Intramolecular Allylstannane−Aldehyde Cyclizations: Stereochemical Results with Flexible Tethers for Reactions Forming Vinylcyclohexanols

Gary E. Keck,* Shawn M. Dougherty,† and Kenneth A. Savin

Contribution from the Department of Chemistry, University of Utah, Salt Lake City, Utah 84112

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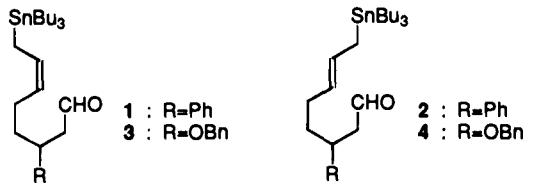
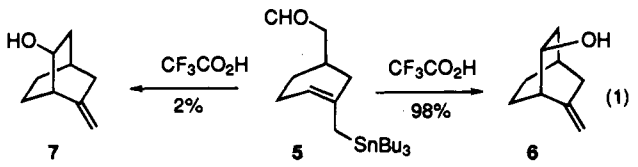
Abstract: Intramolecular Lewis acid-promoted cyclization reactions of both (*Z*)- and (*E*)-3-phenyl-8-(tri-*n*-butylstannyl)oct-6-enal and (*Z*)- and (*E*)-3-(benzyloxy)-8-(tri-*n*-butylstannyl)oct-6-enal have been examined using a variety of Lewis acids, specifically $BF_3{\cdot}Et_2O$, CF_3CO_2H, $SnCl_4$, $TiCl_4$, and $MgBr_2$. Thermally promoted cyclizations were also examined. The results show that product stereochemistry is a sensitive function of both olefin stereochemistry and Lewis acid. The data acquired in these studies also suggest that such reactions are mechanistically more complex than previous studies with more constrained systems have revealed.

Introduction

For several years, our research group has been investigating the synthetic potential and fundamental mechanistic underpinnings of the Lewis acid-promoted reactions of allylstannanes with aldehydes.[1] One of the principal unanswered questions in this area is the preferred transition state structure which leads to product in bimolecular reactions of this type. Since our work to date has indicated that this is a sensitive function of aldehyde structure, stannane structure, and Lewis acid utilized, generalizations are indeed difficult. For this reason, and also to investigate the synthetic potential of intramolecular processes, we have examined in detail the intramolecular cyclizations of substrates **1**−**4** below.



With the reasonable assumption that staggered (or nearly so) transition states will be utilized in such reactions,[2] each reactant has available four limiting transition states (that lead to four chemically distinct products) which correspond to either antiperiplanar or synclinal arrangements of the reacting π systems (*vide infra*). A more constrained system, with two accessible product-forming transition states, has been studied in detail by Denmark[3] (eq 1).



In this case, formation of product **6** from a transition state utilizing a synclinal arrangement of reacting π systems was strongly preferred over an antiperiplanar alternative leading to **7**.

The intramolecular cyclization substrates described herein allow the double bond geometry of the allylstannane to be varied, a feature not possible with substrate **5**. The results obtained with **1**−**4** (*vide infra*) clearly show that double bond stereochemistry in the substrate plays an important role in determining product stereochemistry. The results of bimolecular reactions (*vide infra*) of (*Z*)- and (*E*)-crotylstannanes with various aldehydes also show that olefin geometry, contrary to previous reports,[4] is an important product-determining feature in these reactions as well. Such effects have previously been noted with allylsilanes,[5] although in general the magnitude of such structural effects were considerably smaller than those described herein. Similar stereochemical results have been reported for the intramolecular cyclization of an allylsilane and aldehyde in a related system.[6] The stereochemical course of intramolecular reactions between γ-alkoxystannanes and acetals[7a] and aldehydes[7b] has also been examined. In the latter case, different stereochemical results were obtained in reactions using protic acids vs those using Lewis acids such as $BF_3{\cdot}Et_2O$.

Results

Preparation of Cyclization Substrates. Substrates **1** and **2** (R = Ph) were prepared as shown in Scheme 1. In both cases, the route began with Baeyer−Villiger oxidation of 4-phenylcyclohexanone (**8a**) to afford lactone **9a** (86% yield), which

† Eastman Chemical Co., Kingsport, TN 37662.

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(1) Recent reviews: (a) Yamamoto Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (b) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395.

(2) (a) Cornforth, J. W; Cornforth, R. H; Mathews, K. K. *J. Chem. Soc.* **1959**, 112. (b) Karabatsos, G. J. *J. Am. Chem Soc.* **1967**, *89*, 1367. (c) Cherest, M.; Felkin H.; Prudent, N. *Tetrahedron Lett.* **1968**, *18*, 2199. (d) Ahn, N. T. Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61. (e) Burgi, H. B.; Dunitz, J. D.; Lehn, J. M.; Wipff, G. *Tetrahedron* **1974**, *30*, 1563. (f) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353. (g) Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438.

(3) (a) Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970. (b) Denmark S. E.; Weber, E. J.; Wilson, T. M.; Willson, T. M. *Tetrahedron* **1989**, *45*, 1053.

(4) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.

(5) Hayashi, T.; Kabeta, K.; Itaru, H.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865.

(6) Asao, K.; Iio, H.; Tokoroyama, T. *Tetrahedron Lett.* **1989**, *30*, 6397.

(7) (a) Gevorgyan, V.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **1993**, *34*, 1313. (b) Yamada, J-i.; Asano, T.; Kadota, I.; Yamaoto, Y. *J. Org. Chem.* **1990**, *55*, 6066.

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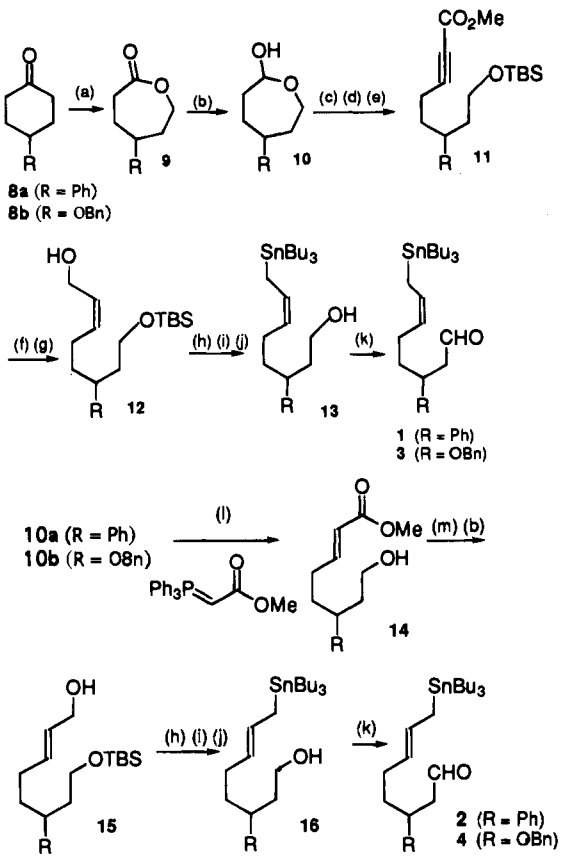
Scheme 1. Preparation of Cyclization Substrates **1**–**4**[a]



[a] Key: (a) *m*-CPBA; (b) DIBAL, 1 equiv; (c) TBSCl; (d) CBr_4, PPh_3; (e) *n*-BuLi, $ClCO_2Me$; (f) H_2, Lindlar catalyst; (g) DIBAL, 2 equiv; (h) pyridine, CCl_4, PBu_3; (i) Bu_3SnLi; (j) NBu_4F; (k) MeMgBr, 1,1-diazodicarbonyldipiperidine; (l) **10b** only, TBDMSCl; (m) **10a** only, TBDMSCl.

was reduced with diisobutylaluminum hydride (DIBAL-H) to give lactol **10a** (97% yield), a significant percentage of which existed in the ring-opened hydroxy aldehyde form. From **10a**, routes to the (*Z*)-allylstannane **1** and the (*E*)-allylstannane **2** diverged. For preparation of the *Z* material, **10a** was first selectively silylated with TBDMS chloride, and the resulting aldehyde was processed according to a protocol developed by Kishi[8] to afford the acetylenic ester **11a** (72% yield for two steps). Lindlar reduction of the alkyne followed by ester reduction with DIBAL-H afforded allylic alcohol **12a** (83% yield for two steps). Reaction of **12a** with tributylphosphine in carbon tetrachloride gave the corresponding allylic chloride, which was reacted with lithiotri-*n*-butylstannane to afford stannane **13a** (79% yield for two steps). Deprotection of **13a** with TBAF proceeded uneventfully,[9] and the resulting alcohol (98% yield) was oxidized by the Saigo–Mukaiyama protocol to afford **1**.[10] It should be noted that this compound was extremely sensitive (due to facile thermal cyclization) and thus was isolated and used *immediately* in the cyclization reactions described herein.

The *E* allylic stannane **2** was prepared from lactol **10a** *via* the stabilized Wittig reaction to afford the *E* unsaturated ester **14a** (87% yield).[11] This material was first silylated and then reduced with diisobutylaluminum hydride to afford allylic alcohol **15a** (86% yield for two steps). Alcohol **15a** was first chlorinated and then stannylated to afford allylstannane **16a** (70% for two steps) *via* procedures previously described in the preparation of **1**. Fluoride-induced removal of the TBS group and oxidation as previously delineated then gave substrate **2**. This material was isolated as a 10:1 mixture of *E* and *Z* geometric isomers, which arose at the stage of stabilized Wittig homologation of the lactol **10a**.

Both the (*E*)-stannane **2** and the (*Z*)-stannane **1** presented special handling problems in that they tended to cyclize on silica gel and had to be chromatographed at −78 °C on basic alumina. Both isomers were utilized immediately; however, this was more critical for the *Z* isomer **1** than for the *E* isomer **2**. It should be noted that reaction temperatures and times preclude any significant thermal contribution to the results of the catalyzed reactions.

Substrates **3** and **4** (R = OBn) were prepared analogously from 4-(benzyloxy)cyclohexanone (**8b**). This material was obtained *via* monobenzylation of 1,4-cyclohexanediol (42% yield)[12] followed by PCC oxidation of the resulting alcohol (91%). As in the phenyl-substituted case, **13** was not contaminated with the *E* isomer; however, **14** was isolated as a 7:1 *E*:*Z* mixture.

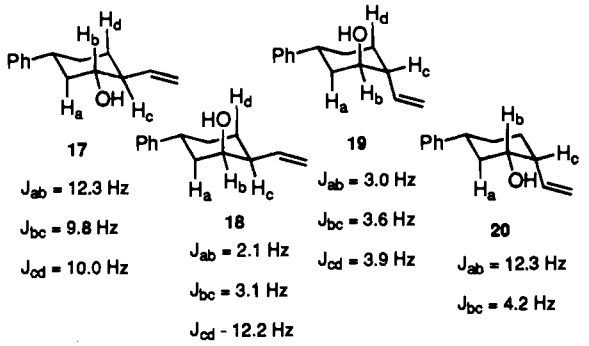
Both the *Z* stannane **3** and the *E* stannane **4** presented additional handling problems in that they tended to cyclize on silica gel and also readily eliminated to produce **26** when chromatographed over basic alumina (−78 °C) or amine-treated silica (−78 °C) (eq 2). Isolation over MeOH-treated silica (−78 °C) solved these problems. Qualitatively, both **3** and **4** cyclized somewhat faster than the phenyl substituted aldehydes **1** and **2**.

Cyclization Reactions Using Substrates 1 and 2. Both **1** and **2** were subjected to Lewis acid-mediated cyclization reactions, using $BF_3{\cdot}Et_2O$, $TiCl_4$, $SnCl_4$, $MgBr_2$, and CF_3CO_2H as Lewis acids. Thermal cyclizations were also investigated; the results obtained with **1** and **2** are tabulated in Tables 1 and 2, respectively. All cyclization reactions were performed at least three times, and the data presented reflect an average of three runs with product distribution agreeing within 2%. Isolated yields were 90% or greater except for the thermal cyclization of **2**. The *Z* substrate was thermally quite labile, with complete cyclization occurring simply on standing in solution at room temperature for 12 h. In contrast, the *E* compound was essentially inert, and the cyclization products observed after heating at toluene reflux for 10 days most probably result from indirect processes.

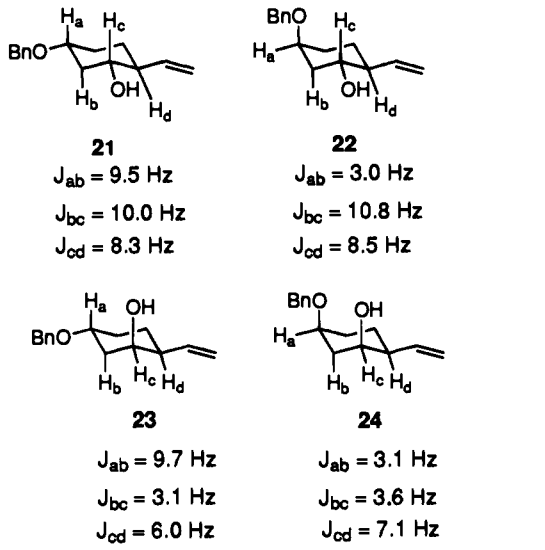
Products **17**–**20** were isolated by HPLC and structures assigned by ^1H NMR decoupling experiments. The methine adjacent to the vinyl group (H_c) was located by irradiation of the vinyl proton at *ca.* 6 δ; the methine adjacent to the hydroxyl moiety (H_b) was clearly visible at *ca.* 4 δ in all cases. In all cases, chair conformations with the phenyl substituent equatorial were observed. Pertinent coupling constants used in structural assignments are given below.

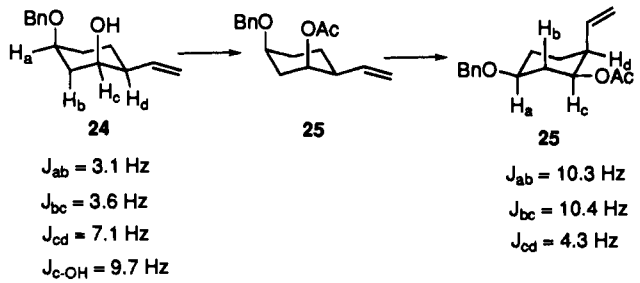
Results for the cyclization of the (*Z*)- and (*E*)-(benzyloxy)-substituted stannanes are tabulated in Tables 3 and 4, respectively. Cyclization occurred in isolated yields greater than 93% for **4** (and yields greater than 95% for **3**). In no case were any side products observed. Products **21**–**24** were isolated by HPLC and structures assigned by ^1H NMR decoupling experiments. Pertinent coupling constants used in structural assignments are given below. The structure of compound **24**, with a hydrogen-bonded diaxial hydroxy–benzyloxy relationship, was further confirmed by acetylating the hydroxyl group. Upon

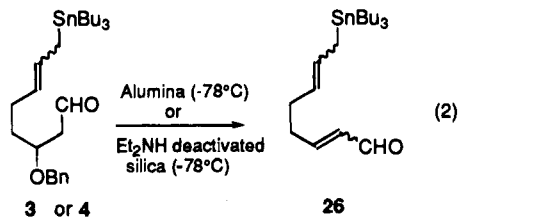
(8) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.
(9) Reaction with 1 equiv of *n*-butylammonium fluoride removed only the TBS group. No products resulting from its reaction with tin were observed.
(10) Narasaka, K.; Morikawa, A.; Saigo, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn* **1977**, *50*, 2773.
(11) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.
(12) Prins, D. A. *Helv. Chim. Acta* **1957**, *168*, 1621.



acetylation ring inversion occurred giving **25** with the coupling constants listed below.







Discussion

1. Thermal Cyclizations. The thermal cyclizations of both the (*Z*)- and (*E*)-stannyl aldehydes **1** and **2** yielded **18** with high selectivity but at drastically different rates. The accepted mechanism[13] for this thermal transformation requires a six-membered ring transition state in which the stannyl substituent is transferred to oxygen as bond formation to the carbonyl carbon occurs from the allyl moiety.

The presence of the *Z* double bond in **1** allows for two accessible transition state geometries, a chairlike array leading to **18**, or a boatlike array leading to **17**. (The conformation of the phenyl-containing six-membered ring at the transition state is of no consequence.) The results shown in Table 1 (*vide infra*) show that the chairlike transition state is preferred over the boatlike alternative to the extent of 95:5, even though this leads to the formation of a thermodynamically less stable product.

In contrast to the very facile thermal cyclization of the (*Z*)-stannane **1**, the *E* isomer **2** proved essentially inert. Heating of **2** at 110 °C in toluene for 17 days led to only a 50% isolated yield of cyclization products **17**−**20**. This stands in marked contrast to the essentially quantitative cyclization of **1** at room temperature.

