Diastereoselectivity in asymmetric allylations: The role of vicinal chirality in the allyl nucleophile for S_E2' reactions with aldehydes[1]

David R. Williams, Kevin G. Meyer, Khalida Shamim, and Samarjit Patnaik

Abstract: A series of nonracemic homoallylic alcohols have been prepared by asymmetric allylation using the (*R*,*R*)- and (*S*,*S*)-1,2-diamino-1,2-diphenylethane bis-sulfonamide controller ligands for in situ formation of chiral B-allyl-1,3,2-diazaborolidines. Diastereofacial selectivity is influenced by adjacent stereochemistry incorporated into the allyl moiety at C-2, in addition to the expected role of the chiral auxiliary. Additional asymmetry in the aldehyde reactant introduces threefold stereodifferentiation. A model is developed to identify reinforcing stereochemical relationships, and examples have ascertained the relative significance of these factors. The methodology supports the construction of complex homoallylic alcohols in a highly convergent fashion.

Key words: asymmetric allylation, diastereofacial selectivity, 1,4-stereocontrol, homoallylic alcohols.

Résumé : On a préparé une série d'alcools homoallyliques non racémiques en procédant à l'allylation asymétrique à l'aide des ligands de contrôle (*R*,*R*)- et (*S*,*S*)-1,2-diamino-1,2-diphényléthane bis-sulfonamide pour la formation in situ de B-allyl-1,3,2-diazaborolidines chirales. La sélectivité diastéréofaciale est influencée par la stéréochimie adjacente qui est incorporée dans la portion allyle au niveau C-2, en plus du rôle attendu de l'auxiliaire chiral. Une asymétrie additionnelle dans l'aldéhyde utilisé comme réactif introduit une triple stéréodifférenciation. On a développé un modèle pour identifier les relations stéréochimiques qui se renforcent et divers exemples ont permis de confirmer la signification relative de ces facteurs. La méthodologie se prête à la construction d'alcools homoallyliques complexes d'une façon extrêmement convergente.

Mots clés : allylation asymétrique, sélectivité diastéréofaciale, stéréocontrôle 1,4, alcools homoallyliques.

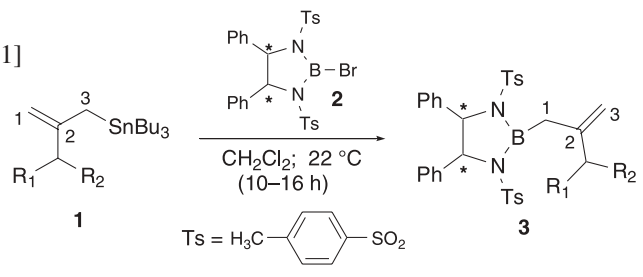
[Traduit par la Rédaction]

Introduction

Asymmetric allylation processes are generally recognized as important tools for stereocontrolled synthesis (1). Impressive levels of stereoselectivity have been achieved for the reactions of allyl and crotyl nucleophiles with aldehydes, leading to the formation of nonracemic homoallylic alcohols (2). Iterations of this scheme are propagated by oxidative cleavage of the terminal olefin and the generation of an aldehyde for sequentially increasing complexity. As often utilized in combination with aldol reactions, asymmetric allylation has provided, in large measure, a significant advance for syntheses of natural products of polyacetate and polypropionate origin (3).

In 1989, Corey and co-workers (4, 5) reported (*R*,*R*)- and (*S*,*S*)-1,2-diamino-1,2-diphenylethane *N*,*N*-sulfonamides as effective chiral auxiliaries to enable enantioselective Diels–Alder, aldol, and allylation reactions. We recognized that the mild conditions needed for transmetalation (eq. [1]) of allylstannanes **1** to nonracemic B-allyl-1,3,2-diazaborolidines **3** with bromoborane **2** would support molecular complexity and functionalization in the allyl segment with substitution at C-2. Thus, asymmetric allylation could prove widely useful for strategic bond formation in a convergent synthesis approach. Recent successes along these lines in our programs, towards hennoxazole A (6), amphidinolide K (7), and phorboxazole A (8), have been encouraging. This study will examine, in detail, the role of vicinal chirality in the allyl component as a result of substitution at the adjacent methylene ($R_1 \neq R_2$ in **1**) of the nascent nucleophile. We will explore the impact of this additional element of asymmetry for stereochemically reinforcing and nonreinforcing relationships with the auxiliary of **3** in the production of diastereomeric alcohols.

[1]



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Dedicated to Professor Ed Piers for his many contributions to organic chemistry.

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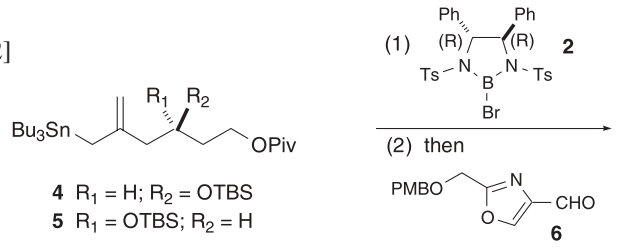
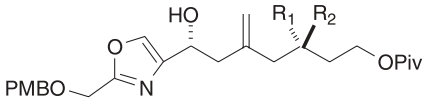
Results and discussion

Our preliminary studies (9) have shown that a range of functionality is tolerated under the ambient conditions of transmetalation of **1** to borane **2**. Examples of compatible functional groups include isolated alkenes, dithioacetals, *para*-methoxybenzyl, and benzyl ethers, esters, vinylstannanes, and most silyl ethers. The presence of Lewis-acid-sensitive protecting groups, such as methoxymethyl (MOM), β-methoxyethoxymethyl (MEM), and tetrahydropyranyl (THP) ethers, as well as other ketals and acetals, are incompatible with bromoborane **2**. Additionally, most allylsilanes do not undergo a productive transmetalation with bromoborane **2**. Upon the in situ formation of allylborane **3** at room temperature, reactions are cooled to –78 °C for the introduction of stoichiometric aldehyde, leading to complete condensations within 2 to 3 h. A variety of functionality may also be incorporated in the aldehyde component. As demonstrated by the reactions of enantiomeric stannanes **4** and **5**, the introduction of a stereogenic center that is separated by at least one methylene unit from the reactive allyl moiety plays little or no role in determining the diastereoselectivity of the condensation. The chiral auxiliary is the major factor to consider in the production of the new chiral alcohols **7** and **8**.

[2]



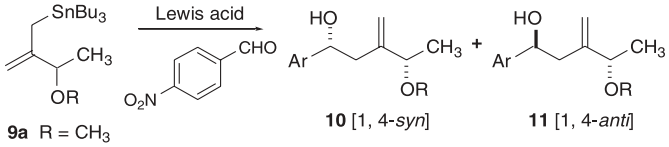
4 R_1 = H; R_2 = OTBS
5 R_1 = OTBS; R_2 = H



7 R_1 = H; R_2 = OTBS
98% yield; >20 : 1 dr
8 R_1 = OTBS; R_2 = H
98% yield; >20 : 1 dr

In previous studies by Nishigaichi et al. (10), moderate stereocontrol in the addition of racemic allylstannanes **9ab** to simple aldehydes was observed. Thus, the placement of methoxy or acetoxy substituents directly adjacent to the reactive allyl component resulted in a diastereofacial preference, which was strongly influenced by the choice of Lewis acid. Related chromium- and indium-mediated allylations (11) have produced 1,4-syn-diol derivatives with diastereomeric excesses of 60–90%.

[3]



9a R = CH_3
9b R = Ac

10 [1, 4-*syn*] **11** [1, 4-*anti*]

With these observations in mind, we have examined the role of adjacent stereogenicity as a control factor for our asymmetric allylations (eq. [1]; $R_1 \neq R_2$). Two general pathways were deployed for the preparation of starting stannanes bearing a chiral carbon at the C-2 allylic position by the introduction of a methyl or hydroxyl substituent.

In the former case, we have utilized our asymmetric conjugate addition methodology (12) for reactions of the alkenylcopper species derived from the Grignard reagent of 2-bromo-3-trimethylsilyl-1-propene (13) with *N*-enoyl-4-phenyl-1,3-oxazolidinone **12**. The imide **13** (diastereomeric ratio (dr) 25:1) was purified by flash chromatography and reduced to yield alcohol **14**, which was subsequently O-protected as the corresponding *tert*-butyldiphenylsilyl ether **15**. Additional complexity was introduced by direct conversion of **14** to the primary iodide **16** for alkylation with 2-lithio-1,3-dithiane, providing the allylsilane **17**. The allylic silanes **15** and **17** were transformed into the desired stannanes **18** and **19** via quantitative, low-temperature reactions to yield the intermediate bromides (R = Br) with subsequent displacement with tri-*n*-butylstannylcopper dimethylsulfide complex (14). In analogous fashion, we also prepared *ent*-**18**.[3] While other routes have been devised and reduced to practice, Scheme 1 offers simplicity and generality.[4]

For the preparation of stannanes bearing an allylic hydroxyl substituent, the aliphatic aldehydes **20** (R = H and R = $CH_2CH{=}CHCH_3$) were converted into the chiral epoxy-alcohols **21** via Wittig olefination, reduction, and Sharpless asymmetric epoxidation (15), as illustrated in Scheme 2.

