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Article

Chiral Allylsilane Additions to Chiral α-Substituted Aldehydes

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Reação do alilsilano quiral **3** com α-metil-β-siloxi-aldeídos fornece os produtos correspondentes com estereoquímica relativa 1,4-*syn* com boa diastereosseletividade, independente da estereoquímica absoluta dos aldeídos. As melhores seletividades são observadas quando ocorre transmetalação do alilsilano **3** usando $SnCl_4$ em CH_2Cl_2, a -78 °C, antes da adição dos aldeídos.

Chiral allylsilane **3** reacted with chiral α-methyl-β-siloxy-aldehydes to afford the corresponding 1,4-syn-products with good diastereoselectivities independent of the absolute stereochemistry of these aldehydes. The best selectivities are observed when the reactions are carried out by transmetallation of the allylsilane **3** using Tin (IV) Chloride in CH_2Cl_2, at -78 °C, before addition of the aldehydes.

Keywords: *chiral allylsilane, transmetallation, 1,4-asymmetric induction, polyacetate derived natural products*

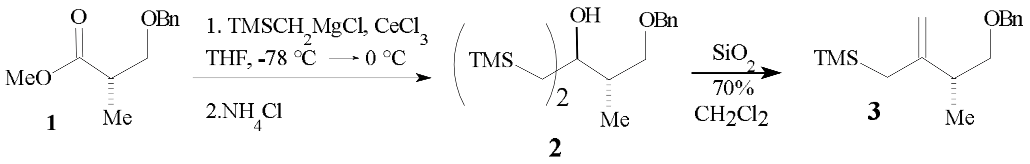
Introduction

The Lewis acid-mediated reaction of allylsilanes with aldehydes is a well-known procedure for the preparation of homoallylic alcohols[1]. The stereochemical outcome of this reaction has been occasionally explained by considering Lewis acid-carbonyl complexation. This type of complexation mainly occurs through two discrete pathways, chelation and non-chelation controlled, depending on the nature of the Lewis acid and on the steric requirements of the carbonyl ligand. Condensation of allylic metals (*e.g.* M: Si, Ti, Sn, B, Cr) with various carbonyl compounds can be used to achieve acyclic stereoselection, and has been applied to the synthesis of natural products[1]. Chiral allylmetal reagents may be thought of as acetate-enolate equivalents for diastereoselective construction of stereochemically well-defined homoallylic alcohols. Because these reactions complement the aldol reactions, they are among the most important groups of organometallic reagents available for the control of acyclic stereochemistry. Many methods can be used to control the configurations of stereogenic centers that are close to each other[2,3]. However relatively few methods are available for control of the stereochemistry of more remote stereogenic centers[4,5].

We describe herein a divergently stereocontrolled reaction between chiral aldehydes and a chiral allylic silane bearing an ethereal functionality, whose coordination to the Lewis acid was found to play a very important role[6]. These allylsilanes offer an attractive site for metal ligation with a benzyloxyl substituent and undergo Lewis acid promoted reactions with chiral aldehydes with efficient 1,4-asymmetric induction[6].

The preparation of chiral allylsilane **3** from methyl ester **1** is detailed in Scheme 1. Allylsilanes can be obtained by the reaction of esters with α-silyl substituted Grignard reagents, but yields in this reaction are typically low due to kinetically-preferred enolization of the intermediate α-silylketone rather than addition of a second equivalent of Grignard reagent[7]. In 1987 Bunnelle and Narayanan reported that this complication can be circumvented in cases of simple esters by premixing the α-silyl Grignard reagent with anhydrous cerium (III) chloride[8]. The yields in this reaction are greatly increased presumably due to suppression of the enolization process[9]. The cerium reagent generated from cerium (III) chloride and trimethylsilylmethyl-magnesium chloride reacts with ester **1** to give *bis*-(silylmethyl)-carbinol **2**[10], which after treatment with silica gel in CH_2Cl_2 affords allylsilane **3**

Dedicated to Prof. José Tércio Barbosa Ferreira (in Memoriam) and to the Brazilian Chemical Society (SBQ)



Scheme 1.

in 70% isolated yield after flash chromatography (Scheme 1)[11].

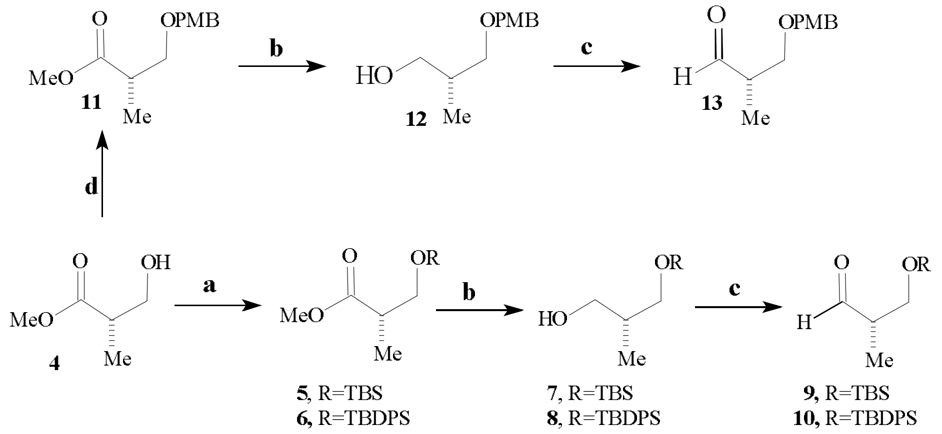
It seems unlikely that the above reaction proceeds *via* the intermediacy of an alkylcerium species, but it is clear that the presence of cerium (III) chloride is essential. It may be that cerium is involved in a direct interaction with the intermediate ketone species which enhances nucleophilic attack at the carbonyl and limits competitive enolization. Control experiments established that the Grignard reagent alone reacts very sluggishly at low reaction temperatures (starting ester along with small amounts of α-silylketone are obtained).

Chiral aldehydes **9**, **10** and **13** and their enantiomers were prepared from methyl 3-hydroxy-2-methylpropionate **4**, both enantiomers of which are commercially available[10,12]. Standard literature methods were employed. The final step in each case was Swern oxidation of alcohols **7**, **8** and **12**. Attempts to purify **9**, **10** and **13** by silica-gel chromatography resulted in partial racemization. Since the diastereoselectivity of the reactions of these aldehydes with allylsilane **3** depends on their enantiomeric purity, crude aldehydes **9**, **10** and **13** were used in all of the studies described in this text. In aldehydes **9** and **10**, chelation is presumably prevented by the use of bulky silyl protecting groups, since silyl ethers, with few exceptions, are recognized generally for their poor coordinating and chelating abilities[13].

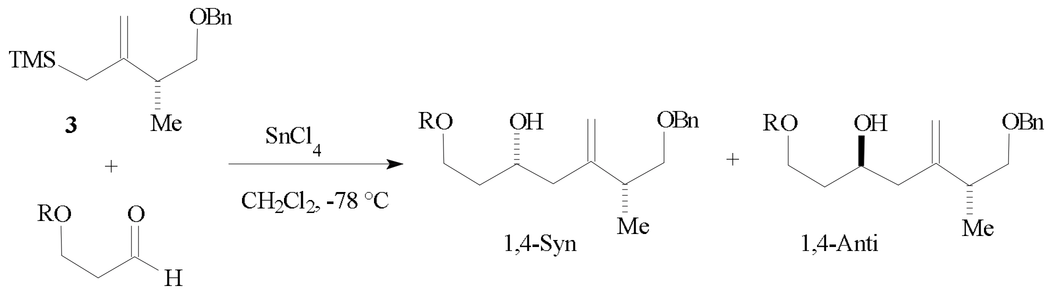
All of the studies were carried out on aldehydes and allylsilane **3** with $SnCl_4$ as the Lewis acid. Tin(IV) chloride promoted reactions of chiral allylsilane **3** with these aldehydes were carried out at 4 different conditions: **1**. Aldehyde and $SnCl_4$ were mixed for 5 min. before the allylsilane addition; **2**. Allylsilane and $SnCl_4$ were mixed for 1 h before the addition of the aldehyde solution; **3**. $SnCl_4$ was added to a mixture of allylsilane and aldehyde in CH_2Cl_2 at -78 °C; **4**. Allylsilane and $SnCl_4$ were mixed for 1 h at -78 °C before the addition of a solution of the aldehyde pre-mixed with $SnCl_4$ at -78 °C.