Transition states C and D (Scheme 2) are bicyclo[4.4.0] systems (isosteric with decalin ignoring bond length differences), and inspection of molecular models clearly reveals that a synchronous (symmetry allowed) six-electron process is more difficult when the double bond is *E*. Thus, as the carbons of the allylstannane and aldehyde are brought within bonding distance, and the carbonyl oxygen and tin atoms are as well, a *trans*-cyclohexene array would be generated in the forming six-membered ring. Thus, it is unlikely that any of the products obtained from the (*E*)-stannane **2** result from direct thermal cyclization. The preponderance of **18** in the mixture is most probably a result of slow isomerization of **2** to **1** followed by intramolecular cyclization. The minor amounts of other products produced may result from other reaction pathways. The key observation, particularly from a synthetic standpoint, is that only the (*Z*)-stannanes are suitable for such intramolecular cyclizations, which occur with a very high degree of stereoselectivity.

Similar results were obtained with the benzyloxy-substituted stannanes **3** and **4**. From the (*Z*)-stannane **3**, product **23** was formed in 93% yield upon thermal cyclization at room temperature. This product would again result from a chairlike transition state as for the cyclization of **1**. Also formed were 5% of **24**, the result of the same chairlike transition state but with the benzyloxy substituent axial, and 4% of **22**.

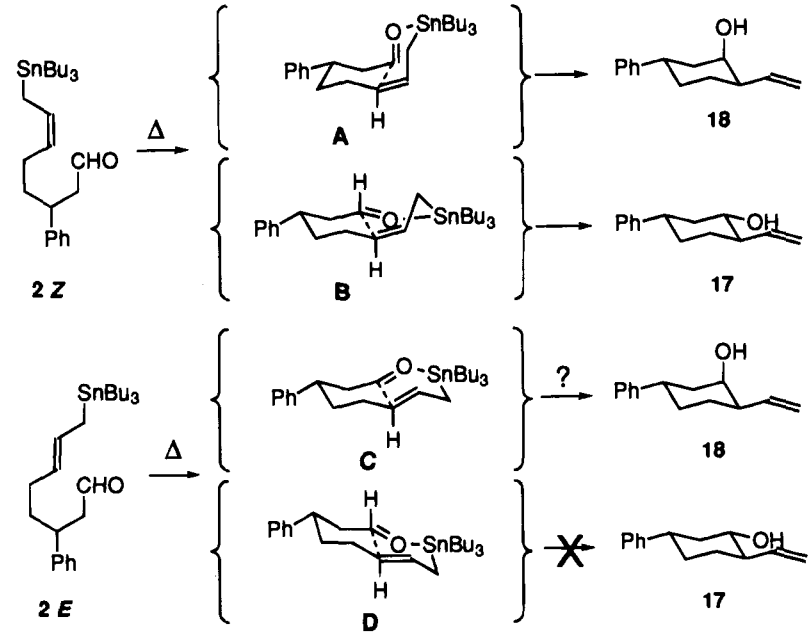
The (*E*)-stannane **4** could not be subjected to thermal cyclization as it decomposed at elevated temperatures. However, after 250 h at room temperature, a bad mixture of **21**−**24** was produced. It seems very likely that this is the result of adventitious acid catalysis, particularly since **4** had to be purified over methanol-deactivated silica gel, which may well have introduced trace acidic contaminants. Indeed, the distribution of products **21**−**24** in the "thermal" cyclization (35:45:9:11) is suspiciously similar to that obtained with CF_3CO_2H (30:48:15:7).

Lewis Acid-Mediated Cyclizations of Stannanes 1 and 2. The Lewis acid-mediated cyclizations of **1** (and **2**) required different conditions than those used for the thermal cyclizations. Freshly chromatographed aldehyde was dissolved in freshly distilled CH_2Cl_2, cooled, and treated with 1 equiv of the appropriate Lewis acid. In most cases the cyclization process was complete almost as soon as the sample could be analyzed. In analogy to the thermal cases, a reactivity difference was again observed between the (*Z*)- and (*E*)-stannanes, although the difference was quite small in the Lewis acid-catalyzed reactions. In the presence of CF_3CO_2H the (*Z*)-stannane cyclized approximately 1 order of magnitude faster than the (*E*)-stannane. Isolated yields for the cyclization of both **1** and **2** with all the Lewis acids were again excellent. Results for cyclization of the (*Z*)- and (*E*)-stannanes **1** and **2** are tabulated in Tables 1 and 2, respectively.

The Lewis acid-mediated cyclizations of **1** and **2** are also mechanistically quite different from the thermal process and require some introduction. In these reactions, complexation of

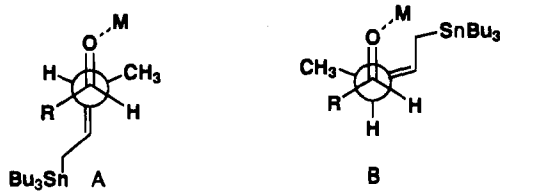
(13) Davis, A. G.; Smith, P. J. In *Comp. Organometallic Chemistry*, 1st ed.; Wilkinson, G., Ed.; New York, 1982; Vol. I, Chapter 11.

Scheme 2 Thermal Cyclization of Substrate **2**



the aldehydic oxygen with the Lewis acid (presumably *anti* to the R group) is followed by nucleophilic addition of the stannane to generate a carbocation intermediate stabilized by strong hyperconjugative donation from the adjacent carbon–tin bond. Loss of the stannyl substituent to a nucleophile (e.g., halide ion) then completes the process.

Two transition state hypotheses for such Lewis acid-promoted reactions of allylstannanes with aldehydes have been advanced. The first, due to Yamamoto,[4] suggests an antiperiplanar arrangement (180° dihedral angle) of the reacting π systems, as shown in structure **A** below for the reaction of an aldehyde with a (*Z*)-crotylstannane. The second, due to Denmark, proposes that a synclinal (60° dihedral angle) arrangement of the reacting π systems is preferred (structure **B**).[3]



Antiperiplanar Transition State **Synclinal Transition State**

Both transition states suggested result in the production of *syn* products. The Yamamoto hypothesis is based upon the stereochemical results obtained in BF_3·Et_2O-mediated bimolecular reactions of crotyltri-*n*-butylstannane with aldehydes and the assumption that the preferred transition state minimizes steric interactions between CH_3 and R. The Denmark hypothesis is based upon results obtained in the intramolecular cyclizations of **5** (note Scheme 1). Although the results obtained with the Denmark substrate **5** demonstrate convincingly that a synclinal orientation of π systems as shown in **B** is strongly preferred over the antiperiplanar arrangement **A**, it has been explicitly noted[3] that these results "do not necessarily negate the Yamamoto hypothesis", since the Yamamoto transition state is inaccessible in the system studied by Denmark, and the same is of course true in the intramolecular systems described herein as well. Such intramolecular substrates incorporate a four-carbon tether between CH_3 and R in structures **A** and **B**, which necessarily precludes structures corresponding to **A**.

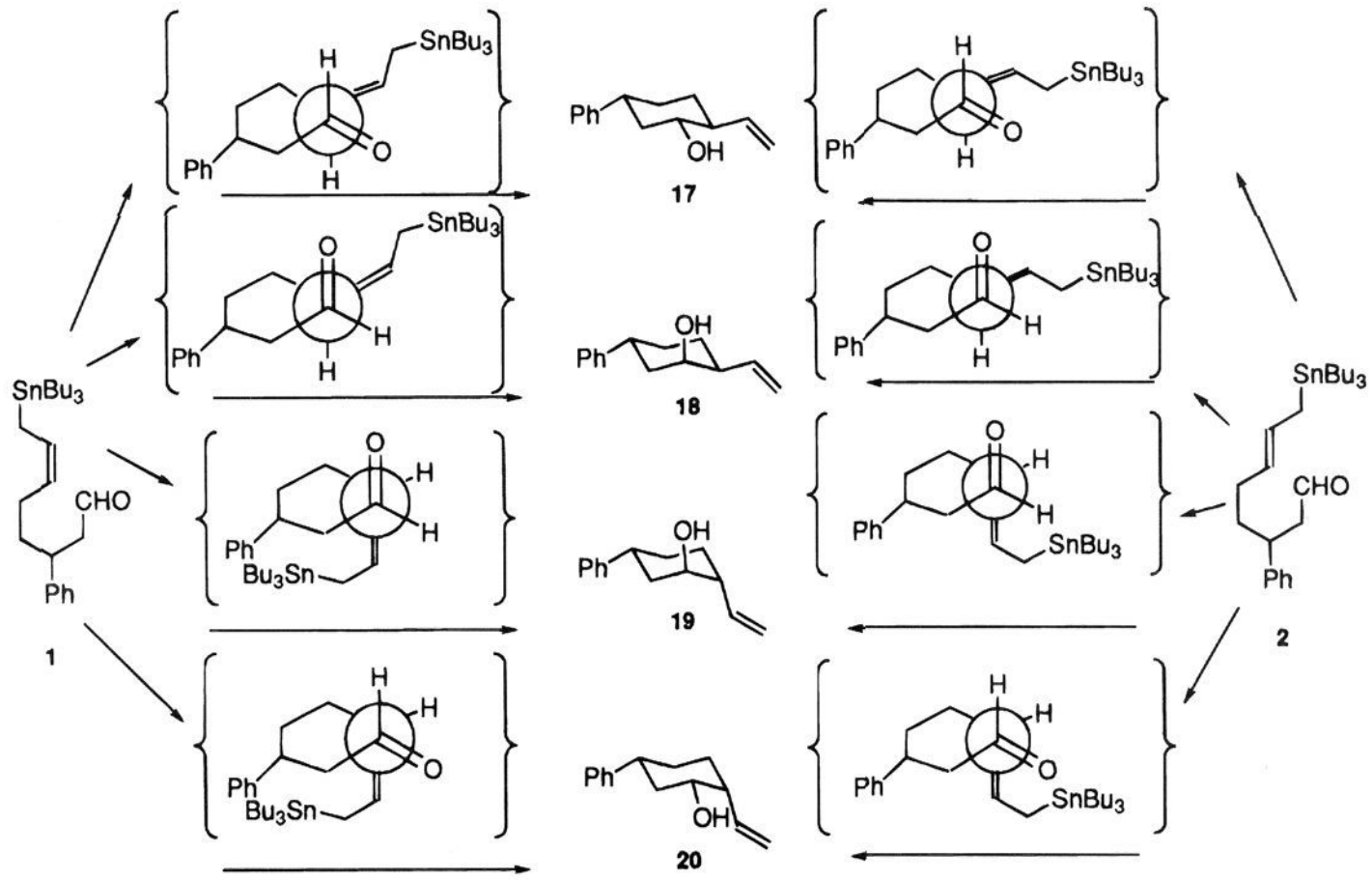
Substrates **1** and **2** can, however, access a *number* of synclinal and antiperiplanar geometries enroute to cyclization products **17**–**20** (Scheme 3). Thus, products **17**, **18**, and **20** result from various synclinal arrangements of the reacting π systems in *Z* stannane **1**, while product **19** would result from an antiperiplanar arrangement. With the *E* stannane **2**, products **17**, **18**, and **20** again are formed *via* synclinal transition states, while **19** again results from an antiperiplanar arrangement. *However, the same transition state geometries do not lead to the same products with stannanes 1 and 2.* Thus, differences in product distributions which might result solely from product stability are, in effect, factored out.

For example, product **17** is formed *via* a synclinal geometry in both cases; with **1** the tin-bearing methylene is *anti* to the carbonyl oxygen, while with **2** it is *syn*. The converse is true for product **18**; with **1** the tin-bearing methylene is *syn* to the carbonyl oxygen, but *anti* with **2**. Similar considerations apply to product **20**. Product **19** is formed *via* antiperiplanar transition states which differ in that the tin-bearing methylene is *syn* to a CH_2 with **1** and *syn* to H with **2**. For convenience, those transition states and structures corresponding to "*syn-synclinal*" arrays (defined here as those synclinal orientations of reacting π systems in which the tin bearing methylene and the carbonyl oxygen are *syn* to one another) are labeled with an asterisk in Tables 1 and 2.

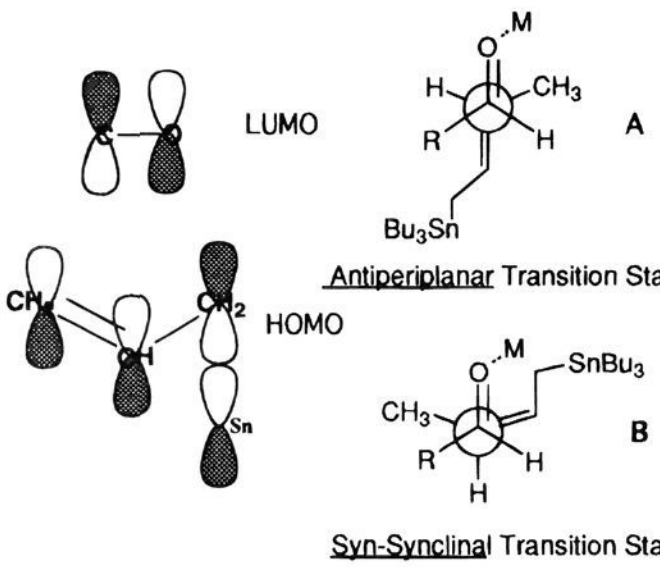
Results for the Lewis acid-mediated cyclization of **1** are summarized in Table 1. Indicated beneath products **17**–**20** are transition state representations, shown as Neuman projections about the forming σ bond, which indicate the relative orientations of the reacting π systems leading to each product. A cursory examination quickly reveals that all of the reactions exhibit quite high levels of stereoselectivity and that product **18** is preferred in all cases. Thus, with CF_3CO_2H, for example, this material accounts for 96% of the four possible diastereomers of product. It is also immediately apparent that the product distribution observed is *not* the result of simple thermodynamic control *via* a Zimmerman–Traxler type of transition state. If this were the case, then product **17**, with both the oxygen and vinyl substituents equatorial on the six-membered ring, should be strongly preferred over **18**, which has the oxygen substituent in an axial position.

The predominance of the "*syn-synclinal*" product **18** can be rationalized using an FMO argument.[3b] The orbital drawing below illustrates the LUMO of the carbonyl interacting with

Scheme 3. Transition State Representations Leading to Products **17**−**20**



the HOMO of the allylstannane. The primary bonding interaction occurs between the carbon of the carbonyl and the terminal carbon of the allylstannane. When the allylstannane is in the geometry indicated, there is a possibility of a secondary orbital overlap (bonding and energy lowering) between the oxygen of the carbonyl and the stannyl methylene carbon. This "*syn-synclinal*" transition state thus may benefit from this secondary orbital overlap stabilization, while the antiperiplanar or *other synclinal* transition states cannot.



Likewise, **2** can cyclize to yield the same four products (Scheme 3). However, in this case two different transition states would be expected to benefit from secondary orbital overlap (i and iv), leading to **17** and **20**, respectively (Table 2). Steric considerations would favor the formation of **17** with exclusively equatorial substitution. Indeed, when the Lewis acid is small (H^+), as in the case of CF_3CO_2H, good selectivity is observed (81% **17**, 8% **20**). However, as the size of the Lewis acid increases (BF_3·OEt_2, $MgBr_2$, $TiCl_4$ to $SnCl_4$), the selectivity for **17** decreases (60%, 55%, 34% to 29%). Comparison with the results for **1** shows that the cyclization of the (*E*)-stannane **2** is much more sensitive to variations in the Lewis acid than is the cyclization of **1**.

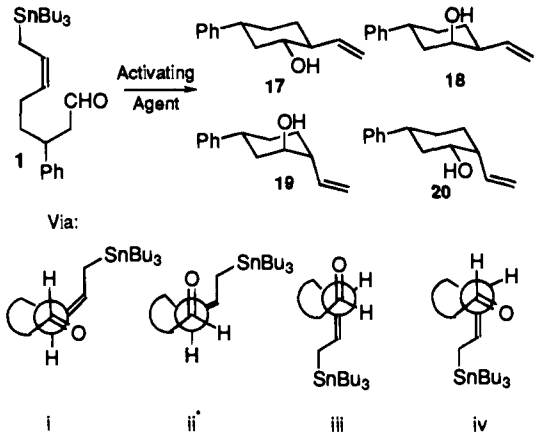
It is interesting to note that when $SnCl_4$ is reacted with the (*E*)-stannane the main product, **19**, obtained in 51% yield, has a diaxial relationship between the hydroxy and vinyl substituent and must result from an antiperiplanar transition state. Perhaps the large steric bulk of this Lewis acid binding anti to the R group on the aldehyde is responsible for a steric preference for this transition state, but the reasons for this result are not really clear. Transmetalation of the allylstannane with $SnCl_4$ is a possibility which cannot be ruled out in this system (*vide infra*), since the intramolecular reactions are too rapid for meaningful spectroscopic investigation.

Lewis Acid-Mediated Cyclization of 3 and 4. With compounds **3** and **4**, the presence of the β-(benzyloxy) substituent could allow for "chelation control" with certain Lewis acids ($MgBr_2$, $SnCl_4$, $TiCl_4$). This possibility would require that the benzyloxy and developing hydroxy substituents occupy axial positions on the forming six-membered ring, leading to products **21** (after ring inversion) or **24** (Scheme 4).