Mesylation and immediate reduction of crude epoxy sulfonate with zinc dust in the presence of sodium iodide (16) gave optically active **22** in excellent yield. The secondary alcohol in **22** was then used to direct allylic lithiation (17) for C-alkylation with tri-*n*-butylstannyl iodide. Acylation with benzoic anhydride led to pure **23a** (R = H) or **23b** (R = $CH_2CH{=}CH{-}CH_3$) for our allylation experiments.[5]

Results of our allylation studies are assembled in Table 1.[6] Data regarding the stereoselectivity of each condensation reaction was obtained by an initial flash silica-gel column to separate product diastereomers from other organic components, including the chiral auxiliary, which can be recovered and recycled. Thus, overall yields of these attempts were readily assessed, and the ratios of diastereomeric products

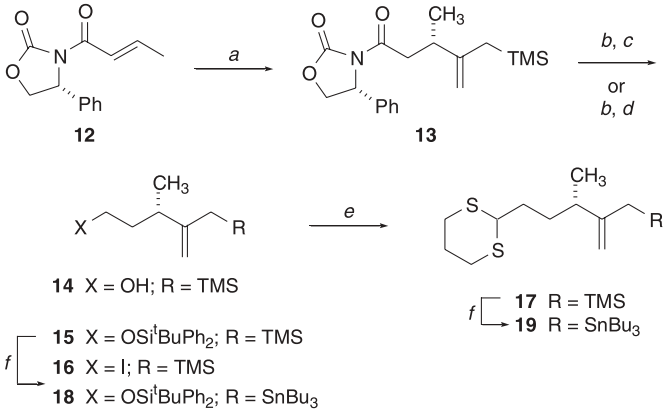
[3] Experimental details for the preparation of allylstannanes **18**, **19**, and *ent*-**18** will be published in the full account of the synthesis of leucascandrolide A.

[4] An alternative method for general introduction of the allylic silane uses methyl ketones for kinetic deprotonation, and transformation to their corresponding vinyl triflates. Cross-coupling with (trimethylsilyl)methyl magnesium chloride in the presence of $Ni(acac)_2$ (THF at 22 °C) yields the C-2-substituted allylic silanes.

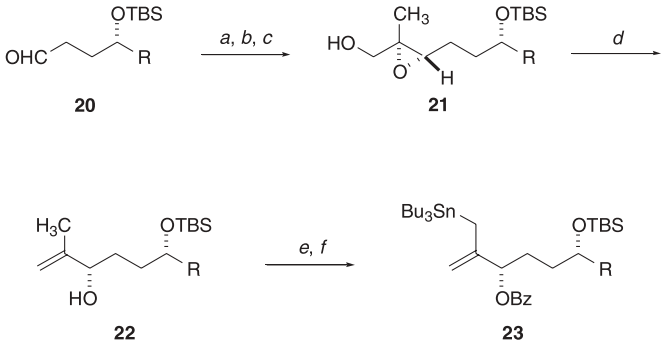
[5] Experimental details for the preparation of stannanes **23a**, **23b**, and (*R*)-**23b** will be published in the full account of our total synthesis of amphidinolide K (see also ref. 7).

[6] We have used a standard set of conditions for these examples of asymmetric allylation, and further attempts to optimize yields or product ratios have not been made in most cases.

Scheme 1. (*a*) CH_2=C(MgBr)CH_2SiMe_3, CuBr·DMS, THF, –78 °C to –30 °C, 90% (>90% diastereomeric excess (de)); (*b*) $LiBH_4$, MeOH, Et_2O, 0 °C, 80%; (*c*) *t*-$BuPh_2SiCl$, imid, DMF, room temperature (rt), 95%; (*d*) DCC·MeI, THF, 88%; (*e*) 2-lithiodithiane, THF, –78 °C to –5 °C, 90%; (*f*) NBS, propylene oxide, –78 °C, CH_2Cl_2:DMF (3:4); then add Bu_3SnLi, CuBr·DMS to crude allyl bromide, 70%–80%.

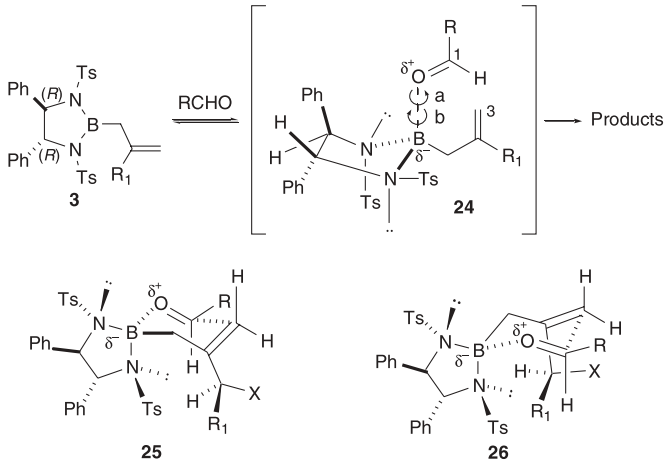


Scheme 2. For R = H or R = CH_2CH=$CHCH_3$; (*a*) $Ph_3PC(CH_3)COOEt$, CH_2Cl_2, rt, 82%; (*b*) DIBAL, CH_2Cl_2, –78 °C, 93%; (*c*) L-(+)-DET, Ti(O-*i*-Pr)$_4$, *t*-BuOOH, CaH_2, 4 Å molecular sieves, CH_2Cl_2, –25 °C, 89% (>97% de); (*d*) MsCl, Et_3N, CH_2Cl_2; then NaI, Zn dust, 2-butanone, 80 °C, 90%; (*e*) *n*-BuLi, TMEDA, Et_2O, rt; then Bu_3SnI, 50%; (*f*) benzoic anhydride, Et_3N, CH_2Cl_2, catalytic amount DMAP, 93%.



were obtained by the integration of selected proton signals in the NMR (400 MHz) spectra. Further confirmations of product ratios in most examples were available via analytical HPLC. In cases that provided a reasonable level of stereoselectivity, the major products were isolated and purified by silica-gel flash chromatography or preparative thin-layer chromatography for complete spectroscopic characterizations. Trace amounts of minor diastereomers or challenging separations from reactions that afforded little selectivity hampered our efforts for full characterization of these materials. However, the stereochemical redundance of our study provided fully characterized major products, which were then compared and identified as minor components in related examples. The assignment of absolute stereochemistry of each purified homoallylic alcohol of Table 1 was determined by Kakisawa analysis of the corresponding Mosher esters (18). Initially, these studies examined reactions with simple aldehydes, as summarized in entries 1 and 2 of Table 1. Reactions were evaluated using bromoborane **2**, bearing the (*R*,*R*)- and the (*S*,*S*)-sulfonamides. The presence of α-stereogenicity in the stannanes **19** and **23a** produced reactions consistent with stereochemically-reinforcing and nonreinforcing relationships with the auxiliaries (19).[7] Best results were obtained using the (*R*,*R*)-**2**, which yielded the 1,4-*syn*-diastereoisomers as major products. The benzoate substituent of **23a** in entry 2 was more effective in reinforcing, as well as countering, the bias of the auxiliary compared with the methyl substitution of **19** in entry 1.

Fig. 1. Diastereofacial selection in allylation reactions.



Our rationale for the stereoselectivity of these reactions is illustrated in the diagrams of Fig. 1. Transmetalation gives the sp^2 hybridized borane **3**, which reversibly binds the aldehyde in the axial orientation **24** and provides a synclinal disposition of the Lewis acid with respect to the aldehydic hydrogen. This complexation serves to activate the electrophilic carbonyl, as well as to trigger nucleophilicity of the allyl moiety. Structure **24** also presents a rehybridization of boron to a tetrahedral geometry, and the five-membered heterocyclic ring assumes a conformation that minimizes the nonbonded interactions of sulfonyl and phenyl substituents. Facial selectivity in **24** is determined by the relative energies of diastereomeric transition states as the reactive C_1 and C_3 carbons approach bonding proximity. Thus, our arguments consider bonding via the closed, chair-like arrangements of **25** and **26** as useful models to depict interactions that may contribute to a difference in transition-state energies. Since facial selectivity is not determined by the initial complexation, we offer the following contrivance to aid the visualization of **24** to **25** and **26** (Fig. 1): This process can be visualized from **24** by a rotation (arrow a) of the carbonyl (approximately 90°) and subsequent attack at the *re* face, as depicted in the favored situation in **25** wherein the illustration of **24** is reoriented by a 90° rotation (allyl is projected forward). On the other hand, rotation of the aldehyde in the clockwise direction in **24** (arrow b) results in the unfavorable nonbonded interactions of the aldehydic hydrogen with the

[7] We have utilized the terms "reinforcing" and "nonreinforcing", as introduced by Evans et al. (19), to describe the relationships of stereochemical elements within a reactant.

Table 1. Asymmetric allylations.

