Remote Conformational Bias Effects on Diastereofacial Selectivity in S_E2' Additions of γ-Oxygenated Allylic Stannanes to Chiral Enals

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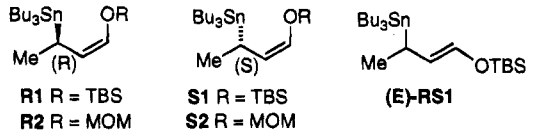
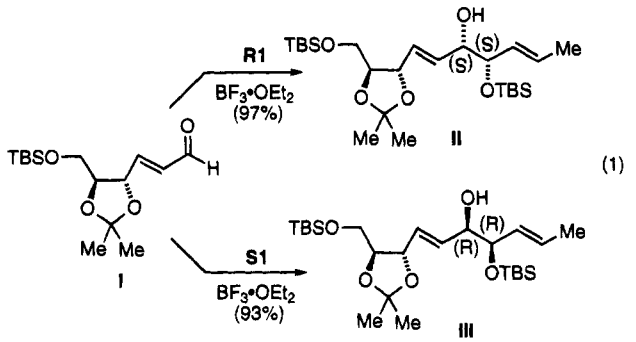
The enal **10** derived from (*R,R*)-diethyl tartrate shows matched/mismatched characteristics in BF_3-promoted additions of the chiral γ-oxygenated allylic stannanes **S1, S2, R1**, and **R2**. Both **S2** and **S1** afford a single *syn* adduct **11** and **14** with enal **10**, whereas **R2** and **R1** give mixtures of *syn* and *anti* products **12/13** and **15/16**. Racemic stannane **RS2** affords a 82:18 mixture of *syn* adducts **11** and **12**; **RS1** gives the two *syn* adducts **14** and **15** as a 77:23 mixture. The observed facial bias in these additions is attributed to conformational effects engendered by the vicinal *syn* OTBS substituents which cause enal **10** to adopt a chair-like conformation. The matched additions proceed by attack on the "outside" face of the carbonyl grouping in the *s-cis* orientation of this chair-like arrangement.

These past several years we have been interested in Lewis acid-promoted additions of the nonracemic γ-oxygenated allylic stannanes **R1/2** and **S1/2**, and more recently **(*E*)-RS1**, to aldehydes as a synthetic route to certain carbohydrate and polyol natural products.[1]

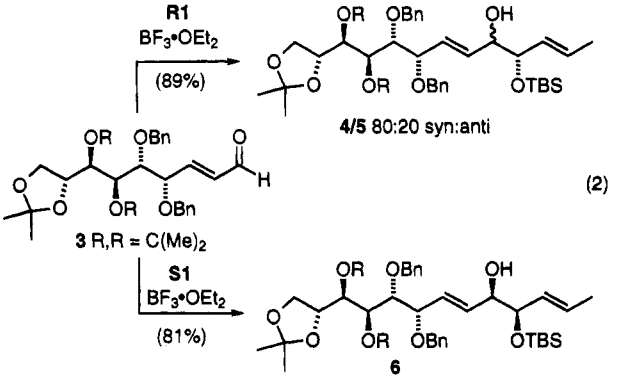


In one application of this approach, we found that stannane **R1** undergoes a stereospecific and highly diastereoselective reagent-controlled addition to the tartrate-derived enal **I** in the presence of BF_3·OEt_2 to afford the (*S,S*)-allylic diol derivative **II**.[2] As expected, under these conditions the enantiomeric stannane **S1** affords the corresponding (*R,R*)-allylic diol derivative **III** with comparable efficiency (eq 1).



(1)

In light of our experience with enal **I**, we were surprised to find that the seemingly related enal **3** yielded an 80:20 mixture of *syn* and *anti* adducts **4** and **5** with stannane **R1** (eq 2).[3] Hoping to clarify this matter, we undertook additional studies on this and related γ-oxygenated enals.



(2)

In contrast to the aforementioned results for stannane **R1**, addition of stannane **S1** to enal **3** afforded alcohol **6** as the sole adduct (see eq 2). Thus **3** appears to be matched with stannane **S1** and mismatched with stannane **R1**. However, as a rule this phenomenon is most common with aldehydes possessing an α stereocenter where direct steric interactions with an attacking chiral reagent are possible.[4] In the case of enal **3** we suspected that the *syn* disposition of the vicinal benzyl ethers might bring about conformational constraints resulting in preferential shielding of one face of the aldehyde carbonyl. Such an effect on additions to the double bonds of *syn* diallylic diol TBS ethers such as **IV** (Figure 1) has been reported by Saito and co-workers.[5] Along these lines, Gung and Wolf have shown that (*E*)-acrylates bearing an OTBS grouping at the gamma (allylic) position (**V**, Figure 1) adopt a favored C/O-eclipsed conformer whereas methyl and benzyl allylic ethers tend to favor the C/H-eclipsed conformer (**VI**, Figure 1).[6]

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(1) Reviews: (a) Marshall, J. A. *Chemtracts–Org. Chem.* **1992**, *5*, 75. Yamamoto, Y.; Shida, N., in *Advances in Detailed Reaction Mechanisms*; JAI press Inc: **1994**; Vol 3, Chap. I. (b) Marshall, J. A.; Seletsky, B. M.; Luke, G. P. *J. Org. Chem.* **1994**, *59*, 3413.

(2) Marshall, J. A.; Beaudoin, S.; Lewinski, K. *J. Org. Chem.* **1993**, *58*, 5876.

(3) Marshall, J. A.; Beaudoin, S. *J. Org. Chem.*, in press.

(4) *Cf.* (a) Aldol reaction: Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1. (b) Allylboronates: Roush, W. R.; Palkowitz, A. D.; Ando, K. A. *J. Am. Chem. Soc.* **1990**, *112*, 6348.

(5) (a) Saito, S.; Morikawa, Y.; Moriwake, T. *J. Org. Chem.* **1990**, *55*, 5424. (b) Saito, S.; Narahara, O.; Ishikawa, T.; Asahara, M.; Moriwake, T.; Gawronski, J.; Kazmiercyak, F. *J. Org. Chem.* **1993**, *58*, 6292.

(6) Gung, B. W.; Wolf, M. A. *J. Org. Chem.* **1993**, *58*, 7038.

