Synthesis of the C1−C21 Fragment of the Serine/Threonine Phosphatase Inhibitor Tautomycin

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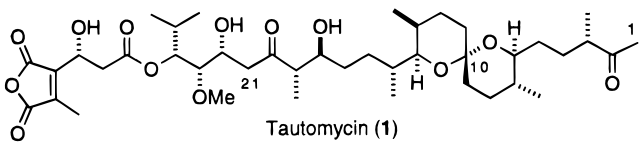
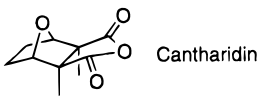
Compound **40** containing the C-1−C-21 region of tautomycin has been synthesized. The two halves (**4** and **5**) of this spirocyclic section were each constructed using Matteson's chloromethylene insertion reaction. Cr/Ni-mediated coupling of compounds **4** and **5** resulted in a structure containing the C-1−C-21 section of tautomycin. Oxidation of the resultant allylic alcohol to the ketone and removal of the α,β unsaturation yielded compound **39**. Treatment with DDQ removed both PMB protecting groups and allowed the spirocyclic ketal to form producing compound **40,** ready for further extension to the natural product tautomycin.

Introduction

Tautomycin (**1**) is a novel secondary metabolite isolated from the fermentation broth of *Streptomyces spiroverticillatus* by Isono et. al. in 1987.[1] Karaki and MacKintosh have shown that tautomycin is a selective inhibitor of serine/threonine phosphatases PP1 and PP2A, two of the four main classes of phosphatases in the cytosol of human cells. The structure of tautomycin shows little similarity to that of other natural products which competitively inhibit PP1 and PP2A. These include the calyculins,[2] microcystins,[3] nodularin,[4] motuporin,[5] and okadaic acid.[6] Of this series, the calyculins, okadaic acid, and tautomycin,[7] all possess at least one spiroketal, though structural similarities resulting from this moiety are difficult to generalize. The unsaturated anhydride found in tautomycin is unique in this series of inhibitors and has been proposed to exist in equilibrium as the diacid in an aqueous solution.[8] The presence of the carboxylate moiety may be critical for activity[9] and is found in all the inhibitors except calyculin, where a phosphate may act as the isostere. The anhydride cantharidin, structurally similar to the anhydride side chain of tautomycin, has also been shown to be an inhibitor of PP1 and PP2A, albeit at substantially reduced potency.[10]



Tautomycin (**1**)



Cantharidin

Our interest in this compound stems from our ongoing work on the synthesis, SAR, and conformational studies of calyculin C and nodularin. Using a combination of molecular modeling and 2D NMR analysis, we have derived an overlay of the proposed ground state structures of tautomycin, calyculin, mycrocystin, nodularin, and okadaic acid in order to understand the common structural motifs associated with these diverse structures. The recent elucidation of the X-ray structure of a cocrystal of PP1 and mycrocystin should further aid in providing a global analysis of these inhibitors.[11] Several groups have reported on their work associated with the total synthesis of tautomycin.[12] This includes the synthesis of a C-1 to C-26 fragment reported by Shibasaki, in addition to the total synthesis of the natural product in 1994 by Oikawa's group.[13] In the context of our abovementioned work on the SAR studies of PP1 and PP2A inhibitors, we focused our work on the synthesis of tautomycin to include a route which would be amenable to isotopic labeling and minor structural modifications. We have used the chemistry developed by Matteson[14] involving the stereospecific insertion of a chloromethylene into a boron−carbon bond directed by

[⊗] Abstract published in *Advance ACS Abstracts,* April 1, 1996.

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(2) (a) Kato, Y.; Fusetani, N.; Matsunaga, S.; Hashimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 2780−2781. (b) Kato, Y.; Fusetani, N.; Matsunaga, S.; Hashimoto, K. *J. Org. Chem.* **1988**, *53*, 3930−3932. (c) Matsunaga, S.; Fujiki, H.; Sakata, D. *Tetrahedron* **1991**, *47*, 2999−3006.

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(7) (a) Ubukata, M.; Cheng, X. C.; Isobe, M.; Isono, *K J. Chem. Soc., Perkin Trans. 1* **1993**, 617−24. (b) Hori, M.; Magae, J.; Han, Y. G.; Heartshorne, D. J.; Karaki, H. *FEBS* **1991**, *25*, 145−148. (c) MacKintosh, C.; Klumpp, S. *FEBS* **1991**, *277*, 137−140.

(8) Ichikawa, Y.; Naganawa, A.; Isobe, M. *Synlett* **1993**, 737−738.

(9) The methyl ester of okadaic acid shows no activity in vitro.

(10) Li, Y. M.; Casida, J. E. *Proc. Natl. Acad. Sci. U.S.A.* **1992**, *89*, 11867−11870.

(11) Goldberg, J.; Huang, H.; Kwon, Y.; Greengard, P.; Nairn, A. C.; Kuriyan, J. *Nature* **1995**, *376*, 745−753.

(12) (a) Oikawa, M.; Ueno, T.; Oikawa, H.; Ichihara, A. *J. Org. Chem.* **1995**, *60*, 5048−5068. (b) Nakamura, S.; Shibasaki, M. *Tetrahedron Lett.* **1994**, *35*, 4145−448. (c) Oikawa, H.; Oikawa, M.; Ueno, T.; Ichihara, A. *Tetrahedron Lett.* **1994**, *35*, 4809−4812. (d) Naganawa, A.; Ichikawa, Y.; Isobe, M. *Tetrahedron* **1994**, *50*, 8969−8982. (e) Oikawa, M.; Oikawa, H.; Ichihara *Tetrahedron Lett.* **1993**, *34*, 4797−4800. (f) Ichikawa, Y.; Naganawa, A.; Isobe, M. *Synlett* **1993**, 737−738. (g) Ichikawa, Y.; Tsuboi, K.; Naganawa, A.; Isobe, M. *Synlett* **1993**, 907−908.

(13) Oikawa, M.; Ueno, T.; Oikawa, H.; Ichihara, A. *J. Org. Chem.* **1995**, *60*, 5048−5068. Oikawa, H.; Oikawa, M.; Ueno, T.; Ichihara, A. *Tetrahedron Lett.* **1994**, *35*, 4809−4812.

(14) (a) Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. *Organometallics* **1983**, *2*, 1536−1543. (b) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, 108, 810−819. (c) Matteson, D. S.; Kandil, A. A.; Soundararajan, R. *J. Am. Chem. Soc.* **1990**, *112*, 3964−3969. (d) Matteson, D. S.: Peterson, M. L. *J. Org. Chem.* **1987**, *52*, 5116−5121.

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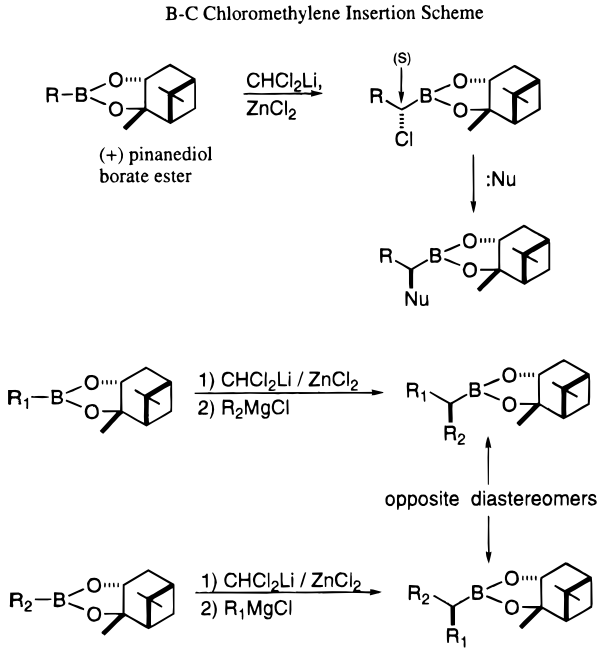
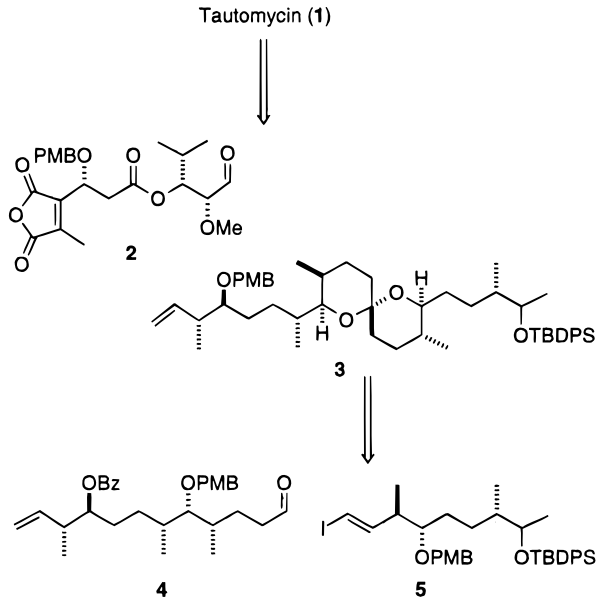
the pinanediol chiral auxiliary to construct stereocenters at carbons 3, 13, 14, and 15 in the spirocyclic half of tautomycin.

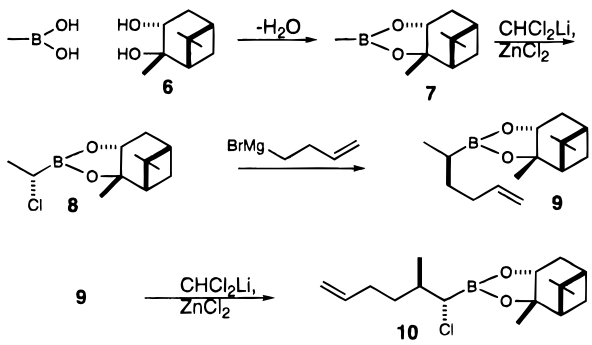


The retrosynthesis we have employed is shown in eq 1. We anticipated that an aldol condensation of the C-1/C-21 methyl ketone with the left half aldehyde could be controlled to afford the correct stereochemistry at C-22. Further disconnection of the spirocyclic half was envisioned to occur at the carbonyl carbon via a Ni/Cr coupling. The stereocenters at C13−C15 could be introduced using Matteson chloromethylene insertion chemistry, and the centers at C18 and C19 could readily be generated using a Brown allylboration. A similar series of transformations were targeted for fragment **5**.



The asymmetric chloromethylene insertion reaction provides a method for introduction of vicinal asymmetric centers by keeping the auxiliary covalently bound to the growing chain. This method seemed like an ideal choice for the "insertion" of contiguous stereocenters in the middle of a larger acyclic fragment (i.e. **4**). This method

Scheme 1



affords an entry to the synthesis of either of the alkyl halide isomers by the use of either the (−)- or (+)-pinanediol auxiliaries. However, continual change of the ligands on boron in a linear synthesis is severely limited by the yields for these transformations. An alternative strategy is to keep the same auxiliary throughout the synthesis and simply vary the order of nucleophiles to suit the stereochemical requirements of the desired diastereomer. Since the (+)-pinanediol chiral auxiliary is reported to consistently give S- chloromethylene insertion product,[15] the construction of the C-10 to C-18 fragment of tautomycin was carried out without changing the chiral auxiliary during the course of synthesis.

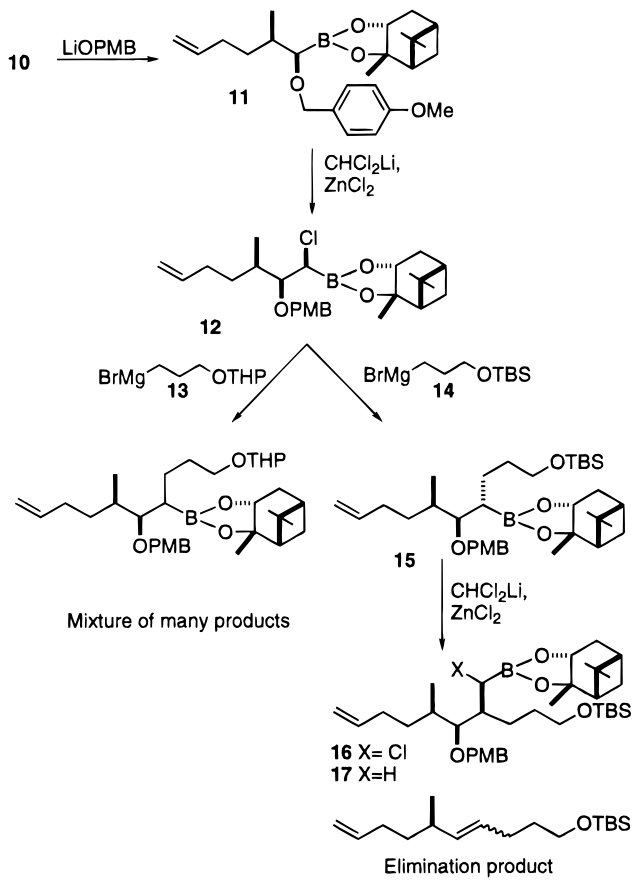
Methaneboric acid was allowed to react with (+)-pinanediol (**6**) to give the pinanediolborate ester (**7**) in almost quantitative yield (Scheme 1). (Dichloromethyl)-lithium is generated by deprotonation of CH_2Cl_2 with *n*-butyl lithium at −100 °C in THF solution following the procedure of Matteson.[16] Addition of compound **7** to the (dichloromethyl)lithium followed by $ZnCl_2$ and warming to rt over several hours yielded chloride **8** in 61% yield along with a large amount of recovered starting material. Compound **8** was treated with homoallylmagnesium bromide, which is titrated into the reaction until TLC analysis showed the starting material had been consumed. After stirring overnight, the reaction yielded 80% of **9**. A second insertion with (dichloromethyl)lithium generated chloride **10** in 92% yield.