The cyclization of **3** yielded four products, **21**−**24**, each containing an equatorial vinyl group. Secondary orbital overlap would favor the formation of products **23** and **24** resulting from cyclization through the transition state labeled ii in Table 3. The data clearly indicate a strong selectivity for the formation of **23** and **24**, with **23** predominating, presumably for steric reasons. The highest selectivity was observed in the CF_3CO_2H case (≅97%). A slight decrease in selectivity is seen in the BF_3·OEt_2 and $MgBr_2$ cases (≅86%), while the lowest selectivity is found in the $SnCl_4$ and $TiCl_4$ cases (≈77%). The good selectivity for the formation of these products provides additional support for our orbital overlap theory.

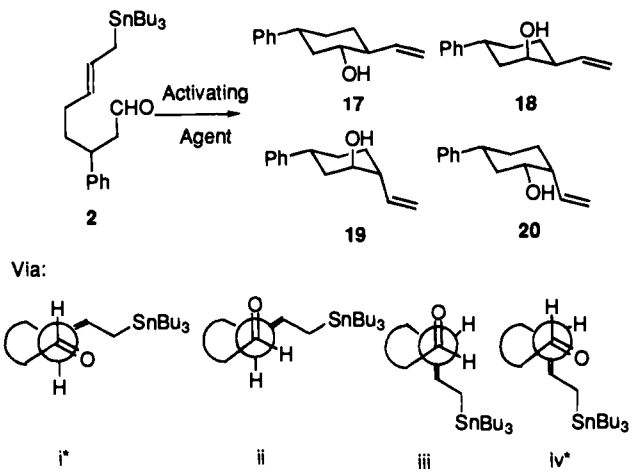
On the other hand, product **24** may also be formed *via* an intermediate chelated structure. $MgBr_2$ gives 84% of this chelation product **24** *via* a pathway which may also benefit from secondary orbital overlap. Compound **21** may also be obtained through a chelation pathway followed by ring inversion and is formed in 11% yield. (It is necessary that the benzyloxy and hydroxy groups be axial on the vinyl-containing six-membered ring for a six-membered chelate to be geometrically feasible.) Both $TiCl_4$ and $SnCl_4$ are also bidentate ligands known to chelate; yet, they only yield 15% and 6% of the chelation product **24** and merely ≈9% of **21**, which may have arisen through a chelated transition state. It seems likely that all three Lewis acids ($MgBr_2$, $TiCl_4$, and $SnCl_4$) react with the aldehyde by initial coordination anti to the R group; however, the $TiCl_4$

Table 1. Products Resulting from the Cyclization of **1**



reagent	17	18*	19	20	time	temp (°C)
CF_3CO_2H	4	96	0	0	<20 min	−78 to +25
$BF_3{\cdot}OEt_2$	15	85	<1	<1	<30 min	−78
$MgBr_2{\cdot}OEt_2$	15	85	0	0	1 h	−23
$TiCl_4$	5	91	≈1	<1	<10 min	−90
$SnCl_4$	10	90	<1	<1	<10 min	−90
thermal	5	95	0	0	<12 h	25

Table 2. Products Resulting from the Cyclization of **2**



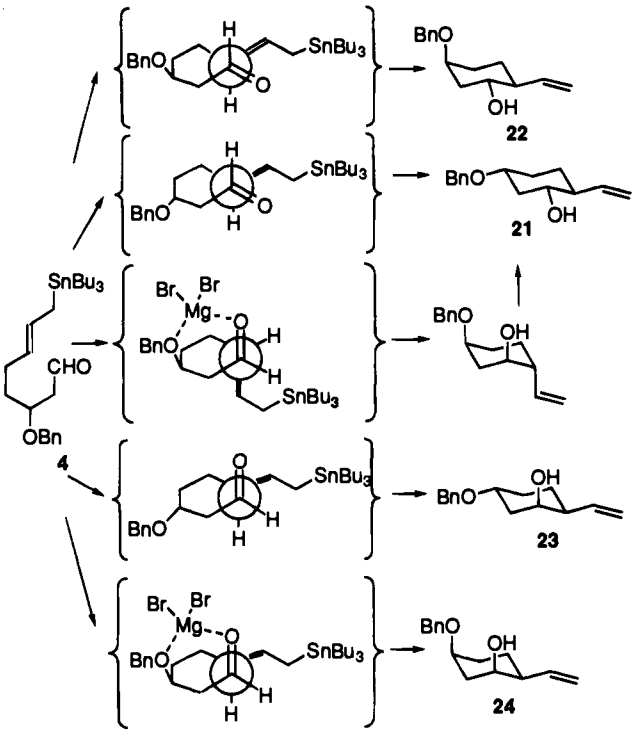
reagent	17*	18	19	20*	time	temp (°C)
CF_3CO_2H	81	6	1	8	3 h	−78 to +25
$BF_3{\cdot}OEt_2$	60	24	6	6	30 min	−78
$MgBr_2{\cdot}OEt_2$	55	32	2	11	1 h	−23
$TiCl_4$	35	39	18	8	<5 min	−90
$SnCl_4$	29	6	51	14	<10 min	−90
thermal	9	80	2	9	≈250 h	110

and $SnCl_4$ complexes are so reactive that cyclization occurs before chelation with the benzyloxy group is established. With the much weaker Lewis acid $MgBr_2$, chelate formation prior to reaction is viable. In this case, it appears that 95% of the products (**24** and **21**) are formed *via* chelation-controlled pathways. The contrast with the CF_3CO_2H-promoted reaction (95% of **23**) is quite dramatic.

These results are supported by an earlier theory proposed by Keck and Castellino in low-temperature NMR studies of the complexation of 3-methoxyoctanal with $SnCl_4$.[14] As the 1:1 chelate was warmed from −90 °C to room temperature, the chemical shift of the methine proton adjacent to the methoxy

(14) Keck, G. E.; Castellino, S.; Andrus M. B. *Selectivities in Lewis Acid Promoted Reactions*; Schinzer, D., Ed.; Series C: Mathematical and Physical Sciences, Vol. 289; NATO ASI Series; 1989; Chapter 5, p 97.

Scheme 4. 21 from Chelation and Ring Flipping or Secondary Orbital Overlap



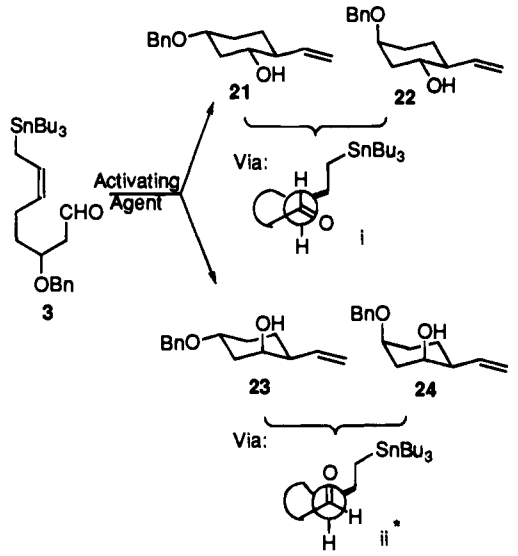
substituent was observed to move upfield considerably more rapidly than that of the methylene group adjacent to the aldehyde, suggested that breakdown of the chelated structure is initiated by loss of the methoxy ligand, *followed* by loss of the aldehyde ligand. By microscopic reversibility this then suggests that $SnCl_4$ initially coordinates anti to the R group on the aldehyde, and then it moves *syn* to the R group (inversion at oxygen), where chelation is geometrically feasible and from which geometry the chelate is obtained.

The results for the cyclization of the (*E*)-stannane **4** are similar in many respects to the results from the cyclization of the phenyl-substituted (*E*)-stannane **2**. Note that secondary orbital overlap would favor the formation of products with equatorial hydroxyl and vinyl substituents (**21** and **22** in Table 4) in this case. Selectivity for these products was very similar to that for the cyclization of the phenyl-substituted *E* case with CF_3CO_2H; 78% from **4** versus 81% from **2**. Again, it was observed that as the size of the Lewis acid increased (CF_3CO_2H, $BF_3{\cdot}OEt_2$ to $TiCl_4$) the selectivity decreased (78%, 46% to 44%). The exceptions to this trend were $SnCl_4$ and $MgBr_2$.

However, the main product from the $SnCl_4$-mediated cyclization of **4** (**22** in 48% yield) is actually just the "ring flipped" version of the main product of the cyclization of **2** (**19** in 51% yield) (Scheme 5)! It thus seems likely that *both* reactions proceeded through an antiperiplanar transition state but the benzyloxy group, unlike the phenyl group, is not constrained to occupy an equatorial position in product. Therefore, **22** simply reflects the more energetically favorable chair conformation of the product.

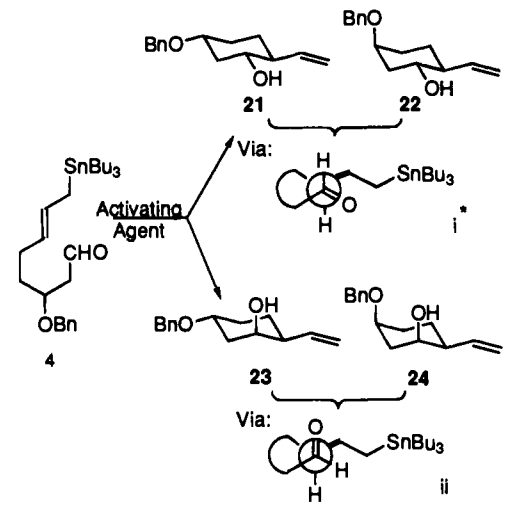
Cyclization mediated by $MgBr_2$ yielded 89% of products which may have resulted from chelation. The product with the diaxial relationship between the two oxygen-bearing centers, **24**, amounts to 30% of this yield, while the product with the diequatorial relationship, **21**, amounts to 59% of the yield. Once again, the exclusively equatorial product may have resulted from ring-flipping of a product that initially formed as an exclusively axial product. It is equally important to note that the all-axial transition state which may have led to the formation of **21** would not benefit from secondary orbital overlap. Therefore two

Table 3. Products Resulting from the Cyclization of **3**



reagent	21	22	23*	24*	time	temp (°C)
CF_3CO_2H	0	2	95	3	<10 min	−78 to +25
$BF_3{\cdot}OEt_2$	4	11	84	1	<10 min	−78
$MgBr_2{\cdot}OEt_2$	11	1	3	85	<20 min	−23
$TiCl_4$	8	13	64	15	<10 min	−90
$SnCl_4$	10	14	70	6	<10 min	−90
thermal	0	3	93	4	<10 h	25

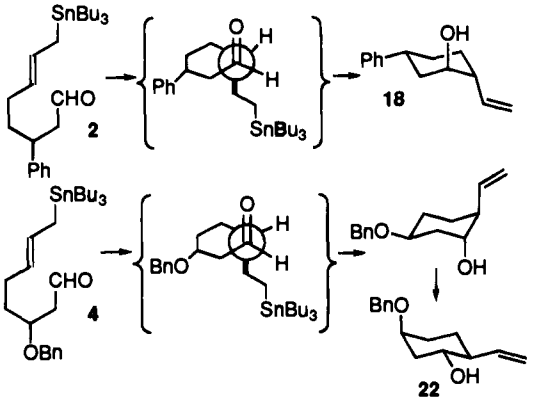
Table 4. Products Resulting from the Cyclization of **4**



reagent	21*	22*	23	24	time	temp (°C)
CF_3CO_2H	30	48	15	7	<1 h	−78 to +25
$BF_3{\cdot}OEt_2$	21	25	50	5	<40 min	−78
$MgBr_2{\cdot}OEt_2$	59	12	4	30	<1 h	−23
$TiCl_4$	11	32	43	14	<10 min	−90
$SnCl_4$	10	48	26	16	<10 min	−90
thermal	35	45	9	11	≈250 h	25

opposing factors contributed to the formation of **21**. If chelation were the sole source of selectivity then one would expect to see more of the lower energy chelation product, **24**. Conversely, if secondary orbital overlap were the main factor, then one would expect to see more of **21** and perhaps **22** (Scheme 5). Although a detailed discussion of the results with **4** is somewhat complicated by the conformational flexibility in this system, it should be noted that the results with **3** and **4** generally parallel those observed with **1** and **2** whether chelation or nonchelation pathways are involved. Thus, cyclizations of the *Z* substrates

Scheme 5. Product **22** May Result from Ring Inversion



1 and **3** are quite stereoselective, while those for the *E* substrates **2** and **4** are much less so.

Further Mechanistic Considerations in the LA-promoted Cyclizations of 1−4. A potentially important factor in the observed selectivity of all the Lewis acid mediated cyclizations is the nature of "MXn" indicated as the Lewis acid in eq 3. With CF_3CO_2H and $BF_3{\cdot}Et_2O$ the situation seems fairly simple: MXn = H^+ and BF_3, respectively. It has been previously documented that aldehydes are preferentially protonated anti to the alkyl substituent,[15] and the same result is observed for BF_3 complexation both in solution and in the solid state.[16] In addition, transmetalation processes are not possible with either CF_3CO_2H or $BF_3{\cdot}Et_2O$. Such a reaction with CF_3CO_2H would lead to simple protiodestannylation and yield a product incapable of subsequent intramolecular cyclization reactions. No products of this sort were observed. $BF_3{\cdot}Et_2O$ does appear capable of catalyzing *Z/E* isomerization of allylstannanes.[3b] This is an issue which is observable in our system: if *Z/E* isomerization of the allylstannane moiety were rapid relative to cyclization, then both geometric pairs, **1** and **2** and **3** and **4**, must yield the same product distributions upon exposure to $BF_3{\cdot}Et_2O$. Our data clearly demonstrate that they do not.

With $SnCl_4$, $TiCl_4$, and $MgBr_2$, the situation is potentially less clear. $SnCl_4$ is known to form bidentate complexes with simple aldehydes, e.g., $(RCHO)_2{\cdot}SnCl_4$, while with aldehydes bearing appropriate α- or β-alkoxy substituents 1:1 chelates are formed at 1:1 stoichiometry.[3b,17] In one case, X-ray crystallography has revealed a *cis* structure for the 2:1 complex.[18] Bidentate complexation is also expected with $TiCl_4$ and $MgBr_2$.[17,19] However, in an intramolecular process, where complexation and reaction are not independent and controllable events, the nature of complexation leading to reaction is an open question. Does cyclization proceed *via* a 5-coordinate metal species (a necessary intermediate enroute to 2:1 complexes) or *via* a 6-coordinate metal species? In principle this question could be addressed *via* spectroscopy; however, the cyclization processes described herein are simply too fast to allow for NMR investigations of the sort used in the study of the bimolecular process.[14,17,19]

One experiment addressing this problem indicated that 1:1 complexes were the reactive species in the $TiCl_4$ case. When

(15) (a) Nobes, R. H.; Rodwell, W. R.; Bouma, W. J.; Radom, L. *J. Am. Chem. Soc.* **1981**, *103*, 1913. (b) Ros, P. *J. Chem. Phys.* **1968**, *49*, 4902. (c) Brouwer, D. M. *Rec. Trav. Chim.* **1967**, *86*, 879.

(16) Reetz, M. T.; Hüllmann, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405.

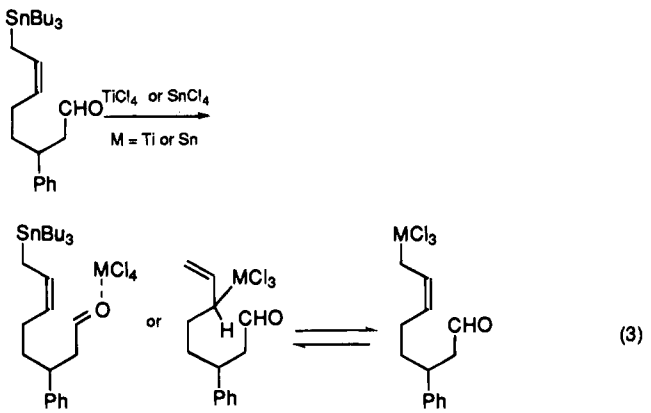
(17) (a) Keck, G. E.; Castellino, S. *J. Am. Chem. Soc.* **1986**, *108*, 3847. (b) Reetz, M. T.; Harms, K.; Reif, W. *Tetrahedron Lett.* **1988**, *29*, 5881.

(18) Denmark, S. E.; Henke, B. R.; Weber, E. *J. Am. Chem. Soc.* **1987**, *109*, 2512.

(19) (a) Keck, G. E.; Castellino, S.; Wiley, M. R. *J. Org. Chem.* **1986**, *51*, 5478. (b) Keck, G. E.; Andrus, M. B.; Castellino, S. *J. Am. Chem. Soc.* **1989**, *111*, 8136.

less than 1 equiv of Lewis acid was added, the reactions did not go to completion, and the selectivity observed did not depend significantly upon stoichiometry. The cyclization studies of **3** and **4** demonstrate that $SnCl_4$ and $TiCl_4$ do not appear to induce cyclization from chelates. This could imply that the compound cyclized from the 1:1 coordinated species and that chelation did not have time to occur. If this is true, i.e., if chelation does not have time to occur, then it is also unlikely that a 2:1 tin or titanium species has time to form.