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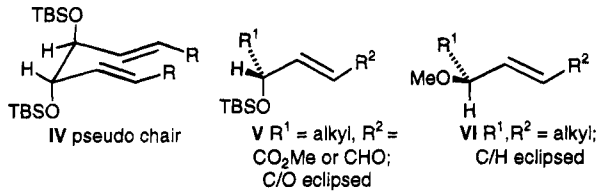
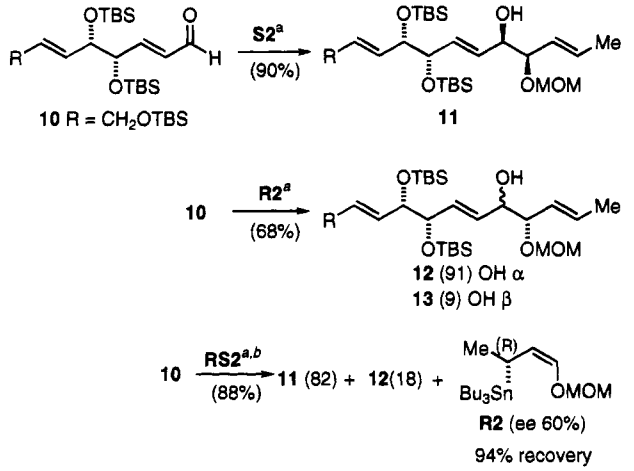


Figure 1. Saito conformation for diallylic diol TBS ethers (**IV**). Gung and Wolff preferred conformers for γ-OTBS acrylates (**V**) and allylic ethers (**VI**).

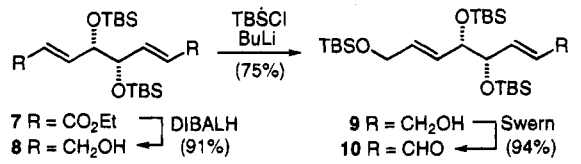
Scheme 1[a]



[a] Key: (a) BF_3·OEt_2, CH_2Cl_2, −78 °C; (b) 2 equiv.

With these considerations in mind, we decided to examine the *bis*-OTBS enal **10** as a substrate for S_E2' additions of stannanes **R1/2** and **S1/2**. Based on reported chemistry, aldehyde **10** should strongly prefer the pseudo chair conformation **IV** (Figure 1), which would accentuate conformationally induced facial bias to carbonyl addition.[5]

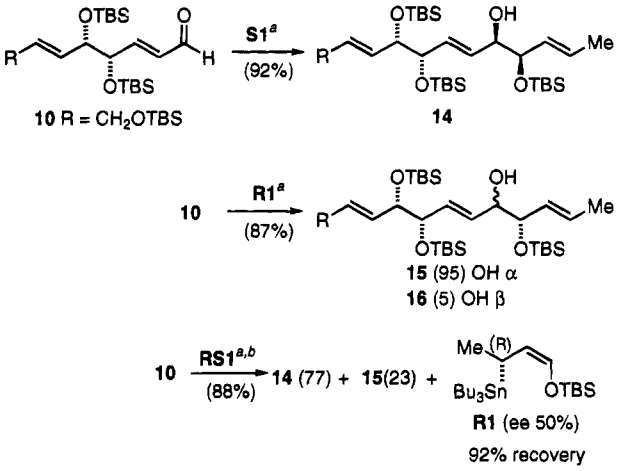
Enal **10** was prepared from the tartrate-derived diester **7**.[5] Reduction with DIBALH led to diol **8**, which was selectively silylated with TBSCl/BuLi. The resulting allylic alcohol **9** was then oxidized by the Swern protocol.[7]



Addition of stannane **S2** to enal **10** in the presence of BF_3·OEt_2 gave rise to the *syn* adduct **11** as the sole detectable product in 90% yield (Scheme 1). Stannane **R2**, on the other hand, afforded a 91:9 mixture of *syn* and *anti* adducts **12** and **13** in only 68% yield under comparable conditions. Upon treatment with excess racemic stannane **RS2**, aldehyde **10** yielded an 82:18 mixture of the two *syn* adducts **11** and **12**. The *anti* adduct **13**, if present, was formed in amounts insufficient for detection by ^1H NMR analysis. As expected, the recovered stannane from this experiment was enriched in the (*R*) enantiomer (*ee* 60%). Thus enal **10**, like its benzyloxy counterpart **3**, shows characteristics typical of α-alkoxy aldehydes in these allylic stannane additions.[1]

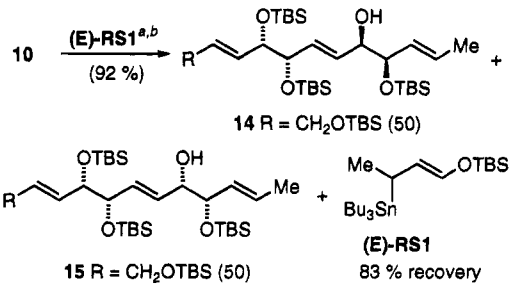
The γ-OTBS allylic stannanes **R1** and **S1** behaved analogously to **R2** and **S2** in BF_3-promoted additions to

Scheme 2[a]



[a] Key: (a) BF_3·OEt_2, CH_2Cl_2, −78 °C; (b) 2 equiv.

Scheme 3[a]



[a] Key: (a) BF_3·OEt_2, CH_2Cl_2, −78 °C; (b) 2 equiv.

enal **10**. Accordingly, stannane **S1** afforded the *syn* adduct **14** in 92% yield, whereas **R1** gave rise to a 95:5 mixture of *syn* and *anti* adducts **15** and **16** (Scheme 2). Treatment of enal **10** with excess racemic stannane **RS1** led to a 77:23 mixture of the two *syn* adducts **14** and **15**, along with recovered **R1** of 50% *ee*.

We also examined the addition of stannane **(E)-RS1** to enal **10** in the presence of BF_3·OEt_2. This stannane, currently available only in racemic form, has been found to react with achiral aldehydes with essentially 100% *syn* diastereoselectivity.[8] The *syn* adducts **14** and **15** were obtained as the sole products of the BF_3-promoted addition. Somewhat surprisingly, these adducts were formed as a 1:1 mixture, with recovered stannane showing no enantioenrichment as judged by the lack of optical rotation at the sodium D line (Scheme 3).