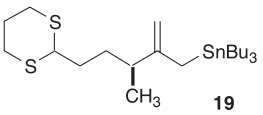
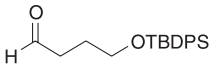
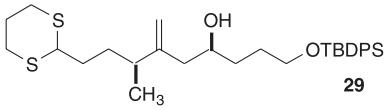
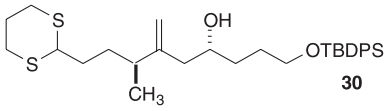
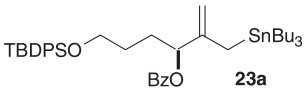
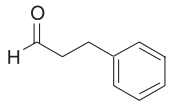
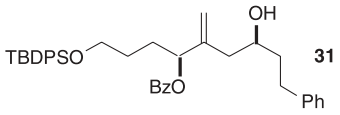
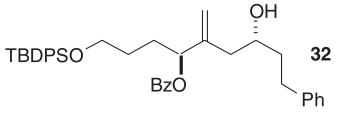
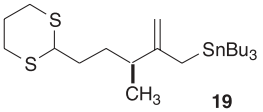
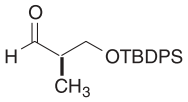
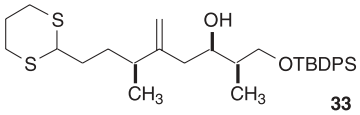
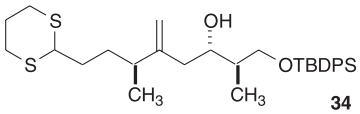
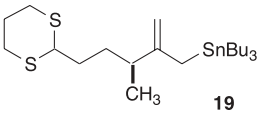
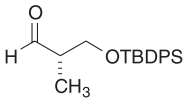
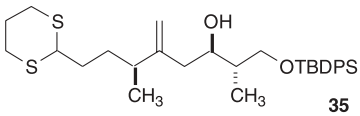
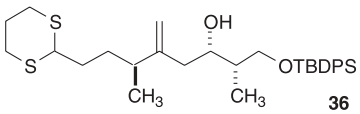
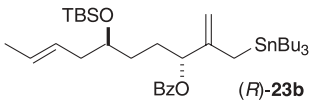
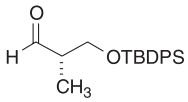
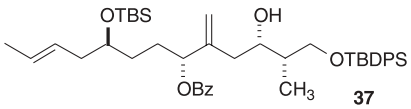
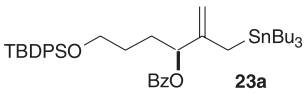
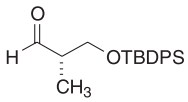
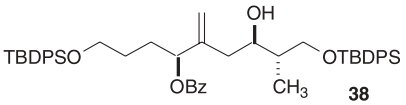
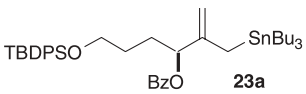
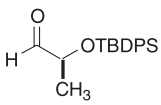
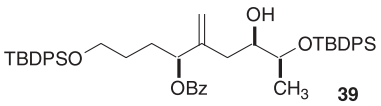
Entry	Stannane	Aldehyde	Sulfonamide	Major Product	Yield[a] dr
1	 **19**		(*R*,*R*)	 **29**	85% 7.7:1[b]
			(*S*,*S*)	 **30**	80% 4:1[b]
2	 **23a**		(*R*,*R*)	 **31**	96% >20:1[c]
			(*S*,*S*)	 **32**	94% 1:1[c]
3	 **19**		(*R*,*R*)	 **33**	77% 15:1[d]
			(*S*,*S*)	 **34**	70% 1.3:1[d]
4	 **19**		(*R*,*R*)	 **35**	75% 5.4:1[d]
			(*S*,*S*)	 **36**	76% 1.7:1[d]
5	 (*R*)-**23b**		(*S*,*S*)	 **37**	56% >25:1[c]
6	 **23a**		(*R*,*R*)	 **38**	83% >20:1[c]
7	 **23a**		(*R*,*R*)	 **39**	56% >20:1[c]

Table 1 (*continued*).

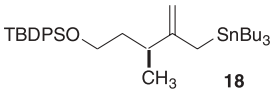
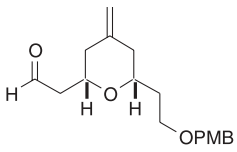
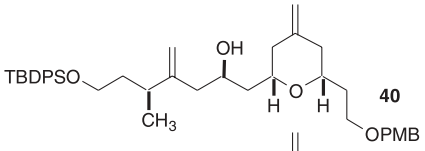
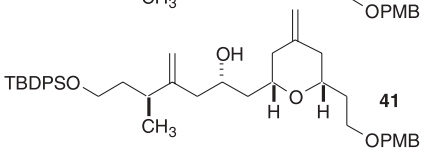
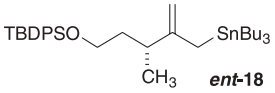
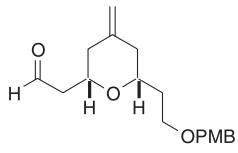
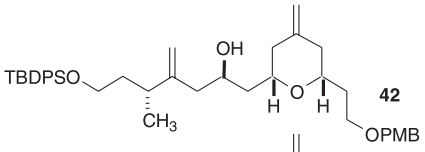
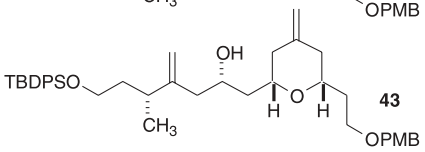
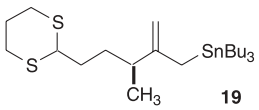
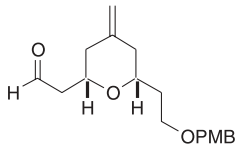
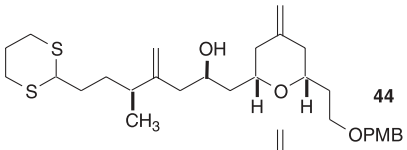
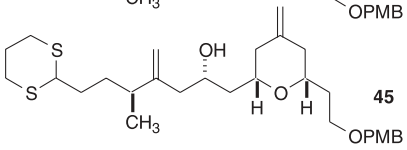
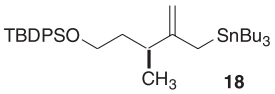
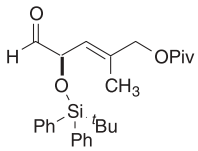
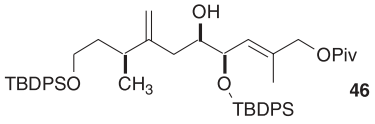
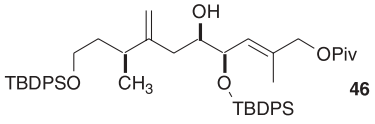
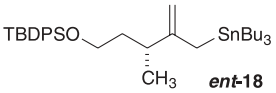
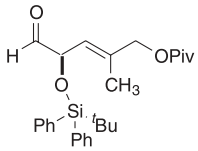
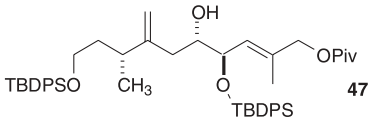
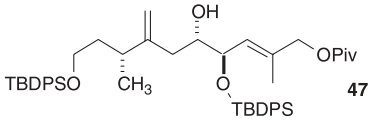
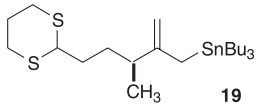
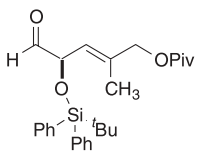
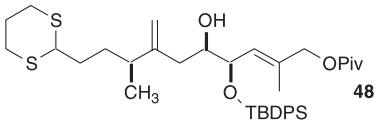
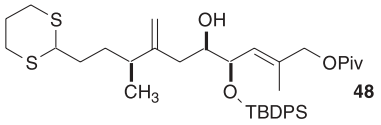
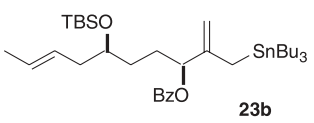
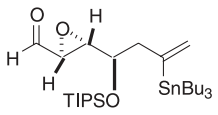
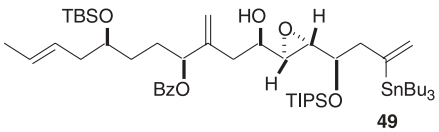
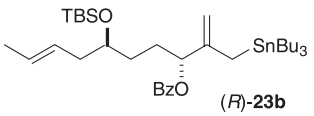
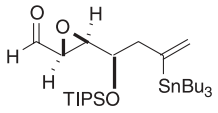
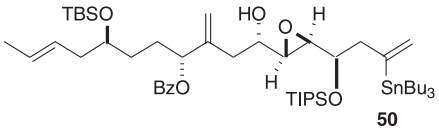
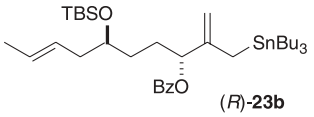
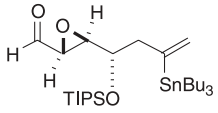
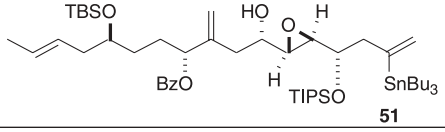
Entry	Stannane	Aldehyde	Sulfonamide	Major Product	Yield[a] dr
8	 **18**		(*R*,*R*)	 **40**	100% 10:1[c]
			(*S*,*S*)	 **41**	98% 2:1[c]
9	 ***ent*-18**		(*R*,*R*)	 **42**	97% 2.2:1[c]
			(*S*,*S*)	 **43**	93% 7:1[c]
10	 **19**		(*R*,*R*)	 **44**	100% 10:1[c]
			(*S*,*S*)	 **45**	78% 2.5:1[c]
11	 **18**		(*R*,*R*)	 **46**	60%[e] 7:1[b]
			(*S*,*S*)	 **46**	77%[e] 1.4:1[b]
12	 ***ent*-18**		(*R*,*R*)	 **47**	80%[e] 1.2:1[b]
			(*S*,*S*)	 **47**	70%[e] 4:1[b]
13	 **19**		(*R*,*R*)	 **48**	82%[e] 4.2:1[b]
			(*S*,*S*)	 **48**	82%[e] 1.5:1[b]

Table 1 (*concluded*).