Reaction of chloride **10** with lithium *p*-methoxybenzyl oxide generated PMB ether **11** in 76% yield (Scheme 2). This material is considerably more polar than the chloride and can be separated by chromatography. To achieve optimum yield, the reaction must be monitored carefully and stopped when all chloride has been consumed. Extended reaction time reduced the yield substantially. A third insertion yielded chloride **12** in 92% yield. At this point, displacement was attempted with the Grignard derived from THP-protected 3-bromo-1-propanol (**13**). Unfortunately this reaction produced a mixture containing at least three different acetals in an inseparable mixture. To avoid this mixture, the THP was replaced with the *tert*-butyldimethylsilyl protecting group (**14**), and the displacement was performed to produce compound **15** in a 71% yield. The fourth insertion proceeded to yield chloride **16**, but with somewhat lower yield of 49% and with the production of 34% of the elimination product involving boron and the PMB ether. More rapid warming of the reaction mixture to rt slightly favored elimination, but slower warming failed to reduce

(15) See reference 14a.

(16) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529−1535.

Scheme 2

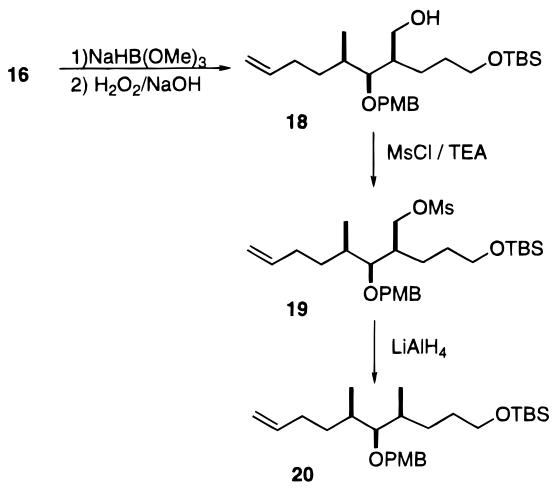


elimination. Compound **16** is readily dechlorinated by treatment with sodium trimethoxyborohydride to yield **17** which is carried on to the next reaction without further purification.

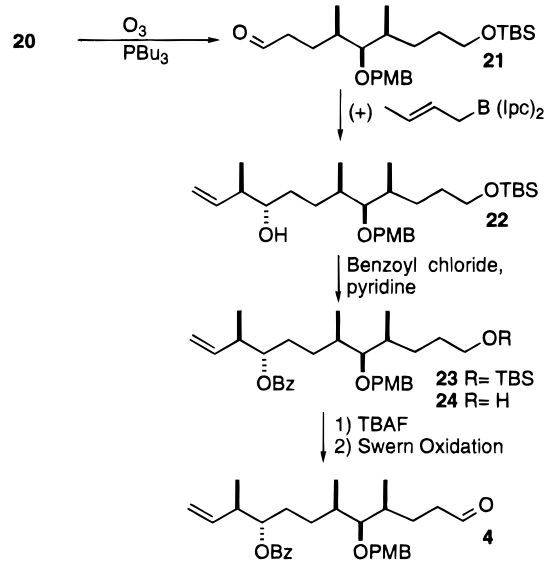
We had originally envisioned the simple removal of the boron functionality by exposure to acid conditions. Unfortunately, while organic acids react quickly with trialkylboranes, reaction with monoalkyl species requires excessively harsh conditions.[17] Since these conditions proved too harsh for these substrates, compound **17** was carried on as a crude mixture and oxidized with basic hydrogen peroxide to yield alcohol **18** in 91% yield (from the starting chloride) (Scheme 3). Alcohol **18** was converted to mesylate **19** in 96% yield by treatment with mesyl chloride and triethylamine. Finally deoxygenation by reduction with lithium aluminum hydride yielded compound **20** in 75% yield.

Compound **20** was readily converted to aldehyde **21** by exposure to ozone followed by tributylphosphine reduction of the resulting ozonide (Scheme 4). Using the allylboration chemistry developed by Brown,[18] aldehyde **21** was converted into alcohol **22** in 71% yield, as a single diastereomer.[19] This alcohol was readily protected with benzoyl chloride in pyridine to yield the benzoate ester **23**. Treatment of compound **23** with TBAF in THF removed the silyl protecting group, and oxidation of the resulting alcohol **24** yielded aldehyde **4** containing the C-21 to C-10 region of tautomycin.

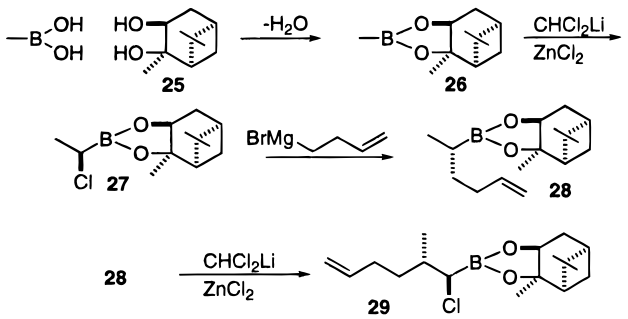
Scheme 3



Scheme 4



Scheme 5



Production of fragment **5** required the enantiomeric pinanediol chiral auxiliary ((−)-pinanediol). Compounds **25**−**29** are exact enantiomers of compounds **7**−**10** and were generated following the same procedures used for the synthesis of these compounds with the substitution of (−)-pinanediol for the (+)-pinanediol chiral auxiliary (Scheme 5).

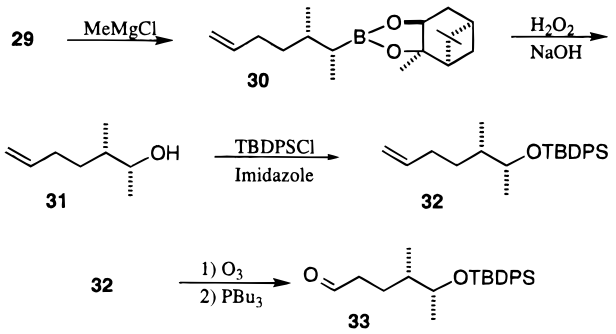
Reaction of **29** with methylmagnesium chloride allowed production of compound **30** in 55% yield (Scheme 6). The natural product contains a ketone at C-2. Because our desired final coupling would involve an aldol condensation of the methyl ketone in fragment **3**, we chose to keep the C-2 carbon at the alcohol oxidation stage. In order

(17) Brown H. C.; Hebert N. C. *J. Organomet. Chem.* **1983**, *255*, 135−141.

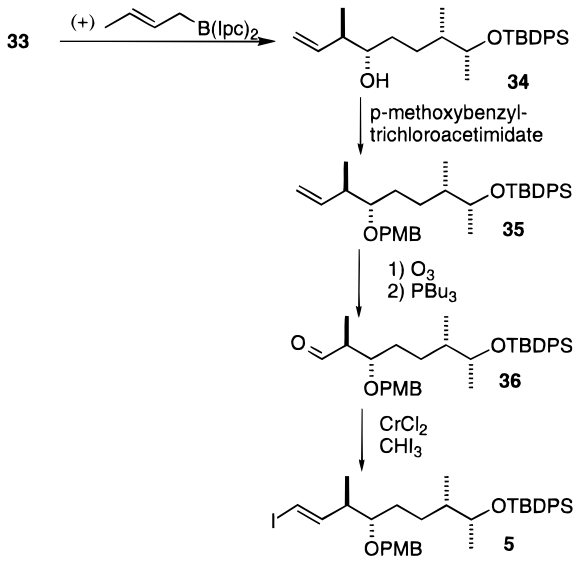
(18) (a) Jadhav, P. K.; Bhat, S. K.; Perumal, P. T.; Brown, H. C. *J. Org. Chem.* **1986**, *51*, 432−439. (b) Brown, H. C.; Jadhav, P. K.; Bhat, S. K. *J. Am. Chem. Soc.* **1988**, *110*, 1535−1538.

(19) Only one diastereomer was observed in the ^{1}H (360 MHz) and ^{13}C (90 MHz) NMR spectra.

Scheme 6



Scheme 7



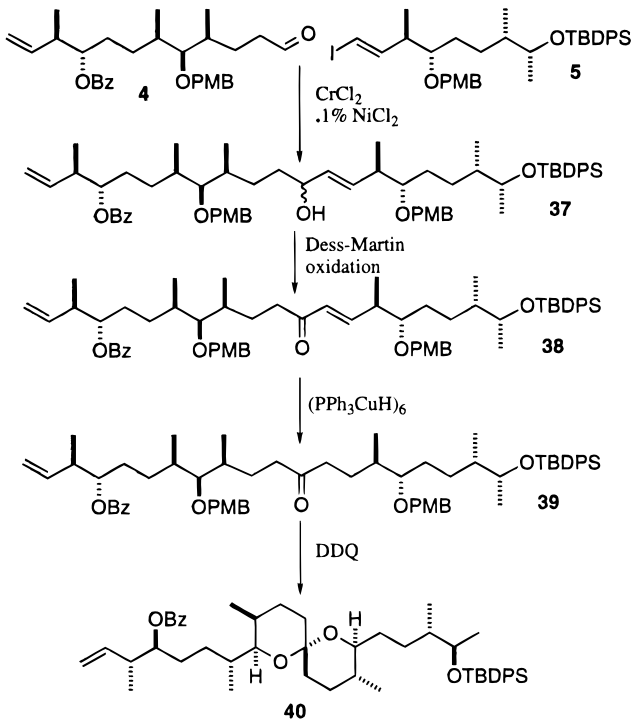
to avoid bringing through a diastereomeric mixture, we introduced the alcohol asymmetically. This significantly simplified NMR interpretation. Oxidative removal of boron with H_2O_2/NaOH led to the volatile alcohol **31** which was converted to its TBDPS ether **32** in 71% overall yield by reaction with *tert*-butyldiphenylsilyl chloride and imidazole in DMF. Ozonolysis of **32** followed by tributylphosphine workup led to the expected aldehyde **33** in 92% yield.

Allylboration converted aldehyde **33** to alcohol **34** in 54% yield (Scheme 7). This alcohol was protected as the *p*-methoxybenzyl ether **35** using the acid-catalyzed trichloroacetimidate procedure of Yonemitsu.[20] The protected compound is subjected to ozonolysis followed by tributylphosphine quench of the resulting ozonide to yield aldehyde **36**. This aldehyde underwent elimination if not subsequently transformed to the vinyl halide in a rapid fashion.

Following the procedures of Takai,[21] the aldehyde was converted to the vinyl iodide **5**. The product vinyl iodide was a mixture containing less than 10% of the cis isomer. This mixture of isomers was not separated and was taken on to be coupled with compound **4** to generate **37** (Scheme 8).

Aldehyde **4** and vinyl iodide **5** were mixed and treated with $NiCl_2$-doped $CrCl_2$ following the procedures of Kishi and Nozaki[22] resulting in a mixture of allylic alcohols **37**.

Scheme 8



Swern oxidation of compounds **37** yielded 61% of the ketone **38** along with 31% of an unidentified rearrangement product. Alternatively, Dess−Martin oxidation[23] afforded unsaturated ketone **37** in 96% yield. It should be noted that the usual Na_2SO_3 quench of the Dess−Martin oxidation causes reduction of the ketone back to the alcohol. This quench is therefore not performed, and the entire reaction mixture is purified by chromatography. We had initially intended to reduce the unsaturated ketone simultaneously with cleavage of the PMB protecting groups via dissolving metal reduction. Unfortunately, compound **38** is not sufficiently robust to survive these conditions, and no identifiable products were isolated from these attempted transformations. Reduction following the dithionite conditions of Gelbard[24] also failed. Reduction of **38** using $NaBH_4$ resulted in mostly 1,2 addition. Removal of the unsaturation was finally accomplished by the use of $(PPh_3CuH)_6$ following the procedure of Stryker,[25] yielding ketone **39**. Treatment of **39** with DDQ removed both PMB protecting groups and afforded spiroketylization to compound **40**.

In order to establish the stereochemistry of the spiroketal and to confirm the relative stereochemistry of the other stereocenters in **40**, extensive ROESY[26] studies were carried out. ROESY cross peaks corresponding to the protons on C-6 and C-14 confirm that the correct spirocycle has formed. The C-14 proton shows both a large (10.1 Hz), and small (2.2 Hz), coupling corresponding to the C-15 and C-13 protons, confirming that it is in the

(20) Nakajima, N.; Horita, K.; Abe, R.; Yonemitsu, O *Tetrahedron Lett.* **1988**, *29*, 4139−4142.

(21) Takai, K., Nitta, K., Utimoto, k. *J. Am. Chem. Soc.* **1986**, *108*, 7408−7410.

(22) Kishi, Y. *Pure Appl. Chem.* **1992**, *64*, 343−350. Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048−6050.

(23) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277−7287.

(24) Louis-Andre, O.; Gelbard, G. *Tetrahedron Lett.* **1985**, *26*, 831−832.

(25) Stryker, J. M.; Brestensky, D. M. *Tetrahedron Lett.* **1989**, *30*, 5677−5680. Stryker, J. M.; Brestensky, D. M.; Mahoney, W. S. *J. Am. Chem. Soc.* **1988**, *110*, 291−293. Churchill, M. R.; Bezman, S. A.; Osborn, J. A.; Wormald, *J. Inorg. Chem.* **1973**, *11*, 1818−1825.

