goal will be reported in due course.

EXPERIMENTRAL

General Details: All reactions were conducted in flame-dried or oven-dried glassware under an atmosphere of dry nitrogen. Diethyl ether and THF were dried by distillation from sodium benzophenone ketyl. Toluene and benzene were dried by distillation from sodium. CH_2Cl_2,

MeCN, Et_3N, and HMPA were distilled from CaH_2. MeOH was distilled from magnesium turnings.

^1H NMR spectra were measured at 400, and 500 MHz on commercial NMR instruments. Chemical shifts are reported in d with coupling constants reported in Hz. Residual $CHCl_3$ (δ 7.26 ppm) or C_6HD_5 (δ 7.15) were used as internal references for spectra measured in these solvents. ^{13}C NMR spectra were measured at 100, or 125 MHz; chloroform (δ 77.0 ppm) or C_6D_6 (δ128.0) were used as internal references. IR spectra were measured with a Perkin-Elmer Spectrum 1000 FT-IR or 1420 Infrared spectrometers using thin film samples on NaCl plates. HRMS were measured at 70 eV on a Micromass Corp. VG 70-250-S at the University of Michigan Mass Spectrometry Laboratory, or on a Kratos GC/MS 80RFA mass spectrometer at the Indiana University Mass Spectrometry Laboratory. Optical rotations were measured on a Rudolph Autopol III polarimeter using a 1 mL quartz cell with a 10 cm path length.

Analytical thin layer chromatography (TLC) was performed using Whatman glass plates coated with a 0.25 mm thickness of silica gel containing PF254 indicator, and compounds were visualized with UV light, potassium iodide/iodine stain, *p*-anisaldehyde stain, ceric ammonium molybdate stain, or phosphomolybdic acid in EtOH. Flash chromatography was performed on Whatman 60 Å (230-400 mesh) silica gel for column chromatography.[72] High pressure liquid chromatography (HPLC) was performed on a system utilizing a Rainin SD-200 pump and a Rainin HPXL pump with a gradient solvent system of hexanes and ethyl acetate, a Rheodyne 7125 injector, and a Rainin UV-C UV detector at 254 nm. Depending on sample size, HPLC purifications were carried out with Rainin Dynamax-60A (Si 83-111-C) 10 mm, Dynamax-60A (Si 83-121-C) 21 mm, or Microsorb (Si 80-140-C8) 41 mm columns. Unless noted otherwise, all compounds purified chromatographically were sufficiently pure (>95%) for use in subsequent reactions.

(2*R*, 2*R*', 4*S*, 5*R*)-Spiro-1-[(*tert*-butyldiphenylsilyloxy)methyl]-2-methyl-5-(2-methylpropen-1-ol)cyclohex-1-ene-(4,5')-2'-*tert*-butyl-1',3'-dioxolan-4'-one (14). A solution of exo-Diels-Alder adduct (**13**)[21] (250 mg, 0.413 mmol) in 8.4 mL of THF was cooled to –78 ˚C. A cooled solution of L-Selectride® (1 M in THF, 826 µL, 0.83 mmol) was added dropwise *via* canula over 30 min. The solution was stirred at –78 ˚C for 1 h, then was allowed to warm slowly to -20˚C, where it was stirred for 30 min. The solution was recooled to –78 ˚C, and a 3:1 MeOH-phosphate buffer solution was added slowly. The solution was then warmed to rt, diluted with brine (5 mL) and extracted with EtOAc (3 x 15 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product by silica gel chromatography (4 :1 hexanes-Et_2O to 1:1 hexanes-Et_2O) provided 199 mg (85%) of **14** as a clear oil. A small amount of the hemi-acetal (**16a**) was present by TLC analysis, but was not isolated: $[\alpha]_D^{23}$ -27.0˚ (c=0.3 in EtOAc); ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 - 7.28 (m, 10 H),

5.38 (dd, *J* = 10.4, 1.3 Hz, 1 H), 5.27 (s, 1 H), 5.10 (s, 1 H), 4.23 (A of AB, J_{AB} = 13.1 Hz, 1 H), 4.12 (B of AB, J_{BA} = 13.1 Hz, 1 H), 4.02 (s, 2 H), 3.48 (d, *J* = 10.3 Hz, 1 H), 2.60 (m, 1 H), 2.15 (dd, *J* = 13.3, 7.1 Hz, 1 H), 1.78 (m, 1 H), 1.68 (s, 3 H), 1.30 (m, 1 H), 1.14 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 9 H), 0.93 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 140.7, 138.9, 135.6, 135.5, 133.7, 129.6, 127.6, 121.8, 120.9, 110.3, 80.6, 68.1, 65.9, 40.8, 37.0, 35.0, 27.8, 26.9, 23.4, 19.6, 19.3, 18.2, 13.9; IR (neat) 3460, 3060, 2821, 1785, 1583, 1459, 1425, 1400 cm^{-1}; HRMS (FAB) calcd for $C_{34}H_{46}O_5NaSi$ $(M+Na)^+$ 585.3012, found 585.3001 m/z.

(2*R*, 2*R*', 3''*S*, 4*S*, 5*R*)-Spiro-1-[(*tert*-butyldiphenylsilyloxy)methyl]-2-methyl-5-(3''-hydroxy-2''-methyl-1'',5''-hexadiene)cyclohex-1-yl-(4,5')-2'-*tert*-butyl-1',3'-dioxolan-4'-one (18). To a –78 °C solution of oxalyl chloride (1.42 mL, 16.2 mmol) in CH_2Cl_2 (50 mL) was added DMSO (1.73 mL, 24.4 mmol). This mixture was stirred at –78 °C for 10 min, then a solution of diol (**16b**)[21] (2.29 g, 4.06 mmol, prepared by DIBAL-H reduction of 2.97 g of **13**, 82% yield) in 10 mL of CH_2Cl_2 was added dropwise. The mixture became cloudy upon addition of **16b**. The mixture was stirred for 1 h at –78 °C, and then triethylamine (5.66 mL 40.6 mmol) was added. This solution was stirred for another hour at –78 °C, and then was allowed to warm slowly to rt. The solution was diluted with Et_2O, and washed with an aqueous salt solution. The aqueous layer was extracted with EtOAc (4 x 25 mL) and the combined organics were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified *via* silica gel chromatography (9 : 1 hexanes-Et_2O, silica gel pre-treated with triethylamine) to yield 2.10 g (92%) of the desired aldehyde (**15**) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 1 H), 7.65-7.35 (m, 10 H), 6.38 (d, *J* = 12.0 Hz, 1 H), 5.36 (s, 1 H), 5.04 (s, 1 H), 4.10 (m, 2 H), 3.78 (m, 1 H), 2.64 (br s, 1 H), 2.04 (m, 1 H), 1.81 (m, 4 H), 1.18 (d, *J* = 6.0 Hz, 3 H), 1.05 (s, 9 H), 0.96 (s, 9 H); IR (neat) 2957, 2845, 1786, 1690 cm^{-1}. This material was used in the subsequent allylboration reaction without further purification.