At this juncture, a comprehensive experimental study of the $SnCl_4$-mediated coupling of chiral allylsilane **3** with achiral aldehydes **14** and **15** was initiated to test the facial selectivity of this allylsilane. Precomplexation of aldehyde **14** or **15** with $SnCl_4$ (1.0 eq.) in CH_2Cl_2 at -78 °C (condition 1) followed by the dropwise addition of allylsilane **3** in CH_2Cl_2 solution led to the isolation of a mixture of diastereomeric homoallylic alcohols **16/17** or **18/19**, respectively, in moderate yields (Scheme 3, Table 1)[14]. Changing the order of addition of allylsilane **3** to $SnCl_4$ (1.0 eq.) for varying periods of time at -78 °C followed by addition of aldehydes **14** or **15** led to the same selectivities as previously observed. Under condition 2, the same selectivity was observed for aldehyde **14** but aldehyde **15** afforded adduct **18** in better selectivity when compared with condition 1. Based on these results we conclude that allylsilane **3** prefers to add to the aldehyde *re* face affording 1,4-*syn* as the major product.

The stereochemical assignment of compound **16** was determined by analysis of the coupling constants in the ^1H-NMR spectrum of the tetrahydropyran derivative **23**. The conversion of **16** to this derivative is illustrated in Scheme 4. Subjection of **16** to standard silylation conditions (TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 20 min) afforded the *bis*-silyl ether **20** in 88% yield. Cleavage of the benzyl ether of **20** by the utilization of the lithium 4,4'-*tert*-butylbiphenyl (LiDBB)



Scheme 2. a. TBSCl, imidazole, DMAP, CH_2Cl_2, 25 °C, 85-89% or TBDPSCl, imidazole, DMAP, CH_2Cl_2, 25 °C, 60-70%; **b.** DIBAL-H, CH_2Cl_2, -23 °C, 88-96%; **c.** Swern, 95-98%; **d.** PMB-acetimidate, CSA, CH_2Cl_2, 80-84%.



14, R = TBS
15, R = PMB

16, R = TBS
18, R = PMB

17, R = TBS
19, R = PMB

Scheme 3.

Table 1. Tin (IV) chloride -promoted additions of allylsilane **3** to unsubstituted aldehydes.

Condition	R = TBS 1,4-Syn (**16**):1,4-Anti (**17**)	Yield (%)	R = PMB 1,4-Syn (**18**):1,4-Anti (**19**)	Yield (%)
1	87:13	42	71:29	40
2	84:16	50	86:14	70

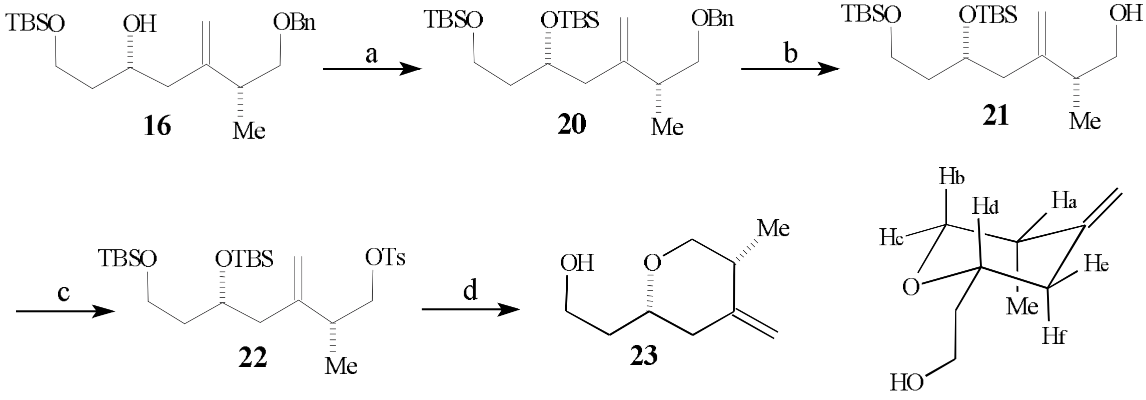
radical anion in THF at -78 °C, afforded the primary alcohol **21** in 50% yield. Tosylation of the primary hydroxyl in **21** gave tosylate **22** in 88% yield. Treatment of **22** with TBAF in THF at room temperature effected smooth deprotection of both silyl ethers with concomitant intramolecular etherification to provide tetrahydropyran **23** in 88% yield. Coupling constants of 11,0 and 3,30 Hz for **Hb**, and 11,0 and 1,83 Hz for **Hc** are indicative of the axial orientation of the methyl group in the ring. In addition, coupling constants of 13,55 and 2,93 Hz for **He** and 13,2 and 11,0 Hz for **Hf** are indicative of the axial orientation of **Hd**, thereby confirming the 1,4-*syn* relationship in homoallylic alcohol **16**.

In order to check the facial selectivity of chiral α-substituted aldehydes they were reacted with commercial allyltrimethylsilane under conditions 1 and 2 (Scheme 5, Table 2). We always isolated a 50:50 mixture of both possible diastereomers in low yields. Based on these results we might conclude that aldehyde **9** has no preference for Felkin or anti-Felkin addition under the present reaction conditions.

The tin (IV) chloride promoted reactions of chiral allylsilane **3** with (S)-α-methyl chiral aldehydes **9** (OTBS) and **10** (OTBDPS) were carried out at the same 4 different experimental conditions described before. Under these conditions

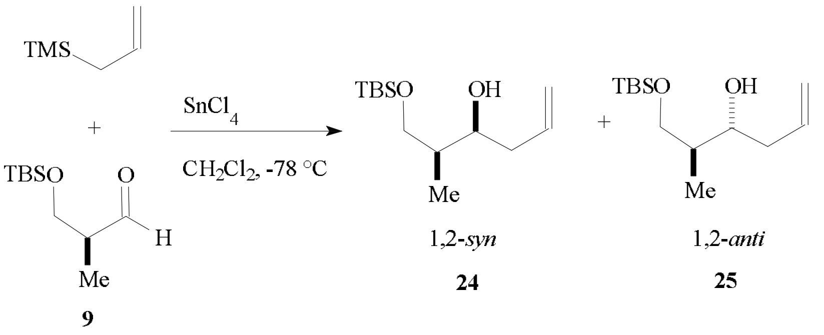
Table 2. Tin (IV) chloride -promoted additions of allyltrimethylsilane to (S)-aldehyde **9**.

Condition	1,2-Syn (**24**):1,2-Anti (**25**)	Yield (%)
1	52:48	50
2	53: 47	55

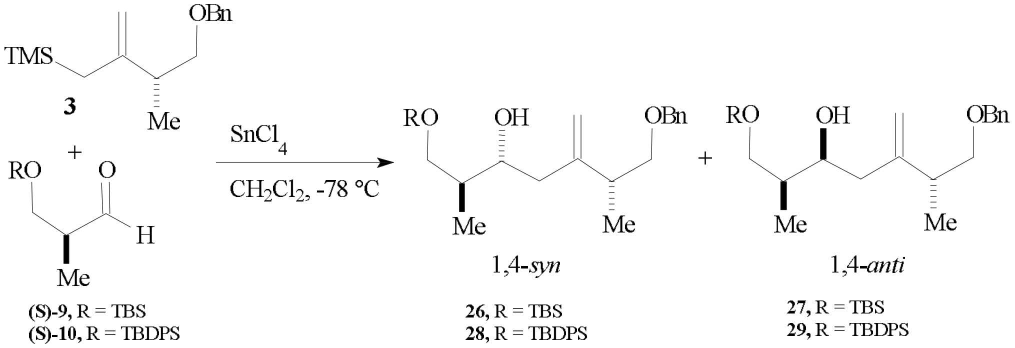


Hb (dd, J=11,0 and 3,3 Hz)
Hc (dd, J=11,0 and 1,83 Hz)
He (dd, J=13,55 and 2,93 Hz)
Hf (ddt, J=13,4; 11,0 and 1,86 Hz)

Scheme 4. a. TBSOTf, 2,6-lutidine, CH_2Cl_2, -10 °C, 88%; **b.** Li°, 4,4'-di-tert-butylbiphenyl, THF, -78 °C, 50%; **c.** TsCl, Pyr, CH_2Cl_2, 25 °C, 88%; **d.** TBAF, THF, 25 °C, 88%.



Scheme 5.



Scheme 6.

the allylsilane **3** reacted with (S)-aldehydes **9** and **10** to give a mixture of the 1,4-syn and 1,4-anti-diastereomers with useful diastereoselectivities (Scheme 6, Table 3), favoring the 1,4-syn-isomer (anti-Felkin addition)[14]. It should be noted that this reaction affords a very important subunit with different protecting groups at the terminus. All of the percentage values represent data obtained from three individual trials. It should be noted that partial racemization of the aldehydes probably occurs during reaction since we observed small peaks at δ 1.0-1.2.