In addition, both $SnCl_4$ and $TiCl_4$ can either complex with the aldehydic oxygen or react with the allylstannane in a transmetalation process to generate a new organometallic species. Both pathways have been observed in previous studies in our laboratories. In bimolecular reactions, one has the opportunity to separate such events in time, but this is not the case in intramolecular reactions where both reactive functionalities are exposed to the Lewis acid simultaneously (eq 3).



(3)

Results obtained in our laboratory for the bimolecular reaction indicate that it is extremely unlikely that transmetalation is occurring with $TiCl_4$ in the intramolecular case.[20] When stannane is added to a 1:1 mixture of cyclohexane carboxaldehyde and $TiCl_4$, good selectivity for *syn* product is obtained (93:7). When aldehyde is added to a mixture of $TiCl_4$ and stannane, good selectivity for the *anti* product is observed (21:1, due to transmetalation). In the example analogous to the intramolecular situation, that is when $TiCl_4$ is added to a mixture of aldehyde and stannane, high *syn* selectivity is again observed. This result is thus inconsistent with the intervention of a transmetalation pathway in these intramolecular reactions using $TiCl_4$.

Conclusion

The studies described herein provide an indication of the stereochemical results which can be anticipated in the preparation of six-membered rings *via* intramolecular allylstannane–aldehyde condensations. A critical and somewhat surprising role of olefin stereochemistry is revealed. Reactions of the (*Z*)-stannanes **1** and **3** occur with much higher stereoselectivity than with their *E* counterparts **3** and **4**, although the reasons for this remain obscure. An important stereoelectronic element in controlling the course of reaction is evident in that such reactions are not governed by simple steric considerations or the relative stability of products. A rationale for this stereoselectivity based upon secondary orbital overlap has been advanced.[21] Although the focus of the discussion in this regard has been upon the potential stabilization due to secondary orbital overlap in a *syn*-synclinal geometry, it should be noted that another important consideration should be the HOMO–LUMO energy gap as a function of Lewis acid utilized. Thus, secondary orbital overlap should be most important for those Lewis acids which result in the largest decrease in energy for the aldehyde π^* LUMO.

Experimental Section

General Information. All reactions were carried out under an atmosphere of nitrogen. Solvents were purified according to the guidelines in *Purification of Common Laboratory Chemicals* (Perrin, Armarego and Perrin, Pergammon Press: Oxford, 1966). Yields were calculated for material judged homogeneous by TLC and NMR. Reactions were performed at room temperature unless otherwise indicated. Solutions were concentrated using a Buchi rotary evaporator under water aspirator vacuum. Unless otherwise indicated, magnetic stirring was used for all reactions. Gas chromatagraphy data were collected under the following conditions: injector temperature was 250 °C, detector temperature was 300 °C, and column program temperature varied according to types of products (vide infra); a DX-4 column 30 m in length with a film thickness of 0.25 μm was employed, using He as the carrier gas (80 psi) and a flame ionization detector fueled by hydrogen (40 psi) and air (60 psi).

Thin layer chromatography was performed on Merck Kieselgel $60F_{254}$ plates, visualizing with a 254 nm UV lamp and staining with either an ethanol solution of 12-molybdophosphoric acid or an ethanol solution of anisaldehyde, H_2SO_4, and acetic anhydride. Flash column chromatography was performed using W. R. Grace Davisil 633 silica gel, slurry packed in glass columns. MPLC, medium-pressure liquid chromatography, implemented Altex columns packed with W. R. Grace Davisil 633 silica gel. Solvents were pumped using a FMI lab pump operating between 10 and 60 psi. HPLC, high-pressure liquid chromatography, was performed with a UV detector (254 nm) utilizing a Rainin 25 cm × 4.6 mm semipreparative column.

NMR spectra were acquired at 300 MHz for ^1H and 75 MHz for ^{13}C. Chemical shifts are reported in parts per million downfield from internal standard, tetramethylsilane (TMS). Abbreviations are as follows: s, singlet; d, doublet; dd, doublet of doublets; ddd, doublet of doublet of doublets; dddd, doublet of doublet of doublet of doublets; t, triplet; dt, doublet of triplets; q, quartet; m, multiplet; br, broad.

Elemental analyses were performed by Desert Analytics of Tuscon, AZ.

4-Phenyl-ϵ-Caprolactone (9a). A solution of 4-phenylcyclohexanone (**8a**) (0.500 g, 2.87 mmol) in 1.5 mL of chloroform was added to a stirring solution of 80% *m*-chloroperbenzoic acid (0.742 g, 3.44 mmol) in 5 mL of chloroform. After 4 h, the mixture was filtered through Celite, washed twice with saturated $NaHCO_3$ and once with brine, dried ($MgSO_4$), and concentrated in vacuo. The lactone was isolated by MPLC (20% EtOAc/hexanes) to yield 0.467 g (86%) of **9a**: R_f = 0.34 (25% EtOAc/hexanes); 300-MHz ^1H NMR ($CDCl_3$) δ 7.26 (m, 5 H), 4.35 (m, 2 H), 2.81 (m, 3 H), 2.0–1.9 (m, 3 H) 1.9–1.7 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 175.5, 144.8, 128.6, 126.7, 126.5, 68.1, 47.1, 36.6, 33.6, 30.2; IR (neat) 3040, 2980, 2300, 1730, 1650, 1420, 1390, 1335, 1240, 1166, 1140, 1070, 995, 960, 890, 870. Anal. Calcd for $C_{12}O_2H_{14}$: C, 75.76; H, 7.42. Found: C, 76.02; H, 7.54.

6-Hydroxy-4-phenylhexanal (10a). DIBAL-H (1.5 M in toluene, 9.67 mL, 14.5 mmol) was slowly (0.25 mL/min) added to a −78 °C solution of 4-phenyl-ϵ-caprolactone (2.50 g, 13.1 mmol) in 250 mL of THF. After 4 h the reaction was quenched with $Na_2SO_4{\cdot}10H_2O$/Celite, warmed to room temperature, and stirred for 4–10 h. The slurry was filtered through Celite, and the cake was washed thoroughly with ether. The filtrate was concentrated in vacuo and purified by MPLC (40% EtOAc/hexanes) to yield 2.45 g (97%) of a 5:1 mixture of aldehyde:lactal as a clear oil: R_f = 0.43 (50% EtOAc/hexanes); 300-MHz ^1H NMR ($CDCl_3$) δ 9.65 (s, 0.5 H), 7.21 (m, 5 H), 3.53 (dt, J = 5.8, 6.5 Hz, 1 H), 3.46 (dt, J = 6.5, 7.3 Hz, 1 H), 2.71 (m, 1 H), 2.28 (q, J = 7.5 Hz, 2 H), 2.07–1.73 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 202.6, 143.8,

(20) Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. *Tetrahedron Lett.* **1984**, *25*, 3927.

(21) (a) It should be noted that the results of the intramolecular reactions described herein and the trends observed do *not* provide suitable models or predictions for the corresponding bimolecular reactions. Thus, in the intramolecular cases described above, it is the *Z* stannanes which provide the higher levels of stereoselectivity in Lewis acid promoted reactions, while in analogous bimolecular reactions, it is generally the *E* stannane which provides the highest *syn*/*anti* stereoselectivity. The same mechanistic hypothesis, however (secondary orbital overlap), proves useful in both circumstances. (b) Keck, G. E.; Savin, K. A.; Cressman, E. N. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889.

128.9, 127.9, 126.9, 60.9, 42.3, 41.7, 39.7, 29.0; IR (neat) 3400 (br), 3020, 2920, 2880, 2720, 1720, 1600, 1490, 1450, 1110, 1040, 905, 760, 730, 700. Anal. Calcd for $C_{12}O_2H_{16}$: C, 74.97; H, 8.39. Found: C, 74.94; H, 8.49.

Methyl 1-[(*tert*-Butyldimethylsilyl)oxy]-3-phenyloct-6-yn-8-oate (11a). A solution of TBDMS chloride (7.28 g, 48.3 mmol) in 75 mL of CH_2Cl_2 was slowly added *via* cannula to a stirring solution of aldehyde **10a** (8.44 g, 43.9 mmol), triethylamine (7.96 mL, 57.1 mmol), and DMAP (0.25 g) in 45 mL of CH_2Cl_2. After 4 h the solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The protected alcohol was purified by MPLC (15% EtOAc/hexanes) to yield 12.6 g (94%) of a clear oil: $R_f = 0.76$ (15% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.67 (s, 1 H), 7.24 (m, 5 H), 3.51 (ddd, J = 1.3, 5.2, 5.2 Hz, 1 H), 3.44 (ddd, J = 1.3, 7.5, 7.5 Hz, 1 H), 2.76 (quint, J = 5.0 Hz, 1 H), 2.30 (q, J = 7.0 Hz, 2 H), 2.08−1.78 (m, 4 H), 0.89 (m, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 203.3, 145.0, 129.7, 128.9, 127.6, 62.1, 43.5, 42.8, 41.0, 30.2, 27.3, 19.6; IR (neat) 3025, 2960, 2925, 2860, 2720, 1728, 1650, 1492, 1470, 1460, 1450, 1388, 1360, 1250, 1100, 1000, 940, 907, 835, 722, 700, 661; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 307 (13), 157 (100), 131 (90), 129 (10), 117 (5), 91 (6), 75 (10); exact mass calcd for $C_{18}O_2H_{30}Si$ 307.208 28, found 307.209 33. To a cold solution of CBr_4 (1.78 g, 5.37 mmol) in CH_2Cl_2 (29 mL) was added triphenylphosphine (2.83 g, 10.8 mmol) portionwise. After 1 h at 0 °C, a solution of the above aldehyde (0.729 g, 2.38 mmol) in CH_2Cl_2 (6 mL) was added dropwise over 30 min. After the addition was complete, the mixture was stirred for 5 min at 0 °C, poured into stirring hexanes (290 mL), and filtered, and the filtrate was concentrated under reduced pressure. The residue was diluted with 55 mL of hexanes, and triphenylphosphine oxide was removed by filtration and washed with hexanes. The filtrate and the washings were combined, concentrated, and purified by MPLC (3% EtOAc/hexanes) to obtain a mixture of dibromide contaminated with a small amount of triphenylphosphine. A small cut of pure dibromide was used for characterization: $R_f = 0.66$ (10% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.24 (m, 5 H), 6.33 (t, J = 7.5 Hz, 1 H), 3.49 (ddd, J = 1.5, 4.3, 6.6 Hz, 1 H), 3.43 (ddd, J = 1.5, 4.0, 7.5, Hz, 1 H), 2.73 (quint, J = 5.0 Hz, 1 H), 1.93 (m, 6 H), 0.89 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 144.2, 138.5, 128.3, 127.7, 126.2, 88.7, 61.0, 41.6, 39.7, 34.7, 31.2, 26.0, 18.4; IR (neat) 3040, 3010, 2940, 2916, 2840, 1595, 1485, 1460, 1455, 1443, 1380, 1350, 1245, 1095, 1019, 995, 928, 825, 795, 765, 690, 655; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 465 (23), 463 (87), 461 (23), 405 (100), 169 (81), 91 (30); exact mass calcd for $C_{15}OH_{21}Br_2Si$ (- 57, t-Bu) 402.970 60, found 402.972 77. To a cold (−78 °C) solution of dibromoolefin obtained from the above reaction, in THF (30 mL), was added 1.48 M *n*-BuLi (3.38 mL, 5.02 mmol) in hexane dropwise. After 20 min at −78 °C, methyl chloroformate (0.92 mL, 11.9 mmol) was added dropwise. The mixture was stirred for 10 min at −78 °C, warmed to room temperature for 45 min, and then poured into ether and brine. The organic layer was washed with $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo. The alkyne was purfied by flash chromatography (3% EtOAc/hexanes) to yield 0.669 g (78% for two steps) of a clear oil: R_f = 0.32 (10% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 5 H), 3.76 (d, J = 2.0 Hz, 3 H), 3.50 (ddd, J = 1.3, 3.5, 5.3 Hz, 1 H), 3.43 (ddd, J = 3.3, 5.0, 6.6 Hz, 1 H), 2.88 (quint, J = 5.0 Hz, 1 H), 2.02 (m, 6 H), 0.89 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 154.0, 143.2, 128.5, 127.7, 126.5, 89.5, 73.1, 61.8, 52.6, 41.2, 39.5, 34.6, 26.0, 18.3, 17.0; IR (neat) 3030, 2955, 2925, 2860, 2240, 1720, 1600, 1490, 1470, 1460, 1451, 1432, 1250, 1100, 1070, 1025, 1000, 940, 832, 762, 750, 700, 660; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 361 (100), 303 (85), 197 (6), 169 (6), 141 (5), 84 (12); exact mass calcd for $C_{21}O_3H_{32}Si$ 361.218 71, found 361.219 90.

(*Z*)-8-[(*tert*-Butyldimethylsilyl)oxy]-6-phenyloct-2-enol (12a). A solution of acetylene **11a** (5.14 g, 14.3 mmol), quinoline (5.23 mL, 44.3 mmol), and Lindlar catalyst (2.61 g) in 400 mL of hexanes was stirred under 1 atm of H_2 (g) for 4.5 h. The solution was filtered through Celite, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The oil was purified by flash chromatography (15% EtOAc/hexanes) to yield 9.10 g (99%) of a clear oil which spotted just below the starting alkyne by TLC: R_f = 0.45 (15% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 5 H), 6.15 (dt, J = 8.0, 11.5 Hz, 1 H), 5.72 (d, J = 11.5 Hz, 1 H), 3.65 (s, 3 H), 3.47 (ddd, J = 2.0, 3.0, 5.0 Hz, 1 H), 3.41 (ddd, J = 1.3, 5.2, 7.5 Hz, 1 H), 2.75 (quint, J = 5.0 Hz, 1 H), 2.60 (dt, J = 7.1, 8.0 Hz, 1 H), 2.44 (q, J = 7.3 Hz, 1 H), 2.00 − 1.60 (m, 4 H), 0.87 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 167.3, 150.9, 145.2, 128.9, 128.4, 126.8, 120.0, 61.7, 51.7, 42.6, 40.3, 36.9, 28.0, 26.8, 19.1; IR (neat) 3025, 2965, 2930, 2860, 1725, 1645, 1495, 1470, 1460, 1452, 1437, 1250, 1200, 1175, 1160, 1100, 833, 772, 700, 662; mass spectrum (CI, isobutane), *m/z* (relative intensity) (M + 1) 363 (70), 305 (100), 131 (4), 91 (9); exact mass calcd for $C_{17}O_3H_{25}Si$ (- 57, *t*-Bu) 305.157 31, found 305.157 30. DIBAL-H in toluene (18.2 mL, 1.0 M, 18.2 mmol) was slowly added to a −35 °C solution of the above ester (3.00 g, 8.28 mmol) in 72 mL of CH_2Cl_2. After 3.5 h the reaction was quenched with MeOH, poured into an Erlenmeyer flask with 200 mL of saturated potassium sodium tartrate, and stirred overnight. The organic phase was washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The alcohol was purified by flash chromatography (20−30% EtOAc/hexanes to yield 2.69 g (97%) of a clear oil: R_f = 0.21 (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 5 H), 5.54 (m, 1 H) 5.50 (m, 1 H), 4.01 (d, J = 6.2 Hz, 2 H), 3.48 (ddd, J = 3.0, 4.8, 5.3 Hz, 1 H), 3.41 (ddd, J = 3.0, 7.0, 7.0 Hz, 1 H), 2.74 (quint, J = 4.8 Hz, 1 H), 1.91 (m, 3 H), 1.71 (m, 4 H), 0.89 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 144.6, 132.3, 128.5, 128.2, 127.6, 126.0, 61.0, 58.4, 41.3, 39.6, 66.4, 26.0, 25.3, 18.3; IR (neat) 3330 (br), 3080, 3060, 3030, 2930, 2860, 1655, 1603, 1493, 1470, 1460, 1450, 1388, 1360, 1255, 1100, 1025, 1002, 935, 900, 835, 810, 730, 700, 660; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 317 (20), 185 (100), 157 (22), 143 (25), 129 (25), 117 (62), 91 (16), 75 (15); exact mass calcd for $C_{20}O_2H_{34}Si$ 335.239 60, found 335.240 63.

(*Z*)-8-Chloro-3-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene. Tributylphosphine (2.89 mL, 11.7 mmol) was slowly added to a solution of CCl_4 (1.14 mL), pyridine (1.80 mL, 11.7 mmol), and alcohol **12a** (3.0 g, 8.97 mmol) in an ice bath. After 10 min the solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated. The chloride was purified by flash chromatography (20% EtOAc/hexanes) to yield 2.25 g (61%) of product and 0.645 g (22%) of recovered starting material: R_f = 0.64 (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 5 H), 5.59 (t, J = 3.3 Hz, 1 H), 5.58 (t, J = 6.5 Hz, 1 H), 3.93 (d, J = 6.8 Hz, 2 H), 3.50 (ddd, J = 1.5, 3.6, 5.3 Hz, 1 H), 3.44 (ddd, J = 1.5, 2.7, 7.0 Hz, 1 H), 2.75 (m, 1 H), 1.80−2.05 (m, 3 H), 1.60−1.80 (m, 3 H), 0.91 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 144.4, 134.7, 128.2, 127.6, 126.1, 125.3, 60.9, 41.5, 39.9, 36.2, 26.0, 25.1, 18.3; IR (neat) 3030, 2960, 2930, 2860, 1600, 1493, 1470, 1460, 1450, 1378, 1250, 1100, 1000, 910, 831, 772, 732, 700, 660; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 353 (95), 317 (30), 185 (100), 157 (55), 143 (45), 128 (28), 117 (53); exact mass calcd for $C_{20}OH_{33}SiCl$ 353.206 74, found 353.206 79.

