Palladium-Catalyzed Trimethylenemethane Reaction To Form Methylenetetrahydrofurans. Reactions of Substituted TMM Precursors and Mechanistic Interpretation[1]

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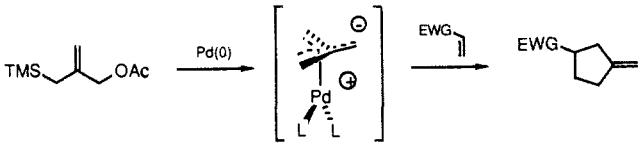
Abstract: Alkyl-, phenyl-, vinyl-, and acetoxy-substituted palladium–trimethylenemethane (Pd–TMM) complexes react with aldehydes in the presence of organotin cocatalysts such as trimethyltin acetate and trimethyltin *p*-toluenesulfonate to give cycloadducts. The reactions of methyl-substituted TMM precursors **2a**, **3**, and **12** were studied most extensively. Two methylenetetrahydrofuran regioisomers, **10k** and **10t**, were produced in mixtures varying from 31:1 to 1:200 depending upon the TMM precursor, aldehyde, and cocatalyst. Conjugating substituents decrease the reactivity of the Pd–TMM complex, and only isomer **10t** is available. The acetoxy substituent increases the reactivity of the organometallic and generated only **9k**; however, the products cannot be isolated due to their lability. Electron-withdrawing substituents cause the complexes to be unreactive. Carveol-derived TMM precursors **23** and **2j** give fused bicyclic products. Stereochemical analysis of these products showed that, contrary to olefin acceptors, aldehydes can, in some cases, attack the Pd complex on either face of the TMM moiety. These results indicate that trimethyltin chloride can be a very potent cocatalyst. The mechanism of the cycloaddition of aldehydes and, in particular, cocatalysis by organostannanes is discussed. The cocatalyst is believed to act by (1) aiding ring closure through the intermediacy of a stannyl ether and (2) acting as a Lewis acid to increase the rate of nucleophilic addition to the aldehyde.

The reaction of tetrakis(triphenylphosphine)palladium(0) with 3-acetoxy-2-[(trimethylsilyl)methyl]-1-propene generates a nucleophilic organometallic complex, **1**, which reacts with olefin and



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carbonyl functionality to yield methylenecyclopentane[3] and methylenetetrahydrofuran[4] products. Our original investigations into this process were conducted with Michael acceptors in the role of the electrophile[5] and suggested that the reactive intermediate is best described as a trimethylenemethane (TMM)[6] complex of palladium in which the four-carbon TMM moiety is bound in a η^3 manner.[7] Thus, the methylene carbons are of two kinds: two that are equivalent and bonded to palladium in a manner very similar to ordinary allyl complexes, and a unique carbon atom that is furthest from the metal. The latter is the nucleophilic center of the complex. Despite the limited symmetry properties of the Pd–TMM intermediate, our studies showed that when specifically deuterated TMM precursors are subjected to cycloaddition reactions, the label is scrambled. On the other hand, when the TMM complex was generated in the presence of diethyl malonate, a proton transfer took place such that the label was completely retained in its original position. We interpreted this data as evidence for a pathway, faster than cycloaddition but slower than deprotonation reactions, which interconverts the methylene carbons by rotation of the carbon umbrella atop the metal center. Fenske–Hall[8] calculations corroborated our supposition that a Pd–TMM species is responsible for the observed chemistry and provided the bonding and charge picture of the parent Pd–TMM complex illustrated in structure **1**.

At first glance, dynamic behavior in the Pd–TMM complex would seem to pose a serious problem for the substituted analogues. Rapid rotation would scramble the position of the substituent and so could yield a regioisomeric mixture of products. Nevertheless, we found that the reaction of either methyl-substituted TMM precursor **2a** or **3** with a Michael acceptor such as cyclopentenone provided chiefly to exclusively a single regioisomer, **5t** (R = Me).[9] The proposed mechanism (Scheme I) implicates rapid interconversion between the two Pd–TMM complexes **4k** and **4t** such that the substituted carbon is selected as the preferred nucleophile. Theory suggests, in fact, that isomer **4t** is the thermodynamically preferred complex. That the first-formed Pd–TMM complexes from **2a** and **3** are not identical can be demonstrated when a very reactive acceptor is employed, wherein cycloaddition becomes competitive with the rotation process: when dimethyl benzylidenemalonate is the electrophile, TMM precursor **2a** yields a 1:3.3 mixture of **6k**/**6t**, while precursor **3** gives a ratio of 1:6.7.

Expanding beyond the parent system, we found that Pd–TMM intermediates can be prepared from precursors bearing a wide variety of substituents, including phenyl, vinyl, cyano, propionyl, and acetoxy, and all react with Michael acceptors to give methylenecyclopentanes.[10] Surprisingly, the product always shows the regiochemical outcome of **4t** in which the substituted TMM carbon has been selected as the preferred nucleophile independent of the nature of the substituent. These results are testament to the powerful control exerted on the reaction pathway by the transition metal.

Considering the employment of aldehydes as the electrophilic component wherein 3-methylenetetrahydrofurans are formed, the question of kinetic versus thermodynamic control of regioselectivity arises once again (see Scheme II). In this paper, we report our synthetic and mechanistic studies of this problem.

† Stanford University.
‡ University of Wisconsin—Madison.

(1) Taken in part from: King, S. A. Ph.D. Thesis, Stanford University, Stanford, CA, 1988.
(2) NSF Graduate Fellow 1985–1988.
(3) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1.
(4) (a) Trost, B. M.; King, S. A. *J. Am. Chem. Soc.* See also: Trost, B. M.; Bonk, P. J. *J. Am. Chem. Soc.* **1985**, *107*, 8277. Trost, B. M.; King, S. A. *Chem. Lett.* **1987**, 15. Trost, B. M.; King, S. A. *Tetrahedron Lett.* **1986**, *27*, 5971. (b) Cf. diastereofacial selectivity of Diels–Alder reaction: Jurczak, J.; Bauer, T.; Jarosz, S. *Tetrahedron* **1984**, *42*, 4809.
(5) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6429. Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315.
(6) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6432.
(7) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1980**, *102*, 6359. Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2326.
(8) Gordon, D. J.; Fenske, R. F.; Nanninga, T. N.; Trost, B. M. *J. Am. Chem. Soc.* **1981**, *103*, 5974. See also: Albright, T. A. *J. Organomet. Chem.* **1980**, *198*, 159.
(9) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1981**, *103*, 5972.
(10) Trost, B. M.; Nanninga, T. N.; Satoh, T. *J. Am. Chem. Soc.* **1985**, *107*, 721.

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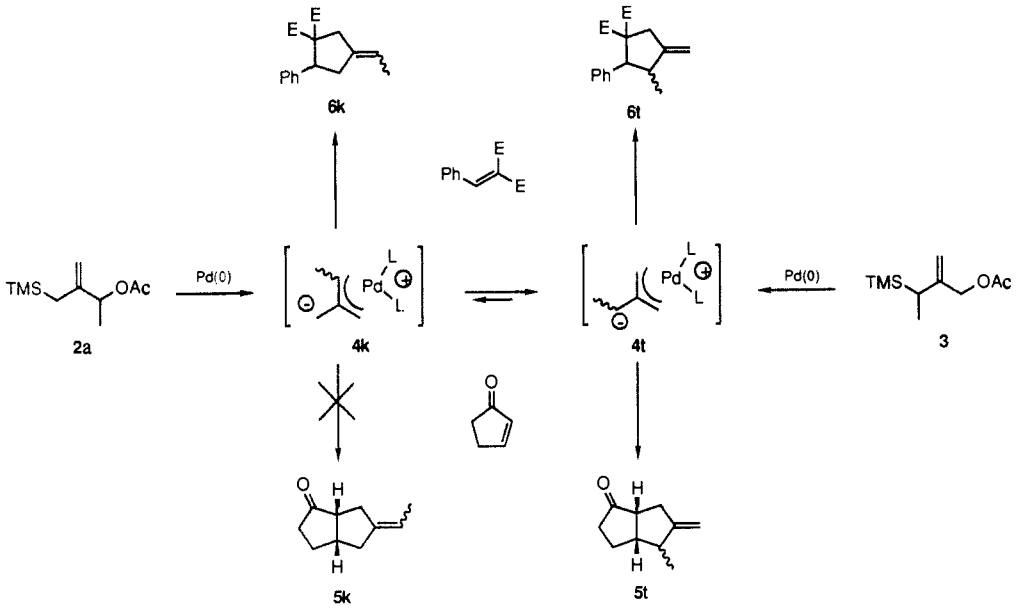
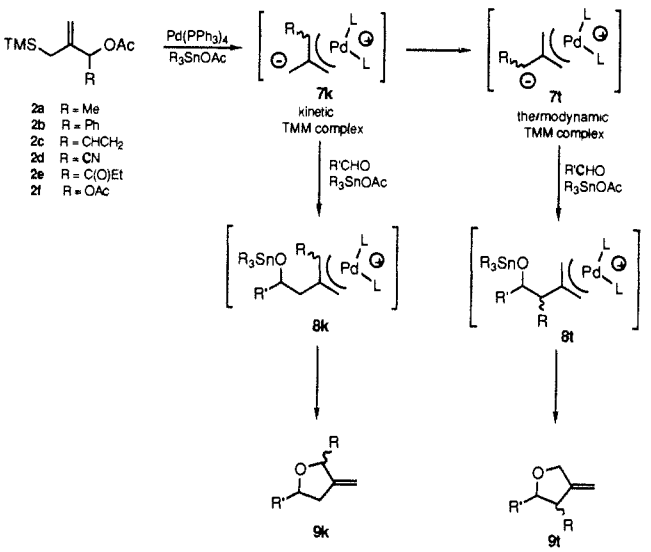
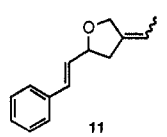
Scheme I. Cycloadditions of Isomeric Substituted TMM–PdL_2 Intermediates



Scheme II. Aldehyde Cycloaddition by Substituted Pd–TMM Complexes



Methyl Substituent. Optimization. We began our investigation with the simple methyl-substituted TMM system since both regioisomeric precursors **2a** and **3** were available. The Pd(0)-catalyzed reaction of **2a** with cinnamaldehyde in dioxane at reflux without tin cocatalysts gave a 30% yield of a mixture of four possible regio- and stereoisomers in a 1:1:1:1 ratio (Table I, entry 1), identified as mixtures of **10k** and **10t**. The absence of vinyl-substituted isomer **11** in complete contrast to electron-deficient



olefin acceptors is noteworthy. Decoupling experiments demonstrated that the stereoisomers **10k**, the products derived from the kinetic TMM complex, were readily identified by their 0.5 ppm downfield shift of the methyl group relative to the regioisomers **10t**. This initial experiment clearly showed that aldehydes were indeed capable of trapping the kinetic TMM complex, but the yield and selectivity were poor.

The establishment of the beneficial effect of tin cocatalysts immediately led to its employment with the substituted TMM precursors. Reaction of 1.7 equiv of **2a** with cinnamaldehyde in THF using palladium acetate/triphenylphosphine as catalyst and tri-*n*-butyltin acetate as cocatalyst gave a 48% yield of a 1.6:1 mixture of regioisomers **10k** to **10t**. Furthermore, while the ratio of stereoisomers of **10t** remained at 1:1, the isomers of **10k** now occurred in a 3:1 ratio. Unfortunately, nuclear Overhauser effect difference spectroscopy (NOEDS) studies failed to define the orientation of the stereoisomer of **10k**, which was present in excess.

As shown in Table I, intensive study was given to the problem of improving the reaction between cinnamaldehyde and the methyl-substituted Pd–TMM complex. Changes of solvent had a large effect on the reaction. DMF (entry 4) and dichloroethane (entries 8 and 9) gave only decomposition of the TMM precursor while leaving the aldehyde untouched. Cyclohexane was also undesirable, at least in part, because the catalyst was barely soluble (entry 12). Benzene, on the other hand, led to a vastly improved yield, generating 85% of a 1.6:1 mixture of regioisomers (entry 3b). Thus, the strong solvating properties of benzene, together with its low dipole moment, proved optimal.

Attention turned to the effects of a variety of cocatalysts. The improved efficacy of trimethyltin acetate compared to the tri-*n*-butyl analogue with the parent precursor **4a** extended to the methyl-substituted system as well (cf. entries 3 and 6). Optimization of the regioselectivity to 8.1–11.8:1 and efficiency (86–93% yield) with precursor **2a** involves use of trimethyltin acetate as cocatalyst in benzene wherein either the concentration of the tin cocatalyst (entry 7c) or acceptor (entry 7d) was increased. Under the same conditions, reaction of the isomeric precursor **3** with cinnamaldehyde gave a 94% yield of a 1:200 mixture favoring the opposite regioisomer **10t** (entry 19). Also apparent in these products was an increase in the ratio of the stereoisomers of **10k**, which now occurred in a 5:1 ratio. The stereoisomers of **10t** maintained their 1:1 ratio. Except for diacetoxytetrabutyldistannoxane (entry 27),[11] other tin carboxylate cocatalysts gave poor yields and/or poor regioselectivity. Variation of the phosphorus ligand either led to poorer selectivity (entry 13) or poorer yields (entries 14, 22, 23, and 26).

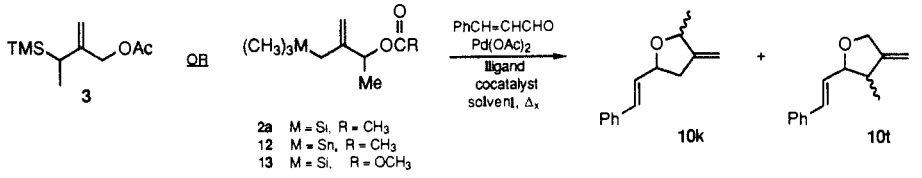
The superior activity of trimethyltin acetate was rationalized to derive from its increased electrophilicity relative to the butyl compounds. Reasoning that yet more electrophilic tin species could be even more effective, trimethyltin sulfonates[14] and trifluoro-

(11) Alleston, D. L.; Davies, A. G.; Figgis, B. N. *Proc. Chem. Soc.* **1961**, 457. Alleston, D. L.; Davies, A. G.; Hancock, D.; White, R. F. M. *J. Chem. Soc.* **1963**, 5469. Alleston, D. L.; Davies, A. G.; Hancock, D. *J. Chem. Soc.* **1964**, 5477.

(12) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158.

(13) Trost, B. M.; Chan, C.; Ruhter, G. *J. Am. Chem. Soc.* **1987**, *109*, 3486.

Table I. Optimization of the Reaction of the Methyl-Substituted TMMs[a]



entry	TMM precursor	ligand	cocatalyst	solvent	10k:10t ratio	yield, %
1	**2a**	PPh_3	no tin	THF	1:1	30[b]
2	**2a**	TIPP	Bu_3SnOAc	THF		NR
3	**2a**	PPh_3	Bu_3SnOAc	THF		
3a			0.2 M		1:1	
3b			0.1 M		1.6:1	48[b]
3c			0.5 M		1.8:1	
4	**2a**	PPh_3	Bu_3SnOAc	DMF		NR
5	**2a**	PPh_3	Bu_3SnOAc	PhH	1.6:1	85[b]
6	**2a**	PPh_3	Me_3SnOAc	THF	3.3:1	95[b]
7	**2a**	PPh_3	Me_3SnOAc	PhH		
7a			0.05 M		1.7:1	91[b]
7b			0.15 M		6.0:1	95[b]
7c			0.30 M		8.1:1	93[b]
7d			0.15 M		11.8:1	86[b,d]
8	**2a**	PPh_3	$In(acac)_3$	DCE		NR
9	**2a**	PPh_3	Me_3SnOAc	DCE		NR
10	**2a**	PPh_3	Ph_3SnOAc	THF		<10[c]
11	**2a**	PPh_3	Ph_3SnOAc	PhH		<10[c]
12	**2a**	PPh_3	Me_3SnOAc	C_6H_{12}	2.6:1	55[c]
13	**2a**	TIPP	Me_3SnOAc	PhH	1.5:1	64[c]
14	**2a**	TDMPP	Me_3SnOAc	PhH		NR
15	**2a**	PPh_3	Me_3SnOMs	PhH		NR
16	**2a**	PPh_3	Me_3SnOTs	PhH		NR
17	**13**	PPh_3	Me_3SnOTs	PhH		NR
18	**12**	PPh_3	Me_3SnOMs	PhH	4:1	50[c]
19	**3**	PPh_3	Me_3SnOAc	PhH	1:200	94[b]
20	**2a**	PPh_3	$Bu_2Sn(OAc)_2$	PhH	3.4:1	<24[c]
21	**2a**	PPh_3	$Me_3SnO_2CCF_3$	PhH		NR
22	**2a**	dppe	Me_3SnOAc	PhH		NR
23	**2a**	dppb	Me_3SnOAc	PhH		NR
24	**12**	PPh_3	none	THF	14.1:1	82[b]
25	**12**	PPh_3	Me_3SnOTs	PhH	31.1:1	82[b]
26	**2a**	$P(O\text{-}(o\text{-tol}))_3$	Me_3SnOAc	PhH		NR
27	**2a**	PPh_3	$(AcOSnBu_2)_2O$	PhH	3.4:1	80[b]
28	**2a**	dppf	Me_3SnOAc	PhH		NR

[a] See Table IV for experimental details for all entries. Yield is based upon TMM precursor; TIPP = triisopropyl phosphite; dppe = 1,2-bis(diphenylphosphino)ethane; dppe = 1,4-bis(diphenylphosphino)butane; dppf = (diphenylphosphino)ferrocene;[12] TDMPP = tris(2,5-dimethoxyphenyl)-phosphine;[13] DCE = 1,2-dichloroethane. [b] By isolation. [c] By GC. [d] Reaction run with 2 equiv of aldehyde (concentration 1 M); all others are run using 1 equiv (concentration 0.5 M).