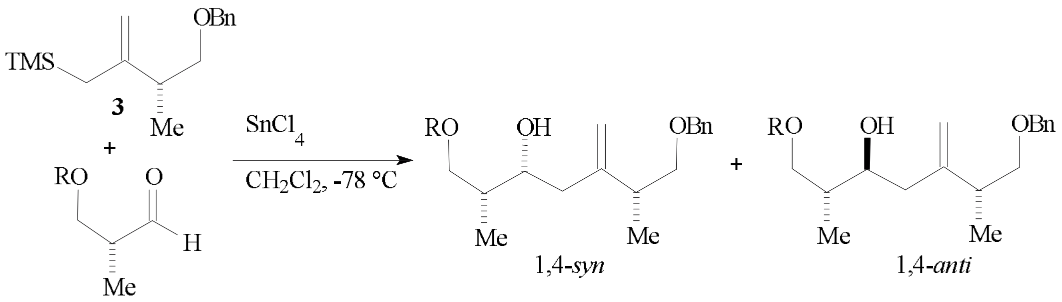
Under the same conditions as described above, allylsilane **3** reacted with the enantiomers of aldehydes **9** and **10** to give 1,4-*syn*-products with Felkin addition (Scheme 7 and Table 4)[10b,11].

In all cases the 1,4-syn products were formed stereoselectively in good yields. Confirmation that the same products were obtained with both TBS and TBDPS protected aldehydes was gained by desylation of **26** and **30** and comparison of these diols with those generated from **28** and **32**, respectively[14]. Based on these results, the chiral aldehydes **9** and **10** would not appear to prefer to react in the Felkin-Anh mode, since similar selectivities for the 1,4-*syn* isomer were obtained with both enantiomers. Although the (R)-aldehydes are matched with (R)-allylsilane **3**, whereas the (S)-enantiomer of these aldehydes are mismatched, it looks as though the allylsilane alone is responsible for the control of the relative stereochemistry.

Table 3. Tin(IV) chloride-promoted additions of allylsilane **3** to (S)-aldehydes **9** and **10**.

Condition[a]	R = TBS[b,c] 1,4-*syn*(**26**):1,4-*anti*(**27**)	Yield (%)[d]	R = TBDPS[c] 1,4-*syn*(**28**):1,4-*anti*(**29**)	Yield (%)[d]
1	52:48	80	85:15	61
2	90:10	70	82:18	35
3	83:17	87	90:10	72
4	84:16	75	54:46	40

a. Reactions were carried out in dichoromethane at -78 °C using molar equivalents of allylsilane, $SnCl_4$ and aldehyde; b. The ratios were determined by ^{1}H- and ^{13}C-NMR spectroscopic analysis of the purified product mixture after protection with TMS-imidazol. Protection as the secondary TMS ether is necessary since the allylsilane reaction afforded mixtures of the secondary silylated (TMS) and non-silylated products; c. The 1,4-*syn* and *anti*-products could not be separated and were characterized as mixtures; Averages of at least three runs with ±3% ratios; d. Combined yields of products isolated chromatographically (SiO_2); e. The minor products corresponded to the 1,4-anti-diastereoisomers of the major products; f. Abbreviations: Bn = $C_6H_5CH_2$-; TBS = t-$BuMe_2Si$-; TBDPS = t-$BuPh_2Si$-.



(R)-9, R = TBS
(R)-10, R = TBDPS

30, R = TBS
32, R = TBDPS

31, R = TBS
33, R = TBDPS

Scheme 7.

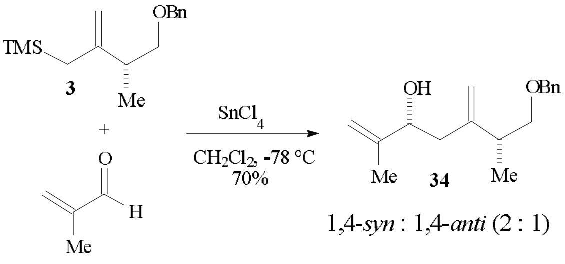
Table 4. Tin(IV) chloride-promoted additions of allylsilane **3** to (R)-aldehydes **9** and **10**.

Condition[a]	R = TBS[b,c] 1,4-*syn*(**30**):1,4-*anti*(**31**)	Yield(%)[d]	R = TBDPS[c] 1,4-*syn*(**32**):1,4-*anti*(**33**)	Yield(%)[d]
1	75:25	90	91:09	54
2	90:10	92	92:08	90
3	85:15	95	89:11	83
4	68:32	66	72:28	36

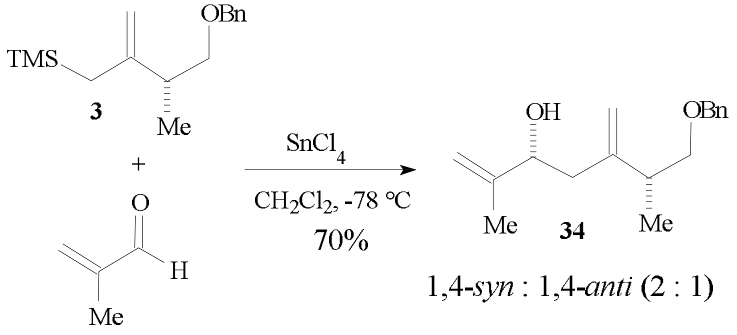
In some of these experiments we observed the formation of small amounts of a by-product (5% yield, 1:1 mixture of diastereomers) that was characterized as being compound **34** (Scheme 8). We believe this compound is formed by the addition of the allylsilane to methacrolein, *in situ* formed from aldehydes and $SnCl_4$. To confirm the structure of this by-product we reacted allylsilane **3** with methacrolein and observed the formation of a 2:1 mixture of adducts **34** in 70% isolated yield (Scheme 8).

The selectivity in this reaction can be explained by invoking transmetalation of the allylsilane **3** with $SnCl_4$ to generate the allyltrichlorotin intermediate **35**, in which the benzyl-protected oxygen atom is coordinated intramolecularly to the electron-deficient tin (Scheme 9)[15]. This species reacts with aldehydes at reasonable levels of 1,4-asymmetric induction in favor of the *syn*-diastereoisomer.

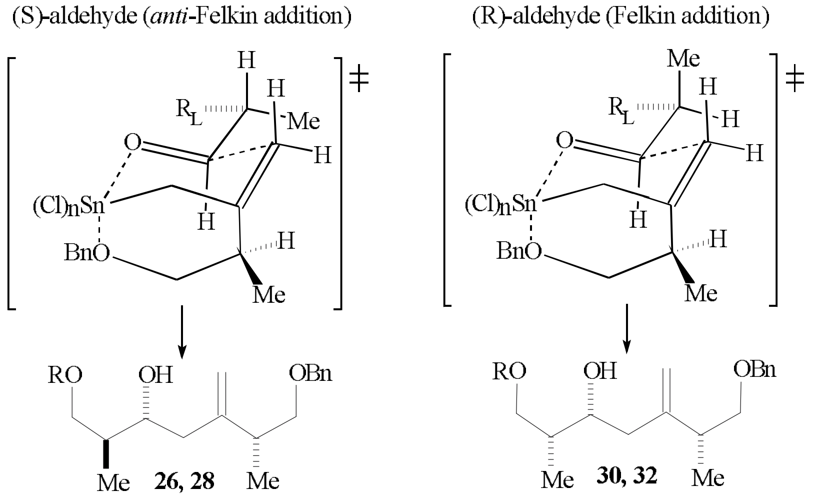
The formation of 1,4-*syn*-products from reactions of the allylsilanes and aldehydes is consistent with the participation of the transition structure involving a coordinated allyltin thrichloride. We believe that entrance of an aldehyde into the coordination sphere of tin does not disrupting the intramolecular chelation to the proximal oxygen. Under these circumstances, π-facial selectivity for attack at the aldehydes is ultimately governed by approach to the less hindered surface of the allyltin reagent. With the $-CH_2OBn$ locked below the developing chair, the methyl substituent could become the key



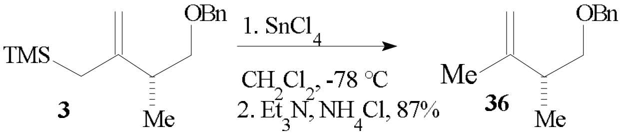
Scheme 9.



Scheme 8.



Scheme 10.



Scheme 11.

factor indictating π-facial diastereoselection. One might anticipate that the inter nally-chelated allylstannane might afford the 1,4-*syn*-diastereoisomer.

The intermediate allyltin trichloride is stabilized by tin-oxygen interaction, and then reacts with the aldehyde *via* a chair-like six-membered ring transition state in which the aldehyde approaches the complex opposite to the methyl group. The preference of the alkyl group of the aldehyde to adopt an equatorial position controls the aldehyde facial selectivity, resulting in the favored 1,4-*syn* stereochemistry in the adduct, independent of the aldehyde absolute configuration (Scheme 10).

