Asymmetric Intramolecular Diels-Alder Cycloadditions of 2-Pyrone-3-Carboxylates and Synthesis of Vitamin D_3 A Ring Phosphine Oxide

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Received April 25, 1998

Intramolecular Diels-Alder cycloadditions of 2-pyrone-3-carboxylates with *trans*-vinyl silaketal groups tethered *via* a chiral, non-racemic 1,3-butanediol auxiliary proceeded in unexpected stepwise cycloadditions through ionic intermediates to provide *cis*-disubstituted bicylolactones. The ratio of two isomers, *exo* and endo, was 5 to 1, and each isomer was found to be diastereomerically pure (>99% de). Their relative and absolute stereochemistries were determined by ^{1}H NMR spectroscopy and confirmed by X-ray crystallography of minor, endo-adduct **9**. The major *exo*-adduct was successfully transformed to (−)-2-butyl substituted A-ring phophine oxide **16**, a key element for the synthesis of 2-butyl vitamin D_3.

Introduction

As a part of the research program involving synthesis of new calcitriol analogs as anticarcinogenic reagents and for chemotherapy of osteoporosis, we were interested in 2-alkyl substituted vitamin D_3 compounds.[1] A simple expansion of our methodology which utilizes intermolecular Diels-Alder cycloadditions of 2-pyrones with silyl enol ethers was not applicable mainly because the reactivity of 2-pyrones is not sufficient to tolerate any substituent groups on the silyl enol ether.[2] High pressure can be used, but from which no asymmetry can be expected.[1b] For both enhancement of chemical reactivity and introduction of chirality,[3] we connected 2-pyrone-3-carboxylates to dienophiles through chiral tether groups for the cycloadditions to occur intramolecularly.[4] Among the systems studied, a vinyl silaketal linked *via* a chiral, non-racemic 1,3-diol gave the best results in both chemical yield and asymmetric induction. We herein report intramolecular cycloadditions of such systems, and propose an explanation for the high diasteroselectivity (>99% de) we observed, as well as the subsequent transformations of the *exo*-cycloadduct **8** into (−)-2-butyl A ring phosphine oxide **16**.

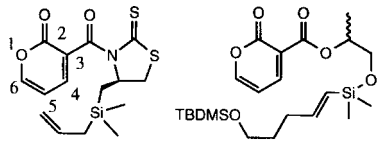
Results and Discussion

System **1** (Table 1) represents a pyrone carboxylate and allylic silane that were connected through a chiral thiazolidinethione.[5] Both thermal (120 °C up to 7 days) and high pressure (140 kpsi up to 7 days) conditions failed to provide the corresponding cycloadducts. Low reactivity of the dienophile, allylic silane, could account for the failures. Cycloadditions of system **2** (Table 1), linked with vinyl silane through 1,2-diol as a tether, also failed under the same conditions. The possible reasons for these failures, however, could be two-fold: 1) the reactivity of the vinyl silane might still be insufficient, and/or 2) the vinyl silane did not match the pyrone electronically.[6] From our earlier study, we learned that the carbon 6 in 2-pyrone-3-carboxylate carries the most positive partial charge.[7] Thus the carbons 6 and 3 in the pyrone would have to line-up to the α-carbon and to the β-carbon next to the silicon, respectively. This alignment would exert too severe distortions, particularly in the portion of the tether group, for a cycloaddition to occur.

The systems in Table 2 were prepared, and this time vinyl silaketals were used as dienophile partners to be consistent with the above electronic factors.[8] The tether groups are chiral 1,2-propanediol for system **3** and chiral 2, 3-butanediol for system **4**.

Attempted thermal cycloaddition reactions led only to the decomposition of the labile vinly silaketal group. When they were pressurized, systems **3** and **4** underwent the desired cycloadditions to provide a mixture of *endo*-**5** and

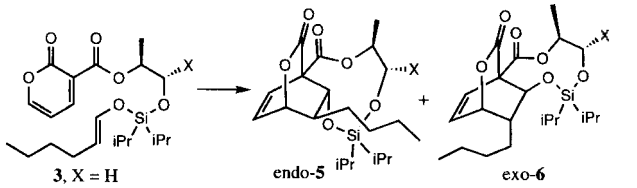
Table 1.



1 **2**

Condition	Result
RT → Δ (up to 7 days)	no reaction
14 kpsi (up to 70 days)	no reaction

Table 2.