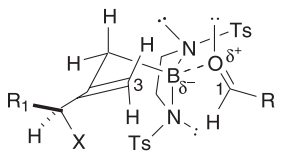
Entry	Stannane	Aldehyde	Sulfonamide	Major Product	Yield[a] dr
14	 **23b**		(*R*,*R*)	 **49**	72% 17:1[b]
15	 (*R*)-**23b**		(*S*,*S*)	 **50**	75% 17:1[b]
16	 (*R*)-**23b**		(*S*,*S*)	 **51**	65% 15:1[b]

Note: TBS = Si-*t*-BuMe$_2$; TBDPS = Si-*t*-BuPh$_2$; Bz = benzoate; Piv = pivaloate.
[a]Yields are based on purified products from flash silica-gel chromatography.
[b]Ratios were determined by HPLC separations of diastereomers on a Zorbax silica column by elution with 1% isopropanol in hexanes.
[c]Ratios were calculated from ^{1}H NMR (400 MHz) data in C_6D_6 via the integration of alkenylic hydrogen signals.
[d]Ratios were determined by HPLC separations on a Chiralpak AD column via elution with 1% isopropanol in hexanes.
[e]Unreacted aldehyde (15%–25%) was recovered in these reactions.

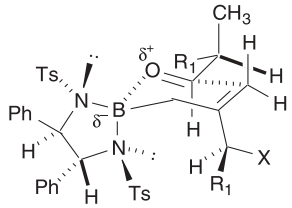
equatorial toluenesulfonyl group of the auxiliary, as shown in **26** (a 90° rotation of **24** with aldehyde projected forward). Thus, our modeling suggests that this nonbonded interaction raises the transition-state energy for *si* face reactions in the case of the (*R*,*R*)-chiral controller (20).

The consequences of steric interactions resulting from allylic branching of the C-2 substituent of **3** introduce an additional level of complexity. As illustrated in Fig. 1, the stereogenic center derived from stannanes such as **19** and **23ab** provides a stereochemically reinforcing scenario in **25** (X = CH_3 or OBz) by a minimization of the A(1,3)-strain, which also directs the methine hydrogen into the region near the sulfonyl group of the auxiliary (21, 22).[8,9] This becomes problematic in the nonreinforcing case, **26**. Aside from steric arguments, the allylic oxygen in the benzoate conformer of **25** (X = OBz) is also anticipated to have electronic effects, which favor the nucleophilic character of the olefin. The composite picture for these allylations suggests that the consequences of isopropyl substitution at C-2 in **25** (X and R_1 = CH_3) is less significant than the interaction of the aldehydic hydrogen and toluenesulfonyl moiety in **26**. This aspect is addressed with greater clarity in Fig. 2, where the proximity of reactive centers at C-1 and C-3 in **27** directs the C-2-branched substituent away from the developing chair. Alternatively, the situation in **26** (Fig. 1) projects the aldehydic hydrogen directly under the six-membered transition state and into the neighboring sulfonyl group. Finally, our models have also incorporated the role of α-chirality in the aldehyde. Diagram **28** in Fig. 2 describes a model for Felkin–Anh addition to the carbonyl while maintaining the favorable relationships of asymmetry, as previously described in **25** (23).[10]

Fig. 2. Preferred transition-state arrangements for asymmetric allylation using (*R*,*R*)-**2**.



27 (Ph's of the (*R*,*R*)-auxiliary have been removed for clarity.)



28

Since the feature of chirality in the aldehyde component multiplies the complexity of the reaction twofold, this aspect was first evaluated with the enantiomerically pure (*R*)- and (*S*)-2-methyl-3-hydroxypropanal derivatives, as shown in entries 3 and 4. The influence of α-stereochemistry in the aldehyde accentuated the reinforcing characteristics of the stannane and the (*R*,*R*)-auxiliary through the expected mode of Felkin–Anh addition (entry 3), yielding predominantly the all-*syn* adduct **33**. On the other hand, it was not sufficient to merely coordinate the chirality of the aldehyde with the (*S*,*S*)-auxiliary **2** in entry 4. This example led to a 1.7:1 mixture of diastereomers; and this points out the importance of allylic stereochemistry in the starting stannane. As observed in reactions with achiral aldehydes, the allylic benzoates **23a** and **23b** led to excellent diastereoselectivity in the matched

[8]The energy requirements for the A(1,3)-strain in **25** (X = CH_3) are estimated to be in the range of 0.4–0.7 kcal/mol, compared with the 1,3-H/H interaction. See ref. 21.
[9]Interestingly, the preferred transition state **25** (X = OBz) may present characteristics that resemble the "inside alkoxy effect" proposed by Stork, Houk, and Jäger for allylic ethers and alcohols. See ref. 22.
[10]Factors for the diastereoselectivity of the aldol reaction using boron enolates derived from chiral ethyl ketones pose some related concerns. Some examples include those found in ref. 23.

cases for Felkin–Anh addition (entries 5 and 7). However, it seems sufficient to coordinate the stereochemically reinforcing asymmetry of the allylic benzoate **23a** with **2** (*R*,*R*) for stereocontrolled condensations via the anti-Felkin mode (entry 6).

Our experiments have also evaluated the effect of β-chirality in the aldehyde, as precipitated by our studies toward leucascandrolide A (24). Tabulated by the results of entries 8, 9, and 10, threefold stereodifferentiation was observed. As documented in previous cases, the cooperation of allylic chirality in the stannane with the auxiliary **2** was a dominant feature. However, the resulting stereochemistry of the major adduct does not conform to the expected result of the Evans polar model for reactions of β-alkoxy aldehydes (19). A challenging situation was also presented by the nonracemic β,γ-unsaturated aldehyde (25)[11] used in entries 11, 12, and 13. Epimerization of this sensitive substrate was avoided, and good yields of condensation products were obtained in spite of considerable steric hindrance. Thus, while the anticipated cooperation of the asymmetry of the stannane and **2** remained intact, the nature of the α-substitution in the aldehyde failed to deliver a clear preference for Felkin or anti-Felkin arrangements. More extensive studies will be needed to probe the issues raised by these entries.

Finally, the versatility of this approach is displayed by the functional complexity of the aldehydes used for entries 14, 15, and 16.[12] Our plans recognized the reinforcing characteristics of stannane **23b** and (*R*,*R*)-**2**, as well as the inherent Felkin–Anh face selectivity for the nonracemic epoxy–aldehyde, as shown in entry 14. This situation is remarkably predictable, as demonstrated by the use of the diastereomeric stannane (*R*)-**23b** in entry 15, which yielded a productive reaction with the (*S*,*S*)-sulfonamide auxiliary and provided for Felkin–Anh addition to give the homoallylic alcohol **50**. The presence of the additional stereocenter at C-4 in the aldehyde (OTIPS of entries 15 and 16) did not impact the stereoselectivity in a major way and demonstrates the flexibility of this methodology for the synthesis of a family of complex diastereoisomers.

Experimental section

General

Infrared spectra were recorded on a Mattson Galaxy 4020 FT-IR instrument with use of an internal standard. Proton and carbon spectra were recorded on a 400 MHz spectrometer in FT mode. Proton chemical shifts are reported in δ, using as a reference the appropriate signal for residual solvent protons, as follows: 7.26 for *d*-chloroform and 7.20 for d_6-benzene. Carbon chemical shifts are reported in δ, using the center peak of the solvent signal as a reference, as follows: 77.0 for $CDCl_3$. Mass spectra were obtained on a Kratos MS80 RFAQQ instrument. Optical rotations were measured using a PerkinElmer 241 polarimeter. Concentration (*c*) is reported as g/100 mL, and temperature is room temperature. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled from sodium benzophenone ketyl. Dimethylformamide (DMF), methylene chloride (CH_2Cl_2), pyridine, oxalyl chloride, triethylamine (Et_3N), benzene, and toluene were distilled from calcium hydride. Ethyl acetate (EtOAc) and hexanes for chromatography were distilled from glass prior to use. Column chromatography was conducted using silica gel 60 (230–400 mesh) from E.M. Science. Precoated glass plates 60F-254 (E. Merck, 0.25 mm and 0.50 mm thickness) were used for analytical and preparative thin layer chromatography (TLC). Reactions were carried out in flame-dried glassware under an inert atmosphere. Elemental analyses were performed by Galbraith Laboratories, Tenn., U.S.A.