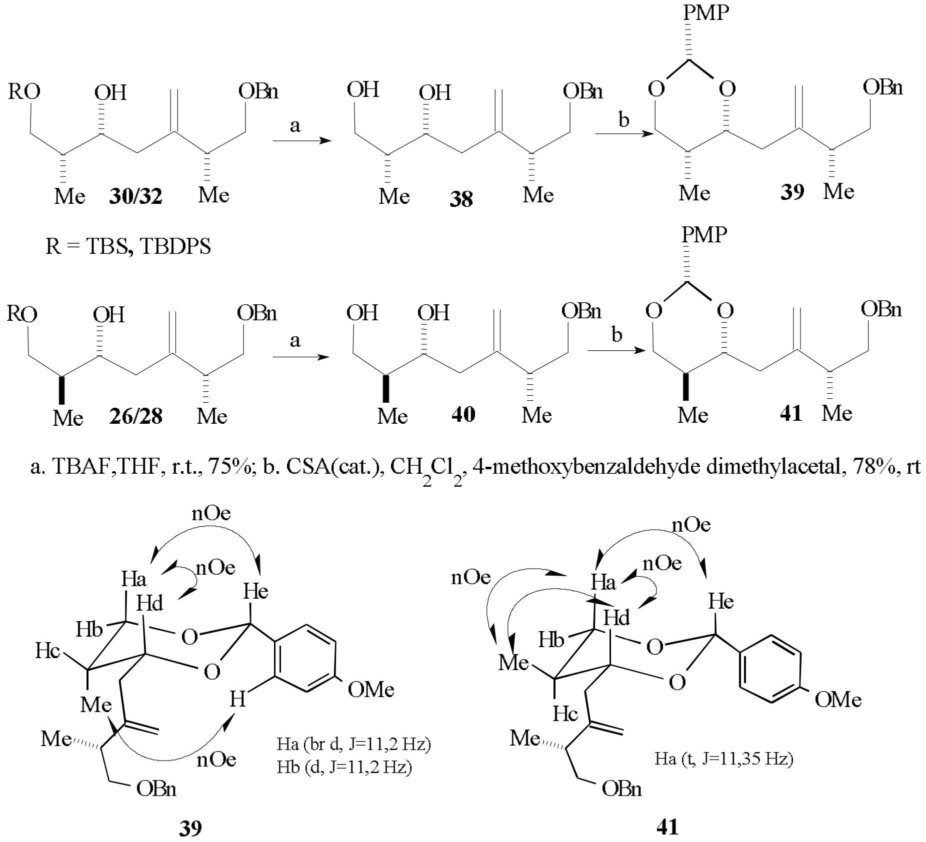
A very interesting experiment was done in order to prove the intermediacy of an allylstannane. Addition of $SnCl_4$ to a solution of chiral allylsilane **3** in CH_2Cl_2 at -78 °C, stirring for 1 h and quenching with Et_3N/NH_4Cl, without the addition of aldehyde, afforded alkene **36** in 87% yield (Scheme 11).

The relative stereochemical assignments of the homoallylic alcohols **26/28** and **30/32** were based on ^{1}H-NMR coupling constant analysis of the derived cyclic *p*-methoxybenzylidene acetals. The indicated vicinal coupling constant data for the benzylidene acetals unambiguously established the configuration of the newly formed stereocenter of the *anti*-felkin adducts **26/28** and the Felkin adducts **30/32**. Average coupling constants of 11 Hz indicate that protons Ha-Hc in **41** are on opposite faces of the heterocyclic ring, and therefore the acetonide is derived from an 1,2-*anti* adduct. In contrast, coupling constants of 1-3 Hz for Ha-Hc in **39** are characteristic of protons residing on the same face of the ring, indicative of a 1,2-*syn* product. In some instances the relative ring stereochemistry was further supported by ^{1}H-^{1}H NOESY measurements. The illustrated NOE measurements on benzylidene acetal established the syn relationship between the newly formed hydroxyl and adjacent methyl bearing stereocenter, thereby securing the stereochemical assignment of these adducts (Scheme 12). Having confirmed the relative (*syn* or *anti*) relationship between allylsilane derived stereogenic centers, the absolute stereochemistry of the newly formed hydroxyl substituent was determined by ascertaining its relationship to the stereocenter originating from the aldehydes, which are of known configuration.

It is interesting to note that reactions of allylsilane **3** with both (R)- and (S)-aldehydes **13** protected with β-OPMB afforded exactly the same mixture of products **42** and **43** in a 50:50 ratio. This result was confirmed by conversion to the corresponding acetonides and comparison to the acetonides obtained in Scheme 12. These results can be explained by racemization of the aldehydes in the presence of $SnCl_4$ and selective reaction of chiral allylsilane with each enantiomer of these aldehydes.

For allylsilane adducts derived from aldehydes possessing the β-OPMB moiety, the strategy to prove the stereochemistry relied on intramolecular oxidative formation of the *p*-methoxybenzylidene acetals **39/41** (Scheme 13)[16]. This was accomplished by treatment of the PMB-ether in **42** and **43** under anhydrous conditions with 2,3-dichlor-5,6-dicyano-benzoquinone (DDQ).

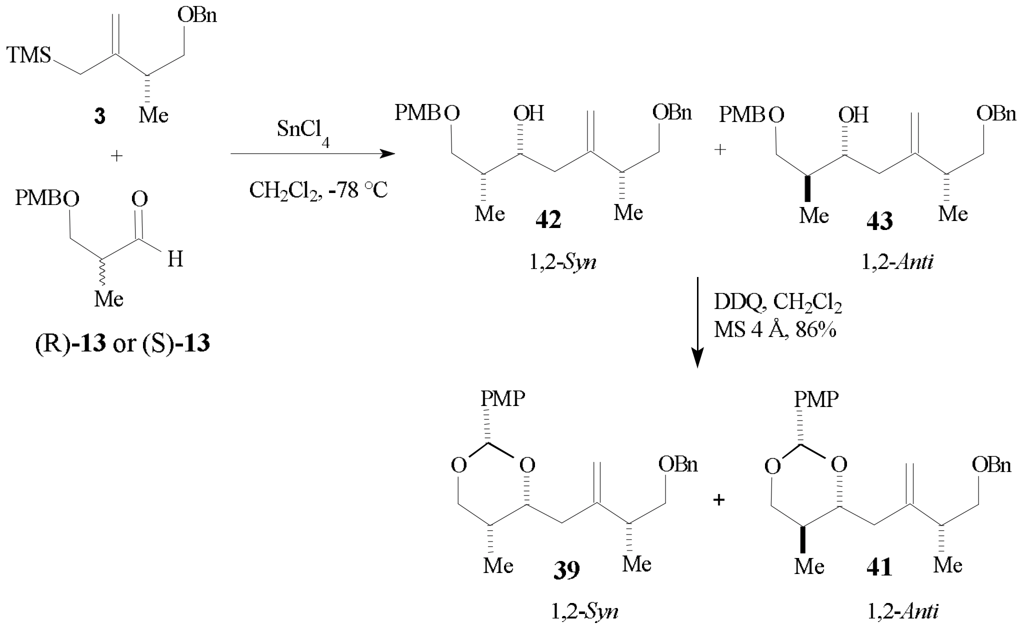
In summary, good levels of 1,4-asymmetric induction were obtained in the reactions of chiral allylsilane **3** and aldehydes. A chelate transition state model, which takes into account dual coordination of tin intramolecularly to nearby oxygen and intermolecularly to activate the aldehyde car-



a. TBAF,THF, r.t., 75%; b. CSA(cat.), CH_2Cl_2, 4-methoxybenzaldehyde dimethylacetal, 78%, rt

39 **41**

Scheme 12.



Scheme 13.

bonyl, is proposed to explain the observed sense of 1,4-asymmetric induction.

The examples presented here show that the levels of π-facial selection are independent of the absolute stereochemistry of the aldehydes. The data support the notion that the stereocenter in allylsilane is primarily responsible for the observed diastereoselection and that these chiral allylsilanes can be used as an effective stereocontrolling element in acyclic diastereoselection. Other Lewis acids could be used to promote this reaction in order to improve yields and selectivities and reduce the amount of racemization in these aldehydes.

We believe that the chemistry involved is truly significant in the context of acyclic diastereoselection and will prove to be exceptionally useful in the synthesis of complex organic molecules like polypropionate and polyacetate-derived natural products. Further exploration of these reagents and their applications is now underway in our laboratories as well as investigations of the mechanistic details.