3, X = H
4, X = CH_3

endo-**5** (diastereomeric mixture)

exo-**6** (diastereomeric mixture)

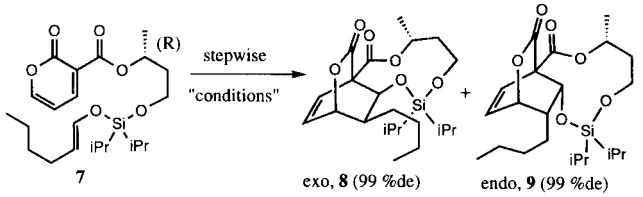
Condition		Total yield (**5**+**6**)
RT → Δ		decomposition
140 kpsi	**3**	50%
	4	50%

exo-**6**, each of which consisted of two diastereomers, in 50% total yield. The 2,3-butanediol tethered system **4** gave the similar results,[9] although it seemed to somewhat increase the rate of the reaction to reach 50% conversion through a buttressing effect. We then increased the length of the tether group to reduce the torsional strain that might exist in the transition state during the intramolecular cycloadditions. System **7** (Table 3)[10] was thus prepared and subjected to the cycloaddition reactions. Thermal reaction conditions resulted in similar breakage of the vinyl silaketal group as was observed in systems **3** and **4**. Upon being pressurized at 140 kpsi for 7 days in toluene, system **7** provided a mixture of the isomeric cycloadducts in 56% total yield.[9] Although we were pleased with these first examples of the intramolecular cycloadditions of the 2-pyrone-3-carboxylates, we decided to run the reactions in the presence of Lewis acids. After 4 days at −30 °C in toluene and ethyl ether, the system **7** underwent a cycloaddition in the presence of $ZnBr_2$ to provide a mixture of *exo*-**8** and *endo*-**9** in 90% total yield with a ratio of 5 : 1. Other Lewis acids $MgBr_2$ and Et_2AlCl gave similar results. The stereochemical assignments of the two isomers were made mainly based on ^1H and ^{13}C NMR spectroscopy, which were further confirmed by single crystal X-ray crystallography of the minor product, *endo*-**9**.[11]

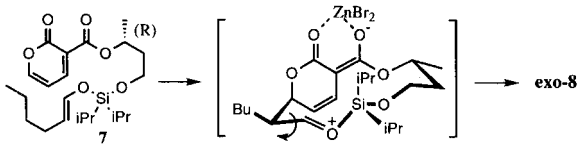
Under the influence of Lewis acid, the cycloaddition proceeded in a stepwise fashion[12] rather than concerted to give rise to *cis*-disubstituted cycloadducts. As outlined in Scheme 1, a zwitterionic species was formed initially *via* 1,6 conjugate addition of the silyl enol ether to C6 on the pyrone system. This intermediate survived long enough to allow a rotation of the siloxy group to relieve the tortional strain in the linker. Upon final cyclization, *cis* adducts were formed. The possible retro-Aldol mechanism was excluded as a possible cause for the formation of *cis*-adducts because the *exo-trans* adduct, prepared earlier, was stable under the same reaction conditions used here. Lewis acid promoted *E*-*Z* isomerization of *E*-silyl enol ether was not observed under the reaction condition. The preferable formation of the *cis*-exo cycloadduct from the system **7** is believed to be due to the more stable endo transition state (secondary orbital interaction, endo TS led to *exo*-**8** because of the bond rotation).

More impressive was that both isolated exo and endo adducts were diastereomerically pure (>99%), not a mixture, based on NMR spectroscopy and their optical rotations. Apparently, the chiral methyl group in the tether served a

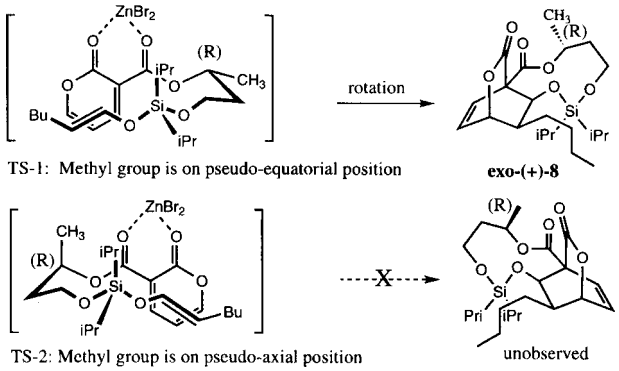
Table 3.