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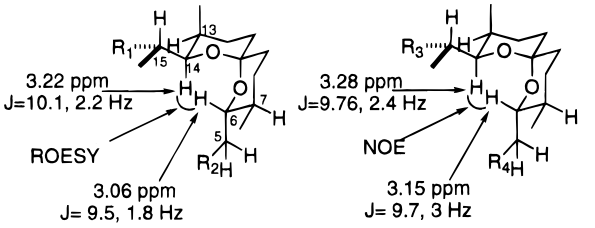
equatorial position. The C-6 proton shows two large couplings (9.5 Hz), and one small coupling (1.8 Hz). The coupling of the proton at C-6 to the proton at C-7 is expected to be large due to the anti relationship in the spirocycle. The other two couplings are expected to come from the methylene protons at C-5. The ROESY cross peaks and the scalar couplings obtained for **40** compare favorably to fragments isolated by Isobe[27] from degradation of isolated natural tautomycin.



Compound **40** Degradation fragment (Isobe et al)

Conclusion

We have synthesized a fragment containing the C1−C21 portion of the natural product tautomycin. Use of Matteson's chloromethylene insertion reaction has allowed us to place a total of five stereocenters early in the synthesis of fragment **40**, each with a minimum de of 95%.[28] The overall yield of the four-insertion chain in compound **16** was 11%, and the two-insertion chain in compound **30** was produced in 22% overall yield. This chemistry will allow us to selectively label these chains at any of these stereocenters by the use of $^{13}CH_2Cl_2$ for future isotope-edited NMR studies of the natural product bound to PP1 and PP2A.

Experimental Section

All reactions were performed under anhydrous conditions under argon, unless otherwise stated. Insertion reactions involving −100 °C baths used a ethanol/liquid nitrogen slurry with a thick syrupy consistency. At this temperature all reagents were added slowly down the chilled wall of the flask to insure that the added solution was cooled to −100 °C prior to entering the reaction mixture. All THF used was distilled from sodium dispersion and benzophenone, methylene chloride was distilled from P_2O_5, toluene and DMF were distilled from CaH_2, methanol was distilled from Mg turnings, and $ZnCl_2$ was dried at 100 °C for 12 h and then fused in vacuum, crushed, and stored (sealed glass ampules) under argon until needed. For EI and CI HRMS $2\sigma = 4$ ppm.

***(S)*−Pinanediol Methylboronate (7).** A mixture of methanboronic acid (1.433 g, 23.94 mmol) and (*S*)-pinanediol (**6**) (3.984 g, 23.39 mmol) in 25 mL diethyl ether was allowed to stir at rt over Na_2SO_4 for 40 min. This mixture was partitioned between 10% saturated Na_2CO_3 solution (50 mL) and CH_2Cl_2 (50 mL). The organic extracts were dried over Na_2SO_4, evaporated, and distilled under vacuum (bp 88 °C, 5 mmHg) to yield 4.286 g (94%) of a clear oil. $[\alpha]^{25}_D = 51.61°$ (*c* = 0.0261 g/mL in benzene) HREIMS *m/z* 194.1480, 194.1478 calcd for (M^+) $C_{11}H_{19}BO_2$; IR (NaCl plates neat cm^{-1}) 2970, 2918, 1475, 1369, 1032; ^1H NMR ($CDCl_3$, 360 MHz) δ 4.23 (dd, 1H, *J* = 8.7, 1.9 Hz), 2.29 (m, 1H), 2.18 (m, 1H) 2.01 (t, 1H), 1.90−1.87 (m, 1H), 1.84−1.79 (m, 1H), 1.79 (s, 3H), 1.26 (s, 3H), 1.10 (d, 1H, *J* = 10.9 Hz), 0.82 (s, 3H), 0.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 85.3, 77.6, 51.2, 39.4, 38.1, 35.4, 28.6, 27.0, 26.4, 23.7

***(S)*-Pinanediol (1*S*)-(1-Chloroethyl)boronate (8).** A mixture of THF (46 mL) and CH_2Cl_2 (1.65 mL, 25.2 mmol) was cooled to −100 °C, butyllithium (10.5 mL 2 M solution in pentane) was added, and the solution was allowed to stir for 14 min. The solution turned cloudy and slightly yellow. Compound **7** (4.070 g, 20.98 mmol) in THF (20 mL) was slowly added and the solution allowed to stir for 10 min at −100 °C. A solution of $ZnCl_2$ (1.624 g, 11.94 mmol) in THF (12 mL) was added, and the mixture was allowed to slowly warm to rt and stirred at rt for 8 h. The mixture was partitioned between acidic NH_4Cl/HCl (100 mL 1.2 M HCl + 200 mL saturated NH_4Cl) and CH_2Cl_2 (300 mL). The organic extracts were dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel, 20% CH_2Cl_2 in pentane) to yield 3.095 g (61%) of a partially purified oil. Typically, 15−20% of compound **7** was also recovered. Data for compound **8**: $[\alpha]^{25}_D = +55.16°$ (*c* = 0.024 g/mL, in benzene); HREIMS *m/z* 243.1278, 242.1245 calcd for (M^+) $C_{12}H_{20}ClBO_2$; IR (NaCl plates neat cm^{-1}) 2970, 2924, 2872, 1448, 1379, 1030, 650; ^1H NMR ($CDCl_3$, 360 MHz) δ 4.33 (d, 1H, *J* = 8.9, 1.9 Hz), 3.52 (q, 1H, *J* = 7.5 Hz), 2.40−2.13 (m, 2H) 2.05 (m, 1H) 1.93−1.80 (m, 1H) 1.53 (d, 3H, *J* = 7.5 Hz), 1.39 (s, 3H) 1.26 (s, 3H) 1.14 (d, 2H, *J* = 11.1 Hz), 0.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 87.5, 79.3, 51.9, 40.0, 39.0, 36.0, 29.1, 27.7, 27.0, 24.7, 21.3.

(2*R*)-2-[(*S*)-Pinanediyldioxy)boryl]-5-hexene (9). A sample of compound **8** (2.845 g, 11.70 mmol) was azeotroped with toluene, dissolved in THF (50 mL) and cooled to −78 °C. 3-Butenylmagnesium bromide was produced by addition of 1-bromo-3-butene (1.90 mL, 18.30 mmol) to magnesium metal (0.600 g, 24.69 g atoms) in THF (5 mL). As necessary THF was used to dilute the mixture, and a cooling bath was used to control the exothermic reaction. The solution was stirred until exotherming ceased and was then titrated into the THF solution of compound **8** until the starting material was consumed (approximately 1.25 equiv was needed). The reaction was allowed to slowly warm to rt (2 h) and then allowed to stir for 15 h at rt. The reaction was then partitioned between HCl (1.2 M, 100 mL), NH_4Cl solution (100 mL saturated), and CH_2Cl_2 (200 mL). The aqueous layer was extracted with CH_2Cl_2 (100 mL), the organic extracts were combined, dried over Na_2SO_4, and evaporated, and the remaining oil was purified by column chromatography (silica gel 2% diethyl ether in hexanes) to yield 2.188 g (80%) of a partially purified oil (95%+ pure). $[\alpha]^{25}_D = +30.50°$ (*c* = 0.0239 g/mL in benzene); HREIMS *m/z* 262.2104, 262.2104 calcd for (M^+) $C_{16}H_{27}BO_2$; IR (NaCl plates neat cm^{-1}) 3076, 2920, 2872, 1642, 1464, 1387; ^1H NMR ($CDCl_3$, 360 MHz) δ 5.80 (m, 1H, 5.01−4.90 (m, 2H), 4.24 (dd, 1H, *J* = 7.7, 0.9 Hz), 2.48−2.28 (m, 1H), 2.25−2.15 (m, 1H), 2.15−2.00 (m, 3H), 1.95−1.80 (m, 3H), 1.67−1.55 (m, 1H), 1.50−1.45 (m, 4H (m 1H, + s 3H)), 1.39 (s, 3H), 1.17−1.05 (m, 1H), 0.98 (d, 3H, *J* = 7.0 Hz), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 140.0, 115.0, 86.0, 78.3, 52.0, 40.2, 38.9, 36.5, 33.9, 33.3, 29.4, 27.8, 27.2, 24.7, 16.3.

(1*S*,2*R*)-1-Chloro-2-methyl-1-[(*S*)-Pinanediyldioxy)boryl]-5-hexene (10). A mixture of THF (21 mL) and CH_2Cl_2 (0.60 mL, 9.176 mmol) was cooled to −100 °C, butyllithium (3.80 mL, 2 M solution in pentane) was added, and the solution was allowed to stir for 14 min. The solution turned cloudy and slightly yellow, and compound **9** (1.999 g, 7.624 mmol, azeotroped with toluene) in THF (10 mL) was slowly added and the solution allowed to stir for 5 min at −100 °C at which point the reaction mixture gelled. After another 5 min at −100 °C a solution of $ZnCl_2$ (0.632 g, 4.644 mmol) in THF (6.2 mL) was added, and the mixture was allowed to slowly warm to rt (the gel rapidly liquefied on addition of $ZnCl_2$, fully liquid by −80 °C) and stirred at rt for 8 h. The mixture was partitioned between acidic NH_4Cl/HCl (100 mL 1.2 M HCl + 100 mL saturated NH_4Cl) and CH_2Cl_2 (200 mL). The aqueous layer was extracted with CH_2Cl_2 (100 mL), and the organic extracts were combined, dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel, 50% CH_2Cl_2 in hexanes) to yield 2.196 g (92%) of a partially purified oil (95+% pure). $[\alpha]^{25}_D = +30.0°$ (*c* = 0.0130 g/mL in benzene); HRCIMS *m/z* 310.1885, 310.1871 calcd for (M^+) $C_{17}H_{28}BClO_2$; IR (NaCl plates neat cm^{-1}) 2972, 2926, 1630, 1475, 1452, 1377, 1030, 909; ^1H NMR ($CDCl_3$, 360 MHz) δ 5.79 (m, 1H) 5.04−4.92 (m, 2H) 4.36 (dd, 1H, 9.0, 2.0 Hz), 3.39 (d, 1H, *J* = 6.6 Hz), 2.40−2.30 (m, 1H) 2.28−1.87 (m, 7H) 1.76−1.65 (m, 1H) 1.40−1.32

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(28) No diastereomers were observed in the ^1H NMR spectra.

(m, 4H) 1.28 (s, 3H) 1.19 (d, 1H, J = 11.0 Hz), 1.02 (d, 3H, 6.7 Hz), 0.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 139.3, 115.3, 87.4, 79.2, 51.9, 40.1, 39.0, 37.1, 36.1, 33.9, 31.9, 29.3, 27.8, 27.2, 24.7, 18.1.

(1*S*,2*R*)-1-[(4-Methoxybenzyl)oxy]-2-methyl-1-[(*S*)-pinanediyldioxy)boryl]-5-hexene (11). To a solution of *p*-methoxybenzyl alcohol (0.960 mL, 7.6428 mmol) in THF (40 mL) at −78 °C was added butyllithium (3.5 mL, 2 M in pentane, 7.00 mmol). The solution was allowed to warm to dissolve frozen p-methoxybenzyl alcohol and then recooled, and DMSO (0.6 mL) was added, followed by compound **10** (2.096 g, 6.747 mmol) in 10 mL of THF. The reaction was allowed to warm to rt and monitored by TLC until the starting chloride had been consumed (about 2 h). The reaction mixture was partitioned between HCl (100 mL, 1.2 M) and CH_2Cl_2 (200 mL), and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The organic extracts were combined, dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel 5% ethyl acetate in hexanes) to yield 2.023 g of pure material (76%) along with 0.210 g (8%) of impure material. $[\alpha]^{25}_D$ = +7.61° (c = 0.0293 g/mL in benzene); HREIMS m/z 412.2785, 412.2784 calcd for (M^+) $C_{25}H_{37}BO_4$; IR (NaCl plates neat cm^{-1}) 2926, 1613, 1514, 1377, 1248, 1076, 1030, 823; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.28 (m, 2H) 6.86 (m, 2H) 5.80 (m, 1H) 5.02−4.90 (m, 2H) 4.56 (d, 1H, J = 11.8 Hz), 4.41 (d, 1H, J = 11.8 Hz), 4.32 (dd, 1H, J = 8.9, 2.0 Hz), 3.80 (s, 3H) 3.22 (d, 1H, J = 4.9 Hz), 2.41−2.30 (m, 1H) 2.30−2.21 (m, 1H) 2.15−2.05 (m, 2H) 2.05−1.75 (m, 4H) 1.71−1.61 (m, 1H) 1.41 (s, 3H) 1.36−1.23 (m, 4H), 1.20 (d, 1H, J = 10.8 Hz), 0.99 (d, 3H, J = 6.8 Hz), 0.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 158.9, 139.1, 131.3, 129.3, 114.0, 113.5, 86.0, 77.9, 72.2, 55.1, 51.0, 39.5, 38.0, 35.4, 34.9, 33.0, 31.6, 28.7, 27.0, 26.5, 24.0, 16.6.