Experimental

General

All experiments were carried out under an argon atmosphere in flame-dried glassware. Dichloromethane, triethylamine, cyclohexane, pyridine, and 2,6-lutidine were distilled from CaH_2. Tin tetrachloride was distilled from P_2O_5 and stored in a Schlenk flask. THF and toluene were distilled from sodium/benzophenone ketyl. Dimethyl sulfoxide was distilled under reduced pressure from calcium hydride and stored over molecular sieves. Trimethylsilil chloride and oxalyl chloride were distilled immediately prior to use. TLC plates were obtained of silica gel 60 and GF (5-40-µm thickness) and visualization was accomplished with either a UV lamp and I_2 staining. ^{1}H-NMR spectra were recorded on a Bruker AC 300/P (300 MHz) or Varian Gemini (300 MHz) spectrometers. Chemical shifts are recorded in ppm with the solvent resonance as the internal standard (deuterochloroform: δ 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, st = sextet, br = broad, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, br d = broad doublet, ddd, doublet of doublet of doublets), integration, coupling constants (Hz), and assignment. ^{13}C-NMR spectra were recorded on a Bruker AC 300/P (75 MHz) or Varian Gemini (75 MHz) spectrometers with complete proton decoupling. Chemical shifts are recorded in ppm with the solvent resonance as the internal standard (deuterochloroform: δ 77.00). Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. Mass spectra were obtained on a GC/MS HP-5988-A. Optical rotations were measured on a polarimeter Polamat A Carl Zeiss Jene using 1 mL capacity quartz cell, using a mercury or sodium lamp, and are reported as follows: $[\alpha]^{t(°C)}_{\lambda}$, (c = g/100 mL, solvent). Chromatography on silica-gel (230-400 mesh) was performed using a forced-flow of the indicated solvent system (flash chromatography)

2-[(1R)-2-benzyloxy-1-methylethyl]allyl(trimethyl) silane (3)

In a 3-necked 500 mL round bottomed flask, powdered $CeCl_3.7H_2O$ (17.6 g, 48 mmol) was heated under vacuum (3 mm Hg) at 160 °C for 10 h with vigorous stirring, resulting in the formation of a white mobile solid. The reaction flask was flushed with argon and allowed to cool to room temperature when 96 mL of dry THF was added to vigorously stirred anhydrous cerium (III) chloride forming a uniform white suspension, which was left stirring for 2 h. During this time, a separate 3-necked 100 mL flask, fitted with a condenser and a pressure equalized dropping funnel, was charged with 1.17 g (48 mmol) of magnesium turnings, and the whole apparatus was flame dried under a flow of argon. A solution of $ClCH_2TMS$ (6.7 mL, 48 mmol) was added to this flask dropwise in 45 mL of dry THF. This mixture was stirred for 1.5 h until almost all of the magnesium was dissolved. The dry cerium (III) chloride suspension was now cooled to -78 °C. To this suspension Grignard reagent (prepared above) was added dropwise forming na off-white suspension which was stirred at -78 °C for 1 h. At this time ester **1** (2.0 g, 9,6 mmol) in 10 mL of THF was added dropwise over 5 min, and the resulting mixture was warmed gradually to room temperature. When consumption of starting ester was complete by TLC (3 h), the resulting gray solution was cooled to 0 °C and quenched by the addition of 10 mL aqueous solution saturated of NH_4Cl (0 °C). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (2 x 50 mL). The combined organic layer was washed with saturated brine (2 x 50 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure affording a slightly yellow liquid which was dissolved in 100 mL of CH_2Cl_2. To this flask 10 g of silica gel was added and this mixture was stirred at room temperature until complete consumption of starting material. The silica gel was then removed by filtration and washed with 300 mL of CH_2Cl_2. The solvent was removed under reduced pressure to give a colorless liquid which was purified by flash chromatography on silica gel (hexanes:ethyl acetate 99:01) to afford 1.76 g in 70% yield. $[\alpha]^{20}_{D}$ = + 12.6 (c 1.3, $CHCl_3$). **TLC**: Rf: 0.26, hexanes:diethyl ether 99:01). **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.03 (9H, s), 1.12 (3H, d, $^3J = 6.59$), 1.57 (2H, d, $^3J = 5.86$), 2.28 (1H, m), 3.26 (1H, dd, $^2J = 9.15$, $^3J = 8.06$), 3.54 (1H, dd, $^2J = 9.15$, $^3J = 4.76$), 4.53 (2H, d, $^3J = 2.56$), 4.63 (2H, d, $^3J = 6.96$), 7.36 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: -1.5 (CH_3), 17.0 (CH_3), 26.6 (CH_2), 40.9 (CH), 72.9 (CH_2), 75.0 (CH_2), 106.5 (CH_2), 127.5 (CH), 127.6 (CH), 128.4 (CH), 138.8 (C_0), 149.9 (C_0). **IR (film)**: 3066, 3030, 2957, 2856, 1631, 1496, 1454, 1419, 1364, 1248, 1158, 1099, 1028, 958, 854, 734, 696, 634 cm^{-1}.

MS (70eV): 45 (13%), 73 (100%), 91 (91%), 156 (14%), 179 (10%).

General procedures for allylsilane reactions

Condition 1

To a solution of 0.25 mmol of aldehyde in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 5 min when 0.25 mmol of allylsilane **3** in 1 mL of CH_2Cl_2 was added. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution.The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded the corresponding homoallylic alcohols.

Condition 2

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 1 h when 0.25 mmol of aldehyde in 1 mL of CH_2Cl_2 was added. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution.The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded the corresponding homoallylic alcohols.

Condition 3

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of aldehyde. To the resulting solution was added 0.25 mmol of $SnCl_4$. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded the corresponding homoallylic alcohols.

Condition 4

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 1 h when was added to a solution 0.25 mmol of aldehyde pre-mixed with $SnCl_4$ in 1 mL of CH_2Cl_2. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded the corresponding homoallylic alcohols.

(3R)-5-[(1R)-2-benzyloxy-1-methylethyl]-1-[tert-butyl (dimethyl)silyloxy]-5-hexen-3-ol (16)

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 1 h when 0.25 mmol of aldehyde **14** in 1 mL of CH_2Cl_2 was added. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded 50 mg of the homoallylic alcohol **16** in 50% yield. $[\alpha]^{20}_{D}$ = +9.9 (c 0.8, $CHCl_3$). **TLC**: Rf: 0.46, hexane:diethyl ether 99:01). **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.06 (6H, s), 0.89 (9H, s), 1.04 (3H, d, ^3J = 6.96), 1.66 (2H, m), 2.20 (2H, d, ^3J = 6.96), 2.48 (1H, sext, ^3J = 6.96), 3.35 (1H, dd, ^2J = 9.15, ^3J = 6.59), 3.49 (1H, dd, ^2J = 9.15, ^3J = 7.32), 3.80 (3H, m), 3.99 (1H, m), 4,50 (2H, s), 4.92 (2H, d, ^3J = 1.46), 7.32 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: -5.8 (CH_3), 17.2 (CH_3), 18.0 (C_o), 25,7 (CH_3), 38.4 (CH_2), 38.9 (CH), 43.7 (CH_2), 61.7 (CH_2), 68.4 (CH), 73.0 (CH_2), 74.6 (CH_2), 112.0 (CH_2), 127.7 (CH), 127.8 (CH), 128.5 (CH), 138.4 (C_o), 149.3 (C_o). **IR (film):** 3482, 2956, 2927, 2855, 1652, 1472, 1456, 1361, 1255, 1092, 1005, 897, 836, 776, 734, 697 cm^{-1}. **MS (70eV):** 77 (23%), 183 (80%), 191 (100%), 239 (51%),269 (73%).

2-[(2R,5R)-5-methyl-4-methylenetetrahydro-2H-2-pyranyl]-1-ethanol (23)

To a solution of compound **16** (60 mg, 0.16 mmol) in 2 mL of CH_2Cl_2 was added 2,6-lutidine (43 mg, 0.4 mmol). This mixture was cooled to -10 °C, and tert-butyldimethylsilyl triflate (48 mg, 0.2 mmol) was added dropwise. After 30 min at -10 °C, the reaction was quenched by the addition of 1.0 mL of H_2O. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 3 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes:ethyl acetate 95:05) afforded 68.2 mg of **20** in 88% yield. **TLC**: Rf: 0.68, hexanes/ethyl acetate 85:15: **IR (film)**: 2955, 2928, 2856, 1734, 1640, 1471, 1389, 1360, 1255, 1091, 1033, 1005, 966, 939, 893, 836, 774, 732, 696 cm^{-1}. To a solution of 4,4-di-tert-butylbiphenyl (0.32 g, 1.2 mmol) in 5 mL of THF at room temperature was added lithium metal (0.17 g, 2.4 mmol) which had been washed with MeOH and THF under argon. This mixture was sonicated at room temperature for 6 h during which time the dark blue color of the anion radical developed. To a -78 °C stirred solution of **20** (60 mg, 0.12 mmol) in 3 mL of THF was added dropwise the LiDBB radical anion solution until a blue color persisted in the reaction mixture. The dark blue solution was then stirred for another