Conditions (4 days)	Total yield	8:9	%de
$ZnBr_2$/ − 30 °C/toluene	67%	2:1	not measured
$MgBr_2$/ − 30 °C/toluene	65%	2:1	not measured
$ZnBr_2$/ − 30 °C/toluene-ether (2:1)	90%	5:1	>99



Scheme 1

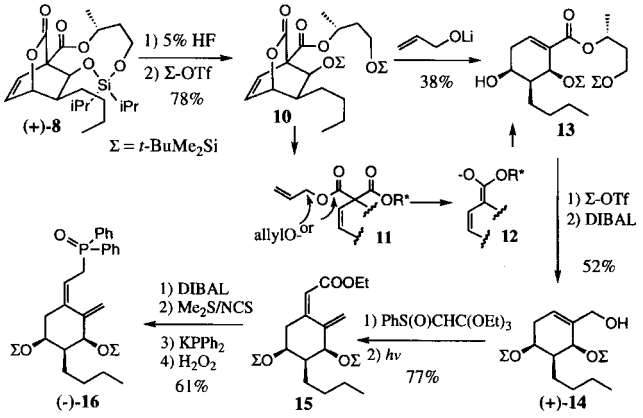


Scheme 2

critical role in this high and almost complete chiral induction. In the formation of the *exo*-adduct, there are two possible transition states, TS-1 and TS-2, which differ in the direction of the approaching vinyl silaketal group with respect to the face of the pyrone (Scheme 2).

TS-1, where the methyl group is in the pseudo-equatorial position, would be at lower energy state than TS-2, where the methyl group is in the pseudo-axial position. This energy difference in the transition state could be large enough at −30 °C, leading to the dominant formation of the single diastereomer whose absolute stereochemistry, assigned spectroscopically and by comparison with similar systems,[11] is as drawn. The same argument can be applied to the exclusive formation of single diasteromeric *endo*-adduct **9** whose absolute stereochemistry is confirmed by X-ray crystallography to be as shown in Table 3.

Diastereomerically pure exo-(+)-**8**, the major adduct, was then carried through for the synthesis of optically active, 2-butyl substituted A-ring phosphine oxide **16** (Scheme 3). Upon silaketal ring openning with 5% HF and subsequent protection of the resulting diols with TBDMS (*t*-butyldimethylsilyl) triflate, the O-silylated cycloadduct **10** was obtained. Lactone ring opening with excess lithium allyl-



Scheme 3

oxide provided unexpected tetrasubstituted cyclohexene **13**, presumably *via* formation of mixed allyl methyl malonate **11**, followed by concomitant deallyloxycarbonylation,[13] resulting from the attack of allyloxide in either direction of the arrows, and double bond conjugation as depicted in Scheme 3. O-silylation and reduction of the conjugated enoate **13** provided allylic alcohol (+)-**14**, which was converted to Z dienoate **15** using our sulfinylated orthoester protocol.[14] In this one-flask reaction, the enoate **13** underwent two-carbon homologation *via* a Claisen rearrangement followed by a spontaneous thermal sulfoxide elimination to give *E* and *Z* mixture of dienoate. The undesired *E* dienoate was photochemically isomerized to *Z* dienoate **15** that was subsequently transformed to optically active, A-ring phosphine oxide (−)-**16** after a few more reactions involving reduction, chlorination, displacement, followed by oxdiation.

The phosphine oxide (−)-**16** can be readily converted to 2β-butyl-1β,25-dihydroxyvitamin D_3 through Lythgoe coupling reaction with CD ring.[15] This highly diastereospecific intramolecular cycloaddition methodology was also successfully applied to construct a new calcitriol analog 2β-(3'-fluoropropyl)-1β,25-dihydroxyvitamin D_3.[1a] Conclusively, 2-pyrone-3-carboxylates with β-substituted vinyl silaketal, connected through 1,3-butanediol linker, underwent smooth intramolecular Diels-Alder cycloadditions with high asymmetric induction. This strategy using chiral, nonracemic 1,3-butanediol as a tether could be further applied to intramolecular cycloadditions of not only pyrone systems, but also other dienes for efficient and high asymmetric control.

