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PALLADIUM CATALYZED COUPLING OF ORGANOSTANNANES WITH VINYL EPOXIDES

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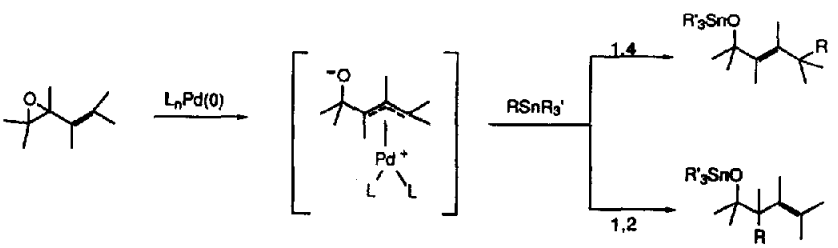
Abstract. The coupling reaction of organotin reagents with vinyl epoxides, catalyzed by palladium, takes place at ambient temperatures, regioselectively, giving predominately the 1,4-addition product. Both aryl- and vinylstannanes undergo coupling in high yields, while acetylenic, allylic and benzylic tin reagents either give low yields or fail to couple. Although the double bond geometry in the vinylstannane partner is maintained in the coupled product, the double bond geometry from the vinyl epoxide is an E/Z mixture. In coupling reactions with cyclic 1,3-diene monoepoxides, the reaction is stereospecific with the organic group from the tin partner coupling trans to the alcohol function.

Introduction

Vinyl epoxides undergo mild, rapid oxidative addition to a variety of palladium(0) complexes, generating a cationic η3-palladium species. This reaction has been utilized in the palladium catalyzed alkylation of vinyl epoxides by soft nucleophiles derived from carbon acids. The coupling reaction is both regioselective, generating the 1,4-addition product and stereospecific, with alkylation occurring at the η3-allyl face opposite to that bonded to palladium.1 The oxidative addition that yields the cationic η3-palladium species also produces an alkoxide derived from the epoxide oxygen, thereby providing a base that abstracts a proton from the carbon acid, generating the carbon nucleophile. The mild, neutral reaction conditions are ideally suited for the synthesis of a variety of organic products.2

Organotin reagents have been utilized in palladium catalyzed coupling reactions with a variety of organic electrophiles.3 Organostannanes become involved in the catalytic cycle through a transmetallation reaction with the transient organopalladium halide in which this palladium(II) species presumably acts as an electrophile in breaking the tin-carbon bond.4 Thus it appeared that the coupling reaction of vinyl epoxide electrophiles with organostannanes would take place by a transmetallation reaction involving the cationic η3-palladium complex (Eq. 1). This reaction also should proceed under mild, neutral reaction conditions but should have the advantage that a wide variety of organostannanes would be available for the coupling.

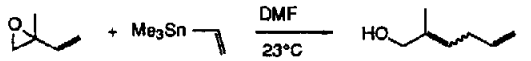


(Eq. 1)

Results and Discussion

Reaction Conditions. The coupling reaction takes place at ambient temperatures in a polar solvent, giving good yields of coupled product, particularly when a catalyst containing weak donor ligands is utilized. The introduction of the palladium(0) complex *via* bis(acetonitrile)dichloropalladium(II) gives the highest yields of product (Table 1).

Table 1. Effect of Catalysts on Coupling Yields[a]

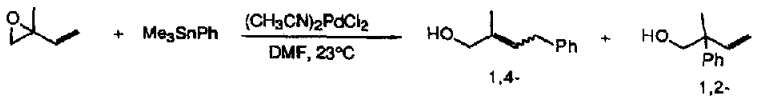


Catalyst	Solvent	Time(h)	Yield(%)
$Pd(dba)_2$	DMF	1	53
$Pd(dba)_2$, dppf	DMF	1	56
$Pd(dba)_2$, dppp	DMF	1	49
$Pd(dba)_2$, $(i\text{-}PrO)_3P$	DMF	1.5	0
$Pd(PPh_3)_4$	THF	1	34
$PdCl_2$(dppp)	THF	36	20
$PdCl_2$(dppf)	DMF	1	34
$Pd(CH_3CN)_2Cl_2$	DMF	1	77

[a] Reactions were carried out with 3 mole % catalyst.

Although the palladium catalyzed coupling reaction of organostannanes with other electrophiles is relatively insensitive to small amounts of water, the presence of water (10 equivalents based on the vinyl epoxide) gave higher yields of coupled product than when the reaction was run under anhydrous conditions (Table 2). Furthermore, in the presence of water, the reaction is more selective, both with respect to the 1,4-:1,2-addition and the E:Z ratios. Other additives, including Lewis acids and bases, protic acids or protic solvents were less effective than water in improving the yields. A similar effect has been noted in the coupling of organomercury reagents with vinyl epoxides.[2j]

Table 2. Effect of Additives on the Coupling Reaction

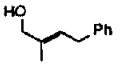
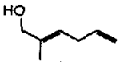
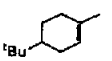
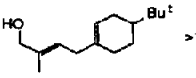
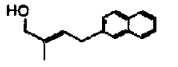
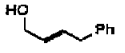
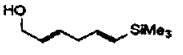
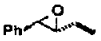
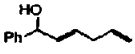
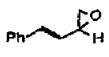
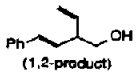
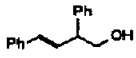


Additive(equiv)	Yield(%)	1,4-:1,2-	E:Z
---	70	27	1.1
H_2O (2)	79	65	2
(10)	85	64	2.2
HOAc (1.1)	22	1	1.1
$ZnCl_2$ (2)	71	50	3
Et_3N (2)	62	65	1.7
Bu_4NF (2)	38	50	2
Bu_3SnOAc (2)	39	100	1.5
$TMSOT_f$ (1.1)	61	10	2
BF_3OEt (1.1)	23	6	2

However, in the coupling reaction of β-naphthyltrimethylstannane with isoprene monoepoxide, water had an adverse effect, the 62% yield obtained in the presence of water being increased to 75% in its absence. Generally, the preferred addition order is catalyst and vinyl epoxide followed by organostannane. Adding the vinyl epoxide to a mixture of catalyst and tin reagent gave lower yields over the same reaction time, presumably because the catalyst was reduced by the tin reagent and in the absence of the vinyl epoxide substrate partially precipitated out of solution as palladium black. This was evident from the immediate blackening of the reaction solution as contrasted to the maintenance of a pale yellow homogeneous solution when the tin reagent was added last.

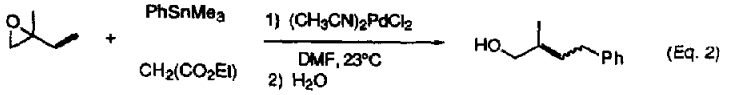
Provided the reaction temperature was kept low, coupling with the organotin reagent was rapid enough such that the competing palladium-catalyzed isomerization of the vinyl epoxides to unsaturated carbonyl

Table 3. Palladium-Catalyzed Coupling of Vinyl Epoxides with Organostannanes

Entry	Epoxide	$RSnR'_3$ R	R'	1,4-Product	(1,4:1,2)	E/Z[d]	Yield (%)[a]
1		Ph	Me Bu		98:2	2.2	85 85
2			Me Bu		>100:1	2	77 80
3		Ph 	Me Bu		87:13	2.2-2.6	63 65
4			Me		>100:1	1.6-1.8	72
5			Me		>100:1	1.8-2	79
6		Bu 	Me		>100:1	2	63
7			Me		>100:1	1.4-2	75
8		Ph	Me		88:12	18	83
9			Me		87:13	10	77
10			Me		88:12	13	65
11			Bu		82:18	7	100
12		Ph	Me		88:12	11	75
13			Me		>100:1	9	80
14			Me		98:2	10	55
15	 E		Bu	 (1,2-product)	9:91	E[b]	83
16		Ph	Me	 (1,2-product)	1:99	E[b]	54
17			Bu		>100:1	19	75

[a] Isolated yields of pure products.
[b] The E-geometry of the vinylepoxide double bond was preserved.

compounds was not observed.[5] Running the reaction at 35°C led to some isomerization. In a competitive coupling reaction of isoprene monoepoxide with equal molar quantities of phenyltrimethylstannane and diethyl malonate, only a single allylic alcohol, 4-phenyl-2-methylbut-2-en-1-ol, was isolated, diethylmalonate being recovered unchanged (Eq. 2).