A solution of aldehyde (**15**) (2.10 g, 3.74 mmol) in toluene (70 mL) containing flame-dried molecular sieves (*ca.* 1 g) was cooled to -78˚C. A solution of the (*R*,*R*)-2,4-dimethylpentyl tartrate allylboronate reagent (**17a**)[26] (10 mL of a 0.6 N toluene solution over 4 Å sieves) was added dropwise *via* canula . The solution was stirred at -78˚C for 5 h, then was allowed to warm slowly to rt overnight. The solution was then filtered (to remove sieves), cooled to 0˚C, diluted with 2 N NaOH (100 mL) and stirred for 3 h. The layers were separated, and the organic layer was washed with a saturated solution of $NaHCO_3$. The combined aqueous fractions were washed several times with Et_2O (4 x 2 mL). The combined organic extracts were dried ($MgSO_4$) filtered and concentrated *in vacuo*. Purification by silica gel chromatography (4 :1 hexanes-Et_2O to 1:1 hexanes-Et_2O) provided the allylation product (**18**) and its alcohol epimer as an inseparable mixture (1.91 g, 85%). The mixture was determined to be >10 : 1 *S*/*R* at the new C(17)-stereocenter by MTPA ester analysis**.** Data for **18**: $[\alpha]_D^{23}$ -67.8º (c=1.0 in $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.37 (m, 10 H), 5.73 (m, 1 H), 5.40

(d, J = 10.4 Hz, 1 H), 5.25 (br s, 1 H), 5.14 (s, 1 H), 5.10 (m, 2 H), 4.22 (A of AB, J_{AB} = 13.2 Hz, 1 H), 4.12 (B of AB, J_{BA} = 13.2 Hz, 1 H), 4.07 (t, J = 6.0 Hz, 1 H), 3.46 (m, 1 H), 2.59 (m, 1 H), 2.31 (m, 2 H), 2.15 (dd, J = 14.0, 6.9 Hz, 1 H), 1.79 (dd, J = 14.0, 1.6 Hz, 1 H), 1.66 (d, J = 1.2 Hz, 3 H), 1.60 (br s, 1 H), 1.13 (d, J = 7.2 Hz, 3 H), 1.05 (s, 9 H), 0.93 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 140.7, 140.6, 135.6, 135.5, 134.1, 133.5, 129.6, 127.6, 127.5, 122.0, 120.7, 118.1, 110.2, 80.6, 76.6, 75.4, 65.8, 40.8, 39.7, 36.9, 35.0, 27.7, 26.8, 23.4, 19.6, 19.2, 15.2, 12.9; IR ($CDCl_3$) 3590, 3050, 2959, 1784, 1605 cm^{-1}; HRMS calcd for $C_{33}H_{41}O_5Si$ (M - C_4H_9)$^+$ 545.2723, found 545.2749 m / z.

MTPA esters of 18: To a solution of alcohol (**18**) (5 mg, 0.007 mmol) in CH_2Cl_2 (0.5 mL) was added MTPA-Cl (4 μL, 0.0231 mmol) and DMAP (4 mg, 0.03 mmol).[31] The mixture was stirred at rt until TLC analysis revealed no starting material remained. The solution was then diluted with Et_2O (5 mL), and washed with 2 mL saturated $NaHCO_3$. The layers were separated, and the aqueous phase was extracted with Et_2O (3 x 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated. Purification of the crude product *via* silica gel chromatography (4:1 hexanes-EtOAc) yielded the desired ester as a clear oil. The diastereomeric MTPA esters are not separable by silica gel chromatography.

Data for (*R*)-MTPA ester (**19a**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.38 (m, 15 H), 5.63 (m, 1 H), 5.51 (d, J = 9.7 Hz, 1 H), 5.43 (s, 1 H), 5.37 (t, J = 7.1 Hz, 1 H), 5.18 (br s, 1 H), 5.06 (m, 2 H), 4.21 (A of AB, J_{AB} = 13.2 Hz, 1 H), 4.14 (B of AB, J_{BA} = 13.2 Hz, 1 H), 3.58 (s, 3 H), 3.39 (d, J = 10.7 Hz, 1 H), 2.49 (m, 2 H), 2.35 (m, 1 H), 2.15 (dd, J = 14.1, 6.9 Hz, 1 H), 1.80 (d, J = 13.8 Hz, 1 H), 1.35 (s, 3 H), 1.14 (d, J = 6.8 Hz, 3 H), 1.05 (s, 9 H), 0.94 (s, 9 H).

Data for (*S*)-MTPA (**19b**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65-7.38 (m, 15 H), 5.52 (m, 2 H), 5.43 (t, J = 7.1 Hz, 1 H), 5.26 (s, 1 H), 5.20 (br s, 1 H), 4.99 (m, 2 H), 4.21 (A of AB, J_{AB} = 13.5 Hz, 1 H), 4.14 (B of AB, J_{BA} = 13.5 Hz, 1 H), 3.45 (m, 4 H), 2.53 (m, 1 H), 2.41 (m, 1 H), 2.31 (m, 1 H), 2.15 (dd, J = 14.1, 7.2 Hz, 1 H), 1.79 (dd, J = 14.1, 1.2 Hz, 1 H), 1.61 (dd, J = 1.2 Hz, 3 H), 1.13 (d, J = 6.8 Hz, 3 H), 1.06 (s, 9 H), 0.89 (s, 9 H).

TBS Ether (20): To a 0 °C solution of alcohol (**18**) (500 mg, 0.83 mmol) in dry CH_2Cl_2 (5.0 mL) under an atmosphere of N_2 was added 2,6-lutidine (290 μL, 2.49 mmol, 3 equiv) and TBSOTf (250 μL, 1.09 mmol, 1.3 equiv). TLC analysis (30% Et_2O-hexane) of the reaction mixture after 15 min showed that the reaction was complete. The mixture was diluted with saturated aq. NH_4Cl (15 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude product was purified by flash column chromatography (10% Et_2O-hexane) through silica gel to afford 591 mg (99%) of the desired silyl ether (**20**) as an oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (m, 4 H), 7.40 (m, 6 H), 5.69 (ddt, J = 17.1, 10.0, 7.1 Hz, 1 H), 5.35 (ap dt, J = 10.5, 1.2 Hz, 1 H), 5.28 (m, 1 H), 5.20 (s, 1 H), 5.01 (m, 1 H), 4.97 (m, 1 H), 4.20 (A of AB, J = 13.3 Hz, 1 H), 4.14 (B of AB, J =