(1*S*,2*S*,3*R*)-1-Chloro-2-[(4-methoxybenzyl)oxy]-3-methyl-1-[(*S*)-pinanediyldioxy)boryl]-9-heptane (12). A mixture of THF (5 mL) and CH_2Cl_2 (0.170 mL, 2.600 mmol) was cooled to −100 °C, and butyllithium (1.10 mL, 1.9 M solution in pentane) was added, and the solution was allowed to stir for 15 min. The solution turned cloudy and slightly yellow. Compound **11** (0.866 g, 2.096 mmol) was azeotroped with toluene, diluted in THF (5 mL) and was slowly added to the solution generated above and allowed to stir for 18 min at −100 °C at which point the reaction mixture slowly gelled. A solution of $ZnCl_2$ (0.734 g, 5.394 mmol) in THF (4.5 mL) was added, and the mixture was allowed to slowly warm to rt (the gel rapidly liquefied on addition of $ZnCl_2$) and was stirred at rt for 7 h. The mixture was partitioned between acidic NH_4Cl/HCl (40 mL saturated + 10 mL 1.2 M) and CH_2Cl_2 (50 mL), and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic extracts were combined, dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel, CH_2Cl_2) to yield 0.886 g (92%) of a partially purified oil. $[\alpha]^{25}_D$ = +9.53° (c = 0.0511 g/mL in benzene); HREIMS m/z 461.2549, calcd for (M^+) 460.2552 $C_{26}H_{38}BClO_4$; IR (NaCl plates neat cm^{-1}) 3076, 2930, 2872, 1615, 1514, 1248, 1030, 911, 824; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.32 (d, 2H, J = 11.2 Hz), 6.87 (m, 2H) 5.83−5.72 (m, 1H) 5.03−4.97 (m, 2H) 4.84 (d, 1H, J = 10.5 Hz), 4.58 (d, 1H, J = 10.5 Hz), 4.36 (dd, 1H, J = 9.0, 1.9 Hz), 3.79 (s, 3H) 3.72 (m, 2H) 2.45−2.30 (m, 1H) 2.28−2.20 (m, 1H) 2.20−1.95 (m, 3H) 1.95−1.88 (m, 2H) 1.80−1.65 (m, 1H) 1.65−1.50 (m, 1H) 1.45−1.30 (m, 7H, 2 singlets overlapping a multiplet), 1.20 (d, 1H, J = 11.0 Hz), 0.93 (d, 3H, J = 6.8 Hz), 0.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.9, 139.0, 131.8, 130.1, 115.4, 114.4, 87.5, 84.4, 79.2, 75.7, 56.0, 51.9, 40.1, 39.0, 37.3, 36.0, 34.3, 32.1, 29.1, 27.8, 27.1, 24.8, 14.5.

(4*S*,5*R*,6*R*)-1-(*tert*-Butyldimethylsiloxy)-5-[(4-methoxybenzyl)oxy]-6-methyl-4-[(*S*)-pinanediyldioxy)boryl]-9-decene (15). Compound **12** (0.788 g, 1.708 mmol) was azeotroped with toluene (10 mL) and then diluted with THF (20 mL) and brought to −78 °C. 3-(*tert*-Butyldimethylsiloxy)-propylmagnesium bromide (**14**) was produced separately from the reaction of Mg metal (0.336 g, 13.840 g atoms) with 1-bromo-3-(*tert*-butyldimethylsiloxy)propane (1.32 g, 5.21 mmol) in THF (10 mL total) at rt. A rt water bath was used to control the exothermic reaction. The Grignard was slowly added to the first solution, at −78 °C, and the solution allowed to warm slowly to rt. The solution was allowed to stir for 5 h and then partitioned between acidic NH_4Cl/HCl (10 mL 1.2 M HCl + 40 mL saturated NH_4Cl) and CH_2Cl_2 (50 mL). The organic extracts were dried over Na_2SO_4, evaporated, and purified by chromatography (50% CH_2Cl_2 in hexanes to 75% CH_2Cl_2 in hexanes) to yield 0.721 g of a thick yellow oil (71%). $[\alpha]^{25}_D$ = +19.32° (c = 0.0446 g/mL in benzene); HREIMS m/z 598.4234, 598.4225 calcd for (M^+) $C_{35}H_{59}BO_5Si$; IR (NaCl plates neat cm^{-1}) 3077, 2930, 2859, 1615, 1514, 1387, 1248, 1097, 835, 775; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.24 (d, 2H, J = 8.5 Hz), 6.38 (m, 2H) 5.84−5.73 (m, 1H) 5.03−4.90 (m, 2H) 4.60 (d, 1H, J = 11.2 Hz), 4.48 (d, 1H, J = 11.2 Hz), 4.21 (dd, 1H, J = 1.8, 8.8 Hz), 3.78 (s, 3H) 3.60 (m, 2H) 3.39 (m, 1H, close to triplet) 2.35−2.20 (m, 1H) 2.20−1.95 (m, 4H) 1.83−1.65 (m, 3H), 1.65−1.40 (m, 6H) 1.35−1.25 (m, 1H, overlaps next two peaks) 1.29 (s, 3H) 1.25 (s, 3H) 1.18 (d, 1H, J = 10.5 Hz), 0.95 (d, 3H, J = 6.8 Hz), 0.89 (s, 9H) 0.81 (s, 3H) 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz, relaxation delay = 7 s) δ 159.4, 139.6, 132.5, 129.4, 115.0, 114.2, 86.1 (two overlapping signals), 78.2, 73.2, 64.1, 56.0, 51.9, 40.2, 38.9, 36.9, 36.2, 34.1, 33.6, 32.6, 29.5, 27.8, 27.0, 26.7, 25.9, 24.8, 19.1, 15.4, −4.5.

(4*S*,5*R*,6*R*)-1-(*tert*-Butyldimethylsiloxy)-4-{chloro-[(*S*)-pinanediyldioxy)boryl]methyl}-5-[(4-methoxybenzyl)-oxy]-6-methyl-9-decene (16). A mixture of THF (2.5 mL) and CH_2Cl_2 (0.10 mL, 1.549 mmol) was cooled to −100 °C, butyllithium (0.61 mL, 1.9 M solution in pentane), was added and the solution was allowed to stir for 10 min. The solution turned cloudy. Compound **15** (0.690 g, 1.154 mmol) was azeotroped with toluene dissolved in THF (5 mL) and then slowly added to the $CHLiCl_2$ solution generated above. The solution was allowed to stir for 16 min at −100 °C. A solution of $ZnCl_2$ (0.595 g) in THF (3 mL) was added, and the mixture was then allowed to slowly warm to rt and stirred at rt for 10 h. The mixture was partitioned between acidic NH_4Cl/HCl (10 mL 1.2 M HCl + 40 mL saturated NH_4Cl) and CH_2Cl_2 (50 mL). The aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic extracts were combined, dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel, CH_2Cl_2 50% in hexanes) to yield 0.447 g (49%, excluding 1.8 equivalents of CH_2Cl_2) of an oil. The B/O elimination product was also isolated in 34% yield. $[\alpha]^{25}_D$ = +19.92° (c = 0.0440 g/mL in benzene); HREIMS m/z 646.3980, 646.3991 calcd for (M^+) $C_{36}H_{60}BClO_5Si$; IR (NaCl plates neat cm^{-1}) 3076, 2930, 1613, 1515, 1387, 1250, 1099, 1032, 835, 775; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.28 (d, 2H, J = 8.6 Hz), 6.85 (m, 2H) 5.85−5.70 (m, 1H) 5.01−4.91 (m, 2H) 4.63 (d, 1H, J = 11.2 Hz), 4.50 (d, 1H, J = 11.2 Hz), 4.30 (dd, 1H, J = 1.9, 8.8 Hz), 3.84 (d, 1H, J = 5.9 Hz), 3.79 (s, 3H) 3.56 (m, 2H) 3.35 (dd, 1H, J = 1.5, 9.2 Hz), 2.35−2.25 (m, 1H) 2.25−1.98 (m, 5H) 1.90−1.75 (m, 2H), 1.75−1.60 (m, 1H) 1.60−1.20 (m, 13H) 0.92 (d, 3H, J = 6.8 Hz), 0.88 (s, 9H) 0.81 (s, 3H), 0.03 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.1, 138.8, 130.8, 129.5, 114.4, 113.7, 86.6, 82.7, 78.3, 74.6, 63.4, 55.2, 53.4, 51.2, 43.6, 39.3, 38.2, 35.3, 35.2, 34.5, 32.0, 30.0, 28.2, 27.0, 26.2, 25.9, 25.8, 24.0, 18.3, 13.6, −5.3. Elimination product: HRCIMS (M + H) m/z 283.2457, 283.2457 calcd for (M + H) $C_{17}H_{35}OSi$; IR (NaCl plates neat cm^{-1}) 3078, 2928, 2857, 1642, 1472, 1255, 1103, 969. 835, 775; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 5.86−5.74 (m, 1H) 5.38−5.27 (m, 1H) 5.26−5.22 (m, 1H) 5.02−4.91 (m, 2H) 3.61 (t, 2H, J = 6.6 Hz), 2.15−1.95 (m, 5H) 1.58 (pent, 2H, J = 6.9 Hz), 1.32 (m, 2H) 0.96 (d, 3H, J = 6.7) 0.90 (s, 9H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 139.1, 136.4, 128.3, 114.1, 62.6, 36.3, 32.7, 31.6, 28.8, 26.0, 20.9, 18.4, −5.3.

(4*S*,5*R*,6*R*)-1-(*tert*-Butyldimethylsiloxy)-5-[(4-methoxybenzyl)oxy]-6-methyl-4-{[(*S*)-pinanediyldioxy)boryl]methyl}-9-decene (17). To compound **16** (0.372 g, 0.575 mmol) in THF (10 mL) was added sodium trimethoxyborohydride (0.464 g, 5.799 mmol), and the resulting solution stirred for 25 min at rt. The reaction mixture was partitioned between a saturated solution of NH_4Cl (50 mL) and CH_2Cl_2 (50 mL), and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic extracts were combined, dried over Na_2SO_4, and evaporated to yield a crude product (ca. 94%) which was used without further purification. Analysis of the crude provided: HRCIMS m/z 612.4369, 612.4381 calcd for (M^+) $C_{36}H_{61}BO_5Si$; IR (NaCl plates neat cm^{-1}) 3075, 2930, 1615, 1514, 1377, 1248, 1097, 835, 775; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.26 (d, 2H, J =

8.6 Hz), 6.84 (d, 2H, J = 8.6 Hz), 5.76 (m, 1H) 5.00−4.91 (m, 2H) 4.58 (d, 1H, J = 11.1 Hz), 4.45 (d, 1H, J = 11.1 Hz), 4.20 (dd, 1H, J = 1.8, 8.7 Hz), 3.79 (s, 3H) 3.57 (t, 2H, J = 6.4 Hz), 3.12 (dd, 1H, J = 4.0, 6.3 Hz), 2.34−2.24 (m, 1H) 2.24−1.88 (m, 5H) 1.88−1.80 (m, 1H) 1.80−1.62 (m, 2H) 1.62−1.43 (m, 4H) 1.40−1.10 (m, 10H), 1.00-0.83 (m, 16H) 0.03 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.6, 139.9, 132.4, 129.7, 115.0, 114.3, 86.8, 85.9, 78.2, 75.0, 64.4, 56.0, 52.0, 40.3, 38.9, 38.1, 36.2, 35.9, 34.8, 32.5, 31.3, 30.9, 29.9, 27.8, 27.2, 26.7, 24.8, 19.1, 15.3, −4.5.

(4*S*,5*R*,6*R*)-1-(*tert*-Butyldimethylsiloxy)-4-(hydroxymethyl)-5-[(4-methoxybenzyl)oxy]-6-methyl-9-decene (18). The preceding crude material (compound **17**) was dissolved in THF (15 mL) and treated with H_2O_2 (0.750 mL, 30% solution in H_2O, 6.617 mmol) and NaOH (0.750 mL, 1.6 M solution, 1.20 mmol) at rt. After stirring for 1 h the reaction mixture was partitioned between NH_4Cl saturated solution (50 mL) and CH_2Cl_2 (50 mL), and the aqueous layer extracted with CH_2Cl_2 (50 mL). The organic extracts were combined, dried over Na_2SO_4, and evaporated, and the resulting mixture purified by column chromatography (silica gel, 20% ethyl acetate in hexanes) to yield 0.245 g (87%, for the two steps) of a thick oil. $[\alpha]^{25}_D$ = +11.30° (c = 0.0415 g/mL in benzene); HRCIMS m/z 451.3227, 451.3244 (MH^+), calcd for $C_{26}H_{47}O_4Si$; IR (NaCl plates neat cm^{-1}) 3453, 2930, 1613, 1514, 1250, 1095, 835, 775; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.25 (d, 2H, J = 8.6 Hz), 6.87 (d, 2H, J = 9.0 Hz), 5.79 (m, 1H) 5.05−4.94 (m, 2H) 4.47 (d, 1H, J = 10.5 Hz), 4.49 (d, 1H, J = 10.5 Hz), 3.79 (s, 3H) 3.63−3.57 (m, 3H) 3.32 (t, 2H, J = 5.2 Hz), 2.95 (s, 1H, broad) 2.25−2.12 (m, 1H) 2.12−2.00 (m, 1H) 1.89−1.78 (m, 1H) 1.78−1.68 (m, 1H) 1.68−1.25 (m, 6H) 0.99 (d, 3H, J = 6.7 Hz), 0.89 (s, 9H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 160.1, 139.4, 131.2, 130.2, 115.4, 114.6, 88.2, 78.2, 75.7, 64.3, 63.9, 56.0, 42.8, 36.5, 34.2, 32.4, 31.2, 26.7, 19.1, 15.5, −4.5.