General allylation procedure

A 35 mL Schlenk flask was charged with (*S*,*S*) or (*R*,*R*)-*N*,*N*′-bis-*para*-toluenesulfonyl-1,2-diamino-1,2-diphenylethane (0.22 g, 0.42 mmol) and heated to ~90 °C under vacuum (30 Pa). After 12 h, the resulting white solid was cooled to room temperature and CH_2Cl_2 (4 mL) was added under an argon atmosphere. The resultant solution was cooled to 0 °C and treated with fresh boron tribromide (0.42 mL of a 1.0 mol L^{-1} solution in CH_2Cl_2 (Aldrich®), 0.42 mmol). The resulting orange solution was stirred at 0 °C for 10 min, warmed to room temperature, and stirred for 1 h. The solvent and HBr were removed carefully under reduced pressure (0.2 mmHg). The resulting solid was dissolved in CH_2Cl_2 (4 mL), stirred for 10 min, and concentrated under high vacuum. The yellow solid was diluted again with CH_2Cl_2 (4 mL) and cooled to 0 °C, and a solution of the allylstannane (0.47 mmol) in CH_2Cl_2 (~1 mL) was added. The yellow solution was stirred for 16 h at room temperature. After this time the reaction was cooled to –78 °C, and a solution of aldehyde (0.31 mmol) in CH_2Cl_2 (~1 mL) was added. The reaction mixture was stirred at –78 °C for 2 h and then quenched with pH 7 buffer (1 mL). The mixture was allowed to warm to room temperature and diluted with CH_2Cl_2 (15 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (15 mL). The aqueous phase was extracted with CH_2Cl_2 (15 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated in vacuo. The resulting solid was dissolved in Et_2O and filtered to recover the sparingly soluble bis-sulfonamide chiral auxiliary. The filtrate was concentrated in vacuo, and the residue was purified by flash silica-gel chromatography to yield the mixture of secondary homoallylic alcohols. Diastereomeric ratios were initially determined by the integration of selected proton signals in NMR (400 MHz) spectra. Product ratios were also obtained by analytical HPLC (see notes of Table 1 for conditions). Major diastereomers were purified by flash column chromatography or preparative TLC (silica gel) for full characterization. Solvents for chromatography and data for full characterization of major adducts are included below.

(4*S*,7*S*)-1-(*tert*-Butyldiphenylsilanyloxy)-9-([1,3]dithian-2-yl)-7-methyl-6-methylene-nonan-4-ol (29)

Application of the allylation procedure above led to the

[11]The route for preparation of the nonracemic β,γ-unsaturated aldehyde (entries 11, 12, and 13 of Table 1) has been previously described; see ref. 25 and also ref. 8.

[12]The preparation of optically active aldehydes for entries 14, 15, and 16 has been described in the course of our total synthesis of amphidinolide K. Experimental details are found in the supporting information of ref. 7.

isolation of **29** (entry 1, Table 1) as the major adduct, which was characterized as follows: R_f = 0.52 in 10% EtOAc–hexanes. IR (neat) (cm^{-1}): 3453, 3070, 3043, 2952, 2926, 2850, 1109. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.70–7.67 (m, 4H), 7.45–7.36 (m, 6H), 4.91 (s, 1H), 4.87 (s, 1H), 4.02 (t, *J* = 6.4 Hz, 1H), 3.78–3.69 (m, 3H), 2.95–2.78 (m, 4H), 2.22 (dd, *J* = 3.8, 14.4 Hz, 1H), 2.18 (br s, 1H), 2.14–2.04 (m, 3H), 1.91–1.78 (m, 1H), 1.77–1.46 (m, 8H), 1.06 (s, 9H), 1.04 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 150.7, 135.5, 133.7, 129.5, 127.6, 110.9, 69.1, 64.0, 47.7, 42.5, 39.4, 33.7, 33.2, 32.0, 30.4, 28.8, 26.8, 25.9, 20.1, 19.1. HR-MS *m/e* calcd. for $C_{31}H_{44}OS_2Si$ ($[M - H_2O]^+$): 524.2603; found: 524.2607.

(4*R*,7*S*)-1-(*tert*-Butyldiphenylsilanyloxy)-9-([1,3]dithian-2-yl)-7-methyl-6-methylene-nonan-4-ol (30)

Application of the allylation procedure above led to the isolation of **30** (entry 1, Table 1) as the major adduct, which was characterized as follows: R_f = 0.54 in 10% EtOAc–hexanes. IR (neat) (cm^{-1}): 3448, 3071, 3045, 2930, 2856, 2850, 1111. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.70–7.65 (m, 4H), 7.45–7.36 (m, 6H), 4.92 (s, 1H), 4.88 (s, 1H), 4.02 (t, *J* = 6.4 Hz, 1H), 3.80–3.68 (m, 3H), 2.90–2.80 (m, 4H), 2.22 (dd, *J* = 3.8, 14.4 Hz, 1H), 2.17 (br s, 1H), 2.15–2.04 (m, 3H), 1.91–1.80 (m, 1H), 1.76–1.48 (m, 8H), 1.08–1.02 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 150.8, 135.5, 133.8, 129.6, 127.5, 111.1, 69.0, 64.1, 47.7, 42.8, 38.9, 33.8, 33.3, 32.4, 30.4, 28.8, 26.8, 26.0, 19.7, 19.1. HR-MS *m/e* calcd. for $C_{31}H_{44}OS_2Si$ ($[M - H_2O]^+$): 524.2603; found: 524.2598.

(3*S*,6*S*)-6-Benzoyloxy-9-(*tert*-butyldiphenylsiloxy)-5-methylene-1-phenyl-nonan-3-ol (31)

The allylation procedure above led to alcohol **31** (entry 2, Table 1) as a single diastereoisomer, characterized as follows: R_f = 0.40 in 30% EtOAc–hexanes. $[\alpha]_D$ +17.6 (*c* 3.95, $CHCl_3$). IR (neat) (cm^{-1}): 3493, 3070, 2930, 2856, 1711, 1502, 1273, 1072. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.04 (m, 2H), 7.75–7.15 (m, 18H), 5.32 (dd, *J* = 8.0, 4.5 Hz, 1H), 5.14 (s, 1H), 4.98 (s, 1H), X of ABX (δ: 3.81, m, 1H), 3.71 (m, 2H), 3.24 (br s, 1H), 2.85 (m, 1H), 2.70 (m, 1H), AB of ABX (δ_A: 2.31, δ_B: 2.03, J_{AB} = 13.8 Hz, J_{AX} = 5.7 Hz, J_{BX} = 6.1 Hz, 2H), 2.00–1.60 (m, 6H), 1.06 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.5, 146.1, 142.3, 135.5, 134.7, 133.9, 133.1, 130.1, 129.6, 128.4, 128.3, 127.7, 127.6, 125.7, 113.2, 77.9, 71.6, 63.4, 41.5, 39.0, 32.1, 29.9, 28.7, 26.8, 19.2. HR-MS *m/z* calcd. for $C_{39}H_{46}O_4Si$ ($[M]^+$): 606.3165; found: 606.3119.

(3*R*,6*S*)-6-Benzoyloxy-9-(*tert*-butyldiphenylsiloxy)-5-methylene-1-phenyl-nonan-3-ol (32)

Application of the allylation procedure above led to compound **32** (entry 2, Table 1), which was characterized as follows: R_f = 0.40 in 30% EtOAc–hexanes. $[\alpha]_D$ +17.2 (*c* 3.67, $CHCl_3$). IR (neat) (cm^{-1}): 3491 (br), 3070, 2937, 1961, 1888, 1822, 1712, 1602, 1471. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.05 (m, 2H), 7.75–7.15 (m, 18H), 5.23 (dd, *J* = 8.0, 3.9 Hz, 1H), 5.13 (s, 1H), 4.98 (s, 1H), X of ABX (δ: 4.00, m, 1H), 3.71 (m, 2H), 2.88 (m, 1H), 2.83 (br s, 1H), 2.70 (m, 1H), AB of ABX (δ_A: 2.30, δ_B: 2.22, J_{AB} = 13.8 Hz, J_{AX} = 5.7 Hz, J_{BX} = 6.1 Hz, 2H), 2.00–1.60 (m, 6H), 1.06 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.4, 144.9, 142.3, 135.5, 134.7, 133.8, 133.1, 130.1, 129.6, 128.4, 128.3, 127.7, 127.6, 125.7, 113.4, 75.9, 67.9, 63.3, 42.5, 38.6, 32.4, 30.2, 28.6, 25.8, 19.2. HR-MS *m/z* calcd. for $C_{39}H_{46}O_4Si$ ($[M]^+$): 606.3165; found: 606.3169.