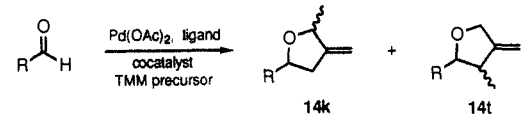
acetate[15] were explored as potential cocatalysts. Mixing of **2a** and cinnamaldehyde with trimethyltin *p*-toluenesulfonate or trifluoroacetate as cocatalyst under the usual conditions led to no reaction. The TMM precursor remained unchanged after refluxing overnight, indicating that the Pd(0) catalyst had been destroyed. On the other hand, the tin reagent **12** reacted well when trimethyltin tosylate was used as cocatalyst yielding a 31.1:1 mixture of regioisomers **10k** to **10t** in 82% yield, the best set of conditions for cycloadditions yielding **10k** as the major product. It seems then that simultaneous presence in the reaction mixture of the trimethylsilyl group and a leaving group like sulfonate or trifluoroacetate leads to catalyst poisoning. Other evidence in our group has indicated that the palladium(0) catalyst is not compatible with trimethylsilyl chloride. Attempted scavenging of the trimethylsilyl group from solution in the form of its methoxide by using TMM precursor **13** was to no avail. Indeed, even the tin sulfonates appeared to have some interaction with the palladium catalyst. When the catalyst mixture of palladium acetate, triphenylphosphine, and trimethyltin tosylate in benzene was exposed to small quantities of oxygen (as in a syringe barrel during transfer), the reversible formation of a bright red solution was observed. Trimethyltin acetate did not cause such behavior.

Methyl Substituent. Variation of Acceptor. Table II summarizes the yields and selectivities using saturated, unsaturated, and α-alkoxyaldehydes. As in the case of the parent TMM system, the reactions of saturated aldehydes proved to be the most challenging and further demonstrate the efficacy of the trimethyl compared to the tri-*n*-butyltin cocatalyst (Table II, entries 4 and 5). Of the data shown in Table II, the formation of methyl-substituted adduct **14k** ($R{=}CH_2{=}CH(CH_2)_8$) from 10-undecenal is a particularly impressive example of the effectiveness of cocatalysis by trimethyltin acetate. We had experienced difficulty in achieving high yields even with the parent TMM precursor and this aldehyde using tributyltin acetate cocatalysis. The isomeric TMM precursor **3**, which directly forms the thermodynamic Pd–TMM complex, cycloadded with 10-undecenal (entry 3) to give a high selectivity (16.2:1) for cycloadduct **14t** ($R{=}CH_2{=}CH(CH_2)_8$) derived from the thermodynamic Pd–TMM complex. The regioisomeric nature of **14k** and **14t** ($R{=}CH_2{=}CH(CH_2)_8$) was easily assigned by the number and multiplicity of the allylic protons occurring from δ 4.0–4.5 in the high-field ^1H NMR spectra. For inexplicable reasons, attempts to cocatalyze the cycloaddition of the tin TMM precursor **12** and saturated aldehyde with trimethyltin *p*-toluenesulfonate failed.

(14) Anderson, H. H. *Inorg. Chem.* **1964**, *3*, 108. Pang, M.; Becker, E. I. *J. Org. Chem.* **1964**, *29*, 1948. Tan, T. H.; Dalziel, J. R.; Yeats, P. A.; Sams, J. R.; Thompson, R. C.; Aubke, F. *Can. J. Chem.* **1972**, *50*, 1843. Harrison, P. G.; Phillips, R. C.; Richards, J. A. *J. Organomet. Chem.* **1976**, *114*, 47.

(15) Poder, C.; Sams, J. R. *J. Organomet. Chem.* **1969**, *19*, 67.

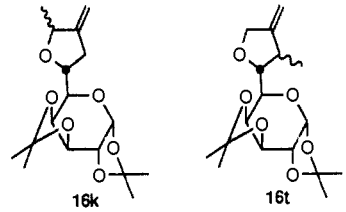
Table II. Reaction of Methyl-Substituted Systems with Various Aldehydes



entry	TMM precursor	RCHO aldehyde	cocatalyst	14k:14t ratio	yield,[a] %
1	**2a**		Me_3SnOAc	3.1:1	89
2	**12**		none	2.9:1	72
3	**3**		Me_3SnOAc	1:16.2	86
4	**2a**		Bu_3SnOAc	1:1.1	46
5	**2a**		Me_3SnOAc	3.1:1	82
6	**2a**		Me_3SnOAc	2.7:1	68
7	**2a**		Me_3SnOAc	7.9:1	90
8	**2a**		Me_3SnOAc	10.8:1	90
9	**3**		Me_3SnOAc	1:95.4	81

[a] See Table V for experimental details for all entries. All reactions were run in benzene with $Pd(OAc)_2/PPh_3$ as catalyst. All yields are of isolated products except entry 6 whose yield was determined by GC.

Exposure of the galactose-derived aldehyde **15** to each of the TMM precursors **2a** and **3** provided **16k** and **16t**, respectively,

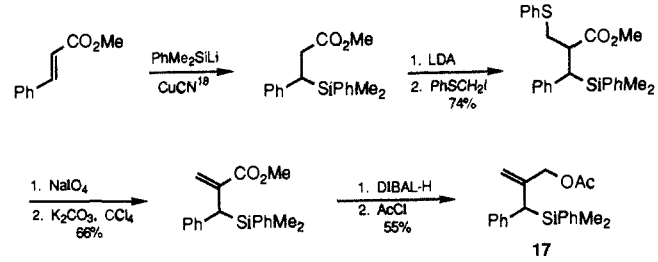


with high yields and very good regioselectivity (Table II, entries 8 and 9). The results correlated well with the high reactivity of α-alkoxy aldehydes. The products were both a mixture of methyl stereoisomers but were of a single orientation at C-6 of the sugar unit as indicated by the H_5–H_6 coupling constant. This stereochemistry was assigned as anti by analogy to the parent TMM cycloadduct.[4,16] As shown in entry 7, the unsaturated aldehyde, 2-hexenal, shows better regioselectivity than the saturated aldehydes.

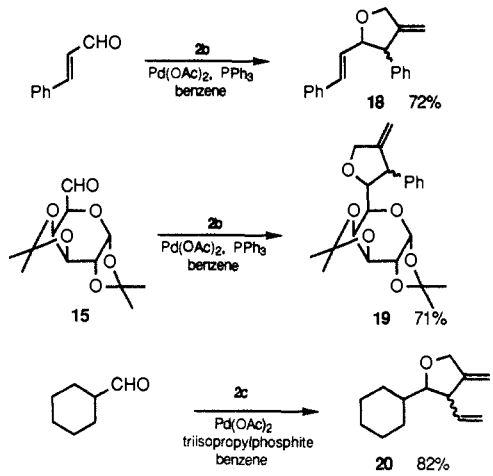
Conjugating Substituents. As conjugating substituents, phenyl and vinyl were envisioned to have marked electronic effects on the properties of the Pd–TMM complex. In order to study the regioselectivity, the pair of phenyl-substituted TMM precursors **2b**, which initially would generate the kinetic TMM complex, and **17**, which would generate the thermodynamic TMM complex, were prepared. While **2b** was a known compound at the outset of our investigation,[10] we explored a new route to TMM precursors substituted at the silylated carbon to demonstrate an ability to conveniently prepare the series of TMM precursors that generates the thermodynamic Pd–TMM complex directly and to demonstrate the ability of the readily available phenyldimethylsilyl moiety

(16) Also see: Czernecki, S.; Valery, J. M. *J. Carbohydr. Chem.* **1988**, *7*, 151; Coutrot, P.; Grison, C.; Tabyaoiu, M.; Czernecki, S.; Valery, J. M. *J. Chem. Soc., Chem. Commun.* **1988**, 1515.

Scheme III. Synthesis of Phenyl-Substituted TMM Precursor **17**



Scheme IV. Reactions of the Phenyl- and Vinyl-Substituted TMM Precursors



to serve in a TMM precursor. The straightforward synthesis of **17** is shown in Scheme III (yields are unoptimized) and depends upon the chemistry of Fleming[17] to put in place the critical silicon substituent.

The phenyl moiety immediately demonstrated a substantial effect upon the reactivity pattern of the Pd–TMM complex. When **2b** was allowed to react with cinnamaldehyde with trimethyltin acetate as cocatalyst in benzene (Scheme IV), a single regioisomer formed in 72% yield as a 1:1 diastereomeric mixture. Spectral data allow assignment of structure **18**, which must arise by rotation of the first-formed TMM complex before cycloaddition. When the reaction was conducted in THF, none of the desired product was obtained, but rather only protodesilylated TMM precursor was produced.[10] Indeed, even in benzene a sizeable amount of protodesilylated material was observed, and use of a 2-fold excess of precursor was necessary to produce good yields. Addition of 0.25 equiv of bis(trimethylsilyl)acetamide (BSA) to the reaction mixture as an acid scavenger did not change this result. Cycloaddition of **17** in the presence of trimethyltin acetate with an excess of cinnamaldehyde gave a 51% yield of **18** identical with that prepared from **2b**. Some protodesilylated precursor was also isolated. The cycloaddition reaction with **17** occurred much faster than with **2b** (2 h versus overnight), perhaps indicating that the phenyldimethylsilyl moiety is more readily cleaved in the initial ionization phase of the reaction pathway. The formation of **18** from **17** demonstrates for the first time the viability of trialkylsilicon groups other than trimethylsilyl in palladium-mediated trimethylenemethane chemistry.[18]

Attempted preparation of the phenyl-substituted adduct of saturated aldehydes such as cyclohexanecarboxaldehyde and hydrocinnamaldehyde was thwarted by protodesilylation. On the other hand, the galactose-derived aldehyde **15** cycloadds readily in benzene to give a 71% yield of the desired product **19**. None of the regioisomer derived from the kinetic TMM complex was

(17) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2520. Fleming, I.; Hill, H. J. M.; Parker, D. C.; Waterson, D. *J. Chem. Soc., Chem. Commun.* **1985**, 318.

(18) Trimethoxysilyl has also been used: Trost, B. M.; Miller, M. L. *J. Am. Chem. Soc.* **1988**, *110*, 3687.

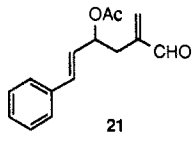
(19) Kobayashi, Y.; Tsuji, J. *Tetrahedron Lett.* **1981**, *22*, 4295.

detected. Again, the product was completely derived from attack upon a single face of the aldehyde. Thus, in the case of the phenyl-substituted complex, rotation is faster than cycloaddition even with the most reactive of aldehydes.

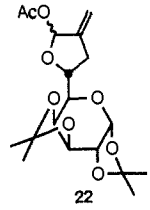
The vinyl-substituted Pd–TMM complex displayed intermediate reactivity. Its reaction with cinnamaldehyde gave a mixture of products that contained all four possible stereo- and regioisomers of the cycloadduct. Cyclohexanecarboxaldehyde failed to give any product when triphenylphosphine was used as ligand. Gratifyingly, however, when triisopropyl phosphite was the ligand, an 82% yield of **20** was obtained as a 4:1 mixture of stereoisomers depicted in Scheme IV. Like the phenyl-substituted cycloadducts, this product must also arise from the thermodynamic TMM complex.

Electron-Withdrawing and Electron-Donating Substituents. The cyano, keto, and acetoxy substituents should impart considerable electronic perturbation to the Pd–TMM complex. In order to determine the effect on the cycloaddition reaction, each of these TMM precursors was reacted with cinnamaldehyde. The cyano- and keto-substituted TMM precursors **2d** and **2e**[10] decomposed under the reaction conditions but failed to generate any desirable product in either THF or benzene even with tin cocatalysis (tri-*n*-butyltin acetate for the cyano-substituted system and trimethyltin acetate for the keto-substituted system). The enhanced carbanion stabilization by cyano or keto sufficiently decreases the nucleophilicity of the carbanion center of the intermediate **7** (Scheme II) that carbonyl addition now fails.

The acetoxy-substituted precursor **2f** was especially interesting since the resultant products are related to deoxypentoses. Unfortunately, **8f** is an allylic, α-alkoxy acetate and should be quite unstable to the palladium(0) catalyst. In the event, reaction of **2f** with cinnamaldehyde gave a messy reaction mixture with only **21** as an identifiable product. This product could easily be formed



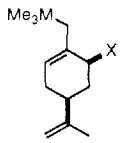
21



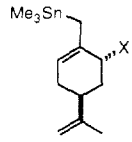
22

through decomposition of the expected cycloadduct by migration of the acetyl group and ring opening. Reaction of **2f** with the aldehyde **15** gave two isolable products, each of which was a stereoisomer of **22**. However, these were hopelessly contaminated by decomposition products and could not be obtained in pure form. It is interesting that these cycloadducts did not also decompose to give products analogous to **21**.

Fused Bicyclic Cycloadducts. In pushing our studies to yet more complex systems, we felt that the cycloaddition reactions of carveol-derived TMM precursors **23** and **24** were most strongly coupled to questions of mechanistic and synthetic interest. Our previous work had shown that olefin electrophiles attack the Pd–TMM complex on the face of the TMM moiety opposite the metal.[20] That is, coordination of the olefin of the acceptor to palladium does not precede reaction. The similarity (or contrast) between carbon–oxygen and carbon–carbon double bonds as electrophiles would shed light upon our earlier speculation regarding internal delivery of conjugated aldehydes. Reactions of **23** and **24** should thoroughly challenge the now-established ability



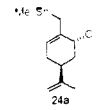
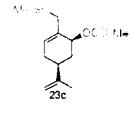
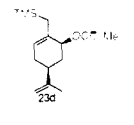
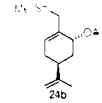
23a M = Sn X = OH
23b M = Sn X = OMS
23c M = Sn X = OCO_2Me
23d M = Si X = OCO_2Me



24a X = Cl
24b X = OAc

(20) Trost, B. M.; Nanninga, T. N. *J. Am. Chem. Soc.* **1985**, *107*, 1075.

Table III. Reactions of Carveol-Derived TMM Precursors with Cinnamaldehyde[a]

entry	TMM precursor	reaction time	product(s) ratio	isolated yield, %
1		8 h	6:1	50%
2		24 h	2:1	49%
3		2 days	9:1	40%
4		24 h	2:1	53%

[a] See text and experimental for details for all entries.

to control regiochemistry. Because the palladium atom must sit in a sterically crowded position under the six-membered ring in the kinetic TMM complex, rotation of the TMM moiety should be quite facile. Lastly, synthetic pathways derived from these precursors would be intriguing since they lead to molecules very similar in structure to the fused bicyclic systems of natural products such as phyllanthocin.[21]

Since we anticipated the need for sulfonate cocatalysts in order to adequately control regiochemistry, we prepared stannylated TMM precursors. Quenching the dianion of *cis*-carveol[22,23] with trimethyltin chloride gave 56% of the stannyl alcohol **23a**. The alcohol was then treated with methanesulfonyl chloride in anticipation that mesylate **23b** would cause a sulfonate cocatalyst, trimethyltin methanesulfonate, to be formed in situ during TMM complex formation. In the event, the actual product of mesylation was the *trans*-chloride **24a** contaminated with about 15% of the epimer. Careful analysis by TLC allowed one to see the intermediate mesylate, which was rapidly further transformed to the chloride.