Experimental Section

Cycloadducts (+)-8 and (−)-9. To a flame dried 50 mL flask charged with 0.310 g (7.3 mmol) of the pyrone enol ether **7**, 3 mL of anhydrous ether and 6 mL of anhydrous toluene was added 0.160 g (7.3 mmol) of $ZnBr_2$. Upon addition, the reaction mixture was cooled to −30 °C and stirred for 4 days. The reaction mixture was then concentrated by rotary evaporator and directly purified by column chromatography (97/3 hexane/EtOAc) to afford 0.233 g of the exo-cycloadduct **8** in 75% yield along with 0.045 g (15% yield) of the crystalline endo-cycloadduct **9**. For (+)-**8**: ^{1}H NMR ($CDCl_3$) δ 6.77 (dt, *J*=8.0, 1.2 Hz, 1H), 6.59 (dd, *J*=8.0, 5.2 Hz, 1H), 5.54-5.46 (m, 1H), 4.98 (dt, *J* =5.2, 1.6 Hz, 1H), 4.38 (s, 1H), 3.89-3.77 (m, 2H), 1.88-1.28 (m, 8H), 1.34 (d, *J*=6.4 Hz, 3H), 1.25-1.16 (m, 1H), 1.03 (d, *J*=3.2 Hz, 3H), 1.01 (d, *J*=3.6 Hz, 3H), 0.92-0.87 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 168.5, 167.0, 130.8, 129.3, 76.4, 75.4, 70.3, 62.6, 59.8, 49.2, 37.7, 30.1, 29.3, 22.4, 20.6, 17.6, 17.4, 17.3, 17.2, 13.8, 12.7, 10.5; FT-IR ($CHCl_3$) 2945, 2868, 1769, 1724, 1464, 1364, 1291 cm^{-1}; HRMS, m/e (M^+-*i*Pr) calc. for $C_{19}H_{31}O_6Si$ 381.1733, found 381.1740; $[\alpha]_D^{24}$ +17.5 (c=22 mg/mL, CH_2Cl_2). For (−)-**9**: ^{1}H NMR ($CDCl_3$) δ 6.83 (dt, *J*=8.0, 1.2 Hz, 1H), 6.51 (dd, *J*=8.0, 5.0 Hz, 1H), 5.60-5.56 (m, 1H), 5.06 (m, 1H), 4.94 (d, *J*=7.6 Hz, 1H), 3.95 (m, 1H), 3.84 (m, 1H), 2.41 (m, 2H), 1.85 (m, 2H), 1.50-1.20 (m, 9H), 1.40 (d, *J*=6.4 Hz, 3H); HRMS, m/e (M^+-*i*Pr) calc. for $C_{19}H_{31}O_6Si$ 381.1733, found 381.1739; $[\alpha]_D^{24}$ −1.8 (c=35 mg/mL, CH_2Cl_2). Single crystal X-ray analysis showed the absolute stereochemistry of (−)-9 to be as shown in Table 3.

Bis-Silyl Ether 12. To a 100 mL round bottomed flask charged with 0.270 g (6.4 mmol) of (+)-**8** was added 27 mL of 5% HF in acetonitrile at RT. After 20 min, the reaction mixture was neutralized with aq. $NaHCO_3$ and extracted with $CHCl_3$ (2×50 mL). The combined solution was dried over $MgSO_4$, concentrated by rotary evaporator and dissolved in 10 mL of DMF. To this solution were added 0.61 mL (2.6 mmol) of *t*-butyldimethylsilyl trifluoromethane sulfonate (TBDMS-OTf) and 0.30 mL (0.26 mmol) of 2,6-lutidine at RT. After 2 hours at RT, the reaction mixture was dumped into 50 mL of H_2O and extracted with ether (2×25 mL). The combined ethereal solution was dried over $MgSO_4$, concentrated and purified by column chromatography (90/10 hexane/ether) to give 0.270 g of the bis-silyl ether **10** as a light green oil in 79% yield from the *exo*-cycloadduct **8**. ^{1}H NMR ($CDCl_3$) δ 6.69 (dt, *J*=7.6, 1.2 Hz, 1H), 6.55 (dd, *J*=7.6, 5.2 Hz, 1H), 5.20-5.12 (m, 1H), 5.02 (dt, *J*=5.2, 1.2 Hz, 1H), 4.16 (bs, 1H), 3.72 (ddd, *J*=7.2, 7.2, 0.8 Hz, 2H), 2.01-1.93 (m, 1H), 1.82-1.73 (m, 1H), 1.65-1.57 (m, 2H), 1.55-1.42 (m, 1H), 1.36 (d, *J*=6.4 Hz, 3H), 1.37-1.27 (m, 4H, overlapped), 0.92 (t, *J* =7.2 Hz, 3H), 0.88 (s, 9H), 0.78 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 167.0, 166.7, 130.4, 130.1, 75.9, 73.6, 71.1, 63.0, 59.6, 49.4, 39.0, 30.0, 29.5, 25.9, 25.5, 22.6, 20.1, 18.2, 17.8, 13.9, −4.3, −5.2, −5.4, −5.4; FT-IR ($CHCl_3$) 2957, 2931, 2858, 1760, 1733, 1472, 1464, 1362, 1288, 1258, 1094 cm^{-1}; HRMS, m/e (M^+-*t*Bu) calc. for $C_{24}H_{43}O_6Si_2$ 483.2598, found 483.2594.