13.3 Hz, 1 H), 4.02 (t, *J* = 5.6 Hz, 1 H), 3.46 (ap dt, *J* = 10.5. 2.0 Hz, 1 H), 2.53 (m, 1 H), 2.24 (dd, *J* = 12.6, 6.0 Hz, 2 H), 2.16 (dd, *J* = 13.9, 7.1 Hz, 1 H), 1.78 (dd, *J* = 14.0, 1.8 Hz, 1 H), 1.62 (d, *J* = 1.5 Hz, 3 H), 1.12 (d, *J* = 7.1 Hz, 3 H), 1.06 (s, 9 H), 0.94 (s, 9 H), 0.88 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 141.0, 140.3, 135.6, 135.5, 134.7, 133.6, 133.5, 129.7, 129.6, 127.7, 127.6, 121.4, 120.6, 116.8, 110.0, 80.7, 76.9, 65.6, 41.1, 40.9, 37.1, 34.9, 27.9, 26.8, 25.8, 23.4, 19.8, 19.2, 18.1, 12.5, -4.6, -5.0; IR (neat film, cm^{-1}) 2959, 2931, 1794, 1472, 1428, 1402, 1258, 1226, 1154, 1112, 1083, 982, 913, 836, 776, 740, 702; HRMS (FAB), calcd for $C_{43}H_{64}O_5NaSi_2$ $[M+Na]^+$ 739.4190, found 739.4156 m / z.

Aldehyde (**21**). To a 25-mL round-bottom flask was added TBS ether (**20**) (720 mg, 1.00 mmol), $(DHQD)_2$-PHAL (78 mg, 0.10 mmol, 0.1 equiv), and *t*-BuOH (4 mL). This mixture was stirred for several min to dissolve **20** and then H_2O (4 mL) and AD-mix β (1.04 g, 1.00 mmol, 1 equiv) were added. After the AD-mix had dissolved, 100 μL (0.02 mmol, 0.02 equiv) of a 0.2 M toluene solution of OsO_4 was added. Analysis of the reaction mixture by TLC (50% EtOAc / Hex, UV, PMA) after 18 h showed some starting material remained, so an additional 50 μL of the 0.2 M toluene solution of OsO_4 was added. The reaction was quenched 6 h later by the addition of 5 mL of 1.0 M aqueous sodium sulfite, and the mixture was stirred at rt for 20 min. The reaction mixture was then partitioned between EtOAc (50 mL) and brine (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography (30% EtOAc-hexane) through silica gel afforded 538 mg (71%) of the intermediate diol as a 1 : 1 mixture of epimers. NMR data for diastereomer A (less polar): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 4 H), 7.39 (m, 6 H), 5.42 (d, *J* = 10.3 Hz, 1 H), 5.25 (br s, 1 H), 5.20 (s, 1 H), 4.27 (dd, *J* = 8.3, 4.2 Hz, 1 H), 4.20 (A of AB, *J* = 13.4 Hz, 1 H), 4.13 (B of AB, *J* = 13.4 Hz, 1 H), 3.82 (m, 1 H), 3.75 (m, 1 H), 3.56 (dd, *J* = 11.0, 3.7 Hz, 1 H), 3.44 (m, 2 H), 2.58 (m, 1 H), 2.14 (dd, *J* = 13.9, 7.1 Hz, 1 H), 1.85 (m, 1 H), 1.82 (dd, *J* = 13.9, 2.4 Hz, 1 H), 1.71 (dt, *J* = 14.4, 8.8 Hz, 1 H), 1.65 (s, 3 H), 1.56 (ddd, *J* = 14.4, 4.2, 2.7 Hz, 1 H), 1.12 (d, *J* = 7.1 Hz, 3 H), 1.05 (s, 9 H), 0.94 (s, 9 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.01 (s, 3 H). NMR data for diastereomer B (more polar): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 4 H), 7.39 (m, 6 H), 5.57 (d, *J* = 10.5 Hz, 1 H), 5.34 (s, 1 H), 5.31 (br s, 1 H), 4.36 (dd, *J* = 3.7, 3.7 Hz, 1 H), 4.19 (A of AB, *J* = 13.4 Hz, 1 H), 4.15 (B of AB, *J* = 13.4 Hz, 1 H), 3.82 (m, 1 H), 3.67 (m, 1 H), 3.57 (m, 1 H), 3.51 (d, *J* = 10.7 Hz, 1 H), 3.39 (dd, *J* = 11.1, 5.3 Hz, 1 H), 2.53 (m, 1 H), 2.18 (dd, *J* = 13.8, 7.3 Hz, 1 H), 1.80 (m, 2 H), 1.68 (m, 2 H), 1.61 (s, 3 H), 1.13 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 9 H), 0.94 (s, 9 H), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.01 (s, 3 H).

To a rt solution of 162 mg (0.22 mmol, 1 equiv) of the diol mixture in dry THF (2 mL) was added periodic acid (64 mg, 0.28 mmol, 1.3 equiv). Upon addition of the periodic acid, the mixture became cloudy and a white solid gradually precipitated. TLC analysis (30% EtOAc / Hex, UV, PMA) of the reaction mixture after 2 h indicated that the reaction was complete.

The mixture was diluted with EtOAc (5 mL) and filtered through a Celite plug in a disposable pipette. The Celite plug was washed with EtOAc (5 mL). The resulting filtrate was washed with H_2O (10 mL) and the aqueous wash was then extracted with EtOAc (4 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography (5% → 10% EtOAc-hexane) gave 146 mg (94%) of **21**: NMR (500 MHz, $CDCl_3$) δ 9.72 (t, *J* = 2.6 Hz, 1 H), 7.67 (m, 4 H), 7.40 (m, 6 H), 5.47 (d, *J* = 10.3 Hz, 1 H), 5.24 (br s, 1 H), 5.14 (s, 1 H), 4.53 (dd, *J* = 7.8, 4.2 Hz, 1 H), 4.20 (A of AB, *J* = 13.4 Hz, 1 H), 4.13 (B of AB, *J* = 13.4 Hz, 1 H), 3.45 (d, *J* = 10.5 Hz, 1 H), 2.57 (m, 2 H), 2.42 (m, 1 H), 2.15 (dd, *J* = 13.9, 7.1 Hz, 1 H), 1.79 (dd, *J* = 13.9, 2.2 Hz, 1 H), 1.67 (s, 3 H), 1.12 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 9 H), 0.94 (s, 9 H), 0.86 (s, 9 H), 0.04 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 175.7, 140.8, 140.3, 135.6, 135.5, 133.6, 133.5, 129.7, 129.6, 127.7, 127.6, 122.3, 119.9, 110.1, 80.4, 72.9, 65.6, 50.2, 40.8, 36.9, 35.0, 27.9, 26.8, 25.7, 23.4, 19.7, 19.3, 18.0, 12.6, -4.5, -5.2; IR (neat film, cm^{-1}) 2959, 2931, 2858, 1793, 1727, 1484, 1472, 1428, 1402, 1361, 1258, 1226, 1153, 1111, 1085, 981, 837, 778, 702; MS (FAB), calcd for $C_{42}H_{62}O_6NaSi$ $[M+Na]^+$ 741.4, found 741.1 m/z.