Cycloaddition of *trans*-chloride **24a** with cinnamaldehyde in benzene using palladium acetate/triphenylphosphine or, better, tetrakis(triphenylphosphine) palladium(0) (7 mol %) and trimethyltin tosylate (7 mol %) produced two tetrahydrofurans in an 85:15 mixture (50% yield) (Table III, entry 1). *^1H and ^{13}C NMR spectroscopy showed that the major product was* ***26***, i.e. *that derived from the kinetic TMM complex*! Specifically, the vinyl protons could be identified at δ 6.61 (d, J = 15.9 Hz, H_9), 6.20 (dd, J = 15.9, 7.4 Hz, H_8), 5.52 (d, J = 1.8 Hz, H_4), 4.81 and 4.66 (two s, H_{10} and H_{10}). The quartet at δ 4.54 (J = 7.3 Hz) was assigned to H_2 and was the first clue to the regiochemistry of the addition. The alternate regioisomer, i.e., **28** or **29**, could have, at most, two couplings to this proton. The only remaining low-field proton is then assigned as H_{7a}. The high-field protons then include a group between δ 2 and 3, the methyl singlet (δ 1.80), and a proton coupled to three other protons at δ 1.54 (ddd, J =

(21) Kupchan, S. M.; LaVoie, E. J.; Braufman, A. R.; Fei, B. Y.; Bright, W. M.; Bryan, R. F. *J. Am. Chem. Soc.* **1977**, *99*, 3199.
(22) Ozawa, S.; Itoh, A.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1979**, 2909.
(23) Trost, B. M.; Nanninga, T. N. *J. Am. Chem. Soc.* **1985**, *107*, 1075. Trost, B. M.; Chan, D. M. T.; Nanninga, T. N. *Org. Synth.* **1984**, *62*, 58. Cf.: Cardillo, G.; Contento, M.; Sandri, S. *Tetrahedron Lett.* **1974**, 2215.

14.3, 9.7, 4.5 Hz). As with the olefin cycloadducts described in our earlier work,[20] decoupling experiments showed that this proton must be the axial proton at C(7). Fully decoupled ^{13}C NMR and INEPT spectroscopy confirmed assignment of the cycloadduct to structure **26**. Ten olefinic and aromatic carbons were all downfield of δ 109. The INEPT experiment indicated that each of the two carbons bonded to oxygen (at δ 77.7 and 74.2) possessed only one attached hydrogen and confirmed the regiochemical assignment. The coupling constant for the axial proton at C(7) with that at C(7a) of 4.5 Hz indicates the latter proton is equatorial and, therefore, β as depicted.

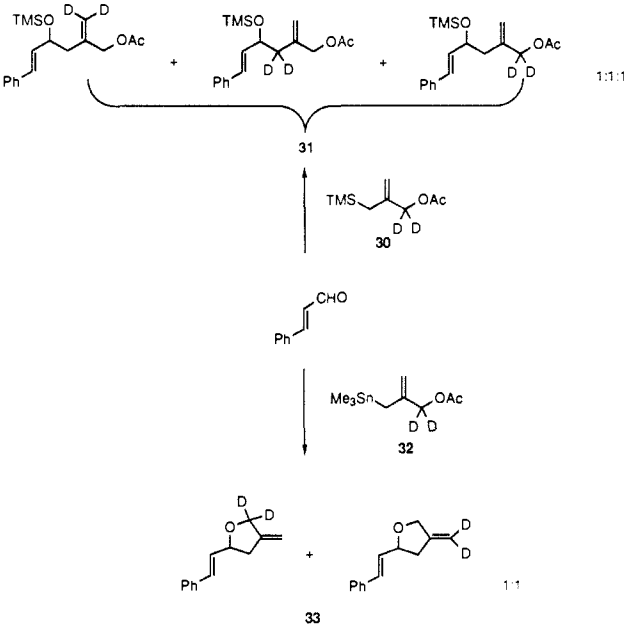
The minor product shared the regiochemistry of **26** and was identified as **27** since the upfield proton ($H_{7\,axial}$) appeared as a quartet with J = 14.3 Hz. This product may have arisen from the stereoisomeric impurity in the starting material. Both **26** and **27** were single stereoisomers at position 2, but NOEDS experiments failed to shed light on their orientation. The carvyl intermediate has a plane of symmetry so either the endo or the exo product is available from the cyclizing intermediate (vide infra). It is thus more reasonable that the stereochemistry is exo as shown in both cases since this orientation should minimize nonbonded interactions.

A *cis*-carveol TMM precursor **23c**, prepared in standard fashion from **23a** in 52% yield, reacted with cinnamaldehyde in the presence of 10 mol % tetrakis(triphenylphosphine)palladium(0), excess triphenylphosphine, and 10 mol % trimethyltin tosylate in benzene to generate a 2:1 mixture of products in 49% yield. The minor compound was identified as **27** by spectral comparison. The major product was a 1:1 mixture of stereoisomers. Each stereoisomer displayed five vinyl protons and three protons α to oxygen: an AB quartet (J = 10.8 Hz) and a triplet (J = 7.3 Hz). These data clearly identify the compounds as belonging to the hexahydroisobenzofuran family of **28** and **29**. The stereochemistry at the ring juncture was assigned by the coupling pattern of the upfield proton as before. This time it appeared as a quartet with J = 12.0 Hz, which identifies the major products as being the stereoisomers of **28**, epimeric at position 1. This compound could be prepared more efficiently by using the trimethylsilyl carbonate **23d** and trimethyltin acetate as cocatalysts (Table III, entry 3).

The preference for formation of the cycloadducts via the thermodynamic TMM–PdL_2 intermediate for Table III, entries 2 and 3, opened the question of the role of chloride in determining the kinetic regioselectivity of entry 1. The reaction PdL_2 intermediate for Table III, entries 2 and 3, opened the question of the role of chloride in determining the kinetic regioselectivity of entry 1. The reaction of the *trans*-carveol[24] stannyl acetate **24b** with cinnamaldehyde and palladium acetate/triphenylphosphine as catalyst generated two compounds. The major isomer was identified as **28a**, one of the previously identified stereoisomers of **28**. The minor isomer was a new product, which displayed the same regiochemistry as **28** but showed a coupling pattern to the upfield axial proton (ddd, J = 14.3, 9.7, 4.5 Hz), which justified its assignment as structure **29**. The assignment of stereochemistry at position 1 derives from the coupling constant (J = 9.6 Hz) for its associated proton with the bridgehead proton.[20] Molecular models suggest a 20–40° dihedral angle for the cis orientation but nearly a 180° angle for its epimer. The unexpected formation of the perhydroisobenzofuran **28a** led us to establish that it could not have arisen by prior isomerization of the starting material.

Cycloadditions of Deuterated TMM Precursors and Related Work. Further insight into the "tin effect" was obtained through deuterium-labeling experiments in which a striking difference between the silicon and tin precursor in the cycloadditions was observed. As illustrated in Scheme V, reaction of the deuterated silicon compound **30** and Pd(0) with cinnamaldehyde in THF at reflux yielded the uncyclized silyl acetate **31**-d_2 with completely scrambled labeling.[7] However, when deuterated stannyl TMM precursor **32** was employed in the same way, the resulting cycloadducts **33**-d_2 retained greater than 95% of the isotopic label at the methylene carbon and the allylic carbon attached to oxygen.

Scheme V. Contrast between the Si- and the Sn-Based Precursors



Reaction through the established TMM manifold could produce the isotopic results of Scheme V if, in the case of the tin-based precursors, the fluxionality of the TMM intermediate was not competitive with nucleophilic attack on the aldehyde as depicted in Scheme VI.

An alternative explanation of the labeling results for the tin substrate invokes a simple allyltin addition[25] followed by palladium-catalyzed ring closure (Scheme VII). Control experiments demonstrated that the hypothetical allyltin addition must be palladium catalyzed. While the likelihood of this seemed remote, it certainly required investigation. A combination of all of the functionality present under TMM cycloaddition conditions did, in fact, lead to an allylstannane addition to an aldehyde. Specifically, reaction of cinnamaldehyde with allyltri-*n*-butyltin and allyl acetate in the presence of $Pd(OAc)_2$ and PPh_3 at 40° in THF gave an 89% yield of the homoallyl alcohol **34** depicted in Scheme VIII. A total of 2 equiv of both allylic compounds was required, however, to force the reaction to completion. Stille has reported the addition of allyltrimethyltin to a π-nitrophenyl ketone in the presence of the palladium(II) complex benzylchlorobis(triphenylphosphine)palladium.[26] This species is notably similar to the allylacetoxybis(triphenylphosphine)palladium complex, which might be produced by the reaction mixture discussed here. Presumably such palladium(II) complexes are capable of acting as a Lewis acid and inducing reaction of allylstannanes with the carbonyl group. Alternatively, the nucleophile might be σ-allyl-π-allyl(triphenylphosphine)palladium. σ-Allyl-π-allyl(trimethylphosphine)palladium is known, but nucleophilic reactivity is not documented.[27] Nevertheless, this reaction failed to extend to allylstannanes other than the parent. The reaction of cinnamyltri-*n*-butyltin with cinnamaldehyde in the presence of palladium acetate and triphenylphosphine left the aldehyde unaffected and only produced coupling[28,29] to 1-phenyl-1,5-hexadiene. Such an allylic coupling process could also be blamed for the excess

(24) Julia, M. Ger. Patent 2162882, 1972; *Chem. Abstr.* **1972**, *77*, 101937.

(25) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107. Pereyre, M.; Quintard, J. P. *Pure Appl. Chem.* **1981**, *53*, 2401. Hoffman, R. W. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 555. Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. *Tetrahedron Lett.* **1984**, *25*, 3927. For an exception to allyl inversion, see: Quintard, J. P.; Elissondo, B.; Peregre, M. *J. Org. Chem.* **1983**, *48*, 1559.

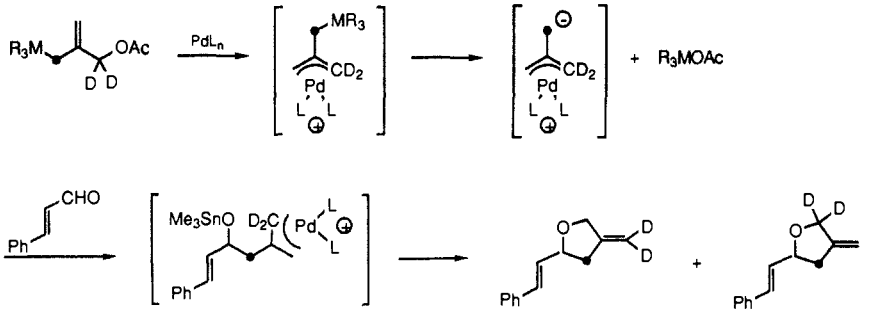
(26) Labadie, J. W.; Tueting, D.; Stille, J. K. *J. Org. Chem.* **1983**, *48*, 4634.

(27) Henc, B.; Jolly, P. W.; Salz, R.; Stobbe, S.; Wilke, G.; Benn, R.; Mynott, R.; Seevogel, K.; Goddard, R.; Kruger, C. *J. Organomet. Chem.* **1980**, *191*, 449.

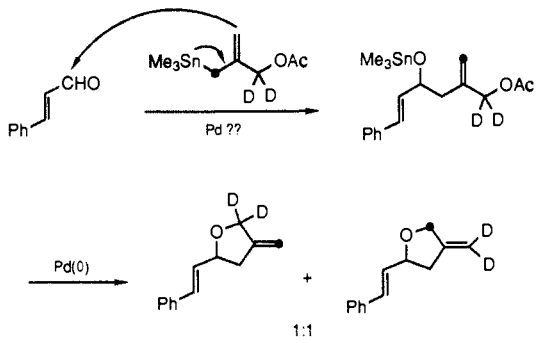
(28) Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2595.

(29) For reviews, see: Stille, J. K. *Pure Appl. Chem.* **1985**, *57*, 1771. Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

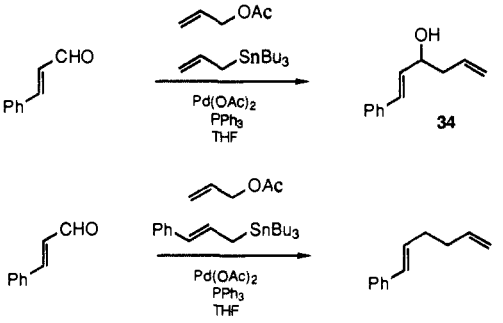
Scheme VI. Trimethylenemethane-Based Explanation of the Results



Scheme VII. Allyltin Addition Mechanism



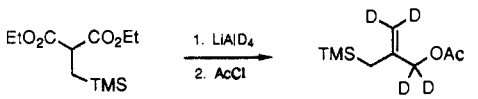
Scheme VIII. Palladium-Catalyzed Allyltin Addition



of allylic starting materials needed to produce **34**. The TMM precursors have never demonstrated any propensity toward such homocoupling reactivity. It seems then that the "allyltin addition" mechanism does not adequately explain the cycloaddition chemistry. Nevertheless, a method was required to better identify the nature of the key steps.

Examination of Schemes VI and VII reveals that the carbon originally bonded to the metal ends up in a different position in each mechanism. Therefore, a TMM precursor, in which the carbon originally bonded to tin is unique, would be highly indicative of the mechanism. TMM precursor **24a** provides such a molecule. Its cycloaddition with cinnamaldehyde under conditions designed to trap the kinetic TMM intermediate (vide infra) and so produce **26** (Table III, entry 1) accomplishes this task. The regiochemistry of **26** clearly indicates that the carbon originally bonded to tin is the nucleophile. Since allylstannane[25] and allylsilane[30] additions are well precedented to proceed via allyl inversion, the carbon atom originally bonded to the tin atom most likely becomes the nucleophilic center through a pathway involving a Pd–TMM complex.

The correlation between utilizing an organostannane as a precursor and a tin carboxylate as a cocatalyst with an organosilane precursor was sought with the deuterated precursor **36**



35 **36**

prepared by LAD reduction of malonate derivative **35**, followed by acetylation. Its reaction with cinnamaldehyde and cyclohexanecarboxaldehyde in the presence of palladium acetate, triphenylphosphine, and trimethyltin acetate demonstrated that the carbon bearing protons (rather than those bearing deuteria) mainly becomes the nucleophilic center (Scheme IX). Integration of the ^1H NMR spectra establishes the distribution of the label as depicted. These results are most consistent with the TMM mechanism in which the major cycloadduct in this unbiased TMM system arises from the kinetic TMM–PdL_2 intermediate in which the carbon originally attached to the group IV metal is the nucleophile. To the extent that the fluxionality of the TMM–PdL_2 competes with cycloaddition, the remaining two products are produced. The higher kinetic trapping with the unsaturated aldehyde acceptor (88:12) compared to the saturated aldehyde acceptor (69:31) correlates with our earlier observations of the greater efficacy of cycloadditions with the unsaturated aldehydes.

Discussion

The striking difference in regioselectivity of cycloadditions of substituted TMM–PdL_2 complexes between electron-deficient olefinic and aldehyde acceptors is accommodated by the notion of a kinetic versus thermodynamic trapping, as depicted in Schemes I and II. The higher electrophilicity of the aldehydes enhances their interception of the kinetic complex. The higher selectivity for the kinetic product as a function of increasing concentrations of reactants and higher electrophilicity of tin species is in accord with this postulate.

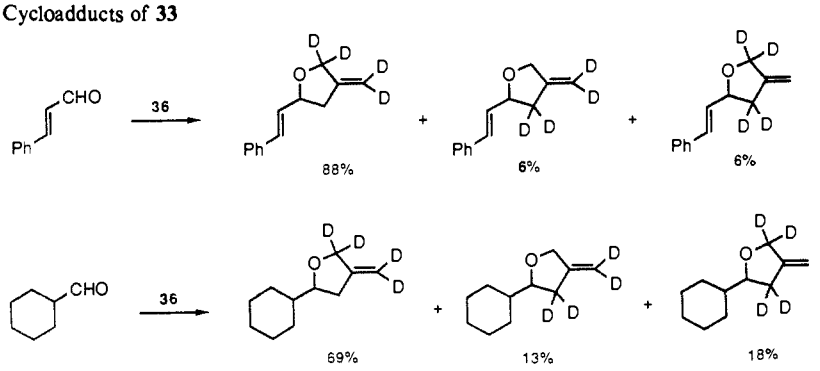
The effect of substituents reinforces the above interpretation. Substituents that either increase the reactivity of the TMM–PdL_2 intermediate or decrease the rate of the migration of palladium in such intermediates enhance kinetic trapping. An alkyl group such as methyl falls into this category. On the other hand, substituents that either decrease the reactivity of the TMM–PdL_2 intermediate or increase the rate of the fluxional processes diminish kinetic interception. Conjugating groups like phenyl and vinyl fall into this category. If the group is too strongly stabilizing like cyano or acyl, then condensation becomes so slow it is negligible.