(*Z*)-8-(Tributylstannyl)-3-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]-oct-6-ene (13a). To a 0 °C solution of DIA (1.41 mL, 10.0 mmol) in 50 mL of THF was slowly added *n*-BuLi (1.4 M, 7.62 mL, 10.7 mmol) and the resultant solution was stirred for 20 min. Tri-*n*-butyltin hydride (2.25 g, 7.70 mmol) was slowly added to the solution of LDA at −78 °C and allowed to stir for 10 min, after which time the above chloride (2.75 g, 7.78 mmol) in 5 mL of THF was added *via* cannula. The reaction was quenched with MeOH 15 min later, diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash chromatography (hexanes) to yield 4.37 g (92%) of a clear oil: R_f = 0.67 (5% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.21 (m, 5 H), 5.51 (dt, J = 9.1, 10.4 Hz, 1 H), 5.03 (dt, J = 7.1, 10.5 Hz, 1 H), 3.44 (m, 2 H), 2.72 (quint, J = 4.7 Hz, 1 H), 2.00−1.60 (m, 6 H), 1.60 (d, J = 9.3 Hz, 2 H), 1.43 (m, 6 H), 1.29 (q, J = 5.0 Hz, 6 H), 0.88 (m, 24 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 145.4, 128.4, 128.0, 126.1, 125.2, 61.5, 42.3, 40.2, 37.4, 29.6, 27.8, 26.3, 25.5, 14.2, 10.8, 9.7; IR (neat) 3050, 3030, 2960, 2930, 2860, 1638, 1600, 1463, 1380, 1365, 1253, 1100, 1000, 940, 830, 770, 700, 662; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 609 (0.1), 317 (66), 291 (25), 289 (16), 185 (100), 157 (25), 117 (25), 91 (13), 75 (14).

(*Z*)-8-(Tributylstannyl)-3-phenyl-1-hydroxyoct-6-ene. A solution of allylstannane **13a** (1.26 g, 2.07 mmol) and TBAF (1.0 M in THF, 2.28 mL) in 60 mL of THF was stirred for 3 h. The solution was

diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The oil was purified by flash chromatography (25% EtOAc/hexanes) to yield 0.99 g (97%) of a clear oil: $R_f = 0.34$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.22 (m, 5 H), 5.50 (dt, $J = 7.9$, 10.6 Hz, 1 H), 5.01 (dt, $J = 6.9$, 10.4 Hz, 1 H), 3.47 (m, 2 H), 2.70 (m, 1 H), 2.00–1.60 (m, 6 H), 1.57 (d, $J = 9.2$ Hz, 2 H), 1.41 (m, 6 H), 1.26 (q, $J = 5.0$ Hz, 6 H), 0.87 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 144.8, 128.6, 128.4, 127.7, 126.2, 123.7, 61.2, 42.3, 39.6, 37.1, 29.1, 27.4, 25.0, 13.7, 10.4, 9.3; IR (neat) 3300 (br), 3000, 2960, 2920, 2890, 2870, 1633, 1600, 1450, 1375, 1045, 1035, 960, 755, 700, 660; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 437 (28), 291 (100), 290 (35), 289 (75), 288 (29), 287 (43), 235 (29), 179 (11), 177 (10); exact mass calcd for $C_{26}OH_{46}Sn$ 494.255 96, found 494.257 05.

(*Z*)-8-(Tributylstannyl)-3-phenyloct-6-enal (1). A THF solution (3 mL) of the above alcohol (300 mg, 0.608 mmol) was slowly added to a THF solution (2 mL) of 3 M MeMgBr (264 μl, 0.790 mmol). After 10 min a THF solution (2 mL) of 1,1-diazodicarbonyldipiperidine (195 mg, 0.773 mmol) was slowly added, and the dark red solution was stirred for 1 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The oil was immediately purified by −78 °C flash column chromatography (alumina 0–5% EtOAc/hexanes) to yield 136 mg (46%) of an unstable oil: $R_f = 0.77$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.65 (s, 1 H), 7.26 (m, 5 H), 5.53 (ddd, $J = 7.7$, 8.7, 10.5 Hz, 1 H), 5.01 (m, 1 H), 2.72 (d, $J = 6.0$ Hz, 2 H), 1.98 (m, 2 H), 1.69 (m, 3 H), 1.57 (d, $J = 9.1$ Hz, 2 H), 1.43 (m, 6 H), 1.26 (q, $J = 7.8$ Hz, 6 H), 0.96 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 201.8, 143.5, 129.0, 128.6, 127.5, 126.6, 123.0, 50.6, 40.0, 36.8, 29.3, 27.5, 24.8, 13.9, 10.7, 9.5; IR (neat) 2960, 2920, 2875, 1728, 1450, 1375, 1015, 700; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 491 (15), 435 (100), 433 (70), 431 (30), 291 (49), 289 (25), 178 (13), 91 (5); exact mass calcd for $C_{22}OH_{35}Sn$ (- 57, *t*-Bu) 435.170 97, found 435.170 35.

Methyl 8-Hydroxy-6-phenyloct-2-enoate (14a). A solution of lactal **10a** (4.70 g, 24.4 mmol) and methyl (triphenylphosphoranylidene)acetate (17.2 g, 51.4 mmol) in 127 mL of chloroform was allowed to stir overnight. The solution was concentrated and filtered to remove triphenylphosphine oxide. The filtrate was concentrated *in vacuo* and purified by MPLC (35% EtOAc/hexanes) to yield 5.69 g (94%) of a 10:1 mixture of *E*:*Z* isomers as a clear oil: $R_f = 0.46$ (50% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5 H), 6.94 (dt, $J =$ 6.9, 15.6 Hz, 1 H), 5.77 (d, $J = 15.6$ Hz, 1 H), 3.73 (s, 3 H), 3.56–3.42 (m, 2 H), 2.75 (m, 1 H), 2.05–1.75 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 166.8, 150.0, 143.7, 128.3, 127.3, 126.2, 120.7, 60.4, 51.3, 41.6, 39.2, 34.9, 30.0; IR (neat) 3400 (br), 2920, 1720, 1650, 1490, 1430, 1255, 1200, 1040, 845, 760, 700. Anal. Calcd for $C_{15}O_3H_{20}$: C, 72.55; H, 8.12. Found: C, 72.31; H, 8.24.

Methyl (*E*)-8-[(*tert*-Butyldimethylsilyl)oxy]-6-phenyloct-2-enoate. A solution of TBDMS chloride (1.82 g, 12.1 mmol) in 25 mL of DMF was slowly added *via* cannula to a stirring solution of ester **14a** (2.50 g, 10.1 mmol) and imidazole (1.02 g, 15.1 mmol) in 15 mL of DMF, and the resulting solution was stirred overnight. The solution was then diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The protected alcohol was purified by MPLC (5–20% EtOAc/hexanes) to yield 3.42 g (94%) of a clear oil: $R_f = 0.84$ (15% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 6.94 (dt, $J = 6.8$, 15.5 Hz, 1 H), 5.77 (d, $J = 15.5$ Hz, 1 H), 3.74 (s, 3 H), 3.49 (ddd, $J = 1.5$, 4.6, 6.6 Hz, 1 H), 3.43 (ddd, $J = 1.5$, 6.4, 7.5 Hz, 1 H), 2.76 (m, 1 H), 2.06 (q, $J = 7.1$ Hz, 2 H), 1.9–1.7 (m, 4 H), 0.90 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 167.0, 149.2, 144.2, 128.3, 127.6, 126.2, 120.9, 60.9, 51.4, 41.5, 39.8, 35.0, 30.3, 26.0, 18.4; IR (neat) 2920, 2858, 1723, 1655, 1490, 1430, 1385, 1359, 1250, 1195, 1150, 1100, 935, 900, 830, 770, 698, 660. Anal. Calcd for $C_{21}O_3H_{34}Si$: C, 69.56; H, 9.45. Found: C, 69.76; H, 9.50.

(*E*)-8-[(*tert*-Butyldimethylsilyl)oxy]-6-phenyloct-2-enol (15a). DIBAL-H in toluene (12.2 mL of a 25% solution, 18.2 mmol) was slowly added to a −25 °C solution of the ester (3.00 g, 8.28 mmol) in 100 mL of THF. After 3.5 h the reaction was quenched with MeOH, poured into 500 mL of CH_2Cl_2 and 200 mL of saturated potassium sodium tartrate, and stirred overnight. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The alcohol was purified by MPLC (20% EtOAc/hexanes) to yield 2.69 g (97%) of a clear oil: $R_f = 0.22$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.19 (m, 5 H), 5.55 (m, 2 H), 4.02 (d, $J = 5.0$ Hz, 2 H), 3.45 (ddd, $J = 3.0$, 5.2, 5.2 Hz, 1 H), 3.39 (ddd, $J = 2.5$, 5.2, 5.9 Hz, 1 H), 2.70 (m, 1 H), 1.95–1.60 (m, 6 H), 1.38 (s, 1 H), 0.86 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 144.9, 133.0, 129.0, 128.3, 127.8, 126.0, 63.8, 61.1, 41.7, 39.9, 36.2, 30.3, 26.1, 18.4; IR (neat) 3300 (br), 3022, 2950, 2925, 2855, 1600, 1490, 1420, 1410, 1400, 1385, 1360, 1250, 1100, 1000, 965, 935, 831, 770, 700, 660. Anal. Calcd for $C_{20}O_2H_{34}Si$: C, 71.80; H, 10.24. Found: C, 71.80; H, 10.19.

(*E*)-8-(Tributylstannyl)-3-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]-oct-6-ene (16a). Tributylphosphine (7.53 mL, 30.2 mmol) was slowly added to a solution of CCl_4 (3.0 mL), pyridine (4.69 mL, 58.1 mmol), and alcohol **15a** (7.5 g, 21.6 mmol) in an ice bath. After 10 min the solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated. The chloride was purified by MPLC (15% EtOAc/hexanes) to yield 5.31 g (67%) of product and 1.40 g (19%) of recovered starting material: $R_f = 0.65$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 5 H), 5.70 (dt, $J = 6.5$, 15.1 Hz, 1 H), 5.53 (dt, 7.0, 15.0 Hz, 1 H), 3.99 (d, $J = 7.0$ Hz, 2 H), 3.52–3.35 (m, 2 H), 2.72 (m, 1 H), 1.94–1.64 (m, 6 H), 0.88 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 144.7, 135.8, 128.3, 127.8, 126.1, 60.9, 45.4, 41.4, 39.7, 35.7, 30.0, 25.9, 18.3; IR (neat) 3030, 2930, 2858, 1665, 1600, 1492, 1430, 1420, 1410, 1385, 1360, 1250, 1100, 1000, 960, 935, 900, 830, 810, 770, 730, 700, 685, 660; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 185 (19), 157 (60), 143 (69), 129 (99), 117 (100) 91 (93); exact mass calcd for $C_{20}OH_{33}SiCl$ 353.206 74, found 353.206 49. *n*-BuLi (2.5 M, 0.640 mL, 1.60 mmol) was slowly added to a 0 °C solution of DIA (206 μL, 1.5 mmol) in 6 mL of THF and allowed to stir for 20 min. Tri-*n*-butyltin hydride (305 μL, 1.13 mmol) was slowly added to the solution of LDA at −78 °C and allowed to stir for 10 min after which time the chloride (400 mg, 1.13 mmol) in 1 mL of THF was added *via* cannula. The reaction was quenched 15 min later, diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by MPLC (hexanes) to yield 0.569 g (89%) of a clear oil: $R_f = 0.75$ (5% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.22 (m, 5 H), 5.48 (dt, $J = 8.4$, 15.0 Hz, 1 H), 5.53 (dt, $J = 7.2$, 15.0 Hz, 1 H), 3.45 (m, 2 H), 2.71 (m, 1 H), 2.00–1.78 (m, 6 H), 1.69 (d, $J = 8.5$ Hz, 2 H), 1.49 (m, 6 H), 1.32 (q, $J = 7.6$ Hz, 6 H), 0.90 (m, 24 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 145.3, 129.2, 128.2, 127.7, 125.9, 125.5, 61.3, 41.7, 39.9, 37.6, 30.8, 29.3, 27.5, 26.1, 18.5, 14.3, 13.9, 9.3; IR (neat) 3020, 2952, 2922, 2850, 1645, 1600, 1455, 1373, 1309, 1250, 1100, 1000, 958, 830, 770, 695, 660. Anal. Calcd for $C_{32}OH_{60}SiSn$: C, 63.26; H, 9.95. Found: C, 63.50; H, 9.95.

(*E*)-8-(Tributylstannyl)-3-phenyl-1-hydroxy-oct-6-ene. A solution of allylstannane **16a** (2.00 g, 3.29 mmol) and TBAF (1.0 M in THF, 3.62 mL) in 100 mL of THF was stirred for 3 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The oil was purified by MPLC (25% EtOAc/hexanes) to yield 1.60 g (99%) of a clear oil: $R_f = 0.17$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.14 (m, 5 H), 5.53 (dt, $J = 8.5$, 14.8 Hz, 1 H), 5.38 (dt, $J = 6.7$, 14.9 Hz, 1 H), 3.39 (m, 1 H), 3.37 (m, 1 H), 2.60 (m, 1 H), 1.90–1.40 (m, 6 H), 1.58 (d, $J =$ 7.9 Hz, 2 H), 1.38 (m, 6 H), 1.21 (q, $J = 7.6$ Hz, 6 H), 0.81 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 144.8, 129.3, 128.3, 127.5, 126.0, 125.1, 61.2, 42.0, 39.7, 37.5, 30.6, 29.2, 27.4, 14.2, 13.8, 9.2; IR (neat) 3300 (br), 3022, 2953, 2922, 2865, 2845, 1645, 1600, 1490, 1450, 1372, 1290, 1040, 958, 870, 860, 753, 700. Anal. Calcd for $C_{26}OH_{46}Sn$: C, 63.40; H, 9.40. Found: C, 63.05; H, 9.37.

(*E*)-8-(Tributylstannyl)-3-phenyloct-6-enal (2). A THF solution (3 mL) of **2** (328 mg, 0.662 mmol) was slowly added to a THF solution (3 mL) of 3 M MeMgBr (285 μL, 0.861 mmol). After 10 min a THF solution (3 mL) of 1,1-diazodicarbonyldipiperidine (213 mg, 0.801 mmol) was slowly added, and the dark red solution was stirred for 1 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The oil was immediately purified by −78 °C flash column chromatography (alumina 0–5% EtOAc/hexanes) to yield 215 mg (66%) of an unstable oil: R_f = 0.75 (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.72 (s, 1 H), 7.31 (m, 5 H), 5.55 (dt, $J = 7.5$, 15.0 Hz, 1 H), 5.22 (dt, $J = 6.3$, 15.0 Hz, 1 H), 3.27 (t, $J = 7.4$ Hz, 2 H), 2.41 (dd, $J = 2.1$, 7.1 Hz, 2 H), 1.91 (m, 1 H), 1.70–1.50 (m, 4 H), 1.74 (d, $J = 8.0$ Hz, 2 H), 1.53

(m, 6 H), 1.36 (q, J = 7.8 Hz, 6 H), 0.96 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 202.0, 143.7, 130.0, 128.6, 127.6, 126.6, 124.6, 50.6, 39.6, 37.1, 30.3, 29.2, 27.4, 14.2, 13.8, 9.2; IR (neat) 2955, 2925, 2870, 1722, 1450, 1375, 1030, 700; mass spectrum (CI, isobutane) m/z (relative intensity) (M + 1) 291 (10), 201 (100), 200 (37), 185 (13), 104 (14); exact mass calcd for $C_{26}OH_{44}Sn$ 493.249 23, found 493.248 75.

5-Phenyl-2-vinylcyclohexanol ((1*R*,2*R*,5*R*)-17), ((1*S*,2*R*,5*R*)-18), ((1*S*,2*S*,5*R*)-19), ((1*R*,2*S*,5*R*)-20). One equiv of Lewis acid or TFA diluted in CH_2Cl_2 was added to a −78 °C solution of 10−35 mg of the aldehyde 1 or 2 in CH_2Cl_2 (2 mL). Thermal reactions were performed in toluene. Reaction times varied with conditions and acid promoters as shown in Tables 1 and 2. All Lewis acid-mediated reactions were performed in CH_2Cl_2 freshly distilled from CaH_2. The reactions were quenched with saturated $NaHCO_3$ and allowed to warm to room temperature. The solution was diluted with ether, washed with $NaHCO_3$, KF (twice), H_2O, and brine, and concentrated in vacuo. Aliquots were analyzed by GC and HPLC to determine isomer ratios. The isomers were separated by HPLC, and the resulting materials were characterized by spectral analysis.