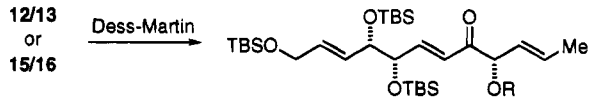
Structure of the Adducts. We have previously shown that additions of stannane **R1** to a variety of aldehydes in the presence of BF_3·OEt_2 leads to *syn* mono TBS diols of (*S,S*) configuration whereas **S1** affords the (*R,R*) enantiomers.[1,2] That such is the case for enal **I** was independently confirmed by conversion of the adduct **II** to a crystalline nonaacetate derivative suitable for X-ray structure analysis.[2] Adduct **III** was converted to the enantiomer of a galaoctonic lactone first prepared from galactose by Fischer.[2] The stereochemistry of adduct **4** was established by conversion to an intermediate employed by Schreiber and co-workers in their synthesis of hikizimycin.[3,9]

The absolute stereochemistry of the carbinol center in adducts **14**, and **15** was confirmed through ^1H NMR

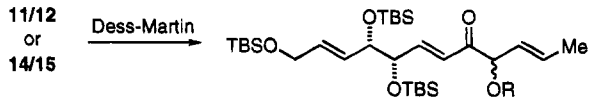
(7) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(8) Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1992**, *57*, 7158.
(9) Ikemoto, N.; Schreiber, S. *J. Am. Chem. Soc.* **1992**, *114*, 2524.

analysis of the *O*-methyl mandelates.[10] In each case, partial racemization of the mandelate α-position occurred under the reaction conditions required for complete esterification. Nonetheless, the assignment of absolute stereochemistry can be judged to be reliable as both the (*R*) and (*S*) mandelates were prepared. Though formed in different ratios, each derivative led to consistent assignments of configuration. The *syn,anti* relationship of carbinols **12/13** and **15/16** was ascertained through oxidation to a single ketone, **17** or **18**, respectively. On the other hand, the mixtures of **11/12** and **14/15** derived from the racemic stannanes afforded a mixture of ketones **19/17** and **20/18** upon oxidation.



17 R = MOM
18 R = TBS



19 OR = β-OMOM
17 OR = α-OMOM
20 OR = β-OTBS
18 OR = α-OTBS

Transition State Considerations. Our previous findings that both (*Z*) and (*E*) OTBS stannanes **R1**, **S1**, and **(*E*)-RS1** show virtually complete *syn* diastereoselectivity in their Lewis acid-promoted additions to achiral aldehydes indicates a preference for an *anti* orientation of the OTBS and aldehyde substituent *and* an antiperiplanar arrangement of the C=C of the stannane with the C=O of the aldehyde.[8] This is the most plausible transition state orientation leading to *syn* products. The formation of *anti* products would proceed by gauche/antiperiplanar or anti/synclinal orientations of the stannane and aldehyde. This arrangement is less disfavored for stannanes **R2** and **S2**, possibly because of the smaller steric requirement of OMOM *vs* OTBS.

The apparent matched pairing of aldehyde **10** with stannanes **S1** and **S2** is in accord with transition state **A** (Figure 2), analogous to that first proposed by Yamamato to explain the *syn* selectivity of BF_3-promoted additions of crotylstannanes to aldehydes and noted above for γ-OTBS stannanes **R1**, **S1**, and **(*E*)-RS1**.[11] In the present case, we assume that attack occurs preferentially on the "outside" face of enal **10**, as suggested by Saito for additions to the double bonds of analogous *bis*-TBS diallylic ethers.[5] We also assume, based on Denmark's findings, that interactions between OR and the Lewis acid BF_3 are relatively unimportant.[12] Given these assumptions, the production of adducts **11** and **14** requires that enal **10** adopt an *s-cis* conformation in the transition state, as illustrated. Reaction through the

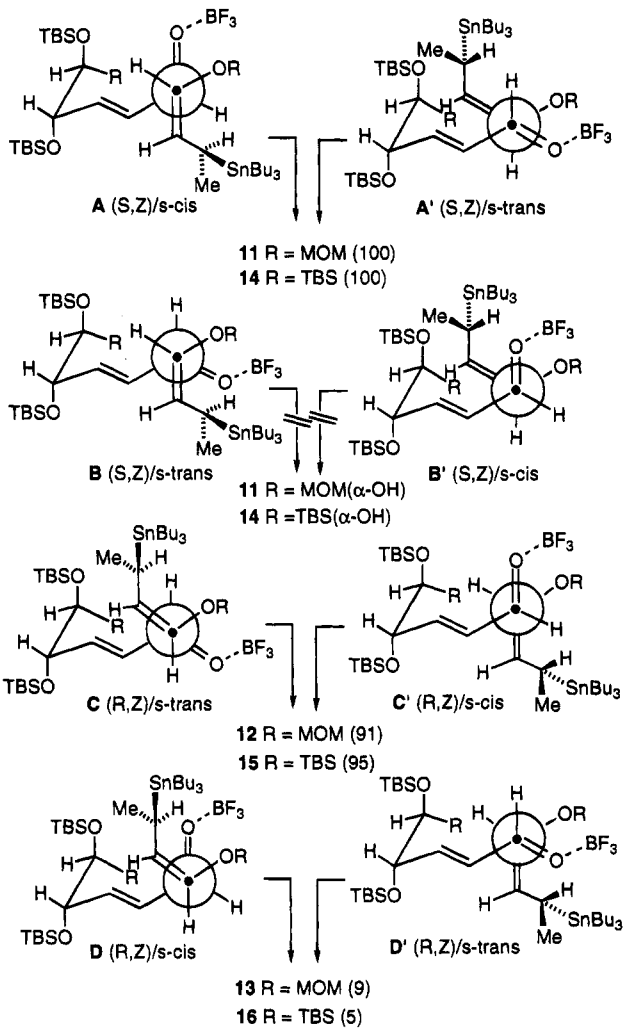


Figure 2. Transition state arrangements for additions of stannanes **R1/2** and **S1/2** to aldehyde **10**.

s-trans conformer **B** would afford the unobserved *anti* adducts. Though theoretically possible, we consider the alternative transition state **A'**, in which stannane **S2** attacks the "inside" face of the *s-trans* conformer of enal **10**, less likely for steric reasons.

The products, **12/13** and **15/16**, of the "mismatched" stannanes **R2** and **R1** could arise through transition states **C/C'** and **D/D'**. The former pair, corresponding to the Yamamoto antiperiplanar arrangement of C=C and C=O, lead to the major products **12** and **15**, respectively. In transition state **C** the aldehyde carbonyl adopts the *s-trans* conformation. An alternative possibility for the genesis of adducts **12** and **15** would entail "inside attack" on the *s-cis* conformer of enal **10** as depicted by **C'**.[13] The minor products **13** and **16** must arise through the less favorable synclinal orientations **D** and **D'**.[14]

The evidence at hand does not permit a clear choice for the mismatched transition states. Our findings to date are most consistent with the pictured arrangements in which the Bu_3Sn grouping adopts an *anti* disposition

(10) (a) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370. (b) Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043.

(11) Yamamoto, Y.; Yatagi, H.; Narita, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.

(12) Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970.