The higher selectivity of the unsaturated aldehydes for the kinetic cycloadducts appears contrary to the fact that they are normally less electrophilic than their saturated counterparts. A rationale suggests that, in such cases, a modified catalyst is generated in which the unsaturated aldehyde is coordinated to palladium during the catalytic cycle.[31] The stereochemical studies of Table III, which indicate that transfer of the TMM fragment to the aldehyde occurs mainly on the face distal to palladium, require condensation with a noncoordinated aldehyde. Within such a picture, the excellent diastereoselectivity with respect to the aldehyde that can be observed can be rationalized as depicted

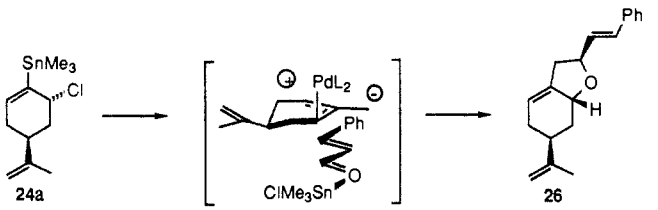
(30) Deleris, G.; Donogues, J.; Calas, R. *J. Organomet. Chem.* **1975**, *93*, 43. Deleris, G.; Donogues, J.; Calas, R. *Tetrahedron Lett.* **1976**, 2449. Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295. Ojima, I.; Kumagai, M.; Miyazawa, Y. *Tetrahedron Lett.* **1977**, 1385. Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, 2589. Yamamoto, Y.; Yatagai, H.; Naruta, K.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.

(31) For a related example, see: Backvall, J. E.; Nordberg, R. E.; Wilhelm, D. *J. Am. Chem. Soc.* **1985**, *107*, 6892.

Scheme IX. Labeling Study of Cycloadducts of **33**

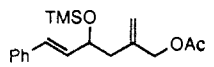


Scheme X. Reaction of Stannyl Chloride **24a**



in Scheme X for **24a** in which one of the ligands in the TMM-PdL_2 intermediate may be a coordinated aldehyde. Furthermore, the anomalous stereochemistry in the cycloaddition of **24b** (Table III) is readily understood as the result of a competition in which the coordinated aldehyde is delivered more rapidly in this case to give adduct **28a**, as depicted in Scheme XI, in contrast to the external delivery to give adduct **29**.

Mechanism of Cocatalysis. The formation of a tin ether as the cyclizing intermediate, as depicted in Scheme XII, for the methyl-substituted case best explains the improved yields and cleanliness of the cocatalyzed aldehyde cycloaddition. A complicating factor in this scenario is the presence in the reaction mixture of trimethylsilyl acetate generated from the starting material in stoichiometric quantities. As is apparent from Scheme VI, trimethylsilyl acetate is capable of trapping the alkoxide to give the open-chain product **31**, which is stable to the reaction



31

conditions and does not cyclize.[4] The implication, then, is that trialkyltin acetate cocatalyst is capable of reacting with the alkoxide intermediate at least 2–3 orders of magnitude faster than trimethylsilyl acetate. The only direct comparisons in the literature of rates of base-induced substitution reactions at silicon and tin involve the alcoholysis of $RMMe_3$ (R = benzyl[32] or allyl,[33] M = Sn or Si). In each case, the stannanes are 20–50 times more reactive than the corresponding silane. The studies of Chipperfield and Prince[34] establish that the reaction of triisopropylgermyl chloride with water is 20 times faster than that of triisopropylsilyl chloride. These results are attributed to the tendency of germanium to become pentacoordinate, therefore, lowering the transition-state energy for the substitution reaction. As previously mentioned, trimethyltin carboxylates also readily become pentacoordinate and indeed are often most stable in that form. This is not true of the trimethylsilyl carboxylates.[35] Some tin carboxylates are even thought to exist in hexacoordinate and heptacoordinate structures.[36] Thus, the ability of tin to expand its valence shell to heteroatoms strongly suggests that in the carbonyl addition process tin ethers rather than silicon ethers would be kinetically formed from an intermediate alkoxide.[37]

A more classical explanation of the tin cocatalyst effect portrays the tin carboxylate as a simple Lewis acid since such species are claimed to exhibit Lewis acid properties.[38] For example, the solution dynamics of trimethyltin acetate and formate examined by NMR spectroscopy suggest these compounds form five-coordinate complexes with pyridine or DMSO in deuterochloroform.[39] Attack of the TMM-PdL_2 on the Lewis acid–Lewis base complex of the aldehyde and the tin carboxylate generates the tin ethers directly. The minor effect observed with organotin species of greatly enhanced Lewis acidity argues against a major role for such an effect. A conclusion that it contributes to the efficacy of the overall process, however, is in agreement with the solvent effect in which the "tin effect" is optimized in a noncoordinating solvent like benzene. A Lewis acid mechanism also means that the direct formation of the trialkylstannyl ether avoids the basic (and apparently problematic) alkoxide.

Either way, capping of the alkoxide to prevent alkoxide-induced alternative modes of reaction, but with a group that still permits the oxygen to display nucleophilic properties toward the π-allylpalladium intermediate,[40] creates an efficient 3-methylenetetrahydrofuran synthesis. By properly choosing the methyl TMM precursor, we can obtain either regioisomeric cycloadduct, as shown in Scheme XII. The regioselectivity of collapse of **38k** is quite interesting since the oxygen nucleophile is attacking the more substituted allyl terminus with complete selectivity. This regioselectivity contrasts with carbon nucleophiles, which normally prefer attacking the less substituted allyl terminus. The variation of regioselectivity of the collapse may derive from the competition between charge or electronic effects, which favor attack of the nucleophile at the most electron-deficient allyl terminus (which is the more substituted one),[41] and steric effects, which favor attack at the sterically more accessible terminus (which is the less substituted one).[42] The sterically nondemanding oxygen nucleophile permits electronic effects to dominate.

We cannot dismiss from consideration for the tin effect the possibility that the organostannane modifies the palladium catalyst. Examples of group IV elements as ligands (e.g., triphenyltin, triphenyllead, trimethyllead) are known in transition-metal chemistry.[43] In the area of palladium chemistry, the trichloro-

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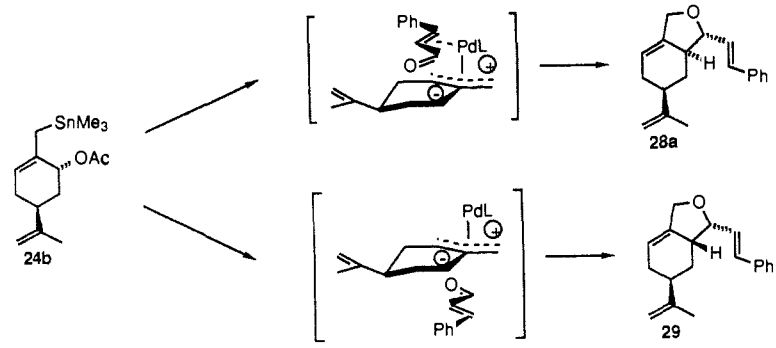
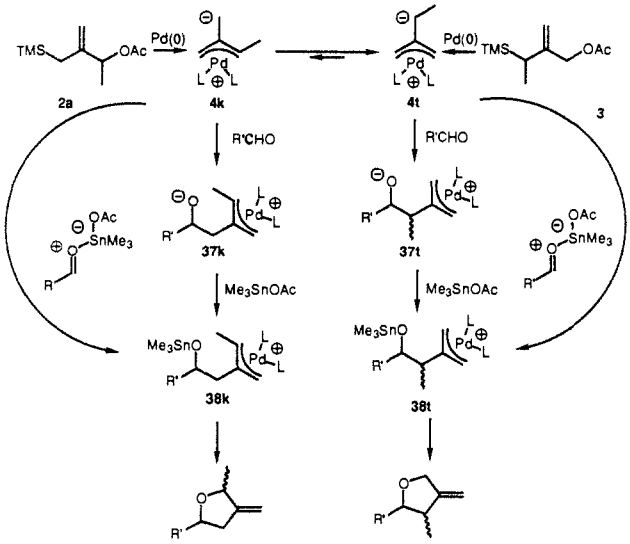
Scheme XI. Reaction of Stannyl Acetate **24b**



Scheme XII. Formation of the Stannyl Ether



stannyl ligand is known, for example, in the complexes (π-allyl)Pd($SnCl_3$)(L), L = Ph_3P or ethylene.[44] However, no examples of trialkylstannyl or triarylstannyl ligands have been reported. Interestingly, the regioselectivity of the hydroformylation of α-olefins is greatly enhanced by the catalyst (H)Pd($SnCl_3$)(PPh_3)$_2$.[45] In the TMM cycloaddition reaction, association of the tin ligand to palladium could hypothetically be accomplished through formation of a complex between the trialkyltin acetate and the Pd–TMM species. Attempts in our laboratories to detect such species under the conditions of the cycloaddition have not been successful and lead us to conclude that this prospect is remote.

Experimental Section

General Procedure for Table I. Development of Regioselective Preparation of *cis*- and *trans*-2-[(*E*)-2-Phenylethenyl]-5-methyl-4-methylenetetrahydrofuran (10k). Palladium acetate (3–7 mol %), the ligand (if a solid, 5 equiv of phosphine/palladium), and a cocatalyst (if a solid) were placed in an oven dried test tube and flushed thoroughly with nitrogen. Solvent (to make a 0.25–0.5 M solution in cinnamaldehyde) was added. The ligand or cocatalyst was added if either was a liquid (triisopropyl phosphite or dibutyltin diacetate). The mixture was stirred and heated at 70 °C until homogeneous. Cinnamaldehyde and the TMM precursor were added, and the vessel was heated at 70 °C. At completion of reaction as judged by TLC and/or GC, the reaction mixture was cooled, diluted with 80:20 hexane/ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent, the residue was flash chromatographed to give a mixture of diastereomers. The ratio of these diastereomers was dependent upon the cocatalyst used: no cocatalyst, 1:1; tributyltin acetate, dibutyltin diacetate, 3:1; trimethyltin acetate, 5:1, R_f 0.49 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): major isomer, δ 7.45–7.21 (m, 5 H), 6.66 (d, J = 15.6 Hz, 1 H), 6.25 (dd, J = 15.6, 7.6 Hz, 1 H), 4.99 (br s, 1 H), 4.87 (br s, 1 H), 4.50–4.40 (m, 2 H), 2.80 (dd, J = 15.4 Hz, 1 H), 2.50 (m, 1 H), 1.39 (d, J = 6.2 Hz, 1 H); minor isomer, δ 7.45–7.21 (m, 5 H), 6.62 (d, J = 15.6 Hz, 1 H), 6.23 (dd, J = 15.6, 7.6 Hz, 1 H), 5.02 (br s, 1 H), 4.88 (br s, 1 H), 4.68 (q, J = 6.2 Hz, 1 H), 4.50–4.40 (m, 1 H), 2.85 (m, 1 H), 2.52 (m, 1 H), 1.33 (d, J = 6.2 Hz, 1 H). IR ($CDCl_3$): 1604, 1499, 1454 cm^{-1}. MS calcd for $C_{16}H_{16}O$: m/e 200.1201. Found: 200.1203. GC retention (50–250 °C, 10 °C/min): major isomer, 11.92 min; minor diastereomer, 12.01 min. The reaction details for each run are summarized in Table IV.

***cis*- and *trans*-2-[(*E*)-2-Phenylethenyl]-3-methyl-4-methylenetetrahydrofuran (10t; Entry 19, Table I).** Palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), and trimethyltin acetate (6 mg, 25 μmol) were placed in an oven-dried test tube and flushed thoroughly with nitrogen. Benzene (0.5 mL) was added and the mixture stirred and heated at 70 °C until homogeneous. Cinnamaldehyde (33 mg, 32 μL, 0.25 mmol) and 2-(acetoxymethyl)-3-(trimethylsilyl)-1-butene (**3**; 75 mg, 85 μL, 0.375 mmol) were added, and the vessel was heated at 70 °C overnight. The reaction mixture was cooled, diluted with 80:20 hexane/ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent the residue was flash chromatographed (96:4 hexane/ethyl acetate) to give 47 mg (94%) of the title compounds as a 1.2:1 mixture of diastereomers, R_f 0.49 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): major isomer, δ 7.45–7.21 (m, 5 H), 6.60 (d, J = 15.6 Hz, 1 H), 6.14 (dd, J = 15.6, 7.6 Hz, 1 H), 5.00–4.90 (m, 2 H), 4.68–4.35 (m, 2 H), 3.91 (dd, J = 8.3, 8.1 Hz, 1 H), 2.89 (m, 1 H), 1.06 (d, J = 6.2 Hz, 3 H); minor isomer, δ 7.45–7.21 (m, 5 H), 6.65 (d, J = 15.6 Hz, 1 H), 6.24 (dd, J = 15.6, 7.6 Hz, 1 H), 5.00–4.90 (m, 2 H), 4.68–4.35 (m, 3 H), 2.42 (m, 1 H), 1.12 (d, J = 6.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture: δ 152.9, 152.9, 136.7, 136.5, 132.6, 132.1, 128.5, 127.7, 127.6, 126.5, 126.4, 103.6, 103.1, 87.3, 83.3, 70.9, 70.3, 44.2, 42.1, 13.9, 13.5. IR (neat) mixture: 1605, 1500, 1454 cm^{-1}. MS (of the mixture) calcd for $C_{14}H_{16}O$: m/e 200.1201. Found: 200.1199. GC retention (50–250 °C, 10 °C/min): major isomer, 12.26 min; minor diastereomer, 12.23 min.

2-[(Trimethylstannyl)methyl]-1-buten-3-ol. To a solution of 14.7 mL (153 mmol) of 10.4 M *n*-butyllithium and 21 g (27 mL, 180 mmol) of TMEDA in 70 mL of ether at 0 °C was added dropwise 5.0 g (58 mmol) of 2-methyl-1-buten-3-ol. Upon completion of the addition, 30 mL of anhydrous THF was added and stirring continued for 24 h during which time the reaction warmed to room temperature. The reaction mixture was cooled to 0 °C, and trimethyltin chloride (12.54 g, 63 mmol) was added rapidly in THF (10 mL). The solution became clear, was allowed to warm to room temperature, and was stirred for 15 min. The reaction mixture was added to 500 mL of ether. The solution was washed with 2 × 100 mL of saturated aqueous copper sulfate, 50 mL of distilled water, and 50 mL of saturated aqueous sodium chloride. The mixture was dried over potassium carbonate, the solvent removed, and the residue flash chromatographed (90:10 hexane/ethyl acetate) to give 6.25 g (43%) of 2-[(trimethylstannyl)methyl]-1-buten-3-ol, R_f 0.14 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.76 (s, 1 H), 4.56 (s, 1 H), 4.14 (m, 1 H), 1.83 (d, J = 17.0 Hz, 1 H), 1.72 (d, J = 17.0 Hz, 1 H), 1.28 (d, J = 6.4 Hz, 3 H), 0.09 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.7, 104.1, 71.6, 22.2, 16.5, –9.2. IR ($CDCl_3$): 3380, 1630, 1439 cm^{-1}. MS calcd for $C_7H_{15}SnO$: m/e 235.0146 ($M^+ - CH_3$). Found: 235.0141.

3-Acetoxy-2-[(trimethylstannyl)methyl]-1-butene (12). 2-[(Trimethylstannyl)methyl]-1-buten-3-ol (498 mg, 2 mmol) was dissolved in methylene chloride (8 mL) at –30 °C. Pyridine (594 mg, 0.60 mL, 7.5 mmol) and acetyl chloride (196 mg, 177 μL, 2.5 mmol) were added sequentially. When TLC showed no starting material remained, the reaction mixture was diluted with ether (50 mL), washed with saturated aqueous sodium bicarbonate (20 mL) and saturated aqueous copper sulfate (2 × 20 mL), dried (potassium carbonate), and concentrated in

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vacuo. The residue was flash chromatographed (95:5 hexane/ethyl acetate) to give 487 mg (84%) of 3-acetoxy-2-[(trimethylstannyl)-methyl]-1-butene, R_f 0.58 (90:10 hexane/ethyl acetate). ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.13 (q, J = 6.5 Hz, 1 H), 4.69 (t, J = 1.1 Hz, 1 H), 4.54 (s, 1 H), 1.97 (s, 3 H), 1.77 (d, J = 12.0 Hz, 1 H), 1.65 (d, J = 12.0 Hz, 1 H), 1.25 (d, J = 6.5 Hz, 3 H), 0.05 (s, 9 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.8, 148.6, 106.1, 73.4, 21.2, 19.2, 16.8, −9.4. IR ($CDCl_3$): 1740, 1632, 1450, 1370 cm^{-1}. MS calcd for $C_{10}H_{20}O_2Sn$: m/e 292.0484. Found: 292.0465.