30 min at -78 °C before being quenched by careful addition of 3 mL of a saturated aqueous NH_4Cl solution. The colorless mixture was extracted with diethyl ether (2 x 5 mL). The combined organic extract was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel (hexane:ethyl acetate 90:10) gave 24 mg of alcohol **21** in 50% yield. **TLC**: Rf: 0.40, hexane:ethyl acetate 85:15. **IR (film)**: 3359, 3081, 2955, 2857, 2738, 1641, 1472, 1463, 1388, 1361, 1255, 1187, 1093, 1033, 1006, 984, 965, 938, 895, 836, 800, 774, 716, 663 cm^{-1}. To a solution of alcohol **21** (20 mg, 0.05 mmol) in 2 mL of CH_2Cl_2 at 0 °C was added pyridine (0.1 mmol), followed by addition of 14 mg (0.07 mmol) of *p*-toluenesulfonyl chloride. The resulting mixture was warmed to room temperature and stirred for 18 h. The reaction was quenched by the addition of ethyl ether (1.0 mL) and H_2O (1 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the crude product by silica gel flash chromatography (hexanes:ethyl acetate 95:05) afforded 24 mg of **22** in 88% yield. **TLC**: Rf = 0.60, hexanes:ethyl acetate 85:15. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.0 (6H, d, $^{3}J = 7.69$), 0.02 (6H, s), 0.85 (9H, s), 0.87 (9H, s) 1.04 (3H, d, $^{3}J = 6.96$), 1.48 (1H, m) 1.65 (1H, m), 2.11 (2H, d, $^{3}J = 6.59$), 2.44 (3H, s), 3.61 (1H, d, $^{3}J = 5{,}86$), 3.64 (1H, d, $^{3}J = 5.86$), 3.74 (1H, m), 3.82 (1H, dd, $^{2}J = 9.15$, $^{3}J = 7.69$), 3.91 (1H, m), 4.00 (1H, dd, $^{2}J = 9.15$, $^{3}J = 5.12$), 4.82 (2H, d, $^{3}J = 17.95$), 7.33 (2H, d, $^{3}J = 8.06$), 7.77 (2H, d, $^{3}J = 8.06$). **IR (film)**: 2955, 2928, 2856, 1735, 1642, 1598, 1472, 1363, 1256, 1189, 1178, 1097, 1034, 1006, 968, 900, 836, 813, 775, 666 cm^{-1}. To a solution of 20 mg (0.04 mmol) of **22** in 1 mL of THF at 0 °C was added 0.16 mL of a 1.0 M solution of TBAF. The solution was warmed to room temperature and stirred for 18 h. The solution was diluted with 2 mL of ethyl ether and washed with aqueous saturated solution of NH_4Cl. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the crude product by silica gel flash chromatography (hexanes:ethyl acetate 95:05) afforded 5 mg of **23** in 88% yield. $[\alpha]^{20}_{D} = +30.4$ (c 0.1, $CHCl_3$). **TLC**: Rf: 0.1, hexanes:ethyl acetate 85:15. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 1.18 (3H, d, $^{3}J = 6.96$), 1.63 (1H, br), 1.71 (1H, m), 1.85 (1H, m), 2.07 (1H, d, $^{2}J = 13.0$) 2.29 (1H, d, $^{2}J = 13.0$), 2.35 (1H, m), 3.50 (1H, m), 3.57 (1H, dd, $^{2}J = 10.6$, $^{3}J = 3.29$), 3.77 (1H, d, $^{2}J = 10.6$), 3.81 (2H, d, $^{3}J = 5.13$), 4.72 (2H, d, $^{2}J = 27.1$). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: 17.7 (CH_3), 37.2 (CH_2), 37.5 (CH_2), 38.2 (CH), 61.3 (CH_2), 73.5 (CH_2), 79.3 (CH), 108.2 (CH_2), 148.3 (C_0). **IR (film)**: 3407, 3071, 2928, 2853, 1724, 1651, 1461, 1430, 1382, 1258, 1178, 1112, 1055, 991, 963, 891 cm^{-1}.

(2R,3R)-5-[(1R)-2-benzyloxy-1-methylethyl]-1-[tert-butyl(dimethyl)silyloxy]-2-methyl-5-hexen-3-ol (26)

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 1 h when 0.25 mmol of aldehyde (S)-**9** in 1 mL of CH_2Cl_2 was added. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution.The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded 68 mg of the alcohol **26** in 70% yield. $[\alpha]^{20}_{D} = -8.7$ (c 0.5, $CHCl_3$). **TLC**: Rf = 0.4, hexanes:diethyl ether 8:2. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.08 (3H, s), 0.91 (9H, s), 0.94 (3H, d, $^{3}J = 6.98$), 1.08 (3H, d, $^{3}J = 6.96$), 1.75 (1H, m), 2.12 (1H, dd, $^{2}J = 14.1$, $^{3}J = 9.86$), 2.34 (1H, dd, $^{2}J = 14.1$, $^{3}J = 2.95$), 2.51 (1H, m), 3.29 (1H, d, $^{3}J = 3.16$), 3.38 (1H, dd, $^{2}J = 9.11$, $^{3}J = 6.63$), 3.52 (1H, dd, $^{2}J = 9.11$, $^{3}J = 7.36$), 3.66 (1H, dd, $^{2}J = 9.95$, $^{3}J = 5.84$), 3.73 (1H, dd, $^{2}J = 9.95$, $^{3}J = 5.35$), 3.74 (1H, m), 4.52 (2H, s), 4.96 (2H, d, $^{3}J = 12.21$), 7.33 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: -5.5 (CH_3), 13.5 (CH_3), 17.6 (CH_3), 18.2 (C_0), 25.9 (CH_3), 38.9 (CH), 40.2 (CH), 41.2 (CH_2), 66.4 (CH_2), 72.2 (CH), 73.0 (CH_2), 74.6 (CH_2), 111.6 (CH_2), 127.5 (CH), 127.6 (CH), 128.3 (CH), 138.3 (C_0), 149,5 (C_0). **IR (film)**: 3482, 2956, 2928, 2857, 1639, 1472, 1389, 1362, 1255, 1093, 1028, 894, 837, 776, 735, 698 cm^{-1}.

1-(2R)-3-[(2R,3S)-4-(tert-butyl(dimethyl)silyloxy)-2-(trimethyl)silyloxy-3-methylbutyl]-2-methyl-3-butenyloxymethylbenzene (26, TMS protected)

To a solution of **26** (100 mg, 0.26 mmol) in 2 mL of dry CH_2Cl_2 at room temperature was added 2 eq. of TMS-imidazole. The resulting solution was stirred for 1 h and filtered in silica gel with CH_2Cl_2. Concentration of the filtrate under reduced pressure and purification by flash chromatography on silica gel (5% EtOAc/hexanes) afforded 83 mg of **26 (TMS protected)** in 70% yield). $[\alpha]^{20}_{D} = +4.2$ (c 2.0, $CHCl_3$). **TLC**: Rf = 0.6, hexanes:ethyl ether 8:2. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.04 (6H, s), 0.09 (9H, s), 0.79 (3H, d, $^{3}J = 6.96$), 0.90 (9H, s), 1.11 (3H, d, $^{3}J = 6.96$), 1.70 (1H, m), 2.19 (1H, dd, $^{2}J = 14.1$, $^{3}J = 6.04$), 2.29 (1H, dd, $^{2}J = 14.1$, $^{3}J = 8.24$), 2.44 (1H, m), 3.31 (1H, dd, $^{2}J = 9.52$, $^{3}J = 7.69$), 3.37 (1H, dd, $^{2}J = 9.52$, $^{3}J = 6.23$), 3.49 (2H, m), 4.10 (1H, m), 4.53 (2H, d, $^{3}J = 1.83$), 4.86 (2H, d, $^{3}J = 6.59$), 7.34 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: -5.7 (CH_3), 0.2 (CH_3), 9.3 (CH_3), 16.8 (CH_3), 18.0 (C_o), 25.7 (CH_3), 39.0 (CH), 39.1 (CH), 41.1 (CH_2), 65.1 (CH_2), 69.8 (CH), 72.9 (CH_2), 74.8 (CH_2), 111.4 (CH_2), 127.6 (CH), 127.7 (CH), 128.5 (CH), 138.9 (C_o), 149.2 (C_o). **IR (film):** 2955, 2856, 1474, 1360, 1250, 1096, 939, 838, 775, 748, 696 cm^{-1}. **MS (70eV)**: 73 (59%), 91 (100%), 147 (20%), 275 (42%).