(4*S*,5*R*,6*R*)-1-(*tert*-Butyldimethylsiloxy)-4-[(methanesulfonyl)methyl]-5-[(4-methoxybenzyl)oxy]-6-methyl-9-decene (19). To a solution of compound **18** (0.216 g, 0.480 mmol, azeotroped with toluene) in CH_2Cl_2 (10 mL) and TEA (1 mL) at 0° C was added methanesulfonyl chloride (0.150 mL, 1.938 mmol). The mixture was allowed to stir at 0 °C for 30 min and was then partitioned between acidic NaCl saturated solution (50 mL of NaCl saturated solution, 10 mL of 1.2 M HCl) and CH_2Cl_2 (50 mL) and the aqueous layer extracted with CH_2Cl_2 (50 mL). The organic extracts were combined, dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel, 20% ethyl acetate in hexanes) to yield 0.240 g (94%) of a clear oil. $[\alpha]^{25}_D$ = +21.63° (c = 47.0 mg/mL in benzene); HRCIMS m/z 527.2871, 527.2863 $(M - H)^+$, calcd for $C_{27}H_{47}O_6SSi$; IR (NaCl plates neat cm^{-1}) 3073, 2932, 1612, 1514, 1464, 1358, 1250, 1176, 1095, 945, 835; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.26 (d, 2H, J = 8.6 Hz), 6.87 (d, 2H, J = 8.6 Hz), 5.80 (m, 1H) 5.06−4.95 (m, 2H) 4.56 (d, 1H, J = 10.6 Hz), 4.47 (d, 1H, J = 10.6 Hz), 4.38−4.30 (m, 2H) 3.80 (s, 3H) 3.62−3.57 (m, 2H) 3.33 (dd, 1H, J = 3.9, 6.6 Hz), 2.93 (s, 3H) 2.25−2.00 (m, 2H) 2.00−1.87 (m, 1H) 1.87−1.71 (m, 1H) 1.70−1.35 (m, 6H) 0.94 (d, 3H, J = 6.7 Hz), 0.90 (s, 9H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.9, 139.4, 131.5, 130.0, 115.5, 114.5, 83.0, 75.3, 70.7, 63.6, 56.0, 41.1, 37.8, 35.8, 34.3, 32.4, 30.7, 26.7, 25.4, 19.1, 14.7, −4.6.

(4*S*,5*R*,6*R*)-1-(*tert*-Butyldimethylsiloxy)-5-[(4-methoxybenzyl)oxy]-4,6-dimethyl-9-decene (20). To a solution of compound **19** (0.222 g, 0.419 mmol, azeotroped with toluene) in THF (20 mL) was added LAH (0.171 g, 4.49 mmol), and the resulting suspension was stirred for 10 min at rt and then heated at 60 °C for a total of 13 min, until TLC indicated the consumption of the starting material. The reaction was then partitioned between acidic NH_4Cl solution (50 mL of saturated NH_4Cl solution, 10 mL of 1.2 M HCl) and CH_2Cl_2 (50 mL). The aqueous layer was extracted with CH_2Cl_2 (50 mL), and the organic extracts were combined, dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel 5% ethyl acetate in hexanes) to yield 0.160 g (88%) of a clear oil. $[\alpha]^{25}_D$ = −2.6° (c = 34.9 mg/mL in benzene); HREIMS m/z 434.3205, 434.3216 calcd for (M^+) $C_{26}H_{46}O_3Si$; IR (NaCl plates neat cm^{-1}) 3077, 2930, 2857, 1615, 1514, 1248, 1095, 835, 775; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.28 (d, 2H, J = 8.6 Hz), 6.87 (d, 2H, J = 8.6 Hz), 5.81 (m, 1H) 5.04−4.93 (m, 2H) 4.51 (s, 2H) 3.80 (s, 3H) 3.60 (t, 2H, J = 6.4 Hz), 3.06 (t, 1H, J = 5.3 Hz), 2.20−1.97 (m, 2H) 1.80−1.67 (m, 2H) 1.67−1.43 (m, 4H) 1.38−1.16 (m, 2H) 0.97 (d, 3H, J = 6.7 Hz), 0.96 (d, 3H, J = 6.7 Hz), 0.91 (s, 9H) 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.7, 139.8, 132.2, 129.8, 115.1, 114.4, 87.6, 75.4, 64.2, 56.0, 36.3, 35.9, 34.4, 32.3, 31.3, 31.1, 26.7, 19.1, 16.0, 15.6, −4.5.

(4*R*,5*R*,6*S*)-9-(*tert*-Butyldimethylsiloxy)-5-[(4-methoxybenzyl)oxy]-4,6-dimethylnonanal (21). A solution of compound **20** (56.0 mg, 0.1288 mmol) in CH_2Cl_2 (10 mL) was cooled to −78 °C and exposed to O_3 gas until the solution turned pale blue (approximately 5 min). Residual ozone was removed with a stream of N_2, and tributylphosphine (40 mL, 0.1621 mol, 92% tech grade) was added. The reaction mixture was allowed to warm to rt and then stirred at rt for 2.5 h. The mixture was vacuum evaporated, and the residues were purified by column chromatography (silica gel 5% ethyl acetate in hexanes) to yield 51.9 mg (93%) of a clear thick oil. $[\alpha]^{25}_D$ = −1.8° (c = 32.6 mg/mL in benzene); HREIMS m/z 379.2305, 379.2304 calcd for $(M - C_4H_9)^+$ $C_{21}H_{35}O_4Si$; IR (NaCl plates neat cm^{-1}) 2955, 2857, 2716, 1726, 1612, 1514, 1248, 1096, 835; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 9.76 (t, 1H, J = 1.7 Hz), 7.26 (m, 2H) 6.86 (m, 2H) 4.55−4.46 (m, 2H, appears as quartet) 3.80 (s, 3H) 3.59 (t, 2H, J = 6.3 Hz), 3.05 (t, 1H, J = 5.0 Hz), 2.55−2.32 (m, 2H) 1.84−1.68 (m, 3H) 1.66−1.41 (m, 4H) 1.29−1.17 (m, 1H) 0.98−0.93 (overlapping doublets, 6H) 0.90 (s, 9H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 203.3, 159.8, 132.0, 129.8, 114.5, 87.3, 75.3, 64.1, 56.0, 42.7, 36.3, 36.0, 31.3, 31.1, 27.2, 26.7, 19.1, 15.9, 15.4, −4.5.

(4*S*,5*R*,6*R*,9*S*,10*R*)-1-(*tert*-Butyldimethylsiloxy)-9-hydroxy-5-[(4-methoxybenzyl)oxy]-4,6,10-trimethyl-11-dodecene (22). To a mixture of potassium *tert*-butoxide (43.5 mg, 0.4223 mmol, freshly sublimed) in THF (1 mL) at −78 °C was added *trans*-2-butene (0.5 mL) followed by *n*-butyllithium (0.150 mL 1.9 M solution in pentane, 0.2850 mmol, Aldrich). The solution was allowed to warm to −40 °C (acetonitrile bath/dry ice) and allowed to stir at −40 °C for 20 min. The solution (now dark yellow) was recooled to −78 °C, and (+)-methoxydiisopinocamphenylborane in THF was slowly added (0.1782 g, 0.5640 mmol in 0.3 mL of THF) quenching the yellow color, and the solution was allowed to stir at −78 °C for 30 min. BF_3-OEt_2 was then added (85 μL, 0.6884 mmol) followed by a THF solution of compound **21** (50.0 mg, 0.1145 mmol, in 1 mL of THF). The resulting reaction mixture was allowed to stir at −78 °C for 4.5 h, and the reaction was quenched at −78 °C by the addition of $Ca(OAc)_2$ solution (2.2 M, 0.50 mL, 1.1 mmol), NaOH solution (5 M, 0.50 mL, 2.5 mmol), and H_2O_2 (30% solution, 0.50 mL, 4.4 mmol) and then warmed to rt for 15 min. The resulting mixture was partitioned between NH_4Cl saturated solution and CH_2Cl_2 (50 mL ea.) and the aqueous layer extracted with CH_2Cl_2 (50 mL × 2). Each extraction caused a severe emulsion which was broken by the addition of hexanes. The organic extracts were combined, dried over Na_2SO_4, and evaporated, and the residue was purified by column chromatography (7.5% ethyl acetate in hexanes) to yield 40.0 mg (71%) of a purified oil. $[\alpha]^{25}_D$ = −11.11° (c = 27.5 mg/mL benzene); HRFABMS m/z 493.3712, 493.3713 calcd for (M + H) $C_{29}H_{53}O_4Si$; IR (NaCl plates neat cm^{-1}) 3461, 2932, 2859, 1615, 1514, 1464, 1248, 1095, 835; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.27 (m, 2H) 6.86 (m, 2H) 5.80−5.71 (m, 1H) 5.14−5.08 (m, 2H) 4.51 (s, 2H) 3.79 (s, 3H) 3.59 (t, 2H, J = 6.4 Hz), 3.38−3.33 (m, 1H) 3.06 (t, 1H, J = 5.2 Hz), 2.21 (hexet, 2H, J = 6.9 Hz), 1.78−1.40 (m, 7H + H_2O peak) 1.40−1.12 (m, 4H) 1.04 (d, 3H, J = 6.8 Hz), 0.97−0.94 (m, 6H, overlapping doublets) 0.89 (s, 9H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.7, 140.9, 132.3, 129.8, 117.1, 114.4, 87.6, 75.9, 75.4, 64.2, 56.0, 44.7, 36.7, 36.4, 32.9, 31.3, 31.3, 31.1, 26.7, 19.1, 17.1, 16.0, 15.7, −4.5.

(4*S*,5*R*,6*R*,9*S*,10*R*)-9-(Benzoyloxy)-1-(*tert*-butyldimethylsiloxy)-5-[(4-methoxybenzyl)oxy]-4,6,10-trimethyl-11-dodecene (23). A solution of compound **22** (30.0 mg, 0.0609 mmol) in pyridine (0.50 mL dry) was treated with catalytic DMAP and benzoyl chloride (28 μL, 0.240 mmol) in four portions over a 4.5 h period. The reaction was quenched by addition of saturated bicarbonate solution (1 mL), and the mixture was partitioned between saturated sodium bicarbon-

ate solution and CH_2Cl_2 (50 mL ea.). The aqueous layer was extracted with CH_2Cl_2 (50 mL × 2). The organic extracts were combined, dried over Na_2SO_4, and evaporated, and the residue was purified by column chromatography ($CHCl_3$, silica gel) to yield the desired product contaminated with benzoic anhydride. Addition of 1-amino-2-propanol (2 equiv per 1 equiv of benzoic anhydride as determined by ^{1}H NMR) and rechromatography yielded 31.0 mg (85%) of oil. $[\alpha]^{25}_D = -18.2°$ (c = 0.0290 g/mL in benzene); HRFABMS m/z 595.3799, 595.3817 calcd for $(M - H)^+$ $C_{36}H_{55}O_5Si$; IR (NaCl plates neat cm^{-1}) 3071, 2955, 28.56, 1717, 1612, 1514, 1271, 1248, 1098, 835, 712; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.05−8.02 (m, 2H) 7.57−7.54 (m, 1H) 7.53−7.40 (m, 2H) 7.23−7.21 (m, 2H) 6.84−6.81 (m, 2H) 5.91−5.82 (m, 1H) 5.12−5.08 (m, 3H) 4.05−4.43 (m, 2H) 3.79 (s, 3H) 3.57 (t, 2H, J = 6.3 Hz), 3.02 (t, 1H, J = 5.2 Hz), 2.60−2.48 (m, 1H) 1.78−1.61 (m, 4H) 1.61−1.38 (m, 4H) 1.35−1.15 (m, 2H) 1.08 (d, 3H, J = 6.9 Hz), 0.93 (d, 6H, J = 6.7 Hz), 0.90 (s, 9H) 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 167.1, 159.7, 140.0, 133.6, 132.1, 131.4, 130.3, 129.9, 129.1, 116.5, 114.4, 87.4, 78.7, 75.4, 64.2, 56.0, 42.2, 36.4, 36.4, 31.3, 31.0, 30.1, 26.7, 19.1, 17.1, 16.0, 15.7, −4.5.

(4*S*,5*R*,6*R*,9*S*,10*R*)-9-(Benzoyloxy)-1-hydroxy-5-[(4-methoxybenzyl)oxy]-4,6,10-trimethyl-11-dodecene (24). Compound **23** (60.1 mg, 0.101 mmol) was dissolved in THF was treated with TBAF (100 μL of 1.0 M solution in THF) at 0 °C and then warmed to rt. After stirring for 45 min, additional TBAF (100 μL) was added. After an additional 2 h the reaction mixture was partitioned between NH_4Cl saturated solution and CH_2Cl_2 (10 mL ea.) and the aqueous layer extracted with CH_2Cl_2 (10 mL) and ethyl acetate (20 mL). The organic extracts were combined, dried over Na_2SO_4, and evaporated, and the resulting crude oil was purified by column chromatography (silica gel, 30% to 50% ethyl acetate in hexanes) to yield 49.4 mg (0.101 mmol, 100%) of a clear oil. $[\alpha]^{25}_D = -13.89°$ (c = 23.8 mg/mL in benzene) HRCIMS 482.3030 m/z, 482.3032 (M^+) calcd for $C_{30}H_{42}O_5$; IR (NaCl plates neat cm^{-1}) 3413, 3067, 2934, 1715, 1613, 1514, 1273, 1111, 712; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.06−8.02 (m, 2H) 7.57−7.53 (m, 1H) 7.45−7.41 (m, 2H) 7.23−7.20 (m, 2H) 6.84−6.81 (m, 2H) 5.86 (m, 1H) 5.13−5.06 (m, 3H) 4.47 (s, 2H) 3.78 (s, 3H) 3.58 (t, 2H, J = 6.4 Hz), 3.02 (t, 1H, J = 5.3 Hz), 2.53 (m, 1H) 1.72−1.39 (m, 9H, 1 from water) 1.29−1.16 (m, 2H) 1.07 (d, 3H, J = 6.9 Hz), 0.93 (d, 6H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 166.2, 158.9, 139.3, 132.7, 131.2, 130.5, 129.4, 129.0, 128.2, 115.7, 113.5, 86.3, 77.8, 74.5, 63.1, 55.1, 41.4, 35.5, 35.5, 30.3, 30.1, 30.1, 29.2, 16.3, 15.1, 14.9.