(13) As we have previously noted, Newman projection representations of these transition states tend to overemphasize certain steric interactions. In C', for example, the Sn reagent approaches the C=O at an angle of 110° rather than 90° along an axis in close proximity to the CH bond of the aldehyde.[8] This arrangement tends to place the γ-vinylic H at some distance from the substituent R.

(14) For a discussion of synclinal *vs* antiperiplanar orientations in such additions, see: Fleming, I. *Chemtracts—Org. Chem.* **1991**, 21.

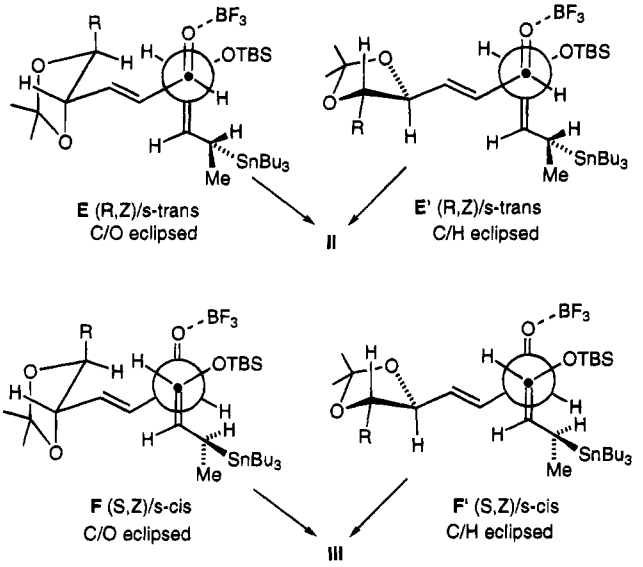
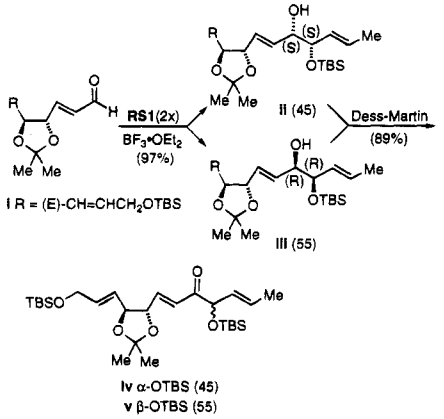


Figure 3. Transition state arrangements for additions of stannanes **R2** and **S2** to aldehyde **I**.

with respect to the forming C—C bond (stereoelectronic effect) and the OR substituent aligns *anti* to the aldehyde substituent (steric effect).[1,8] The antiperiplanar *vs* synclinal orientation of C=C and C=O appears to be of lesser importance.[14] Based on the present results, the *s-cis* conformer of enals may be preferred, when possible, but the effect is secondary to the stereoelectronic and steric factors noted above. With enals such as **10** "inside" *vs* "outside" preferences should not be a major factor unless the steric bulk of the stannane reagent is directed within the cavity of the chair-like arrangement as would be the case for **A'** and **B'** but not **C'** and **D'**.

The additions of stannanes **R1** and **S1** to the acetonide enal **I** can be accommodated by Yamamoto-type transition states **E** and **F** and/or **E'** and **F'** (Figure 3). The acetonide grouping effectively prevents chair-like conformations from impeding attack at the back (*re*) face of the enal carbonyl.[15] Reaction can proceed through the C/O-eclipsed forms **E** and **F** (favored by the electron-withdrawing CHO grouping) or the C/H-eclipsed conformers **E'** and **F'** (favored by the allylic OR grouping), as shown.[6]

(15) It could be argued that the smaller R substituent of **I** (**E/E'** and **F/F'**, R = CH_2OTBS) *vs* **10** (**A/A'**–**D/D'**, R = (E)-CH=$CHCH_2$-OTBS) might be responsible for the lack of facial discrimination in additions to enal **I**. To check this possibility we prepared the enal **i**. Addition of the racemic stannane **RS1** (2×) afforded a 45:55 mixture of the two *syn* adducts **ii** and **iii** along with recovered stannane **R1** (88%) of 8% *ee*. Thus the bulkier side chain does not markedly influence the addition.



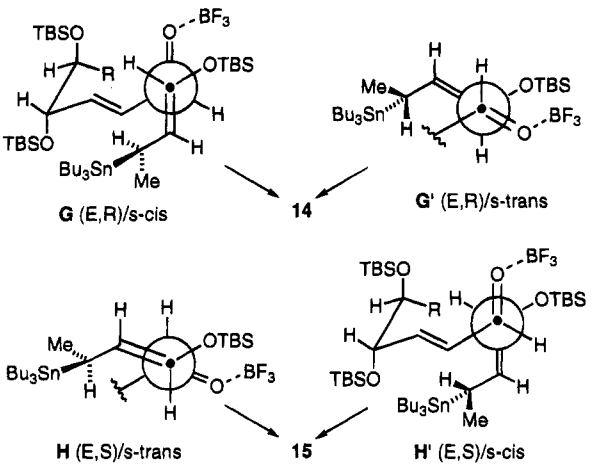


Figure 4. Transition state arrangements for additions of stannanes **(*E*)-RS2** to aldehyde **10**.

The (*E*)-OTBS stannanes **(E)-RS1** afford a 1:1 mixture of the two *syn* adducts **14** and **15**. The former must arise from the (*R*) enantiomer and the latter from the (*S*) enantiomer. The four transition states depicted in Figure 4 incorporate the requisite stereoelectronic and OTBS *anti* orientation considered optimal for the addition. Of the four, **G** would appear to be lowest in energy and, *a priori*, we would expect a predominance of adduct **14**. However, the observed formation of both **14** and **15** in equal amount requires that **H** and **H'** must be considered as well. Presumably the "inside" approach represented by **H'** represents the lower energy option for the pathway leading to **15**.[13]

Conclusions. Though at first sight surprising, the apparent matched/mismatched behavior of enals such as **3** and **10** with regard to chiral allylic stannanes can be explained by consideration of conformational factors engendered by the seemingly remote OR substituents. Thus the choice of OH protecting groups can significantly affect product distributions in such addition reactions. The effect is not seen with the achiral reagents EtMgBr, $Bu_3SnCH_2CH{=}CH_2$, or $Bu_3SnCH_2CH{=}CHCH_3$. All afford 1:1 mixtures upon addition to enal **10**. We might expect *e.g.* chiral enolates[4a] and allylboronates[4b] to also exhibit matching/mismatching effects because of the highly ordered transition states associated with these reactions.