Enoate 13. To a 50 mL flame dried round bottomed flask charged with 37.0 mg (mmol) of the bis-silyl ether **10** was cannulated at 0 °C 2 mL of lithium allylic oxide in allylic alcohol (0.7 M), prepared from 4 mL of nBuLi (1.4 M in hexane) and 4 mL of freshly distilled allylic alcohol at 0 °C. After 30 min. at 0 °C, the reaction mixture was warmed to RT and stirred for 10 hours. Upon quenching with sat NH_4Cl, the product mixture was extracted with CH_2Cl_2 (2×10 mL), dried over $MgSO_4$, concentrated by rotary evaporator and chromatographed (10% EtOAc/hexane) to give 12.3 mg of the enoate 13 in 38% yield. ^{1}H NMR ($CDCl_3$) δ 6.87 (dd, *J*=5.2, 2.4 Hz, 1H), 5.10-5.02 (m, 1H), 4.64 (d, *J*=2.4 Hz, 1H), 4.37 (ddd, *J*=10.8, 6.0, 4.0 Hz, 1H), 3.65 (ddd, *J*=8.4, 6.0, 2.0, 2H), 2.49 (dt, *J*=19.2, 5.6 Hz, 1H), 2.09 (ddd, *J*=19.6, 10.4, 2.8, 1H), 1.95-1.83 (m, 2H), 1.78-1.70 (m, 1H), 1.60-1.23 (m, 7H, overlapped), 1.28 (d, *J*=6.4 Hz, 3H), 0.88 (t, 3H, overlapped), 0.87 (s, 9H), 0.85 (s, 9H), 0.15 (s, 3H), 0.07 (s, 3H), 0.02 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 166.0, 139.1, 131.4, 68.7, 67.7, 65.0, 59.5, 47.2, 39.1, 31.2, 30.4, 25.83, 25.80, 23.1, 22.6, 20.1, 18.2, 17.9, 14.0, 4.5, −4.9, −5.4, −5.5; FT-IR ($CHCl_3$) 3613, 3020, 2957, 2930, 2858, 1704, 1472, 1253 cm^{-1}; HRMS, m/e (M^+-*t*Bu) calc. for $C_{23}H_{45}O_5Si_2$ 457.2806, found 457.2809.

O-Silyl Allylic Alcohol (+)-14. To flask charged with 15.8 mg (0.03 mmol) of the enoate **13** in 0.3 mL of DMF were added 0.014 mL of TBDMS-OTf (0.06 mmol, 2 eq.) and 0.006 mL of 2,6-lutidine at RT. After 4 hours at RT, the product mixture was diluted with ether, washed with H_2O and brine, concentrated by rotary evaporator and chromatographed (10% EtOAc/hexane) to give 30.0 mg of crude O-silylated product contaminated with some high