(4*S*,5*R*,6*R*,9*S*,10*R*)-9-(Benzoyloxy)-5-[(4-methoxybenzyl)oxy]-4,6,10-trimethyl-11-dodeceneal (4). A solution of oxalyl chloride (2.00 mmol in 11 mL of CH_2Cl_2) in CH_2Cl_2 was treated with DMSO (0.30 mL, 4.2 mmol in 0.7 mL of CH_2Cl_2) at −78 °C and the resulting mixture allowed to stir for 20 min. A sample of compound **24** (49.4 mg, 0.1017 mmol) in 2 mL of CH_2Cl_2 was then added (at −78 °C) and the mixture allowed to stir for 1 h, followed by addition of triethylamine (0.86 mL). After stirring for an additional 20 min at −78 °C, the reaction mixture was allowed to warm to 0 °C and partitioned between saturated NH_4Cl solution and CH_2Cl_2 (50 mL ea.) and the aqueous layer extracted with CH_2Cl_2 (50 mL). The organic extracts were combined, dried over Na_2SO_4, and evaporated, and the resulting residue was purified by column chromatography (silica gel, 10% ethyl acetate in hexanes) to yield 33.8 mg (69%) of a clear oil. $[\alpha]^{25}_D = -16.56°$ (c = 43.3 mg/mL in benzene); IR (NaCl plates neat cm^{-1}) 3072, 2964, 2721, 1718, 1613, 1514, 1274, 1249, 1112, 714; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 9.72 (t, 1H, J = 1.6 Hz), 8.04 (m, 2H) 7.58−7.53 (m, 1H) 7.45−7.41 (m, 2H) 7.21 (d, 2H, J = 8.6 Hz), 6.82 (d, 2H, J = 8.6 Hz), 5.91−5.81 (m, 1H) 5.13−5.06 (m, 3H), 4.49−4.43 (m, 2H) 3.78 (s, 3H) 3.02 (t, 1H, J = 5.1 Hz), 2.58−2.48 (m, 1H) 2.48−2.30 (m, 2H) 1.80−1.58 (m, 5H) 1.55−1.35 (m, 2H) 1.29−1.23 (m, 1H) 1.08 (d, 3H, J = 6.8 Hz), 0.94 (d, 3H, J = 6.7 Hz), 0.92 (d, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 202.4, 166.2, 158.9, 139.1, 132.7, 130.9, 130.5, 129.4, 129.0, 128.3, 115.7, 113.6, 86.0, 77.8, 74.4, 55.1, 41.8, 41.4, 35.6, 35.1, 30.2, 29.2, 26.1, 16.3, 14.9, 14.8.

(*R*)-Pinanediol Methylboronate (26). A mixture of methaneboronic acid (1.841 g, 30.75 mmol) and (*R*)-pinanediol (**25**) (5.029 g, 29.52 mmol) in 50 mL of diethyl ether was allowed to stir at rt over Na_2SO_4 until TLC indicated completion of reaction (40 min). The mixture was partitioned between saturated Na_2CO_3 solution (50 mL) and CH_2Cl_2 (100 mL). The organic extracts were dried over Na_2SO_4, evaporated, and distilled under vacuum (bp 93 °C, 9 mmHg) to yield 5.257 g (92%) of a clear oil. $[\alpha]^{25}_D = -51.24°$ (c = 0.0391 g/mL in benzene); HREIMS m/z 194.1474, 194.1478 calcd for (M^+) $C_{11}H_{19}BO_2$; IR (NaCl plates neat cm^{-1}) 2972, 2919, 1476, 1372, 1032; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.24 (dd, 1H, J = 8.6, 1.9 Hz), 2.39−2.25 (m, 1H) 2.25−2.18 (m, 1H) 2.03 (t, 1H, J = 5.9 Hz), 1.95−1.87 (m, 1H) 1.87−1.78 (m, 1H) 1.37 (s, 3H) 1.28 (s, 3H) 1.11 (d, 1H, J = 10.9 Hz), 0.83 (s, 3H) 0.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 85.4, 77.6, 51.2, 39.5, 38.1, 35.4, 28.6, 27.1, 26.4, 24.0.

(*R*)-Pinanediol (1*R*)-(1-Chloroethyl)boronate (27). A mixture of THF (60 mL) and CH_2Cl_2 (2.00 mL, 31.0 mmol) was cooled to −100°C, butyllithium (12.6 mL, 1.9 M solution in pentane, 23.9 mmol) was added, and the solution was allowed to stir for 15 min. The solution turned cloudy and slightly yellow. Compound **26** (4.644 g, 23.93 mmol) in THF (9 mL) was slowly added and the solution allowed to stir for 15 min at −100 °C. A solution of $ZnCl_2$ (1.965 g, 14.45 mmol) in THF (8 mL) was added, and the mixture was then allowed to slowly warm to rt and stirred at rt for 9 h. The mixture was partitioned between acidic NH_4Cl/HCl (50 mL of 1.2 M HCl + 200 mL saturated NH_4Cl) and CH_2Cl_2 (200 mL). The organic extracts were dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel, 25% CH_2Cl_2 in hexane) to yield 3.721 g of a partially purified oil (containing a 60% yield of the desired material). Data for compound **27**: $[\alpha]^{25}_D = -55.28°$ (c = 0.0415 g/mL, in benzene); HREIMS m/z 242.1257, 242.1245 calcd for (M^+) $C_{12}H_{20}ClBO_2$; IR (NaCl plates neat cm^{-1}) 2924, 2872, 1446, 1381, 1287, 1030, 650; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.35 (d, 1H, J = 8.9, 1.9 Hz), 3.55 (q, 1H, J = 7.5 Hz), 2.40−2.30 (m, 1H) 2.30−2.20 (m, 1H) 2.13−2.05 (m, 1H) 1.97−1.85 (m, 2H) 1.55 (d, 3H, J = 7.5 Hz), 1.41 (s, 3H) 1.28 (s, 3H) 1.15 (d, 2H, J = 11.1 Hz), 0.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 87.5, 79.3, 51.9, 40.0, 39.0, 36.0, 29.1, 27.7, 27.0, 24.7, 21.3.

(*S*)-2-[(*R*)-Pinanediyldioxy)boryl]-5-hexene (28). Compound **27** (3.099 g, 12.78 mmol) was azeotroped with toluene, dissolved in THF (50 mL), and cooled to −78 °C. In a separate flask 3-buten-1-ylmagnesium bromide was produced by addition of 1-bromo-3-butene (3.00 mL, 28.89 mmol) to magnesium metal (1.054 g, 43.35 mmol) in THF (5 mL). As necessary THF was used to dilute the mixture, and a cooling bath was used to control the exothermic reaction. The solution was stirred until the exotherm ceased and was then titrated into the THF solution of compound **27** until the starting material was consumed. The reaction mixture was allowed to slowly warm to rt (2 h) and then allowed to stir for 16 h at rt. The reaction was then partitioned between HCl (1.2 M, 10 mL), NH_4Cl solution (200 mL saturated), and CH_2Cl_2 (200 mL). The organic extracts were dried over Na_2SO_4, evaporated, and purified by column chromatography (silica gel 20% CH_2Cl_2 in hexanes) to yield 2.697 g (80%) of a partially purified oil (95%+ pure). Data for compound **28**: $[\alpha]^{25}_D = -30.83°$ (c = 0.0432 g/mL in benzene); HREIMS m/z 262.2115, 262.2104 calcd for (M^+) $C_{16}H_{27}BO_2$; IR (NaCl plates neat cm^{-1}) 3078, 2921, 2872, 1642, 1464, 1389, 1237, 1030, 908; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 5.80 (m, 1H) 5.01−4.90 (m, 2H) 4.24 (dd, 1H, J = 8.7, 2.2 Hz), 2.37−2.28 (m, 1H) 2.25−2.15 (m, 1H) 2.15−2.03 (m, 3H) 1.93−1.85 (m, 1H) 1.85−1.78 (m, 1H) 1.65−1.53 (m, 1H) 1.45−1.35 (m, 4H (m, 1H, + s, 3H)), 1.36 (s, 3H) 1.09 (d, 1H, J = 10.9 Hz), 0.99 (d, 3H, J = 7.0 Hz), 0.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 140.0, 115.0, 86.0, 78.3, 52.0, 40.24, 38.9, 36.4, 33.9, 33.3, 29.4, 27.8, 27.2, 24.7, 16.3.

(1*R*,2*S*)-1-Chloro-2-methyl-1-[(*R*)-pinanediyldioxy)-boryl]-5-hexene (29). A mixture of THF (25 mL) and CH_2Cl_2 (0.85 mL, 13.2 mmol) was cooled to −100°C, butyllithium (5.40 mL, 1.9 M solution in pentane, 10.26 mmol), was added and the solution was allowed to stir for 15 min. The solution turned cloudy and slightly yellow. A solution of compound **28** (2.697 g, 10.29 mmol, azeotroped with toluene) in THF (10 mL) was slowly added and the solution allowed to stir at −100 °C

at which point the reaction mixture gelled. After 5 min at −100 °C a solution of $ZnCl_2$ (0.889 g, 6.539 mmol) in THF (10 mL) was added, and the mixture was then allowed to slowly warm to rt (the gel rapidly liquefied on addition of $ZnCl_2$, fully liquid by −80 °C) and stirred at rt for 9 h. The mixture was partitioned between acidic NH_4Cl/HCl (50 mL of 1.2 M HCl + 150 mL of saturated NH_4Cl) and CH_2Cl_2 (200 mL). The aqueous layer was extracted with CH_2Cl_2 (100 mL), the organic extracts were combined, dried over Na_2SO_4, and evaporated, and the remaining oil was purified by column chromatography (silica gel, 20% CH_2Cl_2 in hexanes) to yield 2.7505 g (86%) of a partially purified oil (85% pure); HRCIMS *m/z* 328.2210, 328.2215 calcd for (M + NH_4) $C_{17}H_{32}BClNO_2$; IR (NaCl plates neat cm^{-1}) 3078, 2971, 2924, 1643, 1377, 1287, 1030, 908; ^1H NMR ($CDCl_3$, 360 MHz) δ 5.79 (m, 1H) 5.04−4.92 (m, 2H) 4.36 (dd, 1H, 9.0, 1.8 Hz), 4.23 (impurity) 3.39 (d, 1H, J = 6.6 Hz), 2.42−2.30 (m, 1H) 2.30−1.87 (m, 7H) 1.76−1.65 (m, 1H) 1.45−1.32 (m, 4H) 1.29 (s, 3H) 1.24 (d, 1H, J = 11.0 Hz), 1.02 (d, 3H, 6.7 Hz), 0.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 139.3, 115.3, 87.5, 79.2, 51.9, 40.1, 39.0, 37.1, 36.4, 36.1, 33.9, 31.9, 29.3, 27.8, 27.2, 24.8, 18.1.

(5*S*,6*R*)-5-Methyl-6-[(*R*)-pinanediyldioxy)boryl]-1-heptene (30). A solution of the previous 85% pure material (2.751 g, 7.53 mmol with 1.33 mmol contaminant) in THF (100 mL) was cooled to −78 °C. A solution of methylmagnesium chloride (3.00 mL 3.0 M solution in THF, 9.00 mmol, Aldrich) was added, and the reaction slowly allowed to warm to rt and stirred at rt for 20 h. The reaction mixture was partitioned between acidic NH_4Cl solution (200 mL of NH_4Cl saturated solution, 10 mL of 1.2 M HCl). The organic layer was extracted with NH_4Cl saturated solution, dried over Na_2SO_4, and evaporated, and the residue was purified by column chromatography (20 to 25% CH_2Cl_2 in hexanes) to yield 1.178 g (54%) of a partially purified oil (95% purity). Data for compound **30**: $[\alpha]^{25}_D$ = −46.65° (c = 0.0382 g/mL in benzene); HRCIMS *m/z* 290.2424, 290.2417 calcd for (M^+) $C_{18}H_{31}BO_2$; IR (NaCl plates neat cm^{-1}) 3076, 2923, 1642, 1458, 1385, 1281, 1032, 909; ^1H NMR ($CDCl_3$, 360 MHz) δ 5.80 (m, 1H) 5.01−4.89 (m, 2H) 4.25 (dd, 1H, J = 2.1, 8.8 Hz), 2.38−2.28 (m, 1H) 2.25−2.17 (m, 1H, 2.17−1.93 (m, 3H) 1.93−1.87 (m, 1H) 1.87−1.79 (m, 1H) 1.70−1.55 (m, 1H) 1.50−1.39 (m, 1H) 1.36 (s, 3H) 1.31−1.20 (m, 1H + s, 3H at 1.28) 1.17-0.95 (m, 2H) 0.92 (d, 3H, J = 7.3 Hz), 0.88 (d, 3H, J = 6.8 Hz), 0.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 140.2, 114.7, 85.39, 78.2, 52.0, 40.3, 38.9, 36.5, 35.9, 35.1, 32.6, 29.5, 27.8, 27.3, 24.8, 18.6, 12.0.

(5*S*,6*R*)-6-(Hydroxy)-5-methyl-1-heptene (31). A solution of compound **30** (1.178 g, 4.060 mmol) in THF (10 mL) at rt was treated with NaOH (1.6 M aqueous solution, 2.5 mL, 4.00 mmol) and H_2O_2 (30% aqueous solution, 0.60 mL, 5.3 mmol) (exothermic reaction) and the resulting suspension allowed to stir at rt for 90 min. The reaction mixture was partitioned between acidic NH_4Cl solution (50 mL of saturated NH_4Cl solution + 5 mL of HCl 1.2 M) and CH_2Cl_2 (50 mL), and the aqueous phase was extracted with CH_2Cl_2 (50 mL). The organic extracts were combined and dried over Na_2SO_4, solvents were removed by careful distillation (1 atm, vigreux column), and the crude mixture was purified by chromatography (silica gel, CH_2Cl_2 followed by 20% ethyl acetate in hexanes.). The fractions containing the desired alcohol were concentrated and used directly in the next step (substantial amounts of CH_2Cl_2 and THF remained). The identity of the alcohol was confirmed by ^1H and ^{13}C NMR. ^1H NMR ($CDCl_3$, 360 MHz) δ 5.79 (m, 1H) 5.03−4.91 (m, 2H) 3.65 (pentet, 1H, J = 6.2 Hz), 2.32−2.10 (m, 1H) 2.05−1.92 (m, 1H) 1.70−1.60 (s, 1H, broad) 1.60−1.45 (m, 2H) 1.19−1.14 (m, 1H) 1.11 (d, 3H, J = 6.3 Hz), 0.86 (d, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 139.7, 115.1, 72.4, 40.2, 32.4, 32.2, 20.1, 15.1.