(2*R*,3*R*,6*S*)-1-(*tert*-Butyldiphenylsilanyloxy)-8-([1,3]dithian-2-yl)-2,6-dimethyl-5-methylene-octan-3-ol (33)

Application of the allylation procedure above led to the isolation of **33** (entry 3, Table 1) as the major adduct, which was characterized as follows: R_f = 0.55 in 25% EtOAc–hexanes. IR (neat) (cm^{-1}): 3504, 3071, 3046, 2955, 2932, 2857, 1639, 1428, 1113. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.70–7.65 (m, 4H), 7.46–7.38 (m, 6H), 4.91–4.86 (m, 2H), 4.07–3.99 (m, 2H), 3.74–3.65 (m, 2H), 2.90–2.76 (m, 4H), 2.47 (br s, 1H), 2.20–2.06 (m, 4H), 1.91–1.61 (m, 5H), 1.61–1.51 (m, 1H), 1.07 (s, 9H), 1.04 (d, *J* = 7.2 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 150.8, 135.6, 135.5, 133.3, 133.1, 129.7, 129.7, 127.6, 110.6, 70.9, 67.9, 47.7, 39.5, 39.2, 33.2, 32.2, 30.4, 26.8, 26.0, 20.1, 19.1, 10.3. HR-MS *m/e* calcd. for $C_{31}H_{44}O_1S_2Si$ ($[M - H_2O]^+$): 524.2603; found: 524.2600.

(2*S*,3*R*,6*S*)-1-(*tert*-Butyldiphenylsilanyloxy)-8-([1,3]dithian-2-yl)-2,6-dimethyl-5-methylene-octan-3-ol (35)

Application of the allylation procedure above led to the isolation of **35** (entry 4, Table 1) as the major adduct, which was characterized as follows: R_f = 0.55 in 25% EtOAc–hexanes. IR (neat) (cm^{-1}): 3506, 3071, 3048, 2958, 2931, 2857, 1639, 1427, 1112. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.71–7.66 (m, 4H), 7.46–7.36 (m, 6H), 4.91 (s, 1H), 4.89 (s, 1H), 4.02 (t, *J* = 6.4 Hz, 1H), 3.84–3.76 (m, 1H), 3.79 (dd, *J* = 4.8, 10.0 Hz, 1H), 3.68 (dd, *J* = 6.2, 10.0 Hz, 1H), 2.90–2.76 (m, 4H), 2.31 (dd, *J* = 2.4, 14.8 Hz, 1H), 2.20–2.05 (m, 3H), 1.90–1.62 (m, 5 H), 1.61–1.51 (m, 1H), 1.07 (s, 9H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 151.0, 135.6, 133.2, 130.0, 127.7, 110.6, 72.3, 67.1, 47.7, 40.2, 39.7, 39.3, 33.3, 32.1, 30.4, 26.8, 26.0, 20.2, 19.2, 13.6. HR-MS *m/e* calcd. for $C_{31}H_{44}O_1S_2Si$ ($[M - H_2O]^+$): 524.2603; found: 524.2609.

(2*S*,3*S*,6*R*,9*S*)-6-Benzoyloxy-9-(*tert*-butyldimethylsilyloxy)-1-(*tert*-butyldiphenylsilyloxy)-2-methyl-5-methylene-tridec-11-(*E*)-en-3-ol (37)

The general allylation procedure described above led to the isolation of **37** (entry 5; Table 1) as a single diastereoisomer, as characterized by the following data: R_f = 0.20 in 5% EtOAc–hexanes. $[\alpha]_D$ –24.1 (*c* 1.10, $CHCl_3$). IR (neat) (cm^{-1}): 3503 (br), 3067, 2933, 2860, 1714, 1464, 1273, 1105, 706. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.15 (m, 2H), 7.68 (m, 4H), 7.56 (m, 1H), 7.41 (m, 8H), 5.42 (m, 2H), 5.33 (m, 1H), 5.15 (s, 1H), 5.01 (s, 1H), 4.10 (m, 1H), 3.70 (m, 3H), 3.36 (d, *J* = 2.4 Hz, 1H), 2.29 (dd, A of ABX, J_{AB} = 14.2 Hz, J_{AX} = 4.1 Hz, 1H), 2.22 (dd, B of ABX, J_{BA} = 14.2 Hz, J_{BX} = 9.2 Hz, 1H), 2.14 (app t, *J* = 5.7 Hz, 2H), 1.90 (m, 1H), 1.79 (m, 1H), 1.63 (d, *J* = 5.1 Hz, 3H), 1.62 (m, 1H), 1.48 (m, 1H), 1.06 (s, 9H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.1, 146.0, 135.7, 135.6, 133.0, 130.3, 129.7, 129.5, 128.3, 127.7, 127.5, 127.4, 112.8, 77.7, 73.0, 71.9, 68.0, 40.4, 39.5, 38.2, 32.5, 29.1, 26.9, 25.9, 19.2, 18.0, 10.5, –4.4, –4.6. HR-MS (FAB, NBA)

m/*z* calcd. for $C_{44}H_{65}O_5Si_2$ ([M + H]$^+$): 729.4371; found: 729.4363.

(2*S*,3*R*,6*S*)-6-Benzoyloxy-1,9-bis-(*tert*-butyldiphenylsilyloxy)-2-methyl-5-methylene-nonan-3-ol (38)

The allylation procedure above led to the isolation of **38** (entry 6, Table 1) as a single diastereoisomer, characterized as follows: R_f = 0.45 in 50% EtOAc–hexanes. $[\alpha]_D$ +22.3 (*c* 2.80, $CHCl_3$). IR (neat) (cm^{-1}): 3504 (br), 3070, 2957, 2930, 2856, 1709, 1427, 1273, 1111, 702. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 7.2 Hz, 2H), 7.74–7.35 (m, 23H), 5.41 (dd, *J* = 7.5, 4.8 Hz, 1H), 5.18 (9s, 1H), 5.06 (s, 1H), 3.86 (m, 1H), 3.72 (m, 4H), 3.63 (br s, 1H), 2.44 (dd, A of ABX, J_{AB} = 14.2 Hz, J_{AX} = 1.9 Hz, 1H), 2.14 (dd, B of ABX, J_{BA} = 14.2 Hz, J_{BX} = 10.0 Hz, 1H), 1.90 (m, 3H), 1.70 (m, 2H), 1.07 (s, 9H), 0.98 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.2, 146.0, 135.6, 135.5, 133.9, 133.8, 133.4, 133.0, 130.3, 129.6, 129.5, 129.5′, 128.4, 127.7, 127.6, 113.2, 77.7, 74.4, 66.9, 63.5, 40.5, 38.3, 29.8, 28.7, 26.8, 19.1, 13.7. HR-MS (FAB, NBA, Na$^+$) *m*/*z* calcd. for $C_{50}H_{62}O_5Si_2Na$ ([M + Na]$^+$): 821.4034; found: 821.4039.

(2*S*,3*R*,6*S*)-6-Benzoyloxy-2,9-bis-(*tert*-butyldiphenylsilyloxy)-5-methylene-nonan-3-ol (39)

The allylation procedure above led to the isolation of **39** (entry 7, Table 1) as a single diastereoisomer, characterized as follows: R_f = 0.45 in 10% EtOAc–hexanes. $[\alpha]_D$ +9.5 (*c* 1.84, $CHCl_3$). IR (neat) (cm^{-1}): 3489 (br), 3070, 2932, 2858, 1718, 1427, 1271, 1109, 702. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (d, *J* = 7.2 Hz, 2H), 7.68 (m, 8H), 7.56 (m, 1H), 7.40 (m, 14H), 5.39 (t, *J* = 6.4 Hz, 1H), 5.13 (s, 1H), 4.94 (s, 1H), 3.86 (m, 1H), 3.78 (m, 1H), 3.69 (app t, *J* = 6.1 Hz, 2H), 2.77 (br s, 1H), 2.34 (dd, A of ABX, J_{AB} = 14.6 Hz, J_{AX} = 3.0 Hz, 1H), 2.08 (dd, B of ABX, J_{BA} = 14.6 Hz, J_{BX} = 9.6 Hz, 1H), 1.86 (m, 2H), 1.64 (m, 2H), 1.08 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.0, 145.1, 135.8, 135.5, 134.3, 133.9, 133.6, 132.9, 130.3, 129.7, 129.6, 128.4, 127.7, 127.5, 113.4, 77.6, 74.7, 72.4, 63.5, 35.5, 29.6, 28.6, 27.0, 26.9, 19.3, 19.2, 17.7. MS (CI, NH_3) *m*/*z* (relative intensity) 606 (25), 349 (42),302 (47), 235 (56). HR-MS *m*/*z* calcd. for $C_{45}H_{51}O_5Si_2$ ([M – *t*-Bu]$^+$): 727.3295; found: 727.3252.