Enal (**22**): A solution of aldehyde (**21**) (146 mg, 0.20 mmol) and triphenylphosphoranylidene propionaldehyde (130 mg, 0.41 mmol, 2.0 equiv) in dry toluene (1 mL) was heated to 85 °C under an N_2 atmosphere. The mixture was stirred for 20 h at 85 °C, at which point ^1H NMR spectral analysis of an aliquot showed that the reaction was complete. The reaction mixture was directly purified by flash column chromatography (10% → 15% Et_2O-hexane) through silica gel to afford 129 mg (83%) of the desired α,β-unsaturated aldehyde (**22**) as an oil: ^1H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1 H), 7.70 (m, 4 H), 7.40 (m, 6 H), 6.46 (t, *J* = 7.3 Hz, 1 H), 5.46 (d, *J* = 10.5 Hz, 1 H), 5.26 (s, 1 H), 5.17 (s, 1 H), 4.15 (m, 3 H), 3.47 (d, *J* = 10.5 Hz, 1 H), 2.57 (m, 1 H), 2.53 (m, 2 H), 2.17 (dd, *J* = 13.9, 7.3 Hz, 1 H), 1.80 (d, *J* = 14.2 Hz, 1 H), 1.73 (s, 3 H), 1.66 (s, 3 H), 1.12 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 9 H), 0.93 (s, 9 H), 0.87 (s, 9 H), 0.02 (s, 3 H), -0.01 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.1, 175.7, 150.5, 140.9, 140.6, 135.6, 135.5, 134.8, 133.6, 129.7, 129.6, 127.7, 127.6, 122.0, 120.1, 110.2, 80.6, 75.6, 65.6, 41.1, 36.9, 36.1, 35.0, 27.9, 26.8, 26.5, 25.8, 23.4, 19.8, 19.3, 18.1, 12.8, 9.4, -4.6, -5.0; IR (neat film, cm^{-1}) 2958, 2930, 2857, 1793, 1689, 1472, 1428, 1361, 1258, 1226, 1111, 940, 837, 776, 740, 702, 668; HRMS (FAB), calcd for $C_{45}H_{66}O_6NaSi_2$ $[M+Na]^+$ 781.4295, found 781.4279 m/z.

Dienyl Iodide (**11**): To a flame-dried 5-mL round-bottom flask was added $CrCl_2$ (674 mg, 5.48 mmol, 10.0 equiv) and dry THF (5 mL) under a nitrogen purge. The $CrCl_2$ aggregated into a single mass and become purple upon the addition of the THF. The mixture was stirred for several min to break up the $CrCl_2$ clump and then a solution of aldehyde (**22**) (416 mg, 0.55 mmol) and CHI_3 (432 mg, 1.10 mmol, 2.0 equiv) in dry THF (3 mL) was added. Transfer of reagents to the flask was completed with a THF rinse (2 mL). The reaction mixture immediately became brown. The mixture was stirred for 1.5 h at rt, at which point TLC

analysis (20% Et_2O-hexane) showed that only a trace of starting material remained. The reaction was quenched by the addition of 1.0 M aqueous sodium serinate (10 mL), and the resulting mixture was stirred for 20 min. The mixture was then partitioned between 40 mL of EtOAc and 40 mL of 1.0 M aqueous sodium serinate. The layers were separated and the aqueous phase was extracted with EtOAc (3 x 40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography through silica gel (2% → 5% Et_2O-hexane) afforded 396 mg (82%) of the desired vinyl iodide (**11**) as an oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 4 H), 7.39 (m, 6 H), 6.98 (d, *J* = 14.7 Hz, 1 H), 6.08 (d, *J* = 14.7 Hz, 1 H), 5.39 (dd, *J* = 7.6, 7.3 Hz, 1 H), 5.33 (d, *J* = 10.5 Hz, 1 H), 5.17 (s, 1 H), 5.16 (s, 1 H), 4.23 (A of AB, *J* = 13.2 Hz, 1 H), 4.11 (B of AB, *J* = 13.2 Hz, 1 H), 4.01 (t, *J* = 5.9 Hz, 1 H), 3.43 (d, *J* = 10.5 Hz, 1 H), 2.60 (m, 1 H), 2.27 (m, 2 H), 2.16 (dd, *J* = 13.9, 7.1 Hz, 1 H), 1.79 (dd, *J* = 13.9, 2.0 Hz, 1 H), 1.66 (s, 3 H), 1.62 (s, 3 H), 1.13 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 9 H), 0.94 (s, 9 H), 0.86 (s, 9 H), 0.00 (s, 3 H), -0.04 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 149.5, 141.1, 140.6, 135.7, 135.62, 135.57, 133.6, 130.4, 129.6, 127.7, 127.6, 121.5, 120.7, 110.1, 80.6, 76.6, 73.3, 65.8, 40.9, 37.0, 35.4, 35.0, 27.7, 26.9, 25.8, 23.5, 19.7, 19.3, 18.1, 12.5, 12.1, -4.7, -5.0; IR (neat film, cm^{-1}) 2958 , 2857, 1794, 1472, 1428, 1361, 1258, 1226, 1153, 1111, 981, 950, 837, 739, 702; HRMS (FAB) calcd for $C_{46}H_{67}O_5INaSi_2$ $[M+Na]^+$ 905.3471, found 905.3494 m / z.

(2*S*, 4*S*, 5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-7-dibromo-2,4-dimethyl-6-hepten-1-ol (24). A solution of dibromo olefin (**23**)[23] (3.64 g, 5.59 mmol) in THF (2 mL) was stirred at 0 °C. EtOH (1 mL) was added, followed by a solution of $LiBH_4$ (3.1 mL of a 2.0 M solution in THF, 6.15 mmol) dropwise *via* syringe. The solution was allowed to warm to rt and stirred for 5 h. The reaction was terminated by the dropwise addition of 2 N aqueous NaOH solution. The clear colorless solution quickly became cloudy, then clear again. The solution was diluted with EtOAc (30 mL), then washed with saturated aq. $NaHCO_3$ (30 mL) and brine (30 mL). The combined aqueous phase was extracted with EtOAc (5 x 50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo.* Purification of the crude oil by silica gel chromatography (4 : 1 hexanes-EtOAc) provided 2.91 mg (94%) of the desired alcohol (**24**) as a colorless oil: $[\alpha]_D^{23}$ -21.1° (c=0.26 in $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.35 (m, 10 H), 6.41 (d, *J* = 8.6 Hz, 1 H), 4.19 (dd, *J* = 8.8, 4.9 Hz, 1 H), 3.31 (m, 2 H), 1.72 (m, 1 H), 1.58 (m, 1 H), 1.40 (m, 1 H), 1.07 (m, 2 H), 1.06 (s, 9 H), 0.90 (d, *J* = 6.8 Hz, 3 H), 0.77 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 135.9, 129.7, 129.6, 127.6, 127.5, 109.0, 90.1, 88.6, 77.6, 68.7, 37.0, 35.4, 33.0, 26.9, 19.3, 16.0, 14.2; HRMS calcd for $C_{21}H_{25}O_2{}^{81}Br_2Si$ $(M - C_4H_9)^+$ 498.9948, found 498.9768 m / z.