General Procedure for Table II. Generalization of the Regioselective Preparation of *cis*- and *trans*-2-Alkyl-5-methyl-4-methylenetetrahydrofurans. Palladium acetate (3–7 mol %), triphenylphosphine (5 equiv of phosphine/palladium), and trimethyltin acetate (5–10 mol %) were placed in an oven-dried test tube and flushed thoroughly with nitrogen. Benzene (to make a 0.25–0.5 M solution in aldehyde) was added. The mixture was stirred and heated at 70 °C until homogeneous. The aldehyde and the TMM precursor (1.2 equiv) were added, and the vessel was heated to 70 °C. At reaction completion as judged by TLC and/or GC, the reaction mixture was cooled, diluted with 80:20 hexane/ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent, the residue was flash chromatographed to give a mixture of diastereomers.

***cis*- and *trans*-2-(9-Decenyl)-5-methyl-4-methylenetetrahydrofuran (14k, R = CH_2=$CH(CH_2)_8$).** A mixture of palladium acetate (5 mg, 22 μmol), triphenylphosphine (30 mg, 114 μmol), and trimethyltin acetate (33 mg, 150 μmol) in benzene (0.5 mL) was heated at 70 °C until homogeneous. 10-Undecenal (126 mg, 156 μL, 0.75 mmol) and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-butene (**2a**; 100 mg, 120 μL, 0.50 mmol) were added sequentially, and the vessel was heated at 70 °C for 2 h. The reaction mixture was cooled, diluted with 80:20 hexane/ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent, the residue was flash chromatographed (98:2 hexane/ethyl acetate) to give 98 mg (89%) of a 3.1:1 (by GC) mixture of regioisomers with the title compounds predominating as a 6.2:1 (by GC) mixture of diastereomers. The major and minor diastereomers were assigned by the ^{1}H NMR methyl doublets at δ 1.30 and 1.32, R_f 0.60 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): major isomer, δ 5.82 (m, 1 H), 5.02–4.83 (m, 4 H), 4.37 (d, J = 13.2 Hz, 1 H), 4.25 (m, 1 H), 3.88 (ddd, J = 10.5, 8.3, 5.8 Hz, 1 H), 2.66 (m, 1 H), 2.02 (q, J = 6.2 Hz, 2 H), 1.64–1.24 (m, 14 H), 1.30 (d, J = 6.2 Hz, 3 H); minor isomer, δ 5.82 (m, 1 H), 5.02–4.83 (m, 4 H), 4.45 (d, J = 13.2 Hz, 1 H), 4.25 (m, 1 H), 3.33 (td, J = 7.5, 3.1 Hz, 1 H), 2.21 (m, 1 H), 2.02 (q, J = 6.2 Hz, 2 H), 1.64–1.24 (m, 14 H), 1.32 (d, J = 6.2 Hz, 3 H). IR (neat): 1648, 1468 cm^{-1}. MS calcd for $C_{16}H_{28}O$: m/e 236.2139. Found: 236.2153. GC retention times (50–250 °C, 10 °C/min): major isomer, 12.70 min; minor diastereomer, 12.82 min.

***cis*- and *trans*-2-(9-Decenyl)-3-methyl-4-methylenetetrahydrofuran (14t, R = CH_2=$CH(CH_2)_8$).** A mixture of palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), and trimethyltin acetate (10 mg, 45 μmol) in benzene (0.5 mL) was heated at 70 °C until homogeneous. 10-Undecenal (42 mg, 52 μL, 0.25 mmol) and 2-(acetoxymethyl)-3-(trimethylsilyl)-1-butene (**3**; 75 mg, 85 μL, 0.375 mmol) were added, and the vessel was heated at 70 °C for 2 h. The reaction mixture was cooled, diluted with 80:20 hexane/ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent, the residue was flash chromatographed (98:2 hexane/ethyl acetate) to give 51 mg (86%) of a 16.2:1 (by GC) mixture of regioisomers with the title compounds predominating as a 1.6:1 (by GC) mixture of diastereomers. The major and minor diastereomers were assigned by the ^{1}H NMR methyl doublets at δ 1.00 and 1.06, R_f 0.60 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): major isomer, δ 5.82 (m, 1 H), 5.02–4.83 (m, 4 H), 4.37 (d, J = 13.2 Hz, 1 H), 4.25 (m, 1 H), 3.88 (ddd, J = 10.5, 8.3, 5.8 Hz, 1 H), 2.66 (m, 1 H), 2.02 (q, J = 6.2 Hz, 2 H), 1.64–1.24 (m, 14 H), 1.00 (d, J = 6.2 Hz, 3 H); minor isomer, δ 5.82 (m, 1 H), 5.02–4.83 (m, 4 H), 4.45 (d, J = 13.2 Hz, 1 H), 4.25 (m, 1 H), 3.33 (td, J = 7.5, 3.1 Hz, 1 H), 2.21 (m, 1 H), 2.02 (q, J = 6.2 Hz, 2 H), 1.64–1.24 (m, 14 H), 1.06 (d, J = 6.2 Hz, 3 H). IR (neat): 1640, 1472, 1443, 1370 cm^{-1}. MS calcd for $C_{16}H_{28}O$: m/e 236.2139. Found: 236.2153. GC retention (100–250 °C, 10 °C/min): major isomer, 13.06 min; minor diastereomer, 13.32 min.

***cis*- and *trans*-2-Cyclohexyl-5-methyl-4-methylenetetrahydrofuran.** Following the above procedure, palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), trimethyltin acetate (33 mg, 150 μmol), cyclohexanecarboxaldehyde (67 mg, 73 μL, 0.60 mmol), and 3-acetoxy-2-[(trimethylsilyl)methyl]-1-butene (**2a**; 100 mg, 120 μL, 0.50 mmol) in 1.0 mL of benzene was heated at 70 °C for 1 h. After the usual workup, flash chromatography (97:3 hexane/ethyl acetate) provided 68 mg (82%) of a 3.1:1 (by GC) mixture of regioisomers with the title compounds predominating as a 1.2:1 (by GC) mixture of diastereomers. The major and minor diastereomers were assigned by the ^{1}H NMR methyl doublets at δ 1.01 and 1.10, R_f 0.53 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.95–4.85 (m, 2 H), 4.30 (m, 1 H), 4.75 (q, J = 7.9 Hz, 0.5 H), 4.57 (q, J = 7.8 Hz, 0.5 H), 2.62–2.25 (m, 2 H), 1.80–1.40 (m, 4 H), 1.38–1.10 (m, 7 H), 1.10 (d, J = 7.2 Hz, 1.5 H), 1.01 (d, J = 7.2 Hz, 1.5 H). IR ($CDCl_3$): 1452, 1250 cm^{-1}. MS calcd for $C_{12}H_{20}O$: m/e 180.1515. Found: 180.1495.

***cis*- and *trans*-2-(1-Pentenyl)-5-methyl-4-methylenetetrahydrofuran.** Following the standard procedure, palladium acetate (5 mg, 22 μmol), triphenylphosphine (30 mg, 114 μmol), trimethyltin acetate (33 mg, 150 μmol), 2-hexenal (98 mg, 116 μL, 1.0 mL), and precursor **2a** (100 mg, 115 μL, 0.50 mmol) in 1.0 mL of benzene was heated at 70 °C for 30 min. After the usual workup, flash chromatography (97:3 hexane/ethyl acetate) gave 70 mg (92%) of a 7.9:1 (by GC) mixture of regioisomers with the title compounds predominating as a 4.0:1 (by GC) mixture of diastereomers. The major and minor diastereomers were assigned by the ^{1}H NMR methyl doublets at δ 1.32 and 1.30, R_f 0.55 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): major isomer, δ 5.75 (dt, J = 15.3, 6.7 Hz, 1 H), 5.49 (ddt, J = 15.3, 7.6, 1.3 Hz, 1 H), 4.92 (br s, 1 H), 4.80 (br s, 1 H), 4.34 (m, 1 H), 4.22 (m, 1 H), 2.65 (dd, J = 15.8, 5.9 Hz, 1 H), 2.35 (m, 1 H), 2.06–1.98 (m, 2 H), 1.40 (q, J = 7.3 Hz, 2 H), 1.32 (d, J = 6.3 Hz, 3 H), 0.90 (t, J = 7.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 134.3, 130.0, 103.8, 79.0, 39.5, 34.3, 22.6, 22.1, 20.3, 13.7. IR (neat): 1656, 1440, 1430, 1359 cm^{-1}. MS calcd for $C_{11}H_{18}O$: m/e 166.1358. Found: 166.1316. GC retention (50–250 °C, 10 °C/min). *cis*- and *trans*-2-(1-Pentenyl)-5-methyl-4-methylenetetrahydrofuran: major diastereomer, 6.10 min; minor diastereomer, 6.21 min. *cis*- and *trans*-2-(1-Pentenyl)-3-methyl-4-methylenetetrahydrofuran: major diastereomer, 6.67; minor diastereomer, 6.67.

Preparation of 16k. Following the standard procedure, palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), trimethyltin acetate (16 mg, 72 μmol), precursor **2a** (87 mg, 100 μL, 0.44 mmol), and aldehyde **15** (74 mg, 0.29 mmol) in 0.5 mL of benzene was heated at 70 °C for 1 h. After the usual workup, flash chromatography (90:10 hexane/ethyl acetate) provided 84 mg (90%) of a 10.8:1 (by GC) mixture of regioisomers with the title compounds predominating as a 5.0:1 (by GC) mixture of diastereomers. The major and minor diastereomers were assigned by the ^{1}H NMR methyl doublets at δ 1.28 and 1.33, R_f 0.44 (70:30 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.49 (d, J = 5.1 Hz, 1 H), 4.96 (d, J = 2.1 Hz, 1 H), 4.81 (d, J = 2.1 Hz, 1 H), 4.60 (dd, J = 8.0, 2.4 Hz, 1 H), 4.42 (dd, J = 8.0, 1.8 Hz, 1 H), 4.29 (dd, J = 4.9, 2.4 Hz, 1 H), 4.10 (m, 1 H), 3.48 (dd, J = 8.9, 1.8 Hz, 1 H), 2.83 (dd, J = 16.0, 7.1 Hz, 1 H), 2.50 (ddd, J = 16.0, 6.4, 2.0 Hz, 1 H), 1.49 (s, 3 H), 1.45 (s, 3 H), 1.36 (s, 3 H), 1.31 (s, 3 H), 1.28 (d, J = 6.2 Hz, 1 H). ^{1}H NMR (400 MHz, C_6D_6): δ 5.48 (d, J = 5.0 Hz, 1 H), 4.81 (q, J = 2.1 Hz, 1 H), 4.64 (q, J = 2.1 Hz, 1 H), 4.55–4.48 (m, 2 H), 4.43 (q, J = 7.3 Hz, 1 H), 4.40 (m, 1 H), 4.16 (dd, J = 4.9, 2.0 Hz, 1 H), 3.82 (d, J = 8.5 Hz, 1 H), 2.80 (ddd, J = 15.9, 6.9, 1.0 Hz, 1 H), 2.73 (ddd, J = 15.9, 7.4, 2.1 Hz, 1 H), 1.47 (s, 3 H), 1.37 (s, 3 H), 1.23 (d, J = 6.2 Hz, 3 H), 1.15 (s, 3 H), 1.03 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 109.2, 108.5, 104.7, 103.7, 96.3, 74.5, 70.8, 70.6, 70.4, 36.8, 26.0, 25.9, 24.9, 24.9, 24.3, 20.5. IR ($CDCl_3$): 1675, 1460, 1445, 1388, 1313 cm^{-1}. MS calcd for $C_{17}H_{26}O_6$: m/e 326.1729. Found: 326.1724. GC retention (100–250 °C, 10 °C/min): major isomer, 6.12 min; minor diastereomer, 6.09 min.

Preparation of 16t. Following the standard procedure, palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), trimethyltin acetate (5 mg, 23 μmol), precursor **3** (26 mg, 30 μL, 0.13 mmol), and aldehyde **15** (26 mg, 0.10 mmol) in 0.5 mL of benzene was heated at 70 °C for 1 h. After the usual workup, flash chromatography (90:10 hexane/ethyl acetate) provided 23 mg (71%) of a 95.4:1 (by GC) mixture of regioisomers with the title compounds predominating as a 1.2:1 (by GC) mixture of diastereomers. The major and minor diastereomers were assigned by the ^{1}H NMR methyl doublets at δ 1.14 and 1.21, R_f 0.43 (70:30 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): major isomer, δ 5.52 (d, J = 2.2 Hz, 1 H), 4.96 (br s, 1 H), 4.89 (br s, 1 H), 4.62 (dd, J = 8.0, 2.4 Hz, 1 H), 4.45–4.29 (m, 2 H), 4.10 (dd, J = 9.5, 5.9 Hz, 1 H), 3.70 (dd, J = 9.5, 1.8 Hz, 1 H), 2.84 (quint, J = 7.0 Hz, 1 H), 1.50 (s, 3 H), 1.46 (s, 3 H), 1.37 (s, 3 H), 1.32 (s, 3 H), 1.14 (d, J = 7.1 Hz, 3 H); minor isomer, δ 5.51 (d, J = 2.2 Hz, 1 H), 4.94 (br s, 1 H), 4.91 (br s, 1 H), 4.59 (dd, J = 8.0, 2.4 Hz, 1 H), 4.45–4.29 (m, 2 H), 3.76 (dd, J = 9.5, 5.5 Hz, 1 H), 3.60 (dd, J = 9.5, 1.8 Hz, 1 H), 2.62 (quint, J = 7.0 Hz, 1 H), 1.48 (s, 3 H), 1.46 (s, 3 H), 1.36 (s, 3 H), 1.32 (s, 3 H), 1.21 (d, J = 6.9 Hz, 3 H). IR ($CDCl_3$): 1477, 1389 cm^{-1}. MS calcd for $C_{17}H_{26}O_6$: m/e 326.1729. Found: 326.1714. GC retention (100–250 °C, 10 °C/min): major isomer, 6.15 min; minor diastereomer, 6.50 min.