(Eq. 2)

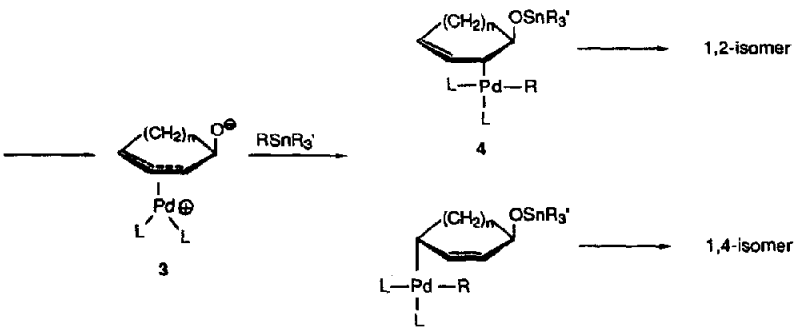
Reaction Characteristics. Vinyl and phenyl tin reagents coupled readily with a variety of vinyl epoxides to give good yields of allylic alcohols (Table 3). Other organostannanes either failed to couple (allyl, benzyl, alkyl) or reacted by other pathways (alkynyl and tributyltin hydride). Epoxides of acyclic alkenes coupled regioselectively. The regioselectivity appears to be controlled by the substitution pattern on the epoxide. Thus, 2-substituted-2-vinyloxiranes (entries 1-7) showed greater 1,4-selectivity than the vinyloxirane unsubstituted in the 2-position (entries 8-11). Substitution at the terminal position of the vinyl group reversed the regioselectivity, generating the 1,2-product (entries 15, 16). Epoxides of cyclic alkenes did not show this high regioselectivity *(vide supra)*. The coupling reaction of vinyl epoxide **1** with phenyltributyltin gave only a 25% yield of a mixture of regioisomers; epoxide **2** failed to undergo coupling.

1 **2**

The geometry of the migrating double bond was an E/Z mixture, particularly in the coupling reactions of 2-methyl-2-vinyloxirane, the E isomer predominating (E/Z = 1-3, Table 3, entries 1-7). High E/Z ratios were obtained, however, in coupling reactions with 2-vinyloxirane (entries 8-11). The geometry of the double bond in the tin reagent was maintained, as has been observed in other coupling reactions with vinylstannanes.[3]

The coupling reactions of several epoxides derived from cyclic 1,3-dienes defined the stereochemistry of this reaction (Table 4). In coupling reactions of cyclopentadiene, 1,3-cyclohexadiene and 1,3-cyclooctadiene monoepoxides with phenyl and vinyl tin reagents, both 1,4- and 1,2-regioisomers were realized, but in both regioisomers, only the *trans*-substituted cycloalkenol was obtained. For example, the *trans* isomers in the cyclohexenols (entry 3) were assigned from the proton NMR spectra in which H_a in the 1,2-isomer couples with H_b (J = 10.5 Hz), H_c (J = 7.7 Hz) and H_d (J = 3.1 Hz), giving a ddd pattern, while H_b was observed as a dm pattern, coupling with H_a (J = 10.5 Hz). The *trans* isomer of the 1,4-addition product was not obvious from the proton NMR spectrum alone. This isomer was hydrogenated to yield *trans*-4-phenylcyclohexanol, which exhibited the same physical and spectroscopic properties as an authentic sample.

This stereochemistry is consistent with an oxidative addition of the vinyl epoxide to palladium to yield an η^3-complex (**3**) with the oxygen from the epoxide on the ring face opposite from palladium. The transmetallation reaction with the tin reagent probably results in the generation of a σ-complexe such as (**4**) which undergoes reductive elimination with retention of configuration[7] at the ring carbon to yield the two regioisomers.



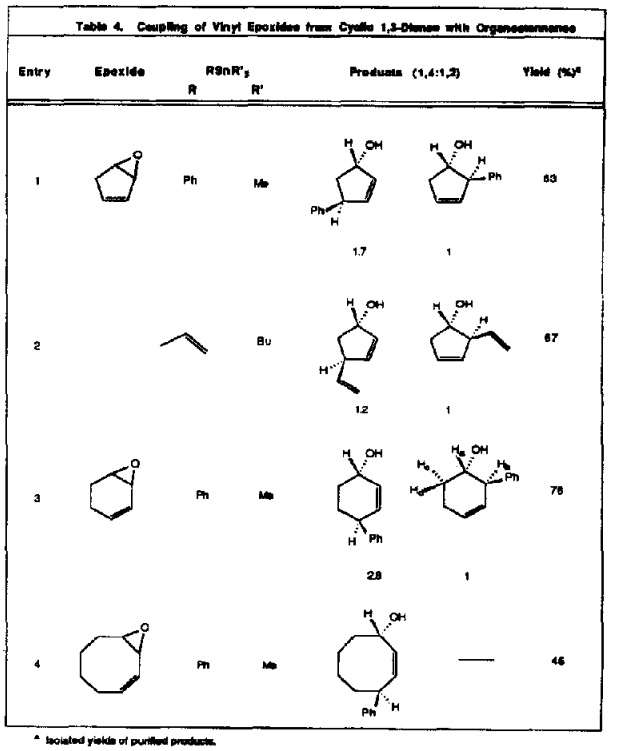


Table 4. Coupling of Vinyl Epoxides from Cyclic 1,3-Dienes with Organostannanes

Entry	Epoxide	RSnR'$_3$ R	R'	Products (1,4:1,2)	Yield (%)[a]
1		Ph	Me	1.7 : 1	83
2			Bu	1.2 : 1	87
3		Ph	Me	2.8 : 1	78
4		Ph	Me	—	46

[a] Isolated yields of purified products.

This coupling yields the *trans*-substituted homoallylic or allylic alcohols, which is opposite to that stereochemistry obtained from the coupling of **3** with a soft nucleophile derived from a carbon acid.[2] In the latter case, a soft nucleophile forms the carbon-carbon bond by approaching from the ring face opposite palladium, displacing palladium(0) in the process.

The by-products of these reactions of the monoepoxides of cyclic dienes were the palladium-catalyzed rearrangement products,[5] and in the case of cyclooctadiene monoepoxide, accounts for the much lower yield of coupled product.

Synthetic Utility. This coupling reaction is regiospecific in coupling reactions with epoxides derived from acyclic 1,3-dienes, giving an allylic alcohol and generating a new carbon-carbon bond. The allylic alcohol can be further elaborated, for example, by a Sharpless oxidation.[8] The synthesis of a variety of natural products can be easily achieved in a few steps.

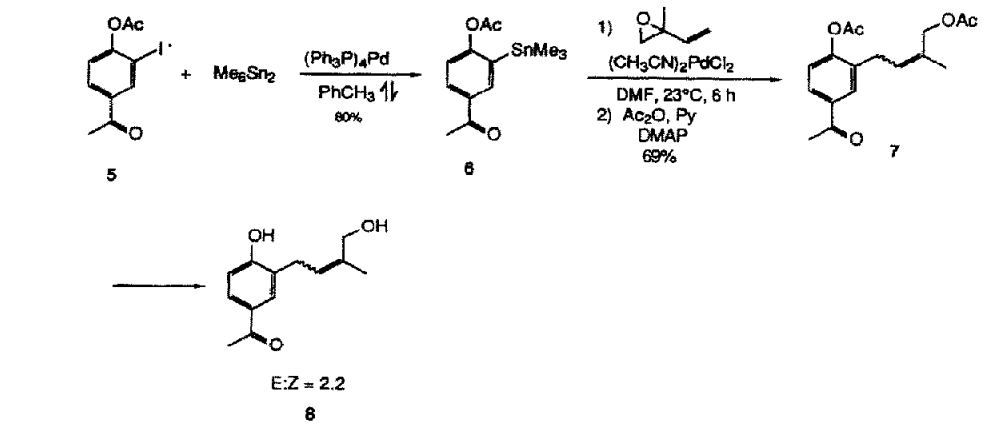
The coupling product, (E)-2-methyl-6-methylene-3,7-octadiene-2-ol (Table 3, entry 17), a pine bark beetle *(Ips confusus)* sex pheromone, has been utilized as a bioassay for monitoring and capture procedures.[9] No 1,2-addition product was isolated from this reaction, the E-isomer was present in >95%.

As expected, the coupling reaction tolerates other reactive functionalities on the tin reagent. The arylstannane (**6**) containing both an acetoxy group and a methyl ketone function can be prepared by the palladium catalyzed reaction of hexamethylditin with 4-acetoxy-3-iodoacetophenone (**5**, Scheme I). Coupling with 2-methyl-2-vinyloxirane followed by acylation (in order to effect purification) gave **7** in 69% yield. Hydrolysis of the acetates gave an E/Z mixture of **8**; the two isomers are identical to E and Z isomers isolated[10] from *Artemisia campestris*.