(2*S*, 4*S*, 5*S*)-5-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethyl-6-heptyn-1-ol (25). A solution of dibromo olefin (**24)**(576 mg, 1.04 mmol) in THF (7 mL) at -78°C was treated with *n*-BuLi (3.10 mL of a 2.0 M solution in hexanes, 6.20 mmol), which was added slowly, dropwise *via* syringe.

The solution was stirred at -78˚C for 15 min, and slowly became light brown in color. The solution was warmed to 0 ºC, and the color quickly deepened to purple. After being stirred at 0 ºC for 1 h, the reaction was quenched by the slow, dropwise addition of H_2O (7 mL) *via* syringe. The layers were separated, and the aqueous was extracted with EtOAc (5 x 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification of the crude product by silica gel chromatography (4 : 1 hexanes-EtOAc) provided 378 mg (93%) of the desired alkynol (**25**): $[\alpha]_D^{23}$ -71.9º (c=2.8 in $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.35 (m, 10 H), 4.25 (dd, *J* = 4.3, 2.1 Hz, 1 H), 3.31 (dd, *J* = 10.5, 5.7 Hz, 1 H), 3.24 (dd, *J* = 10.5, 6.5 Hz, 1 H), 2.30 (d, *J* = 2.2 Hz, 1 H), 1.69 (m, 1 H), 1.52 (m, 1 H), 1.26 (m, 1 H), 1.18 (m, 1 H), 1.10 (s, 9 H), 1.08 (m, 1 H), 1.03 (d, *J* = 6.5 Hz, 3 H), 0.74 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.0, 135.8, 133.9, 133.0, 129.7, 129.6, 127.6, 127.3, 83.0, 73.6, 68.5, 68.3, 36.8, 35.9, 32.8, 26.9, 19.3, 16.1, 13.9; IR (neat) 3400, 3320, 2987, 2760, 1471 cm^{-1}; HRMS calcd for $C_{25}H_{34}O_2Si$ $(M)^+$ 394.2328, found 394.2321 m / z.

Conjugated Triene (10). A Carius tube was charged with a solution of 88 mg (0.22 mmol) of alkyne (**25**) in THF (1 mL) and purged with a continuous stream of N_2 (introduced *via* a septum) Distilled catecholborane (50 µL, 0.46 mmol) was then added slowly, dropwise *via* syringe with a great deal of gas evolution. After 30 min, the flask was sealed and heated to 60 ºC until the reaction was complete by ^{1}H NMR spectral analysis of aliquots. The reaction mixture was cooled to rt and H_2O (1 mL) was added very slowly, dropwise. With addition of H_2O, the solution became cloudy. After being stirred for 1 h, the solution was saturated with NaCl, then extracted with EtOAc (10 x 1 mL). The combined extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the crude vinylboronic acid by silica gel chromatography (4 : 1 hexanes-EtOAc, then 1 : 1 hexanes-EtOAc, then 100% EtOAc) yielded 57 mg (56%) of the boronic acid (**12**) as a white foam: $[\alpha]_D^{23}$ -17.3º (c=0.45 in EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.30 (m, 10 H), 6.47 (dd, *J* = 17.6, 4.3 Hz, 1 H), 5.54 (br d, *J* = 17.7 Hz, 1 H), 4.15 (m, 1 H), 4.03 (br s, 1 H), 3.94 (dd, *J* = 10.0, 3.6 Hz, 1 H), 3.17 (t, *J* = 10.2 Hz, 1 H), 1.54 (m, 2 H), 1.39 (m, 1 H), 1.08 (s, 9 H), 0.72 (d, *J* = 6.6 Hz, 3 H), 0.41 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 135.7, 134.6, 134.2, 129.5, 129.4, 128.3, 127.5, 127.3, 100.2, 78.9, 67.9, 36.7, 35.7, 31.8, 27.1, 19.4, 14.8, 12.0; IR (neat) 3400, 2960, 2927, 1667, 1429 cm^{-1}.

A mixture of vinyl iodide (**11**) (316 mg, 0.36 mmol, 1 equiv) and vinylboronic acid (**12**) (529 mg, 1.21 mmol, 3.4 equiv), distilled THF (15 mL) and distilled H_2O (5 mL) was degassed by 3 freeze-pump-thaw cycles and was then stirred under an inert atmosphere. At this point, $Pd(PPh_3)_4$ (62 mg, 0.05 mmol, 0.15 equiv) and TlOEt (102 µL, 1.43 mmol, 4 equiv) were added.[53] The resulting heterogeneous mixture gradually turned from yellow-orange to brown. TLC analysis (20% Et_2O-hexane) of the reaction mixture after 15 min showed that the vinyl iodide fragment had been consumed. The reaction mixture was filtered through a pad of Celite and the Celite was rinsed with EtOAc (4 x 10 mL). The filtrate was washed with sat.

aqueous NaCl (50 mL) and the aqueous wash was extracted with EtOAc (2 x 50 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography (10% → 30% Et_2O-hexane) through Davisil afforded 342 mg (83%) of the desired conjugated triene (**10**) as an oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (m, 8 H), 7.35 (m, 12 H), 6.04 (m, 2 H), 5.89 (dd, *J* = 15.0, 9.2 Hz, 1 H), 5.57 (dd, *J* = 15.0, 7.4 Hz, 1 H), 5.43 (ap t, *J* = 7.4 Hz, 1 H), 5.39 (d, *J* = 10.5 Hz, 1 H), 5.26 (s, 1 H), 5.18 (s, 1 H), 4.21 (A of AB, *J* = 13.3 Hz, 1 H), 4.12 (B of AB, *J* = 13.3 Hz, 1 H), 4.01 (m, 2 H), 3.45 (d, *J* = 10.5 Hz, 1 H), 3.25 (m, 2 H), 2.56 (m, 1 H), 2.31 (ap t, *J* = 6.7 Hz, 2 H), 2.16 (dd, *J* = 13.8, 7.2 Hz, 1 H), 1.78 (dd, *J* = 13.9, 1.7 Hz, 1 H), 1.71 (s, 3 H), 1.64 (s, 3 H), 1.59 (m, 1 H), 1.47 (m, 1 H), 1.25 (s, 1 H), 1.12 (d, *J* = 7.1 Hz, 3 H), 1.06 (s, 9 H), 1.04 (s, 9 H), 0.92 (s, 9 H), 0.87 (s, 9 H), 0.82 (d, *J* = 6.8 Hz, 3 H), 0.80 - 1.00 (m, 2 H), 0.67 (d, *J* = 6.6 Hz, 3 H), 0.00 (s, 3 H), -0.04 (s, 3 H); IR (neat film, cm^{-1}) 3300 (br), 2930, 1794, 1428, 1111, 836, 668; MS (FAB), calcd for $C_{71}H_{102}O_7NaSi_3$ $[M+Na]^+$ 1173.7, found 1173.8 m/z.