2-Carbomethoxy-1-(dimethylphenylsilyl)-1-phenyl-3-(phenylthio)-propane. In the absence of light, chloromethyl phenyl sulfide (2.00 g, 12.61 mmol) was refluxed overnight with sodium iodide (1.89 g, 12.61 mmol) in acetone (13 mL). The resulting light red suspension was poured into ether (150 mL) and washed with saturated aqueous sodium

Table IV. Experimental Details for Table I

entry	aldehyde, mg (mmol)	TMM, mg (mmol)	solvent (mL)	$Pd(OAc)_2$, mg (mmol)	ligand (mg) [mmol]	cocatalyst (mg) [mmol]	**9k:9t** ratio	yield, mg (%)
1			THF		PPh_3	none		
	66	160	(1.5)	5	(30)		1.6:1	30
	(0.50)	(0.86)		(0.022)	[0.114]			(30)
2			THF		TIPP	Bu_3SnOAc		
	66	100	(1.0)	5	(28)	(35)		NR
	(0.50)	(0.50)		(0.022)	[0.134]	[0.10]		
3a			THF		PPh_3	Bu_3SnOAc		
	66	160	(1.5)	5	(30)	(7)	1:1	
	(0.50)	(0.86)		(0.022)	[0.114]	[0.02]		
3b			THF		PPh_3	Bu_3SnOAc		
	66	160	(1.5)	5	(30)	(35)	1.6:1	48
	(0.50)	(0.86)		(0.022)	[0.114]	[0.10]		(48)
3c			THF		PPh_3	Bu_3SnOAc		
	66	160	(1.5)	5	(30)	(175)	1.8:1	
	(0.50)	(0.86)		(0.022)	[0.114]	[0.50]		
4			DMF		PPh_3	Bu_3SnOAc		
	66	50	(1.0)	5	(30)	(35)		NR
	(0.50)	(0.25)		(0.022)	[0.114]	[0.10]		
5			PhH		PPh_3	Bu_3SnOAc		
	66	50	(1.0)	5	(30)	(35)	1:1	43
	(0.50)	(0.25)		(0.022)	[0.114]	[0.10]		(85)
6			THF		PPh_3	Me_3SnOAc		
	66	140	(1.0)	5	(30)	(11)	3.3:1	95
	(0.50)	(0.70)		(0.022)	[0.114]	[0.05]		(95)
7a			PhH		PPh_3	Me_3SnOAc		
	66	140	(1.0)	5	(30)	(11)	1.7:1	91
	(0.50)	(0.70)		(0.022)	[0.114]	[0.05]		(91)
7b			PhH		PPh_3	Me_3SnOAc		
	66	140	(190)	5	(30)	(33)	1.7:1	95
	(0.50)	(0.70)		(0.022)	[0.114]	[0.15]		(95)
7c			PhH		PPh_3	Me_3SnOAc		
	66	140	(1.0)	5	(30)	(66)	1.7:1	93
	(0.50)	(0.70)		(0.022)	[0.114]	[0.30]		(93)
7d			PhH		PPh_3	Me_3SnOAc		
	132	100	(1.0)	5	(30)	(33)	11.8:1	86
	(1.0)	(0.50)		(0.022)	[0.114]	[0.15]		(86)
8			THF		PPh_3	In(acac)3		
	66	140	(1.0)	5	(30)	(41)		NR
	(0.50)	(0.70)		(0.022)	[0.114]	[0.10]		
9			DCE		PPh_3	Me_3SnOAc		
	66	140	(1.0)	5	(30)	(11)		NR
	(0.50)	(0.70)		(0.022)	[0.114]	[0.05]		
10			THF		PPh_3	Ph_3SnOAc		
	66	140	(1.0)	5	(30)	(41)		
	(0.50)	(0.70)		(0.022)	[0.114]	[0.10]		<10% (GC)
11			PhH		PPh_3	Ph_3SnOAc		
	66	140	(1.0)	5	(30)	(41)		
	(0.50)	(0.70)		(0.022)	[0.114]	[0.10]		<10% (GC)
12			C_6H_{12}		PPh_3	Me_3SnOAc		
	66	140	(1.0)	10	(27)	(33)	2.6:1	55
	(0.50)	(0.70)		(0.010)[a]	[0.103]	[0.15]		(55)
13			PhH		TIPP	Me_3SnOAc		
	66	140	(1.0)	5	(28)	(33)	1.5:1	64
	(0.50)	(0.70)		(0.022)	[0.134]	[0.15]		(64)
14			PhH		TDMPP	Me_3SnOAc		
	66	140	(1.0)	5	(50)	(11)		NR
	(0.50)	(0.70)		(0.022)	[0.111]	[0.05]		
15			PhH		PPh_3	Me_3SnOMs		
	33	50	(0.5)	5	(13)	(*b*)		NR
	(0.25)	(0.25)		(0.005)[a]	[0.050]	[0.10]		
16			PhH		PPh_3	Me_3SnOTs		
	66	100	(1.0)	5	(30)	(50)		NR
	(0.50)	(0.50)		(0.022)	[0.114]	[0.15]		
17			PhH		PPh_3	Me_3SnOTs		
	66	100	(1.0)	5	(30)	(50)		NR
	(0.50)	(0.50)		(0.022)	[0.114]	[0.015]		
18			PhH		PPh_3	Me_3SnOMs		
	66	208	(1.0)	5	(30)		4:1	50
	(0.50)	(0.50)		(0.022)	[0.114]	[0.15]		(50)
19			PhH		PPh_3	Me_3SnOAc		
	33	75	(0.5)	3	(18)	(6)	1:200	47
	(0.25)	(0.375)		(0.013)	[0.069]	[0.025]		
20			PhH		PPh_3	$Bu_2Sn(OAc)_2$		
	33	75	(0.5)	3	(18)	(6)	3.4:1	<25% (GC)
	(0.25)	(0.375)		(0.013)	[0.069]	[0.025]		

Table IV (Continued)

entry	aldehyde, mg (mmol)	TMM, mg (mmol)	solvent (mL)	$Pd(OAc)_2$, mg (mmol)	ligand (mg) [mmol]	cocatalyst (mg) [mmol]	**9k:9t** ratio	yield, mg (%)
21			PhH		PPh_3	$Me_3SnO_2CCF_3$		
	33	75	(0.5)	3	(18)	(21)		NR
	(0.25)	(0.375)		(0.013)	[0.069]	[0.075]		
22			PhH		dppe, PPh_3	Me_3SnOAc		
	66	140	(1.0)	5	(9, 14)	(33)		NR
	(0.50)	(0.70)		(0.022)	[0.022, 0.055]	[0.15]		
23			PhH		dppb, PPh_3	Me_3SnOAc		
	66	140	(1.0)	5	(10, 14)	(33)		NR
	(0.50)	(0.70)		(0.022)	[0.022, 0.055]	[0.15]		
24			PhH		PPh_3	Me_3SnOTs		
	66	100	(1.0)	5	(30)	(50)		NR
	(0.50)	(0.50)		(0.022)	[0.114]	[0.15]		
25			PhH		PPh_3	Me_3SnOTs		
	50	73	(0.5)	3	(18)	(25)	31.1:1	41
	(0.375)	(0.25)		(0.013)	[0.069]	[0.075]		(82)
26			PhH		$P(o\text{-tol})_3$	Me_3SnOAc		
	66	140	(1.0)	5	(40)	(33)		NR
	(0.50)	(0.70)		(0.022)	[0.131]	[0.15]		
27			PhH		PPh_3	$(AcOSnBu_2)_2O$		
	66	100	(1.0)	5	(30)	(48)	3.4:1	80
	(0.50)	(0.50)		(0.022)	[0.114]	[0.075]		(80)
28			PhH		dppf	Me_3SnOAc		
	66	50	(1.0)	5	(15)	(16)		NR
	(0.50)	(0.25)		(0.022)	[0.027]	[0.075]		

[a] Palladium dibenzylideneacetone chloroform complex was used for this run. [b] Prepared in situ from allyltrimethyltin (22 mg, 0.11 mmol) and methanesulfonic acid (9 mg, 0.10 mmol).

Table V. Experimental Details for Table II

entry	aldehyde, mg (mmol)	TMM, mg (mmol)	solvent, mL	$Pd(OAc)_2$, mg (mmol)	ligand (mg) [mmol]	cocatalyst (mg)[mmol]	**13k:13t** ratio	yield, mg (%)
1			PhH		PPh_3	Me_3SnOAc		
	126	100	(1.0)	5	(30)	(33)	3.1:1	98
	(0.75)	(0.50)		(0.022)	[0.114]	[0.15]		(89)
2			PhH		PPh_3	none		
	126	142	(1.0)	5	(30)		2.9:1	79
	(0.75)	(0.50)		(0.022)	[0.114]			(72)
3			PhH		PPh_3	Me_3SnOAc		
	42	75	(0.5)	3	(18)	(10)	1:16.2	51
	(0.25)	(0.38)		(0.013)	[0.069]	[0.045]		(86)
4			PhH		PPh_3	Bu_3SnOAc		
	56	110	(1.0)	5	(30)	(35)	1:1.1	42
	(0.50)	(0.55)		(0.022)	[0.114]	[0.10]		(46)
5			PhH		PPh_3	Me_3SnOAc		
	67	100	(1.0)	3	(18)	(33)	3.1:1	68
	(0.60)	(0.50)		(0.013)	[0.069]	[0.15]		(82)
6			PhH		PPh_3	Me_3SnOAc		
	84	100	(1.0)	5	(30)	(33)	2.7:1	
	(1.0)	(0.50)		(0.022)	[0.114]	[0.15]		68 (by GC)
7			PhH		PPh_3	Me_3SnOAc		
	98	100	(0.5)	5	(30)	(33)	7.9:1	70
	(1.0)	(0.50)		(0.022)	[0.114]	[0.15]		(92)
8			PhH		PPh_3	Me_3SnOAc		
	74	87	(0.5)	3	(18)	(16)	10.8:1	84
	(0.29)	(0.44)		(0.013)	[0.069]	[0.07]		(90)
9			PhH		PPh_3	Me_3SnOAc		
	26	26	(0.5)	3	(18)	(16)	1:95.4	26
	(0.10)	(0.13)		(0.013)	[0.069]	[0.072]		(81)

thiosulfate (50 mL), saturated aqueous sodium bicarbonate (2 × 50 mL), and saturated aqueous sodium chloride (50 mL). The organic layer was dried (magnesium sulfate) and concentrated to yield iodomethyl-phenylsulfide,[46] which was used without further purification. A solution of methyl 3-(dimethylphenylsilyl)-3-phenylpropionate[17] (1.50 g, 4.80 mmol) in THF (4 mL) was added at −78 °C via cannula to a solution of LDA prepared from diisopropylamine (506 mg, 0.70 mL, 5.00 mmol) and *n*-butyllithium (3.05 mL, 1.05 M, 4.80 mmol) in 20 mL of THF. The resulting yellow solution was stirred 5 min and allowed to warm to 0 °C, stirred a further 5 min, and recooled to −78 °C. Iodomethyl phenyl sulfide (1.10 g, 4.40 mmol) in THF (10 mL) was cannulated into the anion solution dropwise. The resulting mixture was stirred 1 h and allowed to warm to room temperature. It was poured into ether (150 mL), washed with saturated aqueous sodium bicarbonate (50 mL) and saturated aqueous sodium chloride (50 mL), dried (magnesium sulfate), and concentrated. Flash chromatography (95:5 hexane/ethyl acetate) yielded 1.41 g (74%) of the desired product. R_f 0.21 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.12 (m, 13 H), 6.79 (d, J = 7.0 Hz, 2 H), 3.22 (s, 3 H), 3.06 (td, J = 3.3, 1.8 Hz, 1 H), 2.90 (dd, J = 13.5, 3.3 Hz, 1 H), 2.81 (dd, J = 13.5, 12.1 Hz, 1 H), 2.62 (d, J = 12.1 Hz, 1 H), 0.26 (s, 3 H), 0.02 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 139.9, 136.6, 135.2, 134.3, 130.4, 129.1, 128.7, 128.4, 127.4, 126.5, 125.5, 51.3, 47.1, 39.3, 36.8, −2.7, −5.2. IR ($CDCl_3$): 1740, 1600, 1584, 1484, 1440, 1432, 1360 cm^{-1}. MS calcd for $C_{25}H_{28}O_2SSi$: m/e 420.1580. Found: 420.1601. Anal. Calcd for $C_{25}H_{28}O_2SSi$: C, 71.38; H, 6.71. Found: C, 71.49; H, 6.74.

2-Carbomethoxy-1-(dimethylphenylsilyl)-1-phenyl-2-propene. A solution of sodium metaperiodate (300 mg, 1.40 mmol) in water (3 mL) was added to a solution of 2-carbomethoxy-1-(dimethylphenylsilyl)-1-phenyl-3-(phenylthio)propane (500 mg, 1.15 mmol) in methanol (15

(46) Trost, B. M.; Kunz, R. A. *J. Org. Chem.* **1974**, *39*, 2648.

mL).[47] The resulting suspension was stirred overnight at room temperature and filtered. The filtrate was concentrated in vacuo to remove most of the methanol and extracted with ether. The combined organic layers were concentrated to yield the sulfoxide, which was carried on without further purification. A solution of the sulfoxide in carbon tetrachloride (20 mL) was heated in the presence of solid potassium carbonate at 70 °C for 24 h. The resulting suspension was filtered, concentrated in vacuo, and flash chromatographed (90:10 hexane/ethyl acetate) to yield 235 mg (66%) of 2-carbomethoxy-1-(dimethylphenylsilyl)-1-phenyl-2-propene. R_f 0.85 (70:30 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.28 (m, 5 H), 7.20 (t, J = 7.5 Hz, 2 H), 7.12 (d, J = 7.2 Hz, 2 H), 6.24 (s, 1 H), 5.60 (s, 1 H), 3.87 (s, 1 H), 3.62 (s, 3 H), 0.31 (s, 3 H), 0.29 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 140.9, 140.5, 137.1, 134.3, 129.2, 128.7, 128.1, 127.6, 125.3, 125.0, 52.0, 38.9, −3.3, −3.6. IR (neat): 1720, 1620, 1600, 1495, 1440 cm^{-1}. MS calcd for $C_{19}H_{22}O_2Si$: m/e 310.1388. Found: 310.1378.

2-(Acetoxymethyl)-1-(dimethylphenylsilyl)-1-phenyl-2-propene (17). 2-Carbomethoxy-1-(dimethylphenylsilyl)-1-phenyl-2-propene (140 mg, 0.45 mmol) was dissolved in ether (1 mL) at −78 °C. Diisobutylaluminum hydride (1.35 mL, 1.0 M in hexane, 1.35 mmol) was added dropwise, and the mixture was allowed to stir for 30 min and warmed to 0 °C for 90 min. The reaction was quenched by dropwise addition of methanol (1 mL). The mixture was poured into ether (20 mL), and saturated aqueous sodium chloride (2 mL) was added to give a gelatinous mixture, which was stirred with Celite for 30 min and filtered. The filtrate was dried (magnesium sulfate), concentrated in vacuo, and immediately subjected to acetylation. The residue was dissolved in methylene chloride (2 mL) and cooled to −20 °C. Pyridine (158 mg, 160 μL, 2.0 mmol) was added followed by dropwise addition of acetyl chloride (70 mg, 64 μL, 0.90 mmol). After 1 h TLC showed the reaction was complete, and saturated aqueous sodium bicarbonate was added as a quench. The mixture was poured into ether (20 mL) and washed with saturated aqueous sodium bicarbonate (5 mL). The organic layer was dried (magnesium sulfate), concentrated in vacuo, and flash chromatographed (95:5 hexane/ethyl acetate) to give 81 mg (55%) of the title compound, R_f 0.41 (70:30 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.30 (m, 5 H), 7.20 (t, J = 6.1 Hz, 2 H), 7.14 (t, J = 7.3 Hz, 1 H), 7.04 (d, J = 7.0 Hz, 2 H), 5.22 (s, 1 H), 5.11 (s, 1 H), 4.37 (s, 2 H), 3.07 (s, 1 H), 1.97 (s, 3 H), 0.36 (s, 3 H), 0.29 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 143.8, 140.2, 137.3, 134.1, 129.1, 128.4, 128.0, 127.5, 125.2, 114.3, 68.0, 41.5, 20.7, −3.2, −3.2. IR (neat): 1745, 1650, 1599, 1490, 1451, 1430, 1375 cm^{-1}. MS calcd for $C_{20}H_{24}O_2Si$: m/e 324.1545. Found: 324.1542.

***cis*- and *trans*-2-[(*E*)-2-Phenylethenyl]-3-phenyl-4-methylenetetrahydrofuran (18). From 3-Acetoxy-3-phenyl-2-[(trimethylsilyl)methyl]-1-propene (2b).** Following the standard procedure, palladium acetate (5 mg, 22 μmol), triphenylphosphine (30 mg, 114 μmol), trimethyltin acetate (20 mg, 90 μmol), precursor **2b**[10] (131 mg, 140 μL, 0.50 mmol), and cinnamaldehyde (33 mg, 32 μL, 0.25 mmol) in 1.0 mL of benzene was heated at 70 °C overnight. After the usual workup, flash chromatography (96:4 hexane/ethyl acetate) provided 47 mg (72%) of the title compounds as a 1:1 mixture (by integration of several signals in the ^{1}H NMR), R_f 0.32 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.14 (m, 10 H), 6.54 (d, J = 15.9 Hz, 0.5 H), 6.49 (d, J = 15.9 Hz, 0.5 H), 6.24 (dd, J = 15.9, 6.2 Hz, 0.5 H), 5.70 (dd, J = 15.9, 6.2 Hz, 0.5 H), 5.12 (q, J = 2 Hz, 0.5 H), 5.08 (q, J = 2 Hz, 0.5 H), 4.99 (q, J = 2 Hz, 0.5 H), 4.80–4.71 (m, 2 H), 4.62–4.54 (m, 1.5 H), 4.44 (dd, J = 9.2, 6.2 Hz, 0.5 H), 4.00 (d, J = 6.2 Hz, 0.5 H), 3.61 (d, J = 9.2 Hz, 0.5 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.4, 151.8, 139.8, 139.1, 136.7, 136.5, 132.2, 129.3, 129.0, 128.6, 128.5, 128.4, 128.2, 127.7, 127.5, 127.0, 126.9, 126.7, 126.6, 126.5, 106.8, 106.3, 87.4, 84.3, 71.7, 71.2, 57.4, 55.2. IR ($CDCl_3$): 1603, 1496, 1455, 1328 cm^{-1}. MS calcd for $C_{19}H_{18}O$: m/e 262.1358. Found: 262.1336.