(5*S*,6*R*)-6-(*tert*-Butyldiphenylsiloxy)-5-methyl-1-heptene (32). The preceding partially evaporated mixture and catalytic DMAP (ca. 5 mg) were dissolved in a mixture of DMF (distilled, dry, 5 mL), 2,6-lutidine (2 mL, 17 mmol), and *tert*-butyldiphenylsilyl chloride (3.0 mL, 12 mmol). The mixture was brought to 85 °C for 12 h. After cooling, the reaction mixture was partitioned between NH_4Cl saturated solution (50 mL) and CH_2Cl_2 (50 mL). The organic extracts were washed with HCl (1.2 M, 50 mL), dried over Na_2SO_4, and evaporated, and the residue was purified by chromatography (silica gel, hexanes to 10% ethyl acetate in hexanes) to yield 0.935 g (66%) of a clear oil. Retreatment of some recovered starting alcohol yielded an additional 0.074 g (5%) of the desired compound. $[\alpha]^{25}_D$ = +9.8° (c = 30.6 mg/mL in benzene); HRCIMS *m/z* 309.1665, 309.1674 calcd for (M − C_4H_9)$^+$ $C_{20}H_{25}OSi$; IR (NaCl plates neat cm^{-1}) 3073, 2961, 2859, 1641, 1589, 1427, 1111, 1039, 910, 702, 613; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.71 (dd, 4H, J = 1.6, 7.9 Hz), 7.46−7.37 (m, 6H) 5.72 (m, 1H) 4.98−4.88 (m, 2H) 3.80 (dq, 1H, J = 2.1, 6.3 Hz), 2.05−1.96 (m, 1H) 1.94−1.82 (m, 1H) 1.67−1.55 (m, 1H) 1.40−1.30 (m, 1H) 1.20−1.11 (m, 1H) 1.09 (s, 9H) 0.97 (d, 3H, J = 6.3 Hz), 0.94 (d, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 139.1, 135.9, 135.0, 134.5, 129.4, 129.3, 127.5, 127.4, 114.1, 72.5, 39.3, 32.2, 31.5, 27.0, 19.3, 18.1, 13.7.

(4*S*,5*R*)-5-(*tert*-Butyldiphenylsiloxy)-4-methylhexanal (33). A solution of compound **32** (0.407 g, 1.104 mmol) in CH_2Cl_2 (30 mL) was cooled to −78 °C and exposed to O_3 gas until the solution turned blue (ca. 5 min). Residual ozone was removed with a stream of N_2, and tributylphosphine (0.325 mL, 1.200 mmol, 92% tech grade) was added. The reaction mixture was allowed to slowly warm to rt and then stirred at rt for 4 h. The mixture was vacuum evaporated, and the residues were purified by column chromatography (silica gel 5% ethyl acetate in hexanes) to yield 0.377 g (92%) of a clear thick oil. $[\alpha]^{25}_D$ = +4.2° (c = 0.0424 g/mL in benzene); HREIMS *m/z* 311.1465, 311.1467 calcd for (M − C_4H_9)$^+$ $C_{19}H_{23}O_2Si$; IR (NaCl plates neat cm^{-1}) 3071, 2932, 2859, 2714, 1728, 1474, 1428, 1381, 1111, 1055, 702, 613; ^1H NMR ($CDCl_3$, 360 MHz) δ 9.66 (t, 1H, J = 1.7 Hz), 7.68 (m, 4H), 7.40 (m, 6H), 3.76 (m, 1H), 2.35−2.15 (m 2H), 1.66−1.56 (m, 1H), 1.56−1.49 (m, 1H), 1.43−1.34 (m, 1H), 1.06 (s, 9H), 0.99 (d, 3H, J = 6.4 Hz), 0.92 (d, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 203.4, 136.7, 136.7, 135.5, 134.99, 130.4, 130.2, 128.3, 128.2, 73.1, 42.6, 40.3, 27.8, 25.6, 20.1, 19.2, 14.7.

(3*R*,4*R*,7*S*,8*R*)-8-(*tert*-Butyldiphenylsiloxy)-4-hydroxy-3,7-dimethyl-1-nonene (34). A mixture of potassium *tert*-butoxide (0.336 g, 3.258 mmol) in dry THF (3 mL) was cooled to −78 °C, *trans*-2-butene was added via cannula (2 mL 29 mmol), *n*-butyllitium was added (1.50 mL of a 1.9 M solution in pentane, 2.85 mmol), and the mixture was brought to −42 °C for 20 min, generating a dark yellow solution. The mixture was recooled to −78 °C, and (+)-methoxydiisopinocampheylborane in THF (1.636 g, 5.176 mmol, in 3 mL of THF) was slowly added, causing the yellow color to fade. The solution was allowed to stir for 40 min, and BF_3OEt_2 was then added (0.70 mL, 5.669 mmol) followed by a THF solution of the aldehyde **33** (0.347 g, 0.9424 mmol, in 2 mL of THF). The reaction mixture was allowed to stir at −78°C for 6 h and was then quenched with excess NaOH/H_2O_2 and allowed to warm to rt for 1.5 h. The mixture was partitioned between CH_2Cl_2 and saturated NH_4Cl solution (100 mL ea.) and the aqueous layer extracted with CH_2Cl_2 (100 mL). The organic extracts were combined, dried over Na_2SO_4, and evaporated, and the resulting residue was purified by chromatography (silica gel, 5% ethyl acetate in hexanes) to yield 0.271 g (54%) of a clear oil. $[\alpha]^{25}_D$ = +4.8° (c = 0.0350 g/mL in benzene); HREIMS *m/z* 367.2099, 367.2093 calcd for (M − C_4H_9)$^+$ $C_{23}H_{31}O_2Si$; IR (NaCl plates neat cm^{-1}) 3424, 3071, 2961, 2859, 1462, 1428, 1379, 1111, 739, 702; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.71−7.68 (m, 4H), 7.42−7.35 (m, 6H), 5.70 (m, 1H), 5.12−5.05 (m, 2H), 3.82−3.75 (m, 1H), 3.23 (q, 1H, J = 5.8 Hz), 2.14 (hexet, 1H, J = 7.1 Hz), 1.60−1.45 (m, 2H), 1.35−1.12 (m, 4H), 1.07 (s, 9H), 0.99 (d, 3H, J = 6.8 Hz), 0.97 (d, 3H, J = 5.2 Hz), 0.91 (d, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 141.1, 136.7, 135.7, 135.3, 130.2, 130.1, 128.2, 128.1, 117.0, 75.4, 73.4, 44.8, 40.6, 32.7, 29.6, 27.8, 20.1, 18.7, 17.0, 14.4.

(3*R*,4*R*,7*S*,8*R*)-8-(*tert*-Butyldiphenylsiloxy)-4-[(4-methoxybenzyl)oxy]-3,7-dimethyl-1-nonene (35). A solution of alcohol **34** (0.392 g, 0.923 mmol) and *p*-methoxybenzyl 2,2,2-trichloroacetimidate (0.285 g, 1.01 mmol) in diethyl ether (18 mL) was treated with trifluoromethylsulfonic acid (0.25 μL, 2.8×10^{-4} mmol in 0.25 mL of ether). The reaction was stirred for 20 min, with the addition of more *p*-methoxybenzyl 2,2,2-trichloroacetimidate (0.122 g, 0.432 mmol, in 2 portions at 10 min and 15 min) during this time. The reaction mixture

was partitioned between CH_2Cl_2 and H_2O (50 mL ea.). The organic extracts were dried over $Na_2SO_4/MgSO_4$ and evaporated, and the remaining oil was purified by column chromatography (silica gel, 5% ethyl acetate/hexanes) to yield a clear colorless oil (0.352 g, 70%) with 0.050 g of recovered starting material (13%) $[\alpha]^{25}_D = +1.06°$ (c = 51.4 mg/ mL in benzene); HREIMS 487.2653 *m/z*, 487.2668 $(M - C_4H_9)^+$ calcd for $C_{31}H_{39}O_3Si$; IR (NaCl plates neat cm^{-1}) 3071, 2963, 2858, 1613, 1514, 1248, 1111, 822, 702; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.75−7.72 (m, 4H), 7.48−7.37 (m, 6H), 7.27−7.25 (m, 2H), 6.91−6.87 (m, 2H), 5.86−5.76 (m, 1H), 5.10−5.01 (m, 2H), 4.45 (d, 1H, J = 11.0 Hz), 4.37 (d, 1H, J = 11.0 Hz), 3.86−3.78 (m, 4H), 3.17 (m, 1H), 2.55−2.42 (m, 1H), 1.60−1.50 (m, 1H), 1.50−1.40 (m, 1H), 1.29−1.21 (m, 3H), 1.11 (s, 9H), 1.03 (d, 3H, J = 8.0 Hz), 0.99 (d, 3H, J = 6.3 Hz), 0.95 (d, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.0, 141.0, 135.8, 134.9, 134.5, 131.1, 129.9, 129.3, 129.2, 127.4, 127.3, 114.3, 113.6, 82.7, 72.6, 71.4, 55.2, 40.4, 39.99, 28.9, 28.4, 27.0, 19.3, 18.0, 14.9, 13.8.

(3*R*,4*R*,7*S*,8*R*)-8-(*tert*-Butyldiphenylsiloxy)-4-[(4-methoxybenzyl)oxy]-3,7-dimethyl-1-octanal (36). A solution of compound **35** (0.676 g, 1.241 mmol) in CH_2Cl_2 was subjected to O_3 gas at −78 °C until a light blue color was discernible. The resulting ozonide was quenched by the addition (at −78 °C) of tributylphosphine (0.318 mL, approximately 1 equiv adjusted for purity) followed by slow warming to rt. After 1.5 h the reaction mixture was evaporated and purified by column chromatography (silica gel 5% ethyl acetate in hexanes) to yield 0.516 g (76%) of aldehyde as a clear oil. This material is unstable to β elimination and is used in the next step without delay. $[\alpha]^{25}_D = +0.9°$ (c = 2.5 mg/mL in benzene); HREIMS 545.3087 *m/z*, 545.3087 $(M - H)^+$ calcd for $C_{34}H_{45}O_4Si$; IR (NaCl plates neat cm^{-1}) 3068, 2933, 2857, 1726, 1613, 1514, 1248, 1109, 1037, 822; ^1H NMR ($CDCl_3$, 360 MHz) δ 9.70 (d, 1H, J = 2.2 Hz), 7.72−7.69 (m, 4H), 7.46−7.36 (m, 6H), 7.22−7.18 (m, 2H), 6.86−6.85 (m, 2H), 4.40 (d, 1H, J = 11.1 Hz), 4.34 (d, 1H, J = 11.0 Hz), 3.82−3.76 (m, 4H), 3.58 (m,-1H), 2.61 (dp, 1H, J = 2.1, 6.8 Hz), 5.55−1.46 (m, 2H), 1.38−1.26 (m, 2H), 1.15−1.11 (m, 1H), 1.09 (s, 9H), 1.05 (d, 3H, J = 7.1 Hz), 0.99 (d, 3H, J = 6.2 Hz), 0.93 (d, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 204.5, 159.1, 135.8, 134.7, 134.4, 130.2, 129.4, 129.3, 129.3, 127.4, 127.3, 113.7, 79.0, 72.5, 71.2, 55.2, 49.2, 40.0, 28.7, 27.6, 27.0, 19.2, 18.1, 13.8, 9.9.

(3*R*,4*R*,7*S*,8*R*)-8-(*tert*-Butyldiphenylsiloxy)-1-iodo-4-[(4-methoxybenzyl)oxy]-3,7-dimethyl-1-nonene (5). Aldehyde **36** (86 mg, 0.1372 mmol) from the previous reaction (freshly prepared) was azeotroped with toluene and then dissolved in THF (1 mL), and iodoform (139 mg, 0.3515 mmol) was added. This solution was added to a suspension of $CrCl_2$ (135. mg, 1.099 mmol) in THF (2 mL) at 0 °C. The reaction mixture rapidly turned brown and was allowed to stir at 0 °C for 3 h. The reaction mixture was then partitioned between diethyl ether and water (50 mL ea.), the aqueous layer extracted with diethyl ether (50 mL × 2) and ethyl acetate (50 mL), the organic extracts were dried over $MgSO_4/Na_2SO_4$ and evaporated, and the residue was taken up in CH_2Cl_2, redried with Na_2SO_4, evaporated, and purified by column chromatography (silica gel, 25% CH_2Cl_2 in hexanes) to yield 44 mg (48%) of a clear oil. $[\alpha]^{25}_D = +9.78°$ (c = 71.7 mg/ mL in benzene); HREIMS 669.2264 *m/z*, 669.2261 $(M - H)^+$ calcd for $C_{35}H_{46}IO_3Si$; IR (NaCl plates neat cm-1) 3070, 2961, 2856, 1612, 1514, 1248, 1109, 1037, 953, 908, 821, 737, 702; ^1H NMR ($CDCl_3$, 360 MHz) δ 7.76−7.72 (m, 4H), 7.48−7.38 (m, 6H), 7.31−7.23 (m, 2H), 6.91−6.88 (m, 2H), 6.55−6.49 (m, 1H), 6.05−6.00 (m, 1H), 4.41 (s, 2H), 3.82 (m, 4H), 3.15−3.10 (m, 1H), 2.45−2.35 (m, 1H), 1.60−1.34 (m, 2H), 1.35−1.11 (m, 3H), 1.11 (s, 9H), 1.06−0.99 (m, 6H), 0.95 (d, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 159.1, 148.7, 135.8, 134.9, 134.4, 133.6, 129.5, 129.4, 129.3, 127.4, 127.3, 113.7, 81.8, 75.0, 72.5, 71.8, 55.2, 43.8, 39.9, 28.9, 28.6, 27.0, 19.3, 18.0, 15.2, 13.8.