(1*R*,2*R*,5*R*)-5-Phenyl-2-vinylcyclohexanol (17): R_f = 0.36 (20% EtOAc/hexanes); t_R = 8.8 min (GC); t_R = 17.3 min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 5 H), 5.74 (ddd, J = 8.5, 10.1, 17.3 Hz, 1 H), 5.23 (dd, J = 1.9, 17.3 Hz, 1 H), 5.19 (dd, J = 1.9, 10.1 Hz, 1 H), 3.45 (dddd, J = 2.6, 4.2, 9.8, 12.3 Hz, 1 H), 2.65 (dt, J = 1.2, 7.0 Hz, 1 H), 2.24 (dddd, J = 1.0, 1.0, 4.0, 12.5 Hz, 1 H), 2.00 (dddd, J = 2.0, 8.5, 10.0, 10.0 Hz, 1 H), 1.95 (d, J = 1.5 Hz, 1 H) 1.88 (dd, J = 2.5, 10.0 Hz, 2 H), 1.52 (m, 3 H); irradiation at δ 1.9 results in collapse of 3.45 to (ddd, J = 4.0, 10.5, 10.5 Hz); irradiation at δ 2.15 results in collapse of 5.74 to (dd, J = 10.1, 17.3 Hz) and 3.45 to (ddd, J = 2.4, 4.4, 11.2 Hz); irradiation at δ 2.25 results in collapse of 3.45 to (ddd, J = 2.3, 9.2, 9.5 Hz) and 2.65 to (t, J = 11.3 Hz); irradiation at δ 2.65 results in collapse of 2.24 to (ddd, J = 1.7, 4.0, 12.0 Hz); irradiation at δ 3.4 results in collapse of 2.24 to (ddd, J = 1.0, 1.0, 12.3 Hz) and 2.00 (ddd, J = 7.0, 7.0, 0.9 Hz); irradiation at δ 5.5 results in collapse of 2.00 to (ddd, J = 2.0, 9.7, 10.0 Hz); ^{13}C NMR ($CDCl_3$) δ 145.9, 140.5, 128.4, 126.7, 126.2, 117.2, 72.7, 50.8, 42.6, 41.0, 33.3, 30.9; IR (neat) 3300 (br); mass spectrum (CI, isobutane) m/z (relative intensity) (M + 1) 202 (6), 184 (10), 133 (31), 105 (35), 104 (100), 91 (35); exact mass calcd for $C_{14}OH_{18}$ 202.135 76, found 202.1357 65.

(1*S*,2*R*,5*R*)-5-Phenyl-2-vinylcyclohexanol (18): R_f = 0.37 (20% EtOAc/hexanes); t_R = 8.8 min (GC); t_R = 12.5 min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 5.97 (ddd, J = 5.3, 10.7, 17.1 Hz, 1 H), 5.21 (ddd, J = 1.5, 1.5, 10.7 Hz, 1 H), 5.16 (ddd, J = 1.5, 1.5, 17.1 Hz, 1 H), 4.09 (dddd, J = 1.3, 2.1, 2.1, 3.1 Hz, 1 H), 3.00 (tt, J = 3.2, 12.2 Hz, 1 H), 2.29 (m, 1 H), 2.12 (dq, J = 3.8, 13.7 Hz, 1 H), 1.97 (ddd, J = 2.9, 3.2, 12.2 Hz, 1 H) 1.82 (dd, J = 3.5, 12.8 Hz, 1 H), 1.72 (ddd, J = 2.5, 2.5, 13.0 Hz, 1 H), 1.66 (ddd, J = 2.5, 2.5, 13.0 Hz, 1 H), 1.56 (d, J = 4.0 Hz, 1 H), 1.55 (ddd, 3.5, 3.5, 12.5 Hz, 1 H); irradiation at δ 1.9 results in collapse of 2.12 to (ddd, J = 3.2, 3.2, 11.5 Hz), 3.00 to (ddd, J = 3.4, 12.2, 12.2) and 4.09 to (t, J = 2.5 Hz); irradiation at δ 2.12 results in collapse of 1.97 to (dd, J = 3.2, 12.2 Hz), 3.00 to (ddd, J = 3.1, 12.1, 12.1 Hz) and 4.09 to (dd, J = 1.3 Hz); irradiation at δ 2.3 results in collapse of 4.0 to (ddd, J = 2.1, 2.1, 3.1 Hz) and 5.97 to (dd, J = 10.7, 17.1 Hz); irradiation at δ 3.00 results in collapse of 1.97 to (dd, J = 2.9, 12.0 Hz) and 2.12 to (ddd, J = 3.1, 3.1, 12.8 Hz); irradiation at δ 4.0 results in collapse of 1.97 to (ddd, J = 2.3, 3.3, 12.7 Hz), 2.12 to (ddd, J = 2.2, 3.4, 13.7 Hz) and 2.29 to (m, J = 1.5, 1.6, 5.3, 12.3 Hz); irradiation at δ 6.0 results in collapse of 2.29 to (ddd, J = 3.9, 12.5, 12.7 Hz); ^{13}C NMR ($CDCl_3$) δ 146.8, 140.6, 128.4, 127.0, 126.0, 115.7, 68.9, 44.7, 40.1, 36.9, 33.3, 24.2; IR (neat) 3300 (br); mass spectrum (CI, isobutane) m/z (relative intensity) (M + 1) 184 (34), 104 (100), 91 (12); exact mass calcd for $C_{14}OH_{18}$ 202.135 76, found 202.1357 65.

(1*S*,2*S*,5*R*)-5-Phenyl-2-vinylcyclohexanol (19): R_f = 0.31 (20% EtOAc/hexanes); t_R = 9.6 min (GC); t_R = 23.7 min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5 H), 5.82 (ddd, J = 7.5, 10.1, 17.3 Hz, 1 H), 5.16 (ddd, J = 1.7, 1.7, 17.3 Hz, 1 H), 5.13 (ddd, J = 1.7, 1.7, 10.1 Hz, 1 H), 3.84 (dddd, J = 2.7, 2.7, 3.0, 3.6 Hz, 1 H), 3.13 (quint, J = 2.5 Hz, 1 H), 2.31 (dddddd, J = 1.0, 1.0, 3.9, 3.9, 4.9, 7.5 Hz, 1 H), 2.11 (ddd, J = 3.0, 9.1, 13.6 Hz, 1 H), 1.91 (dd, J = 1.6, 7.3 Hz, 2 H) 1.70 (m, 3 H), 1.65 (d, J = 3.2 Hz, 1 H); irradiation at δ 1.8 results in collapse of 3.84 to (ddd, J = 2.7, 2.7, 3.7 Hz); irradiation at δ 2.1 results in collapse of 3.84 to (ddd, J = 2.8, 2.8, 3.0 Hz); irradiation of δ 2.3 results in collapse of 3.84 to (ddd, J = 2.8, 2.8, 3.5 Hz) and 5.82 to (dd, J = 10.1, 17.3 Hz); irradiation at δ 3.1 results in collapse of 2.11 to (dd, J = 2.7, 14.0 Hz); irradiation at δ 3.8 results in collapse of 2.11 to (dd, J = 11.0, 14.8 Hz) and 2.31 to (ddddd, J = 1.0, 1.0, 3.9, 4.9, 7.5 Hz); irradiation at δ 5.8 results in collapse of 2.31 to (ddddd, J = 1.0, 1.0, 3.9, 3.9, 4.9 Hz); ^{13}C NMR ($CDCl_3$) δ 145.7, 139.5, 128.4, 127.0, 125.9, 116.2, 70.1, 46.4, 37.2, 36.5, 28.7, 25.5; IR (neat) 3300 (br); mass spectrum (CI, isobutane) m/z (relative intensity) (M + 1) 184 (37), 133 (15), 105 (31), 104 (100), 91 (30); exact mass calcd for $C_{14}OH_{18}$ 202.135 76, found 202.135 764 6.

(1*R*,2*S*,5*R*)-5-Phenyl-2-vinylcyclohexanol (20): R_f = 0.30 (20% EtOAc/hexanes); t_R = 9.3 min (GC); t_R = 26.2 min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 6.12 (ddd, J = 9.0, 10.5, 16.9 Hz, 1 H), 5.28 (dd, J = 1.7, 10.5 Hz, 1 H), 5.13 (dd, J = 1.0, 16.9 Hz, 1 H), 3.82 (dddd, J = 2.6, 4.2, 4.2, 12.3 Hz, 1 H), 2.66 (m, 2 H), 1.97 (dt, J = 3.5, 3.5, 12.3 Hz, 1 H), 1.93 (dq, J = 3.0, 13.5 Hz, 2 H) 1.75 (dt, J = 4.1, 13.0 Hz, 1 H), 1.71−1.50 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 146.0, 135.5, 128.5, 126.7, 126.2, 119.0, 71.6, 44.6, 43.0, 38.3, 29.8, 28.2; IR (neat) 3300 (br); mass spectrum (CI, isobutane) m/z (relative intensity) (M + 1) 202 (14), 184 (7), 133 (15), 104 (100), 91 (11); exact mass calcd for $C_{14}OH_{18}$ 202.135 76, found 202.135 75.

4-(Benzyloxy)cyclohexanone (8b). Sodium (6.5 g, 0.283 mol) was added to a solution of 1,4-cyclohexanediol (30.0 g, 0.258 mol) in 210 mL of dioxane, and the solution was heated at reflux for 4 h . The mixture was then cooled, benzyl bromide was added (30.5 mL, 0.256 mol), and the blue mixture was refluxed for an additional 20 h. The mixture was quenched (MeOH) and poured into 300 mL of acetone. The solid was filtered, and the filtrate was concentrated, dissolved in ether, washed with water (5×), saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The monoprotected alcohol was isolated by MPLC (20% EtOAc/hexanes) to yield 22.4 g (42%) of a clear liquid: R_f = 0.20 (35% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 5 H), 4.50 (s, 2 H), 3.69−3.30 (m, 2 H), 2.90 (sb, 1 H), 2.00 (m, 1 H), 1.88 (m, 2 H), 1.70−1.41 (m, 2 H), 1.29 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.7, 138.5, 128.1, 128.0, 127.2, 127.1, 127.0, 76.1, 73.4, 69.9, 69.3, 69.1, 32.3, 30.2, 29.3, 27.3; IR (neat) 3500−3000, 2805, 2750, 1390, 1255, 1000, 675, 640. PCC (27.0 g, 0.125 mol) was added to a CH_2Cl_2 (580 mL) solution of the above alcohol (23.0 g, 0.111 mol). After 3 h the solution was diluted with Et_2O (600 mL) and filtered through silica and concentrated in vacuo. The ketone was isolated by flash chromatography (15% EtOAc/hexanes) to yield 20.6 g (91%) of **8b**: R_f = 0.63 (35% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 4.55 (s, 2 H), 3.77 (m, 1 H), 2.60 (dd, J = 5.8, 9.6 Hz, 1 H), 2.55 (dd, J = 5.7, 10.3 Hz, 1 H), 2.22 (m, 2 H), 2.11 (q, J = 5.8, 1 H), 2.07 (q, J = 5.7 Hz, 1 H), 1.96−1.89 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 210.5, 138.2, 128.0, 127.2, 127.0, 71.9, 69.9, 37.0, 30.3; IR (neat) 2995, 2970, 2940, 2850, 2775, 2150, 1710, 1450, 1405, 1300, 1050, 1015, 860, 675, 650, 595. Anal. Calcd for $C_{12}O_2H_{14}$: C, 75.76; H, 7.42; mass spectrum (CI, isobutane) m/z (relative intensity) (M + 1) 205 (100), 91 (88); exact mass calcd for $C_{13}O_2H_{16}$ 205.122 22, found 205.122 85.

4-Benzyl-ϵ-Caprolactone (9b). A solution of 4-(benzyloxy)-cyclohexanone (**8b**) (20.6 g, 0.100 mmol) in 210 mL of chloroform was added to a stirring solution of 80% m-chloroperbenzoic acid (26.3 g, 0.121 mmol) in 100 mL of chloroform. After 4 h, the mixture was filtered through Celite, washed twice with saturated $NaHCO_3$ and once with brine, dried ($MgSO_4$), and concentrated in vacuo. The lactone was isolated by flash chromatography (18−36% EtOAc/hexanes) to yield 21.2 g (95%) of a clear liquid: R_f = 0.29 (50% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.34 (m, 5 H), 4.58−4.49 (m, 1 H), 4.54 (s, 2 H), 4.06 (ddd, J = 1.9, 6.2, 13.1 Hz, 1 H), 3.78 (quint, J = 2.7 Hz, 1 H), 3.03 (ddd, J = 1.7, 12.0, 13.9, 1 H), 2.43 (ddd, J = 1.5, 8.2, 14.1, 1 H), 2.09−1.86 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 175.7, 137.8, 133.0, 129.2, 128.1, 124.4, 127.0, 73.0, 69.9, 63.1, 33.9, 27.7, 27.1; IR (neat) 2920, 1725, 1440, 1290, 1150, 1065, 1020, 735, 695; mass spectrum (CI, isobutane) m/z (relative intensity) (M + 1) 221 (20), 91 (100), 57 (112), 43 (126), 42 (82), 41 (118), 39 (41); exact mass calcd for $C_{13}O_3H_{16}$ 221.117 77, found 221.118 33.

6-Hydroxy-4-(benzyloxy)hexanal (10b). DIBAL-H (1.5 M in toluene, 53.1 mL, 79.7 mmol) was slowly (0.25 mL / min) added to a −78 °C solution of 4-(benzyloxy)-ϵ-caprolactone (16.0 g, 72.5 mmol) in 760 mL of CH_2Cl_2. After 1 h the reaction was quenched with MeOH,

poured into 600 mL of saturated potassium sodium tartrate, and stirred (4 h). The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The alcohol was purified by flash chromatagraphy (38% EtOAc/hexanes) to yield 13.2 g (82%) of a clear oil: $R_f = 0.17$ (50% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.74 (s, 0.5 H), 7.32 (m, 5 H), 5.14 (m, 0.4 H), 4.58–4.42 (m, 0.5 H), 4.50 (s, 2 H), 3.80–3.41 (m, 3 H), 2.51 (dt, J = 1.4, 7.1 Hz, 2 H), 2.07–1.55 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 202.1, 138.1, 128.5, 128.0, 127.8, 96.0, 76.4, 71.1, 59.9, 39.6, 36.0, 25.9; IR (neat) 3650–3100, 3015, 2940, 2870, 1720, 1060, 635, 595.

6-[(*tert*-Butyldimethylsilyl)oxy]-4-(benzyloxy)hexanal. A solution of TBDMS chloride (14.2 g, 94.5 mmol) in 200 mL of CH_2Cl_2 was slowly added *via* cannula to a stirring solution of **10b** (17.6 g, 78.7 mmol) and triethylamine (14.9 mL, 106 mmol) in 200 mL of CH_2Cl_2, and the resulting solution was stirred for 6 h. The solution was then diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The protected alcohol was purified by flash chromatagraphy (18% EtOAc/hexanes) to yield 24.9 g (94%) of a clear oil: $R_f = 0.51$ (25% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.68 (t, J =1.6 Hz, 1 H), 7.26 (m, 5 H), 4.45 (d, J = 18.2 Hz, 1 H) 4.41 (d, J = 18.2 Hz, 1 H), 3.66 (m, 2 H), 3.57 (quint, J = 4.8 Hz, 1 H), 2.44 (dt, J = 1.6, 7.3 Hz, 2 H), 2.0–1.50 (m, 4 H), 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 202.1, 138.4, 128.3, 127.8, 127.5, 75.0, 71.1, 59.4, 39.8, 37.1, 26.5, 25.9, 18.2; IR (neat) 3030, 2955, 2925, 2860, 2710, 1725, 1470, 1460, 1450, 1390, 1360, 1250, 1090, 830, 770, 730, 695, 660; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 337 (9), 230 (13), 229 (67), 187 (8), 171 (28), 91 (100), 71 (42), 58 (40), 57 (123), 56 (41), 55 (9); exact mass calcd for $C_{19}O_3H_{32}Si$ 337.219 90, found 337.217 83.