From 3-Acetoxy-3-phenyl-2-[(dimethylphenylsilyl)methyl]-1-propene (18). Following the general procedure, palladium acetate (2.5 mg, 11 μmol), triphenylphosphine (15 mg, 57 μmol), trimethyltin acetate (8 mg, 25 μmol), precursor **18** (50 mg, 0.15 mmol), and cinnamaldehyde (34 mg, 33 μL, 0.25 mmol) in 1.0 mL of benzene was heated at 70 °C for 2 h. After the usual workup, flash chromatography (96:4 hexane/ethyl acetate) provided 20 mg (51%) of product identical with that produced from **2b**.

Preparation of 19. Following the general procedure, palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), trimethyltin acetate (16 mg, 72 μmol), precursor **2b** (65 mg, 69 μ, 0.25 mmol), and hexose **15** in 0.5 mL of benzene was heated at 70 °C for 1 h. After the usual workup, flash chromatography of the residue (90:10 hexane/ethyl acetate) provided 35 mg (71%) of the hexose adduct as a 7:3 (by integration of several signals in the ^{1}H NMR) mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.14 (m, 5 H), 5.48 (d, J = 4.9 Hz, 0.7 H), 5.37 (d, J = 4.9 Hz, 0.7 H), 5.04 (br s, 0.7 H), 4.98 (br s, 0.7 H), 4.97 (br s, 0.6 H), 4.71–4.15 (m, 7 H), 3.87 (br s, 1 H), 3.66 (dd, J = 9.2, 1.7 Hz, 0.7 H), 3.44 (dd, J = 9.5, 1.9 Hz, 0.3 H), 1.53 (s, 2.1 H), 1.46 (s, 0.9 H), 1.39 (s, 2.1 H), 1.36 (s, 0.9 H), 1.35 (s, 2.1 H), 1.34 (s, 2.1 H), 1.12 (s, 0.9 H), 0.59 (s, 0.9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 151.3, 143.2, 129.2, 128.4, 128.3, 127.6, 126.3, 109.3, 108.9, 108.5, 108.0, 107.2, 106.5, 96.3, 95.7, 83.5, 80.7, 71.2, 70.8, 70.5, 70.4, 70.3, 68.7, 66.2, 53.5, 52.7, 26.0, 25.8, 25.1, 25.0, 24.6, 24.5, 24.3. IR ($CDCl_3$): 1477, 1389, 1295 cm^{-1}. MS calcd for $C_{22}H_{28}O_6$: m/e 388.1886. Found: 388.1872. Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 68.57; H, 7.69.

***cis*- and *trans*-2-Cyclohexyl-3-ethenyl-4-methylenetetrahydrofuran (20).** Following the general procedure, palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), trimethyltin acetate (33 mg, 150 μmol), precursor **2c**[10] (205 mg, 230 μL, 0.97 mmol), and cyclohexanecarboxaldehyde (56 mg, 64 μL, 0.50 mmol) in 1.0 mL of benzene was heated at 70 °C for 1 h. After the usual workup, flash chromatography (97:3 hexane/ethyl acetate) provided 79 mg (82%) of a 4:1 (by integration of several signals in the ^{1}H NMR) mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.59 (ddd, J = 16.7, 10.4, 8.7, 1 H), 5.13 (d, J = 16.7 Hz, 1 H), 5.09 (d, J = 10.4 Hz, 1 H), 4.96 (quint, J = 2.2 Hz, 1 H), 4.85 (quint, J = 2.2 Hz, 1 H), 4.43 (br d, J = 13.2 Hz, 1 H), 4.26 (dq, J = 13.2, 2.2 Hz, 1 H), 3.40 (dd, J = 8.6, 5.6 Hz, 1 H), 3.05 (td, J = 8.6, 1.8 Hz, 1 H), 1.90–1.50 (m, 5 H), 1.35–1.10 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 137.6, 117.1, 105.0, 70.6, 52.1, 41.3, 29.7, 28.4, 26.5, 26.2, 26.0, 22.6. IR ($CDCl_3$): 1450, 1058 cm^{-1}. MS calcd for $C_{13}H_{20}O$: m/e 192.1515. Found: 192.1506.

1(*S*)-Hydroxy-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene (23a). *n*-Butyllithium (50 mL, 1.64 M in hexane, 82 mmol) was added to *cis*-carveol[22,23] (5.0 g, 32.8 mmol) in hexane (10 mL) at 0 °C. TMEDA (12.35 mL, 82 mmol) was added, and the mixture was warmed to room temperature and stirred for 24 h. Trimethyltin chloride (10.0 g, 50.0 mmol) was added all at once to the red solution and the reaction mixture decolorized. The solution was poured into ether (200 mL) and washed with saturated aqueous copper sulfate (50 mL) and saturated aqueous sodium bicarbonate (2 × 50 mL). The organic layer was dried (potassium carbonate) and concentrated in vacuo. Column chromatography (85:15 hexane/ethyl acetate) gave 5.8 g (56%) of 1-(*S*)-hydroxy-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene, R_f 0.10 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.31 (br s, 1 H), 4.72 (s, 2 H), 4.10 (br s, 1 H), 2.25–1.92 (m, 4 H), 1.72 (s, 3 H), 1.51 (q, J = 17.0 Hz, 1 H), 1.42 (d, J = 16.5 Hz, 1 H), 0.09 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 139.9, 118.8, 109.1, 70.8, 40.5, 38.1, 31.0, 20.6, 17.5, −9.1. IR (neat): 3311, 1645, 1439, 1378, 1325 cm^{-1}. MS calcd for $C_{13}H_{24}OSn$: m/e 316.0849. Found: 316.0846. Anal. Calcd for $C_{13}H_{24}OSn$: C, 49.26; H, 7.68. Found: C, 49.57; H, 7.59.

1(*R*)-Hydroxy-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene. (1*R*)-(+)-α-Pinene (7.0 g, 8.2 mL, 51.4 mmol) was added to a suspension of benzoyl peroxide (6.0 g, 24.8 mmol), cupric acetate (250 mg, 1.25 mmol), and cuprous chloride (50 mg) in acetonitrile (100 mL). The mixture was stirred at 65–70 °C for 24 h and cooled to room temperature. The solution was diluted with ether (400 mL), washed with 10% sodium thiosulfate (100 mL) and saturated aqueous sodium bicarbonate (2 × 100 mL), dried (magnesium sulfate), and concentrated in vacuo. The crude *trans*-carveol benzoate[24] was dissolved in a methanolic solution of sodium methoxide (prepared by reacting 0.2 g of sodium metal with 100 mL of methanol) and stirred at room temperature for 1 h. At this time, TLC showed no starting material present and the solution was concentrated. Flash chromatography (80:20 hexane/ethyl acetate) yielded 3.00 g (38%) of *trans*-carveol. *trans*-Carveol (1.00 g, 6.57 mmol) was dissolved in dry hexane (5 mL), and *n*-butyllithium (1.64 M, 9.8 mL, 16.0 mmol) was added at 0 °C followed by TMEDA (2.41 mL, 16.0 mmol). The mixture was stirred 24 h at room temperature and quenched with trimethyltin chloride (1.60 g, 8.00 mmol). The resulting solution was diluted with ether (100 mL), washed with saturated aqueous sodium bicarbonate (20 mL), saturated aqueous copper sulfate (20 mL), and water (20 mL), and dried (potassium carbonate). After concentration, the organic layer was flash chromatographed to give 494 mg (36%) of the title compound, R_f 0.11 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39 (d, J = 5 Hz, 1 H), 4.75 (s, 1 H), 4.73 (s, 1 H), 3.91 (m, 1 H), 2.31 (br t, J = 10.1 Hz, 1 H), 2.17 (dt, J = 10.1, 3.2 Hz, 1 H), 1.92–1.85 (m, 2 H), 1.74 (s, 3 H), 1.59 (td, J = 10.1, 3.2 Hz, 1 H), 1.44 (d, J = 6.0 Hz, 1 H), 0.09 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 138.1, 120.4, 108.9, 68.9, 36.8, 35.3, 30.9, 20.9, 19.0, −9.4. IR ($CDCl_3$): 3350, 1642, 1440, 1375 cm^{-1}. MS calcd for $C_{13}H_{24}OSn$: m/e 316.0848. Found: 316.0839.

(47) Cf.: Reich, H. J.; Renga, J. M. *J. Chem. Soc., Chem. Commun.* **1974**, 137. Trost, B. M.; Salzman, T. N. *J. Am. Chem. Soc.* **1973**, *95*, 5321.

1(*R*)-Acetoxy-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene (24b). Acetyl chloride (39 mg, 36 μL, 0.50 mmol) was added to a solution of pyridine (79 mg, 81 μL, 1.0 mmol) and 1(*R*)-hydroxy-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene (130 mg, 0.41 mmol) in methylene chloride (1.0 mL) at −20 °C. The solution was allowed to stir 1 h when TLC showed no starting material remained. The reaction mixture was poured into ether (20 mL) and washed with saturated aqueous sodium bicarbonate (2 × 5 mL). The organic layer was dried (potassium carbonate) and concentrated in vacuo. The residue was flash chromatographed (95:5 hexane/ethyl acetate) to give 141 mg (96%) of the desired product, R_f 0.62 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.53 (dd, J = 5.3, 2.2 Hz, 1 H), 5.16 (t, J = 1.7 Hz, 1 H), 4.73 (s, 1 H), 4.69 (s, 1 H), 2.35–2.18 (m, 2 H), 2.07 (s, 3 H), 1.95–1.85 (m, 2 H), 1.72 (s, 3 H), 1.69 (s, 2 H), 1.60 (ddd, J = 16.8, 12.8, 4.1 Hz, 1 H), 0.09 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 148.8, 134.6, 123.1, 109.1, 71.1, 35.8, 33.7, 30.9, 21.5, 20.9, 18.5–9.5. IR ($CDCl_3$): 1736, 1646, 1440, 1371 cm^{-1}. MS calcd for $C_{15}H_{26}O_2Sn$: m/e 358.0955. Found: 358.0932.

1(*R*)-Chloro-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene (24a). 1(*S*)-Hydroxy-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene (500 mg, 1.59 mmol) was dissolved in methylene chloride at 0 °C, and triethylamine (243 mg, 0.33 mL, 2.40 mL) was added. Methanesulfonyl chloride[48] (229 mg, 155 μL, 2.00 mmol) was added dropwise over 5 min. TLC showed that starting material was not consumed. Triethylamine (120 mg, 0.17 mL, 1.20 mmol) and methanesulfonyl chloride (115 mg, 75 μL, 1.00 mmol) were added again. After 5 min the reaction mixture was poured into ether (50 mL) and washed with saturated aqueous sodium bicarbonate (20 mL). The organic layer was dried (magnesium sulfate) and concentrated in vacuo. Flash chromatography (98:2 hexane/ethyl acetate) yielded 330 mg (53%) of a 85:15 mixture of the isomers, R_f 0.71 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): major, δ 5.42 (m, 1 H), 4.76 (s, 2 H), 4.73 (s, 1 H), 4.41 (br s, 1 H), 2.58 (m, 1 H), 2.31–1.82 (m, 6 H), 1.75 (s, 3 H), 0.10 (s, 9 H); minor, δ 5.45 (m, 1 H), 4.75–4.73 (m, 2 H), 4.52 (vbr s, 1 H), 2.39 (m, 1 H), 2.31–1.82 (m, 6 H), 1.72 (s, 3 H), 0.10 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): major, δ 148.6, 136.8, 122.2, 109.2, 61.2, 37.3, 34.9, 30.8, 20.9, 19.1, −9.2; minor, δ 148.1, 137.2, 121.8, 109.6, 62.2, 42.2, 40.0, 30.9, 20.5, 19.1, −9.2. IR ($CDCl_3$): 1646, 1439, 1375 cm^{-1}. Anal. Calcd for $C_{13}H_{23}ClSn$: C, 46.82; H, 6.95. Found: C, 46.63; H, 7.11.

1(*S*)-Methoxycarboxy-2-[(trimethylstannyl)methyl]-5(*S*)-(2-propenyl)cyclohex-2-ene (23c). Methyl chloroformate (300 mg, 0.25 mL, 3.18 mmol) was added dropwise to a solution of pyridine (628 mg, 0.64 mL, 7.95 mmol) and 1(*S*)-hydroxy-2-[(trimethylstannyl)methyl]-5-(*S*)-(2-propenyl)cyclohex-2-ene (**23a**; 500 mg, 1.59 mmol), in methylene chloride at 0 °C. The reaction was allowed to stir until TLC showed no starting material remained. The reaction mixture was poured into ether (50 mL), washed with saturated aqueous sodium bicarbonate (10 mL), dried (potassium carbonate), and concentrated in vacuo. Flash chromatography (96:4 hexane/ethyl acetate) of the residue gave 304 mg (52%) of the title compound, R_f 0.51 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39 (d, J = 5.2 Hz, 1 H), 5.16 (br s, 1 H), 4.72 (s, 1 H), 4.71 (s, 1 H), 3.78 (s, 3 H), 2.28–2.23 (m, 2 H), 2.10–1.98 (m, 2 H), 1.82 (d, J = 11.9 Hz, 1 H), 1.71 (s, 3 H), 1.64 (d, J = 11.9 Hz, 1 H), 1.55 (q, J = 12.0 Hz, 1 H), 0.09 (s, 9 H). ^{13}C NMR (MHz, $CDCl_3$): δ 155.8, 148.3, 136.1, 121.2, 109.3, 77.7, 54.6, 40.4, 33.9, 30.8, 20.5, 11.8, −9.4. IR ($CDCl_3$): 1739, 1444 cm^{-1}. MS calcd for $C_{15}H_{26}O_3Sn$: m/e 374.0904. Found: 374.0907.

Reaction of 24a with Cinnamaldehyde. Tetrakis(triphenylphosphine)palladium (20 mg, 17 μmol) and trimethyltin tosylate (10 mg, 30 μmol) were placed in an oven-dried test tube and thoroughly flushed with nitrogen. Benzene (0.5 mL) was added, and the mixture was brought to 70 °C until it became homogeneous. The mixture was transferred via syringe to another nitrogen-flushed test tube containing precursor **24a** (80 mg, 0.24 mmol), and cinnamaldehyde (66 mg, 63 μL, 0.50 mmol) was added. The mixture was heated at 70 °C for 8 h. After the usual workup, flash chromatography of the residue (97:3 hexane/ethyl acetate) yielded 32 mg (50%) of the title compound, **26** (contaminated by 15% of **27**), readily identifiable on TLC by the brilliant sky blue nature of its *p*-anisaldehyde stain, R_f 0.32 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 7.2 Hz, 2 H), 7.33–7.20 (m, 2 H), 6.61 (d, J = 15.9 Hz, 1 H), 6.20 (dd, J = 15.9, 7.4 Hz, 1 H), 5.52 (d, J = 1.8 Hz, 1 H), 4.81 (s, 1 H), 4.66 (s, 1 H), 4.54 (q, J = 7.3 Hz, 1 H), 3.99 (br s, 1 H), 2.83 (m, 1 H), 2.53 (br s, 1 H), 2.40–2.15 (m, 4 H), 1.80 (s, 3 H), 1.54 (ddd, J = 14.3, 9.7, 4.5 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.0 (absent), 138.0 (absent), 136.7 (absent), 131.2 (down), 130.3 (down), 128.5 (down), 127.6 (down), 126.5 (down), 117.9 (down), 109.7 (up), 77.7 (down), 74.2 (down), 37.4 (down), 37.1 (up), 30.5 (up), 29.3 (up), 22.0 (down). IR ($CDCl_3$): 1639, 1466 cm^{-1}. MS calcd for $C_{19}H_{22}O$: m/e 266.1670. Found: 266.1676. Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.33. Found: C, 85.46; H, 7.99.

Reaction of 23c with Cinnamaldehyde. Following the above procedure, a solution of tetrakis(triphenylphosphine)palladium (25 mg, 21 μmol), triphenylphosphine (5, mg, 19 μmol), trimethyltin tosylate (5 mg, 22 μmol), 1(*S*)-(methoxycarboxy)-2-[(trimethylstannyl)methyl]-5(*S*)-(1-methylethenyl)cyclohex-2-ene (**23c**; 73 mg, 0.19 mmol), and cinnamaldehyde (66 mg, 63 μL, 0.50 mmol) in 0.5 mL of benzene was heated at 70 °C for 24 h. After the usual workup, flash chromatography of the residue (97:3 hexane/ethyl acetate) yielded 8 mg (16%) of 1(*S**)-(2-phenylethenyl)-6(*S**)-(1-methylethenyl)-1,3,5,6,7,7a(*R**)-hexahydroisobenzofuran (**28a**). The low R_f fraction contained 17 mg (33%) of a 1:1 mixture (by integration of several 1H NMR signals) of hexahydroisobenzofuran **28** and hexahydrobenzofuran **27**, R_f 0.27 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 7.2 Hz, 2 H), 7.33–7.20 (m, 3 H), 6.62 (d, J = 15.9 Hz, 1 H), 6.20 (dd, J = 15.9, 7.4 Hz, 1 H), 5.52 (br s, 1 H), 4.77 (s, 1 H), 4.74 (s, 1 H), 4.61 (q, J = 7.3 Hz, 1 H), 4.23 (br s, 1 H), 2.83 (m, 2 H), 2.40–2.15 (m, 3 H), 1.75 (s, 3 H), 1.43 (q, J = 14.3 Hz, 1 H). IR (neat): 1636, 1483, 1368 cm^{-1}. MS calcd for $C_{19}H_{22}O$: m/e 266.1670. Found: 266.1670.