Aldehyde (**26**): To a 0 °C solution of the Suzuki coupling product (**10**) (44.0 mg, 0.04 mmol) in dry CH_2Cl_2 (1 mL) was added pyridine (25 μL, 0.31 mmol, 8 equiv) and the Dess-Martin periodinane[56] (48 mg, 0.11 mmol, 3 equiv). The mixture was stirred for 15 min at 0 °C, at which point no starting material was observed by TLC analysis (20% Et_2O-hexane). The reaction was quenched with sat. aqueous $NaHCO_3$ (1 mL) and partitioned between EtOAc (10 mL) and brine (10 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. This crude product was purified by flash column chromatography (20% → 30% Et_2O-hexane) to afford 38 mg (86%) of aldehyde (**26**) as an oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.46 (s, 1 H), 7.65 (m, 8 H), 7.36 (m, 12 H), 6.01 (m, 2 H), 5.83 (dd, *J* = 14.4, 9.3 Hz, 1 H), 5.55 (dd, *J* = 15.2, 7.4 Hz, 1 H), 5.43 (ap t, *J* = 7.5 Hz, 1 H), 5.39 (d, *J* = 10.5 Hz, 1 H), 5.26 (s, 1 H), 5.17 (s, 1 H), 4.21 (A of AB, *J* = 13.2 Hz, 1 H), 4.12 (B of AB, *J* = 13.2 Hz, 1 H), 4.00 (m, 2 H), 3.46 (d, *J* = 10.3 Hz, 1 H), 2.56 (ap t, *J* = 6.7 Hz, 1 H), 2.31 (ap t, *J* = 6.6 Hz, 2 H), 2.16 (dd, *J* = 13.8, 7.0 Hz, 1 H), 1.78 (dd, *J* = 13.9, 1.8 Hz, 1 H), 1.71 (s, 3 H), 1.64 (s, 3 H), 1.61 (m, 1 H), 1.34 (m, 1 H), 1.12 (d, *J* = 7.3 Hz, 3 H), 1.12 (m, 2 H), 1.06 (s, 9 H), 1.04 (s, 9 H), 0.92 (s, 9 H), 0.87 (s, 9 H), 0.84 (d, *J* = 6.8 Hz, 6 H), 0.00 (s, 3 H), -0.04 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.0, 176.0, 141.6, 140.5, 137.5, 136.0, 135.9., 135.6, 135.5, 135.1, 134.4, 134.1, 133.6, 132.6, 131.4, 129.6, 129.4, 127.7, 127.6, 127.5, 127.3, 125.9, 121.1, 120.6, 110.1, 80.6, 78.1, 65.7, 43.9, 40.9, 37.1, 36.0, 35.0, 33.3, 27.8, 27.1, 26.8, 25.8, 23.5, 19.8, 19.4, 19.3, 18.1, 13.7, 12.9, 12.5, -4.6, -4.9; IR (neat film, cm^{-1}) 2960, 2931, 2858, 1793, 1726, 1472, 1428, 1361, 1258, 1226, 1111, 985, 836; MS (FAB) calcd for $C_{71}H_{100}O_7NaSi_3$ $[M+Na]^+$ 1171.7, found: 1171.2 m/z.

Hexaenoate (9). A mixture of LiCl (24 mg, 0.57 mmol, 5 equiv, flame dried before use), phosphonate (**38**) (158 mg, 0.57 mmol) and DBU (68 μL, 0.45 mmol, 4 equiv) in dry MeCN (2.5 mL) was cooled to 0 °C. This mixture was stirred at 0 °C for 20 min and then was cooled to

–50 °C. A solution of aldehyde (**26**) (130.4 mg, 0.11 mmol) in a mixture of MeCN (1.0 mL) and THF (1.5 mL) was then added to the mixture. As the substrate precipitated out of solution at –50 °C, it was necessary to warm the reaction mixture to –40 °C to induce **12** to redissolve. The mixture was stirred for 1 h at –40 °C, warmed to –20 °C for 2 h, and finally warmed to 0 °C for 3 h. The reaction was quenched by the addition of sat. aqueous NH_4Cl (3 mL) and the mixture then was partitioned between sat. NH_4Cl (10 mL) and EtOAc (10 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography (2% → 5% Et_2O-hexane) through Davisil afforded the higher R_f *Z* olefin isomer (16.3 mg) and the lower R_f desired *E* olefin isomer (**9**) (85.2 mg, 72% combined yield) as an oil. Data for **9**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (m, 8 H), 7.37 (m, 12 H), 6.50 (d, *J* = 9.8 Hz, 1 H), 5.99 (m, 3 H), 5.80 (dd, *J* = 14.6, 9.6 Hz, 1 H), 5.52 (dd, *J* = 15.1, 7.6 Hz, 1 H), 5.43 (ap t, *J* = 7.6 Hz, 1 H), 5.39 (d, *J* = 10.5 Hz, 1 H), 5.33 (d, *J* = 17.3 Hz, 1 H), 5.27 (s, 1 H), 5.23 (d, *J* = 10.3 Hz, 1 H), 5.18 (s, 1 H), 4.63 (d, *J* = 5.6 Hz, 2 H), 4.21 (A of AB, *J* = 13.4 Hz, 1 H), 4.13 (B of AB, *J* = 13.4 Hz, 1 H), 4.01 (m, 2 H), 3.46 (d, *J* = 10.5 Hz, 1 H), 2.56 (ap t, *J* = 6.5 Hz, 1 H), 2.38 (m, 1 H), 2.31 (ap t, *J* = 6.6 Hz, 2 H), 2.17 (dd, *J* = 13.9, 7.1 Hz, 1 H), 1.78 (dd, *J* = 13. 9, 1.8 Hz, 1 H), 1.71 (s, 6 H), 1.64 (s, 3 H), 1.62 (m, 1 H), 1.26 (m, 1 H), 1.13 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 18 H), 0.98 (m, 1 H), 0.92 (s, 9 H), 0.87 (s, 9 H), 0.85 (d, *J* = 4.6 Hz, 3 H), 0.77 (d, *J* = 6.6 Hz, 3 H), 0.00 (s, 3 H), -0.03 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0,167.9, 148.7, 141.6, 140.4, 137.3, 136.0, 135.9, 135.6, 135.5, 135.1, 134.4, 134.3, 133.6, 132.6, 132.4, 131.5, 129.6, 129.5, 129.4, 127.7, 127.6, 127.4, 127.3, 126.0, 125.5, 121.0, 120.6, 117.7, 110.1, 80.6, 77.9, 76.8, 65.7, 65.1, 40.9, 39.8, 37.3, 37.0, 36.0, 34.9, 31.6, 30.6, 27.8, 27.1, 26.8, 25.8, 23.5, 19.8, 19.4, 19.3, 19.2, 18.1, 14.1, 12.9, 12.5, 12.3, -4.6, -4.9; IR (neat film, cm^{-1}) 2959 , 2931, 2858, 1794, 1713, 1648, 1472, 1428, 1361, 1258, 1225, 1154, 1111, 985, 938, 836, 776; MS (FAB) calcd for $C_{77}H_{108}O_8NaSi_3$ $[M+Na]^+$ 1267.7, found: 1268.1 m / z.