running material. To this crude product in 1.5 mL of anhydrous toluene was added 0.4 mL (0.4 mmol) of DIBAL-H at −78 °C. After 40 min. at −78 °C, the reaction mixture was treated with 1 mL of sodium potassium tartrate (2 M in H_2O and EtOH), and the resulting solution was warmed to RT. After 10 min, the organic layer was decanted, and the aqueous layer was further extracted with 10 mL of CH_2Cl_2. The combined organic solution was dried over $MgSO_4$, filtered through a plug of Celite, concentrated by rotary evaporator and chromatographed (10% EtOAc/hexane) to give 7.0 mg of the allylic alcohol (+)-**14** and 3.5 mg of the monoprotected chiral diol in 52% and 54% overall yield, respectively. ^{1}H NMR ($CDCl_3$) δ 5.67-5.65 (m, 1H), 4.21 (ddd, *J*=9.6, 5.6, 4.0, 1H), 4.14 (d, *J*=2.0 Hz, 1H), 4.06 (d, *J*=1.2 Hz, 2H), 2.14 (dt, *J*=17.2, 5.6 Hz, 2H), 2.03-1.96 (m, 1H), 1.76-1.71 (m, 1H), 1.43-1.22 (m, 7H), 0.91 (t, 3H, overlapped), 0.90 (s, 9H), 0.88 (s, 9H), 0.123 (s, 3H), 0.119 (s, 3H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 137.0, 125.2, 70.4, 66.1, 65.4, 47.5, 31.2, 30.1, 25.8, 23.1, 18.02, 17.93, 14.05, −4.2, −4.6, −4.7, −4.8; FT-IR ($CHCl_3$) 3606, 3015, 2957, 2930, 2858, 1472, 1463, 1256 cm^{-1}; $[\alpha]_D^{23}$ C+32 (c=0.016, CH_2Cl_2); HRMS, m/e (M^+-*t*Bu) calc. for $C_{19}H_{39}O_3Si_2$ 371.2438, found 371.2443.

Z-Dienoate 15. To a 5 mL hydrolysis tube were charged 26 mg (0.06 mmol) of the allylic alcohol (+)-**14**, 100 mg of 1-(phenylsufinyl)-2,2,2-triethoxylethane, 2 mg of 2,4,6-trimethylbenzoic acid and 1.5 mL of CH_2Cl_2. The tube was then sealed and heated at 150 °C for 12 hr. The product mixture was cooled, filtered through a plug of silica gel with ether, concentrated by rotary evaporator and chromatographed (100% hexane → 5% EtOAc/hexane) to give 30 mg of product as a mixture of E and Z-dienoate. A 5 mL borosilicate test tube was charged with the product mixture, 2 mg (0.01 mmol, 0.2 eq) of 9-fluorenone and 2 mL of *tert*-butyl methyl ether. The test tube was then placed in a 2 M aq. solution of sodium orthovanadate (Na_3VO_4) and irradiated with a medium pressure mercury arc lamp for 12 hours. This product mixture was purified by prep TLC (25% EtOAc/hexane) to afford 23 mg of the Z-dienoate **15** in 77% overall yield. ^{1}H NMR ($CDCl_3$) δ 5.60 (t, *J*=1.2 Hz, 1H), 5.16 (dd, *J*=2.0, 1.6 Hz, 1H), 5.04 (dd, *J*=2.0, 1.2 Hz, 1H), 4.24-4.21 (m, 2H), 4.16-4.06 (m, 2H), 2.35 (ddd, *J*=13.2, 6.4, 1.2 Hz, 1H), 2.30-2.26 (m, 1H), 1.61-1.55 (m, 2H), 1.46-1.39 (m, 2H), 1.32-1.20 (m, 6H), 1.23 (t, *J*=7.2, 3H, overlapped), 0.92 (s, 9H), 0.87 (s, 9H), 0.071 (s, 3H), 0.068 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.9, 153.5, 117.3, 111.9, 76.3, 74.4, 68.4, 59.7, 50.9, 44.4, 29.7, 25.83, 25.77, 25.5, 23.0, 18.2, 18.1, 14.2, 14.0, −4.2, −4.6, −5.01, −5.03; FT-IR ($CHCl_3$) 2943, 2857, 1719, 1472 cm^{-1}; HRMS, m/e (M^+) calc. for $C_{27}H_{52}O_4Si_2$ 496.3404, found 496.3410. (M^+-*t*Bu) calc. 439.2700, found 439.2699.