Experimental Section

(4*R*,5*R*,8*S*,9*R*,10*R*,11*R*,12*R*)-8,9-Bis(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)-10,11:12,13-bis-*O*-(1-methylethylidene)-2,6-tridecadien-5-ol (6). To a solution of aldehyde **3**[3] (82 mg, 0.17 mmol) and stannane **S1**[1] (102 mg, 0.21 mmol) in CH_2Cl_2 (2 mL) at −78 °C was added 27 μL (0.22 mmol) of BF_3•OEt_2. After 1.25 h, the reaction mixture was quenched with saturated $NaHCO_3$ (2 mL), allowed to warm to room temperature, diluted with Et_2O (5 mL), washed with H_2O (2 mL) and brine (2 mL), and dried over Na_2SO_4. Flash chromatography on silica gel (2:1, hexanes-Et_2O) gave alcohol **6** (91 mg, 81%) as a colorless oil: $[\alpha]_D$ +28.6 (*c* 1.12, $CHCl_3$); IR (film, cm^{-1}) 3486, 1674; ^1H NMR (400 MHz, $CDCl_3$) δ 0.03 (3 H, s), 0.07 (3 H, s), 0.89 (9 H, s), 1.28 (3 H, s), 1.29 (3 H,s), 1.31 (3 H,s), 1.33 (3 H,s), 1.67 (4 H, dd, *J* = 1.5, 6.5 Hz), 3.62 (1 H, dd, *J* = 4.8, 6.1 Hz), 3.86 (2 H, td, *J* = 1.6, 6.7 Hz), 3.94–3.97 (1 H, m), 3.99–4.04 (2 H, m), 4.08 (1 H, q, *J* = 6.4 Hz), 4.11–4.15 (1 H, m), 4.17 (1 H, t, *J* = 6.5 Hz), 4.36, 4.59 (2 H,

ABq, J_{AB} = 12.0 Hz), 4.66, 4.85 (2 H, ABq, J_{AB} = 11.1 Hz), 5.40 (1 H, qdd, J = 1.5, 7.7, 15.4 Hz), 5.63 (1 H, qd, J = 6.5, 15.4 Hz), 5.78–5.80 (2 H, m), 7.22–7.34 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.74, −3.86, 17.78, 18.16, 25.48, 25.88, 26.37, 27.27, 27.29, 66.59, 70.63, 75.41, 75.43, 76.67, 77.78, 78.05, 79.30, 79.78, 82.83, 109.10, 109.41, 127.36, 127.49, 127.79, 127.95, 128.19, 128.20, 129.20, 129.90, 130.73, 132.94, 138.54, 138.58. Anal. Calcd for $C_{39}H_{58}O_8Si$: C, 68.59; H, 8.56. Found: C, 68.56; H, 8.59.

(2*E*,6*E*,4*S*,5*S*)-4,5-Bis((*tert*-butyldimethylsilyl)oxy)-2,6-octadiene-1,8-diol (8). To a solution of diester **7**[5] (3.65 g, 7.50 mmol) in THF (80 mL) at −78 °C was added 33.0 mL (33.0 mmol) of 1.0 M DIBAL-H in hexanes. After 2 h, the reaction was quenched with Rochelle's salt (50 mL) and H_2O (50 mL), allowed to warm to rt, and stirred overnight. The aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL) and the combined organic extracts were dried over $MgSO_4$. Flash chromatography on silica gel (2:1 hexanes-Et_2O) afforded diol **5** (2.76 g, 91%) as a white solid: mp 60 °C; $[\alpha]_D$ −69.2 (*c* 1.02, $CHCl_3$); IR (KBr, cm^{-1}) 3316; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.02 (6 H, s), 0.04 (6 H, s), 0.87 (18 H, s), 2.57 (2 H, s), 4.06 (4 H, d, J = 4.4 Hz), 4.11 (2 H, d, J = 2.2 Hz), 5.64–5.79 (4 H, m); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.76, −4.59, 18.19, 25.87, 63.07, 75.11, 130.06 , 130.90. Anal. Calcd for $C_{20}H_{42}O_4Si_2$: C, 59.65; H, 10.51. Found: C, 59.82; H, 10.53.

(2*E*,6*E*,4*S*,5*S*)-4,5,8-Tris((*tert*-butyldimethylsilyl)oxy)-2,6-octadien-1-ol (9). To a solution of diol **8** (1.0 g, 2.48 mmol) in THF (12 mL) at 0 °C was added 1.04 mL (2.60 mmol) of 2.5 M n-BuLi in hexanes. After 40 min, TBSCl (411 mg, 2.73 mmol) was added. After 1 h at 0 °C, the reaction mixture was stirred at rt for 4 h, diluted with Et_2O (20 mL), washed with H_2O (10 mL) and brine (10 mL), and dried over Na_2SO_4. Flash chromatography on silica gel (2:1 hexanes-Et_2O) gave alcohol **9** (954 mg, 75%) as a colorless oil: $[\alpha]_D$ −46.6 (*c* 1.54, $CHCl_3$); IR (film, cm^{-1}) 3366; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00 (3 H, s), 0.01 (3 H, s), 0.02 (6 H, s), 0.03 (6 H, s), 0.86 (9 H, s), 0.87 (18 H, s), 1.70 (1 H, bs), 4.06–4.14 (6 H, m), 5.65–5.81 (4 H, m); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −5.22, −5.19, −4.77, −4.60, −4.58 (2 C), 18.13, 18.19, 18.37, 25.85 (3 C), 25.88 (3 C), 25.92 (3 C), 63.36, 63.43, 75.16, 75.25, 128.81, 130.14, 130.23, 130.96. Anal. Calcd for $C_{26}H_{56}O_4Si_3$: C, 60.91; H, 10.92. Found: C, 60.61; H, 10.86.