Reaction of 23d with Cinnamaldehyde. Following the above procedure, a solution of tetrakis(triphenylphosphine)palladium (20 mg, 17 μmol), triphenylphosphine (5 mg, 19 μmol), trimethyltin acetate (5 mg, 22 μmol), 1(*S*)-(methoxycarboxy)-2-[(trimethylsilyl)methyl]-5(*S*)-(1-methylethenyl)cyclohex-2-ene[20] (71 mg, 0.25 mmol) and cinnamaldehyde (40 mg, 38 μL, 0.30 mmol) in 0.5 mL of benzene was heated at 70 °C for 2 days. After the usual workup, flash chromatography of the residue (97:3 hexane/ethyl acetate) yielded a high R_f fraction (15 mg, 25%) identified as 1(*S**)-(2-phenylethenyl)-6(*S**)-(1-methylethenyl)-1,3,5,6,7,7a(*S**)-hexahydroisobenzofuran (**28a**), R_f 0.27 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.22 (m, 5 H), 6.52 (d, J = 15.6 Hz, 1 H), 6.06 (dd, J = 15.6, 7.6 Hz, 1 H), 5.64 (dd, J = 4.0, 2.1 Hz, 1 H), 4.78 (t, J = 7.6 Hz, 1 H), 4.72 (s, 2 H), 4.42 (m, 2 H), 2.96 (br s, 1 H), 2.35–2.15 (m, 2 H), 2.00 (m, 1 H), 1.87 (m, 1 H), 1.73 (s, 3 H), 1.10 (q, J = 12.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6, 139.3, 131.5, 128.5, 127.7, 127.6, 127.3, 126.6, 117.6, 109.0, 82.3, 69.0, 44.4, 41.4, 30.7, 28.5, 20.7. IR (neat): 1636, 1483, 1441, 1368 cm^{-1}. MS calcd for $C_{19}H_{22}O$: m/e 266.1670. Found: 266.1670. The low R_f fraction (12 mg, 20%) contained a 1:5 mixture (by integration of several ^{1}H NMR signals) of the 7a(*S**)-hexahydroisobenzofuran product, **27**, and 1(*R**)-(2-phenylethenyl)-6(*S**)-(1-methylethenyl)-1,3,5,6,7,7a(*S**)-hexahydroisobenzofuran (**28b**), R_f 0.32 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 7.2 Hz, 2 H), 7.33–7.22 (m, 3 H), 6.65 (d, J = 15.9 Hz, 1 H), 6.27 (dd, J = 15.9, 7.3 Hz, 1 H), 5.58 (br s, 1 H), 4.73 (br s, 2 H), 4.53 (br d, J = 10.8 Hz, 1 H), 4.33 (br d, J = 10.8 Hz, 1 H), 3.90 (dd, J = 9.6, 7.9 Hz, 1 H), 2.44 (m, 1 H), 2.33–2.18 (m, 2 H), 2.05–1.90 (m, 2 H), 1.74 (s, 3 H), 1.13 (q, J = 11.9 Hz, 1 H).

Reaction of 24b with Cinnamaldehyde. Following the above procedure, a solution of palladium acetate (3 mg, 13 μmol), triphenylphosphine (30 mg, 114 μmol), trimethyltin tosylate (10 mg, 14 μmol), 1(*R*)-acetoxy-2-[(trimethylstannyl)methyl]-5(*S*)-(1-methylethenyl)cyclohex-2-ene (**24b**; 71 mg, 0.25 mmol), and cinnamaldehyde (36 mg, 33 μL, 0.25 mmol) in 0.5 mL of benzene was heated at 70 °C for 24 h. After the usual workup, flash chromatography of the residue (97:3 hexane/ethyl acetate) yielded 16 mg (31%) of recovered starting material and 20 mg (53%, 77% based on recovered starting material) of two products in a 2:1 ratio (by integration of several ^{1}H NMR signals). The major product was the previously identified 1(*S**)-(2-phenylethenyl)-6(*S**)-(1-methylethenyl)-1,3,5,6,7,7a(*s**)-hexahydroisobenzofuran (**28a**), and the minor product was the 7a epimer, 1(*S**)-(2-phenylethenyl)-6(*S**)-(1-methylethenyl)-1,3,5,6,7,7a(*R**)-hexahydroisobenzofuran (**29**), R_f 0.32 (90:10 hexane/ethyl cetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 7.2 Hz, 2 H), 7.37–7.22 (m, 3 H), 6.61 (d, J = 15.9 Hz, 1 H), 6.23 (dd, J = 15.9, 7.3 Hz, 1 H), 5.58 (br s, 1 H), 4.81 (br s, 1 H), 4.66 (br s, 1 H), 4.50 (br d, J = 10.8 Hz, 1 H), 4.31 (br d, J = 10.8 Hz, 1 H), 3.92 (dd, J = 9.6, 7.9 Hz, 1 H), 2.44 (m, 1 H), 2.33–2.18 (m, 2 H), 2.05–1.90 (m, 2 H), 1.74 (s, 3 H), 1.29 (ddd, J = 14.3, 9.7, 4.5 Hz, 1 H). IR ($CDCl_3$): 1650, 1443, 1252 cm^{-1}. MS calcd for $C_{19}H_{22}O$: m/e 266.1670. Found: 266.1670.

1-Acetoxy-1,1-dideuterio-2-[(trimethylstannyl)methyl]-2-propene (31). Methyl methacrylate (2.40 g, 2.56 mL, 24 mmol) was added dropwise to a suspension of lithium aluminum deuteride (1.00 g, 24 mmol) in ether (150 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred overnight. Excess hydride was quenched by sequential addition of water (1 mL), 10% aqueous sodium hydroxide (1 mL), and water (1 mL). The ether was carefully removed by distillation at atmospheric pressure, and the residue was distilled (bp 115 °C) to give 1.15 g (65%) of 3,3-dideuterio-2-methyl-3-propen-1-ol. *n*-Butyllithium (3.8

(48) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.

mL, 10.4 M, 39.5 mmol) was added at 0 °C to a mechanically stirred solution of the deuterated alcohol (1.15 g, 1.55 mmol) in ether (15 mL). TMEDA (6 mL) and THF (15 mL) were added. After stirring for 24 h at room temperature, the mixture was quenched with trimethyltin chloride (2.98 g, 15 mmol) and diluted with ether. The organic layer was washed with saturated aqueous sodium bicarbonate and saturated aqueous copper sulfate and dried (potassium carbonate). The crude product was dissolved in 60 mL of methylene chloride and cooled to −30 °C. Pyridine (4.74 g, 4.85 mL, 60 mmol) was added followed by dropwise addition of acetyl chloride (1.18 g, 1.08 mL, 15 mmol). The mixture was stirred for 30 min and quenched with saturated aqueous sodium bicarbonate. After diluting with ether (150 mL) the solution was washed with saturated aqueous sodium bicarbonate and saturated aqueous copper sulfate, dried over potassium carbonate, and concentrated. Flash chromatography (90:10 hexane/ethyl acetate) gave 780 mg (25% over two steps) of the title compound, R_f 0.54 (90:10 hexane/ethyl acetate). ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.75 (s, 1 H), 4.69 (s, 1 H), 2.08 (s, 3 H), 0.13 (s, 9 H). MS calcd for $C_9H_{16}D_2O_2Sn$: *m/e* 280.0454. Found: 280.0459; 280 (d_2, 95%).

Reaction of 1-Acetoxy-1,1-dideuterio-2-[(trimethylstannyl)methyl]-2-propene (31) with Cinnamaldehyde. Palladium acetate (5 mg, 22 μmol) and triphenylphosphine (30 mg, 114 μmol) were dissolved in tetrahydrofuran (1 mL), and the mixture was heated until a homogeneous solution was obtained. Cinnamaldehyde (66 mg, 63 μL, 0.50 mmol) and 1-acetoxy-1,1-dideuterio-2-[(trimethylstannyl)methyl]-2-propene (**31**; 140 mg, 0.5 mmol) were added, and the mixture was heated for 1 h. The reaction was diluted with 80:20 hexane/ethyl acetate (2 mL) and filtered through a silica gel plug. Concentration and flash chromatography (97:3 hexane/ethyl acetate) gave 70 mg (80%) of deuterated material. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.40–7.11 (m, 5 H), 6.62 (d, J = 15.9 Hz, 1 H), 6.24 (dd, J = 15.9, 6.7 Hz, 1 H), 5.02 (br s, 0.55 H), 4.94 (br s, 0.55 H), 4.57 (q, J = 7.4 Hz, 1 H), 4.47 (d, J = 13.1 Hz, 0.45 H), 4.32 (d, J = 13.1 Hz, 0.45 H), 2.77 (dd, J = 15.4, 7.4 Hz, 1 H), 2.45 (dd, J = 15.4, 7.4 Hz, 1 H).

Palladium-Mediated Allylation of Cinnamaldehyde. Preparation of 3-Hydroxy-1-phenyl-1,5-hexadiene (34). Palladium acetate (5 mg, 22 μmol) and triphenylphosphine (30 mg, 114 μmol) in 1 mL of THF was heated to 35 °C until homogeneous. Cinnamaldehyde (67 mg, 67 μL, 0.50 mmol), allyl acetate (50 mg, 54 μL, 0.50 mmol), and allyltri-*n*-butyltin (106 mg, 100 μL, 0.50 mmol) were added, and the mixture was stirred for 3 h. At this time TLC showed cinnamaldehyde still remained, so more allyl acetate (50 mg, 54 μL, 0.50 mmol) and allyltri-*n*-butyltin (106 mg, 100 μL, 0.50 mmol) were added and the mixture was heated an additional 3 h. At this time, the reaction mixture was filtered through a silca gel plug and chromatographed (90:10 hexane/ethyl acetate) to give 78 mg (89%) of **34** identical with previously described material.[30] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.50–7.30 (m, 5 H), 6.70 (d, J = 16.8 Hz, 1 H), 6.33 (dd, J = 16.8, 7.2 Hz, 1 H), 5.98 (m, 1 H), 5.28 (br d, J = 16.0 Hz, 1 H), 5.22 (br d, 12.1 Hz, 1 H), 4.42 (br s, 1 H), 2.54 (m, 2 H), 2.10 (br s, 1 H).

1-Phenyl-1,5-hexadiene. Palladium acetate (5 mg, 22 μmol) and triphenylphosphine (30 mg, 114 μmol) in 1 mL of THF was heated to 35 °C until homogeneous. Cinnamaldehyde (67 mg, 67 μL, 0.50 mmol), allyl acetate (50 mg, 54 μL, 0.50 mmol), and cinnamyltri-*n*-butyltin (124 mg, 110 μL, 0.50 mmol) were added, and the mixture was stirred for 3 h. At this time the reaction mixture was filtered through a silica gel plug and chromatographed (hexane) to give 54 mg (62%) of the title compound.[49] R_f 0.75 (hexane). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5 H), 6.40 (d, J = 16.8 Hz, 1 H), 6.20 (dt, J = 16.8, 7.2 Hz, 1 H), 5.85 (m, 1 H), 5.09 (br d, J = 16.0 Hz, 1 H), 5.00 (br d, J = 12.1 Hz, 1 H), 2.24 (m, 2 H).

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1-Acetoxy-1,1,3,3-tetradeuterio-2-[(trimethylsilyl)methyl]-2-propene (36). Sodium hydride (60%, 140 mg, 3.50 mmol) was added to a solution of diethyl [(trimethylsilyl)methyl]malonate[50] (820 mg, 3.33 mmol) in THF (10 mL) at 0 °C. The solution was allowed to warm to room temperature over 2 h, and lithium aluminum deuteride (420 mg, 10 mmol) was added. The reaction mixture was gently refluxed for 48 h and cooled to room temperature. Ether (20 mL) was added, and the excess reagent was quenched sequentially with water (0.42 mL), 20% sodium hydroxide (0.42 mL), and distilled water (1.26 mL). The resulting solid was removed by filtration and washed with ether, and the filtrate was dried (magnesium sulfate). The solvent was removed, and the residue was flash chromatographed (90:10 hexane/ethyl acetate) to give 200 mg (41%) of tetradeuterated alcohol. This material (180 mg, 1.21 mmol) was taken up in methylene chloride (5 mL), and pyridine (0.47 g, 0.49 mL, 6.0 mmol) was added. The mixture was cooled to −30 °C, and acetyl chloride (0.23 g, 0.17 mL, 3.0 mmol) was added dropwise. It was then allowed to warm to 0 °C and quenched with saturated aqueous sodium bicarbonate (1 mL). The mixture was poured into ether (30 mL) and washed with saturated aqueous sodium bicarbonate (5 mL), dried over potassium carbonate, and flash chromatographed (90:10 hexane/ethyl acetate) to yield 200 mg (87%) of the tetradeuterated trimethylenemethane precursor, R_f 0.55 (90:10 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08 (s, 3 H), 1.52 (s, 2 H), 0.03 (s, 9 H). MS calcd for $C_9H_{14}D_4SiO_2$: *m/e* 190.1327. Found: 190.1334; 190 (d_4, >95%).

Reaction of 1-Acetoxy-1,1,3,3-tetradeuterio-2-[(trimethylsilyl)-methyl]-2-propene (36) with Cinnamaldehyde. Following the general protocol, a solution of palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), trimethyltin acetate (16 mg, 70 μmol), cinnamaldehyde (33 mg, 31 μL, 0.25 mmol), and 1-acetoxy-1,1,3,3-tetradeuterio-2-[(trimethylsilyl)methyl]-2-propene (**36**; 23 mg, 27 μL, 0.125 mmol) in 0.5 mL of benzene was heated at 70 °C for 1 h. After the usual workup, preparative thin-layer chromatography (98:2 hexane/ethyl acetate) provided 22 mg (93%) of the deuterated product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.21 (m, 5 H), 6.62 (d, J = 15.9 Hz, 1 H), 6.24 (dd, J = 15.9, 6.7 Hz, 1 H), 5.02 (s, 0.06 H), 4.94 (s, 0.06 H), 4.57 (q, J = 7.4 Hz, 1 H), 4.47 (d, J = 13.1 Hz, 0.06 H), 4.32 (d, J = 13.1 Hz, 0.06 H), 2.77 (dd, J = 15.4, 6.5 Hz, 0.88 H), 2.45 (dd, J = 15.4, 8.1 Hz, 0.88 H). MS calcd for $C_{13}H_{10}D_4O$: *m/e* 190.1295. Found: 190.1289; 190 (d_4, 95%), 189 (d_3, 5%).

Reaction of 1-Acetoxy-1,1,3,3-tetradeuterio-2-[(trimethylsilyl)-methyl]-2-propene (36) with Cyclohexanecarboxaldehyde. Following the general protocol, a solution of palladium acetate (3 mg, 13 μmol), triphenylphosphine (18 mg, 69 μmol), trimethyltin acetate (16 mg, 70 μmol), cyclohexanecarboxaldehyde (28 mg, 30 μL, 0.25 mmol), and 1-acetoxy-1,1,3,3-tetradeuterio-2-[(trimethylsilyl)methyl]-2-propene, **36** (23 mg, 27 μL, 0.125 mmol) in 0.5 mL of benzene was heated at 70 °C for 1 h. After the usual workup, preparative thin-layer chromatography (98:2 hexane/ethyl acetate) gave 16 mg (77%) of the deuterated product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.92 (s, 0.23 H), 4.84 (s, 0.23 H), 4.32 (d, J = 13.1 Hz, 0.18 H), 4.16 (d, J = 13.1 Hz, 0.18 H), 3.59 (m, 1 H), 2.52 (dd, J = 15.6, 5.5 Hz, 0.69 H), 2.23 (dd, J = 15.6, 10.4 Hz, 0.69 H), 1.92–0.95 (m, 11 H). MS calcd for $C_{11}H_{14}D_4O$: *m/e* 170.1604. Found: 170.1611; 170 (d_4, 93%), 169 (d_3, 7%).

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