(2*R*,5*S*)-7-(*tert*-Butyldiphenylsilanyloxy)-1-{(2*S*,6*R*)-6-[2-(4-methoxy-benzyloxy)-ethyl]-4-methylene-tetrahydro-pyran-2-yl}-5-methyl-4-methylene-heptan-2-ol (40)

Application of the allylation procedure above led to the isolation of **40** (entry 8, Table 1) as the major adduct, which was characterized as follows: R_f = 0.45 in 25% EtOAc–hexanes. IR (neat) (cm^{-1}): 3496, 3070, 2932, 2857, 1649, 1610, 1513, 1427, 1248, 1111. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70–7.65 (m, 4H), 7.44–7.35 (m, 6H), 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.83 (s, 1H), 4.80 (s, 1H), 4.71 (app s, 2H), 4.45–4.39 (m, 2H), 4.00 (m, 1H), 3.80 (s, 3H), 3.71–3.63 (m, 2H), 3.67 (br s, 1H), 3.55–3.48 (m, 4H), 2.35 (ddt, *J* = 6.8, 6.8, 6.8 Hz, 1H), 2.27–2.14 (m, 3H), 2.08 (dd, *J* = 6.4, 14.8 Hz, 1H), 2.00–1.93 (m, 2H), 1.88–1.48 (m, 6H), 1.05 (s, 9H), 0.99 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.1, 151.3, 143.8, 135.6, 134.7, 130.6, 129.5, 129.3, 127.6, 113.8, 110.1, 108.9, 79.2, 76.1, 72.7, 70.0, 66.5, 62.1, 55.2, 42.5, 42.3, 41.1, 40.6, 38.4, 36.3, 36.1, 26.9, 19.8, 19.2. HR-MS *m*/*e* calcd. for $C_{37}H_{47}O_5Si$ ([M – *t*-Bu]$^+$): 599.3193; found: 599.3193.

(2*S*,5*R*)-7-(*tert*-Butyldiphenylsilanyloxy)-1-{(2*S*,6*R*)-6-[2-(4-methoxy-benzyloxy)-ethyl]-4-methylene-tetrahydro-pyran-2-yl}-5-methyl-4-methylene-heptan-2-ol (43)

Application of the allylation procedure above led to the isolation of **43** (entry 9, Table 1) as the major adduct, which was characterized as follows: R_f = 0.47 in 25% EtOAc–hexanes. IR (neat) (cm^{-1}): 3477, 3071, 2932, 2857, 1646, 1603, 1513, 1425, 1248, 1111. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70–7.68 (m, 4H), 7.45–7.35 (m, 6H), 7.26 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 4.85 (s, 1H), 4.81 (s, 1H), 4.72 (app s, 2H), 4.44–4.37 (m, 2H), 4.06 (m 1H), 3.80 (s, 3H), 3.72–3.65 (m, 2H), 3.63–3.45 (m, 4H), 2.80 (br s, 1H), 2.36 (ddt, *J* = 6.8, 6.8, 6.8 Hz, 1H), 2.25–1.52 (m, 12H), 1.07 (s, 9H), 1.00 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.1, 151.2, 144.3, 135.5, 134.0, 130.6, 129.5, 129.2, 127.6, 113.8, 110.3, 108.7, 76.0, 75.8, 72.6, 66.6, 66.4, 62.1, 55.2, 42.5, 42.1, 40.7, 40.5, 38.2, 36.4, 36.1, 26.9, 20.0, 19.2. HR-MS *m*/*e* calcd. for $C_{37}H_{47}O_5Si$ ([M – *t*-Bu]$^+$): 599.3193; found: 599.3201.

(2*R*,5*S*)-7-([1,3]Dithian-2-yl)-1-{(2*S*,6*R*)-6-[2-(4-methoxy-benzyloxy)-ethyl]-4-methylene-tetrahydro-pyran-2-yl}-5-methyl-4-methylene-heptan-2-ol (44)

The same procedure for allylation was applied here and led to the isolation of **44** (entry 10, Table 1): R_f = 0.32 in 25% EtOAc–hexanes. IR (neat) (cm^{-1}): 3480, 3070, 2935, 1650, 1607, 1512, 1247, 1095. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.25 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.86 (s, 1H), 4.83 (s, 1H), 4.71 (app s, 2H), 4.45–4.39 (m, 2H), 4.04–3.98 (m, 2H), 3.80 (s, 3H), 3.58–3.50 (m, 4H), 2.90–2.78 (m, 4H), 2.27–2.05 (m, 6H), 2.02–1.92 (m, 2H), 1.89–1.50 (m, 10H), 1.03 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.1, 150.5, 143.7, 130.5, 129.3, 113.7, 110.7, 109.0, 79.4, 76.0, 72.7, 70.1, 66.4, 55.2, 47.8, 42.3, 42.1, 41.0, 40.5, 39.4, 36.2, 33.1, 32.3, 30.4, 26.0, 20.0. HR-MS *m*/*e* calcd. for $C_{29}H_{44}O_4S_2Na$ ([M + Na]$^+$): 543.2591; found: 543.2581.

2,2-Dimethylpropionic acid (4*R*,5*R*,8*S*)-(*E*)-4,10-bis-(*tert*-butyldiphenylsilanyloxy)-5-hydroxy-2,8-dimethyl-7-methylene-dec-2-enyl ester (46)

Application of the allylation procedure above led to the isolation of **46** (entry 11, Table 1) as the major adduct, which was characterized as follows: R_f = 0.68 in 33% EtOAc–hexanes. IR (neat) (cm^{-1}): 3445, 3071, 3049, 2959, 2931, 2857, 1731, 1428, 1282, 1112. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73–7.63 (m, 8H), 7.45–7.30 (m, 12H), 5.38 (d, *J* = 9.6 Hz, 1H), 4.81 (s, 1H), 4.80 (s, 1H), 4.27 (dd, *J* = 6.4, 9.2 Hz, 1H), 4.14 (s, 2H), 3.73–3.60 (m, 3H), 2.54 (d, *J* = 3.6 Hz, 1H), 2.33 (ddt, *J* = 6.8, 6.8, 6.8 Hz, 1H), 2.16 (m, 1H), 1.94 (dd, *J* = 9.6, 14.8 Hz, 1H), 1.79–1.70 (m, 1H), 1.56–1.46 (m, 1H), 1.15 (s, 9H), 1.07–1.02 (m, 21 H), 0.94 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 178.0, 150.7, 135.9, 135.8, 135.5, 134.0, 133.6, 129.8, 129.6, 129.5, 127.7, 127.6, 127.4, 126.0, 72.9, 72.6, 68.8, 62.1, 38.8, 38.1, 36.7, 35.8, 27.2, 27.0, 26.9, 19.9, 19.3, 19.2,

14.2. HR-MS *m/e* calcd. for $C_{46}H_{59}O_5Si$ ([M – *t*-Bu]$^+$): 747.3901; found: 747.3909.

2,2-Dimethylpropionic acid (4*R*,5*S*,8*R*)-(*E*)-4,10-bis-(*tert*-butyldiphenylsilanyloxy)-5-hydroxy-2,8-dimethyl-7-methylene-dec-2-enyl ester (47)

Application of the allylation procedure above led to the isolation of **47** (entry 12, Table 1) as the major adduct, which was characterized as follows: R_f = 0.68 in 33% EtOAc–hexanes. IR (neat) (cm^{-1}): 3513, 3071, 3047, 2959, 2930, 2857, 1731, 1427, 1282, 1149, 1112. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70–7.60 (m, 8H), 7.45–7.34 (m, 12H), 5.52 (d, *J* = 9.2 Hz, 1H), 4.74 (s, 1H), 4.66 (s, 1H), 4.32 (dd, *J* = 4.0, 9.6 Hz, 1H), 4.26 (s, 2H), 3.8 (m, 1H), 3.70–3.60 (m, 2H), 2.28 (br s, 1H), 2.28–2.10 (m, 2H), 2.02 (dd, *J* = 8.8, 15.2 Hz, 1H), 1.74–1.66 (m, 1H), 1.52–1.43 (m, 1H), 1.17 (s, 9H), 1.05–1.02 (m, 21 H), 0.90 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 178.0, 151.1, 135.9, 135.9, 135.5, 133.4, 134.0, 133.4, 129.7, 129.6, 129.5, 127.6, 127.6, 127.4, 126.8, 73.6, 73.5, 68.5, 62.1, 38.8, 38.1, 37.3, 35.5, 27.2, 27.0, 26.9, 20.0, 19.4, 19.2, 14.1. HR-MS *m/e* calcd. for $C_{46}H_{59}O_5Si$ ([M – *t*-Bu]$^+$): 747.3901; found: 747.3897.