IMDA Reaction of 9 and Synthesis of Spirotetronate (40). A Carius tube was soaked overnight in a base bath and then rinsed thoroughly with distilled H_2O and dried in the oven. The tube was then charged with *N,O*-bistrimethylsilyl acetamide (1 mL), evacuated, sealed, and heated at 100 °C for 1.5 h. The tube was then rinsed with hexanes and dried under vacuum. The Carius tube was then charged with allyl ester (**9**) (54.3 mg, 47 mmol), dry toluene (5 mL), and a few crystals of BHT. The resulting solution was degassed by three freeze-pump thaw cycles, flushed with Argon, and then sealed under vacuum. This solution was heated at 180 °C for 24 h at which point ^1H NMR analysis of an aliquot showed that all of the starting material had been consumed. The reaction mixture was cooled to rt, concentrated *in vacuo*, and directly purified by flash column chromatography (2% → 5% Et_2O-hexane) through Davisil to give the IMDA product (**39**) (45.3 mg, 83%) containing significant amounts of

impurities. As a pure sample of **39** could not be obtained, this material was taken on to the next step without further characterization.

A mixture of impure **39** (45.3 mg, 40 μmol) in a mixture of dry THF (500 μL) and MeOH (500 μL) was treated with K_2CO_3 (22 mg, 158 μmol, 4 equiv). The resulting mixture was stirred at rt for 24 h and then was diluted with EtOAc (10 mL) and washed with sat. aq. NH_4Cl (5 mL). The aqueous wash was back extracted with EtOAc (2 x 5 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography (5% → 10% Et_2O-hexane) through Davisil afforded the α-hydroxy methyl ester (30.4 mg, 70%) as an oil: $[\alpha]_D^{25}$ -79.0° (c=0.42 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (m, 8 H), 7.38 (m, 12 H), 6.11 (d, *J* = 10.3 Hz, 1 H), 5.82 (m, 1 H), 5.31 (ap d, *J* = 10.3 Hz, 2 H), 5.26 (br s, 1 H), 5.23 (d, *J* = 17.3 Hz, 1 H), 5.15 (d, *J* = 10.5 Hz, 1 H), 5.05 (dd, *J* = 8.1, 5.4 Hz, 1 H), 4.32 (dd, *J* = 13.3, 6.0 Hz, 1 H), 4.26 (A of AB, *J* = 12.7 Hz, 1 H), 4.26 (m, 1 H), 4.12 (B of AB, *J* = 12.7 Hz, 1 H), 3.95 (dd, *J* = 7.3, 5.9 Hz, 1 H), 3.80 (dd, *J* = 10.5, 4.9 Hz, 1 H), 3.79 (s, 3 H), 3.49 (d, *J* = 8.9 Hz, 1 H), 2.95 (s, 1 H), 2.57 (m, 1 H), 2.47 (m, 1 H), 2.24 (dd, *J* = 13.7, 7.3 Hz, 1 H), 2.09 (m, 2 H), 2.02 (m, 1 H), 1.77 (m, 1 H), 1.69 (m, 2 H), 1.58 (s, 3 H), 1.57 (m, 1 H), 1.37 (s, 3 H), 1.27 (m, 2 H), 1.15 (d, *J* = 7.1 Hz, 3 H), 1.15 (s, 3 H), 1.12 (s, 9 H), 1.06 (s, 9 H), 0.98 (d, *J* = 4.9 Hz, 3 H), 0.86 (s, 9 H), 0.61 (d, *J* = 6.6 Hz, 3 H), 0.00 (s, 3 H), -0.05 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 141.2, 140.2, 136.9, 136.11, 136.08, 135.6, 135.5, 134.7, 134.0, 133.7, 132.3, 129.6, 129.4, 127.62, 127.57, 127.4, 127.3, 126.1, 125.1, 122.9, 121.9, 118.1, 78.4, 77.6, 75.2, 66.0, 64.7, 57.6, 52.7, 49.1, 43.9, 41.5, 41.0, 39.3, 38.6, 35.3, 34.6, 34.4, 31.6, 30.4, 28.2, 27.3, 26.8, 25.8, 25.3, 22.6, 19.9, 19.6, 19.3, 18.3, 18.2, 14.9, 14.1, 13.0, 11.3, -4.7, -5.0; IR (neat film, cm^{-1}) 3530, 2957, 2931, 2857, 1729, 1472, 1462, 1428, 1380, 1362, 1248, 1200, 1144, 1111, 1088, 1006, 889, 837, 823, 777, 740, 702; MS (FAB) calcd for $C_{73}H_{102}O_8NaSi_3$ $[M+Na]^+$ 1213.7, found 1214.0 m/z.

A mixture of α-hydroxy ester (12.0 mg, 10 mmol, from the preceding paragraph), Ac_2O (15 μL, 0.16 mmol, 16 equiv), Et_3N (34 μL, 0.24 mmol, 24 equiv), and a catalytic amount of DMAP in dry CH_2Cl_2 (1.0 mL) was stirred for 24 h at rt. Additional quantities of Ac_2O (15 μL) and Et_3N (34 μL) were added and the mixture was stirred another 16 h. TLC analysis of the reaction mixture showed that the reaction was complete. The mixture was diluted by the addition of sat. aqueous $NaHCO_3$ (1 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) The combined organic layer was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography (5% →10% Et_2O-hexane) through Davisil afforded the intermediate α-acetoxy ester (11.5 mg, 93%): $[\alpha]_D^{25}$ –133.2° (c = 0.22 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (m, 8 H), 7.4 (m, 12 H), 6.09 (d, *J* = 10.3 Hz, 1 H), 5.81 (m, 1 H), 5.36 (d, *J* = 4.6 Hz, 1 H), 5.27 (m, 1 H), 5.25 (s, 1 H), 5.22 (d, *J* = 6.4 Hz, 1 H), 5.15 (d, *J* = 10.5 Hz, 1 H), 5.06 (dd, *J* = 7.6, 5.1 Hz, 1 H), 4.32 (dd (A of ABX), *J* = 12.7, 5.9 Hz, 1 H), 4.25 (m, 1 H), 4.20 (A of AB, *J* = 12.7