(2*E*,6*E*,4*S*,5*S*)-4,5,8-tris((*tert*-butyldimethylsilyl)oxy)-2,6-octadienal (10). To a solution of oxalyl chloride (0.13 mL, 1.49 mmol) in CH_2Cl_2 (7 mL) at −78 °C was added 0.21 mL (2.96 mmol) of DMSO. After 5 min, alcohol **9** (633 mg, 1.22 mmol) in CH_2Cl_2 (3 mL) was added dropwise. After 15 min, 0.85 mL (6.09 mmol) of Et_3N was added. The reaction mixture was stirred at 0 °C for 15 min, diluted with Et_2O (20 mL), then washed with 10% HCl (10 mL), saturated $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (10 mL), and dried over Na_2SO_4. Flash chromatography on silica gel (95:5, hexanes-Et_2O) afforded aldehyde **10** (594 mg, 94%) as a light yellow oil: $[\alpha]_D$ −89.8 (*c* 1.08, $CHCl_3$); IR (film, cm^{-1}) 1698; ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.02 (3 H,s), −0.01 (3 H, s), 0.02 (3 H,s), 0.04 (3 H,s), 0.06 (6 H,s), 0.84 (9 H, s), 0.88 (9 H, s), 0.89 (9 H, s), 4.10–4.11 (2 H, m), 4.20–4.25 (1 H, m), 4.36–4.38 (1 H, m), 5.62–5.71 (2 H, m), 6.23 (1 H, ddd, J = 1.8, 8.2, 15.6 Hz), 6.89 (1 H, dd, J = 3.4, 15.6 Hz), 9.51 (1 H, d, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ −4.90, −4.88, −4.54, −4.51, −4.24, 18.45, 18.51, 18.71, 26.10 (3 C), 26.20 (3 C), 26.23 (3 C), 63.39, 75.17, 75.21, 127.51, 131.65, 132.68, 157.37, 193.88. Anal. Calcd for $C_{26}H_{54}O_4Si_3$: C, 60.64; H, 10.57. Found: C, 60.51; H, 10.60.

(2*E*,6*E*,10*E*,4*R*,5*R*,8*S*,9*S*)-8,9,12-Tris((*tert*-butyldimethylsilyl)oxy)-4-((methoxymethyl)oxy)-2,6,10-decatrien-5-ol (11). A. From Stannane S2. To a solution of aldehyde **10** (150 mg, 0.29 mmol) and stannane **S2**[1] (177 mg, 0.44 mmol) in CH_2Cl_2 (7.5 mL) at −78 °C was added 43 μL (0.47 mmol) of BF_3·OEt_2. After 2 h, the reaction mixture was quenched with saturated $NaHCO_3$ (5 mL) and allowed to warm to rt. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic layers were dried over Na_2SO_4. Purification by flash chromatography on silica gel (4:1, hexanes-Et_2O) gave alcohol **11** (166 mg, 90%) as a colorless oil: $[\alpha]_D$ −65.1 (*c* 1.00, $CHCl_3$); IR (film, cm^{-1}) 3480, 1671; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.00 (3 H,s), 0.01 (3 H, s), 0.03 (9 H, s), 0.04 (3 H, s), 0.86 (9 H, s), 0.87 (9 H, s), 0.88 (9 H, s), 1.70 (3 H, dd, J = 1.6, 6.5 Hz), 1.89 (1 H, bs), 3.36 (3 H, s), 3.78 (1 H, t, J = 7.7 Hz), 4.05–4.14 (5 H, m), 4.54, 4.72 (2 H, ABq, J_{AB} = 6.7 Hz), 5.29 (1 H, qdd, J = 1.7, 8.4, 15.4 Hz), 5.55–5.77 (4 H, m), 5.82 (1 H, ddd, J = 1.3, 4.1, 15.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.85, −4.82, −4.44, −4.36, −4.26, −4.18, 18.25, 18.48, 18.56, 18.72, 26.21, 26.27, 26.29, 55.96, 63.81, 74.29, 75.68, 76.07, 81.13, 93.97, 127.74, 129.29, 129.37, 130.91, 131.58, 132.25. Anal. Calcd for $C_{32}H_{66}O_6Si_3$: C, 60.90; H, 10.54. Found C, 60.81; H, 10.60.

B. From Stannane RS2 (Kinetic Resolution). The procedure described in part A was employed with aldehyde **10** (150 mg, 0.29 mmol) and stannane **RS2**[1] (236 mg, 0.58 mmol) in CH_2Cl_2 (7.5 mL) at −78 °C to which was added 40 μL (0.32 mmol) of BF_3·OEt_2. After 8 h, the reaction mixture was quenched and the product was purified by flash chromatography on silica gel (95:5 then 4:1, hexanes-Et_2O) to give an inseparable mixture of alcohols **11** and **12** (161 mg, 88%, 82:18 by integration of the OMe signals at 3.12 and 3.13 in the ^{1}H NMR spectrum) along with the recovered stannane **R2** (111 mg, 94%, $[\alpha]_D$ −83.1 (*c* 1.95, CH_2Cl_2)): Minor isomer (partial ^{1}H NMR): 0.09 (3 H, s), 0.10 (3 H, s), 0.12 (3 H, s), 3.13 (3 H, s), 3.99 (1 H, t, J = 7.8 Hz), 6.18 (1 H, dd, J = 3.6, 15.7 Hz).

(2*E*,6*E*,10*E*,4*S*,5*S*,8*S*,9*S*)-8,9,12-Tris((*tert*-butyldimethylsilyl)oxy)-4-((methoxymethyl)oxy)-2,6,10-decatrien-5-ol (12). To a solution of aldehyde **10** (150 mg, 0.29 mmol) and γ-stannane **R2** (177 mg, 0.44 mmol) in CH_2Cl_2 (7.5 mL) at −78 °C was added 43 μL (0.47 mmol) of BF_3·OEt_2. After 8 h, an additional 0.21 μL (0.23 mmol) of BF_3·OEt_2 was added. After an additional 19 h, the reaction mixture was quenched with saturated $NaHCO_3$, and the product was isolated as described above and purified by flash chromatography on silica gel (95:5 then 4:1, hexanes-Et_2O) to give alcohol **12** and **13** (125 mg, 68%) as an inseparable 91:9 mixture (^{1}H NMR integration of OCH_3 signals at 3.13 and 3.17 ppm) along with recovered aldehyde **10** (32 mg, 21%): $[\alpha]_D$ −1.0 (*c* 1.12, $CHCl_3$); IR (film, cm^{-1}) 3495, 1672; ^{1}H NMR (400 MHz, C_6D_6) δ 0.09 (3 H, s), 0.10 (3 H, s), 0.12 (6 H, s), 0.14 (3 H, s), 0.15 (3 H, s), 1.00 (9 H, s), 1.01 (9 H, s), 1.02 (9 H, s), 1.56 (3 H, dd, J = 1.6, 6.5), 2.68 (1 H, d, J = 3.1 Hz), 3.13 (3 H, s), 3.99 (1 H, t, J = 7.8 Hz), 4.14 (2 H, d, J = 4.4 Hz), 4.25 (1 H, bt, J = 4.6 Hz), 4.31 (2 H, d, J = 4.3 Hz), 4.40, 4.70 (2 H, ABq, J_{AB} = 6.6 Hz), 5.35 (1 H, qdd, J = 1.6, 8.2, 15.4 Hz), 5.65 (1 H, qd, J = 6.5, 15.7 Hz), 5.88 (1 H, td, J = 4.6, 15.1 Hz), 5.90 (1 H, dd, J = 5.6, 15.6 Hz), 6.01 (1 H, ddd, J = 1.5, 3.5, 15.5 Hz), 6.18 (1 H, dd, J = 3.6, 15.6 Hz); minor isomer (diagnostic signals): δ 0.08 (3 H, s), 3.17 (3 H, s), 4.43, 4.66 (2 H, ABq, J_{AB} = 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.22, −5.19, −4.78, −4.76, −4.67, −4.59, 17.85, 18.10, 18.19, 18.34, 25.82, 25.88, 25.92, 55.57, 63.44, 74.37, 75.40, 75.54, 80.77, 93.75, 126.60, 127.36, 128.91, 129.36, 130.45, 131.56, 131.97. Anal. Calcd for $C_{32}H_{66}O_6Si_3$: C, 60.90; H, 10.54. Found: C, 60.81; H, 10.60.