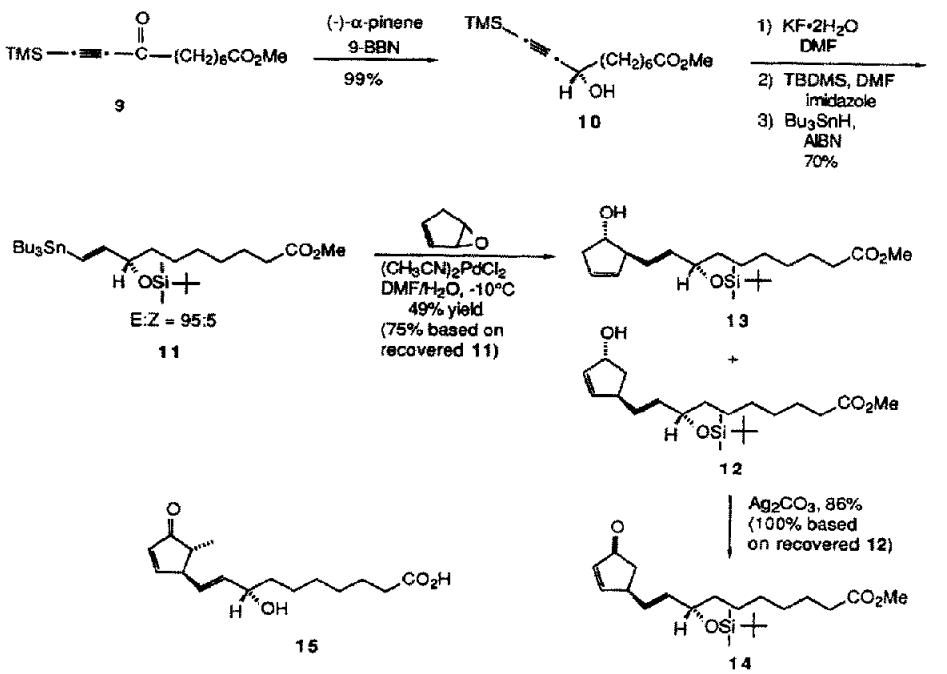
The coupling reactions of cyclopentadiene monoepoxide have potential for the synthesis of a variety of cyclopentanoids, particularly those derived from the *trans* allyl alcohol (1,4-regioisomer). To explore this coupling reaction further, a vinyltin reagent containing a protected chiral alcohol and an ester was selected (Scheme II).

Acetylenic ketone **9** was reduced to the *S*-alcohol (**10**) utilizing enantiomerically pure pinanyl borane.[11] Removal of the acetylenic protecting group, protection of the alcohol and hydrostannation of the acetylene gave vinyltin reagent **11**. Coupling **11** with cyclopentadiene monoepoxide gave the *trans*

Scheme I



Scheme II



regioisomeric (1,4:1,2 = 1.35:1) products (**12**, **13**), in 51% yield, which could be readily separated by column chromatography. The two diastereomers of **12** could not be readily distinguished by NMR, so any diastereoselectivity realized in the coupling reaction is in question. Oxidation of **12** could be carried out to yield ketone **14**, a precursor to hydroxypentenoic acid **15**, isolated recently from a species of aquatic plants *Lemma trisulca*.[12]

Experimental Section

^1H NMR spectra were run on either an IBM WP 270 (270 MHz) or Bruker AC300P (300 MHz) spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded on an IBM WP 270 (68 MHz) or Bruker AC300P (74 MHz) spectrometer using $CDCl_3$ as both solvent and internal standard. Infrared spectra were obtained on a Beckman 4250 spectrometer. Elemental analyses were performed by Atlantic Microlab, Atlanta, Georgia.

Tetrahydrofuran (THF) was distilled from sodium/benzophenone. Dimethylformamide (DMF) was distilled from calcium hydride and stored over 4Å molecular sieves. Dimethyl sulfoxide (DMSO) was distilled from calcium hydride.

Bulb-to-bulb distillations were performed with a Büchi Kügelrohr apparatus. Thin-layer chromatography was performed on aluminum sheets precoated with silica gel 60F-254 (0.2 mm) (Merck). Column chromatographic separations/purifications were run with Woelm 230-400 mesh silica gel using flash column techniques.

Catalysts. Palladium catalysts were prepared according to the published procedures: $Pd(PPh_3)_4$,[13] $Pd(dba)_2$,[14] $Pd_2(dba)_3CHCl_3$,[14] $PdCl_2(dppp)$,[15] $PdCl_2(dppf)$,[16] $Pd(CH_3CN)_2Cl_2$.[17]

Organostannanes. The following organostannanes used in this study were prepared according to published procedures: Phenyltrimethylstannane,[18] phenyltributylstannane,[19] trimethylvinylstannane,[20] tributylvinylstannane,[20] **E**-β-styryltrimethylstannane,[21] **E**-β-styryltributylstannane,[21] isobutenyltrimethylstannane,[22] **E**-1-hexenyltrimethylstannane,[22] (**E**)-1-(trimethylsilyl)-2-(tributylstannyl)ethylene,[23] β-naphyltrimethylstannane,[24] and 2-tributylstannyl-1,3-butadiene.[25] (**E**)-1,2-bis(tributylstannyl)ethylene (gift from Searle) and hexamethylditin (Aldrich) were used as received.

(4-*tert*-Butylcyclohexenyl)trimethylstannane. To a solution of Me_3SnLi (prepared from 3.31 g (16.6 mmol) of Me_3SnCl and 1.12 g (160 mmol) of Li metal in 50 ml of THF) at 0°C, was added dropwise 4.06 g (15.4 mmol) of 4-*tert*-butyl-1-iodocyclohexene in 20 ml of THF over a 1.0 h interval. The gray solution was allowed to warm to 23°C and stirred at that temperature for 16.0 h. The gray suspension was poured into 5 ml of saturated NH_4Cl/25 ml H_2O. The bilayer mixture was extracted with Et_2O (3 x 50 ml). The combined ethereal extracts were washed with 2 x 50 ml H_2O, 2 x 50 ml brine and dried over Na_2SO_4. Solvent removal by atmospheric pressure distillation gave a colorless liquid. Distillation at reduced pressure gave a colorless, clear oil (3.00 g; 65%): b.p. 81-83°C at 1.0 mmHg. ^1H NMR (270 MHz) δ 5.83 (m, 1 H), 2.30-1.72 (m, 5 H), 1.30-1.10 (m, 2 H), 0.82 (s, 9 H), 0.05 (s, 9 H). ^{13}C NMR (68 MHz) δ 140.2, 137.2, 44.4, 32.8, 29.4, 27.1, 25.1, -10.5. Anal. Calcd for $C_{13}H_{26}Sn$: C, 51.88; H, 8.65. Found: C, 51.90; H, 8.73.

4-Acetoxy-3-(trimethylstannyl)acetophenone (5). A solution containing 608 mg (2.00 mmol) of 4-acetoxy-3-iodoacetophenone,[26] 768 mg (2.20 mmol) of hexamethylditin and 56 mg (0.045 mmol; 2.5 mol %) of $Pd(PPh_3)_4$ in 8 ml of toluene was heated to reflux, under air, for 4.0 h. After cooling to 25°C, the black suspension was poured into 50 ml of H_2O. Extraction with 3 x 50 ml Et_2O, washing with 2 x 25 ml brine, drying over $MgSO_4$ and concentration at reduced pressure gave a colorless oil. Chromatography (flash column, hexanes:EtOAc 4:1) gave **5** as a colorless oil (R_F = 0.38). Distillation (bulb-to-bulb) afforded a colorless oil, which solidified upon standing (548 mg; 81%): m.p. 59-61°C; b.p. (bulb-to-bulb) 118-121°C at 0.15 mmHg. ^1H NMR (270 MHz) δ 8.07 (m, 1 H), 7.94 (m, 1 H), 7.21 (m, 1 H), 2.60 (s, 3 H), 2.31 (s, 3 H), 0.35 (s, 9 H). ^{13}C NMR (68 MHz) δ 196.7, 168.4, 159.3, 136.7, 134.4, 130.1, 122.1, 121.0, 26.2, 20.9, -9.27. IR (neat) 3180, 2980, 2910, 1765, 1680, 1580 cm-1. Anal. Calcd for $C_{13}H_{18}O_3Sn$: C, 45.88; H, 5.29. Found: C, 45.83; H, 5.32.

Epoxides. The following epoxides used in this study were prepared according to known procedures: 2-methyl-2-vinyloxirane,[27] 3,4-epoxycyclohex-1-ene,[28] 3,4-epoxycyclopent-1-ene,[28] 3,4-epoxycyclooct-1-ene,[28] (**E**)-2-(2'-phenylvinyl)oxirane,[29] *trans*-2-phenyl-3-vinyloxirane.[30] Vinyloxirane was obtained from Aldrich and used as received.

2,2-Dimethyl-3-vinyloxirane. A suspension containing 3.59 g (5.00 ml, 43.7 mmol) of 4-methyl-1,3-pentadiene (Wiley Organics Inc.) and 200 g (1.89 mol) of solid Na_2CO_3 in 350 ml of CH_2Cl_2 at 0°C was treated with 8.31 g (48 mmol) of 3-chloroperoxybenzoic acid (85%) over 1.0 h. The mixture was stirred at 0°C for 3.0 h and at 23°C for 1.5 h. The mixture was filtered and the filter cake washed with 2 x 50 ml CH_2Cl_2. The filtrate was washed with 100 ml of saturated aqueous K_2CO_3, 2 x 100 ml H_2O, brine and dried over K_2CO_3. Solvent was removed by atmospheric pressure distillation (bath temperature ≤ 50°C). The resulting opaque liquid was distilled to afford the product as a colorless liquid (1.65 g, 38%); b.p. 91-93°C at 650 mmHg. ^1H NMR (270 MHz) δ 5.70 (m, 1 H), 5.42 (m, 2 H), 3.20 (d, J = 7.2 Hz, 1 H), 1.36 (s, 3 H), 1.28 (s, 3 H). IR (neat) 3095, 2980, 2960, 1635, 1455, 1380, 1240, 1110, 980, 915, 865, 795, 728 cm-1. Anal. Calcd for $C_6H_{10}O$: C, 73.46; H, 10.2. Found: C, 72.9; H, 9.96.