Hz, 1 H), 4.01 (B of AB, *J* = 12.7 Hz, 1 H), 3.95 (dd, *J* = 10.0, 4.9 Hz, 1 H), 3.89 (dd, *J* = 7.6, 5.6 Hz, 1 H), 3.79 (dd, *J* = 10.3, 4.9 Hz, 1 H), 3.72 (s, 3 H), 2.42 (br s, 2 H), 2.21 (dd(A of ABX), *J* = 13.1, 6.0 Hz, 1 H), 2.17 (m, 1 H), 2.07 (m, 1 H), 2.00 (s, 3 H), 1.95 (dd, *J* = 13.1, 3.0 Hz, 1 H), 1.89 (m, 1 H), 1.76 (m, 1 H), 1.66 (ap t, *J* = 10.1 Hz, 1 H), 1.58 (s, 3 H), 1.57 (m, 1 H), 1.36 (s, 3 H), 1.26 (m, 2 H), 1.11 (s, 9 H), 1.11 (s, 3 H), 1.06 (d, *J* = 6.8 Hz, 3 H), 1.03 (s, 9 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 0.87 (s, 9 H), 0.62 (d, *J* = 6.6 Hz, 3 H), -0.02 (s, 3 H), -0.04 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 170.0, 139.5, 138.0, 136.8, 136.12, 136.08, 135.6, 135.5, 134.7, 134.1, 133.8, 133.6, 132.4, 129.6, 129.4, 127.7, 127.6, 127.44, 127.41, 125.9, 125.2, 122.6, 122.2, 118.1, 80.9, 77.7, 77.6, 65.5, 64.7, 57.6, 52.4, 49.1, 43.9, 41.5, 39.3, 36.0, 35.6, 34.5, 31.6, 30.4, 28.7, 27.3, 26.7, 25.9, 22.6, 21.1, 19.6, 19.3, 18.6, 18.3, 18.2, 14.1, 13.0, 12.0, -4.6, -4.9; IR (neat film, cm^{-1}) 2975 , 2931, 2858, 1741, 1472, 1462, 1428, 1368, 1247, 1199, 1134, 1112, 1085, 1006, 938, 909, 837, 823, 777, 736, 702; MS (FAB) calcd for $C_{75}H_{104}O_9NaSi_3$ $[M+Na]^+$ 1255.7, found 1256.4 m / z.

A –78 °C solution of α-acetoxy ester (23.5 mg, 19 μmol, from the preceding paragraph) in dry THF (0.5 mL) was treated with KHMDS (113 μL of a 0.5 M toluene solution, 57 μmol, 3 equiv). The reaction mixture was stirred for 1 h at –78 °C and then was warmed to 0 °C. The reaction mixture was quenched with sat. aqueous NH_4Cl (1 mL) and then partitioned between EtOAc (10 mL) and sat. aqueous NH_4Cl (10 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2 x 10 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the crude product by flash column chromatography (1% → 2% MeOH-CH_2Cl_2) through Davisil afforded the desired spirotetronate (**40**) (20.2 mg, 88%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.65 (m, 8 H), 7.43-7.32 (m, 12 H), 6.13 (M, 1 H), 5.82 (m, 1 H), 5.36 (br s, 1 H), 5.31 (m, 1 H), 5.26-5.20 (2 H), 5.17 (br dd, *J* = 10.4, 1.3 Hz, 1 H), 5.10 (s, 1 H), 4.99 (m, 1 H), 4.35 (m, 1 H), 4.28-4.22 (m, 2 H), 4.14 (m, 1 H), 3.93 (m, 1 H), 3.78 (m, 1 H), 3.78 (m, 1 H), 3.48 (m, 1 H), 3.16 (dd, *J* = 22.3, 5.1 Hz, 1 H), 2.94 (dd, *J* = 22.3, 6.8 Hz, 1 H), 2.60 (m, 1 H), 2.46 (m, 1 H), 2.24-2.07 (m,. 2 H), 1.79-1.71 (m, 3 H), 1.66 (m, 1 H), 1.61 (s, 1 H), 1.57 (dd, *J* = 3.3, 1.1 Hz, 1 H), 1.50 (br s, 1 H), 1.44 (s, 1 H), 1.42 (br s, 1 H), 1.36-1.26 (m, 3 H), 1.20 (m, 1 H), 1.17-1.13 (m, 3 H), 1.12 (s, 9 H), 1.09 (m, 1 H), 1.05 (s, 9 H), 1.02 (m, 2 H), 1.00-0.96 (m, 3 H), 0.86 (s, 9 H), 0.62 (br t, J = 3.1 Hz, 3 H), -0.01 (s, 3 H), -0.07 (s, 3 H); IR (neat film, cm^{-1}) 3300, 2929, 2857, 1724, 1703, 1472, 1428, 1250, 1112, 1080, 837, 739, 701; MS (FAB) calcd for $C_{74}H_{100}O_8NaSi_3$ $[M+Na]^+$ 1223.7, found 1223.4 m / z.

Seco Acid (7). A solution of allyl ester (**40**) (7.0 mg, 6 μmol), morpholine (5 μL, 57 mmol, 10 equiv) and $Pd[P(C_6H_5)_3]_4$ (1 mg, 0.9 mmol, 0.15 equiv) in degassed THF (250 μL) was stirred under a N_2 atmosphere for 2 h. The reaction was monitored by TLC (5% MeOH-CH_2Cl_2). The reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with 1 N HCl (2 x 10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. Purification of the crude product by preparative TLC (5% MeOH-CH_2Cl_2 with 5 drops of AcOH in 100 mL of developing solution) afforded seco acid (**7**) (2.7 mg, 41%) as an oil. Partial

data for **7**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (m, 8 H), 7.31 - 7.46 (m, 12 H), 6.10 (d, *J* = 10.8 Hz, 1 H), 5.39 (m, 1 H), 5.36 (m, 1 H), 5.28 (m, 1 H), 5.26 (m, 1 H), 5.02 (ap t, *J* = 6.5 Hz, 1 H), 4.22 (A of AB, *J* = 13.3 Hz, 1 H), 4.13 (B of AB, *J* = 13.3 Hz, 1 H), 3.92 (ap t, *J* = 6.2 Hz, 1 H), 3.79 (dd, *J* = 10.4, 5.0 Hz, 1 H), 3.65 (m, 1 H), 3.48 (d, *J* = 10.3 Hz, 1 H), 3.17 (A of AB, *J* = 22.7 Hz, 1 H), 3.02 (B of AB, *J* = 22.7 Hz, 1 H), 2.60 (m, 1 H), 2.47 (m, 1 H), 2.18 (d, *J* = 14.7 Hz, 1 H), 2.09 (m, 2 H), 2.03 (m, 2 H), 1.78 (d, *J* = 14 Hz, 1 H), 1.54 (s, 3 H), 1.36 (s, 3 H), 1.14 (d, *J* = 7.3 Hz, 3 H), 1.13 (s, 3 H), 1.11 (s, 9 H), 1.05 (s, 9 H), 0.99 (d, *J* = 6.8 Hz, 3 H), 0.85 (s, 9 H), 0.71 (d, *J* = 6 Hz, 3 H), 0.00 (s, 3 H), -0.06 (s, 3 H).

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