Phosphine Oxide (−)-16. To a 25 mL flame dried round bottomed flask charged with 38.0 mg (0.1 mmol) of the Z-dienoate **15** and 2 mL of anhydrous toluene was added 0.33 mL (0.3 mmol, 3 eq.) of DIBAL-H (1.0 M in toluene) at −78 °C. After 55 min. at −78 °C, the reaction mixture was treated with 3 mL of sodium potassium tartrate (2 M in H_2O and EtOH) at −78 °C. The product mixture was then warmed to RT, stirred for 10 min and diluted with H_2O. The solution was extracted with 20 mL of CH_2Cl_2 and 20 mL of $CHCl_3$. The combined organic solution was dried over $MgSO_4$ and concentrated in vacuo to give 35 mg of the crude product allylic alcohol as a tan oil. To a separate 25 mL flame dried round bottomed flask charged with 78.0 mg (0.06 mmol) of NCS (N-chloro succinimide) and 2 mL of CH_2Cl_2 was added 0.05 mL (0.06 mmol) of DMS (dimethylsulfide) at 0 °C (reaction mixture immediately turned to white turbid solution). After 10 min at 0 °C, the reaction mixture was cooled to −20 °C with dry ice-ethylene glycol bath. To this solution was added the crude allylic alcohol dissolved in 1.5 mL of CH_2Cl_2 at −20 °C. After 2 hours, the product mixture was diluted with H_2O and extracted with CH_2Cl_2 (2×20 mL). The combined organic solution was dried over $MgSO_4$, concentrated by rotary evaporator and filtered through a plug of florisil with 20% EtOAc/hexane and concentrated *in vacuo* to give the crude allylic chloride as a tan oil. This crude allylic chloride was then placed in 10 mL flame dried round bottomed flask with 1 mL of THF. To this solution was added of potassium diphenylphosphine (1 M solution in THF) until the red color persisted (about 10 mL was added) at −78 °C. After 1 hour at −78 °C, the reaction mixture was quenched with 2 mL of H_2O, extracted with twice with 10 mL of CH_2Cl_2. The combined solution was dried over $MgSO_4$ and concentrated to reduced volume. To this solution was added 7 to 8 drops of 30% H_2O_2 at RT. After 20 min at RT, the reaction mixture was partitioned into H_2O and CH_2Cl_2. The organic layer was decanted, and the aqueous layer was extracted with 10 mL of CH_2Cl_2. The combined solution was then dried over $MgSO_4$, concentrated by rotary evaporator and purified by prep TLC (70% EtOAc/hexane) to afford 30 mg of the phosphine oxide (−)-**16** as a white, viscous oil in 61% overall yield from the Z-dienoate **15**. ^{1}H NMR ($CDCl_3$) δ 7.74-7.69 (m, 4H), 7.55-7.44 (m, 6H), 5.30 (ddt, *J*=14.0, 7.2, 0.8 Hz, 1H), 5.09 (s, 1H), 4.75 (d, *J*=1.6 Hz, 1H), 4.12 (dt, *J*=6.8, 3.6Hz, 1H), 4.09 (d, *J*=7.2 Hz, 1H), 3.34 (ddd, *J*=22.8, 14.8, 8.4 Hz, 1H), 3.18 (ddd, *J*=22.8, 15.2, 7.2 Hz, 1H), 2.30-2.24 (m, 1H), 2.22-2.17 (m, 1H), 1.57-1.52 (m, 1H), 1.47-1.15 (m, 6H), 0.91 (s, 9H), 0.88 (t, *J*=7.6 Hz, 3H, overlapped), 0.82 (s, 9H), 0.05 (s, 3H), 0.006 (s, 3H), −0.001 (s, 3H), −0.032 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 146.7 (t, *J*=4.4 Hz), 141.4 (d, *J*=45.6 Hz), 133.3 (d, *J*=15.2 Hz), 132.4 (d, *J*=18.4 Hz), 131.74 (d, *J*=9.2 Hz), 131.71 (d, *J*=9.2 Hz), 131.1 (d, *J*=27.6 Hz), 131.0 (d, *J*=27.6 Hz), 128.6 (d, *J*=18.4 Hz), 128.5 (d, *J*=18.0 Hz), 114.3 (d, *J*=30.4 Hz), 111.6-111.4 (m), 74.5 (d, *J*=9.2 Hz), 68.4, 50.9, 43.5, 31.2 (d, *J*=28.2 Hz), 29.7, 25.8, 22.9, 18.2, 18.1, 14.0, −4.3, −4.4, −4.9, −5.0 ; FT-IR ($CHCl_3$) 3018, 2957, 2930, 2857, 1472, 1438 cm^{-1}; $[\alpha]_D^{23}$ C −5 (0.007, CH_2Cl_2); HRMS, m/e (M^+) calc. for $C_{37}H_{59}O_3Si_2P$ 638.3743, found 638.3751.

Acknowledgment. Work at the Johns Hopkins University was supported by N.I.H grant CA 44530.

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