Catalyst Optimization Studies (Table 1). Coupling reactions listed in Table 1 were run according to the general procedure as follows: A stirred solution of the selected catalyst in 4 ml of the indicated solvent, at 0°C, was treated with 2.50 mmol of 2-methyl-2-vinyloxirane followed by 2.75 mol of

trimethylvinylstannane. The pale yellow solution was stirred at 23°C for the specified amount of time. The solution was then filtered (Celite) and the filter cake washed with 3 x 15 ml CH_2Cl_2. The filtrate was washed with 2 x 25 ml H_2O, brine and dried over $MgSO_4$. Concentration at reduced pressure and chromatographic separation afforded 2-methylhexa-2,5-dien-1-ol as a mixture of **E** and **Z** isomers. The **E/Z** isomeric ratio was determined by 1H NMR integration of the vinyl (δ 5.45 **E** and 5.34 **Z**), methylene (δ 4.12 **Z** and 4.01 **E**) and methyl (1.82 **Z** and 1.67 **E**) resonances.

Effects of Additives (Table 2). Coupling reactions listed in Table 2 were run according to the general procedure as follows: A stirred solution of $Pd(CH_3CN)_2Cl_2$ (20.5 mg; 0.08 mmol; 4 mole %) in 4 ml of DMF, cooled to 0°C, was treated with the specified quantity (2.20-20.0 mmol) of the selected additive. To this was added 2-methyl-2-vinyloxirane (167 mg; 2.00 mmol) followed by phenyltrimethylstannane (530 mg; 2.20 mmol). The mixture was stirred at 23°C for 12 h. Dilution with 50 ml CH_2Cl_2, filtration (Celite), washing with 2 x 25 ml H_2O, brine, drying over $MgSO_4$ and concentration at reduced pressure afforded a yellow oil. Chromatographic separation afforded 2-methyl-4-phenylbut-2-en-1-ol as a **E/Z** mixture of isomers and 2-methyl-2-phenylbut-3-en-1-ol. The 1,2-1,4 addition ratio was determined by 1H NMR integration comparison of the vinyl region for 2-methyl-4-phenylbut-2-en-1-ol (1,4 product) (δ 5.64, 5.52); and 2-methyl-2-phenylbut-3-en-1-ol (1,2 product) (δ 6.05, 5.22, 5.11). The E/Z ratio for 2-methyl-4-phenylbut-2-en-1-ol was determined by 1H NMR integration of the vinyl (δ 5.64 **E** and 5.52 **Z**), methylene (δ 4.25 **Z** and 4.06 **E**) and methyl (δ 1.86 **Z** and 1.79 **E**) resonances.

Palladium-Catalyzed Coupling Reaction: General Procedure and Workup (Table 3). (E)- and (Z)-2-Methyl-4-phenylbut-2-en-1-ol (Table 3, Entry 1). (a) Phenyltrimethylstannane: To a stirred solution of 20.5 mg (0.08 mmol; 4 mole %) of $Pd(CH_3CN)_2Cl_2$ in 4 ml of DMF, cooled to 0°C, was added 360 μl (20.0 mmol) of water followed by 167 mg (2.00 mmol) of 2-methyl-2-vinyloxirane. Phenyl trimethylstannane (530 mg; 2.20 mmol) was added and stirring was continued for 12 h. The resulting suspension was diluted with 50 ml of CH_2Cl_2 and filtered through a small pad of Celite. The filtrate was washed with 2 x 25 ml H_2O, brine, dried over $MgSO_4$ and concentrated using a rotary evaporator. Chromatography (flash column, hexanes/EtOAc 4:1, silica gel) gave the desired alcohol as a pale yellow oil (275 mg; 85%): b.p. (bulb-to-bulb) 77-79°C (0.1 mmHg); 1H NMR (270 MHz) δ 7.31-7.16 (m, 5 H), 5.64 (t sext, J = 7.4, 1.4 Hz, 1 H, **E**), 5.52 (tm, J = 7.4 Hz, 1 H, **Z**), 4.25 (s, 2 H, **Z**), 4.06 (s, 2 H, **E**), 3.44-3.39 (m, 2 H, **E** + **Z**), 1.86 (q, J = 0.9 Hz, 3 H, **Z**), 1.79 (s, 3 H, **E**), 1.43 (br, 1 H, exchanges with D_2O, **E** + **Z**). 13C NMR (68 MHz) 140.99 (**E** + **Z**), 135.72 (**E**), 135.38 (**Z**), 128.39 (**E** + **Z**), 128.26 (**E** + **Z**), 126.59 (**Z**), 124.58 (**E** + **Z**), 68.45 (**E**), 61.39 (**Z**), 33.89 (**E**), 33.76 (**Z**), 21.09 (**Z**), 13.62 (**E**). IR (neat) 3400-3240, 3040, 2920, 1605, 1495, 1455, 1025, 990, 735, 690 cm-1. Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.28; H, 8.68.

(b) Phenyltri-n-butylstannane: The coupling was performed as above using 807 mg (2.20 mmol) of the stannane. After stirring for 12 h at 23°C, the mixture was treated with a 1.4 M pyridinium hydrofluoride solution in THF/pyridine (1.60 ml; 2.20 mmol). After 30 min, the thick suspension was diluted with 50 ml CH_2Cl_2 and filtered through a small pad of Celite. The filtrate was washed with 25 ml of 5% HCl (aq), 2 x 25 ml H_2O, brine, dried over $MgSO_4$ and concentrated by rotary evaporation. The crude oil was purified as above to give the expected alcohol (278 mg; 85%).

The following compounds were prepared according to the general procedure:

(E)- and (Z)-2-Methylhexa-2,5-dien-1-ol (entry 2): colorless oil; b.p. (bulb-to-bulb) 50-52°C (0.5 mmHg); 1H NMR (270 MHz) δ 5.80 (ddt, J = 16.9, 10.4, 6.5 Hz, 1 H, **E** + **Z**), 5.45 (t sext, J = 7.2, 1.0 Hz, 1 H, **E**), 5.34 (br t, J = 7.6 Hz, **Z**), 5.03 (dm, J = 17.1 Hz, 1 H, **E** + **Z**), 4.98 (dm, J = 10.2 Hz, 1 H, **E** + **Z**), 4.12 (s, 2 H, **Z**), 4.01 (s, 2 H, **E**), 2.80 (br t, J = 6.2 Hz, 2 H, **E** + **Z**), 1.82 (t, J = 1.1 Hz, 3 H, **Z**), 1.74 (br, 1 H, **E** + **Z**; exchanges with D_2O), 1.67 (s, 3 H, **E**). 13C NMR (68 MHz) δ 137.16 (**Z**), 136.62 (**E**), 136.09 (**Z**), 135.84 (**E**), 125.12 (**Z**), 123.06 (**E**), 114.54 (**E** + **Z**), 68.59 (**E**), 61.46 (**Z**), 31.84 (**E**), 31.73 (**Z**), 21.03 (**Z**), 13.42 (**E**). IR(neat) 3400-3260, 3090, 2980, 2860, 1640, 1430, 1005, 985, 900 cm-1. Anal. Calcd for $C_7H_{12}O$: C, 75.0; H, 10.7. Found: C, 74.3; H, 10.3.

(E,E) and (Z,E)-2-Methyl-6-phenylhexa-2,5-dien-1-ol (entry 3): colorless oil: 1H NMR (270 MHz) δ 7.31-7.16 (m, 5 H); 6.38 (dt, J = 15.2, 1.6 Hz, 1 H, **E**), 6.21 (dt, J = 15.3, 7.5 Hz, 1 H, **E**), 5.51 (br t, J = 7.5 Hz, 1 H, **E**), 5.38 (br t, J = 7.6 Hz, **Z**), 4.18 (s, 2 H, **Z**), 4.04 (s, 2 H, **E**), 2.95 (br m, 2 H, **E** + **Z**), 1.86 (s, 3 H, **Z**), 1.72 (s, 3 H, **E**), 1.50 (br, 1 H, **E** + **Z**, exchanges with D_2O). IR 3470-3280, 3040, 3010, 2920, 1675, 1605, 1490, 1445, 990, 960, 830, 730, 680 cm-1. Anal. Calcd for $C_{13}H_{16}O$: C, 82.97; H, 8.51. Found: C, 82.25; H, 8.56.