(2R,3R)-5-[(1R)-2-benzyloxy-1-methylethyl]-1-[tert-butyl(diphenyl)silyloxy]-2-methyl-5-hexen-3-ol (28)

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of aldehyde (S)-**10**. To the resulting solution was added 0.25 mmol of $SnCl_4$. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution.The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded 91 mg the alcohol **28** in 72% yield. $[\alpha]^{20}_D$ = +13.8 (c 1.8, $CHCl_3$). **TLC**: Rf = 0.38, hexanes:EtOAc 85:15. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.96 (3H, d, ^3J = 6.96), 1,06 (3H, d, ^3J = 7.32), 1.07 (9H, s), 1.86 (1H, m), 2.11 (1H, dd, ^2J = 14.1, ^3J = 10.0), 2.23 (1H, br d, ^3J = 6.28), 2.33 (1H, dl, ^3J = 13.92), 2.51 (1H, m), 3.15 (1H, d, ^3J = 2.93), 3.38 (1H, dd, ^2J = 9.15, ^3J = 6.23), 3.51 (1H, dd, ^2J = 9.15, ^3J = 7.69), 3.70 (1H, dd, ^2J = 10.00, ^3J = 5.86), 3.76 (1H, dd, ^2J = 10.00, ^3J = 5.31), 3.85 (1H, m), 4.52 (2H, s), 4.96 (2H, br d, ^3J = 8.79), 7.38 (10H, m), 7.71 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: 13.2 (CH_3), 17.4 (CH_3), 19.0 (C_o), 26.7 (CH_3), 38.7 (CH), 40.3 (CH), 40.7 (CH_2), 66.8 (CH_2), 71.5 (CH), 73.0 (CH_2), 74.5 (CH_2), 112.0 (CH_2), 127.7 (CH), 127.8 (CH), 128.5 (CH), 129.8 (CH), 133.7 (C_o), 135.0 (CH), 138.4 (C_o), 149.7 (C_o). **IR (film)**: 3069, 2958, 2929, 2856, 1958, 1887, 1821, 1643, 1588, 1471, 1389, 1361, 1308, 1260, 1188, 1111, 1028, 998, 939, 897, 874, 823, 739, 701, 613 cm^{-1}. **MS (70eV)**: 45 (8%), 77 (9%), 199 (100%), 256 (5%).

1-(2R)-3-[(2R,3R)-4-(tert-butyl(dimethyl)silyloxy)-2-(trimethyl)silyloxy-3-methylbutyl]-2-methyl-3-butenyloxymethylbenzene (30, TMS protected)

To a solution of **30** (100 mg, 0.26 mmol) in 2 mL of dry CH_2Cl_2 at room temperature was added 2 eq. of TMS-imidazole. The resulting solution was stirred for 1 h and filtered in silica gel with CH_2Cl_2. Concentration of the filtrate under reduced pressure and purification by flash chromatography on silica gel (5% EtOAc/hexanes) afforded 83 mg of **30** (TMS protected) in 70% yield). $[\alpha]^{20}_D$ = -5.8 (c 2.9, $CHCl_3$). **TLC**: Rf = 0.6, hexanes:ethyl ether 8:2. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.05 (6H, s), 0.08 (9H, s), 0.87 (3H, d, ^3J = 6.96), 0.91 (9H, s), 1.12 (3H, d, ^3J = 6.96), 1.71 (1H, br d, ^3J = 5.86), 2.06 (1H, dd, ^2J = 14.10, ^3J = 8.24), 2.25 (1H, dd, ^2J = 14.1, ^3J = 3.84), 2.48 (1H, m), 3.32 (1H, dd, ^2J = 9.06, ^3J = 7.87), 3.46 (1H, dd, ^2J = 10.16, ^3J = 6.59), 3.53 (1H, dd, ^2J = 9.06, ^3J = 5.13), 3.58 (1H, dd, ^2J = 10.16, ^3J = 6.96), 3.92 (1H, m), 4.53 (2H, d, ^3J = 1.83), 4.86 (2H, d, ^3J = 6.59), 7.35 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: -5.7 (CH_3), 0.2 (CH_3), 12.2 (CH_3), 16.9 (CH_3), 18.0 (C_o), 25.7(CH_3), 38.7 (CH_2), 39.4 (CH), 41.4 (CH), 64.9 (CH_2), 72.9 (CH_2), 73.3 (CH), 74.6 (CH_2), 111.2 (CH_2), 127.6 (CH), 127.7 (CH), 128.6 (CH), 138.9 (C_o), 149.6 (C_o). **IR (film)**: 2957, 2857, 1472, 1362, 1250, 1086, 938, 838, 775, 747, 697 cm^{-1}.

(2S,3R)-5-[(1R)-2-benzyloxy-1-methylethyl]-1-[tert-butyl(diphenyl)silyloxy]-2-methyl-5-hexen-3-ol (32)

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 1 h when 0.25 mmol of aldehyde (R)-**10** in 1 mL of CH_2Cl_2 was added. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution.The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/hexanes) afforded 113 mg of the alcohol **32** in 90% yield. $[\alpha]^{20}_D$ = +2.9 (c 2.9, $CHCl_3$). **TLC:** Rf = 0.38, hexanes:EtOAc 85:15. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.99 (3H, d, ^3J = 7.32), 1.09 (3H, d, ^3J = 6.59), 1.11 (9H, s), 1.81 (1H, m), 2.24 (1H, br), 2.27 (1H, sl), 2.54 (1H, q, ^3J = 6.96), 2.85 (1H, d, ^3J = 2.56), 3.40 (1H, dd, ^2J = 8.97, ^3J = 6.59), 3.53 (1H, dd, ^2J = 8,97, ^3J = 7.32), 3.72 (1H, s), 3.74 (1H, s), 4.09 (1H, m), 4.54 (2H, s), 4.98 (2H, m), 7.45 (10H, m), 7.73 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**, δ: 10.5 (CH_3), 17.3 (CH_3), 19.0 (C_o), 26.7 (CH_3), 38.8 (CH), 39.5 (CH), 40.7 (CH_2), 67.7 (CH_2), 70.5 (CH), 73.0 (CH_2), 74.5 (CH_2), 111.9 (CH_2), 127.7 (CH), 127.8 (CH), 127.9 (CH), 128.0 (CH), 128.5 (CH), 129.9 (CH), 133.6 (C_o), 133.7 (C_o), 135.8 (CH), 135.9 (CH), 138.5 (C_o), 149.5 (C_o). **IR (film)**, 3774, 3070, 2958, 2929, 2856, 1959, 1886, 1643, 1589, 1474, 1454, 1427, 1390, 1361, 1307, 1258, 1188, 1112, 1028, 998, 898, 874, 823, 739, 701, 613 cm^{-1}. **MS (70eV)**, 77 (14%), 91 (82%), 135 (18%), 199 (100%), 239 (13%), 269 (52%).

(1R,S)-3-[(1R)-2-benzyloxy-1-methylethyl]-1-isopropenyl-3-butenyl alcohol (34)

To a solution of 0.28 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.28 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 1 h when 0.28 mmol of methacrolein in 1 mL of CH_2Cl_2 was added. This mixture was stirred at -78 °C for 30 min and quenched by the slow addition of 0.35 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution.The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (20% EtOAc/hexanes) afforded 38 mg of alcohol **34** in 50% yield. **TLC**: Rf: 0.34, hexanes:ethyl acetate 85:15. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 1.05 (3H, d, ^3J = 6.96), 1.76 (3H, d, ^3J = 5.13), 2.19 (1H, m), 2.39 (1H, m), 2.54 (1H, q, ^3J = 6.96), 2.71 (1H, d, ^3J = 2.56), 3.43 (2H, m), 4.21 (1H, m), 4.53 (2H, s), 4.85 (2H, br), 5.01 (2H, br). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: 7.3 (CH_3), 18.0 (CH_3), 38.6 (CH), 42.1 (CH_2), 73.0 (CH), 73.5 (CH_2), 74.3 (CH_2), 110.6 (CH_2), 112.6 (CH_2), 127.8 (CH), 127.9 (CH), 128.1 (CH), 128.5 (CH), 138.2 (C_o), 147.1(C_o), 149.1 (C_o). **IR (film)**: 3438, 3069, 3028, 2963, 2922, 2858, 1644, 1495, 1453, 1369, 1254, 1204, 1090, 1028, 964, 898, 735, 697 cm^{-1}.

1-[(2R)-2,3-dimethyl-3-butenyloxymethyl]benzene (36)

To a solution of 0.25 mmol of allylsilane **3** in 2 mL of dry CH_2Cl_2 at -78 °C was added 0.25 mmol of $SnCl_4$. The resulting solution was stirred at -78 °C for 1 h the reaction was quenched by the slow addition of 0.30 mmol of Et_3N, followed by 5 mL of saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica gel (20% EtOAc/hexanes) afforded 40 mg of **36** in 84% yield. $[\alpha]^{20}_D$ = -15.0 (c 1.4, $CHCl_3$). **TLC**: Rf: 0.34, hexanes:ethyl acetate 85:15. **^{1}H-NMR ($CDCl_3$, 300 MHz)**, δ: 1.07 (3H, d, ^3J = 6.96), 1.73 (3H, s), 2.52 (1H, m), 3.33 (1H, dd, ^2J = 9.15, ^3J = 6.96), 3.48 (1H, dd, ^2J = 9.15, ^3J = 6.59), 4.54 (2H, s), 4.79 (2H, m), 7.36 (5H, m). **^{13}C NMR ($CDCl_3$, 75 MHz)**: δ: 16.6 (CH_3), 20.1 (CH_3), 41.0 (CH), 72.9 (CH_2), 73.9 (CH_2), 110.4 (CH_2), 127.4 (CH), 127.6 (CH), 128.3 (CH), 138.6 (C_o), 147.7(C_o). **IR (film)**: 3066, 3028, 2964, 2854, 1645, 1603, 1495, 1453, 1372, 1248, 1202, 1098, 1028, 1000, 964, 889, 855, 734, 697 cm^{-1}. **MS (70 eV)**: 41 (15%), 69 (19%), 84 (30%), 91 (100%).