(2*E*,6*E*,10*E*,4*R*,5*R*,8*S*,9*S*)-4,8,9,12-Tetrakis((*tert*-butyldimethylsilyl)oxy)-2,6,10-decatrien-5-ol (14). A. From Stannane S1. To a solution of aldehyde **10** (100 mg, 0.19 mmol) and stannane **S1** (177 mg, 0.23 mmol) in CH_2Cl_2 (5 mL) at −78 °C was added 29 μL (0.32 mmol) of BF_3·OEt_2. After 3 h, the reaction mixture was quenched with saturated $NaHCO_3$ (5 mL) and the product was isolated as described above and purified by flash chromatography on silica gel (95:5, hexanes-Et_2O) to give alcohol **14** (126 mg, 92%) as a colorless oil: $[\alpha]_D$ −25.9 (*c* 1.02, $CHCl_3$); IR (film, cm^{-1}) 3568; ^{1}H NMR (400 MHz, C_6D_6) δ 0.07 (3 H, s), 0.08 (3 H, s), 0.09 (6 H, s), 0.14 (3 H, s), 0.15 (3 H, s), 0.16 (6 H, s), 0.95 (9 H, s), 1.01 (9 H, s), 1.03 (9 H, s), 1.05 (9 H, s), 1.58 (3 H, d, J = 6.3 Hz), 2.49 (1 H, d, J = 4.0 Hz), 4.00 (1 H, t, J = 7.2 Hz), 4.14–4.19 (3 H, m), 4.33 (1 H, td, J = 0.9, 5.4 Hz), 4.37 (1 H, t, J = 5.0 Hz), 5.51 (1 H, qdd, J = 1.2, 7.2, 15.4 Hz), 5.62 (1 H, qd, J = 6.3, 15.4 Hz), 5.88 (1 H, tdd, J = 0.9, 4.6, 15.4 Hz), 5.98 (1 H, ddd, J = 1.2, 5.0, 15.6 Hz), 6.00 (1 H, tdd, J = 1.6, 5.4, 15.4 Hz), 6.24 (1 H, ddd, J = 1.5, 5.0, 15.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.21, −5.16, −4.79, −4.72, −4.58, −4.54, −3.89, 17.73, 18.14, 18.20, 18.36, 25.88, 25.91, 25.93, 63.47, 75.21, 75.31, 75.67, 77.75, 128.69, 128.95, 129.08, 130.42, 130.82, 130.91. Anal. Calcd for $C_{36}H_{76}O_5Si_4$: C, 61.65; H, 10.92. Found: C, 61.67; H, 11.01.

***O*-Methyl Mandelate.** To a solution of alcohol **14** (20 mg, 29 μmol) in CH_2Cl_2 (1 mL) was added (*R*)-OMe-mandelic acid (7 mg, 43 μmol), DCC (9 mg, 43 μmol) followed by DMAP (2 mg, 16 μmol). After 1 h, the reaction mixture was diluted with hexanes (5 mL), filtered, washed with 10% HCl, saturated $NaHCO_3$ (1 mL), and H_2O (1 mL), and dried over Na_2SO_4. Flash chromatography on silica gel (95:5, hexanes-Et_2O) gave the mandelate as a colorless oil. Analysis of the ^1H NMR spectra of the (*R*)-mandelate (vinylic CH_3 at 1.44 ppm) and (*S*)-mandelate (vinylic CH_3 at 1.62 ppm) is consistent with the assigned *R* configuration.

B. From Stannane RS1 (Kinetic Resolution). The above procedure was employed with aldehyde **10** (200 mg, 0.39 mmol) and stannane **RS1** (369 mg, 0.78 mmol) in CH_2Cl_2 (10 mL) at −78 °C to which was added 53 μL (0.43 mmol) of BF_3·OEt_2. After 3 h, the reaction mixture was quenched with saturated $NaHCO_3$ (5 mL), and the product was isolated as described and purified by flash chromatography on silica gel (hexanes then 95:5 hexanes-Et_2O) to give a 77:23 mixture (based on integration of signals at 2.48 and 2.46 ppm in the ^1H NMR spectrum) of alcohol **14** and **15** (161 mg, 88%) along with recovered stannane **R1** (111 mg, 92%, $[\alpha]_D$ −86.6 (*c* 1.28, CH_2Cl_2)).

C. From Stannane (*E*)-RS1 (Kinetic Resolution). The above procedure was employed with aldehyde **10** (123 mg, 0.24 mmol) and stannane **(E)-RS1** (228 mg, 0.48 mmol) in CH_2Cl_2 (5 mL) at −78 °C to which was added 0.06 mL (0.48 mmol) of BF_3·OEt_2. After 2 h, the reaction mixture was quenched with saturated $NaHCO_3$ (5 mL), and the product was isolated as described and purified by flash chromatography on silica gel (hexanes then 95:5, hexanes-Et_2O) to give a 50:50 mixture of alcohols **14** and **15** (156 mg, 92%) along with recovered stannane (95 mg, 83%, $[\alpha]_D$ 0.00 (*c* 2.00, CH_2Cl_2)).