Methyl 1-[(*tert*-Butyldimethylsilyl)oxy]-3-(benzyloxy)oct-6-ynoate (11b). To a cold solution of CBr_4 (28.6 g, 86.2 mmol) in CH_2Cl_2 (375 mL) was added triphenylphosphine (45.3 g, 173 mmol) portionwise. After 1 h at 0 °C, a solution of the above aldehyde (12.9 g, 38.2 mmol) in CH_2Cl_2 (50 mL) was added dropwise over 1 h. After addition was complete, the mixture was stirred for 5 min at 0 °C, poured into stirring hexane (3790 mL), and filtered, and the filtrate was concentrated under reduced pressure. The residue was diluted with 600 mL of hexane, triphenylphosphine oxide was removed by filtration, and the residue was washed with hexane. The filtrate and the washings were combined, concentrated, and purified by flash chromatography (4% EtOAc/hexanes) to obtain a mixture of dibromide contaminated with triphenylphosphine. A small cut of pure dibromide was used for characterization: $R_f = 0.60$ (10% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5 H), 6.31 (t, J = 7.3 Hz, 1 H), 4.45 (s, 2 H), 3.67 (t, J = 7.3 Hz, 1 H), 3.65 (t, J = 6.2 Hz, 1 H), 3.53 (quint, J = 5.4 Hz, 1 H), 2.13 (q, J = 7.3 Hz, 2 H), 1.85–1.50 (m, 4 H), 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 138.5, 133.9, 133.6, 128.5, 128.4, 127.9, 127.6, 88.9, 75.2, 71.3, 59.6, 37.2, 32.3, 29.1, 26.0, 18.3; IR (neat) 2960, 2930, 2860, 2240, 1470, 1460, 1450, 1430, 1250, 1100, 905, 835, 770, 730, 695, 645; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 495 (16), 493 (40), 491 (19), 181 (14), 91 (100), 57 (77); exact mass calcd for $C_{20}O_2H_{32}Br_2Si$ 491.061 65. Found: 491.060 88. To a cold (−78 °C) solution of dibromoolefin obtained from the above reaction, in THF (500 mL), was added *n*-BuLi (2.4 M, 32.9 mL, 79.0 mmol) in hexane dropwise. After 20 min at −78 °C, methyl chloroformate (17.7 mL, 188 mmol) was added dropwise. The mixture was stirred for 10 min at −78 °C, warmed to room temperature for 45 min, and then poured into Et_2O and brine. The organic layer was washed with $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo. The alkyne was purfied by flash chromatography (3% EtOAc/hexanes) to yield 6.0 g (41% for the two steps) of a clear oil: $R_f = 0.54$ (18% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 5 H), 4.48 (dt, J = 2.4, 11.5, 1 H), 4.45 (dt, J = 2.4, 11.4, 1 H), 3.68 (m, 6 H), 2.37 (dt, J = 2.4, 7.3 Hz, 2 H), 1.85–1.50 (m, 4 H), 0.84 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 154.1, 138.5, 128.4, 127.8, 127.6, 89.5, 74.6, 73.0, 71.5, 59.4, 52.5, 37.0, 32.2, 25.9, 18.2, 14.8; IR (neat) 2955, 2930, 2860, 2240, 1720, 1475, 1465, 1455, 1435, 1250, 1090, 835, 775, 750, 730, 695, 660. Anal. Calcd for $C_{22}O_4H_{34}Si$: C, 67.65; H, 8.77. Found: C, 67.79; H, 8.76.

(*E*)-8-[(*tert*-Butyldimethylsilyl)oxy]-6-(benzyloxy)oct-2-ynol. DIBAL-H (1.0 M, 31.8 mL, 31.8 mmol) was slowly added to a −25 °C solution of **11b** (5.65 g, 14.4 mmol) in 150 mL of CH_2Cl_2. After 1 h the reaction was quenched with MeOH and then poured into 500 mL of saturated potassium sodium tartrate and stirred for 2 h. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The alcohol was purified by flash chromatagraphy (18% EtOAc/hexanes) to yield 5.11 g (98%) of a clear oil: $R_f = 0.25$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 4.53 (s, 2 H), 4.19 (dt, J = 2.0, 6.0 Hz, 2 H), 3.72 (dt, J = 1.1, 6.0 Hz, 1 H), 3.70 (dt, J = 1.1, 6.0 Hz, 1 H), 3.71 (m, 1 H), 2.32 (tt, J = 2.0, 7.3 Hz, 2 H), 1.80–1.55 (m, 5 H), 0.90 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 138.7, 128.3, 127.8, 127.5, 86.1, 78.6, 74.8, 71.3, 59.6, 51.3, 37.1, 33.2, 25.9, 18.3, 14.9; IR (neat) 3600–3150, 2960, 2925, 2860, 2210, 1470, 1460, 1450, 1360, 1250, 1090, 1020, 835, 770, 730, 695, 660. Anal. Calcd for $C_{21}O_3H_{34}Si$: C, 69.56; H, 9.45. Found: C, 69.41; H, 9.30.

Methyl (*Z*)-8-[(*tert*-Butyldimethylsilyl)oxy]-6-(benzyloxy)oct-2-enoate (12b). A solution of the above alkyne (4.91 g, 13.5 mmol), quinoline (3.88 mL, 32.9 mmol), and Lindlar catalyst (2.55 g) in 200 mL of hexanes was stirred under 1 atm of H_2 (g) for 1 h. The solution was filtered through Celite, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The oil was purified by flash chromatography (10% EtOAc/hexanes) to yield 4.84 g (93%) of a clear oil which spotted just below the starting alkyne by TLC: R_f = 0.21 (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 5 H), 5.59–5.45 (m, 2 H), 4.45 (s, 2 H), 4.11 (t, J = 5.7 Hz, 2 H), 3.68 (t, J = 7.5 Hz, 1 H), 3.66 (t, J = 6.0 Hz, 1 H), 3.56 (quint, J = 6.5 Hz, 1 H), 2.12 (q, J = 7.1 Hz, 2 H), 1.87–1.50 (m, 5 H) 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 150.3, 136.1, 128.9, 128.3, 127.8, 127.5, 75.4, 70.9, 59.7, 58.4, 37.1, 33.8, 26.0, 23.3, 18.3; IR (neat) 3550–3150, 2955, 2930, 2860, 1470, 1460, 14750, 1360, 1250, 1090, 1020, 830, 800, 770, 730, 695, 615. Anal. Calcd for $C_{21}O_3H_{36}Si$: C, 69.18; H, 9.95. Found: C, 69.04; H, 9.73.

(*Z*)-8-Chloro-3-(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene. Tributylphosphine (4.16 mL, 16.7 mmol) was slowly added to a solution of CCl_4 (1.63 mL, 16.7 mmol), pyridine (2.60 mL, 32.2 mmol), and **12b** (4.70 g, 12.9 mmol) in an ice bath. After 10 min the solution was diluted with ether and washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated. The chloride was purified by flash chromotography (5% EtOAc/hexanes) to yield 2.80 g (57%) of product and 0.89 g (19%) recovered starting material: $R_f = 0.67$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.29 (m, 5 H), 5.56 (m, 2 H), 4.48 (d, J = 13.8 Hz, 1 H), 4.44 (d, J = 13.8 Hz, 1 H), 4.00 (d, J = 6.8 Hz, 2 H), 3.68 (t, J = 6.3 Hz, 1 H), 3.65 (t, J = 5.8 Hz, 1 H), 3.55 (quint, J = 5.7 Hz, 1 H), 2.15 (m, 2 H), 1.85–1.55 (m, 4 H), 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 138.9, 135.0, 128.4, 127.8, 127.5, 125.5, 75.5, 71.2, 59.7, 39.4, 37.3, 33.8, 26.0, 23.0, 18.3; IR (neat) 2960, 2930, 2860, 1470, 1460, 1450, 1360, 1250, 1100, 835, 770, 730, 695. Anal. Calcd for $C_{21}O_2H_{35}SiCl$: C, 65.84; H, 9.21. Found: C, 65.82; H, 9.28.

(*Z*)-8-(Tributylstannyl)-3-(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene. *n*-BuLi (2.5 M, 3.80 mL, 9.50 mmol) was slowly added to a 0 °C solution of DIA (1.28 mL, 9.13 mmol) in 50 mL of THF and allowed to stir for 20 min. Tri-*n*-butyltin hydride (1.90 mL, 7.05 mmol) was slowly added to the solution of LDA at −78 °C and allowed to stir for 20 min after which time (*Z*)-8-chloro-3-(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene (2.69 g, 7.02 mmol) in 5 mL of THF was added *via* cannula. The reaction was quenched 15 min later, diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash chromatography (hexanes) to yield 4.09 g (91%) of a clear oil: $R_f = 0.66$ (5% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 5 H), 5.49 (dq, J = 0.5, 10.6 Hz, 1 H), 5.00 (dt, J = 7.0, 10.6 Hz, 1 H), 4.48 (d, J = 15.2 Hz, 1 H), 4.43 (d, J = 15.2 Hz, 1 H), 3.67 (t, J = 7.1 Hz, 1 H), 3.66 (t, J = 5.8 Hz, H), 3.54 (quint, J = 6.3 Hz, 1 H), 2.03 (q J = 7.3 Hz, 2 H), 1.80–1.40 (m, 12 H), 1.23 (q, J = 7.1 Hz, 6 H), 0.84 (m, 24 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 139.1, 128.6, 128.3, 127.7, 127.4, 123.8, 75.9, 71.1, 59.8, 37.5, 34.3, 29.2, 27.4, 26.0, 22.8, 13.7, 10.5, 9.4; IR (neat) 2955, 2920, 2855, 1460, 1250, 1090, 830, 770, 730, 695, 660. Anal. Calcd for $C_{33}O_2H_{62}SiSn$: C, 62.16; H, 9.80. Found: C, 62.12; H, 9.76.

(*Z*)-8-(Tributylstannyl)-3-(benzyloxy)-1-hydroxyoct-6-ene (13b). A solution of (*Z*)-8-(tributylstannyl)-3-(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene (2.00 g, 3.14 mmol) and TBAF (1.0 M in THF, 3.14 mL) in 100 mL of THF was stirred for 1 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The oil was purified by flash

chromatography (15% EtOAc/hexanes) to yield 1.64 g (100%) of a clear oil: $R_f = 0.21$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 5.57 (q, $J = 9.8$ Hz, 1 H), 5.05 (dt, $J = 7.0$, 10.5 Hz, 1 H), 4.57 (d, $J = 33.4$ Hz, 1 H), 4.53 (d, $J = 33.4$ Hz, 1 H), 3.82–3.65 (m, 3 H), 2.54 (t, $J = 5.1$ Hz, 1 H), 2.07 (q, $J = 7.8$ Hz, 2 H), 1.90–1.43 (m, 12 H), 1.29 (q, $J = 7.6$ Hz, 6 H), 0.89 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 138.4, 128.9, 128.4, 127.8, 127.7, 123.4, 78.2, 71.0, 60.7, 36.0, 33.6, 29.2, 27.4, 22.6, 13.7, 10.6, 9.4; IR (neat) 3600–3150, 2955, 2920, 2870, 2850, 1450, 1375, 1070, 730, 695. Anal. Calcd for $C_{27}O_2H_{48}Sn$: C, 61.96; H, 9.24. Found: C, 61.76; H, 9.24.

(*Z*)-8-(Tributylstannyl)-3-(benzyloxy)oct-6-enal (3). MeMgBr (2.9 M, 214 μL, 0.622 mmol) was slowly added to a THF solution (5 mL, 0 °C) of the above alcohol (350 mg, 0.669 mmol). After 20 min a THF solution (5 mL) of 1,1-diazodicarbonyldipiperidine (169 mg, 0.669 mmol) was slowly added, and the dark red solution was stirred for 1 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The oil was immediately purified by −78 °C flash column chromatography (MeOH quenched silica 3% EtOAc/hexanes) to yield 201 mg (58%) of an oil: $R_f = 0.62$ (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.79 (t, $J = 2.2$ Hz, 1 H), 7.32 (m, 5 H), 5.58 (q, $J = 9.0$ Hz, 1 H), 5.03 (dt, $J = 7.0$, 10.5 Hz, 1 H), 4.56 (d, $J = 17.4$ Hz, 1 H), 4.53 (d, $J = 17.4$ Hz, 1 H), 3.98 (quint, $J = 4.8$ Hz, 1 H), 2.68 (ddd, $J = 2.6$, 7.2, 16.2 Hz, 1 H), 2.57 (ddd, $J = 1.9$, 4.8, 16.3 Hz, 1 H), 2.09 (q, $J = 7.2$ Hz, 2 H), 1.83–1.40 (m, 10 H), 1.29 (q, $J = 7.0$ Hz, 6 H), 0.89 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 201.5, 138.2, 129.3, 128.4, 127.8, 122.8, 74.1, 71.3, 48.3, 34.3, 29.2, 27.4, 22.6, 13.7, 10.6, 9.4; IR (neat) 2960, 2930, 2875, 2855, 1730, 1450, 1070, 730, 690; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 465 (70), 463 (49), 464 (34), 289 (30), 235 (30), 233 (29), 179 (32), 177 (42), 175 (27), 92 (28), 91 (100), 39 (139), 37 (88); exact mass calcd for $C_{23}O_2H_{37}Sn$ (- 57, *t*-Bu) 465.181 54, found 465.181 99.

1-(Benzyloxy)-4-vinyl-3-cyclohexanol ((1*R*,3*R*,4*R*)-21), ((1*S*,3*R*,4*R*)-22), ((1*S*,3*S*,4*R*)-23), and ((1*R*,3*S*,4*R*)-24). One equiv of Lewis acid or TFA diluted in CH_2Cl_2 was added to a −78 °C solution of 10–30 mg of the aldehyde **3** or **4** in CH_2Cl_2 (3 mL). Reaction times varied with conditions and acid promoters as shown in Tables 3 and 4. All reactions were performed in CH_2Cl_2 freshly distilled from CaH_2. The reactions were quenched with saturated $NaHCO_3$ and allowed to warm to room temperature. The solution was diluted with ether, washed with $NaHCO_3$, KF (twice), H_2O, and brine, and concentrated in vacuo. Aliquots were characterized by GC and HPLC to determine isomer ratios. The isomers were separated by HPLC and were fully characterized.

(1*R*,3*R*,4*R*)-1-(Benzyloxy)-4-vinyl-3-cyclohexanol (21): $R_f = 0.11$ (20% EtOAc/hexanes); $t_R = 9.2$ min (GC); $t_R = 10.0$ min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 5.65 (ddd, $J = 8.3$, 10.0, 17.3 Hz, 1 H), 5.18 (d, $J = 17.3$ Hz, 1 H), 5.15 (dd, $J = 1.8$, 10.2 Hz, 1 H), 4.57 (s, 2 H), 3.42 (dddd, $J = 3.6$, 3.6, 9.5, 9.5 Hz, 1 H), 3.29 (dddd, $J = 2.8$, 4.0, 9.2, 10.0 Hz, 1 H), 2.44 (dq, $J = 3.0$, 12.1 Hz, 1 H), 2.1–2.0 (m, 2 H), 1.94 (dddd, $J = 3.7$, 8.3, 10.1, 10.1 Hz, 1 H), 1.9–0.85 (m, 4 H); irradiation at δ 3.4 results in collapse of 2.44 to (dt, $J = 1.5$, 12.1 Hz); irradiation at δ 3.29 results in collapse of 2.44 to (dt, $J = 3.0$, 12.1 Hz) and 1.94 to (dt, $J = 3.7$, 9.7, Hz); irradiation of δ 5.65 results in collapse of 1.94 to (dt, $J = 3.9$, 10.1, Hz); ^{13}C NMR ($CDCl_3$) δ 139.9, 138.8, 128.4, 127.5, 117.3, 75.4, 71.0, 70.1, 50.0, 39.3, 30.8, 26.8; IR (neat) 3600–3200, 3060, 3020, 2930, 2860, 1638, 1490, 1450, 1350, 1200, 1190, 1160, 1025, 985, 910, 730, 695. Anal. Calcd for $C_{15}O_2H_{20}$: C, 77.55; H, 8.68. Found: C, 77.64; H, 8.40.

(1*S*,3*R*,4*R*)-1-(Benzyloxy)-4-vinyl-3-cyclohexanol (22): $R_f = 0.19$ (20% EtOAc/hexanes); $t_R = 8.2$ min (GC); $t_R = 7.7$ min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 5.73 (ddd, $J = 8.5$, 10.2, 17.3 Hz, 1 H), 5.18 (dd, $J = 1.1$, 17.4 Hz, 1 H), 5.13 (dd, $J = 1.9$, 10.2 Hz, 1 H), 4.51 (s, 2 H), 3.85 (quint, $J = 3.0$ Hz, 1 H), 3.70 (dddd, $J = 2.6$, 4.1, 9.5, 10.8 Hz, 1 H), 2.33 (dq, $J = 3.4$, 13.6 Hz, 1 H), 2.00–1.89 (m, 2 H), 1.82 (d, $J = 2.6$ Hz, 1 H), 1.65–1.30 (m, 4 H); irradiation at δ 1.82 results in collapse of 3.70 to (ddd, $J = 4.2$, 9.4, 10.1 Hz); irradiation at δ 2.00–1.89 results in collapse of 3.70 to (bd, $J = 10.8$ Hz), 3.85 to (q, $J = 3.1$ Hz) and 5.73 to (dd, $J = 10.2$, 17.2 Hz); irradiation of δ 2.33 results in collapse of 3.70 to (ddd, $J = 2.2$, 9.4, 10.1 Hz) and 3.85 to (bs); irradiation at δ 3.70 results in collapse of 2.00–1.89 to (m) and 2.33 to (dt, $J = 2.5$, 12.7 Hz); irradiation at δ 3.85 results in collapse of 2.00–1.89 to (m) and 2.33 to (ddd, $J = 2.1$, 3.8, 13.4Hz); irradiation at δ 5.70 results in collapse of 2.00–1.89 to (m); ^{13}C NMR ($CDCl_3$) δ 140.5, 128.3, 127.4, 116.9, 74.0, 69.9, 68.6, 50.9, 37.2, 28.7, 25.3.