(E)- and (Z)-2,6-Dimethyl-2,5-heptadien-1-ol (entry 4): colorless oil: b.p. (bulb-to-bulb) 60-62°C (0.1 mmHg) [lit31 105°C/15 mmHg]; 1H NMR (270 MHz) δ 5.36 (tm, J = 7.2 Hz, 1 H, **E**), 5.27 (br t, J = 7.0 Hz, 1 H, **Z**), 5.08 (m, 1 H), 4.12 (s, 2 H, **Z**), 4.02 (s, 2 H, **E**), 2.60 (br, 2 H, **E** + **Z**), 1.80 (s, 3 H, **Z**), 1.70 (s, 6 H), 1.65 (s, 3 H, **E**), 1.30 (br, 1 H, **E** + **Z**, exchanges with D_2O). 13C NMR (68 MHz) δ 127.12; 125.04, 122.73, 122.34, 68.87(**E**), 61.53(**Z**), 26.73, 25.67, 21.28(**Z**), 17.70, 13.65(**E**). IR (neat) 3450-3190, 2970, 2910, 1670, 1450, 1370, 990, 840, 815 cm-1. Spectral data matched that previously reported.32 Our data and that in reference 32 is in disagreement with that reported in reference 31 with respect to the assignment of **E** and **Z** isomers.

(E)- and (Z)-4-(4-*tert*-Butylcyclohex-1-enyl)-2-methylbut-2-en-1-ol (entry 5): colorless oil: b.p. (bulb-to-bulb) 85-87°C (0.1 mmHg); 1H NMR (270 MHz) δ 5.42 (m, 2 H, **E** + **Z**), 4.15 (s, 2 H, **Z**), 4.03 (s, 2 H, **E**), 2.68 (d, J = 7.4 Hz, 2 H, **E** + **Z**), 2.10-1.90 (m, 3 H), 1.83 (s, 3 H, **Z**), 1.70 (s, 3 H, **E**), 1.40-1.10 (m, 5 H), 0.86 (s, 9 H). 13C NMR (68 MHz) δ 136.4(**E**), 135.7(**Z**), 126.2, 124.2, 121.6, 69.0(**E**), 61.7(**Z**), 44.4, 35.6, 32.2, 30.2, 27.3, 26.9, 24.4, 21.2(**Z**), 13.6(**E**). IR (neat) 3490-3160, 2960, 2910, 2830, 1665, 1460, 1005, 985, 850, 790 cm-1. Anal. Calcd for $C_{15}H_{26}O$: C, 81.08; H, 11.71. Found: C, 80.99; H, 11.80.

(E)- and (Z)-2-Methyldeca-2,5-dien-1-ol (entry 6): colorless oil: b.p. (bulb-to-bulb) 64-66°C (0.1 mmHg); 1H NMR (270 MHz) δ 5.40-5.27 (m, 3 H, **E** + **Z**), 4.13 (s, 2 H, **Z**), 4.02 (s, 2 H, **E**), 2.72 (br m, 2 H, **E** + **Z**), 2.00 (m, 2 H), 1.81 (s, 3 H, **Z**), 1.70 (s, 3 H, **E**), 1.40-1.10 (m, 5 H), 0.85 (t, J = 7.0 Hz, 3 H). 13C NMR (68 MHz) δ 135.3(**E**), 135.1(**Z**), 131.0, 128.4, 124.4, 68.8(**E**), 61.6(**Z**), 32.1, 31.7, 30.8, 26.9, 25.9, 22.1, 21.1(**Z**), 13.7, 13.5(**E**). IR (neat) 3490-3190, 2960, 2920, 2860, 1670, 1450, 1370, 1000, 960, 835 cm-1. Anal. Calcd for $C_{11}H_{20}O$: C, 78.57; H, 11.90. Found: C, 78.00; H, 12.20. Mass Spec. Calcd 168.28. Found: 168 (M+).

(E)- and (Z)-2-Methyl-4-(β-napthyl)-but-2-en-1-ol (entry 7): Partial hydrolysis of β-naphyltrimethylstannane was observed when the coupling was run in the presence of water resulting in a lower yield (61%) of alcohol; coupling was run without water to give a 75% yield of the desired alcohol: colorless oil: b.p. (bulb-to-bulb) 93-95°C (0.1 mmHg); 1H NMR (270 MHz) δ 7.80-7.30 (m, 7 H), 5.70 (tm, J = 7.2 Hz, 1 H, **E**), 5.58 (br t, J = 7.3 Hz, 1 H, **Z**), 4.29 (s, 2 H, **Z**), 4.08 (s, 2 H, **E**), 3.56 (br m, 2 H, **E** + **Z**), 1.88 (q, J = 1.1 Hz, 1 H, **Z**), 1.82 (s, 3 H, **E**), 1.39 (br, 1 H, **E** + **Z**, exchanges with D_2O). 13C NMR (68 MHz) δ 138.45, 135.98, 133.60, 132.05, 128.0, 127.57, 127.40, 127.20, 127.11, 126.19, 126.91, 125.17, 124.33, 68.64(**E**), 61.60(**Z**), 34.04 (**E**), 33.93(**Z**), 21.29(**Z**), 13.79(**E**). IR (neat) 3410-3250, 3080, 3000, 2850, 1600, 1480, 1440, 970, 910, 735, 710 cm-1. Anal. Calcd for $C_{15}H_{16}O$: C, 84.90; H, 7.54. Found: C, 84.81; H, 7.57.

(E)-4-Phenylbut-2-en-1-ol (entry 8): colorless oil: b.p. (bulb-to-bulb) 87-89°C (0.1 mmHg); 1H NMR (270 MHz) δ 7.40-7.15 (m, 5 H), 5.86 (dt, J = 15.2, 6.5 Hz, 1 H), 5.70 (dt, J = 15.3, 5.6 Hz, 1 H), 4.12 (d, J = 5.62 Hz, 2 H, **E**), 3.82 (d, J = 7.12 Hz, 2 H), 1.45 (br, 1 H, exchanges with D_2O). 13C NMR (68 MHz) δ 139.96; 130.94, 130.38, 128.36, 128.25, 127.85, 126.59, 125.91, 62.93, 38.42. IR (neat) 3500-3200, 3015, 2910, 1670, 1600, 1490, 1450, 980, 965, 735, 690 cm-1. The 1H NMR and IR matched those reported.33

(**Z**) isomer; 1H NMR (270 MHz) δ 4.31 (d, J = 4.6 Hz, 2 H).

(E)-2,5-Hexadien-1-ol (entry 9): colorless oil: b.p. (bulb-to-bulb) 53-56°C (0.5 mmHg); 1H NMR (270 MHz) δ 5.80-5.63 (m, 3 H), 5.20-5.00 (m, 2 H), 4.12 (d, J = 7.6 Hz, 2 H, **E**), 2.81 (m, 2 H), 1.62 (br, 1 H, exchanges with D_2O). 13C NMR (68 MHz) δ 136.28, 130.24, 130.09, 115.29, 63.2, 36.10. IR (neat) 3480-3210, 3010, 2920, 1650, 1490, 990, 980, 905, 735 cm-1. The 1H and IR matched those reported.34

(**Z**) isomer; 1H NMR (270 MHz) δ 4.20 (d, J = 7.5 Hz, 2 H).

(E,E)-6-Phenylhexa-2,5-dien-1-ol (entry 10): yellow oil: b.p. (bulb-to-bulb) 87-89°C (0.5 mmHg); 1H NMR (270 MHz) δ 7.38-7.14 (m, 5 H), 6.40 (d, J = 15.6 Hz, 1 H), 6.20 (dt, J = 15.5, 7.2 Hz, 1 H), 5.76 (m, 2 H), 4.11 (d, J = 7.0 Hz, 2 H, **E**), 2.95 (m, 2 H), 1.60 (br, 1 H, exchanges with D_2O). 13C NMR (68 MHz) δ 137.74, 132.21, 131.11, 130.54, 130.33, 128.48, 128.14, 127.06, 126.27, 126.10, 63.44, 35.38. IR (neat) 3410-3250, 3018, 2840, 1600, 1485, 1450, 980, 960, 725 cm-1. The 1H NMR and IR spectra matched those reported.35

(**Z**) isomer; 1H NMR (270 Mhz) δ 4.24 (d, J = 7.0 Hz, 2 H).

(E,E)-6-Trimethylsilylhexa-2,5-dien-1-ol (entry 11): colorless oil: b.p. (bulb-to-bulb) 66-68°C (0.3 mmHg); 1H NMR (270 MHz) δ 6.02 (dt, J = 18.5, 6.0 Hz, 1 H), 5.72-5.62 (overlapping, m, 2 H), 5.68 (dt, J = 18.6, 1.5 Hz, 1 H), 4.13 (br d, J = 4.6 Hz, 2 H), 2.86 (t quint, J = 5.0, 1.1 Hz, 2 H), 1.40 (br s, 1 H), 0.05 (s, 9 H). 13C NMR (68 MHz) δ 144.0, 131.23, 130.31, 130.06, 63.26, 39.05, -1.32. IR (neat) 3500-3300, 2950, 1610, 1240, 850, 825 cm-1.

(**Z,E**) isomer; 1H NMR (270 MHz) δ 4.20 (br d, J = 6.9 Hz, 2 H).