(2*E*,6*E*,10*E*,4*S*,5*S*,8*S*,9*S*)-1,4,5-Tetrakis-((*tert*-butyldimethylsilyl)oxy)-2,6,10-decatrien-5-ol (15). The above procedure was employed with aldehyde **10** (123 mg, 0.24 mmol) and stannane **R1** (228 mg, 0.48 mmol) in CH_2Cl_2 (5 mL) at −78 °C to which was added 0.06 mL (0.48 mmol) of BF_3·OEt_2. After 2 h, the reaction mixture was quenched with saturated $NaHCO_3$ (5 mL), and the product was isolated as described and purified by flash chromatography on silica gel (95:5, hexanes-Et_2O) to give alcohol **15** (144 mg, 87%) as a colorless oil: $[\alpha]_D$ −26.8 (*c* 0.96, $CHCl_3$); IR (film, cm^{-1}) 3575, 1673; ^1H NMR (400 MHz, C_6D_6) δ 0.08 (3 H, s), 0.09 (3 H, s), 0.10 (3 H, s), 0.11 (3 H, s), 0.13 (3 H, s), 0.14 (3 H, s), 0.15 (3 H, s), 0.16 (3 H, s), 0.95 (9 H, s), 1.01 (9 H, s), 1.03 (9 H, s), 1.04 (9 H, s), 1.59 (3 H, d, *J* = 6.4 Hz), 2.46 (1 H, d, *J* = 3.6 Hz), 4.05 (1 H, t, *J* = 7.1 Hz), 4.10−4.15 (1 H, m), 4.16 (2 H, d, *J* = 4.5 Hz), 4.33 (2 H, d, *J* = 4.1 Hz), 5.52 (1 H, qdd, *J* = 1.4, 7.1, 15.3 Hz), 5.64 (1 H, qd, *J* = 6.4, 15.3 Hz), 5.89 (1 H, td, *J* = 4.6, 15.0 Hz), 5.94 (1 H, dd, *J* = 5.3, 15.0 Hz), 6.03 (1 H, ddd, *J* = 1.4, 3.6, 15.7 Hz), 6.17 (1 H, dd, *J* = 3.7, 15.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.23, −5.18, −4.84, −4.77, −4.76, −4.59, −4.57, −3.98, 17.68, 18.11, 18.17, 18.34, 25.84, 25.85, 25.87, 25.91, 63.46, 75.50, 75.53, 75.66, 77.51, 128.51, 128.98, 129.53, 130.35, 130.68, 130.73. Anal. Calcd for $C_{36}H_{76}O_5Si_4$: C, 61.65; H, 10.92. Found: C, 61.40; H, 10.95. Analysis of the ^1H NMR spectra of the (*R*)-*O*-methyl mandelate (vinylic CH_3 at 1.62 ppm) and the (*S*)-*O*-methyl mandelate (vinylic CH_3 at 1.43 ppm) is consistent with the assigned *S* configuration.

(2*E*,5*E*,10*E*,4*S*,8*S*,9*S*)-8,9-Bis((*tert*-butyldimethylsilyl)oxy)-4-((methoxymethyl)oxy)-2,6,10-decatrien-5-one (17). To a solution of alcohol **12/13** (30.6 mg, 48 μmol) in CH_2Cl_2 (1 mL) was added 41 mg (96 μmol) of the Dess-Martin periodinane.[16] After 30 min, another portion (20 mg, 47 μmol) of the periodinane reagent was added. After 30 min, $Na_2S_2O_3$ (160 mg, 1.01 mmol), Et_2O (2 mL), and saturated $NaHCO_3$ (2 mL) were added. After stirring for 10 min, the organic layer was washed with H_2O (2 mL) and dried over Na_2SO_4. Purification by flash chromatography on silica gel (4:1, hexanes-Et_2O) gave ketone **17** (24.6 mg, 81%) as a colorless oil: $[\alpha]_D$ +17.0 (*c* 1.00, $CHCl_3$); IR (film, cm^{-1}) 1701, 1634; ^1H NMR (400 MHz, $CDCl_3$) δ 0.0 (3 H, s), 0.01 (6 H, s), 0.02 (3 H, s), 0.04 (3 H, s), 0.05 (3 H, s), 0.86 (9 H, s), 0.88 (9 H, s), 0.90 (9 H, s), 1.71 (3 H, dd, *J* = 1.7 Hz), 3.33 (3 H, s), 4.10−4.11 (2 H, m), 4.18 (1 H, t, *J* = 5.0 Hz), 4.29 (1 H, ddd, *J* = 1.9, 3.4, 5.2 Hz), 4.58, 4.70 (2 H, ABq, J_{AB} = 6.7 Hz), 4.67 (1 H, d, *J* = 7.9 Hz), 5.36 (1 H, qdd, *J* = 1.7, 7.9, 15.3 Hz), 5.58−5.69 (2 H, m), 5.88 (1 H, qdd, *J* = 1.0, 6.5, 15.3 Hz), 6.47 (1 H, dd, *J* = 1.9, 15.7 Hz), 7.06 (1 H, dd, *J* = 3.5, 15.7 Hz). Anal. Calcd for $C_{32}H_{64}O_6Si_3$: C, 61.09; H, 10.25. Found: C, 60.93; H, 10.15.

(2*E*,5*E*,10*E*,4*S*,8*S*,9*S*)-4,8,9-Tris((*tert*-butyldimethylsilyl)oxy)-2,6,10-decatrien-5-one (18). The procedure described for ketone **17** was employed with 50 mg (70 μmol) of alcohol **15/16**. Flash chromatography on silica gel (95:5, hexanes-Et_2O) gave ketone **18** (41 mg, 81%) as a colorless oil: $[\alpha]_D$ −43.2 (*c* 1.14, $CHCl_3$); IR (film, cm^{-1}) 1699, 1633; ^1H NMR (400 MHz, $CDCl_3$) δ 0.00 (3 H, s), 0.01 (3 H, s), 0.02 (9 H, s), 0.03 (3 H, s), 0.04 (3 H, s), 0.05 (3 H, s), 0.86 (9 H, s), 0.87 (9 H, s), 0.88 (9 H, s), 0.90 (9 H, s), 1.68 (3 H, dd, *J* = 6.6 Hz), 4.10 (2 H, d, *J* = 2.8 Hz), 4.17−4.19 (1 H, m), 4.27−4.29 (1 H, m), 4.58 (1 H, td, *J* = 1.3, 6.3 Hz), 5.40 (1 H, qdd, *J* = 1.6, 6.3, 15.2 Hz), 5.58−5.69 (2 H, m), 5.80 (1 H, qdd, *J* = 1.9, 6.6 Hz), 6.56 (1 H, dd, *J* = 1.9, 15.7 Hz), 7.03 (1 H, dd, *J* = 3.6, 15.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.28, −5.20, −4.86, −4.83, −4.76, −4.60, 17.83, 18.10, 18.14, 18.31, 18.35, 25.79, 25.83, 25.86, 25.88, 63.14, 75.14, 75.21, 79.75, 124.43, 127.80, 128.65, 129.06, 131.01, 146.83, 197.84.

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Supplementary Material Available: Experimental procedures for **19/17**, **21/18**, **i−iv/v**, and selected ^1H and ^{13}C NMR spectra (29 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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