(1*S*,3*S*,4*R*)-1-(Benzyloxy)-4-vinyl-3-cyclohexanol (23): $R_f = 0.19$ (20% EtOAc/hexanes); $t_R = 9.1$ min (GC); $t_R = 6.9$ min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 5.91 (ddd, $J = 6.0$, 10.7, 17.4 Hz, 1 H), 5.19 (dd, $J = 1.5$, 17.4 Hz, 1 H), 5.13 (dd, $J = 1.6$, 10.7 Hz, 1 H), 4.55 (s, 2 H), 4.08 (quint, $J = 3.1$ Hz, 1 H), 3.76 (dddd, $J = 3.4$, 3.4, 9.7, 9.7 Hz, 1 H), 2.23–2.30 (m, 2 H), 2.12 (ddd, $J = 12.0$, 3.9, 13.5 Hz, 1 H), 1.73–1.30 (m, 4 H); irradiation at δ 2.23–2.30 results in collapse of 3.76 to (dt, $J = 3.4$, 9.7, 9.7 Hz), 4.08 to (bs) and 5.91 to (dd, $J = 10.7$, 17.4 Hz); irradiation at δ 3.76 results in collapse of 2.12 to (bd, $J = 13.9$ Hz) and 2.23–2.30 to (m); irradiation of δ 4.08 results in collapse of 2.23–2.30 to (m); irradiation at δ 5.91 results in collapse of 2.23–2.30 to (m); ^{13}C NMR ($CDCl_3$) δ 139.4, 128.3, 127.5, 116.3, 73.2, 70.3, 69.4, 44.7, 38.1, 30.9, 22.7.

(1*R*,3*S*,4*R*)-1-(Benzyloxy)-4-vinyl-3-cyclohexanol (24): $R_f = 0.23$ (20% EtOAc/hexanes); $t_R = 7.7$ min (GC); $t_R = 4.8$ min (HPLC); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 6.00 (ddd, $J = 7.1$, 9.8, 17.5 Hz, 1 H), 5.08 (dd, $J = 0.9$, 15.9 Hz, 1 H), 5.07 (dd, $J = 0.9$, 11.8 Hz, 1 H), 4.55 (d, J =27.1 Hz, 1 H), 4.52 (d, $J = 27.1$ Hz, 1 H), 3.86 (dddd, $J = 1.8$, 3.6, 4.1, 10.0 Hz, 1 H), 3.80 (quint, $J = 3.1$ Hz, 1 H), 3.45 (d, $J = 9.4$ Hz, 1 H), 2.20–2.10 (m, 2 H), 2.06 (m, 1 H), 1.85 (dq, $J = 3.0$, 13.5 Hz, 1 H), 1.95–1.20 (m, 3 H); irradiation at δ 1.85 results in collapse of 3.80 to (bs) and 3.86 to (ddd, $J = 1.8$, 4.1, 9.6 Hz); irradiation at δ 2.15 results in collapse of 3.80 to (t, $J = 2.4$ Hz) and 3.86 to (ddd, $J = 1.8$, 3.5, 9.8 Hz); irradiation of δ 3.45 results in collapse of 3.86 to (bs); irradiation at δ 3.83 results in collapse of 2.06 to (m), 2.20–2.10 to (m) and 3.45 to (s); irradiation at δ 6.0 results in collapse of 2.20–2.10 to (bs); ^{13}C NMR ($CDCl_3$) δ 140.8, 128.4, 127.7, 114.5, 74.4, 70.6, 70.2, 46.0, 35.7, 28.3, 20.7.

(1*S*,3*R*,4*S*)-3-(Acetyloxy)-1-(benzyloxy)-4-vinylcyclohexane (25): $R_f = 0.65$ (35% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 5 H), 5.92 (ddd, $J = 6.8$, 10.4, 17.5 Hz, 1 H), 5.12 (d, $J = 10.5$ Hz, 1 H), 5.09 (d, $J = 17.5$ Hz, 1 H), 4.75 (ddd, $J = 4.2$, 4.5, 10.4 Hz, 1 H), 4.47 (s, 2 H), 3.43 (dddd, $J = 5.0$, 5.6, 10.0, 10.5 Hz, 1 H), 2.55 (dddd, $J = 3.4$, 4.0, 4.5, 6.8 Hz, 1 H), 1.93 (s, 3 H), 1.95 (m, 1 H), 1.64 (m, 2 H), 1.46 (m, 2 H), 1.20 (m, 1 H); irradiation at δ 2.55 results in collapse of 5.92 to (ddd, $J = 10.4$, 17.5 Hz) and 4.75 to (dd, $J = 4.2$, 10.4 Hz, 1 H); irradiation at δ 4.75 results in collapse of 2.55 to (ddd, $J = 3.4$, 4.0, 6.8 Hz).

Preparation of Methyl 8-[(*tert*-Butyldimethylsilyl)oxy]-6-(benzyloxy)oct-2-enoate (14). A solution of TBDMS-protected **10b** (10.0 g, 29.7 mmol) and methyl (triphenylphosphoranylidene)acetate (20.0 g, 59.8 mmol) in 300 mL of chloroform was allowed to stir overnight. The solution was concentrated, and excess triphenylphosphine oxide was crystallized and filtered away. The filtrate was concentrated in vacuo and purified by flash chromotography (7% EtOAc/hexanes) to yield 10.7 g (92%) of a 7:1 mixture of *E*:*Z* isomers as a clear oil: R_f-(*E*) = 0.55, R_f(*Z*) = 0.62 (25% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 5 H), 6.91 (dt, $J = 1.5$, 15.7 Hz, 1 H), 5.75 (dt, $J = 7.0$, 15.6 Hz, 1 H), 4.47 (d, $J = 17.1$ Hz, 1 H), 4.43 (d, $J = 17.1$ Hz, 1 H), 3.66 (m, 5 H), 3.56 (quint, $J = 5.0$ Hz, 1 H), 2.24 (dt, $J = 7.0$, 15.3 Hz, 2 H), 1.7–1.5 (m, 4 H), 0.84 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 167.0, 149.2, 138.6, 128.3, 127.7, 127.5, 121.0, 75.2, 71.2, 59.5, 51.3, 37.1, 32.5, 28.0, 25.9, 18.2; IR (neat) 3030, 2950, 2930, 2860, 1728, 1660, 1495, 1470, 1460, 1450, 1435, 1315, 1255, 1200, 1165, 1100, 832, 770, 730, 695, 660. Anal. Calcd for $C_{22}O_4H_{36}$-Si: C, 67.30; H, 9.24. Found: C, 67.57; H, 9.48.

(*E*)-8-[(*tert*-Butyldimethylsilyl)oxy]-6-(benzyloxy)oct-2-enol (15b). DIBAL-H (1.0 M, 62.0 mL, 62.0 mmol) was slowly added to a −25 °C solution of **14b** (11.1 g, 28.0 mmol) in 250 mL of CH_2Cl_2. After 1 h the reaction was quenched with MeOH, poured into 500 mL of saturated potassium sodium tartrate, and stirred for 1.5 h. The organic phase was dried (Na_2SO_4) and concentrated in vacuo. The alcohol was purified by flash chromatagraphy (20% EtOAc/hexanes) to yield 9.73 g (95%) of a clear oil: $R_f = 0.64$ (50% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 5 H), 5.58 (m, 2 H), 4.46 (s, 2 H), 3.98 (d, $J = 4.2$ Hz, 2 H), 3.66 (q, $J = 6$ Hz, 1 H), 3.54 (quint, $J = 5.8$ Hz, 1 H), 2.11 (t, $J = 6.6$ Hz, 1 H), 2.06 (t, $J = 6.6$ Hz, 1 H), 1.80–1.50 (m, 5 H), 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 138.8, 132.7, 129.2, 128.3, 127.7, 127.4, 75.4, 71.0, 63.5, 59.7, 37.2, 33.6, 28.0, 25.9,

18.2; IR (neat) 3600–3150, 3030, 2930, 2955, 2860, 1495, 1470, 1460, 1450, 1360, 1250, 1090, 835, 770, 730, 695, 660. Anal. Calcd for $C_{21}O_3H_{36}Si$: C, 69.18; H, 9.95. Found: C, 69.23; H, 10.01.

(*E*)-8-Chloro-3-(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene. Tributylphosphine (8.44 mL, 34.0 mmol) was slowly added to a solution of CCl_4 (3.30 mL, 34.0 mmol), pyridine (5.27 mL, 65.3 mmol), and **15b** (9.53 g, 26.1 mmol) in an ice bath. After 10 min the solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated. The chloride was purified by flash chromotography (4% EtOAc/hexanes) to yield 7.90 g (79%) of product and 0.982 g (10%) of recovered starting material: R_f = 0.66 (18% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 5 H), 5.69 (dt, J = 6.6, 14.8 Hz, 1 H), 5.53 (dtt, J = 1.2, 6.9, 15.1 Hz, 1 H), 4.47 (d, J = 13.7 Hz, 1 H), 4.43 (d, J = 13.7 Hz, 1 H), 3.94 (d, J = 7.0 Hz, 2 H), 3.66 (q, J = 6.5 Hz, 2 H), 3.53 (quint, J = 5.8 Hz, 1 H), 2.12 (t, J = 6.5 Hz, 1 H), 2.08 (t, J = 6.5 Hz, 1 H), 1.80–1.50 (m, 4 H), 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 139.8, 135.6, 128.3, 127.7, 127.4, 126.1, 75.3, 71.0, 59.6, 45.2, 37.2, 33.3, 27.8, 25.9, 18.2; IR (neat) 3030, 2955, 2925, 2860, 1665, 1495, 1470, 1460, 1450, 1360, 1250, 1090, 830, 770, 730, 695, 680, 660. Anal. Calcd for $C_{21}O_2H_{35}SiCl$: C, 65.84; H, 9.21. Found: C, 65.82; H, 9.16.

(*E*)-8-(Tributylstannyl)-3-(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene. *n*-BuLi (2.5 M, 7.5 mL, 17.7 mmol) was slowly added to a 0 °C solution of DIA (2.39 mL, 17.0 mmol) in 100 mL of THF and allowed to stir for 20 min. Tri-*n*-butyltin hydride (3.53 mL, 13.1 mmol) was slowly added to the solution of LDA at −78 °C and allowed to stir for 20 min after which time the above chloride (5.00 g, 13.1 mmol) in 15 mL of THF was added *via* cannula. The reaction was quenched 15 min later, diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash chromatography (hexanes) to yield 7.92 g (95%) of a clear oil: R_f = 0.73 (5% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.29 (m, 5 H), 5.49 (dt, J = 8.4, 14.9 Hz, 1 H), 5.16 (dt, J = 6.9, 14.9 Hz, 1 H), 4.45 (s, 2 H), 3.67 (q, 2 H), 3.52 (quint, J = 6 Hz, 1 H), 2.05 (t, J= 6.8 Hz, 1 H), 2.01 (t, J = 6.8 Hz, 1 H), 1.80–1.50 (m, 6 H), 1.43 (m, 3 H), 1.25 (q, J = 7.0 Hz, 6 H), 0.85 (m, 24 H), 0.00 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 139.1, 129.4, 128.3, 127.8, 127.4, 126.0, 75.8, 71.1, 59.8, 45.9, 37.4, 34.8, 29.2, 28.6, 27.4, 26.0, 14.2, 13.8, 9.2; IR (neat) 2960, 2925, 2860, 1460, 1250, 1095, 832, 770, 730, 695, 665. Anal. Calcd for $C_{33}O_2H_{62}SiSn$: C, 62.16; H, 9.80. Found: C, 62.17 H, 9.84.

(*E*)-8-(Tributylstannyl)-3-(benzyloxy)-1-hydroxyoct-6-ene (16b). A solution of (*E*)-8-(tributylstannyl)-3-(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]oct-6-ene (2.00 g, 3.14 mmol) and TBAF (1.0 M in THF, 3.14 mL) in 100 mL of THF was stirred for 2 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The oil was purified by flash chromatography (15% EtOAc/hexanes) to yield 1.60 g (97%) of a clear oil: R_f = 0.23 (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 5.47 (dt, J = 8.5, 14.9 Hz, 1 H), 5.12 (dt, J = 6.8, 14.9 Hz, 1 H), 4.47 (d, J = 31.5 Hz, 1 H), 4.43 (d, J = 31.5 Hz, 1 H), 3.8–3.5 (m, 3 H), 2.44 (s, 1 H), 1.96 (q, J = 7.4 Hz, 2 H), 1.80–1.55 (m, 5 H), 1.50–1.40 (m 1 H), 1.39 (m, 6 H), 1.22 (q, J = 7.6 Hz, 6 H), 0.82 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 138.2, 129.6, 128.3, 127.7, 127.5, 124.6, 78.1, 70.9, 60.7, 35.87, 34.0, 28.2, 27.4, 26.4, 14.2, 13.8, 9.2; IR (neat) 3600–3200, 2955, 2920, 2860, 2840, 1450, 1370, 1060, 960, 870, 730, 695. Anal. Calcd for $C_{27}O_2H_{48}Sn$: C, 61.96; H, 9.24. Found: C, 62.25; H, 9.24.

(*E*)-8-(Tributylstannyl)-3-(benzyloxy)oct-6-enal (4). MeMgBr (3 M, 214 μL, 0.622 mmol) was slowly added to a THF solution (5 mL, 0 °C) of the above alcohol (350 mg, 0.669 mmol). After 20 min a THF solution (5 mL) of 1,1-diazodicarbonyldipiperidine (169 mg, 0.669 mmol) was slowly added, and the dark red solution was stirred for 1 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The oil was immediately purified by −78 °C flash column chromatography (MeOH quenched silica 3% EtOAc/hexanes) to yield 230 mg (71%) of an oil: R_f = 0.67 (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.79 (s, 1 H), 7.32 (m, 5 H), 5.55 (dt, J = 8.5, 14.9 Hz, 1 H), 5.18 (dt, J = 6.8, 14.9 Hz, 1 H), 4.55 (d, J = 13.7 Hz, 1 H), 4.51 (d, J =13.7 Hz, 1 H), 3.96 (quint, J = 6.0 Hz, 1 H), 2.66 (dtt, J = 1.5, 7.1, 16.2 Hz, 1 H), 2.56 (ddt, J = 2.0, 4.9, 16.3 Hz, 1 H), 2.04 (m, 2 H), 1.80–1.40 (m, 10 H), 1.29 (q, J = 7.3 Hz, 6 H), 0.89 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 201.5, 138.2, 130.2, 128.4, 127.7, 124.3, 74.0, 71.2, 48.3, 34.8, 29.1, 28.3, 27.3, 14.2, 13.7, 9.1; IR (neat) 2980, 2925, 1725, 1465, 1450, 1375, 1075, 1025, 960, 870, 730, 695; mass spectrum (CI, isobutane) *m/z* (relative intensity) (M + 1) 523 (32), 521 (29), 466 (20), 465 (100), 464 (43), 463 (78), 462 (25), 461 (32), 91 (60), 57 (119); exact mass calcd for $C_{27}O_2H_{46}Sn$ 523.259 79, found 523.259 66.

(*E*)-8-(Tributylstannyl)octa-2,6-dienal (26). MeMgBr (3 M, 171 μL, 0.497 mmol) was slowly added to a THF solution (5 mL) of alcohol **16** (200 mg, 0.382 mmol). After 20 min a THF solution (5 mL) of 1,1-diazodicarbonyldipiperidine (106 mg, 0.420 mmol) was slowly added, and the dark red solution was stirred 1 h. The solution was diluted with ether, washed with H_2O, $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The oil was immediately purified by −78 °C flash column chromatography (diethylamine quenched silica or alumina, 3% EtOAc/hexanes) to yield 141 mg (89%) of an oil: R_f = 0.67 (20% EtOAc/hexanes); 300-MHz ^{1}H NMR ($CDCl_3$) δ 9.49 (d, J = 7.8 Hz, 1 H), 6.87 (dt, J = 6.7, 15.7 Hz, 1 H), 6.12 (ddt, J = 1.5, 7.9, 15.6 Hz, 1 H), 5.60 (dtt, J = 1.3, 8.5, 14.9 Hz, 1 H), 5.19 (dtt, J = 1.2, 6.7, 14.9 Hz, 1 H), 2.37 (q, J = 7.0 Hz, 2 H), 2.18 (q, J = 7.0 Hz, 2 H), 1.69 (d, J = 8.5 Hz, 2 H), 1.46 (m, 6 H), 1.29 (q, J = 7.3 Hz, 6 H), 0.89 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 194.0, 188.3, 158.5, 133.1, 131.2, 123.1, 33.3, 31.0, 29.1, 27.3, 14.2, 13.7, 9.2.

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