(E)-2-Ethenyl-4-trimethylsilylbut-3-en-1-ol (entry 11; 1,2 addition product): 1H NMR (270 MHz) δ 5.93 (dd, J = 18.8, 6.2 Hz, 1 H), 5.82-5.68 (m, 1 H), 5.80 (d, J = 18.4 Hz, 1 H), 5.20-5.17 (m, 1 H), 5.16-5.11 (m, 1 H), 3.58-3.55 (m, 2 H), 2.98 (br quint, J = 6.7 Hz, 1 H), 1.50 (br s, 1 H), 0.07 (s, 9 H). IR (neat) 3440-3280, 3080, 2950, 1635, 1610, 1240, 1030, 980, 905, 860, 815 cm-1. Anal. Calcd for $C_9H_{18}OSi$: C, 63.53; H, 10.58. Found: C, 63.40; H, 10.62.

(E)-1,4-Diphenylbut-2-en-1-ol (entry 12): colorless oil; waxy solid obtained upon standing; b.p. (bulb-to-bulb) 121.123°C (0.05 mmHg); m.p. 38-40°C uncorrected; 1H NMR (270 MHz) δ 7.42-7.28 (m, 10 H), 5.92 (dt, J = 15.7, 6.7 Hz, 1 H), 5.75 (ddt, J = 15.2, 6.5, 1.4 Hz, 1 H), 5.20 (dd, J = 6.3, 2.4 Hz, 1 H), 3.40 (d, J = 6.5 Hz, 2 H), 1.89 (d, J = 3.4 Hz, 1 H, exchanges with D_2O). 13C NMR (68 MHz) δ 143.34, 140.0, 133.90, 130.74, 128.53, 127.47, 126.22, 126.10, 74.79, 38.54. IR (neat) 3430-3250, 3030, 3015, 2850, 1668, 1600, 1490, 1440, 960, 730 cm-1. Anal. Calcd for $C_{16}H_{16}O$: C, 85.71; H, 7.14. Found: C, 85.69; H, 7.24.

(E)-1-Phenyl-2,5-hexadien-1-ol (entry 13): colorless oil; b.p. (bulb-to-bulb) 82-84°C (0.07 mmHg); 1H NMR (270 MHz) δ 7.31-7.25 (m, 5 H), 5.77 (m, 3 H), 5.18 (d, J = 5.6 Hz, 1 H), 5.03 (m, 2 H), 2.81 (m, 2 H), 1.92 (br s, 1 H, exchanges with D_2O). 13C NMR (68 MHz) δ 143.37, 136.22, 133.64, 129.75, 128.41, 127.45, 126.19, 115.53, 74.89, 36.12. IR (neat) 3410-3200, 3025, 3000, 1648, 1620, 1575, 980, 970, 890, 730. Anal. Calcd for $C_{12}H_{14}O$: C, 82.76; H, 8.05. Found: C, 82.81; H, 8.15.

(E,E)-1,6-Diphenyl-2,5-hexadien-1-ol (entry 14): yellow oil; b.p. (bulb-to-bulb) 141-144°C (0.07 mmHg); 1H NMR (270 MHz) δ 7.45-7.15 (m, 10 H), 6.40 (d, J = 15.8 Hz, 1 H), 6.20 (dt, J = 15.9, 2.1 Hz, 1 H), 5.81 (m, 2 H), 5.21 (d, J = 5.8 Hz, 1 H), 2.97 (m, 2 H), 1.91 (br s, 1 H, exchanges with D_2O). 13C NMR (68 MHz) δ 143.4, 137.72, 133.87, 131.23, 129.84, 128.48, 128.01, 127.54, 126.25, 126.13, 74.96, 35.37. IR (neat) 3430-3220, 3020, 3000, 2835, 1620, 980 cm-1. Anal. Calcd for $C_{18}H_{18}O$: C, 86.40; H, 7.20. Found: C, 85.8; H, 7.35.

(E)-4-Phenyl-2-ethenylbut-3-en-1-ol (entry 15): yellow oil; 1H NMR (270 MHz) δ 7.40-7.23 (m, 5 H), 6.50 (d, J = 16.1 Hz, 1 H), 6.16 (dd, J = 16.0, 7.7 Hz, 1 H), 5.81 (ddd, J = 17.7, 10.0, 7.4 Hz, 1 H), 5.25 (dd, J = 17.7, 1.4 Hz, 1 H), 5.19 (dd, J = 10.0, 1.4 Hz, 1 H), 3.65 (d, J = 6.8 Hz, 2 H), 3.14 (m, 1 H), 1.65 (br, 1 H, exchanges with D_2O). IR (neat) 3430-3220, 3040, 3010, 2860, 1632, 1590, 1480, 1440, 1030, 980, 955, 910, 735, 680 cm-1. The 1H NMR and IR spectra matched those reported.[35]

(E)-2,4-Diphenylbut-3-en-1-ol (entry 16): orange oil; 1H NMR (270 MHz) δ 7.41-7.16 (m, 10 H), 6.53 (d, J = 15.9 Hz, 1 H), 6.36 (dd, J = 15.8, 7.6 Hz, 1 H), 3.90 (d, J = 7.4 Hz, 2 H), 3.69 (m, 1 H), 1.55 (br, 1 H, exchanges with D_2O). 13C NMR (68 MHz) δ 141.11, 137.28, 132.10, 130.02, 128.74, 128.48, 128.03, 127.38, 126.88, 126.30, 66.39, 51.76. IR (neat) 3500-3240, 3060, 3020, 2920, 1600, 1490, 1450, 1045, 960, 900, 732, 690 cm-1. Anal. Calcd for : $C_{16}H_{16}O$: C, 85.71; H, 7.14. Found: C, 85.39; H, 7.09.

(E)-2-Methyl-6-methylene-3,7-octadiene-2-ol (entry 17): A solution of $Pd(CH_3CN)_2Cl_2$ (21.0 mg; 0.08 mmol; 4 mole %), 360 µl H_2O, and 1,1-dimethyl-2-vinyloxirane (196 mg; 2.00 mmol) in 4 ml of DMF, cooled to 0°C, was treated with 2-tributylstannyl-1,3-butadiene (720 mg, 2.10 mmol). The orange solution was stirred at 23°C for 3 h. Addition of 1.6 ml of 1.4 N HF•pyridine with stirring for 30 min gave a white thick suspension. Dilution with 50 ml of CH_2Cl_2 and filtration (Celite) afforded a pale yellow filtrate which was washed with 30 ml of 5% HCl (aq), 30 ml H_2O, brine and dried over $MgSO_4$. Concentration gave a colorless oil. Chromatography (flash column, silica gel, hexanes:EtOAc, 4:1, gave pure product as a colorless oil (227 mg; 75%). The resulting synthetic terpene was identical in all respects to the natural product.[9]

1H NMR (270 MHz) δ 6.40 (dd, J = 17.6, 10.6 Hz, 1 H), 5.69 (m, 3 H), 5.24 (d, J = 17.6 Hz, 1 H), 5.05 (m, 2 H), 2.94 (m, 2 H), 1.61 (br, 1 H), 1.32 (s, 6 H). 13C NMR (68 MHz) δ 144.97, 139.92, 138.57, 124.31, 116.24, 113.52, 70.45, 34.24, 29.72. IR (neat) 3450-3240, 3050, 2980, 1675, 1635, 1595, 980, 970, 905, 890 cm-1.

***trans*-4-Phenylcyclopent-2-en-1-ol (A) and *trans*-2-phenylcyclopent-3-en-1-ol (B)** (Table 4, entry 1): yellow oil; **(A)** (R_F = 0.17); b.p. (bulb-to-bulb) 123-126°C (0.1 mmHg); 1H NMR (270 MHz) δ 7.31-7.10 (m, 5 H), 6.00 (m, 2 H), 5.10-5.00 (m, 1 H), 4.18-4.08 (m, 1 H), 2.40-2.02 (m, 2 H), 1.65 (br, 1 H, exchanges with D_2O). **(B)** (R_F = 0.26); b.p. (bulb-to-bulb) 93-95°C (0.1 mmHg); 1H NMR (270 MHz) δ 7.36-7.15 (m, 5 H), 5.90 (m, 1 H), 5.78 (m, 1 H), 4.28 (dt, J = 6.5, 2.5 Hz, 1 H), 3.76 (m, 1 H), 3.85-3.75 (m, 1 H), 2.41-2.31 (m, 1 H), 1.89 (br, 1 H, exchanges with D_2O). The spectra of both **A** and **B** matched those reported.[36]

***trans*-4-Vinylcyclopent-2-en-1-ol (C) and *trans*-2-vinylcyclopent-3-en-1-ol (D)** (Table 4, entry 2): yellow oil; **(C)** (R_F = 0.21): 1H NMR (270 MHz) δ 5.90 (m, 1 H), 5.75-5.60 (m, 1 H), 5.10-4.85 (m, 4 H), 3.55 (m, 1 H), 2.10-1.90 (m, 2 H), 1.73 (br, 1 H, exchanges with D_2O). **(D)** (R_F = 0.28): 93-96°C (0.1

mmHg); 1H NMR (270 MHz) δ 5.83-5.60 (m, 3 H), 5.15-4.95 (m, 2 H), 4.22-4.14 (m, 1 H), 3.23-3.15 (m, 1 H), 2.75-2.65 (m, 1 H), 2.32-2.20 (m, 1 H), 1.80 (br, 1 H, exchanges with D_2O). The spectra of both **C** and **D** matched those reported.[36]