(3*R*,4*S*,7*R*,8*S*,9*S*,15*R*,16*R*,19*S*,20*R*)-4-(Benzoyloxy)-20-(*tert*-butyldimethylsiloxy)-12-hydroxy-8,16-bis[(4-methoxybenzyl)oxy]-3,7,9,15,19-pentamethyl-1,13-henicosadiene (37). A mixture of aldehyde **4** (41.0 mg, 0.0843 mmol) and vinyl iodide (**5**) (134.1 mg, 0.200 mmol) was azeotroped with toluene to assure dryness. In a glove box this mixture was diluted with THF (1.2 mL) and DMF (0.3 mL), and $CrCl_2$[29] doped with 0.1% $NiCl_2$ was added (60 mg, 0.49 mmol). The reaction mixture was allowed to stir for 60 h and then opened to air and partitioned between CH_2Cl_2 and saturated NH_4Cl solution (50 mL ea.). The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL) and ethyl acetate (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated to a green paste, and this was paste purified by column chromatography (silica gel, 10% to 15% ethyl acetate in hexanes) to yield 55.1 mg (65%) of the coupled allylic alcohol as a clear oil containing trace ethyl acetate. This mixture of diastereomers is not separable, and is taken on as a mixture to the next step. HRFABMS 1023.6147 *m/z*, $((M - H)^+)$[30] 1023.6170 calcd for $C_{65}H_{87}O_8Si$; IR (NaCl plates neat cm^{-1}) 3475, 3074, 2932, 1717, 1614, 1514, 1271, 1248, 1109, 821, 702; ^1H NMR ($CDCl_3$, 360 MHz) δ 8.1−8.03 (m, 2H), 7.70−7.67 (m, 4H), 7.57−7.52 (m, 1H), 7.45−7.33 (m, 8H), 7.24−7.19 (m, 4H), 6.85−6.80 (m, 4H), 5.92−5.82 (m, 1H), 5.62−5.53 (m, 1H), 5.47−5.39 (m, 1H), 5.12−5.07 (m, 3H), 4.50−4.43 (m, 2H), 4.38−4.30 (m, 2H), 4.02−3.92 (m, 1H), 3.80-3.73 (m, 7H), 3.14−3.09 (m, 1H, 3.04−3.00 (m, 1H), 2.59−2.49 (m, 1H), 2.45−2.37 (m,1H), 1.73−1.65 (m, 4H), 1.55−1.35 (m, 7H), 1.35−1.10 (m, 4H), 1.08 (d, 3H, J = 7.0 Hz), 1.06 (s, 9H), 1.00−0.89 (m, 15H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 171.1, 166.2, 166.2, 159.0, 158.8, 139.1, 135.8, 134.8, 134.4, 134.2, 133.7, 133.1, 133.0, 132.7, 131.2, 130.9, 130.5, 129.5, 129.4, 129.3, 129.1, 129.1, 129.0, 128.3, 127.4, 127.3, 115.7, 113.6, 113.5, 86.3, 86.3, 82.7, 82.7, 77.8, 74.5, 73.4, 73.0, 72.6, 71.5, 71.4, 60.3, 55.1, 41.4, 41.4, 39.9, 39.3, 39.1, 35.7, 35.6, 35.5, 34.9, 34.8, 30.2, 30.1, 30.0, 29.7, 29.3, 28.6, 28.6, 26.9, 20.9, 19.2, 18.1, 18.0, 16.3, 16.3, 15.8, 15.6, 15.2, 15.2, 15.1, 14.9, 14.8, 14.1, 13.8.

(3*R*,4*S*,7*R*,8*R*,9*S*,15*R*,16*R*,19*S*,20*R*)-4-(Benzoyloxy)-20-(*tert*-butyldimethylsiloxy)-8,16-bis[(4-methoxybenzyl)oxy]-3,7,9,15,19-pentamethyl-1,13-henicosadien-12-one (38). Allylic alcohol **37** (48.3 mg, 0.0471 mmol) was dissolved in CH_2Cl_2 (not distilled) and treated with a solution of Dess−Martin periodinane (0.3878 g, 0.9146 mmol) dissolved in CH_2Cl_2 (10 mL, not distilled) and pyridine (0.80 mL, not distilled). After allowing the reaction mixture to stir for 1 h at rt it was diluted with hexanes (15 mL) and the entire reaction mixture (approximately 31 mL volume) was purified by column chromatography (silica gel, 10% ethyl acetate in hexanes, approximately 30 mL of dry vol silica gel) to yield 39.9 mg (83%) of pure ketone and 6.4 (13%, 0.00625 mmol) mg of ketone containing some aromatic contaminant for an overall yield of 46.3 mg (96%). $[\alpha]^{25}_D = -0.1°$ (c = 39.9 mg/ mL in benzene); HRFABMS 1021.6017 *m/z*, 1021.6014 $(M - H)^+$ calcd for $C_{65}H_{85}O_8Si$; IR (NaCl plates neat cm^{-1}) 3073, 3033, 2963, 1717, 1612, 1514, 1271, 1248, 1111, 824, 708; ^1H NMR ($CDCl_3$, 360 MHz) δ 8.06−8.03 (m, 2H), 7.70−7.66 (m, 4H), 7.57−7.52 (m, 1H), 7.46−7.33 (m, 8H), 7.23−7.18 (m, 4H), 6.86−6.57 (m, 5H), 6.05 (dd, 1H, J = 0.9, 16.1 Hz), 5.92−5.82 (m, 1H), 5.13−5.07 (m, 3H), 4.50−4.43 (m, 2H), 4.35 (s, 2H), 3.80−3.70 (m, 4H), 3.22−3.18 (m, 1H), 3.04 (t, 1H, J = 5.1 Hz), 2.60−2.40 (m, 4H), 1.80−1.60 (m, 5H), 1.55−1.36 (m, 4H), 1.34−1.10 (m, 4H), 1.09−1.01 (m, 15H), 0.96−0.88 (m, 12H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 200.4, 166.2, 159.0, 158.9, 149.1, 139.1, 135.8, 134.8, 134.4, 132.7, 131.1, 130.5, 130.5, 129.9, 129.5, 129.4, 129.3, 129.2, 129.0, 128.2, 127.4, 127.3, 115.7, 113.6, 113.5, 86.4, 82.0, 77.8, 74.5, 72.5, 71.6, 55.1, 53.3, 41.4, 39.9, 37.9, 35.6, 35.4, 30.2, 29.3, 28.9, 28.3, 26.9, 19.2, 18.1, 16.3, 15.0, 15.0, 14.8, 13.8.

(3*R*,4*S*,7*R*,8*R*,9*S*,15*R*,16*R*,19*S*,20*R*)-4-(Benzoyloxy)-20-(*tert*-butyldimethylsiloxy)-8,16-bis[(4-methoxybenzyl)oxy]-3,7,9,15,19-pentamethyl-1-henicosen-12-one (39). Enone **38** (39.3 mg, 0.0383 mmol) was dissolved in degassed benzene-d_6 (1.5 mL) and water (30 μL). A solution of (CuH-

(29) $CrCl_2$ was obtained from RocRic as "anhydrous". This material was green and was heated at 160 °C for 6 days under high vacuum before the gray color, indicating truly anhydrous $CrCl_2$, was obtained.

(30) While it is unusual to observe $(M - H)^+$ in FAB mass spectroscopy we found that vinyl iodide **5** exhibited this ion in both FAB and EI spectra. Additionally in the EI spectra $(M - C_4H_9)^+$ was also found confirming that we have the correct structure. We believe that the anomaly that is causing $(M - H)^+$ to occur in the FAB spectra of **5** is also occurring in this case.

$PPh_3)_6$ in deuterated benzene (0.1068 g, in 3.0 mL of benzene, degassed) was then titrated into the enone solution over 1 h (initial 1.40 mL portion followed by two 0.30 mL portions for an over all 2.00 mL of solution, 0.0328 mmol) until NMR showed complete removal of the enone ^{1}H peak at 6.05 ppm in the ^{1}H NMR spectra. The reaction was opened to air and vacuum evaporated to a paste which was purified by column chromatography (silica gel, 20% ethyl acetate in hexanes and then again in 5−10% ethyl acetate in hexanes) to yield 39.2 mg (99.7%) of a clear oil containing only trace starting material. $[\alpha]^{25}_D = -2.0°$ (c = 39.2 mg/ mL in benzene); HRFABMS 1024.6238 m/z, (M^+) 1024.6248 calcd for $C_{65}H_{88}O_8Si$; IR (NaCl plates neat cm^{-1}) 3073, 2961, 1717, 1613, 1514, 1248, 1111, 822, 708; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10−8.08 (m, 2H), 7.74−7.72 (m, 4H), 7.61−7.58 (m, 1H), 7.49−7.39 (m, 8H), 7.31−7.24 (m, 4H), 6.89−6.83 (m, 4H), 5.95−5.88 (m, 1H), 5.16−5.12 (m, 3H), 4.51 (s, 2H), 4.39 (d, 1H, J = 11.0 Hz), 4.33 (d, 1H, J = 11.0 Hz), 3.83−3.81 (m, 7H), 3.13−3.11 (m, 1H), 3.06 (t, 1H, J = 5.1 Hz), 2.61−2.55 (m, 1H), 2.50−2.32 (m, 4H), 1.80−1.65 (m, 7H), 1.59−1.50 (m, 2H), 1.45−1.20 (m, 7H), 1.13 (d, 3H, J = 6.9 Hz), 1.11 (s, 9H), 1.10-0.93 (m, 12H), 0.87 (d, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 211.1, 166.2, 159.0, 159.0, 139.2, 135.9, 135.0, 134.5, 132.8, 131.2, 131.1, 130.6, 129.5, 129.4, 129.3, 129.3, 129.1, 128.3, 127.5, 127.4, 115.8, 113.7, 113.6, 86.4, 82.9, 77.9, 74.5, 72.7, 71.2, 55.2, 55.2, 41.5, 40.9, 40.6, 40.1, 35.7, 35.4, 34.9, 30.3, 29.4, 28.6, 28.1, 27.6, 27.0, 26.8, 19.3, 18.1, 16.4, 15.0, 14.9, 14.6, 13.8.

Spirocyclic Compound 40. A solution of compound **39** (37.7 mg, 0.0368 mmol) in CH_2Cl_2 (8 mL) and water (0.40 mL) was treated with DDQ (31.5 mg, 0.139 mmol) in CH_2Cl_2 (1 mL), and the resulting mixture was allowed to stir at rt for 40 min. The reaction mixture was partitioned between saturated sodium bicarbonate solution (10 mL) and the aqueous layer extracted with CH_2Cl_2 (4 × 10 mL). The organic extracts were combined, dried over Na_2SO_4, and evaporated, and the resulting oil was purified by column chromatography (silica gel, 5% ethyl acetate in hexanes and then in 2.5% ethyl acetate in hexanes) to yield 19.3 mg (67%) of spirocyclic compound **40**. $[\alpha]^{25}_D = -20.4°$ (c = 19.3 mg/mL in benzene); HRFABMS 765.4894 m/z, 765.4914 $(M - H)^+$ calcd for $C_{49}H_{69}O_5Si$, also possible MH^+ overlapping isotope peak from $(M - H)^+$ 767.5068, 767.5071 calcd for $C_{49}H_{71}O_5Si$; HREIMS found 709.4285 m/z, 709.4288 calcd for $(M - C_4H_9)^+$ $C_{45}H_{61}O_5Si$; IR (NaCl plates neat cm^{-1}) 3071, 2932, 1719, 1271, 1111, 706; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 8.04−8.02 (m, 2H), 7.69−7.65 (m, 4H), 7.55−7.53 (m, 1H), 7.44−7.34 (m, 8H), 5.88−5.81 (m, 1H), 5.08−5.02 (m, 3H), 3.82−3.78 (m, 1H), 3.22 (dd, 1H, J = 2.2, 10.1) 3.06 (ddd, 1H, J = 9.5, 9.5, 1.8) 2.56−1.95 (m, 1H), 1.76−1.65 (m, 2H), 1.60−1.48 (m, 7H), 1.48−1.10 (m, 11H), 1.07−1.03 (m, 12H), 0.97−0.90 (m, 9H), 0.85−0.79 (m, 4H), 0.75 (d, 3H, J = 6.5); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 166.3, 139.1, 135.1, 134.5, 132.8, 130.6, 129.5, 129.4, 129.3, 128.3, 127.4, 127.3, 115.8, 95.5, 77.9, 74.6, 74.6, 72.5, 41.31, 40.2, 36.1, 34.8, 34.8, 31.0, 30.2, 28.7, 28.5, 28.2, 27.5, 27.4, 27.0, 26.6, 19.3, 18.3, 18.0, 16.6, 16.5, 14.4, 10.8.

Supporting Information Available: 90-MHz ^{13}C NMR spectra of new compounds (34 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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