General procedure for the preparation of diols

To a solution of 0.08 mmol of the homoallylic alcohols in 2 mL of dry THF at 0 °C was added 0.24 mL of a 1.0 M solution of TBAF in THF. This mixture was stirred for 1 h at 0 °C and quenched by the addition of a saturated solution of NH_4Cl. The aqueous layer was extracted with 3 x 2 mL of ethyl ether and washed with brine (5 mL). The combined organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification by flash chromatography on silica-gel (20% EtOAc/Hexanes) afforded the corresponding 1,3-diols:

(2R,3R)-5-[(1R)-2-benzyloxy-1-methylethyl]-2-methyl-5-hexene-1,3-diol (38)

Purification by flash chromatography on silica gel (25% EtOAc/hexanes) afforded 17 mg of diol **38** in 75% yield. **TLC**: Rf: 0.26, hexanes:ethyl acetate 1:1. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.95 (3H, d, ^3J = 6.96), 1.02 (3H, d, ^3J = 6.96), 1.69 (1H, br), 1.87 (1H. m), 2,15 (1H, dd, ^2J = 13.8, ^3J = 3.38), 2.24 (1H, dd, ^2J = 13.8, ^3J = 10.0), 2.51 (1H, m), 3.07 (1H, s), 3.41 (1H, dd, ^2J = 8.97, ^3J = 5.49), 3.48 (1H, t, ^3J = 8.97), 3.70 (2H, d , ^3J = 5.49), 4.02 (1H, dt, ^2J = 10.0, ^3J = 3.38), 4.50 (2H, d, ^3J = 1.1), 5.00 (2H, d, ^3J = 2,2), 7.32 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: 10.5 (CH_3), 17.4 (CH_3), 38.5 (CH), 38.6 (CH), 39.5 (CH_2), 67.1 (CH_2), 72.0 (CH), 73.1 (CH_2), 74.4 (CH_2), 112.9 (CH_2), 128.0 (CH), 128.1 (CH), 128.6 (CH), 137.9 (C_o), 149.2 (C_o). **IR (film)**: 3382, 2926, 1716, 1644, 1602, 1454, 1372, 1276, 1177, 1100, 1073, 1028, 901, 752, 714, 699 cm^{-1}.

(2S,3R)-5-[(1R)-2-benzyloxy-1-methylethyl]-2-methyl-5-hexene-1,3-diol (40)

Purification by flash chromatography on silica gel (25% EtOAc/hexanes), afforded 19 mg of diol **40** in 70% yield. $[\alpha]^{20}_D$ = -77.0 (c 0.2, $CHCl_3$). **TLC**: Rf: 0.26, hexanes:ethyl acetate 1:1. **^{1}H-NMR ($CDCl_3$, 300 MHz)**: δ: 0.87 (3H, d, ^3J = 6.96), 1,01 (3H, d, ^3J = 6.96), 1.73 (1H, m), 2.08 (1H, dd, ^2J = 13.5, ^3J = 10.6), 2.39 (1H, br d, ^2J = 13.5), 2.49 (1H, m), 3.48 (4H, m), 3.65 (3H, m), 4.50 (2H, d, ^3J = 4.03), 5.00 (2H, s), 7.31 (5H, m). **^{13}C-NMR ($CDCl_3$, 75 MHz)**: δ: 13.7 (CH_3), 17.5 (CH_3), 38.2 (CH), 40.1 (CH), 42.5 (CH_2), 68.3 (CH_2), 73.2 (CH_2), 74.7 (CH), 74.7 (CH_2), 113.2 (CH_2), 128.0 (CH), 128.1 (CH), 128.6 (CH), 137.7 (C_o), 149.1 (C_o). **IR (film)**: 3382, 2926, 1716, 1644, 1602, 1454, 1372, 1276, 1177, 1100, 1073, 1028, 901, 752, 714, 699 cm^{-1}.

General procedure for p-methoxybenzylidene acetal formation

To a solution of 0.054 mmol of the corresponding diol in 2 mL of CH_2Cl_2 at room temperature was added 0.116 mmol of 4-methoxy-benzaldehyde dimethylacetal, followed by catalytic amounts of camphor sulfonic acid. The mixture was stirred for 3h at room temperature, diluted with 3 mL of CH_2Cl_2 and quenched by the addition of 5 mL of a saturated solution of $NaHCO_3$. The layers were separated and the aqueous layer was extracted with 3 x 2mL of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. An analytical sample was purified by preparative TLC (20% EtOAc/Hexanes) affording the corresponding *p*-methoxybenzylidene acetals:

(4R,5R)-4-2-[(1R)-2-benzyloxy-1-methylethyl]allyl-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (39)

$[\delta]^{20}_D$ = +31.8 (c 0.5, $CHCl_3$). **TLC**: Rf: 0.45, hexanes/ethyl acetate 8:2. **^{1}H-NMR (C_6D_6, 300 MHz)**: δ: 1.10 (3H, s), 1.12 (3H, s), 1.23 (1H, m), 2.05 (1H, dd, ^{2}J = 14.66, ^{3}J = 6.59), 2.44 (1H, dd, ^{2}J = 14.66, ^{3}J = 6.59), 2.53 (1H, q, ^{3}J = 6.40), 3.18 (1H, dd, ^{2}J = 9.06, ^{3}J = 6.40), 3.40 (1H, dd, ^{2}J = 9.06, ^{3}J = 6.40), 3.65 (1H, d, ^{2}J = 11.17), 3.74 (1H, d, ^{2}J = 11.17), 3.88 (1H, t, ^{3}J = 6.59), 4.28 (2H, s), 4.92 (2H, d, ^{3}J = 10.25), 5.34 (2H, s), 6.77 (2H, m), 7.14 (5H, m), 7.59 (2H, m). **^{13}C NMR (C_6D_6, 75 MHz)**: δ: 10.9 (CH_3), 16.9 (CH_3), 31.8 (CH), 39.0 (CH_2), 39.7 (CH), 54.4 (CH_3), 72.8 (CH_2), 73.5 (CH_2), 74.9 (CH_2), 78.7 (CH), 101.8 (CH_3), 111.3 (CH_2), 113.6 (CH_3), 127.6 (CH), 127.8 (CH), 128.5 (CH), 132.4 (C_o), 139.4 (C_o), 149.1 (C_o), 160.4 (C_o). **IR (film)**: 3065, 2962, 2916, 2849, 1734, 1642, 1616, 1588, 1518, 1455, 1395, 1358, 1302, 1249, 1172, 1154, 1118, 1035, 1002, 898, 827, 754, 698 cm^{-1}.

(5S,4R)-4-2-[(1R)-2-benzyloxy-1-methylethyl]allyl-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (41)

TLC: Rf: 0.45, hexanes/ethyl acetate 8:2. **^{1}H-NMR (C_6D_6, 300 MHz)**: δ: 0.34 (3H, d, ^{3}J = 6.59), 1.17 (3H, d, ^{3}J = 6.96), 1.67 (1H, m), 2.21 (1H, dd, ^{2}J = 15.8, ^{3}J = 8.9), 2.36 (1H, dd, ^{2}J = 15.8, ^{3}J = 2.2), 2.68 (1H, m), 3.14 (1H, t, ^{3}J = 11.35), 3.26 (1H, dd, ^{2}J = 7.69, ^{3}J = 8.97), 3.36 (1H, td, ^{2}J = 8.97, J = 2.2), 3.50 (1H, dd, ^{2}J = 6.59, ^{3}J = 8.97), 3.86 (1H, dd, ^{2}J = 11.35, ^{3}J = 4.76), 4.30 (2H, s), 4.98 (2H, d, ^{3}J = 23.0), 5.31 (2H, s), 6.76 (2H, m), 7.14 (5H, m), 7.60 (2H, m). **^{13}C-NMR (C_6D_6, 75 MHz)**: δ: 12.4 (CH_3), 17.1 (CH_3), 33.8 (CH), 38.7 (CH_2), 39.4 (CH), 55.1 (CH_3), 72.8 (CH_2), 72.9 (CH_2), 74.7 (CH_2), 82.5 (CH), 100.7 (CH), 111.4 (CH_2), 113.6 (CH), 127.4 (CH), 127.6 (CH), 127.7 (CH), 128.5 (CH), 131.5 (C_o), 138.9 (C_o), 149.0 (C_o), 160.0 (C_o). **IR (film)**: 3065, 2962, 2916, 2849, 1734, 1642, 1616, 1588, 1518, 1455, 1395, 1358, 1302, 1249, 1172, 1154, 1118, 1035, 1002, 898, 827, 754, 698 cm^{-1}.

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