***trans*-4-Phenylcyclohex-2-en-1-ol (E) and *trans*-2-phenylcyclohex-3-en-1-ol (F)** (Table 4, entry 3): (E) (R_F = 0.19) white prisms m.p. 54-55°C: b.p. (bulb-to-bulb) 123-126°C (0.1 mmHg); 1H NMR (270 MHz) δ 7.32-7.13 (m, 5 H), 5.93-5.79 (m, 2 H), 4.37-4.32 (m, 1 H), 3.44-3.40 (m, 1 H), 2.16-2.07 (m, 2 H), 1.86 (s, 1 H, exchanges with D_2O), 1.65-1.25 (m, 2 H). 13C NMR (68 MHz) δ 145.27, 132.54, 131.67, 128.37, 127.46, 126.19, 66.34, 41.96, 31.78, 30.22. The spectra of E matched those reported.[37]

Comparison of the hydrogenated alcohol with an authentic sample of *trans*-4-phenylcyclohexan-1-ol prepared from 4-phenylcyclohexanone[38] gave identical results: 1H NMR ($CDCl_3$) δ 7.32-7.13 (m, 5 H), 3.68 (tt, J = 10.5, 4.4 Hz, 1 H), 2.49 (tt, J = 11.7, 3.4 Hz, 1 H), 2.12-2.05 (m, 2 H), 1.98-1.90 (m, 2 H), 1.64 (br s, 1 H), 1.60-1.35 (m, 4 H). m.p. 117-118°C (lit.[39] 118-119°C). For a detailed NMR study of stustituted carbocyclic systems, see reference 36.

(F) (R_F = 0.28): yellow oil b.p. (bulb-to-bulb) 100-102°C (0.2 mmHg); 1H NMR (270 MHz) δ 7.35-7.21 (m, 5 H), 5.82 (m, 1 H), 5.55 (m, 1 H), 3.69 (ddd, J = 10.3, 7.7, 3.1 Hz, 1 H), 3.28 (m, 1 H), 2.29-2.21 (m, 2 H), 2.02-1.94 (m, 1 H), 1.91 (br, 1 H, exchanges with D_2O), 1.77-1.63 (m, 1 H). 13C NMR (68 MHz) δ 143.05, 128.62, 128.44, 127.58, 126.83, 73.58, 51.57, 29.46, 24.46. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72, H, 8.10. Found: C, 82.65; H, 8.13.

***trans*-4-Phenylcycloocten-2-en-1-ol** (Table 4, entry 4): colorless oil: b.p. (bulb-to-bulb) 95-98°C (0.15 mmHg); m.p. 36-38°C (solidification on standing); 1H NMR (270 MHz) δ 7.34-7.13 (m, 5 H), 5.66-5.49 (m, 2 H), 5.06-4.97 (m, 1 H), 3.78 (dt, J = 12.4, 4.1 Hz, 1 H), 2.02-1.50 (m, 9 H). 13C NMR (68 MHz) δ 146.1, 133.29, 132.22, 128.42, 127.33, 126.02, 69.14, 45.77, 36.87, 35.55, 26.71, 22.57. IR (neat) 3410-3260, 3010, 2865, 1595, 1440, 1035, 822, 740, 685 cm-1. Anal. Calcd for $C_{14}H_{18}O$: C, 83.16; H, 8.91. Found: C, 82.95; H, 8.99.

(E) and (Z)-3-(4-Hydroxy-3-methyl-2-butenyl)-4-hydroxy acetophenone (8): A solution containing $Pd(CH_3CN)_2Cl_2$ (21.0 mg; 0.08 mmol; 4 mole %), 360 µl H_2O and 2-methyl-2-vinyloxirane (168 mg, 2.00 mmol) in 4 ml of DMF, cooled to 0°C, was treated with 4-acetoxy-3-(trimethylstannyl)-acetophenone **6** (749 mg, 2.20 mmol). The yellow solution was stirred at 23°C for 6 h. Dilution with 75 ml CH_2Cl_2 followed by filtration (Celite) gave a yellow filtrate which was washed with 2 x 25 ml H_2O, brine and dried over $MgSO_4$. Concentration at reduced pressure gave a yellow oil. The crude oil was converted to the diacetyl derivative **7** by stirring with pyridine (237 mg, 3.00 mmol), acetic anhydride (245 mg, 2.40 mmol) and a catalytic amount of 4-dimethyl-aminopyridine (12.2 mg; 0.10 mmol; 5 mole %) in 50 ml of Et_2O at 23°C for 12 h. After the addition of methanol (1.0 ml) to consume excess acetic anhydride, the mixture was added to 50 ml Et_2O, washed with 25 ml of 5% HCl (aq), 2 x 25 ml H_2O, brine and dried over $MgSO_4$. Concentration at reduced pressure gave a yellow oil readily identified as an **E/Z** mixture (2.22:1) of 3-(4-acetoxy-3-methyl-2-butenyl)-4-acetoxyacetophenone (**7**) (397 mg, 69%).[10]

1H NMR (270 MHz) δ 7.98 (m, 2 H), 7.83 (m, 2 H), 7.16 (m, 2 H), 5.55 (t sext, J = 7.24, 1.4 Hz, 1 H, **E**), 5.47 (br t, J = 6.9 hz, 1 H, **Z**), 4.68 (s, 2 H, **Z**), 4.50 (s, 2 H, **E**), 3.38 (m, 4 H, **E** + **Z**), 2.58 (s, 6 H, **E** + **Z**), 2.33 (bs, 6 H, **E** + **Z**), 2.10 (bs, 6 H, **E** + **Z**), 1.82 (s, 3 H, **Z**), 1.77 (s, 3 H, **E**).

Hydrolysis of **7** using KOH-MeOH (10%, 4 ml)[10] gave **8** as a colorless oil (111 mg, 55%). The **E/Z** ratio was determined by 1H NMR integration to be ca. 2.22:1 **E/Z**. Both the **E** and **Z** isomers were identical in all respects to the natural products.[10]

Suberoyl chloride monomethyl ester: A solution of suberic acid monomethyl ester (9.41 g, 50.0 mmol) in 60 ml of dry benzene, cooled to 5°C, was treated with oxalyl chloride (7.61 g, 60.0 mmol) and a catalytic amount of DMF; vigorous evolution of CO_2 was observed immediately. The mixture was stirred at 5°C for 15 min, at 23°C for 2 h and at 60°C for 1 h. Filtration of the mixture through a short plug of Celite followed by solvent removal at reduced pressure gave a colorless oil. Distillation (bulb-to-bulb) gave the acid chloride as a colorless oil (9.90 g, 96%). b.p. (bulb-to-bulb) 83-86°C (0.1 mmHg); 1H NMR (270 MHz) δ 3.67 (s, 3 H), 2.89 (t, J = 7.3 Hz, 2 H), 2.31 (t, J = 7.4 Hz, 2 H), 1.74-1.58 (m, 4 H), 1.40-1.32 (m, 4 H). IR (neat) 2960, 2860, 1808, 1748, 1440, 1250, 1165, 950, 860, 730, 670 cm-1.

Preparation of 9: To a solution of suberoyl chloride monomethyl ether (10.8 g, 52.4 mmol) and bis(trimethylsilyl)acetylene (8.91 g, 52.4 mmol) in 80 mg of CH_2Cl_2, cooled to 0°C, was added $AlCl_3$ (7.68 g, 57.6 mmol) over a 0.5 h interval.[40] The mixture was stirring at 0°C for 3 h, and at 23°C for 4 h. The resulting

red slurry was filtered through a pad of Celite. The filtrate was shaken with 100 ml of cold 10% HCl (aq). The aqueous layer was extracted with 2 x 150 ml of Et_2O. The filtrate and combined ethereal layer was washed with 2 x 100 ml H_2O, brine and dried over $MgSO_4$. Concentration at reduced pressure gave a red oil. Chromatography (flash column, silica gel, hexanes/EtOAc 10:3) gave **9** as a colorless oil (8.42 g, 60%). b.p. (bulb-to-bulb) 108-111°C (0.1 mmHg); 1H NMR (270 MHz) δ 3.67 (s, 3 H), 2.56 (t, J = 7.3 Hz, 2 H), 2.31 (t, J = 7.5 Hz, 2 H), 1.69-1.60 (m, 4 H), 1.37-1.31 (m, 4 H), 0.13 (s, 9 H). IR (neat) 2948, 2118, 1744, 1675, 1435, 1245, 1065, 835, 750 cm-1. Anal. Calcd for $C_{14}H_{24}O_3Si$: C, 62.68; H, 8.95. Found: C, 62.65; H, 9.01.