2,2-Dimethylpropionic acid (4*R*,5*R*,8*S*)-(*E*)-4-(*tert*-butyldiphenylsilanyloxy)-5-hydroxy-10-([1,3]dithian-2-yl)-2,8-dimethyl-7-methylene-dec-2-enyl ester (48)

The same procedure for allylation was applied here and led to the isolation of **48** (entry 13, Table 1): R_f = 0.59 in 33% EtOAc–hexanes. IR (neat) (cm^{-1}): 3551, 3071, 2952, 2929, 2852, 1728, 1432, 1275, 1145, 1110. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69–7.62 (m, 4H), 7.43–7.32 (m, 6H), 5.39 (d, *J* = 9.6 Hz, 1H), 4.85 (s, 1H), 4.84 (s, 1H), 4.29 (dd, *J* = 6.2, 9.4 Hz, 1H), 4.16 (s, 2H), 4.00 (t, *J* = 6.8 Hz, 1H), 3.67 (m, 1H), 2.90–2.76 (m. 4H), 2.53 (d, *J* = 4 Hz, 1H), 2.21–2.05 (m, 3H), 1.95 (dd, *J* = 9.6, 15.2 Hz, 1H), 1.90–1.80 (m, 1H), 1.76–1.60 (m, 2H), 1.55–1.46 (m, 1H), 1.16 (s, 9H), 1.07 (s, 3H), 1.05 (s, 9H), 0.98 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 178.0, 150.5, 136.0, 136.0, 135.9, 134.1, 133.7, 133.5, 129.8, 129.7, 127.7, 127.4, 126.7, 73.8, 73.4, 68.5, 47.8, 39.2, 38.8, 37.0, 33.2, 32.1, 30.4, 27.1, 27.0, 26.0, 20.0, 19.4, 14.1. HR-MS *m/e* calcd. for $C_{34}H_{47}O_4S_2Si$ ([M – *t*-Bu]$^+$): 611.2685; found: 611.2690.

(4*R*,5*R*,6*S*,7*R*,10*S*,13*S*)-10-Benzoyloxy-13-(*tert*-butyldimethylsiloxy)-5,6-epoxy-9-methylene-2-tributylstannyl-4-triisopropylsiloxy-heptadeca-1,15-(*E*)-dien-7-ol (49)

The allylation procedure above led to the isolation of **49** (entry 14, Table 1) as a single diastereoisomer, characterized as follows: R_f = 0.20 in 5% EtOAc–hexanes. $[\alpha]_D$ +6.69 (*c* 1.44, $CHCl_3$). IR (neat) (cm^{-1}): 3489 (br), 2955, 2928, 2854, 1720, 1462, 1271, 1113, 1068. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (d, *J* = 7.2 Hz, 2H), 7.57 (m, 1H), 7.44 (m, 2H), 5.81 (s, 1H), 5.50–5.30 (m, 3H), 5.23 (d, *J* = 2.2 Hz, 1H), 5.18 (s, 1H), 5.06 (s, 1H), 4.12 (m, 1H), 3.90 (m, 1H), 3.69 (dddd, *J* = 5.9, 5.9, 5.7, 5.3 Hz, 1H), 3.15 (dd, *J* = 4.0, 2.0 Hz, 1H), 3.05 (dd, *J* = 2.2, 2.1 Hz, 1H), 2.85 (d, *J* = 2.0 Hz, 1H), 2.71 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.50–2.40 (m, 2H), 2.18 (dd, *J* = 14.2, 9.4 Hz, 1H), 2.14 (m, 2H), 1.84 (m, 2H), 1.62 (d, *J* = 5.9 Hz, 3H), 1.59–1.44 (m, 8H), 1.32 (m, 6H), 1.06 (m, 21H), 0.94–0.86 (m, 24H), 0.04 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.2, 149.9, 144.8, 133.0, 130.2, 129.6, 128.3, 127.5, 127.4, 113.7, 77.7, 71.8, 69.5, 67.9, 57.9, 56.2, 48.5, 40.5, 37.6, 32.4, 29.0, 27.4, 25.9, 18.1, 18.0, 13.6, 12.5, 9.6, –4.4, –4.5. HR-MS (FAB, NBA, Na$^+$) *m/z* calcd. for $C_{52}H_{94}O_6Si_2Sn^{120}Na$ ([M + Na]$^+$): 1013.5509; found: 1013.5549. Anal. calcd. for $C_{52}H_{94}O_6Si_2Sn$ (%): C 63.08, H 9.57; found: C 62.93, H 9.42.

(4*R*,5*S*,6*R*,7*S*,10*R*,13*S*)-10-Benzoyloxy-13-(*tert*-butyldimethylsiloxy)-5,6-epoxy-9-methylene-2-tributylstannyl-4-triisopropylsiloxy-heptadeca-1,15-(*E*)-dien-7-ol (50)

The allylation procedure above led to the isolation of **50** (entry 15, Table 1) as a single diastereoisomer, characterized as follows: R_f = 0.15 in 5% EtOAc–hexanes. $[\alpha]_D$ –25.5 (*c* 2.25, $CHCl_3$). IR (neat) (cm^{-1}): 3483 (br), 2928, 2666, 1720, 1462, 1271, 1113. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (m, 2H), 7.56 (m, 1H), 7.44 (m, 2H), 5.81 (m, 1H), 5.41 (m, 1H), 5.34 (dd, *J* = 7.8, 4.9 Hz, 1H), 5.25 (d, *J* = 2.7 Hz, 1H), 5.17 (s, 1H), 5.05 (s, 1H), 3.86 (m, 1H), 3.75–3.66 (m, 2H), 3.01 (dd, *J* = 3.9, 2.1 Hz, 1H), 2.94 (dd, *J* = 3.9, 2.1 Hz, 1H), 2.89 (d, *J* = 1.7 Hz, 1H), 2.59 (m, 2H), 2.39 (dd, *J* = 14.5, 2.2 Hz, 1H), 2.16–2.10 (m, 3H), 1.89 (m, 1H), 1.75 (m, 1H), 1.63 (d, *J* = 5.3 Hz, 3H), 1.61 (m, 1H), 1.52–1.40 (m, 7H), 1.31 (m, 6H), 1.12–1.02 (m, 21H), 0.98–0.84 (m, 2H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.2, 149.8, 144.9, 133.0, 130.2, 129.6, 129.1, 128.3, 127.4, 127.3, 113.6, 77.8, 71.9, 71.7, 70.0, 59.4, 58.8, 47.3, 40.4, 37.1, 32.5, 29.1, 27.4, 25.9, 18.2, 17.9, 13.7, 12.6, 9.6, –4.4, –4.6.

(4*S*,5*S*,6*R*,7*S*,10*R*,13*S*)-10-Benzoyloxy-13-(*tert*-butyldimethylsiloxy)-5,6-epoxy-9-methylene-2-tributylstannyl-4-triisopropylsiloxy-heptadeca-1,15-(*E*)-dien-7-ol (51)

The allylation procedure above led to the isolation of **51** (entry 16, Table 1) as a single diastereoisomer, characterized as follows: R_f = 0.20 in 5% EtOAc–hexanes. $[\alpha]_D$ –11.2 (*c* 1.35, $CHCl_3$). IR (neat) (cm^{-1}): 3475 (br), 2955, 2928, 2866, 1722, 1462, 1271, 1116. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (m, 2H), 7.57 (m, 1H), 7.44 (m, 2H), 5.81 (s, 1H), 5.42 (m, 2H), 5.35 (m, 1H), 5.24 (d, *J* = 2.2 Hz, 1H), 5.18 (s, 1H), 5.06 (s, 1H), 4.12 (m, 1H), 3.90 (m, 1H), 3.69 (dddd, *J* = 5.9, 5.9, 5.7, 5.3 Hz, 1H), 3.15 (dd, *J* = 4.0, 2.1 Hz, 1H), 3.05 (dd, *J* = 2.4, 2.2 Hz, 1H), 2.87 (d, *J* = 1.9 Hz, 1H), 2.71 (dd, *J* = 13.8, 4.3 Hz, 1H), 2.46 (dd, *J* = 19.0, 9.8 Hz, 1H), 2.44 (dd, *J* = 14.2, 3.1 Hz, 1H), 2.18 (dd, *J* = 14.2, 9.5 Hz, 1H), 2.14 (dd, *J* = 5.7, 5.7 Hz, 2H), 1.90 (m, 1H), 1.76 (m, 1H), 1.63 (d, *J* = 5.2 Hz, 3H), 1.61 (m, 1H), 1.50 (m, 7H), 1.30 (m, 6H), 1.24 (m, 21H), 0.90 (m, 24H), 0.30 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.2, 149.9, 144.8, 133.0, 130.2, 129.6, 128.3, 127.4, 127.3, 113.7, 77.7, 77.2, 71.9, 69.5, 67.9, 57.9, 56.2, 48.5, 40.4, 37.5, 32.4, 29.0, 27.4, 25.8, 18.0, 17.9, 13.6, 12.5, 9.6, –4.4, –4.5. MS (FAB, NBA, Na$^+$) *m/z* ([M – *t*-Bu]$^+$): 933.

Conclusion

In summary, a powerfully convergent strategy for the diastereoselective synthesis of homoallylic alcohols has been described. Our asymmetric allylation reaction incorporates three elements of stereodifferentiation. Optimal results are provided when adjacent asymmetry in the starting stannane

is stereochemically reinforcing with respect to chirality of the bis-sulfonamide auxiliary. Products featuring 1,4-*syn*-stereochemistry are favored. The incorporation of α- or β-stereogenecity in the starting aldehyde has been documented. The diastereofacial selectivity of reactions with α-substituted aldehydes is predicted by the Felkin–Anh model. Overall, this methodology permits the construction of complex arrangements of stereochemistry and functionality as a useful tool for the synthesis of complex natural products.

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