Preparation of 10: A thick, colorless oil of neat B-3-pinnanyl-9-borobicyclo[3.3.1]nonane11 was prepared from (-)-α-pinene (3.23 g, 23.7 mmol) (98% ee) and 9-BBN (2.57 g, 42 ml, 21.0 mmol). To the oil was added, at 0°C, **9** (4.02 g, 15.0 mmol). The mixture was allowed to warm to 23°C and stirred at that temperature for 48 h. The clear oil was diluted with 40 ml of Et_2O, cooled to 0°C, and treated with triethanolamine (4.47 g, 30 mmol) with stirring for 30 min. The suspension was filtered and the white precipitate washed with 2 x 15 ml Et_2O. The filtrate was washed with H_2O, brine and dried over $MgSO_4$. Concentration at reduced pressure gave **10** as a clear oil (4.02 g, 99%). The alcohol may be chromatographed (flash column, silica gel, hexanes/EtOAc 4:1) if desired (R_f = 0.29) 4.34 (m, 1 H), 3.67 (s, 3 H), 2.42 (m, 2 H), 2.31 (t, J = 6.8 Hz, 2 H), 1.93-1.28 (m, 9 H), 0.17-0.15 (9 H). IR (neat) 3460-3880, 2870, 2170, 1748, 970, 835, 750 cm-1.

Preparation of 11: A solution containing **9** (3.00 g, 11.1 mmol) and $KF{\cdot}2H_2O$ (2.07 g, 22.0 mmol) in 30 ml of DMF was stirred at 23°C for 10 h. The yellow solution was poured into 75 ml of H_2O/75 ml of Et_2O. The aqueous phase was extracted with Et_2O (2 x 50 ml). The combined organic phase was washed with 75 ml H_2O, brine and dried over $MgSO_4$. A yellow oil was obtained after concentration at reduced pressure. Chromatography (flash column, silica gel, hexanes/EtOAc 4:1) afforded the product as a colorless oil (R_f = 0.16 (2.04 g, 93%). 1H NMR (270 MHz) δ 4.36 (m, 1 H), 3.67 (s, 3 H), 2.46 (d, J = 2.1 Hz, 1 H), 2.31 (d, J = 7.5 Hz, 2 H), 1.85 (d, J = 5.6 Hz, 1 H), 1.76-1.32 (m, 10 H). IR (neat) 3580-3350, 3210, 2870, 1748, 1415, 1300, 1020 cm-1. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.66; H, 9.09. Found: C, 66.32; H, 8.99.

A mixture of the product (1.70 g, 8.58 mmol), *tert*-butyldimethylchlorosilane (1.55 g, 10.3 mmol) and imidazole (1.46 g, 21.4 mmol) in 7 ml of DMF was stirred at 25°C for 20 h. The yellow solution was poured into 50 ml of H_2O and extracted with 3 x 50 ml Et_2O. The ethereal phase was washed with H_2O, brine, and dried over $MgSO_4$. Concentration at reduced pressure gave a yellow oil. Chromatography (flash column, silica gel, hexanes/EtOAc 5:1) gave the product as a colorless oil (R_F = 0.45) (2.19 g, 82%). The oil may be distilled if desired; b.p. (bulb-to-bulb) 88-90°C (0.1 mmHg). 1H NMR (270 MHz) δ 4.31 (dt, J = 6.4, 1.3 Hz, 1 H), 3.65 (s, 3 H), 2.35 (d, J = 1.3 Hz, 1 H), 2.29 (t, J = 7.4 Hz, 2 H), 1.66-1.29 (m, 10 H), 0.90-0.86 (s, 9 H), 0.12-0.10 (s, 6 H). IR (neat) 3258, 2880, 1745, 1468, 1260, 825, 770 cm-1.

The hydrostannation of this acetylene (1.90 g, 6.09 mmol), was carried out with tributyltin hydride (1.95, 6.69 mmol) and AIBN (10 mg, 10 mole %) heated to 100°C over a 15 min interval. The colorless mixture was maintained at 100°C for 3 h. Chromatography (flash column, silica gel, hexanes/EtOAc 95:5) afforded the stannane **11** as a colorless oil (R_f = 0.63) (3.12 g, 89%). No regioisomer was detected by 1H NMR analysis. The **E/Z** ratio of **11** was determined to be at least ≥ 95:5 **E/Z**. 1H NMR (270 MHz) δ 6.00 (d, J = 19.1 Hz, 1 H), 5.87 (dd, J = 19.0, 5.4 Hz, 1 H), 4.00 (m, 1 H), 3.65 (s, 3 H), 2.29 (t, J = 7.7 Hz, 2 H), 1.63-1.22 (m, 28 H), 0.94-0.82 (m, 18 H), 0.25-0.22 (m, 6 H). IR (neat) 2960, 2940, 1750, 1460, 1260, 1070, 980, 880, 770 cm-1. Anal. Calcd for $C_{29}H_{60}O_3Sn$: C, 60.55; H, 10.44. Found: C, 59.11; H, 9.92.

Synthesis of 12 and 13: To a solution of $Pd(CH_3CN)_2Cl_2$ (55 mg, 0.21 mmol, 4 mole %), 720 µl H_2O, and cyclopentadiene monoepoxide (310 mg, 3.76 mmol) in 10 ml of DMF, cooled to -10°C, was added **11** (2.75 g, 4.56 mmol). The orange solution was stirred at -10°C for 30 min and at 23°C for 16 h. The black mixture was treated with 3.6 ml (5.0 mmol F-) of a 1.4 N HF•pyridine solution with stirring for 30 min. Dilution with 75 ml CH_2Cl_2 and filtration (Celite) gave a clear yellow filtrate which was washed with 50 ml of 5% HCl (aq), H_2O, brine and dried over $MgSO_4$. Concentration at reduced pressure gave a yellow oil. Chromatography (flash column, silica gel, hexanes/EtOAc 4:1) afforded both the 1,4 and 1,2 addition products in a ratio of 1.35:1.00 respectively. Stannane **11** was also recovered (1.27 g, 46%) yield: 1,2 product, 312 mg; 1,4 product, 420 mg. Total combined yield 49% (75% based on recovered **11**).

1,4 Product (12, mixture of diastereomers): 1H NMR (270 MHz) δ 5.84 (m, 2 H), 5.44-5.23 (m, 2 H), 4.89-4.86 (m, 1 H), 4.01-3.95 (m, 1 H), 3.65 (s, 3 H), 3.51-3.44 (m, 1 H), 2.28 (t, J = 7.4 Hz, 2 H), 1.96-1.24

(m, 13 H), 0.85 (s, 9 H), -0.015 (m, 6 H). ^{13}C NMR (68 MHz) δ 174.11, 138.51, 138.42, 133.62, 133.44, 132.63, 77.17, 73.46, 51.23, 46.66, 41.26, 41.20, 38.36, 34.10, 29.20, 29.14, 25.94, 25.11, 24.94, 18.25, -4.11, -4.65. IR (neat) 3440-3250, 3025, 2870, 1740, 1245, 965, 820, 760 cm-1. Anal. Calcd for $C_{22}H_{40}O_4Si$: C, 66.6; H, 10.1. Found: C, 66.54; H, 10.18.

1,2 Product (13, mixture of diastereomers): ^1H NMR (270 MHz) δ 5.73 (m, 1 H), 5.60 (m, 1 H), 5.43 (m, 2 H), 4.13 (m, 1 H), 4.01 (m, 1 H), 3.65 (s, 3 H), 3.15 (m, 1 H), 2.71-2.62 (m, 1 H), 2.28 (t, J = 7.34 Hz, 2 H), 1.71-1.25 (m, 12 H), 0.86 (m, 9 H), 0.02 (m, 6 H). IR (neat) 3470-3260, 2860, 1745, 1255, 995, 968, 835, 765 cm-1.

Oxidation of 12 to 14: A suspension of **12** (264 mg, 0.66 mmol) and Ag_2CO_3 (1.46 g, 5.4 mmol) in 40 ml of benzene was heated to reflux with rapid stirring for 26 h. The gray suspension was filtered through Celite and the filter cake washed with 2 x 50 ml CH_2Cl_2. Concentration of the filtrate at reduced pressure gave a yellow oil. Chromatography (flash column, silica gel, hexanes/EtOAc 4:1) afforded pure **14** (R_F = 0.27) (171 mg, 86% yield, 100% based on recovered **12**). ^1H NMR (270 MHz, mixture of diastereomers) δ 7.54-7.50 (m, 1 H), 6.20-6.17 (m, 1 H), 5.59-5.30 (m, 2 H), 4.08-4.01 (m, 1 H), 3.66 (s, 3 H), 3.60-3.53 (m, 1 H), 2.62 (m, 1 H), 2.30 (t, J = 7.2 Hz, 2 H), 2.10 (m, 1 H), 1.75-1.16 (m, 10 H), 0.88 (s, 9 H), 0.00 (s, 6 H). ^{13}C NMR (68 MHz) δ 209.32, 174.08, 166.16, 135.69, 135.64, 133.90, 129.19, 72.92, 51.30, 43.57, 41.31, 38.17, 34.06, 29.19, 29.09, 25.88, 24.95, 24.88, 18.21, -4.21, -4.71. IR (neat) 2960, 2940, 2860, 1743, 1722, 1590, 1255, 960, 828, 768 cm-1. Anal. Calcd for $C_{22}H_{38}O_4Si$: C, 67.00; H, 9.64. Found: C, 66.80; H, 9.71.

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